Chromosorb W at 150° with a carrier gas flow of 100 ml/min. Accurately weighed samples of pure di-*t*-butyl ketone and crotyldi-*t*-butylcarbinol were analyzed under the same conditions to determine the thermal conductivity correction factor. It was found that the area of the ketone peak had to be multiplied by 1.069 in order to arrive at correct relative per cent values.

Decomposition Reaction.—A mixture[5] of 71.2% *cis*- and 28.8% *trans*-crotyldi-*t*-butylcarbinol was placed in a 15-ml conical flask with a side arm to which a small Friedrichs condenser was attached. To the side arm was connected an open capillary tube with a ground-glass joint, the tip of the capillary being positioned below the surface of the alcohol mixture. At the top of the capillary was a rubber stopple through which a length of 3-mm glass tubing was attached *via* a bubbler to a tank of dry, purified nitrogen which was bubbled slowly through the reaction mixture during heating.

The flask containing the alcohols was lowered into a hot oil bath and that time taken as t_0. Samples were withdrawn at intervals of about 1 hr by puncturing the rubber stopple with a small hypodermic syringe, sliding the needle down through the capillary, and removing about 0.1 ml of the reaction mixture. Aliquots of exactly 4.0 μl were then subjected to vpc analysis, the total areas of ketone and alcohol peaks remaining constant within 2%. Thus it was concluded that no high-boiling products remained behind on the column.

This procedure was continued until the concentration of di-*t*-butyl ketone (bp 153°) became great enough that it was being lost through the condenser. This point was noted by the increase in the relative proportion of *cis*-crotyldi-*t*-butylcarbinol in the reaction mixture. The data are presented in Table I.

Registry No.—Crotyldi-*t*-butylcarbinol: *cis* isomer, 7634-94-8; *trans* isomer, 7634-95-9.

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[5] This mixture was obtained from the reaction of crotylmagnesium chloride with di-*t*-butyl ketone. Separation of the two isomers was effected by vpc (see conditions above). The infrared spectrum of the *cis* isomer showed absorption at 13.8 and no band at 10.3–10.4 μ, whereas the reverse was true for the *trans* isomer. *Anal.* Calcd for $C_{13}H_{26}O$: C, 78.72; H, 13.21. Found (*cis*): C, 78.45; H, 13.39. Found (*trans*): C, 78.20; H, 13.33.

Organic Disulfides and Related Substances. XXI. Sulfuryl Chloride in the Preparation of Thiolsulfonates from Disulfides[1a,b]

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The Douglass–Farah reaction for the preparation of aliphatic thiolsulfonates ($AlkSO_2SAlk$) affords an elegant and valuable synthesis for this class. It involves chlorinolysis of a disulfide in acetic acid and subsequent treatment with water.[2] In a recent communication we showed that this method could be extended to aromatic disulfides and thus is a good general route to symmetrical thiolsulfonates.[3] Since sulfuryl chloride has been used to convert disulfides and thiols to sulfenyl chlorides,[4] key intermediates in the Douglass–Farah reaction,[2] and since it is very easily handled, it presented a useful alternative to chlorine in the Douglass–Farah synthesis; there is also the prospect of greater flexibility in conditions than with a gas, and of useful differences in selectivity. The over-all reaction presumably occurs according to eq 1 and 2 (*cf.* ref 2).

$$\begin{aligned} &\mathrm{RSSR + AcOH + 2SO_2Cl_2} \longrightarrow \\ &\qquad\qquad \underbrace{\mathrm{RS(O)Cl + RSCl + AcCl}}_{\mathrm{2H_2O}\Big\downarrow} + \mathrm{HCl + 2SO_2} \qquad (1) \\ &\qquad\qquad \mathrm{RSO_2SR + AcOH + 3HCl} \qquad (2) \end{aligned}$$

Results are shown in Table I. To test the versatility of the procedure, the reactants were selected to be as diverse as possible in their illustration of various classes of sulfur compounds. No attempt was made to optimize conditions; hence it is likely that improvement in yields would be possible.

