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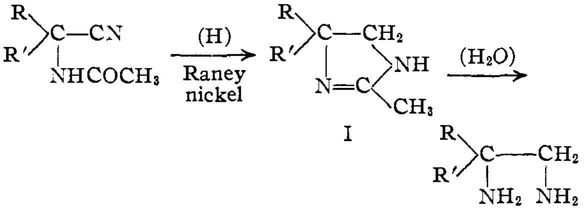
Synthesis of Certain Aliphatic 1,2-Diamines

BY W. LINCOLN HAWKINS AND B. S. BIGGS

The synthesis of 1,2-diamines by reduction of the corresponding α-aminonitriles has not been applied extensively due to the low yields encountered.[1] It has been shown[2] that α-aminonitriles undergo decomposition under the conditions of hydrogenation liberating hydrogen cyanide which poisons the catalyst, but that in acetic anhydride the monoacetyl derivatives can be reduced to diacetyl diamines using platinum oxide as the catalyst. N,N-Dialkylethylene diamines have been prepared by sodium-alcohol reduction of α-aminonitriles in yields as high as 50%, but the monoalkyl ethylenediamines are formed in much lower yield.[3]

In this investigation the monoacetyl derivatives of α-aminonitriles were reduced over Raney nickel to form dihydroimidazoles (I) which were hydrolyzed by acid and alkali to yield the corresponding 1,2-diamines.



By this series of reactions 2-methyl-1,2-diaminobutane was prepared in 53% yield based on 2-methyl-2-aminobutyronitrile as compared with 23% yield of the diamine by direct sodium-ethanol reduction of the aminonitrile. Reduction of 2-methyl-2-methylacetaminobutyronitrile gave a 70% yield of the corresponding N-alkyl-1,2-diamine. Since reduction of acetaminonitriles in the presence of a large excess of ammonia or methylamine did not alter the course of the reaction or the yield, it may be assumed that the imine, the first product of the reduction, undergoes cyclization rather than condensation with a primary amine.

Evidence of hydrogen bonding is observed in comparing the properties of the dihydroimidazoles. In those instances where hydrogen bonding is possible the compound is quite viscous as compared with the limpid oils obtained with dihydroimidazoles in which the labile hydrogen at position three has been replaced by an alkyl or acyl group.

Experimental

2-Methyl-2-acetaminobutyronitrile.—The cyanohydrin prepared from methyl ethyl ketone (72 g.) was transferred to an Aminco pressure bomb, previously chilled in Dry Ice. Liquid ammonia[4] (150 g.) was run in and the reaction mixture kept at room temperature overnight in the sealed bomb. The aminonitrile[5] was distilled in an atmosphere of nitrogen; yield, 71.4 g. or 73%; b. p., 87.5–88.5° (55 mm.); n^{20}D, 1.4302.

The aminonitrile (115 g.) was dissolved in acetic anhydride (600 cc.) while cooling in an ice-water-bath and kept at room temperature overnight. The acetyl derivative was distilled in an atmosphere of nitrogen; yield, 135.7 g., 83% or 61% based on methyl ethyl ketone; b. p., 161–162° (5 mm.); m. p., 42–43°. Reihlen and coworkers[2] reported a melting point of 15–20° for this compound.

Anal. Calcd. for $C_7H_{12}ON_2$: C, 60.00; H, 8.57; mol. wt. (Rast), 140. Found: C, 59.98; H, 8.62; mol. wt., 157.

Acetylation of crude aminonitrile gave a 64% over-all yield of 2-methyl-2-acetaminobutyronitrile based on methyl ethyl ketone.

2,4-Dimethyl-4-ethyldihydroimidazole.—One-half mole (70 g.) of 2-methyl-2-acetaminobutyronitrile in absolute ethanol (30 cc.) was hydrogenated over Raney nickel[6] (100 cc.) in the presence of liquid ammonia (200 g.). Two moles of hydrogen per mole of nitrile were taken up ninety minutes at 90° and 2000 lb. per sq. in. The product was distilled under nitrogen; yield, 55.5 g. or 88%; b. p. 132–133.6° (50 mm.), 203.4–204.4° (747 mm.); n^{20}D, 1.4751.

Anal. Calcd. for $C_7H_{14}N_2$: C, 66.66; H, 11.11. Found: C, 65.03; H, 11.09.

Although numerous attempts to obtain a better check on the above carbon analysis were unsuccessful, the following derivatives of the dihydroimidazole analyzed correctly. The picrate crystallized in thick, yellow needles; yield, 93%; m. p., 123.2–123.8°.

Anal. Calcd. for $C_{13}H_{17}O_7N_5$: C, 43.94; H, 4.79. Found: C, 44.06; H, 5.12.

The dihydroimidazole (11.8 g.) reacted with acetic anhydride (60 cc.) at room temperature forming an acetyl derivative; yield, 14 g. or 89%; b. p. 151.0–151.2° (50 mm.); n^{20}D 1.4884.

