

Rearrangement Studies with Carbon-14. XXXIII. Deamination and Deoxidation Studies on the 1-¹⁴C-1-Propyl System¹

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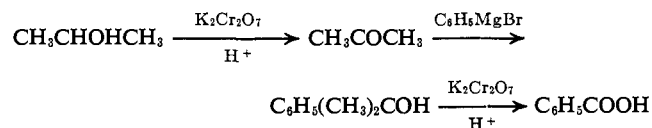
Abstract: The deamination of 1-¹⁴C-1-propylamine gave 1-propanol with 2% rearrangement of the label from C-1 to each of the C-2 and C-3 positions, in complete agreement with an earlier finding. The 2-propanol obtained showed no rearrangement of the label to C-2. Degradation of the propene formed in this reaction indicated about 13% rearrangement of the label from C-1 to C-3, no significant amount of activity being found at C-2. The deoxidation of potassium 1-¹⁴C-1-propoxide in excess 1-¹⁴C-1-propanol as solvent gave propene with 10–12% isotope-position rearrangement from C-1 to C-3. When the deoxidation was carried out in an excess of concentrated KOH, the rearrangement from C-1 to C-3 in the propene was only 4–5%. These results indicate that in both deamination and deoxidation reactions, no propene was formed from protonated cyclopropane, and the rearrangement in the propene from C-1 to C-3 can be readily attributed to the elimination of a proton from the 1-¹⁴C-2-propyl cation formed from the 1-¹⁴C-1-propyl cation. Other mechanistic implications of the results are also discussed.

In 1965, Lee, Kruger, and Wong,² as well as Karabatsos, Orzech, and Meyerson,³ had independently obtained evidence to indicate that a small fraction (4–6%) of the 1-propanol produced in the nitrous acid deamination of 1-propylamine in aqueous HClO₄ was derived from protonated cyclopropane intermediates. When 1-¹⁴C-1-propylammonium perchlorate (I-1-¹⁴C) was deaminated, for example, the resulting 1-propanol (II-¹⁴C) showed that approximately 2% of the isotopic label was rearranged from C-1 to each of the C-2 and C-3 positions.² As propene (III) is a major product in this deamination reaction,^{4,5} it is of interest to determine the isotopic distribution in the propene (III-¹⁴C) obtained from the deamination of I-1-¹⁴C so as to ascertain if any of the III-¹⁴C were derived from protonated cyclopropane.

Skell and Starer^{5,6} have proposed that deoxidation reactions resulting from treatment of alkoxides with bromoform in alkaline media involved carbonium ion intermediates, and that since the precursors to the carbonium ion in the deoxidation (R—O—C⁺: ↔ R—O⁺=C:) and in the deamination (R—N⁺=N: ↔ R—N⁺=N:) are isosteres, it was suggested that the same carbonium ion should be produced upon the loss of CO or N₂, respectively. In support of such a suggestion, Skell and Starer reported, for example, that both deoxidation and deamination reactions with the 1-propyl system gave a hydrocarbon product consisting of 90% propene and 10% cyclopropane. It would, therefore, be also of interest to compare the isotopic scrambling, if any, in the propene obtained from deoxidation of 1-¹⁴C-1-propoxide with the results observed in the deamination studies.

Results and Discussion

The deamination of I-1-¹⁴C was carried out as previously described.^{2,7} The gases evolved were collected in cold traps containing inactive propene (III) as carrier. The alcoholic products, 1-propanol and 2-propanol (II-¹⁴C and IV-¹⁴C), were also recovered with the aid of inactive carriers. By hydroboration, III-¹⁴C was converted to II-¹⁴C. Samples of the alcohols, II-¹⁴C and IV-¹⁴C, after purification by preparative vpc, were degraded to give the isotopic distributions. The degradation of II-¹⁴C has already been described,⁷ while the degradation of IV-¹⁴C was effected as shown. The



benzoic acid obtained from IV-¹⁴C would give a direct measure of any activity located at the C-2 position. As it turned out, essentially inactive benzoic acid was produced from oxidation of the active dimethylphenylcarbinol derived from IV-¹⁴C, indicating that there was no rearrangement of the label to C-2 in the 2-propanol (IV-¹⁴C) obtained in the deamination reaction.⁸ The results from the degradation of II-¹⁴C, obtained either as a deamination product or from the hydroboration of III-¹⁴C, are given in Table I.

