ABSTRACT

PROTONATED CYCLOPROPANE FORMATION IN THE DEAMINATION OF CYCLOPENTYLCARBINYL AMINE

By

Kenneth Edward Martin

The purpose of this investigation was to determine whether protonated cyclopropane intermediates are formed in the deamination of cyclopentylcarbinyl amine. The method used involved first, a study of the classical reaction pathways for the cyclopentylcarbinyl cation, and second, observation of the isotope position rearrangements resulting from deamination of a number of deuterium labeled cyclopentylcarbinyl amines using mass spectroscopy and NMR.

The alcoholic fraction resulting from deamination of cyclopentylcarbinyl amine consisted of 74.8% cyclohexanol, 17.6% 1-methylcyclopentanol, 4.9% cyclopentylcarbinol, and 2.7% trans-2-methylcyclopentanol.

1-methylcyclopentanol could be formed only by classical carbonium ion rearrangement. The lack of isotope position rearrangement occurring in the formation of cyclopentylcarbinol from cyclopentylaminomethane-1,1-d_2 is inconsistent with an equilibrated protonated cyclopropane intermediate, and was interpreted as indicating that this material results from classical intermediates only.

However, the isotope position rearrangements observed in the formation of trans-2-methylcyclopentanol from 1-aminomethylcyclopentanol-1-d are consistent with an equilibrated protonated

cyclopropane intermediate, but inconsistent with a classical 1,3 hydride shift. The possibility of successive 1,2 hydride shifts or equilibration of classical ions involved in the formation of this alcohol was eliminated by deamination of cyclohexyl and 1-methylcyclopentyl amines and supported by the isotope position rearrangement pattern observed in the deamination 1-aminomethylcyclopentane-3,4-$\underline{d}_2$.

For cyclohexanol, the small amount of isotope position rearrangements observed in the deamination of 1-aminomethylcyclopentane-1-$\underline{d}$ are consistent with a protonated cyclopropane intermediate yet inconsistent with an alkyl shift mechanism. The possibility of 1,2 or 1,3 hydride shifts accounting for the observed isotope position rearrangement was eliminated by deamination of cyclopentylaminomethane-1,1-$\underline{d}_2$ and 1-aminomethylcyclopentane-3,4-$\underline{d}_2$. Also deamination of cyclohexyl and 1-methylcyclopentyl amines eliminate equilibration between classical ions as a possible explanation for the observed isotope position rearrangement. Since the isotope position rearrangements found in cyclohexanol resulting from cyclopentylaminomethane-1,1-$\underline{d}_2$ also eliminate equilibrated protonated cyclopropanes as intermediates in the formation of this product, a non-equilibrated protonated cyclopropane is invoked to explain these results.

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By

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To my Parents

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INTRODUCTION

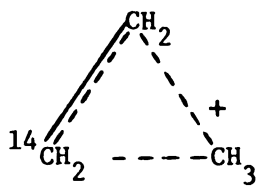
Reports of research concerning the detailed nature of carbonium ion intermediates have occupied a major portion of chemical literature for the past fifty years. Some of this work represents major breakthroughs and classical experiments of our time, but the majority of these efforts have often seemed to be almost trivial further examples of already demonstrated effects. Yet, since conclusions based on a single, perhaps anamolous event have occasionally led chemists astray, these further bits of evidence are necessary to build the strong experimental foundations upon which modern carbonium ion theory is based.

Through the efforts of literally thousands of chemists more is known about the intimate nature, structure, and behavior of carbonium ions than about any of the other types of reactive chemical intermediates. Yet despite this vast body of knowledge there are still many gray areas of misunderstanding that have eluded satisfactory and conclusive explanations.

Perhaps the best known of these is the question of nonclassical ion formation in the norbornyl system. Though the volume of work in this field can only be described as monumental, the question of the existence of these intermediates is almost as hotly debated today as it was ten years ago. It is only in a simpler system that the existence of a species with bonding, delocalized, sigma electrons has been described as resting on "firm experimental ground "(1). The formation of this nonclassical intermediate, a protonated cyclopropane, in a cyclic system is the subject of this thesis.

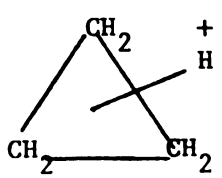
Protonated Cyclopropane Formation in the Propyl System

The concept of protonated cyclopropane intermediates originated in 1953 when Roberts and Halmann (2) discovered that 1-aminopropane-1-^{14}C yielded upon deamination 1-propanol-^{14}C in which 8.5% of the original ^{14}C was not at C-1. They assumed it to be at C-2 and proposed that 17% of the originally formed 1-propyl cation rearranged to a protonated cyclopropane I.



I

Between 1959 and 1962, Skell and Starter (3) deoxidated 1-propanol, demonstrated that the reaction proceeds through carbonium ion intermediates, and isolated cyclopropane from the reaction mixture. The formation of cyclopropane conclusively demonstrated the existence of some type of interaction between C-1 and C-3 of the propyl cation, which Skell originally postulated (3b) as a face-protonated cyclopropane II.



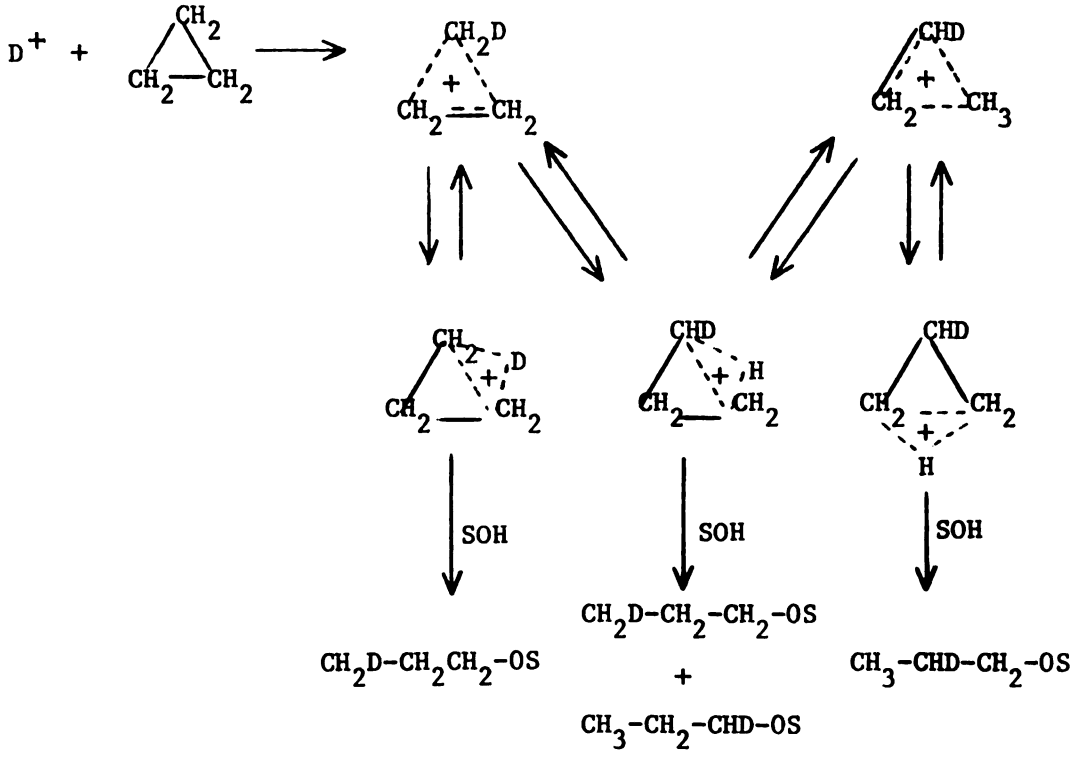
II

In 1962 Reutov and Shatkina repeated Roberts' experiment and

found 8.5% of the ^{14}C in the resulting 1-propanol at C-3. No ^{14}C was found at C-2. Similar results were obtained from the reaction of 1-chloropropane-1-^{14}C and $ZnCl_2/HCl$ (5). In the same year, Karabatsos and Orzech (6) deaminated 1-aminopropane-1,1,2,2-$\underline{d}_4$ and reported that 12% of the resulting 1-propanol had undergone a nominal 1,3 hydride shift. Both Reutov and Karabatsos concluded that 1,3 hydride shifts and not protonated cyclopropane intermediates were responsible for the observed results.

A major breakthrough in protonated cyclopropane chemistry occurred when, in a series of classic experiments, Baird and Aboderin (7) passed cyclopropane through D_2SO_4 and found significant amounts of deuterium incorporated into the cyclopropane ring. Examination of the 1-propanol products in this reaction revealed the following deuterium distribution, based on incorporation of one deuterium per molecule: C_1, 0.38D; C_2, 0.17D; C_3, 0.46D. These results cannot be adequately explained through the usual carbonium ion reactions of a propyl cation. The mechanism suggested for this transformation (See Figure 1) involved edge-protonated cyclopropanes as the product forming intermediates.

This edge-protonated species contains a proton, or deuteron, simultaneously bonded to two carbons; it differs from a face-protonated cyclopropane, that contains a proton symmetrically bonded to all three carbons, and from a corner-protonated cyclopropane that contains protons bonded to only a single carbon atom. A variety of experimental and theoretical data indicate that, in simple acyclic systems, the edge-protonated formulation is superior to the other two. This aspect



D_2SO_4 Solvolysis of Cyclopropane

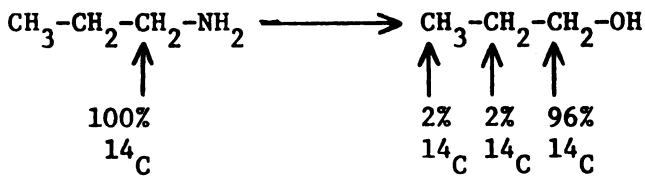
Figure 1 (7b)

will be covered in greater detail later.

In 1964 Baird (8) further revealed that the cyclopropane obtained from the deamination of 1-aminopropane-3,3,3-$\underline{d}_3$ consisted of 43% $C_3H_4D_2$ and 57% $C_3H_3D_3$. Without using protonated cyclopropane intermediates the only possible pathway to cyclopropane-$\underline{d}_3$ involved 1,3 deuteride shifts prior to ring closure. However, such shifts should account for only 12% $C_3H_3D_3$ (6). Hence, to explain the large 57% $C_3H_3D_3$ actually found, a mechanism incorporating protonated cyclopropane intermediates was required.

In 1965 Lee and coworkers again studied the deamination of 1-aminopropane-1-^{14}C (9). Instead of finding 8% ^{14}C at C-3 of the resulting 1-propanol as reported by Roberts and Reutov, Lee found 2%

^{14}C at C-2. In addition, deamination of 1-tritio-1-aminopropane (10)



yielded 1-propanol with 1.5% T at C-3 and 1.5% T at C-2. Since it had already been shown that under these conditions, the 2-propyl cation does not rearrange to the 1-propyl cation (6) Lee's results were best interpreted in terms of protonated cyclopropane intermediates.

The case for protonated cyclopropane was further strengthened when Karabatsos, Orzech, and Meyerson (11) examined the deamination of 1-aminopropanol-2,2-$\underline{d}_2$. The 1-propanol isolated from this reaction was found to have the following deuterium distribution:

$$CH_3\text{-}CD_2\text{-}CH_2\text{-}NH_2 \longrightarrow \underset{97.9\%}{(C_2H_3D_2)CH_2OH} + \underset{1.2\%}{C_2H_5CD_2OH} + \underset{0.9\%}{(C_2H_4D)CHDOH}$$

The migration of deuterium from C-2 to C-1 eliminated a mechanism based solely on 1,3 hydride shifts. The greater abundance of $C_2H_5CD_2OH$ over $(C_2H_4D)DHCOH$ is inconsistent with a series of 1,2 shifts. Hence, a mechanism involving protonated cyclopropanes is required. This conclusion was supported by studying the deamination of 1-aminopropane-1,1-$\underline{d}_2$ (11) and by a reinvestigation of the deamination of 1-aminopropane-1,1,2,2-$\underline{d}_4$ (11).

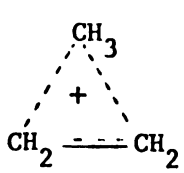
Further reports of the deamination of 1-aminopropane-1-^{14}C (12, 13), 1-aminopropane-1-^{13}C (14), 1-aminopropane-3,3,3-$\underline{d}_3$ (14, 15), 1-aminopropane-2,2-$\underline{d}_2$ (12, 14, 15), 1-aminopropane-1,1-$\underline{d}_2$ (15) and 1-tritio-1-aminopropane (12) served to firmly establish that the

isotope position rearrangements observed in reactions of the 1-propyl cation are characteristic of protonated cyclopropane intermediates rather than any combination of 1,3 with 1,2 hydride shifts (14). In addition, observation of the same general scrambling patterns in the reaction of 1-bromopropane-1-^{13}C (16, 17) 1-aminopropane-2,2-$\underline{d}_2$ (17) and 1-aminopropane-1,1-$\underline{d}_2$ (17) with aluminum bromide, the reaction of 1-chloropropane-1-^{14}C with aluminum chloride (18) and the interaction of 1-propanol-1,1-$\underline{d}_2$ and $ZnCl_2/HCl$ (19) demonstrate that the formation of protonated cyclopropane is characteristic of the 1-propyl cation and not restricted to ions produced by deamination reactions.

It should be pointed out that protonated cyclopropane formation represents at best a minor pathway in the reactions of the 1-propyl cation, accounting for 4%-6% (12, 14) of the product in deamination reactions.

The Structure of Protonated Cyclopropanes

Though the intermediary of protonated cyclopropanes has been firmly established, the question of their exact structural formulation has not been fully resolved. Both theoretical and experimental investigations have attempted to determine whether a corner I, face II, or edge III, protonated structure best represents the actual intermediate.



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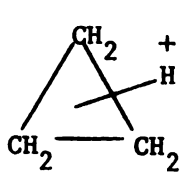

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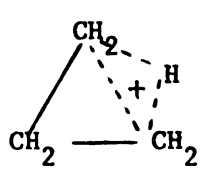


III

In 1964 Hoffmann (20) used extended Huckel theory to calculate that the edge-protonated formulation gives the best picture of the actual intermediate. This conclusion was supported and extended by Petke and Whitten (21) who employed ab-initio-SCF-MO calculations to find that an edge-protonated cyclopropane represented the lowest energy equilibrium geometry for $C_3H_7^+$. Further evidence in favor of the edge-protonated formulation was provided by Smith, Kollman, and coworkers (22), (23), who used modified CNDO and INDO methods of calculation. Their conclusions, summarized in Table 1, also indicate that edge-protonated cyclopropane represents the low energy form of $C_3H_7^+$.

Table 1 (22), (23)

Calculated Energies for $C_3H_7^+$

	Relative energy in Kcal/mole
Face-protonated cyclopropane	62
1-propyl cation	25
2-propyl cation	0
Corner-protonated cyclopropane	- 3
Edge-protonated cyclopropane	-14

More recently, Dewar and Bodor (24) studied this problem by using the MINDO/2 method and established the following order of stability: face-protonated cyclopropane < n-propyl cation < corner-protonated cyclopropane < isopropyl cation < edge-protonated cyclopropane.

The conclusions that an edge-protonated cyclopropane is the energy minimum for $C_3H_7^+$ has been called into question by calculations (25) based on ab-initio-SCF-MO theory with modifications that allowed extensive variations in geometry of the ions involved. Relative energies

found by this method based on the optimized geometry for each species are given in Table II. These results indicate that a corner-proton-

Table 2 (25)

Calculated Energies for $C_3H_7^+$

	Relative energies in Kcal/mole
2-propyl cation	0
1-propyl cation	16.9
Corner-protonated cyclopropane	17.3
Edge-protonated cyclopropane	27.1
Face-protonated cyclopropane	139.6

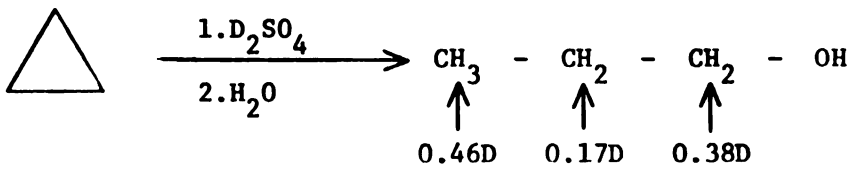
ated species is the most stable of the cyclic $C_3H_7^+$ ions, and that both the 1-propyl cation and 2-propyl cation are more stable than any type of protonated cyclopropane.

It should be pointed out that all of the above calculations are based on isolated molecules in the gas phase. Introduction of an energy of solvation factor could easily alter these results.

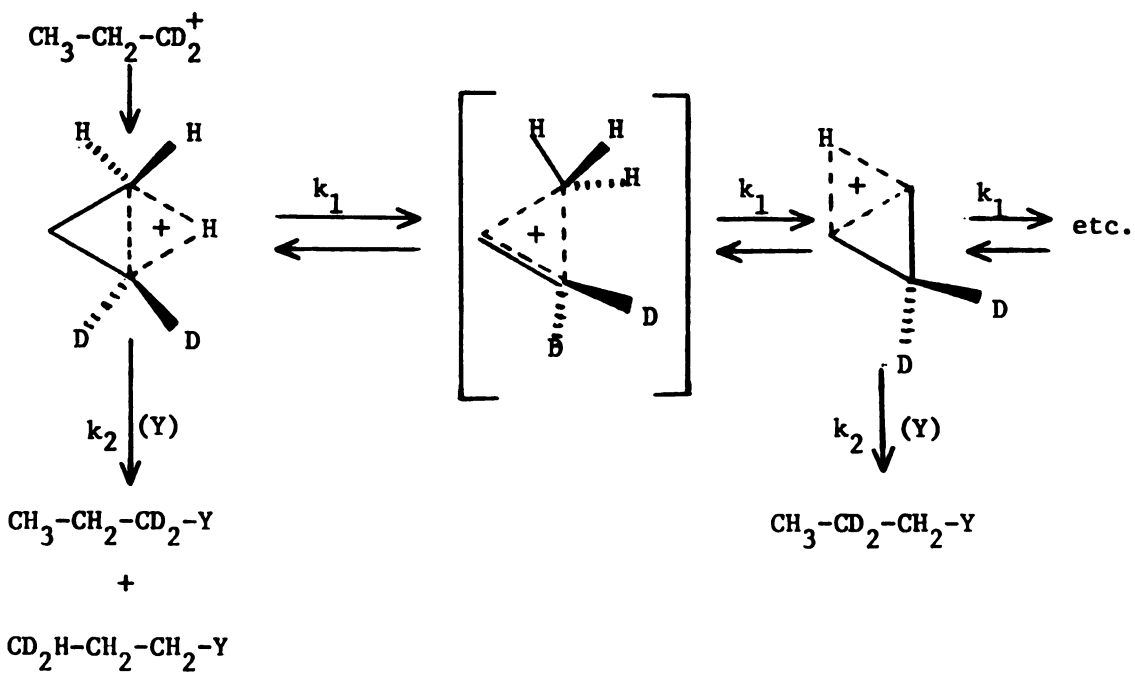
Experimental investigations into the structure of protonated cyclopropanes have attempted to determine if the observed isotope scrambling due to this intermediate more closely fits that predicted by face, edge, or corner-protonated formulations.

