Studies on Sulfate Esters. III. A Comparison of the Solvolyses of Salicyl Sulfate and Sulfur Trioxide

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Abstract: The solvolyses of *o*- and *p*-carboxyphenyl sulfates in aqueous methanol have been investigated. The hydronium ion catalyzed solvolysis of the *para* substrate and the carboxyl-catalyzed solvolysis of the *ortho* isomer yield a similar methyl sulfate/sulfate ratio; the hydronium ion catalyzed solvolysis of the *o*-sulfate gives a significantly lower fraction of methyl sulfate. The threefold selectivities of the former for methanol are comparable to the observed partitioning of monomeric sulfur trioxide in aqueous alcohols. Additional mechanistic evidence is obtained from the effect of various aqueous organic solvents in acclerating the carboxyl group catalyzed solvolysis of the *ortho* isomer. Collectively the data support transition states of considerable sulfur trioxide character for catalysis by hydronium ions and the *o*-carboxyl moiety. The possibility of Lewis acid–base interactions influencing the product composition as in the case of the *ortho* isomer is discussed. A rationale, derived in part from the results on sulfur trioxide partitioning, is proposed for the alcohol selectivity of certain phosphorylating agents and extended hypothetically to sulfating reagents.

Evidence obtained in previous studies on the hydronium ion catalyzed hydrolysis of alkyl and aryl sulfates implicated a transition state of considerable sulfur trioxide character.[1–3] A similar transition state was one of several proposed to account for the participation by the *o*-carboxyl group in salicyl sulfate hydrolysis.[1] We undertook the following study in order to further clarify the mechanism of acid-catalyzed sulfate ester hydrolysis and moreover, to define quantitatively the reactivity pattern of a highly electrophilic species such as sulfur trioxide in a solvolytic medium.

Results and Discussion

Tables given within the Experimental Section list the results of the requisite control experiments designed to investigate the possible interconversion of solvolysis products arising in methanol–water (50% v/v) *via* the following equilibria.

$$CH_3OSO_3H \underset{-H_2O}{\overset{+H_2O}{\rightleftharpoons}} CH_3OH + H_2SO_4 \qquad (1)$$

$$2CH_3OSO_3H \rightleftharpoons (CH_3O)_2SO_2 + H_2SO_4 \qquad (2)$$

$$CH_3OSO_3H \underset{-CH_3OH}{\overset{+CH_3OH}{\rightleftharpoons}} CH_3OCH_3 + H_2SO_4 \qquad (3)$$

No evidence was found for any experimentally significant alteration in the concentrations of methyl sulfate or inorganic sulfate under the conditions and times employed for the solvolysis of the aryl sulfates or sulfur trioxide. These results are consistent with kinetic studies on the pH-dependent hydrolysis of methyl sulfate and the conversion of methyl sulfate to dimethyl ether.[4,5] Presumably the relatively aqueous nature and low acidity of the medium ($[10^{-1}]$–$[10^{-4}]$ in hydronium ion) greatly retard the approach to equilibrium.[6]

Tables I and II record the experimental findings for the solvolysis of salicyl sulfate, *p*-carboxyphenyl sulfate, and sulfur trioxide, respectively, in mixed methanol–water solvents.

Table I. Solvolysis of Salicyl and *p*-Carboxyphenyl Sulfate in Aqueous Methanol[a]

Substrate	Mole fraction CH_3OSO_3H in product	Conditions
Salicyl sulfate	0.585	pH 4.14, μ = 0.16
	(0.565)[b]	t^d = 70 hr
	0.36[c]	pH 1.20, μ = 0.21
	(0.37)[b,c]	t^d = 5.5 hr
p-Carboxyphenyl sulfate	0.53	pH 1.21, μ = 0.21
	(0.545)[b]	t^d = 15 hr

[a] Mole fraction CH_3OH, 0.303, 35°. [b] Duplicate runs. [c] Corrected for contribution arising from intramolecular catalysis, see Figure 2. [d] Analyses performed at t > ten half-lives.

