Tetrahedron, 1967, Vol. 23, pp. 2539 to 2547. Pergamon Press Ltd. Printed in Northern Ireland

EVIDENCE FOR PROTONATED CYCLOPROPANE INTERMEDIATES IN THE DEAMINATION OF 1-PROPYLAMINE AND MECHANISTIC IMPLICATIONS OF PROTONATED CYCLOPROPANES[1]

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(*Received in USA* 18 *October* 1966; *accepted for publication* 7 *November* 1966)

Abstract—The NMR examination of the 1-propanol and 2-propanol obtained from the nitrous acid deamination of 2,2-d_2-1-propylamine, and the isotope position rearrangements observed in the 1-propanol fraction from similar deamination studies with 1-*t*-1-propylamine and 1-^{14}C-1-propylamine showed that about 4–6% of the 1-propanol recovered was derived from protonated cyclopropane intermediates in which all three carbon positions became practically equivalent. A previously suggested direct 1,3-hydride shift as well as the possibility of successive 1,2-hydride shifts have been eliminated. Consideration of the evidence obtained, together with known data from the literature, suggests that equilibration of edge-protonated cyclopropanes may be the best representation of the reactive intermediates responsible for the observed isotopic rearrangements in the 1-propanol from the deamination of 1-propylamine. Probable mechanistic implications of protonated cyclopropanes are discussed.

INTRODUCTION

THE early work on isotope position rearrangements in the nitrous acid deamination of 1-^{14}C-1-propylamine in aqueous perchloric acid[3] reported that the 1-propanol obtained showed about 8% rearrangement of the ^{14}C-label from C-1 to C-2 and C-3. A 1,2-methyl shift in the 1-propyl cation, which would locate the rearranged ^{14}C at C-2, was assumed to be responsible for these results. Some years later, this experiment was repeated[4] with a more complete degradation of the 1-propanol and it was reported that the 8% rearranged ^{14}C was located entirely at C-3, with no activity at C-2. Such a rearrangement could be explained by a 1,3-hydride shift or successive 1,2-hydride shifts, but the 1,3-shift was preferred.[5] The NMR studies[6] on the deamination of 1,1,2,2-d_4-1-propylamine also led to the suggestion that the isotopic rearrangement observed in the 1-propanol had resulted "mainly, if not exclusively" from 1,3-hydride shifts.[6,7] However, the more recent mass-spectral studies[8] on the deamination of 1,1-d_2- or 2,2-d_2-1-propylamine have shown that the earlier conclusion regarding 1,3-shifts was

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[1] Presented in part at the 150th National Meeting of the American Chemical Society, Atlantic City, N.J., September 13–17 (1965).

[2] Holder of a Canadian Industries Ltd. Fellowship, 1963–64, a Canadian Chemicals Ltd. Fellowship, 1964–65 and a National Research Council of Canada Studentship, 1965–66.

[3] J. D. Roberts and M. Halmann, *J. Am. Chem. Soc.* **75**, 5759 (1953).

[4] O. A. Reutov and T. N. Shatkina, *Tetrahedron*, **18**, 237 (1962).

[5] O. A. Reutov, *Congress Lectures, XIXth International Congress of Pure and Applied Chemistry* pp. 203–227. Butterworth, London (1963).

[6] G. J. Karabatsos and C. E. Orzech, Jr., *J. Am. Chem. Soc.* **84**, 2838 (1962).

[7] For a review of suggested 1,3-shifts, see N. C. Deno, *Progr. Phys. Org. Chem.* **2**, 129 (1964).

[8] G. J. Karabatsos, C. E. Orzech, Jr., and S. Meyerson, *J. Am. Chem. Soc.* **87**, 4394 (1965).

in error and that protonated cyclopropane is implicated in the deamination. This finding is in complete agreement with the results from the present work which have been reported as preliminary communications.[9,10] This paper reports the details of the studies on the nitrous acid deamination, in aqueous perchloric acid, of the perchlorate salts of 2,2-d_2-1-propylamine (I-2-d_2), 1-t-1-propylamine (I-1-t) and 1-^{14}C-1-propylamine (I-1-^{14}C).

