

Data for a typical run, no. 4, are given in Table III. The rapid drop in pressure during the first five minutes is attributed to the solution of ethylene in the reaction mixture. The vapor pressure of benzene at 9.2° was calculated to be 43.4 mm.¹⁰; this value was subtracted from the total pressure read. The amount of ethylene dissolved in the benzene could be calculated by assuming that Henry's law applies throughout the reaction. After the ethylene had been recycled for 5 minutes, the pressure drop was slow and steady. The pressure readings could then be extrapolated back to zero time in order to give the pressure which would have been read if the ethylene had not been in solution. The difference in the actual value and the extrapolated value would give the correction for the solubility of ethylene in the reaction mixture. Since this correction would be a constant fraction of the ethylene in a given reaction, it was not used in calculating the reaction rate constants.

(10) T. E. Jordan, "Vapor Pressure of Organic Compounds," Interscience Publishers, Inc., New York, N. Y., 1954, p. 6.

When the logarithm of the pressure of the remaining ethylene is plotted against time, curves as shown in Fig. 1, for four runs are obtained. The slope of the initial part of each curve gives the value for the first-order reaction rate constant listed in Table I.

Radiocarbon Assay Method.—The ethylene-C¹⁴ was counted directly as the gas in an ionization chamber on an Applied Physics Corporation, model 30, vibrating reed electrometer. The apparatus used to prepare the samples for counting was one described by Wilzbach and Sykes¹¹ for assay of carbon-14 samples. The method was shown to give results that varied linearly over the small range of activities expected by making a series of dilutions of ethylene-C¹⁴. Benzene and ethylbenzene were separated by condensation at -100° and 1 micron pressure; the amount of ethylene was determined in a constant-volume manometer. The assay was precise and accurate to ±1.0%.

(11) K. E. Wilzbach and W. Y. Sykes, *Science*, **120**, 484 (1954).
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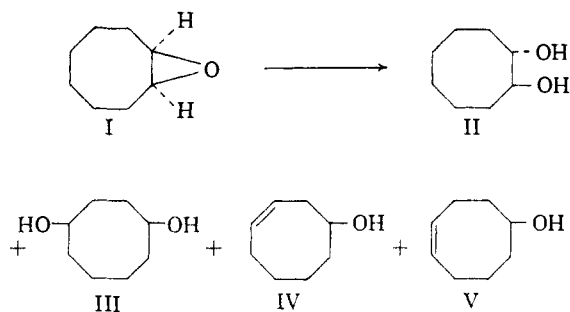
Proximity Effects. XVI. Solvolysis of *cis*-Cyclooctene Oxide with Various Acids^{1,2}

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The extent to which transannular reactions occur on solvolysis of *cis*-cyclooctene oxide with several acids has been determined. With trifluoroacetic acid, products of transannular reactions are formed exclusively; *i.e.*, *cis*-1,4-cyclooctanediol and 3- and 4-cycloocten-1-ol. With acetic acid containing sodium acetate, the product contains 76% of the normal *trans*-1,2-cyclooctanediol and 24% of compounds formed by transannular reactions. Trichloroacetic acid, formic acid and acetic acid form mixtures of products formed by transannular reactions and normal solvolysis lying between these extremes, as shown in Table I.

The solvolysis of *cis*-cyclooctene oxide (I) with formic acid forms *trans*-1,2-cyclooctanediol (II), *cis*-1,4-cyclooctanediol (III) and 3- and 4-cycloocten-1-ol (IV, V).⁴ While II represents the normal solvolysis product of an epoxide, com-



pounds III, IV and V are formed by a "transannular reaction"⁵ involving a shift of a hydrogen atom located in close spatial proximity to the epoxide function across the ring. Such hydrogen atoms are activated by a "proximity effect."^{4a,6}

In the present work, the solvolysis of *cis*-cyclooctene oxide in trifluoroacetic acid, trichloroacetic acid, formic acid, acetic acid, acetic acid containing

sodium acetate and trimethylacetic acid was investigated. The solvolyses were conducted by adding the oxide I to a tenfold molar excess of acid at a constant temperature. After completion of the reactions, the mixtures were neutralized and the esters formed were saponified with cold aqueous sodium hydroxide. The products were then examined by gas chromatography either before or after separation into two fractions by chromatography on alumina, one containing the glycols II and III and the other the unsaturated alcohols IV and V and several secondary products present in small amounts. The products were identified by gas chromatography, physical properties (including infrared spectra) and the preparation of crystalline derivatives, as described in the Experimental section and in Table II. The glycols II and III were separated by converting *trans*-1,2-cyclooctanediol into the isopropylidene ketal, followed by chromatography on alumina.⁷ In each solvolysis gas chromatography was used to detect any *trans*-1,2-cyclooctanediol in the 1,4-glycol fraction, and in cases in which 1,2-glycol was present due to incomplete formation of the isopropylidene ketal, the ketalization procedure was repeated on the mother liquor from crystallization of III.

