acetate in acetic acid as condensing agent[5]; none of the condensation procedures catalyzed by alcoholic potassium hydroxide[6] and alcoholic methylamine,[7] were found suitable.

Experimental

4-Bromo-ω-nitrostyrene.—A mixture of 1 g. of 4-bromobenzaldehyde (m.p. 56°), 2 ml. of nitromethane and 0.2 g. of ammonium acetate in 20 ml. of glacial acetic acid was refluxed for 2 hours. The hot dark mixture was poured into 200 ml. of ice-cold water and allowed to stand 4 hours. The crude yellow product was collected, rinsed thoroughly with water and recrystallized from hot ethanol. Yellow small prisms, melting at 156–158°, were obtained, yield 700 mg. (56%).

Anal. Calcd. for $C_8H_6O_2NBr$ (228.04): N, 6.13. Found: N, 6.01.

4-Iodo-ω-nitrostyrene.—Using the same procedure as described above, 1 g. of 4-iodobenzaldehyde gave 916 mg. (75%) of small yellow needles of 4-iodo-ω-nitrostyrene, melting at 183–184°.

Anal. Calcd. for $C_8H_6O_2NI$ (275.04): N, 5.09. Found: N, 5.14.

Acknowledgment.—The authors express their thanks to Miss Beatriz Gomez for the microanalytical data, to Ing. Carlos Duhne for his encouragement and to Avelino Guerra for preparing the 4-iodobenzonitrile.

[5] (a) M. G. S. Rao, C. Strikantia and M. S. Iyengar, *Helv. Chim. Acta*, **12**, 581 (1924); (b) L. C. Raiford and D. E. Fox, *J. Org. Chem.* **9**, 170 (1944); (c) F. A. Ramirez and A. Burger, THIS JOURNAL, **72**, 2781 (1950); (d) C. B. Gairaud and G. R. Lapping, *J. Org. Chem.*, **18**, 1 (1953); (e) J. H. Mason, *J. Chem. Soc.*, 200 (1953).

[6] J. Thiele, *Ber.*, **32**, 1293 (1899); (b) D. E. Worrall, "Organic Syntheses," Coll. Vol. 1, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 413.

[7] E. Knoevenagel and L. Walter, *Ber.*, **37**, 4502 (1904).

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The Anhydrous Chlorination of Thioesters and Related Compounds[1,2]

BY IRWIN B. DOUGLASS AND CHARLES E. OSBORNE

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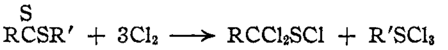
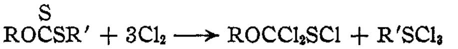
In continuing the study of the action of anhydrous chlorine on different types of organic sulfur compounds,[3] various thioesters and closely related compounds have been treated with anhydrous chlorine in liquid butane near the temperature of solid carbon dioxide. Compounds containing the thiol group are split between the acyl group and sulfur with the formation of an alkylsulfur trichloride from the thiol portion and an acyl chloride or some related compound from the other part of the molecule. When the compound chlorinated is a dithioester, in addition to the removal of the the thiol group as alkylsulfur trichloride, chlorine appears to add to the carbon–sulfur double bond of the thiocarbonyl portion to form a 1,1-dichloroalkanesulfenyl chloride. Alkoxy groups in xanthate esters, which may also be considered as being dithioesters, are not disturbed by the chlorination reaction under the conditions employed.

The following equations illustrate reaction types which have been found to occur and at least one example of each is described in the Experimental part.

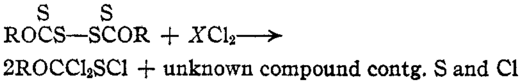
$$\mathrm{RCOSR' + 2Cl_2 \longrightarrow RCOCl + R'SCl_3} \quad (1)$$



$$\mathrm{R\overset{S}{C}SR' + 3Cl_2 \longrightarrow RCCl_2SCl + R'SCl_3} \quad (2)$$



$$\mathrm{RO\overset{S}{C}SR' + 3Cl_2 \longrightarrow ROCCl_2SCl + R'SCl_3} \quad (3)$$

