vapors were driven through an upright water-cooled condenser, a long drying tube containing potassium hydroxide pellets into a receiver containing crushed potassium hydroxide (80 g.) covered with dry ether, the receiver being immersed in a dry-ice–ethylene trichloride bath. Heating was continued until the bulk of the amine had distilled over. Furfuryl bromide solution (prepared according to the method of Zanetti[7] from 38 g. of furfuryl alcohol) was cooled to minus 10° and siphoned into the solution of the amine. The mixture was rocked for several minutes, then removed from the bath and shaken frequently for two hours. It was then allowed to stand overnight. After filtration, the ether was removed by distillation and the product was fractionally distilled *in vacuo*. The fraction boiling 50–57° at 16.5–18 mm. was redistilled; yield, 15 g. (50% of theoretical, assuming 70% yield of bromide). As this amine had been prepared before no analysis was made.

Furfurylethylamine, $C_4H_3OCH_2NHC_2H_5$.—Ethylamine was generated from the hydrochloride (50 g.) in an apparatus consisting of the following train: an ordinary distilling flask equipped with a dropping funnel, a long slightly inclined drying tube containing potassium hydroxide pellets, a water-cooled condenser, and the same receiver as in the preparation of the methylamine. The ethereal furfuryl bromide solution prepared from 25 g. of furfuryl alcohol and precooled to minus 10° was introduced by siphon as before, and the product separated as in the preceding case. The fraction boiling at 63–65° at 17–18 mm. was redistilled; yield, 13 g. (58% on basis of 70% yield of the bromide). This amine having been prepared previously no analysis was made.

Furfurylbutylamine, $C_4H_3OCH_2NHC_4H_9$.—Twenty-five grams of normal butylamine, previously dried over potassium hydroxide and distilled, was added at once to a 20-g. batch of the ethereal furfuryl bromide solution over 50 g. of crushed potassium hydroxide. The whole was stirred for one hour and then allowed to stand overnight. After filtration and removal of the ether, the fraction boiling at 92–95° at 16–18 mm. was redistilled; yield, 13 g. (60% on basis of 70% yield of furfuryl bromide).

Anal. Calcd. for $C_9H_{14}ON$: C, 70.58; H, 9.80; N, 9.15. Found: C, 70.40; H, 9.96; N, 9.29.

Furfurylamylamine, $C_3H_3OCH_2NHC_5H_{11}$.—The procedure was similar to the preceding: 8 g. of amylamine and a 4-g. batch of the furfuryl bromide solution were used. The fraction boiling at 108–111° at 16–18 mm. was redistilled; yield, 3.0 g. (65% on basis of 70% yield of bromide).

Anal. Calcd. for $C_{10}H_{17}ON$: N, 8.48. Found: N, 8.66.

Furfurylphenylamine, $C_4H_3OCH_2NHC_6H_5$.—Forty-five grams of aniline and a 20-g. batch of furfuryl bromide were used in this case. On distillation, the main fraction came over at 113–120° at approximately 1 mm. On redistillation this fraction boiled at 109–110° under 0.5 mm.

Anal. Calcd. for $C_{11}H_{11}ON$: C, 76.30; H, 6.36; N, 8.09. Found: C, 76.51; H, 6.47; N, 8.26.

Summary

1. The action of α-furfuryl bromide in ether solution on primary amines has been studied and found to form secondary amines.

2. The methyl, ethyl, butyl, amyl and phenyl α-furfuryl amines have been prepared by the above method and their properties reported.

NEW YORK, N. Y. RECEIVED SEPTEMBER 7, 1939

(7) Zanetti, THIS JOURNAL, **49**, 1065 (1927).

