Neighboring-Group Participation by Oxirane Oxygen during Oxymercuration of 1,5-Diene Monoxides[1a,b]

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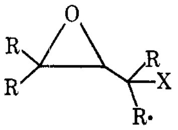
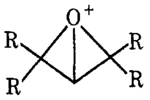
Oxymercuration of the monoepoxides of *cis,cis*-1,5-cyclooctadiene and 1,5-hexadiene takes place with neighboring-group participation of the oxirane oxygen, resulting in formation (after demercuration) of bicyclic and monocyclic ether–alcohols, respectively, in high yield. The rate acceleration caused by this participation is appreciable but less than that of a similarly located hydroxyl group. A stepwise mechanism involving prior hydrolysis to a diol and then oxymercuration is clearly ruled out by the nature of the products and the inertness of similar saturated oxiranes to the reaction conditions. Effects of structure on the oxymercuration rates of a number of substituted *cis*-cyclooctenes are reported.

Neighboring-group participation by ether oxygen has been a topic of interest for more than a decade,[2] but, except for a brief study of the tetrahydrofuran system,[3] participation by the oxygens of cyclic ethers (except for numerous examples of 1–3 participation) has received little attention. A particularly interesting case would be participation by oxirane oxygen. Ethylene oxide is the weakest base toward hydrogen bonding[4] and iodine complexation[5] of the simple cyclic ethers, resembling in this respect ethylenimine.[6] On this basis one might expect oxirane oxygen to be a relatively poor neighboring group during solvolysis reactions. Recently, however, Richey and Kinsman reported evidence for considerable anchimeric assistance by oxygen during solvolysis of esters of substituted 2,3-epoxy-1-propanols (I).[7] The products were substituted 3-oxetanyl derivatives, and 1-oxabicyclobutonium ions (II) were proposed as intermediates.[7] We wish to report additional cases of oxirane oxygen participation which involve epoxy groups quite distant (4,5 position) from the site of the electron-deficient carbon.

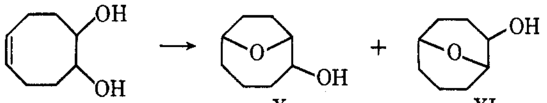


I



II

During the course of some synthetic investigations we noted that the monoepoxide of *cis,cis*-1,5-cyclooctadiene (III) reacted with the complex formed from mercuric acetate in THF–water[8] much more rapidly than expected. Thus, while cyclooctene requires *ca.* 2 hr for decolorization of the complex,[8] III decolorized the reaction mixture in about 5 sec at 25°. (It has been pointed out that this "time to color disappearance" is at least roughly related to the actual oxymercuration rate.[8]) The products from III, after demercuration with sodium borohydride,[8] were shown to consist of the bicyclic ether alcohols IV and V, in a ratio of 1:3. The same products were obtained in the same ratio when the mercuration reaction was carried out in glacial acetic acid. The structures of IV and V were determined by Jones oxidation of the mixture of alcohols and Wolff–Kishner reduction of the ketone mixture to a mixture of the bicyclic ethers VI and VII, which were identified by comparison with known samples obtained by the method of Bordwell and Douglass.[9] The stereochemistry of the hydroxyl groups in IV and V was shown to be trans to the ether oxygen by formation of the same two alcohols through oxymercuration–demercuration of the trans diol VIII. The ratio of IV to V from this route was distinctly different from that obtained from III, being 72:28, almost exactly reversed. (Oxymercuration of VIII with mercuric nitrate in water, however, is an excellent way to prepare pure V. See Experimental Section.) The interrelations are shown in Scheme I. As a further check, the oxymercuration–demercuration of the cis diol IX was examined and found to yield two different ether alcohols, the exo isomers X and XI in a ratio of 88:12.[10]



IX X XI

A mechanism involving rapid prior hydrolysis of III to diol VIII, followed by rapid oxymercuration of VIII, can easily be ruled out, since both cyclooctene oxide and styrene oxide were found to be inert to brief exposure to the reaction conditions. Also, the gross difference in ratio of the two alcohols from III and VIII makes this mechanism untenable.

Another mechanism, suggested by a referee, would involve normal addition of mercuric ion to give the hydroxy epoxide XII, followed by cyclization either at this stage or after demercuration. While such a *trans*-hydroxy epoxide as XII would almost certainly cyclize to a bicyclic ether alcohol,[11] we feel that this mechanism is

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[1] (a) Supported in part by the Alfred P. Sloan Foundation. (b) presented before the Organic Division at the 159th National Meeting of the American Chemical Society, Houston, Tex., Feb 1970. (c) Alfred P. Sloan Research Fellow, 1968–1970.

