ethyl sulfate to a mixture of 20 g. of 6-methyluracil and 17 g. of sodium hydroxide in 100 ml. of H_2O.[4] After 3 hr. of vigorous stirring, the solution was extracted with chloroform, dried over $MgSO_4$, filtered and the chloroform then distilled off, yield 75%, m.p. 52°. The m.p. of a mixture of material prepared by this method and Behrend's method was unchanged.

(g) **1,5-Dimethyl-4-ethoxy-2-pyrimidone.**[8]—The addition of a few drops of pyridine to a solution containing an excess of methyl iodide with 2,4-diethoxypyrimidine,[5] improves the yield materially.

(h) **1-Ethyl-4-ethoxy-2-pyrimidone.**[9]—Slightly better yields were obtained by the addition of a few drops of pyridine to a solution containing an excess of ethyl iodide with 2,4-diethoxypyrimidine. The reaction is complete after 24 hours instead of 7 days.

(i) **1-Tetraacetyl-β-D-glucosido-2-oxy-4-ethoxy-1,2-dihydropyrimidine.**[10]—An improvement in the reported yield of this compound was obtained when a molecular equivalent of pyridine was added to an equimolecular mixture of 1-bromo-tetraacetyl-D-glucose with 2,4-diethoxypyrimidine[5] in chloroform. The yield is increased from 20 to 50% (calculated from the pyrimidine). The bromoacetylglucose need not be recrystallized when this method is used. The intermediate pyrimidium salt of bromoacetylglucose[11] can be isolated when this reaction is carried out in the presence of chloroform and pyridine.

(j) **1-Tetraacetylglucosido-4-ethoxy-6-methyl-2-pyrimidone** or **2-Tetraacetylglucosido-4-ethoxy-6-methylpyrimidine.**—A thick oil was obtained when 9 g. (0.02 mole) of 2,4-diethoxy-6-methyluracil[12] and 9 g. (0.02 mole) of 1-bromotetraacetylglucose were kept in a sealed tube at 65° for four days. The resulting oil was filtered, treated with 30 ml. of ether and chilled for one day. A heavy white crystalline precipitate was filtered and twice recrystallized from EtOH–H_2O using Norite; m.p. 166°, yield 2.9 to 3.2 g. (*ca.* 32%), $[\alpha]^{25}D$ +119.7 (*c*, 0.5 in C.P. chloroform). Similar results have been reported recently by Newmark and Goodman.[13]

Anal. Calcd. for $C_{12}H_{28}O_{11}N_2$: C, 52.06; H, 5.82; N, 5.78. Found: C, 51.96; H, 5.75; N, 5.78–5.71.

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[8] W. Schmidt-Nickels and T. B. Johnson, THIS JOURNAL, **52**, 4511 (1930).

[9] G. E. Hilbert, *ibid.*, **59**, 330 (1937).

[10] G. E. Hilbert and E. F. Jansen, *ibid.*, **58**, 60 (1936).

[11] E. Fisher and K. Raske, *Ber.*, **43**, 1751 (1910).

[12] B.p. 235°, $n^{23}D$ 1.4853. *Anal.* Calcd. for $C_9H_{14}O_2N_2$: C, 59.31; H, 7.74; N, 15.37. Found: C, 59.08; H, 7.62; N, 15.30. The compound was prepared before R. Andrisano's work in *Boll. sci. Facultà chim. ind., univ. Bologna*, **5**, 52 (1944); **5**, 56 (1947), became available.

[13] P. Newmark and I. Goodman, A. C. S. 122nd Meeting, 1952, abstract of Papers, 44C.