The allylic alcohol 2-cycloocten-1-ol was shown by gas chromatography to be absent or present in small amounts in all of the solvolysis products. Secondary rearrangement products (Table II) were formed in the presence of the stronger acids, particularly trifluoroacetic acid, but their formation could be minimized by use of low reaction

(1) Supported in part by a research grant (NSF-G5505) of the National Science Foundation.

(2) Paper XV, A. C. Cope and M. Brown, *THIS JOURNAL*, **80**, 2859 (1958).

(3) National Institutes of Health Postdoctoral Fellow, 1956-1958.

(4) (a) A. C. Cope, S. W. Fenton and C. F. Spencer, *THIS JOURNAL*, **74**, 5884 (1952); (b) A. C. Cope, A. H. Keough, P. E. Peterson, H. E. Simmons and G. W. Wood, *ibid.*, **79**, 3900 (1957).

(5) V. Prelog and K. Schenker, *Helv. Chim. Acta*, **35**, 2044 (1952).

(6) A. C. Cope, R. J. Cotter and G. G. Roller, *THIS JOURNAL*, **77**, 3590 (1955), and later papers in this series.

(7) A. C. Cope and G. W. Wood, *ibid.*, **79**, 3885 (1957).

temperatures. The glycols II and III were shown to be stable under the reaction conditions employed.

The results are summarized in Table I. The solvolysis of *cis*-cyclooctene oxide with trifluoroacetic acid formed exclusively products from transannular reactions (III-V) whereas the product from acetic acid containing sodium acetate contained 76% of the normal product II and only 24% of transannular reaction products. The other acids gave product compositions lying between these two extremes. The glycols were formed stereospecifically and the material balances in the reactions were 80-90%. The reactivities of the acids varied in the following way. *cis*-Cyclooctene oxide was not solvolyzed by trimethylacetic acid at 170°; it was solvolyzed by acetic acid at 120° but not at 60°; it was solvolyzed by formic acid at 60° and 120° but not at 0°; it was solvolyzed by trifluoroacetic acid even at 0°.

TABLE I
SOLVOLYSIS OF *cis*-CYCLOOCTENE OXIDE WITH VARIOUS ACIDS^a

Acid used (undiluted)	Normal reaction, %	Transannular reaction, %
CF ₃ CO ₂ H	0	100
CCl ₃ CO ₂ H	6	94
HCO ₂ H	13	87
CH ₃ CO ₂ H	46	54
CH ₃ CO ₂ H, CH ₃ CO ₂ Na	76	24
(CH ₃) ₃ CCO ₂ H	No reaction	

^a See Table II for details.

The formation of products from transannular reactions can be correlated with the strength of the acids as expressed by their dissociation constants in water (although the solvolyses described in this paper were conducted in undiluted acids).⁸ No obvious correlation appears to exist between the amount of products formed by transannular reactions and the size of the nucleophile⁹ or the dielectric constant of the medium.¹⁰

The transannular reactions can proceed by path a, b or c as shown in Fig. 1. Path a represents an entirely concerted mechanism, while b represents an S_N1 mechanism in which a non-classical ion is formed in the slow step. V. Prelog and S. Borčić showed that acetolysis of cyclodecyl tosylate (that is known to involve a transannular hydride shift)¹¹ proceeds at the same rate as acetolysis of the compound in which the hydrogen that

(8) Dissociation constants in water: trifluoroacetic acid: 5.9×10^{-1} ; A. L. Henne and C. J. Fox, *THIS JOURNAL*, **73**, 2323 (1951), or 18×10^{-1} ; G. C. Hood, O. Redlich and C. A. Reilly, *J. Chem. Phys.*, **23**, 2229 (1955); trichloroacetic acid: 2×10^{-1} ; formic acid: 1.8×10^{-4} ; "Handbook of Chemistry and Physics," Chemical Rubber Publishing Co., Cleveland, Ohio, 1957-1958, p. 1644; trimethylacetic acid: 0.9×10^{-4} ; D. H. Everett, D. A. Landsman and B. R. W. Piusent, *Proc. Roy. Soc., (London)*, **A215**, 403 (1952).

