The remainder of the benzyl halide undergoes the coupling reaction forming ethane and dibenzyl according to the following equation: $2C_6H_5CH_2X + 2CH_3MgI = CH_3CH_3 + C_6H_5CH_2CH_2C_6H_5 + 2MgIX$.

An apparatus is described for measuring the gas evolved by reactions carried out in ethyl ether.

CAMBRIDGE, MASSACHUSETTS

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

THE VALENCE OF NITROGEN IN QUATERNARY AMMONIUM COMPOUNDS

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In quaternary ammonium salts nitrogen has usually been considered as having a valence of five but it has also been recognized that the fifth valence is of a type different from the other four. The older ideas concerning the stereochemistry of quinquivalent nitrogen as advanced by Van't Hoff,[2] Willgerodt[3] and Bischoff[4] predicted many isomers that have never been obtained experimentally. Werner[5] first advances the idea that in ammonium compounds the fifth group is not held directly by the nitrogen atom but rather by the entire ammonium group. He thought that the fourth valence might be different from the first three, but pointed out that if the four are identical, the stereochemistry of nitrogen in the ammonium ion would be the same as that of carbon. This idea is borne out by all the evidence available. Mills and Warren[6] have recently demonstrated that the pyramidal formula of Bischoff is impossible and that the tetrahedral structure of the ammonium ion is probably correct.

Lewis[7] states that in ammonium compounds nitrogen shares four pairs of electrons with other atoms, that is has a valence of four, and that the ammonium ion holds the fifth group by a polar or electrostatic bond. While he believes that phosphorus may share ten electrons, that is, have a true valence of five, as in phosphorus pentachloride, he does not think the shell of the nitrogen atom can ever accommodate more than eight electrons.

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[1] This communication is an abstract of a thesis submitted by F. D. Hager in partial fulfilment of the requirements for the degree of Doctor of Philosophy in Chemistry at the University of Illinois.

[2] Van't Hoff, "Ansichten über die organischen Chemie," Vieweg u. Sohn, Braunschweig, **1878**, vol. 1, p. 80.

[3] Willgerodt, *J. prakt. Chem.*, [2] **41**, 291 (1890).

[4] Bischoff, *Ber.*, **23**, 1967 (1890).

[5] Werner, "Neuere Anschauungen auf dem Gebiete der Anorganischen Chemie," Vieweg u. Sohn, Braunschweig, **1905**, p. 96; "Lehrbuch der Stereochemie," Fischer, Jena, **1904**, p. 311.

[6] Mills and Warren, *J. Chem. Soc.*, **127**, 2507 (1925).

[7] Lewis, "Valence and the Structure of Atoms and Molecules," Chemical Catalog Co., New York, **1923**, p. 111.

W. A. Noyes[8] has recently restated his views concerning the valence of nitrogen in connection with a discussion of the properties of the amine oxides. He points out that there is no reason save the octet hypothesis to suppose that nitrogen may not have a valence of five, that is, be able to share ten electrons with other atoms. He believes that the fifth (polar) atom or group is held by a static charge of the nitrogen atom and not by the ammonium group as a whole.

In all of the ammonium compounds that have been studied carefully, the groups attached to the nitrogen have differed widely in character. It was thought that perhaps more definite information concerning the nature of the fifth valence of nitrogen could be obtained from a study of compounds related to those reported by Schlenk and Holtz.[9] These investigators treated tetramethylammonium chloride with sodium-benzyl and sodium-triphenylmethyl and thus obtained compounds in which the nitrogen is apparently attached to five hydrocarbon radicals. The compounds thus obtained, tetramethylammonium-benzyl and tetramethylammonium-triphenylmethyl, are highly colored and very reactive. They react with water to give tetramethylammonium hydroxide and toluene and triphenylmethane, respectively. Tetramethylammonium-triphenylmethyl in pyridine solution conducts an electric current. There is still considerable difference between the methyl group on the one side and the benzyl or triphenylmethyl group on the other and one cannot be entirely sure from the reactions of these compounds whether the fifth group is held by a valence different from the other four.

