

Anal. Calcd. for $C_8H_{19}N$: N, 10.84. Found: N, 10.51.

Hydrochloride (by treatment of 1 g. of amine in 10 ml. of anhydrous ether with dry hydrogen chloride), crystals which did not melt at 210° .

Anal. Calcd. for $C_8H_{20}NCl$: C, 58.1; H, 12.2; N, 8.47; Cl, 21.5. Found: C, 58.2; H, 12.2; N, 8.70; Cl, 21.5.

Acetyl derivative, m. p. $98-99^\circ$ alone or when mixed with *N-t*-octyl acetamide prepared above.

The ethylene glycol residue from the hydrolysis was diluted with water (800 ml.) and yielded, after twenty-four hours, unhydrolyzed *N-t*-octyl acetamide (5.7 g., 16.6%).

***t*-Amylamine**.—Hydrolysis of *N-t*-amyl acetamide (Table II) in the same manner yielded *t*-amylamine, b. p. $77-78^\circ$ (27%). Acetylation of the amine reformed *N-t*-amyl acetamide, m. p. $78-79^\circ$ alone or mixed with the starting material.

Acid Decomposition of *N-t*-Octyl Acetamide.—*N-t*-Octyl acetamide (5 g.) was boiled with 15% hydrochloric acid in a distilling flask with condenser affixed for distillation. Diisobutene (3 g., calcd. 3.3 g.) was obtained and identified by recondensation with acetonitrile to form *N-t*-octyl acetamide, m. p. $97-98^\circ$.

***N-t*-Amyl Biuret**.—To a mixture of 8.4 g. (0.1 mole) of dicyandiamide and 7.0 g. (0.1 mole) of trimethylethene was added portionwise over one hour, and with mechanical stirring and external ice cooling, a solution of 10 g. (0.1 mole) sulfuric acid in 20 ml. glacial acetic acid. After one additional hour in the ice-bath the mixture, containing solid material, was heated at 60° for four hours during which the solids dissolved. The cooled solution was then poured on cracked ice and neutralized with ammonia. An oil separated, which crystallized on standing overnight. The crystals (9.8 g.) were filtered, washed with ice-water, and air dried. Recrystallization from water yielded 7.0 g. (53.8%), m. p. $148.5-149^\circ$, after drying *in vacuo* at 75° .

Anal. Calcd. for $C_7H_{11}O_2N_2$: N, 24.30. Found: N, 24.25.

***N-t*-Amyl Urea**.—A mixture of 42 g. (1.0 mole) of cyanamide, 70 g. (1.0 mole) of trimethylethene and 300 ml. of glacial acetic acid was stirred mechanically while 205 g. (2.0 mole) of sulfuric acid was added dropwise at $30-40^\circ$. The reaction mixture was poured into water (3500 ml.), neutralized with sodium carbonate, and allowed to stand for several hours. A solid separated; it was filtered, dissolved in hot methanol and refiltered to separate inorganic

matter, and the filtrate was evaporated to dryness under reduced pressure. The crude product remaining was recrystallized from water; yield 14 g. (10%), m. p. 160° in agreement with J. S. Buck and A. M. Hjort.³ By the same procedure, substituting one mole of *t*-amyl alcohol for the trimethylethene used above, the same product was obtained in 30% yield.

***N*- α -Phenethyl Acetamide**.—Styrene (10.4 g., 0.1 mole) and acetonitrile (6.1 g., 0.15 mole) were mixed and added to a solution of 17.1 g. (0.1 mole) of benzenesulfonic acid (94.5%, sulfuric acid-free) in 50 ml. of glacial acetic acid. The resulting solution was allowed to stand for fifteen hours, then poured on 200 g. of cracked ice and neutralized with ammonia. A viscous oil separated; this was extracted with three 100-ml. portions of ether, the combined extracts were dried over anhydrous potassium carbonate, the ether was removed, and the amide was distilled at 7 mm. Seven grams (43%), b. p. $175-180^\circ$, was obtained and recrystallized from petroleum ether. Analogous products from acetonitrile and α -methylstyrene, and from acetonitrile and α -methyl-*p*-methylstyrene were obtained by the same procedure (Table IV).

