[CONTRIBUTION FROM THE COLLEGE OF PHARMACY, UNIVERSITY OF MICHIGAN]

Reaction of Basic Nitriles with Hydrogen Chloride

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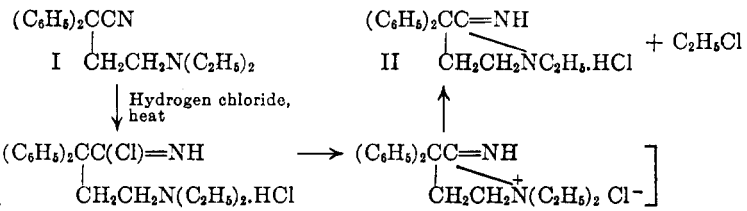
Certain basic nitriles, when heated at an elevated temperature in a steam of hydrogen chloride, yielded 2-iminopolymethylenimine hydrochlorides which, in some cases, could be converted into the corresponding 2-ketopolymethylenimines.

It has been shown[3-6] that α-phenyl- and α,α-diphenyl - γ - dialkylaminobutyronitriles, when heated with concentrated hydrochloric or hydrobromic acid, were converted into salts of 1-alkyl-2-imino-3-phenyl(or 3,3-diphenyl)pyrrolidines or the corresponding 2-pyrrolidone.

It was found[7] that when α,α-diphenyl-γ-diethylaminobutyronitrile (I)[8] was heated at 270–275° in a stream of hydrogen chloride, 1-ethyl-2-imino-3,3-diphenylpyrrolidine hydrochloride (II) was obtained in 70% yield.[9] Hydrolysis of this product yielded the corresponding 2-pyrrolidone.[8]



Since it seemed that this process might be a satisfactory general one for the synthesis of various substituted 2-pyrrolidones, and also 2-piperidones, a number of nitriles were heated in a stream of hydrogen chloride (see Table I for products).

γ-Dimethylaminobutyronitrile,[10] α-phenyl-γ-dimethylaminobutyronitrile,[11] α-phenyl-δ-dimethylaminovaleronitrile,[12] α-phenyl-δ-dibutylaminovaleronitrile and α,α-diphenyl-ε-dimethylaminocapronitrile[13] yielded the hydrochlorides of 1-methyl-2-iminopyrrolidine (III), 1-methyl-2-imino-3-phenylpyrrolidine (IV), 1-methyl-2-imino-3-phenylpiperidine (V), 1-butyl-2-imino-3-phenylpiperidine (VI), and 1-methyl-2-imino-3,3-diphenylhexamethylenimine (VII), respectively (Table II).

α - (3 - Methoxyphenyl) - γ - dimethylaminobutyronitrile[14] did not yield the expected product; instead, 1-methyl-2-(methylimino)-3-(3-methoxyphenyl)pyrrolidine was obtained. It was isolated as the base since the hydrochloride could not be purified.

α,α -Diphenyl - γ - dimethylaminobutyronitrile[8] yielded a mixture of 1-methyl-2-imino-3,3-diphenylpyrrolidine hydrochloride (VIII)[15] and 1 - methyl - 2 - (methylimino) - 3,3 - diphenylpyrrolidine hydrochloride (IX)[15] from which only impure products were obtained by recrystallization. The impure VIII was converted by nitrous acid[4,15,16] into 1-methyl-3,3-diphenyl-2-pyrrolidone[4,8,15,16] for identification. After impure IX had been treated with nitrous acid,[17] it was possible to obtain pure IX by recrystallization.

δ - Dimethylaminovaleronitrile[18] yielded a product, undoubtedly 1-methyl-2-iminopiperidine hydrochloride (X),[19] but the salt could not be purified by recrystallization. For identification, crude X was hydrolyzed to δ-methylaminovaleric acid hydrochloride.[19,20]

(1) This paper represents parts of the dissertations submitted by A. J. Zambito and R. E. Stenseth for the Ph.D. degrees in the University of Michigan.

(2) Parke, Davis and Co. Fellow.

(3) E. Walton, P. Ofner, and R. H. Thorpe, *J. Chem. Soc.*, 648 (1949).

(4) W. Wilson, *J. Chem. Soc.*, 3524 (1952).

(5) M. W. Gittos and W. Wilson, *J. Chem. Soc.*, 2371 (1955).

(6) W. Wilson, *Chem. & Ind.*, 200 (1955).

(7) F. F. Blicke and A. J. Zambito, Abstracts, 111th Meeting of the American Chemical Society, 1947, p. 3K.

(8) D. J. Dupré, J. Elks, B. A. Hems, K. N. Speyer, and R. M. Evans, *J. Chem. Soc.*, 500 (1949).

(9) The nature of the first intermediate, shown in the reaction scheme, is uncertain; it might be a mono- or dihydrochloride.

(10) W. Huber, R. O. Clinton, W. Boehme, and M. Jackson, *J. Am. Chem. Soc.*, **67**, 1618 (1945).

(11) C. E. Kwartler and P. Lucas, *J. Am. Chem. Soc.*, **68**, 2395 (1946).

(12) A. W. D. Adison and A. L. Morrison, *J. Chem. Soc.*, 1474 (1950).

(13) During the preparation of this nitrile, 2,2,7,7-tetraphenyloctanedinitrile was obtained as a by-product. The reduction of this substance to 2,2,7,7-tetraphenyl-1,8-octanediamine is described in the experimental part.

