

General Synthesis of Symmetrical and Unsymmetrical Organic Sulphides under Non-basic Reaction Conditions¹

By A. Johan H. Labuschagne, Johan S. Malherbe, Cornelius J. Meyer, and David F. Schneider,
Chemistry Department, University of Stellenbosch, Stellenbosch 7600, Republic of South Africa

General syntheses of a variety of unsymmetrical methyl and ethyl sulphides, by treatment of the appropriate organic halides or the corresponding sulphonium salts with an excess of dimethyl or diethyl sulphide, are described. When organic halides are treated with the corresponding unsymmetrical methyl sulphides, symmetrical sulphides are produced *via* demethylation of the intermediate methylsulphonium salts by the halide ions.

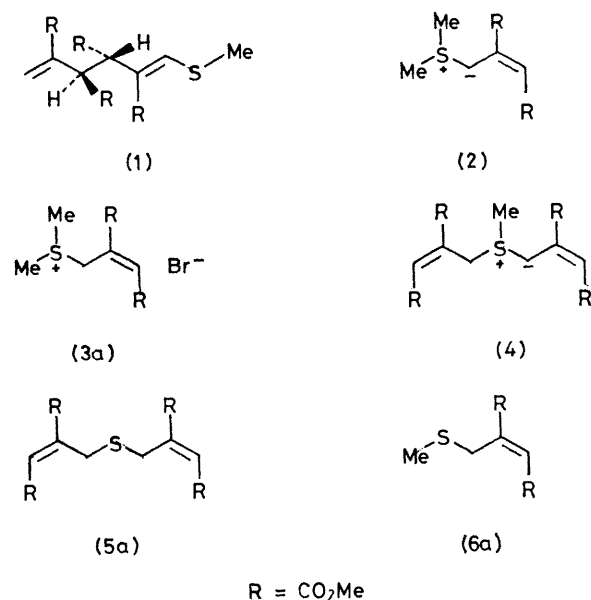
DURING our recent investigations² of the stereospecific formation of the vinyl sulphide (1) *via* Michael addition of the sulphonium ylide (2) to the sulphonium salt (3a), and the sigmatropic rearrangement of the bisallylic sulphonium ylide (4) and related sulphides, we had occasion to synthesize the sulphides (5a) and (6a) as key intermediates.

Symmetrical and unsymmetrical organic sulphides are most commonly synthesized by interaction of strongly basic thiolate anions and appropriate halogen compounds under a variety of reaction conditions.³ Sulphenylation of ester and carbonyl enolates⁴ and other stabilized carbanions⁵ by disulphides, sulphenyl chlorides, and elemental sulphur constitutes another general method for the synthesis of unsymmetrical sulphides. Other general methods include the conjugate addition of thiols to $\alpha\beta$ -unsaturated carbonyl compounds,⁶ free-radical addition of thiols to terminal olefins,⁷ the base-catalysed reaction of thiols with phosphate esters⁸ or dialkyl carbonates,⁹ and the condensation of alcohols utilizing either aminophosphonium salts¹⁰ or dicyclohexylcarbodi-imide.¹¹

Another commonly used general method for the synthesis of symmetrical sulphides comprises treatment of the appropriate organic halide with 0.5 mol. equiv. of sodium sulphide under a variety of conditions.¹² Symmetrical sulphides are also produced by treatment of enolizable substrates with sulphur dichloride.¹³

We regarded the easily accessible bromo-ester (7a) as an obvious starting material for the synthesis of the sulphides (5a) and (6a), but the sensitivity of (7a) to base rendered most of the above-mentioned procedures

unsuitable. The allylic sulphide (6a) could, however, be conveniently synthesized in quantitative yield under non-basic conditions by heating the corresponding dimethylsulphonium salt (3a) with an excess of dimethyl sulphide in Me₂SO. Other sulphonium salts could



equally effectively be demethylated by dimethyl sulphide to produce the corresponding unsymmetrical sulphides in high yield (Table 1). The sulphide (6a) could be synthesized even more conveniently by treatment of the bromo-ester (7a) directly with an excess of dimethyl sulphide (Scheme 1). This method was subsequently developed as a general synthesis for a variety of unsymmetrical alkyl and alkenyl sulphides. Mixtures of

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⁹ Y. Tamura, T. Saito, H. Ishibashi, and M. Ikeda, *Synthesis*, 1975, 641.