Pyrolysis of *N-t*-Octyl Acetamide.—Fifty grams (0.29 mole) of the amide was distilled through a short unpacked steam-jacketed column at a rate to permit a distillate to come over at $50-60^\circ$ (one hour). The distillate (43.3 g.) consisted of an oil (29.5 g.) and a lower aqueous layer. The oil was removed, washed with water, dried (anhydrous sodium sulfate) and distilled, yielding 21.3 g. boiling at $100-101^\circ$. This was identified as diisobutene through its physical constants and by condensation with acetonitrile to reform the original amide. The aqueous layer was saturated with sodium chloride, extracted with ether, and the extract dried and distilled to yield 3.0 g. of acetonitrile, identified by condensation with diisobutene to yield the original amide.

Summary

The interaction of nitriles and alkenes in the presence of concentrated sulfuric acid has been shown to result in *N*-alkyl amides. A series of such amides has been prepared and characterized, and the structures of typical members have been verified by hydrolysis to the corresponding amines.

(3) J. S. Buck and A. M. Hjort, *THIS JOURNAL*, **59**, 2567 (1937).

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NEW YORK UNIVERSITY]

A New Reaction of Nitriles. II. Synthesis of *t*-Carbinamines

BY JOHN J. RITTER AND JOSEPH KALISH¹

The synthesis of *t*-carbinamines R_3CNH_2 has occupied the attention of several investigators² but up to the present no simple general method of synthesis has been reported. In an earlier publication³ was reported the reaction of hydrogen

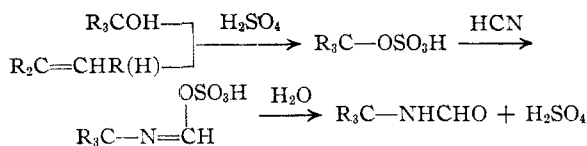
cyanide with diisobutene and with camphene to form *N-t*-alkyl formamides. The ease of hydrolysis of formic acid derivatives in general suggested to the present authors the use of *N-t*-alkyl formamides as a source of *t*-carbinamines. The formamides already reported³ were obtained by addition of hydrogen cyanide to alkene-sulfuric acid-acetic acid mixtures. The present procedure employs a tertiary alcohol or an alkene in acetic acid solution to which one equivalent of sodium cyanide has been added; the reaction occurs spontaneously when sulfuric acid is added, as follows⁴:

(1) Based upon a part of the thesis to be presented by Joseph Kalish to the Graduate Faculty of New York University in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(2) (a) Linnemann, *Ann.*, **192**, 72 (1878); (b) Klages, *et al.*, *ibid.*, **347**, 24 (1941); (c) C. Mentzer, *et al.*, *Bull. soc. chim.*, **9**, 813-818 (1942); (d) H. R. Henze, B. B. Allen and W. B. Leslie, *THIS JOURNAL*, **65**, 87-89 (1943); (e) J. V. Karabinos and K. T. Serijan, *ibid.*, **67**, 1856 (1945); (f) L. I. Smith and O. H. Emerson, *ibid.*, **67**, 1862 (1945); (g) K. N. Campbell, A. H. Sommers and B. K. Campbell, *ibid.*, **68**, 140 (1946); (h) R. Brown and W. E. Jones, *J. Chem. Soc.*, **781-782** (1946).

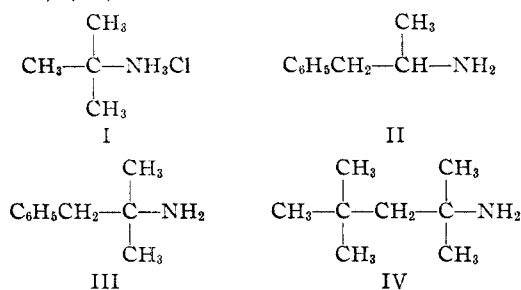
(3) J. J. Ritter and P. P. Miniери, *THIS JOURNAL*, **70**, 4045 (1948).

(4) The use of alcohols in place of alkenes in this method of amide synthesis was developed in collaboration with others (Frederic R. Benson, Ph.D. thesis, 1947; Robert M. Lusskin, research in progress).