Experimental results agree with theoretical calculations in eliminating face-protonated cyclopropanes from consideration. Among many findings that support this conclusion was the discovery of a non-symmetrical incorporation of deuterium when cyclopropane was solvolyzed in D_2SO_4 (7). A face-protonated cyclopropane would have predicted incorporation of equal amounts of deuterium at C-1 and C-2.

A distinction between edge and corner-protonated structures is

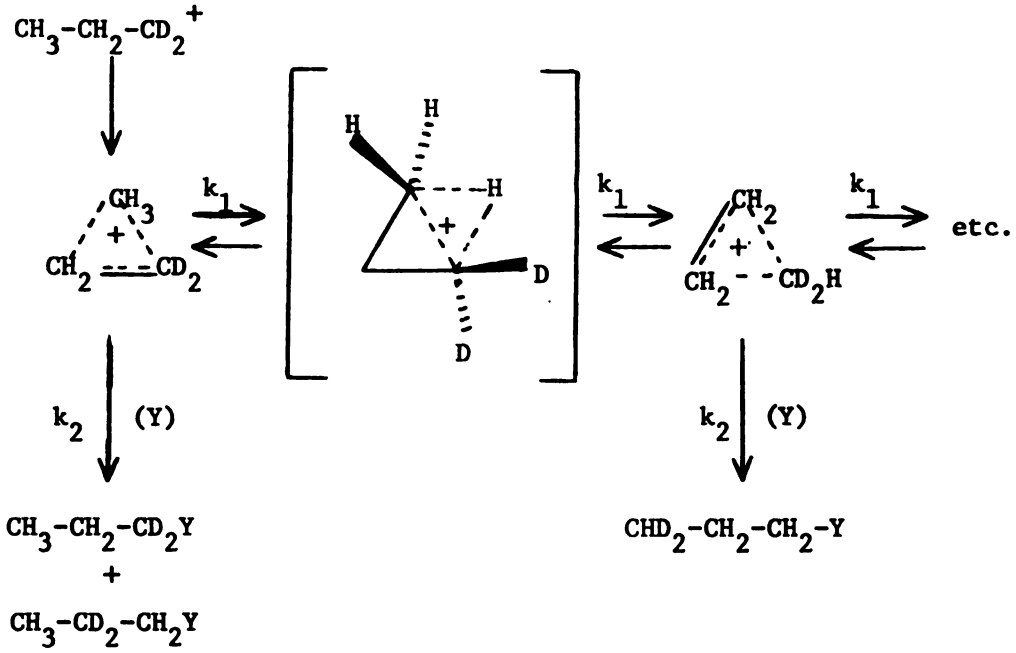


more difficult since both formulations can account for either partial or total scrambling of isotopic labels. Furthermore, since equilibration between two edge-protonated forms can be best pictured as preceding through a corner-protonated transition state (12), (14), (See Figure 2), and because equilibration between two corner-protonated forms would necessitate an edge-protonated transition state (12) (See Figure 3), distinction between the two forms becomes a problem of determining which is the intermediate and which is the transition state (or higher energy intermediate).



Equilibration of an Edge-protonated Cyclopropane

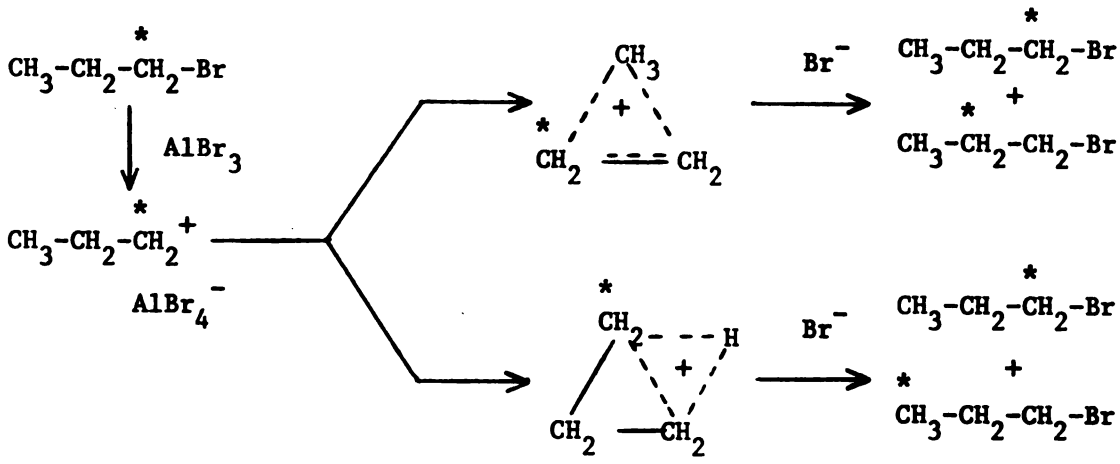
Figure 2 (14)



Equilibration of a Corner-protonated Cyclopropane

Figure 3

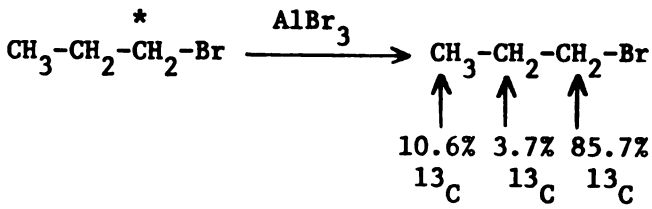
A distinction between these two structures can be made, however, by examining reactions in which only partial equilibration of isotopic labels occurs (18) (19). In these cases, equilibration between the various edge-protonated or corner-protonated structures is competitive with the rate with which the intermediates collapse to products. Consequently, a greater amount of product can be expected to result from the first formed ion rather than any others in equilibrium with it. Hence, in the reaction of 1-bromopropane-1-^{13}C with aluminum bromide (16), for example, a corner-protonated intermediate would give products with a greater amount of ^{13}C at C-2 than at C-3 (See Figure 4), whereas an edge-protonated intermediate would predict the opposite. The actual product from this reaction contains nearly three times as much ^{13}C at C-3 than at C-2. An edge-protonated structure is therefore



Isotopic Distribution Expected from Edge and Corner-protonated Cyclopropanes in Reaction of Aluminum Bromide with 1-bromopropane-1-^{13}C

Figure 4

indicated as the product forming intermediate (16).



This conclusion is supported by a variety of other experiments (7). In fact, all reactions in which a distinction can be made between edge and corner-protonated cyclopropanes indicate that edge-protonated structures are the lower energy intermediates. Figure 2, therefore, gives the best mechanistic picture of reactions involving protonated cyclopropanes.

It should be emphasized that a variety of isotopic scrambling patterns can be expected from this type of intermediate. For example,

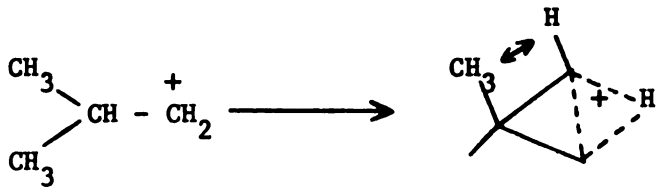
in Figure 2, if $k_1 >> k_2$, any isotopic label will be symmetrically scrambled over all possible positions. The deamination of 1-propyl amines (9) (10) fall into this category. However, if $k_2 >> k_1$, then products will appear to have been derived from a simple 1,3 shift. The reaction of 1-propanol with $ZnCl_2/HCl$ (19) is an example of such a case.

Since the bulk of experimental and theoretical evidence favors the edge-protonated formulation, it will be used through the remainder of this thesis. However, it should be noted that all of the above experiments dealt with acyclic substrates. In view of the relatively small energy difference between edge and corner-protonated species, the various stereochemical constraints imposed by cyclic and polycyclic structures could alter the relative stabilities of these two ions.

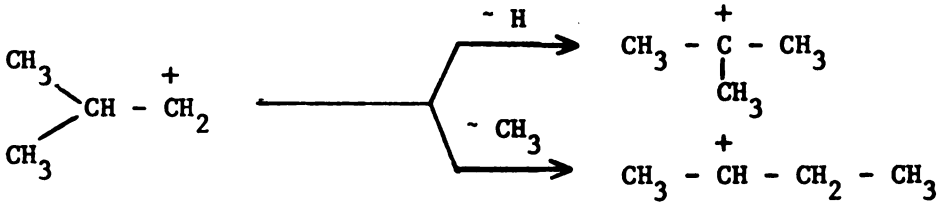
Protonated Cyclopropane Formation in Alkyl Substituted Propyl Systems

As in the propyl system, evidence for protonated cyclopropane intermediates in more highly substituted systems is based on cyclopropane formation and on isotope position rearrangement characteristic of protonated cyclopropane structures. However, the role protonated cyclopropanes play in the reactions of these larger molecules has been found to be sharply reduced. Two explanations have been advanced (26, 27, 28) to explain this phenomenon. First, the introduction of larger groups onto a protonated cyclopropane ring would tend to inhibit the formation of this intermediate because of unfavorable

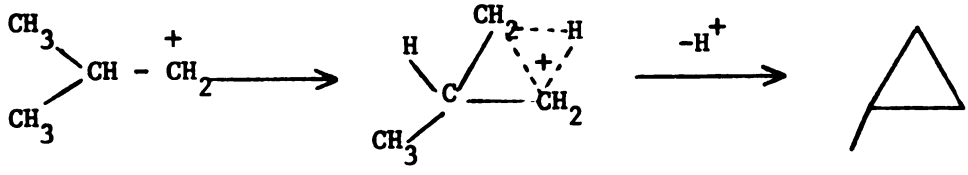
1, 2-eclipsing interactions. And second, other rearrangement paths



leading to relatively stable ions are usually available.



Protonated cyclopropane intermediates have, however, been detected in several systems larger than propyl. For example, in 1965 Friedman and coworkers (29) isolated methylcyclopropane from the deamination of isobutyl amine and based on this evidence, postulated an edge-protonated cyclopropane as its precursor. The possibility



of carbenoid intermediates was eliminated by studying the deamination of isobutyl amine-1,1-$\underline{d}_2$ (30). That protonated cyclopropanes are, however, less important in this system was shown by Skell and Starter (3b), who found that introduction of a single methyl group at C-2 of 1-propanol decreased cyclopropane formation upon deoxidation of the resulting 2-methyl-1-propanol by a factor of approximately 2.5 compared to 1-propanol.

In an extensive study of the isotope position rearrangement occurring in the aqueous acid deamination of isobutyl amine-1,1-$\underline{d}_2$

(26, 31), Karabatsos and coworkers detected no protonated cyclopropane intermediates involved in the formation of alcoholic products. Based on the formation of methyl cyclopropane, however, protonated cyclopropanes were estimated to account for 0.6% of the products derived from this reaction. In comparison, the yield of protonated cyclopropane derived products from 1-propyl amine under similar deamination conditions was found to be 6% (14). It should be pointed out that protonated cyclopropane formation in this system has been found to be highly solvent dependent (32, 33), with higher amounts of methyl cyclopropane formed in solvents of low polarity.

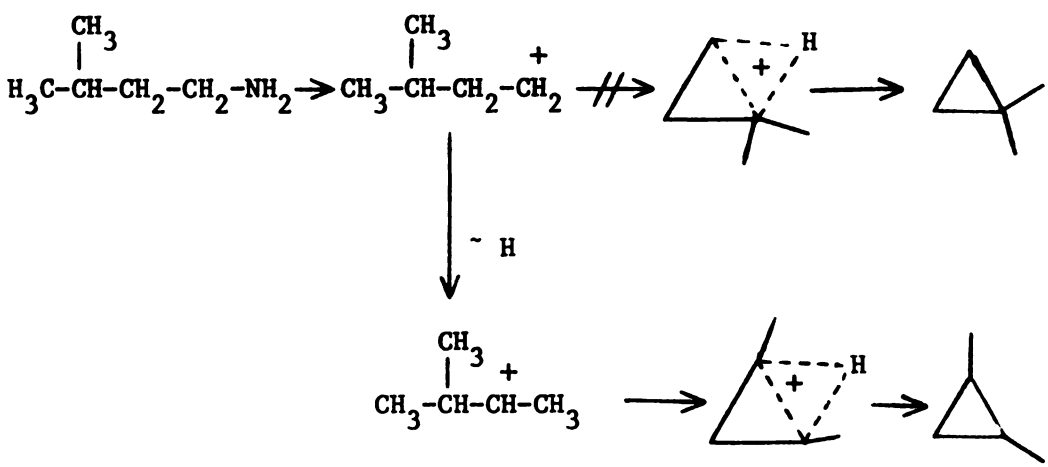
In a related system, Skell and Maxwell (34) isolated ethylcyclopropane and 1,2-dimethylcyclopropane in 3.1% and 2% respective yields from the deoxidation of 2-methyl-1-butanol.

Results from studies of the n-butyl cation paralleled those of the isobutyl system. Initial discovery of 1-methylcyclopropane in the deoxidation of 1-butanol (3b) was followed by confirmation of cyclopropane formation in the deamination of 1-butyl amine (27, 28, 29). But again, extensive studies (28) of the deamination of 1-butyl-1,1-$\underline{d}_2$ amine, 1-butyl-2,2-$\underline{d}_2$ amine, and 1-butyl-3,3-$\underline{d}_2$ amine produced no evidence for protonated cyclopropane precursors to substitution products. As before, addition of a single methyl group to the propyl system reduced the role of protonated cyclopropanes in the reaction mechanism by an approximate factor of 10.

Deamination (35, 36) and solvolysis (36) studies of deuterated 1-pentyl and 1-hexyl amines and tosylates indicate that straight chain compounds longer than four carbons have little or no tendency to form protonated cyclopropane intermediates in these reactions.

Deamination (37) of neopentyl-1-^{13}C amine, and neopentyl-1,1-d_2 amine as well as solvolysis (37) of the corresponding tosylates indicate no protonated cyclopropane precursors to substitution products. In addition, no cyclopropyl compounds were isolated from deamination of neopentyl amine (3b, 37) deoxidation of neopentyl alcohol (3b, 39) or solvolysis of neopentyl tosylate (38).

The absence of products derived from a geminal, dimethyl substituted protonated cyclopropane was observed in the deamination of 3-methyl-1-butyl amine (40, 41). 1,2 dimethylcyclopropane was isolated as 1.5% of the product, and since no 1,1-dimethylcyclopropane, the expected product from direct formation of a protonated cyclopropane by the primary cation, was found, a mechanism using an initial 1,2 hydride shift followed by protonated cyclopropane formation from the secondary ion was suggested (See Figure 5).



Deamination of 3-methyl-1-aminobutane

Figure 5

In agreement with this mechanism, the deamination of 3-methyl-2-aminobutane (40, 41) gave a 15% yield of 1,2-dimethylcyclopropane.

Despite the large amount of cyclopropane formed in the above

reaction, most secondary carbonium ions form smaller amounts of protonated cyclopropanes than do their less stable primary counterparts. For example, while methyl cyclopropane can be isolated as 2% of the hydrocarbon products from the deoxidation of 1-butanol, 2-butanol gives only a trace (<0.5%) of methyl cyclopropane (3b). As expected, a thorough analysis of alcohols obtained from deamination of deuterium labeled 2-butyl amine could detect no involvement of protonated cyclopropanes (28).

Direct formation of protonated cyclopropanes from tertiary ions in normal carbonium ion reactions has never been detected (3b, 39, 42).

Solvent Dependency of Protonated Cyclopropane Formation

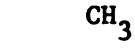
No mention has been made of the role of solvent on the formation and stability of protonated cyclopropane intermediates. In particular, discussion of several significant experiments in "magic acid" solutions have been omitted, since their understanding requires a knowledge of the behavior of protonated cyclopropanes in different types of solvents.

Much of the work in this field (15, 29, 32, 33) has centered on the deamination of deuterated propyl and butyl amines in a variety of different solvents and has resulted in the establishment of two relationships (15) between solvent and protonated cyclopropane formation.

It was found that as the deamination solvent became more protic, the amount of protonated cyclopropane formation, as evidenced by isolation of cyclopropyl products, decreased. Results of studies on isobutyl amine are given in Table 3. The formation of classical type

Table 3 (29, 32)

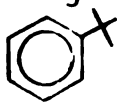
Yield of Methylcyclopropane from the Deamination of Isobutyl Amine in Various Solvents



Amine - $CH_3-CH(CH_3)-CH_2-NH_2$

Diazotizing Agent - Octyl Nitrite - 1.1 equivalents

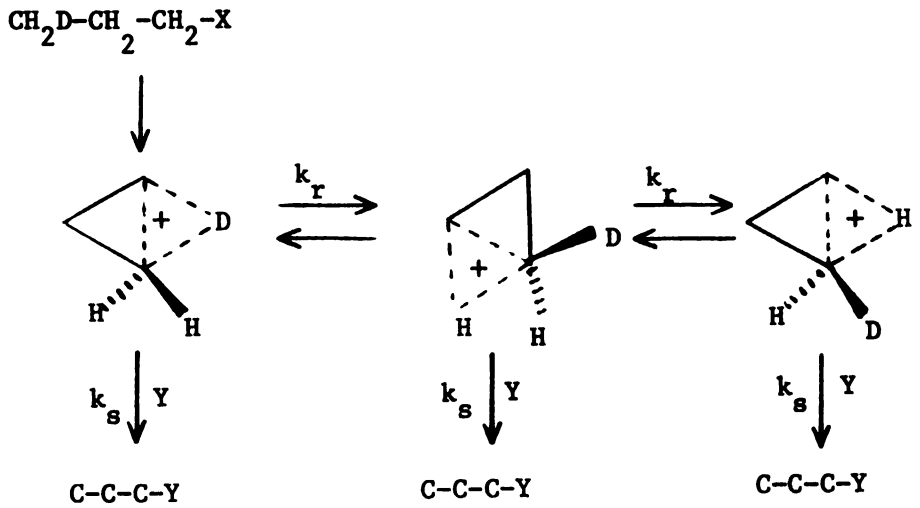
Acid - DOAC - 1.0 equivalents

Solvent	%  in Hydrocarbon Products
$HCCl_3$	14
	12
	11
1-Hexanol	11
Glyme	10
Ethylene Glycol	4
$CH_3-\overset{O}{\overset{\|\|}{C}}-OD$	4
D_2O	2

carbonium ions is favored over the formation of protonated cyclopropanes as the ability of the solvent to stabilize the carbonium ion increases. Since the more charge concentrated classical ions can benefit to a relatively greater extent by increased solvation than protonated cyclopropane intermediates with their more diffuse positive charge, increased solvation favors classical intermediates over the nonclassical counterparts.

