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# REARRANGEMENT OF ALKYL-CATIONS FORMED DURING REACTION BETWEEN NITROUS ACID AND ALKYLAMINE PERCHLORATES

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**Abstract**—In the reaction of nitrous acid with n-propylamine perchlorate labelled with $^{14}C$ at the nitrogen-bonded carbon, no rearrangement of the n-propyl cation chain, but isomerization of the type:

$$CH_3—CH_2—{}^{14}CH_2{}^+ \rightleftarrows {}^+CH_2—CH_2—{}^{14}CH_3$$

with simultaneous isomerization of n-propyl cation to isopropyl cation takes place.

A similar isomerization has been observed in the reaction of nitrous acid with the perchlorate of cyclohexylamine-1$^{14}C$. This results in the linking of the hydroxyl in a portion of the resultant cyclohexanol molecules to carbon atoms not participating in the C-N bond of the original cyclohexylamine.

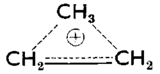
ROBERTS and Halmann have described[1] the rearrangement of the propyl cation

$$CH_3—CH_2—{}^{14}CH_2{}^+ \rightleftarrows {}^+CH_2—{}^{14}CH_2—CH_3$$

during the reaction between $^{14}C$-labelled n-propylamine and nitrous acid:

$$CH_3—CH_2—{}^{14}CH_2—NH_2{\cdot}HClO_4 \xrightarrow{HNO_2} CH_3—{}^{14}CH_2—CH_2—OH$$

This interesting conversion, being the simplest case of a pinacoline rearrangement, attracted the attention of chemists and has taken its place in modern text books of organic chemistry. Its mechanism has been described in terms of the simplest non-classical cation:



It has recently been shown that the propyl free radical in carbon tetrachloride solution does not undergo skeleton rearrangement. Instead isomerization occurs, the hydrogen atom migrating from the $\beta$-position.[2]

$$CH_3—CH_2—{}^{14}CH_2{\cdot} \rightleftarrows {\cdot}CH_2—CH_2—{}^{14}CH_3$$

Bearing in mind the quite frequently observed analogy in behaviour of radicals and cations we have analysed the aforementioned work of Roberts and Halmann[1] and have found their conclusion as to the nature of the propyl cation rearrangement is not the only possible one.

On the basis of the activity of ethylamine formed in the reactions,

$$CH_3—CH_2—{}^{14}CH_2—NH_2{\cdot}HClO_4 \xrightarrow{HNO_2} CH_3—CH_2—CH_2—OH \xrightarrow{KMnO_4}$$

$$CH_3—CH_2—COOH \xrightarrow{HN_3} \underset{\text{active}}{CH_3—CH_2—NH_2} + CO_2$$

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[1] J. Roberts and M. Halmann, *J. Amer. Chem. Soc.* **75**, 5759 (1953).

[2] O. A. Reutov and T. N. Shatkina, *Dokl. Akad. Nauk S.S.S.R.*, **133**, No. 2 (1960); *Tetrahedron* **18**, 305 (1961).

these authors[1] concluded that $^{14}C$ is in the two-position of the resultant n-propyl alcohol ($CH_3—^{14}CH_2—CH_2—OH$). Their assumption that radioactive carbon-14 should be bound to nitrogen in the ethylamine molecule was lacking in experimental evidence.

If $^{14}C$ actually belongs to the methyl group of the ethylamine molecule, then the propyl cation must have undergone isomerization as a result of hydride ion migration. rather than pinacoline rearrangement.*

Repeating the work of Roberts and Halmann under the specified conditions, we found that the propyl cation does not undergo chain rearrangement but isomerization, similar to that shown for the propyl radical†, namely

$$CH_3—CH_2—^{14}CH_2^+ \rightleftarrows {}^+CH_2—CH_2—^{14}CH_3$$

The reaction of n-propylamine perchlorate with nitrous acid affords n-propyl and isopropyl alcohols

$$CH_3—CH_2—^{14}CH_2—NH_2.HClO_4 \xrightarrow{HNO_2} CH_3—CH_2—CH_2OH + CH_3—CH(OH)—CH_3$$

Oxidation of the n-propyl alcohol with potassium permanganate gives propionic acid which is further oxidized by potassium bichromate to acetic acid and carbon dioxide