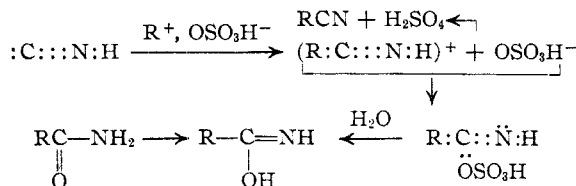
The *N*-alkyl formamides were hydrolyzed with aqueous alkali to *t*-carbinamines.

The preparation of the following compounds is described in this paper: trimethylcarbinamine (*t*-butylamine) hydrochloride (I); methylbenzylcarbinamine (II); dimethylbenzylcarbinamine (III) and dimethylneopentylcarbinamine (*t*-octylamine) (IV).



Methylbenzylcarbinamine (amphetamine) II is included for reasons of general interest and also because of its close relationship to III. It was not obtained from a formamide but by hydrolysis of its acetyl derivative formed from allylbenzene and acetonitrile.⁵

The existence of the tautomeric forms of hydrogen cyanide⁶ suggests the possibility of C-alkylation under the conditions of the reaction formulated above:



In the reaction of diisobutene with hydrogen cyanide to form *N*-*t*-octylformamide the reaction mixture was examined for the presence of a C_9 -acid, amide, or nitrile, but none of these products was isolated.

It may be noted that the ready access to *N*-acyl- β -phenethylamines described here opens a simple route to the isoquinoline series through *o*-ring closure with dehydrating agents.⁷

This is already under investigation in this Laboratory.⁸

Experimental

***N*-*t*-Butylformamide.**—To a mixture of 25 ml. of acetic acid, 15 g. (0.2 mole) of *t*-butanol and 11 g. (0.2 mole)

(5) Joseph Kalish, M.S. thesis, 1946.

(6) Taylor and Baker, "Sidgwick's Organic Chemistry of Nitrogen," Oxford University Press, 1937, p. 321.

(7) (a) Manske, *Chem. Rev.*, **30**, 146; (b) Clemo and Turnbull, *J. Chem. Soc.*, 533 (1945); *ibid.*, 701-705 (1946).

(8) F. X. Murphy, research in progress.

of 90% sodium cyanide was added portionwise (one-half hour) and with shaking a solution of 50 g. of concentrated sulfuric acid in 25 ml. of acetic acid, keeping the temperature at 50–60°. The reaction vessel was stoppered and allowed to stand overnight, and the reaction mixture then poured into 500 ml. of water and neutralized with 15% sodium hydroxide solution by dropwise addition with stirring and ice-cooling. The formamide (with some *N*-*t*-butylamine) was extracted with five 100-ml. portions of ether and distilled after drying (potassium carbonate) and removal of the ether. Ten grams (50%) boiling at 202° (cor.) was obtained. The ether distillate, washed with 20 ml. of 15% hydrochloric acid yielded 2.0 g. (9%) of *t*-butylamine hydrochloride on evaporation of the acid layer.

Anal. (amide) Calcd. for $\text{C}_4\text{H}_{11}\text{ON}$: N, 13.86. Found (Kjeldahl): N, 13.56.

***t*-Butylamine Hydrochloride.**—*N*-*t*-Butylformamide (5 g.) was refluxed five hours with 12.5 g. of sodium hydroxide in 50 ml. of water. The condenser was provided at the exit with a trap containing 20 ml. of 15% hydrochloric acid. The hydrolysis mixture was finally distilled into the acid, from which the amine hydrochloride (4.3 g., 78%) was isolated by evaporation to dryness. On recrystallization from isopropyl alcohol it melted at 310° (cor.). The crude hydrochloride was completely soluble in both cold methanol and boiling isopropyl alcohol and hence free of ammonium chloride.