[CONTRIBUTION FROM THE BIOCHEMICAL RESEARCH FOUNDATION OF THE FRANKLIN INSTITUTE]

Derivatives of Aminomethanethiol

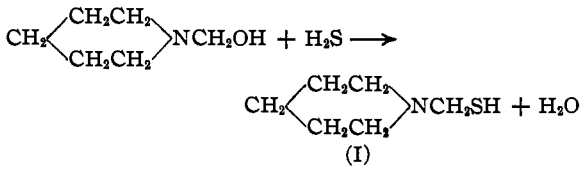
BY ARTHUR BINZ AND LELAND H. PENCE

Hydroxymethanethiol, $HOCH_2SH$, was assumed by Baumann[1] to be formed as an unstable intermediate on treating formaldehyde with hydrogen sulfide, and he showed that the reaction proceeds to insoluble trithioformaldehyde, $HCHO + H_2S \longrightarrow HOCH_2SH \longrightarrow (CH_2S)_3$. Since trithioformaldehyde because of its low solubility and reactivity is of no particular interest for biochemical research, it was considered advantageous to investigate hydroxymethanethiol, either as such or in the form of easily soluble and reactive products obtained from it. For these reasons Binz, Räth, and Walter[2] attempted to isolate hydroxymethanethiol by reducing formaldehyde-sulfoxylate with hypophosphorous acid, $HOCH_2SO_2H \longrightarrow HOCH_2SH$, and obtained a product which appeared to be the desired thiol, but the yield was very small.

In taking up this work again we endeavored to obtain a derivative of the corresponding aminomethanethiol which would be stable, by first condensing formaldehyde-sulfoxylate with piperidine and then reducing the product with hypophosphorous acid in the presence of hydriodic acid according to the reaction $C_5H_{10}NCH_2SO_2H \longrightarrow C_5H_{10}NCH_2SH$. Hydrogen sulfide was also used as a reducing agent, but in both cases the yields of a compound showing the reactions of a thiol were very small.

(1) Baumann, *Ber.*, **23**, 1869 (1890).
(2) Binz, Räth and Walter, *ibid.*, **57**, 1398 (1924).

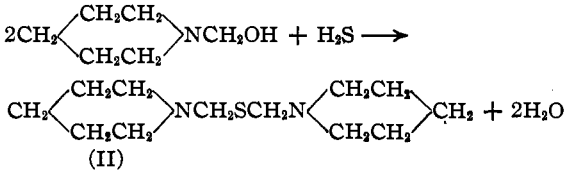
Another method, however, was successful. When piperidine was added to formaldehyde and the 1-piperidinemethanol thus obtained treated with hydrogen sulfide, a vigorous reaction with strong evolution of heat set in and 1-piperidinemethanethiol (I) was obtained in good yield



(I)

It is a clear oil at room temperature, crystallizing in the icebox.

When the reaction was conducted with cooling, 1,3-di-(1′-piperidine)-2-thiapropane (II)[3] was formed:

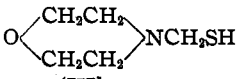


(II)

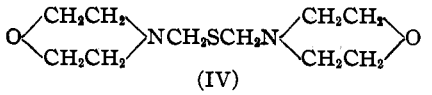
It is probable that the latter reaction is the primary one and that the thiol (I) is produced from the splitting of the sulfide (II) by excess hydrogen sulfide at a higher temperature.

Compound (II) has been obtained by LeFèvre and LeFèvre[4] by saturating an aqueous solution of piperidine with hydrogen sulfide and then adding formaldehyde. These authors had to keep the piperidine at 0° in order to dissolve the necessary amount of hydrogen sulfide and for this reason obtained only the monosulfide (II), not the thiol (I). Furthermore, experiments carried out in this Laboratory by Dr. F. E. Reinhart have shown that our method, even in the case of monosulfides, is more generally applicable than the LeFèvre method, since an excess of hydrogen sulfide must be used in some cases. This is possible only if a stream of the gas is applied to the previously formed aminomethanol.

The application of our procedure to morpholine gave results which closely correspond to those obtained with piperidine. Treatment of morpholine with formaldehyde and hydrogen sulfide yielded 4-morpholinemethanethiol (III); when the reaction was carried out with cooling 1,3-di-(4′-morpholine)-2-thiapropane (IV) was formed.