An attempt has been made to extend this work of Schlenk and Holtz to give compounds in which five closely related aliphatic groups were attached to the nitrogen atom. Lachman[10] attempted to prepare penta-ethyl-nitrogen by the action of zinc-ethyl on tetra-ethylammonium iodide and on triethylamine dibromide. Neither reaction was successful. In this work lithium alkyls[11] were used in place of the sodium derivatives since they can be more easily obtained in a pure condition. It seemed logical to believe that the preparation of R_4NR' by the following methods, $R_4NX + LiR' \longrightarrow R_4NR' + LiX$ and $R_3R'NX + LiR \longrightarrow R_3R'NR + LiX$, would lead to the formation of isomers if the fifth valence of nitrogen were different from the other four, whereas, if the valence shell of the nitrogen may be increased to ten equivalent electrons, the two compounds would be identical.

In our experimental work no penta-alkyl nitrogen could be isolated. The lithium alkyls reacted with more or less ease with the quaternary

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[8] Noyes, This Journal, **47**, 3025 (1925).

[9] (a) Schlenk and Holtz, *Ber.*, **49**, 603 (1916); (b) **50**, 274 (1917).

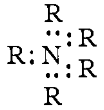
[10] Lachman, *Am. Chem. J.*, **18**, 372 (1896).

[11] Ref 9 b, p. 271.

ammonium halides to give lithium halides. No color was developed during the reaction between lithium-ethyl, -*n*-butyl, -*iso*-amyl or -*n*-heptyl and the tetra-alkylammoniumhalides. In most of our experiments the only organic compounds that could be isolated in the pure state were tertiary amines. There is evidence that hydrocarbons are produced in all of the experiments, but as the reactions were run in petroleum ether, it was usually impossible to isolate them.

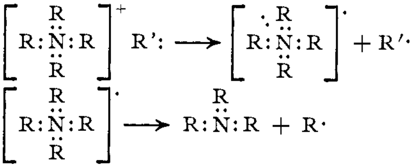
The following reactions have been carried out and the tertiary amines formed have been identified.

$$LiC_2H_5 + (C_2H_5)_3C_4H_9NBr \xrightarrow{70^\circ} (C_2H_5)_2NC_4H_9$$
$$LiC_2H_5 + (C_2H_5)_3C_4H_9NBr \xrightarrow{-70^\circ} (C_2H_5)_2NC_4H_9 + (C_2H_5)_3N$$
$$LiC_5H_{11}\ (iso) + (C_2H_5)_3C_4H_9NBr \xrightarrow{-70^\circ} (C_2H_5)_2NC_4H_9 + (C_2H_5)_3N$$
$$LiC_4H_9 + (C_2H_5)_4NBr \longrightarrow (C_2H_5)_3N$$
$$LiC_4H_9 + (C_2H_5)_3C_6H_5CH_2NBr \longrightarrow (C_2H_5)_2NCH_2C_6H_5$$
$$LiC_4H_9 + (C_4H_9)_3C_7H_{15}NI \longrightarrow (C_4H_9)_2NC_7H_{15}$$
$$LiC_7H_{15} + (C_4H_9)_4NI \longrightarrow (C_4H_9)_3N$$

If, as seems rather likely, a penta-alkyl nitrogen atom is formed as the first product in these reactions, it cannot have the structure  $R:\overset{R}{\underset{R}{\ddot{N}}}\begin{smallmatrix}:R\\:R\end{smallmatrix}$ in which the valences are equivalent, since such a compound should give some tertiary amine containing the alkyl group introduced through the lithium alkyl. This alkyl group never appears in the tertiary amine formed in any of the above reactions unless it was also present in the original quaternary ammonium salt.

