

yield was low or acetals did not form, zinc chloride and anhydrous copper sulfate were used as condensing agents instead of sulfuric acid. Neither of these gave products where sulfuric acid had failed.

### Summary

1. It has been shown that carbonyl compounds such as isobutyraldehyde, valerylaldehyde, isovalerylaldehyde, hydrocinnamaldehyde, diethyl ketone and methyl ethyl ketone will form acetals of dipropenyl glycol in good yield.

2. Carbonyl compounds such as methyl hexyl ketone, pinacolone, acetophenone, benzophenone, methylheptanone, citral, benzylideneacetone, benzylideneacetophenone, *o*-chlorobenzaldehyde, *o*-nitrobenzaldehyde, salicylaldehyde and anisaldehyde gave no acetal or ketal products of dipropenyl glycol.

3. The molecular weights, indices of refraction and densities of all the dipropenyl glycol acetals have been determined and listed.

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## Reactions of Certain Halogen Substituted Aryl, Alkyl and Di-alkyl Sulfides with Benzylamine. I

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**Introduction.**—This investigation was undertaken with the object of obtaining further information concerning the reactions of certain halogen substituted aryl, alkyl and di-alkyl sulfides with benzylamine. The work entailed, as the first step, the preparation of a series of halogen substituted sulfides, three of which have not previously been described in the literature, and, as a second step, the reaction of twelve of these sulfides with benzylamine.

**Historical Part.**—The interaction of bis-( $\beta$ -chloroethyl) sulfide with primary amines to form compounds of the thiazane type was first shown by Clarke.<sup>2</sup> However, the parent substance, 1,4-thiazane, was prepared by Davies<sup>3</sup> by heating bis-( $\beta$ -chloroethyl) sulfide with an excess of alcoholic ammonia in a sealed tube at 60°. Helfrich and Reid<sup>4</sup> also studied the reaction and found that bis-( $\beta$ -chloroethyl) sulfide, sulfoxide, and sulfone react with primary aromatic amines to form aryl derivatives of thiazane and sulfonazane.

The condensation of bis-( $\beta$ -chloroethyl) sulfide with amino bodies has been advanced by Cashmore and McCombie<sup>5</sup> as a possible explanation

(1) Technical Divisions, Chemical Warfare Service, Edgewood Arsenal, Md.

(2) Clarke, *J. Chem. Soc.*, **101**, 1583 (1912).

(3) Davies, *ibid.*, **117**, 297 (1920).

(4) Helfrich and Reid, *THIS JOURNAL*, **42**, 1208 (1920).

(5) Cashmore and McCombie, *J. Chem. Soc.*, **123**, 2884 (1923).

for the extreme vesicant action which characterizes this compound. Lawson and Reid's<sup>6</sup> findings that the non-vesicant sulfoxide also enters into combination with amines demonstrated that other factors, possibly distribution coefficients, would have to be taken into consideration if this theory were correct. The inadequacy of other explanations prompted them to retain the "condensation" theory with the proviso, however, that the toxicity of the sulfide to the individual cells might be due to any reaction disturbing the normal balance of metabolism. Presumably this reaction would entail some type of condensation, for the release of a minute trace of hydrochloric acid seemed to them inadequate as an explanation for the far-reaching results observed.

While the foregoing investigations have included the reactions of various amino compounds with bis-( $\beta$ -chloroethyl) sulfide, sulfoxide and sulfone they have not been extended to include other organic sulfides. The present study is, therefore, an extension of the amine reaction to the homologs of bis-( $\beta$ -chloroethyl) sulfide with the object of obtaining further information concerning this type of reaction.

## Experimental Part

### A. Preparation of Sulfides

1. **Preparation of  $\beta$ -Chloroethyl Aryl and Alkyl Sulfides  $\text{ClCH}_2\text{CH}_2\text{SR}$ .**—The seven sulfides included in this series were all prepared by the method described by Meyer<sup>7</sup> for  $\beta$ -chloroethyl ethyl sulfide. They were all colorless liquids of penetrating odor. Their composition and some of their physical and chemical properties are recorded in Table I.

