Solvolyses of Five- and Six-Membered Sultones

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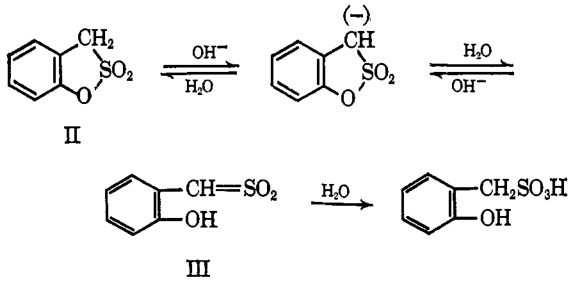
Abstract: The rate constant for the hydroxide ion catalyzed hydrolysis of the five-membered cyclic sulfonate, 1-naphthol-8-sulfonic acid sultone (IV), is comparable to that previously found for another five-membered cyclic ester, *o*-hydroxy-α-toluenesulfonic acid sultone (II). Measurements on the alkaline hydrolysis of the six-membered cyclic sulfonate, β-*o*-hydroxyphenylethanesulfonic acid sultone (V), showed that its second-order rate constant for reaction is reduced by a factor greater than 10^4 from those of the five-membered compounds II and IV.

We have shown that the five-membered cyclic esters of sulfuric and sulfonic acids, catechol cyclic sulfate (I) and *o*-hydroxy-α-toluenesulfonic acid sultone (II), respectively, hydrolyze in alkaline solution at rates which are enormously faster than those of their acyclic analogs.[3,4] Nucleophilic attack at the aromatic carbon atoms in the esters should be very unlikely. Therefore, for I and its analog, diphenyl sulfate, we have concluded that the difference in their rates of hydrolysis represents the difference in the rates of attack of hydroxide ion at the sulfur atoms in a five-membered cyclic sulfate and an open-chain sulfate. However, in the case of II and its acyclic analog, phenyl α-toluenesulfonate, a similar conclusion cannot be drawn without further information since mechanisms can be proposed for the hydrolyses of these compounds which do not involve the direct attack of hydroxide ion at sulfur.

For example, the sulfene (III) could be formed as a reactive intermediate in the hydrolysis of II as outlined in eq 1 and 2.[5] Because the possibility of such alternative pathways exists for II we felt that it would be of interest to determine the rate of hydrolysis of a five-membered sultone which does not have an α-methylene group and is incapable of forming a sulfene by ring opening. Accordingly, we have prepared 1-naphthol-8-sulfonic acid sultone (IV), and we report here our studies on its alkaline hydrolysis (eq 3).

Another problem with which this paper deals is the question of whether the large rate acceleration observed for II is a specific feature of the five-membered ring system or whether a similar acceleration might be found for another ring size. To answer this question we have examined the alkaline hydrolysis of the six-membered ester, β-*o*-hydroxyphenylethanesulfonic acid sultone (V) (eq 4).



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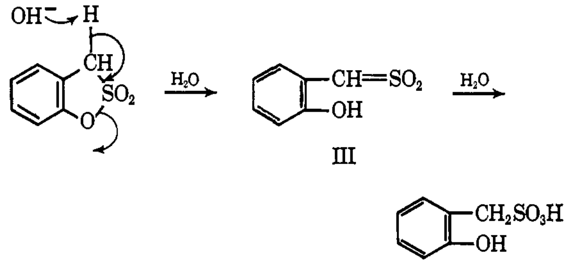

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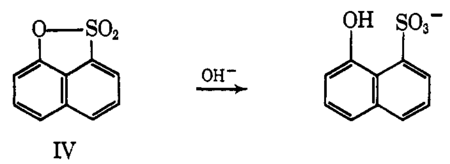
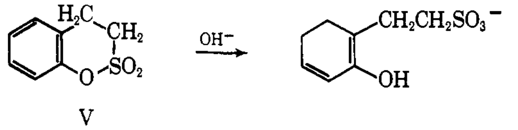


IV

(3)

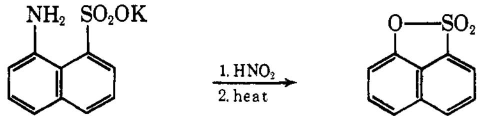


V

(4)

Experimental Section[6]

The preparation of 1-naphthol-8-sulfonic acid sultone (IV) has been carried out by a number of workers.[7,8] The deamination reaction described by Erdmann was performed and gave a good yield of the sultone.



IV

(5)

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[1] To whom inquiries concerning this paper should be addressed.

[2] National Institutes of Health Predoctoral Fellow.

