was grossly different from that of 1-nortricyclylcarbinol,[15] with no bands at 11.78 and 12.74μ, but an intense terminal methylene band at 11.30μ.

This alcohol was converted to its acetate by the same general procedure as outlined for XVI. The acetate thus obtained, b.p. 51–52.5 at 1.8 mm., had an infrared spectrum identical with that obtained from the thermal gas chromatographic rearrangement of XVI (except for a trace band at 12.7 μ in the latter, presumably due to a slight amount of unrearranged XVI).

Analysis of the Acetates from Deamination of XV. (1) **Permanganate Oxidation.**—In order to determine the structure of the non-oxidizable acetate(s), the ester mixture was subjected to limited permanganate oxidation. A solution of 500 mg. of acetate in 5 ml. of ether was stirred at 0° with 10 ml. of 2% aqueous potassium permanganate containing a pinch of detergent. During the 8 hours, three 5-ml. portions of permanganate solution were added. Recovery of the ester from the ether layer (after filtration, water wash and drying) gave material with an infrared spectrum virtually identical with that of authentic 1-nortricyclylcarbinyl acetate. Trace bands at 5.97, 6.02, 6.10 and 8.90 μ were all attributable to slight contamination with material from the original mixture, but were greatly diminished in intensity when compared with the starting acetate mixture.

(2) **Titration for Unsaturates.**—The method of Reid and Beddard,[35] which is designed for determining small amounts of unsaturates in large quantities of saturates, was used. Accurately weighed 0.1-g. samples of ester were dissolved in 25 ml. of methanol, in 500-ml. iodine flasks and chilled to 0° (30 minutes). Standard bromine solution (10 ml. of 0.01155 *N* bromine in glacial acetic acid, standardized with thiosulfate to a starch end-point) was added, mixed thoroughly, kept at 0° for 3 minutes, diluted with 100 ml. of water, 10 ml. of 10% potassium iodide added and the solution titrated with standard 0.01 *N* sodium thiosulfate to a starch end-point. After correction for a small "blank" using pure 1-nortricyclylcarbinyl acetate, the mixture was shown to contain 8.2–8.4% unsaturation.

(3) **Infrared Analysis.**—Infrared spectra of mixtures of known concentrations of 1-nortricyclylcarbinyl acetate (XVI) and 6-acetoxynor-camphene (XVII) were compared with the deamination product. A carbon disulfide solution of deamination product in the "reference" beam and a mixture of 95% XVI and 5% XVII of identical concentration in the "sample" beam showed only two small deflections, at 6.10 and 8.90μ, both apparently due to the nitrate ester. All other bands were compensated.

(35) V. W. Reid and J. D. Beddard, *Analyst*, **79**, 456 (1954).

[Contribution from the Department of Chemistry, Massachusetts Institute of Technology, Cambridge 39, Mass.]

Proximity Effects. XXI. Establishment of 1,3- and 1,5-Hydride Shifts in the Solvolysis of *cis*-Cyclooctene Oxide

By Arthur C. Cope, Glenn A. Berchtold,[1a] Paul E. Peterson[1b] and Samuel H. Sharman[1c]

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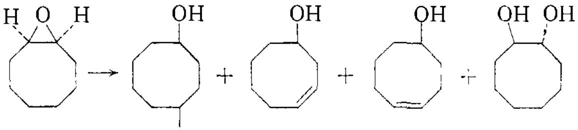
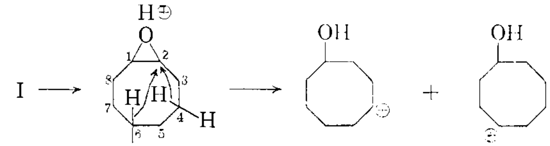
The solvolysis of *cis*-cyclooctene oxide with 90% formic acid has been studied with deuterium labeling on C_5 and C_6 of the epoxide. It has been established that *cis*-1,4-cyclooctanediol is formed to the extent of 61% by a 1,5-hydride shift and 39% by a 1,3-hydride shift, whereas 3-cycloöcten-1-ol is formed to the extent of 94% by a 1,5-hydride shift and 6% by a 1,3-hydride shift.

