RING-OPENING OF NORTRICYCLANES

AT LAST A SOLUTION TO THE NORBORNYL CATION PROBLEM

ACID-CATALYZED RING-OPENING OF 4-HALONORTRICYCLANES

AT LAST A SOLUTION TO THE NORBORNYL CATION PROBLEM

By

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ABSTRACT

The stereochemistry of acid-catalyzed ring-opening of the cyclopropane ring in nortricyclane, 4-chloronortricyclane and 4-bromonortricyclane in D_2SO_4/acetic acid-d_4 medium has been investigated. Stereochemical analysis was carried out by dmr spectroscopy. The endo:exo deuterium ratios, at C6 of the exo-2-norbornyl trideuteroacetates-d_1 are 1.12, 1.35 and 1.61 respectively.

These results conclusively establish that the norbornyl cation formed by edge-protonation is an unsymmetrical, classical and rapidly equilibrating species and not a symmetrical non-classical σ-bridged species.

ACKNOWLEDGEMENTS

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INTRODUCTION

A: CYCLOPROPANES

The chemistry of three-membered ring molecules begins with Freund who synthesized "trimethylene" (or cyclopropane) by reacting zinc dust with bromocyclopropane in aqueous alcohol.[1] A few years later it was Baeyer who observed the unusual reactivity of cyclopropane with electrophiles by noticing that the cleavage of the three-membered ring of cyclopropane with hydrobromic acid was faster than the cleavage of cyclobutane or cyclopentane, under similar conditions.[2] Two years later, Gustavson observed the formation of propyl alcohol and propyl hydrogen sulphate where he treated cyclopropane with aqueous sulphuric acid at room temperature.[3]

The structure of cyclopropane in fact is responsible for its unusual reactivity relative to other saturated compounds. Cyclopropane has a symmetrical D_{3h} structure with the three carbon atoms at the vertices of an equilateral triangle. Experimental and theoretical investigations have established that the carbon-carbon bond lengths (experimentally observed = 1.51 A°, theoretically calculated = 1.50 A°) are shorter than those in acyclic molecules (1.54 A°). The hydrogen-carbon-hydrogen bond angle (experimental 114°, theoretical 115°) is greater than the 109° tetrahedral bond angle.[4-6] Baeyer[2] suggested the greater reactivity of cyclopropane relative to other cycloalkanes due to the increased strain (27.2 kcal/mol[7]) in the cyclopropane. Baeyer's statement is strongly supported by the fact that the bond angle between carbon-carbon-carbon is compressed from the normal tetrahedral angle (109°) to an angle of 60°. To decrease this strain, the molecule can maintain the interorbital angles at ca. 109° to minimize

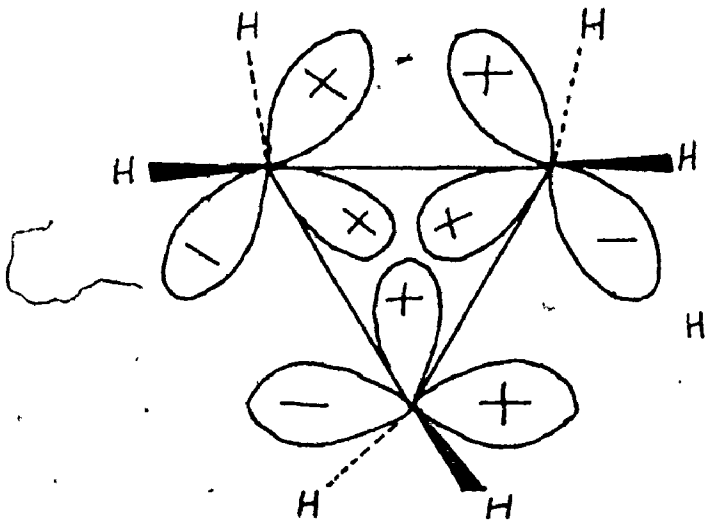
interelectronic repulsions but this would preclude maximum overlap of the bonding orbitals. Alternatively it can maintain maximum overlap by tolerating the greater electrostatic repulsions of orbitals at 60° to each other which result by placing the bonding orbitals co-axial with the line between the nuclei. The actual structure of cyclopropane is likely intermediate between these two extremes and the best possible description of cyclopropane in terms of simple localized hybrid orbitals can assume one of two forms.

In an effort to provide an explanation for the unusual properties and reactivity of cyclopropanes relative to other saturated compounds, Walsh constructed a model of cyclopropane which employed a state of sp^2 hybridization at each carbon center.[8] The Walsh model of cyclopropane (1) consists of the C-C bonds of the ring which are formed from the intra-annular overlap of one of the sp^2-hybridized orbitals on each carbon atom and three p-orbitals. The structure shown in Figure 1 is actually one of three resonance structures necessitated by the fact that one of the three overlaps between p-orbitals is antibonding. The bonds formed by the overlap of the p-orbitals are occupied by four electrons while two electrons are associated with the overlap of the three sp^2-hybridized orbitals in the center of the ring. The orbitals used in forming the C-H bonds are pictured as being sp^2-hybridized. This model provides an explanation for the chemical reactivity of the C-C bonds, which often undergo addition reactions rather than substitution, suggesting that there is more p-character in these bonds than in those of saturated compounds - a fact which is supported by an abundance of experimental data such as dipole moment and nuclear quadrupole resonance

studies of cyclopropyl chloride,[9,10] ability of the cyclopropyl group to enter into "pseudo" conjugation with π-electron systems[11-13], and to stabilize adjacent carbonium ions when properly oriented[14-15]; the postulated ring current[16]; and the shortening of the C-C bond length relative to that in saturated compounds.[6] A state of hybrid orbitals in the C-H bonds close to sp^2 is supported by the chemical reactivity of these bonds;[17] the C-H bond length and HCH bond angle;[6] the C-H stretching frequency (force constant) and the C_{13}-H spin-spin coupling constant (32% 'S' character).[19,20]

The bent bond model of cyclopropane (2) consists of $sp^{4.12}$ orbitals for the carbon-carbon bonds and $sp^{2.28}$ orbitals for the carbon-hydrogen bonds along with an interorbital angle of 104° (cf. 60° for equilateral triangle).[7,21] Bernett[7] has shown that the Walsh and bent-bond models of cyclopropane are really equivalent, i.e., they are just two different interpretations of the same total wave function. Since cyclopropyl bonds have considerable sp^2 character, they can provide a π-cloud for interaction with electrophiles.

Both organic and theoretical chemists have expended considerable time (nearly more than the past two decades) investigating the interaction of electron deficient species (electrophiles) with cyclopropyl groups. Cyclopropanes readily undergo ring cleavage upon treatment with acids, and the nature of the intermediate or intermediates which may be formed in this electrophilic cleavage reaction remains one of the most intriguing unanswered questions in small-ring chemistry. This topic has been the theme of many excellent review articles.[22-27] Cyclopropanes are known to interact with electrophiles both intra- and intermolecularly.



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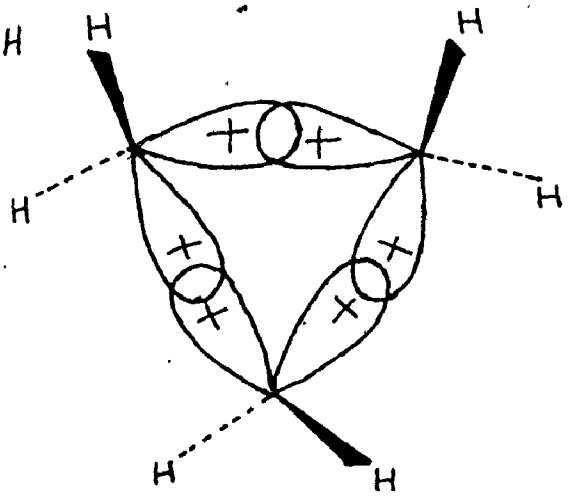
(The Walsh model of cyclopropane)



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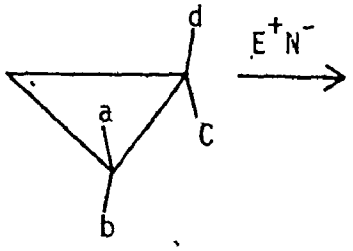
(A bent bond model of cyclopropane)

The well documented stabilities of cyclopropyl carbinyl,[28] homocyclopropyl carbinyl[29,30] and 1-cyclopropylvinyl[31-33] cations attest the nature of intramolecular cyclopropane-electrophile interactions. Intermolecular interactions of cyclopropanes with electrophiles, which normally lead to subsequent ring opening reactions is a reaction of special interest because it remains one of the few in which a carbon-carbon single bond is broken by a proton. While several investigations have been made into the mechanism of these reactions (vide infra), numerous ambiguities remain.

Stereochemistry and mechanism hold prominent positions in any investigation which involves the cleavage of cyclopropyl bonds. The electrophilic cleavage of cyclopropanes offers the unique opportunity to study the stereoelectronic effects in σ bond cleavage. Generally, the electrophile attacks the least substituted carbon atom and breaks the bond which will yield the more stable carbonium ion (Markovnikov's Rule), although exceptions to this rule have been found.[34-37] The stereochemical outcome of attack by electrophiles can range from complete retention of configuration (4 or 6) to complete inversion of configuration (5 or 7) at the carbon atom bearing the electrophile, with the possibility of a mixture resulting from both retention and inversion. Similarly, the nucleophilic portion of the addendum (E^+N^-) can add to give either retention (6 or 7) or inversion (4 or 5) of configuration at the carbon atom undergoing nucleophilic attack, as well as a mixture resulting from both retention and inversion.



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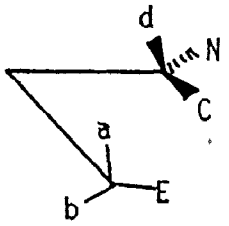
E^+N^-



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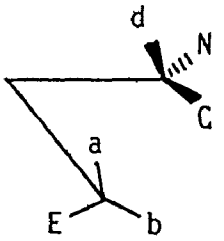

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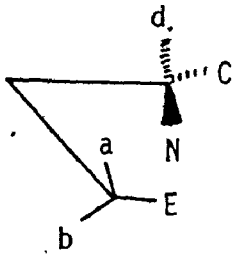

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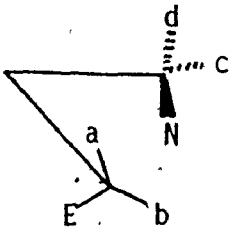

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B. ELECTROPHILIC RING OPENING OF CYCLOPROPANES

1. Cleavage with Acid

Extensive investigations have established that the stereochemistry of electrophilic attack on cyclopropanes occupies a spectrum which ranges from complete retention to complete inversion of configuration at the carbon atom undergoing electrophilic attack.* However, on the basis of experimental studies, it appears that the preferred stereochemical outcome for attack by a proton on cyclopropanes is retention of configuration at carbon.

Addition of deuterium bromide to the cyclopropyl ring of the bicyclo[2.2.2]octane adduct gave the product from anti-Markovnikov addition in which the stereochemistry of attack of the deuterium was retention.[38] It was suggested that the hydrogens alpha to the anhydride carbonyls prevented any solvent-nucleophilic approach towards the potential secondary carbonium ion center to explain the direction of addition, however workers later reported that the anti-Markovnikov's addition was due to the destabilizing inductive effect of the anhydride.[39]

DePuy[40,41] reported that in the acid-catalyzed cleavage of optically active cis-2-phenyl, 1-methylcyclopropanol which produced a 60:40 mixture of 4-phenyl, 2-butanone-d and 3-phenyl-2-butanone-d, the breaking of the C-C single bond which led to 4-phenyl, 2-butanone-d proceeded with retention of configuration.

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* For brevity, electrophilic retention will refer to retention of configuration at the cyclopropyl carbon atom which undergoes electrophilic attack. Electrophilic inversion, nucleophilic retention and nucleophilic inversion will also be used for brevity.

Other relevant examples where in retention by electrophile seems to be the preferred stereochemical course are:

i) the reaction of dibenzotricyclo[3.3.0.$0^{2,8}$]octadiene-d_2 with HBr.[42]

ii) the reaction of 1,2,2-trimethylbicyclo[1.1.0]butane with acetic acid-d_1,[43] and

iii) the reaction of endo and exo-7-hydroxy-1,6-dimethyl bicyclo-[4.1.0]heptane with acid.[44]

In contrast the electrophilic cleavage of the internal cyclopropyl bond of exo-tricyclo[3.2.1.$0^{2,4}$]octane was found to involve electrophilic inversion and nucleophilic inversion.[45,46]. The protonation of this bond in exo-tricyclo[3.2.1.$0^{2,4}$]octane with retention of configuration is subject to severe steric hindrance. Hogeveen has observed electrophilic inversion in the cleavage of 1,2,3,4,5,6-hexamethyl-exo-tricyclo[4.1.0.$0^{2,5}$]hept-3-ene,[47] and Warnet and Wheeler have also observed electrophilic inversion in cyclopropyl ring cleavage.[48]

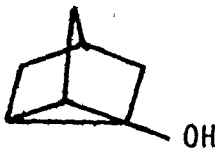
Investigations carried out by Nickon et.al.[49] on the stereochemistry of homoketonization in the norbornyl system by using 1-hydroxy and 1-acetoxynortricyclanes 8 and 9 respectively as model substrates, has indicated that the SE_2 reaction in deuterated acidic medium occurs with electrophilic retention to produce 2-norbornanone endo-6-d (10-endo-6-d) where as the SE_1 reaction in deuterated basic medium occurs with electrophilic inversion to yield 10-exo-6-d. They observed that in various alkaline media the homoketonization produced an exo C-D bond with high stereospecifity (96.5-98%), whereas in acid medium endo attack was favoured to at least 90-95%. Their results concluded that homoenolization at C_6 in bicyclo[2.2.1]heptane-2-one system would involve preferential

abstraction of the exo hydrogen in base and the endo hydrogen in acid. Although high stereospecificity in alkaline homoketonizations can sometimes be diminished by solvent changes, no case has yet been found where it can be completely reversed by change in the alkaline solvent system. In acid media all known cleavages of homoenols and homoenol acetates have proceeded with high stereochemical retention (usually 90-100%) irrespective of substrate or of solvent.[50]

The first example of acid homoketonization that goes by high inversion of configuration has been reported by Nickon et al.[50] More remarkably, it occurs in a system (1-acetoxynortricyclane 9) found earlier to open in D_2SO_4-CH_3CO_2D-D_2O with high retention[49] and they found that the stereospecificity can be varied from high inversion to high retention simply by changing the amount of water in the solvent. Such complete reversal of stereochemical opening with change of solvent is unprecedented in acid or alkaline homoketonizations and has practical utility in preparation of deuterium-labelled, bicyclo[2.2.1]heptyl compounds for mechanistic studies. Whether this unusual behaviour has any generality or is peculiar to 1-acetoxynortricyclane (9) remains yet to be answered. Nickon[50] suggests that possibly in acetic acid the homoketonization involves direct ring cleavage in the homoenol acetate, whereas with water the ester first undergoes hydrolysis (or methanolysis in methanol) and the ring cleavage then takes place in the homoenol. On the other hand if it is so, the behaviour would be just as surprising because it implies fundamentally different stereochemical pathways for two very similar cyclopropyl substrates. The current mechanistic interpretations of cyclopropane cleavages with protonic

acids assign no stereo-influential role to oxygenated groups on the ring, a tacit view that may deserve closer investigation.

The remaining possibility of mixture of inversion and retention in acid-catalyzed ring-openings of the nortricyclane compounds has been reported by Nickon and Hammons.[51] A 50:50 mixture of electrophilic inversion and retention along with predominant nucleophilic inversion was observed by them in the D^+-catalyzed cleavage of tricyclo[2.2.1.$0^{2,6}$]-heptane (nortricyclane, 11a). The mass spectral analysis of 2-norbornanone-d obtained by lithium aluminum hydride reduction of the product which was oxidized by chromium trioxide in acetic acid under conditions known not to induce skeletal change or 6,2-hydrogen shift-indicated less than 3% multiple deuteration. Thus the electrophile D^+ entered the species during ring-opening. If the deuterium had entered the molecule before or after the ring-opening it would have provided a pathway for eventual multiple deuteration whereas repeated treatment of nortricyclane (11a) with DCl gave only exo-norbornyl chloride, whose mass spectrum



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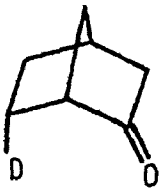
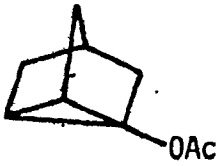


10-endo-6-d



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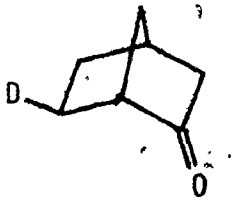
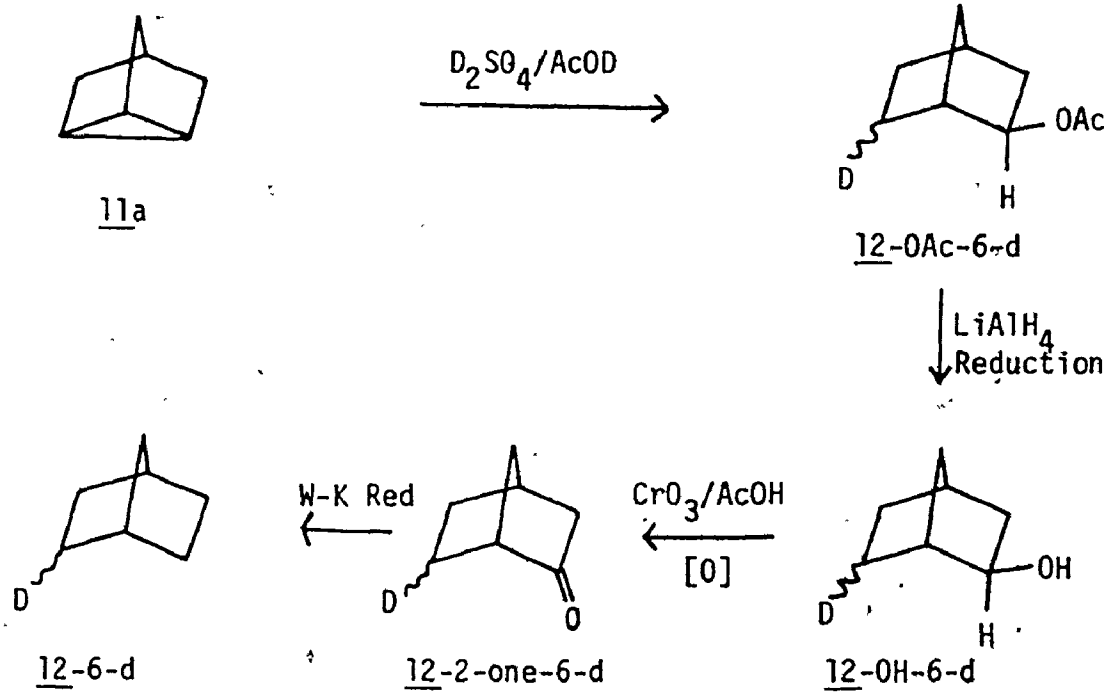


10-exo-6-d

revealed appreciable multiple deuteration, viz. 21.5% no D, 52% 1D, 22.5% 2D, 4% 3D (total 1.09D). The presence of di- and trideuterated species indicated the intervention of reactions other than simple ring cleavage. The extra deuterium could have entered by exchange of cyclopropyl hydrogens prior to ring opening or by the formation of a deuterionorbornene followed by addition of deuterium chloride. The formation of this deuterionorbornene has been attributed to the isomerization of nortricyclane to deuterionorbornene or by elimination of hydrogen chloride from the derived exo-norbornyl chloride.[51] On the basis of their results, the complete selectivity of nucleophilic termination by inversion of configuration together with the virtually equal endo:exo distribution of the electrophile D (1.08±0.15) Nickon and Hammons have suggested that the nortricyclane (11a) is converted to the carbon-bridged norbornyl ion 13 (Scheme 1:2).

Scheme 1:1



11a

12-OAc-6-d

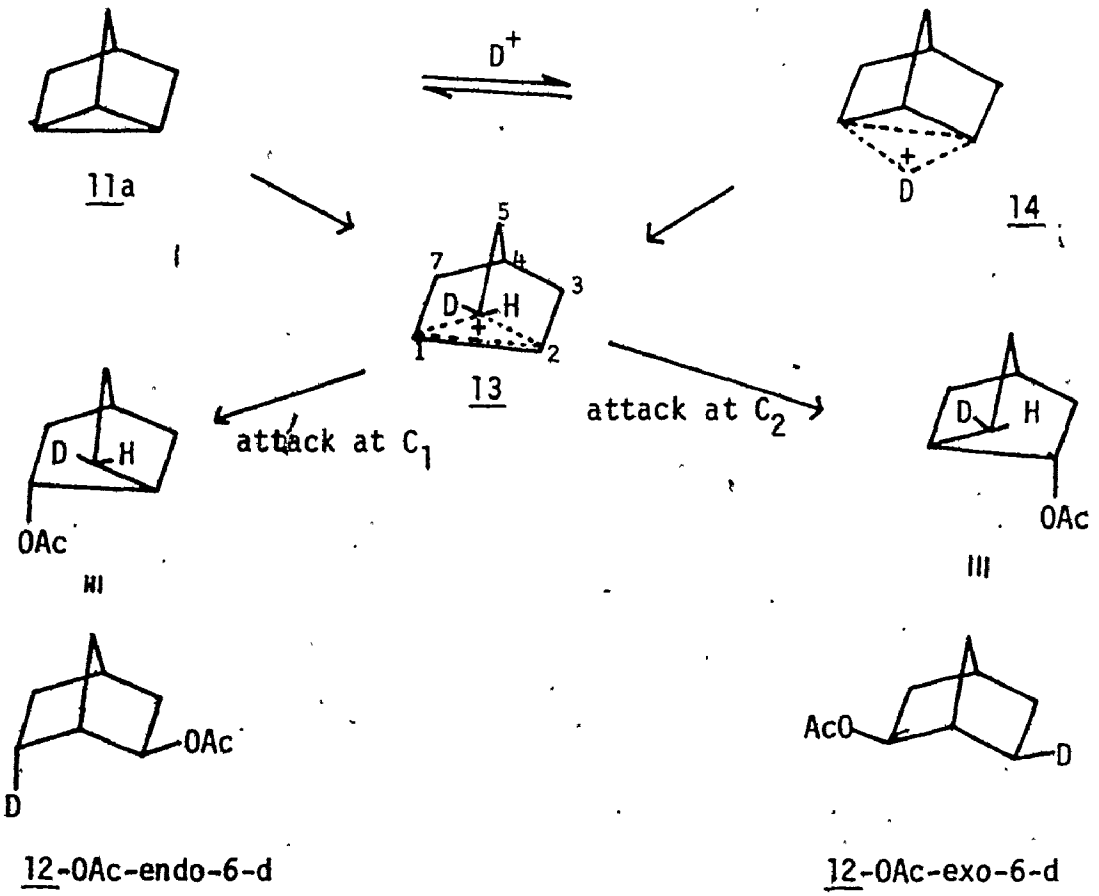
12-6-d

12-2-one-6-d

12-OH-6-d

This bridged cation did not return appreciably to the neutral tricyclic system or to norbornene because proton loss competes with deuteron loss and could provide a means for eventual entry of more than one deuterium. Their results did not rule out formation of other ions (classical or not) prior to the generation of 13 but indicated restrictions on their behaviour. If a reversibly formed deuterium bridged species such as 14 or its equivalent precedes the cation 13 then the rearrangement 14 to 13 must have been essentially irreversible; otherwise multiple deuterium entry could have resulted. The trace amounts of 12-OAc-endo-2-d and 12-OAc-1-d suggested Scheme 1:3 since the so called 6,2-hydrogen shifts transformed ion 13 into the related ions 15 and 16 according to whether H or D migrated, respectively. Ions 13 and 16 are indistinguishable, while ion

Scheme 1:2



12-OAc-endo-6-d

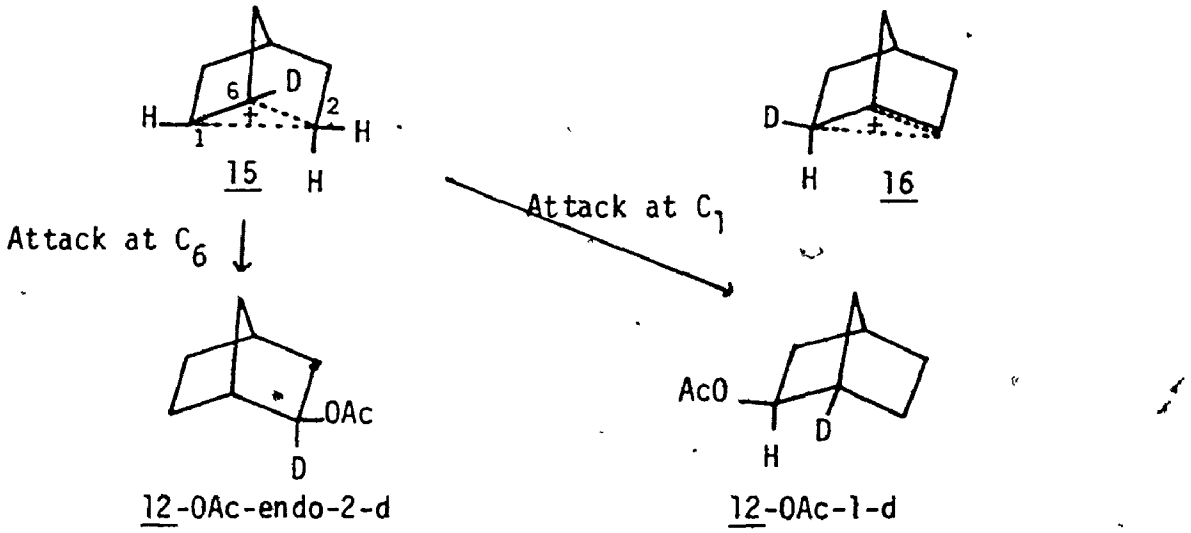
12-OAc-exo-6-d

15 yielded 12-OAc-endo-2-d and 12-OAc-1-d by termination at C-6 and C-1.

However, on the whole the results have been interpreted in terms of corner-protonated nortricyclane intermediates but did not establish whether initial protonation occurred corner-wise or edge-wise.

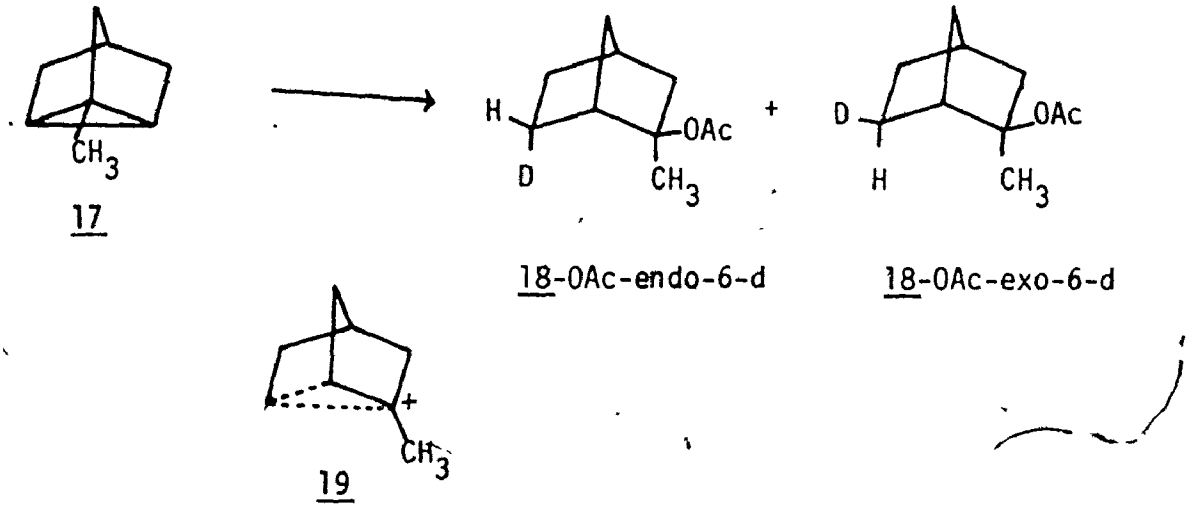
Soon after, Hammons and co-workers[52] have studied the cleavage of the cyclopropyl ring of 1-methyl nortricyclane(17)and found 62:38 mixture of products arising from the electrophilic retention and electrophilic inversion 18-OAc-endo-6-d and 18-OAc-exo-6-d respectively along with predominant nucleophilic inversion. The formation of 18-OAc-exo-6-d and 18-OAc-endo-6-d was found to be accompanied by the incorporation of deuterium into the methyl substituent also via deprotonation-deuteration of the tertiary 2-methylnorbornyl cation (19). Obviously the cleavage

Scheme 1:3



12-OAc-endo-2-d 12-OAc-1-d

of 17 with deuterated acid is not a very suitable route for the incorporation of deuterium stereospecifically at C-6 into 2-methyl-2-norbornyl derivatives. Hammons argued, although the degree of stereoselectivity is low, the dominating path is the sterically unfavourable one of retention. He suggested that the stereoelectronic preference for front-side attack is large enough to override the opposing steric hindrance by a small margin.



17

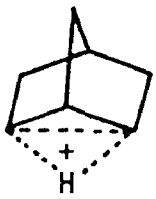
18-OAc-endo-6-d

18-OAc-exo-6-d

19

But regarding the mechanism of the acid-catalyzed ring opening of this methyl nortricyclane these investigations could not establish whether initial protonation occurred corner-wise or edge-wise although the results of these studies have been interpreted in terms of corner-protonated methyl nortricyclane intermediate.

Brown and McIvor's nuclear magnetic resonance studies of addition of deuterium chloride to nortricyclane have shown that nearly all the deuterium is at C-6, and unequally distributed in favour of the endo-position. Their mass spectral analysis indicated incorporation of only one deuterium atom and thus protonation again is essentially irreversible as suggested by Nickon[51] and Hammons.[52] The results also indicated that norbornene and nortricyclane do not intercovert under the reaction conditions and thus their addition products might be considered separately. Brown and McIvor further argued that the results from norbornene addition are not conducive to a unique mechanistic explanation. A bridged ion (21) cannot be the only product-forming ion, but if it is suggested[151] that a rapidly equilibrating localised classical ion (22,23) is solely responsible for these r it



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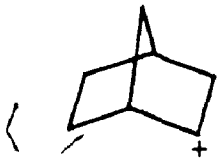
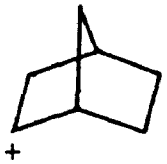




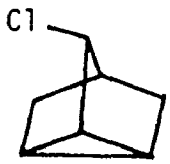
22 23

is necessary to postulate that 1,2-shifts are very much faster than attack of chloride ion in the nonpolar medium. They believe, that if in chloroform solution, the most stable ions were the protonated nortricyclane (20), and scrambling around the cyclopropane ring were slow compared with product formation, then addition of DCl to the nortricyclane would give endo-6-deuterio-exo-2-norbornyl chloride. Also that 20 is the most stable ion in this system was suggested by Klopman's calculations.[176] Since 20 is almost certainly the initial product, they agreed that most of 20 has leaked to 21 or 22-23, with subsequent rapid equilibration, prior to product formation and this leakage is irreversible since no deuterium was observed at positions 1 and 2.

Finally Brown and McIvor[81] have suggested that their investigations favour (but do not require) a greater stability for 21 than for 22 or 20.

Specifically from the investigations carried out by Nickon,[51] Hammons[52] and Brown[81] along with other investigators in this field, it has not been established that whether initial protonation occurred corner-wise or edge-wise, although in all these studies nearly all the deuterium has been detected at C-6, and unequally distributed in favour of the endo-position. All results are explicable on the basis of edge-protonation of the three membered ring.

Studies carried out by Werstiuk and co-workers[53,54] of acid-catalyzed ring-opening of 3-chloronortricyclane (24) and 3-bromonortricyclane (25) in 0.1M H_2SO_4/ACOH medium have established that the ring-opening of the cyclopropyl ring in (24) and (25) occurs with retention and inversion at the carbon atoms bearing the electrophile and nucleophile respectively. Mechanistic investigations pertaining to the electrophilic cleavages in D_2SO_4/ACOD medium of the cyclopropyl ring in 3-chloronortricyclane (24) and 2-methyl-3-chloronortricyclane (26) reported by Werstiuk and Cappelli[54] have shown that for at least 70% of the products the cyclopropyl carbon atom undergoing electrophilic attack experienced predominant retention of configuration (retention: inversion > 14:1) and the site of nucleophilic attack experienced almost exclusive inversion of configuration (inversion:retention ≈ 50:1). Results of their studies[53,54] have established that the σ-bond farthest removed from the electron withdrawing halogen is cleaved preferentially via initial edge-protonation. They concluded that at-



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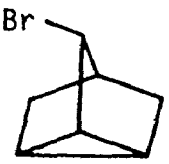

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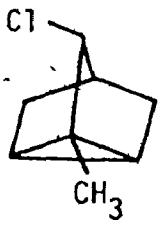

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least 75% of the products arose from initial-edge-protonation of the C_2-C_6 bond which is farthest removed from the halogen. The absence of significant amount of deuterium at exo-6 in the 7-haloacetates established that corner protonation (via paths a, b, d, e, Scheme 1:4) to give 32 and 33 is unimportant unless paths b and d are preferred stereoelectronically.

DePuy[55] has interpreted the results of his recent investigations on the stereochemistry of the attack of electrophile D^+ on cis- and trans-1,2,3-trimethylcyclopropane in terms of an unsymmetrical corner-protonated cyclopropane. Then he suggested that the electrophile enters (probably by way of an edge-protonated species) in the plane of the ring and remains there in the intermediate which leads to ring opening. Finally he says, they in fact believe that the formation of an edge-protonated cyclopropane is probably rate determining, with the proton moving along the edge into the corner.

Investigations of the stereochemistry of the nucleophilic attack have indicated that nucleophilic inversion is the preferred mode of attack with very few cases of nucleophilic retention.[39,42] The chemistry of cleavage of cyclopropanes with electrophilic halogens have also commanded

much interest. Electrophilic cleavage of a strained cyclopropane σ-bond by molecular bromine in the presence of a Lewis acid ($FeBr_3$, $AlCl_3$ or $AlBr_3$) has been studied extensively to determine the site and stereochemistry of addition of the electrophile and nucleophile to establish the nature of the intermediate involved in the ring-opening.[56-68]

The opening of cyclopropane rings by reagents such as mercuric salt,[69-71] diborane,[72,73] palladium chloride,[74] metallic ions such as - silver,[75] thallium[76,77] and lead[78,79] have also been investigated. The ring cleavage by the use of acylium ions have been examined by Hart and Schlosberg.[80].

C. MECHANISM

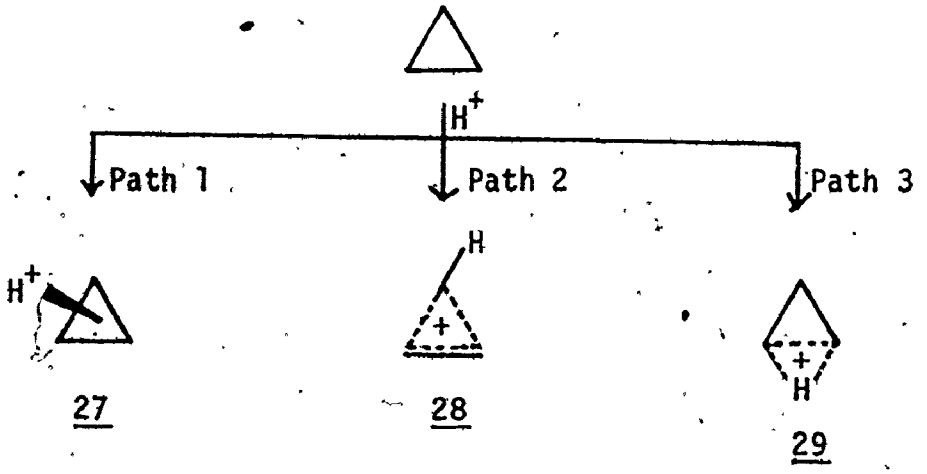
1. Experimental Studies

A cyclopropane ring can be attacked by an electrophile via three possible pathways: (e.g., H^+ is the attacking electrophile, then)

i) face protonation

ii) corner protonation

iii) edge protonation.

