39.05, 39.45, 41.51, 47.90, 69.90. anal. Calcd for $C_{11}H_{20}O$: C, 78.57; H, 11.90. Found: C, 78.63; H, 12.10.

Synthesis of 2-(3-Methylpentyl)-1,3,2-dioxaborinane of Very High Optical Purity. (*S*)-(−)-2-(2-Methylbutyl)-1,3,2-dioxaborinane (10 mmol) of 99% ee, obtained by homologation of (*R*)-(−)-2-(1-methylpropyl)-1,3,2-dioxaborinane, was homologated further by using $LiCHCl_2$ and KIPBH following the general procedure. The crude boronic acid obtained was esterified with 1,3-propanediol and purified by distillation: 1.46 g (86%); bp 106–108 °C (18 torr); ^{11}B NMR δ +31.0 (s); ^1H NMR ($CDCl_3$) δ 0.6–1.7 (m, 11 H), 1.9 (q, J = 6 Hz, 2 H), 3.93 (t, J = 6 Hz, 4 H); $[\alpha]^{23}_D$ −7.73° ± 0.03 (*c* 4, THF).

Oxidation of the boronic ester with alkaline hydrogen peroxide afforded 3-methyl-1-pentanol which was isolated and purified by distillation: 70%; bp 68–70 °C (20 torr); ^1H NMR ($CDCl_3$–D_2O) δ 0.95 (m, 6 H), 1.12–1.82 (m, 5 H), 3.65 (t, J = 6 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 11.0, 18.9, 29.4, 31.0, 39.8, 60.6. Anal. Calcd for $C_6H_{14}O$: C, 70.53; H, 13.81. Found: C, 70.52; H, 13.96.

The alcohol was further purified by preparative GC and dried over 4-Å molecular sieves. The alcohol exhibited α^{23}_D −3.52° ± 0.005 (neat, *l* 0.5), d^{23}_4 0.8227, and $[\alpha]^{23}_D$ −8.53° ± 0.01 (neat), suggesting 99% ee for the boronic ester.[32]

Acknowledgment. We are grateful to the National Science Foundation (Grant CHE 79-18881), the National Institutes of Health (Grant GM 10937-22), and the Ministry of Education, Republic of Korea, for their generous support of this work.

(32) Optical rotations of 3-methyl-1-pentanol of >99% ee: (a) Koppenhoefer, B.; Weber, R.; Schurig, V. *Synthesis* **1982**, 316; $[\alpha]^{20}_D$ +8.24° (neat). (b) Mori, K.; Watanabe, H. *Tetrahedron* **1984**, *40*, 299; $[\alpha]^{20}_D$ −8.5° (neat). (c) Rossi, R.; Carpita, A.; Chini, M. *Ibid.* **1985**, *41*, 627; $[\alpha]^{20}_D$ −8.67° ± 0.02 (neat).

Evidence for an Anionic Sulfene Intermediate in the Alkaline Hydrolysis of Aryl (Methylsulfonyl)methanesulfonate Esters[15]

Sergio Thea,*† Giuseppe Guanti,† Andrew R. Hopkins,‡ and Andrew Williams*‡

Istituto di Chimica Organica dell'Università, CNR Centro di Studio sui Diariloidi e loro Applicazioni, Genova, Italy, and University Chemical Laboratory, Canterbury, England

Received May 22, 1985

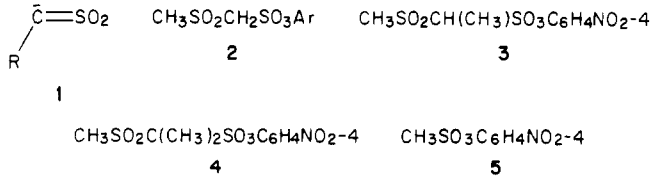
The hydrolysis of aryl (methylsulfonyl)methanesulfonates obeys the kinetic law $k_{obsd} = (k_a + k_b[OH^-])/(1 + [H^+]/K_a)$, where K_a is the ionization constant of the ester. An E1cB mechanism is consistent with the above rate law and the results of studies on Brønsted and Hammett selectivities for variation in the leaving group substituents, entropy of activation data on k_a and k_b, trapping with an amine, oxygen-18 incorporation into the acid products, deuterium exchange from D_2O into the substrates, and the effect on rate constants of substituting one or both hydrogen atoms adjacent to the sulfonate group with methyls. The k_a term involves unimolecular expulsion of the leaving group from the ionized ester to give a sulfene (I). The k_b term is due to further ionization

$CH_3SO_2CH{=}SO_2$ (I) $\qquad$ $CH_3SO_2\bar{C}{=}SO_2$ (II)

of the conjugate base of the ester to give a dianion which expels the leaving group to yield the unprecedented anionic sulfene (II). Deuterium exchange studies indicate that the anion $^-CH_2SO_2CH{=}SO_2$ is not involved kinetically. The variation of effective charge on the leaving oxygen is traced throughout the reaction path.

The reactions of nucleophiles with sulfonate esters and sulfonyl chlorides has been shown in recent years to involve sulfene intermediates provided there is an α hydrogen in the parent acid.[1] Work has progressed to show novel forms of the sulfene mechanism including the S_N2' pathway,[2] the participation of *p*-oxosulfoquinones,[3] and the ketosulfene route.[4]

The present work is aimed at studying systems where a novel anionic sulfene intermediate (**1**) could be formed



1 $\qquad$ 2 $\qquad$ 3 $\qquad$ 4 $\qquad$ 5

from sulfonate esters bearing two α hydrogens. In order to facilitate the formation of the anionic species we looked at the hydrolysis of esters (**2** and **3**) bearing methylsulfonyl activating groups. The hydrolysis of these esters was compared with that for the hydrolysis of esters which should involve regular nucleophilic attack of the hydroxide

† Istituto di Chimica Organica dell'Università.
‡ University Chemical Laboratory.

