2.5 hr. The removal of morpholine under reduced pressure gave white crystals and 5.4 g of red oils. The crystals were filtered, and recrystallization from ethanol gave 6.1 g (91%) of morpholine hydrobromide, mp 202°, lit.[9] mp 202°.

The filtrate was stirred with 2 *N* potassium hydroxide solution for 1 hr at room temperature. The solution was then acidified with hydrochloric acid and extracted with chloroform. After drying, the chloroform was evaporated to dryness and the residue was recrystallized from water to yield 1.1 g (49%) of **1**, mp 104–105.5°.

**Reaction of 2,5-Dibromocyclopentaone (9) with Morpholine.**—To a stirred solution of 21.7 g (0.25 mol) of morpholine in 100 ml of dry ether, 12.1 g (0.05 mol) of **9** was added dropwise with an ice–water bath cooling. The mixture was stirred for several hours at room temperature. The precipitated morpholine hydrobromide was filtered and the removal of ether and surplus morpholine under reduced pressure gave 8.1 g of viscous oils. The oils were crystallized after standing for a few days at −70°. The crystals that formed were recrystallized from a small amount of methanol, affording 4.8 g (57.5%) of 2-morpholino-2-cyclopentenone (**10**): mp 63°; uv max (*n*-hexane) 285 mμ (ε 20,000); ir (KBr) 1690 (C=O), 1613 (C=C), 1110 cm$^{-1}$ (C–O–C); nmr ($CDCl_3$) δ 6.42 (broad s, 1), 3.81 (m, 4), 3.09 (m, 4), 2.47 (almost s, 1).

*Anal.* Calcd for $C_9H_{13}O_2N$: C, 64.65; H, 7.84. Found: C, 64.61; H, 8.02.

**Reaction of 2,6-Dibromocyclohexanone (11) with Morpholine.**—To a solution containing 28.0 g (0.11 mol) of **11** in 100 ml of absolute ether, 47.6 g (0.55 mol) of morpholine was added at room temperature, dropwise and with stirring. After standing overnight, the deposited morpholine hydrobromide was filtered off, and the resulting oil was distilled to yield 5.1 g (25.5%) of 1-cyclopentene-1-carboxymorpholide (**12**): bp 113–114° (0.07 mol); $n^{20}D$ 1.5254; $d^{20}_4$ 1.1326; uv max (EtOH) 213 mμ (ε 10,000); ir (film) 1620 (C=O), 1120 cm$^{-1}$ (C–O–C); nmr ($CCl_4$) δ 5.80 (broad s, 1), 3.57 (sharp s, 8), 2.48 (m, 4), 1.86 (m, 2).

*Anal.* Calcd for $C_{10}H_{15}O_2N$: C, 66.27; H, 7.73. Found: C, 66.04; H, 7.58.

A solution of 1.4 g (0.0077 mol) of **12** in 12 ml of 2 *N* hydrogen chloride was stirred at 80° for 2 hr. The reaction mixture was then cooled and filtered, affording 0.4 g (80%) of 1-cyclopentene-1-carboxylic acid, mp 124°, lit.[10] mp 120–121°.

**Reaction of 2-Bromocyclohexanone with Morpholine.**—To a solution of 9.8 g (0.055 mol) of 2-bromocyclohexanone in 50 ml of dry ether, 14.7 g (0.17 mol) of morpholine was added with an ice–water bath cooling. After standing overnight at room temperature, the reaction mixture was then filtered and the resulting oil was distilled to yield 5.1 g (50.5%) of 2-morpholinocyclohexanone, bp 114–115° (3 mm), lit.[11] bp 148° (20 mm).

*Anal.* Calcd for $C_{10}H_{17}O_2N$: C, 65.54; H, 9.39; N, 7.64. Found: C, 65.40; H, 9.49; N, 7.53.

**Registry No.**—**1**, 80-71-7; **6**, 24454-32-8; **10**, 24454-33-9; **12**, 24454-34-0.

(9) J. Gilbert and H. Gault, *Bull. Soc. Chim. Fr.*, 2975 (1965).

(10) H. Sletter and K. Kiehs, *Ber.*, **98**, 2099 (1965).

(11) M. Mousseron, J. Jullien, and Y. Jolchine, *Bull. Soc. Chim. Fr.*, 757 (1952).

# Mechanism of the Cationic Addition-π,π-Transannular Cyclization of Disubstituted Methanes with 1,5-Cyclooctadiene

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The reaction of 1,5-cyclooctadiene with methoxymethyl acetate, dimethoxymethane, or chloromethyl methyl ether (Lewis acid catalysis) afforded mainly addition-π,π-transannular cyclization products, *cis*-bicyclo[3.3.0]-octane derivatives which exclusively consisted of *endo*-2-methoxymethyl isomers, and bicyclo[3.2.1]octane derivatives. The stereochemistry of the products and the high tendency of cyclization showed that attack of methoxymethyl cation was from the outside of the boat 1,5-cyclooctadiene with a simultaneous nucleophilic attack of the $\Delta^5$ double bond on the transient carbonium ion, which was followed by a partially concerted attack of an anion moiety (Scheme VII).

The well-documented double-bond participation in carbonium ion solvolyses[1] suggests that unconjugated dienes of appropriate configuration and conformation should form cyclized products upon reaction with cationic species.[2] A suitable system for investigating this cationic addition-π,π-transannular cyclization is *cis,cis*-1,5-cyclooctadiene [1,5-COD]. A model indicates that its boat form, shown to be the stable conformer by dipole measurements,[3] affords the close proximity necessary for orbital overlap. In addition, double-bond participation has previously been shown to be important in the solvolysis of the related compounds, $\Delta^4$-cyclooctenyl tosylate and brosylate.[4,5]

In the present paper, reactions of several disubstituted methane–Lewis acid combinations and 1,5-COD are described which afford predominately cyclic products.[6] This high proportion of cyclic products agrees with the previously reported results from the reaction of 1,5-COD with formic acid[7] and acetyl chloride.[8]

However, the stereochemistry of the product reported from the latter reaction is quite contrary to our findings. Results more similar to ours were reported for the reaction of *cis,cis*-1,6-cyclodecadiene with $Br_2$ in methanol[9] although even these results differ in a significant manner.

The following paper describes the reaction of 1,5-COD with methoxymethylacetate, dimethoxymethane, and chloromethyl methyl ether (Lewis acid catalysis). From careful analysis of the stereochemistry of the products, a mechanism for the cationic addition–cyclization reaction is presented. The discussion of this mechanism includes a comparison with results on similar

(1) P. D. Bartlett, "Nonclassical Ions," W. A. Benjamin, Inc., New York, N. Y., 1965.

(2) Cationic addition cyclizations are also known in some instances [*e.g.*, H. F. Tiemann and F. W. Seemler, *Chem. Ber.*, **26**, 2708 (1893); L. Ruzicka, *Helv. Chim. Acta*, **6**, 483 (1923)], but detailed mechanistic investigations are rather scarce [*e.g.*, W. S. Jonnson, A. van der Gen, and J. J. Swoboda, *J. Amer. Chem. Soc.*, **89**, 171 (1967)].

(3) J. D. Roberts, *ibid.*, **72**, 3300 (1950).

(4) W. D. Closson and G. T. Kwiatkowski, *Tetrahedron Lett.*, 6435 (1966).

