Corner Attack on *endo*- and *exo*-Tricyclo[3.2.1.0^{2,4}]oct-6-ene by Deuterium and Mercuric Ions: The Effect of Electrophile on Reaction Course

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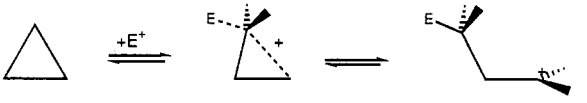
Reaction of *endo*-tricyclo[3.2.1.0^{2,4}]oct-6-ene (1) with mercuric acetate in methanol gave **2b** as the major product of reaction after stereospecific reduction with sodium-mercury amalgam in sodium deuteroxide, along with **3b** and **4b**. In contrast 4-*endo*-deuterio-2-*endo*-methoxybicyclo[3.2.1]oct-6-ene (**2b**) is formed as a minor product from acid-catalyzed reaction of *endo*-tricyclo[3.2.1.0^{2,4}]oct-6-ene (1) with methanol-d_1. Methoxymercuration of *exo*-tricyclo[3.2.1.0^{2,4}]oct-6-ene (8) occurs at the double bond to give 7-*exo*-(acetoxymercurio)-6-*exo*-methoxy-*exo*-tricyclo[3.2.1.0^{2,4}]octane (**9c**; 89%). Acid-catalyzed addition of methanol to *exo*-tricyclo[3.2.1.0^{2,4}]oct-6-ene (8) gave 6-*exo*-methoxy-*exo*-tricyclo[3.2.1.0^{2,4}]octane (**9a**; 15%) and 6-*exo*-methoxytricyclo[3.2.1.0^{2,7}]octane (11) in a process involving corner attack of the electrophile. This tricyclic compound rearranges to 5-*exo*-methoxybicyclo[2.2.2]oct-2-ene (**10a**; 55%). The preference for corner attack by mercuric ion and deuteron with C2-C4 bond cleavage in the reactions of 1 and 8 is rationalized and the competition between reaction at cyclopropane and addition to the double bond discussed.

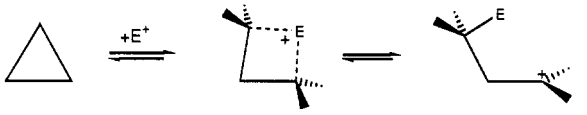
The stereochemistry of proton attack on cyclopropanes and the microscopic reverse process, the formation of cyclopropanes by proton loss from propan-1-yl cation analogues, has been a matter of debate and interest in both chemical[1] and biological systems.[2] Electrophilic addition to cyclopropane or the microscopic reverse process, namely loss of an electrophile, can occur with inversion (Scheme Ia) or with retention[1,3] (Scheme Ib).

In several biochemical pathways the intermediacy of a cyclopropane has been either established or postulated. For example the loss of the 3α-tritium label from [3α-^{3}H]ergosta-7,22-diene-3β,5α-diol upon its conversion into ergosterol by a partially purified yeast enzyme has been postulated to involve the intermediacy of a cyclopropane, which requires edge loss of tritium and edge attack by a proton[4] (Scheme II). Hydrogen loss of one of the two diastereotopic hydrogen atoms at C1 of the prenyl donor in the condensation to the cyclopropyl presqualene pyrophosphate for the biosynthesis of plant and animal steroids occurs with retention of configuration at the carbon from which proton loss occurs[5] (Scheme III). Further along the biological pathway the stereochemical outcome of cyclization and rearrangement of squalene 2,3-epoxide carrying a chiral-labeled C6 methyl group of predominantly *R* absolute configuration with a microsomal preparation from *Ochromonas malhamensis* gives the major species containing exo-tritium and endo-deuterium at the C19 methylene group (Scheme IV). Again the conversion proceeds with retention of configuration.[6] The same conclusion was also derived independently by Arigoni and Blattler[7] from experiments using stereospecifically labeled squalene oxide (*S* configuration at C6) and cyclase obtained from maize. The stereochemistry of ring-opening reactions of several simpler cyclopropanes has been studied.[1,8] Early work in this area favored edge protonation.

Scheme I

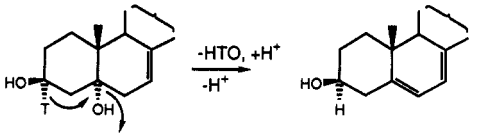


(a) Electrophilic corner attack (loss) with inversion of configuration

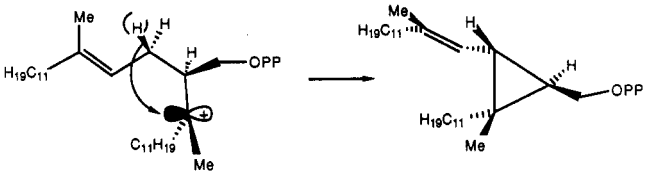


(b) Electrophilic edge attack (loss) with retention of configuration

Scheme II



Scheme III



(1) 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 269.

(2) Liu, H.-W.; Walsh, C. T. In *The Chemistry of the Cyclopropyl Group*; Rappoport, Z., Ed.; Wiley and Sons: New York, 1987; Chapter 16, p 959.

(3) Carpenter, B. K. In *The Chemistry of the Cyclopropyl Group*; Rappoport, Z., Ed.; Wiley and Sons: New York, 1987; Chapter 17, p 1066.

(4) Topham, R. W.; Gaylor, J. L. *Biochem. Res. Commun.* **1972**, *47*, 180.

(5) Donninger, C.; Popjak, G. *Proc. R. Soc. Lond. Ser. B* **1966**, *163*, 465.

(6) Altman, L. J.; Han, C. Y.; Bertolino, A.; Handy, G.; Laungani, D.; Muller, W.; Schwartz, S.; Shanker, D.; de Wolf, W. H.; Yang, F. *J. Am. Chem. Soc.* **1978**, *100*, 3235.

(7) Arigoni, D.; Blattler, W. A. quoted by Floss, H. G.; Tsai, M.-D. *Adv. Enzymol.* **1979**, *50*, 243. Also: Retey, J.; Robinson, J. A. In *Stereospecificity in Organic Chemistry and Enzymology*; Verlag Chemie: Weinhein, 1982, p 236. Reference 2 p 992. The cycloartenol product was after hydrogenation reacted with hydrochloric acid, and the C10 methyl group isolated from Kuhn-Roth degradation was shown to have the same chirality as the methyl group at C6 in the squalene 2,3-oxide. The retention-retention or inversion-inversion pathway was distinguished by acid-catalyzed opening of cycloartenol acetate having tritium and deuterium stereospecifically labeled at C19. From degraditive oxidation of the product the reaction was shown to have undergone addition of the proton with retention at the least substituted carbon. The enzymatic ring closure was therefore established as occurring with retention of configuration.

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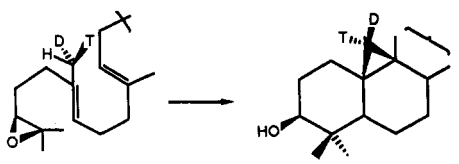
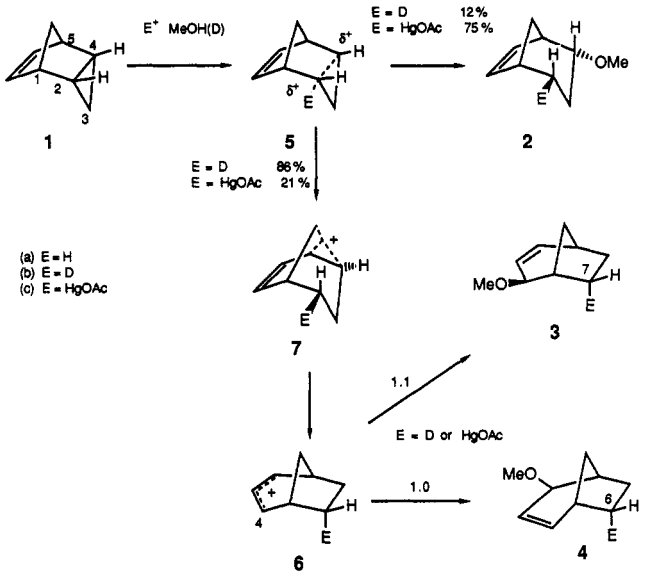
Scheme IV



Scheme V



The discussion has, however, often confused[9] corner-protonated cyclopropane and corner attack with inversion[10] (Scheme Ia).

Little cognizance[11] has been taken of electrophilic attack at cyclopropane at the corner with inversion and the microscopic reverse (Scheme Ia). For the reaction of bromine at cyclopropane the experimental evidence[12] demonstrates that a corner brominated species is not a reaction intermediate, and the reaction proceeds by way of a cation analogous to that shown in Scheme Ia.[13] We have investigated selected tricyclic cyclopropyl compounds[8,11,14] and found that, for reaction with a proton, attack does indeed occur at the corner with inversion. However the generality of these studies remains to be tested.

Results and Discussion

We have previously reported[14] a study of the reaction of *endo*-tricyclo[3.2.1.0^{2,4}]oct-6-ene (**1**) with methanol-d_1, in the presence of catalytic quantities of *p*-toluenesulfonic acid, to probe the stereochemistry of electrophilic attack. In undeuterated methanol the reaction gives three products: 2-*endo*-methoxybicyclo[3.2.1]oct-3-ene, 2-*endo*-methoxybicyclo[3.2.1]oct-6-ene (**2a**), and 2-*exo*-methoxybicyclo[3.2.1]oct-3-ene (**3a**) in the ratio 2:12:86 (>90% material balance). When the reaction was carried out in methanol-d_1, the deuterium in the major product was incorporated endo at C6 and C7, thereby defining the stereochemistry of proton (deuteron) attack on the hydrocarbon at C2 or C4 in the formation of the product. This stereochemistry differs from that observed in the biological investigations reported above, and it is therefore of interest to establish the factors that contribute to the stereochemistry, reactivity, and regiochemistry of cyclopropane cleavage.