The deoxidation was carried out either by the addition of bromoform to potassium 1-¹⁴C-1-propoxide in an excess of 1-¹⁴C-1-propanol (II-1-¹⁴C) as solvent or by adding CHBr₃ to a limited amount of II-1-¹⁴C in an excess of a concentrated solution of KOH. The gaseous products were trapped with inactive propene (III) carrier as described before and the III-¹⁴C was converted by hydroboration to II-¹⁴C for degradation. The results are shown in Table II. The unreacted II-1-¹⁴C re-

(1) Supported by a grant from the National Research Council of Canada; for paper XXXII, see C. C. Lee and R. J. Tewari, *Can. J. Chem.*, **46**, 2314 (1968).

(2) C. C. Lee, J. E. Kruger, and E. W. C. Wong, *J. Amer. Chem. Soc.*, **87**, 3985 (1965); C. C. Lee and J. E. Kruger, *ibid.*, **87**, 3986 (1965).

(3) G. J. Karabatsos, C. E. Orzech, Jr., and S. Meyerson, *ibid.*, **87**, 4394 (1965).

(4) F. C. Whitmore and R. S. Thorpe, *ibid.*, **63**, 1118 (1941).

(5) P. S. Skell and I. Starer, *ibid.*, **82**, 2971 (1960).

(6) P. S. Skell and I. Starer, *ibid.*, **81**, 4117 (1959); **84**, 3962 (1962).

(7) C. C. Lee and J. E. Kruger, *Tetrahedron*, **23**, 2539 (1967).

(8) The degradation of IV-¹⁴C was carried out by Dr. D. J. Woodcock in this laboratory in conjunction with another study in which 2-propanol was degraded. The details of the work of Woodcock will be reported later.

Table I. Activity Data and Rearrangements of the ^{14}C Label in the 1-Propanol- ^{14}C (II- ^{14}C) Obtained from the Deamination of I-1- ^{14}C and from Hydroboration of the Propene- ^{14}C (III- ^{14}C) Formed in the Deamination Reaction

Source of II- ^{14}C	Compd assayed	Specific activity, ^a cpm/mmol		% ^{14}C at C-2 and C-3		% ^{14}C at C-3	
		Run 1	Run 2	Run 1	Run 2	Run 1	Run 2
Deamination product	$\text{CH}_3\text{CH}_2\text{COOH}^b$	218,400	95,900				
	CH_3COOH^b	8,840	3,880	4.1	4.0		
	CH_3NH_2^c	4,320	1,950			2.0	2.0
III- ^{14}C	$\text{CH}_3\text{CH}_2\text{COOH}^b$	32,000	15,900				
	CH_3COOH^b	4,010	2,210	12.5	13.9		
	CH_3NH_2^c	4,030	2,130			12.6	13.4

^a Measured by a liquid scintillation counter. ^b Assayed as the *p*-bromophenacyl ester. ^c Assayed as *N*-methyl-*p*-toluenesulfonamide.

Table II. Activity Data and Rearrangements of the ^{14}C Label in the 1-Propanol- ^{14}C (II- ^{14}C) Derived from Hydroboration of the Propene- ^{14}C (III- ^{14}C) Obtained from Deoxidation Studies with II-1- ^{14}C

Reaction	Compd assayed	Specific activity, ^a cpm/mmol		% ^{14}C at C-2 and C-3		% ^{14}C at C-3	
		Run 1	Run 2	Run 1	Run 2	Run 1	Run 2
$\text{C}_3\text{H}_7\text{OK-1-}^{14}\text{C}$ in excess	$\text{CH}_3\text{CH}_2\text{COOH}^b$	8,850	341,000				
II-1- ^{14}C + CHBr_3	CH_3COOH^b	1,070	3,440	12.1	10.1		
	CH_3NH_2^c	1,050	3,430			11.9	10.1
II-1- ^{14}C in excess KOH + CHBr_3	$\text{CH}_3\text{CH}_2\text{COOH}^b$	90,200	307,900				
	CH_3COOH^b	3,550	17,100	3.9	5.5		
	CH_3NH_2^c	3,810	17,100			4.2	5.5

^{a-c} See footnotes in Table I.

