Trajectory of Electrophilic Attack on Trisubstituted Cyclopropanes

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Received August 22, 1989

In the reactions of 2-*exo*-methyl-*endo*-tricyclo[3.2.1.$0^{2,4}$]octane (**1**) and 2-*exo*-methyl-*endo*-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (**12**) with both mercuric ion and proton, the electrophile attacks the cyclopropane moiety at the corner with inversion. For the reactions with mercuric ion, the propensity toward inversion of configuration at the site of nucleophilic attack is accounted for in terms of the looseness of the transition state and the absence of substantial development of positive charge at the tertiary center. In contrast, the reactions with proton proceed with significant development of positive charge at the tertiary center and occur with reduced regiospecificity and with attack of nucleophile being less stereospecific.

Introduction

We have been interested for some time in the reaction of proton and mercuric ion with cyclopropane derivatives to establish the factors responsible for the regiochemistry of addition to unsymmetrical cyclopropanes and the reaction trajectory for the addition of both electrophile and nucleophile. It is generally believed that the direction of bond cleavage in such reactions can be accounted for by a modified version of Markovnikov's rule[1] which states that the ring opens between the carbons bearing the largest number and smallest number of alkyl substituents. However for almost all systems that have been studied a substantial proportion of product results from rupture of the most substituted carbon–carbon bond of the cyclopropane.[2] In some instances there are no products resulting from cleavage to the least substituted carbon of a substituted cyclopropane.[3] To date no satisfactory explanation has been advanced for the varied behavior observed in cyclopropane ring opening.

In all cases of addition to and rearrangement of cyclopropanes the nucleophile, whether external such as solvent or an internal adjacent σ bond in the molecular framework, always becomes attached or involved with the most substituted carbon of the cyclopropyl ring. Wiberg[4] has noted that while relief of steric strain for acid-catalyzed addition to cyclopropane does not correlate with reaction rate, the reaction develops toward the more stable carbocation.[5] The products are considered to be formed by capture of the protonated cyclopropane before it has become an open carbocation, thereby accounting for stereoselective capture by nucleophile, stereoselective migration, or proton loss. The preference for inversion of configuration at the site of nucleophilic attack in addition to cyclopropanes is consistent with the activation barrier from the reaction intermediate to a classical cation being greater than the barrier to nucleophilic attack at the intermediate with inversion.

When the cyclopropane is in a rigid skeleton, the ability of a σ bond to overlap with retention (syn-periplanar) or inversion (anti-periplanar) with the cyclopropyl bond undergoing cleavage plays a significant role in determining reaction course.[2] The present study reports the electrophilic opening of 2-*exo*-methyl-*endo*-tricyclo[3.2.1.$0^{2,4}$]octane (**1**) and 2-*exo*-methyl-*endo*-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (**12**). A previous study of *exo*- and *endo*-tricyclo[3.2.1.$0^{2,4}$]octane[3,6] and tricyclo[3.2.1.$0^{2,4}$]oct-6-ene[7] has pointed to the importance of the carbon skeleton on the course of the reaction. The *endo*-tricyclo[3.2.1.$0^{2,4}$]octane in contrast to the exo isomer reacts with acid and mercuric acetate exclusively by rupture of the internal cyclopropyl bond. Intramolecular capture of the developing C4 cation with retention dominates the course of the acid-catalyzed reaction and the trajectory of the proton is toward the corner at C2 which results in inversion of configuration at this center in the reaction. Mercuric acetate addition occurs without skeletal rearrangement competing with external nucleophilic addition of solvent.

Since the products of cyclopropane opening are considered to be formed by capture of the protonated cyclopropane before it has become an open carbocation the presence of the methyl in the hydrocarbon **1** and **12** should move the transition-state structure to a more classical carbocation. Such a shift would be expected to affect the stereospecificity of nucleophilic attack. We were therefore interested to establish if the reactions of **1** and **12** with electrophilic reagents proceed by way of a tertiary carbocation with the possibility for interaction with the π-system in hydrocarbon **12** or if residual bridging to C4 dictates the course of reaction.

Results and Discussion

Protonation and Mercuration of 2-Methyl-*endo*-tricyclo[3.2.1.$0^{2,4}$]octane (1). Reaction of **1** with methanol in the presence of catalytic quantities of *p*-toluenesulfonic acid at room temperature for 4 days gave 2-*exo*-methoxy-2-*endo*-methylbicyclo[3.2.1]octane[8,9] (**5a**, 32%), 2-*endo*-methoxy-2-*exo*-methylbicyclo[3.2.1]octane[10] (**3a**, 31%) (1:1 exo/endo attack) and 2-methylbicyclo[3.2.1]-oct-2-ene[11] (**6a**, 18%). The ethers **5a** and **3a** are stable

(1) Zimmerman, M. P.; Li, H.-T.; Duax, W. L.; Weeks, C. M.; Djerassi, C. *J. Am. Chem. Soc.* **1984**, *106*, 5602.

(2) Battiste, M. A.; Coxon, J. M. In *The Chemistry of the Cyclopropyl Group*; Rappoport, Z., Ed.; Wiley and Sons: New York, 1987; Chapter 6, p 255.

(3) Coxon, J. M.; Steel, P. J.; Whittington, B. I.; Battiste, M. A. *J. Am. Chem. Soc.* **1988**, *110*, 2988.

(4) Wiberg, K. B.; Kass, S. R.; de Meijere, A.; Bishop, K. C. *J. Am. Chem. Soc.* **1985**, *107*, 1003.

(5) At the product forming activated complex the structure is considered not to have relaxed to a large extent.[2]

(6) Coxon, J. M.; Steel, P. J.; Whittington, B. I.; Battiste, M. A. *J. Org. Chem.* **1989**, *54*, 1383.

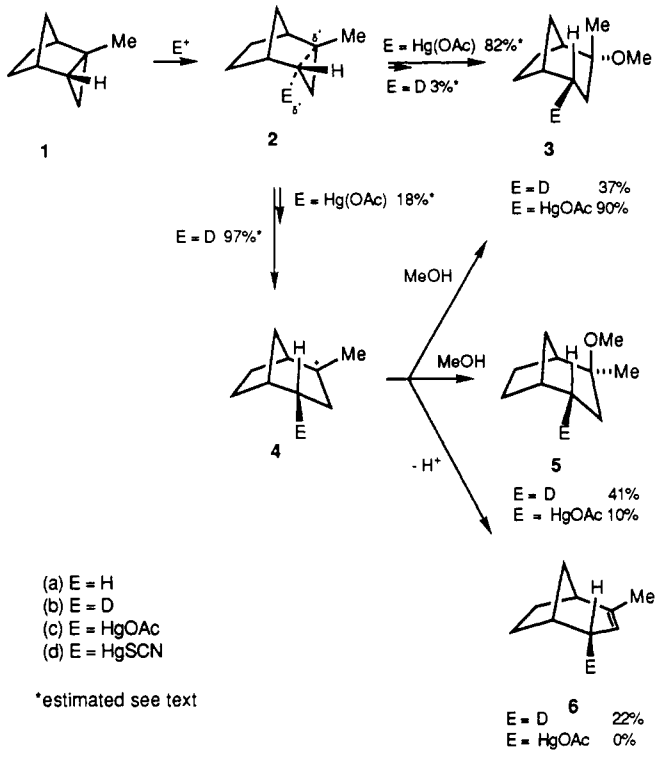
(7) Coxon, J. M.; Steel, P. J.; Whittington, B. I. *J. Org. Chem.* **1989**, *54*, 3702.

(8) The ^{13}C NMR spectrum was assigned by comparison with the known 2-*endo*-methylbicyclo[3.2.1]octan-2-*exo*-ol[9] and a heteronuclear correlation experiment allowed assignment of the chemical shifts of the protons.

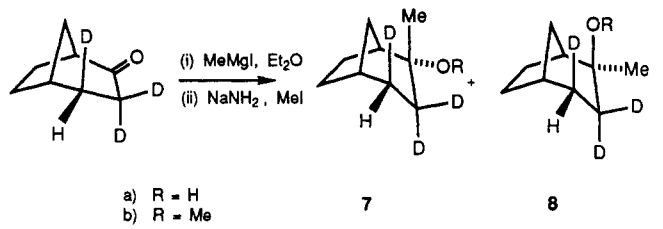
(9) Lippmaa, E.; Pehk, T.; Belikova, N. A.; Bobyleva, A. A.; Kalinichenko, A. N.; Ordubadi, M. D.; Plate, A. F. *Org. Magn. Reson.* **1976**, *8*, 74.

(10) The ^{13}C NMR spectrum of **3a** was assigned by comparison with the reported spectrum of 2-*exo*-methylbicyclo[3.2.1]octan-2-*endo*-ol.[9] The previously reported shifts for C3 and C4 in this alcohol are reversed, as shown by the presence of a triplet at 29.6 ppm for the C4 and apparent absence of a peak at 33.7 ppm due to the D3-*exo*,D3-*endo* in 2-*exo*-methyl-3,3,4-*exo*-trideuteriobicyclo[3.2.1]octan-2-*endo*-ol, **7a**. The carbon–hydrogen connectivities of **3a** were determined from a heteronuclear correlation experiment. A difference NOE spectrum established the exo stereochemistry of the C2-methyl: irradiation of the methyl at 1.20 ppm gave enhancements at 3.17 (OMe), 2.15 (H1, 3.2%), 1.28 (H8s, 3.3%), and 1.45 ppm (H4-exo, 2.6%).

Scheme I. Reaction of 2-Methyl-*endo*-tricyclo[3.2.1.0^{2,4}]octane with H$^+$(D$^+$) and Hg(OAc)$_2$ at 25 °C



Scheme II. Preparation of the Epimeric 3,3,4-*exo*-Trideuterio-2-methoxy-2-methylbicyclo[3.2.1]octanes



under the reaction conditions indicating the ratio is kinetic in origin, and that **6a** does not, at room temperature, arise from the ethers.

To determine the reaction pathway for the methanol addition to **1** the chemical shifts of the C4 protons for each of the primary reaction products **3a**, **5a**, **6a** had to be unambiguously assigned. To achieve this, authentic deuterio isomers **7b** and **8b** of the epimeric 2-methoxy-2-methylbicyclo[3.2.1]octanes were synthesised (Scheme II).[12] Authentic samples of **3a** and **5a** were similarly prepared from bicyclo[3.2.1]octan-2-one. For **5a**, the chemical shifts of the H4-endo and H4-exo are established as 1.26 and 1.65 ppm, respectively. For **6a**, the chemical shifts of H4-exo and H4-endo are determined as 2.30 and 1.75 ppm, respectively.[13]

To observe the effect of temperature on the reaction course and the preference for thermodynamic control vs kinetic control, **1** was reacted with methanol *p*-toluenesulfonic acid at 80 °C for 7 days. In addition to the previously observed **6a** (53%), **3a** (18%), and **5a** (21%), 2-methoxy-1-methylbicyclo[2.2.2]octane[14] (**11a**) (8%) was also present (Scheme III) and was isolated by preparative GLC. The stability of the primary reaction products (from

Scheme III. Rearrangement of Products from the Reaction of 2-Methyl-*endo*-tricyclo[3.2.1.0^{2,4}]octane in Methanol-d_1 at 80 °C

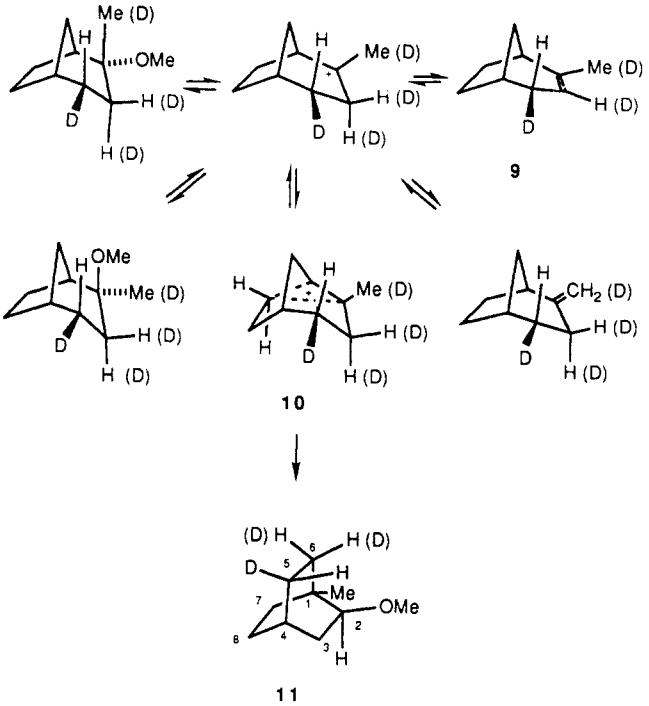


Table I. Stability of the Primary Reaction Products to Methanol and *p*-Toluenesulfonic Acid at 80 °C

		product ratios			
reactant	reaction time	6	11	3	5
3:5 (9:1)	26 h[a]	92	–	4	2
	8 days[a]	67	16	8	9
3:5 (32:68)	25 h[a]	23	7	43	36
	8 days[a]	69	16	8	8
4	8 days[b]	28	2	36	34

[a] [H$^+$] = 0.115 M. [b] [H$^+$] = 0.01 M.