[3] E. T. Kaiser, I. R. Katz, and T. F. Wulfers, *J. Am. Chem. Soc.*, **87**, 3781 (1965).

[4] O. R. Zaborsky and E. T. Kaiser, *ibid.*, **88**, 3084 (1966).

[5] Studies have been done in deuterated solvents to establish the intermediacy of sulfenes in the solvolyses of some sulfonyl halides. See: J. F. King and T. Durst, *J. Am. Chem. Soc.*, **86**, 287 (1964); W. E. Truce, R. W. Campbell, and J. R. Norell, *ibid.*, **86**, 288 (1964); J. F. King and T. Durst, *ibid.*, **87**, 5684 (1965); W. E. Truce and R. W. Campbell, *ibid.*, **88**, 3599 (1966); G. Opitz, M. Kleeman, D. Bücher, G. Walz, and K. Reith, *Angew. Chem. Intern. Ed. Engl.*, **5**, 594 (1966). Preliminary studies by O. Z., however, on the solvolysis of the sultone II have shown that it undergoes very rapid exchange with deuterated solvents such as D_2O and MeOD in the presence of OD^- and OMe^-, respectively. Hence the results of observations made in these solvents may be ambiguous concerning the possible intermediacy of the sulfene III.

[6] Infrared and nmr spectra were obtained for the compounds described and were consistent with the structures given. The instruments used were a Varian A-60 nuclear magnetic resonance spectrometer and a Beckman IR 5-A infrared spectrophotometer. All melting points were taken on a Thomas–Hoover type capillary melting point apparatus and are uncorrected.

[7] G. Schultz, *Ber.*, **20**, 3158 (1887).

[8] H. Erdmann, *Ann.*, **247**, 306 (1888).

However, since the purification of the potassium salt used was tedious, another method was employed. This method consisted of treating 1-naphthol-8-sulfonic acid with phosphorus oxychloride, the reaction conditions being similar to those previously described for the preparation of *o*-hydroxy-α-toluenesulfonic acid sultone (II).

1-Naphthol-8-sulfonic Acid Sultone. To 30.0 g (0.122 mole) of the sodium salt of 1-naphthol-8-sulfonic acid (Eastman, practical grade) was added 90.0 g (0.587 mole) of $POCl_3$. The reaction mixture was heated slowly to 125° and maintained under reflux at that temperature for 2 hr. Excess $POCl_3$ was removed by distillation, and the residue was allowed to cool.

The solidified mass was ground and transferred slowly to 350 g of ice–water, allowed to remain in contact with the water for 3 hr, filtered, washed thoroughly with water, and finally left to air dry. The dry, crude material was recrystallized several times from benzene and yielded 13.5 g (54% yield) of a very slightly yellow product. Final purification was accomplished through column chromatography using Merck acid-washed alumina with benzene–chloroform as the eluent. Recrystallization from benzene of material recovered from the chromatography gave a pure, white, crystalline solid, mp 157.2–157.7° (lit.[7,8] mp 154°).

***o*-Methoxyphenylacetonitrile.** This compound which is used as a precursor in the synthesis of V was prepared by a route similar to that which has been described for *p*-methoxyphenylacetonitrile.[9]

A mixture of 25 g (0.18 mole) of *o*-methoxybenzyl alcohol (Eastman) and 45 ml of concentrated hydrochloric acid was stirred for 20 min and transferred to a separatory funnel. The lower layer was removed, dried over calcium chloride, and filtered. The resultant crude *o*-methoxybenzyl chloride was mixed with 13.3 g (0.27 mole) of sodium cyanide, 1.8 g (0.012 mole) of sodium iodide, and 500 ml of dry acetone in a three-necked flask. The mixture was heated under reflux with vigorous stirring for 20 hr, then cooled and filtered under suction. The solid remaining on the filter was washed with 50 ml of acetone and discarded. The filtrate and washings were combined and distilled under vacuum to remove the acetone. The residual oil was taken up in 54 ml of benzene, filtered to remove precipitate, and washed with three 20-ml portions of water. The benzene solution was dried over anhydrous sodium sulfate, and the solvent was removed by distillation. The residual *o*-methoxyphenylacetonitrile was distilled: bp 88–89° (0.3 mm); mp 69–71° (lit. mp 68°[10] and 71°[11]). The yield of pure compound was 16 g (59% based on *o*-methoxybenzyl alcohol).

