346. *Reactions of Thiols with Tetra-alkylthiuram Disulphides and Related Compounds.*

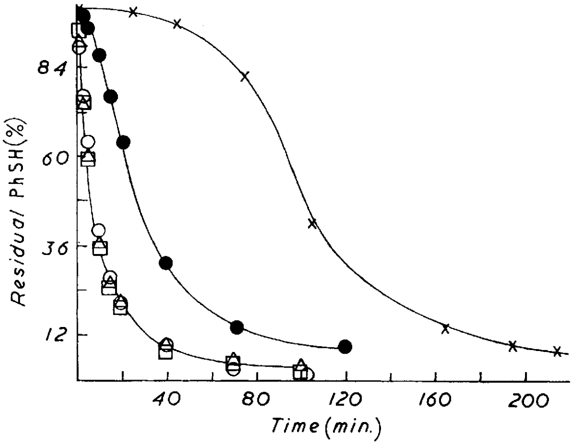
By B. Saville.

Thiols react with tetra-alkylthiuram disulphides at room temperature in solvents such as benzene, ethanol, or chloroform, yielding almost quantitatively dialkylammonium dialkyldithiocarbamate, carbon disulphide, and the disulphide derived from the thiol. The reaction between benzenethiol and tetraethylthiuram disulphide is autocatalytic as the dialkyldithiocarbamate formed is a basic catalyst of the primary reaction. Sodium salts of thiols interchange rapidly with tetra-alkylthiuram disulphides, giving sodium dialkyldithiocarbamates. The course of the reactions between a thiuram trisulphide and thiols seems less certain.

Dodecane-1-thiol has been reported[1] to react with tetramethylthiuram disulphide (TMT), to yield dodecyl disulphide, dimethylammonium dimethyldithiocarbamate, and carbon disulphide according to the equation (R = dodecyl):

$$2RSH + Me_2N{\cdot}C(\colon S)S{\cdot}S(\colon S)C{\cdot}NMe_2 \longrightarrow RS{\cdot}SR + Me_2\overset{+}{N}H_2\ \overset{-}{S}{\cdot}CS{\cdot}NMe_2 + CS_2 \quad . \ . \ . \ . \quad (i)$$

Although experimental details were not given it can be concluded, from analytical studies by Scheele and Gensch,[2] that the reaction is quantitative under mild conditions. For reaction of a number of thiols with tetramethyl- and tetraethyl-thiuram disulphide and certain related compounds, we have found two, apparently general, related reactions, namely: direct reaction of the thiol with the tetra-alkylthiuram disulphide as in (i) (Me may be varied), at room temperature in solvents such as benzene, chloroform, ethanol, or light petroleum but slowly in acetic acid; and an interchange (ii) between the thiol anion and the tetra-alkylthiuram disulphide which occurs rapidly in polar solvents:



Reaction of tetraethylthiuram disulphide (0·025M) *with benzenethiol* (0·05M) *in* 20% (v/v) *acetic acid–ethanol at* 25°.

Catalysts: × *None.* ● 0·05M-*Sodium acetate.* ☐ 0·05M-*Diethylamine.* ○ 0·05M-*Triethylamine.* △ 0·025M-*Diethylammonium diethyldithiocarbamate.*

$$2RS^- + R'_2N{\cdot}C(\colon S)S{\cdot}S(\colon S)C{\cdot}NR'_2 \longrightarrow RS{\cdot}SR + 2R'_2N{\cdot}CS_2^- \quad . \ . \ . \ . \ . \ . \quad (ii)$$

Reactions (i) and (ii) are almost quantitative where R = Ph, CH_2Ph, p-$NO_2{\cdot}C_6H_4{\cdot}CH_2$, or p-$NH_2{\cdot}C_6H_4$, but there is limited evidence for the partial reversal of reaction (ii) when R = p-$NO_2{\cdot}C_6H_4$. This reversal is particularly evident in the reaction of tetrathionate ion (a special example of RS·SR = $^-O_3S_2{\cdot}S_2O_3^-$) with dialkyldithiocarbamate ions, when tetra-alkylthiuram disulphides and thiosulphate ions (*i.e.*, $RS^- = {}^-O_3S{\cdot}S^-$) are formed quantitatively.[3]

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[1] Craig, Davidson, Juve, and Geib, *J. Polymer Sci.*, 1951, **6**, 1.
[2] Scheele and Gensch, *Rubber Chem. Tech.*, 1957, **30**, 728.
[3] Saville, *J.*, 1959, 2749.