TABLE I  
ANALYSES AND PROPERTIES OF  $\beta$ -CHLOROETHYL ALKYL AND ARYL SULFIDES,  
 $\text{ClCH}_2\text{CH}_2\text{SR}$

| R                  | Chlorine, %        |       | Sulfur, % |       | B. p., °C.<br>(press. mm.) | Density,<br>25°/4° <sup>d</sup> | Viscosity<br>coeff.,<br>C. G. S.<br>units 25°<br>$\eta \times 10^3$ |
|--------------------|--------------------|-------|-----------|-------|----------------------------|---------------------------------|---|
|                    | Calcd.             | Found | Calcd.    | Found |                            |                                 |   |
| Ethyl              | 28.46              | 28.54 | 25.74     | 25.30 | 63–65 (47)                 | 1.0663                          | 9.89  |
| <i>n</i> -Propyl   | 25.58              | 25.45 | 23.13     | 22.94 | 43–45 (2)                  | 1.0349                          | 12.92   |
| <i>n</i> -Butyl    | 23.23              | 22.29 | 21.01     | 20.85 | 58–59 (1)                  | 1.0122                          | 15.25   |
| Isoamyl            | 21.28              | 20.63 | 19.24     | 19.14 | 68 (1)                     | 0.9899                          | 18.55   |
| Phenyl             | 20.54              | 20.78 | 18.58     | 18.26 | 88–89 (0.637)              | 1.1769                          | 30.86   |
| Benzyl             | 19.0               | 19.23 | 17.18     | 16.57 | 113–115 (1.01)             | 1.1479                          | 50.61   |
| Ethyl <sup>a</sup> | 47.32 <sup>a</sup> | 47.15 | 18.95     | 19.20 | 57–58 (6)                  | 1.3908                          | 15.55   |

<sup>a</sup> Bromine derivative.

2. **Preparation of  $\beta$ - (and  $\gamma$ )-Chloropropyl Ethyl Sulfide.**—The  $\beta$ -sulfide was prepared by a modification of the method recently described by Kirner<sup>8</sup> for the preparation of chloroalkyl methyl sulfides. Sodium ethyl mercaptide was prepared by adding 50 g. of cold mercaptan to sodium ethylate. Propylene chlorohydrin (72 g.) was then added dropwise with continuous stirring and the mixture heated on a steam-bath for half

(6) Lawson and Reid, *THIS JOURNAL*, **47**, 2821 (1925).

(7) Meyer, *Ann.*, **240**, 310 (1887).

(8) Kirner, *THIS JOURNAL*, **50**, 2446 (1928).

an hour to complete the reaction. The salt was removed and washed with a little hot absolute alcohol, the filtrate and washings combined, the solvent removed by distillation and the residual oil distilled in vacuum. A colorless liquid (81 g.) of b. p.  $83^{\circ}$  at 25.5 mm. was obtained. Redistillation from a 15-cm. Vigreux column yielded a 74 g. fraction of b. p.  $77-78^{\circ}$  at 20 mm. Calcd. for  $C_6H_{12}OS$ : S, 26.66. Found: S, 26.53. The hydroxy compound (63 g.) was chlorinated according to the procedure of Steinkopf, Herold and Stöhr.<sup>9</sup> After one distillation from a 15-cm. Vigreux column, a 70-g. fraction of b. p.  $60^{\circ}$  at 17 mm. was obtained;  $d_4^{25}$  1.0265; viscosity coeff. (C. G. S.)  $25^{\circ}$ ,  $11.15 \times 10^{-3}$ .

*Anal.* Calcd. for  $C_6H_{11}ClS$ : Cl, 25.58; S, 23.13. Found: Cl, 25.35; S, 23.27.

