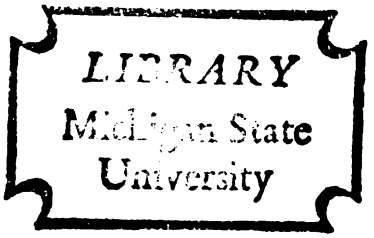
SOME CARBONIUM ION REARRANGEMENTS

Thesis for the Degree of Ph. D.
MICHIGAN STATE UNIVERSITY
Donald Oscar Rickter
1964



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EAST LANSING, MICHIGAN

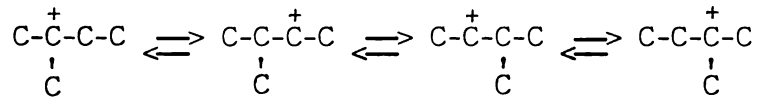
ABSTRACT

SOME CARBONIUM ION REARRANGEMENTS

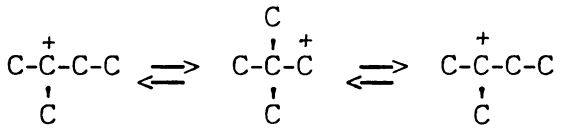
by Donald Oscar Rickter

PART A: THE REACTION OF t-AMYL CHLORIDE WITH ALUMINUM CHLORIDE IN A SOLVENT

The aluminum chloride-catalyzed rearrangement of labeled t-amyl chloride goes largely by equation (1). The existence of other mechanisms was shown by the relative ratio of equilibrations C-2 $\rightleftharpoons$ C-3 and C-1 $\rightleftharpoons$ C-4. Path (1) alone gives a ratio of 2.00, while 1.55 is the actual ratio observed.[1] One explanation[1] is that 13% of the reaction proceeds via equation (2).

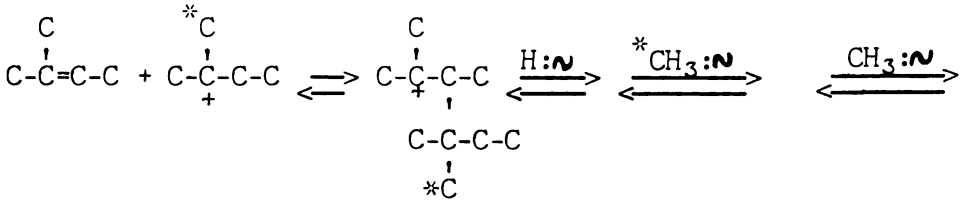


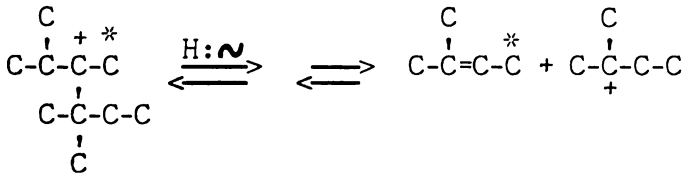
(1)



(2)

However, it has been shown[2] that bimolecular reactions occur:





(3)

Reaction conditions were found under which 1-^{13}C- and 2-^{13}C-t-amyl chlorides were rearranged without appreciable bimolecular reaction.

Ethylene chloride was used as the solvent for the labeled t-amyl chlorides and aluminum chloride at 0° for one to two minutes. The t-amyl chlorides were recovered from the reaction mixture, purified by preparative gas chromatography, and analyzed by mass spectrometry. Scrambling of the labels, C-1 $\rightleftharpoons$ C-4 and C-2 $\rightleftharpoons$ C-3 had occurred. The experimental errors in the mass spectrometric data were too large to permit calculation of the rate ratio $k_{2,3}/k_{1,2}$.

PART B: HIGHER-ORDER WAGNER-MEERWEIN SHIFTS

Examples of 1,2-hydride shifts are well-known, but the existence of a 1,3-hydride shift (cf. a 1,2; 1,2 mechanism) was only recently[3] established. Numerous cyclic systems have transannular 1,5- and 1,6-hydride shifts[4], and several organic ions of special geometry undergo 1,5-hydride shifts[5,6], but the question remained: Do higher-order (1,4; 1,5; 1,6; etc.) hydride shifts occur in simple aliphatic systems?

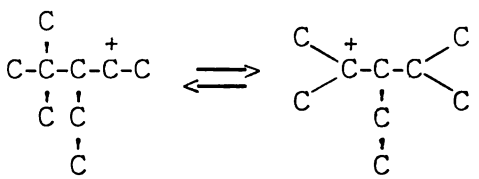
Butylamine-1,1-d_2 and pentylamine-1,1-d_2 were prepared and converted to perchlorate salts. Deamination in water at 25° gave numerous products, which were analyzed by gas chromatography and infrared spectroscopy. The pentyl system gave the following percentage yields: pentenes, 19; 1-pentanol, 22; 2-pentanol, 14; 3-pentanol, 4; 1-pentyl nitrite, 2; 2- and 3-pentyl nitrites, 4; 1-nitropentane, 1; 2- and 3-nitropentanes, 0.1; 1-pentyl nitrate, 1; and 2- and 3-pentyl nitrates, 0.6: a total of 68%. The butyl system gave butenes, 16; 1-butanol, 22; 2-butanol, 20; 1-butyl nitrite, 6; 2-butyl nitrite, 5; 1-nitrobutane, 1; 2-nitrobutane, 1; 1-butyl nitrate, 4; and 2-butyl nitrate, 1: a total of 76%.

Preparative gas chromatography was used to obtain milliliter samples

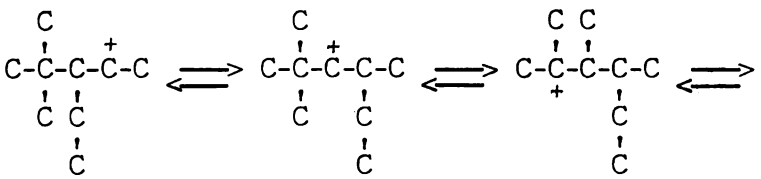
of deuterated 1-pentanol and 1-butanol from the deaminations. The n.m.r. spectra of the neat alcohols showed no α-protons in the labeled 1-pentanol and a slight amount of α-protons in the 1-butanol. The mass spectral analyses of the trimethylsilyl ethers of the alcohols showed that there were actually a few percent of α-protons in both alcohols. Thus some rearrangement of the deuterium did occur. There was no loss of deuterium by exchange with the solvent. The finding of 3-pentanol was unexpected, since Streitwieser[6] stated that it was not a product of the deamination of pentylamine. The distribution of deuterium in the secondary pentanols indicated that there had been successive 1,2-hydride shifts down the chain; i.e., there were 75% 2-pentyl-1,1-d_2, 21% 3-pentyl-1,1-d_2, and 4% 2-pentyl-5,5-d_2. From the mass spectral data it was not possible to tell if a small amount of 1,4- or 1,5-hydride shift occurred in the two systems.

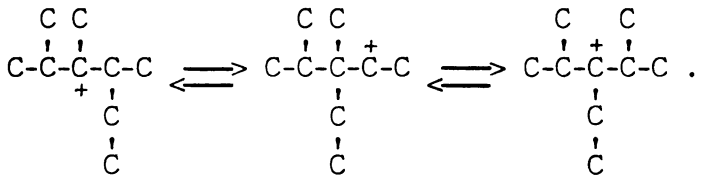
PART C: ALIPHATIC 1,3-METHYL SHIFTS

Several rearrangements could be explained as either 1,3- or 1,2; 1,2-methyl shifts. One case[7], said to require a 1,3-methyl shift,



actually could be explained as a series of 1,2-shifts:





No other examples have required postulation of a 1,3-methyl shift. A system which would favor such a mechanism is a primary carbonium ion which could shift a methyl to form a tertiary ion. The simplest such case is neopentylcarbinyl cation.

Neopentyl cyanide was prepared by nucleophilic displacement on the chloride in dimethylsulfoxide at 100-130° for 24 hours. There was a 44% yield of colorless solid. Reduction with lithium aluminum hydride gave neopentylcarbinylamine. The amine was converted to its perchlorate salt and deaminated in water at 25°. The products were numerous. In a typical run 43% was neopentylcarbinol, 21% t-butyl alcohol, 14% dimethylisopropylcarbinol, 1.3% methyl-t-butylcarbinol, 2% t-butylethylene, and six other compounds. Gas chromatographic analysis showed that there was less than 0.2% of dimethylpropylcarbinol, the alcohol which would form in a 1,3-methyl shift.

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(5) Cohen, T., R. M. Moran, and G. Sowinski, J. Org. Chem., 26, 1 (1961).

(6) Streitwieser, A., Jr., ibid., 22, 861 (1957).

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SOME CARBONIUM ION REARRANGEMENTS

By

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A THESIS

Submitted to
Michigan State University
in partial fulfillment of the requirements
for the degree of

DOCTOR OF PHILOSOPHY

Department of Chemistry

1964

ACKNOWLEDGMENTS

The author is grateful for the opportunity to do research under the direction of Dr. Gerasimos J. Karabatsos. It was a stimulating and rewarding experience to work for a professor who encourages independent thinking and development of responsibility. He and his students, especially Chester Orzech, were very helpful in discussions when progress was stymied.

A research assistantship of the U. S. Atomic Energy Commission (June 1962 to March 1963) and a fellowship of the Petroleum Research Fund--American Chemical Society (March 1963 to September 1964) are thankfully acknowledged.

Seymour Meyerson and John Balka of the American Oil Company are to be thanked for the mass spectral analyses and calculations.

Finally, I am grateful to my wife, PHYLLIS CARLSON RICKTER, whose Patience, Help, and Dedication made my doctoral studies possible.

TABLE OF CONTENTS

PART A

THE REACTION OF t-AMYL CHLORIDE WITH ALUMINUM CHLORIDE IN A SOLVENT

PART B

HIGHER-ORDER WAGNER-MEERWEIN SHIFTS

TABLE OF CONTENTS (Cont.)

LIST OF TABLES

PART A

PART B

LIST OF TABLES (Cont.)

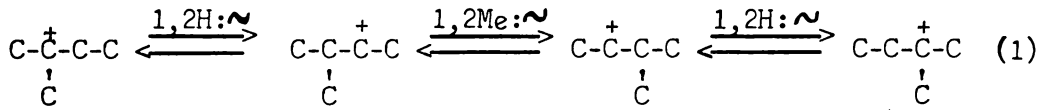
LIST OF FIGURES

PART A

THE REACTION OF t-AMYL CHLORIDE WITH ALUMINUM CHLORIDE IN A SOLVENT

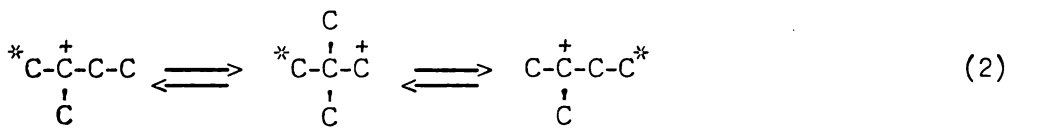
INTRODUCTION

The rearrangement of labeled t-amyl chloride with a catalytic amount of aluminum chloride is complicated. The mechanism is not as simple as equation (1).



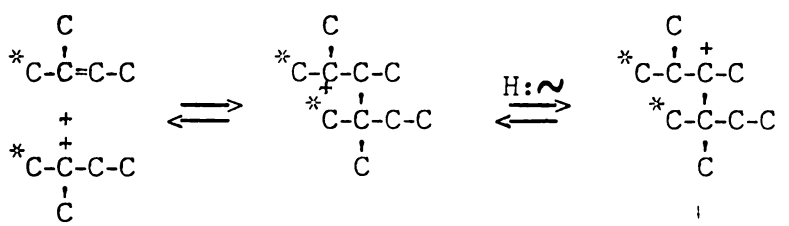
(1)

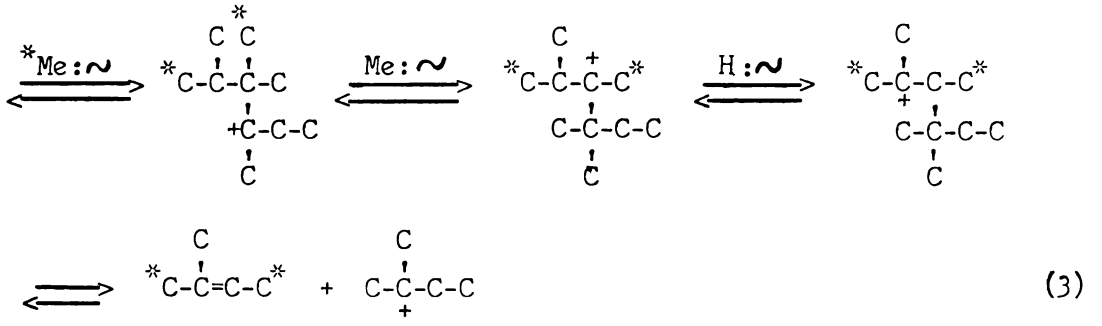
If this were the only mechanism of equilibration of C-1 $\rightleftharpoons$ C-4 and C-2 $\rightleftharpoons$ C-3, the relative rates of equilibration would be 1:2. Experimentally[1] the ratio is $k_{2,3}/k_{1,4} = 1.55$ rather than 2. The explanation given[1] is that a second mechanism is operating: 13% of the equilibration is via the neopentyl cation.



(2)

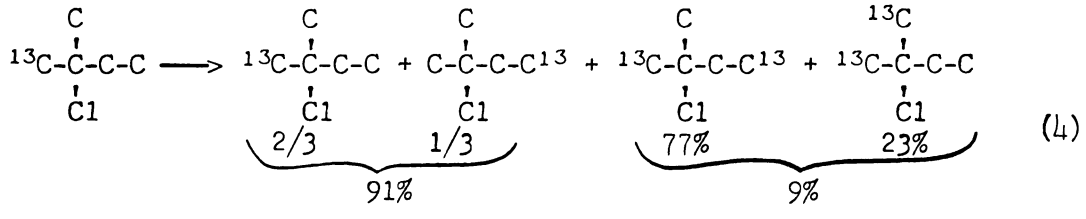
Equation (2) does explain the relative rates. It equilibrates C-1 with C-4 but not C-2 with C-3. However, it is not necessary to postulate the intervention of high-energy primary carbonium ions. Bimolecular reactions also account for the experimental results and have been shown to occur.[2] The simplest of several bimolecular pathways is that shown below -- dimerization followed by a series of 1,3-shifts of hydrides and methyls and then cleavage back to C_5 molecules:





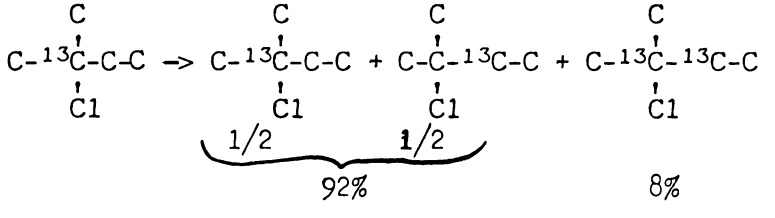
(3)

When 2-methyl-2-chlorobutane-1-^{13}C was stirred with aluminum chloride, several products (besides polymer) were formed.[2] Analysis of the volatile products by gas chromatography showed, in a typical experiment, 63% t-amyl chloride, 22% t-butyl chloride, 7% 2-methyl-2-chloropentane, 2% 3-methyl-3-chloropentane, 4% 2-methyl-3-chlorobutane, 0.9% isopentane, and 0.6% methylpentanes. The t-amyl chloride was separated by preparative gas chromatography and studied with n.m.r. and mass spectrometry. The data and calculations led to the conclusions that the ^{13}C label was completely scrambled between positions 1 and 4 and that about 9% of the molecules were dilabeled:



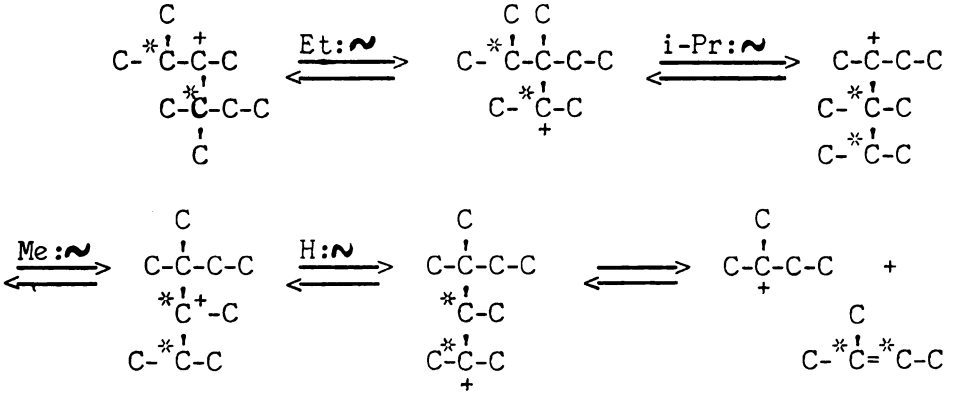
(4)

The reaction of 2-^{13}C-t-amyl chloride gave similar results. The products were the same, and the labeled t-amyl chlorides were as follows:



(5)

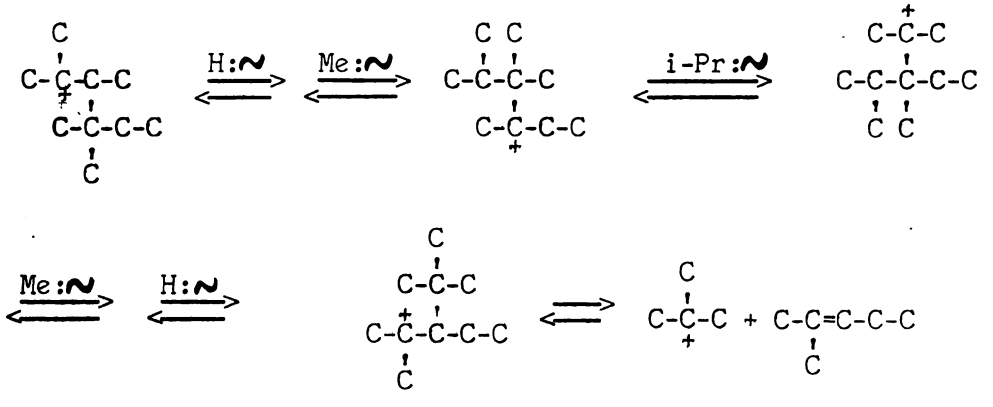
The dilabeled molecules prove that bimolecular reactions occur. Various bimolecular mechanisms can be written. Equation (3) is not an adequate representation. It does account for dilabeled products from C-1 labeled t-amyl chloride but not the dilabeled products from the C-2 labeled compound. Equation (6) results in dilabeled products from the C-2 as well as the C-1 labeled compound.



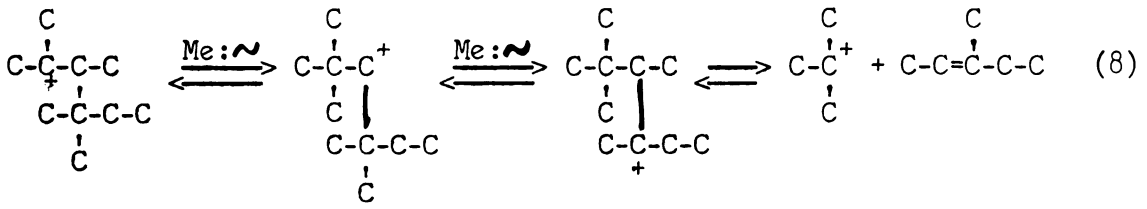
(6)

The effects on isotopic equilibration are the same in equations (2) and (3) (i.e., C-1 $\rightleftharpoons$ C-4 but C-2 $\not\rightleftharpoons$ C-3) and the same in equations (1) and (6) (i.e., C-1 $\rightleftharpoons$ C-4 and C-2 $\rightleftharpoons$ C-3).

