Articles

1,2,3-Benzoxathiazole 2,2-Dioxides: Synthesis, Mechanism of Hydrolysis, and Reactions with Nucleophiles

Kenneth K. Andersen,*[1] Diana D. Bray,[2] Sumalee Chumpradit,[1] Michael E. Clark,[1] Gregory J. Habgood,[1] Colin D. Hubbard,[1] and Kathleen M. Young[1]

Department of Chemistry, University of New Hampshire, Durham, New Hampshire 03824, and Department of Chemistry, Fordham University, Bronx, New York 10458

Received May 21, 1991

The rates of base-induced hydrolysis of some five-membered cyclic sulfamates, X-3-(*p*-tolylsulfonyl)-1,2,3-benzoxathiazole 2,2-dioxides (**1a**, X = H; **1b**, X = 5-Me; **1c**, X = 5-*t*-Bu; **1d**, X = 5-Br; **1e**, X = 5-Cl; **1f**, X = 5-Ac; **1g**, X = 5-NO_2; **8a**, X = 6-NO_2) were measured in aqueous acetonitrile. The hydrolyses occurred with cleavage of the endocyclic N-SO_2 bond. A Hammett plot using σ_m values for **1a-g** and σ_p for **8a** had ρ = +2.20. Activation enthalpies and entropies were measured for **1a** and for 3-methyl-1,2,3-benzoxathiazole 2,2-dioxide (**10**). Volumes of activation were determined for **1g** and for **8a**. The mechanistic profile for hydrolysis resembled that for the saponification of the analogous sultones and cyclic sulfates. These first examples of 1,2,3-benzoxathiazole 2,2-dioxides (**1a-g**, **8a**) were prepared by treating *N*-(2-hydroxyphenyl)-*p*-toluenesulfonamides with sulfuryl chloride and triethylamine or by oxidizing the monoxide precursors using *m*-chloroperbenzoic acid. Treatment of **1a** with potassium fluoride gave 1,2,3-benzoxathiazole 2,2-dioxide (**9**), which was methylated to give **10**. Sulfamate **1a** was treated with various nucleophilic reagents: phenyllithium, methyllithium, potassium fluoride, methylamine, *tert*-butylamine, and sodium methoxide. The first three attacked the tosyl sulfur atom and cleaved the exocyclic N-SO_2 bond. The amines attacked the endocyclic sulfonyl sulfur atom and cleaved the endocyclic N-SO_2 bond. Sodium methoxide attacked both sulfonyl groups.

Introduction

Interest in the reactivity of cyclic sulfur(VI) and sulfur(IV) esters and amides toward nucleophiles in comparison to the reactivity of their acyclic analogues was stimulated by the work of Kaiser.[3] These compounds have been investigated not only to answer questions about structure and reactivity but also to explore their practical uses as reagents in synthesis or as possible medicinal agents.[4] Interest also continues regarding the stereochemistry of nucleophilic substitution at the sulfur atom[5] of these compounds and whether hypervalent intermediates[6] are present or absent, i.e., whether particular reactions are concerted[7] or not.[8]

This paper reports the synthesis of several 1,2,3-benzoxathiazole 2,2-dioxides, five-membered cyclic esters of sulfamic acid, and describes some of their reactions with nucleophiles, particularly hydroxide ion. Five-membered-ring sultones and sulfates, structurally similar to **1a**, as well as analogous cyclic phosphates and phosphonates, undergo basic hydrolysis very rapidly compared to their acyclic counterparts. Kaiser showed that sulfate **2** and sulfonate **3** saponify over 10^6 times faster than their acyclic analogues, **4** and **5**.[3a]

As part of another study, **1a**, the first example of the 1,2,3-benzoxathiazole 2,2-dioxide ring system, was prepared and treated with phenyllithium. It was expected, generalizing from Kaiser's saponification studies of **2** and **3**, that the heterocyclic ring of **1a** would be very reactive toward nucleophiles so that the phenyllithium would attack the ring sulfur atom with initial cleavage of either the ring S-N or S-O bond. Contrary to the anticipated result, the exocyclic sulfonyl group was attacked with formation of phenyl *p*-tolyl sulfone. Therefore, it was of interest to see if the enhanced reactivity toward hydroxide ion associated with five-membered-ring esters such as **2** and **3** carried over the analogous cyclic ester **1a**, if indeed ring opening occurred at all. It was also of interest to examine which sulfonyl group would be attacked by other nucleophiles. Although five-membered cyclic sulfur(VI) esters such as

(1) University of New Hampshire. Most of this research is taken from the theses of S.C. (Ph.D., 1985), M.E.C. (M.S., 1987), G.J.H. (M.S., 1990), and K.M.Y. (B.S., 1986).

(2) Fordham University. Address correspondence concerning X-ray crystal structure to this author.

(3) (a) Kaiser, E. T. *Acc. Chem. Res.* **1970**, *3*, 145-151. (b) Tillett, J. G. *Chem. Rev.* **1976**, *76*, 747-772. (c) Tillett, J. G. *Phosphorus Sulfur* **1976**, *1*, 341-349. (d) Laleh, A.; Ranson, R.; Tillett, J. G. *J. Chem. Soc., Perkin Trans. 2* **1980**, 610-615. (e) Gambarotta, S.; Isoal, M.; Senatore, L.; Ciuffarin, E. *Gazz. Chim. Ital.* **1982**, *112*, 297-300. (f) Izbicka, E.; Bolen, D. W. *J. Am. Chem. Soc.* **1978**, *100*, 7625-7628. (g) Maroni, P.; Calmon, M.; Cazaux, L.; Tisnès, P.; Satoré, G.; Aknin, M. *J. Chem. Soc., Perkin Trans. 2* **1978**, 1207-1210, 1211-1214. (h) Wagner, B. J.; Doi, J. T.; Musker, W. K. *J. Org. Chem.* **1990**, *55*, 5940-5945.

(4) (a) DuBois, G.; Stephenson, R. *J. Org. Chem.* **1980**, *45*, 5371-5373. DuBois, G. *J. Org. Chem.* **1980**, *45*, 5373-5375. (b) Acher, F.; Wakselman, M. *J. Org. Chem.* **1984**, *49*, 4133-4138. (c) Acheson, R. M.; Bite, M. G. *J. Med. Chem.* **1981**, *24*, 1300-1304. (d) Cuthbert, B. K.; Lowe, G. *J. Chem. Soc., Chem. Commun.* **1989**, 1702-1703. (e) Berridge, M. S.; Franceschini, M. P.; Rosenfeld, E.; Tewson, T. J. *J. Org. Chem.* **1990**, *55*, 1211-1217. (f) Gao, Y.; Sharpless, K. B. *J. Am. Chem. Soc.* **1988**, *110*, 7538-7539.

(5) (a) Mikolajczyk, M.; Drabowicz, J. *Top. Stereochem.* **1982**, *13*, 333-468. (b) Mikolajczyk, M. *Phosphorus Sulfur* **1986**, *27*, 31-42. (c) Andersen, K. K.; Chumpradit, S.; McIntyre, D. J. *J. Org. Chem.* **1988**, *53*, 4667-4675.

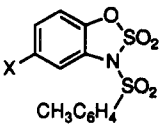
(6) Kice, J. L. *Adv. Phys. Org. Chem.* **1980**, *17*, 65-181.

(7) (a) Luthra, A. K.; Ba-Saif, S.; Chrystiuk, E.; Williams, A. *Bull. Soc. Chim. Fr.* **1988**, 391-394. (b) Lee, I.; Kang, H. K.; Lee, H. W. *J. Am. Chem. Soc.* **1987**, *109*, 7472-7477. (c) Okuyama, T.; Nakamura, T.; Fueno, T. *J. Am. Chem. Soc.* **1990**, *112*, 9345-9349.

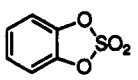
(8) (a) Perkins, C. W.; Wilson, S. R.; Martin, J. C. *J. Am. Chem. Soc.* **1985**, *107*, 3209-3218. (b) Martin, J. C. *Science (Washington, D.C.)* **1983**, *221*, 509-514. (c) Jager, J.; Graafland, T.; Schenk, H.; Kirby, A. J.; Engberts, J. B. F. N. *J. Am. Chem. Soc.* **1984**, *106*, 139-143.

0022-3263/91/1956-6508$02.50/0

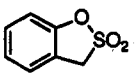
2 and 3 show greatly enhanced reactivity toward hydroxide ion compared to six-membered and acyclic analogues, this is not true for all sulfur(VI) compounds[6,9] nor for similar sulfur(IV) compounds.[10] The cyclic anhydride of 1,2-benzenedisulfonic acid does not exhibit enhanced reactivity toward hydroxide ion.[9b] Five-membered cyclic sulfites hydrolyze much more rapidly than their acyclic analogues in base, but cyclic sulfinates do not.[10b] Dimethyl sulfite hydrolyzes more rapidly than ethylene sulfite in acid.[3c,11] Five-membered cyclic sulfinamides hydrolyze more slowly than acyclic analogues in acid.[3h] However, five-membered cyclic disulfides, examples of sulfur(II) compounds, are more reactive toward nucleophiles than their acyclic analogues.[12]



1 a X = H e X = Cl
b X = Me f X = Ac
c X = t-Bu g X = NO_2
d X = Br



2



3

4

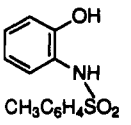
5

Results and Discussion

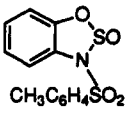
Synthesis. Cyclic sulfamate **1a**, whose structure was confirmed by single-crystal X-ray analysis, was prepared by treating *N*-tosyl-2-aminophenol (**6**) with thionyl chloride and triethylamine to give cyclic sulfimate **7**, which was then oxidized to the sulfamate by *m*-chloroperbenzoic acid. Better yields of **1a** were obtained, in only one step, by treating **6** with sulfuryl chloride and triethylamine. Ring-substituted derivatives (**1b–g**) and the 6-nitro compound **8a** were obtained from substituted *o*-aminophenols via this latter method. It was also possible to obtain the 6-nitro derivative **8a** by nitration of **1a** with sodium nitrite in trifluoroacetic acid.[13] Treatment of **1a** with fuming nitric acid in a mixture of sulfuric acid and methylene chloride gave the dinitro derivative **8b** with one nitro group in the 6-position and the other in the 3′-position of the tolyl ring.

