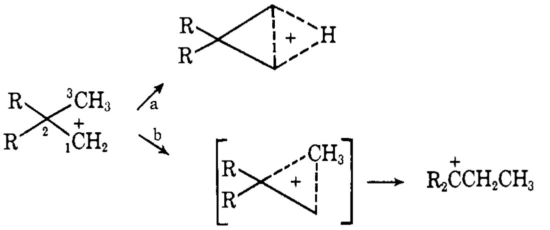
Carbonium Ions. XIV. Effect of Substitution at Carbon-3 of 1-Propyl System on Intermediacy of Protonated Cyclopropanes

Gerasimos J. Karabatsos, Ramon A. Mount, Donald O. Rickter, and Seymour Meyerson

Contribution from the Department of Chemistry, Michigan State University, East Lansing, Michigan, and the Research and Development Department, American Oil Company, Whiting, Indiana. *Received July 2, 1969*

Abstract: The aqueous acid deamination of 1-butylamines labeled with two deuterium atoms at C-1, C-2, or C-3 gave a 50% mixture of butanols consisting of about 65% 1-butanol and 35% 2-butanol. The deamination of 2-butyl-2-d_1-amine and 2-butyl-3,3-d_2-amine gave 2-butanol as the sole alcohol product. Mass spectral analysis of the trimethylsilyl ether derivatives of the 1-butanol products disclosed that these alcohols were exclusively isotope-position unrearranged. This finding ruled out protonated cyclopropanes as intermediates in the path of formation of 1-butanol. Mass spectral and nuclear magnetic resonance analysis of the trimethylsilyl ether derivatives of the 2-butanols obtained from the 1-butyl and the 2-butylamines disclosed that these alcohols were extensively isotope-position rearranged. The rearrangement path responsible for the isotopic scrambling was established to be reversible 1,2-hydride shifts, not involving protonated cyclopropanes. These intramolecular 1,2-hydride shifts are subject to conformational control and to k_H/k_D effects of about 1.2–1.4. A single alkyl substitution at C-3 of the 1-propyl system decreases the product yield arising *via* a protonated cyclopropane to the same extent as a single alkyl substitution at C-2. The overall product yield from the protonated cyclopropane path was estimated to be less than 1%.

The preceding paper of this series[1] reported evidence showing that substitution of an alkyl group for a hydrogen at C-2 of the 1-propyl cation substantially reduces the intervention of intermediate edge-protonated cyclopropanes, so that the ratio of path a [carbon(3)–hydrogen participation] to path b [carbon(2)–carbon(3) participation], eq 1, is probably less than $^1/_{500}$ when both R groups are methyls. This paper will examine the effect that alkyl substitution at C-3 of the 1-propyl system has on the extent of edge-protonated cyclopropane intervention.[2]



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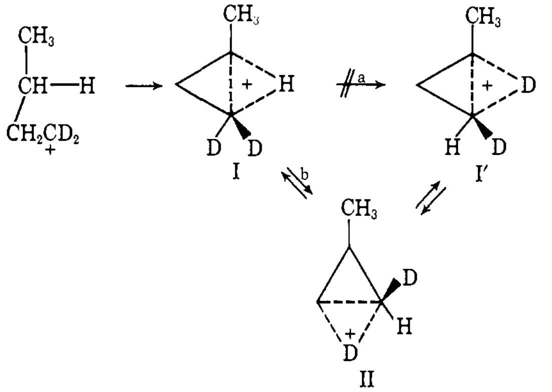
The simplest system suitable for such studies is the 1-butyl. In order to make our comparisons and conclusions more valid, we chose to study the deamination reaction of 1-butylamine. Our experimental approach to the problem consisted again of appropriate deuterium labeling at various positions of the system and determination of the label distribution in the products. Our objective was to clarify the following issues. 1. Extent of edge-protonated cyclopropane intervention during the reaction. 2. Extent of 1,4-hydride shifts. 3. The suggestion[3] that a single process scrambles both the carbon and the hydrogen atoms of the 1-propyl system, *i.e.*, that I does not lead to I′ (eq 2) directly (path a), but indirectly (path b) through the edge-protonated cyclopropane II. If this mechanistic interpretation is correct, then conversion of I to I′ ought to be slow compared to similar conversions in the unsubstituted system, as the activation energy for path b—which leads to the less stable cation II—would be higher than that required for the unsubstituted system. A further consequence of this argument is the good probability that I might lead to II′ (eq 3) much faster than to I′. If so, the isotope-position rearranged 1-butyl products arising through the protonated cyclopropane path would contain mainly two, rather than one, protium atoms at C-1. 4. Assessment of the effect that the precursor leading to the 2-butyl cation has on the intramolecular 1,2-hydride shifts (eq 4) that interconvert 2-butyl cations. Such precursors are the 1-



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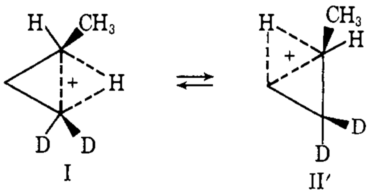

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[1] G. J. Karabatsos, N. Hsi, and S. Meyerson, *J. Amer. Chem. Soc.*, **92**, 621 (1970).

