β,β'-DICHLOROETHYL SULFIDE (MUSTARD GAS)

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I. HISTORY AND PREPARATION

The term "mustard gas," by which β,β'-dichloroethyl sulfide, or bis(β-chloroethyl) sulfide, is most generally known, is an unfortunate one. By this name the most important chemical warfare agent is often confused with the true natural mustard oil which is prepared from black mustard seed and is chemically allyl isothiocyanate, having the following formula, $CH_2:CHCH_2 \cdot N:C:S$. From a purely physical standpoint the classification "mustard gas" is also a misnomer, as the substance under ordinary conditions is a heavy oily liquid.

The early history of bis(β-chloroethyl) sulfide is somewhat involved. The formation of a disagreeable smelling fluid by the action of ethylene upon chloride of sulfur had been observed by Despretz in 1822 (19), though its vesicant action was not noted. Thirty-seven years later Niemann (54) obtained a product by the action of ethylene upon "brown" chloride of sulfur (a mixture of sulfur monochloride and dichloride), which he found to be very toxic: "The most characteristic property of this oil is also a very dangerous one. It consists in the fact that the minutest traces which may accidentally come in contact with any portion of the skin, though at first causing no pain, produce in the course of a few hours a reddening and, on the following day, a severe blister, which suppurates for a long time and is very difficult to heal. Great care is therefore requisite in working with this compound." This product, for which the characteristics of "mustard gas" are so clearly set forth was, according to Niemann's analysis, the disulfide. It is thought that Guthrie in his examination of the action of chloride of sulfur upon ethylene (24) actually possessed some bis(β-chloroethyl) sulfide, for he says: "Its smell is pungent and not unpleasant, resembling that of oil of mustard; its taste is astringent and similar to that of horse-radish. The small quantities of vapor which it diffuses attack the thin parts of the skin, as between the fingers and around the eyes, destroying the epidermis. If allowed to remain in the liquid form on the skin, it raises a blister." Despite the fact that he ascribed to his product the composition of a disulfide and regarded it as different from the product of the reaction of ethylene with sulfur dichloride, his description of the compound as a pale yellow liquid of sp. gr. 1.346 at 19°C. and as highly toxic leaves no doubt but that he actually had some of the compound in hand.

V. Meyer (50) prepared bis(β-chloroethyl) sulfide by allowing ethylene chlorohydrin to react with aqueous potassium sulfide and treating the resulting thiodiglycol with phosphorus trichloride:

$$K_2S + 2CH_2ClCH_2OH \rightarrow S(CH_2CH_2OH)_2 \xrightarrow{PCl_3} S(CH_2CH_2Cl)_2$$

Clarke (13) improved the method by treating the intermediate, thiodiglycol, with concentrated hydrochloric acid on a water bath instead of with phosphorus trichloride, and Gomberg (22), in his studies, found that considerably less of the alkali sulfide could be used and that instead of 80 to 100 per cent of ethylene chlorohydrin a solution of 20 per cent gave as good results.

Gibson and Pope (21) prepared bis(β-chloroethyl) sulfide by the direct addition of ethylene to sulfur dichloride, in accordance with the following equation:

$$2CH_2{:}CH_2 + SCl_2 \rightarrow S(CH_2CH_2Cl)_2$$

The ethylene, freed from alcohol vapor and thoroughly dried, is passed through the agitated sulfur dichloride, maintained at 40–45°C., at such a rate that some escapes unabsorbed. The ethylene is rapidly absorbed from the beginning, and the absorption ceases fairly suddenly when the reaction ends. This method was described in a report to the Chemical Warfare Service under date of January 16, 1918. It gives a better yield and is more expeditious than the method described by V. Meyer and improved by Clarke and Gomberg, which consists in converting (a) ethylene into ethylene chlorohydrin, (b) ethylene chlorohydrin into thiodiglycol by treatment with sodium sulfide, and (c) thiodiglycol into bis(β-chloroethyl) sulfide by the action of hydrochloric acid, as shown in the following equations:

$$\begin{aligned}&(a)\ CH_2{:}CH_2 + HOCl \rightarrow CH_2ClCH_2OH\\&(b)\ 2CH_2ClCH_2OH + Na_2S \rightarrow S(CH_2CH_2OH)_2 + 2NaCl\\&(c)\ S(CH_2CH_2OH)_2 + 2HCl \rightarrow S(CH_2CH_2Cl)_2 + 2H_2O\end{aligned}$$

At the same time, the sulfur dichloride method is difficult to control, because bis(β-chloroethyl) sulfide is acted on rapidly by sulfur dichloride; it is consequently necessary to work under such conditions that little or no sulfur dichloride remains long in contact with the bis(β-chloroethyl) sulfide produced.

Later it was found that by using the monochloride and keeping the temperature between 20°C. and 70°C. the yield of pure bis(β-chloroethyl) sulfide varied between 90 and 98 per cent of that theoretically possible from the sulfur chloride:

$$2CH_2{:}CH_2 + S_2Cl_2 \rightarrow S(CH_2CH_2Cl)_2 + S$$

The day previous to the receipt of a cable from England to the effect that Gibson and Pope had successfully carried out the reaction, this experiment was started by Conant. The sulfur remaining after the distillation retained a mere trace of resinous matter, and no product other than bis(β-chloroethyl) sulfide distilled. The reaction between ethylene and sulfur monochloride is accelerated by rise of temperature, absorption being about three times as rapid at 60°C. as at 30°C.

In place of the simple equation,

$$(1)\ 2CH_2{:}CH_2 + S_2Cl_2 \rightarrow S(CH_2CH_2Cl)_2 + S$$

by which Gibson and Pope represented the reaction between ethylene and sulfur monochloride, Conant, Hartshorn, and Richardson (14) substituted the following:

$$\begin{aligned}&(a)\ S_2Cl_2 \rightleftharpoons S + SCl_2\\&(b)\ CH_2{:}CH_2 + SCl_2 \rightarrow CH_2ClCH_2SCl\\&(c)\ CH_2{:}CH_2 + CH_2ClCH_2SCl \rightarrow S(CH_2CH_2Cl)_2\end{aligned}$$

and a side reaction,

$$(d)\ 2CH_2ClCH_2SCl + xS \rightarrow (ClCH_2CH_2)_2S_x + S_2Cl_2$$

They found evidence favoring their view in determinations of the depression of the freezing point of bis(β-chloroethyl) sulfide by partly ethylerated sulfur monochloride, and concluded that reaction b is dominant until one molecule of ethylene has been absorbed for each one of sulfur monochloride originally present.

Others who prepared bis(β-chloroethyl) sulfide by the same procedure obtained yields of only about 80 per cent. Mann, Pope, and Vernon (46) explained the discrepancy as follows: *when pure ethylene is absorbed by highly purified sulfur monochloride at 60°C., the yield is in the neighborhood of 80 per cent of the theoretical, but when the ethylene carries a small amount of alcohol vapor the yield rises to 99 per cent of the theory.* Insufficient scrubbing of the ethylene, prepared from alcohol, was thus responsible for the high yields.

Steinkopf, Herold, and Stahr (60) prepared bis(β-chloroethyl) sulfide by allowing a chloroform solution of thiodiglycol to stand for one hour with thionyl chloride dissolved in chloroform; after fractionating, a colorless product boiling at 108–109°C. at 15 mm. and melting at 10–12°C. was obtained.

$$S(CH_2CH_2OH)_2 + SOCl_2 \rightarrow S(CH_2CH_2Cl)_2 + SO_2 + H_2O$$

Myers and Stephen (53) obtained bis(β-chloroethyl) sulfide rapidly and continuously by spraying a mixture of 75 per cent sulfur dichloride and 25 per cent of the monochloride into an atmosphere of ethylene. By such a procedure further chlorination was avoided and the yield of bis(β-chloroethyl) sulfide, melting at 8°C., was 93 per cent.

TABLE 1

Variation in density and thermal expansion of bis(β-chloroethyl) sulfide

TEMPERATURE	DENSITY	VOLUME
degrees C.		*cc.*
15	1.2790	1.00000
20	1.2741	1.00324
25	1.2686	1.00824
30	1.2635	1.01226
35	1.2584	1.01642
40	1.2531	1.02067
45	1.2479	1.02497
50	1.2426	1.02901
55	1.2373	1.03372
60	1.2318	1.03830
65	1.2263	1.04295
70	1.2210	1.04747
75	1.2158	1.05193
80	1.2106	1.05648
85	1.2051	1.06133
88	1.2015	1.06452
90	1.1996	1.06614

II. PHYSICAL PROPERTIES

1. *Solubility in water; boiling point; melting point*

Pure bis(β-chloroethyl) sulfide is a colorless, neutral to litmus, almost odorless oil; however, Clarke (13) described it as smelling not unlike α,ε-dichloropentane but far more unpleasant. It is almost insoluble in water, its solubility being 0.07 per cent at 10°C. (33), and 0.0043 moles per liter at 25°C. (68). Its boiling point has been reported as 97°C. at 10 mm. (30), 98°C. at 10 mm. (13), 104–105°C. at 13 mm. (40), 105°C. at 15 mm. (30), 107°C. at 15 mm. (51), 108–109°C. at 15 mm. (60), 120°C. at 34 mm., and 122.5°C. at 37 mm. At atmospheric pressure it decomposes at its boiling point, 217°C. (16). When poured into cold water it rapidly solidifies in long colorless needles which melt over a range of several degrees, as determined by a number of observers: 8°C. (53), 10–12°C. (60), 13.5°C. (16, 67), 13.6°C. (61, 62), 13.82°C. (66), 14.4°C. (51).

2. Density and thermal expansion

Wilkinson and Wernlund (67) found by the use of a dilatometer tube the variation in density of bis(β-chloroethyl) sulfide (m.p., 13.5°C.) and also the thermal expansion as shown in table 1. The variation in density per degree between 15°C. and 90°C. is 0.001058. The variation in volume of 1 gram per degree between the same temperature is 0.0006895 cc. The variation in volume in cubic centimeters per degree is 0.000881 cc.

TABLE 2

Pressures produced by the action of sulfur monochloride on bis(β-chloroethyl) sulfide

TIME	PRESSURE PER 100 G. OF BIS(β-CHLOROETHYL) SULFIDE		
	a	b	c
hours	*mm.*	*mm.*	*mm.*
0	0	0	0
16	64.5	273	328
19	71.8	312	368
22		336	409
25	95.4		
40	115.6	502	636
46	132.8	570	738
70	170.0		
72		791	944
89			944
96	170.0	753	924
136	160.0		
144		609	716
187	160.0	570	656

The curves for the variation in density and thermal expansion of bis(β-chloroethyl) sulfide are both straight lines.

3. Pressure produced by the action of sulfur monochloride on bis(β-chloroethyl) sulfide

Thompson and Kopp (62) determined the pressures produced by the action of relatively small concentrations of sulfur monochloride upon bis(β-chloroethyl) sulfide. Column a of table 2 shows the data resulting from a mixture of 64 g. of the sulfide with 0.64 g. of sulfur monochloride (99:1 per cent); column b the data from a mixture of 41.1 g. of the sulfide with 1.37 g.

of the monochloride (96.78:3.22 per cent); column c shows the data from 49.4 g. of the sulfide with 2.47 g. of the monochloride (95.24:4.76 per cent).