(14) H. Kägi and K. Miescher, *Helv. Chim. Acta*, **32**, 2489 (1949).

(15) F. E. King, K. G. Latham, and M. W. Partridge, *J. Chem. Soc.*, 4268 (1952).

(16) A. L. Morrison and H. Rinderknecht, *J. Chem. Soc.*, 1478 (1950).

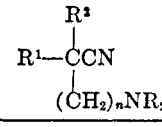
(17) The stability of a 2-(substituted imino)pyrrolidine toward nitorus acid has been reported.[5]

(18) J. M. Stewart, *J. Am. Chem. Soc.*, **76**, 3228 (1954).

(19) J. Renault, *Ann. chim. (Paris)*, **10**, 135 (1955).

(20) C. Rath, *Ann.*, **489**, 107 (1931).

TABLE I



	n	R	R^1	R^2	Base or Salt	Yield, %	B.P.	M.P.
1	2	CH_3	H	H	Base	52	64–66,[a] 10 mm.	
1a	2	CH_3	H	H	Hydrochloride			129–130
2	2	CH_3	C_6H_5	H	Base	63	93–98,[b] 0.3 mm.	
3	2	CH_3	3-$CH_3OC_6H_4$	H	Base	69	122–124,[c] 0.4 mm.	
4	2	CH_3	C_6H_5	C_6H_5	Base	83	146–147,[d] 0.3 mm.	
5	2	C_2H_5	C_6H_5	C_6H_5	Base	72	140–143,[e] 0.1 mm.	
6	3	CH_3	H	H	Base	84	84–86,[f] 14 mm.	
6a	3	CH_3	H	H	Hydrochloride			136–137[f]
7	3	CH_3	C_6H_5	H	Base	82	108–109, 0.5 mm.	
7a	3	CH_3	C_6H_5	H	Hydrochloride			123–124
7b	3	CH_3	C_6H_5	H	Picrate			108–109[g]
8	3	CH_3	C_6H_5	C_6H_5	Base	87		66–68[h]
9	3	C_4H_9	C_6H_5	H	Base	69	136–137, 0.15 mm.	
9a	3	C_4H_9	C_6H_5	H	Acid oxalate			147–148
10	4	CH_3	C_6H_5	C_6H_5	Base	39	161–162, 0.4 mm.	
10a	4	CH_3	C_6H_5	C_6H_5	Hydrochloride			166–167
11	5	CH_3	C_6H_5	C_6H_5	Base	56	163–164, 0.25 mm.	
11a	5	CH_3	C_6H_5	C_6H_5	Hydrochloride			149–150

		Carbon, %		Hydrogen, %		Nitrogen, %		Chloride, %	
	Formula	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
1a	$C_6H_{12}N_2Cl$	48.48	48.86	8.82	8.83	18.85	18.71	23.85	23.97
6	$C_7H_{14}N_2$	66.82	66.53	11.18	10.91				
6a	$C_7H_{15}N_2Cl$	51.68	51.88	9.30	9.18	17.22	17.18	21.80	21.78
7	$C_{13}H_{18}N_2$	77.18	77.06	8.97	8.87	13.85	14.05		
7a	$C_{13}H_{19}N_2Cl$	65.39	65.11	8.02	8.11	11.74	11.77	14.85	14.81
9	$C_{19}H_{30}N_2$	79.66	79.78	10.56	10.62	9.78	9.77		
9a	$C_{21}H_{32}O_4N_2$	66.99	67.05	8.57	8.47	7.44	7.65		
10	$C_{20}H_{24}N_2$	82.15	82.00	8.27	8.39				
10a	$C_{20}H_{25}N_2Cl$	73.04	73.06	7.66	7.65	8.52	8.56	10.78	11.00
11	$C_{21}H_{26}N_2$	82.31	82.36	8.55	8.52				
11a	$C_{21}H_{27}N_2Cl$	73.55	73.75	7.92	8.12	8.17	8.15		

[a] Ref. 10, b.p. 44–47° (1.5 mm.). [b] Ref. 11, b.p. 130° (4 mm.). [c] Ref. 14, b.p. 115–118° (0.05 mm.). [d] Ref. 8, b.p. 150–152° (0.8 mm.). [e] Ref. 8, b.p. 165° (1 mm.). [f] Ref. 18, b.p. 67–68° (3 mm.); hydrochloride, m.p. 138–140°. Analysis of the base was not reported. [g] Ref. 12, m.p. 109–110°. [h] Ref. 21, m.p. 64–65°.

All of the salts except 7b were obtained by addition of an ether solution of hydrogen chloride or oxalic acid to the base dissolved in ether; 7b was obtained by addition of saturated ethanolic picric acid to the base dissolved in absolute ethanol.

All of the salts were recrystallized from absolute ethanol. Compound 8 was recrystallized from petroleum ether (b.p. 90–100°).

Attempts to prepare imino compounds from α,α - diphenyl - δ - dimethylaminovaleronitrile[21] and α,α - diphenyl - ω - dimethylaminoheptylonitrile were unsuccessful.

When the hydrochlorides of α-phenyl-γ-dimethylaminobutyronitrile and α-phenyl-δ-dibutylaminovaleronitrile were heated without the use of a stream of hydrogen chloride, IV and VI, respectively, were obtained again but in lower yields.