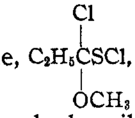


$$\mathrm{RO\overset{S}{C}S{-}S\overset{S}{C}OR + \mathit{X}Cl_2 \longrightarrow 2ROCCl_2SCl + unknown\ compound\ contg.\ S\ and\ Cl} \quad (4)$$

$$\mathrm{RSO_2SR' + 2Cl_2 \longrightarrow RSO_2Cl + R'SCl_3} \quad (5)$$

In equation 1 shown above, the immediate formation of solid $R'SCl_3$ after beginning the passage of chlorine indicates that reaction 1 takes place rapidly. If chlorination is interrupted, however, the solid alkylsulfur trichloride gradually disappears, presumably because a slower reaction takes place between the solid sulfur trichloride and the original thiol ester.

$$\mathrm{RCOSR' + R'SCl_3 \longrightarrow RCOCl + 2R'SCl} \quad (6)$$

An effort was made to study the action of chlorine on methyl thionpropionate, $C_2H_5CSOCH_3$. Reaction occurred and a white solid product with a chlorine content corresponding to $(C_2H_5CSOCH_3)Cl_2$ was formed, but the solid decomposed at 8° and the evolved gas appeared to consist more of chlorine than hydrogen chloride. One does not seem justified in concluding that the chlorination reaction produced 1-chloro-1-methoxypropane-1-sulfenyl chloride,  $\mathrm{C_2H_5\underset{OCH_3}{\overset{Cl}{C}}SCl}$, since the properties of analogous compounds described in this paper lead one to believe that such a compound would be a yellow liquid rather than the white solid obtained.

The formation of an alkylsulfur trichloride precipitate in a chlorination reaction affords a ready means for separating this product of the reaction provided the other product is soluble in liquid butane at the temperature employed.

Experimental Part

Preparation of Intermediates.—The thiol, xanthate and dithio esters, methyl methanethiolsulfonate and the bis-[alkoxythiocarbonyl] disulfides were prepared by standard methods.

Methyl thionpropionate was prepared by a modification of the method of Sakurada.[4] Absolute methyl alcohol, propionitrile and dry hydrogen chloride reacted to form methyl propionimidate hydrochloride. Dry pyridine was added to neutralize the hydrochloride, and hydrogen sulfide was passed into an ether solution of the free imino ether to form the thion ester. Difficulty was encountered in this preparation due to the tendency of the ester to hydrolyze and oxidize. In numerous attempts only a 10% yield was obtained.

Chlorination Procedure.—Ten grams of the ester was dissolved in approximately 50 ml. of liquid C.P. butane in a 30 × 200 mm. culture tube which was cooled in a bath containing solid carbon dioxide and acetone. A gentle stream of chlorine was led into the space above the liquid and was continued until, after alternately shaking and settling, no more solid appeared to form. The mixture was centri-

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[1] This represents a portion of the work done on Project NR-356-165 under Contract N8 onr 647(00) with the Office of Naval Research, United States Navy.

[2] Taken from the master's thesis of Charles E. Osborne.

[3] See I. B. Douglass, K. R. Brower and F. T. Martin, THIS JOURNAL, **74**, 5770 (1952), and preceding papers.

[4] Sakurada, *Mem. Coll. Sci. Kyoto*, **9**, 237 (1926); **10**, 79 (1926); *C. A.*, **21**, 2458, 3609 (1927).

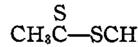
fuged, the liquid decanted into another cooled culture tube, and the solid was washed 2–3 times with butane and centrifuged as before. The combined centrifugates were again chlorinated to cause any ester previously trapped in the solid to react and the solid was removed. After being combined, the butane solutions were allowed to evaporate and the residue was distilled using an 18-in. Vigreux column. Evaporation of the butane tended to sweep out some of the more volatile chlorination products. It was found that this loss could be minimized by condensing the butane in a clean tube, again allowing it to evaporate and combining the residues before distillation.

Substances Chlorinated and Products Formed

1. **Methyl thiolbenzoate**, $C_6H_5COSCH_3$, yielded: (a) benzoyl chloride, b.p. 194–195°, 78–79° (15 mm.), n^{25}_D 1.5498, d^{25}_4 1.21 (86% yield); (b) methylsulfur trichloride, CH_3SCl_3. *Anal.* Calcd. for CH_3Cl_3S: Cl, 69.31. Found: Cl, 68.52, 70.17.

