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Studies of Proton Addition to *exo*- and *endo*-Tricyclo[3.2.1.0^{2,4}]octane

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Abstract: Semiempirical methods have been used to locate the stationary points on the potential energy surface for the reaction of *endo*- and *exo*- tricyclo[3.2.1.0^{2,4}]octanes (1) and (2) with protonated methanol. The calculations show a thermodynamic preference for rupture of the C2C4 bond. The corner transition states for cleavage of the C2C4 bonds show elongation of both the C2C4 and C2C3 cyclopropyl bonds. This is consistent with interaction of the incoming protonated methanol with both the HOMO and HOMO-1 orbitals of the cyclopropanes. For edge attack the semiempirical transition states show elongation of the C2C4 bonds, but not of the C2C3 bonds. Mapping of the HOMO and HOMO-1 orbitals on to the electron density surface provides a simple method of predicting reaction stereochemistry.

INTRODUCTION

The use of cyclopropanes as intermediates in organic syntheses has received considerable attention over recent years as a method for 1,3-difunctionalisation. The reactivity of cyclopropanes often parallels that of alkenes more closely than other cyclic hydrocarbons. When the cyclopropane is fused to other ring systems it can be induced to undergo internal bond rupture with consequent ring enlargement. A knowledge of the factors which effect and control the stereospecificity of cyclopropane ring opening are therefore important in order to be able to fully utilise the unusual reactivity of cyclopropanes as intermediates in organic syntheses.

For sometime we have been interested in the stereospecificity of cyclopropane ring opening. Inclusion of the cyclopropyl moiety into a tricyclic hydrocarbon allows the trajectory of H^+/D^+ addition to be definitively established in an environment where the orbital topology is well defined. The reactions of *endo*- and *exo*-tricyclo[3.2.1.0^{2,4}]octanes (1) and (2) with H^+/D^+ have been examined experimentally and the trajectory of electrophilic attack determined to occur at the corner to the most substituted (C2C4) bond resulting in inversion of configuration at that site.[1] For these systems proton addition to the edge of the C2C4 bond has never been observed, however for tricyclo[3.2.2.0^{2,4}]non-6-ene, edge attack competes with corner attack.[2] We now report studies using semiempirical molecular orbital methods in an attempt to rationalise the orbital effects that control the regio- and stereoselectivity of the addition process.

METHODS

The theoretical methods used in these studies were the semiempirical PM3[3] method and ab initio calculations at the HF/3-21G* level of theory. The PM3 method is a modification of the MNDO method which Stewart[4] considers to be an improvement on the AM1[5] method. The calculations were performed using the Spartan package.[6] Distances are given in angstroms and the mirror image structure that best allow the bond distances to be presented is shown.

RESULTS AND DISCUSSION

In considering the addition of methanol to **1** and **2** the following issues are addressed: the regiochemistry of addition, the stereochemistry of the attack by the electrophile and the stereochemistry of attack by nucleophile. Each of the issues is addressed for **1** then for **2** and the results of the calculations compared with previously reported[1] experimental observations.

The regiochemistry of addition to **1** *and* **2**

Semiempirical calculations (PM3) of **1** and **2** show that the electron density of the HOMO is predominantly associated with the C2C4 bond. From frontier orbital considerations the interaction of the HOMO with the LUMO of an incoming electrophile would be expected to be the dominant orbital interaction in facilitating reaction. Preferential rupture of the internal cyclopropyl bond would therefore be expected.[7] The calculated heats of formation of cations **3**, **4** and **5**, the three possible classical cations that may result from cleavage of the cyclopropane in **1**, show the bicyclo[3.2.1]octanyl cation **5** (from rupture of the C2C4 bond) is the most stable by approximately 49 kJ mol^{-1} (Figure 1). These results[8] are consistent with the experimental observations[1] that cleavage of the C2C4 internal bond of the cyclopropane ring occurs on reaction with $H^+(D^+)$ (see Figures 4 and 5).

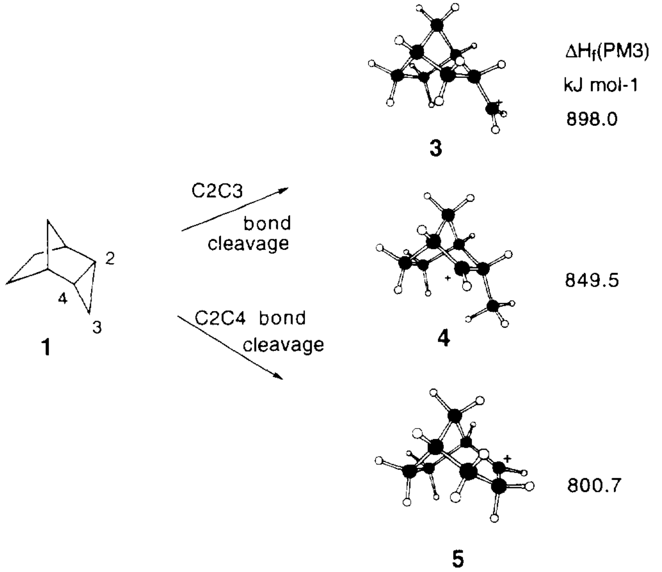


Figure 1. C2C3 and C2C4 bond rupture of **1** on reaction with H$^+$

Similarly, the calculated energies of the classical cations **5**, **6**, and **7** that can be formed from **2**, show cation **5** is favoured by 55 kJ mol^{-1} (Figure 2). This is consistent with the cleavage of the C2C4 bond being the dominant pathway that is observed (76%) for reaction of **2** with acid in methanol.[1] The other significant product (15%) is a result of C2C3 ring cleavage (e.g. **7**) and Wagner Meerwein rearrangement.