A much better explanation of these reactions is that a penta-alkyl nitrogen is formed in which one of the alkyl groups is held by a polar valence to the ammonium ion $[R_4N]^+R'^-$. This compound then at once breaks down into more stable products. Two mechanisms for this decomposition seem more probable than any others. The penta-alkyl nitrogen might first separate into the two ions $[R_4N]^+$ and R'^-. Then the ammonium ion, $[R_4N]^+$, would decompose further to give R_3N and R^+. One would then expect the positive R ion to combine with the negative R' ion to give a hydrocarbon RR'.

The second possible mechanism of decomposition of the penta-alkyl nitrogen involves the intermediate formation of free alkyl groups and a tetra-alkyl ammonium "metal." This may be best shown by the following formulas.



$$\left[\begin{array}{c}R\\R:\ddot{N}:R\\\ddot{R}\end{array}\right]^{+}R'{:}\longrightarrow\left[\begin{array}{c}\cdot\,R\\R:\ddot{N}:R\\\ddot{R}\end{array}\right]^{\cdot}+R'\cdot$$
$$\left[\begin{array}{c}R\\R:\ddot{N}:R\\\ddot{R}\end{array}\right]^{\cdot}\longrightarrow R:\overset{R}{\ddot{N}}:R + R\cdot$$

The free alkyl groups undoubtedly would then undergo disproportionation[12] giving a mixture of saturated and unsaturated hydrocarbons.

In order to see which of these mechanisms is correct, an attempt was made to isolate the hydrocarbons produced in the last two reactions mentioned above; this was unsuccessful. Then the reaction between lithium-ethyl and tetra-ethylammonium bromide was carried out in a heavy paraffin oil solution. The very small quantity of gas produced as a by-product in preparation of the lithium-ethyl was removed before mixing this solution with the tetra-ethylammonium bromide. If the first mechanism mentioned above is correct, butane should be formed in the decomposition of the penta-ethyl nitrogen, whereas if the second mechanism is correct, a mixture of ethane and ethylene should be formed. The reaction was carried out in an apparatus devised so that the gas formed could be collected over water. This gas on analysis was found to consist of 55–56% of ethane and 36–37% of ethylene; no butane was formed. In the collection of the gas a small amount of air was inadvertently admitted and this accounts for the failure of the analysis to add to 100%. One would expect to find the two gases in equivalent amounts. The greater solubility of ethylene in water may account for the loss of some of this gas.

The compounds which Schlenk and Holtz[9] have prepared are stable because the benzyl and the triphenylmethyl groups are stable as ions. That these groups do give fairly stable ions is shown by such facts as the conductance of solutions of sodium-triphenylmethyl[13] and sodium-benzyl.[9b] There is no exchange of groups between the fifth and any of the other four valences since triethylbenzylammonium bromide reacts with lithium-*n*-butyl in the same way that the simple tetra-alkylammonium salts react with lithium alkyls. Yet, as Schlenk and Holtz[9] have shown, when the benzyl group is introduced on the fifth valence, a fairly stable but very reactive ammonium compound is obtained.

These experiments lead to the conclusions that the reaction of a lithium alkyl with a quaternary ammonium salt does not give a compound in which nitrogen has five equivalent valences, and that an alkyl group is unstable as an ion when held by the polar valence of an ammonium group.

In studying these reactions the technique of handling lithium alkyls has been considerably improved. The method described in the experimental part avoids the use of a nitrogen atmosphere and substitutes one of the hydrocarbons that is used as a solvent in the preparation. This offers less opportunity for side reactions. The new lithium alkyls that were prepared were not isolated but were analyzed in solution and used directly.

It is interesting to note that quaternary ammonium bromides apparently react much more readily with lithium alkyls than do the iodides. Also,

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[12] Ziegler and Schnell, *Ann.*, **437**, 233 (1924).

[13] Schlenk and Marcus, *Ber.*, **47**, 1678 (1914).

two of the quaternary ammonium iodides studied, tetra-*n*-butylammonium iodide and tri-*n*-butyl-*n*-heptylammonium iodide, are quite insoluble in water and are very soluble in organic solvents.

Several new compounds were prepared in this work and they are described in the experimental part.