(11) The identity of **6a** followed by comparison with the reported ^{13}C NMR spectrum[9] and by preparation of an authentic sample.

(12) A heteronuclear correlation spectrum of the epimeric ethers **7b** and **8b** showed for **7b** a triplet in the carbon dimension at 29.4 ppm exhibiting connectivity with a proton at 1.42 ppm. The presence of a triplet in the carbon dimension arises from the C4-*exo*-D coupling, C4 exhibiting connectivity with only H4-endo at 1.42 ppm due to the high deuterium incorporation at C4-exo. Thus the chemical shift of H4-endo in **3a** is established as 1.42 coincident with H4-exo. In addition a ^{2}H NMR spectrum of 4-*exo* and 4-*endo*-deuterio-2-*endo*-methoxy-2-*exo*-methylbicyclo[3.2.1]octane, prepared from the nonspecific $NaBD_4$ reduction of 4-*endo*-(acetoxymercurio)-2-*endo*-methoxy-2-*exo*-methylbicyclo[3.2.1]octane, showed a single peak at 1.41 ppm due to D4-exo and D4-endo. For **8b**, the heteronuclear correlation spectrum showed a triplet in the carbon dimension at 28.3 ppm, exhibiting connectivity with H4-endo at 1.26 ppm. As with **7b**, the triplet in the carbon dimension arises from the C4-*exo*-D coupling, no connectivity being observed between C4 and H4-exo due to the high deuterium incorporation at this position.

(13) The mixture of epimeric alcohols **7a** and **8a** was dehydrated by heating with $KHSO_4$ at 160 °C for 30 min (Petit, F.; Evrard, M.; Blanchard, M. *Bull. Soc. Chim. Fr.* **1971**, 4176) to yield 2-methylbicyclo[3.2.1]oct-2-ene, with deuterium present at C3 (5.05 ppm, 25%), C4-exo (2.30 ppm, 53%), C4-endo (1.75 ppm, 29%) and the methyl (1.65 ppm, 0.40 excess deuterium). A heteronuclear correlation spectrum of this compound shows in the carbon dimension, a triplet at 36.5 ppm exhibiting connectivity with H4-endo at 1.75 ppm, no connectivity with H4-exo being observed due to the higher deuterium incorporation at this position.

(14) The partial ^{1}H NMR spectrum of 2-methoxy-1-methylbicyclo-[2.2.2]octane has been reported (Kraus, W.; Chassin, C. *Tetrahedron Lett.* **1970**, 1113) and is consistent with that observed here. The ^{13}C NMR spectrum was assigned from the predicted effect of a methoxy group on the ^{13}C NMR spectrum of 1-methylbicyclo[2.2.2]octane; Pehk, T. I.; Lippmaa, E. T.; Sokolova, I. M.; Vorob'eva, N. S.; Gervits, E. S.; Bobyleva, A. A.; Kalinichenko, A. N.; Belikova, N. A. *Zh. Org. Khim.* **1976**, *12*, 1201.

Table II. Excess Deuterium from the Acid-Catalyzed Addition of Methanol-d_1 to 2-Methyl-*endo*-tricyclo[3.2.1.$0^{2,4}$]octane at 80 °C

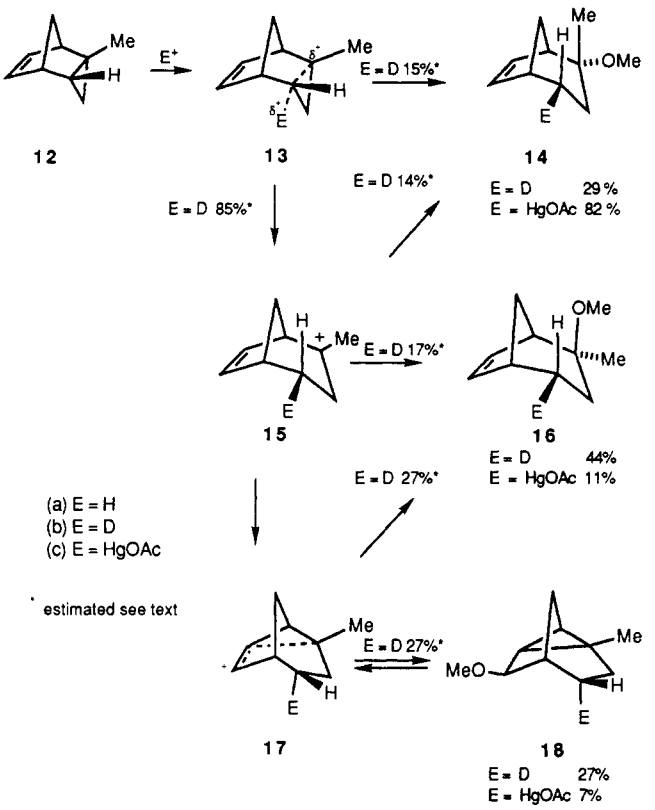
	excess deuterium (atom %)			
compd	D4-endo	D3-exo	D3-endo	methyl
6	98		82	246
3		243		220
5		227		257

the reaction at room temperature) under the more vigorous conditions was tested by separately reacting each of the compounds in methanol *p*-toluenesulfonic acid at 80 °C (Table I). The products interconvert with time at this higher temperature with the gradual appearance of **11a**; this behavior is consistent with **6a**, **3a**, and **5a** being primary products of reaction.

To determine the stereochemistry of proton attack, the reaction of **1** with methanol-d_1 *p*-toluenesulfonic acid was examined at 25 °C, and the products were separated by preparative GLC and investigated by NMR. For deuterated **6b**, the presence of a triplet in the ^{13}C NMR spectrum at 36.3 ppm and a peak in the ^{2}H NMR spectrum at 1.75 ppm indicated the deuterium stereochemistry at C4 as endo. For **5b**, the presence of a triplet in the ^{13}C NMR spectrum at 28.6 ppm and a peak in the ^{2}H NMR spectrum at 1.23 ppm similarly defined the deuterium stereochemistry at C4 in this compound as endo. However, while the ^{13}C NMR spectrum of **3b** indicated the presence of the C4 deuterium by the presence of a triplet at 29.7 ppm, the unfortunate coincidence[12] of the chemical shifts of the 4-exo and 4-endo protons (and hence deuterons), means the deuterium stereochemistry at C4 is indeterminate. To ascertain the stereochemistry of C4-D in **3b**, a 76:24 mixture of **3b** and **5b**, obtained by preparative GLC from the reaction of **1** with methanol-d_1 at room temperature, was reacted with methanol *p*-toluenesulfonic acid at 80 °C for 32 h. GLC and subsequent ^{1}H, ^{2}H, and ^{13}C NMR analyses confirmed the presence of 4-*endo*-deuterio-2-methylbicyclo[3.2.1]oct-2-ene (**6b**) (57%) in a mixture with **5b** (19%) and **3b** (23%). The presence of triplets in the ^{13}C NMR spectrum of the crude reaction mixture corresponding to C4-D for each of **3b**, **5b**, and **6b** and the presence of peaks in the ^{2}H NMR spectrum at 1.72 (**6b**), 1.40 (**3b**), and 1.23 ppm (**5b**) along with the absence of peaks corresponding to 4-*exo*-deuterio-2-methylbicyclo-[3.2.1]oct-2-ene (2.27 ppm) and 4-*exo*-deuterio-2-*exo*-methoxy-2-*endo*-methylbicyclo[3.2.1]octane (1.62 ppm) indicates the deuterium stereochemistry at C4 in **3b** as endo.[15] The observation of C4-*endo*-D in all three of the primary reaction products from the reaction of **1** with methanol-d_1 at room temperature is consistent with corner attack by proton (deuteron) at the cyclopropyl ring. This reflects either an inherent preference for protonation at C4 as compared to C3 or that subsequent reaction at the C4-protonated cation is more facile than reaction at the C3-protonated cation.

The reaction of **1** with methanol-d_1 *p*-toluenesulfonic acid at 80 °C for 7 days yielded deuterated 2-methylbicyclo[3.2.1]oct-2-ene (**6**), 2-*exo*-methoxy-2-*endo*-methylbicyclo[3.2.1]octane (**5**), 2-*endo*-methoxy-2-*exo*-methylbicyclo[3.2.1]octane (**3**), and 2-methoxy-1-methylbicyclo[2.2.2]octane (**11**) in a similar ratio to that previously obtained. The deuterium distribution obtained from mass spectral analysis and ^{2}H and ^{13}C NMR spectra (Table II) is consistent with the multiple addition/elimination mechanism shown in Scheme III. The observation of a deuterium at C5-anti and not C5-syn of deuterio **11** requires nucleophilic attack at the bridged cation **10** to occur before relaxation to the free carbocation. The deuterium incorporation at C3 and the methyl in each of the compounds arises from repeated methanol addition to **6** and **10** and elimination from the epimeric ethers **3** and **5**.[16]

Scheme IV. Reaction of 2-Methyl-*endo*-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene with $H^+(D^+)$ and $Hg(OAc)_2$



In contrast to the acid-catalyzed addition of methanol, reaction of **1** with mercuric acetate in methanol yields, after sodium mercury amalgam reduction in sodium hydroxide, a 9:1 mixture of **3a** and **5a**, respectively.[17,18] Stereospecific reduction[19] of the organomercurial mixture with sodium amalgam in sodium deuteroxide gave a 93:7 mixture of the 4-*endo*-deuterio-2-methoxy-2-methylbicyclo[3.2.1]octanes **3b** and **5b**. The observation of C4-endo deuterium in **5b** from stereospecific reduction of **5c** with sodium amalgam in NaOD and a 4-*exo*-H in **3c** defined the stereochemistry

(15) Resolution of the 4-exo and 4-endo deuterons in the product from nonspecific $NaBD_4$ reduction of 4-*endo*-(acetoxymercurio)-2-*endo*-methoxy-2-*exo*-methylbicyclo[3.2.1]octane by the use of $Eu(fod)_3$ shift reagent was unsuccessful.

(16) The C4-endo deuterium arises from initial deuteron attack with inversion at the cyclopropyl ring.

(17) Separation was achieved by preparative GLC, and the products were identical to those from the acid-catalyzed methanol addition at room temperature.