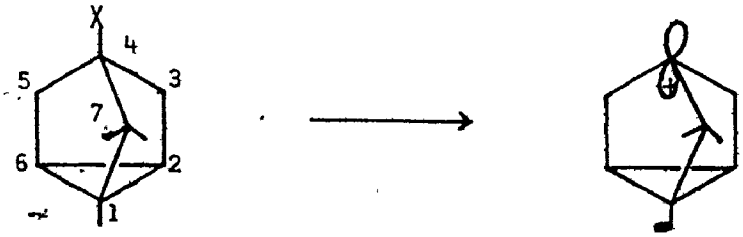


27 28 29

face-protonation corner protonation edge protonation

Roberts and Lee were the first investigators to propose a face protonated cyclopropane as an intermediate to account for their observed isotopic rearrangements which occurred in the solvolysis of 2-norbornyl brosylates-2,3-^{14}C.[89,90] Skell and Starer were the next group to report face protonated cyclopropane intermediates to account for the formation of a small amount of cyclopropane in the deamination of 1-propyl compounds,[91] however they modified this proposal later.[92] Not later than three years, Berson's experimental results indicated that face protonated species were not the important intermediates or transition states during the lactonization of exo-3-methyl-5-norbornene-endo-2-carboxylic acid-endo-3-d in sulphuric acid.[93] Other investigations have also ruled out the importance of face protonated cyclopropanes.[94-96]

Experimental studies have shown that the face of the three-membered ring provides a very little stabilization for an incipient carbonium ion formed during ionization of 4-tricyclyl derivatives 30 giving rise to a positively charged p-orbital, situated directly above the face of a cyclopropane ring.



30 31

Studies done on these derivatives in the early seventies are also against the face protonation of cyclopropyl group. They observed that 4-tricyclyl brosylate underwent slow ionization at 295° in 70%

aqueous dioxane and the corresponding tosylate ionizes at 25° in 60% aqueous ethanol with a half-life of 4 x 10^9 years.[97-99] From these observations, this enormous rate retardation in ionization of the 4-tricyclyl derivatives was attributed to the compression in the C-C-C bond angles at carbons C_3, C_5 and C_7 as well as a flattening at carbon-C_4 as the transition state was approached. Strain energy calculations indicated that the electron withdrawing inductive effect of the cyclopropyl ring was not as important in retarding the ionization as were the angle strain influences.

Also considering the Walsh model[8] for cyclopropane, it is quite understandable that removal of electron density (by an incoming electrophile) from the center of the cyclopropyl ring which has sp^2 like orbitals (ionization potential ≈ 14.7 eV) should be more difficult than removal of electron density from the more p-like orbitals (ionization potential ≈ 11.4 eV) towards the edge of the ring. In view of the foregoing experimental evidence which suggests that the face of a cyclopropane ring does not provide significant stabilization for an incoming electrophile, the further discussion of mechanisms of electrophilic ring opening of cyclopropane will be limited to the corner and the edge protonated species.

Corner protonation implies overlap of the electrophile with a minor σ-bond lobe and edge protonation is the interaction of the incoming electrophile with the protruding center of the bent bond (cf. three-centered bonds in boranes). In unsymmetrically substituted cyclopropanes, approach by electrophile towards one corner might be preferred. Likewise in the case of edge protonation in unsymmetrical cyclopropanes, approach by electrophile towards one edge can be preferred over the other two edges. In fact, the electrophile may perpendicularly approach an

edge of the cyclopropane (in the plane of the ring) along an axis which does not exactly bisect the carbon-carbon bond. Due to the small geometrical differences between 28 and 29, the energy difference between them is probably small, in fact they could possibly represent two extremes of a common mechanism. Although the pathways 1 and/or 2 can rationalize most experimental results which deal with the stereochemistry of cyclopropyl ring cleavage, the reasons for selection between them still remains obscure (vide infra).

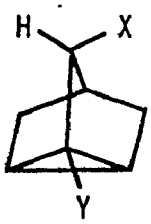
The studies of protonated cyclopropanes generated from aliphatic systems not containing the cyclopropyl group[100-104] has been reviewed by Collins[23] and Lee[24] and the results did not establish whether initial protonation occurred cornerwise or edgewise. In the H-D exchange studies conducted by Baird and Aboderin[105,106] Lee[107,108] and Deno[109] the deuterium distributions were accounted for by the initial equilibration of hydrogen-bridged ions (edge-protonation) via methyl-bridged ions (corner-protonation) with product formation occurring from an edge protonated species. Hendrickson and Boeckman reported edge deuteration as the initial step in the ring opening of cyclopropanes and also the initial edge protonation of the C-C bond followed by collapse via nucleophilic retention as the major product.[38,39,50] However, Cristol has pointed out that although the initial attack may be edgewise, the ultimate ring cleavage might occur after edge to corner isomerization.[42]

Werstiuk and co-workers[53,54] studies of the electrophilic cleavage (H_2SO_4-ACOH, D_2SO_4-ACOD) of the cyclopropane ring in halo-nortricyclanes 24, 25 and 2-methyl, 3-chloronortricyclane (26) have established that the

σ-bond farthest removed from the electron withdrawing halogen is cleaved preferentially via initial edge protonation. All these nortricyclane derivatives opened up to the corresponding acetates via similar scheme as was observed by the nature of the products, and the position and stereochemistry of the deuterium in the syn- and anti-haloacetates.

Since there was no significant amount of deuterium at exo-6 in the 7-haloacetates, the data established that corner protonation (via paths a, b, d, e, as shown in Scheme 1:4 given below) to give 32 and 33 was not important unless paths b and d were preferred stereoelectronically.

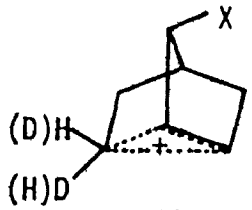
SCHEME 1:4



24 X=Cl, Y=H

25 X=Br, Y=H

26 X=Cl, Y=CH_3



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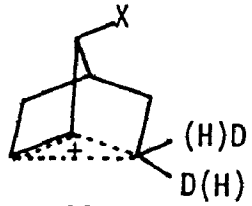

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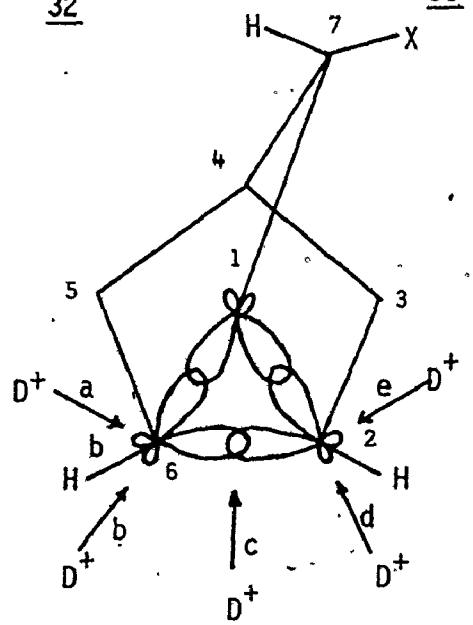
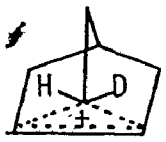


34

The formation of a symmetrical exo-chloronium-3-ion[110] could possibly account for such a stereoelectronic preference for path 'b'. However, they predicted at least 50% of the deuterium in the syn-7-haloacetate would be situated at C_5 if this pathway was important and this was not what was observed experimentally. Furthermore, endo-chloronium-3-ion formation for path 'd' would not be favourable. Therefore, Werstiuk and co-workers postulated that at least 75% of the products arose from initial edge-protonation of the C_2-C_6 bond*. The remaining of the investigations suggested that some leakage to the symmetrical chloronium ion also occurred since they observed the formation of the exo-5-chloroacetates-exo-3-d_1 (3.5%) and endo-3-d_1 (3.5%). But the endo-chloronium-3-ion did not form as was indicated by the lack of deuterium in the 3-position in the endo-5-chloroacetates.[53,54]

For the electrophilic cleavage of nortricyclane (11a), Nickon and Hammonds[51] suggested that the carbon bridged ion (35) was the principal acceptor of nucleophile and they concluded that the product did not arise from ions (36).



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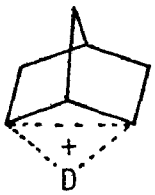
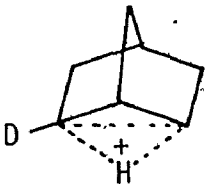


36a



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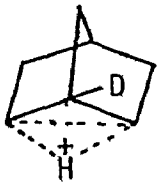

36c

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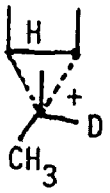
* The numbering system employed for the substituted nortricyclanes was used only for clarity to relate to that of the product haloacetates.

In 1974, DePuy and his co-workers have reported electrophilic (D^+) ring opening of the two isomeric 1,2,3-trimethylcyclopropanes in which they accounted for their data with an unsymmetrical, non-rotating, corner-protonated cyclopropane (37) and rejected the symmetrical non-rotating structure (38) and the edge-protonated species (39).[111] Recently



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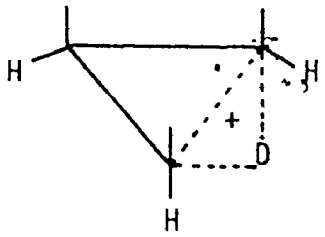
the stereochemical investigations of the electrophilic ring opening of cis-1,2,3-trimethylcyclopropane and trans-1,2,3-trimethylcyclopropane with D^+ done by DePuy and co-workers[55] led to the first and most important conclusion that the activation energies for inversion and retention by electrophile were very nearly the same and yet the reaction did not occur by way of completely symmetrical intermediate which would have led to a 50:50 mixture of products. Since two types of protonated cyclopropanes have been considered previously, edge-protonated (40) and corner-protonated (41),[112,113] it is easy to understand how deuterium could enter with retention of configuration from an edge-protonated intermediate. But in order to get electrophilic inversion from (40) a great deal of molecular motion and change in bonding would have to occur and certainly the structure of an edge-protonated cyclopropane as



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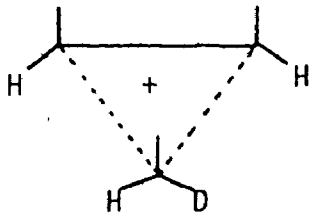

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usually drawn does not make it obvious why the inversion and retention pathways should have nearly the same energy. On the other hand in the symmetrical corner-protonated intermediate retention and inversion pathways are identical (except for isotopic substitution) in energy. The investigators did not find a 50:50 mixture of products and their isotope studies have ruled out an isotope effect as an explanation for the results. They then considered the possibility that ring opening products arose from both an edge and corner protonated intermediate with the former leading to complete electrophilic retention, the latter to an equal mixture of retention and inversion. By choosing the proper mixture of the two pathways many stereochemical results can be accommodated.

Yet two lines of argument can be brought against such a mixture of mechanisms. In the first place it would be extremely surprising if the relative amounts of the two independent pathways would remain constant over a wide range of experimental conditions. Yet DePuy et al.[55] found that the retention:inversion ratio for the cis isomer was unchanged within experimental error whether the reaction was performed in acetic acid, trifluoroacetic acid, methanol or methylene chloride. Secondly one would not expect that the two independent paths would give exactly the same amount of

nucleophilic inversion and retention. Yet in reactions of cis-1,2,3-trimethylcyclopropane DePuy et al. found the same 'D' stereochemistry within the 5% erythro product (from nucleophilic retention) as they did within the 95% threo product from inversion. Considering the above arguments a single intermediate was selected to be most compatible which gives rise to products. In order to accommodate above results this intermediate must be unsymmetrical but only slightly so.

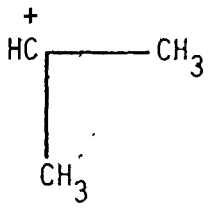
Therefore, DePuy suggested that the electrophile enters probably by way of an edge-protonated species in the plane of the ring and remains there in the intermediate which leads to ring opening. Finally DePuy remarked that they were dealing here with the intermediate which led to products and not necessarily to the intermediate which formed in the rate-determining step. They in fact believe that "the formation of an edge-protonated cyclopropane is probably rate determining with the proton moving along the edge into the corner".

In case of nortricyclane (11a), an interesting hydrocarbon, which has an axis of threefold symmetry and all the cyclopropyl carbons equivalent, fission of any of the cyclopropyl bonds with an unsymmetrical reagent (e.g., DX) would produce a 2,6-disubstituted norbornane in which the electrophile (D) and nucleophile (X) can each have an endo or exo configuration. The stereochemical outcome for each moiety would give information on the intermediates involved in the D^+-ring opening of nortricyclane (11a). The endo:exo deuterium ratio at C6 of exo-2-norbornyl acetate-d_1 (12-OAc-d_1), the product of D^+-catalyzed ring opening of nortricyclane (11a), observed by Nickon and Hammons[51] is (1.08 ± 0.15). This ratio in fact suggests that the D^+-catalyzed ring opening of nortricyclane (11a) occurs via initial edge-protonation since

the ratio of endo:exo deuterium at C6 of the product of ring-opening is not unity. On the other hand, if the ring-opening had occurred via initial corner-protonation the ratio of endo:exo deuterium should have been unity (i.e., 1:1). The cyclopropyl carbon atom undergoing the electrophilic attack would experience predominant retention of configuration and almost exclusive inversion of configuration at the site of nucleophilic attack.

2. Theoretical Studies

The isomeric $C_3H_7^+$ ions (42-44) have been the object of extensive experimental (as described above) and theoretical studies; a number of these studies have resulted in conflicting conclusions.[112-117]



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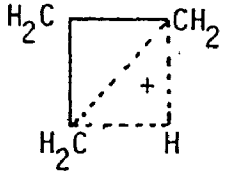
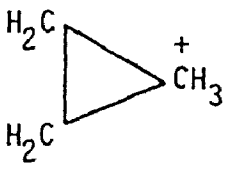
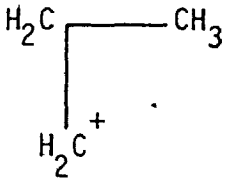


43a



43b



44

Early theoretical studies using extended Hückel theory on protonated cyclopropane ($C_3H_7^+$) implicated that edge-protonation was preferred to corner protonation.[118] Ab-initio calculations have suggested that ($C_3H_7^+$) as an edge-protonated species is 125 kcal/mole more stable than a face protonated species.[119] Semiempirical molecular orbital calculations by the INDO and modified CNDO methods have also favoured edge protonation over corner or face protonation.[120-122] NDDO calculations have shown that edge protonated cyclopropane is more stable than the face

or corner protonated species (by 135 and 20 kcal/mole respectively).[123,124]

Ab-initio molecular orbital calculations with complete geometry optimization have suggested that face protonation is a highly unfavourable geometry for ($C_3H_7^+$), (in agreement with experimental results)[94-99] whereas edge-protonated ($C_3H_7^+$) is less stable than corner protonated species ($C_3H_7^+$).[113,125,126] However, Andrist's theoretical studies have implicated that a cation may experience significant stabilization by the face of a cyclopropane ring.[127]

Molecular orbital calculations of several types now predict[112,113] (Table 1:4), in agreement with experiment,[116,117] that sec-propyl (42) is the most stable ion structure amongst 42-44 structures. Gaseous (n-$C_3H_7^+$) ions have been shown experimentally to be unstable, isomerizing without hydrogen scrambling to (sec-$C_3H_7^+$).[117] MINDO/3 calculations[112] predict the most stable form of the cyclic isomer to be the edge-protonated (43a) cyclopropane structure, deriving a heat of formation value in close agreement with the experimental value determined by Chang and Franklin[116] (Table 1:1) from equilibrium constant measurements of reactions 1 and 2 (Scheme 1:5, A = HCOOH or CH_3OH) at 0.2-0.4 Torr total pressure, assuming the intrinsic entropy changes of these reactions to be zero.

Scheme 1:5

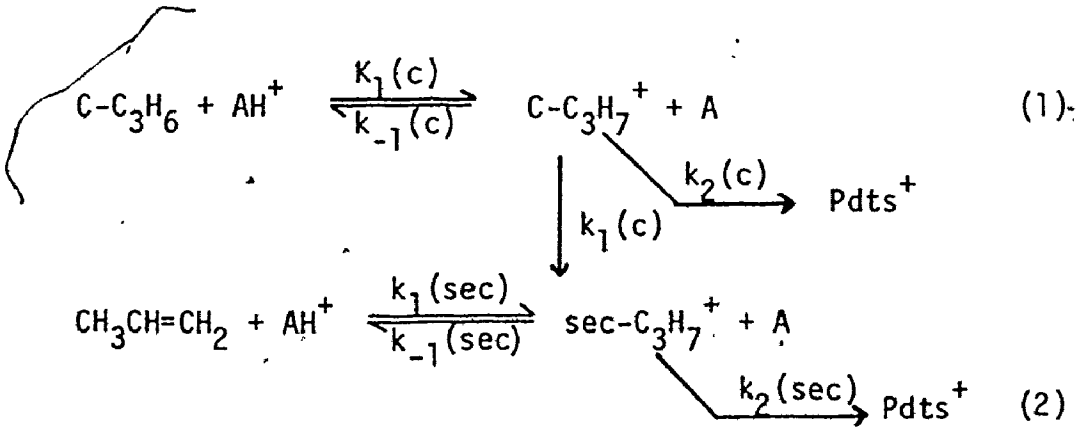


TABLE 1:1: Relative Heats of Formation of ($C_3H_7^+$) Isomers

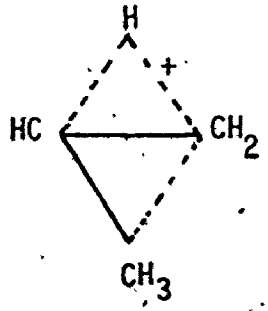
Ion	Heat of formation (Kcal/mole) relative to that of sec-Pr^+		
	MINDO/3[a]	6-31G[b]	Experimental
Sec-Pr^+ (42)	0	0	0
C-Pr^+ (edge) (43-a)	7.5	19.1	8[c]
C-Pr^+ (corner) (43-b)	12.3	13.0	
n-Pr^+ (44)	18.6	17[d]	16[e]

[a] Reference 112. [b]Reference 113; it is predicted that further refinements in geometry optimization and inclusion of p-type orbitals on hydrogen should substantially lower the relative energy of 43-a and, to a lesser extent, that of 43-b. [c]Reference 116. [d]Methyl-staggered form. [e]Reference 130.

Dewar's theoretical calculations [112] also predict the lowest energy form of the cyclic ($C_3H_7^+$) ion (43-a) to be 11 kcal/mole more stable than the n-propyl ion (44); if the latter structure resembles closely the transition state[128] for the rearrangement 43 → 42, this reaction should exhibit a relatively high activation energy. However, interpretations of the experimental results[116,117] differ markedly in the stability indicated for the cyclic ion. In ion cyclotron resonance (ICR) experiments[117] ions formed by the protonation of cyclopropane were found to react with methanol in the same manner as sec-$C_3H_7^+$ ions react; it was concluded that either C-C_3H_6 and $CH_3CH{=}CH_2$ have nearly identical

proton affinities as postulated by Chang and Franklin, or that the ($C\text{-}C_3H_7^+$) ions have isomerized to the ($sec\text{-}C_3H_7^+$) structure before reacting, Scheme II, given above).

McLafferty and his co-workers[129] have found the collisional activation (CA) spectra of gaseous ions formed by the protonation of cyclopropane and propene to be identical, indicating that the isomerization ($C\text{-}C_3H_7^+$) → ($sec\text{-}C_3H_7^+$) occurs in less than 10^{-5} S. However, ion-molecule reactions of ($C_3H_7^+$) at $\sim 10^{-2}$ Torr indicated that ($C\text{-}C_3H_7^+$) ions could have lifetimes of 10^{-7} S, supporting the results of equilibrium constant measurements by Chong and Franklin,[116] who derived $\Delta H_f(c\text{-}C_3H_7^+) - \Delta H_f(sec\text{-}C_3H_7^+)$ = 8 kcal/mole, consistent with the prediction of MINDO/3 calculations;[112] however, the apparent low activation energy for ($C\text{-}C_3H_7^+$) → ($sec\text{-}C_3H_7^+$) indicated by the CA results is not consistent with the MINDO/3 value[112] of $\Delta H_f(n\text{-}C_3H_7^+) - \Delta H_f(C\text{-}C_3H_7^+)$ if the transition state for this reaction was similar to the structure of the ($n\text{-}C_3H_7^+$) ion. Thus the ready isomerization of ($C\text{-}C_3H_7^+$) → ($sec\text{-}C_3H_7^+$) indicated by the CA spectra[129] suggested that $\Delta H_f(n\text{-}C_3H_7^+)$ is lower than the calculated value or that the transition state for 43 → 42 has a substantially lower energy than that of 44. Professor Schleyer has suggested 45 as the alternative transition.[128]



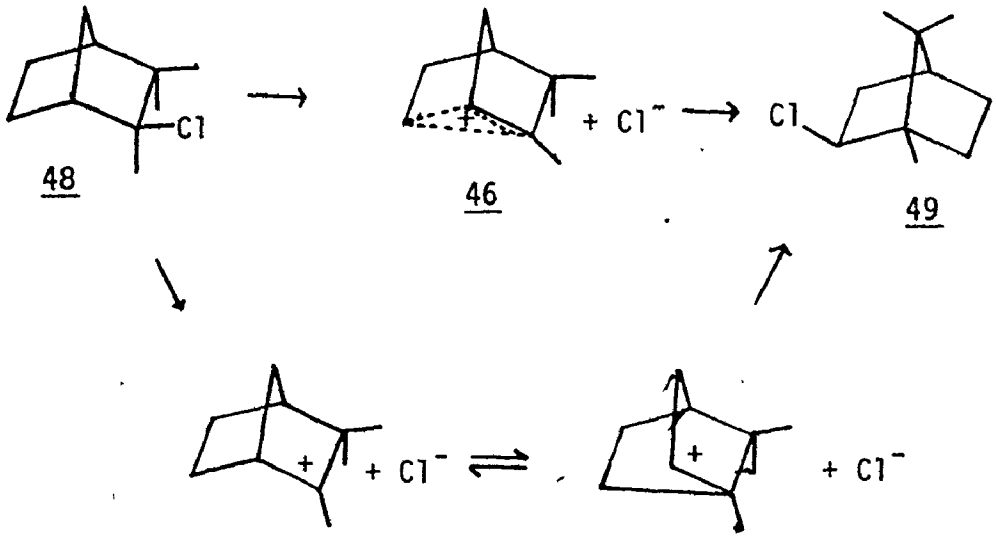
45

D. THE NORBORNYL CATION PROBLEM

1. Experimental Studies

The remarkable facility of skeletal rearrangements in the bicyclo[2.2.1]heptyl (norbornyl) system attracted the early interest of chemists. Wagner realized first in 1899 the general nature of the borneol-camphene type rearrangements and with great foresight related them to the rearrangement which takes place during the dehydration of pinacol to tetramethylethylene.[131] Semmler found tricyclanes in the products of Wagner rearrangements of terpenes.[132] Ruzicka in 1918 suggested a tricyclane-type mechanism for the Wagner rearrangement, without realizing the ionic nature of the process.[133] Meerwein in 1922 reconsidered the mechanism and made the farsighted suggestion that the reaction proceeds through an ionic intermediate, a substituted norbornyl cation.[134] This mechanistic path is now known as the Wagner-Meerwein rearrangement. The structure of the norbornyl cation became controversial, in the "classical-nonclassical ion" controversy,[135,136] following Wilson's original suggestion in 1939 of a mesomeric σ-delocalized, carbonium ion intermediate (46) in the camphene hydrochloride-isobornyl chloride rearrangement,[137] instead of the rapidly equilibrating pair of ions (or ion pairs) (47) proposed by Meerwein and Van Emster.[134]

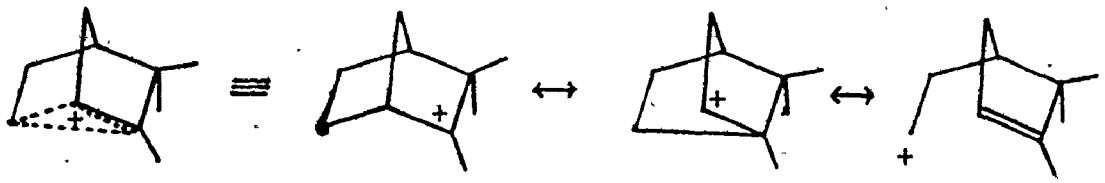
This idea was further developed by Winstein and Trifan[138] and by Ingold and co-workers[139] based on certain stereochemical and kinetic evidence. The solvolyses of exo- and endo-norbornyl brosylates,[138] of isobornyl chloride (49) and camphene hydrochloride (48) were proposed



48 46 49

47

to proceed with participation of the C_1-C_6 bonding pair to produce cationic intermediates possessing the σ-bridged resonance-stabilized structures 50 and 46, respectively.[140]



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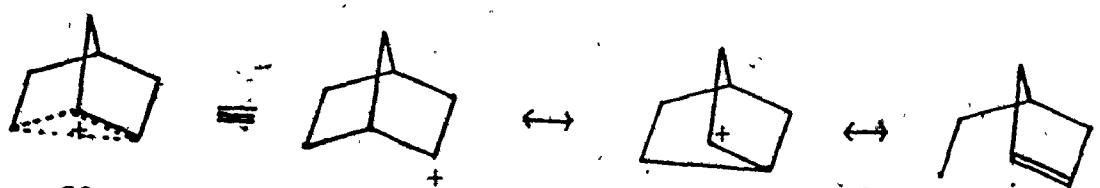

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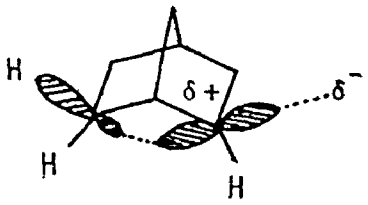
Brown's observation that 2-arylnorbornyl derivatives, which solvolyze to produce classical 2-arylnorbornyl cations, exhibit comparable high exo:endo rate and product ratios demolished the original basis for the proposed σ-bridged structure for the 2-norbornyl cation.[135a] Nevertheless there has been exhibited a major reluctance to surrender this intriguing proposal and there have been numerous attempts to uncover a new basis to support the existence of σ-bridged 2-norbornyl cations.[135a, 140]

Olah, however, has favoured a formulation as a corner-protonated nortricyclane (51), deleting the dashed double bond of Winstein, 50[141a]. In this publication he has also proposed that it is not the C_1-C_6 bonding pair that participates, but the endo lobe of the exo-H on C_6 (see 52). Then two years later he preferred another formulation 53.[141b]



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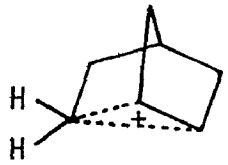

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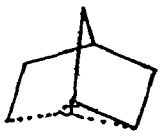

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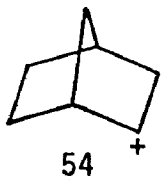
On the other hand, Traylor has supported a formulation of the 2-norbornyl cation as involving vertical stabilization by the C_1-C_6 bonding pair but without σ-bridging or movement of the atoms.[142] In other words, the structure would be that of the classical ion 54 but stabilized by an electronic contribution that does not alter the geometry. It should be pointed out that this particular formulation lacks the plane of symmetry



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possessed by the other proposed structures, 50, 51, 53, 55, 56 and 58. Consequently, there is no lack of formulations for the 2-norbornyl cation. These are lacking only experimental results which require one of these non-classical formulations over the simple classical one.

One might have hoped that the application of various physical methods to the 2-norbornyl cation under stable ion conditions might have solved the problem of the structure of the cation under those conditions. There would then remain only the question as to whether the results could be extrapolated to the structure of the cation under solvolytic conditions. Indeed, Olah and co-workers have applied pmr,[141a,143] cmr,[141a] Raman,[144] and ESCA[145] to the 2-norbornyl cation and have concluded that it possesses structure 53. They have further proposed that the cation formed in the solvolysis of 2-norbornyl derivatives proceeds to give the same species but have not as yet discussed the many experiments which have failed to reveal any experimental evidence for the oft postulated charge delocalization from the C-2 to the C-1 and C-6 positions.[135a] Nor have they

considered Traylor's proposal.[142] Finally, they have ignored Allen's and Dewar's unfavourable calculations although they make frequent reference to Klopman's "remarkable"* calculation.[146]

Major reliance has been placed on the ESCA spectrum in the conclusion that the norbornyl cation is σ-bridged under the experimental conditions. The ESCA technique, as applied to carbonium ions in super-acid media, is fraught with experimental difficulties as remarked in a private communication by Professor Martin Saunders of Yale University to Professor Herbert Brown of Purdue University. Saunders agrees with Brown that the published ESCA data are not conclusive. In Saunders' own ESCA studies he and his co-workers have observed that the peaks vary considerably from experiment to experiment. He believes that "the variability arises from surface effects since the ESCA experiment only looks at about the first 30A° of material." He added it is extremely difficult to prevent small amounts of contamination from entering an ESCA instrument during the sample preparation or afterward. These impurities could very easily destroy carbonium ions. He finally remarked, "It is regretable that no one has yet repeated any of Olah's ESCA experiments in this area".[147] Even more serious is the discovery that such solutions of carbonium ions can involve several equilibria.[148] Consequently, there is no certainty as to the precise solid phase that separates on freezing the solution, the solid phase which is then subjected to ESCA examination.

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* Remarkable, because there was simply no experimental evidence to justify a stabilization of the non-classical structure of some 40 kcal mol^{-1}, as indicated by this calculation.

It has been seen that the original ESCA spectrum[145a] corresponds to a 6:1 distribution of carbon atoms, rather than the 5:2 reported by the authors and required by the σ-bridged formulation.[149] The later ESCA spectrum appears to be that of a mixture.[149]

In spite of these difficulties and uncertainties, not discussed in the publications,[145] the authors have not hesitated to extrapolate their ESCA results in super acid media to the solvolytic field to conclude, "... the long standing controversy as to the nature of the norbornyl cation is unequivocally resolved in favour of the nonclassical carbonium ion".[145b]

Many workers in the field found Goering's solvolysis of optically active 1,2-dimethyl-exo-2-norbornyl p-nitrobenzoate in 90% aqueous acetone to give alcohols with 90% retention[150a] and the methanolysis of optically active 1,2-dimethyl-exo-2-norbornyl chloride to give the methyl ether with 14% retention[150b] more convincing as proof of the classical nature of the 1,2-dimethyl-2-norbornyl cation than the earlier, less direct arguments based on kinetic observations of the effect of the 1-methyl substituent on the rates of solvolysis.[151]

It is clear that the acetolysis of optically active exo-norbornyl brosylate failed to provide optically active acetate.[138] It has often been assumed that the rate of collapse of classical secondary ions to products must be very fast, competitive with the rate of rotation about a single bond.[152] Perhaps the difficulty has been that the solvolysis of 2-norbornyl derivatives do not proceed to the formation of the free carbonium ions which can collapse at the postulated fast rate but proceed instead to tight ion pairs[153] with relatively long lives before collapse occurs. In that event, the intermediate could undergo many Wagner-

Meerwein interconversions before it is finally captured by solvent.

Indeed Olah has calculated that ΔG^* for the capture of the intermediate by solvent is 9.7 kcal/mole.[141a] This compares with a value of $\Delta G^* \leq 4$ kcal/mole estimated for the Wagner-Meerwein interconversion.

The deamination of exo- and endo-norbornylamine appears to involve the formation of carbonium ions not tight ion pairs of such stability.[154] It proceeds to give exo-norbornanol with considerable retention of activity. It was concluded that the reaction does proceed through the formation of the classical 2-norbornyl cation, but it was argued that the exothermic nature of the deamination step made the reaction exceptional so that the result should not be extrapolated to other carbonium ion reactions of the norbornyl system.

In view of the many conflicting conclusions from the various theoretical and experimental approaches considered so far, Brown et al.[147] decided to undertake a direct experimental probe of the question as to whether the norbornyl cation is a symmetrical (non-classical) or an unsymmetrical (classical) species. Brown, in his publications of 1975, concluded that his results as well as related studies, clearly establish that the 2-norbornyl cation can be captured in its unsymmetrical (classical) form. Before additional effort is devoted to the proposal for the existence of a symmetrical σ-bridged (non-classical) intermediate, there is a real need for careful consideration and analysis of the huge mass of data available and a clear statement as to why these data are not convincing to those who continue to favour the symmetrical σ-bridged species.[147]

Recently Olah in his review[155a] again claimed that the structural (spectroscopic) studies of the long lived 2-norbornyl cation fully substantiate Winstein's original views. But in Brown's view the rate of solvolysis of the exo isomer of 2-norbornyl ester is not accelerated; it is the rate for the endo isomer which is slow. Olah adds: study of the long-lived norbornyl cation has resulted in indisputable proof for the σ-bridged nonclassical structure.[155a,b] Olah in support of his direct experimental study of carbocations in highly acidic (and therefore weakly nucleophilic) solvent systems stated, "whereas media of varying nucleophilicity obviously affect solvation of carbocations, the structure of ions observed under stable ion conditions cannot be basically different from that in solvolytic systems". But Brown[147] recently questioned the relevance of direct studies of the norbornyl cation to the behaviour of solvolytic systems: "Finally the point needs to be emphasized that it has not yet been established as to how pertinent are the results and conclusions for studies under stable-ion conditions to the behaviour of cations under solvolytic conditions". Olah in contrast says the answer is obvious. Knowing the structure of the intermediate in any reaction, including solvolysis, has obvious significance to understanding of the path and mechanism of the whole process. What can be argued is to what degree the transition state will resemble the intermediates.[155]

Olah[155] has declared the "classical-nonclassical ion controversy" as concluded not only by overwhelming chemical and structural evidence, but also by consideration of present day understanding of chemical bonding

and charge delocalization. Olah says there is no such thing as a completely "classical" type of carbocation. Charge is always delocalized to a significant degree whenever an electron-deficient center is formed in a molecule. Whenever this happens through π-, n-, or σ-electron pair interactions and to what a degree is dependent of the specific system but not of principle. "The norbornyl cation is only one of the many carbocations showing carbon-carbon σ-bond delocalization and will be remembered in years to come as an interesting but by no means unique member of a substantial class of compounds", Olah further added.[155]

It has long been customary to interpret high exo:endo rate ratios in bicyclic systems in terms of σ-participation leading to the formation of σ-bridged norbornyl cations. But Brown[156] concluded that these high exo:endo rate ratios are presumably the result of decreased rates of reaction in the sterically hindered endo direction of the U-shaped norbornane structure.[159-163]

A basic tenet of carbonium ion chemistry is that the more stable a carbonium ion center, the less demand that center will make on neighbouring groups for additional stabilization through participation.[157] An elegant demonstration of this postulate was made by Gassman and Fentiman[158] in the study of the solvolysis of 7-dehydronorbornyl derivatives. They observed that the participation from the π-electrons of the double bond is a linear function of the electron demand of the incipient carbonium ion. Brown et al. have utilized this tool of increasing electron demand to estimate σ- and π-electronic contributions in a large number of representative systems.[159]

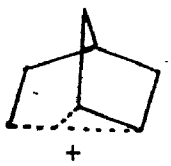
Brown et al. have recently concluded that the tool of increasing electron demand fails to confirm σ-participation in these 2-norbornyl derivatives as the factor responsible for the observed high exo:endo rate and product ratios. The high exo:endo rate and product ratios in these derivatives must instead arise from the unique steric characteristics of the norbornyl system. He finally stresses that in norbornyl system steric effects must contribute a major, if not the only, important factor in the high exo:endo rate and product ratios.[162]

Lambert and Mark[165] have recently observed that even under the inductively enhanced demand in the solvolysis of these derivatives, σ-participation does not contribute significantly to the exo:endo rate ratio.

But Olah[167] in his recent publication has criticized Brown's choice of the "tool of increasing electron demand" as the conclusive proof of nonclassicality by reporting the results of the application of this method by ^{13}C NMR spectroscopic studies of a series of ring-substituted 2-phenyl, 2-norbornyl cations which gives unambiguous evidence for the onset of σ-delocalization, particularly in those ions bearing electron withdrawing substituents. Olah has remarked, "none of Brown's studies ever showed that σ-participation cannot be involved. High exo:endo rates indeed do not per se prove σ-bridging in the 2-norbornyl system, but they are entirely consistent with it and no experimental evidence to the contrary was ever provided".

Olah emphasizes that carbocations observable as stable species in superacidic media are reasonable models for the intermediate ion

like transition states of solvolytic reactions if one takes into account the greater electron demand of carbocations. On the other hand, if the transition states lie earlier on the reaction coordinate, resembling starting materials more than the intermediate ions, then the knowledge of the structure of the ions does not necessarily indicate the nature of the transition state. In other words, if secondary norbornyl systems solvolyze not by a limiting SN_1 mechanism, the transition state can lie earlier on the reaction coordinate and thus not necessarily possess carbocation-like structure (i.e., the solvolysis could show increasing SN_2 characteristic). Olah again declared that the data obtained in their recent studies,[167] however fully support their previous conclusions[155a] reached on the non-classical nature of the parent norbornyl cation (53). They stress, neither the application of Brown's tool of increasing electron demand nor any other experimental data known contradict their conclusion. Olah[167] even questioned Dewar's recent preference for the



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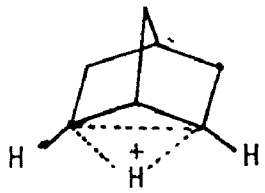
classical structure based on MINDO/3 calculations.[169] Olah's recent words about this mysterious problem are that the so-called 'classical-nonclassical ion controversy' should be considered closed, even when considering Brown's own criterion of the tool of increasing electron

demand.

