CLEAVAGE OF NORTRICYCLENES. γ-ISOTOPE EFFECTS IN HALONORBORNYL BROSYLATES

ELECTROPHILIC CLEAVAGE OF NORTRICYCLENES.

γ-HYDROGEN DEUTERIUM ISOTOPE EFFECTS IN HALONORBORNYL BROSYLATES.

By

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ABSTRACT

Mechanistic investigations pertaining to the electrophilic cleavages (acetic acid containing sulphuric acid) of the cyclopropyl group in 3-chloronortricyclene and 2-methyl-3-chloronortricyclene have been undertaken. For both compounds, the cyclopropyl bond which is furthest removed from halogen is preferentially cleaved. For 3-chloronortricyclene, studies using deuterated acid have established that for at least 70% of the products, the cyclopropyl carbon atom undergoing electrophilic attack experiences predominant retention of configuration (retention:inversion > 14:1). Furthermore, almost exclusive inversion of configuration (inversion:retention ≈ 50:1) was observed at the site of nucleophilic attack. Similarly, for cleavage of 2-methyl-3-chloronortricyclene in deuterated acid, rupture of the cyclopropyl bond furthest removed from halogen occurs with predominant retention of configuration at the site of electrophilic attack and accounts for most of the reaction pathway. Inversion of configuration at the carbon atom undergoing nucleophilic attack was observed.

These results suggest that fission of the cyclopropyl moiety in these systems occurs *via* initial edge protonation.

Syntheses of previously unknown 7-chloro-2-norbornyl brosylates-6-*d* listed below have been carried out. It is suggested that the spectrophotometrically determined γ-hydrogen deuterium isotope effects for

ethanolyses of

(1) *anti*-7-chloro-*exo*-2-norbornyl brosylate-*endo*-6-*d* (1.11 ± 0.01),

(2) *anti*-7-chloro-*exo*-2-norbornyl brosylate-*exo*,*exo*-5,6-d_2 (1.12 ± 0.01),

(3) *syn*-7-chloro-*exo*-2-norbornyl brosylate-*endo*-6-*d* (1.11 ± 0.01),

(4) *syn*-7-chloro-*exo*-2-norbornyl brosylate-*exo*,*exo*-5,6-d_2 (1.11 ± 0.01) and

(5) *anti*-7-chloro-*endo*-2-norbornyl brosylate-*endo*-6-*d* (1.00 ± 0.01)

arise by homohyperconjugative interactions between the bonds at C-6 and the developing *p* orbital at C-2. These results are not consistent with the hypothesis that the γ-effects for solvolyses of *exo*-2-norbornyl brosylate-6-*d* arise by delocalization of the C-1 C-6 bond in the transition state.

From these studies, it was shown that during solvolyses of 7-chloro-*exo*-2-norbornyl brosylates-6-*d*, formation of 3-chloronortricyclene proceeded preferentially from a semi-U arrangement.

ACKNOWLEDGEMENTS

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TABLE OF CONTENTS

		Page
Chapter 1:	INTRODUCTION	1
	A. Cyclopropanes	2
	B. Cleavage of cyclopropanes with electrophiles	6
	C. Effect of substituents on the cleavage of cyclopropanes	18
	D. Mechanisms	20
	E. Kinetic hydrogen deuterium isotope effects	27
	F. Isotope effects in bicyclo{2.2.1}heptanes	32
Chapter 2:	RESULTS	43
	Electrophilic cleavage of nortricyclenes	46
	A. 3-Chloronortricyclene	46
	B. 2-Methyl-3-chloronortricyclene	65
	γ-Hydrogen deuterium isotope effects in bicyclo{2.2.1} heptanes	85
	A. Syntheses	85
	B. Isotope effects for solvolyses of 7-chloro-2-norbornyl brosylates-6-*d*	98
	C. Product identification and product ratios	102
	D. Deuterium losses in the formation of 3-chloronortricyclene	103
Chapter 3:	DISCUSSION OF RESULTS	118
	A. Electrophilic cleavage of nortricyclenes	119
	1) 3-Chloronortricyclene	119
	2) 2-Methyl-3-chloronortricyclene	143
	B. γ-Hydrogen deuterium isotope effects in bicyclo{2.2.1} heptanes	154
Chapter 4:	SUMMARY	184
Chapter 5:	EXPERIMENTAL	187
	General	188
	A. 3-Chloronortricyclene	191
	1) Synthesis	191
	2) Cleavage in non-deuterated acid	191

3) a) *Anti*- and *syn*-7-chloro-*exo*-2-norbornanol (58- and 59-OH)..... 195
b) *Anti*-7-chloro-*exo*-2-norbornyl acetate (58-OAc)..... 196
c) *Syn*-7-chloro-*exo*-2-norbornyl acetate (59-OAc)..... 196
d) *Exo*-3-chloro-2-norbornanone (73)..... 197
e) *Endo*-3-chloro-2-norbornanone (74)..... 197
f) *Exo*-5-chloro-2-norbornanone (65)..... 197
g) *Endo*-5-chloro-2-norbornanone (66)..... 198
h) *Exo*- and *endo*-3-chloro-*exo*-2-norbornyl acetates (71- and 72-OAc)..... 200
j) *Endo*-5-chloro-*exo*-2-norbornyl acetate (61-OAc)..... 201

4) Stability of various chloro acetates to the reaction conditions used for the electrophilic cleavage of 3-chloronortricyclene..... 202

5) Cleavage in deuterated acid..... 202

6) Control experiments to check for deuterium loss. 206

B. 2-Methyl-3-chloronortricyclene..... 207
1) Synthesis..... 207
2) Cleavage in non-deuterated acid..... 209
3) 1-Methyl-*exo*-2-norbornanol..... 214
4) Cleavage in deuterated acid..... 215

C. The preparation of non-deuterated and deuterated chloro alcohols and chloro brosylates for KIE studies..... 218

1) a) *Syn*-7-chloro-*exo*-2-norbornanol (59-OH)..... 219
b) *Syn*-7-chloro-*exo*-2-norbornyl brosylate (59-OBs)..... 219
c) *Syn*-7-chloro-*exo*-2-norbornanol-*endo*-6-*d* (59-OH-*endo*-6-*d*)..... 220
d) *Syn*-7-chloro-*exo*-2-norbornyl brosylate-*endo*-6-*d* (59-OBs-*endo*-6-*d*)..... 220
e) *Syn*-7-chloro-*exo*-2-norbornanol-*exo*,*exo*-5,6-d_2 (59-OH-*exo*,*exo*-5,6-d_2)..... 220
f) *Syn*-7-chloro-*exo*-2-norbornyl brosylate-*exo*, *exo*-5,6-d_2 (59-OBs-*exo*,*exo*-5,6-d_2)..... 224
2) a) *Anti*-7-chloro-*exo*-2-norbornanol (58-OH)..... 224
b) *Anti*-7-chloro-*exo*-2-norbornyl brosylate (58-OBs)..... 227
c) *Anti*-7-chloro-*exo*-2-norbornanol-*endo*-6-*d* (58-OH-*endo*-6-*d*)..... 227

d) *Anti*-7-chloro-*exo*-2-norbornyl brosylate-*endo*-6-*d* (58-OBs-*endo*-6-*d*)..... 228
e) *Anti*-7-chloro-*exo*-2-norbornanol-*exo*,*exo*-5,6-d_2 (58-OH-*exo*,*exo*-5,6-d_2)..... 228
f) *Anti*-7-chloro-*exo*-2-norbornyl brosylate-*exo*, *exo*-5,6-d_2 (58-OBs-*exo*,*exo*-5,6-d_2)..... 230
g) *Anti*-7-chloro-*exo*-2-norbornanol-*exo*-3-*d* (58-OH-*exo*-3-*d*)..... 230
h) *Anti*-7-chloro-*exo*-2-norbornyl brosylate-*exo*-3-*d* (58-OBs-*exo*-3-*d*)..... 232
3) a) *Anti*-7-chloro-*endo*-2-norbornanol (84-OH)..... 232
b) *Anti*-7-chloro-*endo*-2-norbornyl brosylate (84-OBs)... 233
c) *Anti*-7-chloro-*endo*-2-norbornanol-*endo*-6-*d* (84-OH-*endo*-6-*d*)..... 233
d) *Anti*-7-chloro-*endo*-2-norbornyl brosylate-*endo*-6-*d* (84-OBs-*endo*-6-*d*)..... 234
4) 1-Methyl-*exo*-2-norbornanol-*exo*,*exo*-5,6-d_2 (80-OH-*exo*,*exo*-5,6-d_2)..... 234

D. Kinetics..... 235
1) Solvent..... 235
2) General procedure for kinetic runs..... 235
3) Product analysis..... 238

Chapter 6: APPENDICES..... 244

A. Deuterium assay by mass spectrometry..... 245
B. Nmr spectra of selected norbornyl compounds..... 249
C. Kinetics..... 263
D. Kinetic data..... 266
E. Computer programs for analysis of kinetic data..... 275
F. Steady state treatment of the solvolytic ion-pair scheme.... 283

Chapter 7: REFERENCES..... 286

LIST OF TABLES

		Page
1:1	Summary of the stereochemistry of cyclopropyl ring opening with mercuric acetates in methanol	17
1:2	Deuterated compounds for Table 1:3	34
1:3	Hydrogen deuterium isotope effects in solvolysis of *exo*- and *endo*-2-norbornyl compounds	35
2:1	Stability of chloro acetates to the reaction conditions used for electrophilic cleavage of 3-chloronortricyclene (24)	52
2:2	Mass spectrometric deuterium assays on the deuterated chloro ketones 63- to 66-*d*	54
2:3	Distribution of deuterium in the products from electrophilic (CD_3CO_2D,D_2SO_4) cleavage of 3-chloronortricyclene (24)	64
2:4	Distribution of deuterium in the products from electrophilic (CD_3CO_2D,D_2SO_4) cleavage of 2-methyl-3-chloronortricyclene (25)	84
2:5	Extent of deuteration of chloro brosylates	100
2:6	γ-Hydrogen deuterium isotope effects for the solvolysis of 7-chloro-*exo*-2-norbornyl brosylates-6-*d* in 80:20 ethanol-water	101
2:7	β-Hydrogen deuterium isotope effect	102
2:8	Product ratios from solvolyses of 7-chloro-2-norbornyl brosylates	104
2:9	Deuterium losses in the formation of 3-chloronortricyclene (24) from solvolyses of 7-chloro-2-norbornyl brosylates-6-*d*	105
3:1	Conditions required for the cleavage of various nortricyclenes	121

CHAPTER 1

INTRODUCTION

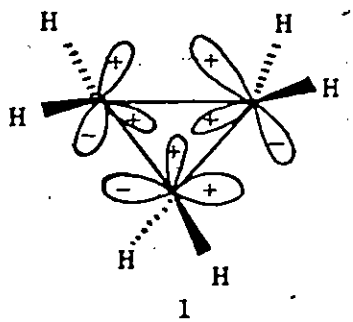
A. Cyclopropanes

Interest in the chemistry of three-membered ring molecules dates back to the nineteenth century (1877) when Freund synthesized "trimethylene" (cyclopropane) by treatment of bromocyclopropane with zinc dust in aqueous alcohol.[1] Eight years later, Baeyer noted that cleavage of the three-membered ring of cyclopropane with hydrobromic acid was easy whereas cleavage of cyclobutane or cyclopentane, under similar conditions, was difficult.[2] Gustavson observed that cyclopropane was easily absorbed at room temperature by aqueous sulphuric acid to produce propyl alcohol and propyl hydrogen sulphate.[3]

Cyclopropane has a symmetrical D_{3h} structure with the three carbon atoms at the vertices of an equilateral triangle. Experimental and theoretical studies have established that the carbon-carbon bond lengths (experimental 1.51 A^{o}, theoretical 1.50 A^{o}) are shorter than those in acyclic molecules (1.54 A^{o}) and that the hydrogen-carbon-hydrogen bond angle (experimental 114°, theoretical 115°) is greater than the 109° tetrahedral bond angle.[4-6] Baeyer[2] attributed the greater reactivity of cyclopropane relative to other cycloalkanes to increased strain (27.2 kcal/mol[7]) in the former. Compression of the carbon-carbon-carbon bond angle from the normal tetrahedral angle (109°) to an angle of 60° accounts for this phenomenon. 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 coaxial with the line between the nuclei. The actual structure of cyclopropane is likely intermediate between these two extremes and it is probably best described as a network of "bent bonds".

A description of cyclopropane in terms of *simple* localized hybrid orbitals can assume one of two forms. The Walsh model of cyclopropane (1) consists of the intra-annular overlap of one of the sp^2 orbitals on each carbon atom and three p orbitals.[8] This description of cyclopropane suggests that there should be extra p character in these bonds - a fact which is supported by an abundance of experimental data such as the carbon-hydrogen bond length and hydrogen-carbon-hydrogen bond angle,[5,6] the carbon-hydrogen stretching frequency[9] and the carbon-13-hydrogen spin-spin coupling constant (32% s character).[10] 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).[7,11] Bernett[7] has shown that the Walsh and bent-bond models are two different descriptions of the same total wave function. Since cyclopropyl bonds have considerable sp^2 character, they can provide a π cloud for interaction with electrophiles.



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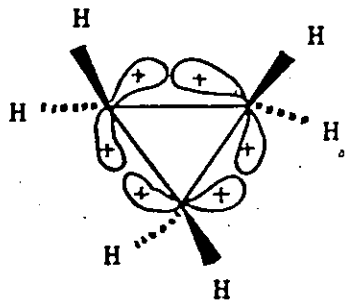

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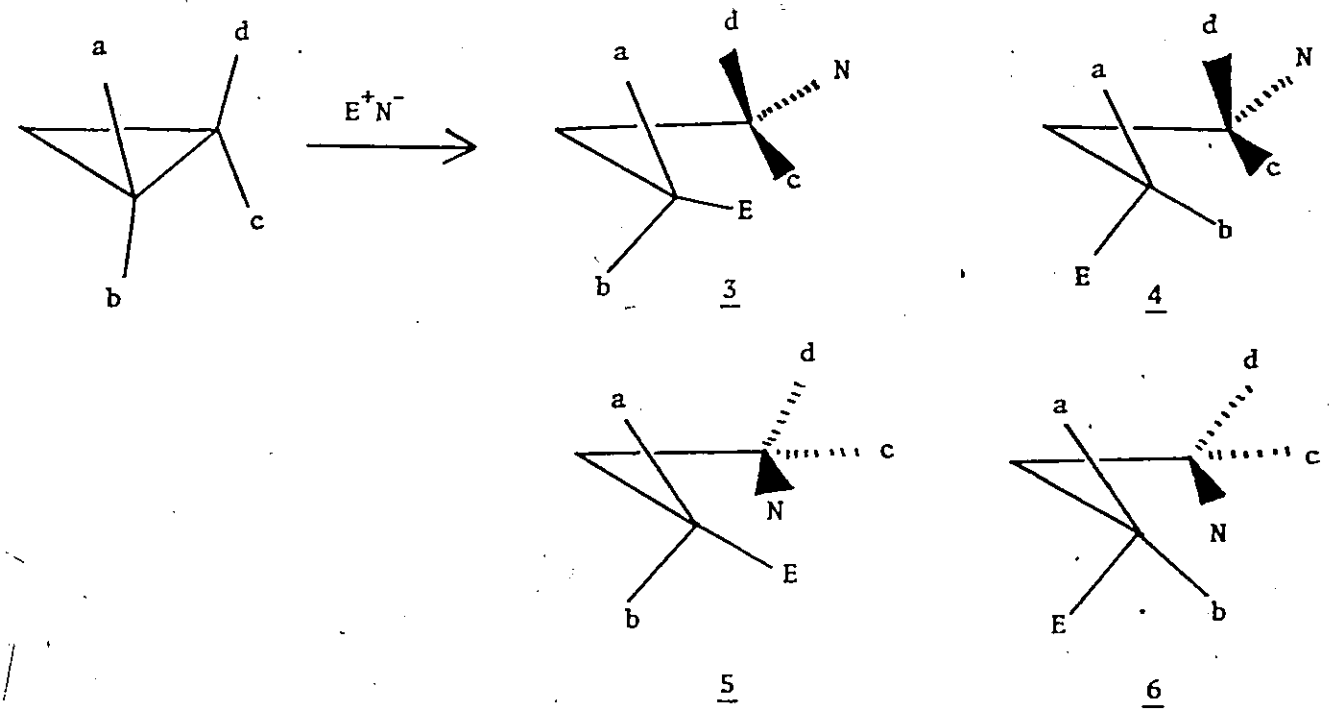
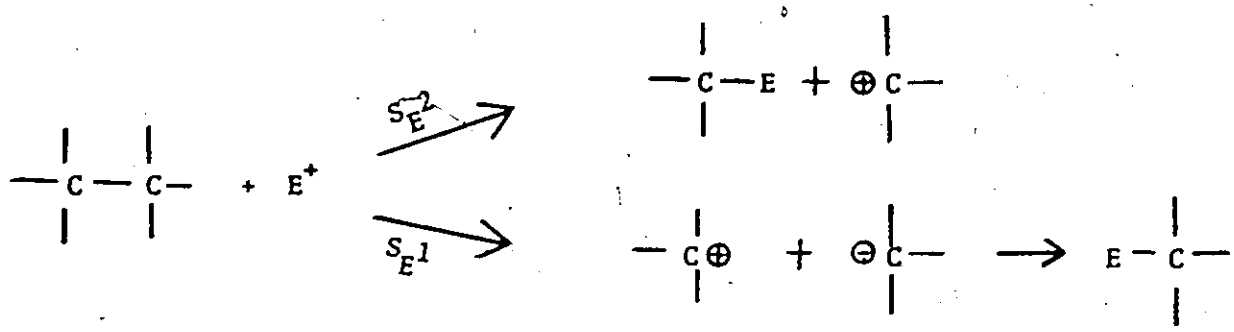
During the past two decades, both organic and theoretical chemists have expended considerable time investigating the interaction of electron deficient species (electrophiles) with cyclopropyl groups. This topic has been the theme of many excellent review articles.[12-17] Cyclopropanes are known to interact with electrophiles both intra- and intermolecularly. The well documented stabilities of cyclopropylcarbinyl,[18] homocyclopropylcarbinyl[19,20] and 1-cyclopropylvinyl[21-23] cations attest the nature of intramolecular cyclopropane-electrophile interactions. Intermolecular interactions of cyclopropanes with electrophiles, which normally lead to subsequent ring opening reactions, have been well-established by experimental observations (*vide infra*) although a general mechanistic pattern has not emerged.

Stereochemistry and mechanism occupy 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 cleaves the bond which will yield the more stable carbonium ion (Markownikov's Rule), although exceptions to this rule have been found.[24-26] The stereochemical outcome of attack by electrophiles can range from complete retention of configuration (3 or 5) to complete inversion of configuration (4 or 6) 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 (5 or 6) or inversion (3 or 4) of configuration at the carbon atom undergoing nucleophilic attack, as well as a mixture resulting from both retention and inversion.



In the Hughes-Ingold terminology, the cleavage of the carbon-carbon single bond of cyclopropanes represents potential bimolecular electrophilic substitution (S_E2). In unimolecular electrophilic substitution (S_E1), cleavage of the carbon-carbon bond precedes the formation of the carbon-electrophile bond.[27]



B. Cleavage of Cyclopropanes with Electrophiles

1) Cleavage with Acid

i) Stereochemistry of the Protonic Attack

Extensive investigations have established that the stereochemistry of protonic (electrophilic) transfer occupies a spectrum which ranges from complete inversion to complete retention of configuration at the carbon atom undergoing electrophilic attack.* Thus the problems associated with mechanistic interpretation can be appreciated. In fact Cristol[33] has remarked ". . . it is clear that inversion or retention of configuration by electrophile and by nucleophile may attend electrophilic addition to cyclopropanes, and that no single mechanism can accommodate these data". However, on the basis of experimental observations, it appears that the preferred stereochemical outcome for attack by a proton on cyclopropanes is retention of configuration at carbon.

For example, De Puy has found that in the acid-catalyzed cleavage of optically active *cis*-2-phenyl-1-methylcyclopropanol (7) which produced

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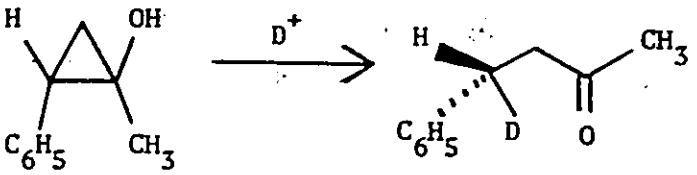
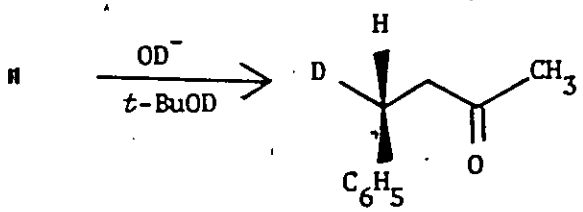
* For brevity, electrophilic inversion will refer to inversion of configuration at the cyclopropyl carbon atom which undergoes electrophilic attack. Electrophilic retention, nucleophilic inversion and nucleophilic retention will also be used for brevity.

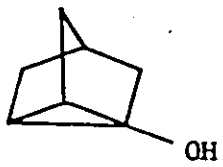
a 60:40 mixture of 4-phenyl-2-butanone-*d* (8) and 3-phenyl-2-butanone-*d* (9), the breaking of the carbon-carbon bond which led to 8 proceeded with retention of configuration.[28,29]



7 8 9



In contrast, the S_E1 process gave inversion of configuration for the formation of deuterated 4-phenyl-2-butanone. Similar work by Nickon on 1-hydroxy-and 1-acetoxynortricyclene (10 and 11) has revealed that the S_E2 reaction (deuterated acidic medium) occurs with electrophilic retention to produce 2-norbornanone-*endo*-6-*d* (12-*endo*-6-*d*) whereas the S_E1 reaction (deuterated basic medium) occurs with electrophilic inversion to yield 12-*exo*-6-*d*.[30,31]



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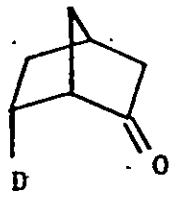
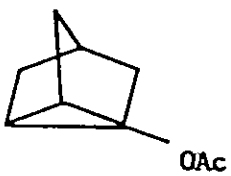


12-*endo*-6-*d*



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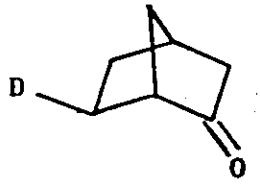
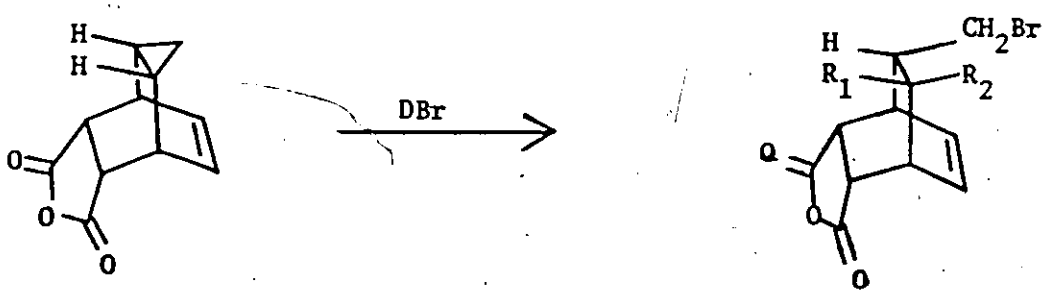


12-*exo*-6-*d*

Addition of deuterium bromide to the cyclopropyl group of compound 13 gave the product 14a, from *anti*-Markownikov addition in which the stereochemistry of attachment of the deuterium was retention.[32] To explain the direction of addition, it was suggested that the hydrogens alpha to the anhydride carbonyls prevented any solvent-nucleophile approach towards the potential secondary carbonium ion center, however the workers later attributed the *anti*-Markownikov addition to the



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14 a R_1 = H, R_2 = D
b R_1 = D, R_2 = H

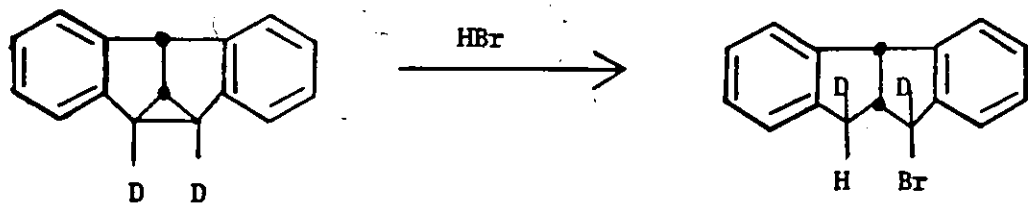
destabilizing inductive effect of the anhydride.[50] Other relevant examples wherein retention by electrophile appears to be the preferred stereochemical course are the following:

1) reaction of dibenzotricyclo{3.3.0.$0^{2,8}$}octadiene-d_2 (15-d_2) with hydrogen bromide[33]

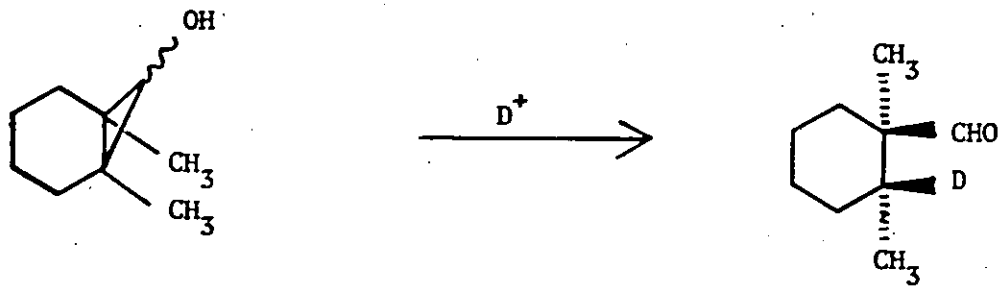
2) reaction of *endo*- and *exo*-7-hydroxy-1,6-dimethylbicyclo{4.1.0} heptane (16) with acid[34]

and

3) reaction of 1,2,2-trimethylbicyclo[1.1.0]butane (17) with acetic acid-O-*d*.[35]



15-d_2



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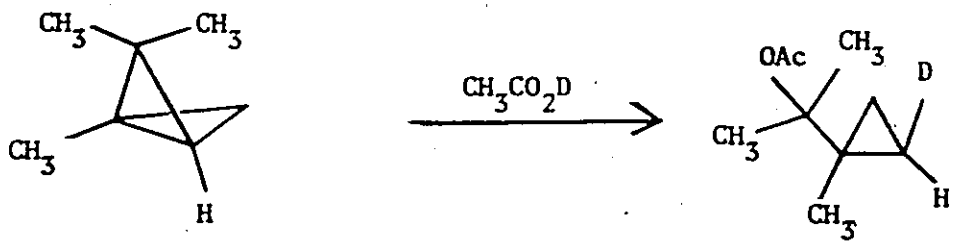

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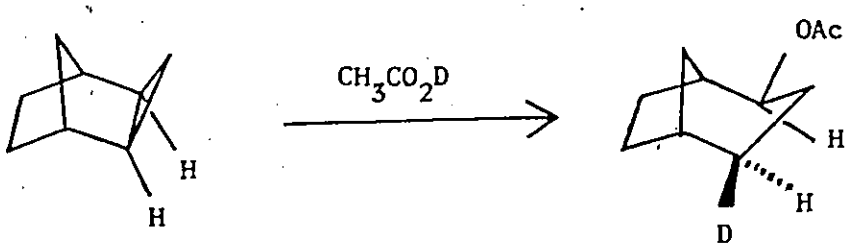
Electrophilic cleavage of the internal cyclopropyl bond of *exo*-tricyclo[3.2.1.$0^{2,4}$]octane (18) was found to involve electrophilic inversion and nucleophilic inversion.[36,37] Protonation of this bond in 18 with retention of configuration is subject to severe steric

hindrance. Recently, Hogeveen has observed electrophilic inversion in the



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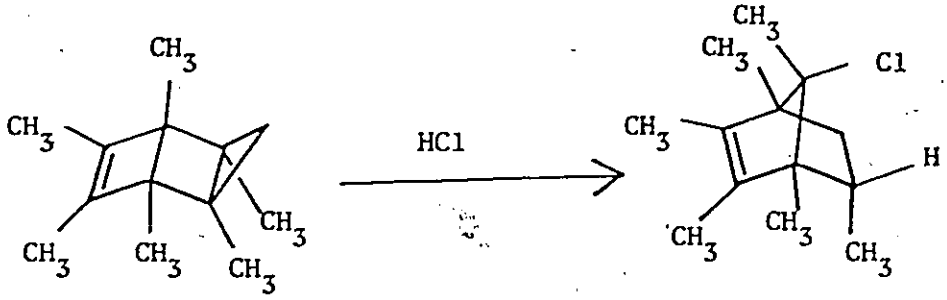

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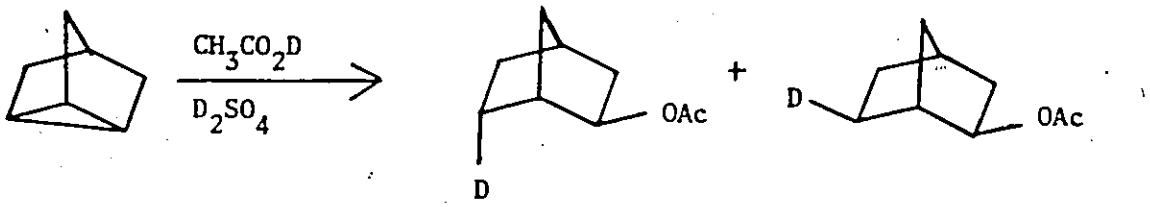
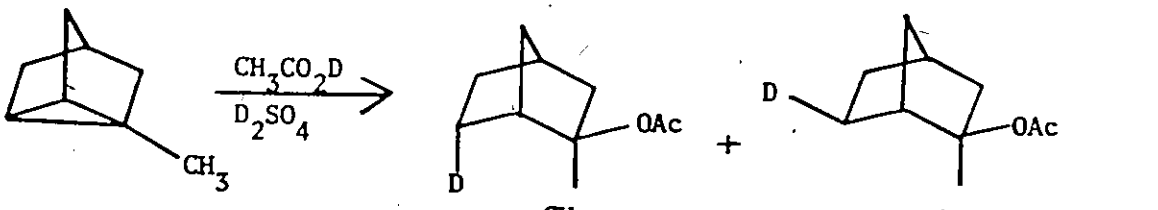
cleavage of 1,2,3,4,5,6-hexamethyl-*exo*-tricyclo[4.1.0.$0^{2,5}$]hept-3-ene (19)[38] and Warnet and Wheeler have also observed electrophilic inversion in cyclopropyl ring cleavage.[39]

The remaining possibility, a mixture of inversion and retention, has been reported for nortricyclene compounds. A 50:50 mixture of electrophilic inversion and retention along with predominant nucleophilic inversion was observed by Nickon and Hammons in the cleavage of tricyclo {2.2.1.$0^{2.6}$} heptane (nortricyclene, 20) by deuterated acid.[40] Mass spectral analyses of the 2-norbornanone-*d* derived from 21-OAc-*exo*-

6-*d* and 21-OAc-*endo*-6-*d* revealed less than 3% multiple deuteration indicating that the electrophile (D^+) entered the molecule during ring opening. If the deuterium entered the molecule before or after ring opening, this would provide a route for eventual multiple deuteration. Hammons and co-workers studied the cleavage of the cyclopropyl group of 1-methylnortricyclene (22) and found a 62:38 mixture of products resulting from electrophilic retention and electrophilic inversion (*i.e.* 23-OAc-*endo*-6-*d* and 23-OAc-*exo*-6-*d*) respectively, along with predominant nucleophilic inversion.[41] The formation of 23-OAc-*exo*- and -*endo*-6-*d* was accompanied by the incorporation of deuterium into



20 21-OAc-*endo*-6-*d* 21-OAc-*exo*-6-*d*

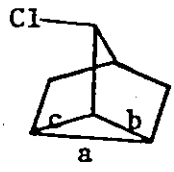


22 23-OAc-*endo*-6-*d* 23-OAc-*exo*-6-*d*

the methyl substituent *via* deprotonation-deuteration of the tertiary 2-methylnorbornyl cation. Apparently, the cleavage of 22 with deuterated

acid is not a suitable route for the incorporation of deuterium stereospecifically at C-6 into 2-methyl-2-norbornyl derivatives.

In view of the threefold axis of symmetry in 20 and the known propensity to rearrangements in bicyclic cations, the 50:50 mixture of electrophilic inversion and retention might not reflect the true stereochemistry of the initial carbon-carbon fission in 20. Introduction of a substituent (chlorine) on a suitable carbon atom of the nortricyclene skeleton destroys the threefold axis of symmetry, creates three chemically different cyclopropyl bonds, allows a means for determining the stereochemistry of the initial deuteration step, acts as a label which allows the detection of hydride (deuteride) shifts and possibly renders alkyl shifts unfavourable in the cation. Therefore, it appeared desirable to examine, in detail, the cyclopropyl bond cleavage of 3-chloronortricyclene (24) with the aim of preparing specifically γ-deuterated 7-chloro-2-norbornyl derivatives. To determine



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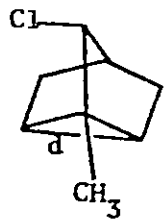


25

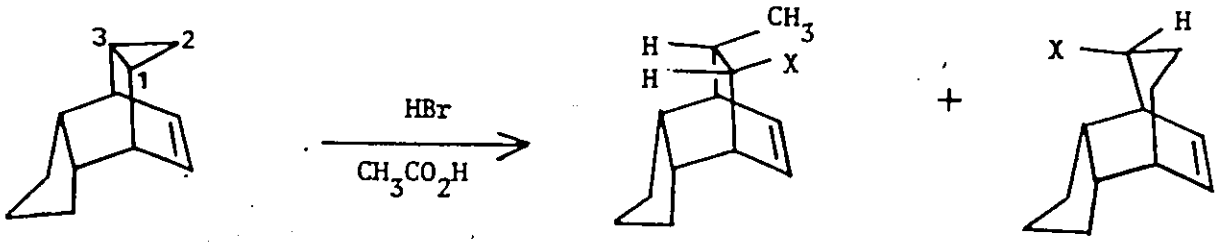
the effect of a methyl substituent directly attached to the cyclopropyl ring on the direction and stereochemistry of cleavage, 2-methyl-3-

chloronortricyclene (25) was used as a model. Once again, our goals were directed towards the synthesis of specifically γ-deuterated 1-methyl-2-norbornyl derivatives *ie* stereospecific cleavage of bond d in 25.

Although the chemical literature contains many other reports of the stereochemical results obtained from cleavage of cyclopropyl groups with electrophiles,[42-49] the extension of conclusions from one system to another, for predictive purposes, is a dangerous art.

ii) Stereochemistry of the Nucleophilic Attack

Present evidence indicates that nucleophilic inversion is the preferred mode of attack with few cases of nucleophilic retention having been observed.[33,50] Ion-pair collapse and steric hindrance have



26 27 28

been proposed as origins of the nucleophilic retention.[33]

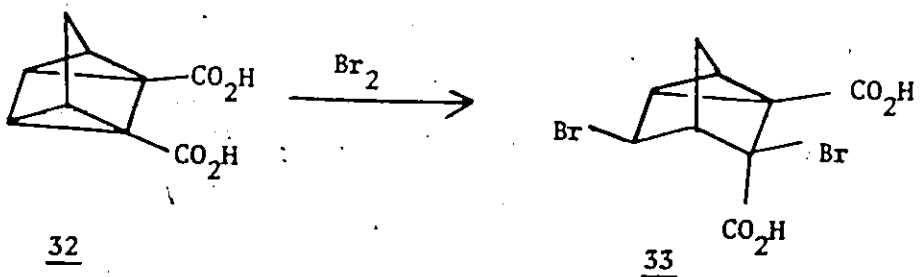
2) Cleavage with Electrophilic Halogen

Molecular bromine, in the presence of a Lewis acid ($FeBr_3$, $AlCl_3$ or $AlBr_3$), adds to cyclopropane (29) to yield a mixture of 1,1-dibromopropane, 1,2-dibromopropane and 1,3-dibromopropane,

probably a result of equilibration between intermediate monobromocyclopropanes ($C_3H_6Br^+$).[51] It was noted that under similar conditions (but at lower temperatures), chlorination of cyclopropane gave only 1,3-dichloropropane. The workers did not elaborate further on the

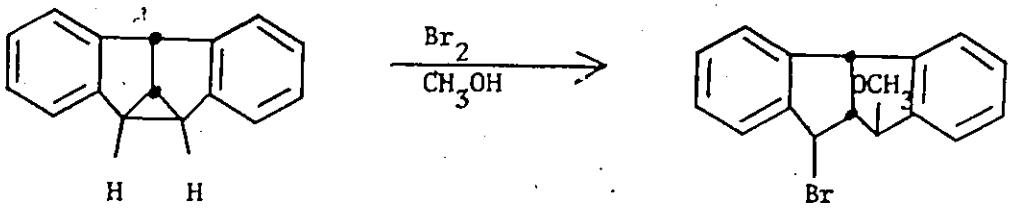
29 30 31

structures of 30 and 31 stating that there was little basis for selection between corner and edge protonated cyclopropanes.[51] Cleavage of the cyclopropyl group of tetracyclo{3.2.0.$0^{2,7}$.$0^{4,6}$}heptane-1,5-dicarboxylic acid (32) with electrophilic bromine gave the dibromo diacid 33, clearly a result of electrophilic inversion and nucleophilic inversion.[52]



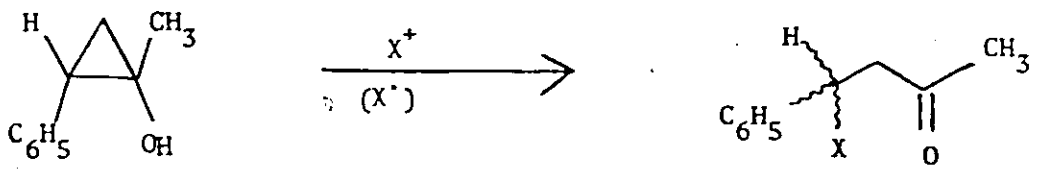
32 33

Cristol and co-workers have reported that for the cleavage of the three-membered ring of dibenzotricyclo{3.3.0.$0^{2,8}$}octadiene (15) with bromine in methanol, the bromo methyl ether (34) was formed by electrophilic retention and nucleophilic inversion.[33]



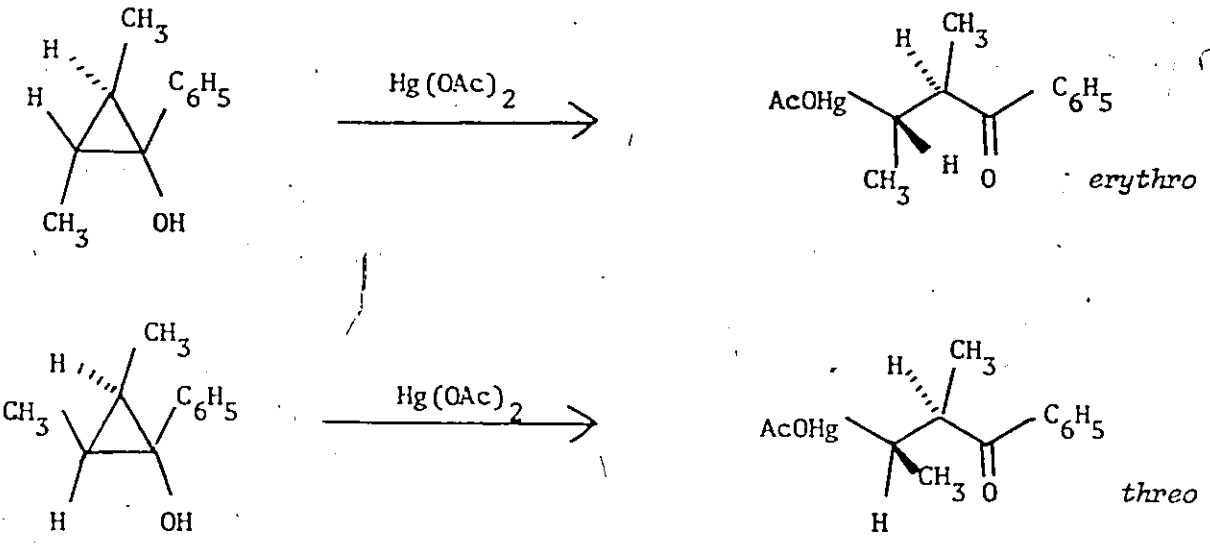
15 34

Halogenation of cyclopropanols has been extensively investigated by De Puy. Using cyclopropanols which were suitably labelled with methyl and phenyl substituents, he found that for addition of electrophilic bromine (generated from n-bromosuccinimide, *t*-butyl hypobromite or molecular bromine), electrophilic inversion was the general rule. However, for addition of electrophilic chlorine (from *t*-butyl hypochlorite or molecular chlorine) there was not any stereochemical preference.[53] *Cis*, *trans*- and *trans*, *trans*-2,3-dimethyl-1-phenylcyclopropanols reacted stereospecifically with electrophilic bromine to yield bromo ketones which arose by electrophilic inversion, whereas both cyclopropanols reacted with chlorine to give identical 50:50 mixtures arising from electrophilic inversion and retention. Comparison of the direction of ring opening of 1,2,2-trimethylcyclopropanol and *trans*-2-phenyl-1-methylcyclopropanol revealed that halogenating agents are more specific than protons in bond breaking (1,3 and 1,2 bond breaking respectively).[53] However, these results must be considered in light of the known tendency of the above sources of electrophilic halogen to initiate free-radical reactions *i.e.* some of these ring cleavages may not proceed through ionic pathways.



3) Cleavage with Mercury(II) Salts

The behaviour of cyclopropanols towards mercury(II) salts was first investigated by De Puy and De Boer who found that cleavage of 1-phenyl- *cis, trans*-2,3-dimethyl- and 1-phenyl-*trans, trans*-2,3-dimethylcyclopropanol (35 and 36) with mercury(II) acetate proceeded with electrophilic inversion.[54] Using mercury(II) trifluoroacetate



35

36

in methanol, the stereochemistry of formation of the carbon-mercury bond in the product for the cleavage of various cyclopropanes was found to depend upon the substitution pattern (Table 1:1).[55,56] Assuming that the electrophile attacks the least hindered bond with the direction of ring opening being towards the benzylic or oxygenated carbon atom and assuming that a *cis* disubstituted cyclopropyl bond is more accessible than a *trans* disubstituted bond, the results in Table 1:1 (see reference 56 for a complete list) are consistent with the following arguments.

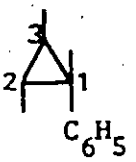
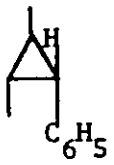
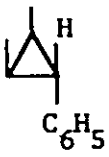
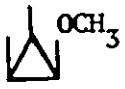
Compound No.	Cyclopropane	Hg^{2+} ret:inv	CH_3OH ret:inv
37		0:100	0:100
38		88:12	10:90
39		28:72	25:75
40		38:62	0:100

Table 1:1 Summary of the Stereochemistry of Cyclopropyl Ring Opening with Mercuric Acetates in Methanol

For compound 37, the electrophile ($^{+}HgOAc$) preferentially attacks through the more accessible disubstituted C-2 C-3 bond with inversion of configuration, whereas predominant attack through the C-1 C-2 bond in 38 leads to electrophilic retention. Electrophilic attack on 40 occurs essentially statistically through all bonds.

From these studies, De Puy concludes that the ultimate stereochemistry of electrophilic attachment is determined by steric effects which determine the bond which is attacked, rather than by a stereochemical demand of the reaction mechanism.

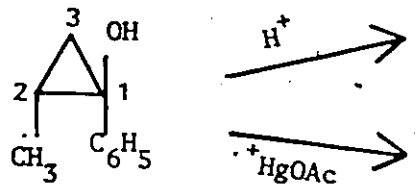
4) Cleavage with Other Electrophiles

Reagents such as diborane[57,58] and palladium chloride[59] in addition to a variety of metallic ions such as silver,[60] thallium[61,62]

and lead[63,64] have been used to rupture cyclopropyl groups. Ring opening has also been achieved by the use of acylium ions.[65,66]

C. Effect of Substituents

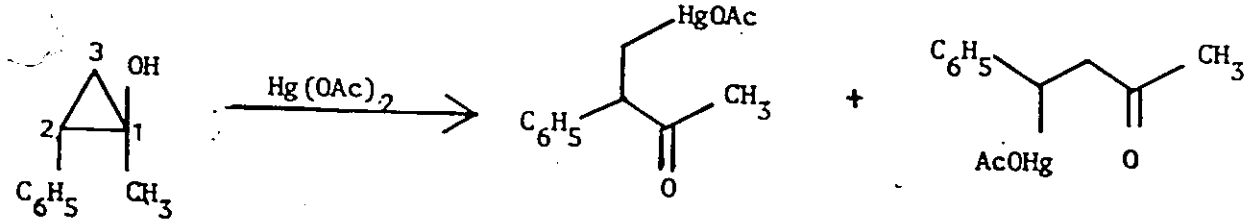
Although protons generally become bonded to the least substituted carbon atom in cyclopropanes, substituents on the ring usually do not have a large effect on this preference. For example, a methyl or phenyl group at C-2 in 41 results in nearly equal amounts of protonic attack at C-2 and C-3.[29,54] In contrast, when mercury(II) salts are used, the electrophile attaches itself predominantly to C-3 indicating that the



	C-2	C-3
H^+	47%	53%
^+HgOAc	1%	99%

41

substitution pattern of the cyclopropane strongly dictates the direction of ring opening when bulky electrophiles are used.[54] However, in certain compounds such as 7, electronic factors may sufficiently offset steric

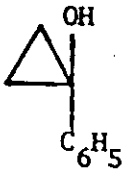


7 75% 25%

factors to decrease the selectivity of attack by ^+HgOAc.

To date, the effect of ring substituents on the rate of cyclopropyl bond cleavage has not been systematically investigated. Cyclopropane reacts with sulphuric acid faster than does ethylene;[67] Peterson has observed that n-butylcyclopropane is more reactive than related alkenes towards acid.[68] In contrast to the hydration of alkenes where introduction of a phenyl substituent can induce a 5000 fold rate acceleration,[69] this effect is not observed when phenyl substituents are placed on cyclopropanes. For example, cyclopropane is about eight times *more reactive* than phenylcyclopropane towards sulphuric acid and from this observation it was concluded that the electron-withdrawing inductive effect of the phenyl group was stabilizing the initial state to a greater extent than the resonance stabilization which the phenyl moiety might impart to the transition state.[70,71]

The relative rate ratios for the reaction of 42, 36 and 43 with mercury(II) acetate were found to be $1:10^{-3}:10^{-6}$ indicating the importance of steric factors in determining the rate of attack by electrophilic mercury.[54]



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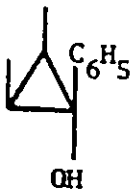

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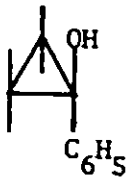


43

D. Mechanism

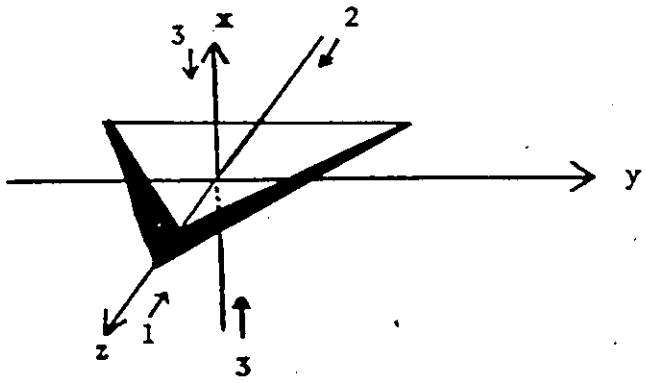
1) Experimental Studies

With reference to mechanism, an electrophile (*eg.* H^+) can approach a molecule of cyclopropane by three possible avenues:

i) corner protonation (approach from the +z axis in the yz plane) - path 1

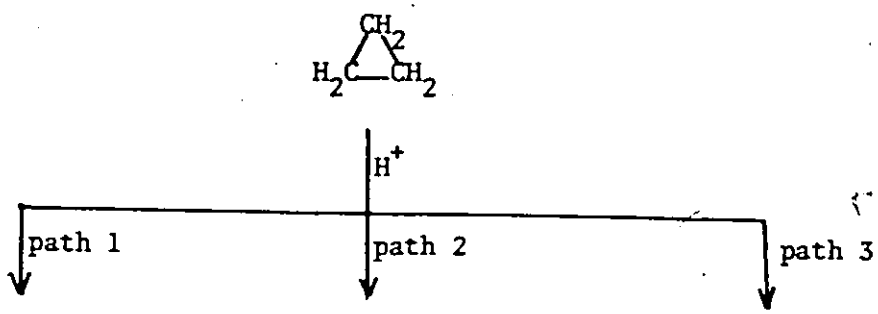
ii) edge protonation (approach from the -z axis in the yz plane) - path 2

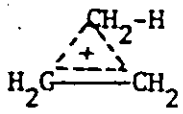
iii) face protonation (approach from the +x or -x axis in the xy plane) - path 3



Corner protonation implies overlap of the electrophile with a minor σ-bond lobe. Edge protonation can be envisaged as the electrophile embedding itself into 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. Similarly, when one speaks 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





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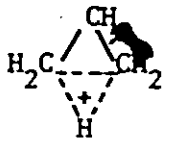
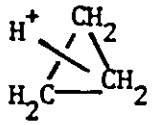
corner protonation



45

edge protonation



46

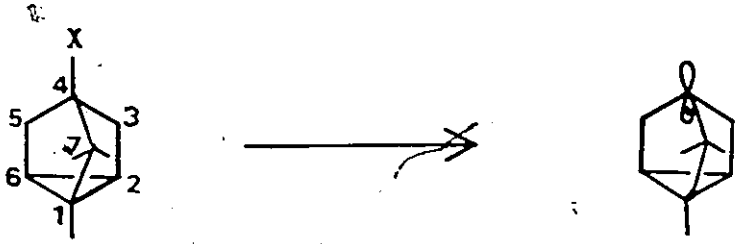
face protonation

differences between 44 and 45, the energy difference between them is probably small, in fact, they could possibly represent two extremes of a common mechanism. Although paths 1 and/or 2 can rationalize most experimental findings which deal with the stereochemistry of cyclopropyl ring cleavage, the reason(s) for selection between them still remains obscure. (*vide infra*).

Roberts initially proposed a face protonated cyclopropane intermediate to account for the observed isotopic rearrangements which accompanied the solvolyses of 2-norbornyl brosylates -2,3-^{14}C.[72,73] Skell and Starer were the next group to invoke face protonated cyclopropane

intermediates to account for the formation of a small amount of cyclopropane in the deamination of 1-propyl compounds,[74] however they later modified this proposal.[75] In 1965, Berson reported experimental evidence which implicated that face protonated species were not important intermediates or transition states during the lactonization of *exo*-3-methyl-5-norbornene-*endo*-2-carboxylic acid-*endo*-3-*d* in sulphuric acid.[76] Other experimental evidence has also discounted the importance of face protonated cyclopropanes.[77-79]

Although ionization of 4-tricyclyl derivatives 47 produces a positively charged *p*-orbital which is situated directly above the face of a cyclopropane ring, experiments have shown that the face of the three-membered



47

ring provides very little stabilization for an incipient carbonium ion. 4-Tricyclyl brosylate undergoes slow ionization at 295° in 70% aqueous dioxane and 4-tricyclyl tosylate ionizes at 25° in 60% aqueous ethanol with a half-life of 4×10^9 years.[80-82] This enormous rate deceleration in ionization of the 4-tricyclyl derivatives was attributed to the compression in the C-C-C bond angles at carbons-3,5 and 7 as well as a flattening at carbon-4 as the transition state is approached. Strain energy calculations indicated that the electron withdrawing inductive effect of the cyclopropyl group was not nearly as important in retarding the ionization as were angle strain influences. In light of the Walsh model[8] for cyclopropane,

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, discussion of mechanisms of electrophile-cyclopropane interactions will be limited to corner and edge protonated species.

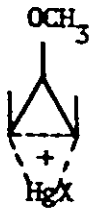
Roberts and Halmann studied the deamination of 1-propylamine-1-^{14}C in 35% perchloric acid and suggested (incorrectly) that in the isolated 1-propanol-^{14}C, the ^{14}C activity was at C-1(91.5%) and C-2(8.5%).[83] To account for these results, they postulated a 1,2 methyl shift *via* a corner protonated ion (also termed methyl-bridged ion). However, subsequent work by Reutov and Shatkina showed that 8.0% of the ^{14}C activity originally present in the 1-propylamine-1-^{14}C had leaked to the C-3 position of the 1-propanol-^{14}C and they proposed a 1,3-hydride shift.[84] This view was supported by the work of Karabatsos and Orzech who found that deamination of 1-propylamine-1,1,2,2-d_4 to 1-propanol-d_4 involved 1,3-hydride shifts (12%) as opposed to successive 1,2-hydride shifts.[85] Since the completion of these pioneering experiments, the study of protonated cyclopropanes generated from aliphatic systems not containing the cyclopropyl group had intensified[86,87] and has been adequately reviewed by Collins[13] and Lee.[14]

Baird and Aboderin reported 21% hydrogen-deuterium exchange when cyclopropane was bubbled through sulphuric acid-d_2.[88] Subsequent work by Baird,[89] Deno[90] and Lee[91,92] on the hydration of cyclopropane in deuterated medium showed that the deuterium distributions could be 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 postulated edge deuteration as the initial step in the opening (with deuterium bromide) of the cyclopropane ring of 13 by reasoning that intervention of a corner protonated species would have led to the partial formation of 14*b*.[32] They also postulated initial edge protonation of the C-1 C-2 bond in 26 followed by collapse *via* nucleophilic retention to yield 27. The minor product 28 was assumed to have arisen by equilibration to a corner protonated species which subsequently captured nucleophile. It was also possible that 28 arose by edge protonation of the C-1 C-3 bond. Alternatively, both 27 and 28 might have been formed by nucleophilic attack on a corner protonated species.[50] However, Cristol has remarked that although the initial attack may be edgewise, the ultimate ring opening might occur after edge to corner isomerization.[33]

De Puy and McGirk favoured a corner mercurated over an edge mercurated cyclopropane intermediate for the reactions of certain cyclopropanes with mercury(II) trifluoroacetate.[55] Although edge mercurated species such as 48 can account for most of the data in Table 1:1, this

type of structure cannot account for the fact that cleavage of 49 yields about twice as much inversion as retention by electrophile (edge mercuration should give rise to predominant electrophilic retention). They concluded



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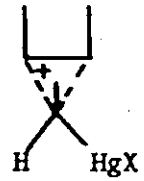
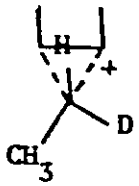


50

that the products arose by nucleophilic attack on a corner mercurated species 50 and that an edge mercurated species could possibly be a transition state.

De Puy has examined the electrophilic (D^+) opening of the two isomeric 1,2,3-trimethylcyclopropanes; he accounted for his data with an unsymmetrical, non-rotating, corner protonated cyclopropane 51 and rejected the symmetrical non-rotating structure 52 as well as the edge protonated



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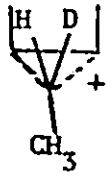

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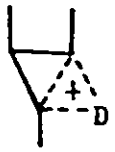
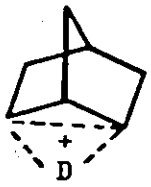


53

structure 53.[93]

For the electrophilic cleavage of nortricyclene (20), Nickon and Hammons suggested that the carbon bridged ion 54-*d* was the principal acceptor of nucleophile and they concluded that product did not arise from ions 55.[40]

54-*d*



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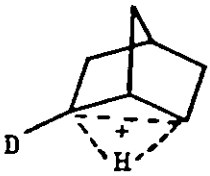

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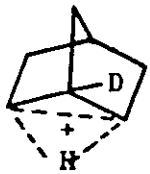


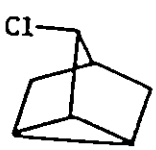
55c

2) Theoretical Studies

Early theoretical studies using extended Hückel theory on protonated cyclopropane ($C_3H_7^+$) implicated that edge protonation was preferred to corner protonation.[94] *Ab initio* calculations have suggested that $C_3H_7^+$ as an edge protonated species is 125 kcal/mol more stable than a face protonated species.[95] Semiempirical molecular orbital calculations by the INDO and modified CNDO methods have also favoured edge protonation over corner or face protonation.[96-98] Recently, NDDO calculations have shown that edge protonated cyclopropane is more stable than the face or corner protonated species (135 and 20 kcal/mol respectively).[99,100]

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 experiment[77-82]), whereas edge protonated $C_3H_7^+$ is less stable than corner protonated $C_3H_7^+$.[101-103] However, a recent theoretical study has implicated that a cation may experience significant stabilization by the face of a cyclopropane ring.[104]

Our interest in the chemistry of cyclopropyl compounds led us to study the acid-catalyzed cleavage of the cyclopropyl groups of 24 and



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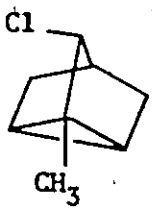

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25 in order to

1) determine the mechanism and stereochemistry of the bond cleavage
2) determine the effect of the methyl substituent in 25 on product distribution, mechanism and stereochemistry of electrophilic cleavage
3) prepare specifically deuterated 7-chloro-2-norbornyl* derivatives -6-*d* from 24 and 1-methyl-2-norbornyl derivatives -6-*d* from 25
4) aid in the understanding of the acid-catalyzed cleavages of nortricyclene (20) and 1-methylnortricyclene (22)

E. Kinetic Hydrogen-Deuterium Isotope Effects

The effect of variation of molecular structure on reaction rate constants and activation parameters is a popular approach to the study of transition state structure and reaction mechanism. Although there are theories which attempt to predict the geometry of transition states from reactant geometry,[105-109] "the theoretical basis for understanding substituent effects does not yet exist".[110] Changes in substitution give rise to different potential energy surfaces even though the mechanism of the reaction could conceivably remain unaltered. A study of substituent effects requires solution of the complex Schrodinger wave equation. Since the initial (1932) spectroscopic observation of heavy hydrogen (deuterium)[111] and the subsequent isolation of heavy water,[112] the use of deuterium for the hydrogen-deuterium isotope effect has been widely used by physical

---

* Bicyclo[2.2.1] heptyl derivatives will be referred to by their trivial names - norbornanes.

organic chemists as a probe for transition state geometry. Eyring and Sherman predicted that hydrogen and deuterium should react at different rates due to the difference in zero-point energy.[113] An experimental kinetic isotope effect was first observed by Washburn and Urey who reported the enrichment of deuterium in the liquid phase in the electrolysis of water.[114] Since then, applications of the kinetic isotope effect to the elucidation of organic reaction mechanisms have been numerous and have been adequately reviewed;[115-131] the following treatment of the theoretical basis for hydrogen-deuterium isotope effects* parallels that given by Saunders.[120]

A fundamental assumption is that the electronic, rotational, vibrational and translational energies of a molecule can be treated separately so that the total molecular energy is a sum of these four individual energies. The electronic energy of any particular arrangement of atoms within a molecule depends only on the Coulombic interaction of the charged particles (nuclei and electrons) with the result that molecules which differ only in isotopic substitution have essentially identical potential energy surfaces. Therefore, isotope effects on reaction rates are not determined by electronic energy differences (there are none) but rather by the differences of nuclear motion such as vibration, rotation and translation. Vibrational motion provides the largest contribution. Differences in rotational and translational energies between isotopically related molecules are usually negligible except in small molecules.

Just as there is quantization of the electronic energy levels of atoms and molecules which dictates that electrons occupy only discrete

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* The theory can also be easily extended to other isotope effects (*eg* ^{12}C and ^{13}C, ^{14}N and ^{15}N, ^{16}O and ^{18}O).

energy levels, there is also quantization of the molecular vibrational energy levels. The energies of these quantized vibrational levels can be derived from solution of the Schrodinger equation for the harmonic oscillator and are given by

$$E = h(m+\tfrac{1}{2})\nu$$

where h is Planck's constant, m is the vibrational quantum number which can assume only the integral values 0,1,2,3. . . and ν is the vibrational frequency. The lowest energy level or the zero-point energy (ZPE) of any bond corresponds to $\frac{1}{2}h\nu$. This is the vibrational energy of the bond at absolute zero, however room temperature is sufficiently close to zero so that most of the bonds (99%) occupy this vibrational energy level. If one considers two isotopically related molecules HA and DA, and assumes that each behaves as a simple harmonic oscillator, then it is possible to calculate their vibrational frequencies ν_{HA} and ν_{DA} from Hooke's Law

$$\nu_{HA} = \frac{1}{2\pi}\sqrt{\frac{k}{\mu_{HA}}}$$

where k is the bond force constant which is independent of isotopic substitution. The reduced mass μ_{HA} is given by

$$\mu_{HA} = \frac{1}{M_H} + \frac{1}{M_A}$$

where M_H and M_A are the masses of H and A, respectively. From these equations it is possible to show that the ZPE of a molecule containing a light isotope is greater than the ZPE of the molecule containing the heavy isotope *ie* $\nu_{HA} > \nu_{DA}$.

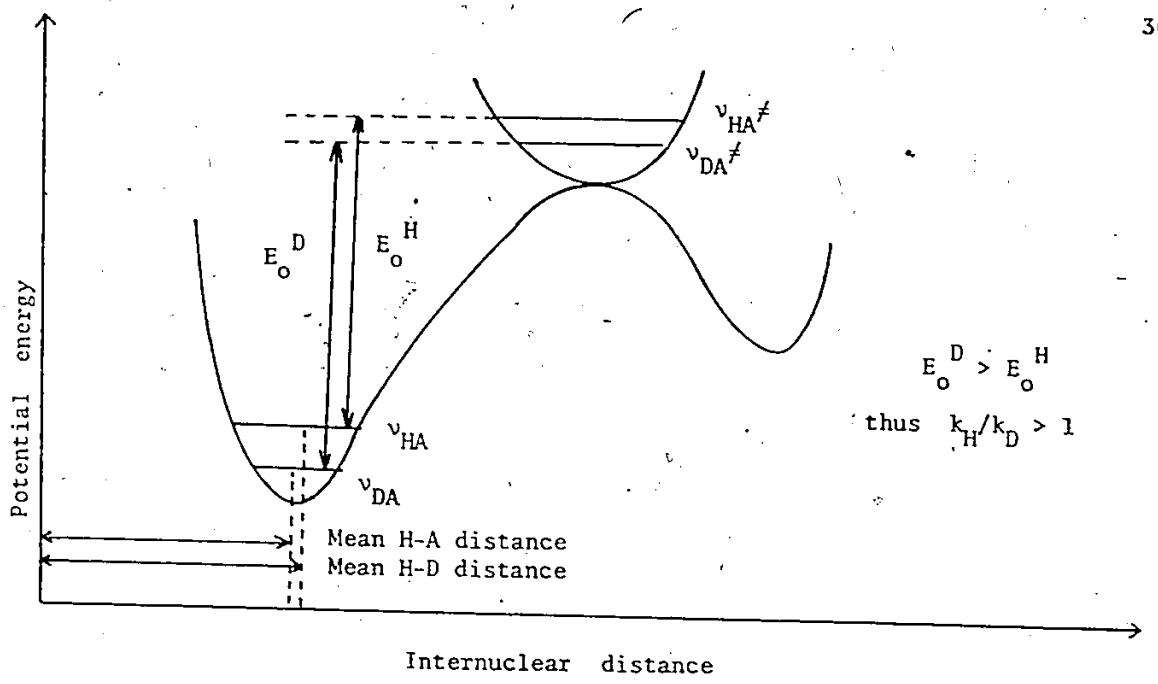

Figure 1:1 Potential Energy Diagram for two isotopically related species (HA and DA). The difference in ZPE between HA and DA in the reactants and the transition state leads to different activation energies which produce a kinetic isotope effect. If $(\nu_{HA}^{\neq} - \nu_{DA}^{\neq}) < (\nu_{HA} - \nu_{DA})$, then $k_H/k_D > 1$ whereas if $(\nu_{HA}^{\neq} - \nu_{DA}^{\neq}) > (\nu_{HA} - \nu_{DA})$, then $k_H/k_D < 1$. Asymmetry of the potential energy curve results in a shorter equilibrium internuclear distance in DA than in HA.

If one considers a reaction wherein the bond to the isotopic atom (H-A or D-A) is cleaved in the transition state in a slow step, then the vibrational energies will vanish as will also the difference in ZPE between the isotopic molecules in the transition state. Since the activation energy for the heavier molecule (see Figure 1:1) is greater than the activation energy for the lighter molecule, the reaction rate of the latter molecule will be greater *ie* $k_H/k_D > 1$. In many reactions the difference in ZPE in the transition state does not disappear completely, however as long as the ZPE difference is smaller in the transition state than in the reactant,

the lighter molecule will still react faster. In the transition state, the difference in ZPE between the labelled and unlabelled molecules decreases with decreasing force constant.* Isotope effects arise principally from changes in vibrational force constants in going from reactant to transition state, in fact, they result from the effects of the rest of the molecule on the vibrational motions of the isotopic atom. Thornton[117] has emphasized that the models of steric[132,133] and inductive[124] isotope effects have vibrational origins.

Mathematical formulation of the equations of isotope effects using the transition state theory of Eyring[134] was first undertaken by Bigeleisen and Mayer[135] and subsequently by other workers.[115,120,129] The maximum hydrogen-deuterium isotope effect at a temperature T is given by

$$k_H/k_D = \exp\{h(\nu_{HA}-\nu_{DA})/2kT\}$$

which near room temperature and in the absence of quantum mechanical tunneling[136-138] is about seven.

Thus, replacement of an atom within a molecule by one of its isotopes represents the smallest molecular perturbation and by this subtle change, the secrets of organic reaction mechanisms have been elegantly exposed in a manner which is presently not feasible by the study of substituent effects. Deuterium is not an "ordinary" substituent.

By definition, a primary isotope effect involves formation or cleavage of a bond to the isotopic atom whereas a secondary isotope effect is one which is not primary.

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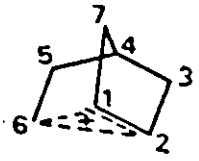
* Westheimer has discussed the isotope effect expected for a three-centered transition state such as in the transfer of hydrogen from one species to another.[119]

F. Isotope Effects in Bicyclo{2.2.1}heptanes

Since the pioneering solvolytic studies by Winstein and Trifan[139-141] on *exo*- and *endo*-2-norbornyl *p*-bromobenzenesulphonates (norbornyl brosylates), there have been numerous kinetic, spectroscopic and theoretical studies aimed at the elucidation of the mechanistic intricacies surrounding the norbornyl system. A large portion of the literature dealing with this molecule has been reviewed.[143-152] Controversy has centered exclusively around the problem of whether the norbornyl cation is best described as non-classical with a highly delocalized, symmetrical electronic structure such as 54 or as classical with the positive charge localized on one carbon atom as in 56. Winstein and his colleagues have advanced the hypothesis that *exo*-2-norbornyl brosylate (21-OBs) ionizes



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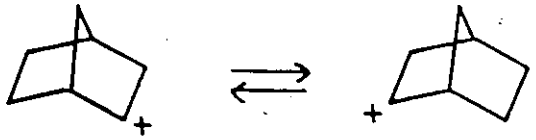


56

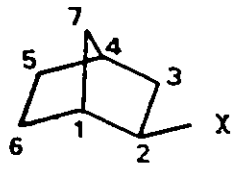
with electronic assistance of the C-1 C-6 σ bond electrons to form the symmetrical norbornonium ion 54, whereas *endo*-2-norbornyl brosylate (57-OBs) ionizes without this type of assistance.[139-143] This has received experimental support by the spectroscopic observation of a σ-bridged 2-norbornyl cation in strongly acidic solutions by Olah and co-workers.[153] However, Brown has argued that both *exo*- and *endo*-2-norbornyl brosylates ionize without anchimeric assistance to a classical ion 56 and that the different rates of ionization can be attributed to steric effects.[149-152]

According to the latter school of thought, the *endo*-epimer undergoes abnormally slow ionization to a set of rapidly equilibrating cations.

Application of the kinetic isotope effect (KIE) to a study of the solvolytic behaviour of norbornyl derivatives has provided a basis for understanding the anomalous character of this system (Table 1:2)[115a,116] The KIE allows an intimate probe into the reaction mechanism which is not possible by a study of substituent effects (*vide supra*).

1) α-Isotope Effects

The rate retardation which is sometimes observed in solvolytic reactions when a hydrogen atom on the carbon bearing the leaving group is replaced by a deuterium atom has been attributed to the decrease in bending force constant from a tetrahedral carbon-hydrogen bending vibration to the lower out-of-plane carbon-hydrogen bending vibration in the transition state leading to the carbonium ion.[165,166] Although a maximum α-KIE of 1.2 has been calculated for a reaction involving a free carbonium ion (S_N1),[166] the smaller observed effect (about 15% per deuterium atom) is usually due to the presence of the leaving group in the transition state which hinders the out-of-plane bending of the carbon-hydrogen bond and also to an inductive effect. For bimolecular processes (S_N2), the presence of the nucleophile and the leaving group in the transition state severely restrict the out-of-plane carbon-hydrogen bending causing the α-KIE to become negligible or slightly inverse.



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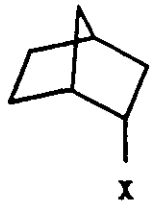

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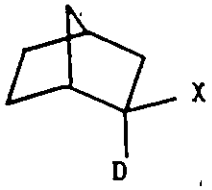
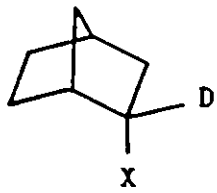
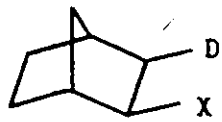


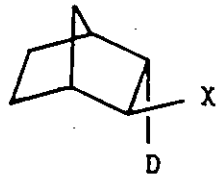
21-2-*d*



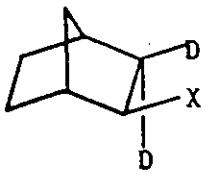
57-2-*d*



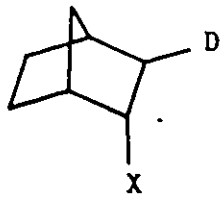
21-*exo*-3-*d*



21-*endo*-3-*d*



21-3,3-d_2



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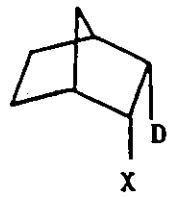

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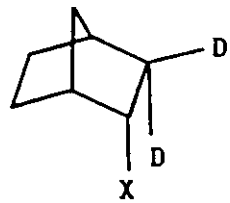
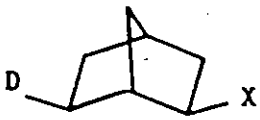
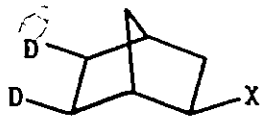


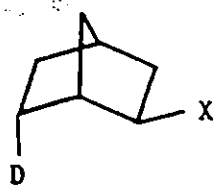
57-3,3-d_2



21-*exo*-6-*d*



21-*exo*,*exo*-5,6-d_2



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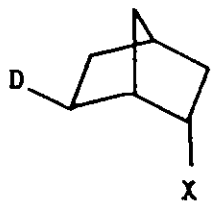
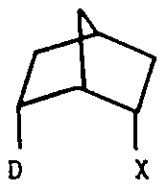
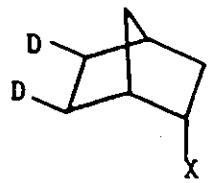


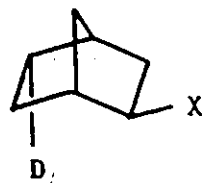
57-*exo*-6-*d*



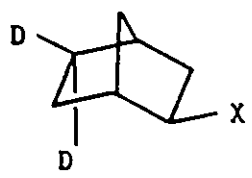
57-*endo*-6-*d*



57-*exo*,*exo*-5,6-d_2



21-*endo*-5-*d*



21-5,5-d_2

Table 1:2 Deuterated compounds for Table 1:3

Table 1:3 Hydrogen Deuterium Isotope Effects in Solvolysis of *exo*- and *endo*-2-Norbornyl Compounds

Compound	X	Solvent	T(°C)	k_H/k_D [a]	Ref
21-2-*d*	OBs	CH_3CO_2H	24.85	1.11	154
	OBs	80%[aq]C_2H_5OH	25	1.125±0.010	156
	OBs	CH_3CO_2H,CH_3CO_2K	25	1.118±0.013	156
57-2-*d*	OBs	CH_3CO_2H	50	1.203	154,155
	OBs	Aq. Dioxane	50.2	1.20	155
	OBs	80%[aq]C_2H_5OH	25	1.193±0.014	156
	OBs	CH_3CO_2H,CH_3CO_2K	25	1.20±0.01	156
	Br	Aq. C_2H_5OH	60.21	1.28	157
21-*exo*-3-*d*	OBs	80% aq.C_2H_5OH	25.0	1.11±0.01	158
	OBs	CH_3CO_2H,CH_3CO_2K	25.0	1.07±0.01	158
21-*endo*-3-*d*	OBs	80% aq. C_2H_5OH	25.0	1.02±0.01	158
	OBs	CH_3CO_2H,CH_3CO_2K	25.0	1.02±0.01	158
21-3,3-d_2	OBs	80% aq.C_2H_5OH	25.0	1.11±0.01[b]	158
	OBs	CH_3CO_2H,CH_3CO_2K	25.0	1.07±0.01[b]	158
	OBs	CH_3CO_2H	44.3	1.014±0.018[b]	159
	Br	Aq. CH_3CO_2H	51.25	1.04	157
57-*exo*-3-*d*	OBs	80% aq.C_2H_5OH	55	1.19±0.01	158
57-*endo*-3-*d*	OBs	80% aq.C_2H_5OH	55	1.12±0.01	158

(continued)

Compound	X	Solvent	T(°C)	k_H/k_D [a]	Ref
57-3,3-d_2	OBs	80% aq.C_2H_5OH	55	1.31±0.01[b]	158
	OBs	CH_3CO_2H	65.0	1.26±0.01[b]	159
	Br	Aq.C_2H_5OH	60.21	1.30±0.01[b]	157
21-*exo*-6-*d*	OBs	CH_3CO_2H,CH_3CO_2K	24.9	1.09±0.03	160
	OBs	80% aq.C_2H_5OH	24.9	1.09±0.01	160
	OBs	CH_3CO_2H,1%$(CH_3CO)_2O$	44.4	1.149±0.016	161
21-*exo*,*exo*-5,6-d_2	OBs	CH_3CO_2H	25.0	1.093±0.049[b]	162
21-*endo*-6-*d*	OBs	CH_3CO_2H,CH_3CO_2K	24.9	1.11±0.01	160
	OBs	80% aq.C_2H_5OH	24.9	1.11±0.01	160
	OBs	CH_3CO_2H,0.7%$(CH_3CO)_2O$	43.3	1.097±0.011	161
57-*exo*-6-*d*	OBs	CH_3CO_2H,CH_3CO_2K	70.1	0.98±0.01	160
	OBs	80% aq.C_2H_5OH	49.1	1.00±0.02	160
	OBs	CH_3CO_2H	65.0	1.021±0.012	161
57-*endo*-6-*d*	OBs	CH_3CO_2H,CH_3CO_2K	70.1	0.99±0.02	160
	OBs	80% aq.C_2H_5OH	49.1	0.97±0.01	160
	OBs	CH_3CO_2H	65.0	0.998±0.012	161
57-*exo*,*exo*-5,6-d_2	OBs	CH_3CO_2H	65.0	1.01±0.02	162
21-*endo*-5-*d*	OBs	CH_3CO_2H,CH_3CO_2K	24.90	1.01±0.01	163,164
21-5,5-d_2	OBs	CH_3CO_2H,CH_3CO_2K	24.90	0.99±0.01[b]	163,164

[a] Per deuterium atom unless otherwise specified

[b] Per two atoms of deuterium

The lower experimental α-KIE (Table 1:3) for solvolysis of *exo*-2-norbornyl brosylate-2-*d*(21-OBs-2-*d*) relative to *endo*-2-norbornyl brosylate-2-*d*(57-OBs-2-*d*),1.12 vs 1.20, was attributed to anchimeric assistance to ionization in 21-OBs-2-*d* by the C-1 C-6 bond (leading to a non-classical ion) which would render S_N2 character to C-2 and decrease the α-KIE.[154,156] Alternatively, the lower α-KIE could have arisen by internal return which scrambles deuterium to C-1. If 21-OBs ionized to a classical ion 56, then deuterium at C-1 would have little effect on the ionization and hence a lower α-KIE would be observed.[154,156] Conceivably, the α-KIE for 57-OBs-2-*d*(k_H/k_D = 1.20)[156] could be abnormally large as is the KIE for ethanolysis of 57-Br-2-*d*(k_H/k_D = 1.28).[157] The effect for 21-OBs-2-*d* is comparable to isotope effects observed in unactivated secondary substrates.[167] Schaefer attributes the large KIE for ethanolysis of 57-Br-2-*d* to a steric interaction between bromine and the C-6 methylene group.[157] However, the observation that the α-KIE for ethanolysis (65% solvolysis of ion pairs, 35% return of ion pairs with C-1 and C-2 equilibration) and acetolysis (22% solvolysis, 78% return) are identical implies that the lower KIE in solvolysis of 21-OBs-2-*d* (relative to 57-OBs-2-*d*) arises from charge delocalization in the transition state and not from the intervention of internal return.[156]

2) β-Isotope Effects

Subsequent to the initial observations of a solvolytic β-KIE,[168,169] it was suggested that hyperconjugation was the source of this effect.[169-172] Carbon-hydrogen hyperconjugation involves the interaction of a *p*-orbital on the carbonium ion with an adjacent

carbon-hydrogen bond. In solvolytic reactions, the magnitude of the β-KIE is dependent on the amount of charge at the carbonium ion center and on the dihedral angle between the *p*-orbital and the β carbon-hydrogen bond.[173] This stereoelectronic requirement for hyperconjugation has been elegantly verified in a rigid bicyclic system by Shiner.[174] β-KIEs for limiting solvolyses usually range from 10 to 20% per deuterium atom.

In the transition state leading to the non-classical norbornyl cation 54, the vacant *p*-orbital at C-2 forms dihedral angles (ϕ) of 180° with H_{3exo} and 60° with H_{3endo} : therefore the C-H_{3exo} bond can provide greater hyperconjugative stabilization to the incipient carbonium ion at C-2 than can the C-H_{3endo} bond. However, in the transition state leading to a classical norbornyl cation 56, the *p*-orbital at C-2 would form similar dihedral angles with both the C-H_{3exo} and C-H_{3endo} bonds (*ca* 30°); therefore each bond should provide equal hyperconjugative stabilization. Thus, ionization of 21-OBs *via* anchimeric assistance to 54 should give a lower β-KIE for 21-OBs-*endo*-3-*d* relative to the KIE for 21-OBs-*exo*-3-*d* due to stereoelectronic factors. Murr and Conkling have found that deuterium at the *endo*-3 and *exo*-3 positions of 21-OBs retards ethanolysis by 2 and 11% respectively (Table 1:3).[158] They attributed the lower KIE in 21-OBs-*endo*-3-*d* relative to 21-OBs-*exo*-3-*d* to possible hindrance to hyperconjugative electron release and/or steric restrictions by the leaving group.[158]

The diminished KIE for 21-OBs-*exo*-3-*d*, the negligible KIE for 21-OBs-*endo*-3-*d* and the similarities of the KIEs for 57-OBs-*endo*-3-*d*

and 57-OBs-*exo*-3-*d* (considering that $\phi=30^{o}$) were used as evidence for charge delocalization, in the transition state for solvolysis of 21-OBs, which reduces the amount of positive charge at C-2.[158] Schaefer has attributed the lower β-KIE observed in 21-Br-3,3-d_2 relative to 57-Br-3,3-d_2 (1.04 vs 1.30) to charge delocalization in the transition state.[157]

3) γ-Isotope Effects

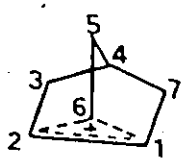
In solvolytic reactions where γ-KIEs have been observed, the origin of the factors which cause the force field changes at the site of isotopic substitution remains obscure. Halevi has suggested that these effects might arise from the greater electropositive nature of the carbon-deuterium bond relative to the carbon-hydrogen bond *ie* inductive effect on the isotopic atom.[122]

The large γ-KIEs for ethanolyses of 21-OBs-*exo*-6-*d* and 21-OBs-*endo*-6-*d* (1.09 and 1.11, respectively) are in contrast to those for the *endo* epimers 57-OBs-*exo*-6-*d* and 57-OBs-*endo*-6-*d* (1.00 and 0.97).[160] Scrambling of deuterium at C-6 to other sites within the molecule was discounted as the source of the large effect for 21-OBs on the basis of detailed considerations. It was concluded that the γ-KIEs for solvolysis of 57-OBs were consistent with a classical transition state whereas the γ-KIEs for 21-OBs were *not* expected on this basis.[160] Dideuteration at C-6 of 1,2-dimethyl-*exo*-2-norbornyl-*p*-nitrobenzoate, which supposedly ionizes without assistance, resulted in a negligible KIE (k_H/k_D = 1.02 for 1.98 atoms of deuterium).[175] This seems to support the view that the large γ-effect for solvolysis of 21-OBs arises from assisted ionization.[160]

4) δ-Isotope Effects

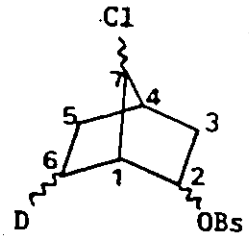
The negligible δ-KIEs for acetolyses of 21-OBs-*endo*-5-*d* and 21-OBs-5,5-d_2 (1.01 and 0.99) were used as evidence to support the view that hyperconjugation to the C-5 hydrogens is unimportant and that hydride (deuteride) shifts followed by internal return to brosylate contribute negligibly to the isotope effects for solvolysis of 21-OBs-*exo*-6-*d* and 21-OBs-*endo*-6-*d*.[163,164]

The purpose of our interest in isotope effects was to intimately probe into the origin of the γ-KIE in the norbornyl system by determining to what extent the large γ-effect arose from charge delocalization in the solvolytic transition state (*cf* 54). It is conceivable that the γ-KIEs for solvolyses of 21-OBs-*exo*- and *endo*-6-*d* (k_H/k_D = 1.09 and 1.11) could arise from a rehydridization at C-6 as the transition state (which might resemble 54) is approached. However, this seems puzzling since in 54, C-6 is probably still very sp^3 like *ie* the hybridizational change in going from the ground state to the transition state can be quite small; the maximum KIE for a sp^3 to sp^2 rehybridization has been calculated to be about 20% per deuterium atom.[166] Thus the γ-KIEs in the norbornyl system appear to be too large to explain on the above basis.



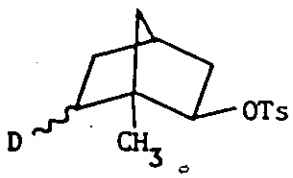
54

Our approach was to place an electron withdrawing substituent (*eg* chlorine) at C-7 in 21 which would destabilize any positive charge which might develop at C-1 during the solvolytic reaction. This would preclude C-1 C-6 σ bond participation in the norbornonium ion sense *ie* the transition state would probably be very unsymmetrical with respect to positive charge distribution at C-1 and C-2. We decided to observe



the effect of this perturbation by measuring the γ-KIE for solvolysis of 7-chloro-2-norbornyl brosylates -6-*d*.

At the other extreme, solvolysis of 1-methyl-2-norbornyl tosylate should proceed with considerable involvement of the C-1 C-6 bond since the methyl substituent at C-1 will stabilize any positive charge which might leak onto this carbon atom in the transition state. Thus, it was decided to investigate the KIE for solvolysis of 1-methyl-2-norbornyl tosylate-6-*d* to determine the effect of involving the C-1 C-6 bond during the ionization.



Jerkunica has measured the γ-KIE for solvolysis of the above compound[115a] however his synthetic route casts doubt upon the authenticity of the deuterated compound.[214]

Gassman has shown that 3-chloronortricyclene (24) is formed in the solvolysis of 7-chloro-2-norbornyl tosylates *via* 1,3 elimination.[176] We decided to investigate the stereochemistry of this 1,3 process by examining the solvolysis of these chloro-brosylates labelled with deuterium at C-6 and determining the preferred stereochemical pathway for formation of the tricyclic material.

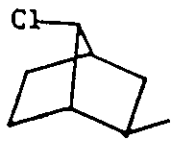
CHAPTER 2

RESULTS

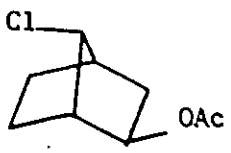
Nomenclature

Throughout this thesis, 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, OBs for brosylate, 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*-3-*d* or *exo,exo*-5,6-d_2 etc.

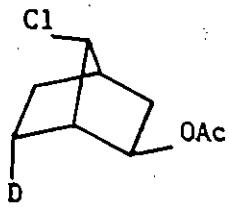
For example, the *anti*-7-chloro-*exo*-2-norbornyl system is denoted by 58 and *anti*-7-chloro-*exo*-2-norbornyl acetate by 58-OAc. To describe a deuterated derivative of 58-OAc, the site of deuteration follows the functional group description. Thus, *anti*-7-chloro-*exo*-2-norbornyl acetate-*endo*-6-*d*



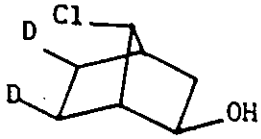
58



58-OAc

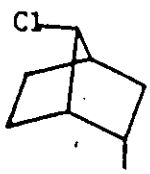


58-OAc-*endo*-6-*d*

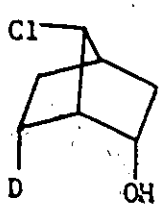


58-OH-*exo,exo*-5,6-d_2

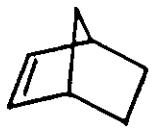
and *anti*-7-chloro-*exo*-2-norbornanol-*exo,exo*-5,6-d_2 are denoted by 58-OAc-*endo*-6-*d* and 58-OH-*exo,exo*-5,6-d_2 respectively. However, *anti*-7-chloro-*endo*-2-norbornyl derivatives are denoted by 84 and hence 84-OH-*endo*-6-*d* describes *anti*-7-chloro-*endo*-2-norbornanol-*endo*-6-*d*.



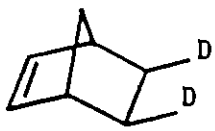
84



84-OH-*endo*-6-*d*

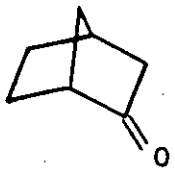


87

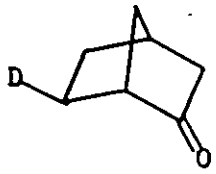


87-*exo,exo*-5,6-d_2

For certain monofunctional compounds, the functional group description is omitted. For example, norbornene is denoted by 87 whereas norbornene-*exo*,*exo*-5,6-d_2 is represented by 87-*exo*,*exo*-5,6-d_2. Similarly 2-norbornanone is denoted by 12 and 2-norbornanone-*exo*-6-*d* by 12-*exo*-6-*d*.

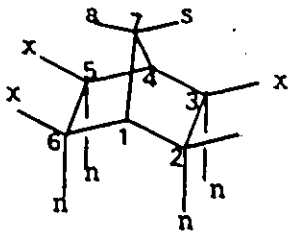


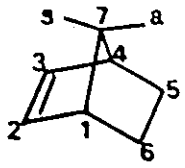
12



12-*exo*-6-*d*

The numbering system which is used for the norbornyl system is as shown below. In nmr spectra (*e.g.* Figures 2:1, 2:2, 2:3), the abbreviated notations 2n, 3x, 7s denote the *endo*-C-2, *exo*-C-3 and *syn*-C-7 positions respectively.



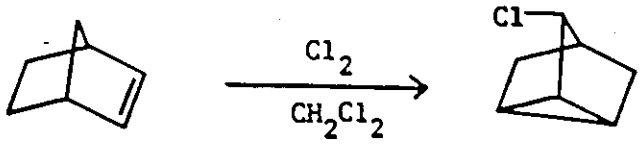


Electrophilic Cleavage of Nortricyclenes

A. 3-Chloronortricyclene (24)

1) Cleavage with Non-Deuterated Acid

Chlorination of norbornene in methylene chloride and pyridine gave 3-chloronortricyclene (24) in 27% yield.[178] Nuclear magnetic



24

resonance (nmr) spectroscopy showed that 24 was not contaminated with isomeric chloronorbornenes, compounds which could lead to misleading results especially in a study dealing with the stereochemistry of the electrophilic cleavage of a cyclopropyl group.

