mp 91–93°. From the ether extract there was recovered 833 mg (40%) of **7a** picrate.

B. From Mercaptans.—A solution of 416 mg (2.83 mmoles) of **7b** and 321 mg (2.83 mmoles) of 2-aminoethanethiol hydrochloride in 15 ml of methanol was refluxed for 4.5 hr. The oily concentrate from the solution was processed by the procedure used in A. Addition of sodium hydroxide afforded, on standing in the air, an 87% yield of disulfide **6c**. No **7b** could be recovered from the ether extract.

Direct treatment of the concentrate from the reaction with ethanolic picric acid gave **2-(3-mercaptopropylamino)-2-thiazoline (5c) picrate** as fine yellow crystals, mp 169.5–171.5°. Its infrared spectrum (KBr) showed a mercaptan band at 3.9 μ.

Anal. Calcd for $C_{12}H_{15}N_5O_7S_2$: C, 35.55; H, 3.73; S, 15.82. Found: C, 35.54; H, 3.70; S, 16.02.

From **7a** and 3-aminopropanethiol hydrochloride[11] there were obtained after 7 hr of refluxing a 54% yield of **6c** and a 14% recovery of **7a** as the picrate. The same mercaptan picrate, after purification by recrystallization from ethanol, was obtained from the reaction.

2-Methylamino-5,6-dihydro-4H-1,3-thiazine.—The method of Gabriel[13] for the preparation of 2-methylamino-2-thiazoline was used. A mixture of 20 ml of cold 30% potassium hydroxide, 30 ml of benzene, and 6.4 g (0.029 mole) of 3-bromopropylamine hydrobromide was shaken in a separatory funnel and the benzene layer was added to 1.8 g (0.025 mole) of methyl isothiocyanate. An aqueous solution of the viscous precipitate that separated during 3 hr at room temperature was treated with 30% potassium hydroxide. The precipitated oil was extracted into benzene and removal of the benzene afforded a solid. The latter was extracted with 20 ml of boiling hexane and 375 mg of long needles, mp 51–54°, was obtained on cooling. Recrystallization from hexane gave colorless needles: mp 57–58.5°; $\lambda_{max}^{CHCl_3}$ 6.10 μ (N=CN); $\lambda_{max}^{H_2O}$ 218 mμ (ε 12,100).[14]

Anal. Calcd for $C_5H_{10}N_2S$: C, 46.12; H, 7.74; N, 21.52. Found: C, 45.92; H, 7.69; N, 21.55.

The picrate crystallized from ethanol as fine yellow needles, mp 189–191°.

Anal. Calcd for $C_{11}H_{13}N_5O_7S$: C, 36.77; H, 3.65; N, 19.49. Found: C, 36.94; H, 3.49; N, 19.20.

(13) S. Gabriel, *Ber.*, **22**, 1139 (1889).

(14) The corresponding absorptions in 2-methylamino-2-thiazoline are at 6.13 μ and 211 mμ (ε 10,200).

Registry No.—**3b**, 13865-94-6; **3b** dipicrate, 13865-95-7; **3c**, 4786-92-9; **3c** dipicrate, 13865-97-9; **5c** picrate, 13865-98-0; **6b**, 13865-99-1; **6b** dipicrate, 13866-00-7; **6c**, 13866-01-8; **6c** dipicrate, 4787-04-6; **9**, 13866-02-9; **9** dipicrate, 13866-03-0; 2-methlamino-5,6-dihydro-4H-1,3-thiazene, picrate of 2-methylamino-5,6-dihydro-4H-1,3-thiazine, 13866-05-2.

Acknowledgment.—We are indebted to Carmine DiPietro of these laboratories for the microanalyses. We also wish to thank Dr. Martin G. Ettlinger for helpful discussions.

A Solvolytic Investigation of Cyclooctyl and *trans*-2-Hydroxycyclooctyl Bromides and *p*-Toluenesulfonates[1]

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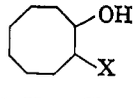
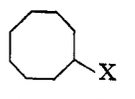
Solvolysis rates of cyclooctyl *p*-toluenesulfonate (**2T**) and bromide (**2B**) and *trans*-2-hydroxycyclooctyl bromide (**1B**) and *p*-toluenesulfonate (**1T**) have been determined in a series of solvents of varying ionizing strength. The kinetic data have been analyzed for neighboring-group, solvent, and leaving-group effects. This analysis, coupled with the partitioning of the activation parameters, suggests a parallel in mechanism between the cyclooctyl and *trans*-2-hydroxycyclooctyl derivatives. Product distribution data have been obtained for solvolysis of **1B** and **1T** in aqueous acetone and the proportions of various products exhibit some sensitivity to leaving group. Comparison with the solvolysis products of the glycol and amino alcohol suggests a product distribution sensitivity to the nature of the cationic intermediate immediately preceding product formation.