Compound III, in the form of the base, was converted into 1-methyl-2-pyrrolidone[22] by the use of Raney nickel.[23]

When IV was heated with aqueous sodium hydroxide solution for three hours, 1-methyl-3-phenyl-2-pyrrolidone (XI)[5] was obtained; hydrolysis for twenty-four hours yielded a mixture of XI and α-phenyl-γ-methylaminobutyric acid. The acid was isolated as the hydrochloride, which was converted by heat into XI. Compound XI was reduced with sodium and butyl alcohol to 1-methyl-3-phenylpyrrolidine.[24]

Heating VI with aqueous sodium hydroxide for three hours yielded α-phenyl-δ-butylaminovaleramide; when the hydrolysis was carried out for a longer time, α-phenyl-δ-butylaminovaleric acid was obtained. The acid was converted by heat into 1-butyl-3-phenyl-2-piperidone.

Attempts to convert III, V, VI, and VII into the corresponding 2-ketopolymethylenimines by the use of nitrous acid[4,5,15] were unsuccessful. Instead of the desired products, only the nitrates[25]

(21) N. R. Easton, J. H. Gardner, M. L. Evanick, and J. R. Stevens, *J. Am. Chem. Soc.*, **70**, 76 (1948).

(22) J. Tafel and O. Wassmuth, *Ber.*, **40**, 2831 (1907).

(23) G. D. Buckley and T. J. Elliott, *J. Chem. Soc.*, 1508 (1947).

(24) F. Bergel, N. C. Hindley, A. L. Morrison, and H. Rinderknecht, *J. Chem. Soc.*, 269 (1944).

of III, V, and VI were obtained; VII yielded an unidentified product.

EXPERIMENTAL

Basic nitriles (1–11) (Table I). The general procedure, used for the preparation of all of the nitriles except 1, 6, 10, and 11, is illustrated in the case of 7.

α-Phenyl-δ-dimethylaminovaleronitrile (7). A solution of 46.8 g. (0.4 mole) of phenylacetonitrile in 100 ml. of dry toluene was added, dropwise, during a period of 30 min., to a stirred suspension of 17.2 g. (0.44 mole) of pulverized sodamide[26] in 100 ml. of toluene. The temperature was maintained at 30–40° during the addition. After stirring for 2 hr., the mixture was stirred and kept below reflux temperature while a solution of 48.6 g. (0.4 mole) of γ-dimethylaminopropyl chloride[27] in 50 ml. of toluene was added, dropwise, during a period of 30 min. After the mixture had been stirred and refluxed for 4 hr., it was cooled and 150 ml. of water was added to the stirred mixture. The layers were separated and the toluene layer was washed with 50 ml. of water, cooled, and extracted with 100 ml. of 20% hydrochloric acid and then with 25 ml. of water. The combined acidic and aqueous extracts were cooled and excess 20% aqueous sodium hydroxide solution was added. The separated oil was extracted with ether, the extract was dried over potassium carbonate, the solvent was removed, and the residue distilled.

Compounds 2, 3, and 4 were prepared from phenylacetonitrile, 3-methoxyphenylacetonitrile[28] and diphenylacetonitrile, respectively, with the use of β-dimethylaminoethyl chloride and sodamide; 5 was prepared from diphenylacetonitrile, β-diethylaminoethyl chloride, and sodamide; 8 was prepared from diphenylacetonitrile, γ-dimethylaminopropyl chloride, and sodamide; 9 was prepared from phenylacetonitrile, γ-dibutylaminopropyl chloride, and sodamide.

γ-Dibutylaminopropyl chloride. A stirred solution of 225 g. (1.2 moles) of γ-di-*n*-butylaminopropanol in 750 ml. of dry chloroform was cooled in an ice-salt bath while a stream of dry hydrogen chloride was passed into the liquid until saturation had occurred. The mixture was then stirred and the temperature was not allowed to exceed 20° during the dropwise addition of 450 g. (3.8 moles) of thionyl chloride. After the mixture had been stirred at room temperature for 4 hr. and refluxed for 12 hr., the solvent and excess thionyl chloride were removed under reduced pressure. The residue was poured into stirred ice water and 28% aqueous ammonium hydroxide solution was added until the mixture was alkaline. The separated oil was extracted with ether, the extract was dried over potassium carbonate, the solvent was removed and the residue distilled; b.p. 109–111° (11 mm.),[29,30] lit.[29] b.p. 109–111° (11 mm.); yield 221 g. (89%).

γ-Dimethylaminobutyronitrile (1). This nitrile was prepared from γ-dimethylaminopropyl chloride (212 g., 1.75 moles) and potassium cyanide (150 g., 2.3 moles) according to a procedure used for the preparation of γ-diethylaminobutyronitrile.[31]

δ-Dimethylaminovaleronitrile (6). An ice-cold solution of 63 g. (1.4 moles) of anhydrous dimethylamine in 60 ml. of dry benzene was added, dropwise, to a stirred, ice-cold solution of 80 g. (0.48 mole) of δ-bromovaleronitrile[32] in 80 ml. of benzene. After the mixture had been stirred at room temperature for 16 hr., the precipitated dimethylamine hydrobromide was removed by filtration. The filtrate was concentrated, filtered, and distilled.