Table II. Solvolysis of Sulfur Trioxide in Aqueous Alcohols (25°)

Alcohol, mole fraction	$[SO_3]$, *M*	$ROSO_3H$[a]
CH_3OH		
0.303	0.072	0.57
	(0.055)[b]	(0.54)[b]
	(0.091)[b]	(0.62)[b]
0.224	0.035	0.51
0.157	0.029	0.45
0.071	0.040	0.20
C_2H_5OH		
0.235	0 029	0.24
	(0.025)[b]	(0.25)[b]
C_3H_7OH		
0.191	0.032	0.12
	(0.043)[b]	(0.16)[b]

[a] Mole fractions in product. [b] Duplicate runs. Plausible causes for the variation in these values are discussed within the Experimental Section.

Inspection reveals that (1) the solvolyses of salicyl sulfate *via* participation by the *o*-carboxyl group (pH 4, see Figure 2), of *p*-carboxyphenyl sulfate through catalysis by hydronium ion, and of sulfur trioxide give

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[1] S. J. Benkovic, *J. Am. Chem. Soc.*, **88**, 5511 (1966).

[2] J. L. Kice and J. M. Anderson, *ibid.*, **88**, 5242 (1966).

[3] B. D. Batts, *J. Chem. Soc.*, 547, 551 (1966).

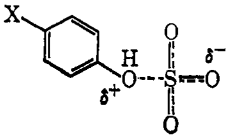
[4] J. L. Kurz, *J. Phys. Chem.*, **66**, 2239 (1962).

[5] R. Kremann and H. Neumann, *Monatsch.*, **31**, 1051 (1910).

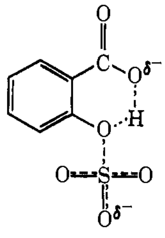
[6] See D. S. Breslow, R. R. Hough, and J. T. Fairclough, *J. Am. Chem. Soc.*, **76**, 5361 (1954), for data on the comparable ethanol–sulfuric acid system.

nearly identical mole fractions of methyl sulfate, 0.57, 0.54, and 0.58 in the same methanol–water solvent; (2) the hydronium ion catalyzed solvolysis of salicyl sulfate yield a significantly lower fraction of methyl sulfate (0.36); and (3) the solvolyses of aryl sulfates and sulfur trioxide give a product composition not identical with the mole fraction solvent composition.

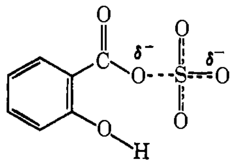
Considering (1) it appears that the product-forming transition states are similar.[7] Since reactions of sulfur trioxide are highly exothermic,[8] it is reasonable to assume that the product-forming transition state for these two aryl sulfate solvolyses resembles the structure of solvated sulfur trixoide monomer.[9] The experimental procedure employed for examining sulfur trioxide reactions generates the monomeric vapor, which is not expected to polymerize prior to solvolysis.[10] With substrate esters in which *ortho* group interactions are precluded, these results demand a considerable degree of S–O bond fission in agreement with an explanation offered by Kice for the electronic effects observed in the hydronium ion catalyzed hydrolysis of *p*-aryl sulfates.[2] The latter transition state may then be represented by A. The mechanisms remaining for *o*-carboxyl group catalyzed solvolysis of salicyl sulfate on the basis of the above and earlier evidence[1] are B and C. Mechanism C must still be considered due to the sulfation of alcohols by acetyl[11] and benzoyl sulfate.[12] The unsuccessful attempts to detect methyl salicylate as one of the products of the methanol–water solvolysis does not eliminate C.