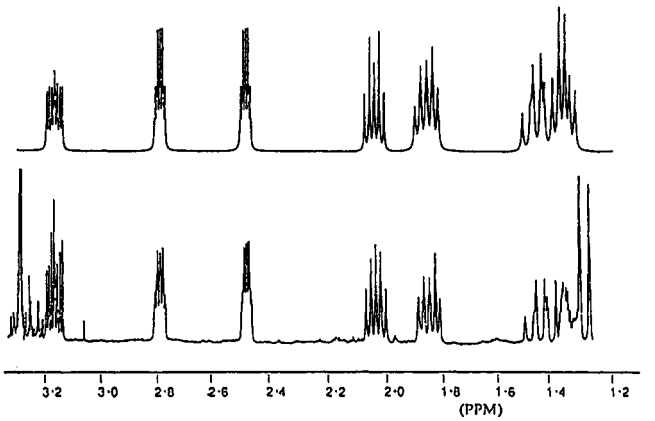


Figure 1. Top: simulated spectrum of 4-*endo*-deuterio-2-*endo*-methoxybicyclo[3.2.1]oct-6-ene. Bottom: actual spectrum (300 MHz).

To probe the role of an electrophile and structure in defining the course of reaction at cyclopropane and to study the comparative reactivity for reaction at alkene vs cyclopropane, we report a further study on the chemistry of *endo*-tricyclo[3.2.1.0^{2,4}]oct-6-ene (**1**) and *exo*-tricyclo[3.2.1.0^{2,4}]oct-6-ene. These compounds were selected for study because of the complimentary relationship of the cyclopropane ring to the skeleton and the presence of an alkene site in each molecule allowing orbital effects to be differentiated from conformational and steric effects while at the same time allowing competition between cyclopropane and double bond to be elucidated.

Reaction of 1 with Mercuric Acetate, H$^+$, and D$^+$ in Methanol-d_1. Reaction of **1** with mercuric acetate in methanol gives 4-*endo*-(acetoxymercurio)-2-*endo*-methoxybicyclo[3.2.1]oct-6-ene (**2c**) as the major product. This compound was not separated from **3c** and **4c** but was formed in sufficiently high yield in the reaction mixture to determine the ^{1}H and ^{13}C NMR parameters and unambiguously establish the structure.[15] The identity of **2a**, isolated when the mercuric adducts are reduced in protic media, follows from the ^{1}H NMR spectrum[16] and was confirmed by hydrogenation to 2-*endo*-methoxybicyclo-

(8) Coxon, J. M.; Steel, P. J.; Whittington, B. I.; Battiste, M. A. *J. Org. Chem.* **1989**, *54*, 1383 and references therein.
(9) Reference 3, p 1066.
(10) A corner protonated species (i) is a necessary structure in the migration of a methyl group in a 1,2-methyl migration but is not a requirement in the opening of a cyclopropane or the reverse process.

i

(11) Battiste, M. A.; Coxon, J. M.; Steel, P. J.; Whittington, B. I. *J. Am. Chem. Soc.* **1988**, *110*, 2988.
(12) Lambert, J. B.; Schulz, W. J.; Mueller, P. H.; Kobayashi, K. *J. Am. Chem. Soc.* **1984**, *106*, 792.
(13) Battiste, M. A.; Coxon, J. M. *Tetrahedron Lett.* **1986**, *27*, 517.
(14) Battiste, M. A.; Coxon, J. M.; King, R. W.; Simpson, G. W.; Steel, P. J.; Jones, A. J. *Tetrahedron* **1984**, *40*, 3137.

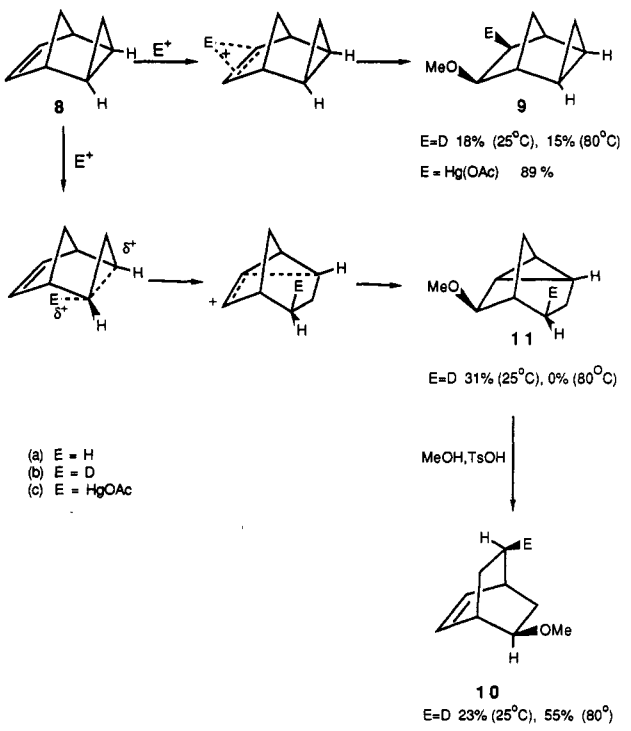
(15) The C2H (3.26 ppm) was axial, coupled with C1H at 2.77 ppm (3.2 Hz), C3-endo-H at 1.95 ppm (9.5 Hz) and C3-exo-H at 2.26 ppm (5.7 Hz); C4H centered at 2.73 ppm was axial, coupled to C5H at 2.88 ppm (2.5 Hz) and with C3-exo-H (5.7 Hz) and C3-endo-H (12.6 Hz). The ^{1}H NMR spectrum established that the mercury and methoxy groups are adjacent to the C3-methylene and defined their stereochemistry. A homonuclear proton–proton correlation 2D NMR experiment further confirmed the structure of **2c**.
(16) H2 (3.19 ppm) was coupled to H1 (J = 2.7 Hz; 2.84 ppm), which is deshielded by the double bond, and to (H3)$_2$ (J = 5.6, 9.3 Hz). The magnitude of the larger coupling to an adjacent H3 establishes the configuration of H2 as pseudoaxial. H1 and H5 are coupled to H8anti (J = 5.5 Hz), and the apparent absence of coupling to H8syn is consistent with the geometry of the bicyclic [3.2.1] skeleton.

[3.2.1]octane, identical by GLC capillary column analysis with an authentic sample.[14]

The mixture of mercuric adducts was reduced with sodium amalgam in sodium deuteroxide[17] to give 2-*endo*-methoxy-4-*endo*-deuteriobicyclo[3.2.1]oct-6-ene (**2b**; 75%), 2-*exo*-methoxy-6-*endo*-deuteriobicyclo[3.2.1]oct-3-ene (**4b**; 10%) and 2-*exo*-methoxy-7-*endo*-deuteriobicyclo[3.2.1]-oct-3-ene (**3b**; 11%). For the deuterated product **2b**, computer simulation using a Fortran LAME[18] program gave excellent agreement (Figure 1) between the experimental[19] and simulated spectrum. The identity of this product also confirms that reduction of **2b** under these conditions is stereospecific since the configuration of the mercury in **2c** was known. The identity of the minor products **3b** and **4b**, separated by preparative GLC, follows from their known ^1H and ^{13}C NMR spectra.[14] The configuration of the deuterium at C6 and C7 follows from the ^2H NMR spectrum,[20] which shows these products to be formed in the ratio 1.1:1.0. Most notable about the formation of **2c** as the major product of reaction is the absence of molecular rearrangement, mercury and methanol adding with rupture of the more substituted cyclopropane bond. Mercury reacts at the corner of the cyclopropane ring with inversion, but not at the least substituted carbon of the ring. The limited extent of rearrangement to the allylic cation **6c** by way of the corner-protonated cyclopropane **7c**, in contrast to the deuterated analogue **5b**, which partitions in favor of rearrangement, indicates the inherent stability of the mercurated cyclopropane **5c**, which undergoes nucleophilic attack more competitively than rearrangement to the allylic cation. The known absence of a conformational preference of mercury as a substituent on cyclohexane[21] suggests that the endo configuration of mercury in **6c** will not be an appreciable barrier to rearrangement. A high degree of orbital interaction between C4 and C2 in the mercurated cation **5c** results in less charge development at C2 compared with the deuterated analogue **5b**, and the reaction is therefore similar to that of alkenes with mercuric acetate where skeletal rearrangement is not normally observed.[22] The product **2c** is therefore formed by capture of the mercurated species **5c** before it relaxes with substantial charge development at C4. The ratio of products **3b** and **4b** is the same as that found[14] for the acid-catalyzed reaction of **1** with methanol-d_1, demonstrating that the cation **6c** exhibits a small memory effect with C4 marginally hindered relative to C2.

In a previous study of the reaction of hydrocarbon **1** with methanol-d_1 and *p*-toluenesulfonic acid,[14] the stereochemistry of deuterium in the minor product **2** was not investigated. We have now isolated this compound by preparative GLC and shown the deuterium substitution to be C4-endo,[23] demonstrating that this product, like the major product(s) **3b** and **4b**, is formed by stereospecific corner

Scheme VI



attack of the cyclopropane at C2(C4) (Scheme V). This is consistent with the reaction partitioning the product from a common intermediate **5b** formed by attack of deuterium at the substituted corner of the cyclopropyl ring.

