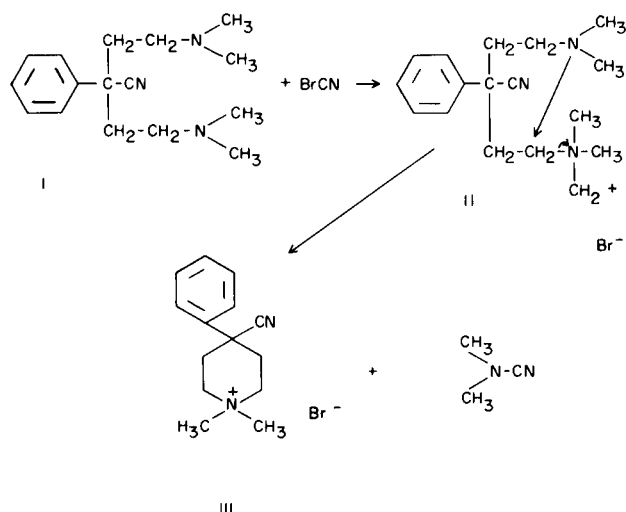


## Ring Closure with Cyanogen Bromide

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During the course of a study on the *N*-demethylation of  $\alpha,\alpha$ -bis(2-dimethylaminoethyl)phenylacetonitrile (I) by means of cyanogen bromide, almost quantitative yields of 4-cyano-1,1-dimethyl-4-phenylpiperidinium bromide (III) and dimethylcyanamide were obtained. Evidently, I reacts with cyanogen bromide to form the cyanodimethyl quaternary ammonium bromide (II), which, being a good leaving group, is displaced by the remaining tertiary amino group, giving rise to III and dimethylcyanamide.



Displacement of cyano quaternary bromide by oxygen function has been reported by Harper, *et al.*,<sup>(1)</sup> Compound III was pyrolyzed to give 4-cyano-1-methyl-4-phenylpiperidine, the hydrochloride salt of which had m.p. 222-224° [lit. (2) m.p. 221-222°].

The reaction of cyanogen bromide with other aliphatic bisdimethylamines was investigated. Only 1,4-bis(dimethylamino)butane and 1,5-bis(dimethylamino)pentane gave cyclic quaternary products, 1,1-dimethylpyrrolidinium bromide and 1,1-dimethylpiperidinium bromide, respectively. When the number of carbons between the two nitrogens was smaller than four or larger than five a complicated mixture was obtained, containing mostly bis(quaternary ammonium) bromides and alkyl cyan-

amides. A small amount of dimethylcyanamide could be detected by vapor phase chromatography, suggesting some cyclization. These results are consistent with the relative ease of ring closure in small common rings (3). Five-membered and six-membered rings are formed much faster than other rings. Primary and secondary bisamines did not give any cyclic product, owing to the lack of a quaternary intermediate.

## EXPERIMENTAL

Melting points were determined on a Mel-Temp apparatus and are uncorrected. The n.m.r. spectrum was determined on a Varian A-60A spectrometer at 60 megacycles in deuterium oxide, containing tetramethylsilane as internal standard.

 $\alpha,\alpha$ -Bis(2-dimethylaminoethyl)phenylacetonitrile (I).

To a stirring mixture of lithium amide (prepared by stirring 6.3 g. of lithium and 100 mg. of ferric chloride in 200 ml. of liquid ammonia for 45 minutes) in liquid ammonia, was added slowly a solution of 152 g. (0.81 mole) of  $\alpha,\alpha$ -bis(2-dimethylaminoethyl)phenylacetonitrile (4) in 150 ml. of toluene. The mixture was stirred for 2 hours. To this mixture was added dropwise 87 g. (0.81 mole) of dimethylaminoethyl chloride in 200 ml. of toluene, and the mixture was stirred for another 2 hours. Ammonia was allowed to evaporate overnight. Water was added, and the toluene layer was removed and dried. The solvent was removed under reduced pressure, and the residue was distilled giving 90 g. (43%) of product, b.p. 97°/0.15 mm.;  $n_D^{25}$  1.5078.

*Anal.* Calcd. for  $C_{16}H_{25}N_3$ : N, 16.20. Found: N, 16.09.

## 4-Cyano-1,1-dimethyl-4-phenylpiperidinium Bromide (III).

To a stirring solution of 14.75 g. (0.14 mole) of cyanogen bromide in 250 ml. of chloroform was added dropwise at room temperature 36.5 g. (0.14 mole) of I in 200 ml. of chloroform. A white precipitate formed almost immediately. After the addition was complete, the mixture was stirred for another hour. The precipitate was filtered, washed with chloroform, and dried *in vacuo* to give 40 g. (63.7%) of III, m.p. 317-320° [lit. (5) m.p. 305-315°].

The filtrate was concentrated under reduced pressure, and the residue was distilled to give 7.5 g. of dimethylcyanamide, b.p. 66°/27 mm.; n.m.r., of III in deuterium oxide, singlet at  $\delta$  7.65 (aromatic); two multiplets  $\delta$  3.6 to 3.97 and  $\delta$  2.4 to 2.73 for the methylene protons, and two singlets  $\delta$  3.3 and  $\delta$  3.48 for the *N*-methyl protons. This n.m.r. agrees with the proposed structure of III.

*Anal.* Calcd. for  $C_{14}H_{19}BrN_2$ : C, 56.96; H, 6.48; N, 9.49;

Br, 27.07. Found: C, 57.16; H, 6.65; N, 9.55; Br, 27.00.  
4-Cyano-1-methyl-4-phenylpiperidine Hydrochloride.

The quaternary bromide (III, 15 g.) in a 200 ml. round-bottom flask fitted for vacuum distillation, *in vacuo*, was heated slowly with a bunsen burner. A mixture of solid and liquid was obtained in the receiver flask. This mixture was diluted with ether and filtered. The ether solution was treated with dry hydrogen chloride; the precipitate was filtered and recrystallized from acetonitrile, m.p. 222-224° [lit. (2) m.p. 221-222°].

#### 1,1-Dimethylpyrrolidinium Bromide.

In a manner similar to that used for the preparation of III, 18.0 g. (0.125 mole) of 1,4-bis(dimethyl)butane (6) was reacted with 13.2 g. (0.125 mole) of cyanogen bromide to give 18 g. (79%) of product, which was recrystallized from 2-propanol, m.p. above 360° [lit. (7) m.p. above 325°]. From the filtrate was isolated 6.5 g. of dimethylcyanamide.

*Anal.* Calcd. for C<sub>6</sub>H<sub>14</sub>BrN: C, 40.00; H, 7.84; N, 7.77. Found: C, 39.76; H, 8.10; N, 7.78.

#### 1,1-Dimethylpiperidinium Bromide.

In a similar manner to that used for the preparation of III, 41 g. (0.26 mole) of 1,5-bis(dimethylamino)pentane (8) was reacted with 27.5 g. (0.26 mole) of cyanogen bromide to give 37 g.

(75.5%) of product, which was recrystallized from acetonitrile, m.p. 347°, sealed tube [lit. (7) m.p. 324°]. From the filtrate was isolated 13 g. of dimethylcyanamide.

*Anal.* Calcd. for C<sub>7</sub>H<sub>16</sub>BrN: C, 43.32; H, 8.30; N, 7.22. Found: C, 43.45; H, 8.55; N, 7.01.

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