Corner Bromination of 2-Methyl-*endo*-tricyclo[3.2.1.0^{2,4}]octane and -oct-6-ene

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Received August 8, 1995 (Revised Manuscript Received February 9, 1996[⊗]*)*

Reaction of 2-methyl-*endo*-tricyclo[3.2.1.0^{2,4}]octane (**1**) with bromine in CCl_4 gave 2-*exo*,3-*endo*-dibromo-2-*endo*-methylbicyclo[3.2.1]octane (**3**) which rearranges on silica to 2-*exo*,6-*endo*-dibromo-1-methylbicyclo[2.2.2]octane (**4**). Reaction in methanol gave 4-*endo*-bromo-2-*exo*-methoxy-2-*endo*-methylbicyclo[3.2.1]octane (**10**) and 4-*endo*-bromo-2-*endo*-methoxy-2-*exo*-methylbicyclo[3.2.1]octane (**11**) formed by corner attack of the bromine electrophile with C2−C4 bond rupture and inversion of configuration at the site of electrophilic attack. Reaction of 2-methyl-*endo*-tricyclo[3.2.1.0^{2,4}]oct-6-ene (**2**) with bromine in CCl_4 and methanol gave products of reaction at the alkene site.

Introduction

Cyclopropanes are important in synthesis as they facilitate 1,3-functionalization involving selective carbon−carbon σ-bond rupture. This is one of only a few methods of functionalizing saturated hydrocarbons, and therefore, understanding the process is important. The reactivity of cyclopropanes resembles that of alkenes more than cyclic hydrocarbons.[1] The strained carbon−carbon bond of the cyclopropane can be involved in pericyclic, radical, and ionic reactions and undergo addition of organometallic compounds. The influences of substituents on geometry,[2] electronic structure,[3] reactivity, stereochemistry, and regiochemistry have been investigated[4] in order to understand and facilitate the use of this functional group for organic synthesis.

Previous studies[5] of the reactions of *exo*- and *endo*-tricyclo[3.2.1.0^{2,4}]octanes and tricyclo[3.2.1.0^{2,4}]oct-6-enes with acid and mercuric acetate have established the stereochemistry and regiochemistry of addition reactions. For *endo*-tricyclo[3.2.1.0^{2,4}]oct-6-ene both acid and mercuric acetate showed a regiochemical preference for exclusive reaction at the cyclopropane ring instead of at the double bond. Electrophilic attack occurs with internal (C2−C4) cyclopropyl bond rupture and inversion of configuration at the site of electrophilic attack (corner attack).[5c,e] This contrasts with *exo*-tricyclo[3.2.1.0^{2,4}]oct-6-ene where mercuration occurs predominantly at the double bond (89%) and protonation of the alkene also competes (18%) with cyclopropane ring opening.

To extend the scope of these investigations, we now report studies of the bromination of 2-methyl-*endo*-tricyclo[3.2.1.0^{2,4}]octane (**1**) and 2-methyl-*endo*-tricyclo[3.2.1.0^{2,4}]oct-6-ene (**2**) directed toward elucidating the factors that effect electrophilic reactions at cyclopropane and where alkene and cyclopropyl groups can compete for the electrophile.

Results and Discussion

For compounds containing a carbon−carbon double bond and a cyclopropane ring, reaction with bromine, in contrast to reaction with proton acids and mercuric acetate, generally take place at the double bond.[6] This is observed, for example, in the bromination of *exo*- and *endo*-tricyclo[3.2.1.0^{2,4}]oct-6-ene[7] where reaction occurs exclusively at the double bond. A substituent at C2, which raises the energy of the HOMO of the cyclopropane moiety, should enhance the reactivity of the cyclopropyl group toward electrophilic attack.[8]

Reaction of 2-methyl-*endo*-tricyclo[3.2.1.0^{2,4}]octane (**1**) with bromine[9] in CCl_4 in the dark gave 2-*exo*,3-*endo*-dibromo-2-*endo*-methylbicyclo[3.2.1]octane (**3**) (ca. 80%),[10] along with several minor products (all less than 5%) (Figure 1). Attempted purification by column chromatography on silica gel (pentane elution) resulted in complete conversion of **3** to 2-*exo*,6-*endo*-dibromo-1-methylbicyclo[2.2.2]octane (**4**). The addition reaction was repeated and **3** isolated by radial chromatography.[11]

The identity of **3** was established from a HMQC experiment that allowed assignment of the $^1H-^{13}C$ one-bond connectivities, a DQCOSY experiment that determined some $^1H-^1H$ connectivities, and a number of HMBC experiments that allowed assignment of a bicyclo[3.2.1]octane carbon skeleton. Of particular note are the correlations of the methyl group (2.08 ppm) to C1, C2,

[⊗] Abstract published in *Advance ACS Abstracts,* April 15, 1996.

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(9) <1.0 mol equiv of bromine was used.

(10) Product ratios were estimated from an ^1H NMR spectrum of the crude reaction mixture due to the instability of the major product to GLC analysis.

(11) **3** was identified as the initial product of bromination reaction by comparison of its ^1H NMR with that of the crude reaction mixture before chromatography.

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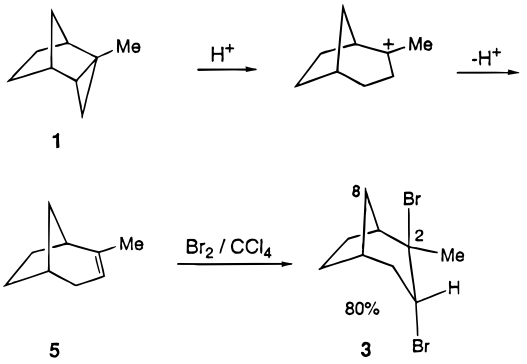

Figure 1. Bromination of 2-methyl-*endo*-tricyclo[3.2.1.$0^{2,4}$]-octane (**1**) in CCl_4.

and C3 and of H3 (4.85 ppm) to C1, C2, C4, and C5 that established the molecular connectivity through the quaternary carbon C2. Irradiation of the proton centred at 2.47 ppm, which had been established as a C4H, resulted in an NOE enhancement in the multiplet at 2.30−2.38 ppm (known to contain H1 and H8*syn* or H8*anti*), thereby establishing the signal as due to H4*exo*. The NOE experiment also determined the *syn* orientation of the C8H in the multiplet. The proton at 4.85 ppm attached to a carbon with a chemical shift of 56.6 ppm identified this proton and carbon as being part of a CHBr group. The DQCOSY and HMBC experiments determined these as H3 and C3. A 5.9 Hz coupling from H4*exo* (2.47 ppm) to H3 and a 1.2 Hz coupling from H4*endo* (2.04 ppm)[12] to H3 is consistent with an *exo* orientation of H3 and, hence, an *endo* orientation of the C3 bromine. The quaternary carbon at 76.7 ppm was identified as having methyl and bromine substituents from its chemical shift and was assigned as C2 from the HMBC experiments.

The stereochemistry of C2 was more difficult to assign due to the similarity of the chemical shifts of the methyl group (2.08 ppm) with H7*endo* (2.12 ppm), H5 (2.03 ppm), and H4*endo* (2.04 ppm), and hence, irradiation of the methyl group in NOE experiments could lead to ambiguous results as any enhancements observed may be due to the partial irradiation of the other protons. Consideration of the effects expected from steric interactions of the bromine or methyl group on the ^{13}C chemical shifts of C8 and C7 also proved inadequate, as the effects are similar in magnitude.[13] Of particular note is the similarity in shielding effects ($\Delta\delta$ values) of an axial methyl or bromine at C2 which result in 6.8 ppm and 4.5−6.6 ppm upfield shifts of C8, respectively.[14] A 1,4-gauche interaction from an equatorial methyl or bromine at C2 also result in similar shielding effects of C7 (4.7 ppm and 4.5−5.1 ppm, respectively).[14] Consideration of the chemical shift of H8*syn* shows an axial methyl group to result in a much smaller downfield shift of this proton than does a bromine in the same position. The chemical shift of H8*syn* in **3** was established at 2.22 ppm when the NMR spectrum is run in $CDCl_3$[15] that compares well to the chemical shift of H8*syn* of 2-*exo*,4-*endo*-dibromobicyclo-[3.2.1]octane (2.30 ppm) and 2-*exo*,3-*endo*-dibromobicyclo-[3.2.1]octane (2.06 ppm) both of which have one axial bromine substituent.[6] The stereochemistry of the bromine substituent of C2 was therefore assigned as *exo* and the methyl group as *endo*.