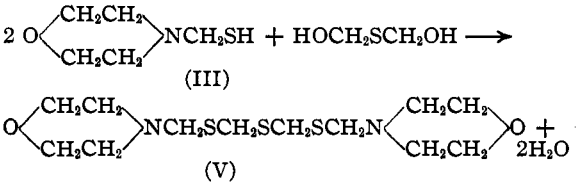


(III)



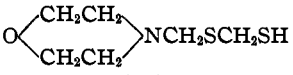
(IV)

One difference in comparison with piperidine was that the formation of compound (III) required the presence of hydrochloric acid. This was unexpected because the addition compounds of amines and aldehydes are sensitive to acids. A greater difference, however, was that compounds (III) and (IV) did not appear as the only reaction products. Simultaneously with (III) was formed 1,7-di-(4′-morpholine)-2,4,6-trithiaheptane (V); apparently di-(hydroxymethyl) sulfide was formed during the reaction and condensed with some of the (III)



(V)

Compound (V) was formed as the chief product, if, instead of equivalent amounts of morpholine and formaldehyde, an excess of the latter was added before the introduction of hydrogen sulfide. Simultaneously with compound (IV), 3-(4′-morpholine)-2-thiapropanethiol (VI) was formed as a by-product.



(VI)

Compounds (V) and (VI) are white flocculent precipitates which show no sharp melting points, and cannot be purified by crystallization. The fact that these compounds are quite soluble in the usual organic solvents precludes the possibility that they are mere mixtures of the amine and trithioformaldehyde.

This tendency to form polymerized thioformaldehyde derivatives was still more pronounced when diethanolamine was treated with formaldehyde and then with hydrogen sulfide. A white flocculent mass (VII) was obtained which according to analysis contained 7 molecules of thioformaldehyde bound to 1 molecule of diethanolamine, although the reaction mixture contained no excess of formaldehyde. This means that some primary compound, perhaps the mono-

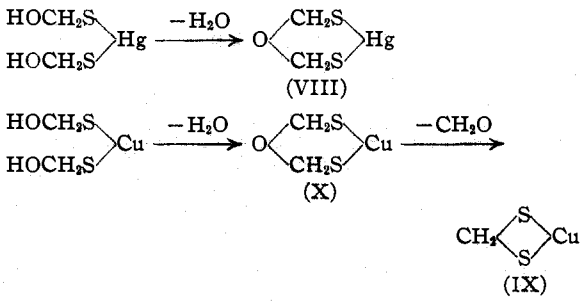
(3) This nomenclature is in conformity with that published in *C. A.* **31**, 9486 (1937), and specifically with Rule 16, THIS JOURNAL, **55**, 3912 (1933).

(4) LeFèvre and LeFèvre, *J. Chem. Soc.*, 1142 (1932).

sulfide $[(HOCH_2CH_2)_2NCH_2]_2S$, has undergone further changes during the reaction. In fact, an oily compound corresponding to this formula was obtained by conducting the reaction between methanoldiethanolamine and hydrogen sulfide at zero degrees. This oil decomposes with water to a white solid mass.

The result of analysis of compound (VII) suggests the formula, $(HOCH_2CH_2)_2N(CH_2S)_7H$. Although this formula might indicate the presence of $2(CH_2S)_3$, trithioformaldehyde could not be extracted with any solvent, nor could it be obtained by sublimation when the compound was heated *in vacuo*.

Most of the compounds give precipitates with the salts of heavy metals. Some of these precipitates have been investigated, and it was found that both 1-piperidinemethanethiol (I) and 4-morpholinemethanethiol (III) with mercuric chloride in alcoholic solution yield the same precipitate, which, according to analysis, appears to be mercuric di-(mercaptomethyl) ether (VIII), $Hg(SCH_2)_2O$. Under the same conditions copper acetate reacts with either (I) or (III) to give a precipitate, the analysis of which indicates it to be cupric methylene dimercaptide (IX), CuS_2CH_2. Perhaps the primary reaction is: $2R_2NCH_2SH + HgCl_2 \longrightarrow (R_2NCH_2S)_2Hg + 2HCl$, a corresponding one occurring with copper acetate. Then the piperidine and morpholine are split off and further changes ensue



We do not consider these conclusions final, as the compounds could not be redissolved and purified. For that reason the possible existence of an equimolecular mixture of the usual cuprous salt of a thiol, in this case $CuSCH_2SCu$, and CH_2S_2 cannot be excluded entirely; this assumption, however, does not appear justified since it would require the two components to have the same high degree of insolubility in order to account for the analytical results obtained (1Cu: 2S).