The amount of isotope position rearrangement resulting from protonated cyclopropane formation also roughly correlates with solvent

proticity. Referring to Figure 6, the extent of isotopic scrambling is directly related to the extent of equilibration between the various protonated cyclopropanes, which in turn depends on the ratio of k_r/k_s. If the protonated cyclopropane has a long life time i.e. k_s/k_r is small, then a large amount of isotopic scrambling is expected. Consequently, reactions in solvents that generally stabilize carbonium ion intermediates, such as more polar and protic solvents, should give larger amounts of isotope position rearranged products.



Relation of Isotopic Scrambling to Equilibration Between Various Protonated Cyclopropanes

Figure 6 (31)

Deamination studies of labeled propyl and butyl amines (15, 33) support this conclusion. For example, deprotonation of the first protonated cyclopropane formed in the deamination of 1-aminopropane-3,3,3-$\underline{d}_3$ should yield only cyclopropane-$\underline{d}_2$. However, as equilibrium between the various protonated cyclopropane structures proceeds, the amount of cyclopropane-$\underline{d}_3$ should increase. This effect was observed

experimentally (See Table 4).

Table 4 (15)

Deuterium Content of Cyclopropane Obtained from Deamination of 1-aminopropane-3,3,3-$\underline{d}_3$ in Various Solvents

Amine - $D_3C-CH_2-CH_2-NH_2$

Diazotizing Agent - Octyl Nitrite - 1.1 equivalents

Acid - 1.0 equivalents

Acid	Solvent	Deuterium Content of △	
		$\%d_2$	$\%d_3$
HOAC	$HCCl_3$	84	16
HOAC	H_2O	52	48
35% $HClO_4$	H_2O	41	59

A similar effect was observed by Deno and coworkers (43) who found that the extent of deuterium scrambling in the solvolysis of cyclopropane with deuterated sulfuric acid increased with increasing acid concentration.

Consequently, a reaction run in an efficient carbonium ion stabilizing solvent would result in relatively little protonated cyclopropane formation, yet the protonated cyclopropane that did form should show extensive isotope position rearrangement. On the other hand, reactions run in solvents that do little to stabilize carbonium ions would show larger amounts of protonated cyclopropane formation but only limited isotope position rearrangement.

An interesting solvent effect with relation to protonated cyclopropane formation occurs in "super" acid reactions. The results observed in these solvents differ markedly from results of reactions

treated thus far. For example, Saunders and coworkers (44) observed an interchange of the two types of protons in the isopropyl cation formed by action of SO_2ClF-SbF_5 on isopropyl chloride. This can be explained by either direct formation of a protonated cyclopropane or by an equilibrium between the 1- and 2-propyl cations. Neither reaction has been observed in more ordinary solvents. The same workers proposed protonated cyclopropane formation to explain complete equilibration of protons in the ion resulting from treatment of sec-butyl chloride with SbF_5-SO_3HF (45).

More surprising are findings (46) that indicate the rearrangement of a tertiary ion to a protonated cyclopropane. When 1-[methyl-^{13}C]-1-chlorocyclopentane is dissolved in SO_2ClF-SbF_5, NMR studies indicate an interchange of methyl and ring carbons. Similar treatment of 1-[methyl-$\underline{d}_3$]-1-chlorocyclopentane results in migration of deuterium into the ring. Consideration of energy parameters for these reactions resulted in a proposal of either direct rearrangement of a tertiary ion to an equilibrating protonated cyclopropane, or initial rearrangement to a secondary ion followed by protonated cyclopropane formation.

Similar results were obtained from studies of t-amyl chloride (46). Interchange of all protons in the corresponding ion was interpreted as resulting from formation of equilibrating cyclopropane intermediates.

Finally, the unusual nature of reactions in super acid solutions is emphasized by solvolysis of a variety of amyl and hexyl halides in SbF_5-SO_3HF (47). While deamination produced no evidence of protonated cyclopropane formation from similar ions, these reactions

resulted in products that indicate substantial intervention of non-classical intermediates. This unusual tendency towards protonated cyclopropane formation in super acid solutions can be rationalized in light of the previous discussion. Because of the extremely low nucleophilicity of these solvents, they can offer little in the way of solvent stabilization for carbonium ions. Consequently, formation of a delocalized protonated cyclopropane would be favored relative to classical ions.

Protonated Cyclopropane Formation from Mono-cyclic Systems

Cyclic systems provide an interesting opportunity to study substituted protonated cyclopropanes. By utilizing a molecule so that the developing protonated cyclopropane is essentially fused onto another ring, the 1, 2-eclipsing interactions that disfavor the formation of the substituted cyclopropyl structure can be minimized, since similar types of interactions exist in both intermediate and ground state. Consequently, protonated cyclopropane formation should occur to a relatively larger extent in such systems than in their open chain counterparts.

In the cyclohexyl cation, for example, formation of a protonated cyclopropane results in little change of any alkyl-alkyl or alkyl-hydrogen interaction. This ion has been extensively studied by

Reutov and coworkers (48), who examined cyclohexanol produced in the deamination and solvolysis of ^{14}C and tritium labeled cyclohexyl amine and tosylate. Typical of their results is that deamination of cyclohexyl amine resulted in nominal 1,2 and 1,3 hydride shifts to the extent of 3.5% and 1.3% respectively. Though these rearrangements were interpreted solely on the basis of classical hydride shifts, they are not inconsistent with a combination of hydride shifts and protonated cyclopropane formation. The intervention of protonated cyclopropanes may be invoked to explain the results of Edwards and Lesage (49) who isolated [3.1.0.]-bicyclohexane in 2% yield from the deamination of cyclohexyl amine.

Since a primary ion can most benefit from stabilization by protonated cyclopropane formation, and because the rigid five membered ring fixes the molecule in the optimum configuration for protonated cyclopropane formation, reactions of cyclopentyl carbinyl derivatives are good potential sources of such non-classical ions. Reutov and coworkers (50) studied the cyclohexanols resulting from the deamination of aminocyclopentylmethane-^{14}C and 1-aminomethylcyclopentane-1-$\underline{t}_1$ and claimed evidence of 9% 1,2 and 1.2% 1,3 hydride shifts and 3.2% 1,2 and 3.4% 1,3 hydride shifts, respectively. Cyclohexanol was the only product examined, and the results were interpreted only in terms of hydride shifts.

In an effort to determine if the formation of protonated cyclopropane is favored in cyclic systems, this thesis will investigate the extent of protonated cyclopropane intervention in the deamination of cyclopentylcarbinyl amine. The fate of cyclopentylcarbinyl cation is also interesting relative to the non-classical ion problem in the

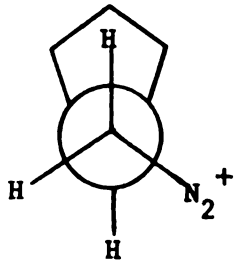
norbornyl system. A protonated cyclopropane resulting from the cyclopentylcarbinyl cation occupies an intermediate position between the well established protonated cyclopropane from the propyl cation and the not so well established protonated cyclopropane from the norbornyl cation. Consequently, significant protonated cyclopropane formation from the cyclopentylcarbinyl cation would imply an even larger amount of non-classical ion intervention in the more rigid norbornyl system. Though a discussion of protonated cyclopropane intermediates in the norbornyl system is beyond the scope of this thesis, it should be noted that the large amount of evidence supporting delocalized ions in this system tends to support the hypothesis that protonated cyclopropane intervention is favored in systems that minimize or eliminate increased steric interactions in the formation of this intermediate.

Results and Discussion

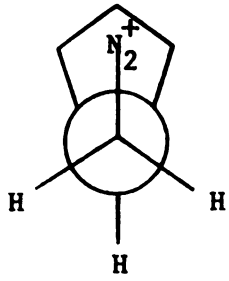
Deamination of Cyclopentylcarbinyl Amine

Cyclopentylcarbinyl amine was prepared by treating cyclopentyl bromide with sodium cyanide in dimethylsulfoxide solution, and reducing the resulting nitrile with lithium aluminum hydride. The amine was deaminated in an aqueous solution, by using perchloric acid and sodium nitrite, under conditions found to maximize yield of alcohols (See experimental). The product mixture was analyzed by gas chromatography and the various alcoholic components identified by comparison of retention times with those of known samples. The results are given in Table 5.

The relatively low yield of 1-methylcyclopentanol can be explained in terms of conformational effects. If the preferred ground state conformation of the diazonium ion intermediate is as shown in V and if carbon - carbon bond rotation in the resulting primary carbonium ion



V

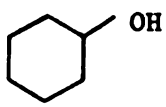


VI

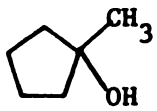
is slow compared to rearrangement, or if rearrangement is concerted with loss of nitrogen, then an alkyl rather than hydride shift will occur. The alkyl shift is also favored by the fact that a hydride shift results in a relatively strained cyclopentyl cation while an

Table 5

Alcoholic Products from Deamination of Cyclopentylcarbinyl Amine



74.8%



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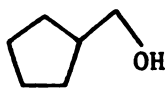
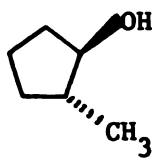


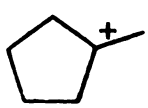
4.9%

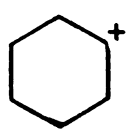


2.7% *

(Based on alcoholic fraction = 100%)

alkyl shift yields a cyclohexyl cation which can more easily accommodate the trigonal carbonium ion center.





Two possible mechanistic schemes (See Figure 7) can account for the above products: one based solely on classical alkyl and hydride shifts, and the other incorporating a protonated cyclopropane intermediate.

Two approaches were used to determine if a protonated cyclopropane

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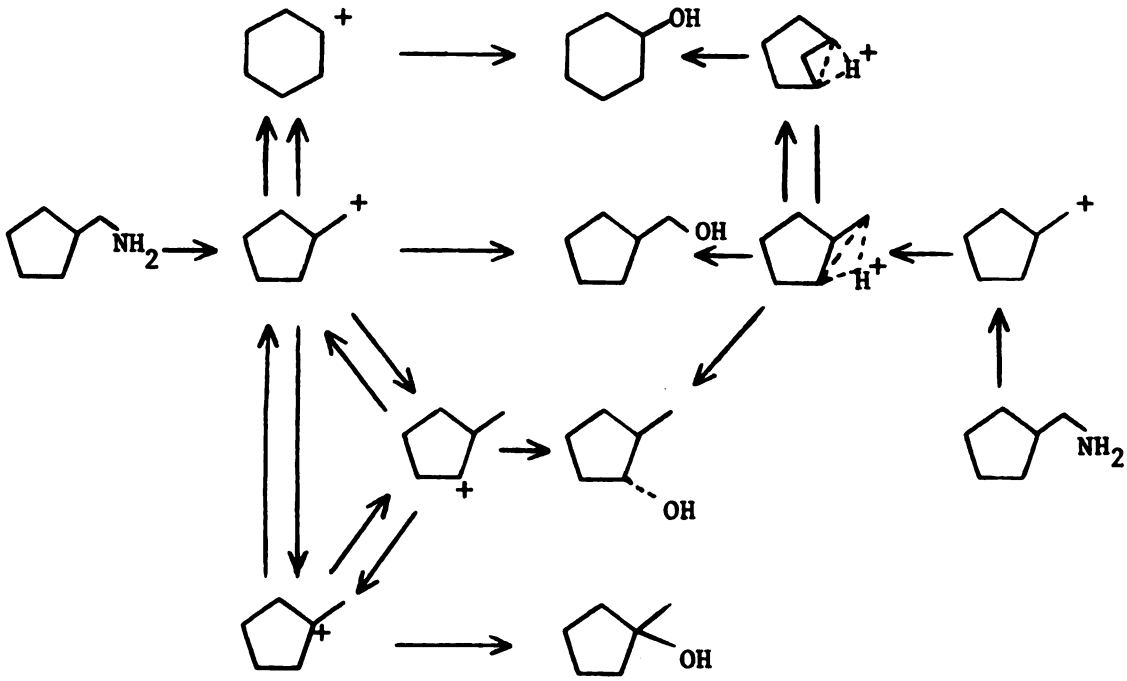
*This product identified as 100% trans-2-methylcyclopentanol by comparison with samples of cis and trans-2-methylcyclopentanol synthesized by other means. See experimental.



Possible Mechanistic Schemes for Deamination of

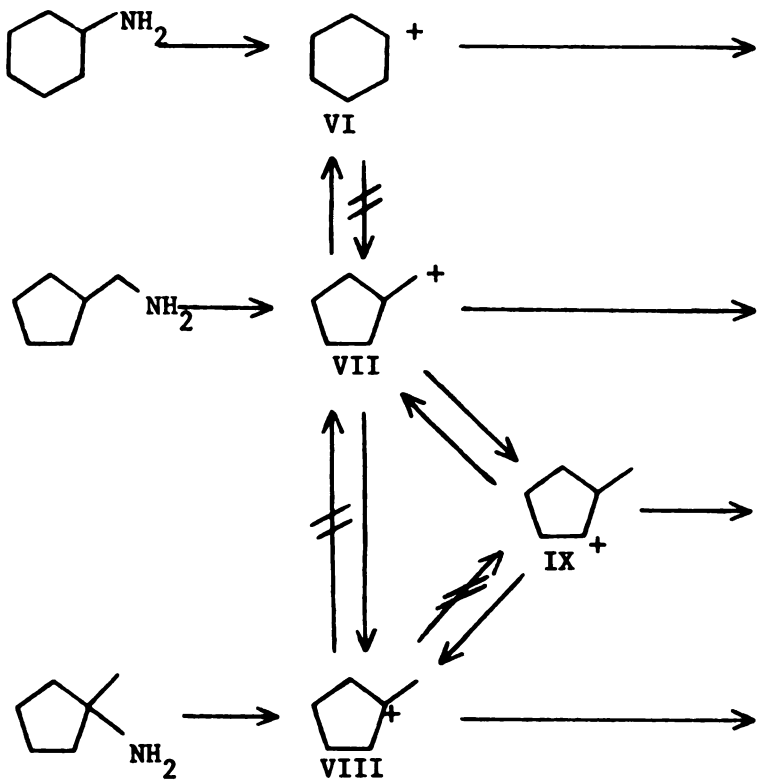
Cyclopentylcarbinyl Amine

Figure 7

intervenes in the rearrangement sequence. First, classical reaction pathways were explored by deamination of cyclohexyl and 1-methylcyclopentyl amines, allowing entrance into the above mechanistic scheme at the corresponding carbonium ions. Second, deamination of several deuterated cyclopentylcarbinyl amines were studied in order to determine if the resulting isotope position rearrangement patterns are more consistent with classical or non-classical intermediates.

Cyclohexyl amine was deaminated under conditions identical to those used for cyclopentylcarbinyl amine, and the resulting material was analyzed by gas chromatography. The only alcohol found was cyclohexanol. 1-methylcyclopentyl amine was deaminated under conditions identical to those used for cyclopentylcarbinyl amine, and the

resulting material was analyzed by gas chromatography. The only alcohol found was 1-methylcyclopentanol. These results allow the left-hand portion of Figure 7 to be modified as follows:



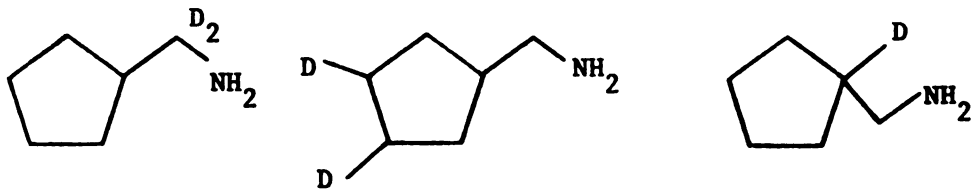
Classical Mechanism for Deamination of Cyclohexyl Amine, Cyclopentylcarbinyl Amine, and 1-methylcyclopentyl Amine

Figure 8

These changes simplify a mechanistic interpretation of this reaction in several ways. First, the possibility of an equilibrium interchange between the three ions VI, VII, and VIII has been eliminated. Second, the possibility of IX arising from VII by a series of 1,2 hydride shifts has also beem eliminated. This conclusion is strongly supported by the 100% trans stereochemistry of IX. Also,

because of this stereospecificity, a classical 1,3 hydride shift giving rise to IX would require attack of solvent to be concerted, or very nearly so, with hydride transfer. The formation of IX from a protonated cyclopropane carries no such restrictions.

The most widely accepted type of evidence for protonated cyclopropane intervention is the observation of isotope position rearrangement patterns typical of this type of intermediate and not consistent with a classical mechanism. Hence, in order to examine the possibility of protonated cyclopropane participation in this rearrangement, the following deuterated cyclopentylcarbinyl amines were prepared and deaminated:



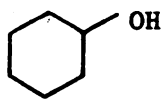
Deamination of Cyclopentylaminomethane-1,1-d_2

Cyclopentylaminomethane-1,1-d_2 was prepared by reduction of cyclopentylnitrile with lithium aluminum deuteride and deaminated under conditions identical to those used for cyclopentylcarbinyl amine. Analysis of the resulting alcohols indicated a product distribution as in Table 6.