(1) (a) King, J. F. *Acc. Chem. Res.* **1975**, *8*, 10. (b) King, J. F.; Beatson, R. P. *Tetrahedron Lett.* **1975**, 973. (c) Davy, M. B.; Douglas, K. T.; Loran, J. S.; Steltner, A.; Williams, A. *J. Am. Chem. Soc.* **1977**, *99*, 1196. (d) Opitz, G. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 107.

(2) King, J. F.; Loosmore, S. M. *J. Chem. Soc., Chem. Commun.* **1976**, 1011.

(3) Thea, S.; Guanti, G.; Hopkins, A. R.; Williams, A. *J. Am. Chem. Soc.* **1982**, *104*, 1128.

(4) Tsuge, O.; Noguchi, M. *J. Org. Chem.* **1976**, *41*, 2438.

(5) Senning, A. *Synthesis* **1973**, 211.

(6) (a) Scott, R. B.; Heller, M. S. *J. Org. Chem.* **1955**, *20*, 1159. (b) Vizgert, R. V. *Usp. Khim.* **1963**, *32*, 1.

(7) (a) Palm, V. A.; Vizgert, R. V. *Dokl. Akad. Nauk SSSR.* **1962**, *142*, 1091. (b) Ciuffarin, E.; Fava, A. *Progr. Phys. Org. Chem.* **1968**, *6*, 81.

(8) (a) Douglas, K. T. *Progr. Bioorg. Chem.* **1976**, *4*, 193. (b) Williams, A.; Douglas, K. T. *Chem. Rev.* **1975**, *75*, 627.

(9) Laleh, A.; Ranson, R.; Tillett, J. G. *J. Chem. Soc., Perkin Trans. 2* **1980**, 610.

(10) Kaiser, E. M.; Petty, J. D.; Knutsen, P. L. A. *Synthesis* **1977**, 509.

(11) Williams, A.; Douglas, K. T. *J. Chem. Soc., Perkin Trans. 2* **1974**, 1727.

(12) (a) Williams, A. *Acc. Chem. Res.* **1984**, *17*, 425. (b) Deacon, T.; Farrar, C. R.; Sikkel, B. J.; Williams, A. *J. Am. Chem. Soc.* **1978**, *100*, 2525.

(13) (a) Thea, S.; Harun, M. G.; Williams, A. *J. Chem. Soc., Chem. Commun.* **1979**, 717. (b) Thea, S.; Williams, A. *J. Chem. Soc., Perkin Trans. 2* **1981**, 72.

0022-3263/85/1950-5592$01.50/0

Table I. Physical and Ionization Constants for the Substrates[a]

$CH_3SO_2CR_1R_2SO_3Ar$						
R_1	R_2	Ar	λ,[b] nm	p$K^{h,i}$	p$K^{c,i}$	mp, °C
H	H	4-$NO_2C_6H_4$	305	9.03	9.00	122–123[f]
H	H	2-$NO_2C_6H_4$	223	8.46	8.70	152–153
H	H	3-$NO_2C_6H_4$	288	9.07	*e*	117–118
H	H	4-CNC_6H_4	250	9.12	*e*	153–154
H	H	2-Cl-4-$NO_2C_6H_3$		8.42[c,d]	8.42	157–158
H	H	4-Cl-2-$NO_2C_6H_3$	340	8.16	8.15	77–79
H	H	2,4-$Cl_2C_6H_3$	245	9.14	*e*	98–99
H	H	3-ClC_6H_4	235	9.59	*e*	89–90
H	H	C_6H_5	230	9.99	*e*	74–75[g]
H	H	2,4-$(NO_2)_2C_6H_3$		*d*	*d*	161–162
CH_3	H	4-$NO_2C_6H_4$		11.24[c,d]	11.24	120–121
CH_3	CH_3	4-$NO_2C_6H_4$				132–133

[a] Temperature 25 °C, ionic strength made up to 1 M with KCl. [b] Wavelength used for spectral determination of pK. [c] Value derived from kinetic data. [d] Value not measured owing to the exceedingly fast hydrolysis of the ester. [e] Reaction was too slow to measure easily in the pK range of the pH profile. [f] Lit. mp 120–121 °C.[5] [g] Lit. mp 72–74 °C.[5] [h] Values of pK obtained from the pH dependence of the absorbance at zero time. [i] Errors are in the third figure only.

ion at the sulfonyl group (4 and 5).

Experimental Section

Materials. Most aryl (methylsulfonyl)methanesulfonates were obtained by adding the appropriate phenol to a mixture of the methanesulfonyl chloride and triethylamine in anhydrous acetonitrile at −40 °C according to the method of Senning.[5] The 2,4-dinitrophenyl sulfonate (2, Ar = 2,4-dinitrophenyl) was prepared by nitrating the 4-nitrophenyl ester, dissolved in a mixture of concentrated sulfuric acid and chloroform, with excess fuming nitric acid. *N*-Benzyl (methylsulfonyl)methanesulfonamide was prepared by adding excess benzylamine to an acetonitrile solution of 2-nitrophenyl (methylsulfonyl)methanesulfonate (2, Ar = 2-nitrophenyl). A precipitate of 2-nitrophenol which soon formed was filtered and the clear acetonitrile solution evaporated to yield a solid. Recrystallization from ethanol afforded the pure sulfonamide, mp 149–151 °C.

