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Intramolecular Nucleophilic Catalysis by the Neighboring Hydroxyl Group in Acid-Catalyzed Benzenesulfonamide Hydrolysis[1]

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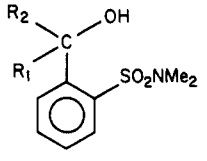
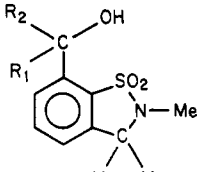
The reactivity toward the neighboring hydroxyl group of two *N,N*-dialkylbenzenesulfonamide systems 1 and 2 is extraordinarily sensitive to structure. In the presence of *o*-CH_2OH, the SO_2NMe_2 group is stable almost indefinitely in 1 M HCl, whereas the corresponding compound with *o*-CMe_2OH cyclizes to the sultone under the same conditions with a half-life of around 20 min. When the sulfonamide group is constrained in a five-membered ring its cleavage must be followed by the stopped-flow technique. These very large variations in reactivity are interpreted primarily in terms of ground-state strain, which is partially relieved in the transition state for cyclization.

The hydrolysis of sulfonamides is an extremely slow reaction, generally requiring strong acid and drastic conditions.[3] However, very large rate accelerations are observed in the presence of a neighboring carboxyl group.[1,4] The reaction involves intramolecular nucleophilic catalysis and features a pentacovalent sulfur intermediate.[4e] We have discussed previously how the effective molarity (EM) of the carboxyl group depends on the subtle interplay of mechanistic and structural factors, and can be as high as 10^{10} M in favorable cases.[1,4]

We present a study of intramolecular catalysis in two *N,N*-dialkylbenzenesulfonamide systems (1 and 2) by the neighboring hydroxyl group. This acid-catalyzed reaction

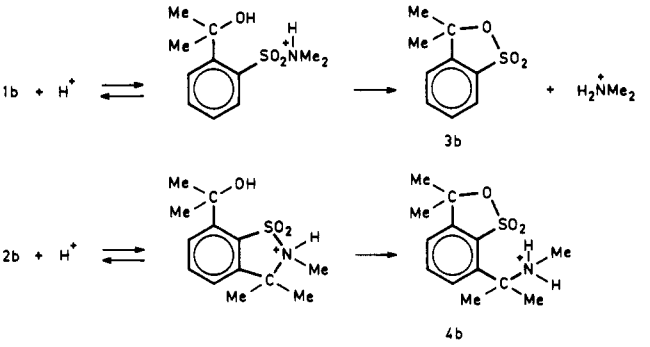


1a, $R_1 = R_2 = H$
1b, $R_1 = R_2 = Me$
1c, $R_1 = H$, $R_2 = Me$



2a, $R_1 = R_2 = H$
2b, $R_1 = R_2 = Me$

Scheme I



involves nucleophilic catalysis. It is extraordinarily sensitive to substituents R_1 and R_2. Thus, the 2-hydroxymethyl compound (**1a**) is unchanged after 7 months at 25 °C in aqueous ethanol containing 1 M HCl, whereas the half-life of **1b** under similar conditions is about 20 min.

Results and Discussion

Sulfonamides **1b** and **2b**, with geminal dimethyl substitution, cyclize irreversibly under acidic conditions to the corresponding sultones (Scheme I). Pseudo-first-order rate constants (k_{obsd}) for both reactions in 1:1 (v/v) EtOH–H_2O at 25.50 °C are given in Table I. Although **2b** is some 4000 times more reactive, the rate constant for the cyclization even of **1b** is far higher than any reasonable estimate for the rate of hydrolysis of *N,N*-dimethylbenzenesulfonamide, for which the half-life in 70% (v/v) CF_3CO_2H–H_2O at 99 °C is 95 h.[5] Evidently the effective

(1) Part 8 in the series on intramolecular-catalyzed sulfonamide hydrolysis. (a) Part 7: Jager, J.; Graafland, T.; Schenk, H.; Kirby, A. J.; Engberts, J. B. F. N. *J. Am. Chem. Soc.* **1984**, *106*, 139. (b) Part 6: Graafland, T.; Nieuwpoort, W. C.; Engberts, J. B. F. N. *J. Am. Chem. Soc.* **1981**, *103*, 4490.