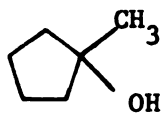
Each of the products, with the exception of 1-methylcyclopentanol which could only arise by a classical 1,2 hydride shift, was further analyzed to determine if the deuterium distribution indicated the presence of protonated cyclopropane intermediates. Table 7 shows the expected deuterium distribution pattern arising

Table 6

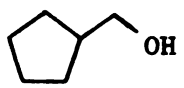
Alcoholic Products from Deamination of Cyclopentylamino-methane-1,1-$\underline{d}_2$



74.8%



17.8%



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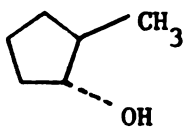


2.6%

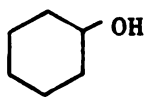
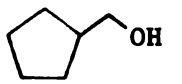
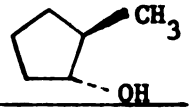
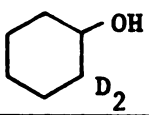
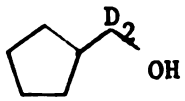
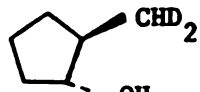
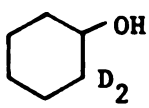
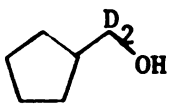
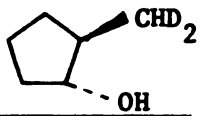
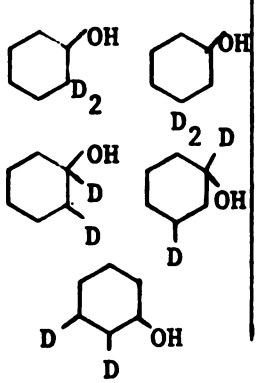
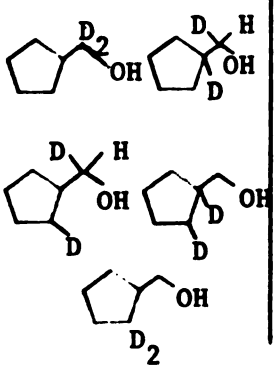
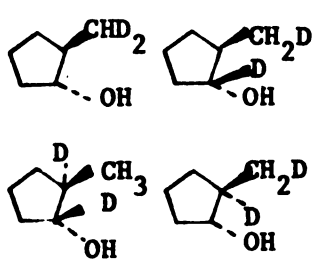
(Based on Alcoholic Fraction = 100%)

from three types of intermediates: (A) a path involving only classical alkyl and hydride shifts, (B) a route in which products are derived from a non-equilibrated protonated cyclopropane (the first non-classical intermediate capable of giving a particular product is the only intermediate involved in the formation of that material), and (C) a mechanism depending only on an equilibrated protonated cyclopropane.

The mass spectrum (See Table 8) of the trimethylsilyl ether of cyclopentylcarbinol-$\underline{d}_2$ isolated from the reaction mixture was compared to the spectra of authentic cyclopentylcarbinol-1,1-$\underline{d}_2$, and of non-deuterated cyclopentylcarbinol (See Tables 9 and 10). These results indicate that cyclopentylaminomethane-1,1-$\underline{d}_2$ showed no loss of deuterium from the one position during deamination.

Table 7

Expected Isotope Distribution in Products from the Deamination of Cyclopentylaminomethane-1,1-d_2

Mechanism	Product		
			
Classical Shifts Only			 *
Non-Equilibrated Protonated Cyclopropane			
Equilibrated Protonated Cyclopropane			

*Product from a classical 1,3 hydride shift.

Though this is perfectly consistent with a classical mechanism involving capture of the primary carbonium ion by solvent, it does not in itself rule out participation of a protonated cyclopropane in the formation of this product. The possibility exists that the protonated cyclopropane did indeed form, but was attacked by solvent before any isotope position rearrangement could occur (a non-equilibrated protonated cyclopropane), as shown in Figure 9. However, in view of work cited earlier (15, 30, 31) concerning solvent effects

Table 8

Mass Spectrum of the Trimethylsilyl Ether of Cyclopentylcarbinol

M/e	Pk. Ht.	Mono.	
107	2.7	1.5	
106	4.1	0.4	
105	44.4	31.0	7.8% of Mono. Σ 99-107
104	35.0	2.8	0.7% "
103	335.0	334.2	83.1% "
102	2.7	1.4	
101	12.1	11.3	
100	2.0	0.3	M/e 103 = $(p\text{-}C_5H_9)^+$
99	15.4	15.4	

Table 9

Mass Spectrum of the Trimethylsilyl Ether of Cyclopentylcarbinol-1,1-$\underline{d}_2$ *

M/e	Pk. Ht.	Mono.	
108	3.9	0.4	
107	42.5	28.7	6.7% of Mono. Σ 99-108
106	37.2	3.0	0.7% "
105	350.0	347.7	80.6% "
104	21.0	20.0	4.4% "
103	9.4	8.7	
102	5.2	4.3	
101	8.4	7.7	
100	5.3	4.8	
99	6.2	6.2	

*Parent ion analysis of this compound gave an isotopic distribution of 95.4% $\underline{d}_2$, 4.6% $\underline{d}_1$

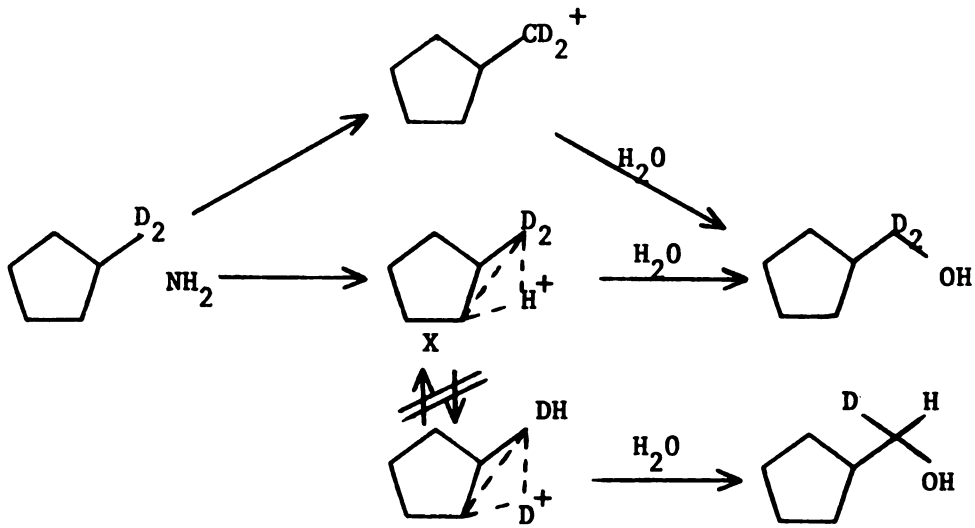
Table 10

Mass Spectrum of the Trimethylsilyl Ether of Cyclopentylcarbinol Isolated from the Deamination of Cyclopentylaminomethane-1,1-$\underline{d}_2$ *

M/e	Pk. Ht.	Mono.	
108	1.4	0.1	
107	15.9	10.8	6.5% Mono. Σ 99-108
106	14.0	1.3	0.8% "
105	129.0	127.5	77.0% "
104	11.3	10.8	6.5% "
103	5.0	4.3	1.6% "
102	3.1	2.3	
101	4.6	4.0	
100	2.3	1.8	
99	2.7	2.7	

* Parent ion analysis of this compound gave an isotopic distribution of 93.0% $\underline{d}_2$, 6.9% $\underline{d}_1$, 0.1% $\underline{d}_0$

and protonated cyclopropane, such a possibility should be judged as unlikely, since maximum isotope position rearrangement occurs in highly polar solvents such as the $H_2O/HClO_4$ system used. Furthermore, solvent attack on an ion such as (X) would be expected at the secondary carbon, yielding trans-2-methylcyclopentenol, rather than at the primary position. Hence, it is unlikely that a protonated cyclopropane intermediate is involved in the formation of this primary alcohol.



Possible Mechanisms for Formation of Cyclopentylcarbinol-1,1-$\underline{d}_2$ from Cyclopentylaminomethane-1,1-$\underline{d}_2$

Figure 9

A search for indications of protonated cyclopropane intermediates in the formation of cyclohexanol also proved fruitless. While a classical alkyl shift would result only in cyclohexanol-2,2-$\underline{d}_2$, a mechanism involving an equilibrated protonated cyclopropane would yield several deuterated cyclohexanols, including a species with a deuterium substituted in the one position. A careful comparison of

the NMR spectra (See Figures 10 and 11) obtained from cyclohexanol and cyclohexanol isolated from the deamination mixture indicated no incorporation of deuterium into the one position. However, due to the large percentage of cyclohexanol formation in this reaction, a small contribution from an equilibrated protonated cyclopropane intermediate could have been masked. And again, the absence of any isotope position rearranged product does not necessarily eliminate the possibility of protonated cyclopropane intermediates, but only of equilibrating protonated cyclopropanes.

In view of experiments cited earlier (50) involving deamination of labeled cyclopentylcarbinyl amine, approximately 3%-9% of the intermediate cyclohexyl cation should have undergone a 1,2 hydride shift, resulting in a substantial amount of deuterium at C-1 in the product alcohol. That this was not observed indicates hydride shifts in the cyclohexyl cation under present conditions occur to either a considerably smaller extent than that reported, or not at all. The significance of this fact will be more fully explored later.

Because of its 100% trans stereochemistry, 2-methylcyclopentanol is the most likely product to examine for evidence of protonated cyclopropane involvement. Though both a concerted 1,3 hydride shift and a non-equilibrated protonated cyclopropane intermediate give the same product, equilibration between various protonated cyclopropane forms will result in loss of deuterium from the methyl group and its accumulation at C-1 and C-2 of the ring. Deuterium at C-2 should be detectable by observation of an NMR splitting pattern for the methyl group consistent with a vicinal deuterium.

Unfortunately the spectrum (See Figure 12) of this product does

Figure 10

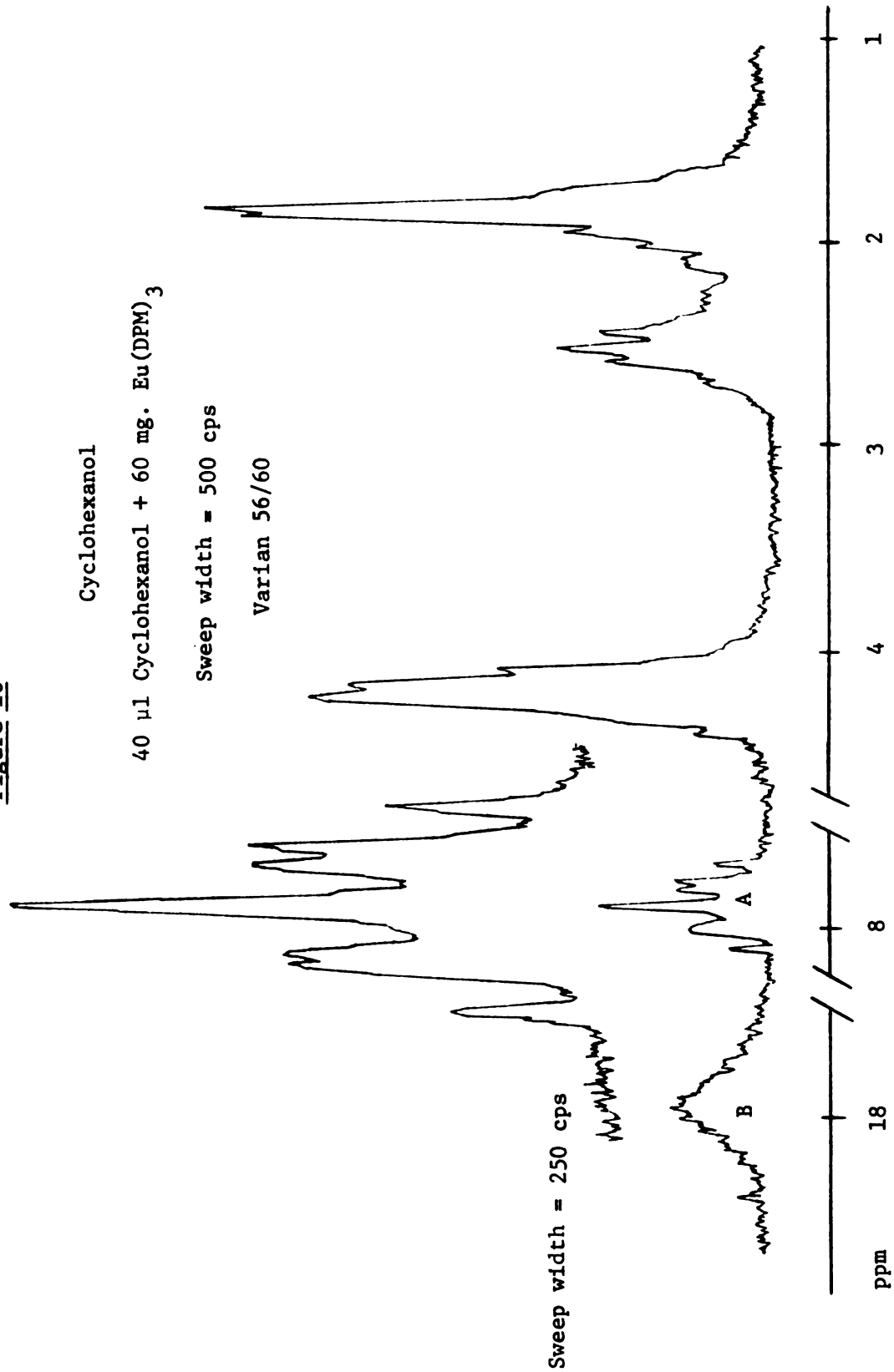

Cyclohexanol
40 µl Cyclohexanol + 60 mg. Eu(DPM)3
Sweep width = 500 cps
Varian 56/60
Sweep width = 250 cps
B
A
ppm
18
8
4
3
2
1

Figure 11

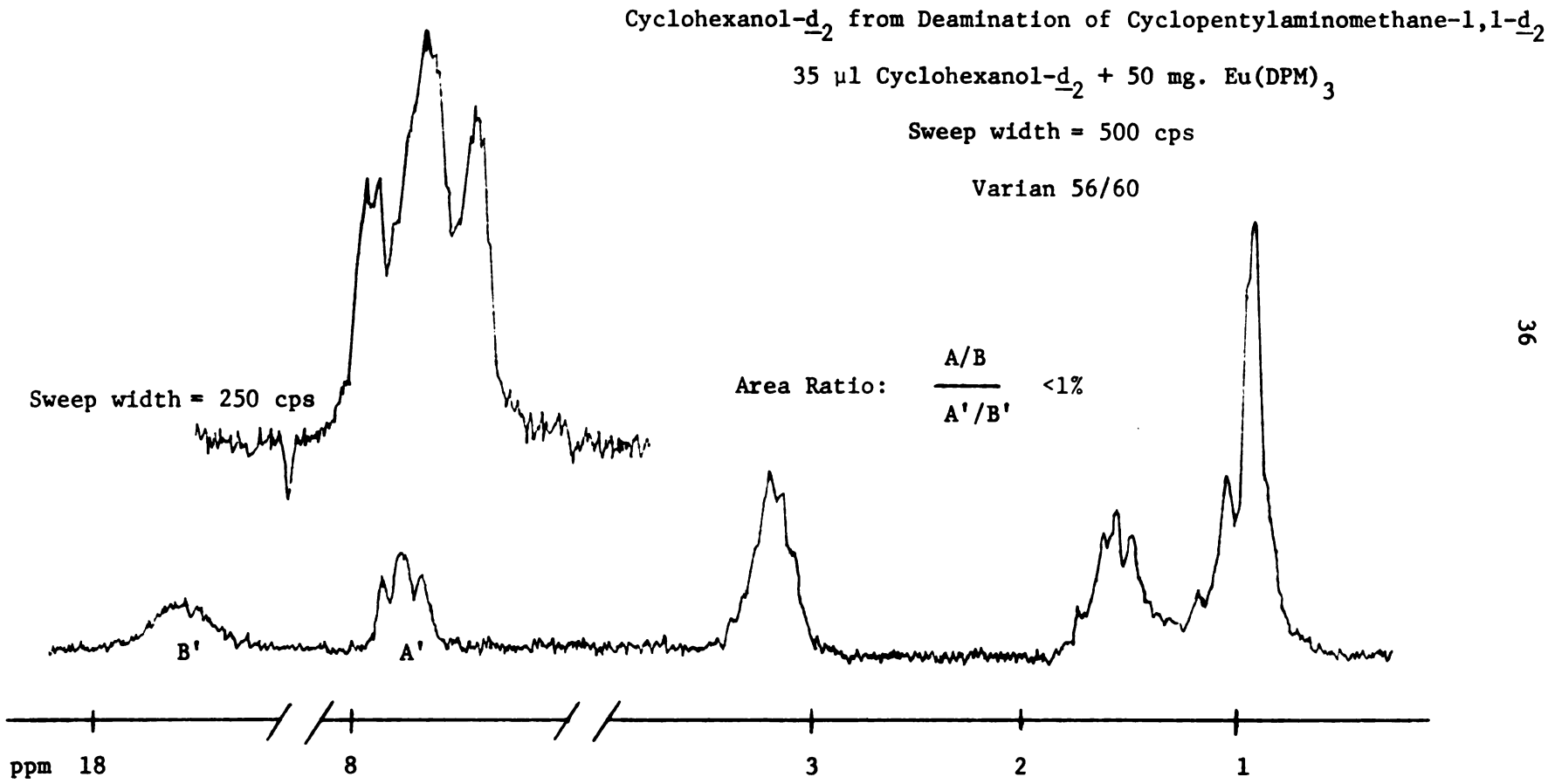
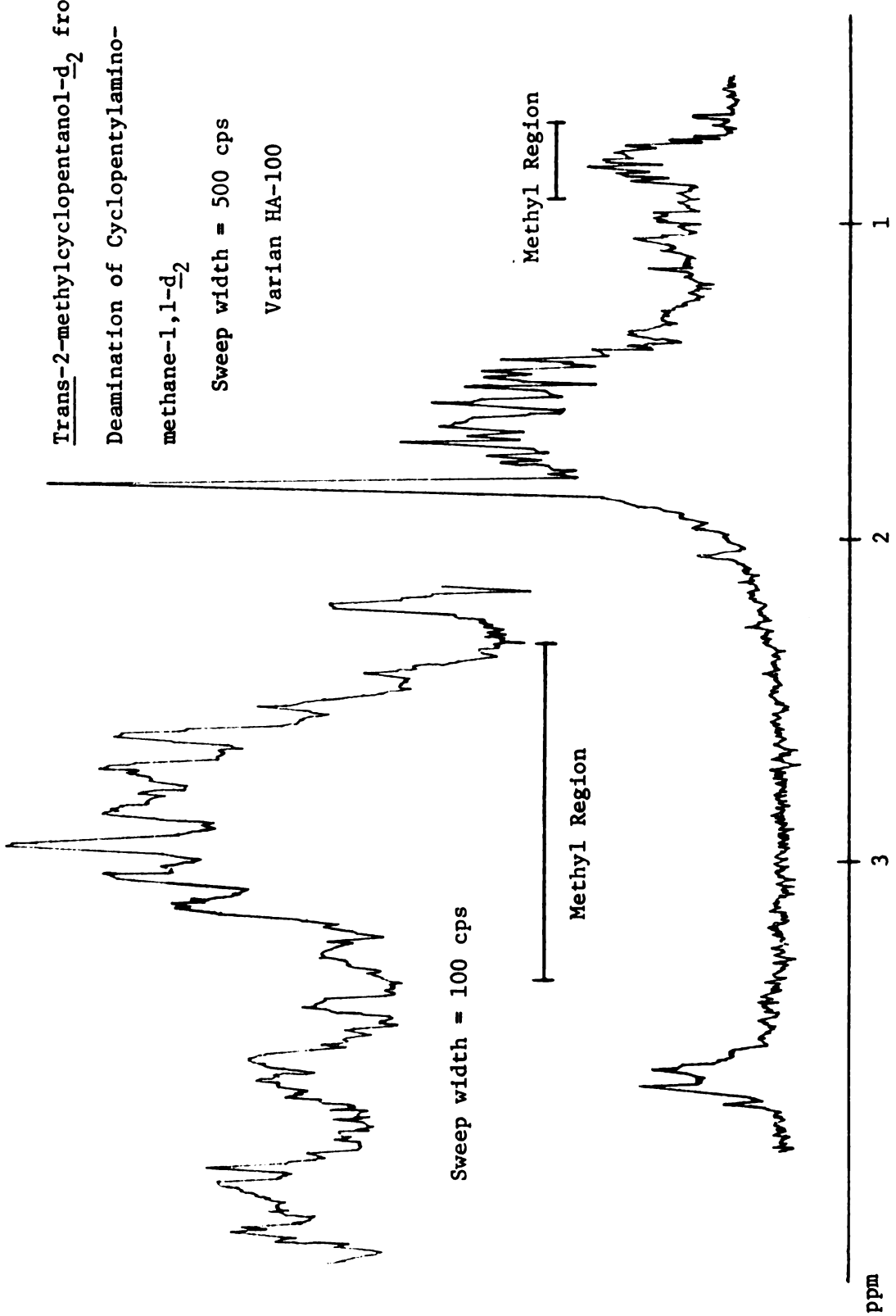