(18) While the intermediate organomercurial mixture was not separated, the major component of this reaction, **3c**, was present in sufficient quantity (ca. 90%) to allow the determination of spectroscopic data. The ^{13}C–^{199}Hg couplings support a 4-*endo*-acetoxymercurio group. The axial nature of the C4H and hence the configuration of the acetoxymercurio group in **3c** was further confirmed by proton–proton couplings (selective decoupling) to the C3-*endo*-H (13.6 Hz), C3-*exo*-H (5.2 Hz), C6-*exo*-H (1.5 Hz), and C5H (1.5 Hz). A difference NOE spectrum, performed on the mixture (9:1) of the thiocyanatomercurials **3d** and **5d**, showed that irradiation of the methyl group at 1.20 ppm gave enhancements at 3.18 (OMe, 5.1%), 2.91 (H4-exo, 5.6%), 2.07 (H1, 2.8%), 1.96 (H3-exo, 3.2%), and 1.56 ppm (H8s, 3.5%), thereby confirming the exo stereochemistry of the methyl and hence the endo nature of the methoxy group.

(19) Kitching, W.; Atkins, A. R.; Wickham, G.; Alberts, V. *J. Org. Chem.* **1981**, *46*, 563.

of the mercuric acetate attack on **1** as at the corner with inversion, the reaction occurring without skeletal rearrangement.

Protonation and Mercuration of 2-Methyl-*endo*-tricyclo[3.2.1.0^{2,4}]oct-6-ene (12). The acid-catalyzed reaction of **12** with methanol at room temperature for 3 days (87% reaction) gave three compounds, **14a**,[20] **16a**,[21] and **18a**,[22] in the ratio 29:38:33, respectively[23] (Scheme IV). While **14a** was stable under the reaction conditions, **16a** gave **18a** along with **16a** in the ratio of 1:9. The greater reactivity of **16a** relative to **14a** reflects the relationship of the double bond to the *exo*-methoxy group. Ether **18a** gave a 1:1 mixture of **16a** and **18a** after 22 h, a product ratio subsequently invariant for 21 days.[24] The solvolysis of **18a** is consistent with the intermediacy of cation **17a**, nucleophilic attack on this species giving **16a** and **18a** in the ratio 1:1. Stereoselective exo attack in the solvolysis of **18a** indicates nucleophilic attack on the classical tertiary cation **15**, if it is indeed present in the solvolysis reaction, is not competitive with attack on **17**.

The reaction of **12** with mercuric acetate in methanol, and subsequent sodium amalgam reduction with sodium hydroxide, gave **14a** (82%), **16a** (11%), and **18a** (7%) identical with those previously obtained from the acid-catalyzed methanol addition at 25 °C. Hydrogenation of the crude reaction mixture gave a mixture containing mainly **3a** identical with an authentic sample. While the original organomercurial mixture was not able to be separated, **14c** was present in sufficient yield to allow determination of its spectroscopic data.[25] To confirm the stereochemistry of the acetoxymercurio group, a sodium amalgam reduction of the crude organomercurial mixture in sodium deuteroxide was carried out to give **14b**, **16b**, and **18b**. The major component **14b** was separated by preparative GLC and the presence of a C4-endo-deuterium after the stereospecific reduction was confirmed[26] by the presence of a triplet in the ^{13}C NMR spectrum at 22.6 ppm and the loss of a coupling from H4-endo to H8a (1.7 Hz) and H3-endo (3.6 Hz). The deuterium stereochemistry in **16b** was similarly established as C4-endo due to the presence of a triplet in the ^{13}C NMR spectrum at 21.7 ppm and a peak in the ^{2}H NMR spectrum at 1.20 ppm corresponding to C4-endo-deuterium. While the deuterium stereochemistry in **18b** was not determined it would be expected, by comparison with **14b** and **13b** that the deuterium be C4-endo. Given the stereospecific nature of the organomercurial reduction, it is therefore apparent that the mercuric salt attacks the cyclopropane ring with inversion of configuration to give **14c** and **16c**, and by implication, **18c**. The higher degree of unrearranged product **14c** as compared to the reaction with proton (deuteron) is indicative of the lack of substantial charge development in the reaction with mercuric acetate.

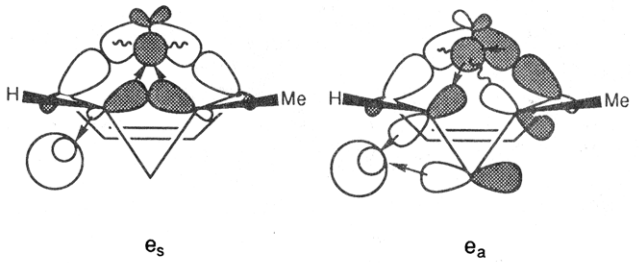


Figure 1. Mixing of C1,C8 and C5,C8 orbitals with cyclopropane orbitals showing interaction with electrophiles at corner and edge.

To determine the stereochemistry of proton attack on the cyclopropane ring, the acid-catalyzed addition of methanol-d_1 to **12** was examined at room temperature. Reaction for 7 days (79% reaction) gave **14b**,[27] **16b**, and **18b** in the ratio 29:44:27, respectively. For product **16b**, the presence of a triplet in the ^{13}C NMR spectrum at 21.7 ppm and a peak at 1.22 ppm in the ^{2}H NMR spectrum along with the loss of a coupling from H8a (1.72 ppm) to H4-endo (2.3 Hz) is consistent with a C4-*endo*-D. For **18b** the presence of a C4-endo deuterium similarly follows from the presence of a triplet in the ^{13}C NMR spectrum at 25.4 ppm and a peak in the ^{2}H NMR spectrum at 1.32 ppm in addition to a loss of a 2.1-Hz coupling from H8a (1.82 ppm) to H4-endo.

The HOMO and subjacent orbital of **1** will contain a contribution from the C1,C8/C5,C8 σ bonds[28] with the cyclopropane e_s and e_a orbitals. An unfavorable secondary

(20) The identity of **14a** was established by methods similar to those described for **16a**.

(21) The identity of **16a** was established from spectral studies and by hydrogenation to **5a**. The ^{1}H NMR spectrum of **16a** was assigned by comparison with that of 2-*endo*-methylbicyclo[3.2.1]oct-6-en-2-*exo*-ol Bohlmann, F.; Rotard, W. *Justus Liebigs Ann. Chem.* **1982**, 1220 and by selective decoupling and difference NOE's. In particular, the exo stereochemistry of the methoxy methyl follows from a difference NOE spectrum. Irradiation of H8s (1.95 ppm), so assigned due to a coupling with H8a (1.72 ppm, 10.0 Hz) and lack of coupling with H1/H5, gives enhancements at the methoxy methyl (3.19 ppm, 0.8%), H1/H5 (2.54 ppm, 1.0%), H8a (1.72 ppm, 12.5%), H4-exo (1.62 ppm, 2.5%), and the methyl (1.03 ppm, 0.4%). A heteronuclear correlation experiment identified connectivities between, among others, H4-exo 1.62 ppm and H4-endo 1.23 ppm/C4, 22.2 ppm and H8s 1.95 ppm and H8a 1.72 ppm/C8, 38.8 ppm. A coupling between C4H at 1.23 ppm and H8a of 2.3 Hz confirms the assignment of this proton as C4-*endo*-H.

(22) The identity of **18a** was determined as follows. Comparison with the ^{1}H NMR spectrum of 6-*exo*-methoxytricyclo[3.2.1.0^{2,7}]octane[7] reveals a loss of coupling of ca. 7 Hz from the cyclopropyl proton at 1.3 ppm, indicating the methyl is substituted at the cyclopropyl ring. A difference NOE spectrum further established the methyl to be at C2. Irradiation of the methyl at 0.92 ppm gave enhancements at H3-exo/H3-endo (1.66–1.60 ppm, 2.2% total), H7 (1.30 ppm, 6.4%), and H1 (1.19 ppm, 5.0%). The methoxy group was established to be at C6-exo by comparison with the couplings at the C6-H observed for 2-methyltricyclo-[3.2.1.0^{2,7}]octan-6-*exo*-ol.[21] H6-endo for both these compounds appears in the ^{1}H NMR spectrum as a singlet, while for 2-methyltricyclo-[3.2.1.0^{2,7}]octan-6-*endo*-ol, H6-exo appears as a quartet with couplings of 4.5 and 4.0 Hz to H5 and H7, respectively. A difference NOE spectrum further confirmed the methoxy stereochemistry: irradiation at H6-endo (3.44 ppm) gave enhancements at the methoxy methyl (3.33 ppm, 4.3%), H5 (1.98 ppm, 1.8%), H4-endo (1.37 ppm, 2.1%), and H7 (1.30 ppm, 2.1%). The NOE experiment in addition to a coupling between the H4-endo and H8a at 1.82 ppm (2.1Hz) allows assignment of H4-endo at 1.37 ppm. A heteronuclear correlation spectrum identified H4-exo at 1.51 ppm. A Eu(Fod)$_3$ study was also performed, the results supporting the assignment of **18a**.

(23) Separation was achieved on a silver nitrate (10%) impregnated column.

(24) Such a rearrangement contrasts with the reaction of 6-*exo*-methoxytricyclo[3.2.1.0^{2,7}]octane to give the bicyclo[2.2.2]octane skeleton upon reaction with *p*-toluenesulfonic acid in methanol for 2 h.[7] Reaction of the *p*-toluenesulfonate of 2-methyltricyclo[3.2.1.0^{2,7}]octan-6-*exo*-ol with *p*-toluenesulfonyl chloride in pyridine has similarly been found to yield 2-*endo*-methylbicyclo[3.2.1]oct-6-en-2-*exo*-ol (11%), in addition to 2-methylbicyclo[3.2.1]octa-2,6-diene (50%) and 2-methylenebicyclo-[3.2.1]oct-6-ene (3%).[21]

(25) The ^{13}C–^{199}Hg couplings are consistent with a 4-*endo*-acetoxymercurio group (J(^{13}C–^{199}Hg): C1, 25 Hz; C2, n.o.; C3, 64 Hz; C4, 1641 Hz; C5, 74 Hz; C6, 34 Hz; C7, n.o.; C8, 299 Hz). A heteronuclear correlation spectrum allowed assignment of the carbon–proton connectivities and, in conjunction with the selective decoupling, assignment of the ^{1}H NMR spectrum. A difference NOE spectrum of the crude organomercurial mixture, with irradiation of H8s at 1.55 ppm, gave enhancements at H4-exo/H5 (c. 2.9 ppm, 11.6% total), H1 (2.56 ppm, 2.7%), H8a (1.97 ppm, ca. 13%), and the methyl (1.29 ppm, 1.8%), further confirming the exo stereochemistry of C4-H (and the methyl).

(26) The magnitude of the coupling from H3-endo to H4-exo (12.5Hz) and also from H3-exo to H4-exo (5.3 Hz) further supports the assignment of the deuterium stereochemistry.

(27) The **14b** was identical in all respects with a sample obtained from sodium mercury amalgam reduction in sodium deuteroxide of the organomercurial mixture from the reaction of **12** with mercuric acetate in methanol.

(28) In a manner similar to *endo*-tricyclo[3.2.1.0^{2,4}]octane.[6]

orbital interaction of the C1,C8/C5,C8 framework with a C2,C4 edge protonated or mercurated species will disfavor edge attack and favor corner attack at C4.[29] For attack by mercuric acetate the preference for corner attack at C4 reflects this favorable cyclopropyl HOMO/mercury 6s LUMO interaction. Edge attack at C2,C4 of the cyclopropyl ring is disfavored due to an unfavorable secondary orbital interaction with the C1,C8/C5,C8 contribution to the HOMO. The lack of rearrangement products resulting from C1,C8 σ bond interaction with the positive charge at C2 indicates electron donation from the C1,C8 bond is no longer necessary as compared with similar reaction of *endo*-tricyclo[3.2.1.$0^{2,4}$]octane. The methyl group is now able to satisfy the bulk of the electronic demand in polarization of the cyclopropyl group upon protonation.

