be determined accurately. These same temperatures 79.1–79.4°, however, coincide definitely with the melting point reported by Hurd,[1] 79.0–79.5°. From a consideration of the combustion analysis (and other data apparently not included in his article) Hurd concludes that the constant melting substance is a mixture or a solid solution, and the freezing point curve might almost be drawn on that basis, since the central portion is so flat. Consideration of the individual cooling curves (Fig. 2), however, each having two definite breaks, many times with supercooling in each, indicates clearly that in our work we are not dealing with a solid solution but with a compound which forms eutectic mixtures with the pure components. The lower break on each curve occurs within limits of the experimental technique, at the same temperature.

A study of the curves obtained by plotting "eutectic halting time" against composition leads to the conclusion, further, that the system forms no solid solutions, the solid phases consisting of the pure components and the compound.

Summary

1. The freezing-point curves of the system acetanilide-propionanilide have been determined.
2. The presence of a compound, almost completely dissociated in the liquid state, is indicated. The central portion of the curve is so flat that the composition of the compound cannot be determined with certainty.
3. The melting point of the compound is 79.2–79.4°.

CORVALLIS, OREGON

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

HALOGENATED TERTIARY AMINES

BY C. S. MARVEL, W. H. ZARTMAN AND O. D. BLUTHARDT

RECEIVED JUNE 6, 1927 PUBLISHED SEPTEMBER 2, 1927

A considerable number of halogenated amines are reported in the literature but as a general rule their properties have not been studied in detail. Gabriel[1] has prepared chloro-ethylamine and bromo-ethylamine and has shown that they undergo internal condensations very easily. Knorr[2] and his students have prepared a few derivatives of the type $XCH_2CH_2NR_2$ and $XCH_2CH_2CH_2NR_2$ and have studied their tendency toward ring formation. The first type forms six-membered piperazine rings and the second type forms eight-membered rings containing two nitrogen atoms. The delta halogenated butylamines have

---

[1] (a) Gabriel, *Ber.*, **21**, 567, 574 (1888); (b) **22**, 1140 (1889).

[2] (a) Knorr, *Ber.*, **37**, 3511 (1904); (b) Knorr and Roth, *Ber.*, **39**, 1424 (1906); (c) Hörlein and Kneisel, *Ber.*, **39**, 1429 (1906).

been studied by several investigators[3] who have found that they are easily converted to pyrrolidines.

More recently a patent[4] describing some halogenated propyl- and butyldiethylamines has appeared. Very little information is given concerning the properties of these compounds. They are said to react as normal alkyl halides in the alkylation of aceto-acetic ester.

From the properties previously recorded for this general class of compounds it was thought that they should be very interesting and useful reagents, if they could be obtained easily. Most of the previous investigators have not given complete directions and yields. Knorr and Roth[2b] prepared 3-chloropropyldimethylamine hydrochloride in yields of about 50% by heating 3-phenoxypropyldimethylamine with concentrated hydrochloric acid in a sealed tube for several hours. We have found that by using hydrobromic acid to open similar ethers, the reactions can be carried out without the use of sealed tubes and yields of 80–88% of the hydrobromides of the bromo-alkylamines can be obtained. In this way 3-bromopropyldiethylamine and 4-bromobutyldiethylamine have been made readily available for use as reagents. The reactions used in the preparation of these two amines are as follows:

$$C_6H_5O(CH_2)_3Br \xrightarrow{(C_2H_5)_2NH} C_6H_5O(CH_2)_3N(C_2H_5)_2$$
$$\xrightarrow{HBr} Br(CH_2)_3N(C_2H_5)_2.HBr \xrightarrow{NaOH} Br(CH_2)_3N(C_2H_5)_2.$$

$$C_6H_5O(CH_2)_3CN \xrightarrow[C_2H_5OH]{Na} C_6H_5O(CH_2)_4NH_2 \xrightarrow{C_2H_5Br} C_6H_5O(CH_2)_4N(C_2H_5)_2$$
$$\xrightarrow{HBr} Br(CH_2)_4N(C_2H_5)_2.HBr \xrightarrow{NaOH} Br(CH_2)_4N(C_2H_5)_2$$

All of the reactions proceed smoothly to give good yields except in the case of the isolation of the free amine. There is considerable loss at this stage on account of the rapid formation of quaternary ammonium salt due to internal condensation.

