The analytical scattering factors of Cromer and Waber[10a] for neutral atoms were used throughout the analysis; both real (D f') and imaginary (i D f''') components of anomalous dispersion were included.[10b]

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Registry No. **1a**, 118895-55-9; **1b**, 118895-56-0; **1c**, 118895-57-1; **1d**, 118895-58-2; **1e**, 118895-59-3; **2**, 118895-60-6; **3a**, 118895-61-7; **3b**, 118920-50-6; **3c**, 118895-62-8; **3d**, 118895-63-9; **3e**, 118895-64-0; **4a**, 118895-65-1; **4b**, 118895-66-2; **4c**, 118895-67-3; **4d**, 118895-68-4; $ZnCl_2$, 7646-85-7; $(CH_3)_3SiCN$, 7677-24-9.

(10) *Internationat Tables for X-Ray Crystallography*; Kynoch Press: Birmingham, England, 1974; (a) pp 99–101; (b) pp 149–150.

Corner Attack on *exo*- and *endo*-Tricyclo[3.2.1.0^{2,4}]octane by Deuteron and Mercuric Ions

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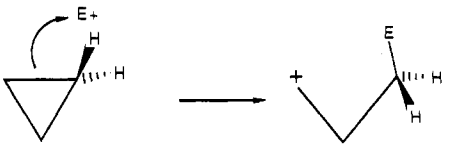
Reaction of *endo*-tricyclo[3.2.1.0^{2,4}]octane (1) with deuteron in methanol-d_1 gave a mixture (62:38) of methoxy ethers **3b** and **4b** from cleavage of the most substituted cyclopropane bond. The reaction proceeds by attack of deuterium at the corner of the cyclopropane. Trapping of the intermediate cation **5b** is competitive with rearrangement to the nonclassical cation **6b**. Reaction of *exo*-tricyclo[3.2.1.0^{2,4}]octane (**2**) under similar conditions gave methoxy ether **11b**, which results from rupture of an external cyclopropyl bond, and methoxy ether **12b** formed from rupture of the internal cyclopropyl bond with inversion at the site of both electrophilic and nucleophilic attack. Reaction of hydrocarbon **1** with mercuric acetate in methanol gave 4-*endo*-(acetoxymercurio)-2-*endo*-methoxybicyclo[3.2.1]octane (**3c**) from attack of the mercuric ion at the corner of the cyclopropane and nucleophilic attack by methanol with inversion without skeletal rearrangement. Similar reaction of the exo hydrocarbon **2** gave product **12c** from internal bond rupture without molecular rearrangement and with inversion of configuration at the site of electrophilic and nucleophilic attack. In addition an almost equal quantity of **11c**, a product of rupture of the external cyclopropyl bond, was formed. The stereochemistry of mercuric ion and deuteron attack at C2 at the corner of the cyclopropane ring of **1** and **2** is rationalized by consideration of the symmetry and energy of the molecular orbitals involved.

Acid- or electrophile-promoted ring cleavage of cyclopropanes has been the subject of considerable speculation.[1] The regiochemistry of reaction is often rationalized by a modified version of Markovnikov's rule, which states[2] that the ring opens between the carbons bearing the largest and smallest number of alkyl substituents. Thus, for cyclopropanes substituted at only one carbon the product(s) can be rationalized by ring opening leading to the more substituted carbocation. However, with substituents on two carbons, products are generally observed to result from both Markovnikov-type addition and from cleavage of the most substituted cyclopropyl bond.[1] The two possible reaction trajectories for electrophilic attack on cyclopropane are shown in Scheme I. For substrates suitably labeled to allow the relative configurations at C1 and C2 in the product to be established, these two processes can be differentiated. For example, DePuy[3] found that *cis*-1,2,3-trimethylcyclopropane reacted with deuteron to give 68% retention of configuration at the site of deuteron attack and 32% inversion, as measured from the ratio of *erythro* and *threo* products. Wiberg[1b] has referred to retention (b, Scheme I) as cleavage of the C–C bond syn to the entering proton and to inversion (a, Scheme I) as cleavage of the C–C bond anti to the entering proton. Subsequent attack by the nucleophile in this system occurred with inversion.

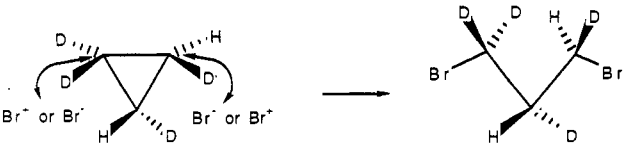
Scheme I

(a) Corner attack by electrophile (with inversion of configuration)



(b) Edge attack by electrophile (with retention of configuration)

Scheme II



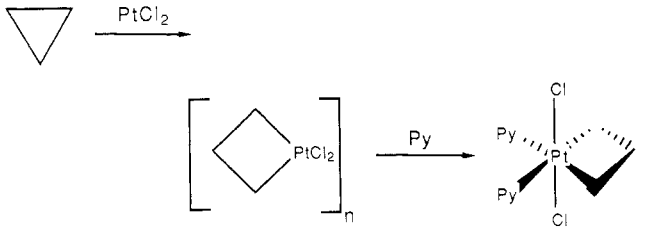
(1) (a) Battiste, M. A.; Coxon, J. M. In *The Chemistry of the Cyclopropyl Group*; Rappoport, Z. Ed.; J. Wiley and Sons: 1987. (b) Wiberg, K. B.; Kass, S. R. *J. Am. Chem. Soc.* **1985**, *107*, 988 and 1005. (c) Lambert, J. B.; Schulz, W. J.; Mueller, P. H.; Kobayashi, K. *J. Am. Chem. Soc.* **1984**, *106*, 792. (d) Battiste, M. A.; Coxon, J. M. *Tetrahedron Lett.* **1986**, *27*, 517. (e) Kirmse, W.; Streu, J. *J. Org. Chem.* **1987**, *52*, 515. (f) Coxon, J. M.; Steel, P. J.; Whittington, B. I.; Battiste, M. A. *J. Am. Chem. Soc.* **1988**, *110*, 2988.

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

(3) DePuy, C. H.; Funfschilling, P. C.; Andrist, A. H.; Olson, J. M. *J. Am. Chem. Soc.* **1977**, *99*, 6297.

0022-3263/89/1954-1383$01.50/0

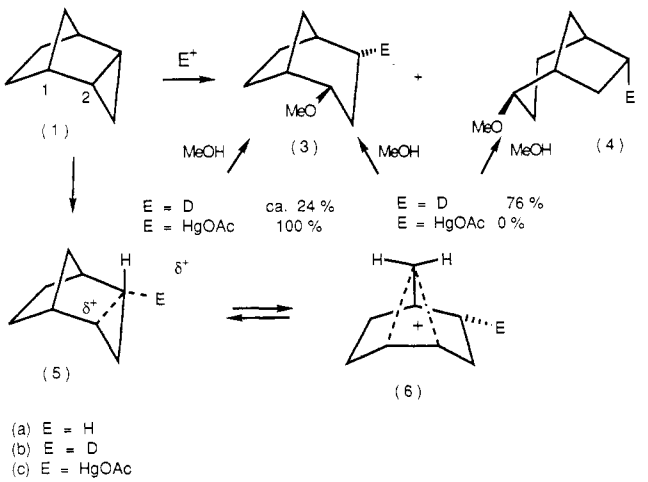
Scheme III



Addition of bromine to cyclopropanes is slow in the absence of light unless the ring is heavily substituted.[4] In the presence of light, reaction is rapid with halogen radical attack on substituted cyclopropanes being fast even at −78 °C. The formation of HBr facilitates reaction by forming the conjugate acid of the cyclopropane. The more facile reaction of cyclopropane with HBr compared with bromine is in contrast to alkene chemistry where bromine addition is more rapid.[1a] Nevertheless, cyclopropane does react with bromine and in an elegant study Lambert[1c] showed that bromination of *trans*-cyclopropane-*1,1,2,3*-d_4 (in an 85:15 mixture with the cis isomer) reacted stereospecifically to give *erythro* product (85%), thereby establishing that inversion of stereochemistry occurred at both the site of electrophilic and nucleophilic attack (Scheme II). In this reaction electrophilic attack occurs at the corner of the cyclopropane with inversion of configuration, and this contrasts with the less stereoselective[3] reaction of trimethylcyclopropane where attack at the edge with retention of configuration competes with reaction with inversion. Cyclopropanes can react with certain metals[5] (e.g., $PdCl_2$, $PtCl_2$, $Rh_2(CO)_4Cl_2$, and $Ph_3PIrClCO$) to undergo oxidative addition at the edge of the cyclopropane with the metal generally becoming attached to the most and least substituted carbon atoms of the ring. The first report of a reaction of a strained alkane with a metal complex was by Tipper[5a] in 1955, who reported the reaction of cyclopropane and $PtCl_2$ (Scheme III) to give a product, the structure of which was first suggested by Chatt and co-workers[5b] in 1961 to be a platinacyclobutane. An X-ray crystal structure by Mason and co-workers[5c] confirmed the structure. For oxidative addition of metals to cyclopropanes,[5c] the metal must of necessity insert into the cyclopropane ring with retention of configuration at each of the carbons. Reactions involving the intermolecular insertion of an organometallic complex into an alkane C–C bond in a homogeneous reaction are rare since there is usually a substantial kinetic and thermodynamic barrier to C–C activation.[5f] A number of examples are known of C–C bond cleavage in ligands.[5g]

To date, no satisfactory explanation has been offered for the varied behavior of cyclopropanes with differing electrophiles.[1,2] There are two important aspects to this problem. The first is to understand when Markovnikov rupture of the cyclopropane is to be observed (i.e., regiochemistry) and the second the reasons for the varied trajectories found for attack of both electrophile and nucleophile (i.e., stereochemistry). For example, why is addition of a proton to 1,2,3-trimethylcyclopropane not stereospecific[3] while intermolecular nucleophilic attack on the resulting cation occurs exclusively with inversion? Why does the addition of bromine to cyclopropane occur with inversion at the sites of electrophilic and nucleophilic attack? Furthermore, oxidative addition of metals to cyclopropanes necessarily occurs with retention of configuration but may involve[5h] initial insertion into a carbon–hydrogen bond and subsequent rearrangement.