RESULTS AND DISCUSSION

Methylmalonic acid was subjected to five successive exchanges with D_2O, and the resulting material was decarboxylated to give 2,2-d_2-propionic acid,[11] which was, in turn, converted to the amide, reduced with LAH and neutralized with perchloric acid to give the perchlorate salt of I-2-d_2. After deamination in aqueous perchloric acid,[3] the 1- and 2-propanol fractions were recovered by preparative VPC and examined by NMR. Pertinent portions of the NMR spectra together with the spectra of the corresponding protio-analogs are shown in Fig. 1.

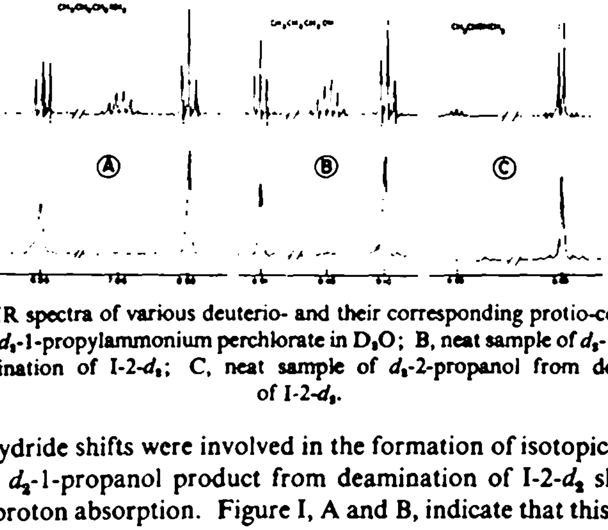

FIG. 1. NMR spectra of various deuterio- and their corresponding protio-compounds. A, 40% 2,2-d_2-1-propylammonium perchlorate in D_2O; B, neat sample of d_2-1-propanol from deamination of I-2-d_2; C, neat sample of d_2-2-propanol from deamination of I-2-d_2.

If only 1,3-hydride shifts were involved in the formation of isotopically rearranged 1-propanol, the d_2-1-propanol product from deamination of I-2-d_2 should show no increase in C-2 proton absorption. Figure I, A and B, indicate that this is not the case. Although the C-2 absorptions appear to be too low to permit accurate and reliable integrations, the spectra clearly suggest the qualitative conclusion that the deuterated 1-propanol product does show stronger C-2 proton absorption (ca. τ 8·45) than the C-2 proton absorption of I-2-d_2 (ca. τ 7·86). Apparently, some of the C-2 deuterium label has rearranged, presumably to C-1 and C-3.

If successive 1,2-hydride shifts were to play a role in the deamination of I-2-d_2, the 2-propanol product obtained should show more C-2 proton absorption than I-2-d_2. From Fig. 1C, it is seen that there is no significant increase in the C-2 proton absorption (ca. τ 6·66) for the 2-propanol product, thus effectively eliminating successive 1,2-hydride shifts as an important process. Such a conclusion has also been reached by Karabatsos *et al.*[6,8]

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[9] C. C. Lee, J. E. Kruger and E. W. C. Wong, *J. Am. Chem. Soc.* **87**, 3985 (1965).

[10] C. C. Lee and J. E. Kruger, *J. Am. Chem. Soc.* **87**, 3986 (1965).

[11] A. Murray, III and D. L. Williams, *Organic Syntheses with Isotopes* Part II pp. 1265, 1266. Interscience, New York, N.Y. (1958).

In order to obtain a more quantitative evaluation of the extents of isotopic rearrangements suggested by the NMR studies, the deamination of I-1-*t* was carried out. I-1-*t* was prepared from the reduction of propionitrile with *t*-labeled LAH, and deaminated in aqueous perchloric acid.[3] The 1-propanol fraction was purified by preparative VPC and degraded by oxidation, first to propionic acid and then to acetic acid.[12] The activity of the propionic acid gave the *t*-content of C-2 and C-3 and the activity of the acetic acid showed the *t*-content of C-3. Each liquid sample was assayed as an appropriate solid derivative which had been repeatedly recrystallized to constant specific activity to ensure radiochemical purity. The results are given in Table 1. It can be seen that only a relatively small amount of about 3% of the *t*-label was rearranged from C-1 to C-2 and C-3, but the rearranged isotope was located at both C-2 and C3. This finding establishes that the rearrangement is not due solely to a 1,3-hydride shift mechanism.