Cyclohexanol-d2 from Deamination of Cyclopentylaminomethane-1,1-d2
35 µl Cyclohexanol-d2 + 50 mg. Eu(DPM)3
Sweep width = 500 cps
Varian 56/60
Sweep width = 250 cps
Area Ratio: A/B / A'/B' <1%
B'
A'
ppm 18
8
3
2
1

Figure 12


Trans-2-methylcyclopentanol-d2 from
Deamination of Cyclopentylamino-
methane-1,1-d2
Sweep width = 500 cps
Varian HA-100
Methyl Region
Sweep width = 100 cps
Methyl Region
3
2
1
ppm

not lend itself to any simple analysis. Coupling between the methyl proton(s) and deuteron(s) result in a highly complex multiplet. In addition, a partial overlap of the methyl resonance and that due to ring protons serves only to further complicate the situation. Formation of trimethylsilyl ether or acetate derivatives did little to improve the spectrum. Though the use of Eu(DPM) chemical shift reagent greatly simplified the spectrum (See Figures 13 and 14), the complex splitting pattern of the methyl proton(s) made conclusive interpretation of the spectra impossible. Furthermore, the unresolvable overlap between ring protons and the methyl group eliminated peak area integration as a method for determining deuterium content of the methyl group.

Deamination of 1-aminomethylcyclopentane-3,4,-d_2

1-aminomethylcyclopentane-3,4-d_2 was prepared from dicyclopentadiene according to the sequence of reactions in Figure 15.

Tris(triphenylphosphine)chlororhodium (I) hydrogenation catalyst (Wilkinson hydrogenation catalyst) has been shown to specifically hydrogenate vinyl carbons and to introduce no hydrogen interchange or scrambling in the remainder of the molecule (51, 52, 53).

The resulting amine was deaminated under the same conditions as before, and the alcoholic products isolated. Yields are given in Table 11.

Table 12 shows expected isotope distribution in products arising from the three possible mechanisms cited earlier.

Figure 13

Trans-2-methylcyclopentanol-$\underline{d}_2$ from Deamination of

Cyclopentylaminomethane-1,1-$\underline{d}_2$

30 µl trans-2-methylcyclypentanol-$\underline{d}_2$ + 35 mg $Eu(DPM)_3$

Sweep width = 500 cps

Varian 56/60

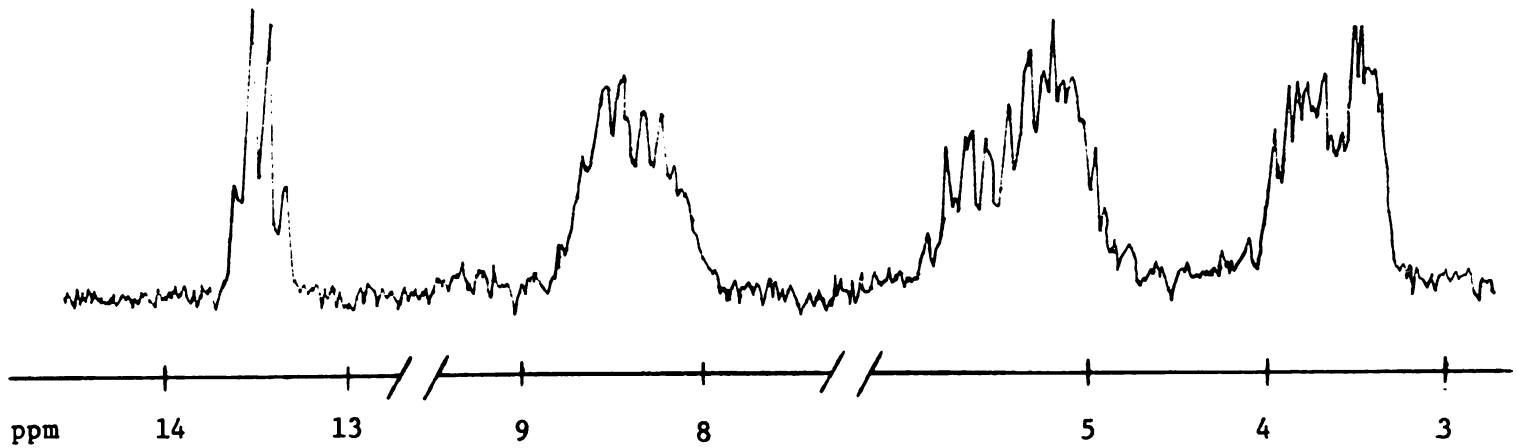


Figure 14

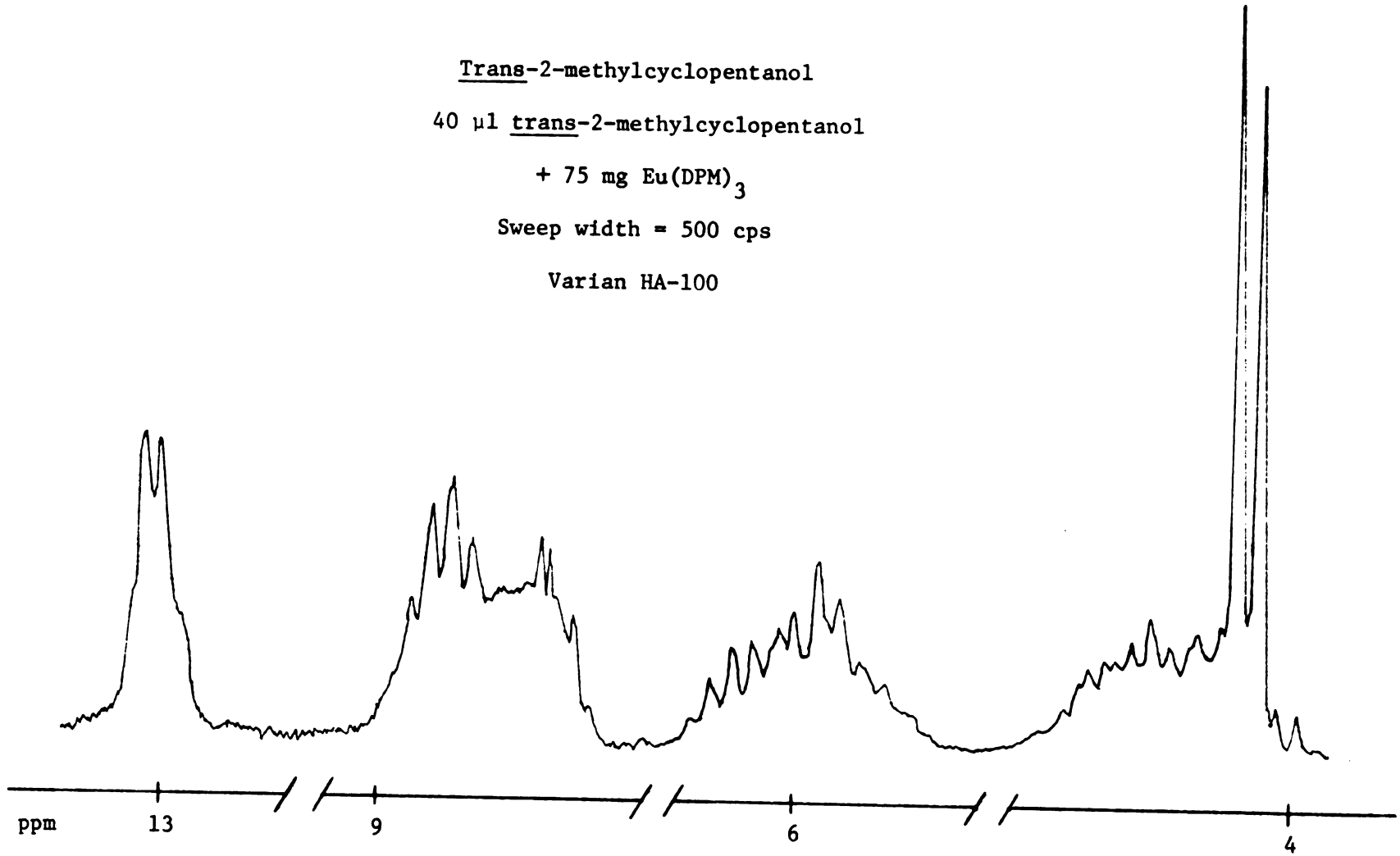
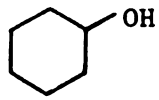

Trans-2-methylcyclopentanol
40 µl trans-2-methylcyclopentanol
+ 75 mg Eu(DPM)3
Sweep width = 500 cps
Varian HA-100
ppm
13
9
6
4

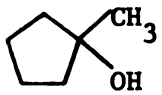
Table 11

Alcoholic Products from Deamination of

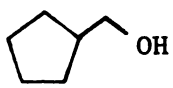
1-aminomethylcyclopentane-3,4-d_2



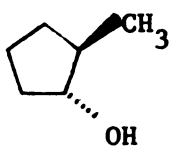
74.8%



17.4%



5.1%



2.8%

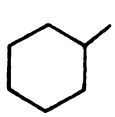
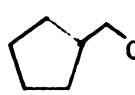
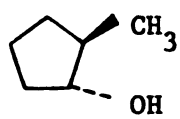
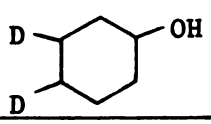
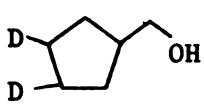
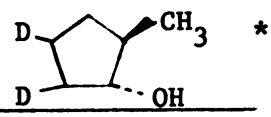
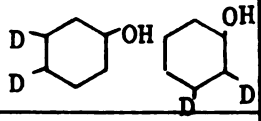
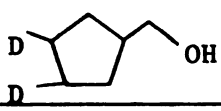
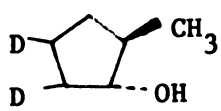
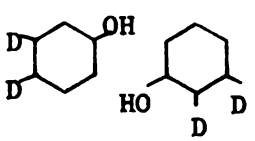
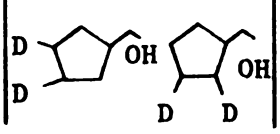
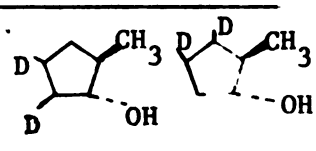
(Based on Alcoholic Fraction = 100%)

Table 12

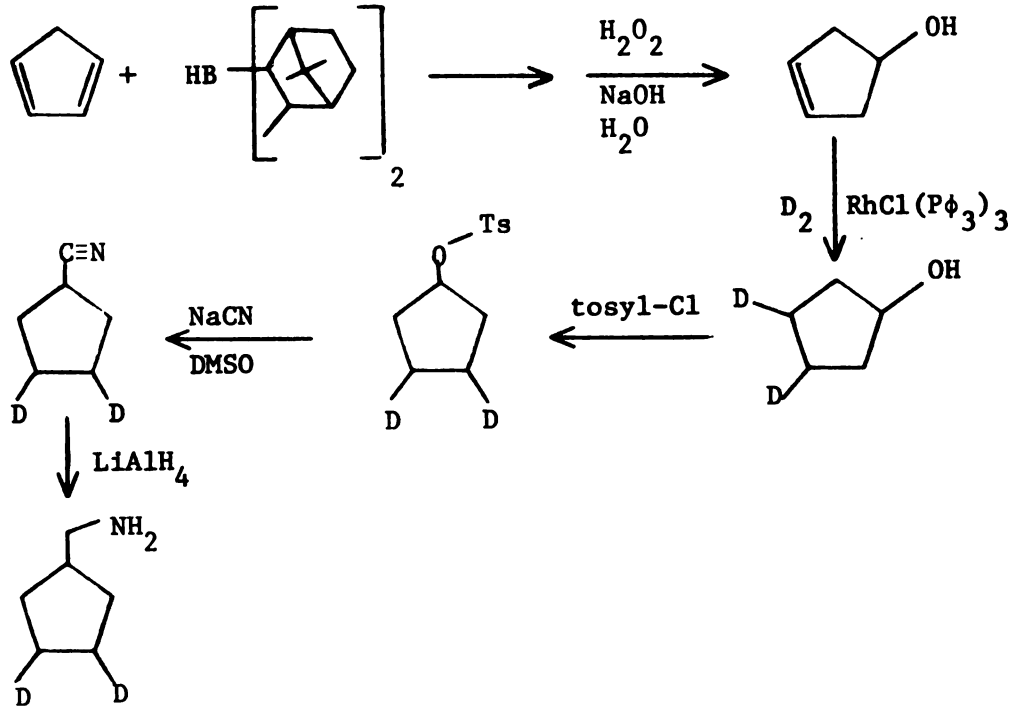
Expected Isotope Distribution in Products from the Deamination

of 1-aminomethylcyclopentane-3,4-d_2

Products

Mechanism			
Classical Shifts Only			 *
Non-Equilibrated Protonated Cyclopropane			
Equilibrated Protonated Cyclopropane			

*Product from a classical 1,3 hydride shift.



Preparation of 1-aminomethylcyclopentane-3,4-$\underline{d}_2$

Figure 15

The mass spectra of the trimethylsilyl ether of cyclopentylcarbinol isolated from the reaction mixture showed no deuterium in the one position (See Tables 13, 14 and 15).

Comparison of NMR spectra (See Figures 10 and 16) of cyclohexanol and cyclohexanol resulting from this reaction indicated no detectable deuterium in the one (by integration) or two position (by lack of deuterium coupling with the one proton).

Though far from exact, the above analysis should have been able to indicate deuterium concentrations of greater than 2%-3% in the one position or greater than 5%-6% at the two position. Consequently, some protonated cyclopropane derived product could have gone undected.

Table 13

Mass Spectrum of the Trimethylsilyl Ether of Cyclopentyl-carbinol

M/e	Pk. Ht.	Mono.	
107	2.5	0.4	
106	6.5	1.7	0.3% of Mono. Σ 99-107
105	71.6	49.2	7.5% "
104	57.0	1.5	0.2% "
103	577.	576.	87.3% "
102	3.4	2.5	
101	14.3	13.7	
100	2.0	0.6	M/e 103 = $(p\text{-}C_5H_9)^+$
99	14.3	14.3	

Table 14

Mass Spectrum of the Trimethylsilyl Ether of 1-aminomethyl-cyclopentane-3,4-$\underline{d}_2$ *

M/e	Pk. Ht.	Mono.	
107	2.3	0.7	
106	10.1	7.1	1.7% of Mono. Σ 99-107
105	38.8	25.0	6.1% "
104	35.3	1.0	0.2% "
103	357.	356.	86.3% "
102	3.9	2.9	
101	9.4	8.8	
100	4.2	3.5	
99	7.3	7.3	

*Parent ion analysis of this compound gave an isotopic distribution of 95.8% $\underline{d}_2$, 3.1% $\underline{d}_1$, 1.1% $\underline{d}_0$