The solvolysis of *cis*-cycloöctene oxide (I) with formic acid has been shown to form *cis*-1,4-cyclooctanediol (II), 3-cycloöcten-1-ol (III), 4-cycloocten-1-ol (IV) and other minor products in addition to the expected *trans*-1,2-cycloöctanediol (V).[2-5]



I II III IV V

Formation of the transannular products (II, III and IV) must involve rearrangement of VI to VII by a 1,3-hydride shift or to VIII by a 1,5-hydride shift. Attack of a solvent molecule at C_4 of VII or at C_6 of VIII would then form II as its monoformate ester, whereas elimination of a proton from C_3 of VII or C_7 of VIII would give rise to III and elimination of a proton from C_5 of VII or VIII would form IV.



VI VII VIII

Deuterium tracer studies were undertaken to determine the relative amounts of 1,3- and 1,5-hydride shifts in this solvolysis. The compound chosen for study was *cis*-cycloöctene-5,6-d_2 oxide (IX). Figure 1 shows the reaction sequence employed. 4-Cycloöcten-1-ol and *trans*-1,2-cyclooctanediol are not shown since no degradation studies were made on these products. Formolysis of IX would yield the glycol X if a 1,3-hydride shift were involved and the glycol XII or XIII by a 1,5-hydride or deuteride shift. Similarly, the 3-cycloöcten-1-ol would be labeled as indicated by XI in the case of the 1,3-hydride shift and as indicated by XIV or XV in the case of the 1,5-hydride or deuteride shift.

Oxidation of the labeled 1,4-cycloöctanediol to adipic acid and esterification with diazomethane would form XVI or a mixture of XVII and XVIII, depending on whether the dimethyl adipate arises from X or a mixture of XII and XIII. Similarly, the labeled 3-cycloöcten-1-ol would be converted to either XVI or a mixture of XVII and XVIII by the same procedure. Finally, equilibration of

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(1) (a) Postdoctoral Fellow, 1959–1960; (b) National Institutes of Health Postdoctoral Fellow, 1956–1958; (c) Postdoctoral Fellow, 1958–1959.

(2) A. C. Cope, S. W. Fenton and C. F. Spencer, This Journal, **74**, 5884 (1952).

(3) A. C. Cope, A. H. Keough, P. E. Peterson, H. E. Simmons and G. W. Wood, *ibid.*, **79**, 3900 (1957).

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

(5) A. C. Cope and R. W. Gleason, to be published.

the α-positions of the dimethyl adipate with methanol would result in an ester containing one atom of deuterium per molecule (XIX) if a 1,3-hydride shift had occurred and no deuterium if a 1,5-hydride shift had occurred (XX). If both 1,3- and 1,5-hydride shifts occur, the quantity of deuterium per molecule in the equilibrated ester would be the fractional amount of product arising from the 1,3-hydride shift.