Scheme IV



(a) E = H
(b) E = D
(c) E = HgOAc

Results and Discussion

We now report the determination of the product(s) and stereochemistry of attack of proton, mercuric ion, and nucleophile in the reaction of *endo*- and *exo*-tricyclo[3.2.1.$0^{2,4}$]octane (**1** and **2**) in methanol. These compounds were selected for study because of the complimentary relationship of the cyclopropane ring to the skeleton allowing orbital effects to be differentiated from conformational and steric effects.

endo-Tricyclo[3.2.1.$0^{2,4}$]octane (**1**) was prepared by hydrogenation of *endo*-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene[6] while the exo isomer **2** was prepared by addition of methylene to norbornene.[7] Methanol was chosen as solvent in preference to acetic acid, and therefore as nucleophile in the reaction with acid and mercuric ion, since an intermediate carbocation when trapped by methanol gives a product that is stable under the reaction conditions. In contrast, acetate products are often unstable[1b] and undergo further rearrangement, which complicates analysis of the primary reaction.

Protonation of 1 in Methanol with H^+ and D^+. Reaction of **1** with methanol and a catalytic quantity of *p*-toluenesulfonic acid[1f] gives a high yield of 2-*endo*-methoxybicyclo[3.2.1]octane (**3a**) when the reaction is carried out at 80 °C for 1 week. A GLC analysis of the reaction mixture indicated that the reaction had occurred to the extent of 80% with less than 2% of other products being formed. The axial nature of C2H in **3a**, and hence the configuration of the methoxy group, was established

(4) Day, J. C.; Shea, K. J.; Skell, P. S. *J. Am. Chem. Soc.* **1973**, *95*, 5089.

(5) (a) Tipper, C. F. H. *J. Chem. Soc.* **1955**, 2045. (b) Adams, D. M.; Chatt, J.; Guy, R.; Sheppard, N. *J. Chem. Soc.* **1961**, 738. (c) Keeton, M.; Mason, R.; Russell, D. R. *J. Organomet. Chem.* **1971**, *33*, 259. (d) Bailey, N. A.; Gillard, R. D.; Keetan, M.; Mason, R.; Russell, D. R. *Chem. Commun.* **1966**, 396. (e) Crabtree, R. H. *Chem. Rev.* **1985**, *85*, 245. (f) Halpern, J. *Acc. Chem. Res.* **1982**, *15*, 238. (g) Crabtree, R. H.; Dion, R. P.; Gibboni, D. J.; McGrath, D. V.; Holt, E. M. *J. Am. Chem. Soc.* **1986**, *108*, 7222. Kang, J. W.; Moseley, R.; Maitlis, D. M. *J. Am. Chem. Soc.* **1969**, *91*, 5970. Benfield, F. W. C.; Green, M. L. H. *J. Am. Chem. Soc.* **1969**, *91*, 5970. Benfield, F. W. C.; Green, M. L. H. *J. Chem. Soc., Dalton Trans.* **1974**, 1325. Eilbracht, P. *Chem. Ber.* **1976**, *109*, 1429, 3136; **1980**, *113*, 542, 1033, 1420, 2211. Grubbs, R. H., Myashita, A. *J. Am. Chem. Soc.* **1978**, *100*, 1200, 7418. Watson, P. L.; Roe, D. C. *J. Am. Chem. Soc.* **1982**, *104*, 6471. Flood, T. C.; Statler, J. A. *Organometallics* **1984**, *3*, 1795. Suggs, J. W.; Cox, S. D. *J. Organomet. Chem.* **1982**, *221*, 199. (h) Periana, R. A.; Bergman, R. G. *J. Am. Chem. Soc.* **1986**, *108*, 7346. (i) Bishop, K. C. *Chem. Rev.* **1976**, *76*, 461. (j) Blomberg, M. R. A.; Siegbahn, P. E. M.; Backvall, J.-E. *J. Am. Chem. Soc.* **1987**, *109*, 4450.

(6) Closs, G. L.; Krantz, K. D. *J. Org. Chem.* **1966**, *31*, 638.

(7) Simmons, H. E.; Cairns, T. L.; Vladuchick, S. A.; Hoiness, C. M. *Org. React.* **1973**, *20*, 1.

from the ^{1}H NMR spectrum.[8] The ^{13}C NMR spectrum could be assigned by comparison with the reported spectrum of 2-*endo*-hydroxybicyclo[3.2.1]octane,[9] and heteronuclear correlation experiments established connectivities.[10] In order to establish the reaction trajectory of the proton in the reaction of *endo*-tricyclo[3.2.1.0^{2,4}]octane (1) with acidic methanol the reaction was carried out in methanol-*d*. The ^{13}C NMR spectrum of the product showed deuterium incorporation at both C4 and C6 (Scheme IV). From the intensities of the signals in the ^{2}H NMR spectrum at 1.41 and 1.34 ppm, the ratio of **3b**:**4b** was established as 62:38. The determination of the configuration of deuterium at C4 and C6 for clarity is discussed separately below.

The formation of the two deuterated products **3b** and **4b** can be accounted for if reaction of deuteron occurs exclusively at the corner of the cyclopropane with rupture of the most substituted adjacent cyclopropane bond. A protonated intermediate (**5b**) can be attacked by methanol to give **3b** or collapse to the protonated species **6b**, which will be attacked with inversion equally at both C1 and C2. A small isotope effect will perturb the symmetry of the cation **6b** but is expected to be sufficiently small as to not effect the partition of the cation to **3b** and **4b** to any significant extent. The preferential attack on protonated hydrocarbon 1 by the nucleophile at C4 compared with C5 (62:38) demonstrates that protonated intermediate **5b** formed by corner attack of deuterium with inversion is trapped by nucleophile to the extent of 24% before conversion to the symmetrical species **6b**. In an independent control experiment, an authentic sample of 2-*endo*-methoxy-3,3,4-*exo*-trideuteriobicyclo[3.2.1]octane was shown to be stable under the reaction conditions, thus establishing the above ratio to be kinetic in origin. Capture of the unsymmetrical protonated cyclopropane **5b** occurs before the activated complex has relaxed to any extent and is competitive with relaxation of the cation intermediate to the symmetrical nonclassical corner-protonated cation **6b**.[1e] Furthermore, the control experiment demonstrates that the reaction cannot proceed by exclusive capture of **5b** followed by subsequent rearrangement. While nucleophilic attack on **5b** occurs with inversion to give **3b**, further intramolecular reorganization of the cation occurs to give **6b** where the configuration at C2 is retained. In this reaction it is apparent that intramolecular reaction with retention at C4 and intermolecular nucleophilic attack at C5 competes successfully with attack of methanol at C4.

Assignment of the NMR Spectrum of 2-*endo*-Methoxybicyclo[3.2.1]octane. The assignment of the chemical shifts of the C4 protons in 2-*endo*-methoxybicyclo[3.2.1]octane was not possible from the chemical shift differences or from difference NOE studies and was determined in the following manner. 2-*exo*-Hydroxybicyclo[3.2.1]heptane was prepared by the method reported by LaLonde[11] and a heteronuclear correlation experiment identified the connectivity of the C4 protons centered at 1.65 and 1.26 ppm with that carbon (28.3 ppm).

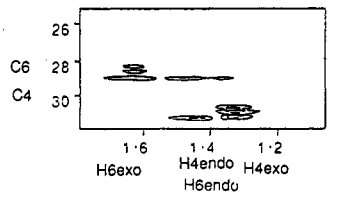
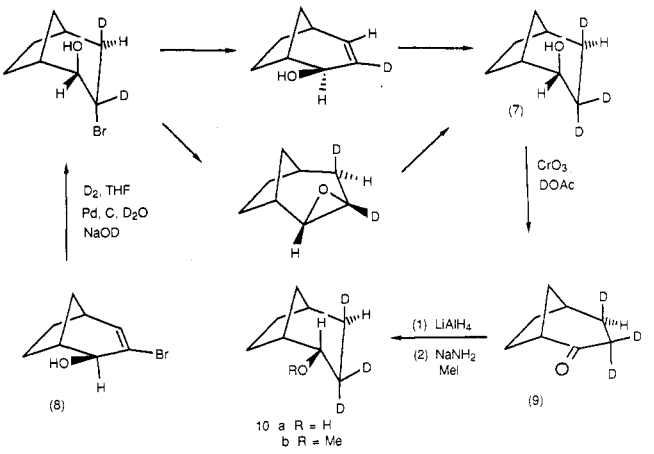


Figure 1. Heteronuclear correlation spectrum of a mixture (62:38) of 4-*endo*- and 6-*endo*-deutero-2-*endo*-methoxybicyclo[3.2.1]octane.

Scheme V



A difference NOE experiment showed that irradiation of the signal centered at 1.92 and identified as H8s due to coupling with H8a resulted in enhancement of the signal at 1.65 ppm, which was therefore assigned to the C4-exo-H.[12] For further confirmation of this assignment, a deuterated analogue of 2-*exo*-hydroxybicyclo[3.2.1]heptane (**7**)[13] was prepared (Scheme V) by reaction of 3-bromo-2-*exo*-hydroxybicyclo[3.2.1]hept-3-ene (**8**) with deuterium gas, sodium deuteroxide (1 M) in deuterium oxide–tetrahydrofuran in the presence of palladium on carbon (10%) as catalyst. Oxidation of the alcohol **7** with chromium trioxide–deuterioacetic acid gave the ketone **9**, shown by analysis of the mass spectrum to contain on average 2.73 deuterium atoms. Lithium aluminum hydride reduction of this ketone where the deuterium configuration at C4 is known gave the endo alcohol **10a** in a mixture (4:1) with the exo alcohol **7**, which was converted to a similar mixture (4:1) of the 2-*endo*-methoxy compound (**10b**) along with the *exo*-methoxy epimer by reaction of sodium amide–methyl iodide. The chemical shifts of the C4 protons of **3a** are centered at 1.33 and 1.41 ppm, and for the deuterated substrate **10b**, with a known exo configuration of deuterium at C4, the presence of a triplet at 1.41 in the proton dimension of a heteronuclear correlation experiment allows the identification of this proton as endo. By exclusion the C4-exo-H of **3a** is centered at 1.33 ppm. The multiplicity in the heteronuclear correlation experiment of the signal at 1.41 as a triplet results from C4-exo-deuterium coupling and connectivity of C4 and the endo proton. This unambiguously establishes the assignment

(8) J = 10.1 Hz C2H to C3-endo-H, J = 5.7 Hz C2H to C3-exo-H, and J = 3.0 Hz to C1H (C1H was further coupled to C8aH (6 Hz) and to the C7-exo-H (6Hz)).