Many of the compounds are lethal. From an investigation carried out under the direction of Dr. J. O. Ely, of our Cytological Department, we submit the following data. 1-Piperidinemethanethiol (I) and 1,3-di-(1′-piperidine)-2-thiapropane (II) in 0.04% water solution killed paramecia immediately, and daphnia in twenty minutes. Lethal doses of 4-morpholinemethanethiol (III), 1,3-di-(4′-morpholine)-2-thiapropane (IV), compound (VII), 1-piperidinemethanethiolhydrochloride (XI), and 1,3-di-(1′-piperidine)-2-thiapropane dihydrochloride (XII), are, respectively, 0.025, 0.021, 0.165, 0.05, and 0.083 mg. per g. of body weight when injected intravenously into mice. The lethal doses of piperidine, 1-methylpiperidine, 1-ethylpiperidine, and coniine, injected subcutaneously into rabbits, have been reported[5] to be 0.5, 0.4, 0.3, and 0.09 mg. per g. body weight, respectively. Thus most of these sulfur compounds are even more poisonous than coniine, without possessing the latter's characteristic side chain. Thioacetic acid, which was tested in comparison, has a lethal dose of 0.125 mg. per g. body weight when injected intravenously in mice, and is tolerated better than our compounds.

It was difficult to obtain several of the compounds analytically pure, as many of them were either insoluble, amorphous, or unstable.

Experimental

1-Piperidinemethanethiol (I).—Piperidine (10 g.) was poured gradually and with cooling into 37% aqueous formaldehyde (20 cc.), and shaken with anhydrous potassium carbonate (10 g.). The 1-piperidinemethanol, $C_5H_{10}N-CH_2OH$, thus formed[6] was separated from the aqueous layer, placed in a large test-tube, weighed, and gassed with hydrogen sulfide. The temperature rose spontaneously to 68°. After fifteen minutes an oily turbidity appeared, and at the end of two and one-half hours the hydrogen sulfide uptake was 3.3 g. The mixture was shaken with 10% sodium hydroxide (25 cc.) to remove unreacted hydrogen sulfide, and the oil was extracted with ether (75 cc.). After separating, drying with sodium sulfate, and evaporating the ether *in vacuo* at room temperature (to prevent decomposition), there remained 13.6 g. (yield, 88%) of 1-piperidinemethanethiol. The oil solidified in the icebox to colorless crystals; m. p. 12.5–15°. It is soluble in the ordinary organic solvents and dilute acid, but insoluble in alkaline solutions.

Anal. Calcd. for $C_6H_{13}NS$: N, 10.68; S, 24.44. Found: N, 9.55; S, 22.65; $n^{21}D$ 1.5552.

Although the analytical results showed a ratio of nitrogen to sulfur of 1:1.03, the values were too low because of the difficulty in removing the last traces of ether from the

(5) Wolffenstein and Wolffenstein, *Ber.*, **34**, 2403 (1901).
(6) L. Henry, *Bull. soc. chim.*, [3] **14**, 157 (1895).

oil at room temperature. A sample of the oily base was therefore converted into the solid hydrochloride for analysis.

1-Piperidinemethanethiol Hydrochloride (XI).—After dissolving 1-piperidinemethanethiol (2.3 g.) in toluene (15 cc.), hydrogen chloride gas was introduced through an inverted funnel with stirring and cooling. The white, solid hydrochloride, which precipitated immediately, was filtered and washed with ether: yield 2.5 g.; m. p. 195–205°.

Anal. Calcd. for $C_6H_{14}NSCl \cdot {}^1/_2H_2O$: N, 7.93; S, 18.15; Cl, 20.07. Found: N, 7.35; S, 18.18; Cl, 20.25.

After dissolving the hydrochloride in water and adding 10% sodium carbonate solution, the oily 1-piperidinemethanethiol was reprecipitated.

It was not possible to purify the 1-piperidinemethanethiol by distillation. On heating 1-piperidinemethanethiol (10 g.) at 4 mm. pressure and 150–170° bath temperature, the main fraction distilled at 75–81° and proved to be di-(1-piperidyl)-methane, $C_5H_{10}NCH_2NC_5H_{10}$, contaminated with a small amount of a sulfur compound.

Anal. Calcd. for $C_{11}H_{22}N_2$: N, 15.4. Found: N, 15.9; S, 0.24; $n^{15}D$ 1.4891.

Putochin[7] found $n^{15}D$ 1.4883 for di-(1-piperidyl)-methane. Piperidine has $n^{15}D$ 1.4538. The residue in the distillation flask consisted of 2.4 g. of a brittle brownish mass; m. p. 228–231°; S found, 58.4%.

