conditions of the analysis. 4-Methylcyclooctene,[4] which has the same retention time as **10** on TCEP, was eliminated as a possible product when the major component was collected from TCEP and reinjected onto a silver nitrate–tetraethylene glycol column (SNTG) at 76°, conditions known to give marked separation of the 1- and 4-methylcyclooctenes.[4] Only one peak was found, with the retention time of **10**. The olefins **10** (83.4% of the solvolysis mixture) and **11** (9.7% of the solvolysis mixture) were collected (SNTG, 40°) and identified by comparison of their infrared spectra with those of authentic samples. The alcohol fraction was separated into two components on a silicone grease column at 140°. The major component (5.5% of the solvolysis mixture) was identified as **12** and the minor one (0.5% of the solvolysis mixture) as mainly **1b** by comparison of retention times and infrared spectra with those of authentic samples.

Solvolysis of 2b.—Tosylate **2b** (m.p. 42.6–44.0° after two recrystallizations from pentane) was prepared from 222.5 mg. of **1b** and 425 mg. of *p*-toluenesulfonyl chloride in 2 ml. of pyridine in the manner described for the preparation of tosylate **2a**.

Anal. Calcd. for $C_{15}H_{24}O_3S$: C, 64.84; H, 8.16. Found: C, 64.72; H, 8.06.

The tosylate **2b** (280 mg., recrystallized twice from pentane) was solvolyzed immediately in 15 ml. of glacial acetic acid–0.5 *M* sodium acetate for 28 hr. at room temperature, then at 40–45° for 22 hr. The products, obtained in the manner described for the solvolysis of **2a**, weighed 180 mg. and still contained some ether (yield as estimated by gas chromatography on TCEP at 105° was 160 mg.).

The procedure for analysis of the olefin fraction was essentially that described for **2a** except that the major product (**11**, 74.0%) was first collected on SNTG at 52°, then reinjected on TCEP at 50° to show the absence of both 3- and 4-methylcyclooctene,[4] and collected again for infrared analysis. The minor olefin product (8.2%) was collected on SNTG at 52° for infrared analysis. When solvolysis products were analyzed on TCEP (105°) before lithium aluminum hydride reduction five components, two major and three minor, were found, exclusive of olefins. The two major products, identified by comparison of infrared spectra and retention times with those of authentic samples, were *cis*- (10.1%) and *trans*-5-methylcyclooctyl acetate (4.6%). The minor components were 1-methylcyclooctyl acetate[25] (1.2%) and two unidentified materials (1.0% and 0.9%). The solvolysis products were reduced with lithium aluminum hydride as described previously, separated by gas chromatography (TCEP, 116°), and identified by comparison of retention times and infrared spectra with those of authentic samples as **1** (mainly *cis*) and **12**. The 2-methylcyclooctanols[4] were eliminated as possible products because no peak was found at their retention time. A sample of **1** was collected and oxidized with chromium trioxide–pyridine[4,26] to 5-methylcyclooctanone, identified by its retention time (TCEP, 140°) and infrared spectrum (comparison with that of an authentic sample). Quantitative infrared studies showed that 3-methylcyclooctanone could not have been present in the sample to an amount >10%.[27]

Stability to the Solvolysis Conditions. A. Olefin Products.—One part of olefin (**10** and **11** in separate experiments) and one part of *p*-toluenesulfonic acid monohydrate were treated with about 50 parts of acetic acid–0.5 *M* sodium acetate for 24.5 hr. at 25° and 24 hr. at 45° and worked up as for the solvolyses. The olefins were recovered unchanged (identified by their retention times and infrared spectra) in high yields.

B. Acetate Products.—*cis*- and *trans*-5-methylcyclooctyl acetates were each shown to be stable to the solvolysis conditions as described above. 1-Methylcyclooctyl acetate[16] was not completely stable, decomposing to **10** to the extent of *ca.* 30%. (Identifications were made by retention times and infrared spectra.) In a typical run, 17 mg. of 1-methylcyclooctyl acetate was treated with 17 mg. of *p*-toluenesulfonic acid monohydrate and 0.80 ml. of acetic acid–0.5 *M* sodium acetate for 25.5 hr. at 25° followed by 21 hr. at 45°. The product (15 mg.) was shown to contain 30.5% of 1-methylcyclooctene and 69.5% of 1-methylcyclooctyl acetate by infrared and gas chromatographic (TCEP, 110°) analyses.

C. 5-Methylcyclooctanols.—The alcohols **1a** and **1b** were shown to be acetylated to the extent of 9% [infrared and gas chromatographic analyses (TCEP, 140°)] when treated with acetic acid–0.5 *M* sodium acetate for 25.5 hr. at 25° followed by 22 hr. at 45°.

(25) Identified by retention time only; the acetate was somewhat unstable to gas chromatography.

(26) G. I. Poos, G. E. Arth, R. E. Beyler, and C. H. Sarett, *J. Am. Chem. Soc.*, **75**, 422 (1953).

(27) This limits the presence of 3-methylcyclooctanone in the solvolysis products to <2.5%, as the sample of 5-methylcyclooctanone used in this study corresponded to about 25% of the solvolysis mixture.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, CAMBRIDGE 39, MASS.]

Proximity Effects. XXXVI. Solvolyses of Deuterium-Labeled Cyclooctyl Brosylate[1,2]

BY ARTHUR C. COPE AND DAVID M. GALE[3]

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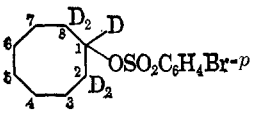
Cyclooctyl brosylate-1,2,2,8,8,-d_5 was solvolyzed in glacial acetic acid–sodium acetate, formic acid–sodium formate, and in trifluoroacetic acid–sodium acetate, and in each case the deuterium distribution in the substitution and elimination products was determined by mass spectrometry. The extents of rearrangement observed were about 53% for the acetolysis, 60% for the formolysis, and >62% for the trifluoroacetolysis. In the first two cases rearrangement proceeded almost exclusively by a transannular 1,5-hydride shift; the extent of 1,3-hydride shift was not appreciable. Conformational and mechanistic implications of the data are discussed.