[2] For a preliminary report of some of the results see G. J. Karabatsos, R. A. Mount, D. O. Rickter, and S. Meyerson, *ibid.*, **88**, 5651 (1966).

[3] G. J. Karabatsos, C. E. Orzech, Jr., J. L. Fry, and S. Meyerson, *ibid.*, **92**, 606 (1970).

Table I. Label Distributions[a] in the Trimethylsilyl Ether Derivatives of 1-Butanols

No.	Compound	Parent − methyl, % d_2	d_1	d_0	Parent − propyl, % d_2	d_1	d_0
1	$CH_3CH_2CH_2CD_2OSi(CH_3)_3$[b]	98.5	1.5	0.0	96.7	3.3	0.0
2	$CCCCOSi(CH_3)_3$[c]	98.4	1.6	0.0	97.7	2.3	0.0
3	$CH_3CH_2CD_2CH_2OSi(CH_3)_3$[d]	97.3	2.7	0.0	0.8	7.2	92.0
4	$CCCCOSi(CH_3)_3$[e]	96.3	3.7	0.0	0.8	7.0	92.2
5	$CH_3CD_2CH_2CH_2OSi(CH_3)_3$[f]	96.5	3.5	0.0	0.3	0.5	99.2
6	$CCCCOSi(CH_3)_3$[g]	95.7	4.3	0.0	0.2	0.4	99.4

[a] Calculated from 70-V mass spectra. [b] Derivative of 1-butanol-1,1-d_2 prepared by reduction of butanoic acid with lithium aluminum deuteride. [c] Derivative of 1-butanol obtained from the deamination of 1-butyl-1,1-d_2-amine. [d] Derivative of 1-butanol-2,2-d_2 prepared by reduction of butanoic-2,2-d_2 acid with lithium aluminum hydride. [e] Derivative of 1-butanol obtained from the deamination of 1-butyl-2,2-d_2-amine. [f] Derivative of 1-butanol-3,3-d_2 prepared by reduction of butanoic-3,3-d_2 acid with lithium aluminum hydride. [g] Derivative of 1-butanol obtained from the deamination of 1-butyl-3,3-d_2-amine.

Table II. Label Distributions[a] in the Trimethylsilyl Ether Derivatives of 2-Butanols

No.	Compound	Parent − methyl, % d_2	d_1	d_0	Parent − ethyl, % d_2	d_1	d_0
1	$CH_3CH_2CD(CH_3)OSi(CH_3)_3$[b]	0.0	99.5	0.5	0.0	99.1	0.9
2	$CH_3CD_2CH(CH_3)OSi(CH_3)_3$[c]	97.4	1.7	0.9	0.1	0.1	99.8
3	$CH_3CH_2CH(CHD_2)OSi(CH_3)_3$[d]	77.4	1.6	21.0	98.1	1.9	0.0
4	$CCC(C)OSi(CH_3)_3$[e]	0.0	99.6	0.4	0.0	99.2	0.8
5	$CCC(C)OSi(CH_3)_3$[f]	82.7	1.6	15.7	75.6	1.6	22.8
6	$CCC(C)OSi(CH_3)_3$[g]	81.0	19.0	0.0	72.0	3.9	24.1
7	$CCC(C)OSi(CH_3)_3$[h]	96.3	3.7	0.0	0.0	19.2	80.8
8	$CCC(C)OSi(CH_3)_3$[i]	97.5	1.6	0.9	0.1	9.5	90.4
9	$CCC(C)OSi(CH_3)_3$[j]	2.4	97.0	0.6	1.9	86.1	12.0

[a] Calculated from analysis of 70-V mass spectra. [b] Derivative of 2-butanol-2-d_1 prepared by reduction of butanone with lithium aluminum deuteride. [c] Derivative of 2-butanol-3,3-d_2 prepared by reduction of butanone-3,3-d_2 with lithium aluminum hydride. [d] Derivative of 2-butanol-1,1-d_2 prepared by reaction of methyl-1,1-d_2 magnesium iodide with butanone. [e] Derivative of 2-butanol-2-d_1 after alcohol (**1**) had been subjected to deamination conditions. [f] Derivative of 2-butanol obtained from the deamination of 1-butyl-1,1-d_2-amine. [g] Derivative of 2-butanol obtained from the deamination of 1-butyl-2,2-d_2-amine. [h] Derivative of 2-butanol obtained from the deamination of 1-butyl-3,3-d_2-amine. [i] Derivative of 2-butanol obtained from the deamination of 2-butyl-3,3-d_2-amine. [j] Derivative of 2-butanol obtained from the deamination of 2-butyl-2-d_1-amine.

butyl, the 2-butyl, and the isobutyl cations generated

$$CH_3CH_2\underset{+}{C}HCH_3 \rightleftharpoons CH_3\underset{+}{C}HCH_2CH_3 \qquad (4)$$

by the deamination of the corresponding amines.

