**2-Chloro-5-aminophenylstibonic Acid** ($2\text{-Cl-5-NH}_2\text{-C}_6\text{H}_3\text{SbO}_2)\text{H}_2\text{O}$.—The method employed for the preparation of this compound was that described by Jacobs, Heidelberger and Rolf.[6] It consisted in the reduction of the nitroarylstibonic acid by means of freshly prepared ferrous hydroxide. The product was purified by precipitating it from an alkaline solution with sulfur dioxide.

**2-Hydroxy-5-nitrophenylstibonic Acid** ($2\text{-HO-5-NO}_2\text{C}_6\text{H}_3\text{SbO}_2)\text{H}_2\text{O}$.—This compound was prepared by heating 2-chloro-5-nitrophenylstibonic acid with 6 *N* potassium hydroxide solution at about 97° for seven hours. The crude product was purified by dissolving it in about 9 *N* hydrochloric acid, boneblacking the solution and diluting the clear filtrate with a large volume of water. The product gave the characteristic ferric chloride test for phenols and showed no qualitative test for halogen.

TABLE II

All of these compounds were obtained as amorphous products not melting below 250°.

| -Phenylstibonic acid | Yield, % | Formula | Antimony analyses, % Calcd. | Found |
|---|---|---|---|---|
| 2-Chloro- | 52 | $C_{18}H_{14}O_7Cl_3Sb_3$ | 44.89 | 44.90 |
| 2-Chloro-5-nitro- | 90 | $C_6H_5O_5NClSb$ | 37.09 | 37.12 |
| 2-Chloro-5-amino- | 40 | $C_6H_7O_3NClSb$ | 41.02 | 41.00 |
| 2-Hydroxy-5-nitro- | 35 | $C_6H_6O_6NSb$ | 39.30 | 39.29 |

**2-Chlorophenylstibinic chloride** $(2\text{-Cl-C}_6\text{H}_4\text{SbCl}_4)\text{H}_2\text{O}$ and **2-chloro-5-nitrophenylstibinic chloride** ($2\text{-Cl-5-NO}_2\text{-C}_6\text{H}_3\text{SbCl}_4$) were prepared by dissolving the respective acids in concentrated hydrochloric acid (sp. gr. 1.18) and cooling the resulting solutions. The products, crystallizing as pale yellow needles, were dried over solid sodium hydroxide and then placed in the air to reach a constant analysis.

**Ammonium 2-chlorophenylchlorostibonate** ($2\text{-Cl-C}_6\text{H}_4\text{SbCl}_5\text{NH}_4$) and **ammonium 2-chloro-5-nitrophenylchlorostibonate** ($2\text{-Cl-5-NO}_2\text{C}_6\text{H}_3\text{SbCl}_5\text{NH}_4$) were prepared according to the method of Schmidt.[4] It consisted of adding an excess of ammonium chloride to a solution of arylstibonic acid in concentrated hydrochloric acid.

TABLE III

| | Yield, % | M. p., °C. | Formula | Sb analyses, % Calcd. | Found |
|---|---|---|---|---|---|
| 2-Chlorophenylstibinic chloride | 95 | 82[a] | $C_6H_6OCl_5Sb$ | 30.98 | 30.98 |
| 2-Chloro-5-nitrophenylstibinic chloride | 95 | 250 | $C_6H_3O_2NClSb$ | 28.99 | 28.90 |
| Ammonium 2-chlorophenylchlorostibonate | 98 | 87–89 | $C_6H_8NCl_6Sb$ | 28.41 | 28.48 |
| Ammonium 2-chloro-5-nitrophenylchlorostibonate | 98 | 250 | $C_6H_7O_2N_2Cl_6Sb$ | 25.71 | 25.90 |

[a] Melted with previous sintering.

## Summary

1. 2-Chloro-5-nitrophenylstibonic acid was condensed with aniline and with a series of aliphatic amines, namely, *n*-propyl, *n*-butyl, *i*-butyl, *n*-amyl and *i*-amylamine.