Treatment of 24 with acetic acid and 0.10M sulphuric acid for 120 hr. at 70° resulted in 97% conversion to

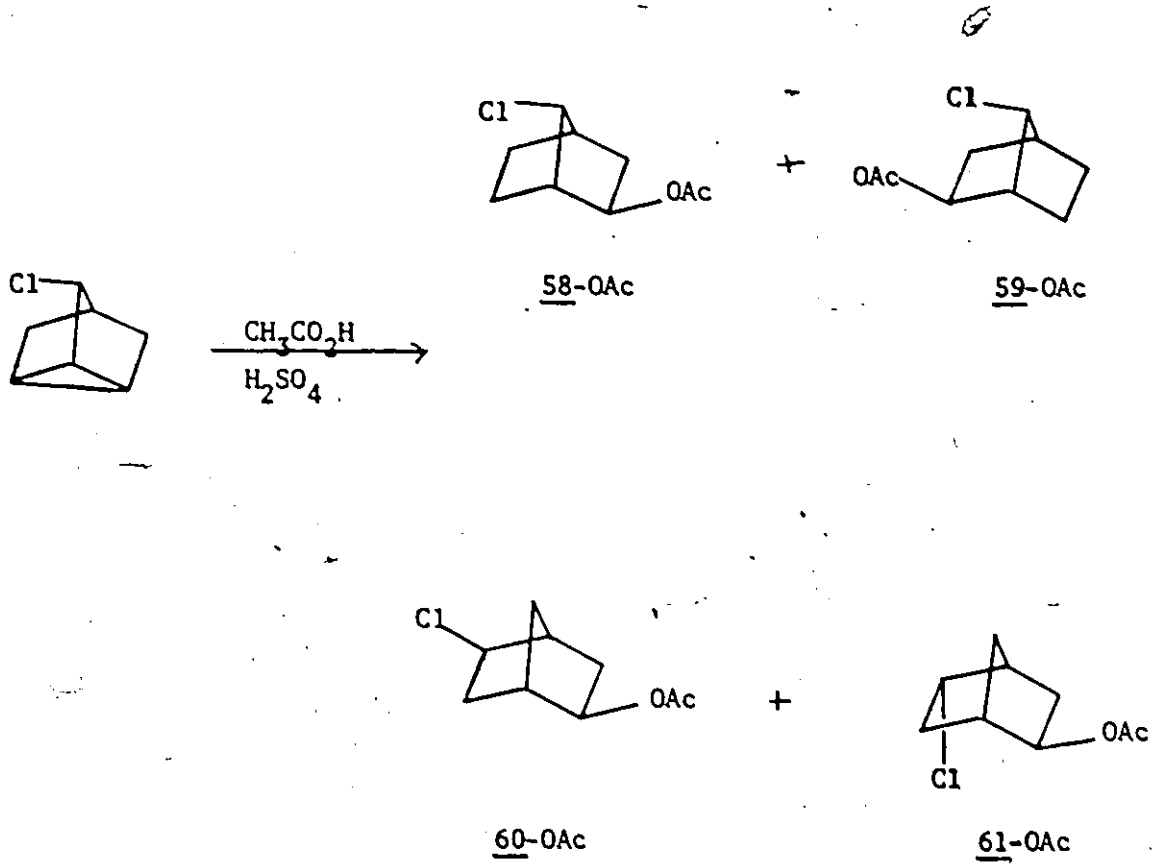
(a) *anti*-7-chloro-*exo*-2-norbornyl acetate (58-OAc),

(b) *syn*-7-chloro-*exo*-2-norbornyl acetate (59-OAc),

(c) *exo*-5-chloro-*exo*-2-norbornyl acetate (60-OAc) and

(d) *endo*-5-chloro-*exo*-2-norbornyl acetate (61-OAc).[179]

When a small portion of the reaction mixture was heated to 100°, isomerization of 58-OAc was noted. Prolonged reaction time at 120° resulted in decomposition (darkening) and the formation of additional products (see Chapter 5). Norbornyl diacetates were not detected in the reaction mixture indicating that solvolysis of chlorine in 24 to produce a



nortricyclyl cation (*cf* cyclopropylcarbinyl cation) does not compete with ring opening.*

An authentic sample of 58-OAc was synthesized by the acetylation

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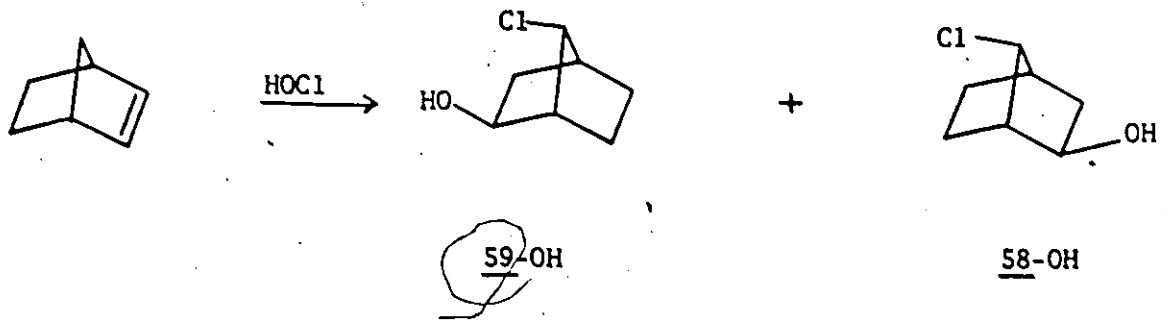
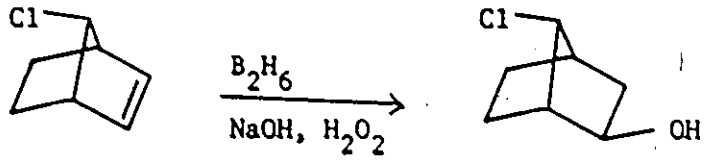
*However, results from this laboratory indicate that when 3-fluoronortricyclene is treated with acid under similar conditions, loss of fluoride ion competes with ring opening and leads to diacetates as products.[180]

of 58-OH which was obtained by one of two routes. Addition of hypochlorous acid to norbornene[178] or alternatively hydroboration-oxidation of *anti*-7-chloronorbornene (62)[181,182] gave the chloro alcohol 58-OH. Since



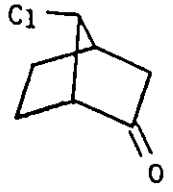
59-OH 58-OH



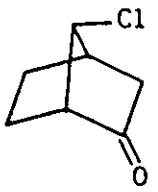
62 58-OH

58-OAc was separable from 59-, 60- and 61-OAc by gas-liquid partition chromatography (glpc), but the latter three compounds could not be resolved from each other, the following scheme was employed to identify these compounds. Reduction with lithium aluminum hydride of 58-,59-,60- and 61-OAc gave a mixture of 58-, 59-, 60- and 61-OH from which it was

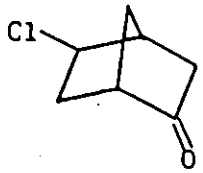
possible to separate only 59-OH. An authentic sample of 59-OH was prepared by the method of Roberts.[178] Oxidation of the mixture of 58-, 59-, 60- and 61-OH with Jones reagent[183] gave 44% *anti*-7-chloro-2-norbornanone (63), 26% *syn*-7-chloro-2-norbornanone (64), 14% *exo*-5-chloro-2-norbornanone (65) and 14% *endo*-5-chloro-2-norbornanone (66) which were separable from each other by glpc.



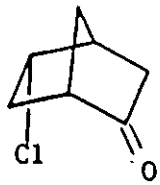
63



64

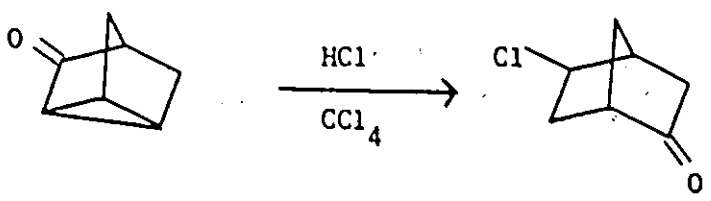


65



66

Preparation of an authentic sample of the chloro ketone 65 was effected in 50% yield by treatment of nortricyclanone[184] with anhydrous hydrogen chloride in carbon tetrachloride. In the nmr spectrum of 65, the triplet at δ 4.0* was assigned to the proton at the *endo*-C-5 position; the carbonyl stretching frequency appeared at 1760 cm^{-1}. Following our



65

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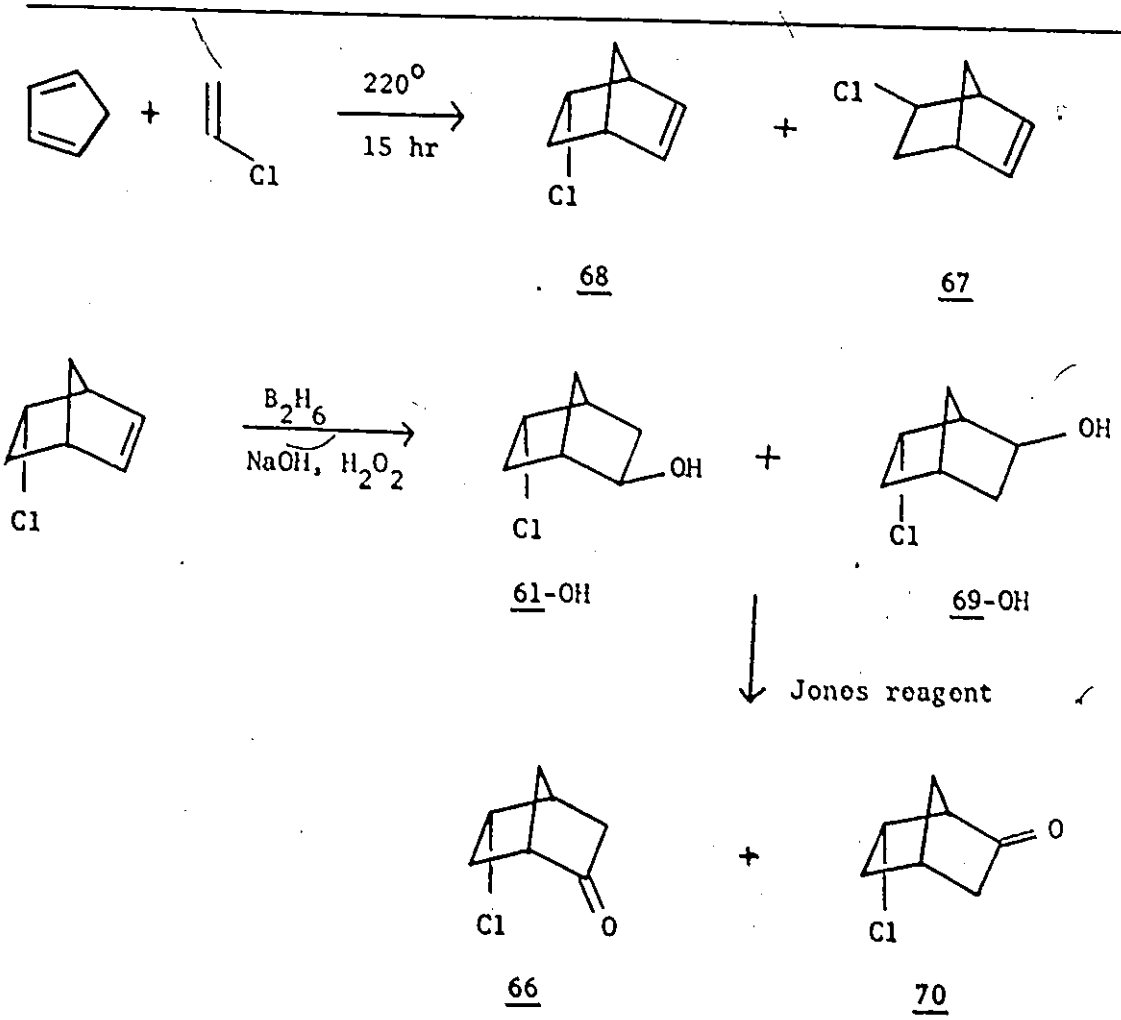
* All chemical shifts are reported as ppm downfield from internal tetramethylsilane.

preparation of 65, Gassman reported an alternate route, however spectral data were not reported.[176]

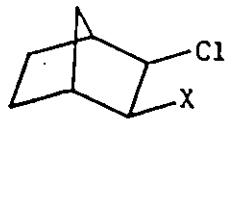
Treatment of cyclopentadiene with vinyl chloride for 15 hr at 220° to give *exo*- and *endo*-5-chloronorbornenes (67 and 68) in the ratio 43:57 was the first step towards the synthesis of 66. Hydroboration-oxidation[185] of the *endo*-chloride 68, which was separated from 67 by spinning band distillation, yielded a mixture of 61- and 69-OH which



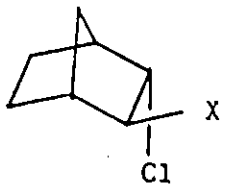
was oxidized directly to a mixture of 66 and *endo*-6-chloro-2-norbornanone (70) respectively, in the ratio 42:58. A one proton multiplet at

δ 4.30 in the nmr spectrum of 66 was due to the proton at *exo*-C-5; the carbonyl stretching frequency appeared at 1750 cm^{-1}.

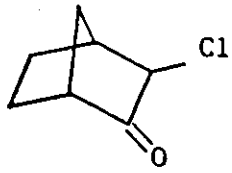
Evidence that *exo*- and *endo*-3-chloro-*exo*-2-norbornyl acetates (71-OAc and 72-OAc) were not formed during the reaction of 24 with acid



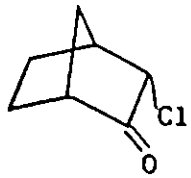
71



72



73



74

came from a comparison of the spectral data of *exo*-3-chloro-2-norbornanone (73) and *endo*-3-chloro-2-norbornanone (74)[186] with those of the chloro ketones (*ie* 63-66) which were derived from the chloro acetates obtained from 24. Chloro ketone 73 was synthesized by treatment of 2-norbornanone (12) with sulphuryl chloride and the *endo*-chloro ketone 74 was obtained by equilibration of 73 in basic solution.[186]

Identification of the *exo*- and *endo*-5-chloro-*exo*-2-norbornyl acetates (60- and 61-OAc), obtained from the electrophilic cleavage of 24, as their chloro ketones 65 and 66 did not yield any information about the stereochemistry of the acetoxy group - *exo* or *endo*. Reduction of an ethereal solution of 58-, 59-, 60- and 61-OAc with lithium aluminum hydride and subsequent reduction of the chloro alcohols with sodium in *iso*-propanol gave a mixture of 98±2% *exo*-2-norbornanol (21-OH) and 2±1% *endo*-2-norbornanol (57-OH) as determined by glpc.* This establishes the *exo*- to *endo*-acetate ratio from the cleavage of 3-chloronortricyclene (24) with acetic acid. Thus the carbon atom which undergoes nucleophilic attack

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* This represents the ratio of 21-OH to 57-OH. The total yield of these compounds was 78%.

experiences predominant inversion of configuration. Another product (<5% yield) with retention time slightly longer than that of the *exo*-2-norbornanol obtained from the above reduction was not identified (see Chapter 5). Conceivably, it arose by solvolysis of chlorine with subsequent fragmentation to a cyclopentenyl derivative.

Control reactions under the conditions used for the electrophilic cleavage of 24 established that 59-OAc underwent 12% isomerization to 58-OAc whereas 61-OAc underwent 15% isomerization to 60-OAc (Table 2:1). Compound 61-OAc which was prepared by the acetylation of 61-OH was contaminated with 69-OAc. Thus, the mixture of 61-OAc and 69-OAc in a known ratio was subjected to the reaction conditions and the per cent isomerization was determined by the change in this ratio. Compounds 58-, 71- and 72-OAc were stable in the acidic medium, less than 3% isomerization to other chloro acetates occurred, discounting the possibility that the latter two compounds might have been formed and undergone rearrangement during the ring opening reaction.

Table 2:1 Stability of Chloro acetates to the Reaction Conditions Used for Electrophilic Cleavage of 24.

Compound	% Rearrangement	Rearrangement Product
58-OAc	<3±1	-
59-OAc	12±1	58-OAc
61-OAc	15±1	60-OAc
71-OAc	<3±1	-
72-OAc	<2±1	-

Treatment of chloro *t*-butyl ethers 71- and 72-O*t*Bu with anhydrous hydrogen chloride gave chloro alcohols 71- and 72-OH which were acetylated with acetic anhydride in pyridine to produce 71- and 72-OAc.[187]

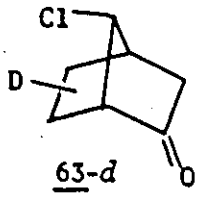
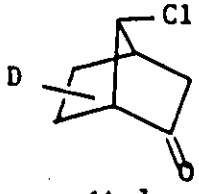
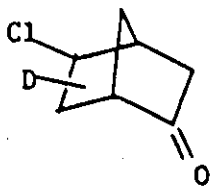
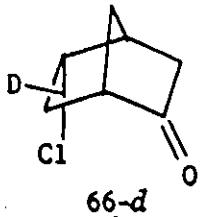
2) Cleavage with Deuterated Acid

To determine the stereochemistry of the attack by electrophile (H^+) on the cyclopropyl group of 24, the reaction was carried out in deuterated medium. 3-Chloronortricyclene (24) was treated with acetic acid-d_4 (99.5 Atom %*d*) and 0.10M sulphuric acid-d_2 for 500 hr at 70° to yield *anti*-7-chloro-*exo*-2-norbornyl trideuteroacetate-d_1 (58-trideuteroacetate-d_1), *syn*-7-chloro-*exo*-2-norbornyl trideuteroacetate-d_1 (59-trideuteroacetate-d_1), *exo*-5-chloro-*exo*-2-norbornyl trideuteroacetate-d_1 (60-trideuteroacetate-d_1), and *endo*-5-chloro-*exo*-2-norbornyl trideuteroacetate-d_1 (61-trideuteroacetate-d_1). The mass spectrum of 58-trideuteroacetate-d_1 indicated appreciable multiple deuteration, *viz* 4% d_3, 94% d_4, 2% d_5 species (av 3.98 *d*/molecule). The amount of deuterium on the norbornyl skeleton of 58-trideuteroacetate-d_1 was ascertained by reduction with lithium aluminum hydride to 58-OH-d_1 followed by reacetylation with acetic anhydride to 58-OAc-d_1. For compound 58-OAc-d_1, deuterium assay by mass spectrometry indicated predominant monodeuteration - 3% d_0, 95% d_1, 2% d_2 species (av 0.99 *d*/molecule).

In view of the difficulties encountered in the separation of the chloro acetates (*vide supra*), the mixture of 58-, 59-, 60- and 61-trideuteroacetates-d_1 was reduced with lithium aluminum hydride to a mixture of the respective deuterated chloro alcohols. This reaction does not affect the stereochemistry of the acetate group or the stereochemistry

of deuterium which is not in the acetate group. Oxidation with Jones reagent gave the deuterated chloro ketones 63-, 64-, 65- and 66-*d*; control experiments with 65-*exo*-3-*d* showed that possible deuterium loss from C-3 *via* acid-catalyzed enolization under the oxidation reaction conditions was negligible. Similarly it was shown that acid-catalyzed homoenolization was negligible when 63-*endo*-6-*d* was subjected to the reaction conditions for oxidation. Mass spectrometry revealed that each of the deuterated chloro ketones 63- to 66-*d* consisted primarily of monodeuterated species (Table 2:2). Compounds 65- and 66-*d* contained

Table 2:2 Mass spectrometric deuterium assays on the deuterated Chloro ketones 63- to 66-*d*

Compound	% d_0	% d_1	% d_2	(av *d*/molecule)
 63-*d*	4	95	1	0.97 ± 0.03
 64-*d*	3	95	2	0.99 ± 0.03
 65-*d*	10	90	-	0.90 ± 0.03
 66-*d*	13	85	2	0.89 ± 0.03

about 10% less deuterium than did 63- and 64-*d* and thus established the deuterium content at C-2.

When the electrophilic cleavage of 24 was carried out in acetic acid-O-*d* and sulphuric acid-d_2, a high percentage of d_o species was found in the deuterated chloro acetates 58- to 61-OAc as determined by mass spectrometric analyses of the corresponding chloro ketones (see Chapter 5). This low incorporation of deuterium was attributed to dilution of the deuterium pool of the reaction medium *via* exchange of the methyl hydrogens of acetic acid-O-*d* with deuterium from solvent.

3) Stereochemistry of Electrophilic Attack

Direct analysis of the complex nmr spectra of 63-, 64-, 65- and 66-*d* did not allow a determination of the sites of deuteration. Recently, the utility of lanthanide shift reagents (LSR) in the "simplification" of the ^{1}H nmr spectra of compounds containing co-ordinating functional groups (alcohol, amine, ether, carbonyl) has been demonstrated.[188-191] Published work by Paasivirta[192] as well as unpublished work from our laboratories[193] have shown that most of the proton resonances of *endo*- or *exo*-2-norbornanol (57- or 21-OH) can be resolved from each other in the presence of the shift reagent Eu(DPM)$_3$*. For these reasons each of the chloro ketones was reduced with lithium aluminum hydride to the deuterated 2-norbornanol and the distribution of deuterium was determined using Eu(DPM)$_3$.

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* Tris-(2,2,6,6-tetramethylheptane-3,5-dionato) europium(III) or tris (dipivalomethanato) europium(III).

When 63- and 66-*d* were treated individually with lithium aluminum hydride for a prolonged period of time, the major product was deuterated *endo*-2-norbornanol (85%) with the minor product being *exo*-2-norbornanol (15%). Reduction of 64-*d* gave deuterated *exo*-2-norbornanol as the expected product which arose by preferential hydride attack from the *endo* side. However, reduction of 65-*d* gave a predominance of *exo*-2-norbornanol; this is surprising because the stereochemical course for reduction of the carbonyl function in 65-*d* should be essentially identical to that for reduction of 2-norbornanone (12) *ie* 85% *endo*-alcohol 57-OH and 15% *exo*-alcohol 21-OH. It is assumed that this anomalous stereochemical outcome arises from initial predominant *exo* attack by hydride on 65-*d* to yield an *endo*-alkoxide and subsequent solvolysis of the chlorine atom followed by a Wagner-Meerwein alkyl shift which converts *endo*-alkoxide to *exo*-alkoxide. Capture by hydride and aqueous workup should give predominantly *exo*-2-norbornanol. This pathway likely competes with direct reduction of the carbon-chlorine bond and thus exclusive formation of *exo*-2-norbornanol is not observed, in fact *exo*-alcohol/*endo*-alcohol = 70:30. The major alcohol product from each reduction was carefully purified by glpc before analysis by nmr.

Figure 2:1 shows the nmr spectrum of *endo*-2-norbornanol complexed with $Eu(DPM)_3$ in carbon tetrachloride (mole ratio LSR/alcohol = 0.64) and Figure 2:2 shows the spectrum of deuterated *endo*-2-norbornanol (derived from 63-*d*) in the presence of shift reagent (mole ratio LSR/alcohol = 0.64).* They reveal that >90% of the deuterium is located at C-6 with at least 95% stereochemical purity. Similarly, comparison of the spectra in Figures 2:3 and 2:4 shows that the deuterated *exo*-2-norbornanol (derived from reduction

* The integrations which appear in these and subsequent spectra represent the average of five scans.

of 64-*d*) contains >90% of the deuterium at C-6 with at least 95% *endo* stereochemical purity. The nmr spectra (in carbon tetrachloride + $Eu(DPM)_3$) of deuterated *exo*- and *endo*-2-norbornanol, derived from 65- and 66-*d* respectively, indicated that the deuterium was scrambled throughout these molecules (Figures 2:5 and 2:6).

The combined mass spectral and nmr data established that the deuterium was distributed as described in Table 2:3.

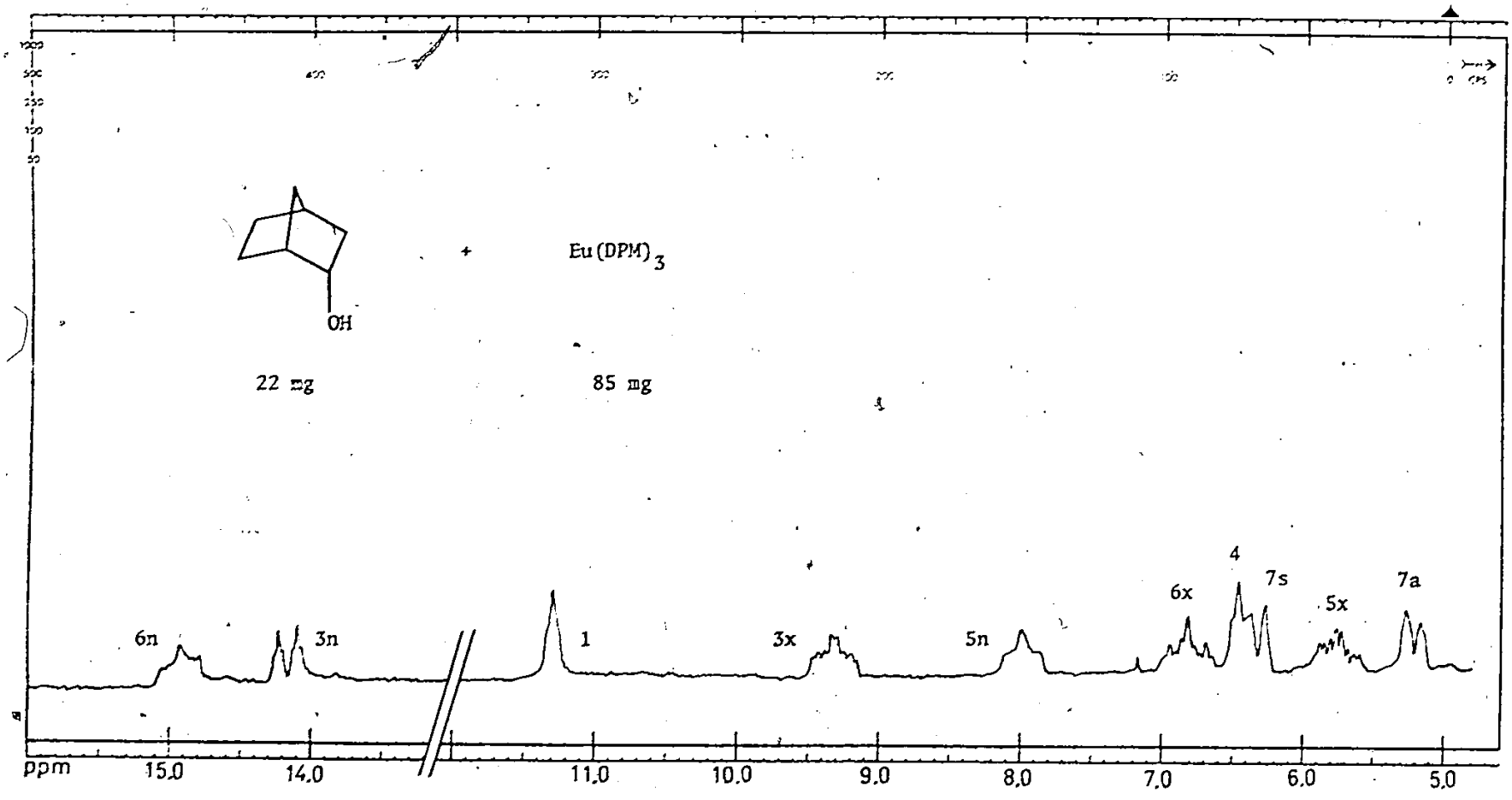


Figure 2:1 Pmr spectrum (100 MHz) of *endo*-2-norbornanol (57-OH) plus $Eu(DPM)_3$ in CCl_4

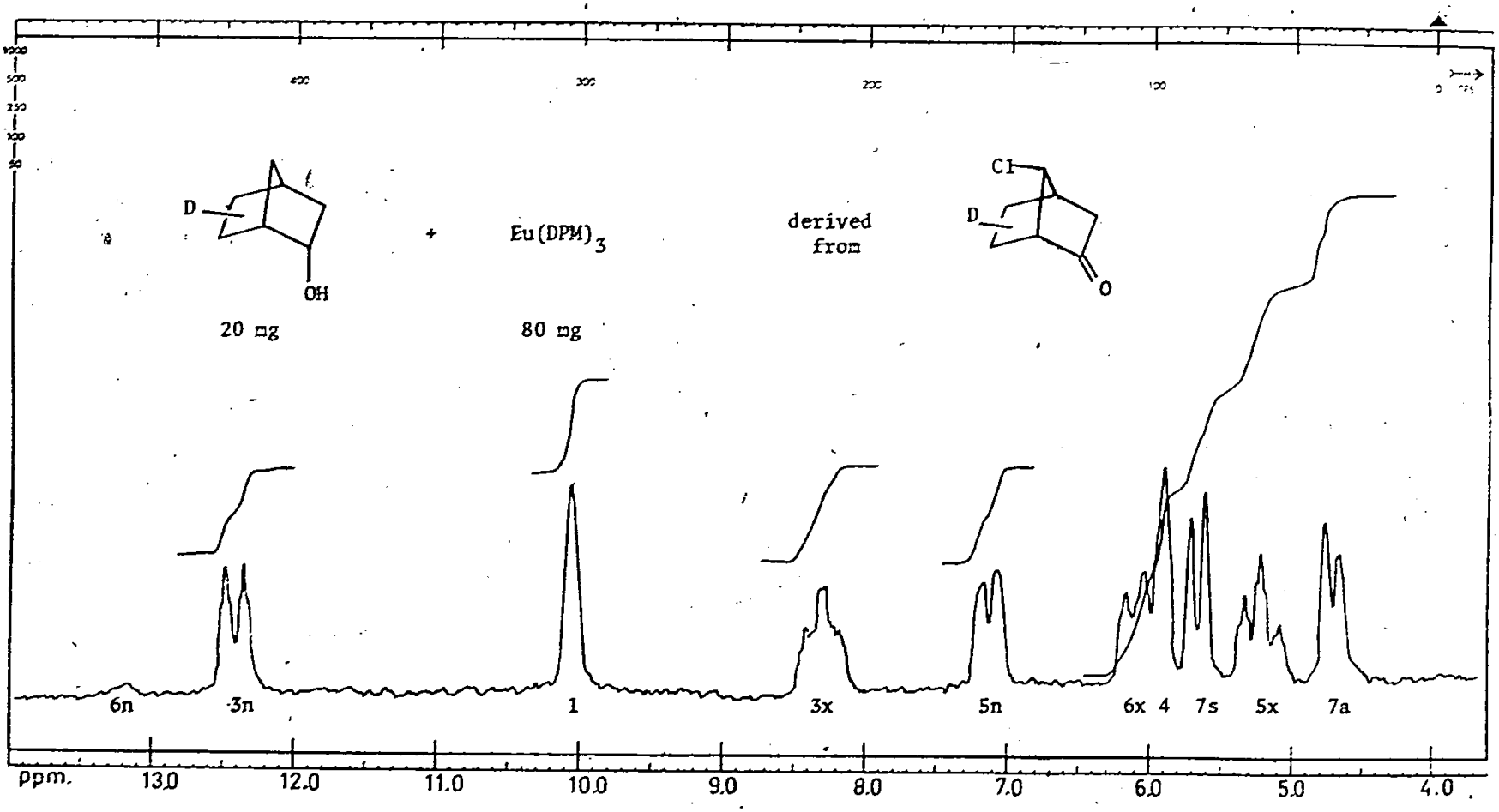


Figure 2:2 Pmr spectrum (100 MHz) of *endo*-2-norbornanol-*d* (derived from *anti*-7-chloro-2-norbornanone-*d*) plus $Eu(DPM)_3$ in CCl_4

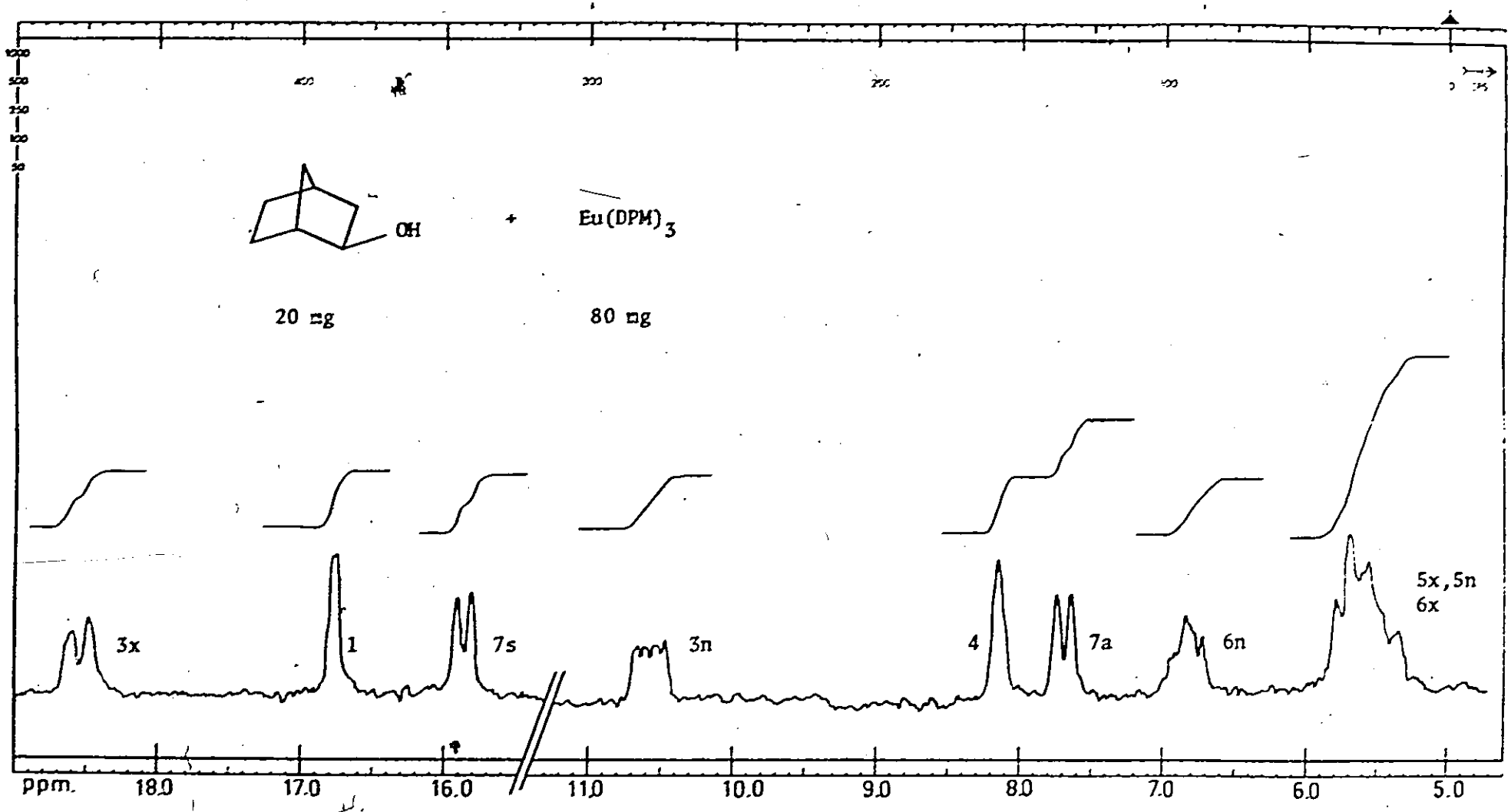


Figure 2:3 Pmr spectrum (100 MHz) of *exo*-2-norbornanol (21-OH) plus $Eu(DPM)_3$ in CCl_4

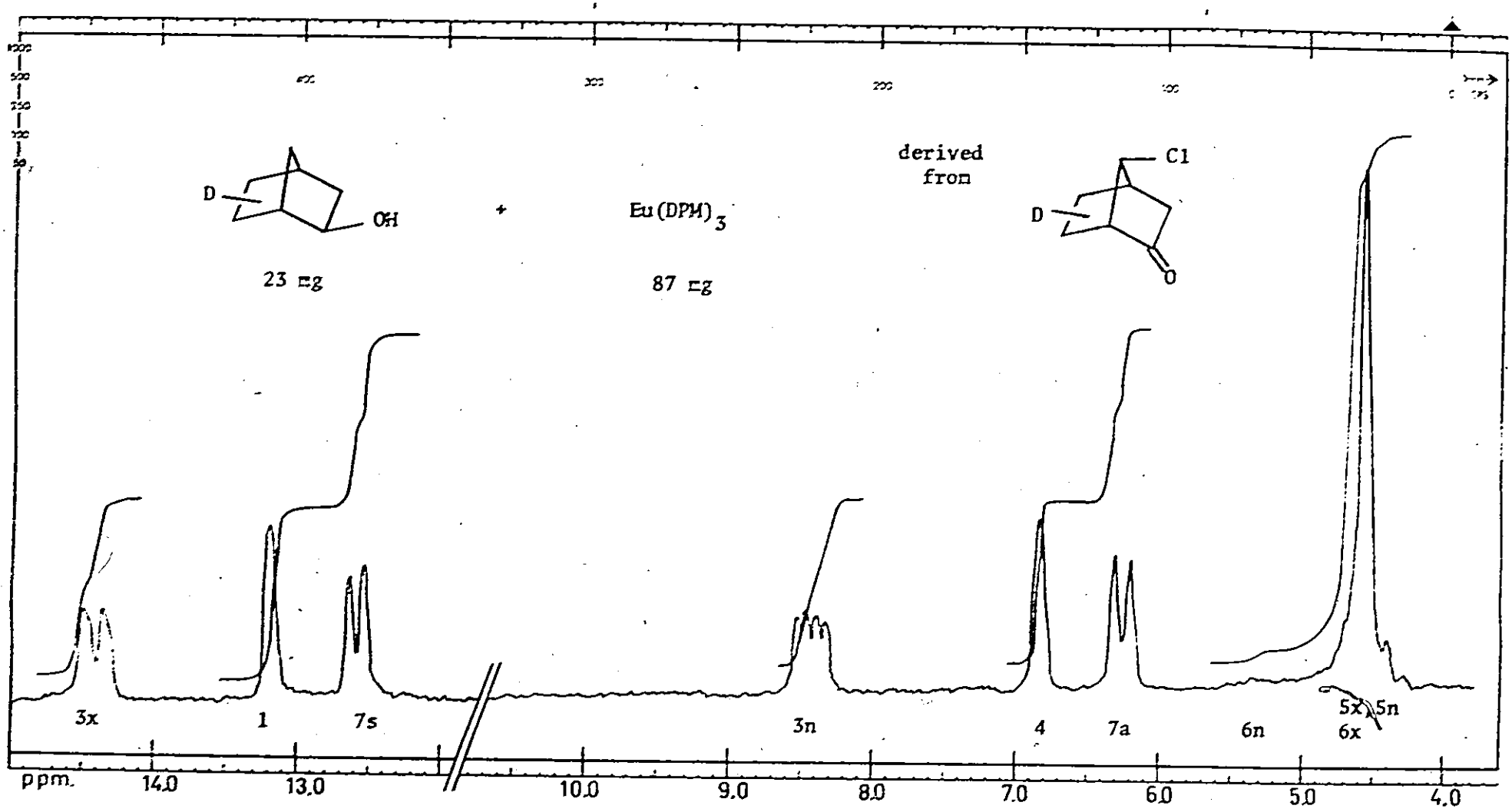


Figure 2:4 Pmr spectrum (100 MHz) of *exo*-2-norbornanol-*d* (derived from *syn*-7-chloro-2-norbornanone-*d*) plus $Eu(DPM)_3$ in CCl_4

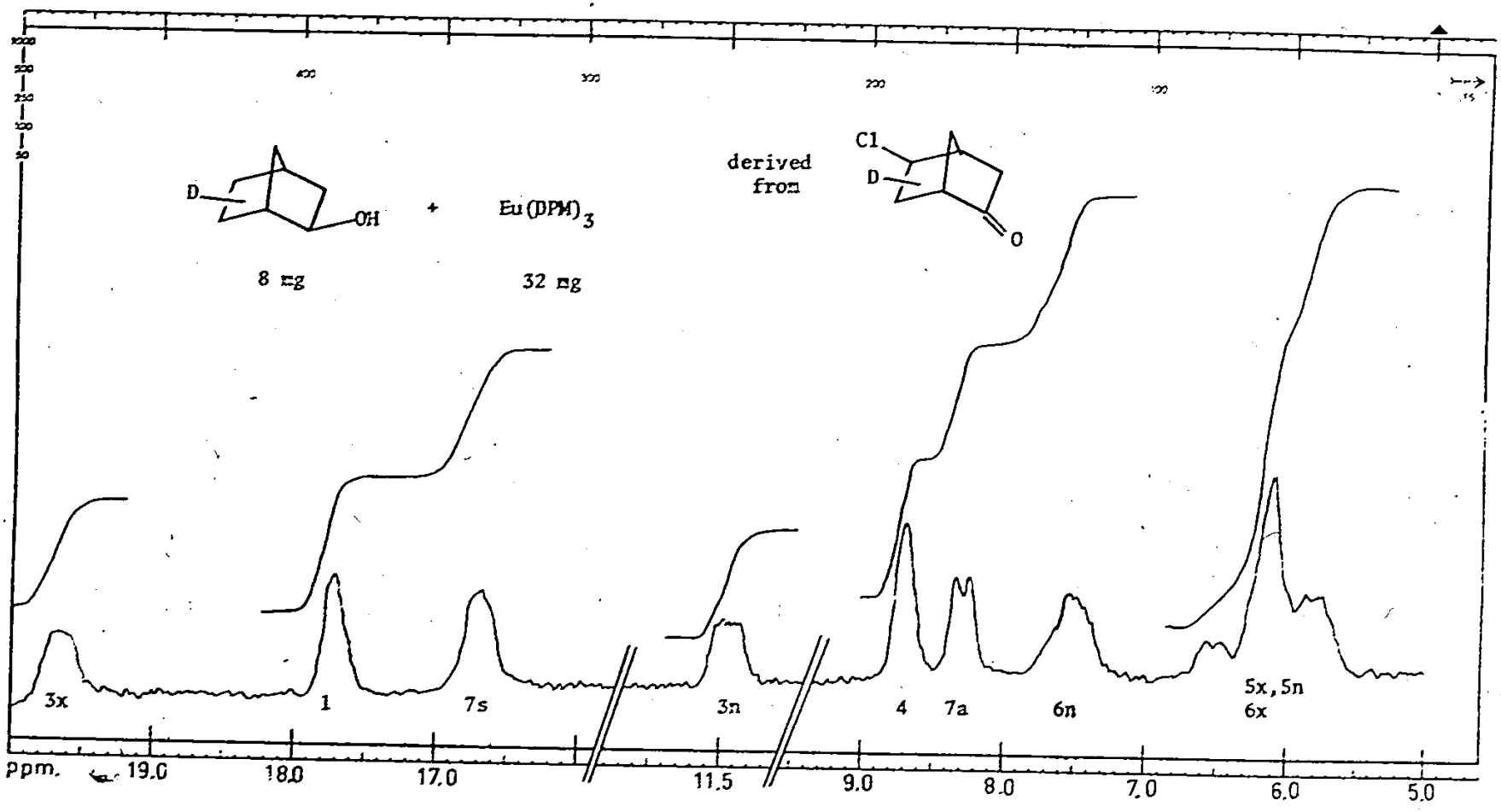


Figure 2:5 Pmr spectrum (100 MHz) of *exo*-2-norbornanol-*d* (derived from *exo*-5-chloro-2-norbornanone-*d*) plus $Eu(DPM)_3$ in CCl_4

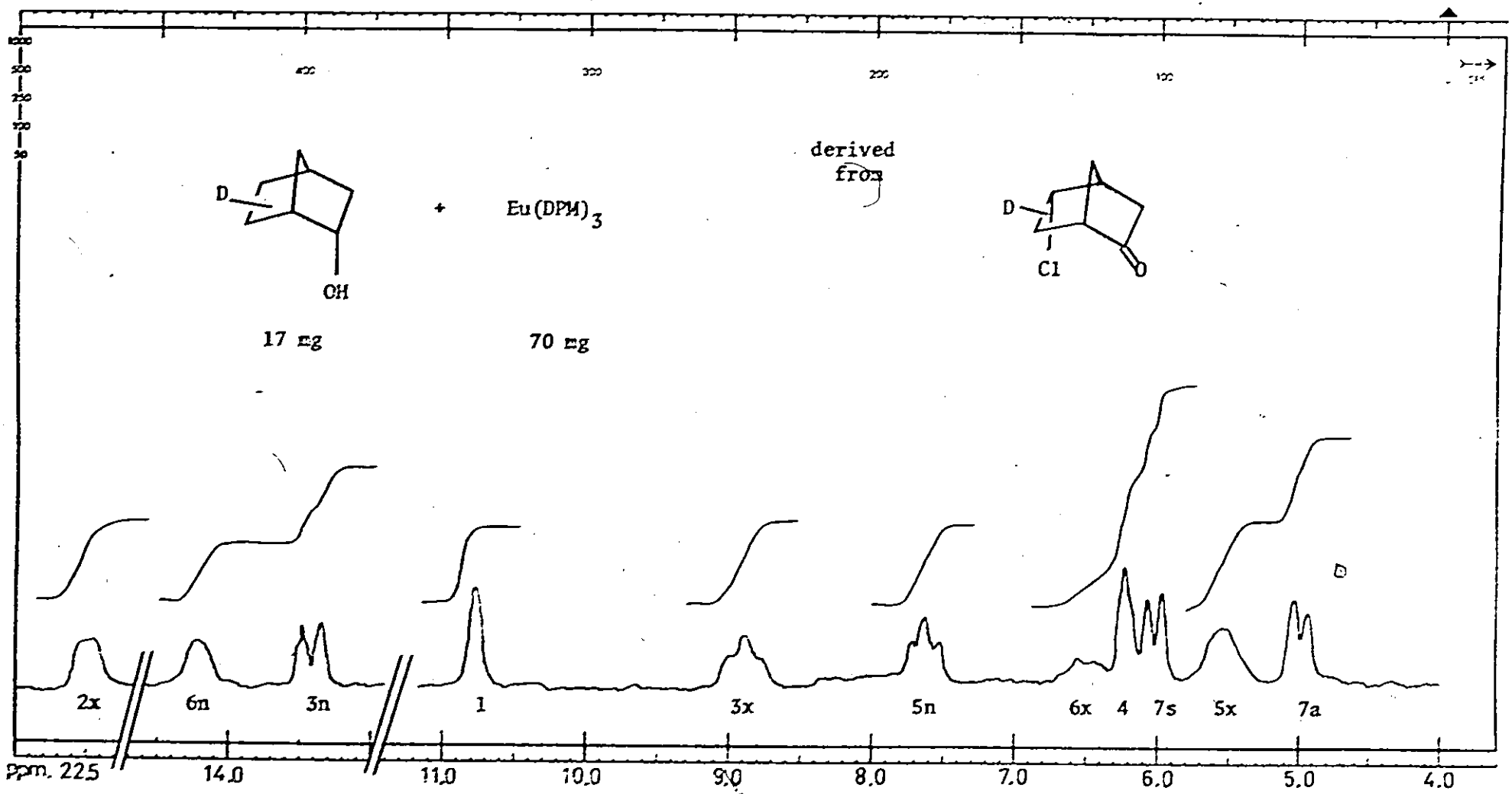
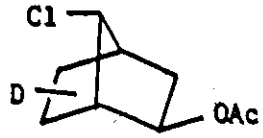
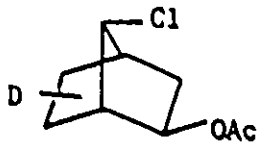
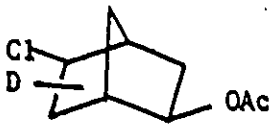
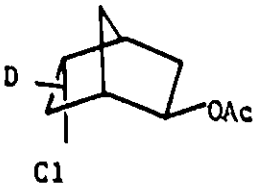


Figure 2:6 Pmr spectrum (100 MHz) of *endo*-2-norbornanol-*d* (derived from *endo*-5-chloro-2-norbornanone-*d*) plus $Eu(DPM)_3$ in CCl_4

Table 2:3 Distribution of Deuterium in the Products from Electrophilic Cleavage (CD_3CO_2D, D_2SO_4) of 3-Chloronortricyclene (24)

Compound	Deuterium Content[a] and Position[b]					
	C-1	C-2	C-3		C-6	
			exo	endo	exo	endo
	-	-	-	-	-[c]	>0.90[c]
	-	-	-	-	-[c]	>0.90[c]
	0.10	0.10	0.20	0.20	0.20	0.20
	0.10	0.15	-	-	0.55	0.25

[a] This table lists the fraction of one deuterium atom which was present at the indicated sites. The error in each number was estimated to be ±0.05 deuterium atom.

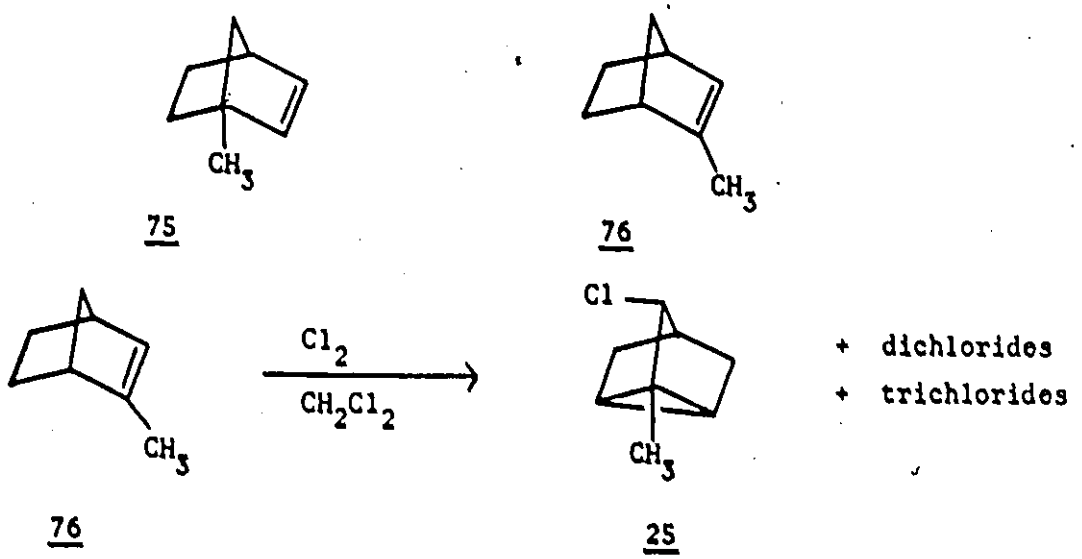
[b] Determined by pmr and ms according to the method described in Chapters 2 and 5.

[c] The spectral data (*vide supra*) indicated that >90% of the deuterium was at C-6 with >95% *endo* stereochemical purity.

B. 2-Methyl-3-chloronortricyclene (25)

1) Synthesis

The Diels-Alder reaction of methylcyclopentadiene with ethylene gave a mixture of 1- and 2-methylnorbornenes (75 and 76) which were separated by spinning band distillation.[194] Their nmr spectra have been previously reported.[195] Chlorination of 76 in methylene chloride containing

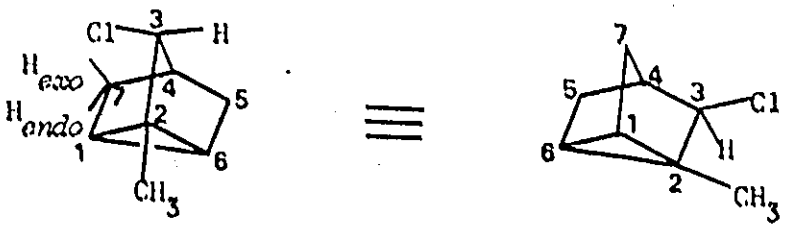


76 25

pyridine gave a 21% yield of 2-methyl-3-chloronortricyclene (25). Strong cyclopropyl-hydrogen stretching and carbon-chlorine stretching absorptions appeared at 3075 and 800 cm^{-1} respectively in the ir spectrum of 25. There were many similarities between the nmr spectrum of 25 (Figure 6:1, Chapter 6) and those of similar nortricyclene compounds.[82,196-198] A doublet (J = 1.5 Hz) at δ 3.65 in the spectrum of 25 was assigned to the proton at C-3 with the small coupling due to the proton at C-4. This was confirmed by irradiation of the broad singlet at δ 2.03 (C-4) which caused the doublet at

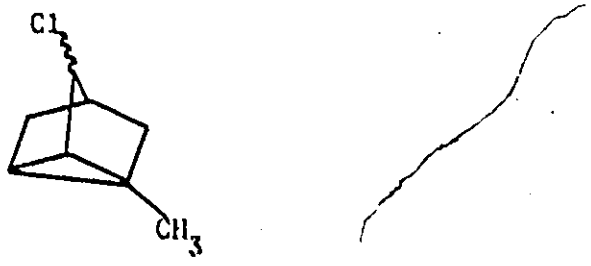
δ 3.65 (C-3) to collapse to a singlet. The methylene protons at C-7 and C-5 appeared as overlapping AB quartets, in agreement with observations from other nortricyclene compounds.[82,196-198] The proton at *exo*-C-7 appeared as half of an AB quartet (J' = 10.5Hz) at δ 2.12 whereas the other half of the quartet due to *endo*-C-7 (δ *ca* 1.4) was obscured by the proton resonances from C-5. Irradiation at δ 1.4 (*endo*-C-7) caused the doublet at δ 2.12 (*exo*-C-7) to collapse to a broad singlet due to loss of the large geminal coupling. A two proton singlet at high field (δ 1.04) was due to the cyclopropyl hydrogens at C-1 and C-6. Coupling between the methylene and cyclopropyl hydrogens was not observed; the methyl protons resonated at δ 1.23.

The nmr data dictate that the methyl group in 25 is situated on the cyclopropane ring whereas simple chemical arguments suggest that the chlorine might be situated on a methylene carbon atom which is adjacent to the



25

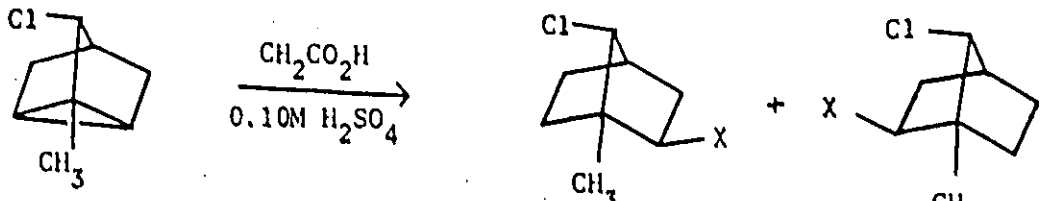
cyclopropyl carbon bearing the methyl substituent. Chlorination of 76 would not be expected to yield 1-methyl-3-chloronortricyclene(77) although this has not been proven conclusively.



77

2) Cleavage with Non-Deuterated Acid

Treatment of 25 with acetic acid ~~and~~ 0.10 M sulphuric acid for 105 hr at 62° gave >93% conversion to 1-methyl-*anti*-7-chloro-*exo*-2-norbornyl acetate (78-OAc) and 1-methyl-*syn*-7-chloro-*exo*-2-norbornyl acetate (79-OAc) in the ratio 76:24. It was shown that the relative product ratios did not



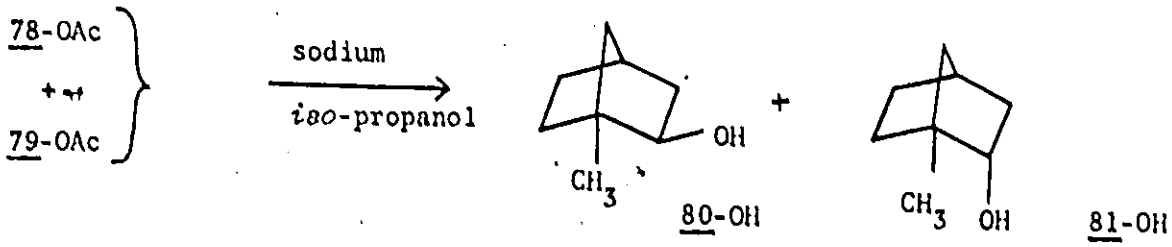
25 78 79

change during the reaction and that the two products were stable during glpc analysis (see Chapter 5).

The C-2 proton of 78-OAc appeared as a doublet of doublets at δ 4.55 and that of 79-OAc as a triplet with fine structure at δ 4.51 indicating that the stereochemistry at C-2 is identical in both compounds. In norbornyl systems, *exo* protons are deshielded relative to *endo* protons[199-201] and thus the chemical shift difference between *exo* -α and *endo* -α protons has been predicted to be about 0.3 to 0.5 ppm.[199] Peaks due to *exo*-C-2 protons are usually more extensively split due to coupling with the bridgehead proton. Thus the proton stereochemistry at C-2 is assigned the *endo* configuration; chemical evidence for this assignment is presented later. The chemical shifts for the *syn*-C-7 and *anti*-C-7 protons in 78- and 79-OAc of 3.77 and 3.51 ppm respectively are in agreement with the

stereochemical assignments at C-7 because in general, C-7 protons *syn* to *exo*-acetate, -hydroxyl or -tosyloxy substituents at C-2 are deshielded relative to *anti*-C-7 protons by about 0.20-0.30 ppm.[181,202-204]

Reduction of the mixture of 78- and 79-OAc with sodium in *iso*-propanol gave 96% 1-methyl-2-norbornanol (80) and 4% unidentified product. Nmr spectroscopy and glpc revealed a 5% maximum of



80-OH 81-OH

1-methyl-*endo*-2-norbornanol (81-OH) thus confirming the *exo*-acetate assignment in 78- and 79-OAc.

When the mixture of chloro acetates 78- and 79-OAc was mildly reduced with lithium aluminum hydride, a 78:22 mixture of 78- and 79-OH was obtained. The ir spectrum of each alcohol showed strong hydroxyl absorption and the nmr spectra corroborated the stereochemical assignments at both C-7 and C-2. Moreover, the chemical shifts for the *endo*-C-2 protons of 78- and 79-OH were 3.35 and 3.52 respectively - a difference of 0.17 ppm (*of* 0.10 ppm for 58- and 59-OH; 0.04 ppm for 78- and 79-OAc). This larger difference in chemical shifts relative to the acetates might possibly be attributed to intramolecular hydrogen-bonding in the chloro alcohols. For 78-OH, the proton at *syn*-C-7 appeared as a broad singlet at δ 3.81 whereas in 79-OH, the *anti*-C-7 proton resonated at δ 3.62.

As a prelude to a study of the electrophilic cleavage of 25 in deuterated medium, it was imperative to be able to unambiguously discern the possible sites and stereochemistry of deuteration on the norbornyl framework. Since the largest paramagnetic shifts have been observed in the nmr spectra of alcohols or amines when complexed with LSR,[188,189] it was decided to examine the behaviour of the proton resonances of 78- and 79-OH in the presence of $Eu(fod)_3$.* A discussion of the factors affecting the lanthanide induced shifts (LIS) is beyond the scope of this thesis. However, suffice it to say that the LIS, which decreases with increased distance of the proton from the co-ordinating group, has been attributed to a through-space dipolar interaction.[205] It has also been shown that nuclear spin-spin coupling constants remain unaffected by contact shifts.[206]

The nmr spectrum of 78-OH in carbon tetrachloride showed only the protons at *syn*-C-7 and *endo*-C-2 as separate signals (Figure 2:7). When $Eu(fod)_3$ was added to the alcohol (mole ratio LSR/alcohol = 0.73), a well-resolved spectrum was observed (Figure 2:8) and the signal assignments were made largely by examination of peak multiplicities, coupling constants and analogy to *exo*-2-norbornanol (Figure 2:3).[192,193] The protons at C-2, C-3 and C-7 appeared furthest downfield since the induced shifts are greatest for protons nearest to the hydroxyl group. Fine structure due to long range W coupling was usually obscured by slight peak broadening. A one proton low field doublet (J = 7 Hz) at δ 17.85 was assigned to the proton at *endo*-C-2 with the splitting due to *cis* vicinal coupling with the *endo*-C-3 proton. In agreement with the well-established relationship

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* Tris-(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyloctane-4,6-dionato) europium(III).

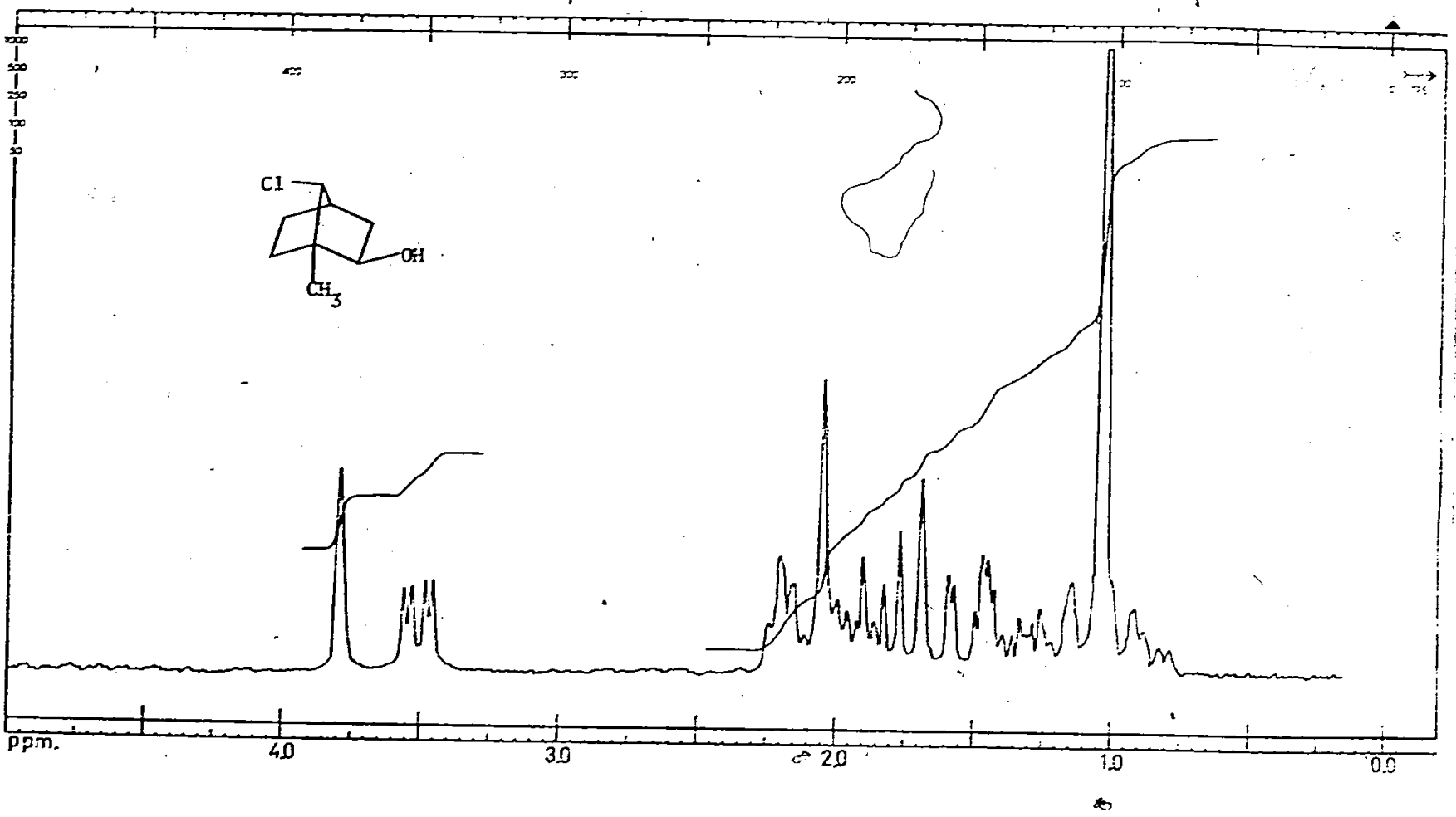


Figure 2:7 Pmr spectrum (100 MHz) of 1-methyl-*anti*-7-chloro-*exo*-2-norbornanol (78-OH) in CCl_4

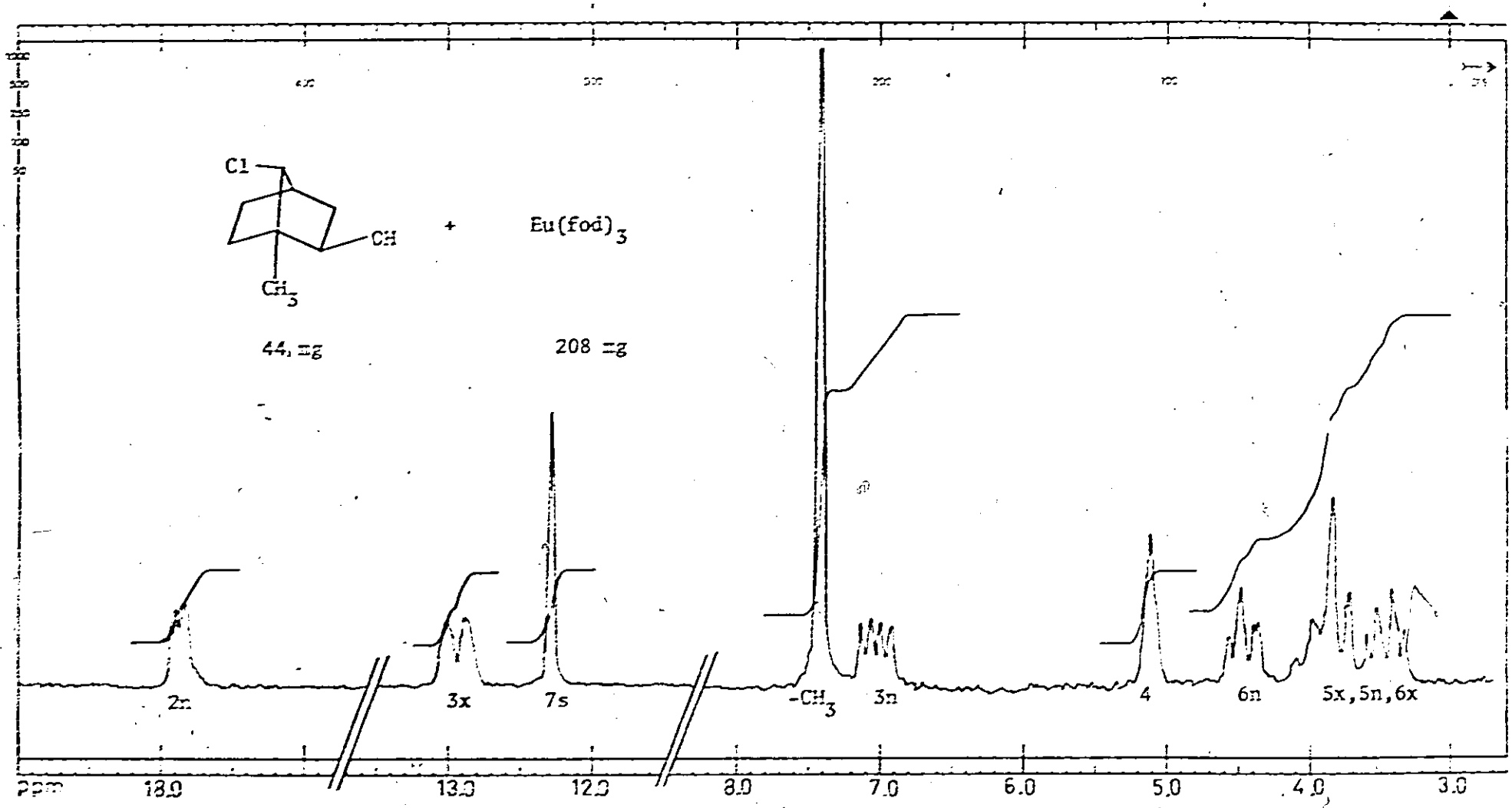


Figure 2:8 Pmr spectrum (100 MHz) of 1-methyl-*anti*-7-chloro-*exo*-2-norbornanol (78-CH) plus $Eu(fod)_3$ in CCl_4

between coupling constants for vicinal protons and dihedral angle,[207] *trans* vicinal coupling between the *endo*-C-2 and *exo*-C-3 protons was small (< 4 Hz). The resonance due to the proton at *exo*-C-3 appeared as a broad doublet (J = 14 Hz, geminal coupling[207] to *endo*-C-3 proton) at δ 12.95. Consistent with these assignments was the observation that the proton at *endo*-C-3, which resonated at δ 7.05, appeared as a doublet of doublets (J = 14 and 7 Hz, geminal and *cis* vicinal coupling respectively). In *exo*-2-norbornanol, the protons at C-7 appear as broad doublets (geminal coupling) with some fine structure (W coupling). However, in 78-OH geminal coupling at C-7 cannot occur and thus *syn*-C-7 appears as a singlet at δ 12.30. A broad singlet at δ 5.10 arose from the sole bridgehead proton. Assignment of the one proton triplet (with fine structure) at δ 4.50 and the three proton multiplet at δ 4.10-3.25 presented problems. Since C-5 is further removed from the hydroxyl group than C-6, the resonance at δ 4.50 was attributed to a proton at C-6, however, there was little basis for determining its stereochemistry.

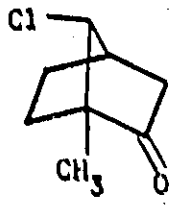
Paasivirta[192] has examined the nmr spectrum of *exo*-2-norbornanol complexed with Eu(DPM)$_3$ but he failed to resolve the high field multiplet which arose from the protons at C-5 and C-6. We have been able to partially resolve this multiplet by using a mole ratio of LSR/alcohol = 0.64 (Figure 2:3). In *exo*-2-norbornanol, a broad triplet was observed at slightly lower field relative to a three proton multiplet (δ 6.80 vs 5.80-5.30) and this was assigned to the proton at *endo*-C-6. This triplet disappeared in the spectrum of an authentic sample of *exo*-2-norbornanol-*endo*-6-*d*. Therefore, it was concluded that for 78-OH plus Eu(fod)$_3$, the

proton at *endo*-C-6 appeared as a triplet at δ 4.50 and the *exo*-C-6, *endo*-C-5 and *exo*-C-5 proton resonances overlapped. Hence it was still possible to discern deuterium at *exo*- or *endo*-C-6, however the differentiation of deuterium simultaneously present at both C-5 and C-6 was impossible. However, we were confident that there was not a mechanistic pathway which would place deuterium at C-5 in the products from the electrophilic cleavage of 25 (see Chapter 3).

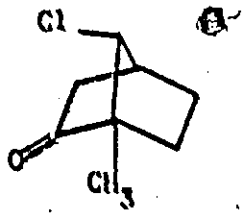
Similarly, the nmr spectrum of 79-OH showed resolution of only the protons at C-7 and C-2 (Figure 2:9), however addition of $Eu(fod)_3$ to the alcohol (mole ratio LSR/alcohol = 0.59) in carbon tetrachloride produced a dramatic change (Figure 2:10). The arguments for proton assignments were identical to those presented above for 78-OH - only the chemical shifts were slightly different. For example, the resonance from *anti*-C-7 appeared at higher field relative to the methyl protons (*cf* for 78-OH plus $Eu(fod)_3$, the methyl protons resonate at higher field). Assignment of the triplet at δ 3.70 to the proton at *endo*-C-6 was made for the reasons given above.

After refrigeration for six months, the samples of the above chloro alcohols plus $Eu(fod)_3$ did not show any changes in their nmr spectra. This indicates that the europium samples are stable over long periods of time.

Oxidation of the mixture of 78- and 79-OH with Jones reagent gave 1-methyl-*anti*-7-chloro-2-norbornanone (82) and 1-methyl-*syn*-7-chloro-2-norbornanone (83) in the ratio 77:23. Spectral data were consistent with



82



83

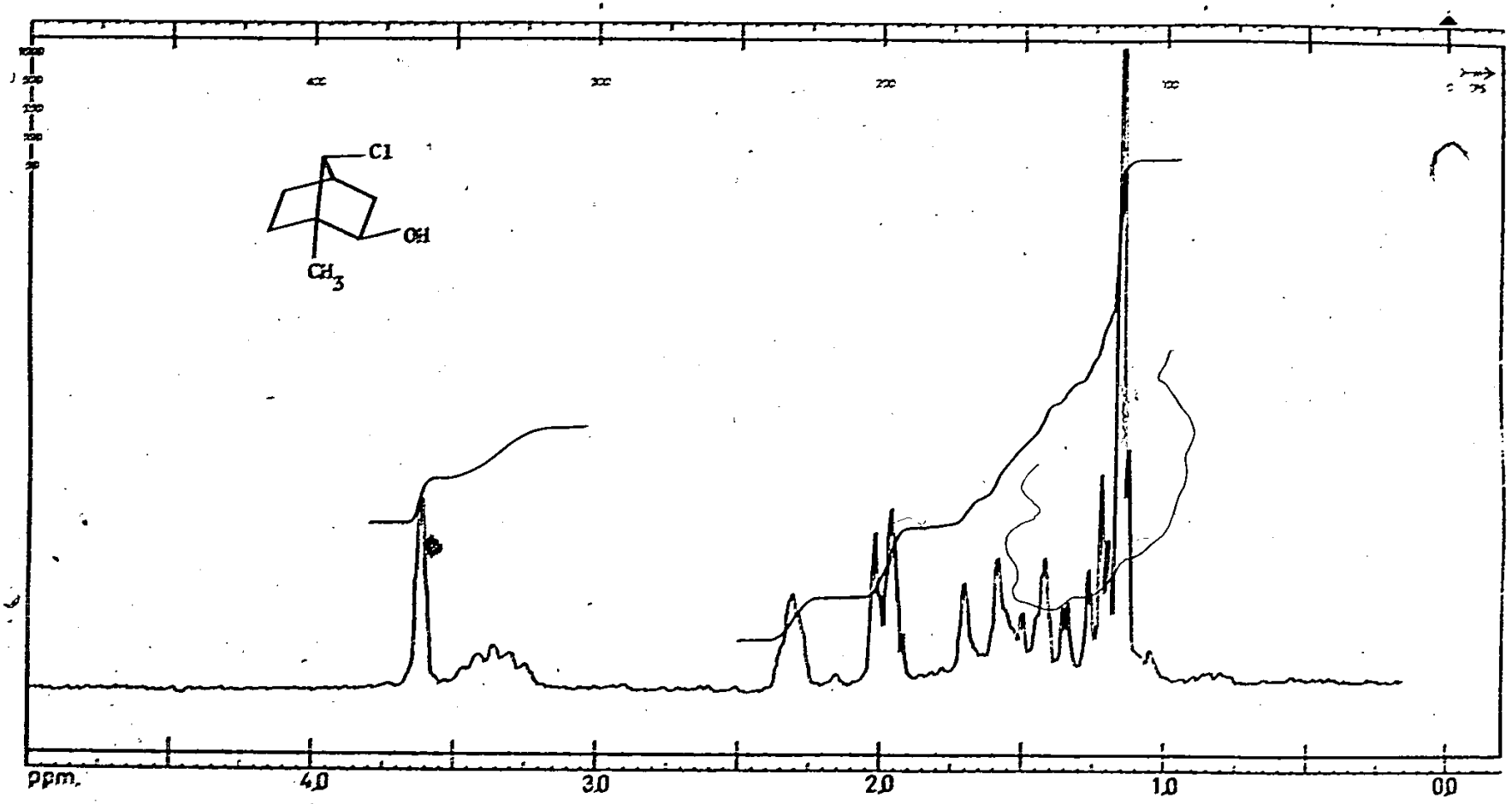


Figure 2:9 Pmr spectrum (100 MHz) of 1-methyl-*syn*-7-chloro-*exo*-2-norbornanol (79-OH) in CCl_4

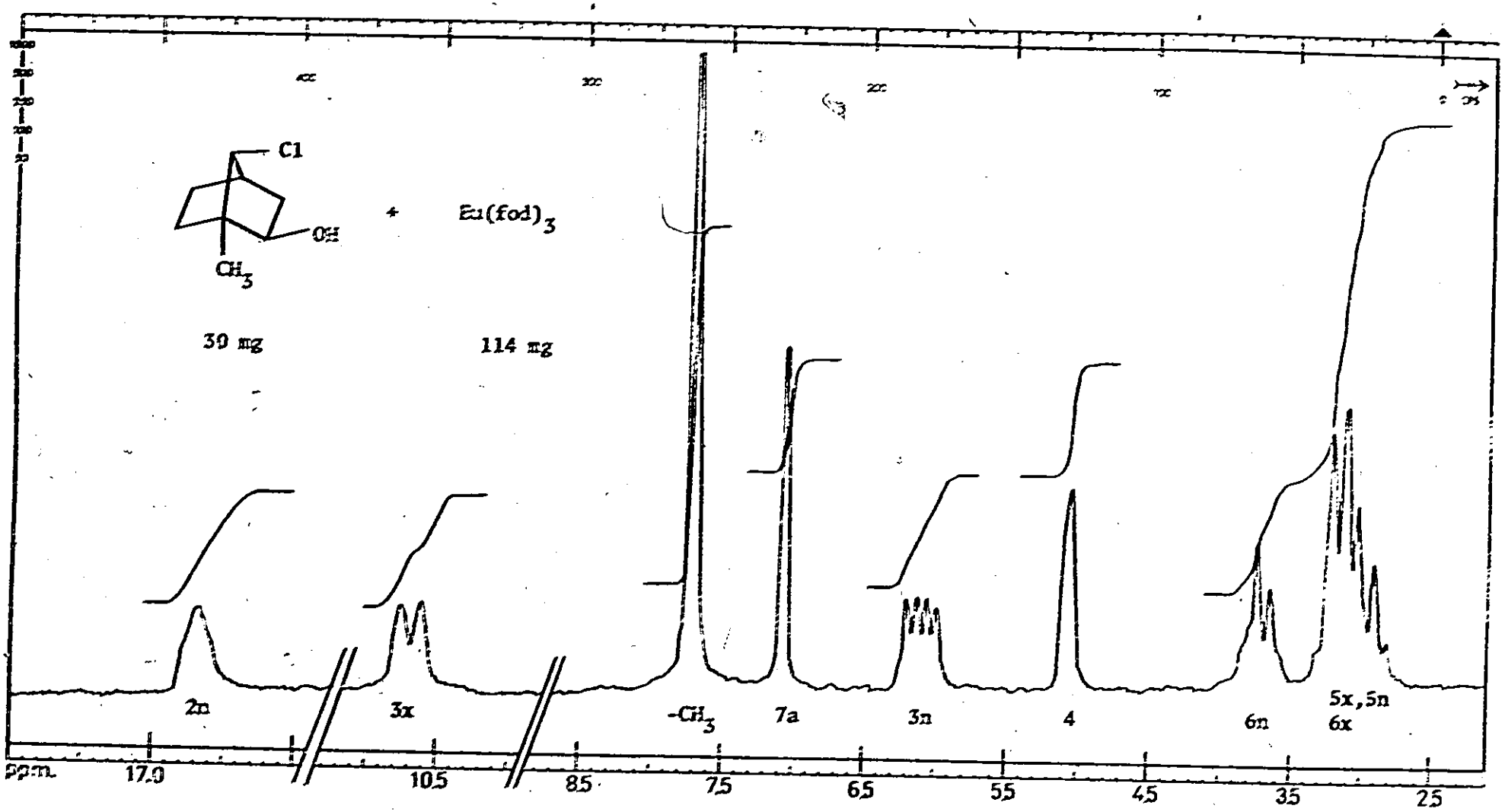


Figure 2:10 Pmr spectrum (100 MHz) of 1-methyl-*syn*-7-chloro-*exo*-norbornanol (79-OH) plus $Eu(fod)_3$ in CCl_4

these structures (see Chapter 5).

3) Cleavage with Deuterated Acid

Treatment of 25 with acetic acid-d_4 and 0.10M sulphuric acid-d_2 for 60 hr at 65° gave 73% 1-methyl-*anti*-7-chloro-*exo*-2-norbornyl trideuteroacetate-*d* (78-trideuteroacetate-*d*) and 27% 1-methyl-*syn*-7-chloro-*exo*-2-norbornyl trideuteroacetate-*d* (79-trideuteroacetate-*d*). This mixture of chloro acetates was reduced with lithium aluminum hydride to 1-methyl-*anti*-7-chloro-*exo*-2-norbornanol-*d* (78-OH-*d*) and 1-methyl-*syn*-7-chloro-*exo*-2-norbornanol-*d*(79-OH-*d*) and then the positions and stereochemistries of deuterium substitution were determined along with the degree of deuterium incorporation. These alcohols were complexed with Eu(fod)$_3$ in carbon tetrachloride and then analyzed by both proton and deuterium magnetic resonance (pmr and dmr) spectroscopy.

4) Stereochemistry of Electrophilic Attack

For 78-OH-*d* (mole ratio LSR/alcohol = 0.88), pmr (Figure 2:11) and dmr (Figure 2:12) analyses revealed that deuterium was distributed as shown in Table 2:4. Mass spectral deuterium assay on 82-*d* which was obtained by oxidation of 78-OH-*d** showed that it contained an average of 1.29 deuterium atoms per molecule (5% d_0, 67% d_1, 22% d_2, 6% d_3).

Similarly 79-OH-*d* was complexed with shift reagent (mole ratio LSR/alcohol = 0.74) and pmr (Figure 2:13) along with dmr (Figure 2:14)

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* It must be emphasized that this reaction removes any deuterium which might have originally been present at the C-2 position of the chloro alcohol.