The tables show that a maximum pressure is reached in approximately seventy-two hours, after which time a steady decrease is noted. When the apparatus was disconnected small amounts of hydrogen chloride and hydrogen sulfide were detected in the gases liberated by the action of the monochloride on the sulfide. Owing to the solubility of hydrogen chloride in the latter substance, the increases in pressures shown in table 2 and the accompanying plot, figure 1, do not actually represent the total gases produced.

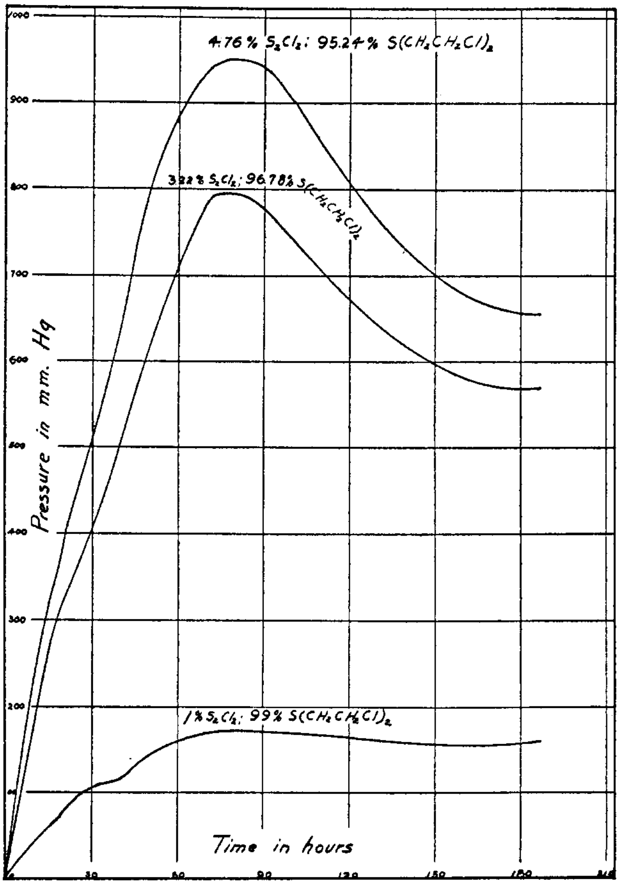


FIG. 1. PRESSURES PRODUCED BY ACTION OF SULFUR MONOCHLORIDE ON BIS(β-CHLOROETHYL) SULFIDE

A secondary reaction takes place between the substances and the gases, as indicated by a decrease in pressure at the end of three days.

4. The intersolubility of bis(β-chloroethyl) sulfide and various solvents

The solubility of bis(β-chloroethyl) sulfide in petroleum hydrocarbons was determined by Thompson and Odeen (63). The data obtained at various temperatures are given in tables 3, 4, 5, and 6 and illustrated by curves in figure 2.

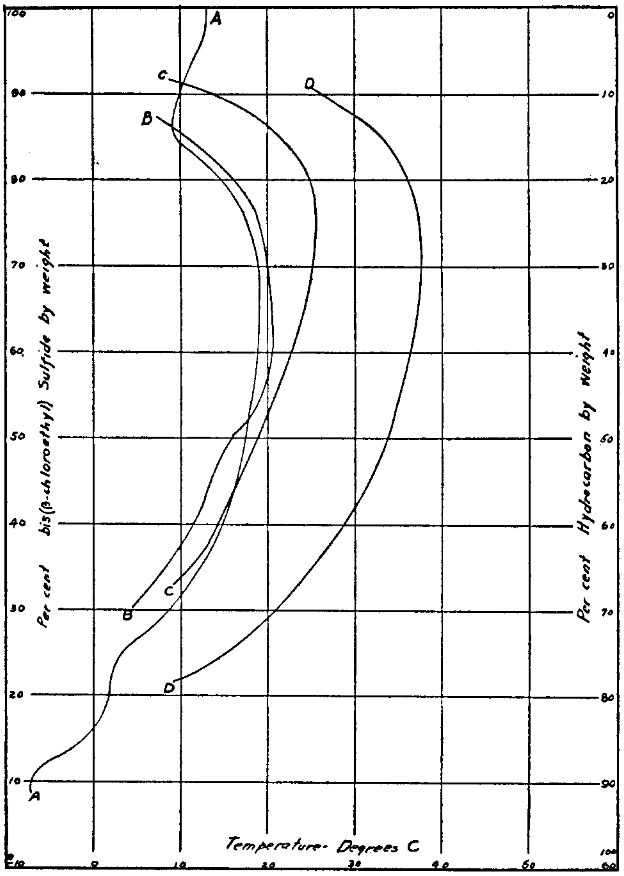


FIG. 2. INTERSOLUBILITY OF BIS(β-CHLOROETHYL) SULFIDE AND HYDROCARBON SOLVENTS

Table 3 shows results obtained from a study of the intersolubility of bis(β-chloroethyl) sulfide and ligroin (b.p. less than 100°C.) at various temperatures and illustrated by the curve AA in figure 2. The critical point of solubility, that is, the temperature above which the two substances would be mutually soluble in all proportions, was found to be 19°C.; the highest temperature at which solid bis(β-chloroethyl) sulfide could exist in the presence of its liquid phase and a ligroin solution of it was 8.8°C.

The critical temperature of solubility of bis(β-chloroethyl) in gasoline (b.p. 60–180°C.) was found to be 20.4°C. The data from their intersolubility is given in table 4 and illustrated by curve BB in figure 2.

Table 5 shows the results secured from a study of the mutual solubilities of bis(β-chloroethyl) sulfide and kerosene (b.p. 160–260°C.) at various temperatures. These determinations indicate that the critical point of solubility of the sulfide and kerosene is 25.6°C. These data are illustrated in figure 2 by curve CC.

TABLE 3

Intersolubility of bis(β-chloroethyl) sulfide and ligroin

TEMPERATURE	LIGROIN		BIS(β-CHLOROETHYL) SULFIDE		SOLUBILITY	
					Ligroin	Bis(β-chloroethyl) sulfide
°C.	*cc.*	*grams*	*cc.*	*grams*	*per cent by weight*	*per cent by weight*
13.0	0	0.00	20	25.44		100.00
13.0	1	0.67	20	25.44	2.6	97.4
12.0	2	1.34	20	25.44	4.9	95.1
10.0	4	2.67	20	25.44	9.5	90.5
9.5	5	3.34	20	25.44	11.6	88.4
9.0	6	4.00	20	25.44	13.6	86.4
9.6	7	4.67	20	25.44	15.5	84.5
12.0	8	5.34	20	25.44	17.4	82.6
14.0	9	6.00	20	25.44	19.1	80.9
17.22	12	8.01	20	25.44	23.9	76.1
19.0	19	12.69	20	25.44	33.3	66.7
19.0	24	16.03	20	25.44	38.6	61.4
18.3	29	19.36	20	25.44	43.2	56.8
17.5	39	26.04	20	25.44	50.6	49.4
16.0	49	32.72	20	25.44	56.3	43.7
14.5	59	39.39	20	25.44	60.7	39.3
10.3	79	52.75	20	25.44	67.5	32.5
6.5	99	66.10	20	25.44	72.2	27.8
2.5	119	79.46	20	25.44	75.8	24.2
0.2	30	20.03	3	3.82	83.9	16.1
−2.5	30	20.03	2.5	3.18	86.3	13.7
−6.5	30	20.03	2	2.54	88.7	11.3
−7.5	30	20.03	1.5	1.91	91.3	8.7

The results secured in experiments on the intersolubility of bis(β-chloroethyl) sulfide and railroad light oil (b.p. 140–315°C.) are shown in table 6 and illustrated by the curve DD in figure 2. The critical point of solubility was found to be 37°C.

From these results it is evident that with the increase in the percentage of high boiling hydrocarbons, the critical temperature of solubility for these solvents and bis(β-chloroethyl) sulfide will also increase. This is very nicely illustrated by a comparison of the solubility curves as shown in figure 2.

TABLE 4

The intersolubility of bis(β-chloroethyl) sulfide and gasoline

TEMPERATURE	BIS(β-CHLOROETHYL) SULFIDE		GASOLINE		SOLUBILITY	
					Bis(β-chloroethyl) sulfide	Gasoline
°C.	*cc.*	*grams*	*cc.*	*grams*	*per cent by weight*	*per cent by weight*
7.3	20.05	25.43	5.00	3.686	87.34	12.66
18.0	20.05	25.43	10.00	7.371	77.53	22.47
20.4	20.05	25.43	17.75	13.095	66.02	33.98
18.7	20.05	25.43	30.00	22.113	53.49	46.51
14.0	20.05	25.43	40.00	29.484	46.32	53.68
9.5	20.05	25.43	60.00	44.226	36.51	63.49
4.5	20.05	25.43	80.00	58.968	30.14	69.86
7.8	15.00	19.03	3.80	2.801	87.17	12.83
13.5	15.00	19.03	30.05	22.150	46.21	53.79
9.0	15.00	19.03	45.00	33.170	36.46	63.54
4.2	15.00	19.03	60.00	44.226	30.08	69.92

TABLE 5

The mutual solubilities of bis(β-chloroethyl) sulfide and kerosene

TEMPERATURE	KEROSENE		BIS(β-CHLOROETHYL) SULFIDE		SOLUBILITY	
					Kerosene	Bis(β-chloroethyl sulfide
°C.	*cc.*	*grams*	*cc.*	*grams*	*per cent by weight*	*per cent by weight*
14.2	60	48.24	25	31.88	60.21	39.79
9.5	80	64.32	25	31.88	66.87	33.13
21.9	7	5.63	25	31.88	15.07	84.93
24.3	9	7.23	25	31.88	18.58	81.42
25.6	12	9.65	25	31.88	23.33	76.67
25.6	13	10.45	25	31.88	24.79	75.21
25.6	14	11.26	25	31.88	26.20	73.80
25.0	18	14.47	25	31.72	31.33	68.67
14.3	6	4.82	33	41.88	10.32	89.68
8.9	6	4.82	43	54.47	8.12	91.88

Thompson, Black, and Sohl (61) determined the intersolubility of bis(β-chloroethyl) sulfide (double-distilled at 13–14 mm. and melting at 13.6°C.) and ethyl alcohol. The solubilities of the alcohol and the sulfide were determined by heating the two substances together in the proportions given in the table until a clear solution was produced. The temperatures at these points were noted. Upon cooling the solution very slowly a characteristic cloudiness appeared, resulting from the formation of two liquid phases. The temperatures at which the cloudiness first appeared were noted. The mutual solubilities of the sulfide and 92.5 per cent alcohol are given in table 7 and the solubilities of the sulfide and absolute alcohol are given in table 8, the data from each being illustrated by the solubility curves in figure 3. The temperature given in the tables, in each case, is the mean obtained from the temperature at which the solution cleared and that at which the cloudiness was produced. Above the curves in figure 3 a homogeneous system exists and below the curves there is a heterogeneous system of the two liquid phases.