Experimental Part

Preparation of Soluble Lithium Alkyls.—The general method of Schlenk and Holtz[11] was followed in the preparation of the lithium alkyls. However, it was found more convenient to modify their apparatus and to use the vapors of the solvent in place of nitrogen to exclude air and moisture. The most convenient solvents are various fractions of petroleum distillate that have been thoroughly treated first with concd. sulfuric acid, then with water, followed by dil. potassium permanganate solution. The solvent should not boil over a range of more than 20°. Before use it was always dried and stored over sodium.

Much of the success of preparing lithium alkyls depends on the fineness of the chips of lithium used in the reaction, since the reaction must all take place on the surface. The pieces of lithium must be scraped to remove the coating of oxide and then sliced under purified ligroin (b. p. $> 100°$) into shavings not more than 0.5 mm. thick or 8 mm. in diameter. Since lithium floats in ligroin, the slices of lithium must be collected in an inverted tube filled with ligroin in order to avoid oxidation. When finely shaved and carefully protected from the air, over half of the lithium used can be converted to the alkyl derivative.

The appropriate mercury dialkyl is placed in the preparation flask (Fig. 1) and covered with a little solvent. The finely sliced lithium is added and then more solvent until the flask is about 80% full. The flask is connected to a suction pump and heated near the top. About 50 cc. of solvent is distilled to remove the air completely from the flask and while the solvent is still boiling the flask is sealed. The flask is then put aside until the reaction is complete. For the preparation of lithium-ethyl, the reaction flask should be incubated at 70° for 3 days, for lithium-*n*-butyl, -*iso*-amyl or -*n*-heptyl at 50° for three days or at 25° for six days.

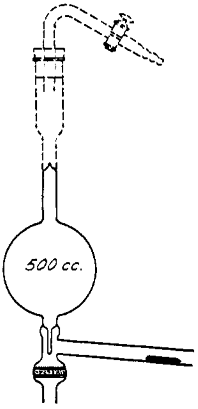

Fig. 1.

The preparation flask is then sealed to the calibrated measuring flask (Fig. 2). The sealed glass capsule of mercury which is later used to open the reaction flask is put in place and the air is expelled from the measuring flask through the valve side arm by displacement with solvent vapor or by evacuating to 10^{-4} mm. or less by means of a mercury-vapor pump.

The side arm is then sealed, the tip of the reaction flask is broken by dropping the mercury slug and the lithium alkyl solution is filtered into the measuring flask. This filtration may be hastened by gently warming the preparation flask.

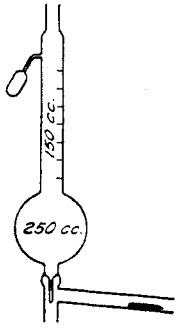

Fig. 2.

After the filtration is complete, the measuring flask is cooled until the internal pressure is below atmospheric pressure and sealed just below the filter. After thoroughly mixing and measuring the contents of the flask, the sampling bulb is filled to the mark with the solution and sealed off. This sample bulb is broken under water and the lithium hydroxide thus formed is titrated. This gives an accurate measure of the amount of lithium alkyl formed in the preparation flask.

The Reaction between a Lithium Alkyl and a Quaternary Ammonium Salt.—The measuring flask containing the lithium alkyl is sealed to the reaction flask (Fig. 3). Through the open side arm the dry, finely powdered ammonium salt (dried at 100° at 5 mm.) and some glass beads are introduced into the top compartment of the reaction flask, this side arm sealed and the flask is freed from air and closed as described before. After the lithium allyl solution has been transferred to the reaction flask it is sealed off from the measuring flask and the solution is cooled to the desired temperature and poured over the quaternary ammonium salt by inverting the reaction flask. The flask is rotated occasionally to prevent the formation of lumps. After standing the desired length of time (two to ten days) the flask is opened, the contents are poured into water and the amine and solvent are steam-distilled. The distillate is acidified and evaporated to dryness and the amine salt is identified.

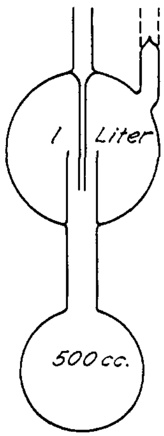

Fig. 3.