1-Piperidinemethanethiol (10 g.) refluxed with dilute hydrochloric acid (25 cc.) at 90° for two hours gradually deposited needles of trithioformaldehyde. The total yield after repeating several times with the filtrate was 3 g.; theoretical, 3.5 g.; m. p. 216–218°. An analogous decomposition had been observed by LeFèvre and LeFèvre[4] with compounds obtained from reactions between dimethyl- and diethylamines, hydrogen sulfide and formaldehyde.

To 1-piperidinemethanethiol (1.3613 g.) dissolved in ethyl alcohol (10 cc.) there was added mercuric chloride (1.409 g.) dissolved in ethyl alcohol (39.2 cc.). A flocculent dark yellow precipitate of mercuric di-(mercaptomethyl) ether (VIII) appeared, which was filtered and washed with absolute ethanol: yield 97%; decomposition at 95–105°. The compound is very insoluble. When hydrogen sulfide gas was passed through an aqueous suspension of this mercury derivative, mercuric sulfide was precipitated immediately, this reaction being characteristic of mercuric mercaptans.

Anal. Calcd. for $HgS_2C_2H_4O$: Hg, 64.97; S, 20.77; C, 7.77; H, 1.31. Found: Hg, 64.51; S, 20.10; C, 6.34, 6.34; H, 1.19, 1.22.

To 1-piperidinemethanethiol (1.8201 g.) dissolved in ethyl alcohol (125 cc.) there was added a saturated alcoholic solution of cupric acetate until a permanent blue color was established. The resulting yellow-tan flocculent precipitate was centrifuged and washed five times with absolute ethanol (150 cc. each), and dried at room temperature *in vacuo;* yield 0.8964 g., (91% based on cupric methylene dimercaptide (IX)); decomposes at 105–110°. Sodium sulfide solution produced a coating of black copper sulfide on the surface of the compound, which hydrogen sulfide would not accomplish. The high insolubility of the compound prevented any further purification.

Anal. Calcd. for CuS_2CH_2: Cu, 44.86; S, 45.24. Found: Cu, 43.74, 43.90; S, 44.09 (Ratio, 1.000 N; 1.995 S).

1,3-Di-(1'-piperidine)-2-thiapropane (II).—1-Piperidinemethanol, prepared from piperidine (10 g.), was treated with hydrogen sulfide at 0° for one and one-half hours, 2.6 g. of the gas being absorbed. The reaction product was extracted with ether (100 cc.), shaken with 10% sodium hydroxide (50 cc.), separated, and dried with calcium chloride. On evaporation of the ether an oil was obtained which crystallized on cooling: yield, 3.2 g.; m. p. 48.5–50.5°. The compound is soluble in the ordinary organic solvents and dilute acid, but insoluble in alkaline solutions.

Anal. Calcd. for $C_{12}H_{24}N_2S$: N, 12.27; S, 14.04. Found: N, 12.38, 12.45; S, 14.56.

1,3-Di-(1'-piperidine)-2-thiapropane Dihydrochloride (XII).—1-Piperidinemethanol, prepared as before from piperidine (10 g.), was dissolved in concd. hydrochloric acid (10 cc.), cooled, and treated with hydrogen sulfide for one hour. The colorless, crystalline mass of 1,3-di-(1'-piperidine)-2-thiapropane dihydrochloride was filtered and washed with acetone; yield, 4.2 g.; m. p. 171–175°, with decomposition.

Anal. Calcd. for $C_{12}H_{26}N_2SCl_2 \cdot H_2O$: N, 8.77; S, 10.04; Cl, 22.21. Found: N, 8.70, 8.60; S, 10.24, 10.33; Cl, 22.01.

An aqueous solution of the hydrochloride, treated with 10% sodium carbonate, yielded a precipitate of the free base (II); m. p. 50–53°.