The identity of **4** was determined by a series of NMR experiments similar to those used to elucidate the structure of **3**. The proton−proton connectivity was established as far as possible from DQCOSY and 2D-TOCSY experiments. An HMBC confirmed the general bicyclo[2.2.2]octane skeleton, and the presence of four correlations from the methyl group protons to carbons in a two- or three-bond relationship established the methyl group to be attached to a bridgehead carbon. The methyl group correlations in the HMBC experiment established the molecular connectivity around the C1 (37.8 ppm) quaternary carbon where connectivity was lost in the DQCOSY experiment due to the lack of a proton at C1. The C1 carbon was shown to be quaternary by the absence of a correlation in an HMQC experiment and the suppression of this signal in a DEPT135 experiment. The one-bond $^1H-^{13}C$ connectivities of **4** were determined from both decoupled and coupled HMQC experiments. The presence of two CHBr groups was established from the chemical shifts of H2 (4.63 ppm) and H6 (4.36 ppm) and from the chemical shifts of the carbons (C2, 56.4 ppm and C6, 59.2 ppm) to which they are attached, as determined from the HMQC experiments. The presence of a 1.5% enhancement of the multiplet at 1.32 ppm on irradiation of H6 in a difference NOE experiment established the *exo* orientation of H6 and the *anti* configuration of the proton at 1.32 ppm (H7*anti*) to the highest priority bridge. The *exo* configuration of H6 was also supported by consideration of its coupling constants to H5*exo*[16] (2.43 ppm) and H5*endo* (2.18 ppm) ($^3J_{6,5exo} = 9.8$ Hz, $^3J_{6,5endo} = 3.9$ Hz). The stereochemistry of C2 was assigned as having an *exo* bromine substituent due to the lack of symmetry in the molecule (nine carbon signals were observed in the ^{13}C NMR spectrum).[17] The stereochemical assignment of C2 was also supported by the presence of a 2.5 Hz coupling of H7*anti* to H2 ($^4J_{7anti,2} = 2.5$ Hz, $^4J_{2,7anti} = 2.5$ Hz), consistent with a "W" coupling of these protons and hence an *endo* orientation of H2.

Dibromide **3** was unexpected and is considered to arise by acid-catalyzed cyclopropane ring opening,[18] by traces of HBr liberated when bromine is added to the reaction mixture, to give 2-methylbicyclo[3.2.1]oct-2-ene[19] (**5**) and *trans* diaxial bromine addition to the double bond. In a separate experiment **1** was allowed to react with a catalytic amount of TFA in CCl_4 for 3 h at room

(12) H4*endo* was identified from the HMQC experiment as a second proton of the C4 methylene group. The assignment was also consistent with the presence of a 2.4 Hz four-bond coupling of this proton to H8*anti* (1.32 ppm) which shows a "W" relationship of these protons.

(13) This can be seen by comparison of the ^{13}C chemical shifts and the differences in chemical shift values of 2-*endo*- and 2-*exo*-methylbicyclo[3.2.1]octane and various bromine-substituted bicyclo-[3.2.1]octane structures with bicyclo[3.2.1]octane.[14]

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(15) The chemical shifts of protons in this molecule are reported in the Experimental Section for benzene-d_6 as solvent because the assignment was easier in this solvent. However, the H and C assignments were also determined in $CHCl_3$ by running NMR spectra, HMQC, and HMBC, etc. in order to allow comparison with other spectra.

(16) A 1.0% enhancement of H5*exo* was observed on irradiation of H8*anti* in the reverse NOE experiment. The multiplet at 2.43 ppm in the ^1H NMR spectrum was assigned H5*exo* by the presence of a small NOE (1.0%) to the multiplet at 1.52 ppm (H8*anti*) on irradiation of H5*exo*.

(17) An *endo* orientation of the bromine at C2 would result in C_s symmetry of the molecule by the presence of a mirror plane through C1, C7, C8, and C4, and hence, only seven signals would be expected in the ^{13}C NMR spectrum.

(18) Due to rapid reaction of **1** with HBr it may have been advantageous to have carried out the reaction in the presence of an acid scavenger, such as *N*-bromosuccinimide.[8] This was not investigated.

(19) The identity of **5** was determined by comparison with the ^1H and ^{13}C NMR data reported.[5c]

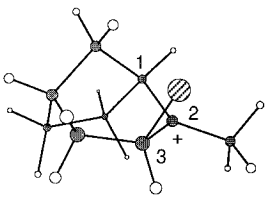
Table 1. Energies of Bromo 2-methylbicyclo[3.2.1]octanes[a]

compd		energy[b]	lengths (Å) and angles (deg)
2-*exo*,3-*endo*-dibromo-2-*endo*-methylbicyclo[3.2.1]octane	(**3**)	−0.596911[c] (−26.43)	C2−Br, 2.003; C3−Br, 1.987; C2−C3−Br, 112.8
2-*endo*,3-*exo*-dibromo-2-*exo*-methylbicyclo[3.2.1]octane		−0.601181[c]	C2−Br, 1.982; C3−Br, 1.963; C2−C3−Br, 112.8
3-*exo*-bromo-2-methylbicyclo[3.2.1]octan-2-yl cation	(**7**)	−0.055763[d] (182.74)	C2−Br, 2.411; C3−Br, 2.010; C2−C3−Br, 86.3
3-*endo*-bromo-2-methylbicyclo[3.2.1]octan-2-yl cation	(**8**)	−0.047420[d] (182.87)	C2−Br, 2.541; C3−Br, 1.990; C2−C3−Br, 93.1
3−**4** TS	(**9**)	−0.500829[d] (43.14)	C2−Br, 2.974; C6−Br, 3.100; C2−C3−Br, 93.1
2-*exo*,6-*endo*-dibromo-1-methylbicyclo[2.2.2]octane	(**4**)	−0.6047275[d] (−26.26)	C2−Br, 1.978; C6−Br, 1.981; C1−C2-Br, 110.7; C1−C6−Br, 111.7

[a] Semiempirical calculations were carried out with MOPAC 93 (Fugitsu Limited). Ab initio (3-21G*) and LST calculations were conducted using SPARTAN (Wavefunction, Irvine, CA). [b] Ab initio energies are in hartrees. PM3 energies (given in parentheses) are in kcal/mol. [c] Prefix digits 5467. [d] Prefix digits 2907.

temperature, after which time it was converted, to the extent of 50%,[20] to **5**. Addition of bromine[21] to **5** gave **3** in a rapid reaction.

The degree of stereospecificity in the addition of bromine to **5** poses interesting questions of mechanism. It is well known that electrophilic attack on the double bond in norbornene is preferentially from the *exo* face of the double bond. This has been attributed[22] to a partial pyramidalization of the olefin carbons due to steric interaction with the bridgehead hydrogens and the bridging methylene group. Examination of the geometry of **5** at the HF/6−31G* level revealed that the hydrogen on C-3 was within 0.6° of the plane of the double bond. We next examined the question of the energy and geometry of the ionic intermediate leading from **5** to **3**. Computations starting from the *exo* and the *endo* bromonium ions utilizing the semiempirical PM3 Hamiltonian and the ab initio HF/3-21G* method indicated the highly asymmetrical ions **7** and **8**. Surprisingly, the *exo* cation **7** computed as 1.5 and 5.2 kcal per mol, respectively, more stable than the expected *endo* cation **8**. When



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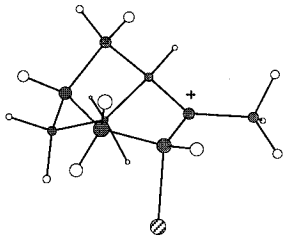

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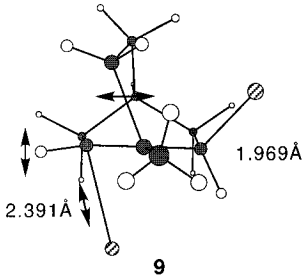

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configuration interaction was introduced in the PM3 calculation at the level of six electrons (HOMO-3 to LUMO+2, 100 configurations) the gap closed to 0.13 kcal/mol. Furthermore, a thermodynamic calculation of the free energy showed the *endo* cation **8** to be the more stable by 0.37 kcal/mol. This emphasizes the necessity of introducing higher levels of computation when dealing with bromine-containing species. The geometries shown are those resulting from the PM3CI calculation. The following data compare the *exo* cation **7** to the *endo* cation **8**, respectively: C3−Br 1.983 and 1.978 Å; C2−Br 2.614 and 2.634 Å; and the C2C3Br angle 97.6 and 98.7°. This type of asymmetry has been noted before as in the bromination of isobutylene.[23] Whether one should call these species bromonian ions is a mute point. A summary of energies and pertinent geometry data are given in Table 1.