Reaction of 8 with Mercuric Acetate, H^+, and D^+ in Methanol-d_1. In contrast to the mercuration of *endo*-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (**1**), the reaction of *exo*-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (**8**) with mercuric acetate in methanol gives 7-*exo*-(acetoxymercurio)-6-*exo*-methoxy-*exo*-tricyclo[3.2.1.$0^{2,4}$]octane (**9c**; 89%), resulting from attack at the double bond rather than at the cyclopropyl ring (Scheme VI).[24] The exo configuration of the cyclopropyl group[25] in **9c** and the acetoxymercurio group follows from the ^1H NMR spectrum,[26] ^{13}C–^{199}Hg couplings,[27] and difference NOE spectra.[28] Reduction[17] of the organomercurial mixture with sodium amalgam in sodium hydroxide gave 6-*exo*-methoxy-*exo*-tricyclo[3.2.1.$0^{2,4}$]octane (**9a**). The ^{13}C NMR data of **9a** were assigned by comparison with the known *exo*-tricyclo[3.2.1.$0^{2,4}$]octan-6-*exo*-ol,[29] a heteronuclear correlation spectrum, proton–proton decoupling, and difference NOE spectra, allowing complete assignment of the ^1H NMR spectral data. Stereospecific reduction of the organomercurial product **9c** with sodium amalgam in sodium deuteroxide gave 7-*exo*-deuterio-**9b**. In contrast, sodium borodeuteride reduction was less stereospecific, yielding a 73:27 mixture of 7-*exo*- and 7-*endo*-deuterio-6-*exo*-methoxy-*exo*-tricyclo-[3.2.1.$0^{2,4}$]octane.

(17) These reaction conditions in related systems have been shown to give reduction with retention of configuration. Kitching, W.; Atkins, A. R.; Wickham, G.; Alberts, V. *J. Org. Chem.* **1981**, *46*, 563.

(18) Castellano, S.; Bothner-By, A. A. *J. Chem. Phys.* **1964**, *41*, 3863. Ferguson, R. C.; Marquardt, D. W. *J. Chem. Phys.* **1964**, *41*, 2087.

(19) The magnitude of the coupling between C3-endo-H and an adjacent C4-H (11.6 Hz) and the relatively small coupling of C3-exo-H and this proton (6.2 Hz) show the configuration of the C4-H (1.32 ppm) to be exo.

(20) Peaks were observed at 1.19 ppm (C6-endo-D) and 1.58 ppm (C7-endo-D).

(21) Jensen, F. R.; Bushweller, C. H. *Adv. Alicycl. Chem.* **1971**, *3*, 139.

(22) de la Mare, P. B. D.; Bolton, R. In *Electrophilic Additions to Unsaturated Systems*, 2nd ed.; Elsevier: Amsterdam, 1982.

(23) The ^2H NMR spectrum of **2b** showed the C4-endo-D at 1.31 ppm and the chemical shifts of the protons H8a, H3-endo, H8s, H1, H2, H5, and H4-exo in the ^1H NMR spectrum were identical with the product of reduction of the organomercurial **2c**.

(24) In addition three minor, unidentified products of 2%, 1%, and 7% were also present.

(25) The similarity in the proton–proton couplings, ^{13}C chemical shifts, and difference NOE spectra of **9c** and *exo*-tricyclo[3.2.1.$0^{2,4}$]octane establish the configuration of the cyclopropyl group.

(26) A coupling of 6.6 Hz between C6-endo-H and C7-endo-H.

(27) $J_{^{13}C^{199}Hg}$: C1, 34 Hz; C2, 296 Hz; C3, 68 Hz; C4, not observed; C5, 39 Hz; C6, 136 Hz; C7, 1762 Hz; C8, 17 Hz.

(28) Irradiation at the C6-endo-H (3.46 ppm) gave enhancements at H7-endo (2.93 pm, 9.2%), H5 (2.55 ppm, 3.2%), and H4 (0.56 ppm, 7.3%), consistent with the exo nature of both the C6-methoxy and the adjacent C7-acetoxymercurio substituents. Irradiation of H8s (0.89 ppm) gave enhancement at H5 (2.55 ppm, 1.9%), H1 (2.51 ppm, 2.5%), H8a (1.05 ppm, 20.0%), and H3-exo (0.68 ppm, 11.1%).

(29) Cheng, A. K.; Stothers, J. B. *Org. Magn. Reson.* **1977**, *9*, 355.

To determine the pathway in the reaction with proton, and in particular the propensity for rearrangement of the intermediate carbocations, the reaction of 8 with methanol was studied (Scheme VI). Reaction at 80 °C for 7 days yielded 5-*exo*-methoxybicyclo[2.2.2]oct-2-ene (**10a**; 55%) and **9a** (15%) in addition to some high retention (by GLC) compounds (30%).[30] The identity of 5-*exo*-methoxybicyclo[2.2.2]oct-2-ene (**10a**) was determined from the ^{1}H NMR analysis.[31] The ^{13}C NMR data was assigned by comparison with that of the known bicyclo[2.2.2]oct-2-en-5-*exo*-ol,[32] a heteronuclear correlation experiment giving the ^{1}H–^{13}C connectivities.[33] This established the chemical shifts of the respective protons, but not their configuration, and therefore selective decoupling was used to assign[34] the stereochemistry of the C7H$_2$. Difference NOE spectra confirmed the assignments.[35] The structure of **9a** was established by comparison with the product obtained from stereospecific sodium amalgam reduction in sodium hydroxide of organomercurial **9c**.

To determine the stereochemistry of proton attack in the acid-catalyzed addition of methanol to 8, reaction was effected in methanol-d_1 at 80 °C. For deuterated **10b**, the presence of a triplet at 25.5 ppm in the ^{13}C NMR spectrum and a peak at 1.60 ppm in the ^{2}H NMR spectrum is consistent with the presence of deuterium at C7-syn.[36] For **9b**, the presence of a triplet at 39.8 ppm in the ^{13}C NMR spectrum and a peak at 1.30 ppm in the ^{2}H NMR spectrum indicates the deuterium is at C7-exo. This compound was identical with the product from stereospecific reduction of organomercurial **9c** in deuterated media.

To establish the preference for proton attack at the double bond or the cyclopropyl ring, the possibility of further reaction at the cyclopropyl ring of **9a** was examined. It would be expected that, given the greater rate of proton attack at an isolated cyclopropyl ring as compared with a double bond, **9a** would be attacked in preference to **10a**. A sample of **9b** obtained from sodium amalgam reduction of **9c** in deuterated media was heated at 80 °C in methanol, *p*-toluenesulfonic acid for 7 days, the same conditions under which the primary reaction was carried out. GLC analysis revealed the presence of starting material (**9b**; 52%) and high-retention compounds (35%). The nonvolatile compounds observed arise from subsequent reaction of **9a**/**b** with methanol to yield more polar dimethoxy products, and therefore the 15% of **9** obtained from reaction of proton (deuteron) with 8 must be regarded as a minimum.

The presence of a 7-syn deuterium in **10b** is consistent with initial attack by a proton (deuteron) at C2(C4) with inversion of stereochemistry, and subsequent W-M rearrangement giving the bicyclo[2.2.2]oct-2-ene system. However, such a rearrangement is unexpected in view of the significant overlap between the C2,C4 bonding orbitals on the cyclopropyl ring with the π system.[29,37-39] To determine the origin of **10b**, the acid-catalyzed reaction of 8 with methanol was examined at room temperature. Reaction for 28 days gave 6-*exo*-methoxytricyclo[3.2.1.0^{2,7}]octane (**11a**; 31%)[40] in addition to the previously observed **9a** (18%), **10a** (23%), and unreacted 8 (23%). 6-*exo*-Methoxytricyclo[3.2.1.0^{2,4}]octane (**11**) is a primary reaction product formed from interaction of the C2,C4 orbitals with the π orbitals and is unstable[41] under the reaction conditions, undergoing solvolysis to **10**.

The acid-catalyzed reaction of 8 in methanol-d_1 at room temperature gave after 72 days (74% reaction) 7-*exo*-deuterio-**9b**, 7-*syn*-deuterio-**10b**, and 4-*exo*-deuterio-**11b**. For **11b**, the presence of a triplet in the ^{13}C NMR spectrum at 26.1 ppm and a peak in the ^{2}H NMR spectrum at 1.52 ppm identifies the deuterium as being at C4-exo, consistent with proton (deuteron) attack at C2(C4) of the cyclopropane ring occurring with inversion.[42] Both **9b** and **10b** obtained from this reaction were identical with isolated samples obtained from the reaction at 80 °C and previously discussed. The stability of **11a** was examined by stirring it at room temperature in methanol in the presence of *p*-toluenesulfonic acid and following the reaction by GLC. Approximately 2 h after the start of the reaction, the mixture contained **11a** (55%) in addition to the **10a** (45%), this product ratio remaining invariant for 16 days. The presence of **10a** demonstrated that it arises from **11a** in the reaction at both 25 °C and 80 °C.

The absence of rearranged product from the proton attack at the double bond in both reaction at 80 °C and room temperature is notable and contrasts with the acetolysis of bicyclo[2.2.1]hepta-2,5-diene,[43] where rearrangement to the tricyclo[2.2.1.0^{2,6}]heptane skeleton accounts for approximately 30% of the reaction. In methanol rearranged product accounts for 13% of the reaction with the diene, 5-*exo*-methoxybicyclo[2.2.1]hept-2-ene comprising the remaining 87%. Given the smaller orbital overlap between the cyclopropyl ring and π system in

(30) Isolation of the volatile components **9a** and **10a** was achieved by preparative GLC.

(31) Müller, E. *Chem. Ber.* **1976**, *109*, 3804.

(32) Stothers, J. B.; Tan, C. T. *Can. J. Chem.* **1976**, *54*, 917.

(33) H1, 2.49 ppm/C1, 29.8 ppm; H2, 6.29 ppm/C2, 136.1 ppm; H3, 6.15 ppm/C3, 131.4 ppm; H4, 2.76 ppm/C4, 33.2 ppm; H5-endo, 3.30 ppm/C5, 78.5 ppm; H6-endo 1.73 ppm and H6-exo 1.17 ppm/C6, 33.5 ppm; H7s 1.60 ppm and H7a 1.25 ppm/C7, 25.9 ppm and H8s 1.90 ppm and H8a 1.05 ppm/C8, 17.6 ppm.

(34) H8a (1.05 ppm), so assigned because of its coupling with H5-endo (3.30 ppm, J = 1.7 Hz), was also coupled to H8s (1.90 ppm, J = 12.7 Hz), H7s (1.60 ppm, J = 3.9 Hz) and H7a (1.25 ppm, J = 12.0 Hz), thereby establishing the chemical shifts of the C7 methylene protons.