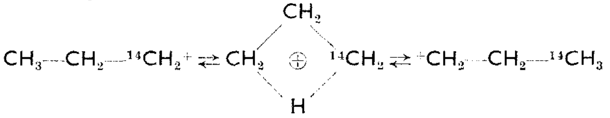
$$CH_3—CH_2—CH_2—OH \xrightarrow{KMnO_4} CH_3—CH_2—COOH \xrightarrow{K_2Cr_2O_7} CH_3—COOH + CO_2$$

The acetic acid activity passes over wholly to methylamine during Schmidt cleavage of the acid and to methane during fusion with alkali as the sodium salt.

$$CH_3—COOH—\begin{cases} \xrightarrow{HN_3} {}^{14}CH_3—NH_2 + CO_2 + N_2 \\ \xrightarrow{NaOH} {}^{14}CH_4 + Na_2CO_3 \end{cases}$$

It is, therefore, clear that the molecules of n-propyl alcohol formed in the reaction of n-propylamine-1 $^{14}C$ with nitrous acid contain radioactive carbon-14 only in the 1 and 3 positions. Similarly, it has been shown that isopropyl alcohol contains $^{14}C$ in 1 and 3 (but not in 2) positions.

The isomerization of the n-propyl cation may be either a single migration of the hydride ion from the $\beta$-position:



$$CH_3—CH_2—^{14}CH_2^+ \rightleftarrows CH_2 \overset{CH_2}{\underset{H}{\oplus}} {}^{14}CH_2 \rightleftarrows {}^+CH_2—CH_2—^{14}CH_3 \qquad (I)$$

or a two stage migration from the $\alpha$-position:

$$\begin{aligned} &(a) \quad CH_3—CH_2—^{14}CH_2^+ \rightleftarrows CH_3—\overset{+}{C}H—^{14}CH_3 \\ &(b) \quad CH_3—\overset{+}{C}H—^{14}CH_3 \rightleftarrows {}^+CH_2—CH_2—^{14}CH_3 \end{aligned} \qquad (II)$$

Evidence in favour of the second mechanism is provided by the the formation of

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* It should be noted that isomerization of n-propyl cation to isopropyl cation during the reaction between n-propylamine and nitrous acid has been reported.[3] Considerable amounts of isopropyl alcohol were revealed among the reaction products, the yield of n-propyl alcohol being 7% and that of isopropyl alcohol 32%).

† Roberts *et al.*[4] in very interesting experiments with other amines (2-aryl-1-ethylamine-1-$^{14}C$) have given irreproachable proof of the existence of skeleton rearrangements in reactions with nitrous acid.

[3] V. Mayer and Fr. Forster, *Chem. Ber.* **9**, 535 (1876); F. C. Whitmore and R. S. Thorpe, *J. Amer. Chem. Soc.* **63**, 1118 (1941).

[4] J. D. Roberts and C. M. Regan, *J. Amer. Chem. Soc.* **75**, 2069 (1953).

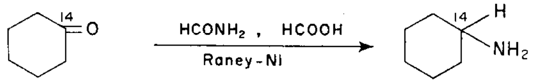
isopropyl alcohol in this reaction and from studies of hydrogen exchange in paraffins.[5] On the other hand, the literature[6] reveals only the formation of isopropyl alcohol (without n-propyl alcohol) from the action of nitrous acid on isopropylamine.*

Hence, whether the isomerization takes place in one or two stages has yet to be determined.

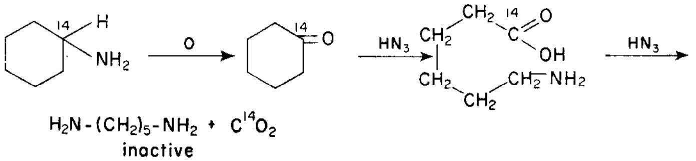
The tendency to isomerize with migration of the hydride ion is doubtlessly more or less a general property of alkyl cations. Roberts *et al.*,[7] for example, have observed such isomerization of ethyl cation in the reaction of ethylamine with nitrous acid. Quite likely such isomerization also takes place during Demyanov interconversion of alicycles.