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

(10) H1, 2.36 ppm/C1, 38.6; H2, 3.18 ppm/C2, 81.9; H3-exo, 1.82 and H3-endo, 1.23 ppm/C3, 25.7; H4-exo 1.33 and H4-endo 1.41/C4, 31.0; H5, 2.12/C5, 34.4; H6-exo 1.65 and H6-endo 1.34/C6, 28.8; H7-exo 1.73 and H7-endo 1.50/C7, 23.9; and H8a 1.59 and H8s 1.28/C8, 37.5.

(11) LaLonde, R. T.; Ding, J.-Y.; Tobias, M. A. *J. Am. Chem. Soc.* **1967**, *89*, 6651. Jefford, C. W.; Mahajan, S.; Waslyn, J.; Waegell, B. *J. Am. Chem. Soc.* **1965**, *87*, 2183.

(12) The reported assignment of the ^{13}C NMR spectrum[9] of this alcohol is incorrect and C4, C6, and C7 are reassigned from coupling data obtained fromthe deuterated analogue.

(13) A signal at 1.26 ppm in the ^{1}H NMR spectrum of **7** and a triplet at 27.7 ppm due to C4 in the ^{13}C NMR spectrum demonstrate not only that this substrate contains deuterium at C4 but that the configuration of the proton at that carbon is endo. The ^{13}C NMR spectrum showed C3 as a multiplet consistent with the presence of two deuterium atoms at this position. The mechanism for formation of **7** may involve either reduction of an intermediate epoxide or loss of HBr and deuterogenation of the resulting alkene.

of the proton spectrum of the C4 protons in compound **3a**. A related procedure for determining deuterium stereochemistry that uses a heteronuclear correlation experiment has recently been reported.[14]

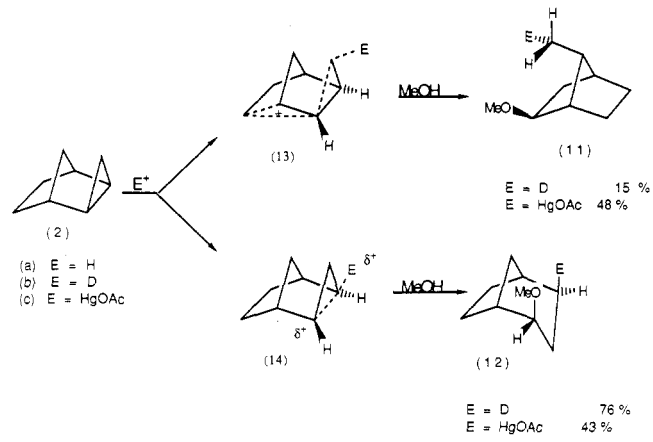
The stereochemistry of the deuterium at C6 (in **4b**) was established as endo from its chemical shift. In the heteronuclear correlation spectrum of the deuterated product mixture (**3b**,**4b**), the connectivities of the protons at C6 with that carbon were observed at 1.65 and 1.34 ppm and the protons at C4 with that carbon in **3b** at 1.33 and 1.41 ppm. The presence of **4b** in the mixture was demonstrated from the heteronuclear correlation spectrum, which exhibited a triplet at 1.65 in the carbon dimension for C6-exo-H, the additional splitting as a 1:1:1 triplet resulting from coupling of C6 to the endo deuterium (Figure 1). The endo configuration of the C6-D eliminated for this compound a signal at 1.34 ppm in the proton dimension and the presence of deuterium at C6 results in the signal at 28.5 for the C6 appearing as a triplet due to carbon–deuterium coupling. The presence of **3b** in the mixture was similarly identified by a triplet in the carbon dimension at 30.3 ppm, resulting from carbon–deuterium coupling and connectivity of C4 and the C4-exo-H. The absence of the endo proton in **3b** eliminates a signal at 1.41 and the signal at 1.33 results from deuterium–carbon coupling and connectivity of C4 and the exo proton.

Methoxymercuration of 1. Reaction of *endo*-tricyclo[3.2.1.$0^{2,4}$]octane (**1**) with mercuric acetate in anhydrous methanol at room temperature gave as a single product 4-*endo*-(acetoxymercurio)-2-*endo*-methoxybicyclo[3.2.1]-octane (**3c**). The identity of this product was established in the following way. Reduction of **3c** with sodium amalgam in sodium hydroxide gave 2-*endo*-methoxybicyclo[3.2.1]octane (**3a**), identical with an authentic sample. The stereochemistry and position of the mercury in **3c** is consistent with the observed ^{1}H NMR couplings (selective decoupling), and ^{13}C–^{199}Hg couplings.[15,16]

Reduction of 4-*endo*-(acetoxymercurio)-2-*endo*-methoxybicyclo[3.2.1]octane (**3c**) with sodium amalgam in sodium deuteroxide gave 4-*endo*-deuterio-2-*endo*-methoxybicyclo[3.2.1]octane (**3b**). The ^{2}H NMR spectrum showed a signal at 1.43 ppm and a two-dimensional ^{1}H–^{13}C heteronuclear correlation experiment identified the C4-exo-H at 1.35 ppm, thereby establishing the configuration of the deuterium.[17] Reduction with sodium borodeuteride was not stereospecific and gave rise to 4-*exo*- and 4-*endo*-deuterio-2-*endo*-methoxybicyclo[3.2.1]octane in the ratio of 45:55, respectively.

Formation of **3c** results from attack of the mercuric ion at the corner of the cyclopropane ring with cleavage of the internal cyclopropyl bond and subsequent attack by methanol with inversion. The unsymmetrical mercurated cation **5c** does not rearrange to the more symmetrical mercurated cation **6c**. A high degree of bond order is maintained between C4 and C2 in the cation **5c** with little charge localization at C4. This reaction is therefore similar to that of alkenes with mercuric acetate[18] where skeletal rearrangement is not normally observed even though charge development on the alkene carbons is observed.

Scheme VI



Protonation of 2 in Methanol with H$^+$ and D$^+$. LaLonde some years ago[19] studied the reaction of *exo*-tricyclo[3.2.1.$0^{2,4}$]octane (**2**) with sulfuric acid in acetic acid and observed by GLC five acetate products, two of which were identified after isolation and hydrolysis as 2-*exo*-bicyclo[3.2.1]octanol (35%) and 2-hydroxybicyclo[2.2.2]-octane (22%). Both of these products result from cleavage of the internal cyclopropyl bond. We decided to reinvestigate the ring-opening reaction of this hydrocarbon with acidic methanol and to contrast its reaction with mercuric acetate in methanol, conditions that would be expected to give a less complex reaction mixture since the initial products are, under these conditions, expected to be stable. The reaction with methanol in the presence of *p*-toluenesulfonic acid was followed by GLC and gave 2-*exo*-methoxybicyclo[3.2.1]octane (**12a**) and 2-*exo*-methoxy-7-*syn*-methylbicyclo[2.2.1]heptane (**11a**) in 76% and 15% yield, respectively. These products were separated by preparative GLC. The identity of 2-*exo*-methoxybicyclo[3.2.1]octane (**12a**) follows from the ^{1}H NMR and ^{13}C NMR spectra and by its identity to an authentic sample prepared by reaction of 2-*exo*-hydroxybicyclo-[3.2.1]heptane prepared as above (Scheme VI) with sodium amide–methyl iodide.[20] The identity of 2-*exo*-methoxy-7-*syn*-methylbicyclo[2.2.1]heptane (**11a**) follows from a heteronuclear correlation experiment and difference NOE studies.[21] The stereospecific formation of 3-*exo*-methoxybicyclo[3.2.1]octane (**12a**) from *exo*-tricyclo-[3.2.1.$0^{2,4}$]octane (**2**) and 3-*endo*-methoxybicyclo[3.2.1]octane (**3a**) from *endo*-tricyclo[3.2.1.$0^{2,4}$]octane (**1**) excludes the intermediacy of a common classical secondary cation from cleavage of the C2–C4 bond of the hydrocarbons since the stereochemistry of nucleophilic attack on such a cation would be independent of the configuration of the starting cyclopropyl ring.

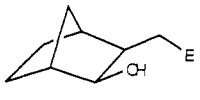
LaLonde[11] and co-workers analyzed the stereochemistry of the incorporated deuterium in the major product, 2-*exo*-acetoxybicyclo[3.2.1]octane, from reaction of hydrocarbon **2** with sulfuric acid-d_2 in acetic acid-d_1. The acetate was converted into hydrocarbon and a comparison of the

(14) Reese, P. B.; Trimble, L. A.; Vederas, J. C. *Can. J. Chem.* **1986**, *64*, 1427.
(15) Kitching, W.; Atkins, A. R.; Wickham, G.; Alberts, V. *J. Org. Chem.* **1981**, *46*, 563.
(16) $J_{^{13}C-^{199}Hg}$ = C1, 25; C2, 310; C3, 97; C4, 1634; C5, 66; C6, 65; C7, n.o.; C8, 310 Hz.
(17) The reduction conditions have been shown in related systems[15] to occur with retention of configuration and therefore the stereochemistry and position of the mercury in **2c** is unambiguous.
(18) Wardell, J. L. *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; 1982; Vol. 2, p 863.
(19) LaLonde, R. T.; Batelka, J. J. *Tetrahedron Lett.* **1964**, 445.
(20) Kirmse, W.; Olbricht, T. *Chem. Ber.* **1975**, *108*, 2606.
(21) The coupling of the C1H (2.10 ppm) to the C6-exo-H (3.1 Hz), and C4H (1.95 ppm) to C3-exo-H (3.0 Hz) and C5-exo-H (3.0 Hz), establishes that either the methyl or the methoxy group is at C2 and in an exo configuration. A difference NOE experiment showed that on irradiation of H4 (1.95 ppm) the signal of the methyl was enhanced as well as the C3H_2 (1.73 ppm), C5-exo-H (1.5 ppm), and C5-endo-H (1.05 ppm). Irradiation of H2 and the methoxymethyl, both centred at 3.3 ppm, caused enhancement of H1 (2.1 ppm), C3H_2 (1.73 ppm), and the methyl at 1.05, thereby establishing that the methoxy group is at C2 and the methyl in a syn configuration at C7.

