

identified and reported in Table I account for 95% of the total product mixture obtained from the *trans*-amino alcohol and for 90% of that from the *cis* isomer.^{9a,b}

Compound **6**, the major product from deamination of *cis*-2-hydroxycyclooctylamine, m.p. 85–86.5°, exhibits ultraviolet absorption (maxima at 360 and 237 m μ) characteristic of an N-nitrosamine²⁴; its infrared spectrum shows no absorptions attributable to O–H or N–H bonds and is consistent with the meager information available for N-nitrosamines.²⁵ The n.m.r. spectrum²⁶ is complex and not particularly helpful;

(24) S. F. Mason, *Quart. Rev.* (London), **15**, 317 (1961).

(25) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1958, pp. 306–307.

(26) We express our appreciation to Dr. William L. Senn, Jr.,

poorly resolved multiplets appear at approximately –1.5, –3.7, –4.2, and –5.2 p.p.m. (peak areas approximately 24–29:1:1:1, respectively), the last one similar in position to the peak for one of the tertiary hydrogens in diisopropyl-N-nitrosamine (–4.97 p.p.m.).²⁷ On the basis of these data, this product is tentatively formulated as **6a** or **6b**.

*Anal.*²⁸ Calcd. for C₁₆H₂₈N₂O₂: C, 68.5; H, 10.1; N, 10.0. Found: C, 68.6; H, 10.3; N, 10.1.

Humble Oil and Refining Co., Baton Rouge, La., and Dr. Fred J. Impastato, Ethyl Corp., Baton Rouge, La., for providing us with n.m.r. and mass spectral data on **6** before instrumentation was operating in our own laboratories (n.m.r. data obtained with CCl₄ solutions, tetramethylsilane internal standard, Varian A-60 instrument).

(27) Unpublished work from this laboratory. See also G. J. Karabatsos and R. A. Taller, *J. Am. Chem. Soc.*, **86**, 4373 (1964).

(28) Microanalyses by Mr. R. Seab of these laboratories.

Solvolyses of *trans*-2-Halocyclooctanols¹

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Product distribution data have been obtained for solvolyses of trans-2-chloro- and -bromocyclooctanols in mixed aqueous solvents and in carboxylic acid solvents. The product mixtures contain substantial amounts of both transannular and nontransannular products. The proportions of the various products are remarkably insensitive to the identity of the halogen, the presence or absence of silver salts or sodium acetate (buffer), temperature, and solvent change. Solvolyses of cis-cyclooctene oxide have been re-examined under these conditions to permit direct comparison of related reactions. The data lead to the conclusion that these halohydrin solvolyses proceed by two competing mechanisms: (1) ionization to an unbridged 2-hydroxycyclooctyl cation, and (2) formation of hydrogen- (or alkyl-) bridged species. The small shift in proportions of products with change of solvent supports the conclusion. Solvolyses of epoxide, glycol, amino alcohol, and halohydrin (all derived from cyclooctene) are compared; the amino alcohol and halohydrin reactions are distinguished from the others by the relative abundance of carbonyl products in the mixtures.

Studies of solvolysis reactions have provided a wealth of information pertinent to considerations of reaction mechanism during the past 40 years. Very recent papers have emphasized the influence of the leaving group on product formation in elimination reactions.³ We have reported some studies of rearrange-

ments of 2-substituted cycloalkanol,^{4,5} and have attributed to medium ring systems a welcome sensitivity to reaction mechanism which is revealed by product distribution data. Acid-catalyzed rearrangements of cyclooctene oxides⁶ and glycols⁴ are highly similar to each other but completely different from rearrangements brought about by nitrous acid deamination of the corresponding amino alcohols.⁵ We have now investigated solvolyses of *trans*-2-chloro- and -bromocyclooctanols (**1** and **2**), both with and without silver ions present, in mixed aqueous solvents and carboxylic acid solvents. Acid-catalyzed hydrolyses of *cis*-cyclooctene oxide under these same conditions have been examined for comparison. Product distribution data for the halohydrin solvolyses, falling in between those for epoxide^{6,7} and glycol⁴ reactions and those for amino alcohol deaminations,⁵ point strongly to an influence of leaving group not only on product formation but on gross reaction mechanism as well.

The halohydrins were prepared by reaction of *cis*-cyclooctene oxide with anhydrous hydrogen halide in carbon tetrachloride solution.⁸ Although the reactions of medium ring epoxides with aqueous acid proceed with extensive transannular rearrangement,^{6,9} the 1,2-product is obtained in nonpolar solvent.⁸ Our confidence in the simplicity of this reaction is supported by the reformation of *cis*-cyclooctene oxide in high yields from the halohydrins and base.

(4) J. G. Traynham and P. M. Greene, *ibid.*, **86**, 2657 (1964).

(5) J. G. Traynham and M. T. Yang, *ibid.*, **87**, 2394 (1965).

(6) (a) A. C. Cope, A. H. Keough, P. E. Peterson, H. E. Simmons, Jr., and G. W. Wood, *ibid.*, **79**, 3900 (1957); (b) A. C. Cope, A. Fournier, Jr., and H. E. Simmons, Jr., *ibid.*, **79**, 3905 (1957); (c) A. C. Cope, J. M. Grisar, and P. E. Peterson, *ibid.*, **81**, 1640 (1959).

(7) This research.

(8) A. C. Cope and H. E. Johnson, *J. Am. Chem. Soc.*, **79**, 3889 (1957).

(9) For a review, see V. Prelog and J. G. Traynham in "Molecular Rearrangements," P. de Mayo, Ed., Interscience Publishers, Inc., a Division of John Wiley and Sons, Inc., New York, N. Y., 1963, Chapter 9.