Based on this assumption it may be concluded that in the formation of cyclohexanol in the reaction of nitrous acid with cyclohexylamine, the hydroxyl group is not necessarily bound only to the carbon which previously participated in the bond with the amine group. This has been proved experimentally. Cyclohexylamine labelled with $^{14}C$ at the N-linked carbon was synthesised according to the following scheme:

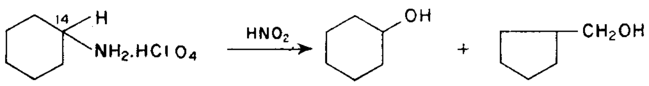
$$Br-(CH_2)_5-Br \xrightarrow[\text{(b) hydrolysis}]{\text{(a) Na}^{14}\text{CN}} HOO^{14}C-(CH_2)_5-{}^{14}COOH \xrightarrow[\text{heating}]{BaCO_3}$$



The following degradation proves that the cyclohexylamine was labelled only at the carbon atom bound to nitrogen. Cyclohexylamine was oxidized to cyclohexanone and the latter converted with hydrazoic acid to aminocaproic acid and then to pentamethylenediamine. The latter was found to be inactive.



The reaction of $^{14}C$ amino-carbon labelled cyclohexylamine perchlorate with nitrous acid leads to a mixture of cyclohexanol and cyclopentylcarbinol



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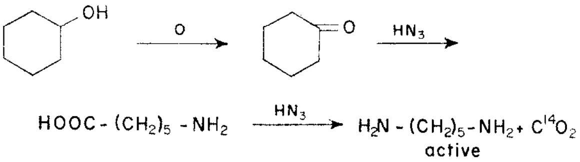
* The results of this investigation require verification. For the n-propyl alcohol to form the more stable isopropyl cation it must isomerize to the less stable n-propyl cation ($CH_3-\overset{+}{C}H-CH_3 \rightarrow {}^{+}CH_2-CH_2-CH_3$) so that if the isomerization does take place at all it should occur only to a small extent and only small amounts of n-propyl alcohol would be present in the reaction mixture.

[5] V. N. Setkina, D. N. Kursanov and E. V. Bochkova, *Prob. Kinet. Katal.* **9**, 234 (1957).

[6] V. Mayer and Fr. Forster, *Chem. Ber.* **9**, 535 (1876).

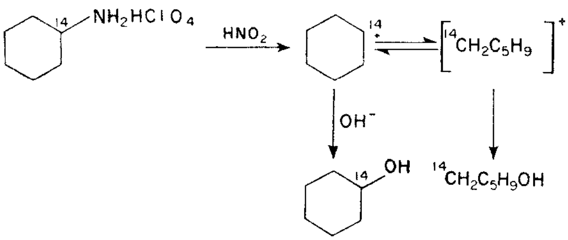
[7] J. Roberts and J. Hancey, *J. Amer. Chem. Soc.*, **74**, 5943 (1952).

In order to ascertain the position of the $^{14}C$ in the cyclohexanol, the latter was subjected to the following degradation:



Pentamethylenediamine was found to active* (3·8 ± 0·3% of the original cyclohexanone activity).

This proves that the hydroxyl of some cyclohexanol molecules is not attached to the amino-binding carbon of the original cyclohexylamine molecule. Hence, the cyclohexyl cation intermediate undergoes isomerization as a result of hydride anion migration.



The rearrangement of the propyl free radical[2] and of alkyl cations considered in the present paper, resulted in an investigation concerning the rearrangement of alkyl anions by the carbonization of n-propylsodium. The action of metallic sodium on propyl-1-$^{14}C$ chloride yields propylsodium-1-$^{14}C$ which on carbonization gives only n-butyric-2-$^{14}C$ acid:

$$CH_3—CH_2—{}^{14}CH_2—Cl \xrightarrow[\text{(toluene)}]{Na} CH_3—CH_2—{}^{14}CH_2^{(-)}Na^{(+)} \xrightarrow[\text{(toluene)}]{CO_2}$$

$$CH_3—CH_2—{}^{14}CH_2—COOH \xrightarrow{HN_3} CH_3—CH_2—{}^{14}CH_2—NH_2 \xrightarrow{O} \underset{\text{inactive}}{CH_3—COOH + {}^{14}CO_2}$$

Hence, the n-propyl anion $CH_3—CH_2—{}^{14}CH_2^{(-)}$ does not undergo rearrangement during carbonization.