Results

Deamination of 1-Butyl- and 2-Butylamines. The deamination of 1-butylamine with sodium nitrite in perchloric acid gave butenes (about 30%), 1-butanol, 2-butanol, 1- and 2-butyl nitrites, and small amounts of 1- and 2-butyl nitrates and 1- and 2-nitrobutanes. The ratio 1-butanol:2-butanol varied with the position of the deuterium label on the starting amine. For example, it was 60:40 from the unlabeled amine, 64:36 from the 1,1-d_2, and 68:32 from the 2,2-d_2 amine. These values compare favorably with the 66:34 value obtained[4] from the deamination in 1 *N* hydrochloric acid and the 65:35 obtained[5] from the deamination in acetic acid. The higher ratio obtained from the deamination of the 2,2-d_2 amine is consonant with the expected k_H/k_D effect for the 1,2-hydride shift.

The deamination of 2-butylamine gave exclusively 2-butanol as the alcohol product (less than 0.2% 1-butanol by vpc).

The product alcohols from the deamination of deuterium-labeled amines were converted to the trimethylsilyl ether derivatives[6] for mass spectral analysis.

Mass Spectral Analysis of the Trimethylsilyl Ethers of 1-Butanols. In Table I are summarized the label distributions in the parent − methyl and parent − propyl ions of the trimethylsilyl ether derivatives of various 1-butanols. Entries **1** and **2** are those of 1-butanol-1,1-d_2 prepared by reduction of butanoic acid with lithium aluminum deuteride and 1-butanol obtained from the deamination of 1-butyl-1,1-d_2-amine, respectively. Entries **3** and **4** are those of the corresponding 2,2-d_2 species (synthetic and product 1-butanol, respectively), and entries **5** and **6** those of the corresponding 3,3-d_2 species. From the results it may be concluded that the 1-butanol product is exclusively isotope-position unrearranged, as shown below for the

$$\underset{100\%\ d_2}{CH_3CH_2CH_2CD_2NH_2} \longrightarrow \underset{100\%\ d_2}{CH_3CH_2CH_2CD_2OH}$$

1,1-d_2 species. The same conclusion was reached by Streitwieser and Schaeffer[5] from the deamination of 1-butyl-1,1-d_2-amine in acetic acid.

Mass Spectral Analysis of the Trimethylsilyl Ethers of 2-Butanols. In Table II are summarized the label distributions in the parent − methyl and parent − ethyl ions in the mass spectra of the trimethylsilyl ethers of various 2-butanols. Entries **1** and **4**, respectively, are those of 2-butanol-2-d_1 prepared by reduction of butanone with lithium aluminum deuteride and of the same 2-butanol after it had been subjected to deamination conditions. This experiment was performed to assess any rearrangement of the 2-butanol product after formation in the reaction. The good agreement between the two rules out any such rearrangement. Entries **2** and **3** are those of authentic samples of 2-butanol prepared by reduction of butanone-3,3-d_2 with lithium aluminum hydride and by reaction of methyl-1,1-d_2-magnesium iodide with propionaldehyde,

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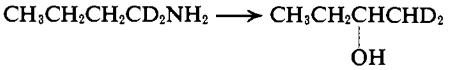
(4) F. C. Whitmore and D. P. Langlois, *J. Amer. Chem. Soc.*, **54**, 3441 (1932).

(5) A. Streitwieser, Jr., and W. D. Schaeffer, *ibid.*, **79**, 2888 (1957).

(6) S. H. Langer, S. Connell, and I. Wender, *J. Org. Chem.*, **23**, 50 (1958).

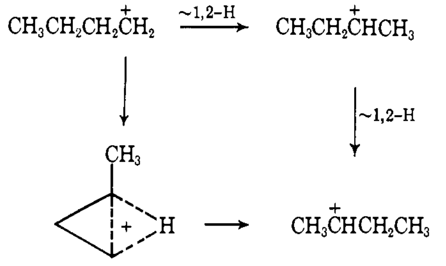
respectively. Entry **5** is that of 2-butanol from the deamination of 1-butyl-1,1-d_2-amine; **6**, that of 2-butanol from the deamination of the 2,2-d_2 amine; and **7**, that of 2-butanol from the 3,3-d_2 amine. Entry **8** is that of 2-butanol from the deamination of 2-butyl-3,3-d_2-amine that was prepared by reduction of the corresponding azide with lithium aluminum hydride. The last entry **9**, is that of 2-butanol from the deamination of 2-butyl-2-d_1-amine prepared by reduction of butanone oxime with lithium aluminum deuteride. The reduction apparently led to about 3% d_2, mainly 2-butyl-1,2-d_2-amine.