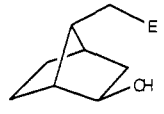
infrared spectrum of the deuterated hydrocarbon with the infrared spectra of authentic *exo*- and *endo*-2-deuteriobicyclo[3.2.1]octane made. This study concluded that the deuterium was exo, consistent with deuterium attack at the corner of the cyclopropyl unit. Our reinvestigation of the stereochemical aspects of the reaction of exo hydrocarbon **2** with methanol-*d* and deuteron were decidedly more straightforward as a consequence of advanced instrumental techniques. The mass spectrum of the product **12b** showed the deuterium content of the sample to be 2% d_0, 90% d_1, and 8% d_2. A heteronuclear correlation experiment on undeuterated sample **12a** established the C4-exo-H at 1.62 ppm and the C4-endo-H at 1.38 ppm. For the deuterated sample a ^{2}H NMR spectrum exhibited a signal for the C4-exo-D at 1.62 ppm and a heteronuclear correlation experiment exhibited a triplet in the carbon dimension exhibiting connectivity with a proton at 1.38 in the proton dimension. The splitting results from coupling of C4 to the exo deuterium. Furthermore, irradiation of H8s at 1.84 ppm caused no enhancement of the signal of the 4-endo-H at 1.38 ppm, further confirming the configuration of deuterium at C4 as exo.

The partition of the reaction of **2** to give a greater yield of **12b** compared with **11b** is either a result of protonation at C2 being more favored than protonation at C3 or alternatively that the C2-protonated species is more rapidly trapped than the C3-protonated species. Failure to observe deuterium at C6 or formation of the *endo*-methoxy isomer of **12** from the reaction with D^+ methanol is consistent with nucleophilic attack on the C2-protonated species occurring before the cation has relaxed to allow conformational change and overlap of the developing cation center with the C1–C8 σ bond. The presence of deuterium in the methyl of **11b** was established from the ^{13}C NMR spectrum, which showed the methyl carbon as a 1:1:1 triplet.

Methoxymercuration of 2. Reaction of the hydrocarbon **2** with mercuric acetate in water followed by reduction of the intermediate hydroxy acetoxymercurio adducts has been reported[22] to give a 1:9 mixture of **15a** and **16a**, both products resulting from external bond rupture involving mercury attack at C3. The stereochemistry of



(15) a E = H
b E = D
c E = HgOAc

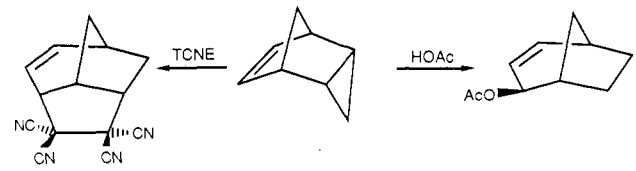


(16) a E = H
b E = D
c E = HgOAc

the alcohol in **15a** was, however, undetermined. Oxidation of a mixture of **15a** and **16a** gave a similar mixture of the corresponding ketones 3-*exo*-methyl- and 7-*syn*-methylbicyclo[2.2.1]heptan-2-ones. When the reaction of **2** with mercuric acetate was repeated, but in methanol as solvent, **11c** and **12c** were formed in approximately equal amounts. The mercuric compounds could not be separated and therefore were reduced to give the corresponding methoxy hydrocarbons **11a** and **12a** in 48% and 43% yields, respectively. These two products were separated by preparative GLC and shown to be identical in all respects with the products obtained from reaction of the hydrocarbon with methanol in the presence of *p*-toluenesulfonic acid. The observation of mercuric ion cleavage of the most substituted cyclopropane bond in the formation of **12c** is in direct conflict with previously stated rules for mercuric ion induced cyclopropane ring opening.[18]

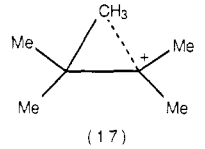
(22) Reutov, O. A.; Rodina, N. B.; Sokolov, V. I. *J. Organomet. Chem.* **1969**, *17*, 477.

Scheme VII

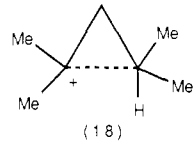


The mixture of mercuric salts from reaction of the exo hydrocarbon **2** with mercuric acetate in methanol was reduced with sodium amalgam in sodium deuteroxide. For the product **11b** the presence of deuterium in the methyl syn to the methoxy group was established from the ^{13}C NMR spectrum, which showed the methyl carbon as a 1:1:1 triplet centered at 12.7 ppm. Notably a 6,2-hydride shift does not compete with the capture of the intermediate cation by methanol for this reaction or for reaction with a proton. This is consistent with delocalization from the C3-mercurated species to C1 and blocking C2 from exo face attack as shown in Scheme VI. The ^{2}H NMR spectrum of 2-*exo*-methoxy-4-*exo*-deuteriobicyclo[3.2.1]octane showed a signal at 1.62 ppm and the product was identical in all respects with that obtained from the reaction with acidic methanol-*d*, thereby establishing that the mercury attacked the cyclopropyl ring with inversion.

Regioselectivity and Stereochemistry of Reactions of 1 and 2. The regioselective cleavage of the C2–C4 bond of hydrocarbon **1** with acid and with mercuric ions in the formation of **3** and **4** (Scheme IV) reflects either (i) that an energy difference of the cations is such that there is a preference for protonation and mercuration at C2 (or C4) as compared with C3 or (ii) that the bond rupture of the C2 (or C4) protonated (mercurated) hydrocarbon is faster than bond rupture of the C3 protonated (mercurated) hydrocarbon. The reaction parallels that of *endo*-tricyclo[3.2.1.0^{2,4}]oct-6-ene with acetic acid[23] and with tetracyanoethene[24] (Scheme VII). In both reactions it is the more substituted bond that is cleaved. This compares with similar reaction of the exo hydrocarbon **2** where external bond cleavage successfully competes with rupture of the internal cyclopropyl bond (Scheme VI). This latter situation finds a parallel in the reaction of 1,1,2,2-tetramethylcyclopropane with acetic acid,[1b] which gives products that result from cleavage of the most substituted bond along with products from rupture of the adjacent bond. Wiberg[1b] has calculated that for the reaction of the tetramethylcyclopropane with a proton there is not a strong preference for which bond is cleaved. He argues that the comparability in calculated energy of cations **17** and **18**,



(17)



(18)

which are presumed to lie along the reaction coordinate, rationalizes the observation that the electrophile does not have a strong preference for which bond is cleaved. Nevertheless these reactions always proceed so that the nucleophile or its equivalent, whether an intermolecular species such as an acetate ion, or intramolecular nucleophile such as a migrating group (H, Me) or an adjacent bond becomes associated with the more substituted cat-

(23) Battiste, M. A.; Coxon, J. M.; Edelman, R. *Tetrahedron Lett.* **1972**, 4577.
(24) Battiste, M. A.; Coxon, J. M.; Posey, R. G.; King, R. W.; Mathew, M.; Palenik, G. J. *J. Am. Chem. Soc.* **1975**, *97*, 945.

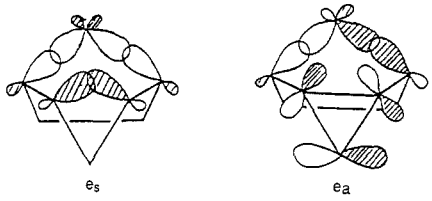


Figure 2. Mixing of the C1, C8/C5, C8 σ orbitals with the cyclopropane orbitals.

ionic center. While the reactions proceed toward the most stable carbocation, at the product-forming activated complex the structure is considered not to have relaxed to a large extent since relief of steric strain does not correlate with reaction rate.[1b] The products are considered to be formed by capture of the protonated cyclopropane before it has become an open carbocation, thereby resulting in stereoselective capture by nucleophile or stereoselective hydrogen migration or loss. A notable feature of the reactions of the endo hydrocarbon 1 is that the attack by an external nucleophile is always observed to occur with inversion of configuration.

Polarization of the cyclopropane ring by an attacking electrophile has been found to be influenced by the low-lying σ orbitals present in the molecule.[1b] For the endo hydrocarbon 1 external bond cleavage does not compete with cleavage of the internal bond. Overlap of the C2–C4 bond with the C1–C8 and C5–C8 bonds will raise the energy of the cyclopropane HOMO's with a C2–C4 component and thereby reduce the energy difference between these orbitals and the LUMO hydrogen 1s orbital favoring cleavage of this more substituted bond. It is noteworthy that for the exo isomer overlap of the C2–C4 bond with the C1–C8 and C5–C8 bonds is not possible and the adjacent external bond cleaves in competition with the internal bond.