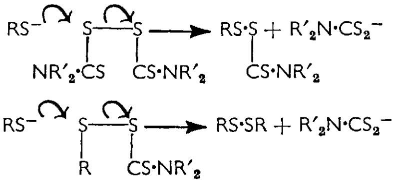
As an example of reaction (i), equivalent quantities of benzenethiol and tetra-ethylthiuram disulphide gave each of the three expected products in 98—100% yield. Reaction in ethanol is too fast to be measured conveniently, and in acetic acid it requires several days for completion, but in 20% (v/v) acetic acid in ethanol it can be measured conveniently. Delay before attainment of maximum rate suggests that one of the products is a catalyst. Adding diethylammonium diethyldithiocarbamate in low concentration to the initial mixture eliminates the induction period; diethylamine and triethylamine also do this but sodium acetate is only moderately effective (see Figure). Reaction (i) is thus interpreted as an ordinary thiol–disulphide interchange in which the hypothetical dialkyldithiocarbamic acid (I) stabilises itself as the equivalent combination of dialkylammonium dialkyldithiocarbamate and carbon disulphide:[4]

$$2RSH + R'_2N{\cdot}C(\!:\!S)S{\cdot}S(S\!:\!)C{\cdot}NR'_2 \longrightarrow RS{\cdot}SR + 2R'_2N{\cdot}CS_2H \quad (I)$$

$$2R'_2N{\cdot}CS_2H \longrightarrow R'_2\overset{+}{N}H_2\ \overset{-}{S}{\cdot}CS{\cdot}NR'_2 + CS_2$$

Since, in solution, this salt can act as a base (*e.g.*, iii) it could convert the thiol into a more nucleophilic entity (*e.g.*, a dialkylammonium mercaptide ion-pair) capable of effecting rapid S–S heterolysis:

$$NH_2R'_2{}^+[NR'_2{\cdot}CS_2]^- + RSH \rightleftharpoons R'_2\overset{+}{N}H_2\ \overset{-}{S}R + NR'_2{\cdot}CS_2H \quad \cdots\cdots\cdots \quad (iii)$$



Reaction between acetone and tetramethylthiuram disulphide[5] is kinetically similar and evidently base-catalysed, and is satisfactorily interpreted in terms of conversion of acetone by bases into reactive nucleophilic intermediates which again effect S–S heterolysis.

Some preliminary results on thiuram trisulphide are also reported. Although bismorpholinothioformyl trisulphide (II) and benzenethiol or toluene-ω-thiol gave morpholinium morpholine-1-carbodithioate according to the equation:

$$2RSH + \{O{<}[CH_2{\cdot}CH_2]_2{>}N{\cdot}C(\!:\!S){\cdot}S{-}\}_2S \longrightarrow O{<}[CH_2{\cdot}CH_2]_2{>}NH_2{}^+\ {}^-S_2C{\cdot}N{<}[CH_2{\cdot}CH_2]_2{>}O + CS_2 + RS{\cdot}S{\cdot}SR$$
(II)

the expected diphenyl and dibenzyl trisulphides were impure and may have been mixtures of disproportionation products. These materials, on treatment with alcoholic sodium cyanide, readily gave the corresponding disulphides and thiocyanate ion.