The rearrangement of dibromides **3** and **4** takes place in the polar milieu on the surface of silica gel. The reaction is reminiscent of the well-known rearrangement of 5α,6*β*-dibromide of cholesterol to its 5*β*,6α-isomer[24] and provides another route to a usefully functionalized bicyclo[2.2.2]octane skeleton. Evidence for the 5α,6*β*-dibromide rearrangement supports the four-center pathway proposed by Grob and Winstein[25] against a prior dissociation to bromide ion and a bromonium ion. Attempts to minimize an analog of the 2-norbornyl cation formed by loss of the C2−Br and bridging between the methylene at C7 with carbons 1 and 2 at the PM3 or HF/3-21G* levels invariably gave the tertiary 3-bromo-2-methyl-2-cation. It seemed unreasonable to expect this ion to rearrange to the less stable secondary ion. Consequently, the rearrangement of **3** to **4** was modeled as a one-step rearrangement. Initial thinking suggested structure **6**. Linear strategic transit calculations for the conversion of **3** to **4** were carried out at both the PM3 and HF/3-31G* levels, respectively, giving structure **9**. Both calculations met the usual requirement of one imaginary vibrational frequency corresponding to the reaction coordinate. The normal modes of vibration along this reaction coordinate are indicated above as are the pertinent C−Br distances.

Acid-catalyzed ring opening of **1** is suppressed when the reaction is performed in methanol (Figure 2). Reaction with bromine[9] in dry methanol in the dark gave 4-*endo*-bromo-2-*exo*-methoxy-2-*endo*-methylbicyclo[3.2.1]-octane (**10**) (50%) and 4-*endo*-bromo-2-*endo*-methoxy-2-*exo*-methylbicyclo[3.2.1]octane (**11**) (45%) and two minor

(20) Determined from a ^{1}H NMR spectrum.

(21) Examples of *cis* bromine additions are known. Ruasse, M.-F. *Acc. Chem. Res.* **1990**, *23*, 87.

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(25) Grob, C. A.; Winstein, S. *Helv.* **1952**, *99*, 782.

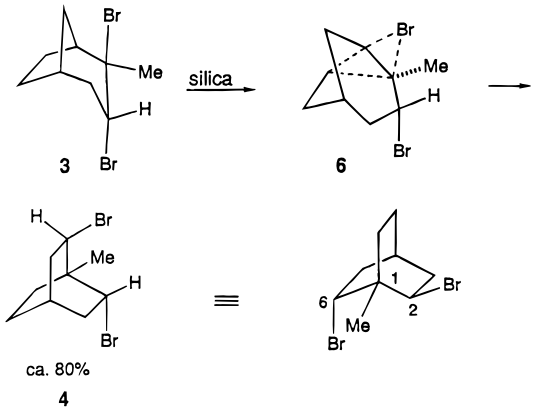

Figure 2. Rearrangement of 2-*exo*,3-*endo*-dibromo-2-*endo*-methylbicyclo[3.2.1]octane (**3**).

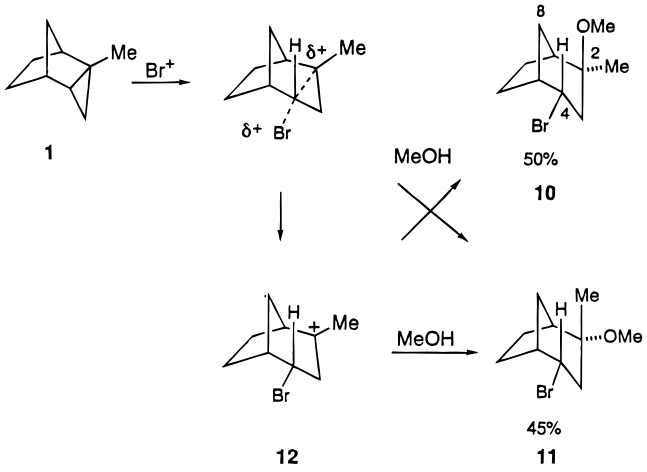

Figure 3. Reaction of 2-methyl-*endo*-tricyclo[3.2.1.0^{2,4}]octane (**1**) with bromine in methanol.

products that were not identified. The identity of **10** was determined as follows: a DQCOSY experiment established the ^{1}H−^{1}H connectivity and an HMQC determined the one-bond ^{1}H−^{13}C assignments. An HMBC experiment confirmed the general bicyclo[3.2.1]octane structure from the presence of correlations from H8*anti*[26] (1.37 ppm) to C1 (42.0 ppm), C5 (43.2 ppm), C4 (55.7 ppm), and C2 (78.2 ppm) and from H8*syn* (2.04 ppm) to C6 (24.2 ppm) and C7 (26.2 ppm). The HMBC also showed correlations to C1, C2, C4, and C5 from H3*exo* (2.14 ppm) and hence established the molecular connectivity through the quaternary carbon C2. The presence of the *C*(OMe)-Me (C2) and *C*HBr (C4) groups was determined from consideration of the ^{13}C chemical shifts and from the chemical shift of H4 (4.40 ppm). The stereochemistry of C4 was assigned by the presence of a 1.8% enhancement of the multiplet at 2.04 ppm on irradiation of H4 (4.40 ppm) in a difference NOE experiment that establishes the multiplet centred at 2.04 ppm as H8*syn* and the *exo* orientation of H4 (a 1.7% enhancement of H4 was observed on irradiation of H8*syn*). This therefore requires an *endo* orientation of the C4 bromine substituent.[27] An *exo* orientation of the methoxy group of C2 was established from the presence of an NOE (1.2%) to H8*syn* on irradiation of the methoxy group at 3.16 ppm and the presence of a 1.7% enhancement of H7*endo* (1.42 ppm) on irradiation of the methyl group attached to C2, hence confirming an *endo* orientation of this group.[28]

The structure of **11** was determined from the following: a DQCOSY and selective decoupling experiments established the proton−proton connectivity and an HMQC experiment established the ^{1}H−^{13}C one-bond connectivities. The one-bond ^{1}H−^{13}C connectivities of the carbons at 23.9 and 23.8 ppm could not be resolved due to the similarity of the chemical shifts of both the carbons and their attached protons, whose correlations overlapped in the HMQC.[29] An HMBC experiment confirmed the general bicyclo[3.2.1]octane structure of the molecule and identified the chemical shift of the quaternary carbon (C2, 76.8 ppm) which was not observed in the ^{13}C NMR spectrum.[30] Irradiation of the multiplet corresponding to H8*syn* and H8*anti*[31] at 1.55 ppm in a difference NOE experiment gave a 0.7% enhancement of the methyl group of C2 and a 2.7% enhancement of H4, thereby establishing the *exo* orientation of H4 and giving a tentative assignment of an *exo* orientation of the methyl substituent of C2. Irradiation of H4 gave an enhancement to the multiplet centered at 1.55 ppm, but this could not be measured due to the presence of water in the ^{1}H NMR spectrum that partially obscured the multiplet. In the same irradiation a 0.9% NOE to the methyl group of C2 was observed. Irradiation of the methyl signal at 1.20 ppm gave a 2.6% enhancement of H4, and an enhancement of the multiplet centered 1.55 ppm was also observed. This confirmed the *exo* orientation of the methyl substituent and hence an *endo* orientation of the methoxy group attached to the same carbon.[32] The chemical shift of H8*syn* at approximately 1.55 ppm is significantly (0.5 ppm) upfield from H8*syn* in compound **10**. Thus, the presence of an axial methyl group leads to a smaller downfield shift of this proton than does an axial methoxy group and bromine substituent[14] and hence further supports the assignment of an *exo* bromine at C2 in **3** due to the large downfield shift of H8*syn* observed (2.22 ppm in $CDCl_3$ solution).

The methoxy bromides **10** and **11** are formed by corner attack of the bromine electrophile at the C2−C4 bond of the cyclopropane ring with inversion of configuration (Figure 3). This is followed by nucleophilic attack with both inversion and retention of configuration. A small preference is observed for axial attack (retention).[33] The formation of both tertiary epimers is at first sight

(26) The assignment of the multiplet at 1.37 ppm stemmed from the presence of a 5.1 Hz coupling of this proton to H1 and H5. The proton at 2.04 ppm was established from the HMQC to be the second proton of the C8 methylene group and hence was assigned to H8*syn*.