2. THEORETICAL STUDIES

At one time, empirical calculations leased on the Foote-Schleyer correlation appeared to support the σ-bridged formulation.[172] However, this correlation proved incapable of handling steric hindrance to ionization in certain norbornyl derivatives, and it was concluded that the correlation could not resolve the problem.[173] Then it was argued that the observed degree of racemization in the solvolysis of 2-norbornyl derivatives would require a rate of equilibration of 10^{12} sec^{-1}. It was considered that such a rate was not compatible with formulation as an equilibrating pair of classical cations.[152] However, Fong has applied relaxation theory to the problem and has concluded that a rate of equilibration of 10^{12} sec^{-1} is precisely what should be anticipated for a pair of equilibrating classical 2-norbornyl cations.[174] The introduction of representative substituents in appropriate positions have failed to detect the proposed charge delocalization to the 1 and 6 positions.[135a] However, it has been argued that it is a characteristic of nonclassical delocalization that it cannot be detected by such methods.[175]

However, calculations by Klopman indicated that the nonclassical structure be favoured over the classical structure by some 40 kcal mol^{-1} and also revealed that the edge-protonated structure (55) is favoured over the face-protonated (56) species.[176] On the other hand, on the basis of a more refined ab-initio calculation, Goetz and Allen



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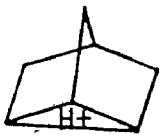

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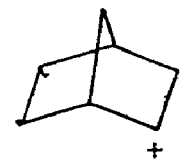
concluded that the classical structure was more favoured by some 5 kcal mol^{-1}.[177] It has been argued, if the classical structure were correct, the norbornyl cation should be a regular secondary carbocation with no additional stabilization provided by σ delocalization (such as the cyclopentyl ion). The facts are, however, to the contrary. Several direct measurements related to the stability of the 2-norbornyl cation, such as Hogeveen's measurement of rates and equilibria of carbonylation[178] and the rates of hydrogenation,[179] Arnett and Larsen's calorimetric data on the heats of formation of stable carbocations from alcohols in FSO_3H-SbF_5,[180a] as well as Arnett and Petro's preliminary measurements of related ionization of chlorides in CH_2Cl_2-SbF_5 solution,[180b] show the norbornyl cation to be substantially more stable (by 6-8 kcal mol^{-1}) than other secondary cations. Regular secondary cations (other than the norbornyl cation), such as the isopropyl, sec-butyl, or cyclopentyl cations, are not stable in methylene chloride solution. However, Arnett was able to study in SbF_5-SO_2ClF solution (in which secondary alkyl cations are

stable at low temperature) the heat of isomerization of the sec-butyl cation to the tert-butyl cation, and found it to be about 14 kcal mol^{-1}. This value is contrasted with the difference in heat of formation of the 2-methylnorbornyl and parent norbornyl cation, which is about 8 kcal mol^{-1}. Thus, the secondary norbornyl cation is substantially more stable than a simple secondary alkyl cation. Solution studies, including direct comparison, through halonium ion formation of stable ions with each other,[181] are also in accord with recent gas-phase ICR and chemical ionization mass spectrometric measurements of relative ion stabilities.[182a] Recently time-resolved high pressure mass spectrometric studies carried out by Field has indicated that the norbornyl cation has 10 kcal/mol more stability than that which would be expected for a secondary species.[182b] Of course, these kinds of studies cannot be sure of the structure of the ions involved.

Dewar's recent remarks about the what he called long standing and not very interesting problem, the two considerations (accuracy and cost) eliminate nearly all the procedures currently available. Conventional semi-empirical treatments (EH, CNDO, INDO) are too inaccurate, as also are ab-initio methods based on the Roothan-Hall[183] (RH) SCF approach unless a very large basis set (6-31G*)[113] is used. The only promising approach currently available is that based on the recently developed MINDO/3 semi-empirical SCF MO method.[184] This has given good results for a very large number of "normal" molecules and ions and also for the three "non-classical" species[186] (CH_5^+,[185] $C_2H_7^+$,[185] protonated

cyclopropane[116]). Dewar admits that the accuracy of MINDO/3 is less than one would like, but still it does at least seem to be much the same for molecules of most kinds. However it produced very meaningful results in comparisons of "classical" and "nonclassical" ions.

So recently, by using MINDO/3, Dewar et al.[169a] have calculated the geometries and energies of 57-61 and of the transition states involved in the degenerate rearrangements of 51 via 59, 60 and 61. The three latter species represent local minima on the potential surface. On the other hand 58 is not a stable species, according to MINDO/3, but rather the symmetrical transition state for the corresponding degenerate rearrangement 57 ⇌ 62.



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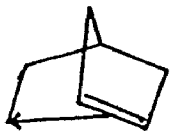

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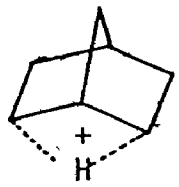

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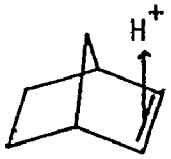

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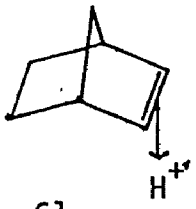

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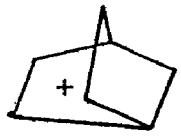

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Their calculated energies, relative to that of 57, of various stable species and transition states are shown in Figure 1, together with experimental values derived from measured activation energies. MINDO/3 predicted the most stable of the isomers to be the "classical ion (57)", the π-complex (58) lying higher in energy although by less than 2 kcal/mol.[169a] But again like always, Olah[155a,167] et al. have criticised

Dewar's recent results which favour the classical structure based on MINDO/3 calculations[169] where minima found corresponding to both classical and nonclassical structures differ by 2 kcal mol^{-1}. Olah adds even when

FIG.1

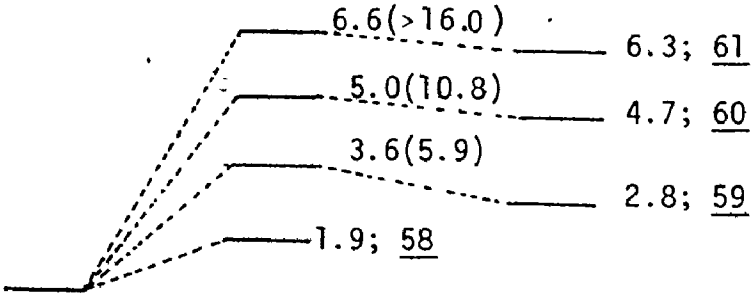


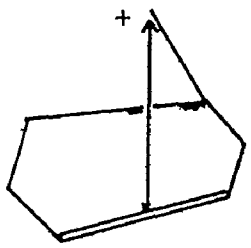
Fig. 1: Relative energies (Kcal/mol) for the 2-norbornyl cation isomers 57-61 and for the transition states for their interconversions; experimental values in parenthesis.

considering that these calculations relate only to the idealized gas phase and refinements may somewhat change values, the energy differences are small, not unlike in the case of the $C_3H_7^+$ system. As, however, similar MINDO/3 calculations by Dewar himself of the heat of formation of the parent neutral hydrocarbon i.e., norbornane gave an error in excess of 20 kcal mol^{-1} compared with the experimentally measured value,[169b] it must be concluded that the limitations of his MINDO/3 calculations at the present time vastly exceed the energy differences involved.[169c] Olah further says that the validity of their reported ESCA spectral studies are recently fully justified by Allen and Goetz,[170] who carried out an extensive non-empirical LCAO-MO-SCF investigation at the STO-3G and STO-4.31G level on the electronic structures of the classical and nonclassical norbornyl cation. Clark, Cromarty and Colling[171] using these parameters were also able to carry out a detailed interpretation of the experimental ESCA data for the core-hole spectra at the ΔSCF STO 4.31G level and calculated equivalent cores at the STO-3G level. Agreement between experimental spectra and those calculated for the nonclassical ion are good

but dramatically different from those calculated for the classical ion.

Finally, the most important conclusion Dewar et al.[169a] established is that the claim by Olah et al. that they had concluded the nonclassical ion controversy by proving the 2-norbornyl cation to have the π-complex structure (58) (or σ-bridged cation 53), was somewhat premature. They[169a] hesitate to claim that they in turn have solved this long standing problem, but however, from their recent studies it does now seem likely that the ion in fact has the classical structure (57), as Brown has been maintaining for years and has succeeded.[162]

Dewar has also suggested that their MINDO/3 studies indicates that the species 63, the unsymmetrical π complex, might be another reasonably stable isomer of 57 which is derived from 57 by passage of C_7 to a bridging position between C_1 and C_2, on the exo side of 57, whereas conversion of 57 to 58 involves an endo migration of C_6. In fact, the calculations they carried out for 63 in the hope that its energy might be low enough for it to



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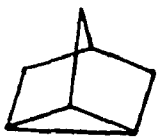
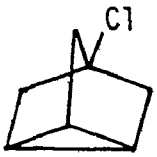
be a possible intermediate in reactions of 57 have indicated to a great surprise that it not only is a stable species but more stable than any of the other 2-norbornyl isomers, 57-61. Even the calculated heat of formation was less than that of 57 by 3.5 kcal mol^{-1}. It is curious that this possibility has never been seriously considered, and also it appears to be consistent with all the available experimental evidence (except perhaps the ESCA spectrum). While it seems unlikely that the ion really is 63,

it is to the credit of MINDO/3 to have drawn attention to the possibility regardless of the final outcome, remarked Dewar.[169a]

Our interest in the chemistry of cyclopropyl compounds led us to study the electrophilic (D^+) cleavage of the cyclopropyl ring of nortricyclane (11a), 4-chloronortricyclane (11b), and 4-bromonortricyclane (11c) in order to:



11a



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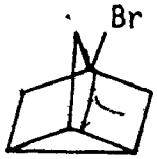


11c

i) understand the electrophilic ring openings of the symmetrical 4-halonortricyclanes and more importantly

ii) to bring the "classical-nonclassical ion controversy" to an end by establishing the structure of the intermediate cation (2-norbornyl cation) generated by ring opening.

Experimental investigations to date have quite well established that the acid-catalyzed ring opening of the nortricyclane occurs via initial edge protonation of the carbon-carbon single bonds of the cyclopropane moiety. In the hope of avoiding some of the complications inherent in the use of these unsymmetrical substituted nortricyclanes we decided to utilize the symmetrical nortricyclane (11a), 4-chloronortricyclane (11b) and 4-bromonortrieyclane (11c), since all three possess an axis of threefold

symmetry and therefore all the cyclopropyl carbons are equivalent. Clearly C_4 is the only carbon centre where substitution of hydrogen does not complicate the situation like in cases of unsymmetrically substituted nortricyclanes. The fission of any of the cyclopropyl bonds of the nortricyclanes 11a, 11b and 11c with an unsymmetrical reagent D^+X^- would yield a 2,6-disubstituted norbornane in which the electrophile (D) and nucleophile (X) can each have an endo or exo configuration. The stereochemical outcome for each moiety would provide information on the intermediates involved in the D^+-ring opening of these symmetrical nortricyclanes 11a, 11b and 11c. The objective of investigating D^+-catalyzed ring-opening of the symmetrical nortricyclanes 11a, 11b and 11c was that by establishing the effect of the mass of the substituent at C_4 (i.e., Ponderal Effect) of these nortricyclanes would clarify the nature of the intermediate via which the protonation occurs viz edge-deuterated or corner-deuterated. "The ponderal effect is defined by de la Mare and co-workers as the effect of added masses which depends upon their weight but not their volume." When the behaviour of molecules having different masses are being compared, the ponderal effect must enter the picture as it depends exclusively upon the distribution of masses in the reactants and in the activated complex as well. The ponderal effect operates only on the entropies of activation almost invariably decreasing the rates of reactions of heavier compounds in comparison to lighter compounds. Ponderal effects have been estimated theoretically[187] for some particular systems.

The study of acid-catalyzed ring-opening of nortricyclane (11a), 4-chloronortricyclane (11b) and 4-bromonortricyclane (11c) is of interest

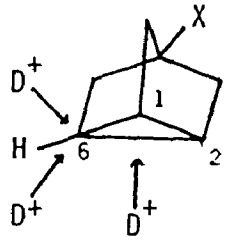
to us for the reason that, the results of these studies would establish the nature of the first formed intermediate resulting either from initial edge or corner protonation.

If the ring opening of nortricyclane, 4-chloronortricyclane and 4-bromonortricyclane in D_2SO_4/CD_3COOD medium occurs via initial corner protonation (or corner deuteration) the product of each ring-opening would be expected to contain an equal amount of deuterium in exo and endo positions at the carbon atom attacked by the electrophile D^+ (e.g., C_6 in Scheme 1:6). But if the ring opening occurs via intial edge-protonation (of C_2-C_6 bond for instance), the resulting product should contain more of deuterium in the endo position than in the exo position of C_6, (Scheme 1:6).

Moreover the ratio of endo:exo deuterium should increase as the mass of the substituent at C_4 increases due to the ponderal effect since the rate of conversion of 64-endo-6-d to 64-exo-6-d would decrease as the mass of substituent at C_4 increases.

The essential feature of our studies was to establish the structure of the norbornyl cation i.e., whether it is a rapidly equilibrating classical ion[162] or a σ-bridged nonclassical cation.[167] In all the studies reported to date, the central issue in the conflict is whether the σ-bridged norbornonium ion (65a) is an intermediate or it best represents the transition state between classical cations (66a) and (67a). To date the chemists have been utilized unsymmetrically substituted norbornyl compounds, substituted with electron withdrawing or electron donating groups, at most sites, in the bicyclic[2.2.1]framework and thereby destroyed the symmetry inherent in 65a and in the 66a - 67a pair of ions. As C_4 is the only carbon centre where substitution of hydrogen does not destroy the symmetry and thereby

SCHEME 1:6

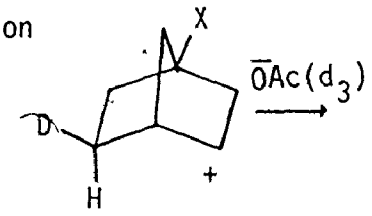


11a ; X=H

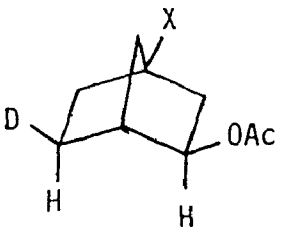
11b ; X=Cl

11c ; X=Br

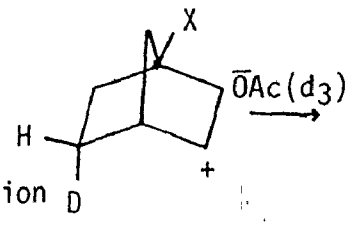
Corner-deuteration
Exo attack
of D^+ at C_6



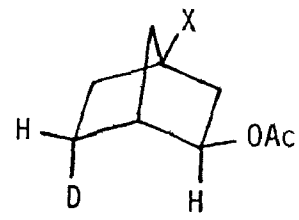
64-exo-6-d



11-OAc-exo-6-d



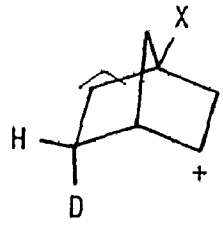
64-endo-6-d



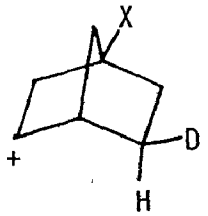
11-OAc-endo-6-d

Corner deuteration
Endo attack
of D^+ at C_6

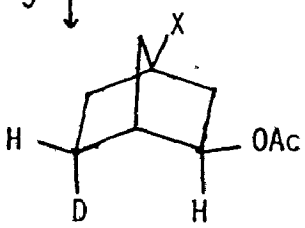
Edge-deuteration
of C_2-C_6 bond
by D^+



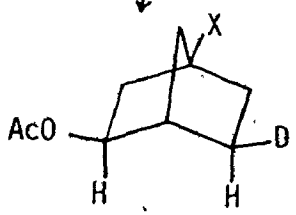
64-endo-6-d



64-exo-6-d

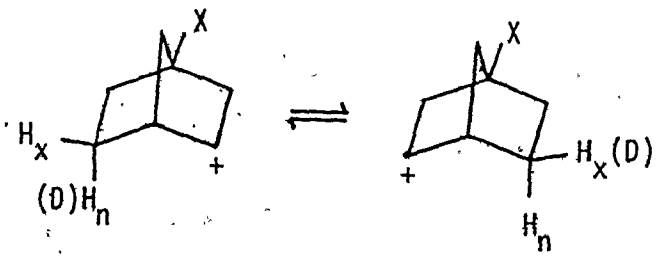


11-OAc-endo-6-d



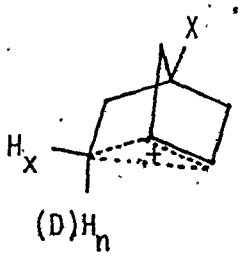
11-OAc-exo-6-d

avoids complicating the situation, we reasoned that to answer the critical question (vide supra) of structure of the long-lived norbornyl cation - the stereochemistry of the ring opening of 4-halonortricyclanes should be established, which would provide solution to the critical classical-nonclassical cation problem for the reason that: if the σ-bridged species (65a) is the intermediate, the stereochemistry of the deuteration of these 4-halonortricyclanes, as determined by the endo:exo deuterium ratio at C_6, would be independent of the substituent at C_4. However, if the intermediate in the acid-catalyzed ring-opening is the rapidly equilibrating classical cation 66 ⇌ 67 and 65 best represents the transition state between classical cations 66 and 67, the rate of isomerization of 66 to 67 should decrease as the ponderal effect[187] of substituent at C_4 increases. The collapse of the first formed classical ion with solvent would compete more effectively with its equilibration and a change would be detected in the stereochemistry of the acid-catalyzed ring opening of the symmetrical 4-halonortricyclanes 11a, 11b and 11c. The stereochemistry of the deuteration of 4-halonortricyclanes



66 ⇌ 67

Classical ions



65

a; X=H

b; X=Cl

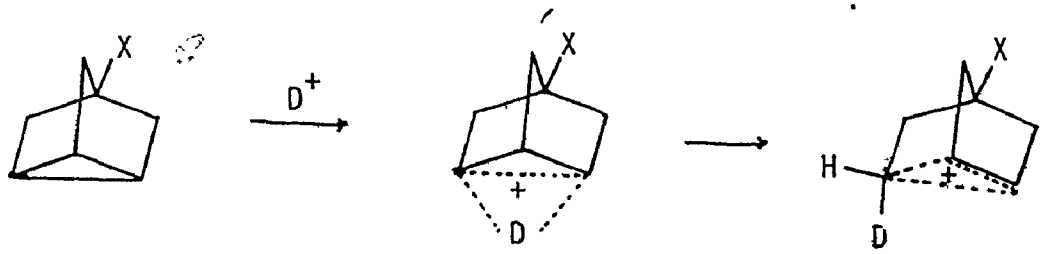
c; X=Br

Nonclassical ions

depends upon the ponderal effect of the substituents at C_4 because of changes in nuclei involved during generation of the intermediate classical ions 66 and 67, via the transition state 65, from the D^+-catalyzed ring opening of 11a, 11b and 11c, since the transition state 65 has to undergo structural change/s in order to give the intermediate ions 66 and 67.

All the studies reported to date indicate that the acid-catalyzed ring-opening of the symmetrical 4-halonortricyclanes (11a), 11b and 11c which have an axis of three-fold symmetry, occur via initial edge-protonated species as the transition state rearranging into either non-classical ion (65) or a rapidly equilibrating pair of classical ions (66) and (67) as the intermediates of the ring opening, (Scheme 1:7).

Scheme 1:7



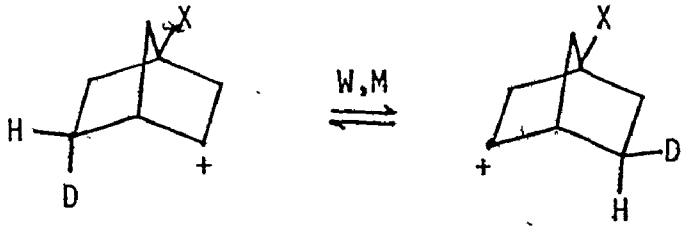
11a ; X=H

11b ; X=Cl

11c ; X=Br

Transition state

65



66

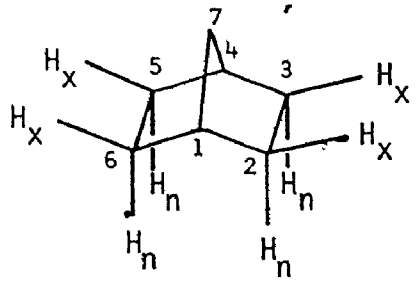
67

CHASPTER 2

RESULTS AND DISCUSSION

Nomenclature

The numbering system which is used for the norbornyl system is as shown below. Throughout this thesis, the abbreviated notations H_n, H_x etc. denote hydrogen in endo and exo-positions with respect to the parent ring system. Reference is repeatedly made to certain compounds



which possess identical skeletons but different functionalities and deuterium substitution. Thus the following system will be used to refer to such compounds. The basic skeleton will be assigned a number and then the functionality will be written immediately following the number (e.g., OAc for acetate, OH for alcohols, etc.) and finally the deuterium substitution (if any) will be described in terms of stereochemistry and site by phrases such as endo-6-d or exo-6-d etc. For example, exo-2-norbornyl system is denoted by 21 and exo-2-norbornyl acetate (or trideuteroacetate) by 21-OAc. To describe a deuterated derivative of 21-OAc, the site of deuteration follows the functional group description. Thus, exo-2-norbornyl acetate-endo-6-d is denoted by 21-OAc-endo-6-d.

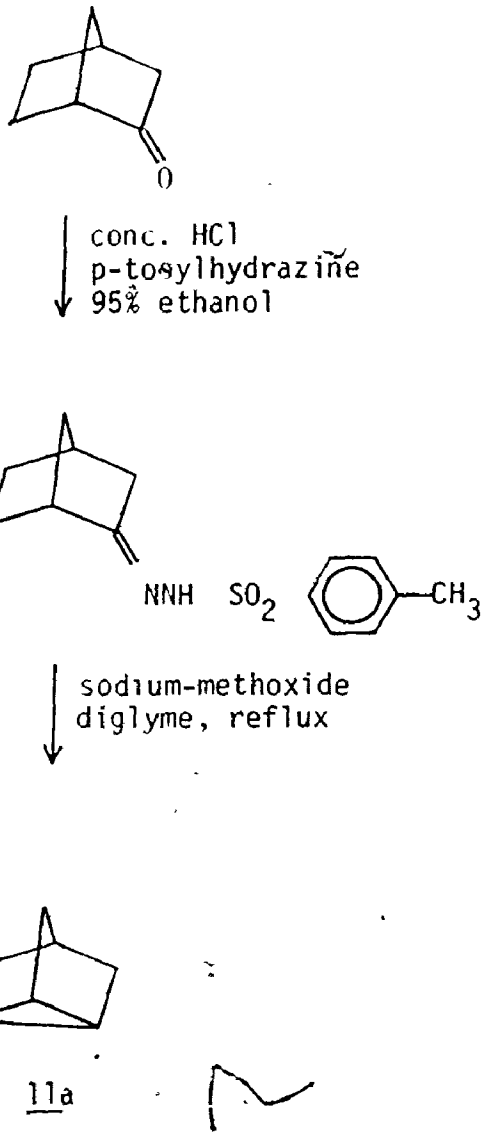
For certain monofunctional compounds, the functional group description is omitted. For example, 2-norbornanone is denoted by 71 and 2-norbornanone-endo-6-d by 71-endo-6-d.

I. Synthesis of Nortricyclanes

A. Nortricyclane (11a)

Nortricyclane (11a) was prepared from the tosylhydrazone of 2-norbornanone[191,192] (Scheme 2:1).

Scheme 2:1

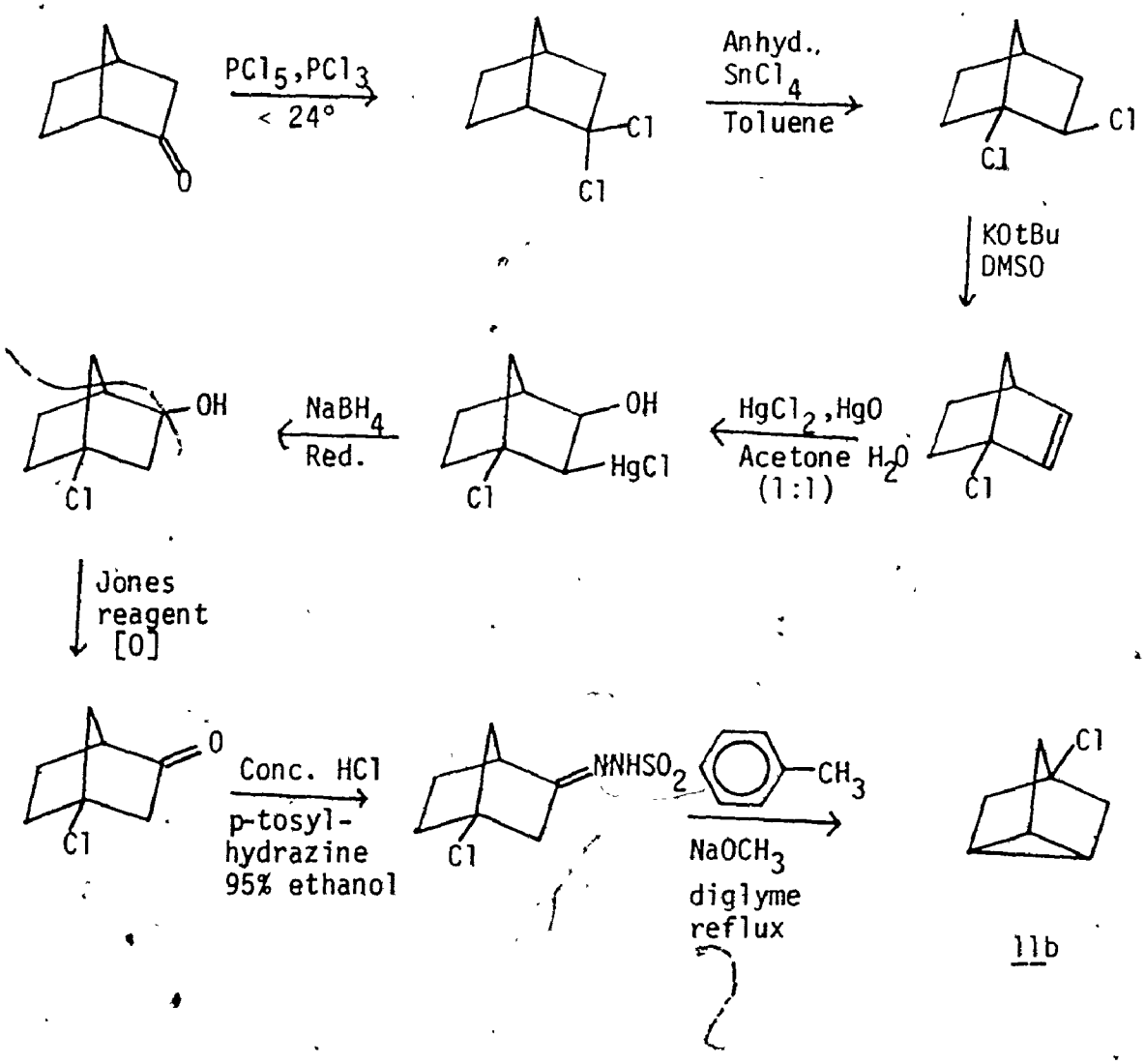


11a

B. 4-Chloronortricyclane (11b)

4-Chloronortricyclane (11b) was synthesized from 2-norbornanone by a route which was modified from the one described by Sauer et al.[199] 1-Chloronorbornene was prepared from 2-norbornanone by the procedure described by Wilt et al.[194] and 4-chloro-exo-2-norborneol was obtained from 1-chloronorbornene by oxymercuration,[195,196] which in turn was oxidized to 4-chloro-2-norbornanone by Jones reagent.[54] 4-Chloronortricyclane was finally obtained from the tosylhydrazone of 4-chloro-2-norbornanone in 40% yield[191,192] (Scheme 2:2).

Scheme 2:2



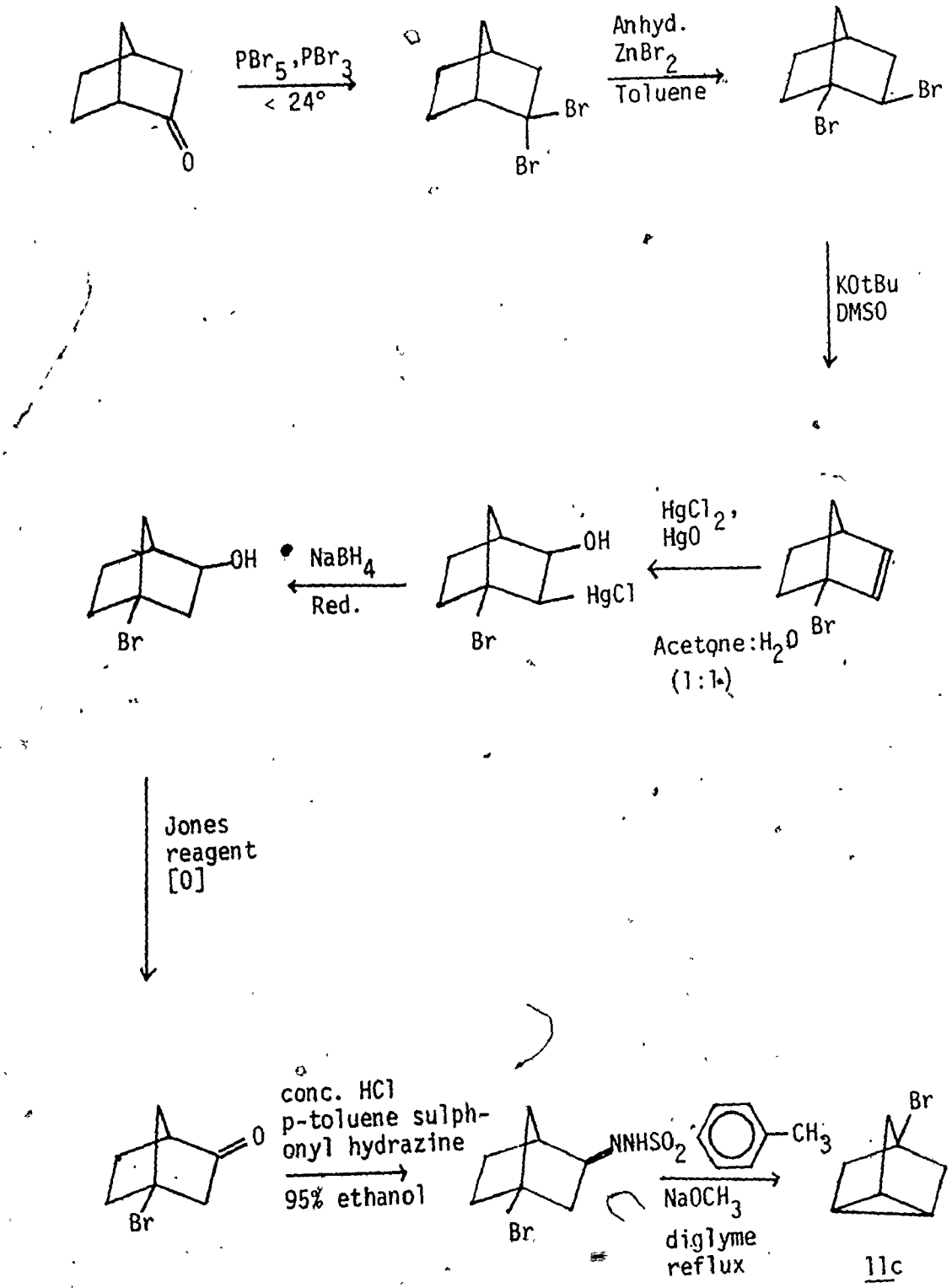
C.1 4-Bromonortricyclane (11c)

4-Bromonortricyclane (11c) was synthesized from 2-norbornanone by a similar route as described for the preparation of 4-chloronortricyclane (11b) with few modifications. 2-Norbornanone was treated with PBr_5 in PBr_3 to give the gem-dibromide of norcamphor which was rearranged to 1, exo-2-dibromonorbornane with anhydrous zinc bromide in toluene. Treatment of this 1, exo-2-dibromonorbornane with potassium tert butoxide in dimethyl sulphoxide produced 1-bromonorborn-2-ene (1-norbornenyl bromide). Oxymercuration of 1-norbornenyl bromide followed by sodium borohydride reduction of organomercurial resulted into 4-bromo-exo-2-norborneol which on oxidation gave 4-bromo -2-norbornanone. The solution of 4-bromo - 2-norbornanone on treatment with p-toluene sulphonylhydrazine in the presence of concentrated hydrochloric acid yielded 4-bromo-2-norbornyltosylhydrazone, which in turn gave 4-bromonortricyclane on refluxing with sodium methoxide in pure diglyme in 42% yield, as summarized in Scheme 2:3.

2. Synthesis of 4-bromonortricyclane from 4-chloronortricyclane

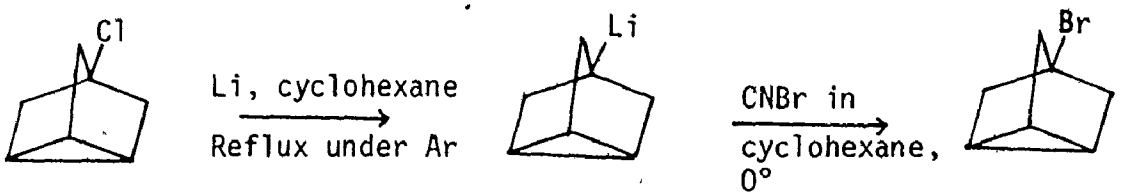
Nortricyclyl lithium[201] was obtained by refluxing 4-chloronortricyclane (11b) with a five fold excess of a dispersion of lithium metal in purified dry cyclohexane under argon for 5-6 hours. 4-Nortricyclyl lithium prepared as such was then quenched with a solution of cynogen bromide in cyclohexane at a temperature of 0° which yielded 4-bromonortricyclane in 41% yield (Scheme 2:4).

Scheme 2:3



11c

Scheme 2:4



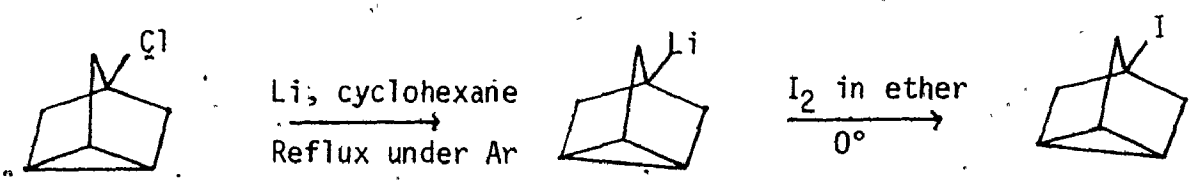
11b 11c

The ir and nmr spectra were identical to that obtained in the previous synthesis of 4-bromonortricyclane from 2-norbornanone as summarized in Scheme 2:3.

D.1. Synthesis of 4-iodonortricyclane (11d) from 4-chloronortricyclane (11a).

4-Nortricyclyl lithium was obtained by refluxing 4-chloronortricyclane (11a) with a five-fold excess of a dispersion of lithium metal prepared, as described in the experimental section, under argon. 4-Iodonortricyclane was obtained by quenching the 4-nortricyclyl lithium with freshly sublimed iodine in ether at 0°, in 40% yield, Scheme 2:5.

Scheme 2:5



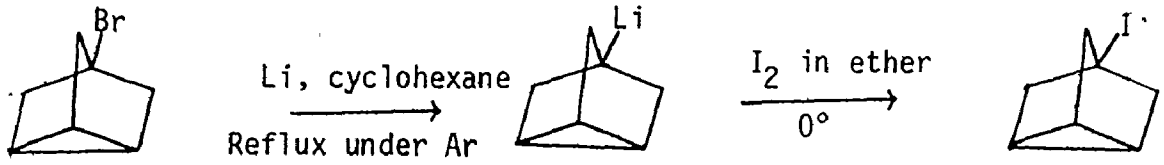
11b 11d

The ir and nmr spectra were obtained and were found to be quite similar to those of 4-chloronortricyclane and 4-bromonortricyclane.

2. Synthesis of 4-iodonortricyclane (11d) from 4-bromonortricyclane (11c).

A five-fold excess of lithium dispersion was refluxed with 4-bromonortricyclane (11c) in cyclohexane under argon. The 4-nortricyclyl lithium obtained as such gave 4-iodonortricyclane (11d) when quenched with freshly sublimed iodine in ether at 0°, Scheme 2:6.