TABLE 6

The intersolubility of bis(β-chloroethyl) sulfide and railroad light oil

TEMPERATURE	RAILROAD LIGHT OIL		BIS(β-CHLOROETHYL) SULFIDE		SOLUBILITY	
					Railroad light oil	Bis(β-chloroethyl) sulfide
°C.	*cc.*	*grams*	*cc.*	*grams*	*per cent by weight*	*per cent by weight*
25.0	2.45	1.926	14.95	18.966	9.22	90.78
28.0	5.12	4.024	25.00	31.715	11.26	88.74
31.3	3.74	2.940	14.95	18.966	13.42	86.58
37.0	13.69	10.760	14.95	18.966	36.20	63.80
35.0	20.19	15.869	14.95	18.966	45.52	54.48
33.0	26.19	20.585	14.95	18.966	52.05	47.95
23.6	38.57	30.316	14.95	18.966	61.51	38.49
20.9	56.62	44.503	14.95	18.966	70.12	29.88
14.5	75.07	59.005	14.95	18.966	75.67	24.33
9.3	87.42	68.692	14.95	18.966	78.36	21.64

The effect of water upon the critical point of solubility is very decided. With 92.5 per cent alcohol a critical temperature of solubility of 38.6°C. was secured, but with absolute alcohol the critical temperature was 15.6°C.

5. *Freezing point constant; vapor pressure; heat of combustion; refractive index*

Delépine, Fleury, and Ville (18) determined the freezing point constant, K, of bis(β-chloroethyl) sulfide. Raoult's law gives $K = 60 - 2$, but this value diminishes very rapidly with moderate increases of the concentration. When Louguinine and DuPont's modified formula (42), $dt = Kn/(n + N)$ is applied, better agreement is realized and $K = 38$.

Herbst reports the measurements, by an air-saturation method, of the vapor pressure of an impure specimen of bis(β-chloroethyl) sulfide (m.p. 12.85°C.) at 22°C. and 39°C. as 0.087 and 0.358, respectively. Apart from this, there appears to be no record of the determination of the vapor pressure of this substance at ordinary temperatures until a study was made by Mumford, Phillips, and Ball (52), though a number of values are quoted in the literature. These, however, are very discordant, ranging from 0.01 mm. (55) to 0.051 mm. (34) at 10°C., and from 0.06 mm. (55) to 0.11 mm. (64) at 20°C.

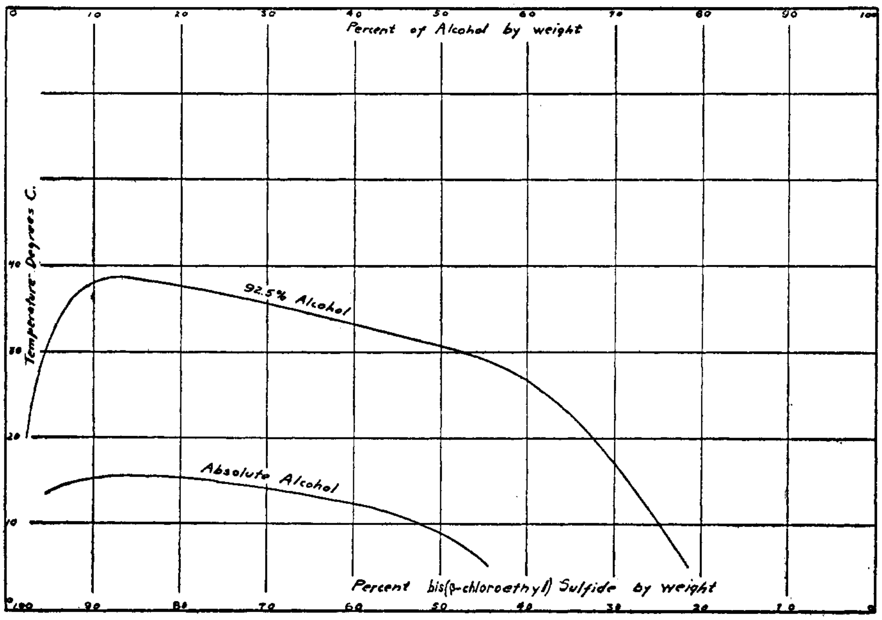


FIG. 3. INTERSOLUBILITY OF ALCOHOL AND BIS(β-CHLOROETHYL) SULFIDE

The results of the vapor pressure determinations, represented by the equation,

$$\log_{10} p = 8.3937 - 2734.5/T$$

are given in table 9 and illustrated by graph in figure 4.

The heat of combustion of liquid bis(β-chloroethyl) sulfide in the calorimetric bomb was determined as 743.3 Calories at constant volume by Heycock and Mills (31). They also determined its heat of formation from rhombic sulfur, amorphous carbon, and gaseous hydrogen and chlorine as 67.9 Calories.

Refractive indices were determined by Palmer (56) as 1.52776 for H_c, 1.53125 for Na_D, and 1.53999 for H_F at 15°C. The molecular depression of the freezing point by benzene was determined as 54.6; the latent heat of fusion is hence calculated as about 30 Calories.

6. Surface tension determinations

Harkins and Ewing (26) made the surface tension determinations between bis(β-chloroethyl) sulfide and various aqueous solutions by the drop-weight method, using the proper precautions as determined by Harkins and Brown (25). The radius of the tip used was 0.24995 cm. for all the interfacial work, except when a 0.1 per cent solution of turkey-red oil was used in the absence of sodium hydroxide, when the radius was 0.275 cm. For bis(β-chloroethyl) sulfide alone a tip of 0.27441 cm. radius was used.

TABLE 7

Mutual solubility of bis(β-chloroethyl) sulfide and 92.5 per cent alcohol

TEMPERATURE	BIS(β-CHLOROETHYL) SULFIDE	92.5 PER CENT ALCOHOL	SOLUBILITY	
			Bis(β-chloroethyl) sulfide	92.5 per cent alcohol
°C.	*grams*	*grams*	*per cent by weight*	*per cent by weight*
19.9	31.97	0.81	97.53	2.47
30.9	31.97	1.62	95.18	4.82
35.7	31.97	2.43	92.93	7.07
37.8	31.97	3.24	90.80	9.20
38.4	31.97	4.05	88.75	11.25
38.5	31.97	4.86	86.80	13.20
38.6	31.97	5.67	84.93	15.07
37.9	31.97	7.29	81.42	18.58
37.6	31.97	8.91	78.20	21.80
36.7	31.97	10.53	75.22	24.76
35.8	31.97	12.15	72.45	27.55
35.2	31.97	14.58	68.67	31.33
34.4	31.97	17.02	65.27	34.73
33.6	31.97	19.45	62.18	37.82
33.0	31.97	21.88	59.37	40.63
32.5	31.97	24.31	56.76	43.24
31.0	31.97	26.74	54.45	45.55
31.4	31.97	29.17	52.29	47.71
30.6	31.97	32.42	49.66	50.34
29.9	28.13	32.42	46.47	53.53
28.3	24.30	32.42	42.84	57.16
25.6	20.46	32.42	38.70	61.30
21.7	16.62	32.42	33.91	66.09
17.6	14.06	32.42	30.26	69.74
12.8	11.51	32.42	26.20	73.80
5.1	8.95	32.42	21.64	78.36

The density of this latter liquid was 1.2732 g. per cubic centimeter. In all of the experiments the aqueous solution was dropped upward through this liquid without allowing time for mixing. The values for r/a and $r/v^{\frac{1}{3}}$ indicate the shape of the drop (25).

TABLE 8

Mutual solubility of bis(β-chloroethyl) sulfide and absolute alcohol

TEMPERATURE	BIS(β-CHLOROETHYL) SULFIDE	ABSOLUTE ALCOHOL	SOLUBILITY	
			Bis(β-chloroethyl) sulfide	Absolute alcohol
°C.	*grams*	*grams*	*per cent by weight*	*per cent by weight*
13.6	31.9	1.57	95.31	4.69
14.5	31.9	2.35	93.13	6.87
14.8	31.9	3.14	91.04	8.96
15.3	31.9	4.71	87.13	12.87
15.6	31.9	6.48	83.12	16.88
15.5	31.9	7.85	80.25	19.75
14.8	31.9	10.20	75.76	24.24
14.2	31.9	12.56	71.75	28.25
13.6	31.9	15.70	67.00	33.00
12.2	31.9	19.62	61.91	38.09
11.8	31.9	23.55	57.52	42.48
10.6	31.9	27.47	53.73	46.27
9.1	31.9	31.40	50.39	49.61
7.5	31.9	35.32	47.45	52.55
5.6	31.9	39.25	44.83	55.17

TABLE 9

Experimental vapor pressure of bis(β-chloroethyl) sulfide

TEMPERATURE	MEAN PRESSURE	MAXIMUM DEVIATION FROM MEAN, ±	VAPOR PRESSURE (CALCULATED)
°C.	*mm.*		
0	0.035	0.007	0.024
10	0.055	0.005	0.054
15	0.075	0.008	0.079
20	0.115	0.007	0.115
30	0.225	0.025	0.230
40	0.450	0.050	0.450
50	0.830	0.100	0.850
60	1.550	0.150	1.520

The surface tension at 20°C. between bis(β-chloroethyl) sulfide and water is 28.36 dynes per centimeter, or about 5 dynes less than that between benzene and water. The surface tension of this liquid toward its vapor is

42.82 dynes per centimeter, which is 14 dynes higher than that of benzene. One of the most important characteristics of a liquid in this connection is the amount of work done when 1 sq. cm. of the surface of the liquid approaches 1 sq. cm. of a water surface. This value is 87.26 ergs in the case of bis(β-chloroethyl) sulfide, which indicates that this liquid, while only very slightly soluble in water, has a high attraction for it, although the magnitude of the work done is slightly less than that found for alcohol.

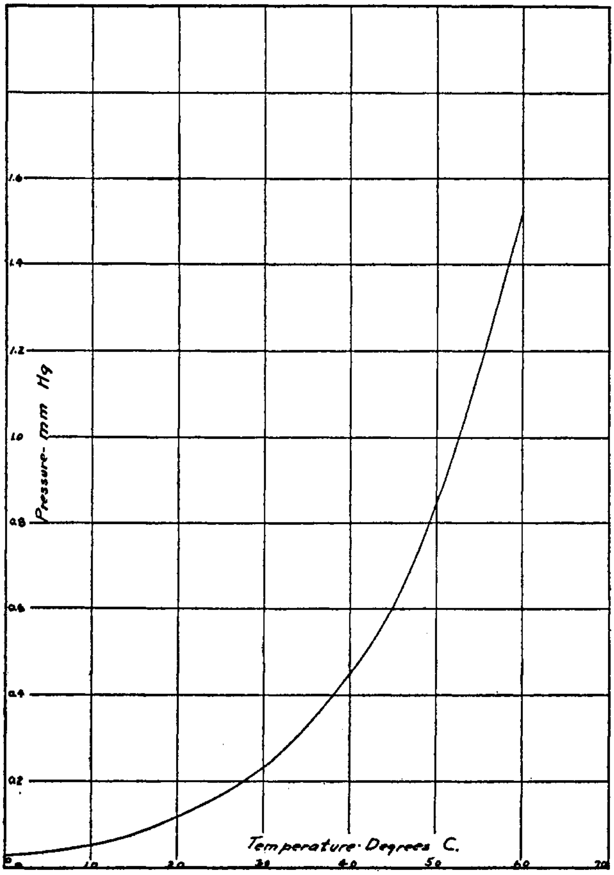


FIG. 4. VAPOR PRESSURE OF BIS(β-CHLOROETHYL) SULFIDE

7. *The compressibility of bis(β-chloroethyl) sulfide*

The compressibility of bis(β-chloroethyl) sulfide was determined by Adams and Williamson (2) after the method of Adams, Williamson, and Johnson (3). The sulfide was surrounded by kerosene in the interior of a thick-walled steel cylinder, one end being closed while the other was fitted with a piston and leak-proof packing. By means of a hydraulic press the piston was forced into the cylinder, thus subjecting the kerosene and the sulfide to hydrostatic pressure and thereby decreasing the volume of each.