Anal. Calcd. for $C_9H_{16}ON_2$: C, 64.29; H, 9.52. Found: C, 64.03; H, 9.53.

2-Methyl-1,2-diaminobutane. (a) Sodium-Alcohol Reduction of 2-Methyl-2-acetaminobutyronitrile.—2-Methyl-2-acetaminobutyronitrile (56 g.) was dissolved in absolute ethanol (1 liter) and the solution heated to reflux. Metallic sodium (100 g.) was added at such a rate as to maintain a vigorous reflux without external heat. The reaction mixture was cooled to room temperature and diluted with water (2.5 liters). This aqueous ethanol solution was taken to dryness catching the distillate under hydrochloric acid (500 cc. of 1:1). The distillate was taken to dryness and the viscous, reddish residue treated with strong potasium hydroxide solution (80 g. of potassium hydroxide in 80 cc. of water) while cooling in an ice-water bath. The basic fraction separated out as an oil which on distillation yielded, along with an unidentified high boiling fraction, the diamine; yield, 9.1 g., or 23%; b. p. 142.4–143.8° (752 mm.); n^{20}D, 1.4483.

Anal. Calcd. for $C_5H_{14}N_2$: C, 58.82; H, 13.72. Found: C, 58.71; H, 13.87.

The diamine formed a crystalline dipicrate identical with that obtained from the acid hydrolysis product below.

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(1) McMeeking and Stevens, *J. Chem. Soc.*, 347 (1933); Winans and Adkins, THIS JOURNAL, **55**, 4172 (1933).

(2) Reihlen, von Hessling, Hühn and Weinbrenner, *Ann.*, **493**, 2032 (1932).

(3) Bloom, Breslow and Hauser, THIS JOURNAL, **67**, 539 (1945).

(4) Menge, *ibid.*, **56**, 2197 (1934).

(5) Biltz and Slotta, *J. prakt. Chem.*, **113**, 233 (1926).

(6) Pavlic and Adkins, THIS JOURNAL, **68**, 1471 (1946).

(b) **Hydrolysis of 2,4-Dimethyl-4-ethyldihydroimidazole.**—2,4-Dimethyl-4-ethyldihydroimidazole (20 g.) was added to a 30% solution (100 cc.) of potassium hydroxide. After refluxing under nitrogen for five hours, the reaction mixture was homogeneous. While cooling in an ice-water-bath potassium hydroxide pellets (70 g.) were added and the diamine which separated out as an oily layer dried over potassium hydroxide pellets and distilled in an atmosphere of nitrogen; yield 13.5 g. or 83%. This diamine gave a crystalline picrate identical with that obtained by acid hydrolysis.

Hydrolysis of the dihydroimidazole (1.5 g.) with concentrated hydrochloric acid (10 cc.) in a sealed glass tube at 175–180° for twelve hours gave a 72% yield of 2-methyl-1,2-diaminobutane from which a crystalline picrate was formed; m. p., 228.6–229.3° with decomposition.

Anal. Calcd. for $C_{17}H_{20}O_{14}N_8$: C, 36.43; H, 3.59. Found: C, 36.50; H, 3.80.

2-Methyl-2-methylacetaminobutyronitrile.—One mole (72 g.) of methyl ethyl ketone was converted to the cyanohydrin and this product treated with methylamine (180 g.) in an Aminco pressure bomb at room temperature overnight. 2-Methyl-2-methylaminobutyronitrile was distilled under nitrogen; yield, 78.2 g. or 70%; b. p., 153–154.5°.[7] The aminonitrile (67.5 g.) was acetylated as described previously and the product distilled under nitrogen; yield, 87 g. or 95% (66.5% based on methyl ethyl ketone); b. p., 119–120° (7 mm.); $n^{20}D$, 1.4671.

Anal. Calcd. for $C_8H_{14}ON_2$: C, 62.30; H, 9.15. Found: C, 62.78; H, 9.37.

2-Methyl-2-methylacetaminobutyronitrile formed a crystalline picrate; m. p., 187–188°.

Anal. Calcd. for $C_{14}H_{17}O_8N_5$: C, 43.85; H, 4.46. Found: C, 44.12; H, 4.49.

2,3,4-Trimethyl-4-ethyldihydroimidazole.—One-half mole (77 g.) of 2-methyl-2-methylacetaminobutyronitrile in absolute ethanol (30 cc.) was hydrogenated over Raney nickel catalyst (100 cc.) at an initial pressure of 2030 lb. per sq. in. and a temperature of 140°. The product was distilled in an atmosphere of nitrogen; yield, 65.7 g. or 94%; b. p., 118.5–119.4° (50 mm.). The picrate of this dihydroimidazole crystallized in yellow needles; m. p., 161–162.5°.

