# Synthesis of Unsymmetrical Disulphides

By **D. A. Armitage,* M. J. Clark, and C. C. Tso,** Department of Chemistry, Queen Elizabeth College, Atkins Building, Campden Hill, London W8 7AH

The synthesis of unsymmetrical disulphides by cleaving sulphenamides and sulphenic esters with alkyl- and aryl-thiosilanes and thiols is reported. Alkyl phenyl disulphides and unsymmetrical diaryl disulphides can be prepared conveniently and in 80—90% yield by the interaction of methyl benzenesulphenate and a thiol. Unsymmetrical dialkyl disulphides result from dimethyl or diethyl disulphide and a thiol.

THE synthesis of unsymmetrical disulphides usually involves the oxidation of a mixture of thiols, or the rearrangement of two disulphides.[1] Yields are low, but can be improved if a sulphenyl chloride and a thiol, or its sodium derivative are used. n-Butyl phenyl disulphide was obtained in 60% yield from benzenesulphenyl chloride and n-butanethiol, but allyl phenyl disulphide proved elusive,[2] probably because of the ready addition of the chloride to the double bond.[3]

The role of sulphenamides in rubber technology has stimulated interest in their reactions; notably, unsymmetrical disulphides are formed with thiols.[4] They also result from methyl benzenesulphenate and the esters of thioboric, thioboronic, and thioborinic acids,[5] and from 2,4-dinitrobenzenesulphenyl chloride and tin–sulphur compounds.[6]

Low yields of ethyl phenyl disulphide result from ethylthiotrimethylsilane and *NN*-dimethylbenzenesulphenamide [7] or benzenesulphenyl chloride.

$$\mathrm{PhSX + Me_3Si{\cdot}SEt \longrightarrow PhS{\cdot}SEt + Me_3SiX}$$
$$\mathrm{(X = Cl\ or\ NMe_2)}$$

Benzenethiol cleaves the sulphur–nitrogen bond in sulphenamides exothermically, and methyl n-propyl disulphide is formed from n-propanethiol and *NN*-diethylmethanesulphenamide.

$$\mathrm{RS{\cdot}NEt_2 + PhSH \longrightarrow RS{\cdot}SPh + Et_2NH}$$
$$\mathrm{(R = Me\ or\ Ph)}$$
$$\mathrm{MeS{\cdot}NEt_2 + Pr^nSH \longrightarrow MeS{\cdot}SPr^n + Et_2NH}$$

The reaction of methyl benzenesulphenate with alkyl- and aryl-thiosilanes gives high yields of the disulphides. The formation of low-boiling methoxytrimethylsilane assists separation in this strongly thermodynamically favoured reaction.

$$\mathrm{PhS{\cdot}OMe + RS{\cdot}SiMe_3 \longrightarrow PhS{\cdot}SR + Me_3Si{\cdot}OMe}$$
$$\mathrm{(R = Et\ or\ Ph)}$$

However, the most convenient synthetic route to alkyl aryl disulphides involves the reaction of the sulphenate ester with the thiol directly. All the reactions are exothermic and yields of the disulphides are high. Allyl phenyl disulphide can be conveniently prepared by this method.

$$\mathrm{PhS{\cdot}OMe + RSH \longrightarrow PhS{\cdot}SR + MeOH}$$
$$\mathrm{(R = alkyl)}$$

A strongly exothermic reaction occurred between benzenethiol and methyl benzenesulphenate, to give methanol and disulphide in almost quantitative yields.

$$\mathrm{PhS{\cdot}OMe + PhSH \longrightarrow Ph_2S_2 + MeOH}$$

The isomeric tolyl and benzyl phenyl disulphides can all be prepared by the same method. These reactions were not strongly exothermic and the methanol, which slowly separated from the liquid disulphide, formed as the upper layer. With the alkyl aryl disulphides, it was completely miscible. The high-boiling disulphides prepared this way showed little tendency to disproportionate, unlike the diaryl disulphides prepared from *N*-arylthiophthalimides and thiols in boiling benzene.