(1) (a) We gratefully acknowledge partial support of this research by grants from the National Science Foundation and the Petroleum Research Fund administered by the American Chemical Society. (b) Presented in part at the Southwest Regional Meeting of the American Chemical Society, Shreveport, La., Dec. 1964.

(2) National Science Foundation Cooperative Fellow, 1964–1965.

(3) (a) D. J. Cram and M. R. V. Sahyun, *J. Am. Chem. Soc.*, **85**, 1257 (1963); (b) M. Cocivera and S. Winstein, *ibid.*, **85**, 1702 (1963); (c) P. S. Skell and W. L. Hall, *ibid.*, **85**, 2851 (1963).

Table I. Product Distribution from Solvolyses of 2-Hydroxycyclooctyl Halides in Mixed Aqueous Solvents

Halide	Solvent ^a	Salt	Time, hr.	Product distribution, mole %								
				3	4	5	6	7	8	9	10, 11 ^b	12 ^t
Cl	THF	None	335	15	8	0	7	4	28	9	15	3.5
Cl	THF	AgNO ₃	27	16	0	8	1	2	38	4	25	1
Br	THF	None	44	21	3	0.4	7	5	32	7	17	3.5
Br	THF	AgNO ₃	4	24	0	6	1	1	34	2	28	1
Br	THF	NaOAc ^c	54	24	6	0	6	4	30	10	9	5
Br	HOAc	AgNO ₃	6	23	11	3	1	1	26	4	24	1
Br	HOAc ^d	AgNO ₃	52	25	11	1	1	1	36	2	21	1
Br	1 M H ₂ SO ₄ ^e	AgNO ₃	22	24	0	10	1	0	9	3.5	47	1

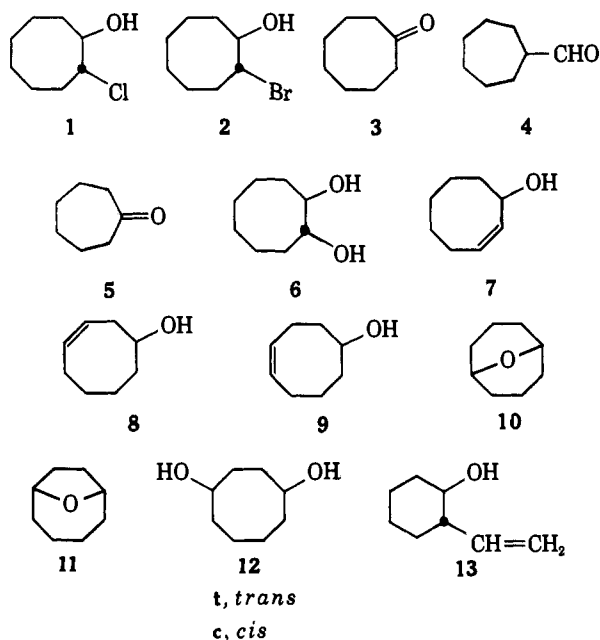
^a Organic solvent indicated was mixed with water in the following proportions by volume: 2 THF-1 HOH; 1 HOAc-1 HOH. Reaction temperature 66° unless otherwise noted. ^b Mixture on basis of infrared spectrum; not resolved on g.c. ^c Product mixture also contained 13.5% of *cis*-cyclooctene oxide; product distribution data reported are calculated for remainder of the mixture. ^d Reaction temp., 0°. ^e Reaction temp., 100°.

Table II. Product Distribution from Solvolyses of 2-Hydroxycyclooctyl Bromide in Carboxylic Acid Solvents

Solvent	Salt	Product distribution, mole %								
		3	4	5	6	7	8	9	10, 11 ^a	12 ^t
CH ₃ COOH ^b	CH ₃ COOAg	35	0.2	1	15	1	11	4	1	28
CF ₃ COOH ^c	CF ₃ COOAg	20	2	4	Tr ^d	0	29	4	15	21
HCOOH ^e	CH ₃ COOAg	10	1.5	3	4	0	37	4	3	37
HCOOH ^f	CH ₃ COOAg	10	Tr ^d	4	4.5	0	37	4	2	37.5

^a Mixture on basis of infrared spectrum; not resolved on g.c. ^b Glacial acetic acid, 10°, 24 hr. ^c Anhydrous acid, 0°, 3.5 hr. ^d Trace detected by g.c. ^e Commercial 97-100% formic acid, 0°, 10 hr. ^f Commercial 97-100% formic acid, 38°, 6.5 hr.

Solvolyses of the halohydrins were carried out, both with and without added silver ions, in aqueous tetrahydrofuran (THF), aqueous acetic acid, and nearly anhydrous carboxylic acid solvents. Some experiments were performed to evaluate the effects of temperature and buffer on the solvolysis reactions. Product mixtures were analyzed by capillary column gas chromatography, and component identities were established by use of preparative gas chromatography, infrared spectroscopy, preparation of derivatives, and comparison with authentic samples and mixtures.^{4,5} Tables I and II summarize the product data.



Discussion of Results

Aqueous Solvents. The data for the several runs are remarkably similar. About two-thirds to three-fourths

of each product mixture consists of diols, unsaturated alcohols, and bicyclic ethers, products mainly transannular in nature and obtained in acid-catalyzed rearrangements of cyclooctene oxides^{6,7,9} and glycols.⁴ The remaining one-third to one-fourth of each mixture consists of carbonyl compounds (which represent migration of neighboring hydrogen or alkyl), products formed almost exclusively by nitrous acid deamination of 2-hydroxycyclooctylamines⁵ but virtually absent in mixtures from the rearrangements of cyclooctene oxides^{6,7,9} and glycols.⁴ The change from chloro to bromo as leaving group, the presence or absence of silver nitrate, or the change of solvent from aqueous THF to aqueous acetic acid affects the composition of the product mixtures but little.