Phenyl 1-(methylsulfonyl)ethanesulfonate was prepared by methylating the parent ester (2, Ar = phenyl). Anhydrous K_2CO_3 (0.97 g, 7 mmol) was added portionwise over 8 h to a solution of phenyl (methylsulfonyl)methanesulfonate (1.75 g, 7 mmol) and dimethyl sulfate (0.88 g, 7 mmol) in dry acetone (100 mL) while the reaction mixture was refluxed with stirring on a steam bath. The mixture was stirred overnight at room temperature and 4% HCl was added after the solvent had been evaporated. The aqueous mixture was extracted with dichloromethane to give the ester, which was pure enough to be used to prepare the 4-nitrophenyl ester without further purification. A solution of KNO_3 (0.6 g, 6.1 mmol) in concentrated H_2SO_4 (2.4 g) was added dropwise to a solution of phenyl 1-(methylsulfonyl)ethanesulfonate (1 g, 3.8 mmol) in concentrated H_2SO_4 (3.15 g). The mixture was stirred overnight at room temperature and then cautiously poured onto crushed ice; the solid, which separated, was extracted into chloroform to give the 4-nitrophenyl 1-(methylsulfonyl)ethanesulfonate (3) on evaporation and recrystallization. 4-Nitrophenyl 1-(methylsulfonyl)-1-methylethanesulfonate (4) was prepared by nitration of the corresponding phenyl ester by the above technique. The phenyl ester was prepared by refluxing phenyl (methylsulfonyl)methanesulfonate (1.75 g, 7 mmol) and dimethyl sulfate (3.45 g, 27.3 mmol) in anhydrous acetone (100 mL) in the presence of anhydrous K_2CO_3 (2.0 g, 14.4 mmol) over a 12-h period. The ester was obtained as above and was pure enough to proceed to the nitration to afford pure 4-nitrophenyl ester on recrystallization.

Sodium (methylsulfonyl)methanesulfonate was prepared by the method of Senning.[3] Physical data on the above derivatives are given in Table I. Elemental analyses (supplementary table), IR (Perkin-Elmer 257), and NMR (Varian FT80 or EM360A) spectra are fully consistent with the proposed structures of the esters. Buffer components were of analytical reagent grade or were purified by redistillation or recrystallization of the bench grade materials. Dioxane and dimethoxyethane were dried and freed from peroxides by rapid filtration under pressure of nitrogen through a neutral activated alumina column. The absence of peroxides was routinely checked with aqueous KI solution. Water used in the experiments was obtained by glass distillation of deionized water.

Methods. Kinetic measurements were carried out spectrophotometrically with Gilford 2400S or Perkin-Elmer 554 UV–vis instruments fitted with thermostatted cell compartments. The substrate (10 to 50 μL of stock solution in dioxane) was added to the appropriate buffer (2.5 mL) in a silica cell on the flattened tip of a glass rod and mixed by rapid vertical motions. Suitable wavelengths for the kinetic studies were selected by repetitive spectral scanning of the reaction in the Perkin-Elmer instrument. Pseudo-first-order rate constants were calculated from the changes in absorbance at the constant wavelength by plotting $A_\infty - A_t$ vs. time on semilogarithmic graph paper. Very low rate constants were measured by the method of initial rates; infinity values were calculated from the known extinction coefficients of the components of the products or were measured for the reaction solution "forced" to completion at high pH and then adjusted to the pH under investigation.

Ionization constants were determined spectrophotometrically; when a fast reaction occurred, the absorbance was extrapolated to zero time with the aid of a Kipp and Zonen recorder operated at its highest chart speed. Measurements of pH were performed with a Radiometer PM62 instrument fitted with either type C or B electrodes. Values of pH for alkaline solutions from 0.01 to 1 M were calculated from the ionic product at the temperature of the experiment.

Thin layer chromatography and UV and NMR spectroscopy were used to demonstrate (methylsulfonyl)alkanesulfonic acids and the phenol were the only products of the hydrolyses.

The effect of benzylamine concentration on product composition and rate constant was studied for the reaction of water (2, Ar = 4-nitrophenyl) by extracting the acidified reaction mixture into chloroform and submitting the extract to ^1H NMR analysis (Varian FT 80 machine). Comparison of the signals of sulfonamide with those of 4-nitrophenol made it possible to calculate the yield of the former relative to the latter. Control experiments employing "mock" infinity solutions showed the method to be reliable.

The H/D exchange reaction was studied for selected substrates by recording the ^1H NMR spectrum at ca. 5-min intervals. Deuterium oxide (99.7% D) and DCl (37%) in D_2O (99% D) were obtained from Merck. Substrates were dissolved at 0.01 M concentration in 1.0 M NaOD. This technique made it possible to follow the H/D exchange process at the acyl moiety of the selected esters and the hydrolytic reaction simultaneously because the hydrogen atoms of the leaving phenol undergo a large change in their chemical shifts during hydrolysis. We could also monitor the disappearance of the substrate and the appearance of the phenoxide ion products simultaneously.

Trapping with ^{18}O-enriched water (obtained from Prochem) was carried out with the ester 4. The ester (0.5 g) was added to 15 mL of a 1 M solution of NaOH in 50% (v:v) dimethoxy-

(14) Al-Rawi, H.; Williams, A. *J. Am. Chem. Soc.* **1977**, *99*, 2671.
(15) Preliminary account of this work: Thea, S.; Guanti, G.; Williams, A. *J. Chem. Soc., Chem. Commun.* **1981**, 535.