$$\mathrm{PhS{\cdot}OMe + ArSH \longrightarrow PhS{\cdot}SAr + MeOH}$$
$$\mathrm{(Ar = \mathit{o}\text{-}, \mathit{m}\text{-}, or\ \mathit{p}\text{-}tolyl)}$$
$$\mathrm{PhS{\cdot}OMe + PhCH_2{\cdot}SH \longrightarrow PhS{\cdot}S{\cdot}CH_2Ph + MeOH}$$

---

[1] E. E. Reid, ' Organic Chemistry of Bivalent Sulphur,' vol. III, Chemical Publishing Co., Inc., New York, 1960, p. 367.

[2] G. Jacini and F. Lauria, *Gazzetta*, 1950, **80**, 762 (*Chem. Abs.*, 1952, **46**, 4499d).

[3] E. E. Reid, ' Organic Chemistry of Bivalent Sulphur,' vol. 1, Chemical Publishing Co. Inc., New York, 1958, p. 276.

[4] (*a*) K. S. Boustany and A. B. Sullivan, *Tetrahedron Letters*, 1970, 3547; (*b*) D. N. Harpp, D. K. Ash, T. G. Back, J. G. Gleason, B. A. Orwig, and W. F. VanHorn, *ibid.*, p. 3551.

[5] R. H. Cragg, J. P. N. Husband, and A. F. Weston, *Chem. Comm.*, 1970, 1701.

[6] J. L. Wardell and P. L. Clarke, *J. Organometallic Chem.*, 1971, **26**, 345.

[7] D. A. Armitage and M. J. Clark, *J. Organometallic Chem.*, 1970, **24**, 629.

While the medium is only weakly basic, the comparatively high acidity of arenethiols compared with aliphatic ones could account for this tendency, especially as high-boiling aliphatic disulphides can be readily prepared this way,

$$\textit{e.g. } N\text{-PhS-phthalimide} + p\text{-MeC}_6\text{H}_4\cdot\text{SH} \longrightarrow \text{Ph}_2\text{S}_2 + \text{PhS}\cdot\text{S}\cdot\text{C}_6\text{H}_4\text{Me-}p + (p\text{-MeC}_6\text{H}_4)_2\text{S}_2 \quad (\text{ratio } 1:5:1)$$

Allyl phenyl and *m*-tolyl phenyl disulphides appear not to have been previously reported; others have been tested as insecticides, acaricides, and rubber additives but not fully characterised.

The difficulties encountered in preparing the chlorides [8] and esters [9] of alkanesulphenic acids render the synthesis of asymmetrical dialkyl disulphides from either a laborious task.

The ready exchange between symmetrical disulphides in the presence of traces of thiol or a basic catalyst (*e.g.* NaSR) or photolytically provides a useful route to unsymmetrical dialkyl disulphides [10] and has been studied kinetically.[11] Prolonged heating of the product can result in rearrangement of the substituents and a lowering of the overall yield of the unsymmetrical product.[12] While direct oxidation of a mixture of thiols gives only low yields of the mixed compound,[13] stepwise oxidation with diethyl azodicarboxylate and two different thiols [14] separately produces the unsymmetrical disulphide in high yield.

Thiol exchange with dialkyl disulphides by use of alkanethiols occurs only slowly, but the unsymmetrical dialkyl disulphides are readily formed if small quantities of triethylamine are added. The thiol and disulphide are usually heated for a few hours with the disulphide in excess. The unsymmetrical disulphide is formed in high yield in this way, though significant rearrangement occurs if the compound is heated for several days.

$$\text{Me}_2\text{S}_2 + \text{RSH} \xrightarrow{\text{Et}_3\text{N}} \text{MeSH} + \text{MeS}\cdot\text{SR} \quad (\text{R} = \text{Bu}^{\text{n}} \text{ or } \text{Bu}^{\text{t}})$$

$$\text{R}_2\text{S}_2 + \text{PhCH}_2\cdot\text{SH} \xrightarrow{\text{Et}_3\text{N}} \text{RSH} + \text{RS}\cdot\text{SCH}_2\text{Ph} \quad (\text{R} = \text{Me or Et})$$