The major differences between experiments with silver nitrate and those without it are in the relative proportions (A) of 4 to 5, and (B) of diols (6 and 12) to 10 and 11. The shift from 4 to 5 with addition of silver nitrate probably represents secondary processes unassociated with the halohydrin solvolyses themselves. In our studies of deaminations of 2-hydroxycyclooctylamines,⁵ we detected the surprising transformation of cycloheptanecarboxaldehyde (4) into cycloheptanone (5) under acidic conditions.¹⁰ Apparently silver ion, or silver halide, is an unusually effective catalyst for this degradation. For the present considerations, the solvolysis reactions, products 4 and 5 should be combined and regarded as 4 alone. The shift from diols to bicyclic ethers (10 and 11) may reflect influence of salt on the lifetime and consequent fate of intermediate carbonium ions. A similar, though less extensive, shift was found for solvolysis of cyclooctene oxide in 50% acetic acid containing either silver nitrate or sodium nitrate (Table III), although sodium acetate did not cause such a shift with bromohydrin solvolysis (Table I).

(10) This transformation is currently under study in our laboratory. All preparations of cycloheptanecarboxaldehyde which we have attempted so far have given mixtures of 4 and 5.

Table III. Product Distribution from Acid-Catalyzed Rearrangements of *cis*-Cyclooctene Oxide

Solvent	Product distribution, mole %						
	3	6	8	9	10,11 ^a	12c	13
2THF-1HOH ^b	Tr ^c	39	16	8	1	30	Tr ^c
50% HOAc ^d	1.5	33	28	9	1.5	19	...
50% HOAc ^e	1.5	34	29	9	6	17	1
50% HOAc ^f	2	33	29	9	4.5	17	1
90% HCOOH ^g	1	23	22	14	4	27	7.5
1 M H ₂ SO ₄ ^h	7	10	4	2	30	24	20
HCOOH ⁱ	8	20	23	8	...	39	...
CF ₃ COOH ^j	2	4	40	3	0.5	48	1

^a Mixture on basis of infrared spectrum; not resolved on g.c. ^b 20 mmoles of epoxide in 150 ml. of solvent, 6 drops of concentrated H₂SO₄, refluxing for 5 days; product mixture also contained 1% of 7. ^c Trace detected by g.c. ^d 0.1 mole of epoxide in 300 ml. of solvent, refluxing for 72 hr. ^e Same as *d* but with 0.1 mole of AgNO₃ added. ^f Same as *d* but with 0.1 mole of NaNO₃ added. ^g 0.1 mole of epoxide in 50 ml. of commercial solvent, steam bath for 3.5 hr. ^h 24 mmoles of epoxide in 100 ml. of solvent, refluxing for 15 hr. ⁱ 10 mmoles of epoxide in 35 ml. of commercial 97-100% solvent, refluxing for 3 hr. ^j 0.1 mole of epoxide in 65 g. of solvent, 3 hr. at 0°.

Although cyclooctene oxide and glycol and 3- and 4-cyclooctenols all yield small amounts of cyclooctanone (3) in hot aqueous sulfuric acid solutions,^{4,7} none of these materials is changed by the solvolysis reaction conditions.¹¹ Cyclooctanone then must be a primary reaction product in the solvolyses. Cycloheptanecarboxaldehyde (4) is not formed in acid-catalyzed rearrangements of cyclooctene oxide and glycol and cyclooctenols. The relatively high proportion of cyclooctanone together with cycloheptanecarboxaldehyde in all of the solvolysis reaction mixtures is significant for descriptions of mechanism, we believe. These are the products which are formed almost exclusively during nitrous acid deaminations of 2-hydroxycyclooctylamines.⁵ Although one can attribute such products to the intervention of a "hot" carbonium ion in deamination,¹² it is extremely unlikely that anything like a "hot" carbonium ion is formed during solvolysis of the halohydrins, most particularly in aqueous solvent without added silver nitrate (no less 3 and 4 than with silver nitrate). Since the products that distinguish amino alcohol deaminations and halohydrin solvolyses from acid-catalyzed rearrangements of glycols and epoxides are the same, the temptation to blame their appearance on the same mechanistic feature, in the absence of any evidence to the contrary, is indeed strong.

Even with the similarity of products, however, certain features distinguish the amino alcohol deaminations and halohydrin solvolyses. *trans*-2-Hydroxycyclooctylamine leads mainly to cycloheptanecarboxaldehyde (ratio of 3 to 4, 1:5.5),⁵ but *trans*-2-hydroxycyclooctyl halides give mainly cyclooctanone (ratio of 3 to 4, 2-3:1). If these carbonyl products are indeed formed by essentially the same kind of process in the different reactions, this reversal of product ratios may be associated with ring conformation preferences.^{13a,14}

(11) *cis*-Cyclooctene oxide is rearranged under the solvolysis conditions but so slowly that it cannot figure in the halohydrin reactions.

(12) For a list of pertinent references, see footnote 6 in ref. 5.

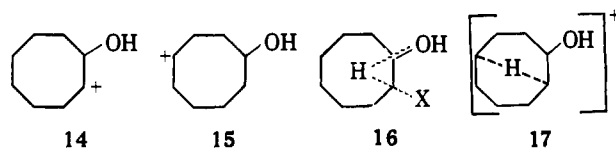
(13) (a) J. B. Hendrickson, *J. Am. Chem. Soc.*, **86**, 4854 (1964), reports that calculations indicate two conformations of about equal minimum energy for unsubstituted cyclooctane. His calculated minimum-energy form for cyclodecane has the same geometry as that revealed by X-ray analysis of derivatives of 1,6-cyclodecanediamine.^{13b} (b) E. Huber-

Alternatively, halide may leave mostly from one substituent conformation (favoring ketone formation), while deamination of amine can involve intermediates with a different substituent conformation.¹⁴

In some cases, a major influence of incompletely departed leaving group on the reactions of a carbonium ion has been reported.³ Ascribing very similar influences, however, to associated halide being removed by solvent alone, halide being removed by silver ion, and nitrogen does not seem reasonable.