1,2,3-Benzoxathiazole 2,2-dioxide (**9**) was prepared by treatment of **1a** with potassium fluoride in aqueous acetonitrile, which removed the *N*-tosyl group; N-methylation of **9** gave *N*-methyl-1,2,3-benzoxathiazole 2,2-dioxide (**10**).

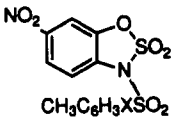
N-Benzyl- and *N*-4-tolyl-1,8-naphthosultam (**11** and **12**) were obtained by treatment of 1,8-naphthosultam (**13**) with benzyl chloride and with tosyl chloride,[14] respectively. Phenyl *N*-methyl-*N*-phenylsulfamate (**14**) was prepared from phenyl *N*-phenylsulfamate by alkylation with methyl iodide under phase-transfer conditions.[15]



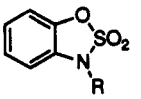
6



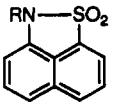
7



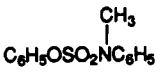
8 a X = 3′-H
8 b X = 3′-NO_2



9 R = H
10 R = CH_3



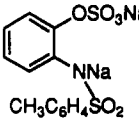
11 R = $C_6H_5CH_2$
12 R = $CH_3C_6H_4SO_2$
13 R = H



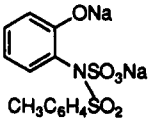
14

Reaction with Hydroxide Ion. Sulfamate **1a** reacted readily with sodium hydroxide in aqueous acetonitrile to give the disodium salt, initially of unknown structure, but either **15a** or **15b**. Partial saponification gave a mixture of **1a** and sodium salt **15**, the latter identified by its elemental analysis and spectra. Aqueous acid transformed salt **15** to sulfonamide **6** by loss of sulfate ion, which was identified by its conversion to barium sulfate. The UV spectrum of salt **15** had a λ_{max} at 242 nm ($\epsilon = 4.62 \times 10^4$) with a shoulder at 284 nm.

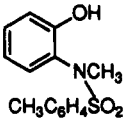
In order to ascertain which structure, **15a** or **15b**, correctly represented **15** and so to identify which ring bond had been cleaved, S–N or S–O, the UV spectra of three model compounds were measured in basic aqueous acetonitrile. The dianion of **6** showed a λ_{max} at 299 nm ($\epsilon = 4.86 \times 10^4$), the monoanion of **16**, a λ_{max} at 235 nm ($\epsilon = 4.89 \times 10^4$) with a shoulder at 301 nm, and the monoanion of **17**, a λ_{max} at 245 nm ($\epsilon = 4.62 \times 10^4$) with a shoulder at 284 nm. The spectrum obtained for **17** in base matched closely the spectrum obtained for sodium salt **15**; thus, the structure of **15** is **15a** and not **15b**. Had the structure been **15b**, a spectrum resembling that obtained for **16** in base should have been observed. No evidence for loss of the tosyl group during saponification was found.



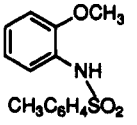
15 a



15 b



16



17

Kinetics. The rate of saponification of **1a** in aqueous acetonitrile containing a large excess of sodium hydroxide was followed for 10 or more half-lives by observing the increase in absorption at 294 nm. The development of an isosbestic point at 282 nm makes it unlikely that buildup of an intermediate occurred in the reaction mixture. The observed rates followed pseudo-first-order kinetics, being first order in sulfamate **1a**. The pseudo-first-order rate constants varied linearly with the hydroxide ion concen-

(9) (a) Chau, M. M.; Kice, J. L.; Margolis, H. C. *J. Org. Chem.* **1978**, *43*, 910–914. (b) Laird, R. M.; Spence, M. J. *J. Chem. Soc. B* **1971**, 1434–1440.
(10) (a) Bristow, P. A.; Tillett, J. G.; Wiggins, D. E. *J. Chem. Soc. B* **1968**, 1360–1363. (b) Najam, A.; Tillett, J. G. *J. Chem. Soc., Perkin Trans. 2* **1975**, 858–860.
(11) Bunton, C. A.; de la Mare, P. B. D.; Tillett, J. G. *J. Chem. Soc.* **1959**, 1766–1774.
(12) (a) Ravenscroft, M.; Roberts, R. M. G.; Tillett, J. G. *J. Chem. Soc., Perkin Trans. 2* **1982**, 1569–1572. (b) Singh, R.; Whitesides, G. M. *J. Am. Chem. Soc.* **1990**, *112*, 6304–6309.
(13) Uemura, S.; Toshimitsu, A.; Okano, M. *J. Chem. Soc., Perkin Trans. 1* **1978**, 1076–1079.
(14) Mustafa, A.; Ali, M. I. *J. Am. Chem. Soc.* **1955**, *77*, 4593–4596.
(15) Burke, P. O.; Spillane, W. J. *Synthesis* **1985**, 935–937.

Table I. Rate Constants for the Reaction of 1a with NaOH in MeCN/H_2O, 1:5 v/v

T, °C	[OH^-], mol dm^{-3}	$k_{obsd} \times 10^2$, s^{-1}	k_2, mol dm^{-3} s^{-1}
30	0.041	12.9 ± 2.7[a]	3.09[b] ± 0.35
	0.050	16.6 ± 1.7	
	0.082	25.8 ± 2.0	
20	0.050	8.67 ± 0.11	1.77 ± 0.24
	0.060	10.6 ± 0.3	
	0.10	17.6 ± 2.8	
10	0.050	4.45 ± 0.15	0.828 ± 0.052
	0.060	5.40 ± 0.14	
	0.10	8.63 ± 0.57	
0	0.050	1.79 ± 0.05	0.375 ± 0.028
	0.060	2.11 ± 0.05	
	0.10	3.64 ± 0.32	

[a] Standard deviation. [b] k_2 values obtained from the slopes of plots of k_{obsd} vs [OH^-].

Table II. Second-Order Rate Constants versus Solvent Composition (v/v) for the Reaction of 1a and 1g with NaOH at 20 °C

compd	MeCN/H_2O	k_2, mol dm^{-3} s^{-1}	compd	MeCN/H_2O	k_2, mol dm^{-3} s^{-1}
1a	1:5	1.77	1g	3:7	28.7
	1:3	1.18		2:3	22.7
	1:1	0.57		1:1	8.24
	3:1	0.29			

tration over the experimentally accessible range; thus, the kinetics were second-order overall (Table I). The second-order rate constant for **1a** (2.7 mol dm^{-3} s^{-1}, obtained by linear extrapolation of k_2 to pure water using the data given in Table II and then to 25 °C) is of the same magnitude as that observed for **2** (18.8 mol dm^{-3} s^{-1} in water at 25 °C),[16] **3** (33.6 mol dm^{-3} s^{-1} in 3% acetonitrile at 25 °C),[17] and **18a** (22.1 mol dm^{-3} s^{-1} extrapolated to pure water from aqueous acetonitrile at 25 °C).[18a] In the linear plot of pseudo-first-order rate constants, k_{obsd}, versus hydroxide ion, the intercept was 0; that is, there is no detectable spontaneous hydrolysis.

Rate constants for **1a** and **1g** decreased as the concentration of acetonitrile increased (Table II). Such a decrease would be anticipated for a reaction in which there is charge development overall in the transition state compared with the initial state. This implies that if this explanation is applicable here, the hydroxide ion may retain its negative character but induces polarization in the sulfur-containing ring. A decrease was also observed by Kaiser for the saponification of **3** in going from 8 to 24% 1,2-dimethoxyethane[17] and for **18a** in going from 8 to 20% aqueous acetonitrile.[18a]

Known quantities of an aqueous sodium hydroxide solution were added to an aqueous acetonitrile solution of **1a**. After each addition, the solution was allowed to stand until the UV absorbance became constant. The absorbance increased until 2 equiv of base had been added; then no further increase occurred with additional base, confirming that the ring opening to give **15a**, which requires 2 equiv of base, was rapid compared to further reaction.

Acid Stability. Sulfamate **1a** is stable to aqueous acid. No change occurred in the UV spectrum of a solution of **1a** in aqueous ethanol after several hours standing. In a scaleup of this experiment, thin-layer chromatography did not reveal the formation of any new substances. As described above, **1a**, **1g**, **8a**, and **8b** survive acidic nitration conditions.

Table III. Rate Constants for the Reaction of 1a–g and 8a with NaOH in MeCN/H_2O (1:1 v/v) at 25 °C

compd[a]	X	$k_{obsd} \times 10^3$, s^{-1}	k_2, mol dm^{-3} s^{-1}
1a	H	13.8 ± 0.4	0.44 ± 0.01
1b	CH_3	9.6 ± 0.4	0.30 ± 0.01
1c	$(CH_3)_3C$	9.9 ± 0.2	0.314 ± 0.008
1d	Br	62.1 ± 3.6	1.97 ± 0.25
1e	Cl	61.1 ± 1.9	1.94 ± 0.06
1f	$CH_3C{=}O$	67.1 ± 2.2	2.13 ± 0.08
1g	NO_2		14.8 ± 0.1
8a	6-NO_2		34.1 ± 0.1

[a] Rates for **1a–f** were measured in 0.0315 mol dm^{-3} NaOH. Rates for **1g** and **8a** were measured by stopped-flow techniques in various concentrations of NaOH at 20 and 30 °C and interpolated to 25 °C. Plots of k_{obsd} versus [OH^-] were linear with negligible intercepts.

Hammett Plot. Pseudo-first-order rate constants were obtained for the saponification of 5-substituted sulfamates **1b–g** and for 6-nitro sulfamate **8a**. A plot of pseudo-first-order rate constants versus hydroxide ion concentration was linear with an intercept of 0 for 5-chloro sulfamate **1e** and 5-nitro sulfamate **1g** as it was for **1a**, so we assume that all of the remaining sulfamates saponify similarly. The calculated second-order rate constants shown in Table III were used to construct two Hammett plots. A good correlation (correlation coefficient = 0.983) was found using σ_m values for **1a–g** and σ_p for **8a**. When σ_p values for **1a–g** and σ_m for **8a** were used to construct the plot, the points for the nitro sulfamates **1g** and **8a** deviated considerably from the regression line (correlation coefficient = 0.921). The better fit in the first case supports the conclusion that endocyclic S–N, and not S–O, bond cleavage occurs. The moderately large ρ value of +2.20 shows that an increase of electron density adjacent to the aromatic ring in the transition state compared with the initial state is occurring. Although the positive ρ value indicates the buildup of negative charge in the transition state relative to the initial state, it is not clear whether the reaction is concerted, proceeding from reactants directly to products, or a pentacoordinate intermediate is formed. The positive ρ value is consistent with rate-determining formation of a pentacoordinate intermediate, if one is actually formed, but not with its decomposition. The ρ value of +2.20 is the same as the value of +2.2 for the alkaline hydrolysis of $ArSO_2OPh$ in 70% dioxane.[6] Kaiser reported a ρ of +1.23 for the saponification of substituted sultones (**3**). A better correlation (correlation coefficient = 0.995) with ρ = 1.32 is obtained when his data is plotted versus more recent σ_p constants including σ^- for 4-nitro-substituted **3**.[19]

It is interesting that the S–N rather than the S–O bond was cleaved in the saponification reactions of **1a–g** and **8**. The *N*-tosyl group is doubtless responsible for this, accepting negative charge in the transition state, but one might have expected that S–O bond cleavage would have been favored in **1g** by the presence of the electron-withdrawing nitro group.

