Carbonium Ions. XIII. Effect of Substitution at C-2 of the 1-Propyl System on the Formation of Protonated Cyclopropanes

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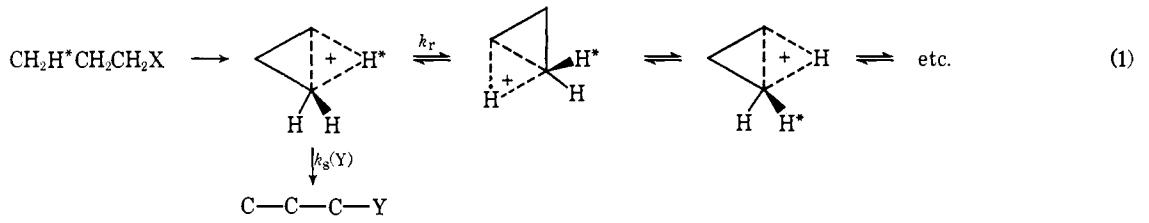
Abstract: The aqueous acid deamination of isobutyl-1,1-d_2-amine gave a 70% yield of alcohols with the composition 72.5% *t*-butyl alcohol, 18.0% *sec*-butyl alcohol, and 10.5% isobutyl alcohol. The composition of the mixture obtained from deamination of the corresponding 2-*d*-amine was 64.0% *t*-butyl alcohol, 24.5% *sec*-butyl alcohol, and 11.5% isobutyl alcohol. The difference in the ratio of *t*-butyl to *sec*-butyl alcohol obtained from the two amines is ascribed to a k_H/k_D isotope effect of about 1.5 for the intramolecular 1,2-hydride shift. The isobutyl alcohols were found to be exclusively isotope-position unrearranged, thus excluding protonated cyclopropane intermediates in their path of formation. The *sec*-butyl alcohols from the 1,1-d_2, and 2-*d*-amines were both isotope-position rearranged, about 7.6% and 9.1%, respectively. The path responsible for this rearrangement was established to be exclusively intramolecular 1,2-hydride shifts with a k_H/k_D of about 1.3. Substitution of a methyl group for a hydrogen (isobutyl system) at C-2 of the 1-propyl system decreases the over-all product arising from the protonated cyclopropane path from 6% in the deamination of *n*-propylamine to 0.6% in the deamination of isobutylamine. Substitution of two methyl groups (neopentyl system) decreases it to the point where no products arising from the protonated cyclopropane path have been detected. These differences have been explained in terms of the relative stabilities of the protonated cyclopropanes and their classical carbonium ion counterparts.

In the preceding two papers[2a,b] we discussed the intermediacy by the "σ route" of the unsubstituted protonated cyclopropane, by emphasizing its structure (edge-protonated), the mechanism of carbon–carbon and hydrogen–hydrogen scrambling, and the effect that X and reaction conditions play on its stability relative to other processes, such as nucleophilic capture and rearrangements (eq 1). It was established that the protonated cyclopropane leaks neither to the 1-propyl nor to the 2-propyl cation, that a single process is probably responsible for both carbon–carbon and hydrogen–hydrogen scrambling, and that the ratio k_r/k_s (rate of rearrangement *vs.* rate of nucleophilic capture) is probably greater when the protonated cyclopropane is generated by deamination than by the reaction of 1-bromopropane with aluminum bromide. In the deamination reaction k_r/k_s was estimated to be about 5–10. It was also pointed out that the over-all contribution of the protonated cyclopropane path to product formation was about 6% (*ca.* 1% 1-propanol and 5% cyclopropane) in the deamination of *n*-propylamine.



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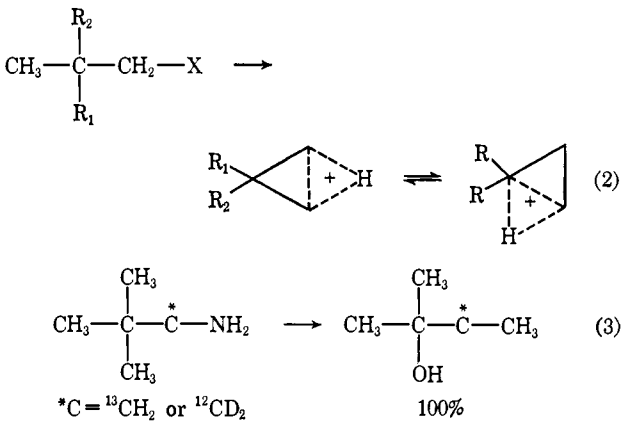
In this paper we will deal with the question of what effect alkyl substitution at C-2 has on the relative stability of the edge-protonated cyclopropane (eq 2) with respect to other processes available to the system. Specifically, we will discuss the behavior of the isobutyl system (R_1 = H; R_2 = CH_3) in the deamination of isobutylamine.