[2] (a) S. Winstein, E. Allred, R. Heck, and R. Glick, *Tetrahedron*, **3**, 1 (1958). (b) For a review of this area, see B. Capon, *Quart. Rev.* (*London*), **18**, 45 (1964). (c) For a recent study involving methoxy oxygen participation, see J. R. Hazen, *J. Org. Chem.*, **35**, 973 (1970).

[3] G. T. Kwiatkowski, S. J. Kavarnos, and W. D. Closson, *J. Heterocycl. Chem.*, **2**, 11 (1965).

[4] S. S. Searles and M. Tamres, *J. Amer. Chem. Soc.*, **73**, 3704 (1951).

[5] M. Brandon, M. Tamres, and S. Searles, *ibid.*, **82**, 2129 (1960); M. Tamres and M. Brandon, *ibid.*, **82**, 2134 (1960).

[6] H. C. Brown and M. Gerstein, *ibid.*, **72**, 2926 (1950).

[7] H. G. Richey, Jr., and D. V. Kinsman, *Tetrahedron Lett.*, 2505 (1969).

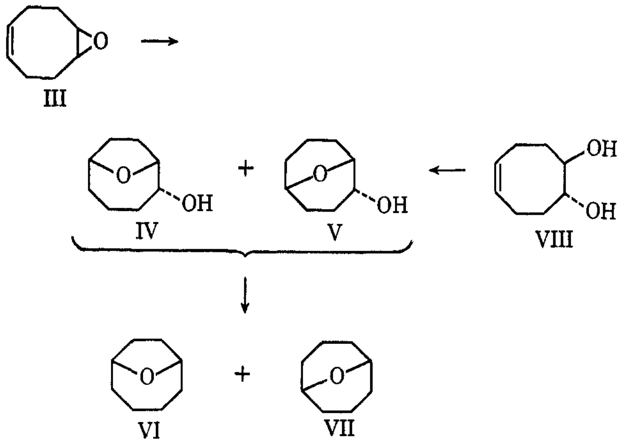
[8] H. C. Brown and P. Geoghegan, Jr., *J. Amer. Chem. Soc.*, **89**, 1522 (1967); *J. Org. Chem.*, **35**, 1844 (1970).

[9] F. G. Bordwell and M. L. Douglass, *J. Amer. Chem. Soc.*, **88**, 993 (1966).

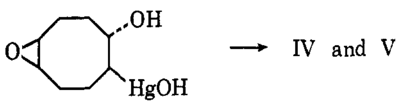
[10] Authentic samples of IV, V, and X were obtained from Professor Leo Paquette of the Department of Chemistry, The Ohio State University, and were shown to be identical with our compounds by comparison of gc retention times on several columns. We thank Professor Paquette for his generous help. See L. A. Paquette and P. C. Storm, *J. Amer. Chem. Soc.*, **92**, 4295 (1970).

[11] Epoxidation of 4-cyclooctenol with *m*-perbenzoic acid yields directly a mixture of IV and V, and *cis*-4-cycloocten-1-ol oxide: unpublished work of J. L. Jernow. See also J. K. Crandall, J. P. Arrington, and C. F. Mayer, *J. Org. Chem.*, **36**, 1428 (1971).

SCHEME I



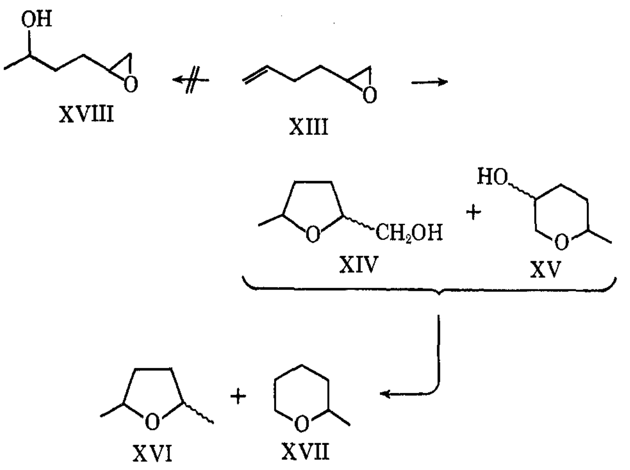
also unlikely. First, it would require very stereospecific oxymercuration to give exclusively XII, since the *cis*-hydroxy epoxide would probably survive and be easily detectable. Second, such a mechanism would not explain the enhanced reaction rate of III (*vide infra*). Third, oxymercuration of III in anhydrous methanol yields a mixture of ethers, after demercuration, which appear to be simply the methoxy analogs of IV and V. No evidence for a cyclooctene oxide group, easily detectable by nmr (δ 3.0–3.1), could be found in this latter reaction product. Clearly, one would not expect a methoxy group to open an epoxide ring under these mild conditions. (The *trans*-4,5-epoxycyclooctyl acetate is known to be fairly stable.)[12]