The results clearly indicate that the 2-butanol is not solely the species expected from a simple 1,2-hydride shift (1-butyl to 2-butyl), as shown below, but a mixture of isotope-position labeled species. For example,



$$CH_3CH_2CH_2CD_2NH_2 \longrightarrow CH_3CH_2\underset{\displaystyle OH}{\underset{|}{C}}HCHD_2$$

observe the differences in the parent − ethyl ion label distributions between **3** and **5**. The task was now to establish the identity of the various species, as this could shed light on how much of the isotope-position rearranged species arose by successive 1,2-hydride shifts and how much through a protonated cyclopropane path (eq 5). In our previous paper[1] we established that the 2-butyl cation generated from the deamination of isobutylamine underwent 1,2-hydride shifts that were competitive with capture of the cation by water. The only labeled species that could give information on whether any of the 2-butanol arose by by 1,3-hydride shifts (protonated cyclopropane path), is the 1-butyl-3,3-d_2-amine, as shown in Scheme I.



(5)

Whereas intramolecular 1,2-hydride (deuteride) shifts lead to 2-butanols III and IV that contain no deuterium in the methyl groups, the protonated cyclopropane path leads to 2-butanols V and VI that *contain* deuterium in the methyl groups. Our data show that V and VI are not present. (1) The trimethylsilyl ether of the 2-butanol obtained from the deamination of 1-butyl-3,3-d_2-amine (95.7% d_2 and 4.3% d_1, entry **6**, Table I) gave 96.3% d_2 and 3.7% d_1 for the parent − methyl ion (entry **7**, Table II). The 3.7% d_1 ion can arise from the 4.3% 1-butyl-3-d_1-amine present in the starting amine and from species VI, as none of the species III, IV, and V can give rise to d_1 parent − methyl ion. Had VI been present to any significant extent, the d_1 contribution to the parent − methyl ion of **7** would have been appreciably higher than 3.7%. (2) Under our instrumental conditions, the integrated area ratio of the signals of the 1-methyl and 4-methyl groups of **7** was 1.06:1.00 from the 2-butanol product derivative and 1.07:1.00 from the ether of unlabeled 2-butanol. This result rules out more than 3–5% of V.

Scheme I

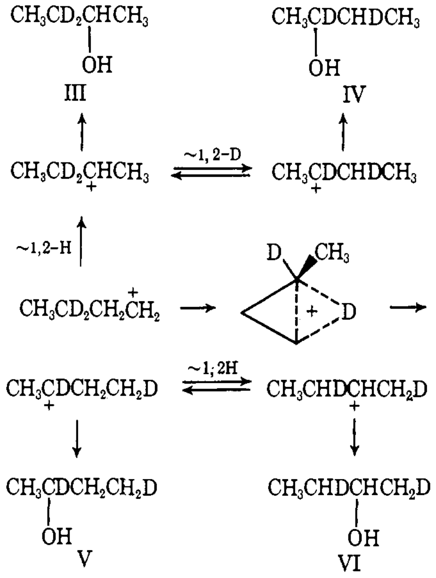


Table III summarizes the 2-butanol isotope-position labeled species obtained from the deaminations of the various butylamines. For the first five entries, the percentages were calculated from the mass spectral data of Table II. The last two entries are those from ref 1 and are included for purposes of comparison and later discussion. The following observations are pertinent to subsequent discussion. (1) In all cases the major species is that from the 2-butyl cation formed first in the reaction. Those species arising by subsequent 1,2-hydride (deuteride) shifts are found in smaller concentrations. (2) The ratio of major to minor product depends not only on whether the minor product is formed subsequent to a hydride or deuteride shift (compare entry **3** with **1** and **2**; entry **5** with **4**; and entry **7** with **6**), but also on the source leading to the 2-butyl cation (compare entries **3**, **5**, and **7**; and entries **4** and **6**). (3) The percentage of the product derived after two rearrangements, 1.3% (entry **2**), is very small when compared to the relative percentages of those derived prior to and after one rearrangement, *i.e.*, the ratio 1.3:24.0 is much smaller than the ratio 24.0:74.7.