The product data from these related reactions appear to demand two distinct, competing mechanisms, alternate descriptions of which are as follows: (I) (a) formation of a 2-hydroxycyclooctyl cation (14) which gives products almost exclusively after transannular hydride shift (to 15, for example), and (b) concurrent migration of hydrogen or alkyl during departure of the leaving group, before substantial carbonium ion development has occurred (16); (II) (a) direct formation of a hydrogen-bridged carbonium ion (such as 17) which gives mostly or exclusively transannular products,⁶ and (b) formation of a 2-hydroxycyclooctyl cation (14) in which combination with solvent and 1,2-shifts rather than transannular shifts lead to products.

These alternate descriptions clearly assign completely different roles to intermediate 2-hydroxycyclooctyl cations 14 and to hydrogen-bridged species 16 and 17. Personal tastes will favor one or the other, but the demands of the experimental data are for the moment less clear-cut. Cyclooctene oxide and glycol rearrange almost completely by path Ia or IIa, amino alcohol almost completely by path Ib or IIb, and halohydrins by both Ia and Ib or IIa and IIb.¹⁵



The stereochemistry of 1,4-diol formation from halohydrins as well as from epoxide favors, but does not demand, path IIa for the major part of these reactions. The stereoselective formation of *cis*-1,4-diol from *cis*-epoxide⁶ and of *trans*-1,4-diol from *trans*-halohydrins is precisely what an ion such as 17 leads one to expect, but, in these crowded eight-membered rings, such stereoselectivity with unbridged carbonium ions is entirely reasonable.¹⁶

Buser and J. D. Dunitz, *Helv. Chim. Acta*, **44**, 2027 (1961); J. D. Dunitz and K. Venkatesan, *ibid.*, **44**, 2033 (1961).

(14) Deamination studies with *cis*-2-hydroxycyclohexylamine and *cis*-2-hydroxycycloheptylamine have led to the conclusion that an intermediate, presumably diazo hydroxyde, undergoes conformational re-equilibration: M. Chérest, H. Felkin, J. Sicher, F. Šipoš, and M. Tichý, *J. Chem. Soc.*, in press. We gratefully acknowledge private communication from Professor J. Sicher about these studies. See also J. W. Huffman and J. E. Engle, *J. Org. Chem.*, **24**, 1844 (1959).

(15) Of course, different nonionizing processes may be operative. Elimination of hydrogen halide (to give initially enol which tautomerizes to ketone) could be largely a *cis* process, whereas migration during loss of nitrogen from diazonium cation would be *trans*. Models suggest strongly that *trans* migration will favor carbon rather than hydrogen migration⁵ and that *cis* elimination of hydrogen halide is reasonable. We expect our projected studies with the less accessible *cis* halohydrins to provide clues about these details.

(16) In spite of several published claims of completely or nearly completely stereoselective¹⁷ reactions of (unbridged) carbonium ions, discussion during a symposium session at a recent meeting of the American Chemical Society¹⁸ indicated a persistent belief, even among distinguished chemists, in the incompatibility of carbonium ion formation and subse-

The formation of *trans*-1,2-diol (**6**) from *trans*-halohydrin excludes an S_N2 type replacement and signals a stereoselective combination of intermediate cation with solvent. The same stereoselective formation of 1,2-diol is observed in acid-catalyzed reactions of the corresponding epoxides and glycol: *cis*-epoxide gives only *trans*-1,2-diol,⁶ and *trans*-1,2-diol is not isomerized to *cis*-1,2-diol.⁴ Formation of *trans*-1,2-diol from *trans*-halohydrin has far more mechanistic significance than formation of *trans*-1,2-diol from *cis*-epoxide: the epoxide can react by S_N2 displacement or by 2-hydroxycyclooctyl cations to give the same 1,2-diol, but all *trans*-1,2-diol from halohydrin must come from intermediate cations. A comparison of the relative proportions of various products from epoxide and halohydrin reactions, respectively, reveals, we believe, that very little 1,2-diol is formed from 2-hydroxycyclooctyl cations, and nearly all of the 1,2-diol formed from epoxide is an S_N2 displacement product. If we choose mechanism description I, which would couple 1,2-diol and transannular product formation through intermediate 2-hydroxycyclooctyl cations **14**, comparison of the ratio of 1,2-diol to transannular products **8–12** obtained from bromohydrin and from epoxide under comparable conditions indicates that only 2–10% of the 1,2-diol from epoxide is formed from **14**. If we choose the alternate description (II) which would couple 1,2-diol and carbonyl products through **14**, appropriate comparison of bromohydrin and epoxide rearrangements indicates that less than 0.5% of the 1,2-diol obtained from epoxide is formed through 2-hydroxycyclooctyl cations. Formation of 1,2-diol from an intermediate like **17** is apparently unlikely, since that path should lead to *cis*-1,2-diol, not the *trans*-1,2-diol actually obtained, from *cis*-epoxide. Before these data for halohydrin solvolysis became available, no good estimation of the proportions of transannular and nontransannular reactions for the cation **14** was possible.