Lithium-ethyl with Triethyl-*n*-butylammonium Bromide.—Lithium-ethyl, prepared from 2 g. of lithium and 31 g. of diethyl-mercury in about 150 cc. of ligroin was allowed to react at 70° with 11 g. of triethyl-*n*-butylammonium bromide. Considerable pressure was developed and one run of this size exploded. The volatile amine obtained in this reaction was converted to the hydrobromide, dried and analyzed.

Anal. Subs., 0.4374: 37.8 cc. of 0.0550 *N* $AgNO_3$. Calcd. for $(C_2H_5)_2C_4H_9N.HBr$; Br, 38.03. Found: 37.97.

A duplicate run, in which the first part of the reaction was carried out at about —70° in a carbon dioxide snow and acetone slush cooling-bath and gradually allowed to come to room temperature during about 72 hours, gave a mixture of volatile amines which were converted to the hydrochlorides and analyzed.

Anal. Subs., 0.5668: 69.05 cc. of 0.0528 *N* $AgNO_3$. Calcd. for $(C_2H_5)_3N.HCl$: Cl, 25.76. Calcd. for $(C_2H_5)_2C_4H_9N.HCl$: Cl, 21.40. Found: 22.81.

Lithium-*iso*-Amyl with Triethyl-*n*-butylammonium Bromide.—This reaction was carried out exactly as the preceding one. Lithium-*iso*-amyl was prepared from 2 g. of lithium and 38 g. of di-*iso*-amyl-mercury in 150 cc. of ligroin. It was not isolated or analyzed, but at once allowed to react with 12 g. of triethyl-*n*-butylammonium bromide. The volatile amine formed by the reaction was converted into the hydrochloride, dried and analyzed. The analysis indicated a complex mixture so an attempt was made to purify the amine. The hydrochloride was treated with alkali and then with benzenesulfonyl chloride to test for primary and secondary amines. Neither was present. Some water-insoluble amine was then isolated and converted into the hydrobromide. Analysis shows that this is fairly pure diethyl-*n*-butylamine hydrobromide.

Anal. Subs., 0.7604: 69.65 cc. of 0.0528 N $AgNO_3$. Calcd. for $(C_2H_5)_2C_4H_9N.HBr$: Br, 38.03. Calcd. for $(C_2H_5)_3N.HBr$: Br, 43.88. Found: 38.65.

Lithium-*n*-butyl with Tetra-ethylammonium Bromide.—Two reactions were carried out, one at 0° and one at —70°. In each case the materials used were 2 g. of lithium, 32 g. of di-*n*-butyl-mercury, 10 g. of tetra-ethylammonium bromide and 150 cc. of solvent. The volatile amine was the same in each run. The hydrobromide was prepared and analyzed.

Anal. Subs., 0.5885: 58.85 cc. of 0.0550 N $AgNO_3$. Calcd. for $(C_2H_5)_3N.HBr$: Br, 43.88. Found: 43.93.

This experiment shows that the butyl radical from the lithium-butyl is not left on the nitrogen after the reaction.

Lithium-*n*-butyl with Triethylbenzylammonium Bromide.—The materials used were 2.2 g. of lithium, 20 g. of di-*n*-butyl-mercury, 24 g. of ammonium salt and 150 cc. of solvent. The reaction was carried out at about 70°. A slight color developed during the run, but not the deep color described by Schlenk and Holtz[9] in the similar run of sodium-benzyl on tetramethylammonium bromide. The volatile amine was converted to the hydrochloride, dried and analyzed.

Anal. Subs., 0.4743: 44.45 cc. of 0.0528 N $AgNO_3$. Calcd. for $(C_2H_5)_2C_6H_5CH_2N.HCl$: Cl, 17.63. Found: 17.55.