EXPERIMENTAL

Materials.—Thiols. Toluene-ω-thiol, toluene-*p*-thiol, benzenethiol, mercaptoacetic acid, and *o*-aminobenzenethiol were commercial specimens redistilled before use. *p*-Nitrotoluene-ω-thiol was made by alkaline hydrolysis of *S*-*p*-nitrobenzylthiuronium chloride[6] in the presence of a trace of sodium cyanide as antioxidant, or hydrolysis of *S*-*p*-nitrobenzyl thiosulphate[7] in 6N-hydrochloric acid overnight at room temperature. Both products, crystallised from aqueous methanol, had m. p. 52—53°. Attempts to make *p*-aminotoluene-ω-thiol by reduction of *p*-nitrotoluene-ω-thiol or of di-*p*-nitrobenzyl disulphide in acetic–hydrochloric acid with zinc dust gave only uncharacterised red compounds. *p*-Nitrobenzenethiol was obtained as the sodium salt[8] and converted into the free thiol (m. p. 75°; from ethanol) by hydrochloric acid.

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[4] Bedford and Gray, *Ind. Eng. Chem.*, 1923, **15**, 720.
[5] Robinson, Craig, and Fowler, *Canad. J. Chem.*, 1956, **34**, 1596, 1601.
[6] Momose and Tanaka, *Pharm. Bull.* (*Japan*), 1954, **2**, 152; *Chem. Abs.*, 1955, **49**, 11,501.
[7] Price and Twiss, *J.*, 1909, **95**, 1727.
[8] Waldron and Reid, *J. Amer. Chem. Soc.*, 1923, **45**, 2401.

p-Aminobenzenethiol was first made by the reduction[9] of *p*-thiocyanatoaniline (obtained in only 25% yield by Kaufmann's method[10]) by sodium sulphide. A better procedure was that of Kurihara, Ro, and Chiba,[11] modified to give the thiol hydrochloride which crystallised in needles, m. p. 207—208° (99% pure by titration with iodine) from 10% aqueous hydrochloric acid.

Thiuram sulphides. Tetramethylthiuram disulphide and tetraethylthiuram disulphide were purified as previously.[3] Bispiperidinothioformyl disulphide, purified commercial material, had m. p. 118—120°. Bismorpholinothioformyl disulphide was made by oxidising an aqueous solution of morpholinium morpholine-1-carbodithioate [from morpholine (2 mols.) and carbon disulphide (1 mol.) in light petroleum (b. p. 40—60°) at 0°] with potassium ferricyanide at 50°. The precipitated product was washed several times with warm water, dried, and recrystallised twice from chloroform–ethanol as light-yellow plates, m. p. 145° (Found: C, 37·0; H, 5·0. Calc. for $C_{10}H_{16}N_2O_2S_4$: C, 37·0; H, 4·9%). The trisulphide (II) was synthesised by Blake's method.[12]

Solvents.—Apart from methanol and ethanol, which were dried by the conventional magnesium–iodine procedure, all solvents were "AnalaR" materials redistilled before use.

Direct Reactions between Thiols and Thiuram Sulphides.—General procedures. (A) For water-immiscible solvents. Solutions of the thiol and of the thiuram sulphide in the appropriate solvent, usually at 30—40°, were mixed under nitrogen. After 1 hr., unless otherwise stated, the mixtures were cooled to 10°. In most experiments light petroleum (b. p. 40—60°) (twice the volume of the reaction mixture) was then added, precipitating the bulk of the dialkylammonium dialkyldithiocarbamate which was removed, washed with a little light petroleum, and dried. More of this was extracted from the filtrate with water (2 × 50 ml. per 0·01 mole of original thiuram sulphide) and determined gravimetrically as the lead or zinc salt which was precipitated quantitatively upon the addition of excess of aqueous lead or zinc acetate.

Carbon disulphide in the organic layer from the extraction above was most conveniently determined by distilling it into ice-cold 30% v/v aqueous diethylamine (30 ml. per 0·01 mole of original thiuram sulphide), the original solvent being continuously replaced by ethanol. The distillate then consisted of two layers: the aqueous one contained diethyldithiocarbamate ion equivalent to the carbon disulphide distilled over. Addition of excess of aqueous ammoniacal copper sulphate gave copper diethyldithiocarbamate which was determined gravimetrically. [Copper diethyldithiocarbamate is usually precipitated in a very fine form which makes washing and drying of the filtered product difficult. The aqueous suspensions were therefore heated on a water-bath for 1 hr. after addition of chloroform (5—10 ml.).] Removal of solvent from the distillation residue gave the disulphide corresponding to the thiol taken; this was usually fairly pure, but yields were noted only for recrystallised products for which satisfactory analytical and m. p. data had been obtained.