TABLE 1. ACTIVITY DATA AND TRITIUM REARRANGEMENTS IN THE 1-PROPANOL FROM DEAMINATION OF I-1-*t*

Compd. assayed	Specific activity,[a] cpm/mmole Run 1	Specific activity,[a] cpm/mmole Run 2	%T in C-2 and C-3 Run 1	%T in C-2 and C-3 Run 2	%T in C-3 Run 1	%T in C-3 Run 2
C_3H_7OH[b]	3,450,000	2,750,000				
C_2H_5COOH[c]	101,000	81,000	2·9	2·9		
CH_3COOH[c]	55,700	45,400			1·6	1·7

[a] Measured by a liquid scintillation counter.
[b] Assayed as the α-naphthylurethan.
[c] Assayed as the *p*-bromophenacyl ester.

The isotopic rearrangements observed in the studies with I-2-d_2 and I-1-*t* may be most logically explained by assuming some involvement of protonated cyclopropane[13–15] (II) in the deamination reaction. However, the work[4] with I-1-^{14}C has apparently eliminated this possibility since involvement of II would result in the location of the rearranged ^{14}C at both C-2 and C-3, not solely at C-3 as reported. It is, therefore, of interest to investigate once more the nitrous acid deamination of I-1-^{14}C in aqueous perchloric acid. I-1-^{14}C was prepared from potassium ^{14}C-cyanide as described.[3] After deamination, the 1-propanol fraction was purified by VPC and degraded according to the procedures[4] involving oxidation of the 1-propanol to propionic acid and then to acetic acid, followed by the conversion of the latter to methylamine *via* the Schmidt reaction. Again, to ensure radiochemical purity, the samples were assayed as solid derivatives which had been recrystallized until their specific activities were constant. The results, summarized in Table 2, showed that about 4% of the C-1 label was rearranged and the rearranged ^{14}C was almost equally distributed at C-2 and C-3. The difference between the presently observed rearrangements and the earlier reported higher value of about 8% probably may be due to

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[12] The degradation procedures were those reported[4] with the exception that, in the oxidation to propionic acid, $KMNO_4$ in dil H_2SO_4, instead of in dil Na_2CO_3aq, was employed in order to minimize any possibility of hydrogen exchange.

[13] R. L. Baird and A. Aboderin, *Tetrahedron Letters* 235 (1963).

[14] R. L. Baird and A. Aboderin, *J. Am. Chem. Soc.* **86**, 252 (1964).

[15] A. Aboderin and R. L. Baird, *J. Am. Chem. Soc.* **86**, 2300 (1964).

inadequate purification of some of the compounds in the earlier work.[3,4] For example, if the 1-propanol were contaminated with some 2-propanol and if the 2-propanol were oxidized to acetic acid during the degradation, a higher rearrangement with an apparent preponderance of activity at C-3 would result.

TABLE 2. ACTIVITY DATA AND REARRANGEMENTS OF THE ^{14}C-LABEL IN THE 1-PROPANOL FROM DEAMINATION OF I-1-^{14}C

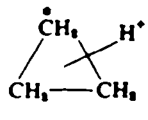
Compd. Assayed	Specific activity,[a] cpm/mmole Run 1	Run 2	%^{14}C in C-2 and C-3 Run 1	Run 2	%^{14}C in C-3 Run 1	Run 2
CH_3CH_2COOH[b]	7340	194,700				
CH_3COOH[b]	297	8,030	4·1	4·1		
CH_3NH_2[c]	109	3,600			1·5	1·9

[a] Measured by a liquid scintillation counter.

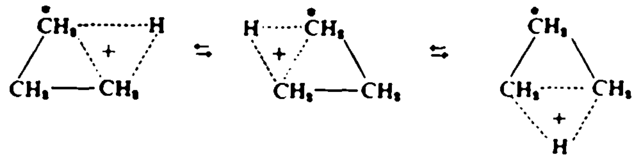
[b] Assayed as the *p*-bromophenacyl ester.

[c] Assayed as N-methyl-*p*-toluenesulfonamide.