In 1964, we reported[3] that the deamination of neopentylamine (R_1 = R_2 = CH_3) labeled at C-1 with either deuterium or carbon-13 led to *t*-amyl alcohol (eq 3) labeled exclusively at C-3. This observation, coupled



(2)

(3)

with the fact that the deamination gave no detectable dimethylcyclopropane,[4] established that the neopentyl

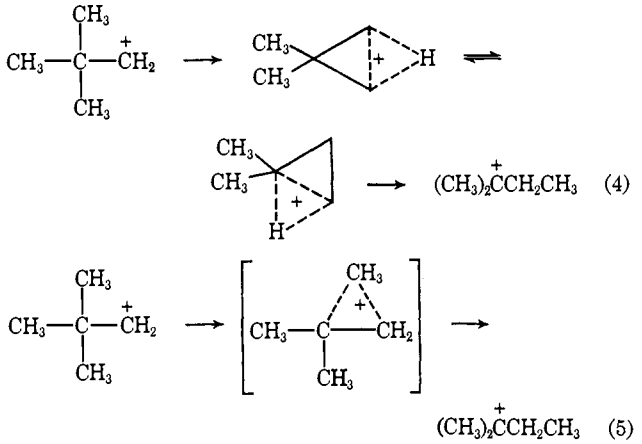
(1) Research and Development Department, American Oil Company, Whiting, Ind.

(2) (a) G. J. Karabatsos, C. E. Orzech, Jr., J. L. Fry, and S. Meyerson, *J. Amer. Chem. Soc.*, **92**, 606 (1970); (b) G. J. Karabatsos, J. L Fry, and S. Meyerson, *ibid.*, **92**, 614 (1970).

(3) G. J. Karabatsos, C. E. Orzech, Jr., and S. Meyerson, *ibid.*, **86**, 1994 (1964).

(4) (a) P. S. Skell and I. Starer, *ibid.*, **82**, 2971 (1960); (b) M. S. Silver, *ibid.*, **82**, 2971 (1960); (c) J. H. Bayless, F. D. Mendicino, and L. Friedman, *ibid.*, **87**, 5790 (1965); (d) J. H. Bayless, A. T. Jurewicz, and L. Friedman, *ibid.*, **90**, 4466 (1968).

cation (or its precursor) did not lead to the *t*-amyl cation *via* the edge-protonated cyclopropane (eq 4), but instead by carbon–carbon bond participation (eq 5). The bridged species pictured in process 5 may be either

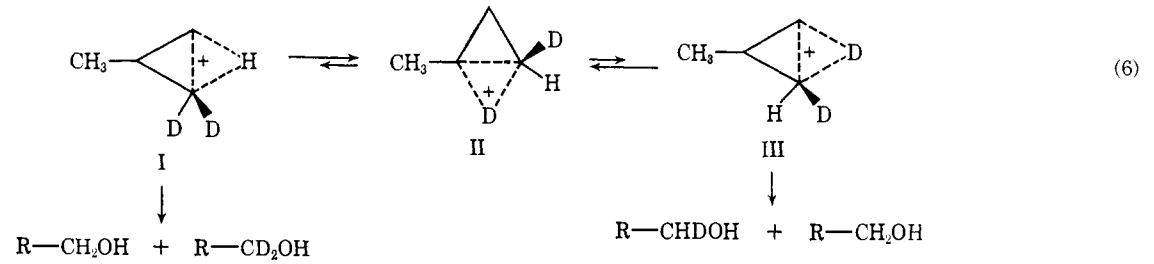


(4)

(5)

a transition state or an intermediate, and it may arise either from the neopentyl cation or from a suitable precursor. This behavior of the neopentyl system was observed in several other reactions,[3,5] including the deoxidation of neopentyl alcohol.[6] A rationale for the difference in behavior between the *n*-propyl and the neopentyl system has been offered.[3]