Preparation of the  $\gamma$ -sulfide was identical with that just described for the  $\beta$ -compound. The materials and quantities used were also identical except that trimethylene chlorohydrin was substituted for propylene chlorohydrin. The hydroxy compound was obtained as a colorless liquid of b. p.  $95^{\circ}$  at 12 mm.; yield 75 g. It was not analyzed for purity, but chlorinated directly to form the chloro derivative, which was obtained as a colorless liquid of b. p.  $72^{\circ}$  at 17 mm.;  $d_4^{25}$  1.0427; viscosity coeff. (c. g. s.)  $25^{\circ}$ ,  $13.30 \times 10^{-3}$ .

*Anal.* Calcd. for  $C_6H_{11}ClS$ : Cl, 25.58; S, 23.13. Found: Cl, 24.77; S, 23.01.

**3. Preparation of Bis-( $\beta$  (and  $\gamma$ )-chloropropyl) Sulfide.**—The method described by Coffey<sup>10</sup> for the preparation of the  $\beta$ -compound was followed in detail. The product was obtained as a colorless liquid of b. p.  $94-95^{\circ}$  at 7 mm.;  $d_4^{25}$  1.1569; viscosity coeff. (C. G. S.)  $25^{\circ}$ ,  $33 \times 10^{-3}$ .

*Anal.* Calcd. for  $C_6H_{12}Cl_2S$ : Cl, 37.91; S, 17.14. Found: Cl, 37.95; S, 16.98.

The method described by Bennett and Hock<sup>11</sup> for the preparation of the  $\gamma$ -compound was followed in detail. The product was obtained as a colorless liquid of b. p.  $111-112^{\circ}$  at 7 mm.;  $d_4^{25}$  1.1774; viscosity coeff. (C. G. S.)  $25^{\circ}$ ,  $41.87 \times 10^{-3}$ .

*Anal.* Calcd. for  $C_6H_{12}Cl_2S$ : Cl, 37.91; S, 17.14. Found: Cl, 37.02; S, 17.10.

**4. Preparation of Bis-(chloromethyl) Sulfide.**—The method described by Bloch and Höhn<sup>12</sup> for the preparation of this compound was followed in detail. The product was obtained as a colorless liquid of b. p.  $51^{\circ}$  at 11 mm.;  $d_4^{20}$  1.4065; viscosity coeff. (C. G. S.)  $20^{\circ}$ ,  $18.09 \times 10^{-3}$ .

*Anal.* Calcd. for  $C_2H_4Cl_2S$ : Cl, 54.13; S, 24.47. Found: Cl, 54.74; S, 24.41.

**5. Preparation of Bis-( $\beta$ -chloroethyl) Disulfide.**—The method described by Bennett<sup>13</sup> for the preparation of this compound was followed in detail. The product was obtained as a colorless liquid of b. p.  $124-127^{\circ}$  at 10 mm.;  $d_4^{20}$  1.3375; viscosity coeff. (C. G. S.)  $20^{\circ}$ ,  $83.06 \times 10^{-3}$ .

*Anal.* Calcd. for  $C_4H_8Cl_2S_2$ : Cl, 37.11; S, 33.56. Found: Cl, 35.95; S, 33.40.

**6. Preparation of  $\beta$ -Chloroethyl Mono- and Dichlorovinyl Sulfides.**—The method as described by Lawson and Dawson<sup>14</sup> for the preparation of  $\beta$ -chloroethyl  $\alpha$ -(and  $\beta$ )-chlorovinyl sulfides was followed in detail, except in this work the compounds were not isolated as the  $\alpha$ - and  $\beta$ -isomers, but as a mixture of the two. The boiling point observed for this mixture,  $83-84^{\circ}$  at 4 mm., was considerably higher than that obtained for either of the isomers in the pure state. As indicated by the analysis, it still contained traces of undecomposed trichlorodiethyl sulfide. However, it was sufficiently pure for our use.