A

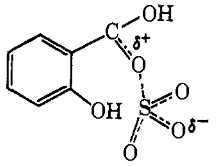


B



C

It is evident from (2) that the hydronium ion catalyzed solvolysis of salicyl sulfate results in a markedly lower percentage of methyl sulfate product. Earlier kinetic studies indicated *ortho* effects,[13] especially manifested by substituents with available nonbonded electrons which served to accelerate the rate of hydrolysis and increase the deuterium solvent isotope effect (k_{H_2O}/k_{D_2O}) relative to the identical *para* substituent.[1,14] The facile formation of Lewis acid–base adducts with sulfur trioxide which attenuate the solvolytic reactivity of the free reagent[10] suggests that the product-forming species may be represented by D. There is ample evidence for a variety of sulfur trioxide complexes with electron donors ranging from dimethylformamide[15] and dioxane[16] to trimethylamine.[17] All act to moderate the reactivity of sulfur trioxide and therefore such complexes exhibit more specific sulfating properties. Although it is problematic whether a discrete acyl sulfate is generated during hydronium ion catalyzed solvolysis, the evidence clearly implicates a donor–acceptor interaction. On the basis of the above data it is anticipated that the proposed acyl sulfate intermediate C should partition in aqueous alcohol to a product composition more nearly like that resulting from transition state D rather than B. Subject to this condition the mechanism of carboxyl group catalyzed salicyl sulfate hydrolysis then appears to involve intramolecular general acid catalyzed sulfur trioxide expulsion. This condition will be tested.



D

It is noteworthy from (3) that the solvolysis of sulfur trioxide exhibits a molar product ratio differing from that of the mole composition of the solvent. This selectivity is represented graphically in Figure 1 which plots the concentration ratio of products against the ratio of solvent compositions. Although there is some scatter in the data due to inherent experimental difficulties, the plot is satisfactorily linear indicating that sulfur trioxide is *ca.* 3.5-fold more reactive with methanol than with water.[18] This selectivity decreases with increasing substitution on the α-carbon of the alcohol until the predominant reaction is hydrolysis (methanol > ethanol ≈ water > 2-propanol). The results, therefore, indicate that if one assumes the solvated sulfur trioxide monomer, to be similar to the planar triangular structure of sulfur trioxide vapor[19a] then this planarity is not sufficient for nonselectivity. Nor does it appear that the ground-state energy of sulfur trioxide is sufficient to exert a leveling effect on the nucleophilicity of the solvent components. Thus steric effects within the nucleophile become the controlling factors and with their increase partitioning of the reagent is directed to the hydrolysis product. The greater nucleophilicity of the alcohols is

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[7] It is possible that the close numerical agreement between the aryl sulfate and sulfur trioxide solvolyses is fortuitous because of the slight difference in conditions (μ, *t*) and the dependence on reactant concentration for the latter experiments. If this be the case, the above arguments still pertain except for the degree of sulfur trioxide character in the aryl sulfate transition state.

[8] T. Moeller, "Inorganic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1952, p 530.

[9] G. S. Hammond, *J. Am. Chem. Soc.*, **77**, 334 (1955).

[10] E. E. Gilbert, *Chem. Rev.*, **62**, 549 (1962).

[11] A. J. van Peski, *Rec. Trav. Chim.*, **40**, 103 (1921).

[12] W. A. McRae and S. S. Alexander, *Chem. Abstr.*, **55**, 8703*d* (1961).

[13] R. W. Taft, "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1956, Chapter 3.

[14] G. N. Burkhardt, C. Horrex, and D. I. Jenkins, *J. Chem. Soc.*, 1649 (1936).

[15] D. W. Clayton, J. A. Farrington, G. W. Kenner, and J. M. Turner, *ibid.*, 1398 (1957).

[16] E. E. Gilbert, B. Veldhuis, E. J. Carlson, and S. L. Giolito, *Ind. Eng. Chem.*, **45**, 2065 (1953).

[17] A. B. Burg, *J. Am. Chem. Soc.*, **65**, 1629 (1943).

[18] If one assumes a linear extrapolation of the sulfur trioxide solvolysis data to zero sulfur trioxide concentration (50% methanol–water) the reagent is twofold more reactive with methanol than with water. This would be the minimum selectivity.

[19] The sulfur is at the center of an equilateral triangle with S–O bond distances of 1.43 Å.[19b] (b) F. A. Cotton and G. Wilkinson, "Advanced Inorganic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1966, p 542.

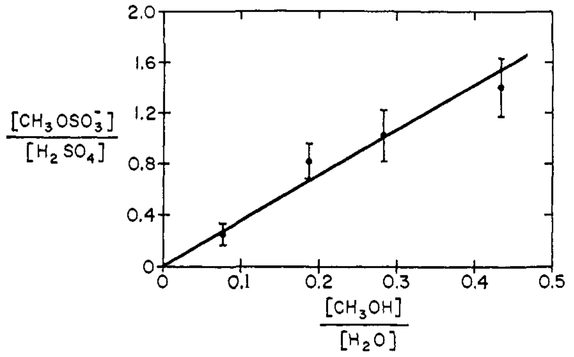

Figure 1. Plot of the molar ratio of methyl sulfate to inorganic sulfate as a function of the molar ratio of solvent composition for the solvolysis of sulfur trioxide in aqueous methanol solutions.

generally of less significance in regard to product composition.