The formation of t-butyl chloride was explained[2] by disproportionation of the intermediate $C_{10}H_{21}^{+}$ to the tertiary butyl cation and a branched hexene:



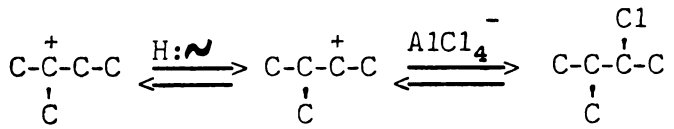
(7)



(8)

Equation (7) gives 2-methyl-2-chloropentane, while (8) gives 3-methyl-3-chloropentane.

The presence of 3-chloro-2-methylbutane is probably due to this path:



(9)

The 2-methylbutane arises from hydride abstraction by either of the carbonium ions in equation (9).

While it has been clearly shown[2] that bimolecular reactions occur, the intervention of neopentyl cation has not been excluded. The amount of rearrangement *via* neopentyl cation had not been established. The mechanistic picture would be simplified by finding suitable conditions, such as running the reaction in a solvent, under which *t*-amyl chloride rearranges but bimolecular reactions do not occur. (The criterion for occurrence of bimolecular reactions is the formation of C_4 and C_6 fragments; *i.e.*, *t*-butyl chloride and methylchloropentanes.) Under such conditions the ratio $k_{2,3}/k_{1,4}$ would be higher than the 1.55 found[1] earlier, since bimolecular reactions lower the ratio. The amount of rearrangement by way of neopentyl cation would be measured by the decrease in the ratio below the value 2.00.

A suitable solvent for the study would be polar enough to dissolve a catalytic amount of aluminum chloride and a high concentration of

t-amyl chloride. It would not react with the catalyst, the substrate, or any of the products. Finally, it would be easily separated from the rearranged t-amyl chloride and would not mask the presence of t-butyl chloride or methylchloropentanes. (Solvents are discussed further in the Appendix.)

RESULTS

Tables Ia and IIa show conditions under which t-amyl chloride and aluminum chloride were in solution with little or no bimolecular rearrangement occurring. Similar conditions were used with labeled t-amyl chloride (Tables IIIa-IVa). In run 6 there was no detectable reaction. The isotopic distribution was shown by mass spectrometry (Tables Va and VIa) to be the same before and after the treatment with aluminum chloride. In runs 7 and 8 the amount of catalyst and the duration of treatment were both increased. The result was scrambling of label--to a small extent, about equal to the experimental uncertainty, in run 7, and to a very large extent in run 8. Mass spectrometry data (Tables Va and VIa) indicated that equilibration in run 8 went beyond statistical distribution of label! Apparently the data contain experimental error almost as large as the values obtained. An attempt to calculate[1] the rate ratio was unsuccessful; the ratio came out

$$\frac{k_{1,4}t}{k_{2,3}t} = \frac{-\frac{1}{3}\log(-0.246)}{-\frac{1}{2}\log(0.190)} = 0.562 - 1.846 \log i.$$

No polymerization was apparent in any of the runs. (No polymer precipitated out and no water-insoluble residue was left after distillation of the volatile products.)

Table Ia. Runs with unlabeled t-amyl chloride in 1,2-dichloroethane at 0°.

Run No.	Conc. of t-AmCl (Wt.%)	Wt. $AlCl_3$ (mg.)	Mole Ratio of $AlCl_3$ to t-AmCl	Reaction Time (sec.)	Products Formed
1	6.6	70	0.032	300	$\leq$ 0.1%
2	6.6	31	0.014	20	< 0.01%
3	6.6	17	0.0077	60	< 0.01%
4	15.0	6	0.0046	90	$\leq$ 0.05%
5	4.4	7	0.011	15	< 0.01%

Table IIa. Gas chromatographic analyses of unlabeled solutions (using 30% silicone DC-550 column in Perkin-Elmer 154L at 8 p.s.i.)

Compound	Time (min.) at 45°	Run 1 Product	Run 2 Product	Solvent
CH_2ClCH_2Cl	55	93.9 %	93.0 %	99.7 %
t-AmCl	40	5.8	6.8	0.00
t-BuCl	12	0.3	0.2	0.2
Unknown W	12			
Unknown X	5	0.03	0.007	0.00
Unknown Y	7	0.00	0.007	0.00
Unknown Z	9	0.00	0.07	0.1

Compound	Time (min.) at 80°	Run 3 Reactant	Run 3 Product	Run 4 Product	Run 5 Product
CH_2ClCH_2Cl	14	93.0 %	92.6 %	86.5 %	96. %
t-AmCl	12	7.0	7.4	13.	4.
t-BuCl	4	0.02	0.02	0.00	0.2
Unknown W	4				
Unknown X	5	0.04	0.04	0.01	0
Unknown Y	6	0.1	0.09	0.15	0
Unknown Z	10	0.02	0.02	0.04	0

Table IIIa. Runs with labeled t-amyl chloride in 1,2-dichloroethane at 0°.

Run No.	Conc. of t-AmCl (Wt.%)	Mole Ratio of $AlCl_3$ to t-AmCl	Reaction Time (sec.)	Products Formed
6	14	0.0056	15	< 0.1%
7	15	0.0087	60	< 0.1%
8	15	0.012	120	1% 2-methyl-2-butene

Table IVa. Gas chromatographic analyses of products (20% SE-30 prep. column at 52° and 8 p.s.i. in Perkin-Elmer 154L)

Compound	Time (min.)	Run 6	Run 7	Run 8
2-Methyl-2-butene	6	< 0.1%	< 0.1%	1%
t-Amyl chloride	17	15	15	14
CH_2ClCH_2Cl	13	85	85	85

Table Va. Mass spectral data for labeled t-amyl chlorides

	Run 6		Run 7		Run 8	
	React-ant	Prod-uct	React-ant	Prod-uct	React-ant	Prod-uct
Sample Number	131-1	132-3	135-1	136-1	135-1	139-1
$C_5H_9^+, C_5H_{10}^+, C_5H_{11}^+$						
69	8.0	7.0	6.9	7.0		9.3
70	67.0	58.5	55.8	56.6		65.5
71	189.2	181.2	180	187.9		193.4
72	141.5	141.6	145.6	153.6		144.5
73	- .9	- .9	- .8	- .8		2.9
% labeled	53.6	53.5	54.0			51.3
% doubly labeled						1.0
$C_3H_4Cl^+, C_3H_5Cl^+, C_3H_6Cl^+$						
75	1.9	1.9	2.0	2.0		2.2
76	69.8	70.9	72.1	78.8		109.4
77	195.7	198.0	203	215.8		230
78	137.1	136.1	144.8	144.6		83.7
79	-1.0	-1.3	-1.3	-1.3		.2
% labeled	54.2	53.1	55.4			31.8
% doubly labeled						0.1
$C_4H_7Cl^+, C_4H_8Cl^+$						
90	2.8	2.8	2.7	2.8		2.8
91	26.5	26.9	27.4	28.4		27.1
92	17.3	17.3	18.4	19.2		19.9
93	- .2	- .2	- .4	- .3		0.2
94	.1	.1	- .2	.0		0.1
% labeled	41.4	40.9	42.0			44.3
% doubly labeled						0.4

Table VIa. Positions of labeling (atom percent ^{13}C) in t-amyl chlorides

	C-1	C-2	C-3	C-4
Run 6 (Reactant)	26.0	27.9	0	0
(Product)	25.8	27.5	0	0
Run 7 (Reactant)	26.4	28.3	0	0
(Product)	24.5	27.8	1.9?	0.5?
Run 8 (Reactant)	26.4	28.3	0	0
(Product)	15.2	16.6	11.3	10.8

DISCUSSION

Conditions were found for the rearrangement of t-amyl chloride in the absence of bimolecular paths. Fifteen percent solutions of t-amyl chloride in 1,2-dichloroethane were stirred at 0^0 for 60 or 120 seconds. The amount of catalyst was about one molecule of Al_2Cl_6 per two hundred molecules of alkyl halide.

The experiments with labeled t-amyl chloride were not completely satisfactory. It was difficult to isolate the substrate in pure form from the reaction mixture. There was appreciable dehydrochlorination before or during the mass spectrometric determinations. This problem complicated the calculations. The determination of the amount of ^{13}C label at positions 3 and 4 were made by subtracting values with relatively large experimental uncertainties. The isotopic enrichments at C-1 and C-2 were only about 25%, so each percent of error constitutes an uncertainty of 1/25 or 4%. However, after extensive scrambling of the label the uncertainties are worse--of the order of twice as large.

It would be possible to improve the situation considerably if compounds with higher ^{13}C-enrichment were available. Another possibility is to use dilabeled molecules. For example, methylation of propionyl chloride-1-^{13}C with methylcadmium,[3] condensation of the methyl ketone with methylmagnesium iodide-^{13}C, and distillation from hydrochloric acid, should give a good yield of t-amyl chloride labeled at positions 1 and 2. (There would actually be four kinds of molecules. If the labeled barium carbonate and methyl iodide each had sixty atom-percent ^{13}C, the t-amyl chloride molecules would be 36% dilabeled, 24% labeled at C-1, 24% at C-2, and 16% unlabeled. This is better than the

30% C-1, 30% C-2, and 40% unlabeled molecules obtained by synthesizing the 1-^{13}C- and 2-^{13}C-compounds separately and then mixing them.)

Actually bimolecular reactions are not absolutely excluded by this investigation. There could be a subliminal amount. The threshold of detection by gas chromatography is high enough to allow 0.1% t-butyl chloride in a 15% solution. This represents about one molecule out of 150 molecules of t-amyl chloride. The mass spectrometric data for run 8 indicated the presence of dilabeled material (approximately 1.0% of the C_5^+ fragments, 0.4% of the C_4^+, and 0.1% of the C_3^+). The values were of the same magnitude as the uncertainties to which they were subject.

EXPERIMENTAL

Studies of Dichloromethane

Methylene chloride from Matheson, Coleman, and Bell was purified[17] by shaking it with 5% aqueous sodium carbonate and with water, drying over calcium chloride, and distilling at 39-40°. Five ml. of the distillate was tested with 1.3 g. of anhydrous aluminum chloride (Mallinckrodt AR grade). The liquid was colorless at first, yellow after one or two minutes, and bright yellow-orange within fifteen minutes.

Another purification method was tried. The solvent was shaken with concentrated sulfuric acid and then twice with water. The resulting emulsion was dried over calcium chloride for three hours and distilled. The distillate reacted with aluminum chloride as before. Drying the distillate over phosphorus pentoxide did not change the situation.

The more elaborate procedure of Harmon[18] (successive treatments with sulfuric acid, water, sodium bicarbonate solution, and calcium chloride, distillation from phosphorus pentoxide, and storage over Linde 4A molecular sieve) was not tried. Prins[27] purified methylene chloride by repeatedly boiling it with, and distilling it from, aluminum chloride. The pure solvent remained colorless when treated with aluminum chloride.

Gas chromatographic studies of solutions were made. None of the available columns would completely resolve the peaks due to t-butyl chloride and the solvent. The best separation was obtained with a 30% silicone DC-550 column at low temperature and low pressure. There was inversion in the order of appearance of the first two compounds.

Table VIIa. Retention times (minutes) on Silicone DC-550 analytical columns in Perkin-Elmer Model 154L.

Compound	B.P.	20% 80° 8 p.s.i.	20% 59° 8 p.s.i.	30% 78° 8 p.s.i.	30% 45° 8 p.s.i.	30% 32° 5 p.s.i.
CH_2Cl_2	40°	3.4	5.1	5.5	11.6	30
t-BuCl	51°	3.6	5.8	5.0	12.6	27
$(CH_2Cl)_2$	83°	8	14	17	44	115
t-AmCl	86°	9	16	14	35	85

Studies of 1,2-Dichloroethane

Analytical gas chromatographic conditions were found that separated completely the peaks due to t-amyl chloride and this solvent. (See Table VIIa.) The peaks came off in opposite sequence on 30% and 20% silicone DC 550 columns.

Commercial 1,2-dichloroethane (Matheson, Coleman and Bell) was purified by shaking with concentrated sulfuric acid and with water, drying over calcium chloride, and distilling.[19] The distillate turned to a pale yellow after five or ten minutes over aluminum chloride. (Thomas[20] reported a pale straw color and a 3° rise in temperature for this mixture.)

The solvent for the runs described was distilled from phosphorus pentoxide before use. Despite repeated distillation, however, the solvent always had detectable impurities (See Table IIa.)

Synthesis of 1-^{13}C-t-Amyl Chloride

The method was that used by Roberts[1] and by Vane[2b]. Preparation of methyl iodide-^{13}C from labeled barium carbonate was considered. (Nystrom[22] reduced carbon dioxide with lithium aluminum hydride in diethylcarbitol to methanol in 81% yield. Tolbert[23] prepared methyl iodide-^{14}C from labeled methanol, red phosphorus, iodine, and water on a vacuum line in 95% yield. He obtained yields of 80-90% when he hydrogenated carbon dioxide-^{14}C over a copper-alumina catalyst at 460 atmospheres.) However, commercial methyl iodide-^{13}C (Bio-Rad Laboratories) was finally obtained and used.

Ordinary methyl iodide (1.30 g.; 0.00915 mole) was used to start a Grignard reaction with 1.105 g. of magnesium (0.0455 g. at.; Domal) in dry ether under dry nitrogen. Then 5.20 g. (0.0364 mole) of labeled methyl iodide in 12 ml. of ether was added with stirring. The resulting methyl Grignard reagent had $62.4 \times \frac{0.0364}{0.0455} = 50.0$ atom percent ^{13}C.

After 1.5 hours of stirring the solution, 2.96 g. (0.0410 mole) of methyl ethyl ketone in 15 ml. of ether was added slowly. The reaction mixture stood overnight. The complex was decomposed with a solution of 5.14 g. of ammonium chloride (0.096 mole) in 31.5 ml. of water. The colorless layers were separated. The aqueous layer was extracted four times with ether. The ethereal solutions were dried and distilled at 34-35°. The residue was vacuum distilled: 3.3 g. at 47-51° (80 mm.). The distillate was 75% t-amyl alcohol (thus 2.5 g.: 69% yield from the ketone) and 25% ether by gas chromatography (30% silicone DC-550 at 79° and 8 p.s.i.).

A mixture of 2.2 g. of the labeled alcohol (0.025 mole) and 6.9 ml. of concentrated hydrochloric acid (0.082 mole) was heated for 60 min. Collected was 2.17 g. colorless liquid at 75-79°. Gas chromatographic analysis showed it was 95% t-amyl chloride, 0.5% 2-methyl-2-butene, and 4% ether. The yield was thus 2.06 g. (78%).

Synthesis of 2-^{13}C-t-Amyl Chloride

Propionic acid. The reaction system consisted of Pyrex glassware connected by Tygon tubing, with all joints and stoppers tightly wired. A flask containing barium carbonate-^{13}C was fitted with a dropping funnel and an outlet tube going to a sintered glass tube in concentrated sulfuric acid in a gas-washing bottle. This bottle was followed by a second one which held only glass wool. The exit led to a 10 mm. tube which was to be just below the surface of the stirred Grignard solution. The tube was wide open at its tip. (Use of a sintered glass tip in the first seven runs resulted in yields below 50%.) The reaction flask had a Hershberg stirrer, a dropping funnel, and condenser leading to a calcium sulfate drying tube and then to a trap filled with saturated barium hydroxide solution.

The system was flushed with dry nitrogen while being flamed and cooled. Then 6.46 g. of magnesium (0.266 g. at.; Domal) was added to the reaction flask. Thirty ml. of redistilled ethyl bromide in 100 ml. of dry ethyl ether was added with stirring in 0.5 hr. Another 0.5 hr. of stirring was needed for the last of the metal to react. Another 450 ml. of dry ether was added to decrease the concentration below 0.5 M. Dry nitrogen was bubbled through the solution while dry ice was added to an acetone bath around it to lower the bath temperature to -30°.

Seventy-five ml. of 40% perchloric acid was dripped onto 26.2 g. (0.133 mole) of barium carbonate in the first flask. The acid was added in 12 min. For 10 min. nitrogen was used to flush the carbon dioxide through the Grignard solution.

Eighty ml. of 10% aqueous sulfuric acid was added to the cold reaction mixture in 8 min. The layers were separated. The aqueous layer was extracted three times with 50-ml. portions of ether. The combined ether solutions were dried over calcium sulfate, filtered and distilled. Obtained was 8.42 g. of propionic acid at 80° (80 mm.). Gas chromatographic analysis (10% silicone column in Beckman GC-2 at 70° and 30 p.s.i.) showed that it was 99% pure (1% ether). Thus the yield was 85%.

Some of the carbon dioxide was recovered as a precipitate of barium carbonate. It weighed 0.91 g. when dry. (This was 1.7% of the original amount.)

1-^{13}C-Propionic Acid

The above procedure was followed with 26.3 g. of barium carbonate-^{13}C (57.7 atom % ^{13}C; 0.133 mole). The yield was 7.14 g. at 79-80° (77 mm.) or 72%. Another 3.5% of the carbon dioxide-^{13}C was recovered as 0.91 g. of dry barium carbonate-^{13}C. Gas chromatographic analysis (20% silicone column in Beckman GC-2 at 100°) showed that the distillate was 98.7% propionic acid and 1.3% ether.

2-^{13}C-t-Amyl Alchol

Diazomethane was prepared from 10.3 g. nitrosomethylurea,[24] dried over potassium hydroxide, and used to esterify the labeled propionic acid in ether.

A methyl Grignard reagent was made from 4.60 g. of magnesium (0.19 g.at.; Domal), 20 ml. of methyl iodide, and 100 ml. of dry ether.

The ester solution was added slowly to the Grignard solution with stirring, which was continued for another two hours. The mixture stood overnight, was stirred another hour, and was then treated with 35 ml. of saturated ammonium chloride solution. The ether layer was decanted. The white aqueous paste was extracted twice with 25 ml. portions of ether. The ether solutions were dried, filtered, and distilled through a packed column. After removal of most of the ether, the liquid was distilled under vacuum. The product was 3.34 g. at 53-54° (90 mm.). Gas chromatographic analysis (15% LAC 446 in an Aerograph at 70° and 27 ml./min.) showed that no methyl propionate was present and the alcohol was 95% pure (5% ethyl ether). Thus the yield was 74.6%. Infrared analysis confirmed the absence of carbonyl compounds.

2-^{13}C-t-Amyl Chloride

A mixture of 3.05 g. of the labeled alcohol (0.034 mole) and 9.0 ml. of concentrated hydrochloric acid (0.108 mole) was heated for 45 min. Obtained was 2.35 g. colorless liquid at 74-78°. Gas chromatographic analysis showed it was more than 99.5% t-amyl chloride with a trace of ether. The yield was 64%.

Runs with t-Amyl Chloride and Aluminum Chloride in 1,2-Dichloroethane at 0°C

The procedure was based on that of Vane.[2b] A solution of 1.75 g. of t-amyl chloride (16.4 m. mole) in 25 g. of purified 1,2-dichloroethane in a 50 ml. flask in an ice bath was stirred magnetically while 70.0 mg. (0.525 m. mole) of aluminum chloride (Mallinckrodt AR grade)

was added through a side-arm. (The catalyst was weighed in a 7 mm. Pyrex tube that was sealed at one end and tightly closed with a Tygon cap. The cap was made by welding Tygon tubing with hot crucible tongs.) After 5:00 min. of stirring, the reaction was quenched by the addition of 0.10 ml. (0.79 m. mole) of dimethylaniline. The ice bath was removed, and the liquid was vacuum distilled into a receiver cooled with a slush of dry ice-trichloroethylene. The distillate was 25.37 g. of colorless liquid (95% recovery). It was analyzed by gas chromatography. The results of this first run are in Tables Ia and IIa. There was no evidence of polymer-formation. Remaining in the reaction flask after the distillation was 0.23 g. of pale yellow solid on the walls; it was water-soluble and smelled like the amine. Found in the first of two liquid nitrogen traps following the receiver was 0.26 g. of colorless liquid with composition similar to that of the distillate.