Scheme 2:6



11c 11d

II. Electrophilic Ring-Opening of Nortricyclanes

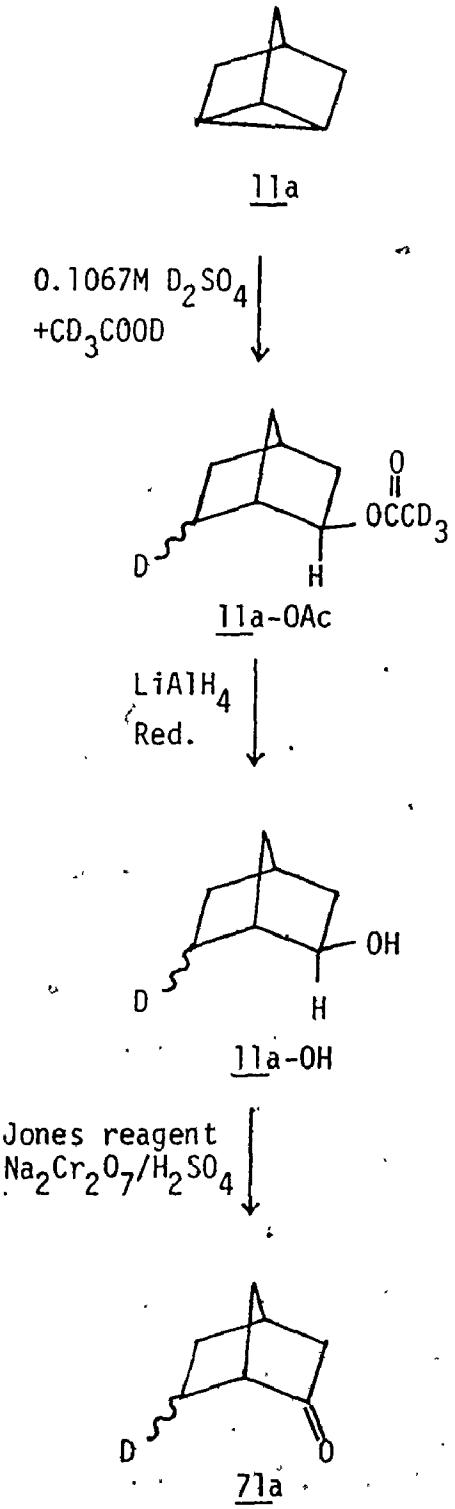
A. Ring-opening of nortricyclane (11a) with deuterated acid.

Nortricyclane (11a) was treated with acetic acid-d_4 (99.5 atom % d) and 0.1067 M sulphuric acid-d_2 for 17 hr at 24° to yield exo-2-norbornyl trideuteroacetate-d_1 (11a-OAc) as identified by nmr spectroscopy (Fig. 2:1). Reduction of an ethereal solution of exo-2-norbornyltrideuteroacetate-d_1 with $LiAlH_4$ gave a mixture of 98 ± 2% exo-2-norborneol-d_1 (11a-OH) and 2 ± 1% endo-2-norborneol-d_1 as determined by analytical glpc.* The reduction of exo-2-norbornyltrideuteroacetate-d_1 (11a-OAc) with $LiAlH_4$ to the corresponding exo-2-norborneol-d_1 (11a-OH) does not affect the stereochemistry of the acetate group or that of deuterium which is not in the acetate group.[51,53,54] Oxidation of the exo-2-norborneol-d_1 with

* See experimental section for estimation of exo- and endo-2-norborneol-d_1.

Jones reagent gave deuterated norbornanone-d_1 (Scheme 2:7).

Scheme 2:7



The amounts of exo-2-norbornyl trideuteroacetate-d_1 (≃ 98%) and endo-2-norbornyl trideuteroacetate-d_1 (≃ 2%) obtained from the D^+-catalyzed ring-opening of nortricyclane (11a) establish that the carbon atom undergoing nucleophilic attack experiences predominant inversion of configuration.

Exo-2-norborneol-d_1 (11a-OH) was purified by preparative glpc. The i.r. and nmr spectroscopy identified it to be exo-2-norborneol-d_1 (11a-OH). Fourier transform dmr spectroscopy was employed for determining the distribution of deuterium at C_6 and more importantly the endo:exo deuterium ratio at C_6. The dmr spectrum of exo-2-norborneol-d_1 (11a-OH) (Fig. 2:4) showed endo:exo deuterium ratio at C_6 to be 1.12. The deuterium distribution in exo-2-norborneol-d_1 (11a-OH) indicated by the dmr spectrum is given in Table 2:1.

Table 2:1: Deuterium distribution and endo:exo deuterium ratio at C_6 of deuterated exo-2-norborneol-d_1 (11a-OH).

Substrate	% Deuterium at				Endo/Exo* Ratio of D at C_6
	C_1	C_2	Endo-C_6	Exo-C_6	
Nortricyclane 11a	9.2±0.6	8.2±2.0	43.6±1.5	39.0±1.3	1.12±0.09

Mass spectrometry indicated that 2-norbornanone-d_1 71a consisted primarily of monodeuterated species (Table 2:2).

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* The results are averages of two ring-openings and five spectrum acquisitions of each of the deuterated exo-norborneols. Errors are expressed as average deviations.

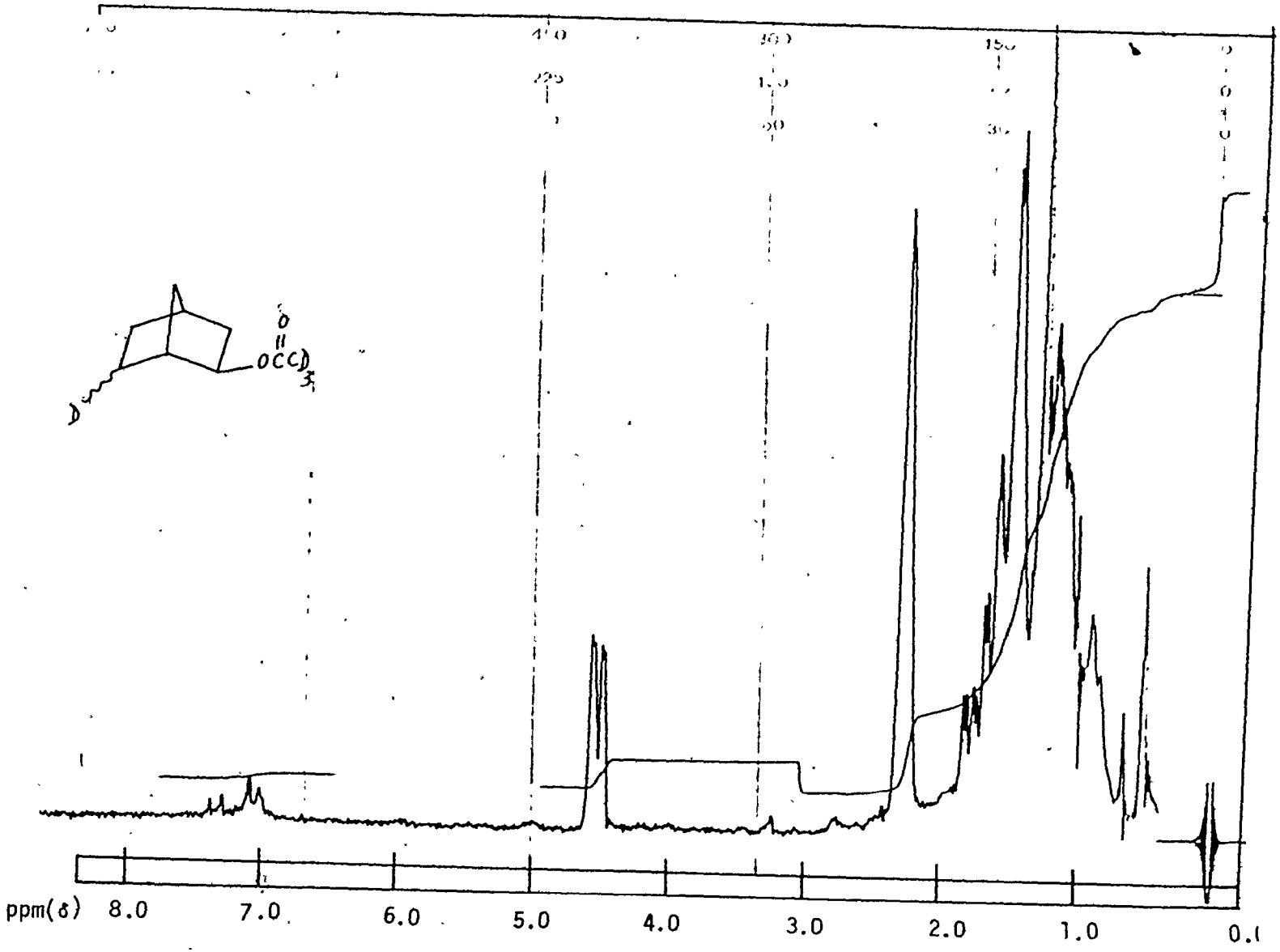


Fig. 2:2. Pmr spectrum (90 MHz) of <u>exo</u>-2-norbornyl trideuteroacetate-d_1 (11a-OAc) in CCl_4.

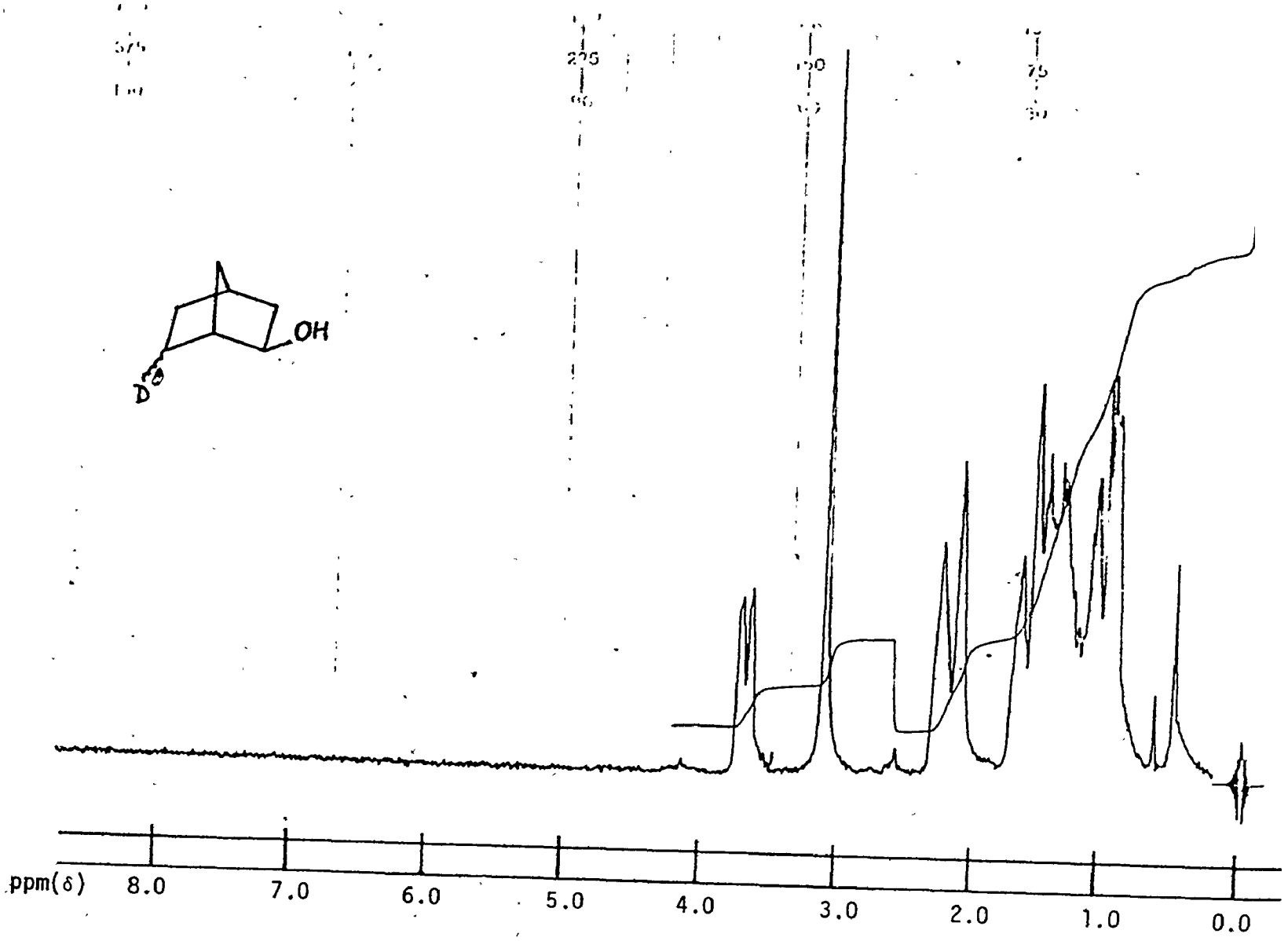


Fig. 2:3. Pmr spectrum (90 MHz) of exo-2-norborneol-d_1 (11a-OH) in CCl_4.

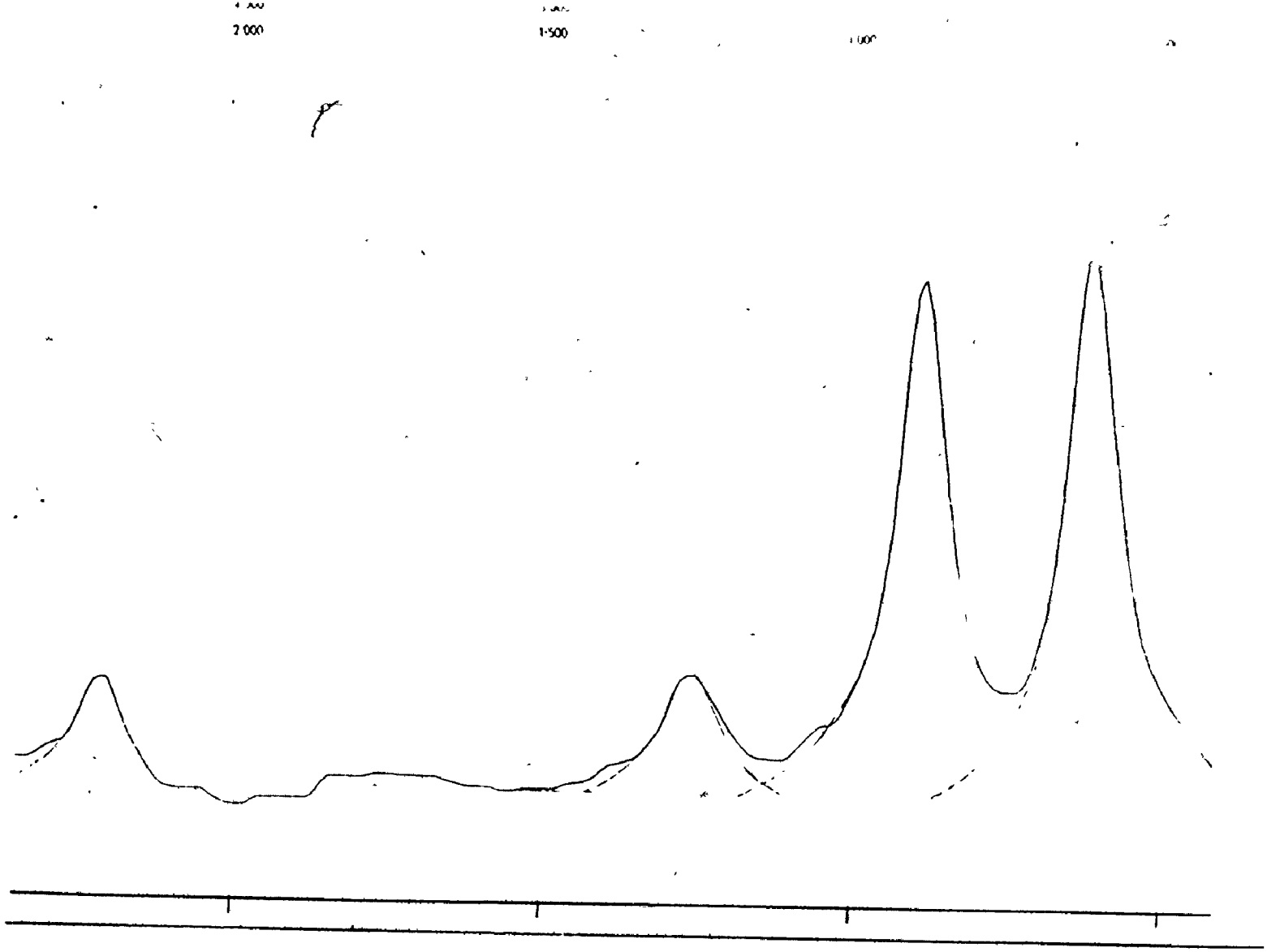


Fig. 2.4. Dmr spectrum of exo-2-norborneol-d_1 (11a-OH) obtained from D^+-catalyzed ring-opening of nortricyclane (11a).

Table 2:2: Mass spectrometric deuterium assay on 2-norbornanone-d_1 71a.

	% d_0	% d_1	% d_2	Average d/molecule
2-norbornanone-d_1 71a	44.24	55.76	0	0.56

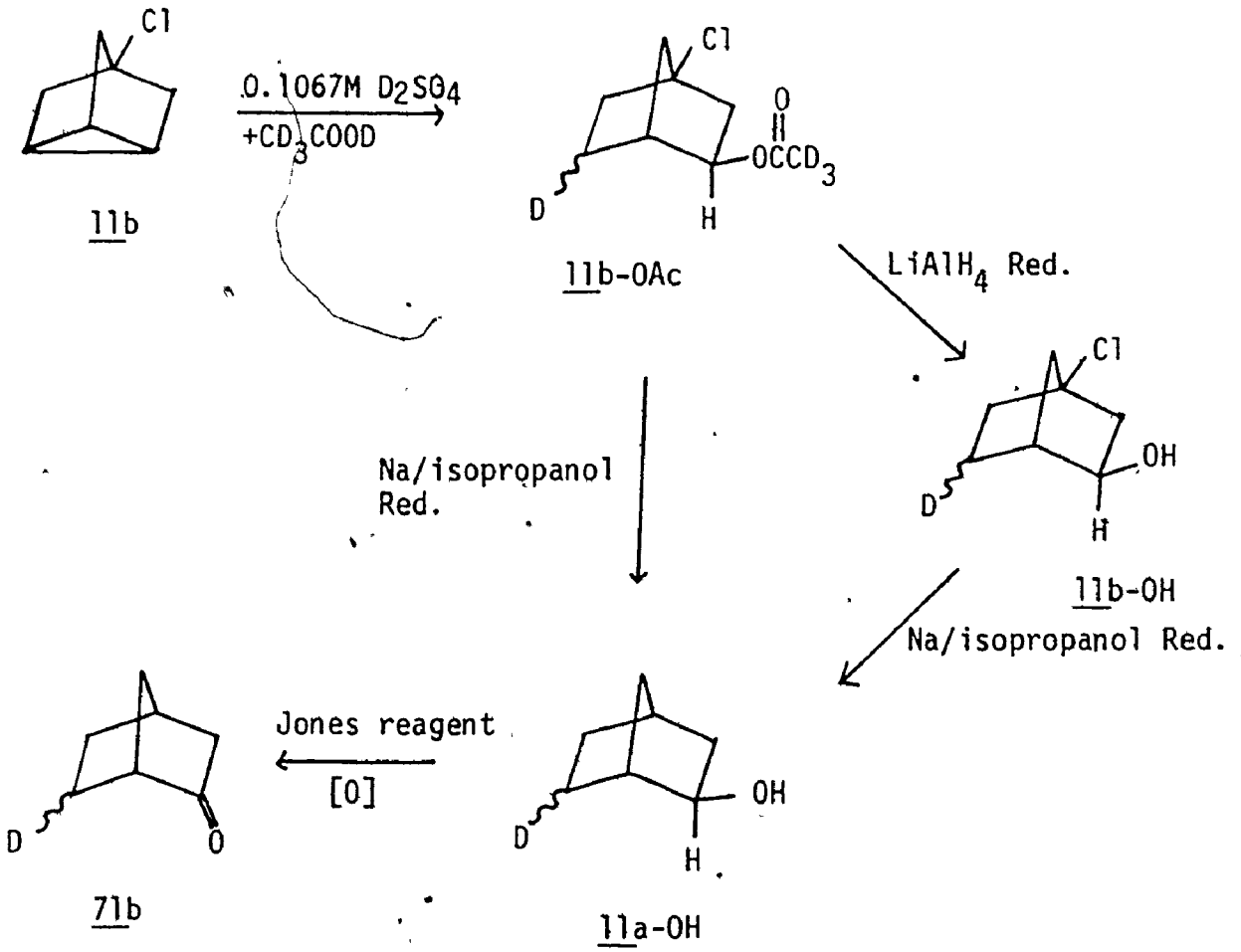
B. Ring-opening of 4-chloronortricyclane (11b) with deuterated acid.

4-Chloronortricyclane (11b) was treated with acetic acid-d_4 (99.5 atom % d) and 0.1067 M sulphuric acid-d_2 for 94 hours at (50° ± 1) to yield 4-chloro-exo-2-norbornyl trideuteroacetate-d_1 (11b-OAc) as identified by nmr spectroscopy (Fig. 2:6). Reduction of the above 4-chloro-exo-2-norbornyl trideuteroacetate-d_1 (11b-OAc) in ether with lithium aluminum hydride gave more than 97% of 4-chloro-exo-2-norborneol-d_1 (11b-OH) and the remaining undetectable (<3%) 4-chloro-endo-2-norborneol-d_1. 4-Chloro-exo-2-norborneol-d_1 (11b-OH) was purified by preparative glpc (15% carbowax, 160°). The nmr spectrum indicated as pure chlorohydrin and identified as to be 4-chloro-exo-2-norborneol-d_1, (Fig. 2:7).

To keep consistency in comparisons of dmr analysis of exo-2-norborneols, 4-chloro-exo-2-norbornyl trideuteroacetate-d_1 was reduced to exo-2--norborneol-d_1 by sodium in isopropanol. The exo-2-norborneol-d_1 obtained as such was purified by preparative glpc (15% carbowax, 140°). The proton nmr spectrum of the exo-2-norborneol-d_1 (11a-OH) obtained from 4-chloro-exo-2-norbornyl trideuteroacetate-d_1 (11b-OAc) was identical to that given in Fig. 2:3.

The dmr spectrum of exo--2-norborneol-d_1 (11a-OH) was obtained by fourier transform dmr spectroscopy (Fig. 2:8). Exo-2-norborneol-d_1 was then oxidized to 2-norbornanone-d_1 (71b) by Jones reagent (Scheme 2:8).

Scheme 2:8



The deuterium distribution in exo-2-norborneol-d_1 obtained from 4-chloro-exo-2-norbornyltrideuteroacetate-d_1 (11b-OAc), the product of D^+-catalyzed ring-opening of 4-chloronortricyclane (11b), as determined from the dmr spectrum (Fig. 2:8) is given in Table 2:3.

Table 2:3: Deuterium distribution and endo:exo deuterium ratio at C_6 of exo-2-norborneol-d_1 obtained from 4-chloro-exo-2-norbornyl-trideuteroacetate-d_1.

Substrate	% Deuterium at				
	C_1	C_2	Endo-C_6	Exo-C_6	$\frac{\text{Endo}}{\text{Exo}}$ Ratio of D at C_6
4-chloronortricyclane, (11b)	3.3±0.6	2.6±0.3	54.0±0.8	40.1±0.9	1.35±0.03

Mass spectrometric deuterium assay of 2-norbornanone-d_1 obtained from 4-chloro-exo-2-norbornyl trideuteroacetate-d_1 (11b-OAc) as shown in (Scheme 2:8) indicated that the deuterated norbornanone was primarily a monodeuterated species (Table 2:4).

Table 2:4: Mass spectrometric deuterium assay on 2-norbornanone-d_1 71b.

	% d_0	% d_1	% d_2	Average d/molecule
2-norbornanone-d_1 71b	11.8	86.8	1.3	0.9

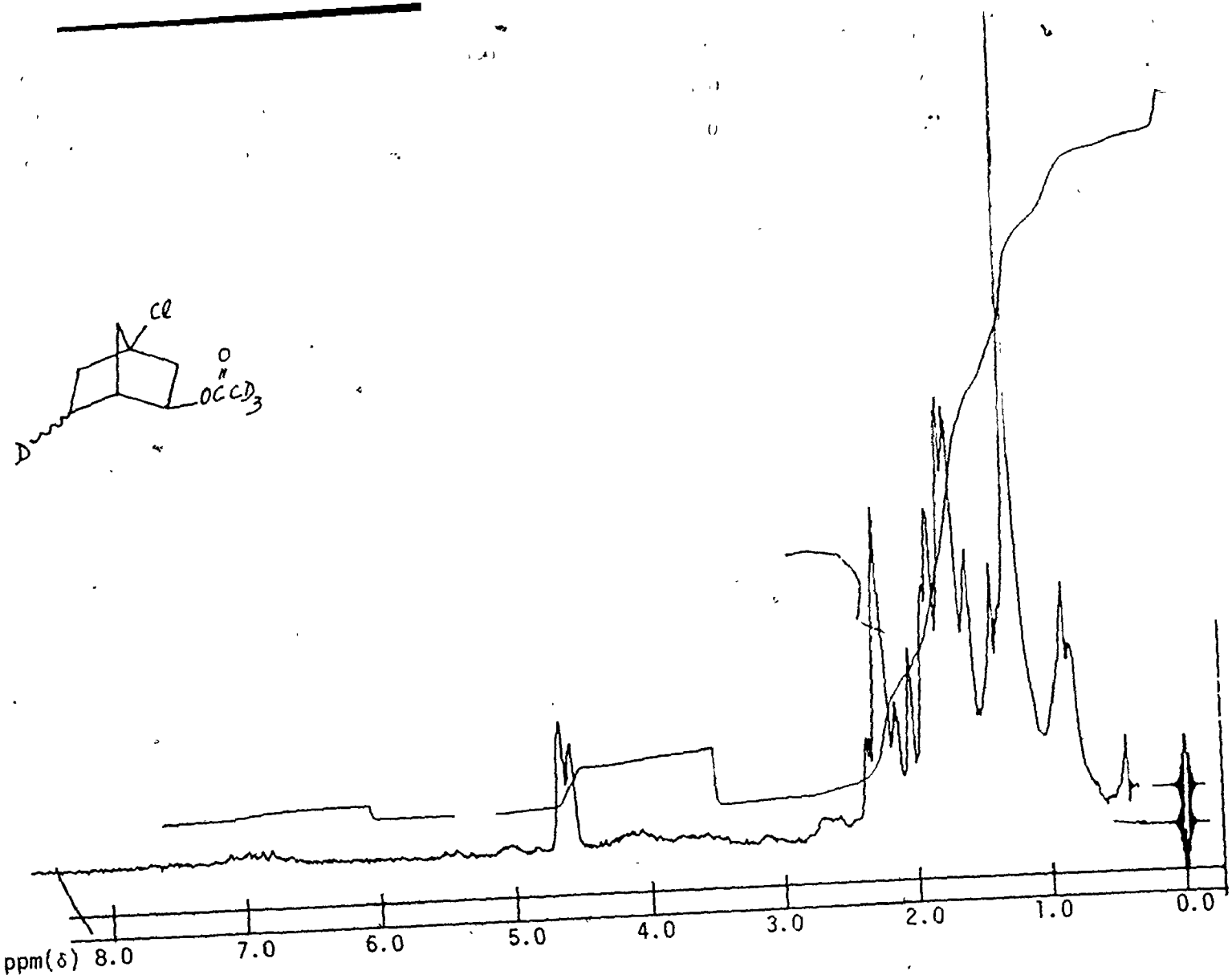


Fig. 2:6. Pmr spectrum (90 MHz) of 4-chloro-exo-2-norbornyl trideuteroacetate-d_1 (11b-OAc) in CCl_4.

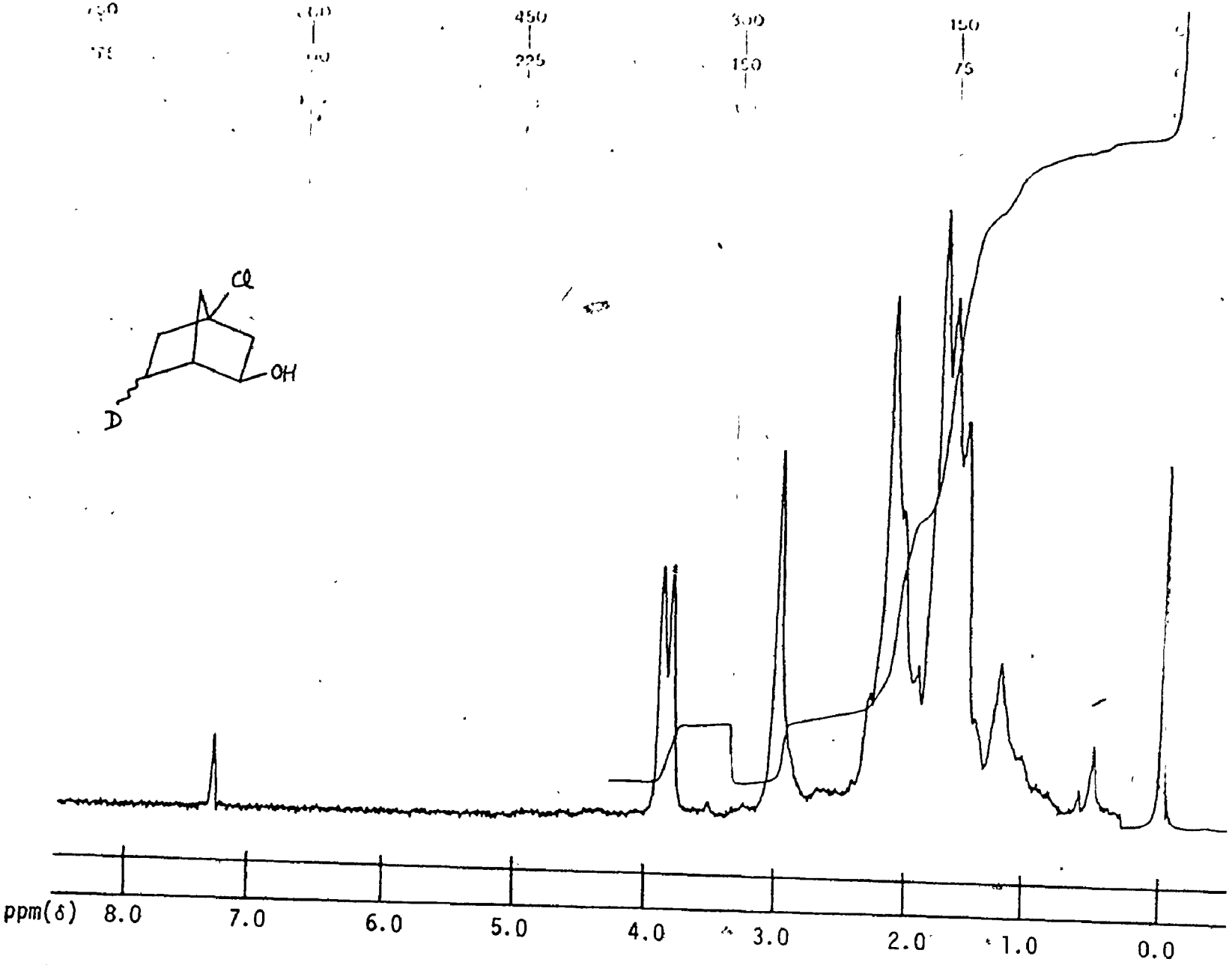


Fig. 2:7. Pmr spectrum (90 MHz) of 4-chloro-exo-2-norborneol-d_1 (11b-OH) in CCl_4.

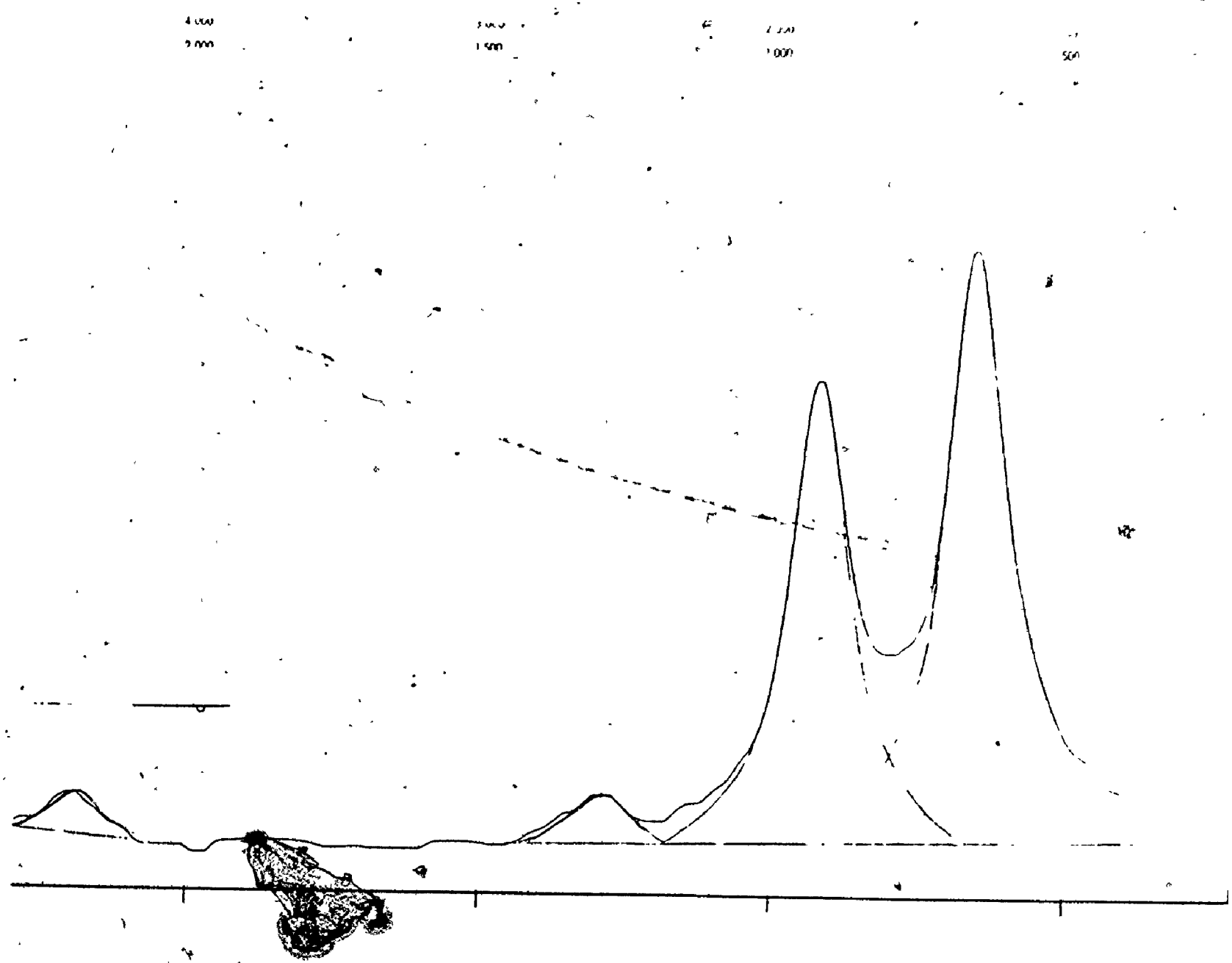


Fig. 2:8. dmr of exo-2-norborneol-d_1 (11a-OH) obtained from the D^+-catalyzed ring-opening of 4-chloronortricyclane (11b).