Anal. Calcd. for $C_{14}H_{19}O_7N_5$: C, 45.51; H, 5.21. Found: C, 45.60; H, 5.26.

2-Methyl-2-methylamino-1-aminobutane. (a) **Alkaline Hydrolysis.**—The dihydroimidazole (14 g.) was hydrolyzed with 30% potassium hydroxide. After refluxing seven hours, the reaction mixture, which was not completely homogeneous, was treated as above and the resulting, oily layer fractionated; yield, 5.0 g. or 43%. (Unreacted dihydroimidazole (3.0 g.) was recovered from this reaction.) The diamine was redistilled in an atmosphere of nitrogen; b. p. 154–155° (737 mm.); $n^{20}D$ 1.4502, and from this product a crystalline dipicrate was prepared; m. p. 201–203° with decomposition.

Anal. Calcd. for $C_{18}H_{22}O_{14}N_8$: C, 37.62; H, 3.87. Found: C, 37.02; H, 4.09.

(b) **Acid Hydrolysis.**—2,3,4-Trimethyl-4-ethyldihydroimidazole (6.4 g.) was hydrolyzed with concentrated hydrochloric acid as above. The diamine, recovered in the usual way, was distilled in an atmosphere of nitrogen; yield, 4.3 g. or 74%. Identity of the diamine was established by comparison of its picrate with the sample obtained by alkaline hydrolysis.

2-Acetaminobutyronitrile.—One mole (58 g.) of propionaldehyde was converted to the cyanohydrin and from this product 2-aminobutyronitrile was prepared by treating with liquid ammonia (150 g.). After removal of the excess ammonia, the product was distilled under nitrogen; yield, 28.7 g. or 35%; b. p. 94.3° (50 mm.). The nitrile (17.5 g.) which had been described previously[8] was acetylated; yield, 13.2 g. or 50%; b. p. 152–153° (5 mm.).

Anal. Calcd. for $C_6H_{10}ON_2$: C, 57.10; H, 8.01. Found: C, 56.27; H, 8.17.

This acetyl derivative was unstable under the conditions of distillation (50% recovery on redistillation) and did not form a picrate in ethanol solution.

2-Methyl-4-ethyldihydroimidazole.—2-Acetaminobutyronitrile (15.2 g.) in absolute ethanol (420 cc.) and in the presence of Raney nickel (50 cc.) was hydrogenated at an initial pressure of 1970 lb. per sq. in. and at 150°. The product was distilled under nitrogen; yield, 7.1 g. or 53%; b. p., 95–96° (7 mm.). The dihydroimidazole formed a crystalline picrate; m. p. 103–104°.

Anal. Calcd. for $C_{12}H_{15}O_7N_5$: C, 42.22; H, 4.43. Found: C, 42.16; H, 4.53.

1,2-Diaminobutane.—2-Methyl-4-ethyldihydroimidazole (2.5 g.) was hydrolyzed with 30% potassium hydroxide; yield, 1.2 g. or 61%; b. p. 135–137°. This diamine formed a picrate,[9] m. p., 256° with decomposition.

Anal. Calcd. for $C_{16}H_{18}O_{14}N_8$: C, 35.15; H, 3.33. Found: C, 35.09; H, 3.39.

2-Ethylacetaminobutyronitrile.—The cyanohydrin of methyl ethyl ketone was converted to 2-ethylaminobutyronitrile by treating with ethylamine; yield, 75%; b. p., 85–87° (45 mm.). The aminonitrile (33.5 g.) was acetylated with acetic anhydride (200 cc.); yield, 23.3 g. or 51%; b. p., 117–118° (10 mm.).

Anal. Calcd. for $C_9H_{16}ON_2$: C, 64.29; H, 9.52. Found: C, 64.03; H, 9.65.

2,4-Dimethyl-3,4-diethyldihydroimidazole.—2-Ethylacetaminobutyronitrile (42 g.) in absolute ethanol (200 cc.) and with Raney nickel catalyst (50 cc.) was hydrogenated at an initial pressure of 2100 lb. per sq. in. and at 150°; yield, 32 g.; b. p. 128.0–128.4° (50 mm.). This dihydroimidazole formed a crystalline picrate melting at 129–130°.

Anal. Calcd. for $C_{15}H_{21}O_7N_5$: C, 46.97; H, 5.53. Found: C, 47.06; H, 5.60.

Summary

1. α-Aminonitriles have been converted to 1,2-diamines through hydrogenation of their monoacetyl derivatives followed by hydrolysis of the resulting dihydroimidazoles.

2. It has been shown that the course of this hydrogenation is not affected by the presence of liquid ammonia or methylamine.

MURRAY HILL, N. J. RECEIVED JANUARY 27, 1949

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[7] Immendörfer, *Ber.*, **48**, 608 (1915).

[8] Zelinsky and Stadnikoff, *Ber.*, **41**, 2062 (1908).

[9] Demjanow, *ibid.*, **40**, 246 (1907).