2. Hydrolysis of 2-chloro-5-nitrophenylstibonic acid was carried out in 6 *N* potassium hydroxide solution, producing 2-hydroxy-5-nitrophenylstibonic acid.

3. 2-Chloro-5-aminophenylstibonic acid was prepared by reduction of the nitro compound.

4. 2-Chlorophenylstibonic acid, 2-chloro-5-nitrophenylstibonic acid, and the chlorides and ammonium chlorostibonates of each were also prepared for the first time.

LINCOLN, NEBRASKA

RECEIVED MARCH 5, 1935

---

[6] Jacobs, Heidelberger and Rolf, THIS JOURNAL, **40**, 1581 (1918).

---

[CONTRIBUTION FROM THE HERCULES EXPERIMENT STATION, HERCULES POWDER CO.]

# The Chlorinated Ethylamines—A New Type of Vesicant

BY KYLE WARD, JR.

This paper describes the preparation and properties of $\beta$-chloroethylamine, $\beta,\beta'$-dichlorodiethylamine, $\beta,\beta',\beta''$-trichlorotriethylamine and a few of their derivatives. The primary[1] and secondary[2] derivatives have been prepared previously. The tertiary derivatives are new. Both the tertiary amine and its hydrochloride exhibit a marked vesicant action.

These three bases have all been prepared from the corresponding ethanolamines or their hydrochlorides. This is very easily accomplished by means of thionyl chloride. Phosphorus pentachloride also proved suitable in the only case where it was tried, namely, with triethanolamine.

The chlorination of monoethanolamine hydrochloride proceeds much more smoothly than that of the free base. The yield is better, also, and the purification of the chlorinated product easier. Formation of thionylamine may be causing the difficulty in this case.

While this paper was being written, an article[3] by F. G. Mann appeared describing the preparation of $\beta,\beta'$-dichlorodiethylamine by the same method used in the present work. The only

---

[1] Gabriel, *Ber.*, **21**, 566, 1049 (1888); Seitz, *ibid.*, **24**, 2624 (1891).

[2] Prelog, Dříza and Hanousek, *Coll. Czech. Chem. Comm.*, **3**, 578 (1931).

[3] Mann, *J. Chem. Soc.*, 464 (1934).

appreciable difference lies in the recovery of the chlorinated product. Mann accomplishes this by cooling and crystallizing from the reaction mixture, while the writer distilled off the solvent and volatile reaction products.

The tertiary compound, either as free base or as hydrochloride, proved to have a marked vesicant action. The primary and secondary compounds have no such action. This action appears analogous to that of the mustard gas vesicants and, like that, apparently hinges upon the presence of $\beta$-chloroethyl groups. It is the first case where the sulfur has been replaced by an element of the fifth group, the chlorovinylarsines differing in several respects. Whereas in the case of sulfur both the mercaptan and sulfide are vesicant, in the case of nitrogen three $\beta$-chloroethyl groups are necessary before vesicant action is noticed.

A few tests on the reactivity of these chloro derivatives show that they react readily with sodium phenolates and sodium mercaptides, but only one of the resulting products, that obtained from sodium amyl mercaptide and $\beta,\beta'$-dichlorodiethylamine, was purified sufficiently to be described here.

## Experimental Part

The hydrochlorides, free bases and picrates corresponding to $\beta$-chloroethylamine, $\beta,\beta'$-dichlorodiethylamine and $\beta,\beta',\beta''$-trichlorotriethylamine were all prepared by the same methods, with the exception noted below. For this reason, only the preparation of the tertiary derivatives will be given in detail. The use of phosphorus pentachloride was tried only on three compounds.

**Reaction of Triethanolamine with Thionyl Chloride.**—Forty-six grams of triethanolamine (0.3 mol) was dissolved in 40 cc. of chloroform and added, drop by drop, with mechanical stirring to a solution of 147 g. of thionyl chloride (1.2 mol or 33% excess) in 60 cc. of chloroform. When all the amine had been added, the volatile products were distilled off and the remaining crystalline mass recrystallized from acetone. The melting points and analyses are given in the table.