(27) The axial orientation of H4 was also supported by the presence of a 12.0 Hz coupling to H3*endo* (1.62 ppm), consistent with a *trans* relationship of these protons, and a smaller 5.4 Hz coupling to H3*exo* (2.14 ppm).

(28) The chemical shift of H8*syn* showed a significant downfield shift to 2.04 ppm similar to that observed for 2-*exo*,4-*endo*-dibromobicyclo-[3.2.1]octane and 2-*exo*,3-*endo*-dibromobicyclo[3.2.1]octane (2.06 ppm and 2.30 ppm, respectively),[6] both of which have a single axial bromine substituent at C2, and hence supports the *exo* assignment of the methoxy group.

(29) The carbons at 23.9 and 23.8 ppm were confirmed as the carbons of methylene groups by a DEPT135 experiment. The chemical shifts of the methylene protons were identified from the DQCOSY.

(30) H3*exo* (2.10 ppm) showed correlations to C1 (42.0 ppm), C4 (54.6 ppm), C5 (44.0 ppm), and a fourth carbon, which after taking into account foldback, was calculated to have a chemical shift of 76.8 ppm, similar to that observed for C2 (78.2 ppm) of **10**, and is consistent with a quaternary carbon with methoxy and methyl substituents.

(31) C8 showed only one correlation in the HMQC experiment, to a multiplet centered at 1.55 ppm, but was confirmed as the carbon of a methylene group from a DEPT135 experiment.

(32) The assignment of an axial orientation of H4 was also supported by the presence of a 12.2 Hz coupling to H3*endo*, consistent with a *trans* arrangement of the two protons.

(33) This was also observed for the reaction of **1** with MeOD−D$^+$.[5c,e]

consistent with the intermediacy of a tertiary carbocation. However, the carbocation **12** is expected to react preferentially with nucleophile from the axial direction.[34] The formation of such significant quantities of **11** would therefore not be expected and suggests some proportion of the reaction with methanol may occur before the protonated cyclopropane is relaxed to the tertiary carbocation.[5e]

The regiochemistry of addition of cyclopropanes is often rationalized by a modified version of Markovnikov's rule that states[35] that "the ring opens between the carbons bearing the largest and smallest number of alkyl substituents". With substituents on two carbons, products are generally observed to result from Markovnikov-type addition and from cleavage of the most substituted cyclopropyl bond. For the reaction of **1** with bromine in CCl_4 or methanol no products are formed from rupture toward C3, which would be the case if the modified version of Markovnikov's rule were to operate. Electrophilic attack by bromine to **1** results only in cleavage of the most substituted cyclopropyl bond, the C2−C4 bond.

The preference for corner attack is consistent with the results of Skell[8] for the bromination of dehydroadamantane. This corner trajectory of attack by bromine contrasts with the mechanism reported by Lambert[36] for bromination of cyclopropane-*cis*-*1*,*2*,*3*-d_3 who reported that edge attack of electrophile (retention) followed by nucleophilic attack with inversion occurred.

The predominance of acid-promoted ring opening of **1** in CCl_4 contrasts with the reaction in methanol where proton acid-catalyzed ring opening is not observed. In methanol, any HBr that is formed will be competitively solvated by methanol. Acid-catalyzed ring opening in methanol will therefore be slower, and electrophilic opening with bromine is exclusively observed. In methanol any intermediate cation is expected to benefit from solvation more than in CCl_4 where intramolecular proton loss to give alkene **5** competes with intermolecular capture by nucleophile; the latter is not observed.

The reaction of **2** with bromine[9] in CCl_4 proceeded instantaneously at room temperature to give 7-*exo*-8-*anti*-dibromo-2-methylbicyclo[3.2.1]oct-2-ene (**13**) (ca. 80%)[37] and a number of minor products (1−5% each) (Figure 4). The identity of **13** was determined as follows: a HETCOR established the $^1H-^{13}C$ one-bond connectivities and a COSY experiment determined the proton−proton connectivity. The chemical shift of H7 at 4.27 ppm established this proton as part of a CHBr group, and the absence of a measurable coupling to H1 determined the *endo* orientation of this proton and hence an *exo* orientation of the bromine substituent of C7. The *endo* orientation of H7 was confirmed from consideration of its coupling constants to H6*endo* (2.43 ppm) and H6*exo* (2.88 ppm) ($^3J_{7,6endo}$ = 8.3 Hz, $^3J_{7,6exo}$ = 3.8 Hz, $^3J_{6endo,7}$ = 8.3 Hz). The *exo* orientation of the C6 proton centered at 2.88 ppm was assigned due to the presence of a correlation to H5 in the COSY. No correlation from H5 to the multiplet centred at 2.43 ppm was observed in the COSY; hence, this proton was assigned to H6*endo*. The HETCOR experiment had previously established the geminal relationship of these protons. The *anti* stereochemistry of the bromine at C8 (55.9 ppm) was established by the lack of coupling of H8 (4.42 ppm) to H5 or H1 that is characteristic of a proton attached to C8 in a *syn* orientation with respect to the largest bridge in bicyclo-[3.2.1]octane systems.[5]

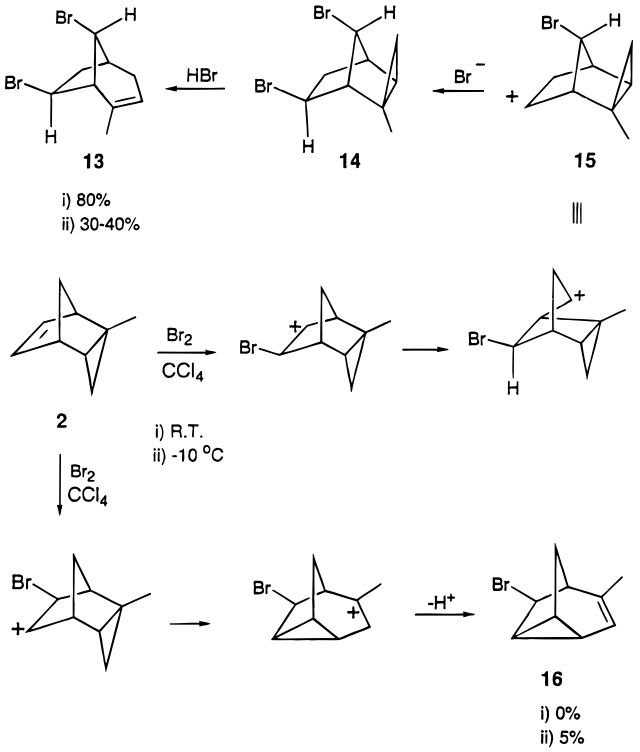

Figure 4. Bromination of 2-methyl-*endo*-tricyclo[3.2.1.0^{2,4}]oct-6-ene (**2**) in CCl_4.

The dibromide **13** is considered to be formed by way of 7-*exo*,8-*anti*-dibromo-2-methyl-*exo*-tricyclo[3.2.1.0^{2,4}]-octane (**14**), a product of addition−rearrangement of bromine to the alkene, followed by acid-catalyzed ring opening with traces of HBr formed by elimination processes. Attack of the bromine nucleophile on cation **15** from an *exo* trajectory is consistent with that observed for norbornane systems—the *syn* bromine does not restrict this trajectory.[38] An attempt was made to isolate **14** by performing the reaction at −10 °C. This resulted in the formation of **13** but in a reduced yield (30−40%) along with 6-*exo*-bromo-4-methyltricyclo[3.2.1.0^{2,7}]oct-3-ene (**16**) (ca. 5%)[39] and a number of other minor products.[40]

The identity of 6-*exo*-bromo-4-methyltricyclo[3.2.1.0^{2,7}]-oct-3-ene (**16**) was determined from the following:[41] the presence of a cyclopropane ring was established by the chemical shift of C1 and C2 at 15.4 and 18.5 ppm, respectively. The third carbon of the cyclopropane ring

(34) Coxon, J. M.; Houk, K. N.; R. T. Luibrand, R. T. *J. Org. Chem.* **1995**, *60*, 418.

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

(36) Lambert, J. B.; Chelius, E. C.; Schulz, Jr., W. J.; Carpenter, N. E. *J. Am. Chem. Soc.* **1990**, *112*, 3156.