TABLE 10

The surface tension between bis(β-chloroethyl) sulfide and various aqueous solutions

SUBSTANCE	VOLUME OF 1 DROP	DENSITY OF SUBSTANCE	r/a	SURFACE TENSION
	cc.			*degrees per cm.*
Vapor	0.03555		1.04	42.82
Water	0.10620	0.9982	0.595	28.36
0.1 *N* hydrochloric acid	0.10900	1.00011	0.5385	28.90
0.1 *N* sodium hydroxide	0.04612	1.0032	0.8066	12.78
0.1 *N* sodium carbonate	0.06950	1.0025	0.6635	18.82
1 per cent turkey-red oil	0.05670	1.0000	0.6070	14.47
1 per cent turkey-red oil in 0.1 *N* sodium carbonate	0.02977	1.0035	1.0000	8.35
			$r/v^{\frac{1}{3}}$	
1 per cent Twitchell's solution	0.04384	0.99924	0.7088	12.32
1 per cent Twitchell's solution in 0.1 *N* sodium carbonate	0.04663	1.00311	0.6944	12.89
1 per cent corn oil solution	0.45770	0.99840	0.6980	12.94
1 per cent corn oil solution in 0.1 *N* sodium carbonate	0.03936	1.00360	0.7350	10.91

TABLE 11

Decrease in volume of bis(β-chloroethyl) sulfide under pressure

PRESSURE	$-\Delta v/v_0$ (OBSERVED)		$-\Delta v/v_0$ (CALCULATED)
	1	2	
megabars			
392	0.0000	0.0000	0.0000
840	0.0175	0.0179	0.0177
1280	0.0327	0.0331	0.0326
1713	0.0447	0.0450	0.0450

The decrease in the volume of the sulfide for each increment of pressure was determined from a pair of readings of pressure and corresponding piston displacement. Pressures were measured by an electric method, the precision being such that one scale division was equal to about one megabar; the displacement of the piston was read on a dial micrometer which was graduated to 0.01 mm. Temperature regulation was obtained by an electric heating coil of asbestos-covered "nichrome" wire wrapped about the heavy steel cylinder and covered with an insulating layer of felt. About 10 g. of bis(β-chloroethyl) sulfide was contained in a steel capsule closed at the top and terminating in a capillary which dipped into a cup containing mercury. Pressure could thus be transmitted through the mercury seal to the interior of the capsule.

Table 11 shows the results for the decrease in volume at 31.5°C. of the bis(β-chloroethyl) sulfide; the second and third columns of the table give for two separate runs the value of $-\Delta v/v_0$, where Δv is reckoned from the initial pressure, $P_0 = 392$ megabars, and v_0 is the volume of the liquid at 31.5°C. and atmospheric pressure. The value of Δv as a function of P may be represented by a power series yielding the equation

$$\Delta v/v_0 = 4.24 \times 10^{-5}\,(P - P_0) - 6.3 \times 10^{-5}\,(P - P_0)^2$$

However, the results are expressed equally well by the exponential equation,

$$-\Delta v/v_0 = 0.118\,[I - e^{-0.364 \times 10^{-3}(P-P_0)}] \qquad (1)$$

which gives a more reasonable course to the compressibility curve and hence is to be preferred for extrapolating to zero pressure. In the third column are shown the values of $-\Delta v/v_0$ calculated from equation 1.

By differentiation this equation becomes

$$-\mathrm{d}v/\mathrm{d}P = 49.5e^{-0.364 \times 10^{-3} P} \qquad (2)$$

from which the compressibility ($-\mathrm{d}v/\mathrm{d}P$) at $P = 0$ was found to be 495×10^{-6} per megabar, while at 1000 and 2000 megabars, respectively, the compressibility is 34.4×10^{-6} and 23.9×10^{-6}.

8. *Freezing pressure; freezing point–solubility curve*

After the conclusion of the measurements of compressibility the freezing pressure and resultant change of volume at a few temperatures were determined; this could be done without removing the material from the apparatus. The desired quantities may be obtained from a series of readings, at constant temperature, of pressure P and piston-displacement R. When freezing or melting of the substance in the capsule takes place, P remains constant while R increases or decreases, and the resulting discontinuity at once locates the freezing pressure for the given temperature.

It was found that the necessary readings had to be taken with decreasing pressure since, on account of the propensity of liquids for undercooling to a temperature several degrees below their melting point, they will generally support a pressure far beyond the true freezing pressure before solidification takes place. Bis(β-chloroethyl) sulfide requires at ordinary temperatures about 1000 megabars superpressure to start it freezing, which corresponds to an undercooling of 14°C.

The results for the freezing points at several pressures are shown in table 12, which also gives the change of volume $V - V^s$ in cubic centimeters per gram. From these results it may be seen that the compressibility measurements of table 11 were extended by about 500 megabars into the region of undercooled liquid.

In order to test for the possible existence of other solid modifications of this substance, the pressure on it was increased to 12,000 megabars at 38°C., but no new forms were discovered.

TABLE 12

Results for freezing pressures, and change of volume on freezing

TEMPERATURE	FREEZING PRESSURE	$V_l - V_s$	dP/dT	ΔH (CALCULATED)
°C.	*megabars*	*cc. per gram*	*megabars per degree*	
13.9	1	(0.054)*	68	
21.9	570	0.050	71	25
29.6	1110			
31.4	1210	0.047	74	25
38.9	1800	0.042	77	25

* By extrapolation.

From the data contained in table 12 the latent heat of melting was calculated by the Clausius-Clapeyron equation. Thus

$$\Delta H = 0.02391T\ (V_l - V_s)\ dP/dT$$

where ΔH is the latent heat in calories per gram, T is the absolute temperature, $V_l - V_s$ is the change of volume on melting in cubic centimeters per gram, and dP/dT is the slope of the $P - T$ curve expressed in megabars per degree; practically it is the pressure in megabars required to raise the melting point one degree. Over the range of temperature covered by the measurements of Adams and Williamson it was found that ΔH = 25 calories per gram. This is a value which is higher than the latent heat of melting of most substances but, on the other hand, the compressibility and change of volume upon freezing do not differ markedly from the average for organic liquids.

Wilkinson, Neilson, and Wylde (66) in determining the freezing point solubility curve for bis(β-chloroethyl) sulfide used a product melting at 13.82°C., high-grade roll sulfur, and especially purified rhombic, monoclinic, and amorphous sulfur. These determinations were made by mixing equal amounts of the two substances in a test tube and heating slowly (2°C. per 5 minutes), noting the temperature at which the two phases become one, then cooling and observing the temperature at which the second phase appeared. These results are shown graphically in figure 5.

TABLE 13

Solubility of roll sulfur

SULFUR	NATURE OF THE SOLID PHASE AT GIVEN TEMPERATURE		
	Solid bis(β-chloroethyl) sulfide	Solid sulfur	Liquid phase
per cent	*°C.*	*°C.*	*°C.*
0.00	13.82		
0.10	13.79		
0.30	13.75		
0.70	13.70		
0.90	13.66		
1.48		24.0	
2.44		43.0	
3.38		54.0	
4.31		61.0	
6.10		74.0	
9.09		85.0	
16.66		99.0	
20.00		102.5	
25.18			110.0
31.00			120.0
32.00			122.0
35.00			127.0
40.00			133.5
60.00			143.5
78.00			135.0
85.00			124.0
87.00			117.0
90.00			105.0
94.00		108.0	
100.00		114.0	

Rhombic and monoclinic sulfur were found to have the same solubility, while amorphous sulfur had a solubility of less than 0.14 per cent below 120°C.; below 78°C. the solid phase which separated was rhombic sulfur, while above this temperature it was monoclinic.

Attempts to determine accurately the partition coefficient of bis(β-chloroethyl) sulfide have not been highly successful, owing to the rapidity with which it hydrolyzes, but using xylene and water at 20°C. Lynch, Smith, and Marshall (43) determined it as over 200.

III. CHEMICAL PROPERTIES

1. *Action with metals*

Aluminum, lead, brass, iron, bronze, zinc, and tin are not acted on by bis(β-chloroethyl) sulfide at ordinary temperatures; with the first three metals no appreciable action is noted at 100°C., but the others named are attacked at this temperature, the action being most rapid in the case of tin. Titanic and stannic chlorides yield additive compounds with the substance. Sulfur dichloride acts vigorously on bis(β-chloroethyl) sulfide at ordinary temperatures (21).

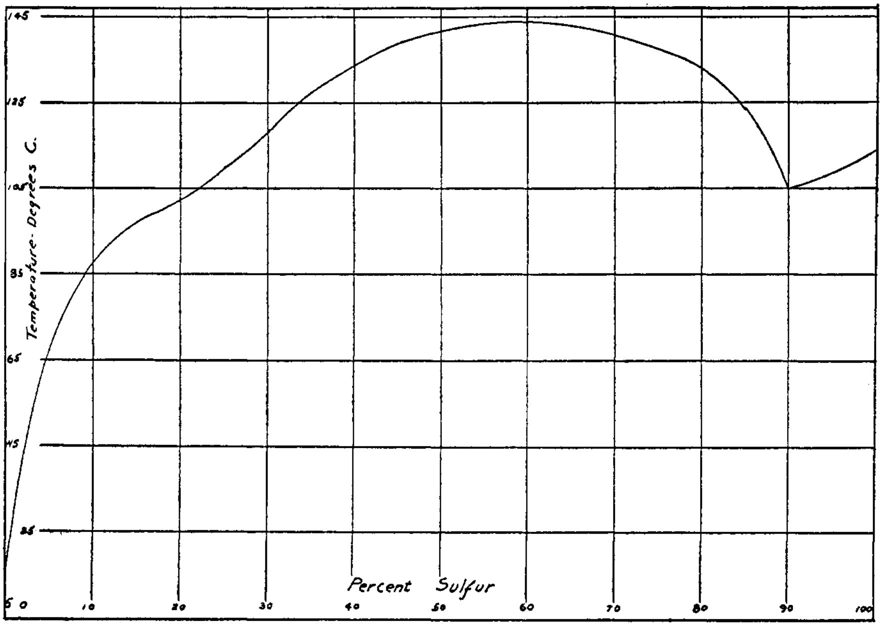


FIG. 5. SOLUBILITY-FREEZING POINT CURVE OF SULFUR IN BIS(β-CHLOROETHYL) SULFIDE

Kretov (36) investigated the interaction between bis(β-chloroethyl) sulfide and zinc dust and found it to be a complex reaction resulting in the formation of a large number of compounds. The sulfide is entirely decomposed with formation of ethylene, hydrogen sulfide, diethylene disulfide, zinc chloride, divinyl sulfide, diethyl sulfide, and ethyl vinyl sulfide. The decomposition is caused by metallic zinc and not by zinc oxide present as an impurity. The principal products of the reaction between bis(β-chloroethyl) sulfide and zinc in the presence of alcohol are esters of thiodiglycol of the general formula $S(CH_2CH_2OR)_2$, which are stable liquid compounds, capable of distillation under atmospheric pressure without decomposition.