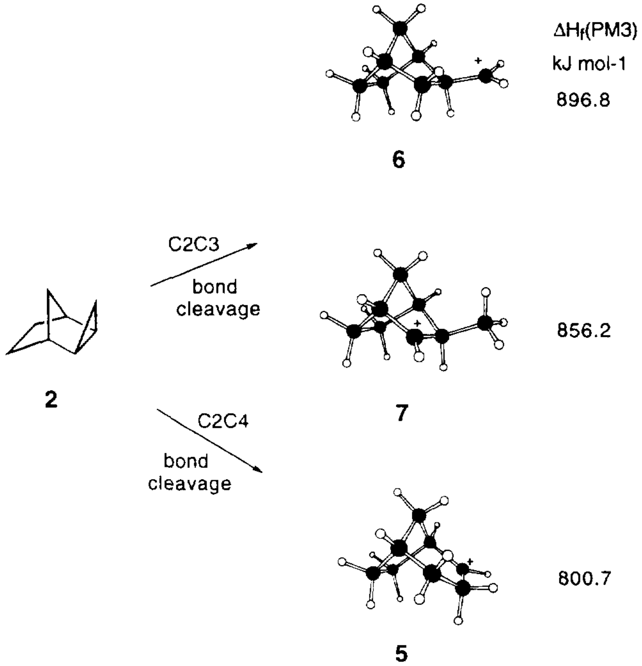


Figure 2 C2C3 and C2C4 bond rupture of **2** on reaction with H^+

Frontier orbital analysis of **1** and **2** and PM3 calculations of the possible classical ions **3**-**7** that may result from rupture of C2C4 and C2C3 bonds are consistent with the preference observed in the experiments for products of rupture of the internal C2C4 cyclopropyl bond. Cation **5** might be expected to be initially formed as a chair conformation in the reaction of **1**, and in a boat conformation from reaction of **2** (Figures 3).

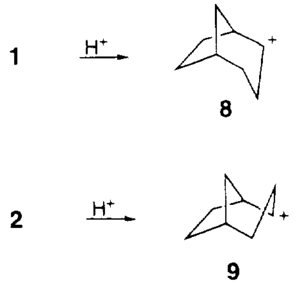


Figure 3. Least motion conformations of cations formed from **1** and **2** by C2C4 bond rupture.

When either the chair or the boat conformation is used as an input geometry for a PM3 calculation, minimisation gives the cation **5** in a pseudo planar conformation. The semiempirical method therefore predicts the open cation formed from cleavage of the C2C4 bond of **1** and **2** to be identical. If cation **5** were common to both the reactions of **1** and **2**, its intermediacy can not account for the stereospecific attack of a nucleophile in the reaction of each hydrocarbon with protonated methanol. For each substrate methanol addition occurs with inversion of configuration[1] (Figures 4 and 5). The stereochemistry of nucleophilic attack is discussed in detail later.

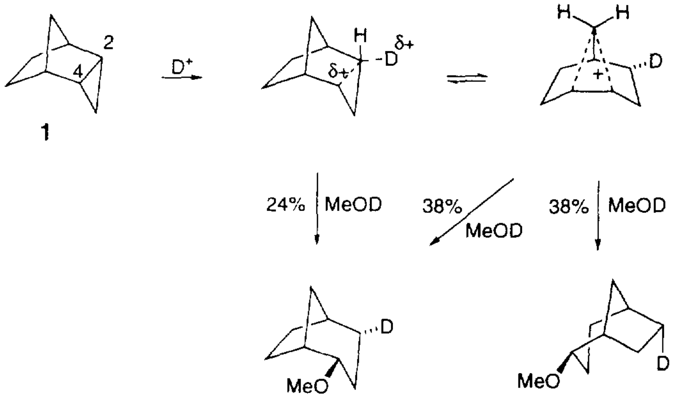


Figure 4. Reaction of **1** with acid in methanol.

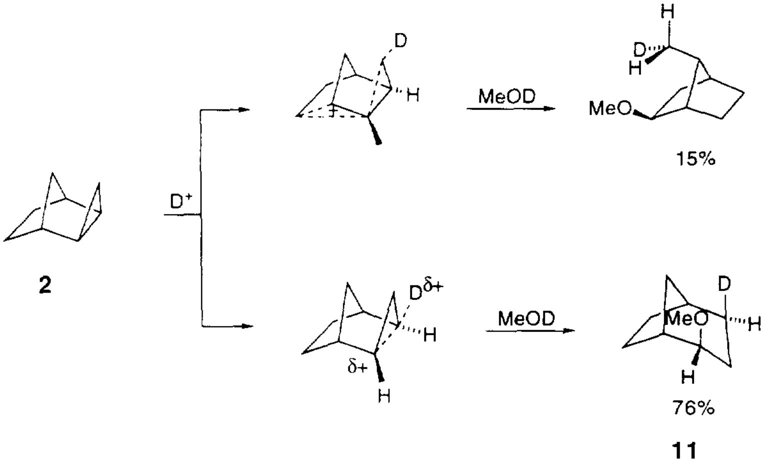
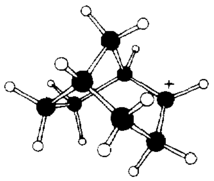


Figure 5. Reaction of **2** with acid in methanol.

Optimisation of a chair conformation of cation **5** at the HF/3-21G* level of theory retains the chair like



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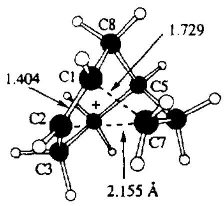


10

conformation **8** (E = -308.52998 hartrees). In contrast optimisation of the cation **9** with the three carbon bridge as part of a boat conformation (HF/3-21G* basis set) led to the collapse of the structure to a unsymmetrical nonclassical cation **10** (E = -308.52938 hartrees) as an intermediate. For ion **8** the p-orbital on the face *syn* to C8 is more hindered that the *anti* face and this is consistent with the stereochemistry observed for nucleophilic attack of methanol on **1** (Figure 4). For ion **10** which is non-classical but with greater charge at C2 than C1, the C2C7 bond is longer (2.155 Å) than C1C7 (1.729 Å), and hence nucleophilic attack will be expected at C2. The bridged nature of the cation will ensure that nucleophilic attack occurs with inversion of configuration and this is consistent with experiment (Figure 5). This suggests that ion **10** may be an intermediate on the reaction pathway of **2** to **11**. Ion **10** can rearrange by way of transition state **12** (E = -308.52875 hartrees) to the bicyclo[2.2.2]octan-2-yl cation (**13**) (E = -308.52990 hartrees) but products resulting from nucleophilic capture of this cation are not observed experimentally (Figure 6).