Solvolysis of deuterium-labeled *cis*-cyclooctene oxide in formic acid has shown that both 1,5- and 1,3-hydride shifts occurred. The 1,5-shift predominated by 61 to 39 in the formation of *cis*-1,4-cyclooctanediol, and by 94 to 6% in the formation of 3-cycloocten-1-ol.[4,5] On the other hand, 1,5-hydride shift took place to the exclusion of 1,3-hydride shift in the acetolysis of 5-methyl- and 5-*t*-butylcyclooctyl tosylates.[6,7] Conformational and electronic effects due to the epoxide ring may be expected to change the nature of the hydride shifts in the case of *cis*-cyclooctene oxide. Likewise, the solvolysis of 5-alkylcyclooctyl tosylates may be influenced by electronic and conformational effects of the alkyl groups.

This paper reports an investigation of the transannular hydride shifts that occur in cyclooctyl brosylate modified only by the deuterium substitution shown in formula **1**.



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(1) Supported in part by a research grant (NSF-G5055) of the National Science Foundation.

(2) Paper XXXV, *J. Am. Chem. Soc.*, **85**, 3743 (1963).

(3) National Institutes of Health Predoctoral Fellow, 1961–1963; National Science Foundation Summer Fellow, 1961.

(4) A. C. Cope, G. A. Berchtold, P. E. Peterson, and S. H. Sharman, *J. Am. Chem. Soc.*, **82**, 6366 (1960).

(5) The possible influence of isotope effects was not considered in arriving at these figures, but would not substantially alter the data. For example, if deuteride should migrate rather than hydride, the maximum probable value for rate decrease is threefold; see C. G. Swain, R. A. Wiles, and R. W. Bader, *J. Am. Chem. Soc.*, **83**, 1945 (1961), and references cited therein. Using this value and assuming equal numbers of deuterium and hydrogen atoms in the 5- and 6-positions with the proper stereochemistry for migration, the corrected percentages of 1,5-hydride shift are 70% for the formation of *cis*-1,4-cyclooctanediol and 96% for the formation of 3-cycloocten-1-ol.

(6) A. C. Cope and D. M. Gale, *J. Am. Chem. Soc.*, **85**, 3743 (1963).

(7) N. L. Allinger and S. Greenberg, *ibid.*, **84**, 2394 (1962).

The acetolysis of cyclodecyl[8] and cyclononyl[9] tosylates has been investigated, employing C^{14}-labeling techniques. Deuterium labeling proved to be a convenient method of detecting various types of hydride migration in the present case. Solvolyses were conducted in three acids, since it has been shown previously that the extent of transannular reactions in the solvolysis of cyclooctene oxide increases with the strength of the acid.[10]

Cyclooctanone-2,2,8,8-d_4 was prepared by five or six successive equilibrations of cyclooctanone in refluxing deuterium oxide containing potassium carbonate. Mass spectrometric analysis of the ketone after five equilibrations showed that it contained 97% d_4-species and 3% d_3-species. The absence of d_5-species in the deuterated cyclooctanone shows that no deuterium was incorporated in positions other than those α to the carbonyl function under the conditions employed. Reduction of the deuterated cyclooctanone with lithium aluminum deuteride in refluxing ether gave cyclooctanol-1,2,2,8,8-d_5 containing 98.6% of the theoretical amount of deuterium, as determined by combustion analysis. A sample of the brosylate of this deuterated alcohol also was reduced with lithium aluminum hydride to cyclooctane, which was analyzed by mass spectrometry and found to contain 95% of d_5-species. The acetolysis of the brosylate **1** gave cyclooctyl acetate (53%) which was separated from *cis*-cyclooctene (47%) by chromatography on alumina and then reduced with lithium aluminum hydride. Conversion of this deuterated cyclooctanol to the tosylate, followed by reduction with lithium aluminum hydride, gave cyclooctane with the same deuterium distribution as cyclooctane obtained from the original brosylate, showing that no deuterium was lost to the solvent during acetolysis.

Oxidation of the cyclooctanol formed on solvolysis with chromic acid in acetone gave partially deuterated cyclooctanone. Equilibration of this cycloöctanone with water and sodium carbonate removed the deuterium present in the α-positions. Use of a large excess of water made it possible to remove the α-deuterium atoms completely in one equilibration. The conditions necessary were determined by equilibration of authenic cyclooctanone-2,2,8,8-d_4. Table I shows the deuterium

TABLE I

DEUTERATED CYCLOOCTANOLS (AND CYCLOOCTANONES DERIVED FROM THEM) FROM POSSIBLE HYDRIDE SHIFTS IN SOLVOLYSIS OF BROSYLATE 1

Shift	Cyclooctanol formed	Cyclooctanone formed by oxidn. of the cyclooctanol—Before equil.	After equil.	*d*-Species in the equil. cyclooctanone
None	1,2,2,8,8-d_5	2,2,8,8-d_4	d_0	d_0
1,2-	1,2,2,3,3-d_5	2,2,3,3-d_4	3,3-d_2	d_2
Direct 1,3-	2,2,3,4,4-d_5	2,2,3,3,4,4-d_5	3,4,4-d_3	d_3
Apparent 1,3-[a]	2,3,3,4,4-d_5	2,3,3,4,4-d_5	3,3,4,4-d_4	d_4
1,4-	3,3,4,5,5-d_5	3,3,4,5,5-d_5	3,3,4,5,5-d_5	d_5
1,5-	4,4,5,6,6-d_5	4,4,5,6,6-d_5	4,4,5,6,6-d_5	d_5

[a] By two successive 1,2-shifts.

content that would be present (before and after equilibration) in the ketone formed from cyclooctanol produced without hydride shift and with various transannular hydride shifts. Any 1,4-hydride shift that occurred would give a product that could not be distinguished by this scheme from the product of 1,5-hydride shift. However, 1,4-shifts have not been observed previously and further results obtained in this study indicate that none takes place here.

Results of mass spectrometric analysis of partially deuterated cyclooctanone samples obtained by oxidation of the cyclooctanols formed by solvolysis of the brosylate **1** in three acids are summarized in Table II.