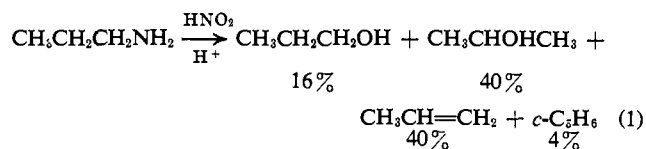
covered from the deoxidation reaction mixtures was also degraded and found to be isotopically unrearranged (in the case of deoxidation effected in concentrated KOH with a limited amount of II-1- ^{14}C , inactive carrier was used to aid the recovery of unreacted II-1- ^{14}C).

From Table I, it is seen that the 1-propanol- ^{14}C (II- ^{14}C) obtained as a product in the deamination of I-1- ^{14}C showed rearrangements of 2% of the label from C-1 to each of the C-2 and C-3 positions. Previously, Lee and Kruger^{2,7} reported that for two runs of a similar deamination of I-1- ^{14}C , the data from the more reliable run, which utilized a sample of I-1- ^{14}C of higher specific activity, showed rearrangements of 2.2 and 1.9%, respectively, from C-1 to C-2 and C-3. It was concluded that "the results indicate a total of about 4% rearrangement, with the rearranged ^{14}C approaching equal distribution in C-2 and C-3."² The present results are in complete agreement with this conclusion, the isotope-position rearrangements in the II- ^{14}C obtained from deamination of I-1- ^{14}C being apparently $2.0 \pm 0.2\%$ from C-1 to each of the C-2 and C-3 positions. With regard to the propene- ^{14}C (III- ^{14}C) produced in the deamination, about 13% rearrangement of the label from C-1 to C-3 was noted, and essentially no significant amount of activity was found at C-2. These observations show that no detectable amount of III- ^{14}C was derived from protonated cyclopropane intermediates, and that the rearrangement of the label from C-1 to C-3 resulted from elimination after the 1- ^{14}C -1-propyl cation has been converted to the 1- ^{14}C -2-propyl cation, the latter giving rise to equal amounts of 1- ^{14}C -propene and 3- ^{14}C -propene.

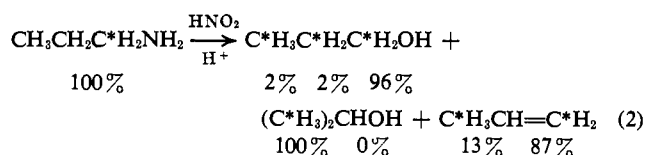
After consideration of the relevant known data,^{4,5,9} Karabatsos¹⁰ has estimated that the approximate product distribution from the deamination of I may be as shown (eq 1). From the present work, the isotopic

(9) G. J. Karabatsos and C. E. Orzech, Jr., *J. Amer. Chem. Soc.*, **84**, 2838 (1962).

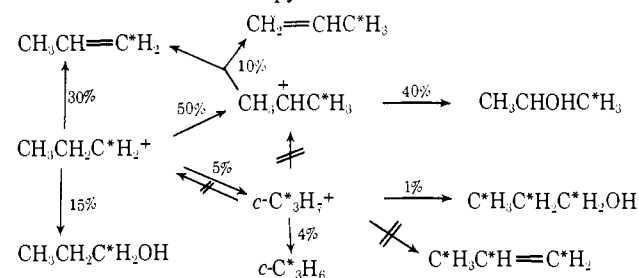
(10) G. J. Karabatsos, private communications.



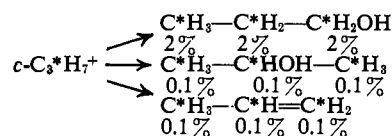
distributions in the products from the deamination of I-1- ^{14}C may be summarized by eq 2. Considering to-



gether the data given above in eq 1 and 2, it is possible to give a reasonable and complete description of the fate of the 1-propyl cation from the deamination of 1-propylamine as shown in Scheme I.