The above arguments may be extended to include the product composition observed in the hydronium ion catalyzed solvolysis of the *p*-aryl sulfates and the carboxyl group catalysis in the hydrolysis of salicyl sulfate. The selectivity for methanol may be attributed to the change from the tetrahedral geometry of the sulfate moiety[19b] to a more planar and nucleophile accessible sulfur trioxide like transition state. The product-determining step becomes increasingly bimolecular when a neighboring *ortho* group can function as a Lewis base and methanolysis is less favorable. Steric effects should predominate in a bimolecular (solvolysis as evidenced by reactions in aqueous alcohols of diisopropyl phosphorochloridate,[20] phosphoramidate[21] (hydronium ion catalyzed), ethyl benzenesulfonate,[22] and *n*-butyl bromide;[22] in all cases the hydrolysis $\lesssim$ alcoholysis (ethanol or methanol).

One may compare the solvolytic behavior of sulfur trioxide with that of the presumed metaphosphate species generated in unimolecular phosphate monoester and dianion solvolyses with the reservation as to whether these latter reactions lead to products *via* transition states in which no interaction exists between the leaving group and phosphoryl moieties. A parallel but not quantitatively identical selectivity pattern (methanol > ethanol > water > 0 ≈ 2-propanol) is found.[23] The selectivity for methanol ranges from *ca.* 1 to 4 depending on whether the monoanion or dianion species is solvolyzed; however, the latter may have. some bimolecular character. Admittedly the comparison is tenuous—for example, metaphosphate bears a formal charge—but its merits are that sulfur trioxide is an accessible reagent model for solvolytic studies of this type. The decreased selectivity for alcohols relative to water exhibited by the "metaphosphate species" may be attributed to its higher (compared to SO_3) ground-state energy, acting to level differences in nucleophilicity but to accentuate differences in accessibility to the nucleophilic atom.

In order to accommodate the solvolysis of aryl phosphoramidates[24] within this framework it is necessary to assume that the product composition resulting from mixed transition states, *i.e.*, those exhibiting both unimolecular and bimolecular character, is not a linear function of the two limiting cases. Recall from the aforementioned that the bimolecular (phosphorochloridates) and unimolecular (metaphosphate) solvolyses are approximately nonselective. In contrast the solvolyses of aryl phosphoramidates[24] and phosphoramidate[21] reveal a tenfold selectivity for methanol relative to water, a preference that extends for the former to 2-propanol (twofold). It is possible to rationalize these results by involing a transition state in which the configuration of the atoms bonded to phosphorus are in a trigonal bipyramid array in contrast to the tetrahedral ground-state geometry.[19b,25] Consequently the phosphorus, like the aforementioned sulfur, is more accessible to the nucleophile. However, it is also necessary that in this transition state the bond between phosphorus and the leaving group though extended is not broken.[24,26] Thus it appears possible to achieve selective phosphorylation and possibly sulfation *via* mixed transition states.

The above represent a working hypothesis; the data are insufficient to allow a quantitative analysis. It remains to be determined whether selectivity greater than tenfold may be achieved with other phosphorylating species that lie between unimolecular and bimolecular solvolysis, or whether a pronounced selectivity phenomenon will occur with sulfating agents that may exhibit this characteristic.