The isobutyl system is structurally intermediate between the *n*-propyl and the neopentyl. On deamination isobutylamine gives methylcyclopropane, which comprises about 4% of the hydrocarbon fraction. Since the hydrocarbon fraction comprises about 13% of the over-all product[7] when the deamination is carried out at 38°—the remaining 87% are butanols—the per cent methylcyclopropane in the product is only 0.5 to 0.6%. This value should be contrasted with 5% in the deamination of *n*-propylamine and 0% in that of neopentylamine. These results suggest that the isobutyl system should be closer in behavior, in regard to intervention of protonated cyclopropanes, to the neopentyl than to the *n*-propyl system. With respect to the mechanism proposed[2a] for carbon–carbon and hydrogen–hydrogen scrambling, in which the isomerization of I to III is not direct but proceeds through II, the sequence shown below (eq 6) suggests that the major isotope-position rearranged isobutyl alcohol from the deamination of isobutyl-1,1-d_2-amine might be the one with two protons at C-1, accompanied by very little with one proton and one deuterium at C-1, as the conversion of II to III would be energetically unfavorable. If, however, the conversion of I to III is direct, *i.e.*, without the intervention of II, substantial amounts of isobutyl alcohol with one deuterium at C-1 might be obtained. We therefore chose to study the isobutyl system in order to assess the factors associated with the relative stability of edge-protonated cyclopropanes with respect to intermediates arising from competing paths, and to check the proposed mechanism for carbon–carbon and hydrogen–hydrogen scrambling.



(6)

Results

The aqueous acid deamination of isobutylammonium-1,1-d_2 perchlorate at 35–40° gave a 70% yield of alcohol mixture, whose composition by gas chromatographic analysis was found to be 71.5% *t*-butyl alcohol, 18.0% *sec*-butyl alcohol, and 10.5% isobutyl alcohol. These values agree with the 71%, 19%, and 10% values reported by Cannell and Taft for the deamination of the unlabeled amine.[7] The corresponding values from the deamination of isobutylammonium-2-*d* perchlorate were 64.0%, 24.5%, and 11.5%, respectively.

The alcohols were converted to the trimethylsilyl ether derivatives[8] for mass spectral analysis.

Mass Spectral Analysis of Butyl Alcohols from Deamination of Isobutylamines. In Table I are summarized the label distributions in the trimethylsilyl ethers of various butyl alcohols. Entry 1 is that of isobutyl alcohol prepared by the reduction of isobutyric acid with lithium aluminum deuteride. Entry 2 is that of isobutyl alcohol obtained from the deamination at 40° of isobutyl-1,1-d_2-amine. It is clear from the results that the product alcohol is exclusively (over 99.9%) isotope-position unrearranged and that no protium–deuterium exchange between solvent and substrate occurred during the reaction. The same conclusions can be reached from entries 8 and 9, which refer to isobutyl-2-*d* alcohol prepared by the reduction of isobutyric-2-*d* acid with lithium aluminum hydride and to that recovered from the deamination of isobutyl-2-*d*-amine. These results are summarized below

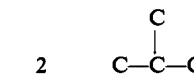
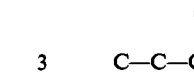
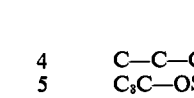
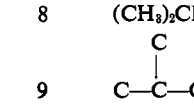
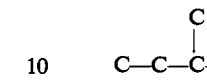
$$\underset{100\%\ d_2}{(CH_3)_2CHCD_2NH_2} \longrightarrow \underset{>99.9\%}{(CH_3)_2CHCD_2OH}$$

$$\underset{100\%\ d_1}{(CH_3)_2CDCH_2NH_2} \longrightarrow \underset{100\%}{(CH_3)_2CDCH_2OH}$$

Entry 7 in Table I is that of *t*-butyl alcohol prepared by addition of methylmagnesium iodide to hexadeuterioacetone. From the label distribution in the parent less-methyl ion it can be concluded that 74.1% of this ion yield arises by methyl loss from the *t*-butyl group and 25.9% from the trimethylsilyl group. Entries 5 and 6 are those of *t*-butyl alcohols obtained from the deamination of isobutyl-1,1-d_2-amine, with the isotopic composition 97.8% d_2 and 2.2% d_1 (see entry 2). On the basis that 74.1% of this ion arises by loss from the *t*-butyl

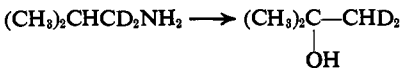
(5) G. J. Karabatsos and J. D. Graham, *J. Amer. Chem. Soc.*, **82**, 5250 (1960).
(6) P. S. Skell, I. Starer, and A. P. Krapcho, *ibid.*, **82**, 5257 (1960).
(7) L. G. Cannell and R. W. Taft, Jr., *ibid.*, **78**, 5812 (1956).
(8) S. H. Langer, S. Connell, and I. Wender, *J. Org. Chem.*, **23**, 50 (1958).