¹⁰ Y. Tanigawa, H. Kanamura, and S.-I. Murahashi, *Tetrahedron Letters*, 1975, 4655.

¹¹ E. Vowinkel and C. Wolff, *Chem. Ber.*, 1974, **107**, 496.

¹² (a) L. A. Paquette, R. E. Wingard, jun., J. C. Phillips, G. L. Thompson, L. K. Read, and J. Clardy, *J. Amer. Chem. Soc.*, 1971, **93**, 4508; (b) R. H. Schlessinger and I. S. Ponticello, *Tetrahedron Letters*, 1967, 4057; (c) H. Müller, *Angew. Chem. Internat. Edn.*, 1971, **10**, 652; (d) D. Landini and F. Rolla, *Synthesis*, 1974, 565.

¹³ (a) J. J. D'Amico and W. E. Dahl, *J. Org. Chem.*, 1975, **40**, 1224; (b) S. K. Gupta, *ibid.*, 1974, **39**, 1944.

¹ Preliminary report, A. J. H. Labuschagne, J. S. Malherbe, C. J. Meyer, and D. F. Schneider, *Tetrahedron Letters*, 1976, 3571.

² (a) C. F. Garbers, A. J. H. Labuschagne, C. J. Meyer, and D. F. Schneider, *J.C.S. Perkin I*, 1973, 2016; (b) A. J. H. Labuschagne, C. J. Meyer, H. S. C. Spies, and D. F. Schneider, *ibid.*, 1975, 2129; (c) C. J. Meyer and D. F. Schneider, *ibid.*, 1977, 1073.

³ (a) M. K. Kaloustian, N. Dennis, S. Mager, S. A. Evans, F. Alcludia, and E. L. Eliel, *J. Amer. Chem. Soc.*, 1976, **98**, 956; (b) A. W. Herriott and D. Picker, *Synthesis*, 1975, 447; (c) E. G. Wilson, jun., and J. G. Riley, *Tetrahedron Letters*, 1972, 379; (d) K. Mori and Y. Nakamura, *J. Org. Chem.*, 1969, **34**, 4170.

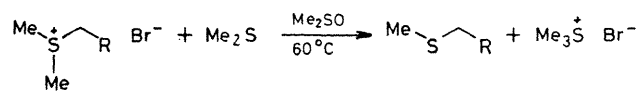
⁴ (a) B. M. Trost, T. N. Salzmann, and K. Hiroi, *J. Amer. Chem. Soc.*, 1976, **98**, 4887; (b) D. Seebach and M. Teschner, *Chem. Ber.*, 1976, **109**, 1601.

⁵ S. J. Slikson and D. S. Watt, *Tetrahedron Letters*, 1974, 3029.

⁶ (a) P. Grieco and M. Miyashita, *J. Org. Chem.*, 1975, **40**, 1181; (b) I. Kuwajima, T. Murofushi, and E. Nakamura, *Synthesis*, 1976, 602; (c) I. Vlattas and L. DellaVecchia, *Tetrahedron Letters*, 1974, 4459.