Kinetics. Figure 2 illustrates the pH–log rate profile of salicyl sulfate in various mixed aqueous solvents. In all cases the rate of intramolecular carboxyl group catalysis is increased relative to the purely aqueous medium. The observed rate in a nucleophilic solvent such as methanol may be described in terms of a two-parameter rate equation ($k_{CH_3OH} + k_{H_2O}$) provided k_{H_2O} is increased by an order of magnitude in aqueous alcohol in order to account for the product distribution. The increase in k_{H_2O} observed in aqueous dioxane, which is also found for hydronium ion catalyzed hydrolysis of methyl sulfate,[3] was previously rationalized on the basis of decreasing charge density (neutralization of the zwitterion) as the transition state is approached.[3] The dioxane–water solvent effects on inter- and intramolecular acid catalysis are in the opposite direction to those commonly observed for reactions in which a water molecule attacks a formally unsaturated electrophilic atom, as in the spontaneous hydrolysis of derivatives of organic and inorganic acids.[27] This effect corroborates other evidence—positive $\Delta S^{\neq}$, $-\rho$, and $k_{H_2O}/k_{D_2O} < 0.5$ (hydronium ion catalysis)—that the transition states for the inter- and intramolecular acid catalyzed hydrolysis of aryl sulfates feature a small degree of covalent bonding between solvent and substrate.[28a]

The variation in k_{obsd} for the hydronium ion catalyzed hydrolysis of methyl sulfate in dioxane–water mixtures

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(20) I. Dostrovsky and M. Halmann, *J. Chem. Soc.*, 502 (1953).

(21) J. D. Chanley and E. Feageson, *J. Am. Chem. Soc.*, **85**, 1181 (1963).

(22) A. Streitwieser, *Chem. Rev.*, **56**, 607 (1956).

(23) A. J. Kirby and A. G. Varvoglis, *J. Am. Chem. Soc.*, **89**, 415 (1967).

(24) S. J. Benkovic and P. A. Benkovic, *ibid.*, **89**, 4714 (1967).

(25) T. C. Bruice and S. J. Benkovic, "Bioorganic Mechanisms," Vol. II, W. A. Benjamin, Inc., New York, N. Y., 1966, Chapter 5, and references therein.

(26) W. P. Jencks and M. Gilchrist, *J. Am. Chem. Soc.*, **86**, 1410 (1964).

(27) C. A. Bunton and G. Schwerin, *J. Org. Chem.*, **31**, 842 (1966), and references therein.

(28) (a) It is noteworthy that the solvolysis of alkyl chlorosulfates proceeds with C–O bond fission and expulsion of chlorosulfate anion thereby demonstrating the high $\Delta F^{\neq}$ associated with nucleophilic attack on quadravalent sulfur.[28b] (b) E. Buncel and J. P. Millington, *Can. J. Chem.*, **43**, 547 (1965).

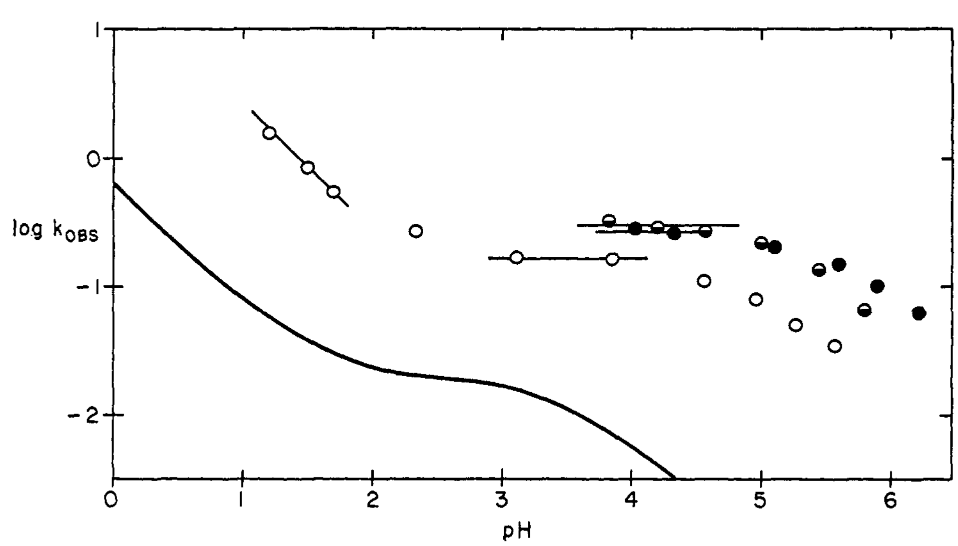

Figure 2. The log k_{obsd}–pH rate profile for the solvolysis of salicyl sulfate in 50% v/v dioxane–water (◒), 50% v/v dimethylformamide–water (●), and 50% v/v methanol–water (○) at 35°, μ = 0.2. The solid line represents salicyl sulfate hydrolysis.