Table I. Label Distributions[a] in Various Butyl Alcohols

No.	Compound	Parent less-methyl, % d_2	d_1	d_0	Parent less-ethyl, % d_2	d_1	d_0	Parent less-propyl, % d_2	d_1	d_0
1	$(CH_3)_2CHCD_2OSi(CH_3)_3$[b]	97.8	2.2	0.0				97.0	2.8	0.2
2	 [c]	97.8	2.2	0.0				96.8	2.9	0.3
3	 [d]	97.5	2.2	0.0	0.0	7.7	92.3			
4	 [d]	98.1	1.9	0.0	0.0	7.5	92.5			
5	$C_3C—OSi(CH_3)_3$[e]	73.8	1.6	24.6						
6	$C_3C—OSi(CH_3)_3$[e]	73.6	1.7	24.7						
7	$(CD_3)_2C(CH_3)—OSi(CH_3)_3$[f]	49.2(d_6), 1.4(d_5) 48.7(d_3), 0.7(d_2)								
8	$(CH_3)_2CDCH_2OSi(CH_3)_3$[g]	0.0	95.8	4.2				0.0	0.0	100.0
9	 [h]	0.0	97.1	2.9				0.0	0.0	100.0
10	 [i]	0.0	97.6	2.4	0.0	88.7	11.3			

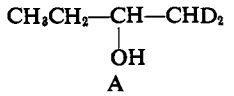
[a] Calculated from 70-V mass spectra. [b] Derivative of isobutyl alcohol sample synthesized by reduction of isobutyric acid with lithium aluminum deuteride. [c] Derivative of isobutyl alcohol obtained from the deamination at 40° of isobutyl-1,1-d_2-amine. [d] Derivatives of *sec*-butyl alcohol obtained from the deamination of same amine as in *c*. [e] Derivatives of *t*-butyl alcohols from deaminations of same amine as in *c*. [f] Derivative of *t*-butyl alcohol synthesized by reduction of hexadeuterioacetone with lithium aluminum hydride. [g] Derivative of isobutyl alcohol prepared by reduction of isobutyric-2-*d* acid with lithium aluminum hydride. [h] Derivative of isobutyl alcohol from the deamination at 40° of isobutyl-2-*d*-amine. [i] Derivatives of *sec*-butyl alcohol from the deamination of same amine as in *h*.

group and 25.9% from the trimethylsilyl, the 1.6% and 1.7% d_1 distributions are as anticipated (0.022[25.9 + 2(74.1)/3] = 1.66%). So are the 24.6 and 24.7% d_0 values (74.1/3 = 24.7). The *t*-butyl alcohol is, therefore, exclusively isotope-position unrearranged, as shown. This finding corroborates the observation by

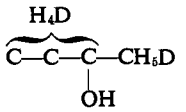


Cannell and Taft[7] that no deuterium was incorporated in the methyl groups of *t*-butyl alcohol when the deamination was carried out in deuterium oxide.

Entries 3 and 4 are those of the *sec*-butyl alcohol products obtained from two deaminations of isobutyl-1,1-d_2-amine. The label distribution in the parent less-methyl ion, 0.0% d_0 and 2.2% d_1 from the first deamination, and 0.0% d_0 and 1.9% d_1 from the second, rules out species A (<0.5%) and B. Species A would contribute d_0 to the parent less-methyl ion, as about 21% of