TABLE II

DEUTERIUM CONTENT OF CYCLOOCTANONE SAMPLES OBTAINED BY OXIDATION OF THE CYCLOOCTANOL ISOLATED FROM SOLVOLYSIS OF THE BROSYLATE 1

Acid used in solvolysis	Deuterated species in cyclooctanone after equilibration, % d_0	d_1	d_2	d_3	d_4	d_5
Acetic	45	0	<1	<1	<2	52
Formic	40	0	<2	<1	<2	56
Trifluoroacetic	30	3	5	7	6	49

The extents of rearrangement for the acetolysis and formolysis were determined simply as 100 minus the percentage of d_0-species in each case, the values being 55 and 60%, respectively. The trifluoroacetolysis was complicated by the facile addition of trifluoroacetic acid to *cis*-cyclooctene.[11] Therefore the data in Table II could not be used to determine extent of rearrangement or types of hydride shifts occurring in trifluoroacetic acid. However an estimation of the minimum extent of rearrangement could be made in the following manner: the increase of d_4-species in the trifluoroacetate from solvolysis as compared to the initial brosylate (determined in both cases by conversion to partially deuterated cyclooctane; see Table VII, Experimental) represented the maximum amount of normal elimination product (8%). Normal elimination (followed by addition of trifluoroacetic acid) would have to result in loss of a deuterium atom to the solvent with the conversion of brosylate-d_5 to trifluoroacetate-d_4. A normal substitution reaction would give trifluoroacetate-d_5 which would be converted to undeuterated cyclooctanone after equilibration (30% d_0-species from Table II). Thus the minimum extent of rearrangement is estimated as $100 - (8 + 30) = 62\%$.

Samples of *cis*-cyclooctene obtained from the acetolysis and the formolysis of brosylate **1** were oxidized with potassium permanganate to suberic acid samples which were esterified with diazomethane. The dimethyl suberate samples were treated with sodium methoxide in methanol to remove the deuterium atoms from the α-positions. A sample of α-deuteriodimethyl suberate was prepared from dimethyl suberate and methanol-O-*d* in the presence of sodium methoxide and was used as a standard to determine the conditions needed for exchange. Table III shows the deuterium distribution expected in dimethyl suberate from *cis*-cyclooctene produced without rearrangement and with various transannular hydride shifts.

Table IV indicates the deuterium content of the dimethyl suberate samples derived from the olefin from the solvolyses, after equilibration.[12] From the infor-

(8) V. Prelog, V. Jünig, and T. Tomljenovic, *Helv. Chim. Acta.*, **45**, 1352 (1962). Data obtained from earlier studies with deuterium labeling are summarized in this reference.

(9) V. Prelog, H. H. Kugi, and E. H. White, *ibid.*, **45**, 1658 (1962).

(10) A. C. Cope, J. M. Grisar, and P. E. Peterson, *J. Am. Chem. Soc.*, **81**, 1640 (1959).

(11) P. E. Peterson and G. Allen, *J. Org. Chem.*, **27**, 1505 (1962). We have verified that complete addition occurs under our solvolysis conditions, and have also shown that addition of formic acid does not take place under the conditions of the formolysis.

(12) Dimethyl suberate does not show a molecular ion peak [R. Ryhage and E. Stenhagen, *Arkiv. Kemi*, **14**, 497 (1959)]. Therefore the peak at $M - 31 = 171$ was used for deuterium analysis. This peak arises from the well-established loss of ·OMe. To establish that no exchange of methyl for methylene hydrogen atoms occurred in the instrument, dimethyl suberate-d_6 was prepared and analyzed by mass spectrometry. It showed the expected peak at m/e 174 due to loss of ·OCD$_3$ and no peaks (except isotopes) at higher mass numbers. The validity of the mass spectrometric method was also demonstrated by the agreement with combustion analysis in the case of a sample of α,α'-dideuteriodimethyl suberate.

TABLE III

DEUTERATED *cis*-CYCLOOCTENES (AND DIMETHYL SUBERATES DERIVED FROM THEM) FROM POSSIBLE HYDRIDE SHIFTS IN SOLVOLYSIS OF BROSYLATE 1

Shift	*cis*-Cyclooctene formed	Dimethyl suberate formed from methyl *cis*-cyclooctene— Before equil.	After equil.	*d*-Species in equilibrated dimethyl suberate
None or 1,2-	1,2,3,3-d_4	α,α-d_2	d_0	d_0
1,2- or apparent 1,3-[a]	2,3,3,4,4-d_5	$\alpha,\alpha,\beta,\beta$-$d_4$	β,β-d_2	d_2
Apparent 1,3-[a]	3,3,4,4-d_4	$\alpha,\alpha,\beta,\beta$-$d_4$	β,β-d_2	d_2
1,3-	2,3,4,4-d_4	α,β,β-d_3	β,β-d_2	d_2
1,3- or 1,4-	3,3,4,5,5-d_5	$\alpha,\alpha,\beta,\gamma,\gamma$-$d_5$	β,γ,γ-d_3	d_3
Apparent 1,3-[a]	3,4,4,5,5-d_5	$\alpha,\beta,\beta,\gamma,\gamma$-$d_5$	$\beta,\beta,\gamma,\gamma$-$d_4$	d_4
1,5- or 1,4-	4,4,5,6,6-d_5	$\beta,\beta,\gamma,\delta,\delta$-$d_5$	$\beta,\beta,\gamma,\delta,\delta$-$d_5$	d_5

[a] By two successive 1,2-shifts.