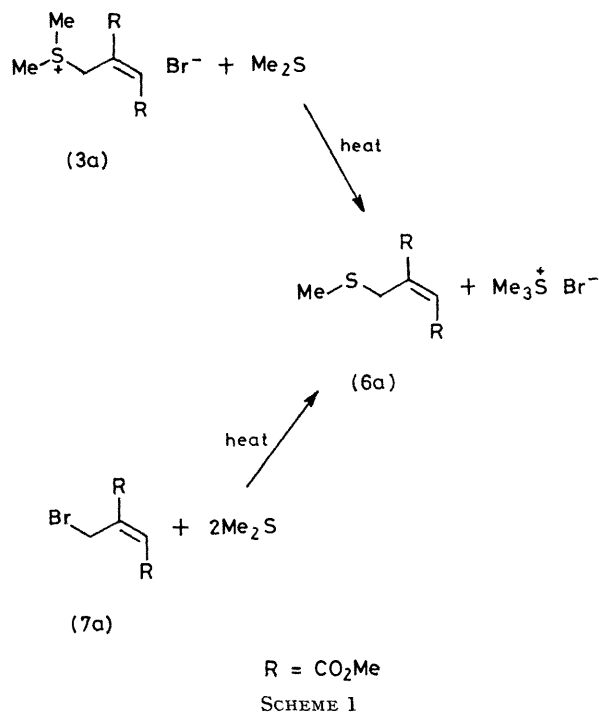
the appropriate halogen compounds (7a—g) and a four-fold molar excess of dimethyl or diethyl sulphide

TABLE 1



(3a—c) Sulphonium salt	R	(6a—c) Sulphide	Yield (%)
(3a)		(6a)	100
(3b)		(6b)	89
(3c)		(6c)	83

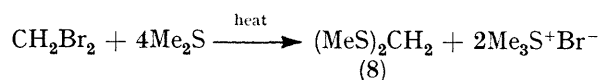
were heated in a Pyrex pressure vessel at 60 °C to produce the corresponding sulphides (6a—h) in excellent yields (Table 2).^{*} Only in the syntheses of (6g and h) did the utilization of Me₂SO as solvent appear to be



advantageous. The thioacetal (8) could also be synthesized in reasonable yield (65%) by heating dibromomethane with a 12-fold molar excess of dimethyl sulphide at a higher temperature (120 °C).

^{*} Pertinent to this general synthesis is the observation^{14a} that the sulphide (6b) and trimethylsulphonium bromide were undesirable by-products of Kornblum oxidation of ethyl bromoacetate. Ray and Levine^{14b} furthermore reported the unexpected formation of methyl phenylfluoren-2-ylmethyl sulphide instead of the corresponding dimethylsulphonium salt upon treatment of phenylfluoren-2-ylbromomethane with an excess of dimethyl sulphide.

Furthermore, diethyl (methylthio)malonate (6e) could be alkylated and sulphenylated under unusually mild conditions. When a mixture of the sulphide (6e), methyl iodide, and sodium hydrogen carbonate in



Me₂SO was stirred for 24 h at room temperature, the alkylated sulphide (9) was produced. In the absence of methyl iodide and at higher temperature (85 °C), however, diethyl bis(methylthio)malonate (10) was produced, evidently as the result of sulphenylation of the sulphur-stabilized anion (11) by the sulphide (6e) with concomitant formation of diethyl malonate (Scheme 2). This observation offers an alternative explanation for the formation of the bis-sulphide (10) as an undesirable by-product during the synthesis of the sulphide (6e) *via*

TABLE 2

Halide	R ¹	R ²	R ³	Time (h)	Sulphide	Yield (%)
(7a)	H		Me	12	(6a)	79 (ref. 2a)
(7b)	H		Me	24	(6b)	89
(7c)	H		Me	48	(6c)	94
(7d)	H		Me	24	(6d)	91
(7e)	CO ₂ Et	CO ₂ Et	Me	96	(6e)	83
(7f)	H	CO ₂ Et	Et	72	(6f)	95
(7g)	H	Ph	Me	24	(6g)	100
(7g)	H	COPh	Me	12	(6h)	63