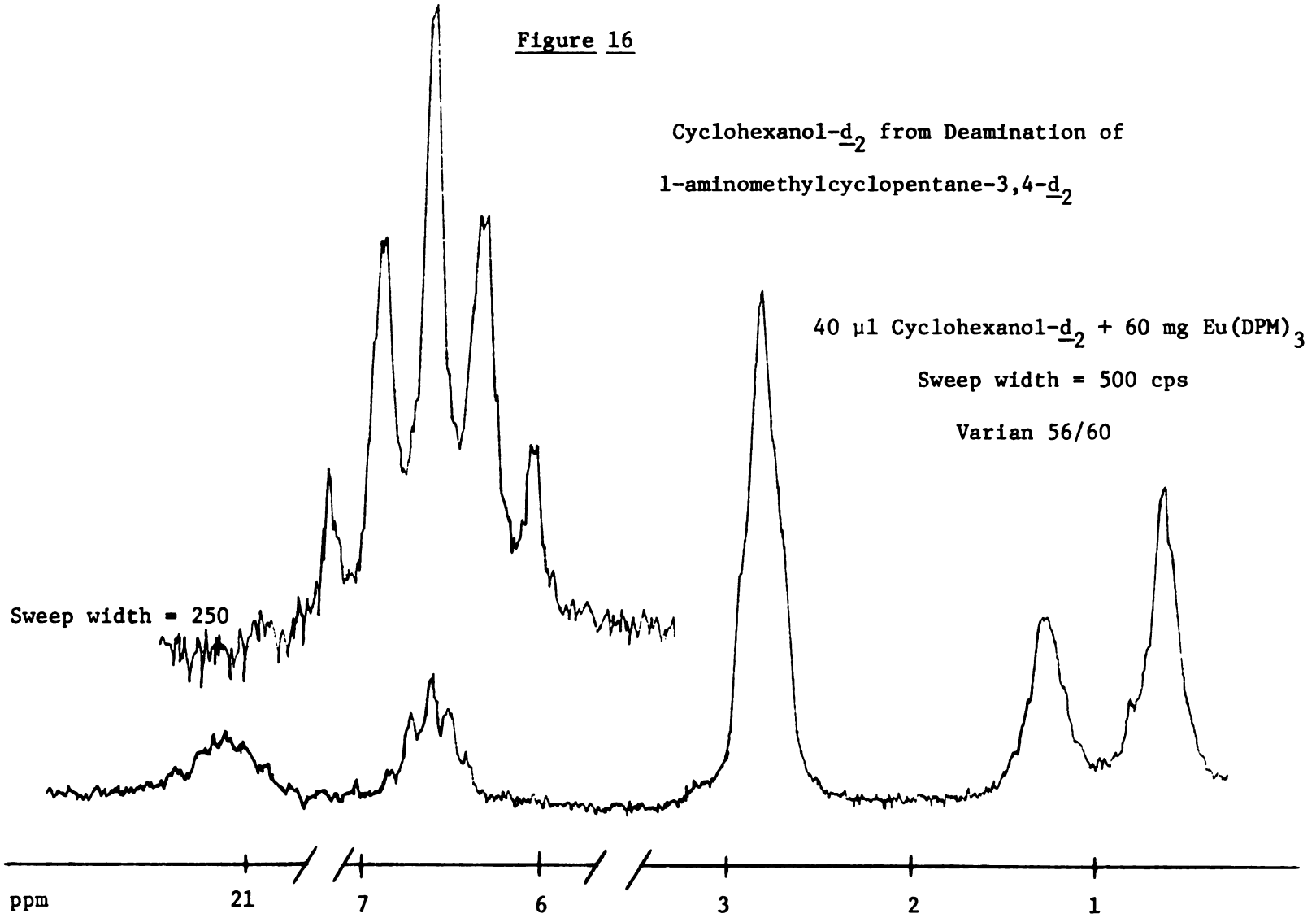
Table 15

Mass Spectrum of the Trimethylsilyl Ether of Cyclopentylcarbinol* isolated from Deamination of 1-aminomethylcyclopentane-3,4-$\underline{d}_2$

M/e	Pk. Ht.	Mono.		
107	2.7	0.5		
106	13.4	9.3	1.5% of Mono.	Σ 99-107
105	53.5	33.9	5.5%	"
104	49.5	0.4	0.1%	"
103	510.	508.	81.9%	"
102	10.9	6.8		
101	40.9	39.7		
100	8.0	6.5		
99	15.2	15.2		

*Parent ion analysis of this compound gave an isotopic distribution of 95.8% $\underline{d}_2$, 3.1% $\underline{d}_1$, 1.1% $\underline{d}_0$

Figure 16


Cyclohexanol-d2 from Deamination of
1-aminomethylcyclopentane-3,4-d2
40 µl Cyclohexanol-d2 + 60 mg Eu(DPM)3
Sweep width = 500 cps
Varian 56/60
Sweep width = 250
ppm
21
7
6
3
2
1

These results do, however, support the earlier conclusion that the relatively large amounts of 1,2 hydride shifts previously observed in these systems (50) are much less important under present conditions.

As expected, the NMR spectra (See Figures (17 and 18) of trans-2-methylcyclopentanol isolated from the reaction mixture showed no deuterium at either C-2 of the ring or in the methyl group. This indicates the absence of any significant amount of successive 1,2 or 1,3 hydride shifts which would interfere in the analysis of isotope position rearrangements in the formation of this product from other deuterated cyclopentylcarbinyl amines.

Deamination of 1-aminomethylcyclopentane-1-d

1-aminomethylcyclopentane-1-d was synthesized by treatment of cyclopentanone with lithium aluminum deuteride, conversion of the resulting alcohol to the tosylate, reaction of the tosylate with sodium cyanide, and reduction of the nitrile to the desired amine. Deamination was accomplished under the same conditions as before, and the resulting alcohols were isolated by gas chromatography.

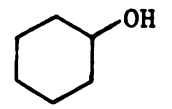
The expected isotope distribution in products arising from three possible mechanisms is given in Table 17.

Comparison of the NMR spectra (See Figures 10, 19, 20) of cyclohexanol and authentic cyclohexanol-1-d with that of cyclohexanol isolated from the reaction indicated a 10% loss of deuterium from C-1. Since it has already been shown that under present conditions, 1,2 hydride shifts could not account for such a large amount of

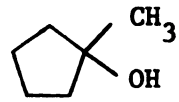
Table 16

Alcoholic Products from Deamination of

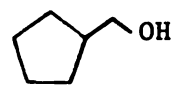
1-aminomethylcyclopentane-1-d



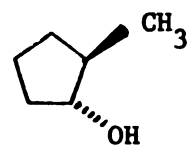
74.7%



17.7%



4.8%



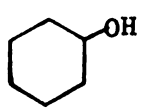
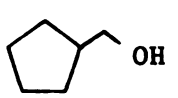
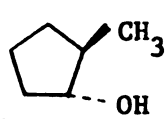
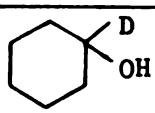
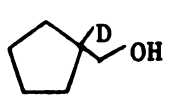
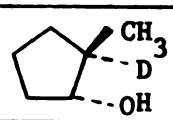
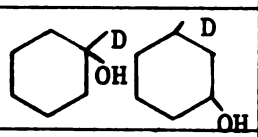
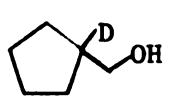
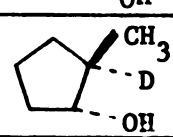
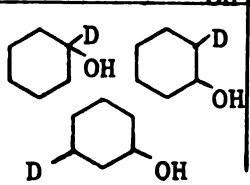
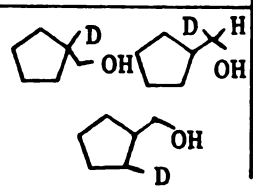
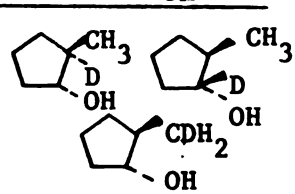
2.9%

(Based on Alcohols = 100%)

Table 17

Expected Isotope Distribution in Products from Deamination

of 1-aminomethylcyclopentane-1-d

	Product		
Mechanism			
Classical Shifts Only			 *
Non-Equilibrated Protonated Cyclopropane			
Equilibrated Protonated Cyclopropane			

*Product from a classical 1,3 hydride shift.

Figure 17

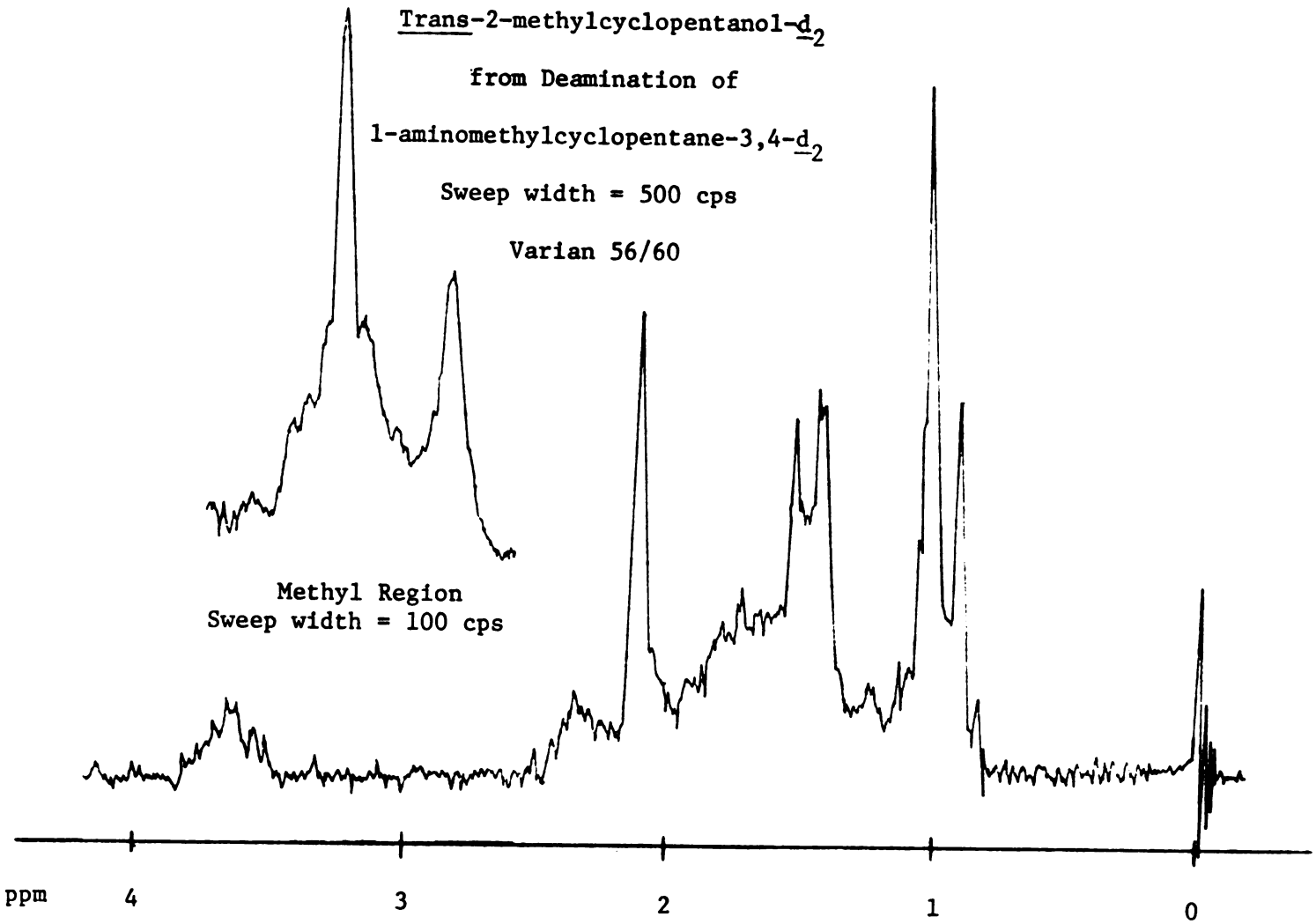
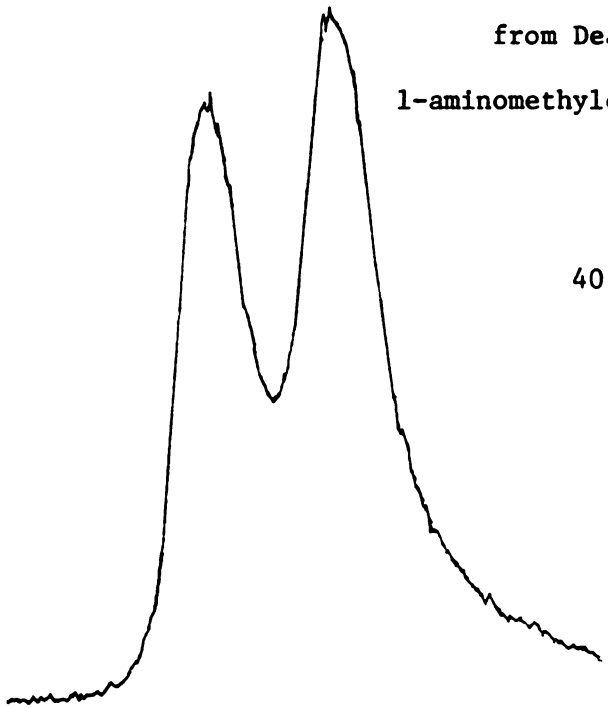

Trans-2-methylcyclopentanol-d2
from Deamination of
1-aminomethylcyclopentane-3,4-d2
Sweep width = 500 cps
Varian 56/60
Methyl Region
Sweep width = 100 cps
ppm
4
3
2
1
0

