[Contribution from the Stamford Research Laboratories, Research Division,
American Cyanamid Co.]

REACTIONS OF SOME AMINES WITH HYDROGEN CYANIDE

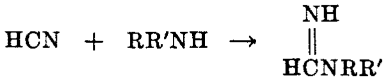
JOHN G. ERICKSON[1]

Received July 18, 1955

The reactions of amines with hydrogen cyanide have been virtually unexplored. Indeed, the literature suggests that amines and hydrogen cyanide do not react, even to the limited extent of forming salts in alcoholic solution (1). Upon investigation, however, we have found that hydrogen cyanide reacts readily with aliphatic and heterocyclic amines. The nature of the final products depends to a great extent upon the structures and relative amounts of the amines used.

In the presence of small amounts of aliphatic amines, especially tertiary amines, hydrogen cyanide is polymerized. Gryszkiewicz-Trochimowski (2) has studied this polymerization, which may be of nearly explosive speed under certain conditions, and has shown that it is catalyzed by alkaline materials. He found that most of the polymer is a coke-like substance of unknown structure. A tetramer is formed in small amounts and has been shown to be diaminomaleonitrile or a tautomer (2–4). We did not investigate the polymerization in the present study.

If the amine is present in molar excess over the hydrogen cyanide, the polymerization is avoided. Instead, with some primary and secondary amines (butylamine, diethylamine, and piperidine), addition of the amines to the triple bond of hydrogen cyanide then takes place and an unstable substituted formamidine is formed. Although we had no success in isolating pure formamidines or their hydrochlorides, there is no doubt that the reactions follow this course.



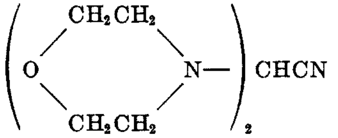
$$\mathrm{HCN} + \mathrm{RR'NH} \rightarrow \mathrm{H\overset{\overset{NH}{\|}}{C}NRR'}$$

The hydrogen cyanide in a freshly prepared mixture with an amine, as butylamine, reacts readily with dilute silver nitrate solution, forming a precipitate of silver cyanide. With the passage of time, the hydrogen cyanide becomes steadily less available for this reaction and, after several days at room temperature, there is virtually no activity in this respect. Addition of water to the amine-hydrogen cyanide reaction mixtures at this point gives good yields of the corresponding substituted formamides, as well as ammonia. Other reactions occur at the same time, giving small amounts of dark-colored products which were not studied.

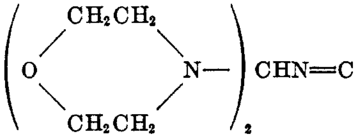
Morpholine differs from the other amines in that, as it reacts with hydrogen cyanide, much ammonia is evolved and a more complex product, $C_{10}H_{17}N_3O_2$, is formed. The structure of the compound $C_{10}H_{17}N_3O_2$ was elucidated in the following manner. Its empirical formula was firmly established by excellent carbon, hydrogen, nitrogen, and molecular weight determinations. It supplied one mole of hydrogen cyanide and two moles of morpholine upon hydrolysis.

---

[1] Present address: Research Dept., General Mills, Inc., Minneapolis, Minn.

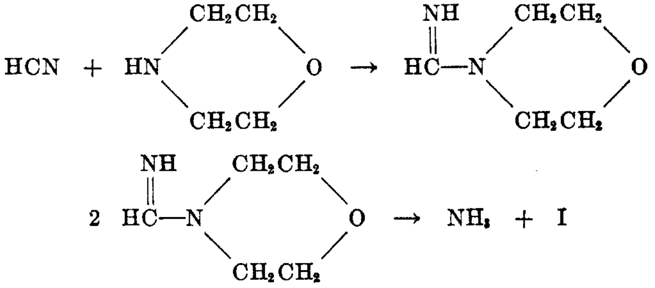


I

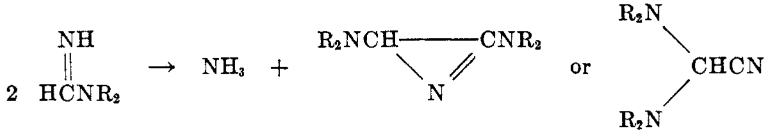


II

These facts limit the possibilities to I or II. Since the infrared spectrum of $C_{10}H_{17}N_3O_2$ shows an absorption band (2242 cm.$^{-1}$) characteristic of the $C\equiv N$ group but none corresponding to double bonds, I is indicated as the correct structure. The $C\equiv N$ band is weak but Dr. R. C. Gore suggests that this may be due to the symmetry of the compound. Attempts to confirm the structure by hydrogenation to 4-(2-aminoethyl)morpholine were not successful.