Acyclic Sulfamate. Since an acyclic model compound for **1a** was not available, the extent to which the saponification of **1a** is accelerated over that of an acyclic analogue could not be determined. To see what effect the *N*-tosyl

(16) Kaiser, E. T.; Katz, I. R.; Wulfers, T. F. *J. Am. Chem. Soc.* **1965**, *87*, 3781–3782.
(17) Zaborsky, O. T.; Kaiser, E. T. *J. Am. Chem. Soc.* **1966**, *88*, 3084–3087.
(18) (a) Kaiser, E. T.; Kudo, K.; Zaborsky, O. T. *J. Am. Chem. Soc.* **1967**, *89*, 1393–1395. (b) Tamagaki, S.; Hirota, H.; Oae, S. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 1247–1249.
(19) (a) Zaborsky, O. T.; Kaiser, E. T. *J. Am. Chem. Soc.* **1970**, *92*, 860–862. (b) Carey, F. A.; Sundberg, R. J. *Advanced Organic Chemistry, Part A: Structure and Mechanisms*; 3rd ed.; Plenum Press: New York, 1990; p 201.

Table IV. Rate Constants for the Reaction of 1a and 10 with NaOH in H_2O/EtOH, 1:1 v/v

compd	T, °C	[OH⁻], mol dm⁻³	$k_{obsd} \times 10^4$, s⁻¹	k_2, mol dm⁻³ s⁻¹
1a[a]	-4.6	0.0037	16.7 ± 1.5	0.45 ± 0.04
	1.5	0.0037	27.2 ± 0.58	0.73 ± 0.02
	5.6	0.0037	36.8 ± 1.2	0.99 ± 0.03
10[a]	29.5	0.16	6.60 ± 0.16	$4.12 \pm 0.10 \times 10^{-3}$
	35.2	0.10	5.64 ± 0.47	
		0.13	7.90 ± 0.17	$5.86 \pm 0.59 \times 10^{-3}$
		0.16	9.15 ± 0.14	
	40.5	0.16	16.0 ± 1.3	$9.92 \pm 0.79 \times 10^{-3}$

[a] Concentration: 1a, 2.7×10^{-4} mol dm⁻³; 10, 3.7×10^{-5} mol dm⁻³.

group had on the rate of saponification, the rate constant for the hydrolysis of **10** was measured. The rate was lessened to such an extent that the aqueous acetonitrile solution of sodium hydroxide was not sufficiently stable to permit reliable UV measurements, so this solvent was replaced by aqueous ethanol. Second-order rate constants for **1a** and **10**, obtained in aqueous ethanol (1:1 v/v) at three temperatures for each and extrapolated to 25 °C, were 4.2 mol dm⁻³ s⁻¹ for **1a** and 2.5×10^{-3} mol dm⁻³ s⁻¹ for **10**; **1a** saponifies 1700 times faster than **10** (Table IV). However, S–O and not S–N bond cleavage would be expected in the case of **10**, since a phenoxide ion is a better leaving group than an anilide ion. The UV spectrum of the reaction mixture bears out this expectation. With time, an absorption maximum arose at 297 nm, one at 270 nm decreased, and two isosbestic points appeared, one at 254 nm and one at 286 nm. Thus, the cleavage of the S–N bond in **10** compared to **1a** is decreased more than 1700-fold.

Sulfamate **14**, an acyclic model for **10**, was synthesized. It hydrolyzed very slowly in boiling aqueous ethanolic sodium hydroxide, so no rate was measured. A very crude estimate for a rate constant, 1.4×10^{-6} mol dm⁻³ s⁻¹, was made on the basis of the amount of unhydrolyzed **14** recovered from the ethanolic base solution. This compares reasonably well with the rate constant of 2.4×10^{-6} mol dm⁻³ s⁻¹ for the alkaline hydrolysis of the sulfamate *p*-$NO_2C_6H_4OSO_2NMe_2$ in 1:1 ethanol/water at 60 °C.[20] It is clear that five-membered-ring formation greatly accelerates the saponification of sulfamate esters reacting through nucleophilic attack at sulfonyl sulfur.

Naphthosultams. 1,8-Naphthosultone (**18a**)[18a] and its nitrated derivatives[4b] saponify at accelerated rates compared to their acyclic analogues, whereas thiosulfonate **18b** and thiosulfinate **18c** react much more slowly than do their acyclic analogues, $PhSO_2SPh$ and PhSOSPh.[18b] Therefore, some 1,8-naphthosultams were investigated to see how they behaved. The saponification of 1,8-naphthosultam **13** could not be studied, since its acidic N–H proton (pK_a = 6.2)[21] is removed by base, forming an anion which is resistant to further nucleophilic attack. *N*-Benzyl-1,8-naphthosultam (**11**) is also resistant to S–N bond cleavage. No change was observed in the UV spectrum of **11** in aqueous ethanolic base over a 5-h period, nor did TLC reveal any products being formed when **11** was heated with alkaline ethanol for several days. This is not unexpected, since both **13** and *N*-methyl-1,8-naphthosultam are unreactive toward phenylmagnesium bromide,[22] which is an indication of the poor leaving-group ability of the anilide anion. N-Sulfonation transforms the nitrogen into a much better leaving group. Thus, N-benzenesulfonated **13** reacts with both phenylmagnesium bromide and lithium aluminum hydride[23] in processes involving endocyclic S–N bond cleavage; the exocyclic S–N bond remains intact. Sultam **12** reacts similarly with hydroxide ion; the endocyclic sulfonyl group is attacked preferentially with S–N bond cleavage. An 82% yield of the endocyclic S–N cleavage product (**19**) and an 8% yield of the exocyclic S–N cleavage product (**13**) were obtained when **12** was heated with sodium hydroxide in ethanol.

Table V. Activation Parameters[a] at 25 °C

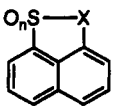
compd	solvent[b]	$\Delta H^{\ddagger}$, kJ mol⁻¹	$\Delta S^{\ddagger}$, J K⁻¹ mol⁻¹
1a	$EtOH/H_2O$	45 ± 0.1	-82 ± 0.4
1a	$MeCN/H_2O$	44 ± 2	-91 ± 6
10	$EtOH/H_2O$	63 ± 7	≈-84
3	$MeCN/H_2O$	42 ± 2	-74 ± 5
5	DME/H_2O	94 ± 4	-9.3 ± 14
20	$MeCN/H_2O$	64 ± 3	-85 ● 8
21	$DMSO/H_2O$	73 ± 2	-94 ± 7
22	dioxane/H_2O	70 ± 0.4	-82 ± 1

[a] Values for **3**, **5**, **20**, **21**, and **22** recalculated from data in ref 3d. [b] For **1a** and **10** in $EtOH/H_2O$: 1:1 v/v. For **1a** in $MeCN/H_2O$: 1:5 v/v. For remaining entries: 4% organic solvent.

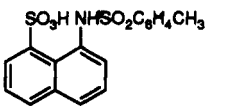
Table VI. Rate Constants for the Reaction of 1g and 8a with NaOH in $MeCN/H_2O$ (1:1 v/v) versus Pressure[a]

compd	P, bar	k_{obsd}, s⁻¹	compd	P, bar	k_{obsd}, s⁻¹
1g	52	0.981	8a	50	1.42
	254	1.13		250	1.64
	503	1.32		500	1.94
	750	1.50		750	2.25
	1000	1.76		1000	2.59

[a] [NaOH] = 0.050 mol dm⁻³; [sulfamates] = 1.0×10^{-4} mol dm⁻³; T = 24.4 ± 0.2 °C. Average rate constants from four or five runs with a deviation typically of ±1–3%.

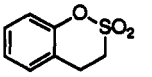


18

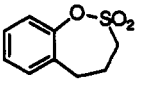


19

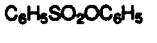
18a, n = 2, X = O
18b, n = 2, X = S
18c, n = 1, X = S



20



21



22

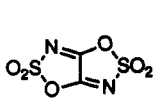
Activation Parameters. Values of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ for saponification were determined for **1a** in 1:5 acetonitrile/water and in 1:1 ethanol/water and for **10** in the latter solvent. Essentially there is no difference in the activation parameters determined for **1a** in the two solvents. The values are similar to those obtained by Tillet in dilute organic solvents for the saponification of sultones **3**, **20**, and **21** and for sulfonate **22** (Table V).[3d] Sulfonate **5** has quite different values, reflecting the change in mechanism from nucleophilic substitution at sulfur to an elimination–addition pathway proceeding via a sulfene. Most of

(20) Williams, A.; Douglas, K. T. *J. Chem. Soc., Perkin Trans 2* **1974**, 1727–1732.
(21) Kanety, H.; Kosower, E. M. *J. Phys. Chem.* **1982**, *86*, 3776–3780.
(22) Mustafa, A.; Hishmat, O. H. *J. Am. Chem. Soc.* **1953**, *75*, 4647–4649.
(23) Mustafa, A.; Asker, W.; Hishmat, O. H.; Shalaby, A. F. A.; Kamel, M. *J. Am. Chem. Soc.* **1954**, *76*, 5447–5452.
(24) (a) van Eldik, R.; Asano, T.; LeNoble, W. J. *Chem. Rev.* **1989**, *89*, 549–688. (b) Asano, T.; LeNoble, W. J. *Chem. Rev.* **1978**, *78*, 407–489.

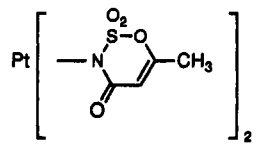
the reduction in rate of saponification in going from **1a** to **10** can be accounted for by an increase in enthalpy rather than an increase in entropy.