2. Hydrolysis

It was generally assumed and later proved (57) that the hydrolysis of bis(β-chloroethyl) sulfide occurs in two stages:

$$S(CH_2CH_2Cl)_2 + HOH \rightarrow ClCH_2CH_2 \cdot S \cdot CH_2CH_2OH + HCl$$

$$ClCH_2CH_2 \cdot S \cdot CH_2CH_2OH + HOH \rightarrow S(CH_2CH_2OH)_2 + HCl$$

Wilson, Fuller, and Schur (68) showed that the hydrolysis of bis(β-chloroethyl) sulfide in contact with water is a two-stage reaction which affects only the molecules dissolved in the aqueous phase.

The rate of the first stage of the reaction determines that of the second. Once steady conditions are established, the concentration of the intermediate compound automatically increases or decreases, keeping the rate of the second stage just equal to that of the first. The amount of intermediate compound present at any time is extremely small, and the time required to build up the equilibrium concentration is generally negligible.

The simplest expression for the rate of hydrolysis at 25°C. in alkaline solutions, where there is no tendency toward reversal, is:

$$\mathrm{d}C/\mathrm{d}t = 2K_1 - (M) = 0.304\ (M)$$

where $\mathrm{d}C/\mathrm{d}t$ is the rate of hydrolysis in millimoles of hydrogen chloride produced per liter per minute and (M) is the concentration of bis(β-chloroethyl) sulfide in millimoles per liter.

The second stage of the hydrolysis reaction is substantially non-reversible except in very strong hydrochloric acid solutions. The first stage is, however, reversible to a considerable extent in the presence of even dilute acids. This reversibility of one stage serves to retard but not to stop the reaction, because the intermediate hydrolysis compound is being continually destroyed by the irreversible second stage.

The mathematical expression for the rate of hydrolysis in acid solutions is, therefore,

$$\mathrm{d}C/\mathrm{d}t = K_1(M) - k_1(I)(H^+)(Cl^-) + K_2^1(I)(H^+)$$

A simpler but less obviously rational form of this equation is:

$$\mathrm{d}C/\mathrm{d}t = 2k_1(M)/[1 + k_3(Cl^-)] = 0.304(M)/[1 + 6.14(Cl^-)]$$

This equation has been found to hold with satisfactory accuracy for a wide variety of acid solutions.

Helfrich and Reid (29) state that when bis(β-chloroethyl) sulfide is acted on with 20 per cent sodium ethoxide, the sodium hydroxide present hydrolyzes the sulfide with separation of sodium chloride from the alcohol solution, the reaction going for the most part according to the equation

$$S(CH_2CH_2Cl)_2 + 2NaOH \rightarrow S(CH_2CH_2OH)_2 + 2NaCl$$

However, another reaction takes place to some extent, forming an easily polymerizable liquid, which they surmised to be divinyl sulfide, thus:

$$S(CH_2CH_2Cl)_2 + 2NaOEt \rightarrow S(CH{:}CH_2)_2 + 2NaCl + 2EtOH$$

This was later confirmed by Bales and Nickelson (5).

Bales and Nickelson (6) increased the 26 per cent yield of divinyl sulfide by distilling bis(β-chloroethyl) sulfide with 20 per cent potassium hydroxide without previous heating under reflux. Hydrolysis with alcoholic potassium hydroxide containing water causes the product to increase in density as the proportion of water increases, until, when the alcohol contains 20 per cent water, the hydrolysis product has a density greater than that of water. The yield is almost constant up to this concentration of water, but with higher concentration the yields are smaller and the product more dense as shown in table 14. With alcoholic sodium ethoxide, the yield was 36 per cent.

TABLE 14

Hydrolysis of bis(β-chloroethyl) sulfide with 20 per cent potassium hydroxide in alcohol-water mixtures

WATER	YIELD	DENSITY
per cent	*per cent**	
5	35.0	0.931
15	33.5	0.941
17	33.6	0.960
20	33.5	1.014
24	21.0	1.034
43	16.0	1.050

* The percentage of the product of hydrolysis calculated on the weight of bis(β-chloroethyl) sulfide taken.

When the product obtained by the hydrolysis of bis(β-chloroethyl) sulfide with 20 per cent potassium hydroxide in 80:20 or 57:43 alcohol-water was heated and carefully purified, a clear, colorless liquid boiling at 152–154°C., $d_{4^\circ}^{15^\circ} = 1.110$, was obtained. This liquid, which contained chlorine and which regenerated bis(β-chloroethyl) sulfide on treatment with phosphorus trichloride, was thought to be β-chloro-β′-hydroxydiethyl sulfide, $ClCH_2CH_2 \cdot S \cdot CH_2CH_2OH$; this was later confirmed by Peters and Walker (57).

Boulin and Simon (9) found that when 1 part of the sulfide was dissolved in 200 parts of water, the ratio of the length of time for complete hydrolysis at 20°, 50°, and 100°C. is 1:7.5:30. A longer time is required if less water is used. The sulfide decomposes and distils with the water vapor at 100°C. Acids and ammonium hydroxide (1 mole per liter) slightly retard the decomposition; 100 cc. of water containing 100 millimoles of potassium hydroxide per liter decomposed 7.5 millimoles of the sulfide in 50 hours at 50°C.; 3 hours suffice in the absence of the hydroxide, the retardation being due to the potassium chloride formed.

Kramer (35) has shown that when bis(β-chloroethyl) sulfide is shaken with a 1 per cent solution of sodium silicate, after the elapse of two hours each drop of the sulfide is surrounded by a sheath of colloidal silicic acid, and in 48 hours the whole tube is filled with colloidal silicic acid gel. The sulfide is hydrolyzed to dihydroxydiethyl sulfide, and the hydrogen chloride set free liberates colloidal silicic acid.

Davies and Oxford (17) hydrolyzed bis(β-chloroethyl) sulfide with 4 moles of 20 per cent potassium hydroxide in alcohol-water and obtained therefrom several compounds: divinyl sulfide, $S(CH:CH_2)_2$, boiling at 85°C., a colorless, highly refractive, mobile oil; β-ethoxyethyl vinyl sulfide, $CH_2:CH \cdot S \cdot CH_2CH_2OEt$, a colorless mobile liquid with a curious, pungent, camphor-like odor, boiling at 65°C. at 8 mm., $d_{4°}^{20°} = 0.9532$; β-ethoxy-β'-hydroxydiethyl sulfide, $HOCH_2CH_2 \cdot S \cdot CH_2CH_2OEt$, boiling at 117.5°C. at 4 mm. pressure; bis(β-ethoxyethyl) sulfide, $S(CH_2CH_2OEt)_2$, boiling at 101–102°C. at 4 mm., $d_{4°}^{20°} = 0.9658$. Using 1 mole of 20 per cent potassium hydroxide in alcohol-water, β-chloroethyl vinyl sulfide, $CH_2:CH \cdot S \cdot CH_2CH_2Cl$, boiling at 71–72°C. at 50 mm. and at 151.5–152.5°C. at 764 mm., is obtained.

Wilson, Fuller, and Schur (68) determined the acceleration of the hydrolysis of bis(β-chloroethyl) sulfide by alkaline colloidal solutions. With a solution containing 3 per cent sulfonated corn oil and 2 per cent sodium carbonate the hydrolysis of bis(β-chloroethyl) sulfide on cloth is completed in 35 minutes at 85°C. The alkaline sulfonated corn oil accelerates only the specific rate of solution per unit area of interface, by acting as carrier to transport the sulfide from the very thin aqueous layer through which the gas was diffusing before hydrolysis was complete; it has no tendency to increase the specific rate of hydrolysis nor the solubility of the gas in the aqueous phase. Alkaline soap solutions do not complete the hydrolysis of the sulfide on cloth, because of the formation of a gummy compound, probably a fatty acid ester of thiodiglycol, between the hydrolysis product of the gas and soap, which deposits on the films of the cloth.

3. Oxidation

Bis(β-chloroethyl) sulfide is ultimately oxidized by various reagents to the corresponding sulfone:

$$(ClCH_2CH_2)_2S \rightarrow (ClCH_2CH_2)_2SO \rightarrow (ClCH_2CH_2)_2SO_2$$

When pure bis(β-chloroethyl) sulfide is dropped into concentrated nitric acid at room temperature, there is an energetic reaction with evolution of heat and formation of a light green solution (21, 29, 44). From this solution, after diluting with water, the sulfoxide separates as white crystalline plates which melt at 109.5–110°C.; so far as can be judged by handling, it is entirely without effect upon the human skin. The sulfoxide is soluble in water, concentrated mineral acids, alcohol, ether, benzene, carbon disulfide, and acetone. It can not be distilled without partial decomposition even at reduced pressure, the chief decomposition product being the sulfide; it seems that during the distillation the sulfoxide dissociates into the sulfide and oxygen, the former appearing in the distillate and the latter escaping as such or effecting a destructive oxidation of the sulfoxide. Upon brominating an ice-cold chloroform solution of the sulfide a deep orange-colored precipitate quickly separates which, after drying and purifying, results in a bright yellow solid which yields the sulfoxide upon treatment with dilute sodium hydroxide solution (21). The sulfoxide is also prepared by slowly treating the sulfide in cold acetic acid with 30 per cent hydrogen peroxide and allowing to stand overnight (60).

When the sulfoxide is further oxidized by the use of fuming nitric acid, potassium permanganate, or chromic acid, the chief product is the corresponding sulfone which, when recrystallized from water or alcohol, appears as beautiful thin white leaflets melting at 48°C. (60), 53.5°C. (16), 56°C.; it distils *in vacuo* without decomposition at 183°C. at 20 mm. (29). Its solubility in water and dilute acids is much less than that of the sulfoxide. Bennett (7) obtained β-chloroethanesulfonic acid, $ClCH_2CH_2SO_3H$, when he treated the sulfoxide with fuming nitric acid in a sealed tube for 10 hours at 100°C.

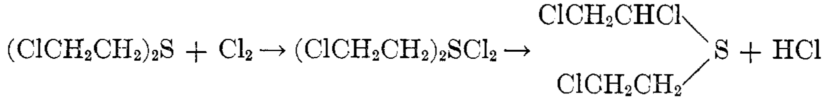
The sulfone produces, on contact with the skin, blisters and persistent sores; its vapors are lachrymatory, causing a copious flow of tears and a soreness of the eyes, and are also somewhat sternutatory, causing sneezing and a slight burning in the nostrils, but as its vapor pressure is low at ordinary temperatures no inconvenience is experienced in handling it. That these unpleasant properties should reoccur in the sulfone after disappearing in the sulfoxide is peculiar. The theory has been advanced (48) that hydrolysis is one of the main factors entering into the action of the sulfide on the human body. It is of interest to note that hydrolysis of the sulfide by water is greatest, the sulfone next, and the sulfoxide least. These factors are in accord with the theory as applied to the observed physiological effects of the sulfoxide and sulfone.