Table II. Rate Parameters for Hydrolysis of the Substrates[a,j]

$CH_3SO_2CR_1R_2SO_3Ar$						
R_1	R_2	Ar	λ^{kin}, nm	k_a, s^{-1}	k_b, M^{-1} s^{-1}	k_aK_a/K_w or k_{OH^-}[b]
H	H	4-$NO_2C_6H_4$	400	3.1×10^{-4}	9.72×10^{-3}	29
H	H	2-$NO_2C_6H_4$	414	2.2×10^{-3}	5.16×10^{-2}	763
H	H	3-$NO_2C_6H_4$	388	1.7×10^{-6}	9.4×10^{-5}	0.14
H	H	4-CNC_6H_4	275	1.5×10^{-5}	4.95×10^{-4}	1.14
H	H	2-Cl-4-$NO_2C_6H_3$	402	0.1	1.30	37200
H	H	4-Cl-2-$NO_2C_6H_3$[c]	*h*	1.5×10^{-2}	0.301	10600
H	H	2,4-$Cl_2C_6H_3$	305	8.2×10^{-6}	2.31×10^{-4}	0.59
H	H	2,4-$(NO_2)_2C_6H_3$[d]	*e*	*f*	*f*	2.62×10^8
CH_3	H	4-$NO_2C_6H_4$	400	0.151		87
CH_3	CH_3	4-$NO_2C_6H_4$	400			2.5×10^{-7}[g]
$CH_3SO_3C_6H_4NO_2$-4			400			6.7×10^{-2}[g,i]

[a] Temperature 25 °C, ionic strength made up to 1 M with KCl. [b] Equivalent second-order rate constant for reaction of OH^- with the neutral ester; units in M^{-1} s^{-1}. [c] $k_{H_2O} = 6 \times 10^{-7}$ s^{-1}. [d] $k_{H_2O} = 3 \times 10^{-5}$ s^{-1}. [e] Wavelength employed in the kinetic study varied according to pH (pH >4.2, λ = 360 nm; 4.2 > pH > 2.0, λ = 340 nm; pH <2.0, λ = 325 nm). [f] Rates too high to measure. [g] This term is unambiguously bimolecular. [h] Wavelengths employed in kinetics were 430 nm for pH >6; 360 nm for pH <6. [i] This agrees with previous data.[1c] [j] Errors in the derived parameters (k_{H_2O}, k_a, k_b, k_{OH^-}, and k_ak_a/K_w) are no more than 5%. The pH ranges are shown in Figures 1 and 2.

ethane/water; the aqueous component was at 3.636% ^{18}O-enrichment. The resulting suspension was stirred at room temperature until no more of the initial solid was left. Standard TLC techniques demonstrated that the reaction was complete. The solution was then acidified with dilute HCl and extracted with dichloromethane. The organic phase was dried with $CaCl_2$ and evaporated, and the residue was submitted to mass spectral analysis (AEI 902 high resolution mass spectrograph under the supervision of Dr. J. F. J. Todd). The 4-nitrophenol molecular ion was identified in the recorder trace and the ratio (M + 2)/M obtained from the peak heights.

Results

The release of substituted phenols in the decomposition of the aryl sulfonates (esters **2**, **3**, **4**, and **5**) took place quantitatively in each case and obeyed pseudo-first-order kinetics over at least 80% of the total reaction. Good isosbestic points were observed during the spectral scanning, indicating the absence of an absorbing intermediate at a concentration comparable with that of reactant or products.

In the case of the esters **2** and **3** the absorbance at a selected wavelength at zero time varied with pH according to the ionisation law (eq 1),

$$pK = pH + \log (A_H - A_{pH})/(A_{pH} - A_L) \quad (1)$$

which was employed to estimate p*K* (Table I). The values A_H, A_{pH}, and A_L are respectively the absorptions when the ester is completely ionized, is at the pH in question, and is unionized.

The pseudo-first-order rate constants are independent of buffer concentration even when nucleophilic species such as primary and secondary amines are employed. The rate constants for the esters **2** and **3** varied with pH according to the rate law (eq 2). Values for the kinetic

$$k_{obsd} = k_{H_2O} + (k_a + k_b[OH^-])/(1 + [H^+]/K_a) \quad (2)$$

parameters are collected in Tables I and II. Table I indicates good agreement between kinetically and spectroscopically measured p*K* values. The acidity of the esters varies according to the Brønsted-type relationship (eq 3);

$$pK = (0.49 \pm 0.08)pK^{ArOH} + (5.13 \pm 0.62) \quad r = 0.935 \quad (3)$$

$$pK = (1.29 \pm 0.07)\sigma + (10.01 \pm 0.42) \quad r = 0.995 \quad (4)$$

an improved correlation (eq 4) results if Hammett σ values for only meta and para substituents are employed.

The rate constants k_a and k_b for the methanesulfonate esters **2** obeyed the Brønsted-type relationships (eq 5 and 6) but gave poor Hammett σ relationships (eq 7 and 8) when ortho substituents were neglected. Better fit is seen when Hammett σ^- values are employed (eq 9 and 10).

$$\log k_a = (-1.71 \pm 0.21)pK^{ArOH} + (8.83 \pm 0.87) \quad r = 0.961 \quad (5)$$

$$\log k_b = (-1.52 \pm 0.23)pK^{ArOH} + (8.88 \pm 1.70) \quad r = 0.946 \quad (6)$$

$$\log k_a = (12.29 \pm 14.26)\sigma - (13.5 \pm 10.3) \quad r = 0.653 \quad (7)$$

$$\log k_b = (11.99 \pm 11.97)\sigma - (11.7 \pm 8.64) \quad r = 0.706 \quad (8)$$

$$\log k_a = (4.17 \pm 0.47)\sigma^- - (8.63 \pm 0.46) \quad r = 0.994 \quad (9)$$

$$\log k_b = (3.78 \pm 0.15)\sigma^- - (6.68 \pm 0.15) \quad r = 0.999 \quad (10)$$

The pH dependence of the hydrolysis of the ethanesulfonate ester **3** is illustrated in Figure 2 and obeys the rate law (eq 2) where the k_b term is absent. The rate and p*K* parameters are reported in Table II.

The pH profiles for the hydrolysis of the 1-methylethanesulfonate (**4**) and of the parent methanesulfonate ester (**5**) are shown in Figure 2 and indicate a simple second-order rate law in hydroxide ion and ester concentrations. The derived second-order rate parameters are collected in Table II.