Figure 18



Methyl Region of

Trans-2-methylcyclopentanol-$\underline{d}_2$

from Deamination of

1-aminomethylcyclopentane-3,4-$\underline{d}_2$

40 µl of Trans-2-methylcyclopentanol-$\underline{d}_2$

+ 60 mg $Eu(DPM)_3$

Sweep width = 100 cps

Varian HA-100

Figure 19

Cyclohexanol-1-d

Sweep width = 500 cps

Varian 56/60

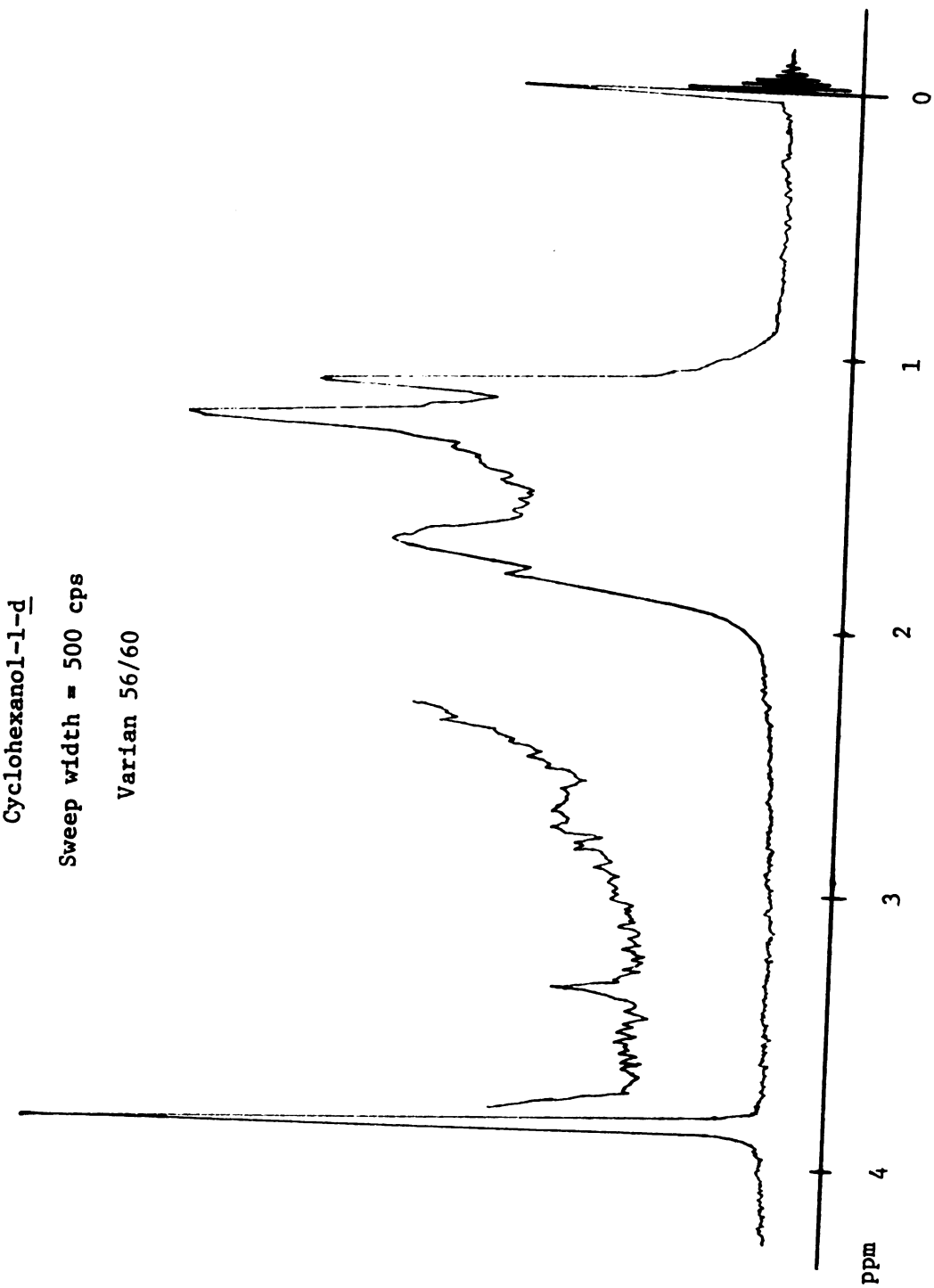


Figure 20

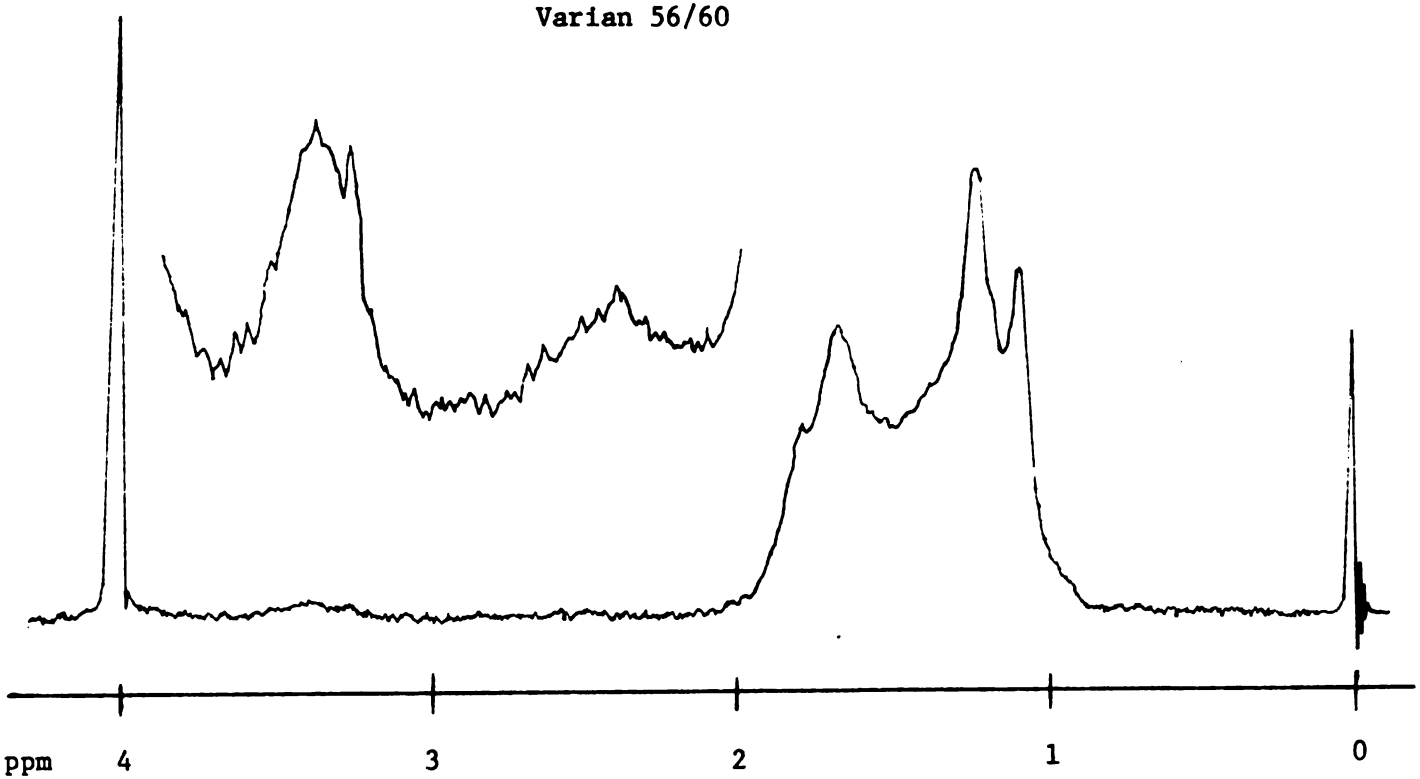
Cyclohexanol-d

from Deamination of

1-aminomethylcyclopentane-1-d

Sweep width = 500 cps

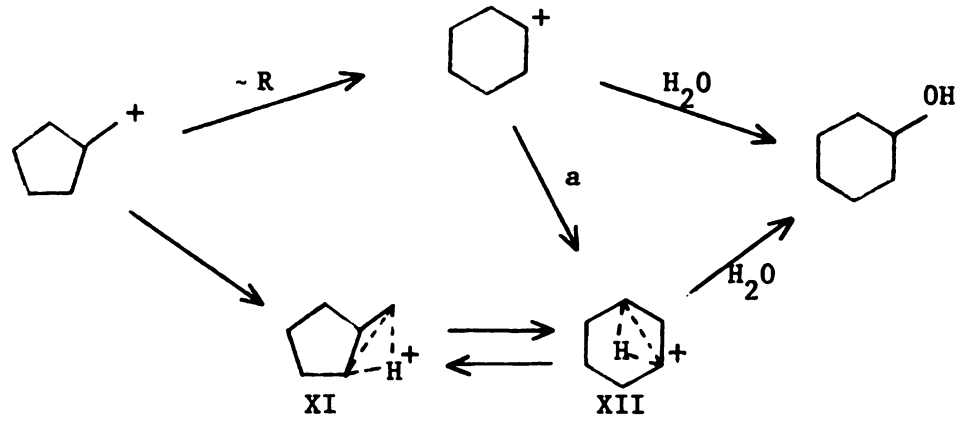
Varian 56/60



rearrangement, a protonated cyclopropane intermediate must be invoked to explain these results.

Since no cyclohexanol with deuterium at C-1 was isolated from the deamination of cyclopentylaminomethane-1,1-$\underline{d}_2$, the protonated cyclopropane intermediate that leads to cyclohexanol in this reaction must be non-equilibrated, $\underline{i.e.}$, cyclohexanol must arise from the first nonclassical intermediate capable of giving this product, and not from any other intermediate resulting from equilibrating protonated cyclopropanes.

It should be pointed out that protonated cyclopropanes could arise from two sources in this reaction as shown in Figure 21.



Possible Mechanisms for Formation of Cyclohexanol from the Cyclopentylcarbinyl Cation

Figure 21

The data of Edwards and Lesage (49) could be interpreted as if path $\underline{a}$ accounted for approximately 2% of the cyclohexyl cation with respect to elimination reactions. Furthermore, it is logical to

expect that ion XII is more stable than ion XI, since XII carries a positive charge dispersed over two secondary carbons while XI has the charge spread over one secondary and one primary carbon. Hence, a considerable portion of the first formed protonated cyclopropane, XI , would be expected to rearrange to XII, and give cyclohexanol as product. Therefore, a relatively large amount of protonated cyclopropane intervention in the formation of cyclohexanol is not unreasonable.

More conclusive evidence for the existence of protonated cyclopropane intermediates in this reaction results from examination of 2-methylcyclopentanol-d isolated from this product mixture. As shown in Table 17 only an equilibrated protonated cyclopropane could yield a product mixture containing deuterium at both C-1 and C-2 of the cyclopentyl ring. The NMR (See Figures 22 and 23) of trans-2-methylcyclopentanol-d clearly shows the methyl region as a triplet (J = 0.9) resulting from methyl-deuterium coupling, superimposed on a doublet (J = 6.0) resulting from methyl-proton coupling. Hence an equilibrating protonated cyclopropane must be an intermediate in the formation of this alcohol from cyclopentylcarbinyl amine.

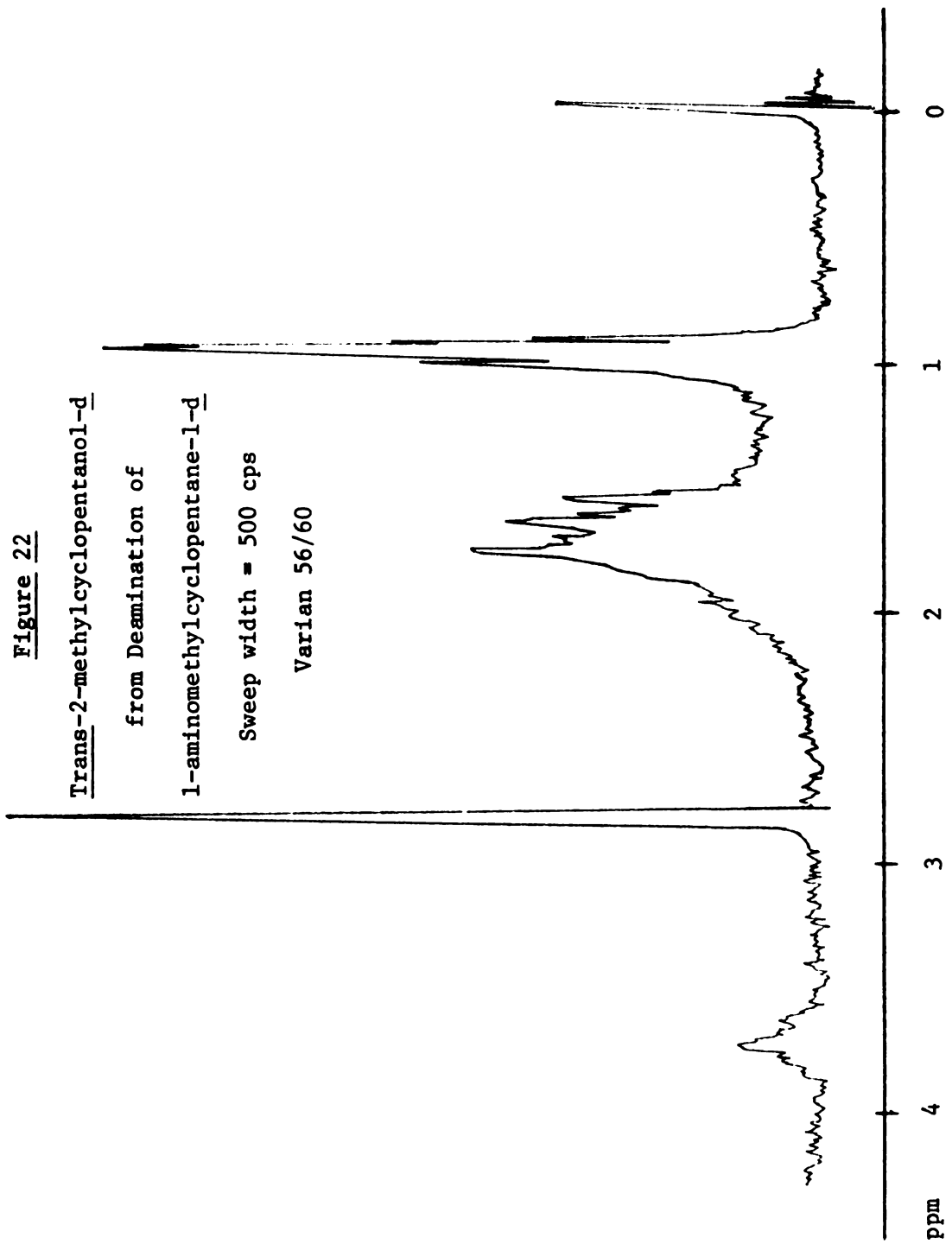


Figure 22

Trans-2-methylcyclopentanol-d

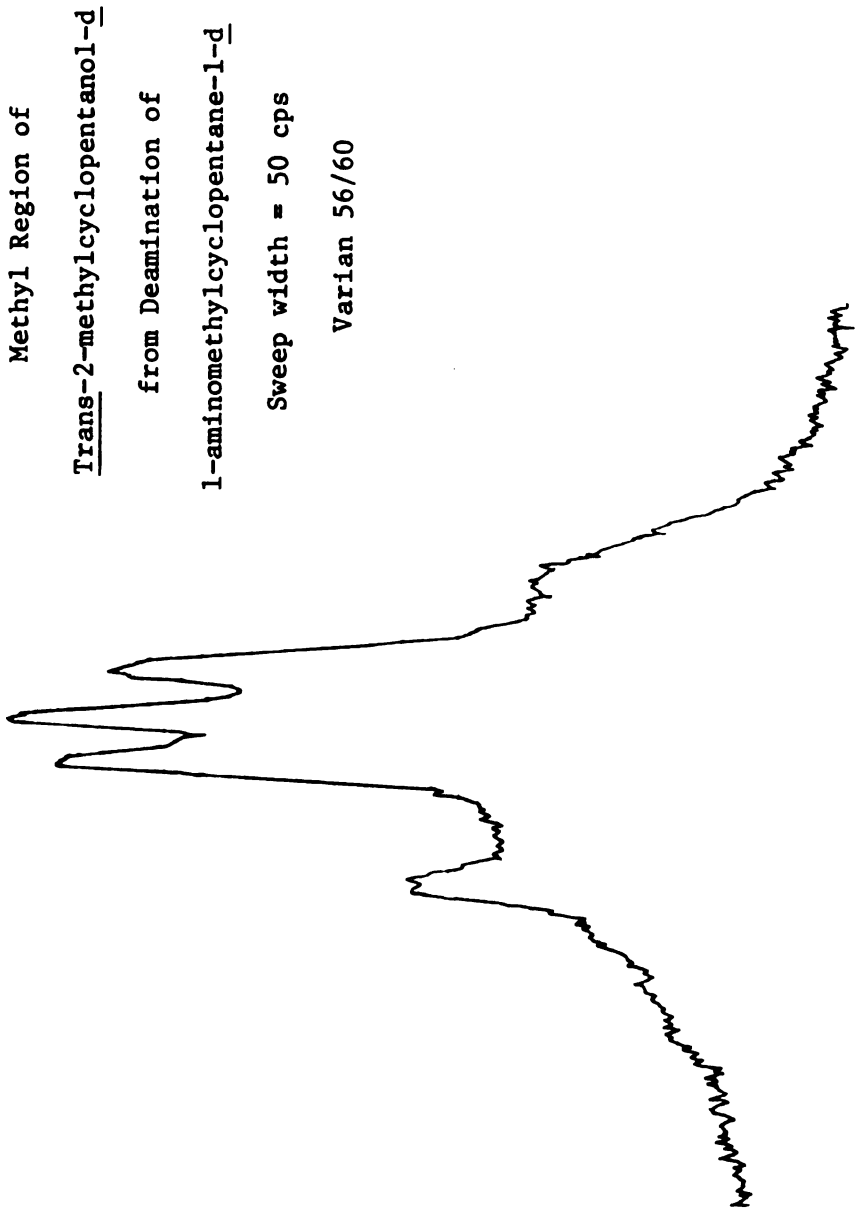
from Deamination of

1-aminomethylcyclopentane-1-d

Sweep width = 500 cps

Varian 56/60

Figure 23

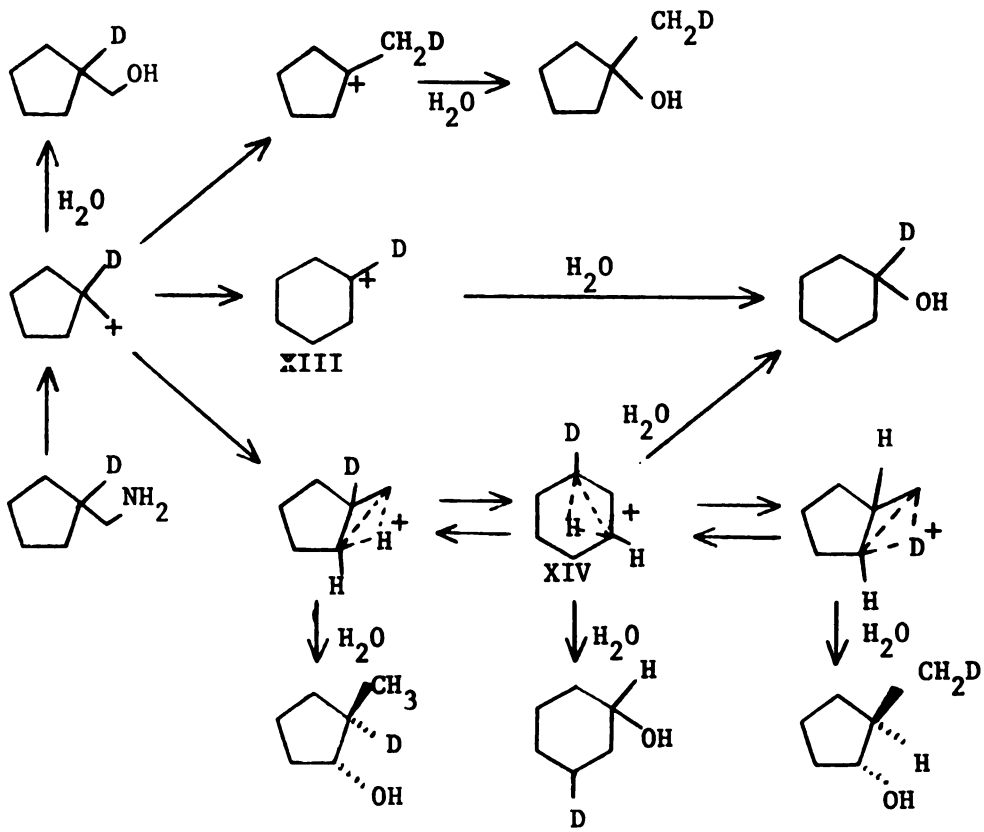

Methyl Region of
Trans-2-methylcyclopentanol-d
from Deamination of
1-aminomethylcyclopentane-1-d
Sweep width = 50 cps
Varian 56/60

Summary and Conclusions

The foregoing results conclusively demonstrate that protonated cyclopropane intermediates are involved in the formation of cyclohexanol and trans-2-methylcyclopentanol in the deamination of cyclopentylcarbinyl amine. This conclusion was reached in the following manner. The isotope position rearrangements observed in the formation of trans-2-methylcyclopentanol from 1-aminomethylcyclopentanol-1-d are consistent with an equilibrated protonated cyclopropane intermediate, but inconsistent with a classical 1,3 hydride shift. The possibility of successive 1,2 hydride shifts or equilibration of classical ions involved in the formation of this alcohol was eliminated by deamination of cyclohexyl and 1-methylcyclopentyl amines and supported by the isotope position rearrangement pattern observed in the deamination 1-aminomethylcyclopentane-3,4-d_2. For cyclohexanol, the isotope position rearrangements observed in the deamination of 1-aminomethylcyclopentane-1-d are consistent with a protonated cyclopropane intermediate yet inconsistent with an alkyl shift mechanism. The possibility of 1,2 or 1,3 hydride shifts accounting for the observed results were eliminated by deamination of cyclopentylaminomethane-1,1-d_2 and 1-aminomethylcyclopentane-3,4-d_2. The isotope position rearrangements found in cyclohexanol resulting from cyclopentylaminomethane-1,1-d_2 also eliminate equilibrated protonated cyclopropanes as intermediates in the formation of this product. Deamination of cyclohexyl and 1-methylcyclopentyl amines eliminate equilibration between classical ions as a possible

explanation for the observed isotope position rearrangement.

A mechanistic scheme, shown in Figure 24, can thus be written that is consistent with the above observations.



Mechanism for Deamination of 1-aminomethylcyclopentane-1-d

Figure 24

The above outline shows 1-aminomethylcyclopentane-1-d as the starting amine. Similar sequences could be drawn for the other cyclopentylcarbinyl amines discussed in this thesis. Also, protonated cyclopropane equilibration sequences slightly different than that shown, yet also consistent with the data, could be drawn. Any such sequences, however, must account for the non-equilibrated

nature of the protonated cyclopropane precursor to cyclohexanol. For example, an ion such as XIV resulting from cyclopentylaminomethane-1,1-$\underline{d}_2$ would yield only cyclohexanol-2,2-$\underline{d}_2$ and give no alcohol with deuterium at C-1, as observed.

It is difficult to estimate the exact amount of protonated cyclopropane formation in this reaction. Because of the large amount of isotope rearrangement found in trans-2-methylcyclopentane (See Figures 22 and 23) and because of the 100% trans stereochemistry of this product, it is assumed that all of this compound comes from protonated cyclopropanes. Though classical shifts are undoubtedly responsible for the bulk of cyclohexanol formation, the surprisingly large amount of isotope position rearranged product isolated from 1-aminomethylcyclopentane-1-$\underline{d}$, coupled with the necessary occurrence of a protonated cyclopropane capable of giving cyclohexanol in the equilibrating system necessary to explain the isotope position rearrangement in the formation of trans-2-methylcyclopentanol, indicate that a substantial amount, at least 3%-10%, of cyclohexanol formed in this reaction results from protonated cyclopropanes.

Consequently, a minimum of approximately 5% of the total products derived from the deamination of cyclopentylcarbinyl amine can be said to result from protonated cyclopropane. This large amount of nonclassical ion formation in competition with classical pathways that result in relatively stable secondary and tertiary ions furnishes ample support for the hypothesis that protonated cyclopropane formation is enhanced in sterically favorable cyclic systems.

EXPERIMENTAL

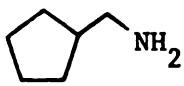
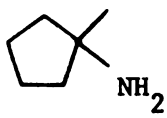
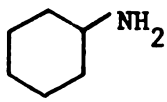
NMR Spectra. All NMR Spectra were taken on either a Varion 56/60 or HA-100 spectrometers, at room temperature, and as 10%-30% carbon tetrachloride solutions. Integrations were made both electronically and with a planimeter.