A solvolysis study of *trans*-2-hydroxycyclooctyl halides **1C** and **1B** led to the proposal that products are formed by two competing pathways, One leading largely to normal 1,2-rearrangement products and the other, largely to transannular products.[2] The alternate pathways, differing principally in the descriptions of cationic intermediates, were not specifically identified with the two groups of products, and a more detailed mechanistic investigation was needed. Because chemical kinetics is particularly useful for measuring substrate response to medium and substituent effects[3a,b] and to change in leaving group,[3c] a kinetic investigation of the solvolytic reactions of both the cyclooctyl and 2-hydroxycyclooctyl systems was undertaken. The data indicates that the reactions studied proceed through cationic intermediates and that a *trans*-2-hydroxy substituent does not alter the nature of the intermediate.



1C, X = Cl
B, X = Br
T, X = OTs



2B, X = Br
T, X = OTs

The first-order rate constants for solvolysis of **1B**, **1T**, **2B**, and **2T** in various solvents are summarized in Table I. The acetolysis reactions of **1B**, **2B**, and **1T** yielded integrated first-order rate constants that tended to decrease as the reaction progressed; consequently, the rate constant was calculated from the initial slope of a plot of log $(a - x)$ *vs.* time. All other reactions were first order in *p*-toluenesulfonate or bromide up

(1) This research was supported in part by Grant No. GP 5749 from the National Science Foundation to Louisiana State University.

(2) J. G. Trahnham and J. Schneller, *J. Am. Chem. Soc.*, **87**, 2398 (1965).

(3) (a) A. Streitwieser, Jr., "Solvolytic Displacement Reactions," McGraw-Hill Book Co., Inc., New York, N. Y., 1962; (b) E. R. Thornton, "Solvolysis Mechanisms," The Ronald Press Co., New York, N. Y., 1964; (c) H. M. R. Hoffmann, *J. Chem. Soc.*, 6748, 6753, 6762 (1965).

TABLE I

RATES OF REACTION OF CYCLOOCTYL AND *trans*-2-HYDROXYCYCLOOCTYL DERIVATIVES[a] IN A VARIETY OF SOLVENTS

Compd	Temp, °C	Solvent, vol. %[b]	k_1, sec^{-1}[c]	ΔH^*, kcal/mole	ΔS^*, eu
Cyclooctyl tosylate	35.2	EtOH	1.29×10^{-5}	23.6	−4.5
	45.0	EtOH	4.6×10^{-5}		
	55.0	EtOH	14.5×10^{-5}		
	30.2	80% aq EtOH	1.83×10^{-4}	20.5	−7.9
	35.2	80% aq EtOH	3.46×10^{-4}		
	45.0	80% aq EtOH	9.25×10^{-4}		
	55.0	80% aq EtOH	26.0×10^{-4}		
	25.0	60% aq EtOH	5.8×10^{-4}		
	45.0	60% aq EtOH	41.0×10^{-4}		
	35.2	70% aq acetone	21.0×10^{-5}	20.4	−9.1
	45.0	70% aq acetone	63.0×10^{-5}		
	55.0	70% aq acetone	16.9×10^{-4}		
	30.0	AcOH	5.5×10^{-5}	21.8	−7.2
	35.0	AcOH	10.0×10^{-5}		
	55.0	AcOH	92.0×10^{-5}		
	5.0	HCO_2H[d]	6.4×10^{-3}	14.5	−16.3
	10.0	HCO_2H[d]	10.0×10^{-3}		
	15.0	HCO_2H[d]	16.0×10^{-3}		
	20.0	HCO_2H[d]	26.0×10^{-3}		
	25.0	HCO_2H[d]	40.0×10^{-3}		
Cyclooctyl bromide	35.0	EtOH	4.4×10^{-8}	21.6	−12.2
	45.0	EtOH	1.4×10^{-7}		
	55.0	EtOH	4.0×10^{-7}		
	65.0	EtOH	11.3×10^{-7}		
	30.2	80% aq EtOH	5.65×10^{-7}	24.7	−5.4
	35.2	80% aq EtOH	12.1×10^{-7}		
	45.0	80% aq EtOH	40.3×10^{-7}		
	55.0	80% aq EtOH	13.7×10^{-6}		
	45.0	60% aq EtOH	3.8×10^{-5}		
	32.2	70% aq acetone	1.92×10^{-6}		
	45.0	70% aq acetone	6.1×10^{-6}		
	55.0	70% aq acetone	19.2×10^{-6}		
	55.0	AcOH[e]	3.0×10^{-7}	27.8	−3.0
	65.0	AcOH[e]	12.0×10^{-7}		
	73.4	AcOH[f]	38.4×10^{-7}		

[a] Initial concentration: 0.03 − 0.04 *M*. [b] Vol. % (*X*) aqueous organic solvent (A) means *X* volumes of A plus 100*X* volumes of water, HCO_2Li. [c] Initial rate constants, as determined by graphical analysis. [f] Taken from data of A. C. Cope and P. E. Petersen, *J. Am.*

to 80% conversion. The activation parameters were obtained by IBM 1620 computer regression analyses.