In later runs there were different concentrations of t-amyl chloride, amounts of catalyst, and duration of run.

First Run with 1-^{13}C-t-Amyl Chloride and 2-^{13}C-t-Amyl Chloride

A mixture was made by adding $\frac{57.7}{107.7}$ x 0.80 ml. = 0.43 ml. of 1-^{13}C-t-amyl chloride with 50.0 atom percent ^{13}C to $\frac{50.0}{107.7}$ x 0.80 ml. = 0.37 ml. of 2-^{13}C-t-amyl chloride with 57.7 atom percent ^{13}C. Measurement was with a 1.00 ml. syringe graduated in hundredths of a ml. The 0.80 ml. was injected into a 20% silicone SE-30 preparative column (1 in. x 100 in.) at 52° and 8.5 p.s.i. in a Perkin-Elmer model 154L. Collected from 15.0 to 21.0 min. was 441.3 mg. of t-amyl chloride.

A solution of 356 mg. (3.33 m. mole) of the labeled t-amyl chloride in 2.02 g. of 1,2-dichloroethane was treated with 2.5 mg. (0.0188 m. mole)

of aluminum chloride for 15 sec. and then quenched with 9.0 μl. (0.071 m. mole) of dimethylaniline. Ninety-five percent of the organic halides was recovered for purification by preparative gas chromatography. The 2.48 g. was injected in three installments into a 20% SE-30 column at 50° and 8 p.s.i. Unfortunately the large solvent peak preceded the solute peak and tailed into it. The material collected at 17 to 24 minutes was only 80% pure. About 0.15 ml. of it was put through the column a second time, giving 35.6 mg. for mass spectral analysis. The final sample was shown to be free of solvent by analysis with a 30% silicone DC-550 column.

Second and Third Runs with ^{13}C-t-Amyl Chlorides

A mixture of 0.99 g. of 1-^{13}C- and $\frac{50.0}{57.7}$ x 0.99 g. = 0.86 g. of 2-^{13}C- t-amyl chloride was purified by preparative gas chromatography as before.

A solution of 350 mg. (3.26 m. moles) of labeled t-amyl chloride in 2.02 g. of 1,2-dichloroethane (freshly distilled from phosphorus pentoxide) was stirred with 3.8 mg. (0.0285 m. mole) of aluminum chloride for 60 sec. Six μl. of dimethylaniline (0.047 m. mole) was added to quench any reaction. The volatile liquids were pumped out and separated by two passes through the preparative gas chromatograph.

A solution of 436 mg. (4.07 m. moles) of labeled t-amyl chloride in 2.46 g. of 1,2-dichloroethane (freshly distilled from phosphorus pentoxide) was stirred with 6.6 mg. (0.050 m. mole) of aluminum chloride for 120 sec. Quenching was by 8.3 μl. (0.065 m. mole) of dimethylaniline. Ninety percent of the volatile liquids was recovered by vacuum distillation. The distillate was purified with preparative gas chromatography.

APPENDIX

Solvents for Carbonium Ion Rearrangements

Methylene chloride is a non-nucleophilic solvent that has been used for Friedel-Crafts acylations,[5] for cationic polymerizations of isobutylene (with aluminum chloride),[4] and for studies of carbonium ions.[18] It was the solvent for a Prins reaction of hexachloropropene and 1,2-dichloroethylene[14] at 5°. Methylene chloride adds to 1,2-dichloroethylene at 40-60°.[15] This solvent has dielectric constant 9.14 at 20° and 10.02 at 0°,[16] nearly the same as that of t-amyl chloride (9.3 at 16°).[6] It would have been used in these studies if it had been possible to separate it from t-butyl chloride on the gas chromatographic columns available.

Ethylene chloride has dielectric constant 10.65 at 20°[6] and 11.66 at 1°.[7] Waterman et al.[26] found that it reacted with 10% aluminum chloride (thus 0.0825 mole $AlCl_3$ per mole of CH_2ClCH_2Cl) at 45-55° to give resin in 40% yield. A more remarkable reaction was reported by Sisido and Yosikawa.[8] The same concentration of aluminum chloride was used at 26° for 75 min. The products included bibenzyl and m-bis (β-phenylethyl) benzene! Apparently the chlorocarbon condensed to benzene, which underwent Friedel-Crafts alkylations. The total yield of condensation products was about 12%. In spite of these reports, ethylene chloride has been used as a solvent for Friedel-Crafts acylations[5] and Fries rearrangements.[76] It did not react under the conditions used in this study. There was the disadvantage of difficulty of separation. The best preparative gas chromatography column gave a large solvent peak followed by a small solute peak in its tail.

Other solvents were not tried. Possibly one of the Friedel-Crafts solvents with high gas chromatographic retention time would be more satisfactory. Several possibilities are tabulated below with three major components of the reaction mixture. The gas chromatography data[10] are for two columns: A, 20% β,β'-oxypropionitrile on Chromosorb and B, 20% tri-m-tolyl phosphate on Chromosorb. Both were at about 50 ml./min. in a Burrell Kromo-Tog K-2.

Carbon disulfide has very recently[29] been used in a study of isomerization of butyl bromides. When 0.31 mole of aluminum bromide and 7.6 moles of carbon disulfide per mole of n-butyl bromide were stirred at 0°, eighty percent of the butyl bromide was isomerized in about ten minutes. Small amounts of t-amyl bromide and neopentyl bromide said to be present were rationalized with bimolecular mechanisms incorrectly based on those of Karabatsos et al.[2d]

Chloroform[20,31,32] and nitro compounds form soluble solid complexes with aluminum chloride. The complexes with nitromethane[30] and nitrobenzene[20] are excellent catalysts for alkylating aromatic compounds.

Aluminum chloride rapidly exchanges chlorine with carbon tetrachloride and chloroform, even at their melting points.[28]

Olah's comprehensive new source book on electrophilic organic reactions[97] includes numerous discussions of solvents for aluminum chloride.

Table II

Compo
2-Me-2-B
t-BuCl
t-AmCl
CS_2
$CHCl_3$
CCl_4
CH_2Cl_2
$(CH_2Cl$
CH_3NO_2
Cl_2CC
C_6H_5NO

[a] Refe

[b] Valu
0.00

Table VIIIa. Comparison of possible solvents.

Compound	B.P.	Dielectric Constant[a] 0°	20°	Solubility[a] of $AlCl_3$ (g./l.)	Retention Times (min.)[10] $A_{53°}$	$B_{93°}$
2-Me-2-butene	38.4	---	---	---	1.8	1.2
t-BuCl	51.2	10.95	---	---	2.3	---
t-AmCl	86.0	---	9.3 (16°)	---	4.0	4.0
CS_2	46.3	2.69	2.64	0.2	2.0	2.2
$CHCl_3$	61.2	5.16	4.81	1.00 at 0°	10.6	5.5
CCl_4	76.8	2.28	2.24	0.74[b]	4.0	4.3
CH_2Cl_2	40.1	10.02[16]	9.08	---	6.8	2.8
$(CH_2Cl)_2$	83.5	11.66(1°)[7]	10.65	< 4%	22.0	7.0
CH_3NO_2	101.0	---	37.5	600	63.1	7.9
Cl_2CCCl_2	121.0[9]	---	2.46	---	---	12.5
$C_6H_5NO_2$	210.9	39.34[11]	35.7	v.s.	---	---

[a] Reference 6 unless otherwise noted.

[b] Value given for 4°. Others state[28] that solubility is less than 0.0033M (0.44 g./l.) at 0°.

PART B

HIGHER-ORDER WAGNER-MEERWEIN SHIFTS

INTRODUCTION

Examples of 1,2-hydride shifts have been well-known for years; the question of whether there is a 1,3-hydride shift in an open chain system has been settled only recently. Karabatsos and Orzech[33] showed that rearrangement of 1-propyl cation is almost all by a 1,3-hydride shift rather than by two successive 1,2-shifts. Their experimental method was to deaminate deuterium-labeled propylamine, collect the 1-propanol, and study its n.m.r. spectrum. The results clearly showed that equation (1) rather than (2) describes the rearrangement.

$$CH_3CD_2\overset{+}{C}D_2 \xrightarrow{1,3\text{-H:}\sim} \overset{+}{C}H_2CD_2CD_2H \xrightarrow{H_2O} HOCH_2CD_2CD_2H \quad (1)$$

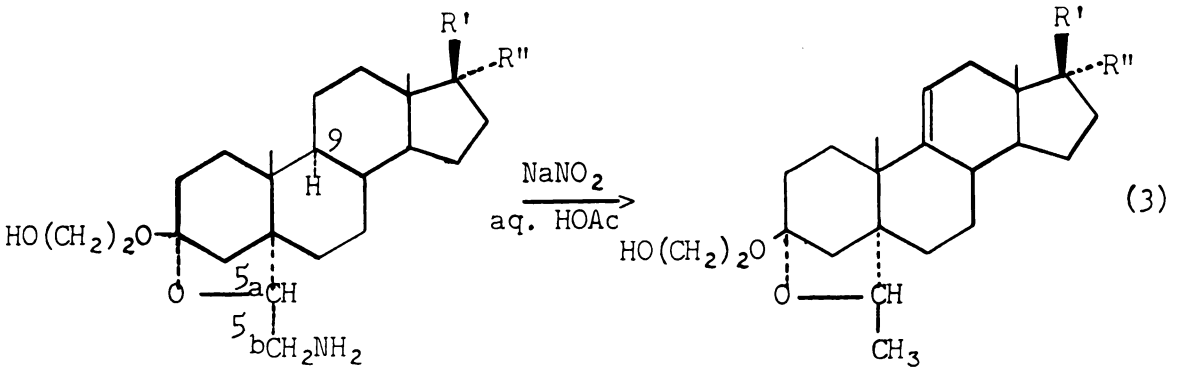
$$CH_3CD_2\overset{+}{C}D_2 \xrightarrow{1,2\text{-H:}\sim} CH_3\overset{+}{C}DCD_3 \xrightarrow{1,2\text{-H:}\sim} \overset{+}{C}H_2CHDCD_3 \xrightarrow{H_2O} HOCH_2CHDCD_3 \quad (2)$$

After noting the importance of 1,2- and 1,3-hydride shifts, it is reasonable to look for 1,4- and 1,5-hydride shifts. Do they occur? If so, to what extent and under what conditions?

There are numerous examples of 1,5- and 1,6-hydride shifts in medium-sized rings -- dating back twelve years to independent discoveries of transannular hydride shifts by Cope[34] and by Prelog.[35] The electron-deficient carbons have been generated by several means: hydroxylation of olefins with performic acid, solvolyses of cycloalkyl tosylates, and nitrous acid deaminations of cycloalkylamines. This field has been reviewed recently.[36]

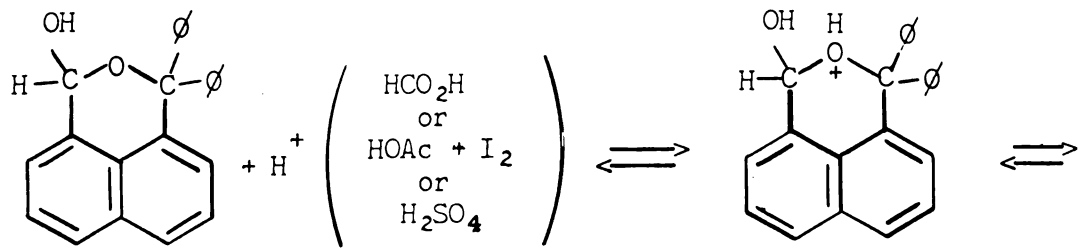
Few higher-order (1,4; 1,5; 1,6; etc.) hydride shifts have been reported for aliphatic noncyclic systems. Deamination of some steroids

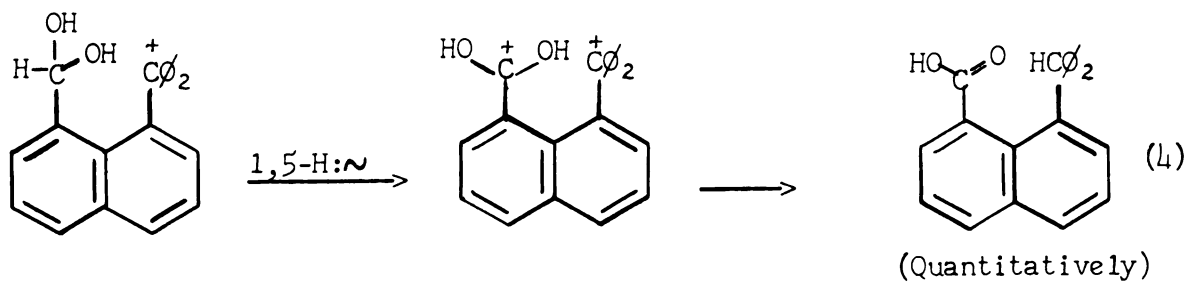
with especially favorable geometry goes via a 1,5-hydride shift:[59]



(3)

Letsinger and coworkers[49,50] have found 1,5-hydride shifts in peri-substituted naphthalenes. For example,

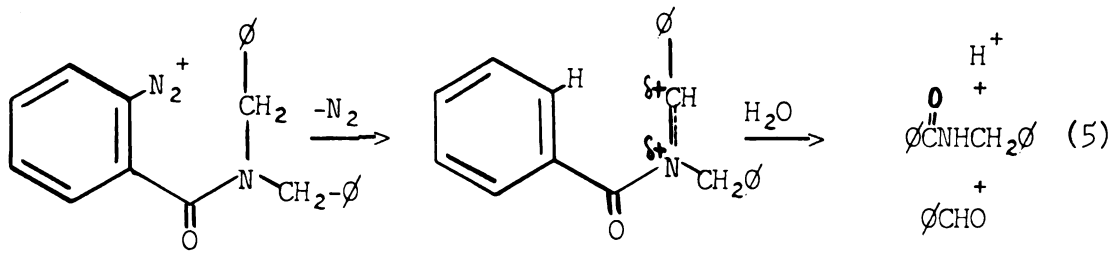




(4)

(Quantitatively)

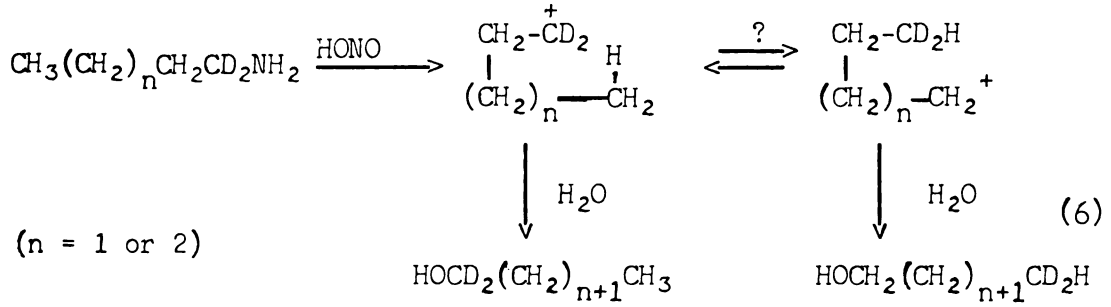
Cohen et al. have referred to four other nontransannular 1,5-hydride shifts[63] and have demonstrated a new example:[64]



(5)

In most of these examples a 1,5-hydride shift is facilitated by a molecular framework that favors the formation of a six-membered cyclic transition state.

The simplest systems to check for 1,4- and 1,5-hydride shifts are 1-butylamine and 1-pentylamine, respectively. If each amine is labeled with deuterium at carbon no. 1 and deaminated, the reaction paths of interest are



(n = 1 or 2) (6)

Rearrangement is indicated by the presence of protons on the carbon bearing the hydroxyl (easy to spot by n.m.r.).

RESULTS

The deamination of aqueous solutions of pentylamine gave 1-pentanol, 2-pentanol, 3-pentanol, pentenes, pentyl nitrites, pentyl nitrates, and nitropentanes. Similarly, butylamine gave 1-butanol, 2-butanol, butenes, butyl nitrites, butyl nitrates, and nitrobutanes. Tables Ib, Vb, and IXb-XIIb summarize the product analyses of some of the deaminations. Identification of products was by gas chromatography supplemented by infrared analysis. Known samples of alcohols, olefins, and nitrite esters were used for comparison.

Preparative gas chromatography was used to obtain milliliter samples of 1-pentanol and 1-butanol from deamination of pentylamine-1,1-d_2 and butylamine-1,1-d_2. The n.m.r. spectra (Fig. 2b and 5b) of the neat alcohols showed no α-protons in the 1-pentanol and only a slight amount in the 1-butanol (τ = 6.43 p.p.m.).

The deuterium contents of the starting material and products were determined by mass spectrometry. The labeled amines were run as the diacetylated derivatives (N-alkyldiacetamides), and the alcohols as trimethylsilyl ethers. Tables IIb-IVb and VIb-VIIIb outline the analyses obtained.

Table Ib. Percentage yields of deamination products from pentylamine and pentylamine-1,1-d_2 (second deamination)

	Pentylamine	Pentylamine-1,1-d_2 (Second Deamination)	B.P.
Pentenes	7	19	20-38°
2-AmONO* and	25	4	96°
3-AmONO			98°
2-AmOH* and		14	119°
3-AmOH		4	116°
1-AmONO	21	2	104°
1-AmOH		22	138°
1-$AmNO_2$	3	1	172°
1-$AmONO_2$		1	157°
2-$AmNO_2$* and	3	0.1	150°
3-$AmNO_2$			152°
2-$AmONO_2$* and		0.6	144°
3-$AmONO_2$			140°
Totals	59	68	

*The analyses did not distinguish between 2-pentyl and 3-pentyl compounds. Mass spectrometry and gas chromatography (10 ft. Carbowax 20M at 68°) showed that the secondary pentanol was 22% 3- and 78% 2-pentanol.

Table IIb. Mass spectra of N-pentyldiacetamide and of N-pentyl-1,1-d_2-diacetamide.