A high-pressure stopped-flow spectrophotometer was used to obtain the rate constants for the reaction of 0.050 mol dm^{-3} sodium hydroxide (1:1 acetonitrile/water) with the nitrosulfamates **1g** and **8a** were obtained at pressures up to 1 kbar (Table VI). The volumes of activation, $\Delta V^{\ddagger}$, obtained in the standard way, are pressure independent and are -15.1 ± 0.3 and -15.7 ± 0.5 cm^3 mol^{-1} for the reactions of **1g** and **8a**, respectively. A typical value for an associative reaction[24] is -10 cm^3 mol^{-1}. The evidence from the rate law (second order overall, first order in each reactant) is that the reactions of hydroxide ion are bimolecular; consequently, either the intrinsic volume change upon reaching the transition state is larger than normally encountered or there is a contribution from a solvation change. This latter effect could be the reason for the additional volume of contraction of about 5 cm^3 mol^{-1}. The incoming hydroxide ion may induce polarization within the nonaromatic ring which gives rise to increased solvent water electrostriction. This explanation also requires that the charge is still largely held by the hydroxide ion; otherwise, a significant change in the volume will occur as a consequence of loss of electrostricted water from the incoming nucleophile. We assume that in the solvent mixture partially or fully developed charged species are solvated by water rather than by acetonitrile.

Crystal Structure. The crystal structure of **1a**[25] showed the N–S–O internal ring angle to be 95.0° compared to 97.1° for the O–S–O ring angle in cyclic sulfate **2**,[26] 96.1° for the O–S–C ring angle in sultone **3**[27] (96.7° in 6-nitro-**3**[28]), and 97.4° for the N–S–O ring angle in **23**.[29] All of these angles are considerably less than the analogous angles found in related acyclic and six-membered-ring compounds. For example, sultone **20**[23] has a C–S–O angle of 101.4°, and sulfamates **24**,[30] **25**,[31] and **26**[32] have N–S–O angles of 104.1°, 101.4°, and 101.1°, respectively.



23



24

$ROSO_2N(CH_3)_2$ **25**

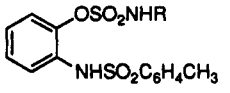
$ArOSO_2NHCOR$ **26**

A plot of S=O bond lengths vs O=S=O bond angles for a number of sulfonyl compounds is linear, albeit with a fair amount of scatter, and shows that as O=S=O bond angles increase, S=O bond lengths decrease.[33] For **1a**, the ring S=O bond lengths of 1.421 and 1.407 Å and O=S=O bond angle of 119.4° yield two points that fall within the domain of points of the plot. The two points for the tosyl group, obtained from S=O bond lengths of 1.428 and 1.425 Å and an O=S=O bond angle of 122.0°, also fall within this domain. But in the case of **1a**, the larger O=S=O angle is associated with the longer, not the shorter, S=O bond lengths.

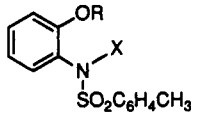
The five-membered ring in **1a** is not planar, but has the conformation of a distorted envelope with the sulfur atom at the apex. The sum of the five internal ring angles is 537.9° and not 540° as required for a planar structure. The trigonal nitrogen atom approaches planarity with the sum of the angles equal to 353.7°, close to 360° and some distance from 328.5°, the sum of three tetrahedral angles. This is not unexpected, since the nitrogen is planar in both dibenzenesulfonamide ($C_6H_5SO_2NHSO_2C_6H_5$)[34] and methanesulfonanilide ($CH_3SO_2NHC_6H_5$).[35] In acyclic sulfamate **25**, however, the sum of the angles around nitrogen is 348°; the nitrogen is nonplanar. The five-membered-ring O–C–C and N–C–C angles of 112.5° and 110.6°, respectively, are indicative of strain although the sum of the three bond angles around each carbon equals 360°, as required by planarity.

The torsion angle (82.0°) around the exocyclic S–N bond (ipso-C–S–N–S) is such that the two exo sulfonyl oxygens are bisected by a plane approximately perpendicular to the plane defined by the contiguous C–N–S atoms of the ring. The similarity in the bond lengths and angles between **1a** and **2** is noteworthy.

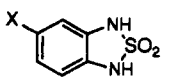
Reaction of 1a with Various Nucleophiles. Reaction at the Exocyclic Sulfonyl Sulfur Atom. Treatment of **1a** with phenyllithium in THF gave *p*-tolyl phenyl sulfone in 78% yield. A similar reaction of **1a** with methyllithium gave a 49% yield of bis(*p*-tolylsulfonyl)methane (**27**), $(p\text{-}TolSO_2)_2CH_2$. Apparently, methyl *p*-tolyl sulfone, formed initially by methyllithium attack at the *N*-tosyl sulfur, was converted to the anion, which then functioned as a nucleophile to give **27**. Treatment of **1a** with potassium fluoride in aqueous acetonitrile gave *p*-toluenesulfonyl fluoride in 87% yield and N-unsubstituted sulfamate **9**. Although it appears that the fluoride ion attacked the *N*-tosyl sulfur, it is possible that the fluoride ion also opened the ring, but that this process was rapidly reversible and the ring was reclosed. However, only signals for the fluoride ion and for *p*-toluenesulfonyl fluoride were observed when the reaction was monitored by ^{19}F NMR.



28 R = CH_3
29 R = t-Bu



30 R = H, X = CH_3
31 R = SO_2OCH_3, X = Na



32

Reaction at the Endocyclic Sulfonyl Sulfur Atom. Methylamine in aqueous acetonitrile reacted with **1a** overnight at room temperature to give an 89% yield of **28**. A similar reaction of **1a** with *tert*-butylamine proceeded more slowly and gave only a 44% yield of the analogue **29**,

(25) Bray, D. D.; Andersen, K. K.; Chumpradit, S. *Acta Crystallogr.* **1989**, *C45*, 537–538.
(26) Boer, F. P.; Flynn, J. J. *J. Am. Chem. Soc.* **1969**, *91*, 6604–6609.
(27) Fleischer, E. B.; Kaiser, E. T.; Langford, P.; Hawkinson, S.; Stone, A.; Dewar, R. *J. Am. Chem. Soc.* **1967**, *89*, 197–198.
(28) (a) Huu-Dau, E. T.; Guilhem, J.; Acher, F.; Wakselman, M. *J. Chem. Res., Miniprint* **1985**, 1501–1535. (b) Huu-Dau, E. T.; Guilhem, J.; Acher, F.; Wakselman, M. *J. Chem. Res., Synop.* **1985**, 126–127.
(29) Gieren, A.; Riemann, U.; Dederer, B. *Z. Anorg. Allg. Chem.* **1980**, *468*, 15–26.
(30) Beck, W.; Ambach, E.; Nagel, U. *Chem. Ber.* **1985**, *118*, 444–449.
(31) Potekhin, K. A.; Sedov, B. B.; Struchkov, Yu. T.; Zyk, N. V.; Kutateladze, A. G.; Lapin, Yu. A.; Zefirov, N. S. *Dokl. Akad. Nauk SSSR* **1986**, *290*, 627–630.
(32) Schaumann, E.; Kausch, E.; Imbert, J. P. *Chem. Ber.* **1978**, *111*, 1475–1485.
(33) Gillespie, R. J.; Robinson, E. A. *Can. J. Chem.* **1963**, *41*, 2074–2085.
(34) Cotton, F. A.; Stokely, P. F. *J. Am. Chem. Soc.* **1970**, *92*, 294–302.
(35) Klug, H. *Acta Crystallogr.* **1968**, *B24*, 792–802.

the remainder being starting material. Thus, these amines reacted at the ring sulfur as did the hydroxide ion.

Reaction at Both the Exo- and Endocyclic Sulfur Atoms. When **1a** was treated with sodium methoxide in methanol, three products, sulfonamide **6** (57%), its *N*-methyl derivative **30** (8%), and methyl *p*-toluenesulfonate (34%), were isolated in yields that accounted for 99% of the *p*-toluenesulfonyl group of the starting material. Methyl *p*-toluenesulfonate arose from attack by the methoxide ion on the *N*-tosyl sulfur. Compounds **6** and **30** arose from ring S–N bond cleavage to give **31**. Compound **31**, formed initially in 65% (57% + 8%) yield, was then responsible for the formation of the small amount of **30** though N-methylation of **31**, probably bimolecularly. Ultimately, loss of the sulfate group from **31** to give **6** would have taken place during the aqueous workup, and not sooner, since no O-methylated product was observed. The methoxide ion cleaved the endocyclic sulfonyl S–N bond about twice as often as it did the exocyclic sulfonyl S–N bond.

The endocyclic or ring sulfonyl sulfur of **1a** is the site of reaction when the nucleophile is OH^-, $MeNH_2$, or *t*-$BuNH_2$, but it is the endocyclic or tosyl sulfur that reacts when the nucleophile is PhLi, MeLi, or F^-. In the case of MeO^-, reaction occurs at both sulfonyl groups. The 2,1,3-benzothiadiazole 2,2-dioxide ring (**32**) is quite acidic (pK_a 4.7) compared to a typical sulfonamide; e.g., methanesulfonanilide has a pK_a of 8.85.[4c] By analogy, sulfamate **9** would be expected to be quite acidic, and therefore, its conjugate base would act as a good leaving group. This may be the reason why the exocyclic sulfonyl sulfur undergoes nucleophilic attack.

Conclusions. Cyclic sulfamates **1a–g**, **8a**, and **10** resemble their sulfate and sulfonate analogues **2** and **3** in mechanistic profiles, including undergoing rapid alkaline hydrolysis compared to their acyclic counterparts **4**, **5**, and **14**. It should be emphasized that this finding was not a foregone conclusion. As mentioned earlier, various five-membered cyclic sulfonic anhydrides, sulfinates, and sulfinamides do not exhibit enhanced reactivity compared to their acyclic analogues. The variable chemoselectivity exhibited by the two sulfonyl groups of **1a** remains unexplained.

Experimental Section

General Methods. Elemental analyses were performed by D. Cardin. NMR spectra, obtained on spectrometers operating at 60, 90, or 360 MHz for ^1H NMR and at 22.5 and 90.6 MHz for ^{13}C NMR, all in $CDCl_3$ unless otherwise noted, are reported in parts per million from internal TMS. Solvents were purified and dried via standard techniques. Reactions were usually run under nitrogen and worked up by the addition of water, extraction with an organic solvent, drying of the extracts over magnesium sulfate, filtration, and concentration on a rotary evaporator.