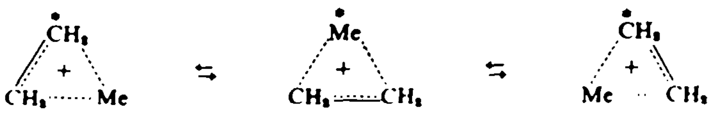
The present results indicate that the major pathway in the formation of 1-propanol from the deamination of 1-propylamine results in no isotopic rearrangement, but for that portion of the reaction leading to isotopically rearranged 1-propanol, involvement of a protonated cyclopropane, in which all three carbon positions become equivalent or are approaching equivalence, is strongly indicated. On the basis of the present results alone, however, it is not possible to differentiate between face-protonated cyclopropane IIa or the equilibration of edge-protonated cyclopropanes IIb–d (asterisk denoting an isotopic label, ^{14}C, D or T). Moreover, the complete equivalence of all three carbon positions in the resulting 1-propyl product may also be explained by the equilibration of methyl-bridged ions IIIa–c.[16] Indeed the equilibration between edge-protonated cyclopropanes may proceed *via* Me-bridged ions and *vice versa*, and interconversions between IIb–d and IIIa–c likely occur with relative ease.[14–16] In the following discussion, some pertinent literature is considered in conjunction with the present results in an attempt to give some clarification on the relative importance of IIa, IIb–d and IIIa–c in the deamination of 1-propylamine as well as to indicate some possible mechanistic implications of protonated cyclopropanes.



IIa



IIb IIc IId



IIIa IIIb IIIc

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[16] N. C. Deno, *Lecture given at the 152nd Meeting, American Chemical Society*, New York, N.Y., September 12–16 (1966), and by private communications.

In 1960, it was reported[17] that the deamination of 1-propylamine and the deoxidation of 1-propanol both gave a hydrocarbon fraction consisting of 90% propene and 10% cyclopropane. A completely symmetrical protonated cyclopropane, IIa, was suggested as a possible intermediate. These workers, however, later stated a preference for the 1,3-hydride shift[18] because the I-1-^{14}C studies[4] had apparently excluded any process involving protonated cyclopropane. Significant roles for protonated cyclopropane intermediates were clearly established and reported in an important series of papers.[13–15] Thus in the solvolysis of cyclopropane in deuteriosulfuric acid,[14] deuterium was incorporated into all three positions of the 1-propanol obtained, the average distribution in the C-1, C-2 and C-3 positions, respectively, being 0·38, 0·17 and 0·46 deuterium atom. A mechanism involving both edge-protonated cyclopropanes and Me-bridged ions was proposed, but to account for the experimental results, solvolytic ring opening was assumed to occur primarily with the edge-protonated cyclopropanes rather than with Me-bridged ions.[14] If there were a competition between solvolytic ring opening and further scrambling of the isotopic label, then the finding of a lesser amount of deuterium at C-2 would be reasonable because incorporation of deuterium into C-2 would require more extensive rearrangements from IIb to IId.

Aboderin and Baird[15] also reported that the deamination of 3,3,3-d_3-1-propylamine (I-3-d_3) gave a cyclopropane fraction consisting of 57% d_3-cyclopropane and 43% d_2-cyclopropane. These data, when considered in the light of the present results from the deamination of I-2-d_2, I-1-t and I-1-^{14}C, may be reinterpreted as a confirmation of the conclusion that the deamination of 1-propylamine involves protonated cyclopropane intermediates in which all three carbon positions (and all hydrogens) are approaching complete equivalence. Since there are four hydrogen and three deuterium atoms in any protonated cyclopropane from I-3-d_3, loss of a proton or a deuteron would give rise to d_3-cyclopropane or d_2-cyclopropane respectively. On purely statistical grounds, if the hydrogen and deuterium atoms were equivalent, the ratio of d_3-cyclopropane to d_2-cyclopropane should be 4:3, which is almost exactly the same as the observed ratio of 57%:43%. It is also of interest to point out that in the deoxidation of 1,1-d_2-1-propanol,[18] the cyclopropane obtained was found to contain about 94% d_2-cyclopropane and only 5–6% d_1-cyclopropane. Under the highly basic medium of deoxidation, it is not surprising that hydrogen mixing through equilibration of edge-protonated cyclopropanes would compete less effectively with deprotonation.