(37) The yield of **13** was not reproducible and ranged from approximately 50 to 80%. **13** was unstable to the GLC conditions.

(38) Traylor, T. G. *Acc. Chem. Res.* **1969**, *2*, 152. Kwart, H.; Kaplan, L. *J. Am. Chem. Soc.* **1954**, *76*, 4072. Kwart, H.; Miller, R. K. *J. Am. Chem. Soc.* **1956**, *78*, 5678. Kaplan, L.; Kwart, H.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1960**, *82*, 2341.

(39) Compound **16** was not isolated from this reaction but was identified from a ^1H NMR spectrum of the crude reaction mixture by comparison with an authentic sample.

(40) Column chromatography on silica gel with gradient elution with ether−pentane mixtures gave little separation, and the products were not further investigated.

(41) A COSY experiment in conjunction with difference NOE experiments established the $^1H-^1H$ connectivity, and a HETCOR allowed determination of the one bond $^1H-^{13}C$ connectivities.

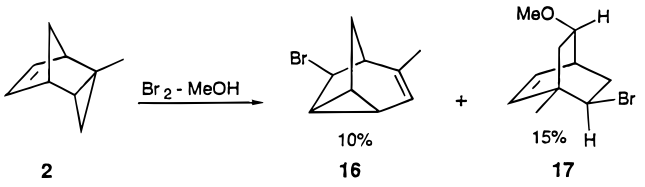

Figure 5. Bromination of 2-methyl-*endo*-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (**2**) in MeOH.

(C7, 22.5 ppm) was shifted downfield due to the presence of a α-CHBr group. The proton of the CHBr group (H6) appeared as a singlet at 3.69 ppm ($W_{h/2}$ = 2.5 Hz) with no apparent coupling to H5 (2.53 ppm) or H7 (1.68 ppm) consistent with an *endo* orientation. The chemical shift of 3.69 ppm is significantly upfield from that usually observed for protons of CHBr groups[42] and is consistent with the proximity of this proton to a cyclopropane ring and with its relationship to the double bond. The relationship of H6 to H5 and H7 was confirmed by the presence of a small enhancement of these protons on irradiation of H6 in a difference NOE experiment. Further support for the *exo* orientation of the bromine at C6 came from the downfield shift of H8*anti* (2.22 ppm) which is consistent with deshielding due to the proximity of the bromine in this orientation and from comparison of the chemical shift of C8 in **16** (25.5 ppm) with C8 in 6-*exo*-bromotricyclo[3.2.1.$0^{2,7}$]oct-3-ene (25.4 ppm).[7]

Bromination[9] of **2** was repeated in methanol where the electrophile can be distinguished from the nucleophile. The reaction gave a complex mixture of products from which 7-*anti*-bromo-5-*endo*-methoxy-1-methylbicyclo[2.2.2]-oct-2-ene (**17**) (ca. 15%) and 6-*exo*-bromo-4-methyltricyclo-[3.2.1.$0^{2,7}$]oct-3-ene (**16**) (ca. 10%) were separated (Figure 5).[43]

The identity of **17** was established from the following: a COSY established the ^{1}H−^{1}H connectivity and a HETCOR determined the one-bond ^{1}H−^{13}C assignments. Irradiation of H5 (3.69 ppm) showed a 2.2% enhancement of the multiplet at 1.81 ppm in a difference NOE experiment (3.4% enhancement of H5 was observed in the reverse irradiation) and hence established the *exo* orientation of H5 and determined the multiplet at 1.81 ppm to be H8*anti*. The chemical shift of H5 (3.69 ppm) and its attached carbon C5 (80.1 ppm) is diagnostic of a *CH*OMe group, with the methoxy group evident as a singlet in the ^{1}H NMR at 3.29 ppm and its corresponding carbon at 55.8 ppm in the ^{13}C NMR spectrum. The HETCOR experiment established a geminal relationship between the protons at 2.25 ppm and 1.81 ppm and hence in conjunction with the NOE data allowed the assignment of the multiplet at 2.25 ppm as H8*syn*. The chemical shift of C7 at 58.1 ppm and its attached proton H7 at 3.80 ppm (determined from the HETCOR experiment) established the presence of a CHBr group. The stereochemistry of the bromine substituent at C7 was determined from the coupling constants of H7 to H8*syn*

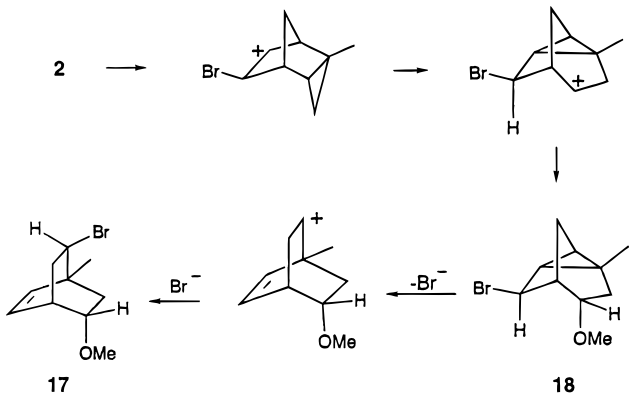

Figure 6. Conversion of **2** to **17**.

($^3J_{7,8syn}$ = 10.1 Hz, $^3J_{8syn,7}$ = 10.2 Hz) and H8*anti* ($^3J_{7,8anti}$ = 4.3 Hz, $^3J_{8anti,7}$ = 4.3 Hz) which established a *cis* relationship of H7 and H8*syn* and therefore determined the orientation of the bromine substituent at C7 to be *anti* with respect to the carbon−carbon double bond.

A possible mechanism for the formation of **17** is by solvolysis of 6-*exo*-bromo-4-*endo*-methoxy-2-methyltricyclo-[3.2.1.$0^{2,7}$]octane (**18**) followed by nucleophilic addition of bromine (Figure 6). The reaction was repeated at lower temperatures (−20, −78 °C) in an attempt to reduce rearrangement and in methanol-d_4 to allow direct examination of the reaction mixture by ^{1}H NMR. These studies showed the reaction to be complex even at low temperature.

All the products isolated in these studies of the bromination of **2** result form bromine addition to the double bond rather than to the cyclopropane. This is consistent with the observations for the bromination of *endo*- and *exo*-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene.[7] The methyl group at C2 of **2** is insufficiently activating to direct attack to the cyclopropane ring, and reaction occurs at the alkene, not at the cyclopropane.

Conclusions

These studies of bromination of **1** and **2** demonstrate that when bromine attacks the cyclopropane ring the trajectory of attack is to the corner resulting in inversion of configuration. Where the developing cation is tertiary, nucleophilic attack occurs with both retention and inversion. In the bromination of **1** nucleophilic attack occurs to the brominated cyclopropane in part before it is fully relaxed to the tertiary cation. The methyl group in **2** provides insufficient activation for cyclopropane ring opening to compete in the first instance with reaction of the alkene.

Experimental Section

NMR spectra were recorded on Varian XL-300 or Varian Unity 300 spectrometers equipped with a 5 mm probe and operating at 300 and 75 MHz for ^{1}H and ^{13}C, respectively. Chemical shifts are reported in ppm relative to tetramethylsilane. Difference NOE spectra were obtained in arrayed experiments with the decoupler offset 10 000 Hz and then cycled with low power over the multiplet peaks of the desired proton for irradiation, a procedure based on that of Kinns and Sanders.[44] Carbon-detected heteronuclear proton−carbon correlated (HETCOR) spectra were recorded using a pulse

(42) The HETCOR confirmed this proton as part of a CHBr group by the presence of a correlation to C6 at 56.5 ppm. The downfield chemical shift of C6 identified this carbon as having a bromine substituent. The chemical shift is also similar to that reported for H6 (3.64 ppm) of 6-*exo*-bromotricyclo[3.2.1.$0^{2,7}$]oct-3-ene. Japenga, J.; Klumpp, G. W.; Stapersma, J. *Tetrahedron* **1977**, *33*, 2847.

(43) Attempted separation by radial chromatography on a 2 mm silica plate with gradient elution with ether/pentane followed by further purification by dry column flash chromatography gave two products. The percentage composition of the products was estimated from a ^{1}H NMR spectrum of the crude reaction mixture due to the overlap of peaks and instability of products.