The lack of sterespecificity observed in nucleophilic attack on hydrocarbon **1**, as represented by the ratio of **3a**:**5a**, cannot be explained by the intermediacy of cation **2** alone. However, the results can be accommodated by inclusion of the free tertiary carbocation **4** as an intermediate in competition with attack at the bridged species **2**. An indication of the degree of nucleophilic attack on cations **4** and **2** was obtained as follows. Solvolysis of the *p*-nitrobenzoate of 1-methylbicyclo[2.2.2]octan-2-ol in either acetone/water or acetic acid has been found to give only 2-*exo*-methylbicyclo[3.2.1]octan-2-*endo*-ol (45%) and 2-*endo*-methylbicyclo[3.2.1]octan-2-*exo*-ol (55%), the products from kinetic attack at cation **4**.[30] If methanol attack on **4** proceeds with a similar ratio, then the product ratios observed in the acid-catalyzed methanol addition of **1** at 25 °C require nucleophilic attack at the corner protonated species **2** to account for only ca. 3% of the reaction pathway. Collapse of this species to the tertiary carbocation **4** and subsequent proton elimination or nucleophilic attack accounts for the remaining 97% of the reaction pathway.[31] The higher ratio of nucleophilic capture to elimination in the addition of methanol to **4**; 78:22 as compared to that in the reported acetolysis of 2-(4-methylcyclohex-3-enyl)ethyl brosylate[32] (18:55) is a reflection of the better nucleophilicity of methanol as compared with acetic acid.

In the reaction of **1** with mercuric acetate, the 9:1 ratio of **3c**:**5c** requires nucleophilic capture of the corner mercurated species **2c** to the extent of ca. 82%. This reflects the lesser charge development at C2 (i.e. greater orbital interaction between C2 and C4 in **2c**) in the oxymercuration reaction, a consequence of the poor overlap of the mercury 6s atomic orbital with the HOMO of **1** (Figure 1).

In the reactions of **12** nucleophilic attack at the initially formed protonated cyclopropane **13a** is competitive with collapse to the free tertiary cation **15a** in a manner similar to that observed in the protonation of **1**. However, the tertiary cation **15a** is sufficiently stable and long lived to allow conformational change and interaction of the positive charge at C2 and the π-system, resulting in the formation of **17a**.[33] Given the instability of **18a** to the reaction conditions, the degree of involvement of the two cations **15** and **17** cannot be stated with any certainty, since **16a** may arise from either initial methanol addition to hydrocarbon **12** or from subsequent decomposition of **18a**. However if we assume 27% of **16b** arises from subsequent decomposition of **18b** then, under kinetic control, approximately 54% of the reaction pathway will proceed through cation **17b**. Therefore nucleophilic attack at the protonated cyclopropane **13b** occurs to the extent of ca. 15%, nucleophilic attack at **15b**[34] accounting for the remaining 31%. This requires a greater degree of nucleophilic attack (ca. 15:3) at the protonated cyclopropane **13a** than is the situation with **1** and is not inconsistent with a electron-withdrawing inductive effect by the double bond, initially disfavoring the development of positive charge at C2.

In all of the products from the acid-catalyzed methanol-d_1 addition to **12**, the deuterium is at C4-endo, consistent with initial corner attack by the deuteron. Similarly to the analogous *endo*-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene, the HOMO of **12** would be expected to contain a contribution from the Walsh e_s orbital, the C6,C7 π-bond, and the C1,C8/C5,C8 σ orbitals, in addition to a contribution from the methyl group (Figure 1). Electrophilic attack at the edge of the C2,C4 cyclopropyl bond of **12** is unfavorable due to a secondary orbital interaction between the electrophile LUMO and the C1,C8/C5,C8 contribution to the HOMO as outlined in the discussion of the reaction of **1**. The methyl will also offer some hinderance to attack at the edge of the C2–C4 bond. There are no significant unfavorable frontier orbital interactions for protonation (mercuration) at the corner of C4, and therefore attack at this position is observed. The observation of exclusive protonation at the cyclopropyl ring and not at the double bond reflects the kinetic favorability of this process, further enhanced by the presence of a methyl group at C2. Mercuration similarly occurs at the cyclopropyl ring as a consequence of the greater charge stabilization possible with the C2-methyl.

Experimental Section

General Methods. NMR spectra were obtained on a Varian T-60 or Varian XL-300 (300-MHz ^{1}H, 75-MHz ^{13}C, 46-MHz ^{2}H). All ^{2}H NMR spectra were run unlocked with broad-band proton decoupling and an acquisition time of 4 s and using 2 drops of $CDCl_3$ (7.27 ppm) as an internal reference. LB in the ^{13}C NMR data shows the presence of peak broadening due to ^{13}C–^{2}H coupling. Heteronuclear proton–carbon correlation spectra were obtained using a relaxation time of 4 s between scans, 64 values of t_1, and zero filling to 256 points in f_1 (^{1}H). NOE's were obtained by difference spectroscopy, the decoupler offset for the reference spectrum being 10000 Hz. A delay time of 20 s was incorporated to ensure complete relaxation, along with a line broadening of 1 Hz and an acquisition time of 1.5 s with zero filling to 16384 points. Mass spectra were run on AEI MS902 spectrometer. A Hewlett-Packard HP 5890A GLC was used in both analytical and preparative modes. For preparative separations 1.5% OV-17 and 1.95% QF-1 on Chromosorb W in a column of 5 mm external

(29) For edge attack the electrophile interacts unfavorably with the antisymmetric filled orbital while corner attack is favorable.[3]

(30) Kraus, W. *Justus Liebigs Ann. Chem.* **1967**, *708*, 127.

(31) The requirement for a free tertiary carbocation in the acid catalyzed addition to **1** while being unusual for proton attack on cyclopropanes is not unique. The acetolysis of 5,5-dimethylbicyclo[2.1.0]-pentane proceeds by way of a tertiary cation. Wiberg, K. B.; Kass, S. R.; Bishop, K. C. *J. Am. Chem. Soc.* **1985**, *107*, 996.

(32) The acetolysis of 2-(4-methylcyclohex-3-enyl)ethyl brosylate at 80 °C for 28 h has been reported to yield 2-methylbicyclo[3.2.1]oct-2-ene (55%), 2-*endo*-acetoxy-2-*exo*-methylbicyclo[3.2.1]octane (8%), 2-*exo*-acetoxy-2-*endo*-methylbicyclo[3.2.1]octane (10%), and 2-(4-methylcyclohex-3-enyl)ethyl acetate (27%). Felkin, H.; Lion, C. *Tetrahedron* **1971**, *27*, 1375. 2-Acetoxy-1-methylbicyclo[2.2.2]octane was not observed. However, it is to be noted that leakage from the tertiary cation to the bicyclo[2.2.2]octane occurs in our reaction only after prolonged periods at 80 °C. Berson, J. A.; Gajewski, J. J.; Donald, D. S. *J. Am. Chem. Soc.* **1969**, *91*, 5550, and references therein.

(33) This interconversion is similar to that observed in the reaction of hydrocarbon **12** with tetracyanoethylene (TCNE). Unlike the reaction of TCNE, nucleophilic attack at **15a** is competitive with rearrangement. Coxon, J. M.; de Bruijn, M.; Lau, C. K. *Tetrahedron Lett.* **1975**, 337.

(34) This calculation assumes the ratio of exo to endo attack at cation **15b** by methanol to be similar to the 55:45 ratio observed for nucleophilic attack at the analogous cation **4**.

diameter and length 3 m was used. Unless otherwise stated all preparative separations employed this column.

2-Methyl-*endo*-tricyclo[3.2.1.0^{2,4}]oct-6-ene (12). 1-Methylcyclopropene[35] was bubbled with N_2 into a solution of cyclopentadiene (30 g) in methylene chloride (50 mL) at −78 °C for 6 h. The solvent was removed by distillation through a Vigreux column, and the residue was purified by spinning band distillation to give **12**: ^{1}H NMR ($CDCl_3$) δ_H 5.88 (dd, $^3J_{7,1}$ = 3.5 Hz, $^3J_{7,6}$ = 5.5 Hz, H7), 5.68 (dd, $^3J_{6,7}$ = 5.5 Hz, $^3J_{6,5}$ = 3.2 Hz, H6), 2.84 (s, $W_{h/2}$ = 8 Hz, H5), 2.44 (s, $W_{h/2}$ = 6 Hz, H1), 1.92 (dt, $^2J_{8s,8a}$ = 6.8 Hz, $^3J_{8s,5}$ = $^3J_{8s,1}$ = 1.8 Hz, H8s), 1.65 (dd, $^2J_{8a,8s}$ = 6.8 Hz, $^5J_{8a,3exo}$ = 2.0 Hz, H8a), 1.32 (s, $W_{h/2}$ = 2 Hz, CH_3), 1.00 (dt, $^3J_{3endo,3exo}$ = 7.0 Hz, $^3J_{3endo,4}$ = ^4J = 3.5 Hz, H3-end), 0.56 (dd, $^2J_{4,3endo}$ = 3.1 Hz, $^3J_{4,3exo}$ = 5.1 Hz, H4), 0.48 (m, $^2J_{3exo,3endo}$ = 7.2 Hz, $^3J_{3exo,4}$ = 5.1 Hz, $^5J_{3exo,8a}$ = 2.6 Hz, H3-exo); ^{13}C NMR as published.[33]

2-Methyl-*endo*-tricyclo[3.2.1.0^{2,4}]octane (1). To a suspension of activated palladium on carbon (5%, 80 mg) in pentane was added **12** (1 g) in pentane (30 mL), and the mixture was stirred in a hydrogen atmosphere until 1 molar equiv of hydrogen had been adsorbed. The mixture was filtered, and the solvent was removed by distillation through a Vigreux column. The residual liquid was left in an open flask for a few hours to remove the last traces of pentane to give **1** (0.76 g, 76%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ_H 2.26 (s, $W_{h/2}$ = 9 Hz, H5), 1.97 (s, $W_{h/2}$ = 7 Hz, H1), 1.92 (m, $^2J_{8s,8s}$ = 8.3 Hz, $^3J_{8s,1}$ = $^3J_{8s,5}$ = $^4J_{8s,6endo}$ = $^4J_{8s,7endo}$ = 2.2 Hz, H8s), 1.38–1.27 (H8a, H6exo, H7-exo), 1.15 (s, Me), 1.10–0.95 (H6-endo, H7-endo, H4, H3-endo), 0.56 (m, $^2J_{3exo,3endo}$ = 7.8 Hz, $^3J_{3exo,4}$ = 5.6 Hz, $^5J_{3exo,8a}$ = 2.2 Hz, H3-exo); the following assignments were obtained from a heteronuclear correlation experiment: 1.33 (H8a), 1.32 (H6-exo), 1.28 (H7-exo), 1.07 (H6-endo), 1.00 (H4, H7-endo), 0.94 (H3-endo); ^{13}C NMR ($CDCl_3$) δ_C 50.8 (C8), 42.3 (C1), 38.3 (C5), 29.8 (C4), 27.1 (C6), 26.2 (C7), 24.3 (C3), 22.5 (Me), C2 not observed.