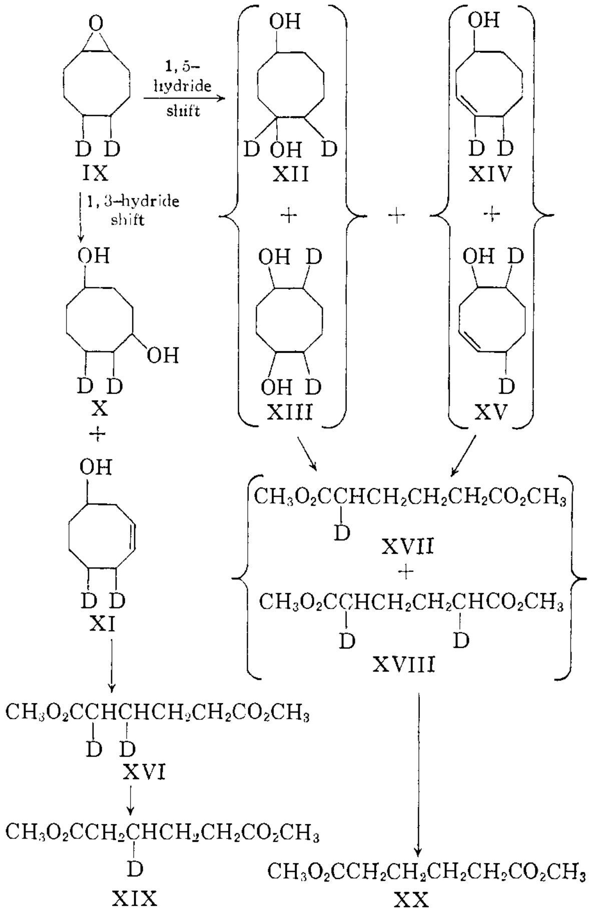


Fig. 1.—Reaction scheme for determining the extent of 1,3- and 1,5-hydride shifts during the solvolysis of IX.

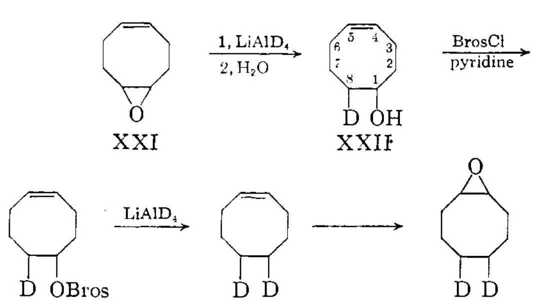
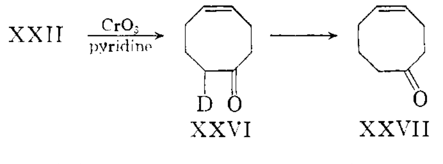


Fig. 2.—Synthesis of XXV.



cis-Cycloöctene oxide, deuterated on C_5 and C_6, was prepared by the sequence indicated in Fig. 2. The reaction of lithium aluminum deuteride with *cis-cis*-1,5-cycloöctadiene monoepoxide (XXI) gave XXII in 94% yield. Mass spectrograph analysis indicated XXII to consist of 13% undeuterated, 74% monodeuterated and 13% dideuterated species, thereby indicating that exchange had occurred during the reaction. Since XXI was treated with a stoichiometric amount of lithium aluminum deuteride, the total amount of deuterium in XXII is one atom of deuterium per molecule even though exchange is occurring. The facts that the amounts of undeuterated and dideuterated species were equal and there was no evidence of any trideuterated species indicated that the exchange was occurring with the hydrogen atoms on the carbon atoms of the epoxide ring before cleavage and all the deuterium would therefore be on C_1 and C_8 of XXII.[6] This was established by oxidation of XXII to XXVI by chromic anhydride in anhydrous pyridine, a method previously shown not to equilibrate deuterium atoms on the α-positions of ketones,[7] and subsequent equilibration of XXVI to 4-cycloöcten-1-one containing no deuterium (XXVII). Compound XXVI was found by analysis to contain 0.91 atom of deuterium per molecule, XXVII contained no deuterium, thereby establishing that all the deuterium is located on C_1 and C_8 of XXII.[8] The deuterium distribution for XXII should then be that indicated in Fig. 3, and it is therefore expected that a loss of 6.5% of the deuterium would occur during the oxidation of XXII to XXVI, which is essentially the observed result.

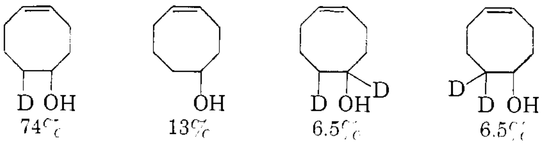


Fig. 3.—Distribution of deuterium in XXII.

