ficients of sodium bicarbonate. They found over the wide range of protein concentrations studied, and at reactions from *p*H 7 to 8, that $-\log \gamma/C_{\mathrm{Hb}}$ had the value 14 for carboxyhemoglobin and 20 for reduced hemoglobin, where the concentration C_{Hb} was based on a molecular weight of 16,700. Assuming a molecular weight of 66,700 the corresponding values are 56 and 80. Comparison with our results is however difficult, since the ratio of ionic to dipolar ionic hemoglobin changes markedly over the *p*H range studied by them.

Solubility studies on insoluble salts in the presence of hemoglobin may be more directly compared. Pauli and Stenzinger[34] observed a 5% increase in the solubility of calcium sulfate in 0.5% oxyhemoglobin. This leads to a very high value of the slope $(\log S/S_0)/C_{\mathrm{Hb}}$. Stone and Failey's[35] more recent study upon the solubility of thallous chloride in the presence of concentrations of electrodialyzed reduced hemoglobin ranging from 1 to 3% yields far lower values for the slope, increasing with increasing concentration of from 14 to 26. At the ionic strength of saturated thallous chloride, slightly greater than 0.016, the slope calculated from the final column of Table IV is approximately eleven.

Summary

1. The solubility of horse carboxyhemoglobin has been studied at $-5°$ in 25 and 35% ethanol containing sodium chloride at ionic strengths from 0.01 to 0.2.

2. Under these conditions the solubilities of carboxyhemoglobin are 0.081 and 0.085 $\times 10^{-5}$ mole per liter at an ionic strength of 0.01 in 25 and 35% ethanol, or far lower than in aqueous solution Solubility ratios may therefore be considered to yield activity coefficients.

3. The experimentally determined activity coefficients have been compared with the expectation on the basis of Kirkwood's theory, assuming hemoglobin to be a double dipole with a moment of 500 $\times 10^{-18}$ e. s. u. Effects due to electric moments of higher order and to "salting-out" have also been considered.

4. Activity coefficients for hemoglobin in aqueous sodium chloride at 25° have been estimated and compared with the measurements of Green in such systems, and the activity coefficients of the sodium chloride estimated and compared with the measurements of Stone and Failey on thallous chloride.

5. The possibility of change in the nature of the saturating body under these various conditions is not excluded.

BOSTON, MASS.

RECEIVED MARCH 16, 1938

[34] Pauli and Stenzinger, *Biochem. Z.*, **205**, 71 (1929).

[35] Stone and Failey, *J. Phys. Chem.*, **37**, 935 (1933).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY]

The Interaction of Chlorine with Different Types of Organic Sulfur Compounds

BY IRWIN B. DOUGLASS[1] AND TREAT B. JOHNSON

As a result of the recent researches conducted in this Laboratory on the production of sulfonyl chlorides by the chlorination of isothiourea salts[2] in aqueous solution, we have been led to a study of the action of aqueous chlorine at low temperatures on various other types of sulfur compounds. In this paper the authors describe results of the chlorination of certain representations of the following types: mercaptans, disulfides, thiol esters, alkyl thiosulfate salts, a thiosulfonate ester, alkyl ethylxanthates, potassium xanthates, and an acyldithiocarbamate.

Schiller and Otto[3a] reported that diphenyl disulfide interacted with chlorine in the presence of water to give phenylsulfonyl chloride. They also treated phenylthiol benzoate[3b] with aqueous chlorine and obtained benzoic acid, phenylsulfonyl chloride, and phenylsulfonic acid. They postulated that the first action of the halogen is to produce benzoyl chloride and diphenyl disulfide, but they did not report the isolation of benzoyl chloride.

Zincke and others in a series of papers dealing with the chemistry of aryl sulfur chlorides[4]

[1] Sterling Professorship of Chemistry Research Assistant 1937-1938.

[2] Johnson and Sprague, THIS JOURNAL, (a) **58**, 1348 (1936); (b) **59**, 1837 (1937); (c) **59**, 2439 (1937).

[3] (a) Schiller and Otto, *Ber.*, **9**, 1638 (1876); (b) *ibid.*, 1635 (1876).