4. Chlorination

Chlorine is slowly but steadily absorbed when passed through bis(β-chloroethyl) sulfide; after a short time hydrogen chloride is evolved and the temperature rises to about 50°C. The product boils with partial decomposition under atmospheric pressure, and when distilled under reduced pressure yields no constant-boiling compound. On distillation under 15 mm. through a 65 mm. Dufton column at the rate of one drop each three seconds, Mann and Pope (44) resolved the mixtures, and after several similar fractional distillations the following three compounds were obtained in a state of purity: (a) α,β,β'-trichlorodiethyl sulfide, $ClCH_2$-$CH_2 \cdot S \cdot CHClCH_2Cl$, boiling at 106.5–108°C. at 15 mm., $d_{4^\circ}^{21.8^\circ} = 1.4219$; (b) $\alpha,\beta,\beta,\beta'$-tetrachlorodiethyl sulfide, $ClCH_2CH_2 \cdot S \cdot CHClCHCl_2$, boiling at 123–125°C. at 15 mm., $d_{4^\circ}^{15.2^\circ} = 1.5441$; (c) $\alpha,\alpha,\beta,\beta,\beta,\beta'$-hexachlorodiethyl sulfide, $ClCH_2CH_2 \cdot S \cdot CCl_2CCl_3$, boiling at 160–161°C. at 15 mm., $d_{4^\circ}^{10.6^\circ} = 1.6944$. These three chlorinated diethyl sulfides are colorless liquids which slowly acquire a light green tint when exposed to sunlight; they possess a faint odor similar to the parent dichloro compound, but are devoid of vesicant properties and have much lower melting points. As the number of chlorine atoms in the molecule increases, the sulfur atom shows increasing reluctance to become quadrivalent.

On passing dry chlorine into bis(β-chloroethyl) sulfide, allowing the liquid to warm up spontaneously, and finally heating at 100°C. in the current of chlorine, sulfur dichloride distils over, the absorption ceasing after about twenty-two hours; the product, on distillation, yields a mixture of sulfur monochloride and dichloride followed by an oil boiling at 130–175°C. Above this temperature the distillate solidifies in the condenser, the crystalline substance being identified as perchloroethane, melting at 185°C. The liquid boiling at 130–175°C. separates sharply, on distillation through a Dufton column, into α,β,β,β-tetrachloroethane, boiling at 129–130°C., and pentachloroethane, boiling at 159–161°C., while a crystalline residue of perchloroethane remains in the distilling flask.

Because of the ease and rapidity with which bis(β-chloroethyl) sulfide is chlorinated, Lawson and Dawson (37) suggest that a preliminary addition of the chlorine followed by a molecular rearrangement involving substitution of one atom of chlorine and elimination of one molecule of hydrogen chloride takes place as follows:



$$(ClCH_2CH_2)_2S + Cl_2 \rightarrow (ClCH_2CH_2)_2SCl_2 \rightarrow \begin{matrix} ClCH_2CHCl \\ ClCH_2CH_2 \end{matrix}\!\!>\!S + HCl$$

Mumford and Phillips (51) advanced the view that the products of chlorination of bis(β-chloroethyl) sulfide described by Mann and Pope (44) as α,β,β′-trichloro- and α,β,β,β′-tetrachlorodiethyl sulfides were α,β-dichloro- and α,β,β-trichlorovinyl β-chloroethyl sulfide respectively.

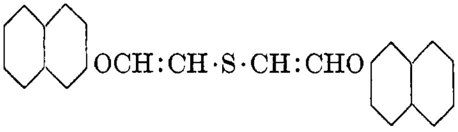
Bis(β-chloroethyl) sulfide in carbon tetrachloride and chlorine at −5°C. to 0°C. gives the chlorine intermediate addition product in the process of chlorination, bis(β-chloroethyl) sulfonium chloride, $(ClCH_2CH_2)_2SCl_2$, which Lawson and Dawson (37) crystallized as white needles and which was found to decompose at room temperature to give hydrogen chloride, α,β,β′-trichlorodiethyl sulfide, and dichloroethyl sulfoxide. Distillation of α,β,β′-trichlorodiethyl sulfide gave two isomeric vinyl compounds, β-chloroethyl β-chlorovinyl sulfide and β-chloroethyl α-chlorovinyl sulfide. These investigators found that on distillation of this relatively pure trichlorodiethyl sulfide, great quantities of hydrogen chloride were evolved but no definite boiling point was observed. After ten distillations two distinct fractions were obtained which analysis showed to have the same empirical formula corresponding to chloroethyl chlorovinyl sulfide.

The instability of α,β,β′-trichlorodiethyl sulfide and its decomposition on distillation to give two isomers affords an explanation for the failure of Mann and Pope to isolate the pentachlorodiethyl sulfide. They found the trichlorodiethyl sulfide so unstable that it was impossible to isolate it by distillation at pressures as low as 3.5 mm.; the compound isolated by Mann and Pope could not, therefore, have been the trichlorodiethyl sulfide. They postulated the splitting-out of hydrogen chloride from tetrachlorodiethyl sulfide to give a chloroethyl dichlorovinyl sulfide, and similarly the decomposition of pentachlorodiethyl sulfide to give chloroethyl vinyl sulfide, which was afterwards confirmed by Phillips, Davies, and Mumford (58). An explanation was thus afforded for the inability of Mann and Pope to isolate the pentachloro derivative.

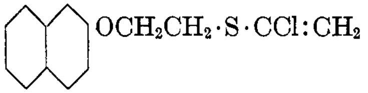
Contrary to previous views Phillips, Davies, and Mumford (58) proved that chlorination is not confined to one chain but occurs in both chloroethyl groups.

Besides compounds heretofore mentioned the following bis(β-chloroethyl) sulfide chlorinated products have been prepared and identified (37): α,β,β′-trichlorodiethyl sulfide, $CHCl_2CHCl \cdot S \cdot CH_2CH_2Cl$, a colorless liquid, decomposing at room temperature with evolution of hydrogen chloride, $d_4^{20°} = 1.4038$, $n_D^{22.5°} = 1.5309$; β-chloroethyl β-chlorovinyl sulfide, $CHCl{:}CH \cdot S \cdot CH_2CH_2Cl$, a colorless oil, boiling at 73.5–74.5°C. at 4 mm.,

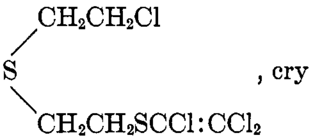
$d^{20°} = 1.3280$, $n_D^{22.5°} = 1.5483$; β-chloroethyl α-chlorovinyl sulfide, $CH_2ClCH_2 \cdot S \cdot CH_2:CCl$, a colorless liquid, boiling at 69.5–70.5°C. at 4 mm., $d_{4°}^{20°} = 1.3193$, $n_D^{22.5°} = 1.550$; α-bromo-β, β'-dichloroethyl sulfide, $CH_2ClCHBr \cdot S \cdot CH_2CH_2Cl$, a yellow oil, unstable at room temperature; bis(β-naphthoxy)ethyl vinyl sulfide,



tiny diamond-shaped plates, melting at 129.5°C.; β-naphthoxyethyl α-chlorovinyl sulfide,



an oil which crystallizes from petroleum ether giving crystals melting at 56–57°C.; α,β,β,β'-tetrachlorodiethyl sulfide, $CHCl_2CHCl \cdot S \cdot CH_2CH_2Cl$, boiling at 118.5–119°C. at 3 mm.; α,α,β,β'-tetrachlorodiethyl sulfide, $CH_2ClCCl_2 \cdot S \cdot CH_2CH_2Cl$, too unstable for isolation; β-chloroethyl α,β-dichlorovinyl sulfide, $CH_2ClCH_2 \cdot S \cdot CCl:CHCl$, a colorless mobile liquid, boiling at 79.7–80.5°C. at 4 mm., $d_{4°}^{20°} = 1.4315$; $\eta^{20°} = 0.028$ dynes per square centimeter (58); β-chloroethyl β,β-dichlorovinyl sulfide, $CH_2ClCH_2 \cdot S \cdot CH:CCl_2$, boiling at 90–91°C. at 3.5 mm.; β-chloroethyl α,β,β-trichlorovinyl sulfide, $CH_2ClCH_2 \cdot S \cdot CCl:CCl_2$, boiling at 97–98°C. at 4 mm., and at 123.5–124.5°C. at 15 mm.; α,α,β,β,β'-pentachlorodiethyl sulfide, $CHCl_2CCl_2 \cdot S \cdot CH_2CH_2Cl$, an unstable yellow oil; α,α,β,β,β,β'-hexachlorodiethyl sulfide, $CCl_3CCl_2 \cdot S \cdot CH_2CH_2Cl$, boiling at 131–132°C. at 4.5 mm., and at 159.5–60°C. at 15 mm., $d_4^{20°} = 1.6849$, $\eta^{20°}$ 0.254 dynes per square centimeter (58). β(β-Chloroethylthiol)ethyl trichlorovinyl sulfide,

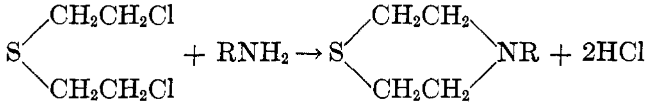


$$S \begin{cases} CH_2CH_2Cl \\ CH_2CH_2SCCl:CCl_2 \end{cases}$$

, crystallizes from alcohol in long flat needles, boils at 157–167°C. at 2.5 mm., melts at 70.5°C.; α,α,β-trichloroethyl β-chlorovinyl sulfide, $CH_2ClCCl_2 \cdot S \cdot CH:CHCl$, a colorless mobile liquid, boiling at 122–123°C. at 15 mm., $d_{4°}^{20°} = 1.5404$, $\eta^{20°} = 0.057$ dynes per square centimeter; α,β-dichloroethyl α,β-dichlorovinyl sulfide, $CHCl:CCl \cdot S \cdot CHClCH_2Cl$ a colorless liquid, boiling at 120–121°C. at 15 mm., $d_{4°}^{15.2°} = 1.544$; α,α,α'β,β',β'-hexadichlorodiethyl sulfide, $CH_2ClCCl_2 \cdot S \cdot CHClCHCl_2$, a colorless liquid, boiling at 159–160°C. at 15 mm., $d_{4°}^{20°} = 1.6841$, $\eta^{20°} = 0.294$ dynes per square centimeter; α,β,β-trichloroethyl α,β-dichlorovinyl sulfide, $CHCl{:}CCl \cdot S \cdot CHClCHCl_2$, a colorless liquid, boiling at 134–135°C. at 15 mm., $d_{4^\circ}^{20^\circ} = 1.6293$, $\eta^{20^\circ} = 0.065$ dynes per square centimeter; α,α,α',β,β,β',β'-heptachlorodiethyl sulfide, $CHCl_2CCl_2 \cdot S \cdot CHClCHCl_2$, a colorless viscid liquid, boiling at 170–172°C. at 15 mm., $d_{4^\circ}^{20^\circ} = 1.7473$, $\eta^{20^\circ} = 0.427$ dynes per square centimeter; α,α,α',β,β,β'-hexachlorodiethyl sulfide, $CHCl_2CCl_2 \cdot S \cdot CHClCH_2Cl$, boiling at 157–159°C. at 15 mm., $d_{4^\circ}^{20^\circ} = 1.6825$, $\eta^{20^\circ} = 0.273$ dynes per square centimeter; α,β-dichloroethyl α,β,β-trichlorovinyl sulfide, $CCl_2{:}CCl \cdot S \cdot CHClCH_2Cl$, boiling at 133–134°C. at 15 mm., $d_{4^\circ}^{20^\circ} = 1.6190$, $\eta^{20^\circ} = 0.063$ dynes per square centimeter; α,α,α',β,β,β,β'-heptachlorodiethyl sulfide, $CCl_3CCl_2 \cdot S \cdot CHClCH_2Cl$, boiling at 132–134°C. at 2 mm., $d_{4^\circ}^{20^\circ} = 1.7430$, $\eta^{20^\circ} = 0.382$ dynes per square centimeter; α,α,α,β-tetrachloroethane, CCl_3CH_2Cl, b.p. 35–36°C. at 20 mm., 129–129.7°C. at 760 mm.; α,β-dichloroethyl α,β,β'-trichlorovinyl sulfide, $CCl_2{:}CCl \cdot S \cdot CHClCH_2Cl$, boiling at 133.5–134° at 15 mm., $d_4^{20^\circ} = 1.6183$, 1.6183, $\eta^{20^\circ} = 0.069$ dynes per square centimeter.