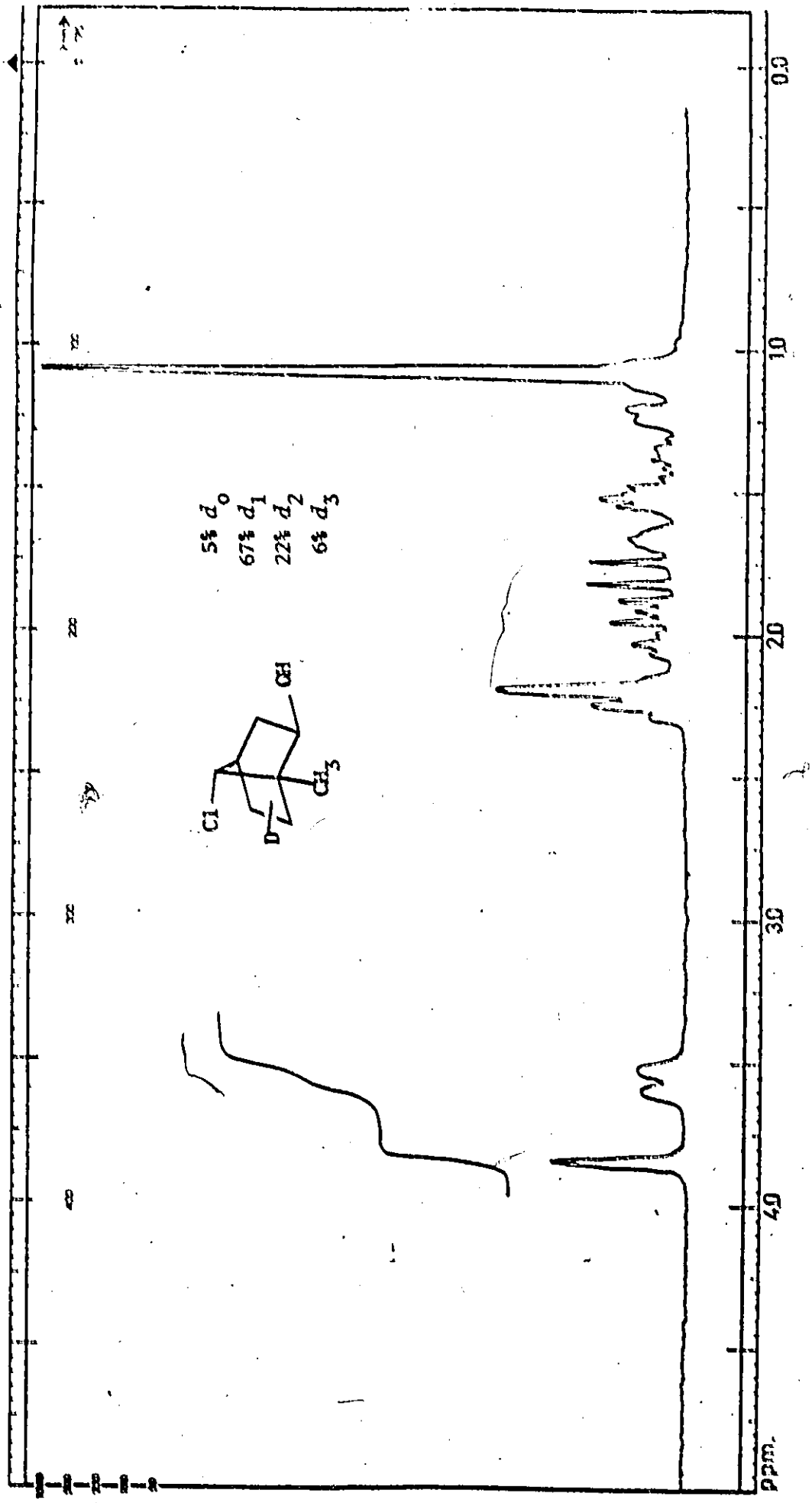


Figure 2:11a Pmr spectrum (100 MHz) of 1-methyl-*anti*-7-chloro-*exo*-2-norbornanol-*d* in CCl_4

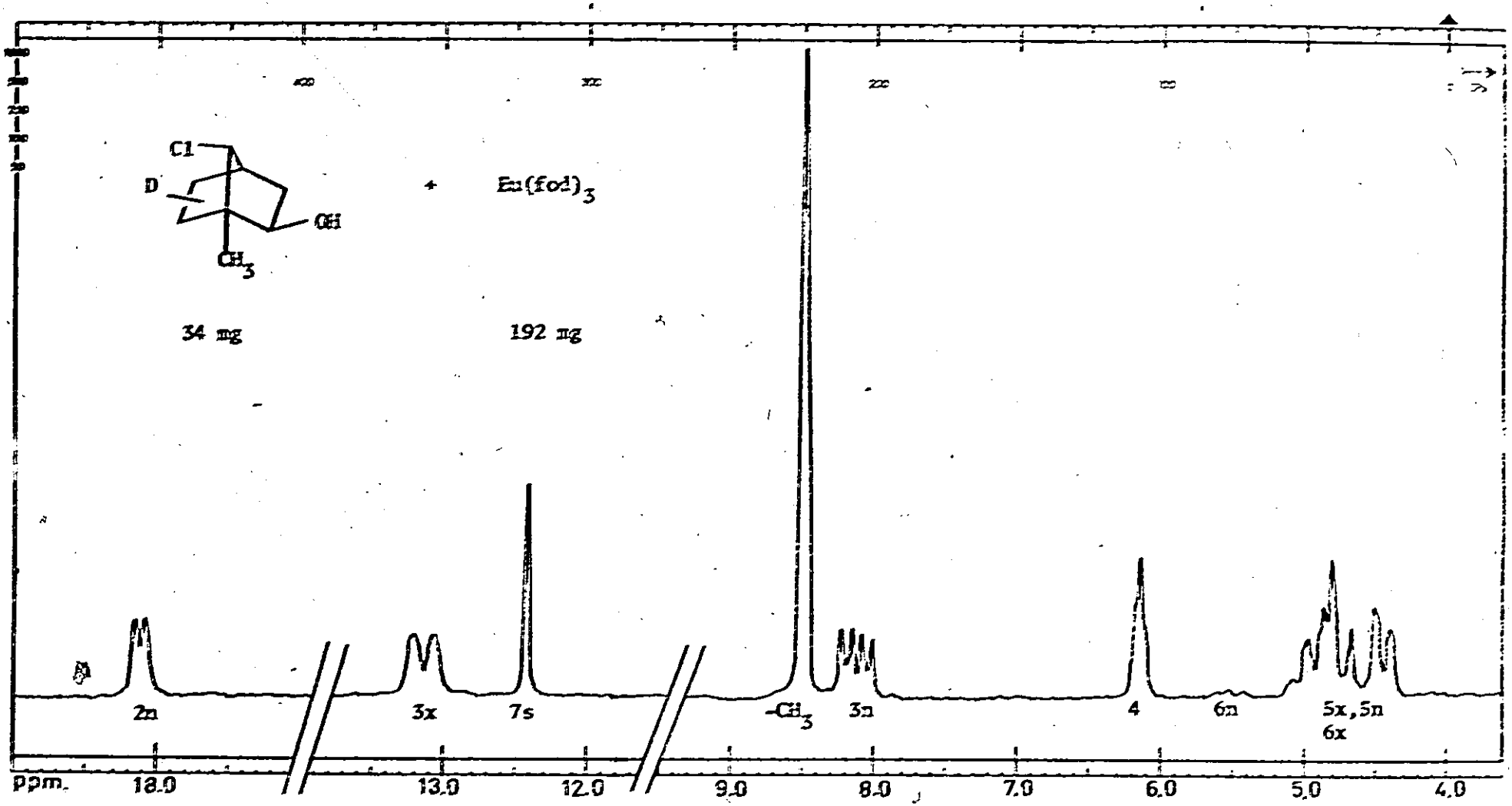


Figure 2:11b Pmr spectrum (100 MHz) of 1-methyl-*anti*-7-chloro-*exo*-2-norbornanol-*d* plus $Eu(fod)_3$ in CCl_4

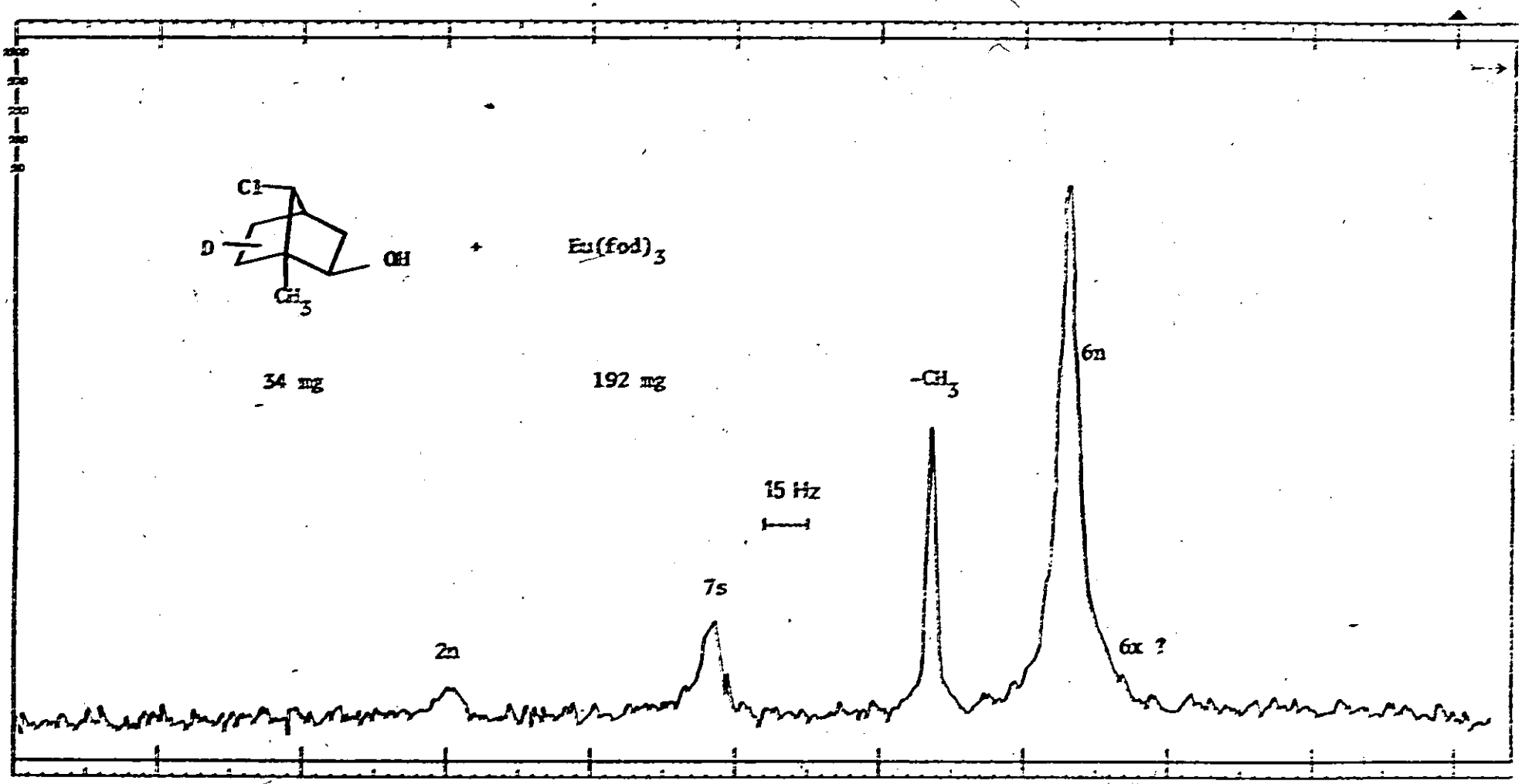


Figure 2:12 Dmr spectrum of 1-methyl-*anti*-7-chloro-*exo*-2-norbornanol-*d* plus $Eu(fod)_3$ in C_6H_6 and $CHCl_3$

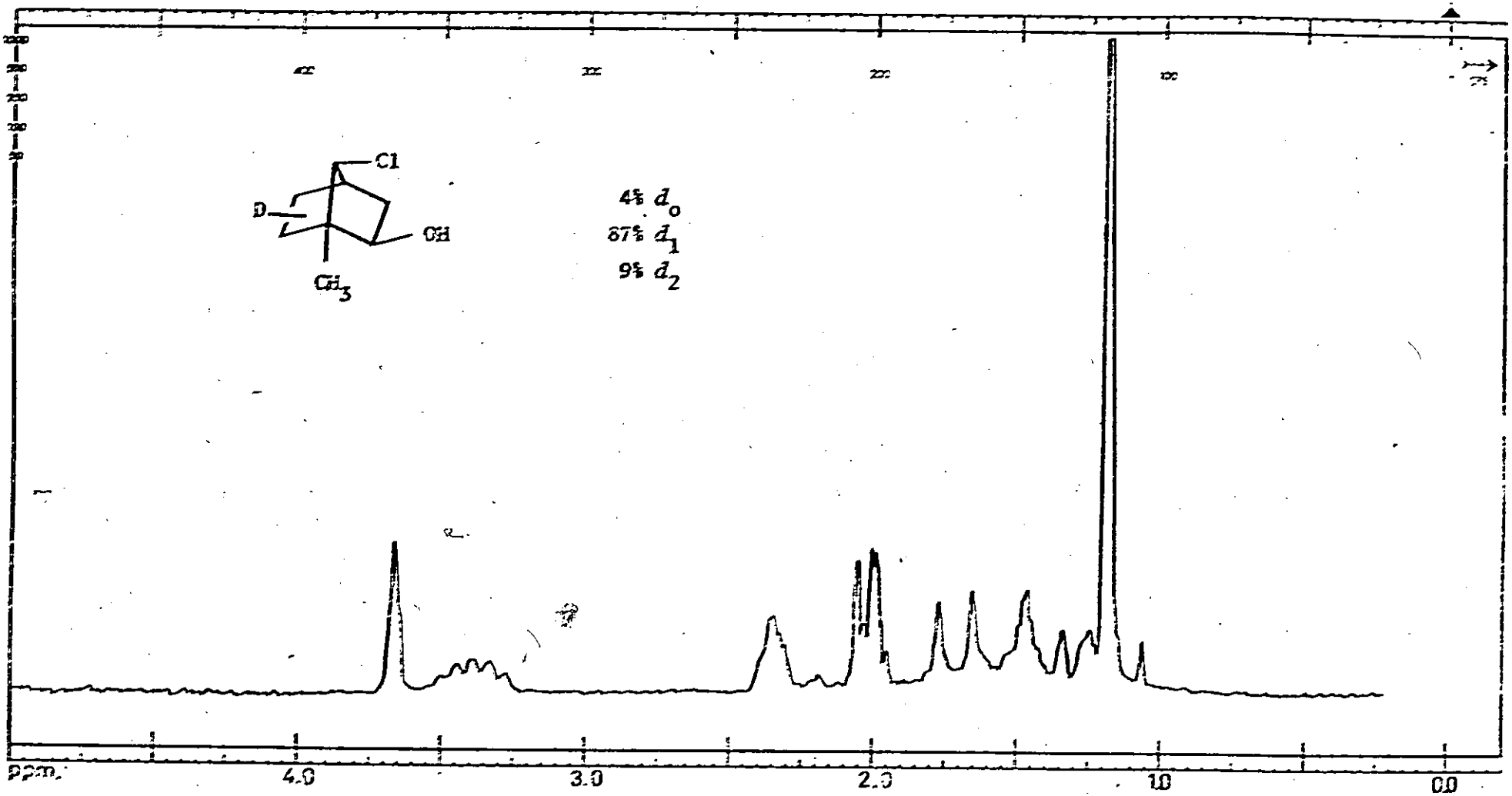


Figure 2:13a Pmr spectrum (100 MHz) of 1-methyl-*syn*-7-chloro-*exo*-2-norbornanol-*d* in CCl_4

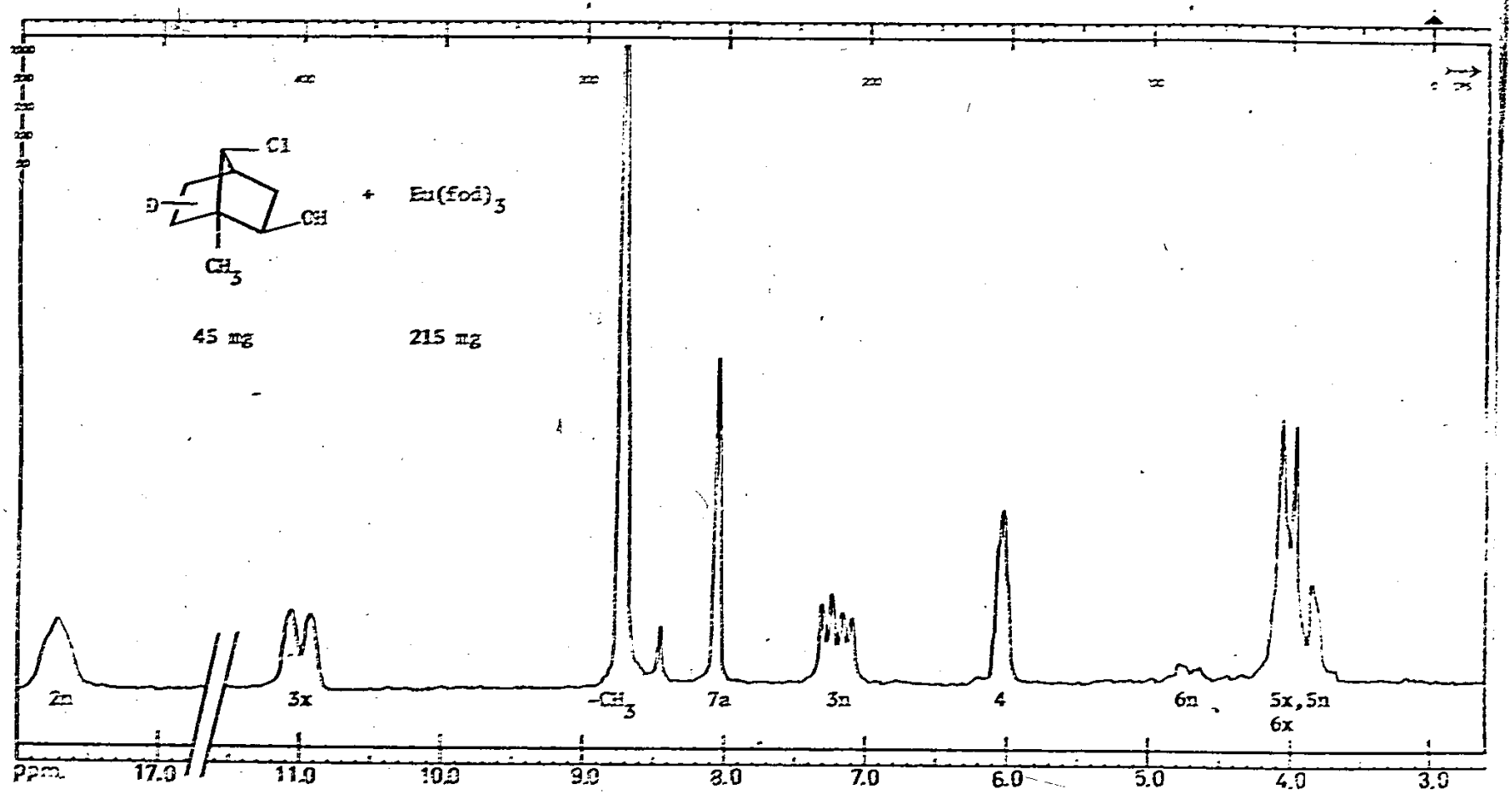


Figure 2:13b Pmr spectrum (100 MHz) of 1-methyl-*syn*-7-chloro-*exo*-2-norbornanol-*d* plus $Eu(fod)_3$ in CCl_4

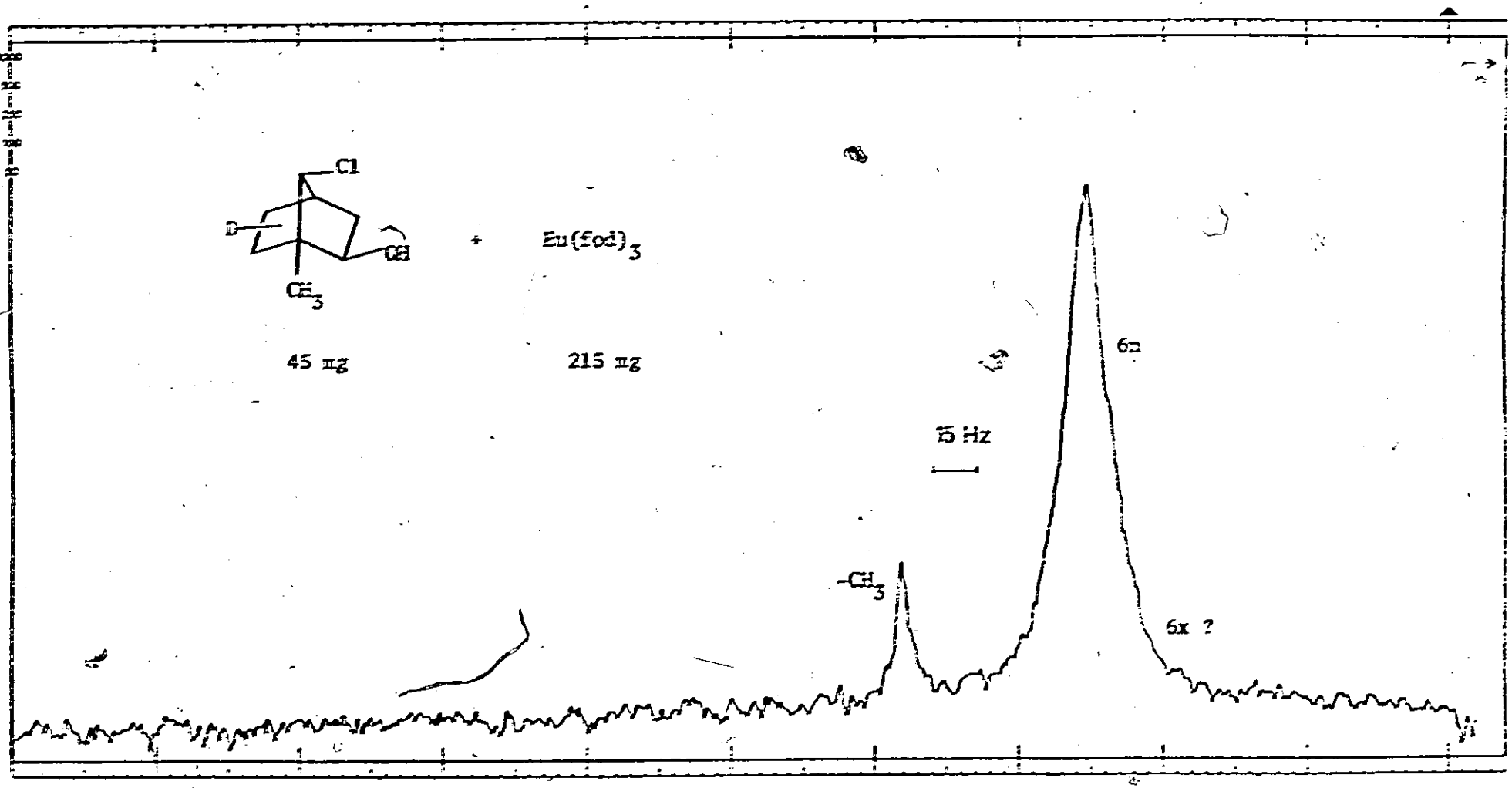
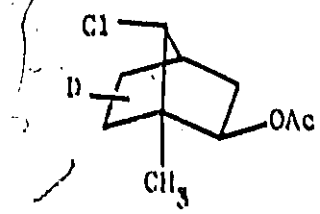
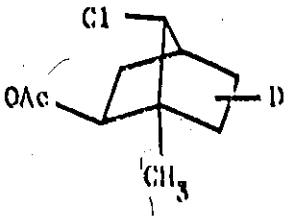


Figure 2:14 Pmr spectrum of 1-methyl-*syn*-7-chloro-*exo*-2-norbornanol-*d* plus $Eu(fod)_3$ in C_6H_6 and $CHCl_3$

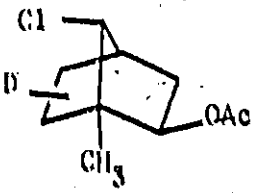
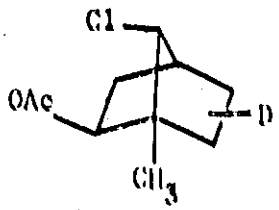
analyses established that the deuterium was distributed as shown in Table 2:4. Oxidation of 79-OH-*d* gave a sample of 83-*d* which was found to contain an average of 1.05 deuterium atoms per molecule (4% d_0, 87% d_1, 9% d_2).

Table 2:4 Distribution of Deuterium in the Products from Electrophilic Cleavage (CD_3CO_2D, D_2SO_4) of 2-methyl-3-chloronortricyclene (25)

a) Determination of Labelled Sites by Proton Magnetic Resonance Spectroscopy (pmr)

Compound	Deuterium Content and Position				
	$-CH_3$	C-2	C-6		C-7
			exo	*endo*	
	0.17±0.03	0.05±0.02	0.04±0.02	0.83±0.03	0.13±0.03
	0.11±0.02		0.06±0.03	0.88±0.06	

b) Determination of Labelled Sites by Deuterium Magnetic Resonance Spectroscopy (dmr)

Compound	Deuterium Content and Position				
	$-CH_3$	C-2	C-6		C-7
			exo	*endo*	
	0.22±0.02	0.05±0.01	0.88±0.05[a]		0.14±0.01
	0.09±0.01	-	0.96±0.04[a]		-

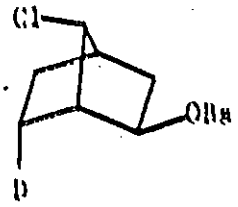
[a] These two resonances were not resolved from each other and hence this number represents total deuterium at C-6.

γ-Hydrogen Deuterium Isotope Effects in Bicyclo(2.2.1)heptanes

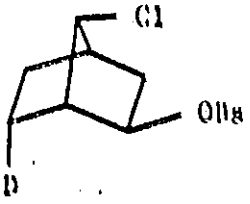
A. Syntheses

For our studies on γ-isotope effects in bicyclic systems, it was decided to investigate the solvolytic behaviour of some isomeric 7-chloro-2-norbornyl brosylates-6-*d*. In two cases it was necessary to use brosylates which were specifically labelled at both C-5 and C-6 with deuterium. KIHs were measured for the solvolyses of

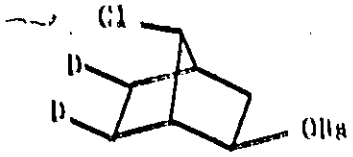
1. *anti*-7-chloro-*exo*-2-norbornyl brosylate-*endo*-6-*d* (58-OBs-*endo*-6-*d*),
2. *syn*-7-chloro-*exo*-2-norbornyl brosylate-*endo*-6-*d* (59-OBs-*endo*-6-*d*),
3. *anti*-7-chloro-*exo*-2-norbornyl brosylate-*exo*,*exo*-5,6-d_2 (58-OBs-*exo*,*exo*-5,6-d_2),
4. *syn*-7-chloro-*exo*-2-norbornyl brosylate-*exo*,*exo*-5,6-d_2 (59-OBs-*exo*,*exo*-5,6-d_2), and
5. *anti*-7-chloro-*endo*-2-norbornyl brosylate-*endo*-6-*d* (84-OBs-*endo*-6-*d*).



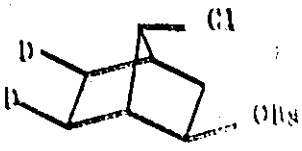
58-OBs-*endo*-6-*d*



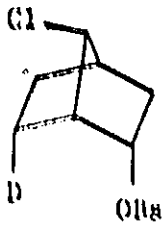
59-OBs-*endo*-6-*d*



58-OBs-*exo*,*exo*-5,6-d_2



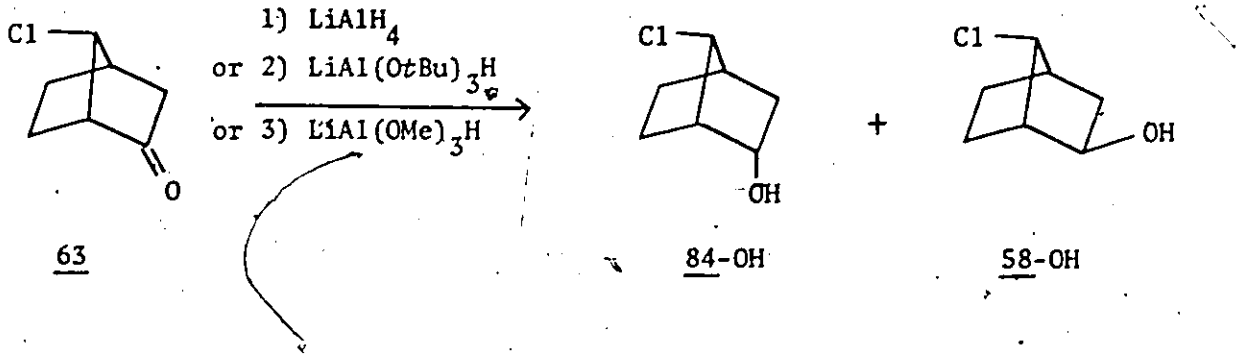
59-OBs-*exo*,*exo*-5,6-d_2



84-OBs-*endo*-6-*d*

In all cases, the brosylates were prepared by treatment of the corresponding alcohols with brosyl chloride in pyridine. Therefore only the syntheses of the appropriate bicyclic alcohols will be described. Each alcohol was purified by glpc before preparation of the brosylate and it was assumed that the brosylation reaction did not alter the stereochemistry of deuterium.

Compounds 58- and 59-OH were prepared by the literature method of Roberts[178] and their nmr spectra appear in Chapter 6 (Figures 6:2 and 6:3). For the preparation of the known alcohol 84-OH,[176] the chloro ketone 63 was reduced with lithium tri-*t*-butoxyaluminum hydride. Surprisingly, this reaction gave a 92:8 mixture of 84-OH and 58-OH which is quite similar to the ratio of 90:10 which was obtained by Gassman[176] when lithium aluminum hydride was used as the reducing agent and identical to the ratio of 92:8



63 84-OH 58-OH

obtained with lithium trimethoxyaluminum hydride. The similar stereochemical outcome for reduction with lithium trimethoxyaluminum and tri-*t*-butoxyaluminum hydrides has been attributed to the tendency of the former compound to form aggregate dimeric or trimeric species.[208] Glpc was the most effective method for purification of 84-OH. In the nmr spectrum of 84-OH (Figure 6:4,

Chapter 6), a quintet (with fine structure) at δ 4.00 was attributed to the proton at *exo*-C-2 whereas the proton at *syn*-C-7 appeared as a broad singlet at δ 3.70 (*cf* in 58-OH, the protons at *endo*-C-2 and *syn*-C-7 resonate at δ 3.75 and 4.19 respectively).

For the deuterated alcohols, the degree of deuterium incorporation was assayed by mass spectrometry. However, since the mass spectra of the alcohols displayed weak parent ions due to the loss of water, it was felt that analysis for deuterium on the corresponding ketones would provide a more reliable indication of the extent of deuteration. Problems with this approach could arise if deuterium is present alpha to the hydroxy group (C-2) but in all cases the absence of deuterium at C-2 in the alcohols was ascertained by nmr spectroscopy.

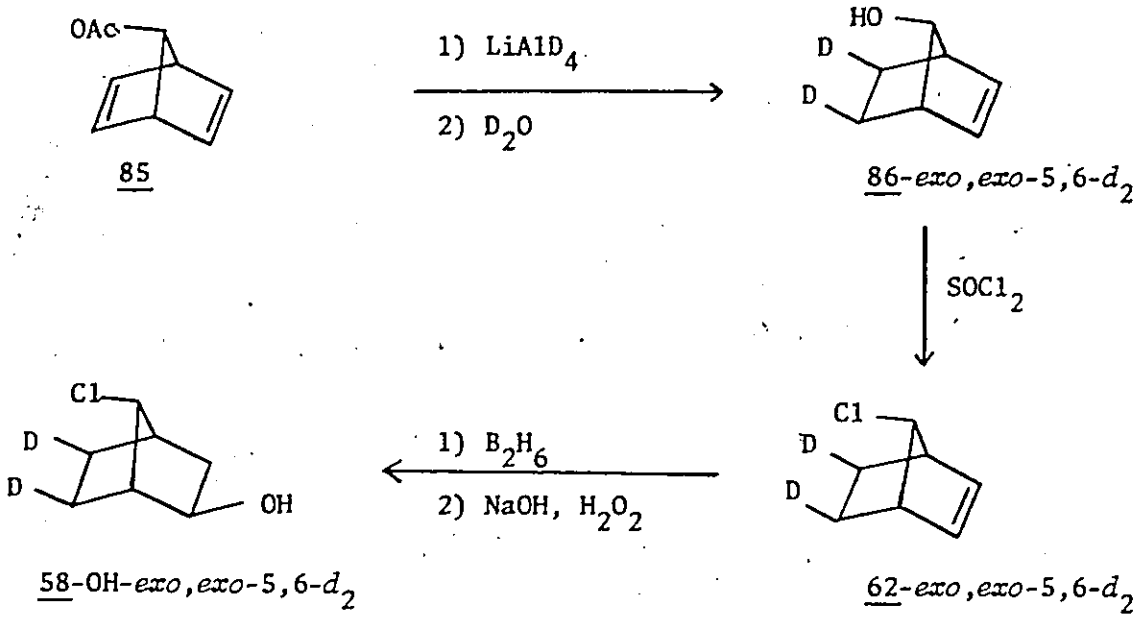
Reduction with lithium aluminum hydride of 58-trideuteroacetate-*endo*-6-*d* gave 58-OH-*endo*-6-*d* which was found to contain an average of 0.99 deuterium atoms per molecule. The nmr spectrum of this alcohol is presented elsewhere (Figure 6:5, Chapter 6).

Similarly, 59-OH-*endo*-6-*d* was prepared by the reduction with lithium aluminum hydride of 59-trideuteroacetate-*endo*-6-*d* and it contained 0.97 deuterium atoms per molecule. Both 58- and 59-trideuteroacetates-*endo*-6-*d* were obtained as the major products from the electrophilic cleavage of 24 with acetic acid-d_4 and sulphuric acid-d_2.

In the first step towards the synthesis of 58-OH-*exo*,*exo*-5,6-d_2,7-acetoxynorbornadiene (85) was treated with lithium aluminum deuteride and then the aluminum salts were decomposed with deuterium oxide and then

the alcohol was washed with water to produce *anti*-7-norbornenol-*exo*,*exo*-5,6-d_2 (86-*exo*,*exo*-5,6-d_2).[209,210]

Scheme 2:1 Synthesis of *anti*-7-chloro-*exo*-2-norbornanol-*exo*,*exo*-5,6-d_2 (58-OH-*exo*,*exo*-5,6-d_2)



85

86-*exo*,*exo*-5,6-d_2

58-OH-*exo*,*exo*-5,6-d_2

62-*exo*,*exo*-5,6-d_2

Alcohol 86-*exo*,*exo*-5,6-d_2 was converted to 62-*exo*,*exo*-5,6-d_2 by treatment with thionyl chloride.[182] The nmr spectrum of the chloride (Figure 6:6, Chapter 6) showed that the deuterium at C-5 and C-6 was at least 93% stereochemically pure *exo*. Deuterium assay showed that the chloride contained an average of 1.83 deuterium atoms per molecule and nmr integration showed that 0.12 hydrogen atom was present at *exo*-C-5 and *exo*-C-6. Hydroboration of 62-*exo*,*exo*-5,6-d_2 and subsequent oxidation of the organoborane with alkaline hydrogen peroxide resulted in a 90% yield of *anti*-7-chloro-*exo*-2-norbornanol-*exo*,*exo*-5,6-d_2

(58-OH-*exo*,*exo*-5,6-d_2). Its nmr spectrum (Figure 6:7, Chapter 6) showed a broad singlet with fine structure at δ 4.16 (*syn*-C-7) and a doublet of doublets (J = 3 and 7 Hz) at δ 3.75 (*endo*-C-2). For the latter resonance, the small coupling was attributed to *trans* vicinal coupling with the proton at *exo*-C-3 and the larger coupling arose from *cis* vicinal coupling with the proton at *endo*-C-3. Resonances due to the bridgehead protons at C-1 and C-4 appeared at δ 2.11 as a broad singlet and at δ 2.24 as a doublet (J = 4 Hz) respectively. The resonances due to the protons at *exo*-C-3 and *endo*-C-3 formed an AB quartet. A doublet of doublets (J = 7 and 13 Hz) at δ 1.75 constituted the lower field portion of the AB quartet which arose from the proton at *endo*-C-3. Large geminal coupling (13 Hz) with *exo*-C-3 and smaller *cis* vicinal coupling (7 Hz) to *endo*-C-2 accounted for the multiplicity of the peak. Moreover, a doublet of triplets (J = 3 and 13 Hz) centered at δ 1.40 which comprised the high field portion of the AB quartet was attributed to the proton at *exo*-C-3. Once again, large geminal coupling (13 Hz) with *endo*-C-3 and smaller *trans* vicinal coupling (3 Hz) with *endo*-C-2 could account for the multiplicity. At highest relative field, δ 1.05, there appeared a broad singlet due to the two protons at *endo*-C-5 and *endo*-C-6.

For the synthesis of 59-OH-*exo*,*exo*-5,6-d_2, hypochlorous acid was added to norbornene-*endo*,*endo*-5,6-d_2 (87-*endo*,*endo*-5,6-d_2). Olefin 87-*endo*,*endo*-5,6-d_2 was prepared by a four step scheme starting with norbornadiene as shown in Scheme 2:2. Addition of deuterium gas to norbornadiene gave 71% norbornene-*exo*,*exo*-5,6-d_2 (87-*exo*,*exo*-5,6-d_2),

17% norbornane-*exo*, *exo*, *exo*', *exo*'-d_4 and 12% starting material.[211] Bromination of this mixture in methylene chloride gave *syn*-7-*exo*-2-dibromonorbornane-*endo*, *endo*-5,6-d_2 (88-*endo*, *endo*-5,6-d_2) as one of the products.[212] Treatment of this deuterated dibromide with potassium-*t*-butoxide in *t*-butanol for 33 hr at reflux gave a 70% yield of *syn*-7-bromonorbornene-*endo*, *endo*-5,6-d_2 (89-*endo*, *endo*-5,6-d_2). The nmr spectrum of 89-*endo*, *endo*-5,6-d_2 was consistent with that which has been reported[212] and furthermore the integration showed that the deuterium at

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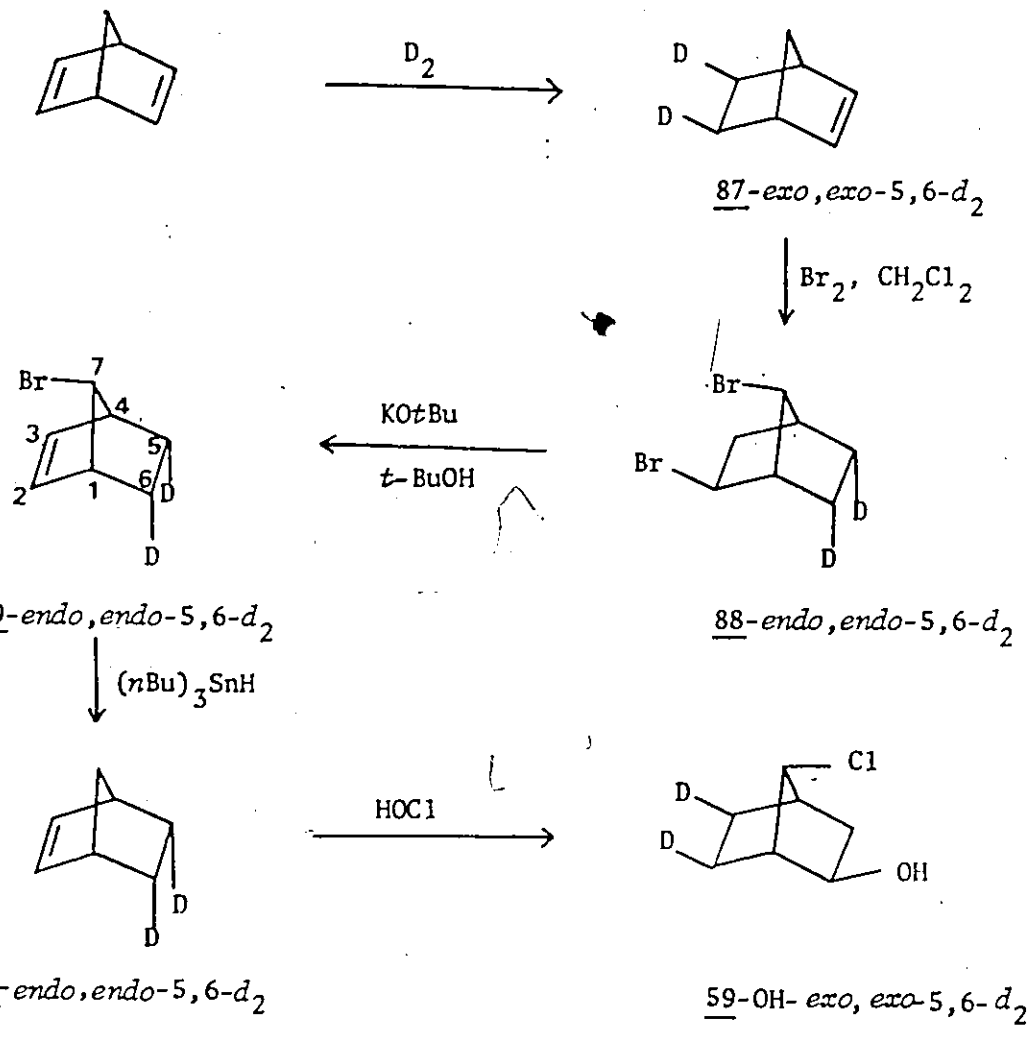
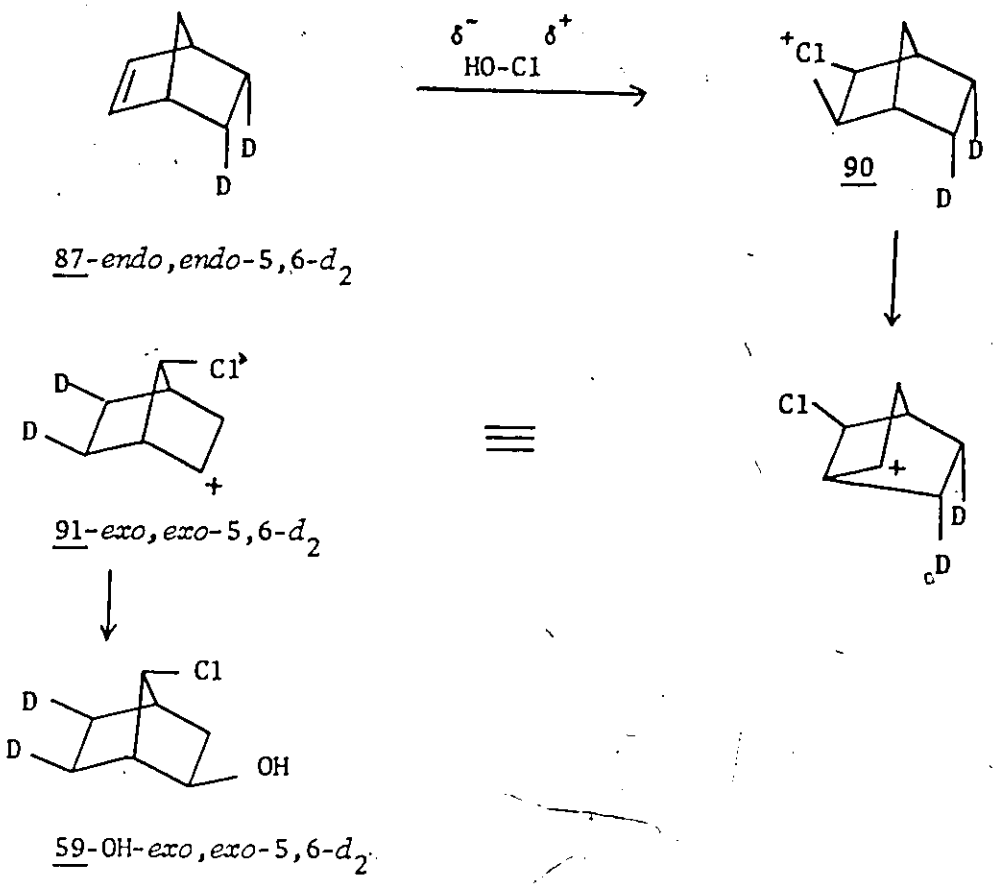
Scheme 2:2 Synthesis of *syn*-7-chloro-*exo*-2-norbornanol-*exo*, *exo*-5,6-d_2 (59-*exo*, *exo*-5,6-d_2)



C-5 and C-6 was at least 92% stereochemically pure *endo*. It was also found that 0.08 hydrogen atom remained at the *endo*-C-5 and *endo*-C-6 positions. When tri-*n*-butyl tin hydride[213] was caused to react with 89-*endo*,*endo*-5,6-d_2 in a sealed tube for 36 hr at steam bath temperature,[212] 87-*endo*,*endo*-5,6-d_2 was formed in 75% yield based on the bromide and 7% overall yield based on norbornadiene. Deuterium assay by mass spectrometry revealed that the deuterated olefin contained an average of 1.90 deuterium atoms per molecule. Finally, treatment of 87-*endo*,*endo*-5,6-d_2 with hypochlorous acid[178] gave the desired chloro alcohol 59-OH-*exo*,*exo*-5,6-d_2. This reaction inverts the stereochemistry of deuterium at C-5 and C-6 from

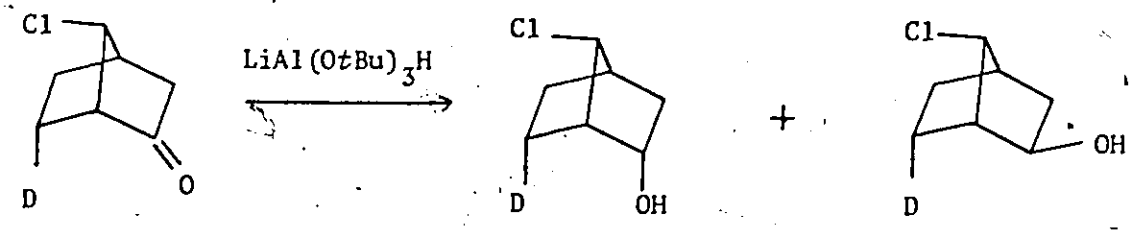


Scheme 2:3 Addition of Hypochlorous Acid to norbornene-*endo*,*endo*-5,6-d_2

endo,endo to *exo,exo via* an alkyl shift (Scheme 2:3). Addition of chlorine to the deuterated olefin 87 yields a species probably resembling 90 which can undergo a Wagner-Meerwein rearrangement to 91* and then be captured by solvent. Even if cation 91 undergoes a 2,6 *endo,endo*-hydride shift, this would not present any problems because capture by solvent would produce the *anti*-alcohol 58-OH-*d*. In other words, the *syn*-alcohol 59-OH-*exo*, *exo*-5,6-d_2 can only arise by one stereochemical pathway.

Additional proof for the deuterium stereochemistry in 59-OH-*exo*, *exo*-5,6-d_2 came from its nmr spectrum (Figure 6:8, Chapter 6). A two proton broad singlet at δ 1.11 was attributed to the protons at *endo*-C-5 and *endo*-C-6 whereas the multiplet due to the *exo*-C-5 and *exo*-C-6 protons at δ 1.52 was missing in the spectrum of the deuterated compound. Deuterium assay by mass spectrometry on the corresponding chloro ketone 64-*exo,exo*-5,6-d_2 showed that it contained an average of 1.84 deuterium atoms per molecule.

For the preparation of 84-OH-*endo*-6-*d*, the known chloro ketone 63-*endo*-6-*d* was reduced with lithium tri-*t*-butoxyaluminum hydride. The alcohol was separated from small amounts of 58-OH-*endo*-6-*d* by glpc. It



63-*endo*-6-*d* 84-OH-*endo*-6-*d* 58-OH-*endo*-6-*d*

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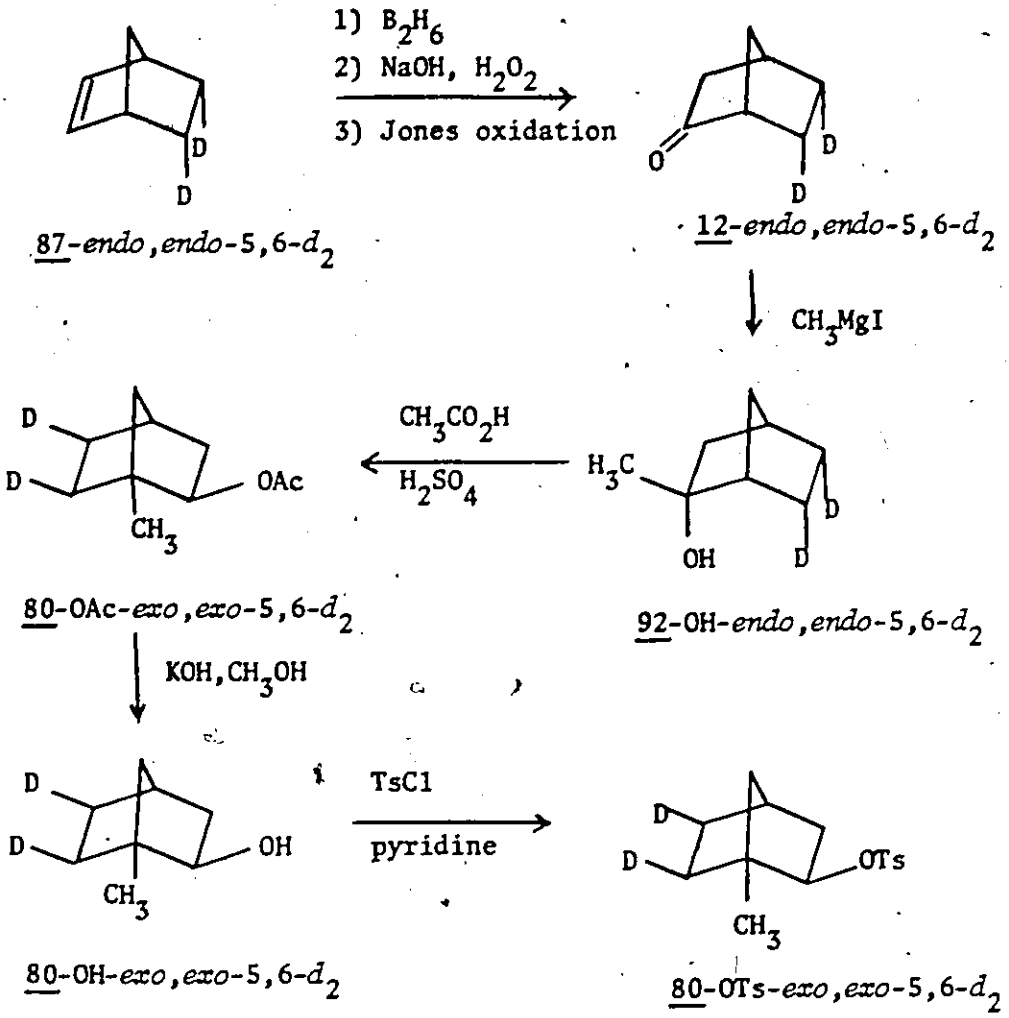
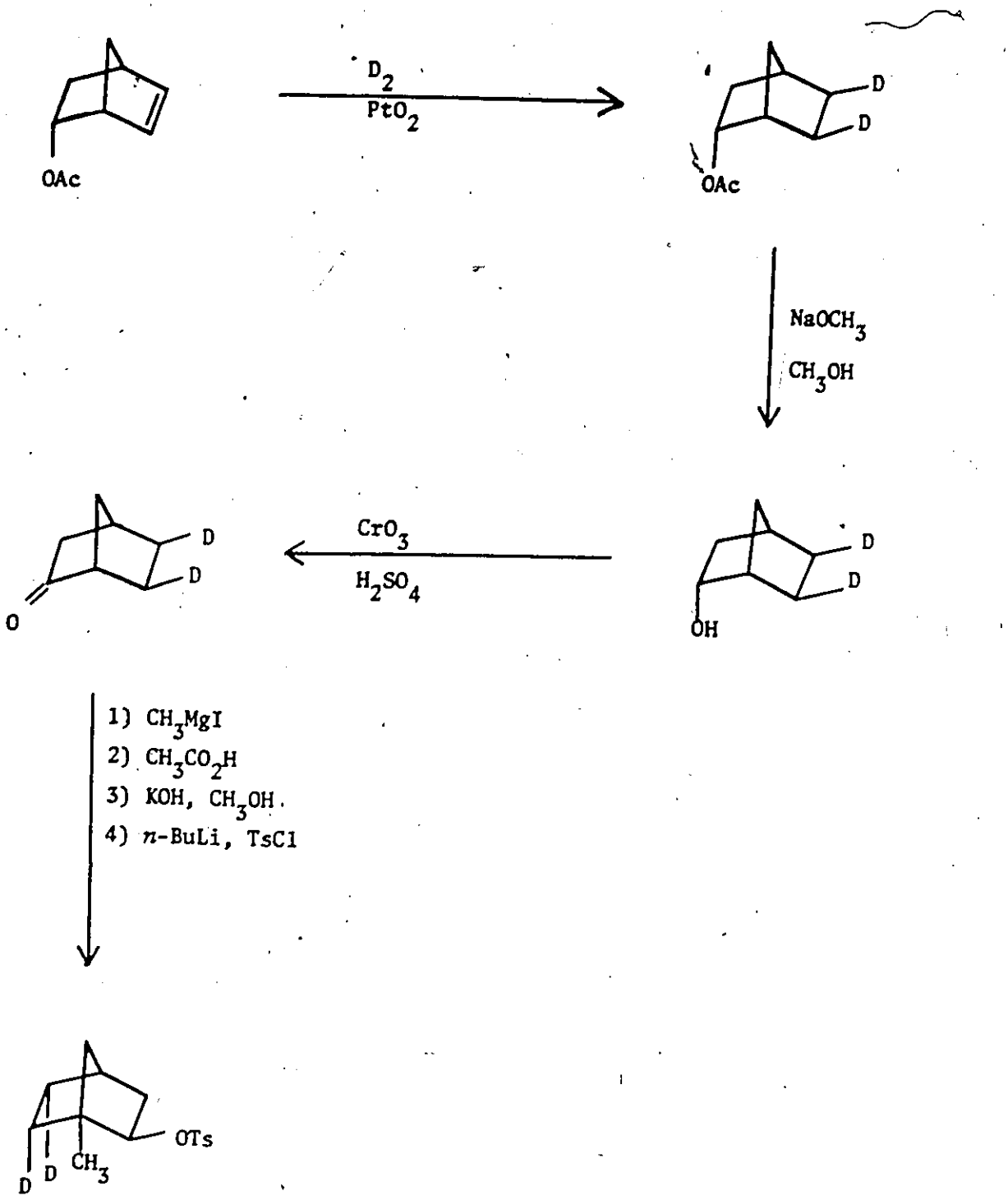
* This structure is *not* intended to represent an opinion on the norbornyl cation controversy.

was not possible to ascertain the position and stereochemistry of deuterium in 84-*endo*-6-*d* by nmr spectroscopy (Figure 6:9, Chapter 6). A quintet with fine structure centered at δ 4.00 indicated that the proton at C-2 was *exo*. It was assumed that in the reduction of the known chloro ketone 63-*endo*-6-*d*, the stereochemical integrity of the deuterium was maintained.

As part of these studies on γ-isotope effects in bicyclic systems,

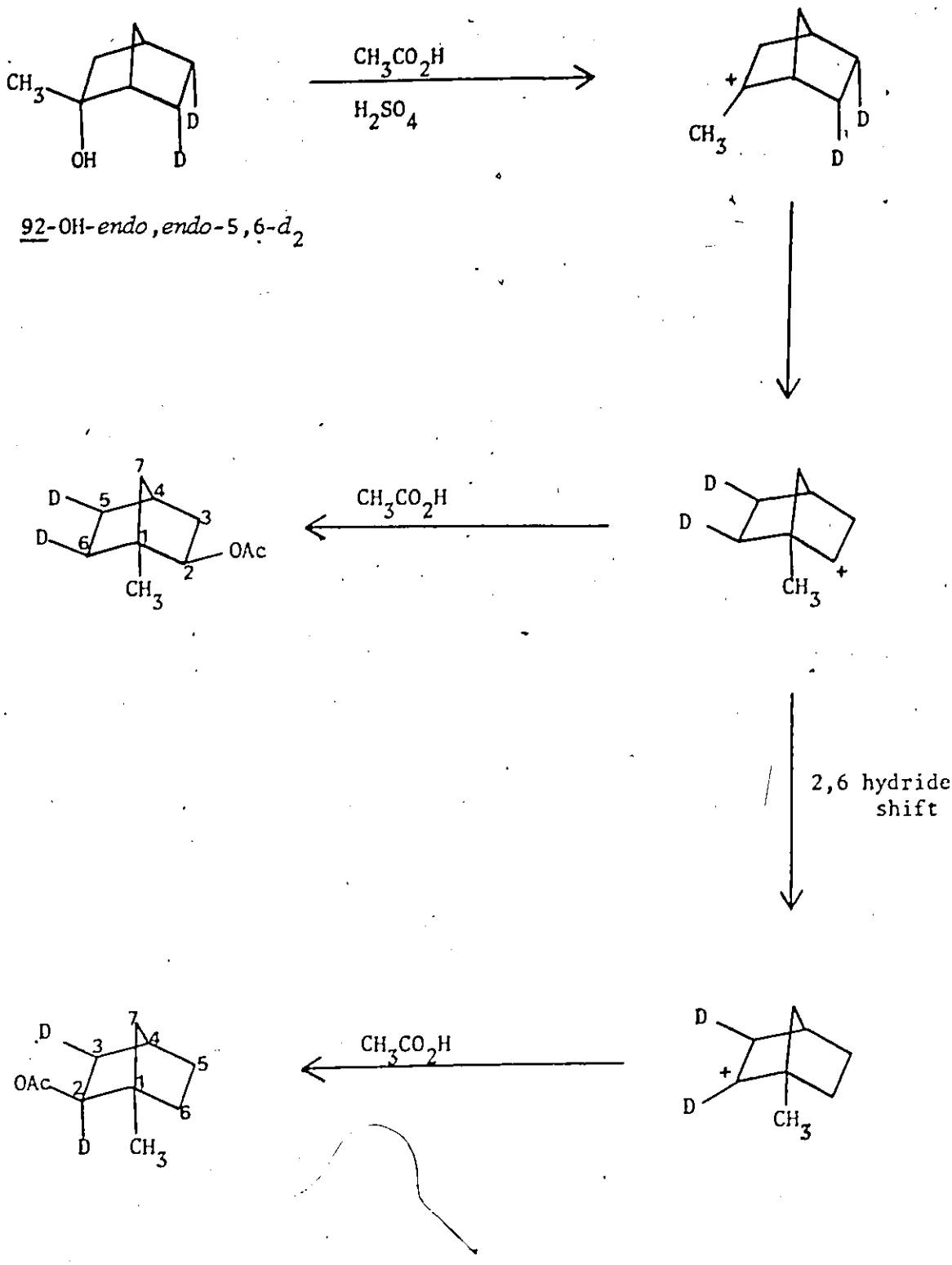


Scheme 2:4 Synthesis of 1-methyl-*exo*-2-norbornyl tosylate-*exo*,*exo*-5,6-d_2



80-OTs-*endo*,*endo*-5,6-d_2

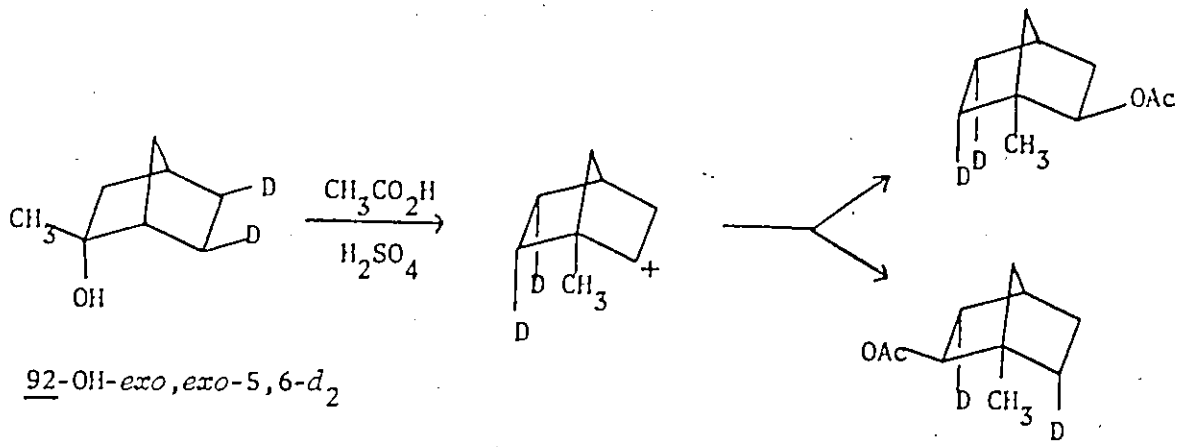
Scheme 2:5 Synthesis of 1-methyl-*exo*-2-norbornyl tosylate-*endo*,*endo*-5,6-d_2[214]



92-OH-*endo*,*endo*-5,6-d_2

Scheme 2:6 Deuterium scrambling during the acid catalyzed rearrangement of *exo*-2-methyl-*endo*-2-norbornanol-*endo*,*endo*-5,6-d_2

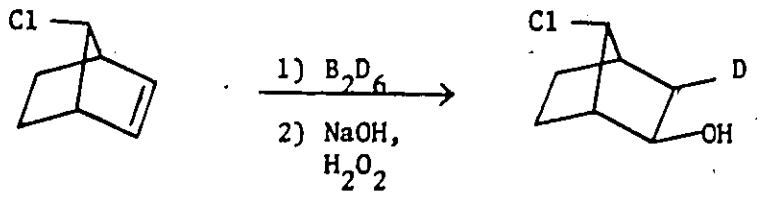
an attempt was made to prepare 1-methyl-*exo*-2-norbornyl tosylate-*exo*, *exo*-5,6-d_2 (80-OTs-*exo*,*exo*-5,6-d_2) by the route in Scheme 2:4 which is similar to the route used by Jerkunica[214] for the preparation of 80-OTs-*endo*, *endo*-5,6-d_2 (Scheme 2:5). As shown in Scheme 2:4, the deuterated ketone 12-*endo*,*endo*-5,6-d_2 was prepared from 87-*endo*,*endo*-5,6-d_2[212] by known reactions. Treatment of 12-*endo*,*endo*-5,6-d_2 with methyl magnesium iodide gave 92-OH-*endo*,*endo*-5,6-d_2[215,216] which was subsequently rearranged in acetic acid and sulphuric acid to 80-OAc-*exo*,*exo*-5,6-d_2.[215,216] Saponification of this acetate[41,217] with methanolic potassium hydroxide was expected to produce specifically labelled 80—OH-*exo*,*exo*-5,6-d_2. However, nmr analysis of the alcohol revealed that there was about 0.30 deuterium atom at *endo*-C-2. This arises *via* a 2,6 *endo*,*endo*-hydride shift during the acid catalyzed rearrangement of 92-OH-*endo*,*endo*-5,6-d_2 to 80-OAc-*exo*, *exo*-5,6-d_2 (Scheme 2:6). This rearrangement must also occur when 92-OH-*exo*, *exo*-5,6-d_2 is treated with acid and this also results in deuterium scrambling (Scheme 2:7). Thus, the value of the γ-KIE for solvolysis of " 80-OTs-*endo*,*endo*-5,6-d_2 " as prepared and measured by Jerkunica is suspect.[115a]



92-OH-*exo*,*exo*-5,6-d_2

Scheme 2:7 Deuterium scrambling during the acid catalyzed rearrangement of *exo*-2-methyl-*endo*-2-norbornanol-*exo*,*exo*-5,6-d_2

To complement the γ-KIE studies in bicyclic molecules, a preliminary investigation of a β-KIE was undertaken. In view of the availability of *anti*-7-chloronorbornene (62),[182] it was decided to prepare 58-OH-*exo*-3-*d*. Deuteroboration of 62 followed by oxidation of the



62 58-OH-*exo*-3-*d*

intermediate organoborane with alkaline hydrogen peroxide gave nearly quantitative conversion to 58-OH-*exo*-3-*d*. In the nmr spectrum of 58-OH-*exo*-3-*d* (Figure 6:10, Chapter 6), the proton at *endo*-C-2 appeared at δ 3.77 as a doublet with J = 7 Hz (*cf* for 58-OH, the *endo*-C-2 proton appears as a doublet of doublets). This doublet arises from *cis* vicinal coupling; deuterium at *exo*-C-3 precludes smaller *trans* vicinal coupling. This stereochemical assignment of deuterium was confirmed by use of LSR. When $Eu(fod)_3$ was added to 58-OH (mole ratio LSR/alcohol = 0.55) in carbon tetrachloride, nmr spectroscopy showed that all the proton resonances, except those due to C-5 and C-6, were well resolved from each other (Figure 6:11, Chapter 6). All coupling constants and peak multiplicities were consistent with the assigned structure. Alcohol 58-OH-*exo*-3-*d* (37 mg) was complexed with 160 mg of $Eu(fod)_3$ (mole ratio LSR/alcohol = 0.61) in carbon tetrachloride and the nmr spectrum (Figure 6:12, Chapter 6) showed that the resonance due to the proton at *exo*-C-3 had disappeared. Furthermore,

at δ 6.60; the *endo*-C-3 proton resonated as a doublet (J = 7 Hz, *cis* vicinal coupling with the *endo*-C-2 proton). Deuterium assay (by mass spectrometry) on the corresponding chloro ketone 63-*exo*-3-*d* indicated that it contained an average of 0.93 deuterium atoms per molecule.

B. Isotope Effects for Solvolyses of 7-Chloro-2-norbornyl brosylates-6-*d*

The γ-isotope effects were determined in 80:20 ethanol-water buffered with 0.04 M sodium acetate by simultaneously observing the solvolysis of the non-deuterated and deuterated chloro brosylates.[218] By monitoring changes in absorbance as a function of time, first order rate constants (k) were calculated by a least squares program from the $-\ln(A_t-A_\infty)$ vs time graphs where A_t is absorbance at time t and A_∞ is absorbance at time infinity (usually ~ 10 half-lives). The derivation and validity of this relationship are discussed in Chapter 6. This method was used for the various deuterated analogs of 58- and 59-OBs. Due to the unreactive solvolytic behaviour of 84-OBs at 80° ($t_{½}$ ≈ 12 hr), it was impractical to spectrophotometrically determine A_∞. The reaction rate constants for solvolysis of 84-OBs were determined by a computer program[219] which fits absorbance and time data to an equation of the form

$$A_t = be^{-kt} + d$$

where b and d are constants. Thus, the best k was obtained for a given set of (t, A_t).

For all the compounds which were studied, linear first-order plots were obtained. Runs with deuterated substrates were carried out only after control runs with the non-deuterated substrates consistently gave identical

rate constants ie $k_H/k_H = 1.00 \pm 0.01$. Table 2:5 summarizes the deuterium content of the chloro brosylates and Table 2:6 lists the γ-KIEs. Typical first-order plots for solvolysis of each substrate (non-deuterated vs non-deuterated and non-deuterated vs deuterated) are illustrated in Figures 2:15 - 2:34.

The β-KIE for solvolysis of 58-OBs-*exo*-3-*d* is shown in Table 2:7 and typical first-order plots are illustrated in Figures 2:35 - 2:36.

Table 2:5

Extent of Deuteration of Chloro Brosylates[a]

Compound	% d_0	% d_1	% d_2	average d/molecule
58-OBs-*endo*-6-d	4	95	1	0.97
59-OBs-*endo*-6-d	3	95	2	0.99
58-OBs-*exo*,*exo*-5,6-d_2	7	3	90	1.83
59-OBs-*exo*,*exo*-5,6-d_2	5	6	89	1.84
84-OBs-*endo*-6-d	4	95	1	0.97
58-OBs-*exo*-3-d	7	93	-	0.93

[a] Determined by mass spectrometry at low voltage on appropriate derivatives (see text)

Table 2:6

γ-Hydrogen Deuterium Isotope Effects for the Solvolysis of 7-Chloro-2-Norbornyl Brosylates-6-*d* in 80:20 Ethanol-Water[a]

Compound	k x 10^2 (min^{-1})[b]	k_H/k_D[c,d]	T[e]
58-OBs	2.056±0.004	1.11±0.01	60.0°
58-OBs-*endo*-6-*d*	1.846±0.002		
59-OBs	0.987±0.005	1.11±0.01	50.0°
59-OBs-*endo*-6-*d*	0.889±0.005		
58-OBs	1.652±0.004	1.12±0.01	57.8°
58-OBs-*exo*,*exo*-5,6-d_2	1.471±0.002		
59-OBs	1.001±0.004	1.11±0.01	51.1°
59-OBs-*exo*,*exo*-5,6-d_2	0.904±0.004		
84-OBs	5.27±0.03[f]	1.00±0.02	80°
84-OBs-*endo*-6-*d*	5.29±0.02		

[a] Measured by the spectrophotometric method of Swain.[218]

[b] These are representative runs. A complete tabulation of rate constants appears in Chapter 6.

[c] Mean of at least 3 runs: the errors in the ratios are the sums of the standard deviations in k_H and k_D.

[d] Corrected for incomplete deuteration.

[e] This represents the approximate temperature (±2°). However, temperature control was ±0.05°.

[f] The units are hr^{-1}.

Table 2:7

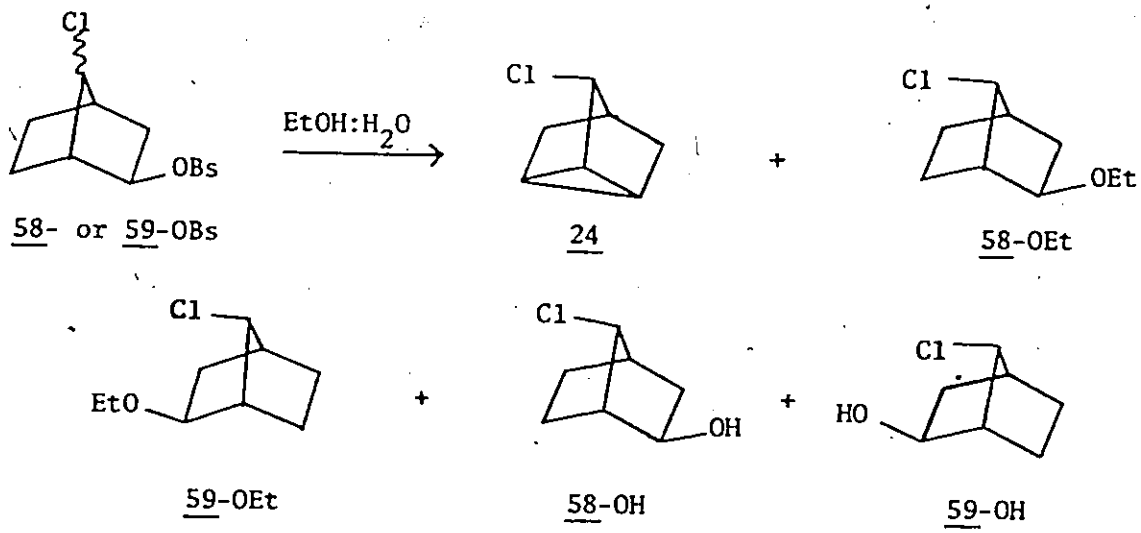
β-Hydrogen Deuterium Isotope Effect[a]

Compound	k x 10^2(min^{-1})[b]	k_H/k_D[c,d]	T[e]
58-OBs	1.725±0.003	1.09±0.01	57.8°
58-OBs-*exo*-3-*d*	1.576±0.004		

a,b,c,d,e, See footnotes of Table 2:6

C. Product Identification and Product Ratios

Solvolysis of 58- and 59-OBs in the ethanol-water mixture gave 24, 58-OEt, 59-OEt, 58-OH and 59-OH as products. These were identified by comparison to authentic samples. For solvolysis of the deuterated substrates,



58- or 59-OBs — 24 — 58-OEt — 59-OEt — 58-OH — 59-OH

we did not attempt to locate the site of deuterium substitution within the products. Relative product ratios are tabulated in Table 2:8. Product

identification from the reaction of 84-OBs was hampered by the formation of secondary products.

D. Deuterium Losses in the Formation of 3-Chloronortricyclene

Table 2:9 lists the fractional percentage loss of deuterium in the formation of 24 from the solvolysis of the deuterated chloro brosylates. The deuterated chloride 24 was isolated by glpc under carefully controlled conditions which excluded the possibility of contamination by chloronorbornene (62) which could arise *via* 1,2 elimination. Also, isolation of 24 from a large scale solvolytic reaction and subsequent nmr analysis showed that there were not any olefinic protons.

Table 2:8

Product Ratios from Solvolysis of 7-Chloro-2-Norbornyl Brosylates[a]

	Relative % Yield[b,c]					
Compound	24	58-OEt	59-OEt	58-OH	59-OH	Other[i]
58-OBs[d]	21	36	5	29	4	5
58-OBs-*endo*-6-*d*	13	40	4	33	3	7
59-OBs[g]	30	11	24	8	23	4
59-OBs-*endo*-6-*d*	20	10	31	8	30	1
58-OBs[e]	20	39	7	23	5	6
58-OBs-*exo*,*exo*-5,6-d_2	22	38	6	23	4	7
59-OBs[h]	35	11	21	11	19	3
59-OBs-*exo*,*exo*-5,6-d_2	20	11	27	17	25	0
58-OBs[f]	19	40	7	22	5	7
58-OBs-*exo*-3-*d*	28	36	7	18	5	6

[a] Solvolysis in 80:20 ethanol-water with 0.04 M sodium acetate

[b] Determined by glpc by electronic integration

[c] Average of 4-5 determinations: these numbers have a tolerance of 10%

[d,e,f] Product ratios from these runs are not exactly identical because they were determined at different time periods. Comparison of these numbers indicates their reproducibility over long time intervals.

[g,h] See footnotes d,e,f.

[i] Unidentified

Table 2:9

Deuterium Losses in the Formation of 3-Chloronortricyclene (24) from Solvolysis of 7-Chloro-2-Norbornyl Brosylates-6-*d*

Compound	Deuterium Content of Brosylate[a]				Deuterium Content of 24[b]				Fractional % Loss of 1 Deuterium Atom
	% d_0	% d_1	% d_2	*d*/molecule	% d_0	% d_1	% d_2	*d*/molecule	
58-OBs-*endo*-6-*d*	4	95	1	0.97	77	23	-	0.23	76
59-OBs-*endo*-6-*d*	3	95	2	0.99	78	22	-	0.22	79
58-OBs-*exo*,*exo*-5,6-d_2	7	3	90	1.83	7	4	89	1.82	1[c]
59-OBs-*exo*,*exo*-5,6-d_2	5	6	89	1.84	7	9	84	1.77	8[c]

[a] See Table 2:5, footnote a

[b] Determined mass spectrometrically at low voltage

[c] The calculations assume equal distribution of label between C-5 and C-6 and exclusive loss of deuterium from C-6 during elimination.

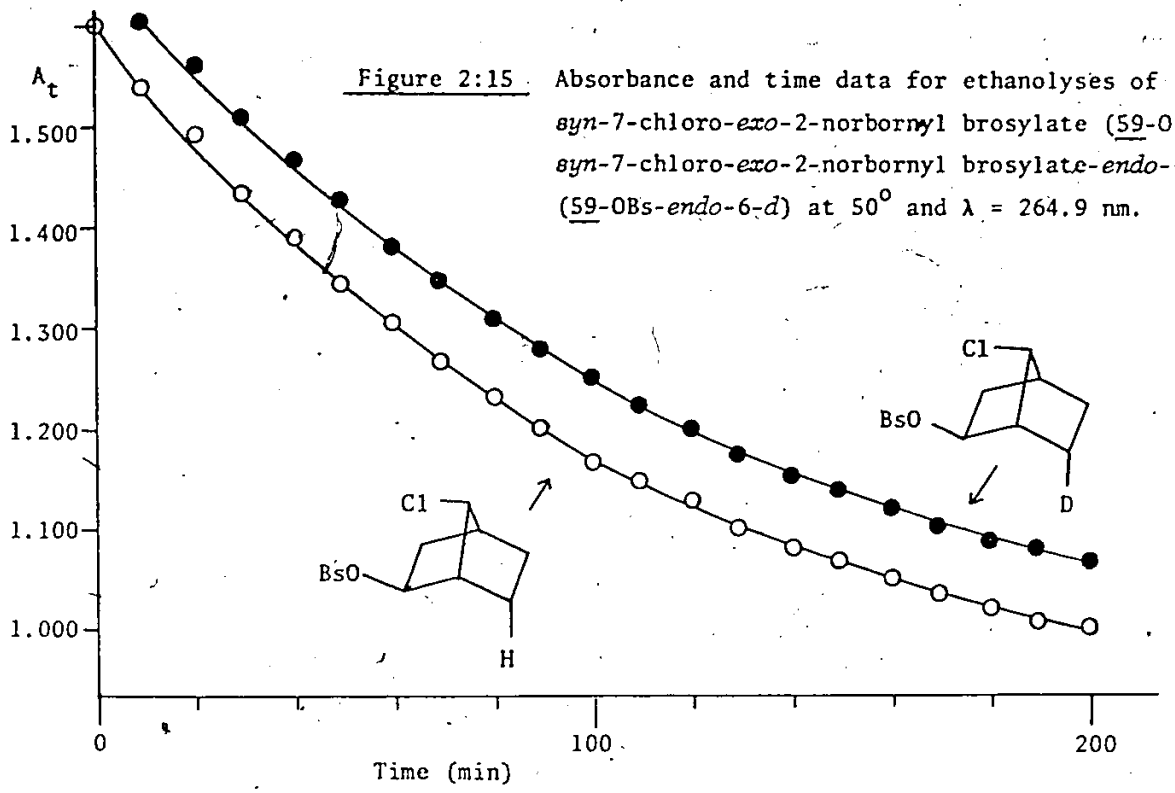


Figure 2:15 Absorbance and time data for ethanolyses of *syn*-7-chloro-*exo*-2-norbornyl brosylate (59-OBs) and *syn*-7-chloro-*exo*-2-norbornyl brosylate-*endo*-6-*d* (59-OBs-*endo*-6-*d*) at 50° and λ = 264.9 nm.

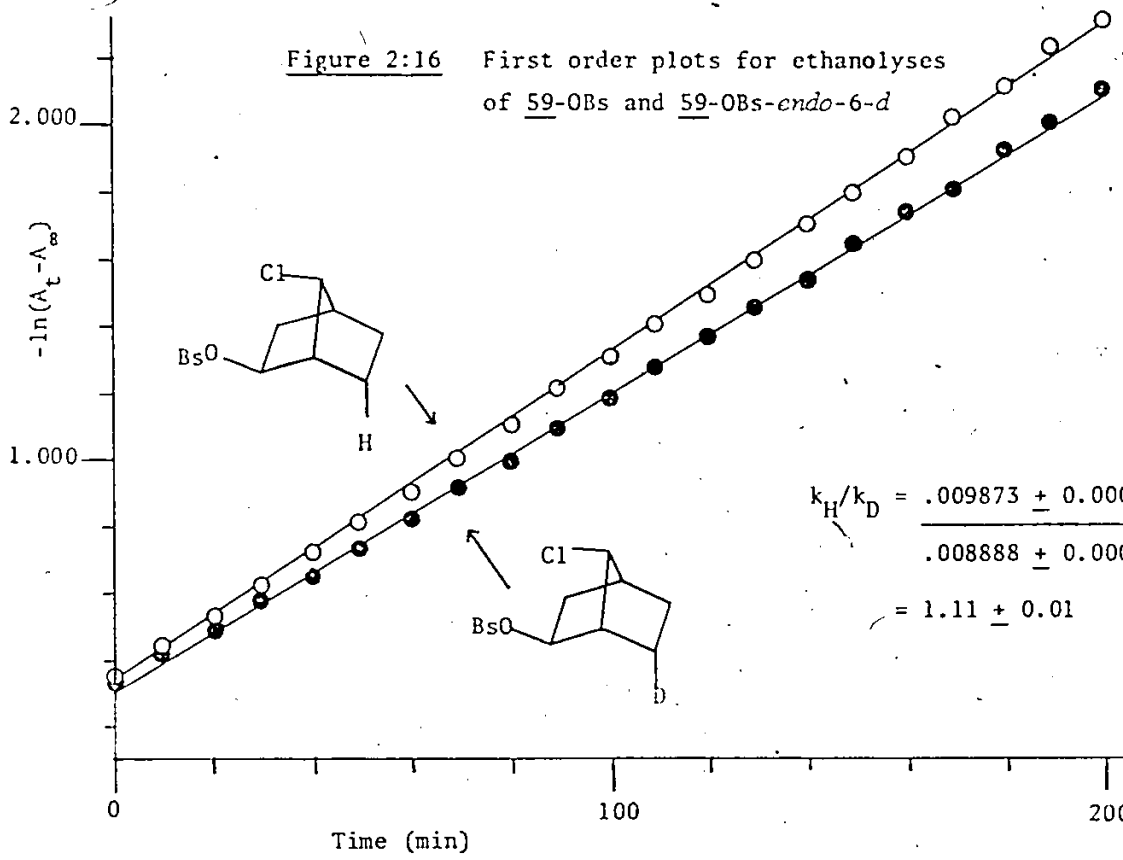


Figure 2:16 First order plots for ethanolyses of 59-OBs and 59-OBs-*endo*-6-*d*

$$k_H/k_D = \frac{.009873 \pm 0.000054 \text{ min}^{-1}}{.008888 \pm 0.000050 \text{ min}^{-1}}$$

$$= 1.11 \pm 0.01$$

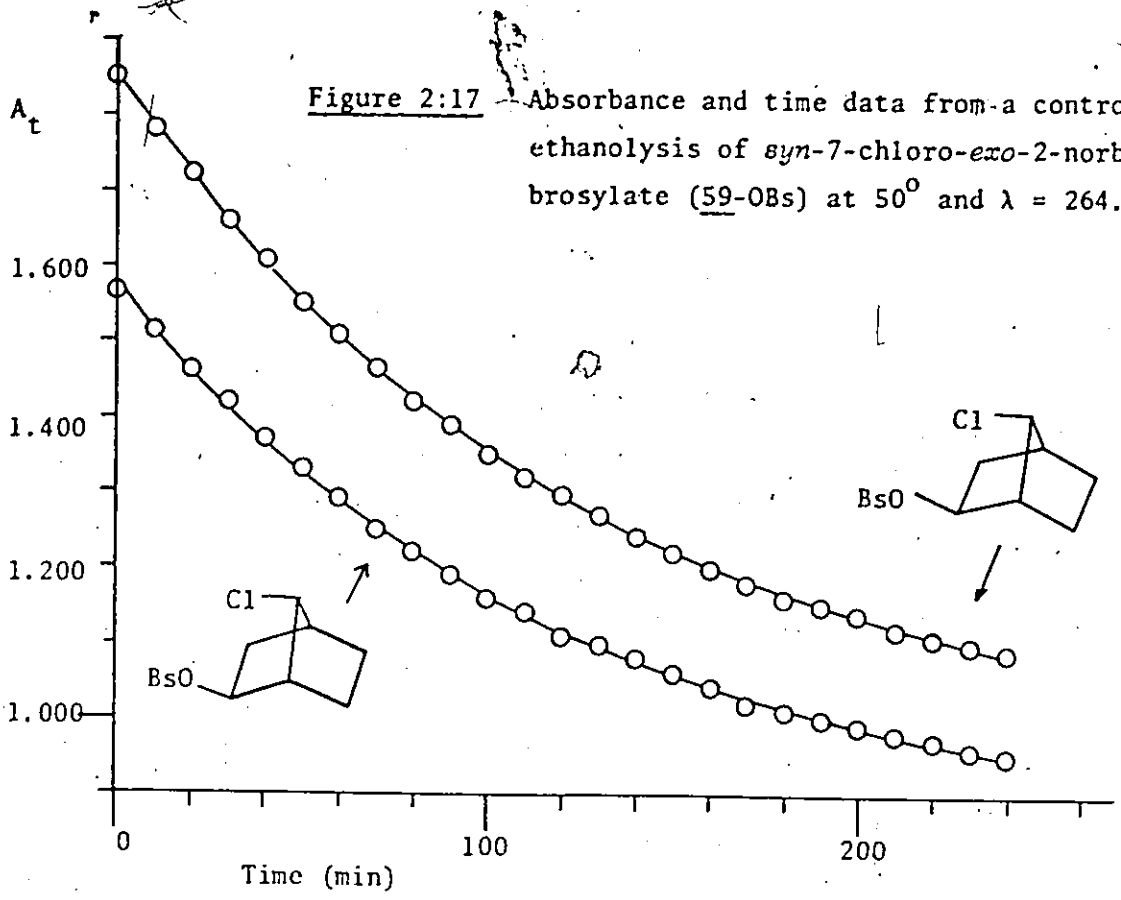


Figure 2:17 Absorbance and time data from a control run for ethanolysis of *syn*-7-chloro-*exo*-2-norbornyl brosylate (59-OBs) at 50° and λ = 264.9 nm.

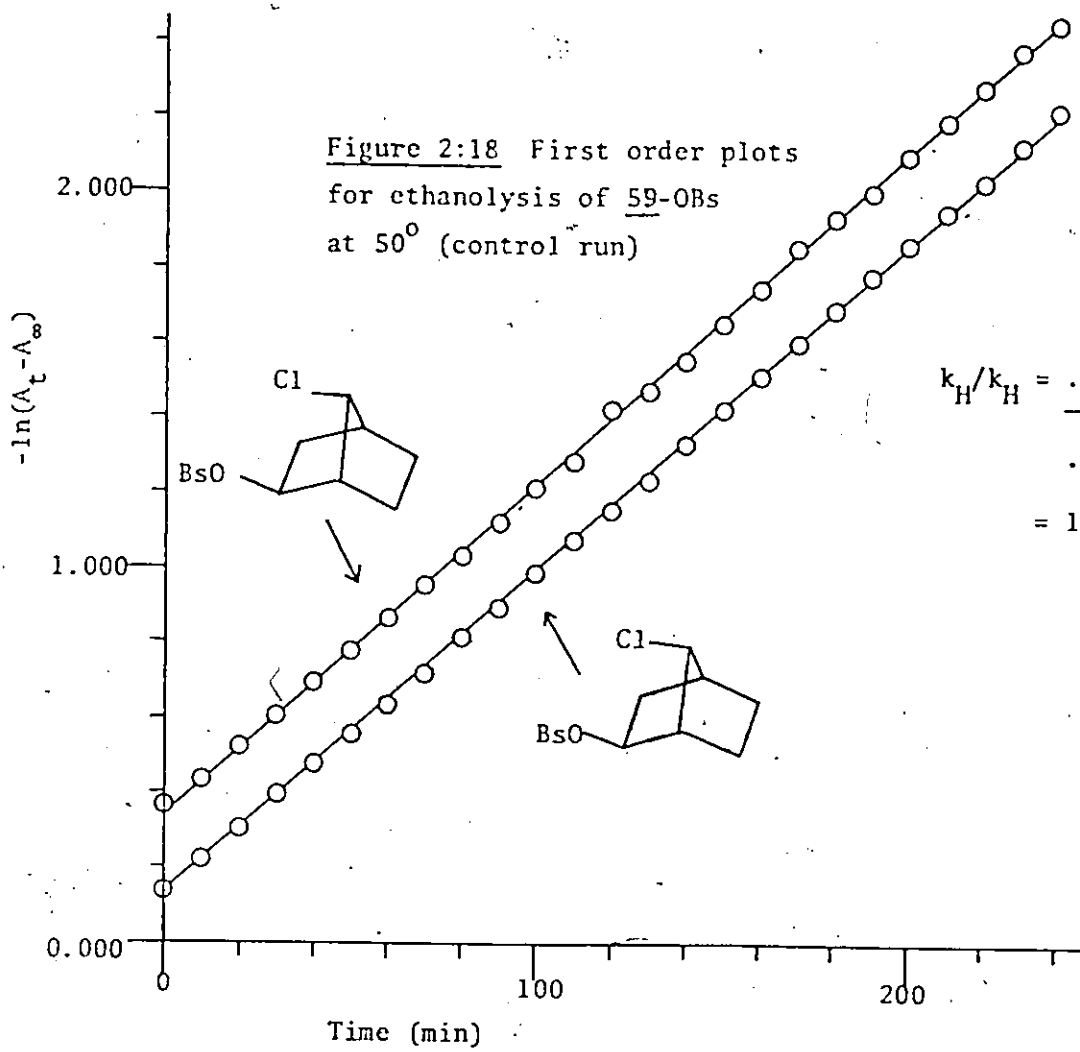


Figure 2:18 First order plots for ethanolysis of 59-OBs at 50° (control run)

$$k_H/k_H = \frac{.00881 \pm .000034 \text{ min}^{-1}}{.00868 \pm .000026 \text{ min}^{-1}}$$

$$= 1.01 \pm 0.01$$

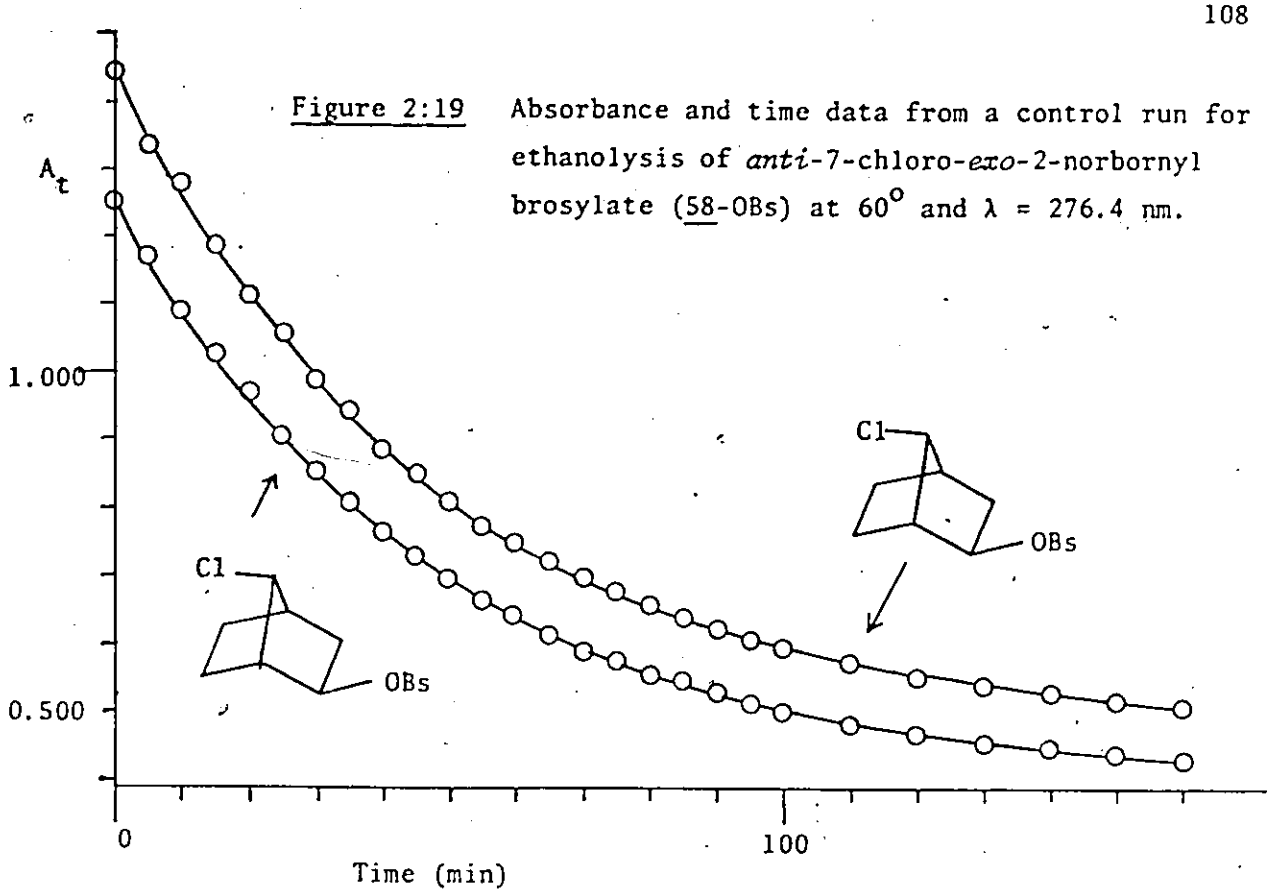


Figure 2:19 Absorbance and time data from a control run for ethanolysis of *anti*-7-chloro-*exo*-2-norbornyl brosylate (58-OBs) at 60° and λ = 276.4 nm.

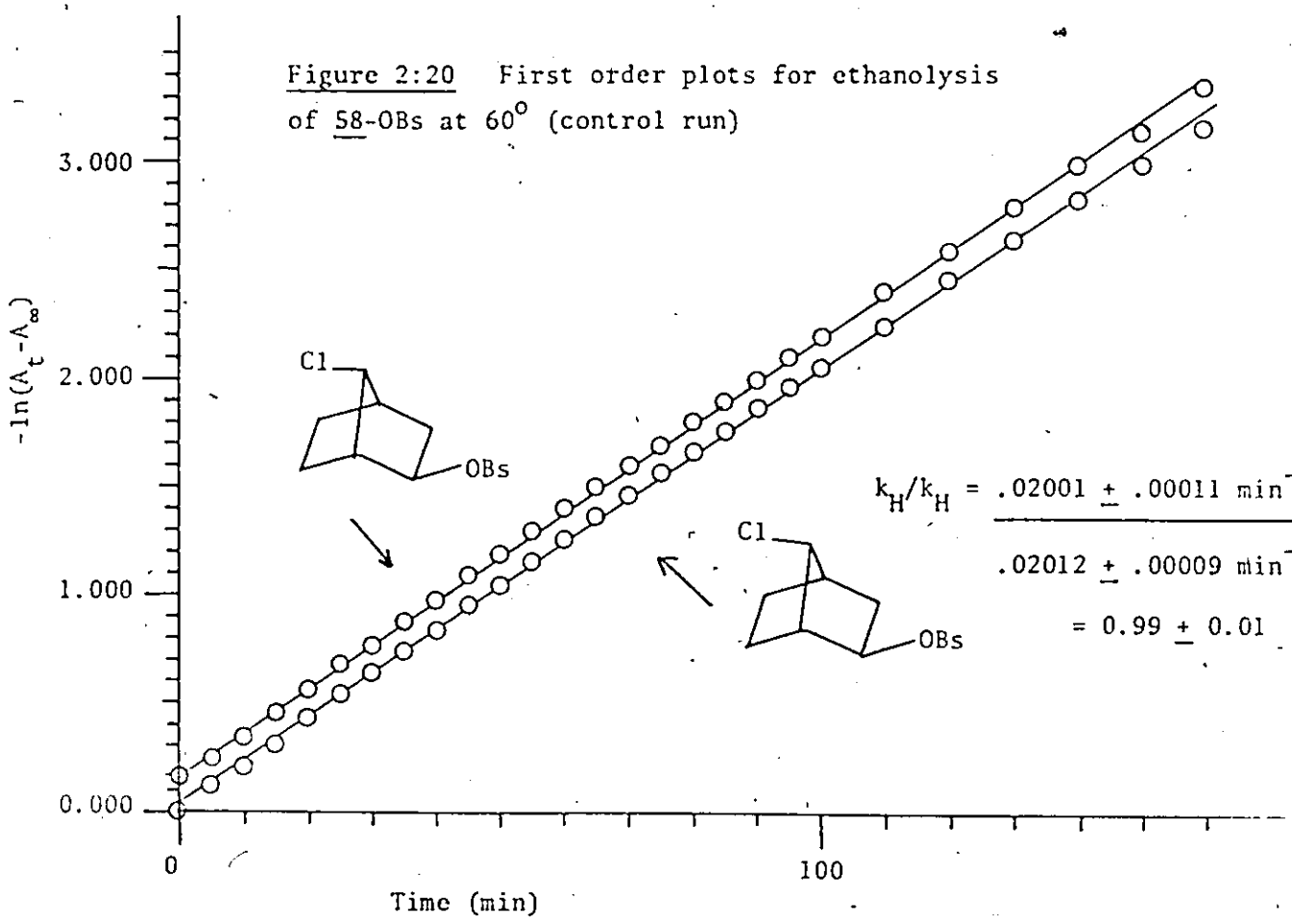


Figure 2:20 First order plots for ethanolysis of 58-OBs at 60° (control run)

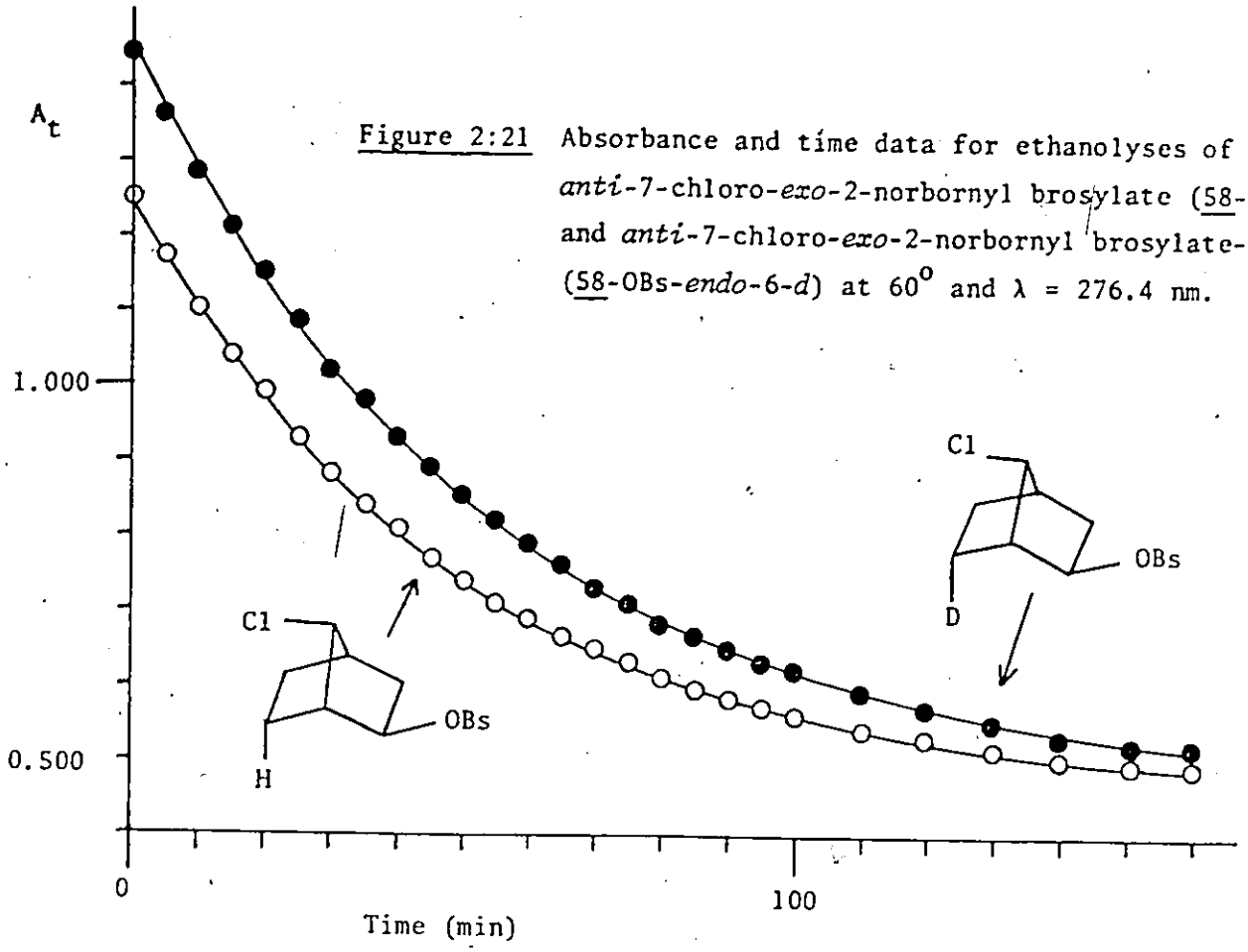


Figure 2:21 Absorbance and time data for ethanolyses of *anti*-7-chloro-*exo*-2-norbornyl brosylate (58-OBs) and *anti*-7-chloro-*exo*-2-norbornyl brosylate-*endo*-6-*d* (58-OBs-*endo*-6-*d*) at 60° and λ = 276.4 nm.

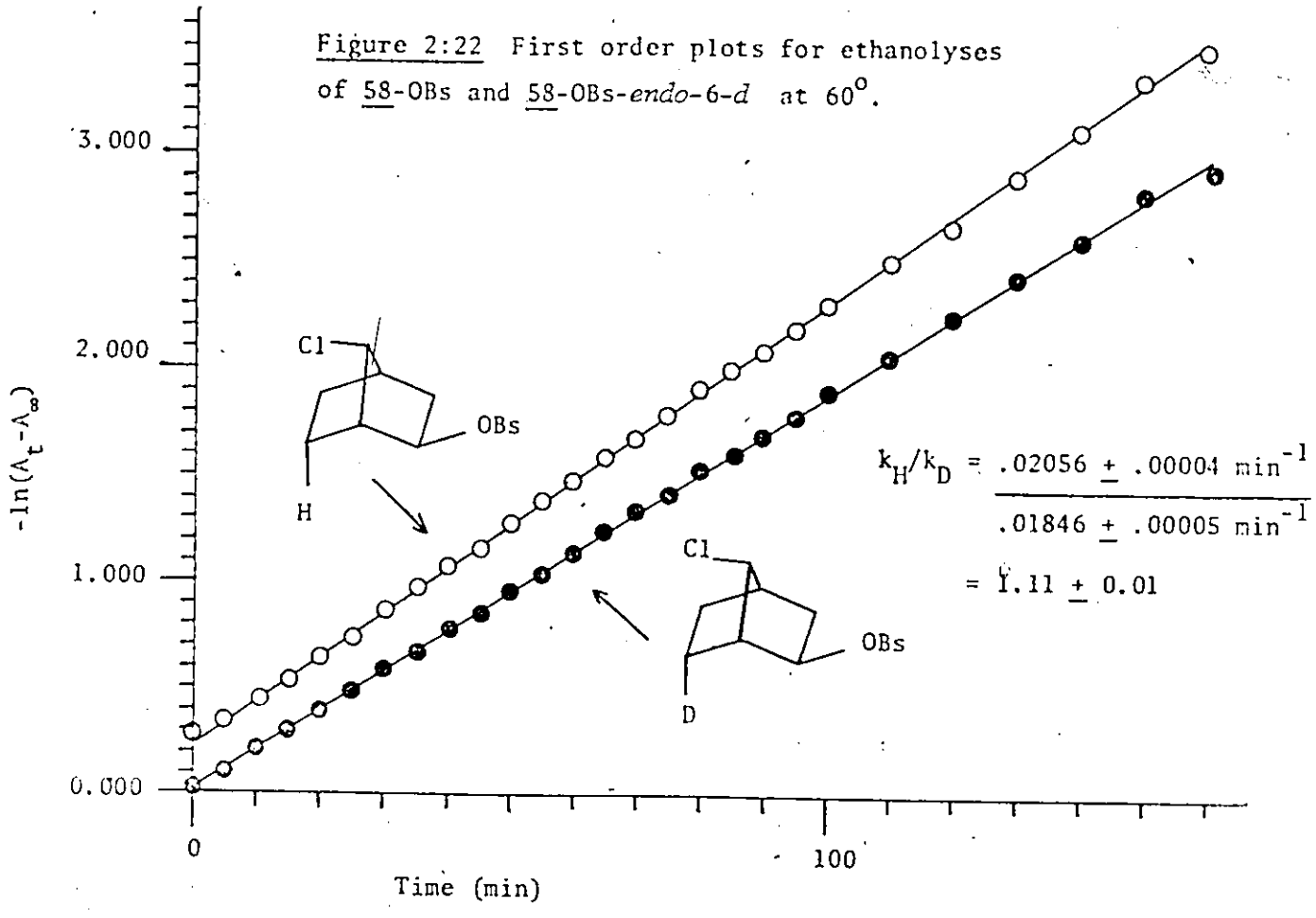


Figure 2:22 First order plots for ethanolyses of 58-OBs and 58-OBs-*endo*-6-*d* at 60°.