(2) (a) University of Groningen. (b) University of Cambridge.

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(5) Wagenaar, A.; Kirby, A. J.; Engberts, J. B. F. N., to be published. Compare: Vinnik, M. I.; Ryabova, R. S.; Lazareva, V. T. *Zh. Org. Khim.* **1970**, *6*, 1434, 1438.

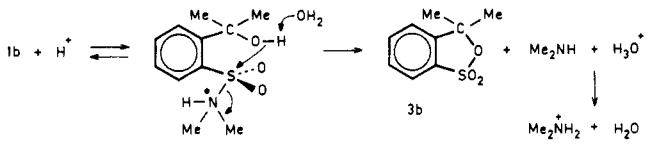
0022-3263/84/1949-3445$01.50/0

Table I. Pseudo-First-Order Rate Constants for the Acid-Catalyzed Hydrolysis of 1b,c and 2b in 1:1 (v/v) EtOH–H_2O at 25.50 °C

compd	[HCl], M	10^2k_{obsd}, s^{-1}
1b[a]	0.1352	0.0054
	0.3367	0.0147
	1.009	0.0610
	2.159	0.279
1c	1.009	0.00026
	2.159	0.00103
	4.138	0.00594
2b[b]	0.0107	1.82
	0.0216	2.65
	0.0320	4.77
	0.0424	5.62
	0.0541	10.3
	0.1352	24.2
	0.3367	68.6
	0.5221	111
	0.7120	166
	1.009	257
	1.327	463
	1.850	752
	2.159	1070

[a] $\Delta H^{\ddagger}$ = 68.3 ± 1.2 kJ mol^{-1}, $\Delta S^{\ddagger}$ = −80 ± 4 J mol^{-1} K^{-1} (0.0541 M HCl). [b] $\Delta H^{\ddagger}$ = 35.1 ± 1.2 kJ mol^{-1}, $\Delta S^{\ddagger}$ = −121 ± 4 J mol^{-1} K^{-1} (0.0541 M HCl).

Scheme II



molarity of the neighboring hydroxyl group of **1b** is far greater than that of solvent water.

The rate constants for hydrolysis of **1b** and **2b** show almost identical dependencies on acid concentration[6] (**1b**, $\log k_{obsd} = -0.93H_0 - 2.46$, $r^2 = 1.00$; **2b**, $\log k_{obsd} = -0.90H_0 + 1.14$, $r^2 = 1.00$). The small inverse solvent deuterium isotope effect for the reaction of **2b** (k_{H_2O}/k_{D_2O} = 0.84 in 0.05 M aqueous HCl at 25.50 °C) is also consistent with specific acid catalysis of the intramolecular reaction.

The simplest mechanism consistent with these facts is outlined in Scheme II for the reaction of **1b**. We have no evidence to support or rule out a pentacovalent sulfur intermediate in the reaction, but the involvement of a water molecule, acting as a general base, is consistent with the substantial negative entropies of activation observed for the reactions of both **1b** and **2b** (Table I). Normally, if water acts as general base, other, more basic components of the reaction medium, should do also. Consistently, we find significant rate increases with increasing concentrations of carboxylate–carboxylic acid buffers (Table II), which are clearly proportionately greater for the more basic acetate than for chloroacetate, and greater also than might be expected for specific salt effects; but we have not investigated this question in detail.

The very efficient intramolecular participation[7] of the hydroxy groups of **1b** and **2b** is in line with similar behavior in the lactonization of structurally related hydroxy acids.[8] *gem*-Dialkyl substitution generally provides a powerful driving force for the formation of small rings.[7] In many cases the explanation is that ground-state strain is partly relieved in the transition state for (lactone or sultone) ring formation.[7,9,10]

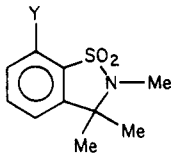
Table II. Pseudo-First-Order Rate Constants for Hydrolysis of 2b in Aqueous Buffer Solutions[a] at 25.50 °C

X	$[XCO_2H]$, M	$[XCO_2Na]$, M	pH	10^4k_{obsd}, s^{-1}
Me	0.050	0.025	4.08	5.86
	0.100	0.050	4.10	7.72
	0.500	0.250	4.22	22.1
CH_2Cl	0.050	0.025	2.45	177
	0.100	0.050	2.37	180
	0.500	0.250	2.37	241

[a] Ionic strength, 1.000 M (NaCl).