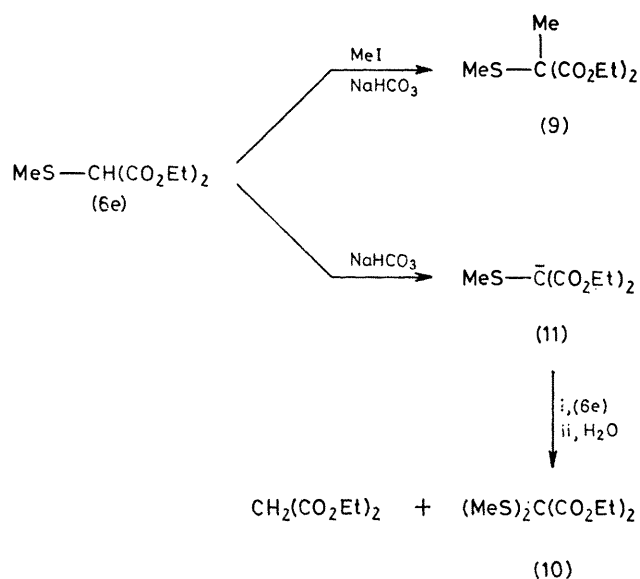
sulphenylation of the anion of diethyl malonate by methanesulphenyl chloride.¹⁵

As an extension of this investigation a general method, based on the known labile character of sulphonium halides in solution,¹⁶ was elaborated for the synthesis of symmetrical dialkyl and dialkenyl sulphides under non-basic conditions. The very simple procedure involves heating a mixture of an unsymmetrical sulphide and the corresponding alkyl or alkenyl halide in a 1:1 molar ratio without solvent. We believe that the corresponding sulphonium halides (12) are formed as intermediates, which are demethylated by the bromide ions to produce the desired symmetrical sulphides. By utilizing this general method a variety of symmetrical sulphides

¹⁴ (a) I. M. Hunsberger and J. M. Tien, *Chem. and Ind.*, 1959, 88; (b) F. E. Ray and I. Levine, *J. Org. Chem.*, 1937, **2**, 267.

¹⁵ E. L. Eliel and S. A. Evans, jun., *J. Amer. Chem. Soc.*, 1972, **94**, 8587.

¹⁶ (a) E. J. Corey and M. Jantelat, *Tetrahedron Letters*, 1968, 5787; (b) P. Mamalis, *J. Chem. Soc. (C)*, 1960, 4747; (c) F. Krollpfeiffer and H. Hartmann, *Chem. Ber.*, 1950, **83**, 90.



SCHEME 2

(5a—f) could be synthesized in reasonable yields (Table 3). The desired symmetrical sulphide (5a) was synthesized in 66% yield according to this method, despite the fact that no such product was obtained upon treatment of the bromo-ester (7a) with sodium sulphide under the usual conditions.^{12a,c}

The foregoing results prompted us to study briefly

TABLE 3

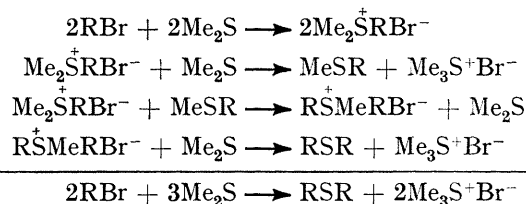
$$\begin{array}{c}
 \text{MeS}-\text{CH}_2\text{R} + \text{RCH}_2\text{Br} \xrightarrow{\text{heat}} \text{R}-\overset{\text{Me}}{\text{S}}-\text{R} + \text{Br}^- \\
 \text{(6)} \quad \quad \quad \text{(7)} \quad \quad \quad \text{(12)} \\
 \downarrow \\
 \text{MeBr} + \text{R}-\text{S}-\text{R} \\
 \text{(5a—f)}
 \end{array}$$

Halide	R	Sulphide	Temperature °C	Time days	Symmetrical sulphide	Yield %
(7a)		(6a)	60	7	(5a)	66
(7b)		(6b)	60	10	(5b)	76
(7c)		(6c)	60	7	(5c)	43
(7d)		(6d)	60	10	(5d)	48
(7f)	Ph	(6g)	120	2	(5e)	80
(7g)	COPh	(6h)	20	1	(5f)	61

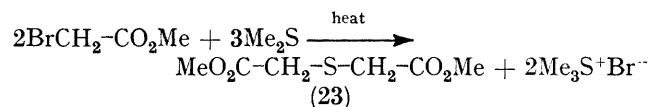
the possible extension of this procedure to the synthesis of unsymmetrical sulphides of type (16) from sulphides (13) and halides (14). Demethylation of the intermediate sulphonium salts (15) by the bromide ion should lead to the desired unsymmetrical sulphides (16), although it was realized that the dissociation equilibria leading to the sulphides (17) and the bromide (18) and eventually to the symmetrical sulphides of types (19) and (20), respectively, might also be operative.

