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[Contribution from the Chemistry Department of the University of Michigan]

Preparation of Alkyl Azides from Hydrazine Derivatives[1]

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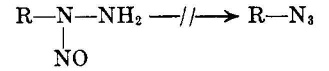
N-Alkyl-*N*-acylhydrazines have been found to give alkyl azides in poor to satisfactory yields by treatment with nitrous acid. Isobutyl and hexahydrobenzyl azides were prepared by this method from the corresponding 2-alkylsemicarbazides, and the adducts of these azides with acetylenedicarboxylic acid, dicyclopentadiene, or bicycloheptadiene were prepared as characterizing derivatives. *N*-*tert*-Butyl-*N*-benzoylhydrazine has been prepared by benzoylation of acetone *N*-*tert*-butylhydrazone followed by selective hydrolysis; nitrosation converts it in small part to *tert*-butyl azide.

The reaction of arylhydrazines with nitrous acid has been recognized for a long time as a useful method for the synthesis of aryl azides.[2] The nitrogen atom from the nitrous acid has been shown to become the outer, terminal atom of the azide chain,[3] and the initial attack by nitrous acid is therefore presumably on the unsubstituted amino group.

$$\text{Ar—NH—NH}_2 + \text{HNO}_2 \longrightarrow [\text{Ar—NH—NH—NO}] \longrightarrow \text{Ar—N}_3 + \text{H}_2\text{O}$$

Alkyl hydrazines, due to their more difficult accessibility, have been much less studied regarding their behavior on nitrosation. The available information shows that their nitrosation is not a useful synthesis of alkyl azides and that, indeed, azides are rarely formed at all. The primary nitrosation products that have been isolated appear to be 1-nitroso-1-alkylhydrazines,[4] which obviously cannot give rise to azides without rearrangement, and not surprisingly they decompose in other ways.



$$\text{R—NH—NH}_2 + \text{HNO}_2 \longrightarrow \underset{\text{NO}}{\underset{|}{\text{R—N}}}\text{—NH}_2 \;\text{—//}\!\!\longrightarrow \text{R—N}_3$$

The explanation for this difference in behavior between aryl- and alkylhydrazines appears to be in the effect of the substituents on the relative basicity of the two hydrazine nitrogens. Inasmuch as aryl groups are base-weakening and alkyl groups are base-strengthening when attached to an amine nitrogen, one might reasonably expect the substituted nitrogen of alkylhydrazines to be more basic than the unsubstituted one, and the reverse to be true for arylhydrazines. The very reasonable assumption that nitrosation occurs on the more basic nitrogen then explains the observed behavior.

In order to bring about nitrosation on the unsubstituted nitrogen of alkylhydrazines, we prepared 1-alkyl-1-acylhydrazines. The base-weakening acyl group would be expected to prevent nitrosation at the alkylated nitrogen, but would be removable hydrolytically at a suitable time. Nitrosation on the unsubstituted nitrogen would then give rise to the three-nitrogen chain of the azide system, and subsequent elimination of the acyl group should produce an alkyl azide. A solitary exemplification of this is the reported formation of a keto azide from a fused-ring *N*-aminoimidazolidone or a related oxime.[5]

1-Alkyl-1-acylhydrazines might be prepared by acylation of an alkylhydrazine, or by nitrosation of an *N*-alkyl amide followed by reduction of of the *N*-nitroso group. The latter was investigated first, because of the more readily accessible starting

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[2] J. H. Boyer and F. Canter, *Chem. Revs.*, **54,** 1 (1954).

[3] K. Clusius and H. R. Weisser, *Helv. Chim. Acta*, **35,** 1548 (1952); *Naturwissenschaften*, **39,** 42 (1952).

[4] J. Thiele, *Ann.*, **376,** 239 (1910).

[5] M. O. Forster and H. E. Fierz, *J. Chem. Soc.*, **87,** 826 (1905); **91,** 867 (1907).