[4] Zincke and Frohneberg, *ibid.*, **42**, 2728 (1909), and later papers by Zincke and co-workers.

showed that mercaptans and disulfides, when chlorinated in glacial acetic acid, likewise produced sulfonyl chlorides. Fries and Schurmann[5] made the same observation in a study dealing with the chlorination of certain anthraquinone disulfides. Pollak, Riesz, and Nadel[6] also produced sulfonyl chlorides by chlorinating aryl mercaptans in concentrated hydrochloric acid suspension. They utilized the reaction to prove the constitution of a commercial sulfur dyestuff. In fact, a patent has been issued for the commercial production of aryl sulfonyl halides by application of this reaction.[7] Our survey of the literature has failed to reveal any record of the action of aqueous chlorine and aliphatic mercaptans.

Price and Twiss[8] in producing disulfides by the action of iodine on sodium alkyl thiosulfates also tried the action of chlorine in place of iodine. They reported, however, that the disulfide obtained was contaminated to a considerable extent with mercaptan and the yield was always poor.

Mylius[9] treated a solution of potassium isobutyl xanthate with chlorine and obtained dicarbobutoxydisulfide but he did not continue the chlorination to the point of further oxidation of the sulfur atoms.

Experimental Part

Chlorination Procedure.—Five to ten grams of the sulfur compound to be chlorinated was suspended in about 100 cc. of water in a flask cooled externally by an ice-bath and fitted with chlorine inlet tube and a mechanical stirrer. The chlorine was passed in at such a rate that the temperature did not rise above 10°. The reaction was assumed to be complete when a strong, greenish yellow color appeared in the aqueous layer. The products of the reaction were extracted with ether and the excess of chlorine removed by treatment with sodium bisulfite and sodium bicarbonate solutions. In order to identify the products of reaction the ether solution was dried and the product distilled, or allowed to interact directly with an ether solution of an amine to obtain a solid derivative.

Chlorination of Mercaptans.—Ethyl and *n*-amyl mercaptans readily formed sulfonyl chlorides in yields of over 70%. Benzyl mercaptan did not proceed completely to the sulfonyl chloride. Soon after beginning the passage of chlorine the liquid mercaptan changed to the solid disulfide. By repeatedly filtering out this solid and grinding, a product was finally obtained which melted within a few degrees of the melting point of benzyl sulfonyl chloride. Its identity was determined by the formation of the anilide, m. p. 103°, which was compared to an authentic sample. In another experiment the repeated grinding of the solid product was omitted. It was filtered out, dried, and treated with ether. A portion that remained undissolved was recrystallized from alcohol and proved to be benzyl benzylthiosulfonate, m. p. 108°, and was identified by a mixed melting point with an authentic sample. The ether solution was treated with aniline and allowed to stand for several hours over sodium bicarbonate solution. After removing the excess of aniline with acid, the benzylsulfonyl anilide was extracted with dilute sodium hydroxide and the remaining ether solution was allowed to evaporate. From the solid residue was obtained dibenzyl disulfide, m. p. 71°, identified by a mixed melting point.

In chlorinating phenylmercaptan, the liquid soon changed to the solid diphenyl disulfide. This solid soon became yellow on the edges of the lumps and in twenty to thirty minutes had all turned to a bright yellow liquid having the appearance of phenyl sulfur chloride,[10] which in another experiment was found to be only slowly decomposed by water at the temperature employed. The yellow color gradually faded to the water white color of the phenylsulfonyl chloride.

Chlorination of Di-*n*-butyl Disulfide.—When chlorine was passed into the suspension of di-*n*-butyl disulfide the oil acquired a yellowish orange color as though some *n*-butyl sulfur chloride was being formed. The final product showed the following constants: b. p. 70–71° at 3 mm., n^{24}_D 1.4552. Since Sprague and Johnson[2b] report n^{25}_D 1.4524 for *n*-butylsulfonyl chloride our compound was analyzed with the following results. Calcd. for $C_4H_9ClO_2S$: S, 20.47; Cl, 22.64. Found: S, 19.47; Cl, 23.52. These analytical results seem to indicate that there had been some substitutions of chlorine in the butyl radical.

The change of color on first adding chlorine is not conclusive evidence of the formation of butyl sulfur chloride, but would cause one strongly to suspect its presence. In another experiment an attempt was made to prepare *n*-amyl sulfur chloride, $C_5H_{11}SCl$, by chlorinating amyl mercaptan in carbon tetrachloride solution. No pure compound was obtained but an analysis showed that the middle fraction of the product contained approximately three chlorine atoms per mole instead of the expected one, indicating that this alkyl sulfur chloride was readily chlorinated in the alkyl radical.