The hydrobromide salts of the halogenated amines are very hygroscopic and very hard to purify. In the open air they take up water so rapidly that it seriously interferes with their purification and analysis. The crude salts can be used in absolute alcohol solution with two moles of sodium malonic ester to give typical malonic ester condensations. These reactions show that these compounds can be used as other alkyl halides in order to introduce the groups $—(CH_2)_3N(C_2H_5)_2$ and $—(CH_2)_4N(C_2H_5)_2$.

Experimental Part

3-Phenoxypropyldiethylamine.—To 73 g. of boiling diethylamine in a 500cc. flask fitted with a reflux condenser was added 100 g. of phenoxypropyl bromide over a period

---

[3] (a) Gabriel, *Ber.*, **24**, 3232 (1891). (b) Blank, *Ber.*, **25**, 3044 (1892). (c) von Braun, *Ber.*, **39**, 4121 (1906).

[4] Eng. pat., 167,781; *Chem. Zentr.* (4), **1921**, 1223.

of about thirty minutes. The reaction mixture was heated for about twelve hours when the reaction was complete and the contents of the flask appeared to be almost solid. The reaction mixture was extracted with 200 cc. of ether and the diethylamine hydrobromide was filtered and washed with about 100 cc. of ether. The ether extract and washings were combined and distilled. After the ether was removed, the phenoxypropyldiethylamine was distilled under reduced pressure. The yield was 80–123 g. (84–94% of the theoretical amount); b. p. 147–150° at 20 mm.; d_4^{20}, 0.9425; n_D^{20}, 1.4987. M_D, calcd., 64.39; observed, 64.43.

A small amount of the amine was dissolved in dry ether and converted to the hydrochloride by passing dry hydrogen chloride into the solution. The salt which separated melted at 98–102° with some decomposition.

Anal. (Volhard). Subs., 0.5071 g.: 19.93 cc. of 0.1034 *N* $AgNO_3$. Calcd. for $C_{13}H_{22}ONCl$: Cl, 14.56. Found: 14.41.

In a few runs of the amine another substance which was insoluble in ether and only slightly soluble in water was isolated. On recrystallization from hot water this product separated in long, white needles which melted at 77.5–79°. It seemed to be diphenoxypropyldiethylammonium bromide.

Anal. (Volhard). Subs. 0.7000 g.: 16.85 cc. of 0.0981 *N* $AgNO_3$. Calcd. for $C_{22}H_{32}O_2NBr$: Br, 18.95. Found: 18.89.

3-Bromopropyldiethylamine Hydrobromide.—A solution of 88 g. of phenoxypropyldiethylamine in 100 cc. of 40% hydrobromic acid was placed in a 500cc. flask, fitted by means of a ground glass connection to a 45cm. fractionating column which in turn was connected with a condenser set for distillation. The flask was placed in an oil-bath heated to 180–210°. Water, hydrobromic acid and phenol distilled from the reaction mixture. More hydrobromic acid was added from time to time until a total of 350–400 cc. was used. It was important to have an excess of hydrobromic acid present at all times as tarry products were formed when the reaction mixture was heated too long without the presence of hydrobromic acid solution. After about twelve to fifteen hours no more phenol came over in the distillate. The residue in the reaction flask was dissolved in about 100 cc. of water and most of the color removed by boiling with decolorizing carbon (Norit). The solution was then evaporated under reduced pressure until all of the water was removed. On standing the residue crystallized slowly. The color varied from gray to brown with different runs. The yield of crude product was about 88 g. (80% of the theoretical amount).

This product was very hygroscopic and attempts to recrystallize the material from solvents were not particularly successful on this account. It was found that dissolving the crude product in absolute butyl alcohol and precipitating with anhydrous ether gave colorless crystals. They were filtered out of contact with air and dried in a desiccator over phosphorus pentoxide and sulfuric acid. There was considerable loss in purification. This product melted at 91–94°.