TABLE IV

DEUTERIUM CONTENT OF DIMETHYL SUBERATE SAMPLES OBTAINED BY DEGRADATION OF *cis*-CYCLOOCTENE FROM SOLVOLYSIS OF BROSYLATE 1

Acid used in solvolysis	Deuterated species after equilibration, % d_0	d_1	d_2	d_3	d_4	d_5
Acetic	51	<1	<1	<2	<1	46
Formic	39	<1	<1	<3	<1	56

mation in Tables III and IV certain conclusions may be drawn: (1) The contribution of 1,2-hydride shift to the undeuterated dimethyl suberate (d_0) was probably small; if 1,2-hydride shift occurred to a large extent one would expect a larger amount of dimethyl suberate-d_2. (2) Likewise, the contribution of 1,4-hydride shift to dimethyl suberate-d_5 was probably small; if 1,4-shift were a major pathway, one would expect a larger amount of dimethyl suberate-d_3. (3) Apparent 1,3-hydride shift (two successive 1,2-hydride shifts) is not an important process since the amounts of d_2- and d_4-species in the dimethyl suberate were very small. (4) 1,5-Hydride shift predominated to a large extent over 1,3-hydride shift and is the major pathway of transannular reaction. For the formation of *cis*-cyclooctene from brosylate **1**, the extent of rearrangement may be determined in three ways. Table V shows the extent of rearrangement calculated from the mass spectra of *cis*-cyclooctene, dimethyl suberate before equilibration, and dimethyl suberate after equilibration. The mass spectrometric data needed to calculate these values are found in Table VI. The extent of rearrangement was found to increase from about 50% to about 60% when the medium was changed from acetic to formic acid.

TABLE V

EXTENT OF REARRANGEMENT FOR *cis*-CYCLOOCTENE ISOLATED FROM SOLVOLYSIS OF BROSYLATE 1

Acid used in solvolysis	From *cis*-cyclooctene (100% − % d_4-species)	From dimethyl suberate Before equilibration (100% − % d_2-species)	After equilibration (100% − % d_0-species)
Acetic	50	50	49
Formic	58	60	60

TABLE VI[a]

Acid	Process	$(d_4 + d_5)/d_0$
Acetic	Substitution	1.21 ± 0.08
	Elimination	0.90 ± .02
Formic	Substitution	1.47 ± .18
	Elimination	1.42 ± .01

[a] The ratios are given as $(d_4 + d_5)/d_0$ rather than d_5/d_0 because the d_4-species was probably due to incomplete deuteration. Error is expressed as standard deviation. For calculated values of this type, including the average values reported in previous tables, the mass spectrometric data used were essentially those reported in the Experimental section (Table VII), but before rounding off.

The information in Tables I–V suggests that the rearrangement during solvolysis of brosylate **1** proceeded almost exclusively by a transannular 1,5-hydride migration, and that the extent of rearrangement increased somewhat with increased acidity of the medium. These conclusions may be applied without alteration to undeuterated cyclooctyl brosylate. (See the discussion of isotope effects below.)

The absence of appreciable 1,3-hydride migration during the solvolysis of cyclooctyl brosylate suggests that the 3-position is less favored as a site of migration initiation than the 5-position. Examination of Barton or Dreiding models reveals that, if a crown conformation is assumed, a 1,5-hydride migration can proceed by a (presumably more favorable) *trans* coplanar path while 1,3-hydride migration cannot; on this basis the 1,3-shift should be less favored. A small amount of 1,3-shift seems to be indicated, however, suggesting that the difference in migratory aptitude may not be overwhelming. According to models, *cis*-cyclooctene oxide cannot be made to assume a crown conformation. Therefore it is not surprising that the epoxide cleavage reaction gives somewhat different results from the brosylate solvolysis. A high energy intermediate in the epoxide cleavage could account for a decrease in selectivity.

Before semiquantitative conclusions can be drawn concerning undeuterated cyclooctyl brosylate, the influence of isotope effects must be considered. The solvolysis of **1** might be expected to exhibit kinetic primary and secondary α- and β-deuterium isotope effects.[13] The primary isotope effect which most concerns us here is the possible slowing of the normal elimination reaction (E2) and the decreasing of its extent with respect to transannular rearrangement.[14,15]

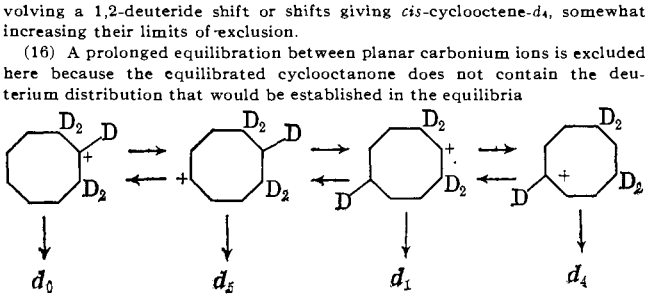
Secondary isotope effects are usually small.[13b] The solvolysis of **1** is subject to possible α- and β-effects, the β-effects most important as there are four β-deuterons. The magnitude of these secondary effects lies within the variance of the $(d_4 + d_5)/d_0$ ratio from unity (Table VI). To interpret the results, one might envision the solvolysis of **1** to proceed *via* ions **2a** and **2b**, which may interconvert but have not completely lost their tetrahedral geometry.[16] These ions are probably not completely free of leaving group or solvent. Because of its deuterium distribution, ion **2b** is slightly favored, and when equilibrium is reached, amounts of products from **2b** will exceed those derived from **2a**. If insufficient interconversions have occurred, ion **2a**, formed first, may be present in excess of its equilibrium value and

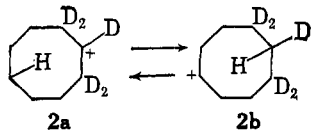
(13) (a) F. H. Westheimer, *Chem. Rev.*, **61**, 265 (1961), and references therein; (b) A. Streitwieser, Jr., "Solvolytic Displacement Reactions," McGraw–Hill Book Co., Inc., New York, N. Y., 1962; *Chem. Rev.*, **56**, 571 (1956).

(14) The extent of normal elimination is also in doubt because of the known autodecomposition of **1** even at room temperature [A. C. Cope and P. E. Peterson, *J. Am. Chem. Soc.*, **81**, 1643 (1959)].

(15) Other primary isotope effects might also occur in the processes involving a 1,2-deuteride shift or shifts giving *cis*-cyclooctene-d_4, somewhat increasing their limits of exclusion.