(5) A. C. Cope, J. M. Crisar, and P. E. Peterson, *J. Amer. Chem. Soc.*, **82**, 4299 (1960).

(6) Preliminary reports have been presented on the subject: I. Tabushi, K. Fujita, and R. Oda, *Tetrahedron Lett.*, 3815, 3755 (1967).

(7) A. C. Cope and P. E. Peterson, *J. Amer. Chem. Soc.*, **81**, 1643 (1959).

(8) T. S. Cantrell, *J. Org. Chem.*, **32**, 1669 (1967); only formation of the cyclized product was described.

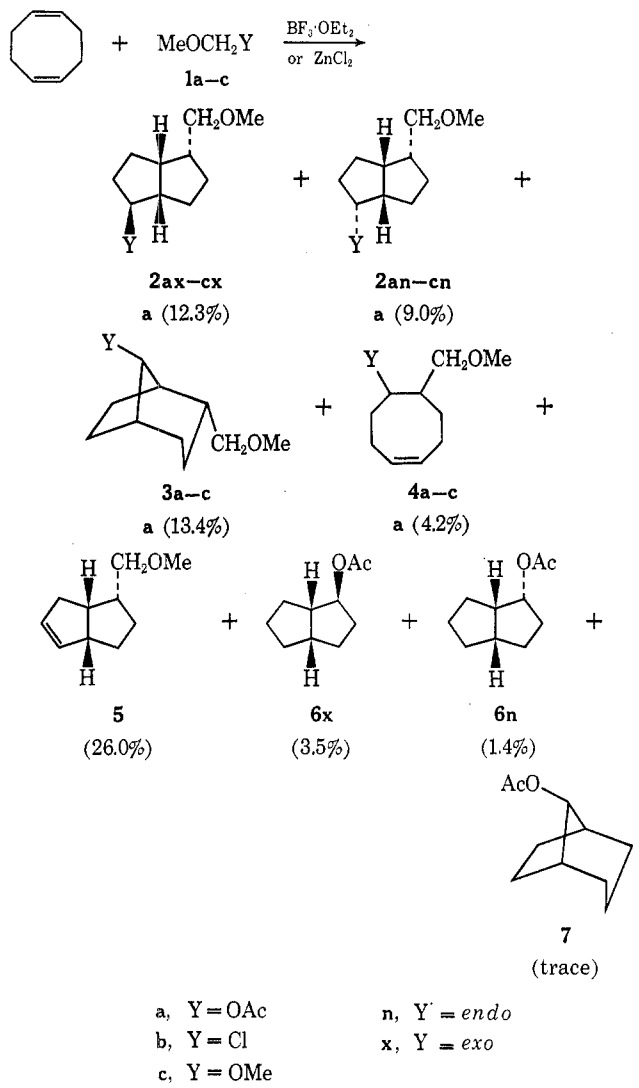
(9) F. M. Gipson, H. W. Guin, S. H. Simonsen, C. G. Skinner, and W. Shive, *J. Amer. Chem. Soc.*, **88**, 5366 (1966).

systems and an interpretation of the correlations and discrepancies.

## Results and Discussion

**Reaction of 1,5-COD with Methoxymethyl Acetate.**—The reaction gave the products shown in Scheme I.

SCHEME I




a, Y = OAc
b, Y = Cl
c, Y = OMe

n, Y = *endo*
x, Y = *exo*

The skeletal structure, *endo*-2-methoxymethyl-*cis*-bicyclo[3.3.0]octane, was determined for **2ax** and **2an** by the chemical conversion shown in Scheme II. Saponification of the isomeric acetates **2ax** and **2an** gave the alcohols **8ax** and **8an** which were converted to the tosylates, **9x** and **9n**, and reduced with lithium aluminum hydride. The main product **10n** was identified by comparison with an authentic sample prepared as shown in Scheme III. Further, the brosylates **11x** and **11n** from the mixture of alcohols **8x** and **8n** were treated with trifluoroacetic acid and then hydrogenated on $PtO_2$ to give **10n** as the major product.

Oxidation of the mixture of alcohols **8n** and **8x** with the chromic oxide–pyridine complex gave a single ketone, **12**, indicating that the acetates **2ax** and **2an** were stereoisomers. The two were distinguished by comparison of nmr spectra of the alcohols. By analogy to the nmr absorptions of the known *exo*- and *endo*-*cis*-bicyclo[3.3.0]oct-2-yl alcohols,[10] the absorption in **8n** at $\tau$ 5.95 (broader) was assigned to the *exo* proton, $\alpha$ to the hydroxyl, and the absorption in **8x** at $\tau$ 6.40 to the *endo* proton.

The assignment of the structure for **3a** was based mainly on spectroscopic evidence. The infrared spectrum of **3a** showed the presence of methoxyl (1100 $cm^{-1}$) and acetoxyl (1700 and 1245 $cm^{-1}$). The nmr spectrum showed a singlet for the $\alpha$ proton to the acetoxyl group, very similar to the absorption reported in the spectrum of *anti*-bicyclo[3.2.1]oct-8-yl acetates, **7**.[6] Hydrolysis of **3a** produced the alcohol **13**. Oxidation of alcohol **13** to the corresponding ketone was much slower than oxidation of alcohol **8**, a fact consistent with the assigned structure for **13**.[11]

The acetates **6x**, **6n**, and **7** were not soluble in aqueous silver nitrate and were unreactive toward $Br_2$–$CH_2Cl_2$. These saturated acetates were identified by comparison of their vapor phase chromatographs and infrared spectra with those of authentic samples.

The olefin **5** was soluble in aqueous silver nitrate and reacted readily with $Br_2$–$CH_2Cl_2$. Hydrogenation on $PtO_2$ converted the olefin to **10n**, identical with the authentic sample from Scheme III.

Contrary to the previous report of a single product **17b**,[12] dehydration of cyanohydrin **16** produced two cyanides **17a** and **17b** in a ratio of 55:45 as determined by analysis of either the nmr spectrum or the vapor phase chromatograph. This mixture of products is more reasonable since simple *trans* elimination should lead to both isomers. The mixture of cyanides was hydrolyzed to a mixture of isomeric carboxylic acids **18a** and **18b** present in a ratio of 56:44; hydrogenation of this mixture quantitatively produced a single saturated carboxylic acid **19n**. Completion of the reaction scheme produced a mixture of saturated ethers **10n** and **10x**, the latter compound also being synthesized by another reaction sequence shown in Scheme IV.

**Reaction of 1,5-COD with Chloromethyl Methyl Ether or Dimethoxymethane.**—The reactions gave the products shown in Scheme I.

Comparison of the product composition for these two reactions and the previously discussed reaction with methoxymethylacetate are shown in Table I. Product determinations were made by chemical conversions to appropriate derivatives and by nmr measurements.