Figure 2:23 Absorbance and time data for ethanolyses of *syn*-7-chloro-*exo*-2-norbornyl brosylate (59-OBs) and *syn*-7-chloro-*exo*-2-norbornyl brosylate-*exo*,*exo*-5,6-d_2 (59-OBs-*exo*,*exo*-5,6-d_2) at 51° and λ = 264.9 nm.

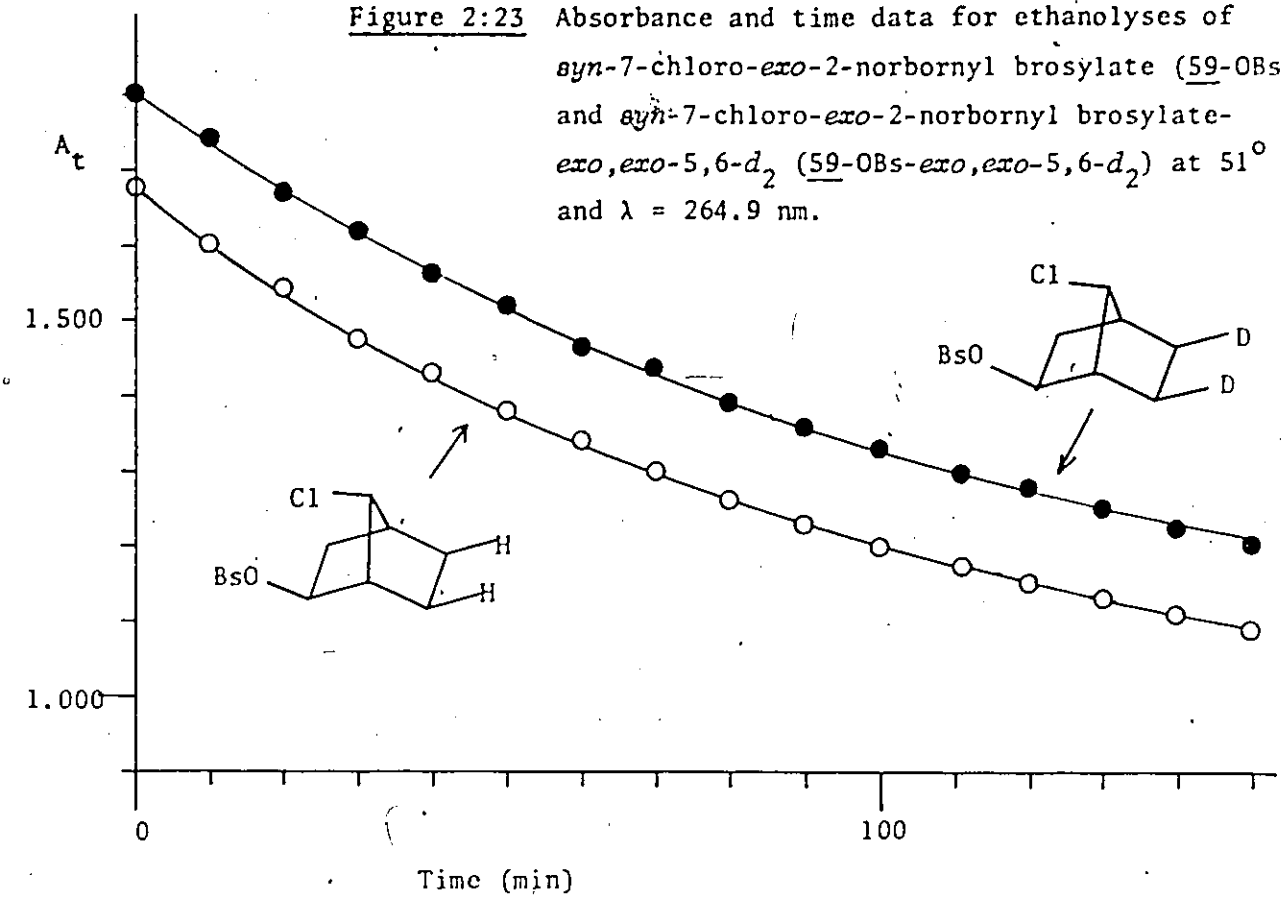
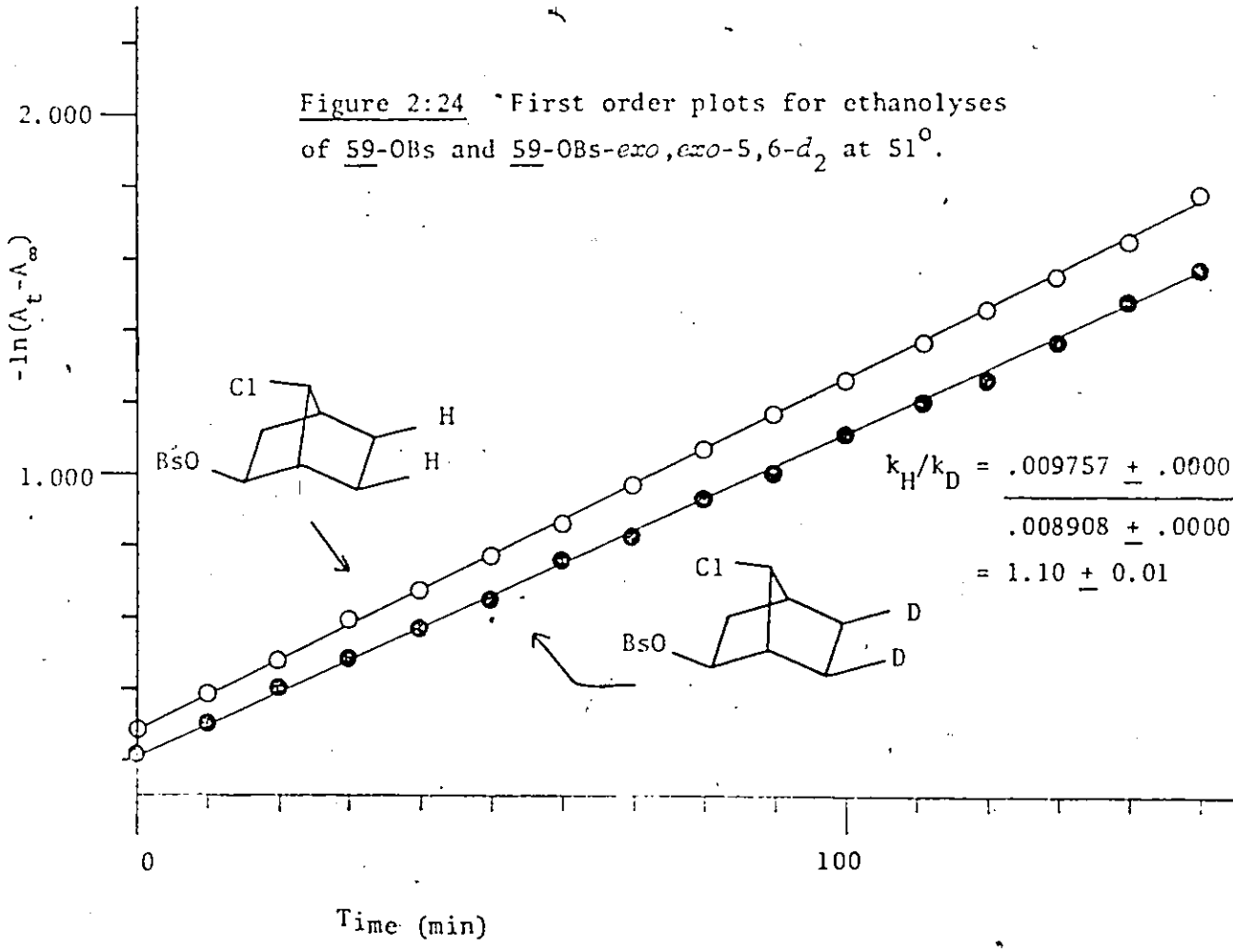


Figure 2:24 First order plots for ethanolyses of 59-OBs and 59-OBs-*exo*,*exo*-5,6-d_2 at 51°.



$$k_H/k_D = \frac{.009757 \pm .000030 \text{ min}^{-1}}{.008908 \pm .000064 \text{ min}^{-1}} = 1.10 \pm 0.01$$

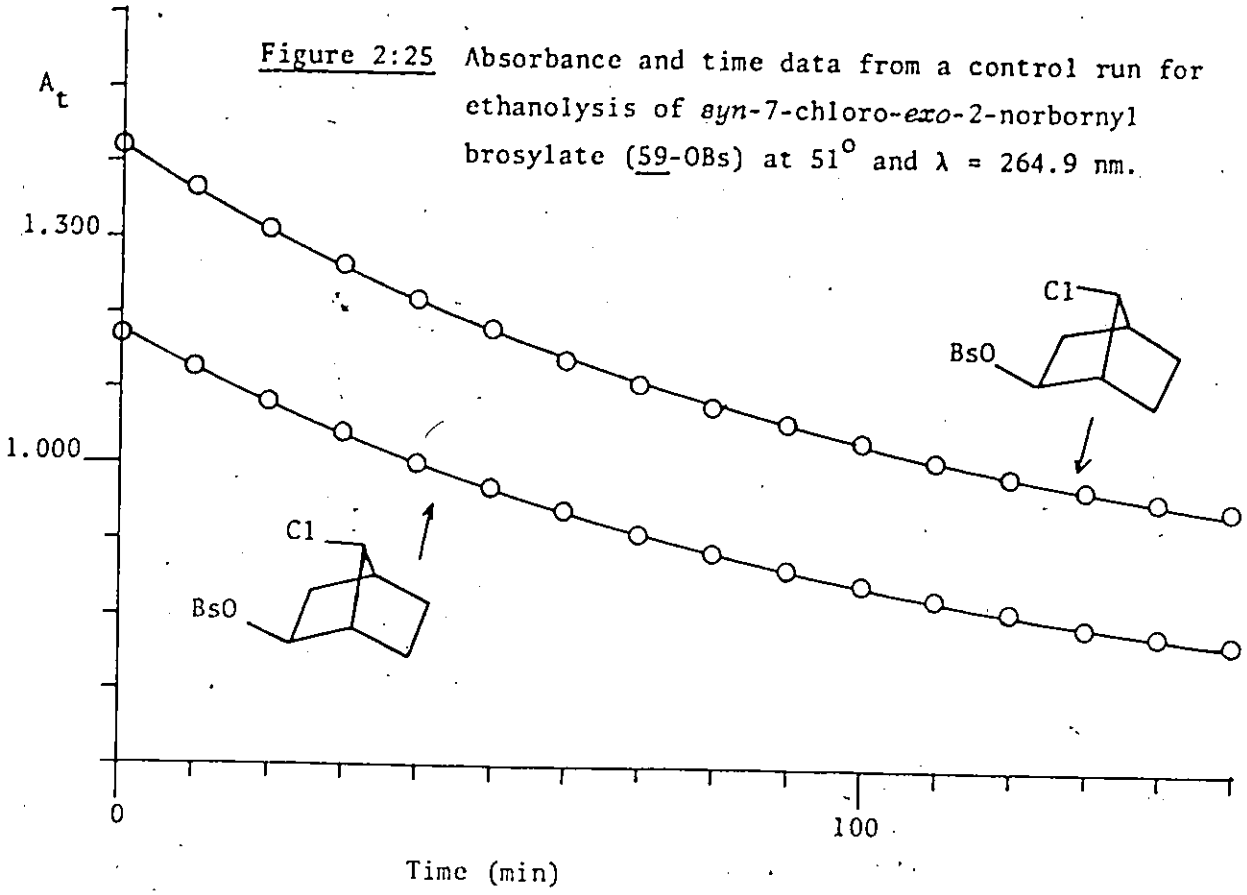


Figure 2:25 Absorbance and time data from a control run for ethanolysis of *syn*-7-chloro-*exo*-2-norbornyl brosylate (59-OBs) at 51° and λ = 264.9 nm.

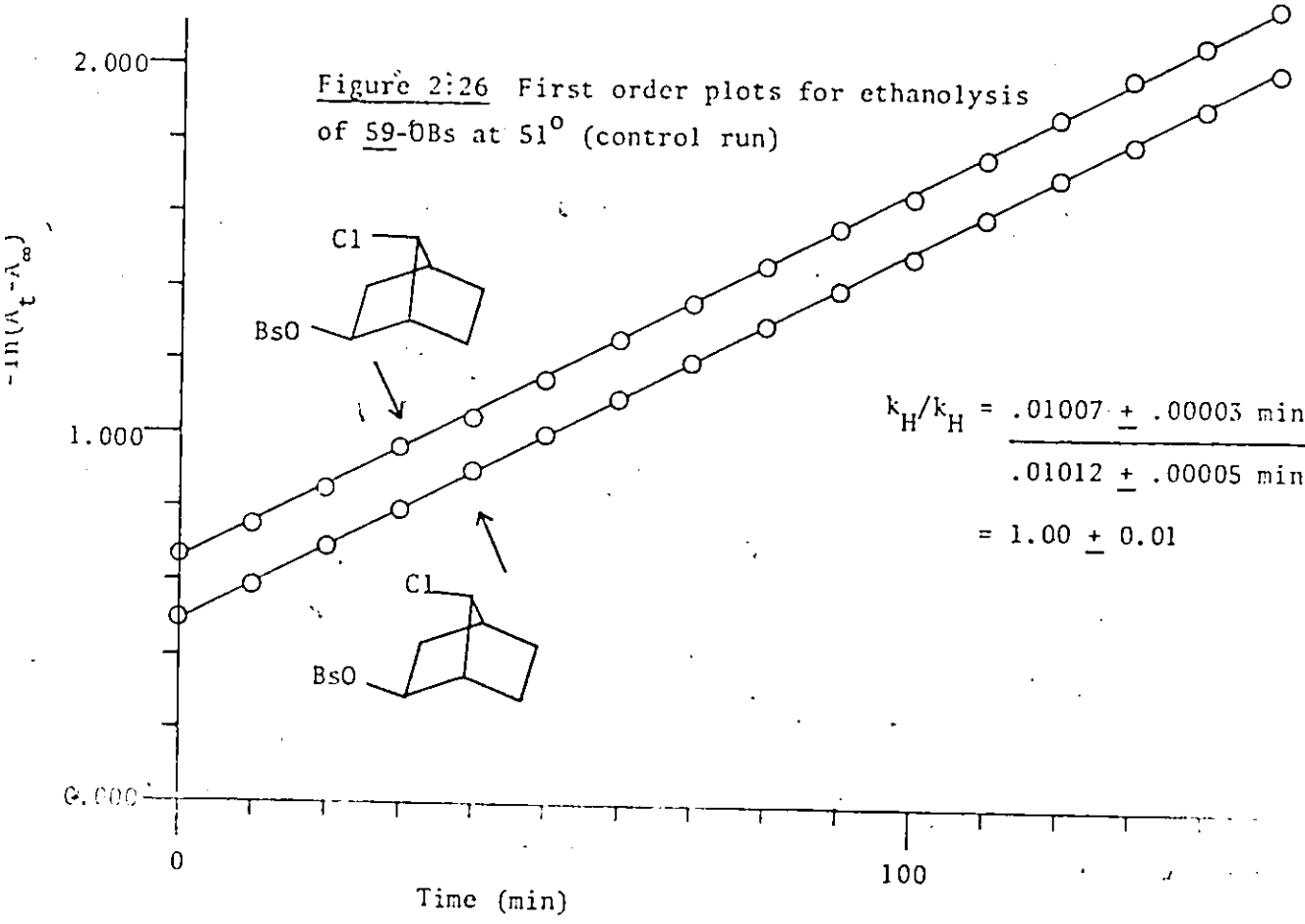


Figure 2:26 First order plots for ethanolysis of 59-OBs at 51° (control run)

$$k_H/k_H = \frac{.01007 \pm .00003 \text{ min}^{-1}}{.01012 \pm .00005 \text{ min}^{-1}}$$

$$= 1.00 \pm 0.01$$

Figure 2: 27 Absorbance and time data from a control run for ethanolysis of *anti*-7-chloro-*endo*-2-norbornyl brosylate (84-OBs) at 80° and λ = 266.0 nm.

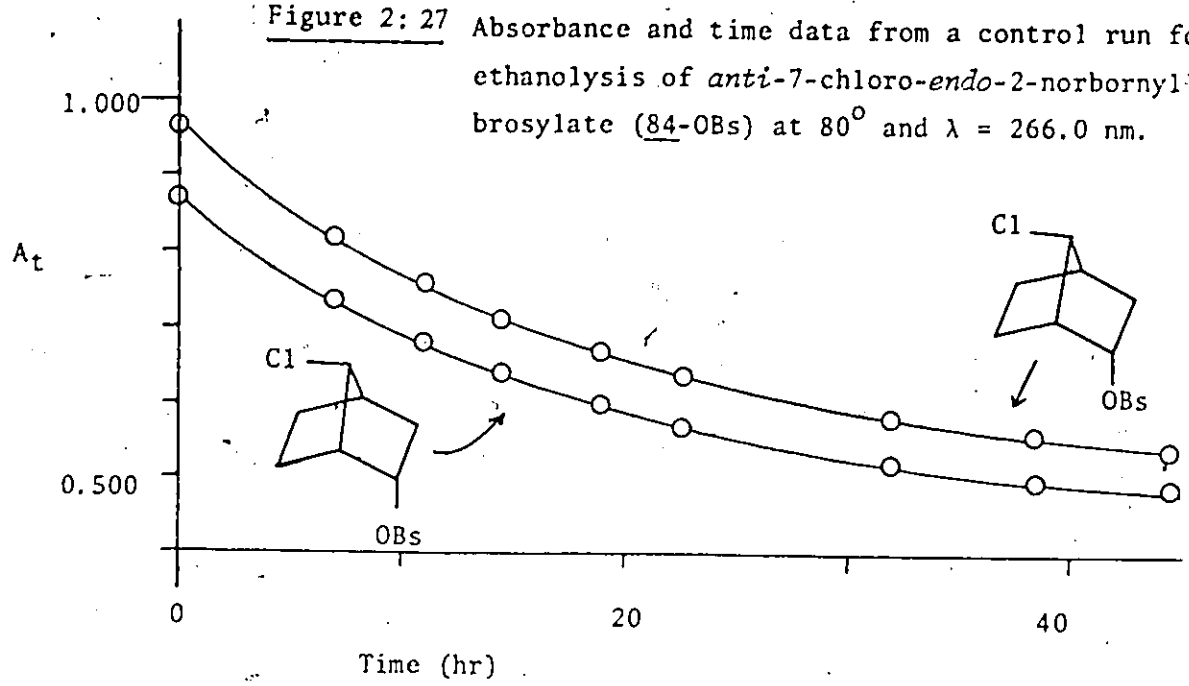
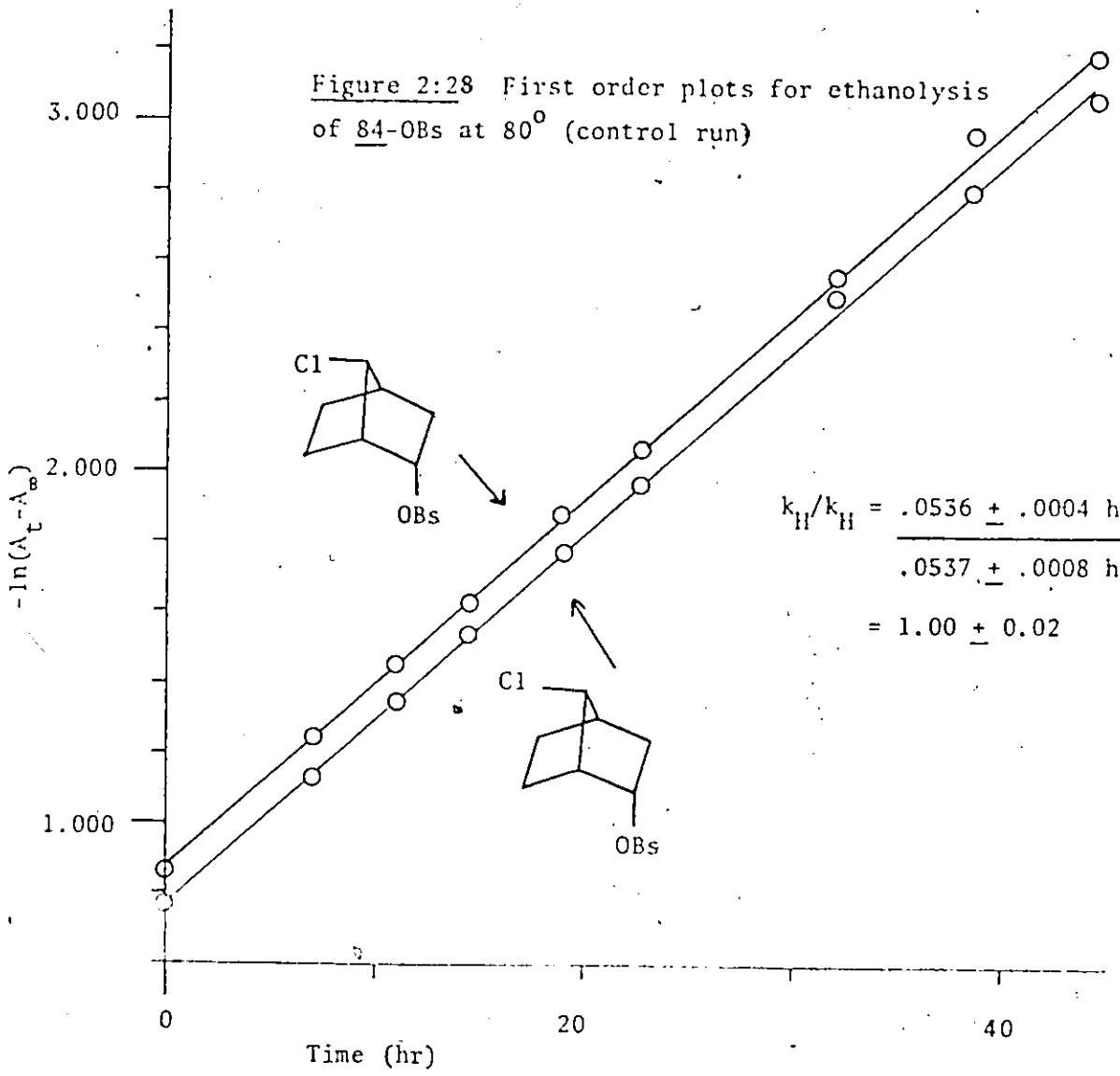


Figure 2:28 First order plots for ethanolysis of 84-OBs at 80° (control run)



$$k_H/k_H = \frac{.0536 \pm .0004\ hr^{-1}}{.0537 \pm .0008\ hr^{-1}}$$

$$= 1.00 \pm 0.02$$

Figure 2:29 Absorbance and time data for ethanolyses of *anti*-7-chloro-*endo*-2-norbornyl brosylate (84-OBs) and *anti*-7-chloro-*endo*-2-norbornyl brosylate-*endo*-6-*d* (84-OBs-*endo*-6-*d*) at 80° and λ = 266.0 nm.

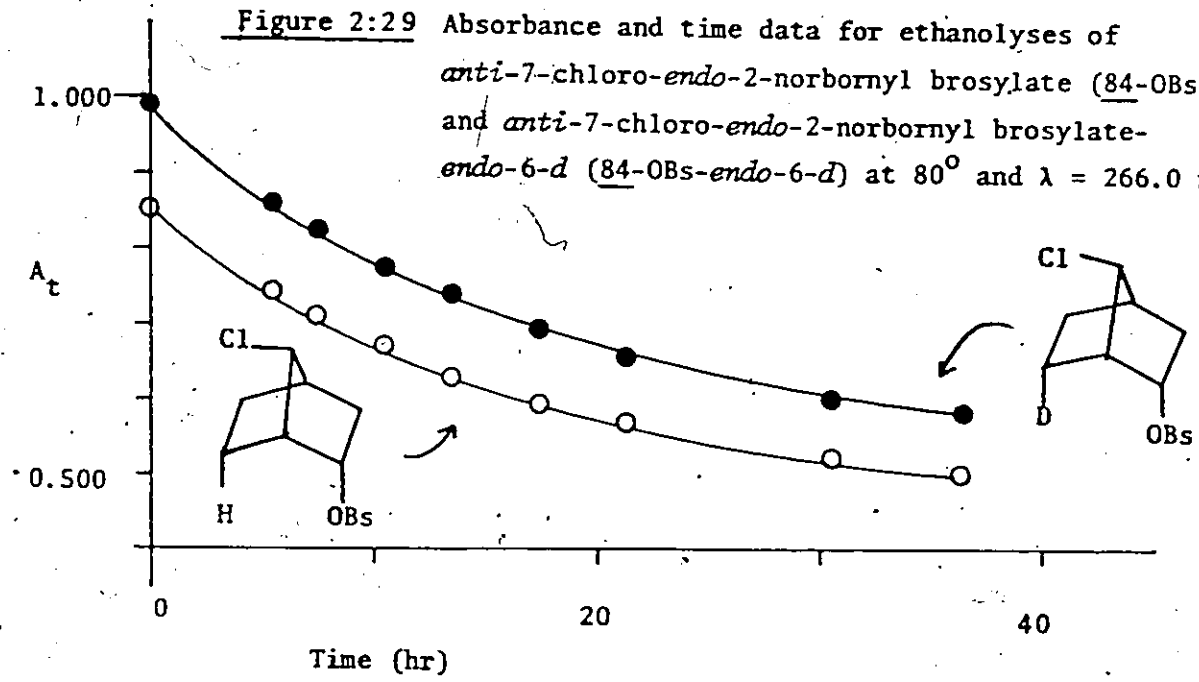
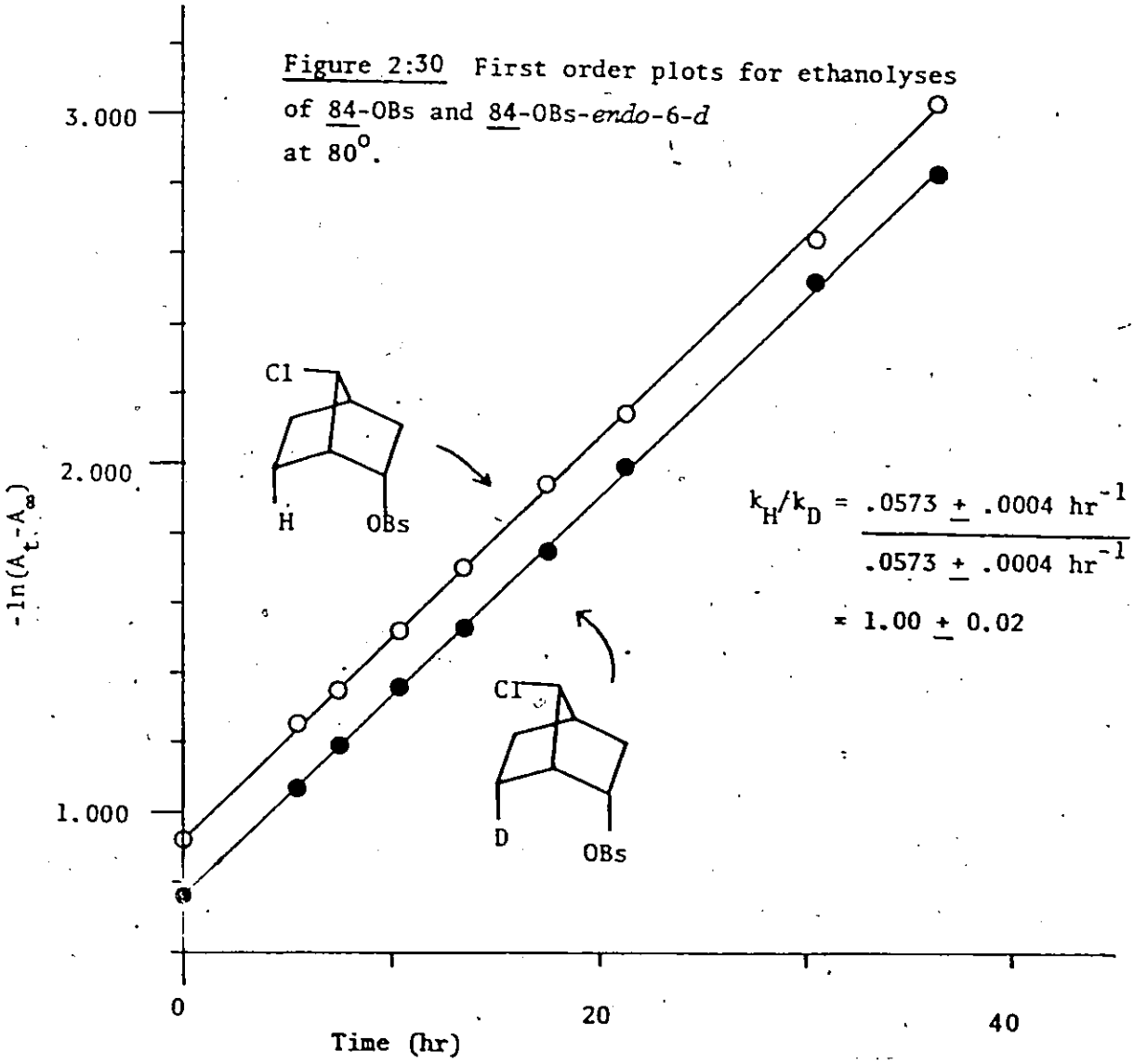


Figure 2:30 First order plots for ethanolyses of 84-OBs and 84-OBs-*endo*-6-*d* at 80°.



$$k_H/k_D = \frac{.0573 \pm .0004\ hr^{-1}}{.0573 \pm .0004\ hr^{-1}}$$

$$= 1.00 \pm 0.02$$

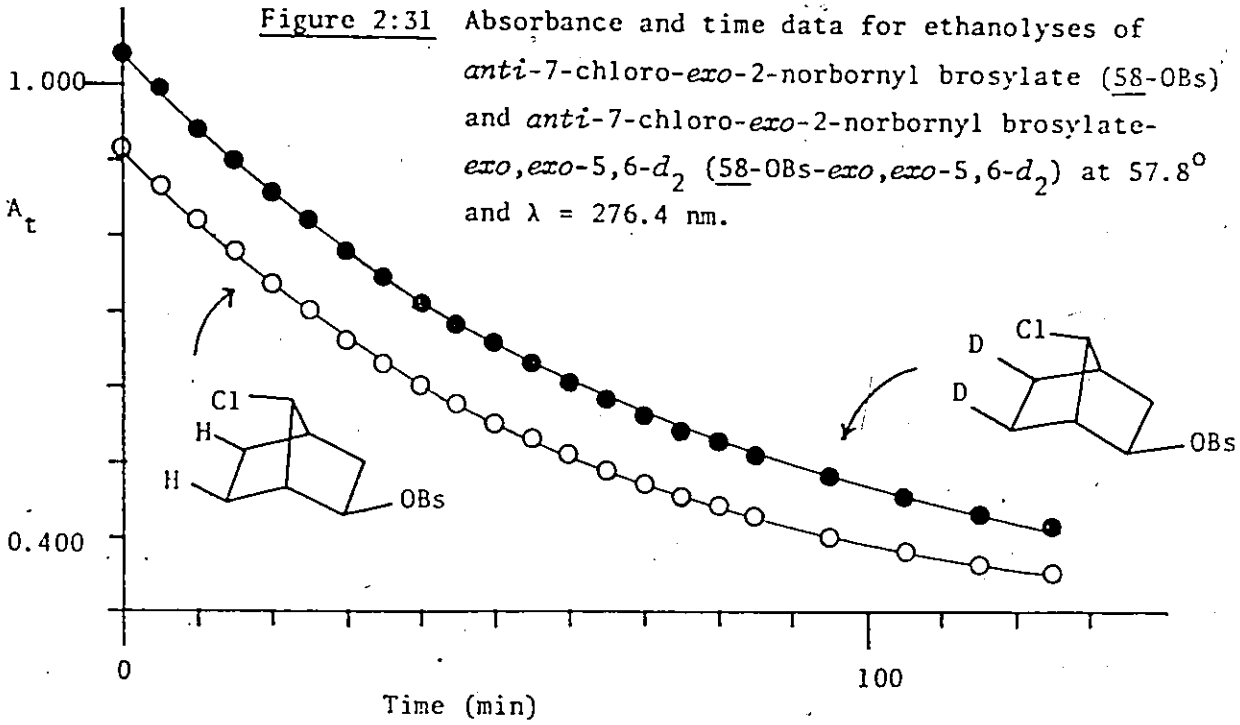


Figure 2:31 Absorbance and time data for ethanolyses of *anti*-7-chloro-*exo*-2-norbornyl brosylate (58-OBs) and *anti*-7-chloro-*exo*-2-norbornyl brosylate-*exo*,*exo*-5,6-d_2 (58-OBs-*exo*,*exo*-5,6-d_2) at 57.8° and λ = 276.4 nm.

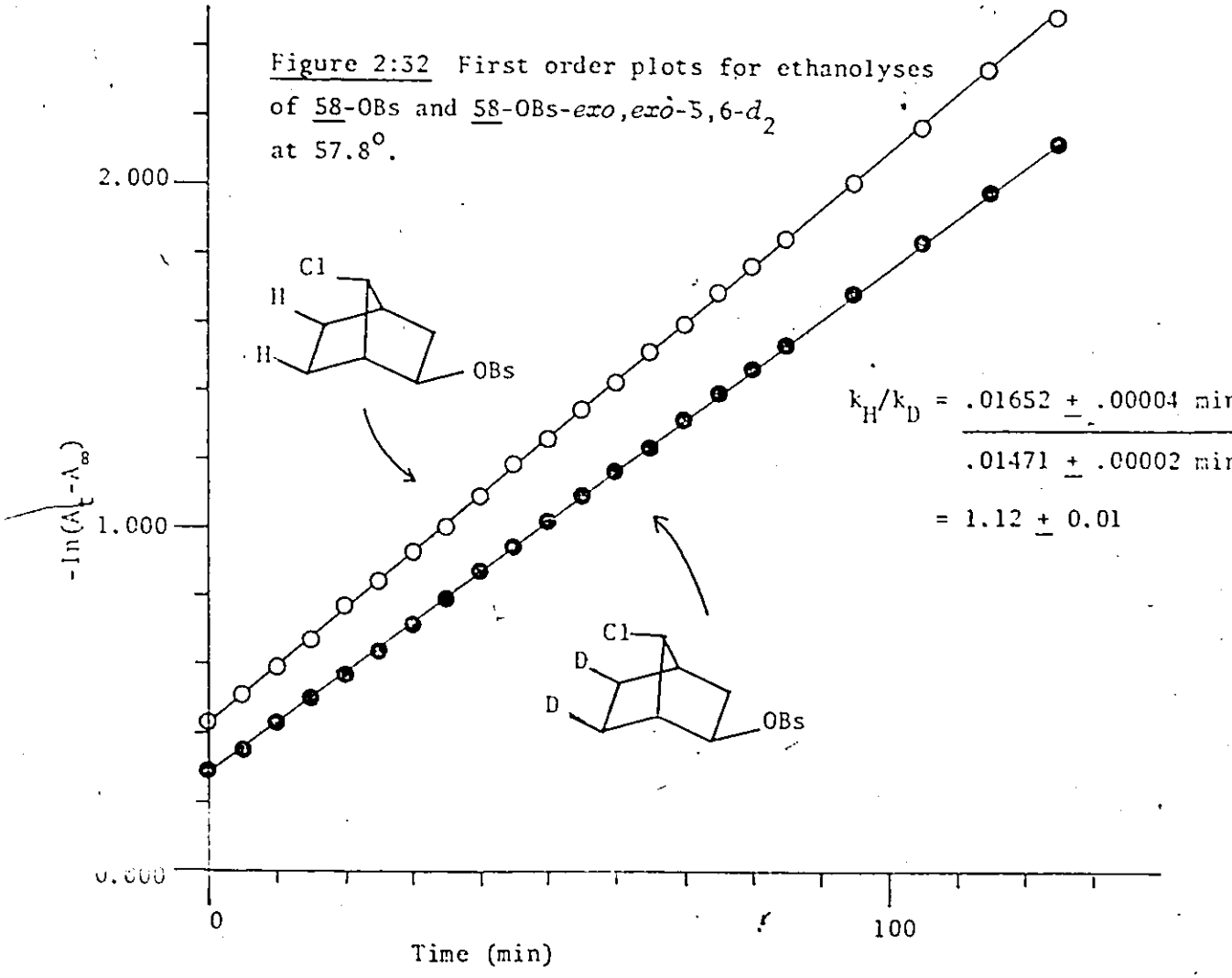


Figure 2:32 First order plots for ethanolyses of 58-OBs and 58-OBs-*exo*,*exo*-5,6-d_2 at 57.8°.

$$k_H/k_D = \frac{.01652 \pm .00004 \text{ min}^{-1}}{.01471 \pm .00002 \text{ min}^{-1}}$$

$$= 1.12 \pm 0.01$$

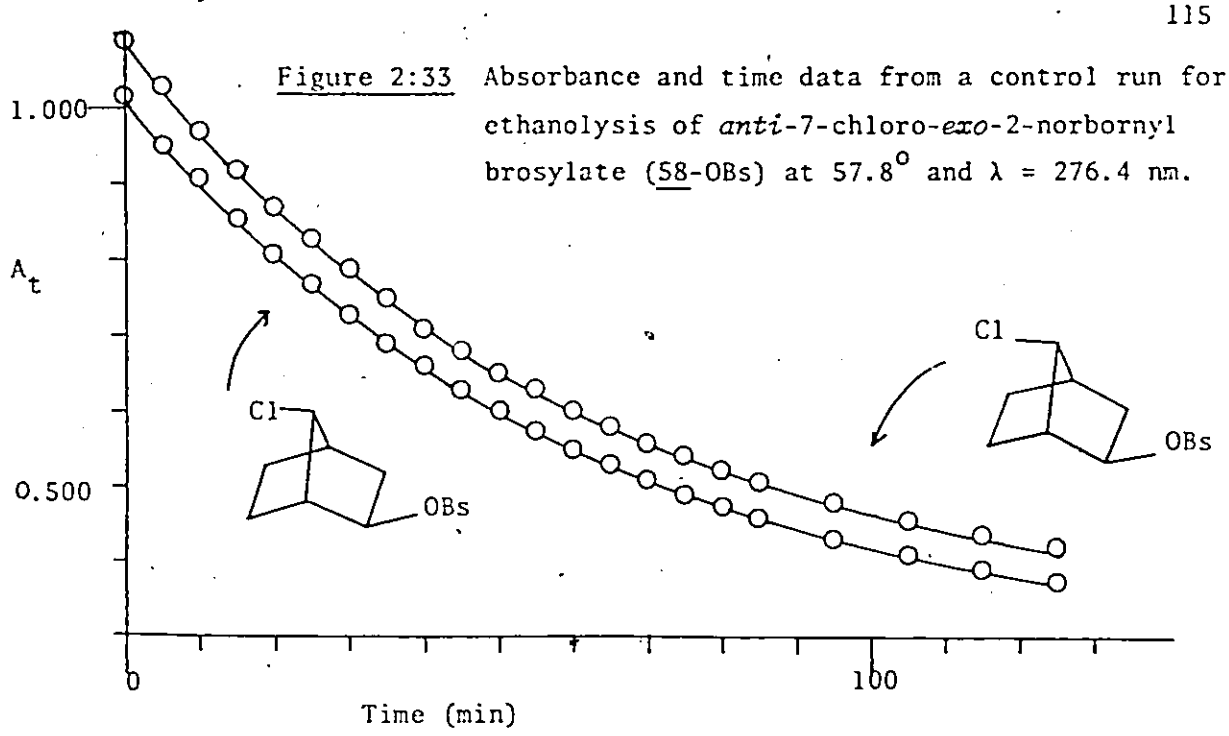


Figure 2:33 Absorbance and time data from a control run for ethanolysis of *anti*-7-chloro-*exo*-2-norbornyl brosylate (58-OBs) at 57.8° and λ = 276.4 nm.

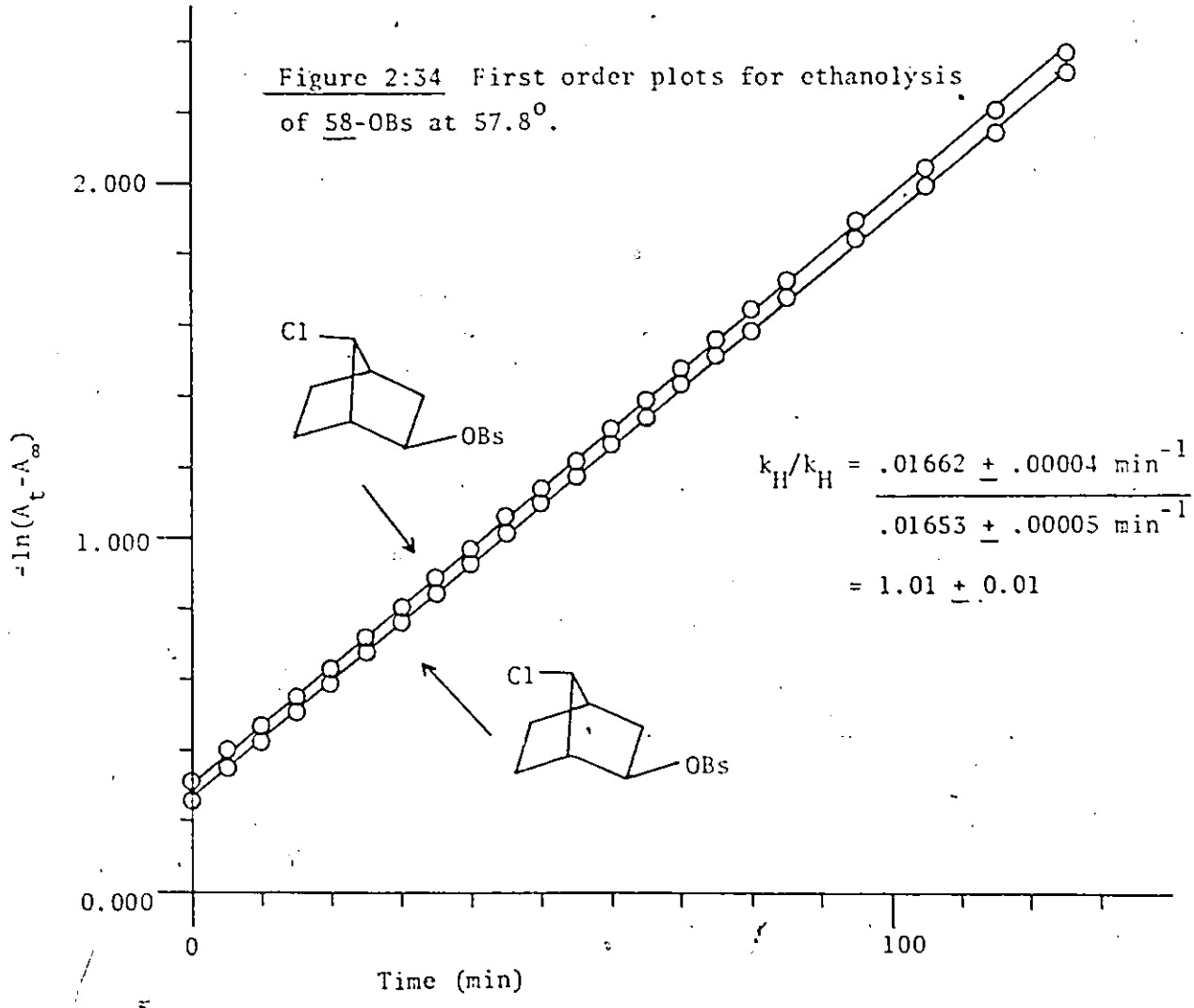


Figure 2:34 First order plots for ethanolysis of 58-OBs at 57.8°.

$$k_H/k_H = \frac{.01662 \pm .00004 \text{ min}^{-1}}{.01653 \pm .00005 \text{ min}^{-1}}$$

$$= 1.01 \pm 0.01$$

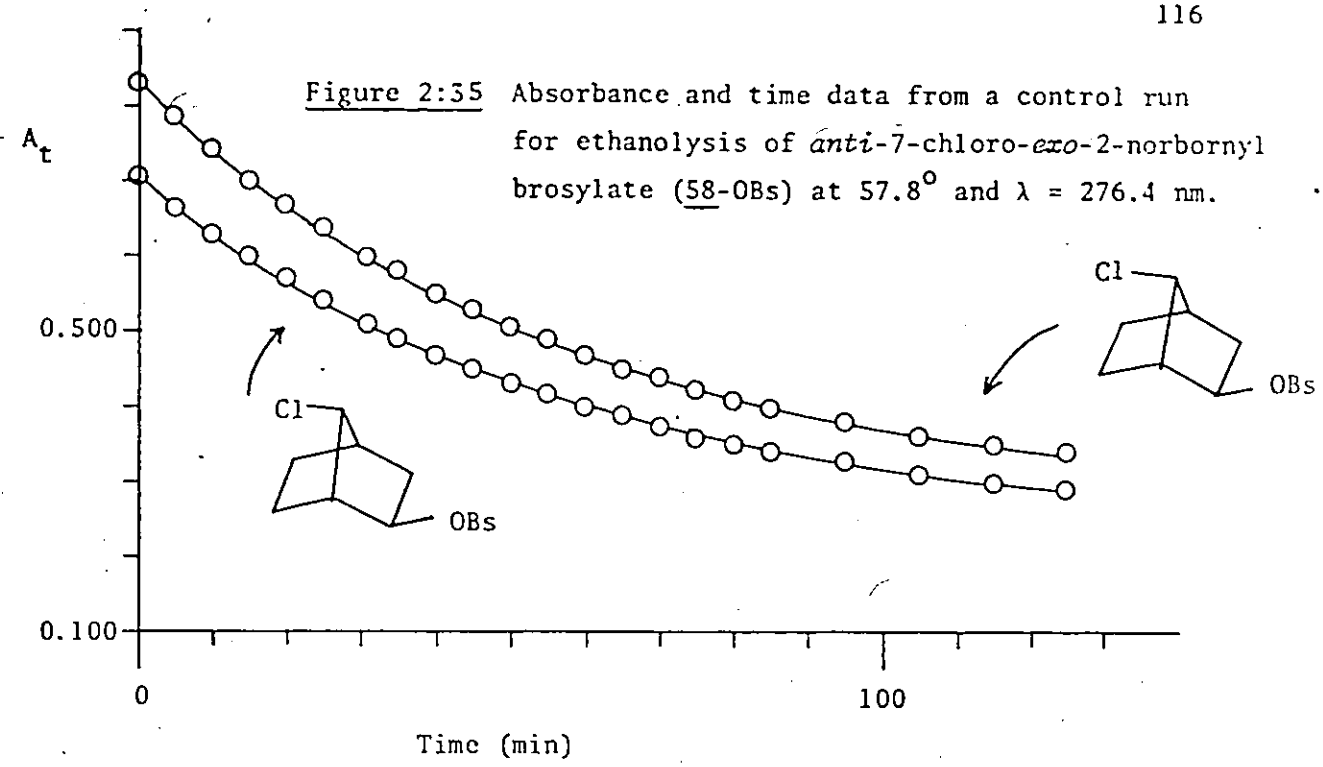


Figure 2:35 Absorbance and time data from a control run for ethanolysis of *anti*-7-chloro-*exo*-2-norbornyl brosylate (58-OBs) at 57.8° and λ = 276.4 nm.

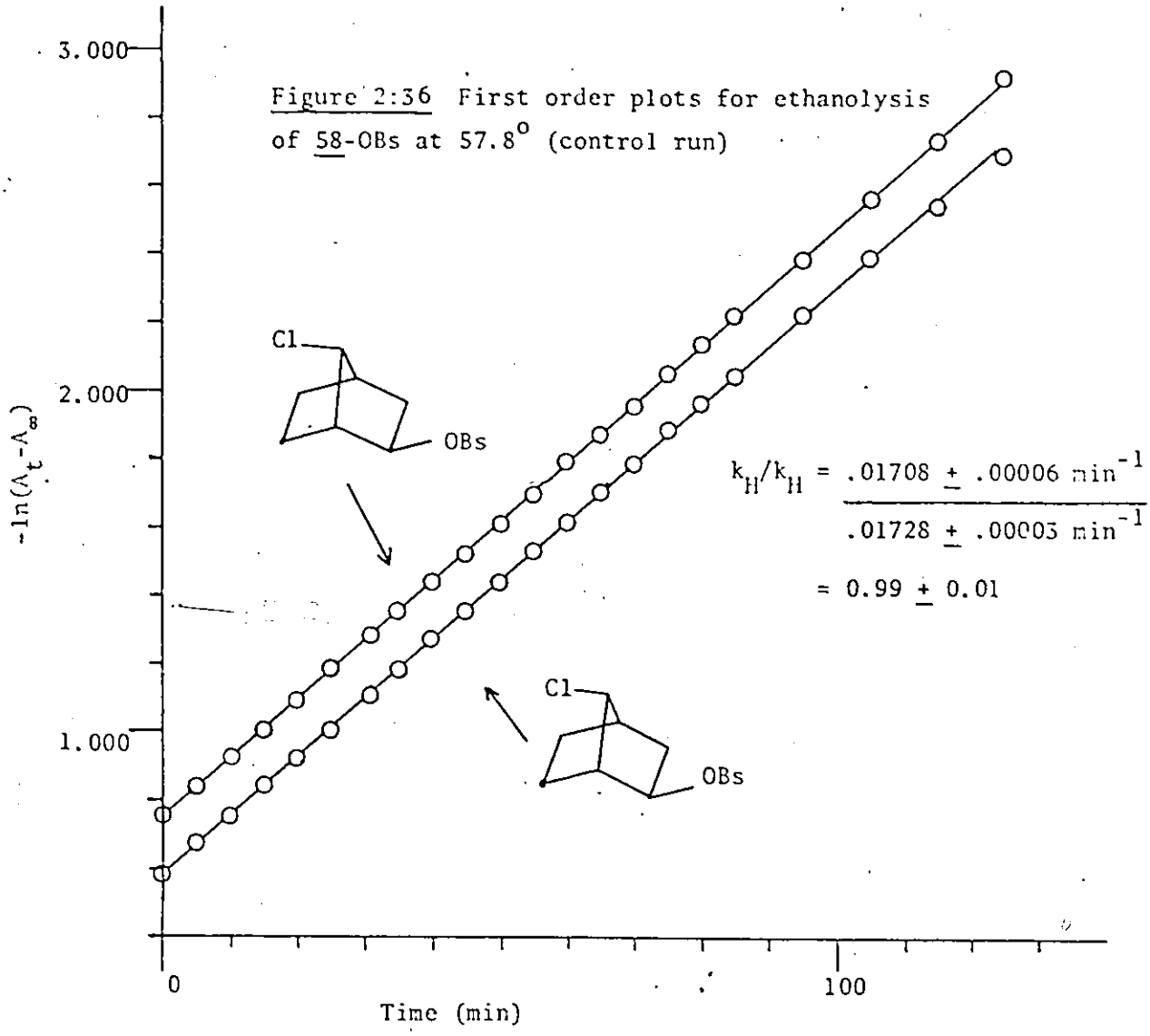


Figure 2:36 First order plots for ethanolysis of 58-OBs at 57.8° (control run)

$$k_H/k_H = \frac{.01708 \pm .00006 \text{ min}^{-1}}{.01728 \pm .00003 \text{ min}^{-1}}$$

$$= 0.99 \pm 0.01$$

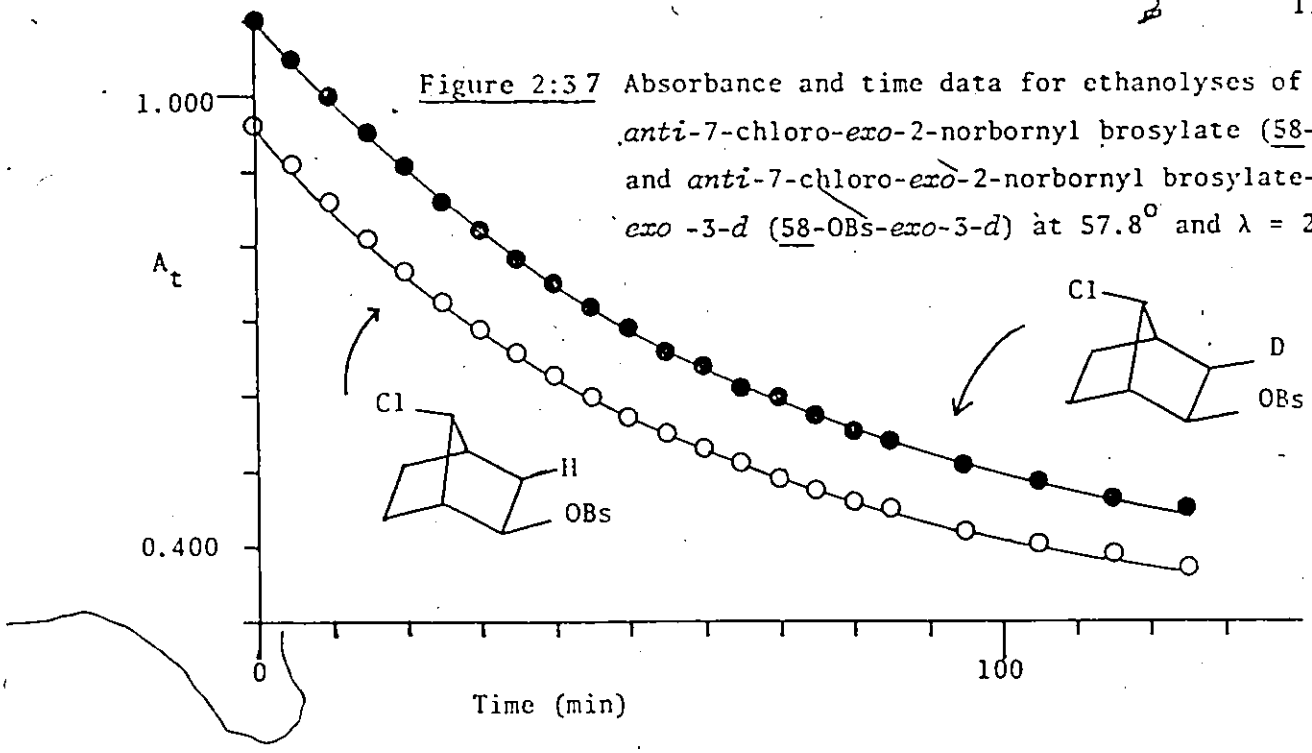


Figure 2:37 Absorbance and time data for ethanolyses of *anti*-7-chloro-*exo*-2-norbornyl brosylate (58-OBs) and *anti*-7-chloro-*exo*-2-norbornyl brosylate-*exo*-3-*d* (58-OBs-*exo*-3-*d*) at 57.8° and λ = 276.4 nm.

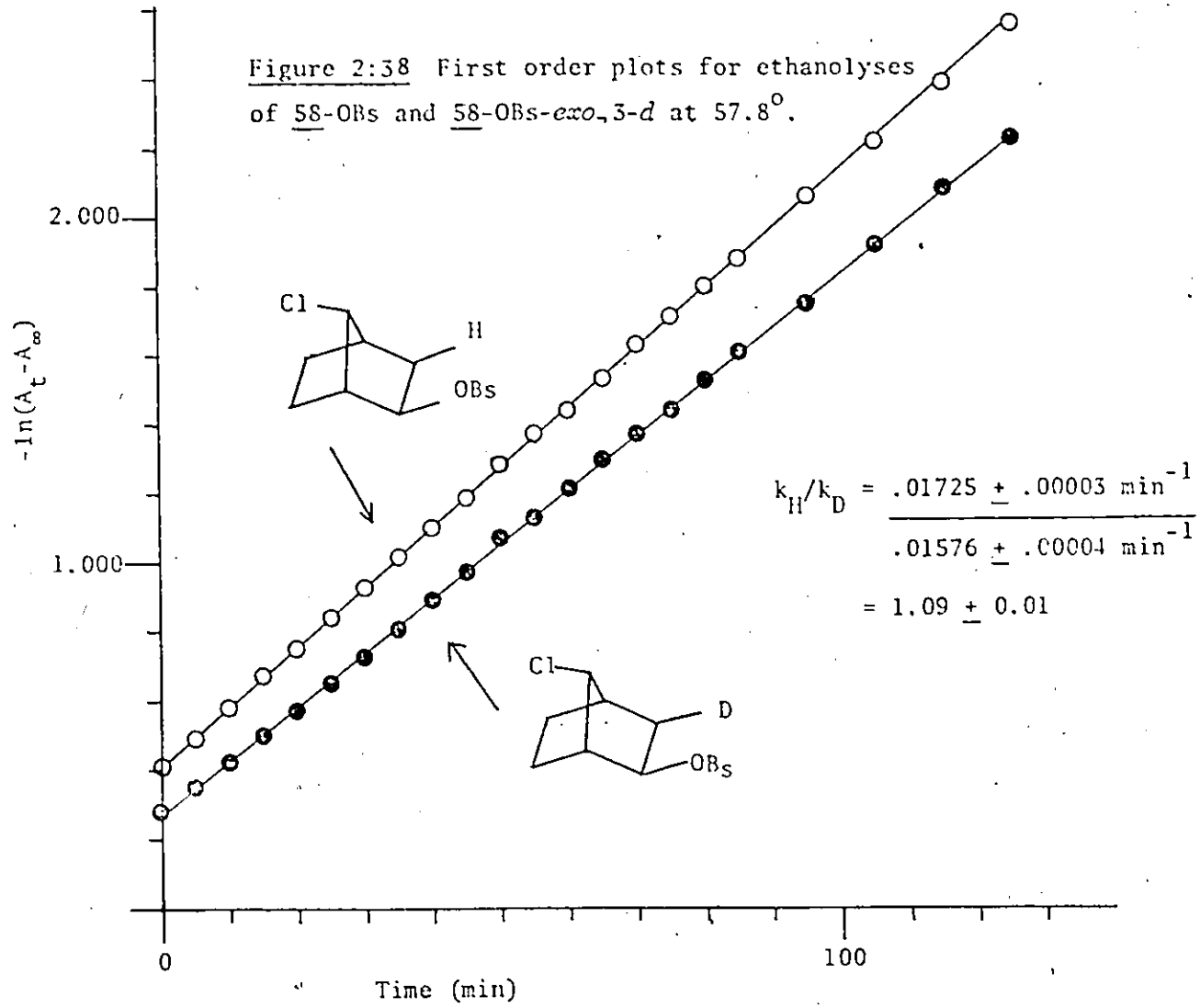


Figure 2:38 First order plots for ethanolyses of 58-OBs and 58-OBs-*exo*-3-*d* at 57.8°.

$$k_H/k_D = \frac{.01725 \pm .00003 \text{ min}^{-1}}{.01576 \pm .00004 \text{ min}^{-1}}$$

$$= 1.09 \pm 0.01$$

CHAPTER 3

DISCUSSION OF RESULTS

A. Electrophilic Cleavage of Nortricyclenes

1) 3-Chloronortricyclene (24)

Accurate rate constants for the electrophilic cleavage of 3-chloronortricyclene (24) in acetic acid containing sulphuric acid under the conditions previously described were not obtained. However, from Table 3:1 it is apparent that 24 is less reactive than nortricyclene (20) or 1-methylnortricyclene (22) with respect to rupture of the cyclopropyl bonds. This is not surprising when one considers that in the absence of resonance stabilization by chlorine, the inductive effect of this halogen destabilizes positively charged species. Solvolysis of 24 (*via* loss of chloride) to produce the nortricyclyl cation in which there is a *p*-orbital adjacent to the cyclopropyl group (*cf* cyclopropylcarbinyl cation) does not compete with ring cleavage. This corroborates the experimental observations of Roberts[221,222] which have established that the solvolytic reactivity of 24 is extraordinarily low ($k = 0.019\ hr^{-1}$, in 80:20 ethanol-water at 85°) relative to other cyclopropylcarbinyl-type compounds. It is likely that introduction of severe strain by the sp^3 to sp^2 hybridizational change which occurs during solvolysis outweighs any cyclopropylcarbinyl stabilization in the transition state.

Product ratios from the electrophilic cleavage of 24, *inter alia* 58-OAc : 59-OAc = 44:26*, suggest that for steric reasons attack by acetate on the chloronorbornonium ions 93 and 94 or conceivably on the edge-protonated 3-chloronortricyclene 95 is preferred from the side *anti* to chlorine. This

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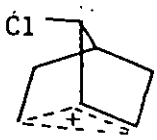
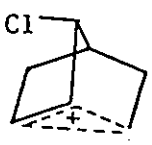
* These numbers are based on the relative ratio of the corresponding chloro ketones 63 and 64.

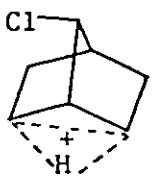
point is examined in more detail in a subsequent section.



93



94



95

Since predominantly *exo*-acetate products are observed (*exo*-acetate: *endo*-acetate = 98±2:2±1), this shows that the carbon atom which undergoes nucleophilic attack experiences net inversion of configuration, a phenomenon also observed in other nortricyclenes[40,41,180] as well as in a multitude of other compounds containing cyclopropyl groups.[36,37,52,55,56] However, the stereospecificity of nucleophilic attack could be peculiar to this system since *exo*-attack in the norbornyl system is favoured.[144] In deuterated medium, ring rupture of 24 gives monodeuterated products with minor multiple labeling (<3%) and establishes that the intermediate cationic species do not return appreciably to 24 or to chloronorbornenes.

In view of the spectral data in Table 2:3 (Chapter 2) which quantitatively establishes the distribution of deuterium within the products, a mechanism for electrophilic cleavage of 3-chloronortricyclene (24) is presented in Scheme 3:1. A,B,C,D,E, and F represent either the chloronorbornonium ion or the appropriate pair of classical ions. Since there was 10-15% isomerization of *endo*-5-chloro-*exo*-2-norbornyl acetate (61-OAc) to the *exo*-5-chloro isomer 60-OAc, the partitioning of A,B,C,D,E and F to 60- and 61-OAc-*d* is not exactly that given by deuterium positional analysis and therefore is represented as totals leading to A,B,C,D,E and F.

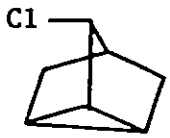
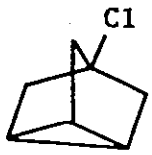
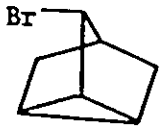
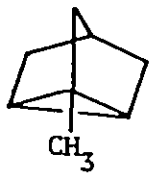
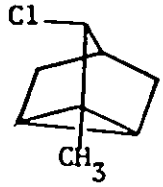
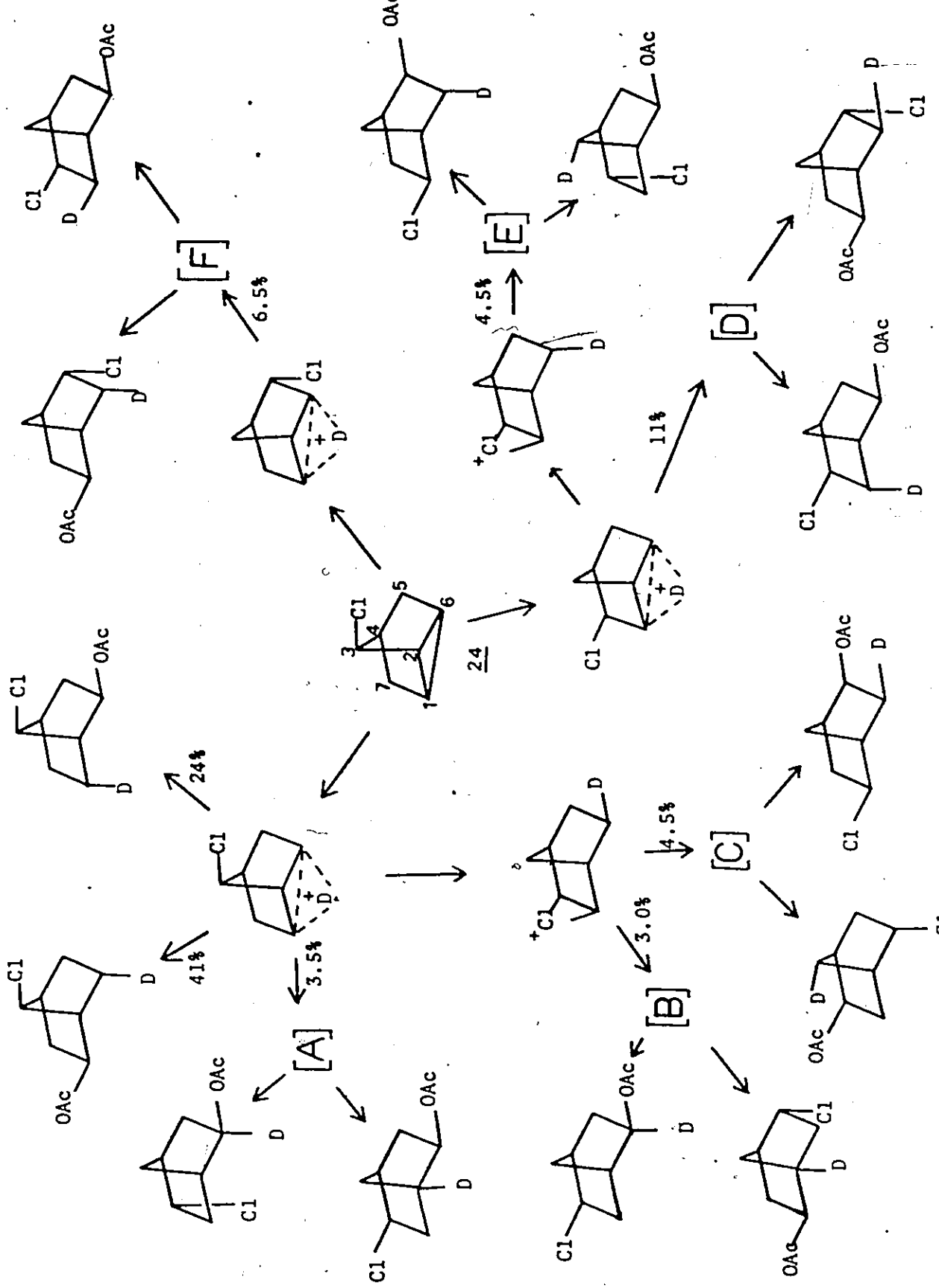
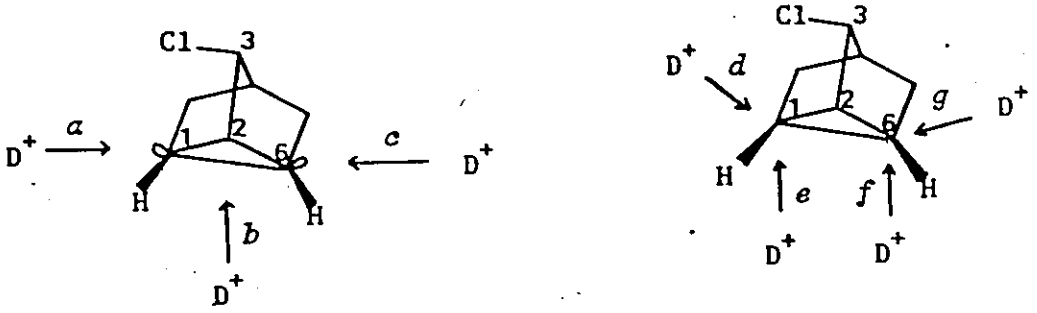
Compound	Acid Medium	Temp	Time(% Reaction)	Ref
 24	CH_3CO_2H + 0.10M H_2SO_4	70°	120 hr (>95)	this work
	CH_3CO_2H + 0.10M H_2SO_4	45°	96 hr (>95)	180
	CH_3CO_2H + 0.10M H_2SO_4	75°	45 hr (98)	180
 20	CH_3CO_2H + 0.08M H_2SO_4	23°	24 hr (≈95)	40
 22	CH_3CO_2H + 0.0052M H_2SO_4	24°	2 hr (15)	41
 25	CH_3CO_2H + 0.10M H_2SO_4	62°	105 hr (>93)	this work

Table 3:1 Conditions required for the cleavage of various nortricyclenes



Scheme 3:1 Mechanism for the electrophilic (D^+) cleavage of 3-chloronortricyclene (24)

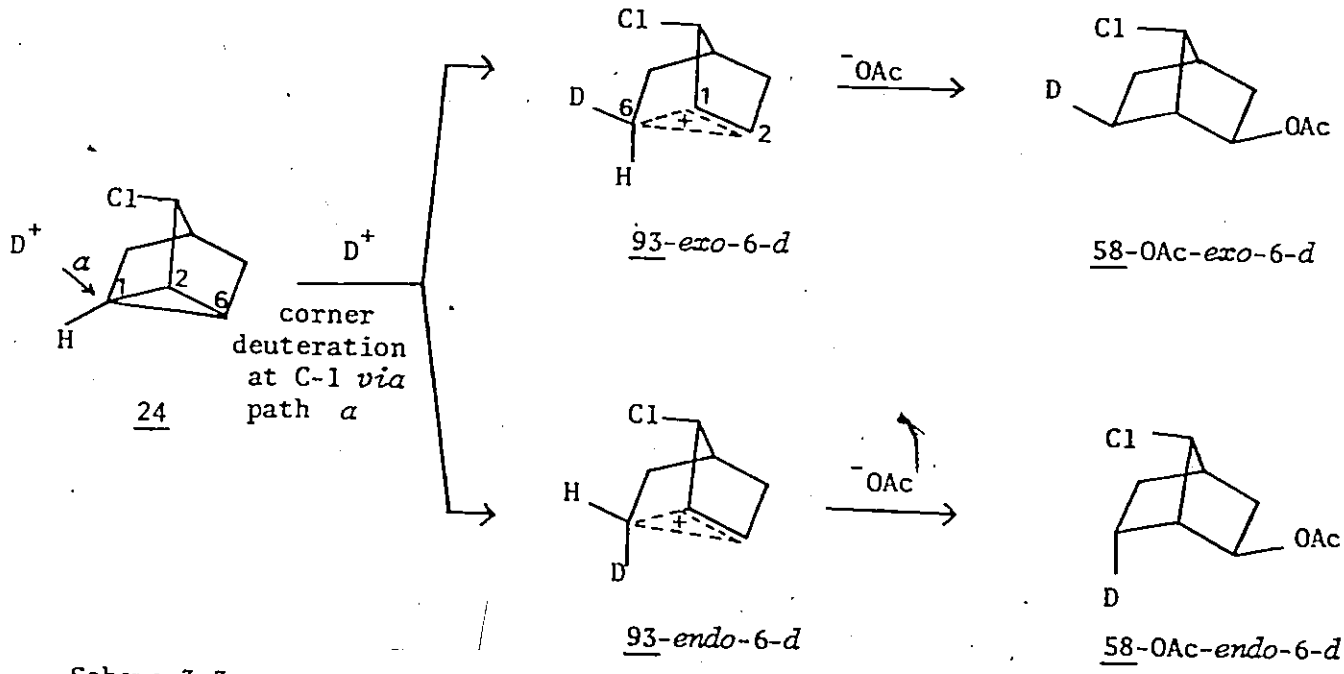
Since electrophilic (D^+) cleavage of 24 gave *anti*-7-chloro-*exo*-2-norbornyl acetate-*endo*-6-*d* (58-OAc-*endo*-6-*d*) with only small amounts of deuterium at *exo*-C-6 (*endo*-6-*d*:*exo*-6-*d*>14), this suggests that *initial corner deuteration* at C-1 (path a, Scheme 3:2) of the cyclopropyl group with subsequent cleavage of the C-1 C-6 bond is not an important path leading to this product. If one accepts the Walsh model[8] for cyclopropane (*cf* 1) as being representative of the cyclopropyl bonding in 3-chloronortricyclene (24), then corner deuteration at C-1 actually implies electrophilic attack directed towards a back lobe of the sp^2 orbital at C-1 (path a, Scheme 3:2). This minor lobe is situated in a plane defined by the C-7, C-1, C-1-H atoms and almost bisects the angle formed by these three atoms. By definition,



Scheme 3:2

corner deuteration at C-1 *via* this route involves the simultaneous development of positive charge at the two carbon atoms which are opposite to that being attacked, namely C-2 and C-6. Neglecting isotope effects, attack in this manner should give equal probabilities for formation of ions 93-*exo*-6-*d* and 93-*endo*-6-*d* (Scheme 3:3) and therefore equal amounts of chloro acetates 58-OAc-*exo*-6-*d* and 58-OAc-*endo*-6-*d*. The experimental data in Table 2:3 (Chapter 2) do not support these predictions. Alternatively, if one considers the bent bond model[11] for cyclopropane (*cf* 2) as being an accurate

representation of bonding in 3-chloronortricyclene, then corner deuteration at C-1 implies electrophilic approach by paths d and e (Scheme 3:2).



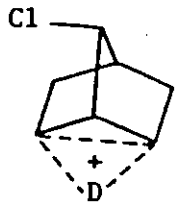
Scheme 3:3

ie approach by electrophile towards the back lobes of the C-1 C-6 and C-1 C-2 bonds respectively. Conceivably, the chlorine atom at C-3 could impede approach of electrophile by path d and hence initial corner deuteration at C-1 by path e could predominate. This particular preferred pathway could easily account for the predominant formation of 58-OAc-*endo*-6-*d*. However, this possibility can be excluded since Brown[223,224] has demonstrated that the *gem*-dimethyl groups of 7,7-dimethylnorbornene do not reverse the *exo* stereospecificity[144] for reactions proceeding through non-cyclic processes. Since a methyl group and a chlorine atom occupy approximately the same volume in space, there would be a negligibly small steric difference between corner deuteration at C-1 *via* paths d and e. Once again this should result in a

virtually equal probability for formation of ions 93-*exo*-6-*d* and 93-*endo*-6-*d* and therefore equal amounts of 58-OAc-*exo*-6-*d* and 58-OAc-*endo*-6-*d*.

Formally, whether corner deuteration at C-1 in 24 occurs by path a or by paths d and e, the intermediate cations should be identical. In Scheme 3:2, the representation of approach by D^+ towards C-1 by paths d and e emphasizes the fact that two stereochemical outcomes are possible for formation of ion 93, namely *exo*- and *endo*-6-*d*. However, it must also be stressed that corner deuteration by path a (Scheme 3:2) also allows for the same two stereochemical outcomes for the formation of ion 93.

Initial edge deuteration (path b, Scheme 3:2) of the C-1 C-6 bond in 3-chloronortricyclene to yield 95-*d* and subsequent collapse with nucleophile (acetate) accounts for formation of 58-OAc-*endo*-6-*d*.

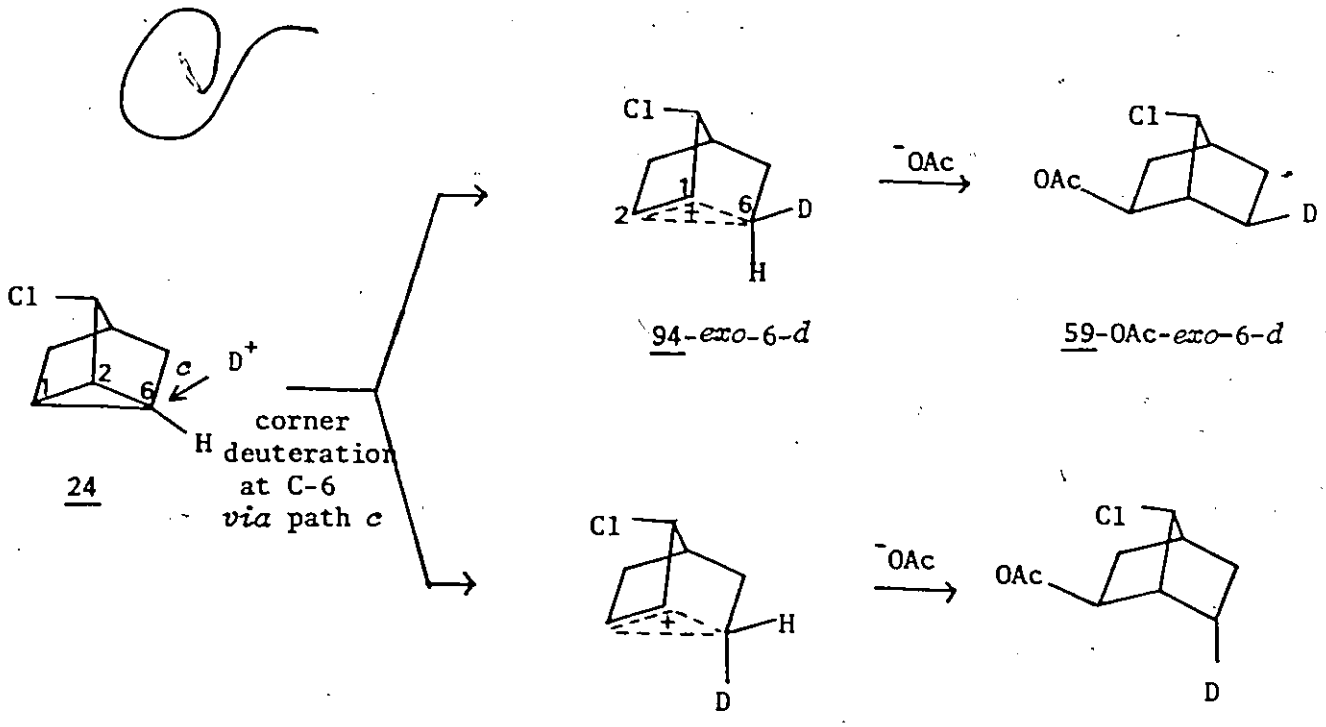


95-*d*

In Scheme 3:3, corner deuteration of 24 at C-1 is depicted as giving rise to norbornonium-type ion 93 in order to conform to the concept that cornerwise attack by an electrophile at a particular cyclopropyl carbon atom induces simultaneous development of positive charge at the two opposite carbon atoms. Ion 93 would be unsymmetrical with respect to charge distribution between C-1 and C-2 *ie* most of the positive charge probably resides on C-2 since this carbon atom is further removed than C-1 from the chlorine substituent. This prediction is supported by the observation that

significant amounts of *endo*-3-chloro-*exo*-2-norbornyl acetate (72-OAc) were not formed (< 3%) during the electrophilic (CH_3CO_2H, H_2SO_4) cleavage of 3-chloronortricyclene; this chloro acetate would have arisen as a result of nucleophilic attack by acetate at C-1 in ion 93. In fact, Gassman[176] has recently suggested that ion 93, which was generated by solvolysis of *anti*-7-chloro-*exo*-2-norbornyl tosylate (58-OTs), is classical. Therefore substituents at C-6 in 93 assume their respective *endo*- and *exo*-like character which is maintained in the reaction leading to product (*e.g.* 58-OAc-*exo*-6-*d*).

Similarly, the predominant formation of *syn*-7-chloro-*exo*-2-norbornyl acetate-*endo*-6-*d* (59-OAc-*endo*-6-*d*) with only small amounts of 59-OAc-*exo*-6-*d* being present (*endo*-6-*d*:*exo*-6-*d*>14) dictates that corner deuteration at C-6 in 3-chloronortricyclene (path c, Scheme 3:2) is not an important path leading to this product. Neglecting isotope effects, attack at C-6 by path c



Scheme 3:4

should give equal probabilities for formation of 94-*exo*-6-*d* and 94-*endo*-6-*d*; therefore equal amounts of 59-OAc-*exo*-6-*d* and 59-OAc-*endo*-6-*d* should be formed (Scheme 3:4). Once again, if one prefers to envisage corner deuteration at C-6 as involvement of paths f and g (Scheme 3:2), then there should not be a steric preference for either path and hence virtually identical amounts of 59-OAc-*exo*-6-*d* and 59-OAc-*endo*-6-*d* should be formed. The data in Table 2:3 (Chapter 2) do not support these contentions.

Therefore, *initial edge deuteration* of the C-1 C-6 bond in 3-chloronortricyclene (path b, Scheme 3:2) to give 95-*d* and subsequent collapse with acetate accounts for the formation of 59-OAc-*endo*-6-*d*. Corner deuteration at C-6 in 24 is depicted in Scheme 3:4 as yielding the norbornonium-type ion 94 for reasons identical to those put forth for ion 93 (*vide supra*).

Possibly, corner deuteration *via* path f (Scheme 3:2) followed by cleavage of the C-2 C-6 bond might be stereoelectronically favoured relative to corner deuteration *via* path g, due to formation of an *exo*-chloronium ion 90. This pathway (Scheme 3:5) could also account for formation of 59-OAc-*endo*-6-*d*. If initial corner deuteration of 24 by path f gave the symmetrical ion 90 directly, then neglecting isotope effects, equal amounts of 59-OAc-*endo*-6-*d* and 59-OAc-*endo*-5-*d* would be formed. Clearly this is not borne out by the experimental results in Table 2:3. Moreover, it is difficult to rationalize why path g should be totally suppressed. Thus the initial interaction of electrophile (D^+) with 3-chloronortricyclene occurs in an edge-deuterated fashion to give 95-*d*, in order to account for the distribution of label (*ie* predominantly *endo*-C-6) within the two major products 58- and 59-OAc-*d*. In contrast to nortricyclene (20)[40] and 1-methylnortricyclene (22)[41]

Figure 3:1

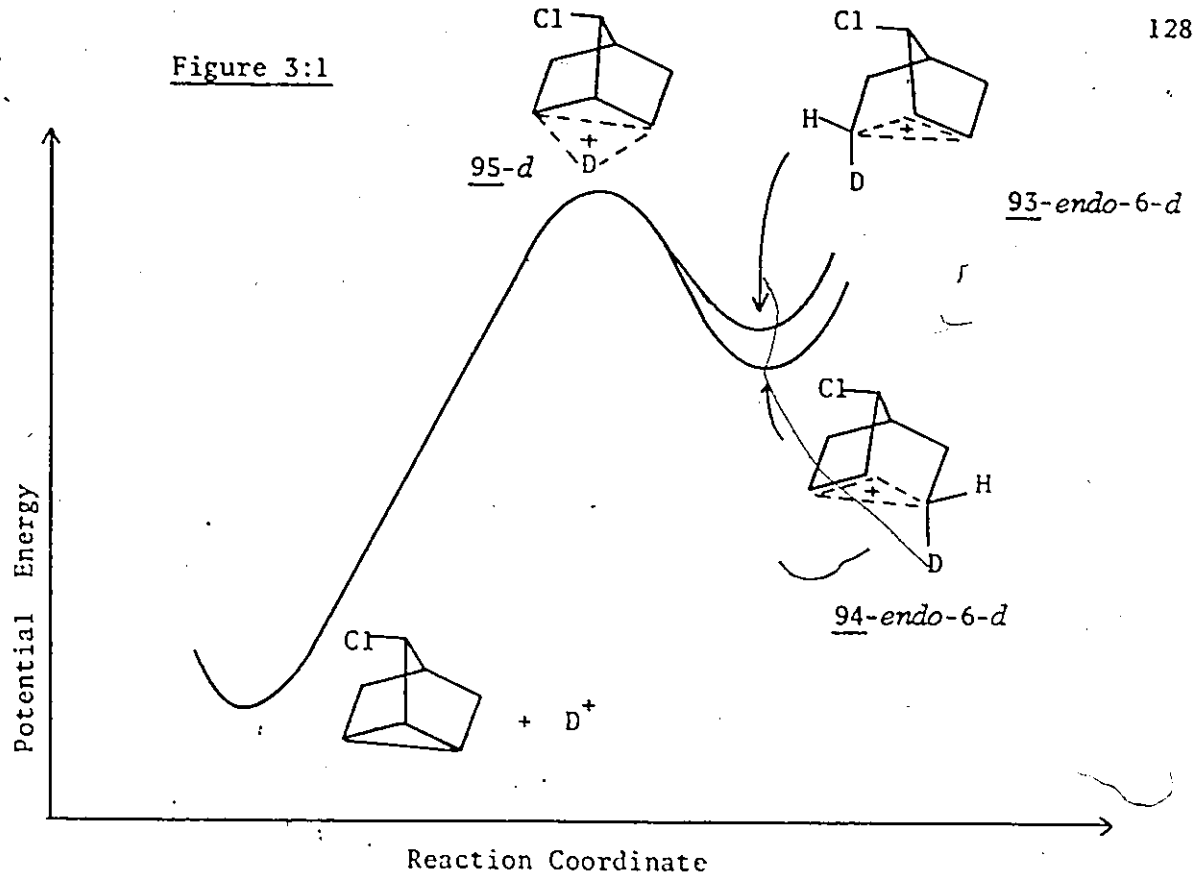
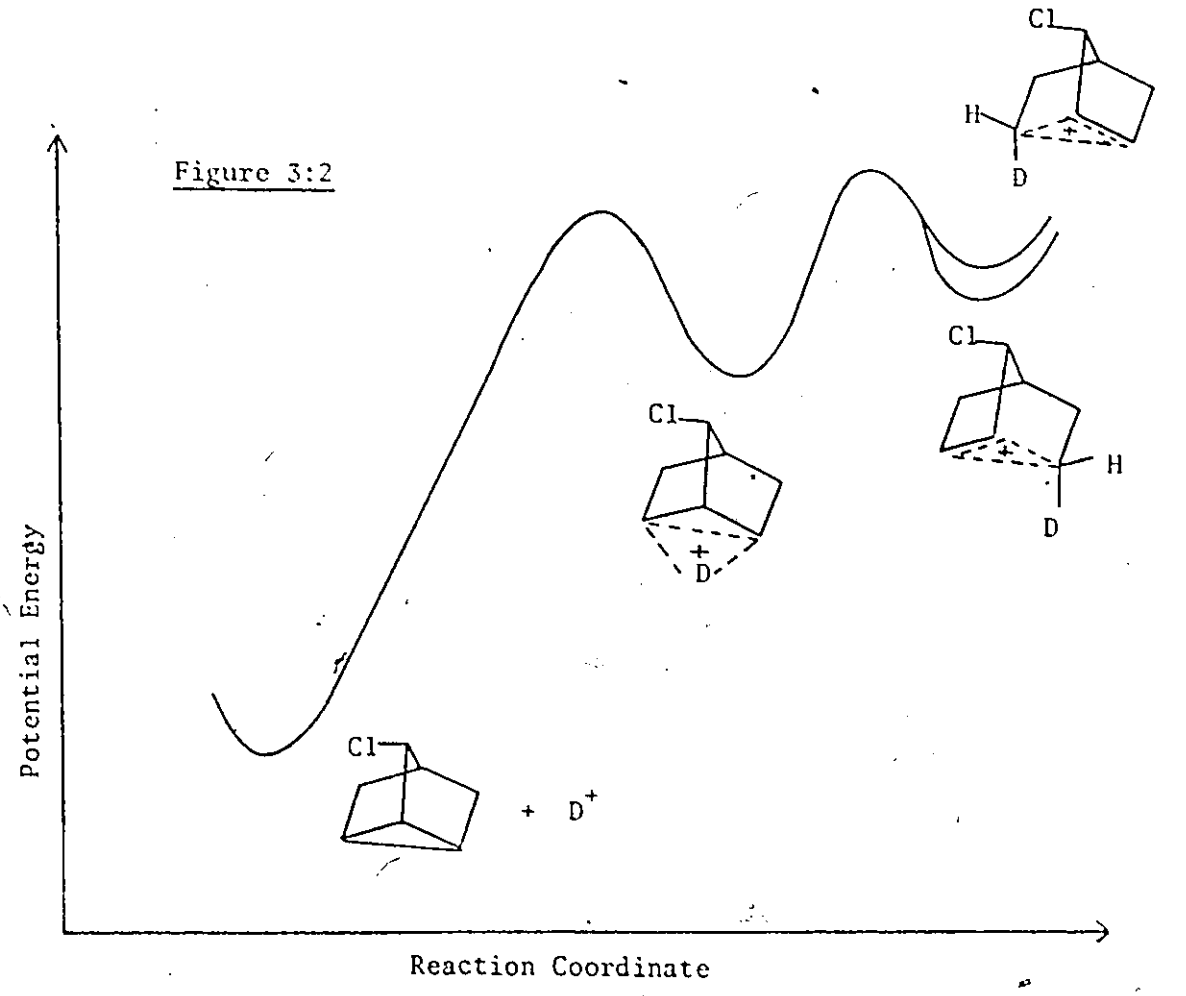
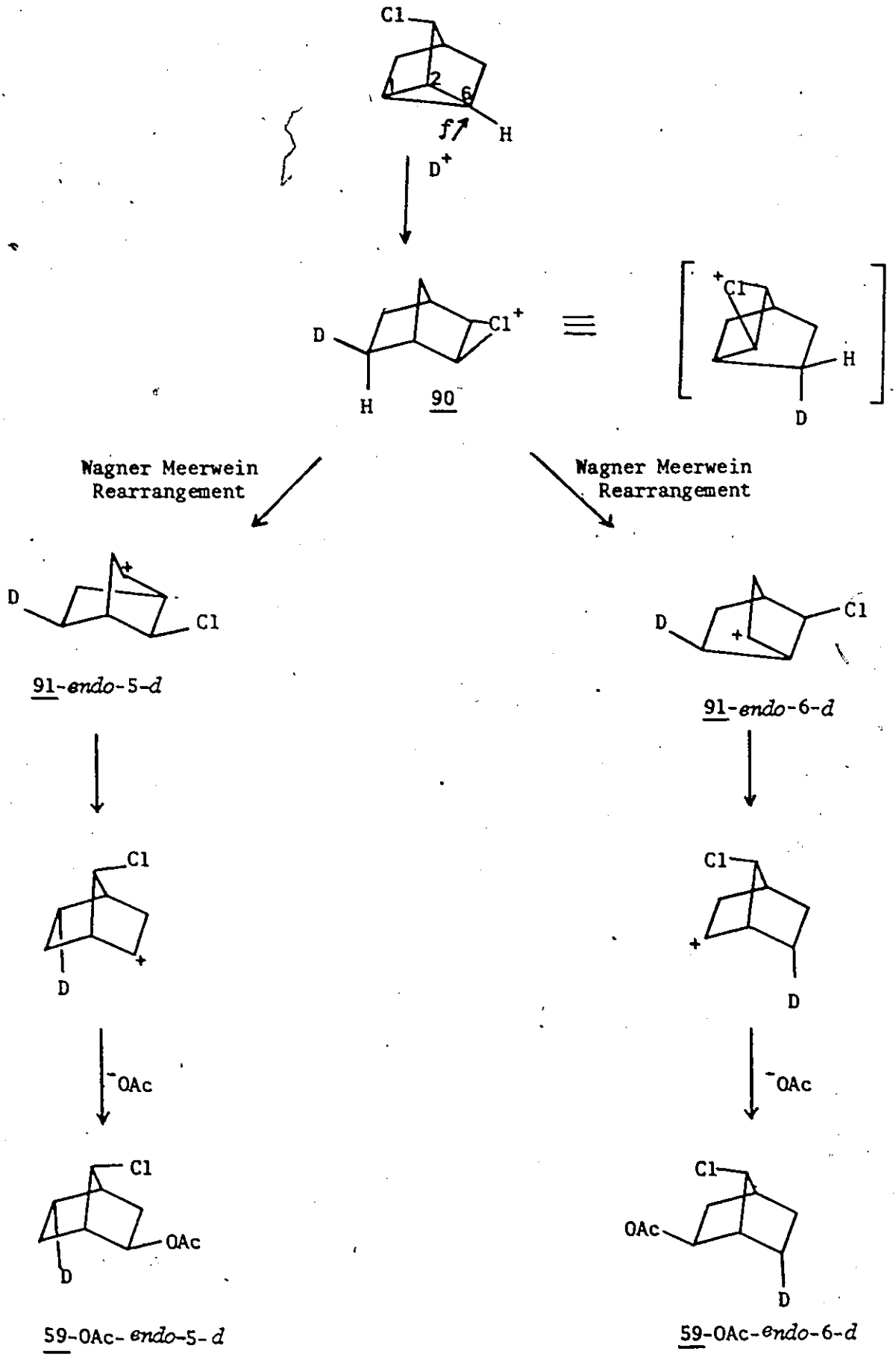


Figure 3:2



Scheme 3:5



59-OAc-*endo*-5-*d*

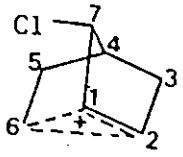
59-OAc-*endo*-6-*d*

where substantial electrophilic inversion was observed, the C-1 C-6 bond in 3-chloronortricyclene undergoes cleavage with predominant electrophilic retention (this contrast is discussed later).

