From the neutral fraction the starting amide (20%) was recovered. The small amount of remaining liquid showed a medium infrared absorption band at 4.55 μ (nitrile).

A small sample of the amine hydrochloride was refluxed with *p*-nitrobenzoyl chloride in benzene–pyridine for several hours to give N-(2,3,5,6-tetramethylbenzyl)-*p*-nitrobenzamide, m.p. 218.0–218.6° (recrystallized from alcohol).

Anal. Calcd. for $C_{18}H_{20}N_2O_3$: C, 69.2; H, 6.5; N, 9.0. Found: C, 69.1, 69.3; H, 6.4, 6.7; N, 8.9, 8.9.

Benzonitrile (Expt. 5).—The sample withdrawn as soon as possible after the addition had a weak absorption band at 4.5 μ (nitrile). The intensity of this band increased as the reaction proceeded while a band at 6.0 μ (amide) became weaker.

The reaction product was mixed with petroleum ether (b.p. 35–55°) and cooled in a Dry Ice–acetone-bath to separate the starting amide (35%). The mother liquor was washed with 6 *N* hydrochloric acid and distilled to give a mixture of benzonitrile and benzaldehyde. The distillate was then oxidized with alkaline permanganate according to a conventional method[23] to give benzoic acid (4%) and benzonitrile (45%), b.p. 75–76° at 20 mm.

In experiment 6, samples withdrawn after various periods of time had no infrared absorption band at 4.5 μ (nitrile). Although no pure component was isolated from the reaction mixture the neutral fraction had a weak band at 4.5 μ (nitrile) and a strong band at 5.9 μ (aldehyde).

2,2,2-Triisopropylethylamine (Expt. 7).—Distillation of the reaction product gave crude 2,2,2-triisopropylethylamine (97%), b.p. 87–90° at 8 mm., which solidified into a wax-like solid, m.p. 40–45°. N-(2,2,2-Triisopropylethyl)-*p*-nitrobenzamide, m.p. 124.5–125.5° (recrystallized from alcohol), was prepared by refluxing with *p*-nitrobenzoyl chloride in benzene for 20 minutes.

Anal. Calcd. for $C_{18}H_{28}N_2O_3$: C, 67.5; H, 8.8; N, 8.7. Found: C, 67.3; 67.5; H, 8.7, 8.9; N, 8.8, 8.8.

Treatment of the crude amine with concentrated hydrochloric acid caused an exothermic reaction, followed by precipitation of crystalline amine hydrochloride. Recrystallization from hot water afforded 2,2,2-triisopropylethylamine hydrochloride, m.p. in the region of 355° in a sealed tube.

Anal. Calcd. for $C_{11}H_{26}NCl$: C, 63.6; H, 12.6; N, 6.7; Cl, 17.1. Found: C, 63.6, 63.7; H, 12.9, 12.7; N, 6.7, 6.7; Cl, 17.0, 17.3.

Triisopropylacetaldehyde (Expt. 8).—The reaction product was distilled to give a colorless oil, b.p. 105–110° at 4 mm. A part of the distillate was refluxed with 2,4-dinitrophenylhydrazine and a small amount of concentrated hydrochloric acid in alcohol. The crystals were dissolved in benzene and chromatographed on alumina. On evaporating the benzene the 2,4-dinitrophenylhydrazone in 46% yield of triisopropylacetaldehyde, m.p. 152.0–152.8° (recrystallized from alcohol), was obtained.

Anal. Calcd. for $C_{17}H_{26}N_4O_4$: C, 58.3; H, 7.5; N, 16.0. Found: C, 58.4, 58.4; H, 7.7, 7.6; N, 15.9, 16.0.

A part of the distillate yielded a mixture of picrates, m.p. 185–197°, after treatment with picric acid in alcohol. This mixture contained picrates of both imine and amine. The amount of amine listed in Table I was obtained by subtracting the weight of imine picrate calculated on the basis of aldehyde isolated above.

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[23] R. L. Shriner and R. C. Fuson, "The Systematic Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1948, p. 170.

[CONTRIBUTION FROM THE ORGANIC CHEMISTRY DEPARTMENT, RESEARCH DIVISION, ABBOTT LABORATORIES]

Synthesis of Primary 1,2-Diamines by Hydrogenation of α-Aminonitriles[1]

BY MORRIS FREIFELDER AND RICHARD B. HASBROUCK

RECEIVED JULY 6, 1959

In the catalytic hydrogenation of α-aminonitriles to 1,2-diamines, hydrogenolysis is a competing reaction. Successful low pressure reduction of unsubstituted α-aminonitriles in alcoholic hydrogen chloride in the presence of platinum oxide is reported.