Gas Chromatography. Gas chromatographic analyses were preformed on an Aerograph A-90-P by using a 1/4" x 20' column packed with 20% carbowax 20-M on 60/80-AW/HMDS-chromasorb W. Unless otherwise noted, preparative scale gas chromatography was done on the same instrument by using either the above column or a 1/4" x 6' column packed with the same material.

Deamination Procedure. All deaminations were carried out in the following manner. A 0.100 mole of amine was dissolved in 75 ml of distilled water. The solution was contained in a round-bottomed flask, immersed in an ice bath, and fitted with an addition funnel, condenser, nitrogen inlet tube, and magnetic stirrer. A mixture of 0.130 moles of perchloric acid (as standard 70% solution) and 25 ml H_2O was added, and the resulting salt solution stirred at 0° for one-half hour. Deamination was then accomplished by very slow addition of 0.210 moles of sodium nitrite in 32 ml of water. The reaction was warmed to room temperature and stirred for four - six hours. The entire procedure was carried out under a nitrogen atmosphere.

The reaction mixture was saturated with sodium chloride and extracted with 5 x 75 ml of ether. The ether solution was washed with a saturated sodium bicarbonate-sodium chloride solution, dried over sodium sulfate and concentrated to approximately 15 ml by careful distillation. This crude product was than analyzed and various fractions purified and isolated as needed by gas chromatography.

Yields were normally between 70% and 80% with typical product composition as follows:

Amine	% Alcohols	% Alkenes	% Unidentified Components *
	88	4	8
	89	2	9
	95	3	2

* Presumably composed of nitrite esters and unreacted amine.

Preparation of Trimethylsilyl Ethers. The trimethylsilyl ethers of alcohols to be analyzed by mass spectroscopy were prepared in the following manner. Approximately 100 micro-liters of alcohol was placed in a small tube equipped with a cold finger-reflux condenser, and immersed in an oil bath at 60° - 90°. To this was added 130 micro-liters of hexamethyldisilazane followed by 10 micro-liters of dimethylchlorosilane, and the mixture was allowed to react for twelve to twenty-four hours. The resulting trimethylsilyl ether

was purified by preparative gas chromatography.

Preparation of Cyclopentyl Cyanide. A mixture of 15.77 g (0.32 moles) of sodium cyanide and 95 ml of dimethylsulfoxide (freshly distilled from calcium hydride) was heated to 70° - 80° in a 500 ml 3-necked flask, fitted with a mechanical stirrer, reflux condenser and addition funnel. To this was added 40.00 g (0.27 moles) of cyclopentyl bromide over a period of three hours and the resulting mixture was stirred at 70° - 80° for an additional three hours. After the reaction mixture was cooled and a vacuum distillation head attached, the product was distilled under water aspirator pressure. Approximately 60 ml of material was collected between 63° and 76°.

The resulting nitrile was purified on an F & M Model 760 preparative gas chromatograph by using a 1" x 10' carbowax 20-M column at 140°. This resulted in 14.30 g (55% yield) of pure cyclopentyl cyanide.

Preparation of Cyclopentylcarbinyl Amine. To 2.5 g (0.066 moles) of lithium aluminum hydride in 30 ml of ether 6.0 g (0.063 moles) of cyclopentyl cyanide dissolved in 20 ml of ether was added over a period of forty minutes. The reaction was contained in an ice-cooled, 3-necked flask fitted with an addition funnel, stirrer, condenser, and drying tube.

The mixture was stirred for three hours at room temperature, cooled in ice, and hydrolyzed by dropwise addition of 4 ml water followed by 4 ml of 5% sodium hydroxide solution. The ether layer was separated, dried over sodium sulfate, and carefully distilled. About

4.9 g (77% yield) of cyclopentylcarbinyl amine was collected at 135° - 136°.

Preparation of Trans-2-Methylcyclopentanol. To an ice-cooled solution of 8.00 g (0.098 moles) of 1-methylcyclopentene and 1.11 g (0.029 moles) of sodium borohydride dissolved in 50 ml of tetrahydrofuran, 5.62 g (0.039 moles) of boron trifluoride etherate dissolved in 10 ml of tetrahydrofuran was added over a period of thirty minutes. The resulting mixture was warmed to room temperature and stirred for three hours. The entire reaction was carried out under a nitrogen atmosphere.

Next, the reaction vessel was cooled in ice and 2 ml of water was added, followed by 10.0 ml of 5% sodium hydroxide and 10.0 ml of 30% hydrogen peroxide. The reaction mixture was stirred for several hours, the THF layer was removed, dried over magnesium sulfate, and evaporated. Distillation of the residue at water aspirator pressure yielded 3. 18 g (32% yield) of trans-2-methylcyclopentanol, collected at 65° - 70°.

Preparation of N-(1-methylcyclopentyl) Formamide (54). To 38 ml of glacial acetic acid contained in a 500 ml round-bottomed flask fitted with a stirrer, condenser, addition funnel, and thermometer was added 28.5 g of 1-methylcyclopentene (0.303 moles) and 5.3 g of sodium cyanide (0.303 moles). Next, 78.6 g of sulfuric acid dissolved in 38 ml of glacial acetic acid was added over one hour while the reaction temperature was maintained at 40° - 50° by use of ice bath cooling.

After the resulting mixture was stirred for eighteen hours at room temperature, it was then diluted with 300 ml of water, neutralized with a $NaOH/H_2O$ solution, and extracted with 5 x 100 ml of ether. The ether solution was dried over magnesium sulfate, the ether was evaporated, and the residue was distilled at 12 - 15 mm pressure to give 27.7 g (63% yield) of N-(1-methylcyclopentyl) formamide, boiling at 130° - 135°.

Preparation of 1-methylcyclopentyl Amine. A solution of 31.78 g (0.250 moles) of N-(1-methylcyclopentyl) formamide and 118 g potassium hydroxide in 480 ml of water was refluxed for six hours. The reaction mixture was then steam distilled, and the distillate was salted and extracted with 4 x 100 ml of ether. The ether solution was dried over sodium sulfate and after distillation yielded 10.34 g (42% yield) of 1-methylcyclopentyl amine, collected at 112° - 114°.

Preparation of Cyclopentylaminomethane-1,1-d_2. An amount of 2.00 g (0.0477 moles) of lithium aluminum deuteride was mixed with 30 ml of ether (freshly distilled from lithium aluminum hydride) contained in a 3-necked round-bottomed flask, fitted with a stirrer, addition funnel, condenser, and drying tubes, and immersed in an ice bath. To this was added, over an hour, 4.60 g (0.0485 moles) of cyclopentyl cyanide dissolved in 20 ml of ether (freshly distilled from lithium aluminum hydride). The resulting mixture was stirred at room temperature for four hours.

The reaction was again cooled in an ice bath and 4 ml of water

followed by 4 ml of a 5% sodium hydroxide solution was added. Stirring was continued for 12 hours. The ether layer was then removed, dried over sodium sulfate, stripped, and distilled to yield 3.41 g (71% yield) of cyclopentylaminomethane-1,1-d_2 boiling at 136° - 138°.

Preparation of Cyclopentanecarboxylic Acid. A hot (65° - 70°) solution of 63.2 g (0.40 moles) potassium permanganate in 330 ml water was added over two hours to 30.0 g (0.30 moles) of cyclopentylcarbinol dissolved in 100 ml of water contained in a 3-necked round-bottomed flask fitted with a stirrer, condenser, thermometer, and heated addition funnel. The reaction was stirred for an additional two hours at 50° - 60°.

The mixture was filtered and concentrated to approximately 150 ml on a rotary evaporator and the resulting solution was acidified and extracted with ether. The ether solution was dried over magnesium sulfate and distilled at 12 - 15 mm pressure. The fraction boiling between 95° - 113° was collected and redistilled to give 14.0 g (33% yield) of cyclopentanecarboxylic acid, collected at 112° - 113°.

Preparation of Cyclopentylmethanol-1,1-d_2. A solution of 6.5 g (0.058 moles) of cyclopentylcarboxylic acid dissolved in 25 ml of ether (freshly distilled from lithium aluminum hydride) was added over a period of forty minutes to a mixture of 2.4 g (0.058 moles) lithium aluminum deuteride and 40 ml of ether (freshly distilled from lithium aluminum hydride).

The reaction was stirred for sixteen hours and hydrolyzed by slow

addition of 5 ml water followed by 5 ml of a 5% sodium hydroxide solution. After an additional three hours stirring, the ether layer was removed, dried over magnesium sulfate and distilled at 12 - 15 mm to yield 4.64 g (82% yield) of the desired alcohol, collected at 80° - 85°.

Preparation of Diborane (55). A solution of 47.5 g sodium borohydride in 900 ml of diglyme (freshly distilled from lithium aluminum hydride) was added over a period of four to five hours to 337 g of boron trifluoride etherate (freshly distilled from calcium hydride). The resulting diborane was bubbled through a solution of sodium borohydride in diglyme to remove traces of boron trifluoride and into 700 ml of ice-cooled tetrahydrofuran. After the addition of sodium borohydride was complete, the generating flask was heated to 50° for an additional two hours. The entire reaction was carried out under nitrogen using a mercury safety valve, and a mercury/acetone trap to remove any escaping diborane, as described in Reference 55. The resulting B_2H_6/THF solution was found to be 1±0.1 molar by titration with a tetrahydrofuran/water solution.

Preparation of Δ^3-cyclopentenol (56). A one molar solution of diborane in tetrahydrofuran (400 ml, 0.8 moles of BH_3) was added over a period of fifteen minutes to an ice-cooled 1 liter flask containing 239.5 g of α-pinene (1.76 moles, 10% excess, freshly distilled from lithium aluminum hydride). The mixture was stirred at 0° for two hours and 105.7 g (1.6 moles) of freshly distilled cyclopentadiene was added and

stirring continued at room temperature for thirty hours. The entire reaction was carried out under nitrogen.

The reaction vessel was cooled in ice and 30 ml of water added to decompose any excess hydride. The organoborane was oxidized by dropwise addition of 256 ml of sodium hydroxide and 256 ml of hydrogen peroxide. The aqueous layer was well salted, and the organic layer removed. Excess cyclopentadiene and tetrahydrofuran were removed under vacuum, and the resulting mixture diluted with 200 ml of ether.

This solution was then stirred for one hour with 750 ml of 1 molar aqueous silver nitrate. The organic layer was removed and extracted twice more with 200 ml of silver nitrate solution. The water solutions were combined and washed twice with ether. An excess of sodium chloride was added to completely precipitate silver chloride, and the unsaturated alcohol extracted with ether. The ether solution was dried over magnesium sulfate, the ether removed, and the resulting material distilled to give 14.54 g (21.5% yield) of Δ^3-cyclopentenol.

Preparation of Tris(triphenylphosphine)chloroRhodium (I) (51, 52, 53). Freshly recrystallized triphenylphosphine (6 g) dissolved in 130 ml of degassed ethanol was heated to reflux in a nitrogen atmosphere. Rhodium chloride trihydride (1 g) was added, and refluxing continued for one-half hour. The mixture was filtered and the precipitate washed with degassed ether and dried under vacuum to yield 3.44 g (99% yield) of tris(triphenylphosphine)chloroRhodium (I).

Preparation of Cyclopentanol-3,4-d_2 (51, 52, 53). Rhodium chloride

triphenylphosphine (1.2 g) was placed in a 500 ml filter flask fitted with a rubber septum cap. The flask was repeatedly evacuated and flushed with deuterium gas. Degassed benzene (375 ml) was injected and the solution stirred for one hour. Δ^3-cyclopentenol (12.0 g) was injected and the reaction mixture stirred for five hours. The solvent was removed by distillation at atmospheric pressure, and then at reduced pressure to yield 9.29 g (71%) of cyclopentanol-3,4-$\underline{d}_2$.

Preparation of Cyclopentyltosylate-3,4-$\underline{d}_2$ (57). p-Toluenesulfonyl chloride (121 g, 0.635 moles) was dissolved in 300 ml of cold pyridine, and 28.29 g (0.318 moles) of cyclopentanol-3,4-$\underline{d}_2$ added and the resulting solution allowed to react at 0° for 24 hours. The reaction mixture was then poured into 1500 ml of a stirred ice/water mixture and stirring continued for one-half hours. The tosylate was extracted five times with 300 ml of ether, the ether solution washed with cold 1:1 hydrochloric acid/water, then with water, and dried over Na_2SO_4/K_2CO_3. The ether was removed to yield 61.18 g (73.5%) of crude tosylate.

Preparation of Cyclopentyl-3,4-$\underline{d}_2$ Cyanide. A solution of powdered sodium cyanide (15.45 g, 0.315 moles) in 100 ml dimethyl sulfoxide (freshly distilled from CaH_2) was heated to 50° - 60° and 61.18 g (0.252 moles) of crude cyclopentyltosylate added over a period of two hours. An additional portion of 50 ml of dimethyl sulfoxide was added, and the reaction maintained at 50° - 60° for five hours. The resulting mixture was cooled to approximately 40° and set up for

distillation under water aspirator pressure. Distillation was continued until approximately 60 ml had been collected. This material was redistilled twice more to yield 11.51 g (47.5% yield) of cyclopentyl-3,4-$\underline{d}_2$ cyanide.

Preparation of 1-aminomethylcyclopentane-3,4-$\underline{d}_2$. To an ice-cooled mixture of 5.90 g (0.155 moles) of lithium aluminum hydride and 70 ml of ether, 11.52 g (0.119 moles) of cyclopentyl-3,4-$\underline{d}_2$ cyanide in 50 ml of ether was added over a period of approximately one hour. The reaction was stirred at room temperature for eighteen hours. cooled in ice, and carefully hydrolyzed with 14 ml of water followed by 14 ml of a 5% sodium hydroxide solution.

The resulting mixture was stirred at room temperature for six hours. The ether layer removed, dried over sodium sulfate, and distilled to yield 7.32 g (61% yield) of 1-aminomethylcyclopentane-3,4-$\underline{d}_2$.

Preparation of Cyclopentanecarboxylic Acid-3,4-$\underline{d}_2$. A solution of 3.32 g (0.0342 moles) of cyclopentyl-3,4-$\underline{d}_2$ cyanide, 3.74 g (0.0935 moles) of sodium hydroxide and 40 ml of a 70% ethanol - 30% water solution was refluxed for four hours. Ethanol was removed on a rotary evaporator and the residue acidified with a 50% hydrochloric acid solution.

The reaction mixture was extracted with 3 x 30 ml ether, the ether solution dried over magnesium sulfate, and evaporated to yield 2.70 g (68% yield) of the deuterated acid.

Preparation of Cyclopentylcarbinol-3,4-d_2. A solution of 2.70 g (0.0233 moles) of cyclopentanecarboxylic acid-3,4-d_2 and 10 ml of ether was slowly added to an ice-cooled mixture of 1.50 g (100% excess) lithium aluminum hydride and 50 ml of ether. The reaction was stirred at room temperature for fifteen hours and hydrolyzed by careful addition of 5 ml of water followed by 5 ml of a 5% sodium hydroxide solution.

The ether layer was removed, dried over magnesium sulfate, and evaporated to yield 1.86 G (91% yield) cyclopentylcarbinol-3,4-d_2.

Preparation of Cyclopentanol-1-d. A solution of 23.90 g (0.286 moles) of freshly distilled cyclopentanone and 50 ml ether (freshly distilled from lithium aluminum hydride) was added over a period of ninety minutes to an ice-cooled mixture of 3.00 g (0.0715 moles) lithium aluminum deuteride and 100 ml of ether (freshly distilled from lithium aluminum hydride). The reaction was stirred at room temperature for sixteen hours and hydrolyzed by careful addition of 6 ml water followed by 6 ml of a 5% sodium hydroxide solution.

The ether layer was separated, dried over sodium sulfate, and evaporated to yield 22.97 g (92%) of deuterated alcohol.

Preparation of Cyclopentyltosylate-1-d. An ice cold solution of 100.00 g (0.528 moles) of p-toluenesulfonylchloride in 320 ml of pyridine was combined with 22.97 g (0.264 moles) of cyclopentanol-1-d and the reaction allowed to stand at 0° for twenty-four hours. The mixture was then poured into 2000 ml of ice water and stirred

vigorously. The resulting crystals were collected by vacuum filtration, washed with water, and dried in a vacuum desicator to yield 38.9 g (61% yield) of cyclopentyltosylate-1-d.

Preparation of Cyclopentyl-1-d Cyanide. A mixture of 38.9 g (0.161 moles) of cyclopentyltosylate-1-d , 9.46 g (0.193 moles) of powdered sodium cyanide, and 200 ml of dimethylsulfoxide (freshly distilled from calcium hydride) contained in a 500 ml round-bottomed flask, fitted with a stirrer and reflux condenser, was allowed to react at room temperature for eighteen hours, and then at 50° - 60° for four hours.

This material was distilled at 12 - 15 mm until approximately 110 ml of distillate had been collected. The impure cyanide was redistilled three additional times resulting in 12.11 g of 70% pure (by VPC) cyclopentyl-1-d cyanide. Boiling range: 54° - 62° at 12 - 15 mm. Yield - 55%.

Preparation of 1-aminomethylcyclopentane-1-d. To a mixture of 7.18 g (0.189 moles) of lithium aluminum hydride in 250 ml of ether, 12.11 g of 70% pure cyclopentyl-1-d cyanide (0.126 moles) dissolved in 30 ml of ether was added over a period of thirty minutes at 0° and the reaction stirred at room temperature for eighteen hours. Hydrolysis was accomplished by careful addition of 16 ml water followed by 16 ml of a 5% sodium hydroxide solution.

The ether layer was removed, dried over sodium sulfate, and distilled to give 7.91 g (91% yield) of 1-aminomethylcyclopentane-1-d

collected at 135° - 139°.

Preparation of Cyclohexanol-1-d. A solution of 6.85 g (0.070 moles) of freshly distilled cyclohexanone and 20 ml of ether (freshly distilled from lithium aluminum hydride) was carefully added to an ice-cooled mixture of 1.00 g (0.0238 moles) lithium aluminum deuteride and 30 ml of ether (freshly distilled from lithium aluminum hydride). The reaction was stirred at room temperature for eighteen hours and then hydrolyzed by careful addition of 2 ml water followed by 2 ml of a 5% sodium hydroxide solution.

The ether layer was separated, dried over magnesium sulfate, and evaporated to yield 6.1 g (87% yield) of cyclohexanol-1-d. The crude alcohol was purified by preparative gas chromatography as needed.

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