(35) Irradiation at H8s (1.90 ppm) gave enhancements at the OMe (3.30 ppm, 1.0%), H4 (2.76 ppm, 2.1%), H7s (1.60 ppm, 2.4%), H7a (1.25 ppm, 1.4%), and H8a (1.05 ppm, 14.4%). In addition, irradiation at H1 (2.49 pm) gave enhancements at H2 (6.29 pm, 2.9%), H3 (6.15 ppm, 1.0%), H6endo (1.73 ppm, ca. 2.6%), H7s (1.60 ppm, ca. 1.4%) and H7a, H6exo (1.3–1.1 ppm, 2.8% total).

(36) Additional evidence for the deuterium stereochemistry arises from the extensive broadening of H8s at 1.90 ppm, due to the close proximity of the 7-syn deuterium, and the loss of a large coupling from H7-syn to H7-anti at 1.23 ppm.

(37) Bruckmann, P.; Klessinger, M. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 524.

(38) Bischof, P.; Heilbronner, E.; Prinzbach, H.; Martin, H. D. *Helv. Chim. Acta* **1971**, *54*, 1072.

(39) Srinivasan, R.; Ors, J. A.; Brown, K. H.; Baum, T.; White, L. S.; Rossi, A. R. *J. Am. Chem. Soc.* **1980**, *102*, 5297.

(40) The identity of **11a** was determined from a difference NOE spectrum, which showed that irradiation at H6-endo (3.52 ppm) gave enhancement at the methoxy methyl (3.34 ppm, 1.2%), H5 (1.96 ppm, 1.3%), H3-endo (ca. 1.74 ppm, 0.8%), H7 (1.51 ppm, 1.1%), and H4-endo (1.32 ppm, 2.3%). Irradiation at H2 (0.92 ppm) gave enhancements at H3-exo and H3-endo (1.7% total), H7 (ca. 3.4%) and H1 (ca. 5.7%). The configuration of the C6-H was established as endo from its presence as a singlet in the ^{1}H NMR, this being similar to the corresponding 2-methyltricyclo[3.2.1.0^{2,7}]octan-6-*exo*-ol (Bohlmann, F.; Rotard, W. *Justus Liebigs Ann. Chem.* **1982**, 1220) and tricyclo[3.2.1.0^{2,7}]octan-6-*exo*-ol (Kirmse, W.; Wahl, K.-H. *Chem. Ber.* **1974**, *107*, 2768). The C2-H at 0.92 ppm was assigned from the NOE and also from coupling with H3-exo and H3-endo (ca. 1.75 ppm, J = 2.7 Hz each), H7 (1.51 ppm, 8.0 Hz), and H1 (1.41 ppm, 8.0 Hz). This is consistent with the presence of the C2-H as an endocyclic cyclopropyl proton adjacent to the C3 methylene at 1.75 ppm.

(41) Such behavior is found in the solvolysis of tricyclo[3.2.1.0^{2,7}]octan-6-*exo*(and *endo*)-ol, quantitatively yielding bicyclo[2.2.2]oct-2-en-5-*exo*-ol. LeBel, N. A.; Huber, J. E. *J. Am. Chem. Soc.* **1963**, *85*, 3193.

(42) Assignment of the 4-endo proton at 1.32 ppm in **11a** follows from NOE enhancement of the H6-endo (2.3%) and coupling with H8a at 1.88 ppm (2.2 Hz), H8a being assigned from its coupling with H5 (1.96 ppm, 5.7 Hz), H8s (1.51 ppm, 11.4 Hz), and H1 (1.40 ppm, 3.4 Hz), in addition to coupling with H4-endo. A heteronuclear correlation spectrum allowed assignment of the carbon–hydrogen connectivities and in particular, those of H4-exo 1.58 ppm and H4-endo 1.32 ppm/C4, 26.5 ppm.

(43) Cristol, S. J.; Morrill, T. C.; Sanchez, R. A. *J. Org. Chem.* **1966**, *31*, 2733.

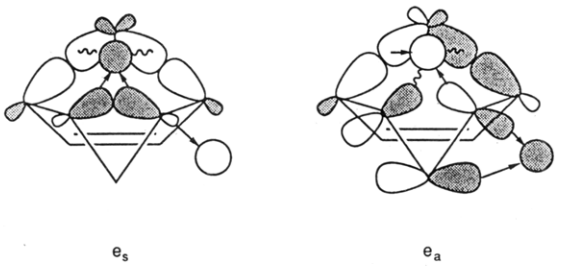


Figure 2. Mixing of C1C8 and C5C8 orbitals with cyclopropane orbitals showing interaction with electrophiles at corner and edge.

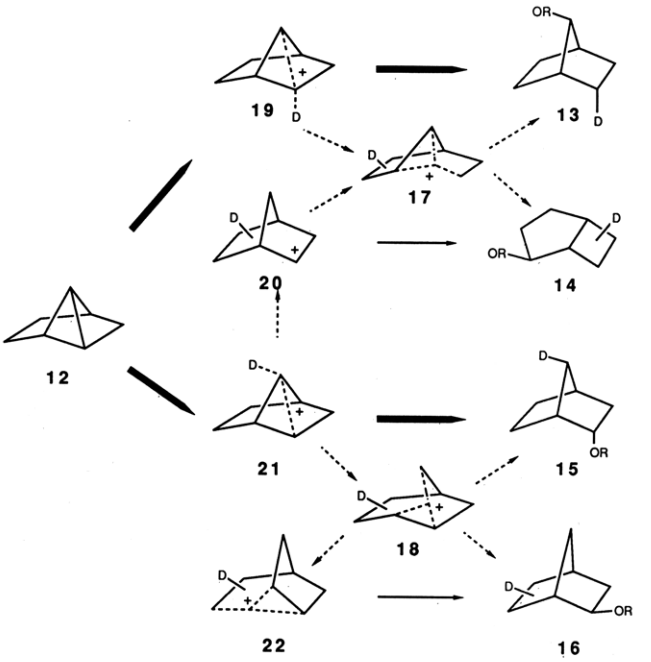
hydrocarbon 8 than that of the π system for norbornadiene[39] the absence of rearrangement is expected in the methanolysis of 8. When the reaction is effected with stronger acids rearrangement would be expected to become increasingly important.[43]

Discussion of Regiochemistry and Stereochemistry of Reactions of 1 and 8. The unique orbital topology of hydrocarbon 1 results in mixing of the degenerate cyclopropane 3e′ orbitals with the C1C8 and C5C8 σ bonds with consequent increase in energy of the cyclopropane orbitals and removal of their degeneracy.[39] Photoelectron spectroscopy shows that the two highest occupied molecular orbitals of 1, assigned to the π and e_s orbitals,[38] are relatively similar in energy (−9.05 and −9.5 eV, respectively) when compared with the e_a orbital (−10.30 eV). It is notable that reaction at the double bond of hydrocarbon 1 with a proton and mercuric ion does not compete with reaction at the corner of the cyclopropane ring despite the fact that the π orbital contributes to the HOMO. Furthermore both the reaction with acid and with mercuric ion effect rupture of the more substituted cyclopropane ring and products from electrophilic attack in a Markovnikov manner at the least substituted carbon of the cyclopropane ring are not observed. Mixing of the C2C4 bond with the framework of the molecule with consequent raising in energy of the 3e′ (*S*) orbital facilitates internal cyclopropyl bond rupture relative to the C2C3 and C4C3 bonds and accounts for internal cyclopropyl bond cleavage being favored over external bond cleavage.

The stereochemistry of deuterium in the products from reaction of hydrocarbon 1 with deuteron in methanol-d_1 precludes edge attack of deuteron on the C2–C3 bond and reorganization to a corner species since such a process would require deuterium to be exo in the products. Likewise mercuric acetate reacts stereospecifically at C2 with inversion of configuration. The corner attack of the electrophiles, deuterium and mercuric ion, parallels the reaction of tetracyanoethylene with hydrocarbon 1[44] and 2-methyl-*endo*-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene[45] and of cyclopropane[12,13] and bicyclobutane[46] with bromine. However these reactions are in direct contrast with the observed stereochemistry of the microscopically reverse ring closure observed for squalene oxide[6] with *Ochromonas malhamensis* and cyclase from maize, the postulated scheme to account for the loss of the 3a-tritium in the yeast-catalyzed formation of ergosterol[14] and the stereochemistry of proton loss in the formation of presqualene pyrophosphate.[5]

Interaction of the antisymmetric filled cyclopropane orbital with the LUMO of the electrophile dictates that corner attack is favored to C2C4 edge attack in the absence

Scheme VII



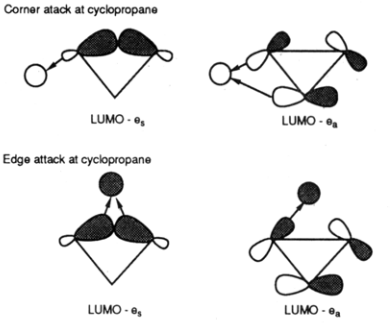
of overriding steric factors.[11,47] The antibonding interaction in the transition state for edge attack between the electrophile and the C1C8 and C5C8 framework of hydrocarbon 1 further disfavors edge attack at the C2C4 bond (Figure 2). Such an antibonding interaction is not present for corner attack with inversion.

For attack of a proton at a cyclopropane ring, a favorable carbon–electrophile overlap results in a substantial decrease in bonding between C1 and C2 and therefore charge development at C2. For attack by mercury the overlap between the mercury and the cyclopropane 3e′ (*S*) orbital is less efficient than for a proton. As a consequence the bonding between C1 and C2 is reduced to a lesser extent with less positive charge development at C4 in hydrocarbon 1 upon reaction at C2 by mercury as compared with proton attack.