## EXPERIMENTAL

### I. *Synthesis of propylamine-*1-$^{14}C$ *perchlorate*

1. *Preparation of propionitrile*-1-$^{14}C$.[1] To a solution of 21·6 g (0·33 mole)K $^{14}CN$ (total activity 10 mc) in 35 ml water and 35 ml ethylene glycol 43 ml (0·33 mole) diethyl sulphate was added dropwise at 35°. After 18 hr at 20°, the 85–100° fraction was distilled off. Sulphuric acid (15 ml 18 N) was then added, and the supernatant layer separated and dried (fused $CaCl_2$). The fraction boiling at 94–97° was collected. Weight 5·4 g (30% of the theoretical), total activity 3 mc (Reported[9]: b.p. 97–97·2°).

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* The low percentage of rearrangement of the cyclohexyl cation may perhaps be explained by its rapid reaction with the solvent to form cyclohexanol.

A similar view has been advanced by Streitwieser and Coverdall[8] to explain the fact that not less than 94% *cis*-cyclohexanol-2-d is formed in the reaction of *cis*-cyclohexylamine 2-d perchlorate with nitrous acid.

[8] A. Streitwieser and C. E. Coverdall, *J. Amer. Chem. Soc.* **81**, 4275 (1959).

[9] R. Schiff, *Chem. Ber.* **19**, 567 (1886).

2. *Hydrogenation of propionitrile*-1-$^{14}$C. Propionitrile-1-$^{14}$C (4 g; 0·07 mole); total activity 1 mc* in 15 ml absolute ether was added with stirring to 6 g (0·16 mole) $LiAlH_4$ in 200 ml absolute ether at 0°. The mixture was stirred for 3 hr, followed by the dropwise addition of 3 ml water, 2 ml 20% NaOH and an additional 9 ml water. Propylamine was distilled from the reaction mixture into 7 ml perchloric acid and the solution evaporated to dryness *in vacuo* at 30–35°. Weight 5·15g (50% of theoretical), radioactivity presented in Table 1.

II. *Reaction of propylamine*-1-$^{14}$C *and nitrous acid*[1]

To a solution of 5·13 g (0·05 mole) propylamine-1-$^{14}$C in 4·5 ml 35% perchloric acid at 25°, a solution of 4·8 g (0·07 mole) sodium nitrite in 7 ml water was added over a period of 1 hr and the mixture maintained for another hr at 25°, and then 10 ml propyl and 10 ml isopropyl alcohols were added to the carriers and 28 ml of the mixture distilled off. The distillate was acidified with conc HCl, redistilled and then saturated with anhydrous $K_2CO_3$. After removal of the aqueous layer, the isopropyl alcohol (10·4 g) at 81–83° and propyl alcohol (4·41 g) at 97–98·5° was collected. (Reported[10] b.p. of isopropyl alcohol 80·7–81·4° and propyl alcohol 97·2–97·25°).

TABLE 1. DISTRIBUTION OF RADIOACTIVITY IN PROPYL-$^{14}$C ALCOHOL OBTAINED IN THE REACTION OF PROPYLAMINE-1-$^{14}$C WITH $HNO_2$

| Compound | Radioactivity pulses/min mmole |
|---|---|
| 1. Propylamine-1-$^{14}$C | 295 . 10$^3$ |
| 2. Propionic acid | 10·9 . 10$^3$ |
| 3. Acetic acid | 0·879 . 10$^3$ |
| 4. Methylamine | 0·877 . 10$^3$ |
| 5. Sodium carbonate | 0·0 |
| % Rearrangement | 8·0 ± 0·8 |

$$\% \text{ Rearrangement} = \frac{\text{pulses/min mmole } CH_3COOH\cdot 100}{\text{pulses/min mmole } CH_3CH_2COOH}$$

III. *Determination of position of carbon* 14 *in propyl*-$^{14}$C *alcohol*

1. *Oxidation of propyl*-$^{14}$C *alcohol.* Propyl alcohol (4 g; 0·066 mole) prepared as in II was mixed with a solution of 4 g (0·038 mole) anhydrous sodium carbonate in 15 ml water and cooled in ice. A solution of 14 g (0·09 mole) potassium permanganate in 300 ml water (kept below 5°) was added and the mixture allowed to stand 12 hr at 20°. The filtrate from the $MnO_2$ was concentrated *in vacuo* at 35–40° to 30–40 ml and acidified with 66% $H_2SO_4$. Propionic-$^{14}$C acid was extracted with ether and the ethereal extract dried (fused $Na_2SO_4$). After removal of the solvent on a water bath, the acid (2·15 g; 43%), was distilled at 140–141°, $n_D^{15}$ 1·3894 . (Reported b.p. 140·9°, $n_D^{28}$ 1·3859). The radioactivity of propionic-$^{14}$C acid is given in Table 1.