Lithium-*n*-heptyl with Tetra-*n*-butylammonium Iodide.—The lithium-*n*-heptyl was prepared from 5.2 g. of lithium and 48 g. of di-*n*-heptyl-mercury in 300 cc. of solvent. The solvent used was petroleum ether which boiled at 15–36°. Titration of a sample of the solution showed the yield of lithium-*n*-heptyl was practically that calculated based on the di-*n*-heptyl-mercury. The lithium-*n*-heptyl was then allowed to react with 94 g. of dry tetra-*n*-butylammonium iodide which was previously powdered to pass a 30-mesh sieve. The temperature was held at —10° for about 24 hours. No apparent reaction was noted so the mixture was allowed to come to room temperature and stand for four weeks during occasional shaking. In this run an attempt was made to separate all of the products of the reaction. The amine isolated weighed 24 g. It boiled at 212–215°, and agreed in all respects with tri-*n*-butylamine. By distillation of the solvent through a good fractionating column, 8.5 cc. of hydrocarbon boiling at 95–100° was obtained. This agrees fairly well with the boiling point of *n*-heptane. No unsaturation could be detected by tests with bromine in carbon tetrachloride or with potassium permanganate. The hydrocarbon boiling above 100° amounted to only 0.5 cc. and could not be identified. The heptane may have been formed from unreacted lithium-*n*-heptyl since titration of the alkalinity due to the formation of lithium hydroxide by treatment with water showed that 9 cc. of heptane should have been produced.

Lithium-*n*-butyl with Tri-*n*-butyl-*n*-heptylammonium Iodide.—The materials used were 5 g. of lithium and 35 g. of di-*n*-butyl-mercury in 300 cc. of solvent (b. p., 15–36°). The yield of lithium-*n*-butyl was practically quantitative based on the di-*n*-butyl-mercury. The solution of lithium-*n*-butyl was added to a suspension of 95 g. of dry tri-*n*-butyl-*n*-heptylammonium iodide in 250 cc. of solvent. The reaction mixture was allowed to stand for six weeks at ordinary room temperatures. The amine isolated from the filtered solvent before treatment of the reaction mixture with water agreed in properties with known di-*n*-butyl-*n*-heptylamine. No attempt was made to isolate the hydrocarbon on account of the large amount of solvent used in this experiment.

Lithium-ethyl and Tetra-ethylammonium Bromide.—Lithium-ethyl was prepared from 3.6 g. of lithium and 26 g. of diethyl-mercury in about 160 cc. of high-boiling paraffin oil. The solvent had been previously heated over sodium to 225° under a pressure of 10 mm. to remove any volatile material. The air was removed from the reaction flask by a water pump and the flask was sealed and incubated at 70° for three days. A slight accident necessitated a transfer of the contents to a second flask and, before sealing this, it was evacuated to less than 1 mm. pressure. The lithium-ethyl solution was filtered and allowed to react with 40 g. of tetra-ethylammonium bromide in an apparatus constructed in such a way that the gases produced could escape through a mercury trap and then be collected over water. In collecting the gas a small amount of air was admitted.

The gas was then analyzed for saturated and unsaturated hydrocarbons, the former by combustion after the latter had been removed by absorption in 12% fuming sulfuric acid. Several analyses were run of which a typical example follows. Volume of gas, 44.4 cc. Gas absorbed by fuming sulfuric acid, 16.2 cc. Oxygen introduced, 96.7 cc. Contraction after explosion, 61.3 cc. Volume of carbon dioxide, 48.8 cc. This gives the percentage of ethane as 55.8 with no butane and of ethylene (assuming that the absorption was all due to ethylene) as 36.4. Explosion of samples of the mixed gases calculated for ethylene and ethane gave similar results. While these values do not check so closely as would be desirable, they indicate that no other hydrocarbons are present.