2. **Ethyl thiolacetate**, $CH_3COSC_2H_5$, yielded: (a) acetyl chloride, CH_3COCl; reacted readily with aniline to form acetanilide, m.p. 112°, mixed m.p. with an authentic sample 112°; (b) ethylsulfur trichloride, $C_2H_5SCl_3$. The white solid was hydrolyzed in cold sodium bicarbonate solution and the solution treated with benzyl chloride to form ethyl benzyl sulfone, $C_2H_5SO_2CH_2C_6H_5$, m.p. 84.5, mixed m.p. with authentic sample 84.5°.

3. **Methyl dithiopropionate**, $C_2H_5\overset{S}{C}—SCH_3$, yielded: (a) 1,1-dichloropropane-1-sulfenyl chloride, $C_2H_5CCl_2SCl$, yellow liquid, b.p. 69.5° (29 mm.), 65° (27 mm.), n^{25}_D 1.510; d^{25}_4 1.361, d^{0}_4 1.391 (27% yield). *Anal.* Calcd. for $C_3H_5Cl_3S$: Cl, 59.26; *MR*D 38.7; mol. wt., 179.5. Found: Cl, 59.64; *MR*D 39.4; mol. wt., 175.7. (b) Methylsulfur trichloride, CH_3SCl_3, which was hydrolyzed to sodium methanesulfinate and caused to react with benzyl chloride to form benzyl methyl sulfone, m.p. 126° and unchanged when mixed with an authentic sample.



4. **Methyl dithioacetate**, $CH_3\overset{S}{C}—SCH_3$, yielded: (a) yellow liquid boiling 46° (28 mm.), presumably methyldichloromethanesulfenyl chloride, CH_3CCl_2SCl, but which decomposed with the evolution of hydrogen chloride too readily to be purified; (b) methylsulfur trichloride which was identified as methyl benzyl sulfone.

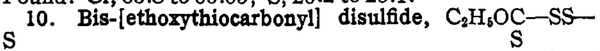
5. **Methyl methylxanthate**, $CH_3OCSSCH_3$, yielded: (a) methoxydichloromethanesulfenyl chloride, CH_3OCCl_2SCl, yellow liquid, b.p. 77° (35 mm.), 82° (40 mm.), n^{25}_D 1.518, d^{25}_4 1.522, d^{0}_4 1.555 (70% yield). *Anal.* Calcd. for $C_2H_3OCl_3S$: Cl, 58.62; S, 17.61; *MR*D 35.8; mol. wt., 185.1. Found: Cl, 59.06, 58.30; S, 17.4; *MR*D 36.2; mol. wt., 181.5; (b) methyl sulfur trichloride, CH_3SCl_3, identified as methyl benzyl sulfone as described above.

6. **Ethyl ethylxanthate**, $C_2H_5OCSSC_2H_5$, yielded: (a) ethoxydichloromethanesulfenyl chloride, $C_2H_5OCCl_2SCl$, yellow liquid, b.p. 88° (33 mm.), n^{25}_D 1.507, d^{25}_4 1.422, d^{0}_4 1.454. *Anal.* Calcd. for $C_3H_5OCl_3S$: Cl, 54.40; *MR*D 40.5; mol. wt., 195.5. Found: Cl, 54.55; *MR*D 40.9; mol. wt., 195.1. (b) Ethylsulfur trichloride, $C_2H_5SCl_3$. *Anal.* Calcd. for $C_2H_5Cl_3S$: Cl, 63.5. Found: Cl, 61.7, 62.2.

7. **Methyl 1-propylxanthate**, $CH_3CH_2CH_2OCSSCH_3$, yielded: (a) 1-propoxydichloromethanesulfenyl chloride, $CH_3CH_2CH_2OCCl_2SCl$, yellow liquid, b.p. 95.5° (26 mm.), n^{25}_D 1.498, d^{25}_4 1.353, d^{0}_4 1.383. *Anal.* Calcd. for $C_4H_7OCl_3S$: Cl, 50.77; *MR*D 45.1; mol. wt., 209.5. Found: Cl, 50.95; *MR*D 45.4; mol. wt., 203.1. (b) Methyl sulfur trichloride, CH_3SCl_3, identified by transforming to methyl benzyl sulfone.