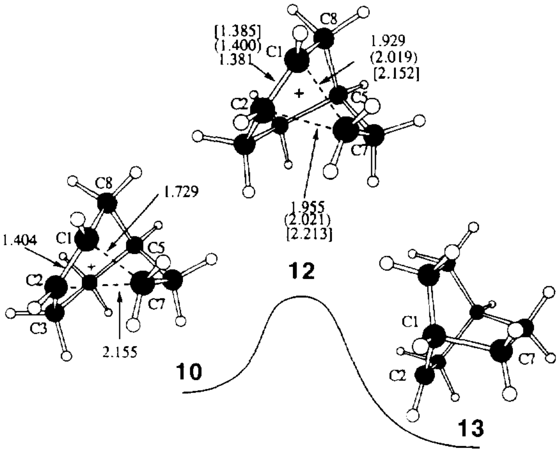


Figure 6 Structure of transition state **12** 3-21G* basis set, (PM3) [AM1] between **10** and **13**.

Trajectory of electrophilic attack on 1

We now report calculations of the relative energies of edge and corner trajectories for proton attack on **1** and **2**.[9] Attack of H$^+$ on **1** is predicted[10] by the PM3 method to occur without an activation barrier in the gas phase. We therefore examined the transfer of a proton from protonated methanol to **1** and **2** as a more appropriate model for the experimental studies and where a transition structure might be able to be identified.

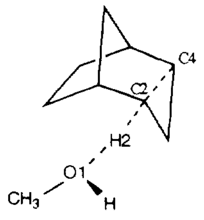


Figure 7. Input geometry of the grid calculation for corner attack of MeOH$_2^+$ on **1**.

(i) Corner attack: Attack of protonated methanol at the corner of the cyclopropane was modelled by first evaluating the PM3 heat of formation of geometries at varying lengths of the H2O1 and H2C2 distances (Figure 7), after initially placing the proton from the MeOH$_2^+$ moiety that is to be transferred to the cyclopropane in the plane of the cyclopropane ring. A possible transition state was identified at an O1H2 distance of 1.3 Å and a C2H2 distance of 1.5 Å. Starting from this geometry the structure was refined by a gradient norm minimisation procedure to locate a transition structure which showed one imaginary frequency characteristic of a transition structure.[11] The oxygen of the methanol group is enantiotopic (see figure 7). The methyl and the proton on the oxygen not being transferred to the cyclopropane ring were interchanged. This resulting structure was investigated in some detail. The O1H2 bond of this structure was systematically rotated through 360° in 30° increments while the O1CH$_3$ bond rotated through 120° with 10° increments. The O1H2 and C2-H2 distances fixed at the transition structure values. The resulting potential energy surface is relatively flat. The lowest energy structure identified on the potential energy surface was refined by gradient minimisation with no geometric constraints imposed. The resulting structure **14** was shown to be a transition structure by the presence of one negative force constant (Figure 8). The corresponding imaginary frequency showed a simultaneous elongation of the O1H2, C2C4, and C2C3 distances and contraction of H2C2. The transition structure therefore corresponds to a structure that leads directly to ring opening.[12] The potential energy surface for the rotation of the methanol moiety in the initial structure was searched by rotating the O1H2 bond through 360° with 90° increments and reoptimising at each point. The surface was relatively flat. Three of the four initial structures converged to the same final geometry, **15** (731.8 kJ mol^{-1}) and the fourth collapsed to a transition structure that was 0.8 kJ mol^{-1} higher in energy. The methanol moiety would therefore be expected to rotate without a significant barrier. The transition structure **14** is lower in energy (1.9 kJ mol^{-1})

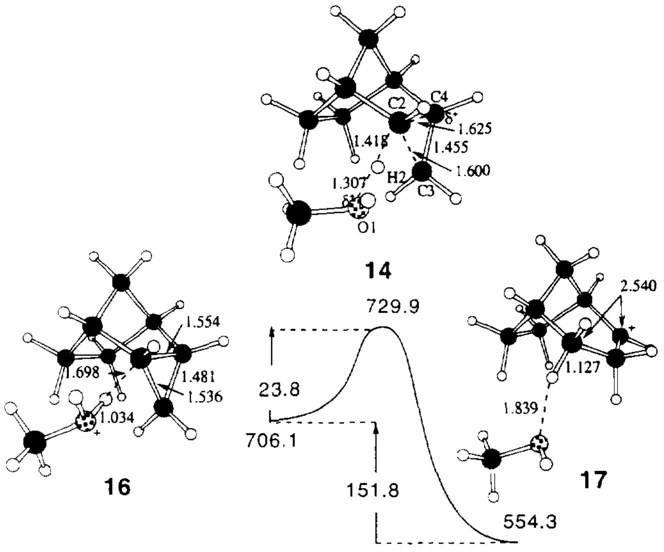
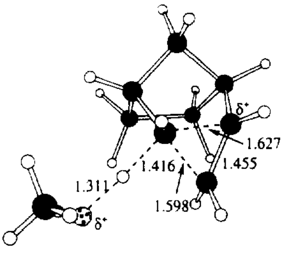


Figure 8. Corner proton transfer from MeOH$_2^+$ to **1**



15

than **15**, and was the lowest energy transition state found. The configuration at the oxygen therefore has only a small effect on the energy of the transition structure.