The question arises as to whether the protonated cyclopropane intermediates in the deamination of 1-propylamine should be represented by IIa or by the equilibration of IIb–d. From theoretical considerations, Hoffman[19] has concluded that the edge-protonated structure is preferred. Moreover, a completely symmetrical intermediate IIa cannot account for the data from the solvolysis of cyclopropane in deuteriosulfuric acid.[14] Recent studies in this laboratory on the solvolysis of 1-^{14}C-1-propyl tosylate (IV) of high specific activity have shown that formolysis gave a small amount of isotopic rearrangement in the resulting 1-propyl formate, the distribution of the

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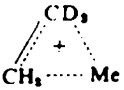
[17] P. S. Skell and I. Starer, *J. Am. Chem. Soc.* **82**, 2971 (1960).

[18] P. S. Skell and I. Starer, *J. Am. Chem. Soc.* **84**, 3962 (1962).

[19] R. Hoffmann, *J. Chem. Phys.* **40**, 2480 (1964).

rearranged ^{14}C being 0·15% and 0·68%, respectively, in the C-2 and C-3 positions.[30] The unequal distribution of the rearranged isotopic label is not compatible with IIa, but an explanation based on the equilibration of IIb–d is feasible. As in the case of solvolysis of cyclopropane,[14] the initially formed edge-protonated cyclopropane from IV would be IIb, which would give 1-propyl formate with the label at C-1 and C-3. Further scrambling to IId, possibly *via* IIIb, IIc and IIIc, would be required in order to have the ^{14}C located at the C-2 position of the product. If more product is formed from the first intermediate IIb, more of the rearranged ^{14}C would be located at C-3 than at C-2 as observed. These considerations also argue against product formation from equilibrating Me-bridged ions IIIa–c. In the formolysis of IV, the initially formed Me-bridged ion would be IIIa which would give a product with the ^{14}C-label at C-1 and C-2. Further rearrangement to IIIb is required to give a product with the ^{14}C rearranged to C-3. If product formation were more rapid than further rearrangement, one would expect more of the rearranged ^{14}C at C-2 than at C-3. On the other hand, if further rearrangement were faster than product formation, all carbon positions would become equivalent and the rearranged ^{14}C would be equally located at C-2 and C-3. Neither of these possibilities agree with the observed rearranged ^{14}C distribution in the 1-propyl formate from the formolysis of IV. It appears that the best representations of the product forming protonated cyclopropane intermediates may be the equilibrating edge-protonated cyclopropanes. In the deamination reaction, the energetics of the various species involved may be such that equilibration is more complete than in the case of solvolysis.

Interconversion between edge-protonated cyclopropanes may proceed via Me-bridged ions.[14,15] In a careful mass spectral study on the deamination of I-1-d_2 and I-2-d_2, it was noted[8] that among the isotopically rearranged 1-propanol, both systems gave the same amount of $C_2H_4DCHDOH$ (0·9–1·0%). One proposed explanation suggested that the deamination of I-1-d_2 and of I-2-d_2 both first gave the same Me-bridged ion V which then further rearranges to edge-protonated cyclopropanes before formation of isotopically rearranged 1-propanol. If both edge-protonated cyclopropanes and methyl-bridged ions were involved and products could arise only from the edge-protonated intermediates, the Me-bridged ions may be of somewhat higher energy and may be regarded as transition states in the interconversions between edge-protonated cyclopropanes.[16] Theoretical calculations[19] regarding the relative stabilities of the Me-bridged ion and the edge-protonated cyclopropane, unfortunately, led to apparently inconclusive results.



V

From the present experimental data and other results already reported in the literature, it may be concluded that the 1-propyl cation derived from deamination of 1-propylamine may (1) react with water to give 1-propanol without rearrangement and deprotonate to propene; (2) undergo irreversible 1,2-hydride shift to the 2-propyl

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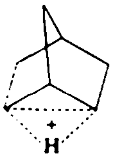
[30] C. C. Lee and J. E. Kruger, *Canad. J. Chem.* **44**, 2343 (1966).