4-Morpholinemethanethiol (III).—To morpholine (17.5 cc.) there was added slowly with cooling 37% aqueous formaldehyde (18 cc.), followed by concd. hydrochloric acid (17 cc.); *p*H 3.5. On treatment with hydrogen sulfide at 55° for two hours, the solution absorbed 5.1 g. of the gas (calcd., 6.8 g.). The reaction mixture was treated with 10% sodium hydroxide (100 cc.), and extracted with ether (200 cc.). The extract, which was dried with calcium chloride, and concentrated, deposited crystals of 4-morpholinemethanethiol; yield 8 g. Recrystallization from methanol (15 cc.) gave 5.3 g. of fine prisms; m. p. 86–88°. Cooling below room temperature during the recrystallization was avoided to prevent the precipitation of the by-product (V) of the reaction.

Anal. Calcd. for $C_5H_{11}NSO$: N, 10.52; S, 24.07. Found: N, 10.46, 10.50; S, 24.14, 24.08.

When the thiol (1.85 g.) was refluxed for one hour with concd. hydrochloric acid (25 cc.), trithioformaldehyde (0.6 g. or 94%) was obtained; m. p. 219°. S, calcd. 69.6; found, 69.0.

To 4-morpholinemethanethiol (1.3309 g.) dissolved in ethyl alcohol (30 cc.) there was added mercuric chloride (1.3575 g.) dissolved in ethyl alcohol (37.7 cc.). A flocculent canary-yellow precipitate of mercuric (di-mercaptomethyl) ether (VIII) appeared immediately. After purification by washing with absolute ethanol and centrifuging several times, the precipitate was dried: yield 94%; decomposition at 110–115°. When an aqueous suspension of the compound was treated with hydrogen sulfide, mercuric sulfide was precipitated.

(7) Putochin, *Ber.*, **55**, 2749 (1922).

Anal. Calcd. for $HgS_2C_6H_4O$: Hg, 64.97; S, 20.77; C, 7.77; H, 1.31. Found: Hg, 65.08, 65.10; S, 20.70; C, 5.26, 5.27; H, 1.03, 1.04.

To 4-morpholinemethanethiol (0.6655 g.) dissolved in ethyl alcohol (15 cc.) there was added a saturated alcoholic solution of cupric acetate until a permanent blue color was imparted to the solution. The flocculent yellow precipitate was purified as much as possible by washing several times with absolute ethanol, centrifuged, and dried at room temperature: yield, 94% based on cupric methylene dimercaptide (IX); decomposition at 100–110°. When suspended in sodium sulfide solution the compound immediately acquired a black coating of copper sulfide; hydrogen sulfide had no effect.

Anal. Calcd. for CuS_2CH_2: Cu, 44.86; S, 45.24; C 8.47; H, 1.43. Found: Cu, 45.79; S, 43.71; C, 5.98, 6.08; H, 1.78, 1.60.

In these cases also the mercury and copper derivatives were too insoluble for further purification, and the values found for carbon are too low, presumably because of the difficulty of obtaining complete combustion.

The ether filtrate obtained after removal of the 8 g. of crude 4-morpholinemethanethiol (III) was cooled to 0°, yielding 5 g. of an amorphous white compound. The latter was purified by dissolving in hot ethanol and cooling, followed by two similar treatments from acetone, and gave a precipitate which melted at 72–80°. This is apparently the same compound which is formed when the reaction between morpholine, formaldehyde, and hydrogen sulfide is carried out without hydrochloric acid, but with twice as much formaldehyde as was previously used. Morpholine (8.75 g.) was added gradually with cooling to 37% formaldehyde (18 cc.), followed by benzene (40 cc.). Hydrogen sulfide was then passed in, with moderate cooling, until 5 g. was absorbed. After the reaction mixture was shaken with 10% sodium hydroxide (25 cc.), the benzene layer was separated, washed with water, concentrated, and cooled to 0°. A colorless, amorphous solid (7.6 g.) was obtained; m. p. 67–78°. Successive purifications with hot methanol, and acetone, raised the melting point to 77–84°.

Anal. Calcd. for $C_{12}H_{24}N_2S_3O_2$: N, 8.64; S, 29.60. Found: N, 8.88, 8.78; S, 30.21.

According to this analysis the compound is probably 1,7-di-(4′-morpholine)-2,4,6-trithiaheptane (V).