Preparation of *p*-tolyl *p*-toluenethiolsulfonate (**1**) shows that an aromatic thiol can be used. Oxidation of the thiol to the disulfide presumably occurs according to eq 3. The preparations of **1** and of *p*-nitrophenyl *p*-nitrobenzenethiolsulfonate (**2**) show that aromatic thiolsulfonates with either electron-donating or electron-attracting groups can be made. However, the low yield of **2** shows that sulfuryl chloride is less effective in this instance than chlorine (75% yield),[3] and thus its use should be considered an alternative to chlorine and not a substitute for it. Possibly the low yield of **2** is a consequence of lower electrophilic character of sulfuryl chloride than of chlorine toward the sulfur atom with its reduced basicity caused by the nitro group. The low yield of 21% with a 20% excess of sulfuryl chloride suggests that the yield might be further improved by a greater excess; pure **2** could not be isolated when no excess was used.

$$\mathrm{2RSH + SO_2Cl_2 \longrightarrow RSSR + 2HCl + SO_2} \qquad (3)$$

Ethyl ethanethiolsulfonate (**3**), a primary alkyl thiolsulfonate, and isopropyl 2-propanethiolsulfonate (**4**), a secondary alkyl thiolsulfonate, were made from the disulfides. However, the reaction shown in eq 4[5]

$$\mathrm{(RCH_2S)_2 + SO_2Cl_2 \longrightarrow 2RCH(Cl)SCl} \qquad (4)$$

conceivably could become troublesome in the preparation of certain alkanethiolsulfonates and is worth being kept in mind as a possible side reaction with alkyl disulfides.

Treatment of ethanethiol by the process using sulfuryl chloride also gave thiolsulfonate **3** in reasonable yield, showing the reaction can be extended to the use of alkanethiols as starting materials. However, treatment of 2-acetamidoethanethiol failed to give the

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[1] (a) This investigation was supported by the U. S. Army Medical Research and Development Command, Department of the Army, under Research Contract No. DA-49-193-MD-2030. Taken partly from the Ph.D. dissertation of J. D. B., Vanderbilt University, June 1966. (b) Paper XX: J. D. Buckman and L. Field, *J. Org. Chem.*, **32**, 454 (1967). (c) Du Pont Postgraduate Teaching Assistant, 1964–1965. (d) To whom correspondence should be addressed.

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[3] L. Field and T. F. Parsons, *ibid.*, **30**, 657 (1965).

[4] N. Kharasch, U. S. Patent 2,929,820 (1960); *Chem. Abstr.*, **54**, 15318 (1960).

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TABLE I

OXIDATION TO THIOLSULFONATES USING SULFURYL CHLORIDE

Thiolsulfonate no.	Reactant	Reactant, mole	Sulfuryl chloride, moles	Methylene chloride, ml	Acetic acid, mole	Water, mole	Product		Lit. mp or bp (mm), °C
							Yield, %[a]	Mp or bp (mm), °C	
1	p-$CH_3C_6H_4SH$	0.80	1.23	200	0.40	1.00	91	74–76	78.5–79.5[b]
2	$(p\text{-}NO_2C_6H_4S)_2$	0.02	0.048	10	0.02	0.04	21	181–183	180–180.5[c]
3	$(C_2H_5S)_2$	0.25	0.50	100	0.25	0.50	60	112 (5)	56 (0.2)[d]
	C_2H_5SH	0.50	0.75	100	0.25	0.62	47	132–134 (20)	*d*
4	$[(CH_3)_2CHS]_2$	0.25	0.50	100	0.25	0.50	66	82–83 (0.45)	96–97 (1–2)[e]
5	$(CH_2)_5CH(CH_2)_4NH_2^+$-$(CH_2)_2SSO_3^-$[f]	0.10	0.125	150	0.05	0.19	75[g]	195–196 dec[h]	
6	$(Cl^-H_3N^+CH_2CH_2S)_2$	0.03	0.06	100	0.03	0.06	67	162–164 dec	165–166[i]