(9) Steinkopf, Herold and Stöhr, *Ber.*, **553**, 1010 (1920).

(10) Coffey, *J. Chem. Soc.*, **119**, 94 (1921).

(11) Bennett and Hock, *ibid.*, **127**, 2673 (1925).

(12) Bloch and Höhn, *Ber.*, **55**, 53 (1922).

(13) Bennett, *J. Chem. Soc.*, **119**, 423 (1921).

(14) Lawson and Dawson, *This Journal*, **49**, 3119 (1927).

*Anal.* Calcd. for  $C_4H_8Cl_2S$ : Cl, 45.16; S, 20.42. Found: Cl, 46.42; S, 19.03.

The preparation of  $\beta$ -chloroethyl- $\alpha,\beta$ -dichlorovinyl sulfide as described by the above authors was followed in detail. The product was obtained as a colorless liquid of b. p. 79.5–80.5° at 4 mm.;  $d_4^{20}$  1.4581; viscosity coeff. (C. G. S.) 20°,  $31.98 \times 10^{-3}$ .

*Anal.* Calcd. for  $C_4H_8Cl_3S$ : Cl, 55.55; S, 16.74. Found: Cl, 55.51; S, 16.43.

7. **Preparation of Ethyl Allyl Sulfide.**—Although this compound was prepared in connection with other work, its preparation is included in this investigation since it has not previously been recorded in the literature. A brief description follows: ethyl mercaptan (50 g.) was added to a cold solution of sodium ethylate and 97 g. of allyl bromide added dropwise with stirring. After addition of the bromide was complete, the reaction mixture was poured into a large volume of water and the oil which separated was extracted with ether and dried over anhydrous sodium sulfate. After removal of ether the residue was fractionated from a Vigreux column until a constant boiling fraction was obtained. The pure compound was a colorless liquid of b. p. 115–116°;  $d_4^{20}$  0.8676; viscosity coeff. (c. g. s.) 20°,  $5.97 \times 10^{-3}$ .

*Anal.* Calcd. for  $C_6H_{10}S$ : S, 31.39. Found: S, 31.25.

#### B. Preparation of Benzylaminoaryl, Alkyl and Dialkyl Sulfides and their Hydrochlorides

The benzylamino derivatives were all prepared by the following general method. To a 25-g. sample of the sulfide dissolved in 100 cc. of absolute ethyl alcohol, the molecular equivalent of benzylamine and of anhydrous sodium carbonate was added. The mixture was refluxed on the steam-bath from one to ten hours, depending on the ease with which condensation was accomplished. With the unsaturated chlorinated derivatives it was necessary to conduct the reaction under pressure. Sealed tubes of about 200 cc. capacity were used; fused sodium acetate was substituted for sodium carbonate and the volume of alcohol was reduced from 100 to 50 cc. The tubes were heated for five hours at 110°. After they had cooled sufficiently, they were opened and their contents washed out with hot absolute alcohol. The salt was filtered off and extracted twice with hot alcohol. The filtrate and washings were combined, the solvent removed by distillation and the alcoholic residue poured into a 50% aqueous solution of potassium hydroxide. The amino sulfide which separated out as a heavy oil was extracted with ether and dried overnight with stick potassium hydroxide. The procedure as above outlined was also carried out when the experiment was conducted in a flask at atmospheric pressure. After removal of ether the residue was distilled once in vacuum and the free base dissolved in dry toluene and hydrogen chloride passed in until precipitation was complete. The hydrochlorides were obtained in good yield and of high purity when the above method was carried out. However, if the free base could not be distilled due to decomposition and the hydrochloride was prepared from the crude product, purification was more difficult and lower yields resulted. The hydrochlorides were all white crystalline solids of definite melting point. Their analyses and some of their properties are recorded in Table II.