(44) Kinns, M.; Sanders, J. K. M. *J. Magn. Reson.* **1984**, *56*, 518.

sequence which ensures full $^1H-^1H$ decoupling.[45] All other experiments were recorded using standard pulse sequences and parameters available with the XL-300 or Unity 300 systems. Proton chemical shifts marked with an asterisk were estimated from NOE or two-dimensional NMR experiments (COSY, DQCOSY, HETCOR, or HMQC experiments). Proton chemical shifts marked with a superscript hash mark (#) were determined from 1D- or 2D-TOCSY experiments.

Mass spectra were run by GCMS using a Kratos MS80RFA spectrometer directly coupled to a Carlo Erba 500 Series GLC fitted with a Restex R_{tx}1 30 m × 0.32 mm capillary column. A programmed run was used for the GCMS (an initial temperature of 60 °C was held for 1 min and then the column temperature increased at the rate of 20 °C per minute up to 260 °C) to ensure that the sample and all impurities passed through the column to the MS instrument. In some cases molecular ion peaks were not observed in the high-resolution mass spectra (HRMS) but were identified in the low-resolution spectra (LRMS). In these cases the LRMS and HRMS spectra are shown along with a number of fragment ion peaks which were observed.

A Hewlett-Packard HP5890A GLC was used in both analytical and preparative modes with either a 1.5% OV-17, 1.25% QF-1 chromosorb W packed column of 5 mm external diameter and 3.0 m length or a 1.5% OV-17, 1.95% QF-1 chromosorb W packed column of 10 mm external diameter and 2.5 m length. Melting points were determined on an electrothermal melting point apparatus and are uncorrected. Elemental analyses were performed at the Department of Chemistry, University of Otago, Dunedin. Radial chromatography was performed on a chromatotron (Harrison and Harrison) using Merck grade 60PF_{254} silica gel or poly(ethylene glycol) (PEG, molecular weight 6000 g mol^{-1}) coated silica plates.

Preparation of 2-Methyl-*endo*-tricyclo[3.2.1.0^{2,4}]oct-6-ene (2). 2-Methyl-*endo*-tricyclo[3.2.1.0^{2,4}]oct-6-ene (**2**) was prepared by the literature procedure[5c] from the Diels−Alder reaction of cyclopentadiene and 2-methylcyclopropene[46] at −78 °C and was identified by comparison of its ^1H and ^{13}C NMR spectra with literature values.

Preparation of 2-Methyl-*endo*-tricyclo[3.2.1.0^{2,4}]octane (1). Compound **1** was synthesized by the literature procedure,[5] whereby **2** was hydrogenated over 5% palladium on carbon until 1 equiv of hydrogen was taken up. Product **1** was identified by comparison of its ^1H and ^{13}C NMR spectra with literature values.

Reaction of 2-Methyl-*endo*-tricyclo[3.2.1.0^{2,4}]octane 1 with Bromine in Carbon Tetrachloride. To a stirred solution of **1** (100 mg, 0.82 mmol) in CCl_4 (5 mL) was added bromine (121 mg, 0.76 mmol, 0.93 mole equiv) in CCl_4 (5 mL) dropwise over 10 min. The reaction was stirred in the absence of light for 1.5 h after which time the colorless solution was washed with water (7 mL). The organic extract was separated and dried over $MgSO_4$ and the solvent carefully removed under reduced pressure to give a brown oil (207 mg, ca. 97% recovery). A ^1H NMR spectrum showed the oil to consist of 2-*exo*,3-*endo*-dibromo-2-*endo*-methylbicyclo[3.2.1]octane (**3**) (ca. 80%). A number of minor products were also present (all less than 5%) but were not identified. Purification was effected by radial chromatography (2 mm PEG-coated silica plate, pentane elution) to give **2-*exo*,3-*endo*-dibromo-2-*endo*-methylbicyclo[3.2.1]octane** (**3**) as a colorless oil. ^1H NMR δ_H (C_6D_6): 4.85 (d, $^3J_{3,4exo}$ = 5.8 Hz, H3), 2.47 (m, $^2J_{4exo,4endo}$ = 16.6 Hz, $^3J_{4exo,3}$ = 5.9 Hz, $^3J_{4exo,5}$ = 3.7 Hz, $^4J_{4exo,6exo}$ = 1.2 Hz, H4*exo*), 2.34* (H1), 2.33* (H8*syn*), 2.25* (H6*endo*) 2.12* (H7*endo*), 2.08 (s, $W_{h/2}$ = 1.0 Hz, Me), 2.04 (m, $^2J_{4endo,4exo}$ = 16.6 Hz, $^3J_{4endo,3}$ = 1.2 Hz, $^3J_{4endo,5}$ = 4.9 Hz, $^4J_{4endo,8anti}$ = 2.4 Hz, H4*endo*), 2.03* (H5), 1.50* (H6*exo*), 1.43* (H7*exo*), 1.32 (m, $^2J_{8anti,8syn}$ = 11.6 Hz, $^3J_{8anti,1}$ = $^3J_{8anti,5}$ = 4.9 Hz, $^4J_{8anti,4endo}$ = 2.4 Hz, H8*anti*). ^{13}C NMR δ_C (C_6D_6): 76.7 (C2), 56.6 (C3), 50.6 (C1), 38.7 (C8), 38.3 (C4), 35.6 (Me), 34.6 (C5), 27.8 (C6), 26.7 (C7). LRMS: $C_9H_{14}{}^{81}Br_2$ M$^{\bullet+}$ requires 284, found 284; $C_9H_{14}{}^{79}Br^{81}Br$ M$^{\bullet+}$ requires 282, found 282; $C_9H_{14}{}^{79}Br_2$ M$^{\bullet+}$ requires 280, found 280; $C_9H_{14}{}^{81}Br$ [M − Br]$^{\bullet+}$ requires 203, found 203; $C_9H_{14}{}^{79}Br$ [M − Br]$^{\bullet+}$ requires 201, found 201; C_9H_{14} [M − Br_2]$^{\bullet+}$ requires 122, found 122; C_9H_{13} [M − HBr_2]$^{\bullet+}$ requires 121, found 121. HRMS: $C_9H_{14}{}^{81}Br$ [M − Br]$^{\bullet+}$ requires 203.0260, found 203.0263; C_9H_{14} [M − Br_2]$^{\bullet+}$ requires 122.1096, found 122.1059; C_9H_{13} [M − HBr_2]$^{\bullet+}$ requires 121.1018, found 121.1026.

The products from the reaction of 2-methyl-*endo*-tricyclo[3.2.1.0^{2,4}]octane (**1**) with bromine in carbon tetrachloride (207 mg, containing approximately 80% **3**) were subjected to column chromatography (silica gel, 100:1 ratio absorbent to sample loaded, pentane elution). The resulting major product was identified as 2-*exo*,6-*endo*-dibromo-1-methylbicyclo[2.2.2]octane (**4**) as white crystals: mp 60−61 °C (pentane). ^1H NMR δ_H ($CDCl_3$): 4.63 (d of t, $^3J_{2,3endo}$ = 9.8 Hz, $^4J_{2,7anti}$ = 2.5 Hz, H2), 4.36 (d of d, $^3J_{6,5endo}$ = 3.9 Hz, $^3J_{6,5exo}$ = 9.8 Hz, H6), 2.59 (m, $^2J_{3endo,3exo}$ = 15.1 Hz, $^3J_{3endo,2}$ = 9.8 Hz, $^3J_{3endo,4}$ = 2.6 Hz, $^4J_{3endo,8anti}$ = 2.6 Hz, H3*endo*), 2.43 (m, $^2J_{5exo,5endo}$ = 15.2 Hz, $^3J_{5exo,4}$ = 2.7 Hz, $^3J_{5exo,6}$ = 9.8 Hz, $^4J_{5exo,3exo}$ = 2.7 Hz, H5*exo*), 2.19* (H3*exo*), 2.18* (H5*endo*), 2.10* (H7*syn*), 1.77* (H8*syn*), 1.71* (H4), 1.52 (m, H8*anti*), 1.32 (m, $^2J_{7anti,7syn}$ = 13.6 Hz, $^3J_{7anti,8anti}$ = 11.3 Hz, $^3J_{7anti,8syn}$ = 2.5 Hz, $^4J_{7anti,2}$ = 2.5 Hz, H7*anti*), 1.08 (s, $W_{h/2}$ = 1.0 Hz, Me). ^{13}C NMR δ_C ($CDCl_3$): 59.2 (C6), 56.4 (C2), 39.9 (C5), 39.2 (C3), 37.8 (C1), 28.3 (C7), 26.7 (C4), 26.4 (Me), 24.5 (C8). LRMS: $C_9H_{14}{}^{81}Br_2$ M$^{\bullet+}$ requires 284, found 284; $C_9H_{14}{}^{79}Br^{81}Br$ M$^{\bullet+}$ requires 282, found 282; $C_9H_{14}{}^{79}Br_2$ M$^{\bullet+}$ requires 280, found 280; $C_9H_{14}{}^{81}Br$ [M − Br]$^{\bullet+}$ requires 203, found 203; $C_9H_{14}{}^{79}Br$ [M − Br]$^{\bullet+}$ requires 201, found 201. HRMS: $C_9H_{14}{}^{81}Br$ [M − Br]$^{\bullet+}$ requires 203.0260, found 203.0222.