In order to locate the species that interconverted by way of **14** the following calculations were performed. On lengthening the H2C2 bond of **14** to 1.8 Å and decreasing the O1-H2 bond length to 1.2 Å, followed by geometry optimisation on an energy criterion, the structure collapsed to complex **16** consisting of a complex of protonated methanol and **1**. This structure corresponds to a minimum on the potential energy surface formed on approach of protonated methanol to **1**. In a second series of calculations the transition state **14** was reoptimised by an energy criterion and give **17** which was shown to be a minimum on the potential energy surface (all force constants were positive) and is in effect a complex of cation **5** and methanol formed after proton transfer. The barrier to activation for proton transfer from the complex of protonated methanol and **1** (ΔH_f(**14**) - ΔH_f(**16**)) is 23.8 kJ mol^{-1} and the overall enthalpy change for proton transfer (ΔH_f(**17**) - ΔH_f(**16**)) is -151.8 kJ mol^{-1}. Comparison of the relative charges of C3 and C4 (-0.002 and 0.030, respectively) of **14** shows more positive charge development at C4 than at C3 due to the greater ability of the hydrocarbon skeleton to donate electron density to C4. Transition state **14** therefore collapses to form carbocation **5**.[1]

(ii) Edge attack: In order to model the attack of protonated methanol on **1** from an edge trajectory, an approximation to the transition structure was derived from building the hydrocarbon skeleton onto a previously obtained edge transition state for $MeOH_2^+$ addition to cyclopropane. In the transition structure model O1-H2, H2C2, and H2C4 distances were fixed and the remaining parts of the structure allowed to minimise using molecular mechanics methods. The resulting structure was reoptimised by a gradient norm minimisation procedure using the PM3 parameterised Hamiltonian. The methanol moiety in the structure was rotated about the O1H2 bond in 90° increments through 360°. Full transition structure optimisation was effected at each point. The lowest energy transition structure obtained, **18**, has one imaginary frequency. The single imaginary frequency corresponds to a symmetrical contraction of H2C2 and H2C4 distances and elongation of the H2O1 and C2C4 bonds. This is consistent with the structure being a transition structure for edge attack of protonated methanol on the C2C4 bond of **1** (Figure 9). Epimerisation at oxygen followed by geometry optimisation resulted in a structure that is virtually a mirror image of **18**.

The minima **19** and **20** on either side of the transition structure were determined using similar procedures to those described above. Optimisation of transition structure **18** on an energy criterion after lengthening the H2C2 and H2C4 distances to 1.8 Å and decreasing H2O1 to 1.2 Å, gave **19** that corresponds to an edge complex of protonated methanol and **1**. The minimum **20** was found by geometry optimisation of the transition structure **18** on an energy criterion.[13] The structure is unsymmetrical and corresponds to the

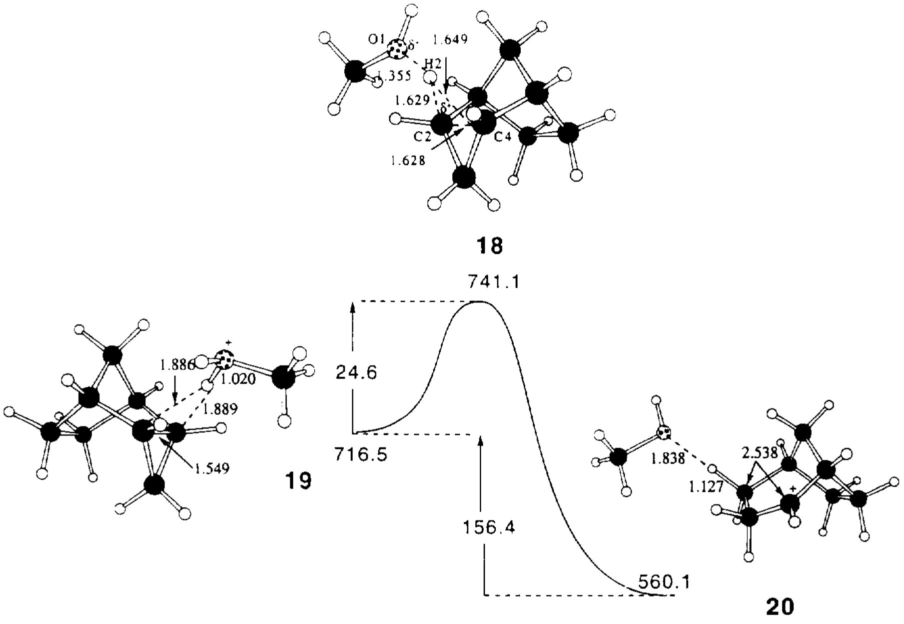


Figure 9. Edge proton transfer from MeOH$_2^+$ to **1**.

complex of protonated methanol and the open bicyclic cation formed after proton transfer from MeOH$_2^+$ to **1** had occurred. The activation barrier for edge proton addition to **1** (ΔH_f(**18**) - ΔH_f(**19**)) is 24.6 kJ mol^{-1} and the overall enthalpy change for the proton transfer (ΔH_f(**20**) - ΔH_f(**19**)) is -156.4 kJ mol^{-1}.

The relative energies of the transition structures and minima found for both corner and edge attack of MeOH$_2^+$ on **1** are summarised in Figure 10. The calculations indicate that the activation barriers between **19** and **18** and **16** to **14** are similar (24.6 kJ mol^{-1} and 23.8 kJ mol^{-1}, respectively) while the energies of the two minima **16** and **19** differ significantly (706 kJ mol^{-1} and 716 kJ mol^{-1}, respectively). If it is assumed that the density of states of **18** and **14** are comparable and represent the dynamics of the system, the corner protonated pathway (channel) for the reaction is favoured (i.e. **1-16-14-17-5**). This is supported by the experimental results that show exclusive corner addition of an electrophile (H^+/D^+)[1].

The electron distribution in the HOMO of **1** shows no obvious reason for the predominance of corner attack over edge attack. When the HOMO of **1** is mapped onto the electron density surface in Spartan[6] the areas of high correlation show little variation between the sites of corner and edge attack of the C2C4 bond. The HOMO-1 orbital of **1** forms the C2C3 (C4C3) bond. When in addition to mapping the HOMO orbital the HOMO-1 orbital is simultaneously mapped onto the electron density surface the area of high correlation at the edge of the C2C3 bond overlaps with the area of high correlation of corner attack at C2C4.