Chlorination of Thiol Esters.—Ethyl thiolacetate chlorinated smoothly to give a 71% yield of ethylsulfonyl chloride.

Benzyl thiolacetate gave the same mixture of product, *i. e.*, dibenzyl disulfide, benzyl benzylthiosulfonate, and benzyl sulfonyl chloride, as was obtained by chlorinating benzylmercaptan.

Benzyl thiolbenzoate yielded as principal products benzoyl chloride and benzylsulfonyl chloride with a small amount of benzoic acid as by-product. No disulfide or thiobenzoate was found in this case, probably because the benzoyl chloride kept the products in a pasty condition and in the efficient stirring all portions were able to come in contact with the chlorine water.

Chlorination of Sodium Alkylthiosulfates.—Methyl sulfate (25.2 g.) was stirred vigorously with a solution of 50 g. of sodium thiosulfate in 200 cc. of water. In twenty minutes all had dissolved and the temperature of the solu-

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(5) Fries and Schurmann, *Ber.*, **52**, 2183 (1919).

(6) Pollak, Riesz, and Nadel, *Monatsh.*, **53/54**, 97 (1929).

(7) Ohse, *C. A.* **26**, 4828 (1932); German Patent 550,685 (1928).

(8) Price and Twiss, *J. Chem. Soc.*, **95**, 1490 (1909).

(9) Mylius, *Ber.*, **5**, 976 (1872).

(10) Lecher and Holschneider, *ibid.*, **57**, 755 (1924).

TABLE I

THE ACTION OF CHLORINE ON SULFUR COMPOUNDS

	Compound chlorinated	Conditions	Products identified
1	C_2H_5SH[11]	5–10°	$C_2H_5SO_2Cl$ (73%)
2	*n*-$C_5H_{11}SH$	1–5	$C_5H_{11}SO_2Cl$ (78%)
3	C_6H_5SH	5–10	$C_6H_5SO_2Cl$ (55%)
4	$C_6H_5CH_2SH$	5–12	$(C_6H_5CH_2S)_2$, $C_6H_5CH_2SO_2SCH_2C_6H_5$, $C_6H_5CH_2SO_2Cl$[12]
5	(*n*-$C_4H_9S)_2$	1–6	$C_4H_9SO_2Cl$ (contaminated with some nuclear substituted product)
6	$CH_3COSC_2H_5$	2–10	$C_2H_5SO_2Cl$ (71%)
7	$CH_3COSCH_2C_6H_5$	2–10	$(C_6H_5CH_2S)_2$, $C_6H_5CH_2SO_2SCH_2C_6H_5$, $C_6H_5CH_2SO_2Cl$[12]
8	$C_6H_5COSC_2H_5$	1–3	C_6H_5COOH, C_6H_5COCl,[12] $C_2H_5SO_2Cl$[12]
9	$C_6H_5COSCH_2C_6H_5$	1–3	C_6H_5COOH, C_6H_5COCl,[12] $C_6H_5CH_2SO_2Cl$[12]
10	$C_6H_5CH_2SO_2SCH_2C_6H_5$	1–6	$C_6H_5CH_2SO_2Cl$[12]
11	CH_3SSO_3Na	1–10	CH_3SO_2Cl (54%)
12	$C_2H_5SSO_3Na$	5–20	$C_2H_5SO_2Cl$ (55%)
13	$C_6H_5CH_2SSO_3Na$	0–5	$(C_6H_5CH_2S)_2$, $C_6H_5CH_2SO_2SCH_2C_6H_5$, $C_6H_5CH_2SO_2Cl$[12]
14	$C_2H_5OCSSC_2H_5$	3–7	C_2H_5OCOCl,[12,13] $C_2H_5SO_2Cl$[13]
15	$C_2H_5OCSSCH_2C_6H_5$	1–3	C_2H_5OCOCl,[13] $C_6H_5CH_2SO_2Cl$[13], $C_6H_5CH_2Cl$ (?)
16	C_2H_5OCSSK	1–8	C_2H_5OCOCl (33%)
17	$C_6H_5CONHCSSC_2H_5$	0–1	$C_6H_5CONCCl_2$,[14] (70%), $C_2H_5SO_2Cl$[13] (60%)