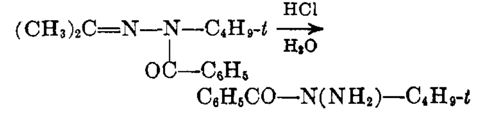
materials. Alkylurethans and alkylureas were chosen, since their nitrosation behavior has been fairly well studied. Difficulty was encountered in converting the urethans to 1-alkyl-1-carboalkoxyhydrazines, so attention was concentrated on the ureas, which could be converted to 1-alkyl-1-carbamylhydrazines in satisfactory yield. The difference in behavior between the urethans and the ureas may be due either to an intrinsic difference in the ease of reductive cleavage of the N=N bond, or may perhaps be due to the greater ease of handling the urea derivatives, which were all solids in contrast to the liquid urethan derivatives.

Nitrosation of the 2-alkylsemicarbazides obtained gave rise to azides without isolation of intermediates; the reactions were not clean-cut, as shown by the somewhat low yields, but elimination of the carbamyl group was spontaneous under the conditions used. The two successful examples both involved primary alkyl groups (isobutyl and hexahydrobenzyl).

$$H_2N{-}NR{-}CO{-}NH_2 \xrightarrow{HNO_2} R{-}N_3 + CO_2 + N_2$$

Attempts to extend the reaction to the secondary and tertiary class, represented by cyclohexyl- and *tert*-butyl-semicarbazides, were at first thwarted by our failure to obtain the required semicarbazides by the nitrosation and reduction route. However, 2-substituted semicarbazides can also be prepared by a different route, the key step of which is the reaction of a carbamyl chloride with the magnesium derivative of a benzophenone *N*-alkylhydrazone, obtained by the addition of a Grignard reagent to diphenyldiazomethane.[6] We found that *tert*-butylmagnesium chloride added readily to diphenyldiazomethane, but the resulting salt could not be made to react with acid chlorides.

Since it appeared probable that the unreactivity was steric in origin, and in part due to the size of the phenyl groups as well as the *tert*-butyl, we next investigated acetone *tert*-butylhydrazone, which was prepared from *tert*-butylhydrazine. We were able to benzoylate this compound successfully, and to hydrolyze the product selectively to *N*-benzoyl-*N*-*tert*-butylhydrazine. Treatment of this with nitrous acid then brought about some conversion to *tert*-butyl azide, but the yields were too low to permit its isolation in pure form.



$$(CH_3)_2C{=}N{-}NH{-}C_4H_9\text{-}t \longrightarrow (CH_3)_2C{=}N{-}\underset{\displaystyle OC{-}C_6H_5}{N}{-}C_4H_9\text{-}t \xrightarrow[H_2O]{HCl} C_6H_5CO{-}N(NH_2){-}C_4H_9\text{-}t$$

tert-Butylhydrazine was required in quantity for these experiments. Since previously published syntheses of this compound[7,8] did not seem satisfactory, we explored most of the synthetic methods that have been used for other alkylhydrazines. Most failed altogether or gave only negligible yields, but the seldom used method discovered by Zerner[9] and developed by Coleman, Gilman, Adams, and Pratt,[6] utilizing the reaction of Grignard reagents with diphenyldiazomethane, worked well, and we were able to carry it out on a scale of several moles and to characterize pure *tert*-butylhydrazine for the first time. However, the hydrolysis of the intermediate benzophenone *tert*-butylhydrazone had to be carried out at room temperature for success; hot acid caused elimination of the *tert*-butyl group.

$$(C_6H_5)_2C{=}N_2 \xrightarrow{t\text{-}C_4H_9MgCl} (C_6H_5)_2C{=}N{-}NH{-}C_4H_9\text{-}t \xrightarrow[H_2O]{HCl} (C_6H_5)_2CO + H_2N{-}NH{-}C_4H_9\text{-}t$$

Although the route to alkyl azides developed here is not a generally useful synthetic method, it has the potentially important characteristic of allowing the aliphatic azide group to be built up one atom at a time. This makes it in principle possible to prepare aliphatic azides with a specific nitrogen atom isotopically tagged, a feat hitherto possible only for aryl azides.