Table II compares the neighboring hydroxyl substituent effect upon the cyclooctyl system in solvents varying in polarity from weakly ionizing, nucleophilic ethanol to strongly ionizing, weakly nucleophilic formic acid. It is readily apparent that the order of magnitude of the expected[4] rate retardation is not observed; only in formic acid is the reduction significant. The remarkedly slight influence on the rate of reaction in aqueous ethanol, aqueous acetone, and acetic acid has previously been observed[2] in aqueous tetrahydrofuran.

TABLE II

COMPARISON OF REACTION RATES OF *trans*-2-HYDROXYCYCLOOCTYL AND CYCLOOCTYL BROMIDES AND TOSYLATES IN VARIOUS SOLVENTS AT 45°

Solvent	k^{OH}/k^H, tosylates	k^{OH}/k^H, bromides
EtOH	0.78	0.88
70% aq acetone	0.51	0.49
80% aq EtOH	0.42	0.38
60% aq EtOH	0.38	0.31
AcOH	0.38	1.0
HCO_2H	0.025[a]	

[a] Rate ratio at 25°.

By analogy to the solvolytic behavior of *trans*-2-hydroxycyclopentyl and *trans*-2-hydroxycyclohexyl chlorides,[5a] the apparent absence of the substituent effect can be rationalized in terms of a balance between opposing neighboring-group assistance and electronic effects upon the free energy of activation. Thus, the reduced ability of *trans*-2-hydroxycyclooctyl derivatives to accommodate the positive charge (due to the electron-withdrawing influence of the hydroxyl group) is almost compensated by the enhanced ability of the substrate to disperse charge (due to hydroxyl group participation[5b,6]).

The greater sensitivity of the substrate to the electronic influence of the OH group in formolysis re-

(4) S. Winstein and E. Grunwald (*J. Am. Chem. Soc.*, **70**, 828 (1948)) calculated, for the electrostatic effect of a neighboring hydroxyl group, a rate-retarding factor of about 10^{-2}.

(5) (a) H. Bodat, J. Jullien, and M. Mousseron, *Bull. Soc. Chim. France*, 1101, 1110 (1958). (b) Work in progress by one of us (D. D. R.) reveals that both the response and magnitude of the k^{OH}/k^H value to variable solvent ionizing strength is very similar in the five-, seven- and eight-membered ring tosylates. Since the variation in geometry and conformational factors among these three-ring systems is substantial, the insensitivity of the k^{HO}/k^H value to ring size over a wide spectrum of solvents suggests that conformational factors do not have a significant influence upon the hydroxyl neighboring-group effect.

(6) Participation by the hydroxyl group, however, is less than complete covalency, since 1,2-epoxycyclooctane is not a reaction product although it is reasonably stable under the reaction conditions.

TABLE I
(*Continued*)

Compd	Temp. °C	Solvent, vol. %[b]	k_1, sec^{-1} [c]	ΔH^*, kcal/mole	ΔS^*, eu
Cyclooctyl bromide	90.0	AcOH[f]	256×10^{-7}		
	20.0	HCO_2H[d]	2.9×10^{-5}	20.2	−8.0
	30.0	HCO_2H[d]	12.0×10^{-5}		
	40.0	HCO_2H[d]	26.0×10^{-5}		
	50.0	HCO_2H[d]	78.0×10^{-5}		
trans-2-Hydroxycyclooctyl tosylate	35.2	EtOH	1.04×10^{-5}	24.4	−2.3
	45.0	EtOH	3.60×10^{-5}		
	55.0	EtOH	12.8×10^{-5}		
	30.2	80% aq EtOH	7.1×10^{-5}	20.9	−8.4
	35.2	80% aq EtOH	12.2×10^{-5}		
	45.0	80% aq EtOH	39.0×10^{-5}		
	55.0	80% aq EtOH	107×10^{-5}		
	45.0	60% aq EtOH	15.5×10^{-4}		
	35.2	70% aq acetone	11.5×10^{-5}	20.2	−11.0
	45.0	70% aq acetone	31.9×10^{-5}		
	55.0	70% aq acetone	91.0×10^{-5}		
	30.0	AcOH[e]	2.5×10^{-5}	23.0	−4.3
	35.0	AcOH[e]	3.8×10^{-5}		
	50.0	AcOH[e]	20.0×10^{-5}		
	55.0	AcOH[e]	30.0×10^{-5}		
	20.0	HCO_2H[d]	6.1×10^{-4}	16.8	−16.0
	30.0	HCO_2H[d]	18.0×10^{-4}		
	40.0	HCO_2H[d]	44.0×10^{-4}		
	50.0	HCO_2H[d]	91.0×10^{-4}		
trans-2-Hydroxycyclooctyl bromide	45.0	EtOH	1.25×10^{-7}	19.4	−21
	65.0	EtOH	8.2×10^{-7}		
	35.2	80% aq EtOH	3.8×10^{-7}	25.3	−6.0
	45.0	80% aq EtOH	15.1×10^{-7}		
	55.0	80% aq EtOH	53.0×10^{-7}		
	45.0	60% aq EtOH	1.2×10^{-5}		
	35.2	70% aq acetone	9.0×10^{-7}	22.7	−13
	45.0	70% aq acetone	30.0×10^{-7}		
	55.0	70% aq acetone	92.5×10^{-7}		
	65.0	AcOH[e,g]	7.5×10^{-7}	24.0	−16
	75.0	AcOH[e,g]	24.0×10^{-7}		