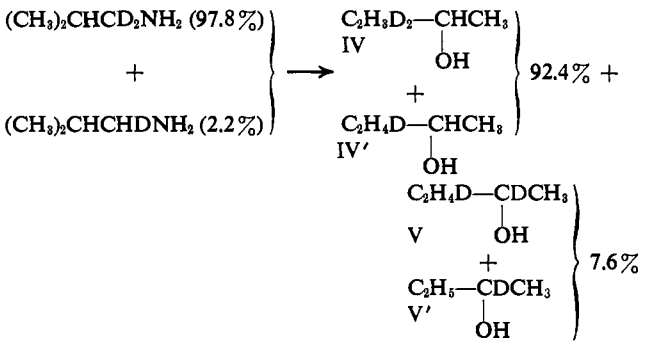


A



B

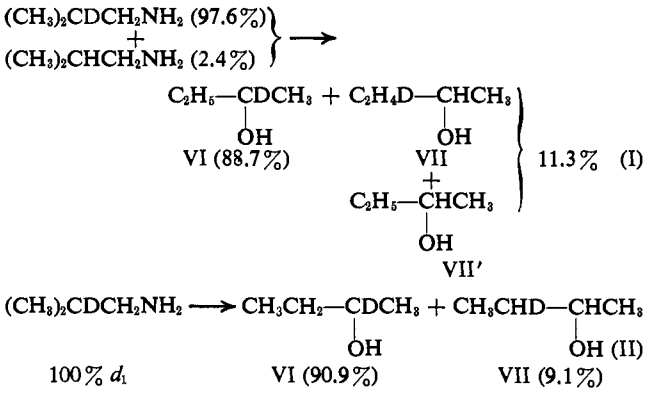
this ion yield arises by loss of methyl from the 2-butyl group and 79% by loss from the trimethylsilyl group;[9] species B would contribute d_1. However, no d_0 was detected, and the per cent d_1 is not larger than the amount of d_1 in the starting amine (see entry 2). The parent less-ethyl label distributions are interpreted as follows



Crucial to the question of the protonated cyclopropane intermediacy is the determination of the position of the two deuterium atoms in the ethyl group of IV and the position of the one deuterium atom in the ethyl group of IV′. Examination of the nmr spectrum of the trimethylsilyl ether derivative of the *sec*-butyl alcohol product showed that—within experimental error—all the deuterium label in question was at the methylene group, none at the C-4 methyl. No deuterium was detected at the C-1 methyl group, either. The ratio (IV + IV′):(V + V′) calculated from the nmr was 93:7, in good agreement with the more accurate 92.4:7.6 value from the mass spectral analysis.

Entry 10 is that of *sec*-butyl alcohol obtained from the deamination of isobutyl-2-*d*-amine. The results from this entry may be analogously treated to yield eq I. Assuming that the secondary deuterium isotope effect (deuterium at C-2) for the migration of the methyl group is negligible, and normalizing the results to 100% d_1, give the results shown in eq II. Significantly, the VI:VII ratio of 90.9:9.1 is smaller than the corresponding (IV + IV′):(V + V′) ratio of 92.4:7.6.

(9) G. J. Karabatsos, R. A. Mount, D. O. Rickter, and S. Meyerson, *J. Amer. Chem. Soc.*, **88**, 5651 (1966).



Discussion

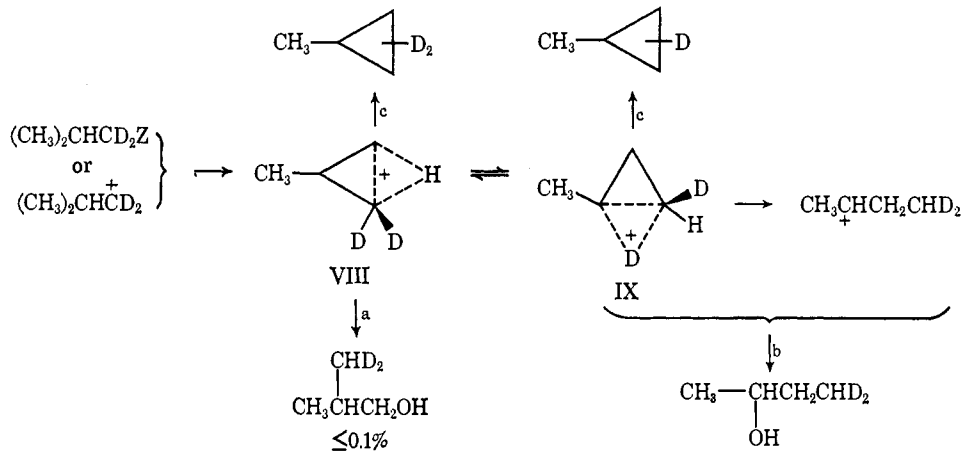
Protonated Cyclopropanes. The failure to detect any isotope-position rearranged isobutyl alcohol, or any deuterium label at the methyl groups of the *sec*-butyl alcohol, does not exclude the intermediacy of protonated cyclopropanes in the deamination of isobutylamine. Thus, the results are not incompatible with those obtained from the deamination of *n*-propylamine. As pictured in Scheme I, the protonated methylcyclopropanes would lead to methylcyclopropane (path c) and to isotope-position rearranged isobutyl (path a) and *sec*-butyl (path b) alcohols. In the case of the unsubstituted protonated cyclopropane, the ratio of cyclopropane to isotope-position rearranged 1-propanol was about 5:1. If the protonated methylcyclopropane were to lead to similar ratios of methylcyclopropane–isotope-position rearranged alcohols, then the isotope-position rearranged alcohols would constitute about 0.1% (0.5:5) of the over-all product. The *sec*-butyl alcohol fraction, therefore, with deuterium at the C-4 methyl would constitute less than 0.3% of the over-all *sec*-butyl alcohol product, and the isotope-position rearranged isobutyl alcohol less than 0.5% of the over-all isobutyl alcohol product. Although our experimental techniques cannot detect 0.3% *sec*-butyl alcohol with deuterium label at C-4, they can detect as much as 0.2% isobutyl alcohol with two protons at C-1. The fact that the concentration of the latter was $\leq 0.1\%$ is not surprising because: (a) the ratio of methylcyclopropane–isotope-position rearranged alcohol should be larger than the corresponding one from the deamination of *n*-propylamine, as a methyl substituent on the protonated cyclopropane would sterically retard nucleophilic attack at one of the carbon atoms and facilitate attack on the acidic hydrogen to yield methylcyclopropane; (b) most of the isotope-position rearranged alcohol should be *sec*-butyl alcohol, not isobutyl alcohol, as a result of IX being more stable than VIII. The absence of any *n*-butyl alcohol product should not be construed as evidence against the intermediacy of IX. From the fact that in the acid-catalyzed ring opening of propylene oxide[10] water attack at the secondary carbon is favored over attack at the primary carbon by 7:3, one would expect XI to lead to *sec*-butyl, not *n*-butyl alcohol.