Kinetic data offer promise of aiding our choice of mechanisms. In the absence of anchimeric assistance, a vicinal OH group is strongly rate retarding in solvolysis reactions,²⁰ and a comparison of rates of reaction of bromocyclooctane and 2-bromocyclooctanol should reveal the effect of the hydroxyl substituent. If the major parts of the solvolyses of these two bromides are alike in mechanism, for intermediates like **14** and

quent reaction to yield a single stereoisomer as product. It seems in order to emphasize that a carbonium ion intermediate can react in a completely stereoselective manner if certain conditions prevail: among others, rotation in the carbonium ion is slow compared to product-forming processes (for example, in 1-hydroxy-1,1-diphenyl-2-propyl cation)^{19a}; rapid equilibration, such as has been suggested for 2-norbornyl cation,^{19b} effectively protects one side of the cationic center from attack by external reagent; or one lobe of the unoccupied p-orbital extends into a ring and is inaccessible (in some medium ring cations, for example⁹). Complete stereoselectivity of product formation merely signals asymmetric combination of intermediate with reagent. It does not appear able to distinguish (open) carbonium ions from alternate descriptions of the reaction intermediates, however frustrating this acknowledgment may be for our efforts to make such distinctions.

(17) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, pp. 436, 437.

(18) Symposium on Electrophilic Addition to Olefins, 148th National Meeting of the American Chemical Society, Chicago, Ill., Sept. 1964.

(19) (a) B. M. Benjamin, H. J. Schaeffer, and C. J. Collins, *J. Am. Chem. Soc.*, **79**, 6160 (1957); (b) H. C. Brown, Special Publication No. 16, The Chemical Society, London, 1962, pp. 140–158, 175–178.

(20) 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.

17 the effect of the hydroxyl group should be strongly rate retarding. Only for an intermediate such as **16**, possibly favored for the bromohydrin but not for the bromide, should the electrostatic effect of the hydroxyl be offset to some degree by a rate enhancement due to assistance by migrating hydrogen (or alkyl). When the rates of solvolysis of the two compounds in refluxing aqueous THF were compared, only a small rate retardation (factor of 0.82) was found. Such a result clearly implies some actual rate acceleration and tends to implicate mechanism I rather than II. Since mechanism I would ascribe **16** to only one-fourth of the total reaction (see Table I, mole per cent of carbonyl products), combination of an experimental rate retardation factor of 0.82 and an expected one of 10⁻² indicates that the actual rate acceleration factor for **16** is 325. One cannot account for the acceleration as a result of participation of hydroxyl itself, leading to epoxide which then reacts further, because the distributions of even the noncarbonyl products from epoxide and bromohydrin are quite different (compare entries in Tables I and III) and epoxide rearranges too slowly under these conditions.¹¹

Carboxylic Acid Solvents. Solvolyses of bromohydrin in three nearly anhydrous carboxylic acid solvents show more solvent influence than do the reactions in the aqueous solvents. Even so, the general pattern of the aqueous solvolyses is followed except that the relative proportions of 1,4-diol (**12t**) to other transannular products (**8–11**) are reversed. Substantial but differing proportions of carbonyl compounds are found in the product mixtures.

High proportions of 1,4-diol in carboxylic acid solvents have also been reported for cyclooctene oxide solvolyses.⁶ Since either **15** or **17** is a reasonable precursor for all the transannular products **8**, **9**, **10**, and **12t**, it is unexpected that the less nucleophilic carboxylic acid solvents favor **12t** more than do the more nucleophilic aqueous solvents. In view of the great number of studies of effects of solvent change on rates of solvolyses of various compounds, we are surprised by the paucity of data which reveal effects of solvent change on composition of product mixtures from solvolyses. Data particularly pertinent to the present considerations, namely, change from aqueous to carboxylic acid solvents, are not readily available, but two studies may be cited. Solvolysis of *t*-butyl chloride in aqueous methanol is reported to yield, along with substitution products, small proportions of olefin which increase slightly with decreasing water content in the mixed solvent.²¹ In solvents containing substantial amounts of bases (CaCO₃ in aqueous acetone, RCO₂Na in acetic and formic acid), 4-*t*-butylcyclohexyl tosylate undergoes solvolysis to yield product mixtures containing slightly increasing amounts of olefin with change from aqueous acetone to acetic acid to formic acid.²² In both these cases, which show the trend opposite to our data, the shift from substitution to elimination product in the solvolyses is most probably determined mainly or wholly by the relative nucleophilicities of the solvents used. Abstraction of proton (to give olefin) will be a function of basicity, which is

(21) F. Spieth, W. C. Ruebsamen, and A. R. Olson, *ibid.*, **76**, 6253 (1954).

(22) S. Winstein and J. J. Holness, *ibid.*, **77**, 5562 (1955).

about the same in the solvents compared in each study. In our solutions however, with substantial differences in basicity of solvent molecules and with no other good base present, the alternate fates of **15** or **17** once formed will depend on both the relative nucleophilicities and relative basicities of the solvents. Water is a better nucleophile than carboxylic acid, but it is also a far better base. The competing roles of solvent molecules (combination with cation and abstraction of proton) then can account for the relative proportions of diol and enol products in these different solvent systems.

The major difference among the carboxylic acid solvents themselves, a difference more salient to our considerations of solvolysis mechanisms, lies in the relative abundance of carbonyl and transannular products formed during reaction. The highest proportion of **3-5** is obtained in acetic acid, the lowest in formic acid. These relative proportions support our inference of duality of mechanism in these halohydrin solvolyses, but do not point to a clean choice between mechanism descriptions I and II. For description I, the competitive pathways involve a carbonium ion (**14**) and a hydrogen-bridged, neutral species (**16**). As the ionizing power^{23a} of the solvent increases, the carbonium ion forming pathway is augmented at the expense of the carbonyl-forming one. For description II, the competition is between cationic intermediate formation with and without transannular hydrogen participation. For solvolysis of 1-phenyl-2-propyl tosylate, to which has been attributed competition between neighboring phenyl participation and more conventional carbonium ion formation, change of solvent from ethanol to acetic acid to formic acid was found to favor phenyl participation.^{24a} Similarly, a shift to more limiting conditions (metal ion catalysis) favored phenyl-assisted solvolysis over unassisted processes with 1,1,2-triphenyl-2-bromoethanol.^{24b} The same kind of shift, toward bridged ions at the expense of unbridged ones, can be read into the small solvent effects observed here. Although these effects do not firmly support the choice of mechanism indicated by the kinetic data (namely, I), they do permit that choice.