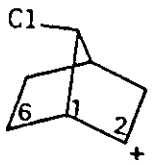
Although the present work dictates intervention of edge deuteration, it does not differentiate whether this is a transition state or an intermediate along the reaction coordinate, or if an edge deuterated species is converted into a corner deuterated species. In fact, subsequent arguments (*vide infra*) suggest that corner deuteration is likely not important in this system. Figures 3:1 and 3:2 illustrate two possible potential energy profiles for the electrophilic cleavage of 24:

a) an edge deuterated transition state preceding ionic intermediates and b) an edge deuterated intermediate preceding ionic intermediates.

The potential energy diagrams depict ion 94-*endo*-6-*d* as being more stable than ion 93-*endo*-6-*d* because of possible stabilization of the positive charge by chlorine *via* halonium ion participation. Once again, it must be



93



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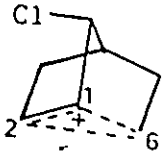
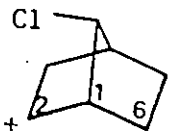


94

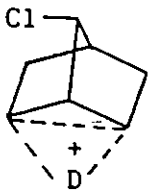


91

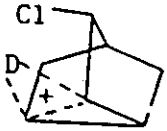
remembered that more accurate descriptions of 93 and 94 would place most of the positive charge at C-2 so that ions 96 and 91 respectively are probably truer representations. Experimental evidence for halonium ion participation in 91 was recently reported by Gassman who found that acetolyses of *anti*-7-chloro-*exo*- and *endo*-2-norbornyl tosylates gave virtually identical product mixtures whereas acetolyses of *syn*-7-chloro-*exo*- and *endo*-2-norbornyl tosylates gave different product mixtures.[176] Neighbouring group participation or intramolecular interaction of the *syn* chlorine atom with the *p*-orbital was invoked as an explanation for the above behaviour.

In Figures 3:1 and 3:2, edge deuterated ion 95-*d* rearranges only to 93- and 94-*endo*-6-*d* because transformation into 93- and 94-*exo*-6-*d* would require large atomic rearrangements of the hydrogen and deuterium atoms at C-6. Therefore *if* the electrophilic cleavage of 24 does in fact involve the intervention of corner deuterated species, our results impose one important restriction, namely edge deuteration must precede corner deuteration.

The reaction products could arise by nucleophilic attack on edge and/or corner deuterated and/or ionic species. Baird and Aboderin studied the electrophilic cleavage of cyclopropane and concluded that solvolytic ring opening occurred primarily from hydrogen-bridged ions (edge protonation, 45).[89] In the 3-chloronortricyclene - CD_3CO_2D, D_2SO_4 system, the twelve hydrogen- (and deuterium) bridged ions formally derivable are 95-*d*, 97-107 (Table 3:2). Initial edge deuteration of the C-1 C-6 bond gives 95-*d* which can conceivably rearrange *via* corner deuterated ions 93-*endo*-6-*d* and 94-*endo*-6-*d* to the edge protonated ions 101 and 106 respectively. Further rearrangement *via* other corner protonated ions can convert 101 into 105 and 106 into 102. Similarly,

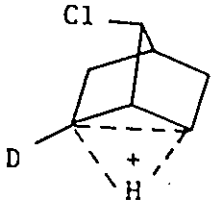


95-*d*



100

104



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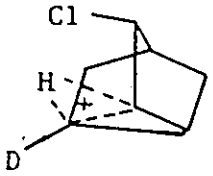

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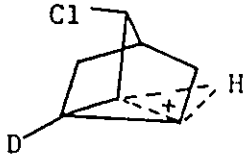

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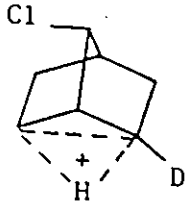

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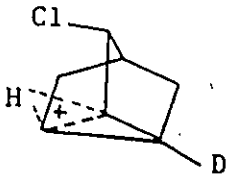
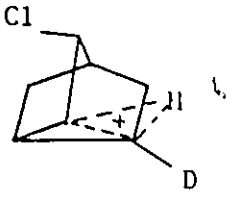


102



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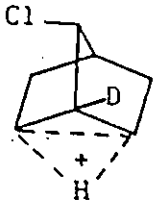

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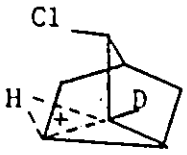
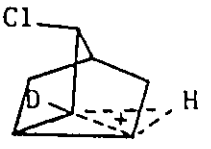


103

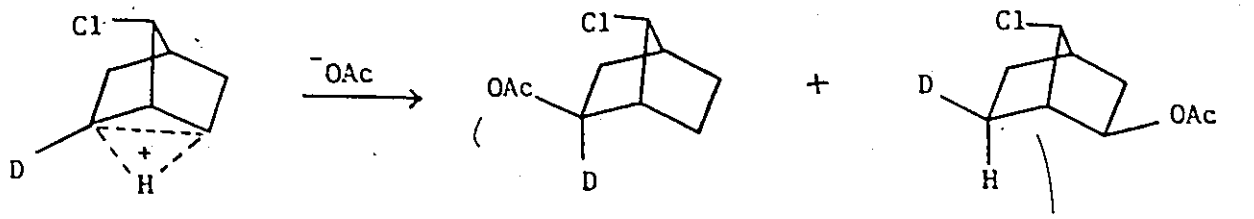


107

Table 5:2 Possible hydrogen (deuterium) bridged ions for D^+ and 3-chloronortricyclene (24)

initial edge deuteration of the C-1 C-2 bond in 3-chloronortricyclene gives 100 which can be converted into ions 99 and 105 *via* ions 107 and 97 respectively. If nucleophilic attack occurs directly on these ions from the sides opposite to those of the delocalized bonds, then attack by acetate on ion 95-*d* would yield both *syn*- and *anti*-7-chloro-*exo*-2-norbornyl acetate-*endo*-6-*d*. However, attack by acetate could also occur on unsymmetrical ions such as 93-*endo*-6-*d* and/or 94-*endo*-6-*d* which might arise from 95-*d*. This work does not distinguish between these possibilities.

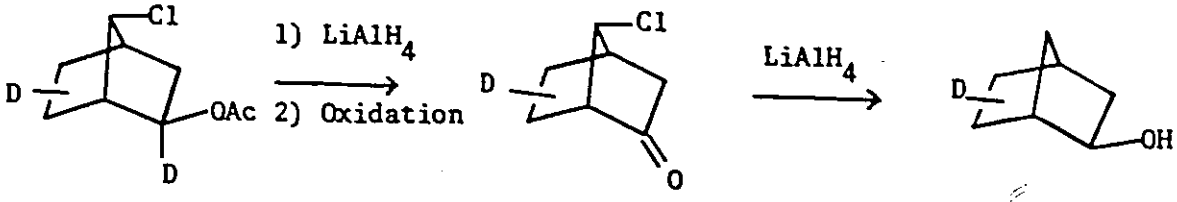
If products were formed solely by nucleophilic attack on the ions shown in Table 3:2, then attack by acetate on 97 should give a mixture of 59-OAc-*endo*-2-*d* and 58-OAc-*exo*-6-*d*. As shown in Table 2:3 (Chapter 2), it was



97 59-OAc-*endo*-2-*d* 58-OAc-*exo*-6-*d*

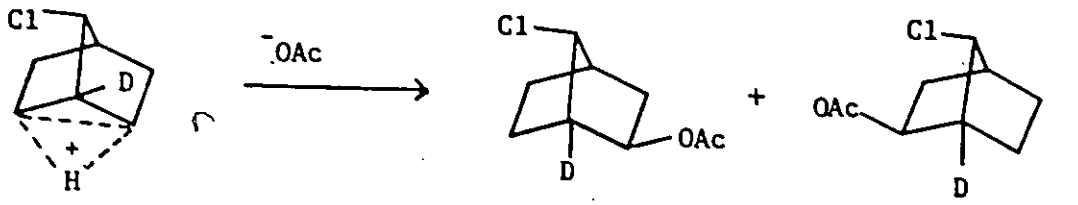
estimated that less than 5% of the deuterium at C-6 in 58-OAc-*d* was positioned at *exo*-C-6. If this small amount of deuterium at *exo*-C-6 arose by nucleophilic attack by acetate on ion 97, then one should expect deuterium at C-2 in 59-OAc-*d*. However, the analysis for deuterium was carried out on the deuterated norbornanol which was derived from 59-OAc-*d* by (a) reduction with lithium aluminum hydride to 59-OH-*d* (b) oxidation

to 64-*d* and (c) reduction of 64-*d* with lithium aluminum hydride. The oxidation would remove any deuterium which was originally present at C-2



and thus would not be detected.

Attack by acetate on ion 99 would produce 58-OAc-1-*d* and 59-OAc-1-*d*.



99 58-OAc-1-*d* 59-OAc-1-*d*

Within the limits of detection by pmr spectroscopy*, these two products were not observed.

Formation of *exo*-5-chloro-*exo*-2-norbornyl acetate-*exo*-3-*d* (60-OAc-*exo*-3-*d*) cannot be explained in terms of nucleophilic attack on any of the ions shown in Table 3:2. However, transformation of ion 95-*d* into ion 90 which undergoes a hydride shift and then reacts with acetate accounts for 60-OAc-*exo*-3-*d* (Scheme 3:6). Formation of 60-OAc with deuterium at both

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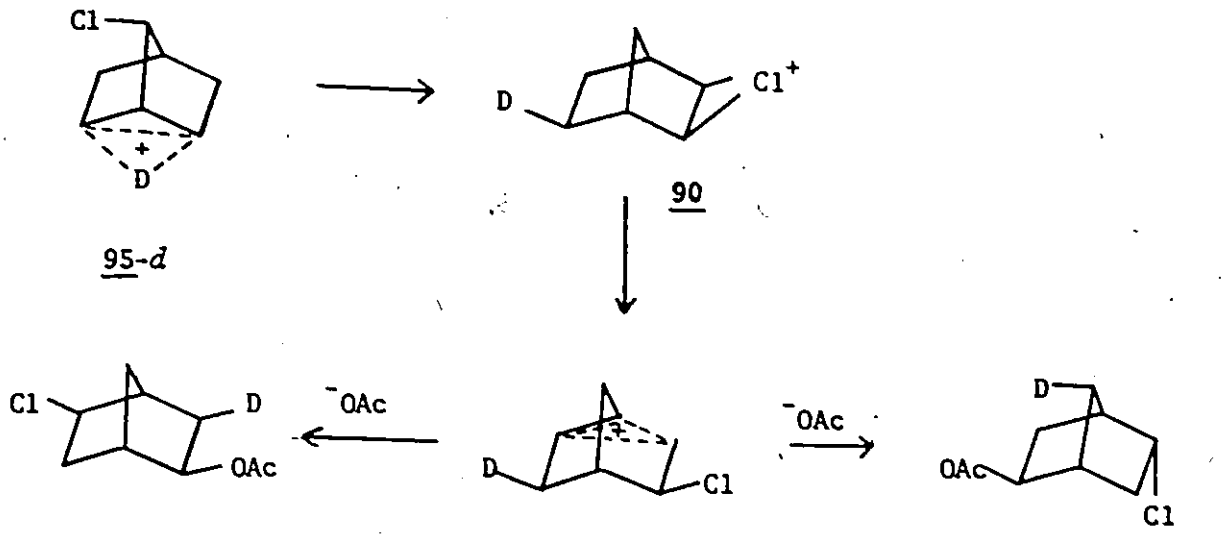
* It must be emphasized that detection of small amounts of deuterium, within these compounds, by pmr spectroscopy is usually quite difficult.

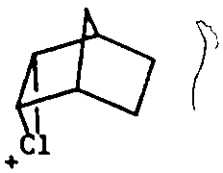
exo- and *endo*-C-3 shows that some leakage to the *exo*-chloronium ion 90



60-OAc-*exo*-3-*d* 61-OAc-*syn*-7-*d*

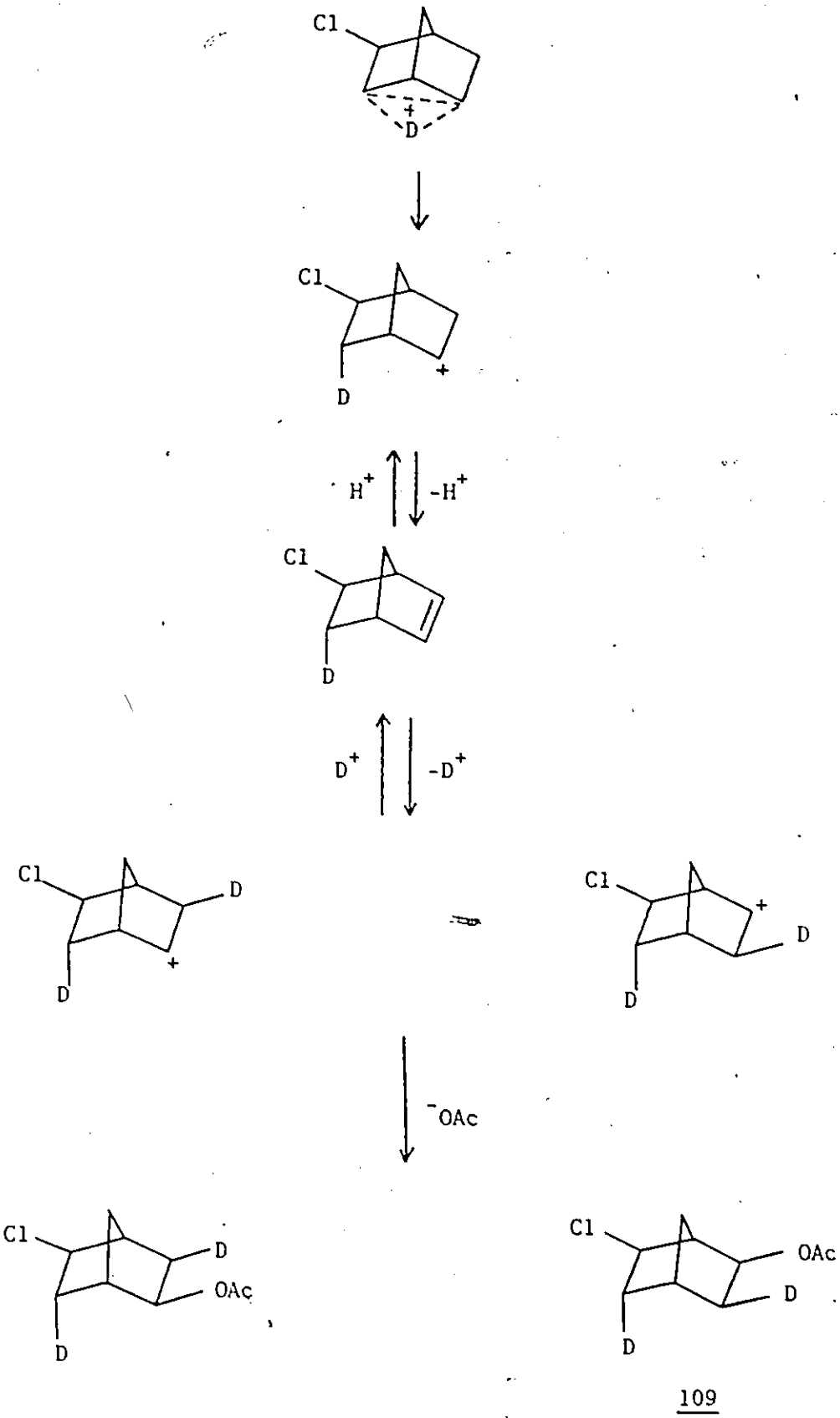
Scheme 3:6

occurs whereas lack of deuterium at the C-3 position in 61-OAc-*d* shows, by analogy, that leakage to an *endo*-chloronium ion 108 does *not* occur.



108

Deuterium is not introduced into C-3 of 60-OAc-*d* by the deprotonation-deuteration path shown in Scheme 3:7 since this would require that the amount of d_2 species in *exo*-5-chloro-*exo*-2-norbornyl acetate-*d* would equal the amount of deuterium at C-3. Experimentally, it was found that there

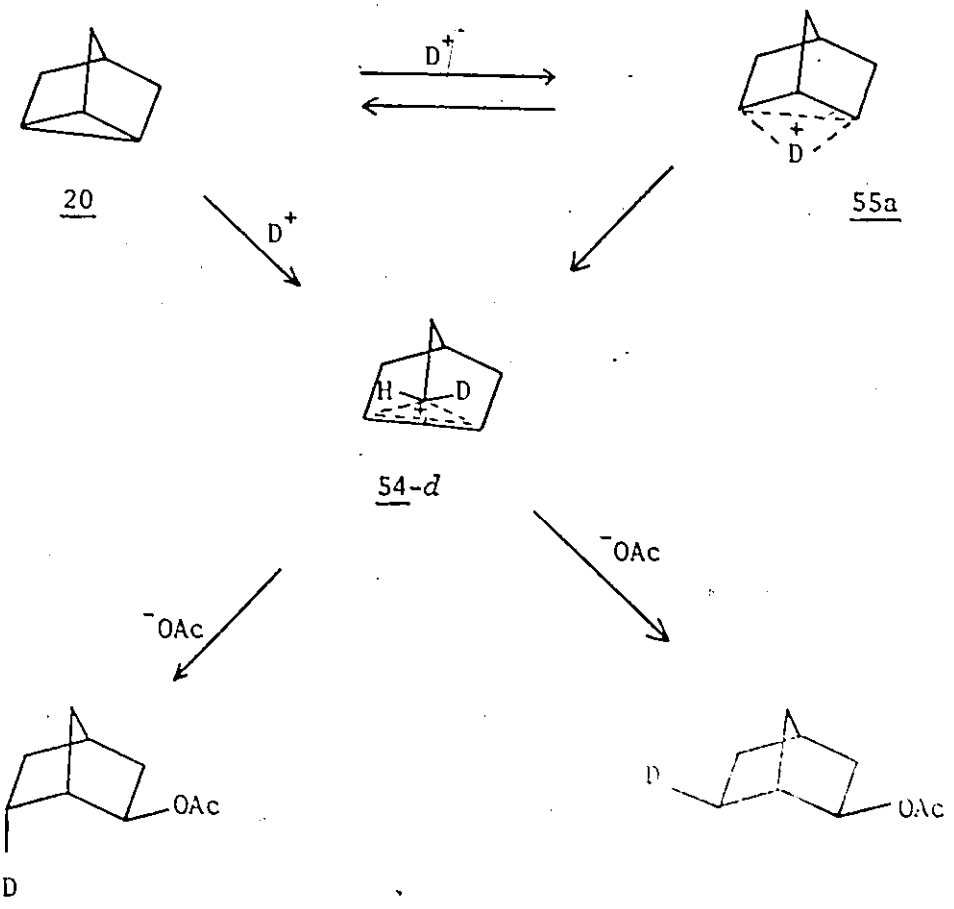


109

Scheme 3:7

were not any d_2 species and there was 0.40±0.10 deuterium atoms at C-3 in 60-OAc-*d* (Table 2:3, Chapter 2). The mechanism shown in Scheme 3:7 would allow for formation of *exo*-6-chloro-*exo*-2-norbornyl acetate (109); this compound was not detected among the reaction products.

For electrophilic (D^+) cleavage of nortricyclene (20), Nickon and Hammons found an equal distribution of deuterium at the *exo*- and *endo*-C-6 positions of the product - *exo*-2-norbornyl acetate.[40] They suggested that 20 was converted to a carbon-bridged norbornyl cation (54-*d*) which subsequently reacted with acetate; they further argued that if edge deuterated nortricyclene (55a) preceded formation of the carbon-bridged ion 54-*d*, then rearrangement of the former to the latter must be irreversible (Scheme 3:8).

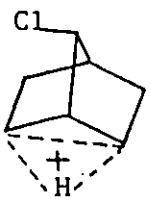


Scheme 3:8

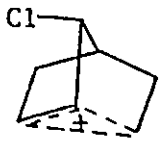
Since 20 has a plane of symmetry, it was not possible to discern whether the initial electrophilic attack was edge-wise or corner-wise, however, it was necessary to invoke the carbon-bridged ion 54-*d* as an intervening species.

In 3-chloronortricyclene, the chlorine substituent destroys the symmetry of the cyclopropyl ring and this should allow differentiation of initial edge and corner deuteration. However, such a molecular perturbation creates three chemically distinct cyclopropyl bonds and thus, extension of conclusions concerning this system (*ie* 24) to others (*e.g.* 20) can present problems. On the basis of the present work which has implicated initial edge deuteration for electrophilic (D^+) cleavage of 24, it appears desirable to suggest that nortricyclene also undergoes initial edge deuteration to give 55a which then rearranges to the corner deuterated species 54-*d*.

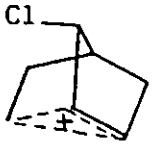
If by definition, corner protonation at a cyclopropyl carbon atom necessarily involves simultaneous development of positive charge more or less equally at the two carbon atoms opposite to that which is attacked, then it can be argued (validly) that predominant edge protonation of 3-chloronortricyclene (24) to give 95 occurs only because the chlorine substituent makes corner protonation (to yield 93 and/or 94) such an unfavourable process. Corner protonation at C-1 or C-6 in 3-chloronortricyclene would place some positive charge adjacent to the halogen; the edge protonated



95



94



93

ion 95 should be more stable than the corner protonated ions 93 or 94 because the positive charge in 95 is delocalized further away from chlorine. This possibility would invalidate any mechanistic comparison of the electrophilic cleavages of 3-chloronortricyclene and nortricyclene.

The energy barrier separating edge and corner protonated nortricyclene (54 and 55) is probably small so that conversion of the former to the latter is rapid. In 3-chloronortricyclene, an appreciable energy barrier probably exists between edge and corner protonation with the result that rearrangement of 95 to 93 and/or 94 might become unfavourable. It was previously suggested that *if* corner protonated 3-chloronortricyclene (93 or 94) was an important species in the reaction, then it must be preceded by an edge protonated species 95 (*vide supra*).

Recently, LCAO SCF MO calculations were performed for three-membered ring compounds in order to evaluate the electrostatic potentials produced in the neighbouring space by the nuclear and electronic charge distributions. These potentials were used to predict the molecular sites most likely to undergo electrophilic attack.[227] The electrostatic potential energy maps for the ring plane of cyclopropane are shown in Figures 3:3 and 3:5. They clearly show three energy minima (-22.3 kcal/mol) on the ring plane symmetrically placed with respect to the ring plane and in the region of the C-C bonds. Initial approach by the electrophile towards an edge produces a more negative potential (-22.3 kcal/mol) relative to initial corner-wise approach (-3.8 kcal/mol). Conversion of an edge protonated to a corner protonated species may then be facile provided that the potential energy barrier separating them

is small. This supports the contention that electrophilic cleavage of 3-chloronortricyclene involves initial edge protonation. However in this system, edge and corner protonated ions are probably separated by an appreciable energy barrier (*vide supra*).

Figure 3:4 provides support to the experimental observations that electrophiles are not stabilized by the face of cyclopropanes.[80-82] Approach towards the cyclopropyl face produces a positive potential.

The above electrostatic picture presented for cyclopropane represents a hypothetical gas-phase reaction and the actual potentials in solution may require modification, however the difference in potentials between edge- and corner-wise attack should still exist.

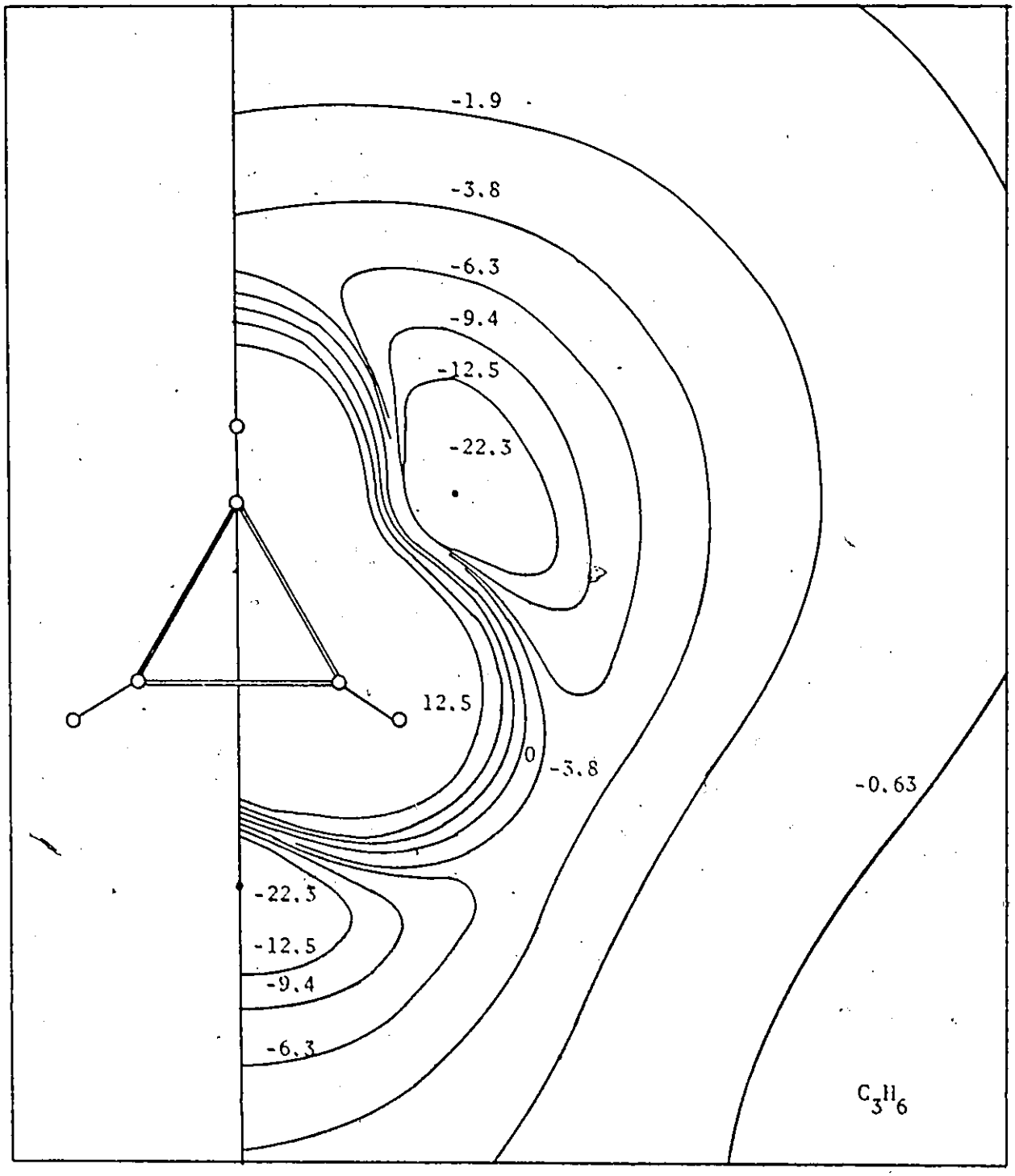


Figure 3:3 Potential-energy map for cyclopropane in the ring plane. From reference 227.

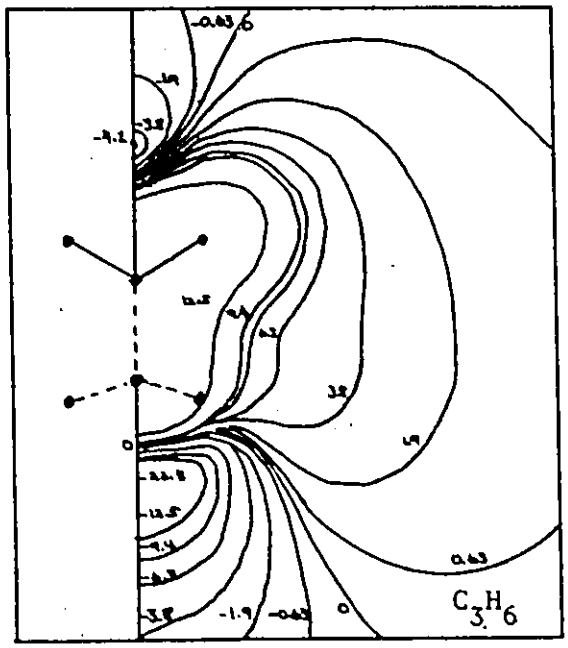


Figure 3:4 Electrostatic potential-energy map for cyclopropane. From reference 227.

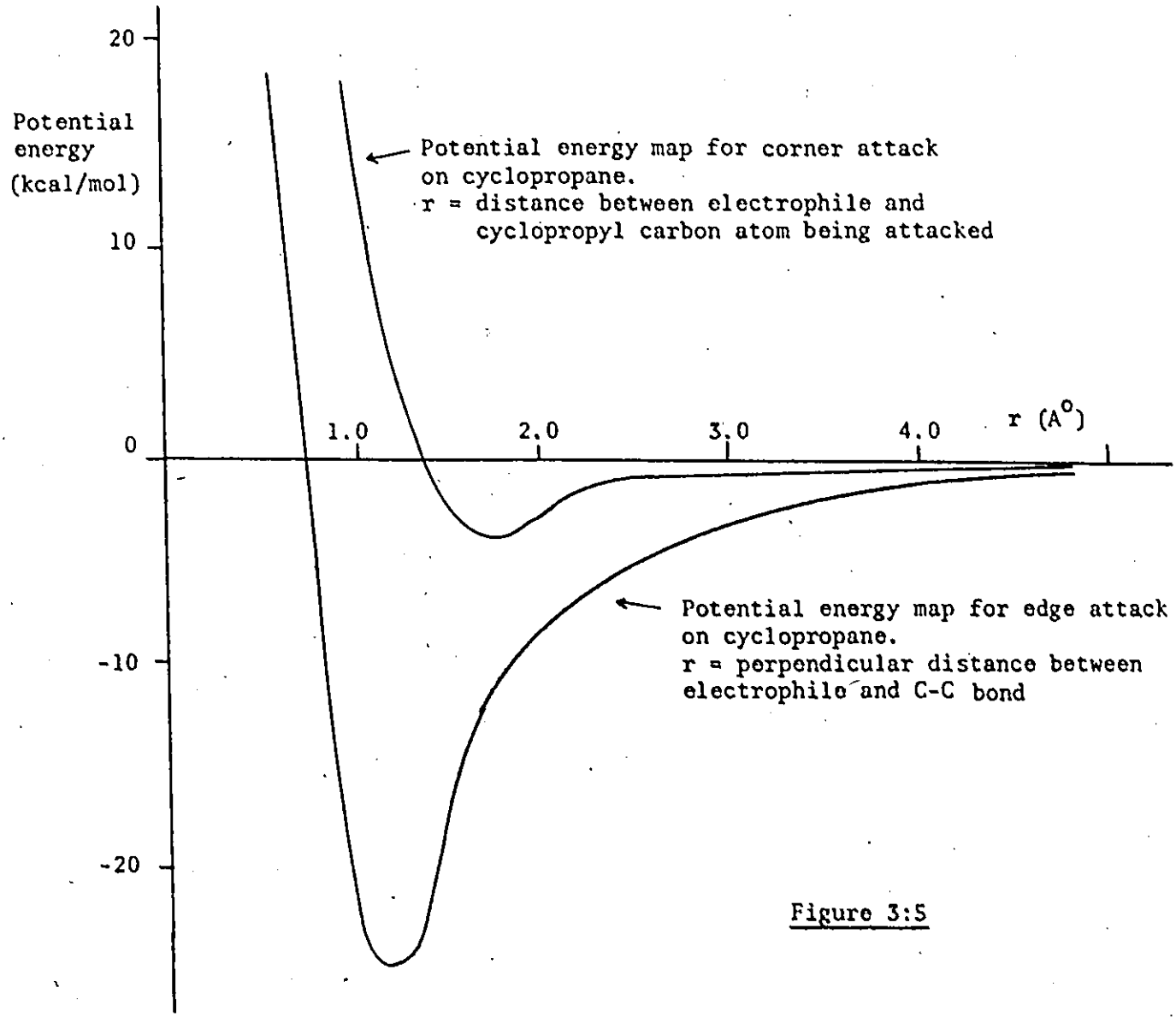
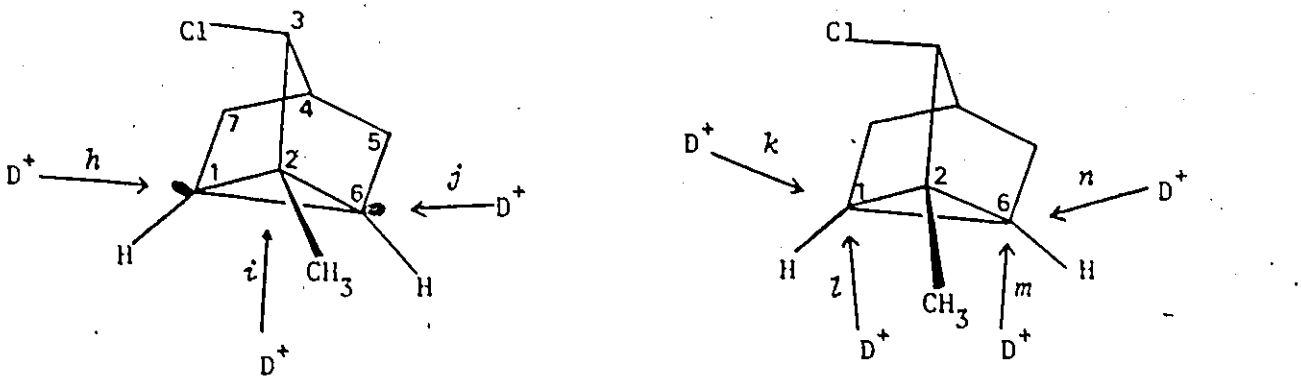


Figure 3:5

2) 2-Methyl-3-Chloronortricyclene (25)

2-Methyl-3-chloronortricyclene possesses three chemically distinct cyclopropyl bonds and predictions concerning which bond will be preferentially protonated must take into account two opposing effects, (i) electron

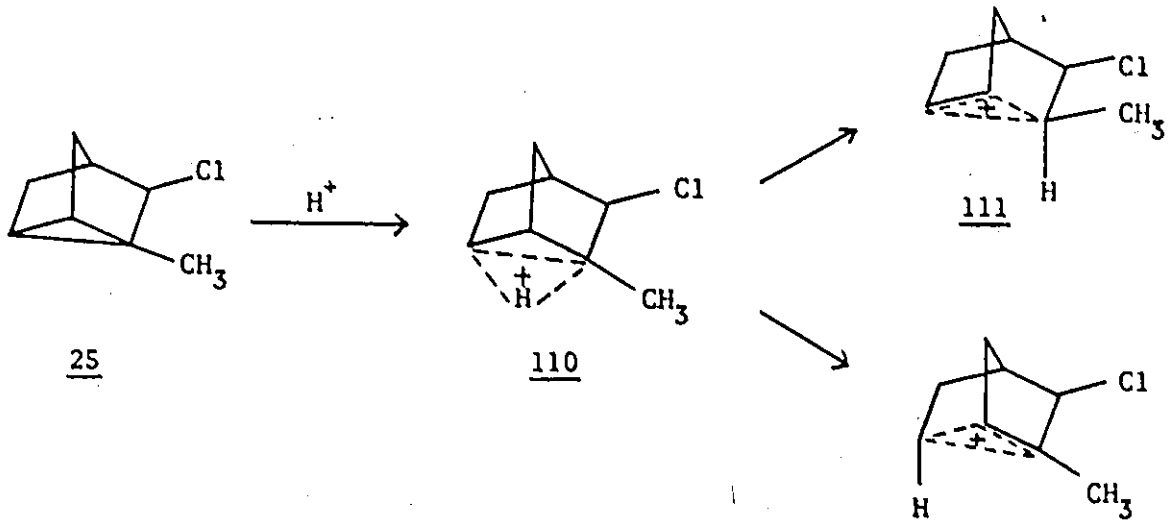


Scheme 3:9

withdrawing effect of chlorine and (ii) electron donating effect of the methyl group. Although protonation of the cyclopropyl bond furthest removed from halogen is definitely preferred for 3-chloronortricyclene, it is possible that in 25, cleavage of the C-1 C-2 and/or C-2 C-6 bonds with the charge residing at C-2 might actually become a favourable process due to formation of a tertiary cation although the positive charge is situated beta to chlorine. Although accurate rate constants are lacking, qualitative comparison of the data in Table 3:1 shows that the reactivity of 25 towards acid is similar to that of 24. This suggests that in 25 the methyl group exhibits a negligible directive effect relative to chlorine with respect to direction of cyclopropyl

bond cleavage. Furthermore, methyl does not drastically enhance the rate of the reaction.* However, it is also possible that favourable formation of a tertiary cation by possible C-1 C-2 bond cleavage is overpowered by the energetically unfavourable development of positive charge at a center adjacent to chlorine. This point is examined in detail (*vide infra*) in conjunction with the stereochemistry of deuteration.

Electrophilic cleavage of 25 in protic medium gives only 1-methyl-*anti*- and *syn*-7-chloro-*exo*- 2- norbornyl acetates without any indication of methyl-5-chloro-*exo*-2-norbornyl acetates. This behaviour clearly contrasts that of 24 where *exo*- and *endo*-5-chloro-*exo*-2-norbornyl acetates were obtained in addition to other products (*vide supra*). These latter two compounds were formed from 24 by protonation of the C-1 C-2 and C-2 C-6 bonds as illustrated in Scheme 3:1. For cleavage of 25, the analagous route is shown in Scheme 3:10



25 110 111 112

Scheme 3:10

* Reports concerning substituent effects on the rate of cyclopropyl bond cleavage have been scant. However, it has been observed that substituents on the ring do not induce the expected rate changes. For example, phenylcyclopropane is eight times *less* reactive than cyclopropane towards acid.[70,71]

where an edge protonated species (*ie* 110) is depicted for reasons to be discussed later. This shows the controlling effect of the methyl group situated at C-2 which blocks formation of methyl-5-chloro-*exo*-2-norbornyl acetates since chloronium ion formation and hydride shifts which are necessary precursors of these compounds do not occur. If edge protonation is accepted as the initial step, then ion 111 is not formed because it is well known that for electrophilic attack at a cyclopropyl bond, the electrophile generally becomes attached to the least substituted carbon atom.[55,56] If corner protonation is the first step in this reaction, apparently conversion of ion 112 to 111 does not occur because methylated-5-chloro-*exo*-2-norbornyl acetates were not formed from electrophilic (H^+) cleavage of 25.

Solvolysis of 25 under the reaction conditions was not observed for reasons which have been previously discussed in relation to the cleavage of 24. Since predominantly *exo*-acetates were observed (*exo*:*endo* = 95±1:5±1), the carbon atom undergoing nucleophilic attack experiences inversion of configuration; this behaviour is common in norbornyl systems.[40,41]

Treatment of 25 with deuterated acid gave 78-OAc-*d* which contained an average of 1.29 deuterium atoms per molecule* suggesting that a significant amount of deuterium entered the molecule after ring cleavage. The other product 79-OAc-*d* contained 1.05 deuterium atoms per molecule.*

Pmr analysis of both 78- and 79-OH-*d* in the presence of shift reagent $Eu(fod)_3$ revealed that most of the deuterium was situated at the *endo*-C-6 position (*endo*-6-*d*:*exo*-6-*d* = 15-20, Table 2:4). Assuming that this

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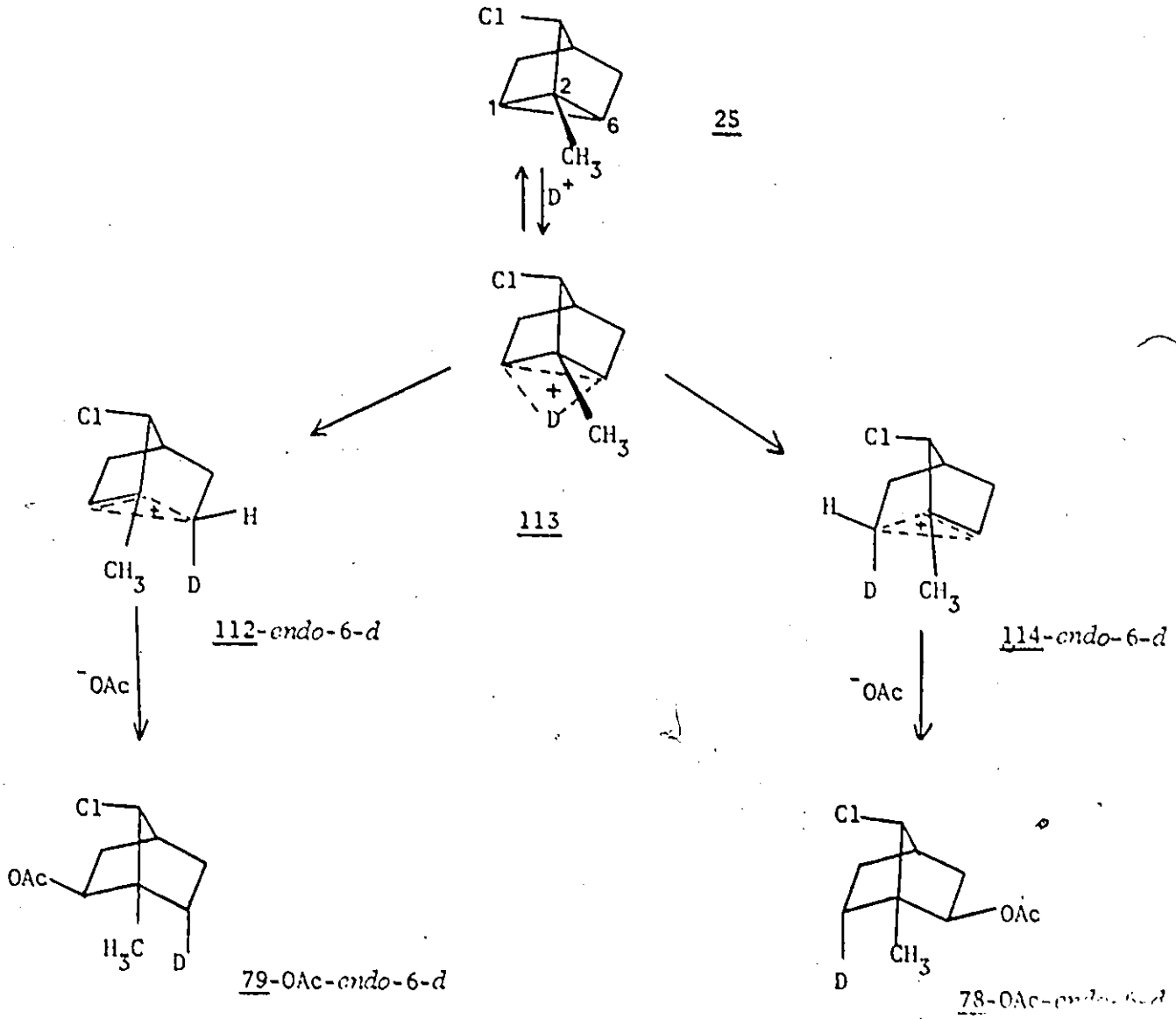
* These numbers are based on mass spectrometric analysis of the corresponding chloro ketones.

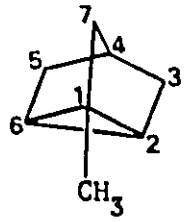
stereochemistry in the product represents that of the initial deuteration step and is not determined by a series of subsequent rearrangements, it is clear that electrophilic retention predominates. This sharply contrasts the behaviour of 1-methylnortricyclene (22) towards acid where a 62:38 mixture resulting from electrophilic retention and inversion was observed for formation of the kinetic product.[41]



Scheme 3:11

Initial edge deuteration of the C-1 C-6 bond in 2-methyl-3-chloronortricyclene (path i, Scheme 3:9) to yield ion 113 and subsequent formation of ions 112-*endo*-6-*d* and 114-*endo*-6-*d* which are then captured by acetate can account for formation of 78- and 79-OAc-*endo*-6-*d* respectively as shown in Scheme 3:11. Since the reactivity of 25 is similar to that of 24, the mechanistic pathway shown in Scheme 3:11 is reasonable *ie* predominant deuteration of the cyclopropyl bond which is furthest removed from the halogen substituent.

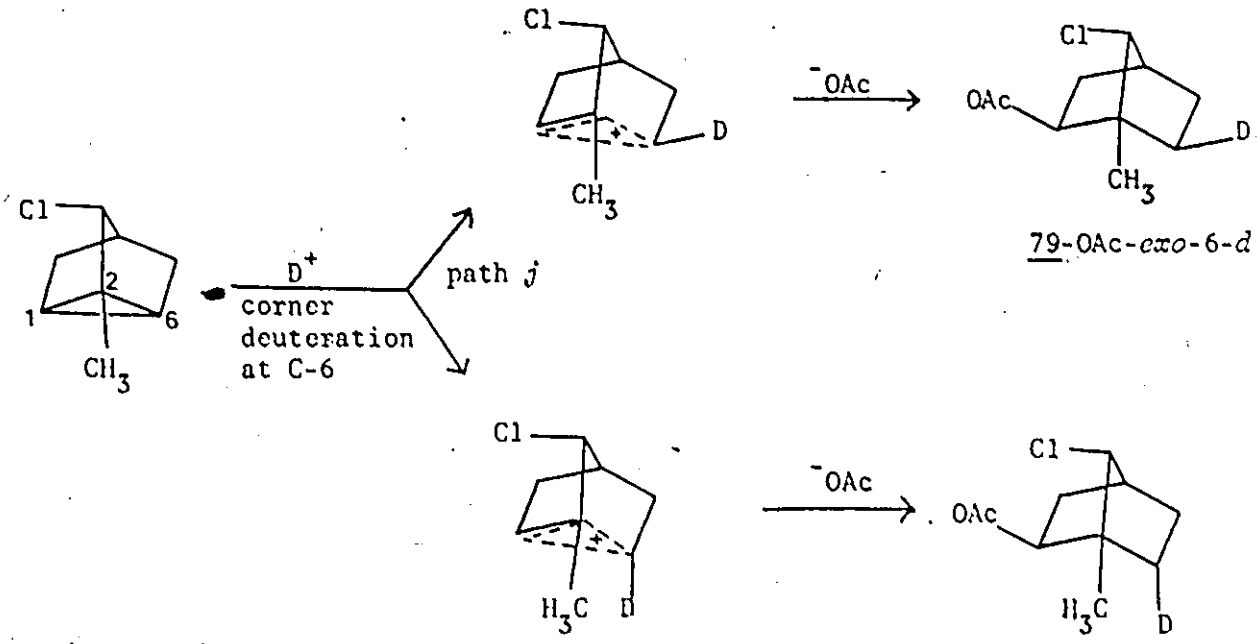
Any attempt to rationalize the predominant formation of 79-OAc-*endo*-6-*d* from 25 by corner deuteration at C-6 (path j, Scheme 3:9) followed by cleavage of the C-1 C-6 bond fails to explain why 79-OAc-*exo*-6-*d* is not formed. Alternatively, if one adopts the bent bond model for the cyclopropyl group in 25, then corner deuteration at C-6 implies electrophilic approach through paths m and n (Scheme 3:9). It can be argued that path n might become sterically unfavourable because the methyl group at C-2 hinders attack on C-6 from the C-2 side whereas the hydrogen atom at C-1 presents less of an obstacle to attack



22

on C-6 from the C-1 side. However, in 1-methylnortricyclene (22), it was found that this preference is not very large; almost equal amount of attack at

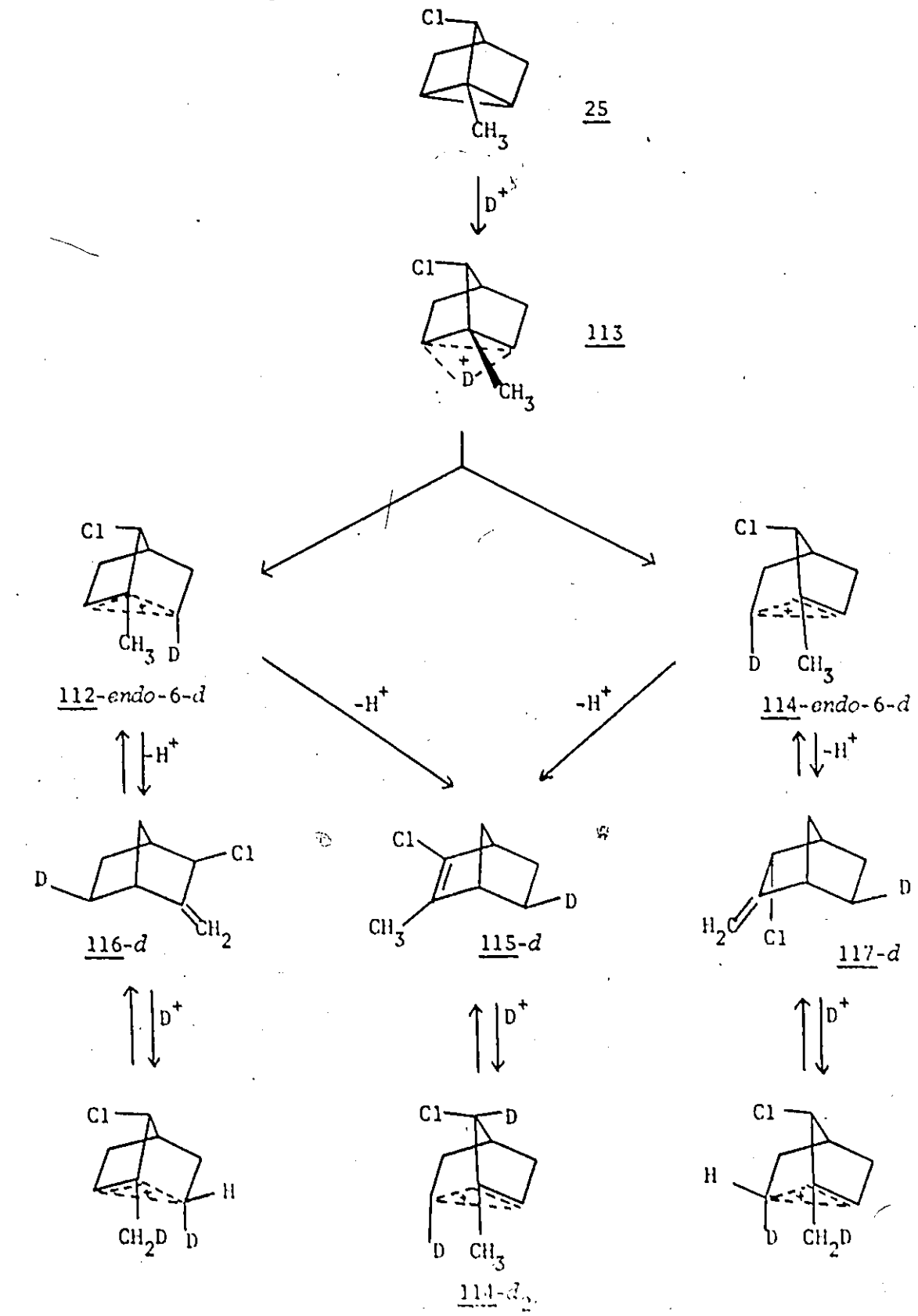
C-6 from the C-1 and C-2 sides was observed.[41] In compound 25, corner protonation at C-6 should be sterically (although perhaps not stereoelectronically) identical to protonation at C-6 in 22 and therefore if such a mechanism was operative for the electrophilic cleavage of 25, significant amounts of 79-OAc-*exo*-6-*d* would be formed in deuterated medium (Scheme 3:12). This is



Scheme 3:12

not confirmed by the data in Table 2:4. The small amount of 79-OAc-*exo*-6-*d* (0.06*d*) could arise from a minor contribution through path n (Scheme 3:9).

The other deuterium incorporation results shown in Table 2:4 are readily explainable in terms of bridged methylnorbornyl cations 112-*endo*-6-*d* and 114-*endo*-6-*d* or a pair of classical ions interconvertible by Wagner-Meerwein rearrangement (Scheme 3:13). Deuteration of 25 at C-6 gives ion 112-*endo*-6-*d* (*via* initial edge deuteration). Deprotonation from the methyl group to give deuterated *exo*-3-chloro-2-methylenenorbornane (116-*d*) followed

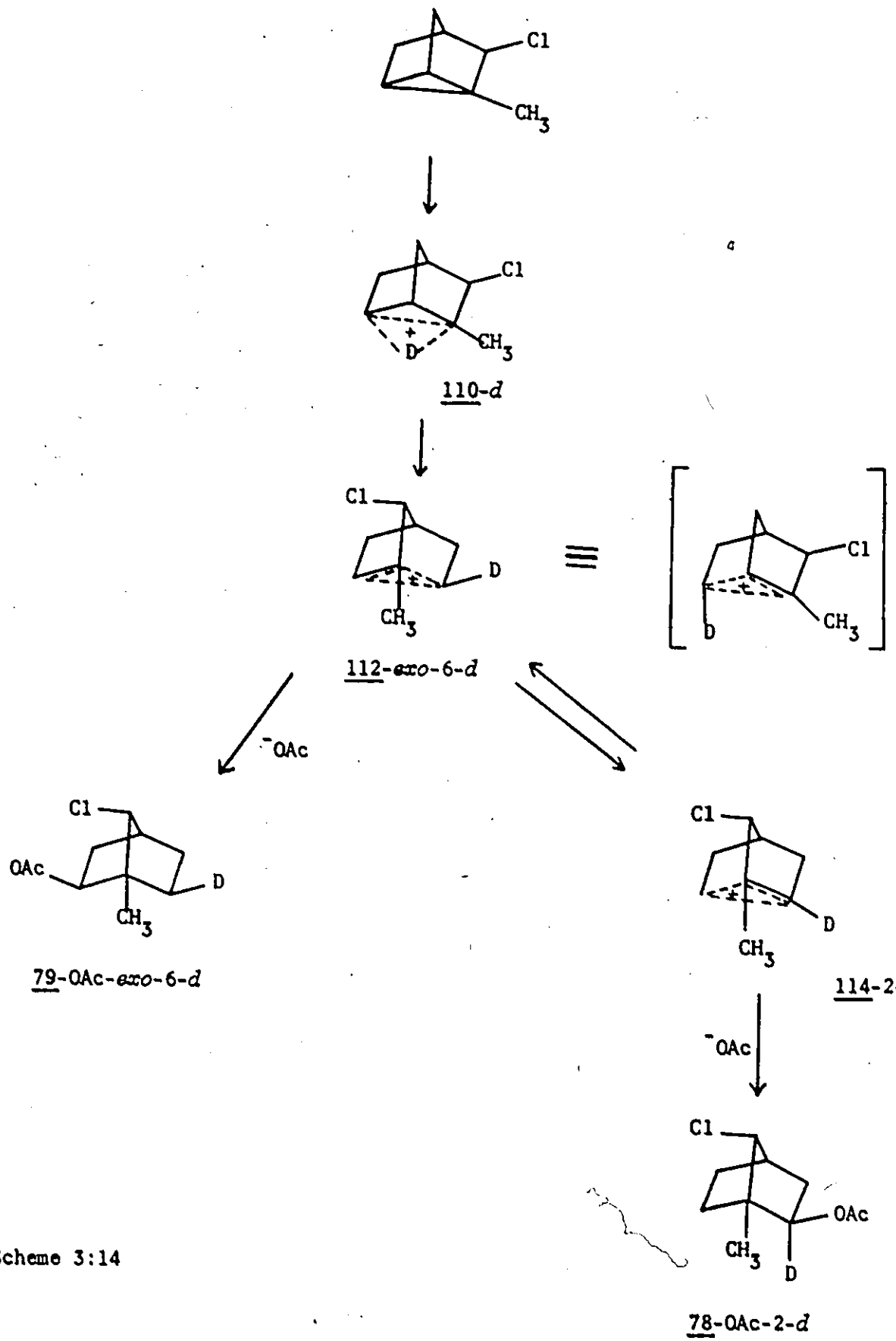

Cl
CH3
25
D+
Cl
D
CH3
113
Cl
CH3 D
112-endo-6-d
-H+
-H+
Cl
D
CH3
114-endo-6-d
H+
-H+
D
Cl
CH2
116-d
Cl
CH3
D
115-d
D
H2C
Cl
117-d
D+
D+
D+
Cl
H
CH2D D
Cl D
D CH3
114-d2
Cl
H
D CH2D

Schemo 3:13

by addition of D^+ to the methylene carbon atom results in introduction of deuterium into the methyl group. Similarly, deuterium is introduced into the methyl group of ion 114-*endo*-6-*d*. Deprotonation from the carbon atom bearing chlorine in either 112- or 114-*endo*-6-*d* produces deuterated 2-methyl-3-chloronorbornene (115-*d*) which can be attacked by D^+ from the preferred *exo* side[225,226] to regenerate the carbonium ion 114-d_2. Collapse of 114-d_2 with acetate yields 78-OAc-*d* which contains deuterium at *endo*-C-6 and *syn*-C-7. Loss of a proton from 114-*endo*-6-*d* to give 115-*d* should be preferred relative to loss of a proton from 112-*endo*-6-*d*.[225]

The small amount of 79-OAc-*exo*-6-*d* which was formed from electrophilic cleavage of 25 could have arisen by edge deuteration of the C-2 C-6 bond (Scheme 3:14). Rearrangement of ion 110-*d* would give 112-*exo*-6-*d* which upon reaction with acetate gives 79-OAc-*exo*-6-*d*. Ion 112-*exo*-6-*d* can undergo a 2,6 hydride shift to yield ion 114-2-*d* which upon capture by acetate produces 78-OAc-2-*d*. Similarly, edge deuteration of the C-1 C-2 bond in 25 can account for the formation of small amounts of 78-OAc-*exo*-6-*d* (Table 2:4). These two routes can also account for introduction of deuterium into sites other than at *endo*-C-6. For example, ions 112-*exo*-6-*d* and 114-2-*d* (Scheme 3:14) can individually deprotonate-redeuterate and introduce deuterium into C-7 and $-CH_3$ in a manner similar to that shown in Scheme 3:13.

In 3-chloronortricyclene, protonation of the C-1 C-2 and C-2 C-6 accounted for the formation of 5-chloro-*exo*-2-norbornyl acetates (28%, Scheme 3:1). If for electrophilic (D^+) attack it is assumed that any deuterium which is not present at *endo*-C-6 in the products was introduced *via* cleavage of the C-1 C-2 and C-2 C-6 bonds, then from the data in Table 2:4 it can be shown that



Scheme 3:14

this constitutes about 27% of the total reaction. For 78-OAc-*d*, the contribution from deuteration of the C-1 C-2 and C-2 C-6 bonds would be

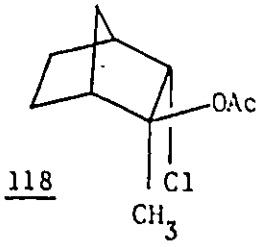
$$\{(0.17\pm0.03) + (0.05\pm0.02) + (0.04\pm0.02) + (0.13\pm0.03)\} \times 75 \times \frac{1}{1.29}\% = 23 \pm 5\%$$

Similarly, for 79-OAc-*d*, it would be

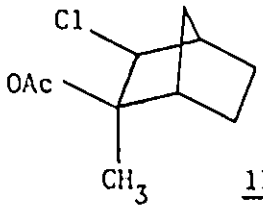
$$\{(0.11\pm0.02) + (0.06\pm0.03)\} \times 25 \times \frac{1}{1.05}\% = 4 \pm 1\%$$

Therefore the total contribution from these routes is 27 ± 6%. This adds further support to the contention that 2-methyl-3-chloronortricyclene behaves similar to 3-chloronortricyclene with respect to cleavage of the cyclopropyl bonds by a proton *ic* for both compounds, about 72% of the products arise by cleavage of the bond furthest removed from chlorine and about 28% of the products arise from cleavage of the other two bonds.

Attack by acetate on ions 114 or 112 at the tertiary cationic center



118



119

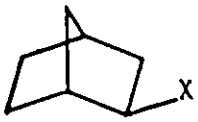
would yield the tertiary acetates 118 and 119. These acetates would probably be unstable under the reaction conditions with respect to the thermodynamically more stable secondary acetates 78- and 79-OAc. Hammons has observed that electrophilic (H^+) cleavage of 1-methylnortricyclene (22) gave

endo-2-methyl-*exo*-2-norbornyl acetate as the kinetic product which slowly rearranged to 1-methyl-*exo*-2-norbornyl acetate and *exo*-2-methyl-*endo*-2-norbornyl acetate under the reaction conditions.[41] For cleavage of 2-methyl-3-chloronortricyclene (25), tertiary acetates 118 and 119 were not detected. Although experimental evidence is lacking, it is unlikely that the solvolytic reactivity of these tertiary chloro acetates is so great that detection of these compounds was precluded.

Therefore the preferred stereochemical course for cleavage of the cyclopropyl group in 2-methyl-3-chloronortricyclene (25) involves electrophilic retention. Once again, this contrasts the behaviour of other nortricyclenes (*e.g.* nortricyclene and 1-methylnortricyclene) where electrophilic inversion and retention are almost equally favoured.[40,41]

B. γ-Hydrogen Deuterium Isotope Effects in Bicyclo[2.2.1]heptanes

Before undertaking a discussion of the mechanistic implications of the solvolytic γ-isotope effects for 7-chloro-2-norbornyl brosylates-6-*d* as they relate to the effects observed for 2-norbornyl brosylates-6-*d*, it is essential to examine in detail the solvolytic mechanism associated with the former system. Roberts[228] has reported that 58- and 59-OTs undergo acetolysis approximately 280 times slower than 21-OTs. Since the product



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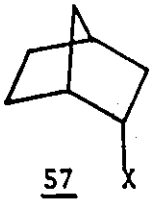

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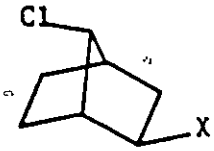

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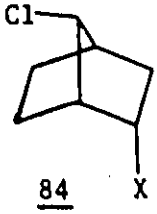

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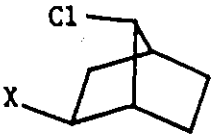
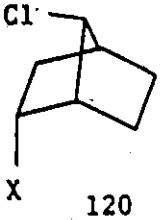


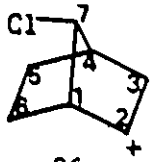
59



120

mixture contained only small amounts of 3-chloro-*exo*-2-norbornyl acetates (71- and 72-OAc), it was concluded that this was probably due to the low cationic character at C-1 during ionization of the chloro tosylates. The inductive effect of the adjacent chlorine caused this phenomenon. Gassman[176] has found that although the solvolytic reactivities of 58- and 59-OTs are decreased by factors of 531 and 346 respectively, relative to 21-OTs, the

two epimeric *exo-endo* pairs 59- and 120-OTs along with 58- and 84-OTs have *exo*:*endo* rate ratios which are similar to that for 21- and 57-OTs. It is an accepted fact that solvolysis of *endo*-2-norbornyl tosylates[139-152] and related compounds such as 84- and 120-OTs yield classical ions similar to



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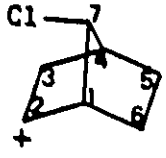

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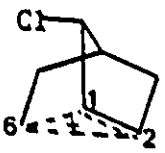

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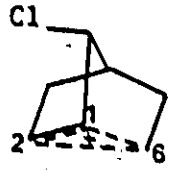


94

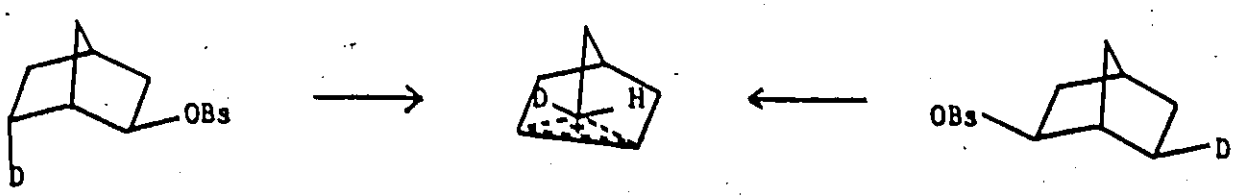
96 and 91 whereas controversy exists concerning the mechanism of solvolysis of compounds related to 21. Since the electron-withdrawing substituent (chlorine) had little effect on the *exo*:*endo* rate ratios, it was concluded that the transition states for solvolyses of 58- and 59-OTs have very little accumulation of positive charge at C-1. If there was appreciable charge development at C-1 in the transition state for ionization of 58- and 59-OTs, then chlorine at C-7 would certainly retard solvolyses of these epimers more than of the *endo*-epimers 84- and 120-OTs. Thus the *exo*:*endo* rate ratio would be dramatically different than that for 21- and 57-OTs.

Similar work by Goering and Degani[181] has also shown that for acetolyses of 58- and 59-OTs, capture of ions 93 and 94 at C-1 was minor relative to capture at C-2 and C-6. Once again this was attributed to the low cationic

character at C-1 due to the inductive effect of the adjacent chlorine atom. These systems have been described as being "locked". A locked norbornyl system is one in which neighbouring group participation (1,2 Wagner-Meerwein shift) is made unfavourable by the introduction of charge destabilizers at C-1 or C-7.[229] For example, a carbomethoxy[229] or cyano[230] group at C-1 would be a more effective lock than chlorine at C-7.

As shown in Table 2:6 (Chapter 2), deuteration at C-6 in 7-chloro-*exo*-2-norbornyl brosylates (58- and 59-OBs-6-*d*) causes a rate retardation of 11-12% per deuterium atom for solvolysis in buffered 80:20 ethanol-water.[231] Presently, the variation in γ-KIEs with solvent and temperature is not known, however assuming that it is negligible, it appears that the solvolytic KIEs for these chloro brosylates are similar to those for *exo*-2-norbornyl brosylates-6-*d*.[160,161] Interestingly, Halevi[124] has tentatively suggested that in systems which do not present mechanistic ambiguities, γ-effects in solvolysis arise from the inductive effect of deuterium *ie* $k_H < k_D$. Obviously this generalization does not apply to the systems studied in this present work.

It has been suggested that the γ-KIEs for 21-OBs-*endo*-6-*d* and 21-OBs-*exo*-6-*d* arise from rate-determining formation of the norbornonium ion



21-OBs-*endo*-6-*d* 54-*d* 21-OBs-*exo*-6-*d*

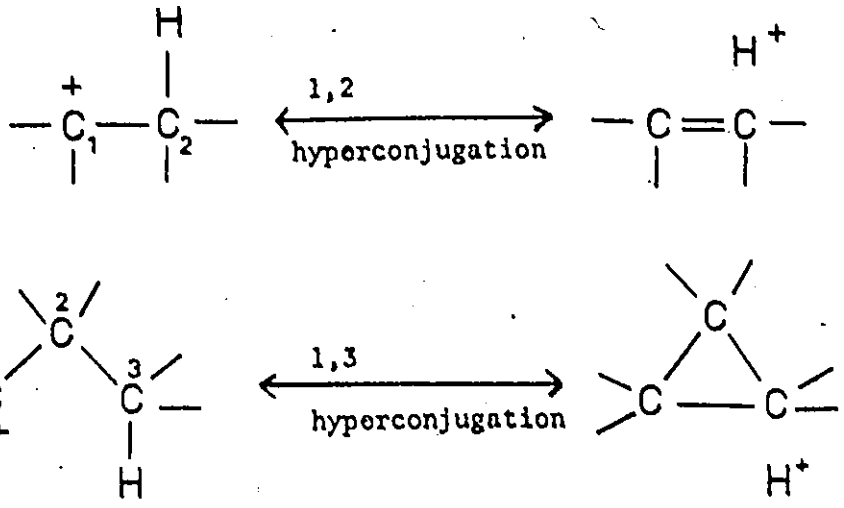
54-*d*.[161] It was argued that the similarity (?) of the isotope effects for 21-OBs-*endo*-6-*d* (1.097±0.011) and 21-OBs-*exo*-6-*d* (1.149±0.016) is expected because in cation 54-*d*, the distinction between *exo*- and *endo* deuterium at C-6 is lost. In light of these arguments, the γ-KIEs in Table 2:6 (Chapter 2) are quite surprising. For solvolyses of 58- and 59-OBs, the cationic character at C-1 is certainly minimal[176,181,228] and thus in terms of relative charge at C-1 and C-2, the transition states probably resemble ions 96 and 91 respectively. Therefore during the ionization step, the degree of neighbouring group participation (*via* involvement of C-1 C-6 bond) in compounds 58- and 59-OBs is less than that in compound 21-OBs. Yet the solvolytic γ-KIEs for 58- and 59-OBs-6-*d* are similar to those for 21-OBs-6-*d*. Within experimental error, the isotope effects for the chloro brosylates were identical regardless of stereochemistry of deuterium at C-6.

In some cases (*e.g.* 58- and 59-OBs-*exo*,*exo*-5,6-d_2) the γ-effects were determined for compounds which were deuterated at both C-5 and C-6. In view of previous work which has established that acetolyses of *exo*-2-norbornyl brosylates-5-*d* results in a negligible δ-KIE (Table 1:3, Chapter 1),[163,164] it was assumed that these effects should also be small for 58- and 59-OBs-5-*d*. Therefore the observed rate retardation for ethanolyses of 58- and 59-OBs-*exo*, *exo*-5,6-d_2 arose only as a result of the deuterium atom at C-6.

Changes in non-bonding interactions at the γ-hydrogen (deuterium) atoms must certainly be small since the only nuclei changing their positions are three atoms removed. Models indicate that the substituents at C-6 are not crowded. Quantum mechanical tunnelling should also be unimportant in this system although it can be significant in reactions where a C-H(C-D) bond

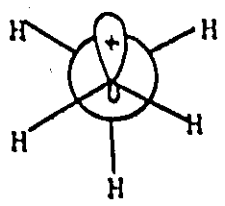
is cleaved in a slow step. Anharmonicity and inductive effects may be present however they are less important than the total effect and in the opposite direction. Conceivably, the Y-effects for solvolyses of 58- and 59-OBs-6-*d* arise by *homohyperconjugative* interaction of the incipient *p* orbital at C-2 with the C-H(C-D) bonds at C-6. Hyperconjugative interactions refer to 1,2 processes whereas homohyperconjugative interactions refer to 1,3 processes (*vide infra*).

Ample experimental evidence exists which suggests that for reactions involving rate-limiting formation of a carbonium ion, replacement of a β hydrogen atom which is in a position capable of hyperconjugating, by a deuterium atom causes a rate retardation.[169-172] Hyperconjugation refers to partial withdrawal of electron density from a single bond (*e.g.* C-H) into a neighbouring vacant orbital. This reduces the force constants associated with the C-H bond and therefore substitution of deuterium for hydrogen will produce a change in the difference in zero point energies between ground state and transition state. In this case, the ΔZPE is usually smaller in the transition state than in the ground state and thus $k_H/k_D > 1.00$. This type of overlap has also been termed σ-π conjugation or vertical stabilization.[232,233] Traylor describes this phenomenon as delocalization of a σ bond *without* a change in bond length or angle. The limiting resonance contributors associated with 1,2 hyperconjugation are depicted below. To date most examples of hyperconjugation have involved 1,2 interactions with only relatively few cases of 1,3 interactions (homohyperconjugation) having been reported. For example, Paquette[234] invoked this latter type of interaction as a possible mechanism



for delocalization of positive charge into the aryl group of benzo-7-oxa-*exo*-2-norbornyl brosylate during acetolysis. Recently, the mechanism of long range interactions between hydrogen atoms and the electron spin in bicyclic systems was discussed in terms of homohyperconjugation.[235]

Quantum mechanical calculations have implicated that hyperconjugative stabilization of incipient carbonium ion centers by neighbouring hydrogen involves a *trans* effect.[94] For example in $C_2H_5^+$, a hydrogen atom which is



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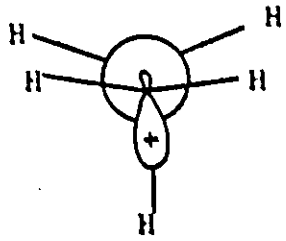
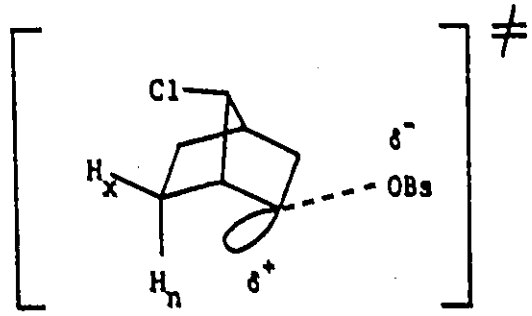


122

trans to the developing *p* orbital, as in 121, acquires more positive charge relative to the other hydrogens. Furthermore, conformation 121 is preferred over 122 because the former possesses a *trans* β bond whereas the latter has

a *cis* β bond. Experimental evidence in support of these calculations has shown that *trans* overlap is favoured relative to *cis* overlap for interaction of β C-H bonds with vacant orbitals.[236] Similar conclusions should qualitatively apply to 1,3 interactions.

In view of the stereoelectronic requirements for hyperconjugative stabilization of positive charge by neighbouring carbon-hydrogen (deuterium) bonds[174] as well as the proximity of the developing *p* orbital (at C-2) to C-6 during ionization of 58- or 59-OBs-6-*d*, it is not surprising that the γ-KIEs are similar regardless of stereochemistry at C-6. The transition state for ionization of 58-OBs probably resembles 123 however, for clarity with respect to subsequent arguments, ion 96 will be used. In the transition state, the developing *p* orbital on the *endo* side of C-2 can be stabilized



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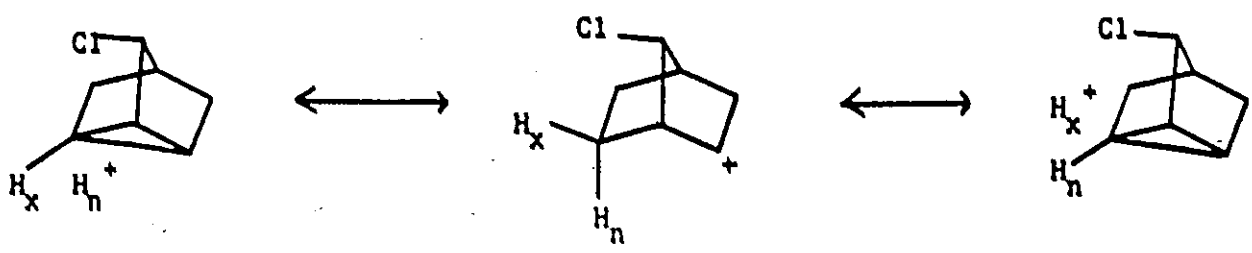
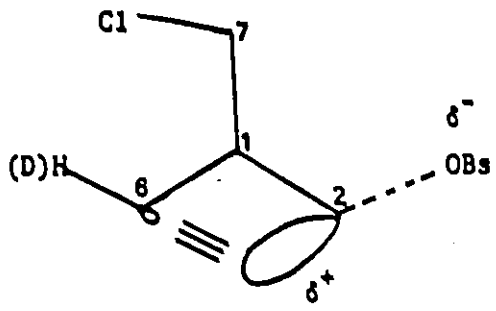
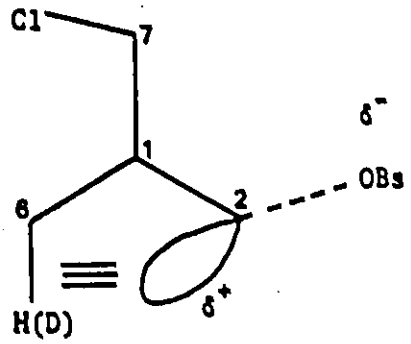


124 96 125

homohyperconjugatively by the C-H(C-D) bonds at C-6. For ion 96, the limiting resonance contributors are 124 and 125. Once again, these represent delocalization of charge *via* 1,3 interactions, a process which is made favourable by the rigid geometry of the norbornyl framework. It is attractive to suggest that the similarity of the γ-KIEs for ethanolyses of 58-OBs-*endo*-6-*d* and 58-OBs-*exo*,*exo*-5,6-d_2 arises due to equal contributions from both 124 and 125. The C-H(C-D) bond at *exo*-C-6 is approximately *trans* periplanar to the *p* orbital at C-2 with respect to an imaginary line joining C-2 and C-6. Withdrawal of electron density from this bond by the charge at C-2 is similar to the *trans* effect (*of* 121) which was previously discussed. This is illustrated by



126



127

structure 126 which shows the transition state for ionization of 58-OBs-*exo*, *exo*-5,6-d_2 as viewed along the C-1 C-4 axis. The limiting resonance contributor associated with this *trans* effect resembles 125.

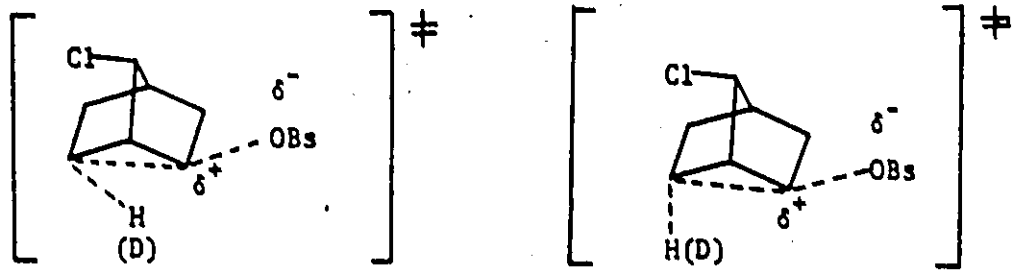
Stabilization of the cationic center at C-2 *via* homohyperconjugation with the C-H(C-D) bond at the *endo*-C-6 position (*cis* effect, *of* structure 122) which gives 124 as a resonance contributor should be less important than

stabilization from the C-H(C-D) bond at *exo*-C-6 (*trans* effect, *cf* structure 121).[94] At present it is difficult to quantify the relative importance of the *cis* and *trans* effects as they relate to 1,3 interactions in 58- and 59-OBs. Present evidence (Table 2:6, Chapter 2) suggests that within experimental error, these two phenomena are similar. Using the spectrophotometric technique,[218] small differences in γ-KIEs (1-2%) between the *exo*- and *endo*-C-6 positions of 58- or 59-OBs-6-*d* could not be detected.

In this context it is interesting that one group of workers has found that the γ-KIE for acetolysis of *exo*-2-norbornyl brosylate-*exo*-6-*d* (1.146±0.016) was greater than that for *exo*-2-norbornyl brosylate-*endo*-6-*d* (1.097±0.011).[161] Once again, the vacant *p* orbital at C-2 is approximately *trans* periplanar with respect to the C-H(C-D) bond at *exo*-C-6 and *cis* with respect to the C-H(C-D) bond at *endo*-C-6. These kinetic observations corroborate the prediction that the *trans* effect should be more important relative to the *cis* effect. However, a second group has reported that within experimental error, the γ-KIEs for acetolyses of 21-OBs-*exo*-6-*d* and 21-OBs-*endo*-6-*d* are identical.[160]

Homohyperconjugative stabilization of ion 96 by the C-H(C-D) bond at *endo*-C-6 implies that the distance between the hydrogen (deuterium) atom and the developing *p* orbital at C-2 does not *appreciably* change. This is depicted by structure 123. However, it is also possible that the hydrogen (deuterium) atom at *endo*-C-6 can directly participate by moving closer to C-2 in the solvolytic transition state as depicted by 128. Direct participation of hydrogen (deuterium) at *endo*-C-6 during solvolysis of 21-OBs has been considered.[72,73] In the 7-chloro-2-norbornyl system, the measured isotope effects are much too small compared with those in systems where such

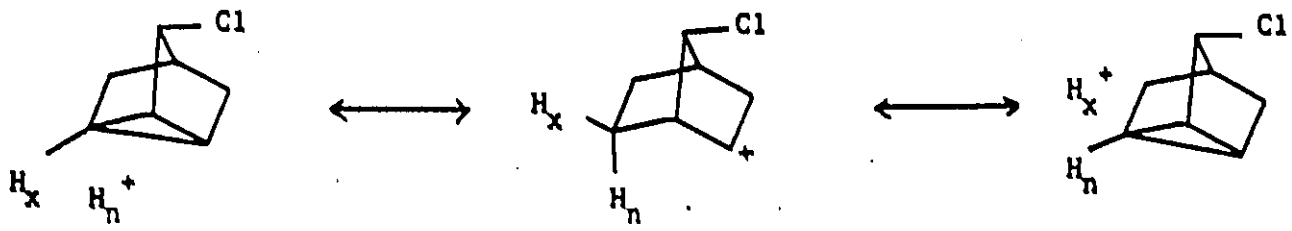
participation has been established.[237] Therefore, 128 should not contribute significantly to the observed effect. Using the arguments presented by



128 123

Traylor,[232,233] it is suggested that most of the stabilization energy in the transition state can be provided without nuclear movement of the substituents at C-6, since little is gained by moving atoms. Structures 128 and 123 are not resonance forms since geometrical changes are implied. For a transition state resembling 128, a much larger γ-KIE is expected; furthermore since deuterium at *exo*-C-6 is not able to participate directly, it should give rise to a smaller KIE relative to deuteration at *endo*-C-6. These predictions are not borne out by the experimental results in Table 2:6 (Chapter 2).

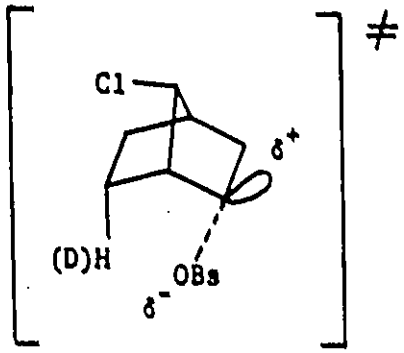
Similarly, the γ-KIEs observed for 59-OBs-6-*d* can be explained on the basis of the preceding arguments. Possible complications in interpretation



of the γ-effects for this system due to deuterium scrambling are discussed in a subsequent section.

Interestingly, the γ-KIEs for ethanolyses of *anti*-7-bromo-*exo*-2-norbornyl brosylate-*endo*-6-*d* (1.13±0.01) and *syn*-7-bromo-*exo*-2-norbornyl brosylate-*endo*-6-*d* (1.05±0.01) are significantly different.[231] Possibly, the lower γ-effect for ethanolysis of the *syn* bromo brosylate is due to steric interaction of *syn* bromine and *exo* brosylate which distorts the norbornyl system and thereby alters favourable alignment of the C-H(C-D) bond at *endo*-C-6 and the developing *p* orbital. Molecular models reveal that such a distortion would force the *p* orbital into a more favourable position with respect to the bond at *exo*-C-6 to overlap in a *trans* periplanar fashion should be more favourable than in the undistorted system. Therefore it is predicted that a larger γ-KIE should be observed for *syn*-7-bromo-*exo*-2-norbornyl brosylate-*exo*-6-*d* relative to the *endo*-6-*d* isomer.

Further evidence which supports the contention that the degree of homohyperconjugative stabilization depends on stereoelectronic factors comes from the γ-KIE for ethanolysis of *anti*-7-chloro-*endo*-2-norbornyl brosylate-*endo*-6-*d* (84-OBs-*endo*-6-*d*; k_H/k_D = 1.00±0.02). In the transition state for ionization, the C-H(C-D) at *endo*-C-6 does not have the proper



129

alignment which is necessary to stabilize the developing *p* orbital at C-2 (see 129) and thus deuteration should not cause a significant rate retardation. On steric grounds it can be argued that as a result of the smaller size of deuterium relative to hydrogen, an inverse effect ($k_H/k_D<1$) should be observed if there was considerable interation between the substituent at *endo*-C-6 and the leaving group. Such a small effect would likely escape kinetic detection.

Since ionization of 7-chloro-*exo*-2-norbornyl brosylates-6-*d* does not involve participation of the C-1 C-6 bond and yet the γ-KIEs are essentially identical to those for *exo*-2-norbornyl brosylates-6-*d*, it is suggested that the γ-effects for the latter compound arise *via* homohyperconjugative stabilization of the vacant *p* orbital at C-2 by C-H(C-D) bonds at C-6. Thus, the transition state for ionization of *exo*-2-norbornyl brosylate probably possesses minimal positive charge at C-1. However, absence of non-classical character* in the transition state does not imply absence of such character in a subsequent intermediate ion. In fact, it is reasonable to assume that a more electron-demanding ion would derive more stabilization energy from neighbouring bonds than would a transition state. In the solvolytic transition state, delocalization of positive charge at C-2 likely arises *via* the C-H bonds at C-6 and not *via* the C-1 C-6 bond. This is clearly represented by resonance contributor 132 wherein positive charge development at C-1 does not play a significant role. These arguments are consistent with the high *exo*:*endo* rate ratios for solvolyses of 58- and 84-OTs as well as 59- and 120-OTs.[176]

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*With respect to norbornyl systems, the term non-classical has been taken to mean a significant geometrical reorganization with an increase in bonding between C-2 and C-6, a decrease in bonding between C-1 and C-6 and dispersal of charge to C-1 from C-2.[238]

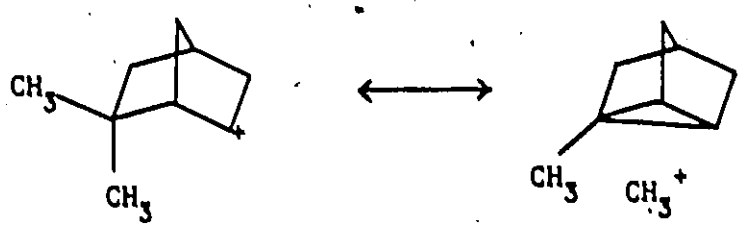
Experimental evidence concerning substituent effects at C-1 in *exo*-2-norbornyl tosylate on solvolytic rates suggest that charge development at this site might be unimportant during ionization. For example, a methyl substituent at C-1 enhances solvolysis by only a factor of 51 whereas methyl substitution at *endo*-C-2 enhances solvolysis 63,000 fold.[147] Also, acetolysis of 1-phenyl-*exo*-2-norbornyl tosylate is only 3.9 times faster than that of *exo*-2-norbornyl tosylate.[147] For the latter reaction, the solvolytic rate constants were well correlated by the Hammett σ-ρ treatment when σ values were used. On this basis, charge development in the transition state should be minimal. However, Sargent has emphasized that in order for mesomeric stabilization by aryl substituents at C-1 to be felt in the transition state, significant rehybridization at C-1 must occur to generate an orbital with proper geometry for overlap.[147] He concluded that the hybridization at this carbon atom did not permit overlap with the aryl π system. In sharp contrast, *endo*-2-phenyl-*exo*-2-norbornyl chloride solvolyzes 39,000,000 times faster than *exo*-2-norbornyl chloride.[239]

It is possible that *part* of the rate enhancement observed for solvolysis of *exo*-2-norbornyl brosylate relative to *endo*-2-norbornyl brosylate (*ca* 300:1)[141] arises from homohyperconjugative stabilization in the transition state during ionization of the former compound. This type of stabilization is not possible during ionization of the latter compound.

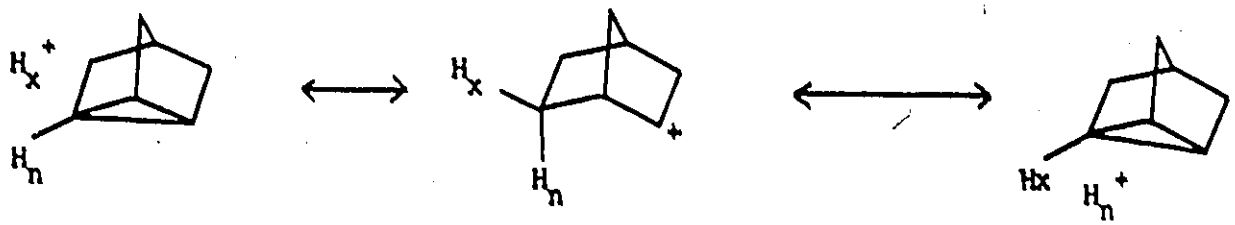
For 21-OBs, the lower isotope effects at C-7 relative to C-3 were attributed to a smaller initial-state zero point energy of the C-H bonds at C-7 or alternatively to lack of equivalence of C-3 and C-7 in the transition state.[158] This latter possibility seems especially attractive in view of

structure 132. Furthermore, it was stated that equality of the γ-KIEs for 21-OBs-*endo*-6-*d* and 21-OBs-*exo*-6-*d* do not require equivalence of C-3 and C-7 in the transition state since these effects are determined by a weakening of the C-1 C-6 bond which equally affects both C-H bonds at C-6.[158] However, this contention cannot explain why the γ-KIEs still remain at about 11% in systems (*ie* 58- and 59-OBs-*endo*-6-*d*, 58- and 59-OBs-*exo*,*exo*-5-,6-d_2) where delocalization of the C-1 C-6 bond is precluded.