cation which will lead to 2-propanol as well as propene; and (3) give rise to equilibrating edge-protonated cyclopropane intermediates which will deprotonate to cyclopropane and react with water to give 1-propanol. If isotopically labelled 1-propylamine were the starting material, isotopically rearranged 1-propanol would result from the process involving equilibrating edge-protonated cyclopropanes. Since the total isotope position rearrangements from C-1 to C-2 and C-3 in the deamination of I-1-*t* and I-1-^{14}C amounted to about 3–4% (Tables 1 and 2), the major portion of the 1-propanol was formed without rearrangement and only about 4–6% of the 1-propanol recovered was derived from equilibrating edge-protonated cyclopropanes such as IIb–d. The present results thus have eliminated the possibility of a direct 1,3-hydride shift in the 1-propyl cation. It may be worthwhile to re-examine other previously proposed 1,3-hydride shifts such as those quoted in Refs. 5 and 7.

In recent years, products having the cyclopropane ring structure have been reported in a number of reactions including deoxidation,[17,18,21,22] deamination,[17,23–26] cationic decomposition of tosylhydrazones,[27] and aprotic diazotization of amines.[28] Protonated cyclopropanes likely play a role in these reactions as reactive intermediates, and indeed this was the conclusion reached by some of the authors.[26,28] Finally, some comments may be made on the extensively studied 2-norbornyl system. The overall 6,2-hydride shift originally observed[29,30] is now generally believed to proceed via edge-protonated nortricyclene (VI). In the acetolysis of *exo*-2-norbornyl brosylate, previously undetected elimination products have recently been reported as amounting 4%, and significantly, the composition of this hydrocarbon fraction was found to be 98% nortricyclene and 2% norbornene.[31] Evidence has also been presented to indicate that the 6,2- (or 6,1-) hydride shift takes place following 1,2-carbon bridging to give the norbornonium ion.[32] Recent studies on the norbornyl cation generated by both the σ- and π-routes have delineated more clearly the various processes contributing to the observed overall isotope position rearrangements.[33,34] A major portion of the



VI

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[21] P. S. Skell and I. Starer, *J. Am. Chem. Soc.* **81**, 4117 (1959).

[22] P. S. Skell and R. J. Maxwell, *J. Am. Chem. Soc.* **84**, 3963 (1962).

[23] M. S. Silver, *J. Am. Chem. Soc.* **82**, 2971 (1962).

[24] M. S. Silver, *J. Org. Chem.* **28**, 1686 (1963).

[25] W. G. Dauben and P. Lang, *Tetrahedron Letters* 453 (1963).

[26] O. E. Edwards and M. Lesage, *Canad. J. Chem.* **41**, 1592 (1963).

[27] L. Freidman and H. Shechter, *J. Am. Chem. Soc.* **81**, 5512 (1959).

[28] J. H. Bayless, F. D. Mendicino and L. Friedman, *J. Am. Chem. Soc.* **87**, 5790 (1965).

[29] J. D. Roberts and C. C. Lee, *J. Am. Chem. Soc.* **73**, 5009 (1951).

[30] J. D. Roberts, C. C. Lee and W. H. Saunders, Jr., *J. Am. Chem. Soc.* **76**, 4501 (1954).

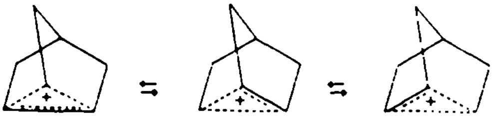
[31] S. Winstein, E. Clippinger, R. Howe and E. Vogelfanger, *J. Am. Chem. Soc.* **87**, 376 (1965).

[32] A. Colter, E. C. Friedrich, N. J. Holness and S. Winstein, *J. Am. Chem. Soc.* **87**, 378 (1965).

[33] C. C. Lee and L. K. M. Lam, *J. Am. Chem. Soc.* **88**, 2831 (1966).

[34] C. C. Lee and L. K. M. Lam, *J. Am. Chem. Soc.* **88**, 2834 (1966).

solvolysis product arises from the equilibration of carbon-bridged norbornonium ions VIIa–c. These equilibrations take place through 6,2- and 6,1-hydride shifts, presumably via edge-protonated nortricyclene (VI). In contrast to the 1-propyl system where products are formed from the edge-protonated species, the carbon-bridged ions in the norbornyl case may be of greater stability, and a major part of the solvolysis product results from reaction of the solvent with norbornonium ions VIIa–c rather than from reaction with edge-protonated nortricyclene.