Mixing of the Walsh 3e′(S) and 3e′(A) orbitals of *endo*-tricyclo[3.2.1.$0^{2,4}$]octane (1) with the low-lying C1–C8/C5–C8 orbitals gives rise to the e_s and e_a molecular orbitals shown in Figure 2. From photoelectron spectroscopy, the e_s orbital can be assigned as the HOMO at −9.40 eV, the e_a orbital at −10.20 eV.[25] Attack at the e_s orbital of necessity results in C2–C4 bond cleavage, and attack could occur with either retention or inversion. For edge attack, while there is a favorable interaction with the cyclopropyl 3e′(S) component of e_s, an unfavorable secondary orbital interaction with the C1–C8/C5–C8 orbitals disfavors such attack. This edge attack is also disfavored by the unfavorable interaction of the proton 1s orbital with the e_a orbital. For attack at the corner no large antibonding interaction is present, and hence this pathway is favored. As interaction of orbitals of similar energy produces the greatest orbital energy stabilization gain influencing transition-state energy, overlap of the electrophile LUMO with the energetically lower e_a molecular orbital, which could give external bond cleavage, is not as important as overlap with the e_s HOMO, and therefore cleavage of an external cyclopropyl bond is not observed.

For hydrocarbon 2, mixing of the Walsh 3e′(S) and 3e′(A) orbitals with the C1–C7/C5–C6 orbitals of the correct symmetry gives rise to the HOMO e_s and the e_a orbitals shown in Figure 3. The separation between the e_s and e_a orbitals for 2 is not as large as for 1.[25] For attack at the e_s orbital, corner attack is more favored since edge

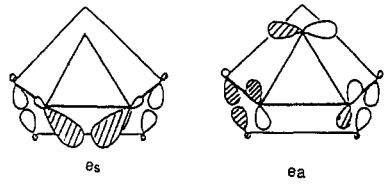


Figure 3. Mixing of the 3e′(S) and 3e′(A) orbitals with the C1, C7/C5, and C6 σ orbitals to give the e_s HOMO and the e_a molecular orbital.

attack at C2–C4 is disfavored by an unfavorable secondary orbital interaction with the C1–C7/C5–C6 orbitals. External cyclopropyl bond cleavage attack at the e_a orbital could result in either retention or inversion; however, determination of the stereochemistry of electrophile attack was not possible due to the presence of the prochiral C8 methylene in product 11. For proton attack at hydrocarbon 2, the preference for corner attack at the e_s HOMO reflects the favorable stabilization to the transition state from this HOMO/LUMO interaction. However since the energy gap between e_s and e_a is not large, and delocalization stabilizes cation **13a** produced from attack at the e_a orbital, this pathway is competitive. For attack by mercuric acetate on 2, any steric hindrance to corner attack at the e_s orbital is offset by the gains in the favorable e_s HOMO/mercury 6s LUMO interaction. Attack by mercuric acetate at the e_a orbital is, however, more competitive than proton attack at 2.[26]

The stereochemistry observed for proton and mercuric ion attack at C2(C4) of both the exo and endo hydrocarbons 1 and 2 parallels that found for attack of bromine on *trans*-1,1,2,3-tetradeuteriocyclopropane where the formation of *erythro* product excludes the intermediacy of a symmetrical corner-brominated cyclopropane intermediate[1c,d] and dictates that the reaction pathway is unsymmetric. Lambert[1c] has interpreted the reaction to require a corner-brominated cyclopropane, which by definition is symmetrical. For this to be the case rotation of the pentacoordinated carbon would have to be slow with respect to the rate of nucleophilic attack. Furthermore, the initial configuration of the bromine atom in the species would have to dictate which of the adjacent carbon sites is attacked by nucleophile. The favored attack by the electrophiles deuteron and mercuric ion and bromine at the corner of the cyclopropane ring with inversion reflects in general the favorable interaction of both the degenerate HOMO's of the cyclopropane with the hydrogen 1s or LUMO 6s of the mercuric ion or the 4p orbital of bromine respectively (Figure 4). For edge attack the HOMO/LUMO interaction with the symmetric Walsh orbital is favorable for proton, mercuric ion, or bromine, but this is not the case with the unsymmetric orbital.

A favorable interaction of the LUMO Walsh orbital of cyclopropane with the d orbitals of electron-donor metals allows oxidative addition[27] at the edge of the cyclopropane. This interaction compensates for the more favored σ interaction at the corner of cyclopropane between the HOMO Walsh orbitals and the LUMO orbitals of the electrophile. The low promotion energy generally observed for electron donation from the *n*d orbital to the $(n + 1)$p

(25) (a) Bischof, P.; Heilbronner, E.; Prinzbach, H.; Martin, H. D. *Helv. Chim. Acta* **1971**, *54*, 1072. (b) Jonkers, G.; Van der Meer, W. J.; DeLange, C. A.; Baerends, E. J.; Stapersma, J.; Klumpp, G. W. *J. Am. Chem. Soc.* **1984**, *106*, 587.

(26) Exclusive external cyclopropane ring cleavage has been reported[14] for reaction of hydrocarbon 2 with mercuric acetate in water. The cationic nature of **14c** is low with the positive charge residing at mercury. Cation **13c**, from which rearrangement occurs, is therefore expected to be more sensitive to stabilization by a more polar solvent.

(27) (a) Campbell, W. H.; Jennings, P. W. *Organometallics* **1983**, 2, 1460. (b) Waddington, M. D.; Campbell, J. A.; Jennings, P. W.; Campana, C. F.; *Organometallics* **1983**, *10*, 1269. (c) Wiberg, K. B.; McClusky, J. V.; Schulte, G. K. *Tetrahedron Lett.* **1986**, *27*, 3083.

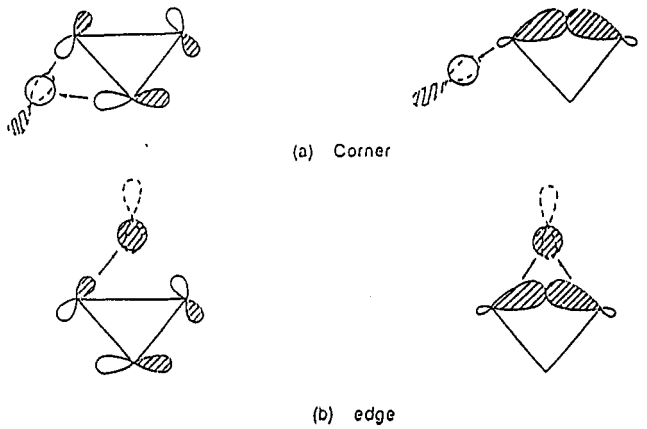


Figure 4. σ interaction of LUMO of electrophile with degenerate HOMO's of cyclopropane.

orbital[5i] indicates that these orbitals are energetically similar. It is therefore valid to consider interaction between the cyclopropyl 3e' HOMO and the metal $(n + 1)$p LUMO orbitals. For mercury the donor ability[28] of the d_π orbitals is small and thus the d_π HOMO–cyclopropane LUMO interaction is unimportant and the reaction stereochemistry parallels the reaction with deuteron.

Conclusion

The general preference for corner attack[1f] at cyclopropane by protons and mercuric ions reflects the favorable interaction for both degenerate HOMO orbitals of the cyclopropane with the LUMO of the electrophile. For the molecules **1** and **2** where the 3e'(S) and 3e'(A) Walsh orbitals are no longer degenerate (see Figures 2 and 3), the reactions with electrophiles are most influenced by the HOMO, since this interaction will give the greatest energy gain upon interaction with the LUMO of the electrophile. The next lower occupied molecular orbital, in the absence of any antibonding interactions, becomes important as the energy difference between this orbital and the HOMO decreases.

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) instrument. All ^{2}H NMR spectra were run unlocked with broadband proton decoupling, an acquisition time of 4 s and using 2 drops of $CDCl_3$ (7.27 ppm) as an internal reference. Heteronuclear proton–carbon correlation spectra were obtained by 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 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 instrument 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. Radial chromatography was performed on a Chromatatron (Harrison and Harrison) using Merck type 60 PF_{254} silica gel.

***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 *endo*-tricyclo[3.2.1.0^{2,4}]oct-6-ene[6] (1 g) in pentane (20 mL). The mixture was stirred vigorously in a hydrogen atmosphere until 1 mol of hydrogen had been adsorbed. The mixture was filtered and the solvent removed by distillation through a Vigreux column. The residual liquid was left in an open flask for a few hours to remove the remaining traces of pentane to give *endo*-tricyclo[3.2.1.0^{2,4}]octane (0.90 g, 90%) as a low melting glass, mp 71–72 °C: ^{1}H NMR δ_H ($CDCl_3$) 2.21 (s, $W_{h/2}$ = 7 Hz, H1, H5), 1.88 (m, $^2J_{8s,8a}$ = 8.3 Hz, $^3J_{8s,1} = {}^3J_{8s,5} = {}^3J_{8s,6endo} = {}^3J_{8s,7endo}$ = 2.1 Hz, H8s), 1.44 (dd, $^2J_{8a,8s}$ = 8.3 Hz, $^5J_{8a,3exo}$ = 2.4 Hz, H8a), 1.36–1.30 (m, H2, H4, H6exo, H7exo), 1.01 (dd, $^2J_{6endo,6exo}$ = 7.3 Hz, $^3J_{6endo,7exo}$ = 2.3 Hz, H6endo, H7endo), 0.88 (dt, $^2J_{3endo,3exo}$ = 5.9 Hz, $^3J_{3endo,2} = {}^3J_{3endo,4}$ = 2.4 Hz, H3endo), 0.72 (m), $^2J_{3exo,3endo}$ = 5.9 Hz, $^3J_{3exo,2} = {}^3J_{3exo,4}$ = 7.4 Hz, $^5J_{3exo,8a}$ = 2.3 Hz, H3exo); ^{13}C NMR, see ref 29.