Further evidence which justifies the premise that limiting resonance contributors for homohyperconjugation in this system are best represented as 124 and 125 comes from acetolysis of 6,6-dimethyl-*exo*-2-norbornyl tosylate.[240] Replacement of the hydrogens at C-6 in 21-OTs with methyl groups produces a 25 fold rate retardation on acetolysis. The rate depression was assigned to unfavourable methyl group steric interactions with both C-1 and C-2 in a non-classical transition state. However, since hyperconjugation of unstrained

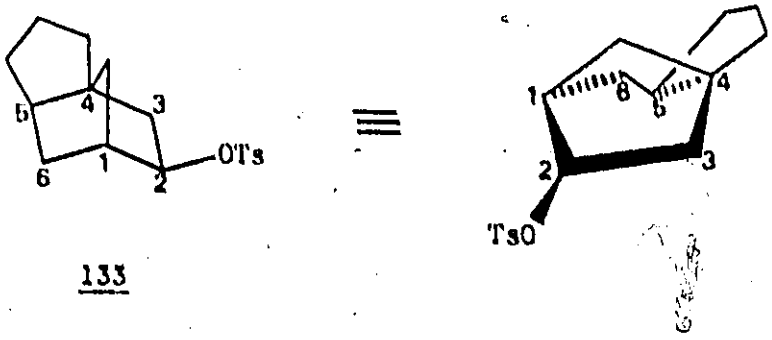


130 131



132 56 132

C-C bonds is less important relative to C-H bonds,[170,171,232,233] delocalization of electron density from the C-CH_3 bond in 130 to C-2 is not as facile as delocalization from the C-H bond of 56 to C-2 *ie* more effective hyperconjugation by C-H *vs* C-CH_3. In other words, resonance contributor 131 does not play an important role in stabilization of ion 130 whereas 132 contributes significantly to stabilization of ion 56. Furthermore, it is predicted that the δ-KIE for solvolysis of 6,6-di(trideuteromethyl)-*exo*-2-norbornyl tosylate should be inverse. Similar arguments can account for the fact that *exo*-6-methoxy-*exo*-2-norbornyl tosylate solvolyzes seven times slower than *exo*-2-norbornyl tosylate.[241] Also, on the above basis, the solvolytic behaviour of 5,6-trimethylene-2-norbornyl tosylates[147] can be explained. Corey[242] has found that the ratio of rate constants for acetolyses of *exo*-4,5-trimethylene-*exo*-2-norbornyl tosylate (133) and *exo*-2-norbornyl tosylate is 1:85. Part of this rate retardation can be attributed to a geometrical distortion in the [2.2.1] skeleton (induced by the trimethylene

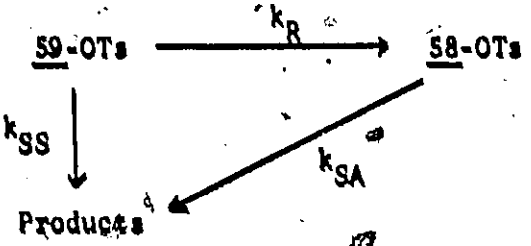


133

group) which destroys suitable overlap between an incipient *p*-orbital at C-2 with the substituents at C-6.

Goering and Degani[181] have found that acetolysis of *exo*-3-chloro-*exo*-2-norbornyl tosylate (71-OTs) was at least 239 times slower than 58- or 59-OTs. Even after 70% reaction for solvolysis of these latter two chloro tosylates, there was not any 71-OTs present in the reaction mixture. Similar behaviour is expected for the corresponding chloro brosylates. In relation to the present work, this suggests that if 71-OBs-*exo*-6-*d* was formed from 59-OBs-*endo*-6-*d* by ion-pair return, it would accumulate during the reaction. In fact, about 10 half-lives for 59-OBs corresponds to <3% reaction for 71-OBs. Similarly, *endo*-3-chloro-*exo*-2-norbornyl brosylate (72-OBs) should be unreactive.

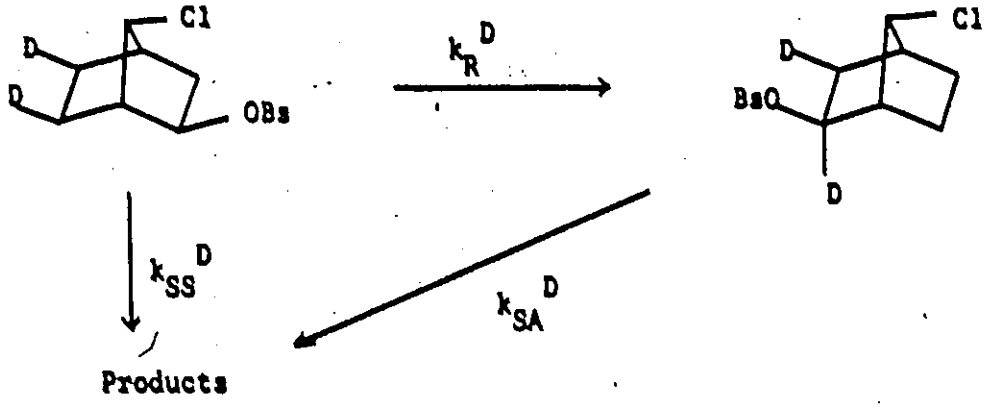
Acetolysis of *syn*-7-chloro-*exo*-2-norbornyl tosylate (59-OTs) is accompanied by isomerization to the *anti* isomer 58-OTs.[181] After 10% reaction there was 6% 58-OTs and after 70% reaction there was 29% 58-OTs. This rearrangement is associated with internal return from intimate ion-pairs. Isomerization of 58-OTs to 59-OTs was not observed. In buffered acetic acid, the ratio of solvolysis to rearrangement (k_{SS}/k_R) for 59-OTs was calculated



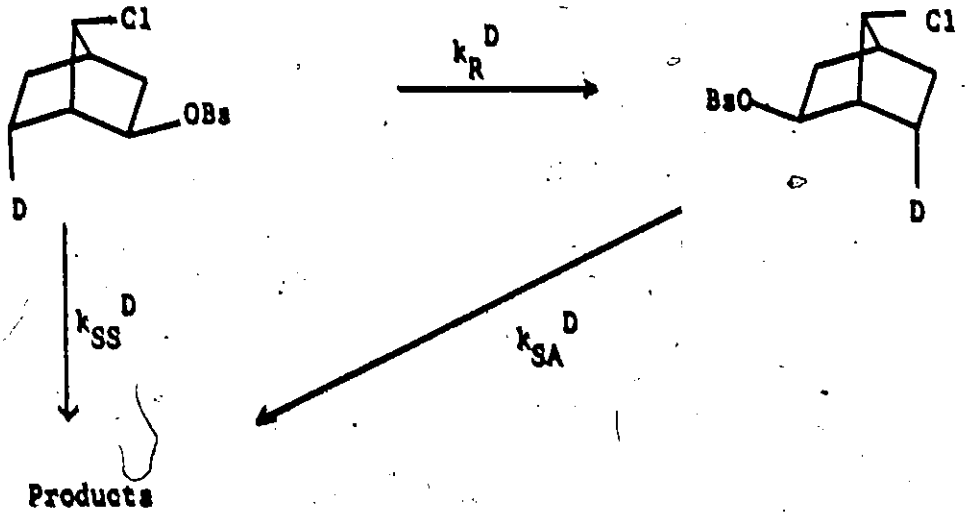
Scheme 3:15

to be 4.1 (Scheme 3:15). For 59-OBs-*exo*,*exo*-5,6-d_2 this isomerization has serious implications since it places deuterium at C-2 and C-3 in the rearrangement product 58-OBs (Scheme 3:16). Similarly, 59-OBs-*endo*-6-*d*

could rearrange to 58-OBs-*endo*-6-*d* (Scheme 3:17) *via* a 6,2 deuteride shift within an intimate ion-pair. Although four types of 6,2 hydride (deuteride)



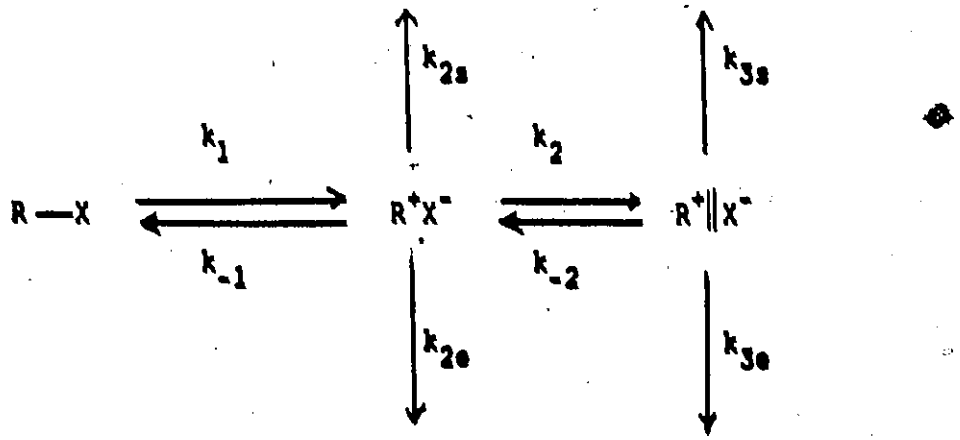
Scheme 3:16



Scheme 3:17

shifts are conceivable (*exo,exo*; *endo,endo*; *exo,endo*; *endo,exo*), the preferred path is the *endo,endo* one.[41,76,243] In aqueous ethanol, internal return from intimate ion-pairs is known to be less important than in acetic acid.[156] For example, acetolysis of *exo*-2-norbornyl brosylate involves 22% solvolysis of ion-pairs and 78% return of ion-pairs to covalent material whereas ethanolysis involves 65% solvolysis and 35% internal return.[156] Therefore it is reasonable to assume that, in Scheme 3:16, $k^D_{SS}/k^D_R \approx 10$. Since $k^D_{SS}/k^D_{SA} = 1.4$*, it appears unlikely that the γ-KIE measured for 59-OBs-*exo,exo*-5,6-d_2 arises *solely* from solvolysis of rearranged chloro brosylate. If this was true, then the first order plots would show considerable curvature.

The foregoing analysis of γ-KIEs in the 7-chloro-2-norbornyl brosylate system assumes that the observed isotope effect is determined solely by the ionization isotope effect *i.e.* $(k_H/k_D)_{OBS} = k^H_1/k^D_1$. Examination of the ion-pair scheme (Scheme 3:18) reveals that the solvolytic isotope effect could arise



Scheme 3:18

* This number represents the approximate *observed* relative rate ratio for ethanolyses of the *syn*- and *anti*-7-chloro brosylates 59- and 58-OBs.

from 1,3 elimination (*ie* from k_e) which only occurs *after* ion-pair formation is complete. Steady state treatment of this scheme establishes that the observed γ-effect is a composite of the ionization isotope effect (IIE) and the terms a and b as described in Equation 3:1.* This scheme does not directly include rate constants for hydride shifts since the species which are formed from R^+X^- or $R^+\|X^-$ *via* hydride shifts should react like SSIP and therefore are totalled into $R^+\|X^-$. In the event that IIE = 1.00, then

$$(k_H/k_D)_{OBS} = \frac{k_1^H}{k_1^D}\left(\frac{a^H}{a^D}\right)\left(\frac{a^D + b^D}{a^H + b^H}\right) \qquad \text{Equation 3:1}$$

where

$$a^H = (k_{2e}^H + k_{2s}^H)\,(k_{-2}^H + k_{3e}^H + k_{3s}^H) + (k_{3e}^H + k_{3s}^H)k_2^H \qquad \text{Equation 3:2}$$

and

$$b^H = k_{-1}^H(k_{-2}^H + k_{3e}^H + k_{3s}^H) \qquad \text{Equation 3:3}$$

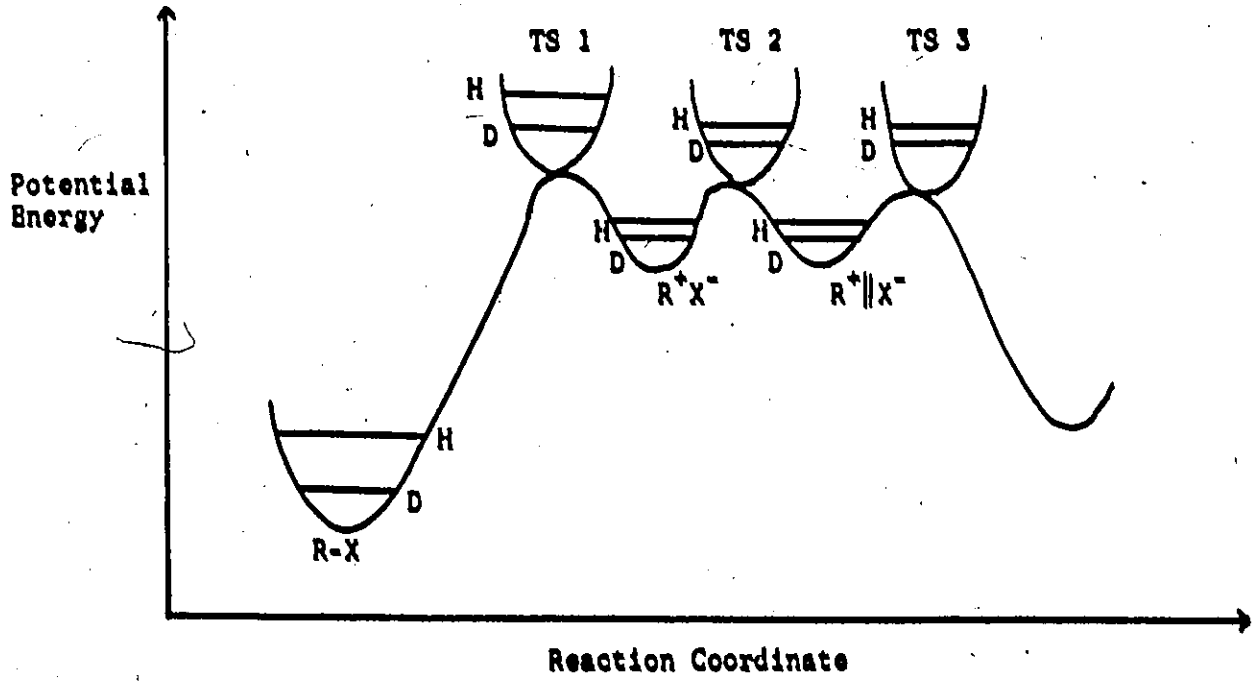
$(k_H/k_D)_{OBS}$ would arise from contributions of the a and b terms.

If internal return from intimate ion-pairs to covalent material does not occur *ie* $k_{-1}^H = k_{-1}^D = 0$, then $b^H = b^D = 0$ and from Equation 3:1, it follows that the observed isotope effect equals the ionization isotope effect. In the special case that $a^H = b^H$ and $a^D = b^D$, then as above, the observed effect equals the IIE. If these two conditions are not met, then the observed

* Derivation of this equation appears in Chapter 6.

effect is a composite of the IIE and contributions from a and b. In this case it becomes necessary to compare a^H to a^D and b^H to b^D in order to determine the origin(s) of the observed effect.

Since the structure of R^+ should be identical in both the intimate ion-pair (IIP) and the solvent separated ion-pair (SSIP), the difference in zero-point energy (ΔZPE) for the protio and deuterio substrates in each case should be similar. The transition state for conversion of IIP to SSIP (TS 2)



should resemble the IIP or SSIP and there should not be a significant change in ΔZPE as a result of γ-deuterium; therefore $k_2^H \approx k_2^D$ and $k_{-2}^H \approx k_{-2}^D$. In the case of α-isotope effects, however, this is not necessarily true because the α-effect would be more sensitive to the tightness of IIP and to congestion due to solvent molecule(s) in SSIP.[244] Since the C-H(C-D) bond

at C-6 should experience a greater perturbation in the IIP than in TS 1, the ΔZPE for TS 1 ≥ ΔZPE for IIP and thus $k_{-1}^{D} \geq k_{-1}^{H}$. Since product forms inevitably from SSIP,[245] therefore $k_{2s}^{H} = k_{2s}^{D} = 0$. It is expected that $k_{2e}^{H} \geq k_{2e}^{D}$ and $k_{3e}^{H} \geq k_{3e}^{D}$. For identical reasons to those discussed in relation to the relative magnitudes of k_{-1}^{H} and k_{-1}^{D}, $k_{3s}^{D} \geq k_{3s}^{H}$. This assumption is justified because the proportion of solvolytic products relative to 1,3 elimination product increases for reaction of 58- or 59-OBs *vs* 58- or 59-OBs-6-*d* (Table 2:8, Chapter 2).

For solvolysis of *exo*-2-norbornyl brosylate, little elimination product (<4%) is formed and thus k_{2e} and k_{3e} are negligible. Therefore, equation 3:1 can be simplified to equation 3:4. However since solvolysis of 58- or 59-OBs proceeds with a considerable contribution from 1,3 elimination

$$\left(\frac{k_H}{k_D}\right)_{OBS} = \left(\frac{k_1^H}{k_1^D}\right)(1)\left(\frac{k_{3s}^D k_2^H + k_{-1}^D(k_{-2}^D + k_{3s}^D)}{k_{3s}^H k_2^H + k_{-1}^H(k_{-2}^H + k_{3s}^H)}\right) \qquad \text{Equation 3:4}$$

and since at present there does not exist any experimental evidence which relates the relative importance of k_{2e} and k_{3e}, it is not possible to discount elimination as a partial source of the observed isotope effect. Also, although the *relative* magnitudes of a^H and a^D can be deduced by qualitative comparison of the individual rate constants within each term (similarly for b^H and b^D), before the contribution of the terms containing a and b to $(k_H/k_D)_{OBS}$ can be assessed it is essential to know a^H/a^D and b^H/b^D. For example, from equation 3:1 it can be shown that for $a^H/a^D = 1.10$, by changing b^H/b^D from 1.20 to 1.00 causes $(a^H/a^D)((a^D + b^D)/(a^H + b^H))$ to

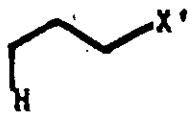
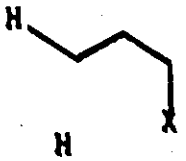
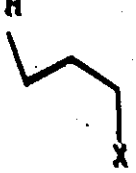
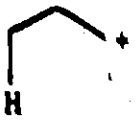
change from 1.15 to 1.08 whereas for a^H/a^D = 1.20, a change in b^H/b^D from 1.20 to 1.00 causes the above term to change from 1.20 to 1.09.

Experimental evidence which suggests that the a and b containing terms in total do not contribute significantly to $(k_H/k_D)_{OBS}$ comes from the γ-KIEs for solvolysis of *exo*-2-norbornyl brosylate. While the γ-effects for acetolysis and ethanolysis of this compound are essentially identical within experimental error, the k_{-1}/k_2 ratio varies from 4.6 to 1.53.[160] Similar arguments should apply to the chloro brosylates 58- and 59-OBs. That the observed γ-KIE might possibly be insensitive to the k_e's is suggested by the fact that although the (k_H/k_D)'s for 58- and 59-OBs-6-*d* are essentially identical, the k_e's differ substantially as indicated by the relative amount of product arising by 1,3 elimination (Table 2:8, Chapter 2).

Strong support for the premise that the k_e's and therefore the a and b terms do not contribute significantly to the observed γ-KIE would have been obtained if ethanolysis of 84-OBs gave 3-chloronortricyclene (24) as a product and furthermore if the amount of 24 obtained from 84-OBs-*endo*-6-*d* was less than that obtained from 84-OBs (*ie* if there is still an isotope effect on the relative amount of elimination product). Unfortunately, product ratios from solvolyses of 84-OBs and 84-OBs-*endo*-6-*d* were not obtainable because under the conditions used to ensure complete reaction (80° ± 4° for 8 days), the primary products were not stable and underwent further reaction. However, it has been reported that acetolysis of 84-OTs yields 7% 24 relative to other products.[176]

The preceding analysis of the ion-pair scheme for solvolytic reactions is not intended to be exact; it only reveals the complexity involved in interpretation of isotope effects.

An interesting feature of these solvolytic reactions is the formation of 3-chloronortricyclene (24) since this process involves the making of a cyclopropyl bond *via* 1,3 elimination. This complements the first part of this thesis which deals with the stereochemistry of cleavage of the cyclopropyl bonds in 24. Use of specifically deuterated 58- and 59-OBs-6-*d* allowed investigation of the preferred stereochemistry of 1,3 elimination. Recent developments suggest that these processes are more likely to occur by two-step mechanisms than are 1,2 eliminations due to the greater separation of the leaving groups.[246-249] The one-step mechanism is rare or non-existent. Concise notation which describes the various possible conformations for 1,3 eliminations has been proposed[250] and is shown below.

Short Notation	Terminology
	U
	W
	*exo*-sickle
	*endo*-sickle
	*apo*-sickle
	semi-U
	semi-W

In relation to the 7-chloro-2-norbornyl brosylate-6-*d* system, the preferred arrangement for E-1-like 1,3 eliminations was investigated by determining deuterium losses during formation of 24-*d*. The data in

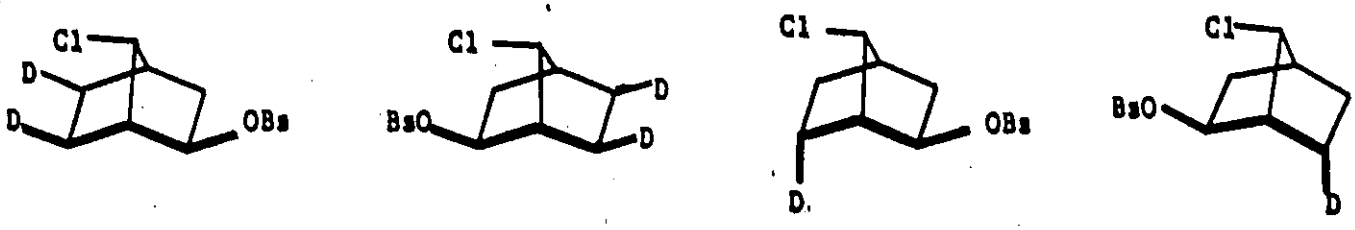


Table 2:9 (Chapter 2) show that elimination from the semi-U arrangement is preferred *to endo* stereochemical preference.* This stereochemical preference suggests that elimination occurs from an edge-protonated (deuterated) species such as 95. Since 58- and 59-OBs-*endo*-6-*d* produced 24-*d* which within experimental error had lost identical amounts of deuterium *to ca* 77% (Table 2:9, Chapter 2), this requires that 1,3 elimination occur from a common species (Scheme 3:16). In contrast, the other solvolytic products do not arise from a common ion because product ratios from solvolyses of 58- and 59-OBs are different (Table 2:8, Chapter 2). This work is unable to differentiate whether 95-*d* is an intermediate or a transition state for the elimination process.

Similarly, the fact that 58- and 59-OBs-*exo*,*exo*-5,6-d_2 both

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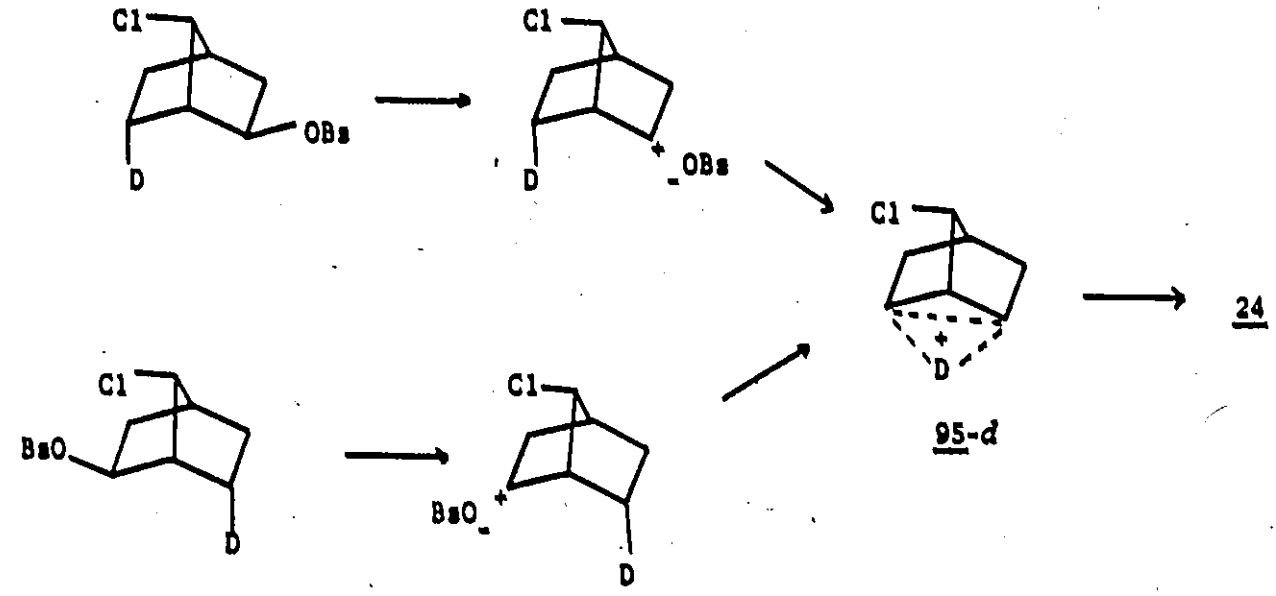
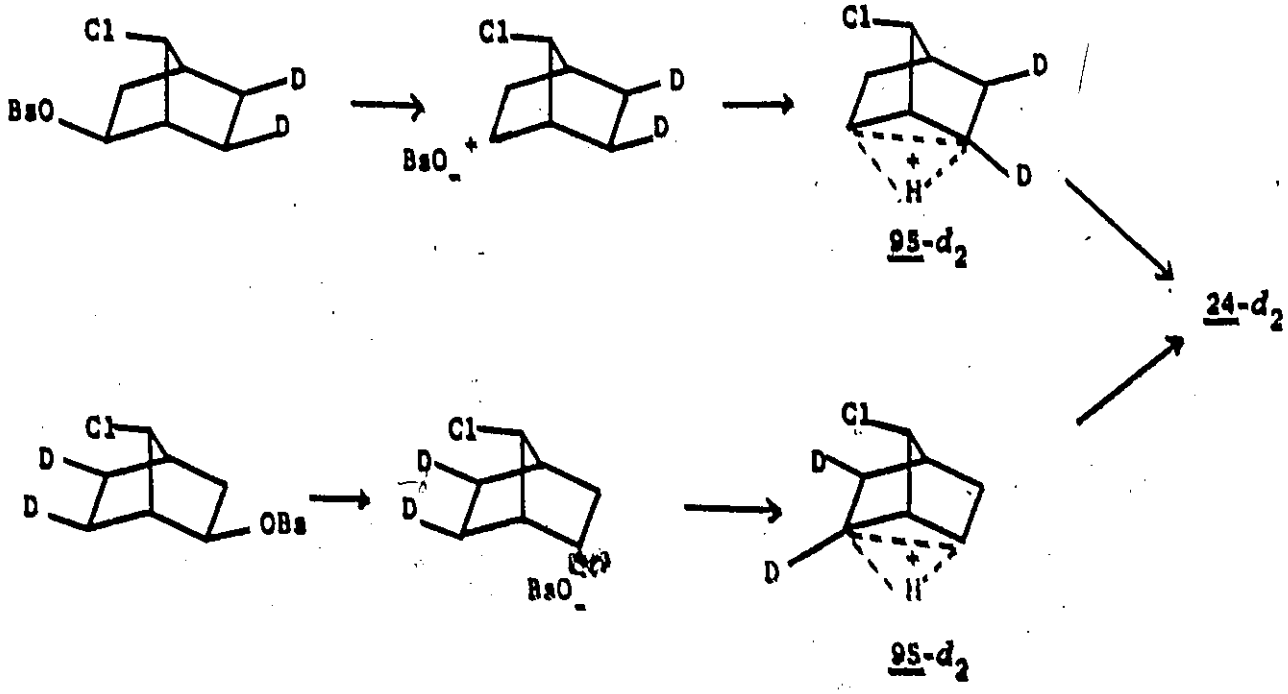
*Under E-1 type conditions, identical fractional percentages of deuterium were lost from *exo*-2-norbornyl tosylate-*endo*- and *exo*-6-*d* in formation of nortricyclene. Under E-2 type conditions, elimination from *exo*-2-norbornyl tosylate-*endo*-6-*d* (*of exo*-sickle arrangement) was preferred relative to elimination from the *exo*-6-*d* isomer (*of* W arrangement).[250]

gave rise to essentially similar fractional percentages of deuterium loss in formation of 24-*d* *ie* *ca* 0-10% (Table 2:9, Chapter 2) during



Scheme 3:16



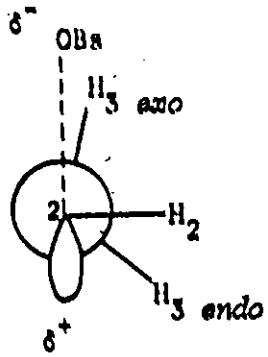
Scheme 3:17

ethanolysis, necessitates intervention of an edge-protonated species such as 95-d_2. Although these species as depicted in Scheme 3:17 are not identical with respect to stereochemistry of deuterium, their stabilities should be similar (neglecting isotope effects). Therefore each should deprotonate in a similar fashion and most of the deuterium originally present in the starting material should be retained in the product arising from 1,3 elimination. The small amounts of deuterium lost may reflect contributions from small amounts of 58- or 59-OBs-*endo,endo* 5,6-d_2 present as contaminants in starting material. Alternatively, it could represent the fact that *endo* elimination is not totally preferred.

A calculation of the *endo:exo* preference for C-H(C-D) bond cleavage at C-6 for ethanolyses of 58- and 59-OBs-6-*d* is not feasible at present. Recently, the *endo:exo* preference for solvolysis of *exo*-2-bromonorbornane-1-carboxylic acid methyl ester-*endo,endo*-5,6-d_2 was calculated to be at least 15:1.[251] This preference is calculated from an assumed isotope effect for the 1,3 elimination based upon the relative ratio of tricyclic material and solvolytic products formed from the non-deuterated and deuterated substrates. Since large errors arose in the determination of product ratios (see Table 2:8, footnotes d,e and f, Chapter 2) from solvolyses of 58- and 59-OBs, it was felt that the above analysis would not be meaningful in this case.

The β-KIE for solvolysis of 58-*exo*-3-*d* (Table 2:7, Chapter 2) at 57.8° is 1.09 ± 0.01. Neglecting temperature effects, within experimental error it is similar to that for 21-OBs-*exo*-3-*d* (1.11 ± 0.01).[158] In the transition state for solvolysis of the former compound, the

developing *p* orbital at C-2 is properly aligned in an *anti* periplanar sense with respect to the C-H(C-D) bond at *exo*-C-3. Newman projection along the C-2 C-3 bond axis shows that the C-H bond at *exo*-C-3 and the developing *p* orbital at C-2 form a dihedral angle of 180°. Therefore



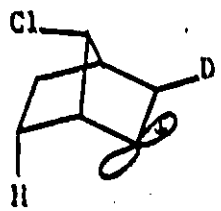
135

the charge at C-2 should be more effectively stabilized by the C-H bond at *exo*-C-3 relative to the C-H bond at *endo*-C-3. Verification of this prediction must await a determination of the β-KIE for 58-OBs-*endo*-3-*d*. The major contribution to the β-effect for 58-OBs-*exo*-3-*d* is hyperconjugation.

It has been argued that during solvolysis of 21-OBs, charge delocalization onto C-1 and C-2 *via* involvement of the C-1 C-6 bond should reduce the β-KIE whereas the absence of charge delocalization during solvolysis of 57-OBs should lead to a larger β-KIE.[116] The β-effects for ethanolyses of 21- and 57-OBs-*exo*-3-*d* are 1.11 ± 0.01 and 1.19 ± 0.01 respectively.[158] For ionization of 58-OBs, delocalization onto C-1 is not important[176,181,228] and yet the β-KIE is similar to that for 21-OBs-*exo*-3-*d*. The reduced β-effect for 58-OBs-*exo*-3-*d* (relative to 57-OBs-*exo*-3-*d*)

is attributed to delocalization of charge in the transition state onto the C-H bonds at C-6 and *not* from delocalization of the C-1 C-6 bond. This delocalization reduces the amount of positive charge at C-2 and lessens the demand for hyperconjugative stabilization from the bonds (C-H) at C-3.

Comparison of product ratios from solvolyses of 58-OBs and 58-OBs-*exo*-3-*d* (Table 2:8, Chapter 2) reveals that the relative amount of 1,3 elimination product (3-chloronortricyclene, 24) increases for the latter chloro brosylate. From these observations it is suggested that in ion 96-*exo*-3-*d*, a decrease in hyperconjugative stabilization of the *p* orbital at C-2 by introduction of deuterium at *exo*-C-3 causes an increase

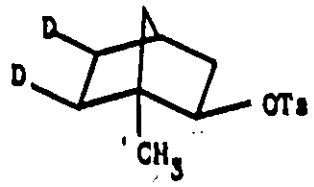


96-*exo*-3-*d*

in the demand for homohyperconjugative stabilization from the C-H bonds at C-6. Therefore the acidity of these bonds increases as does also the relative amount of 1,3 elimination product.

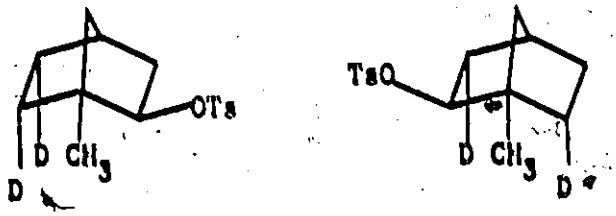
Originally, measurement of the γ-KIE for solvolysis of 1-methyl-*exo*-2-norbornyl tosylate-*exo*,*exo*-5,6-d_2 (80-OTs-*exo*,*exo*-5,6-d_2) was planned since ionization of this compound likely involves a great degree of C-1 C-6 bond participation in the transition state. It is likely that weakening of the C-1 C-6 bond is appreciable during ionization and

hence both bonds at C-6 should be affected considerably. Therefore the γ-KIE should be significant (*ca* 10%). The γ-KIE for acetolysis of "80-OTs-*endo*,*endo*-5,6-d_2" at 25° was found to be 1.03.[115b] However,



80-OTs-*exo*,*exo*-5,6-d_2

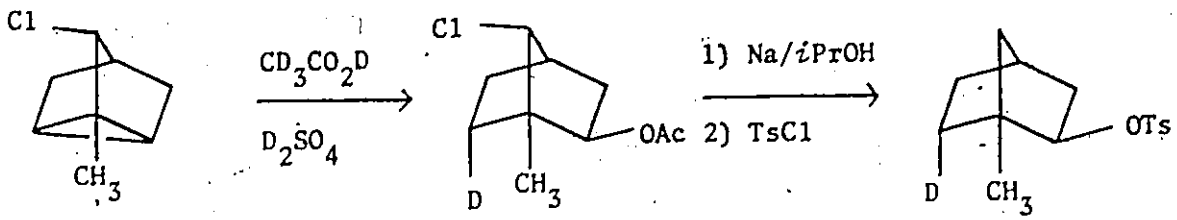
as a result of a private communication from the worker,[214] it was found that the synthetic route leading to this deuterated tosylate was complicated by rearrangement processes (Schemes 2:4 to 2:7, Chapter 2). As a result, the γ-KIE represents contributions from the two species shown below.



80-OTs-*endo*,*endo*-5,6-d_2

Initially, we expected that electrophilic cleavage (D^+) of 2-methyl-3-chloronortricyclene (25) would yield specifically deuterated 1-methyl-7-chloro-*exo*-2-norbornyl acetate-6-*d* as shown below. However, Table 2:4 (Chapter 2) shows that about 10% of the deuterium at C-6 is *exo*. Presently this route is the most effective method for preparation of 80-OTs-*endo*-6-*d* despite the small amount of 80-OTs-*exo*-6-*d* which is

formed. The γ-KIE for solvolysis of this compound is certainly low[115b]



despite the fact that an accurate value is not available. Although the lower γ-effect can be explained by a reduced degree of bridging in the transition state, it certainly is not consistent with the proposal that the γ-KIEs for 21-OBs-6-*d* arise from weakening of the C-1 C-6 bond.

CHAPTER 4

SUMMARY

Electrophilic(D^+) cleavage of 3-chloronortricyclene (24) gives 44% *anti*-7-chloro-*exo*-2-norbornyl acetate-*endo*-6-*d*, 26% *syn*-7-chloro-*exo*-2-norbornyl acetate-*endo*-6-*d*, 14% *exo*-5-chloro-*exo*-2-norbornyl acetate-*d* and 14% *endo*-5-chloro-*exo*-2-norbornyl acetate-*d*. At least 70% of the products arise from initial *edge protonation* of the cyclopropyl bond which is furthest removed from halogen (*ie* C-1 C-6 bond). Cleavage of this bond occurs with predominant retention of configuration (retention:inversion>14:1) at the site of electrophilic attack and predominant inversion of configuration (inversion:retention = *ca* 50:1) at the site of nucleophilic attack.

Electrophilic(D^+) cleavage of 2-methyl-3-chloronortricyclene (25) gives 73% 1-methyl-*anti*-7-chloro-*exo*-2-norbornyl acetate and 27% 1-methyl-*syn*-7-chloro-*exo*-2-norbornyl acetate in which most of the deuterium is situated at *endo*-C-6. Furthermore, the reactivity of 25 towards acid is closer to that of 3-chloronortricyclene than that of 1-methylnortricyclene (22). Once again, these facts suggest that cleavage of 25 proceeds *via* initial *edge protonation* (*deuteration*) of the cyclopropyl bond which is furthest removed from halogen. The stereochemistry of deuterium within the products suggests that rupture of this cyclopropyl bond occurs with retention of configuration by electrophile and accounts for most of the reaction pathway. Inversion of configuration at the carbon atom undergoing nucleophilic attack was observed.

The KIEs for ethanolyses of

(a) *anti*-7-chloro-*exo*-2-norbornyl brosylate-*endo*-6-*d* (1.11±0.01),

(b) *anti*-7-chloro-*exo*-2-norbornyl brosylate-*exo*,*exo*-5,6-d_2 (1.12±0.01),

(c) *anti*-7-chloro-*endo*-2-norbornyl brosylate-*endo*-6-*d* (1.00±0.02),

(d) *syn*-7-chloro-*exo*-2-norbornyl brosylate-*endo*-6-*d* (1.11±0.01),

(e) *syn*-7-chloro-*exo*-2-norbornyl brosylate-*exo*,*exo*-5,6-d_2 (1.11±0.01) and

(f) *anti*-7-chloro-*exo*-2-norbornyl brosylate-*exo*-3-*d* (1.09±0.01)

have been determined spectrophotometrically. Homohyperconjugative interactions between the bonds at C-6 and the developing *p*-orbital at C-2 in the solvolytic transition state can account for the γ-KIEs. These results cast doubt on the premise that delocalization of the C-1 C-6 bonding electrons is the source of the γ-KIE at C-6 in norbornyl systems. It is suggested that the γ-KIEs for ethanolyses of *exo*-2-norbornyl brosylate-*exo*-6-*d* (1.09±0.01) and *exo*-2-norbornyl brosylate-*endo*-6-*d* (1.11±0.01)[160] do not arise from delocalization of the C-1 C-6 bond but rather from homohyperconjugative interactions in the transition state.

From the solvolytic studies with 7-chloro-*exo*-2-norbornyl brosylates-6-*d*, it was found that the preferred stereochemical arrangement for 1,3 elimination (to yield 3-chloronortricyclene) is a semi-U arrangement. Furthermore, it is suggested that elimination occurs from an edge-protonated species.

CHAPTER 5

EXPERIMENTAL

General

Nuclear magnetic resonance (nmr) spectra were recorded on Varian T-60, A-60 and HA-100 spectrometers with tetramethylsilane (TMS) as the internal standard. Samples were dissolved in either carbon tetrachloride or carbon disulphide. Deuterium magnetic resonance (dmr) spectra were recorded on chloroform solutions using an XL-100 spectrometer with ^{19}F as the internal lock signal (perfluorobenzene) by Professor J.B. Stothers at the University of Western Ontario. 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.

Infrared spectra were recorded with Perkin Elmer 337 and Beckman IR-5 infrared spectrometers and the samples were dissolved in carbon tetrachloride or carbon disulphide. Absorption frequencies were calibrated with a polystyrene thin film and are expressed in reciprocal centimeters (cm^{-1}). For brevity, the notation cm^{-1} is excluded.

Ultraviolet spectra were recorded on a Cary Spectrophotometer Model 14.

Mass spectra were taken on a Hitachi Perkin Elmer RMU-6A spectrometer at 80 eV. Deuterium assay analyses were performed at 13 or 14 eV and are expressed as atoms of deuterium per molecule in excess of natural abundance deuterium. Chapter 6 presents sample calculations.

Analytical gas liquid partition chromatography (analytical glpc) was performed on a Varian Aerograph Model 204B dual column analytical gas chromatograph equipped with dual flame ionization detectors using helium as the carrier gas. The gas flow rate was usually 20-30 ml/min. 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 flow rate of 50-60 ml/min. Chromosorb W (Chromatographic Specialties Ltd) of mesh size 60/80 was used as the solid phase in all cases. The liquid phases were varied and will be designated as follows:

a% SE-30	refers to a% SE-30 on Chromosorb W
b% Carbowax	refers to b% Carbowax 20M on Chromosorb W
c% FFAP	refers to c% FFAP on Chromosorb W
d% Ucon Polar	refers to d% Ucon Polar 50-HB-2000 on Chromosorb W
e% GE-XF 1150	refers to e% GE-XF 1150 on Chromosorb W

Analytical columns (stainless steel) were 10' x 1/8" and preparative columns (glass) were 10' x ¼". Thus, "analytical glpc (5% SE-30,125°)" describes a chromatographic analysis on a Varian Model 204B instrument using a 5% SE-30 on Chromosorb W column (10' x 1/8") at a column temperature of 125°.

Relative product ratios were usually obtained by cutting out the peak on the chromatogram and weighing the paper on an analytical balance; however, product ratios from the solvolytic reactions (Table 2:8, Chapter 2) were determined by an Aerograph Model 475 Electronic Digital Integrator.

Spinning band distillations were performed on a Nester/Faust auto annular 30" teflon spinning band distillation column.

Melting points were recorded on a Kofler hot-stage apparatus and are uncorrected. Boiling points are also uncorrected.

Pentane was stirred vigorously over fuming sulphuric acid, washed

with sodium bicarbonate solution, dried and then distilled. Dry ether refers to ether which was distilled from lithium aluminum hydride. Pyridine was refluxed in barium oxide for 48 hr and then distilled.

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

Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tennessee.

A. 3-Chloronortricyclene (24)

1) Synthesis

Norbornene (Aldrich Chemical Co., 88.0 gm, 0.936 mol) in methylene chloride and pyridine was chlorinated by the method of Roberts[178] to yield 32.4 gm (27%) of 3-chloronortricyclene (24): bp 68-70° (31mm) (lit[178] bp 64-65° (27mm)); ir (neat) 3075 (cyclopropyl C-H), 815 (C-Cl); nmr (CCl_4, 100 MHz) δ 3.74 (s, 1H, H-C-Cl), 1.92 and 1.26 (m, 2H and 6H, norbornyl envelope). Nmr analysis revealed that 24 was not contaminated with isomeric chloronorbornenes.

2) Cleavage in Non-Deuterated Acid

a) Electrophilic cleavage of 3-chloronortricyclene (24) with sulphuric acid in acetic acid

3-Chloronortricyclene (10.13 gm, 79 mmol), sulphuric acid (1.311 gm) and 150 ml of acetic acid (distilled from acetic anhydride) were mixed in a 250 ml flask fitted with a calcium chloride drying tube and a magnetic stirrer. The flask was placed into an oil bath at 70° ± 3° and the progress of the reaction was monitored by glpc. After 120 hr the reaction was estimated to be >97% complete. Three-quarters of the reaction mixture was neutralized by slow addition to a saturated sodium bicarbonate solution and then the products were extracted into ether (3x150 ml). The ethereal extracts were washed with water (75 ml), saturated bicarbonate solution (75 ml) and water (75 ml). After the solution was dried and the solvent was removed, there remained 10.9 gm (98%) of chloro acetates. Glpc analysis (10% Carbowax, 180°) showed at least three products and only the product with shortest retention time (7 min) was resolved from the others. Isolation of this compound by prep glpc (15% Carbowax, 175°, rt 13 min)

gave *anti*-7-chloro-*exo*-2-norbornyl acetate (58-OAc) which was identified by comparison of spectral data to those of an authentic sample.[181]

When the remaining one-quarter of the reaction mixture was heated to $100^{\circ} \pm 5^{\circ}$, after 198.5 hr the relative product ratios were altered as determined by analytical glpc. Notably, the relative amount of 58-OAc had decreased and on raising the temperature to $120^{\circ} \pm 5^{\circ}$ considerable darkening of the reaction mixture as well as additional products were noted after 314.5 hr (glpc). These observations were not further investigated.

b) Reduction of the chloro acetate mixture with lithium aluminum hydride

Into a 125 ml three necked flask fitted with a condenser (with calcium chloride drying tube), adding funnel and magnetic stirrer was placed a slurry of lithium aluminum hydride (1.92 gm, 51 mmol) in dry ether (55 ml). The chloro acetate mixture from above (4.46 gm, 24 mmol) was dissolved in dry ether (10 ml) and slowly added to the slurry. Then the mixture was refluxed for 4 hr. The reaction flask was cooled in ice and excess hydride was *carefully* destroyed by the dropwise addition of water. After the white precipitate was filtered off, the filtrate was acidified with hydrochloric acid (10%, 20 ml) and then the ethereal layer was separated. The aqueous layer was extracted with ether (2x75 ml) and the combined ethereal layers were washed with water (50 ml), dried ($MgSO_4$) and concentrated to yield 3.3 gm (94%) of chloro alcohols (foul odour). Analysis by glpc (10% Carbowax, 178°) revealed at least three products but again only the product with shortest retention time (5 min) was resolved from the others. This product was isolated by prep glpc (15% Carbowax, 175°, rt 12 min) and identified as *syn*-7-chloro-*exo*-2-

norbornanol (59-OH), mp 88-92°, by comparison of spectral data to those from an authentic sample.[181] Similarly, the other chloro alcohol products which will be designated "other chloro alcohols" were collected by prep glpc (rt 22-30 min).

It was noted that excessive reaction time (>5 hr) led to the formation of *exo*-2-norbornanol (21-OH) as determined by both glpc and nmr spectroscopy.

c) Oxidation of "other chloro alcohols"

The oxidizing agent[183] was prepared as follows: sodium dichromate (10 gm) 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 the "other chloro alcohols" (0.20 gm, 1.4 mmol) in ether (5 ml, pretreated with oxidizing agent) in a 50 ml flask equipped with a condenser and magnetic stirrer, the oxidizing agent (0.8 ml) was slowly added. After the solution was vigorously stirred for 6.5 hr, the ethereal layer was separated and the aqueous layer was extracted with ether (5x20 ml). The combined ethereal layers were washed with saturated bicarbonate (2x15 ml), water (2x20 ml) and then dried. Analytical glpc (10% Carbowax, 190° and 20% Ucon Polar, 180°) showed three products and each was collected by prep glpc (15% Carbowax, 170°). The product with shortest retention time (12 min) was *anti*-7-chloro-2-norbornanone (63): ir (CS_2) 1760 (C=O); nmr (CCl_4, 60 MHz) δ 4.2 (s with fine structure, 1H, *syn*-C-7), 2.6 (broad s, 2H, C-1 and C-4), 2.5-1.5 (m, 6H, norbornyl envelope).

The product with intermediate retention time (15 min) was *exo*-5-chloro-2-norbornanone (65) and the product with longest retention time (19 min) was *endo*-5-chloro-2-norbornanone (66). The identities of these latter two compounds were verified by comparison of spectral data (ir, nmr) to those from authentic samples whose syntheses are subsequently described.

In a separate experiment, a small portion of the chloro alcohol mixture which was obtained from the chloro acetates by reduction but which was not subjected to prep glpc was oxidized as described above. This reaction gave 44% *anti*-7-chloro-2-norbornanone (63), 14% *exo*-5-chloro-2-norbornanone (65), 26% *syn*-7-chloro-2-norbornanone (64) and 14% *endo*-5-chloro-2-norbornanone (66) as determined by analytical glpc (10% Carbowax, 192°). None of the above chloro ketones had retention time identical to that of an authentic sample of *exo*-3-chloro-2-norbornanone (73).

d) Reduction of the chloro alcohols with sodium

To a stirred solution of the chloro alcohols obtained from part 2b (0.75 gm, 5.2 mmol) in *i*-propanol (50 ml, reagent grade) were slowly added small pieces of sodium metal (1.0 gm, 43 mmol). The mixture was stirred magnetically and refluxed during the addition; the colour changed from pale yellow to brown. After the sodium completely dissolved, the solution was refluxed for a further 3.0 hr and then the brown solid which formed when the mixture was cooled, was dissolved in water (50 ml) and the aqueous solution was extracted with pentane (4x70 ml). The combined pentane extracts were washed with dilute hydrochloric acid (10%, 40 ml),

water (2x40) and then dried and concentrated to yield 0.45 gm (78%) of a white solid. Analytical glpc (10% Carbowax, 132°) showed one major product (>95%) and after isolation by prep glpc (15% Carbowax, 139°), its properties were shown to be identical to those of *exo*-2-norbornanol (21-OH): ir(CS_2) 3600 (free OH), 3600-3200 (hydrogen bonded OH); nmr (CCl_4, 60 MHz) δ 3.6 (d, 1H, *endo*-C-2), 2.2 and 2.0 (broad s, each 1H, bridgeheads), 1.9-0.7 (m, 9H, norbornyl envelope and OH). Another product (<5%) with retention time slightly longer than that of *exo*-2-norbornanol was not identified.

By analytical glpc (10% FFAP, 105°) it was estimated that the ratio of *exo*-2-norbornanol : *endo*-2-norbornanol (rt 54 and 58 min respectively) was 98±2 : 2±1.

3) a) *Anti*- and *syn*-7-chloro-*exo*-2-norbornanols (58-OH and 59-OH)

Alcohols 58-OH and 59-OH were prepared by the addition of hypochlorous acid to norbornene according to the procedure of Roberts[178] and purified by prep glpc (15% Carbowax, 160°). *Syn*-7-chloro-*exo*-2-norbornanol (59-OH) had the following properties: mp 87-91° (lit[178] mp 89-90°); ir (CCl_4) 3590 (OH); nmr (CS_2, 100 MHz) δ 3.86 (m, 1H, *anti*-C-7), 3.60 (broad quintet, 1H, *J*=6 Hz, *endo*-C-2), 2.25 (m, 2H, C-1 and C-4), 1.88 (m, 3H, *exo*-C-3, *endo*-C-3 and -OH), 1.53 (m, 2H, *exo*-C-5 and *exo*-C-6), 1.10 (m, 2H, *endo*-C-5 and *endo*-C-6).[181] These assignments are based upon comparison to spectra of specifically deuterated 59-OH (*vide infra*).

Anti-7-chloro-*exo*-2-norbornanol (58-OH) had the following properties: ir (CCl_4) 3620 (free OH), 3650-3200 (hydrogen bonded OH); nmr (CCl_4, 100 MHz)

δ 4.19 (broad s with fine structure, 1H, *syn*-C-7), 3.75 (d of d, 1H, *J*=7.5 and 2.5 Hz, *endo*-C-2), 2.69 (broad s, 1H, OH), 2.26 and 2.14 (broad s, each 1H, bridgeheads), 2.00-1.67 (m, 3H, *exo*-C-3, *exo*-C-5 and *exo*-C-6), 1.40 (broad d, 1H, *J*=15 Hz, *endo*-C-3), 1.10 (m, 2H, *endo*-C-5 and *endo*-C-6). These assignments were confirmed by synthesis of specifically deuterated 58-OH (*vide infra*).

Independent synthesis of the *anti*-alcohol 58-OH was also effected by the hydroboration-oxidation of *anti*-7-chloronorbornene (62).[181]

b) *Anti*-7-chloro-*exo*-2-norbornyl acetate (58-OAc)

Anti-7-chloro-*exo*-2-norbornanol (58-OH, 25 mg, 0.1 mmol) was dissolved in pyridine (7 ml) and acetic anhydride (7 ml) and stirred at room temperature for 48 hr. Then the solution was added to crushed ice (*ca* 15 cc) and extracted with ether. The extracts were washed with dilute hydrochloric acid (10%), saturated bicarbonate, water and then dried and concentrated to yield *anti*-7-chloro-*exo*-2-norbornyl acetate (58-OAc): ir (CCl_4) 1750 (C=0), 1235 (acetate); nmr (CCl_4, 60 MHz) δ 4.6 (d of d, 1H, *endo*-C-2), 4.1 (s with fine structure, 1H, *syn*-C-7), 2.3 (broad s, 2H, C-1 and C-4), 1.9 (s, 3H, OAc), 2.2-1.0 (m, 6H, norbornyl envelope).[181]

c) *Syn*-7-chloro-*exo*-2-norbornyl acetate (59-OAc)

Syn-7-chloro-*exo*-2-norbornanol (59-OH) was acetylated by the method above to yield *syn*-7-chloro-*exo*-2-norbornyl acetate (59-OAc) : ir (CS_2) 1730 (C=0), 1240 (acetate); nmr (CCl_4,60 MHz) δ 4.5 (m, 1H, *endo*-C-2), 3.8 (s with fine structure, 1H, *anti*-C-7), 2.3 (broad s, 2H, C-1 and C-4), 1.9 (s, 3H, OAc), 2.2-1.0 (m, 6H, norbornyl envelope).[181]

d) *Exo*-3-chloro-2-norbornanone (73)

2-Norbornanone (Aldrich Chemical Co., 11.7 gm, 0.11 mol) was treated with sulphuryl chloride (15.0 gm, 0.11 mol) in carbon tetrachloride (20 ml) at 25° for 195 hr.[187] The major product (73, >90%) which was purified by prep glpc (15% Carbowax, 168°) had infrared absorptions as reported[187]: nmr (CS_2, 60 MHz) δ 3.5 (d, 1H, J=3 Hz, *endo*-C-3), 2.6 (broad s, 2H, C-1 and C-4), 2.4-1.3 (m, 6H, norbornyl envelope). The minor product was identified as 3,3-dichloro-2-norbornanone : ir (CS_2) 1760 (C=0), 850, 750, 700 (C-Cl); nmr (CS_2, 60 MHz) δ 3.0 and 2.7 (broad s, each 1H, bridgeheads), 2.5-1.5 (m, 6H, norbornyl envelope).

e) *Endo*-3-chloro-2-norbornanone (74)

The chloro ketone 74 was prepared according to the procedure reported by McDonald and Tabor[186] by refluxing a solution of lithium carbonate (1.7 gm), water (60 ml) and *exo*-3-chloro-2-norbornanone (636 mg) for 21 hr. The infrared spectrum of 74 was identical to that which was reported[187]: nmr (CS_2, 60 MHz) δ 4.0 (d with fine structure, 1H, J=*ca* 4 Hz, *exo*-C-3), 2.8 and 2.6 (broad s, each 1H, bridgeheads), 2.2-1.5 (m, 6H, norbornyl envelope).

f) *Exo*-5-chloro-2-norbornanone (65)

Nortricyclanone[184] (370 mg, 3.4 mmol) was dissolved in carbon tetrachloride (25 ml) and placed into a 50 ml round bottom flask fitted with a condenser and a magnetic stirrer. The solution was heated to 71°±5° in an oil bath. Anhydrous hydrogen chloride was bubbled through the solution

for 67 hr (>90% complete as determined by glpc) and then the mixture was neutralized with saturated sodium bicarbonate. The aqueous solution was extracted with carbon tetrachloride (4x55 ml) and the combined extracts were washed with saturated bicarbonate (40 ml), water (3x25 ml) and then dried. After the organic solvent was removed by distillation through a 15 cm column packed with glass helices, analysis by glpc (10% Carbowax, 185°) revealed one product (rt 4 min). Purification by prep glpc (15% Carbowax, 188°) gave 240 mg (49%, corrected for losses during collection) of a waxy solid which was identified as *exo*-5-chloro-2-norbornanone (65): ir (CS_2) 1760 (C=O), 1310, 1300, 1275, 1245, 1175, 1130, 1125, 1090, 955, 945, 880, 860, 710, 690, 565; nmr (CS_2, 60 MHz) δ 4.0 (t with fine structure, 1H, *endo*-C-5), 2.8 and 2.5 (broad s, each 1H, bridgeheads), 2.3-1.5 (m, 6H, norbornyl envelope).

g) *Endo*-5-chloro-2-norbornanone (66)

i) *Endo*-5-chloronorbornene (68)

To three thick-walled glass tubes were added 11.7, 11.7 and 10.3 gm of vinyl chloride along with 8.8, 8.8 and 7.8 gm of freshly distilled cyclopentadiene respectively. The tubes were sealed and then heated in a Monel Pressure Reaction Apparatus (Parr-Model 4914) at 220° for 15 hr, opened and the solutions were combined. Distillation through a 30 cm Vigreux column yielded 39 gm of a mixture containing *exo*- and *endo*-5-chloronorbornene (67 and 68); bp 95-97° (54-59 mm). The ratio of 67 to 68 was 43:57 as determined by nmr spectroscopy. Spinning band distillation under reduced pressure was used to separate 67 from 68. The lower boiling

fraction was *exo*-5-chloronorbornene (67): ir (neat) 3050 (olefinic C-H), 800, 725, 690; nmr (CCl_4, 100 MHz) δ 6.14 (quartet, 1H, C-3), 5.94 (quartet, 1H, C-2), 3.67 (t with fine structure, 1H, *endo*-C-5), 2.92 and 2.85 (broad s, each 1H, bridgeheads), 1.90-1.40 (m, 4H, *exo*-C-3, *endo*-C-3, *syn*-C-7 and *anti*-C-7).[252] The higher boiling fractions contained *endo*-5-chloronorbornene (68) with 15-20% contamination by *exo*-5-chloronorbornene (67) as determined by analytical glpc (5% SE-30, 90°). Distillation of the pot residue (enriched in 68) through an 8 cm Vigreux column yielded 3.6 gm of *endo*-5-chloronorbornene (68): bp 60-68° (33 mm); ir (neat) 3050 (olefinic C-H), 815, 770, 725, 695; nmr (CCl_4, 100 MHz) δ 6.25 (quartet, 1H, C-3), 6.00 (quartet, 1H, C-2), 4.30 (m, 1H, *exo*-C-5), 3.06 (broad s, 1H, C-4), 2.82 (broad s, 1H, C-1), 2.20 and 1.60-1.00 (m, 1H and 3H, *exo*-C-3, *endo*-C-3, *syn*-C-7, *anti*-C-7).

ii) Hydroboration-oxidation of *endo*-5-chloronorbornene (68)

Into a 250 ml flask fitted with a magnetic stirrer and a pressure equalizing funnel were placed *endo*-5-chloronorbornene (1.92 gm, 15.0 mmol) dissolved in tetrahydrofuran (40 ml, freshly distilled) along with sodium borohydride (1.21 gm, 31.8 mmol).[185] After the flask was purged for 10 min with nitrogen, boron trifluoride etherate (6.5 gm, 46 mmol, freshly distilled) in tetrahydrofuran (20 ml) was slowly added to the stirred solution containing olefin and after the addition was complete, the mixture was stirred for 1.5 hr at room temperature. The funnel was replaced with a condenser and water was added to the mixture until hydrogen was no longer evolved. Sodium hydroxide (10%, 30 ml) was added, then hydrogen peroxide (30%, 6 ml) was slowly added (maintaining a mild reflux rate). After being stirred for 3.0 hr,

the solution was extracted with ether (3x80 ml) and the extracts were washed with dilute hydrochloric acid (10%, 10 ml), water (2x20 ml) and then dried and concentrated to yield a white solid (1.3 gm, 59%). The two expected products *endo*-5-chloro-*exo*-2-norbornanol (61-OH) and *endo*-6-chloro-*exo*-2-norbornanol (69-OH) could not be separated by prep glpc (10% Carbowax, 180°).

iii) *Endo*-5-chloro-2-norbornanone (66) and *endo*-6-chloro-2-norbornanone (70)

The mixture of chloro alcohols 61-OH and 69-OH was oxidized as described in part 2c to a mixture of 66 and 70 in the ratio 42:58. Each chloro ketone was purified by prep glpc (15% Carbowax, 170°); the ketone with shorter retention time (17 min) was *endo*-5-chloro-2-norbornanone (66): ir (CS_2) 1750 (C=O), 1310, 1280, 1260, 1180, 1150, 1075, 1060, 960, 940, 915, 890, 865, 770, 695, 675; nmr (CS_2, 100 MHz) δ 4.30 (m, 1H, *exo*-C-5), 2.80-1.30 (m, 8H, norbornyl envelope). The ketone with longer retention time (23 min) was *endo*-6-chloro-2-norbornanone (70): ir (CS_2) 1760 (C=O), 1300, 1280, 1260, 1230, 1190, 1150(s), 1120, 1070(s), 1030, 970, 945, 925, 885, 865, 765, 735, 640; nmr (CS_2, 100 MHz) δ 4.30 (m, 1H, *exo*-C-6), 2.70-1.40 (m, 8H, norbornyl envelope).

h) *Exo*-3-chloro-*exo*-2-norbornyl acetate (71-OAc) and *endo*-3-chloro-*exo*-2-norbornyl acetate (72-OAc)

i) *Exo*-3-chloro-*exo*-2-norbornyl *t*-butyl ether (71-O*t*Bu) and *endo*-3-chloro-*exo*-2-norbornyl *t*-butyl ether (72-O*t*Bu)

Compounds 71-O*t*Bu and 72-O*t*Bu were prepared by the treatment of norbornene with *t*-butyl hypochlorite.[187] The *endo*-3-chloro ether 72-O*t*Bu

was isolated by prep glpc (15% FFAP, 155°): ir (neat) 1120 and 1075 (C-O); nmr (CCl_4, 60 MHz) δ 3.8 (m, 1H, *exo*-C-3), 3.2 (t, 1H, *endo*-C-2), 1.2 (s, 9H, $-C(CH_3)_3$), 2.3-1.0 (m, 8H, norbornyl envelope). Similarly, the *exo*-3-chloro ether 71-O*t*Bu was isolated by prep glpc: ir (neat) 1090 (C-O); nmr (CCl_4, 60 MHz) δ 3.8 (d of d, 1H, *J=ca* 6 and 1 Hz, *endo*-C-3), 3.5 (d of d, 1H, *J=ca* 6 and 1 Hz, *endo*-C-2), 1.2 (s, 9H, $-C(CH_3)_3$), 2.4-0.9 (m, 8H, norbornyl envelope).

ii) *Exo*-3-chloro-*exo*-2-norbornanol (71-OH) and *endo*-3-chloro-*exo*-2-norbornanol (72-OH)

Chloro alcohols 71-OH and 72-OH were prepared according to the literature method[187] by treatment of the corresponding chloro-*t*-butyl ethers 71-O*t*Bu and 72-O*t*Bu with anhydrous hydrogen chloride. The nmr spectra of 71-OH and 72-OH were identical to the reported spectra.[187]

iii) *Exo*-3-chloro-*exo*-2-norbornyl acetate (71-OAc) and *endo*-3-chloro-*exo*-2-norbornyl acetate (72-OAc)

The chloro alcohols 71-OH and 72-OH were individually acetylated using acetic anhydride in pyridine to yield the corresponding chloro acetates 71-OAc and 72-OAc. Analytical glpc (10% Carbowax, 190°) revealed that each acetate was >97% pure.

j) *Endo*-5-chloro-*exo*-2-norbornyl acetate (61-OAc)

Acetylation with acetic anhydride of a mixture of *endo*-5-chloro-*exo*-2-norbornanol (61-OH) and *endo*-6-chloro-*exo*-2-norbornanol (69-OH) (see section 3,g,i) gave a mixture of the chloro acetates 61-OAc and

69-OAc. Compound 61-OAc was isolated by prep glpc (15% Carbowax, 175°) however it was contaminated with 69-OAc (*ca* 18%).

4) Stability of various chloro acetates to the reaction conditions used for the electrophilic cleavage of 3-chloronortricyclene (24)

In a typical control reaction, 100-200 mg of the chloro acetate was dissolved in acetic acid containing 0.10 M sulphuric acid (*ca* 5 ml) and heated to 70° ± 5° in an oil bath for 500 hr. The extent of isomerization was monitored by analytical glpc (15% Carbowax, 150-185°) and the stabilities of the following chloro acetates were determined: *syn*-7-chloro-*exo*-2-norbornyl acetate (59-OAc) underwent 12% isomerization to *anti*-7-chloro-*exo*-2-norbornyl acetate (58-OAc), *endo*-5-chloro-*exo*2-norbornyl acetate (61-OAc) underwent 15% isomerization to *exo*-5-chloro-*exo*-2-norbornyl acetate (60-OAc). *Exo*-3-chloro-*exo*-2-norbornyl acetate (71-OAc), *endo*-3-chloro-*exo*-2-norbornyl acetate (72-OAc) and *anti*-7-chloro-*exo*-2-norbornyl acetate (58-OAc) each underwent <3% rearrangement.

5. Cleavage in Deuterated Acid

a) Electrophilic cleavage of 3-chloronortricyclene (24) with deuteroacetic acid containing deuterosulphuric acid

3-Chloronortricyclene (18.5 gm, 145 mmol) was dissolved in 80 ml of acetic acid—d_4 (Merck, Sharp and Dohme of Canada Ltd., 99.5 Atom % *d*) and 0.82 gm of sulphuric acid—d_2 (Merck, Sharp and Dohme) in a 250 ml flask fitted with a calcium chloride drying tube and then was heated in an oil bath to 70° ± 3° for 504 hr. Sodium acetate-d_3 (1.7 gm) was added to the reaction mixture to act as a buffer and acetic acid—d_4 (55 ml) was

removed by distillation under reduced pressure (5-7 mm). The remaining solution was neutralized with saturated sodium bicarbonate and extracted with ether. After the extracts were washed with water and dried, evaporation of solvent left 26.5 gm (95%) of deuterated chloro acetates: *anti*-7-chloro-*exo*-2-norbornyl trideuteroacetate-*d*, *syn*-7-chloro-*exo*-2-norbornyl trideuteroacetate-*d*, *exo*-5-chloro-*exo*-2-norbornyl trideuteroacetate-*d* and *endo*-5-chloro-*exo*-2-norbornyl trideuteroacetate-*d*. A small sample of deuterated *anti*-7-chloro-*exo*-2-norbornyl acetate was isolated by prep glpc (15% Carbowax, 175°) and deuterium assay by mass spectrometry indicated 4% d_3, 94% d_4, 2% d_5 species (av 3.98 *d*/molecule). When several milligrams of the deuterated *anti*-7-chloro-acetate 58-OAc was reduced with lithium aluminum hydride to the *anti*-7-chloro-alcohol 58-OH-*d* and then acetylated with acetic anhydride in pyridine, deuterium assay by mass spectrometry revealed 3% d_0, 95% d_1, 2% d_2 species (av 0.99 *d*/molecule).

b) Reduction of deuterated chloro acetates with lithium aluminum hydride

The deuterated chloro acetate mixture from above (17.6 gm, 92 mmol) was dissolved in dry ether (20 ml) and reduced with lithium aluminum hydride (1.89 gm, 50 mmol) as previously described. After workup, 12.7 gm (94%) of deuterated chloro alcohols were obtained. Some deuterated *syn*-7-chloro-*exo*-2-norbornanol (59-OH-*d*) was collected by prep glpc (15% Carbowax, 175°) and acetylated (acetic anhydride in pyridine), however deuterium assay by mass spectrometry was unreliable due to a weak parent ion.

c) Oxidation of the deuterated chloro alcohols

The deuterated chloro alcohols from above (12.7 gm, 86 mmol) were oxidized by the method previously described (44 ml oxidizing agent) to yield 12.0 gm (97%) of deuterated chloro ketones. Each of the four compounds was collected by prep glpc (15% Ucon Polar, 130°) and deuterium assay by mass spectrometry gave the following results: *anti*-7-chloro-2-norbornanone (63-*d*), 4% d_0, 95% d_1, 1% d_2 species (av 0.97 *d*/molecule); *exo*-5-chloro-2-norbornanone (65-*d*), 10% d_0, 90% d_1 species (av 0.90 *d*/molecule); *syn*-7-chloro-2-norbornanone (64-*d*), 3% d_0, 95% d_1, 2% d_2 species (av 0.99 *d*/molecule); *endo*-5-chloro-2-norbornanone (66-*d*), 13% d_0, 85% d_1, 2% d_2 species (av 0.89 *d*/molecule).

When the electrophilic cleavage of 3-chloronortricyclene was carried out in acetic acid-O-*d* (prepared from distilled acetic anhydride and deuterium oxide) and 0.10 M sulphuric acid-d_2 at 70° ± 3° for 332 hr, considerable acid-catalyzed hydrogen-deuterium exchange within the methyl group of the acetic acid caused the deuterium pool to become diluted. Mass spectrometric deuterium assay on the deuterated *anti*-7-chloro-*exo*-2-norbornyl acetate which was collected by prep glpc (15% Carbowax, 175°) revealed that it consisted of 19% d_0, 75% d_1, 6% d_2 species (av 0.87 *d*/molecule). The four deuterated chloro acetates which were obtained from the electrophilic (CH_3CO_2D,D_2SO_4) cleavage of 3-chloronortricyclene (24) were converted to the corresponding chloro alcohols and then oxidized to the corresponding chloro ketones. Deuterium assays by mass spectrometry showed the following results: *anti*-7-chloro-2-norbornanone (63-*d*), 20% d_0, 80% d_1 species (av 0.80 *d*/molecule); *exo*-5-chloro-2-norbornanone (65-*d*), 32% d_0, 68% d_1

species (av 0.68 *d*/molecule); *syn*-7-chloro-2-norbornanone (64-*d*), 21% d_0, 78% d_1, 1% d_2 species (av 0.80 *d*/molecule); *endo*-5-chloro-2-norbornanone (66-*d*), 30% d_0, 68% d_1, 2% d_2 species (av 0.72 *d*/molecule).

d) Location of deuterium within the deuterated chloro ketones 63-, 64-, 65, and 66-*d*.

To determine the location of the deuterium, the deuterated chloro ketones which had been previously separated by prep glpc (15% Ucon Polar, 130°) were individually reduced with lithium aluminum hydride to a mixture of *exo*- and *endo*-2-norbornanol. In a typical reaction, the deuterated chloro ketone (*ca* 100 mg) in ether (15 ml) was reduced with lithium aluminum hydride (reflux for 15 days) to the deuterated 2-norbornanols. Reduction of deuterated *anti*-7-chloro-2-norbornanone (63-*d*) and *endo*-5-chloro-2-norbornanone (66-*d*) gave *endo*-2-norbornanol-*d* (57-OH-*d*) as the major product (minor product was the *exo*-alcohol 21-OH-*d*) whereas reduction of deuterated *syn*-7-chloro-2-norbornanone (64-*d*) and *exo*-5-chloro-2-norbornanone (65-*d*) gave *exo*-2-norbornanol-*d* (21-OH-*d*) as the major product (minor product was the *endo*-alcohol 57-OH-*d*). In each case about 20 mg of the major norbornanol isomer was isolated by prep glpc (15% Carbowax, 110°), dissolved in a solution of $Eu(DPM)_3$ (*ca* 80 mg) in carbon tetrachloride (*ca* 1 ml) and then subjected to nmr (100 MHz) deuterium position analysis.[192,193] The combined mass spectral and nmr data (Table 2:3, Chapter 2) established that (a) the deuterium in the *syn*-7- and *anti*-7-chloro-*exo*-2-norbornyl acetates (59- and 58-OAc-*d*) was situated at C-6 (>90%) with at least 95% *endo* stereochemical purity, (b) the deuterium in the *exo*-5-chloro-*exo*-2-norbornyl acetate (60-OAc-*d*) was positioned at C-1 (0.10 ± 0.05), *endo*-C-2 (0.10 ± 0.05), *exo*-C-3 (0.20 ± 0.05), *endo*-C-3 (0.20 ± 0.05), *exo*-C-6 (0.20 ± 0.05), *endo*-C-6 (0.20 ± 0.05) and (c) the deuterium in *endo*-5-chloro-*exo*-2-norbornyl acetate (61-OAc-*d*) was positioned at C-1 (0.10 ± 0.05), *endo*-C-2 (0.15 ± 0.05), *exo*-C-6 (0.55 ± 0.05), *endo*-C-6 (0.25 ± 0.05).

6) Control experiments with *anti*-7-chloro-2-norbornanone-*endo*-6-*d* (63-*endo*-6-*d*) and *exo*-5-chloro-2-norbornanone-*exo*-3-*d* (65-*exo*-3-*d*) to check for deuterium losses

a) Check for deuterium loss during prep glpc

A sample of 63-*endo*-6-*d* which was collected by prep glpc (15% Ucon Polar, 130°) was analyzed mass spectrometrically for deuterium: 5% d_0, 95% d_1, species (av 0.95 *d*/molecule). Reinjection of a small portion of the above chloro ketone and collection by glpc, followed by mass spectral analysis revealed 5% d_0, 94% d_1, 1% d_2 species (av 0.96 *d*/molecule).

Similarly, the chloro ketone 65-*exo*-3-*d* was tested for deuterium loss during isolation by prep glpc. After one injection and collection, 65-*exo*-3-*d* was assayed as 10% d_0, 90% d_1 species (av 0.90 *d*/molecule) and after reinjection and collection, the ketone was found to be composed of 10% d_0, 90% d_1 species (av 0.90 *d*/molecule).

b) Check for deuterium loss during oxidation

Anti-7-chloro-2-norbornanone-*endo*-6-*d* (*ca* 10 mg, av 0.95 *d*/molecule) in ether (3 ml, pretreated with oxidizing agent) and oxidizing agent[183] (2 ml) were vigorously stirred together for 3.5 hr at room temperature. Workup was as previously described and the product was isolated by prep glpc (15% Ucon Polar, 140°). Mass spectral analysis indicated 5% d_0, 94% d_1, 1% d_2 species (av 0.96 *d*/molecule).

Similarly deuterated *exo*-5-chloro-2-norbornanone (av 0.90 *d*/molecule) which contained some deuterium at *exo*-C-3 was subjected to the chromic acid oxidation reaction conditions and deuterium assay by mass spectrometry

revealed 11% d_0, 88% d_1, 1% d_2 species (av 0.90 d/molecule).

B. 2-Methyl-3-chloronortricyclene (25)

1) Synthesis of 25

a) 2-Methylnorbornene (76)

In a typical run, ethylene (800 psi) and methylcyclopentadiene dimer (Aldrich, 125 gm) were caused to react at 200° for 12 hr[194] in a Monel Pressure Apparatus (Parr-Model 4914) fitted with a glass liner. The reaction vessel was cooled to room temperature and the excessive ethylene was released. From eight runs, the mixtures were combined, filtered and then distilled through a 30 cm vacuum jacketed Vigreux column. The fraction boiling between 110° and 120° was collected. Redistillation at atmospheric pressure was effected with a Nester-Faust spinning band distillation unit. After a forerun of 5 gm was collected, the first fraction (100 gm, head temperature 80-102°) was 1-methylnorbornene (75): nmr (CCl_4, 100 MHz) δ 5.98 (quartet, 1H, J= 5.0 and 2.5 Hz, C-3), 5.75 (d, 1H, J= 5.0 Hz, C-2), 2.78 (broad s, 1H, C-4), 1.37 (s, 3H, $-CH_3$), 1.90-0.95 (m, 6H, norbornyl envelope). The second fraction (50 gm, head temperature 105°) was a mixture of 1- and 2-methylnorbornenes. The third fraction (160 gm, head temperature 106-112°) was 2-methylnorbornene (76): ir (neat) 3060 (olefinic C-H); nmr (CCl_4, 100 MHz) δ 5.48 (broad s, 1H, C-3), 2.75 and 2.58 (broad s, each 1H, bridgeheads), 1.74 (d, 3H, J= 1.5 Hz, $-CH_3$), 1.74-0.85 (m, 6H, norbornyl envelope).[195]

b) Chlorination of 2-methylnorbornene (76)

2-Methylnorbornene (110 gm, 1.02 mol) was dissolved in methylene chloride (500 ml) and pyridine (105 ml) in a three-necked flask fitted with

a mechanical stirrer along with a gas inlet and outlet. The flask was cooled in an ice bath and then chlorine gas (passed through concentrated sulphuric acid) was bubbled into the stirred solution until the mixture turned yellow permanently. It was allowed to warm to room temperature and then it was washed with water (150 ml), dilute hydrochloric acid (10%, 2x200 ml), saturated bicarbonate solution (2x200 ml) and water (2x200 ml). After the organic layer was dried and concentrated, a yellow oil (150 gm) was obtained and analytical glpc (5% SE-30, 140°) showed a product (35%) with short retention time (2 min) along with at least six other products having longer retention times. Analysis on a different chromatographic column (10% Carbowax, 175°) revealed that the product with shortest retention time (2 min) was the major product (75%) and the others were minor. A glass insert in the injector block of the gas chromatograph did not darken after several injections of the reaction mixture. Separation of the tricyclic compound was attempted by fractional column distillation through a glass column (30 cm) packed with glass helices and wrapped several times with aluminum foil.

During the early stages of the distillation, a white substance solidified in the column and caused the forerun to become cloudly. The first fraction consisted of thirty grams of a colourless liquid bp 35-40° (20-25 mm) which was shown by analytical glpc (10% Carbowax, 190°) and nmr spectroscopy to be >96% pure. This compound was labile on a 5% SE-30 column (100°) when the injector and detector block temperatures were high (>200°). The second fraction was a clear yellow liquid (47 gm): bp 80-90° (20-25 mm); nmr (CCl_4, 60 MHz) δ 4.1 and 3.3 (AB quartet, each 1H, J= 11 Hz),

3.9 (s with fine structure, 1H), 2.3-1.2 (m, 7H). After the second fraction was collected, a yellow substance solidified in the condenser and the distillation was stopped. Further attempts were not made to separate the compounds remaining in the pot (*ca* 70 gm).

The first fraction was further purified by spinning band distillation under reduced pressure with pressure control ± 2 mm. The head temperature was 51° (*ca* 80 mm) and the pot temperature was 56°. After 2 ml of forerun, four separate fractions were collected and each was estimated by analytical glpc (5% SE-30, 100°) to be at least 97% pure. The spectral data which were consistent with 2-methyl-3-chloronortricyclene (25) were as follows: ir (neat) 3075 and 3010 (cyclopropyl C-H), 1455, 1445, 1310, 1295, 1240, 925, 905, 850, 800, 775; nmr (CCl_4, 100 MHz, Figure 6:1, Chapter 6) δ 3.65 (d, 1H, J= 1.5 Hz, H-C-Cl), 2.12 and *ca* 1.4 (AB pattern, each 1H, J= 10.5 Hz, *exo*-C-7 and *endo*-C-7), 2.03 (broad s, 1H, C-4), 1.40 (m, 2H, *exo*-C-5 and *endo*-C-5), 1.23 (s, 3H, $-CH_3$), 1.04 (s, 2H, C-1 and C-6). Spin decoupling experiments corroborated the above assignments. For example, irradiation at δ 2.03 caused the peak at δ 3.65 to collapse to a singlet. Irradiation at δ 1.4 caused the doublet at δ 2.12 to collapse to a singlet.

Strong mass spectrum peaks were *m/e* 142, 107, 91 and 79.

2) Cleavage in Non-Deuterated Acid

a) Electrophilic cleavage of 2-methyl-3-chloronortricyclene (25) with sulphuric acid in acetic acid

2-Methyl-3-chloronortricyclene (5.47 gm, .39 mmol) was dissolved in acetic acid (75 ml) containing 0.10 M sulphuric acid and the mixture was

heated to 62° ± 2°, under an atmosphere of nitrogen, in an oil bath. The progress of the reaction was monitored by analytical glpc (15% Carbowax, 180°) and was estimated to be >93% complete after 105 hr. The excess of acid was quenched with saturated sodium bicarbonate solution and the products were extracted into ether (3x350 ml). The combined extracts were washed with water (4x100 ml), dried and then concentrated to yield 7.7 gm (97%) of chloro acetates. Analytical glpc (15% Carbowax, 180°) showed two products (ratio 76:24) whose ratio did not change through the course of the reaction. To check for decomposition and/or rearrangement of the reaction products during analysis by gas chromatography, the injector and detector block temperatures were altered to observe the effect on the product ratio.

Injector Temp.	Detector Temp.	Column Temp.	Product Ratio
215°	225°	180°	76:24
160°	170°	180°	76:24
160°	170°	150°	79:21
130°	140°	175°	78:22

The two products were isolated by prep glpc (15% FFAP, 150°) and the compound with shorter retention time (13 min) was identified as 1-methyl-*anti*-7-chloro-*exo*-2-norbornyl acetate (78-OAc): ir (CS_2) 1740 (C=0), 1380, 1235(s), 1060, 1025, 860(s), 695; nmr (CS_2 100 MHz) δ 4.55 (d of d, 1H, J= 8,0 and 3.0 Hz, *endo*-C-2), 3.77 (broad s, 1H, *syn*-C-7), 1.89 (s, 3H, -OAc), 0.97 (s, 3H, $-CH_3$), 2.25-1.00 (m, 7H, norbornyl envelope); mass spectrum (70 eV) *m/e* (relative intensity) 202(2), 160(4), 142(11), 124(25), 109(22), 80(100). The compound with longer retention time (15 min) was

1-methyl-*syn*-7-chloro-*exo*-2-norbornyl acetate (79-OAc): ir (CS_2) 1740 (C=O), 1375, 1240(s), 1065, 1030, 860(s), 695; nmr (CS_2, 100 MHz) δ 4.51 (t with fine structure, 1H, *J=ca* 6 Hz, *endo*-C-2), 3.51 (broad s, 1H, *anti*-C-7), 2.22 (broad s, 1H, C-4), 1.87 (s, 3H, -OAc), 1.02 (s, 3H, $-CH_3$), 2.02-0.95 (m, 6H, norbornyl envelope); mass spectrum (70 eV) *m/e* (relative intensity) 142(10), 107(91), 81(75), 80(100). Only at low ionizing voltage (10 eV) was the peak at *m/e* 202 discernable.

b) Reduction with lithium aluminum hydride of the mixture of 1-methyl-*anti*-7-chloro-*exo*-2-norbornyl acetate (78-OAc) and 1-methyl-*syn*-7-chloro-*exo*-2-norbornyl acetate (79-OAc)

To a slurry of lithium aluminum hydride (0.95 gm, 25 mmol) and dry ether (50 ml) in a 125 ml flask fitted with a reflux condenser, calcium chloride drying tube and magnetic stirrer were slowly added 3.28 gm (16 mmol) of the mixture of methyl chloro acetates 78-OAc and 79-OAc dissolved in dry ether (20 ml). The mixture was refluxed for 3.0 hr; upon cooling, excessive hydride was *carefully* destroyed with water and the products were extracted into ether (3x100 ml). After the ethereal extracts were washed with water (1x50 ml), dried and concentrated, an oily residue (2.5 gm, 97%) with a foul odour was obtained. Analytical glpc (15% Carbowax, 180°) revealed two products (ratio 22:78, rt 3 and 5 min respectively) which were separable by prep glpc (15% FFAP, 170°). The product with shorter retention time was collected as a white waxy solid and was identified as 1-methyl-*syn*-7-chloro-*exo*-2-norbornanol (79-OH): ir (CS_2) 3600(OH), 1305, 1265, 1245, 1210, 1145, 1095, 1080(s), 1030, 1015, 980, 940, 860, 830, 805, 770; nmr (CS_2, 100 MHz, Figure 2:9, Chapter 2)

δ 3.62 (broad s with fine structure, 1H, *anti*-C-7), 3.35 (broad quintet, 1H, *endo*-C-2), 2.31 (broad s, 1H, C-4), 1.16 (s, 3H, $-CH_3$), 2.03-1.05 (m, 7H, norbornyl envelope and OH). Anal: Calc'd for $C_8H_{13}OCl$: C, 59.81; H, 8.10; Cl, 22.12. Found: C, 59.63; H, 8.02; Cl, 22.28.

The compound with longer retention time was collected as a white waxy solid and identified as 1-methyl-*anti*-7-chloro-*exo*-2-norbornanol (78-OH): ir (CS_2) 3625 (Free OH), 3700-3250 (hydrogen bonded OH), 1340, 1310, 1290, 1270, 1235, 1195, 1075, 1005, 965, 915, 905, 840, 740; nmr (CS_2, 100 MHz, Figure 2:7, Chapter 2) δ 3.81 (broad s, 1H, *syn*-C-7), 3.52 (d of d, 1H, J= 8.0 and 3.0 Hz, *endo*-C-2), 1.05 (s, 3H, $-CH_3$), 2.25-0.75 (m, 7H, norbornyl envelope and OH). Anal: Calc'd for $C_8H_{13}OCl$: C, 59.81; H, 8.10; Cl, 22.12. Found: C, 59.68; H, 8.13; Cl, 21.96.

It was noted by both glpc and nmr spectroscopy that long reaction times led to the formation of 1-methyl-*exo*-2-norbornanol (80-OH) as a secondary reaction product.

When 30 mg of the *syn*-7-chloro alcohol 79-OH was complexed with 114 mg of $Eu(fod)_3$ in carbon tetrachloride (*ca* 0.5 ml), nmr spectral analysis (100 MHz, Figure 2:10, Chapter 2) revealed that most of the proton resonances were resolved: δ 16.66 (broad s, 1H, *endo*-C-2), 10.70 (d, 1H, J= 14 Hz, *exo*-C-3), 7.72 (s, 3H, $-CH_3$), 7.08 (s, 1H, *anti*-C-7), 6.10 (d of d, 1H, J= 14 and 7 Hz, *endo*-C-3), 5.06 (broad s, 1H, C-4), 3.70 (m, 1H, *endo*-C-6), 3.30-2.80 (m, 3H, *exo*-C-5, *exo*-C-6 and *endo*-C-5).

Similarly, 44 mg of the *anti*-7-chloro alcohol 78-OH was complexed with 208 mg of $Eu(fod)_3$ in carbon tetrachloride (*ca* 0.5 ml) and analyzed

by nmr spectroscopy (100 MHz, Figure 2:8, Chapter 2): δ 17.85 (d, 1H, J= 7 Hz, *endo*-C-2), 12.95 (d, 1H, J= 14 Hz, *exo*-C-3), 12.30 (s, 1H, *syn*-C-7), 7.44 (s, 3H, $-CH_3$), 7.05 (d of d, 1H, J= 14 and 7 Hz, *endo*-C-3), 5.10 (broad s, 1H, C-4), 4.50 (t with fine structure, 1H, J= 8 Hz, *endo*-C-6), 4.10-3.25 (m, 3H, *exo*-C-5, *exo*-C-6 and *endo*-C-5).

c) Oxidation of the mixture of 1-methyl-*anti*-7-chloro-*exo*-2-norbornanol (78-OH) and 1-methyl-*syn*-7-chloro-*exo*-2-norbornanol (79-OH).

A mixture (3.0 gm) of the chloro alcohols 78-OH and 79-OH was oxidized as previously described to a mixture of the chloro ketones 82 and 83 in 95% yield. Analytical glpc (15% Carbowax, 165°) showed two products (ratio 77:23, rt 3 and 5 min respectively) which were separated by prep glpc (15% FFAP, 140°). The product with shorter retention time was identified as 1-methyl-*anti*-7-chloro-2-norbornanone (82): ir (CS_2) 1760 (C=O), 1305, 1280, 1090, 1055(s), 1005, 975, 905, 855(s), 800, 740, 615; nmr (CS_2, 100 MHz) δ 3.75 (s with fine structure, 1H, *syn*-C-7), 2.58 (broad s with fine structure, 1H, C-4), 1.04 (s, 3H, $-CH_3$), 2.35-1.15 (m, 6H, norbornyl envelope); mass spectrum (70 eV) *m/e* (relative intensity) 158(6), 114(12), 81(100). The product with longer retention time was 1-methyl-*syn*-7-chloro-2-norbornanone (83): ir (CS_2) 1760 (C=O), 1340, 1315, 1300, 1265(s), 1240, 1165, 1130, 1065(s), 1030, 965, 950, 930, 895, 875, 865, 835, 790, 760; nmr (CS_2, 100 MHz) δ 3.98 (m, 1H, *anti*-C-7), 1.06 (s, 3H, $-CH_3$), 2.65-1.45 (m, 7H, norbornyl envelope); mass spectrum (70 eV) *m/e* 158 (parent), 114, 81 (base).

d) Reduction with sodium in *i*-propanol of a mixture of 1-methyl-*anti*-7-chloro-*exo*-2-norbornyl acetate (78-OAc) and 1-methyl-*syn*-7-chloro-*exo*-2-norbornyl acetate (79-OAc)

The mixture of chloro acetates 78-OAc and 79-OAc (*ca* 500 mg) was reduced with sodium in *i*-propanol, as described previously. Analytical glpc (15% Carbowax, 150°) revealed one major product (>95%) which was isolable by prep glpc (15% FFAP, 130°) and was shown to be 1-methyl-*exo*-2-norbornanol (80-OH) by comparison of spectral data to those from an authentic sample. The minor product (<4%) was not conclusively identified; possibly it arose *via* solvolysis of chlorine followed by fragmentation to a cyclopentenyl derivative. Its nmr spectrum (100 MHz) displayed a one proton multiplet at δ 5.17 and a two proton triplet (J=*ca* 6 Hz) at δ 3.50 as well as a multi proton multiplet at high field.

Analytical glpc and nmr spectroscopy indicated that a 5% maximum of 1-methyl-*endo*-2-norbornanol (81-OH) was present in the reaction mixture.