This is generally a poor synthetic route to alkyl aryl disulphides, with or without the catalyst, probably owing to the greater acidity of the arenethiols catalysing the rearrangement to the two symmetrical disulphides.

$$2\ \text{AlkylS}\cdot\text{SAryl} \xrightarrow{\text{ArylSH}} \text{Alkyl}_2\text{S}_2 + \text{Aryl}_2\text{S}_2$$

Methyl and ethyl phenyl disulphides can be made this way, though yields of *o*- and *m*-tolyl methyl disulphides are not high whether triethylamine is added or not.

$$\text{Me}_2\text{S}_2 + \text{ArSH} \longrightarrow \text{MeSH} + \text{ArS}\cdot\text{SMe} \quad (\text{Ar} = o\text{- or } m\text{-tolyl})$$

## EXPERIMENTAL

The alkylthiosilanes,[15] *NN*-dimethylbenzenesulphenamide,[16a] methyl benzenesulphenate,[16b] and *NN*-diethylmethanesulphenamide [17] were prepared by reported methods. The reactions were conducted under anhydrous conditions.

*Reaction of Benzenesulphenyl Chloride with Ethylthiotrimethylsilane.*—Benzenesulphenyl chloride (4·45 g) was slowly added to ethylthiotrimethylsilane (4·08 g, 1 mol. equiv.) with cooling. An exothermic reaction occurred and subsequent distillation gave trimethylchlorosilane (2·5 g, 75%) b.p. 58°, $n_D^{24}$ 1·3877; and ethyl phenyl disulphide [7] (2·45 g, 47%), b.p. 46° at 0·01 mmHg, $n_D^{24}$ 1·5989 (Found: C, 56·4; H, 5·85; S, 37·5. Calc. for $C_8H_{10}S_2$: C, 56·5; H, 5·88; S, 37·7%); the residual oil distilled up the column and solidified.

*Interaction of* NN-*Diethylbenzenesulphenamide with Benzenethiol.*—The sulphenamide (7·6 g) was added slowly to benzenethiol (4·6 g, 1 mol. equiv.) in xylene (20 cm³) with cooling. The solvent was then pumped off, leaving a pale yellow crystalline solid. This was washed with small amounts of benzene and acetone and recrystallised from acetone to give white crystals of diphenyl disulphide (6·3 g, 69%), m.p. 58—59° (Found: C, 66·5; H, 4·6. Calc. for $C_{12}H_{10}S_2$: C, 66·0; H, 4·6%).

*Interaction of* NN-*Diethylmethanesulphenamide with Benzenethiol.*—The sulphenamide (26·1 g) was added slowly to benzenethiol (24·1 g, 1 mol. equiv.) with cooling. The mixture was then heated and diethylamine (10·2 g, 63%), b.p. 56°, $n_D^{25}$ 1·3840, was collected. Distillation of the residue gave methyl phenyl disulphide (13·2 g, 39%), b.p. 64—66° at 0·01 mmHg, $n_D^{25}$ 1·6140. N.m.r. spectra confirmed the presence of the disulphide [τ 2·75 (5H, m, Ph) and 7·81 (3H ⊣, Me)], which exploded on attempted analysis. Its properties are in accord with those of an authentic sample prepared later.

*Interaction of* NN-*Diethylmethanesulphenamide with n-Propanethiol.*—The sulphenamide (5·2 g) and thiol (3·3 g, 1 mol. equiv.) were mixed and heated at 100° for 4 h. Distillation gave diethylamine (1·5 g, 47%), b.p. 56°, $n_D^{25}$ 1·3895, and various higher-boiling fractions containing dimethyl and di-n-propyl disulphides, methyl n-propyl disulphide, and unchanged starting materials. These were analysed by g.l.c., v.p.c., and n.m.r. spectroscopy; subsequent distillation of the middle fractions gave methyl n-propyl disulphide [18a] (2·6 g, 49%), b.p. 46—48° at 10 mmHg,

---

[8] I. B. Douglass, R. V. Norton, R. L. Weichman, and R. B. Clarkson, *J. Org. Chem.*, 1969, **34**, 1803.