[a] After recrystallization from a suitable solvent. [b] L. Field, *J. Am. Chem. Soc.*, **74**, 394 (1952). [c] G. Bulmer and F. G. Mann, *J. Chem. Soc.*, 680 (1945). [d] $n^{25}D$ found, 1.4980; bp and $n^{25}D$ of 1.4972, reported by L. D. Small, J. H. Bailey, and C. J. Cavallito, *J. Am. Chem. Soc.*, **71**, 3565 (1949). *Anal.* Calcd for $C_4H_{10}O_2S_2$: C, 31.14; H, 6.54. Found: C, 31.12; H, 6.44. [e] $n^{25}D$ found, 1.4885; bp and $n^{20}D$ of 1.4942, reported by B. G. Boldyrev and T. A. Trofimova, *Zh. Obshch. Khim.*, **27**, 1006 (1957); *Chem. Abstr.*, **52**, 3663 (1958). *Anal.* Calcd for $C_6H_{14}O_2S_2$: C, 39.53; H, 7.74. Found: C, 39.34; H, 7.61. [f] Kindly provided by Dr. T. R. Sweeney of the Walter Reed Army Institute of Research, Washington, D. C. [g] Based on the Bunte salt. However, SO_2Cl_2 or AcOH probably actually was the limiting reagent, so that the true yield probably actually exceeded 75%. [h] *Anal.* Calcd for $C_{24}H_{50}Cl_2N_2O_2S_2$, *i.e.*, $(CH_2)_5CH(CH_2)_4NH(CH_2)_2SO_2S(CH_2)_2NH(CH_2)_4CH(CH_2)_5\cdot 2HCl$: C, 54.01; H, 9.44; N, 5.25; S, 12.02. Found: C, 53.69; H, 9.52; N, 5.37; S, 11.85. [i] L. Field, T. C. Owen, R. R. Crenshaw, and A. W. Bryan, *J. Am. Chem. Soc.*, **83**, 4414 (1961).

corresponding thiolsulfonate (use of the corresponding disulfide also failed with chlorine).[6] To test the possible preparation of a tertiary thiolsulfonate, *t*-butyl mercaptan was used; no pure product could be isolated and elementary sulfur precipitated, suggesting that C–S cleavage occurred, as happens with *t*-butyl disulfide which gives with chlorine *t*-butyl chloride at 0°F and 2-methyl-2-propanesulfenyl chloride at 80–90°F.[7]

The successful oxidation of the Bunte salt S-2-(4-cyclohexylbutylamino)ethylthiosulfuric acid to thiolsulfonate **5** is noteworthy, since Bunte salts are themselves often intermediates in the synthesis of disulfides; use of sulfuryl chloride thus offers a direct route to thiolsulfonates not requiring separate conversion to the disulfide. However, oxidation of the phosphate Bunte-type salt (**7**) gave only the corresponding disulfide (the low yield of 23% suggested that further effort with the disulfide was not worthwhile). The higher yield of 2-aminoethyl 2-aminoethanethiolsulfonate dihydrochloride (**6**) obtained by the use of sulfuryl chloride (67%) shows that this reagent can give better results than chlorine, since use of chlorine gave only a 23% yield.[6]

$$H_2N(CH_2)_3NH_2^+(CH_2)_2SPO_3^-\cdot H_2O$$

7

Solid products **1**, **2**, and **6** were characterized by identity of infrared spectra and by mixture melting point. The liquids (**3** and **4**) had physical constants in reasonable agreement with reported values, but were further characterized by elemental analyses and determination of purity (both were 98% pure) by thioalkylation of a thiol.[8] The infrared spectra of all compounds showed strong bands at about 1150 and 1340 cm^{-1}, characteristic of thiolsulfonates.[9]

Experimental Section[10]

General Procedure for Preparing Thiolsulfonates.—The general method can be exemplified by the oxidation of *p*-toluenethiol to thiolsulfonate **1**. Other products were prepared similarly except for the different amounts of reagents specified in Table I.