Catalytic hydrogenation of α-aminonitriles has not led directly to primary diamines. Reduction has been accomplished only when at least one alkyl substituent has been present on the amino nitrogen.[2a,b] Yields as high as 50% have been obtained when a tertiary aminonitrile has been hydrogenated.[2a,c] There are a few instances of better than average yields.[3a–d]

The difficulty in obtaining good yield is due to the small difference between the rates of hydrogenation and hydrogenolysis. That hydrogenolysis is a problem is shown by Winans and Adkins,[4] who report a 37% yield of β-diethylaminoethylamine from high pressure reduction of diethylaminoacetonitrile with Raney nickel. They also found in the case of four different α-piperidinonitriles that rapid hydrogenolysis of the nitrile group occurred without any of the desired β-piperidinoethylamines being formed. In this Laboratory we have attempted to hydrogenate piperidinoacetonitrile under various conditions with palladium and platinum catalysts and have obtained only piperidine.

Reitsema[5] reports a 37% yield of N-β-aminoethylpyrrolidine from high pressure reduction of pyrrolidinoacetonitrile with a nickel catalyst. In the work of Leonard and his co-workers[6] extensive hydrogenolysis is encountered in the reduction of α-acetanilinophenylacetonitrile. They obtained a 20% yield of desired product I plus 60% of aniline and 10% of benzylaniline.

Reduction leading to primary diamines involves acylation of the aminonitrile, followed by

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[1] Presented at the Atlantic City Meeting, American Chemical Society, September, 1959.

[2] (a) W. L. Hawkins and B. J. Biggs, THIS JOURNAL, **71**, 2530 (1949); (b) R. A. Turner, *ibid.*, **68**, 1607 (1946); (c) I. G. Farbenind., German Patent 561,156, Sept. 22, 1932, reports yields of 20-40% in high pressure reductions of various mono- and di-N-substituted α-aminonitriles using nickel-on-kieselguhr.

[3] (a) F. E. King and R. M. Acheson, *J. Chem. Soc.*, 683 (1946), obtained a 61% yield of β-diethylaminoethylamine by a high pressure reduction of diethylaminoacetonitrile in ether in the presence of Raney nickel. (b) Union Carbide and Carbon Corp., British Patent 745,684, Feb. 29, 1946, noted 90% yields after successful high pressure hydrogenation of dialkylaminoacetonitriles with a cobalt catalyst. (c) J. Corse, J. T. Bryant and H. A. Shonle, THIS JOURNAL, **68**, 1907 (1946), obtained yields ranging from 34–88% in catalytic reductions of mixed dialkylsubstituted-α-aminonitriles in ether in the presence of Raney nickel and ammonia at 125°. (d) H. Baganz and H. Milster, *Arch. Pharm.*, **291**, 118 (1958), report 82 and 79% yields of N-β-aminoethylmorpholine and N-β-aminoethylpiperidine by reduction of the corresponding nitriles with nickel and ammonia.

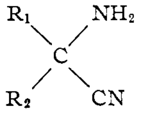
[4] C. F. Winans and H. Adkins, THIS JOURNAL, **55**, 4172 (1933).

[5] R. H. Reitsema, U. S. Patent 2,496,955, Feb. 7, 1950.

[6] N. J. Leonard, G. W. Leubner and E. H. Burk, Jr., *J. Org. Chem.*, **15**, 982 (1950).