No overlap of the area of high correlation at the edge of the C2C4 bond with the corner of the HOMO-1 of the C2C3 bond was observed and therefore including the HOMO-1 in edge attack at C2C4 provides little benefit. Interaction of the attacking electrophile with the HOMO-1 orbital results in a stabilising effect on the corner attack trajectory that is not present in the edge attack pathway. Interaction with the HOMO-1 orbital

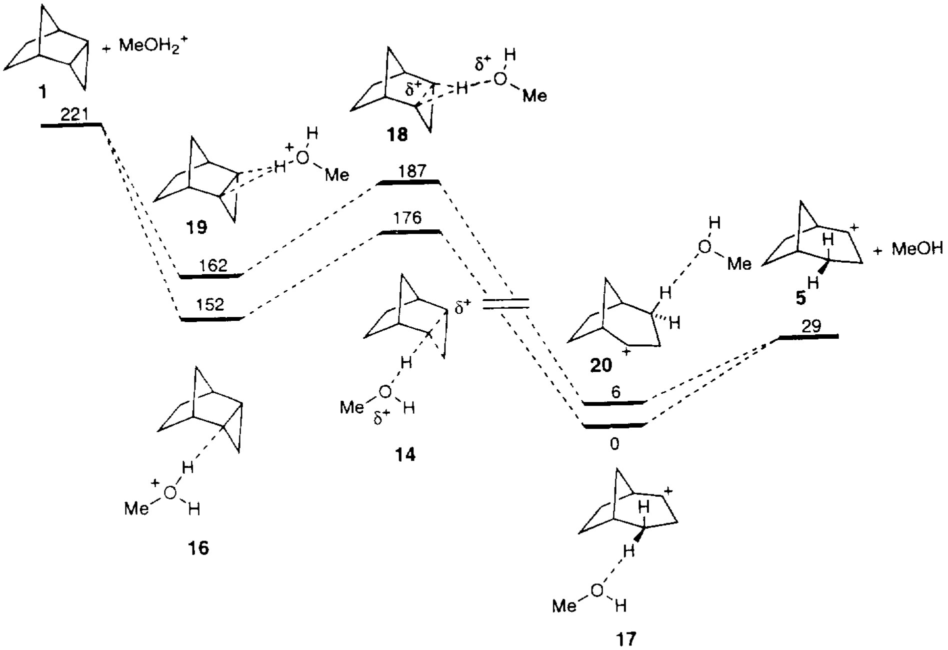


Figure 10. The relative energies of the species (PM3) involved in edge and corner protonation of **1**. Energies are in kJ mol^{-1} relative to intermediate **17**.

would favour corner attack with rupture of the C2C4 bond.[14] In a frontier orbital analysis, it is apparent that orbital interactions with the HOMO-1 as well as the HOMO may play an important part in determining the stereoselectivity. In the process of corner attack, both the C2C4 and C2C3 bonds are partially broken at the transition structure and not just the bond (C2C4) *anti* to the incoming electrophile.[1] In transition structure **14** both the C2C4 and C2C3 bond lengths are lengthened to 1.625 Å and 1.600 Å, respectively and the C4C3 bond is significantly shortened (1.455 Å). In **1** the C2C3 bond length is 1.503. This supports the assumption that the HOMO-1 orbital is involved in the proton transfer, as this orbital is predominantly responsible for formation of the C2C3 bond. The importance of the interaction of orbitals other than the HOMO with incoming electrophiles has previously been suggested by Wiberg,[7] who found that in some cases the HOMO is responsible for only half of the electron density contributed to the attacking proton on addition to a cyclopropane ring.

Nucleophilic attack in the reaction of **1**

In this system the possibility of rearrangement to a nonclassical species **21** or rapid inter-conversion of cations, **5** or **8** to their enantiomers (Figure 11), can explain the observation that nucleophilic attack occurs exclusively with inversion. Calculations of the non classical structure **21** at PM3 and HF/3-21G* level of theory show it to be a transition structure. Barriers to the interconversion of **5** with its enantiomer are high at the PM3 level (54.4 kJ ml^{-1}) but lower for **8** at the HF/3-21G* level (7 kJ mol^{-1}). The geometry of cation **8** where the ring is in chair shows the LUMO to be more open to 'bottom' face attack (*anti* to C8) than from the

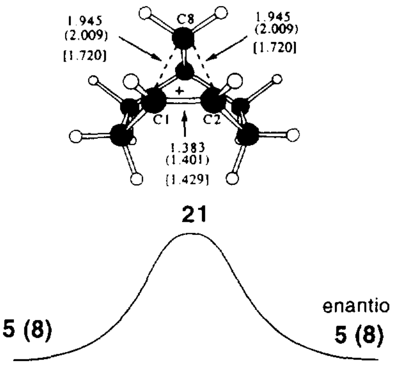


Figure 11. Structure of cation **21** from ab initio 3-21G* basis set, (PM3) and [MINDO/3].

'top' face (*syn* to C8). Nucleophilic capture would therefore be expected to occur with inversion of configuration as was observed by experiment.[1] Also mapping of the LUMO orbital of **8** onto the electron density surface shows nucleophilic attack to the bottom" of the carbocation p-orbital to be sterically less hindered than attack at the top and this is also consistent with the experimental results (see Figure 4).

Proton transfer from protonated methanol to 2.

The reaction of protonated methanol with **2** from both corner and edge trajectories was considered in a similar way to that of **1**. The cations resulting from cleavage of the C2C4 or C2C3 (C3C4) bonds of **2** were discussed earlier. Rupture of the internal C2C4 bond results in formation of the most stable carbocation **5**.

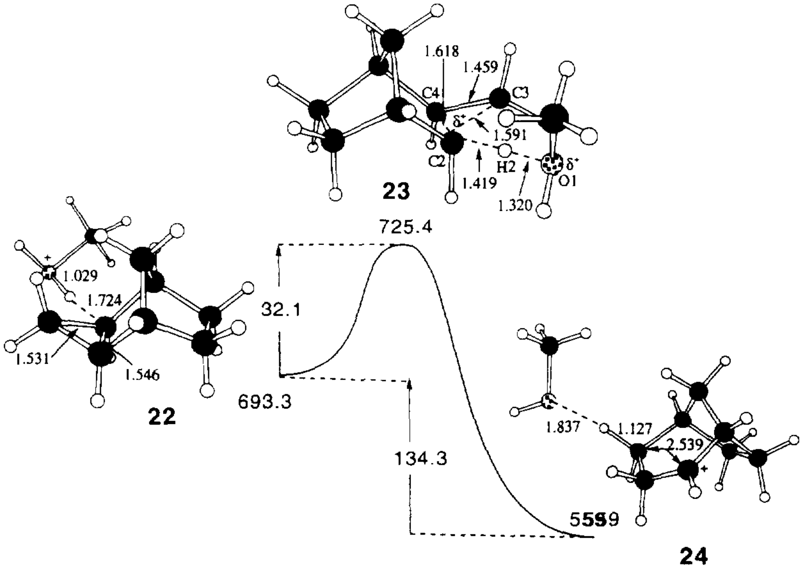


Figure 12. Corner proton transfer from $MeOH_2^+$ to **2**.