3) 1-Methyl-*exo*-2-norbornanol (80-OH)

a) *Exo*-2-methyl-*endo*-2-norbornanol (92-OH)

The alcohol 92-OH was prepared by treatment of 2-norbornanone (10 gm, 91 mmol) with methyl magnesium iodide by the procedure of Toivonen *et al.*[216, 217] The yield was 11.3 gm (98%); mp 30-32° (lit[216] 34-35): ir (CS_2) 3600 (free OH), 3650-3150 (hydrogen bonded OH); nmr (CS_2, 100 MHz) δ 2.16 (s, 1H, -OH), 2.10 and 1.88 (broad s, each 1H, bridgeheads), 1.21 (s, 3H, $-CH_3$), 1.60-1.00 (m, 8H, norbornyl envelope).

b) 1-Methyl-*exo*-2-norbornyl acetate (80-OAc)

Exo-2-methyl-*endo*-2-norbornanol (8.6 gm, 68 mmol) was rearranged and acetylated at room temperature for 11 hr with Bertram-Walbaum solution (85 ml of acetic acid and 15 ml of 50% v/v sulphuric acid and acetic acid) by the method of Toivonen[216] to yield 11.1 gm (97%) of 1-methyl-*exo*-2-norbornyl acetate (80-OAc). A small portion of the acetate was purified by prep glpc (15% FFAP, 150°) and it had the following spectral properties: ir (CS_2) 1740 (C=O), 1240 (acetate); nmr (CS_2, 100 MHz) δ 4.40 (d of t, 1H, *J*= 7 Hz, *endo*-C-2), 2.12 (unresolved t, 1H, C-4), 1.88 (s, 3H, -OAc), 1.03 (s, 3H, $-CH_3$), 1.85-0.90 (m, 8H, norbornyl envelope).

c) 1-Methyl-*exo*-2-norbornanol (80-OH)

1-Methyl-*exo*-2-norbornyl acetate (10.5 gm, 63 mmol) was hydrolyzed by treatment with potassium hydroxide (27.3 gm) in water (50 ml) and methanol (70 ml) on a steam bath for 24 hr.[41,217] The product was extracted into pentane (3x150 ml) and after the extracts were washed with water and dried, evaporation of solvent left 4.0 gm (50%) of 1-methyl-*exo*-2-norbornanol (80-OH): mp 73-74° (lit[216] 70-71°); ir (CS_2) 3600 (free OH), 3650-3250 (hydrogen bonded OH), 1245 (C-O); nmr (CS_2, 100 MHz) δ 3.31 (d with fine structure, 1H, *J*= 7 Hz, *endo*-C-2), 2.25 (broad s, 1H, -OH), 2.16 (unresolved t, 1H, C-4), 1.06 (s, 3H, $-CH_3$), 1.77-0.83 (m, 8H, norbornyl envelope).

4) Cleavage in Deuterated Acid

a) Electrophilic cleavage of 2-methyl-3-chloronortricyclene (25) with deuterosulphuric acid and deuteroacetic acid

Into a three necked flask fitted with a condenser and a calcium

chloride drying tube were placed 50 ml of acetic acid-d_4 (Merck, Sharp and Dohme of Canada Ltd, 99.5 Atom %d) and sulphuric acid-d_2 (0.516 gm). Nitrogen gas was slowly bubbled through the acid which was heated to $65^{\circ}\pm2^{\circ}$ in an oil bath. 2-Methyl-3-chloronortricyclene (2.99 gm, 21 mmol) was added to the flask, the mixture was magnetically stirred and the progress of the reaction was monitored by analytical glpc (15% Carbowax, 175°). After 5 hr, a small sample was withdrawn and glpc revealed a minor product peak (*ca* 10%), with retention time slightly longer than that of starting material, which disappeared with time. After 60 hr, the reaction was estimated to be complete and the excess of acid was neutralized with a saturated solution of sodium bicarbonate. The products were extracted into ether and after the ethereal extracts were washed, dried and concentrated, 4.1 gm (91%) of 1-methyl-*anti*-7-chloro-*exo*-2-norbornyl trideuteroacetate-*d* (78-trideuteroacetate-*d*) and 1-methyl-*syn*-7-chloro-*exo*-2-norbornyl trideuteroacetate-*d* (79-trideuteroacetate-*d*) in the ratio 73:27 were obtained.

b) Reduction with lithium aluminum hydride of the mixture of deuterated chloro acetates

The deuterated chloro acetate mixture from above (4.0 gm, 19 mmol) was reduced with lithium aluminum hydride (0.84 gm, 22 mmol) as previously described, to 3.0 gm (97%) of a mixture containing 1-methyl-*anti*-7-chloro-*exo*-2-norbornanol-*d* (78-OH-*d*) and 1-methyl-*syn*-7-chloro-*exo*-2-norbornanol-*d* (79-OH-*d*). Each product was isolated by prep glpc (25% GE XF-1150, 170°). When 1-methyl-*syn*-7-chloro-*exo*-2-norbornanol-*d* (45 mg) was complexed with Eu(fod)$_3$ (215 mg) in carbon tetrachloride (*ca* 0.5 ml), analysis by proton magnetic resonance spectroscopy (100 MHz, Figure 2:13, Chapter 2)

revealed the following distribution of deuterium (Table 2:4, Chapter 2); $-CH_3$ (0.11 ± 0.02), *exo*-C-6 (0.06 ± 0.03), *endo*-C-6 (0.88 ± 0.06). Analysis of this sample by deuterium magnetic resonance spectroscopy (Figure 2:14, Chapter 2) showed that the deuterium was distributed as follows (Table 2:4, Chapter 2); $-CH_3$ (0.09 ± 0.01), C-6 (0.96 ± 0.04). Complexation of 1-methyl-*anti*-7-chloro-*exo*-2-norbornanol-*d* (34 mg) with 192 mg of $Eu(fod)_3$ in carbon tetrachloride (*ca* 0.5 ml) and analysis by proton magnetic resonance spectroscopy (100 MHz, Figure 2:11 Chapter 2) revealed the following distribution of deuterium (Table 2:4, Chapter 2); $-CH_3$ (0.17 ± 0.03), *endo*-C-2 (0.05 ± 0.02), *endo*-C-6 (0.83 ± 0.03), *exo*-C-6 (0.04 ± 0.02), *syn*-C-7 (0.13 ± 0.03). Analysis by deuterium magnetic resonance spectroscopy (Figure 2:12, Chapter 2) gave the following results (Table 2:4, Chapter 2); $-CH_3$ (0.22 ± 0.02), *endo*-C-2 (0.05 ± 0.01), C-6 (0.88 ± 0.05), *syn*-C-7 (0.14 ± 0.01).

c) Oxidation of a mixture of 1-methyl-*anti*-7-chloro-*exo*-2-norbornanol-*d* (78-OH-*d*) and 1-methyl-*syn*-7-chloro-*exo*-2-norbornanol-*d* (79-OH-*d*)

A mixture of 1-methyl-*anti*-7-chloro-*exo*-2-norbornanol-*d* and 1-methyl-*syn*-7-chloro-*exo*-2-norbornanol-*d* was oxidized (*vide supra*) to a mixture of 1-methyl-*anti*-7-chloro-2-norbornanone-*d* (82-*d*) and 1-methyl-*syn*-7-chloro-2-norbornanone-*d* (83-*d*) respectively. After workup, each product was isolated by prep glpc (25% GE XF-1150, 175°) and then analyzed by mass spectrometry for deuterium. Compound 82-*d* was a composite of 4% d_0, 87% d_1, 9% d_2 species (av 1.05 *d*/molecule) and compound 83-*d* was a composite of 5% d_0, 67% d_1, 22% d_2, 6% d_3 species (av 1.29 *d*/molecule).

C The preparation of non-deuterated and deuterated chloro alcohols and chloro brosylates for KIE studies

This section describes the syntheses of the various non-deuterated and deuterated chloro brosylates and the corresponding alcohol precursors. The same general procedure was used for the preparation of all chloro brosylates.

In a typical brosylation reaction, the chloro alcohol was dissolved in dry pyridine (distilled from barium oxide) and the solution was cooled in an ice bath. A 10-20% mole excess of freshly recrystallized brosyl chloride* (petroleum ether 30-60°, mp 73-74°) was slowly added to the ice cold solution of chloro alcohol which was then placed in the refrigerator at 0° for at least one week whereupon the solution usually turned pink or yellow. The product was isolated in the following manner. Several small pieces of ice were added to the solution and the reaction vessel was allowed to warm to room temperature. After the ice had melted, the solution was diluted with water (turned cloudy) and then it was extracted with chloroform. The combined extracts were washed successively with cold water, *cold dilute* hydrochloric acid (10%) saturated bicarbonate solution, cold water and then dried. After the solvent was removed under reduced pressure, the solid (or oil) which remained was decolourized with carbon and then recrystallized from a suitable solvent system to constant melting point. Crude yields were generally 80-95%.

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*p-Bromobenzenesulphonyl chloride

Since both the deuterated chloro alcohols and their corresponding chloro brosylates gave weak parent ions when analyzed by mass spectrometry, the determination of deuterium content directly from these compounds by this method was not reliable. Therefore, the extent of deuteration was determined mass spectrometrically on the corresponding deuterated chloro ketone which was obtained by oxidation of the deuterated chloro alcohol. It was assumed that the deuterium contents of the deuterated chloro ketones and the corresponding chloro brosylates were identical. This assumption is valid provided that deuterium is not situated on the hydroxylated carbon atom (C-2) since it (deuterium) would be lost during oxidation. However, in all cases, the lack of deuterium at C-2 was ascertained by nmr spectroscopy.

1) a) *Syn*-7-chloro-*exo*-2-norbornanol (59-OH)

Syn-7-chloro-*exo*-2-norbornanol (59-OH) was prepared according to the procedure reported by Roberts.[178] The nmr spectrum of 59-OH appears in Chapter 6 (Figure 6:3).

b) *Syn*-7-chloro-*exo*-2-norbornyl brosylate (59-OBs)

This brosylate was recrystallized from pentane-ether and had the following characteristics: mp 112-113°; ir (CS_2) 1375, 1350, 1315, 1190 (-SO_2-O), 1100, 1075,1040, 1020, 970, 940, 895, 875, 825, 775, 750, 640, 620, 600, 550; nmr (CS_2, 100 MHz) δ 7.63 (m, 4H, arom), 4.50 (m, 1H, *endo*-C-2), 3.76 (broad s with fine structure, 1H, *anti*-C-7), 2.43 and 2.28 (broad s, each 1H, bridgeheads), 2.20-1.10 (m, 6H, norbornyl envelope).

Anal: Calc'd for $C_{13}H_{14}SO_3Br$: C, 42.69; H, 3.83.

Found C, 42.57, H, 3.84.

c) *Syn*-7-chloro-*exo*-2-norbornanol-*endo*-6-*d* (59-OH-*endo*-6-*d*)

The deuterated alcohol 59-OH-*endo*-6-*d* was obtained by reduction with lithium aluminum hydride of *syn*-7-chloro-*exo*-2-norbornyl trideuteroacetate-*endo*-6-*d*. This latter chloro acetate was a product from the electrophilic cleavage (D^+) of 3-chloronortricyclene with deuteroacetic and deuterosulphuric acid (*vide supra*). A small sample of the chloro alcohol 59-OH-*endo*-6-*d* was oxidized to the chloro ketone *syn*-7-chloro-2-norbornanone-*endo*-6-*d* and deuterium assay by mass spectrometry revealed 3% d_o, 95% d_1, 2% d_2 species (av 0.99 *d*/molecule).

d) *Syn*-7-chloro-*exo*-2-norbornyl brosylate-*endo*-6-*d* (59-OBs-*endo*-6-*d*)

Chloro brosylate 59-OBs-*endo*-6-*d* had the following properties: mp 112-112.5°; ir (CS_2) 1360, 1310, 1190(s), 1100, 1070, 1040, 1015, 970, 935, 890, 870, 820, 775(s), 635, 610, 595, 550; nmr (CCl_4, 100 MHz) δ 7.68 (m, 4H, arom), 4.60 (m,1H, *endo*-C-2), 3.79 (broad s, 1H, *anti*-C-7), 2.50 and 2.30 (broad s, each 1H, bridgeheads), 2.20-1.05 (m, 5H, norbornyl envelope).

e) *Syn*-7-chloro-*exo*-2-norbornanol-*exo*,*exo*-5,6-d_2 (59-OH-*exo*,*exo*-5,6-d_2)

The addition of hypochlorous acid to norbornene-*endo*,*endo*-5,6-d_2 (87-*endo*,*endo*-5,6-d_2) yielded *syn*-7-chloro-*exo*-2-norbornanol-*exo*,*exo*-5,6-d_2 (59-OH-*exo*,*exo*-5,6-d_2) as one of the products.

Norbornene-*endo*,*endo*-5,6-d_2 (87-*endo*,*endo*-5,6-d_2)

i) Norbornene-*exo*,*exo*-5,6-d_2 (87-*exo*,*exo*-5,6-d_2)

Norbornadiene (Frinton Chemicals Ltd, 50.0 gm, 0.54 mol) was dissolved in methanol (75 ml) and 3 gm of palladium on powdered

charcoal (10% catalyst) was added to the solution. The mixture was reduced with deuterium gas (13.2 litres, 0.54 mol, C.P. Grade, Matheson) at *ca* 1.0 atm.[211] Another similar run was performed; the mixtures were combined and filtered. Water (300 ml) was added and the products were extracted into pentane (3x300 ml). After the extracts were washed with water (2x50 ml) and then dried, the organic solvent was removed by distillation through a 71 cm glass column filled with glass helices. Short path distillation of the products into a flask cooled in solid carbon dioxide yielded 100 gm of material. Analytical glpc (5% SE-30, 60°) showed that the reaction mixture consisted of 12% norbornadiene, 71% norbornene-*exo*,*exo*-5,6-d_2 and 17% norbornane-*exo*,*exo*,*exo'*,*exo'*-2,3,5,6-d_4.

ii) *Syn*-7-*exo*-2-dibromonorbornane-*endo*,*endo*-5,6-d_2 (88-*endo*,*endo*-5,6-d_2)

To 100 gm of the mixture containing 71% norbornene-*exo*,*exo*-5,6-d_2 (87-*exo*,*exo*-5,6-d_2) in methylene chloride (300 ml) and pyridine (70 ml) cooled in an ice-water bath, was slowly added bromine (161 gm, 1.0 mol) in methylene chloride (50 ml) over a period of three hours. After the addition was complete, the organic layer was washed with dilute sodium thiosulphate solution (2x100 ml), water (2x100 ml), dilute hydrochloric acid (10%, 2x70 ml), saturated sodium bicarbonate solution (100 ml) and water (2x100 ml). The organic layer was dried and methylene chloride was removed by distillation through a 30 cm glass column filled with glass helices. Distillation of the pot residue through a 30 cm vacuum jacketed Vigreux column

afforded 24 gm of deuterated 3-bromonortricyclene (bp 48-50°(6 mm)) and 53.2 gm of *syn*-7-*exo*-2-dibromonorbornane-*endo*,*endo*-5,6-d_2 (88-*endo*, *endo*-5,6-d_2): bp 80-85°(0.7 mm), {lit[253] bp 70-74°(0.25-0.30 mm)}. Redistillation of this last fraction afforded 42.0 gm of the dibromide 88-*endo*,*endo*-5,6-d_2: bp 80-83°(0.7 mm); nmr (CCl_4, 100 MHz) δ 3.90 (m, 2H, *anti*-C-7 and *endo*-C-2), 2.70-2.10 (m, 4H, *exo*-C-3, *endo*-C-3, C-1 and C-4), 1.65 (broad s, 2H, *exo*-C-5 and *exo*-C-6). Isomerization of 88 occurs during analysis by glpc unless the injector and detector block temperatures are kept below 160°.

iii) *Syn*-7-bromonorbornene-*endo*,*endo*-5,6-d_2 (89-*endo*,*endo*-5,6-d_2)

Syn-7-*exo*-2-dibromonorbornane-*endo*,*endo*-5,6-d_2 (35.6 gm, 139 mmol) was dissolved in a saturated solution of potassium *t*-butoxide in *t*-butanol (1M, 350 ml) and the mixture was refluxed for 33 hr on a steam bath.[212] The brown solution was poured into water (350 ml) and extracted with pentane (3x300 ml). After the extracts were washed with water (150 ml), dilute hydrochloric acid (10%, 100 ml), saturated sodium bicarbonate solution (100 ml), water (2x100 ml) and dried, pentane was removed by distillation through a 30 cm Vigreux column. The brown oily residue which remained was distilled under reduced pressure to yield 17.0 gm (70%) of *syn*-7-bromonorbornene-*endo*,*endo*-5,6-d_2 (89-*endo*,*endo*-5,6-d_2): bp 67-68°(20 mm) {lit[253] bp 68-70°(13 mm)}; nmr (CCl_4, 100 MHz) δ 5.95 (s with fine structure, 2H, C-2 and C-3), 3.79 (s, 1H, *anti*-C-7), 2.95 (m, 2H, C-1 and C-4), 1.72 (broad s, 2H, *exo*-C-5 and *exo*-C-6), 1.10 (m, 0.08H, *endo*-C-5 and *endo*-C-6). The integrals showed that the deuterium at C-5 and C-6 was at least 92% stereochemically pure *endo*.

iv) Norbornene-*endo*,*endo*-5,6-d_2 (87-*endo*,*endo*-5,6-d_2)

Syn-7-bromonorbornene-*endo*,*endo*-5,6-d_2 (17.0 gm, 97 mmol) and tri-*n*-butyl tin hydride[213] (85.9 gm, 0.30 mol) were sealed in a thick walled glass tube under vacuum. After being heated over a steam bath for 36 hr, the tube was opened and its contents were poured into a 250 ml three necked flask which was connected to three gas dispersion bottles. The first bottle was empty, the second contained water and the third contained sodium hydroxide pellets. The flask was heated gently with a hair dryer and nitrogen gas was bubbled directly through the reaction mixture. At the end of the three gas dispersion bottles, 7.0 gm (75%) of norbornene-*endo*,*endo*-5,6-d_2 (87-*endo*,*endo*-5,6-d_2) were collected in a receiver cooled in solid carbon dioxide. The nmr spectrum of 87-*endo*,*endo*-5,6-d_2 was identical to that which has been reported.[212] nmr (CCl_4, 100 MHz) δ 5.90 (t, 2H, C-2 and C-3), 2.80 (m, 2H, C-1 and C-4), 1.55 (broad s with fine structure, 2H, *exo*-C-5 and *exo*-C-6), 1.31 and 1.04 (d with fine structure, each 1H, J = *ca* 8 Hz, *syn*-C-7 and *anti*-C-7). Mass spectral analysis for deuterium revealed 3% d_o, 4% d_1, 93% d_2 species (av 1.90 *d*/molecule).

v) Addition of hypochlorous acid to norbornene-*endo*,*endo*-5,6-d_2

Hypochlorous acid {hydrochloric acid (10%,10 ml) and sodium hypochlorite (40 ml)} was vigorously stirred with norbornene-*endo*,*endo*-5,6-d_2 (0.74 gm, 8.0 mmol) at 0° for 24 hr.[178] Deuterated 3-chloronortricyclene and *syn*-7-chloro-*exo*-2-norbornanol-*exo*,*exo*-5,6-d_2 59-OH-*exo*,*exo*-5,6-d_2) were the major products as determined by glpc.

Deuterated 3-chloronortricyclene was a composite of 5% d_0, 35% d_1, 61% $d_2$species (av 1.57 *d*/molecule) as determined mass spectrometrically. This represents a 35% fractional percent loss of deuterium. The chloro alcohol 59-OH-*exo*,*exo*-5,6-d_2 was isolated by prep glpc (15% FFAP, 150°): nmr (CS_2, 100 MHz, Figure 6:8, Chapter 6) δ 3.85 (m, 1H, *anti*-C-7), 3.62 (broad m, 1H, *endo*-C-2), 2.30 (d, 1H, C-4), 2.25 (broad s, 1H, C-1), 2.00 (broad s, 1H, -OH), 1.90 (m, 2H, *exo*-C-3 and *endo*-C-3), 1.11 (broad s with fine structure, 2H, *endo*-C-5 and *endo*-C-6). Mass spectrometric deuterium assay on the corresponding chloro ketone (*syn*-7-chloro-2-norbornanone-*exo*,*exo*-5,6-d_2) showed 5% d_0, 6% d_1, 89% d_2 species (av 1.84 *d*/molecule).

f) *Syn*-7-chloro-*exo*-2-norbornyl brosylate-*exo*,*exo*-5,6-d_2 (59-OBs-*exo*,*exo*-5,6-d_2)

Syn-7-chloro-*exo*-2-norbornyl brosylate-*exo*,*exo*-5,6-d_2 had mp 112-113°; nmr (CCl_4, 100 MHz) δ 7.64 (m, 4H, arom), 4.52 (m, 1H, *endo*-C-2), 3.75 (broad s with fine structure, 1H, *anti*-C-7), 2.43 and 2.26 (broad s, each 1H, bridgeheads), 2.15-1.70 (m, 2H, *exo*-C-3 and *endo*-C-3), 1.15 (s, 2H, *endo*-C-5 and *endo*-C-6).

2) a) *Anti*-7-chloro-*exo*-2-norbornanol (58-OH)

Anti-7-chloro-*exo*-2-norbornanol (58-OH) was prepared by one of three methods.

i) Alcohol 58-OH was prepared by treatment of norbornene (87) with hypochlorous acid as reported by Roberts[178]

ii) Alcohol 58-OH was prepared by the reduction with lithium

aluminum hydride of *anti*-7-chloro-*exo*-2-norbornyl acetate (58-OAc) which was obtained from the electrophilic (CH_3CO_2H, H_2SO_4) cleavage of 3-chloronortricyclene (*vide supra*).

iii) Hydroboration-oxidation of *anti*-7-chloronorbornene (62) gave the alcohol 58-OH.[181,182] *Anti*-7-chloronorbornene (62) was prepared by the procedure described below.

Anti-7-norbornenol (86)

To a slurry of lithium aluminum hydride (6.8 gm, 0.18 mol) and ether (50 ml) was added a solution of norbornadienyl acetate (Frinton Chemicals Ltd, 22.0 gm, 0.15 mol) dissolved in ether (90 ml). The addition was carried out under an atmosphere of nitrogen and the solution was stirred for 4 hr at room temperature. Excessive hydride was carefully destroyed by addition of wet pieces of sodium sulphate until gas was no longer evolved; the reaction mixture was allowed to stand overnight. The inorganic salts were filtered off and the ethereal layer was separated. After the aqueous layer was extracted with ether (3x200 ml), the combined ethereal layers were washed with water (2x100 ml), dried and concentrated. Ether was removed by distillation through a 30 cm glass column packed with glass helices; a white waxy solid (14.3 gm) remained.[210]

Anti-7-chloronorbornene (62)

Into a three necked flask fitted with a reflux condenser, magnetic stirrer and nitrogen inlet was placed *anti*-7-norbornenol (14.3 gm, 0.13 mol) dissolved in anhydrous ether (50 ml). To this solution was added thionyl chloride (18.5 gm, 0.16 mol) by means of a dropping funnel; after the addition was complete, the mixture was refluxed under an atmosphere of nitrogen for 1.75 hr. The mixture was washed with cold water; then the ethereal layer was dried and ether was removed by distillation through a 15 cm Vigreux column. The remaining oil (dark yellow) was distilled under reduced pressure through a 8 cm vacuum jacketed Vigreux column to yield 10.5 gm (61%) of *anti*-7-chloronorbornene (62): bp 75-80°(70 mm), {lit[182] bp 70.5-71.5°(60 mm)} whose nmr spectrum was in agreement with the published spectrum.[254]

nmr (CS_2, 100 MHz, Figure 6:13, Chapter 6) δ 6.06 (t, 2H, J = 2 Hz, C-2 and C-3), 3.62 (s, 1H, *syn*-C-7), 2.70 (m, 2H, C-1 and C-4), 2.00 (m, 2H, *exo*-C-5 and *exo*-C-6), 1.04 (m, 2H, *endo*-C-5 and *endo*-C-6).

Hydroboration-oxidation of *anti*-7-chloronorbornene (62)

Anti-7-chloronorbornene was hydroborated and then the organoborane was treated with alkaline hydrogen peroxide according to the published procedure[181] to give a 95% yield of *anti*-7-chloro-*exo*-2-norbornanol (58-OH). The product was shown to be homogeneous by means of

glpc (3% GE-XF1150, 155°) as well as by nmr spectroscopy (Figure 6:2, Chapter 6).

b) *Anti*-7-chloro-*exo*-2-norbornyl brosylate (58-OBs)

Anti-7-chloro-*exo*-2-norbornyl brosylate was recrystallized from ether:petroleum ether 30-60° (1:2) and had mp 69.5-71.0°; ir (CS_2) 1375, 1190(s), 1180, 1100, 1075, 1065, 1015, 970, 940, 920, 890, 870, 825, 780, 605, 550; nmr (CCl_4, 100 MHz) δ 7.75 (m, 4H, arom), 4.47 (m, 1H, *endo*-C-2), 4.16 (broad s, 1H, *syn*-C-7), 2.42 and 2.30 (broad s, each 1H, bridgeheads), 2.05-1.60 and 1.20 (m, 6H, norbornyl envelope).

Anal: Calc'd for $C_{13}H_{14}SO_3Br$: C, 42.69; H, 3.83
Found C, 42.72, H, 3.88.

c) *Anti*-7-chloro-*exo*-2-norbornanol-*endo*-6-*d* (58-OH-*endo*-6-*d*)

Reduction with lithium aluminum hydride of *anti*-7-chloro-*exo*-2-norbornyl trideuteroacetate-*endo*-6-*d*, which was obtained from the electrophilic (CD_3CO_2D, D_2SO_4) cleavage of 3-chloronortricyclene (*vide supra*), gave *anti*-7-chloro-*exo*-2-norbornanol-*endo*-6-*d*: ir (CS_2) 3600 (free OH), 3650-3100 (hydrogen bonded OH), 1310, 1280, 1265, 1225, 1085, 1070, 1030, 995, 940, 910, 870, 850, 815, 805, 785, 700; nmr (CCl_4, 100 MHz, Figure 6:5, Chapter 6) δ 4.18 (s with fine structure, 1H, *syn*-C-7), 3.75 (d of d, 1H, J= 7.5 and 2.5 Hz, *endo*-C-2), 2.23 and 2.11 (broad s, each 1H, bridgeheads), 2.00-1.00 (m, 6H, norbornyl envelope and -OH). A small sample of 59-OH-*endo*-6-*d* was oxidized to *anti*-7-chloro-2-norbornanone-*endo*-6-*d* and deuterium assay by mass spectrometry revealed 4% d_o, 95% d_1, 1% d_2 species (av 0.97 d/molecule).

d) *Anti*-7-chloro-*exo*-2-norbornyl brosylate-*endo*-6-*d* (58-OBs-*endo*-6-*d*)

Chloro brosylate 58-OBs-*endo*-6-*d* had the following properties: mp 72°; ir (CS_2) 1320, 1310, 1190(s), 1100, 1070, 1055, 1015, 980, 965, 935, 915, 890, 870(s), 825, 790, 740, 700, 640, 625, 605, 550; nmr (CCl_4, 100 MHz) δ 7.76 (s, 4H, arom), 4.46 (m, 1H, *endo*-C-2), 4.15 (s, 1H, *syn*-C-7), 2.40 and 2.30 (broad s, each 1H, bridgeheads), 2.00-1.79 and 1.15 (m, 5H, norbornyl envelope).

e) *Anti*-7-chloro-*exo*-2-norbornanol-*exo*,*exo*-5,6-d_2 (58-OH-*exo*,*exo*-5,6-d_2)

i) *Anti*-7-norbornenol-*exo*,*exo*-5,6-d_2 (86-*exo*,*exo*-5,6-d_2)

7-Acetoxynorbornadiene (20 gm, 0.13 mol) was treated with lithium aluminum deuteride (Ventron, 6.0 gm, 0.14 mol) in dry ether (125 ml) for 4.5 hr at room temperature under an atmosphere of nitrogen (*vide supra*). A paste of sodium sulphate (dried at 150° for 3 days) and deuterium oxide (Merck, Sharp and Dohme of Canada Ltd, 99.7 atom %*d*) was carefully added to the reaction mixture until gas was no longer evolved. The mixture was stirred overnight (13 hr) and then the inorganic salts were filtered off. The ethereal layer was separated and the aqueous phase was extracted with ether. After the combined organic layers were washed with water, solvent was removed by distillation through a 30 cm glass column filled with glass helices to leave *anti*-7-norbornenol-*exo*,*exo*-5,6-d_2 (86-*exo*,*exo*-5,6-d_2).[209]

ii) *Anti*-7-chloronorbornene-*exo*,*exo*-5,6-d_2 (62-*exo*,*exo*-5,6-d_2)

Anti-7-chloronorbornene-*exo*,*exo*-5,6-d_2 was prepared in 50% yield by treatment of *anti*-7-norbornenol-*exo*, *exo*-5,6-d_2 with thionyl chloride according to the literature method[182] (*vide supra*): nmr (CCl_4, 100 MHz, Figure 6:6, Chapter 6) δ 6.00 (t, 2H, *J*=2 Hz, C-2 and C-3), 3.67 (s with fine structure, 1H, *syn*-C-7), 2.70 (m, 2H, C-1 and C-4), 2.00 (m, 0.12 H, *exo*-C-5 and *exo*-C-6), 0.98 (s, 2H, *endo*-C-5 and *endo*-C-6). The integrals showed that deuterium at C-5 and C-6 was at least 93% stereochemically pure *exo*. Deuterium assay by mass spectrometry showed that 62-*exo*,*exo*-5,6-d_2 was a composite of 7% d_o, 3% d_1, 90% d_2 species (av 1.83 *d*/molecule).

iii) Hydroboration-oxidation of *anti*-7-chloronorbornene-*exo*, *exo*-5,6-d_2

Hydroboration of *anti*-7-chloronorbornene-*exo*,*exo*-5,6-d_2 with subsequent oxidation by alkaline hydrogen peroxide[181] gave a 90% yield of *anti*-7-chloro-*exo*-2-norbornanol-*exo*, *exo*-5,6-d_2 (58-OH-*exo*,*exo*-5,6-d_2) which was purified by prep glpc (25% GE XF-1150, 180°): nmr (CCl_4, 100 MHz, Figure 6:7, Chapter 6) δ 4.16 (broad s with fine structure, 1H, *syn*-C-7), 3.75 (d of d, 1H, *J*=7 and 3 Hz, *endo*-C-2), 2.24 (d, 1H, *J*=*ca* 4 Hz, C-4), 2.11 (broad s, 1H, C-1), 2.06 (s, 1H, -OH), 1.75 (d of d, 1H, *J*=7 and 13 Hz, *endo*-C-3),

1.40 (d of t, 1H, J=3 and 13 Hz, *exo*-C-3), 1.05 (broad s, 2H, *endo*-C-5 and *endo*-C-6).

f) *Anti*-7-chloro-*exo*-2-norbornyl brosylate-*exo*,*exo*-5,6-d_2 (58-OBs-*exo*,*exo*-5,6-d_2)

Anti-7-chloro-*exo*-2-norbornyl brosylate-*exo*,*exo*-5,6-d_2 was recrystallized from ether-petroleum ether 30-60° (1:2). It had the following properties: mp 69-70°; nmr (CCl_4, 100 MHz) δ 7.65 (s, 4H, arom), 4.45 (d of d, 1H, J=4 and 6 Hz, *endo*-C-2), 4.10 (broad s with fine structure, 1H, *syn*-C-7), 2.39 (broad s, 1H, C-1), 2.27 (m, 1H, C-4), 1.75 (m, 2H, *exo*-C-3 and *endo*-C-3), 1.11 (s, 2H, *endo*-C-5 and *endo*-C-6).

g) *Anti*-7-chloro-*exo*-2-norbornanol-*exo*-3-*d* (58-OH-*exo*-3-*d*)

Into a three necked flask fitted with a magnetic stirrer, condenser, addition funnel, drying tube and nitrogen inlet were placed *anti*-7-chloronorbornene (2.0 gm, 16 mmol), diglyme (7 ml, distilled from lithium aluminum hydride) and sodium borodeuteride (Ventron, 0.34 gm, 8 mmol). Freshly distilled boron trifluoride etherate (1.4 gm, 10 mmol) dissolved in diglyme (6 ml) was slowly added to the flask[181,185] at room temperature and then the mixture was stirred for 3 hr. Water was added to the reaction mixture followed by sodium hydroxide (3N, 7 ml) and hydrogen peroxide (33%, 7 ml). After the mixture was stirred for 14 hr, the products were extracted into ether. A 90% yield of *anti*-7-chloro-*exo*-2-norbornanol-*exo*-3-*d* was obtained: nmr (CCl_4, 100 MHz, Figure 6:10, Chapter 6) δ 4.19 (broad s, 1H, *syn*-C-7), 3.77 (d, 1H, J=7 Hz, *endo*-C-2),

2.60 (broad s, 1H, -OH), 2.26 and 2.14 (broad s, each 1H, bridgeheads), 2.05-1.70 and 1.10 (m, 3H and 2H, norbornyl envelope).

The position of deuterium was verified by complexation of the chloro alcohols 58-OH and 58-OH-*exo*-3-*d* with $Eu(fod)_3$. When 134 mg of $Eu(fod)_3$ was complexed with 34 mg of *anti*-7-chloro-*exo*-2-norbornanol (58-OH) in carbon tetrachloride (*ca* 0.5 ml), nmr analysis revealed that most of the proton resonances were resolved from each other: nmr (CCl_4, 100 MHz, Figure 6:11, Chapter 6) δ 16.90 (d, 1H, *J*=7 Hz, *endo*-C-2), 12.40 (s, 1H, *syn*-C-7), 10.84 (broad d with fine structure, 1H, *J*=14 Hz, *exo*-C-3), 10.25 (broad s, 1H, C-1), 6.38 (d of d, 1H, *J*=7 and 14 Hz, *endo*-C-3), 5.10 (broad s, 1H, C-4), 3.80-3.00 (m, 4H, C-5 and C-6). Complexation of *anti*-7-chloro-*exo*-2-norbornanol-*exo*-3-*d* (37 mg) with $Eu(fod)_3$ (160 mg) in carbon tetrachloride (*ca* 0.5 ml) ie mole ratio LSR/alcohol = 0.61 and subsequent analysis by nmr spectroscopy revealed that the proton at *exo*-C-3 (δ 11.20) had disappeared: nmr (CCl_4, 100 MHz, Figure 6:12, Chapter 6) δ 17.90 (d, 1H, *J*=7 Hz, *endo*-C-2), 12.90 (s, 1H, *syn*-C-7), 10.80 (broad s, 1H, C-1), 6.60 (d, 1H, *J*=7 Hz, *endo*-C-3), 5.17 (broad s, 1H, C-4), 4.00-3.00 (m, 4H, C-5 and C-6). Notably, the resonance due to the proton at *endo*-C-3 (δ 6.60) appeared as a doublet due to loss of geminal coupling with the proton at *exo*-C-3.

A small sample of *anti*-7-chloro-*exo*-2-norbornanol-*exo*-3-*d* was oxidized to *anti*-7-chloro-2-norbornanone-*exo*-3-*d* and deuterium assay by mass spectrometry showed 7% d_0, 93% d_1 species (av 0.93 *d*/molecule).

h) *Anti*-7-chloro-*exo*-2-norbornyl brosylate-*exo*-3-*d* (58-OBs-*exo*-3-*d*)

Chloro brosylate 58-OBs-*exo*-3-*d* had the following properties: mp 70-71°; nmr (CCl_4, 100 MHz) δ 7.70 (s, 4H, arom), 4.45 (d, 1H, J=7 Hz, *endo*-C-2), 4.13 (broad s, 1H, *syn*-C-7), 2.41 and 2.29 (broad s, each 1H, bridgeheads), 2.15-1.80 (m, 3H, *exo*-C-5, *exo*-C-6 and *endo*-C-3), 1.15 (m, 2H, *endo*-C-5 and *endo*-C-6).

3) a) *Anti*-7-chloro-*endo*-2-norbornanol (84-OH)
Anti-7-chloro-2-norbornanone (63)

The chloro ketone 63 was obtained as described in the section of this chapter dealing with the electrophilic (CH_3CO_2H,H_2SO_4) cleavage of 3-chloronortricyclene.

Reduction with lithium tri-*t*-butoxyaluminum hydride of *anti*-7-chloro-2-norbornanone (63)

Anti-7-chloro-2-norbornanone (0.61 gm, 4 mmol) in tetrahydrofuran (20 ml) was added to a stirred solution of lithium tri-*t*-butoxyaluminum hydride (1.3 gm, 5 mmol) and tetrahydrofuran (15 ml). The yellow solution was refluxed and after 7.5 hr it was estimated by analytical glpc that the reaction was >95% complete. Water (50 ml) and dilute hydrochloric acid (10%, 20 ml) were added to the reaction mixture and then the products were extracted into ether (4x50 ml). The combined ethereal extracts were washed with water (50 ml), saturated bicarbonate solution (50 ml), water (50 ml) and then dried. Evaporation of solvent under reduced pressure left a white solid (0.56 gm). Analytical glpc

(3% GE XF-1150, 155°) revealed that there was 92% *anti*-7-chloro-*endo*-2-norbornanol (84-OH) and 8% *anti*-7-chloro-*exo*-2-norbornanol (58-OH). When the chromatographic analysis was carried out using a different column (15% Carbowax, 185°), the ratio of 84-OH to 58-OH was about 85:15. By prep glpc (25% GE XF-1150, 160°) it was possible to obtain a pure sample of *anti*-7-chloro-*endo*-2-norbornanol: mp 83-84° (lit[176] 84-86°); nmr (CCl_4, 100 MHz, Figure 6:4, Chapter 6) δ 4.00 (quintet with fine structure, 1H, *exo*-C-2), 3.70 (broad s with fine structure, 1H, *syn*-C-7), 2.83 (s, 1H, -OH), 2.25-0.85 (m, 8H, norbornyl envelope).

When the reduction was carried out with lithium trimethoxyaluminum hydride, the ratio of 84-OH to 58-OH was 92:8 as determined by analytical glpc (3% GE XF-1150, 155°).

b) *Anti*-7-chloro-*endo*-2-norbornyl brosylate (84-OBs)

Chloro brosylate 84-OBs was purified by recrystallization from ether-petroleum ether 30-60° (1:2) and had mp 49-51°: nmr (CCl_4, 100 MHz) δ 7.70 (m, 4H, arom), 4.75 (quintet with fine structure, 1H, *exo*-C-2), 3.80 (broad s, 1H, *syn*-C-7), 2.50-1.20 (m, 8H, norbornyl envelope). It was shown by nmr spectroscopy that 84-OBs was not contaminated with 58-OBs.

Anal: Calc'd for $C_{13}H_{14}SO_3Br$: C, 42.69; H, 3.83
Found: C, 42.83; H, 3.79

c) *Anti*-7-chloro-*endo*-2-norbornanol-*endo*-6-*d* (84-OH-*endo*-6-*d*)

Anti-7-chloro-2-norbornanone-*endo*-6-*d* (63-*endo*-6-*d*)

Chloro ketone 63-*endo*-6-*d* was obtained as described in the section of this chapter dealing with the electrophilic (CD_3CO_2D,D_2SO_4)

cleavage of 3-chloronortricyclene and by mass spectrometry it was found to be a composite of 4% d_0, 95% d_1, 1% d_2 species (av 0.97 d/molecule).

Reduction of *anti*-7-chloro-2-norbornanone-*endo*-6-*d* (63-*endo*-6-*d*) with lithium tri-*t*-butoxyaluminum hydride

Chloro ketone 63-*endo*-6-*d* was reduced by the similar procedure used for the reduction of the non-deuterated chloro ketone 63 (*vide supra*). A pure sample of *anti*-7-chloro-*endo*-2-norbornanol-*endo*-6-*d* was isolated by prep glpc (25% GE XF-1150, 160°): nmr (CCl_4, 100 MHz, Figure 6:9, Chapter 6) δ 4.00 (quintet with fine structure, 1H, *exo*-C-2), 3.70 (broad s with fine structure, 1H, *syn*-C-7), 2.52 (s, 1H, -OH), 2.20-0.85 (m, 7H, norbornyl envelope).

d) *Anti*-7-chloro-*endo*-2-norbornyl brosylate-*endo*-6-*d* (84-OBs-*endo*-6-*d*)

The chloro brosylate 84-OBs-*endo*-6-*d* had mp 48-50°: nmr (CCl_4, 100 MHz), δ 7.70 (m, 4H, arom) 4.75 (quintet with fine structure, 1H, *exo*-C-2), 3.80 (s, 1H, *syn*-C-7), 2.50-1.25 (m, 7H, norbornyl envelope).

4) 1-Methyl-*exo*-2-norbornanol-*exo*,*exo*-5,6-d_2 (80-OH-*exo*,*exo*-5,6-d_2)

Hydroboration-oxidation[185] of norbornene-*endo*,*endo*-5,6-d_2[212] gave *exo*-2-norbornanol-*endo*,*endo*-5,6-d_2 which was oxidized[183] to 2-norbornanone-*endo*,*endo*-5,6-d_2. This ketone was converted to *exo*-2-methyl-*endo*-2-norbornanol-*endo*,*endo*-5,6-d_2 by treatment with methyl magnesium iodide[41] and then this alcohol was rearranged in sulphuric

acid and acetic acid[41] to deuterated 1-methyl-*exo*-2-norbornyl acetate. Hydrolysis of the acetate with methanolic potassium hydroxide gave deuterated 1-methyl-*exo*-2-norbornanol. Nmr spectroscopy showed about 30% deuterium at *endo*-C-2. This probably arises *via* a 2,6-*endo*, *endo*-hydride shift during the rearrangement of deuterated *exo*-2-methyl-*endo*-2-norbornanol to 1-methyl-*exo*-2-norbornanol (Scheme 2:6 and 2:7, Chapter 2): nmr (CCl_4, 100 MHz) δ 3.38 (d, 0.70 H, J=*ca* 7 Hz, *endo*-C-2).

D. KINETICS

1) Solvent

The solvolytic reactions were carried out in 80:20 ethanol-water (v/v before mixing) containing 0.04 M sodium acetate. Water was refluxed in potassium permanganate for several hours and then distilled five times. Ethanol was purified by two distillations. An ultraviolet spectrum of the solvent mixture did not reveal any interfering absorptions.

2) General procedure for kinetic runs

Solvolytic isotope effects were obtained by simultaneously observing the solvolyses of the non-deuterated and deuterated substrates spectrophotometrically[218] in a Cary Spectrophotometer Model 14. By circulating water from a Haake Model NBe bath through the thermostattable cell compartment, the desired temperature and temperature control were achieved during the reaction. The water bath specifications claim temperature control to be $\pm 0.01^{\circ}$. Inside the actual cell compartment of the spectrophotometer, the sample cells as well as several Pasteur pipettes

(wrapped with aluminum foil) were allowed to equilibrate for at least ten hours with the temperature of the circulating water. Generally, the actual temperature within the cell compartment was about 3-5° lower than that of the water bath. Before a solvolysis reaction was performed, the appropriate chloro brosylates were purified by recrystallization to constant melting point and then dried under vacuum (*ca* 1 mm) at room temperature for 0.5 hr. The brosylates (2-3 mg) were weighed into 2 ml volumetric flasks and then allowed to equilibrate in the water bath for 0.5 hr. Another flask containing about 20 ml of the ethanol-water solution was also allowed to come into thermal equilibrium with the temperature of the circulant.

Solvent (*ca* 3 ml) was rapidly transferred into the volumetric flasks containing the brosylates, then the flasks were vigorously shaken in order to ensure complete solution and they were allowed to equilibrate in the water bath for 5 minutes. The solutions were rapidly transferred, with insulated Pasteur pipettes, to the 1.00 cm cells in the cell compartment. After ten minutes, readings were taken at an absorbance maximum at 5, 10 and 20 minute intervals by running the pen and chart paper from 10 seconds before to 10 seconds after the minute. The slit controls were shut off to avoid fluctuations. Absorbance readings were taken for at least three half-lives. A check of the zero reading on the instrument after the infinity reading was taken (*ca* 24 hr) revealed a negligible baseline drift of less than ±0.003 of an absorbance unit from the original zero. The graphs of $-\ln(A_t-A_\infty)$ vs time* which usually

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* A_t = absorbance at time t

A_∞ = absorbance at time ∞ (*ca* 10 half-lives)

consisted of 20-30 sets of data points were analyzed on an IBM CDC6400 computer for slopes and standard deviation in the slopes by a least squares program. A copy of this program appears in Chapter 6. Slopes from the $-\ln(A_t-A_\infty)$ vs time graphs gave the first-order rate constants for the solvolysis reactions. Derivation of this relationship appears in Chapter 6.

Changes in absorbance as a function of time were monitored for *anti*-7-chloro-*exo*-2-norbornyl brosylate (58-OBs) at 276.4 nm and for *syn*-7-chloro-*exo*-2-norbornyl brosylate (59-OBs) at 264.9 nm.

Runs on deuterated material were performed only after control runs with non-deuterated brosylates showed that a ratio of the rate constants between 0.99±0.01 to 1.01±0.01 was routinely obtainable. Corrections due to incomplete deuteration were usually small because of the high degree of deuterium incorporation in the compounds.

The kinetic runs for non-deuterated and deuterated *syn*-7-chloro-*exo*-2-norbornyl brosylate were carried out at a cell temperature of *ca* 50°. Half-lives were generally 50-60 minutes. For *anti*-7-chloro-*exo*-2-norbornyl brosylates, the solvolyses were performed at *ca* 60° with a half-life of 35-40 minutes. A complete tabulation of rate constants along with sample calculations appears in Chapter 6.

The kinetic procedure for *anti*-7-chloro-*endo*-2-norbornyl brosylate was slightly different from that described above. Water at 80° was circulated through thermostattable cell adapters (Varian Instruments, Part No. 1444300, ±0.03° at ambient temperatures from -10° to 40°) and the thermostattable cell compartment was kept at 71° with

water from a Haake Model NBe circulating bath. Absorbance readings (266.0 nm) were taken as a function of time for about 36 hr at approximately 4-6 hr intervals and 9-10 points were used to determine the first-order reaction rate constant. Since the half-life of the solvolytic reaction was about 12 hr, A_∞ and the rate constant (k) were calculated from the (A_t, t) readings by a computer program written especially for the IBM CDC 6400.[219] The data were fitted to an equation of the form $A_t = ce^{-kt}+d$ where A_t = absorbance at time t, k = first-order rate constant and c,d = constants. A copy of this program appears in Chapter 6. To check the accuracy of this program, all the solvolytic data for *anti*- and *syn*-7-chloro-*exo*-2-norbornyl brosylates were analyzed by this method *ie* for a given set of (A_t, t) readings, the best A_∞ and k were calculated. Excellent agreement between calculated and experimental A_∞ was found in all cases. There was also excellent agreement between the calculated and experimental rate constants (k).

3) Product analysis

a) Identification

Syn-7-chloro-*exo*-2-norbornyl brosylate (5.5 gm) and buffered ethanol-water solvent (75 ml) were magnetically stirred in a round bottomed flask and heated with an oil bath at 56±2° for 36 hr. All the brosylate dissolved after several hours. After the reaction mixture cooled to room temperature, it was extracted with pentane (3x200 ml). Water (700 ml) was added to the aqueous layer and further extractions with ether (3x250 ml) were carried out. The pentane and ether extracts were combined and washed with water (2x100 ml), saturated

bicarbonate solution (2x100 ml), water (2x150 ml) and then dried. After the solvent was removed under reduced pressure, a yellow residue remained which was found by analytical glpc (10% Carbowax, 170°) to contain five major products. Each product was collected by prep glpc (15% FFAP, 175°). In order of increasing retention time, the products were identified as the following: 3-chloronortricyclene (24), *anti*-7-chloro-*exo*-2-norbornyl ethyl ether (58-OEt), *syn*-7-chloro-*exo*-2-norbornyl ethyl ether (59-OEt), *syn*-7-chloro-*exo*-2-norbornanol (59-OH) and *anti*-7-chloro-*exo*-2-norbornanol (58-OH). Except for 58-OEt, the identities of the compounds were ascertained by comparison of spectral data (ir, nmr) to those from authentic samples. Careful analysis of the nmr spectrum of 24 revealed that chloronorbornenes (products from 1,2 elimination) were not present. From past experience it was known that 3-chloronortricyclene and the isomeric chloronorbornenes such as *anti*-7-chloronorbornene (62) or *exo*-5-chloronorbornene (67) have similar retention times under the chromatographic conditions described above. When the fourth product *ie* *syn*-7-chloro-*exo*-2-norbornanol (59-OH) was subjected to analytical glpc (10% Carbowax, 175°), the peak due to the above compound had an appreciable "shoulder". A small portion of this sample was oxidized as previously described to the corresponding chloro ketones. By comparison of retention times, it was shown with analytical glpc (10% Carbowax, 145°) that the "contaminant" was *exo*-3-chloro-2-norbornanone (73). The relative ratio of *syn*-7-chloro-2-norbornanone (64) to *exo*-3-chloro-2-norbornanone (73) was determined to be 90:10. This establishes that the solvolysis of *syn*-7-chloro-*exo*-2-norbornyl brosylate yields small amounts of *exo*-3-chloro-*exo*-2-norbornanol (71-OH) and this

demands that *exo*-3-chloro-*exo*-2-norbornyl ethyl ether (71-OEt) also be formed during the reaction. Likely, the retention time of 71-OEt is similar to that of either 58- or 59-OEt. It is conceivable that 5-10% 71-OEt would not be detected in the nmr spectrum of 58- or 59-OEt.

The products from solvolysis of *anti*-7-chloro-*exo*-2-norbornyl brosylate (58-OBs) were identical to those obtained from 59-OBs.[176]

For solvolysis of 84-OBs, product identification and relative ratios were not obtained. Since 84-OBs is unstable with respect to analysis by glpc, it was necessary to heat the solutions from the kinetic runs in sealed glass tubes at $80^{\circ}\pm4^{\circ}$ for 8 days in order that the reaction go to about 99% completion. Upon workup (*vide supra*) of the mixtures, analytical glpc (15% Carbowax, 130°) showed that the five expected products (3-chloronortricyclene, *anti*- and *syn*-7-chloro-*exo*-2-norbornyl ethyl ethers and *anti*- and *syn*-7-chloro-*exo*-2-norbornanol) were not present. There appeared to be only one major product (rt 6 min) which did not have retention time similar to that of 3-hydroxynortricyclene. Under these conditions, the primary reaction products probably underwent fragmentation (*via* solvolysis of chlorine) to yield cyclopentenyl compounds. At present, this proposal cannot be verified.

b) *Syn*-7-chloro-*exo*-2-norbornyl ethyl ether (59-OEt)

Syn-7-chloro-*exo*-2-norbornanol (100 mg, 0.7 mmol) was dissolved in methylene chloride (3 ml) in a round-bottomed flask fitted with a nitrogen inlet and a calcium chloride drying tube. The system was flushed with nitrogen for 15 min. To this solution was added about 120 mg of triethyloxonium fluoroborate and the mixture was magnetically stirred for 24 hr at 25°. After this time, water (10 ml) was added and the solution

was extracted with methylene chloride (3x15 ml). The combined extracts were washed with water (2x10 ml) and then dried. After the solution was concentrated under reduced pressure, analytical glpc (15% FFAP, 190°) showed one major product and one minor product with retention time similar to that of solvent. The major product was isolated by prep glpc (15% FFAP, 175°) as a clear liquid and it was identified as *syn*-7-chloro-*exo*-2-norbornyl ethyl ether (59-OEt): ir (CS_2) 1350, 1320, 1310, 1265, 1245, 1190, 1115(s), 1070, 860, 830, 695; nmr (CS_2, 100 MHz) δ 3.72 (s with fine structure, 1H, *anti*-C-7), 3.32 (m, 3H, *endo*-C-2 and $-CH_2-$), 2.33 and 2.30 (broad s, each 1H, bridgeheads), 2.12-1.02 (m, 6H, norbornyl envelope), 1.09 (t, 3H, J=8 Hz, $-CH_3$).

c) *Anti*-7-chloro-*exo*-2-norbornyl ethyl ether (58-OEt)

An authentic sample of this ether was not synthesized, however the spectral data obtained from the sample isolated from the solvolysis reaction are as follows: ir (CS_2) 1320, 1245, 1170, 1100(s), 1060, 860, 690; nmr (CS_2, 100 MHz) δ 4.02 (s, 1H, *syn*-C-7), 3.30 (m, 3H, *endo*-C-2 and $-CH_2-$), 2.23 and 2.12 (broad s, each 1H, bridgeheads), 1.90-0.90 (m, 6H, norbornyl envelope), 1.09 (t, 3H, J=8 Hz, $-CH_3$).

d) Product ratios from solvolytic reactions

Determination of the relative product ratios was carried out by the following typical procedure. Measurement of the γ-KIE for ethanolysis of *syn*-7-chloro-*exo*-2-norbornyl brosylate-*endo*-6-*d* (59-OBs-*endo*-6-*d*) involved four control runs (non-deuterated *vs* non-deuterated) and three non-control runs (non-deuterated *vs* deuterated) as shown in Table 6:5 of

Chapter 6. Therefore, the solutions (from a total of 7 cells) containing products from solvolysis of non-deuterated brosylate 59-OBs were combined and similarly the solutions (from a total of 3 cells) containing products from solvolysis of deuterated brosylate 59-OBs-*endo*-6-*d* were combined.

Water (20 ml) was added to the non-deuterated mixture and then the products were extracted into ether (2x80 ml, 1x30 ml). The combined extracts were washed with water (20 ml), saturated bicarbonate solution (2x35 ml) and water (3x30 ml). After the organic layer was dried, the solvent was removed by careful distillation through a glass column (30 cm) filled with glass helices. Similarly, water (10 ml) was added to the deuterated mixture, the products were extracted with ether (2x40 ml, 1x15 ml) and then the combined extracts were washed with water (10 ml), saturated bicarbonate solution (2x20 ml) and water (3x15 ml). After being dried, the solvent was removed as described above.

Relative product ratios from non-deuterated and deuterated mixtures were determined by analytical glpc (10% Carbowax, 155°) by electronic area integration and are tabulated in Table 2:8 (Chapter 2). They represent averages of the results from 4-5 injections. Sample concentrations were usually approximately similar to each other.

e) Deuterium losses in the 1,3 elimination process

The preferred stereochemical course for formation of 3-chloronortricyclene (24) from *anti*- and *syn*-7-chloro-*exo*-2-norbornyl brosylate (58- and 59-OBs) was determined by detection of deuterium losses associated with the formation of this compound from solvolyses of

specifically deuterated 58- and 59-OBs-6-*d*.

In a typical reaction, the solution of buffered 80:20 ethanol-water (35-45 ml) was heated to $63^{\circ}\pm5^{\circ}$ (oil bath) in a round-bottomed flask equipped with a reflux condenser and a calcium chloride drying tube. The chloro brosylate (*ca* 500 mg of 58-OBs-6-*d* or *ca* 170 mg of 59-OBs-6-*d*) was added to the solution and the mixture was heated for about 40-50 hr. Workup was as previously described, however before the products were extracted into ether, a large volume of water (about 500 ml) was added to prevent miscibility problems. After removal of solvent, the total reaction mixture was subjected to prep glpc (15% Carbowax, 110°) in one injection (50 μl) and the fraction corresponding to 3-chloronortricyclene was collected in a U-shaped tube cooled in liquid nitrogen. Injection of an authentic sample containing 3-chloronortricyclene, *exo*-5-chloronorbornene and *endo*-5-chloronorbornene into the gas chromatograph under the conditions described above revealed that these compounds were separable from each other. Therefore the possibility of contamination of 3-chloronortricyclene (1,3 elimination) by isomeric chloronorbornenes (1,2 elimination) was excluded.

Deuterium assay on deuterated 3-chloronortricyclene was performed mass spectrometrically at low ionizing voltage. The results are presented in Table 2:9 (Chapter 2).

CHAPTER 6

APPENDICES

A Deuterium Assay by Mass Spectrometry

Mass spectrometric analyses for deuterium were determined on a Hitachi Perkin Elmer RMU-6A spectrometer at low voltage (13-14 eV). Isotopic distributions were calculated by comparison of relative peak heights of the unlabelled (natural abundance) and labelled species as described by Biemann.[220] Mass spectral peak intensities of selected compounds in the region of the molecular weight are tabulated in Table 6:1a. Two typical sample calculations are illustrated in Tables 6:1b and 6:1c.

Although isotopic distributions were repeatedly determined for certain deuterated compounds, in all cases the natural abundance spectrum was always recorded before the spectrum of the deuterated species was taken. It was found that the reproducibility of the relative ion intensities over long periods of time was satisfactory. Average deuterium contents, which refer to deuterium in excess of natural abundance, were determined from summation of the deuterium content of the individual species ($\%d_1 \times .01 + \%d_2 \times .02 + \%d_3 \times .03 + \ldots\ldots$). 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.[220]

Table 6:1a Relative Ion Intensities for Various Norbornyl Compounds in the Region of the Molecular Weight[a,b,c]

Compound	M^+	$M^+ + 1$	$M^+ + 2$	$M^+ + 3$
3-chloronortricyclene (24)	100.0	8.8	32.5	2.8
anti-7-chloronorbornene (62)	100.0	8.8	32.6	5.0
anti-7-chloro-*exo*-2-norbornyl acetate (58-OAc)[d]	100.0	10.9	32.9	4.0
anti-7-chloro-*exo*-2-norbornyl ethyl ether (58-OEt)[d]	100.0	17.9	34.1	6.1
anti-7-chloro-2-norbornanone (63)	100.0	8.1	32.9	3.0
syn-7-chloro-2-norbornanone (64)	100.0	8.4	32.4	2.8
exo-5-chloro-2-norbornanone (65)	100.0	8.2	32.9	3.0
endo-5-chloro-2-norbornanone (66)	100.0	9.3	33.0	3.2
1-methyl-*anti*-7-chloro-*exo*-2-norbornyl acetate (78-OAc)	100.0	12.0	32.9	4.0
1-methyl-*anti*-7-chloro-2-norbornanone (82)	100.0	9.6	32.5	3.0
1-methyl-*syn*-7-chloro-2-norbornanone (83)	100.0	9.3	33.3	3.2

[a] Determined at low ionizing voltage (13-14 eV)

[b] Average of five scans

[c] These numbers were reproducible to within 3-5% over long periods of time and with different samples of the same compound

[d] The *syn*-isomer displayed a weak molecular ion

Table 6:1b Sample calculation involving deuterium assay by mass spectrometry

Relative peak intensities (%)[a]

m/e	3-chloronortricyclene (24)	3-chloronortricyclene-*d* (24-*d*)[b]
128	100.0	100.0
129	8.8	36.6
130	32.5	35.2
131	2.8	11.9

Corrections

m/e	Uncorrected intensity of polyisotopic species	Contribution from $M^+ + 1$	Contribution from $M^+ + 2$	Contribution from $M^+ + 3$	Corrected intensity
128	100.0	-	-	-	100.0
129	36.6	(0.88)(100.0)	-	-	27.8
130	35.2	(0.88)(27.8)	(.325)(100.0)	-	0.3
131	11.9	(0.88)(0.3)	(.325)(27.8)	(.028)(100.0)	0.1

These numbers indicate 78% d_0 and 22% d_1 species or an average of 0.22 deuterium atoms per molecule.

---

a These numbers represent the average of five scans

b This compound was obtained from solvolysis of *syn*-7-chloro-*exo*-2-norbornyl brosylate-*endo*-6-*d*(59-OBs-*endo*-6-*d*)

Table 6:1c Sample calculation involving deuterium assay by mass spectrometry

Relative peak intensities (%)[a]

m/e	*anti*-7-chloronorbornene (62)	*anti*-7-chloronorbornene-*exo,exo*-5,6-d_2 (62-*exo,exo*-5,6-d_2)
128	100.0	8.0
129	8.8	4.4
130	32.6	100.0
131	5.0	10.0
132	-	32.0
133	-	3.0

Corrections

m/e	Uncorrected intensity of polyisotopic species	Contribution from $M^+ + 1$	Contribution from $M^+ + 2$	Contribution from $M^+ + 3$	Corrected intensity
128	8.0	-	-	-	8.0
129	4.4	(.088)(8.0)	-	-	3.7
130	100.0	(.088)(3.7)	(.326)(8.0)	-	97.1
131	10.0	(.088)(97.1)	(.326)(3.7)	(.05)(8.0)	-0.1
132	32.0	(.088)(0)	(.326)(97.1)	(.05)(3.7)	0.2
133	3.0	(.088)(0.2)	(.326)(0)	(.05)(97.1)	-1.9

These numbers indicate 7% d_0, 3% d_1 and 90% d_2 species (average 1.83 deuterium atoms per molecule)

[a] These numbers represent the average of five scans

B Nmr spectra of selected norbornyl compounds

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

(1) 2-methyl-3-chloronortricyclene (25)

(2) *anti*-7-chloro-*exo*-2-norbornanol (58-OH)

(3) *syn*-7-chloro-*exo*-2-norbornanol (59-OH)

(4) *anti*-7-chloro-*endo*-2-norbornanol (84-OH)

(5) *anti*-7-chloro-*exo*-2-norbornanol-*endo*-6-*d* (58-OH-*endo*-6-*d*)

(6) *anti*-7-chloronorbornene-*exo*,*exo*-5,6-d_2 (62-*exo*,*exo*-5,6-d_2)

(7) *anti*-7-chloro-*exo*-2-norbornanol-*exo*,*exo*-5,6-d_2 (58-OH-*exo* *exo*-5,6-d_2)

(8) *syn*-7-chloro-*exo*-2-norbornanol-*exo*,*exo*-5,6-d_2 (59-OH-*exo*,*exo*-5,6-d_2)

(9) *anti*-7-chloro-*endo*-2-norbornanol-*endo*-6-*d* (84-OH-*endo*-6-*d*)

(10) *anti*-7-chloro-*exo*-2-norbornanol-*exo*-3-*d* (58-OH-*exo*-3-*d*)

(11) *anti*-7-chloro-*exo*-2-norbornanol plus $Eu(fod)_3$

(12) *anti*-7-chloro-*exo*-2-norbornanol-*exo*-3-*d* plus $Eu(fod)_3$

(13) *anti*-7-chloronorbornene (62)

The extent of deuteration in the deuterated compounds was determined by the method described in Chapter 5, Section C.

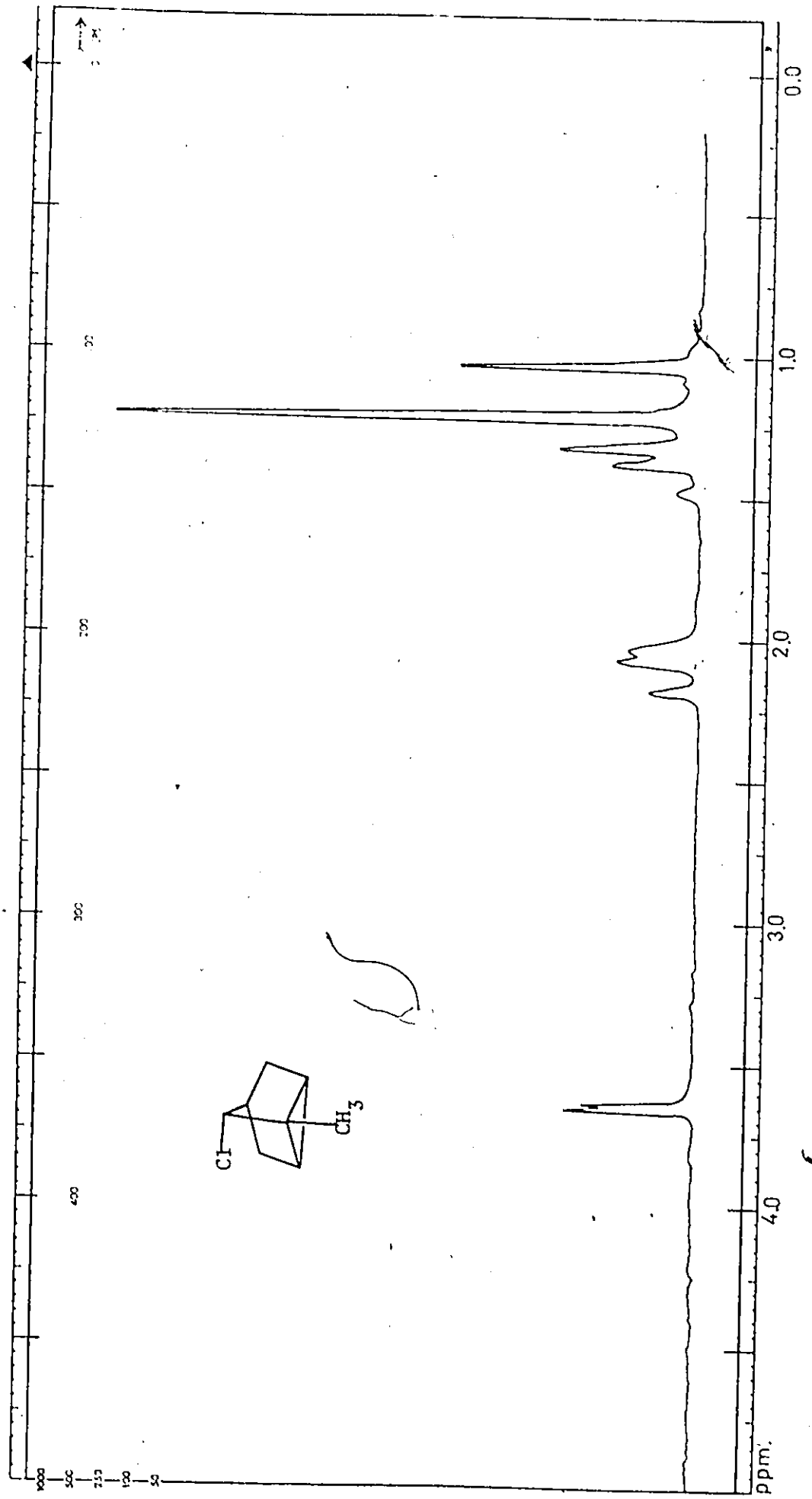


Figure 6:1 Pmr spectrum (100 MHz) of 2-methyl-3-chlorononortricyclene (25) in CCl_4

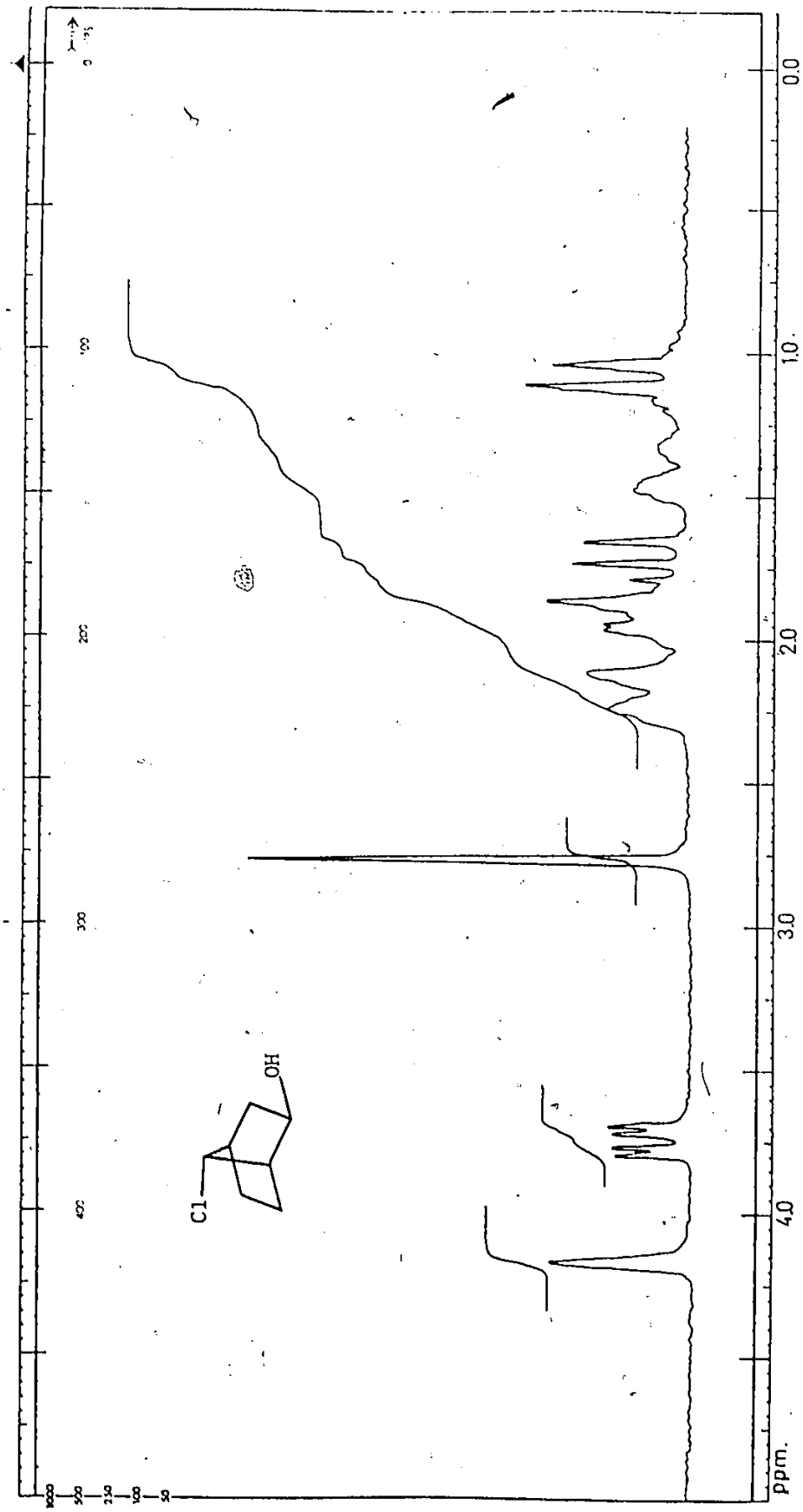


Figure 6:2 Pmr spectrum (100 MHz) of *anti*-7-chloro-*exo*-2-norbornanol (58-OH) in CCl_4

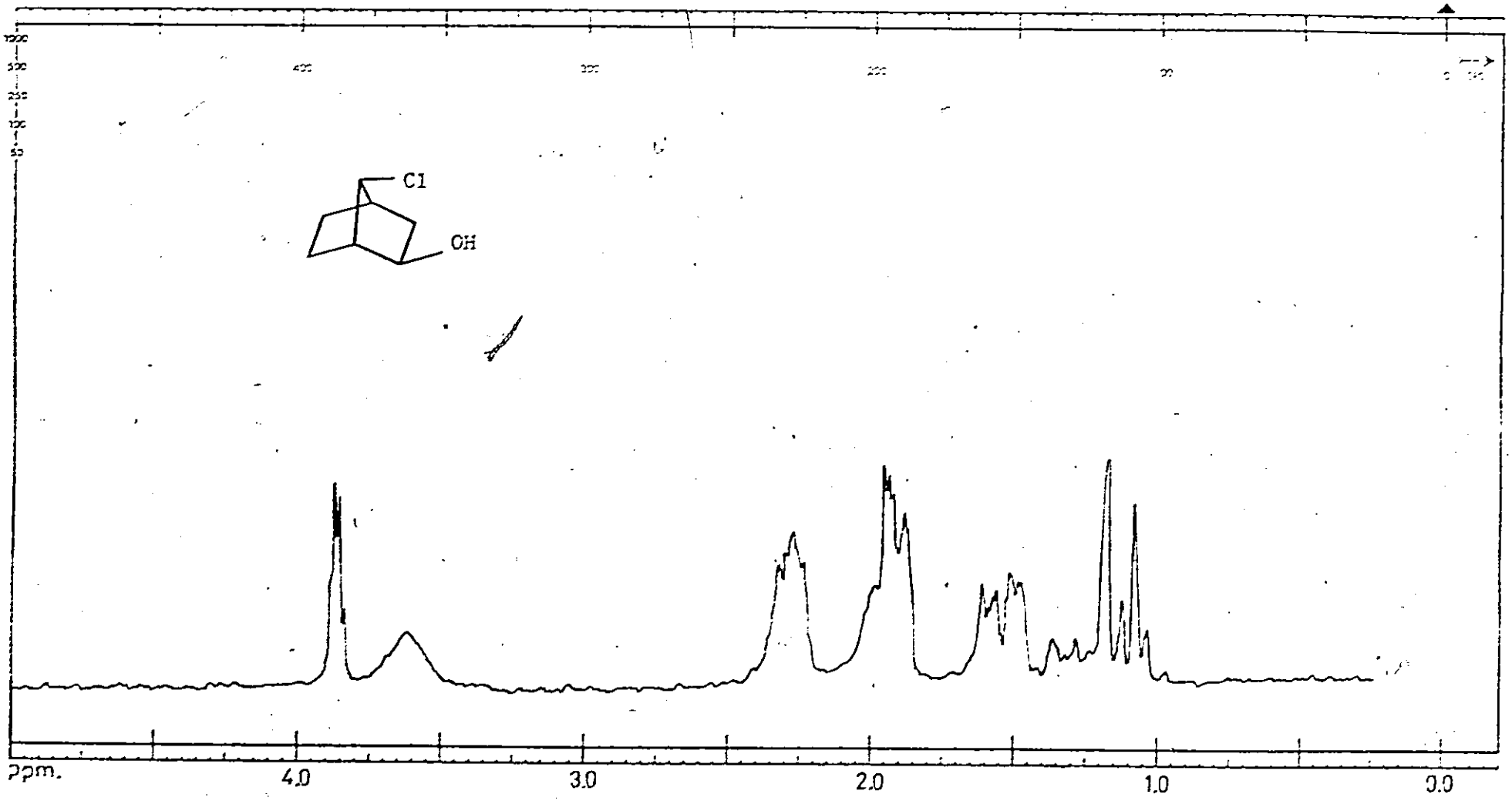


Figure 6:3 Pmr spectrum (100 MHz) of *syn*-7-chloro-*exo*-2-norbornanol (59-OH) in CS_2

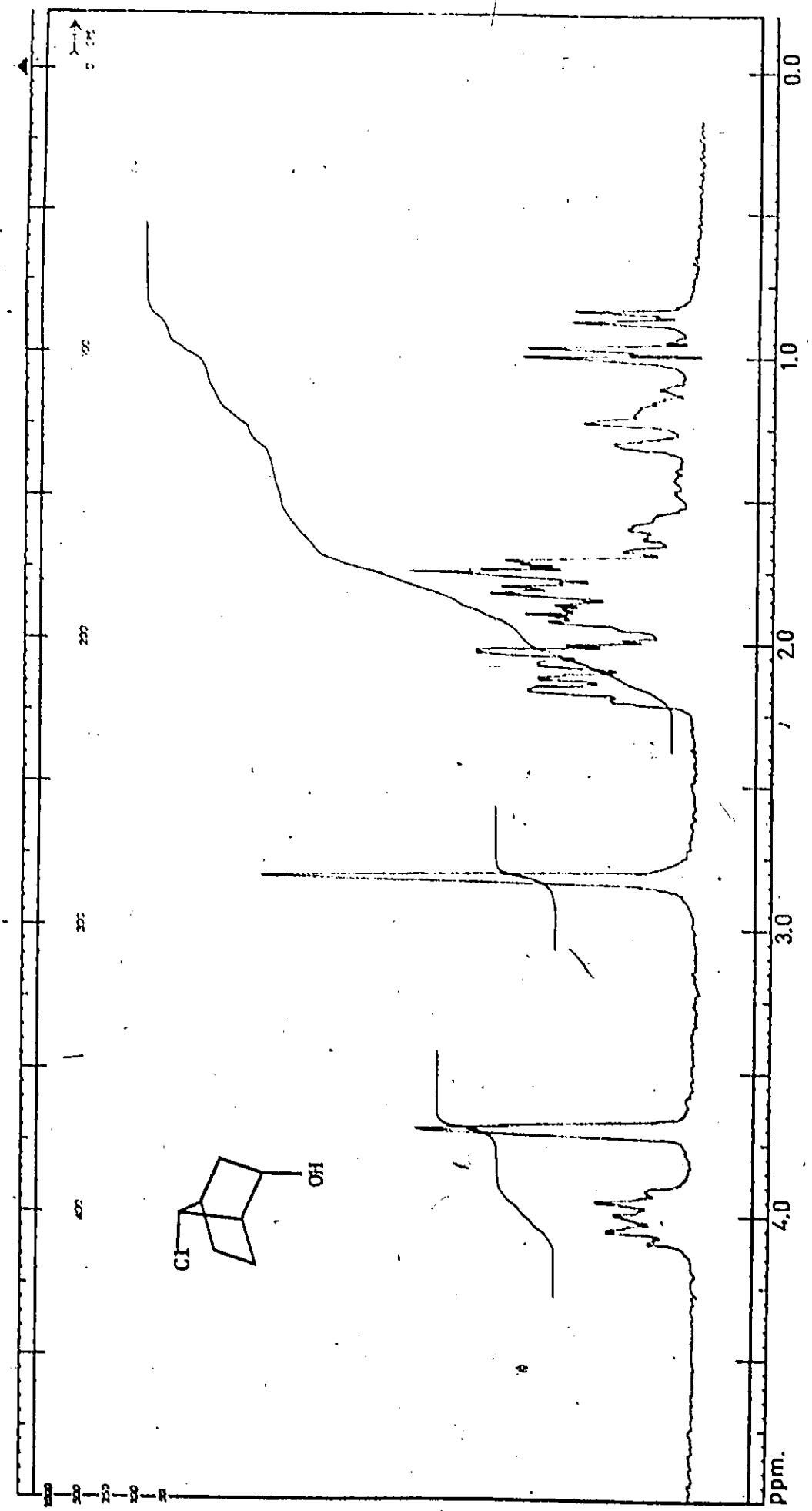


Figure 6:4 Pmr spectrum (100 MHz) of *anti*-7-chloro-*endo*-2-norbornanol (84-OH) in CS_2

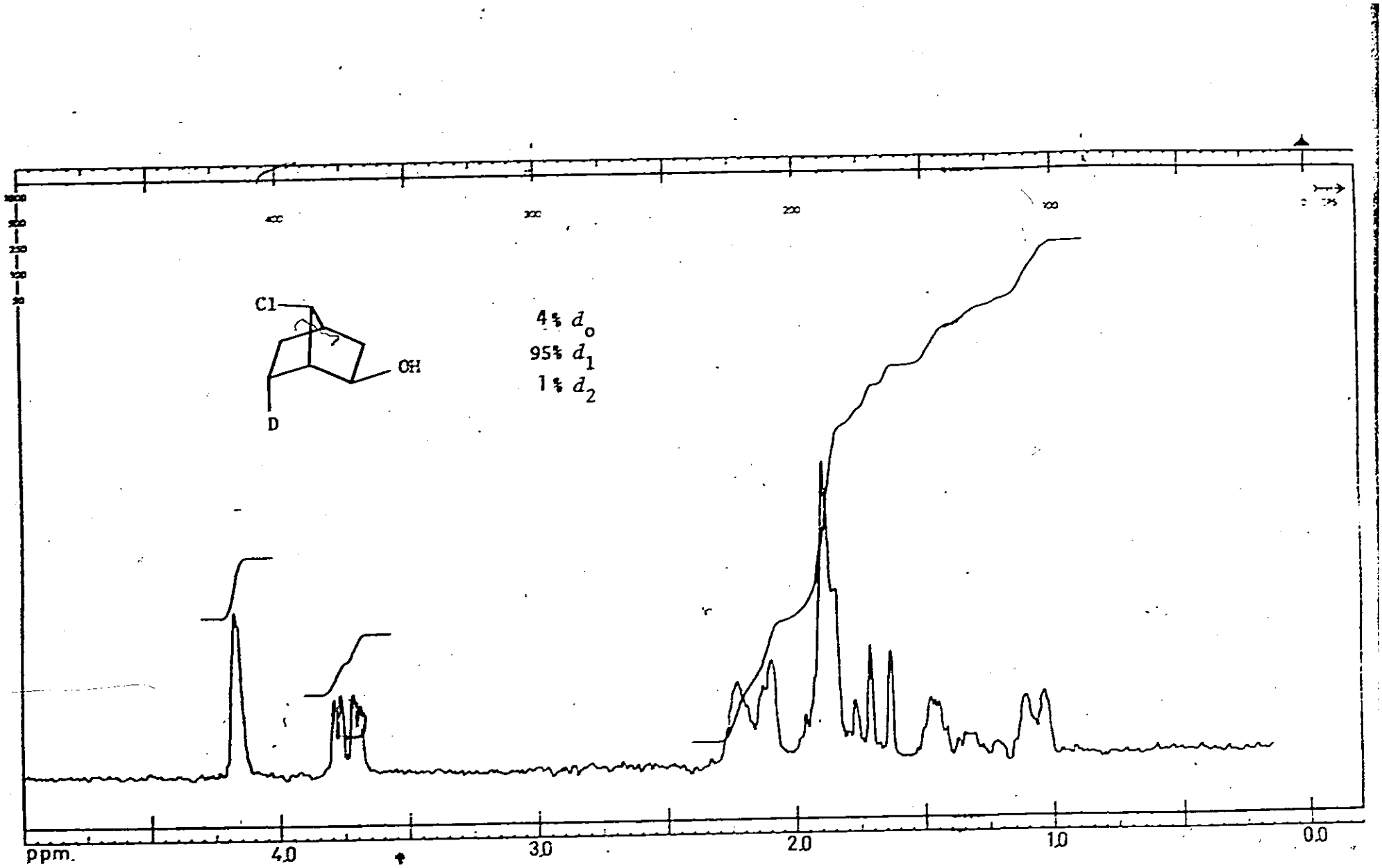


Figure 6:5 Pmr spectrum (100 MHz) of *anti*-7-chloro-*exo*-2-norbornanol-*endo*-6-*d* (58-OH-*endo*-6-*d*) in CCl_4

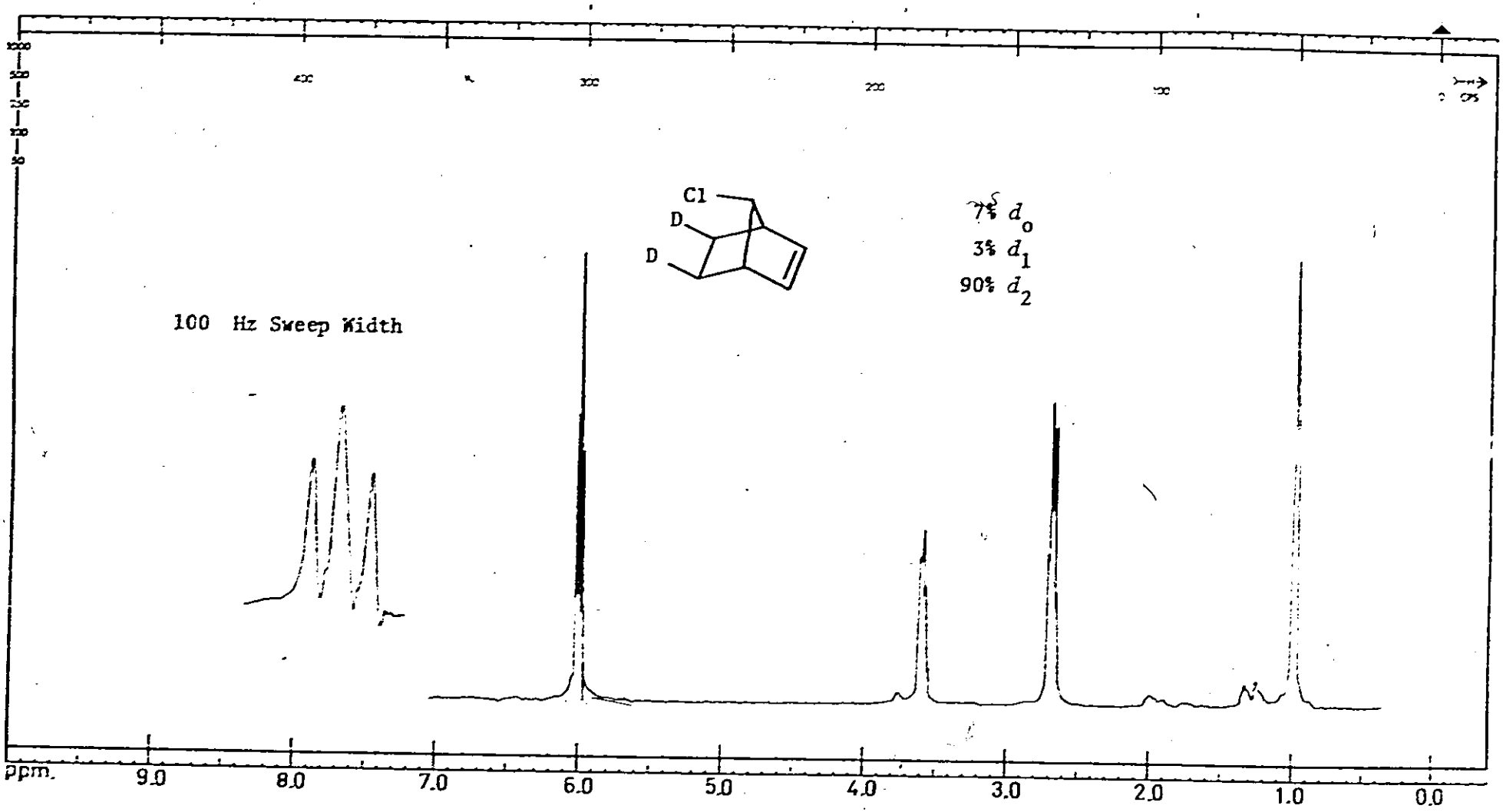


Figure 6:6 Pmr spectrum (100 MHz) of *anti*-7-chloronorbornene-*exo*,*exo*-5,6-d_2 (62-*exo*,*exo*-5,6-d_2) in CCl_4

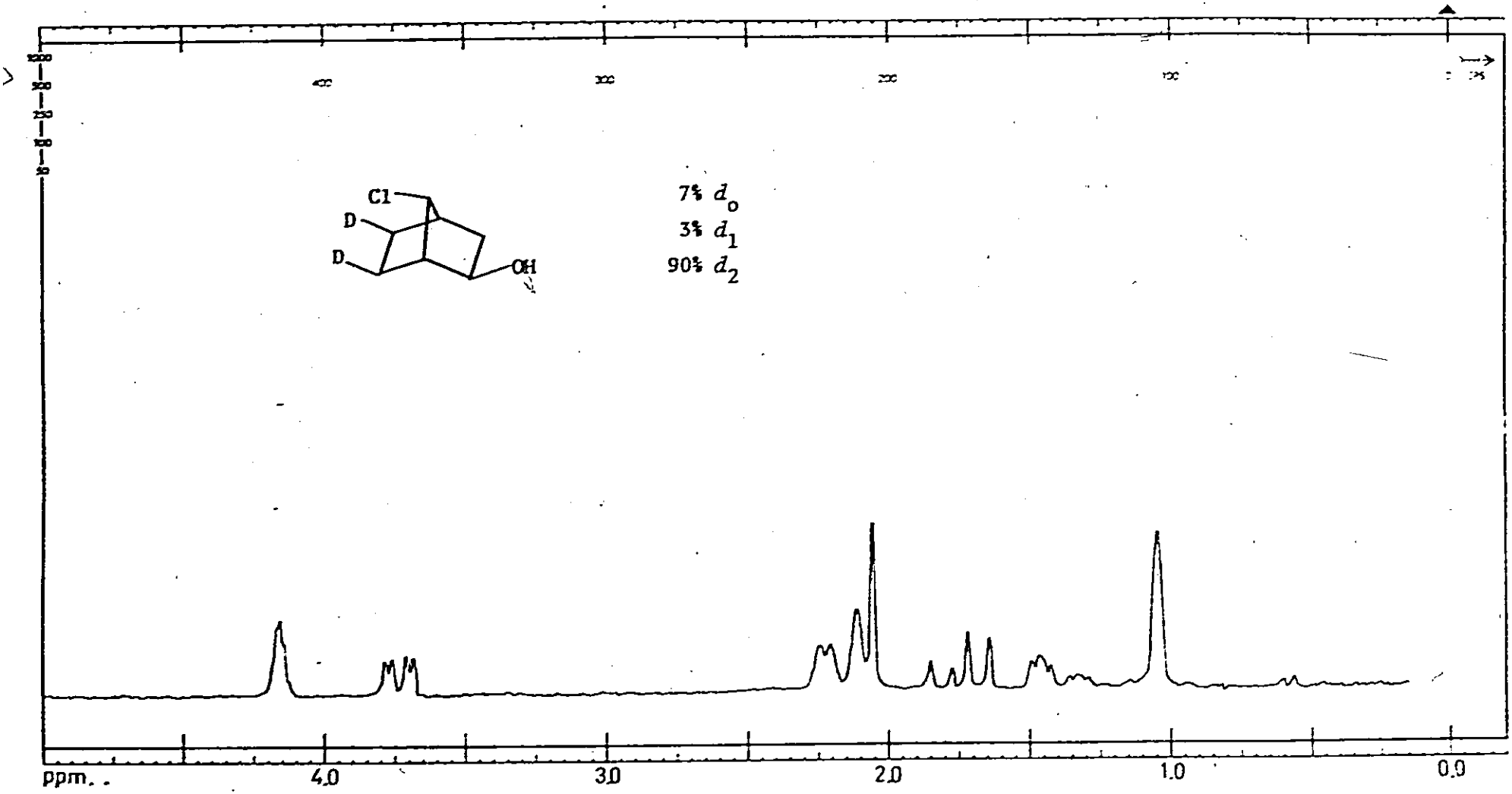


Figure 6:7 Pmr spectrum (100 MHz) of *anti*-7-chloro-*exo*-2-norbornanol-*exo*,*exo*-5,6-d_2 (58-OH-*exo*,*exo*-5,6-d_2) in CCl_4

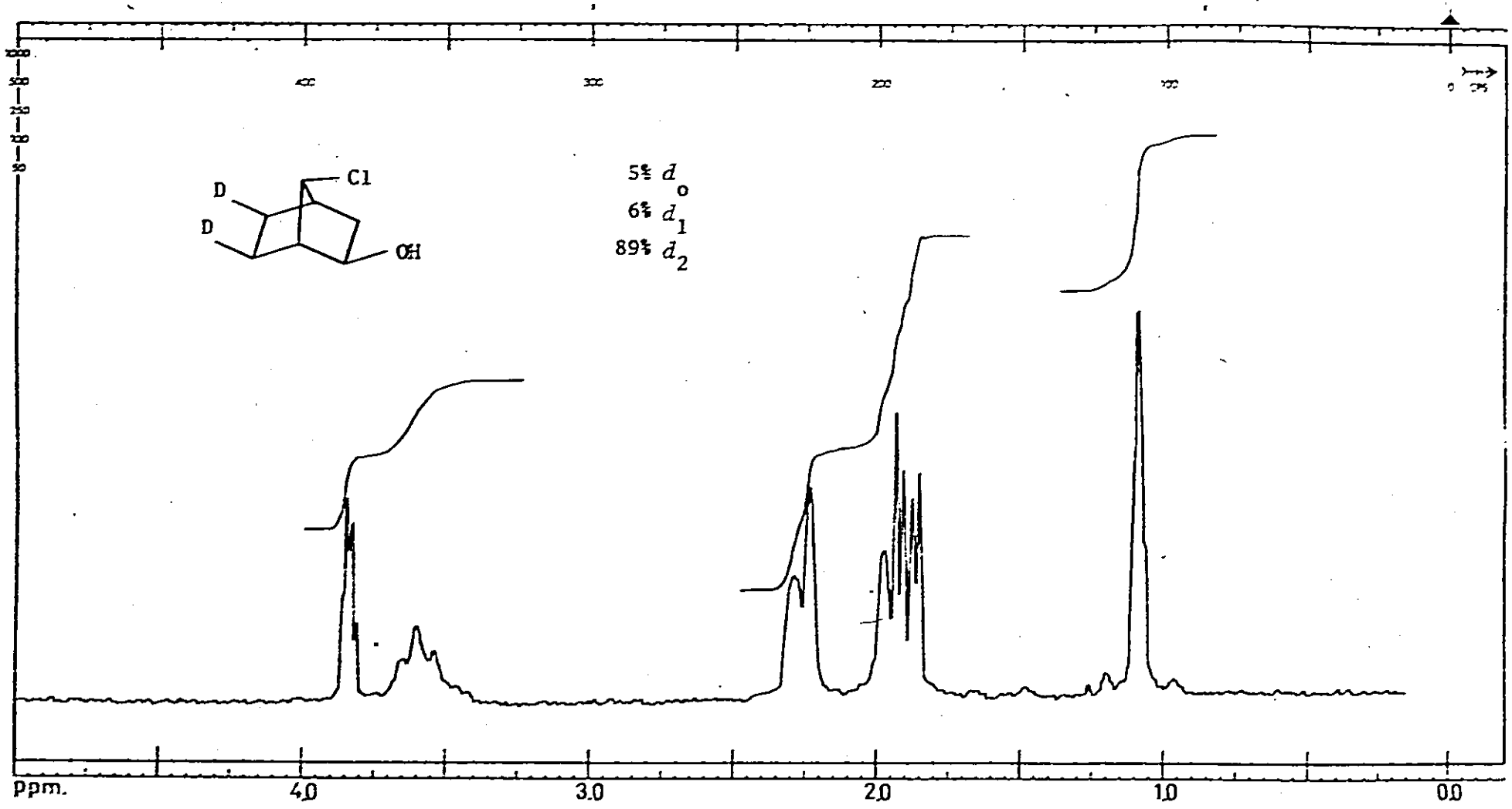


Figure 6:8 Pmr spectrum (100 MHz) of *syn*-7-chloro-*exo*-2-norbornanol-*exo*,*exo*-5,6-d_2 (59-OH-*exo*,*exo*-5,6-d_2) in CS_2