Mass	Ion	Unlabeled	Labeled	Mass	Ion	Unlabeled	Labeled
58		27.7	21.1	114	$C_5H_8NO_2^+$	79.1	10.2
59		8.62	14.6	115		5.33	4.21
60	$C_2H_6NO^+$	114.	129.	116		-0.07	81.1
61		0.59	12.9	117		--	5.49
62		0.14	0.50	118		--	0.08
---				---			
70		14.0	8.23	125		5.64	--
71		11.1	13.3	126		0.80	
72	$C_3H_6NO^+$	519.	20.7	127		0.59	6.14
73		201.	37.0	128		78.1	1.00
74		2.25	497.	129	$C_7H_{15}NO^+$	96.3	9.66
75		0.14	209.	130		6.12	57.1
76		0.07	1.82	131		0.03	86.0
77		0.69	0.73	132		--	7.77
---				133		--	0.35
96		1.38	--	---			
97		0.93	0.70	153		4.50	--
98		1.63	1.04	154		0.31	0.62
99		0.97	1.51	155		0.0	3.86
100	$C_4H_6NO_2^+$	59.0	4.83	156	$C_8H_{14}NO_2^+$	100.0	0.46
101		12.0	12.3	157		-0.10	5.40
102		92.6	143.	158		-0.07	100.0
103		-0.07	7.73	159		--	0.12
104		--	4.44	160		--	0.04
105		--	1.35	---			
106		--	0.27	171	$C_9H_{17}NO_2^+$	17.4p	0.89
107		--	0.19	172		1.49	0.62

110		0.69	--	173		0.03	15.6p
111		7.09	--	174		--	2.98
112		9.13	1.66	175		--	0.19
113		1.11	5.56				

Table IIIb. Mass spectra of trimethylsilyl ethers of labeled 1-pentanol from deamination of pentylamine-1,1-d_2 and of unlabeled 1-pentanol.[a]

	Labeled			Unlabeled		
Mass	Raw Peaks	Monoisotopic		Raw Peaks	Monoisotopic	
99	13.0	13.0		44.7	44.4	
100	19.2	17.7		6.8	0.1	
101	16.8	14.4		182.1	177.5	819.8
102	24.0	20.6	757.2	27.0	7.1	
103	165.0	162.4		600.0	589.2	= 71.9%
104	43.6	27.1		58.2	0.2	
105	511.	502.	= 66.3%	27.1	1.4	
106	49.5	-0.2		1.3	-0.2	
107	20.0	0.4		0.2	0	
115	3.0	2.8			22.5	
116	5.0	4.6			5.3	
117	15.3	14.4			6.7	
118	5.0	3.3			0.4	
119	6.1	5.6			3.2	
120	1.1	0.4			-0.1	
129	0.9	0.8			26.0	
130	2.0	1.8			0.1	
131	19.0	17.8			1.8	
132	2.5	0.1			0.1	
133	2.2	1.1			0.7	
143	--	--		17.0	17.0	
144	1.7	1.7		2.7	0.5	2326.6
145	3.3	3.1		2310.0	2309.1	= 99.3%
146	77.0	76.6	2243.7	297.0	-2.8	
147	2196	2164	= 96.5%	424.0	-0.05	
148	288			58.4	0.6	
149	93.9			28.0	2.3	
150	7.0			2.9	0.1	
151	0.9			0.8	0.2	
159	0.9	0.9		10.3	9.6	
160	2.4	2.3		19.2	17.6p	
161	1.3	0.9		3.0	0.1	
162	15.5	15.3p		1.0	0.2	
163	2.7	0.5		0.2	0.1	
164	0.8	0.1		--	--	

[a]Monoisotopic peak intensities are corrected for presence of hexamethyldisiloxane (0.3 volume percent of the labeled sample and 5.0 volume percent of the unlabeled sample).

Table IVb. Mass spectra of trimethylsilyl ethers of labeled 2-pentanol and 3-pentanol from deamination of pentylamine-1,1-d_2, unlabeled 2-pentanol, and unlabeled 3-pentanol.[a]

Mass	Labeled Mixture Raw Peaks	Labeled Mixture Monoisotopic		Unlabeled Monoisotopic 2-Pentanol	Unlabeled Monoisotopic 3-Pentanol
99		8.3		7.5	28.3
100		3.1		1.1	-0.5
101		21.9		71.3	65.7
102		19.4		40.4	0.5
103		62.8		36.6	5.2
104		38.1		-0.2	0.5
105		8.2		0.8	0.3
115	10.0	9.8		11.8	50.1
116	6.2	5.0		8.9	13.9
117	135.0	133.6	6.3% $C_5H_{13}OSi^+$	2233.2	10.9
118	96.0	81.3	3.8% $C_5H_{12}DOSi^+$		0.1
119	1914	1900	89.8% $C_5H_{11}D_2OSi^+$		0.6
120	207	-0.7			
121	76.0	-0.1			
122	4.0	0.6			
123	0.4	0.3			
129	6.0	6.0		14.0	4.1
130	2.7	2.0		1.3	7.6
131	279.6	277	48.4% $C_6H_{15}OSi^+$	0.2	2226.6
132	44.5	11.4	2.0% $C_6H_{14}DOSi^+$	0.6	-1.0
133	297	283.5	49.6% $C_6H_{13}D_2OSi^+$	0.5	1.5
134	35.0	0.2			
135	12.0	0.2			
136	1.0	0.3			
143	--	--		4.3	3.5
144	--	--		1.0	1.3
145	129.0	129.0	20.3% $C_7H_{17}OSi^+$	594.6	286.6
146	35.0	18.8	3.0% $C_7H_{16}DOSi^+$	-0.7	-0.3
147	547	486.3	76.7% $C_7H_{15}D_2OSi^+$	0	0
148	72.0	-0.5			
149	25.0	0.1			
150	2.0	0.0			
159	1.1	1.1		22.3	19.5
160	1.9	1.7		0.1p	0.1p
161	25.4	25.1		0.9	0.03
162	3.9	0.2p		0	0
163	1.9	0.7		0	0

[a]Monoisotopic peak intensities are corrected for presence of hexamethyldisiloxane (0.8 volume percent in the labeled mixture, 0.8 volume percent in the unlabeled 2-pentyl ether, and 9.4 volume percent in the unlabeled 3-pentyl ether).

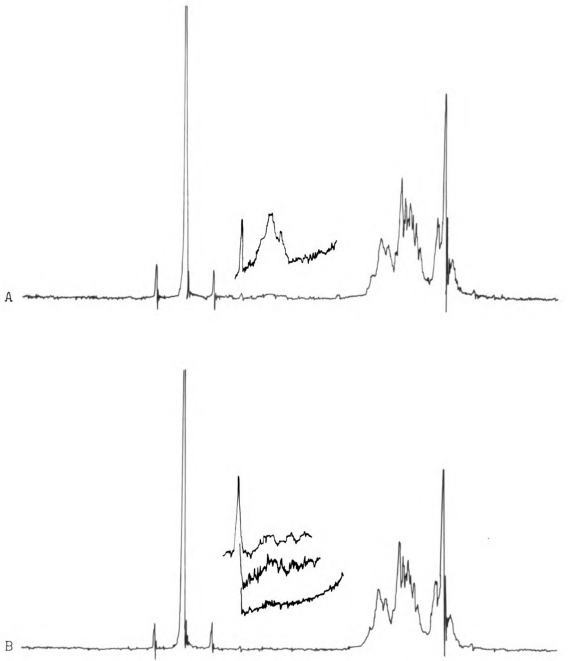


Figure 1b. N.m.r. spectra of pentylammonium perchlorates (80% solutions in deuterium oxide): (A) 10% unlabeled salt and 90% 1,1-dideuterated salt; (B) 1,1-dideuterated salt.

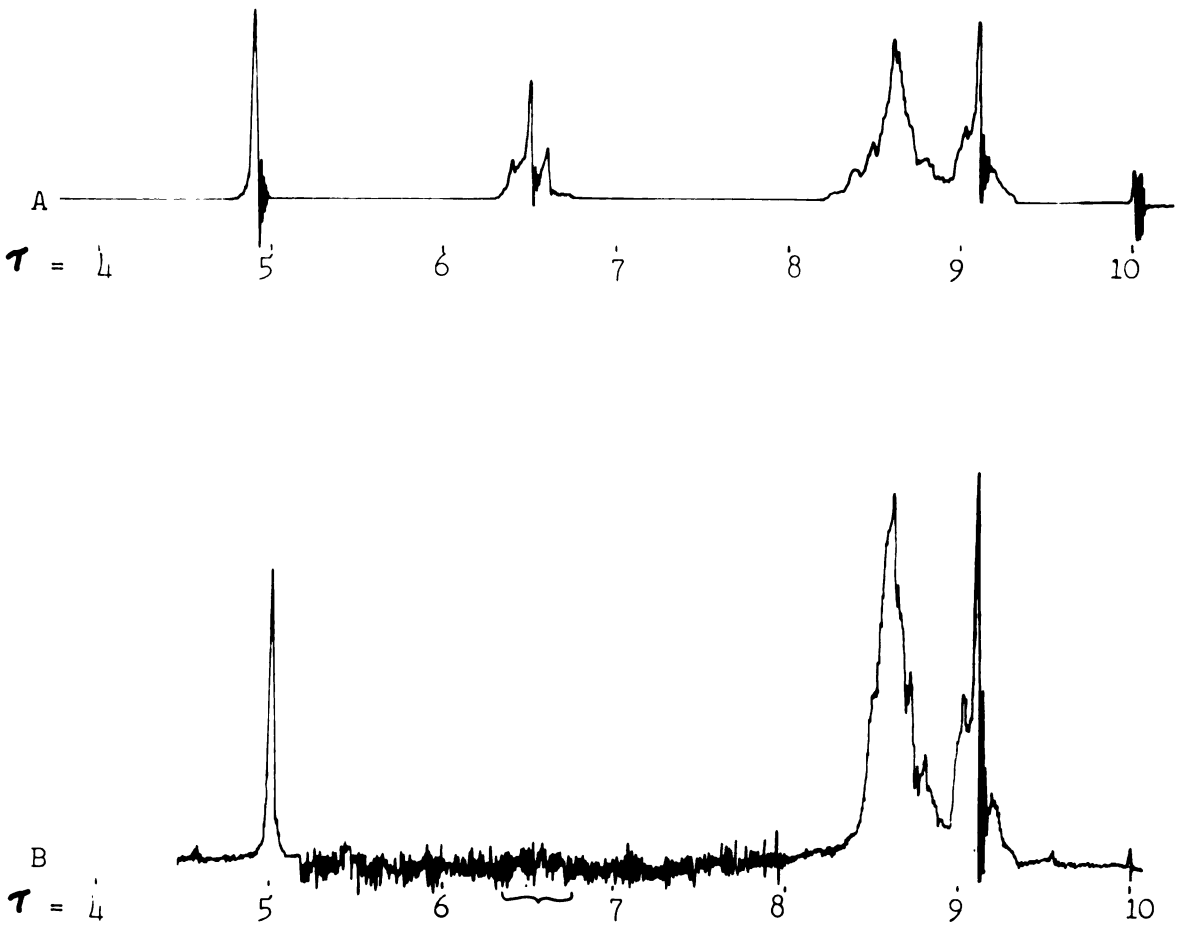


Figure 2b. N.m.r. spectra of 1-pentanols (neat samples): (A) unlabeled; (B) product of deamination of pentylamine-1,1-d_2.

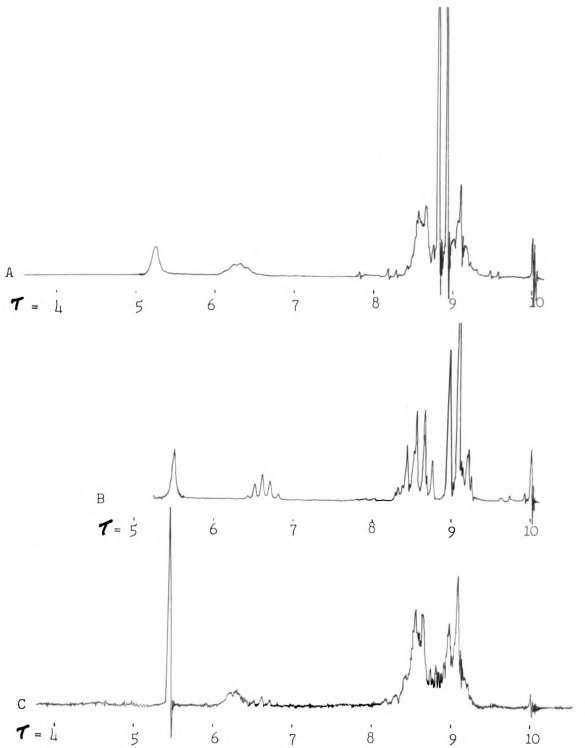


Figure 3b. N.m.r. spectra of secondary pentanols (neat samples): (A) unlabeled 2-pentanol; (B) unlabeled 3-pentanol; (C) products of deamination of pentylamine-1,1-d_2.

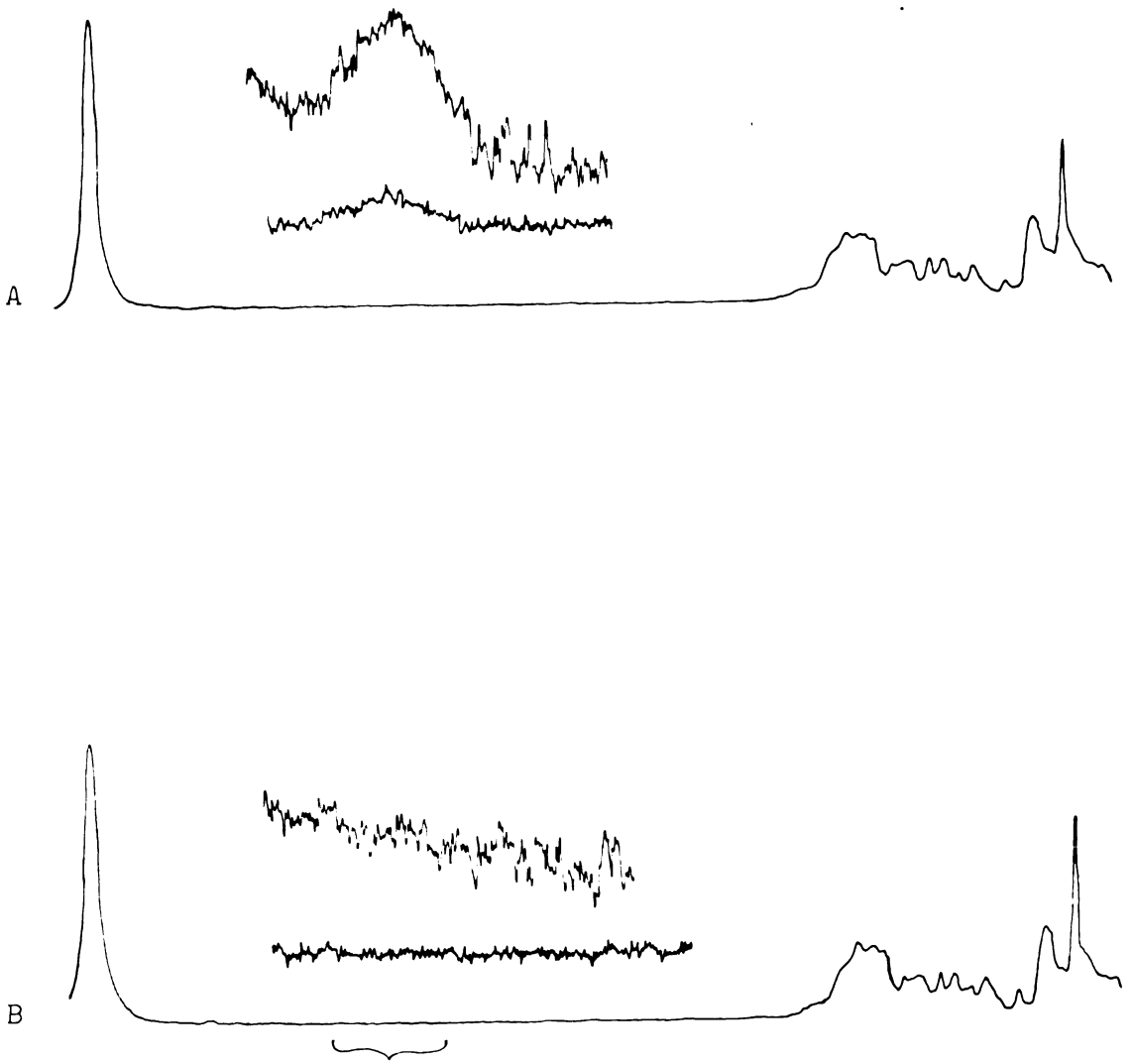


Figure 4b. N.m.r. spectra of butylammonium perchlorates (82% solutions in deuterium oxide): (A) 4.9% unlabeled salt and 95.1% 1,1-dideuterated salt; (B) 1,1-dideuterated salt.

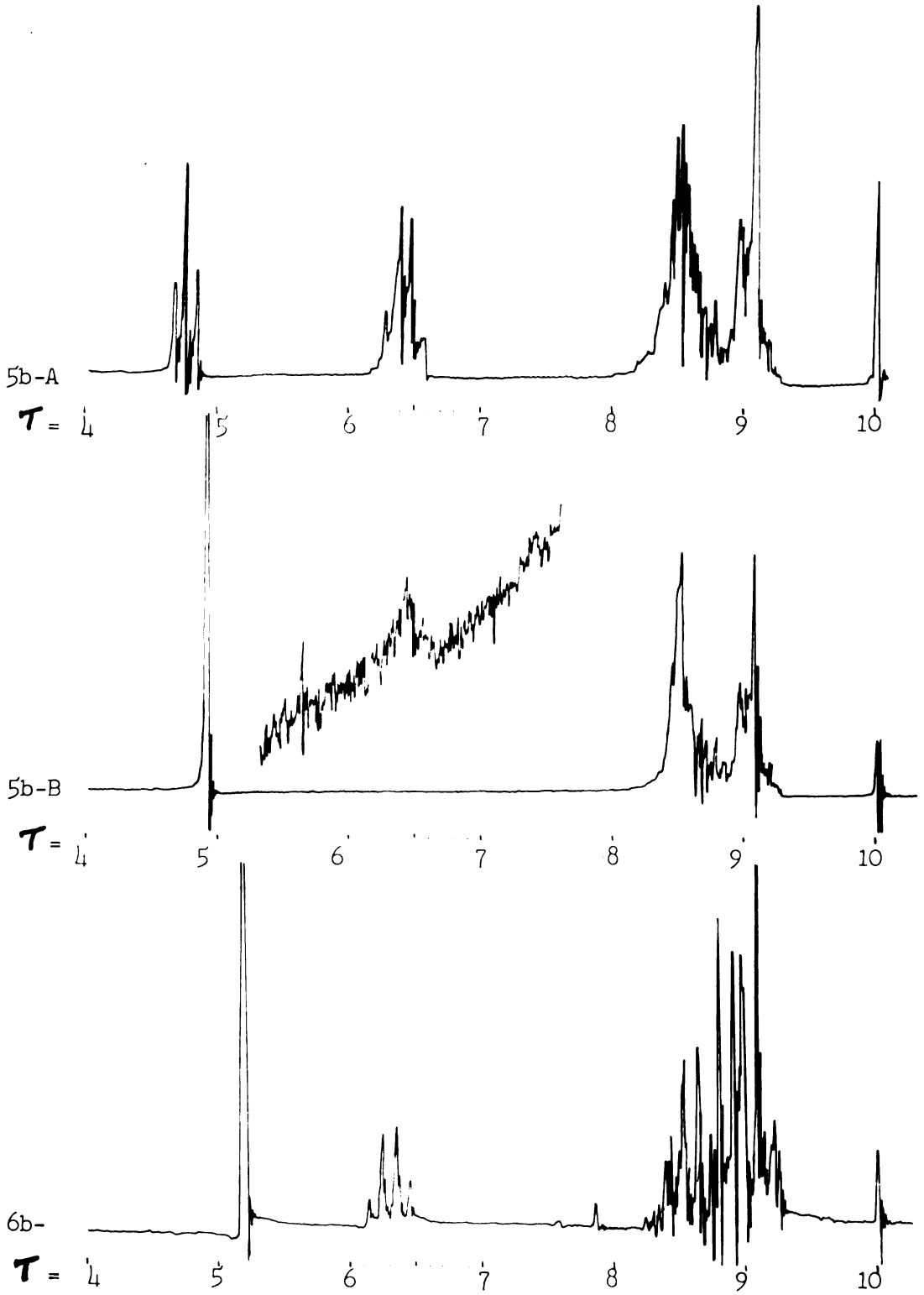


Figure 5b. N.m.r. spectra of 1-butanols (neat samples): (A) unlabeled; (B) product of deamination of butylamine-1,1-d_2.

Figure 6b. N.m.r. spectrum of labeled 2-butanol (neat sample) from deamination of butylamine-1,1-d_2.

Table Vb. Percentage yields of deamination products from butylamine and butylamine-1,1-d_2.