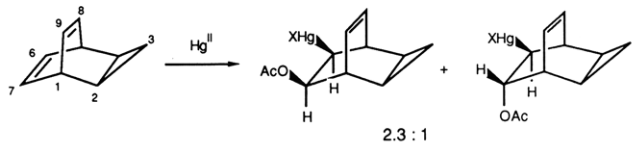
Reaction of 1 with mercuric acetate gives 21% of **3c** and **4c**, contrasting with the similar reaction of the saturated analogue where rearrangement is not observed and only 1,3-methoxymercuration occurs.[8] The double bond of 1 is considered to influence the extent of charge development at C4 in cation **5c**, which will be greater for the unsaturated compound because of homoallylic stabilization of the cation center. As a consequence rearrangement becomes competitive with 1,3-addition for hydrocarbon 1. The driving force for this rearrangement is the development of the allylic cation in **6**.

(44) Battiste, M. A.; Coxon, J. M.; Posey, R. G.; King, R. W.; Mathew, M.; Palenik, G. J. *J. Am. Chem. Soc.* **1975**, *97*, 945.
(45) Coxon, J. M.; de Bruijn, M.; Lau, C. K. *Tetrahedron Lett.* **1975**, 337.
(46) Hoz, S.; Livneh, M.; Cohen, D. *J. Am. Chem. Soc.* **1987**, *109*, 5149.

(47) For edge attack the electrophile interacts unfavorably with the antisymmetric filled orbital while corner attack is favorable.[11]



Scheme VIII



A preference for corner attack has similarly been reported[48] for reaction of tricyclo[3.2.0.0^{2,7}]heptane (**12**) with D_2SO_4–dioxane, which was shown to give **13**, **14**, **15**, and **16**. Products **13** and **15** were established to arise by corner attack with inversion of electrophile and similar attack of the nucleophile with inversion. While the nonclassical corner–deuterated species **17** and **18** are drawn by Kirmse et al.,[48] as intermediates in the formation of **13** and **15**, the products can arise directly from **19** and **21** where only one of the cyclopropyl bonds is stretched as shown in Scheme VII. Cations **19** and **21** are analogous to cation **5** in Scheme V. The reaction intermediate **21** is trapped competitively with rearrangement to the 2-norbornyl cation **22**. The study does not establish the stereochemistry and distribution of the deuterium label in the products **16** or **14** so it is not known if ion **19** rearranges to **17** and product **14** in competition with trapping to **13** or if **14** is formed from **21** without involvement of cation **17**.

External cyclopropyl bond cleavage does not compete with C2C4 bond cleavage in the reaction of *endo*-tricyclo[3.2.1.0^{2,4}]octane with acid or mercuric acetate in methanol while similar reactions of *exo*-tricyclo[3.2.1.0^{2,4}]octane result in products from external bond cleavage.[8] For *exo*-tricyclo[3.2.1.0^{2,4}]octane, the HOMO (e_s) differs in energy from the e_a orbital by 0.6 eV,[38] and external bond rupture competes with C2C4 bond cleavage. This contrasts with the reaction of **8** where no products of external bond rupture are observed and the HOMO π_s differs in energy from the e_a orbital by 1.3 eV.[38] For both **8** and **1** it is the interaction of the LUMO of an electrophile with the e_a orbital, the orbital most responsible for bonding C2 and C4 with C3, that is important for facilitating rupture of the external cyclopropyl bond since for the e_s orbital electron density is localized in the C2C4 bond. The large difference between the energy of the e_a and the HOMO π orbital is consistent with the absence of external bond cleavage on reaction of *exo*-tricyclo[3.2.1.0^{2,4}]oct-6-ene (**8**) and similarly *endo*-tricyclo[3.2.1.0^{2,4}]oct-6-ene (**1**) with acid or mercuric acetate in methanol.

The methoxymercuration of *exo*-tricyclo[3.2.1.0^{2,4}]oct-6-ene (**8**) parallels acetoxymercuration of tricyclo[3.2.2.0^{2,4}]nona-6,8-diene[49] (Scheme VIII) where addition occurs at the C6C7 double bond and not at the cyclopropyl ring or the C8C9 double bond. The calculated orbital contributions to the HOMO of tricyclo[3.2.2.0^{2,4}]nona-6,8-diene indicate a substantial contribution from the C6C7 π system, a result of a large through space interaction between the C6C7 π orbitals and the cyclopropyl e_s orbital. The large overlap integral $\langle\pi|\sigma_s\rangle$ of 0.06[39] for tricyclo[3.2.2.0^{2,4}]nona-6,8-diene compares with 0.052 and 0.012 for hydrocarbons **8** and **1**, respectively.

The larger orbital coefficients[50] at the C6C7 π orbitals in the HOMO's of **8** and tricyclo[3.2.2.0^{2,4}]nona-6,8-diene results in better overlap between the Hg^{2+} LUMO and the hydrocarbon HOMO at the π orbitals. However the low orbital coefficients for the π orbitals in the HOMO of **1** result in exclusive cyclopropyl ring opening. A through bond interaction can similarly increase the π orbital coefficients in the HOMO and in the acetoxymercuration of tricyclo[3.2.1.0^{2,7}]oct-3-ene[48] only products from double bond attack were reported. While the charge development is low for mercuration and orbital overlap appears to determine the reaction pathways, cation stabilities also play a role in the protonation reactions. Here the "nonclassical" nature of the protonated cyclopropane as compared with the classical protonated alkene favors cyclopropyl attack over π attack. This kinetic factor explains the cyclopropyl attack observed at hydrocarbons **8** and **1** by proton and contrasts with the orbital overlap controlled methoxymercuration observed at the double bond for **8**. It is notable that proton attack on the double bond with cyclopropyl participation in **8** to give a C2C7 bond is not observed. This is similar to bicyclohepta-2,5-diene, where the π-orbital overlap is greater, which gives only a limited amount of tricyclic product on reaction with acid.

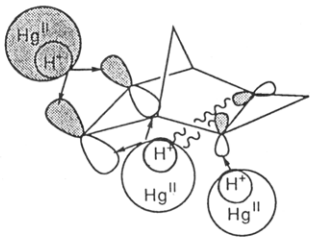


Figure 3. Electrophilic attack on the HOMO of *exo*-tricyclo[3.2.1.0^{2,4}]oct-6-ene.

For *exo*-tricyclo[3.2.1.0^{2,4}]oct-6-ene (**8**) the HOMO is shown in Figure 3, schematically indicating the orbital preference for exo addition, an effect operating in sympathy with torsional factors. The e_s orbital of **8** is lower in energy than the HOMO π orbital by 0.7 eV, while for tricyclo[3.2.2.0^{2,4}]nona-6,8-diene the difference between the HOMO π and e_s is 1.2 eV,[37] accounting for the absence of cyclopropyl ring cleavage in the reaction of the cyclopropyldiene with mercuric acetate in acetic acid.

Reaction of **8** with acid in methanol occurs predominantly by proton attack at the more substituted positions of the cyclopropane (Scheme VI). This kinetic preference for proton attack at the cyclopropane ring compared with attack at the double bond is reflected by the relative ratios of **9a** to (**10a** + **11a**) being 18:54 in the reaction at room temperature. The cleavage of the cyclopropyl ring between C2 and C4 results from the relatively high energy of the e_s orbital relative to the e_a orbital. Edge attack at this bond is disfavored due to an unfavorable secondary orbital interaction of the electrophile with the framework of the molecule and corner attack at C2(C4) results.

Experimental Section

General Methods. NMR spectra were obtained on a Varian T-60 or a Varian XL-300 (300-MHz ^1H, 75-MHz ^{13}C, 46-MHz ^2H). All ^2H NMR spectra were run unlocked with broadband proton decoupling, an acquisition time of 4 s, and 2 drops of $CDCl_3$ (7.27 ppm) as an internal reference. Heteronuclear proton–carbon correlation spectra were obtained with a relaxation time of 4 s between scans, 64 values of t_1, and zero filling to 256 points in f_1 (^1H). NOE's were obtained by difference spectra, the decoupler offset for the reference spectrum being 10 000 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 an 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 diameter and length 3 m was used. *endo*-Tricyclo[3.2.1.0^{2,4}]oct-6-ene (**1**) was prepared from the re-

(48) Kirmse, W.; Streu, J. *J. Org. Chem.* **1987**, *52*, 515.
(49) Müller, E. *Chem. Ber.* **1976**, *109*, 3793.
(50) Gleiter, R.; Böhm, M. C.; de Meijere, A.; Preuss, T. *J. Org. Chem.* **1983**, *48*, 796.

action of cyclopropene with cyclopentadiene at −78 °C.[14] *exo*-Tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (**8**) was prepared from norbornene by addition of methylene carbene generated by a zinc/copper couple.[51]