The temperature dependence of the parameters for the hydrolysis of 2-nitro-4-chlorophenyl (methylsulfonyl)-methanesulfonate was measured, and the resulting Arrhenius parameters are reported in Table III.

The reaction rate constant for 4-nitrophenyl (methylsulfonyl)methanesulfonate is independent of benzylamine concentration at pH 10.09, although significant yields of sulfonamide were observed; at pH 13.0 the rate constant decreased significantly when the benzylamine concentration was above 0.1 M, probably due to a solvent effect. An almost quantitative yield of sulfonamide was, however, observed at pH 13 for a benzylamine concentration of 1 M. The data are recorded in Table IV.

4-Nitrophenol recovered from the hydrolysis of the ester **4** in enriched water (^{18}O = 3.636%) in 1 M NaOH gave an abundance of the M + 2 molecular ion of 0.833 compared with a value calculated for cleavage of the S–O bond in the enriched water (0.883) and with a value calculated for Ar–O cleavage in enriched water (4.313). A control value for

Table III. Activation Parameters for the Hydrolysis of 4-Chloro-2-nitrophenyl (Methylsulfonyl)methanesulfonate[a,b]

rate parameter	$\Delta H^{\ddagger}$, kcal mol	$\Delta S^{\ddagger}$, eu/mol	r^f	rate constants[g]
k_aK_a/K_w	13.8 ± 0.3	+6.1 ± 1.1	0.9995	1.01×10^{4}[c] (25.0)
				2.38×10^{4}[c] (36.6)
				6.58×10^{4}[c] (49.9)
k_a	17.6 ± 0.1	−8.0 ± 0.2	0.9998	1.47×10^{-2}[d] (25.0)
				4.58×10^{-2}[d] (36.6)
				0.156[d] (49.9)
k_b	18.6 ± 0.6	+1.7 ± 1.9	0.9991	0.115[e] (15.0)
				0.385[e] (25.0)
				1.21[e] (36.8)

[a] Kinetics were followed at 430-nm wavelength. [b] Activation parameters are relative to a standard state of 1 M in each reactant. Entropy values are for 25 °C. [c] Dimensions are M^{-1} s^{-1}; pH at 25.0 °C 6.07, phosphate buffer at 0.01 M total concentration. [d] Dimensions are s^{-1}; pH at 25.0 °C 9.79, K_2CO_3 buffer at 0.01 M total concentration. [e] Dimensions are M^{-1} s^{-1}; KOH buffer. [f] Correlation coefficient. [g] Figures in parentheses are temperatures.

Table IV. Effect of Benzylamine Concentration on Rate of 4-Nitrophenoxide Liberation from 4-Nitrophenyl (Methylsulfonyl)methanesulfonate and Formation of *N*-Benzyl (Methylsulfonyl)methanesulfonamide[a]

	pH	10^4k_{obsd}, s^{-1}	[100 amide]/[4-nitrophenol]
Benzylamine in 0.1 M Potassium Hydroxide Solution			
[amine]			
0.0	13.02	12.8	
0.06	13.01	12.3	
0.10	13.05	11.9	30
Benzylamine Buffers, Fraction of Base 0.8			
[buffer]			
0.04	10.08	2.83	
0.20	10.09	2.72	
1.00	10.09	2.93	60[b]

[a] Ionic strength made up to 1.0 M with KCl, temperature 25 °C. [b] An error is noted in the preliminary account where we quote 70%.

Table V. Hydrolysis and Hydrogen-Deuterium Exchange at the CH_3 Group of Some (Methylsulfonyl)methanesulfonic Acid Derivatives in Alkaline Solution in D_2O[a]

substrate	k_{hydrol}, M^{-1} s^{-1}	k_{exch},[b,d] s^{-1}
$CH_3SO_2CH_2SO_3C_6H_4CN$-4	5.5×10^{-4}	8.1×10^{-4}
$CH_3SO_2CH_2SO_3C_6H_5$	[c]	8.2×10^{-4}
$CH_3SO_2CH_2SO_3Na^+$		fast[e]

[a] NaOD 1 M; reactions followed by NMR spectrometry, sample temperature 31.4 °C, sodium 3-(trimethylsilyl)tetradeuteriopropanoate as internal reference. [b] k_{exch} refers to the methyl group and was measured from the disappearance of its signal from the NMR spectrum. Exchange at the CH_2 group was virtually instantaneous, even in the absence of the added base, as the corresponding signal was never observed in the spectrum. [c] No reaction was observed within an hour after the reagents were mixed. [d] k_{exch} represents the rate constant per proton, which is one third of the rate constant for the formation of the dicarbanion in the present case (= 2.4×10^{-3} s^{-1}). [e] Complete exchange occurred before the spectrum was recorded (less than 1 min). In neutral D_2O incorporation of deuterium into the CH_3 group was negligible.

natural 4-nitrophenol M + 2 ion abundance was shown to be (0.891). The results indicate that no more than 1% of the reaction involves Ar–O fission.

Deuterium exchange experiments were carried out on the 4-cyanophenyl and phenyl (methylsulfonyl)methanesulfonate esters in D_2O in the presence of 1 M NaOD where k_b is the major contributor to hydrolysis. Exchange occurs at the methyl group with a rate constant essentially independent of the aryl substituent. The value of the rate constant for hydrolysis for the cyanophenyl ester ($5.5\ 10^{-4}$ M^{-1} s^{-1}) is close to the value of k_b for the same ester ($4.95\ 10^{-4}$ M^{-1} s^{-1}), giving us confidence in the method. The slightly different values are probably due to differences in temperature (31.4 °C and 25 °C) and solvent (D_2O and H_2O). Experiments with sodium (methylsulfonyl)methanesulfonate show that, in strong alkali, incorporation of deuterium in the CH_3 group is much faster than that for the esters. Exchange at the CH_2 group of both the sodium sulfonate and the esters was too fast to follow kinetically by NMR and it is likely that this is due to the slightly basic internal reference employed. The data are presented in Table V.