Di-*n*-heptyl-mercury.—This product was made according to the general procedure of Marvel and Gould.[14] The Grignard reagent was obtained from 36 g. of magnesium and 270 g. of *n*-heptyl bromide in 60% yields. To this was added 108 g. of dry mercuric chloride. The reaction mixture was stirred and refluxed gently for four days. The mixture was then worked up in the usual way and the di-*n*-heptyl-mercury distilled under a pressure of 0.005 to 0.01 mm. Some heptyl-mercuric halide came over first and then di-*n*-heptyl-mercury distilled at 119–122° (bath at 126°); the yield was 144 g., or 90%; n_D^{21}, 1.4935; d_0^0, 1.474.

Anal. Subs., 0.5136: HgS, 0.2985. Calcd. for $(C_7H_{15})_2Hg$: Hg, 50.30. Found: 49.71.

Triethyl-*n*-butylammonium Bromide.—In this preparation and the other ammonium salts described, pure samples rather than high yields were sought. The exact yields, therefore, are not recorded. Equal molecular amounts of diethyl-*n*-butylamine and ethyl bromide were allowed to react in an alcohol solution in a sealed flask at 90–100° for about a week. The alcohol and unreacted reagents were then removed by distillation under reduced pressure and the residue was recrystallized from ethyl acetate. The product melts with decomposition at 212–215°.

Anal. Subs., 0.3735: 27.9 cc. of 0.0528 *N* $AgNO_3$. Calcd. for $(C_2H_5)_3C_4H_9NBr$: Br, 33.56. Found: 33.56.

Equally good results were obtained by using *n*-butyl bromide and triethylamine.

Triethyl-*n*-butylammonium Iodide.—The residues from crystallizing the bromide were dissolved in water and treated with silver oxide to convert them to the hydroxide. After filtering, the solution was neutralized with hydriodic acid and evaporated. The residue was crystallized from ethyl acetate; the product melted at 205° with decomposition.

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[14] Marvel and Gould, THIS JOURNAL, **44**, 153 (1922).

Anal. Subs., 0.5210: 34.5 cc. of 0.0528 *N* $AgNO_3$. Calcd. for $(C_2H_5)_3C_4H_9NI$: I, 44.50. Found: 44.40.

Triethylbenzylammonium Bromide.—Diethylbenzylamine was dissolved in benzene and treated with ethyl bromide. After heating the mixture under pressure at 100° for about three weeks, the product that had separated was collected on a filter and then recrystallized from ethyl acetate. It melted at 195° with decomposition.

Anal. Subs., 0.4220: 29.4 cc. of 0.0528 *N* $AgNO_3$. Calcd. for $(C_2H_5)_3C_6H_5CH_2NBr$: Br, 29.36. Found: 29.40.

Triethylbenzylammonium Iodide.—This was prepared from the bromide residues in a manner similar to that used for the iodide described before. The product melted at 128–135°.

Anal. Subs., 0.5524: 32.7 cc. of 0.0528 *N* $AgNO_3$. Calcd. for $(C_2H_5)_3C_6H_5CH_2NI$: I, 39.76. Found: 39.65.

Tetra-*n*-butylammonium Halides.—The bromide was prepared by heating tri-*n*-butylamine with *n*-butyl bromide in alcohol solution in a sealed flask at 100° for about five days. It is very soluble in water, alcohol and ethyl acetate and pure crystals could not be obtained. The chloride prepared from the bromide through the free base also failed to crystallize.

The iodide was prepared from the crude bromide through the free base; it crystallized well from hot water or benzene. It was dried at 100° under a pressure of 10^{-4} mm. The product melted at 144–145°.

Anal. Subs., 0.5704: 29.25 cc. of 0.0528 *N* $AgNO_3$. Calcd. for $(C_4H_9)_4NI$: I, 34.37. Found: 34.36.

Tri-*n*-butyl-*n*-heptylammonium Halides.—The iodide was prepared from tri-*n*-butylamine and heptyl iodide and from di-*n*-butylheptylamine and *n*-butyl iodide in alcohol solution in a sealed flask at 100° for about a week; it was very hard to purify. The most satisfactory method was to dissolve the salt in alcohol and then pour this solution with stirring into four volumes of warm water. The milky solution thus obtained was allowed to settle until it was clear and reached a temperature of 25–30°. The clear upper solution was then decanted through a filter paper moistened with water, and the filtrate was cooled to about —15°. The white crystals were separated from the mother liquors in a centrifuge and finally dried at room temperature under a pressure of less than 1 mm. for several hours.