4. Formation of primary amines

Primary amines, thiazanes, are prepared from bis(β-chloroethyl) sulfide and the amine in ethyl alcohol containing sodium carbonate.



They are colorless, mobile oils with densities less than 1 (except the benzyl derivative).

The following thiazanes have been prepared: *methyl* (13), completely miscible with water and organic solvents, a powerful base fuming in the presence of acid vapors, b.p. 163–164°C. at 757 mm., $d_{4^\circ}^{15^\circ} = 0.99596$; *ethyl* (13), insoluble in water, b.p. 184°C. at 763 mm., $d_{4^\circ}^{15^\circ} = 0.99295$; *isoamyl* (13), oil with characteristic odor, almost insoluble in water, b.p. 105–106°C. at 13 mm.; *benzyl* (13), insoluble in water but soluble in organic solvents, b.p. 154°C. at 13 mm., 152.5°C. at 10 mm. (39), $d_{4^\circ}^{15^\circ} = 1.08328$. *Propyl*, soluble in water, b.p. 82.5–83.5°C. at 12 mm.; *isopropyl*, soluble in water, b.p. 74.5–75°C. at 9 mm.; *butyl*, b.p. 118°C. at 33 mm., 101–102°C. at 19 mm.; *isobutyl*, b.p. 93°C. at 17 mm.; *amyl*, b.p. 119°C. at 15 mm., 104°C. at 9 mm., $d_{4^\circ}^{4^\circ} = 0.9485$ (39).

5. Formation of secondary amines

These are prepared in the same manner as the corresponding primary amines except that two molecular equivalents of secondary amine are used for each equivalent of sulfide.

$$S(CH_2CH_2Cl)_2 + 2HNR_2 \rightarrow S(CH_2CH_2NR_2)_2 + 2HCl$$

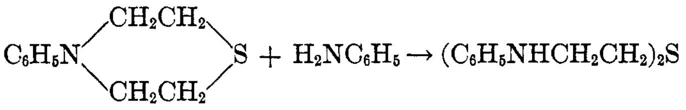
All the bis(β-dialkylaminoethyl) sulfides are colorless oils, soluble in organic solvents but almost insoluble in water except for the diethyl derivative, which has a solubility of about 0.1 per cent (39). The following have been prepared: *Dimethylaminoethyl vinyl sulfide,* one amino group was lost thus forming the unsaturated compound, b.p. 168.5°C. at 763 mm.; *ethyl,* b.p. 139–140°C. at 9 mm.; *propyl,* b.p. 194°C. at 19 mm., $d_{4^\circ}^{4^\circ} = 0.9007$; *butyl,* b.p. 205–206°C. at 10 mm.; *piperidyl,* b.p. 174.5–176°C. at 15 mm.; *phthalimide,* m.p. 125°C., fine, pale cream-colored needles (11).

6. Formation of tertiary amines

Condensation with tertiary amines is by addition, unaccompanied by the elimination of any by-product. When trimethylamine and bis(β-chloroethyl) sulfide are heated in a sealed tube for 6 hours at 100°C., crystals of $S(CH_2CH_2ClNMe_3)_2$ are formed, which melt at 135.5°C. (39).

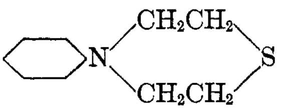
7. Formation of aromatic amines

The aromatic derivatives are prepared with difficulty, this difficulty being based on two facts: (1) their insolubility (which causes inconvenience in purification), and (2) their secondary reaction with excess aromatic amines, apparently to break open the heterocyclic ring:



The compound resulting from the secondary reaction is easily soluble in dilute hydrochloric acid (quite in contrast with the thiazanes), yielding in alkaline solution an oil heavier than water, which is only slightly volatile in steam.

4-Phenyl-1-thiazane,



a dull white powder, not pure, soluble in hot toluene, m.p. 108–111°C.

8. Condensation with sodium thiophenate and phenates

The fundamental reaction is the formation of sodium chloride with the simultaneous condensation of the organic residues:

$$2C_6H_5SNa + S(CH_2CH_2Cl)_2 \rightarrow (C_6H_5SCH_2CH_2)_2S + 2NaCl$$

$$2C_6H_5ONa + S(CH_2CH_2Cl)_2 \rightarrow (C_6H_5OCH_2CH_2)_2S + 2NaCl$$

Thus it is seen that the condensation with sodium thiophenate gives complex trisulfides or related compounds, while with the phenates it produces various mixed sulfide-ethers. All that have been prepared by Helfrich and Reid (29) are white, or nearly white, crystalline bodies and most of them can be recrystallized from alcohol but are insoluble in water (see table 15).

9. Condensation with sodium mercaptides (29)

The condensation of bis(β-chloroethyl) sulfide with sodium mercaptides is quite similar to that with sodium thiophenate already considered:

$$S(CH_2CH_2Cl)_2 + 2NaSR \rightarrow S(CH_2CH_2SR)_2 + 2NaCl$$

The reaction is rapid in the hot alcohol solution and the yield nearly quantitative. The stability of these multiple sulfides and their oxidation products is again an outstanding feature. Data concerning them are given in table 16.

10. Miscellaneous reactions

Upon distilling at reduced pressure Mann and Pope (44) obtained a trichlorodiethyl sulfide and tetrachlorodiethyl sulfide from a mixture of bis(β-chloroethyl) sulfide and sulfur monochloride; it thus appears that sulfur monochloride acts as a chlorinating agent on bis(β-chloroethyl) sulfide.

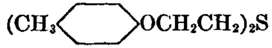
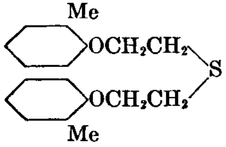
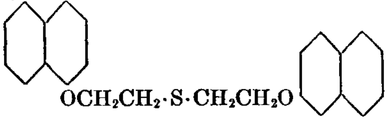
Upon heating bis(β-chloroethyl) sulfide under pressure with alcoholic ammonia Clarke (13) obtained 1,4-thiazane, $\underline{CH_2 \cdot S \cdot CH_2CH_2NHCH_2}$, a colorless liquid, boiling at 169°C. at 758 mm., miscible with water and organic solvents, possessing an odor similar to, yet more unpleasant than, that of pyridine. It is a very strong base, very rapidly absorbing carbon dioxide from the air, and reacts vigorously with metallic potassium on gentle warming.

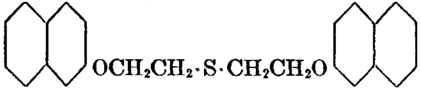
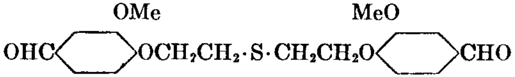
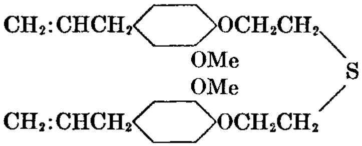
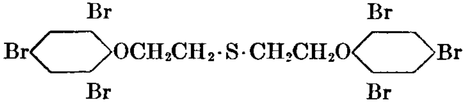
Bis-β-thioethyl acetate, $S(CH_2CH_2OOCMe)_2$, is prepared (29) by distilling *in vacuo* the oil obtained after anhydrous sodium acetate and bis(β-chloroethyl) sulfide have been heated; b.p. 155–156°C. at 20 mm., $d^{20°} = 1.132$, $n^{22.5°} = 1.4720$.

β,β′-Dichlorodiethylsulfine-*p*-toluenesulfonylimine,

TABLE 15

Products formed by condensation of bis(β-chloroethyl) sulfide with sodium thiophenate and phenates

NAME AND FORMULA	MELTING POINT	SOLUBILITY IN 100 CC. ALCOHOL		REMARKS
		Cold (18°C.)	Hot (75°C.)	
	°C.	*grams*	*grams*	
Bis(β-phenylmercaptoethyl) sulfide $(C_6H_5SCH_2CH_2)_2S$	57.5	0.65	10.00	Lustrous white leaflets
Bis(β-phenoxyethyl) sulfide $(C_6H_5OCH_2CH_2)_2S$	54.2	1.42	20.00	Fine white needles
Bis(β-*p*-cresoxyethyl) sulfide 	78.0	0.20	Soluble	Lustrous needles
Bis(β-*o*-cresoxyethyl) sulfide 	46.5	0.30	Soluble	White needles
Bis(β,α-naphthoxyethyl) sulfide 	94.5	Insoluble	Slightly soluble	Light brown crystals

Bis(β, β-naphthoxyethyl) sulfide 	129.0	Insoluble	0.60	Small crystals
Bis(β-vanilloxyethyl) sulfide 	131.5	Insoluble	2.00	Gray needles
Bis(β-eugenoxyethyl) sulfide 	113.5	0.10	2.00	Yellow powder
Bis(β-tribromophenoxyethyl) sulfide 	118.5	Insoluble	0.50	White powder

is obtained (45) in the form of fine white needles, m.p. 144–145°C., upon shaking bis(β-chloroethyl) sulfide with an aqueous solution of chloramine-T.

Cashmore and McCombie (11) prepared the ethyl ester of bis(β-chloroethyl) sulfide, $(CH_2CH_2NHCH_2CO_2Et)_2S$, from bis($\beta$-chloroethyl) sulfide and glycine ester hydrochloride in 98 per cent ethyl alcohol containing anhydrous sodium acetate. It is an oil boiling at 159–160°C. at 15 mm.

By boiling for several hours a mixture of potassium cyanide and bis(β-chloroethyl) sulfide the nitrile, probably $(CH_2SCH_2CH_2CN)_2$, is obtained (16). It crystallizes in colorless microneedles from benzene, melting at 91–91.5°C., and readily soluble in alcohol but insoluble in water.