G.l.c. analysis of the mixture produced when a 1 : 1 mixture of ethyl bromoacetate (7b) and ethyl γ -(methylthio)crotonate (6c) was heated at 150 °C for 7 h without solvent revealed that the unsymmetrical sulphide (21) was indeed produced in 43% yield together with the symmetrical sulphides (5b) (20%) and (5c) (7%). The yield of the unsymmetrical sulphide (21) was significantly increased to 55%, with concomitant production of the sulphides (5b) (15%) and (5c) (12%), when a mixture of ethyl γ -bromocrotonate (7c) and ethyl methylthioacetate (6b) was heated in a 2 : 1 molar ratio. Similar treatment of a *ca.* 2 : 1 mixture of methyl benzyl sulphide (6g) and the bromo-ester (7b) gave the corresponding unsymmetrical sulphide (22) (38%) and the symmetrical sulphides (5e) (27%) and (5b) (5%) (Scheme 3).

The foregoing results demonstrate that unsymmetrical sulphides can be synthesized in high yields by treatment of organic halides with an excess of dimethyl or diethyl sulphide. It occurred to us that treatment of an organic halide with 1.5 mol. equiv. of dimethyl sulphide might constitute an attractive direct route to the corresponding symmetrical sulphide, provided that the reaction proceeds *via* the following sequence:



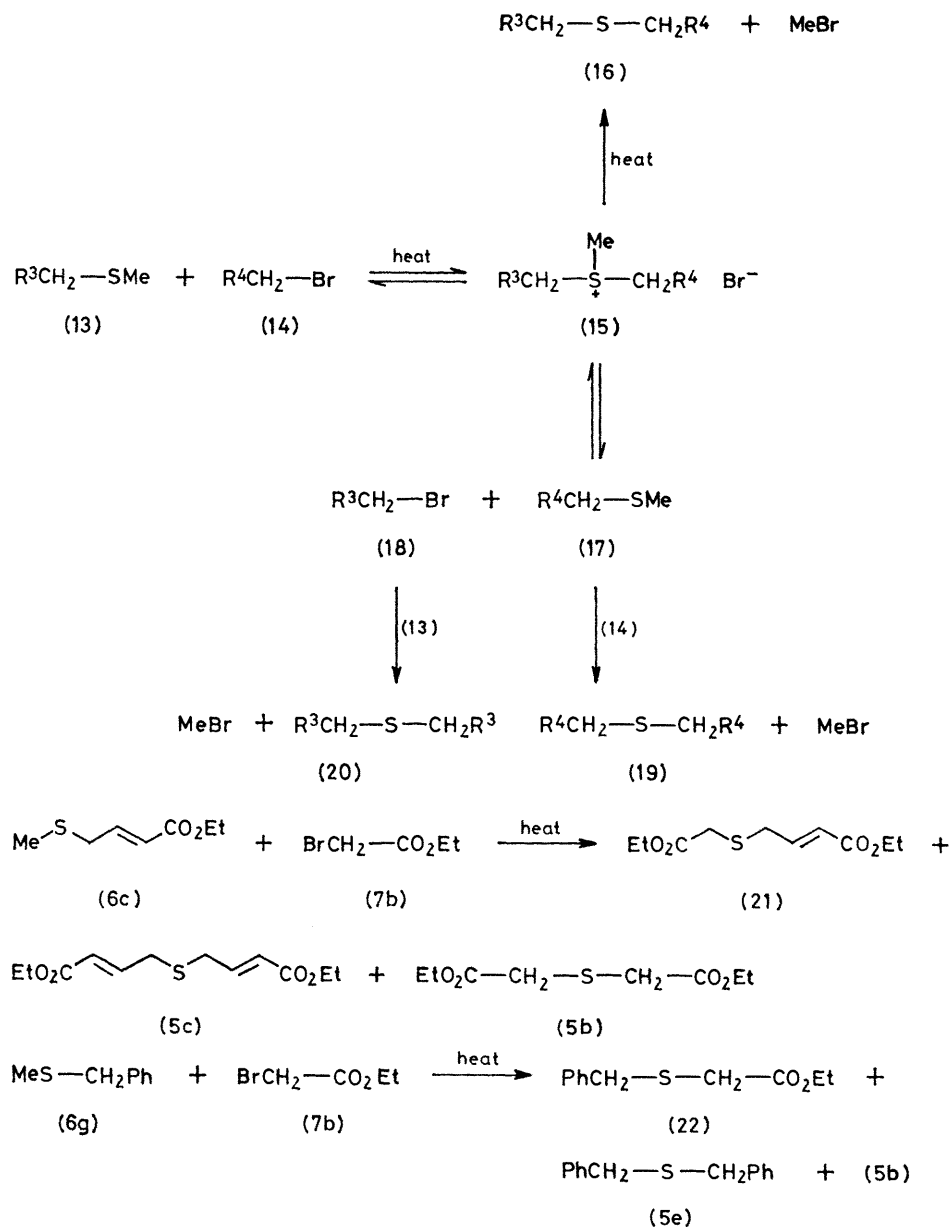
The symmetrical sulphide (23) was indeed produced in 96% yield when a mixture of methyl bromoacetate and dimethyl sulphide (molar ratio 2 : 3) was heated in a pressure vessel at 60 °C. Similar treatment of ethyl bromoacetate (7b) and the bromo-ester (7c), however,