We are now in a position to summarize and explain the differences in the behavior of the 1-propyl, 2-methyl-1-propyl (isobutyl), and 2,2-dimethyl-1-propyl (neopentyl) systems with respect to the extent of protonated cyclopropane intervention. For clarity and simplicity of presentation, we have constructed Scheme II, which shows the relevant rearrangement paths of the three classical carbonium ions. Path a of the 1-propyl cation is responsible for 6% of the over-all product.[2a] If all the 2-propyl cation, path b, were converted to 2-propanol, *i.e.*, if propene formation were disregarded, then the ratio a:b would be about 1:7. Since some propene would arise from the 2-propyl cation, the ratio 1:7 is a maximum; it may be as small as 1:14.

In the 2-methyl-1-propyl (isobutyl) system, the competition facing path a is much more formidable than before. Path b leads to the highly stable *t*-butyl cation and path c to a secondary cation. On this basis alone, the ratio a: (b + c) should be smaller than it is in the case of the 1-propyl cation. Furthermore, the protonated methylcyclopropane formed in path a should be less stable than the unsubstituted protonated cyclopropane, as a result of two 1,2-eclipsing methyl-hydrogen interactions. It is not surprising, therefore, that the ratio a:(b + c) has now dropped from 1:7 to about 1:80.

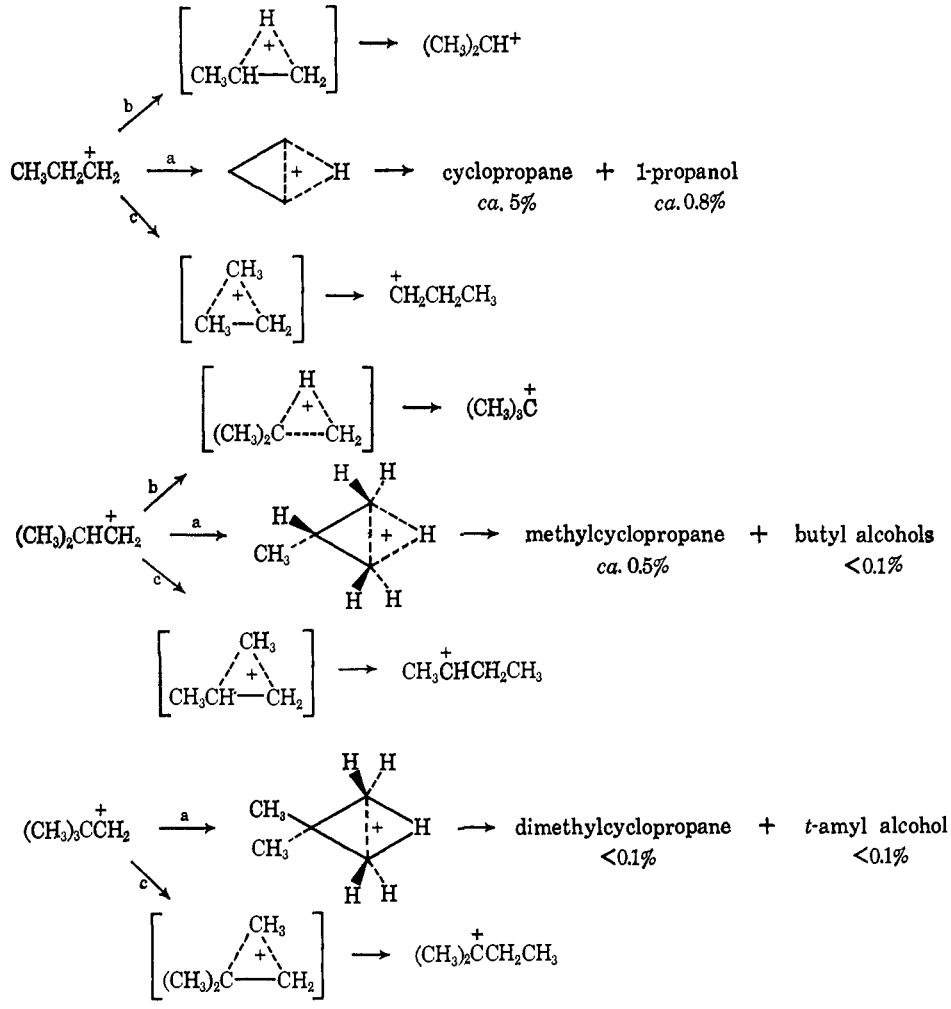
The same arguments can be extended to cover the case of the 2,2-dimethyl-1-propyl (neopentyl) system. There are now four 1,2-eclipsing methyl-hydrogen interactions and path c leads to the highly stable *t*-amyl cation. It should be made clear that under different deamination conditions the relative contributions of the various paths may change. In fact, the ratio a:(b + c) of the isobutyl system is much higher in