***exo*-Tricyclo[3.2.1.0^{2,4}]octane (2).** *exo*-Tricyclo[3.2.1.0^{2,4}]-octane was prepared from norbornene by addition of methylene carbene generated by using a zinc/copper couple:[7] ^{1}H NMR δ_H ($CDCl_3$) 2.21 (s, $W_{h/2}$ = 5.1 Hz, H1, H5), 1.43 ($W_{h/2}$ = 18 Hz, H6exo, H7exo), 1.24 ($W_{h/2}$ = 13 Hz, H6endo, H7endo), 0.92 (dt, $^2J_{8s,8a}$ = 10.4 Hz, $^4J_{8s,6endo} = {}^4J_{8s,7endo}$ = 2.1 Hz, H8s), 0.66 (dd, $^3J_{2/4,3endo}$ = 7.3 Hz, $^3J_{2/4,3exo}$ = 3.2 Hz, H2, H4), 0.57 (d, $^2J_{8a,8s}$ = 10.4 Hz, H8a), 0.28 (dt, $^2J_{3exo,3endo}$ = 6.0 Hz, $^3J_{3exo,2} = {}^3J_{3exo,4}$ = 3.1 Hz, H3exo), –0.11 (m, $^2J_{3endo,3exo}$ = 6.1 Hz, $^3J_{3endo,2} = {}^3J_{3endo,4}$ = 7.0 Hz, H3endo); partial ^{1}H NMR, see ref 30; ^{13}C NMR, see ref 29.

Reaction of 1 with *p*-Toluenesulfonic Acid/Methanol. *endo*-Tricyclo[3.2.1.0^{2,4}]octane (120 mg), anhydrous methanol (3 mL), and *p*-toluenesulfonic acid monohydrate (8 mg) were placed in an ampule (5 mL) and kept at 80 °C for 7 days. The mixture was diluted with water (5 mL) and the product extracted into pentane. The pentane extracts were washed with aqueous sodium carbonate solution and dried over $MgSO_4$, and the solvent was removed under reduced pressure to give an oil (130 mg, 81%) shown by GLC analysis to be at least 95% pure and shown to be 2-*endo*-methoxybicyclo[3.2.1]octane (**3a**): ^{1}H NMR δ_H ($CDCl_3$) 3.30 (s, OMe), 3.18 ($^3J_{2exo,3endo}$ = 10.1 Hz, $^3J_{2exo,3exo}$ = 5.7 Hz, $^3J_{2exo,1}$ = 3.0 Hz, H2exo), 2.36 ($^3J_{1,2exo}$ = 3.0 Hz, $^3J_{1,7exo}$ = 6.0 Hz, $^3J_{1,8a}$ = 6.0 Hz, H1), 2.12 (s, $W_{h/2}$ = 7 Hz, H5), 1.9–1.2 (m, 10 H's). The following assignments were obtained from a heteronuclear correlation experiment: 1.82, H3exo; 1.73, H7exo; 1.65, H6exo; 1.59, H8a; 1.50, H7endo; 1.41, H4endo; 1.34, H6endo; 1.33, H4exo; 1.28, H8s; 1.23, H3endo. ^{13}C NMR: δ_C ($CDCl_3$) 81.9 (C2), 55.7 (OMe), 38.6 (C1), 37.5 (C8), 34.4 (C5), 31.0 (C4), 28.8 (C6), 25.7 (C3), 23.9 (C7).

Preparation of 2-*endo*-Methoxybicyclo[3.2.1]octane and the Deuterated Analogue (10b). A solution of 3-bromobicyclo[3.2.1]oct-3-en-2-*exo*-ol (**8**)[11] (4 g) in tetrahydrofuran (30 mL) with aqueous sodium hydroxide (30 mL, 1 M) was shaken with prehydrogenated palladium on carbon (2.4 g, 10%) under hydrogen at 1.5 atm. After the addition of hydrogen was complete, the mixture was diluted with water and saturated with NaCl, and the product was extracted with ether. The solvent was removed by distillation and the crude product steam distilled to give bicyclo[3.2.1]octan-2-*exo*-ol[11] (1.88 g, 75%) as a white solid: ^{1}H NMR δ_H ($CDCl_3$) 3.73 (s, $W_{h/2}$ = 8 Hz, H2), 2.21 (H1), 2.16 (H5), 1.92 (d, $^2J_{8s,8a}$ = 10.0 Hz, H8s), 1.75 (s, $W_{h/2}$ = 3 Hz, OH), 1.69 (m, H4exo, H6exo, H7exo, H3exo), ca. 1.5 (H7endo), 1.39 (m, H6endo, H3endo), 1.26 (m, H4endo), 1.19 (m, H8a). The position of H4exo was obtained by an NOE experiment using the alcohol-OD. ^{13}C NMR: δ_C ($CDCl_3$) (revised from ref 9) 71.3 (C2), 41.6 (C1), 34.3 (C5), 32.1 (C8), 28.3 (C4), 26.8 (C7), 26.7 (C6), 26.4 (C3).

The reaction of 3-bromobicyclo[3.2.1]oct-3-en-2-*exo*-ol (**4g**) was repeated by using deuterium, NaOD, and D_2O to give 3,3,4-*exo*-trideuteriobicyclo[3.2.1]octan-2-*exo*-ol (**7**) (1.6 g, 63%): ^{2}H NMR δ_D ($CHCl_3$) 1.64 (2 D, D3exo, D4exo), 1.38 (1 D, D3exo), 1.25 (0.34 D, D4endo); ^{13}C NMR δ_C ($CDCl_3$) 71.2 (L.B., C2), 41.5 (C1), 34.1 (L.B., C5), 32.0 (C8), 27.6 (t, $J_{^{13}C,^2H}$ = 18.7 Hz, C4), 26.7 (C7), 26.6 (L.B., C6), 25.8 (m, C3) (L.B. indicates the presence of a small ^{13}C–^{2}H coupling[31]).

Bicyclo[3.2.1]octan-2-*exo*-ol (1.54 g) was oxidized by chromium trioxide in acetic acid to give bicyclo[3.2.1]octan-2-one (1.2 g, 79%) as a white solid: ^{1}H NMR δ_H ($CDCl_3$) 2.69 (t, $^3J_{1,7exo} = {}^3J_{1,8a}$ =

(28) Nyholm, R. S. *Proc. Chem. Soc.* **1961**, 273.

(29) (a) Cheng, A. K.; Stothers, J. B. *Org. Magn. Reson.* **1977**, *9*, 355. (b) Bicker, R.; Zimmermann, G.; Kessler, H. *Chem. Ber.* **1978**, *111*, 3200.

(30) (a) Freeman, P. K.; Hutchinson, L. L.; Blazevich, J. N. *J. Org. Chem.* **1974**, *39*, 3606. (b) Freeman, P. K.; Hutchinson, L. L. *J. Org. Chem.* **1980**, *45*, 3191. H3exo and H3endo reassigned.

(31) A similar line broadening (i.e., a small $J_{^{13}C,^2H}$) is observed in the 4-deuteriobicyclo[3.2.1]octan-2-one system. Patel, V.; Ragauskas, A. J.; Stothers, J. B. *Can. J. Chem.* **1986**, *64*, 1440.

4.6 Hz, H1), 2.44 (m, H5), 2.37 (m, H3exo), 2.19 (q, $^2J_{3endo,3exo}$ = 16.0 Hz, $^3J_{3endo,4endo}$ = 7.0 Hz, H3endo), ca. 2.0 (H6exo), ca. 1.8 (H4endo, H4exo, H7exo, H7endo), ca. 1.7 (H6endo); ^{13}C NMR, see ref 9.

3,3,4-*exo*-Trideuteriobicyclo[3.2.1]octan-2-one (**9**) was prepared as above but by oxidation with chromium trioxide in deuterioacetic acid: ^{13}C NMR δ_C ($CDCl_3$) 210.9 (C2), 51.1 (C1), 38.2 (C8), 33.8 (L.B., C5), 31.6 (t, $J_{^{13}C,^2H}$ = 19.4 Hz, C4), 28.0 (C7), 27.9 (L.B., C6); ^2H NMR δ_D ($CHCl_3$) 2.33 (0.92 D, D3exo), 2.16 (0.88 D, D3endo), 1.77 (0.28 D, D4endo), 1.69 (0.73 D, D4exo); mass spectrum shows 3% D_0, 5% D_1, 22% D_2, 61% D_3, 6% D_4, 1% D_5, 0.6% D_6.

To 3,3,4-*exo*-trideuteriobicyclo[3.2.1]octan-2-one (**9**) (100 mg) in anhydrous ether (10 mL) was added with stirring $LiAlH_4$ (140 mg). After stirring for 3 h, the excess $LiAlH_4$ was destroyed by the careful addition of sodium sulfate decahydrate crystals. Water (10 mL) was added and the aqueous layer extracted with ether. The combined ether extracts were washed with a brine solution and dried over Na_2SO_4. Removal of the solvent at reduced pressure gave a mixture (4:1; 82 mg, 81%) of 3,3,4-*exo*-trideuteriobicyclo[3.2.1]octan-2-*endo*-ol (**10a**) [^{13}C NMR δ_C ($CDCl_3$) 72.4 (C2), 42.5 (C1), 37.1 (C8), 33.4 (C5), 30.0 (t, $J_{^{13}C,^2H}$ = 20.0 Hz, C4), 28.4 (C6), 23.2 (C7, C3, not obsd); ^2H NMR δ_D ($CHCl_3$) 1.74 (0.85 D), 1.67 (0.3 D, D4endo), 1.35 (0.90 D), 1.24 (0.75 D)] and 3,3,4-*exo*-trideuteriobicyclo[3.2.1]octan-2-*exo*-ol.

3,3,4-*exo*-Trideuteriobicyclo[3.2.1]octan-2-*endo*-ol (**10a**) (94 mg) in dry benzene (5 mL) was added dropwise with vigorous stirring to sodium amide (200 mg) in dry benzene (5 mL). The mixture was heated under reflux for 16 h and the benzene removed by draining the water out of the condenser. Methyl iodide (3.4 g, 1.5 mL) in anhydrous ether (5 mL) was added and the mixture heated under reflux for 8 h. Water (10 mL) was carefully added and the ether layer separated. The aqueous layer was extracted with ether, and the combined ether extracts were washed with a brine solution and dried over $MgSO_4$. Removal of the solvent at reduced pressure gave 2-*endo*-methoxy-3,3,4-*exo*-trideuteriobicyclo[3.2.1]octane (**10b**) (48 mg, 47%) as a pale yellow oil: ^1H NMR δ_H ($CDCl_3$) 3.30 (OMe), 3.16 ($W_{h/2}$ = 6 Hz, H2), 2.35 ($^4J_{1,5}$ = 2.1 Hz, $^3J_{1,8a}$ = 6.1 Hz, $^3J_{1,7exo}$ = 6.1 Hz, H1); 2.10 (s), $W_{h/2}$ = 15.8 Hz, H5), 1.85–1.20 (m, 7.2 H); ^{13}C NMR δ_C ($CDCl_3$) 81.8 (C2), 55.6 (OMe), 38.5 (C1), 37.4 (C8), 34.3 (C5), 30.4 (t, $J_{^{13}C,^2H}$ = 19.1 Hz, C4), 28.8 (C6), 23.9 (C7, C3, not observed); ^2H NMR δ_D ($CHCl_3$) 1.78 (0.90 D, D3exo), 1.42 (0.25 D, D4endo), 1.33 (0.71 D, D4exo), 1.23 (0.90 D, D3endo).