Reaction of 1 with Mercuric Acetate. To a solution of *endo*-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (**1**) (200 mg) in anhydrous methanol (4 mL) was added, with stirring, mercuric acetate (600 mg), and the mixture was stirred at room temperature overnight. The solvent and acetic acid were removed under reduced pressure to give a colorless oil (795 mg, 95%) identified as 4-*endo*-(acetoxymercurio)-2-*endo*-methoxybicyclo[3.2.1]oct-6-ene (**2c**) (75%) and 6- and 7-*endo*-(acetoxymercurio)-2-*endo*-methoxybicyclo-[3.2.1]oct-3-ene (**4c** and **3c**) (10% and 11%, respectively). 4-*endo*-(Acetoxymercurio)-2-*endo*-methoxybicyclo[3.2.1]oct-6-ene (**2c**): ^{1}H NMR δ_H ($CDCl_3$) 6.08 (d of d, $^3J_{7,6}$ = 5.5 Hz, $^3J_{7,1}$ = 2.5 Hz, H7), 6.02 (d of d, $^3J_{6,7}$ = 5.7 Hz, $^3J_{6,5}$ = 2.5 Hz, H6), 3.30 (OMe), 3.26 (m, $^3J_{2exo,1}$ = 3.2 Hz, $^3J_{2exo,3endo}$ = 9.5 Hz, $^3J_{2exo,3exo}$ = 6.0 Hz, H2exo), 2.88 (d of t, $^3J_{5,4exo}$ = $^4J_{5,6}$ = 2.5 Hz, $^3J_{5,8a}$ = 5.2 Hz, H5), 2.77 (d of t, $^3J_{1,2exo}$ = 3.0 Hz, $^3J_{1,7}$ = 2.0 Hz, $^3J_{1,8a}$ = 3.6 Hz, H1), 2.73 (m, $^3J_{4exo,3exo}$ = 5.6 Hz, $^3J_{4exo,3endo}$ = 12.3 Hz, $^3J_{4exo,5}$ = 2.0 Hz, H4exo), 2.26 (d of t, $^2J_{3exo,3endo}$ = 13.1 Hz, $^3J_{3exo,4exo}$ = $^3J_{3exo,2exo}$ = 5.6 Hz, $H3_{exo}$), 2.13 (d of t, $^2J_{8a,8s}$ = 11.1 Hz, $^3J_{1,8a}$ = $^3J_{5,8a}$ = 5.6 Hz, H8a), 2.02 (OAc), 1.95 (d of t, $^2J_{3endo,3exo}$ = $^3J_{3endo,4exo}$ = 12.8 Hz, $^3J_{3endo,2exo}$ = 9.5 Hz, H3endo), 1.30 (d, $^2J_{8a,8s}$ = 10.7 Hz, H8s); ^{13}C NMR δ_C ($CDCl_3$) 176.8 (OAc), 133.6 (C6), 132.4 (C7), 80.0 (C2), 55.8 (OMe), 44.6 (C5), 43.3 (C8), 43.1 (C1), 42.1 (C4), 32.3 (C3), 23.0 (OAc).

Reduction of the Organomercurials (2c, 3c, and 4c). (a) With Sodium Amalgam. Mercury (50 g) was cautiously added dropwise to molten sodium (0.75 g) under Shell Ondina 17 (20 mL). The resulting amalgam was left to cool before being transferred to a mortar where it was broken into small pieces under pentane. To the sodium amalgam (5 g, 1.5%), previously washed with pentane and dried under vacuum for 1 h, in NaOD, D_2O (2 mL, 2 M) was added the organomercurial (110 mg). The mixture was stirred for 3 h, and water (4 mL) was added. The product was extracted with pentane, the combined extracts were dried over $MgSO_4$, and the solvent was removed under reduced pressure to give a mixture (23 mg, 64%) of 6-*endo*- and 7-*endo*-deuterio-2-*exo*-methoxybicyclo[3.2.1]oct-3-ene (**4b** and **3b**) (10% and 11%, respectively) and 4-*endo*-deuterio-2-*endo*-methoxybicyclo-[3.2.1]oct-6-ene (**2b**) (75%), identical with that obtained from the acid-catalyzed reaction of *endo*-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (**1**) with methanol-d_1. The 6-*endo*- and 7-*endo*-deuterio-2-*exo*-methoxybicyclo[3.2.1]oct-3-ene (**4b** and **3b**) and 4-*endo*-deuterio-2-*endo*-methoxybicyclo[3.2.1]oct-6-ene (**2b**) were separated by preparative GLC. The ^{1}H NMR, ^{2}H NMR, and ^{13}C NMR spectra of 6-*endo*- and 7-*endo*-deuterio-2-*exo*-methoxybicyclo[3.2.1]oct-3-ene (**4b** and **3b**) were as reported:[14] ^{2}H NMR δ_D ($CHCl_3$) 1.58 (D7endo), 1.19 (D6endo). 4-*endo*-Deuterio-2-*endo*-methoxybicyclo[3.2.1]oct-6-ene (**2b**): ^{1}H NMR δ_H ($CDCl_3$) 5.92 (d of d, $^3J_{6,7}$ = 5.8 Hz, $^3J_{6,5}$ = 2.2 Hz, H6), 5.86 (d of d, $^3J_{7,6}$ = 5.8 Hz, $^3J_{7,1}$ = 2.2 Hz, H7), 3.34 (OMe), 3.19 (m, $^3J_{2exo,3endo}$ = 9.3 Hz, $^3J_{2exo,1}$ = 2.7 Hz, $^3J_{2exo,3exo}$ = 5.6 Hz, H2exo), 2.82 (d of t, $^3J_{1,2exo}$ = 2.7 Hz, $^3J_{1,7}$ = 2.6 Hz, $^3J_{1,8a}$ = 5.5 Hz, H1), 2.50 (d of t, $^3J_{5,4exo}$ = $^3J_{5,6}$ = 2.6 Hz, $^3J_{5,8a}$ = 5.5 Hz, H5), 2.02 (d of t, $^2J_{8a,8s}$ = 10.3 Hz, $^3J_{8a,1}$ = $^3J_{8a,5}$ = 5.5 Hz, H8a), 1.84 (d of t, $^2J_{3exo,3endo}$ = 13.0 Hz, $^3J_{3exo,2exo}$ = 5.6 Hz, $^3J_{3exo,4exo}$ = 6.2 Hz, H3exo), 1.42 (m, $^2J_{3endo,3exo}$ = 13.0 Hz, $^3J_{3endo,2exo}$ = 9.3 Hz, $^3J_{3endo,4exo}$ = 11.6 Hz, H3endo), 1.32 (H4exo), 1.28 (d, $^2J_{8a,8s}$ = 10.3 Hz, H8s); ^{13}C NMR δ_C ($CDCl_3$) 133.8 (C6), 130.3 (C7), 76.4 (C2), 55.4 (OMe), 42.4 (C1), 41.9 (C8), 38.9 (C5), 25.3 (C3), 22.9 (t, $J_{^{13}C,^2H}$ = 19.5 Hz, C4); ^{2}H NMR δ_D ($CHCl_3$) 1.34 (D4endo). Mass spectrum shows 1% D^0, 95% D^1, 4% D^2. The ^{13}C NMR data of 2-*endo*-methoxybicyclo[3.2.1]oct-6-ene (**2a**) were assigned by comparison with the corresponding bicyclo[3.2.1]oct-6-en-2-*endo*-ol.[52]

Computer simulations using the Fortran LAME program[18] for 4-*endo*-deuterio-2-*endo*-methoxybicyclo[3.2.1]oct-6-ene (**2b**) gave excellent agreement with the observed ^{1}H NMR spectrum for the following values: linewidth 1.2 Hz; 3.19 ($^3J_{2exo,3endo}$ = 9.3 Hz, $^3J_{2exo,3exo}$ = 5.6 Hz, $^3J_{2exo,1}$ = 2.7 Hz, H2exo), 2.80 ($^3J_{1,2exo}$ = 2.7 Hz, $^3J_{1,7}$ = 2.6 Hz, $^3J_{1,8a}$ = 5.5 Hz, H1), 2.50 ($^3J_{5,4exo}$ = $^3J_{5,6}$ = 2.6 Hz, $^3J_{5,8a}$ = 5.5 Hz, H5), 2.02 ppm ($^3J_{8a,1}$ = $^3J_{8a,5}$ = 5.5 Hz, $^2J_{8a,8s}$ = 10.3 Hz, H8a); linewidth 2.2 Hz; 1.83 ($^2J_{3exo,3endo}$ = 13.0 Hz, $^3J_{3exo,2exo}$ = 5.6 Hz, $^3J_{3exo,4exo}$ = 6.2 Hz, H3exo), 1.42 ($^2J_{3endo,3exo}$ = 13.0 Hz, $^3J_{3endo,2exo}$ = 9.3 Hz, $^3J_{3endo,4exo}$ = 11.6 Hz, H3endo), 1.32 ppm ($^3J_{4exo,3endo}$ = 11.6 Hz, $^3J_{4exo,3exo}$ = 6.2 Hz, H4exo). Note: H4exo is present only to induce second-order effects at H3endo (1.42 ppm) and consequently does not give an accurate simulation in this part of the spectrum.

(b) With Sodium Borodeuteride. To the crude mixture of the organomercurials (77 mg) in methanol (1 mL) was added with stirring 1 M NaOH (1 mL), followed by sodium borodeuteride (40 mg). The mixture was stirred for 30 min. The mercury was decanted off, and the liquid was extracted with pentane, washed with water, and dried over $MgSO_4$. The solvent was removed under reduced pressure to yield a mixture of 4-*exo*- and 4-*endo*-deuterio-2-*endo*-methoxybicyclo[3.2.1]oct-6-ene, 6-*exo*-, 6-*endo*-, 7-*exo*-, and 7-*endo*-deuterio-2-*endo*-methoxybicyclo-[3.2.1]oct-3-ene (16 mg, 62%). Mass spectrum shows 2% D^0, 95% D^1, 3% D^2.

Reaction of 1 with Methanol-d_1, *p*-Toluenesulfonic Acid. The reaction was carried out as described previously.[14] Repetitive preparative GLC gave 4-*endo*-deuterio-2-*endo*-methoxybicyclo-[3.2.1]oct-6-ene (**2b**), whose ^{1}H NMR spectrum was identical with that obtained from the sodium amalgam reduction of 4-*endo*-(acetoxymercurio)-2-*endo*-methoxybicyclo[3.2.1]oct-6-ene (**2c**) above.