Reaction of 1 with Methanol *p*-Toluenesulfonic Acid. (a) At Room Temperature. To **1** (118 mg) was added 2 mL of a solution containing *p*-toluenesulfonic acid (181 mg) in methanol (10 mL). The mixture was kept at room temperature for 4 days and diluted with water (5 mL), the product was extracted into pentane, washed with aqueous sodium carbonate, and dried over $MgSO_4$, and the solvent was removed under reduced pressure to give a colorless oil (103 mg, 75%) shown to contain **1** (19%), 2-methylbicyclo[3.2.1]oct-2-ene (**6a**) (18%), 2-*exo*-methoxy-2-*endo*-methylbicyclo[3.2.1]octane (**5a**) (32%), and 2-*endo*-methoxy-2-*exo*-methylbicyclo[3.2.1]octane (**3a**) (31%) separated by preparative GLC. 2-Methylbicyclo[3.2.1]oct-2-ene (**6a**): ^{1}H NMR ($CDCl_3$) δ_H 5.03 (br s, $W_{h/2}$ = 8 Hz, H3), 2.27 ($W_{h/2}$ = 16 Hz, H4-exo, H5), 2.12 (t, $^3J_{1,8a}$ = $^3J_{1,7exo}$ = 4.2 Hz, H1), 1.8–1.3 (m, 10 H); the following assignments were determined from a heteronuclear correlation experiment 1.76 (H6-exo), 1.73 (H4-endo), 1.70 (H7-exo, H7-endo), 1.65 (Me), 1.50 (H8s, H8a), 1.40 (H6-endo); ^{13}C NMR ($CDCl_3$) δ_C 141.9 (C2), 116.6 (C3), 40.7 (C1), 36.8 (C4), 35.3 (C8), 34.5 (C7), 33.2 (C5), 30.5 (C6), 22.6 (Me). **3a** (93% pure GLC): ^{1}H NMR ($CDCl_3$) δ_H 3.17 (s, OMe), 2.13 ($W_{h/2}$ = 11 Hz, H1, H5), 1.84 (m, H7-exo), 1.68–1.55 (m, 2 H, H8a, H6-exo), 1.5–1.3 (m, 7 H's, H8s, H4-exo, H4-endo, H3-exo, H3-endo, H7-endo, H6-endo), 1.20 (s, Me); the following assignments were determined from a heteronuclear correlation experiment 1.65 (H6-exo), 1.56 (H8a), 1.51 (H7-endo), 1.55–1.45 (H3-exo, H3-endo), 1.43 (H4-exo, H4-endo, H6-endo), 1.28 (H8s); ^{13}C NMR ($CDCl_3$) δ_C 76.8 (C2), 48.0 (OMe), 42.9 (C1), 35.5 (C8), 34.5 (C5), 31.4 (C3), 30.0 (C4), 27.6 (C6), 24.5 (C7), 20.9 (Me). **5a** (75% pure GLC): ^{1}H NMR ($CDCl_3$) δ_H 3.18 (OMe), 2.10 ($W_{h/2}$ = 15 Hz, H5, H1), 1.94 (dt, $^2J_{8s,8a}$ = 11 Hz, $^4J_{8s,6endo}$ = $^4J_{8s,7endo}$ = 1.5 Hz, H8s), 1.7–1.55 (m, 3 H's, H4-exo, H7-exo, H6-exo), 1.50–1.35 (m, 3 H's, H6-endo, H3-exo, H7-endo), 1.30–1.15 (m, 3 H's, H4-endo, H3-endo, H8a), 1.06 (s, Me); the following assignments were determined from a heteronuclear correlation experiment 1.73 (H6-exo, H7-exo), 1.65 (H4-exo), 1.50–1.26 (H3-exo, H3-endo), 1.42 (H6-endo, H7-endo), 1.26 (H4-endo), 1.19 (H8a); ^{13}C NMR ($CDCl_3$) δ_C 77.2 (C2), 48.5 (OMe), 43.4 (C1), 33.6 (C5), 33.3 (C8), 29.7 (C3), 29.0 (C4), 28.0 (C6), 26.8 (C7), 22.3 (Me).

(35) Fisher, F.; Applequist, D. E. *J. Org. Chem.* **1965**, *30*, 2089. Magid, R. M.; Clarke, T. C.; Duncan, C. D. *J. Org. Chem.* **1971**, *36*, 1320.

(b) At 80 °C. A solution of **1** (240 mg) in anhydrous methanol (2 mL) and *p*-toluenesulfonic acid (9 mg) was placed in an ampoule (5 mL) and kept at 80 °C for 7 days. The mixture was extracted in the usual manner to give a light yellow oil (247 mg, 82%), shown to contain **6a** (53%), 2-methoxy-1-methylbicyclo[2.2.2]octane (**11a**) (8%), **5a** (21%), and 2-*endo*-methoxy-2-*exo*-methylbicyclo[3.2.1]octane (**3a**) (18%). Separation was achieved by preparative GLC. **11a**: ^{1}H NMR ($CDCl_3$) δ_H 3.32 (s, OMe), 3.02 (m, $^3J_{2endo,3endo}$ = 9.0 Hz, $^3J_{2endo,3exo}$ = 3.5 Hz, $^3J_{2endo,6a}$ = 1.7 Hz, H2-endo), 1.84 (m, $^2J_{3endo,3exo}$ = 12.4 Hz, $^4J_{3endo,2endo}$ = 8.6 Hz, $^3J_{3endo,4}$ = $^4J_{3endo,5a}$ = 2.9 Hz, H3-endo), 1.64 (m, H4, H6s), 1.55–1.38 (m, 6 H's, H5s, H3-exo, H5a, H7-exo, H8-exo, H8-endo), 1.28 (m, $^2J_{7endo,7exo}$ = 12 Hz, $^3J_{7endo,8endo}$ = 7.8 Hz, $^3J_{7endo,8exo}$ = 3.6 Hz, $^4J_{7endo,6s}$ = 1.2 Hz, H7-endo), 1.08 (m, H6a), 0.83 (s, Me); the following assignments were determined from a heteronuclear correlation experiment 1.54 (H5s), 1.51 (H8-exo), 1.49 (H3-exo), 1.46 (H5a), 1.43 (H7-exo), 1.41 (H8-endo); ^{13}C NMR ($CDCl_3$) δ_C 82.8 (C2), 56.3 (OMe), 34.5 (C3), 32.1 (C7), 26.2 (C6), 26.0 (C5), 25.6 (C8), 24.8 (C4), 24.7 (Me), C1 not observed; MS $C_{10}H_{18}O$ requires ($M^{\cdot+}$) 154.1358, found ($M^{\cdot+}$) 154.1354, 155 (9), 154 (25), 123 (19), 122 (51), 107 (13), 95 (23), 94 (100), 93 (36), 81 (47), 79 (30). The spectral data for **6a**, **3a**, and **5a** are identical with those reported above.

Reaction of 1 with Methanol-d_1 *p*-Toluenesulfonic Acid. (a) At Room Temperature. The reaction of **1** (268 mg) with methanol-d_1 was carried out as above for 7 days to give a colorless oil (230 mg, 68%) shown to contain **1** (26%), 4-*endo*-deuterio-2-methylbicyclo[3.2.1]oct-2-ene (**6b**) (16%), 4-*endo*-deuterio-2-*exo*-methoxy-2-*endo*-methylbicyclo[3.2.1]octane (**5b**) (30%), and 4-*endo*-deuterio-2-*endo*-methoxy-2-*exo*-methylbicyclo[3.2.1]octane (**3b**) (28%). Separation was achieved by preparative glc to give 4-*endo*-deuterio-2-methylbicyclo[3.2.1]oct-2-ene (**6b**): ^{1}H NMR ($CDCl_3$) δ_H 5.03 (br s, $W_{h/2}$ = 8 Hz, H3), 2.27 ($W_{h/2}$ = 16 Hz, H4-exo, H5), 2.12 (t, $^3J_{1,8a}$ = $^3J_{1,7exo}$ = 4.2 Hz, H1), 1.8–1.3 (m, 9 H's); the spectrum was almost identical with that of the nondeuterated compound; ^{13}C NMR ($CDCl_3$) δ_C 141.9 (C2), 116.3 (C3), 40.4 (C1), 36.3 ($J_{13C,2H}$ = 19.8 Hz, C4), 35.4 (LB, C8), 34.5 (C7), 33.0 (LB, C5), 30.5 (C6), 22.6 (Me); ^{2}H NMR ($CHCl_3$) δ_D 1.75 (D4-endo). **5b**: ^{1}H NMR ($CDCl_3$) δ_H 3.18 (OMe), 2.10 ($W_{h/2}$ = 11.8 Hz, H5, H1), 1.94 ($^2J_{8s,8a}$ = 11 Hz, $^4J_{8s,6endo}$ = $^4J_{8s,7endo}$ = 1.5 Hz, H8s), 1.7–1.55 (m, 3 H's, H4-exo, H7-exo, H6-exo), 1.50–1.35 (m, 3 H's, H6-endo, H3-exo, H7-endo), 1.30–1.15 (m, 2 H's, H3-endo, H8a), 1.06 (s, Me); the spectrum was almost identical with that of the nondeuterated compound; ^{13}C NMR ($CDCl_3$) δ_C 77.2 (C2), 48.5 (OMe), 43.4 (C1), 33.5 (LB, C5), 33.3 (LB, C8), 29.6 (C3), 28.6 $J_{13C,2H}$ = 19.8 Hz, C4), 28.0 (C6), 26.9 (C7), 22.4 (Me); ^{2}H NMR ($CHCl_3$) δ_D 1.23 (D4-endo). The spectral data for 4-*endo*-deuterio-2-*endo*-methoxy-2-*exo*-methylbicyclo[3.2.1]octane (**3b**) are identical with those reported in the major product from the sodium mercury reduction of the organomercurial mixture below. The C4-*endo*-H and C4-*exo*-H both absorb at 1.42 ppm in the nondeuterated compound.[36]

(b) At 80 °C. The reaction of **1** (240 mg) with methanol-d_1 *p*-toluenesulfonic acid was carried out as above, but at 80 °C for 7 days. The product was isolated as a light yellow oil (247 mg, 82%) and shown by GLC analysis to contain four compounds (42%, 21%, 19%, 17%). The products were separated by preparative GLC. 3,4-*endo*,9,9-tetradeuterio-2-methylbicyclo[3.2.1]oct-2-ene (**6**) (42%): ^{1}H NMR ($CDCl_3$) δ_H essentially as reported above, except 5.01 ppm (0.13 H, H3); ^{13}C NMR ($CDCl_3$) δ_C 40.4 (C1), 36.5 ($J_{13C,2H}$ = 18.9 Hz, C4), 35.3 (C8), 34.5 (C7), 32.7 (C5), 30.5 (C6), C2, C3, Me not observed; ^{2}H NMR ($CHCl_3$) δ_D 5.08 (0.82 D, D3), 1.78 (0.98 D, D4-endo), 1.62 (2.46 D, Me); mass spectrum shows 1% D^0, 7% D^1, 14% D^2, 10% D^3, 30% D^4, 38% D^5. 3,3,4-*endo*-9,9-Pentadeuterio-2-*endo*-methoxy-2-*exo*-methylbicyclo[3.2.1]octane (**3**) (17%): ^{1}H NMR ($CDCl_3$) δ_H essentially as above, except 1.18 (m, 0.68 H, Me); ^{13}C NMR ($CDCl_3$)

(36) A study of the spectrum of a mixture of 4-*exo*- and 4-*endo*-deuterio-2-*endo*-methoxy-2-*exo*-methylbicyclo[3.2.1]octane, obtained from the sodium borodeuteride reduction of the reaction products from the reaction of 2-*endo*-methyltricyclo[3.2.1.0^{2,4}]octane with mercuric acetate in methanol (carried out as outlined in the reduction of 4-*endo*-(acetoxymercurio)-2-*endo*-methoxybicyclo[3.2.1]octane), with Eu(fod)$_3$ was carried out. To a $CHCl_3$ solution of 8.6 mg of the reduction products was added, incrementally, a total of 78 mg of Eu(fod)$_3$, and the ^{2}H NMR spectrum recorded (with heteronuclear proton-deuteron decoupling). No resolution of the 4-exo and 4-endo deuterons was observed.