Sulfonamide **1c**, with only one methyl group on the alcohol side chain, is much less reactive then **1b** (Table I, $\log k_{obsd} = -0.74H_0 - 4.97$, $r^2 = 1.00$). In 1:1 (v/v) EtOH–H_2O, 4.32 M in HCl, $k_{obsd} = 5.9 \times 10^{-5}$ s^{-1} at 75 °C. Extrapolation of k_{obsd} for **1b** to these reaction conditions gives a ratio k_{obsd} (**1b**)/k_{obsd} (**1c**) = 1.4×10^5. For comparison, the introduction of the second methyl group into the corresponding *o*-(hydroxymethyl)benzoic acid increases the rate of lactonization by less than 10^3-fold,[8] so the sulfonamide reaction is substantially more sensitive to this mode of substitution.

The hydrolysis of **1a** is extremely slow, no reaction being detectable after a period of 7 months in 3:1 (v/v) CD_3C-D_2OD–D_2O containing 1.26 M DCl at 25.50 °C. After 17 h in 70% (v/v) CF_3CO_2H–H_2O at 75 °C about 10% hydrolysis occurred in addition to ca. 65% esterification of the hydroxy function. Similarly, **2a** reacts much more slowly than **2b**, but now an equilibrium mixture containing cyclic sulfonamide and sultone is formed.[11] The equilibrium constant depends on acid concentration and solvent. Therefore, we also examined the acid-catalyzed hydrolysis of **5a,b**. In 70% (v/v) CF_3COOH-H_2O at 99 °C the



5a, Y = H
5b, Y = Me

half-life ($t_{1/2}$) for hydrolysis of **5a** is ca. 167 h, the *o*-methyl substituent in **5b** further increases $t_{1/2}$ by a factor of more than 100. These very slow reactions fully substantiate the large effective molarity of the neighboring hydroxy group in the case of *gem*-dimethyl substitution. It may well be that, particularly in **2b**, the enthalpy barrier involved in the positioning of the hydroxy function for effective nucleophilic attack on the sulfonyl sulfur is already partly overcome in the initial state.

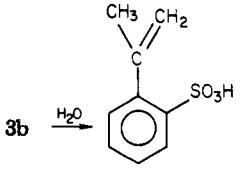
The substantially (over 4000-fold) greater reactivity of **2b** compared with **1b** is of interest, because in the reaction catalyzed by a neighboring carboxyl group, incorporation of the leaving group into a ring in this way (viz., **5**, Y = CO_2H) lowers the reactivity by a factor of 15.[4e] We have suggested that this latter effect is the result of a change in rate-determining step to the hydrolysis of the cyclic

(6) We have used the H_0 function for HCl in 51% (v/v) EtOH–H_2O. Satchell, D. P. N. *J. Chem. Soc.* **1957**, 3524.
(7) Kirby, A. J. *Adv. Phys. Org. Chem.* **1980**, *17*, 183.
(8) (a) Milstein, S.; Cohen, L. A. *J. Am. Chem. Soc.* **1972**, *94*, 9158. (b) Danforth, C.; Nicholson, A. W.; James, J. C.; Loudon, G. M. *Ibid.* **1976**, *98*, 4275. (c) Winans, R. E.; Wilcox, C. F., Jr. *Ibid.* **1976**, *98*, 4281. (d) Caswell, M.; Schmir, G. L. *Ibid.* **1980**, *102*, 4815.
(9) DeTar, D. F.; Luthra, N. P. *J. Am. Chem. Soc.* **1980**, *102*, 4505.
(10) The conversion of sulfonamide **2c** (R_1 = R_2 = Ph) into the corresponding sultone upon adding a solution of **2c** in cold, concentrated sulfuric acid to methanol, has been noted previously: Watanabe, H.; Schwarz, R. A.; Hauser, C. R. *J. Chem. Soc., Chem. Commun.* **1969**, 287.
(11) Reversible hydrolysis has also been observed in the intramolecular carboxyl-catalyzed hydrolysis of sulfonamides when the leaving group is incorporated in a cyclic structure (cf. ref 4e). The hydrolysis of **2b** is completely irreversible.

mixed anhydride that is the initial product of the cyclization of **5** (Y = CO_2H).[4e] No such second step is involved in the reaction of **2b**, so the factor of 4000 represents the true relative reactivity of sulfonamide groups in **2b** and **1b**.