Reaction of 2-Methyl-*endo*-tricyclo[3.2.1.0^{2,4}]octane (1) with Trifluoroacetic Acid and Bromine in Carbon Tetrachloride. 2-Methyl-*endo*-tricyclo[3.2.1.0^{2,4}]octane (**1**) (50 mg, 0.41 mmol) was added to a stirred solution of TFA (5 mg, 0.04 mmol) in CCl_4 (3 mL). The solution was stirred at room temperature for 3 h, after which time a ^1H NMR spectrum of a sample (0.4 mL) showed that approximately 50% of the starting material had been consumed. The major product was identified as 2-methylbicyclo[3.2.1]oct-2-ene (**5**) (ca. 80% of the observed reaction gave this product) by comparison of its ^1H and ^{13}C NMR spectra with those published.[5c] The remaining solution was stirred for a further 1 h before bromine (39 mg, 0.24 mmol) in CCl_4 (0.8 mL) was added dropwise. The solution was stirred at room temperature for 15 min after which time all of the starting material had been consumed (^1H NMR). The major product, 2-*exo*,3-*endo*-dibromo-2-*endo*-methylbicyclo[3.2.1]octane (**3**) (ca. 80%), was identified by comparison of its ^1H and ^{13}C NMR spectra with those reported above. A small amount of **5** (ca. 2%) was also present, along with a number of minor products which were not identified.

Reaction of 2-Methyl-*endo*-tricyclo[3.2.1.0^{2,4}]octane (1) with Bromine in Methanol. Bromine (181 mg, 1.13 mmol) in dry methanol (5 mL) was added dropwise over 10 min to a stirred solution of **1** (154 mg, 1.26 mmol, 1.1 mol equiv) at room temperature. The reaction was stirred in the dark for 30 min, diluted with water (7 mL), and extracted with pentane (8 mL) and ether (2 × 8 mL). The organic extracts were combined and dried over $MgSO_4$, and the solvent was carefully removed under reduced pressure to give a pale yellow oil (258 mg, ca. 98% recovery). GLC analysis showed the presence of two major products, 4-*endo*-bromo-2-*exo*-methoxy-2-*endo*-methylbicyclo[3.2.1]octane (**10**) (50%) and 4-*endo*-bromo-2-*endo*-methoxy-2-*exo*-methylbicyclo[3.2.1]octane (**11**) (45%), and two minor products which were not isolated. The two major products were separated by preparative GLC. **4-*endo*-Bromo-2-*exo*-methoxy-2-*endo*-methylbicyclo[3.2.1]octane** (**10**) was obtained as a colorless oil. ^1H NMR δ_H ($CDCl_3$): 4.40 (m, $^3J_{4,1}$ = 3.0 Hz, $^3J_{4,3endo}$ = 12.0 Hz, $^3J_{4,3exo}$ = 5.4 Hz, $^4J_{4,6exo}$ = 1.0 Hz, H4), 3.16 (s, $W_{h/2}$ = 0.6 Hz, OMe), 2.49 (m, H5), 2.17* (H1), 2.14 (d of d, $^2J_{3exo,3endo}$ = 14.2 Hz, $^3J_{3exo,4}$ = 5.4 Hz, H3*exo*), 2.04 (d, $^2J_{8syn,8anti}$ = 12.2 Hz, H8*syn*), 1.84* (H6*endo*), 1.69* (H7*exo*), 1.64* (H6*exo*), 1.62* (H3*endo*), 1.42* (H7*endo*), 1.37 (d of t, $^2J_{8anti,8syn}$ = 11.8 Hz, $^3J_{8anti,1}$ = $^3J_{8anti,5}$ = 5.1 Hz, H8*anti*), 1.08 (s, $W_{h/2}$ = 1.0 Hz, Me). ^{13}C NMR δ_C ($CDCl_3$): 78.2 (C2), 55.7 (C4), 48.6 (OMe), 43.2 (C5), 42.0 (C1), 41.5 (C3), 33.5 (C8), 26.2 (C7), 24.2 (C6), 21.5 (Me). LRMS: $C_{10}H_{17}{}^{81}BrO$ M$^{\bullet+}$ requires

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234, found 234; $C_{10}H_{17}{}^{79}BrO$ $M^{\bullet+}$ requires 232, found 232; $C_9H_{14}{}^{81}BrO$ $[M - 15]^{\bullet+}$ requires 219, found 219 (10%); $C_9H_{14}{}^{79}BrO$ $[M - 15]^{\bullet+}$ requires 217, found 217. HRMS: $C_9H_{14}{}^{81}BrO$ [M - 15]$^{\bullet+}$ requires 219.0209; found 219.0219. **4-*endo*-Bromo-2-*endo*-methoxy-2-*exo*-methylbicyclo[3.2.1]-octane** (**11**) was obtained as a colorless oil. ^1H NMR δ_H ($CDCl_3$): 4.18 (m, $^3J_{4,3endo} = 12.2$ Hz, $^3J_{4,3exo} = 5.4$ Hz, $^3J_{4,5} = 2.4$ Hz, H4), 3.16 (s, $W_{h/2} = 0.6$ Hz, OMe), 2.50 (m, H5), 2.18 (m, H1), 2.10 (m, $^2J_{3exo,3endo} = 13.2$ Hz, $^3J_{3exo,4} = 5.4$ Hz, $^4J_{3exo,1} = {}^4J_{3exo,5} = 1.4$ Hz, H3*exo*), 1.84* (H6*endo*), 1.83* (H3*endo*), 1.82* (H7*endo*), 1.65* (H7*exo*), 1.50−1.58 (H8*anti*, H8*syn*), 1.50* (H6*exo*), 1.20 (Me). ^{13}C NMR δ_C ($CDCl_3$): 76.8 (C2), 54.6 (C4), 48.5 (OMe), 44.0 (C5), 43.0 (C3), 42.0 (C1), 34.7 (C8), 23.9_4 (C6 or C7), 23.8_5 (C7 or C6), 21.3 (Me). The quaternary carbon (C2, 76.8 ppm) was not observed in the ^{13}C NMR spectra but its chemical shift was calculated from a correlation observed in an HMBC experiment. LRMS: $C_{10}H_{17}{}^{81}BrO$ $M^{\bullet+}$ requires 234, found 234; $C_{10}H_{17}{}^{79}BrO$ $M^{\bullet+}$ requires 232, found 232; $C_9H_{14}{}^{81}BrO$ $[M - 15]^{\bullet+}$ requires 219, found 219; $C_9H_{14}{}^{79}BrO$ $[M - 15]^{\bullet+}$ requires 217, found 217. HRMS: $C_9H_{14}{}^{81}BrO$ $[M - 15]^{\bullet+}$ requires 219.0209, found 219.0208.