2. *Oxidation of propionic*-$^{14}$C *acid.*[12] Propionic-$^{14}$C acid (1 g; 0·013 mole), 12·8 g (0·043 mole) potassium dichromate and 120 ml 18 N $H_2SO_4$ were heated in a current of $N_2$ at 100° for 3 hr. Acetic acid was removed by steam distillation with ca. one l. water, the solution made alkaline with 0·1 N NaOH (simultaneous determination of acid) was concentrated *in vacuo* at 40–50° to ca. 10 ml. The residue was quantitatively transferred into a volumetric flask of such volume that the acetic acid concentration was ca. 10 mg/ml. The radioactivity of the acid is given in Table 1.

3. *Schmidt conversion of acetic acid to methylamine.*[1] To 88·5 mg (0·001 mole) sodium acetate-$^{14}$C in 0·5 ml absolute chloroform with stirring and cooling, 0·5 ml conc $H_2SO_4$ and then at 45–55° 2 ml 1·3 N hydrazoic acid in chloroform was added and the mixture maintained for 1 hr at 45–55°. The

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* Propionitrile-1-$^{14}$C (1·8 g) diluted with 2·2 g inactive propionitrile.

[10] W. Atkins and T. Wallace, *J. Chem. Soc.* **103**, 1471 (1913).

[11] A. Zander, *Liebigs Ann.* **224**, 62 (1887); P. Guye and E. Mallet *Ch. Zbl. I.* 1314 (1902).

[12] P. Nahinsky and S. Ruben, *J. Amer. Chem. Soc.* **63**, 2275 (1941).

solution was made alkaline with 10% aqueous NaOH during cooling with ice, the chloroform layer was removed and the methylamine steam distilled into 5 ml 5 N HCl. The solution of methylamine hydrochloride was evaporated to dryness and the salt purified by repeated addition of water and evaporation. After recrystallization from absolute alcohol, 67·7 mg (93%), m.p. 232–233° was obtained. (Reported[13] m.p. 232–233·5°). Results of activity measurements given in Table 1.

4. *Fusion of sodium acetate-*$^{14}$*C with sodium hydroxide.* Sodium acetate-$^{14}$C (85 mg; 0·001 mole) was fused with 80 mg (0·002 mole) NaOH until cessation of methane evolution; the residue was dissolved in 12 ml water and the activity of the resultant sodium carbonate measured. Results are given in Table 1.

## IV. *Synthesis of cyclohexylamine-*1-$^{14}$C

1. *Preparation of pimelic-*1,7-$^{14}$*C acid.*[14] A mixture of 2·86 g (0·044 mole) K$^{14}$CN (total activity 55 mc) 4·6 g (0·040 mole) distilled pentamethylene bromide, 3 ml water and 13 ml alcohol was boiled for 3 hr; the solvent evaporated *in vacuo*; 10 ml conc HCl added and the mixture boiled again for 2 hr. Pimelic-1,7-$^{14}$C acid was extracted with ether and the ethereal extract dried ($Na_2SO_4$). After removal of the solvent in a current of nitrogen, pimelic-1,7,-$^{14}$C acid (3·02 g) was dried in a vacuum desiccator. According to titrimetric data the acid is 94%, i.e. the yield is 81% of theoretical.

2. *Preparation of cyclohexanone-*1-$^{14}$C.[14] A mixture of 3·0 g (0·019 mole) pimelic-1,7,-$^{14}$C acid and 0·1 g (0·005 mole) barium carbonate was gradually heated (1 hr) to and then maintained at 325° for 3 hr. During the heat treatment 1.7 g cyclohexanone-1-$^{14}$C (79%) was distilled over, $n_D^{20}$ 1·4498, m.p. 2,4-dinitrophenylhydrazone 161–163°. (Reported[15] $n_D^{21}$ 1·4503, m.p. of 2,4-dinitrophenylhydrazone 162°.)