***t*-Butylbenzamide,** made from the amine hydrochloride by treatment with benzoyl chloride and sodium hydroxide, melted at 134–135° alone, in agreement with Campbell, Sommers and Campbell²⁰ or when mixed with the product obtained from benzonitrile and isobutene.³ The over-all yield of the amine was increased considerably by direct hydrolysis of the initial reaction mixture without isolating the formamide. The mixture was dissolved in water (100 ml.) and sodium hydroxide (120 g.) in 250 ml. of water was added with cooling. It was then hydrolyzed as in the preceding paragraph. The amine (b. p. 45°) was distilled off into the trap at intervals until completion of the reaction. The yield of amine hydrochloride was 18 g. (81%).

***N*-*t*-Octylamine (IV).**—*N*-*t*-Octylformamide was prepared as in the preceding experiment, substituting diisobutene (22.4 g., 0.2 mole) for the *t*-butanol used therein. Sodium hydroxide (120 g.) in 250 ml. of water was then added, without special precaution to avoid temperature rise (amine, b. p. 137–138°). *t*-Octylformamide (b. p. 110° (2 mm.))³ may be isolated at this point by ether extraction and distillation; in the present experiment it was hydrolyzed without isolation, by refluxing for five hours. The amine was removed by steam distillation, dissolved in ether, dried (potassium carbonate) and distilled after removal of the ether. Sixteen grams (62%) boiling at 137–138° was obtained. The ether-containing forerun of the distillate (100–137°) was dissolved in 10 ml. of 15% hydrochloric acid and the solution evaporated to yield 3 g. (9%) of the amine hydrochloride.

***N*-(Benzylmethylcarbonyl)-acetamide.**—A solution of 45 g. of concentrated sulfuric acid in 40 g. of acetonitrile was prepared by slow addition of the acid with stirring and cooling (5–10°). Allylbenzene⁹ (23.6 g., 0.2 mole) was added and the stirring continued without cooling. The mixture, orange-colored and turbid at first, became homogeneous and darker as the temperature rose slowly to 50° and then more rapidly to 80°. It was then cooled and poured into 400 ml. of 15% sodium hydroxide solution. An upper layer separated as a pale yellow oil which solidified after several hours. The solid (14 g., 40%) was filtered, washed with water and air-dried. On recrystallization from hexane it melted at 88–89°. The product is conveniently purified also by distillation (b. p., 180–185° (13 mm.)). The distilled material is subject to supercooling but quickly crystallizes on seeding.

(9) Prepared according to C. Weygand, "Organisch-chemische Experimentierkunst," Interscience Publishers, New York, N. Y., 1945, p. 356.

Anal. Calcd. for $C_{11}H_{15}ON$: N, 7.91. Found (Kjeldahl): N, 7.84.

Methylbenzylcarbinamine (Amphetamine) (II).—The distilled amide (15.4 g.) was boiled under reflux with 100 ml. of 15% hydrochloric acid for eleven hours. The mixture was then cooled, washed with benzene, and the aqueous layer separated and made alkaline with sodium hydroxide. The amine separated as an oil which was extracted with benzene, the extract dried (sodium sulfate), the benzene removed and the amine (7.0 g., 67%) boiling at 205–210° distilled at ordinary pressure. The benzoyl derivative melted at 134–135° alone or when mixed with an authentic sample prepared from phenylacetone.

N-(Dimethylbenzylcarbinol)-formamide.—Sodium cyanide (90%, 11 g., 0.2 mole) and 25 ml. of acetic acid were mixed with cooling and stirring. A solution of sulfuric acid (50 g.) in 25 ml. of acetic acid was then added with continued stirring at 20°. Dimethylbenzylcarbinol (30 g., 0.2 mole) was then added and the temperature permitted to rise spontaneously to 40–50° as the carbinol, insoluble at first, passed into solution. The mixture was then heated to 70° during one-half hour, stoppered, allowed to stand for two hours, diluted with 300 ml. of water, and neutralized with sodium carbonate. The formamide (21.5 g., 61%) separated as a viscous oil which was extracted with ether and distilled (b. p. 183–185° (15 mm.)) after drying (sodium sulfate) and removal of the ether.

Anal. Calcd. for $C_{11}H_{15}ON$: N, 7.81. Found (Kjeldahl): N, 7.55.

The formamide was also prepared by the same procedure

with substitution of methallylbenzene and also 2-methyl-3-phenyl-2-propene for the dimethylbenzylcarbinol used above with practically identical result.