Compound XXII was converted to its brosylate XXIII, which was cleaved by lithium aluminum deuteride to form XXIV. Analysis of XXIV showed it to contain 1.98 atoms of deuterium per molecule and to have the expected deuterium distribution, *i.e.*, 13% monodeuterated, 74% dideuteriated and 13% trideuterated species. Epoxidation of XXIV with monoperphthalic acid gave XXV which contained 1.99 atoms of deuterium per molecule.

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[6] It is interesting to note that E. L. Eliel and D. W. Delmonte, THIS JOURNAL, **80**, 1744 (1958), report only the monodeuterated species formed in the reduction of styrene oxide and isobutylene oxide with lithium aluminum deuteride in the presence of aluminum chloride and found over 90% of the deuterium to be on the carbinol carbon atom, establishing that the epoxide undergoes an intramolecular hydride shift to form the aldehyde which is then reduced to the primary alcohol.

[7] Cyclodecanone-2,2,10,10-d_4 was reduced to cyclodecanol-2,2,10,10-d_4 with lithium aluminum hydride and oxidized back to the ketone by chromic anhydride in pyridine. The deuterium lost was less than 1.6%.

[8] It is argued that no deuterium could have been on C_2 of XXVI since if any had been present a corresponding amount would have been on C_7 and would not have been removed by the equilibration.

The epoxide XXV is then composed of the species indicated in Fig. 4. Since C_5 and C_6 are equivalent positions in *cis*-cycloöctene oxide, the unequal distribution of deuterium in XXV will have no effect on the procedure for determination of the extent of 1,3- and 1,5-hydride shifts during the solvolysis of XXV as outlined in Fig. 1. It is expected from the method of synthesis of XXV that the deuterium atoms on C_5 and C_6 are *cis* to each other.

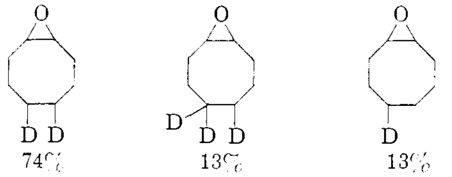

Fig. 4.—Distribution of deuterium in XXV.

The solvolysis of XXV with 90% formic acid and the product isolation were carried out as previously described for *cis*-cycloöctene oxide.[3] The *cis*-1,4-cycloöctanediol contained 2.00 atoms of deuterium per molecule, thereby showing no loss of deuterium during the solvolysis. This glycol was oxidized with potassium permanganate, the acidic products were esterified with diazomethane, and the dimethyl adipate was isolated by gas chromatography. Since no good method has been developed for the separation of 3- and 4-cyclo-octen-1-ol in pure form without considerable loss, the mixture was oxidized and the acidic products were esterified by the same procedure used for the glycol. The dimethyl adipate was again collected by gas chromatography. All of the dimethyl adipate must arise from the 3-cycloöcten-1-ol. The dimethyl adipate from both sources was equilibrated with sodium methoxide in methanol to remove the deuterium in the α-positions (see Experimental for details of the equilibration).

The dimethyl adipate from the *cis*-1,4-cyclo-octanediol contained 1.65 atoms of deuterium per molecule before equilibration and 0.39 atom of deuterium per molecule after equilibration. It may therefore be concluded that *cis*-1,4-cyclo-octanediol is formed to the extent of 39% by a 1,3-hydride shift and to the extent of 61% by a 1,5-hydride shift. Since loss of deuterium by equilibration during the oxidation and esterification is highly improbable, the analysis of the unequilibrated dimethyl adipate indicates that the glycol consisted of 39% X and 61% of approximately equal amounts of XII and XIII.[9] The equal amounts of hydride and deuteride shifts in the 1,5-hydride shift indicates that half of the molecules of XXV have the deuterium atoms on the same side of the cycloöctane ring as the epoxide group and the other half are on the opposite side.