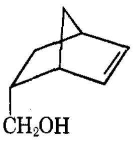
XII

To test whether oxirane-oxygen participation would compete with normal oxymercuration in an acyclic system, the reaction of the monoxide of biallyl (1,5-hexadiene) (XIII) was examined. From treatment of XIII with mercuric acetate in THF–water and demercuration of the products was obtained a complicated mixture of alcohols. The nmr spectrum of this mixture was devoid of the characteristic terminal epoxide proton resonances in the δ 2.5–3.0 region.[13] Conversion of the alcohol mixture to tosylates and reduction with lithium aluminum hydride yielded a mixture of *cis*- and *trans*-2,5-dimethyltetrahydrofuran (XVI) and 2-methyltetrahydropyran (XVII) in about 60:40 ratio, implying that the initially obtained alcohol products are probably XIV and XV, as indicated in Scheme II. It should be noted that the tosylates of XIV and XV could conceivably equilibrate under the conditions of reduction, and that epoxy alcohol XVIII, if present, might also be converted to XVI and/or XVII under these conditions. Clearly, though, the bulk of the reaction must proceed generally as indicated in Scheme II.

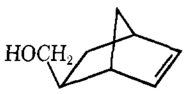
SCHEME II



Neighboring-group participation during oxymercuration often leads to considerable rate acceleration, *e.g.*, *endo*-5-hydroxymethyl-2-norbornene (XIX), which yields a ring-closed ether, reacts at least 10^2 times faster than its exo epimer (XX),[14] and both 4-penten-1-ol and 5-hexen-1-ol undergo oxymercuration at accelerated rates relative to unsubstituted 1-alkenes and yield cyclic oxymercuri ethers.[15] The approximately 10^3-fold increase in reactivity of III over that of *cis*-cyclooctene, mentioned previously, is probably not a good measure of the anchimeric effect of the oxirane oxygen, however. This is clearly indicated by the relative rate data in Table I. From the *ca.* 10^2-fold acceleration of bicyclo[6.1.0]non-4-ene (XXI) over *cis*-cyclooctene, it is clear that a major portion of the reactivity of III must be geometric in origin. It should be noted that XXI yields only a mixture of normal oxymercuration products and the cyclopropane ring survives intact.[16] The geometries about the double bonds in III and XXI should be essentially identical. The 50-fold difference in rate between III and XXI is probably much closer to a true measure of the anchimeric effect, but does not take into account the rate-retarding inductive effect of the oxygen in III. Halpern and Tinker report that oxymercuration in aqueous acid media is rather sensitive to inductive effects ($\rho^* = -3.3$)[15] and one would expect a modest effect in III. Crude kinetic data also indicate that the acyclic epoxy olefin XIII exhibits enhanced reactivity relative to an unsubstituted terminal alkene, but is apparently less reactive than analogous



XIX



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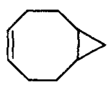
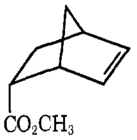
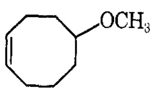


XXI



XXII



XXIII

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[12] A. C. Cope, B. S. Fisher, W. Funke, J. M. McIntosh, and M. A. McKervey, *J. Org. Chem.*, **34**, 2231 (1969).

[13] N. S. Bhacca, D. P. Hollis, L. F. Johnson, and E. A. Pier, "NMR Spectra Catalog," Varian Associates, Palo Alto, Calif., 1963, Spectra No. 193, 558.

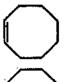
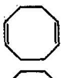
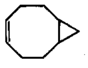
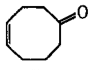
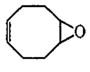
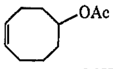
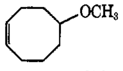
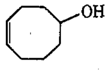
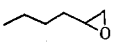
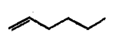
[14] A. Factor and T. G. Traylor, *J. Org. Chem.*, **33**, 2607 (1968).

[15] J. Halpern and H. B. Tinker, *J. Amer. Chem. Soc.*, **89**, 6427 (1967).

[16] Strained cyclopropanes have been observed to react with mercuric ion in water; see V. I. Sokolov, N. B. Rodina, and O. A. Reutov, *J. Organometal. Chem.*, **17**, 477 (1969), and R. Y. Levina, V. N. Kostin, D. G. Kim, and T. K. Ustynyuk, *Zh. Obshch. Khim.*, **29**, 1956 (1959). Also, at higher temperatures unstrained cyclopropyl rings may be oxymercurated; see R. J. Ouellette and C. Levin, *J. Amer. Chem. Soc.*, **93**, 471 (1971).