**Reaction of Triethanolamine Hydrochloride with Thionyl Chloride.**—The triethanolamine hydrochloride was prepared according to the process described by Germann and Knight.[4] Forty-six g. (0.25 mol) was treated with a solution of 119 g. of thionyl chloride (1 mol or 33% excess) in 75 cc. of benzene. The reaction went smoothly and was complete after letting stand overnight at about 30°. The volatile portion was distilled off and the residual colorless crystals recrystallized from acetone. The yield was 42 g. (70%).

**Reaction of Triethanolamine Hydrochloride with Phosphorus Pentachloride.**—Thirty-seven grams of triethanolamine hydrochloride (0.2 mol) was treated with a chloroform solution of 62.5 g. of phosphorus pentachloride (0.3 mol, theoretical amount). The mixture was refluxed overnight on the steam-bath. The volatile material was then distilled and the crude product dissolved in water. A solution of calcium hydroxide was added to precipitate the phosphoric acid. This also threw out the free amine as an oily liquid. The calcium phosphate was filtered off with a fritted glass funnel and washed free of the amine with chloroform, which dissolves the free base readily. The aqueous and chloroform layers in the filtrate were separated and the former extracted several times with fresh chloroform. The combined chloroform solution was evaporated with an excess of hydrochloric acid. The $\beta,\beta',\beta''$-trichlorotriethylamine hydrochloride so obtained was recrystallized from acetone with a yield of 32 g. (66%).

**$\beta,\beta',\beta''$-Trichlorotriethylamine.**—The free base separates as a pale yellowish oil of unpleasant odor if the aqueous solution of the hydrochloride is treated with an alkali, even with sodium bicarbonate.

**$\beta,\beta',\beta''$-Trichlorotriethylamine Picrate.**—This was prepared by mixing cold saturated aqueous solutions of picric acid and of trichlorotriethylamine hydrochloride. The picrate was recrystallized from acetone, as recrystallization from water tends to split off the chlorine atoms.

**$\beta,\beta'$-Dichlorodiethylamine and Derivatives.**—The procedures used here were similar to those described for the tertiary compounds. The reaction of diethanolamine with thionyl chloride gives 60% of the theoretical yield of dichlorodiethylamine hydrochloride, colorless crystals. If the reaction is carried out on diethanolamine hydrochloride, a dark liquid obtained by evaporating diethanolamine with the required amount of hydrochloric acid, 87% of the theoretical yield is obtained. The melting point of dichlorodiethylamine hydrochloride after one recrystallization from acetone is 208–209°, but this can be raised by further recrystallizations to 216°.

**$\beta$-Chloroethylamine and Derivatives.**—These were prepared similarly to the corresponding tertiary derivatives. A much nicer product and a higher yield (87%) was obtained from monoethanolamine hydrochloride, hygroscopic crystals obtained by evaporating monoethanolamine with the required amount of hydrochloric acid, than from the free monoethanolamine.

Recrystallization can be carried out with amyl alcohol (as did Seitz) or with ethyl alcohol–ether.[5] The hydrochloride, colorless crystals, melts higher than Seitz observed, but the melting point of the picrate and the analysis make it evident that the compound is that which is sought (see table below). Possibly Seitz's material contained traces of amyl alcohol, as he crystallized from that solvent and dried at a low temperature, 60°. The free base is an oily liquid of unpleasant odor. It is quite soluble in water and is not thrown out by alkali from moderately dilute solutions. The picrate crystallizes with one-half molecule of water of crystallization. This was removed by boiling up the crystals suspended in toluene and removing the water by distillation of this suspension.

The table will serve to compare the derivatives of the three bases.

---

[4] Germann and Knight, THIS JOURNAL, **55**, 4150 (1933).