Scheme I. The Fate of the 1-Propyl Cation from Deamination of 1- ^{14}C -1-Propylamine¹¹

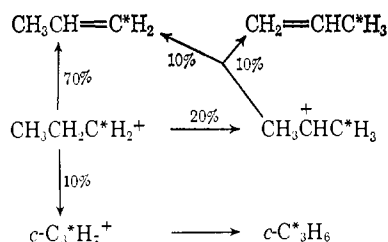
(11) The maximum amount of rearrangement to C-2 in the 2-propanol (IV- ^{14}C) or propene (III- ^{14}C) that might have gone undetected in the present work is estimated to be 0.1%. Thus one might set upper limits for the partitioning of *c*-C * ₃H * ₇⁺ as shown. Such considerations would



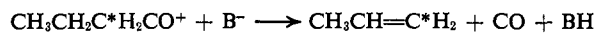
According to Scheme I, the ^{14}C content at C-3 of the propene (III- ^{14}C) would be $(5/40) \times 100 = 12.5\%$, and the rearrangement to C-2 or C-3 in the 1-propanol (II- ^{14}C) would be $(0.33/16) \times 100 = 2\%$. It is of interest to note that some 50% of the 1-propyl cation rearranges to the 2-propyl cation while only about 5% of the 1-propyl cation is converted to protonated cyclopropane. These results clearly establish the order of relative stability as $2\text{-C}_3\text{H}_7^+ > c\text{-C}_3\text{H}_7^+ > 1\text{-C}_3\text{H}_7^+$. Of some interest also is the relatively large amount of unrearranged propene present in the product, some 30% being ascribed to the conversion of $\text{CH}_3\text{CH}_2\text{C}^*\text{H}_2^+$ to $\text{CH}_3\text{CH}=\text{C}^*\text{H}_2$. Although there are no direct data relating to the details of this conversion to unrearranged propene, it is possible that this process may include some E2-type of elimination involving the immediate precursor to the 1-propyl cation ($\text{CH}_3\text{CH}_2\text{C}^*\text{H}_2\text{N}_2^+ \xrightarrow{\text{B}^-} \text{CH}_3\text{CH}=\text{C}^*\text{H}_2 + \text{N}_2 + \text{BH}$).

The data from the deoxidation studies (Table II) also indicate that the propene (III- ^{14}C) obtained showed rearrangement of the label only from C-1 to C-3. Again no detectable amount of III- ^{14}C was derived from protonated cyclopropane. When the reaction was carried out with potassium 1- ^{14}C -1-propoxide in excess II-1- ^{14}C as solvent, this rearrangement amounted to about 10–12%. Since the hydrocarbons produced in such a deoxidation would consist of 90% propene and 10% cyclopropane,⁵ Scheme II can be devised to account for the observed results.

Scheme II. The Fate of the 1-Propyl Cation from Deoxidation of Potassium 1- ^{14}C -1-propoxide in Excess 1- ^{14}C -1-propanol as Solvent



When the deoxidation was carried out in concentrated KOH, a lesser amount of rearrangement from C-1 to C-3 (4–5%) was observed in the resulting III- ^{14}C . In Scheme II, some 70% of the over-all processes could be assigned to the formation of unrearranged III-1- ^{14}C . For the reaction in concentrated KOH, the relative contribution of this process to unrearranged III-1- ^{14}C would be still greater. As mentioned earlier, perhaps the formation of III-1- ^{14}C without rearrangement may include an E2-type of reaction involving the precursor to the carbonium ion



Possibly, such an E2 process may be of greater importance in a medium of excess concentrated KOH than in a medium with 1-propanol as solvent. The possibility

suggest that a maximum of about $(0.3/6.3) \times 100 = 5\%$ of the protonated cyclopropane intermediates could have been converted to IV- ^{14}C or III- ^{14}C without being detected by the present experiments. Very recently, L. Friedman and A. Jurewicz, *J. Amer. Chem. Soc.*, **91**, 1800 (1969), reported that deaminations of 1-propyl-3,3,3- d_3 -amine and 1-propyl-2,2- d_2 -amine under aprotic conditions gave samples of propene whose deuterium contents suggested that some propene was formed from equilibrating protonated cyclopropane intermediates. Studies on the aprotic deaminations of I-1- ^{14}C are currently in progress in our laboratory.