In the course of this work, the need to characterize liquid azides by conversion to a solid derivative arose. Three reagents were investigated: acetylenedicarboxylic acid, which gives rise to 1-alkyltriazole-4,5-dicarboxylic acids; and bicyclo[2.2.1]-heptadiene and dicyclopentadiene, which would be expected to give bicyclic fused-ring triazolines. All three reagents were successful in giving crystalline derivatives readily. The triazoledicarboxylic acids were rather unsatisfactory in that they readily form hydrates, which may have indefinite melting points. The bicycloheptadiene adducts showed addition at both double bonds, giving products which are presumably bis(triazolino)-bicycloheptanes, the positions of substitution on the two triazoline rings relative to each other being unknown. These are high-melting, crystalline substances which appear to be stable to storage, and make suitable derivatives for characterization. *tert*-Butyl azide, however, did not form such derivatives satisfactorily. It was therefore characterized by rearrangement to acetone *N*-methylimine with concentrated sulfuric acid, and isolating acetone dinitrophenylhydrazone.

EXPERIMENTAL

2-Isobutylsemicarbazide was prepared in 54% yield by reduction of *N*-nitroso-*N*-isobutylurea[8] with zinc and acetic acid; it had m.p. 89-91° (reported[10] 91.5-92°).

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(6) G. H. Coleman, H. Gilman, C. E. Adams, and P. E. Pratt, *J. Org. Chem.*, **3**, 99 (1938).

(7) F. Klages, *Ann.*, **547**, 25 (1941).

(8) L. F. Audrieth and K. H. Diamond, *J. Am. Chem. Soc.*, **76**, 4869 (1954).

(9) E. Zerner, *Monatsh.*, **34**, 1609 (1913).

(10) K. Taipale, *J. Russ. Phys. Chem. Soc.*, **56**, 81 (1925); *Chem. Zentr.*, 1926, I, 872.

Isobutyl azide. A solution of 26.2 g. (0.2 mole) of 2-isobutylsemicarbazide in 50 ml. of concentrated hydrochloric acid and 50 ml. of water was cooled to 0° and a solution of 19.3 g. (0.28 mole) of sodium nitrite in 35 ml. of water was added dropwise; the solution became bright green. It was stirred an additional hour and then urea was added to destroy the excess nitrous acid; the green color disappeared. The solution was made basic, causing the separation of a second layer, and the mixture was then distilled, the product being codistilled with the water. The distillate was extracted with ether and the extracts were dried over calcium chloride. The solution was fractionally distilled at 752.5 mm., giving 7.59 g. of b.p. 40–53°, 3.40 g. of b.p. 53–93°, 5.53 g. of b.p. 93–95°, and 3.08 g. of b.p. >95°. The 93–95° fraction was taken up in petroleum ether (b.p. 30–37°) and washed twice with 5% hydrochloric acid, once with water, dried and redistilled at 751.5 mm., giving 1.50 g., b.p. 45–53°; 2.90 g., b.p. 93–94°; and 0.62 g., b.p. >94°. The middle fraction, which reacted vigorously with concentrated sulfuric acid and flashed in a flame, was taken as isobutyl azide (it is not clear whether the small discrepancy in the carbon analysis should be attributed to impurity in the azide or to its immoderate behavior on combustion).

Anal. Calcd. for $C_4H_9N_3$: C, 48.46; H, 9.15. Found: C, 49.18; H, 9.06.

1-Isobutyl-1,2,3-triazole-4,5-dicarboxylic acid. The foregoing isobutyl azide, 2.80 g., was taken up in petroleum ether (b.p. 30–60°), washed with two portions of 10% hydrochloric acid, once with water, and dried over magnesium sulfate. To this was added 4.55 g. (0.034 mole) of acetylenedicarboxylic acid hydrate and 20 ml. of dry ether, and the solution was refluxed for one hour, cooled, and petroleum ether was added until a white solid precipitated; yield 5.94 g. (74.7%), m.p. 50–95°.