The preparation of 10 and 11 is illustrated in the case of 11.

α,α-Diphenyl-ω-dimethylaminoheptylonitrile (11). α,α-Diphenyl-ω-bromoheptylonitrile was prepared from 96.6 g. (0.5 mole) of diphenylacetonitrile, 21.5 g. (0.55 mole) of pulverized sodamide, and 345 g. (1.5 moles) of 1,5-dibromopentane. In this preparation, a toluene suspension of the sodio derivative of diphenylacetonitrile was added to the bromide in refluxing toluene[33]; yield 164 g.

A solution of 82 g. of the crude bromonitrile in 200 ml. of dry benzene was added, dropwise, during a period of 1 hr., to a stirred, ice-cold solution of 45 g. (1 mole) of anhydrous dimethylamine in 100 ml. of benzene. The mixture was stirred at room temperature for 24 hr. and then refluxed for 4 hr. After cooling and adding water to the stirred mixture, the layers were separated and the benzene layer was extracted with 20% hydrochloric acid. The acidic extract was cooled and excess 20% aqueous sodium hydroxide solution was added. The separated oil was extracted with ether, the extract was dried over potassium carbonate, the solvent was removed, and the residue distilled (56% yield based on diphenylacetonitrile).

For the preparation of 10, dimethylamine was allowed to react with α,α-diphenyl-ε-bromocapronitrile.[8] The bromonitrile, in crude form, was prepared by interaction of diphenylacetonitrile, 1,4-dibromobutane and sodamide in the manner mentioned above for the corresponding heptylonitrile; a by-product, 2,2,7,7-tetraphenyloctanedinitrile,[34] was also obtained. It was recrystallized from chloroform; m.p. 226–228°, lit.[8] m.p. 224–228°; yield 12%.

2,2,7,7-Tetraphenyl-1,8-octanediamine. A suspension of 13 g. (0.03 mole) of 2,2,7,7-tetraphenyloctanedinitrile in 600 ml. of dry toluene was added slowly, through a large bore dropping funnel, to a stirred suspension of 6.85 g. (0.18 mole) of lithium aluminum hydride in 600 ml. of dry ether. The mixture was stirred and refluxed for 22 hr. After the dropwise addition of 14 ml. of water to the stirred mixture, stirring was continued for 24 hr. The solid material (A) was removed by filtration and retained, and the solvents were removed from the filtrate. The product (1.3 g.) was recrystallized from chloroform; m.p. 206–208°.

The dried filter cake (A) was placed in a Soxhlet extractor and extracted with chloroform for 4 hr. After concentration of the extract, the product precipitated. The combined material was recrystallized from chloroform; m.p. 208–210°; total yield 9.2 g. (69%).

Anal. Calcd. for $C_{32}H_{36}N_2$: C, 85.67; H, 8.09; N, 6.24. Found: C, 85.45; H, 8.04; N, 6.28.

(25) During the treatment of a 2-iminopyrrolidine hydrochloride with nitrous acid, the formation of a 2-iminopyrrolidine nitrate has been reported.[5]

(26) F. W. Bergstrom, *Org. Syntheses*, **20**, 86 (1940).

(27) This base was liberated from the hydrochloride immediately before use by R. R. Burtner's method (*J. Am. Chem. Soc.*, **71**, 2578 (1949)), and the toluene solution was kept ice cold to prevent cyclization of the base.

(28) W. S. Rapson and R. Robinson, *J. Chem. Soc.*, 1533 (1935).

(29) A. Marxer (*Helv. Chim. Acta*, **24**, 209E (1941)) prepared this compound in 54% yield from 1-bromo-3-chloropropane and dibutylamine.

(30) R. R. Adams and F. C. Whitmore (*J. Am. Chem. Soc.*, **67**, 735 (1945)) obtained this compound in 68% yield by the method of A. Marxer (ref. 29); b.p. 118–130° (25 mm.).

(31) W. J. Humphlett, J. Weiss, and C. R. Hauser, *J. Am. Chem. Soc.*, **70**, 4021 (1948).

(32) N. J. Leonard and W. C. Wildman, *J. Am. Chem. Soc.*, **71**, 3100 (1949).

(33) The detailed procedure was similar to that employed by L. C. Cheney, W. B. Wheatley, M. E. Speeter, W. M. Byrd, W. E. Fitzgibbon, W. F. Minor, and S. B. Binkley (*J. Org. Chem.*, **17**, 770 (1952)) for the preparation of crude α,α-diphenyl-ε-chlorocapronitrile and crude α,α-diphenyl-ω-chloroheptylonitrile from diphenylacetonitrile, lithium amide, and the required dichloroalkanes.

(34) This nitrile[8] was obtained as a by-product in 29.6% yield when α,α-diphenyl-ε-bromocapronitrile was prepared by addition of 1,4-dibromobutane to the sodio derivative of diphenylacetonitrile.

The dihydrochloride, prepared in chloroform-ether, was recrystallized from methyl ethyl ketone–methanol; m.p. 336–338° dec.

Anal. Calcd. for $C_{32}H_{38}N_2Cl_2$: C, 73.69; H, 7.34; N, 5.37. Found: C, 73.74; H, 7.38; N, 5.31.