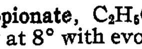
8. **Methyl 2-propylxanthate**, $(CH_3)_2CHOCSSCH_3$, yielded: (a) methylsulfur trichloride, CH_3SCl_3, identified by transforming to methyl benzyl sulfone; (b) a yellow liquid boiling 87° (25 mm.) and presumably 2-propoxydichloromethanesulfenyl chloride, $(CH_3)_2CHOCCl_2SCl$, but the product lost hydrogen chloride so readily that purification was impossible.

9. **Bis-[methoxythiocarbonyl] disulfide**, $CH_3O\overset{S}{C}S S\overset{S}{C}OCH_3$, yielded: (a) methoxydichloromethanesulfenyl chloride, CH_3OCCl_2SCl, yellow liquid, n^{25}_D 1.518 (53% yield); (b) a white solid of unknown identity melting with decomposition at 15° and hydrolyzing in water to give a sulfur-like yellow solid. The gases from the decomposition liberated iodine from potassium iodide. The original white solid was analyzed repeatedly but with inconsistent results. Found: Cl, 55.8 to 60.65; S, 20.2 to 25.1.



10. **Bis-[ethoxythiocarbonyl] disulfide**, $C_2H_5O\underset{S}{C}—SS—\overset{S}{C}OC_2H_5$, yielded: (a) ethoxydichloromethanesulfenyl chloride, $C_2H_5OCCl_2SCl$, yellow liquid, b.p. 83° (27 mm.), n^{25}_D 1.507, d^{25}_4 1.421; (b) a white solid of unknown identity, similar to that obtained from the chlorination of bis-[methoxythiocarbonyl] disulfide.

11. **Methyl methanethiosulfonate**, $CH_3SO_2SCH_3$, yielded: (a) methanesulfonyl chloride, CH_3SO_2Cl, which was allowed to react with aniline to form methanesulfonanilide, $CH_3SO_2NHC_6H_5$, m.p. 97–98° and unchanged when mixed with an authentic sample; (b) methylsulfur trichloride, CH_3SCl_3, which was identified by transformation to methyl benzyl sulfone.



12. **Methyl thionpropionate**, $C_2H_5\overset{S}{C}OCH_3$, yielded: a white solid, decomposing at 8° with evolution of a gas which fumed slightly in moist air but which also liberated iodine from potassium iodine–starch paper. *Anal.* Calcd. for $C_2H_5CSOCH_3Cl_2$: Cl, 44.57. Found: Cl, 44.2.

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The Reaction of 2,4-Dinitrobenzenesulfonic Acid with Free Amino Groups of Proteins

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In a previous communication[1] which dealt with the combination of a series of substituted 2,4-dinitrobenzenes with tissue proteins *in vivo*, it was reported that the sodium or potassium salts of 2,4-dinitrobenzene sulfonate formed a stable derivative *in vitro* with bovine gamma globulin. Because the reaction between this compound and protein may readily be carried out under conditions which cause little or no denaturation of many proteins, we have examined this reaction in greater detail.

Dinitrobenzene sulfonate reacts readily with bovine gamma globulin at *p*H 10–11 at room temperature; at *p*H 7, however, under otherwise similar conditions, protein is not derivatized after 24 hours. Since dinitrobenzene sulfonate is appreciably water soluble, the reaction may be carried out in an aqueous system, in which case the derivatized protein is soluble at *p*H 7.0 as well as at higher *p*H values.

The derivatization involves the splitting out of sulfonate and the substitution of dinitrophenyl in free NH_2 groups, yielding the same derivative as in the reaction with 2,4-dinitrofluorobenzene.[2] This conclusion is based upon evidence from three sources.

(1) Bovine gamma globulin was reacted with dinitrobenzene sulfonate and, after purification by extensive dialysis, the protein was hydrolyzed in 6 *N* HCl. After ether extraction, the hydrolysate was examined chromatographically on buffered silica gel columns.[2,3] A single yellow band was obtained with the same R_f as a sample of ε-dinitrophenyllysine prepared by the method of Porter and Sanger[4]; a mixed chromatogram of the latter

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[1] H. N. Eisen, L. Orris and S. Belman, *J. Exp. Med.*, **95**, 473 (1952).

[2] F. Sanger, *Biochem. J.*, **39**, 507 (1945).

[3] S. Blackburn, *ibid.*, **45**, 579 (1949).

[4] R. R. Porter and F. Sanger, *ibid.*, **42**, 287 (1948).