of some contribution from concerted processes in deoxidation reactions has also been suggested by Sanderson and Mosher¹² and by Lee and Hahn.¹³

The overall fates of the 1-propyl cation from deamination and from deoxidation are necessarily different since in the deamination, besides the hydrocarbon product, 1- and 2-propanols (II and IV) are also produced. From Schemes I and II, it is seen that in partitioning the 1-propyl cation into the various processes, in the deoxidation, a greater proportion of the ion gives rise to unrearranged III-1- ^{14}C than to the 2-propyl cation, while the reverse is true for the 1-propyl cation derived from deamination. Although a contributing factor for this difference may be a greater amount of E2-type of elimination in the deoxidation, a comparison of Schemes I and II appears to indicate that the carbonium ions formed in deamination and in deoxidation behave in similar, but not identical, manners.

In a deoxidation study with 2-phenyl-1- ^{14}C -ethanol carried out in concentrated KOH, Lee and Hahn¹³ have noted that the labeled 2-phenylethanol recovered from the deoxidation reaction mixture showed some rearrangement of the isotopic label from C-1 to C-2. This was the first observation of the formation of a rearranged alcohol in a deoxidation reaction. In the present work, the recovered II-1- ^{14}C was isotopically unrearranged, indicating, not surprisingly, that no 1-propanol was formed from protonated cyclopropane in the deoxidation. Since the observed rearrangement in III- ^{14}C from C-1 to C-3 apparently resulted from elimination of proton from the 1- ^{14}C -2-propyl cation, it would be of interest to find out if any 2-propanol (IV) could be formed in the deoxidation reaction mixture. In the two runs effected in concentrated KOH, both inactive alcohols II and IV were added to the reaction mixture as carriers. Both of the recovered alcohols, after purification by preparative vpc, were found to be radioactive. Isotope dilution calculations (see Experimental Section) indicate that under the reaction conditions employed, about 15% unreacted II-1- ^{14}C was recovered, and the secondary alcohol, IV-1- ^{14}C , present in the two runs effected in KOH, amounted to 0.06 and 0.09% of the originally used II-1- ^{14}C . Thus, with the relatively sensitive tracer technique, it is possible to detect the formation of rearranged alcohols from the reaction of rearranged cations with the hydroxide ions in the alkaline medium of the deoxidation reaction.

Experimental Section

Deamination. The deamination of I-1- ^{14}C was carried out as described previously,⁷ but with modifications in the apparatus to allow for the collection of the gaseous products by equipping the reaction flask with gas inlet and outlet tubes. During the course of the reaction, a gentle stream of nitrogen was passed over the reaction mixture to sweep out the gases into a series of traps cooled in Dry Ice-acetone, the first of these traps containing about 12 g of condensed inactive propene as carrier. Both inactive 1-propanol (4.0 g) and 2-propanol (2.0 g) were also added as carriers to the resulting reaction mixture to aid the isolation of these liquid products, which were finally separated and purified by preparative vpc with a Carbowax 20 M column.⁷

Deoxidation. Method A. A solution of potassium 1- ^{14}C -1-propoxide was prepared by adding 3.00 g (0.077 g-atom) of K to 21 ml (16.9 g, 0.28 mol) of 1- ^{14}C -1-propanol (II-1- ^{14}C) in a 100-ml three-necked round-bottomed flask equipped with magnetic stirrer,

(12) W. A. Sanderson and H. S. Mosher, *J. Amer. Chem. Soc.*, **83**, 5033 (1961); **88**, 4185 (1966).

(13) C. C. Lee and B. S. Hahn, *Can. J. Chem.*, **45**, 2129 (1967).

reflux condenser, dropping funnel, and gas inlet and outlet tubes, the gas outlet tube being connected to the top of the condenser. The stirred reaction mixture was heated at reflux while 19.5 g (0.077 mol) of CHBr_3 was added slowly over a period of 1 hr and then the mixture was allowed to reflux for an additional 0.5 hr. Throughout the process, a gentle stream of nitrogen was introduced into the system to sweep out the gases into Dry Ice-acetone cooled traps containing about 12 g (0.28 mol) of propene carrier as described under deamination. After cooling, water was added to the resulting reaction mixture until all the solids were dissolved. The solution was neutralized with dilute HCl and then continuously extracted with ether for 24 hr. The extract was dried and fractionally distilled to give recovered 1-propanol. The recovered 1-propanol was subjected to purification by preparative vpc, only an amount sufficient for the subsequent degradation (about 3 g) being so purified.