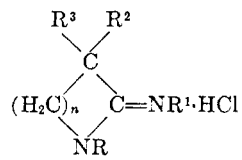
Substituted 2-iminopolymethylenimine hydrochlorides (1–8) (Table II). The general procedure, used for the preparation of the imine hydrochlorides, is illustrated in the case of 1; modifications are mentioned below.

mixture was kept at this temperature[37] for 5 to 10 min. to complete conversion of the nitrile into the molten hydrochloride. The temperature was then raised quickly to 270–275°[38] and held there for 5 to 10 min., continuing the stream of hydrogen chloride throughout this time. The dark, viscous oil was cooled somewhat and rubbed under acetone. The solid material which formed was filtered and recrystallized.

The general procedure was modified for the isolation of 3, 4, and 8.

TABLE II

SUBSTITUTED 2-IMINOPOLYMETHYLENIMINE HYDROCHLORIDES



	n	R	R^1	R^2	R^3	Yield, %	M.P.
1	2	CH_3	H	H	H	46	182–183
2	2	CH_3	H	C_6H_5	H	54[a]	214–215 dec.
3	2	CH_3	CH_3	3-$CH_3OC_6H_4$	H		223
3a (base)	2	CH_3	CH_3	3-$CH_3OC_6H_4$	H	40	151–153
4	2	CH_3	CH_3	C_6H_5	C_6H_5	26	285–286 dec.[b]
4a (base)	2	CH_3	CH_3	C_6H_5	C_6H_5		105–106[c]
5	2	C_2H_5	H	C_6H_5	C_6H_5	70	261–262
5a (base)	2	C_2H_5	H	C_6H_5	C_6H_5		97–88
6	3	CH_3	H	C_6H_5	H	50	241–243
7	3	C_4H_9	H	C_6H_5	H	54[d]	188–189
8	4	CH_3	H	C_6H_5	C_6H_5	19	155–156

		Carbon, %		Hydrogen, %		Nitrogen, %		Chloride, %	
	Formula	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
1	$C_5H_{11}N_2Cl$	44.61	44.66	8.24	8.26	20.81	20.89	26.34	26.28
2	$C_{11}H_{15}N_2Cl$	62.70	62.86	7.17	7.28	13.30	13.15	16.83	16.85
3	$C_{13}H_{19}ON_2Cl$	61.28	61.38	7.52	7.60	11.00	11.14	13.92	14.15
3a	$C_{13}H_{18}ON_2$	71.52	71.64	8.31	8.22	12.83	12.56		
4	$C_{18}H_{21}N_2Cl$	71.86	71.46	7.04	6.89	9.31	9.38	11.79	11.85
4a	$C_{18}H_{20}N_2$	81.77	81.81	7.63	7.75	10.60	10.51		
5	$C_{18}H_{21}N_2Cl$	71.86	71.96	7.04	7.07	9.31	9.20	11.79	11.84
5a	$C_{18}H_{20}N_2$	81.77	81.87	7.63	7.59	10.60	10.82		
6	$C_{12}H_{17}N_2Cl$	64.13	64.23	7.62	7.62	12.47	12.52	15.78	15.76
7	$C_{15}H_{23}N_2Cl$	67.52	67.43	8.69	8.59	10.50	10.62	13.29	13.12
8	$C_{19}H_{23}N_2Cl$	72.48	72.48	7.36	7.39	8.90	8.82	11.26	11.55

[a] The yield obtained by heating (275–280°) the hydrochloride of the nitrile without the use of a stream of hydrogen chloride was 11%. [b] Ref. 15, m.p. 292–293° dec. [c] Ref. 15, m.p. 106°. [d] The yield obtained by heating (280–290°) the hydrochloride of the nitrile without the use of a stream of hydrogen chloride was 32%.

All of the compounds except 4a and 5a were recrystallized with the use of Norite. Compounds 1, 2, 5, 6, 7, and 8 were recrystallized from isopropyl alcohol; 3 and 4 from bsolute ethanol; 3a from methanol; 4a from methanol-water; 5a from petroleum ether (b.p. 60–75°).

1-Methyl-2-iminopyrrolidine hydrochloride (1). γ-Dimethylaminobutyronitrile (22.4 g., 0.2 mole) was placed in an 8-inch Pyrex test tube made from standard wall 41 mm. tubing and fitted with a rubber stopper through which were inserted an inlet tube, an outlet tube, and a thermometer. The thermometer and inlet tube extended almost to the bottom of the test tube. A rapid stream of dry hydrogen chloride was passed into the liquid[35] and it was heated with a free flame until the temperature reached 155–160°.[36] The

The melt obtained during the preparation of 3 was dissolved in water. After the addition of excess 20% aqueous sodium hydroxide solution, the separated oil was extracted with ether. The extract was dried over magnesium sulfate, concentrated, and refrigerated. The precipitate (crude base 3a) was filtered and recrystallized. The hydrochloride (3) was prepared in absolute ethanol-ether and recrystallized.

The viscous oil obtained during the preparation of 4 formed a glassy solid. When it was recrystallized from isopropyl alcohol, crude 4, m.p. 255–275°, separated in 46% yield. After concentration of the filtrate, a lower melting portion was obtained which represented a 29% crude yield of 1-methyl-2-imino-3,3-diphenylpyrrolidine hydrochloride; m.p. 205–225°, lit.[4] m.p. 223.5–224°. Neither compound could be purified by recrystallization. In a separate experi-

(35) In some instances, the material solidified as its transformation into the hydrochloride began.