δ_C 76.8 (C2), 48.0 (OMe), 42.9 (C1), 35.4 (C8), 34.3 (C5), 27.6 (C6), 24.5 (C7), C3, C4, Me not observed; ^{2}H NMR ($CHCl_3$) δ_D 1.42 (2.43 D, D4-endo, D3-exo, D3-endo), 1.18 (2.20 D, Me); mass spectrum shows 1% D^0, 10% D^1, 1% D^2, 4% D^3, 16% D^4, 35% D^5, 33% D^6. 3,3,4-*endo*-9,9-Pentadeuterio-2-*exo*-methoxy-2-*endo*-methylbicyclo[3.2.1]octane (**5**) (19%): ^{1}H NMR ($CDCl_3$) δ_H almost identical with the nondeuterated compound except the loss of H4-endo, 1.18 ($^2J_{8a,8s}$ = 11.0 Hz, $^3J_{8a,1}$ = $^3J_{8a,5}$ = 5.4 Hz, H8a), 1.02 (m, 0.35 H, Me); ^{13}C NMR ($CDCl_3$) δ_C 77.2 (C2), 48.5 (OMe), 43.3 (C1), 35.5 (C5), 33.2 (C8), 27.9 (C6), 26.8 (C7), C3, C4, Me not observed; ^{2}H NMR ($CHCl_3$) δ_D 1.42 (D3-exo), 1.23 (D4-endo), 1.18 (D3-endo), 1.04 (2.57 D, Me); mass spectrum shows 6% D^0, 5% D^3, 16% D^4, 35% D^5, 35% D^6, 2% D^7. 6,6,5a,9,9-Pentadeuterio-2-*exo*-methoxy-1-methylbicyclo[2.2.2]octane (**11**) (21%): ^{1}H NMR ($CDCl_3$) δ_H essentially as for the nondeuterated compound, except the signal centered at 3.02 had lost the $^4J_{2,6a}$ coupling of 1.7 Hz (H2), 1.85 had lost $^4J_{3endo,5a}$ = 2.9 Hz (H3-endo), 1.22 lost $^4J_{7endo,6s}$ = 1.2 Hz (H7-endo), 1.03 (0.21 H, H6a), 0.77 (m, 0.5 H, Me); ^{13}C NMR ($CDCl_3$) δ_C 82.9 (C2), 56.4 (OMe), 34.5 (C3), 32.0 (LB, C7); 25.7 (C8), 24.8 (C4), C1, C6, C5, Me not observed; ^{2}H NMR ($CHCl_3$) δ_D 1.64 (D6s), 1.46 (ca. 0.95 D, D5a), 1.08 (D6a), 0.78 (2.43 D, Me).

Stability of 3a, 5a, and 6a under Reaction Conditions. (a) 2-*endo*-Methoxy-2-*exo*-methylbicyclo[3.2.1]octane (3a). (i) At Room Temperature. To a solution of 2-*endo*-methoxy-2-*exo*-methylbicyclo[3.2.1]octane (85 mg, prepared from the $NaBH_4$ reduction of 4-*endo*-(acetoxymercurio)-2-*endo*-methoxy-2-*exo*-methylbicyclo[3.2.1]octane (**3c**)) was added 1.3 mL of a solution containing *p*-toluenesulfonic acid (493 mg) in anhydrous methanol (25 mL). GLC analysis showed the epimer ratio was invariant for 21 days.

(ii) At 80 °C. To an ampoule containing 2-*endo*-methoxy-2-*exo*-methylbicyclo[3.2.1]octane (85 mg, prepared as above) was added 0.7 mL of a solution containing *p*-toluenesulfonic acid, and the solution kept at 80 °C for 8 days. GLC showed a mixture of **6a**, **11a**, **5a**, and **3a** in the ratio of 67:16:9:8, respectively. The product mixture was isolated and ^{1}H and ^{13}C NMR analysis was consistent with the GLC analysis. In a separate experiment, but after 26 h, the product was a mixture (92:0:4:2) of **6a**, **11a**, **3a**, and **5a**, respectively.

(b) 4-Deuterio-2-*endo*-methoxy-2-*exo*-methylbicyclo[3.2.1]octane (3b). To an ampoule (1 mL) containing **3b** (26 mg, obtained by preparative GLC of the products of the reaction of **1** with methanol-d_1 at room temperature and contaminated with 24% **5b**) was added 0.7 mL of a solution containing *p*-toluenesulfonic acid (54 mg) in methanol (5 mL). The ampoule was sealed and placed in an oven at 80 °C for 32 h. The product was isolated in the usual manner and GLC and ^{1}H and ^{13}C NMR analyses confirmed the presence of 4-deuterio-2-methylbicyclo[3.2.1]oct-3-ene (57%), 4-deuterio-2-*exo*-methoxy-2-*endo*-methylbicyclo[3.2.1]octane (23%), and 4-deuterio-2-*endo*-methoxy-2-*exo*-methylbicyclo[3.2.1]octane (19%). ^{2}H NMR ($CDCl_3$) δ_D 1.75, **6b**; 1.41, 4-*endo*-deuterio-2-*endo*-methoxy-2-*exo*-methylbicyclo[3.2.1]octane (**3b**); 1.24, 4-*endo*-deuterio-2-*exo*-methoxy-2-*endo*-methylbicyclo[3.2.1]octane (**5b**).

(c) 2-*exo*-Methoxy-2-*endo*-methylbicyclo[3.2.1]octane (5b). (i) At Room Temperature. To 4-*endo*-deuterio-2-*exo*-methoxy-2-*endo*-methylbicyclo[3.2.1]octane (16 mg, obtained by preparative GLC of the reaction mixture of **1** with methanol-d_1 at room temperature and contaminated with 32% of **3b**) was added 1.0 mL of a solution containing *p*-toluenesulfonic acid as above. GLC analysis showed the ratio of epimers to be invariant for 21 days.

(ii) At 80 °C. 2-*exo*-Methoxy-2-*endo*-methylbicyclo[3.2.1]-octane (**5a**) (16 mg, prepared as above) was kept at 80 °C for 8 days and shown to give a mixture of **6a**, **11a**, **5a**, and **3a** in the ratio of 69:16:8:8, respectively.

(d) 2-Methylbicyclo[3.2.1]oct-2-ene (6a) (22 mg) (obtained by preparative glc from the reaction of **1** and methanol at 80 °C) was added to an ampoule containing anhydrous methanol (3 mL) and *p*-toluenesulfonic acid (5 mg) and kept at 80 °C for 7 days. GLC analysis revealed the presence of **11a**, **5a**, **3a**, and **6a** in the ratio 2:34:36:28, respectively. The product mixture was isolated and ^{1}H and ^{13}C NMR spectra confirmed the above results.

Preparation of 7b and 8b. 3,3,4-*exo*-Trideuteriobicyclo-[3.2.1]octan-2-one[6] (370 mg) was reacted with MeMgI (prepared from 300 mg of magnesium and 0.6 mL of CH_3I) in ether to give a mixture of 2-*exo*-methyl-3,3,4-*exo*-trideuteriobicyclo[3.2.1]octan-2-*endo*-ol (**7a**) and 2-*endo*-methyl-3,3,4-*exo*-trideuteriobicyclo[3.2.1]octan-2-*exo*-ol (**8a**) (272 mg, 65%; 66:34) as a white solid. **7a**: ^{13}C NMR ($CDCl_3$)[37] δ_C 72.8 (C2), 47.6 (C1), 35.9 (C8), 33.8 (C5), 29.6 (t, $J_{13C,2H}$ = 19.4 Hz, C4), 27.5 (Me), 26.9 (C6), 24.9 (C7). **8a**: ^{13}C NMR ($CDCl_3$) δ_C 72.9 (C2), 46.8 (C1), 33.4 (C5), 29.0 (C6, C8), 28.3 (t, $J_{13C,2H}$ = 19.0 Hz, C4), 27.1 (Me), 24.9 (C7), C3 not observed.

The mixture (100 mg) was methylated with sodium amide/methyl iodide to give a mixture of 2-*exo*-methoxy-2-*endo*-methyl-3,3,4-*exo*-trideuteriobicyclo[3.2.1]octane (**8b**) and 2-*endo*-methoxy-2-*exo*-methyl-3,3,4-*exo*-trideuteriobicyclo[3.2.1]-octane (**7b**) as an oil (75 mg, 70%).[38] **7b**: ^{13}C NMR ($CDCl_3$) δ_C 76.5 (C2), 47.9 (OMe) 42.8 (C1), 35.4 (C8), 34.3 (C5), 29.4 (t, $J_{13C,2H}$ = 19.0 Hz, C4), 27.5 (C6), 24.4 (C7), 20.7 (Me), C3 not observed. **8b**: ^{13}C NMR ($CDCl_3$) δ_C 76.7 (C2), 48.3 (OMe), 43.3 (C1), 33.4 (C5), 33.2 (C8), 28.3 (t, $J_{13C,2H}$ = 19.0 Hz, C4), 27.9 (C6), 26.7 (C7), 22.2 (Me), C3 not observed.

Authentic samples of **3a** and **5a** were obtained from bicyclo-[3.2.1]octan-2-one by the above procedure.

Preparation of Deuterio-2-methylbicyclo[3.2.1]oct-2-ene. A mixture of **8a** and **7a** (260 mg, obtained from the reaction of 3,3,4-*exo*-trideuteriobicyclo[3.2.1]octan-2-one[6] with MeMgI) was heated under reflux with potassium hydrogen sulfate (200 mg) at 160 °C for 30 min. Isolation of the product gave 2-methyl-3,4-*exo*-dideuteriobicyclo[3.2.1]oct-2-ene (200 mg, 85%): ^{13}C NMR ($CDCl_3$) δ_C 116.5 (C3), 48.4 (C1), 36.5 ($J_{13C,2H}$ = 18.1 Hz, C4), 35.3 (C8), 34.4 (C7), 32.7 (C5), 30.5 (C6), 22.5 (Me); ^{2}H NMR ($CHCl_3$) δ_D 5.05 (0.25 D, D3), 2.30 (0.53 D, D4-exo), 1.75 (0.29 D, D4-endo), 1.65 (0.40 D, Me).

Reaction of 1 with Mercuric Acetate. To a solution of **1** (120 mg) in anhydrous methanol (1 mL) was added, with stirring, mercuric acetate (320 mg). After 4 h the unreacted mercuric acetate was removed by filtration, and the solvent was removed under reduced pressure to give a mixture (9:1) of 4-*endo*-(acetoxymercurio)-2-*endo*-methoxy-2-*exo*-methylbicyclo[3.2.1]octane (**3c**) and 4-*endo*-(acetoxymercurio)-2-*exo*-methoxy-2-*endo*-methylbicyclo[3.2.1]octane (**5c**) (310 mg, 82%) as a white solid. **3c**: ^{1}H NMR ($CDCl_3$) δ_H 3.16 (OMe), 2.83 (m, $^3J_{4exo,3end3}$ = 13.6 Hz, $^3J_{4exo,3exo}$ = 5.2 Hz, $^3J_{4exo,5}$ = $^4J_{4exo,6exo}$ = 1.5 Hz, H4-exo), 2.49 ($^3J_{5,6exo}$ = $^3J_{5,8a}$ = 5.1 Hz, $J_{199Hg,H5}$ = 120 Hz, H5), 2.07 (m, H1), 2.02 (s, OAc), 1.98 (m, H7-exo), 1.90–1.78 (m, H3-exo, H3-endo, H6-exo), 1.6–1.45 (m, H8a, H8s, H6-endo, H7-endo), 1.20 (s, Me); the following assignments were determined from a heteronuclear correlation experiment 1.92 (H3-exo), 1.85 (H3-endo), 1.79 (H6-exo), 1.56 (H8s), 1.52 (H8a), 1.48 (H7-endo), 1.45 (H6-endo); ^{13}C NMR ($CDCl_3$) δ_C 176.1 (OAc), 76.9 ($J_{199Hg,13C}$ = ca. 284 Hz, C2), 51.7 ($J_{199Hg,13C}$ = 1662 Hz, C4), 48.0 (OMe), 43.2 ($J_{199Hg,13C}$ = 27 Hz, C1), 40.5 ($J_{199Hg,13C}$ = 74 Hz, C5), 38.1 ($J_{199Hg,13C}$ = 67 Hz, C3), 36.8 ($J_{199Hg,13C}$ = 255 Hz, C8), 30.2 ($J_{199Hg,13C}$ = 28 Hz, C6), 24.2 (no ^{199}Hg–^{13}C coupling observed, C7), 23.4 (OAc), 20.5 (Me). Anal. Calc for $C_{12}H_{20}O_3Hg$: C, 34.91; H, 4.88. Found: C, 34.89; H, 4.91. A solution of the organomercurial mixture above (300 mg), dissolved in a minimum amount of methanol, was shaken with a saturated solution of potassium thiocyanate in water (2 mL). The mixture was extracted with chloroform and dried over $MgSO_4$, and the solvent was removed under reduced pressure to give a product enriched (ca. 90%) in 2-*endo*-methoxy-2-*exo*-methyl-4-*endo*-(thiocyanatomercurio)bicyclo[3.2.1]octane (**3d**) as an oil (285 mg): ^{1}H NMR ($CDCl_3$) δ_H 3.18 (s, OMe), 2.91 (m, $^3J_{4exo,3endo}$ = 13.7 Hz, $^3J_{4exo,3exo}$ = 5.2 Hz, $^3J_{4exo,5}$ = $^4J_{4exo,6exo}$ = 1.6 Hz, H4-exo), 2.57 (br s, $W_{h/2}$ = 13.4 Hz, H5), 2.14–1.80 (m, H1, H7-exo, H3-exo, H3-endo, H6-exo), 1.6–1.50 (m, H7-endo, H8s, H8a, H6-endo), 1.23 (s, Me); the following assignments were determined from a heteronuclear correlation experiment 2.10 (H1), 1.99 (H7-exo, ca. 1.96, Ho-exo, H3-endo), 1.88 (H6-exo), 1.54 (H7-endo, H8s, H8a), 1.53 (H6-endo); ^{13}C NMR ($CDCl_3$) δ_C 61.9 (C4), 48.1 (OMe), 43.0 (C5), 41.0 (C1), 38.2 (C3), 37.2 (C8), 30.5 (C6), 24.3 (C7), 20.6 (Me), C2 not observed.