	Butylamine		Butylamine-1,1-d_2		B.P.
Butenes		6		16	-6° to 4°
2-Butyl nitrite	ca. 8	23		5	68°
2-Butanol	ca. 15			20	100°
1-Butyl nitrite		10		6	76°
1-Butanol		14		22	118°
2-Butyl nitrate		0.7		1	124°
1-Butyl nitrate		2		5	130°
2-Nitrobutane		0.2			140°
1-Nitrobutane		0.4		1	153°
Butylammonium perchlorate		0.2		0.8	--
Totals		56		77	

Table VIb. Mass spectrum of N-butyl-1,1-d_2-diacetamide

Mass	Raw Peaks	Monoisotopic		
113	2.0	2.0		
114	1.9	1.8		
115	13.0	12.9		
116	155.4	154.6		
117	158.4	149.1		
118	38.6	28.8		
119	3.6	0.9		
120	1.6	1.2		
140	1.0	1.0		
141	14.3	14.2		
142	6.0	4.8	1.2%d_0	
143	12.0	11.5	3.0%d_1	3.0%d_1
144	368.0	367.0	95.8%d_2	97.0%d_2
145	30.0	-0.3		
146	2.9	0.3		
147	0.3	-0.2		
157	0.8	0.8	1.3%d_0	
158	4.3	4.2	7.1%d_1	
159	54.6	54.2p	91.6%d_2	
160	14.7	9.6		
161	1.7	0.4		
162	1.3	1.1		

Table VIIb. Mass spectra of trimethylsilyl ethers of labeled 1-butanol from deamination of butylamine-1,1-d_2 and of unlabeled 1-butanol.

Mass	Labeled Raw Peaks	Labeled Monoisotopic[a]		Unlabeled Raw Peaks	Unlabeled Monoisotopic[b]	
99	5.0	5.0		3.9	3.8	
100	5.0	4.5		0.9	0	
101	7.3	6.7		19.0	17.8	156.8
102	14.8	14.0	685.7	28.0	25.3	
103	22.5	20.9		114.3	109.9	=70.1%
104	62.8	60.2		12.2	0.4	
105	581.0	574.4	= 83.8%	6.3	0.8	
106	57.6	0.04		0.3	0	
107	23.0	0.7		--	--	
108	1.0	-0.05		--	--	
129	--	--		1.8	1.8	
130	7.0	7.0		0.3	0.1	
131	5.0	2.7	2808.6	578.0	572.1	= 99.7%
132	79.2	78.4		68.5	-0.2	
133	2730.0	2720.5	= 97.1%	26.7	0.9	
134	324.0	-1.6		2.4	0.6	
135	111.6	-0.2		1	0	
136	7.0	0.5		--	--	
137	0.6	0.6		--	--	
145	0.6	0.6		3.3	3.3	
146	19.0	18.9		3.3	2.8p	
147	26.2	23.7		124.8	0	
148	14.1	10.2p		19.6	0	
149	3.7	1.3		9.8	0	
150	0.8	0.1		1.0	0	

[a] A very small impurity of hexamethyldisiloxane was not corrected for.

[b] Correction was made for the 1.9 volume percent of hexamethyldisiloxane present.

Table VIIIb. Mass spectra of trimethylsilyl ethers of labeled 2-butanol from deamination of butylamine-1,1-d_2 and of unlabeled 2-butanol.

Mass	Labeled Raw Peaks	Labeled Monoisotopic[a]		Unlabeled Raw Peaks	Unlabeled Monoisotopic[b]	
114	0.9	0.8		--	--	
115	9.3	7.7		6.0	5.1	
116	4.0	3.4	2052	2.0	1.1	421.4
117	539.0	535.9		417.0	415.2	= 98.5%
118	112.2	54.1		44.8	0	
119	1470.0	1451.1	= 70.7%	17.4	0.8	
120	159.0	-0.2		1.0	0.9	
121	58.0	-0.1		--	--	
122	3.4	0.8		--	--	
129	0.7	0.6		1.8	1.8	
130	1.9	1.7	800.7	1.0	0.8	183.0
131	136.8	127.2		186.0	180.4	= 98.6%
132	38.3	21.8		22.0	-0.2	
133	661.0	649.4	= 98.6%	10.6	1.0	
134	78.6	-0.05		0.8	0.5	
135	26.9	-0.04		0.1	0	
136	1.8	0.2		--	--	
144	--	--		0.1	0.1	
145	0.4	0.4		6.9	6.9	
146	2.6	2.5		1.0	0.9p	
147	203.4	5.0		116.7	0	
148	31.1	0p		18.3	0	
149	15.6	0		9.2	0	
150	1.7	-0.2		0.9	0	

[a]Correction was made for the 3.1 volume percent of hexamethyldisiloxane present.

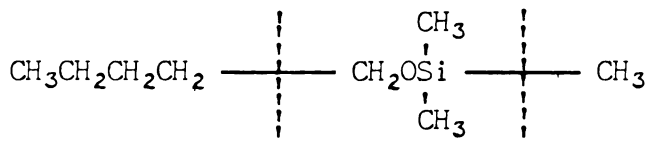
[b]Correction was made for the 1.8 volume percent of hexamethyldisiloxane present.

DISCUSSION

Pentyl System

The mass spectrum of the diacetylated starting material (Table IIb) shows that the labeled molecules are mostly dilabeled. The major fragmentation path is loss of methyl (from an acetyl group), giving peaks at 156-158. Calculation from their intensities gives 94.5% d_2, 5.1% d_1, and 0.4% d_0. The 0.4% is probably not real. Recalculation without it brings the figures to 94.9% d_2 and 5.1% d_1. The parent peak (at mass 173) is less reliable; its low intensity makes for larger experimental error. It indicates that the labeling is 91.2% d_2, 3.6% d_1, and 5.2% d_0. Dropping the d_0 and renormalizing give the values 96.2% d_2 and 3.8% d_1.

The 1-pentanol from deamination showed no α-protons in the n.m.r. (Figure IIb), but the more sensitive mass spectral analysis (Table IIIb) showed there was actually some monodeuterated compound. The fragmentation of trimethylsiloxypentane can be as follows:



Loss of methyl (Si–C cleavage) leaves an ion of mass 145, while the loss of butyl (C–C cleavage) leaves mass 103. The peaks in the region of 145 indicate 97.1% d_2 and 2.9% d_1. The interpretation of the 103 region required the mass spectrum of the unlabeled 1-pentyl ether. It had a peak intensity at 103 which was 71.9% of the total intensity of the 99-105 region. The corresponding parent-less-butyl peak from the labeled ether (at 105) had 66.3% of the total intensity of its region. Thus

66.3/71.9 = 92.2% of the α-methylenes were dideuterated. Further calculations gave 5.0% d_1 and 2.8% d_0 at this position. Comparison of these figures with those from the 145 region showed that the distribution of label was as follows:

92.2% $C_4H_9CD_2OH$

2.8% $C_4H_7D_2CH_2OH$

2.1% $C_4H_8DCHDOH$

2.9% C_4H_9CHDOH.

Recalculation without the contribution of the monodeuterated species gave:

95.0% $C_4H_9CD_2OH$

2.9% $C_4H_7D_2CH_2OH$

2.1% $C_4H_8DCHDOH$.

The loss of deuteriums from the α-carbon is probably due to reversible hydride shifts within the pentyl system. Less likely are alkyl shifts such as 1,2-propyl or 1,3-ethyl. There was no loss of deuteriums by exchange with the solvent.

The data of Table IVb are consistent with the amount of monodeuteration previously found. The peaks at 131 and 133 are clearly due to the loss of C_2H_5 or $C_2H_3D_2$ from the 3-pentyl ether with about equal probability. The data indicated very little deuterium at position 3, which means little reversible 1,2; 1,2- or 1,3-hydride shift. The amount of 3-pentyl ether can be calculated on the basis that the 2-pentyl ether readily loses propyl but not ethyl, while the 3-pentyl ether loses ethyl and cannot lose propyl. Using sensitivities derived from the spectra of unlabeled compounds, the calculation of the composition of the labeled mixture was:

$$\% \text{ 3-Am} = \frac{\text{intensities at 131 to 133}}{24.6} = \frac{571.9}{24.6} = 23.2$$

$$\% \text{ 2-Am} = \frac{\text{intensities at 117 to 119}}{27.3} = \frac{2114.5}{27.3} = 77.5$$

Normalizing and omitting the 0.8% of hexamethyldisiloxane bring the figures to 23.0% 3-pentyl and 77.0% 2-pentyl.

The finding of 3-pentyl compounds was not expected, since Streitwieser[44] has stated that no 3-pentanol is formed in the deamination of 1-pentylamine. Gas chromatographic analysis of the intractable pair of secondary alcohols showed that 21.7% was 3-pentanol and 78.3% 2-pentanol.

The peak at 117 shows that there is some 2-pentyl-5,5-d_2 ether present with the 2-pentyl-1,1-d_2 ether. This suggests that there were successive 1,2-hydride shifts down the pentyl chain -- past the midpoint -- to give all three secondary carbonium ions: 75% 2-pentyl-1,1-d_2, 21% 3-pentyl-1,1-d_2, and 4% 2-pentyl-5,5-d_2. The over-all pattern for the deamination of pentylamine-1,1-d_2 is summarized in the following outline.

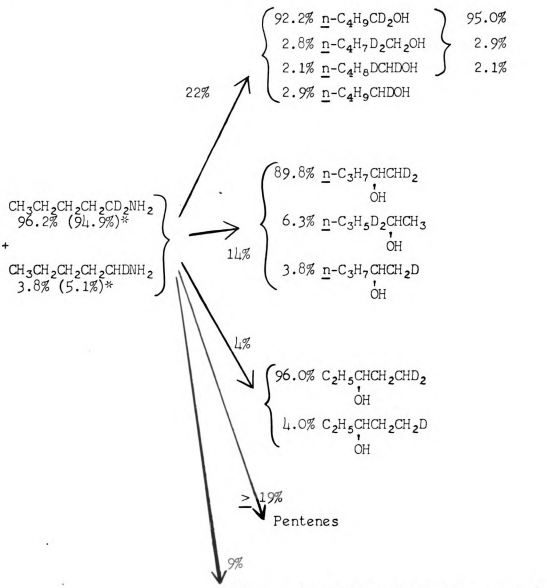
Butyl System

The n.m.r. spectrum of the primary alcohol from the deamination had a slight amount of α-protons. (See Fig. Vb.)

The mass spectrum of the diacetylated starting material (Table VIb) shows that 97.0% is dideuterated and 3.0% monodeuterated. (These figures are from the parent-less-methyl region of masses 142-144.)

It was not possible to calculate the results from the mass spectral analysis of the labeled 1-butyl silyl ether. The spectrum of the unlabeled ether was not comparable with that of the labeled ether in the

Figure 7b. Outline of the deamination of pentylamine-1,1-d_2.



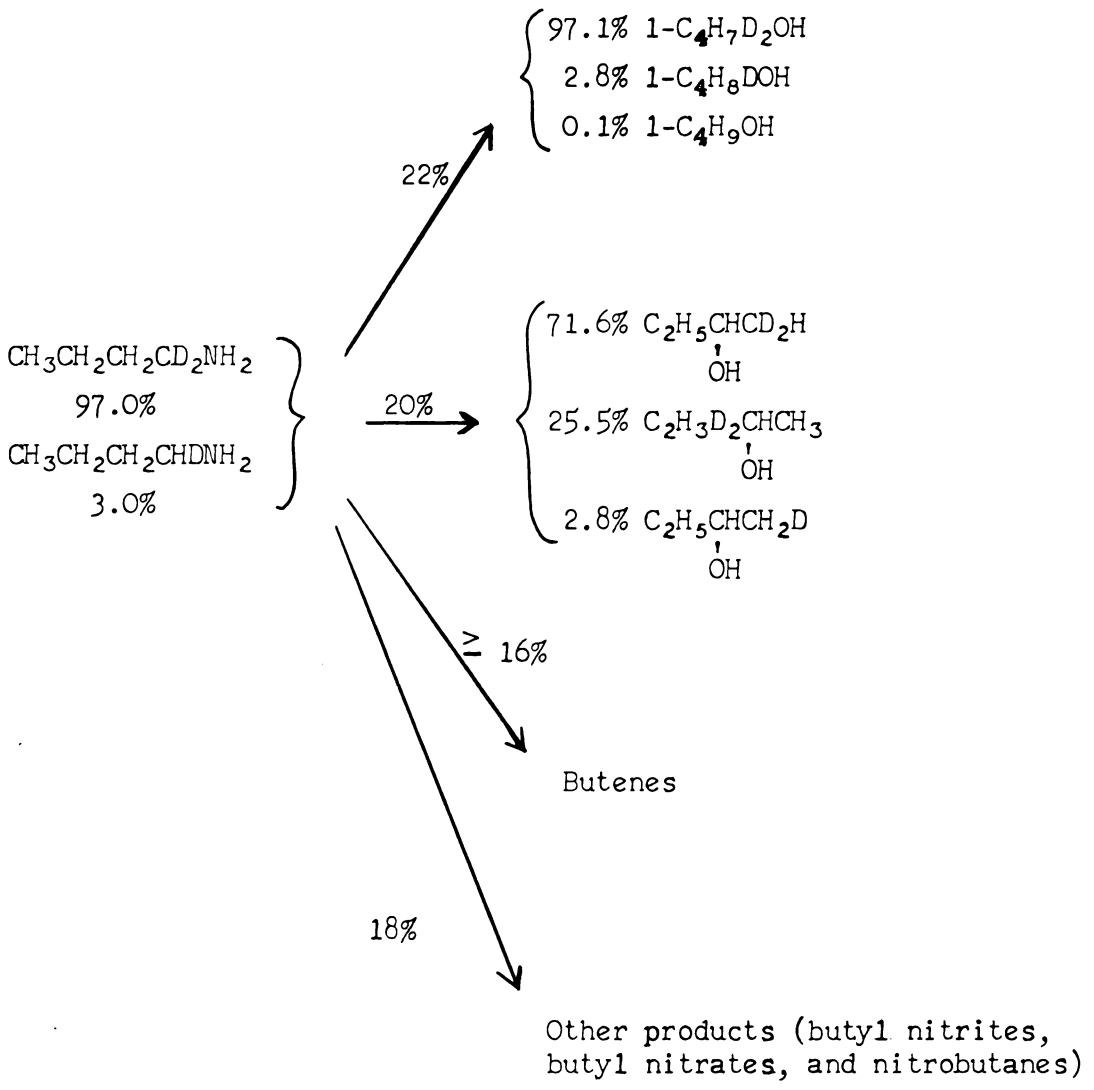
*Parenthetical figures are from parent-less-methyl peaks of pentyldiacetamide.

103 region. Comparison with the published spectrum[93] of 1-butoxytrimethylsilane indicated that the unlabeled sample had impurities with masses 101 and 102.

The 2-butyl silyl ether was simpler than the 2-pentyl (since there is only one secondary butyl cation). Calculations from the intensities in the 117 region (loss of ethyl) show that 70.7/98.5 = 71.8% of the ions are dideuterated, 2.7% are monodeuterated, and 25.5% are undeuterated. Thus 25.5% of the labeled 2-butyl ether molecules had two deuterium atoms in the ethyl group. The 131 region (loss of methyl) gave the distribution 82.3% d_2, 2.8% d_1, and 15.0% d_0. This means that 15.0% of the methyl groups lost were CD_2H. It does not tell what fraction of the no. 1 carbons of butyl were dideuterated, since methyls were lost from the trimethylsilyl as well as from butyl. If the isotopic purity is assumed to be the same in the 2-butyl ester as in the 1-butyl ester (97.0% d_2 and 3.0% d_1), then 97.0-25.5 = 71.5% of the 2-butyl groups contained CD_2H. This implies that 15.0/71.5 = 21.0% of the methyl groups lost came from butyl and 79.0% from trimethylsilyl. The information obtained on the deamination of butylamine is summarized in Figure 8b.

Streitwieser and Schaeffer[94] reported that deamination of butylamine-1,1-d_2 in anhydrous acetic acid gave no ethyl rearrangement. They converted the esters formed into alcohols and analyzed the 1-butanol for deuterium by mass spectrometry. (No results were given for 2-butanol.) The 1-butanol from the reaction gave intensities 12.3 at 31 $(CH_2OH)^+$, 26.1 at 32 $(CHDOH)^+$, and 63.6 at 33 $(CD_2OH)^+$. The 1-butanol-1,1-d_2 from which the butylamine was made gave intensities 13.3, 25.4, and 66.8, respectively. Thus there seemed to be no rearrangement (within experimental error). However, mass spectrometric studies of alcohols

Figure 8b. Outline of the deamination of butylamine-1,1-d_2.



are known to be fraught with difficulties.

This thesis reports more products of deamination than previous studies in the literature. In the definitive study,[85] 3.5 moles of butylamine in 1 l. of water was deaminated with 3.5 moles of hydrochloric acid and 10.5 moles of sodium nitrite. No reaction occurred "in the cold". Heating to boiling gave these percentage yields:

1-butanol	25.0
2-butanol	13.2
1-butyl chloride	5.2
2-butyl chloride	2.8
butenes	36.5
high-boiling material	7.6
butyl nitrites	(traces)
Total	90.3

(Reports[82,83] of isobutyl alcohol's being a product have been disproved.[84,85]) Streitwieser[94] obtained a 40% yield of butyl esters (mostly acetates but including 4 to 8% nitrates), which were hydrolyzed to 65% 1-butanol and 35% 2-butanol. There was also an unspecified amount of butenes: 71% 1-butene, 9% cis-2-butene, and 20% trans-2-butene. Deamination of butylamine in aqueous acetic acid at 70° gave butenes (60% 1-butene, 15% cis, and 25% trans) in 26% yield.[95] (No other products were discussed.)

Pentylamine has been deaminated by converting its hydrochloride to the nitrite and then heating. The yields of products were:[67]

alcohols ("perhaps one-third" secondary)	50.0
olefins	30.1
nitroso-secondary amine	1.9
primary amine	1.7
primary ammonium chloride	0.7
Total	84.4

The formation of nitrite and nitrate esters is readily explained by the reaction of the alcohols with nitrous acid and its decomposition

product, nitric acid. Some of the nitrite ester may be due to nucleophilic displacement by nitrite ion, which according to ambident anion theory,[68] should form more nitrite ester than nitroalkane when it attacks either a carbonium ion or a diazonium ion.

The low material balances found in this study are probably due to loss of olefins. Deaminations are known to give a larger proportion of elimination compared to nucleophilic displacement than these results indicate.

EXPERIMENTAL

Synthesis of Pentylamine[37]

Valeronitrile (Eastman white label) seemed pure by gas chromatographic analysis: one peak (at 20.0 min. on 30% silicone DC-550 column at 105° and 8 p.s.i.). One-tenth of a mole of it (8.31 g.) in 30 ml. of dry ether was added dropwise (in 35 min.) with stirring to ice-cold dry ether (250 ml.) and 3.8 g. of lithium aluminum hydride (lumps; 0.10 mole). The white suspension stood overnight. Four ml. of water, 3 ml. of 20% aqueous sodium hydroxide, and 14 ml. of water were added slowly with ice-cooling and stirring. The clear and colorless ether layer was decanted from the white solid. The solid was stirred three times with ether. The ether solutions were combined, dried over calcium sulfate, and filtered. The filtrate was refluxed one hour with barium oxide and then distilled at 35° through a 5-inch packed column. The residual 13 ml. was filtered and distilled, giving ether and three fractions:

152-2	1.03 g.	92-102°
152-3	2.85 g.	102.0-102.5°
152-4	1.41 g.	ca. 80° (reduced pressure)
Total	5.29 g.	

Each of the fractions was about 95% pure pentylamine by gas chromatography (30% silicone DC-550 at 111° and 8 p.s.i.). The yield of amine was 58%.