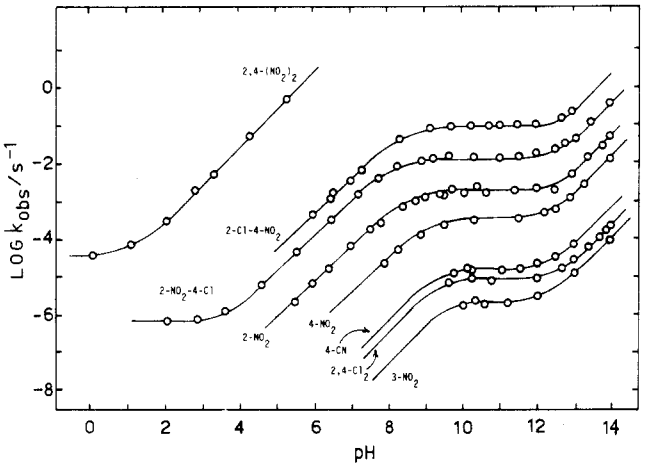


Figure 1. Dependence on pH of the hydrolysis of aryl (methylsulfonyl)methanesulfonates **2** at 25 °C and ionic strength 1 M made up with KCl. Lines are calculated from eq 2 with parameters from Tables I and II.

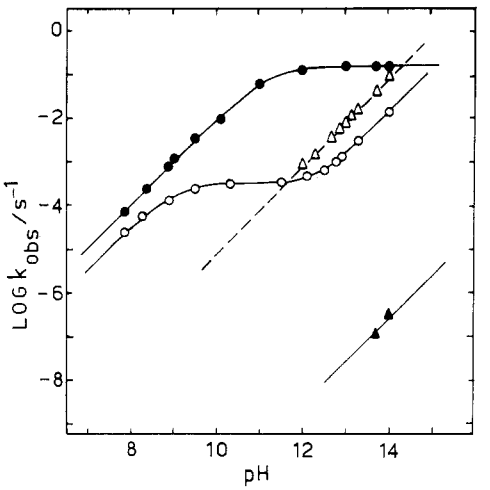
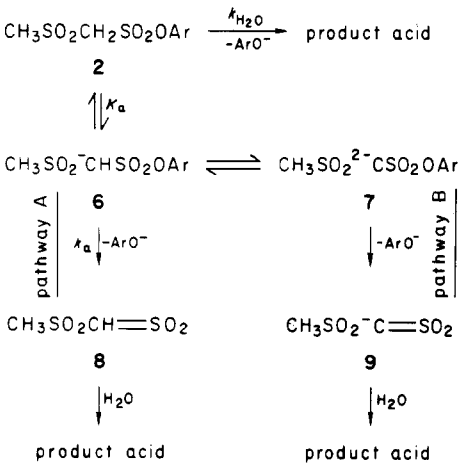


Figure 2. The hydrolysis, as a function of pH, of the 4-nitrophenyl esters of (methylsulfonyl)methanesulfonic acid (○) (**2**, Ar = 4-nitrophenyl), 1-(methylsulfonyl)ethanesulfonic acid (●) (**3**), 1-(methylsulfonyl)-1-methylethanesulfonic acid (▲) (**4**), and methanesulfonic acid (△) (**5**). Conditions are 25 °C and ionic strength made up to 1 M with KCl. Lines are calculated from eq 2 with parameters from Tables I and II.

Scheme I



Discussion

The dependence on pH (Figure 1 and eq 2) of the hydrolysis of the aryl (methylsulfonyl)methanesulfonate esters **2** indicates at least two mechanisms which we ascribe to those in Scheme I. At low pH the reaction flux goes through the neutral sulfene intermediate (path A) and at high pH through the charged sulfene (path B).

The following arguments provide evidence that the k_a term of eq 2 arises from pathway A in Scheme I. 4-Nitrophenyl (methylsulfonyl)methanesulfonate (Table I) possesses an apparent bimolecular reactivity toward hydroxide ion some 10^8-fold larger than that of the corresponding 1,1-dimethyl-substituted ester **4**. The alkaline hydrolysis of the latter esters is presumably through a bimolecular mechanism comprising attack of the hydroxide ion on the sulfonate group because it cannot follow the mechanisms of Scheme I. Incorporation studies with ^{18}O-enriched water indicate exclusive S–OAr fission in the alkaline hydrolysis of **4**, excluding an S_NAr mechanism in which OH^- attacks the nitrophenol moiety. This conclusion must hold for all the nitrophenyl esters reported here as they are more reactive than is **4** to hydroxide ion attack and have less steric hindrance (arising from substitution at the 1-position) than that in ester **4**. The sparse data from the literature[6] indicate that the dramatic rate retardation from the (methylsulfonyl)methanesulfonate to the 1,1-dimethyl ester **4** is too high to arise from steric effects. It is very unlikely that a bimolecular mechanism carries the reaction flux for the unsubstituted esters **2**. Such a conclusion is strongly supported by the observation that the 1-methyl-substituted analogue **3** has an apparent bimolecular reactivity to OH^- 3-fold higher than that of the parent 4-nitrophenyl ester **2**. Ester **3** hydrolyzes in alkali through path A in Scheme I but path B is excluded.