C. Ring-opening of 4-bromonortricyclane (11c) with deuterated acid.

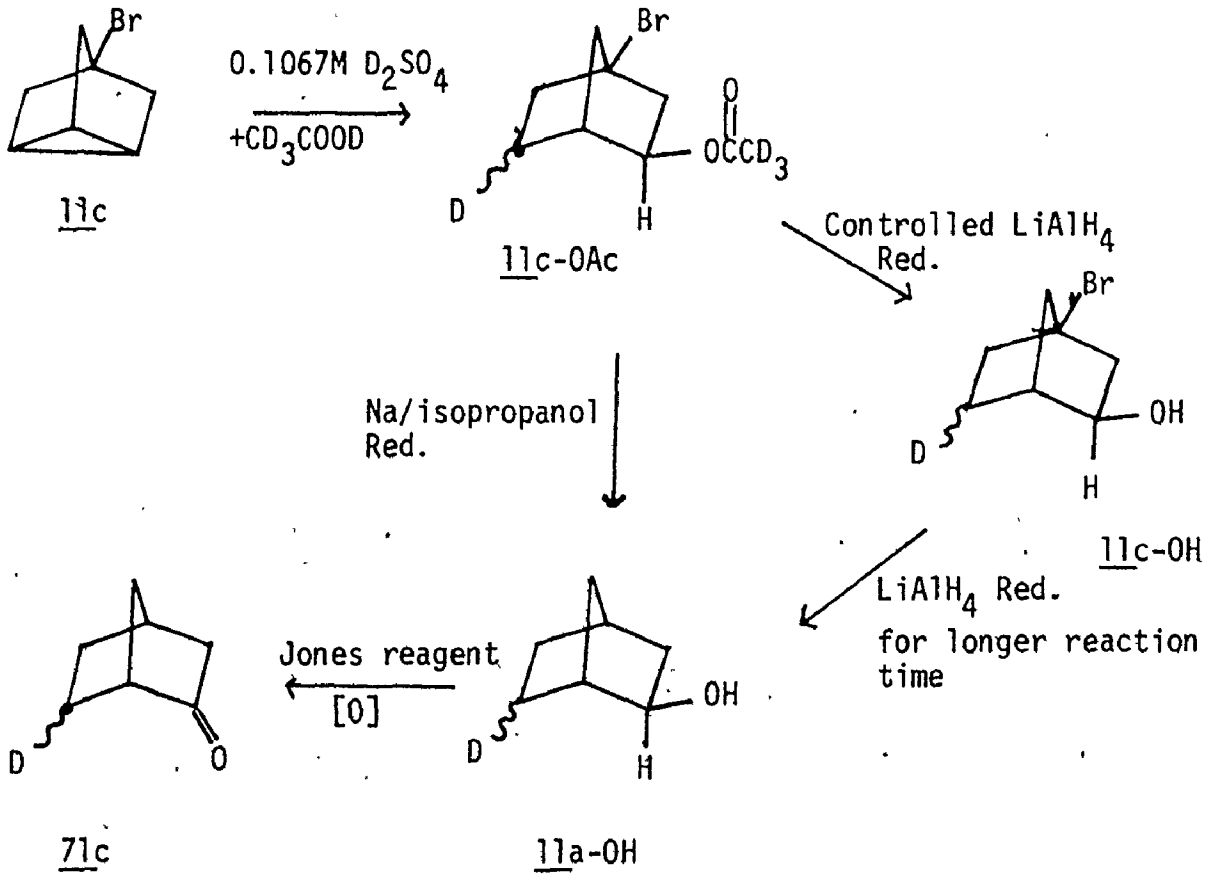
4-Bromonortricyclane (11c) was treated with acetic acid-d_4 (99.5 atom % d) and 0.1067 M sulphuric acid-d_2 for 90 hours at (50°±1) to yield 4-bromo-exo-2-norbornyl trideuteroacetate-d_1 (11c-OAc). The formation of 4-bromo-endo-2-norbornyl trideuteroacetate-d_1 was checked by analytical glpc (10% carbowax, 122°). This analysis indicated that ≈ 2% of 4-bromo-endo-2-norbornyl trideuteroacetate-d_1 was present. The product 4-bromo-exo-2-norbornyl trideuteroacetate-d_1 (11c-OAc) was identified by ir and nmr spectroscopy. Fig. 2:10 shows the proton nmr spectrum of 4-bromo-exo-2-norbornyl trideuteroacetate-d_1 (11c-OAc).

Lithium aluminum hydride reduction of 4-bromo-exo-2-norbornyl trideuteroacetate-d_1 (11c-OAc) in ether gave a mixture of 4-bromo-exo-2-norborneol-d_1 (11c-OH) and exo-2-norborneol-d_1 (11a-OH) in 10-15 minutes of reaction time. Under longer reaction times reduction was complete to exo-2-norborneol-d_1.

A portion of 4-bromo-exo-2-norbornyl trideuteroacetate-d_1 (11c-OAc) was reduced with sodium in isopropanol to yield exo-2-norborneol-d_1 (11a-OH). The exo-2-norborneol-d_1 obtained via two different reductions (viz. $LiAlH_4$ reduction and Na reduction) were found to have identical spectral characteristics. After obtaining the dmr spectrum of the exo-2-norborneol-d_1, it was oxidized by Jones reagent to give 2-norbornanone-d_1 (71c), Scheme 2:9.

The dmr spectrum of exo-2-norborneol-d_1 (Fig. 2:11) was used to establish the deuterium distribution and the endo:exo deuterium ratio at C_6, Table 2:5.

Scheme 2:9



11c

11c-OAc

11c-OH

7lc

11a-OH

Table 2:5: Deuterium distribution and endo:exo deuterium ratio at C_6 of exo-2-norborneol-d_1 obtained from 4-bromo-exo-2-norbornyl-trideuteroacetate-d_1.

Substrate	% Deuterium at				$\frac{\text{Endo}}{\text{Exo}}$ Ratio of 'D' at C_6
	C_1	C_2	Endo-C_6	Exo-C_6	
4-bromonortricyclane (11c)	2.6±0.5	1.9±0.3	58.9±0.8	36.6±0.4	1.61±0.03

Mass spectrometric deuterium assay of 2-norbornanone-d_1 (7lc), revealed that the deuterated norbornanone was primarily a monodeuterated species (Table 2:6).

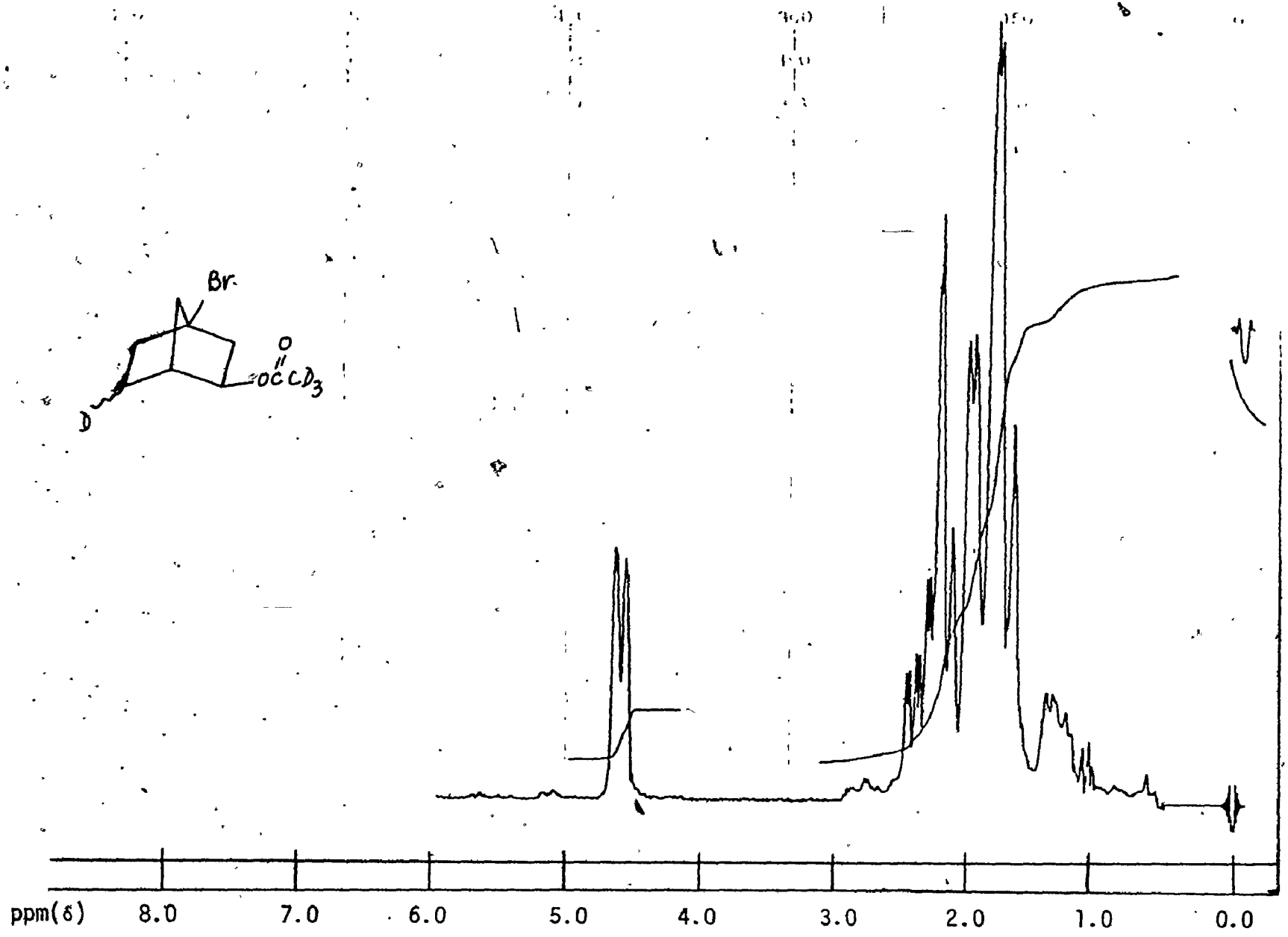


Fig. 2:10. Pmr spectrum (90 MHz) of 4-bromo-exo-2-norbornyl trideuteroacetate-d_1 (11c-OAc) in CCl_4.

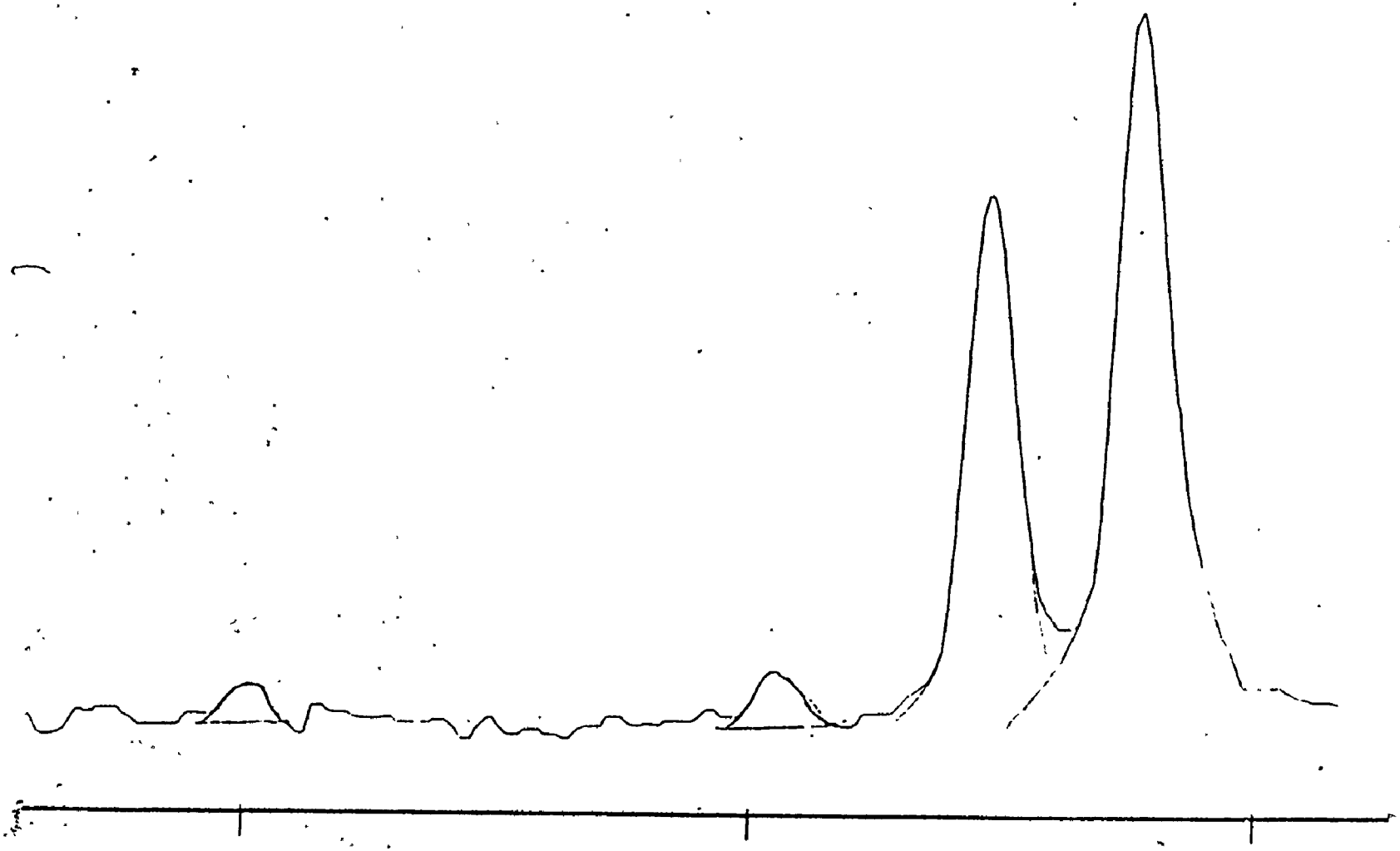


Fig. 2:11. Dmr spectrum of exo-2-norborneol-d_1 (11a-OH) obtained from D^+-catalyzed ring-opening of 4-bromonortricyclane (11c).

Table 2:6: Mass spectrometric deuterium assay on 2-norbornanone-d_1 (71c).

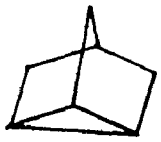
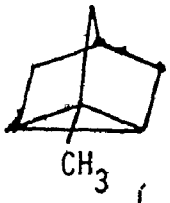
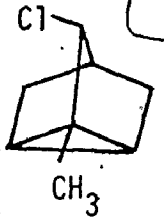
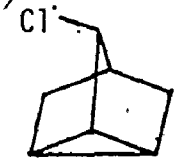
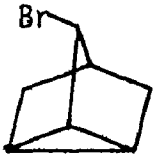
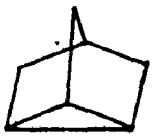
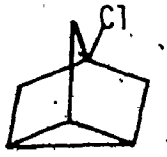
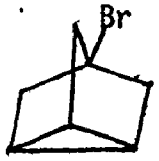
	% d_0	% d_1	% d_2	Average d/molecule
2-norbornanone-d_1 (71c)	9.6	90.4	0	0.9

DISCUSSION OF RESULTS

Accurate rate constants for the acid-catalyzed (D^+) ring opening of nortricyclane (11a), 4-chloronortricyclane (11b) and 4-bromonortricyclane (11c) in acetic acid-d_4 containing sulphuric acid-d_2 under the conditions previously described were not obtained. However, from Table 2:7 it is apparent that halo-nortricyclanes are less reactive than nortricyclane (11a) or 1-methyl nortricyclane (17) with respect to rupture of the cyclopropyl bonds. This is quite acceptable when one considers that in the absence of resonance stabilization by halogen atoms (Cl and Br), the inductive effect of this halogen destabilizes positively charged species, the intermediate of the reaction.

Since predominantly exo-acetate products are observed, this indicates that the carbon atom which undergoes the nucleophilic attack experiences net inversion of configuration, a phenomenon also observed in other nortricyclanes[51,52] as well as in a multitude of other compounds containing cyclopropyl groups.[45,46,54,55,65,70,71] This is not really surprising since this stereospecificity of nucleophilic attack being peculiar to this system because it has been established that exo-attack in the norbornyl system is favoured.[162]

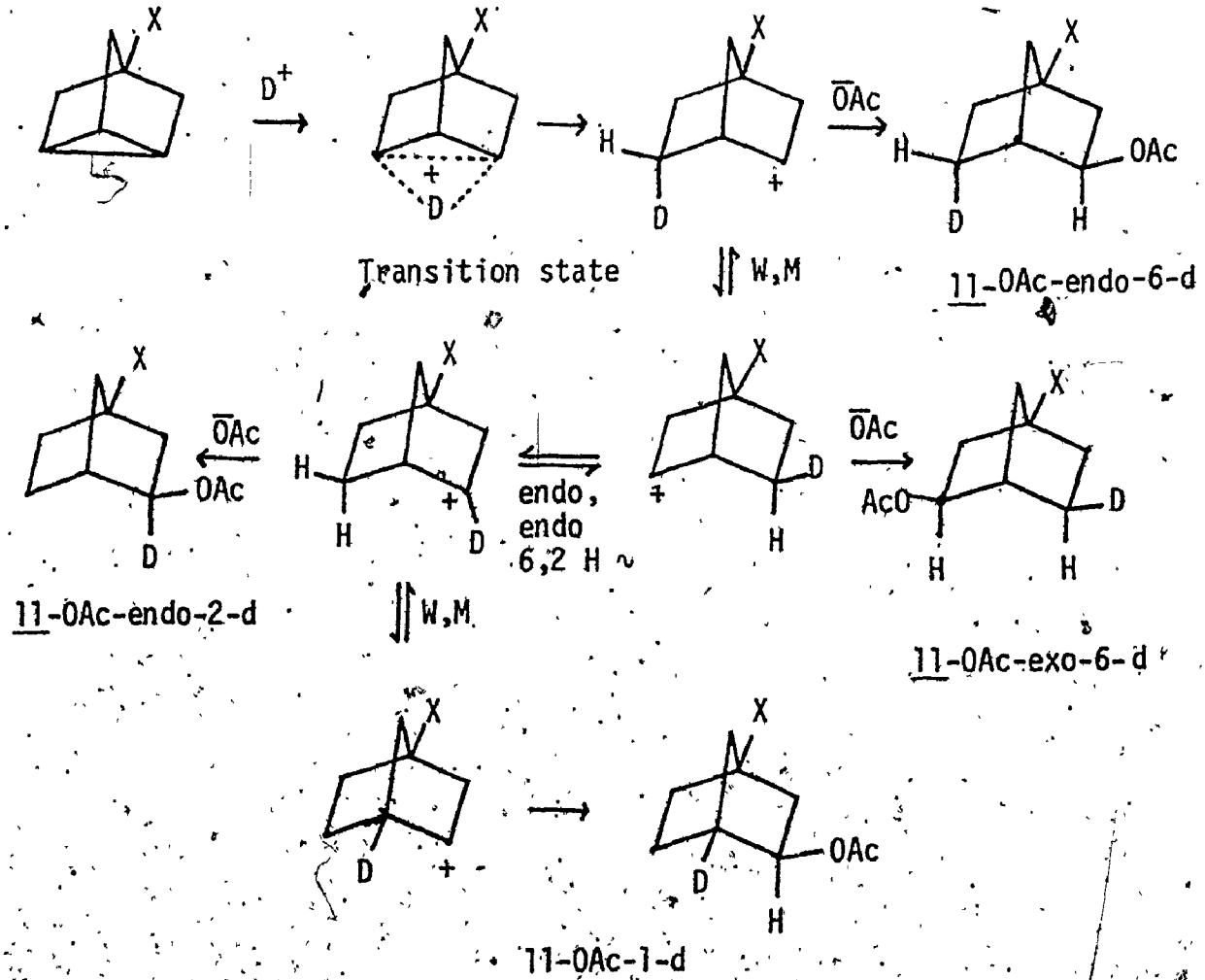
Table 2:7: Conditions required for the cleavage of various nortricyclanes.

Compound	Acid Medium	Temp.	Time (% Reaction)	Ref.
	CH_3COOH + 0.08M H_2SO_4	23°	24 hr (≈95)	51
	CH_3COOH + 0.0052M H_2SO_4	24°	2 hr (15)	52
	CH_3COOH + 0.10M H_2SO_4	62°	105 hr (>93)	54a
	CH_3COOH + 0.10 M H_2SO_4	70°	120 hr (>95)	54a
	CH_3COOH + 0.10M H_2SO_4	75°	45 hr (98)	54b
	CD_3COOD + 0.106M D_2SO_4	24°±1	17 hr (≈99)	This work
	CD_3COOD + 0.106M D_2SO_4	50°±1	92 hr (≈99)	This work
	CD_3COOD + 0.106M D_2SO_4	50°±1	<90 hr (≈99)	This work

In D^+-catalyzed ring opening of various nortricyclanes 11a, 11b, and 11c the formation of monodeuterated products with minor or no multiple deuteration establishes that the intermediate cationic species do not return appreciably to the starting substrate viz. nortricyclane (11a), 4-chloronortricyclane (11b), 4-bromonortricyclane (11c) and/or norbornene or halonorbornenes.

In view of the spectral data tabulated in Tables 2:1-2:6 which quantitatively establish the distribution of deuterium within the products of D^+-catalyzed ring-opening of nortricyclane (11a), 4-chloronortricyclane (11b), and 4-bromonortricyclane (11c), a mechanism for this electrophilic cleavage of these symmetrical nortricyclanes is presented in Scheme 2:10.

Scheme 2:10



The deuterium distribution in mono deuterated exo-2-norborneols obtained from the products of electrophilic ring-opening of nortricyclane (11a), 4-chloronortricyclane (11b) and 4-bromonortricyclane (11c) in D_2SO_4/CD_3COOD, is given in Table 2:8 as determined by the dmr analysis.

Table 2:8: Deuterium distribution and endo:exo deuterium ratio at C_6 of exo-2-norborneols-d_1.

Substrate	% Deuterium at				Endo/Exo* Ratio of 'D' at C_6
	C_1	C_2	Endo-C_6	Exo-C_6	
Nortricyclane (11a)	9.2±0.6	8.2±2.0	43.6±1.5	39.0±1.3	1.12±0.09
4-Chloronortricyclane (11b)	3.3±0.6	2.6±0.3	54.0±0.8	40.1±0.9	1.35±0.03
4-Bromonortricyclane (11c)	2.6±0.5	1.9±0.3	58.9±0.8	36.6±0.4	1.61±0.03

Since D^+-catalyzed ring-opening of 11a, 11b and 11c gave more endo deuterium than exo deuterium at C_6 of the products 11a-OAc, 11b-OAc and 11c-OAc, this suggests that initial deuteration at C_6 (path a, Scheme 2:11) of the cyclopropyl ring with subsequent cleavage of the C_2-C_6 bond is not an important path leading to these products.

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* The results are averages of two ring-openings and five spectrum acquisitions of each of the deuterated exo-2-norborneols. Errors are expressed as average deviations.

Since 11a, 11b and 11c have an axis of threefold symmetry, all the cyclopropyl carbons are equivalent. Fission of any of the cyclopropyl bonds with an unsymmetrical reagent (e.g., D^+X^-) would produce a 2,6-disubstituted norbornane.

If one accepts the Walsh model[8] for cyclopropane (cf. 1) as being representative of the cyclopropyl bonding in nortricyclanes (11a), (11b) and (11c), then corner deuteration at C_6 actually implies electrophilic attack directed towards a back lobe of the sp^2 orbital at C_6 (path a, Scheme 2:11). This minor lobe is situated in a plane defined by the C_5, C_6, C_6-H atoms and almost bisects the angle formed by these three atoms. Since cyclopropyl carbons C_1, C_2 and C_6 in 11a,

Scheme 2:11

11a ; X=H

11b ; X=Cl

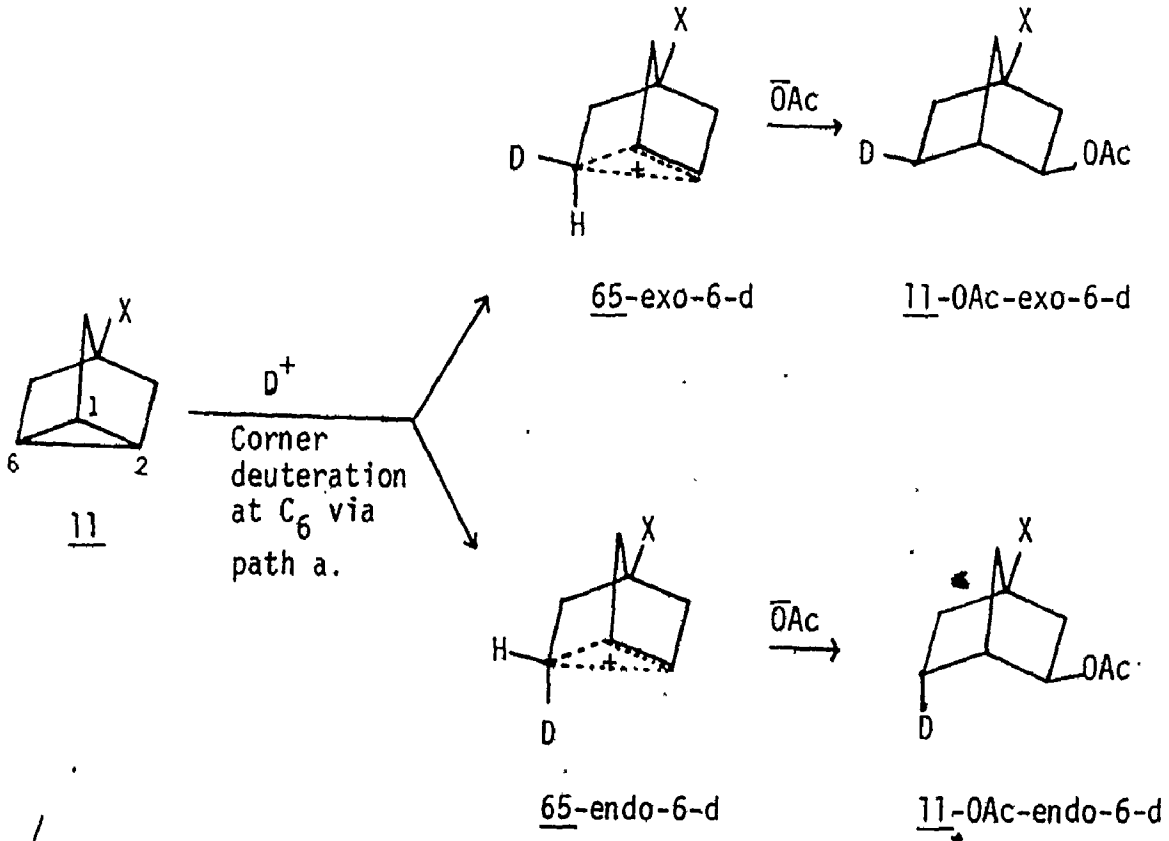
11c ; X=Br

11b and 11c are equivalent, attack of the electrophile at any of the minor back lobes of sp^2 orbital at C_1, C_2 or C_6 would produce the same ionic species. By definition, corner deuteration at C_6 via (path a) involves the simultaneous development of positive charge at the two

oms ich are that att C_1 and

C_2. Neglecting isotope effects, attack in this manner should give equal probabilities for formation of ions 65-exo-6-d and 65-endo-6-d (Scheme 2:12) and therefore equal amounts of products 11-OAc-exo-6-d and 11-OAc-endo-6-d. The experimental data in Table 2:8 do not support these predictions.

Scheme 2:12



Alternatively, if one considers the bent bond model[21] for cyclopropane (cf. 2) as being an accurate representation of bonding in the nortricyclanes (11a), (11b) and (11c), then corner deuteration at C_6 implies electrophilic approach by paths c and d (Scheme 2:11) i.e., approach by electrophile towards the back lobes of the C_6-C_2 and C_6-C_1 bonds respectively. Once again this should result in equal probability for of and and

amounts of 11-OAc-exo-6-d and 11-OAc-endo-6-d.

Formally, whether corner deuteration at C_6 in 11's occurs by path 'a' or by paths 'c' and 'd', the intermediate cations should be identical. In Scheme 2:11, the representation of approach by D^+ towards C_6 by paths c and d emphasizes the fact that two stereochemical outcomes are possible for formation of ion 65, namely exo- and endo-6-d. However, it must also be stressed that corner deuteration by path a (Scheme 2:11) also allows for the same two stereochemical outcomes for the formation of ion 65.

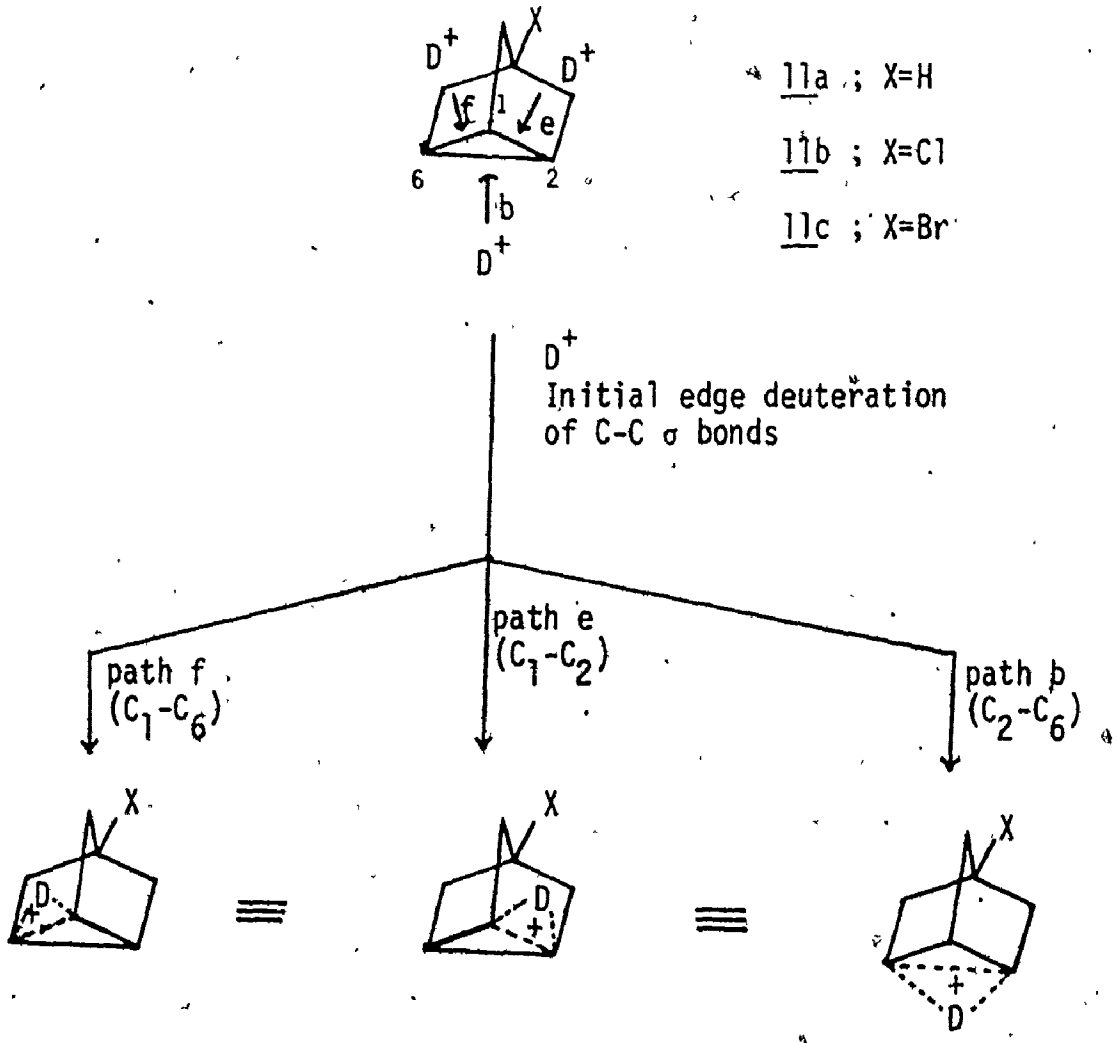
As 11a, 11b and 11c possess an axis of three-fold symmetry, all three strained σ bonds, namely C_1-C_2, C_2-C_6 and C_1-C_6 are equivalent. The initial edge deuteration of any of these three C-C σ-bonds would yield identical cationic intermediates.

Initial edge deuteration (e.g., path b, Scheme 2:10) of the C_2-C_6 σ-bond in 11a, 11b and 11c to yield ionic intermediates 66, 67, 69 and 70 via the transition state 68-d and subsequent collapse with nucleophile (trideuterated acetate in our work) accounts for the deuterium distribution in 11a-OAc, 11b-OAc and 11c-OAc, the products of D^+-catalyzed ring-opening of nortricyclane (11a), 4-chloronortricyclane (11b) and 4-bromonortricyclane (11c) respectively. Scheme 2:13 describes the mechanism for the electrophilic (D^+) ring-opening of 11a, 11b and 11c. The ions 66-endo-6-d and 67-exo-6-d account for the distribution of deuterium at C_6 and the ions 70-1-d and 69-2-d account for the distribution of deuterium at C_1 and C_2 respectively of the products in Scheme 2:13.

It is clear from the (Table 2:8) that the electrophilic (D^+) r of and in

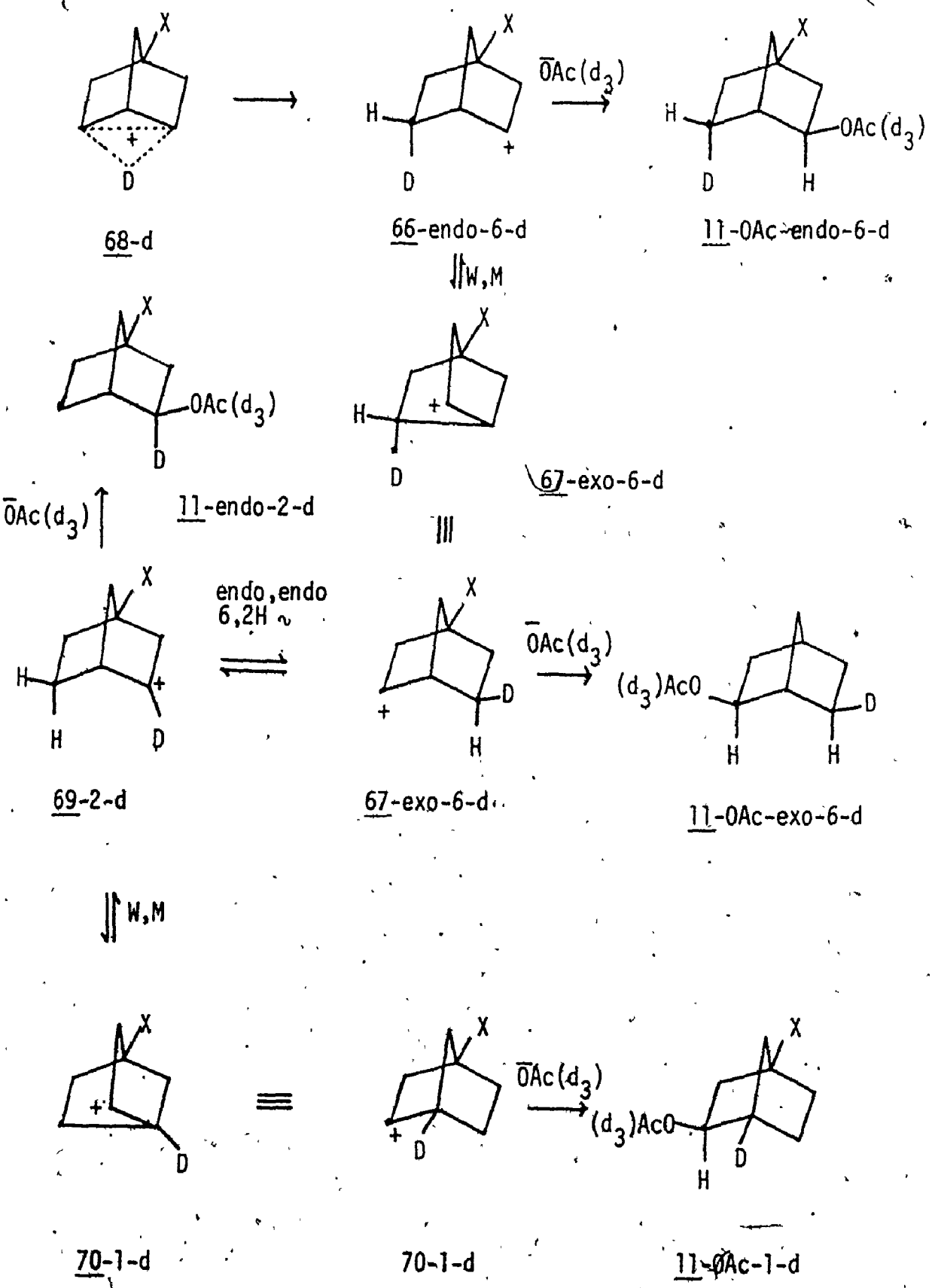
electrophilic attack. So our results of D^+-catalyzed ring-opening of nortricyclane (11a), 4-chloronortricyclane (11b) and 4-bromonortricyclane (11c) conclusively establish that the ring opening occurs via initial edge deuterated (or initial edge protonated) cyclopropyl moiety of 11a, 11b and 11c. The D^+-catalyzed ring-opening does not occur via initial corner deuterated species, which is in accord with Werstiuk's results of acid-catalyzed ring-opening studies of the unsymmetrical 3-halo-nortricyclanes.[53,54]

Scheme 2:13



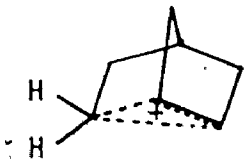
state

Scheme 2:13 (continued)

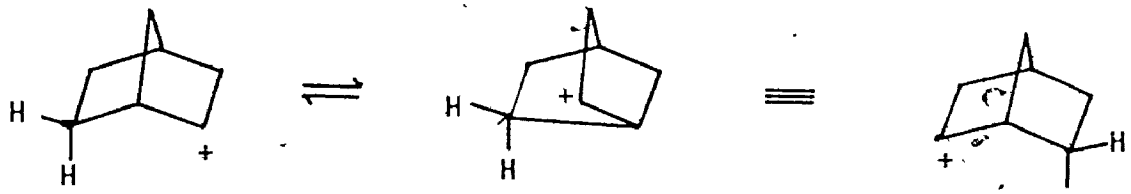


Solution to the "Norbornyl Cation Problem"

We, along with a good number of other chemists, were drawn into the see-saw battle of the past twenty-five years between the classical[159,162] and the non-classical[155-167] groups over the nature of the norbornyl cation. As it is known to almost every physical-organic chemist in this area of cation chemistry that the central issue in the conflict is whether the symmetrical non-classical norbornonium ion (65a) is an intermediate or it best represents the transition state between the unsymmetrical classical cations 66a and 67a.