The dimethyl adipate from the 3-cycloöcten-1-ol contained 1.55 atoms of deuterium per molecule before equilibration and 0.06 atom of deuterium per molecule after equilibration. Thus, 3-cycloöcten-1-ol is formed to the extent of 6% by a 1,3-hydride shift and 94% by a 1,5-hydride shift. Analysis of the unequilibrated dimethyl adipate indicates that the 3-cycloöcten-1-ol consisted of 6% XI and 94% of approximately equal amounts of XIV and XV.

This difference in the relative amounts of 1,3- and 1,5-hydride shifts in the formation of *cis*-1,4-cycloöctanediol and 3-cycloöcten-1-ol establishes that 3-cycloöcten-1-ol is not formed by dehydration of the glycol, and gives further evidence that there are no free carbonium ions in the reaction and the reaction is therefore concerted. The formation of *cis*-1,4-cycloöctanediol to the extent of 61% by a 1,5-hydride shift and 39% by a 1,3-hydride shift is not surprising since Dreiding models indicate that either shift might occur, the 1,5-shift appearing to be somewhat more favorable. Since there appears to be no hindrance to attack by solvent at C_4 of VII or C_6 of VIII, the relative amounts of hydride shifts are apparently controlled by the relative ease of hydride ion migration from each position. 3-Cycloöcten-1-ol formation, however, requires that the ring adopt a conformation with a planar configuration involving the two carbon atoms of the double bond being formed, the hydride ion shifting and the hydrogen ion being eliminated. Examination of Dreiding models indicates such a conformation is much more favorable in the 1,5-hydride shift than in the 1,3-hydride shift.

Experimental[10]

Ring Opening of *cis-cis*-1,5-Cycloöctadiene Monoepoxide with Lithium Aluminum Deuteride.—*cis-cis*-1,5-Cycloöctadiene monoepoxide[11] (63.2 g., b.p. 114–115° at 73 mm., n^{25}_D 1.4930) was added dropwise to a slurry of 5.35 g. of lithium aluminum deuteride[12] in 300 ml. of tetrahydrofuran over a period of 2.5 hours while the mixture was kept at room temperature by a water-bath. The mixture was stirred for 22 hours, after which time a solution of 10 ml. of water in 40 ml. of tetrahydrofuran was added dropwise while the reaction mixture was cooled in an ice-bath. The mixture was poured into 800 ml. of cold 10% sulfuric acid and extracted with one 300-ml. portion and two 100-ml. portions of ether. The combined extracts were washed with water and dried over sodium sulfate. Removal of the ether and fractionation of the residue yielded 57.6 g. (94%) of deuterated 4-cyclo-octen-1-ol, b.p. 87.5–90° (10 mm.), mass spectrograph analysis: 13% d_0, 74% d_1, 13% d_2 species.

Oxidation of XXII with Chromic Anhydride–Pyridine Complex.—A solution of 1.00 g. of XXII in 10 ml. of dry pyridine was added to the preformed complex[13] prepared from 1.50 g. of chromic anhydride and 16 ml. of dry pyridine. The mixture was stirred for 8.5 hours, poured into 200 ml. of water and extracted with five 100-ml. portions of ether. The combined extracts were washed with 15% acetic acid, dilute sodium bicarbonate and water and dried over calcium chloride. The ether was removed and the residue was distilled in a short-path still. The 4-cycloöcten-1-one was collected by gas chromatography on Silicone oil,[14] wt. 697 mg.

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[9] The unequal distribution of deuterium in XXV is neglected in this consideration.

[10] Melting points are corrected and boiling points are uncorrected. All deuterium analyses indicating the number of atoms of deuterium per molecule were determined by the falling drop method; these analyses were performed by Mr. Josef Nemeth, Urbana, Ill. Mass spectrographic analyses were determined with a C. E. C. type 21-103C instrument with a heated inlet system. We are indebted to Drs. K. Biemann and J. Seibl for these analyses.

[11] A. C. Cope and B. S. Fisher, to be published.

[12] Metal Hydrides, Inc., Beverly, Mass.; purity: 95.5%; minimum isotopic purity: 99%.