TABLE II

NEW COMPOUNDS PREPARED AS INTERMEDIATES OR MADE FOR PURPOSES OF IDENTIFICATION

	Compound	M. p. or b. p., °C.	Analyses, % Calcd.	Found
1	*n*-$C_5H_{11}SO_2Cl$	B, 77–78 (3 mm.) n^{25}_D 1.4547	S, 20.77	S, 20.67
2	$C_2H_5OCSSCH_2C_6H_5$	B, 143 (3 mm.)	S, 30.21	S, 29.47
3	$C_2H_5SO_2NHC_6H_4CH_3$-*p*	M, 81	N, 7.03	N, 6.91
4	$C_6H_5CON{=}C(NHC_6H_4CH_3\text{-}p)_2\cdot HCl$	M, 193–194	Cl, 10.08 N, 11.09	Cl, 9.86 N, 11.05

tion, which had arisen slightly, had started to fall. After cooling the solution to 4° it was chlorinated. A 54% yield of methylsulfonyl chloride was obtained.

In some runs the sodium alkylthiosulfate was formed by mixing the alkyl halide or sulfate (0.1 mole) with an equivalent amount of 20% sodium thiosulfate solution and 50–75 cc. of acetone. When the formation of a homogeneous solution indicated complete reaction the acetone was removed with steam and the solution cooled and chlorinated as usual. In this manner a 55% yield of ethylsulfonyl chloride was obtained. An attempt to form sodium cyclohexyl thiosulfate using cyclohexyl chloride was unsuccessful.

Ethyl chloroacetate readily united with sodium thiosulfate but on chlorination no sulfonyl chloride was obtained.

Sodium benzyl thiosulfate yielded a mixture of dibenzyl disulfide, benzyl benzylthiosulfonate, and benzyl sulfonyl chloride. These were separated and identified as already described.

Chlorination of Benzyl Benzylthiosulfonate.—In order to establish definitely that benzyl benzylthiosulfonate (dibenzyl disulfoxide) was an intermediate product in the formation of benzylsulfonyl chloride from dibenzyl disulfide, some of the thiosulfonate was prepared by the method of Hinsberg.[15] Five grams of this solid, m. p. 108°, was chlorinated in the usual manner. The crude product after drying in the air melted 70–85°. By dissolving in ether and treating with aniline it was possible to isolate the known benzyl sulfonyl anilide, and some unchanged starting material. Both compounds were identified by mixed melting points.

Chlorination of Alkyl Xanthates.—The alkyl xanthates employed were prepared by the action of the required alkyl bromide or chloride on potassium ethylxanthate in acetone solution.

Ethyl ethylxanthate (20 g.) was chlorinated to complete saturation and extracted with ether. After removing the ether from the dried solution on a water-bath, the residue was distilled from an oil-bath and yielded 4.90 g. of a liquid, boiling at 92–95° at atmospheric pressure, and 9.60 g. of a liquid, boiling at 60–63° at 12 mm. The liquid boiling at 92–95° had the sharp, musty odor characteristic of ethyl chloroformate and when it was added to an ether solution of *p*-toluidine it reacted almost explosively. After removing the excess of *p*-toluidine, *p*-tolylurethan, $C_2H_5OCONHC_6H_4CH_3$-*p* of m. p. 52–53°, was obtained by evaporating the ether. The original ether distillate smelled strongly of ethyl chloroformate and after treatment with aniline yielded 4.82 g. of phenylurethan, m. p. 51–52°. The liquid boiling at 60–65° at 12 mm. was practically pure ethylsulfonyl chloride and was identified by the formation of ethylsulfonyl *p*-toluidide, m. p. 80–81°.[16]

Benzyl ethylxanthate was chlorinated in the same man-

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[11] First chlorinated by Dr. James M. Sprague in this Laboratory.

[12] Identified as the anilide.

[13] Identified as the *p*-toluidide.

[14] Identified as benzoyl di-*p*-tolylguanidine hydrochloride.

[15] Hinsberg, *Ber.*, **41**, 2839 (1908).