Some reports have indicated an unusually strong promotion of ionic reactions by trifluoroacetic acid solvent. For example, solvolysis of *cis*-cyclooctene oxide with trifluoroacetic acid gives transannular products more extensively than with acetic or formic acid.^{6c,7} Contrasting with these reports, our data place trifluoroacetic acid in between acetic and formic acid in promoting ion-forming reactions in competition with concerted ones and suggest strongly that the epoxide reactions are best accounted for by differences in nucleophilicity of trifluoroacetic and formic acid solvents. As we have already pointed out, the bulk of 1,2-diol formed from cyclooctene oxide most likely comes from an S_N2 type reaction between solvent and epoxide and not from an intermediate 2-hydroxycyclooctyl cation. Formic acid, weakly nucleophilic though

(23) (a) *Y* values for 50% acetic acid, 100% acetic acid, and 100% formic acid are +1.9, -1.4, and +2.1, respectively.^{23b} A *Y* value for trifluoroacetic acid was not found, but *Y* for heptafluorobutyric acid is estimated^{23b} to be +1.7. (b) A. H. Fainberg and S. Winstein, *J. Am. Chem. Soc.*, **78**, 2770 (1956).

(24) (a) S. Winstein, M. Brown, K. C. Schreiber, and A. H. Schlesinger, *ibid.*, **74**, 1140 (1952); (b) J. F. Lane and D. R. Walters, *ibid.*, **73**, 4234, 4238 (1951).

it may be, is a better nucleophile and will react more by displacement on epoxide than trifluoroacetic acid. We believe that the relative proportions of 1,2-diol and transannular products from epoxide solvolysis with these two solvents are poor measures of the relative ionizing power of the solvents. The cautionary note²⁵ about claiming maximum ionizing power for trifluoroacetic acid is supported by our data.

Epoxide Rearrangements. Rearrangements of cyclooctene oxides in carboxylic acid solvents have been investigated elegantly by Cope and co-workers.⁶ In order that we might compare more directly rearrangements of epoxide and 2-substituted cyclooctanols, however, rearrangement of *cis*-cyclooctene oxide was re-examined under the aqueous conditions chosen for the other studies.^{4,5,7}

Some uncertainty figures in the comparison. We can only presume that the preferred conformation of a leaving group is one which will lead to relief of intramolecular strain; we are further uncertain about the preferred conformation of the *ring*¹³ for reaction and what changes (if any) in that conformation occur during cation formation. Models alone leave us unconvinced whether *trans*-amino alcohol and *trans*-halohydrin should be compared more appropriately with *cis*- or with *trans*-epoxide, but reaction products clearly favor *cis*-epoxide. Although the 1,4-diols obtained from *trans*-halohydrin and *cis*-epoxide, respectively, are geometrical isomers, the other components of the two reaction mixtures are quite similar and are unlike those obtained from formolysis of *trans*-epoxide.^{6b} We therefore used the far more accessible *cis*-cyclooctene oxide.

Just as was found in carboxylic acid solvents,⁶ transannular rearrangements dominate the reactions of *cis*-cyclooctene oxide in the mixed aqueous solvents, and cyclooctanone is a minor component in the product mixtures (Table III).²⁶ In addition to the relative importance of carbonyl products from the two reactions, these halohydrin and epoxide solvolyses are distinguished from each other by the relative proportions of different transannular products: from epoxide, large amounts of 1,4-diol **12** and small amounts of bicyclic ethers **10** and **11** are obtained, while from halohydrin the opposite is true. This difference, together with the opposite stereoselectivity in 1,4-diol formation, indicates that the interpretation of these reactions in terms of rather simple carbonium ions suffers some inadequacy.

Added silver nitrate or sodium nitrate does not affect significantly the product distribution from epoxide in 50% acetic acid solution. A change in proportions of isomeric cyclooctenols **8** and **9** in going from acidified aqueous THF or 50% acetic acid to 90% formic acid and a slight decrease in proportions of glycols **6** and **12c** with change to less nucleophilic solvent occur, but the general patterns of product distribution for the three solvents are notably similar. A higher proportion of *trans*-1,2-diol (**6**) is formed in each of these solvents than in nearly anhydrous carboxylic acid solvents.^{6,7} As we have already pointed

(25) P. E. Peterson, *ibid.*, **82**, 5834 (1960).

(26) Our data for rearrangement of *cis*-cyclooctene oxide in nearly anhydrous formic acid and trifluoroacetic acid essentially reproduce those published earlier,^{6c} except for the estimation of larger proportions of cyclooctanone and 1,2-diol in our mixtures.

out, we believe this result stems from a competition between direct displacement (on epoxide by solvent) and formation (and subsequent rearrangement) of 2-hydroxycyclooctyl cations. Better competition by the displacement path is expected with the more nucleophilic water present than with the less nucleophilic carboxylic solvents alone.

The product distribution in 1 *M* sulfuric acid solution is like that found for rearrangement of **6** in the same solvent.⁴ The shift of product distribution from **8** and **9** to **3**, **10**, **11**, and **13** simply reflects the reactions of **8** and **9** in sulfuric acid,⁴ secondary effects not germane to the rearrangement of the epoxide.

These results clearly show that the major course of acid-catalyzed reaction of the epoxide is not particularly solvent dependent. Some S_N2-type displacement by solvent does occur, to extents affected by the relative nucleophilicity of the solvent, but the main reaction is transannular rearrangement, with solvent playing a minor role in shifting exact product proportions. Except in hot, strongly acidic solutions favoring secondary reactions, cyclooctanone is formed in hardly more than detectable amounts from the epoxide, and cycloheptanecarboxaldehyde was not even detected in any of the epoxide or glycol rearrangements. The appearance then of both of these carbonyl products in substantial amounts among the products from amino alcohol deamination⁵ and halohydrin solvolysis must necessarily denote a change in mechanism of rearrangement.