Another run, using twice as much material and similar procedures, gave 11.43 g. of distillate at 94-103° which was 97% pentylamine and 3% ether by gas chromatography. The yield was therefore 64%.

First Synthesis of Pentylamine-1,1-d_2

Valeronitrile (9.91 g.; 0.119 mole; Eastman white label, not distilled) was reduced with 5.01 g. (0.119 mole) of lithium aluminum deuteride (from Metal Hydrides). The solvent was anhydrous ethyl ether that was freshly distilled from lithium aluminum hydride. Obtained was 6.78 g. of amine, 90-102°. It was 95% pentylamine and 5% ether by gas chromatography. (Yield 60%).

Second Synthesis of Pentylamine-1,1-d_2

The valeronitrile was distilled after it was found to have one impurity. Gas chromatographic analysis with a 20% SE-30 preparative column showed two peaks: 99% valeronitrile at 25 min. and 1% unknown at 62 min. The column was at 72° and 8 p.s.i.) The fraction at 89-90° (102 mm.) was collected. Bad frothing during distillation was controlled with one drop of General Electric Antifoam 66.

Quantities of reactants in this run were just twice those of the previous run. The yield of labeled amine was 14.50 g., which was pure by gas chromatography (68.5% yield).

Deamination of Unlabeled Pentylamine

One fortieth of a mole (2.18 g.) of pentylamine was added to an equivalent amount of perchloric acid (2.10 ml. of 71.6% acid). The liquid was removed with a Rinco evaporator, leaving white crystals, which were dried in a vacuum desiccator. The yield was 4.42 g. (94%) with m.p. 225-231°.

One fiftieth of a mole (3.75 g.) of pentylammonium perchlorate was deaminated,[40] giving 0.22 g. of alcohols (ca. 12% yield). Gas

chromatographic analysis of them (30% silicone DC-550 at 110° and 8 p.s.i.) gave:

			time (min.)
ca.	49%	1-pentanol	12.6
ca.	46%	2-pentanol	7.9
ca.	4%	less volatile unknown	23.5

The deamination product distilled from the reaction mixture was mostly water under a frothy emulsion of alcohols. Several methods were tried to dry the emulsion layer. A successful way was to add the emulsion to molecular sieve 4A (Linde), using 10 g. of sieve for each gram of water, let it stand for 45 min., and pump off the alcohol at room temperature and < 1 mm. Hg. (This gave 85% recovery of alcohol as a single phase from a mixture of 2.0 ml. of alcohol and 0.5 ml. of water.)

One twentieth of a mole (4.36 g.) of pentylamine was reacted with an equivalent amount of perchloric acid (4.20 ml. of 71.6% acid), giving a colorless liquid and a chunk of white solid. To this mixture was added 3.75 ml. of 71.6% perchloric acid (0.045 mole), 25 ml. of water, and then, dropwise, a solution of 7.50 g. of sodium nitrite (0.109 mole) in 10.0 ml. of water. The resulting reaction mixture was blue. It was distilled to give an organic layer and an aqueous layer. Saturation with potassium fluoride and separation of layers gave 2.5 ml. (2.02 g.) of organic liquid. (This would be a 46% yield if only pentyl alcohols were present.) During the reaction and distillation the gases and more volatile liquids were collected in dry ice traps: blue liquid. After evaporation of the blue N_2O_3 (b.p. 3.5°C) there was 0.4 ml. of yellow liquid. (This was a 7% yield of pentenes if it was hydrocarbons only.)

The distillate was fractionated by preparative gas chromatography. (The analysis is included in Table IXb.) Washing with 5% hydrochloric acid did not change the gas chromatographic analysis; little amine was present and little hydrolysis of nitrite esters occurred.

First Deamination of Labeled Pentylamine

The amine was converted to its perchlorate salt in two batches. In the first, 2.9 ml. of 71.6% perchloric acid was added dropwise to 3.19 g. of pentylamine-1,1-d_2 (0.035 mole). Vacuum pumping on the product left 6.44 g. of colorless crystals with m.p. 214-219° (98% yield). More salt was made from 1.47 ml. of 71.6% perchloric acid and 1.62 g. of pentylamine-1,1-d_2 (0.018 mole). This salt was added to 6.20 g. from the first batch, giving an estimated 9.48 g. (0.050 mole) of pentylammonium-1,1-d_2 perchlorate, which was dissolved in 3.75 ml. of 71.6% perchloric acid and 20 ml. of water. To this pale brown solution was added a solution of 7.50 g. sodium nitrite (0.108 mole) in 15 ml. of water over a half-hour period. The reaction mixture was blue-green. Distillation from a 105-125° oil bath gave 2.5 ml. yellow organic liquid and 6.0 ml. colorless aqueous layer at 76-97°. The organic layer was dried over magnesium sulfate. Two liquid nitrogen traps were used to collect volatile liquids from the reaction and distillation. In the first was collected a deep blue liquid. Evaporation of nitrogen oxides left 0.65 g. of liquid which was analyzed by gas chromatography (See Table IXb.) The organic layer was separated into five fractions by preparative gas chromatography: pentenes, 2-pentanol, 1-pentanol, and two unknowns. The 2-pentanol fraction contained a large amount of impurity (at least twice as much as in the

Table IXb. Products of deaminations of pentylamines (gas chromatographic analyses and separations, using a 100 in. x 1 in. 20% SE-30 on Chromosorb W column).

Compounds	72° and 8 p.s.i. Time (min.)	Pentylamine (distillate)	Pentylamine-1,1-d_2 (First Run) (Distillate)	(Trap)	95° and 3 p.s.i. Pentylamine-1,1-d_2 (Second Run) (Distillate)	Time (min.)
Pentenes	3.1	1%	4%	15%	1 5	5.8 6.4
Unknown	7.2	0	0	7	0	--
2°-AmONO*	11.4	45	39	46	39	19
2°-AmOH*	12.0			0		
1-AmONO	15	13	26	31	8	22
1-AmOH	21	35	22	0	38	32
2°-AmONO_2* +2°-AmNO_2*	41	2	2	0	2	58
1-AmONO_2 +1-AmNO_2	62	4	7	0	8	84 89

*The analyses did not distinguish between 2-pentyl and 3-pentyl compounds.

previous deamination.) The identity of the impurity was uncertain. One possibility with the right retention time was pentylamine. The 2-pentanol fraction was washed with 5% aqueous hydrochloric acid, dried, and analyzed again by gas chromatography: There was no change. One curious result was the gas chromatogram of a known sample containing 0.2 ml. of pentylamine, 0.2 ml. of 1-pentanol, and 0.2 ml. of 2-pentanol. These compounds had retention times 16 min., 20 min., and 12 min., respectively, but the mixture gave only the two alcohol peaks.

An infrared spectrum of the impure 2-pentanol had very strong absorption at 6.05 μ, indicating nitrite ester. The two likely nitrites, 1-pentyl and 2-pentyl were synthesized by a method based on that for 1-butyl nitrite.[38] Yields of 76% and 88%, respectively, were obtained on a scale of 0.05 mole (cf. 81-86% for 5 moles[38]). Although nitrite esters are said[39] to be extremely easy to saponify, several experiments showed that the nitrites of 1-pentanol, 2-pentanol, and 3-methyl-1-butanol resisted hydrolysis in refluxing 20% aqueous sodium hydroxide for several hours. Refluxing for about 18 hours was required to saponify 95% of 1-pentyl nitrite.

Second Deamination of Labeled Pentylamine

A sample of 14.22 g. of pentylamine-1,1-d_2 (0.160 mole) was added slowly (in 30 min.) to 13.0 ml. of 71.6% perchloric acid (0.160 mole), giving a pale pink slush, which was pumped on (< 1 mm.) until it solidified to a mass of pale pink crystals, m.p. 209-229°. After storage in an evacuated desiccator for two days, the crystals were white, weighed 28.94 g. (95% yield) and had m.p. 223-228°. Recrystallization from 66 ml. of heptanol (on steam bath) by addition of 1500 ml. of purified

petroleum ether gave 26.40 g. (93% recovery) of white crystals, m.p. 225-229°. (The "30-60° pet. ether" from the stockroom was shaken with concentrated sulfuric acid (twice in this case) until the acid layer was colorless and then distilled slowly. The 40-55° cut was used.)

Another 3.08 g. of pentylammonium-1,1-d_2 perchlorate, m.p. 223-225°, was obtained by careful addition of perchloric acid to the ether fractions from the distillation of the labeled pentylamine and recrystallization as described above. N.m.r. spectra (Fig. 1b) were run on saturated solutions (80 wt.%) of pentylammonium perchlorates in deuterium oxide.

To 27.31 g. of pentylammonium-1,1-d_2 perchlorate (0.144 mole) in dilute perchloric acid (10.8 ml. of 71.6% perchloric acid and 60 ml. of water) in a 3-necked, 24/40, 300 ml. flask, was added, from a dropping funnel, a solution of 21.60 g. sodium nitrite in 45 ml. of water. The reaction proceeded at room temperature for 2.5 hrs. Distillation at 73-98° then gave two liquid phases. The distillate was saturated with potassium fluoride and separated, giving 7.5 ml. of yellow organic liquid. During the reaction and distillation all effluent gases were passed through two dry ice traps. The second trap was empty. The first held 4 ml. of blue liquid which formed brown gas in air ($N_2O_3 \rightarrow NO_2$). After 15 min. of standing at room temperature, the blue liquid became 3.5 ml. of yellow liquid. The two liquids were analyzed immediately by gas chromatography. (See Table Xb for the results.) N.m.r. spectra were run with the neat samples of labeled pentanols collected by preparative gas chromatography. (See Figures 2b and 3b.) The primary and secondary pentanols had n_D^{24} 1.4074 and 1.4010, respectively. Each sample (1.11 ml.

Table Xb. Products of second deamination of pentyl amine-1,1-d_2.

	Analyses with 10 ft. x 1/4 in. column of 20% Carbowax 20M on Chromosorb W at 118° in Aerograph			Separations with 100 in. x 1 in. column of 20% SE-30 on Chromosorb W at 95° and 3 p.s.i. in Perkin-Elmer 154L		
Compounds	Time (min.)	Distillate	Trap	Distillate	Time (min.)	Fraction
Pentenes	2	5%	70%	1% 4%	5.8 6.4	173-0
Unknown	7.8	0.6	0	0	---	
2°-AmONO*	10	5	12	39	19	173-2
2°-AmOH*	11.5	38				
1-AmONO	17.4	4	2	8 (shoulder)	22	
1-AmOH	22.2	46	12	38	32	173-3
2°-$AmONO_2$*	14	2	0	2	58	173-4
+2°-$AmNO_2$*	---	---	---			
1-$AmONO_2$	---	---	---	8	84	173-5
+1-$AmNO_2$	---	---	---		89	
		(Nothing from 22 to 97 min.)	(Nothing from 22 to 75 min.)			

*The analyses did not distinguish between 2-pentyl and 3-pentyl compounds.

of labeled 1-pentanol and 1.10 ml. of labeled 2-pentanol*) was refluxed for 16 hrs. with 1.2 ml. of hexamethyldisilazane (0.0058 mole for 0.010 mole of alcohol) and one drop of trimethylchlorosilane.[48] The trimethylsilyl ethers were purified by preparative gas chromatography (15 to 20 min. and 20 to 28 min. peaks at 102° and 9 p.s.i.). The mass spectrometric data are in Tables IIIb and IVb. Unlabeled 1-pentanol and 2-pentanol were converted to their trimethylsilyl ethers in the same way, but it was found that the long refluxing period[48] was not necessary; the composition of the reaction mixture was the same after two hours as after twenty hours of refluxing.

The problem of determining 3-pentanol in samples of 2-pentanol was solved as described below. The available gas chromatographic columns for Perkin-Elmer, Wilkens, and Beckman instruments were tried with a known mixture of the two alcohols. Only one gave the slightest separation. A 10 ft. x 1/4 in. column packed with 20% Carbowax 20M on Chromosorb gave 22.3% resolution[41] at 94°. The peaks were at 20.6 and 22.0 min. The Wilkens Company[42] obtained 78.8% resolution with a 20 ft. x 3/8 in. 30% Zonyl E-7 column at 92°. (Zonyl E-7 is the ester of pyromellitic acid with four molecules of $H(CF_2)_nCH_2OH$.)[42b] (Later it was learned that complete separation could be obtained with 20 ft. Carbowax 400 columns.)[43]

No 3-pentanol was found in the deamination products of 1-pentylamine when they were analyzed with the 10 ft. Carbowax 20M column. This result agreed with that of Streitwieser.[44] Mass spectrometric analysis

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*It was later found that 3-pentanol was also present.

(Table IIIb) of the trimethylsilyl ether of supposedly pure 2-pentanol from deamination showed that the 3-pentyl ether was also present. This prompted the reexamination of the 2-pentanol sample. It was 21.7% 3-pentanol by gas chromatographic analysis with the same Carbowax column but with a lower temperature, 68°. The alcohols had retention times 42.7 and 47.7 min. The resolution was 71.4%.

Preparation of N-Pentylacetamide

Two methods were tried for the preparation of N-pentylacetamide. Each gave a mixture of monoacetylation and diacetylation. The first method was that of Smith and Adkins:[44] acetic anhydride and pentylamine at 0°. To 1.47 g. (0.0169 mole) of pentylamine was added dropwise 1.71 g. (0.0169 mole) of acetic anhydride (freshly distilled at 135.0-137.0°) at 0°. The mixture was set aside for several days. The work-up was washings with 10 ml. of water, 10 ml. of 5% sodium hydroxide, 10 ml. of 5% hydrochloric acid, and 10 ml. of water, drying over calcium sulfate, and distillation. Gas chromatographic analysis (20% SE-30 preparative column at 128° and 8 p.s.i.) showed two peaks: 65% at 44 min. and 35% at 74 min. Preparative gas chromatography resulted in separation but extensive decomposition--brown liquids were collected when colorless samples were injected. Infrared analysis of the distillate showed strong N-H absorption at 3.03 μ.

The second method[46] was to use acetyl chloride in toluene at 60°. A solution of 1.47 g. pentylamine (0.0169 mole), 1.80 ml. acetyl chloride (0.025 mole), and 3.51 ml. pyridine (0.044 mole), in 17 ml. toluene was stirred magnetically in a 70-80° oil bath for 25 min. The reaction mixture (massive white precipitate and yellow liquid) was washed four times

Table XIb. Minor products of deamination of pentylamine-1,1-d_2 (fractions collected by preparative gas chromatography).

1. Gas chromatographic analyses.

(20% SE-30 at 110°)				(20% Carbowax 20M at 128°)	
173-4	Compound	Time (min.)	173-5	173-5	Time (min.)
0	Unknown	1.0	0	2%	5.5
0	2°-AmOH*	1.5	0	1%	9.7
73%	2°-$AmONO_2$*	3.0	0	12%	13.7
12%	1-AmOH	2.0	1%	0	16.5
0	1-$AmONO_2$	4.1	43%	34%	17.3
0	1-$AmNO_2$	3.7	43%	51%	38.5
15%	2°-$AmNO_2$*	6.2	1%	0	est.20
0	Unknown	8.3	11%		

*The analyses did not distinguish between 2-pentyl and 3-pentyl compounds.

2. Infrared analyses (10% solutions in carbon tetrachloride) (wavelengths in microns)

173-4	173-5
No RONO (6.20)	No RONO (6.20)
Strong $RONO_2$:	Strong $RONO_2$:
6.10	6.05
7.80	7.66
11.48	11.55
Medium RNO_2:	Strong RNO_2:
6.40	6.42
7.20	7.18
7.32	

with 20 ml. each time: water, 5% sodium hydroxide, 5% hydrochloric acid, and water. The organic layer was dried over calcium sulfate and distilled. Bad frothing was eliminated with one small drop of General Electric antifoam 66. Toluene came over at 64-65° (122 mm.), leaving a pale yellow liquid residue, 0.70 g. with n_D^{24} 1.4497 (cf. lit.[47] n_D^{25} 1.4412 for N-pentylacetamide). Gas chromatographic analysis of this liquid showed only a trace of toluene (ca. 0.3%), 29% at 17.5 min., and 71% at 29.0 min. (20% SE-30 prep. column at 160° and 8 p.s.i.). Several attempts to collect pure fractions gave decomposition at higher temperatures and very high retention times at lower temperatures (e.g., nothing came through in 3 hours at 90° and 8 p.s.i.).

Preparation of Labeled N-Pentyldiacetamide

The second method[46] was chosen, since it gave a greater proportion of diacetamide, which was more convenient for mass spectrometry.

Some of the sample of pentylamine-1,1-d_2 that was used for the second deamination had been set aside. A solution was made from 1.54 g. of the amine (0.0169 mole), 3.51 ml. of pyridine, and 17 ml. of toluene. Acetyl chloride (1.80 ml.; 0.025 mole) was added dropwise at room temperature. The reaction mixture (white solid plus liquid) was stirred and heated in a 70-100° oil bath for 30 min. It was washed with 20 ml. volumes of water, 5% sodium hydroxide, 5% hydrochloric acid, and water and dried over calcium sulfate. Toluene was distilled at about 70° (150 mm.), but the liquid residue still had about 15% toluene (by gas chromatographic analysis). Another hour of pumping (ca. 1 mm.) and heating (oil bath up to 150°) brought the toluene content down to 1.5%. Pumping (at the capacity of the vacuum pump) and heating (oil bath up

to 170°) were continued until all of the liquid vaporized and condensed on the walls of the vigreux column. This liquid, 0.21 g. (n_D^{24} 1.4498), was allowed to drain into a clean flask. It was 90% pentyldiacetamide and 10% pentylacetamide by gas chromatographic analysis. The mass spectral analysis is in Table IIb.

Preparation of Butylamine

Butyronitrile (Eastman white label) was distilled at 114.5-115.0°. A tenth of a mole (6.91 g.) in 30 ml. of ether was added slowly to 3.8 g. of powdered lithium aluminum hydride in 250 ml. of ether with ice-bath cooling. (The ether had just been distilled, from lithium aluminum hydride.) The mixture was stirred and refluxed for four hours. It was then chilled in ice and treated with 4 ml. of water, 3 ml. of 20% sodium hydroxide, and 14 ml. of water. The ether layer and three ether extracts of the aqueous paste were combined; dried, and distilled. Only 0.4 ml. of amine was obtained. However, the ether that had been distilled off was treated with perchloric acid until the mixture was barely acidic. Vacuum pumping removed the ether and water, leaving white crystals. After drying in a vacuum desiccator overnight the crystals weighed 11.85 g. and had m.p. 193-198° (lit.[77] 195-197°). This was a yield of 68.4% (cf. lit.[37] 57% yield of amine).

Deamination of Butylamine

No reaction occurred in the first three attempts, when the quantities of reactants were 0.050 mole of butylammonium perchlorate, 0.18 mole of perchloric acid, and 0.108 mole of sodium nitrite. Decreasing the amount of acid brought success.

A clear, colorless solution was prepared from 8.83 g. of the perchlorate salt of butylamine (m.p. 194-196°; 0.0508 mole), 3.75 ml. of 71.6% perchloric acid (0.045 mole), and 20 ml. of water. Sodium nitrite (7.50 g.; 0.108 mole) in 10 ml. of water was added in 20 min. at 25° with magnetic stirring. After two hours the reaction mixture was distilled at 62-98° (oil bath 115-140°). The distillate was saturated with potassium fluoride, and the yellow oil separated. Obtained was 1.4 ml. (1.57 g.) of oil 220-A. Its analysis is in Table XIIb. Further distillation gave only water and a solid residue.