TABLE I

PRODUCT COMPOSITION (PER CENT)

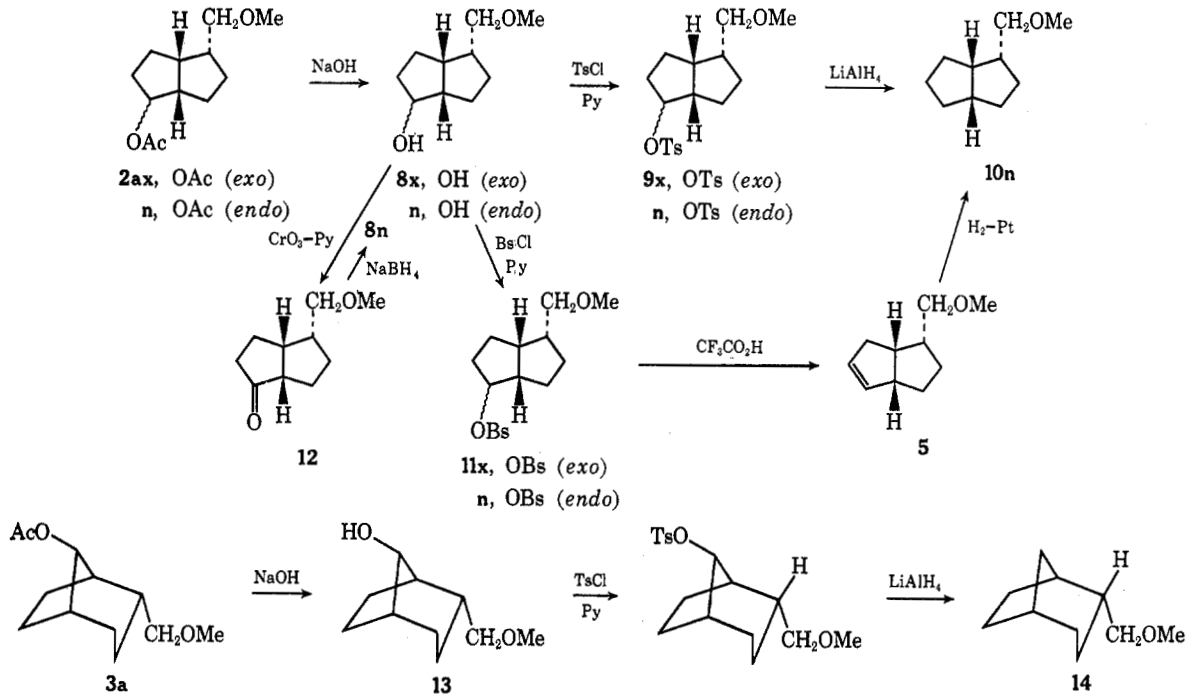
| Product | 2x | 2n | 3 | 4 |
|---|---|---|---|---|
| a | 31.6 | 23.9 | 34.4 | 10.8 |
| b | 22.6 | 26.4 | 12.2 | 38.8 |
| c | 15.2 | 24.2 | 17.9 | 42.7 |

(10) E. W. C. Wong and C. C. Lee, *Can. J. Chem.*, **42**, 1245 (1964); the $\alpha$ proton to the hydroxyl group in *exo*-*cis*-bicyclo[3.3.0]oct-2-yl alcohol absorbs at $\tau$ 6.27; the absorption for the corresponding proton in the *endo* isomer is broader and is at $\tau$ 5.91.

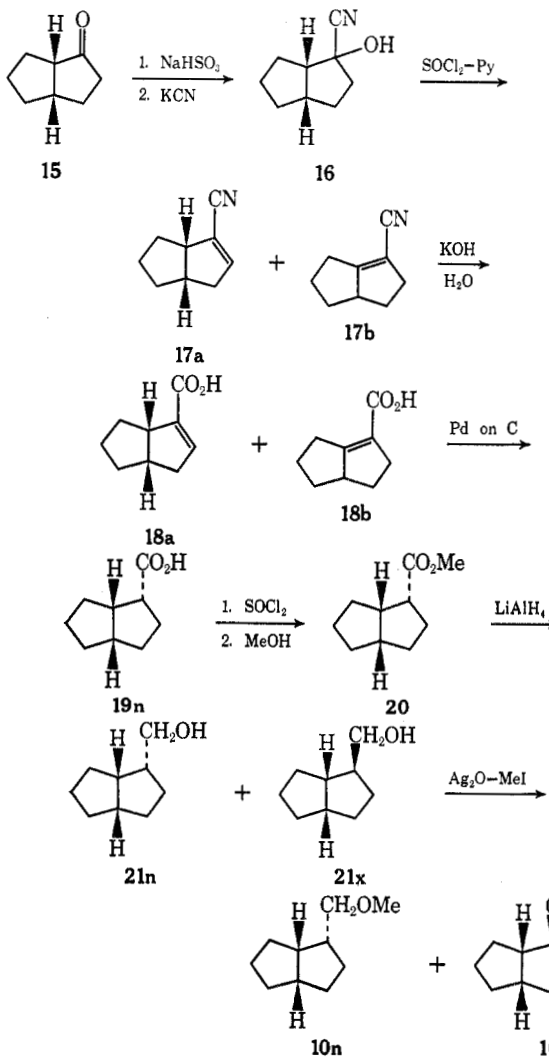
(11) The hydroxyl function on the highly strained bridge of the bicyclic compound (*e.g.*, bicyclo[3.2.1]oct-8-yl alcohol) is reasonably expected to be oxidized more slowly than that of relatively less strained compounds (*e.g.* *cis*-bicyclo[3.3.0]oct-2-yl alcohol), because oxidation to ketone increases bond angle strain. *syn*-Bicyclo[3.2.1]oct-8-yl alcohol is oxidized 16.1 times faster than the *anti* isomer (ref 5). Therefore, it is reasonable that **13** was recovered under the reaction condition where **2ax** and **2ax** were completely oxidized.

(12) A. C. Cope and M. Brown, *J. Amer. Chem. Soc.*, **80**, 2859 (1958).