Discussion

Protonated Cyclopropanes. The failure to detect any isotope-position rearranged 1-butanol and 2-butanol from the deamination of deuterium-labeled 1-butylamines excludes protonated cyclopropanes as important intermediates in the paths leading to the formation of these alcohols. However, it does not necessarily exclude their intervention in this reaction. As was the case with isobutylamine, the results are compatible with those obtained from the deamination of *n*-propylamine. In terms of Scheme II, the protonated methylcyclopropanes would lead to methylcyclopropanes (path a) and to isotope-position rearranged butanols (path b and c). The percentage of methylcyclopropane in the overall product under our deamination conditions is estimated to be about 0.6%, on the basis that the hydrocarbon fraction was about 30% of the overall product, and of this fraction not more than 2% is methylcyclopropane.[7] If, now, the

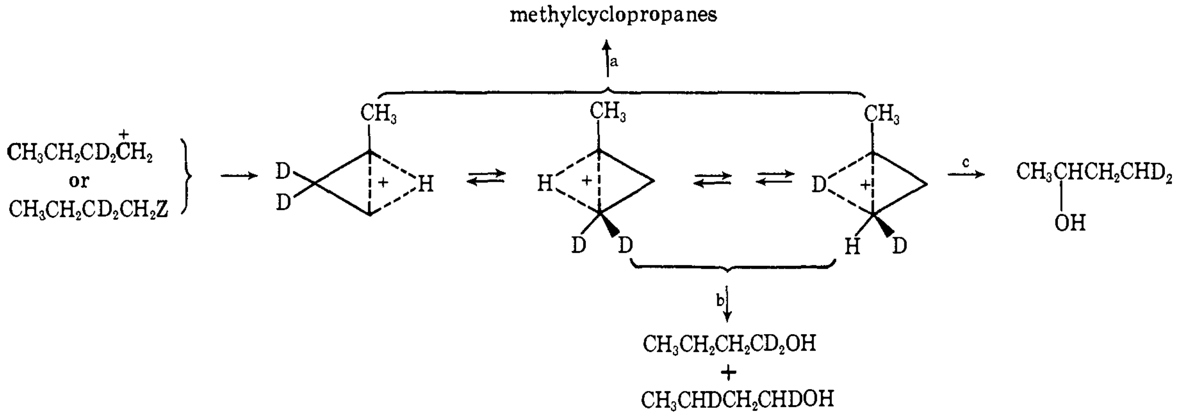
Table III. Isotope-Position Labeled 2-Butanols from the Deamination of Butylamines

No.	Amine	2-Butanol
1	$CH_3CH_2CH_2CD_2NH_2 \rightarrow$	$CH_3CH_2\underset{OH}{C}HCHD_2$ 76.8% $+$ $CH_3\underset{OH}{C}HCH_2CHD_2$ 23.2%
2	$CH_3CH_2CD_2CH_2NH_2 \rightarrow$	$CH_3CH_2\underset{OH}{C}DCH_2D$ 74.7% $+$ $CH_3\underset{OH}{C}HCHDCH_2D$ 24.0% $+$ $\left.\begin{array}{c} CH_3CHD\underset{OH}{C}HCH_2D \\ + \\ CH_3\underset{OH}{C}DCH_2CH_2D \end{array}\right\}$ 1.3%
3	$CH_3CD_2CH_2CH_2NH_2 \rightarrow$	$CH_3CD_2\underset{OH}{C}HCH_3$ 80.8% $+$ $CH_3\underset{OH}{C}DCHDCH_3$ 19.2%
4	$CH_3CH_2\underset{NH_2}{C}DCH_3$	$\rightarrow CH_3CH_2\underset{OH}{C}DCH_3$ 88.3% $+$ $CH_3\underset{OH}{C}HCHDCH_3$ 11.7%
5	$CH_3CD_2\underset{NH_2}{C}HCH_3$	$\rightarrow CH_3CD_2\underset{OH}{C}HCH_3$ 90.4% $+$ $CH_3\underset{OH}{C}DCHDCH_3$ 9.6%
6	$(CH_3)_2CDCH_2NH_2$[a]	$\rightarrow CH_3CH_2\underset{OH}{C}DCH_3$ 90.9% $+$ $CH_3\underset{OH}{C}HCHDCH_3$ 9.1%
7	$(CH_3)_2CHCD_2NH_2$[a]	$\rightarrow CH_3CD_2\underset{OH}{C}HCH_3$ 92.5% $+$ $CH_3\underset{OH}{C}DCHDCH_3$ 7.5%

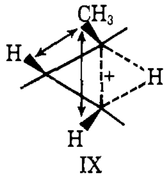
[a] Reference 1.

protonated cyclopropanes were to lead to similar ratios of methylcyclopropane:alcohol as in the deamination of 1-propylamine, then about 0.1% (0.6:5) alcohol would result from this path. Since the alcohols constitute about 50% of the overall product, not more than 0.2–0.3% of the alcohols would be isotope-position rearranged. Such percentages are within experimental error of our measurements. The only available experimental evidence for the intermediacy of protonated methylcyclopropanes in the *aqueous* acid deamination of 1-butylamine is, therefore, the formation of methylcyclopropane. Thus, a single methyl substitution at C-3 of the 1-propyl system reduces the overall product yield from the protonated cyclopropane path to the same extent as a single methyl substitution[1] at C-2.