Reduction of 3c with Sodium Mercury Amalgam. Mercury (50 g) was cautiously added to molten sodium (0.75 g) under

(37) The ^{13}C NMR spectrum is revised from that reported.[9]
(38) The spectral analysis is obtained from the mixture of epimers.

paraffin oil (20 mL), and the resulting amalgam was broken into small pieces under pentane and dried under vacuum for 1 h. To sodium amalgam (5 g, 1.5%) in NaOD D_2O (2 mL, 2 M) was added the organomercurial (106 mg), the mixture was stirred for 3 h, and water (4 mL) was added. The mixture was extracted with pentane to give a colorless oil (27 mg, 68%) shown to consist of **3b** (93%) and **5b** (7%). The major product, **3b**, was separated by preparative GLC: ^{1}H NMR ($CDCl_3$) δ_H 3.17 (s, OMe), 2.13 ($W_{h/2}$ = 16 Hz, H1, H5), 1.84 (m, H7-exo), 1.68–1.55 (m, 2 H, H8, H6-exo), 1.5–1.3 (m, 6 H, H8, H4-exo, H4-endo, H3-exo, H3-endo, H7-endo, H6-endo), 1.20 (s, Me); the spectrum was almost identical with that of the nondeuterated compound; ^{13}C NMR ($CDCl_3$) δ_C 76.8 (C2), 48.0 (OMe), 43.0 (C1), 35.5 (LB, C8), 34.4 (C5), 31.4 (C3), 29.7 ($J_{13C,2H}$ = 19.6 Hz, C4), 27.7 (C6), 24.6 (C7), 21.0 (Me); ^{2}H NMR ($CHCl_3$) δ_D 1.41 (D4-endo).

Reaction of 12 at Room Temperature with *p*-Toluenesulfonic Acid. (i) In Methanol. To **12** (215 mg) was added a solution of *p*-toluenesulfonic acid (12 mg) in anhydrous methanol (4 mL). After 3 days of stirring at 25 °C GLC analysis showed the presence of starting material (13%), 2-*exo*-methoxy-2-*endo*-methylbicyclo[3.2.1]oct-6-ene (**16a**) (33%), 2-*endo*-methoxy-2-*exo*-methylbicyclo[3.2.1]oct-6-ene (**14a**) (25%), and 6-*exo*-methoxy-2-methyltricyclo[3.2.1.$0^{2,7}$]octane (**18a**) (28%). The product mixture was extracted to give a colorless oil (199 mg, 73%). Chromatography on a silver nitrate (40 mL) impregnated silica column[39] and elution with pentane gave **12** and **18a** of varying purity. Further elution with pentane/ether (50:50) gave **16a**, followed by **14a**: ^{1}H NMR ($CDCl_3$) δ_H 6.03 (dd, $^3J_{7,6}$ = 5.7 Hz, $^3J_{7,1}$ = 2.8 Hz, H7), 5.88 (dd, $^3J_{6,7}$ = 5.8 Hz, $^3J_{6,5}$ = 2.7 Hz, H6), 3.20 (s, OMe), 2.59 (dd, $^3J_{1,7}$ = 2.5 Hz, $^3J_{1,8a}$ = 5.5 Hz, H1), 2.52 (s, $W_{h/2}$ = 10 H, H5), 1.87 (m, $^2J_{8s,8a}$ = 10.7 Hz, $^3J_{8a,5}$ = $^3J_{8a,1}$ = 5.3 Hz, $^4J_{8a,4endo}$ = 1.7 Hz, H8a), 1.65 (t d, $^2J_{3endo,2exo}$ = 11.6 Hz, $^3J_{3endo,4endo}$ = 3.6 Hz, $^3J_{3endo,4exo}$ = 11.6 Hz, H3-endo), 1.49 (d, $^2J_{8s,8a}$ = 11.0 Hz, H8s), 1.48 (m, H3-exo), 1.42–1.34 (m, H4-exo, H4-endo), 1.27 (s, Me); ^{13}C NMR ($CDCl_3$) δ_C 133.8 (C_7), 133.0 (C6), 48.2 (OMe), 47.5 (C1), 40.7 (C8), 39.1 (C5), 32.2 (C3), 23.0 (C4), 21.6 (Me), C2 not observed; MS $C_{10}H_{16}O$ requires ($M^{\bullet+}$) 152.1201, found ($M^{\bullet+}$) 152.1195. **16a**: ^{1}H NMR ($CDCl_3$) δ_H 5.94 (dd, $^3J_{7,1}$ = 2.8 Hz, $^3J_{7,6}$ = 5.7 Hz, H7), 5.88 (dd, $^3J_{6,5}$ = 2.6 Hz, $^3J_{6,7}$ = 5.4 Hz, H6), 3.19 (OMe), 2.54 ($W_{h/2}$ = 15.8 Hz, H1, H5), 1.95 (d, $^2J_{8s,8a}$ = 10.0 Hz, H8s), 1.72 (m, $^2J_{8a,8s}$ = 10.0 Hz, $^3J_{8a,1}$ = $^3J_{8a,5}$ = 5.1 Hz, $^4J_{8a,4endo}$ = 2. Hz, H8a), 1.62 (m, H4-exo), 1.55–1.50, H3-exo, H3-endo), 1.23 (m, H4-endo), 1.03 (Me); ^{13}C NMR ($CDCl_3$) δ_C 135.5 (C7), 133.4 (C6), 48.8 (OMe), 47.5 (C1), 38.8 (C8), 38.6 (C5), 31.2 (C3), 23.9 (Me), 22.2 (C4), C2 not observed; MS $C_{10}H_{11}O$ requires ($M^{\bullet+}$) 152.1201, found ($M^{\bullet+}$) 152.1207. **18a**: ^{1}H NMR[40] ($CDCl_3$) δ_H 3.44 (s, $W_{h/2}$ = 2 Hz, H6), 3.33 (OMe), 1.98 (s, $W_{h/2}$ = 8.8 Hz, H5), 1.82 (m, $^2J_{8a,8s}$ = 11.6 Hz, $^3J_{8a,1}$ = 3.7 Hz, $^3J_{8a,5}$ = 5.6 Hz, $^4J_{8a,4endo}$ = 2.1 Hz, H8a), 1.66–1.61 (H3-exo, H3-endo), 1.51 (m, H4-exo), 1.45 (d, $^2J_{8s,8a}$ = 11.7 Hz, H8s), 1.37 (m, H4-endo), 1.29 ($^3J_{7,1}$ = 5.5 Hz, H7), 1.19 (dd, $^3J_{1,7}$ = 5.4 Hz, $^3J_{1,8a}$ = 3.8 Hz, H1), 0.92 (Me); ^{13}C NMR ($CDCl_3$) δ_C 85.4 (C6), 55.6 (OMe), 34.9 (C5), 29.8 (C7), 27.9 (C8), 25.7 (C4), 25.0 (C1), 24.4 (Me), 23.3 (C3), 21.8 (C2); MS $C_{10}H_{16}O$ requires ($M^{\bullet+}$) 152.1201, found ($M^{\bullet+}$) 152.1213.

Hydrogenation of the Products. To prehydrogenated palladium on carbon (100 mg, 10%) in pentane was added a pentane solution of the crude reaction mixture (140 mg). The mixture was shaken under a hydrogen atmosphere for 30 min to give a colorless oil (80 mg, 57%). GLC and ^{1}H and ^{13}C NMR analyses showed this to contain **5a** and **3a** in the ratio of 1.37:1, respectively. The data (GLC and ^{1}H, ^{13}C NMR) for **5a** and **3a** are identical with those obtained from the products of reaction of **1** with methanol at room temperature.

(ii) In Methanol-d_1. The acid-catalyzed methanol-d_1 addition to **12** (845 mg) was carried out as above for 7 days to give a colorless oil (854 mg, 79%), shown by GLC analysis to contain **12** (21%), deuterio-2-methylbicyclo[3.2.1]octa-2,6-diene (7%), 4-*endo*-deuterio-2-*exo*-methoxy-2-*endo*-methylbicyclo[3.2.1]octane (**16b**) (30%), 4-*endo*-deuterio-2-*endo*-methoxy-2-*exo*-methylbicyclo[3.2.1]octane (**14b**) (17%), and 4-*endo*-deuterio-6-*exo*-methoxy-2-methyltricyclo[3.2.1.$0^{2,7}$]octane (**18b**) (17%). Separation was effected on a silver nitrate impregnated silica column. 4-*endo*-Deuterio-2-*endo*-methoxy-2-*exo*-methylbicyclo[3.2.1]oct-6-ene (**14b**):[41] mass spectrum shows 2% D^0, 95% D^1, 3% D^2. **16b**: ^{1}H NMR ($CDCl_3$) δ_H 5.94 (dd, $^3J_{7,1}$ = 2.8 Hz, $^3J_{7,6}$ = 5.7 Hz, H7), 5.88 (dd, $J_{6,5}$ = 2.6 Hz, $J_{6,7}$ = 5.4 Hz, H6), 3.19 (OMe), 2.54 ($W_{h/2}$ = 12.4 Hz, H1, H5), 1.95 (d, $^2J_{8s,8a}$ = 10.0 Hz, H8s); 1.72 (dt, $^2J_{8a,8s}$ = 10.0 Hz, $^3J_{8a,1}$ = $^3J_{8a,5}$ = 5.1 Hz, H8a), 1.62 (m, H4-exo), 1.55–1.50, H3-exo, H3-endo), 1.03 (Me); ^{13}C NMR ($CDCl_3$) δ_C 135.4 (C7), 133.3 (C6), 48.8 (OMe), 47.5 (LB, C1), 38.8 (LB, C8), 38.5 (LB, C5), 31.0 (C3), 23.8 (Me), 21.7 ($J_{13C,2H}$ = 19.6 Hz, C4), C2 not observed; ^{2}H NMR ($CHCl_3$) δ_D 1.22 (H4-endo); mass spectrum shows 1% D^0, 98% D^1, 1% D^2. **18b**: ^{1}H NMR ($CDCl_3$) δ_H 3.44 (s, $W_{h/2}$ = 2 Hz, H6), 3.33 (OMe), 1.94 (dd, $^3J_{5,4exo}$ = 4.6 Hz, $^3J_{5,8a}$ = 5.2 Hz, H5), 1.82 (m, $^2J_{8a,8s}$ = 11.6 Hz, $^3J_{8a,1}$ = 3.m Hz, $^3J_{8a,5}$ = 5.6 Hz, H8a), 1.66–1.61 (H3-exo, H3-endo), 1.51 (br d, $^3J_{4exo,3exo}$ = ca. 12 Hz, H4-exo), 1.45 (d, $^2J_{8s,8a}$ = 11.6 Hz, H8s), 1.29 (d, $^3J_{7,1}$ = 5.6 Hz, H7), 1.18 (dd, $^3J_{1,7}$ = 5.5 Hz, $^3J_{1,8a}$ = 3.8 Hz, H1), 0.91 (Me); ^{13}C NMR ($CDCl_3$) δ_C 85.3 (C6), 55.6 (OMe), 34.8 (LB, C5), 29.8 (C7), 27.8 (LB, C8), 25.4 ($J_{13C,2H}$ = 19.3 Hz, C4), 25.0 (C1), 24.4 (Me), 23.2 (C3), 21.8 (C2); ^{2}H NMR ($CHCl_3$) δ_D 1.32 (4-endo); mass spectrum shows 6% D^0, 92% D^1, 2% D^2.