Recrystallization from ether–petroleum ether mixture gave white needles which lost water at 121° and melted at 136–137°. The neutral equivalent was 109.3 (calcd. 106.5). The sample was allowed to stand open to the air until the weight was constant. The neutral equivalent was then found to be 118 (calcd. for the monohydrate 115.5).

Anal. Calcd. for $C_8H_{11}O_4N_3 \cdot H_2O$: C, 41.56; H, 5.67. Found: C, 41.92; H, 5.62.

Isobutyl azide–bicycloheptadiene adduct. A mixture of 1.50 g. (0.015 mole) of isobutyl azide and 0.70 g. (0.0076 mole) of bicycloheptadiene was allowed to stand at room temperature for several days. The addition of a small amount of methylene chloride and sufficient petroleum ether (b.p. 40–60°) to cause some precipitation gave 0.16 g. (7.3%) of colorless crystals, m.p. 186–188°; presumably, more could have been obtained from the mother liquors. Recrystallization from the same solvents gave an analytical sample, m.p. 188–191°.

Anal. Calcd. for $C_{15}H_{26}N_6$: C, 62.02; H, 9.02. Found: C, 62.05; H, 9.18.

Nitrosohexahydrobenzylurea (1-cyclohexanemethyl-1-nitrosourea). A mixture of 78 g. (0.5 mole) of hexahydrobenzylurea,[11] 150 ml. of ether, 50 g. of ice, and 160 g. (2.25 moles) of sodium nitrite in 250 ml. water was acidified by dropwise addition of 150 g. of concentrated nitric acid and 150 g. of ice. More ice was added as needed, to keep the temperature below 5°. The product which precipitated was filtered off and washed with cold water, and the mother liquors were extracted with ether. The ethereal solution was dried and evaporated. The total yield was 47.1 g. (51%), m.p. 118–121°. Recrystallization from ethanol-water mixture gave an analytical sample, m.p. 120–123° dec.

Anal. Calcd. for $C_8H_{15}O_2N_3$: C, 51.87; H, 8.16. Found: C, 52.00; H, 8.14.

2-Hexahydrobenzylsemicarbazide (2-cyclohexanemethylsemicarbazide). A solution of 18.5 g. (0.1 mole) of nitrosohexahydrobenzylurea in 100 ml. of glacial acetic acid and 50 ml. of water was added dropwise to 30 g. of zinc dust and 100 ml. of 50% acetic acid, while the temperature was kept below 20°. After the addition was completed, the mixture was allowed to warm to room temperature and was then filtered. The filtrate was made basic and the product was filtered and washed with water. The filtrate was extracted with ether, which was then dried and evaporated. The combined yield of 2-hexahydrobenzylsemicarbazide was 11 g. (64.5%), m.p. 154–162°. Recrystallization twice from absolute alcohol gave an analytical sample, m.p. 160.5–163°.

Anal. Calcd. for $C_8H_{16}ON_3$: C, 56.11; H, 10.01. Found: C, 56.28; H, 10.04.

Hexahydrobenzyl azide (cyclohexanemethyl azide). One-fifth mole (34.2 g.) of 2-hexahydrobenzylsemicarbazide was triturated with 50 ml. of concentrated hydrochloric acid and heated on a steam bath. To the hot suspension was added 50 ml. of water, and the mixture was cooled to 0°. The solution was stirred mechanically while a solution of 20.7 g. (0.3 mole) of sodium nitrite in 35 ml. of water was added dropwise. Stirring was continued for an additional hour, and the solution was made basic and then filtered to remove a small amount of solid material.

The filtrate was steam-distilled and the distillate was extracted with ether. The extracts were dried over calcium chloride, the ether was removed at the aspirator and the residue distilled at 0.15-mm. pressure; the entire amount distilled at 30–34°/0.15 mm. The distillate, wt. 14.5 g. (48.6%), gave a very vigorous reaction with concentrated sulfuric acid.