3-(*p*-Tolylsulfonyl)-1,2,3-benzoxathiazole 2,2-Dioxide (1a). Method A. *m*-Chloroperbenzoic acid (0.52 g, 3.0 mmol) in chloroform (45 mL) was added dropwise to 3-(*p*-tolylsulfonyl)-1,2,3-benzoxathiazole 2-oxide[36] (**7**) (0.927 g, 2.70 mmol) in chloroform (30 mL) with stirring at 10 °C or lower. After 11 h the mixture was passed through basic alumina and concentrated, and the residual solid was purified by column chromatography (silica gel/chloroform) to give **1a** (0.44 g, 45%), mp 130–131 °C.

Method B. Freshly distilled sulfuryl chloride (4.59 g, 2.73 mL, 34.0 mmol) in dichloromethane (10 mL) was added dropwise with stirring over a 30-min period to *N*-(2′-hydroxyphenyl)-4-toluenesulfonamide[37] (**6**) (9.0 g, 34 mmol) and triethylamine (9.48 mL, 68 mmol) in dichloromethane (110 mL) at −78 °C. After an additional 15 min, the mixture was allowed to warm to 5 °C. Following an aqueous workup, the organic layer gave a solid, which was purified by chromatography (silica gel/chloroform) to give **1a** (9.50 g, 85%): mp 130–131 °C; MS, *m/z* (relative intensity) 325 (7.8, M^+), 91 (100); ^1H NMR ($CDCl_3$) δ 8.07–7.03 (m, 8 Ar H, Ar), 2.38 (s, 3 H, Ar CH_3); ^{13}C NMR (acetone-d_6) δ 148.5, 141.8, 133.2, 131.2, 129.6, 128.0, 127.9, 126.9, 116.5, 113.1, 21.7; ($CDCl_3$) δ 21.8, 111.9, 115.6, 125.5, 126.2, 126.4, 128.7, 130.1, 132.6, 141.1, 147.0; UV [1:1 ethanol/H_2O (v/v)] λ_{max} (nm) 223.5 (log ε 4.15), (point of inflection) 267.0 (3.40); UV (CH_3CN) λ_{max} (nm) 224.0 (log ε 4.70). Anal. Calcd for $C_{13}H_{11}NO_5S_2$: C, 47.99; H, 3.41; N, 4.31. Found: C, 48.02; H, 3.44; N, 4.28.

The following compounds were prepared via method B.

3-(*p*-Tolylsulfonyl)-5-methyl-1,2,3-benzoxathiazole 2,2-dioxide (1b): mp 166–168 °C; MS, *m/z* (relative intensity) 339 (15, M^+), 91 (100). ^1H NMR (acetone-d_6) δ 8.05–7.15 (m, 7 H, Ar H), 2.40 (s, 6 H, Ar CH_3); ^{13}C NMR (acetone-d_6) δ 148.4, 139.8, 137.4, 133.3, 131.0, 129.5, 128.1, 126.5, 116.8, 112.6, 21.6, 21.3. Anal. Calcd for $C_{14}H_{13}NO_5S_2$: C, 49.54; H, 3.86; N, 4.13. Found: C, 49.66; H, 3.97; N, 4.05.

3-(*p*-Tolylsulfonyl)-5-*tert*-butyl-1,2,3-benzoxathiazole 2,2-dioxide (1c): mp 112–124 °C; MS, *m/z* (relative intensity) 381 (15, M^+), 155 (100); ^1H NMR (acetone-d_6) δ 8.10–7.30 (m, 7 H, Ar H), 2.40 (s, 3 H, Ar CH_3), 1.40 [s, 9 H, $C(CH_3)_3$]; ^{13}C NMR (acetone-d_6) δ 150.6, 148.5, 139.9, 133.2, 131.2, 129.7, 126.5, 124.9, 113.7, 112.5, 35.8, 31.5, 21.7. Anal. Calcd for $C_{17}H_{19}NO_5S_2$: C, 53.53; H, 5.02; N, 3.67. Found: C, 53.72; H, 5.13; N, 3.65.

3-(*p*-Tolylsulfonyl)-5-bromo-1,2,3-benzoxathiazole 2,2-dioxide (1d): mp 182–184 °C. MS, *m/z* (relative intensity) 403 (7, M^+), 155 (100), 91 (100); ^1H NMR (acetone-d_6) δ 8.10–7.30 (m, 7 H, Ar H), 2.45 (s, 3 H, Ar CH_3); ^{13}C NMR (acetone-d_6) δ 148.9, 140.8, 131.5, 131.3, 130.6, 129.7, 127.8, 118.9, 115.0, 21.7. Anal. Calcd for $C_{13}H_{10}NBrO_5S_2$: C, 38.63; H, 2.49; N, 3.46. Found: C, 38.65; H, 2.50; N, 3.44.

3-(*p*-Tolylsulfonyl)-5-chloro-1,2,3-benzoxathiazole 2,2-dioxide (1e): mp 142–144 °C; MS, *m/z* (relative intensity) 359 (5.6, M^+), 155 (100), 91 (100); ^1H NMR (acetone-d_6) δ 8.25–7.20 (m, 7 H, Ar H), 2.45 (s, 3 H, Ar CH_3); ^{13}C NMR (acetone-d_6) δ 148.9, 140.3, 133.2, 131.7, 131.4, 129.7, 127.7, 124.7, 116.2, 114.6, 21.7. Anal. Calcd for $C_{13}H_{10}NClO_5S_2$: C, 43.40; H, 2.80; N, 3.89. Found: C, 43.36; H, 2.84; N, 3.89.

3-(*p*-Tolylsulfonyl)-5-acetyl-1,2,3-benzoxathiazole 2,2-dioxide (1f): mp 153–154 °C; MS, *m/z* (relative intensity) 367 (4, M^+), 91 (100); ^1H NMR (acetone-d_6) δ 8.40–7.45 (m, 7 H, Ar H), 2.70 (s, 3 H, $CH_3C{=}O$), 2.45 (s, 3 H, Ar CH_3); ^{13}C NMR (acetone-d_6) δ 195.7, 148.8, 144.4, 136.0, 133.0, 131.3, 129.6, 128.6, 127.1, 115.5, 113.2, 26.7, 21.7. Anal. Calcd for $C_{15}H_{13}NO_6S_2$: C, 49.04; H, 3.57; N, 3.81. Found: C, 48.99; H, 3.78; N, 3.71.

3-(*p*-Tolylsulfonyl)-5-nitro-1,2,3-benzoxathiazole 2,2-dioxide (1g): mp 177–178 °C dec; MS, *m/z* (relative intensity) 370 (2, M^+), 91 (100); ^1H NMR (acetone-d_6) δ 8.60–7.40 (m, 7 H, Ar H), 2.40 (s, 3 H, Ar CH_3); ^{13}C NMR (acetone-d_6) δ 149.2, 131.5, 129.8, 126.5, 123.6, 120.0, 116.0, 114.1, 111.5, 21.7. Anal. Calcd for $C_{13}H_{10}N_2O_7S_2$: C, 42.16; H, 2.72; N, 7.56. Found: C, 42.38; H, 2.81; N, 7.50.

3-(*p*-Tolylsulfonyl)-6-nitro-1,2,3-benzoxathiazole 2,2-dioxide (8a): mp 140 °C dec; ^1H NMR δ 8.22–7.25 (m, 7 H, Ar H), 2.5 (s, 3 H, Ar CH_3). Anal. Calcd for $C_{13}H_{10}N_2O_7S_2$: C, 42.16; H, 2.72; N, 7.56. Found: C, 42.20; H, 2.74; N, 7.58. Sultam **8a** was also prepared by the nitration of **1a**.

Kinetic Procedure. Typically, aliquots (2.5 mL) of standardized carbonate-free sodium hydroxide solutions (0.05, 0.06, or 0.10 mol dm^{-3}) in distilled deionized water were added quickly by syringe to 6.77×10^{-4} mol dm^{-3} solutions (0.5 mL) of **1a** in spectrophotometric grade acetonitrile (Aldrich) in UV cuvettes thermostated at 0, 10, or 20 °C. Temperatures were controlled to ±0.1 °C with fluid circulated from thermostat baths. The absorbance was monitored at 294.0 nm with a Cary 219 spectrophotometer. A Durrum-Gibson stopped-flow spectrophotometer with a Kel-F flow path of 0.02 m was used to gather the kinetic data at 30 °C by following the change in absorbance, *A*, at 390 nm for **1g** and at 396 and 440 nm for **8a**. Absorbance data were obtained from photographs of oscilloscope traces. Rate constants, k_{obsd}, were obtained from the slopes of linear plots of log ($A_\infty - A_0$) versus *t* by the method of least squares and are reported in Table I. To obtain the kinetic data for the Hammett plot given

(36) Capuano, L.; Urhahn, G.; Willmes, A. *Chem. Ber.* **1979**, *112*, 1012–1022.
(37) Kurita, K. *Chem. Ind. (London)* **1974**, 345.

in Table III, the aqueous sodium hydroxide (1.5 mL) was added to the sulfamates **1a–f** in acetonitrile (1.5 mL) and the absorbance values, measured over time with a Cary 219 spectrophotometer, were fed to an Apple IIe computer, which calculated the first-order rate constants by a least-squares iterative procedure using the Varian Advanced Order Kinetics Calculations program. At least four (five in the Hammett plot study) runs were performed to obtain each average rate constant. The reactions were followed for at least 10 half-lives. Kinetics at pressures above atmospheric were studied in a stopped-flow instrument in which reacting solutions could be subjected to pressures up to 1 kbar as previously described.[38] Volumes of activation were obtained from plots of ln k_{obsd} versus pressure. Since these plots are linear over the range of pressure studied, the compressibility of activation is essentially 0 and $\Delta V^{\ddagger}$ refers to the value at 1 bar. Enthalpies and entropies of activation were obtained from plots of ln k versus $1/T$.[39]

Reaction of 1a with Sodium Hydroxide. Excess 0.05 mol dm^{-3} aqueous sodium hydroxide was added to **1a** (0.200 g) in a mixture of acetonitrile/95% ethanol (3:2 v/v). After 3 h, the solution was acidified with hydrochloric acid, and then it was extracted with chloroform to yield sulfonamide **6**. Addition of barium chloride to the aqueous layer gave a precipitate of barium sulfate.