TABLE 16

Compounds formed by the condensation of bis(β-chloroethyl) sulfide with sodium mercaptides

NAME AND FORMULA	BOILING POINT	MELTING POINT	REMARKS
	degrees C.	*degrees C.*	
Bis(β-ethylmercaptoethyl) sulfide $(EtSCH_2CH_2)_2S$	173–175 at 21 mm.	17.0	$n^{22.5°} = 1.5151$; odor rather unpleasant and persistent
Bis(β-propylmercaptoethyl) sulfide $(PrSCH_2CH_2)_2S$	193–195 at 22 mm.	27.5	
Bis(β-butylmercaptoethyl) sulfide $(BuSCH_2CH_2)_2S$	222–223 at 21 mm.	17.5	Oil; unpleasant, persistent odor; $d^{20°} = 1.102$; $n^{22.5°} = 1.5455$
Bis(β-amylmercaptoethyl) sulfide $(isoAmSCH_2CH_2)_2S$	170 at 4 mm.	20.0	

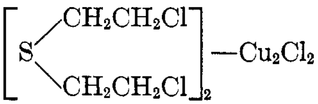
γ-Thiodibutyric acid, $S(CH_2CH_2CH_2COOH)_2$, is formed when the product of the condensation of the sulfide with ethyl malonate (or ethyl acetoacetate) and sodium ethoxide is subjected to alkaline hydrolysis (16). The acid, obtained as colorless leaves with a nacreous luster, m.p. 97–98°C., is fairly soluble in hot water, moderately so in alcohol, ether, and benzene, and does not distil in a current of steam or under diminished pressure.

Diiodoethyl sulfide, $(CH_2CH_2I)_2S$, results from the condensation of bis(β-chloroethyl) sulfide with an alcoholic solution of sodium iodide (29). It is a yellowish white crystalline material, m.p. 55–60°C., darkens slowly at room temperature, is insoluble in water and only slightly soluble in cold and moderately soluble in hot alcohol.

When bis(β-chloroethyl) sulfide is heated several hours on a water bath with a 20 per cent solution of sodium thiocyanate there is formed bis(β-thiocyanoethyl sulfide, $S(CH_2CH_2SCN)_2$, which crystallizes as light yellow crystals from ether, m.p. 35°C. (33).

IV. DETECTION AND DETERMINATION

The usual procedure for the estimation of bis(β-chloroethyl) sulfide in a sample is to distil a known volume under diminished pressure and to collect the fraction boiling at 125–130°C. at 40 mm. This product is fairly pure, and the volume obtained affords an approximation of the purity of the crude product. This procedure involves personal risks, and gives no accurate figure for the absolute percentage of bis(β-chloroethyl) sulfide, as the latter fraction also contains higher chlorinated compounds and other impurities. With the object of overcoming these difficulties Hollely (32) devised the following volumetric method for the estimation of bis(β-chloroethyl) sulfide with or without solvents. This method depends upon the fact that the sulfide forms a definite double salt with cuprous chloride, of the constitution



As the higher chlorinated compounds do not react with cuprous chloride, the method is applicable for the absolute estimation of the sulfide.

When a 10 per cent solution of bis(β-chloroethyl) sulfide in glacial acetic acid is heated with a 67 per cent solution of hydriodic acid at 50–70°C., a yellowish oil is deposited which solidifies on cooling to a crystalline mass of diiodoethyl sulfide, melting at 62°C. Grignard, Rivat, and Scatchard (23) make use of this in the determination of bis(β-chloroethyl) sulfide. About 1 g. (weight = P) of sample is introduced into a small flask fitted with an air condenser and containing 15 g. of glacial acetic acid and exactly 5 cc. of 54 per cent hydriodic acid; the whole is heated 15 minutes at 70°C. After cooling, the contents of the flask is washed into a 500-cc. volumetric flask containing exactly 100 cc. of carbon tetrachloride and about 200 cc. of water. After dissolving the precipitate, the flask is filled to the mark with water, shaken well, and 50 cc. of the aqueous layer treated with 10 cc. of 10 per cent sodium nitrite. The liberated iodine is extracted with carbon tetrachloride which is then washed with 100 cc. of water, and the iodine titrated with 0.1 N sodium thiosulfate, the volume used being A_1 cc. The carbon tetrachloride solution in the 500-cc. flask is then separated carefully, the aqueous solution washed with a little carbon tetrachloride, which is added to the main solution, and the combined carbon tetrachloride extracts are titrated with 0.1 N sodium thiosulfate, the volume consumed being A_2 cc. A blank determination of the total iodine in 5 cc. of the hydriodic acid solution used is made, the 0.1 N sodium thiosulfate consumed being A_0 cc. The percentage of bis(β-chloroethyl) sulfide in the sample is then $0.82/P\ [10A_0 + 1.5 - (8A_1 + A_2)]$.

Yablick, Perrott, and Furman (69) determined quantitatively the presence of traces of bis(β-chloroethyl) sulfide in the air by reducing a 1 per cent solution of selenious acid in dilute sulfuric acid by means of the sulfide vapor to an orange-red suspension of selenium. Amounts of the sulfide as small as 0.005 mg. can be detected in this way. The amount of suspension produced is nearly directly proportional to the amount of the sulfide present, and 0.10 to 0.01 mg. can be established nephelometrically with a fair degree of accuracy (±0.005 mg.). This method is remarkably free from the necessity for extreme purity of original solutions, cleanliness of glassware, etc., but the selenious acid reagent is *not* specific to bis(β-chloroethyl) sulfide, for arsine and the substituted arsines and several other toxic gases react with it vigorously.

Spica (59) finds nitrosyl iodide to be the *only* specific reagent proposed for detection of bis(β-chloroethyl) sulfide which gives the corresponding diiodo compound.

Maxim (49) oxidizes the sulfur of the sulfide by heating with potassium permanganate, then passing the gas into barium chloride solution containing hydrogen peroxide. The barium sulfate precipitated is washed, dried, and weighed.

On account of the solubility and hydrolysis of bis(β-chloroethyl) sulfide it is quite difficult to estimate with any degree of accuracy small amounts of the sulfide, yet Hopkins (33) introduced a new rapid method whose principle is dependent upon the increase in the hydrogen-ion concentration. By this means a sample can be taken and determination made within five minutes.

V. PROPOSED THEORIES TO ACCOUNT FOR VESICANT ACTION

Several theories have been advanced to explain the remarkable vesicant action of bis(β-chloroethyl) sulfide. Each fits certain facts but none is entirely satisfactory. The oldest and probably most generally accepted theory is that the vesicant action is due to the formation of free hydrochloric acid within the cell. This was suggested by Marshall (48) and others (43) and substantially supported by Lillie, Clowes, and Chambers (41), but has been opposed by a number of investigators. Warthin and Weller (65) and Arbuckle (4) took exception to it from a pathological standpoint. Peters and Walker (57) showed that the rate of hydrolysis of lipoid-soluble substituted diethyl sulfides is not a critical factor.

Flury (20) advanced the theory that the vesicant action was due to the reactivity of the sulfur atom, but when it was found that the sulfoxide containing quadrivalent sulfur was non-vesicant it lost much of its probability. The idea that the unlooked-for reaction of bis(β-chloroethyl) sulfide with sodium alcoholate to give the highly toxic divinyl sulfide (5, 29) might have a bearing on the vesicant action was discounted by the later investigations of Bales and Nickelson (6), who found that the yield of divinyl sulfide decreases markedly when the per cent of alcohol drops below 80, and of Lawson and Dawson (38) who obtained no trace of divinyl sulfide from bis(β-chloroethyl) sulfide when using secondary sodium phosphate and sodium carbonate in 50 per cent alcohol, which substance gives hydrogen-ion concentrations approaching those in body tissues.

Cashmore and McCombie (11) suggest that the vesicant action of bis(β-chloroethyl) sulfide might be due to the product formed by its reaction with the amino acids present in the skin. The results obtained by Lawson and Reid (39) are consistent with the theory that the vesicant action of bis(β-chloroethyl) sulfide is due to its reactions with the living cells.

It has also been suggested that the vesicant action is due to the oxidation of the sulfide in the animal system with subsequent hydrolysis of the oxidation product (10).

Arbuckle (4) is of the opinion that the vesicant action is due to the integrity of the entire molecule, that is, the toxicity is maintained only as long as the sulfide remains in the original state.

VI. PHYSIOLOGICAL PROPERTIES

The symptoms which arise from exposure to bis(β-chloroethyl) sulfide consist essentially of local irritation of the upper respiratory tract, eyes, and skin, giving rise to conjunctivitis and superficial necrosis of the cornea, hyperemia, edema, vesication, and later necrosis of the skin, leading to a skin lesion of great chronicity, and congestion and necrosis of the epithelial lining of the pharynx, trachea, and bronchia. In the skin the cells of the epidermis are damaged, following which there is injury to the capillaries with edema, bleb formation, and exudation. The poison may gain entrance to the blood through the injured epithelium and capillaries, and circulatory injury and damage to internal organs result. Injury to the blood itself and particularly the red blood cells consisting of intravascular destruction is evidenced by hemosiderin deposits in the spleen and liver. The severity of the injury to the skin, respiratory organs, and blood corpuscles results in general toxic phenomena manifested by a rapid disappearance of fat from the fat depôts, atrophic changes in the heart and liver, and deposition of waste pigments. In animals exposed to high concentrations of this gas, vomiting and diarrhea, hyperexcitability and convulsions, and effects on the heart suggest an absorption into the blood stream and a systematic action.

Experiments demonstrate clearly that there is an absorption of dichloroethyl sulfide through the lungs. When this substance is injected either subcutaneously or intravenously into a dog, the following symptoms make their appearance after a latent period: salivation, hyperexcitability, and convulsions, vomiting and bloody diarrhea, a slow and irregular heart, which becomes rapid before death, muscular weakness, and finally, coma and death. Further proof of the absorption through the lungs is furnished by the detection of one of its decomposition products, dihydroxyethyl sulfide, in the urine of the gassed animals (27, 48).

Dichloroethyl sulfide profoundly modifies the leucocyte count of the blood in dogs as well as in rabbits and human beings, and Hektoen and Corper (28) place the sulfide in the same class with the leucotoxic agents: benzene, the radioactive preparation of which thorium X is an example, and the Roentgen ray, all of which have a profound effect on the hemapoietic organs, the leucocytes and specific antibody formation.

Dichloroethyl sulfide is a protoplasmic poison and affects all cells with which it comes in contact (20).

The toxicity of bis(β-chloroethyl) sulfide, as determined by Chlopin (12), is 15.3 when compared with chlorine as unity.

VI. APPLICATIONS

The Mexican bean weevil (Epilachna corrupta Muls.) is killed in from three to six hours when 0.01 per cent of the sulfide with a little ether adsorbed on charcoal is dusted over a bean plant. A 4 per cent solution without ether was no more effective; as high as 16 per cent bis(β-chloroethyl) sulfide on charcoal did not injure plants. The results with 0.01 per cent sulfide adsorbed on charcoal on the cotton boll weevil (Anthonomus grandis Boh.) are also quite promising (47).

Bis(β-chloroethyl) sulfide is found to have a direct retarding influence on the development of tuberculosis (15). Adair and Bagg (1) have been able to control tar cancers in mice by the surface application of bis(β-chloroethyl) sulfide in absolute alcohol. In human beings it is thought that the sulfide offers another agent for fighting cancer provided the lesion is localized, and Berenblum (8) is able to bring about the inhibition of carcinogenic tar by the addition of a small amount of bis(β-chloroethyl) sulfide to the tar.

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