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Rearrangement in the Reaction of C^{14}-Labeled *n*-Propylamine (1-Aminopropane-1-C^{14}) with Nitrous Acid[1]

BY JOHN D. ROBERTS[2] AND MARTIN HALMANN[3]

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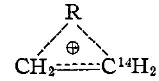
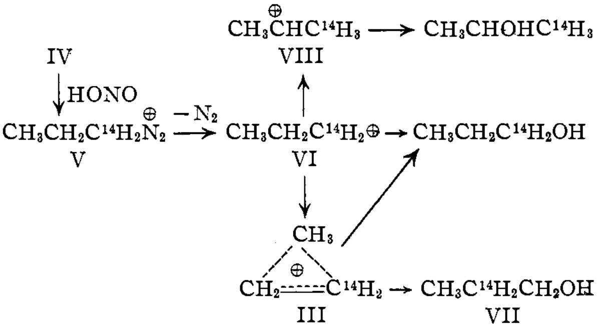
Ethylamine-1-C^{14} on treatment with aqueous nitrous acid has been shown[4] to yield, besides ethylene, a mixture of 98.5% of ethanol-1-C^{14} and 1.5% of ethanol-2-C^{14}. It was concluded that if the ethyl cation is an important intermediate in the reaction of ethylamine with nitrous acid it reacts with water considerably more rapidly than it is converted to the ethyleneprotonium ion (I). Much more rearrangement is found with 2-phenylethylamine-1-C^{14} with nitrous acid and about 56% of the 2-phenylethanol formed appears to result from a symmetrical intermediate such as II.[5]



I, R = H
II, R = C_6H_5
III, R = CH_3

Alkyl-bridged cations analogous to III ("ethylenealkonium" ions) have been proposed[6] to account for a wide variety of rearrangement reactions of alkyl derivatives but there are very few data which indicate the degree of stability of such ions relative to the isomeric classical carbonium ions like R–$CH_2CH_2^{\oplus}$.

In the present research, the tendency of the *n*-propyl cation to be converted to III was tested in the reaction of 1-propylamine-1-C^{14} (IV) with nitrous acid. The reaction is complicated by elimination and rearrangement to 2-propyl derivatives,[7] but if III is formed from the *n*-propyldiazonium ion (V) or cation VI the 1-propanol obtained from IV should contain at least some 1-propanol-2-C^{14} (VII). A possible reaction sequence for propanol formation is given below in which, for simplicity, it has been assumed that all of the cation isomerization processes are irreversible[8] and further that all of the propanol is formed by carbonium ion processes. The validity of the latter assumption has been discussed before.[4,5]



The following reactions were carried out in the present investigation. The substances represented by formulas in bold-face type were analyzed for radioactive carbon. The degradation procedure was checked for rearrangement as indicated by a blank experiment on authentic 1-propanol-1-C^{14}. The results are presented in Table I. The 1-propanol from the amine–nitrous acid reaction was found to contain 8.5% of isotope-position rearrangement product such as would be expected from hav-

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[1] Supported in part by the program of research of the U. S. Atomic Energy Commission.

[2] Gates and Crellin Laboratories, California Institute of Technology, Pasadena 4, Calif.

[3] Foreign Students Summer Project, Massachusetts Institute of Technology, 1952. The Weizmann Institute of Science, Rehovoth, Israel.

[4] J. D. Roberts and J. A. Yancey, THIS JOURNAL, **74**, 5943 (1952).

[5] J. D. Roberts and C. M. Regan, *ibid.*, **75**, 2069 (1953).

[6] (a) A number of references have been given previously[4,5]; (b) D. P. Stevenson, C. D. Wagner, O. Beeck and J. W. Otvos, *ibid.*, **74**, 3269 (1952).

[7] A. Siersch, *Ann.*, **144**, 137 (1867); F. C. Whitmore and R. S. Thorpe, THIS JOURNAL, **63**, 1118 (1941).

[8] The assumption only becomes important to the qualitative interpretation of the tracer results if VI and VIII are in rapid equilibrium, which event is unlikely since 2-propylamine with nitrous acid gives no 1-propanol and, in other processes, primary and secondary cations do not appear to be at all readily interconvertible; *cf.* J. D. Roberts, R. E. McMahon and J. S. Hine, *ibid.*, **72**, 4237 (1950).

ing 17% of the 1-propanol originating from III[9] and 83% by way of VI.