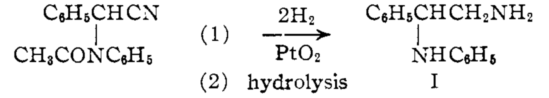
TABLE I

α-AMINONITRILES

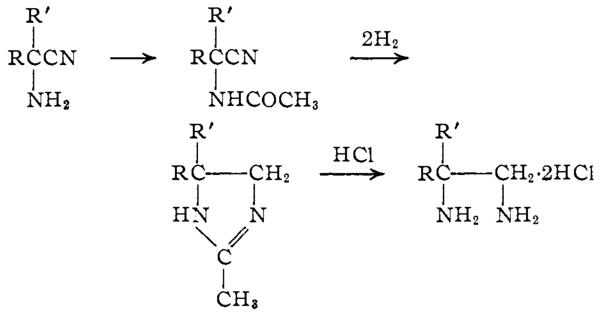


R_1	R_2	Method (equation)	Yield, %	B.p. °C.	B.p. Mm.	Melting point, °C. B·HCl	Formula	Nitrogen, % Calcd.	Nitrogen, % Found
CH_3	CH_3	A[a,b]	55	64–67	39		$C_4H_8N_2$	33.30	33.38
CH_3	C_2H_5	A[a,c]	53	75.5–76.5	30		$C_5H_{10}N_2$	28.55	28.63
C_2H_5	C_2H_5	A[a,d]	37	82–83	25		$C_6H_{12}N_2$	24.98	25.21
CH_3	n-C_3H_7	A[a,e]	37	87–90	40		$C_6H_{12}N_2$	24.98	24.66
n-$C_4H_9C(Et)H$	H	A[a,f]	13			131–132	$C_9H_{19}N_2Cl$	14.70	14.68
C_2H_5	H	B[g]	38			143–145	$C_4H_9N_2Cl$	23.24	22.69
CH_3	n-C_9H_{19}	C[h]	12			101–103	$C_{12}H_{25}N_2Cl$	12.04	12.04
$C_6H_5CH_2$	H	C[h]	36			167–168 dec.	$C_9H_{11}N_2Cl$	15.34	15.46
$C_6H_5CH_2$	CH_3	C[h]	18			135–136 dec.	$C_{10}H_{13}N_2Cl$	14.25	14.25

[a] Procedure of Biltz and Slotta[10] modified as follows: The ammonium sulfate was added to the sodium cyanide solution at 12–15°. The ketone was added to this solution at 15–20° over 10–15 min. [b] Reaction stood for 24 hr. at 25°; product (lit.)b. p. 55–60° (20 mm.). [c] Reaction stirred 10 hr. at 25°; product (lit.) b.p. 72° (20 mm.). [d] Reaction stirred 3.5 hr. at 25°; product (lit.) b.p. 81° (15 mm.). [e] Reaction stirred 10 hr. at 25°. [f] Sodium cyanide solution added to all other reactants at 7–10° over 25 min. with vigorous stirring. Stirred 2.5 hr. longer at 7–10°. Diluted with water, separated, dried upper layer and treated with alcoholic HCl at 10°. Concentrated *in vacuo* and precipitated product with ether. [g] The methanolic solution of crude aminonitrile (prepared by the method of ref. 11b) was concentrated to a residue *in vacuo* at 30°, dissolved in ethanol and precipitated with ethereal HCl; it was recrystallized from ethanol. [h] See Experimental section.



high pressure hydrogenation in the presence of nickel.[2a,7a,7b] The resultant imidazoline is then hydrolyzed to give the 1,2-diamine.

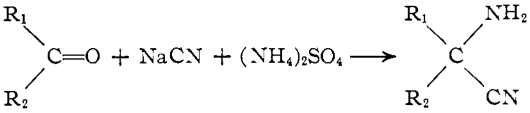


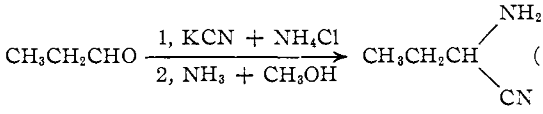
Reihlen and his co-workers[8] report that α-aminonitriles undergo decomposition under hydrogenation conditions liberating HCN which poisons the catalyst. However, in acetic anhydride the acetylaminonitrile can be reduced to the diacetylamine using platinum oxide. Hydrolysis is required as in the work of Hawkins and Biggs.

In this investigation low pressure reduction in the presence of platinum oxide was carried out using the aminonitrile base or the hydrochloride in alcoholic hydrogen chloride. Yields were generally good, ranging from 60–82%. In addition to the advantage of reduction at low pressure, this method tends to minimize hydrogenolysis of the nitrile group. Furthermore, the use of the acid medium described here eliminates the acylation and hydrolysis steps noted in other procedures.[2a,7a,7b,8]

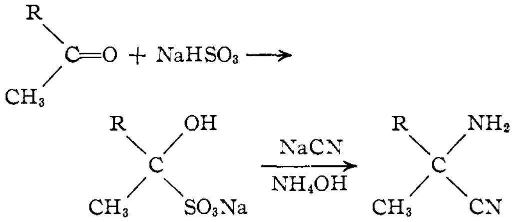
The low pressure procedure does not appear to be applicable to α-aminonitriles in which the amino group is substituted. Extensive hydrogenolysis occurred during the reduction of 1-cyclohexyl-2,5-dicyano-2,5-dimethylpyrrolidine, yielding 89% of methylamine hydrochloride and 69% of 1-cyclohexyl - 2,5 - dimethylpyrrolidine. Similar reductions attempted on 1-dimethylamino-1-cyclohexanecarbonitrile and diethylaminoacetonitrile also resulted in hydrogenolysis of the nitrile group.