Gases evolved during the reaction and distillation had been passed through two dry ice traps. The second trap was empty. The first held blue liquid. It was possible to weigh 0.7 g. of it in a vial cooled in dry ice and analyze it by gas chromatography. Its composition was 22% butenes, 1% unknown compound, 39% 2-butyl nitrite, and 38% 1-butyl nitrite. This sample (220-C) was sealed in a glass tube. Two days later the liquid contained a few sharp needles, presumably polymerized olefins.

The residue from distillation was dissolved in water and made alkaline to phenolphthalein with less than 1 ml. of 20% sodium hydroxide. Ether extractions gave an amine which reacted with 0.12 millimole of perchloric acid to form 0.02 g. of amine salt (0.2% of the starting material).

The total yields of deamination products are summarized in Table Vb.

Preparation of Butylamine-1,1-d_2

Ten grams of lithium aluminum deuteride (0.238 mole; Metal Hydrides) was used to reduce 16.42 g. of butyronitrile (0.238 mole) in the manner

used for the unlabeled amine. Obtained were 1.53 g. of butylamine-1,1-d_2 (0.020 mole) and 29.47 g. of dry, white, crystalline perchlorate salt (0.168 mole; m.p. 194-198°), a total yield of 79.0%. N.m.r. spectra (Fig. 4b) were run on saturated solutions (82 wt.%) of the salt in deuterium oxide.

Deamination of Butylamine-1,1-d_2

A solution was prepared from 26.55 g. of butylammonium-1,1-d_2 perchlorate (0.151 mole), 11.3 ml. of 71.6% perchloric acid (0.136 mole) and 20 ml. of water. A solution of 22.6 g. of sodium nitrite (0.330 mole; Mallinckrodt AR grade) in 32 ml. of water was added dropwise with stirring. The reaction mixture was stirred in a 24-26° water bath for two hours. Distillation at 74-97° and saturation of the distillate with potassium fluoride gave 4.41 g. of yellow oil, 226-A. Further distillation gave 1.75 g. of organic layer 226-B. Ether extraction of the aqeuous phases of the distillates gave organic liquid (.35 g.).

Gases evolved during the deamination and distillations were passed through dry ice traps. There was 3.0 g. of yellow-green condensate.

The solid residue from distillation was dissolved in water, made alkaline to phenolphthalein (with 3.2 ml. of 1M sodium hydroxide), and extracted with ether. Distillation, neutralization, and drying gave 0.2 g. of colorless amine perchlorate (0.8% recovery).

A preparative gas chromatographic column packed with 20% silicone SE-30 on Chromosorb W was used at 70°. An experiment with a 50-50 mixture of 1-butanol and 2-butanol showed that the recovery of alcohols was only 50% at 8 p.s.i. but increased with decreasing pressure. The optimum was 3 p.s.i., where there was 79% recovery of 0.75 ml. of injected alcohols.

The deamination product 226-A was fractionated under these conditions. There were three injections (0.6, 0.7, and 0.7 ml.). Obtained were six fractions, including labeled 2-butanol at 18-26 min. and labeled 1-butanol at 30-39 min. The analyses are summarized in Table XIIb. The n.m.r. spectra of the two alcohols are shown in Figures 5b and 6b. The total yields of deamination products are outlined in Table Vb.

Preparation of Silyl Ethers

Unlabeled trimethylsilyl ethers were prepared from 1-butanol and 2-butanol by refluxing 0.30 g. of each alcohol with 0.50 ml. of hexamethyldisilazane and a small drop of trimethylchlorosilane for two hours. The products were purified by preparative gas chromatography (20% SE-30 at 133° and 8 p.s.i.). The ethers were collected at 37-44 min. and at 29-35 min. The impurities were 2-butanol at 17 min. and hexamethyldisiloxane at 23 min. The collected samples had only traces of impurities by gas chromatographic analysis (10 ft. 20% Carbowax 20M in Aerograph).

The labeled alcohols obtained from deamination were converted to trimethylsilyl ethers in the same way. All four ethers were analyzed mass spectrometrically by Mr. S. Meyerson. The results are in Tables VIb-VIIIb.

Acetylation of Butylamine-1,1-d_2[46]

The 1.53 g. of butylamine-1,1-d_2 (0.020 mole) mentioned above was dissolved in 4 ml. of pyridine and 20 ml. of toluene and treated with 6.6 ml. of acetyl chloride (0.093 mole). The semi-solid mixture was stirred magnetically for 30 min. in a 70-90° oil bath. It was then

Table XIIb. Products of deaminations of butylamines.

1. Gas chromatographic analyses, using a 100 in. x 1 in. 20% SE-30 column at 73° and 8 p.s.i.

Compounds	Time (min.)	Butylamine (Distillate 220-A)	Butylamine-1,1-d_2 (Distillate 226-A)
Gases	0.7	--	--
Butenes	2.1	2%	4%
	2.4		
2-BuOH	7.6	38	38
1-BuONO	9.2	17	0.2
1-$BuNH_2$	9.4	0	0
1-BuOH	12	29	39
2-$BuONO_2$	27	3	4
1-$BuONO_2$	37	8	15
2-$BuNO_2$	46	1	
1-$BuNO_2$	64	1	0.4

2. Infrared analyses of products of deamination of butylamine-1,1-d_2 fractionated by gas chromatography (wavelengths of strongest absorption in microns)

	References (unlabeled compounds)
2-BuOH: 3.03, 3.50, 6.87, 7.33, 7.79, 8.87	81(no. 75)
1-BuOH: 3.1, 3.5, 4.60, 4.80, 6.87, 7.27, 8.92, 9.35, 10.42	81(no. 5278)
2-BuONO and 1-BuONO: (not collected; seen only as trace impurities in the alcohols, ca. 6.18)	91
2-$BuONO_2$: 6.16, 7.85, 11.57	69
1-$BuONO_2$ } 6.15, 6.86, 7.26, 7.85, 10.8, 11.8	87;81(no. 13495)
2-$BuNO_2$ } 6.52, 7.26, 8.80	69
1-$BuNO_2$: 4.65, 4.83, 6.12, 6.47, 6.83, 7.25, 8.59, 8.86	69; 89

washed with 20 ml. volumes of water, 5% sodium hydroxide, 5% hydrochloric acid, and water. Drying, filtration, and distillation gave colorless liquids:

0.30 g.	223-2	70° (0.8 mm.)	n_D^{24} 1.4467
0.16 g.	223-3	65° (0.4 mm.)	1.4486
0.26 g.	223-4	hold-up	1.4497

The literature gives comparable boiling points for butylacetamide:[78] 230° (760 mm.) and 140-141° (21 mm.) but n_D^{25} 1.4391. The only data for butyldiacetamide are nitrogen analysis (9.11%; calc. 8.91%)[79] and boiling point (48-62° at 0.2 mm.)[80] The infrared spectrum of 223-3 had a barely detectable N-H absorption and differed from the spectrum of butylacetamide.[81] The gas chromatogram of 223-3 (20% SE-30 preparative column at 150°) showed no toluene, 0.9% at 10 min., and 99.1% at 27 min.

Preparation of Butyl Nitrites

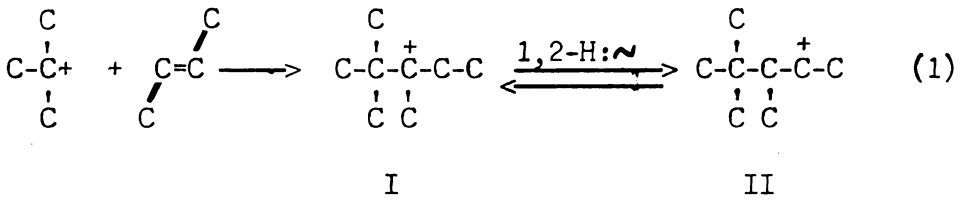
The directions[38] for preparing butyl nitrite were modified for use with only 3.70 g. (0.050 mole) of each butanol. The yields obtained were 63% with 1-butanol and 58% with 2-butanol.

PART C

ALIPHATIC 1,3-METHYL SHIFTS

INTRODUCTION

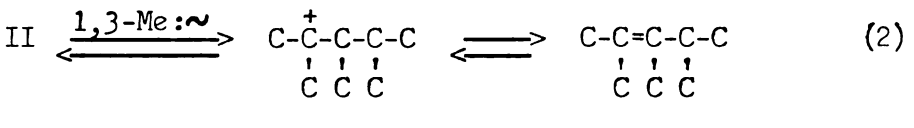
Several carbonium ion rearrangements have been reported as possible 1,3-methyl shifts. The earliest was discussed in the 1933 doctoral thesis of Laughlin and published after repeated verification.[51] The reaction sequence began with the acid-catalyzed copolymerization of s-butyl alcohol and t-butyl alcohol:



(1)

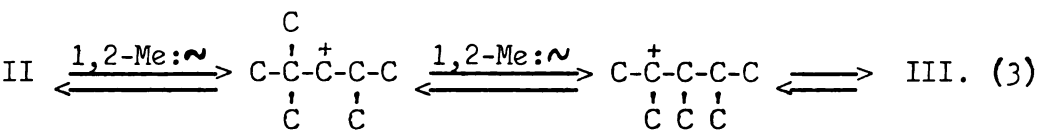
I II

The major product was 3,4,4-trimethyl-2-pentene, formed by simple loss of a proton from I or II. However, another octene, III, was found. It was explained by the rearrangement of II, either by a 1,3-methyl shift or by two successive 1,2-methyl shifts:



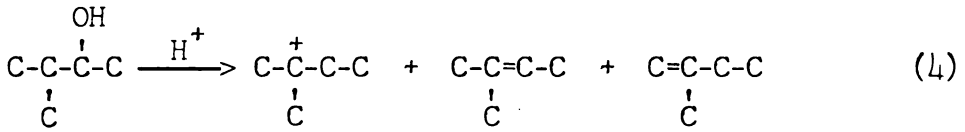
(2)

III

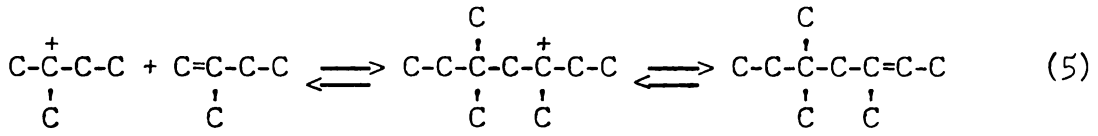


III. (3)

The second system was also described by Whitmore and his students.[52]

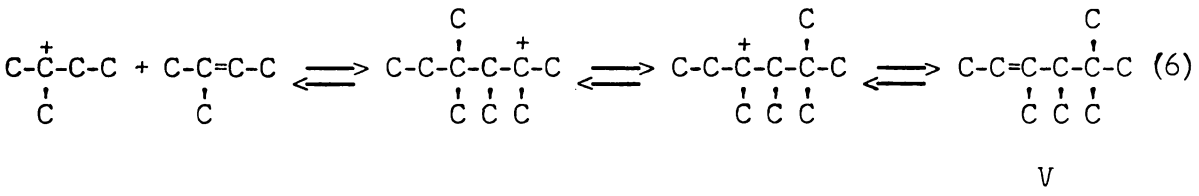


(4)



(5)

IV



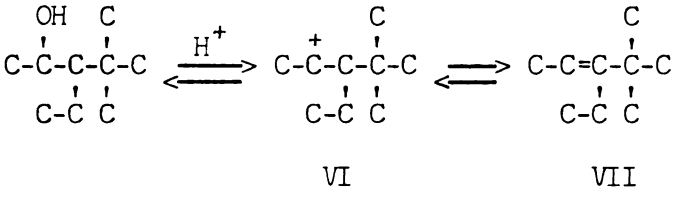
(6)

V

The only decenes found were IV and V. Careful fractional distillation separated them: 45% yield of IV and 35% yield of V. The pure fractions were ozonized and identified as carbonyl derivatives.

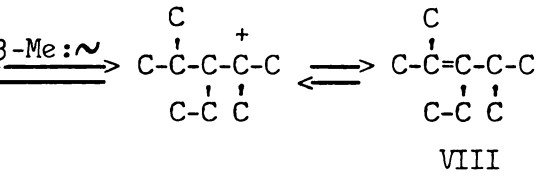
Whitmore's work[52] has been criticized by Johnson,[71] who treated t-amyl alcohol with sulfuric acid, hydrogenated the mixture of decenes, and found by analytical distillation that five decanes were present. Whitmore's failure to find more decenes was explained by resistance of some of them to ozonolysis, incomplete separation of decenes by distillation, and presence of smaller amounts of rearranged products because more dilute sulfuric acid was used.

In 1950 Mosher and Cox[53] reported a rearrangement which they claimed had to be explained as a 1,3-methyl shift. They said that successive 1,2-alkyl shifts would give a different product, IX, which was not found.



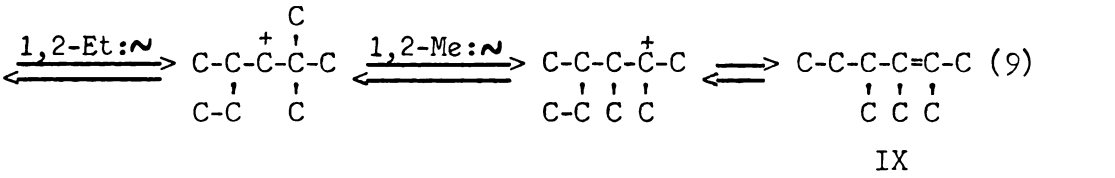
(7)

VI VII



(8)

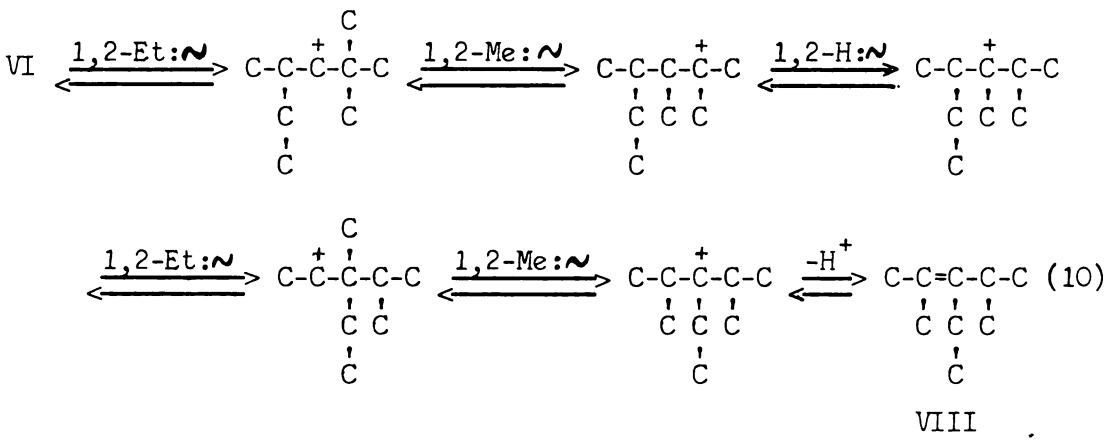
VIII



(9)

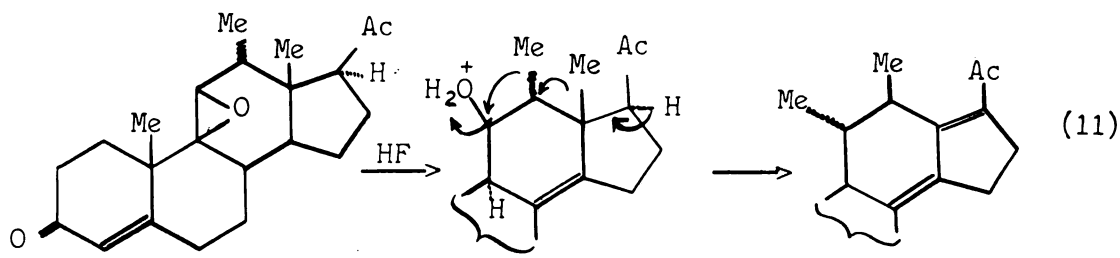
IX

The product obtained was a mixture of three parts of VII and four parts of VIII. Product analysis was by ozonolysis of the mixture and identification of acetaldehyde, acetone, and ethyl isopropyl ketone as their derivatives. Ethyl t-butyl ketone was not mentioned. It would be worthwhile to repeat the rearrangement of VI and study the products with newer instrumental methods, especially gas chromatography. However, it is not necessary to presume that VI ⟶ VIII proves the existence of a 1,3-methyl shift. Other reasonable mechanisms can be written for VI ⟶ VIII. For example,



(10)

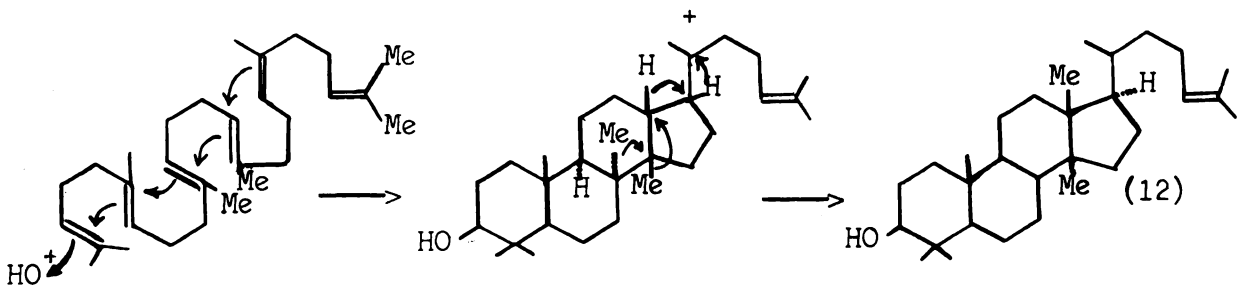
The literature is sprinkled with rearrangements which are 1,2; 1,2-methyl shifts rather than 1,3-shifts. One example[54] is that of 12α-methyl-9β,11β-oxidoprogesterone, X:



(11)

X XI XII

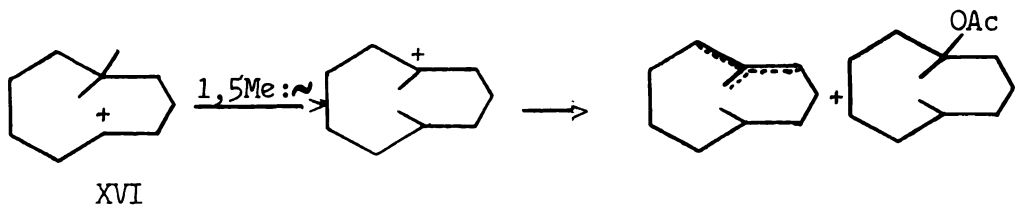
Another case is the final steps in the biosynthesis of lanosterol, XV, from squalene, XIII:[55]



XIII XIV XV

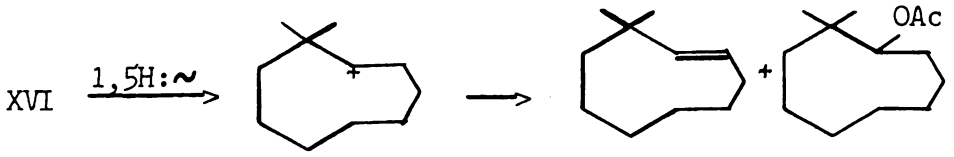
Elaborate work with ^{13}C-labeled precursors led to the conclusion that the mechanism of XIV ⟶ XV was 1,2; 1,2-methyl shifts, not 1,3.