[5] Contrary to the findings of Seitz, the hydrochloride proved only very slightly soluble in ether.

| Derivative | M. p., ° C. Found | M. p., ° C. Previous value | Nitrogen, % Calcd. | Nitrogen, % Found | Chlorine, % Calcd. | Chlorine, % Found |
|---|---|---|---|---|---|---|
| $ClCH_2CH_2NH_2 \cdot HCl$ | 144 | 119–123 | 12.09 | 11.93 | 61.1 | 61.0 |
| $(ClCH_2CH_2)_2NH \cdot HCl$ | 216 | 216–217 | 7.85 | 7.78 | 59.6 | 59.3 |
| $(ClCH_2CH_2)_3N \cdot HCl$ | 130–131 | ..... | 5.80 | 5.66 | 58.8 | 58.9 |
| Picrates | | | | | | |
| $ClCH_2CH_2NH_2–C_6H_3N_3O_7–{}^1/_2\ H_2O$ | 107–110 | above 100 | | | | |
| $ClCH_2CH_2NH_2–C_6H_3N_3O_7$ | 143 | 142–143 | | | | |
| $(ClCH_2CH_2)_2NH–C_6H_3N_3O_7$ | 112–113 | 111–112 | | | | |
| $(ClCH_2CH_2)_3N–C_6H_3N_3O_7$ | 136.5–137 | ..... | | | 24.6 | 24.9 |

The melting points in the second column are taken from the work of Gabriel (the primary picrate), Seitz (the primary derivatives), Prelog and co-workers (the secondary picrate), and Mann (the secondary hydrochloride).

**Reactions of the Chloroethylamines.**—The chlorine atoms in these derivatives react readily with sodium alcoholates, sodium phenolates and sodium mercaptides, as was shown by a few tests. In only one case, however, was the reaction mixture worked up to identify the final product. This reaction will be described here as typical.

Four grams of sodium was dissolved in 167 cc. of alcohol and 8.7 g. of amyl mercaptan added. To this solution 5 g. of β,β'-dichlorodiethylamine hydrochloride was added and the mixture refluxed for half an hour. On distillation of the resulting mixture, the fraction boiling about 214° at 25 mm. pressure was taken and analyzed for the diamyl thioether of diethanolamine.

*Anal.* Calcd. for $C_{14}H_{31}NS_2$: N, 5.05; S, 23.1. Found: N, 4.85, S, 22.5.

**Physiological Action of the above Bases and their Hydrochlorides.**—Symptoms of poisoning were noted with the first preparation of the tertiary derivative. About five hours after it had been handled irritation between the fingers had been noticed and the next morning large red welts and blisters had formed in several places on the hands and arms. These were very slow to heal, blisters reforming soon after they were emptied. The worst burns required several months to heal completely and left brown discolorations. These symptoms are very similar to those produced by the action of mustard gas.

In order to eliminate the possibility of sulfur compounds as the cause, tests were run on the pure materials, using samples of the tertiary base and hydrochloride prepared by means of phosphorus pentachloride. Ten per cent. aqueous solutions of the three hydrochlorides and 3% chloroform solutions of the three bases were used. One drop was placed upon the forearm, left for ten minutes and washed away. After an hour a slight redness was evident where the tertiary hydrochloride had been placed. After two hours this was also evident where the chloroform solution had been spotted. During the evening, some five hours later, itching was noticed on both of these spots. The next day both places had blistered. The 3% solution of the free base, however, did not cause as bad a burn as the other. It was healed in a day or two, leaving a brown discoloration. The blister caused by the hydrochloride persisted for two weeks and was not entirely healed for five further days. None of the other spots produced any effect whatever.

## Conclusions

1. β-Chloroethylamine, β,β'-dichlorodiethylamine and β,β',β''-trichlorotriethylamine have been prepared with their hydrochlorides and picrates. The tertiary compounds have not been prepared previously.
2. The melting point of β-chloroethylamine hydrochloride has been found to be 144°, about twenty-five degrees higher than that obtained by Seitz.
3. The tertiary amine and its hydrochloride have been shown to be strongly vesicant.
4. The diamyl thioether of diethanolamine has been prepared from the secondary chloroethylamine.

WILMINGTON, DELAWARE

RECEIVED MARCH 11, 1935