The reaction of morpholine with hydrogen cyanide no doubt gives the formamidine as the first product. Two molecules of this compound then react, forming ammonia and di-4-morpholinylacetonitrile (I). It is not clear what the mechanism of the second reaction might be. That such reactions do occur, however, is shown by the work of Pinner (5), who prepared N,N-dialkylformamidines from imido esters and dialkylamines. These dialkylformamidines were found to be unstable, splitting out ammonia upon standing and forming new products, to which Pinner assigned cyclic structures (III). We feel that the correct structures of Pinner's compounds are more likely analogous to that of di-4-morpholinylacetonitrile (IV). Pinner's compounds, which appear to have been liquids, were not stable. The superior stability of di-4-morpholinylacetonitrile, which can be kept indefinitely if dry, may be ascribed to the fact that it is a solid. In the presence of moisture, it generates hydrogen cyanide, a reaction very similar to the behavior of the dialkoxyacetonitriles (6).



III IV

Acknowledgment. I wish to thank Dr. R. C. Gore for determining and interpreting the infrared absorption spectrum of di-4-morpholinylacetonitrile. Analyses were performed by the Microanalytical Group of these laboratories.

EXPERIMENTAL

Melting points are corrected. The hydrogen cyanide was over 99% pure, containing a small amount of water and stabilized with a trace of sulfur dioxide.

Reaction of butylamine with hydrogen cyanide. A mixture of hydrogen cyanide (13.5 g., 0.50 mole) and *n*-butylamine (73.0 g., 1.0 mole) was allowed to stand at room temperature for 25 days. Water (9 ml., 0.5 mole) then was added. After another 3 days at room temperature, the mixture was distilled to yield 36.0 g. (71%) of butylformamide, b.p. 63–69° (1 mm.). It was redistilled, b.p. 62° (0.5 mm.), n_D^{25} 1.4424.

Anal. Calc'd for $C_5H_{11}NO$: C, 59.41; H, 10.89; N, 13.86; Mol. wt., 101.

Found: C, 60.90; H, 11.18; N, 14.62; Mol. wt. (benzene f.p.), 105.

The following experiment was carried out to demonstrate that hydrogen cyanide is actually consumed by reaction with butylamine. Hydrogen cyanide (6.8 g., 0.25 mole) was added to *n*-butylamine (36.5 g., 0.50 mole). Three drops of this mixture, added to water (readily soluble) and treated with several drops of dilute silver nitrate-nitric acid solution, gave an insoluble white precipitate. After 35 days at room temperature, however, the mixture had become a dark brown liquid, insoluble in water. It no longer reacted readily with silver nitrate-nitric acid solution.

Reaction of diethylamine with hydrogen cyanide. Hydrogen cyanide (40.5 g., 1.50 moles) was added to cold diethylamine (146 g., 2.00 moles). The mixture, completely solid at first, gradually became liquid after standing several days at 25°. After 11 days water (27 ml., 1.50 moles) was added to the reaction mixture. After a further period of 3 days, the mixture was distilled under atmospheric pressure. Much ammonia was evolved and so much diethylamine was recovered that it appears that the hydrolysis was incomplete. The distillation was completed under water pump pressure, leaving 29.0 g. of a viscous black residue. The distillate was redistilled under atmospheric pressure, yielding 33.2 g. (22%) of diethylformamide, b.p. 176–179° (758 mm.), n_D^{25} 1.4328. It was redistilled to give an analytical sample, b.p. 29° (0.5 mm.), n_D^{25} 1.4318.

Anal. Calc'd for $C_5H_{11}NO$: C, 59.41; H, 10.89; N, 13.86; Mol. wt., 101.

Found: C, 59.32; H, 10.94; N, 14.20; Mol. wt. (benzene f.p.), 92.

The yield of diethylformamide was subsequently raised to 46% by allowing 13 days for the hydrolysis.

An attempt was made to prepare the hydrochloride of the formamidine. A reaction mixture of hydrogen cyanide and diethylamine, prepared as described above, was subjected to water pump pressure at 25°. After distillation of the volatile components had ceased, the dark liquid residue was poured into a mixture of concentrated hydrochloric acid and isopropyl alcohol. Only amine hydrochloride, identified by analysis, was recovered.

Anal. Calc'd for $C_5H_{13}ClN_2$: Cl, 25.97; N, 20.52.