[9] Ref. 3, pp. 267, 284.

[10] W. A. Proell, U.S.P. **2**,521,870 (*Chem. Abs.*, 1951, **45**, P8027f); M. Kleiman, U.S.P. 2,474,849 (*Chem. Abs.*, 1950, **44**, 653); U.S.P. 2,610,967 (*Chem. Abs.*, 1954, **48**, 8812); U.S.P. 2,510,893 (*Chem. Abs.*, 1951, **45**, 636b).

[11] G. Gorin, G. Dougherty, and A. V. Tobolsky, *J. Amer. Chem. Soc.*, 1949, **71**, 3551; A. Fava, A. Iliceto, and E. Camera, *ibid.*, 1957, **79**, 833.

[12] M. Kleiman, U.S.P. 2,510,893 (*Chem. Abs.*, 1951, **45**, 636b).

[13] C. J. M. Stirling, *J. Chem. Soc.*, 1957, 3597.

[14] T. Mukaiyama and K. Takahashi, *Tetrahedron Letters*, **1968**, 5907.

[15] E. W. Abel and D. A. Armitage, *Adv. Organometallic Chem.*, 1967, **5**, 1.

[16] Ref. 3, (*a*) p. 279; (*b*) p. 284.

[17] D. A. Armitage and M. J. Clark, *J. Chem. Soc.* (*C*), 1971, 2840.

[18] (*a*) W. A. Proell, U.S.P. 2,521,870 (*Chem. Abs.*, 1951, **45**, 8027f); (*b*) K. Bundo, R. Sugawara, and T. Muto, *Noyaku Seisan Gijutsu*, 1967, **18**, 1 (*Chem. Abs.*, 1968, **69**, 75,902d); (*c*) A. Jumer, P. Held, and W. Schultz, East Ger.P. 19,932 (*Chem. Abs.*, 1962, **56**, P3416b); (*d*) Japan Soda Co. Ltd., Jap.P. 15,646 (*Chem. Abs.*, 1963, **59**, P8071a).

$n_D^{25}$ 1·5050 (Found: C, 39·8; H, 8·4; S, 52·1. Calc. for $C_4H_{10}S_2$: C, 39·3; H, 8·2; S, 52·4%).

*Reaction of Trimethylphenylthiosilane with Methyl Benzenesulphenate.*—The sulphenate (0·73 g) was added slowly to the phenylthiosilane (0·95 g, 1 mol. equiv.) with cooling. The mixture was warmed for 1 h, and the methoxytrimethylsilane was pumped off (0·4 g, 74%), $n_D^{25}$ 1·3660. The crude residue of diphenyl disulphide (1·1 g, 96%) was recrystallised from ethanol–water, m.p. 60°.

TABLE 1

Disulphides from methyl benzenesulphenate and alkane thiols

| R in PhS·SR | Yield [g (%)] | B.p. [°C (mmHg)] | $n_D^{25}$ | Calc. (%) C | Calc. (%) H | Calc. (%) S | Found (%) C | Found (%) H | Found (%) S |
|---|---|---|---|---|---|---|---|---|---|
| Et * | 6·95 (84) | 48 (0·005) | 1·5980 | | | | | | |
| Pr$^n$ † | 11·20 (93) | 52 (0·01) | 1·5850 | 58·7 | 6·5 | 34·8 | 58·8 | 6·5 | 35·0 |
| Pr$^i$ ‡ | 10·0 (96) | 48—50 (0·01) | 1·5819 | 58·7 | 6·5 | 34·8 | 58·3 | 6·6 | 35·6 |
| Bu$^n$ | 7·8 (81) | 68 (0·005) | 1·5746 | 60·6 | 7·05 | 32·3 | 59·9 | 7·05 | 33·1 |
| Bu$^t$ † | 5·7 (94) | 48 (0·003) | 1·5714 | 60·6 | 7·05 | 32·3 | 60·7 | 7·0 | 32·5 |
| Allyl | 12·5 (66) | 75 (0·6) | 1·6021 | 59·3 | 5·5 | 35·2 | 59·5 | 5·6 | 34·2 |