[13] G. I. Poos, G. E. Arth, R. E. Beyler and L. H. Sarett, This Journal, **75**, 422 (1953).

[14] Gas chromatography columns were 8-mm. Pyrex tubes of 190-cm. length containing 30% by weight of liquid phase absorbant on a 60–80 mesh firebrick support. The liquid phase absorbants employed were the following: Dow-Corning Silicone oil no. 550 (column temperature 170–180°) and 4-methyl-4-nitropimelonitrile (column temperature 25–50°). Helium at 15 p.s.i. was the carrier gas and thermistors were employed for detecting sample peaks.

(71%); deuterium analysis: 0.91 atom of deuterium per molecule.

Equilibration of XXVI.—A solution of 650 mg. of XXVI in 2 ml. of methanol and 1 ml. of 0.5 *N* aqueous sodium hydroxide was sealed in an ampoule and placed in an oil-bath at 40–45° for 48 hours. The reaction mixture was acidified with hydrochloric acid, mixed with 5 ml. of water and extracted with three 25-ml. portions of ether. The combined extracts were dried and the ether removed under reduced pressure. The ketone was then collected for deuterium analysis by gas chromatography on Silicone oil[14]; deuterium analysis after four equilibrations: 0.00 atom of deuterium per molecule.

The brosylate of XXII was prepared from 31.8 g. of XXII by the same procedure used for the undeuterated compound.[15] The yield was 54.7 g. (63%), m.p. 71.5–72.0°.

Reaction of XXIII with Lithium Aluminum Deuteride.—A solution of 52.0 g. of XXIII in 750 ml. of ether was stirred under a nitrogen atmosphere at −10° while a slurry of 4.75 g. of lithium aluminum deuteride[12] in 100 ml. of ether was added dropwise over a period of 2 hours. The mixture was stirred at −10° for 6 hours and then at room temperature for 22 hours. A saturated solution of water in ether (100 ml.) was added while the mixture was cooled in an ice-bath. The mixture was poured into 500 ml. of 10% aqueous sulfuric acid, shaken, and the ether layer removed. The aqueous layer was extracted with 100 ml. of ether. The combined extracts were washed with water and dried over magnesium sulfate. The drying agent was removed by filtration and the ether was removed by distillation through a 90 × 2-cm. spinning band column. The residue was distilled through a 45 × 0.5-cm. spinning band column to obtain 12.3 g. of colorless liquid, b.p. 73–76° (92 mm.). Gas chromatography on 4-methyl-4-nitropimelonitrile[14] indicated the mixture consisted of 77% *cis*-cycloöctene and the other products were principally *cis*-bicyclo[3.3.0]octane, cycloöctane and *cis-cis*-1,5-cycloöctadiene. The olefin was not separated from these impurities since the purification of its epoxide is a more convenient method. A pure sample of the deuterated *cis*-cycloöctene was collected by gas chromatography; deuterium analysis: 1.98 atoms of deuterium per molecule; mass spectrograph analysis: 13% monodeuterated, 74% dideuterated and 13% trideuterated species.

Epoxidation of XXIV.—A sample of the mixture obtained from the reaction of XXIII with lithium aluminum deuteride which weighed 11.3 g. and contained 8.40 g. of XXIV was dissolved in 190 ml. of ether and added to 380 ml. of an ethereal solution containing 27.2 g. of monoperphthalic acid. The reaction vessel was covered with aluminum foil to exclude light and the reaction was followed by iodometric titration until no more peracid was being used. The solution was filtered from the precipitated phthalic acid, extracted three times with 200-ml. portions of 5% sodium hydroxide, once with water, and dried. The ether was removed by distillation through a Vigreux column and the residue was distilled through a 45 × 0.5-cm. spinning band column to obtain 8.69 g. (91%) of *cis*-cycloöctene-5,6-d_2 oxide, b.p. 93–94° (33 mm.); deuterium analysis: 1.99 atoms of deuterium per molecule.