TABLE I

RELATIVE RATES OF OXYMERCURATION AT 25° [a]

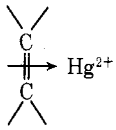
Compd	Registry no.	Relative rate[b]	Time, sec[c]	K_{Ag^+}, 1/M[d]
	931-87-3	0.0005	7200[e]	0.005[f]
	1552-12-1		15	
	31598-69-3	0.02	60	
	31598-70-6		840	1.30
	31598-71-7	1.0	5	0.10
	31598-73-9		5650	<0.10
	31598-72-8		1680	
	31598-74-0		2	29
	1436-34-6	1.1		
	821-41-0	3.3[g] 0.92[h]		29
			90	0.095[i]

[a] Reactions run in 50% THF–water, unless otherwise specified. [b] From competition reactions; precision is about ±20%. [c] Time required for decolorization of mercuric complex in THF–water; determined under conditions specified in ref 8. [d] Formation constants for silver ion π complex in water at 25°; from ref 20b unless otherwise specified. [e] From ref 8. [f] J. G. Traynham and J. R. Olechowski, *J. Amer. Chem. Soc.*, **81**, 571 (1959). [g] Absolute rate in 0.01 M aqueous perchloric acid is 10^5 l. mol sec^{-1}; see ref 14. [h] Competition against 1,5-cyclooctadiene monoxide in glacial acetic acid. [i] S. Winstein and H. J. Lucas, *J. Amer. Chem. Soc.*, **60**, 836 (1938).

hydroxyalkenes. One interesting feature is that participation by oxirane oxygen appears to be relatively independent of solvent, XIII and III both yielding cyclic products in glacial acetic acid as well as in the THF–water mixture, unlike participation by the ester carbonyl in XXII, which occurs only in aqueous media.[14]

The data in Table I also give interesting information on the effects of other neighboring groups and trigonal atoms in the cyclooctane ring. Neither reaction rate nor products reflect participation in the case of a 5-acetoxy substituent, no bicyclic material being observed after demercuration. Presumably the carbonyl oxygen, the more basic site in the acetoxy group, is too remote to interact. The slightly greater reactivity of *cis*-4-cyclooctenyl acetate, as measured by its rate of decolorization of the mercuric ion complex, may simply be due to greater solubility in 50% THF–water. Oxymercuration of *cis*-5-methoxycyclooctene (XXIII) is significantly enhanced, and yields a mixture of products containing about 30% of the bicyclic ethers VI and VII, after demercuration. The rest is a higher boiling fraction, presumably a mixture of 4- and 5-methoxycyclooctanols. The corresponding alcohol reacts extremely rapidly (as do the diols VIII and IX) and yields only VI and VII, as reported previously by Bordwell and Douglass.[9] Introduction of two trigonal atoms, as in *cis*-1,5-cyclooctadiene, leads to very rapid reaction as noted previously,[9] but replacing the double bond by a fused cyclopropane ring (as in XXI) is almost as efficient at enhancing reactivity. One trigonal atom, as in *cis*-4-cycloocten-1-one, is considerably less rate enhancing, but the ketone is still *ca.* ten times as reactive as cyclooctene in spite of an adverse inductive effect. These effects of trigonal or "semitrigonal" carbons in the cyclooctene ring are probably due to diminution of unfavorable torsional interactions and angle strain that normally occur when one of the trigonal carbons of cyclooctene is converted to tetrahedral geometry.[17]

In Table I the silver ion complexation constants (K_{Ag}) are given for several of the compounds investigated. These have generally been regarded as being indicative of rates of oxymercuration,[15,18] due to the similarity of the chemistry and electronic structures of Ag(I) and Hg(II), and it has often been postulated that oxymercuration proceeds through a mercurinium π-complex intermediate (XXIV).[19] Halpern and Tinker concluded that XXIV might be formed in a rapid preequilibrium, followed by rate-controlling rearrangement, or reaction with solvent, to yield product.[15] (The large value of ρ^* would favor rate-controlling formation of a carbon–mercury σ bond.) Since remote functional groups, particularly hydroxyl, often confer considerable stabilization on silver–olefin π complexes, presumably through chelation,[20] one might expect similar stabilization of the corresponding mercurinium π complexes. This could lead to rate enhancement by increasing the concentration of XXIV. This seems clearly *not* the case for the epoxy compounds, since III has a very low K_{Ag}, and neighboring-group participation, as discussed earlier, must be a major cause of rate acceleration. The case of the hydroxyl-substituted systems is less clear, and a portion of their enhanced reactivity may be due to stabilization of XXIV by bonding of the hydroxyl to mercuric ion, though this would require considerable reorientation of groups in the following step leading to cyclized products. Henbest and Nicholls have postulated such chelation effects to explain the stereochemistry of oxymercuration of 3-cyclohexenyl derivatives and related compounds,[21] but recent work strongly implies that the stereoselectivity of these reactions is due primarily to inductive and steric effects.[22]



XXIV

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[17] E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill, New York, N. Y., 1962, Chapter 9.