Trajectory of electrophilic attack

(i) Corner attack: For corner attack, an initial complex of **2** and protonated methanol, namely **22**,[15] is related by the transition structure **23**[16] with the product complex **24**[17] (Figure 12). The transition structure **23** is slightly lower in energy than its diastereoisomer **25**.

(ii) Edge attack: For edge attack, the initial complex **26**[18] is related by the transition structure **27**[19] to the complex **28**.[20] The activation barrier for edge addition of $MeOH_2^+$ to the C2C4 bond of **2** was calculated to be (ΔH_f(**27**) - ΔH_f(**26**)) 28.5 kJ mol^{-1} and the overall enthalpy change for the reaction to be -131 kJ mol^{-1} (ΔH_f(**28**) - ΔH_f(**26**)) (Figure 13).

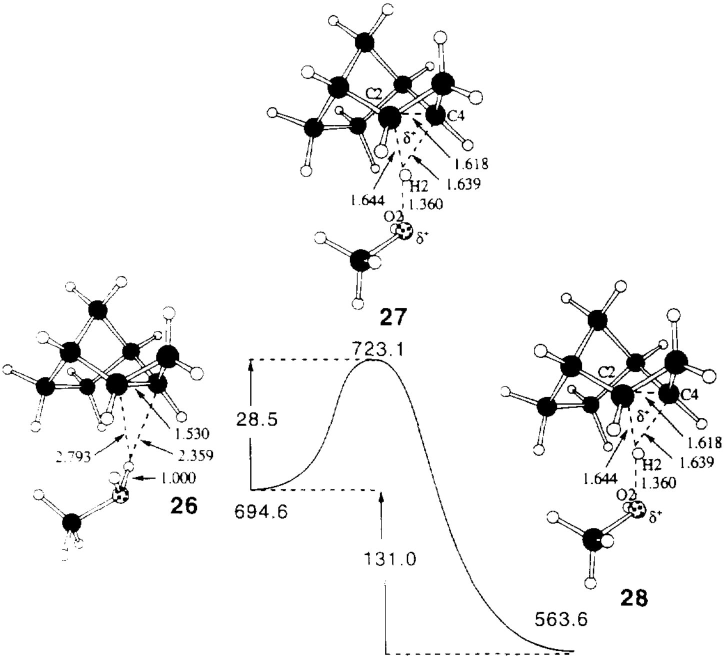


Figure 13. Edge proton attack from $MeOH_2^+$ to 2.

The results of the semiempirical calculations for proton transfer to **2** are summarised in Figure 14. The corner and edge trajectories for addition to the C2C4 bond are calculated to have similar activation barriers of 32.1 kJ mol^{-1} and 28.5 kJ mol^{-1}, respectively for the rearrangement reactions from the complex. The population of the initially formed complex is weighted towards the corner attack complex **22**. However the difference in energy between **22** and **23** is greater than between **26** and **27** and if it is assumed that the densities of states of **27** and **23** are similar and reflect in the dynamics of the transformation then the edge and corner pathways are not easy to differentiate.[21] The experimental results however show attack occurs from a corner trajectory at the C2C4 bond[1] and cleavage of the C2C3 bond does compete with C2C4 bond rupture. Mapping the HOMO orbital of **2** onto the electron density surface[4] shows there is little reason for preference between corner and edge of the C2C4 bond at the sites of their respective maximum correlation. For corner attack the areas of high correlation of the two orbitals, HOMO-1 and HOMO, and the electron density surface

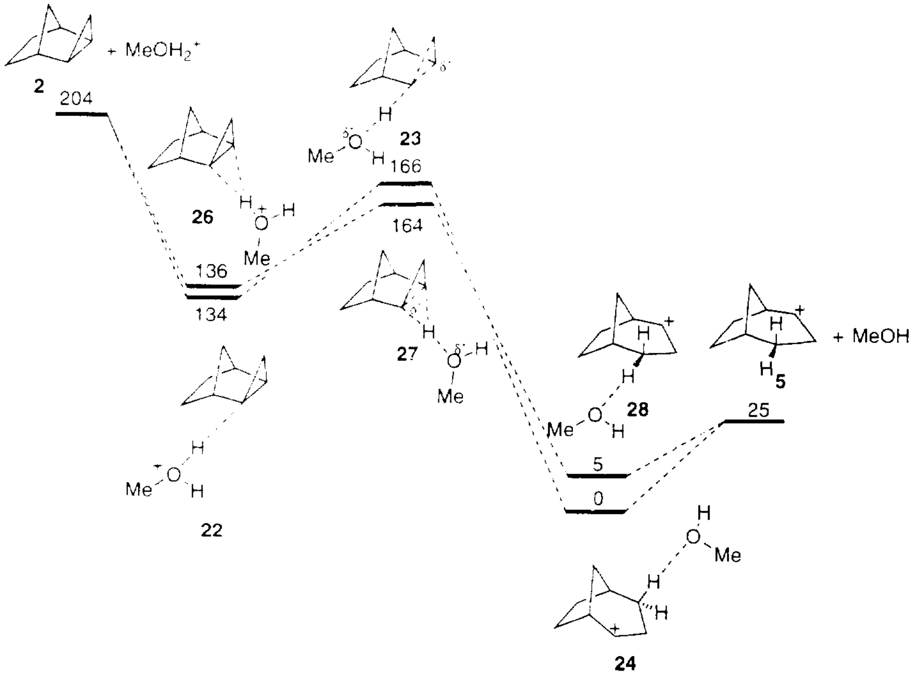
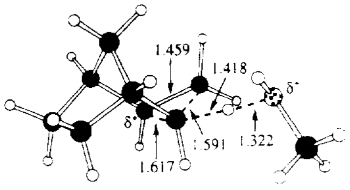