Anal. (Parr bomb). Subs. 0.3155 g.: 22.38 cc. of 0.1010 *N* $AgNO_3$. Calcd. for $C_7H_{17}NBr_2$: Br, 58.18. Found: 57.29.

The low result for bromine was undoubtedly due to the presence of moisture. The range over which the product melted was also probably due to moisture taken up during handling of the product.

3-Bromopropyldiethylamine.—The crude hydrobromide was suspended in ether and this suspension was treated with a large excess of cold, concentrated sodium hydroxide solution. The ether solution was separated, dried over solid sodium hydroxide and the ether distilled under reduced pressure. The residue was distilled at 7 mm. and the fraction boiling at 60–64° was collected. The product came over clear but soon became cloudy, due to formation of some of the quaternary ammonium compound produced by the reaction of one molecule of the bromo-amine with another. The physical properties and analysis were taken on samples freshly prepared and distilled; d_4^{25}, 1.1524; n_D^{25}, 1.4580. M_D, calcd., 46.40; observed, 45.81.

Anal. (Parr bomb). Subs. 0.8068 g.: 40.43 cc. of 0.1010 *N* $AgNO_3$. Calcd. for $C_7H_{16}NBr$: Br, 41.23. Found: 40.19.

On standing overnight the liquid amine changed to a solid quaternary ammonium salt, presumably the eight-membered ring analogous to that which Knorr and Roth[2b] found to be formed from 3-chloropropyldimethylamine. The salt melted at 180–185° and the bromine could be titrated directly.

Anal. (Volhard). Subs. 0.4002 g.: 20.37 cc. of 0.1010 *N* $AgNO_3$. Calcd. for $(C_7H_{16}NBr)$: Br, 41.23. Found: 41.12.

Diethyl 3-Diethylaminopropyl Malonate.—In a 1-liter round-bottomed flask connected to a good reflux condenser was placed 500 cc. of absolute ethyl alcohol which had been dried by refluxing with magnesium methylate and distilling. Through the condenser 15 g. of sodium was added in small pieces as rapidly as possible. When the sodium had reacted, 120 g. of diethyl malonate was added and then a solution of 88 g. of crude bromopropyldiethylamine hydrobromide in 100 cc. of absolute alcohol. The mixture was refluxed for six to eight hours. Sodium bromide separated during this time. Most of the alcohol was distilled and the sodium bromide was dissolved in water. The ester layer was collected in ether and separated from the water layer. The amino ester was extracted from the ether with dilute hydrochloric acid solution, separated from the ether layer and then liberated with alkali. The amino ester was extracted with ether, the ether was distilled and then the residue was distilled under reduced pressure. The product boiled at 163–170° at 23 mm. The yield was 52 g. (62% of the theoretical amount); d_4^{25}, 0.9686; n_D^{25}, 1.4380. M_D, calcd., 74.28; observed, 73.98.

Anal. (Kjeldahl). Subs. 0.4212 g.: 18.08 cc. of 0.1745 *N* HCl. Calcd. for $C_{14}H_{27}O_4N$: N, 5.12. Found: 5.18.

4-Phenoxybutyldiethylamine.—In a 500cc. flask fitted with a reflux condenser was placed 85 g. of phenoxybutylamine and to it was added 56 g. of ethyl bromide and 21 g. of sodium hydroxide dissolved in 50 cc. of water. The reaction mixture was shaken for a short time. Considerable heat developed. The reaction mixture was allowed to stand for a day and then 56 g. of ethyl bromide and a solution of 25 g. of sodium hydroxide were added. The mixture was again allowed to stand for a day and finally refluxed for about a half hour to complete the reaction. Usually three layers appeared at this stage. The amine layer was on top, the aqueous solution was on the bottom and in between was an oily layer which was probably the quaternary ammonium salt. It was not purified. The amine layer was extracted with ether and the ether distilled. The residue was distilled under reduced pressure and the product boiling at 152–158° at 21 mm. was collected. The yield was 83–91 g. (73–80% of the theoretical amount). Occasionally the yields were higher or lower depending on the amount of quaternary ammonium salt formed; d_4^{25}, 0.9424; n_D^{25}, 1.4975. M_D, calcd., 69.01; observed, 68.51.