(36) In some experiments, an initial temperature rise to 200° or higher occurred spontaneously before heat had been applied. The temperature was allowed to fall to the desired level.

(37) In a few cases (3, 4, and 8), a higher temperature was required.

(38) A temperature higher than 270–275° was required for the preparation of 3, 4, 6, 7, and 8; in these instances, the temperature was maintained at 285–295°.

ment in which the pyrolysis was conducted at 305–315°, crude 4 was obtained in 69% yield. It was purified in the following manner.

A solution of 3.3 g. of crude 4 in 15 ml. of 5% hydrochloric acid, 10 ml. of ethanol and 5 ml. of water was stirred at 65–70° during the dropwise addition of a solution of 3.5 g. of sodium nitrite in 10 ml. of water. After stirring at 65–70° for 15 min., the mixture was cooled and allowed to remain at room temperature for 12 hr. The crystals which separated were filtered and recrystallized; yield of pure 4, 1.9 g. (26% from the nitrile).

The base 4a was obtained by the addition of excess 10% aqueous sodium hydroxide solution to an aqueous solution of 4, extracting with ether, drying the extract with magnesium sulfate and removing the solvent. The residue (base 4a) was recrystallized.

The picrate of 4a, prepared in absolute ethanol, was recrystallized from absolute ethanol; m.p. 180–181°, lit.[15] m.p. 180–182°.

In order to isolate 8, the crude product, a viscous liquid, was dissolved in methyl ethyl ketone. The gummy precipitate obtained upon the addition of ether was dissolved in hot isopropyl alcohol. Upon the addition of ether to the cooled solution, crystalline material was obtained.

1-Methyl-2-pyrrolidone. 1-Methyl-2-iminopyrrolidine hydrochloride (4 g.), after treatment with an equivalent amount of aqueous sodium hydroxide solution, was converted into 1-methyl-2-pyrrolidone with the use of 0.1 g. of moist Raney nickel[23,39,40]; b.p. 89–90° (20 mm.), lit.[22] b.p. 197–202° (736 mm.); yield 2.4 g. (80%).

The hydrochloride, prepared in ether, was recrystallized from acetone-ether; m.p. 87–88°, lit.[41] m.p. 86–88°.

Upon exposure to air or by treatment with carbon dioxide, an ether solution of 1-methyl-2-iminopyrrolidine yielded an ether-insoluble, water-soluble substance, undoubtedly a carbonate.[42] This substance softened at 105° and melted at 115–125° with the evolution of a gas. It decomposed upon attempted recrystallization. A precipitate was obtained upon the addition of barium chloride solution to an aqueous solution of the substance. Treatment of an aqueous solution with hydrochloric acid and evaporation to dryness yielded 1-methyl-2-iminopyrrolidine hydrochloride.

1-Methyl-2-iminopyrrolidine nitrate. 1-Methyl-2-iminopyrrolidine hydrochloride was treated with sodium nitrite and hydrochloric acid according to a procedure[15] used for the hydrolysis of certain 2-iminopyrrolidines. The only product isolated was the nitrate of the pyrrolidine. It was obtained after neutralization (alkacid test ribbon) of the acidic solution with aqueous sodium hydroxide solution, evaporation to dryness and extraction with ethanol. After concentration of the extract, addition of ether and refrigeration, the precipitated nitrate was recrystallized from absolute ethanol; m.p. 115–117°; yield 25%. The nitrate ion brown ring test was positive.

An authentic sample of the nitrate was prepared from the base and an equivalent amount of nitric acid. It was recrystallized from absolute ethanol; m.p. 116–117°; mixed m.p. 115–117°.

Anal. Calcd. for $C_6H_{11}O_3N_1$: C, 37.26; H, 6.88; N, 26.08. Found: C, 37.36; H, 6.81; N, 26.18.

1-Methyl-3-phenyl-2-pyrrolidone. (A) A mixture of 27 g. (0.128 mole) of 1-methyl-2-imino-3-phenylpyrrolidine hydrochloride, 25.6 g. (0.64 mole) of sodium hydroxide and 200 ml. of water was stirred and refluxed for 3 hr. The cooled mixture was extracted with ether and the solvent was removed from the extract. The oily residue solidified after some time. The product was recrystallized from anhydrous ether; m.p. 60–61°, lit.[5] m.p. 58–59°; yield 18.0 g. (80%).

(B) When the hydrolysis described above was carried out for 24 hr., a mixture of 1-methyl-3-phenyl-2-pyrrolidone (35%) and α-phenyl-γ-methylaminobutyric acid, isolated as the hydrochloride (18%), was formed. The pyrrolidone was isolated from the ether layer. The aqueous layer was acidified with hydrochloric acid, evaporated to dryness, and extracted with absolute ethanol. The extract was concentrated and ether was added until a precipitate began to form. After refrigeration for 24 hr., the precipitated butyric acid hydrochloride was filtered and recrystallized from absolute ethanol; m.p. 177–179°.

Anal. Calcd. for $C_{11}H_{16}O_2NCl$: N, 6.11; Cl, 15.49. Found: N, 6.20; Cl, 15.31.