Anal. Calcd. for $C_7H_{13}N_3$: C, 60.40; H, 9.41. Found: C, 60.58; H, 9.64.

The solid which had been filtered from the basic solution weighed 2.62 g. and melted at 100–120°. Two recrystallizations from absolute alcohol gave 1.08 g. (4.3%), m.p. 144–147°, of *sym*-dihexahydrobenzylurea.

Anal. Calcd. for $C_{15}H_{28}ON_2$: C, 71.38; H, 11.18. Found: C, 71.21; H, 11.41.

Upon the addition of water to the mother liquors, a second solid was obtained. This material was recrystallized from ethanol-water to give a yellowish solid, m.p. 94° dec., weight 1.38 g. (3.5%), which gave a Liebermann nitroso test. Repeated recrystallization did not give an apparently pure sample.

Anal. Found: C, 55.35; H, 9.08; N, 21.64.

Hexahydrobenzyl azide–bicycloheptadiene adduct. This material was prepared in the same manner as the isobutyl azide adduct; the yield was 53%, m.p. 208–212°.

Anal. Calcd. for $C_{21}H_{34}N_6$: C, 68.07; H, 9.37. Found: C, 68.15; H, 9.37.

Hexahydrobenzyl azide–dicyclopentadiene adduct. A mixture of 5.0 g. (0.036 mole) of hexahydrobenzyl azide, 2.38 g. (0.018 mole) of dicyclopentadiene and 10 ml. of ether was allowed to stand for several days. Evaporation of the ether caused a white solid (2.30 g., 31.2%) to separate, m.p. 108–114° after washing with petroleum ether (b.p. 40–60°).

Anal. Calcd. for $C_{17}H_{25}N_3$: C, 75.23; H, 9.28. Found: C, 75.35; H, 9.17.

sym-Dihexahydrobenzylurea (1,3-biscyclohexanemethylurea). To a stirred suspension of 33.9 g. (0.3 mole) of hexahydrobenzylamine and 16.8 g. (0.3 mole) of potassium hydroxide in 100 ml. of water, was slowly added 17 g. (0.15 mole) of phosgene in 100 ml. of reagent benzene. The white solid which formed was filtered off, and a small additional amount was obtained by evaporating the benzene solution. The total yield of crude *sym*-dihexahydrobenzylurea was 21.2 g. (56.2%), m.p. 117–124°. Recrystallization from ethanol-water gave fine white platelets, m.p. 148–150°, undepressed when mixed with the *sym*-dihexahydrobenzylurea obtained from the hexahydrobenzyl azide preparation.

2-Ethylsemicarbazide. To a stirred suspension of 20 g. of zinc dust in 70 ml. of 50% acetic acid there was added dropwise a solution of 10 g. (0.085 mole) of *N*-nitroso-*N*-methylurea in 50 ml. of glacial acetic acid and 25 ml. of water. The temperature of the reaction was kept at about 20°

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(11) O. Wallach, *Ann.*, **353**, 299 (1907).

during the addition, and then raised to 50–60° for 1 hr. The zinc dust was filtered from the hot solution, and the filtrate was made basic (dissolving all the zinc hydroxide) and extracted continuously with ether. After several days, the ether extract had precipitated 0.57 g. of a substance which melted at 97–103°. Recrystallization of 0.47 g. from ethylene glycol dimethyl ether gave 0.15 g., m.p. 105.5–107.5°, and a second crop weighing 0.05 g. By continuing the ether extraction, a total of 2.73 g. (31%) was obtained.

Anal. Calcd. for $C_3H_9ON_3$: C, 34.94; H, 8.80. Found: C, 35.02; H, 8.70.

Because of the difficulties of preparing sufficient quantities, this semicarbazide was not investigated further than the preparation of derivatives.