The α-aminonitriles were prepared by slight modifications of standard methods based on the Strecker[9] synthesis. The procedures include those of Biltz and Slotta[10] (equation A), Tiemann[11a,11b] (equation B) and Knoevenagel[12a,12b] (equation C).


(A)



(B)



(C)

Most of the preparations were carried out on a one- or two-mole scale and were run only once or twice. Yields ranged from 12 to 55% and could probably be improved by further study of the reactions.

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(7) (a) W. L. Hawkins, U. S. Patent 2,587,043, Feb. 26, 1952; (b) G. Erhard and F. Nolte, German Patent 830,954, Feb. 7, 1952.

(8) H. Reihlen, G. von Hessling, W. Hühn and E. Weinbrenner, *Ann.*, **493**, 20 (1932).

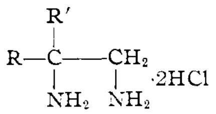
(9) A. Strecker, *ibid.*, **75**, 28 (1850).

(10) H. Biltz and K. Slotta, *J. prakt. Chem.*, **113**, 241, 249, 251 (1926).

(11) (a) F. Tiemann and L. Friedländer, *Ber.*, **14**, 1970 (1881); (b) H. T. Clarke and H. J. Bean, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 29.

(12) (a) E. Knoevenagel and E. Mercklin, *Ber.*, **37**, 4089 (1904); (b) C. F. H. Allen and J. A. Van Allan, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 275.

TABLE II



1,2-DIAMINES $R-C(R')(NH_2)-CH_2(NH_2)\cdot 2HCl$

R	R′	Yield, %	M.p., °C.	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
C_2H_5[a]	H	76[c]	186–187	$C_4H_{12}N_2\cdot 2HCl$	29.82	29.94	8.76	8.75	17.40	17.87
$C_6H_5CH_2$[b]	H	64[c]	246–248 dec.	$C_9H_{14}N_2\cdot 2HCl$	48.43	48.36	7.13	7.12	12.55	12.66
CH_3[a]	CH_3	82.5[c]	306 dec.[k]	$C_4H_{12}N_2\cdot 2HCl$	29.82	30.04	8.76	8.69	17.40	17.36
C_2H_5[a]	CH_3	68	[g,h]	$C_5H_{14}N_2$						
C_3H_7[a]	CH_3	75	[g,i]	$C_6H_{16}N_2\cdot 2HCl$						
C_9H_{19}[b]	CH_3	10[j]		$C_{12}H_{28}N_2\cdot 2HCl$	52.72	52.73	11.07	11.08	10.27	10.19
$C_6H_5CH_2$[b]	CH_3	60[d,e]	240–241	$C_{10}H_{16}N_2\cdot 2HCl$[l]	50.62	50.53	7.64	7.65	11.81	11.65
C_2H_5[a]	C_2H_5	61.5[d]	179–181	$C_6H_{16}N_2\cdot 2HCl$	38.16	38.38	9.59	9.89	14.82	14.87
C_4H_9[b]	C_2H_5	65[f]	246.5 dec.	$C_8H_{20}N_2\cdot 2HCl$	46.75	46.60	10.46	10.27	12.12	12.10

[a] Method 1. [b] Method 2. [c] Recrystallized from absolute alcohol. [d] Recrystallized from alcohol and acetone. [e] Recrystallized further by dissolving in water and adding solution to 10 volumes of acetone. [f] Recrystallized from hot isopropyl alcohol. [g] Could not obtain solid salt. [h] Obtained base, b.p. 149–153° (755 mm.), n^{25}D 1.4442. Hawkins and Biggs, THIS JOURNAL, **71**, 2530 (1949), give b.p. 142.4–143.5° (752 mm.), n^{20}D 1.4483. [i] After long standing the material showed signs of solidifying. It was, however, converted to the base and distilled, b.p. 90° (30 mm.), n^{25}D 1.4433. [j] Slow decomposition begins at 188.5–193°. Difficulty in obtaining a crystalline hydrochloride probably accounts for the low yield. [k] Reihlen, Hessling, Hühn and Weinbrenner, *Ann.*, **493**, 20 (1932), give analytical data but no melting point for this compound. [l] The salt must be dried thoroughly since it tends to form a hydrate.