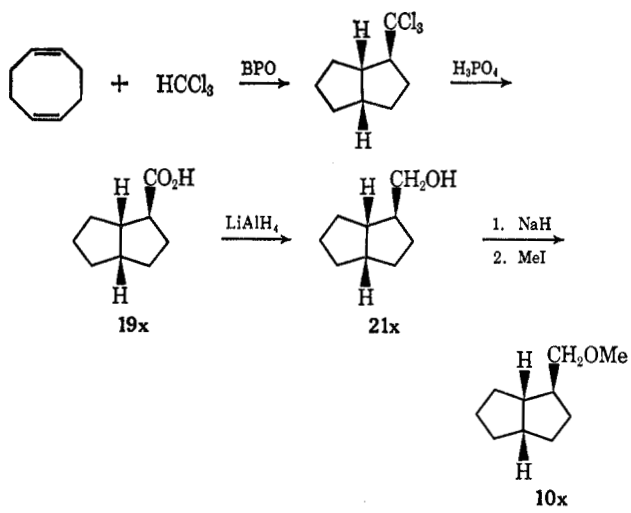
SCHEME II




SCHEME III




SCHEME IV



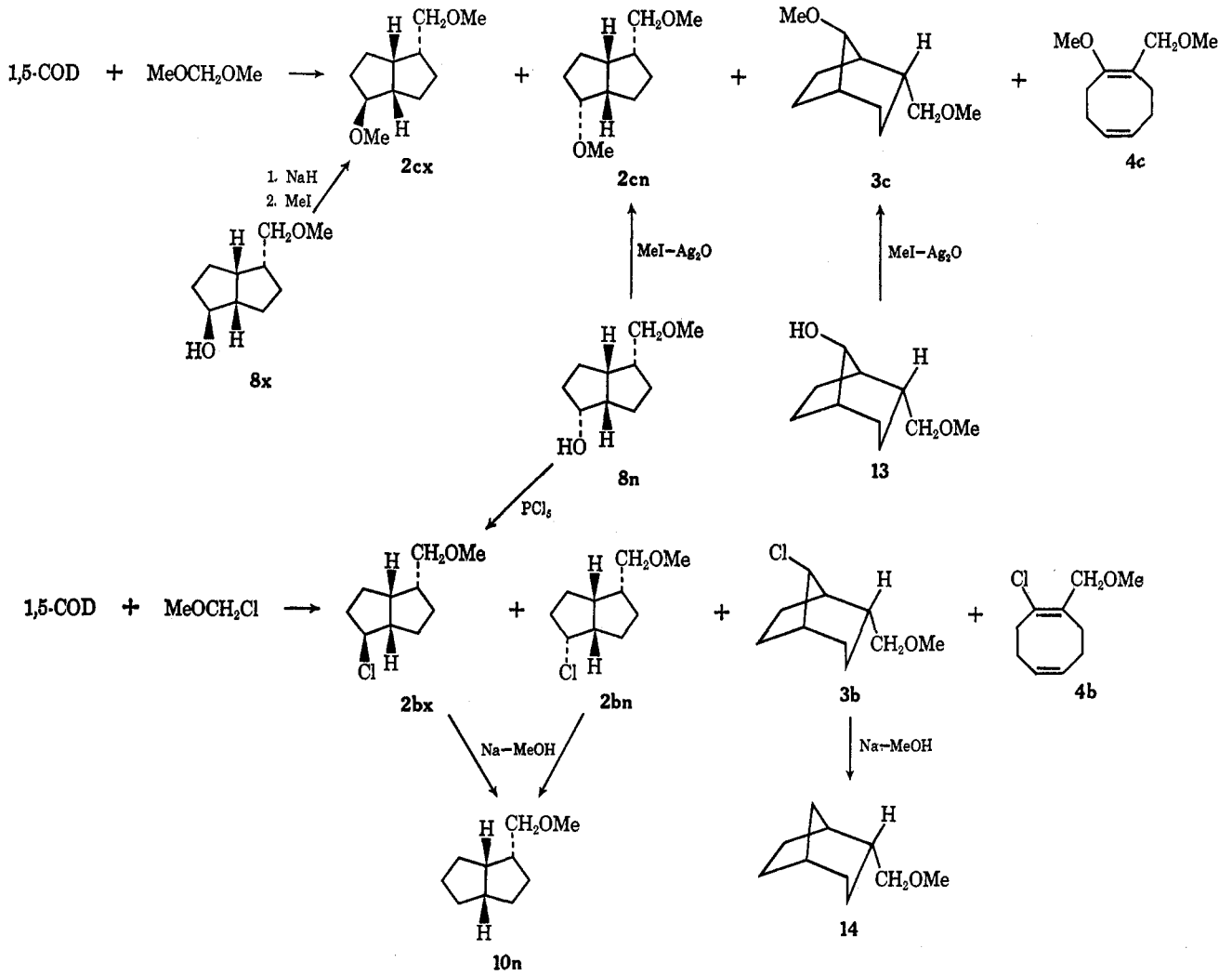

The chemical conversions and interconversions are summarized in Scheme V.

**Mechanism of the Reaction.**—The formation of the methoxymethyl cation from methoxymethyl acetate and a Lewis acid and its attack on a double bond have been previously reported.[13]

After the attack of methoxymethyl cation on one double bond, the resultant carbonium ion was attacked competitively by an anion to give the noncyclized product or by $\Delta^5$ double bond to give the cyclized product. Therefore, the amount of the cyclized product formed in the reactions of 1,5-COD with $CH_3OCH_2Y$ depends on the nucleophilicity of the anions: $BF_3$–$AcOCH_2OCH_3$, 89.8%; $ZnCl_2$–$ClCH_2OCH_3$, 61.2%; and $BF_3$–$(CH_3O)_2CH_2$, 57.3%. As the nucleophilicity

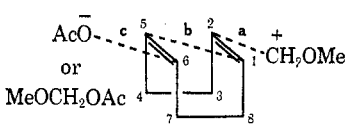
(13) R. Oda, K. Fujita, and I. Tabushi, *J. Chem. Soc. Jap., Pure Chem. Sect.*, **87**, 756 (1966).

SCHEME V



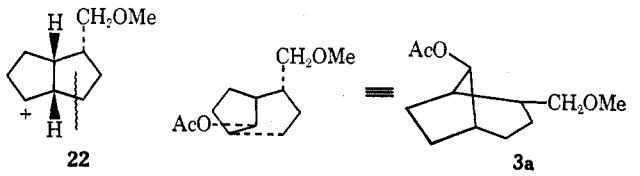

of $Y^-$ increases, $OAc^- < Cl^- < OMe^-$, the cyclization tendency (cyclizability) of 1,5-COD decreases. This is consistent with the idea that the stronger nucleophile competes more effectively with the $\Delta^5$ double bond, resulting in decreased cyclizability. In the attack of methoxymethyl cation on one double bond of 1,5-COD, exclusive formation of the *endo*-methoxymethyl isomer results despite its expected thermodynamic instability[14] relative to the *exo* isomer. Thus, the product is kinetically controlled, and attack by the methoxymethyl cation is from the outside of the preferred boat form of 1,5-COD with a simultaneous nucleophilic attack of the $\Delta^5$ double bond on the transient carbonium ion (step b), leading to new bond formation between $C_1$ and $C_5$ as shown in Scheme VI.

SCHEME VI




The stereochemistry of the acetoxyl group shows that step c, the attachment of the acetate ion, is not completely concerted with steps a and b. If step c were concerted with a and b, the acetate ion should attack the *endo* position of $C_6$ (as shown in step c of Scheme VI); if step c is nonconcerted, the thermodynamically favored *exo* product should predominate. The observed *exo/endo* ratio of 1.37 to 1.00 indicates that step c is only partially concerted with a and b. Also supporting this contention by indicating the formation of free *endo*-6-methoxymethyl-*cis*-bicyclo[3.3.0]oct-2-yl cation, (**22**) is the isolation of **3a** and **5**. The latter, a bicyclic olefin, is the result of loss of a proton from this carbonium ion **22**. The former, a bicyclo[3.2.1] derivative, results from the breaking of the $C_8$–$C_1$ bond of the carbonium ion **15** with subsequent formation of a bond from $C_8$–$C_2$ and concerted attack of acetate ion at the $C_1$ position (see Scheme VII).

SCHEME VII

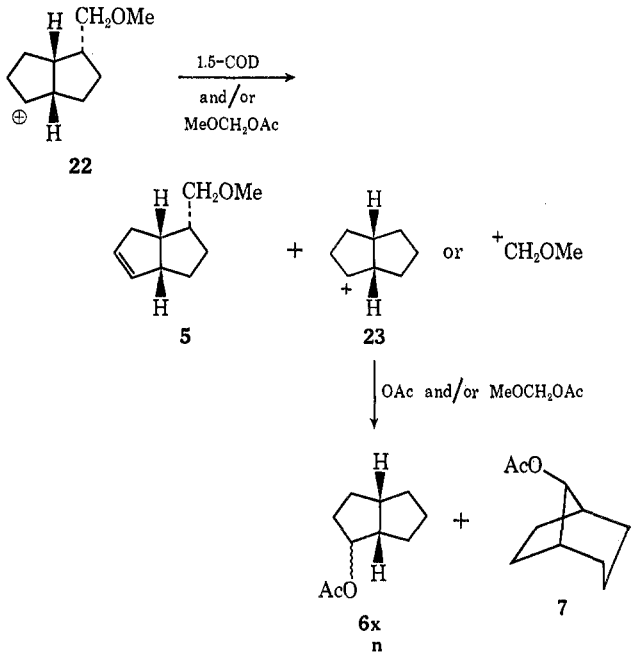



22 3a

(14) *endo-cis*-Bicyclo[3.3.0]oct-2-yl alcohol gave a mixture of 61% *exo* alcohol and 39% *endo* alcohol upon refluxing with aluminum isopropoxide in isopropyl alcohol. Also, *endo-cis*-bicyclo[3.3.0]octane-2-carboxylic acid was readily converted to the *exo* isomer on treatment with hot alcoholic base: A. C. Cope, M. Brown, and H. E. Petree, *J. Amer. Chem. Soc.*, **80**, 2852 (1958).