1,3-Di-(4′-morpholine)-2-thiapropane (IV).—Morpholine (35 cc.) was added gradually with cooling to 37% formaldehyde (36 cc.). The reaction mixture was shaken with anhydrous potassium carbonate (20 g.), to give an upper layer of 4-morpholinemethanethiol which was separated and treated with hydrogen sulfide at 0°. The crystalline precipitate of 1,3-di-(4′-morpholine)-2-thiapropane formed almost at once. After fifteen minutes the yield of filtered crystals was 12.8 g. The filtrate on treatment with hydrogen sulfide gave a second crop of 11.6 g. and a third crop of 2.6 g. After recrystallizing the product twice from acetone and once from ether the 1,3-di-(4′-morpholine)-2-thiapropane separated as colorless, cube-like crystals, melting at 107–108°.

Anal. Calcd. for $C_{10}H_{20}N_2SO_2$: N, 12.06; S, 13.80. Found: N, 12.16; S, 13.85.

In preparing 1,3-di-(4′-morpholine)-2-thiapropane, a certain amount remains dissolved in the aqueous filtrate after the crystals have been removed. This filtrate on standing deposits a white flocculent precipitate which appears to be identical with a compound obtained from 1,3-di-(4′-morpholine)-2-thiapropane directly by dissolving 3.7 g. in 75 cc. of water at room temperature. After twenty-four hours 0.15 g. of a white precipitate had formed, m. p. 72–82°. The filtrate after warming on the water-bath gave an additional 1.6 g.

Anal. Calcd. for $C_6H_{13}NS_2O \cdot {}^1/_2H_2O$: N, 7.44; S, 34.06. Found: N, 7.41; S, 33.58, 33.51.

According to this analysis the compound is probably 3-(4′-morpholine)-2-thiapropanethiol (VI), $OC_4H_8NCH_2SCH_2SH$.

The Reaction between Diethanolamine, Formaldehyde, and Hydrogen Sulfide.—According to German Patent 564,787 (1931) (I. G. Farbenindustrie), diethanolamine and formaldehyde, when warmed for one-half hour at 50°, form hydroxyethyloxazolidine. We have added diethanolamine to formaldehyde[8] in the cold, thus avoiding the formation of the oxazolidine ring, and have treated the resulting methanoldiethanolamine with hydrogen sulfide.

Gradually and with cooling diethanolamine (5.2 g.) was poured into 37% aqueous formaldehyde (4.5 cc.). Hydrogen sulfide was passed into the solution and within one-half hour a white mass filled the test-tube. The entire reaction mixture was digested with boiling ethanol, in which it did not dissolve, and was then filtered and washed with alcohol and ether: yield, 3.3 g. of compound (VII); m. p. 224–226°.

Anal. Calcd. for $(HOCH_2CH_2)_2N(CH_2S)_7H$: N, 3.28; S, 52.47. Found: N, 3.03; S, 52.39.

Compound (VII) can be dissolved in 20 parts of boiling diethanolamine and remains in solution on addition of water. Since the melting point is near that of trithioformaldehyde (216°) the question arises, whether trithioformaldehyde (S calcd. 69.7) has formed during the reaction and become part of the compound. This is doubtful, as trithioformaldehyde when dissolved in 20 parts of boiling diethanolamine is precipitated by adding water.

Another preparation made from diethanolamine (21 g.) and aqueous formaldehyde (18 cc.) was treated with hydrogen sulfide for one hour. The absorbed gas amounted to 6.8 g. when the tube began to fill with the white semi-solid mass. This was boiled in acetone (600 cc.), in which most of it dissolved. The filtrate on cooling gave 6.7 g. of (VII) as a white precipitate, m. p. 218–221°. When the compound was placed in a bath at 170° it melted immediately to a clear liquid, then solidified, and remelted at 218–228°.

Anal. Calcd. for $(HOCH_2CH_2)_2N(CH_2S)_7H$: N, 3.28; S, 52.47. Found: N, 3.46, 3.43, 3.37; S, 52.00.

We tried to ascertain whether it was possible to obtain the same compound by using the components in the ratio suggested by the above formula. Into 37% formaldehyde (18 cc.) was poured diethanolamine (3 g.). In order to

(8) The reaction between diethanolamine and formaldehyde has been studied by Lyubomudrov, *Ukrain. Khem. Zhur.*, **11**, Wiss. Tl. 119 (1936); *C. A.*, **30**, 5957 (1936).

keep the resulting compound more dispersed, water was added (175 cc.), and the hydrogen sulfide was passed into the suspension at 65°. Within one hour 7.4 g. of the gas had been absorbed. The resulting suspension of white precipitate was made alkaline with 10% sodium hydroxide (20 cc.) and then washed with water by centrifuging. After drying *in vacuo* a yield of 7 g. was obtained; m. p. 220–224°. When placed in the bath at 180°, the compound did not melt until 230–233° Found: N, 1.56; S, 51.08.