[18] C. Heathcock, *Angew. Chem., Int. Ed. Engl.*, **8**, 134 (1969).

[19] H. Lucas, F. Hepner, and S. Winstein, *J. Amer. Chem. Soc.*, **61**, 3102 (1939); N. S. Zefirov, *Russ. Chem. Rev.*, **34**, 527 (1965). For recent discussions of mercurinium ions, see W. Kitching, *Organometal. Chem. Rev.*, **3**, 61 (1968); G. A. Olah and P. R. Clifford, *J. Amer. Chem. Soc.*, **93**, 2320 (1971); and J. E. Byrd and J. Halpern, *ibid.*, **92**, 6967 (1970).

[20] (a) B. Franzus, W. C. Baird, Jr., E. I. Snyder, and J. H. Surridge, *J. Org. Chem.*, **32**, 2845 (1967); (b) D. Gray, R. A. Wies, and W. D. Closson, *Tetrahedron Lett.*, 5639 (1968); (c) See, however, C. F. Wilcox, Jr., and W. Gaal, *J. Amer. Chem. Soc.*, **93**, 2453 (1971).

[21] H. B. Henbest and B. Nicholls, *J. Chem. Soc.*, 227 (1959).

[22] (a) J. Klein and R. Levene, *Tetrahedron Lett.*, 4833 (1969); (b) M. R. Johnson and B. Rickborn, *Chem. Commun.*, 1073 (1968); (c) P. Chamberlain and G. H. Whitham, *J. Chem. Soc. B*, 1382 (1970).

Experimental Section[23]

***cis,cis*-1,5-Cyclooctadiene monoxide (III)** was prepared by the method of Traynham and Greene[24] with the following modifications: molar ratio of diene to peracid was 2.5:1 and chloroform was used as solvent. A 63% yield of III was obtained, bp 95° (30 mm) [lit.[24] bp 97–100° (40 mm)].

***cis*-Cyclooctene-*trans*-5,6-diol (VIII).**—A solution of 12.4 g (0.100 mol) of III in a mixture of 30 ml of tetrahydrofuran (THF), 120 ml of water, and about 0.5 ml of concentrated sulfuric acid was stirred at 25° for 24 hr. The mixture was then saturated with sodium carbonate and extracted several times with ether. The extract was dried with magnesium sulfate and concentrated, and the residual oil distilled, yielding 12.3 g (0.87 mol) of the diol: bp 84–87° (0.05 mm); nmr ($CDCl_3$) δ 1.3–2.5 (m, 8 H), 3.4–3.7 (m, 2 H), 3.8 (s, 2 H), and 5.4–5.7 (m, 2 H).

The dibrosylate, mp 132.5–133.5°, and its analysis have been described previously.[25]

***cis*-Cyclooctene-*cis*-5,6-diol (IX).**—To a solution of 65 g (0.60 mol) of 1,5-cyclooctadiene in 100 ml of acetone, kept at −5 to −10°, was slowly added a solution of 39 g (0.20 mol) of potassium permanganate in a mixture of 1 l. of acetone and 100 ml of water. After addition was complete (1.5 hr) the solution was allowed to warm to room temperature and then filtered through Supercel. The filtrate was concentrated under reduced pressure to *ca.* 150 ml and then extracted with five 50-ml portions of ether. The ether extract was dried with magnesium sulfate and the solvent and unreacted diene were removed under reduced pressure. The residue, after recrystallization from ether, yielded 0.89 g (6.3 mmol, 3.1% yield) of diol IX: mp 104.5–106°; nmr (DMSO-d_6) δ 1.3–2.8 (m, 8 H), 3.5 (s, 2 H), 3.8 (m, 2 H), and 5.5 (m, 2 H).

The dibrosylate, mp 146–147°, and its analysis have been described elsewhere.[25] The bis phenylurethane melted at 188–190°.

Anal. Calcd for $C_{22}H_{24}N_2O_4$: C, 69.46; H, 6.36. Found: C, 69.27; H, 6.42.

1,5-Hexadiene monoxide (XIII) was prepared in a manner similar to that of Everett and Kon[26] from biallyl and *m*-chloroperbenzoic acid. The monoxide was obtained in 44% yield, bp 119–120° (760 mm) [lit.[26] bp 119–121° (760 mm)].

***cis*-Bicyclo[6.1.0]non-4-ene (XXI)** was prepared by the procedure of Cope, *et al.*,[27] bp 167° (760 mm) [lit.[27] bp 65–68° (22 mm)].