The remaining products isolated, **6x**, **6n**, and **7**, arise from a secondary reaction in which the elements of acetic acid are added to 1,5-COD. The best rationalization of this is that it involves proton transfer from carbonium ion **22** to 1,5-COD, resulting in olefin **5** and a new carbonium ion, bicyclo[3.3.0]oct-2-yl cation (**23**), which reacts with acetic acid to give **6x**, **6n**, and **7** (see Scheme VIII).[6]

SCHEME VIII

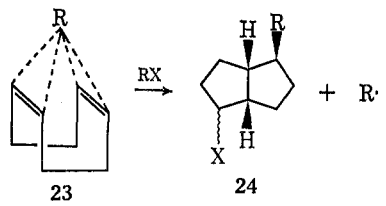



The *exo/endo* ratio of the bicyclic esters **2a** also depends on the nucleophilicity of the anion in the system. Thus, the addition of methoxymethyl acetate ($BF_3$–$OEt_2$ catalyzed) gives the acetates **2a** with an *exo/endo* ratio of 1.37. For acetic acid addition ($BF_3$–$OEt_2$ catalyzed), this ratio is 1.67,[6] while for formic acid addition (perchloric acid catalyzed) it is 2.26. This increasing *exo/endo* ratio reflects a decreasing amount of concerted character of step c.

The outside cationic attack on a cyclic diene system (step a) with concerted cyclization (step b) is similar to that reported recently for the addition of $Br_2$ in methanol to *cis,cis*-1,6-cyclodecadiene.[9] The isolation of only *endo*-2-bromo-*endo*-7-methoxymethyl-*cis*-bicyclo[4.4.0]decane, indicating a concerted step c, is contrary to expectation based on our results; it is quite possible that only the major product was isolated and reported. A more serious discrepancy exists in the finding of Cantrell[8] that *exo*-2-acetyl-6-chloro-*cis*-bicyclo[3.3.0]octane was formed in the reaction of 1,5-COD with acetyl chloride under $AlCl_3$ catalysis. Two possibilities may explain this contradiction: (1) heterogeneity of the reaction or (2) isomerization from *endo* to *exo* isomer in his procedure for the replacement of chlorine with hydrogen using sodium in *t*-butyl alcohol.

An interesting difference exists in the free-radical addition of $CHCl_3$, $HCNMe_2$, and $CH_3\overset{O}{\overset{\|}{C}}H$ to 1,5-COD as reported by Dowbenko.[15] The isolation of *exo*-2-substituted *cis*-bicyclo[3.3.0]octanes indicates that the radical attacked the boat form of 1,5-COD from the inside of the double bonds, just the opposite of cationic attack (Scheme IX). In the cationic addition, the

SCHEME IX




outside attack of the cation with concerted intramolecular participation of the double bond seems to decrease remarkably the energy of the transition state relative to that of the nonconcerted process. In the radical reaction, on the other hand, the energy decrease of the transition state in the concerted addition is less important; instead, the free-radical intermediate is best stabilized when it is on the $\pi$-electron cloud.

In contrast to the high cyclizability of 1,5-COD in reaction with methoxymethyl acetate, 1,5-hexadiene shows little cyclization (<10.3%) under the same conditions. The marked difference in their cyclizabilities may be ascribed to differences in their entropies of activation. In order to achieve $\pi$ overlap with the carbonium ion, the open-chain diene loses 2 degrees of internal rotational freedom, resulting in a considerable decrease in the preexponential factor. The importance of this entropy factor may be seen in the amount of cyclized product of the following solvolyses: formolysis of $\Delta^4$-pentenyl nosylate, 0%,[16] compared with $\Delta^4$-cyclooctenyl brosylate, 89%;[5] acetolysis of $\Delta^5$-hexenyl nosylate, 73%,[16] compared with $\omega$-($\Delta^2$-cyclopentenyl)-propyl-1 brosylate, 100%;[17] acetolysis of $\Delta^4$-cycloheptenyl-methyl brosylate, 90%,[18] compared with $\Delta^5$-cyclodecenyl nitrobenzoate, 100%.[19]

## Experimental Section[20]

**Reaction of *cis,cis*-1,5-Cyclooctadiene with Methoxymethyl Acetate.**—A solution of 10.8 g (0.1 mol) of 1,5-COD in 20 g of 1,2-dichloroethane was added over 1 hr at 68° to a mixture of 10.4 g (0.1 mol) of methoxymethyl acetate, 2.8 g (0.02 mol) of boron trifluoride–ether complex (47 wt %), and 20 g of 1,2-dichloroethane. After refluxing for 12 hr, the reaction mixture was poured into saturated sodium bicarbonate and extracted with ether. The ether layer was washed with water, dried ($Na_2SO_4$), and concentrated. Upon distillation, 3.0 g of a mixture of *endo*-6-methoxymethyl-*cis*-bicyclo[3.3.0]oct-2-yl acetates (**2ax** and **2an**) and *endo*-2-methoxymethyl-bicyclo[3.2.1]oct-*anti*-8-yl acetate (**3a**) was obtained at 91–92° (3 mm). The lower boiling distillate (5.0 g), bp 66° (15 mm) and 94° (12 mm), contained *endo*-6-methoxymethyl-*cis*-bicyclo[3.3.0]oct-2-ene (**5**), *cis*-bicyclo[3.3.0]oct-2-yl acetates (**6x** and **6n**), and *anti*-bicyclo[3.2.1]oct-

(15) R. Dowbenko, *Tetrahedron*, **20**, 1843 (1964).

(16) W. D. Johnson, D. M. Bailey, R. Owyang, R. A. Bell, B. Jaques, and J. K. Crandall, *J. Amer. Chem. Soc.*, **86**, 1959 (1964).

(17) W. D. Closson and G. T. Kwaitkowsky, *ibid.*, **86**, 1887 (1964).

(18) G. LeNy, *C. R. Acad. Sci., Paris*, **251**, 1526 (1961).

(19) P. D. Bartlett and S. Bank, *J. Amer. Chem. Soc.*, **83**, 2591 (1961).

(20) Analyses were by the Microanalytical Laboratory, Department of Pharmaceutical Sciences, University of Kyoto, Japan. Boiling points are uncorrected. Nmr spectra were determined with a JMN-3H-60 recording spectrometer. Ir spectra were determined with a Nihon Bunko Model IR-S spectrometer. For vpc, columns (210 cm, 3.0-mm i.d.) packed with silicone DC 550, PEG 20M, or Apiezon L were used. In the descriptions of nmr absorptions, s, d, t, m, and b correspond to singlet, doublet, triplet, multiplet, and broad, respectively.

