3,4-Diacetoxy-6-bromonitrobenzene (XIIIb). A solution composed of 3,4-(dimethylmethylenedioxy)-6-bromonitrobenzene (XVII, 1.05 g.),[13] concd. hydrochloric acid (4 ml.) and dioxane was heated at steam bath temperature for 15 min. The solvent was removed (*in vacuo*) and replaced with acetic anhydride–pyridine. Heating (steam bath) was continued for 30 min. and the solid which separated upon cooling the acetylation mixture collected and discarded. Evaporation (*in vacuo*) of the filtrate to dryness and recrystallization of the residue, 0.91 g. (74.6%), from benzene (Norit A)–petroleum ether (b.p. 60–90°) gave a specimen of the acetate XIIIb, m.p. 120–122° (lit.,[13] m.p. 122°).

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[CONTRIBUTION FROM THE STAMFORD LABORATORIES, CENTRAL RESEARCH DIVISION, AMERICAN CYANAMID COMPANY]

Cyanoethylation. I. The Selective Cyanoethylation of 2-Aminoethanethiol Hydrochloride

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Received November 19, 1959

Over the *p*H range of 3.2 to 6.9 aqueous solutions of 2-aminoethanethiol hydrochloride react with acrylonitrile exclusively on the sulfhydryl group to give good yields of 3-(2-aminoethylthio)propionitrile hydrochloride. The selective sulfhydryl cyanoethylation is most rapid in the *p*H range of 6 to 6.9. In basic solutions a rapid and nonselective reaction is observed.

An obscure literature observation interpreted the fact that 2-aminoethanethiol (m.p. 99°[2]) melted nearly 30° higher than its hydrochloride (m.p. 70°[3]) as indicating that the free base existed as the Zwitterion Ib. This statement prompted us to utilize the cyanoethylation of 2-aminoethanethiol as a means of investigating this problem.

If the above rationalization is correct, then aqueous solutions of 2-aminoethanethiol, and similarly constituted mercaptoamines, should behave as shown. As the *p*H of the solution is increased the predominant species should pass from the ammonium salt (Ia) through the Zwitterion (Ib) to the free amine (Ic).

$$\underset{\text{Ia}}{HSCH_2CH_2NH_3^+} \rightleftharpoons \underset{\text{Ib}}{{}^-SCH_2CH_2NH_3^+} \rightleftharpoons \underset{\text{Ic}}{{}^-SCH_2CH_2NH_2}$$

From the accumulated data on the behavior of mercaptans and amines toward acrylonitrile, we would predict the following:

1. In strongly acid solution Ia would predominate and cyanoethylation either would not occur or would take place slowly and exclusively on sulfur.
2. As the *p*H is increased progressively more of Ib would be formed. The rate of the reaction should increase and reach a maximum at the *p*H corresponding to the isoelectric point. Addition should occur exclusively to the mercaptide anion.
3. In basic solution, where Ic would predominate, the reaction would, likewise, be rapid but completely nonselective.

To test these predictions, aqueous solutions of 2-aminoethanethiol covering the *p*H range 1.5–8.8 were allowed to react with excess acrylonitrile for at least one hour. The results are summarized in Table I.

At *p*H 1.5 no reaction was observed. At *p*H 3.6 a moderate reaction produced exclusively 3-(2-aminoethylthio)propionitrile hydrochloride as inferred from analytical data and failure of the product to give a color reaction with sodium nitroprusside.[4] The rate of the reaction increased, with retention of selectivity, up to *p*H 6.8 and, from our qualitative data, reached a maximum in the *p*H region 6–6.8.

In alkaline solution a fast, nonselective reaction produced an uncrystallizable sirup. To eliminate disulfide formation *via* air oxidation of 2-aminoethanethiol in alkaline solution, another reaction was run first at *p*H 6.4 then at *p*H 8.8. The same sirupy product was obtained.

The above evidence supports the postulate that aminoethanethiol exists as the internal salt both in the solid state and in solution and suggests that the cyanoethylation of similarly constituted aliphatic mercaptoamines[5] in slightly acid solutions should give good yields of the *S*-monocyanoethylated products.

EXPERIMENTAL

3-(2-Aminoethylthio)propionitrile hydrochloride. Acrylonitrile (63.6 g., 1.2 moles) was added at once to a stirred solution of 34 g. (0.3 mole) of 2-aminoethanethiol hydrochlo-

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(2) S. Gabriel and J. Coleman, *Ber.*, **45**, 1643 (1912).

(3) E. J. Mills, Jr., and M. T. Bogert, *J. Am. Chem. Soc.*, **62**, 1173 (1940).

(4) M. D. Cheronis and J. B. Entriken, *Semimicro Qualitative Organic Analysis*, T. Y. Crowell Co., N. Y., 1947, p. 141.

(5) Mercapto-*t*-carbinamines might possibly be an exception since the cyanoethylation of *t*-carbinamines is acid catalyzed, *cf.*, L. S. Luskin, M. J. Culver, G. E. Gantert, W. E. Craig, and R. S. Cook, *J. Am. Chem. Soc.* **78**, 4042 (1956); E. Profft, *Ber.*, **90**, 1734 (1957).