β-*o*-Hydroxyphenylethanesulfonic Acid Sultone. The preparation of this compound from *o*-methoxyphenylacetonitrile followed the route which has been described in the literature.[11,12] First, the nitrile was converted to ethyl *o*-methoxyphenyl acetate[10] which was reduced to give β-*o*-methoxyphenylethyl alcohol. The latter compound was treated with phosphorus tribromide to give β-*o*-methoxyphenylethyl bromide which was in turn converted to sodium β-*o*-methoxyphenylethanesulfonate.[11] From the reaction of this compound with 48% hydrobromic acid, sodium β-*o*-hydroxyphenylethanesulfonate was obtained. Cyclization of the latter material to β-*o*-hydroxyphenylethanesulfonic acid sultone was achieved using phosphorus oxychloride.[12] The sultone had mp 110–111.5° (lit.[12] mp 111–112°).

Kinetic Methods

1-Naphthol-8-sulfonic Acid Sultone (IV) Hydrolysis. The rate of hydrolysis of IV was monitored by means of an Applied Physics Corp. Cary 14 recording spectrophotometer equipped with an expanded scale slidewire and a thermostated cell compartment maintained at 25.0 ± 0.1°. Borate buffers were employed in the kinetic measurements and these were prepared essentially according to the directions given by Clark and Lubs.[13,14] All buffers used in the kinetic work were 0.5 *M* in $NaClO_4$, and the boric acid and perchlorate were recrystallized from water. The procedure for a typical kinetic run was as follows.

With a 500-μl syringe the appropriate amount of acetonitrile (Eastman Spectro quality) was added to a clean, dry, 5-ml volumetric flask. Then 6–12 μl of a stock solution of IV in acetonitrile (3.75×10^{-2} *M*) was added, and the volume was brought up to the mark with the desired buffer of constant ionic strength ($\mu = 0.5$). The flask was shaken vigorously, and some of the clear solution was transferred to a stoppered, quartz cell. The solution was allowed to equilibrate in the Cary cell compartment, and then a continuous plot of the absorbance increase at 325 mμ (the wavelength at which the maximum change occurred) was recorded.

β-*o*-Hydroxyphenylethanesulfonic Acid Sultone (V) Hydrolysis. The rate of the hydrolysis of V was determined from the increase in absorption at 290 mμ as a function of time, measured with a Beckman DU spectrophotometer equipped with a cell compartment maintained at 25.0°. In a typical run, 50 μl of a stock solution (3.0×10^{-2} *M*) of V in acetonitrile was added to a vial containing 5 ml of a sodium hydroxide solution (Fisher Certified) of an appropriate concentration. The vial was shaken vigorously, and the resultant solution was transferred to a spectrophotometer cell. After the equilibration of the solution in the Beckman cell compartment, measurements were periodically taken. All solutions were adjusted to an ionic strength of 0.5 with $NaClO_4$.

Kinetic Results and Discussion

Because of the low solubility of IV in water, acetonitrile had to be added as cosolvent. Since the hydroxide ion concentrations were kept constant during the course of a given run by the use of buffers, pseudo-first-order kinetics were observed in these individual determinations. The hydroxide ion concentrations employed in reaction mixtures ranged from 5.37×10^{-6} to 24.0×10^{-6} *M*, and the initial concentrations of IV ranged from 4.5×10^{-5} to 9×10^{-5} *M*. Calculation of the second-order rate constants for the hydroxide ion catalysis at various acetonitrile concentrations from the pseudo-first-order rate constants measured at different hydroxide ion concentrations gave the values tabulated in Table I. Extrapolation of these results to 0% acetonitrile led to a value of 22.1 M^{-1} sec^{-1} for the rate constant (Figure 1).

Table I. Effect of Acetonitrile Concentration on Second-Order Alkaline Rate Constant for the Hydrolysis of IV

Acetonitrile, %, v/v	Second-order alkaline rate constant, M^{-1} sec^{-1}
8	19.4_0
12	18.4_5
16	17.0_0
20	15.8_5

The rate constant for the hydroxide ion catalyzed hydrolysis of 1-naphthol-8-sulfonic acid sultone (IV), a five-membered cyclic sulfonate which cannot react *via* the intermediate formation of a sulfene, is compara-

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[9] K. Rorig, J. D. Johnston, R. W. Hamilton, and T. J. Telinski, "Organic Syntheses," Coll. Vol. IV, N. Rabjohn, Ed., John Wiley and Sons, Inc., New York, N. Y., 1963, p 576.

[10] R. Pschorr, O. Wolfes, and W. Burkow, *Ber.*, 33, 162 (1960).

[11] S. Sugasawa and H. Shigehara, *ibid.*, 74, 459 (1941).