gave the corresponding unsymmetrical sulphides (6b) and (6c) as major products, while the symmetrical sulphides (5b) and (5c) were produced in unpromisingly low yields. It therefore appears that alkylation of the sulphide (25) by the sulphonium salt (24), followed by demethylation of the resulting sulphonium salt (26), proceeds much faster than demethylation of salt (24) to the unsymmetrical sulphide (25) (Scheme 4). The

validity of this statement was supported by the observation that the symmetrical sulphide (23) was produced in 43% yield even upon treatment of methyl bromoacetate with a four-fold molar excess of dimethyl sulphide.

methylsulphonium Salts. General Procedure.—A solution of the sulphonium salt and dimethyl sulphide in Me_2SO was heated for 5 h at 60 °C in a pressure vessel. The resultant rimethylsulphonium bromide^{2a} was filtered off and washed with acetone-ether (1:1). The combined filtrates were



SCHEME 3

EXPERIMENTAL

U.v. spectra were recorded for solutions in 96% ethanol with a Unicam SP 1800 spectrometer. ^1H N.m.r. spectra were recorded for solutions in $[\text{2H}]$ chloroform with a Varian HA-60IL spectrometer and SiMe_4 as internal standard. Mass spectra were determined with A.E.I. MS 902 and Varian MAT 311A spectrometers. Silica gel (0.05–0.2 mm; Merck) was used for column chromatography. No attempts were made to optimize yields.

Unsymmetrical Sulphides from the Corresponding Di-

repeatedly extracted with water to remove the Me_2SO and distillation of the residue from the dried (Na_2SO_4) organic phase gave the pure sulphide (Table 1).

(a) (2,3-Bismethoxycarbonylprop-2-enyl)dimethylsulphonium bromide (3a)^{2a} (12 g, 0.04 mol) and dimethyl sulphide (19 g, 0.3 mol) in Me_2SO (19 g) gave dimethyl α -(methylthiomethyl)fumarate (6a) (8 g, 100%), b.p. 90 °C (air-bath temperature, 0.1 mmHg), which exhibited spectral data identical with those of an authentic sample.^{2a}