(16) A prolonged equilibration between planar carbonium ions is excluded here because the equilibrated cyclooctanone does not contain the deuterium distribution that would be established in the equilibria





2a **2b**

may give rise to increased amounts of normal product. Reaction of the ions before equilibrium is reached may explain why acetic acid, the stronger nucleophile[13b] and base,[10] shows a smaller $(d_4 + d_5)/d_0$ ratio than does formic acid (Table VI).[17] The formation of **2a** in the rate-determining step is consistent with the absence of a kinetic primary isotope effect for the acetolysis of cyclodecyl tosylate when hydrogen atoms known to migrate transannularly were replaced by deuterium.[18] The close agreement between the $(d_4 + d_5)/d_0$ ratios for the elimination and substitution reactions also tends to support this carbonium ion mechanism. An alternative concerted mechanism might be expected to produce a substantially larger ratio for the elimination reaction, because a large primary isotope effect would slow normal elimination (E2).[19,20] The carbonium ion mechanism also seems more reasonable because it is well known that transannular rearrangements require "SN1 conditions" and will not proceed under "SN2 conditions."

The extent of transannular rearrangement found here is somewhat larger than that reported for the acetolyses of cyclononyl[9] and cyclodecyl[8,18b] tosylates (about 20% and 16%, respectively), but less than that reported for the acetolyses of *cis*-5-*t*-butylcyclooctyl tosylate (80%)[7] and *cis*-5-methylcyclooctyl tosylate (90%).[6]

Experimental[21]

Mass spectrometric data for the solvolyses of brosylate 1 are given in Table VII.

Cyclooctanone-2,2,8,8-d_4.—The general procedure for each equilibration was to treat about 25 g. of cyclooctanone with 10 g. of anhydrous potassium carbonate in 100 g. of deuterium oxide at reflux for 3 days. The product was isolated by extraction with ether and recycled. Samples were collected by gas chromatography (silicone grease at 180 or 150°) and analyzed by mass spectrometry. The infrared spectra (carbon disulfide) showed considerable changes in the fingerprint region as deuterium was incorporated. After five or six equilibrations the product was distilled, b.p. 97–104° (40 mm.). This material was shown to contain 97% d_4-species and 3% d_3-species when it was introduced

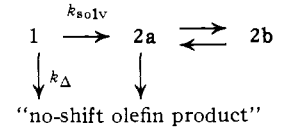
TABLE VII

MASS SPECTROMETRIC DATA[a]

Compound	Percentages of deuterated species[b] d_0	d_1	d_2	d_3	d_4	d_5	d_6[c]
Cyclooctanone							
2,2,8,8-d_4 (solid)	...	...	...	3	97	..	...
(liquid)	<2	<1	<2	10	86	..	...
Before equilibration							
a, 1	<1	...	...	5	37	57	...
2	...	...	...	8	39	55	2
f, 1	...	...	...	6	36	58	...
2	...	...	...	5	34	61	...
t, 1[d]	...	...	1	9	36	50	3
2	...	...	...	7	34	59	...
After equilibration							
a, 1	45	...	<1	<1	<2	53	...
2	46	...	<2	<1	<2	51	...
f, 1	42	...	<2	<1	<2	55	...
2	38	...	<2	1	<2	58	...
t, 1	31	2	5	7	6	48	...
2	30	3	5	7	5	50	...
Cyclooctane							
From 1, 1	<1	<1	<1	...	4	95	...
2	...	...	...	1	4	96	...
3	...	...	...	...	4	96	...
From cyclooctanol, a	...	...	...	1	4	95	...
f	...	...	...	<1	4	96	...
t	...	...	...	1	12	88	...
cis-Cyclooctene							
a, 1	<1	<1	<1	2	50	48	...
2	<1	<1	<1	2	48	49	...
3	...	...	...	1	52	47	...
f, 1	...	...	...	2	43	55	...
2	...	...	...	2	42	56	...
3	...	...	...	1	42	57	...
4	...	...	...	1	42	57	...
Dimethyl suberate							
α-d[e]	4	19	37	31	9	..	...
Dimethyl-d_6	1	...	6	93	...	..	...
Before equilibration							
a, 1	3	1	50	<2	<1	44	<1
2	1	...	51	<1	<1	46	...
3	1	<1	50	<2	<1	45	...
f, 1	3	...	39	1	1	56	...
3	<1	<1	42	<2	<1	55	...
4	<1	<1	40	<2	<1	57	...
After equilibration							
a, 1	51	...	...	<2	...	47	...
3	51	<1	<1	2	...	45	...
f, 3	40	...	...	<3	...	56	...
4	40	<1	<1	<3	...	57	...

[a] Thel etter a under the compound heading refers to acetolysis, f to formolysis, and t to trifluoroacetolysis; arabic numbers indicate determination number; dashes represent zero or negligible percentages. [b] Maximum estimated error ±3% for cyclooctanone only; somewhat <±3% for the other compounds analyzed. The M^+ peak was used for analysis of all compounds except dimethyl suberate, in which case the $M-31^+$ peak was used. For a detailed discussion of sources of error and methods of calculation, see K. Biemann, "Mass Spectrometry," McGraw-Hill Book Co., Inc., New York, N. Y., 1962. [c] "d_6-Species" probably appear due to inaccuracies in the method. [d] Partially equilibrated. [e] 2.26 D atoms/molecule, as determined by combustion analysis.

(17) The situation is not completely straightforward. The increased effective nucleophilicity and basicity of acetic acid (compared to formic acid) can account for the lower $(d_4 + d_5)/d_0$ ratios in acetic acid, but not for the decreased ratio of elimination to substitution in acetic acid. This observation is explained by the thermal decomposition of **1** at room temperature,[14] the temperature used for solvolysis.



"no-shift olefin product"

The no-shift olefin product, then, can arise in two ways: one from **2a** and the other directly from brosylate **1**. Since the *p*-bromobenzenesulfonic acid is taken up by the buffer present, no acid-catalyzed rearrangement of the olefin can occur. The rate of thermal decomposition will be essentially independent of the media (rate = $k_\Delta[1]$), while the solvolysis (acid-catalyzed) would be expected to proceed faster in formic than in acetic acid.[13b] Thus, more no-shift olefin product is formed in acetic acid than in formic acid.

(18) (a) 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). See, however, (b) V. Prelog, *Bull. soc. chim. France*, 1433 (1960). A small isotope effect (k_H/k_D = 1.08) is reported, but this is considered consistent with an "E1" reaction.

(19) K. Wiberg, *Chem. Rev.*, **55**, 713 (1955); see Tables 5 and 6 in this reference.