TABLE I

CYANOETHYLATION PRODUCTS OF 2-AMINOETHANETHIOL

pH	Exotherm $^{\circ}_{max}$/min	Product	Yield, %	M.P.[a]
1.5	None	$HCl \cdot H_2NCH_2CH_2SH$[b]	—	69.5–70.3
3.6	36/30	$HCl \cdot H_2NCH_2CH_2SCH_2CH_2CN$	69	81.3–83.1
6.0	52/6	$HCl \cdot H_2NCH_2CH_2SCH_2CH_2CN$	81.4	81.5–83.5
6.8	52/<1	$HCl \cdot H_2NCH_2CH_2SCH_2CH_2CN$	77.8	77.5–78.8
8.8	52/<1	$NCCH_2CH_2SCH_2CH_2NHCH_2CH_2CN \cdot HCl$ $NCCH_2CH_2SCH_2CH_2N(CH_2CH_2CN)_2 \cdot HCl$	82.4[c]	Sirup

[a] All melting points are corrected. [b] Recrystallized from ethanol-ether. [c] Yield calculated as tricyanoethylation product.

ride[6] in 100 ml. of deionized water which had been adjusted to *p*H 6.8 with sodium hydroxide. A strongly exothermic reaction brought the temperature to 52° within 45 sec. After 60 min. the mixture was acidified with hydrochloric acid and vacuum concentrated (90°, 20 mm.) to a sirup. This was treated successively with several portions of ethanol-benzene, with removal of precipitated sodium chloride and further vacuum concentration, to give 50.6 g. (100%) of pale yellow sirup which crystallized on cooling. Recrystallization from ethanol-benzene afforded 38.9 g. (77.8%) of colorless crystals, m.p. 77.5–78.8°.

An analytical sample, m.p. 83.1–83.7°, was obtained after two recrystallizations from ethanol-benzene.

Anal. Calcd. for $C_5H_{11}N_2SCl$: C, 36.03; H, 6.65; N, 16.81. Found: C, 35.96; H, 6.62; N, 16.55.

3-(2-Aminoethylthio)propionic acid hydrochloride. A solution of 33.3 g. (0.2 mole) of 3-(2-aminoethylthio)propionitrile hydrochloride in 50 ml. of concd. hydrochloric acid was heated under reflux for 3 hr. The resulting solution was vacuum concentrated to a sirup which was dissolved in 100 ml. of boiling absolute ethanol. After removal of the precipitated ammonium chloride (9.4 g., 87.8%), the filtrate was again vacuum concentrated. Several successive treatments with ethanol-benzene and, finally, benzene alone gave 36 g. (97.1%) of crude acid, m.p. 116–120°. Recrystallization from ethanol-hexane afforded 27.4 g. (73.8%) of colorless crystals, m.p. 120.5–122.2°.

Analytical material, m.p. 124.7–125.3°, was obtained after two more recrystallizations from ethanol-hexane.

Anal. Calcd. for $C_5H_{12}ClNO_2S$: C, 32.34; H, 6.52; Cl, 19.10. N. 7.55; S, 17.27; Found: C, 32.55; H, 6.72; Cl, 18.83. N, 7.83; S, 17.33.

Hydrolysis of the product from reaction at pH 8.8. A solution of 42.5 g. of the uncrystallizable sirup in 100 ml. of concd. hydrochloric acid was heated under reflux for 4 hr. Upon chilling, 17.9 g. (74.6% of theory for tricyanoethylated product) of ammonium chloride was removed. Vacuum concentration of the filtrate gave 46.9 g. (94.7% of theory for tricarboxylic acid) of uncrystallizable yellow sirup.

Acknowledgment. The authors wish to thank Dr. Julius Kuck and the members of the Microanalytical Laboratory for their contributions.

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(6) Obtained from Evans Chemetics, Inc., Waterloo, N. Y.

[CONTRIBUTION FROM THE RADIUM INSTITUTE OF THE UNIVERSITY OF PARIS]

Some Homologs of α,α-Dimethyl-β-phenethylamine

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Received August 18, 1959

A number of homologs of α,α-dimethyl-β-phenethylamine bearing substituents on the aromatic nucleus have been synthesized, starting from the corresponding benzyl chlorides, for investigation of their sympatho-mimetic activity. α,α-Dimethyl-β-(2-chlorophenyl)propionamide has been found to undergo Hofmann degradation to the corresponding symmetrical urea.

β-Arylethylamines containing a quaternary carbon atom *alpha* to the amine radical are interesting sympatho-mimetic substances with a wide range of secondary activities. The naphthyl derivatives, for instance, also possess local anesthetic properties greater than that of cocaine,[1] and *N*-methyl-α,α-dimethyl-β-phenethylamine is a valuable nasal shrinker causing no cerebral stimulation.[2]

It was deemed of interest to prepare a number of new β-arylethylamines for biological investigation, especially those bearing alkyl or halogen substituents on the aromatic nucleus. Recently, α,α-dimethyl-β-(3,4-dimethylphenethyl)amine was prepared in the course of a study of the Bischler-Napieralski reaction;[3] we now record the synthesis of two of its position isomers, starting from the chloromethylation-products of *m*- and *p*-xylene. These underwent Haller condensation[4] with isobutyrophenone in the presence of sodium amide to

(1) P. Cagniant, C. Mentzer, and N. P. Buu-Hoï, *Bull. Soc. Chim. France*, **10** [5], 145 (1943).

(2) *Cf.* A. Burger, *Medicinal Chemistry*, Interscience Publishers Inc., New York, 1951, p. 311.

(3) N. P. Buu-Hoï, C. T. Long, and N. D. Xuong, *J. Org. Chem.*, **23**, 12 (1958).

(4) A. Haller, *Bull. Soc. Chim. France*, **31**, [4], 1073 (1902).