***cis*-4-Cycloocten-1-ol,** its acetate, and the corresponding ketone were available from previous work.[20b]

5-Methoxycyclooctene (XXIII).—To 2.5 g (0.020 mol) of *cis*-4-cycloocten-1-ol in 20 ml of ether was added slowly 20 ml of 5% methyllithium in ether (1.0 g, 0.040 mol) at 25° with stirring. After addition was complete, 5.5 g (0.050 mol) of dimethyl sulfate (neat) was added dropwise. The mixture was then heated at reflux for 24 hr. It was then cooled and drowned in ice–water, and the ether layer was separated, dried, and concentrated. Distillation of the residual oil gave 2.1 g (0.015 mol, 75%) of XXIII: bp 77° (26 mm); ir (neat) 1473 (m), 1097 (s), and 728 cm^{-1} (m); nmr (CCl_4) δ 1.2–2.4 (m, 10 H), 3.0–3.3 (m, 1 H), 3.2 (s, 3 H), and 5.2–5.8 (m, 2 H).

Anal. Calcd for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 76.85; H, 11.21.

Preparative oxymercuration reactions were mostly carried out by the method of Brown and Geoghegan.[8] The olefin (0.01 mol) was added neat to a rapidly stirred mixture of 0.01 mol of mercuric acetate in 20 ml of 50% (v/v) THF–water at 25°. The times required for disappearance of the yellow mercuric complex, which are roughly related to the rate and extent of reaction,[8] are reported in Table I. Reduction and isolation of products were as described previously.[8]

Oxymercuration of *cis,cis*-1,5-Cyclooctadiene Monoxide (III).—By Brown's procedure,[8] 1.3 g (92%) of material, bp 125–128° (8 mm), was obtained. Analysis by gc on a 12 ft × 0.25 in. column of 10% tris-1,2,3-cyanoethoxypropane (TCEP) showed it to be a mixture of 24% *endo*-9-oxabicyclo[4.2.1]non-2-ol (IV) and 76% *endo*-9-oxabicyclo[3.3.1]non-2-ol (V). The identities of IV and V were confirmed both by comparison of gc retention times with those of authentic samples,[10] and by removal of the hydroxyl groups (Jones oxidation, Wolff–Kishner reduction) yielding a mixture of 9-oxabicyclo[4.2.1]nonane (VI) and 9-oxabicyclo[3.3.1]nonane (VII) in *ca.* a 1:3 ratio. These ethers were identified by comparison of ir spectrum of the ether mixture and gc retention times 6 ft × 0.125 in. column of 10% diglycerol) with those of an authentic mixture of VI and VII prepared from 1,5-cyclooctadiene by the method of Bordwell and Douglass.[9]

Oxymercuration of III in acetic acid was carried out by adding 2.5 g (0.020 mol) of III to a suspension of 6.4 g (0.020 mol) of mercuric acetate in 10 ml of acetic acid at 25°. After 3 min of stirring, the solution became clear and slightly warm. After an additional 10 min of stirring, the mixture was poured into 250 ml of saturated sodium chloride solution and allowed to stand overnight. A white solid was then collected by filtration, dissolved in 40 ml of 1.5 *N* sodium hydroxide, and treated with 20 ml of 0.5 *N* sodium borohydride in 3 *N* sodium hydroxide. Workup according to the usual procedure[8] yielded 1.9 g (0.013 mol, 65%) of a mixture of IV (29%) and V (71%), as shown by gc.

Oxymercuration of III in anhydrous methanol was carried out in a manner similar to that carried out in acetic acid, except that the reaction mixture, after 10 min, was treated directly with aqueous sodium hydroxide and sodium borohydride. Workup in the usual procedure yielded 2.5 g (0.016 mol, 80%) of a mixture of what appeared to be methyl ethers: bp 94–96° (16 mm); nmr ($CDCl_3$) δ 1.3–2.3 (m, 10 H), 3.35 (s, 3 H), 3.8–4.1 (m, 3 H) (the region δ 2.4–3.1, where epoxide protons would be expected, was entirely clear); ir (neat) 1110 (s), 1070 (m), 1049 (w), 1002 (m), 991 (m), 901 (m), 872 cm^{-1} (m). (Compare nmr and ir with that of V, for example.)

Oxymercuration of *cis*-cyclooctene-*trans*-5,6-diol (V,III) by Brown's procedure[8] yielded 0.78 g (5.5 mmol, 55%) of a mixture of ether-alcohols, bp 130–132° (10 mm), shown to consist of 77% IV and 23% V by gc on a TCEP column.