8-yl acetate (7) together with many minor unknown products. The products were identified by comparison with the vapor phase chromatographs, infrared spectra, and nmr spectra of authentic samples. The infrared spectrum of the mixture of **2ax**, **2an**, and **3a** had strong bands at 1740, 1245, and 1100 $cm^{-1}$. The nmr spectrum ($CCl_4$) of the mixture exhibited absorptions at $\tau$ 6.87 (s, $OCH_3$), 6.67–7.25 (b, $OCH_2$), 8.14 (s, $CH_3CO_2$), and 7.25–9.0 (b, other protons). The absorption for the H $\alpha$ to the acetoxy group varied: **2ax** $\tau$ 5.35 (b, *endo*-**H**), **2an** 4.95 (b, *exo*-**H**), **3a** 5.44 (singlet, *syn*-**H**).

*Anal.* Calcd for $C_{12}H_{20}O_3$ (mixture of **2ax**, **2an**, and **3a**): C, 67.89; H, 9.50. Found: C, 67.72; H, 9.47.

**Hydrolysis of *endo*-6-Methoxymethyl-*cis*-bicyclo[3.3.0]oct-*exo*- and -*endo*-2-yl Acetates (2ax and 2an) and *endo*-2-Methoxymethylbicyclo[3.2.1]oct-*anti*-8-yl Acetate (3a).**—One gram of the mixture of the acetates **2ax**, **2an**, and **3a** was hydrolyzed with methanolic sodium hydroxide (5 g of sodium hydroxide, 25 g of methanol, and 5 g of water) to give 0.8 g of the corresponding alcohols, bp 90–97° (7 mm). The infrared spectrum of this mixture **8x**, **8n**, and **13** exhibited strong bands at 3360 and 1100 $cm^{-1}$. The nmr spectrum ($CCl_4$) of each acetate isolated from the mixture by the following procedures exhibited absorptions at $\tau$ 6.85 (s, $OCH_3$), 6.60–7.15 (b, $OCH_2$), and 7.3–9.3 (b, other protons). The absorption of the H $\alpha$ to the hydroxy function varied: **8x** $\tau$ 6.40 (b, *endo*-**H**), **8n** 5.95 (b, *exo*-**H**), **13** 6.47 (singlet, *syn*-**H**).

**Oxidation of the Mixed Alcohols 8x, 8n, and 13 with Chromic Oxide in Pyridine.**—A solution of 3.7 g of the mixed alcohols in 37 ml of pyridine was stirred with a mixture of 5.94 g of chromic oxide in 74 ml of pyridine at room temperature for 8 hr. The reaction mixture was poured into ice–water and extracted with ether. The ether extract was washed with 6 *N* hydrochloric acid and saturated sodium bicarbonate and was dried ($MgSO_4$). Distillation afforded the following: fraction A, bp 85–109° (7 mm), 1.28 g; fraction B, bp 109–111° (7 mm), 0.47 g; fraction C, pb 111° (7 mm), 0.19 g. Fraction A was shown by vpc on PEG 20M and Apiezon L to be a single ketone, *endo*-6-methoxymethyl-*cis*-bicyclo[3.3.0]octan-2-one (**12**): ir (neat) 2940, 1738, and 1100 $cm^{-1}$; nmr ($CCl_4$) $\tau$ 6.85 (s, $OCH_3$), 6.5–7.1 (b, $OCH_2$), 7.1–9.0 (b, other protons). Fraction C was unreacted *anti*-bicyclo[3.2.1]oct-8-yl alcohol (**3a**) of which nmr spectrum is cited above.

**Reduction of *endo*-6-Methoxymethyl-*cis*-bicyclo[3.3.0]octan-2-one (12) with Sodium Borohydride.**—A solution of 1.0 g of the ketone **12** in 7.5 ml of methanol was stirred with 0.9 g of sodium borohydride in 19 ml of methanol at room temperature for 3 hr. After removal of the methanol under reduced pressure, the residue was carefully acidified with 2 *N* hydrochloric acid. This solution was extracted with ether. The ether extract was dried ($MgSO_4$) and evaporated to give 0.8 g of an alcohol **8n**. The infrared spectrum of the product showed complete conversion of the ketone to the alcohol **8n**. This alcohol, distilled at 90–97° (7 mm), was determined as **8n** by analysis of nmr spectrum (*vide supra*). The structural assignment is supported by the fact that the hydride reduction of *cis*-bicyclo[3.3.0]octan-2-one gives mainly *endo-cis*-bicyclo[3.3.0]oct-2-yl alcohol.[21]

**Reduction of the Tosylates of the Mixed Alcohols 8x, 8n, and 13, with Lithium Aluminum Hydride.**—A solution of 5 g of the mixed alcohols **8x**, **8n**, and **13** in 24.5 ml of pyridine was added dropwise to 11.5 g of *p*-toluenesulfonyl chloride in 24.5 ml of pyridine at 0°. After standing at room temperature overnight, 150 ml of water was added, and the mixture was extracted with ether. The ether extract was washed with 6 *N* hydrochloric acid and aqueous saturated sodium bicarbonate and was dried. Removal of the ether at reduced pressure produced a pasty oil. Its infrared spectrum showed complete conversion of the alcohols to their tosylates (from the disappearance of the OH stretching band). Dissolution of the oil in ether and reduction with 0.1 g of lithium aluminum hydride gave two hydrocarbons, neither of which reacted with $Br_2$–$CH_2Cl_2$. These were tentatively identified as *endo*-2-methoxymethyl-*cis*-bicyclo[3.3.0]octane (**10n**) and *endo*-2-methoxymethylbicyclo[3.2.1]octane (**14**). The product composition was determined by vapor phase chromatography (silicone DC 550): **10n** (53.2%), **14** (13.7)%, starting alcohols (11.9%), and two unknown products (5.0%). **10n** was identical with an authentic sample (*vide infra*) by vapor phase chromatography (PEG 20 M, silicone DC 550, and Apiezon L) and infrared spectroscopy.

**Trifluoroacetolysis of the Brosylates of the Mixed Alcohols, 8x, 8n, and 13.**—A solution of 1.02 g of the mixed alcohols **8x**, **8n**, and **13** in 4.9 ml of pyridine was added dropwise at 0° to 3.05 g of *p*-bromobenzenesulfonyl chloride in 4.9 ml of pyridine. After stirring for 16 hr, water was added, and the reaction mixture was extracted with ether. The ether extract was washed with 6 *N* hydrochloric acid and saturated aqueous sodium bicarbonate and was dried ($MgSO_4$). Evaporation of the ether gave a viscous oil, a mixture of the *p*-bromobenzenesulfonates. This oil was added at 0° to a mixture of 1.08 g of sodium acetate and 27.36 g of trifluoroacetic acid, and the mixture was stirred at 0° for 2 hr. Water was added and the mixture was extracted with ether. The oil obtained by evaporation of the ether was hydrolyzed with 1.2 g of sodium hydroxide, 12 ml of water, and 20 ml of methanol at 50° for 1 hr. The hydrolysis mixture was extracted with ether, and the extract was dried ($MgSO_4$). Evaporation of ether gave an oily residue which contained 16.1% mixed alcohols **8x**, **8n**, and **13** and 70.4% (combined) two olefinic products which readily reacted with $Br_2$–$CH_2Cl_2$. The olefinic products were hydrogenated over $PtO_2$ catalyst at atmospheric pressure to give 2-*endo*-methoxymethyl-*cis*-bicyclo-[3.3.0]octane (**10n**) as one of the major products.