One equivalent of 0.060 mol dm^{-3} sodium hydroxide (4.6 mL) was added with vigorous shaking to **1a** (0.089 g, 0.275 mol) in acetonitrile (10 mL). Water (5 mL) was then added, and the mixture was extracted with chloroform (3 × 5 mL). The organic layer yielded starting material **1a** (0.0307 g, 35%). The water layer was concentrated, washed three times with ether, and then dried in vacuo over phosphorus pentoxide to give **15a** (0.045 g, 45%): ^{1}H NMR (D_2O) δ 7.79–6.75 (m, Ar H). Anal. Calcd for $C_{13}H_{11}NO_6S_2Na_2 \cdot H_2O$: C, 38.52; H, 3.23; N, 3.46. Found: C, 38.38; H, 2.96; N, 3.41.

Treatment of 1a with Hydrochloric Acid. A 1.54×10^{-4} mol dm^{-3} solution of **1a** in ethanol containing excess hydrochloric acid was scanned at 330–220 nm. No change in the spectrum was observed over the course of 3 h. A similar treatment of a more concentrated solution of **1a** was monitored by TLC. No evidence of reaction was observed.

Reaction of 1a with Phenyllithium. A solution of standardized phenyllithium solution in ether/hexane (8.40 mL, 3.08 mmol), prepared from bromobenzene and *n*-butyllithium in hexane, plus THF (4.2 mL) at −12 °C was added to **1a** (0.500 g, 1.54 mmol) in THF at −78 °C. The dark-red mixture was stirred for 40 min, quenched with 3 drops of water, filtered to remove a white precipitate, and concentrated. The residue was taken up in dichloromethane, washed with water, dried over magnesium sulfate, and concentrated to give phenyl *p*-tolyl sulfone (0.280 g, 78%), mp 124–125 °C from ethanol (lit.[40] mp 124–125 °C), with IR and ^{1}H NMR spectra identical with those obtained from an authentic sample.

Reaction of 1a with Methyllithium. A solution of methyllithium (1.32 mL, 2.77 mmol) was added to a solution of **1a** (0.300 g, 0.923 mmol) in THF (15 mL) at room temperature. TLC indicated that the reaction was complete within 5 min. After 15 min, 8 drops of water were added and the volatiles were removed in vacuo. Extraction of the residue with methylene chloride gave a solid, which, upon recrystallization from ethanol, yielded bis(*p*-tolylsulfonyl)methane (**27**) (0.0722 g, 49%), mp 132–33 °C (lit.[41] mp 135 °C), whose IR and ^{1}H NMR spectra matched those in the literature.

Reaction of 1a with Methylamine. Aqueous methylamine (40% by weight, 0.0116 g, 0.0290 mL, 0.400 mmol) was added to **1a** (0.13 g, 0.40 mmol) in acetonitrile (10 mL). After being stirred overnight, the mixture was concentrated and the residue was extracted with methylene chloride. The extracts yielded a solid identified as **28** (0.127 g, 89%): mp 121–122 °C (EtOH); IR (KBr) 3320 (s, NH) cm^{-1}; ^{1}H NMR δ 7.89–7.00 (m, 9 H, Ar H and NH), 5.27 (br s, 1 H, NH), 2.83 (d, 3 H, NCH_3), 2.36 (s, 3 H, CH_3); ^{13}C NMR δ 144.2, 140.7, 135.9, 129.7, 127.5, 127.3, 125.7, 122.6, 30.5, 21.5. Anal. Calcd for $C_{14}H_{16}N_2O_5S_2$: C, 47.18; H, 4.52; N, 7.86. Found: C, 47.05; H, 4.44; N, 7.81.

Reaction of 1a with *tert*-Butylamine. A reaction analogous to the one with methylamine yielded a solid identified as **29** (44%): mp 105–106 °C (EtOH); IR (KBr) 3320 and 3280 (s, NH) cm^{-1}; ^{1}H NMR δ 7.76–7.12 (m, 9 H, Ar H and NH), 5.47 (s, 1 H, NH), 2.34 (s, 3 H, CH_3), 1.35 [s, 9 H, $C(CH_3)_3$]; ^{13}C NMR δ 144.0, 140.8, 135.9, 129.9, 129.6, 127.3, 125.5, 123.1, 122.7, 56.2, 21.5. Anal. Calcd for $C_{17}H_{22}N_2O_5S_2$: C, 51.24; H, 5.56; N, 7.03. Found: C, 50.95; H, 5.66; N, 6.99.

Reaction of 1a with Sodium Methoxide. A 2 mol dm^{-3} solution of sodium methoxide (2.0 mL, 0.40 mmol), prepared from sodium and methanol, was added to **1a** (0.130 g, 0.400 mmol) in methanol/acetonitrile (12 mL of 3:2 v/v), and the reaction mixture was stirred at room temperature for 12 h. Water (10 mL) was added, and the organic solvents were removed in vacuo. Extraction with methylene chloride yielded methyl *p*-toluenesulfonate (25.1 mg, 34%). The aqueous layer was acidified with 3 mol dm^{-3} hydrochloric acid and concentrated to give a solid. The acetone-soluble extract of this solid was separated by preparative TLC on silica gel (ether/hexanes) to give **30** (9.3 mg, 8.4%) and **6** (58.5 mg, 56.5%). These compounds were identified by their physical and spectral properties.

3-H-1,2,3-Benzoxathiazole 2,2-Dioxide (9). Potassium fluoride (0.0376 g, 0.800 mmol) in water (5 mL) was added to **1a** (0.13 g, 0.40 mmol) in acetonitrile (15 mL). The solution was stirred overnight, concentrated, and extracted with dichloromethane. The organic layer yielded *p*-toluenesulfonyl fluoride (0.060 g, 87%), mp 40–41 °C (lit.[42] mp 43–44 °C), whose IR and ^{1}H NMR spectra matched those in the literature. The ^{19}F NMR spectrum observed at 84.26 MHz during the course of the reaction showed resonances only for the product at δ 142.9 ppm from external trifluoroacetic acid and for the fluoride ion. The reaction was repeated on a larger scale. Upon acidification of the extracted aqueous solution with 1 mol dm^{-3} HCl solution, a white precipitate formed, which was recovered by extraction with dichloromethane. Workup of the extracts gave **9** (0.97 g, 93%): mp 76–79 °C; IR (Nujol) 3320 (sharp, NH), 1480, 1365 (SO_2), 1300, 1240, 1180 (SO_2), 1160, 1090, 1005, 845, 800, 740, 730 cm^{-1}; ^{1}H NMR δ 7.01 (m, 1 H, Ar *H*), 7.06–7.14 (m, 4 H, Ar *H* and N*H*); ^{13}C NMR δ 111.4, 113.5, 124.3, 124.9, 129.1, 143.6; MS *m/z* (relative intensity) 171 (35, M^+), 106 (6), 79 (100).

3-Methyl-1,2,3-benzoxathiazole 2,2-Dioxide (10). 3-H-1,2,3-Benzoxathiazole 2,2-dioxide (**9**, 0.91 g, 5.3 mmol) in THF (10 mL) was added with stirring to a suspension of hexane-washed sodium hydride (0.26 g of a 60% dispersion in mineral oil, 6.4 mmol) in anhydrous THF (15 mL) at 0 °C. After 5 min, iodomethane (3.76 g, 1.65 mL, 26.5 mmol) was added, whereupon a white solid precipitated. After 12 h, the mixture was concentrated and triturated with hot ethyl acetate, and the insoluble material was removed by gravity filtration. TLC (1:3 ethyl acetate/hexanes) of the filtrate showed one major spot plus a spot at the base line. Elution through silica gel (1:1 chloroform/ethyl acetate), followed by recrystallization from ethyl acetate/hexanes, gave **10** (0.47 g, 48%): mp 75–77 °C; IR (KBr) 2940, 1625, 1600, 1590, 1360 (SO_2), 1215, 1175 (SO_2), 865, 790, 740, 605 cm^{-1}; ^{1}H NMR δ 3.30 (s, 3 H, CH_3), 6.81 (dd, 1 H, Ar *H*, J = 1.2, 7.8 Hz), 7.02 (dt, 1 H, Ar *H*, J = 1.3, 7.9 Hz), 7.11 (dd, 1 H, Ar *H*, J = 1.3, 7.9 Hz), 7.16 (dt, 1 H, Ar *H*, J = 1.3, 7.8 Hz); ^{13}C NMR δ 29.9, 109.3, 111.1, 122.3, 125.0, 132.5, 141.5; UV (1:1 ethanol/water) λ_{max} (nm) 228 (log ε 3.83), 276 (3.28); MS *m/z* (relative intensity) 185 (65, M^+), 120 (100), 93 (56), 92 (30). Anal. Calcd for $C_7H_7NO_3S$: C, 45.39; H, 3.81; N, 7.56. Found: C, 45.44; H, 3.89; N, 7.56.

6-Nitro-3-(*p*-tolylsulfonyl)-1,2,3-benzoxathiazole 2,2-Dioxide (8a). Sodium nitrite (0.21 g, 3.0 mmol) was added to **1a** (0.32 g, 1.0 mmol) in trifluoroacetic acid (10 mL) with stirring.[43] After 48 h, TLC analysis (1:1 ethyl acetate/cyclohexane) showed two spots, one yellow and one for unreacted **1a**. After an additional 5 days, TLC showed **1a** to be present, so an additional 4

(38) van Eldik, R.; Palmer, D. A.; Schmidt, R.; Kelm, H. *Inorg. Chim. Acta* **1981**, *50*, 131–135.
(39) Robinson, P. J. *J. Chem. Educ.* **1978**, *55*, 509–510.
(40) *Dictionary of Organic Compounds*; Buckingham, J., Ed.; Chapman and Hall: New York, 1982; Vol. 4, p 3837.
(41) Fromm, E.; Forster, A.; Scherschewitzki, B. V. *Justus Liebigs Ann. Chem.* **1912**, *394*, 343–349.
(42) *Dictionary of Organic Compounds*; Buckingham, J., Ed.; Chapman and Hall: New York, 1982; Vol. 4, p 3749.
(43) Uemura, S.; Toshimitsu, A.; Okano, M. *J. Chem. Soc., Perkin Trans. 1* **1978**, 1076–1079.

equiv of sodium nitrite (0.27 g, 3.9 mmol) was added. After an additional 6 days, **1a** was still noted by TLC, so the solution was heated to 40 °C for 3 days and then allowed to cool. One day later, the reaction was quenched by water (75 mL). Extraction with dichloromethane gave **8a** as a yellow solid, which was recrystallized from ethyl acetate/cyclohexane (0.22 g, 59%): mp 167–169 °C dec; IR (Nujol) 3100, 1590, 1520 (NO_2), 1470, 1400, 1385 (SO_2), 1335 (NO_2), 1215 (SO_2), 1165 (SO_2), 890, 820, 745 cm^{-1}; ^1H NMR δ 2.45 (s, 3 H, CH_3), 7.38 (d, 2 H, Ar *H*, J = 8.0 Hz), 7.76 (d, 1 H, Ar *H*, J = 8.8 Hz), 7.94 (d with fine splitting, 2 H, Ar *H*, J = 8.7 Hz), 7.99 (d, 1 H, Ar *H*, J = 2.2 Hz), 8.20 (dd, 1 H, Ar *H*, J = 2.3, 9.0 Hz); ^{13}C NMR δ 21.9, 108.1, 114.0, 121.4, 128.8, 130.5, 131.0, 132.3, 139.8, 144.5, 148.0; MS m/z (relative intensity) 370 (9, M^+), 216 (27), 200 (10), 155 (738), 149 (17), 91 (1000), 77 (102), 65 (210). Anal. Calcd for $C_{13}H_{10}N_2O_7S_2$: C, 42.16; H, 2.72; N, 7.56. Found: C, 42.18; H, 2.74; N, 7.32.