Solvolysis of XXV with Formic Acid.—Compound XXV (6.17 g.) was solvolyzed with 90% formic acid to obtain 1.29 g. of a mixture of 3- and 4-cycloöcten-1-ol and 3.01 g. of *cis*-1,4-cycloöctanediol, m.p. 82.6–83.3°, by the procedure previously described for the undeuterated compound[3]; deuterium analysis of the *cis*-1,4-cycloöctanediol: 2.00 atoms of deuterium per molecule.

Permanganate Oxidation of the Deuterated *cis*-1,4-Cycloöctanediol.—The deuterated glycol (2.80 g.) was dissolved in 280 ml. of water and 1 ml. of 5% potassium hydroxide was added. The mixture was stirred while 22 g. of potassium permanganate was added over a period of 15 minutes, the temperature being kept at 27–31°. Stirring was continued 1.5 hours after the addition was completed. The solution was acidified to *p*H 1 with hydrochloric acid and the excess permanganate and manganese dioxide were destroyed by the addition of sodium bisulfite. Nitrogen was bubbled through the solution to remove sulfur dioxide. The aqueous solution was extracted continuously with ether for 36 hours. The ether solution was dried and treated with an excess of diazomethane. The ether was removed by distillation and the residue was distilled in a short-path still. Dimethyl adipate (702 mg.) was isolated from the product mixture by gas chromatography on Silicone oil[14]; deuterium analysis: 1.65 atoms of deuterium per molecule. A sample of the dimethyl adipate which was recollected by gas chromatography contained 1.67 atoms of deuterium per molecule, thereby showing that no loss of deuterium occurred during the vapor phase purification.

Permanganate Oxidation of Deuterated 3-Cycloöcten-1-ol.—The mixture of deuterated 3- and 4-cycloöcten-1-ols (1.29 g.) was oxidized with 11.0 g. of potassium permanganate and the acidic product mixture esterified as described above for the oxidation products of the glycol. Dimethyl adipate (356 mg.) was isolated by gas chromatography on Silicone oil[14]; deuterium analysis: 1.55 atoms of deuterium per molecule.

Equilibration of Deuterated Dimethyl Adipate.—The general procedure used for equilibration of the α-positions of dimethyl adipate was: the sample of ester (300–700 mg.) was sealed in an ampoule with 3.0 ml. of 0.17 *M* sodium methoxide in methanol and placed in an oil-bath at 40° for 5–6 days. The ampoule was opened and its contents were mixed with 5 ml. of water, acidified to congo red with hydrochloric acid and extracted with four 10-ml. portions of ether. The extract was washed with 10 ml. of 5% sodium bicarbonate, 10 ml. of water and dried. The ether was removed under reduced pressure and the ester was collected by gas chromatography on Silicone oil.[14] A sample was then removed for deuterium analysis and the remainder was equilibrated again by the same procedure. Preliminary experiments indicated that this procedure gave approximately 85–90% equilibration.[16]

Table I lists the results of consecutive equilibrations.

TABLE I

EQUILIBRATION OF DEUTERATED DIMETHYL ADIPATE SAMPLES

Number of equilibrations	Atoms of deuterium per molecule in dimethyl adipate from indicated source		
	Standard[16]	*cis*-1,4-Cycloöctanediol	3-Cycloöcten-1-ol
0	3.01	1.65	1.55
1	0.54	0.57	..
2	.07	.40	0.06
3	.01	.39	.06
4	.00	.39	

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[15] A. C. Cope and P. E. Peterson, THIS JOURNAL, **81**, 1648 (1959).

[16] Dimethyl adipate containing 3.01 atoms of deuterium in the α-positions was prepared by essentially the same procedure using 0.17 *M* sodium methoxide in methanol-O-*d*. This sample was equilibrated with methanol under identical conditions to the samples of dimethyl adipate obtained from the oxidations in order to ensure complete equilibration.