Scheme I

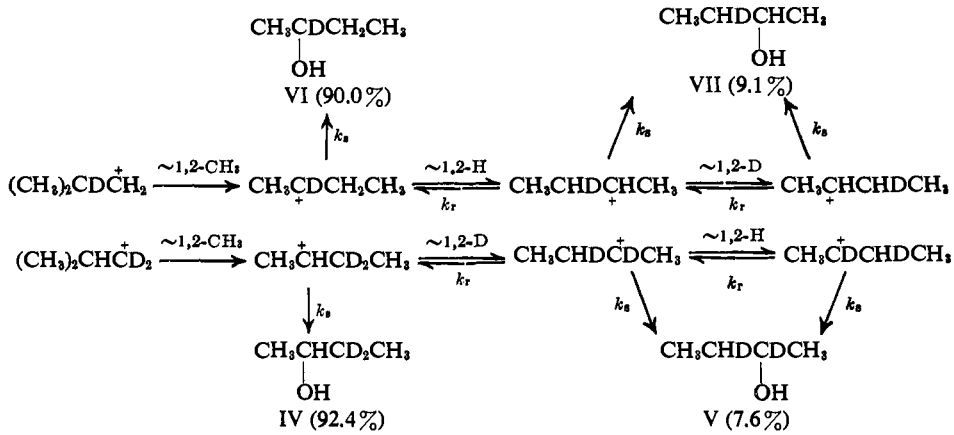


(10) J. G. Pritchard and F. A. Long, *J. Amer. Chem. Soc.*, 78, 2667 (1956).

Scheme II



Scheme III



nonhydroxylic solvents than it is in aqueous hydroxylic solvents.[4c,d]

Extrapolation of the conclusions drawn from this work to systems where the alkyl substituent at C-2 is part of a ring system should be made cautiously. For example, the methylcyclopentyl–cyclohexyl interconversion proceeds through a detectable protonated cyclopropane mechanism.[11]

Intramolecular 1,2-Hydride Shifts and Isotope Effects. As pointed out, the product *sec*-butyl alcohols obtained from the deaminations of the 1,1-d_2- and the 2-*d*-isobutylamines are 7–10% isotope-position rearranged. Protonated cyclopropane intermediates having been excluded, intramolecular 1,2-hydride shifts interconverting 2-butyl cations remain as the only reasonable path responsible for the rearrangement. We will discuss now the rate of the 1,2-hydride shift relative to that of the capture of the 2-butyl cation by nucleophile (water), and the kinetic k_H/k_D isotope effect of this shift. To assist in the discussion, we have constructed Scheme III.