3. *Preparation of cyclohexylamine-*1-$^{14}$C.[16] To 50 g (1 mole) of the formamide-formate mixture, 50 g (1 mole) 85% formic acid and 0·5 g Raney nickel, during 1·5 hr, 24 g (0·25 mole) cyclohexanone-1-$^{14}$C* was added dropwise, the reaction mixture heated for 2·5 hr at ca. 115° and then evaporated to dryness after addition of 250 ml conc HCl. Excess 50% KOH was added to the residue and the mixture boiled 18–20 hr until complete elimination of ammonia. Cyclohexylamine-1-$^{14}$C was separated from the aqueous layer and distilled into 130 ml 18% perchloric acid. The solution was evaporated to dryness, the residue (16·08 g; 50%) washed with benzene and with ether and dried in a vacuum desiccator.

## V. *Reaction of cyclohexylamine-*1-$^{14}$*C with nitrous acid*[8]

To an ice cooled solution of 15·7 g (0·08 mole) cyclohexylamine-1-$^{14}$C in 50 ml water and 7 ml 60% perchloric acid, a solution of 6·5 g (0·09 mole) sodium nitrite in 30 ml water was added dropwise. After stirring for 6 hr at 0°, another 1 g (0·014 mole) sodium nitrite was added. The mixture was allowed to stand for 18 hr at 0–2° and then for 24 hr at 20°. The supernatant layer of cyclohexanol-$^{14}$C and cyclopentylcarbinol-$^{14}$C was removed and the lower layer, after saturation with sodium chloride, was extracted with ether. The combined ethereal extract and upper alcohol layer was washed with 10% $H_2SO_4$ and with water and dried ($Na_2SO_4$). After removal of the ether, 1 g of cyclohexanol carrier was added and the 159–161° fraction (2·88 g) collected. (Reported[17,18] b.p. cyclohexanol 160·5°; cyclopentylcarbinol 162·5–163·5°.)

## VI. *Determination of carbon-*14 *position in cyclohexanol-*$^{14}$C

1. *Oxidation of cyclohexanol-*$^{14}$*C and cyclopentylcarbinol-*$^{14}$C.[19] To 2·88 g of the alcohol mixture in 15 ml water and 1·8 ml conc $H_2SO_4$, 2·2 g (0·022 mole) $CrO_3$ in 50 ml water was added dropwise and the mixture left overnight at 20°. After distilling off ca. 20 ml, the distillate was saturated with anhydrous $K_2CO_3$ and the separated layer of cyclohexanone-$^{14}$C and cyclopentaldehyde-$^{14}$C extracted with ether. The ethereal solution was evaporated and the residue in 20 ml water was boiled for 1·5 hr

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* 1·7 g Cyclohexanone-1-$^{14}$C were diluted to 24 g by reagent cyclohexanone.

[13] M. Sommelet, *C.R. Acad. Sci. Paris*, **178**, 219 (1924).

[14] R. J. Speer, M. Z. Humphries and A. Roberts, *J. Amer. Chem. Soc.* **74**, 2443 (1952).

[15] O. Wallach, *Liebigs Ann.* **353**, 331 (1907).

[16] A. N. Kost and I. I. Grandberg, *Zh. Obschii. Khim.* **25**, 1432 (1955).

[17] V. V. Markovnikov, *Liebigs Ann.* **302**, 21 (1898).

[18] N. D. Zelinski, *Chem. Ber.* **41**, 2629 (1908).