The Brønsted and Hammett coefficients for the k_a term for esters **2** are very large ($\beta = -1.71$ and $\rho^- = +4.2$). The Hammett coefficient for the apparent bimolecular reactivity of these esters to OH^- (k_aK_a/K_w) may be calculated from the individual parameters for k_a and K_a; the derived value (+5.49) is very much larger than that (2.73) reported for a bona fide bimolecular process, namely, the alkaline hydrolysis or aryl benzenesulfonates.[7] The very high sensitivity to the electronic effect of the substituents in the leaving group and the Hammett σ^- dependence of k_a (and hence of the apparent bimolecular parameter) are consistent with an E1cB mechanism (path A) where the S–OAr bond fission would be well advanced in the transition state of the rate-controlling step.[1c]

The Brønsted coefficient for the k_{H_2O} term ($\beta = -0.72$), although not very accurate as it is based on a two-point correlation, suggests the occurrence of a bimolecular mechanism where water attacks the neutral substrates.

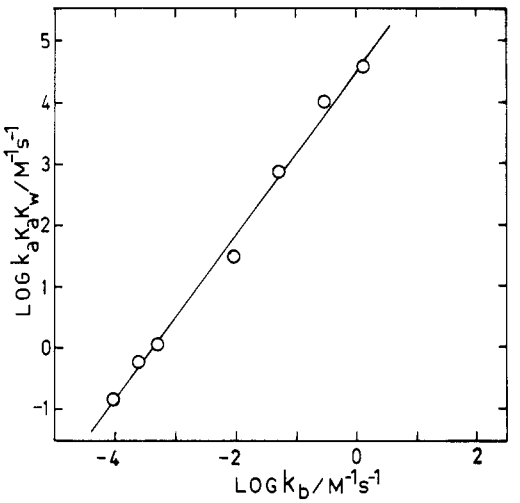


Figure 3. Plot of log k_aK_a/K_w vs. log k_b for the hydrolysis of aryl (methylsulfonyl)methanesulfonate esters **2**. Conditions are 25 °C and ionic strength made up to 1 M with KCl. Data are from Table II and the correlation has a slope +1.34 ± 0.05.

Trapping experiments with benzylamine and 4-nitrophenyl (methylsulfonyl)methanesulfonate (Table IV) at pH 10.09 where essentially k_a is measured indicate that the yield of the trapped sulfonamide is independent of the rate constant for disappearance of the ester; the mechanism must therefore involve a rate-limiting step prior to the step forming the sulfonamide, consistent with path A of Scheme I where benzylamine traps the sulfene.

The entropy of activation for k_aK_a/K_w, the apparent bimolecular rate constant, for 2-nitro-4-chlorophenyl (methylsulfonyl)methanesulfonate is +6.1 eu mol^{-1}, providing excellent confirmation of the dissociative nature of the mechanism.[8] Tillett[9] measured a slightly positive value for the entropy of activation (+0.7 eu mol^{-1}) for the alkaline hydrolysis of phenyl phenylmethanesulfonate, a mechanism known to be $E1cB_R$.[1c] The alkaline hydrolysis of phenyl benzenesulfonate has $\Delta S^{\ddagger} = -17.0$ eu mol^{-1}, consistent with an associative pathway. Participation of water molecules in the transition state may be responsible for the slightly negative value of the entropy of activation (−8.0 eu mol^{-1}) observed for the E1 step, k_a.

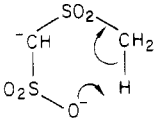
The k_b term cannot be a simple hydroxide ion attack on the sulfonate function of the ionised ester because the reactivity for the 4-nitrophenyl (methylsulfonyl)-methanesulfonate ester compared with the 1,1-dimethyl ester **4** is too high (see Table II). The Brønsted coefficient ($\beta = -1.52$) and the Hammett slope ($\beta^- = +3.78$) for leaving group variation are well outside the range typical of a bimolecular mechanism as explained for the k_a term. The absence of downward curvature in the k_b-controlled limb of the pH profile, together with no spectral changes at zero time as a function of pH, rule out the buildup of stoichiometric proportions of the dianion of the ester in aqueous solution even at 1 M KOH. Preparation of dicarbanionic species normally requires the use of very strong bases such as *n*-butyllithium in tetrahydrofuran.[10] Supporting evidence for path B is the positive entropy of activation for the 4-chloro-2-nitrophenyl (methylsulfonyl)methanesulfonate (+1.7 eu mol^{-1}). Trapping experiments with benzylamine on the 4-nitrophenyl ester (Table IV) in the presence of 0.1 M KOH, where k_b is the major contributor to the reaction flux, are consistent with a rate-limiting step prior to the addition of the benzylamine. Mechanistic similarity with the pathway for the k_a path is indicated by the excellent correlation between

the two processes (Figure 3).

Although there is no doubt about the identity of the monoanion resulting from the first ionization of esters of type **2**, it is not trivial to discuss the site of the second ionization which could occur at $-^{-}CH-$ or at CH_3. Exchange is observed at the CH_3 group in esters undergoing hydrolysis in D_2O-containing solvents (Table V). Were the second hydrolysis correct, the dianion lying on the reaction pathway would be $^{-}CH_2SO_2{}^{-}CHSO_2OAr$ (**10**) rather than