Oxymercuration of 7.1 g (0.050 mol) of VIII by adding it neat to 16.2 g of mercuric nitrate in 120 ml of water and stirring at 25° for 2 hr yielded, after treatment with 120 ml of 3 *N* sodium hydroxide and 100 ml of a 0.5 *M* sodium borohydride in 3 *N* sodium hydroxide solution and isolation of the organic material in usual fashion, 5.2 g (0.041 mol, 82%) of *endo*-9-oxabicyclo[3.3.1]-nonan-2-ol (V), bp 130–135° (10 mm), mp 73–73.5°. Analysis by gc (TCEP column) showed a single peak with retention time identical with that of authentic V:[10] ir ($CHCl_3$) 1073 (s), 1045 (s), 992 (m), 897 (m), and 862 cm^{-1} (m); nmr (CCl_4) δ 1.4–2.2 (m, 10 H), 3.5–4.0 (m, 4 H).

Oxymercuration of *cis*-cyclooctene-*cis*-5,6-diol (IX) by Brown's procedure[8] yielded 0.85 g (6.0 mmol, 60%) of a mixture of ether–alcohols, bp 120–122° (7 mm). The major component (88%) had a gc retention time (TCEP column) identical with that of authentic[10] *exo*-9-oxabicyclo[4.2.1]non-2-ol (X). The minor component (12%) was assumed to be *exo*-9-oxabicyclo[3.3.1]-non-2-ol (XI).

Oxymercuration of bicyclo[6.1.0]non-4-ene (XXI) by Brown's procedure[8] gave a 60% yield of a mixture of alcohols, bp 117–122° (22 mm). The nmr spectrum of the mixture was identical with that of the starting material except for the absence of vinyl protons and the presence of –CHOH protons. Oxidation (Jones method) of 3.5 g (0.025 mol) of the alcohol mixture yielded a single ketone (4-bicyclo[6.1.0]nonanone)[28] (XXVI) in 60% yield (2.0 g, 0.0145 mol), bp 118–120° (35 mm), whose 2,4-dinitrophenylhydrazone melted at 160.5–161.5° (ethanol).

Anal. Calcd for $C_{15}H_{18}N_4O_4$: C, 56.60; H, 5.70. Found: C, 56.44; H, 5.73.

Wolff–Kishner reduction of the ketone XXV on a small scale yielded a hydrocarbon, bicyclo[6.1.0]nonane, identical (gc, nmr) with that obtained from XX by catalytic hydrogenation.

Oxymercuration of 1,5-hexadiene monoxide (XIII) by the usual procedure yielded a complicated mixture of alcohols in 65% yield, bp 85–91° (12 mm). Conversion of this mixture to

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(23) All nmr spectra were recorded using a Varian A-60A spectrometer with tetramethylsilane as internal standard. Infrared (ir) spectra were recorded on a Beckman IR-10 spectrometer. Gas chromatographic (gc) analyses were performed using Hewlett-Packard 5750 and Varian A-90 gas chromatographs. Melting and boiling points are uncorrected. Unless otherwise specified, all materials were obtained from commercial sources.

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(28) This ketone has been prepared previously [K. B. Wiberg and A. Demeijere, *Tetrahedron Lett.*, 59 (1969)], but its properties were not described.

tosylates and reduction with lithium aluminum hydride in the usual manner gave a mixture of 2,5-dimethyltetrahydrofuran (cis and trans) and 2-methyltetrahydropyran (*ca.* 6:4 ratio by gc) identical by nmr and gc with a similarly proportioned authentic mixture.

Oxymercuration of 5-methoxycyclooctene (XXIII) (Brown's procedure[8]) gave a 70% yield of a mixture consisting of about 30% of ethers VI and VII and 70% of material of longer gc retention time, presumably a mixture of 4- and 5-methoxycyclooctanols.

Oxymercuration of 5-acetoxycyclooctene was carried out in usual fashion. The product (*ca.* 60%) contained a fair amount of unreacted unsaturated acetate, no bicyclic ethers VI or VII, but a considerable amount of material of very long gc retention time. This latter fraction was presumably a mixture of various cyclooctanediols and monoacetates thereof.

Stabilities of Oxides to Reaction Conditions.—Cyclooctadiene monoxide was found to be stable to glacial acetic acid at 25° for periods of up to 2 hr, and to 50% THF–water for even longer periods of time, as measured by gc analysis of sample mixtures. Saturated olefin oxides, such as cyclooctene oxide, styrene oxide, and propylene oxide, were unaffected by several minutes of exposure to 0.005 M mercuric acetate in 50% THF–water. Cyclooctene oxide could be recovered in 75% yield after 72 hr of exposure to these conditions.

Competition Experiments.—In aqueous THF, a solution of *ca.* 1 mmol of each of the competing olefins in 1 ml of THF was stirred at 25° while 1.0 ml of 0.1 M mercuric acetate in water was added. After a period of 0.5–3 min, 1 ml of 3 N sodium hydroxide followed by 1 ml of sodium borohydride solution was added, the aqueous layer was saturated with sodium hydroxide pellets, and the THF layer was analyzed by gc.