Sulfuryl chloride (166 g, 1.23 moles)[11] was added over a 3-hr period to a rapidly stirred solution (or suspension, for certain other compounds) of *p*-toluenethiol (100 g, 0.80 mole) and acetic acid (24.0 g, 0.40 mole) in methylene chloride (200 ml) at 0 to −5°. The reaction mixture was allowed to warm to room temperature. Water (18 ml, 1.0 mole) then was added dropwise during 15 min, after which the heterogeneous mixture was stirred overnight. The methylene chloride solution was washed with three 100-ml portions of water, dried over anhydrous magnesium sulfate, and then evaporated to give 107 g (96%) of *p*-tolyl *p*-toluenethiolsulfonate (**1**), mp 72–74°. Recrystallization from cyclohexane (240 ml) gave 102 g (91%) of thiolsulfonate **1**, mp 74–76°, which had an identical infrared spectrum and undepressed mixture melting point with an authentic sample.

With the nitro compound (**2**), a solid appeared when the water was added. Solvent therefore was removed under vacuum and the residue was rubbed with methanol–chloroform–water (1:1:1), dried, and recrystallized from dioxane–ether.

In the conversion of cystamine dihydrochloride to **6** and of S-2-(4-cyclohexylbutylamino)ethylthiosulfuric acid to **5**, the procedures for isolation were slightly modified to avoid possibility of anion exchange with sulfuric acid present in the solution. With these, the reaction mixture was evaporated, and the residue was crystallized from an HCl (concentrated)–acetic acid mixture.

2-(3-Aminopropylamino)ethyl Disulfide Tetrahydrochloride.—2-(3-Aminopropylamino)ethylthiophosphonic acid hydrate (**7**, 23.1 g, 0.1 mole)[12] was treated as described for S-2-(4-cyclohexylbutylamino)ethylthiosulfuric acid. Crude product was obtained as a thick, viscous gum. Trituration with glacial acetic acid and crystallization from HCl (concentrated)–acetic acid gave colorless needles (4.7 g, 23%), mp 262° dec. Further crystallizations failed to alter the melting point.

Anal. Calcd for $C_{10}H_{30}Cl_4N_4S_2$: C, 29.13; H, 7.33; N, 13.59; S, 15.56. Found: 29.26; H, 7.38; N, 13.69; S, 15.60.

Registry No.—Sulfuryl chloride, 7791-25-5; **5**, 10027-64-2; 2-(3-aminopropylamino)ethyl disulfide tetrahydrochloride, 10027-65-3; **1**, 2943-42-2; **2**, 1041-15-2; **3**, 682-91-7; **4**, 10027-69-7; **6**, 10027-70-0.

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(7) W. A. Schulze, G. H. Short, and W. W. Crouch, *Ind. Eng. Chem.*, **42**, 916 (1950).

(8) D. Barnard and E. R. Cole, *Anal. Chim. Acta*, **20**, 540 (1959).

(9) J. Cymerman and J. B. Willis, *J. Chem. Soc.*, 1332 (1951).

(10) Melting points are corrected and boiling points are uncorrected. Elemental analyses were performed by Galbraith Microanalytical Laboratories, Knoxville, Tenn. Infrared spectra were obtained using a Perkin-Elmer Model 137B or a Beckman IR 10 spectrophotometer with liquids neat and with solids in Nujol mulls or KBr pellets.

(11) Purchased from Distillation Products Industries, Rochester, N. Y.

(12) Kindly provided by Dr. T. R. Sweeney of the Walter Reed Army Institute of Research, Washington, D. C.