6-Nitro-3-[(3-nitro-*p*-tolyl)sulfonyl]-1,2,3-benzoxathiazole 2,2-Dioxide (8b). Concentrated sulfuric acid (10 mL) and 90% fuming nitric acid (5 mL) were added with stirring to sulfamate **1a** (1.63 g, 5.01 mmol) in dichloromethane (10 mL) with cooling by a water bath.[44] The two-phase mixture was stirred vigorously for 2 days, diluted with water, and extracted. Workup gave a yellow solid (1.12 g). Recrystallization from ethyl acetate gave **8b** (0.32 g, 15%): mp 192–193 °C dec; IR (Nujol) 3120, 1605, 1535 (br, NO_2), 1480, 1415 and 1390 (SO_2), 1345 (br, NO_2), 1220, 1190 and 1180 (SO_2), 1060, 950, 910, 880, 820, 730 cm^{-1}; ^1H NMR δ 2.71 (s, 3 H, CH_3), 7.63 (d, 1 H, Ar *H*, J = 8.3 Hz), 7.83 (d, 1 H, Ar *H*, J = 9.0 Hz), 8.03 (d, 1 H, Ar *H*, J = 2.3 Hz), 8.16 (dd, 1 H, Ar *H*, J = 2.1, 8.2 Hz), 8.26 (dd, 1 H, Ar *H*, J = 2.3, 9.0 Hz), 8.58 (d, 1 H, Ar *H*, J = 2.1 Hz); ^{13}C NMR δ 21.0, 108.5, 114.3, 121.8, 125.1, 130.4, 132.1, 134.4, 134.8, 139.9, 142.6, 145.2, 149.2; MS m/z (relative intensity) 415 (5, M^+), 216 (2), 200 (100), 136 (46), 89 (43). Anal. Calcd for $C_{13}H_9N_3O_9S_2$: C, 37.59; H, 2.18; N, 10.12. Found: C, 37.25; H, 2.13; N, 10.19.

Phenyl *N*-Methyl-*N*-phenylsulfamate (14). A mixture of phenyl *N*-phenylsulfamate (3.4 g, 14 mmol), anhydrous sodium carbonate (10.0 g, 0.100 mol), benzyltriethylammonium chloride (3.1 g, 14 mmol), iodomethane (9.6 g, 68 mmol), and benzene (50 mL) was stirred vigorously for 24 h, and then additional iodomethane (11.5 g, 81.0 mmol) was added.[45] After an additional 24 h, the mixture was filtered and concentrated to give 3.0 g of a brown oil, which slowly partially crystallized. The crystals were recovered by vacuum filtration, rinsed with cold cyclohexane, and then recrystallized from dichloromethane/cyclohexane to give **14** (0.38 g, 11%): mp 70–72 °C; IR (Nujol) 3050, 1590, 1585, 1485, 1365 (SO_2), 1255, 1195 (SO_2), 1060, 885, 850, 725, 680 cm^{-1}; ^1H NMR δ 3.40 (s, 3 H, CH_3), 7.24–7.45 (complex, m, 10 H, Ar *H*); ^{13}C NMR δ 40.1, 121.8, 126.2, 126.9, 127.8, 129.4, 129.8, 141.2, 150.2; UV (1:1 ethanol/water) λ_{max} (nm) (point of inflection) 238.5 (log ϵ 3.58); MS m/z (relative intensity) 263 (71, M^+), 183 (3), 170 (2), 106 (100), 93 (4), 77 (60). Anal. Calcd for $C_{13}H_{13}NO_3S$: C, 59.30; H, 4.98; N, 5.32. Found: C, 59.40; H, 5.09; N, 5.24.

Reaction of Phenyl *N*-Methyl-*N*-phenylsulfamate (14) with Excess NaOH. Sodium hydroxide (1.0 g, 25.0 mmol) was added to **14** (0.9 g, 3 mmol) in absolute ethanol (50 mL), and the mixture was heated under reflux. After 3 days, TLC showed a major spot (3:1 hexanes/ethyl acetate) corresponding to unreacted starting material, a minor spot, and a strong spot at the base line. The reaction was monitored by TLC for several days. No change was observed, so, after 11 days, the reaction was quenched with water. Extraction with dichloromethane gave 0.3 g (33%) of a brown oil that slowly solidified upon standing and whose IR spectrum matched that of the starting material **14**. The remaining aqueous solution was acidified with 3 mol dm^{-3} HCl and extracted to give 0.14 g (45%) of a dark oil whose IR spectrum matched that of phenol.

***N*-Benzyl-1,8-naphthosultam (11).** Triethylamine (0.25 g, 0.34 mL, 2.5 mmol) followed by benzyl chloride (9.38 g, 8.53 mL, 74.1 mmol) was added to 1,8-naphthosultam (**13**) (0.50 g, 2.5 mmol) in benzene (30 mL), and the solution was then heated to reflux. After 18 h, a precipitate that had formed was filtered, and the filtrate was concentrated. The solid residue was chromatographed on silica gel (2:1 cyclohexane/ethyl acetate) to give **11** (0.43 g, 59%): mp 159–161 °C; IR (Nujol) 1625, 1585, 1485, 1460, 1380, 1350, 1340, 1300 and 1170 (SO_2), 1130, 800 (SN), 740 cm^{-1}; ^1H NMR δ 4.98 (s, 2 H, CH_2), 6.47 (dd, 1 H, Ar *H*, J = 6.5, 1.4 Hz), 7.23–7.41 (m, 5 H, Ar *H*), 7.51 (br d, 2 H, Ar *H*, J = 7.0 Hz), 7.73 (t, 1 H, Ar *H*, J = 8.0 Hz), 7.99 (d, 1 H, Ar *H*, J = 7.2 Hz), 8.03 (d, 1 H, Ar *H*, J = 8.2 Hz); ^{13}C NMR δ 45.4, 103.8, 118.3, 119.1, 119.9, 127.5, 127.9, 128.0, 128.9, 129.3, 130.1, 130.5, 131.2, 135.2, 136.2; UV (1:1 acetonitrile/water) λ_{max} (nm) 243.5 (log ϵ 4.19), (point of inflection) 254.5 (4.04), 341.5 (3.48); MS m/z (intensity) 295 (20, M^+), 230 (1), 204 (1), 140 (2), 126 (4), 91 (100). Anal. Calcd for $C_{17}H_{13}NO_2S$: C, 69.13; H, 4.44; N, 4.74. Found: C, 68.91; H, 4.34; N, 4.72.

***N*-(*p*-Tolylsulfonyl)-1,8-naphthosultam (12)** was prepared from triethylamine (1.01 g, 1.40 mL, 10.0 mmol), *p*-toluenesulfonyl chloride (1.91 g, 10.0 mol), and 1,8-naphthosultam (**13**, 2.05 g, 10.0 mol) in dichloromethane (20 mL). Recrystallization from ethyl acetate gave **12** (1.51 g, 42%): mp 210–211 °C (lit.[14] mp 208–209 °C); IR (Nujol) 3100, 3060, 1590, 1580, 1455, 1370 (SO_2), 1345 (SO_2), 1210, 1180 (br, SO_2), 1100, 1075, 950, 875 (br, SN), 800 cm^{-1}; ^1H NMR δ 2.34 (s, 3 H, CH_3), 7.27 (d, 2 H, Ar *H*, J = 8.4 Hz), 7.58–7.65 (m, 3 H, Ar *H*), 7.74 (t, 1 H, Ar *H*, J = 7.8 Hz), 7.93 (d, 1 H, Ar *H*, J = 7.3 Hz), 8.07 (d, 2 H, Ar *H*, J = 8.4 Hz), 8.08 (d, 1 H, Ar *H*, J = 8.2 Hz); ^{13}C NMR δ 21.6, 109.3, 118.2, 120.2, 121.9, 128.1, 128.6, 129.2, 129.3, 129.8, 130.6, 130.7, 131.8, 134.2, 145.9; UV (1:1 acetonitrile/water) λ_{max} (nm) 239.5 (log ϵ 4.66), 309.5 (3.70); MS m/z (relative intensity) 359 (2, M^+), 204 (4), 188 (6), 172 (6), 155 (100), 113 (11), 91 (100). Anal. Calcd for $C_{17}H_{13}NO_4S_2$: C, 56.81; H, 3.64; N, 3.90. Found: C, 56.98; H, 3.82; N, 4.01.

Treatment of *N*-Benzyl-1,8-naphthosultam (11) with NaOH. Sodium hydroxide (0.80 g, 20 mmol) was added to sultam **11** (0.11 g, 0.37 mmol) suspended in 95% ethanol (10 mL), and the mixture was heated under reflux for several days. TLC (2:1 hexanes/ethyl acetate) of the suspension taken over this period continued to show starting material. After 1 week, the mixture was extracted with ethyl acetate and worked up to give 0.21 g of a solid. Recrystallization from ethyl acetate gave **11** (40 mg, 36%), mp 160–161 °C, whose melting point and IR and NMR spectra matched those of an authentic sample. No other compounds were isolated. In addition, the absorbance versus time of **11** was recorded using a 500-fold excess of hydroxide ion in 60:40 acetonitrile/water. Successive spectra scanned between 450 and 260 nm at 25 °C at 1-h intervals over an 11-h period showed no change in absorption.