correlates linearly with the inverse of the dielectric constant of the solvent. The rates depicted in Figure 2, however, are in the order DMF–H_2O ≈ dioxane–H_2O[29] > CH_3OH–H_2O[29] > H_2O whereas the order of decreasing dielectric is H_2O > DMF–H_2O[30] ≈ CH_3OH–H_2O[31] > dioxane–H_2O.[32] A second factor in the increased rate may be the basicity of the organic solvent component in which case DMF is more basic on the H_0 scale.[33] The relative basicity of water, alcohols, and ethers is quite sensitive to the choice of medium[33] although in terms of inductive effects the order anticipated is dioxane > methanol > water. Since the formation of a zwitterion either as a metastable species or by its transient generation along the reaction coordinate leading to the transition state is disfavored in solvents of lower ϵ, the rate acceleration observed must arise from an overcompensation. In addition to the electrostatic effect another factor may be the more effective interaction of the organic solvent with a sulfur trioxide transition state rather than the initial sulfate state, thus reducing the number of solvent–solute or solvent–solvent interactions.[34a] This argument is akin to the breakdown of the "initial state solvation shell" advocated by Robertson.[35]

The effect of increasing k_{H_2O} through solvolysis in mixed aqueous solvents is to furnish a model system that begins to approach aryl sulfatase activity. Intramolecular carboxyl group catalysis in 50% v/v dioxane–water ($t_{1/2} \approx$ 3 hr) is some 4000-fold faster than the bimolecular hydronium ion catalyzed hydrolysis of *p*-carboxyphenyl sulfate.

Experimental Section

Materials. The *o*- and *p*-carboxyphenyl sulfates were those employed in a previous study.[1] The sodium salt of methyl sulfate was synthesized by the method of Calhoun and Burwell.[36] Its purity (100.5%) was established by ion-exchange conversion to the acid followed by titration with standardized base. Kinetic solutions were prepared from freshly boiled distilled water. Reagent grade salts, acids, and solvents (Fisher, Baker) were used without further purification. Methanol was spectrophotometric grade (Baker).

Apparatus. Instrumentation was identical with that already reported. A Sargent Model V chemical oscillometer with cell Type B was utilized in the analyses of the solvolysis experiments.

Kinetics. The solvolysis of salicyl sulfate was monitored at 296 mμ following the increase in absorption due to salicylic acid formation. Reactions were initiated by adding *ca.* 1 mg of substrate directly to a cuvette containing the temperature-preequilibrated solvolytic medium (35°, 0.1 *M* in total buffer species; μ = 0.2, KCl). Buffers employed were identical with those utilized in the previous hydrolysis experiments. No buffer effects in the mixed solvents were noted (fourfold dilution). The pH of the kinetic runs was measured at 35° upon initiation and after completion of the runs. The pH drift was generally less than ±0.02 units; for runs with pH drift >0.02 units the average pH value was employed. The observed first-order rate constants were calculated from slopes of plots of log $[OD_\infty/OD_\infty - OD_t)]$ *vs.* time.

Solvolyses. The solvolysis of *p*- and *o*-carboxyphenyl sulfates was carried out in Kimax (No. 45066) screw-cap tubes maintained at reaction temperature (35°) by immersion in a circulating water bath. To 4 cc of 50% methanol–aqueous buffer was added 23–24 mg of the desired sulfate and the run thermostated until t_∞, as determined by the observed rates in aqueous and mixed aqueous media. The pertinent data for duration of runs, μ, and pH are recorded in Table I. Hydrochloric acid and sodium formate (0.2 *M*) were the buffer systems at low and high pH, respectively. Differences in μ between runs was dictated by ionic strength effects on the solubility of the solvolysis products.