Figure 14. Relative energies (PM3) of the species involved in edge and corner addition of $MeOH_2^+$ to **2**. Energies are in kJ mol^{-1} relative to intermediate **24**.

partially overlap, supporting corner attack. This is not the case for edge attack. The area of high correlation of the HOMO-1 and electron density surface partially overlaps with the area of high correlation of the HOMO so therefore as the electrophile approached the HOMO orbital from the corner of the C2C4 bond it also experiences a favourable interaction with the HOMO-1. The corner attack transition structure **23** showed an increase in length of both the C2C3 and C2C4 bonds (C2C3 1.591 Å, C2C4 1.618 Å) (similar to those observed for **14**) consistent with the importance of the donation of electrons to the electrophile from both the HOMO and HOMO-1 orbitals to the incoming proton.

The edge **29** (ΔH_f 960.0 kJ mol^{-1}) or corner **30** (ΔH_f 917.6 kJ mol^{-1}) protonated species in the absence of methanol were investigated and located not as intermediates on the potential energy surface but were shown to be transitions states. Structure **29** was a transition structure on the PM3 potential energy surface for a 1,3-hydride migration from C2 to C4. Structure **30** was identified as a transition structure leading to the primary cation **6** rather than cation **5**.

The semiempirical corner transition states **14** from **1** and **23** from **2** show elongation of both the C2C4 and C2C3 cyclopropyl bonds. This is consistent with interaction of the incoming protonated methanol with



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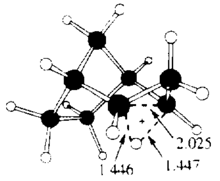

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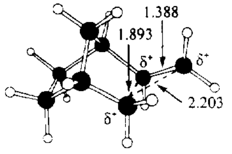

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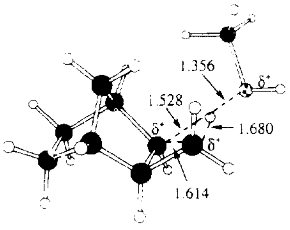
both the HOMO and HOMO-1 orbitals of **1** and **2** respectively. For edge attack the semiempirical transition states **18** from **1** and **27** from **2** show elongation of the C2C4 bonds but show no elongation of the C2C3 bonds. These results support the value of mapping of the HOMO and HOMO-1 orbitals on to the electron density surface as a simple method of predicting reaction chemistry. The transition states for edge and corner proton transfer from protonated methanol to **1** with rupture of the C2C4 bond are consistent with the observed experimental results where corner attack and C2C4 bond rupture occurs exclusively. The semiempirical calculation of the transition states for edge and corner proton transfer from protonated methanol to **2** with rupture of the C2C4 bond show similarity in energies.

The experimental results[1] for the acid catalysed ring opening of **2** showed some cleavage of the C2C3 (C3C4) bond to also occur. Results of PM3 calculations to model edge addition to the C2C3 bond indicate the transition state **31** ($\Delta H_f = 726.9$ kJ mol^{-1}) to be similar in energy to transition states **23** and **27** ($\Delta H_f = 725.4$ kJ mol^{-1}, $\Delta H_f = 723.1$ kJ mol^{-1}, respectively) and hence some addition from this trajectory would be expected.



31

Nucleophilic attack on **1** *and* **2**

Nucleophilic attack on protonated cyclopropanes is often considered to occur to an unrelaxed protonated cyclopropane and is supported by the stereospecificity of the nucleophilic attack and the exclusion of a common intermediate **5** from both **1** and **2**. As outlined earlier optimisation of the open carbocation **5** with a boat and chair conformation by ab initio methods (3-21G* basis set) gave **10** and **8** respectively. If the interconversion of **8** and **10** were high in energy then this could account for the different stereochemistries of nucleophilic attack from **1** and **2**. The geometry of **8** is such that the LUMO to more open to 'bottom' face attack (*anti* to C8) than from 'top' face attack (*syn* to C8). Nucleophilic capture would therefore be expected to occur with inversion of configuration and this is consistent with experiment.[1] Consideration of the carbon charges in **10** that would be formed from **2** showed C2 to be more highly charged than C1 (0.252 and -0.315, respectively) and bond lengths are consistent with this. Therefore nucleophilic capture would be expected to occur at C2 in preference to C1 and retention of the bicyclo[3.2.1]octane carbon skeleton would be expected. Comparison of the high correlation areas of the LUMO / electron density map for the possible trajectories of nucleophilic attack at C2 and C3 of cation **10** show that attack on C2 with inversion is favoured and this is consistent with experiment.

CONCLUSIONS

PM3 calculations of the possible classical ions resulting from rupture of the C2C4 and C2C3 bonds for reaction **1** and **2** with a proton show a thermodynamic preference for formation of ion **5** involving rupture of the C2C4 bond. This ion is common to both the reactions of **1** and **2** and can not account for the stereospecific attack of a nucleophile in the reaction of **1** and **2** with protonated methanol, where for each substrate methanol addition occurs with inversion of configuration.

Ab initio calculations at the HF/3-21G* level of theory for chair and boat conformations of ion **5** that would be expected to be the conformations that the ions might initially be formed in from **1** and **2** respectively, afford **8** and **10** respectively. For ion **8** the carbocation p-orbital on the face *syn* to C8 is more hindered than the *anti* face, consistent with the stereochemistry observed for nucleophilic attack of methanol in the reaction of **1**. For the non classical ion **10** the greater charge at C2 than C1 and greater bond length of the C2C7 bond length (2.155 Å) than that of C1C7 (1.729 Å) will direct nucleophilic attack to C2. The bridging nature of the cation will ensure inversion of configuration. This is consistent with the experimental result.