This salt is quite soluble in alcohol, benzene, ethyl acetate and carbon tetrachloride. It is slightly soluble in water and insoluble in petroleum ether.

Anal. Subs., 0.8895: AgI, 0.5082. Calcd. for $(C_4H_9)_3C_7H_{15}NI$: I, 30.86. Found: 30.88.

The chloride and bromide were never obtained in a crystalline condition.

Diethyl-*n*-butylamine.—Two molecular proportions of diethylamine in benzene solution was treated with one of *n*-butyl bromide in a sealed flask at 100° for about one week. The flask was cooled and opened. The solid diethylamine hydrobromide was removed by filtration, the amine was converted to the hydrochloride by treating with hydrochloric acid and the benzene was evaporated. The free amine was then obtained by treating the salt with concd. sodium hydroxide solution, separating and drying over metallic sodium. The product boiled at 136–137°; d_0^0, 0.7614.

Anal. Subs., 0.6113: 50.2 cc. 0.0929 *N* H_2SO_4. Calcd. for $C_8H_{19}N$: neut. equiv., 129.2. Found: 131.7.

It was not analyzed but there is no question concerning its purity since with ethyl bromide it gave pure triethyl-*n*-butylammonium bromide.

Di-*n*-butyl-*n*-heptylamine.—In a similar way di-*n*-butylamine and heptyl bromide gave this amine, which boils at 119–120° at 7 mm.; n_D^{15}, 1.4389; d_0^0, 0.8088.

Anal. Subs., 1.0587: 47.5 cc. of 0.0929 *N* H_2SO_4. Calcd. for $C_{15}H_{33}N$: neut. equiv., 227.3. Found: 239.

Treatment with *n*-butyl iodide gave tri-*n*-butyl-*n*-heptylammonium iodide which was analyzed, giving the calculated results.

Summary

1. A modified and more satisfactory technique for the preparation of lithium alkyls has been developed.
2. Attempts have been made to prepare penta-alkyl nitrogen compounds from quaternary ammonium halides and lithium alkyls. These products, if formed, are very unstable and at once yield tertiary amines and hydrocarbons.
3. The evidence obtained indicates that the fifth valence of nitrogen in ammonium compounds retains its unique character even under conditions most favorable for its being otherwise, and at no time does it become equivalent to or is there any exchange of groups between it and any of the other four valences.

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THE BASIS FOR THE PHYSIOLOGICAL ACTIVITY OF -ONIUM COMPOUNDS. VII. DERIVATIVES OF BETAINES[1]

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Several phases of the problem of determining the basis for the physiological activity of the -onium compounds have been discussed in earlier papers.[2]

A number of years ago Hunt and Taveau[3] in a study of over seventy derivatives and homologs of choline showed that the muscarine effect (stimulation of the inhibitory nerves to the heart and other organs with a production of a lowering of the blood pressure) is most marked in those compounds that depart least from the choline type of structure, that is, have the grouping  $(CH_3)_3\underset{\displaystyle X}{N}CH_2CH_2O—$ Betaine salts such as the

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[1] This problem is being carried out in coöperation with Dr. Reid Hunt of the Harvard Medical School. The physiological data are the basis of another series of papers published elsewhere by him.

[2] Renshaw, *Science*, **62**, 384 (1925). Bencowitz and Renshaw, THIS JOURNAL, **47**, 1904 (1925). Renshaw and Ware, *ibid.*, **47**, 2989 (1925). Renshaw, Bacon and Roblyer, *ibid.*, **48**, 517 (1926). Renshaw and Bacon, *ibid.*, **48**, 1726 (1926). Bencowitz and Renshaw, *ibid.*, **48**, 2146 (1926).

[3] Hunt and Taveau, *U. S. Pub. Health Hyg. Bull.*, **73** (1911).