[12] W. E. Truce and F. D. Hoerger, *J. Am. Chem. Soc.*, 76, 5357 (1954).

[13] W. M. Clark and H. A. Lubs, *J. Bacteriol.*, 2, 1, 109, 191 (1917).

[14] I. M. Kolthoff, "Acid-Base Indicators," Macmillan and Co., New York, N. Y., 1937, p 245.

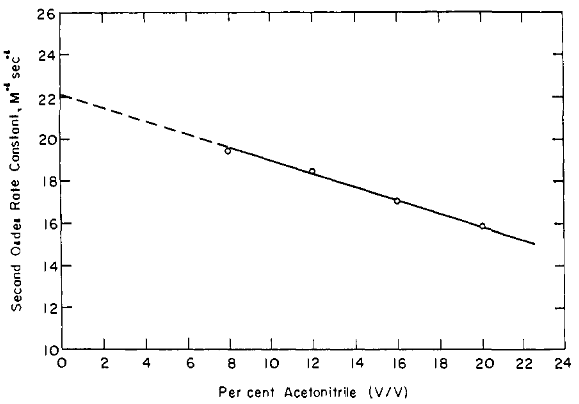

Figure 1. Effect of acetonitrile concentration on second-order alkaline rate constant.

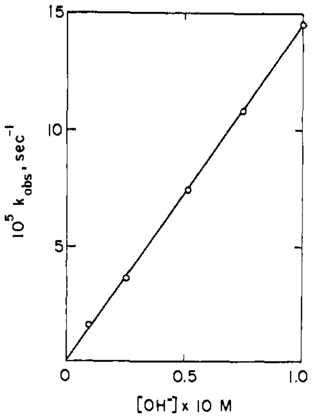

Figure 2. The hydroxide ion catalyzed hydrolysis of β-o-hydroxyphenylethanesulfonic acid sultone at 25°, ionic strength 0.5.

ble to that (33.6 M^{-1} sec^{-1}) found earlier[4] for o-hydroxy-α-toluenesulfonic acid sultone (II), an ester for which the possibility of such intermediate formation exists.[15] Of course, since there are considerable differences in the structures of the sultones II and IV and since the factors responsible for the unusual lability of a five-membered sultone or a corresponding cyclic sulfate are incompletely understood, it is probably wise at the present time not to put too much emphasis on the extremely close similarity of the alkaline reactivity of II and IV. Nevertheless, at the very least we can say from our study of IV that we have observed a large rate constant for the alkaline hydrolysis of a five-membered cyclic sulfonate in a case in which this rate constant should reflect the susceptibility of the sulfur atom in the ring to attack by hydroxide ion. An alternative route of attack like that illustrated above for II can be ruled out for IV since a sulfene cannot be formed from the latter compound. Hence, the analogy between the five-membered cyclic sulfonate and sulfate[3] esters is reinforced; for both types of ester we have found that rapid attack of hydroxide ions at the sulfur atoms in the rings occurs.

At this point we should return to a question raised earlier. Is the alkaline lability of the five-membered cyclic sulfonates a specific feature of this ring size or can another larger ring ester show a similar reactivity? The results of our kinetic measurements on the hydroxide ion catalyzed hydrolysis of the six-membered cyclic ester, β-o-hydroxyphenylethanesulfonic acid sultone (V), are relevant to this question.

The hydroxide ion concentrations employed in the determination of the rate of the alkaline hydrolysis of V ranged from 0.01 to 0.1 M, and the initial concentration of the sultone was on the order of 10^{-4} M. Since there was a large excess of base present, in individual measurements pseudo-first-order kinetics were observed. Figure 2 shows a plot of the pseudo-first-order rate constants measured at 25.0° vs. the hydroxide ion concentration. The slope of the line which is the second-order rate constant for hydroxide ion catalysis is 14.5×10^{-4} M^{-1} sec^{-1}. This value is approximately an order of magnitude greater than that found previously for the open-chain compound, phenyl α-toluenesulfonate,[4] but it is smaller by a factor of more than 10^4 than the second-order rate constants measured for the five-membered sultones II[4] and IV. Thus, we have established that very high lability to alkaline attack is a particular property of the five-membered sultones and that it does not occur in the larger ring six-membered system. We are continuing to investigate the reasons for the unusual reactivity of the five-membered cyclic sulfur-containing esters.[16]

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(15) The second-order rate constant for the alkaline hydrolysis of catechol cyclic sulfate (I) is 18.8 M^{-1} sec^{-1}, a very similar value also (see ref 3).

(16) The support of the National Science Foundation is gratefully acknowledged.