Scheme II



Less than 1% product arises from this path. This decreased contribution, when compared to that of the unsubstituted protonated cyclopropane (*ca.* 6%), may be partly ascribed to vicinal methyl-hydrogen nonbonded interactions in IX, analogous to those suggested for the isobutyl and neopentyl systems.[1] It



IX

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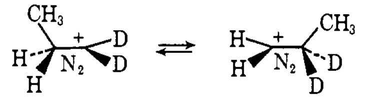
[7] No accurate figure of the per cent methylcyclopropane is available under conditions of aqueous acid deamination. On the assumption that the deoxidation and deamination reactions lead to the same percentage of cyclopropane in the hydrocarbon fraction [see P. S. Skell and I. Starter, *J. Amer. Chem. Soc.*, **82**, 2971 (1960)], only 2% of this fraction is methylcyclopropane.

should be emphasized, however, that the contribution of the protonated cyclopropane path to product formation depends on solvent and increases with decrease of the water concentration, as shown by Friedman and his coworkers.[8]

Although the results do not resolve the question of the mechanism of protonated cyclopropane equilibration (eq 2), they do offer indirect evidence against a classical carbonium ion mechanism for the formation of isotope-position rearranged 1-propanol from the deamination of 1-propylamine. Such a mechanism requires that the reversible 1,2-methyl shift (eq 6) be about five to ten



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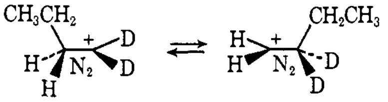
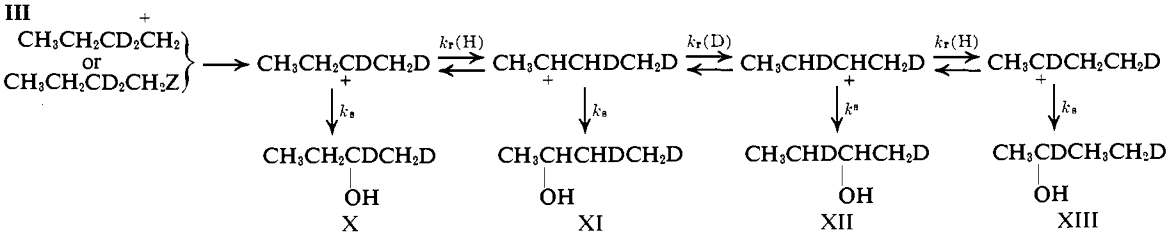
times faster than capture of the 1-propyl cation by water.[3] The 1,2-ethyl shift (eq 7), in view of the con-



(7)

formational requirement of the classical carbonium ion mechanism (migrating group *trans* to the nitrogen), would seem even better suited for rearrangement. But to be compatible with our data, it would have to proceed at least five to ten times slower than capture of the 1-butyl cation by water.