Two factors seem likely contributors to the increased reactivity of **2b**. It is well-known that 5-ring sultones, like other sulfur–oxy acid esters, are substantially more reactive than comparable acyclic esters.[12] It is likely that the same effect increases the reactivity of N-protonated[13] **2b**. Secondly, we have presented evidence[4e] that there is a significant steric interaction between the amine leaving group and the *o*-hydrogen atom in the transition state for the cyclization of *o*-carboxybenzenesulfonamides. This factor may be presumed to reduce the reactivity in the series **1a–c** also, but is absent in **2a** and **2b**, where the sulfonamide ring holds the amine leaving group in the correct position in the ground state.

Finally, we note that sultone **3b** is slowly hydrolyzed[14] to the sulfonic acid **6** under the conditions used for the sulfonamide hydrolysis. In water at 25.50 °C the rate



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constant is almost independent of the acid concentration (k_{obsd} = 4.8 ± 0.2 × 10^{-5} s^{-1} between pH 1.3 and 4.2) and the reaction is possibly of the S_N1 type. Under the conditions employed for the hydrolysis of **2b**, sultone **4b** was found to be stable.

Experimental Section

Melting points were measured on a Kofler hot-stage and are uncorrected. Proton NMR spectra were measured at 60 MHz with a Hitachi-Perkin-Elmer R24B spectrometer by using solutions in $CDCl_3$. ^{13}C NMR spectra were obtained (solutions in $CDCl_3$) by using a Varian XL 100/15 spectrometer. Elemental analyses were performed by H. Draayer, J. Ebels, and J. E. Vos of the analytical section of the department.

Materials. The sulfonamides **1a** and **2a** were prepared from *N,N*-dimethylbenzenesulfonamide and **5a**, respectively, via lithiation at the ortho position to the sulfonamide function followed by reaction with formaldehyde. All reactions were carried out under an atmosphere of dry nitrogen.

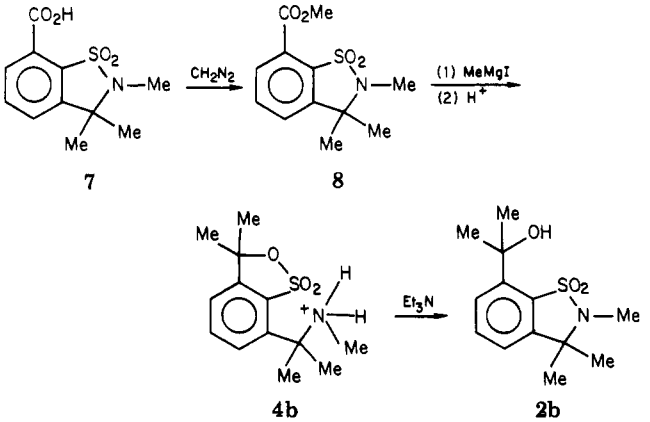
***o*-(Hydroxymethyl)-*N,N*-dimethylbenzenesulfonamide (1a).** A 1.6 M solution (3.5 mL) of *n*-BuLi in *n*-hexane was added dropwise at 0 °C to a solution of *N,N*-dimethylbenzenesulfonamide (926 mg, 5 mmol) in DME (10 mL). This mixture was added by means of a syringe to a suspension of paraformaldehyde (1.5 g) in DME (15 mL). After stirring for 1 h, the reaction mixture was poured into water, neutralized with HCl, and extracted with CH_2Cl_2. Evaporation of the solvent gave crude **1a**. After purification by column chromatography (silica gel, 60–120 μm, CH_2Cl_2 as eluent), pure **1a** was obtained as a colorless, hygroscopic liquid (75%) yield): ^1H NMR δ 2.73 (s, 6 H), 3.13 (br s, 1 H), 4.75 (s, 2 H), 7.03–7.73 (m, 4 H); ^{13}C NMR δ 140.2 (q), 133.9 (q), 132.83, 129.51, 129.11, 127.17, 61.55, 36.65. Anal. Calcd for $C_9H_{13}NO_3S$: C, 50.22; H, 6.09; N, 6.51; S, 14.89. Found: C, 49.93; H, 6.14; N, 6.33; S, 14.81.