Stability of 14b, 16b, and 18b under the Reaction Conditions at Room Temperature. (i) **14b** (18 mg, obtained from the acid-catalyzed reaction of **12** with methanol-d_1 at room temperature) in 0.7 mL of a solution containing *p*-toluenesulfonic acid (493 mg) in anhydrous methanol (25 mL) was shown by GLC not to react after 21 days.

(ii) **16b** (10 mg, obtained as above) was added to 0.7 mL of *p*-toluenesulfonic acid in anhydrous methanol. After 21 days, the mixture contained **18b** and **16b** in the ratio of 1:9.

(iii) **18b** (10 mg, obtained as above) was added to 0.5 mL of a solution containing *p*-toluenesulfonic acid (94 mg) in anhydrous methanol (25 mL). After 22 h reaction, the mixture contained **16b** and **18b** in the ratio of 1:1. This product ratio was invariant for 21 days.

Reaction of 12 with Methanol Mercuric Acetate. To a stirred solution of **12** (275 mg) in anhydrous methanol (18 mL) was added mercuric acetate (900 mg). After 2 h the suspension was filtered, and the solvent was removed under reduced pressure for 12 h to give a pale, viscous oil (840 mg, 89%) consisting mainly of 4-*endo*-(acetoxymercurio)-2-*endo*-methoxy-2-*exo*-methylbicyclo[3.2.1]oct-6-ene (**14c**): ^{1}H NMR ($CDCl_3$) δ_H 6.20 (dd, $^3J_{7,6}$ = 5.8 Hz, $^3J_{7,1}$ = 2.8 Hz, H7), 6.00 (dd, $^3J_{6,7}$ = 5.8 Hz, $^3J_{6,5}$ = 2.6 Hz, H6), 3.19 (s, OMe), 2.90 ($W_{h/2}$ = 12 Hz, H5), 2.86 (m, $^3J_{4exo,3endo}$ = 12.5 Hz, $^3J_{4exo,3exo}$ = 5. Hz, $^3J_{4exo,5}$ = 2.0 Hz, H4-exo), 2.56 ($W_{h/2}$ = 12 Hz, H1), 2.21 (t, $^2J_{3endo,3exo}$ = 13.0 Hz, $^3J_{3endo,4exo}$ = 12.9 Hz, H3-endo), 2.02 (s, OAc), 1.97 (m, H8a), 1.89 (dd, $^2J_{3exo,3endo}$ = 13.0 Hz, $^3J_{3exo,4exo}$ = 5.5 Hz, H3-exo), 1.55 (d, $^2J_{8s,8a}$ = 9.1 Hz, H8s), 1.29 (s, Me); ^{13}C NMR ($CDCl_3$) δ_C 176.2 (OAc), 135.3 ($J_{199Hg,13C}$ not observed, C7), 132.7 ($J_{199Hg,13C}$ = 34 Hz, C6), 77.2 (C2), 48.3 (OMe) 47.6 ($J_{199Hg,13C}$ = 25 Hz, C1), 45.1 ($J_{199Hg,13C}$ = 74 Hz, C5), 42.7 ($J_{199Hg,13C}$ = 1640.9 Hz, C4), 41.8 ($J_{199Hg,13C}$ = 299 Hz, C8), 38.7 ($J_{199Hg,13C}$ = 64 Hz, C3).

Reduction with Sodium Mercury Amalgam. Reduction of the organomercurial mixture (477 mg) in sodium deuteroxide was carried out as previously described to give an oil (150 mg, 85%), shown to contain **16b** (11%), **14b**, (82%) and **18b** (7%). **14b** was separated by preparative GLC: ^{1}H NMR ($CDCl_3$) δ_H 6.03 (dd, $^3J_{7,6}$ = 5.7 Hz, $^3J_{7,1}$ = 2.8 Hz, H7), 5.88 (dd, $^3J_{6,7}$ = 5.8 Hz, $^3J_{6,5}$ = 2.7 Hz, H6), 3.20 (s, OMe), 2.59 (dd, $^3J_{1,7}$ = 2.5 Hz, $^3J_{1,8a}$ = 5.9 Hz, H1), 2.52 (dt, $^3J_{5,4exo}$ = $^3J_{5,6}$ = 2.5 Hz, $^3J_{5,8a}$ = 5.3o Hz, H5), 1.87 (dt, $^2J_{8s,8a}$ = 10.6 Hz, $^3J_{8a,5}$ = $^3J_{8a,1}$ = 5.3 Hz, H8a), 1.65 (t, $^2J_{3endo,3exo}$ = $^3J_{3endo,4exo}$ = 12.5 Hz, H3-endo), 1.49 (d, $^2J_{8s,8a}$ = 11.4 Hz, H8s), 1.48 (m, H3-exo), 1.42–1.34 (m, H4-exo), 1.27 (s, Me); ^{13}C NMR ($CDCl_3$) δ_C 133.8 (C7), 133.0 (C6), 77 (C2), 48.2 (OMe), 47.5 (C1), 40.7 (LB, C8), 39.0 (LB, C5), 32.1 (LB, C3), 22.6 ($J_{13C,2H}$ = 19.8 Hz, C4), 21.5 (Me); ^{2}H NMR ($CHCl_3$) δ_D 1.35 (D4-endo). **Hydrogenation of the Reduction Products.** To prehydrogenated palladium on carbon (10%, 100 mg) in pentane was added the products from the sodium mercury reduction in sodium hydroxide (225 mg). The mixture was shaken under a hydrogen atmosphere for 1 h and filtered, and the solvent was removed under reduced pressure to give an oil (164 mg, 73%)

(39) **14a** and **18a** are only partially separated by GLC for retention times upwards of 60 min.

(40) A $Eu(fod)_3$ study was performed on this compound (12.5 mg), $Eu(Fod)_3$ being added incrementally to 13.7 mg total.

(41) The spectral data are presented in the sodium amalgam reduction in sodium deuteroxide of the crude organomercurial mixture.

shown by GLC analysis and ^{13}C NMR to contain **5a** (10%), unknown compounds (12%), and **3a** (78%). The data (GLC and ^{13}C NMR) are identical with those from the products from reaction of 1 with methanol at room temperature.

Acknowledgment. We acknowledge grants from the Research Committee of the New Zealand Universities Grants Committee and helpful discussions with Professor M. A. Battiste.

Supplementary Material Available: ^{13}C and ^{1}H NMR spectra for compounds 1, **3a-d**, **5a,b**, **6a,b**, **12**, **14a-c**, **16a,b**, and **18a,b** (26 pages). Ordering information is given on any current masthead page.

Reaction of Carbonyl Compounds with Ethyl Lithiodiazoacetate. Studies Dealing with the Rhodium(II)-Catalyzed Behavior of the Resulting Adducts†

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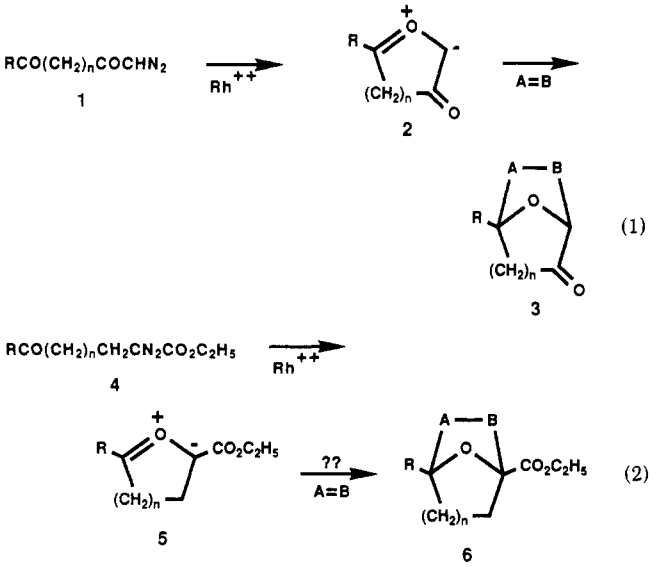
Received December 5, 1989

The carbenoid intermediate derived by treating ethyl 2-diazo-4-phthalimidobutyrate with rhodium(II) octanoate undergoes transannular cyclization onto the adjacent imido carbonyl group. The resulting cyclic carbonyl ylide dipole was trapped with several dipolarophiles. In an attempt to prepare related substrates for cyclization studies, the reaction of ethyl lithiodiazoacetate with various aldehydes and ketones was studied. Treatment of the α-diazo-β-hydroxy ester derived from acetone or cyclopentanone with rhodium(II) octanoate gave rise to a β-keto ester. The exclusive phenyl shift encountered with acetophenone is in keeping with migration to an electron-deficient center. The reaction works well with acrolein, leading to high yields of 3-oxo-4-pentenoate. The 1,2-hydrogen shift pathway was found to proceed much faster than intramolecular cyclopropanation. Dehydration of the α-diazo-β-hydroxy esters generates vinyl diazo esters, which readily cyclize to 1*H*-pyrazoles on thermolysis.

α-Diazo carbonyl compounds have found numerous applications in organic synthesis, and their use in either heterocyclic or carbocyclic ring formation is well documented.[1-14] Most of the early work has centered on the cyclopropanation and C-H insertion reactions of the resulting carbenes or metallocarbenoids.[15-18] Recently, we described the formation of oxabicyclo compounds from the rhodium(II) acetate catalyzed reaction of 1-diazoalkanediones.[19] The reaction involves the formation of a rhodium carbenoid and subsequent transannular cyclization of the electrophilic carbon onto the adjacent keto group to generate a cyclic carbonyl ylide followed by 1,3-dipolar cycloaddition (eq 1).[20,21] The ease with which α-diazo ketones 1 undergo this tandem cyclization-cycloaddition sequence suggested that a similar transformation should also occur with the related α-diazo keto ester system 4 (eq 2). We thought that this latter reaction could be of some synthetic value as it permits for the synthesis of novel functionalized THF derivatives of type **6**. The importance of tetrahydrofuran ring systems in natural products, interwoven with their rich diversity of molecular architecture, has continued to challenge the current level of synthetic methodologies.[22-25] Although a variety of methods exist



†Dedicated with respect and admiration to Professor Ernest Wenkert, one of the leading pioneers in the area of diazocarbonyl chemistry, on the occasion of his 65th birthday.

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