VIIc VIIa VIIb

EXPERIMENTAL

$2,2\text{-}d_2$-*Propionic acid.*[11] Ethyl methylmalonate[25] was hydrolyzed in 25% KOH soln to give VIII which, after crystallization from ether–pet. ether, melted at 135° dec (lit.[26] m.p. 135° dec). A sample of VIII (35·0 g, 0·30 mole) was dissolved in 30 g D_2O (99·7%) in a 100-ml flask and heated at 55° for 12 hr. The D_2O (containing some H_2O derived from exchange) was then evaporated off under vacuum at 55°, with the last traces removed by storing the product over P_2O_5 in a vacuum desiccator. The procedure was repeated successively 5 times, each time using fresh D_2O, after which exchange was essentially complete as indicated by the NMR spectrum of the resulting IX.

Compound IX was placed in a Claisen flask set up for vacuum distillation. Decarboxylation was effected by heating the flask and its content at 135° under mild vacuum for 7 hr. The resulting product was vacuum distilled into a receiver cooled in a Dry Ice-acetone bath. Redistillation over a helix-packed column gave 19·2 g (86%) of $2,2\text{-}d_2$-propionic acid, b.p. 138–140° (lit.[26] b.p. 140°).

$2,2\text{-}d_2$-1-*propylamine* ($I\text{-}2\text{-}d_2$). The deuterated propionic acid was converted to $2,2\text{-}d_2$-propionamide.[27] The deuterated amide (9·75 g, 0·13 mole) was added, in small portions, to a stirred suspension of 12 g of LAH in 600 ml anhydrous ether in a 2-l. flask equipped with reflux condenser. The reaction mixture was stirred at room temp for 40 hr and then decomposed by the addition of cold water and 10% NaOHaq. The volatile materials were distilled into a receiver containing 12 ml of cold and stirred 70% aqueous perchloric acid. The recovered materials were then fractionated to remove the ether and the remaining soln was evaporated under reduced press at 35–40°. The residual solid was recyrstallized 3 times from 1-hexanol–heptane, giving 13·7 g (65%) of the perchlorate salt of $I\text{-}2\text{-}d_2$, m.p. 166° (lit.[8] m.p. 167°).

1-t-1-*Propylamine* (I-1-t). A suspension of 12·0 g of *t*-labelled LAH (containing about 10 mc. of tritium) in 800 ml of anhydrous ether was placed in a 2-l. flask cooled in an ice bath and equipped with magnetic stirrer, reflux condenser and dropping funnel. A soln of 24·4 g (0·44 mole) propionitrile in 110 ml of anhyd ether was added dropwise with stirring. Following this, a further 10·8 g of ordinary LAH was introduced portionwise. Stirring was continued for 3 hr. The resulting mixture was decomposed and the product recovered as described under the preparation $I\text{-}2\text{-}d_2$, 40 ml of 70% aqueous perchloric acid being used to trap the amine. The perchlorate salt of I-1-*t* so obtained, m.p. 166°, weighed 55·0 g (78%).

$1\text{-}^{14}C$-1-*Propylamine* ($I\text{-}1\text{-}^{14}C$). $1\text{-}^{14}C$-Propionitrile was prepared from potassium ^{14}C-cyanide (about 2 mc.) and Et_2SO_4 as described.[8] The reduction of the nitrile to $I\text{-}1\text{-}^{14}C$ was effected in the same way as in the preparation of I-1-*t*, except that the soln of 24·4 g of the nitrile was added dropwise to a single suspension of 22·8 g of LAH. The yield of the perchlorate salt of $I\text{-}1\text{-}^{14}C$, m.p. 166° was 53·0 g (75%).

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[25] A. H. Blatt, Ed., *Organic Synthesis* Coll Vol. II, p. 279. Wiley, New York, N.Y. (1943).

[26] R. L. Shriner, R. C. Fuson and D. Y. Curtin, *The Systematic Identification of Organic Compounds* (4th Edition) Wiley, New York, N.Y. (1956).

[27] G. E. Philbrook, *J. Org. Chem.* 19, 623 (1954).