Of the mono-halogen substituted sulfides examined  $\beta$ -bromoethyl ethyl sulfide reacted most readily with benzylamine. A one-hour reaction period was used as compared with a four-hour period for the corresponding chloro derivative. A yield of 80% based on the fraction boiling at 162–164° at 13 mm. was obtained. With  $\beta$ -chloroethyl *n*-propyl and  $\beta$ -(and  $\gamma$ )-chloropropyl ethyl sulfides, six-hour reaction periods were used; the corresponding amino sulfides were obtained in good yield and distilled with but little decomposition.  $\beta$ -Chloroethyl *n*-butyl and isoamyl sulfides were less reactive; reaction periods of eight and ten hours, respectively, were used. The corresponding amino derivatives were also less stable toward heat. Yields of 51% based on the once distilled products were obtained.  $\beta$ -Chloroethyl phenyl sulfide was the least reactive of the

TABLE II  
ANALYSES AND PROPERTIES OF BENZYLAMINOARYL, ALKYL AND DIALKYL SULFIDES AND  
OF THE HYDROCHLORIDES

| Sulfide hydrochlorides  | Form                     | B. p. <sup>a</sup> (press. mm.), °C. | M. p., °C. |
|---|--------------------------|--------------------------------------|------------|
| 1 $\beta$ -Benzylaminoethyl ethyl                                 | Rectangular plates       | 162-164 (13)                         | 214-215    |
| 2 $\beta$ -Benzylaminoethyl <i>n</i> -propyl                      | Clusters of flat plates  | 167-169 (13)                         | 175        |
| 3 $\beta$ -Benzylaminoethyl <i>n</i> -butyl                       | Flat plates              | 172-230 (13)                         | 152-153    |
| 4 $\beta$ -Benzylaminoethyl isoamyl                               | Clusters of flat plates  | 190-250 (17)                         | 161-162    |
| 5 $\beta$ -Benzylaminoethyl phenyl                                | Silky needles            | Decomposes                           | 152-153    |
| 6 $\beta$ -Benzylaminopropyl ethyl                                | Needles                  | 157-158 (11)                         | 115        |
| 7 $\gamma$ -Benzylaminopropyl ethyl                               | Needles                  | 163-165 (12)                         | 172        |
| 8 3-Benzyl-1,3-thiazetidine                                       | Clusters of small plates | 175-185 (16)                         | 201-203    |
| 9 Bis-( $\beta$ -benzylaminopropyl)                               | Crystalline rods         | Decomposes                           | 239-240    |
| 10 Bis-( $\beta$ -benzylaminoethyl)di-                            | Hexagonal plates         | Decomposes                           | 269        |
| 11 $\beta$ -Benzylaminoethyl $\alpha$ -(and $\beta$ )-chlorovinyl | Needles                  | Decomposes                           | 211-212    |
| 12 $\beta$ -Benzylaminoethyl $\alpha\beta$ -dichlorovinyl         | .....                    | Decomposes                           | 174-176    |

<sup>a</sup> The boiling points are those of the free bases; all other data recorded in this table are for the hydrochlorides.

|    | Total chlorine, % |       | Sulfur, % |       | Ionizable chlorine, % |       |
|----|-------------------|-------|-----------|-------|-----------------------|-------|
|    | Calcd.            | Found | Calcd.    | Found | Calcd.                | Found |
| 1  | 15.31             | 15.33 | 13.84     | 13.56 | ...                   | ...   |
| 2  | 14.43             | 14.27 | 13.05     | 11.99 | 14.43                 | 14.16 |
| 3  | 13.65             | 14.14 | 12.35     | 11.40 | 13.65                 | 13.90 |
| 4  | 12.95             | 13.20 | 11.71     | 11.62 | 12.95                 | 13.21 |
| 5  | 12.68             | 12.73 | 11.47     | 11.54 | 12.68                 | 12.88 |
| 6  | 14.43             | 14.50 | 13.05     | 14.50 | 14.43                 | 13.57 |
| 7  | 14.43             | 14.08 | 13.05     | 12.71 | ...                   | ...   |
| 8  | 17.59             | 17.85 | 15.90     | 15.71 | ...                   | ...   |
| 9  | ...               | ...   | 7.99      | 8.04  | 17.68                 | 17.72 |
| 10 | 17.50             | 17.67 | 15.82     | 15.66 | 17.50                 | 17.77 |
| 11 | 26.85             | 27.13 | 12.14     | 11.97 | 13.43                 | 13.31 |
| 12 | 35.63             | 34.47 | 10.74     | 10.24 | 11.88                 | 12.06 |