***endo*-2-Methoxymethyl-*cis*-bicyclo[3.3.0]octane (10n).**—The cyanohydrin **16** was prepared from the sodium bisulfite adduct of *cis*-bicyclo[3.3.0]octan-2-one (**15**) with potassium cyanide by Cope's procedure.[22] To a stirred solution of 5.5 g of the cyanohydrin **16** in 10 g of pyridine and 20 ml of ether was added 7.9 g of thionyl chloride with ice cooling. After refluxing for 2 hr, the mixture was poured onto 100 g of ice. The ether layer was separated, washed with water and saturated aqueous sodium bicarbonate, and was dried ($MgSO_4$). Distillation at 80–90° (5 mm) produced 2.7 g of a mixture of two cyanides **17a** and **17b**.

The nmr spectrum ($CCl_4$) of the mixed cyanides exhibited absorptions at $\tau$ 3.80 (t, with an intensity corresponding to 55.4% of olefinic protons) and 6.05–9.20 (b, other protons). Thus the ratio **17a**:**17d** was determined as 55.4:44.6 from nmr, which was supported by vpc (54.8:45.2).

The mixture of cyanides (5.3 g) was refluxed with 4.5 g of potsssium hydroxide, 0.85 g of water, and 22 ml of diethylene glycol for 48 hr. The solution was poured into 140 ml of water which was washed with benzene. After acidification with 6 *N* hydrochloric acid, the aqueous layer was again extracted with benzene. The benzene extract was washed with saturated sodium chloride and dried ($MgSO_4$). Distillation at 112.5–114.0° (0.65 mm) gave 2.8 g of a mixture of the two acids **18a** and **18b**.

The nmr spectrum ($CCl_4$) of the mixed acids exhibited absorptions at $\tau$ 2.11 (s, COOH), 3.35 (d, olefinic proton, with an intensity corresponding to 56% of olefinic protons), and 6.20–9.00 (b, other protons). Thus the ratio **18a**:**18b** was determined as 56:44 from nmr.

The mixture of the two acids (1.2 g) was hydrogenated over 0.14 g of 10% Pd-on-Norit catalyst in 13 ml of absolute ethanol at atmospheric pressure to give 1.1 g of the saturated *endo*-carboxylic acid **19n**.

One gram of this acid was refluxed for 3 hr with 19 ml of thionyl chloride. After removal of the thionyl chloride *in vacuo*, 2 ml of methanol was added to the residue with ice cooling and stirring. Ether was added, and the solution was washed with water and saturated aqueous sodium bicarbonate and was dried ($MgSO_4$). On distillation, the methyl ester **20** was obtained at 79–80° (3 mm) together with a small amount of an unknown ester. The ester was used in the following reaction without further purification.

A solution of 0.7 g of **20** in 20 ml of ether was added below −10° to a suspension of 0.095 g of lithium aluminum hydride in 20 ml of ether, and the mixture was stirred at room temperature overnight. After the usual work-up, a mixture of the alcohols **21n** and **21x** (in ratio of 70.0:30.0 as determined by vpc) was obtained. These alcohols were treated with 0.6 g of methyl iodide and 1.5 g of silver oxide to give the methyl ethers **10n** and **10x**, bp 70° (17 mm) and 65° (10 mm), in a ratio of **10n**:**10x** of 68.2:31.8 (determined by vapor phase chromatography with PEG 6000 column). The spectral data on the mixed ethers follow: ir (neat) 1100 $cm^{-1}$; nmr ($CCl_4$) $\tau$ 6.75 (superposition of the singlet from $CH_3O$ and the multiplet from $OCH_2$) and 7.3–9.2

(21) H. C. Brown and W. J. Hammar, *J. Amer. Chem. Soc.*, **89**, 6378 (1967).

(22) A. C. Cope and W. R. Schmitz, *ibid.*, **72**, 3056 (1950).

(other protons). **10x** was identical with authentic ether as shown by vpc (PEG 6000, silicone DC 550, and Apiezon L).

*exo*-**2-Methoxymethyl-*cis*-bicyclo[3.3.0]octane (10x).**—The *exo*-carboxylic acid **19x** was obtained from hydrolysis of *exo*-2-trichloromethyl-*cis*-bicyclo[3.3.0]octane by Dowbenko's procedure.[15] A solution of 3.4 g of this acid in 20 ml of tetrahydrofuran was added to a suspension of 4.3 g of lithium aluminum hydride in 20 ml of tetrahydrofuran with stirring and cooling in an ice bath. The mixture was then stirred at 40° for 22 hr. After the usual work-up, the *exo* alcohol **21x** which was obtained, was dissolved in 20 ml of ether and stirred with 0.28 g of sodium hydride overnight at room temperature. A solution of 39.7 g of methyl iodide in 50 ml of tetrahydrofuran was added to the reaction mixture, and the mixture was heated at reflux overnight. After addition of water, the mixture was extracted with ether. The ether layer was dried ($MgSO_4$), concentrated, and distilled to give the *exo*-methyl ether **10x**, bp 90–93° (42 mm). This was shown to be a single product by vpc (PEG 8000, silicone DC 550, and Apiezon L). The spectral data follow: ir (neat) 2860, 1455, 1385, 1260, 1190, and 1100 $cm^{-1}$; nmr ($CCl_4$) $\tau$ 6.75 [superpositon of singlet ($OCH_3$) and multiplet ($OCH_2$)] and 7.3–9.2 (other protons).

*exo-cis*-**Bicyclo[3.3.0]oct-2-yl Acetate (6x).**—*exo-cis*-Bicyclo-[3.3.0]oct-2-yl alcohol was prepared by the reductive cleavage of *cis*-bicyclo[3.3.0]oct-2-ene oxide with lithium aluminum hydride.[23] A mixture of 0.5 g of the alcohol and 2.1 g of acetic anhydride was maintained at 60° overnight. The mixture was poured into saturated sodium bicarbonate and extracted with ether. The ether layer was washed with water, dried ($Na_2SO_4$), and concentrated to give the practically pure acetate (shown by vpc analysis).

*endo-cis*-**Bicyclo[3.3.0]oct-2-yl Acetate (6n).**—*cis*-Bicylco-[3.3.0]octan-2-one (**15**) was reduced with sodium borohydride to give *endo-cis*-bicyclo[3.3.0]oct-2-yl alcohol.[21] The acetate was obtained as described above for **6x**.

*anti*-**Bicyclo[3.2.1]oct-8-yl Acetate (7).**—Addition of formic acid to 1,5-COD (perchloric acid catalysis) followed by hydrolysis gave a mixture of alcohols.[7] 4-Cyclooctenol-1 was removed from the mixture as previously described.[7] A solution of 15 g of the remaining alcohols in 200 ml of pyridine was added to a mixture of 32 g of chromic oxide in 400 ml of pyridine. The reaction mixture was stirred at room temperature for 4 days. The mixture was poured into ice–water and extracted with ether, the extract being washed with saturated aqueous sodium bicarbonate, dried ($MgSO_4$), and concentrated. Distillation gave a first fraction composed of a mixture of oxidized products, bicyclo-[3.3.0]octan-2-one (**15**) and bicyclo[3.2.1]octan-8-one and a second fraction, bp 60° (5 mm), of unoxidized *anti*-bicyclo-[3.2.1]oct-8-yl alcohol. This solid alcohol had the following nmr spectrum ($CCl_4$): $\tau$ 6.47 (s, $C_8$-**H**), 7.50–8.75 (b, other protons). The corresponding acetate **7** was obtained from the reaction of the alcohol with acetic anhydride as described for **6x**.