[16] The *p*-toluidide is the best derivative to use for identifying ethyl sulfonyl chloride.

ner. Without attempting to distil the dried ether extract it was added to an ether solution of *p*-toluidine. Benzylsulfonyl *p*-toluidide, m. p. 113–114°, was obtained by alkaline extraction and after removing the excess of *p*-toluidine and evaporation of the ether solution an oily residue remained which gave a strong test for halogen and smelled strongly of benzyl chloride. After standing for two days *p*-tolylurethan, m. p. 50–52°, crystallized from the oil and was identified by a mixed melting point with the known substance.

Chlorination of Acyldithiourethans.—Ethyl benzoyldithiocarbamate was chlorinated and the resulting oil, dissolved in ether, was added cautiously to an ether solution containing three equivalents of *p*-toluidine and the solution allowed to stand over sodium bicarbonate solution for twenty-four hours. Ethylsulfonyl *p*-toluidide was obtained from the mixture by extraction with sodium hydroxide. On adding 6 *N* hydrochloric acid to the remaining ether solution a white solid separated, particularly on diluting the acid. This solid was practically insoluble in water or dilute acid and crystallized from alcohol as glass-like prisms, softening slightly at 190° and melting at 193–194°. Analysis for chlorine and nitrogen gave results indicating that this compound was the monohydrochloride of benzoyl di-*p*-tolylguanidine.

In Table I are registered the representatives of the different types of sulfur compounds exposed to the action of chlorine gas, and the different products formed by such drastic treatment. In Table II are recorded several new compounds that were obtained during the progress of our research.

Summary

1. A study of the action of chlorine in aqueous solution on different organic sulfur compounds has been continued.

2. In this paper is described the behavior of chlorine gas toward sulfur compounds of the thiol type or their derivatives, and derivatives of the xanthate series, thiosulfonates and acyl dithiourethans.

3. Further research is in progress and will be reported later.

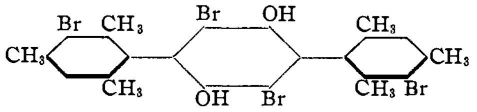
NEW HAVEN, CONN. RECEIVED APRIL 16, 1938

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

Stereochemistry of Biphenyls.[1] XLIV. *Meso* and Racemic Isophthalamides of 3-Nitro-3′-aminobimesityl

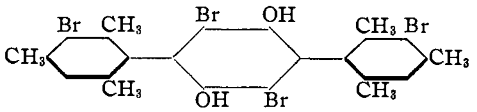
BY ROGER ADAMS AND R. M. JOYCE, JR.*

Several molecules previously have been described in which two points of restricted rotation occur.[2] These were found to exist in two diastereoisomeric forms as anticipated and since the molecules were symmetrical one was *meso* and other racemic. In all these cases, however, the two points of restriction were on a single benzene nucleus as illustrated by the two 3,6-di-(3-bromo-2,4,6-trimethylphenyl)-2,5-dibromohydroquinones I and II. These substances were widely different in solubility. Compound II was resolved, while compound I resisted resolution.



I

trans-meso



II

cis-racemic

A study now has been made to determine the characteristics of molecules with two points of restricted rotation not as closely adjacent as in diphenyl benzenes. Such a molecule was conveniently prepared by condensation of isophthalyl chloride and 3-nitro-3′-aminobimesityl. Two diastereoisomers were isolated which may be assigned the formulas III and IV. It is thus evident that separation of the points of restricted rotation in a molecule does not alter the number of stereoisomers to be expected.

These isomers showed a marked difference in solubility; the higher-melting was six times as soluble in toluene as the lower-melting. A mixed melting point of 90% of the lower and 10% of the higher showed a depression.

The compound III may be divided into two identical halves (dotted line in III) and is therefore *meso*. The compound IV has no elements

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* Submitted in partial fulfilment of the requirements for the Degree of Doctor of Philosophy in Chemistry. Chemical Foundation Fellow, 1936–1938.

(1) For previous paper in this series see Adams and Snyder, THIS JOURNAL, **60**, 1411 (1938).

(2) Browning and Adams, THIS JOURNAL, **52**, 4098 (1930); Shildneck and Adams, *ibid.*, **53**, 343, 2203 (1931); Knauf, Shildneck and Adams, *ibid.*, **56**, 2109 (1934); Chang and Adams, *ibid.*, **56**, 2089 (1934).