1-(p-Chlorobenzylidene-2-ethylsemicarbazide). A mixture of 0.1 g. (0.0085 mole) of 2-ethylsemicarbazide and 0.14 g. (0.001 mole) of *p*-chlorobenzaldehyde with 10 ml. of absolute alcohol was refluxed for 10 min., allowed to cool, and slowly diluted with water until needles formed. The crude, colorless product weighed 0.12 g. (63%), m.p. 153–154°. Recrystallization from the same solvents gave an analytical sample, m.p. 153.5–154°.

Anal. Calcd. for $C_{10}H_{12}ON_3Cl$: C, 53.20; H, 5.76. Found: C, 53.19; H, 5.48.

1-Benzylidene-2-ethylsemicarbazide. Ten grams of *N*-nitroso-*N*-ethylurea was reduced in the same manner as described above. Instead of the usual work-up, 10 g. of benzaldehyde was added to the filtered mixture and the flask was shaken on a mechanical shaker overnight. The solid which formed was filtered off and washed with water and a very small portion of ether; wt. 7.14 (44%), m.p. 135–139°. Recrystallization from alcohol-water gave fine white needles, m.p. 137.5–139°.

Anal. Calcd. for $C_{10}H_{13}ON_3$: C, 62.80; H, 6.85. Found: C, 62.80; H, 6.75.

1-Ethyl-1,2,3-triazole-4,5-dicarboxylic acid. A mixture of 4 g. (0.0565 mole) of ethyl azide,[12] 6.4 g. (0.0565 mole) of acetylenedicarboxylic acid and 10 ml. of ether was allowed to reflux under the heat of the reaction, and then heated on a steam bath for about 15 min. longer. Upon evaporation of the solvent, the hydrated triazole was obtained as a white solid, 7.57 g. (66%), which started to soften at 85° when heated slowly. Recrystallization from ether–petroleum ether mixture gave the anhydrous material, m.p. 106–109° (reported[13] 108–110°).

Benzophenone tert-butylhydrazone. A solution of 814 g. (4.18 moles) of diphenyldiazomethane[14] in 2 lb. of ether was slowly added with stirring to a solution of *tert*-butylmagnesium chloride, cooled by ice, prepared from 585 g. (6 moles) of *tert*-butyl chloride. Upon completion of the addition, the mixture was allowed to stand overnight; the red solution became nearly colorless and a yellow precipitate formed. The mixture was hydrolyzed with ammonium chloride and ice, the ether layer was separated, and the water layer was extracted twice with more ether. The combined ethereal layers were dried over calcium chloride and then evaporated. There remained 948 g. (87.5%) of benzophenone *tert*-butylhydrazone as a yellow solid, m.p. 68–72°. Recrystallization of a portion from alcohol gave light yellow needles, m.p. 73.5–75°.

Anal. Calcd. for $C_{17}H_{20}N_2$: C, 80.91; H, 7.99; N, 11.10. Found: C, 81.02; H, 7.79; N, 11.17.

tert-Butylhydrazine. Initial attempts to hydrolyze benzophenone *tert*-butylhydrazone with refluxing 20% or 50% hydrochloric acid gave only hydrazine hydrochloride, while distillation from 10% sodium hydroxide solution produced no volatile base of any kind.

A mixture of 7.0 g. of benzophenone *tert*-butylhydrazone, 10 ml. of concd. hydrochloric acid and 15 ml. of alcohol was allowed to stand at room temperature overnight. The alcohol was then evaporated in a stream of air, and the remainder was extracted twice with ether, diluted with 10 ml. of water, and again extracted twice with ether. The combined extracts were washed twice with water, and the washings were added to the ether-insoluble residue. Evaporation of the ethereal extracts gave 3.94 g. (78%) of benzophenone. The aqueous layers on evaporation left 2.07 g. (60%) of *tert*-butylhydrazine hydrochloride; recrystallization of a portion from alcohol gave colorless plates, m.p. 189° (reported m.p. 187°;[8] 191–192°[7]).