(B) For water-miscible solvents. After the thiol and thiuram sulphide had been allowed to react in the solvent (total volume *ca.* 50—100 ml. per 0·01 mole of original thiuram sulphide) the mixture was cooled to 10° and an equal volume of water added. The crude disulphide corresponding to the thiol taken was then filtered off, washed with a little aqueous ethanol, dried, and recrystallised. The filtrate and washings were combined and extracted with light petroleum (50 ml.) to remove traces of disulphide before the addition of an excess of aqueous zinc acetate to precipitate the zinc dialkyldithiocarbamate equivalent to the dialkylammonium dialkyldithiocarbamate present. The zinc salt was redissolved in hot chloroform, the solution filtered, and solvent removed. This procedure invariably gave an analytically pure product. Carbon disulphide was not determined in this procedure.

The results obtained for several examples of these procedures are submitted in Table 1.

Reactions of Bismorpholinothioformyl Trisulphide in Benzene.—Procedure A was used. The products from benzenethiol (0·02 mole) and the trisulphide (3·56 g., 0·01 mole) were morpholinium morpholine-1-carbodithioate (I) (2·48 g., 99%) and a substance, m. p. 36—39° (2·54 g.), believed to be diphenyl trisulphide. This was evidently impure (Found: C, 59·2; H, 4·1; S, 36·1.

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[9] Clayton and Bann, B.P. 546,279/1942.

[10] Kaufmann, *Ber.*, 1929, **62**, 390.

[11] Kurihara, Ro, and Chiba, *J. Pharm. Soc. Japan*, 1953, **73**, 725.

[12] Blake, *J. Amer. Chem. Soc.*, 1943, **65**, 1267.

Calc. for $C_{12}H_{10}S_3$: C, 57·6; H, 4·0; S, 38·4%) but gave diphenyl disulphide, m. p. and mixed m. p. 59—60° (1·07 g., 90% from 1·37 g. of substance), on treatment with sodium cyanide (0·4 g.) in ethanol (10 ml.). Thiocyanate ion (Fe^{3+} test) was also formed but not determined.

A similar experiment with toluene-ω-thiol gave the salt (I) (100%), carbon disulphide (76%), and impure dibenzyl trisulphide (Found: C, 62·2; H, 5·1; S, 32·2. Calc. for $C_{14}H_{14}S_3$: C, 60·4; H, 5·04; S, 34·6%). The trisulphide gave dibenzyl disulphide, m. p. and mixed m. p. 69—70° (85%), on treatment with alcoholic sodium cyanide.

Reactions of Salts of Thiols with Thiuram Sulphides.—No simple procedure can be given but the following approach, with individual modifications, was adopted. An alcoholic solution of the sodium derivative of the thiol was prepared by mixing the equivalent quantity of sodium alkoxide with the thiol in order to establish the equilibrium, $RSH + R'O^- \rightleftharpoons RS^- + R'OH$. To this solution, under nitrogen, was added the thiuram disulphide in warm alcohol, and after a few minutes the mixture was cooled and water was added. The disulphide derived from the