Dimethylbenzylcarbinamine (III).—The formamide (10 g.) obtained as in the preceding paragraph was refluxed for five hours with 85 ml. of 20% sodium hydroxide solution. The mixture was then steam distilled, the distilled amine dissolved in ether, dried (sodium sulfate) and the amine (7.5 g., 89%) distilled at 85–90° (10 mm.) after removal of the ether. Zenitz, Macks and Moore¹⁰ reported the boiling point as 89–90° (10 mm.). The amine was dissolved in warm concentrated hydrochloric acid, the solution decolorized with carbon and allowed to cool to crystallize the hydrochloride, m. p. 198–198.5°. Zenitz, Macks and Moore¹⁰ reported the melting point as 200–201°; Shelton and van Campen,¹¹ 195–196°.

Anal. Calcd. for $C_{10}H_{15}N$: N, 9.39. Found (Kjeldahl): N, 9.12.

Summary

A convenient general method for the preparation of *t*-carbinamines, and also a new synthesis of β -phenethylamines of interest as medicinals has been described.

(10) Zenitz, Macks and Moore, *THIS JOURNAL*, **70**, 955 (1948).

(11) Shelton and Van Campen, U. S. Patent 2,408,345 (Sept. 1946).

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

The Identity of Müller's *iso*-Inositol with Racemic Inositol¹

BY HEWITT G. FLETCHER, JR.,² AND GORDON R. FINDLAY³

In 1912 Hugo Müller⁴ reported that the treatment of *meso*-inositol (m. p. 225°) or scyllitol with hydrogen halides in acetic acid solution at an elevated temperature gave a mixture from which, after hydrolysis with barium hydroxide, were isolated two hexahydroxycyclohexanes which he named *iso*- and *pseudo*-inositols. The marked similarity between the physical constants which Müller reported for *iso*-inositol and those which had previously been recorded for racemic inositol^{5,6,7} has led to the suggestion⁸ that the two cyclitols may be identical. It is the purpose of the present communication to present the evidence which verifies this identity.

Müller⁴ described several processes leading to

(1) A portion of the material of this paper is taken from a thesis submitted by Gordon R. Findlay to the Department of Chemistry of the Massachusetts Institute of Technology in October, 1944, in partial fulfillment of the requirements for the degree of Bachelor of Science.

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(3) Present address: Findlay Science Engineering Co., Watertown, Massachusetts.

(4) H. Müller, *J. Chem. Soc.*, **101**, 2383 (1912).

(5) L. Maquenne and C. Tanret, *Compt. rend.*, **110**, 86 (1890).

(6) G. Wyruboff, *Bull. soc. franc. minéral.*, **25**, 165 (1902); *Chem. Zentr.*, **73**, II, 1498 (1902).

(7) G. Tanret, *Compt. rend.*, **145**, 1196 (1907).

(8) H. G. Fletcher, Jr., *Advances in Carbohydrate Chem.*, **3**, 45 (1948).

his *iso*- and *pseudo*-inositols. Hydrogen chloride, hydrogen bromide and hydrogen iodide were all employed and both *meso*-inositol and its hexaacetate as well as scyllitol were used; in each case the solvent was glacial acetic acid and the initial reaction product was treated with boiling aqueous barium hydroxide. For the present work *meso*-inositol was heated with glacial acetic acid which had been saturated with hydrogen chloride at room temperature. After sixty-nine hours at a temperature of 160° the solvent was removed *in vacuo* and the residue boiled with aqueous barium hydroxide. Removal of barium, deionization and finally concentration *in vacuo* yielded a residue which deposited from aqueous alcoholic solution a crude crystalline product representing twelve per cent. of the starting material. After recrystallization from water the substance was found to possess the same melting point as racemic inositol; a mixed melting point with authentic racemic inositol was undepressed. Comparison of the optical crystallographic properties of *iso*-inositol with those of racemic inositol showed the two to be identical. Further comparison of *iso*-inositol with racemic inositol was made through their hexaacetates and hexabenzates. In both cases mixed melting points between the corresponding derivatives were undepressed.