(20) A deuteron might be expected to be lost somewhat more slowly than a proton[18f,19] even from a carbonium ion, producing an increase in the $(d_4 + d_5)/d_0$ ratio for elimination as compared to substitution. The thermal decomposition reaction could compensate for this (and though it appears unlikely, might possibly compensate for a full E2 isotope effect). The absence of a large isotope effect therefore does not completely exclude a concerted mechanism.

(21) Melting points are corrected and boiling points are uncorrected. Deuterium analyses (falling drop method) were performed by Mr. Josef Nemeth, Urbana, Ill. Mass spectrometric analyses were performed by Miss Jean King with a CEC 21-130 instrument. We are grateful to Prof. Herbert O. House for assistance in interpreting the mass spectrometric data. Methods used for gas chromatography were those described in ref. 14, footnote 24.

into the mass spectrometer as a solid. Collection of a sample by gas chromatography (silicone grease, 155°) and introduction as a liquid gave some loss of deuterium.

Cyclooctanol-1,2,2,8,8-d_5.—All precautions were taken to exclude water and air. To a stirred slurry of 1.88 g. of lithium aluminum deuteride (Metal Hydrides Corp., 98.8% chemical purity; 99 + % isotopic purity) in 200 ml. of ether was added dropwise over 0.5 hr. 8.11 g. of cyclooctanone-2,2,8,8-d_4 in 75 ml. of ether. After refluxing for 20.5 hr., the suspension was decomposed at 0° with 150 ml. of 3 *N* hydrochloric acid. The aqueous layer was extracted twice with ether and the combined ether solutions were washed with cold saturated sodium bicarbonate solution and twice with water and dried over magnesium sulfate. The residue obtained on removal of ether was distilled through a semimicro column; b.p. 103.5–106.0° (14 mm.), n^{25}D 1.4808–1.4813. The fractions were shown to be free from the initial ketone by gas chromatography (TCEP, 110°) and infrared analysis. The yield was 7.45 g. (90%). The fraction boiling at 105.5–105.6° (14 mm.), n^{25}D 1.4813, was found to contain 30.80 atom % excess deuterium by combustion analysis, which indicated 98.6% d_5-species and 1.4% d_0-species.

Cyclooctyl Brosylate-1,2,2,8,8-d_5 (1) and its Acetolysis.—The brosylate 1 was prepared (80% yield) essentially as for the nondeuterated species[1b,22] and was solvolyzed immediately. A 3.68-g. sample was treated with 48.9 g. of glacial acetic acid–0.5 *M* sodium acetate for 51 hr. at room temperature. The mixture, including a white precipitate, was diluted with 300 ml. of ice–water and extracted with three 100-ml. portions of ether. The ether extracts were washed successively with ice–water, cold saturated sodium bicarbonate solution and again with ice–water, and dried over magnesium sulfate. The ether solution was concentrated and the residue (1.67 g.) was shown by gas chromatographic analysis (silicone grease, 147°) to contain 4.3% of ether, 40.0% of *cis*-cyclooctene, and 45.7% of cyclooctyl acetate. The products were isolated by chromatography on alumina, the olefin (692 mg.) being eluted with pentane and the acetate (736 mg.) with ether.

A 100-mg. sample of this brosylate was reduced to cyclooctane by treatment with 183 mg. of lithium aluminum hydride in 10 ml. of ether at 0° for 2 hr., then at room temperature for 10 hr. Work-up of the mixture as described in the paragraph below led to cyclooctane as well as some *cis*-cyclooctene (gas chromatographic analysis on NMPN, 31°). The cyclooctane was shown to contain *ca.* 95% d_5-species by mass spectrometric analysis.

Deuterated Cyclooctanol from the Acetolysis of 1.—To a stirred, cooled solution of 730 mg. of cyclooctyl acetate (from the acetolysis of 1) in 40 ml. of ether was added 250 mg. of lithium aluminum hydride. After stirring at 0° for 5 min. and at room temperature for 20 hr., the suspension was decomposed with 250 μl. of water, 250 μl. of 15% aqueous sodium hydroxide solution, and three 250-μl. portions of water. After stirring at room temperature for 1 hr., magnesium sulfate was added and the ether solution was filtered. The residue after removal of most of the ether weighed 590 mg. and was shown to be essentially homogeneous by gas chromatography (silicone grease, 147°).

To determine the deuterium content of the cyclooctanol by mass spectrometry, a 78-mg. sample was treated with 284 mg. of *p*-toluenesulfonyl chloride in 5 ml. of pyridine as previously described[6] for the preparation of tosylates. The crude tosylate (169 mg.) was reduced with 278 mg. of lithium aluminum hydride by a procedure similar to that described above for the brosylate. The cyclooctane obtained was shown to contain 95% d_5-species by mass spectrometric analysis.[23,24]

Deuterated Cyclooctanone from the Acetolysis of 1.—A chromic acid solution was prepared from 69 g. of chromium trioxide, 138 ml. of water, and 58 ml. of concentrated sulfuric acid at 0°. A solution of 490 mg. of deuterated cyclooctanol in 50 ml. of acetone was cooled to 0° and titrated with the chromic acid solution (about 1 ml. added), the end point being taken when the acetone solution remained brown for a few minutes. The solution was diluted with water and extracted with ether. The ether extracts were washed with cold saturated sodium bicarbonate solution, then with water, and dried over magnesium sulfate. The residue obtained on evaporation of the ether weighed 416 mg. (85%) and was shown to be essentially homogeneous by gas chromatographic analysis on a silicone grease column at 147°.

Equilibration of Deuterated Cyclooctanone from the Acetolysis of 1.—The equilibration of deuterated cyclooctanone was carried out at reflux with a large excess of 10% sodium carbonate solution for 3 days. A sample of cyclooctanone-2,2,8,8-d_4 was converted to cyclooctanone-d_0 by the same procedure. In a typical run, 200 mg. of the ketone was refluxed with 50 ml. of 10% sodium carbonate solution. The product was isolated by extraction with ether. Samples were collected by gas chromatography (silicone grease, 147°) for mass spectrometric analysis.