This compound (XIII) has a ratio N:S = 1:14.4, which shows that this preparation is different from the one mentioned above.

However, as in the case of (VII), it is not likely that this compound (XIII) is a molecular combination of diethanolamine with trithioformaldehyde. Both are much less soluble in acetone, ether, absolute alcohol, and benzene, and far more soluble in hot diethanolamine than the trithioformaldehyde. Furthermore, the three substances show a marked difference when submitted to sublimation, as is shown in the table.

	100°	230°
$(CH_2S)_3$	Started to sublime	Completely sublimed
(VII)	Slight sublimation with subsequent melting of sublimate	Residue melted with decomposition
(XIII)	Nothing sublimed	Residue unchanged

The analyses were done by Dr. H. K. Alber of our Microchemical Department.

Summary

Piperidine, morpholine, and diethanolamine were treated with aqueous formaldehyde to form the corresponding aminomethanols.

The 1-piperidinemethanol, 4-morpholinemethanol, and methanoldiethanolamine were treated with hydrogen sulfide under varying conditions, yielding 1-piperidinemethanethiol, 1,3-di-(1-piperidine)-2-thiapropane, 4-morpholinemethanethiol, 1,3-di-(4′-morpholine)-2-thiapropane, and polymerized thioformaldehyde derivatives of methanoldiethanolamine, respectively.

The lethal doses of the sulfur derivatives of piperidine, morpholine, and diethanolamine were determined by intravenous injections in mice.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING OF THE UNIVERSITY OF PENNSYLVANIA]

The Alkylation of α-Sulfonylamides[1]

BY AUSTIN POMERANTZ[2] AND RALPH CONNOR

A number of α-sulfonyl-α-alkylacetamides recently were prepared[3] by the alkylation of α-sulfonylacetamides. While this method was adequate for the compounds previously investigated, continuation of the earlier work disclosed that in certain cases the yields were low and the products difficult to purify. Since the alkylation products were of some interest as hypnotics,[4] a more complete study of this reaction was undertaken. The discussion will be limited to the ethylation of α-*n*-butylsulfonylacetamide (I) but examples of other alkylations will be given in the experimental part.

In several ethylations of α-*n*-butylsulfonylacetamide under the conditions previously used (sodium ethoxide and an alkyl halide in alcohol solution), a considerable amount of unchanged I was always present and consequently the purification of the product (α-*n*-butylsulfonyl-*n*-butyramide, II) was very difficult. The recovered starting material was not present in the reaction mixture as unreacted sodium derivative, for the solution was refluxed until it became neutral. It therefore seemed likely that the methylene group of I was not sufficiently activated to compete successfully for the sodium with the large excess of alcohol that was present[5] and that the true situation might be represented according to the equations[6]

(1) This communication is constructed from a thesis submitted by Austin Pomerantz in partial fulfilment of the requirements for the degree of Doctor of Philosophy at the University of Pennsylvania in June, 1939.

(2) Harrison Fellow in Chemistry, 1938–1939; Harrison Scholar in Chemistry, 1937–1938.

(3) d'Ouville and Connor, THIS JOURNAL, **60**, 33 (1938).

(4) A pharmacological examination of the compounds reported in this paper is being made under the direction of Dr. Robert S. Shelton of the Wm. S. Merrell Company and will be reported elsewhere.

(5) Tröger and Lux [*Arch. Pharm.*, **247**, 618 (1909)] reported that α-phenylsulfonylacetamide ($C_6H_5SO_2CH_2CONH_2$) formed no sodium derivative with alcoholic sodium ethoxide. However, the alkylations of α-*p*-tolylsulfonylacetamide previously reported[3] were carried out in alcoholic solution and appeared to be more satisfactory than the alkylation of I.

(6) The weak acidity of the methylene group of I is not surprising in view of the fact that both the sulfone and carbonamide groups are generally considered to be relatively weak labilizing groups.[5,7] It is interesting to note, however, that when a methylene group