Calc'd for $C_4H_{12}ClN$: Cl, 32.35; N, 12.78.

Found: Cl, 32.21; N, 12.46.

Reaction of morpholine with hydrogen cyanide. A completely liquid mixture of hydrogen cyanide (13.5 g., 0.50 mole) and morpholine (87.0 g., 1.0 mole), after standing for two months at 25°, had become partly solid and much ammonia had evolved. The unreacted morpholine was distilled out of the mixture under water-pump pressure. The solid residue, pressed on a porous plate to remove a dark oil, gave 38.6 g. (36% crude yield) of dark red product. Two recrystallizations from *tert*-butyl alcohol gave white crystals, m.p. 123.5–124.5°. It was later found that the reaction time may be greatly decreased. Thus, a reaction mixture similar to that described above gave, after two weeks, a 62% yield of recrystallized product.

Anal. Calc'd for $C_{10}H_{17}N_3O_2$: C, 56.85; H, 8.11; N, 19.89; Mol. wt., 211.

Found: C, 57.08; H, 8.16; N, 19.47; Mol. wt. (benzene f.p.), 200.

It was noted that this product is easily hydrolyzed to hydrogen cyanide in dilute acid. The hydrogen cyanide so produced was determined quantitatively by titration with silver nitrate solution, using potassium iodide as indicator (7). In two experiments it was found that one mole of $C_{10}H_{17}N_3O_2$ gave 0.982 and 0.984 mole of hydrogen cyanide, respectively.

In other words, one mole of $C_{10}H_{17}N_3O_2$ yields, upon hydrolysis, one mole of hydrogen cyanide.

Another hydrolysis product is morpholine. This was determined in the following manner. Three grams of $C_{10}H_{17}N_3O_2$ were mixed with water (20 ml.) but did not dissolve. Eight pellets of sodium hydroxide were added, whereupon rapid solution took place. The mixture was allowed to stand at 25° for 13 days, then was distilled under water-pump pressure. To the distillate was added 4.5 g. of benzoyl chloride and 4.0 g. of sodium hydroxide. The mixture was shaken vigorously, cooled, and extracted with ether to yield 3.1 g. of N-benzoylmorpholine, m.p. 73–76°. Reported m.p. for this compound is 74–75° (8). The 3.1 g. of N-benzoylmorpholine accounts for 57% of the morpholine groups in $C_{10}H_{17}N_3O_2$.

Reaction of piperidine with hydrogen cyanide. Hydrogen cyanide (6.8 g., 0.25 mole) was added to piperidine (43.0 g., 0.50 mole). The mixture, which was largely a solid, presumably amine hydrocyanide, was allowed to stand at 25°. After 4 days it was completely liquid and had become dark-colored. There was no sign of the evolution of any ammonia. After 8 days water (4.5 ml., 0.25 mole) was added and the mixture was allowed to stand at 25° for 26 days, then was distilled to yield 25.4 g. of N-formylpiperidine, b.p. 111–112° (24.5 mm.), n_D^{25} 1.4826. This is a 90% yield from the hydrogen cyanide used.

Anal. Calc'd for $C_6H_{11}NO$: N, 12.38. Found: N, 12.05.

An attempt to isolate the formamidine hydrochloride was no more successful than in previous experiments.

SUMMARY

Primary and secondary aliphatic amines, including piperidine, react with hydrogen cyanide to form substituted formamidines. The reaction of hydrogen cyanide with morpholine goes further to give ammonia and di-4-morpholinylacetonitrile

STAMFORD, CONNECTICUT

REFERENCES

(1) STEWART AND FONTANA, *J. Am. Chem. Soc.*, **62**, 3281 (1940).

(2) GRYSZKIEWICZ-TROCHIMOWSKI, *Roczniki Chem.*, **8**, 165 (1928); *Chem. Abstr.*, **22**, 4475 (1928).

(3) HINKEL, RICHARDS, AND THOMAS, *J. Chem. Soc.*, 1432 (1937).

(4) HINKEL AND WATKINS, *J. Chem. Soc.*, 1206 (1940).

(5) PINNER, *Die Imidoäther und Ihre Derivative*, Robert Oppenheim, Berlin, 1892, pp. 100, 101.

(6) ERICKSON, *J. Am. Chem. Soc.*, **73**, 1338 (1951).

(7) KOLTHOFF AND SANDELL, *Textbook of Quantitative Inorganic Analysis*, Macmillan, 1943, p. 574.

(8) HEILBRON, *Dictionary of Organic Compounds*, Oxford University Press, N. Y., 1936, vol. II, p. 840.