2,3,3-Trimethyl-7-(hydroxymethyl)benzisothiazoline 1,1-dioxide (2a) was prepared similarly, starting from 2,3,3-trimethylbenzisothiazole 1,1-dioxide.[4e] The reaction mixture was deluted with ether (50 mL), washed with water, and dried over $MgSO_4$. Evaporation of the solvent gave the crude **2a**. Pure **2a** was obtained (85% yield) after crystallization from benzene: mp 162–164 °C; ^1H NMR δ 1.50 (s, 6 H), 2.77 (s, 3 H), 4.87 (s, 2 H), 7.03–7.47 (m, 3 H); ^{13}C NMR δ 144.2 (q), 136.9 (q), 133.22, 127.8, 121.46, 62.37 (q), 60.35, 25.19, 22.54. Anal. Calcd for $C_{11}H_{15}NO_3S$: C, 54.75; H, 6.27; N, 5.80; S, 13.29. Found: C, 54.75; H, 6.29; N, 5.75; S, 13.20.

***o*-(1-Methyl-1-hydroxyethyl)-*N,N*-dimethylbenzenesulfonamide (1b).** NaOH (160 mg, 4 mmol) was added to a solution of *o*-(1-methyl-1-hydroxyethyl)-*N*-methylbenzenesulfonamide[15] (1 g, 4 mmol) in 75% (v/v) EtOH–H_2O (20 mL). After dissolution of the NaOH, methyl iodide (2 mL) was added dropwise and then the mixture was kept at 40 °C for a few hours. Crude **1b** was obtained after evaporation of the solvent. It was dissolved in ether and washed with water, and the solution was dried over $MgSO_4$. The oil (1.17 g), obtained after removal of the solvent in vacuo, was purified by Kügelrohr distillation [(bp 150 °C (10^{-3} mm Hg)] to afford pure **1b** as a colorless, hygroscopic oil: ^1H NMR δ 1.65 (s, 6 H), 2.78 (s, 6 H), 6.88–7.52 (m, 4 H); ^{13}C NMR δ 149.1 (q), 136.5 (q), 132.2, 129.9, 128.2, 126.8, 72.38 (q), 37.46, 31.68. Anal. Calcd for $C_{11}H_{17}NO_3S$: C, 54.30; H, 7.04; N, 5.76; S, 13.18. Found: C, 54.05; H, 7.02; N, 5.84; S, 13.17.

***o*-(1-Hydroxyethyl)-*N,N*-dimethylbenzenesulfonamide (1c).** A 1.6 M solution (7 mL) of *n*-BuLi in *n*-hexane was added at 0 °C to a solution of *N,N*-dimethylbenzenesulfonamide (1.85 g, 10 mmol) in 20 mL of THF. After stirring for 0.5 h, the mixture was added (by means of a syringe) to a solution of a 10-fold excess of freshly distilled acetaldehyde in 10 mL of ether. The reaction mixture was poured into water, carefully neutralized with dilute HCl, and extracted with three portions of ether (25 mL). After drying ($MgSO_4$) and evaporation of the solvent the crude product (2.48 g) was purified by Kügelrohr distillation. A byproduct distilled at 70 °C, unreacted starting material (38%) at 120 °C, and **1c** at 130 °C (0.708 g, 30%). Crystallization from ether–*n*-hexane gave white crystals: mp 56–57 °C; ^1H NMR δ 1.50 (d, 3 H), 2.80 (s, 6 H), 5.61 (q, 1 H), 7.20–7.97 (m, 4 H); ^{13}C NMR δ 145.57 (q), 134.24 (q), 133.20, 128.94, 127.70, 127.19, 64.9 (q), 36.91, 23.95. Anal. Calcd for $C_{10}H_{15}NO_3S$: C, 52.38; H, 6.59; N, 6.11; S, 13.98. Found: C, 52.33; H, 6.60; N, 6.09; S, 14.00.