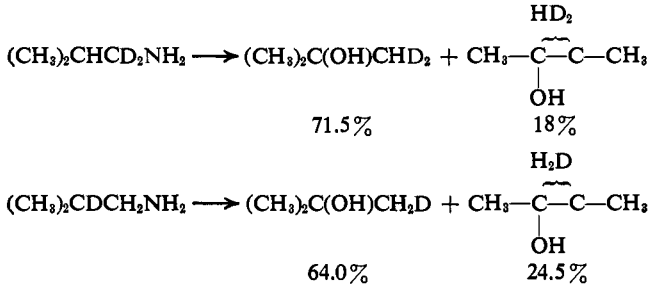
From the concentrations of the product alcohols VI and VII, the ratio k_s/k_r (with k_s containing a nucleophile concentration term) may be roughly estimated as 9:1. An exact evaluation of this ratio is impossible,

(11) G. J. Karabatsos and R. A. Mount, unpublished results.

not only because of the possibility that part of VI might arise from a direct path not involving the 2-butyl cation, *i.e.*, by concerted methyl migration and nucleophilic attack, but also because the carbonium ion precursors to VI and VII might give butenes at different rates, as a result of isotope effects and differences in their ion pair structures. These limitations notwithstanding, it is clear that the 2-butyl cation reacts with water faster than it rearranges to another 2-butyl cation by an intramolecular 1,2-hydride shift.

The k_H/k_D isotope effect accompanying the rearrangement of one 2-butyl to another 2-butyl cation (secondary-to-secondary) can be estimated from the relative ratios IV:V and VI:VII to be about 1.3. Again, this isotope effect cannot be accurately calculated, not only for the same reasons given in discussing k_s/k_r but also because the 92.4:7.6 ratio does not truly represent IV:V. As pointed out, it represents (IV + IV′):(V + V′). Since the carbonium ion leading to V is formed by an 1,2-deuteride shift, whereas that leading to V′ is formed by a 1,2-hydride shift, the ratio IV′:V′ would be smaller than the IV:V ratio and, consequently, IV:V would be larger than the assumed 92.4:7.6 value. In view, however, of the fact that the starting amine is mainly doubly labeled (97.8%), the true IV:V ratio cannot be much greater than the 92.4:7.6 value.

The k_H/k_D isotope effect for the 1,2-hydride shift leading to the formation of the *t*-butyl cation (primary-to-tertiary) can be estimated from the results shown below (relative amounts of *sec*-butyl and *t*-butyl alcohol from the 1,1-d_2- and 2-*d*-labeled amines) to be about 1.5. A value of 1.2 was estimated from deu-



terium content analysis of the isobutylenes obtained from the same labeled isobutylamines.[4d]

The above isotope effects are within the range of primary k_H/k_D isotope effects observed for intramolecular 1,2-hydride shifts. For example, the isomerization of 1-propyl-2-*d* bromide to 2-propyl bromide with aluminum bromide at −20° proceeds with a k_H/k_D of 3.3 ± 0.2.[12] The reaction of 1-propanol-2-*d* with boron trifluoride and benzene to give cumene shows an isotope effect of 1.4 ± 0.1.[13] The isotope effects for pinacol rearrangements are 1.5–1.8 for 2-methylbutane-2,3-diol[14] and 2.2–3.3 for 1,2,2-triphenylethanol.[15] That for the formation of the 2-propyl cation from the deamination of *n*-propylamine was estimated to be 1.5–2.0.[2a]

Experimental Section

Preparation of Labeled Compounds. All labeled compounds used in this study were prepared by established procedures. The isobutyl-1,1-d_2-amine was prepared by reduction of isobutyronitrile with lithium aluminum deuteride (for the procedure used see ref 2a). The isobutyl-2-*d*-amine was prepared by reduction of isobutyronitrile-2-*d* with lithium aluminum hydride. The isobutyronitrile-2-*d* was synthesized as follows: dimethylmalonic acid was converted to dimethylmalonic-2-*d* acid-d_2 by repeated exchange with deuterium oxide at about 105°. The exchanged acid was converted to isobutyric-2-*d* acid-*d* by heating the solid with a sand bath until evolution of carbon dioxide had ceased. The purified isobutyric acid was converted to the acid chloride with thionyl chloride, the chloride was converted to the amide with ammonium hydroxide, and the amide to the nitrile with thionyl chloride.

Deamination of Isobutylamines. For the procedure used to deaminate the isobutylamines see ref 2a.

Preparation of trimethylsilyl ether derivatives of the butyl alcohols was carried out as in ref 2a.

Mass Spectral Analysis. Mass spectral analysis of the isotopically labeled compounds was done with 70-V electrons on a Consolidated Model 21-103C instrument.

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