α-Phenyl-γ-methylaminobutyric acid hydrochloride (1.0 g.) was heated at 190–200° for a few minutes. Water and hydrogen chloride were evolved. The crude, oily 1-methyl-3-phenyl-2-pyrrolidone was dissolved in ether, filtered and the filtrate was concentrated. Upon refrigeration, 0.3 g. of the pyrrolidone was precipitated; m.p. and mixed m.p. 60–61°.

1-Methyl-3-phenylpyrrolidine. Sodium (25 g.) was added to a hot solution of 16.5 g. (0.94 mole) of 1-methyl-3-phenyl-2-pyrrolidone in 300 ml. of butyl alcohol. The mixture was refluxed for 1.5 hr., cooled, and treated slowly with water. After filtration, the filtrate was acidified with hydrochloric acid and evaporated to dryness. The residue was dissolved in the minimum volume of water and solid sodium hydroxide was added until the mixture was strongly alkaline. The separated oil was extracted with ether, the extract was dried over magnesium sulfate, the solvent was removed, and the residue distilled; b.p. 200–215°, lit.[24] b.p. 105–110° (11 mm.); yield 10 g. (66%)

The picrate melted at 157–159°, lit.[24] m.p. 155–158°.

1-Methyl-3,3-diphenyl-2-pyrrolidone. Crude 1-methyl-2-imino-3,3-diphenylpyrrolidine hydrochloride (2.8 g.) was treated with dilute hydrochloric acid and sodium nitrite (3.0 g.) in a manner similar to a described procedure[4]; the product melted at 144–145°, lit.[4] m.p. 144°; mixed m.p. 144–145°[43]; yield 1.1 g. (approximately 45%).

1-Methyl-2-imino-3-phenylpiperidine nitrate. When 1-methyl-2-imino-3-phenylpiperidine hydrochloride was subjected to nitrous acid in the manner used to convert 2-iminopyrrolidines into 2-pyrrolidones,[15] only the piperidine nitrate was obtained. It was isolated in 62% yield in the same manner as 1-methyl-2-iminopyrrolidine nitrate. It melted at 138–139° after recrystallization from absolute ethanol.

Anal. Calcd. for $C_{12}H_{17}O_3N_3$: C, 57.34; H, 6.82; N, 16.72. Found: C, 57.01; H, 6.71; N, 16.62.

An authentic sample of the nitrate was prepared from the base and an equivalent amount of nitric acid. It was recrystallized from absolute ethanol; m.p. and mixed m.p. 138–139°.

1-Ethyl-3,3-diphenyl-2-pyrrolidone. A mixture of 22.5 g. (0.075 mole) of 1-ethyl-2-imino-3,3-diphenylpyrrolidine hydrochloride, 56.1 g. (1.0 mole) of potassium hydroxide, 45 ml. of water, and 225 ml. of ethylene glycol was refluxed for 30 hr. The cooled mixture was diluted with 750 ml. of water, the precipitate was filtered, triturated with dilute

(39) We used the sponge nickel catalyst, preserved under water, purchased from the Davison Chemical Co., Division of W. R. Grace and Co., Cincinnati Plant, Box 75, Station 1, Cincinnati 29, Ohio.

(40) An attempt to convert 1-ethyl-2-imino-3,3-diphenylpyrrolidine into 1-ethyl-3,3-diphenyl-2-pyrrolidone by the use of Raney nickel was unsuccessful.

(41) S. M. McElvain and J. F. Vozza, *J. Am. Chem. Soc.*, 71, 896 (1949).

(42) The formation of carbonates from certain imino derivatives has been reported. See A. Pinner (*Die Imidoäther und Ihre Derivate*, Oppenheim, Berlin, 1892, p. 120), A. E. Chichibabin, R. A. Konovalova, and A. A. Konovalova (*Ber.*, 54B, 814 (1921)) and Y. L. Gol'dfarb and M. S. Kondakova (*Compt. rend. acad. sci. U.R.S.S.*, 49, 421 (1945); *Chem. Abstr.*, 40, 6489 (1946)).

(43) An authentic sample (m.p. 144–145°) was prepared by a described method.[5]

hydrochloric acid, filtered, and recrystallized from petroleum ether (b.p. 90–100°); m.p. 113–114°, lit.[8] m.p. 111.5–113°; yield 14.5 g. (73%).

δ-Methylaminovaleric acid hydrochloride. Crude 1-methyl-2-iminopiperidine hydrochloride (1.55 g.) (m.p. 140–147°[44]) was converted into the amino acid hydrochloride by a described procedure[19]; m.p. 96–97°, lit.[19,20] m.p. 93°; yield 0.4 g. (approximately 24%).

Anal. Calcd. for $C_6H_{14}O_2NCl$: C, 42.98; H, 8.42; N, 8.36; Cl, 21.15. Found: C, 42.95; H, 8.43; N, 8.60; Cl, 21.06.

α-Phenyl-δ-butylaminovaleramide. A mixture of 2.7 g. (0.01 mole) of 1-butyl-2-imino-3-phenylpiperidine hydrochloride, 2.0 g. (0.05 mole) of sodium hydroxide, and 20 ml. of water was stirred, refluxed for 3 hr., cooled, and extracted with ether. The extract was dried over magnesium sulfate and the solvent was removed. The oily residue, which partially solidified, was triturated with ether and filtered; the product melted at 90–91°; yield 1.5 g. (60%). Recrystallization from absolute ethanol did not raise the melting point.