We are continuing our study of rearrangements of 2-substituted cycloalkanol.

Experimental

Gas chromatographic (g.c.) analyses were carried out with a Barber Colman Model 20 instrument equipped with a hydrogen-flame detector and a 100-ft. capillary column coated either with GE-96 silicone or poly(propylene glycol). An Aerograph Autoprep Model A-700 instrument equipped with a 3/8 in. × 10 ft. Carbowax 20-M column or a 3/8 in. × 20 ft. SE-30 silicone column was used for preparative gas chromatography (g.c.). Capillary melting points were obtained with a Thomas-Hoover apparatus and are uncorrected. Infrared spectra were obtained mainly with a Beckman IR-5 spectrophotometer. Microanalyses were performed in these laboratories by Mr. R. Seab.

trans-2-Halocyclooctanols. Anhydrous hydrogen halide was passed slowly into an ice-chilled solution of *cis*-cyclooctene oxide⁵ (0.1 mole) in carbon tetrachloride (100 ml.) until the solution was obviously saturated.²⁷ The solution was then washed with water, sodium bicarbonate solution, and water, dried over magnesium sulfate, and distilled. G.c. analyses indicated minimum purity of 98 and 99% for chloro- and bromohydrin, respectively.

trans-2-Chlorocyclooctanol²⁸ was obtained in 85% yield, b.p. 61° (0.06 mm.). *Anal.* Calcd. for C₈H₁₅ClO: C, 59.1; H, 9.29. Found: C, 58.8; H, 9.45. The

chlorohydrin was converted to solid ester derivatives²⁹: benzoate, m.p. 60–61° (lit.³⁰ m.p. 61°); 3,5-dinitrobenzoate, m.p. 96–97° (*Anal.* Calcd. for C₁₅H₁₇ClN₂O₆: C, 50.5; H, 4.81. Found: C, 50.6; H, 4.84); and *p*-nitrobenzoate, m.p. 86–87° (*Anal.* Calcd. for C₁₅H₁₈ClNO₄: C, 57.8; H, 5.82. Found: C, 57.6; H, 6.15).

trans-2-Bromocyclooctanol²⁷ was obtained in 91% yield, b.p. 75–76° (0.2 mm.). *Anal.* Calcd. for C₈H₁₅BrO: C, 46.4; H, 7.31. Found: C, 46.4; H, 7.30. The 3,5-dinitrobenzoate derivative had m.p. 94–96° (lit.²⁷ m.p. 95–96°).

Each of the halohydrins was readily converted to *cis*-cyclooctene oxide in high yield by treatment with aqueous sodium hydroxide (5–10%) at 38° for 5–8 hr.

Solvolyses of Halohydrins. Solvolyses of the halohydrins were carried out under a variety of conditions: refluxing (66°) aqueous THF (2 THF–1 HOH, v./v.), both with and without added silver nitrate; 50% aqueous acetic acid (v./v.), with added silver nitrate (66° and ice-chilled) or sodium acetate (66°); 1 *M* sulfuric acid at 100°, with silver nitrate; and nearly anhydrous acetic, trifluoroacetic, and formic acid solvents (10, 0, and 0°, respectively), with added silver carboxylate. The solutions were approximately 0.1 *M* in halohydrin, 0.12 *M* in silver salt, and 0.2 *M* in sodium acetate. A nitrogen atmosphere was used. Reaction times were varied to reflect the different apparent rates of reaction; g.c. analysis was used with the slow reactions to determine extent of reaction.

Each reaction mixture was diluted with water, filtered to remove silver halide if necessary, saponified if carboxylic acid solvent had been used, and extracted several times with ethyl ether or petroleum ether (b.p. 60–70°). The extract solution was washed with water and dried over magnesium sulfate. After removal of solvent by rotary evaporation, the residue was weighed and analyzed by g.c. A portion of the residue was treated in pyridine solution to convert alcohol components to their trimethylsilyl ether derivatives,³¹ which were satisfactorily resolved by g.c.⁵ By comparison with authentic samples^{4,5} and mixtures, identities and yields of components were established. Some components were separated by preparative g.c. for spectroscopic examination and preparation of solid derivatives. *trans*-1,4-Diol, identified by melting point (90–91°, lit.^{6a} m.p. 90–91°) and preparation of derivatives (bis-*p*-nitrobenzoate m.p. 154–155°, lit.^{6a} m.p. 156.2–156.7°, and bisphenylurethan m.p. 179–179.5°, lit.^{6a} m.p. 180.2–181.7°), was isolated directly from some of the nonaqueous solvolysis mixtures. (Mixture melting points with *cis*-1,4-diol, from epoxide solvolysis, and its derivatives, were strongly depressed.) Unlike the case with the isomeric 1,2-diols,⁵ neither the isomeric 1,4-diols nor their trimethylsilyl ether derivatives are resolved on our g.c. column. No evidence for *cis*-1,4-diol from these halohydrins was obtained. The yield of 1,2-diol was determined by titration of a portion of the original residue with

(27) A. C. Cope and H. E. Johnson, *J. Am. Chem. Soc.*, **79**, 3889 (1957).

(28) M. Godchot, M. Mousseron, and R. Granger, *Compt. rend.*, **200**, 748 (1935); M. Mousseron, R. Granger, F. Winternitz, and G. Combes, *Bull. soc. chim. France*, **13**, 610 (1946).

(29) J. H. Brewster and C. J. Ciotti, Jr., *J. Am. Chem. Soc.*, **77**, 6214 (1955).