$^{-}CH_2SO_2{}^{-}CHSO_2OAr$

10



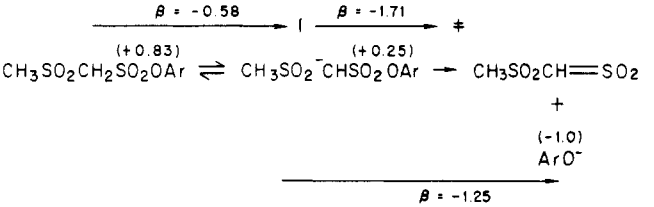
11

$CH_3SO_2{}^{2-}CSO_2OAr$ (**7**), and the sulfene would be $^{-}CH_2SO_2CH{=}SO_2$. The absence of a k_b term from the rate for the methylmethanesulfonate **3** ester hydrolysis suggests but does not prove that the kinetically important dianion is **7**. Hydrogen/deuterium exchange data for the 4-cyanophenyl and phenyl (methylsulfonyl)methanesulfonate esters displayed in Table V show that the rate of hydrolysis depends on pK^{ArOH} as expected from the high Brønsted coefficient of the reaction but the rate constant for 1,3-dianion formation is independent of the phenol residue. Under the same conditions (1 M NaOD in D_2O) exchange at the CH_3 group is much faster for $CH_3SO_2CH_2SO_3Na$ than for each of the two esters. This rules out the possibility that the observed exchange in the esters occurs *after* hydrolysis has taken place. We suggest that the sulfonate group acts as an intramolecular catalyst as shown in **11**. The velocity of exchange at CH_3 is very low in neutral D_2O solution and the negative charge on the C-1 carbon is a prerequisite for catalysis. It is reasonable to assume from our data that the rate constant for ionization of the CH_3 group in alkali is independent of the phenol substituents in the esters **2** and comparison of the data in Table V with those in Table II indicates that some of the esters hydrolyze faster than they will yield the 1,3-dianion **10**. This species is therefore a very unlikely candidate as an intermediate; very fast exchange at the CH_2 group is consistent with the intermediacy of **7**.

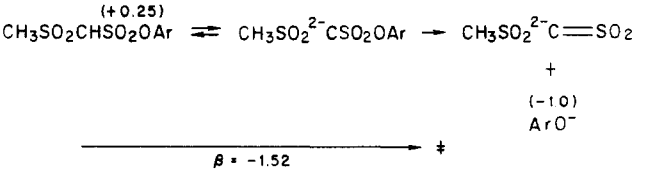
Studies with space-filling molecular models indicate that no significant differences in steric strain exist between the two anionic derivatives of the 4-nitrophenyl esters **2** and **3** and between the related sulfenes. It is therefore probable that electronic factors reflected in the dissimilar pK's are responsible for the reactivity difference. The dependence of log k_a on the ester pK ($\beta = +1.1$) suggests that most of the negative charge is removed from the α-carbon atom in the transition state. This corresponds to a well-advanced C=S double bond formation in the transition state of the rate-controlling step and implies advanced fission of the S–OAr bond. It is interesting that the anion of 4-nitrophenyl (methylsulfonyl)methanesulfonate has a k_a value (3.1×10^{-4} s^{-1}), only an order of magnitude less than that of the conjugate base of 4-nitrophenyl *N*-methylamino sulfonate (8.4×10^{-3} s^{-1}).[11] Both acids have similar pK values of about 9.

Evaluation of the effective charge on the leaving oxygen is possible since we know the effect of substituents in the leaving group on both the ionization of the proton on the α-carbon and on the elimination reactivity; we know, moreover, the overall effective charge change for a sulfonate group transfer.[12] Scheme II illustrates the effective charges on the oxygen and the related β values for the mechanism through the neutral sulfene, and Scheme III those for the anionic sulfene mechanism. The decrease in positive charge on the oxygen on ionization of the neutral ester is similar to that involved at the ether oxygen of other esters where the hydrogen on the α-atom ionizes.[11,12a,14]

Scheme II



Scheme III



The negative charge on the leaving oxygen in the transition state for both k_a and k_b exceeds that in the product phenolate ion. A similar observation was made for the E1 step in displacements at phenylmethanesulfonate esters; the simplest explanation is that the transition state is less solvated than is the phenoxide ion in the bulk solvent.[13] This implies that, formally at least, there is a solvent reorganization step following the expulsion of the phenoxide ion from the anion (**6** or **7**); such a step would not be rate limiting (eq 11). Trapping evidence will not clearly distinguish whether nucleophiles attack the sulfene before or after it leaves its "cage" with the phenoxide ion.

$$CH_3SO_2{}^{-}CHSO_2OAr \rightleftarrows [CH_3SO_2CH{=}SO_2{}^{*-}OAr] \xrightarrow[\text{nucleophile}]{\text{water or}} \text{products} \quad (11)$$

The greater charge change on the oxygen from ground to transition state in the k_a step compared with that in the k_b step is consistent with a more advanced S–O bond fission; this would be expected due to the greater propensity of the dianion to expel the phenoxide ion in the latter case. The difference in selectivity in the two mechanisms is illustrated in Figure 3.

Acknowledgment. We thank the SERC (United Kingdom) and CNR (Italy) for their support of this work and N.A.T.O. for a travel grant (RG 115.80).

Registry No. $CH_3SO_2CH_2SO_2O$-*p*-$C_6H_4NO_2$, 13165-89-4; $CH_3SO_2CH_2SO_2O$-*o*-$C_6H_4NO_2$, 99097-74-2; $CH_3SO_2CH_2SO_2O$-*m*-$C_6H_4NO_2$, 99127-90-9; $CH_3SO_2CH_2SO_2O$-*p*-C_6H_4CN, 99097-75-3; $CH_3SO_2CH_2SO_2O$-2-Cl-4-$NO_2C_6H_3$, 99097-76-4; $CH_3SO_2CH_2SO_2O$-4-Cl-2-$NO_2C_6H_3$, 99097-77-5; $CH_3SO_2CH_2SO_2O$-2,4-$Cl_2C_6H_3$, 99097-78-6; $CH_3SO_2CH_2SO_2O$-*m*-C_6H_4Cl, 99097-79-7; $CH_3SO_2CH_2SO_2OPh$, 42008-59-3; $CH_3SO_2CH_2SO_2O$-2,4-$(NO_2)_2$-C_6H_4, 99097-80-0; $CH_3SO_2CH(CH_3)SO_2O$-*p*-$C_6H_4NO_2$, 79108-29-5; $CH_3SO_2C(CH_3)_2SO_2O$-*p*-$C_6H_4NO_2$, 79108-30-8; H_2, 1333-74-0.

Supplementary Material Available: Analytical data (1 page). Ordering information is given on any current masthead page.