Anal. Calcd. for $C_{15}H_{24}ON_2$: C, 72.54; H, 9.74; N, 11.28. Found: C, 72.59; H, 9.79; N, 11.45.

The hydrochloride, prepared in absolute ethanol-ether, was recrystallized from isopropyl alcohol–ether; m.p. 135–136°.

Anal. Calcd. for $C_{15}H_{25}ON_2Cl$: C, 63.25; H, 8.85; N, 9.84; Cl, 12.45. Found: C, 63.24; H, 8.60; N, 9.96; Cl, 12.45.

α-Phenyl-δ-butylaminovaleric acid. After the hydrolysis described above had been carried out for 17 hr., ether was added and three layers formed. The middle layer was neutralized with hydrochloric acid whereupon a white precipitate formed. Without filtration, the mixture was evaporated to dryness and extracted with absolute ethanol. The crude valeric acid obtained, upon concentration and refrigeration of the extract, was recrystallized from absolute ethanol; m.p. 184°; yield 30%.

Anal. Calcd. for $C_{15}H_{23}O_2N$: C, 72.25; H, 9.30; N, 5.62. Found: C, 72.28; H, 9.40; N, 5.60.

Identifiable products were not obtained from the top or lower layers.

1-Butyl-3-phenyl-2-piperidone. α-Phenyl-δ-butylaminovaleric acid (3.5 g.) was placed in a distillation flask to which a condenser was attached and heated at 190–200° for 15 min. Water collected in the condenser. The residue in the flask, the piperidone, was distilled; b.p. 138–140° (0.4 mm.); yield 2.9 g. (90%).

Anal. Calcd. for $C_{15}H_{21}ON$: C, 77.88; H, 9.15; N, 6.06. Found: C, 77.68; H, 8.99; N, 6.18.

When an attempt was made to obtain the piperidone by treatment of 1-butyl-2-imino-3-phenylpiperidine hydrochloride with nitrous acid[15] at 85° for 10 hr., 1-butyl-2-imino-3-phenylpiperidine nitrate precipitated in 68% yield when the reaction mixture was cooled; m.p. 149–150° after recrystallization from absolute ethanol.

Anal. Calcd. for $C_{15}H_{23}O_3N_3$: C, 61.41; H, 7.90; N, 14.33. Found: C, 61.54; H, 7.73; N, 14.10.

(44) The monohydrate of this substance melted at 157°.[19]

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[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

Reaction of Diazo Compounds with Nitroolefins. VII. The Thermal Decomposition of Nitropyrazolines

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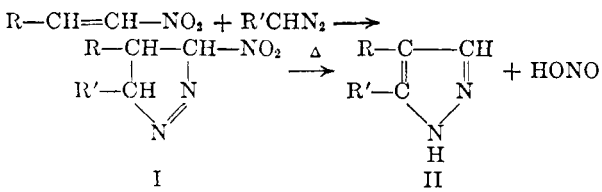
The course of thermal decomposition of nitropyrazolines of type III, in which the diazonitrogen is attached to the β-carbon of the nitroolefin from which the pyrazoline was prepared, is dependent upon the nature of the substituent in the 3-position. When this substituent is alkyl (methyl or ethyl), thermal decomposition leads to nitrocyclopropanes. When the substituent is hydrogen, the intermediate pyrazoline has not been isolated, and the nitrocyclopropane results directly from the reaction of diphenyldiazomethane and the nitroolefin. When the substituent is phenyl, nitrocyclopropanes do not result. Products isolated from the thermal decomposition of 4-nitro-3,3,5-triphenylpyrazoline are discussed.

The thermal decomposition of nitropyrazolines (I), derived from nitroolefin and diazomethane or diazoacetic ester, is known[2] to result in the elimination of the elements of nitrous acid with the formation of pyrazoles of type II.[3] The conversion of I to II is also known to be catalyzed by acid or base.[2] Hitherto the only nitrocyclopropanes that have been prepared by the reaction of nitroolefin with diazo compounds are those reported by Mustifa[4] from diazofluorene and nitroolefins.



We have recently shown that diphenyldiazomethane adds to nitroolefins to give pyrazolines of type III, in which the diazo nitrogen atom is attached to the *beta*-carbon atom of the nitroolefin.[5,6]

(1) From the Ph.D. theses of Henry G. Braxton, Jr., and Carl Serres, Jr., The University of Minnesota, 1960 and 1956, respectively.

(2) W. E. Parham and J. L. Bleasdale, *J. Am. Chem. Soc.*, **72**, 3813 (1950); **73**, 4664 (1951).

(3) Type II pyrazoles are designated as those in which the diazonitrogen becomes attached to the α-carbon of the nitroolefin. The double bonds in such pyrazoles can lie in any of the three possible positions.

(4) A. Mustifa and A. Harbash, *J. Am. Chem. Soc.*, **76**, 1383 (1954).

(5) W. E. Parham, C. Serres, Jr., and, P. R. O'Connor, *J. Am. Chem. Soc.*, **80**, 588 (1958).

(6) W. E. Parham, H. G. Braxton, Jr., and, P. R. O'Connor, *J. Org. Chem.*, **26**, 1805 (1961).