The solvolysis of sulfur trioxide in aqueous alcohols was accomplished by syringe injecting Sulfan (Allied) into a three-necked microware flask fitted with a nitrogen inlet tube, an injection port, and a glass flow tube. The latter was connected to an adjacent two-necked microware flask containing the aqueous alcohol (20 ml) with the remaining neck closed with a drying tube. The glass flow tube was drawn out to a fine capillary tip and maximally submersed in the reaction medium. The aqueous alcohol was agitated by means of an external magnetic stirrer. The entire apparatus was flamed before addition of either reagent and purged with dry nitrogen. The aqueous alcohol reagent was introduced while maintain-

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(29) The difference in k_{obsd} for dioxane–H_2O and CH_3OH–H_2O solvents is unchanged upon extrapolation to zero ionic strength.

(30) Estimated from data of A. J. Parker, *Advan. Phys. Org. Chem.*, **5**, 175 (1967).

(31) P. S. Albright and L. J. Gosting, *J. Am. Chem. Soc.*, **68**, 1061 (1946).

(32) F. E. Critchfield, J. A. Gibson, and J. L. Hall, *ibid.*, **75**, 1991 (1953).

(33) E. M. Arnett, *Progr. Phys. Org. Chem.*, **1**, 223 (1963).

(34) (a) The possibility of interactions of the organic solvent with a sulfur trioxide transition state has been cited in the solvolysis of steroidal sulfate in aqueous organic solvents.[34b] (b) S. Burstein and S. Lieberman, *J. Am. Chem. Soc.*, **80**, 5235 (1958).

(35) R. E. Robertson, *Progr. Phys. Org. Chem.*, **4**, 213 (1967).

(36) G. M. Calhoun and R. L. Burwell, Jr., *J. Am. Chem. Soc.*, **77**, 6441 (1955).

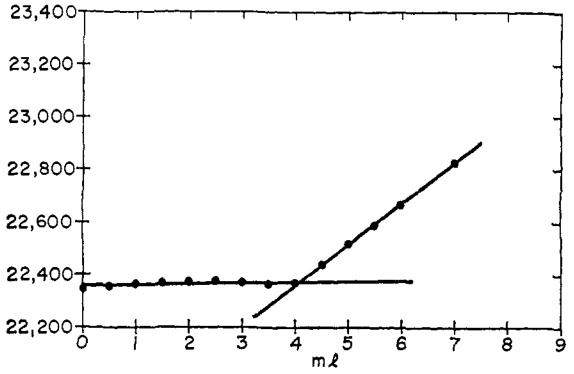

Figure 3. A typical plot of oscillometer resonance settings against milliliters of (0.1 N) $BaCl_2$ for the titration of inorganic sulfate. The inflection point yields the equivalents of inorganic sulfate.

ing the system under a positive nitrogen pressure followed by injection of the Sulfan into the remaining empty flask. No fuming of Sulfan was noted, if this sequence of operations was followed. The Sulfan was vaporized to sulfur trioxide by gently flaming the reaction vessel with the nitrogen now acting as a carrier gas. Fuming was noted over the aqueous alcohol solution particularly in the case of methanol, as the sulfur trioxide was discharged through the capillary. The slight but significant increase in methyl sulfate formed in those solutions with increasing sulfur trioxide concentration may be attributed to vapor-phase sulfation. The volume of Sulfan initially injected was calculated to yield products within the limits of the analytical techniques and to obviate side reactions. Total concentrations of generated sulfur trioxide ranged from 3 to 9 × 10^{-2} M. No attempts were made to control ionic strength by addition of external salts. The final μ is calculated to range from 0.05 to 0.16 assuming the products to be completely ionized. Data on product composition and controls are communicated in the Products section.

Table III. Oscillometry Data on Standard Solutions

Composition, mmol			Determined, mmol of SO_4^{2-}
SO_4^{2-} [a]	$NaOSO_3CH_3$	o-HOC_6H_4-COOH	
0.077	...	...	0.077
0.088	0.16	...	0.084
0.088	0.24	...	0.086
0.082	0.097	...	0.082
0.082	0.095_5	0.11	0.082
0.041[b]	0.021	0.058	0.041
0.041[b]	0.022_5	0.066	0.040

[a] Added as 1.029 N H_2SO_4. [b] Titrated solution contains 0.5 ml of 0.2 M formate, μ = 0.4.