Scheme III

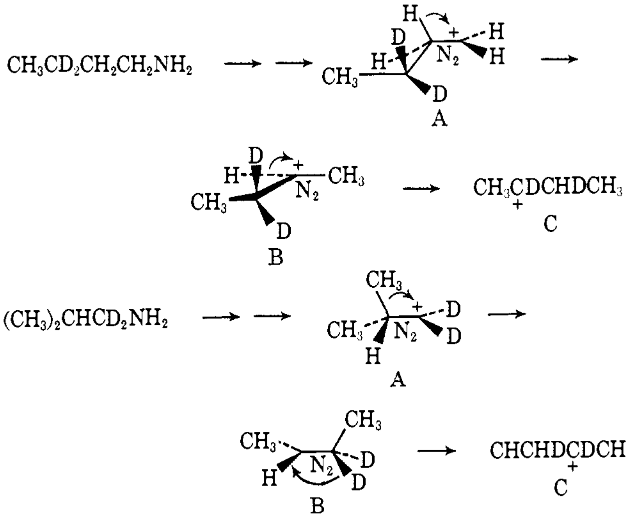


Intramolecular 1,2-Hydride Shifts and Isotope Effects. Our data furnish a basis for estimating isotope effects on the intramolecular 1,2-hydride shifts that interconvert 2-butyl cations. We consider first cases **1** and **2** in Table III, and illustrate our points with case **2** in terms of Scheme III. From the concentrations of alcohols X and XI, the rates of solvent capture of the 2-butyl cations relative to the rate of intramolecular 1,2-hydride shift, k_s/k_r(H), are about 2–2.5:1. An exact evaluation of this ratio cannot be made not only because part of X might come from a direct path not involving the cation, *i.e.*, concerted hydrogen migration and nucleophilic attack, but also because the carbonium ions precursor to the alcohol will probably give butenes at different rates as a result of isotope effects. The most significant result, however, is the finding that the concentration of (XII + XIII) is only 1.3%. If all k_s constants were the same and all k_r(H) constants were the same, with k_r(H)/k_r(D) of about 1.3, the concentration of (XII + XIII) should have been greater than 3%. Two rationalizations can be offered for the low concentration of these two products. Either the first 2-butyl cation rearranges faster than the second, *i.e.*, it is "hotter," or the rate of capture by water of the first 2-butyl cation is slower than that of the second, as the result of the first being less solvated (nitrogen molecule still in the vicinity) than the second.

The next point of interest in the results of Table III is the finding that the 2-butyl cation from the deamination of 1-butyl-3,3-d_2 amine, case **3**, has undergone less rearrangement than that from the other two amines (cases **1** and **2**). So has the one from **5** when compared to that from **4**; and that of **7** when compared to that of **6**. These results are readily accommodated by a k_H/k_D effect of about 1.2–1.3 for the intramolecular 1,2-hydride shift. Such values appear reasonable[1,8] for reactive carbonium ions like those produced in the deamination reaction.

The final point here is the finding that the ratios of the isotope-position labeled 2-butanol obtained from the same 2-butyl cations, cases **3**, **5**, and **7**, differ from one another. Cases **3** and **7** are rationalized best in terms of conformational control of the 1,2-hydride shifts, as shown in Scheme IV. The carbonium ions responsible for the 2-butanol species are B and C. The two cations B arise from the corresponding A by a 1,2-hydride and a 1,2-methyl shift, respectively. Whereas the cation B from the 1-butyl system is now in a good position for deuterium migration to lead to C, the same cation from the isobutyl system is not, because of the position of the nitrogen molecule with respect to the deuterium needed to rearrange. This explanation

Scheme IV



could be extended to furnish a third possible rationalization for the low concentration of alcohol XII (case **2**).

The small amount of rearrangement observed in the case of the 2-butyl cation generated from the 2-butylamine in case **5** is best rationalized in terms of backside capture of the first 2-butyl cation by water, or direct

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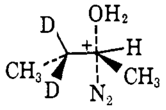
[8] L. Friedman and A. T. Jurewicz, *J. Amer. Chem. Soc.*, 91, 1803 (1969), and references cited therein.

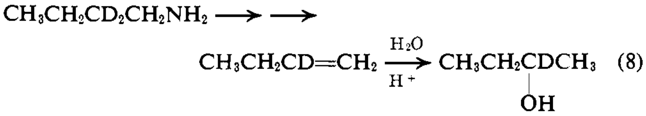
solvent displacement on the diazonium ion, leading to inverted 2-butanol.[9] Furthermore, the presence of a solvent molecule near the developing positive charge, and on the opposite side of the leaving group, will hinder the rearrangement of the deuterium (XIV).



XIV

The 11.7% isotope-position rearranged 2-butanol from the deamination of 2-butyl-2-d_1 amine, case **4**, compares favorably with the 9% isotope-position rearranged 2-butyl acetate obtained in the limiting solvolysis of 2-butyl-1-^{14}C tosylate in acetic acid.[10] The fact that the former is higher than the latter is presumably further testimony of the higher reactivity of carbonium ions generated in deamination reactions.

As was the case with similar studies on deamination reactions,[1,6,11] no detectable amount of alcohol arises by hydration of the olefins produced in the reaction. For example, had any 2-butanol arisen by eq 8, then its presence would have been detected in the label distribution of the parent – methyl ion (d_1 contribution). Such was not the case.



$$CH_3CH_2CD_2CH_2NH_2 \longrightarrow \longrightarrow CH_3CH_2CD{=}CH_2 \xrightarrow[H^+]{H_2O} CH_3CH_2\underset{\displaystyle OH}{\underset{|}{C}}DCH_3 \quad (8)$$

Experimental Section

Preparation of Labeled Compounds. (a) **1-Butyl-1,1-d_2-ammonium Perchlorate.** Lithium aluminum deuteride (40 g) reduction of 6.6 g of butyronitrile in anhydrous ether gave, after treatment with 71% perchloric acid, 15 g (90% yield) of 1-butyl-1,1-d_2-ammonium perchlorate, mp 186–188°.