**Reaction of 1,5-COD with Chloromethyl Methyl Ether.**—A solution of 25.9 g of 1,5-COD in 25 g of 1,2-dichloroethane was added at room temperature over 2 hr to a solution of 19.2 g of chloromethyl methyl ether and 1.5 g of zinc chloride in 25 g of 1,2-dichloroethane. The reaction mixture was stirred at room temperature for 38 hr after which it was poured into saturated aqueous sodium bicarbonate and extracted with ether. The ether layer was washed with water, dried ($MgSO_4$), and concentrated. Distillation at 121–169° (10 mm) produced 14.3 g of a mixture of the *endo*-6-methoxymethyl-*cis*-bicyclo[3.3.0]oct-2-yl chlorides (**2bx**[24] and **2bn**), *endo*-2-methoxymethyl-bicyclo[3.2.1]-oct-*anti*-8-yl chloride (**3b**), and an olefinic product **4b** which was removed from the mixture by extraction with aqueous silver nitrate. The mixture of **2bx**, **2bn**, and **3b** had the following spectral properties: nmr ($CCl_4$) of $\alpha$ proton to chlorine, $\tau$ 5.6 (m, **2bx**), 5.9 (m, **2bn**), and 6.06 (s, **3b**); ir (neat) 1100, 755, and 725 $cm^{-1}$.

*Anal.* Calcd for $C_{10}H_{17}OCl$: C, 63.83; H, 9.04; Cl, 18.62. Found: C, 63.36; H, 9.19; Cl, 18.24.

The skeletons of **2bx** and **2bn** were ascertained by the reduction to **10n**. The stereochemistry and the product composition of **2bx**, **2bn**, and **3b** were determined by the nmr measurement of the $\alpha$ proton to chlorine. The chloride **2bx** was shown by vpc (Apiezon L and PEG 20M) to be identical with an authentic sample obtained from the chlorination of **8n** with phosphorus pentachloride.[24]

**Reduction of 2bx, 2bn, and 3d with Sodium in Methanol.**—To a solution of 1.9 g of the mixture of chlorides **2bx**, **2bn**, and **3d** in 6.4 g of methanol was added 2.3 g of sodium metal in small portions with stirring. After the spontaneous refluxing ceased, the mixture was heated to maintain reflux until the sodium disappeared. The mixture was neutralized with dilute hydrochloric acid with ice cooling and was extracted with ether. After evaporation of the ether, the residue was shown by vpc (silicone DC 550) to consist of two products (53.3 and 46.7%). One was identical with an authentic sample of **10n** as demonstrated by vpc (PEG 20M and silicone DC 550), and the other was assumed to be **14**.

**Reaction of 1,5-COD with Dimethoxymethane.**—A solution of 21.6 g of 1,5-COD in 30 g of dichloromethane was added to a solution of 15.6 g of dimethoxymethane and 5.6 g of boron trifluoride–ether complex (47 wt %) in 30 g of dichloromethane with stirring at 31–41° over 7 hr. Stirring was continued for 93 hr at 35–37°. Then the mixture was poured into saturated aqueous sodium bicarbonate and was extracted with ether. The ether extract was washed with water, dried ($MgSO_4$), and concentrated. Distillation at 112–114° (10 mm) afforded 4.93 g of a mixture of the *endo*-6-methoxymethyl-*cis*-bicyclo[3.3.0]oct-2-yl methyl ethers (**2cx** and **2cn**), *endo*-2-methoxymethyl-bicyclo[3.2.1]oct-*anti*-8-yl methyl ether (**3c**), and an olefin **4c**, which was removed from the mixture by extraction with aqueous silver nitrate. The nmr spectrum ($CCl_4$) of the mixture of isomers exhibited absorptions at $\tau$ 6.55–7.20 (b, OCH and $OCH_2$), 6.75 (s, $OCH_3$), and 7.20–9.20 (b, other protons). Since the nmr absorptions of OCH were not separated from those of $OCH_2$, the nmr measurement did not define the stereochemistry of 6-methoxyl group.

*Anal.* Calcd for $C_{11}H_{20}O_2$: C, 71.69; H, 10.94. Found: C, 71.43; H, 10.85.

By comparison of the infrared spectra and vapor phase chromatographs (Apiezon L and PEG 20M), the products were shown to be identical with the ether from the hydrolysis products of **2ax**, **2an**, and **3a** obtained in the reaction of 1,5-COD with methoxymethyl acetate.

*endo*-**6-Methoxymethyl-*cis*-bicyclo[3.3.0]oct-2-yl Methyl Ethers (2cx and 2cn) and *endo*-2-Methoxymethyl-bicyclo[3.2.1]oct-*anti*-8-yl Methyl Ether (3c) from 8x, 8n, and 13.**—To a solution of 1.7 g of the mixture of **8x**, **8n**, and **13** (obtained from the hydrolysis of **2ax**, **2an**, and **3a**) in 20 ml of tetrahydrofuran was added 2.4 g of sodium hydride (50%). After the mixture was stirred at reflux for 5 hr, the mixture was cooled in an ice bath, and 14.2 g of methyl iodide was added. After reflux for 24 hr, water was added to the mixture, and the mixture was extracted with ether. The ether extract was dried ($MgSO_4$) and concentrated to give the methyl ethers **2cx**, **2cn**,[25] and **3c**.[26] Vapor phase chromatography (PEG 20M) showed complete conversion of the alcohols to their methyl ethers.

**Registry No.**—*cis*,*cis*-1,5-COD, 1552-12-1; methoxymethyl acetate, 4382-76-7; chloromethyl methyl ether, 107-30-2; dimethoxymethane, 109-87-5.

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(23) I. Tabushi, K. Fujita, and R. Oda, unpublished data.

(24) **2bx** from **8n**. A solution of 0.2 g of **8n** in 2 ml of dichloromethane was heated to reflux for 2 hr with 0.3 g of phosphorus pentachloride. The mixture was poured into water and extracted with dichloromethane. The dichloromethane extract was washed with saturated aqueous sodium bicarbonate and was concentrated to give the chloride **2bx**. The product was contaminated by a small amount of impurity as shown by vpc (PEG 20M and Apiezon L).

(25) **2cn** from **8n**. A mixture of 0.5 g of **8n**, 1 ml of methyl iodide, and 0.1 g of silver oxide was refluxed for 4 hr. Ether (six washings) was used to dissolve the organic product from the precipitate, and the ether extracts were dried ($MgSO_4$). Evaporation of ether gave practically pure *endo* methyl ether **2cn**, as demonstrated by vpc (PEG 20M).

(26) **3c** from **13**. A mixture of 0.19 g of **13**, 1 ml of methyl iodide, and 0.1 g of silver oxide was refluxed for 4 hr. The procedure described above for the conversion of **2cn** to **8n** produced practically pure methyl ether, **3c** (shown by vpc on PEG 20M).