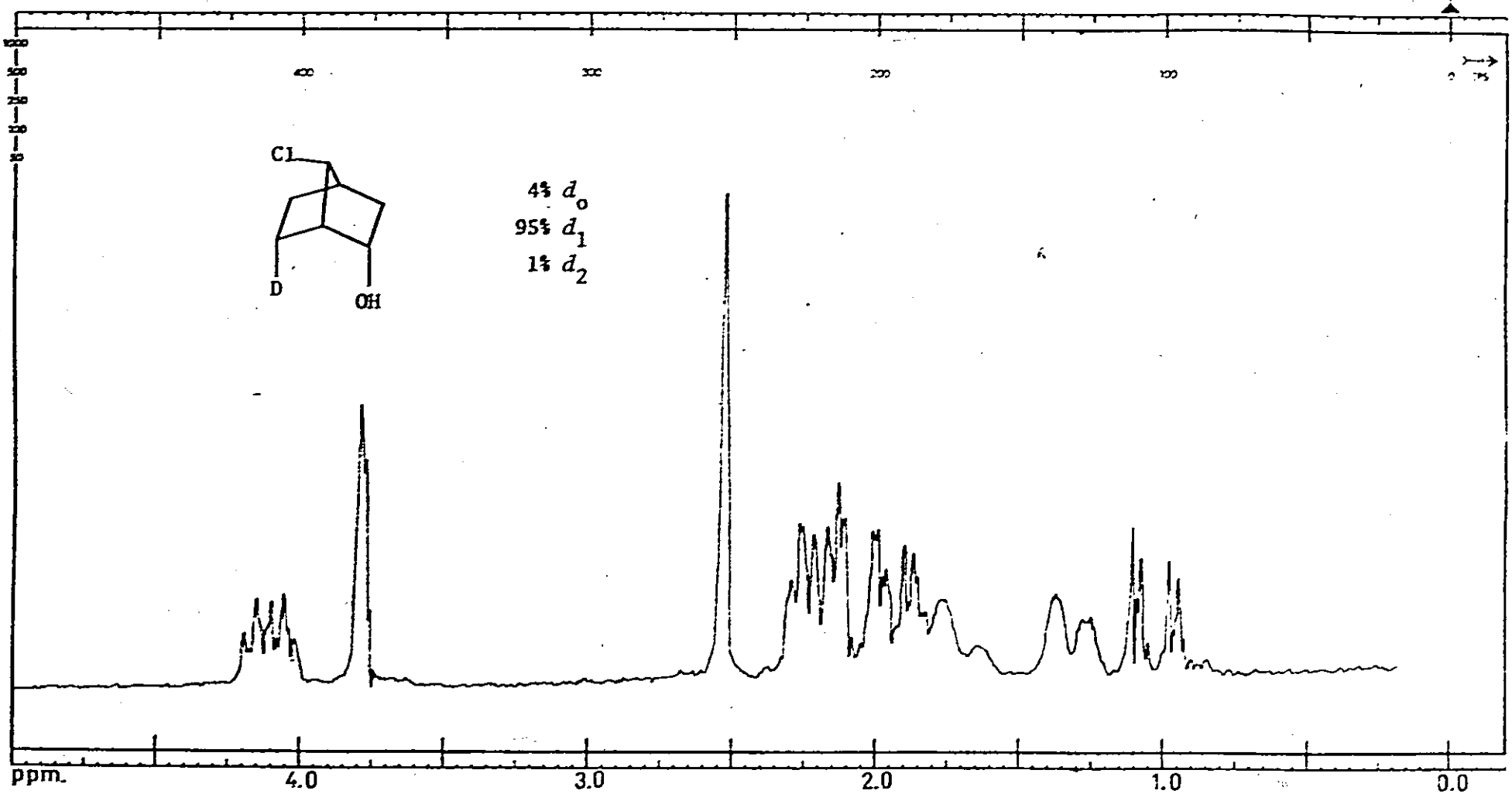


Figure 6:9 Pmr spectrum (100 MHz) of *anti*-7-chloro-*endo*-2-norbornanol-*endo*-6-*d* (84-OH-*endo*-6-*d*) in CS_2

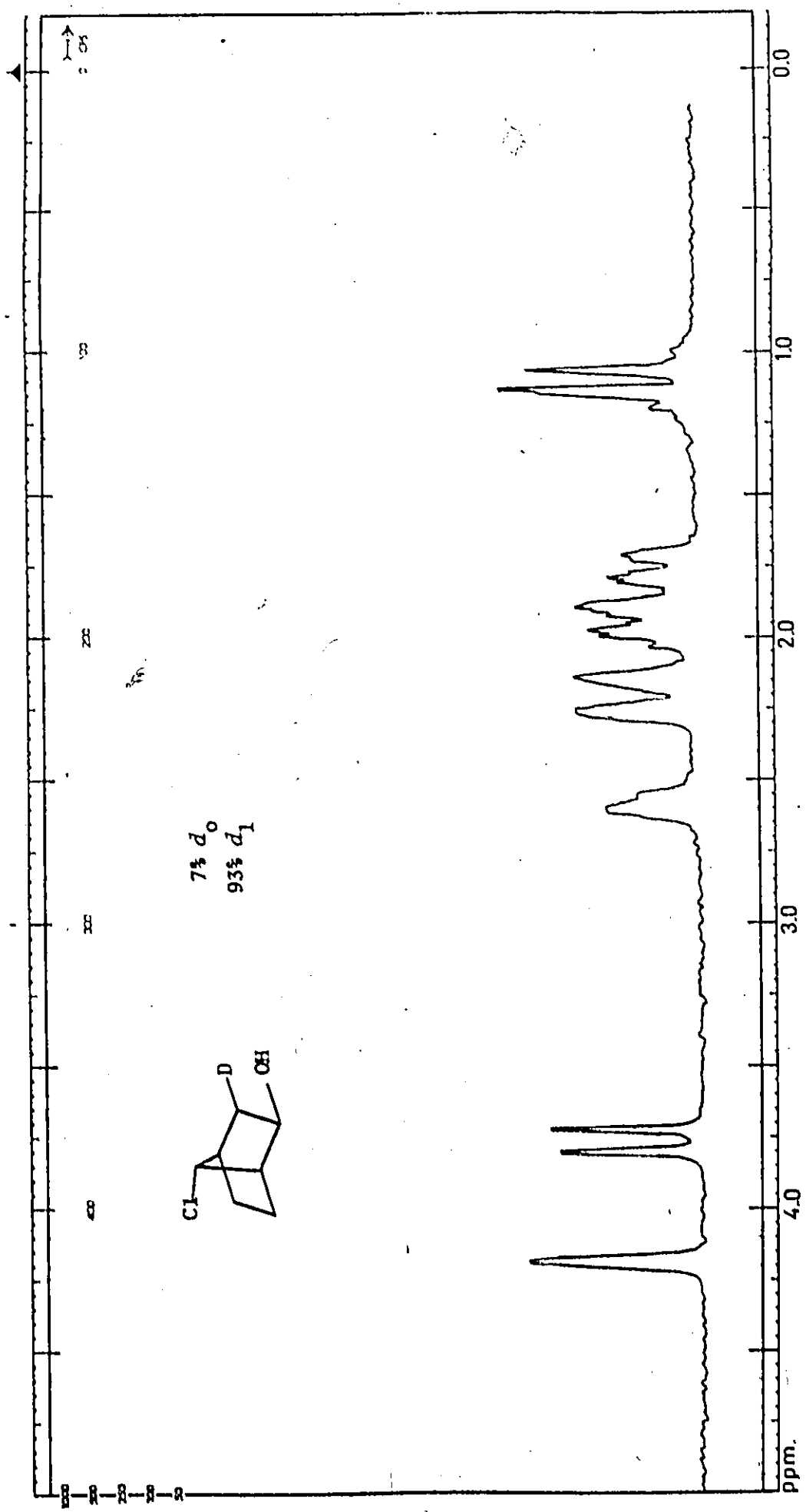


Figure 6:10 Pmr spectrum (100 MHz) of *anti*-7-chloro-*exo*-2-norbornanol-*exo*-3-*d* (58-OH-*exo*-3-*d*) in CCl_4

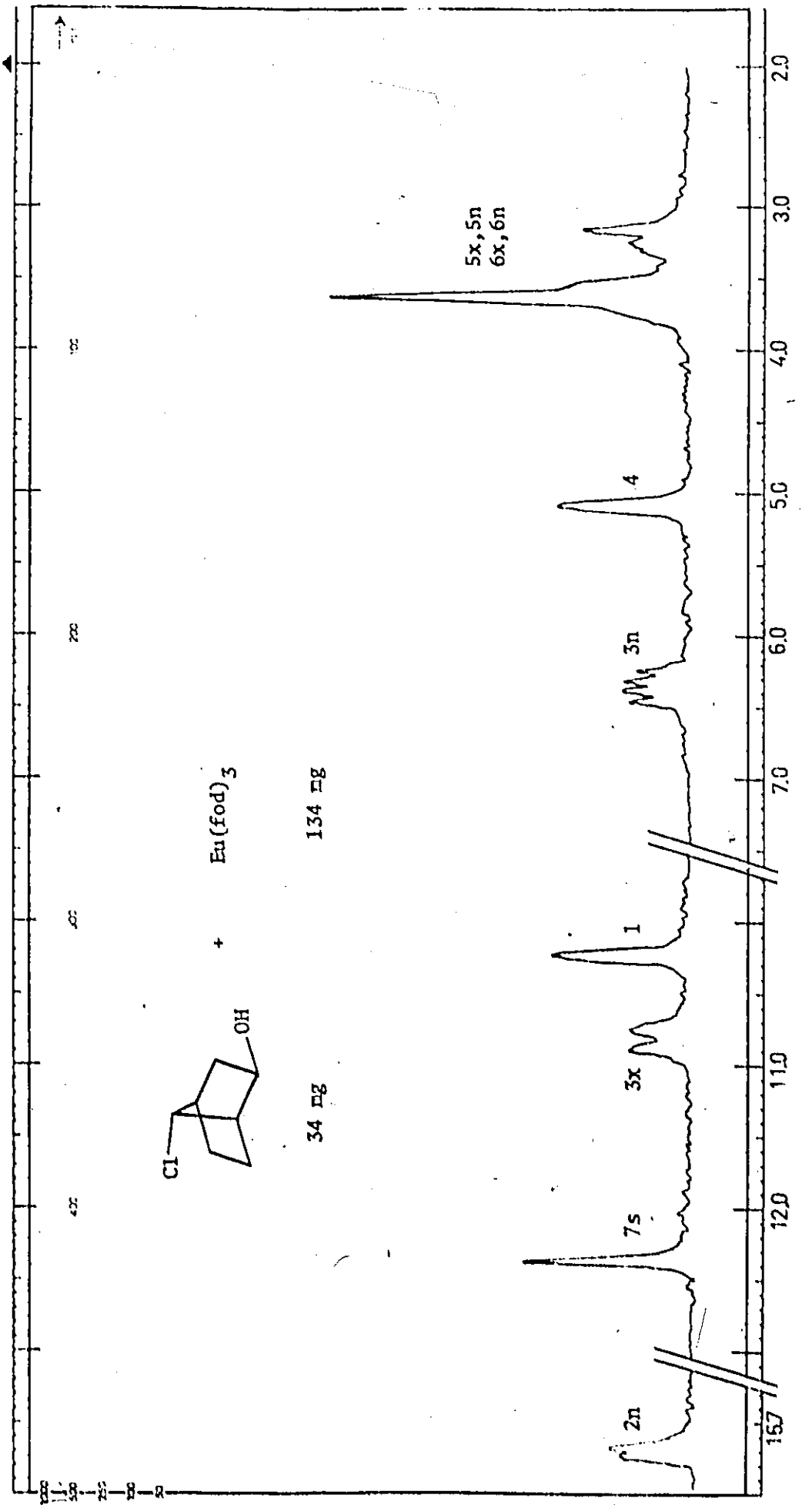


Figure 6:11 Pmr spectrum (100 MHz) of *anti*-7-chloro-*exo*-2-norbornanol (58-OH) plus $Eu(fod)_3$ in CCl_4

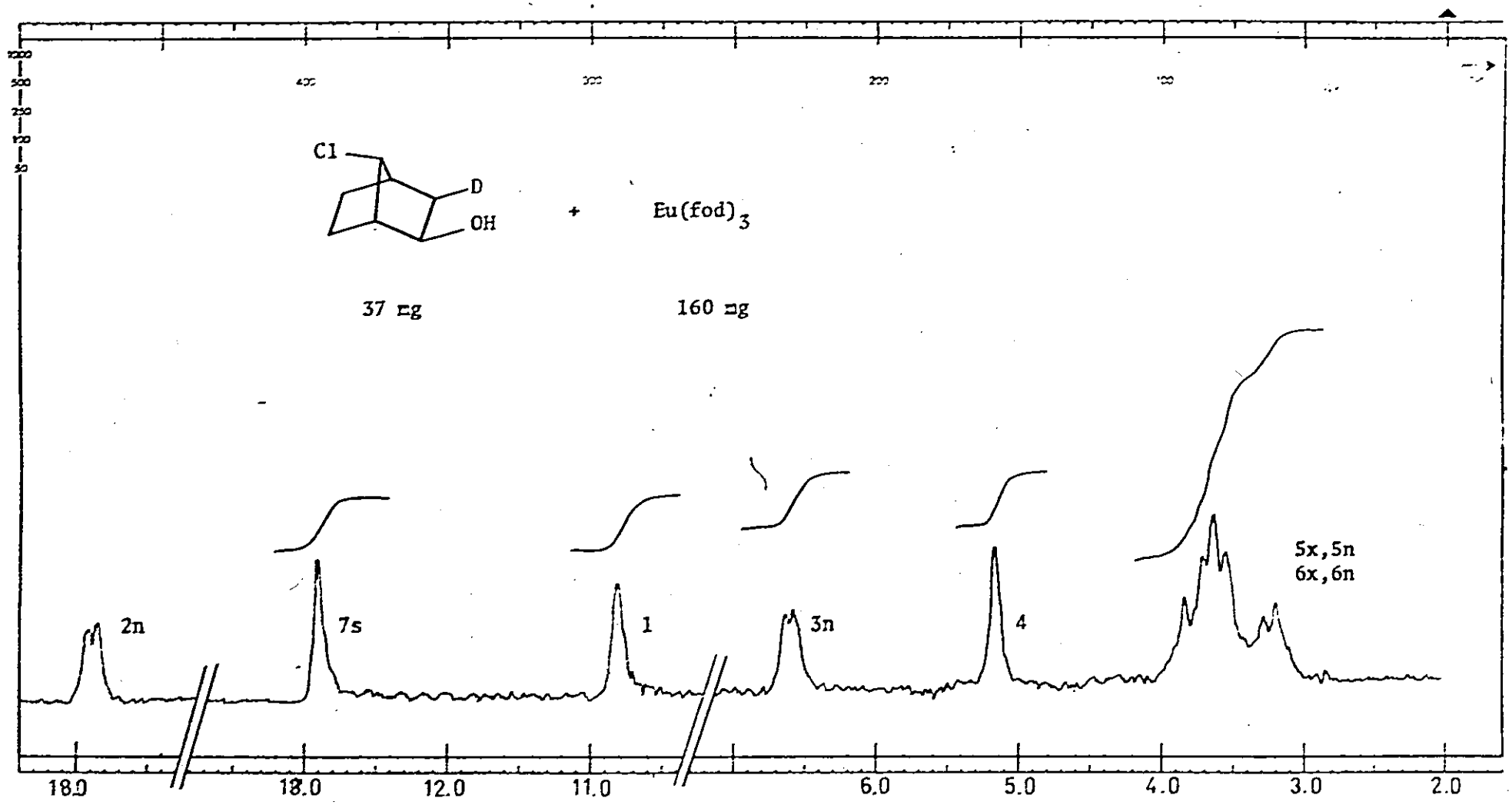


Figure 6:12 Pmr spectrum (100 MHz) of *anti*-7-chloro-*exo*-2-norbornanol-*exo*-3-*d* (58-OH-*exo*-3-*d*) plus $Eu(fod)_3$ in CCl_4

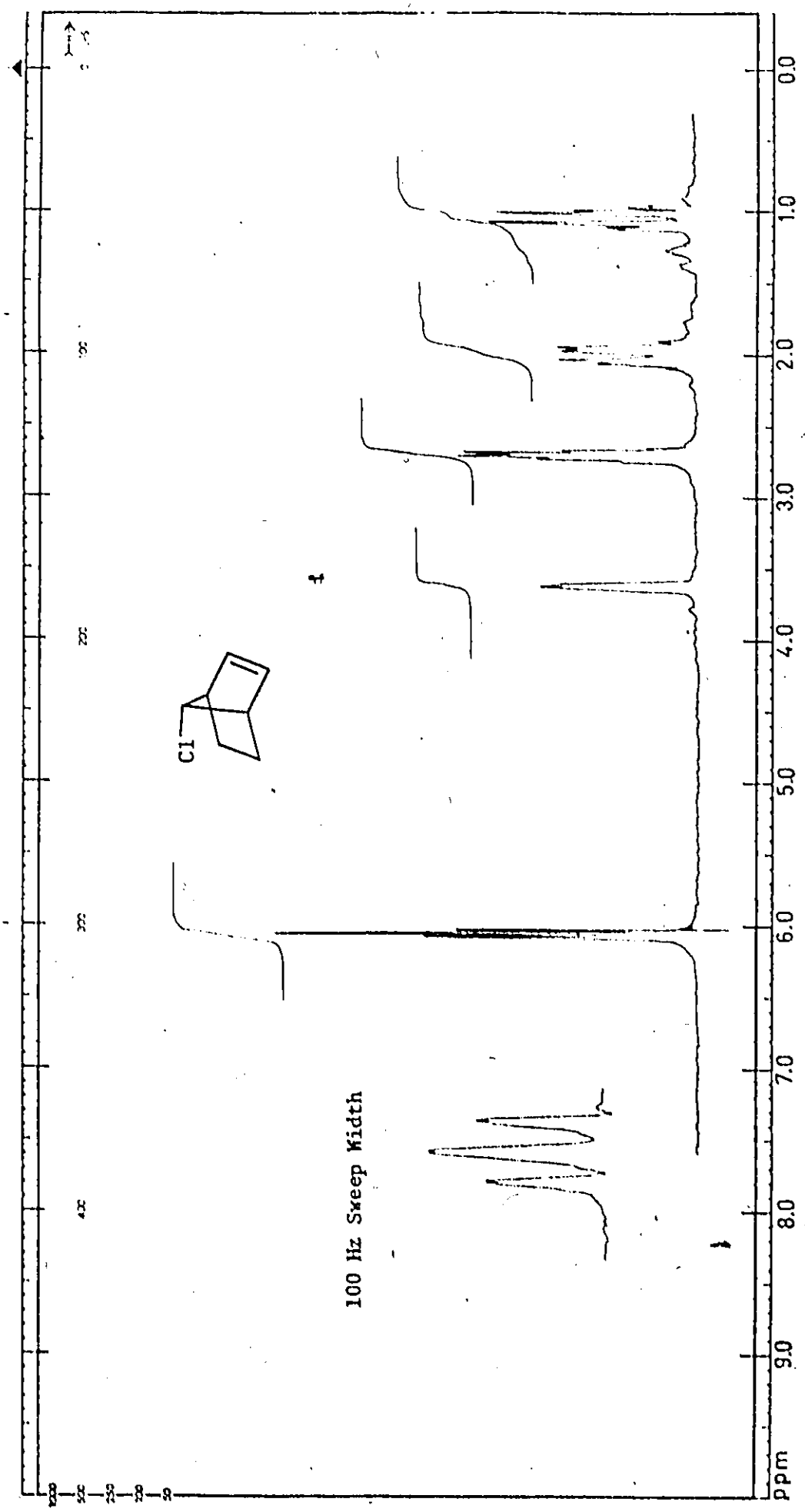


Figure 6:13 Pmr spectrum (100 MHz) of *anti*-7-chloronorbornene (62) in CCl_4

C Kinetics

First order rate constants (k) for the solvolytic reactions were determined from the slopes of the graphs of $-\ln(A_t-A_\infty)$ vs time where A_t and A_∞ are the absorbances at time t and time ∞ respectively. This A_∞ term takes into account the fact that the sodium brosylate which is produced as the reaction progresses has a finite absorption at the same wavelength at which the decrease in concentration of alkyl brosylate was monitored. Derivation of this relation is shown below and $[ROBs]_0$, $[ROBs]_t$, $[ROBs]_\infty$ denote the concentrations of alkyl brosylate at time 0, t, ∞ respectively whereas $[NaOBs]_0$, $[NaOBs]_t$, $[NaOBs]_\infty$ denote the concentrations of sodium brosylate at the appropriate times. Experimentally, $t = \infty$ was taken to be about ten half-lives.

$$-\frac{d[ROBs]}{dt} = k[ROBs]$$

$$\frac{d[ROBs]}{[ROBs]} = -kdt$$

$$\int_0^t \frac{d[ROBs]}{[ROBs]} = -\int_0^t kdt$$

$$\ln\left\{\frac{[ROBs]_t}{[ROBs]_0}\right\} = -kt$$

$$\frac{[ROBs]_t}{[ROBs]_0} = e^{-kt}$$

$$[ROBs]_t = [ROBs]_0 e^{-kt} \qquad \text{Eq. 6:1}$$

The concentration of sodium brosylate at time t is given by

$$[NaOBs]_t = [ROBs]_o - [ROBs]_t$$

$$[NaOBs]_t = [ROBs]_o - [ROBs]_o e^{-kt}$$

$$[NaOBs]_t = [ROBs]_o(1-e^{-kt}) \qquad \text{..... Eq. 6:2}$$

At time t, the absorbance reading is

$$A_t = \varepsilon c_t l \qquad \text{where } l = \text{cell path length}$$

where c_t (concentration of absorbing species at time t) includes contributions from both NaOBs and ROBs.

$$c_t = [NaOBs]_t + [ROBs]_t$$

Thus

$$A_t = \varepsilon_{NaOBs}[NaOBs]_t l + \varepsilon_{ROBs}[ROBs]_t l \qquad \text{..... Eq. 6:3}$$

Substitution of Eq's 6:1 and 6:2 into Eq 6:3 yields

$$A_t = \varepsilon_{NaOBs}[ROBs]_o(1-e^{-kt})l + \varepsilon_{ROBs}[ROBs]_o e^{-kt} l \qquad \text{.....Eq. 6:4}$$

At time ∞, the absorbance reading is

$$A_\infty = \varepsilon c_\infty l$$

where

$$c_\infty = [NaOBs]_\infty + [ROBs]_\infty$$

Thus

$$A_\infty = \varepsilon_{NaOBs}[NaOBs]_\infty l + \varepsilon_{ROBs}[ROBs]_\infty l \qquad \text{..... Eq. 6:5}$$

But

$$[NaOBs]_\infty = [ROBs]_o \qquad \text{..... Eq. 6:6}$$

and

$$[ROBs]_\infty = 0 \qquad \text{..... Eq. 6:7}$$

Substitution of Eq's 6:6 and 6:7 into Eq 6:5 yields

$$A_\infty = \varepsilon_{NaOBs}[ROBs]_o l \qquad \text{..... Eq. 6:8}$$

Subtraction of Eq 6:8 from Eq 6:7 gives

$$(A_t - A_\infty) = \varepsilon_{NaOBs}[ROBs]_o l - \varepsilon_{NaOBs}[ROBs]_o e^{-kt} l + \varepsilon_{ROBs}[ROBs]_o e^{-kt} l - \varepsilon_{NaOBs}[ROBs]_o l$$

$$(A_t - A_\infty) = (\varepsilon_{ROBs}[ROBs]_o l - \varepsilon_{NaOBs}[ROBs]_o l) e^{-kt}$$

$$-\ln(A_t - A_\infty) = -\ln\left\{\frac{\varepsilon_{ROBs}[ROBs]_o l}{\varepsilon_{NaOBs}[ROBs]_o l}\right\} + kt$$

$$\frac{d}{dt}(-\ln(A_t - A_\infty)) = +k$$

$$d((-\ln(A_t - A_\infty)) = kdt$$

Integrating both sides over time t yields

$$-\ln(A_t - A_\infty) = kt + \text{constant}$$

and thus shows that a plot of $-\ln(A_t - A_\infty)$ versus time should yield the rate constant k.

For the solvolysis of *anti*-7-chloro-*endo*-2-norbornyl brosylate (84-OBs), the rate constant was determined by fitting the set of data (A_t, t) to an equation of the form

$$A_t = be^{-kt} + d$$

where b and d are constants.[219]

D Kinetic data

Typical first order plots for each solvolytic reaction are shown in Chapter 2 (Figures 2:15 to 2:38). A typical set of absorbance and time data along with the calculated rate constants and standard deviations are presented in Table 6:2 (see also Table 6:3). This section also lists the kinetic data for each solvolytic run of each chloro brosylate (Tables 6:4 to 6:9).

Table 6:2 Absorbance and time data for a typical solvolytic reaction[a,b]

59-OBs				59-OBs-*endo*-6-*d*			
T(min)	A_t[c]	(A_t-A_∞)	$-\ln(A_t-A_\infty)$	T(min)	A_t[c]	(A_t-A_∞)	$-\ln(A_t-A_\infty)$
0	1.604	0.704	0.351	0	1.664	0.722	0.326
10	1.544	0.644	0.440	10	1.610	0.668	0.403
20	1.488	0.588	0.531	20	1.557	0.615	0.486
30	1.436	0.536	0.624	30	1.510	0.568	0.566
40	1.389	0.489	0.715	40	1.465	0.523	0.648
50	1.345	0.445	0.810	50	1.422	0.480	0.734
60	1.307	0.407	0.899	60	1.383	0.441	0.819
70	1.268	0.368	1.000	70	1.345	0.403	0.909
80	1.232	0.332	1.102	80	1.312	0.370	0.994
90	1.199	0.299	1.207	90	1.278	0.336	1.091
100	1.172	0.272	1.302	100	1.250	0.308	1.178
110	1.147	0.247	1.398	110	1.224	0.282	1.266
120	1.125	0.225	1.492	120	1.199	0.257	1.359
130	1.104	0.204	1.590	130	1.177	0.235	1.448
140	1.083	0.183	1.698	140	1.159	0.217	1.528
150	1.067	0.167	1.790	150	1.137	0.195	1.635
160	1.050	0.150	1.897	160	1.120	0.178	1.726
170	1.033	0.133	2.017	170	1.108	0.166	1.796
180	1.021	0.121	2.112	180	1.089	0.147	1.917
190	1.008	0.108	2.226	190	1.079	0.137	1.988
200	0.999	0.099	2.313	200	1.064	0.122	2.104
∞[d]	0.900	-	-	∞[d]	0.942	-	-

* * * * * * * * * * * * * * * * * * * *

Slope[e]	
9.873×10^{-3} min^{-1} (k_H)	8.888×10^{-3} min^{-1} (k_D)
Standard deviation	
5.394×10^{-5} min^{-1}	4.981×10^{-5} min^{-1}

$k_H/k_D = 1.11 \pm 0.01$

[a] Solvolyses of 59-OBs and 59-OBs-*endo*-6-*d* in buffered 80:20 ethanol-water at 50.0° at λ = 264.9 nm.

[b] See Table 6:5, Run #8

[c] The error in these numbers is estimated to be ± 0.003 absorbance unit.

[d] Determined after more than ten half-lives

[e] This denotes the slope of the $-\ln(A_t-A_\infty)$ vs time data and it also represents the first order rate constant.

Table 6:3 Absorbance and time data for a typical solvolytic reaction[a,b]

84-OBs		84-OBs-*endo*-6-*d*	
Time (hr)	A_t[c]	Time (hr)	A_t[c]
0.00	0.847	0.00	0.988
5.50	0.738	5.50	0.862
7.50	0.711	7.50	0.824
10.50	0.669	10.50	0.775
13.50	0.633	13.50	0.736
17.50	0.595	17.50	0.693
21.25	0.568	21.25	0.656
30.50	0.522	30.50	0.599
36.50	0.499	36.50	0.578
∞[d]	0.451	∞[d]	0.519

* * * * * * * * * * * * * * * * * * *

Slope

5.73×10^{-2} hr^{-1} 5.73×10^{-2} hr^{-1}

Standard deviation

4.28×10^{-4} hr^{-1} 3.75×10^{-4} hr^{-1}

$k_H/k_D = 1.00 \pm 0.02$

---

[a] Solvolyses of 84-OBs and 84-OBs-*endo*-6-*d* in buffered 80:20 ethanol-water at 80° at λ = 266.0 nm.

[b] See Table 6:8, Run #36

[c] The error in these numbers is estimated to be ± 0.005 absorbance unit.

[d] Determined by computer fit to an exponential equation as described elsewhere.

Table 6:4 First order rate constants for solvolyses of *anti*-7-chloro-*exo*-2-norbornyl brosylate (58-OBs) and *anti*-7-chloro-*exo*-2-norbornyl brosylate-*endo*-6-*d* (58-OBs-*endo*-6-*d*)[a,b] at 60.0°[c]

Run	Substrates[d]	$k_H \times 10^2$	SD $\times 10^5$	$k_H \times 10^2$	SD $\times 10^5$	$k_D \times 10^2$	SD $\times 10^5$	k_H/k_H	k_H/k_D
10	H and H	0.665	2.959	0.675	2.953	-	-	0.99 ± 0.01	-
12	H and D	2.087	4.097	-	-	1.872	3.177	-	1.11 ± 0.01
13	H and D	2.095	5.722	-	-	1.900	1.931	-	1.10 ± 0.01
14	H and D	2.020	8.056	-	-	1.816	5.763	-	1.11 ± 0.01
15	H and H	2.001	10.95	2.012	9.454	-	-	0.99 ± 0.01	-
16	H and D	2.056	3.809	-	-	1.846	4.548	-	1.11 ± 0.01

a Solvolysis in buffered 80:20 ethanol-water; units are min^{-1}

b Determined spectrophotometrically at λ = 276.4 nm.

c See Table 2:6, footnote e.

d H and D refer to the non-deuterated and deuterated brosylates respectively.

Table 6:5 First order rate constants for solvolyses of *syn*-7-chloro-*exo*-2-norbornyl brosylate (59-08s) and *syn*-7-chloro-*exo*-2-norbornyl brosylate-*endo*-6-*d* (59-08s-*endo*-6-*d*)[a,b] at 50.0° [c]

Run	Substrates[d]	$k_H \times 10^3$	SD $\times 10^5$	$k_H \times 10^3$	SD $\times 10^5$	$k_D \times 10^3$	SD $\times 10^5$	k_H/k_H	k_H/k_D
3	H and H	4.710	1.686	4.717	1.020	-	-	1.00 ± 0.01	-
4	H and H	4.593	2.832	4.623	3.029	-	-	0.99 ± 0.01	-
5	H and D	10.36	4.680	-	-	9.244	2.670	-	1.12 ± 0.01
6	H and D	9.435	3.157	-	-	8.525	2.670	-	1.11 ± 0.01
7	H and H	8.347	3.579	8.318	2.550	-	-	1.00 ± 0.01	-
8	H and D	9.873	5.394	-	-	8.888	4.981	-	1.11 ± 0.01
9	H and H	8.808	3.369	8.680	2.553	-	-	1.01 ± 0.01	-

a Solvolysis in buffered 80:20 ethanol-water; units are min^{-1}

b Determined spectrophotometrically at λ = 264.9 nm.

c See Table 2:6, footnote e.

d H and D refer to the non-deuterated and deuterated brosylates respectively.

Table 6:6 First order rate constants for solvolyses of *anti*-7-chloro-*exo*-2-norbornyl brosylate (58-OBs) and *anti*-7-chloro-*exo*-2-norbornyl brosylate-*exo*,*exo*-5,6-d_2 (58-OBs-*exo*,*exo*-5,6-d_2)[a,b] at 57.8° [c]

Run	Substrates[d]	$k_H \times 10^2$	SD $\times 10^5$	$k_H \times 10^2$	SD $\times 10^5$	$k_D \times 10^2$	SD $\times 10^5$	k_H/k_H	k_H/k_D
49	H and D	1.671	4.080	-	-	1.512	4.290	-	1.11 ± 0.01
50	H and D	1.696	5.288	-	-	1.492	4.011	-	1.13 ± 0.01
51	H and D	1.680	2.854	-	-	1.491	2.413	-	1.13 ± 0.01
52	H and H	1.672	4.222	1.665	3.071	-	-	1.00 ± 0.01	-
53	H and D	1.671	3.883	-	-	1.489	3.693	-	1.12 ± 0.01
54	H and D	1.652	3.602	-	-	1.471	2.306	-	1.12 ± 0.01
55	H and H	1.662	3.635	1.652	4.685	-	-	1.01 ± 0.01	-

a Solvolysis in buffered 80:20 ethanol-water; units are min^{-1}

b Determined spectrophotometrically at λ = 276.4 nm.

c See Table 2:6, footnote e.

d H and D refer to the non-deuterated and deuterated brosylates respectively.

Table 6:7 First order rate constants for solvolyses of *syn*-7-chloro-*exo*-2-norbornyl brosylate (59-OBs) and *syn*-7-chloro-*exo*-2-norbornyl brosylate-*exo*,*exo*-5,6-d_2 (59-OBs-*exo*,*exo*-5,6-d_2)[a,b] at 51.1° [c]

Run	Substrates[d]	$k_H \times 10^2$	SD $\times 10^5$	$k_H \times 10^2$	SD $\times 10^5$	$k_D \times 10^2$	SD $\times 10^5$	k_H/k_D	k_H/k_D
18	H and H	1.016	3.148	1.003	4.145	-	-	1.01 ± 0.01	-
19	H and H	1.008	4.222	1.021	4.524	-	-	0.99 ± 0.01	-
21	H and D	0.986	4.077	-	-	0.883	3.609	-	1.12 ± 0.01
22	H and D	0.976	2.979	-	-	0.891	6.423	-	1.10 ± 0.01
23	H and H	1.014	8.778	1.008	4.902	-	-	1.00 ± 0.01	-
24	H and H	1.007	3.012	1.012	4.549	-	-	1.00 ± 0.01	-
25	H and D	1.001	3.612	-	-	0.904	4.153	-	1.11 ± 0.01
26	H and D	1.008	5.950	-	-	0.919	5.240	-	1.10 ± 0.01
27	H and H	1.020	4.335	1.033	5.335	-	-	0.99 ± 0.01	-

[a] Solvolysis in buffered 80:20 ethanol-water; units are min^{-1}

[b] Determined spectrophotometrically at λ = 264.9 nm.

[c] See Table 2:6, footnote e.

[d] H and D refer to the non-deuterated and deuterated brosylates respectively.

Table 6:8 First order rate constants for solvolyses of *anti*-7-chloro-*endo*-2-norbornyl brosylate (84-OBs) and *anti*-7-chloro-*endo*-2-norbornyl brosylate-*endo*-6-*d* (84-OBs-*endo*-6-*d*)[a,b] at 80° [c]

Run	Substrates[d]	$k_H \times 10^2$	SD $\times 10^4$	$k_H \times 10^2$	SD $\times 10^4$	$k_D \times 10^2$	SD $\times 10^4$	k_H/k_H	k_H/k_D
29	H and H	4.67	3.58	4.51	4.76	-	-	1.03 ± 0.02	-
30	H and H	3.07	2.87	3.05	3.87	-	-	1.00 ± 0.02	-
31	H and H	2.89	2.95	2.93	10.5	-	-	0.99 ± 0.05	-
33	H and H	5.36	4.01	5.37	8.18	-	-	1.00 ± 0.02	-
34	H and D	5.19	5.83	-	-	5.47	2.10	-	0.95 ± 0.02
35	H and D	5.27	3.20	-	-	5.29	2.05	-	1.00 ± 0.02
36	H and D	5.73	4.28	-	-	5.73	3.75	-	1.00 ± 0.02
37	H and D	5.39	6.07	-	-	5.64	5.04	-	0.97 ± 0.02
38	H and D	5.01	7.76	-	-	4.93	3.73	-	1.01 ± 0.02

[a] Solvolysis in buffered 80:20 ethanol-water; units are hr^{-1}

[b] Determined spectrophotometrically at λ = 266.0 nm.

[c] See Table 2:6, footnote e.

[d] H and D refer to the non-deuterated and deuterated brosylates respectively.

Table 6:9 First order rate constants for solvolyses of *anti*-7-chloro-*exo*-2-norbornyl brosylate (58-OBs) and *anti*-7-chloro-*exo*-2-norbornyl brosylate-*exo*-3-*d* (58-OBs-*exo*-3-*d*)[a,b] at 57.8° [c]

Run	Substrates[d]	$k_H \times 10^2$	SD $\times 10^5$	$k_H \times 10^2$	SD $\times 10^5$	$k_D \times 10^2$	SD $\times 10^5$	k_H/k_H	k_H/k_D
40	H and H	1.708	5.815	1.728	3.467	-	-	0.99 ± 0.01	-
41	H and H	1.714	6.543	1.697	6.853	-	-	1.01 ± 0.01	-
42	H and D	1.717	6.123	-	-	1.588	3.808	-	1.09 ± 0.01
43	H and D	1.725	3.120	-	-	1.576	3.572	-	1.09 ± 0.01
44	H and D	1.715	4.872	-	-	1.574	2.860	-	1.09 ± 0.01
45	H and D	1.712	3.499	-	-	1.582	3.270	-	1.08 ± 0.01
46	H and H	1.678	5.549	1.677	5.295	-	-	1.00 ± 0.01	-
47	H and D	1.679	4.583	-	-	1.524	3.546	-	1.10 ± 0.01
48	H and D	1.735	3.695	-	-	1.569	3.440	-	1.10 ± 0.01

a Solvolysis in buffered 80:20 ethanol-water; units are min^{-1}

b Determined spectrophotometrically at λ = 276.4 nm.

c See Table 2:6, footnote e.

d H and D refer to the non-deuterated and deuterated brosylates respectively.

E Computer programs for analysis of kinetic data

First order rate constants along with standard deviations for solvolyses of 7-chloro-*exo*-2-norbornyl brosylates (58- and 59-OBs) were calculated from sets of $-\ln(A_t-A_\infty)$ and time(t) data by a least squares program which follows. First order rate constants for solvolysis of *endo*-7-chloro-*endo*-2-norbornyl brosylate (84-OBs) were determined by computer by fitting the absorbance (A_t) and time data to an exponential curve of the form $y = Ae^{-Bx} + C$. For a given set of y and x (*ie* absorbance and time respectively), the best C(A_∞) and B(rate constant k) were obtained. A copy of this program follows.[219]

For 58- and 59-OBs, the reliability of the solvolytic first order rate constants is partially dependent upon the reliability of the experimentally determined absorbance reading at infinity (A_∞). In order to check the reliability of the rate constants and the A_∞'s which were obtained experimentally from solvolyses of 58- and 59-OBs, these numbers were calculated independently by fitting the (A_t,t) data to an exponential curve as described above. From a given set of (A_t,t) data from a particular run, A_∞ and k were calculated by computer. Comparison of these calculated and experimental values (Tables 6:10 to 6:13) shows that agreement was generally satisfactory. Although in most cases the absolute values of the two experimental and calculated rate constants (k_H and k_H or k_H and k_D) from a kinetic run were not identical, the ratios of these numbers were usually similar to each other *ie* $(k_H/k_H)_{exp't} = (k_H/k_H)_{calc'd}$ and $(k_H/k_D)_{exp't} = (k_H/k_D)_{calc'd}$.

Table 6:10 Comparison of calculated and experimental kinetic data from solvolysis of *syn*-7-chloro-*exo*-2-norbornyl brosylate (59-08s)

Run[a]	Substrate[a]	Experimental[a,b] A_∞	Experimental[a,b] $k(\text{min}^{-1})$	Experimental[c] k_1/k_2	Calculated[d] A_∞	Calculated[d] $k(\text{min}^{-1})$	Calculated[c] k_1/k_2
3	H	0.636	4.710×10^{-3}	1.00	0.628	4.551×10^{-3}	0.98
3	H	0.853	4.717×10^{-3}		0.848	4.650×10^{-3}	
4	H	0.719	4.593×10^{-3}	0.99	0.689	4.032×10^{-3}	1.02
4	H	0.634	4.628×10^{-3}		0.605	3.968×10^{-3}	
5	H	0.781	1.036×10^{-2}	1.12	0.775	0.980×10^{-2}	1.10
5	D	0.762	0.924×10^{-2}		0.756	0.888×10^{-2}	
6	H	0.996	9.435×10^{-3}	1.11	0.986	8.825×10^{-3}	1.11
6	D	0.922	8.525×10^{-3}		0.909	7.974×10^{-3}	
7	H	0.484	8.347×10^{-3}	1.00	0.479	8.033×10^{-3}	1.01
7	H	0.560	8.318×10^{-3}		0.554	7.937×10^{-3}	
8	H	0.900	9.873×10^{-3}	1.11	0.872	8.864×10^{-3}	1.13
8	D	0.942	8.888×10^{-3}		0.905	7.869×10^{-3}	

[a] See Table 6:5

[b] A_∞ was determined spectrophotometrically; k was obtained by least squares treatment of the kinetic data.

[c] This represents the ratio of the two rate constants from the run. For run #5, experimental $k_1/k_2 = 1.036 \times 10^{-2}/0.924 \times 10^{-2} = 1.12$; calculated $k_1/k_2 = 0.980 \times 10^{-2}/0.888 \times 10^{-2} = 1.10$.

[d] A_∞ and k were determined by data fitting of (A_t, t) to an exponential curve.

Table 6:11 Comparison of calculated and experimental kinetic data from solvolysis of *anti*-7-chloro-*exo*-2-norbornyl brosylate (53-OBs)

Run[a]	Substrate[a]	Experimental[a,b] A_∞	Experimental[a,b] $k(\sec^{-1})$	Experimental[a,b] k_1/k_2[c]	Calculated[d] A_∞	Calculated[d] $k(\sec^{-1})$	Calculated[d] k_1/k_2[c]
I0	H	0.408	6.653×10^{-3}	0.99	0.413	6.794×10^{-3}	1.00
I0	H	0.340	6.748×10^{-3}		0.341	6.818×10^{-3}	
I2	H	0.412	2.987×10^{-2}	1.11	0.408	2.040×10^{-2}	1.11
I2	D	0.414	1.872×10^{-2}		0.409	1.831×10^{-2}	
I3	H	0.480	2.096×10^{-2}	1.10	0.481	2.112×10^{-2}	1.12
I3	D	0.438	1.900×10^{-2}		0.437	1.888×10^{-2}	
I4	H	0.411	2.020×10^{-2}	1.11	0.413	2.054×10^{-2}	1.11
I4	D	0.463	1.816×10^{-2}		0.465	1.843×10^{-2}	
I5	H	0.467	2.001×10^{-2}	0.99	0.474	2.100×10^{-2}	0.99
I5	H	0.393	2.012×10^{-2}		0.400	2.121×10^{-2}	

[a] See Table 6:4

[b,c,d] See corresponding footnotes in Table 6:10.

Table 6:12 Comparison of calculated and experimental kinetic data from solvolysis of *syn*-7-chloro-*exo*-2-norbornyl brosylate (59-OBs)

		Experimental[a,b]			Calculated[d]		
Run[a]	Substrate[a]	A_∞	$k(min^{-1})$	k_1/k_2[c]	A_∞	$k(min^{-1})$	k_1/k_2[c]
18	H	0.776	1.016×10^{-2}	1.01	0.770	0.988×10^{-2}	0.99
18	H	0.906	1.003×10^{-2}		0.904	0.998×10^{-2}	
21	H	0.780	0.986×10^{-2}	1.12	0.774	0.967×10^{-2}	1.11
21	D	0.728	0.883×10^{-2}		0.725	0.868×10^{-2}	
25	H	0.676	1.001×10^{-2}	1.13	0.663	0.951×10^{-2}	1.07
25	D	0.683	0.904×10^{-2}		0.679	0.890×10^{-2}	

[a] See Table 6:7

[b,c,d] See corresponding footnotes in Table 6:10.

Table 6:13 Comparison of calculated and experimental kinetic data from solvolysis of *anti*-7-chloro-*exo*-2-norbornyl brosylate (58-OBs)

		Experimental[a,b]			Calculated[d]		
Run[a]	Substrate[a]	A_∞	$k(min^{-1})$	k_1/k_2[c]	A_∞	$k(min^{-1})$	k_1/k_2[c]
41	H	0.316	1.714×10^{-2}	1.01	0.319	1.746×10^{-2}	0.99
41	H	0.298	1.697×10^{-2}		0.304	1.760×10^{-2}	
42	H	0.356	1.717×10^{-2}	1.09	0.370	1.830×10^{-2}	1.12
42	D	0.278	1.588×10^{-2}		0.282	1.625×10^{-2}	
44	H	0.282	1.715×10^{-2}	1.09	0.286	1.768×10^{-2}	1.11
44	D	0.295	1.574×10^{-2}		0.299	1.599×10^{-2}	
46	H	0.282	1.678×10^{-2}	1.00	0.278	1.650×10^{-2}	0.99
46	H	0.290	1.677×10^{-2}		0.288	1.665×10^{-2}	
47	H	0.312	1.679×10^{-2}	1.10	0.313	1.693×10^{-2}	1.11
47	D	0.291	1.524×10^{-2}		0.289	1.518×10^{-2}	

a See Table 6:9

b,c,d See corresponding footnotes in Table 6:10.

Least Squares Program .

```
      PROGRAM TST (INPUT,OUTPUT,TAPE5=INPUT,TAPE6=OUTPUT)
C-----LEAST SQUARES PROGRAM.
      DIMENSION X(40), Y(40)
  100 READ 1, N
      IF(N.EQ.0) GO TO 101
    1 FORMAT(I3)
      DO 2 J = 1,N
    2 READ 3, X(J), Y(J)
    3 FORMAT(2F10.0)
      A = N
      SIGX = 0.0
      SGDXY = 0.0
      SGDX2 = 0.0
      SIGY = 0.0
      SIGY2 = 0.0
      SIGXY = 0.0
      DO 4 I = 1,N
    4 SIGX = SIGX + X(I)
      XBAR = SIGX/A
      DO 5 L = 1,N
      DELX = X(L) - XBAR
      SGDXY = SGDXY + Y(L)*DELX
      SGDX2 = SGDX2 + DELX**2
      SIGY2 = SIGY2 + Y(L)**2
      SIGY = SIGY + Y(L)
      SIGXY = SIGXY + X(L)*Y(L)
    5 CONTINUE
      SLOPE = SGDXY/SGDX2
      SYDX2 = (SIGY2 - ((SIGY**2)/A) - SLOPE*SIGXY + (SLOPE*SIGX*SIGY/A)
     1)/(A - 2.0)
      SB = SQRT(SYDX2/SGDX2)
      YBAR = SIGY/A
      CEPT = YBAR - SLOPE*XBAR
      SA = SQRT(SYDX2/A)
      PRINT 6, SLOPE, SB
    6 FORMAT(1H0,4X,8HSLOPE   =,E14.6,5X,28HSTANDARD DEVIATION =,E13.6)
      PRINT 7, CEPT, SA
    7 FORMAT(1H0,12HINTERCEPT  =,E14.6,5X,28HSTANDARD DEVIATION =,E13.6)
      PRINT 8
    8 FORMAT(1H0,15X,10H**********)
      GO TO 100
  101 CALL EXIT
      END
```

Program for data fitting to an exponential curve of the general form

$$y = Ae^{-Bx} + C$$

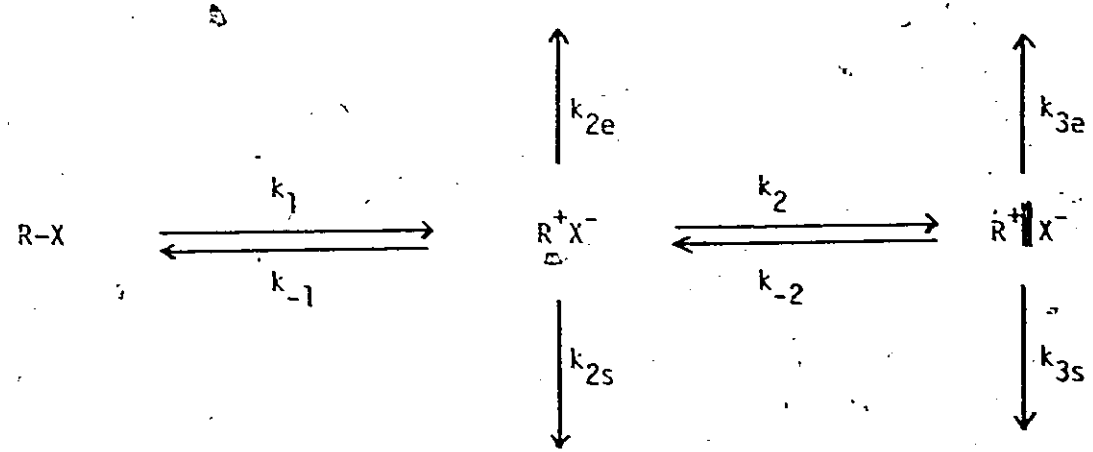
```
      PROGRAM TST (INPUT,OUTPUT, TAPE5 = INPUT)
C     EXPONENTIAL CURVE FIT OF Y= A * EXP(-B*X) + C
      DIMENSION X(100),Y(100)
C     READ IN NUMBER OF OBSERVATIONS N  (RIGHT ADJUSTED COL. 5)
C           NUMBER OF ITERATIONS LMAX AND EPSILON
  345 READ 1,5, N, LMAX, EPSILON
      IF(EOF(5)) 30,33
   33 IFLAG = 0
C     READ IN X AND Y INPUT DATA
      READ 101, (X(I),I=1,N)
      READ 101, (Y(I),I=1,N)
      PRINT 512, (X(I),I=1,N)
      PRINT 661, (Y(I),I=1,N)
C     STANDARD DEVIATION
      A=N
      SIGX = 0.0
      SGGXY = 0.0
      SGGX2 = 0.0
      SIGY = 0.0
      SIGY2 = 0.0
      SIGXY = 0.0
      DO 44 I = 1,N
   44 SIGX = SIGX + X(I)
      XBAR = SIGX/A
      DO 5 L = 1,N
      DELX = X(L) - XBAR
      SGGXY = SGGXY + Y(L)*DELX
      SGGX2 = SGGX2 + DELX**2
      SIGY2 = SIGY2 + Y(L)**2
      SIGY = SIGY + Y(L)
      SIGXY = SIGXY + X(L)*Y(L)
    5 CONTINUE
      SLOPE = SGGXY/SGGX2
      SY2X2 = (SIGY2 - ((SIGY**2)/A) - SLOPE*SIGXY+(SLOPE*SIGX*SIGY/A)
     1)/(A - 2.0)
      SB = SQRT(SY2X2/SGGX2)
      PRINT 6, SB
    6 FORMAT(1HJ,5X,20HSTANDARD DEVIATION =,E13.6)
      P=(Y(N)-Y(N-1))*(X(2)-X(1))
      Q = (Y(2)-Y(1))*(X(N)-X(N-1))
      R=ABS(P/Q)
      S=X(N)+X(N-1)-X(2)-X(1)
      B=2.*ALOG(R)/S
      E=(Y(N)-Y(N-1))*EXP((+B)*(X(N)+X(N-1))/2.0)*(+B)
      A=(Y(N)-Y(N-1))/E
      M=(N+1)/2
      C=Y(M)-A*EXP((+B)*X(M))
C     COMPUTATION OF CORRECTIONS FOLLOWS
```

continued →

```
      DO 2 L=1, LMAX
      H0=H1=H2=H3=H4=H5=H6=H7=0.0
      DO 3 I=1,N
      EX1 = EXP((+B)*X(I))
      EX2=EX1*EX1
      XIEX1=X(I)*EX1
      XIEX2 = X(I)*EX2
      XI2EX2=X(I)*XIEX2
      H0  = H0  + EX1
      H1  = H1  + EX2
      H2  = H2  + XIEX1
      H3  = H3  + XIEX2
      H4  = H4  + XI2EX2
      H5  = H5  + Y(I)
      H6  = H6  + Y(I)*EX1
      H7  = H7  + Y(I)*XIEX1
    3 CONTINUE
C
CC    COMPUTATION OF SUM TERMS IN NORMAL EQUATIONS
C
      D11=H1
      D12=H3*A
      D13=H0
      D22=H4*A*A
      D23=H2*A
      D33 = N
      F1  = -H1*A-H0*C + H6
      F2  = -H3*A*A-H2*C*A + H7*A
      F3  = -H0*A-D33*C + H5
      DELTA11 = D22*D33-D23*D23
      DELTA12 = D13*D23-D12*D33
      DELTA13 = D12*D23-D13*D22
      DELTA22 = D11*D33-D13**2
      DELTA23 = D12*D13-D11*D23
      DELTA33 = D11*D22-D12**2
      DELTA = D11*DELTA11 + D12*DELTA12 + D13*DELTA13
      U  = (F1*DELTA11+F2*DELTA12+F3*DELTA13)/DELTA
      V  = (F1*DELTA12 + F2*DELTA22 + F3*DELTA23)/DELTA
      W  = (F1*DELTA13 + F2*DELTA23 + F3*DELTA33)/DELTA
      A  = A+U
      B  = B+V
      C  = C+ W
      ESQ = 0.0
      DO 4 I=1,N
      ESQ = ESQ + (Y(I)-C-A*EXP((+B)*X(I)))**2
    4 CONTINUE
      IF(L.EQ.1) GO TO 510
      IF(ABS(SAVE-ESQ).LT.EPSILON) GO TO 73
      IF(L.LT.LMAX) GO TO 500
      GO TO 600
  500 SAVE = ESQ
    2 CONTINUE
  600 IFLAG = 1
   73 PRINT 102, IFLAG,L,A,B,C
      GO TO 345
   20 STOP

  100 FORMAT(2I5,F10.0)
  101 FORMAT(8F10.0)
  102 FORMAT(*0THE FOLLOWING ARE THE FINAL RESULTS IF IFLAG=0 CALCULATIO
     -N IS 0.K.*/* IF IFLAG=1 CALCULATION IS NOT FINISHED YET BUT THE EP
     -SILON IS TOO SMALL PLEASE CHANGE EPSILON AND RERUN THIS JOB*/
     -*0IFLAG = *I3/*0AFTER*I3*ITERATIONS*/*0          A(0) =*E16.8/
     -*0          ALPHA =*E16.8/*0A(INFINITY) =*E16.8)
  510 FORMAT(41H1EXPONENTIAL CURVE FIT OF Y=A*EXP(-B*X)+C/* INPUT DATA O
     -F X */(1X,10F10.5))
  501 FORMAT(*0INPUT DATA OF Y */(1X,10F10.5))
  502 FORMAT(*0STANDARD DEVIATION = *E15.5//)
      END
```

F Steady state treatment of the solvolytic ion-pair scheme



P = product

$$\frac{dP}{dt} = k_{2e}[R^+X^-] + k_{2s}[R^+X^-] + k_{3e}[R^+\|X^-] + k_{3s}[R^+\|X^-] \qquad \text{Eq. 6:10}$$

$$\frac{d[R^+X^-]}{dt} = k_1[RX] + k_{-2}[R^+\|X^-] - k_{-1}[R^+X^-] - k_{2e}[R^+X^-] - k_{2s}[R^+X^-] - k_2[R^+X^-] = 0$$

$$[R^+X^-] = \frac{k_1[RX] + k_{-2}[R^+\|X^-]}{k_{-1} + k_{2e} + k_{2s} + k_2} \qquad \text{Eq. 6:11}$$

$$\frac{d[R^+\|X^-]}{dt} = k_2[R^+X^-] - k_{-2}[R^+\|X^-] - k_{3e}[R^+\|X^-] - k_{3s}[R^+\|X^-] = 0$$

$$[R^+\|X^-] = \frac{k_2[R^+X^-]}{k_{-2} + k_{3e} + k_{3s}} \qquad \text{Eq. 6:12}$$

Substitution of Eq 6:12 into Eq 6:11 yields

$$[R^+X^-] = \frac{k_1[RX] + \dfrac{k_{-2}k_2[R^+X^-]}{k_{-2} + k_{3e} + k_{3s}}}{k_{-1} + k_{2e} + k_{2s} + k_2}$$

$$[R^+X^-] = \frac{(k_{-2} + k_{3e} + k_{3s})k_1[RX] + k_{-2}k_2[R^+X^-]}{(k_{-1} + k_{2e} + k_{2s} + k_2)(k_{-2} + k_{3e} + k_{3s})}$$

$$[R^+X^-] = \frac{(k_{-2} + k_{3e} + k_{3s})k_1[RX]}{(k_{-1} + k_{2e} + k_{2s} + k_2)(k_{-2} + k_{3e} + k_{3s}) - k_2k_{-2}} \qquad \text{Eq. 6:13}$$

Substitution of Eq 6:13 into Eq 6:12 yields

$$[R^+\|X^-] = \frac{k_1 k_2 [RX]}{(k_{-1} + k_{2e} + k_{2s} + k_2)(k_{-2} + k_{3e} + k_{3s}) - k_2 k_{-2}} \qquad \text{Eq. 6:14}$$

Substituting Eq's 6:13 and 6:14 into Eq. 6:10 gives

$$\frac{dP}{dt} = \frac{(k_{2e} + k_{2s})(k_{-2} + k_{3e} + k_{3s})k_1[RX]}{(k_{-1} + k_{2e} + k_{2s} + k_2)(k_{-2} + k_{3e} + k_{3s}) - k_2 k_{-2}} + \frac{(k_{3e} + k_{3s})k_1 k_2 [RX]}{(k_{-1} + k_{2e} + k_{2s} + k_2)(k_{-2} + k_{3e} + k_{3s}) - k_2 k_{-2}}$$

$$k_{total} = k_1 \left(\frac{(k_{2e} + k_{2s})(k_{-2} + k_{3e} + k_{3s}) + (k_{3e} + k_{3s})k_2}{(k_{-1} + k_{2e} + k_{2s} + k_2)(k_{-2} + k_{3e} + k_{3s}) - k_2 k_{-2}} \right)$$

$$k_t = k_1 \left(\frac{(k_{2e} + k_{2s})(k_{-2} + k_{3e} + k_{3s}) + (k_{3e} + k_{3s})k_2}{(k_{2e} + k_{2s})(k_{-2} + k_{3e} + k_{3s}) + (k_{3e} + k_{3s})k_2 + k_{-1}(k_{-2} + k_{3e} + k_{3s})} \right)$$

$$\frac{k_t^H}{k_t^D} = \frac{k_1^H}{k_1^D} \left(\frac{(k_{2e}^H + k_{2s}^H)(k_{-2}^H + k_{3e}^H + k_{3s}^H) + (k_{3e}^H + k_{3s}^H)k_2^H}{(k_{2e}^D + k_{2s}^D)(k_{-2}^D + k_{3e}^D + k_{3s}^D) + (k_{3e}^D + k_{3s}^D)k_2^D} \right) \times$$

$$\left(\frac{(k_{2e}^D + k_{2s}^D)(k_{-2}^D + k_{3e}^D + k_{3s}^D) + (k_{3e}^D + k_{3s}^D)k_2^D + k_{-1}^D(k_{-2}^D + k_{3e}^D + k_{3s}^D)}{(k_{2e}^H + k_{2s}^H)(k_{-2}^H + k_{3e}^H + k_{3s}^H) + (k_{3e}^H + k_{3s}^H)k_2^H + k_{-1}^H(k_{-2}^H + k_{3e}^H + k_{3s}^H)} \right)$$

CHAPTER 7

REFERENCES

1. A. Freund, *J. prakt. Chem.*, (2) 26, 367 (1877).

2. A Baeyer, *Chem. Ber.*, 18, 2277 (1885).

3. G. Gustavson, *J. prakt. Chem.*, (2) 36, 300 (1887).

4. W.A. Lathan, L. Radom, P.C.Hariharan, W.J. Hehre and J.A. Pople, *Fortschr. Chem. Forsch.*, 40, 1 (1973).

5. L. Radom, W.A. Lathan, W.J. Hehre and J.A. Pople, *J. Amer. Chem. Soc.*, 93, 5339 (1971).

6. E. Goldfish, *J. Chem. Educ.*, 36, 408 (1959).

7. W.A. Bernett, *J. Chem. Educ.*, 44, 17 (1967).

8. A.D. Walsh, *Trans. Faraday Soc.*, 49, 179 (1949).

9. K.B. Wiberg and B.J. Nist, *J. Amer. Chem. Soc.*, 83, 1226 (1961).

10. J.J. Burke and P.C. Lauterbur, *J. Amer. Chem. Soc.*, 86, 1870 (1964).

11. C.A. Coulson and W.E. Moffitt, *Phil. Mag.*, 40, 1 (1949).

12. C.H. DePuy, *Accounts Chem. Res.*, 1, 33 (1968).

13. C.J. Collins, *Chem. Rev.*, 69, 543 (1969).

14. C.C. Lee, *Progr. Phys. Org. Chem.*, 7, 129 (1970).

15. J.L. Fry and G.J. Karabatsos in *Carbonium Ions*, Vol. 2, G.A. Olah and P.von R. Schleyer, Ed., Wiley-Interscience, New York, N.Y., 1970, Chapter 4.

16. M. Saunders, P. Vogel, E.L. Hagen and J. Rosenfeld, *Accounts Chem. Res.*, 6, 53 (1973).

17. C.H. DePuy, *Fortschr. Chem. Forsch.*, 40, 73 (1973).

18. P. von R. Schleyer and G.W. van Dine, *J. Amer. Chem. Soc.*, 88, 2321 (1966).

19. M.J.S. Dewar and J.M. Harris, *J. Amer. Chem. Soc.*, 90, 4468 (1968).

20. Y.E. Rhodes and T. Takino, *J. Amer. Chem. Soc.*, 90, 4469 (1968).

21. R.G. Bergman and D.R. Kelsey, *J. Amer. Chem. Soc.*, 93, 1941 (1971).

22. R.G. Bergman and S.A. Sherrod, *J. Amer. Chem. Soc.*, 93, 1925 (1971).

23. S. Sarel, J. Yovell and M. Sarel-Imber, *Angew. Chem. Internat. Edit.*, 7, 577 (1968).

24. R.T. LaLonde and L.S. Forney, *J. Amer. Chem. Soc.*, 85, 3767 (1963).

25. R. Criegee and A. Rimmelin, *Chem. Ber.*, 90, 414 (1957).

26. E.J. Corey, M. Ohno, S.W. Chow and R.A. Scherrer, *J. Amer. Chem. Soc.*, 81, 6305 (1959).

27. D.J. Cram, *Fundamentals of carbanion Chemistry*, Academic Press Inc., New York, N.Y., 1965, Chapter 4.

28. C.H. DePuy and F.W. Breitbeil, *J. Amer. Chem. Soc.*, 85, 2176 (1963).

29. C.H. DePuy, F.W. Breitbeil and K.R. DeBruin, *J. Amer. Chem. Soc.*, 88, 3347 (1966).

30. A. Nickon, J.H. Hammons, J.L. Lambert and R.O. Williams, *J. Amer. Chem. Soc.*, 85, 3713 (1963).

31. A. Nickon, J.L. Lambert, R.O. Williams and N.H. Werstiuk, *J. Amer. Chem. Soc.*, 88, 3354 (1966).

32. J.B. Hendrickson and R.K. Boeckman, *J. Amer. Chem. Soc.*, 91, 3269 (1969).

33. S.J. Cristol, W.Y. Lim and A.R. Dahl, *J. Amer. Chem. Soc.*, 92, 4013 (1970).

34. P.S. Wharton and T.I. Bair, *J. Org. Chem.*, 31, 2480 (1966).

35. W.R. Moore, K.G. taylor, P. Muller, S.S. Hall and Z.L. Gaibel, *Tetrahedron Letters*, 2365 (1970).

36. R.T. LaLonde and J.J. Batelka, *Tetrahedron Letters*, 445 (1964).

37. R.T. LaLonde, J. Ding and M.A. Tobias, *J. Amer. Chem. Soc.*, 89, 6651 (1967).

38. H. Hogeveen, C.F. Roobeek and H.C. Volger, *Tetrahedron Letters*, 221 (1972).

39. R.J. Warnet and D.M.S. Wheeler, *Chem. Commun.*, 547 (1971).

40. A. Nickon and J.H. Hammons, *J. Amer. Chem. Soc.*, 86, 3322 (1964).

41. J.H. Hammons, E.K. Probasco, L.A. Sanders and E.J. Whalen, *J. Org. Chem.*, 33, 4493 (1968).

42. R.T. LaLonde and A.D. Debboli, *J. Org. Chem.*, 35, 2657 (1970).

43. S.J. Cristol, J.K. Harrington, T.C. Morrill and B.E. Greenwald, *J. Org. Chem.*, 36, 2773 (1971).

44. R.T. LaLonde and L.S. Forney, *J. Amer. Chem. Soc.*, 85, 3767 (1963).

45. R.C. Cookson, D.P.G. Hamon and J. Hudec, *Chem. Commun.*, 5782 (1963).

46. H.H. Wasserman and D.C. Clagett, *Tetrahedron Letters*, 341 (1964).

47. J. Paasivirta, *Acta Chem. Scand.*, 27, 374 (1973).

48. J. Paasivirta and P. Hirsjarvi, *Acta Chem. Scand.*, 27, 1098 (1973).

49. T.C. Morrill and B.E. Greenwald, *J. Org. Chem.*, 36, 2769 (1971).

50. J.B. Hendrickson and R.K. Boeckman, *J. Amer. Chem. Soc.*, 93, 4491 (1971).

51. N.C. Deno and D.N. Lincoln, *J. Amer. Chem. Soc.*, 88, 5357 (1966).

52. S.J. Cristol and R.T. LaLonde, *J. Amer. Chem. Soc.*, 80, 4355 (1958).

53. C.H. DePuy, W.C. Arney and D.H. Gibson, *J. Amer. Chem. Soc.*, 90, 1830 (1968).

54. A. De Boer and C.H. DePuy, *J. Amer. Chem. Soc.*, 92, 4008 (1970).

55. C.H. DePuy and R.H. McGirk, *J. Amer. Chem. Soc.*, 96, 1121 (1974).

56. C.H. DePuy and R.H. McGirk, *J. Amer. Chem. Soc.*, 95, 2366 (1973).

57. W.A.G. Graham and F.G.A. Stone, *Chem. Ind.*, 1096 (1957).

58. B. Rickborn and S.E. Wood, *J. Amer. Chem. Soc.*, 93, 3940 (1971).

59. R.J. Ouellette and C. Levin, *J. Amer. Chem. Soc.*, 90, 6889 (1968).

60. L.A. Paquette, *Accounts Chem. Res.*, 4, 280 (1971).

61. A. South Jr. and R.J. Ouellette, *J. Amer. Chem. Soc.*, 90, 7064 (1968).

62. R.J. Ouellette and S. Williams, *J. Org. Chem.*, 35, 3210 (1970).

63. S. Moon, *J. Org. Chem.*, 29, 3456 (1964).

64. R.J. Ouellette, D. Miller, A. South Jr. and R.D. Robins, *J. Amer. Chem. Soc.*, 91, 971 (1969).

65. H. Hart and R.H. Schlosberg, *J. Amer. Chem. Soc.*, 88, 5030 (1966).

66. H. Hart and R.H. Schlosberg, *J. Amer. Chem. Soc.*, 90, 5189 (1968).

67. R.L. Baird and A.A. Aboderin, *J. Amer. Chem. Soc.*, 86, 252 (1964).

68. P.E. Peterson and G. Thompson, *J. Org. Chem.*, 33, 968 (1968).

69. P.B.D. de la Mare and R. Bolton, *Electrophilic Additions to Unsaturated Systems*, Elsevier, New York, N.Y., 1965, p. 26.

70. M.A. McKinney, S.H. Smith, S. Hempelman, M.M. Gearon and L. Pearson, *Tetrahedron Letters*, 3657 (1971).

71. M.A. McKinney and E.C. So, *J. Org. Chem.*, 37, 2818 (1972).

72. J.D. Roberts and C.C. Lee, *J. Amer. Chem. Soc.*, 73, 5009 (1951).

73. J.D. Roberts, C.C. Lee and W.H. Saunders Jr., *J. Amer. Chem. Soc.*, 76, 4501 (1954).

74. P.S. Skell and I. Starer, *J. Amer. Chem. Soc.*, 82, 2971 (1960).

75. P.S. Skell and I. Starer, *J. Amer. Chem. Soc.*, 84, 3962 (1962).

76. J.A. Berson and P.W. Grubb, *J. Amer. Chem. Soc.*, 87, 4016 (1965).

77. B.M. Benjamin, B.W. Ponder and C.J. Collins, *J. Amer. Chem. Soc.*, 88, 1558 (1966).

78. B.M. Benjamin and C.J. Collins, *Tetrahedron Letters*, 5477 (1966).

79. C.J. Collins and B.M. Benjamin, *J. Amer. Chem. Soc.*, 89, 1652 (1967).

80. S.A. Sherrod, R.G. Bergman, G.J. Gleicher and D.G. Morris, *J. Amer. Chem. Soc.*, 92, 3469 (1970).

81. R.C. Bingham, W.F. Sliwinski and P.v.R. Schleyer, *J. Amer. Chem. Soc.*, 92, 3471 (1970).

82. S.A. Sherrod, R.G. Bergman, G.J. Gleicher and D.G. Morris, *J. Amer. Chem. Soc.*, 94, 4615 (1972).

83. J.D. Roberts and M. Halmann, *J. Amer. Chem. Soc.*, 75, 5759 (1953).

84. O.A. Reutov and T.N. Shatkina, *Tetrahedron*, 18, 237 (1962).

85. G.J. Karabatsos and C.E. Orzech,Jr., *J. Amer. Chem. Soc.*, 84, 2838 (1962).

86. G.J. Karabatsos and J.D. Graham, *J. Amer. Chem. Soc.*, 82, 5250 (1960).

87. P.S. Skell, I. Starer and A.P. Krapcho, *J. Amer. Chem. Soc.*, 82, 5257 (1960).

88. R.L. Baird and A. Aboderin, *Tetrahedron Letters*, 235 (1963).

89. R.L. Baird and A.A. Aboderin, *J. Amer. Chem. Soc.*, 86, 252 (1964).

90. N.C. Deno, D. LaVietes, J. Mockus and P.C. Scholl, *J. Amer. Chem. Soc.*, 90, 6457 (1968).

91. C.C. Lee and L. Gruber, *J. Amer. Chem. Soc.*, 90, 3775, 3778 (1968).

92. C.C. Lee, L. Gruber and K.M. Wan, *Tetrahedron Letters*, 2587 (1968).

93. C.H. DePuy, A.H. Andrist and P.C. Funfschilling, *J. Amer. Chem. Soc.*, 96, 948 (1974).

94. R. Hoffmann, *J. Chem. Phys.*, 40, 2480 (1964).

95. J.D. Petke and J.L. Whitten, *J. Amer. Chem. Soc.*, 90, 3338 (1968).

96. H. Fischer, H. Kollmar, H.O. Smith and K. Miller, *Tetrahedron Letters*, 5821 (1968).

97. H. Kollmar and H.O. Smith, *Tetrahedron Letters*, 1833 (1970).

98. H. Kollmar and H.O. Smith, *Angew. Chem., Int. Ed. Engl.*, 9, 462 (1970).

99. J.E. Williams, R. Sustmann, L.C. Allen and P.v.R. Schleyer, *J. Amer. Chem. Soc.*, 91, 1037 (1969).

100. R. Sustmann, J.E. Williams, M.J.S. Dewar, L.C. Allen and P.v.R. Schleyer, *J. Amer. Chem. Soc.*, 91, 5350 (1969).

101. L. Radom, J.A. Pople, V. Buss and P.v.R. Schleyer, *J. Amer. Chem. Soc.*, 93, 1813 (1971).

102. L. Radom, J.A. Pople, V. Buss and P.v.R. Schleyer, *J. Amer. Chem. Soc.*, 94, 311 (1972).

103. P.C. Hariharan, L. Radom, J.A. Pople and P.v.R. Schleyer, *J. Amer. Chem. Soc.*, 96, 599 (1974).

104. A.H. Andrist, *J. Amer. Chem. Soc.*, 95, 7531 (1973).

105. G.S. Hammond, *J. Amer. Chem. Soc.*, 77, 334 (1955).

106. K.B. Wiberg, *Chem. Rev.*, 55, 713 (1955).

107. E.R. Thornton, *J. Amer. Chem. Soc.*, 89, 2915 (1967).

108. G.J. Frisone and E.R. Thornton, *J. Amer. Chem. Soc.*, 90, 1211 (1968).

109. J.C. Harris and J.L. Kurz, *J. Amer. Chem. Soc.*, 92, 349 (1970).

110. E.M. Kosower, *Introduction to Physical Organic Chemistry*, J. Wiley and Sons, Inc. New York, 1968, p. 54.

111. H.C. Urey, F.G. Brickwedde and G.M. Murphy, *Phys. Rev.*, 39, 164 (1932).

112. G.N. Lewis and R.T. MacDonald, *J. Chem. Phys.*, 1, 341 (1933).

113. H. Eyring and A. Sherman, *J. Chem. Phys.*, 1, 335 (1933).

114. E.R. Washburn and H.C. Vroy, *Proc. Natl. Acad. Sci.*, 18, 496 (1932).

115. *Isotope Effects in Chemical Reactions*, ACS Monograph 167, C.J. Collins and N.S. Bowman, Ed., Van Nostrand-Reinhold, New York, N.Y., 1970.

a) Chapter 3
b) page 205, reference 80

116. S.E. Scheppele, *Chem. Rev.*, 72, 511 (1972).

117. E.R. Thornton, *Ann. Rev. Phys. Chem.*, 17, 349 (1966).

118. E.R. Thornton, *Solvolysis Mechanisms*, Ronald Press, New York, 1964.

119. F.H. Westheimer, *Chem. Rev.*, 61, 265 (1961).

120. W.H. Saunders Jr., *Surv. Prog. Chem.*, 3, 109 (1966).

121. J. Bigeleisen and M. Wolfsberg, *Adv. Chem. Phys.*, 1, 15 (1958).

122. J. Bigeleisen, *Science*, 147, 463 (1965).

123. C.J. Collins, *Advan. Phys. Org. Chem.*, 2, 1 (1964).

124. E.A. Halevi, *Prog. Phys. Org. Chem.*, 1, 109 (1963).

125. R.E. Weston, Jr., *Science*, 158, 332 (1967).

126. R.E. Robertson, *Prog. Phys. Org. Chem.*, 4, 213 (1967).

127. M.J. Goldstein, *Science*, 154, 1616 (1966).

128. H. Simon and D. Palm, *Angew. Chem. Internat. Ed. Eng.*, 5, 920 (1966).

129. K.B. Wiberg, *Chem. Rev.*, 55, 713 (1955).

130. L. Melander, *Isotope Effects on Reaction Rates*, Ronald Press, New York, 1960.

131. M. Wolfsberg, *Ann. Rev. Phys. Chem.*, 20, 449 (1969).

132. L.S. Bartell, *J. Amer. Chem. Soc.*, 83, 3567 (1961).

133. L.S. Bartell, *Tetrahedron*, 17, 177 (1962).

134. S. Glasstone, K. Laidler and H. Eyring, *The Theory of Rate Processes*, McGraw Hill, New York, 1941.

135. J. Bigeleisen and M.G. Mayer, *J. Chem. Phys.*, 15, 261 (1947).

136. E.S. Lewis and J.K. Robinson, *J. Amer. Chem. Soc.*, 90, 4337 (1968).

137. E.S. Lewis and L.H. Funderburk, *J. Amer. Chem. Soc.*, 89, 2322 (1967).

138. E.F. Caldin and M. Kasparian, *Discuss. Faraday Soc.*, 39, 25 (1965).

139. S. Winstein and D. Trifan, *J. Amer. Chem. Soc.*, 71, 2953 (1949).

140. S. Winstein, B.K. Morse, E. Grunwald, H.W. Jones, J. Corse, D. Trifan and H. Marshall, *J. Amer. Chem. Soc.*, 74, 1127 (1952).

141. S. Winstein and D. Trifan, *J. Amer. Chem. Soc.*, 74, 1147, 1154 (1952).

142. S. Winstein, E. Clippinger, R. Howe and E. Vogelfanger, *J. Amer. Chem. Soc.*, 87, 376 (1965).

143. S. Winstein, *J. Amer. Chem. Soc.*, 87, 381 (1965).

144. J.A. Berson in *Molecular Rearrangements*, Part 1, P. de Mayo, Ed., Interscience, New York, N.Y., 1963, Chapter 3.

145. P.D. Bartlett, *Nonclassical Ions*, W.A. Benjamin, New York, N.Y. 1965.

146. G.D. Sargent, *Quart. Rev., Chem. Soc.*, 20, 301 (1966).

147. G.D. Sargent in *Carbonium Ions*, Vol. 3, G.A. Olah and P.v.R. Schleyer, Ed., Interscience, New York, N.Y., 1972, Chapter 24.

148. G.E. Gream, *Rev. Pure Appl. Chem .*, 16, 25 (1966).

149. H.C. Brown, *Chem. Soc.*, Spec. Publ., No. 16, 140 (1962).

150. H.C. Brown, *Chem. Eng. News*, 45, 87 (1967).

151. H.C. Brown, *Accounts Chem. Res.*, 6, 377 (1973).

152. H.C. Brown, *Chem. Brit.*, 199 (1966).

153. G.A. Olah, A.M. White, J.R. DeMember, A. Commeyras and C.Y. Lui, *J. Amer. Chem. Soc.*, 92, 4627 (1970).

154. C.C. Lee and E.W.C. Wong, *J. Amer. Chem. Soc.*, 86, 2752 (1964).

155. C.C. Lee and E.W.C. Wong, *Can. J. Chem.*, 43, 2254 (1965).

156. B.L. Murr and J.A. Conkling, *J. Amer. Chem. Soc.*, 92, 3462 (1970).

157. J.P. Schaefer, M.J. Dagani and D.S. Weinberg, *J. Amer. Chem. Soc.*, 89, 6938 (1967).

158. B.L. Murr and J.A. Conkling, *J. Amer. Chem. Soc.*, 92, 3464 (1970).

159. J.M. Jerkunica, S. Borcic and D.E. Sunko, *Chem. Commun.*, 1302 (1967).

160. B.L. Murr, A. Nickon, T.D. Swartz and N.H. Werstiuk, *J. Amer. Chem. Soc.*, 89, 1730 (1967).

161. J.M. Jerkunica, S. Borcic and D.E. Sunko, *J. Amer. Chem. Soc.*, 89, 1732 (1967).

162. S. Borcic, V. Belanic-Lipovac and D.E. Sunko, *Croat. Chem. Acta*, 33, 35 (1961).

163. N.H. Werstiuk, R.R. MacDonald, R.W. Ouwehand, W.L. Chan, F.P. Cappelli, J.G. Ballard, R.E. Young, R.E. Massey and G. Timmins, *Tetrahedron Lett.*, 49, 4363 (1970).

164. N.H. Werstiuk, R.R. MacDonald, R.W. Ouwehand, W.L. Chan, F.P. Cappelli, J.G. Ballard, R.E. Young, R.E. Massey, G. Timmins, I. Goodwin, A. Walling and Y. Teruta, *Can. J. Chem.*, 50, 618 (1972).

165. A. Streitweiser, Jr., *Solvolytic Displacement Reactions*, McGraw-Hill Book Co., New York, 1962, pp. 172-175.

166. A. Streitweiser, Jr., R.H. Jagow, C.R. Fahey and S. Suzuki, *J. Amer. Chem. Soc.*, 80, 2326 (1958).

167. V.J. Shiner, Jr., R. Fisher and W. Dowd, *J. Amer. Chem. Soc.*, 91, 7748 (1969).

168. V.J. Shiner, Jr., *J. Amer. Chem. Soc.*, 74, 5285 (1952).

169. E.S. Lewis and C.E. Boozer, *J. Amer. Chem. Soc.*, 74, 6306 (1952).

170. V.J. Shiner, Jr., *J. Amer. Chem. Soc.*, 75, 2925 (1953).

171. V.J. Shiner, Jr., *Tetrahedron*, 5, 243 (1959).

172. E.S. Lewis, *Tetrahedron*, 5, 143 (1959).

173. V.J. Shiner, Jr., W.E. Buddenbaum, B.L. Murr and G. Lamaty, *J. Amer. Chem. Soc.*, 90, 418 (1968).

174. V.J. Shiner, Jr. and J.S. Humphrey, Jr., *J. Amer. Chem. Soc.*, 85, 2416 (1963).

175. H.L. Goering and K. Humski, *J. Amer. Chem. Soc.*, 91, 4594 (1969).

176. P.G. Gassman and J.M. Hornback, *J. Amer. Chem. Soc.*, 94, 7010 (1972).

177. P.G. Gassman and J.M. Hornback, *J. Amer. Chem. Soc.*, 91, 4280 (1969).

178. J.D. Roberts, F.O. Johnson and R.A. Carboni, *J. Amer. Chem. Soc.*, 76, 5692 (1954).

179. F.P. Cappelli, G. Timmins and N.H. Werstiuk, *Can. J. Chem.*, 50, 2163 (1972).

180. N.H. Werstiuk, *personal communication.*

181. H.L. Goering and M.J. Degani, *J. Amer. Chem. Soc.*, 91, 4506 (1969).

182. H. Tanida and Y. Hata, *J. Org. Chem.*, 30, 977 (1965).

183. H.C. Brown and C.P. Garg, *J. Amer. Chem. Soc.*, 83, 2952 (1961).

184. J. Meinwald, J. Crandall and W.E. Hymans, *Org. Syn.*, 45, 77 (1965).

185. H.C. Brown and B.C. Subba Rao, *J. Amer. Chem. Soc.*, 81, 6428 (1959).

186. R.N. McDonald and T.E. Tabor, *J. Org. Chem.*, 33, 2934 (1968).

187. E. Tobler, D.E. Battin and D.J. Foster, *J. Org. Chem.*, 29, 2834 (1964).

188. C.C. Hinckley, *J. Amer. Chem. Soc.*, 91, 5160 (1969).

189. J.K.M. Sanders and D.H. Williams, *Chem. Commun.*, 422 (1970).

190. J.K.M. Sanders and D.H. Williams, *J. Amer. Chem. Soc.*, 93, 641 (1971).

191. A.F. Cockerill, G.L.O. Davies, R.C. Harden and D.M. Rackham, *Chem. Rev.*, 73, 553 (1973).

192. J. Paasivirta, *Suomen Kemistilehti*, 44B, 131 (1971).

193. T. Kadai, *Ph.D. Dissertation*, McMaster University (1973).

194. C.W. Jefford, S. Mahajan, J. Waslyn and B. Waegell, *J. Amer. Chem. Soc.*, 87, 2183 (1965).

195. C.K. Alden and D.I. Davies, *J. Chem. Soc.*, C, 709 (1968).

196. R.A. Finnegan and R.S. McNees, *J. Org. Chem.*, 29, 3234 (1964).

197. A.T. Blomquist and R.J. Himics, *Tetrahedron Lett.*, 3947 (1967).

198. R.R. Sauers and R.J. Kiesel, *J. Amer. Chem. Soc.*, 89, 4695 (1967).

199. E.W.C. Wong and C.C. Lee, *Can. J. Chem.*, 42, 1245 (1964).

200. J.I. Musher, *Mol. Phys.*, 6, 93 (1963).

201. P. Laszlo and P.v.R. Schleyer, *J. Amer. Chem. Soc.*, 86, 1171 (1964).

202. S.J. Cristol and G.W. Nachtigall, *J. Org. Chem.*, 32, 3738 (1967).

203. E.I. Snyder and B. Franzus, *J. Amer. Chem. Soc.*, 86, 1166 (1964).

204. J.C. Davis, Jr., and T.V. Van Auken, *J. Amer. Chem. Soc.*, 87, 3900 (1965).

205. W. DeW. Horrocks, Jr., *Inorg. Chem.*, 9, 690 (1970).

206. D.R. Eaton, A.D. Josey, W.D. Phillips and R.E. Benson, *J. Chem. Phys.*, 39, 3513 (1963).

207. R.M. Silverstein and G.C. Bassler, *Spectrometric Identification of Organic Compounds*, John Wiley and Sons, Inc., New York, 1968. p. 132

208. H.O. House, *Modern Synthetic Reactions*, Second Edition, W.A. Benjamin, Inc., Menlo Park, California, 1972. pp. 62-64.

209. B. Franzus and E.I. Snyder, *J. Amer. Chem. Soc.*, 87, 3423 (1965).

210. P.R. Story, *J. Org. Chem.*, 26, 287 (1961).

211. B. Franzus and J.H. Surridge, *J. Org. Chem.*, 33, 1288 (1968).

212. N.H. Werstiuk, *Can. J. Chem.*, 48, 2310 (1970).

213. C.R. Warner, R.J. Strunk and H.G. Kuivila, *J. Org. Chem.*, 31, 3381 (1966).

214. J.M. Jerkunica, *Personal Communication*, 1973.

215. J. Paasivirta, *Suomen Kemistilehti* 36B, 156 (1963).

216. N. Toivonen, E. Siltanen and K. Ojala, *Ann. Acad. Sci. Fennicae*, A II 64, (1955).

217. P. Hirsjarvi, H.L. Kauppinen and S. Paavolainen, *Suomen Kemistilehti* B 42, 236 (1969).

218. G.C. Swain and C.R. Morgan, *J. Org. Chem.*, 29, 2097 (1964).

219. Kindly written for us by Mr. Michael S. Yu, Department of Applied Mathematics, McMaster University.

220. K. Biemann, *Mass Spectrometry, Organic Chemical Applications*, McGraw-Hill Book Co., Inc., New York, N.Y., 1962. Chapter 5.

221. J.D. Roberts and W. Bennett, *J. Amer. Chem. Soc.*, 76, 4623 (1954).

222. J.D. Roberts, W. Bennett and R. Armstrong, *J. Amer. Chem. Soc.*, 72, 3329 (1950).

223. H.C. Brown, J.H. Kawakami and K.T. Liu, *J. Amer. Chem. Soc.*, 95, 2209 (1973).

224. H.C. Brown, J.H. Kawakami and S. Ikegami, *J. Amer. Chem. Soc.*, 89, 1525 (1967).

225. A.F. Thomas and B. Willham, *Tetrahedron Lett.*, 1309 (1965).

226. H.C. Brown and K.T. Liu, *J. Amer. Chem. Soc.*, 89, 3900 (1967).

227. R. Bonaccorsi, E. Scrocco and J. Tomasi, *J. Chem. Phys.*, 52, 5270 (1970).

228. W.G. Woods, R.A. Carboni and J.D. Roberts, *J. Amer. Chem. Soc.*, 78, 5653 (1956).

229. N.H. Werstiuk, *Chem. Commun.*, 1499 (1970).

230. R. Muneyuki and T. Yano, *J. Amer. Chem. Soc.*, 92, 746 (1970).

231. N.H. Werstiuk, G. Timmins and F.P. Cappelli, *Can. J. Chem.*, 51, 3473 (1973).

232. W. Hanstein, H.J. Berwin and T.G. Traylor, *J. Amer. Chem. Soc.*, 92, 829 (1970).

233. T.G. Traylor, W. Hanstein, H.J. Berwin, N.A. Clinton and R.S. Brown, *J. Amer. Chem. Soc.*, 93, 5715 (1971).

234. L.A. Paquette and I.R. Dunkin, *J. Amer. Chem. Soc.*, 95, 3067 (1973).

235. G.A. Russell, G.W. Holland, K.W. Chang, R.G. Keske, J. Mattox, C.S.C. Chung, K. Stanley, K. Schmitt, R. Blankespoor and Y. Kosugi, *J. Amer. Chem. Soc.*, 96, 7237 (1974).

236. R.C. Bingham and P.v.R. Schleyer, *Tetrahedron Lett.*, 23 (1971).

237. S. Winstein and J. Takahashi, *Tetrahedron*, 2, 316 (1958).

238. D.G. Farnum and A.D. Wolf, *J. Amer. Chem. Soc.*, 96, 5166 (1974).

239. H.C. Brown, F.J. Chloupek and M.H. Rei, *J. Amer. Chem. Soc.*, 86, 1246 (1964).

240. P. von R. Schleyer, M.M. Donaldson and W.E. Watts, *J. Amer. Chem. Soc.*, 87, 375 (1965).

241. P.v.R. Schleyer, P.J. Stang and D.J. Raber, *J. Amer. Chem. Soc.*, 92, 4725 (1970).

242. E.J. Corey and R.S. Glass, *J. Amer. Chem. Soc.*, 89, 2600 (1967).

243. B.M. Benjamin and C.J. Collins, *J. Amer. Chem. Soc.*, 88, 1556 (1966).

244. B.L. Murr and M.F. Donnelly, *J. Amer. Chem. Soc.*, 92, 6686, 6688 (1970).

245. S. Winstein and G.C. Robinson, *J. Amer. Chem. Soc.*, 80, 169 (1958).

246. S.J. Cristol, A.R. Dahl and W.Y. Lim, *J. Amer. Chem. Soc.*, 92, 5670 (1970).

247. F.G. Bordwell, *Accounts Chem. Res.*, 3, 281 (1970).

248. F.G. Bordwell and B.B. Jarvis, *J. Amer. Chem. Soc.*, 95, 3585 (1973).

249. W.H. Saunder, Jr. and A.F. Cockerill, *Mechanisms of Elimination Reactions*, J. Wiley and Sons, New York, 1973.

250. A. Nickon and N.H. Werstiuk, *J. Amer. Chem. Soc.*, 89, 3914, 3915, 3917 (1967).

251. N.H. Werstiuk, in press, *Can. J. Chem.*

252. P. Laszlo and P.v.R. Schleyer, *J. Amer. Chem. Soc.*, 85, 2709 (1963).

253. H. Kwart and L. Kaplan, *J. Amer. Chem. Soc.*, 76, 4072 (1954).

254. L. Kaplan, H. Kwart and P. von R. Schleyer, *J. Amer. Chem. Soc.*, 82, 2341 (1960).