both at 25° before mixing. [c] The standard deviation of these rate constants ranged from +0.3 to ±1.5%. [d] Contained 0.050 *M* *Chem. Soc.*, **81**, 1643 (1959). [g] Contained 0.050 *M* AcONa.

actions is in accord with the more ionic transition state expected in this solvent; however, the fact that the rate retardation is 40% of the expected value[4,5] further supports the presence of the opposing acceleration effect.

The rates of ionization of *p*-methoxyneophyl *p*-toluenesulfonate in several solvents provide a useful scale of solvent polarity for measuring the response of a given reaction to solvent variation.[7] Accordingly, the kinetic data presented in Table I were analyzed by use of eq 1[7] where log k_1 is the rate constant for *p*-methoxyneophyl tosylate in a given solvent, and the *a* value is a measure of relative sensitivity of a reaction to solvent ionizing power.

$$\log k_{\text{reaction}} = a \log k_1 + b \qquad (1)$$

The good correlation of log k_{reaction} with log k_1 (*cf.* Figure 1) for cyclooctyl tosylate establishes that this ester suffers solvolysis throughout the entire solvent variation by a limiting of SN1 mechanism.[8]

The log k_1 plot for **1T** exhibits a noticeable downward deviation from linearity in solvents of high ionizing strength. This reduced response to change in solvent polarity or alternatively, this enhanced sensitivity to the presence of the neighboring hydroxyl group, is in agreement with the expected greater importance of the rate-retarding electronic effect upon a more ionic transition state.

The log *k* data for **2B** and **1B** fail to correlate with k_1 (*cf.* Figure 2) revealing that the change in the X portion of substrate *RX* is too great a change to leave $\log(f_{RX}/f_*)$ linearly related to $\log(f_{ROTs}/f_*)$ for *p*-methoxyneophyl tosylate over the range of solvent variation. A similar situation is evidenced by the neophyl substrate, the tosylate[7] correlates well with log k_1 while the bromide[9] yields a scatter diagram.

Recently, Hoffmann[3c] published a series of papers in which the ratio of k_{OTs}/k_{Br} for a given substrate was used as a mechanistic criterion. It was demonstrated in a rather dramatic fashion that the k_{OTs}/k_{Br} ratio increases with increasing ionizing tendency of the substrate. The consistency of the proposal, however, requires that initial and transition-state solvation differences between the tosylate and bromide make only a minor and approximately constant contribution

(7) S. G. Smith, A. H. Fainberg, and S. Winstein, *J. Am. Chem. Soc.*, **83**, 618 (1961).

(8) According to ref 7, eq 1 is equivalent to a linear relation between log (f_{RX}/f_*) for the substrate RX and that of the reference substrate, *p*-methoxyneophyl tosylate. The fact that a limiting SN1 mechanism has been convincingly established for the reference ester in a variety of solvents argues for a correspondence in mechanism for these compounds which are correlated by eq 1.

(9) A. H. Fainberg and S. Winstein, *ibid.*, **79**, 1602, 1608 (1957).

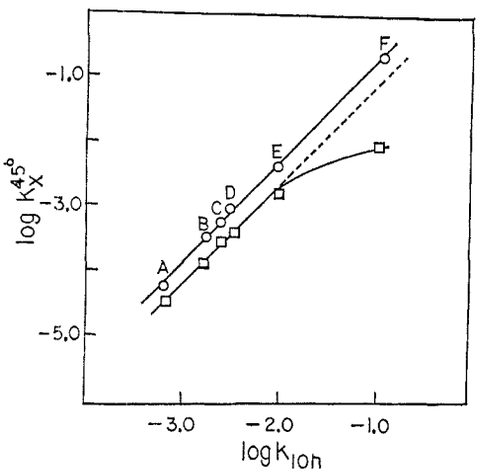


Figure 1.—Plot of log k for cyclooctyl, O, and *trans*-2-hydroxycyclooctyl, □, tosylates *vs.* log k for *p*-methoxyneophyl tosylate in the following solvents: A, ethanol; B, acetic acid; C, 70% aqueous acetone; D, 80% aqueous ethanol; E, 60% aqueous ethanol; and F, formic acid. Data taken from Table I and ref 7.