2,3,3-Trimethyl-7-(1-methyl-1-hydroxyethyl)benzisothiazoline 1,1-dioxide (2b) was prepared according to the procedure:



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2,3,3-Trimethyl-7-(carboxymethyl)benzisothiazoline 1,1-Dioxide (8). To a solution of 2,3,3-trimethyl-7-carboxybenzisothiazoline 1,1-dioxide (7, 1.6 g, 6 mmol) in CH_3OH (25 mL) was added an excess of diazomethane dissolved in ether. Evaporation of the solvent gave **8**, which was recrystallized from benzene (93% yield), mp 164–165 °C; ^1H NMR δ 1.53 (s, 6 H), 2.87 (s, 3 H), 4.00 (s, 3 H), 7.5–8.2 (m, 3 H). Anal. Calcd for $C_{12}H_{15}NO_4S$: C, 53.52; H, 5.61; N, 5.20; S, 11.91. Found: C, 53.43; H, 5.63; N, 5.19; S, 11.98.

4b. A solution of **8** (1.077 g, 4 mmol) in warm benzene (25 mL) was added dropwise to the Grignard reagent prepared from Mg (243 mg, 10 mmol) and methyl iodide (1.70 g, 12 mmol) in ether

(12) Kaiser, E. T. *Acc. Chem. Res.* **1970**, *3*, 145.
(13) Protonation of sulfonamides has been studied by the following groups: (a) Laughlin, R. G. *J. Am. Chem. Soc.* **1967**, *89*, 4268. (b) Menger, F. M.; Mandell, L. *J. Am. Chem. Soc.* **1967**, *89*, 4424.
(14) For a recent discussion of sultone hydrolysis, see: Laleh, A.; Ranson, R.; Tillett, J. G. *J. Chem. Soc., Perkin Trans. 2* **1980**, 610 and references cited therein.
(15) Sachs, F.; von Wolff, F.; Ludwig, A. *Chem. Ber.* **1904**, *37*, 3257.

(10 mL) under an atmosphere of dry nitrogen. The reaction mixture was refluxed for 2 h and then poured into cold, 2 N H_2SO_4. The aqueous layer was separated, neutralized carefully with a solution of $NaHCO_3$, and extracted with CH_2Cl_2 (50 mL). After drying over $MgSO_4$, the solvent was evaporated. The crude sultone **4b** was crystallized from EtOH (85% yield): mp 143–147 °C; ^1H NMR δ 1.60 (s, 6 H), 1.78 (s, 6 H), 2.28 (s, 3 H), 7.0–7.8 (m, 3 H); ^{13}C NMR δ 148.4 (q), 146.9 (q), 133.5, 130.4, 127.0, 120.5, 85.58, 56.43, 29.7, 28.8, 28.5; mass spectrum, *m/e* (relative intensity) 254 (M^+, 100), 223 (27), 72 (61), 56 (23), 43 (45). Treatment of **4b** with triethylamine in boiling EtOH afforded **2b**. After crystallization from EtOH, pure **2b** was obtained in 95% yield: mp 182 °C; ^1H NMR δ 1.42 (s, 6 H), 1.66 (s, 6 H), 2.77 (s, 3 H), 3.50 (s, 1 H), 7.07–7.50 (m, 3 H); ^{13}C NMR δ 147.0 (q), 146.0 (q), 132.7, 130.6 (q), 126.0, 121.2, 73.13 (q), 61.06 (q), 31.25, 25.18; mass spectrum, *m/e* (relative intensity) 254 (M^+, 100), 236 (25), 223 (16), 91 (28), 57 (20), 56 (42), 55 (19), 44 (64), 43 (55), 41 (25), 39 (20), 28 (62). Anal. Calcd for $C_{13}H_{19}NO_3S$: C, 57.97; H, 7.11; N, 5.20; S, 11.90. Found: C, 58.02; H, 6.99; N, 5.36; S, 11.99.

Reaction Products. This sultone **3b**, isolated in high yield after hydrolysis of **1b**, was synthesized independently according to Sachs et al.[15] The sultone **4b** is an intermediate in the synthesis of **2b** (vide infra) and was identical with the product isolated upon hydrolysis of **2b** in the presence of HCl. The product of hydrolysis of **2a**, the N-protonated sultone **4b**, was characterized by its ^1H NMR spectrum in 1:1 (v/v) EtOD–D_2O: δ 2.03 (s, 6 H), 2.57 (t, 3 H), 5.63 (s, 2 H), 7.40–8.07 (m, 4 H). Treatment of **4b** with NaOH gave **6** in high yield. The sulfonic acid was isolated in quantitative yield as the corresponding sodium salt. ^1H NMR (1:1 (v/v) EtOD–D_2O) δ 2.07 (br s, 3 H), 4.77 (br s, 1 H), 5.00 (br s, 1 H), 6.73–7.23 (m, 3 H), 7.57–7.80 (m, 1 H). Anal. Calcd for $C_9H_9O_3SNa$: C, 49.09; H, 4.12. Found: C, 48.70; H, 4.04.