There seem to be no alkyl or aryl transannular shifts.[56] For example, the search for a 1,5-methyl shift in the acetolysis of 5,5-dimethylcyclononanol tosylate was fruitless; infrared analysis showed that there was less than five per cent (if any) 1,5-methyl shift (equation 13).[57]



(13)

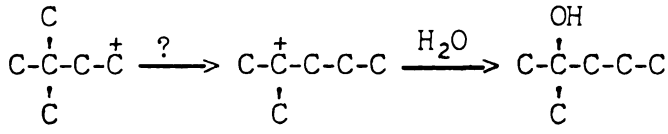
XVI



(14)

Meinwald[70] conclusively proved that a 1,5-methyl migration does not occur in the acid-catalyzed rearrangement of cinenic acid. Letsinger[49] found 1,5-phenyl and 1,5-hydride but no 1,5-methyl shift in peri-substituted naphthalenes.

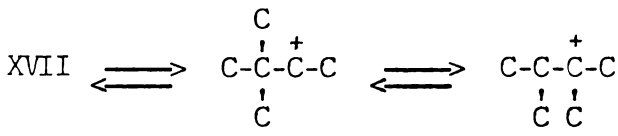
A model which is simpler than those mentioned above and which favors the possibility of a 1,3-methyl shift in an acyclic system is the neopentylcarbinyl cation:



(15)

XVII XVIII XIX

It is to be expected that 1,2-hydride and 1,2-methyl shifts also occur:



(16)

XX XXI

Thus the products should include alcohols and olefins formed from ions XVIII, XX, and XXI.

RESULTS AND DISCUSSION

The deamination of neopentylcarbinylamine gave several products. Their analysis is outlined in Tables Ic and IIc. Identification of products was by means of gas chromatography. Samples of known alcohols were run at the same conditions as neat samples and as additives to the mixtures of reaction products. Generally the retention times varied slightly, but the peaks were easily recognized by their sizes, shapes, and order of appearance.

In the first deamination, using conditions based on those of Roberts *et al.*,[40] the major product was the unrearranged alcohol, neopentylcarbinol. Because the yield was low, the reaction conditions were changed. In the second deamination the acid was added to the aqueous mixture of ammonium salt and sodium nitrite.[73] In this case the major product was *t*-butyl alcohol and the over-all yield was still low.

Two deaminations were performed with α,α-dideuterated amine, using the original reaction conditions. After three hours of reaction the main product was neopentylcarbinol. Extended contact with aqueous acid increased the amount of *t*-butyl alcohol and dimethylisopropylcarbinol.

Several attempts to identify the minor products were unsuccessful, because the quantities were too small for collection of fractions by gas chromatography. Some of the compounds shown to be absent are listed in Table IIc.

Complete gas chromatographic separation of the two tertiary alcohols, dimethylisopropylcarbinol and dimethylpropylcarbinol was difficult to

Table Ic. Deamination products of neopentylcarbinylamine and neopentylcarbinylamine-1,1-d_2 (gas chromatographic analyses)[a]

Compound	Time (min.)	First Run[b] (%)	Second Run[c] (%)	Third Run[d] (% at 3 hr.)	Run[d] (% at 24hr.)	Fourth Run[d]
Gases	1.2	trace	1.6	--	1.6	8
(Isobutylene)[e]	1.4	trace	0	0	0	0
t-Butylethylene	1.6	trace	0	2	0.2	7
(2,3-Dimethyl-1-butene)	3.0	0	1.5	0.3	0	2
Tetramethylethylene t-Butyl nitrite }	4.5	1.6	0.13	1.2	0.3	6
	7.5	2.3	1.4	4.6	3.2	5
t-Butyl alcohol	11	0.4	56	21	51	9
	14	0.3	6.4	0.8	13	4
(t-Butyl nitrate)	17	2.2	1.5	0.4	0	2
(2-Nitro-2-methylpropane)	18	1.6	1.1	4.6	1.7	2
	22	0.2	0	0	0.1	1
Dimethylisopropylcarbinol	39	8.3	16	14	23	2
Dimethylpropylcarbinol	41	<0.2	0	0	0	0
Methyl-t-butylcarbinol	48	5.4	1.4	1.3	0	2
(Neopentyl cyanide)	54	1.3	1.4	0	0	2
(2,3-Dimethyl-2-butylnitrate)	76	5	0.5	6.5	2	7
(2-Nitro-2,3-dimethylbutene)	88	6	1.8	0	1	0
(Neopentylcarbinyl nitrite)	100	0	1.3	0	0	0
Neopentylcarbinol	120	68	11	43	2	40

[a]Using 10 ft. x 1/4 in. 20% Carbowax column in an Aerograph at 70° and 30 p.s.i.

[b]Distillate from unlabeled amine.

[c]Oil layer (not distilled) from unlabeled amine.

[d]Oil layer (not distilled) from labeled amine.

[e]Tentative identifications are given in parentheses.

Table IIc. Compounds shown to be absent in deamination products of neopentylcarbinylamine. (Analyses under the conditions of Table Ic.)

Compound	Time (min.)
2-Methyl-1-pentene	2.8
2-Methyl-2-pentene	3.1
2-Ethyl-1-butene	3.2
cis-3-Methyl-2-pentene	3.4
trans-3-Methyl-2-pentene	3.5
3-Methyl-3-pentanol	37
2-Methyl-3-pentanol	57
4-Methyl-2-pentanol	58
n-Heptanol	250

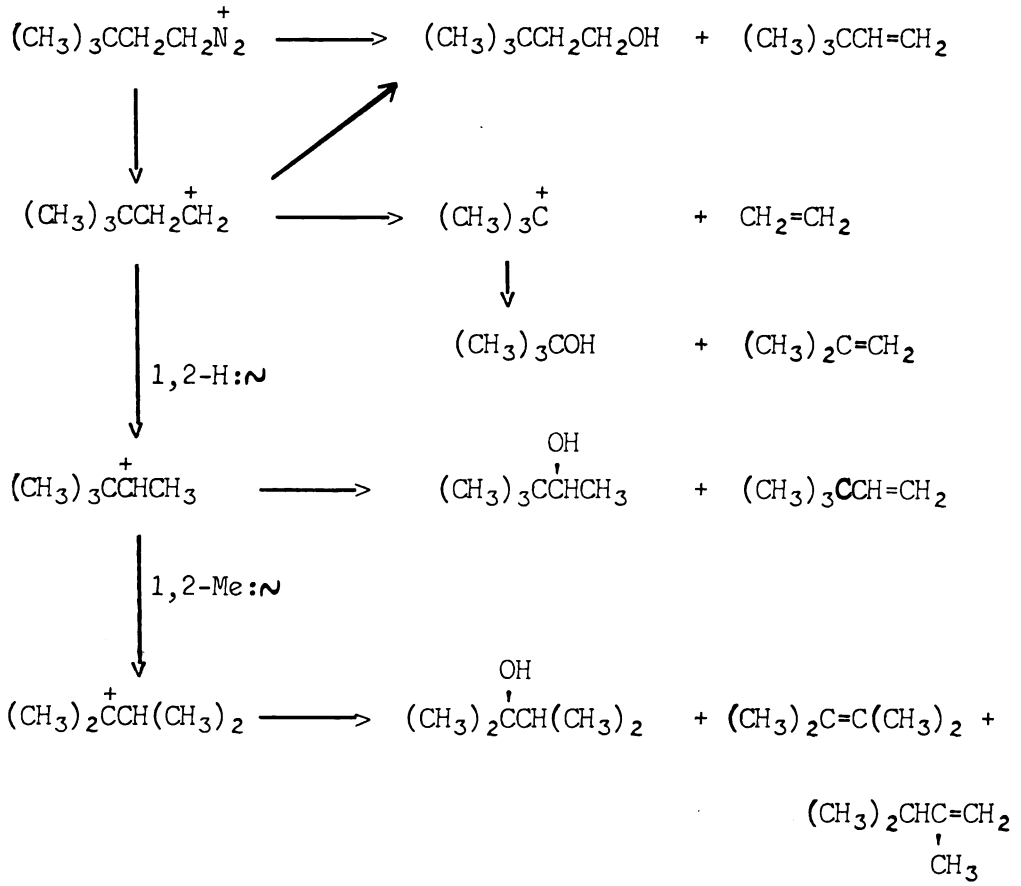
achieve. The analytical results are only good enough for the unequivocal statement that less than 0.2% of the deamination product was the latter alcohol.

The analysis of olefins by gas chromatography was not definitive. No attempt was made to collect ethylene, which must have formed when neopentylcarbinyl ions cleaved to form t-butyl cations. The peak at 1.4 min. is probably due to isobutylene. The peak at 3.0 min. is probably due to 2,3-dimethyl-1-butene. The olefins 2-methyl-1-pentene and 2-methyl-2-pentene had retentions times 2.8 and 3.1 min., respectively.

The retention times of t-butyl nitrite and tetramethylethylene were too close (4.4 and 4.8 min. under the conditions used) for conclusive determination of each. It is likely that t-butyl nitrate and 2-nitro-2-methylpropane are represented by the partially resolved pair of peaks at 17 and 18 min.

The compounds at 76 and 88 min. are probably 2,3-dimethyl-2-butyl nitrate and 2-nitro-2,3-dimethylbutane. The broad peak around 54 min. might be due to a small impurity of neopentyl cyanide. Dimethylisopropylcarbinyl nitrite had retention time 33 min., but small amounts were not separable from the parent alcohol. Dimerization products (branched dodecenes) are possible but not very likely. They would have fairly long retention times in view of their boiling in the range 180-200°; 1-dodecene, b.p. 213°, had retention time 123 min.

From these data it is evident that a 1,3-methyl shift did not occur in the deamination of neopentylcarbinylamine. The following mechanistic scheme is a reasonable representation of the reactions of neopentylcarbinyldiazonium ion. (The scheme does not include the formation of the esters and the nitroalkanes.)



The purpose of the deuterium labeling was to determine whether there was a t-butyl shift. Before these experiments were completed, however, it was found that Saunders[96] had done a similar study. He diazotized neopentylcarbinylamine-1-^{14}C and separated the products by distillation. The neopentylcarbinol-^{14}C had less than one percent rearrangement of its radiocarbon label. Only two products were found--a 20% yield of neopentylcarbinol and a 16% yield of dimethylisopropylcarbinol.

EXPERIMENTAL

Synthesis of Neopentyl Cyanide

Dimethylsulfoxide (m.p. 18°; Matheson) was dried over calcium hydride overnight and vacuum distilled from a 60° water bath.[60] Sodium cyanide (Baker reagent) was dried[58] for 24 hours in a 110° oven. Neopentyl chloride (K and K Laboratories) gave a single peak on a silicone SE-30 gas chromatographic column, but this is not proof of purity; t-amyl chloride had the same retention time on this column. The neopentyl chloride was therefore tested by shaking it with 0.10 M silver nitrate. There was no visible reaction. (t-Amyl chloride reacts instantaneously.)

Forty grams of dried sodium cyanide was stirred with 230 ml. of freshly distilled dimethylsulfoxide. The suspension was heated to 90° on a steam bath and stirred while 53.30 g. of neopentyl chloride was added without heating. There was no evidence of reaction. On heating with a mantle the reaction mixture (yellow liquid and white suspended solid) quickly darkened to yellow-brown after it reached reflux temperature (85°). Stirring and heating (100 to 130°) were continued for 24 hours. When it cooled to room temperature it was a brown slush, too thick to pour, so 350 ml. of water was added to it. After separation of the organic layer the water layer was extracted with 100 ml. portions of ethyl ether. The organic layer was combined with the ether extracts, washed three times with 50 ml. portions of saturated aqueous sodium chloride, dried over calcium chloride, and distilled through a 6-inch vigreux column. After collection of fractions containing ether and neopentyl chloride, the water was turned off and the condenser

jacket drained, because the fraction at 134-135° solidified as it cooled to room temperature. (Neopentyl cyanide boils[61] at 137° and melts at 28-30°.) Obtained was 18.79 g. The lower boiling fractions were redistilled slowly and another 2.82 g. was collected at 133-135°. Thus the total yield of neopentyl cyanide was 21.61 g. (44.4% yield) of colorless solid. Some unreacted neopentyl chloride (15%) was recovered.

Reduction of Neopentyl Cyanide

A colorless solution of 8.75 g. (0.0900 mole) of neopentyl cyanide in 25 ml. of dry ether was added in 25 min. to a stirred and ice-cooled mixture of 3.4 g. (0.090 mole) of powdered lithium aluminum hydride in 250 ml. of dry ether. (The ether had just been distilled from lithium aluminum hydride.) There was no sign of reaction occurring. The mixture was stirred and refluxed (steam bath) for four hours. After cooling it with ice, it was successively treated with 4 ml. of water added dropwise, 3 ml. of 20% aqueous sodium hydroxide, and 14 ml. of water. The clear ether layer was decanted, and the white solid residue was extracted three times with 30 ml. volumes of ether. The ether solutions were dried over calcium sulfate, filtered, and distilled through a 5-inch packed column. After removal of most of the ether at 35°, there was 25 ml. of residue, which was distilled in a smaller apparatus. Obtained at 111-112° (745 mm.) was only 3.96 g. of neopentylcarbinylamine with n_D^{23} 1.4130. (Theoretical yield: 9.11 g.; literature[92] values 112.8-.9° (745) and n_D^{25} 1.4122.) More of the amine was recovered from the lower-boiling fractions by gradual addition of 35% perchloric acid until the liquid was acidic to pHydrion indicator paper. The white, deliquescent crystals were first dried in an evacuated desiccator. When

heated on a Fisher hot stage, they lost liquid around 160°, and the remaining dry, white crystals melted at 280-284°. Recrystallization from 30 ml. of n-heptanol, using 750 ml. of 30-60° pet. ether, gave 8.50 g. with m.p. 290-294°. The yield of the purified ammonium salt from the nitrile was 46.9%.

First Deamination of Neopentylcarbinylamine

(The proportions of reactants were the same as those used by Roberts.[40])

A mixture of 8.07 g. of neopentylcarbinylammonium perchlorate (0.040 mole) and 4.80 g. of 71.6% perchloric acid (0.0343 mole) was diluted with water to 70 ml. To this mixture was added 5.93 g. of sodium nitrite in 10 ml. of water, with magnetic stirring, during 20 min. The reaction flask was in a 1 l. 25° water bath during the reaction. Only a faint blue color was seen in the reaction mixture. During the two hours of stirring after addition an oil formed above the aqueous layer. The mixture was saturated with sodium chloride, 20 ml. of ether was added, and the layers were separated. The aqueous layer was extracted three times with 20 ml. volumes of ether. The combined ether solutions were dried over calcium sulfate. As the ether dried, 1.95 g. of unreacted ammonium salt precipitated. On distillation the filtered ether solution gave 0.98 g. of colorless liquid with odor of camphor and 1.03 g. yellow solid residue. The distillate was analyzed by gas chromatography. (See Table Ic.) The deamination yield was only about 25% with recovery of 37% of the unreacted ammonium salt.

Second Deamination of Neopentylcarbinylamine

Zollinger[72] quotes the statement of Austin[73] that the correct method of deamination is slow addition of mineral acid to a solution of the alkylammonium salt and sodium nitrite. This method was tried with about 1.6 g. of impure neopentylcarbinylammonium perchlorate (m.p. 245-255°). This salt (0.008 mole) and 1.66 g. of sodium nitrite (0.024 mole) were dissolved in water, forming 33 ml. of solution. A capillary dropper was inserted through a cork in the sidearm of a 50 ml. reaction flask holding the solution. Dilute perchloric acid (0.96 g. of the 71.6% acid diluted to 5.6 ml.; 0.0069 mole) was added through the capillary, which extended below the surface of the stirred solution, in five minutes.

The mixture was stirred for two hours at 25°. It was then saturated with sodium chloride. The yellow oil layer was removed with a dropper and dried over calcium sulfate. It weighed 0.2 g. Analysis of this product was by gas chromatography. (See Table Ic.)

Preparation of Neopentylcarbinylammonium-1,1-d_2 Perchlorate

An ether solution of 9.30 g. of neopentyl cyanide (0.0958 mole) was reduced with 4.02 g. of lithium aluminum deuteride (0.0958 mole). The deuterated amine was converted to its perchlorate salt (m.p. 281-284° (dec.)), which was not recrystallized. The yield from nitrile to ammonium salt was 78.8%.

Third Deamination (Using Deuterated Amine)

One twentieth of a mole (10.18 g.) of neopentylcarbinylammonium-1,1-d_2 perchlorate was stirred with 6.00 g. of 71.6% perchloric acid (0.0429

mole) diluted to 200 ml. Almost all of the salt dissolved. A solution of 7.41 g. of sodium nitrite (0.1076 mole) in 10 ml. of water was added in twenty minutes. There was little evidence of reaction. After three hours a sample of the small oil layer was removed and analyzed by gas chromatography. (See Table Ic.) One hour later another 6.00 g. of 71.6% perchloric acid and then 7.41 g. of sodium nitrite in 10 ml. of water were added dropwise. Five hours later a third addition of 6.00 g. of acid was made. The mixture was stirred for thirteen hours and then treated with 7.41 g. of sodium nitrite. Indicator paper showed that the pH changed from 3 to 5 on addition of the nitrite. The reaction mixture was saturated with sodium chloride 24 hours after the reaction was started. The oil layer was separated and dried over calcium sulfate. There was 1.72 g. (See Table Ic.)

Gases evolved during the reaction were passed through two dry ice traps. The second was empty. The first held blue liquid (largely nitrogen sesquioxide), which was washed by passing it through a 10% solution of sodium hydroxide. Obtained in a dry ice trap was about fifty microliters of yellow liquid. Gas chromatographic analysis showed that it had the same composition as the oil layer.

Fourth Deamination (Using Deuterated Amine)

Five grams (0.0246 mole) of neopentylcarbinylammonium-1,1-d_2 perchlorate was deaminated under conditions similar to those of Roberts,[40] avoiding the excess acid which rearranged the product in the third run. The 5.00 g. of salt and 2.94 g. of 71.6% perchloric acid was diluted to a volume of 40 ml. with water, the minimum amount which would permit the magnetic stirrer to turn in the sediment of undissolved salt. A

solution of 3.64 g. of sodium nitrite (0.053 mole) in 5 ml. of water was added in 20 min. The mixture became pale blue and evolved colorless and brown gases. The gases were passed through a vigreux column, a condenser, a gas-washing bottle containing 200 ml. of 10% sodium hydroxide solution, an empty bottle, and two dry ice traps.

After two hours of stirring at 25°, the reaction mixture was saturated with sodium chloride. The 1.25 g. of yellow oil layer was removed with a capillary dropper and dried over calcium sulfate, giving 0.83 g. of oil. (See Table Ic for its analysis.)

The dry ice traps were completely empty. The alkali washing solution was saturated with sodium chloride and extracted three times with ether. Distillation of the ether extracts gave 0.30 ml. of liquid which was about half methyl-t-butylcarbinol and half dimethylisopropylcarbinol.

Ether extraction of the aqueous part of the reaction mixture gave 0.40 g. of yellow slush which was washed with benzene, leaving 0.20 g. of colorless crystals (the unreacted ammonium perchlorate). The benzene solution contained approximately equal amounts of methyl-t-butylcarbinol and dimethylisopropylcarbinol.

Preparation of Known Compounds for Gas Chromatography

Pyrolysis of 2.2 g. of bis(1,1-dimethylbutyl) oxalate in an oil bath at 140-150° gave 0.15 g. of olefin in a receiver cooled in dry ice-trichloroethylene. There were two products: 40% 2-methyl-2-pentene at 2.8 min. and 60% 2-methyl-1-pentene at 3.1 min. on the gas chromatographic column used for product analysis.

Five millimoles of t-butyl alcohol was converted to its nitrite ester.[38]

A mixture of 0.07 g. of neopentylcarbinol, 0.12 g. of methyl-t-butylcarbinol, and 0.18 g. of dimethylisopropylcarbinol was treated by the same conditions.[38] The products were t-butyl nitrite and t-butyl alcohol from the primary alcohol, a compound with retention time 14 min. from the secondary alcohol, and apparently dimethylisopropylcarbinyl nitrite with retention time 33 min.

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