65a



66a 67a 67a

In all the studies reported to date, investigators have substituted hydrogen at most sites in the norbornyl frame-work with either electron donating or electron-withdrawing substituents and thereby destroyed the symmetry inherent in 65a and in 66a-67a pair. Since C_4 is the only carbon centre where substitution of hydrogen does not destroy the symmetry of the molecule and thereby does not complicate the situation, we made use of that to answer the critical question

(vide-supra) by studying the effect of the size and mass of the substituent at C_4 on the chemistry of the norbornyl cation. Specifically, the determination of the stereochemistry of D^+-catalyzed ring-opening of 4-halonortricyclanes* (11a), 11b and 11c would be of interest for the reason that if 65a is the intermediate, the stereochemistry of the deuteration of the nortricyclane (11a), 4-chloronortricyclane (11b) and 4-bromonortricyclane (11c) - monitored by the endo:exo deuterium ratio at C_6 would be independent of the substituent at C_4. If, however, the intermediate in the ring-opening is the rapidly-equilibrating classical cations (66 ⇌ 67) and 65 best describes the transition state between classical cations, the rate of conversion of 66 into 67 should decrease as the Ponderal Effect of substituent at C_4 increases. Thus the collapse of the first formed classical cation with solvent would compete more effectively with its equilibration and a change would be observed in the stereochemistry of the ring-opening of the series of nortricyclanes.

We have observed a significant increase in the ratio of endo:exo deuterium at C_6 of the exo-trideuteroacetates, obtained by D_2SO_4 catalyzed ring-opening in acetic acid-d_4, of nortricyclane (11a), 4-chloronortricyclane (11b) and 4-bromonortricyclane (11c), (Table 2:7). That this increase in the endo:exo deuterium ratio at C_6 of 11a, 11b and 11c, as

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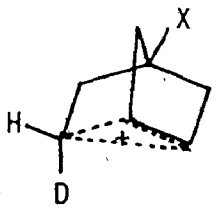
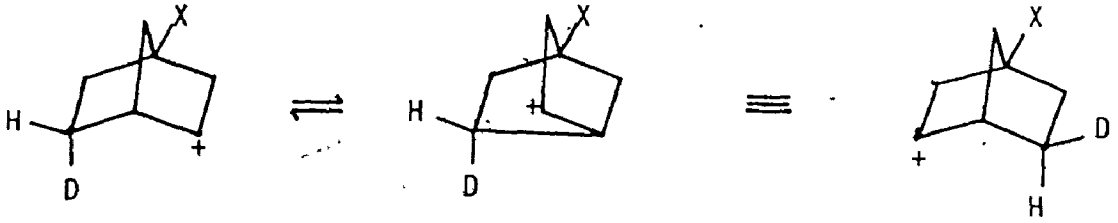
* For brevity nortricyclane (11a) is included in 4-halonortricyclanes since these possess the same symmetrical structure. It would be interesting to study D^+-catalyzed ring-opening of 4-iodonortricyclane (11d).



65a ; X=H

65b ; X=Cl

65c ; X=Br



66a ; X=H

66b ; X=Cl

66c ; X=Br

67a; X=H

67b; X=Cl

67c; X=Br

established by the dmr analysis, is supported by the work of Nickon and Hammons,[51] who determined the endo:exo deuterium ratio (1.08±0.03) at C_6 of exo-2-norbornylacetate-d_1 obtained from the ring-opening of the nortricyclane (11a) by infrared spectroscopy. Furthermore they established that optically active exo-2-norbornyl acetate does not racemize in the acidic medium i.e., isomerization of the norbornyl acetates is not important in this reaction.

The fact established by our present studies that there is a progressive increase in the endo:exo deuterium ratio as the atomic weight of the substituent at C_4 increases (Table 2:7) conclusively establishes that the norbornyl cation is a classical and rapidly-

equilibrating species. That the degree of 6,2-hydride shift decreases with the increase in atomic weight of the C_4-substituent which is also in accord with the fact that the norbornyl cation is classical (not non-classical, the σ-bridged ion). The rate of the 6,2-hydride shift is sensitive to the ponderal effect[187] of the substituent at C_4 of the 4-halonortricyclanes 11a, 11b and 11c because the transition state is an edge-protonated nortricyclane.

The deuterium distribution at C_1 and C_2 also supports the classical structure of the norbornyl cation. As it is evident from Scheme 2:12 that 11-OAc-endo-2-d results from the reaction of the cation 69-2-d with solvent, the cation 69-2-d in turn is the result of endo-endo 6,2-hydride shift in 67-exo-6-d. Wagner-Meerwein rearrangement of 66-endo-6-d ion which is generated by the initial edge-wise attack of D^+ on the cyclopropyl rings of 11a, 11b and 11c, gives rise to the ion 67-exo-6-d.

Thus the amount of deuterium at C_2 would in fact be a function of the ponderal effect. It is clear from Scheme 2:12 that the amount of deuterium at C_1 of norbornyl acetates would be sensitive to the ponderal effect at C_4. That the amount of product 11-OAc-1-d decreases with the increase in the ponderal effect of substituent at C_4 of 11a, 11b and 11c.

In brief, the overall distribution of deuterium in the product of D^+-catalyzed ring-opening of 11a, 11b and 11c is in fact governed by the mass of the substituent at C_4 (ponderal effect).

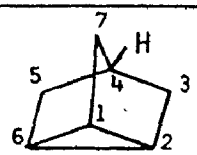
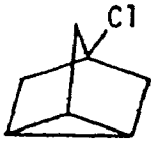
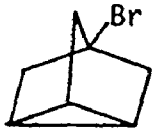
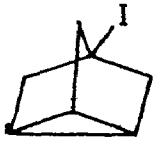
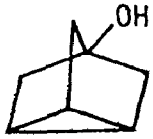
These results conclusively establish that the norbornyl cation/s formed by edge-protonation of 11a, 11b and 11c is/are unsymmetrical classical and rapidly equilibrating species and not symmetrical non-classical σ-bridged species.

Further the formation of alcohol and methyl ether with 9% and 14% retention of configuration respectively in solvolysis of optically active 1,2-dimethyl-exo-2-norbornyl-p-nitrobenzoate in 90% aqueous acetone carried out by Goering and Humski[150a] and 1,2-dimethyl exo-2-norbornyl chloride in methanol carried out by Goering and Clevenger[150b] may also be a consequence of the ponderal effect of the methyl groups on the 1,2-alkyl shifts. Thus this work in fact supports Brown's suggestion that the difference in the stereochemistry of solvolysis of the parent system and the 1,2-dimethyl-substrates is due to the rate of equilibration of the classical norbornyl cations, the rate being faster. The classical nature of the long lived norbornyl cation has also been supported by the solvolytic studies of 7-halonorbornyl brosylates done by Cappelli, Timmins and Werstiuk.[53b] Recently Banerjee and Werstiuk[188] have applied the so-called log k_{exo} vs. log k_{endo} correlation to the mechanisms of solvolysis of norbornyl derivatives and have concluded in conjunction with other results and viewpoints[166b,174] that the σ-bridged norbornyl cation is an unnecessary and improbable species in solvolytic processes.

DISCUSSION OF NMR DATA OF 4-HALONORTRICYCLANES

The proton nmr data of nortricyclane (11a, Fig. 2:1), 4-chloronortricyclane (11b, Fig. 2:5), 4-bromonortricyclane (11c, Fig. 2:9), 4-iodonortricyclane (11d, Fig. 2:12) and 4-hydroxynortricyclane (11e, Fig. 2:13) are recorded in Table 2:9.

Table 2:9. NMR Chemical Shifts of 4-Halonortricyclanes

Substrates	Chemical shifts (δ) of:		
	Cyclopropyl Protons at C_1, C_2 and C_6. (δ)	Methylene protons at C_3, C_5 and C_7. (δ)	Proton at C_4 (δ)
11a 	0.97	1.18	1.92
11b 	1.2	1.66	-
11c 	1.12	1.68	-
11d 	0.95	1.70	-
11e 	1.07	1.4	1.2

4-Hydroxynortricyclane (11e) was synthesized from 4-chloronortricyclane (11b) by the use of lithium as in the syntheses of 4-bromonortricyclane (11c) and 4-iodonortricyclane (11d) from 4-chloronortricyclane (11b).

Table 2:9 shows that the protons on the cyclopropyl ring at C_1, C_2 and C_6 are structurally identical and all yield the same resonant frequency and that the methylene protons at C_3, C_5 and C_7 are also structurally undistinguishable and yield the same absorption signal.

Table 2:9 reveals the electron withdrawl by the attached electronegative atoms (Cl, Br, I, OH) causes deshielding of the methylene protons at C_3, C_5 and C_7 more than for the cyclopropyl protons at C_1, C_2 and C_6.

This indicates that in saturated C-H cases electron withdrawal (σ-bond dipoles) by attached electronegative atoms causes deshielding. The same kind of deshielding is produced when the electronegative atom is one carbon further removed but the magnitude is then very small.

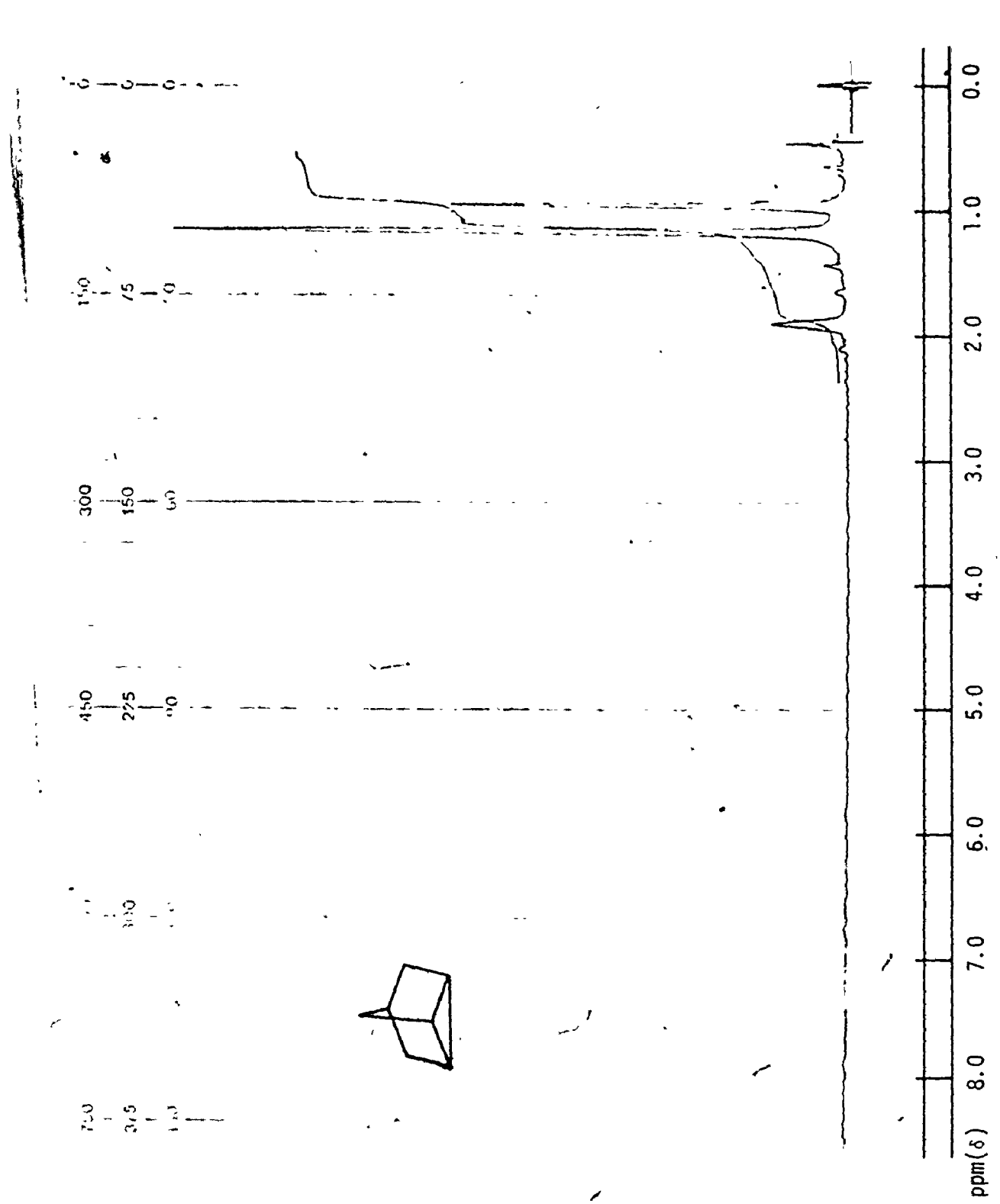


Fig. 2:1. Pmr spectrum (90 MHz) of nortricyclane (11a) in CCl_4.

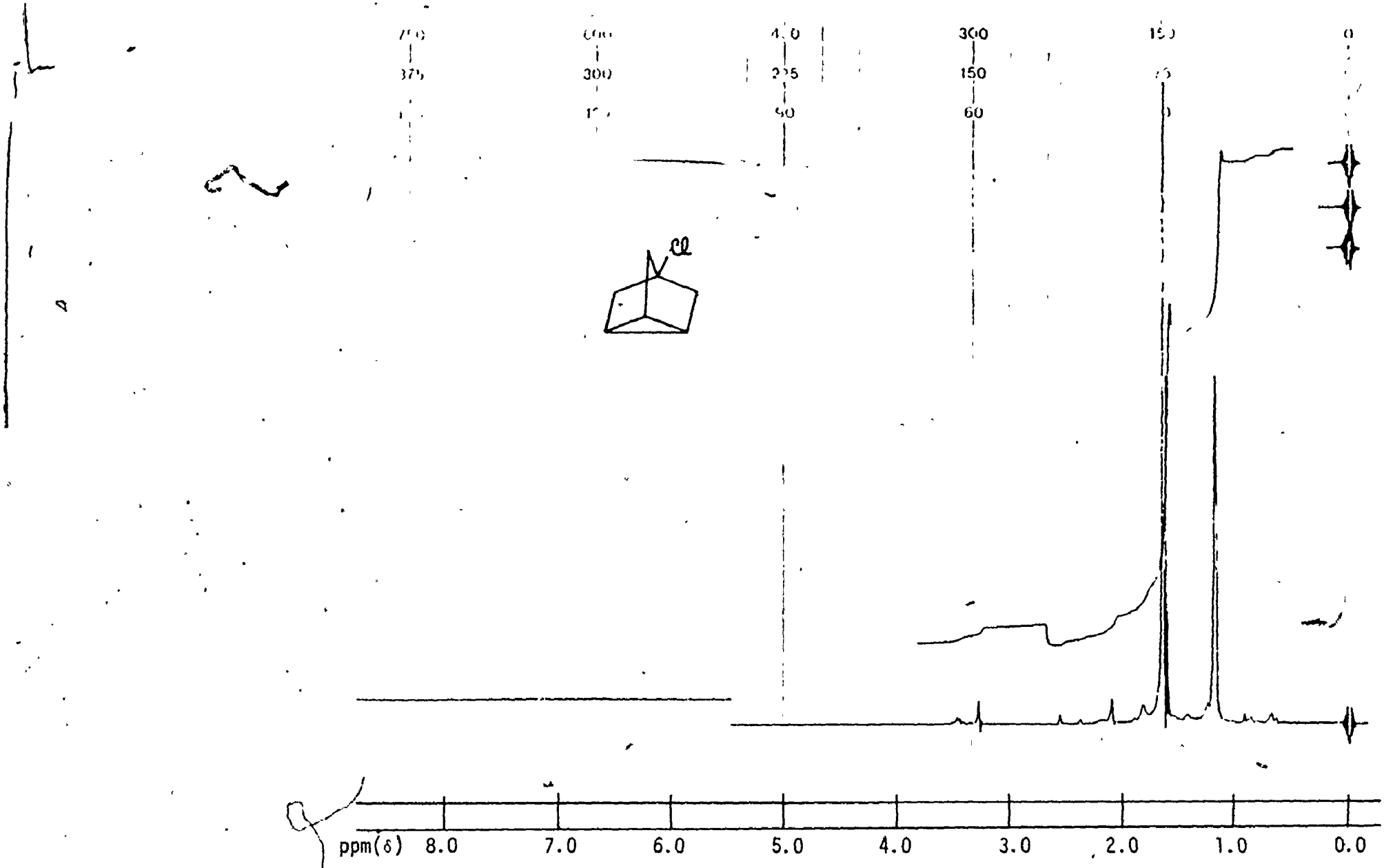


Fig. 2:5. Pmr spectrum (90 MHz) of 4-chloronortricyclane (11b) in CCl_4.

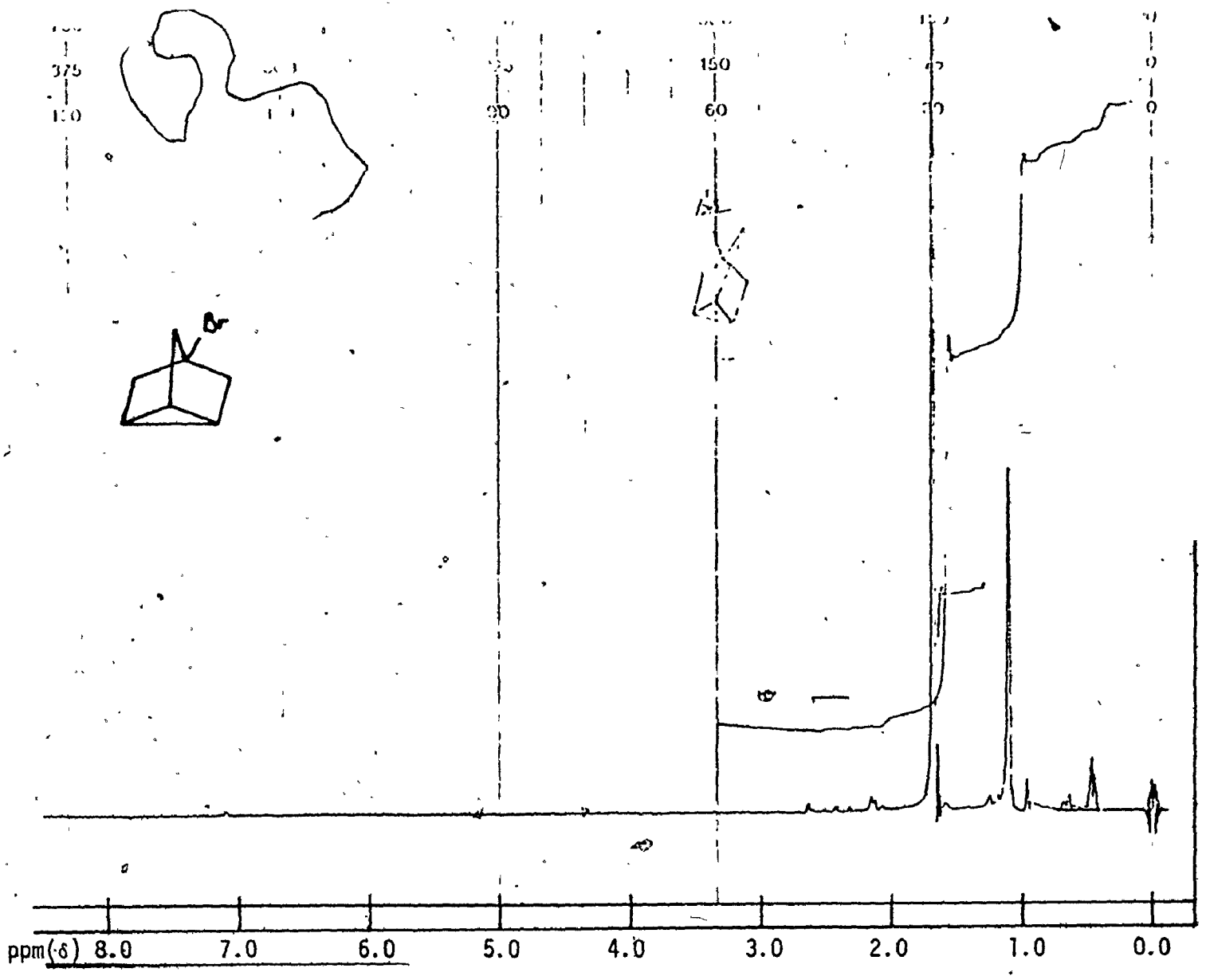


Fig. 2:9. Pmr spectrum (90 MHz) of 4-bromonortricyclane (11c) in CCl_4.

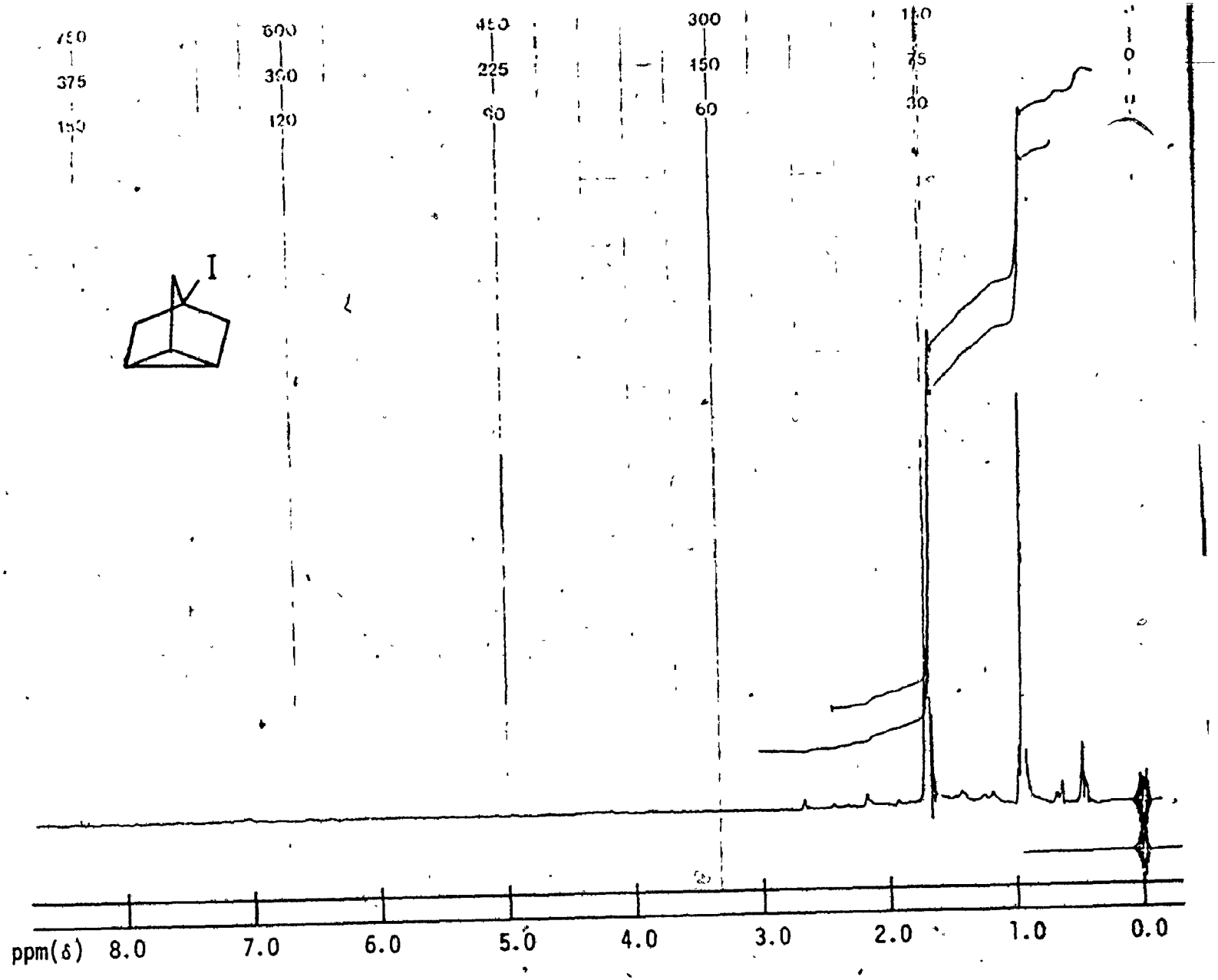


Fig. 2:12. Pmr spectrum (90 MHz) of 4-iodonortricyclane (11d) in CCl_4.

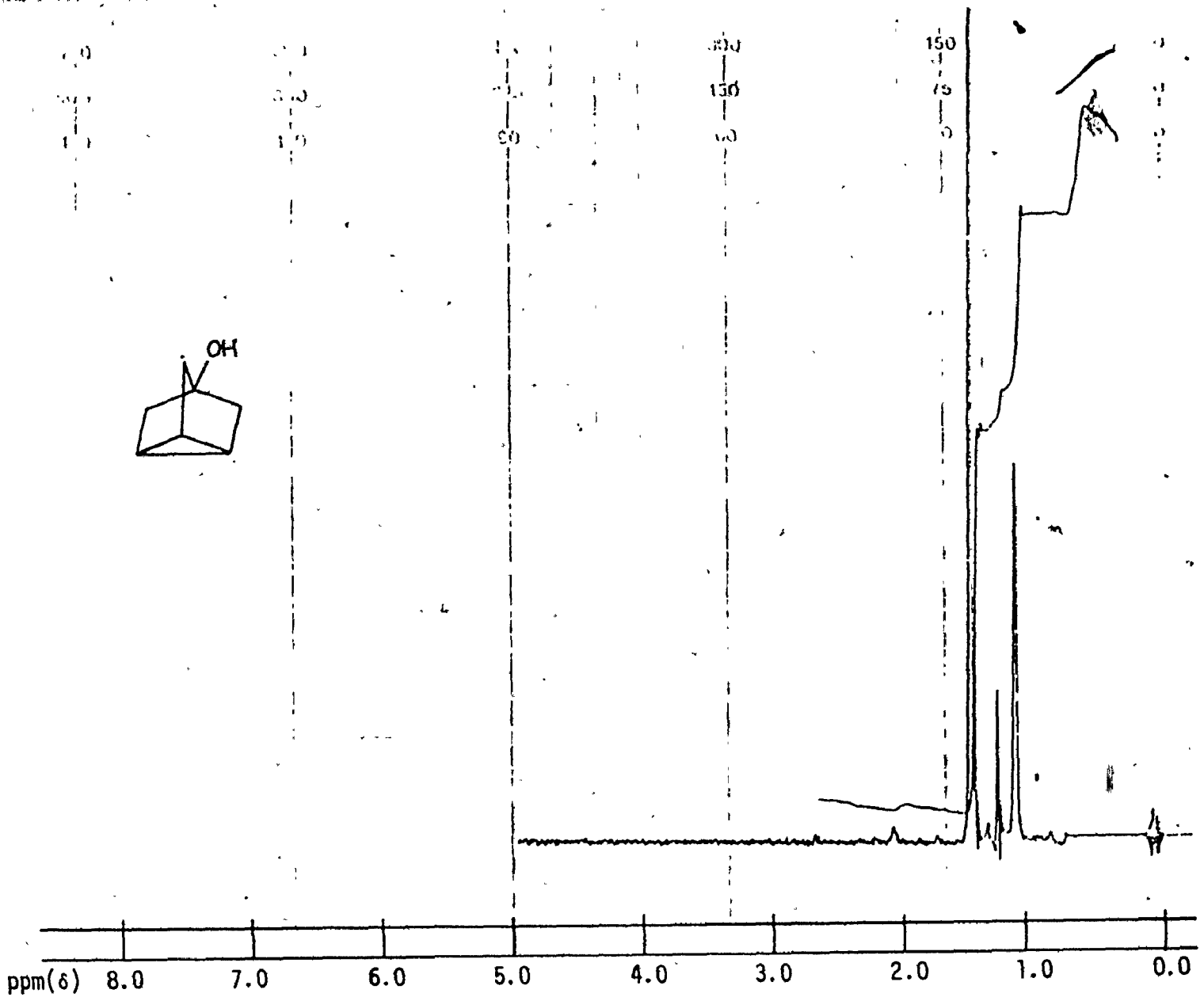


Fig. 2:13. Pmr spectrum (90 MHz) of 4-hydroxynortricyclane (11e) in CCl_4.

CHAPTER 3

EXPERIMENTAL

General

Nuclear magnetic resonance (nmr) spectra were recorded on Varian T-60 and EM-390 with tetramethylsilane (TMS) as the internal standard. Samples were dissolved in either carbon tetrachloride or deuterated chloroform (d_1) or deuterated acetone (d_6). Deuterium magnetic resonance (dmr) spectra were recorded on either carbon tetrachloride or chloroform solutions using an XL-100 spectrometer with ^{19}F as the internal lock signal (perfluorobenzene) by Brian Sayer of McMaster University. Chemical shifts are expressed in parts per million downfield from internal tetramethylsilane (δ 0.0). In nmr descriptions, S = singlet, d = doublet, t = triplet, m = multiplet, d,d = doublet of doublets, dt = doublet of triplets, etc.

Infrared spectra were recorded with Perkin Elmer 337 and Perkin-Elmer 283 infrared spectrometers and the samples were dissolved in carbon tetrachloride or carbon disulphide. Absorption frequencies were calibrated with a polystyrene thin film (wherever possible and necessary) and are expressed in reciprocal centimeters (cm^{-1}). For brevity, the notation cm^{-1} is excluded.

Mass spectra were recorded on consolidated Electrodynamics Corporation Mass Spectrometer. Deuterium assay analyses were performed at $\sim$ 10 eV on Hitachi Perkin-Elmer RMH-6A Mass Spectrometer and are expressed as atoms of deuterium per molecule in excess of natural abundance deuterium.

Analytical gas-liquid partition chromatography (analytical glpc) was performed on a Varian Aerograph Model 200 analytical gas chromotograph

equipped with dual flame ionization detectors using helium as the carrier gas and on a Tracor 560 gas chromatograph equipped with dual flame ionization detectors using helium as the carrier gas in this gas chromatograph as well. Preparative gas liquid partition chromatography (prep glpc) was carried out on a Varian Aerograph Model A-90-P gas chromatograph with a thermal conductivity detector and a helium gas as carrier. Chromosorb W (Chromatographic Specialties Ltd) of mesh size $\frac{60}{80}$ was used in all cases except for the two columns used for Tracor-560 gas chromatograph for which mesh size $(\frac{80}{100})$ was used.

The liquid phases were varied and will be designated as follows:

Columns used for VA Model 204B:

a% SE-30 — refers to a% SE-30 on chromosorb W $(\frac{60}{80})$, of stainless steel and (5' x 1/4") in size.

b% carbowax — refers to b% carbowax 20M on chromosorb W $(\frac{60}{80})$ of stainless steel and (5' x 1/4") in size.

c% FFAP — refers to c% FFAP on chromosorb W $(\frac{60}{80})$ of stainless steel and (10' x 1/4") in size.

Columns used for Tracor-560:

d% OV-1 — refers to d% OV-1 on chromosorb W $(\frac{80}{100})$ of glass and (6' x 1/4") in size.

e% carbowax — refers to e% carbowax 20M on chromosorb W $(\frac{80}{100})$ of glass and (6' x 1/4") in size.

Columns used for preparative VA Model A-90-P:

f% GE-XF 1150 — refers to f% GE-XF 1150 on chromosorb W $(\frac{60}{80})$ of stainless steel and (10' x 1/4") in size.

g% carbowax : refersto g% carbowax 20M on chromosorb W $(\frac{60}{80})$ of stainless steel and (5' x 1/4") in size.

All organic solutions were dried with either anhydrous sodium sulphate or magnesium sulphate.

A. NORTRICYCLANE

1) SYNTHESIS

a) Norcamphor tosylhydrazone

Concentrated hydrochloric acid (3 ml) was added to tosyl hydrazine (Aldrich Chemical Co., 19 g, 0.102 mole, m.p. 110°) and norcamphor (Aldrich Chemical Co., 11.4 g, 0.104 mole, m.p. 90-92°) dissolved in 95% ethanol (300 ml). The mixture was refluxed overnight and poured into water (1-1). The resultant precipitate was collected and recrystallized from 95% ethanol to give norcamphor tosylhydrazone (16.5 g, 58%, m.p. 206-208°, lit. m.p. 206.5-208°[189] and 205-208°[190]); i.r. ($CHCl_3$): 3300, 3200 (N-H); 1660 (C=N), 1160 (S=O).

b) Nortricyclane (11a)

Nortricyclane (11a) was prepared from norcamphor-p-toluene sulphonyl hydrazone.[190-192] Norcamphor tosylhydrazone (15.0 g, 0.054 mole, m.p. 206-208°) was added to purified diglyme (250 ml) in a three-necked round bottomed flask equipped with a stoppered condenser and a nitrogen inlet and outlet. Sodium methoxide (J.T. Baker Chemicals Co., 24.3 g, 0.45 mole) was added and the reaction mixture was heated to reflux. As nitrogen was vented through the solution, the product was carried through a water wash, a KOH pellet drying system, and collected in a small flask and U-tube cooled in dry ice-acetone bath. Analytical glpc analysis (3% OV-1, 67°) indicated pure nortricyclane: i.r. (CCl_4): 3070 (cyclopropyl C-H); 1450, 1355, 1304, 1254, 1225.

nmr (90 MHz, CCl_4): δ 1.92 (s, 1H, C_4-H); δ 1.18 (s, 6H, methylene protons at C_3, C_5 and C_7); δ 0.97 (s, 3H, cyclopropyl protons at C_1, C_2 and C_6). The nmr spectrum revealed nortricyclane free from norbornene (Fig. 2:1).

2. CLEAVAGE IN DEUTERATED ACID

a. Electrophilic cleavage of nortricyclane (11a) with sulphuric acid-d_2 in acetic acid-d_4.

Nortricyclane (0.2824 g, 3.004 millimole) was dissolved in 24.7 ml of stock solution,* which was a mixture of 0.32 g of sulphuric acid-d_2 (Merck, Sharp and Dohme of Canada, Ltd.) and 30 ml of acetic acid-d_4 (Merck, Sharp and Dohme of Canada, Ltd., 99.5 atom % d), in a 50 ml flask fitted with a calcium chloride drying tube and was stirred at room temperature. Analytical glpc analysis of the first aliquot taken out after 17 hrs indicated the completion of the reaction with only one major product. The remaining reaction mixture was neutralized with saturated sodium bicarbonate solution. The product exo-2-norbornyl trideuteroacetate-d_1 was extracted with ether. After the extracts were washed with water and dried over anhydrous sodium sulphate, the ether was removed by distillation via a 2 ft glass helices packed column leaving behind (0.43 g, 2.7 mmole, 91%) of exo-2-norbornyl trideuteroacetate-d_1 (11a-OAc) which was identified by m.s., i.r. and nmr spectroscopy.

The nmr spectrum of exo-2-norbornyltrideuteroacetate-d_1 (11a-OAc) is shown in Fig. 2.2.

i.r. (CCl_4): 1750 (C=O)

n.m.r. (90 MHz, CCl_4): δ 4.5 (dd, 1H, H at C_2); δ 2.25 (s, H bridgehead H's at C_1 and C_4); δ 1.8-0.7 (m, 7H, H's at C_3, C_5 and C_7).

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* Stock solution contains 0.1067 M D_2SO_4 + $ACOH-d_4$.

b) Reduction of exo-2-norbornyl trideuteroacetate-d_1 (11a-OAc) with lithium aluminum hydride.