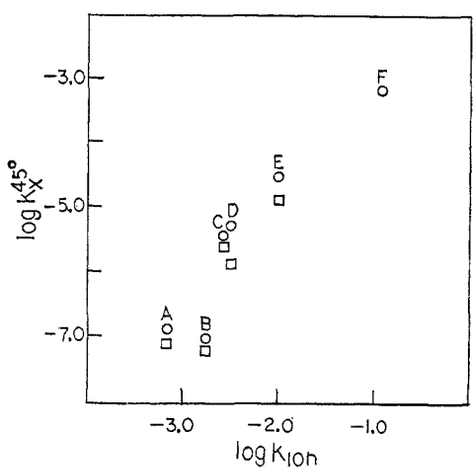


Figure 2.—Plot of log k for cyclooctyl, O, and *trans*-2-hydroxycyclooctyl, □, bromides *vs.* log k for *p*-methoxyneophyl tosylate in the following solvents: A, ethanol; B, acetic acid; C, 70% aqueous acetone; D, 80% aqueous ethanol; E, 60% aqueous ethanol; and F, formic acid. Data taken from Table I and ref 7.

to the free energy of activation change. That this is not always the case is also demonstrated by Hoffmann's work,[3c] and care, therefore, must be taken in the application of this mechanistic probe.

Nevertheless, in spite of the limitations, some meaningful information relevent to charge development is obtainable from the data reported in Table III. For example, the fact that the k_{OTs}/k_{Br} ratios for the cyclooctyl and *trans*-2-hydroxycyclooctyl compounds reflect a similar response to changing medium strongly indicates similar charge development and, consequently, similar reaction mechanism.

Further evaluation of the leaving-group response to varying solvent is afforded by a treatment of Fainberg and Winstein.[9] A plot of log k (neophyl bromide) *vs.* log k (neophyl chloride) revealed a separation of the aqueous alcohols from the carboxylic acid solvents which was attributed to a leaving-group specificity to solvation effects, particularly hydrogen bonding. In agreement with this finding and the reported[10] order

(10) S. Winstein, A. H. Fainberg, and E. Grunwald, *J. Am. Chem. Soc.*, **79**, 4151 (1957).

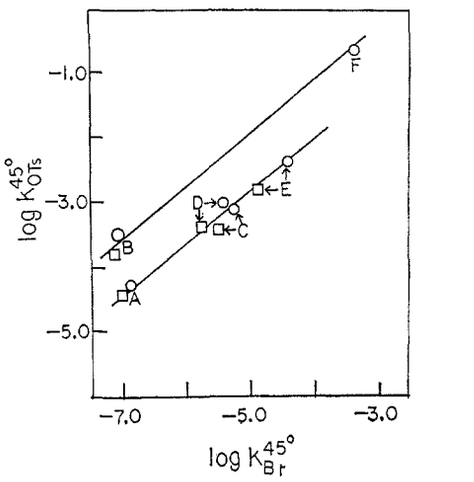


Figure 3.—Plot of log k for cyclooctyl tosylate *vs.* log k for *trans*-2-hydroxycyclooctyl tosylate, O, and log k for cyclooctyl bromide *vs.* log k for *trans*-2-hydroxycyclooctyl bromide, □, in the following solvents: A, ethanol; B, acetic acid; C, 70% aqueous acetone; D, 80% aqueous ethanol; E, 60% aqueous ethanol; and F, formic acid. Data taken from Table I.

TABLE III

k_{OTs}/k_{Br} RATIOS FOR THE SOLVOLYSIS OF SOME ALKYL DERIVATIVES AT 45°

Solvent	k_{OTs}/k_{Br} (2T, 2B)	k_{OTs}/k_{Br} (1T, 1B)	k_{OTs}/k_{Br} R = neophyl
EtOH	330	290	106[a]
70% aq acetone	100	100	
80% aq EtOH	230	260	22[a]
60% aq EtOH	110	130	
AcOH	4100	1500	163[a]
HCO_2H	380		14[b]

[a] At 50°. [b] At 25°.

of hydrogen bonding (F ≫ OTs > Cl > Br > I) a similar sorting of the solvents into two families is demonstrated by Figure 3, once again establishing a continuity of mechanism between the cyclooctyl and *trans*-2-hydroxycyclooctyl compounds.

The presence of a linear relationship[11] between activation enthalpy and entropy with changing medium or substrate structure provides another criterion for establishing continuity of interaction mechanism for a given variable. From Figures 4 and 5, it is quite clear that the data for both the cyclooctyl and *trans*-2-hydroxycyclooctyl tosylates are regularly correlated by the isokinetic treatment with solvent as a variable. This sufficiently uniform behavior of the activation parameters warrants their use in comparing transition state geometries of the two tosylates. With both esters, the increase in rate with increasing ionizing strength of solvent is associated with a decreasing ΔH^* compensating for a corresponding decrease in ΔS^*. This close parallel in the partitioning of the activation parameters supports an equally close parallel in the transition-state molecular reorganization.