TABLE 1. *Direct reaction of thiols with thiuram disulphides.*

Thiol		Thiuram disulphide			Products						
					$XH_2^+[X{\cdot}CS_2]^-$						
					Precipd.			Dissd.	CS_2	RS·SR	
R in RSH	Mole	X in $[X{\cdot}CS_2]_2$	Mole	Sol-vent[a]	M. p.	(%)		(%)	(%)	M. p.	(%)
Ph[b]	0·04	Me_2N	0·02	B 50	125°	93		6	96	60°	99
Ph	0·04	Et_2N	0·02	B 50	80—81	48		51	95	60	98
Ph	0·02	Et_2N	0·01	L 150	81	89		n.d.	97	60	100
Ph	0·04	Et_2N	0·02	M 25	—	—		100	n.d.	60	99
Ph	0·02	Mor[c]	0·01	B 50	Subl.	98		n.d.	—	59—60	99
Ph[d]	0·02	,,	0·01	B 50	>150	99		n.d.	—	59—60	99
CH_2Ph	0·02	Me_2N	0·01	B 50	—		99		80—84[e]	68—69	97
CH_2Ph	0·02	Et_2N	0·01	B 50	81	77		n.d.	n.d.	69—70	96
p-$NO_2{\cdot}C_6H_4{\cdot}CH_2$	0·02	Me_2N	0·01	B 50	—		99		97	126·5	91
p-$NO_2{\cdot}C_6H_4{\cdot}CH_2$	0·02	Me_2N	0·01	C 60	—		86		75	126·5	95
p-$NH_2{\cdot}C_6H_4$	0·02	Et_2N	0·01	B 30	80—81	92		n.d.	n.d.	92—93	91
o-$NH_2{\cdot}C_6H_4$	0·02	Et_2N	0·01	B 30	—	—		—	—	75—76	94

[a] B, L, M and C denote respectively benzene, light petroleum (b. p. 60—80°), methanol, and chloroform. The number following is volume (ml.). [b] Typical elemental analyses on the products for this expt. are as follows: $Me_2NH_2^+Me_2N{\cdot}CS_2^-$: Found: C, 36·1; H, 8·5; S, 38·6. Calc.: C, 36·2; H, 8·4; S, 38·6%. $(Me_2N{\cdot}CS_2)_2Pb$: Found: C, 16·3; H, 2·6. Calc.: C, 16·1; H, 2·7%. $(Et_2N{\cdot}CS_2)_2Cu$ (eq. to CS_2): Found: C, 33·5; H, 5·5. Calc.: C, 33·4; H, 5·6%. PhS·SPh: Found: C, 65·9; H, 4·6; S, 29·3. Calc.: C, 66·0; H, 4·6; S, 29·4%. [c] Morpholino. [d] In this expt. morpholine (0·022 mole) was added to the reaction after 1 hr. to convert the CS_2 into further $XH_2^{+-}S_2C{\cdot}X$. The total yield of the latter was calculated from eq. (i) together with $2XH + CS_2 \longrightarrow XH_2^+\,{}^-S_2C{\cdot}X$. This gives convincing evidence for the quantitative formation of CS_2. [e] CS_2 probably not completely determined in these experiments. n.d. = not determined.

TABLE 2. *Reaction of thiol salts* (RS^-M^+) *with thiuram sulphides.*

Thiol salt			Thiuram disulphide			Products		
						$X{\cdot}CS_2^-$	RS·SR	
R	M^+	Mole	X in $[X{\cdot}CS_2]_2$	Mole	Solvent[b]	(%)	M. p.	(%)
Ph	Na^+	0·02	Me_2N	0·01	M 40	100[c]	60°	97
Ph	Na^+	0·02	Et_2N	0·01	E 50	99[d]	60	98
p-$NO_2{\cdot}C_6H_4$	Na^+	0·002	Et_2N	0·001	E 20	92[d]	181	92
p-C_6H_4Me	$C_5H_{10}{\cdot}NH_2^+$	0·02	Mor[g]	0·01	B 50	85·5[e] + 11·5[c]	46	97

[a] In a small-scale qualitative experiment it was shown that di-β-naphthyl disulphide (m. p. 139°) is rapidly precipitated on mixing of methanolic solutions of tetramethylthiuram disulphide and the sodium salt of β-naphthalenethiol. [b] M, E, and B denote respectively methanol, ethanol, and benzene. The number following is volume (ml.) used. [c] Isolated as Zn^{++} salt. [d] Isolated as Pb^{++} salt. [e] Isolated as piperidinium salt formed directly during reaction. [f] In a complementary experiment it was found that a yellow colour resulted on adding solid $NaS{\cdot}CS{\cdot}NEt_2$ to a saturated ethanolic solution of di-p-nitrophenyl disulphide. This colour was probably due to p-nitrobenzenethiol ion and indicates minor reversal of reaction (ii). [g] Morpholino.

thiol taken was usually isolated by filtration and purified. The filtrate contained sodium dialkyldithiocarbamate which was determined gravimetrically as the zinc derivative. The piperidine salt of toluene-*p*-thiol was soluble in benzene and the reaction with the thiuram sulphide was performed essentially by method A except that the distillation for carbon disulphide did not apply. For the examples of Table 2, product yields were calculated on the basis of equation (ii).