[19] N. Ya. Demyanova, *Sbornik Izbrannykh Trudov Akademika* pod (red. A. E. Favorskovo) p. 266 (1936).

with excess freshly precipitated silver oxide. Cyclohexanone-$^{14}$C was steam distilled from the reaction mixture and 1·8 g isolated after saturating the solution with anhydrous $K_2CO_3$. To the aqueous layer, 0·5 g of cyclohexanone carrier was added, the mixture shaken vigorously, and the cyclohexanone (0·45 g) again isolated. Sodium bisulphite (14 ml; 36% solution) was added to the combined cyclohexanone-$^{14}$C layers and the mixture left overnight. The bisulphite–cyclohexanone-$^{14}$C compound was washed with ether and the cyclohexanone-$^{14}$C liberated by addition of 20 ml boiling saturated $K_2CO_3$ solution. The cyclohexanone-$^{14}$C (1·16 g) was isolated by cooling and a further quantity (0·28 g) was obtained by addition of 0·5 g cyclohexanone carrier. For the activity measurements, cyclohexanone-$^{14}$C was converted to the 2,4-dinitrophenylhydrazone, m.p. 161–162° (from alcohol). The radioactivity is presented in Table 2.

TABLE 2

| Reaction<br>Activity of products pulses/min. mmole | Deamination of cyclohexylamine-1-$^{14}$C I | Oxidation of cyclohexylamine-1-$^{14}$C II |
|---|---|---|
| Cyclohexanone (as 2,4-dinitrophenyl-hydrazone) | 355 . $10^3$ | 405 . $10^3$ |
| Pentamethylene-diamine (as picrate) | 13·4 . $10^3$ | 0·0 |
| % Rearrangement | 3·8 ± 0·3 | 0·0 |

2. *Reaction of cyclohexanone-$^{14}$C with hydrazoic acid.*[20] A solution of 1·39 g (0·014 mole) cyclohexanone-$^{14}$C in 20 ml water was saturated at 0° with hydrogen chloride and then 1·5 g (0·023 mole) sodium azide added in portions. The mixture was stirred for 4 hr at 20°, the temp. was then gradually raised to and maintained at 90° for 4 hr and finally the solution was evaporated to dryness *in vacuo*. The hydrochloride of δ-amino-n-caproic acid was extracted with boiling absolute alcohol and after distillation of the solvent the hydrochloride (1·93 g) was dried in a vacuum desiccator.

3. *Reaction between δ-amino-n-caproic acid and hydrazoic acid.*[20] The hydrochloride of δ-amino-n-caproic-$^{14}$C acid (0·8 g; 0·006 mole) was heated *in vacuo* with 1·5 ml conc $H_2SO_4$ until complete elimination of HCl and 5 ml (0·01 mole) 2 N hydrazoic acid in benzene added to the residue. The liberated $CO_2$ was absorbed in sodium carbonate-free sodium hydroxide. The mixture was allowed to stand 24 hr at 20°, heated 3 hr at 50° and the benzene finally removed *in vacuo*. Water (30 ml) and ca. 11 g barium carbonate (until complete precipitation of $SO_4^{-2}$ ions) was added to the residue, barium sulphate was filtered off, washed repeatedly with water and the filtrate after acidification evaporated to dryness.

In order to measure the radioactivity of pentamethylenediamine hydrochloride it was converted to the picrate, m.p. 226–228°. The latter was recrystallized twice from alcohol; m.p. 228–229°. (Reported[21] m.p. 225–230°). The results of the activity measurements are given in Table 2.

VII. *Experiments showing the original cyclohexylamine to be labelled only at the amino-linked carbon*

1. *Oxidation of cyclohexylamine-*1-$^{14}$C *to cyclohexanone.*[22] To a solution of 10·4 g (0·05 mole) cyclohexylamine-1-$^{14}$C perchlorate in 30 ml water, 200 ml 5% potassium permanganate was added; the mixture brought to pH 8 with 40% NaOH and a further 4 ml 0·5N of alkali added. The mixture was heated for 30 min at 90–100°. Cyclohexanone was steam distilled from the acidified solution; the distillate saturated with anhydrous $K_2CO_3$ and the cyclohexanone-1-$^{14}$C (1·5 g; 32%) isolated, $n_D^{16}$ 1·4495, m.p. 2,4-dinitrophenylhydrazone 160–161°.

2. *Determination of position of carbon-*14 *in cyclohexanone-*1-$^{14}$C. This was carried out as in Experiments VI 2, 3. Results of activity measurements are given in Table 2 (column II).

[20] R. B. Loftfield, *J. Amer. Chem. Soc.* **73**, 4707 (1951).
[21] K. Yoshimira, *Biochem. Z.* **28**, 19 (1910).
[22] E. F. Phares, *Arch. Biochem. Biophys.* **33**, 176 (1951).