Reaction of 1 with Mercuric Acetate. To a solution of *endo*-tricyclo[3.2.1.$0^{2,4}$]octane (100 mg) in anhydrous methanol (4 mL) was added, with stirring, mercuric acetate (300 mg), and the mixture was stirred for 3 h. The mixture was filtered to remove unreacted mercuric acetate, the solvent removed under reduced pressure, and the organomercurial placed under high vacuum for 12 h to remove acetic acid. The residue, a pale green viscous oil, was identified as 4-*endo*-(acetoxymercurio)-2-*endo*-methoxybicyclo[3.2.1]octane (**3c**) (275 mg, 95%): ^1H NMR δ_H ($CDCl_3$) 3.40 (s, OMe), 3.18 (m, $^3J_{2exo,1}$ = 2.6 Hz, $^3J_{2exo,3exo}$ = 5.4 Hz, $^3J_{2exo,3endo}$ = 9.8 Hz, H2exo), 2.75 (qt, $^3J_{4exo,3endo}$ = 13.6 Hz, $^3J_{4exo,3exo}$ = 4.7 Hz, $^3J_{4exo,5}$ = 1.7 Hz, $^4J_{4exo,6exo}$ = 1.6 Hz, $J_{^{199}Hg,H4}$ = 192 Hz, H4), 2.50 (t, $^3J_{5,6exo}$ = $^3J_{5,8a}$ = 6.0 Hz, H5), 2.33 (s, $W_{h/2}$ = 11.9 Hz, H1), 2.25 (m, H6exo), 2.00 (s, OAc), 1.9–1.75 (m, H7exo, H3exo, H6endo), 1.68 (m, $^2J_{8s,8a}$ = 12.0 Hz, $^3J_{8a,1}$ = $^3J_{8a,5}$ = 5.0 Hz, H8a), 1.55 (m, H3endo, H7endo), 1.38 (d, $^2J_{8a,8s}$ = 12.0 Hz, H8s); ^{13}C NMR δ_C (CD_3OD) 178.4 (OAc), 82.5 ($J_{^{199}Hg,^{13}C}$ = 310 Hz, C2), 55.7 (OMe), 50.3 ($J_{^{199}Hg,^{13}C}$ = 1634 Hz, C4), 40.8 ($J_{^{199}Hg,^{13}C}$ = 66 Hz, C5), 39.3 ($J_{^{199}Hg,^{13}C}$ = 25 Hz, C1), 38.8 ($J_{^{199}Hg,^{13}C}$ = 310 Hz, C8), 32.7 ($J_{^{199}Hg,^{13}C}$ = 65 Hz, C6), 31.2 ($J_{^{199}Hg,^{13}C}$ = 97 Hz, C3), 23.8 ($J_{^{199}Hg,^{13}C}$ not obs, C7), 22.9 (OAc). Note: The $^{199}Hg,^{13}C$ coupling constants are the averages obtained from three separate spectra.

Reaction of 1 with Methanol-*d*/*p*-Toluenesulfonic Acid. The reaction of *endo*-tricyclo[3.2.1.$0^{2,4}$]octane (120 mg) with methanol-*d* was carried out as previously described for the reaction with methanol. The product was isolated after 7 days to give 4-*endo*- and 6-*endo*-deuterio-2-*endo*-methoxybicyclo[3.2.1]octane (**3b** and **4b**) (120 mg, 79%) in the ratio of 62:38 (±4%), respectively: mass spectrum 15% D_0, 84% D_1, 1% D_2; $C_9H_{15}OD$ requires $M^{+\cdot}$ 141.1264, found $M^{+\cdot}$ 141.1269; ^2H NMR δ_D ($CHCl_3$) 1.41 (D4endo), 1.34 (D6endo). 4-*endo*-Deuterio-2-*endo*-methoxybicyclo[3.2.1]octane (**3b**): ^{13}C NMR δ_C ($CDCl_3$) 81.6 (C2), 55.4 (OMe), 38.4 (C1), 37.2 (C8), 34.1 (C5), 30.3 (t, $J_{^{13}C,^2H}$ = 20.4 Hz, C4), 28.5 (C6), 25.3 (C3), 23.6 (C7). 6-*endo*-Deuterio-2-*endo*-methoxybicyclo[3.2.1]octane (**4b**): ^{13}C NMR δ_C ($CDCl_3$) 81.6 (C2); 55.4 (OMe), 38.4 (C1), 37.2 (C8), 34.1 (C5), 30.7 (C4), 28.2 (t, $J_{^{13}C,^2H}$ = 19.9 Hz, C6), 25.4 (C3), 23.5 (C7).

Reduction of the Organomercurial 3c with (a) Sodium Borohydride. To the crude 4-*endo*-(acetoxymercurio)-2-*endo*-methoxybicyclo[3.2.1]octane (275 mg) in methanol (4 mL) was added with stirring aqueous NaOH (5 mL, 1 M), followed by a solution of NaOH (5 mL, 1 M) and sodium borohydride (80 mg). After 30 min the mixture was extracted with pentane, washed with water, and dried over $MgSO_4$. The solvent was removed under reduced pressure to give 2-*endo*-methoxybicyclo[3.2.1]octane (**3a**) (68 mg, 66%), identical with a sample obtained by the reaction of *endo*-tricyclo[3.2.1.$0^{2,4}$]octane with toluenesulfonic acid in methanol.

(b) With Sodium Borodeuteride. To the crude 4-*endo*-(acetoxymercurio)-2-*endo*-methoxybicyclo[3.2.1]octane (**3c**) (100 mg) dissolved in methanol (1 mL) was added with stirring aqueous NaOH (1 mL, 1 M) and sodium borodeuteride (20 mg). After 30 min of stirring, the liquid was extracted with pentane, washed with water, and dried over $MgSO_4$. The solvent was removed under reduced pressure to give a mixture (45:55; 25 mg, 65%) shown to be 4-*exo*- and 4-*endo*-deuterio-2-*endo*-methoxybicyclo[3.2.1]octane, respectively. ^2H NMR δ_D ($CHCl_3$) 1.40 (D4endo), 1.33 (D4exo). Mass spectrum shows 6% D_0, 94% D_1.

(c) 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 **3c** (100 mg). The mixture was stirred for 3 h and water (4 mL) was added. The mixture was extracted with pentane, the combined extracts were dried over $MgSO_4$, and the solvent was removed under reduced pressure to give 4-*endo*-deuterio-2-*endo*-methoxybicyclo[3.2.1]-octane (**3b**) (23 mg, 64%) as an oil: ^2H NMR δ_D ($CHCl_3$) 1.39 (D4endo); ^{13}C NMR δ_C ($CDCl_3$) 81.6 (C2), 55.4 (OMe), 38.4 (C1), 37.2 (C8), 34.1 (C5), 30.3 (t, C4, $J_{^{13}C,^2H}$ = 20.4 Hz), 28.5 (C6), 25.3 (C3), 23.6 (C7); mass spectrum 6% D_0, 94% D_1.

Reaction of 2 with *p*-Toluenesulfonic Acid/Methanol at 80 °C. Reaction of *exo*-tricyclo[3.2.1.$0^{2,4}$]octane (150 mg) with methanol and *p*-toluenesulfonic acid was carried out as previously described for the reaction with *endo*-tricyclo[3.2.1.$0^{2,4}$]octane. The product was isolated after 7 days to give an oil (174 mg, 89%), shown by GLC to contain three compounds (15%, 9%, 76%). Separation of the two major products was achieved by preparative GLC. The minor product was not obtained pure and was not identified. The major product was 2-*exo*-methoxybicyclo-[3.2.1]octane (**12a**) (76%): ^1H NMR δ_H ($CDCl_3$) 3.30 (s, OMe), 3.18 ($W_{h/2}$ = 8 Hz, H2endo), 2.38 (s, $W_{h/2}$ = 9.5 Hz, H1), 2.14 ($W_{h/2}$ = 10.4 Hz, H5), 1.84 (d, $^2J_{8s,8a}$ = 10.9 Hz, H8s), 1.7–1.5 (m, H4exo, H6exo, H7exo, H7endo), 1.55–1.42 (m, H3exo, H3endo, H6endo), 1.38 (m, H4endo), 1.16 (m, H8a); ^{13}C NMR δ_C ($CDCl_3$) 80.2 (C2), 55.8 (OMe), 37.9 (C1), 34.2 (C5), 32.2 (C8), 28.7 (C4), 27.3 (C7), 26.6 (C6), 23.1 (C3). 7-*syn*-Methyl-2-*exo*-methoxybicyclo-[2.2.1]heptane (**11a**) (15%): ^1H NMR δ_H ($CDCl_3$) 3.28 (m, $^3J_{2endo,3endo}$ = 7.5 Hz, $^3J_{2endo,3exo}$ = 3.2 Hz, H2endo), 3.26 (s, OMe), 2.10 (br d, $^3J_{1,6exo}$ = 3.1 Hz, H1), 1.95 (t, $^3J_{4,5exo}$ = $^3J_{4,3exo}$ = 3.0 Hz, H4), 1.8–1.65 (H3exo, H3endo), 1.65 (m, H7anti), 1.55–1.45 (H5exo, H6exo), 1.09–1.05 (H5endo, H6endo), 1.05 (d, $^3J_{CH_3,7anti}$ = 7.2 Hz, CH_3); ^{13}C NMR δ_H ($CDCl_3$) 85.6 (C2), 56.0 (OMe), 43.6 (C1, C7), 40.3 (C4), 36.9 (C3), 28.9 (C5), 26.4 (C6), 12.8 (CH_3).