Into a 100 ml three necked flask equipped with a condenser along with a drying tube, adding funnel and magnetic stirrer, was placed a slurry of lithium aluminum hydride (0.218 g, 5.79 millimole) in dry ether (50 ml). The exo-2-norbornyl trideuteroacetate-d_1 (11a-OAc) from the previous experiment (0.43 g, 2.72 millimole) was dissolved in dry ether (5 ml) and slowly added to the slurry. Then this mixture was refluxed for 15 minutes. The reaction flask was cooled in ice and excess hydride was destroyed very carefully by the dropwise addition of water. After the white ppt. was filtered off, the filtrate was acidified with hydrochloric acid (10%, 3 ml) and then the ethereal layer was separated. The aqueous layer was extracted with ether (4 x 25 ml) and the combined ethereal layers were washed with water (50 ml) dried over anhydrous sodium sulphate and concentrated to yield (0.29 g, 2.5 millimole, 94%) of exo-2-norborneol-d_1 (11a-OH). Analytical glpc analysis (3% OV-1, temperature programme: initial temperature 67°, final temperature 175°, programme rate 75°/min, initial hold 4 min, final hold 5 min) revealed only one major product, i.e. exo-2-norborneol-d_1 as determined by i.r. and proton nmr spectroscopy (Fig. 2:3).
nmr (90 MHz, CCl_4): δ 3.65 (dd, 1H, H at C_2); δ 3.05 (s, 1H, OH); δ 2.3-2.0 (m, 2H, bridgehead H's at C_1 and C_4); δ 1.8-0.5 (m, 7H, H's at C_3, C_5 and C_7).

c) Oxidation of exo-2-norborneol-d_1 (11a-OH)

The oxidizing agent[54] was prepared as follows: sodium dichromate (10 g) was dissolved in water (20 ml) and then sulphuric acid (7.5 ml) was added. For each millimole of alcohol to be oxidized 0.5 ml of solution

is used. To a solution of exo-2-norborneol-d_1 (0.10 g, 0.90 millimole) in ether (10 ml, pretreated with oxidizing agent) in a 50 ml flask equipped with a condenser and magnetic stirrer, the oxidizing agent in excess (1 ml) was slowly added. After the solution was vigorously stirred overnight, the ethereal layer was separated and the aqueous layer was extracted with ether (5 x 20 ml). The combined ethereal layers were washed with saturated bicarbonate (2 x 15 ml), water (2 x 20 ml) and then dried over anhydrous sodium sulphate. The ether was distilled off through a 2 ft glass helices packed column. Analytical glpc (3% OV-1, 70°) showed only one product which had the same retention time as that of norcamphor under identical conditions. The oxidation of exo-2-norborneol-d_1 (11a-OH) gave 2-norbornanone-d_1 (71a), (0.06 g, 0.54 millimole, 61%).

nmr (90 MHz, CCl_4): δ 2.65 (m, 1H, bridgehead H at C_1); δ 2.5 (m, 1H, bridgehead H at C_4); δ 2.2-0.9 (m, 8H, H's at C_2, C_5, C_6 and C_7).

B. 4-CHLORONORTRICYCLANE

1. SYNTHESIS

a) 2,2-Dichloronorbornane

2,2-Dichloronorbornane was obtained by the procedure adopted by Wiberg et al.[193] To a solution of norcamphor (350 g, 3.18 moles) in 300 ml of phosphorus trichloride in a three-necked three litre flask which was cooled in an ice-salt bath and equipped with a magnetic stirrer and reflux condenser, was added in small portions phosphorus pentachloride (747 g, 3.58 moles) over the period of 4 hrs. The reaction mixture was allowed to warm slowly to room temperature and was allowed to stir overnight. The reaction mixture was poured onto 3-4 kg of ice. The organic products, i.e. dichlorides of norcamphor were extracted with (10 x 200 ml) portions of pentane. The pentane layer was then washed with water (2 x 200 ml) and dried over anhydrous sodium sulphate. After removal of the pentane via a 12" glass helices packed column the residue was distilled under reduced pressure until a solid distillate appeared. The 12" vigreux column used had to be heated to prevent the crystallization in it during distillation. The solid fraction, b.p. 40-45°, under 1.5 mm (lit. b.p. 77-79°, 19 mm) was then collected to give (446 g, 2.7 mole, 85%) of norcamphor dichloride. Analytical glpc analysis (5% SE-30, 100°), indicated the product free from other dichlorides and norcamphor.

b) 1-Exo-2-Dichloronorbornane[194]

To the solution of 2,2-dichloronorbornane (365g, 2.21 mole) in 750 ml. of toluene was added 150 ml of anhydrous stannic chloride in small portions over a course of 2 hrs into a 2 litre three necked round bottomed flask equipped with a reflux condenser, a drying tube, a dropping funnel and a magnetic stirrer. The contents of the reaction flask were stirred at a temperature of 55-57° for 50 hrs. Then the entire contents were carefully

poured onto 1-2 litres of ice-water and the organic product was extracted with (6 x 500 ml) portions of benzene. The solvents were distilled off after drying the extracts over anhydrous sodium sulphate. Analytical glpc analysis (5% SE-30, 100°) of the residual oil revealed the complete conversion of 2,2-dichloronorbornane to 1-exo-2-dichloronorbornane. Distillation under reduced pressure gave a solid fraction (277.4 g, 1.68 mole, 76%) of b.p. 55-57°, 1.1 mm (lit. b.p. 77°, 11 mm, n_D^{25} 1.5019; m.p. 6-7°). nmr (60 MHz, CCl_4): δ 3.87 (m, 1H, H at C_2), δ 2.4-1.3 (m, 9H, H's at C_3, C_4, C_5, C_6 and C_7).

c) 1-Norbornenyl chloride[194,198]

A two fold excess of potassium tertiary butoxide (373.3 g, 3.33 mole, Ventron Chemical Ltd.) was added in portions into a 3 litre round bottomed flask containing solution of 1-exo-2-dichloronorbornane (275 g, 1.66 mole) in 1600 ml of dimethyl sulphoxide, equipped with a drying tube and a magnetic stirrer. The contents of the reaction flask were stirred for 50 hrs. This reaction mixture was then poured carefully onto a mixture of water:ether (1ℓ:1ℓ). The ethereal layer was separated and the aqueous layer was extracted with (6 x 500 ml) portions of ether. The combined ethereal extracts were washed with (3 x 200 ml) water and dried over anhydrous magnesium sulphate. After the removal of solvents the distillation of the slightly yellow oil provided 1-norbornenyl chloride (170 g, 1.32 mole, 79% yield) as a colourless oil of b.p. 136-138° at atmospheric pressure, lit. b.p. 139.5-141°, 750 mm). Analytical glpc analysis (5% SE-30, 60°) revealed the only product 1-chloronorbornene: i.r. (neat): 3070 (=C-H), 1452 (C=C), 790 (C-Cl), 710 (cis CH=CH).

nmr (60 MHz, $CDCl_3$): δ 6.2-5.9 (m, 2H, olefinic H's); δ 2.9 (m, 1H, bridgehead H) δ 2.5-1.0 (m, 6H, H's at C_5, C_6 and C_7).

d) 1-Chloro-exo-cis-3-hydroxy-2-norbornyl mercuric chloride and 4-chloro-exo-2-norborneol.

i) To prepare 1-chloro-exo-cis 3-hydroxy-2-norbornyl mercuric chloride from 1-chloronorbornene the method of oxymercuration of norbornene by Traylor and Baker[195] was modified.

A solution of 1-chloronorbornene (168 g, 1.31 mole), mercuric oxide (141.5 g, 0.655 mole) and of mercuric chloride (178.2 g, 0.656 mole) in 3 litres of 50% aqueous acetone, was refluxed for 48 hours in a 5 litre round bottomed flask equipped with a mechanical stirrer and a reflux condenser. A light yellow precipitate remained. The acetone was evaporated leaving a solid organomercurial (398.5 g, 1.04 mole, 80%).

ii) This crude organomercurial was mixed with 1600 ml of (1:3) mixture of ether:methanol in a large round bottomed flask equipped with a stirrer and a reflux condenser. Sodium borohydride (88.2 g, 2.33 mole) was added to the reaction flask in small portions and the contents were then refluxed overnight. After the reaction mixture was acidified the product was extracted with (6 x 500 ml) portions of anhydrous ether. The ethereal extracts were then washed with (2 x 250 ml) saturated sodium bicarbonate solution and (2 x 250 ml) water. After drying the ethereal extracts over anhydrous magnesium sulphate the ether was evaporated by distillation via a 2 ft glass helices packed column which left behind the 4-chloro-exo-2-norborneol (126 g, 0.86 mole, 82%). Analytical glpc analysis (3% OV-1, 160°) indicated the only product as determined by nmr and i.r. spectroscopy. i.r (CCl_4): 3625 (free O-H); 3560-3160 (broad, bonded O-H).

nmr (90 MHz, $CDCl_3$): δ 3.85 (dd, 1H, H at C_2); δ 2.98 (s, 1H, -OH), δ 2.35-1.0 (m, 9H, H's at C_1, C_3, C_5, C_6 and C_7).

e) 4-Chloro-2-norbornanone

4-Chloro-2-norbornanone was prepared by oxidizing 4-chloro-exo-

2-norborneol by Jones reagent. The oxidizing agent[197] was prepared by dissolving sodium dichromate (10 g) in water (20 ml) and then sulphuric acid (7.5 ml) was added. For each millimole of alcohol to be oxidized, 0.5 ml of solution is used.

To the solution of chlorohydrin (125.5 g, 0.856 mole) in ether (1 litre, pretreated with oxidizing agent) in a 2 litre flask equipped with a condenser and a magnetic stirrer, the oxidizing agent (428.5 ml) was added carefully in small fractions. After stirring the solution vigorously for 96 hrs, the ethereal layer was separated and the aqueous layer was extracted with ether (5 x 200 ml). The combined ethereal layers were washed with saturated sodium bicarbonate solution (2 x 150 ml), water (2 x 200 ml) and then dried over anhydrous magnesium sulphate. Removal of the solvent by distillation via a 2 ft glass helices column gave a slightly dirty white solid (106.5 g, 0.737 mole, 86%) of m.p. 80-82°; lit.[193] m.p. 80.6-82°. The analytical glpc analysis (5% SE-30, 105°) indicated only one product which was identified by i.r. and nmr spectroscopy to be 4-chloro-2-norobrnanone.

i.r. (CCl_4): 1750 (C=O).

nmr (60 MHz, $CDCl_3$): δ 2.70 (s broad, 1H, bridgehead H at C_1); δ 2.50 (s, 2H, H at C_3); δ 1.30-0.60 (m, 6H, H's at C_5, C_6 and C_7).

f) 4-Chloro-2-norbornyl tosylhydrazone

It was prepared by the method described for the preparation of norcamphor tosylhydrazone from norcamphor. Concentrated hydrochloric acid (10 ml) was added to tosylhydrazine (136.5 g, 0.73 mole) and 4-chloro-2-norbornanone (106 g, 0.73 mole) dissolved in 95% ethanol (1500 ml) in a 3 litre flask equipped with a reflux condenser and stirrer. The mixture was refluxed for 48 hours and poured onto water (2-3 litre). The resultant precipitate was collected and the aqueous solution was extracted with (3 x 1 litre) portions of methylene chloride. The extracts were washed with 1 litre

of water and then dried over anhydrous sodium sulphate. The solvents were then removed by distillation via 12" glass helices column and the entire precipitates were recrystallized from 95% ethanol to give 4-chloro-2-norbornyl tosylhydrazone (137.6 g, 0.44 mole, 60%, m.p. 176.5-179°). i.r. ($CHCl_3$): 3690, 3630 (N-H); 1675, 1600 (C=N); 1335, 1170 (S=O).

g) 4-Chloronortricyclane (11b)

4-Chloro-2-norbornyl tosylhydrazone (90.0 g, 0.288 mole m.p. 174.5-176.5°) was added to purified diglyme* (1200 ml) in a flask equipped with a condenser, a safety trap, a gas bubbler and a drying tube at the end of the system. Sodium methoxide (J.T. Baker Chemicals, 136.7 g, 2.53 mole) was added. The mixture was refluxed (150-170°) until a vigorous evolution of N_2 gas was noticed. After the evolution of N_2 was over, the reaction flask was allowed to attain the room temperature. The contents were then poured onto 1 litre of water. The organic product was extracted with (10 x 500 ml) portions of ether. The ethereal extracts were washed with (5 x 500 ml) portions of water and then were dried over anhydrous sodium sulphate. After concentrating the ethereal extracts, the analytical glpc analysis revealed 50% diglyme along with the product. To remove the diglyme, the above concentrated solution was dissolved in n-pentane (1500 ml) which was then washed with water again (5 x 100 ml). Pentane containing the product was dried and then evaporated by distillation via a 2 ft glass helices packed column. The analytical glpc analysis (3% OV-1, 70°) indicated the product 4-chloronortricyclane completely free of diglyme without any significant loss of 4-chloronortricyclane. The reaction yielded 4-chloronortricyclane (14.9 g, 0.116 mole, 40%), b.p. 142-144.5°; lit.[199,200] b.p. 142-144°. i.r. (CS_2): 3070 (cyclopropyl C-H); 2960, 2900, 2870, 1350,

* Diglyme was purified as described by Fieser and Fieser in "Reagents for Organic Synthesis, 1967" by John Wiley and Sons, Inc., on page 255.

1285, 1264, 1252, 1010, 798 (C-Cl).

nmr (90 MHz, CCl_4): δ 1.66 (s, 6H, methylene H's at C_3, C_5 and C_7), δ 1.2 (s, 3H, cyclopropyl H's at C_1, C_2 and C_6). The nmr spectrum (Fig. 2:5) and the b.p. were identical to that reported in literature which confirmed the compound as 4-chloronortricyclane.

2) CLEAVAGE IN DEUTERATED ACID

a) Electrophilic cleavage of 4-chloronortricyclane (11b) with sulphuric acid-d_2 in acetic acid-d_4.

4-Chloronortricyclane (0.4950 g, 3.852 millimole) purified by preparative glpc (25% GEXF-1150, 110°) was dissolved in (31.7 ml) of stock solution (0.1067 M D_2SO_4 in acetic acid-d_4) in a 50 ml flask equipped with a drying tube and a magnetic stirrer. This flask was then placed into an oil bath maintained at a constant temperature of 50°±2. The reaction was followed by glpc. After 92 hours the ring-opening was found out to be complete. The entire reaction mixture was neutralized with saturated sodium bicarbonate solution and the product was extracted with ether. The ethereal extract was washed with water and dried. The ether was removed by distillation via a 2 ft glass helices packed column which left behind (0.6745 g, 3.5038 millimole, 91%) of 4-chloro-exo-2-norbornyl trideutero-acetate-d_1 (11b-OAc) which was identified by i.r. and nmr spectroscopy (Fig. 2:6). i.r. (CCl_4): 1750 (C=O.

nmr (90 MHz, CCl_4): δ 4.6 (dd, 1H, H at C_2); δ 2.4-0.7 (m, 8H, H's at C_1, C_3, C_5, C_6, and C_7).

b) Reduction of 4-chloro-exo-2-norbornyl trideuteroacetate-d_1 (11b-OAc) with sodium in isopropyl alcohol.

To a stirred solution of the 4-chloro-exo-2-norbornyl trideutero-

acetate-d_1 (0.6745 g, 3.504 millimile) in isopropanol (50 ml) were slowly added small pieces of sodium (1.34 g, 58.26 millimole).[54] The mixture was stirred magnetically and refluxed during the addition. After the sodium completely dissolved the solution was refluxed for 6 hours and then the pale yellow solid obtained on cooling was dissolved in water (50 ml) and the aqueous solution was extracted with n-pentane (4 x 75 ml). The combined pentane extracts were washed with dilute HCl (10%, 40 ml), water (2 x 40 ml) and then dried and concentrated to yield (0.2852 g, 2.5238 millimole, 72%) of a white solid. The analytical glpc (3% OV-1, 70°) indicated only one major product (> 97%) and after isolation by preparative glpc (15% carbowax, 140°) it was found to have identical spectral characteristics to those of exo-2-norborneol-d_1 (11a-OH). i.r. (CCl_4): 3625 (free OH), 3600-3300 (H bonded OH).
nmr (90 MHz, CCl_4): δ 3.65 (dd, 1H, H at C_2); δ 3.05 (s, 1H, OH); δ 2.3-2.0 (m, 2H, bridgehead H's at C_1 and C_4); δ 1.8-0.5, (m, 7H, H's at C_3, C_5, C_6 and C_7); (Fig. 2:3).

c) Estimation of 4-chloro-endo-2-norbornyl trideuteroacetate-d_1

Since the reduction of the products of D^+-catalyzed ring-opening of 4-chloronortricyclane (11b), the 4-chloro-exo-2-norbornyl trideuteroacetate-d_1 and 4-chloro-endo-2-norbornyl trideuteroacetate-d_1 does not change the distribution of these exo and endo isomers, the estimation of amount of the endo-isomer as endo-2-norborneol-d_1 would give the amount of 4-chloro-endo-2-norbornyl trideuteroacetate-d_1. The analytical glpc analysis (10% carbowax, 122°) of mixture of these endo and exo-2-norborneols obtained from 4-chloro-exo- and 4-chloro-endo-2-norbornyl trideuteroacetates-d_1 by sodium in isopropanol reduction was compared with that of the standard mixture of 95% of exo-2-norborneol

and 5% endo-2-norborneol. This comparison indicated that D^+-catalyzed ring-opening in fact produced ≈ 2% of the 4-chloro-endo-2-norbornyl trideuteroacetate-d_1 and ≈ 98% of 4-chloro-exo-2-norbornyl trideuteroacetate-d_1.

d) Oxidation of exo-2-norborneol-d_1.

After the dmr spectrum of exo-2-norborneol-d_1 was obtained the solvent was removed and the alcohol was oxidized with Jones reagent. To solution of exo-2-norborneol-d_1 (0.10 g, 0.9 millimole) in ether (10 ml, pretreated with the oxidizing agent) in a 50 ml flask equipped with a condenser and magnetic stirrer, the oxidizing agent (1 ml) was slowly added. After the solution was vigorously stirred overnight, the ethereal layer was separated and the aqueous layer was extracted with ether (5 x 20 ml). The combined ethereal layers were washed with saturated bicarbonate (2 x 15 ml), water (2 x 20 ml), and then dried over anhydrous sodium sulphate.

Analytical glpc (3% OV-1, 70°) indicated only one product with retention time identical to that of norcamphor. The oxidation of exo-2-norborneol-d_1 yielded (0.065 g, 0.58 millimole, 66%) of 2-norbornanone-d_1 (71b).

nmr (90 MHz, CCl_4): δ 2.65 (m, 1H, bridgehead H at C_1); δ 2.5 (m, 1H, bridgehead H at C_4); δ 2.2-0.9 (m, 8H, H's at C_2, C_5, C_6 and C_7).

C. 4-BROMONORTRICYCLANE (11c)

1. SYNTHESIS

a) Phosphorus pentabromide

The reagent phosphorus pentabromide was prepared by the procedure as described by Fieser and Fieser* by slowly adding PBr_3 (270.7 g, 1 mole) to a cold, vigorously stirred solution of bromine (160 g, 1 mole) in petroelum ether (600 ml) placed into a 2 litre flask. The solvent was decanted and the phosphorus pentabromide washed several times with fresh solvent. Removal of the solvent under vacuum gave (406 g, 0.943 mole, 94%) of yellow phosphorus pentabromide.

b) 2,2-Dibromonorbornane

A solution of norcamphor (80 g, 0.727 mole) in phosphorus tribromide (225 g, 0.83 mole) in a 2 litre flask equipped with a magnetic stirrer and a reflux condenser, was placed into an ice-salt bath. To the above solution was added phosphorus pentabromide (355 g, 0.82 moles) carefully in small portions over the course of 2-3 hr. The mixture was allowed to warm slowly to room temperature and stir for 48 hr. The mixture was poured onto ice (1.5 Kg). The porduct was carefully extracted with pentane (10 x 200 ml). The pentane extracts were dried and the solvent was then distilled out via a 12" glass helices column. Analytical glpc analysis (5% SE-30, 100°) indicated the formation of 2,2-dibromonorbornane (132.9 g, 0.52 mole, 72%).

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* Reagents for "Organic Synthesis" by Fieser and Fieser, p. 865, (1967), by John Wiley and Sons, Inc.

c) 1-Exo-2-dibromonorbornane

To the solution of 2,2-dibromonorbornane (132.7 g, 0.52 mole) in toluene (250 ml) was added anhydrous zinc bromide[193] (Ventron Chemicals, 75 g, 0.33 mole) into a flask equipped with a magnetic stirrer and a drying tube. The progress of the reaction was monitored by analytical glpc (5% SE-30, 100°). The mixture was allowed to stir very slowly for one week at room temperature. The rearranged product was extracted with (10 x 200 ml) portions of pentane and after drying the pentane extracts the solvents were evaporated via 12" vigreux column by distillation which left behind the product 1-exo-2-dibromonorbornane (124.7 g, 0.49 mole, 94%).
nmr (60 MHz, CCl_4): δ 4.15 (m, 1H, H at C_2), δ 2.8-1.3 (m, 9H, H's at C_3, C_4, C_5, C_6 and C_7).

d) 1-Norbornenyl bromide

This elimination reaction was conducted as described in the synthesis of 1-norbornenyl chloride. A two fold excess of potassium tert. butoxide (110 g, 0.98 mole) was added in portions into a 1 litre flask containing a solution of 1-exo-2-dibromonorbornane (124 g, 0.488 mole) in dimethyl sulphoxide (600 ml) equipped with a drying tube and a magnetic stirrer. The contents of the reaction flask were stirred for 24 hr which were then poured onto 1 litre 1:1 mixture of water and ether. The ethereal layer was separated and the aqueous layer was extracted with (6 x 500 ml) portions of ether again. The combined ethereal extracts were washed with (3 x 200 ml) portions of water and dried over anhydrous magnesium sulphate. After the removal of the solvents, the distillation at atmospheric pressure resulted into the product 1-norbornenyl bromide (67.7 g, 0.39 mole, 80%) as a colourless oil, b.p. 148° at atmospheric pressure. The analytical glpc (5% SE-30, 100°) indicated only one product as determined by i.r. and nmr

spectroscopy. i.r. (neat): 3070 (olefinic C-H); 1452 (C=C); 790 (C-Br), 710 (cis CH=CH).

nmr (90 MHz, CCl_4):δ 6.0 (m, 2H, olefinic H's at C_2 and C_3); δ 2.95-2.7 (m, 1H, bridgehead H at C_4); δ 2.2-1.0 (m, 6H, H's at C_5, C_6 and C_7).

e) 1-Bromo-exo-cis-3-hydroxy-2-norbornyl mercuric chloride and 4-bromo-exo-2-norborneol.

i) The oxymercuration of 1-bromonorbornene was conducted as described previously.[195] A solution of 1-bromonorbornene (67.2 g, 0.388 mole), mercuric oxide (42 g, 0.194 mole) and of mercuric chloride (52.7 g, 0.194 mole) in 1 litre of 50% aqueous acetone, was refluxed with stirring for 48 hr in a 2 litre flask equipped with a mechanical stirrer and a reflux condenser. A yellow solid was obtained upon cooling the reaction flask. Removal of the acetone and water gave 1-bromo-exo-cis-3-hydroxy-2-norbornyl mercuric chloride (133 g, 0.312 mole, 80%).

ii) Sodium borohydride reduction of the organomercurial was conducted as described previously in the synthesis of 4-chloro-exo-2-norborneol. The organomercurial was mixed with 1600 ml of 1:3 mixture of ether:methanol in a 1 litre flask equipped with a reflux condenser and a magnetic stirrer. Sodium borohydride (26.4 g, 0.698 mole) was added to the reaction flask in small portions and the contents were then refluxed overnight. After the reaction mixture was acidified the product was extracted with (6 x 250 ml) fractions of anhydrous ether. The ethereal extracts were then washed with (2 x 125 ml) saturated sodium bicarbonate solution and water (2 x 125 ml). After drying the ethereal extracts over anhydrous magnesium sulphate the solvent ether was distilled off via a 2 ft glass helices column. The removal of ether gave 4-bromo-exo-2-norborneol (49 g, 0.256 mole, 82%).

The analytical glpc (3% OV-1, 160°) revealed only one product as determined by i.r. and nmr spectroscopy. i.r. (CS_2): 3585 (free O-H); 3550-3180 (broad, bonded O-H);

nmr (90 MHz, acetone-d_6): δ 3.83 (dd, 1H, H at C_2); δ 2.97 (s, 1H, OH); δ 2.35-0.7 (m, 9H, H's at C_1, C_3, C_5, C_6 and C_7).

f) 4-Bromo-2-norbornanone

4-Bromo-2-norbornanone was prepared by the oxidation of 4-bromo-exo-2-norborneol. The oxidizing agent (Jones reagent) was prepared by dissolving sodium dichromate (10 g) in water (20 ml) and sulphuric acid (7.5 ml) again.[54] For each millimole of alcohol to be oxidized, 0.5 ml of solution was used.

To the solution of 4-bromo-exo-2-norborneol (48 g, 0.25 mole) in 500 ml of ether pretreated with oxidizing agent in a 1 litre flask equipped with a condenser and a magnetic stirrer, 126 ml of oxidizing agent was added carefully in small portions. The reaction mixture was stirred for 96 hr. After separating the ethereal layer, the aqueous layer was extracted with ether (5 x 100 ml). The combined ethereal extracts were washed with saturated solution of sodium bicarbonate (2 x 75 ml), water (2 x 100 ml) and then were dried over anhydrous sodium sulphate. Removal of the solvent yielded a shite solid (41 g, 0.217 mole, 86%), m.p. 60-61.5°.

i.r. ($CDCl_3$): 1755 (C=O).

nmr (90 MHz, acetone-d_6): δ 2.45 (s, 1H, H at C_1); δ 2.3-1.9 (m, 2H, H's at C_3); δ 1.75-0.6 (m, 6H, H's at C_5, C_6 and C_7).

g) 4-Bromo-2-norbornyl tosylhydrazone

Concentrated hydrochloric acid (5 ml) was added to tosylhydrazine (39.5 g, 0.212 mole) and 4-bromo-2-norbornanone (40 g, 0.212 mole) dissolved

in 95% ethanol (500 ml) in a 1 litre flask equipped with a reflux condenser and a magnetic stirrer. The reaction mixture was refluxed for 40 hr and poured onto water (800 ml). The resultant precipitates were separated and the aqueous solution was further extracted with (4 x 250 ml) portions of methylene chloride. The extracts were washed with water (1 x 500 ml) and then dried. The solvent was removed by distillation via a 12" glass helices packed column. The precipitates were recrystallized from 95% ethanol to give 4-bromo-2-norbornyl tosylhydrazone (45.5 g, 0.127 mole, 60%); m.p. 189.5-190.5°. i.r. ($CHCl_3$): 3300, 3210 (N-H); 1670, 1600 (C=N); 1340, 1165 (S=O).

h) 4-Bromonortricyclane (11c).

The reaction was conducted as described in the formation of 4-chloronortricyclane. 4-Bromo-2-norbornyl tosylhydrazone (36 g, 0.1 mole, m.p. 190°) was added to purified diglyme (600 ml) in a 1 litre flask equipped with a condenser and safety trap, a gas bubbler and a drying tube. Sodium methoxide (47.5 g, 0.88 mole) was added to the reaction flask. The reaction mixture was refluxed until a vigorous evolution of N_2 gas was noticed. The contents were cooled down to room temperature after refluxing for 3-4 hrs. The dark brown reaction mixture was poured onto water (500 ml). The product was extracted with (10 x 250 ml) portions of ether. The ethereal extracts were washed with water (5 x 250 ml) and then dried. The analytical glpc analysis of the concentrated ethereal extracts (3% OV-1, 67°) indicated the presence of diglyme with 4-bromonortricyclane. To remove diglyme, the above concentrated mixture was dissolved in n-pentane (800 ml) and then was washed with water (6 x 50 ml). The pentane was dried and then distilled off

via a 2 ft glass helices column. The analytical glpc analysis (3% OV-1, 70°) revealed the product 4-bromonortricyclane free from diglyme.

The distillation under reduced pressure yielded 4-bromonortricyclane (7.4 g, 0.043 mole, 42%), b.p. 36° under 1.8 mm. i.r. (CS_2): 3070 (cyclopropyl C-H); 2960-2940, 2900, 2870, 1280, 1262, 1250, 1240, 990; and 798 (C-Br).

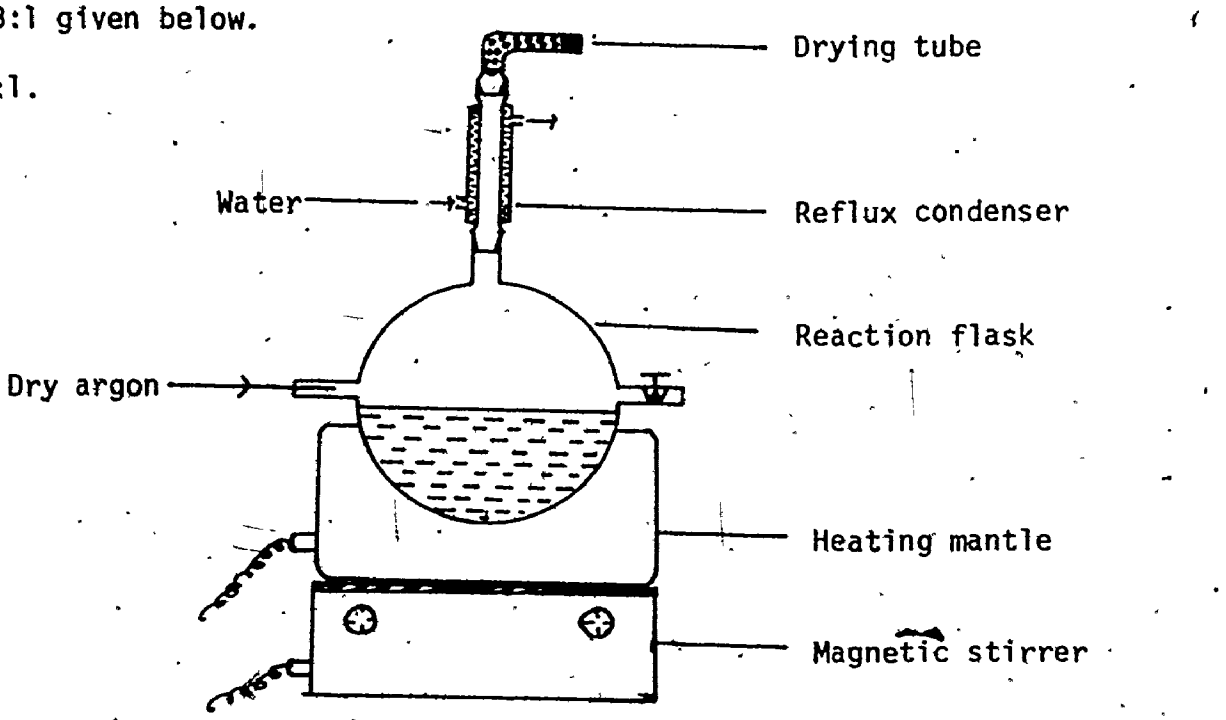
nmr (90 MHz, CCl_4): δ 1.68 (s, 6H, methylene H's at C_3, C_5 and C_7); δ 1.12 (s, 3H, cyclopropyl H's at C_1, C_2 and C_6); Fig. (2:9).

i) 4-Bromonortricyclane from 4-chloronortricyclane

4-Nortricyclyl lithium was prepared according to Bixler and Niemann[201] from 4-chloronortricyclane and lithium sand as described below.

A five-fold excess of lithium (0.123 g, 17.57 millimole) was heated in 25 ml of mineral oil under argon gas in a 300 ml flask equipped with a magnetic stirrer and a reflux condenser with a drying tube as shown in Fig. 3:1 given below.

Fig 3:1.



To prevent the coagulation of lithium melt[202] a few drops of oleic acid were added. The reaction flask was heated to 185-187°. As lithium melted the mixture was stirred very vigorously to form a fine shining dispersion. The mineral oil was drained out through the bottom stopcock. The lithium dispersion was washed four times with purified cyclohexane from calcium hydride.. To the lithium dispersion in the reaction flask under Ar, was introduced a solution of 4-chloronortricyclane (0.4495, 3.5 millimole) in cyclohexane by the use of a syringe needle. All the chemicals and the equipment must be free of moisture since lithium as well as 4-nortricyclyl lithium are very reactive towards moisture. The reaction contents were then refluxed for 6 hrs under argon. 4-Nortricyclyl lithium obtained as such was then quenched with a solution of cyanogen bromide (0.4 g, 3.7 millimole) in pure cyclohexane at 0°. The reaction mixture was washed with water (3 x 15 ml) after quenching the unreacted lithium with water carefully. The cyclohexane extracts were dried and then concentrated by distilling off cyclohexane via a 12" glass helices packed column. The analytical glpc analysis (5% SE-30, 60°) indicated only one major product with retention time equal to that of 4-bromonortricyclane. This product was further purified by preparative glpc (25% GEXF-1150, 150°) which gave (0.2769, 1.6 millimole, 41%) of 4-bromonortricyclane as identified by i.r. and nmr spectroscopy. The spectral characteristics of 4-bromonortricyclane obtained by two different synthetic routes were found to be identical. i.r. (CS_2): 3070 (cyclopropyl C-H); 2960-2940, 2900, 2870, 1280, 1262, 1250, 1240, 990; 798 (C-Br).

nmr (90 MHz, CCl_4): δ 1.68 (s, 6H, methylene H's at C_3, C_5 and C_7); δ 1.12 (s, 3H, cyclopropyl H's at C_1, C_2 and C_6).

2. CLEAVAGE IN DEUTERATED ACID

a) Electrophilic cleavage of 4-bromonortricyclane (11c) with sulphuric acid-d_2 in acetic acid-d_4.

4-Bromonortricyclane (0.6637 g, 3.839 millimole) was dissolved in (31.6 ml) of stock solution (0.1067 M D_2SO_4 in acetic acid-d_4) in a 50 ml flask equipped with a drying tube and a magnetic stirrer. The flask was then placed into an oil bath maintained at a constant temperature of (50°±1). The ring-opening was found completed after 90 hrs. The entire reaction mixture was neutralized with a saturated solution of sodium bicarbonate and the products were extracted with ether. The ethereal extracts were washed with water and then dried. The ether was removed by distillation via a 2 ft glass helices packed column. Removal of ether yielded (0.827 g, 4.783 millimole, 91%) of 4-bromo-exo-2-norbornyl trideuteroacetate-d_1 (11c-OAc) as identified by i.r. and nmr (Fig. 2:10) spectroscopy. i.r. (CCl_4): 1750 (C=O).

nmr (90 MHz, CCl_4): δ 4.58 (dd, 1H, H at C_2); δ 2.5-1.1 (m, 8H, H at C_1, C_3, C_5, C_6 and C_7).

b) Reduction of 4-bromo-exo-2-norbornyl trideuteroacetate-d_1 (11c-OAc) with sodium and isopropanol.

Small pieces of sodium (1.23 g, 53.48 millimole) were slowly added to a stirred solution of 4-bromo-exo-2-norbornyl trideuteroacetate-d_1 (0.827 g, 4.78 millimole) in isopropanol (50 ml). After the sodium metal was dissolved completely the reaction mixture was refluxed for 6 hrs. A light yellow solid was obtained on cooling down the reaction mixture. This solid was dissolved in water (50 ml) and the aqueous solution was extracted with (4 x 75 ml) portions of n-pentane. The entire pentane extracts were

washed with dilute hydrochloric acid (10%, 40 ml), water (2 x 40 ml) and then dried. Removal of the solvent gave (0.2850 g, 2.522 millimole, 72%) of a white solid. The analytical glpc analysis (3% OV-1, 70°) indicated only one major product more than 97%. The i.r. and nmr spectral characteristics were found identical to that of the exo-2-norborneol-d_1 (11a-OH).

i.r. (CCl_4): 3625 (free O-H); 3600-3300 (bonded O-H).

nmr (90 MHz, CCl_4): δ 3.65 (dd, 1H, H at C_2); δ 3.05 (s, 1H, OH); δ 2.3-2.0 (m, 2H, bridgehead H's at C_1 and C_4); δ 1.8-0.5 (m, 7H, H's at C_3, C_5, C_6 and C_7).

c) Estimation of 4-bromo-endo-2-norbornyl trideuteroacetate-d_1

The mixture of 4-bromo-exo-2-norbornyl trideuteroacetate-d_1 and 4-bromo-endo-2-norbornyl trideuteroacetate-d_1 obtained from the D^+-catalyzed ring-opening of 4-bromonortricyclane (11c) was reduced with sodium in isopropanol to endo and exo-2-norborneol-d_1 as described above. The analytical glpc analysis (10% carbowax, 122°) indicated a minor product with a major product, exo-2-norborneol-d_1. The analytical glpc analysis (10% carbowax, 122°) of the standard mixture of 95% exo-2-norborneol and 5% endo-2-norborneol showed a little larger peak for endo-2-norborneol with a little longer retention time than exo-2-norborneol. The comparison of both the mixtures under identical conditions indicated 2% of endo-2-norborneol-d_1 and 98% of exo-2-norborneol and that 2% of 4-bromo-endo-2-norbornyl trideuteroacetate-d_1 and 98% of 4-bromo-exo-2-norbornyl trideuteroacetate-d_1.

d) Oxidation of exo-2-norborneol-d_1

After the dmr spectrum for this exo-2-norborneol-d_1 was obtained, exo-2-norborneol-d_1 was oxidized to 2-norbornanone-d_1 by Jones reagent as previously described. To a solution of exo-2-norborneol-d_1 (0.1 g, 0.9 millimole) in (10 ml) of ether, pretreated with oxidizing agent in a 50 ml flask equipped with a condenser and magnetic stirrer, the oxidizing agent (1 ml) was added. After the reaction mixture was stirred overnight, the ethereal layer was separated and the aqueous layer was extracted with ether (5 x 20 ml). The combined ethereal extracts were washed with a saturated solution of sodium bicarbonate (2 x 15 ml), water (2 x 20 ml) and then dried over anhydrous sodium sulphate.