Disodium Mercaptoacetate and Tetraethylthiuram Disulphide.—The technique was different in this case. To a solution of sodium (4·6 g., 0·2 g.-atom) in methanol (100 ml.) was added mercaptoacetic acid (9·21 g., 0·1 mole), followed by the disulphide (14·8 g., 0·05 mole) in hot methanol (50 ml.). After cooling, disodium dithio(diacetate), $(\cdot S\cdot CH_2\cdot CO_2Na)_2$, was filtered off, dissolved in water (100 ml.), and treated with concentrated sulphuric acid (7 ml.). Extraction with ether (3 × 100 ml.) gave crude dithio(diacetic acid) (6·74 g.) which, recrystallised from benzene–acetic acid, had m. p. 105—106° (Found: C, 26·3; H, 3·4; S, 34·8. Calc. for $C_4H_6O_4S_2$: C, 26·4; H, 3·3; S, 35·2%). The first methanol filtrate, on treatment with zinc sulphate (17·3 g., 0·06 mole) in water (100 ml.), gave a precipitate which was washed, dried, and redissolved in hot chloroform. The chloroform solution on evaporation to dryness gave zinc diethyldithiocarbamate, m. p. and mixed m. p. 176—177° (17·02 g.), equivalent to a 94·5% yield of sodium diethyldithiocarbamate. The aqueous filtrate from the zinc salt was combined with the aqueous phase from the ether-extraction and treated with zinc dust (10 g.) to reduce any soluble dithio(diacetic acid) to mercaptoacetic acid, which was estimated iodometrically. This analysis corresponded to 0·702 g. of original dithiodiacetic acid. Thus the total dithiodiacetic acid accounted for in this experiment is 6·74 + 0·70 = 7·44 g. (82%). The reason for this low recovery is obscure. Further experiments gave no better yields.

Kinetic Examination of the Reaction between Benzenethiol and Tetraethylthiuram Disulphide.—In preliminary experiments it was shown that benzenethiol (up to 0·0005 mole) can be accurately determined in mixtures with diethylammonium diethyldithiocarbamate and diphenyl disulphide dissolved in ethanol or glacial acetic acid (25 ml.) by dissolution in a mixture of water (80 ml.), glacial acetic acid (19 ml.), and concentrated hydrochloric acid (1 ml.) and titration with 0·1N-iodine to a starch end-point (the acid solvent instantly decomposes diethyldithiocarbamate ions which would otherwise react with iodine). The iodine titre for constant quantities of benzenethiol added to this solvent containing various suspended quantities of tetraethylthiuram disulphide was unchanged for at least 30 min., *i.e.*, thiol–disulphide reaction is effectively stopped in this solvent.

Suitability of Solvents.—Only water-miscible solvents were considered. Equal volumes of 0·1M-benzenethiol and 0·05M-tetraethylthiuram disulphide in ethanol were combined under nitrogen at room temperature. At intervals, aliquot parts (10·0 ml.) were removed and added to the titrating solvent (100 ml.) to stop the reaction and were then titrated with 0·1N-iodine. The reaction was approximately 50% and 96% complete in 1 and 3 min. respectively. In glacial acetic acid no reaction was detectable in 2 hr.

Final procedure. Solutions of benzenethiol (0·1M) and tetraethylthiuram disulphide (0·05M) were made up separately in freshly prepared 20% (v/v) acetic acid in ethanol containing, in some cases, basic catalysts. They were allowed to reach thermal equilibrium in a thermostat at 25°, then equal volumes were mixed under nitrogen. Aliquot parts (10·0 ml.) of the mixture were removed at intervals, added to cold titrating solvent (100 ml.), and titrated with 0·1N-iodine to determine residual thiol. The reaction was followed to about 98% completion. Results are given graphically in the Figure.

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