Reaction of 8 with Mercuric Acetate. To a stirred solution of *exo*-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (**8**) (285 mg) in anhydrous methanol (10 mL) was added mercuric acetate (950 mg). After 2 h the mixture was filtered, and the solvent was removed under reduced pressure before being placed under high vacuum for 12 h to remove acetic acid. The residue, a pale green viscous oil (89%), was identified as 7-*exo*-(acetoxymercurio)-6-*exo*-methoxy-*exo*-tricyclo[3.2.1.$0^{2,4}$]octane (**9c**) (991 mg, 95%): ^{1}H NMR δ_H ($CDCl_3$) 3.46 (d of d, $^3J_{6endo,7endo}$ = 6.6 Hz, $^4J_{6endo,8s}$ = 1.5 Hz, H6endo), 3.37 (OMe), 2.93 (d of d, $^3J_{7endo,6endo}$ = 6.6 Hz, $^4J_{7endo,8s}$ = 2.9 Hz, H7endo), 2.55 (s, $W_{h/2}$ = 4 Hz, H5), 2.51 (s, $W_{h/2}$ = 4 Hz, H1), 2.04 (s, OAc), 1.05 (d, $^2J_{8a,8s}$ = 11.1 Hz, H8a), 0.89 (d, $^2J_{8s,8a}$ = 11.2 Hz, H8s), 0.77 (t of d, $^3J_{2,3endo}$ = 6.8 Hz, $^3J_{2,3exo}$ = 3.2 Hz, $^3J_{2,4}$ = 6.8 Hz, H2), 0.68 (d of t, $^2J_{3exo,3endo}$ = 6.5 Hz, $^3J_{3exo,2}$ = 3.2 Hz, $^3J_{3exo,4}$ = 3.2 Hz, H3exo), 0.56 (t of d, $^3J_{4,2}$ = 7.0 Hz, $^3J_{4,3exo}$ = 3.3 Hz, $^3J_{4,3endo}$ = 6.9 Hz, H4), 0.26 (m, $^2J_{3endo,3exo}$ = 6.7 Hz, $^3J_{3endo,2}$ = 6.5 Hz, $^3J_{3endo,4}$ = 6.5 Hz, H3endo); ^{13}C NMR δ_C ($CDCl_3$) 176.7 (OAc), 86.1 ($J_{^{199}Hg,^{13}C}$ = 136.3 Hz, C6), 60.1 ($J_{^{199}Hg,^{13}C}$ = 1761.8 Hz, C7), 56.2 (OMe), 39.1 ($J_{^{199}Hg,^{13}C}$ = 34.4 Hz, C1), 38.6 ($J_{^{199}Hg,^{13}C}$ = 38.6 Hz, C5), 24.4 ($J_{^{199}Hg,^{13}C}$ = 16.8 Hz, C8), 22.3 (OAc), 18.0 ($J_{^{199}Hg,^{13}C}$ = 296.2 Hz, C2), 11.2 ($J_{^{199}Hg,^{13}C}$ not obsd, C4), 6.2 ($J_{^{199}Hg,^{13}C}$ = 67.8 Hz, C3).

Reduction of the Organomercurials. (a) With Sodium Amalgam. The reduction of the organomercurial mixture (480 mg) from above was carried out as described earlier to give a colorless oil (165 mg, 58%), consisting of 7-*exo*-deuterio-6-*exo*-methoxy-*exo*-tricyclo[3.2.1.$0^{2,4}$]octane (**9b**) (89%): ^{1}H NMR δ_H ($CDCl_3$) 3.35 (d of d, $^3J_{6endo,7endo}$ = 7.1 Hz, $^4J_{6endo,8s}$ = 1.4 Hz, H6endo), 3.29 (OMe), 2.38 (s, $W_{h/2}$ = 3 Hz, H5), 2.21 (s, $W_{h/2}$ = 5 Hz, H1), 1.70 (d of t, $^2J_{7endo,D7exo}$ = $^4J_{7endo,8s}$ = 2.5 Hz, $^3J_{7endo,6endo}$ = 6.7 Hz, H7endo), 0.94 (d, $^2J_{8a,8s}$ = 10.9 Hz, H8a), 0.83 (d of t, $^2J_{8s,8a}$ = 11.1 Hz, $^4J_{8s,6endo}$ = 1.8 Hz, $^4J_{8s,7endo}$ = 1.8 Hz, H8s), 0.69 (t of d, $^3J_{2,3endo}$ = 7.3 Hz, $^3J_{2,3exo}$ = 3.7 Hz, $^3J_{2,4}$ = 6.8 Hz, H2), 0.54 (H3exo, H4), 0.12 (m, $^2J_{3endo,3exo}$ = 6.4 Hz, $^3J_{3endo,2}$ = 6.4 Hz, $^3J_{3endo,4}$ = 6.4 Hz, H3endo); ^{2}H NMR δ_D ($CHCl_3$) 1.30 (D7exo); ^{13}C NMR δ_C ($CDCl_3$) 83.9 (l.b., C6), 56.2 (OMe), 39.8 ($J_{^{13}C,^2H}$ = 19.8 Hz, C7), 39.4 (l.b., C5), 34.8 (C1), 23.4 (C8), 15.9 (l.b., C2), 11.3 (C4), 4.0 (C3) [(l.b.) indicated the presence of a small ^{13}C–^{2}H coupling]; MS $C_9H_{13}OD$ requires $M^{\bullet+}$ 139.1107, found $M^{\bullet+}$ 139.1106.

(b) With Sodium Borodeuteride. The organomercurial mixture (600 mg) dissolved in methanol (6 mL) was added with stirring to aqueous NaOH (6 mL, 1 M) and sodium borodeuteride (120 mg). The mixture was stirred for 30 min, and the product was extracted with pentane, washed with water, and dried over $MgSO_4$. The solvent was removed under reduced pressure to give a mixture (73:27) of 7-*exo*- and 7-*endo*-deuterio-6-*exo*-methoxy-*exo*-tricyclo[3.2.1.$0^{2,4}$]octane (119 mg, 58%): ^{2}H NMR δ_D ($CHCl_3$) 1.71 (D7endo), 1.31 (D7exo).

Reaction of 8 with H^+ and D^+. (a) In Methanol at 80 °C. *exo*-Tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (**8**) (260 mg), anhydrous methanol

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(4 mL), and *p*-toluenesulfonic acid (15 mg) were placed in an ampoule (5 mL) and kept at 80 °C for 7 days. The mixture was diluted with water (5 mL), the product was extracted into pentane, washed with aqueous sodium carbonate solution, and dried over $MgSO_4$, and the solvent was removed under reduced pressure to give an oil (243 mg, 73%), shown by GLC analysis to contain 5-*exo*-methoxybicyclo[2.2.2]oct-2-ene (**10a**) (55%), 6-*exo*-methoxy-*exo*-tricyclo[3.2.1.0^{2,4}]octane (**9a**) (15%), and some high polarity compounds of longer retention times (30%). Separation of the volatile ethers was effected by preparative GLC. 5-*exo*-Methoxybicyclo[2.2.2]oct-2-ene (**10a**): ^{1}H NMR δ_H ($CDCl_3$) 6.29 (t, $^3J_{2,3}$ = 7.7 Hz, $^3J_{2,1}$ = 7.7 Hz, H2), 6.15 (t of d, $^3J_{3,2}$ = $^3J_{3,4}$ = 7.5 Hz, $^4J_{3,1}$ = 1.8 Hz, H3), 3.30 (OMe, H5endo), 2.76 (s, $W_{h/2}$ = 11 Hz, H4), 2.49 (s, $W_{h/2}$ = 13 Hz, H1), 1.90 (m, $^2J_{8s,8a}$ = 12.7 Hz, $^3J_{8s,4}$ = 2.3 Hz, $^3J_{8s,7a}$ = 2.3 Hz, $^3J_{8s,7s}$ = 8.1 Hz, H8), 1.73 (m, $^2J_{6endo,6exo}$ = 13.2 Hz, $^3J_{6endo,1}$ = 3.4 Hz, $^3J_{6endo,5endo}$ = 9.7 Hz, $^3J_{6endo,7a}$ = 3.4 Hz, H6endo), 1.60 (m, $^2J_{7a,7s}$ = 11.8 Hz, $^3J_{7a,1}$ = 2.6 Hz, $^3J_{7a,8s}$ = 3.9 Hz, $^3J_{7a,8a}$ = 9.0 Hz, H7s), 1.25 (m, $^2J_{7a,7s}$ = $^3J_{7a,8s}$ = 12.0 Hz, $^3J_{7a,1}$ = 3.1 Hz, $^3J_{7a,8s}$ = 4.4 Hz, H7a), 1.17 (d of t, $^2J_{6exo,6endo}$ = 13.2 Hz, $^3J_{6exo,1}$ = 2.5 Hz, $^3J_{6exo,5endo}$ = 2.5 Hz, H6exo), 1.05 (m, $^2J_{8a,8s}$ = 12.3 Hz, $^3J_{8a,4}$ = 2.8 Hz, $^3J_{8a,7a}$ = 12.3 Hz, $^3J_{8a,7s}$ = 4.4 Hz, $^4J_{8a,5endo}$ = 1.7 Hz, H8a); ^{13}C NMR δ_C ($CDCl_3$) 136.1 (C2), 131.4 (C3), 78.5 (C5), 56.0 (OMe), 33.5 (C6), 33.2 (C4), 29.8 (C1), 25.9 (C7), 17.6 (C8); MS $C_9H_{14}O$ requires $M^{\cdot+}$ 138.1045, found $M^{\cdot+}$ 138.1043.

6-*exo*-Methoxy-*exo*-tricyclo[3.2.1.0^{2,4}]octane (**9a**): ^{1}H NMR δ_H ($CDCl_3$) 3.35 (d of t, $^3J_{6endo,7endo}$ = 6.6 Hz, $^3J_{6endo,7exo}$ = $^4J_{6endo,8s}$ = 1.8 Hz, H6endo), 3.29 (OMe), 2.38 (s, $W_{h/2}$ = 4 Hz, H5), 2.21 (s, $W_{h/2}$ = 7 Hz, H1), 1.73 (m, $^2J_{7endo,7exo}$ = 12.3 Hz, $^3J_{7endo,6endo}$ = 6.8 Hz, $^4J_{7endo,8s}$ = 2.6 Hz, H7endo), 1.31 (d of t, $^2J_{7exo,7endo}$ = 12.4 Hz, $^3J_{7exo,1}$ = $^3J_{7exo,6endo}$ = 3.1 Hz, H7exo), 0.95 (d, $^2J_{8a,8s}$ = 11.0 Hz, H8a), 0.84 (d of t, $^2J_{8s,8a}$ = 11.0 Hz, $^4J_{8s,6endo}$ = $^4J_{8s,7endo}$ = 2.1 Hz, H8s), 0.70 (t of d, $^3J_{2,3endo}$ = 7.3 Hz, $^3J_{2,3exo}$ = 3.6 Hz, $^3J_{2,4}$ = 7.3 Hz, H2), 0.54 (m, H3exo, H4), 0.12 (m, $^2J_{3endo,3exo}$ = $^3J_{3endo,2}$ = 6.4 Hz, $^3J_{3endo,4}$ = 6.4 Hz, H3endo); ^{13}C NMR δ_C ($CDCl_3$) 84.0 (C6), 56.3 (OMe), 40.2 (C7), 39.5 (C5), 34.9 (C1), 23.5 (C8), 16.0 (C2), 11.3 (C4), 4.1 (C3); MS $C_9H_{14}O$ requires $M^{\cdot+}$ 138.1045, found $M^{\cdot+}$ 138.1045.