Table IV. Data on Controls for Solvolysis Experiments in Methanol–Water (50% v/v, 35°)

Composition, M		Determined, M		Conditions	
SO_4^{2-} [a]	$NaOSO_3CH_3$ [b]	SO_4^{2-} [a]	$NaOSO_3CH_3$ [b]	pH	Hr
	0.026	0	...	4.55[c]	66
0.072_5	...	0.071_5	...	4.43[d]	48
0.075	...	0.075	...	4.14[e]	118
0.075	...	0.075 0.075_5	...	1.21[f]	5, 21
	0.026	0	...	1.21[g]	144
	0.500	...	0.500, 0.505	1.21[h,i]	4, 10

[a] Added as 1.029 N H_2SO_4. [b] Added as $NaOSO_3CH_3$. [c] 0.2 M formate, μ = 0.13 (K^+). [d] 0.2 M formate μ = 0.15 (K^+). [e] 0.2 M formate, μ = 0.19 (Na^+). [f] HCl, μ = 0.24. [g] HCl, μ = 0.18. [h] Determined by ion-exchange titration. [i] HCl, μ = 0.65.

Products. The product composition of the solvolysis experiments employing o- and p-carboxyphenyl sulfates in aqueous methanol was determined by oscillometry and ultraviolet spectroscopy. The results of controls on the analysis for inorganic sulfate in the presence of other compounds found in the solvolyses are listed in Table III. The recovery of added sulfate averaged 98.2%; no interference from other compounds present in the solvolysis medium was noted. The oscillometric procedure employed was similar to that of Harris and Himmelblau[37] except that methanol-water (50% v/v) solutions, total volume 100 ml, served as the analytical medium. The titrant was standardized $BaCl_2$ solution (0.01 or 0.02 N). The above control concentrations were selected on the basis of a 2.0-ml sampling of the solvolytic reaction. A typical oscillometry plot of resonance setting against milliliters of $BaCl_2$ is shown in Figure 3. The initial concentrations of o- and p-carboxyphenyl sulfates were determined from spectrophotometric assay of the solvolysis solutions at t_∞, the observed OD being related to the concentration of the organic acid product through standard plots of OD $vs.$ concentration of o- and p-hydroxybenzoic acids at identical pH, measured at 296 and 282 mμ, respectively. A check on the initial concentrations of o- and p-carboxyphenyl sulfates was obtained by direct weighing of the samples on a Sartorius semimicro balance (±0.01 mg). The concentration of methyl sulfate was then calculated as the difference between the concentration of inorganic sulfate determined at t_∞ and the initial concentrations of the aryl sulfates. The results are listed in Table I.

The product composition in the sulfur trioxide solvolyses was determined by acid–base titration and oscillometry. Generally 0.5–1.0-ml aliquots of reaction solution were titrated in an enclosed vessel under nitrogen with standardized potassium hydroxide (0.01 N) to a phenolphthalein end point. Oscillometric measurements for inorganic sulfate were carried out, as above, on 1-ml aliquots. Duplicate determinations after 1 hr revealed no change in product composition upon standing. The amount of methyl sulfate is then calculated from the mass balance relationship.

$$[CH_3OSO_3^-] = [H^+]_t - 2[SO_4^{2-}]$$

The results are recorded in Table II.

The solutions from the solvolysis of o-carboxyphenyl sulfate and sulfur trioxide in aqueous methanol were also analyzed by descending paper chromatography (solvent: n-propyl alcohol–ammonia–water; 6:3:1). The paper employed was S & S 589, orange ribbon. The sodium salts of methyl and inorganic sulfate served as internal standards. Inorganic sulfate was detected after air drying of the chromatograms by the method of Burma.[38] Sulfate esters were determined after hydrolysis to inorganic sulfate by the technique of Schneider and Lewbart[39] (24-hr hydrolysis period). Only methyl sulfate and inorganic sulfate were formed as products of the solvolysis reactions, (R_f 0.67; R_f 0.24, respectively). Concentrations employed were 6 μg/μl.

The possibility of the solvolysis interconversions or further reaction of methyl sulfate and inorganic sulfate was investigated in the control experiments described in Table IV. No significant change in the concentrations of either product was detected over the times and conditions employed in the above experiments. All ionic strengths quoted in the footnotes to Table IV are based on the sum total of substrate and buffer.

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