(9) Size of the unsolvated nucleophiles: trimethylacetic acid > trichloroacetic acid > trifluoroacetic acid > acetic acid > formic acid.

(10) Dielectric constants: formic acid: 57.9 (20°), acetic acid: 6.15 (20°); J. Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1956, p. 43; trifluoroacetic acid: 8.42 (20°); W. Dannhauser and R. H. Cole, *THIS JOURNAL*, **74**, 6105 (1952); trichloroacetic acid: 4.5 (60°); P. Walden, *Z. physik. Chem.*, **70**, 569 (1910).

(11) (a) H. J. Urech and V. Prelog, *Helv. Chim. Acta*, **40**, 477 (1957); (b) V. Prelog and S. Borčić, *ibid.*, **41**, 199 (1958).

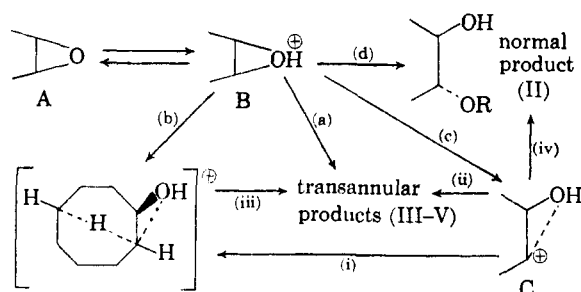


Fig. 1.—Possible reaction paths for solvolysis of *cis*-cyclooctene oxide.

shifts is replaced by deuterium.¹² Accordingly, our results are interpreted in terms of a mechanism (path c) in which no hydride shift occurs in the slow step, although the mechanism of solvolysis of the oxide I does not necessarily parallel the mechanism of acetolysis of cyclodecyl tosylate. The "classical" carbonium ion C must preserve some tetrahedral configuration by partial bonding to the adjacent hydroxyl group as shown, to account for the stereospecific formation of the *cis*-

TABLE II
PERCENTAGE YIELDS OF PRODUCTS OF SOLVOLYSIS OF *cis*-CYCLOOCTENE OXIDE WITH VARIOUS ACIDS

Acid	Normal product, <i>trans</i> -1,2-cyclooctane-diol	Products of transannular reactions			Other products ^a	Total yield
		<i>cis</i> -1,4-cyclooctane-diol	3- and 4-cycloocten-1-ols			
Trifluoroacetic acid ^b	0 ^c	45	34 ^d	1	80	
Trichloroacetic acid	5	37	28 ^e	8 ^f	78	
Formic acid	12	48	30 ^e	..	90	
Acetic acid	41	21	26 ^e	2	90	
Acetic acid containing sodium acetate	71	9	10 ^e	3	93	

^a The secondary products described in ref. 4b and others being investigated currently. ^b Products formed in 3 hours at 0-5°; the composition was very sensitive to the reaction temperature. ^c Less than 1%. ^d Composition of this mixture was 90% of 3-cycloocten-1-ol, 10% of 4-cycloocten-1-ol; less than 3% of 2-cycloocten-1-ol. ^e Composition of this mixture was 75% of 3-cycloocten-1-ol, 25% of 4-cycloocten-1-ol; less than 3% of 2-cycloocten-1-ol. ^f Contains a small amount of cyclooctanone. ^g The ratio of 3-cycloocten-1-ol to 4-cycloocten-1-ol in this mixture was 3/1. Gas chromatography showed a peak corresponding in retention time to 2-cycloocten-1-ol, which if present amounted to less than 15% of the fraction.

glycol III. Formation of C can be followed by fast steps ii or i (followed by iii) leading to products of transannular reactions, or iv leading to the normal glycol II. Another path to II is normal displacement (d). In either case the intermediate is diverted to the normal product II in the more nucleophilic medium. In the first case, two *fast* steps, ii and iv, are competing and the nucleophilic contribution of the migrating hydrogen becomes more important in the less nucleophilic medium in analogy to medium effects in neighboring group participation of carbon and hydrogen.^{12a} In the second case, two *slow* steps, c and d, are

(12) V. Prelog, *Experientia*, Suppl. No. 7 (1957); *Angew. Chem.*, **70**, 145 (1958); English translation in *Record Chem. Progr. (Kresge-Hooker Sci. Lib.)*, **18**, 247 (1957).

(12a) A. Streitwieser, Jr., *Chem. Revs.*, **56**, 571 (1956), and references given there.

competing, one of SN1 character, the other of SN2 character. The fact that transannular reaction is favored by SN1 conditions is in agreement with other experiments cited in earlier papers in this series and by Prelog.