(b) With Methanol-d_1 at 80 °C. The acid-catalyzed reaction of *exo*-tricyclo[3.2.1.0^{2,4}]oct-6-ene (**8**) (273 mg) with methanol-d_1 at 80 °C for 7 days was carried out as above to give a mixture (56:12) of 7-*syn*-deuterio-5-*exo*-methoxybicyclo[2.2.2]oct-2-ene (**10b**) and 7-*exo*-deuterio-6-*exo*-methoxy-*exo*-tricyclo[3.2.1.0^{2,4}]-octane (**9b**) (304 mg, 87%), which were separated by careful preparative GLC. 7-*syn*-Deuterio-5-*exo*-methoxybicyclo[2.2.2]-oct-2-ene (**10b**): ^{1}H NMR δ_H ($CDCl_3$) 6.29 (t, $^3J_{2,3}$ = $^3J_{2,1}$ = 7.7 Hz, H2), 6.15 (t of d, $^3J_{3,2}$ = $^3J_{3,4}$ = 7.5 Hz, $^4J_{3,1}$ = 1.3 Hz, H3), 3.30 (OMe, H5endo), 2.76 (s, $W_{h/2}$ = 12 Hz, H4), 2.49 (s, $W_{h/2}$ = 11 Hz, H1); 1.90 (m, $^2J_{8s,8a}$ = 12.3 Hz, $^3J_{8s,4}$ = 2.3 Hz, $^3J_{8s,7a}$ = 2.3 Hz (broadened due to its proximity to ^{2}H7s), H8s), 1.73 (m, $^2J_{6endo,6exo}$ = 13.2 Hz, $^3J_{6endo,1}$ = 3.4 Hz, $^3J_{6endo,5endo}$ = 9.7 Hz, $^3J_{6endo,7a}$ = 3.4 Hz, H6endo), 1.23 (H7a), 1.17 (d of t, $^2J_{6exo,6endo}$ = 13.1 Hz, $^3J_{6exo,1}$ = 2.2 Hz, $^3J_{6exo,5endo}$ = 3.3 Hz, H6exo), 1.05 (m, $^2J_{8a,8s}$ = 12.2 Hz, $^3J_{8a,4}$ = 3.1 Hz, $^3J_{8a,7a}$ = 12.2 Hz, $^4J_{8a,5endo}$ = 1.6 Hz, H8a); ^{2}H NMR δ_D ($CHCl_3$) 1.60 (D7s); ^{13}C NMR δ_C ($CDCl_3$) 136.1 (l.b., C2), 131.5 (C3), 78.5 (C5), 56.2 (OMe), 33.5 (C6), 33.2 (C4), 29.7 (l.b., C1), 25.5 ($J_{^{13}C,^2H}$ = 19.7 Hz, C7), 17.5 (C8); MS $C_9H_{13}OD$ requires $M^{\cdot+}$ 139.1107, found $M^{\cdot+}$ 139.1103; mass spectrum shows 7% D^0, 77% D^1, 16% D^2.

7-*exo*-Deuterio-6-*exo*-methoxy-*exo*-tricyclo[3.2.1.0^{2,4}]octane (**9b**): all spectral data are identical with those reported in the sodium mercury amalgam reduction in NaOD, D_2O of 7-*exo*-(acetoxymercurio)-6-*exo*-methoxy-*exo*-tricyclo[3.2.1.0^{2,4}]-octane (**9c**).

(c) With Methanol at Room Temperature. A solution of *exo*-tricyclo[3.2.1.0^{2,4}]oct-6-ene (**8**; 1.156 g) and *p*-toluenesulfonic acid (384 mg) in anhydrous methanol (10 mL) was kept at room temperature, and the reaction was monitored by GLC. After 28 days (77% reaction) the product was isolated with pentane, the combined pentane extracts were washed with aqueous sodium bicarbonate solution and dried over $MgSO_4$, and the solvent was removed under reduced pressure to give a pale yellow oil (1.035 g, 80%), consisting of *exo*-tricyclo[3.2.1.0^{2,4}]oct-6-ene (**8**) (23%), 5-*exo*-methoxybicyclo[2.2.2]oct-2-ene (**10a**) (23%), 6-*exo*-methoxy-*exo*-tricyclo[3.2.1.0^{2,4}]octane (**9a**) (18%), and 6-*exo*-methoxytricyclo[3.2.1.0^{2,7}]octane (**11a**) (31%). In addition there were two unidentified compounds (2% and 3%). 6-*exo*-Methoxytricyclo[3.2.1.0^{2,7}]octane (**11a**) was isolated by preparative GLC: ^{1}H NMR δ_H ($CDCl_3$) 3.52 (s, $W_{h/2}$ = 2.0 Hz, H6endo), 3.34 (s, OMe), 1.96 (br s, $W_{h/2}$ = 11.4 Hz, H5), 1.88 (m, $^2J_{8a,8s}$ = 11.4 Hz, $^3J_{8a,1}$ = 3.4 Hz, $^3J_{8a,5}$ = 5.7 Hz, $^4J_{8a,4endo}$ = 2.2 Hz, H8a), 1.78–1.68 (m, H3exo, H3endo), 1.58 (H4exo), 1.51 (H7, H8s), 1.40 (H1), 1.32 (H4endo), 0.92 (m, $^3J_{2,1}$ = 8.0 Hz, $^3J_{2,3exo}$ = $^3J_{2,3endo}$ = 2.7 Hz, $^3J_{2,7}$ = 8.0 Hz, H2); ^{13}C NMR δ_C ($CDCl_3$) 85.5 (C6), 55.7 (OMe), 34.9 (C5), 27.4 (C8), 26.5 (C4), 22.0 (C7), 16.9 (C1), 16.5 (C2), 16.1 (C3). The spectral data for 5-*exo*-methoxybicyclo[2.2.2]oct-2-ene (**10a**) and 6-*exo*-methoxytricyclo[3.2.1.0^{2,7}]octane (**9a**) were identical with those reported in the acid-catalyzed methanol addition at 80 °C.

(d) With Methanol-d_1 at Room Temperature. To *exo*-tricyclo[3.2.1.0^{2,4}]oct-6-ene (**8**) (55 mg) was added a solution of *p*-toluenesulfonic acid (25 mg) in methanol-d_1 (2 mL), and the mixture was stirred for 72 days (75% reaction). Isolation of the products in the usual manner gave 7-*syn*-deuterio-5-*exo*-methoxybicyclo[2.2.2]oct-2-ene (**10b**) (28%), 7-*exo*-deuterio-6-*exo*-methoxy-*exo*-tricyclo[3.2.1.0^{2,4}]octane (**9b**) (16%), and 4-*exo*-deuterio-6-*exo*-methoxytricyclo[3.2.1.0^{2,7}]octane (**11b**) (31%). 4-*exo*-Deuterio-6-*exo*-methoxytricyclo[3.2.1.0^{2,7}]octane (**11b**): ^{13}C NMR δ_C ($CDCl_3$) 85.5 (C6), 55.7 (OMe), 34.7 (C5), 27.4 (C8), 26.1 ($J_{^{13}C,^1H}$ = 19.9 Hz, C4); 22.0 (C7), 16.9 (C1); 16.5 (C2); 16.2 (C3); ^{2}H NMR δ_D ($CHCl_3$) 1.52 (D4exo).

Stability of 9b and 11a under the Reaction Conditions: (a) 7-*exo*-Deuterio-6-*exo*-methoxytricyclo[3.2.1.0^{2,4}]octane (9b). To an ampoule containing 7-*exo*-deuterio-6-*exo*-methoxy-*exo*-tricyclo[3.2.1.0^{2,4}]octane (45 mg), prepared from the sodium amalgam reduction of the organomercurial **9c** in NaOD (0.7 mL), was added of a solution of *p*-toluenesulfonic acid (21 mg) in methanol (10 mL). The ampoule was sealed and placed in an oven at 80 °C for 7 days, after which time GLC analysis revealed the presence of 7-*exo*-deuterio-6-*exo*-methoxy-*exo*-tricyclo-[3.2.1.0^{2,4}]octane (**9b**) (52%), high retention time compounds (35%), and three other compounds (2%, 8%, and 2%).

(b) 6-*exo*-Methoxytricyclo[3.2.1.0^{2,7}]octane (11a). To a flask containing 6-*exo*-methoxytricyclo[3.2.1.0^{2,7}]octane (5 mg; obtained by preparative GLC from the products of the acid-catalyzed reaction of *exo*-tricyclo[3.2.1.0^{2,4}]oct-6-ene with methanol at 25 °C), was added 0.6 mL of a solution of *p*-toluenesulfonic acid (215 mg) in methanol (10 mL). The solution was stirred and monitored by GLC. After 2 h the mixture was shown to contain 5-*exo*-methoxybicyclo[2.2.2]oct-2-ene (**10a**) (45%) and 6-*exo*-methoxytricyclo[3.2.1.0^{2,7}]octane (**11a**) (55%). This product ratio was invariant for 16 days.

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