The semiempirical corner transition states **14** and **23** show elongation of both the C2C4 and C2C3 cyclopropyl bonds, consistent with interaction of the incoming protonated methanol with both the HOMO and HOMO-1 orbitals of **1** and **2**, respectively. For edge attack the semiempirical transition states **18** from **1** and **27** from **2** show elongation of the C2C4 bonds but show no elongation of the C2C3 bonds. The transition states for edge and corner proton transfer from protonated methanol to **1** with rupture of the C2C4 bond are consistent with the observed experimental results where corner attack occurs and C2C4 bond rupture occurs exclusively. The semiempirical calculation of the transition states for edge and corner proton transfer from protonated methanol to **2** with rupture of the C2C4 bond show similarity in energies.

For **1** and **2** mapping of the HOMO and HOMO-1 orbitals of the cyclopropane onto the electron density surface shows the areas of high correlation of these orbitals at the corner of the C2C4 bond (edge of C2C3 and corner of C2C4) overlap. For both substrates no overlap of the HOMO and HOMO-1 correlations were observed at the edge of the C2C4 bond (edge C2C4 and corner C2C3). These results are consistent with the regiochemistry and stereochemistry of proton addition.

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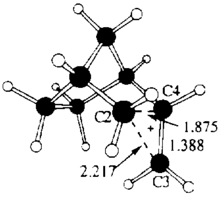
8 Attempts to locate a corner protonated intermediate, were unsuccessful using PM3. However, transition structure **32** (ΔH_f = 915.7 kJ mol^{-1}) similar in geometry to that expected for a corner protonated species was identified. Structure **32** showed both the C2C4 and C2C3 bonds to be lengthened (1.875 Å and 2.217 Å, respectively) with relative charge development greater at C3 than C4 (0.239 an -0.133, respectively) reflecting the constraints of the rest of the molecule. It is therefore unlikely that structure **32** could lead to cation **5** and would show a preference to give the primary cation **3** on the PM3 potential energy surface.



32

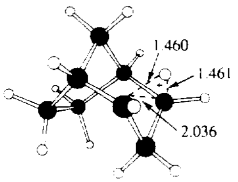
9 From CPK space filling models of **1** both edge and corner trajectories would appear accessible. A similar model of **2** shows a difference in the accessibility for corner and edge attack with the corner trajectory appearing the more favourable.

10 The heat of formation was evaluated when a proton is placed in the pane of the cyclopropane at a fixed distance from C2 (C4) and the structure optimised. As the distance of the proton to C2 was decreased the heat of formation continually decreased until the open cation **5** was reached.

11 The six vibrational modes corresponding to the rotation and translation of the structure as a whole were all small and hence characteristic of a stationary point.

12 Optimisation of this structure with AM1 failed to converge to a transition structure.

13 Geometry optimisation of **18** did not lead to a symmetrical edge protonated complex of the cation **33** and methanol. In a separate calculation structure **33** (ΔH_f 971.2 kJ mol^{-1}) without methanol present was shown to be a transition structure for *exo* hydride migration in cation **5** from C2 to C4. Attempts to locate a minimum formed by an edge protonated structure **33** and methanol after proton transfer was unsuccessful.



33

14 This, in conjunction with corner attack being marginally more sterically favoured, results in attack exclusively from a corner trajectory.

15 Geometry optimisation of **23** by an energy criterion after increasing the H2C2 distance to 1.6 Å and decreasing the H2O1 distance to 1.2Å gave structure **22** the minimum formed on approach of protonated methanol and **2** before proton transfer occurs.

16 An approximate transition structure for corner addition of protonated methanol to **2** was constructed by using as a model the transition structure obtained for cyclopropane and building the rest of the hydrocarbon framework around this structure. The transition structure distances were fixed and the structure minimised with molecular mechanics. The structure was optimised with the PM3 semiempirical method without any geometrical constraints imposed to give a transition structure. The conformers formed by rotation of the O1H2 bond in 90° increments through 360° led to the collapse of all four structures to **23**. The potential energy surface for rotation of this bond was therefore assumed to be relatively flat. The configuration at the oxygen of **23** was epimerised by exchange of the Me and H not being transferred. The above procedure repeated to search for the lowest energy conformation of the transition state, namely **25**. Structures **23** and **25** differ in energy by only 0.4 kJ mol^{-1}. Both structures showed one imaginary frequency that corresponded to an increase in length of the C2C3, C2C4, and H2O1 bonds and a decrease in length of the C3C4 and C2H2 bonds consistent with corner transition structures.

17 Geometry optimisation of **23** after decreasing the H2C2 and increasing the H2O1 bond lengths gave structure **24** that is a minimum on the potential energy surface and is the structure formed after proton transfer from protonated methanol to **2**.

18 The minimum **26** formed on approach of $MeOH_2^+$ to **2** before proton transfer occurred, was located by increasing the C2H2 and C4H2 distances and shortening the H2O1 distance of **27**, followed by geometry optimisation by an energy criterion.

19 Edge attack of protonated methanol on the C2C4 bond of **26** was modelled in a similar way to that of edge attack on **1**, by using the edge transition structure obtained from addition of protonated methanol to cyclopropane and building the rest of the hydrocarbon skeleton around this structure. Optimisation by a gradient norm minimisation procedure gave a transition structure that was examined by rotation of the O1H2 bond through 90° increments for 360° and complete structure optimisation performed for each conformer. The lowest energy transition structure **27** showed one imaginary frequency which corresponded to the simultaneous decrease of the H2C2 and H2C4 bond lengths and an increase in length of the H2O2 and C2C4 bonds. The vibration is therefore consistent with a transition structure for edge attack of protonated methanol on **2**.

20 Increasing the H2O1 distance and decreasing the H2C2 and H2C4 bond lengths of **27** followed by geometry optimisation by an energy criterion gave **28**. Structure **28** was identified as a minimum on the potential energy surface and corresponded to the complex formed after proton transfer from $MeOH_2^+$ to **2**.

21 The PM3 calculations may underestimate the steric effects (i.e. proton-proton nuclear repulsions) in the case of edge attack or overestimate the electronic stabilisation gained from attack at the edge of the C2C4 bond.

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