The analytical glpc analysis (3% OV-1, 70°) indicated a product with retention time identical to that of norcamphor under identical conditions. Thus the oxidation of exo-2-norborneol-d_1 yielded (0.06 g, 0.54 millimole, 61%) of 2-norbornanone-d_1 (71c).

nmr (90 MHz, CCl_4): δ 2.65 (m, 1H, bridgehead H at C_1); δ 2.5 (m, 1H, bridgehead H at C_4); δ 2.2-0.9 (m, 8H, H's at C_2, C_3, C_5, C_6 and C_7).

D. 4-IODONORTRICYCLANE

1. SYNTHESIS

a) 4-Iodonortricyclane from 4-chloronortricyclane

A five-fold excess of lithium (0.136 g, 19.43 millimole) was melted in 25 ml of moisture free mineral oil under argon in a 300 ml flask (Fig. 3:1) equipped with a magnetic stirrer and a reflux condenser with a drying tube. Again to prevent the coagulation of lithium melt[202] a few drops of oleic acid were introduced. The reaction flask was heated with stirring to melt lithium into a fine dispersion. The mineral oil was drained out through the bottom outlet of the reaction flask. The lithium dispersion was washed four-five times with pure and dry cyclohexane. To this washed lithium dispersion in the reaction flask under argon was introduced a solution of 4-chloro-nortricyclane (0.5 g, 3.891 millimole) in cyclohexane by the use of a syringe needle. The reaction contents were then refluxed for 6 hrs under argon. 4-Nortricyclyl lithium obtained as such was quenched with a solution of freshly sublimed iodine (1 g, 3.937 millimole) in ether at 0°. The reaction mixture was washed with water (3 x 15 ml) after quenching the unreacted lithium with water carefully. The cyclohexane extracts were dried and then the solvents were distilled off via a 12" glass helices packed column. The analytical glpc analysis (5% SE-30, 60°) indicated only one major product with retention time longer than 4-chloro-nortricyclane and 4-bromonortricyclane as well. The product was purified by preparative glpc (25% GEXF-1150, 150°) which gave (0.1 g, 0.45 millimole, 12%) of 4-iodonortricyclane as identified by i.r. and nmr (Fig. 2:12). i.r. (CS_2): 3070 (cyclopropyl C-H). nmr (90 MHz, CCl_4): δ 1.70 (s, 6H, methylene H's at C_3, C_5 and C_7); δ 0.95 (s, 3H, cyclopropyl H's at C_1, C_2 and C_6).

b) 4-Iodonortricyclane from 4-bromonortricyclane

Lithiation of 4-bromonortricyclane was conducted as described in the lithiation of 4-chloronortricyclane.

Again a five-fold excess of lithium (0.102 g, 14.57 millimole) was heated in 25 ml of mineral oil under argon in a 300 ml flask equipped with a magnetic stirrer and a reflux condenser with a drying tube as shown in (Fig. 3:1). To prevent the coagulation of lithium melt[202] a few drops of oleic acid were added. The reaction flask was heated with stirring to melt lithium into a fine dispersion. The mineral oil was drained out through the bottom outlet of the flask. The lithium dispersion was washed four times with cyclohexane. To this washed lithium dispersion in the reaction flask under argon was introduced a solution of 4-bromonortricyclane (0.5 g, 2.892 millimole) in cyclohexane by the use of a syringe needle. The reaction mixture was then refluxed for 6 hrs under argon to produce 4-nortricyclyl lithium. It was then quenched with freshly sublimed iodine (0.75 g, 2.953 millimole) in ether at 0°. The reaction mixture was washed with water (3 x 15 ml) after quenching the excess of lithium with water. The organic solvent layer was dried over anhydrous sodium sulphate. The solvents were distilled off via a 12" glass helices packed column. The analytical glpc analyses (5% SE-30, 60°) indicated only a product and starting material 4-bromonortricyclane. The product was isolated by preparative glpc (25% GEXF-1150, 150°) which resulted in (0.05 g, 0.23 millimole, 8%) of 4-iodonortricyclane as identified by i.r. and nmr spectroscopy. The 4-iodonortricyclane (11c) prepared by lithiation of 4-chloronortricyclane and 4-bromonortricyclane, was found to have identical i.r. and nmr spectra, (Fig. 2:12).

E. STEREOCHEMISTRY OF DEUTERIUM INCORPORATION DURING D^+-CATALYZED RING OPENING.

Fourier transform dmr spectroscopy was used to obtain the dmr spectra of deuterated exo-2-norborneols obtained from the D^+-catalyzed ring-opening of nortricyclane (11a), 4-chloronortricyclane (11b) and 4-bromonortricyclane (11c).

The deuterium distribution and endo:exo deuterium ratio at C_6 of the deuterated exo-2-norborneols, the products of D^+-catalyzed ring opening of nortricyclane (11a), 4-chloronortricyclane (11b) and 4-bromo-nortricyclane (11c) is given in (Table 3:1).

TABLE 3:1 Deuterium distribution and endo:exo deuterium ratio at C_6 of deuterated exo-2-norborneols

Substrate	% Deuterium* at				Endo:Exo ratio of 'D' at C_6
	C_1	C_2	Endo-C_6	Exo-C_6	
Nortricyclane (11a)	9.2±0.6	8.2±2.0	43.6±1.5	39.0±1.3	1.12±0.09
4-Chloronortricyclane (11b)	3.3±0.6	2.6±0.3	54.0±0.8	40.1±0.9	1.35±0.03
4-Bromonortricyclane (11c)	2.6±0.5	1.9±0.3	58.9±0.8	36.6±0.4	1.61±0.03

* The results are averages of two ring-openings and five spectrum acquisitions of each of the deuterated exo-2-norborneols. Errors are expressed as average deviations.

CHAPTER 4

APPENDICES

A. Deuterium Assay by Mass Spectrometry

Mass spectrometric analysis for deuterium was determined on a Hitachi Perkin Elmer RMU-6A spectrometer at low voltage (10 eV). Isotopic distributions were calculated by comparison of relative peak heights of the unlabelled (natural abundance) and labelled species as described by Biemann.[205] Mass spectral peak intensities of 2-norbornanone-d_1 in the region of the molecular weight are tabulated in tables given below. Average deuterium contents which refer to deuterium in excess of natural abundance, were determined from summation of the deuterium content of the individual species (% d_1 x .01 + % d_2 x .02 + % d_3 x .03 + ...). This type of analysis for total deuterium content is subject to greater errors than the combustion analysis method. Some sources of error and limitations of this method for deuterium assay have been discussed by Biemann.[205]

1. Deuterium assay by mass spectrometry for 2-norbornanone-d_1 (71a), obtained from acid-catalyzed ring-opening of nortricyclane (11a).

TABLE 3:2. Relative peak intensities (%)[a]

m/e	2-norbornanone	2-norbornanone-d_1 (71a)
110	91.36	39.23
111	8.64	54.61
112		5.49
113		0.67

[a] These numbers represent the average of seven scans.

The calculations indicated that 2-norbornanone-d_1 (71a) contained 44.24% of d_0 and 55.76% of d_1 species.

2. Deuterium assay for 2-norbornanone-d_1 (71b) obtained from the acid-catalyzed ring-opening of 4-chloronortricyclane (11b).

TABLE 3:3. Relative peak intensities (%)[a]

m/e	2-norbornanone	2-norbornanone-d_1 (71b)
109	0.698	0.179
110	100.0	13.432
111	9.87	100.0
112	0.698	11.417
113		1.007

[a] These numbers represent the average of seven scans.

The calculations indicated 11.8% d_0, 86.8% d_1 and 1.39% d_2 species or an average of 0.9 deuterium atom per molecule in 2-norbornanone-d_1 (71b).

3. Deuterium assay for 2-norbornanone-d_1 (71c) obtained from the acid-catalyzed ring-opening of 4-bromonortricyclane (11c).

TABLE 3:4. Relative peak intensities (%)[a]

m/e	2-norbornanone	2-norbornanone-d_1 (71c)
110	91.36	8.55
111	8.64	81.3
		8.64
		1.5

[a] These numbers represent the average of seven scans.

The calculations indicated 9.6% d_0, 90.4% d_1 and 0% d_2 species or an average of 0.9 deuterium atom per molecule in 2-norbornanone-d_1 (71c).

B. Nmr Spectra of Selected Norbornyl Compounds

This section of the Appendix contains the nmr spectra of the following compounds.

1) 1-Norbornenyl chloride
2) 4-Chloro-exo-2-norborneol
3) 4-Chloro-2-norbornanone
4) 1-Norbornenyl bromide
5) 4-Bromo-exo-2-norborneol
6) 4-Bromo-2-norbornanone

C. Dmr Spectra of Monodeuterated Exo-2-Norborneols

Dmr spectra of monodeuterated exo-2-norborneols obtained individually from

i) D^+-catalyzed ring opening of 4-chloronortricyclane (11b) and
ii) D^+-catalyzed ring opening of 4-bromonortricyclane (11c).

Fig. 4:7 shows more of endo-D in exo-2-norborneol-d_1 obtained from ring opening of 4-bromonortricyclane (11c) than that in exo-2-norborneol-d_1 obtained from the ring opening of 4-chloronortricyclane (11b).

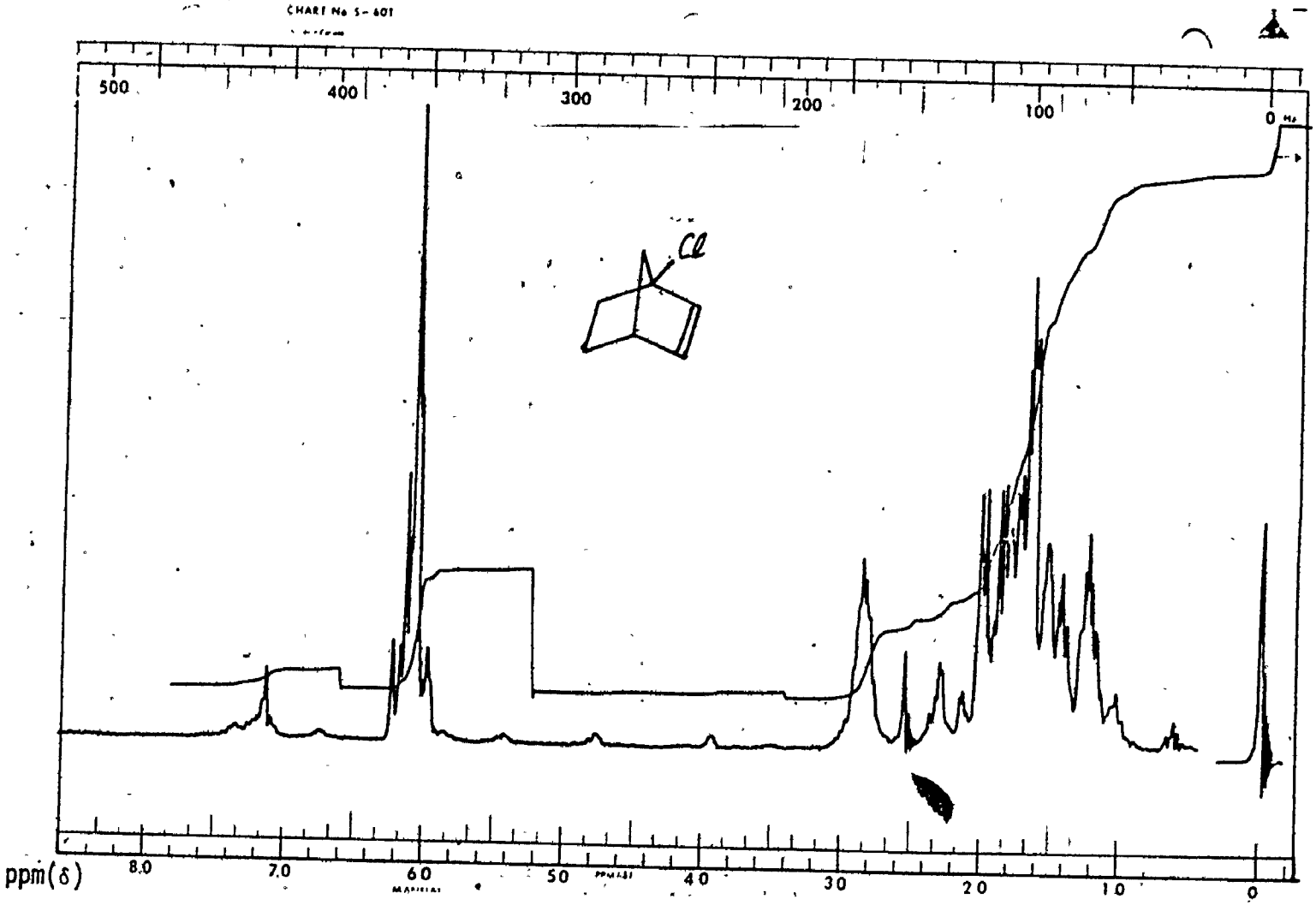


Fig. 4:1. Pmr spectrum (60 MHz) of 1-norbornyl chloride in $CDCl_3$.

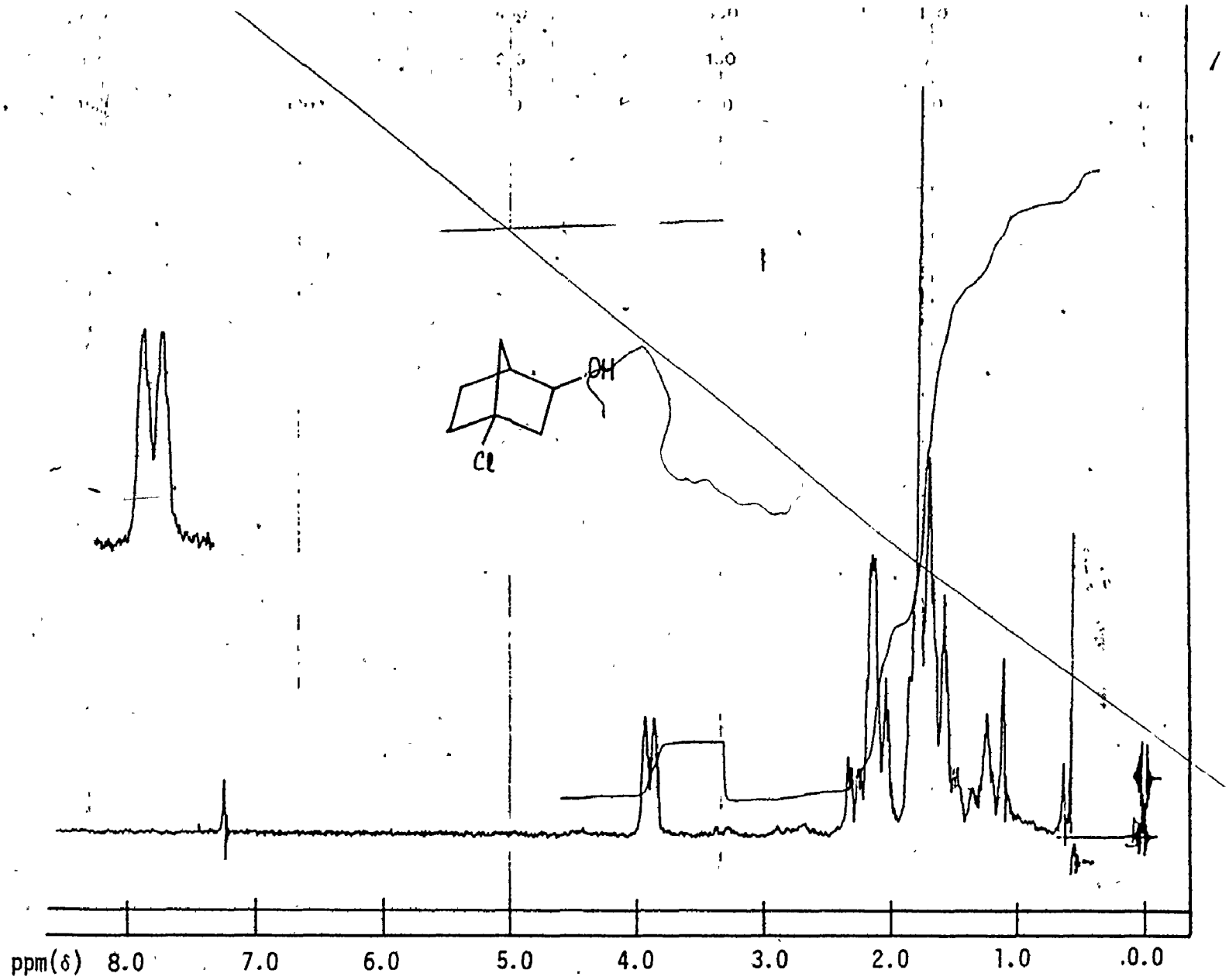


Fig. 4:2. Pmr spectrum (60 MHz) of 4-chloro-exo-2-norborneol in $CDCl_3$ and D_2O.

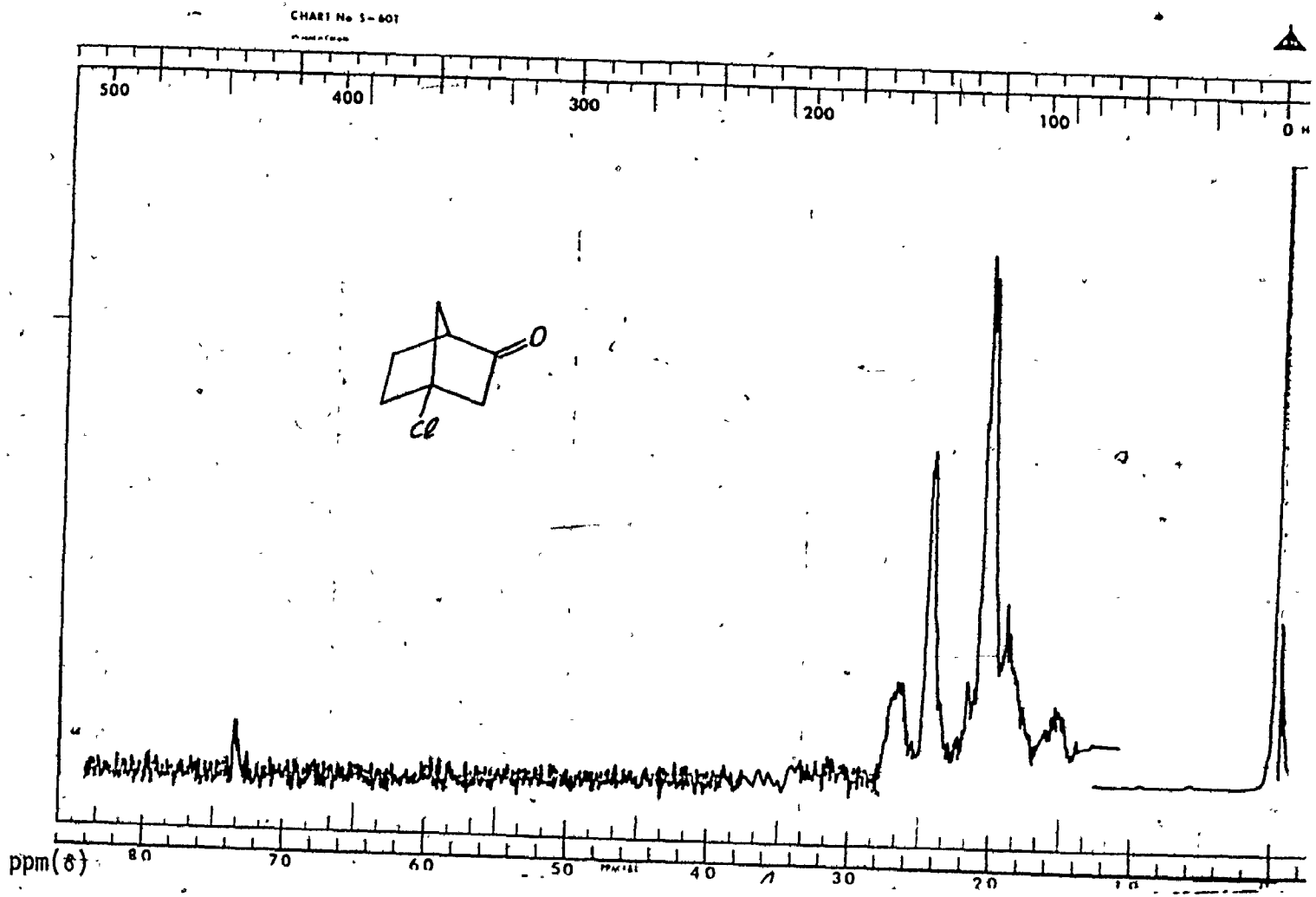


Fig. 4:3. Pmr spectrum (60 MHz) of 1-norbornenyl bromide in $CDCl_3$.

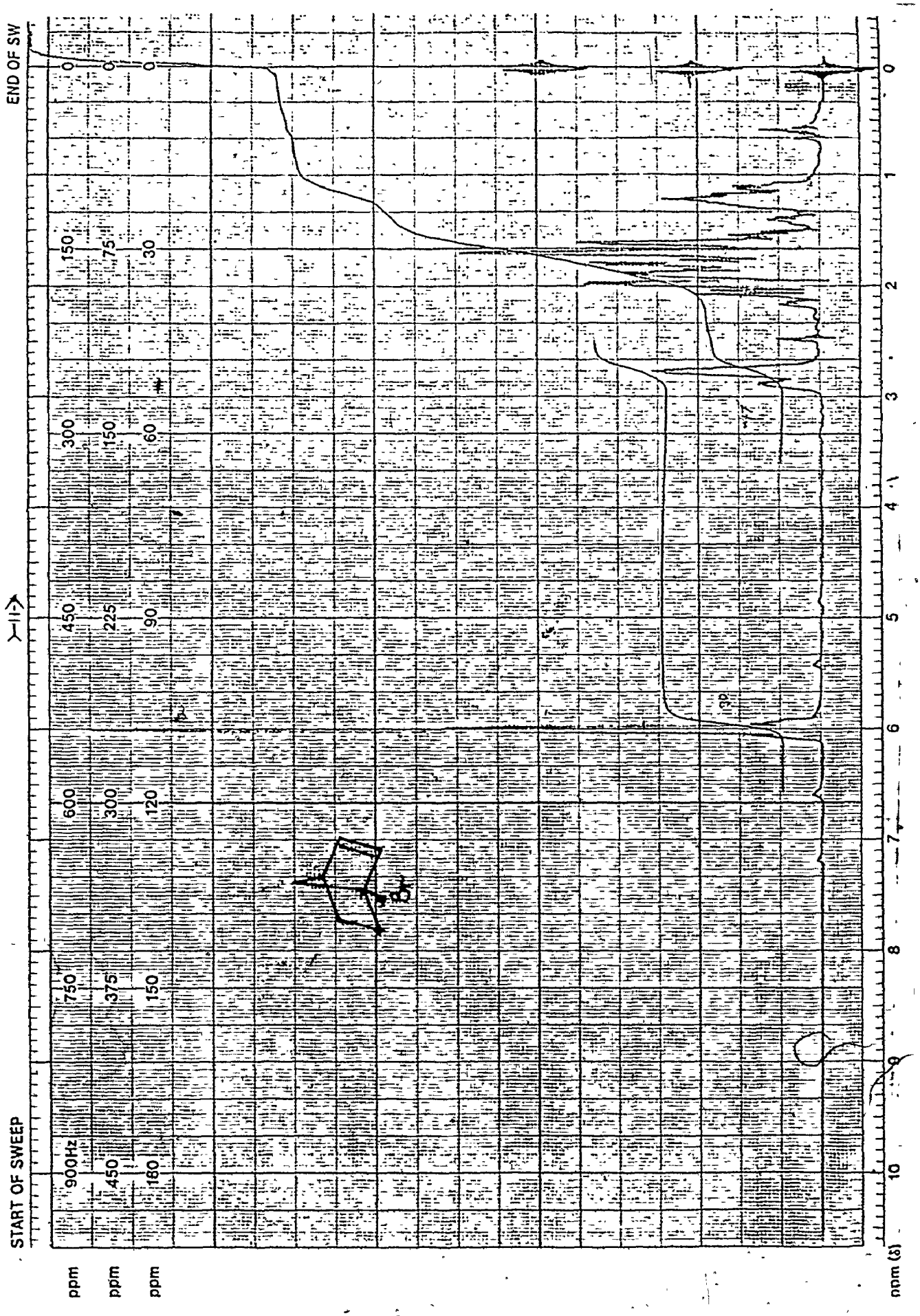


Fig. 4:4. Pmr spectrum (90 MHz) of 1-norbornenyl bromide in $CDCl_3$.

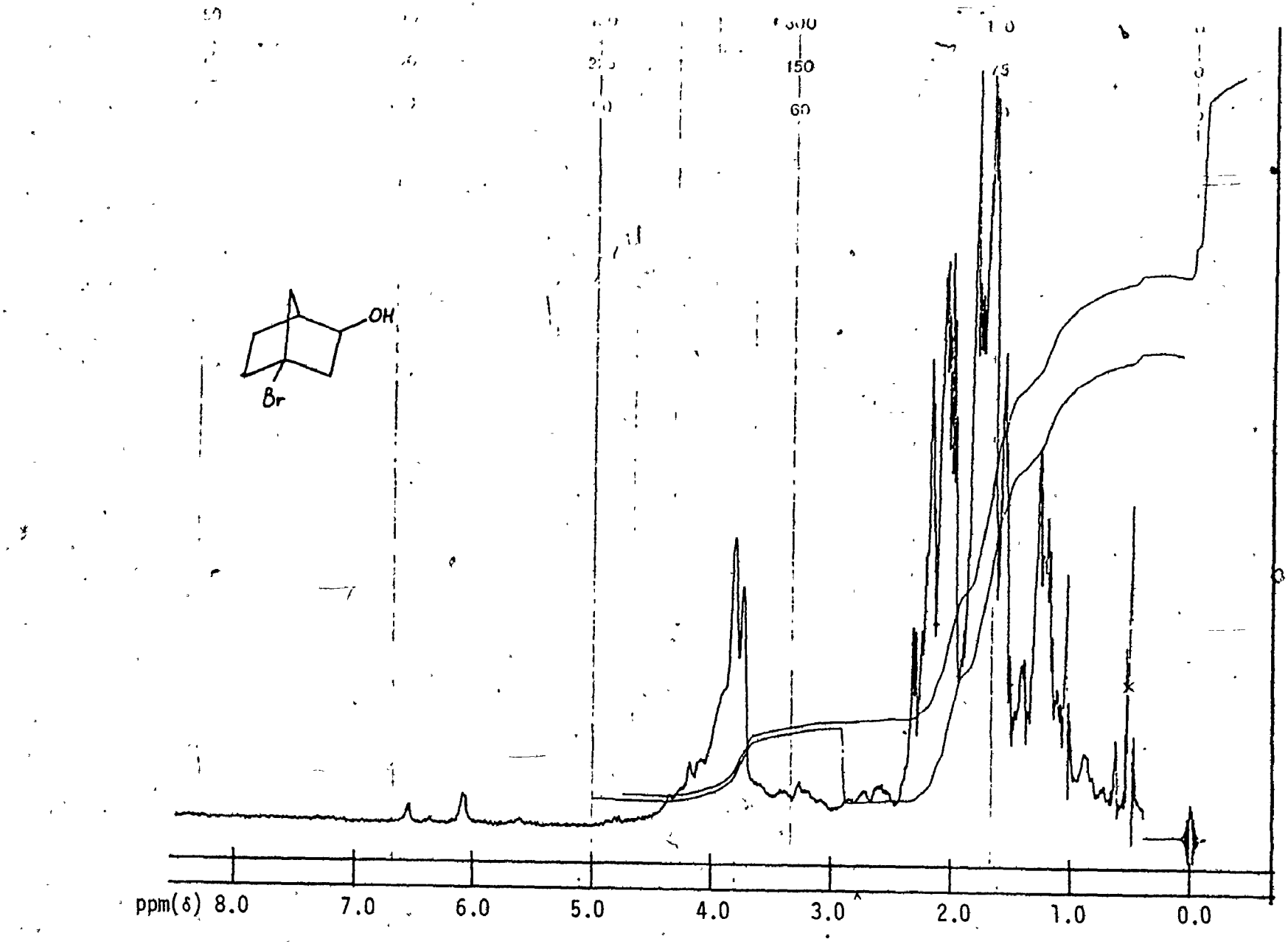


Fig. 4:5. Pmr spectrum (90 MHz) of 4-bromo-exo-2-norborneol in acetone-d_6 and D_2O.

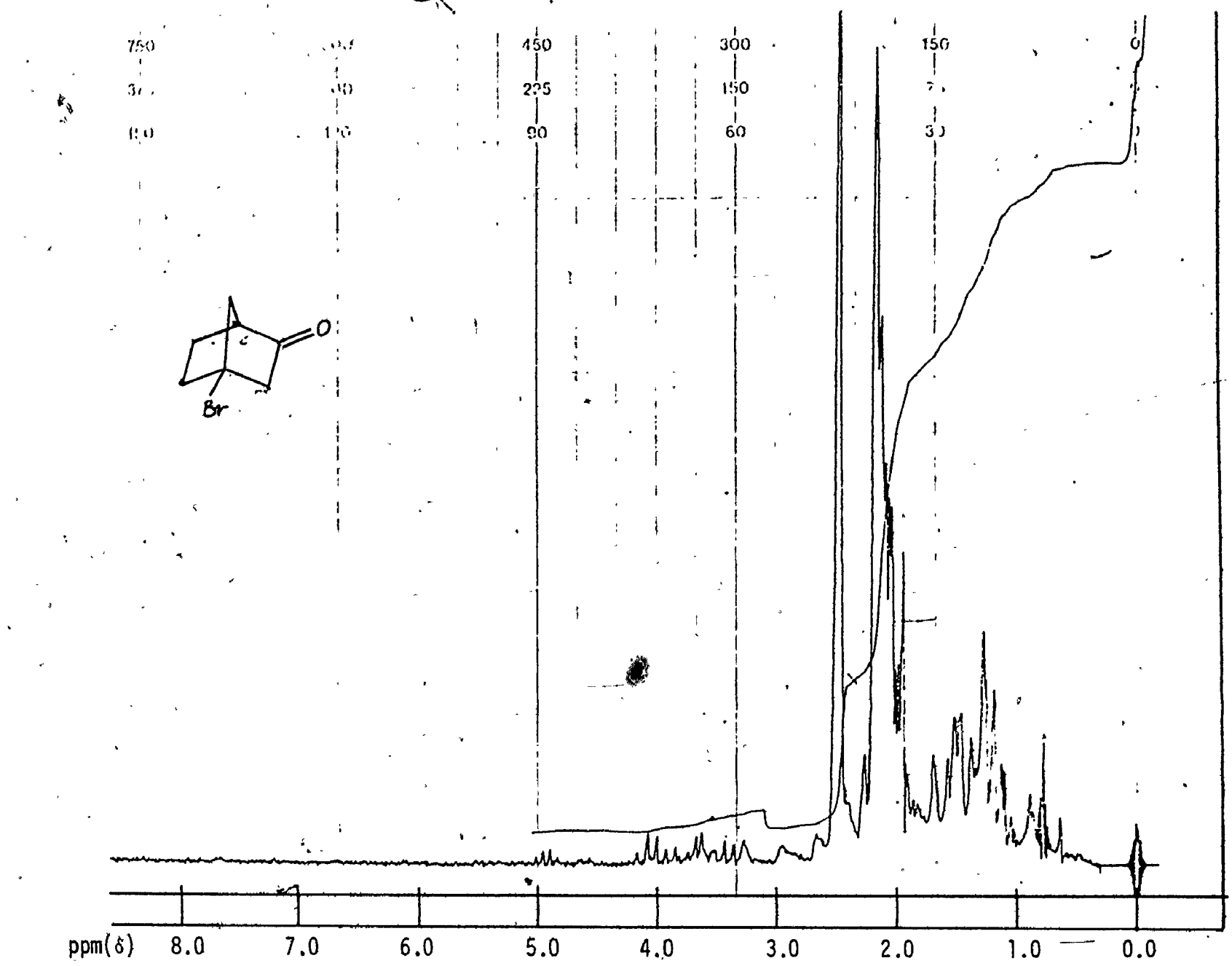


Fig. 4:6. Pmr spectrum (90 MHz) of 4-bromo-2-norbornanone in acetone-d_6.

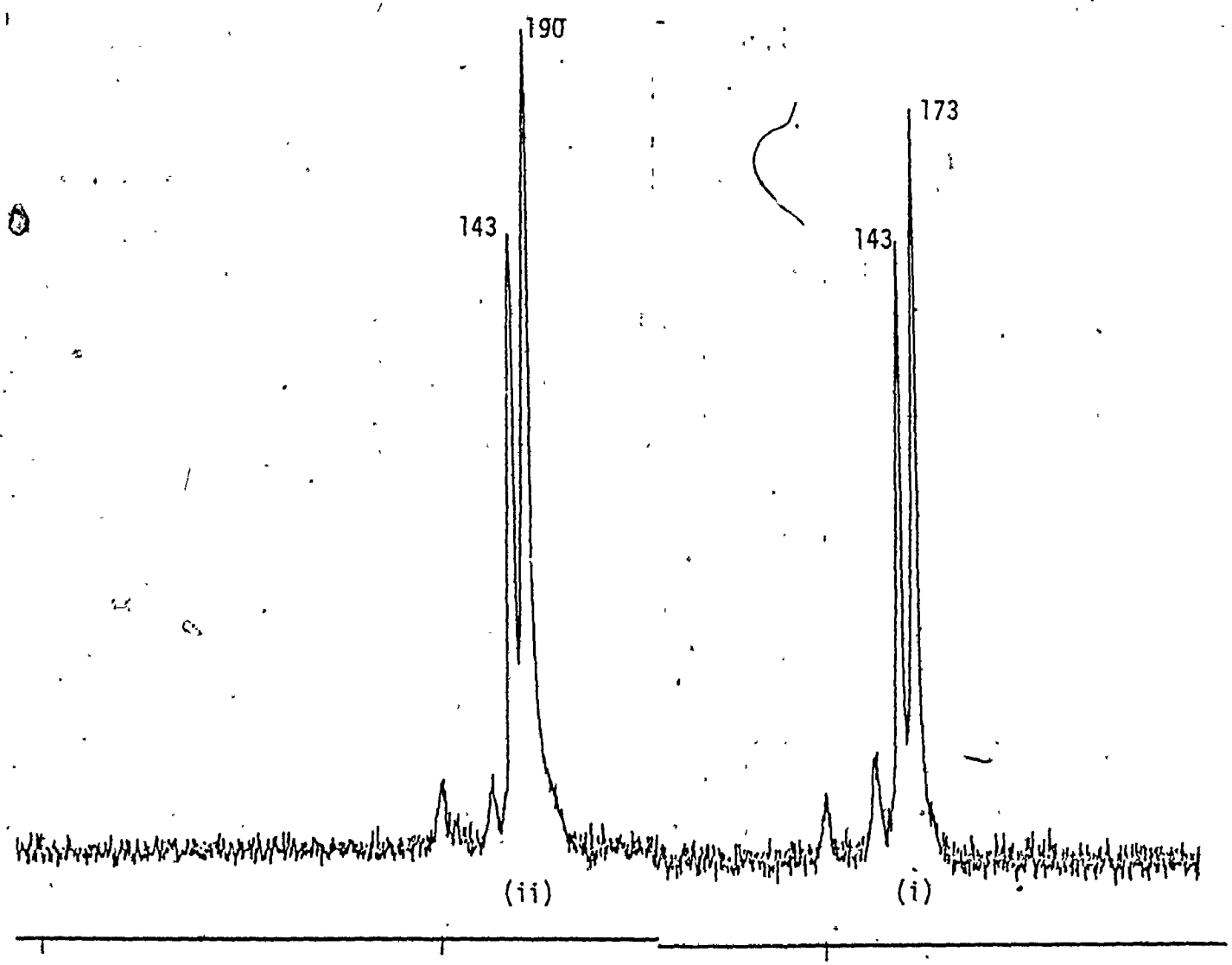


Fig. 4:7. Dmr spectra of (i) exo-2-norborneol-d_1 obtained from D^+-catalyzed ring-opening of 4-chloronortricyclane (11b) and (ii) exo-2-norborneol-d_1 obtained from D^+-catalyzed ring opening of 4-bromonortricyclane (11c).

CHAPTER 5

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