Reaction of *N*-(*p*-Tolylsulfonyl)-1,8-naphthosultam (12) with Sodium Hydroxide. A suspension of sultam **12** (0.72 g, 2.0 mmol) and sodium hydroxide (0.85 g, 21 mmol) in 95% ethanol (10 mL) was refluxed with stirring for 24 h. TLC showed complete consumption of **12**. Water was added to form a solution, which was then acidified with 2 mol dm^{-3} HCl. Extraction and workup gave 30 mg of a black, tar-like solid, which was shown by IR analysis to be **13**. The remaining aqueous solution was concentrated to give 1.0 g of a black, tarry material. Approximately 0.5 g of this material was chromatographed on silica gel with acetone. A pale yellow oil, 0.33 g (82%), was recovered. Treatment of 0.15 g of this oil with *S*-benzylthiouronium chloride immediately produced a white precipitate. Recrystallization from 1-butanol gave the *S*-benzylthiouronium salt of *N*-(*p*-tolylsulfonyl)-1-naphthylamine-8-sulfonic acid (**19**) (30 mg), mp 173–175 °C, which was identical with an authentic sample whose preparation is described below. Anal. Calcd for $C_{25}H_{25}N_3O_5S_3$: C, 55.23; H, 4.63; N, 7.73. Found: C, 55.67; H, 4.62; N, 7.74.

***S*-Benzylthiouronium Salt of *N*-(*p*-Tolylsulfonyl)-1-naphthylamine-8-sulfonic Acid (19).** *N*-(*p*-Tolylsulfonyl)-1-naphthylamine-8-sulfonic acid (**19**) was prepared from 1-naphthylamine-8-sulfonic acid (1.06 g, 4.70 mmol), sodium carbonate (0.48 g, 4.5 mmol), water (50 mL), and *p*-toluenesulfonyl chloride (0.88 g, 4.6 mmol) as a pink, glassy solid (0.72 g, 42%). An attempt to recrystallize this solid from ethyl acetate failed, with a purple, viscous oil being recovered. This oil was then treated with *S*-benzylthiouronium chloride[46] to give the title salt (0.24 g from 1-propanol, 9.6% based on *p*-toluenesulfonyl chloride): mp 172–175 °C; IR (Nujol) 3340 (br, NH), 3180 (br, NH),

(44) Davis, G.; Cook, N. *Chemtech* **1977**, *7*, 626–629.
(45) Burke, P. O.; Spillane, W. J. *Synthesis* **1985**, 1851–1854.
(46) Pasto, D. J.; Johnson, C. R. *Laboratory Text for Organic Chemistry*; Prentice-Hall Inc.: Englewood Cliffs, NJ, 1971; p 494.

1660, 1460, 1340 (SO_2N), 1305, 1220, 1155 (SO_3), 1115 (SO_2N), 1045 (SO_3), 945, 855, 760, 655 (SO_3) cm^{-1}; ^1H NMR (DMSO-d_6) δ 2.23 (s, 3 H, CH_3), 4.48 (s, 2 H, CH_2), 7.19 (d, 2 H, Ar *H*, *J* = 8.1 Hz), 7.27-7.46 (m, 7 H, Ar*H*), 7.57 (d, 1 H, Ar *H*, *J* = 7.8 Hz), 7.87 (d, 1 H, Ar *H*, *J* = 8.4 Hz), 7.90 (d, 2 H, Ar *H*, *J* = 8.0 Hz), 8.27 (d, 1 H, Ar *H*, *J* = 7.3 Hz), 8.95 (br s, 2 H, NH_2), 9.20 (br s, 2 H, NH_2), 12.82 (s, 1 H, N*H*); ^{13}C NMR (DMSO-d_6) δ 20.9, 34.3, 116.0, 120.9, 124.4, 124.5, 125.6, 127.5, 128.0, 128.1, 128.9, 129.0, 129.2, 131.9, 133.6, 134.9, 135.9, 136.6, 141.7, 143.0, 169.0. Anal. Calcd for $C_{25}H_{25}N_3O_5S_3$: C, 55.23; H, 4.63; N, 7.73. Found: C, 55.26; H, 4.67; N, 7.75.

Acknowledgment. We acknowledge generous support from the National Science Foundation for Grant CHE 8308245 to K.K.A. and for Grants CHE 7908399 and CHE 86 14606 enabling purchase of UV and NMR spectrometers, respectively; from the U.S. Department of Defense for Grant US DOD DAAL03-88-G-0100 enabling purchase of a mass spectrometer; and from the Central University Research Fund of the University of New Hampshire to G.J.H. We thank Dr. Achim Gerhard for assistance in conducting the high pressure kinetics experiments and Professor Dr. R. van Eldik of the University of Witten/Herdecke, Germany, for access to the instrument and for hospitality (C.D.H.).

Registry No. **1a**, 107555-82-8; **1b**, 136061-81-9; **1c**, 136061-82-0; **1d**, 136061-83-1; **1e**, 136061-84-2; **1f**, 136061-85-3; **1g**, 136061-86-4; **b**, 3897-39-0; **7**, 70376-37-3; **8a**, 136061-87-5; **8b**, 136061-96-6; **9**, 136061-92-2; **10**, 136061-95-5; **11**, 136061-98-8; **12**, 109593-01-3; **13**, 603-72-5; **14**, 136061-97-7; **15a**, 136088-51-2; **19**, 130955-98-5; **19**·$PhCH_2SC{=}NH(NH_2)$, 136061-99-9; **28**, 136061-93-3; **29**, 136061-94-4; **30**, 81256-17-9; SO_2Cl_2, 7791-25-5; C_6H_5Li, 591-51-5; CH_3Li, 917-54-4; CH_3NH_2, 74-89-5; *t*-$BuNH_2$, 75-64-9; CH_3ONa, 124-41-4; KF, 7789-23-3; $C_6H_5SO_2C_6H_4$-4-CH_3, 640-57-3; $CH_2(S{-}O_2C_6H_4$-4-$CH_3)_2$, 15310-28-8; $C_6H_5OSO_2NHC_6H_5$, 85599-60-6; $C_6H_5CH_2SC{=}NH(NH_2)$·HCl, 538-28-3; *N*-(2-hydroxy-5-methylphenyl)-4-toluenesulfonamide, 81256-11-3; *N*-(5-*tert*-butyl-2-hydroxyphenyl)-4-toluenesulfonamide, 136061-88-6; *N*-(5-bromo-2-hydroxyphenyl)-4-toluenesulfonamide, 136061-89-7; *N*-(5-chloro-2-hydroxyphenyl)-4-toluenesulfonamide, 136061-90-0; *N*-(5-acetyl-2-hydroxyphenyl)-4-toluenesulfonamide, 136061-91-1; *N*-(2-hydroxy-5-nitrophenyl)-4-toluenesulfonamide, 91956-17-1; *N*-(2-hydroxy-4-nitrophenyl)-4-toluenesulfonamide, 91956-16-0; 1-naphthylamine-8-sulfonic acid, 82-75-7.

An Efficient Synthesis of 2-Vinylbenzimidazoles from 1-(2-Benzimidazol-2-ylethyl)pyridinium Salts Using an Anion-Exchange Resin

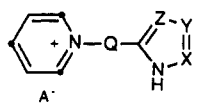
Ermitas Alcalde,*[†] Lluïsa Pérez-García,[†] Immaculada Dinarés,[†] and Jordi Frigola[‡]

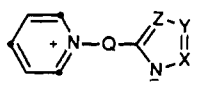
Laboratorio de Química Orgánica, Facultad de Farmacia, Universidad de Barcelona, 08028-Barcelona, Spain, and Departamento de Química Médica, Laboratorios Dr. Esteve S.A., 08026-Barcelona, Spain

Received March 11, 1991

Transformation of several 1-(2-benzimidazol-2-ylethyl)pyridinium salts, obtained by two different procedures, into their corresponding 2-vinylbenzimidazoles either using an anion-exchange resin (OH^- form) or in the solid state is described. This approach now allows a facile entry into the almost unknown 2-vinylbenzimidazole monomers.

As part of an ongoing research project in the quest for novel organic substrates with large dipole moments, we have reported[1,2] the transformation of *N*-azolylpyridinium **1** and (azolylmethyl)pyridinium salts **2** into their corresponding heterocyclic betaines **3** and **4**.[3] A logical extension of the preceding studies is to consider an ethylene moiety as the interannular linkage, leading to the (azolylethyl)pyridinium salts **5**, potential precursors of ethylenepyridinium azolate inner salts **6**.



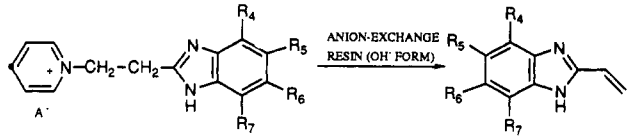


1 Q: -
2 Q: CH_2
5 Q: CH_2CH_2

3 Q: -
4 Q: CH_2
6 Q: CH_2CH_2

X, Y, Z: = CR-; =N-
•: = CR-

During the course of this investigation it became apparent that the almost unknown title pyridinium salts **7** could be efficiently prepared by two methods which have sufficient flexibility to allow conveniently substituted benzimidazoles to be generated from a variety of *o*-arylenediamines. Once synthesis was achieved, this class of pyridinium salts **7** was quantitatively transformed at room temperature into the corresponding 2-vinyl-1*H*-benzimidazoles **8** using an anion-exchange resin (OH^- form).



7 **8**

To the best of our knowledge, only three 2-vinyl-1*H*-benzimidazoles and a few 1-alkyl derivatives have been described since the work of Bachman,[4] seeking 2-vinyl

[†] Laboratorio de Química Orgánica.
[‡] Departamento de Química Médica.

(1) (a) Alcalde, E.; Dinarés, I.; Elguero, J.; Fayet, J.-F.; Vertut, M. C.; Miravitlles, C.; Molins, E. *J. Org. Chem.* **1987**, *52*, 5009. (b) Alcalde, E.; Dinarés, I.; Elguero, J.; Frigola, J.; Osuna, A.; Castanys, S. *Eur. J. Med. Chem.* **1990**, *25*, 309.

(2) Alcalde, E.; Pérez, L.; Fayet, J.-P.; Vertut, M.-C. *Chem. Lett.* **1991**, 845.

(3) The method of choice for this transformation was found to be the use of an anion-exchange Amberlite IRA-401 resin (OH^- form) in over 90% yield and also applied to other betaines or compounds with a betaine character.

0022-3263/91/1956-6516$02.50/0