Kinetic Measurements. Pseudo-first-order rate constants (k_{obsd}) for reactions having half-lives longer than 1 min were determined by using the UV (Beckman model 24 spectrophotometer) and NMR methods outlined previously.[4e] Faster reactions were followed by using an Aminco-Morrow stopped-flow apparatus, equipped with a data acquisition storage and retrieval (DASAR) system. The optical path length of the mixing chamber was 1.0 cm. Thermodynamic activation parameters were calculated from second-order rate constants ($k_2 = k_{obsd}[H^+]^{-1}$) at seven different temperatures in the temperature range 25–54 °C for **1b** and at six temperatures in the range 21–43 °C for **2b**.

Registry No. **1a**, 91190-73-7; **1b**, 91190-74-8; **1c**, 91190-75-9; **2a**, 91190-76-0; **2b**, 91190-77-1; **3b**, 81403-42-1; **4b**, 91190-82-8; **4b**·HCl, 91190-83-9; **5a**, 91190-78-2; **5b**, 91190-79-3; **6**, 79347-33-4; **7**, 72519-75-6; **8**, 91190-81-7; *N,N*-dimethylbenzenesulfonamide, 14417-01-7; *o*-(1-methyl-1-hydroxyethyl)-*N*-methylbenzenesulfonamide, 91190-80-6; acetaldehyde, 75-07-0.

Mechanism of Base-Catalyzed Reactions in Phase-Transfer Systems with Poly(ethylene glycols) as Catalysts. The Isomerization of Allylanisole

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The mechanism of base-catalyzed reactions with poly(ethylene glycol) (PEG) as phase-transfer catalysts was studied by using the isomerization of allylanisole as a model reaction. The reaction kinetics showed the reaction to be chemical reaction controlled. The reaction system was a three-phase system consisting of an organic solvent phase, a PEG–potassium hydroxide complex phase, and a basic aqueous phase. The reaction mechanism included diffusion of the substrate from the solvent to the complex phase reaction and back diffusion of the product. The concentration of the aqueous phase is also important. When the aqueous phase is unsaturated there is no reaction. Concentrations above saturation increase rate because the basic complex becomes more potent under anhydrous conditions. The chain length and chain end moiety of the PEG catalysts have significant influence on the reaction rate. In general, short chain catalysts were more effective per gram but not per mole of catalyst. Etherification of the terminal hydroxyl group reduced activity. When alkoxide species were used as bases the trends were reversed, long chain catalysts being more effective and etherification increasing activity.

Introduction

In recent years since the first published paper by Lehmkuhl et al.[1] poly(ethylene glycols) (PEG) and their ethers (PEGE) have received increasing attention as phase-transfer catalysts. They have been used in a wide variety of reactions including Williamson ether synthesis,[2-5] reductions,[6-8] oxidations,[2,7,9] eliminations,[10] and substitution reactions.[2,7,11-13] Poly(ethylene glycol) appears to be especially attractive for base-catalyzed reactions as it is stable to base, a condition under which the better known quaternary ammonium salts undergo Hofmann elimination and therefore deactivation. In addition, the low price and nontoxicity of the PEG catalyst may enable its use in industrial reactions. Despite the considerable number of syntheses reported using PEG as catalyst, little is known or understood about the kinetics and mechanism of a PEG-catalyzed reaction. Recently, Gokel and his coworkers[14] have investigated some mechanistic and kinetic aspects of aliphatic nucleophilic substitutions (cyanation of octyl chloride) but to the best of our knowledge no such studies have been made in base-catalyzed reactions.

In order to investigate the base-catalyzed, poly(ethylene glycol) phase-transfer catalytic system we have chosen as a model reaction the double bond olefin isomerization of

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