* N.m.r. spectrum like that of sample obtained from PhSCl and EtS·SiMe$_3$. † Ref. 5. ‡ Ref. 18*b*.

TABLE 2

Disulphides from methyl benzenesulphenate and thiocresols or toluene-α-thiol

| R in PhS·SR | Yield (%) | B.p. [°C (mm)] | $n_D^{24}$ | Calc. (%) C | Calc. (%) H | Calc. (%) S | Found (%) C | Found (%) H | Found (%) S |
|---|---|---|---|---|---|---|---|---|---|
| *o*-Tolyl *† | 77 | 102 (0·01) | 1·6513 | 67·3 | 5·15 | 27·6 | 66·7 | 5·2 | 28·1 |
| *m*-Tolyl | 88 | 107 (0·01) | 1·6481 | | | | 67·04 | 5·1 | 27·7 |
| *p*-Tolyl † | 86 | 110 (0·005) | 1·6479 | | | | 67·1 | 5·05 | 27·8 |
| Benzyl ‡ | 87 | 112 (0·01) | 1·6429 | | | | 67·1 | 5·2 | 27·7 |

* Diphenyl disulphide was slowly precipitated from the forerun. † Ref. 18*c*. ‡ Ref. 18*d*.

TABLE 3

Reaction of disulphides with thiols

| R in RSH (wt. in g) | Me$_2$S$_2$ | Product | Time of heating | Wt. (g) | Yield (%) | MeS·SR b.p. [°C (mm)] | $n_D$ ($T$/°C) | Calc. (%) C | Calc. (%) H | Calc. (%) S | Found (%) C | Found (%) H | Found (%) S |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bu$^n$ (12·6) | Excess | MeS·SBu$^n$ [9] | 20 h | 15·5 | 90 | 58 (10) | 1·5008 (24) | 44·1 | 8·9 | 47·1 | 44·0 | 8·7 | 47·2 |
| Bu$^t$ (13·65) | Excess | MeS·SBu$^t$ [9] | 4 h | 16·5 | 81 | 70 (38) | 1·4973 (24) | 44·1 | 8·9 | 47·1 | 44·3 | 8·85 | 47·3 |
| PhCH$_2$ (11·15) | Excess | MeS·S·CH$_2$Ph [19] | 12 h | 11·8 | 77 | 64 (0·2) | 1·5996 (24) | 56·5 | 5·9 | 37·7 | 56·4 | 5·85 | 37·8 |
| Ph *† (12·0) | Excess | MeS·SPh [5] | 5 days | 12·35 | 72 | 60 (0·2) | 1·6148 (25) | | | | | | |
| *o*-Tolyl * (9·3) | Excess | MeS·S-*o*-tolyl ‡ | 3 days | 3·7 | 29 | 66 (0·1) | 1·6063 (24) | 56·5 | 5·9 | 37·7 | 56·4 | 5·95 | 37·9 |
| *o*-Tolyl (10·75) | Excess | MeS·S-*o*-tolyl ‡ | 2 h | 9·2 | 62 | 60 (0·2) | 1·6030 (28·5) | | | | | | |
| *m*-Tolyl * (9·2) | Excess | MeS·S-*m*-tolyl ‡ | 7 days | 3·5 | 40 | 58 (0·07) | 1·6040 (22) | 56·5 | 5·9 | 37·7 | 56·7 | 6·0 | 37·9 |
| *m*-Tolyl (9·2) | Equimolar | MeS·S-*m*-tolyl ‡ | 3 h | 6·5 | 52 | 60 (0·05) | 1·6026 (24·5) | | | | | | |
| PhCH$_2$ (7·3) | Et$_2$S$_2$ equimolar | EtS·S·CH$_2$Ph [13,14] | 2 h | 4·3 | 41 | 75 (1) | 1·5853 (23) | 58·7 | 6·55 | 34·8 | 58·6 | 6·65 | 34·9 |
| Ph *† (5·26) | Et$_2$S$_2$ § excess | EtS·SPh [7] | 3 days | 4·3 | 53 | 48 (0·04) | 1·5998 (23) | | | | | | |