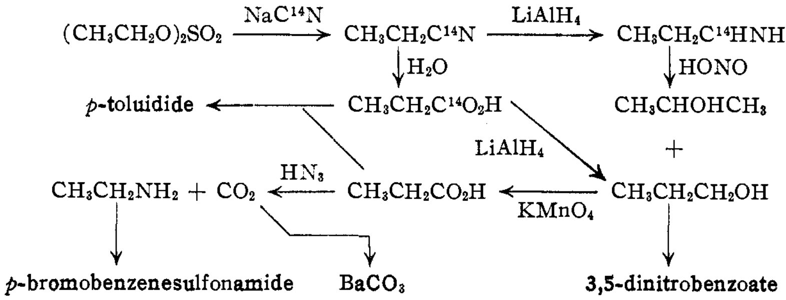

TABLE I

RADIOACTIVITY DETERMINATIONS

Reaction		1-Amino-propane-1-C^{14} + nitrous acid	Degradation of 1-propanol-1-C^{14}
C^{14}-Activities,[a] mc. per millimole × 10^3	1-Propanol[b]	139	......
	Propionic acid[c]	142 ± 4^f	11380
	Barium carbonate[d]	127 ± 2^f	11070
	N-Ethyl-*p*-bromobenzenesulfonamide	12 ± 1^f	16
	Rearrangement,[e] %	8.5 ± 1	0.15

[a] Measured by the procedure of O. K. Neville, THIS JOURNAL, **70**, 3051 (1948), using a vibrating reed electrometer (Applied Physics Corp.). Corrected for background. [b] Assayed as the 3,5-dinitrobenzoate. [c] Assayed as the *p*-toluidide. [d] Since the barium carbonate samples are particularly subject to contamination their activities are only considered to be useful as a qualitative check on the other activities. [e] % rearrangement = activity of N-ethyl-*p*-bromobenzenesulfonamide/activity of *p*-toluidide × 100. [f] Average of four to five different combustions with standard deviations.

It is clear that rather more rearrangement (8.5%) occurs in the process of forming 1-propanol through the reaction of 1-propylamine with nitrous acid than in the corresponding reaction (1.5%) with ethylamine.[4] The results probably reflect a greater stability of III compared to I under similar reaction conditions. This amounts to saying that the intrinsic migratory aptitude of methyl is likely to be greater than that of hydrogen in circumstances where the degree of substitution of the methylene groups of the intermediates (I or III) is the same.

Experimental

Propionitrile-1-C¹⁴.—Ethyl sulfate (66 ml.) was added dropwise to a solution of 25 g. of sodium cyanide[10] containing 1 mc. of C^{14} in 50 ml. of water and 50 ml. of ethylene glycol at 35°. The mixture was allowed to stand overnight and the low-boiling material was distilled out. The distillate was diluted with 20 ml. of 18 N sulfuric acid, the upper layer separated, dried over calcium chloride and distilled. The yield of propionitrile-1-C^{14} was 12.1 g. (44%), b.p. 94–97°.

1-Propyl-1-C¹⁴-ammonium Perchlorate.—The procedure was based on that of Amundsen and Nelson.[11] Propionitrile-1-C^{14} (12.1 g.) dissolved in 30 ml. of ether was added dropwise with stirring to 9 g. of lithium aluminum hydride in 300 ml. of dry ether in a flask cooled in ice-water. After 3 hours, 8 ml. of water, 6 ml. of 20% sodium hydroxide solution and 25 ml. more of water were added successively. The mixture was distilled and the distillate collected in a flask containing 20 ml. of 70% perchloric acid. The volatile material was removed at 30–35° under reduced pressure and the residual perchlorate salt recrystallized from *n*-hexyl alcohol by adding *n*-heptane. The yield of 1-propyl-1-C^{14}-ammonium perchlorate was 11 g. (31%), m.p. 167°.