In acetic acid, a mixture of the two olefins (*ca.* 1 mmol each) was added to a stirred solution of 0.2 mmol of mercuric acetate in 1 ml of acetic acid at 25°. After 3 min of stirring, the flask was chilled and 3 N sodium hydroxide was added until basic. Reduction was then carried out with 0.5 M sodium borohydride in 3 N sodium hydroxide, the products were extracted with ether, and analysis was performed by gc.

Variation of reaction times between 0.5 and 3 min had no apparent effect on product composition. Each reported relative rate is the average of at least two experiments using different proportions of reactants. Reproducibility was at least of the order of 20%. It has been shown that relative rates measured under these conditions correlate excellently with measured absolute rates.[22c]

Registry No.—IV, 29359-88-4; IV (methoxy analog), 31598-89-7; V, 31598-90-0; V (methoxy analog), 31662-28-9; VIII, 31598-91-1; IX, 31603-51-7; IX bisphenylurethane, 31603-52-8; X, 29359-87-3; XI, 31598-76-2; XXVI, 28405-47-2; XXVI 2,4-DNPH, 31603-54-0.

Replacement of the Carbonyl Oxygen of Hydroxy Ketones by Methylene and 1,1-Ethano Groups by Reaction with the Simmons–Smith Reagent[1]

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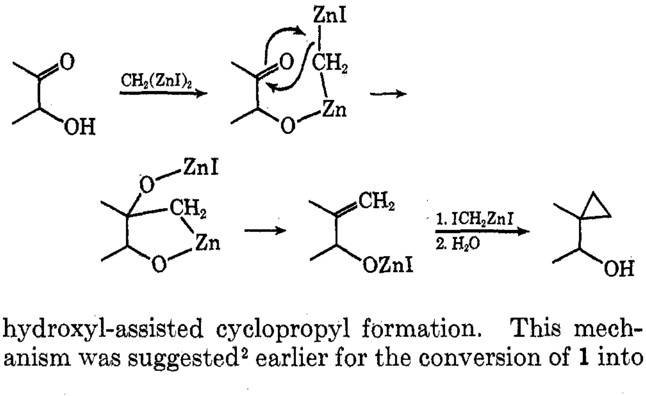
The reagent prepared from methylene iodide and zinc–copper couple replaces the carbonyl oxygen of ketones containing a neighboring hydroxyl group by the methylene and 1,1-ethano groups. Reaction conditions have been defined which allow the formation of either one of these products.

In a previous communication we reported[2] the unexpected formation of methylene and ethano derivatives **2** and **3** by reaction of 17β-acetoxy-11β-hydroxyestr-5(10)-en-3-one (**1**) with a reagent derived from methylene iodide and zinc–copper couple (Simmons–Smith reagent). Further work has shown that the reaction is not limited to hydroxy ketones; for example, 5α-androstan-3-one (**4**) was converted into a mixture of 3,3-methylene-5α-androstane (**5**), 3,3-ethano-5α-androstane (**6**), and other unidentified products. However, good yields were obtained only in the cases where assistance by hydroxyl is sterically allowed. No reaction was observed with α,β-unsaturated carbonyl groups, although the dienone **7** gave the derivatives **8a** and **8b** by by a normal cyclopropyl-forming reaction on the more nucleophilic, terminal double bond.

The reaction of α-hydroxy ketones with the Simmons–Smith reagent prepared in the usual manner led to mixtures of the methylene and ethano derivatives. For example, 17α-hydroxypregn-4-ene-3,20-dione (**9**) gave a mixture of **10** and **11**. Variation of the reaction conditions indicated that the relative yields of the two products were critically but reproducibly dependent on the procedure by which the reagent was prepared. A reagent formed *in situ* or by refluxing an ether solution of methylene iodide with zinc–copper couple for up to 1 hr reacted with the ketone **9** to give the ethano derivative **11** in high yield, whereas a reagent preformed by refluxing for 2–4 hr reacted to give the methylene derivative **10**, also in high yield. These results can be rationalized in terms of an inhomogeneous and time-variable composition for the reagent.

Olefination of aldehyde and ketone carbonyls by *gem*-dimetallic reagents of the type MCH_2M is quite general;[3] we therefore attribute the formation of ethano derivatives from hydroxy ketones to hydroxyl-assisted methylenation of the carbonyl by a species of the general structure $\cdots ZnCH_2Zn \cdots$, followed by a typical hydroxyl-assisted cyclopropyl formation. This mechanism was suggested[2] earlier for the conversion of **1** into



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(1) Publication no. 385 from the Syntex Institute of Organic Chemistry. For publication no. 384, see L. Tökés, "Photochemical Cycloadducts," part VI, in press.

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