An authentic sample of 2-*exo*-methoxybicyclo[3.2.1]octane was prepared from bicyclo[3.2.1]octan-2-*exo*-ol (172 mg) by methylation with sodium amide/methyl iodide to give a yellow oil (124 mg, 65%) consisting of 2-*exo*-methoxybicyclo[3.2.1]octane (**12a**) (ca. 56%), 2-*endo*-methoxybicyclo[3.2.1]octane (ca. 26%), and unreacted starting material. The ^1H and ^{13}C NMR data are identical with those obtained above.

Reaction of 2 with Mercuric Acetate in Methanol and Subsequent Reduction. To a solution of *exo*-tricyclo-[3.2.1.$0^{2,4}$]octane (**2**) (150 mg) in anhydrous methanol (4.5 mL) was added mercuric acetate (580 mg), and the mixture was stirred for 48 h. The mixture was filtered and the solvent removed under

reduced pressure. To the crude mixture was added sodium amalgam (8 g, 1.5% Na/Hg) with NaOD/D_2O (5 mL, 1 M), and the reaction was stirred for 3 h. The mixture was diluted with water, the mercury decanted off, and the product extracted into pentane. The combined pentane extracts were dried over $MgSO_4$ and filtered and the solvent removed under reduced pressure to yield an oil (142 mg, 73%) shown to be a mixture of 7-*syn*-(deuteriomethyl)-2-*exo*-methoxybicyclo[2.2.1]heptane (**11b**) (43%) and 4-*exo*-deuterio-2-*exo*-methoxybicyclo[3.2.1]octane (**12b**) (48%). Separation was effected by preparative GLC. 4-*exo*-Deuterio-2-*exo*-methoxybicyclo[3.2.1]octane (**12b**): ^{1}H NMR δ_H ($CDCl_3$) 3.30 (s, OMe), 3.18 ($W_{h/2}$ = 6 Hz, H2endo), 2.38 (s, $W_{h/2}$ = 9.6 Hz, H1), 2.14 (s, $W_{h/2}$ = 16.2 Hz, H5), 1.84 (d, $^2J_{8s,8a}$ = 10.9 Hz, H8s), 1.65 (m, H6exo, H7exo, H7endo), 1.55–1.42 (H3exo, H3endo, H6endo), 1.38 (d, $^3J_{4endo,3endo}$ = 9.1 Hz, H4endo), 1.16 (m, $^3J_{8a,5}$ = $^3J_{8a,1}$ = 5.7 Hz, H8a); ^{2}H NMR δ_D ($CHCl_3$) 1.62 (D4exo); ^{13}C NMR δ_C ($CDCl_3$) 80.4 (C2), 55.8 (OMe), 38.0 (C1), 34.2 (C5), 32.3 (C8), 28.5 (t, $J_{^{13}C,^2H}$ = 18.9 Hz, C4), 27.3 (C7), 26.8 (C6); MS, $C_9H_{15}OD$ requires $M^{+\cdot}$ 141.1264, found $M^{+\cdot}$ 141.1264.

7-*syn*-(Deuteriomethyl)-2-*exo*-methoxybicyclo[2.2.1]heptane (**11b**): ^{1}H NMR δ_H ($CDCl_3$) 3.28 (m, $^3J_{2endo,3endo}$ = 7.5 Hz, $^3J_{2endo,3exo}$ = 3.2 Hz, H2endo), 3.26 (s, OMe), 2.10 (br d, $^3J_{1,6exo}$ = 3.1 Hz, H1), 1.95 (t, $^3J_{4,5exo}$ = $^3J_{4,3exo}$ = 3.0 Hz, H4), 1.8–1.65 (H3exo, H3endo), 1.65 (t, $^3J_{7anti,CH_2D}$ = 6.6 Hz, H7anti); 1.55–1.45 (H5exo, H6exo), 1.09–1.05 (H5endo, H6endo, CH_2D); ^{2}H NMR δ_D ($CHCl_3$) 1.07 (CH_2D); ^{13}C NMR δ_C ($CDCl_3$) 85.7 (C2), 56.2 (OMe), 43.8 (L.B., C1), 43.6 (L.B., C7), 40.5 (L.B., C4), 37.1 (C3), 29.0 (C5), 26.6 (C6), 12.7 (t, $J_{^{13}C,^2H}$ = 19.1 Hz, CH_2D) (L.B. indicates the presence of a small ^{13}C–^{2}H coupling).

Reaction of 2 with Methanol-*d*/*p*-Toluenesulfonic Acid. Reaction of *exo*-tricyclo[3.2.1.$0^{2,4}$]octane (**2**) (150 mg) with methanol-*d* was carried out as previously described to give a pale yellow oil (174 mg, 91%), shown to consist of 7-*syn*-(deuteriomethyl)-2-*exo*-methoxybicyclo[2.2.1]heptane (**11b**) (15%) and 4-*exo*-deuterio-2-*exo*-methoxybicyclo[3.2.1]octane (**12b**) (76%). Separation was effected by preparative GLC. The spectral data for these compounds are identical with those obtained from the sodium amalgam reduction of the products from reaction of *exo*-tricyclo[3.2.1.$0^{2,4}$]octane (**2**) with mercuric acetate/methanol above. 4-*exo*-Deuterio-2-*exo*-methoxybicyclo[3.2.1]octane (**12b**): MS 3% D_0, 90% D_1, 7% D_2.

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Registry No. **1**, 22389-16-8; **2**, 13377-46-3; **3a**, 85698-98-2; 4-*endo*-**3b**, 113925-23-8; 4-*exo*-**3b**, 118760-52-4; **3c**, 118716-26-0; **4b**, 113947-64-1; **7**, 118716-27-1; **8**, 2565-97-1; **9**, 118722-48-8; **10a**, 118760-53-5; **10b**, 118716-28-2; **11a**, 118716-29-3; **11b**, 118716-30-6; **12a**, 85698-97-1; **12b**, 118722-49-9; *endo*-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene, 3635-94-7; bicyclo[3.2.1]octan-2-*exo*-ol, 1965-38-4; bicyclo[3.2.1]octan-2-one, 5019-82-9; mercuric acetate, 1600-27-7; methanol-*d*, 1455-13-6.

Selective Carriers of Ammonium Ions. 1. Synthesis and Template Effect of CsCl and X-ray Structure and Ionophoric Properties of Polyether Crowns Containing 1-Methyl-3,5-bis(methylene)-1*H*-pyrazole Units

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A new series of asymmetric crown ethers of cyclic (**7**, **8**) and acyclic structure (**9**) containing 1-methyl-3,5-bis(methylene)-1*H*-pyrazole units have been synthesized. Crowns **7** and **8** having 18 and 36 ring atoms have been obtained in 24% and 25% yields respectively by 1:1 and 2:2 cyclization of 1-methyl-3,5-bis(chloromethyl)-1*H*-pyrazole and disodium tetraethylene glycolate under the template effect of CsCl. When the Cs^+ cation was not present in the above reaction, the crowns **7** and **8** were formed in lower yields. The X-ray structure of smaller crown **7** showed a flexible irregular cavity which presents an internal overall twist that changes the pseudo-2-fold axis of symmetry in the neighborhood of the pyrazole ring into a pseudo mirror plane for the rest of it. A ^{1}H and ^{13}C NMR study has shown that in the Eu(fod)$_3$–crown **7** complex, the pyrazolic sp^2 nitrogen and the oxygens belonging to the polyether cavity are cooperatively acting as donor sites, the Eu^{3+} being near the pyrazole side least hindered by the methyl group. The transport rates of alkali and ammonium ions are much higher for all polyether ligands **7**–**9** than for ester crowns **3** and **4** evaluated before. The larger crown, **8**, is a selective carrier of NH_4^+ in relation to K^+ and Na^+ ions. However, the smaller crown, **7**, and its acyclic analogue **9** (which shows a "plateau" selectivity toward NH_4^+ and alkali ions) are better carriers of K^+ ions.

Introduction

In view of the important role played by substituted ammonium ions in chemistry and biology, the development of receptor molecules capable of recognizing and transport of such substrates is of special interest.[1,2]

Macrocyclic polyethers bind primary ammonium ions by anchoring the NH_4^+ group into their circular cavity via three $^+$N–H···O hydrogen bonds[3–6] and are able to carry organic ammonium cations, in particular, physiologically active ones.[7] In general, however, these polyethers bind the alkali cations K^+ and Rb^+ appreciably stronger than R–NH_3^+ groups[8] whereas the opposite selectivity would

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(1) Lehn, J. M. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 89.
(2) Izatt, R. M.; Bradshaw, J. S.; Nielsen, S. A.; Lamb, J. D.; Christensen, J. J.; Sen, D. *Chem. Rev.* **1985**, *85*, 271.
(3) Stoddart, J. F. *Chem. Soc. Rev.* **1979**, *7*, 85; *Annu. Rep. Prog. Chem., Sect. B* **1983**, 353.
(4) Cram, D. J.; Cram, J. M. *Acc. Chem. Res.* **1978**, *11*, 8.
(5) Hayward, R. C. *Chem. Soc. Rev.* **1983**, *12*, 285.
(6) Sutherland, I. O. *Chem. Soc. Rev.* **1986**, *15*, 63.
(7) Bacon, E.; Jung, L.; Lehn, J. M. *J. Chem. Res., Synop.* **1980**, 136; *J. Chem. Res., Miniprint* **1980**, 1964.
(8) Izatt, R. M.; Terry, R. E.; Haymore, B. L.; Hansen, L. D.; Dalley, N. K.; Avondet, A. G.; Christensen, J. J. *J. Am. Chem. Soc.* **1976**, *98*, 7620.

0022-3263/89/1954-1391$01.50/0