***n*-Propylamine–Nitrous Acid Reaction.**—To a stirred solution at 25° of 22.5 g. of 1-propyl-1-C^{14}-ammonium perchlorate in 20 ml. of 35% perchloric acid was added dropwise over 2 hours 21 g. of sodium nitrite dissolved in 30 ml. of water. The solution was then distilled until 25 ml. of distillate was collected. The distillate was acidified with hydrochloric acid and redistilled to remove any excess amine. Potassium fluoride was added to the distillate to salt out the organic products which were then separated and diluted with 2.0 ml. of 1-propanol as a carrier. The products were fractionated through a Podbielniak Micro Column and yielded, besides 3.4 g. (41%) of 2-propanol with b.p. 80–84°, 0.76 g. of pure 1-propanol, b.p. 95–96°. The 1-propanol was diluted with 20 g. of carrier 1-propanol for the degradation reactions. Part of the 1-propanol was converted to the 3,5-dinitrobenzoate, m.p. 73°, for radioactive assay.

Degradation Procedure.—A stirred solution of 20 g. of labeled propanol in 300 ml. of water containing 30 ml. of concd. sulfuric acid was cooled to 5° with an ice-bath and 54 g. of potassium permanganate added in small portions at a rate slow enough to keep the temperature below 15°. The mixture was stirred for 1.5 hours, after which time sulfur dioxide was passed in until the manganese dioxide dissolved. The solution was extracted continuously with ether for 10 hours. The extract was dried with sodium sulfate and distilled. The yield of propionic acid, b.p. 135.5–139.5°, was 8.1 g. (42%). The product was assayed as the *p*-toluidide, m.p. 124°.

A mixture of 1.44 g. of labeled propionic acid, 5 ml. of chloroform and 3 ml. of concd. sulfuric acid was stirred magnetically at 45–55° in a 200-ml. flask equipped with a dropping funnel and gas inlet and outlet tubes while a stream of carbon dioxide-free nitrogen was passed through. The outlet was connected to two absorption flasks containing 0.07 N barium hydroxide solution. The nitrogen flow was stopped and 35 ml. of a solution of 1.2 N hydrazoic acid in chloroform added over 70 minutes. After two additional hours at 50°, nitrogen was passed through to sweep out the balance of the carbon dioxide. The barium carbonate precipitate in the absorption flasks was filtered, washed with boiling water and acetone, then dried at 120°. The yield was 2.8 g. (73%). The material in the reaction flask was cooled with ice, cautiously basified with 5% sodium hydroxide solution and stirred with a solution of 2 g. of *p*-bromobenzenesulfonyl chloride in 5 ml. of chloroform. After 2 hours, the mixture was acidified with concd. hydrochloric acid, the chloroform layer separated, dried over sodium sulfate and evaporated to dryness. The residue was dissolved in 5% sodium hydroxide solution, the crude N-ethyl *p*-bromobenzenesulfonamide precipitated with hydrochloric acid, dried and crystallized from a benzene–*n*-hexane mixture. The yield was 1.4 g. (30%), m.p. 80.5°.

The degradation procedure was checked in the following way. 1-Propionitrile-1-C^{14} (see above) was hydrolyzed with 90% sulfuric acid to propionic-1-C^{14} acid in 67% yield. The acid was reduced with lithium aluminum hydride to give a 50% yield of 1-propanol-1-C^{14}. The above degradation was then carried through on the 1-propanol-1-C^{14} and, as may be seen from the data given in Table I, a negligible fraction of the activity of the N-propionyl-*p*-toluidide was found in the N-ethyl-*p*-bromobenzenesulfonamide.

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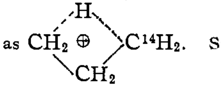
[9] It is possible that some or all of the rearranged 1-propanol might arise from an intermediate such as  Such intermediates may be important in special sterically favorable conditions; J. D. Roberts and C. C. Lee, *ibid.*, **73**, 5009 (1951), J. D. Roberts and J. A. Yancey, *ibid.*, **75**, 3165 (1953), but are rendered unlikely with alkyl derivatives by the finding[4] that the presumably more stable ion I does not seem to play a very important role in the reaction of ethylamine with nitrous acid.

[10] The radioactive sodium cyanide was obtained from Tracerlab, Inc., Boston, Mass., on allocation from the U. S. Atomic Energy Commission.

[11] L. H. Amundsen and L. S. Nelson, *ibid.*, **73**, 282 (1951).