The effect of leaving group and neighboring hydroxyl substituent upon the activation enthalpy and entropy is summarized in Table IV. It is quite evident that, as one traverses the spectrum of solvent polarity, the rate dependency for the cyclooctyl derivatives varies in a regular fashion from a favorable entropy change to a favorable enthalpy change in 80%

(11) J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1963, Chapter 9.

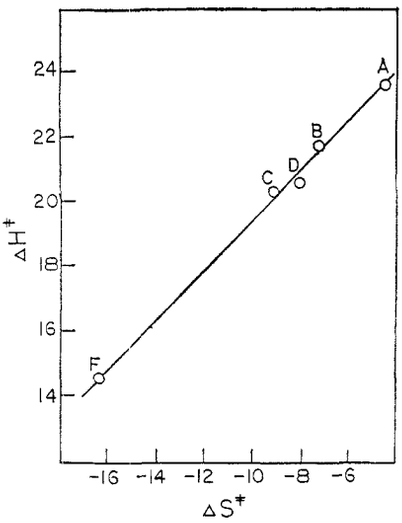


Figure 4.—Isokinetic correlation of cyclooctyl tosylate activation parameters in the following solvents: A, ethanol; B, acetic acid; C, 70% aqueous acetone; D, 80% aqueous ethanol; and F, formic acid. Data taken from Table I.

TABLE IV

THE INFLUENCE OF LEAVING GROUP AND NEIGHBORING HYDROXYL GROUP UPON PARTITIONING OF THE ACTIVATION PARAMETERS

Solvent	$\Delta(\Delta H^*)$ $\Delta H^*_{ROTs} - \Delta H^*_{RBr}$	$\Delta(\Delta S^*)$ $\Delta S^*_{ROTs} - \Delta S^*_{RBr}$	Rate-controlling parameter
	R = Cyclooctyl		
EtOH	2.0	7.7	Entropy
70% aq acetone	−1.9	2.8	Entropy and enthalpy
80% aq EtOH	−4.2	−2.5	Enthalpy
AcOH	−6.0	−4.0	Enthalpy
HCO_2H	−7.5	−14.4	Enthalpy
	R = *trans*-2-hydroxycyclooctyl		
EtOH	5.0	18.7	Entropy
70% aq acetone	−2.5	1.6	Entropy and enthalpy
80% aq EtOH	−4.4	−2.4	Enthalpy

Solvent	$\Delta(\Delta H^*)$ $\Delta H^*_{1T} - \Delta H^*_{2T}$	$\Delta(\Delta S^*)$ $\Delta S^*_{1T} - \Delta S^*_{2T}$	Rate-controlling parameter
EtOH	0.8	2.2	Enthalpy
70% aq acetone	−0.2	−2.8	Entropy
80% aq EtOH	0.5	−0.5	Enthalpy and entropy
AcOH	1.2	2.9	Enthalpy
HCO_2H	2.3	0.5	Enthalpy

ethanol and acetic and formic acids. The $\Delta(\Delta H^*)$ and $\Delta(\Delta S^*)$ values for the hydroxy-substituted ring compound parallel this behavior; *i.e.*, the substituent effect tends to be dominated by an unfavorable enthalpy change.

The product mixtures obtained by solvolyzing **1B** and **1T** in 70% aqueous acetone were analyzed by capillary column gas chromatography and component identities were established by use of infrared and nuclear magnetic resonance spectroscopy and by comparison with authentic samples and mixtures.[2] Product stability to the reaction conditions was established by the similar product composition in both the buffered (sodium acetate) and unbuffered runs and also by previously reported work.[2]

Table V affords a comparison of the product data from the present study with the previously reported[2] solvolysis data. Once again, the remarkable similarity in the distribution between transannular and nontransannular products is noted; however, the change from bromo to tosylate as leaving group affects the composition of the product mixtures by increasing the proportion of cyclooctanone, a nontransannular product, at the expense of bicyclic ethers, **5** and **6**, products of a transannular reaction.[12]