Reaction of 2-Methyl-*endo*-tricyclo[3.2.1.0^{2,4}]oct-6-ene (2) with Bromine in Carbon Tetrachloride. (i) At Room Temperature. A solution of bromine (396 mg, 2.48 mmol) in CCl_4 (10 mL) was added dropwise over 10 min to a stirred solution of **2** (320 mg, 2.66 mmol, 1.1 mol equiv) in CCl_4 (5 mL) at room temperature. After 1 h the solvent was removed under reduced pressure to give a brown oil (696 mg, ca. 100% recovery). A ^1H NMR spectrum showed the oil to consist of one major product which was identified as 7-*exo*,8-*anti*-dibromo-2-methylbicyclo[3.2.1]oct-2-ene (**13**) (ca. 80%). The major product was purified by rapid radial chromatography (2 mm silica plate, 10% ether/pentane elution). The product ratios could not be determined by GLC analysis due to the instability of the major product (GLC analysis showed five products, 10−20% each, to be present which was not in agreement with the ^1H NMR spectrum). A large number of minor products were also present, but these were estimated (^1H NMR) to comprise not more than 20% of the overall reaction mixture. **7-*exo*,8-*anti*-Dibromo-2-methylbicyclo-[3.2.1]oct-2-ene** (**13**) was obtained as a colorless oil. ^1H NMR δ_H ($CDCl_3$): 5.14 (s, $W_{h/2} = 8.0$ Hz, H3), 4.42 (s, $W_{h/2} = 3.1$ Hz, H8), 4.27 (m, $^3J_{7,6endo} = 8.3$ Hz, $^3J_{7,6exo} = 3.8$ Hz, H7) 2.88 (m, $^2J_{6exo,6endo} = 14.8$ Hz, H6*exo*), 2.84 (s, $W_{h/2} = 4.1$ Hz, H1), 2.71 (m, H5), 2.54 (m, $^2J_{4exo,4endo} = 17.9$ Hz, H4*exo*), 2.43 (d of d, $^2J_{6endo,6exo} = 14.9$, $^3J_{6endo,7} = 8.3$ Hz, H6*endo*), 1.92 (m, $^2J_{4endo,4exo} = 17.8$ Hz, H4*endo*), 1.73 (d of d, $^4J_{Me,3exo} = 3.9$ Hz, $^4J_{Me,3endo} = 3.9$ Hz Me). ^{13}C NMR δ_C ($CDCl_3$): 140.0 (C2), 119.1 (C3), 57.5 (C1), 55.9 (C8), 48.9 (C7), 44.8 (C5), 43.3 (C6), 36.2 (C4), 22.2 (Me). HRMS: $C_9H_{12}{}^{81}Br_2$ $M^{\bullet+}$ requires 281.9267, found 281.9244; $C_9H_{12}{}^{79}Br^{81}Br$ $M^{\bullet+}$ requires 279.9287, found 279.9241; $C_9H_{12}{}^{79}Br_2$ $M^{\bullet+}$ requires 277.9307, found 277.9240.

(ii) At −10 °C. The reaction procedure was similar to that used for the reaction of **2** with bromine in carbon tetrachloride at room temperature, except that the reaction was carried out at −10 °C (ice−NaCl bath) with **2** (126 mg, 1.05 mmol) and bromine (138 mg, 0.86 mmol, 0.82 mol equiv) and gave a yellow oil (309 mg). A ^1H NMR spectrum showed a complex reaction mixture consisting of 7-*exo*,8-*anti*-dibromo-2-methylbicyclo-[3.2.1]oct-2-ene (**13**) (30−40%), two other major products (ca. 10% and 20%), 6-*exo*-bromo-4-methyltricyclo[3.2.1.0^{2,7}]oct-3-ene (**16**) (ca. 5%), and other minor products. Attempted purification by column chromatography on silica gel (by gradient elution with ether/pentane mixtures) failed to give any significant separation. Compound **16** was not isolated, but was identified from a ^1H NMR spectrum of the crude reaction mixture with that of authentic samples.

Reaction of 2-Methyl-*endo*-tricyclo[3.2.1.0^{2,4}]oct-6-ene (2) with Bromine in Methanol. (i) At Room Temperature. A solution of bromine (280 mg, 1.75 mmol) in dry methanol (10 mL) was added dropwise over 10 min to a stirred solution of **2** (235 mg, 1.96 mmol, 1.1 mol equiv) in dry methanol (5 mL) at room temperature. The reaction was stirred for 2.5 h after which time the methanol was removed under reduced pressure to give a yellow oil (669 mg, some methanol still present). A ^1H NMR spectrum of the oil showed a complex reaction mixture with numerous products. Attempted separation by radial chromatography (on a 2 mm silica plate, gradient elution with ether/pentane mixtures) followed by further purification by dry column flash chromatography gave two products, 7-*anti*-bromo-5-*endo*-methoxy-1-methylbicyclo[2.2.2]oct-2-ene (**17**) (ca. 15%) and 6-*exo*-bromo-4-methyltricyclo[3.2.1.0^{2,7}]oct-3-ene (**16**) (ca. 10%). No other products were isolated. **6-*exo*-Bromo-4-methyltricyclo-[3.2.1.0^{2,7}]oct-3-ene** (**16**) was obtained as a colorless oil. ^1H NMR δ_H ($CDCl_3$): 5.51 (m, $^3J_{3,2} = 4.8$ Hz, $^4J_{3,Me} = 1.6$ Hz, H3), 3.69 (s, $W_{h/2} = 2.5$ Hz, H6), 2.53 (d, $^3J_{5,8anti} = 4.9$ Hz, H5), 2.22 (m, $^2J_{8anti,8syn} = 11.8$ Hz, $^3J_{8anti,1} = 2.3$ Hz, $^3J_{8anti,5} = 4.7$ Hz, H8*anti*), 1.72 (d, $^4J_{Me,3} = 1.7$ Hz, Me), 1.68* (H7), 1.63* (H2), 1.59* (H1), 0.91 (d, $^2J_{8syn,8anti} = 11.8$ Hz, H8*syn*). ^{13}C NMR δ_C ($CDCl_3$): 136.5 (C4), 115.9 (C3), 56.5 (C6), 47.2 (C5), 25.5 (C8), 22.5 (C7), 20.1 (Me), 18.5 (C2), 15.4 (C1). **7-*anti*-Bromo-5-*endo*-methoxy-1-methylbicyclo[2.2.2]oct-2-ene** (**17**) was obtained as a colorless oil. ^1H NMR δ_H ($CDCl_3$): 6.23 (t, $^3J_{3,2} = {}^3J_{3,4} = 8.1$ Hz, H3), 6.07 (d, $^3J_{2,3} = 8.0$ Hz, H2), 3.80 (m, $^3J_{7,8syn} = 10.1$ Hz, $^3J_{7,8anti} = 4.3$ Hz, $^4J_{7,6endo} = 2.4$ Hz, H7), 3.69 (d of t, $^3J_{5,4} = {}^3J_{5,6endo} = 3.0$ Hz, $^3J_{5,6exo} = 8.1$ Hz, H5), 3.29 (s, $W_{h/2} = 0.6$ Hz, OMe), 2.82 (m, H4), 2.36 (d of d, $^2J_{6exo,6endo} = 13.7$ Hz, $^3J_{6exo,5} = 8.1$ Hz, H6*exo*), 2.25 (m, $^2J_{8syn,8anti} = 14.4$ Hz, $^3J_{8syn,7} = 10.2$ Hz, $^3J_{8syn,4} = 4.1$ Hz, H8*syn*), 1.81 (m, $^2J_{8anti,8syn} = 14.6$ Hz, $^3J_{8anti,7} = 4.3$ Hz, $^3J_{8anti,4} = 2.1$ Hz, H8*anti*), 1.24 (s, $W_{h/2} = 1.1$ Hz, Me), 1.07 (d of t, $^2J_{6endo,6exo} = 13.7$ Hz, $^3J_{6endo,5} = {}^3J_{6endo,7} = 2.7$ Hz, H6*endo*). ^{13}C NMR δ_C ($CDCl_3$): 136.7 (C2), 132.4 (C3), 80.1 (C5), 58.1 (C7), 55.8 (OMe), 39.4 (C1), 37.3 (C6), 36.8 (C8), 34.8 (C4), 24.1 (Me). LRMS: $C_{10}H_{15}{}^{81}BrO$ $M^{\bullet+}$ requires 232, found 232; $C_{10}H_{15}{}^{79}BrO$ $M^{\bullet+}$ requires 230, found 230. HRMS: $C_{10}H_{15}{}^{79}BrO$ $M^{\bullet+}$ requires 230.0307, found 230.0259.

(ii) at −20 and −78 °C. A procedure similar to that used for the reaction of **2** with bromine in MeOH at room temperature was used except that the reactions were cooled to −20 °C (CCl_4/dry ice bath) or −78 °C (acetone/dry ice bath) and performed in methanol-d_4 to allow analysis of the reaction mixtures by NMR directly without workup. ^1H NMR spectra of the crude reactions showed the formation of a complex mixture of products in both cases. The products were not further investigated.

Acknowledgment. We acknowledge grants from the New Zealand Lotteries Board.

Supporting Information Available: Copies of ^1H and ^{13}C NMR spectra of all new compounds and details of the computations (25 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO951470S