Free *tert*-butylhydrazine was obtained in 94% yield by distilling larger quantities of the hydrochloride from 25% sodium hydroxide solution, treating the distillate with successive portions of solid sodium hydroxide until a water layer no longer appeared, and distilling the dried material from barium oxide through a Podbielniak column. The colorless, pungent *tert*-butylhydrazine so obtained had b.p. 109°/749 mm., n_D^{25} 1.4270, and density 0.82264 at 25°, and evolved gas slowly when in contact with impurities. A boiling point of 129–134° has been reported[7] for alleged *tert*-butylhydrazine whose identity was not supported by analysis.

Anal. Calcd. for $C_4H_{12}N_2$: C, 54.50; H, 13.72; N, 31.78. Found: C, 54.31, 54.27; H, 13.73, 13.77; N, 31.55, 31.66.

Acetone tert-butylhydrazone. A mixture of 5.0 g. of *tert*-butylhydrazine and 6.6 g. of acetone, prepared with cooling, was allowed to stand for a short time, and ether and potassium hydroxide pellets were then added. The lower, aqueous layer was removed and fresh potassium hydroxide pellets were added; the procedure was repeated until no more water could be removed. The ethereal layer was then distilled from barium oxide to yield 5.41 g. (74%) of a colorless strong-smelling liquid, b.p. 132–134°.

Anal. Calcd. for $C_7H_{16}N_2$: C, 65.57; H, 12.58. Found: C, 65.68; H, 12.66.

Acetone N-tert-butyl-N-benzoylhydrazone. A mixture of 2.0 g. of acetone *tert*-butylhydrazone with 4.4 g. of benzoyl chloride was agitated with 15 ml. of 10% sodium hydroxide solution until the odor of benzoyl chloride was gone. The product was taken up in ether and dried over magnesium sulfate. Evaporation left 3.65 g. (100%) of a viscous, light yellow oil. Distillation at 0.1 to 0.15-mm. pressure gave without appreciable loss a colorless product, b.p. 100–103°, which soon crystallized. After recrystallization from aqueous methanol it had m.p. 70–70.5°.

Anal. Calcd. for $C_{14}H_{20}N_2O$: C, 72.30; H, 8.68. Found: C, 72.28; H, 8.90.

N-Benzoyl-N-tert-butylhydrazine. A solution of 0.5 g. of acetone *N*-*tert*-butyl-*N*-benzoylhydrazone in 3 ml. of 10% hydrochloric acid and 3 ml. of alcohol was allowed to stand at room temperature for 11 hr., and was then made basic with dilute sodium hydroxide. The alcohol was evaporated in an air stream, and the solid which separated was filtered off. It weighed 0.35 g. (85%), and had m.p. 117–123°. Recrystallization from aqueous alcohol gave an analytical sample, m.p. 131–132°.

Anal. Calcd. for $C_{11}H_{16}N_2O$: C, 68.72; H, 8.39. Found: C, 68.67; H, 8.34.

Nitrosation of N-benzoyl-N-tert-butylhydrazine. A solution of 1.33 g. of nitrogen tetroxide in 15 ml. of dioxane was chilled in a Dry Ice–alcohol bath, 2.4 g. of anhydrous sodium acetate was added and the mixture was allowed to warm to 0°. While this solution was being stirred, 0.8 g. of *N*-benzoyl-*N*-*tert*-butylhydrazine was added in portions, after which the mixture was kept at room temperature for 34 hr.

Distillation of the mixture then gave a 10-ml. fraction of b.p. 85–95° before dioxane began to distill. This fraction, which should have contained any *tert*-butyl azide, was added dropwise to 10 ml. of concd. sulfuric acid with stirring; gas

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(12) E. Oliveri-Mandalà and G. Caronna, *Gazz. chim. ital.*, 71, 182 (1941); H. Staudinger and E. Hauser, *Helv. Chim. Acta*, 4, 861 (1921).

(13) F. von Bruckhausen and H. Hoffmann, *Ber.*, 74, 1593 (1941).