(b) **1-Butyl-2,2-d_2-ammonium Perchlorate.** Diethyl ethylmalonate was prepared in 95% yield from diethyl malonate and ethyl bromide in a sodium methoxide–ethanol medium. Basic hydrolysis, deuterium exchange of the resulting ethylmalonic acid in deuterium oxide, and decarboxylation of the diacid gave butyric-2,2-d_2 acid-d_1. The corresponding amide, prepared by way of the acid chloride, was dehydrated by heating with thionyl chloride, yielding butyronitrile-2,2-d_2 (48% yield from butyric-2,2-d_2 acid-d_1). The nitrile was reduced with lithium aluminum hydride to give, after neutralization with 71% perchloric acid, a 65% yield of 1-butyl-2,2-d_2-ammonium perchlorate, mp 192–193°.

(c) **1-Butyl-3,3-d_2-ammonium Perchlorate.** Diethyl methylmalonate was hydrolyzed with base to methylmalonic acid, which was subjected to deuterium exchange and then was decarboxylated to propionic-2,2-d_2 acid-d_1. This acid was reduced with lithium aluminum hydride to 1-propanol-2,2-d_2 in 85% yield. The alcohol was converted with no isotopic scrambling to the corresponding bromide by using phosphorus tribromide (80% yield). Treatment of the bromide with sodium cyanide in aqueous methanol gave an 80% yield of butyronitrile-3,3-d_2. The nitrile was reduced with lithium aluminum hydride to give 1-butyl-3,3-d_2-amine. Neutralization with 71% perchloric acid gave 1-butyl-3,3-d_2-ammonium perchlorate, mp 189–191°.

(d) **2-Butyl-2-d-ammonium Perchlorate.** Ten grams of butanone oxime was reduced with lithium aluminum deuteride by refluxing for 5 hr in di-*n*-butyl ether. Basic work-up was followed by perchloric acid neutralization of the resulting amine to give a slurry of 2-butyl-2-d-ammonium perchlorate (50% yield) in di-*n*-butyl ether. Because removal of the last traces of solvent was difficult, the salt was dissolved in water and organic materials were removed by extraction with ether. The resulting aqueous solution was then subjected to the deamination conditions.

(e) **2-Butyl-3,3-d_2-ammonium Perchlorate.** Reduction of acetic anhydride with lithium aluminum deuteride gave a 62% yield of ethanol-1,1-d_2. Treatment of the alcohol with phosphorus tribromide gave a 60% yield of bromoethane-1,1-d_2. The corresponding Grignard reagent was prepared and treated with acetaldehyde to give a 54% yield of 2-butanol-3,3-d_2, from which 2-butyl-3,3-d_2 *p*-toluenesulfonate was made (in 90% yield) by using *p*-toluenesulfonyl chloride in pyridine. The *p*-toluenesulfonate group was displaced by azide upon treatment with sodium azide in aqueous methanol. The resulting 2-butyl-3,3-d_2 azide was not isolated because of its instability. Rather, it was taken up in ether and reduced directly with lithium aluminum hydride. Neutralization of the resulting amine with 71% perchloric acid gave a slurry of 2-butyl-3,3-d_2-ammonium perchlorate (30% yield from the *p*-toluenesulfonate). The perchlorate salt was not isolated, but was dissolved in water and deaminated.

All other deuterium-labeled compounds used in this study were prepared by well-established standard procedures.

Deaminations of butylamines were carried out using the conditions of Roberts and Halmann.[12] The reaction temperature was generally 35–40°. Product alcohols were extracted from the aqueous reaction mixture with ether; then, after solvent removal, they were collected by preparative gas chromatography through a 9-ft column of 25% Carbowax 20M on Chromosorb W at 115°.

Trimethylsilyl ethers of the butanols were prepared by refluxing overnight hexamethyldisilazane (Metallomer Laboratories) and the appropriate alcohol in a 1:2 molar ratio. The ethers were purified and collected by gas chromatography through a 20-ft Carbowax 20M column at 85°.

Mass Spectral Analysis. Mass spectral analysis of the isotopically labeled compounds was done with a Consolidated Model 21-103C instrument at 70 ionizing V, with the source and inlet systems both at 250°.

Nuclear magnetic resonance spectra were determined at 60 Mc on a Model A-60 spectrometer (Varian Associates, Palo Alto, Calif.).

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[9] The yield of inverted 2-butanol from optically active 2-butylamine is reported to be about 22% (K. B. Wiberg, Ph.D. Thesis, Columbia University, 1950, as cited in ref 5).

[10] J. D. Roberts, W. Bennett, R. E. McMahon, and E. W. Holroyd, Jr., *J. Amer. Chem. Soc.*, 74, 4283 (1952).

[11] J. D. Roberts and Y. A. Yancey, *ibid.*, 74, 5943 (1952).

[12] J. D. Roberts and M. Halmann, *ibid.*, **75**, 5759 (1953).