Experimental¹³

Solvolytic with Formic Acid.—A solution of 2.00 g. of *cis*-cyclooctene oxide in 2 ml. of ether was added dropwise through a capillary with stirring to 7.32 g. of 98–100% formic acid at 60°. The oxide was rinsed into the solution with two 2-ml. portions of ether, and the mixture was heated at 60° for 3 hours. Sodium hydroxide (30 g.) in 100 ml. of water was added with cooling in ice, and the mixture was shaken overnight to saponify esters. The products were extracted continuously with methylene chloride for 22 hours, and the extract was dried over magnesium sulfate. Concentration under reduced pressure left a residue of 2.192 g., which was dissolved in a small amount of methylene chloride and placed on a chromatographic column containing 100 g. of activity II alumina (Merck, acid-washed) suspended in petroleum ether. Elution with 50% ether in petroleum ether gave fraction 1, 0.609 g. The infrared spectrum of this fraction showed that it contained approximately 75% of 3-cycloöcten-1-ol and 25% of 4-cycloöcten-1-ol, while gas chromatography on a column at 165° containing tetrahydroxyethylenediamine showed that less than 3% of 2-cycloöcten-1-ol was present. Fraction 2, 1.360 g., was eluted from the alumina with 10% methanol in ether, and shown by gas chromatography on Silicone oil at 205° to contain 20% of *trans*-1,2-cycloöctanediol and 80% of *cis*-1,4-cycloöctanediol. This fraction was shaken overnight with 50 ml. of dry acetone and 5 g. of anhydrous copper sulfate. After filtration and concentration, chromatography on 60 g. of alumina separated 0.224 g. of *trans*-1,2-cycloöctanediol isopropylidene ketal,⁷ identified by its infrared spectrum, and 0.776 g. of *cis*-1,4-cycloöctanediol, m.p. after recrystallization from ethyl acetate, 83.2–84.0° (mixed m.p. with an authentic sample showed no depression).

An attempted solvolysis under conditions similar to those described above but with a reaction temperature of 0–5° resulted in no reaction and the *cis*-cycloöctene oxide was recovered.

In an inverse addition procedure, in which formic acid was added to *cis*-cycloöctene oxide at room temperature and the solution was heated at 60° for 3 hours, the same products were isolated in practically the same yield as with the other order of addition (described above).

Solvolytic with Acetic Acid.—A solution of 2.00 g. of *cis*-cycloöctene oxide in 6 ml. of ether was added to a solution of 2.94 g. of anhydrous sodium acetate in 25 ml. of glacial acetic acid and the mixture was heated to 60° for 22 hours and then refluxed for 74 hours. The products listed in Table II were isolated as described for the formic acid solvolysis, except that the residue after concentrating the extract was treated with acetone and copper sulfate to convert the 1,2-glycol to isopropylidene ketal prior to chromatography on alumina. Two such treatments were required to convert all of the glycol to ketal. The products were identified as described above.

This procedure is a convenient one for the preparation of *trans*-1,2-cycloöctanediol, which in a reaction conducted on a larger scale (25.2 g. of the oxide) was obtained in 60% yield.

cis-Cycloöctene oxide (2.00 g.) also was treated with 9.6 g. of glacial acetic acid at the reflux temperature for 20 hours in the absence of added sodium acetate. The products were isolated as described for the solvolysis with acetic acid containing sodium acetate. The crude product (2.33 g.) was separated into three fractions by chromatography on 100 g. of activity II alumina, and the fractions were analyzed and the components identified as previously described.

Solvolytic with Trifluoroacetic Acid.—Trifluoroacetic acid (18.1 g.) was cooled to 0° with stirring and a solution of 2.00 g. of *cis*-cycloöctene oxide in 2 ml. of ether was added through a capillary with stirring during a period of 30 minutes, and rinsed into the solution with two 2-ml. portions of ether. The mixture was stirred at 0–5° for 3 hours. It was made alkaline by adding a solution of 30 g. of sodium hy-