Deuterated Dimethyl Suberate from the Acetolysis of 1.—To a stirred, ice-cooled solution of 250 mg. of deuterated *cis*-cyclooctene in 50 ml. of acetone containing 6 drops of 15% aqueous sodium hydroxide solution was added 2.5 g. of solid potassium permanganate in portions over 20 min. After stirring for 2 hr. at 0°, the mixture was stirred for 15 hr. longer while the ice was allowed to melt (final temperature, 30°). The flask was allowed to stand stoppered for 2 days, after which the acetone was removed under reduced pressure. Then 250 ml. of 10% aqueous sodium bisulfite solution was added (cooling) followed by 30 ml. of 6 *N* hydrochloric acid at 0°. Nitrogen was bubbled through to remove dissolved gases, and the colorless solution was extracted four times with ether. The ether was dried and evaporated to give 475 mg. of semisolid suberic acid, which was dissolved in 150 ml. of ether and treated with excess diazomethane in ether at 0°. The resulting yellow solution stood at room temperature for 17 hr., after which excess diazomethane was removed with a nitrogen stream. The residue (532 mg.) after removal of the ether was shown by gas chromatography (silicone grease, 185°) to be mainly dimethyl suberate, which was collected for mass spectrometric analysis. Small amounts of shorter-chained dimethyl esters (due to over-oxidation) were also probably present (identified by retention times only).

Equilibration of Deuterated Dimethyl Suberate from the Acetolysis of 1.—One part of deuterated dimethyl suberate (purified by short-path distillation) was treated in a closed flask with 50 parts of 0.17 *M* sodium methoxide in methanol for 1 week at 50 ± 2°. The colorless solution was acidified to pH 1 with concentrated hydrochloric acid (cooling), diluted with water, and extracted with ether. The ether extracts were washed with water until neutral and dried over magnesium sulfate. The ether was evaporated and the residue was purified by short-path distillation. The recovery after distillation was about 40%. A standard sample was shown to lose 96.5% of its exchangeable deuterium by this procedure. An additional equilibration was used to remove the remainder of the α-deuterons. A standard sample containing 1.82 D-atoms/molecule (mass spectrometric analysis) gave >99% dimethyl suberate-d_0 after two equilibrations at 44°.[25]

Dimethyl-d_6 Suberate.—A solution of 1.0 g. of suberic acid and 1.0 ml. of methanol-C-d_3 (minimum isotopic purity 99%) in 5 ml. of dry benzene containing 0.25 ml. of concentrated sulfuric acid was heated at reflux with stirring for 23 hr. and then stirred at room temperature for 3 days. The mixture was diluted with 50 ml. of ice–water and extracted twice with ether. The ether extracts were washed with cold saturated sodium bicarbonate solution, water, and dried over magnesium sulfate. The residue obtained on evaporation of the solvents weighed 972 mg. A sample (n^{25}D 1.4312) was collected for mass spectrometric analysis by gas chromatography on silicone grease at 180°.

α-Deuterated Dimethyl Suberate.—A 1.71-g. sample of dimethyl suberate was dissolved in 5 ml. of methanol-O-*d* (prepared by three successive equilibrations of methanol with deuterium oxide). A 1-ml. portion of 1 *M* sodium methoxide in methanol-O-*d* was added and the colorless solution was allowed to stand at room temperature for 109 hr. After dilution with 10 ml. of deuterium oxide, the solution was extracted with three 30-ml. portions of anhydrous ether. The ether extracts were washed with 15 ml. of deuterium oxide, dried over magnesium sulfate, and evaporated under reduced pressure to a residue of 1.66 g. Samples were collected by gas chromatography (silicone grease, 150°) for mass spectrometric analysis and deuterium analysis by combustion. A 250-mg. portion of the residue was purified by short-path distillation, giving 225 mg. of dimethyl suberate, n^{25}D 1.4310. Combustion analysis showed 12.00 atom % excess deuterium (2.26 D atoms/molecule), and mass spectrometric analysis showed 2.22 D atoms/molecule.

Formolysis of 1 and Subsequent Degradations.—Brosylate 1 was treated for the formolysis essentially as for the acetolysis described above, except that pentane was used to extract the products. The reaction was carried out in 98–100% formic acid–0.5*M* sodium formate at room temperature for 24 hr. The formates were saponified in 10% sodium hydroxide solution (1:1 water–methanol) at room temperature for 2 days.[4] The deuterated cyclooctanol (eluted with ether) and deuterated *cis*-cyclooctene (eluted with pentane) thus obtained were separated by chromatography on alumina and degraded as described for the acetolysis.

Attempted Addition of Formic Acid to *cis*-Cyclooctene.—A mixture of 148 mg. of sodium *p*-bromobenzenesulfonate, 50 mg.

(22) See also ref. 6 for general procedure.

(23) It is worthy of note that in addition to the cyclooctane and a small amount of *cis*-cyclooctene, a large amount of toluene was also isolated and identified by infrared comparison. This observation is in disagreement with the common belief[24] that *p*-thiocresol, the primary reduction product of *p*-toluenesulfonic acid, is stable to further reduction with hydride.

(24) N. G. Gaylord, "Reduction with Complex Metal Hydrides," Interscience Publishers, Inc., New York, N. Y., 1956, p. 855.

(25) The exclusion of moisture during these equilibrations was of extreme importance. Apparently water destroys an equivalent amount of dicarboxylic ester, converting it to a monoester–monoacid salt. While re-esterification with diazomethane is possible, the sodium salt formed on saponification will not have exchanged appreciable deuterium.

of sodium formate, 3.5 g. of 98–100% formic acid, and 50 mg. of *cis*-cyclooctene was allowed to stand at room temperature for 24 hr. *cis*-Cyclooctene was recovered in more than 90% yield and was identified by comparison of its infrared spectrum with that of an authentic sample. Cyclooctyl formate was not detected (gas chromatographic analysis on silicone grease at 155°).

Trifluoroacetolysis of 1 and Subsequent Degradation of Deuterated Cyclooctanol.—The trifluoroacetolysis of 1 was carried out as described for the formolysis at 0° for 3.5 hr. in trifluoroacetic acid–0.5 *M* sodium acetate. The only trifluoroacetolysis product isolated (after saponification) was partially deuterated cyclooctanol. The procedure used for its isolation and subsequent degradation was that described for the formolysis.