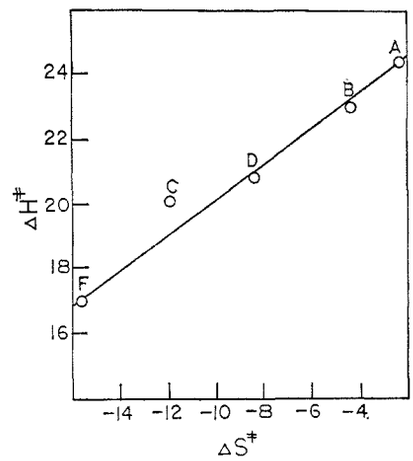
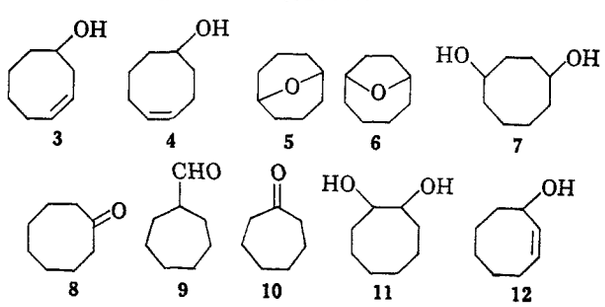


Figure 5.—Isokinetic correlation of *trans*-2-hydroxycyclooctyl tosylate activation parameters in the following solvents: A, ethanol; B, acetic acid; C, 70% aqueous acetone; D, 80% aqueous ethanol; and F, formic acid. Data taken from Table I.

TABLE V

PRODUCT DISTRIBUTION FROM SOLVOLYSES OF *trans*-2-HYDROXYCYCLOOCTYL BROMIDE AND TOSYLATE IN MIXED AQUEOUS SOLVENTS



		Product distribution, mole %									
		Transannular				Nontransannular					
Solvent[a]	Salt	3, 4	5, 6	7	Total	8	9	10	11	12	Total
THF[b]	None	39	17	3.5	60	21	3	0.4	7	4	36
THF[b]	NaOAc[c]	40	9	5	54	24	6	0	6	4	40
Me_2CO	None[d]	33	22	0	55	32	2	...	0	10	44
Me_2CO	None[d]	31	12	0	43	42	8	...	0	12	57
Me_2CO	NaOAc	35	9	0	44	42	2	...	0	12	56

[a] Organic solvent indicated was mixed with water in the following proportions by volume: 2:1 THF:HOH; 7:3 Me_2CO:HOH. [b] Data taken from ref 2. [c] Product mixture also contained 13.5% of *cis*-cyclooctene oxide; product distribution data reported are calculated for remainder of the mixture. [d] Product mixture also contained 11–12% of the *trans*-1,2-cyclooctyl ketal of acetone; product distribution data reported are calculated for the remainder of the mixture.

We believe this result to be significant for establishing an inverse relationship between the extent of transannular reaction and the ease of charge development in the transition state. Thus, the acid-catalyzed rearrangements of cyclooctene glycols[13] yield products

(12) A. C. Cope, A. H. Keough, P. E. Petersen, H. E. Simmons, Jr., and G. W. Wood, *J. Am. Chem. Soc.*, **79**, 3900 (1957).
(13) J. G. Traynham and P. M. Greene, *ibid.*, **86**, 2657 (1964).

primarily transannular in nature while nitrous acid deaminations of the corresponding amino alcohols[14] lead almost exclusively to normal (nontransannular) products.

In summary, the probability of a dual mechanism as originally postulated[2] for the halohydrin solvolyses appears unlikely in view of the evidence for a single ionizing mechanism for the cyclooctyl and *trans*-2-hydroxycyclooctyl derivatives. However, the product distribution is apparently related to the activation energy of the cationic intermediate immediately preceding product formation; as the activation increases, there is a larger solvent participation and a formation of the more transannular products.

Experimental Section

Gas chromatographic analyses (glpc) were carried out with a Barber–Coleman Model 20 instrument with a hydrogen-flame detector and a 100-ft capillary column coated with SE-96 silicone. Infrared spectra were obtained mainly with a Perkin-Elmer Infracord spectrophotometer and nuclear magnetic resonance spectra were obtained with a Varian HA-60 spectrometer.

Cyclooctyl *p*-toluenesulfonate (2T) was prepared several times in 75–85% yield by the method of Heck and Prelog.[15] The crude ester was washed with cold petroleum ether (bp 60–70°) to yield samples of 95–99% purity by "infinity" titers. The infrared spectrum—ν_{SO_2} (*asym*) 1345 cm^{-1} and ν_{SO_2} (*sym*) 1165 cm^{-1}—and the nmr spectrum—δ 1.50 (multiplet, 14 methylene H), 2.38 (singlet, 3 methyl H), 4.65 (1 H multiplet, CHOTs), 7.58 (2 doublets, J = 8 cps, 4 aryl H)—were consistent with the assigned structure.

Cyclooctyl bromide (2B) was prepared in 60% yield by treatment of cyclooctanol with phosphorus tribromide: bp 97–98° (15 mm); lit.[16] bp 97° (15 mm). Purity was established by glpc analysis at 100°.