Deamination of I-2-d_2. To a stirred soln of 24·0 g (0·15 mole) of 2,2-d_2-1-propylammonium perchlorate in 21 ml of 35% aqueous perchloric acid, maintained at 25° in a water bath, was added dropwise over 2 hr 22·1 g (0·32 mole) of $NaNO_2$ dissolved in 32 ml water. The reaction mixture was stirred for an additional 2 hr at 25°. The soln was then distilled until about 25 ml distillate was collected. The distillate was acidified with HCl and redistilled to remove any excess amine. KF was added to salt out the organic layer containing the 1-propanol and 2-propanol. This mixture of products, after drying over Na_2SO_4, weighed 3·43 g (37%). Pure 1-propanol and 2-propanol were obtained by preparative VPC. A preliminary separation was effected in a Beckman GC-2A chromatograph with a 10 ft column packed with 20% didecyl phthalate on acid washed chromosorb P. Each of the 1-propanol and 2-propanol fractions was then purified once more by passage through a 10 ft column packed with 20% Carbowax 20 M on chromosorb P, using an Aerograph Autoprep. The deuterated 1-propanol and 2-propanol so obtained were examined with a Varian Associates HR100 spectrometer.[28]

Deamination of I-1-t *and* I-1-^{14}C. These deaminations were effected in the same way as in the deamination of I-2-d_2, except that in the final isolation of the desired product, some inactive 1-propanol was added as carrier,[29] and only one VPC separation using the Carbowax 20 M column in the Aerograph Autoprep was necessary. Starting from 27·0 g (0·17 mole) of the perchlorate salt of I-1-*t* or I-1-^{14}C, with 1·2 g of inactive 1-propanol carrier added, the recovery of VPC purified active 1-propanol was about 2·7 g. This was further diluted with inactive carrier to give a sufficient amount of 1-propanol for degradation.

The experimental conditions used in the deamination reactions were essentially the same as those reported,[8] except that in the present case, purification was by preparative VPC, and the reaction time was extended to include an additional 2 hr of stirring at 25° after the dropwise addition of the $NaNO_2$aq has been completed. The yields of 1-propanol, assuming a quantitative recovery of the added carrier, was about 15%. Most probably, under the conditions of nitrous acid deamination, some of the alcohol formed likely has been destroyed, presumably by oxidation, as was observed[24] in similar studies. The isotopically labeled 1-propanol obtained from the present experiments likely represents the alcohol that has survived under the present experimental conditions.

Degradation of 1-*propanol from the deamination of* I-1-t *or* I-1-^{14}C. A small amount (about 0·5 g) 1-propanol from each run was converted in the conventional way[30] to a solid derivative, the α-naphthylurethan, m.p. 80° (lit.[30] m.p. 80°). The remainder of each sample was first oxidized by $KMnO_4$ in dil H_2SO_4 to give propionic acid as described.[8] The propionic acid was steam distilled, neutralized, and recovered as sodium propionate. A small portion of each sodium propionate sample was converted[30] to *p*-bromophenacyl propionate, m.p. 63° (lit.[30] m.p. 63°), and the remainder was utilized for oxidation to AcOH. A control oxidation of an authentic sample of 1-*t*-1-propanol gave a completely inactive propionic acid derivative, indicating that this oxidation causes no isotopic rearrangements.

The oxidation of sodium propionate to AcOH was effected by $K_2Cr_2O_7$ in 18N H_2SO_4 as described.[6] The AcOH was steam distilled, neutralized and recovered as AcONa, a sample of which was converted to *p*-bromophenacyl acetate, m.p. 85–86° (lit.[30] m.p. 85°).

With the 1-propanol derived from the deamination of I-1-^{14}C, the AcONa obtained as outlined above was further degraded *via* the Schmidt reaction, as described[6] to give $MeNH_2$, recovered as the hydrochloride. The $MeNH_2 \cdot HCl$ was converted[30] to a solid deriv, the N-methyl-*p*-toluenesulfonamide, m.p. 75° (lit.[30] m.p. 75°).

All solid derivatives of the various samples were sublimed and recrystallized 3 to 6 times to give samples of constant specific activity for radioactivity assays.

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[28] The NMR spectra were obtained by G. W. Bigam at the University of Alberta through arrangements with Professor R. U. Lemieux.

[29] This expedient was also employed by previous workers.[8,6]