(30) W. Reppe and O. Schlichting, German Patent 923,185 (1958); *Chem. Abstr.*, **52**, 4685g (1958).

(31) C. C. Sweeley, R. Bentley, M. Makita, and W. W. Wells, *J. Am. Chem. Soc.*, **85**, 2497 (1963).

periodic acid,³² and this yield was used with relative g.c. responses to estimate the yield of 1,4-diol. The product composition data are summarized in Tables I and II. The average of the total yields of identified products in each solvolysis is 89%, the median being 91%. The lowest total yield (79%) was from chlorohydrin without silver nitrate, and the highest (96%) was from chlorohydrin with silver nitrate.

When 2- and 3-cyclooctenol were subjected separately to the aqueous solvolysis conditions (75 ml. of THF-HOH solvent, 10 mmoles of cyclooctenol, 2 mmoles of AgNO₃, 10 mmoles of AgCl, and 10 mmoles of HNO₃; reflux for 4 hr.), each was recovered unchanged in about 95% yield. Other solvolysis products were not detected by g.c.

Kinetic Data. The rates of solvolysis of bromocyclooctane and *trans*-2-bromocyclooctanol in refluxing aqueous THF (2 THF-1 HOH, v./v.) were followed titrimetrically. Dilute solutions (approximately 0.01 *M*) were prepared by adding the required amount of bromide to refluxing solvent. Aliquots (5 ml.) were withdrawn periodically (1-2-hr. intervals) through a septum seal with a hypodermic syringe, and the product acid was titrated with 0.0025 *M* sodium hydroxide. Treated in a pseudo-first-order fashion (ln concentration vs. time), the data gave good linear plots from which rate constants were calculated. For bromocyclooctane,

(32) S. Siggia, "Quantitative Organic Analysis via Functional Groups," 3rd Ed., John Wiley and Sons, Inc., New York, N. Y., 1963, p. 39.

$k = 0.0570 \pm 0.0002 \text{ hr.}^{-1}$ and for *trans*-2-bromocyclooctanol, $k = 0.0466 \pm 0.0016 \text{ hr.}^{-1}$.

Rearrangements of *cis*-Cyclooctene Oxide. Solutions of *cis*-cyclooctene oxide in mixed aqueous and in 97-100% formic acid solvents were heated until the epoxide was all rearranged, and a solution in trifluoroacetic acid was stirred at 0° for 3 hr. Periodic g.c. analysis was used to follow disappearance of epoxide. One solution (50% acetic acid) contained silver nitrate and another sodium nitrate to permit evaluation of the effect of salts on epoxide solvolysis. The solutions were extracted with ethyl ether after appropriate dilution with water or saponification. Each extract was dried, the solvent was removed by rotary evaporation, and the product mixture was analyzed as were the mixtures from halohydrin solvolyses. *cis*-1,4-Diol, identified by melting point (84-84.5°, lit.^{6a} m.p. 85-86.5°) and derivatives (bis-*p*-nitrobenzoate, m.p. 156.5-157.5°, lit.^{6a} m.p. 161.5-162.7°, and bisphenylurethan, m.p. 182-183°, lit.^{6a} m.p. 186.0-186.7°), was isolated directly from some of the mixtures; no evidence for *trans*-1,4-diol was obtained. Total yields of identified products averaged about 85%. Product distribution data are summarized in Table III.

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Rates of Reaction of 4-Substituted Bicyclo[2.2.2]octylmethyl Tosylates with Sodium Thiophenolate. The Role of Polar Effects in the Displacement Reaction¹

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Contribution from the George Herbert Jones Laboratory of the University of Chicago, Chicago 37, Illinois. Received January 30, 1965

The reaction of sodium thiophenolate with 4-substituted 1-bicyclo[2.2.2]octylmethyl tosylates is second order and yields unrearranged phenyl thioethers. Relative rate data for the reaction in ethanol at 75° indicate that electron-withdrawing substituents accelerate this reaction. The influence of saturated dipolar substituents on the energy requirements for SN2 reactions is discussed.

Introduction

The influence of structure on the rate of SN2 reactions has received considerable attention and excellent discussions of the work in this area are available.³⁻⁸

(1) Chemistry of the bicyclo[2.2.2]octanes, part IV. This research was supported by Grants G14211 and G25190 from the National Science Foundation.

(2) Esso Educational Foundation Fellow, 1961-1962; Union Carbide Corporation Fellow, 1962-1963.

(3) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, pp. 316-338.

However, the role of saturated, dipolar substituents in these reactions remains uncertain. The interpretation of the available data is difficult because conflicting steric and resonance effects introduce serious ambiguities. Thus, saturated β-substituents slow the displacement reactions of aliphatic molecules. The major importance of steric effects is recognized, but opinions differ concerning the polar effect.³⁻⁹ Steric effects are

(4) A. Streitwieser, "Solvolytic Displacement Reactions," McGraw-Hill Book Co., Inc., New York, N. Y., 1962.

(5) J. Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, pp. 169-178.

(6) C. A. Bunton, "Nucleophilic Substitution at Saturated Carbon," Elsevier Publishing Co., New York, N. Y., 1963, Chapter 2.

(7) F. G. Bordwell and W. T. Brannen, *J. Am. Chem. Soc.*, **86**, 4645 (1964).

(8) E. R. Thornton, "Solvolysis Mechanism," The Ronald Press, New York, N. Y., 1964.

(9) (a) C. K. Ingold, *Quart. Rev. (London)*, **11**, 1 (1957); (b) J. Hine and W. H. Brader, *J. Am. Chem. Soc.*, **75**, 3964 (1953); (c) J. Hine and R. G. Ghirardelli, *J. Org. Chem.*, **23**, 1550 (1958); (d) E. T. McBee, R. D. Battershell, and H. F. Braendlin, *J. Am. Chem. Soc.*, **84**, 3157 (1962).