4-Bromobutyldiethylamine Hydrobromide.—This product was prepared by the same method used for the corresponding propyl compound. From 100 g. of phenoxybutyldiethylamine and 350 cc. of 40% hydrobromic acid, there was obtained 103–115 g. (79–88% of the theoretical amount) of crude bromobutyldiethylamine hydrobromide. This product was also very hygroscopic and consequently very hard to purify. After crystallizing from anhydrous butyl alcohol and anhydrous ether, crystals which melted at 62–68° were obtained. These were dried in a desiccator over phosphorus pentoxide and sulfuric acid.

Anal. (Parr bomb). Subs. 0.5864 g.: 39.74 cc. of 0.1010 *N* $AgNO_3$. Calcd. for $C_8H_{19}NBr_2$: Br, 55.36. Found: 54.75.

4-Bromobutyldiethylamine.—The free bromo-amine was isolated as described for the propyl compound. It boiled at 68–70° at 6 mm.; d_4^{25}, 1.0187; n_D^{25}, 1.4415. M_D, calcd., 52.38; observed, 53.92.

Anal. (Parr bomb). Subs. 0.3197: 15.43 cc. of 0.1010 *N* $AgNO_3$. Calcd. for $C_8H_{18}NBr$: Br, 38.46. Found: 38.49.

This amine gradually became opaque and after about twelve hours crystals of the quaternary ammonium compound, which was presumably diethyl pyrrolidinium bromide, began to separate. This product melted at 170–175°.

Anal. (Volhard). Subs. 0.2958 g.: 14.07 cc. of 0.1010 *N* $AgNO_3$. Calcd. for $C_8H_{18}NBr$: Br, 38.46. Found: 38.43.

Diethyl 4-Diethylaminobutyl Malonate.—This ester was prepared by the same method used for the corresponding propyl derivative. From 16 g. of sodium, 600 cc. of absolute alcohol, 128 g. of diethyl malonate and 100 g. of crude bromobutyldiethylamine hydrobromide, there was obtained 23 g. (23% of the theoretical amount) of the amino malonic ester, which boiled at 170–175° at 24 mm.; d_4^{25}, 0.9621; n_D^{25}, 1.4468. M_D, calcd., 78.90; observed, 80.46.

Anal. (Kjeldahl). Subs., 0.4047 g.: 17.93 cc. of 0.1745 *N* HCl. Calcd. for $C_{15}H_{29}O_4N$: N, 4.88. Found: 4.90.

Summary

3-Bromopropyldiethylamine and 4-bromobutyldiethylamine have been prepared by general reactions and some of their properties and reactions have been studied.

URBANA, ILLINOIS

[CONTRIBUTION NO. 16 FROM THE MASSACHUSETTS INSTITUTE OF TECHNOLOGY, RESEARCH LABORATORY OF ORGANIC CHEMISTRY]

ALKYL-NITROGUANIDINES

BY TENNEY L. DAVIS AND STEWART B. LUCE

RECEIVED JUNE 11, 1927 PUBLISHED SEPTEMBER 2, 1927

Nitroguanidine in aqueous solution at 60–70° appears to dearrange in the expected manner[1] to produce, on the one hand, ammonia and nitrocyanamide and, on the other, nitro-amide and cyanamide. If the solution is digested with ammonia, the ammonia inhibits the first of the above-mentioned dearrangements and combines with the cyanamide produced by the second to form guanidine, while the nitro-amide which is liberated at the same time decomposes to produce nitrous oxide, which escapes from the solution. By working with ammonium carbonate, guanidine carbonate is obtained in a yield amounting to 90% of the theoretical, and the by-products are a small amount of melamine from the polymerization of cyanamide, and a smaller amount of urea, from the cyanic acid which results apparently from the loss of nitrous oxide from nitrocyanamide. With aniline a small amount of phenylguanidine is produced, but

---

[1] Davis and Abrams, *Proc. Am. Acad. Arts Sci.*, **61**, 437 (1926).