Several of the lower molecular weight aminonitriles were isolated as the free bases by distillation. The others were obtained as the crystalline hydrochlorides. Physical data and yields of the α-aminonitriles are presented in Table I.

Acknowledgments.—The authors gratefully acknowledge the assistance of Messrs. F. C. Garven and T. S. Wang in preparing several of the α-aminonitriles and that of Mr. G. R. Stone in aiding with the catalytic hydrogenations. They also thank Messrs. E. F. Shelberg and O. L. Kolsto and their staff for the microanalytical assays.

Experimental

α-Aminonitriles.—Method A, see footnotes *a–f*, Table I; method B, see footnote *g*, Table I. Method C is an adaptation of those of Knoevenagel and Mercklin[12a] and Allen and Van Allan.[12b]

One mole of aldehyde or methyl ketone was added to a solution of one mole of sodium bisulfite in 160 cc. of water over 30 min. The temperature rose to 60° and in some cases a crystalline solid separated. One mole of 28% ammonium hydroxide was added to the reaction mixture and the whole heated at 55–60° for one hour. It was then cooled to 6° and a solution of one mole of sodium cyanide in 140 cc. of water was added dropwise (stirring) over 30 min. The mixture was stirred at 6° for an additional 30 min. and then warmed to 30° over a one-hour period. The reaction was diluted with 100 cc. of water and the upper layer separated and dried over anhydrous magnesium sulfate. The crude product was cooled in ice and to it was added one mole of alcoholic hydrogen chloride over a 30-min. period. The major part of the alcohol was distilled *in vacuo* at about room temperature and ether was added to the residue to complete crystallization.

Preparation of the Diamine Dihydrochlorides. Method 1.—A solution of 235 cc. of 14% alcoholic hydrogen chloride (0.9 mole) was cooled in a Parr shaker bottle. Three-tenths of a mole of an aminonitrile was added in portions while keeping the temperature below 10°. One gram of platinum oxide was added carefully and the mixture hydrogenated under 3 atmospheres pressure. After hydrogen uptake was complete the solution was filtered from the catalyst and the filtrate concentrated to a thick mass. This was then treated with isopropyl alcohol, cooled and filtered.

Method 2.—A solution or suspension of 0.1 mole of the aminonitrile hydrochloride in 150 cc. of absolute ethanol was cooled in a Parr shaker bottle and 0.1 mole of alcoholic hydrogen chloride was added in portions while the temperature was kept below 10°. Then 0.75 g. of platinum oxide was added carefully and the mixture hydrogenated as in method 1. After reduction was complete it was often necessary to add some water to dissolve the diamine dihydrochloride. If water was added it was necessary to concentrate the solution to dryness, add benzene and azeotropically remove the water. The salt was then isolated as in method 1.

The use of one extra equivalent of hydrogen chloride appeared to increase the solubility of the starting material and aid in isolation of the diamine dihydrochloride.

Hydrogenation of 1-Cyclohexyl-2,5-dicyano-2,5-dimethylpyrrolidine.—A solution of 11.55 g. (0.05 mole) of the dinitrile[13] in 150 cc. of absolute alcohol was treated with 0.2 mole of alcoholic hydrogen chloride as in method 1. It was then hydrogenated in the presence of 0.6 g. of platinum oxide. When hydrogen uptake was complete the solution was filtered from the catalyst and concentrated to about 25 cc. under reduced pressure. When anhydrous ether was added a mushy solid was obtained which became filterable on the addition of acetone. The solid was shown to be methylamine hydrochloride by its melting point and mixed melting point with an authentic sample. The yield amounted to 89%.

The filtrate was concentrated, treated with water and made strongly basic with solid sodium hydroxide. The oily residue was extracted with benzene and then dried, filtered and distilled. After removal of solvent the material boiled at 70° (1.4 mm.), n^{25}D 1.4734. Analytical values corresponded to those calculated for 1-cyclohexyl-2,5-dimethylpyrrolidine. The yield was 69%.

Anal. Calcd. for $C_{12}H_{23}N$: C, 79.54; H, 12.70; N, 7.74. Found: C, 79.11; H, 12.49; N, 8.21.

NORTH CHICAGO, ILL.

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[13] Described by P. L. de Benneville and J. S. Strong, U. S. Patent 2,580,738, Jan. 1, 1952.