* No catalyst used. † Properties identical with those of samples already characterised. ‡ Compound not previously reported. § EtSH (1·9 g, 66%), b.p. 34°, $n_D^{23}$ 1·4311, also obtained.

*Reaction of Ethylthiotrimethylsilane with Methyl Benzenesulphenate.*—The silane (4·5 g) and ester (4·7 g, 1 mol. equiv.) heated together, yielded methoxytrimethylsilane (2·4 g, 69%), b.p. 56—57°, $n_D^{25}$ 1·3662. Vacuum distillation of the residual oil gave ethyl phenyl disulphide (3·5 g, 62%), b.p. 77° at 0·8 mmHg, $n_D^{25}$ 1·5979.

*Reaction of Methyl Benzenesulphenate with Methanethiol.*—Methyl benzenesulphenate (9·6 g) was slowly added to an excess of methanethiol at −70°. An exothermic reaction occurred and after stirring for 1 h the mixture was allowed to warm to room temperature. After the excess of methanethiol had evaporated the methanol was pumped off; vacuum distillation of the residue gave methyl phenyl disulphide[5] (8·9 g, 89%) b.p. 52° at 0·005 mmHg, $n_D^{25}$ 1·6135 (Found: C, 53·9; H, 5·15; S, 41·0%. Calc. for $C_7H_8S_2$: C, 53·9; H, 5·1; S, 41·0%), τ 2·75br (5H, m) and 7·82 (3H, s).

*Reaction of Methyl Benzenesulphenate with Alkanethiols.*—The thiol (*ca.* 0·05 mol) was slowly added to the sulphenic ester (*ca.* 0·05 mol) with cooling. An exothermic reaction occurred, the methanol formed was pumped off, and the residual oil was distilled under vacuum. With prop-2-enethiol, a 50% excess of thiol was used. Details are given in Table 1; all the disulphides had characteristic n.m.r. spectra.

*Reaction of Methyl Benzenesulphenate with Benzenethiol.*—Benzenethiol (2·4 g) was slowly added to the ester (3·05 g, 1 mol. equiv.) with cooling. The reaction was exothermic; pumping and trapping yielded crude methanol (0·7 g, 99%) which was redistilled, b.p. 64°, $n_D^{25}$ 1·3265. The solid residue (4·7 g, 98%) was recrystallised from ethanol–

---

[19] W. L. Fierce and R. L. Weichman, U.S.P. 3,153,078 (*Chem. Abs.*, 1965, **62**, 488f).

water giving white needles of diphenyl disulphide, m.p. 59—60°.

*Reactions of Methyl Benzenesulphenate with the Thiocresols and Toluene-α-thiol.*—The thiol was added to an equimolar quantity of the ester. The mixture slowly became cloudy and was left for 1 week. Two layers formed. Pumping under vacuum removed the upper methanolic layer and distillation gave the disulphide. Details are in Table 2.

*Reaction of Disulphides with Thiols* (*Table* 3).—The unsymmetrical disulphides were prepared by heating the thiols with an excess of dimethyl disulphide or diethyl disulphide in the presence of triethylamine (1 ml) except where indicated. The mixtures were heated to constant weight then the disulphide mixture was vacuum distilled. Products had n.m.r. spectra in accordance with their structure; where possible, reference is made to previous reports of the compounds.

[1/1523 *Received*, 23*rd August*, 1971]