Acknowledgment.—We are grateful to Dr. Richard L. Schowen for discussions concerning isotope effects.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, CAMBRIDGE 39, MASS.]

Proximity Effects. XXXVII. Proximity Effects in the Solvolysis of 1-Octene Oxide[1,2]

BY ARTHUR C. COPE, LEE J. FLECKENSTEIN, SUNG MOON, AND HARRIS E. PETREE

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The reaction of 1-octene oxide with trifluoroacetic acid yields small amounts of abnormal products, 1,3-, 1,4-, 1,5-, 1,6-, and 1,7-octanediol, in addition to the normal product, 1,2-octanediol. This may be interpreted as evidence for the operation of a proximity effect in acyclic compounds. From hydroxylation of 1-octene with performic acid or peracetic acid only 1,2-octanediol was isolated.

The reaction of *cis*-cyclooctene with performic acid gave principally the abnormal product *cis*-1,4-cyclooctanediol,[3] and the solvolysis of *cis*-cyclooctene oxide with trifluoroacetic acid gave exclusively products of transannular hydride shifts.[4] To determine whether such a proximity effect was operative in acyclic compounds that could assume conformations similar to those of medium-ring compounds, the solvolysis of 1-octene oxide with trifluoroacetic acid and the hydroxylation of 1-octene with performic and peracetic acid were studied.

In this study several methods were considered which might permit the isolation and identification of extremely small amounts of isomeric octanediols present in a large amount of 1,2-octanediol. The selective formation of a cyclic ketal, used for the separation of *trans*-1,2-cyclooctanediol and *cis*-1,4-cyclooctanediol, was not applicable because 1,2-, 1,3-, and 1,4-octanediol formed such ketals on treatment with copper sulfate and acetone. The method which ultimately proved successful was separation of 1,2-octanediol from the reaction product by repeated crystallization and gas chromatography of the diacetates prepared from glycols present in the mother liquor.

The reaction product of 1-octene oxide with trifluoroacetic acid was hydrolyzed and repeatedly recrystallized to separate 1,2-octanediol. Glycols in the mother liquor were converted to diacetates and the diacetates were fractionally distilled. Gas chromatography showed that there were several minor peaks in addition to a major peak due to 1,2-octanediol diacetate. These minor components were 1,3- (0.7%), 1,4- (0.5%), 1,5- (0.3%), 1,6- (0.2%), and 1,7-octanediol diacetate (0.1%).[5] The first four compounds were isolated by gas chromatography and identified by comparison of the infrared spectra with the spectra of authentic samples and by comparison of the retention times with the retention times of authentic samples on four different gas chromatographic columns. The last compound was identified only by comparison of the retention time with an authentic sample on four different gas chromatographic columns.

The small amount of additional material (*ca.* 1%) was probably a mixture of octenyl acetates on the basis of its analysis and its infrared spectrum, which was similar to that of *trans*-2-octen-1-yl acetate. Gas chromatography on 1,2,3-tris-(2-cyanoethoxy)-propane showed a broad peak corresponding in retention time to a mixture of *cis*- and *trans*-2-octen-1-yl acetate.

Hydroxylation of 1-octene with formic acid and hydrogen peroxide or with peracetic acid and treatment of the products in the manner described above gave only 1,2-octanediol and no detectable amount of any other glycol.

Formation of 1,3-, 1,4-, 1,5-, 1,6-, and 1,7-octanediol can be formulated as the result of 1,2-, 1,3-, 1,4-, 1,5-, and 1,6-hydride shifts in an intermediate carbonium ion resulting from the protonated 1-octene oxide. Alternatively, they may have been formed by a series of 1,2-hydride shifts. It has been shown that trifluoroacetic acid promotes 1,2-hydride shifts.[6] Detection of 1,3-octanediol among the solvolysis products demonstrates that a 1,2-hydride shift has occurred.

However, the following argument suggests that a series of 1,2-shifts would give a different distribution of products. The total amount of the abnormal products is less than 2%. Using 2% as a representative amount of 1,2-hydride shift in secondary cations, it may be estimated that the amounts of 1,3-, 1,4-, 1,5-, 1,6-, and 1,7-octanediol formed by successive 1,2-shifts in the reaction of 1-octene oxide would be 2, 0.04, 0.0008%. . . . Experimentally, the yields of isomeric octanediols does not decrease this sharply. Accordingly, one-step hydride shifts appear to explain our results more satisfactorily.

Experimental[7]

***cis*-2-Octen-1-ol.**—Commercial 2-octyn-1-ol (Farchan Research Laboratories) was hydrogenated in methanol using 1.5% palladium chloride on calcium carbonate as catalyst, giving *cis*-2-octen-1-ol, $n^{25}D$ 1.4465 (lit.[8,9] $n^{20}D$ 1.44609).

The alcohol was treated with acetic anhydride in pyridine, giving *cis* 2-octen-1-yl acetate, $n^{25}D$ 1.4348.

Anal. Calcd. for $C_{10}H_{18}O_2$: C, 70.54; H, 10.66. Found: C, 70.27; H, 10.54.

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(2) Paper XXXVI: *J. Am. Chem. Soc.*, **85**, 3747 (1963).

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

(4) A. C. Cope, J. M. Grisar, and P. E. Peterson, *ibid.*, **81**, 1640 (1959).

(5) The percentages are based on 1-octene oxide.

(6) P. E. Peterson, *J. Am. Chem. Soc.*, **82**, 5834 (1960).

(7) Melting points are corrected and boiling points are uncorrected. We are indebted to Dr. S. M. Nagy and his associates for analyses. Footnote 24 of A. C. Cope and P. E. Peterson, *J. Am. Chem. Soc.*, **81**, 1643 (1959), describes the conditions and equipment used for gas chromatography.

(8) G. Smets, *Acad. Roy. Belg., Classe Sci., Mem., Collection in 8°*, **21**, 3 (1947); *Chem. Abstr.*, **44**, 8315 (1950).

(9) J. Colonge and G. Poilane, *Compt. rend.*, **238**, 1821 (1954).