sulfides examined. After refluxing for ten hours, approximately 25% of the sulfide was recovered unchanged. The condensation product was also unstable on distillation in vacuum at 11.5 mm.

Of the di-halogen substituted sulfides examined, bis-( $\beta$ -chloroethyl) disulfide reacted most readily with benzylamine. The crude amino derivative was obtained in good yield after refluxing for four hours on the steam-bath, but readily decomposed on distillation in vacuum at 13 mm. Bis-(chloromethyl) and bis-( $\beta$ -chloropropyl) sulfides were less reactive, requiring ten-hour reaction periods. Of the corresponding amino derivatives, the former was obtained in 70.5% yield based on the once distilled product; the latter was unstable when purification was attempted in vacuum at 13 mm. The unsaturated sulfides failed to condense with benzylamine to any appreciable extent after refluxing for thirty hours on the steam-bath at atmospheric pressure. A condensation was effected, however, by conducting the reaction under pressure for five hours at 110°. The crude products were quite impure as evidenced by the difficulty experienced in preparing their hydrochlorides. The free bases decomposed completely on attempting to distil in a vacuum at 8 mm.

### Discussion

The data obtained from these reactions may be regarded as further substantiating the condensation theory of vesicant action, but they entirely eliminate thiazane formation as an important factor and appear to demand a new limitation, that of a reactive halogen on the beta carbon atom. That the formation of ring compounds of the thiazane type is not essential is demonstrated by the reaction of mono-halogen substituted alkyl sulfides and of bis-( $\beta$ -chloropropyl) sulfide with benzylamine to form open-chain derivatives. The limitation to a reactive halogen attached to the beta carbon atom appears necessary in view of the condensation of both bis-(chloromethyl) sulfide and of ethyl  $\gamma$ -chloropropyl sulfide with benzylamine. Neither of these compounds is vesicant, yet both undergo reaction with amino compounds of the type of benzylamine.

The author is exceedingly grateful to Dr. Walter E. Lawson, who offered much valuable assistance during the course of this work.

### Summary

1. The preparation of ethyl allyl sulfide and fifteen halogen substituted aryl, alkyl and di-alkyl sulfides is described, three of which have not previously been recorded in the literature.
2. The viscosity and the density of each have been determined.
3. The preparation of a new series of benzylaminoaryl, alkyl and di-alkyl sulfides together with their hydrochlorides is described.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE STATE UNIVERSITY OF IOWA]

## The Reaction of Monobromoamine with Grignard Reagents

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Previous work in this Laboratory has shown that monochloroamine reacts with Grignard reagents to form primary amines and ammonia.<sup>1</sup>

The present investigation was prompted by the thought that monobromoamine should undergo a reaction with Grignard reagents similar to that of monochloroamine and that a comparison of the results obtained in the two cases would be of interest.

Monobromoamine has been prepared by Moldenhauer and Burger<sup>2</sup> by the reaction of ammonia with bromine in ether solution at 0°. The reaction is represented by the equation



(1) Coleman and Hauser, *THIS JOURNAL*, **50**, 1193 (1928); Coleman and Yager, *ibid.*, **51**, 567 (1929).

(2) Moldenhauer and Burger, *Ber.*, **62**, 1615 (1929).