(14) L. I. Smith and K. L. Howard, *Org. Syntheses*, Coll. Vol. III, 352 (1955).

was evolved. The mixture was then diluted with 30 ml. of water and distilled. Treatment of the distillate with 2,4-dinitrophenylhydrazine reagent solution gave an orange precipitate, which was purified by chromatography on an alumina column. Elution with benzene gave 0.08 g. (8.5%) of acetone dinitrophenylhydrazone, m.p. 115–120°, undepressed by mixture with an authentic sample. Furthermore, the infrared spectrum of this product was identical with that of an authentic sample.

Benzoic acid (0.33 g., 65%) was isolated from the higher boiling part of the dioxane solution and from the undistilled part of the sulfuric acid reaction mixture.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF MICHIGAN]

Investigation of Some Dialkylamino Isocyanides[1]

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Some 3-dialkylaminopropylamines and 2-dialkylaminoethylamines have been converted to the corresponding isocyanides by the Hofmann synthesis. Neither hydroxyalkylamines nor *N,N*-dialkylhydrazines could be converted to isocyanides. In several Hofmann syntheses formamides were formed. *N*-Dialkylaminoalkylcarbonimidyl chlorides and 1-dialkylaminoalkyltetrazoles were prepared by treating the corresponding isocyanides with chlorine or hydrogen azide.

Isocyanides have been known for 90 years due to their discovery independently by Hofmann[2] and Gautier.[3] In that time two general syntheses have been developed: the action of silver cyanide on alkyl iodides,[2–5] and the action of alkali on a mixture of chloroform and an amine.[2,5–8] Aryl isocyanides with various functional groups on the benzene nucleus have been prepared, but no aliphatic isocyanides with other functional groups have yet been reported. This paper reports the synthesis and properties of a group of dialkylaminoalkyl isocyanides, and the attempted preparation of some hydroxyalkyl isocyanides and isocyanoamines by the known general methods.

The Hofmann synthesis was used successfully to prepare 3-diethylaminopropyl isocyanide (IIa), 3-dimethylaminopropyl isocyanide (IIb), and 2-diethylaminoethyl isocyanide (IIc) from the corresponding amines (Ia, b, c). The adaptation described by Malatesta[8] was found to be the most convenient for carrying out the reaction. The yields were low, and the products were accompanied by unreacted amine and tar.

$$\underset{(I)}{R{-}NH_2} \xrightarrow[KOH]{CHCl_3} \underset{(II)}{R{-}NC}$$

a, R = $(C_2H_5)_2NCH_2CH_2CH_2{-}$;
b, R = $(CH_3)_2NCH_2CH_2CH_2{-}$;
c, R = $(C_2H_5)_2NCH_2CH_2{-}$.

A black, tarry mass remained after the isocyanides and unreacted amines were distilled from the reaction mixtures. Attempts to remove any higher boiling component from the tar by further distillation resulted, in the case of IIa, only in extensive decomposition. However, from the tar obtained in the preparation of IIb there was obtained a small amount of impure carbonyl compound. Cuprous chloride successfully freed it from an isocyanide impurity by complex formation.[9] Comparison of the boiling point and infrared spectrum with those of 3-dimethylaminopropylformamide suggests that they are the same substance. Analysis, however, indicated an impurity low in nitrogen. This is also indicated by a comparison of the relative intensities of the C—H bond N—H stretching bands in the infrared with those of an authentic sample.

The Hofmann synthesis with 3-diethylaminopropylamine (Ia) and methanolic potassium hydroxide produced no isocyanide. Besides unreacted amine, there was isolated a small amount of high-boiling material, identified as 3-diethylaminopropylformamide (III) by analysis, infrared spectrum and comparison with an authentic sample.

$$\underset{(Ia)}{(C_2H_5)_2N(CH_2)_3NH_2} \xrightarrow{CHCl_3,\ KOH} \underset{(III)}{(C_2H_5)_2N(CH_2)_3NHCHO}$$

No isocyanides were isolated when 1-amino-2-propanol or 3-aminopropanol were subjected to the Hofmann synthesis. In the latter case, however,

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