Deoxidation. Method B. A mixture of 1.80 g (0.030 mol) of $\text{II-1-}^{14}\text{C}$ and a concentrated solution of 20 g of KOH in 10 ml of water was refluxed for 0.5 hr in the same apparatus described under method A. Bromoform (15.2 g, 0.060 mol) was then slowly added over a period of 1 hr and the resulting mixture was allowed to reflux for a further 0.5 hr. A gentle stream of nitrogen was again used to sweep out the gaseous products. The reaction flask was then cooled to room temperature, and water together with inactive alcohol carriers (6.00 g of 1-propanol and 4.00 g of 2-propanol) were introduced. The two isomeric alcohols were then recovered and purified by preparative vpc as previously described.⁷ From the activities of the resulting alcohols, isotope-dilution calculations showed that for the two runs, respectively, the recoveries of unreacted 1-propanol were 17 and 15% and the formation of 2-propanol amounted to 0.06 and 0.09% of the 1-propanol originally present.

As an illustration of the isotope-dilution calculations, take, for example, run 1 in which the originally used 1.80 g of $\text{II-1-}^{14}\text{C}$ had a specific activity of 3,585,000 cpm/mmol. After dilution with 4.00 g of inactive 2-propanol carrier, the specific activity of the recovered 2-propanol was 1080 cpm/mmol. If $x = \text{mg of active 2-propanol produced in the reaction}$, $(3,585,000)(x/60) = (1080)(x + 4000)/60$, and $x = 1.2 \text{ mg}$, which corresponds to $(1.2/1800) \times 100 = 0.06\%$ of the $\text{II-1-}^{14}\text{C}$ originally present.

Hydroboration.¹⁴ The reaction was carried out in a 500-ml three-necked round-bottomed flask equipped with reflux condenser, thermometer, a gas inlet tube reaching to the bottom of the flask, and a gas outlet tube connected to the top of the condenser and leading to a series of traps cooled in Dry Ice-acetone. A mixture of 2.85 g (0.075 mol) of sodium borohydride and 100 ml of diglyme was placed in the flask and then cooled in an ice bath. When the temperature reached 5° , a solution of 14.2 g (0.10 mol) of boron trifluoride diethyl etherate in 20 ml of diglyme was added. The propene (about 12 g, 0.28 mol) from the deamination or deoxidation reaction that was collected in the cold traps was swept into the reaction mixture by a gentle stream of nitrogen. During this period, the temperature of the traps was allowed to rise gradually to room temperature. The unreacted gas that escaped from the reaction mixture was trapped again and recycled. The resulting material was stirred for 2 hr at $0-5^\circ$, and then for an additional hour at room temperature. The excess hydride was decomposed with 10 ml of water. The organoborane was oxidized at $30-40^\circ$ by the dropwise addition of 32 ml of 3 N NaOH followed by 32 ml of 30% H_2O_2 . The temperature was maintained at about 45° for an additional hour and then the mixture was continuously extracted with ether. The extract was washed with a saturated NaCl solution, dried over anhydrous MgSO_4 , and fractionally distilled, the fraction boiling between 83 and 98° being collected. The 1-propanol was separated from the 2-propanol (5-7%) by preparative vpc. The overall yields from deamination or deoxidation to propene to 1-propanol, estimated by isotope dilution, ranged from 20 to 40%, the higher values being observed in the deoxidations.

Degradations. The samples of 1-propanol- ^{14}C from the deamination or hydroboration were degraded to give the isotopic distributions in the same way as described previously.⁷ The results are summarized in Tables I and II. For the unreacted 1-propanol- ^{14}C recovered from the various deoxidation experiments, no significant rearrangement of the isotopic label from C-1 to C-2 and C-3 was observed.

(14) G. Zweifel and H. C. Brown, *Org. Reactions*, 13, 1 (1963).