***trans*-2-Hydroxycyclooctyl *p*-toluenesulfonate (1T)** was prepared several times. In a typical run, 4.9 g (37.5 mmoles) of 1,2-epoxycyclooctane, 6.7 g (37.5 mmoles) of lithium tosylate, and 6.5 g (37.5 mmoles) of *p*-toluenesulfonic acid were stirred together in 100 ml of acetone at room temperature for 10 hr. The slurry was then diluted fourfold with ice water and extracted three times with ether. The ether extracts were washed twice with cold, dilute hydrochloric acid, twice with cold sodium bicarbonate solution, and once with cold water, dried over anhydrous sodium sulfate, and concentrated by rotary evaporation to yield 7.5 g of an oil. This crude ester was dissolved in hot petroleum ether (bp 60–70°) and cooled to −78°. The solvent was removed from the precipitated ester by decantation and rotary evaporation to yield 6.0 g of an oil. The purities, calculated from "infinity" titers, ranged from 90–95%. Analysis by glpc at 100° revealed that the impurity was primarily oxide. The infrared spectrum—ν_{SO_2} (*asym*) 1345 cm^{-1}, ν_{SO_2} (*sym*) 1170 cm^{-1}, ν_{OH} = 3400 cm^{-1}—and the nmr spectrum—δ 1.50 (multiplet, 12 H), 2.38 (singlet, 3 methyl H), 3.30 (1 H singlet, OH), 3.80 (1 H multiplet, CHOH), 4.60 (1 H multiplet, CHOTs), 7.58 (2 doublets, J = 8 cps, 4 aryl H)—were consistent with assigned structure. The *trans* configuration was confirmed by reformation of the *cis*-cyclooctene oxide in 95% yield by treatment with 10% sodium hydroxide at room temperature for 5 hr.

***trans*-2-Hydroxycyclooctyl bromide (1B)** was prepared as previously reported.[2]

Solvents.—Absolute ethanol was prepared according to the method of Fieser.[17] Aqueous ethanol solvents (60 and 80% by volume) were prepared volumetrically from absolute ethanol and distilled water. Aqueous acetone (70% by volume) was prepared from distilled water and acetone purified by distillation from potassium permanganate. Acetic acid solvent was prepared from 985 ml of glacial acetic acid (Du Pont, 99.7% min) and 15 ml of acetic anhydride. Formic acid solvent was stored several days over boric anhydride, decanted, and distilled from fresh anhydride.

Rate Measurements.—The rates of solvolysis were followed titrimetrically. At appropriate times, 2-ml aliquots were analyzed for either liberated hydrobromic or *p*-toluenesulfonic acid. In ethanol, aqueous ethanol, and aqueous acetone, aliquots were analyzed for developed acid by titrating with aqueous sodium hydroxide to a bromothymol blue end point. In acetic acid, aliquots were analyzed for developed acid by titrating with standard sodium acetate in acetic acid to the yellow end point of bromophenol blue. The rate of the reaction in formic acid was followed in the same manner except that the 2-ml aliquots were quenched in 10 ml of chilled acetic acid containing a known quantity of standardized perchloric acid in acetic acid.

Product Studies.—Solvolyses of **1T** were carried out in 70% (v/v) aqueous acetone at 50° for 15 half-lives, both with and without added sodium acetate. Each reaction was diluted threefold with ice water and extracted five times with petroleum ether (bp 60–70°). The extract solution was washed with water and dried over anhydrous sodium sulfate. After removal of solvent by rotary evaporation, the residue was weighed (average yield of 95%) and analyzed by glpc at 100°. A portion of the residue was treated in pyridine solution to convert alcohol components to their trimethylsilyl ether derivatives,[18] which were satisfactorily resolved by glpc[14] at 150°. By comparison with authentic samples[2,13,14] and mixtures, identities and yields of components were established with the exception of the *trans*-1,2-cyclooctyl ketal of acetone; identity of this component (isolated by preparative glpc) was established first by structure assignment consistent with its nmr spectrum—δ 1.28 (singlet, 6 methyl H), 1.50 (multiplet, 12 methylene H), 3.72 (2 H multiplet, CHOC)—and then comparison with the authentic sample prepared almost quantitatively by allowing a solution of *trans*-1,2-cyclooctanediol and *p*-toluenesulfonic acid in acetone to stand at room temperature for 3 hr.

Two solvolyses of **1B** were carried out in 70% (v/v) aqueous acetone at 50° for 15 half-lives. Each reaction was worked up (average yield of 93%) and the component products were identified as above. The product distribution of the two runs agreed within experimental limits.

Registry No.—**1B**, 1502-14-3; **1T**, 13448-99-2; **2B**, 1556-09-8; **2T**, 6597-09-7.

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(16) L. Ruzicka, P. Barman, and V. Prelog, *ibid.*, **34**, 401 (1951).
(17) L. F. Fieser, "Experiments in Organic Chemistry," 3rd ed, D. C. Heath and Co., Boston, Mass., 1957, p 285.
(18) C. C. Sweeley, R. Bently, M. Makita, and W. W. Wells, *J. Am. Chem. Soc.*, **85**, 2497 (1963).