droxide in 100 ml. of water with cooling, and shaken overnight at room temperature to saponify esters. The products were separated by continuous extraction with methylene chloride for 26 hours. The extract was dried over magnesium sulfate and concentrated under reduced pressure, leaving a residue of 1.963 g. Gas chromatography on Silicone oil at 205° showed that this was a mixture of *cis*-1,4-cycloöctanediol (there was no peak corresponding to *trans*-1,2-glycol) and cycloöctenols. The residue was chromatographed on 100 g. of activity II alumina (Merck, acid-washed). Elution with 50% ether in petroleum ether separated fraction 1 (0.707 g., 35%), while 3–10% methanol in ether eluted fraction 2 (1.062 g., 45%). The infrared spectrum of fraction 1 showed that it contained approximately 90% of 3-cycloöcten-1-ol and 10% of 4-cycloöcten-1-ol, and gas chromatography at 165° on a column containing tetrahydroxyethylenediamine showed that less than 3% of 2-cycloöcten-1-ol was present. Crystallization of fraction 2 gave 0.775 g. of *cis*-1,4-cycloöctanediol, m.p. 80.5–82.5°, identified by mixed m.p. The residue from the mother liquor (0.210 g.) was treated with acetone and copper sulfate under conditions that would convert 1,2-glycols to isopropylidene ketals,^{4,7} and the product was chromatographed on 40 g. of activity II alumina. Practically no material (ketal) was eluted with 50% ether in petroleum ether, while 0.187 g. of crude *cis*-1,4-glycol was eluted with 5% methanol in ether.

Solvolytic of *cis*-cycloöctene oxide with refluxing trifluoroacetic acid (72°) under conditions otherwise similar to those described above gave a total yield of products of only 26%, and the remainder was polymerized to high-boiling material.

In an inverse addition procedure, 2.00 g. of *cis*-cycloöctene oxide was heated to 60° and 25 g. of trifluoroacetic acid was added dropwise with stirring. The fractions obtained by chromatography on alumina were analyzed by gas chromatography on the columns specified above. The total yield of product was 73% and its composition in mole per cent. was 20% of II, 24% of III, 16% of a mixture of IV and V, and 13% (calculated as C₈H₁₆O) of five unidentified compounds. The *trans*-1,2-cycloöctanediol (II) was identified as its bisphenylurethan, m.p. 174.5–175.8° (not depressed on admixture with an authentic sample), and by the infrared spectrum of its isopropylidene ketal. When the acid was added in one portion to the oxide at room temperature, followed by heating at 60° for 3 hours, less of the *trans*-1,2-glycol II was formed. It is concluded that the reaction with trifluoroacetic acid is so rapid that the normal product II is formed early in the addition when the medium is largely the relatively non-polar *cis*-cycloöctene oxide.

Solvolytic with Trichloroacetic Acid.—A solution of 2.00 g. of *cis*-cycloöctene oxide in 2 ml. of ether was added dropwise with stirring to 26.0 g. of trichloroacetic acid at 60°, rinsed in with two 2-ml. portions of ether, and the mixture was heated at 60° for 3 hours. The products (Table II) were isolated and identified as in the trifluoroacetic acid solvolysis.

Attempted Solvolysis with Trimethylacetic Acid.—*cis*-Cycloöctene oxide failed to react with trimethylacetic acid at 100° for periods of 2 to 46 hours, under reflux (169°) for 23 hours, or at 135° for 24 hours in the presence of two molar equivalents of water per mole of oxide. In all cases the oxide was recovered.

Stability of Cycloöctanediols to Acids.—*trans*-1,2-Cycloöctanediol (2.00 g.) was refluxed with 25 ml. of glacial acetic acid for 23 hours. The glycol was recovered quantitatively after saponification. *cis*-1,4-Cycloöctanediol (1.00 g.) was stirred with 9.0 g. of trifluoroacetic acid for 3 hours at 0–5°, after which it was recovered practically quantitatively.

Analysis of Mixtures of 2-, 3- and 4-Cycloöcten-1-ols.—Infrared spectra of mixtures of 3- and 4-cycloöcten-1-ol of known composition were determined and used as standards for the analysis of mixtures obtained by solvolysis. The absorption bands of 3-cycloöcten-1-ol at 705 and 760 cm.⁻¹ and of 4-cycloöcten-1-ol at 725 cm.⁻¹ were used in the analyses reported in Table II, which are estimated to be accurate to within ±5%.

A mixture of 2- and 3-cycloöcten-1-ol was shown to be separated by gas chromatography on tetrahydroxyethylenediamine at 160–170°. Mixtures containing 3% of 2-cycloöcten-1-ol showed a distinct shoulder (due to this component) on the principal peak, while mixtures containing 6% gave separate peaks for each component. 3- and 4-cycloöcten-1-ol were not separated by this column.

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(13) Melting points are corrected and boiling points are uncorrected. The columns used for gas chromatography are identified in each instance, and are described in footnote 24 of the following paper.