(b) (Ethoxycarbonylmethyl)dimethylsulphonium bro-

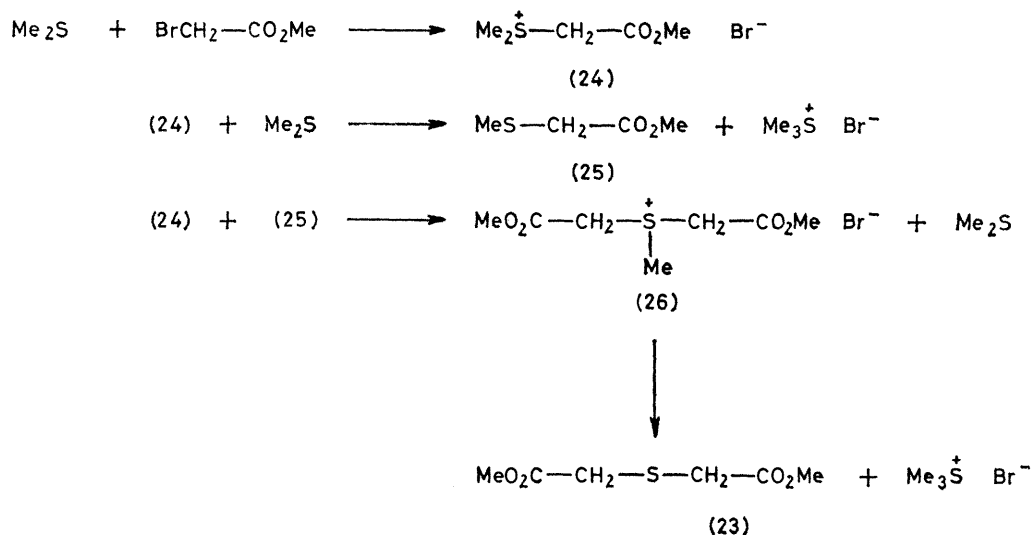
mide (3b)¹⁷ (25 g, 0.11 mol) and dimethyl sulphide (34.8 g, 0.56 mol) in Me₂SO (50 g) gave ethyl (methylthio)acetate (6b)¹⁸ (13 g, 89%), b.p. 75 °C (18 mmHg) (lit.,¹⁸ 66 °C at 12 mmHg) (Found: C, 44.4; H, 7.5. Calc. for C₅H₁₀O₂S: C, 44.75; H, 7.5%).

(c) A solution of ethyl γ -bromocrotonate (7c) (96 g, 0.5 mol) and dimethyl sulphide (62 g, 1.0 mol) in acetone (200 ml) was kept at room temperature for 48 h. The resulting hygroscopic crystals were filtered off, washed with acetone, and dried *in vacuo* to yield (3-ethoxycarbonylprop-2-enyl)dimethylsulphonium bromide (3c) (79 g, 62%), m.p. 76–78 °C, δ 6.93 (1 H, dt, *J* 15.4 and 7.2 Hz), 6.48 (1 H, d, *J* 15.4 Hz), 4.97 (2 H, br d, *J* 7.2 Hz), 4.22 (2 H, q, *J* 7 Hz), 3.36 (6 H, s), and 1.29 (3 H, t, *J* 7 Hz). The sulphonium salt (3c) (25 g, 0.1 mol) and dimethyl sulphide

(b) Ethyl γ -bromocrotonate (7c) (25 g, 0.1 mol) and dimethyl sulphide (40.3 g, 0.6 mol) gave ethyl γ -(methylthio)crotonate (6c) (19.5 g, 94%).

(c) Ethyl α -(bromomethyl)acrylate (7d)¹⁹ (10 g, 60 mmol) and dimethyl sulphide (17 g, 280 mmol) gave ethyl α -(methylthiomethyl)acrylate (6d) (8 g, 91%), b.p. 50 °C at 0.7 mmHg, λ_{\max} 207 nm (ϵ 7 478), δ 6.21 (1 H, d, *J* 1.4 Hz), 5.62 (1 H, br d, *J* 1.4 Hz), 4.25 (2 H, q, *J* 7.1 Hz), 3.36 (2 H, br s), 2.03 (3 H, s), and 1.31 (3 H, t, *J* 7.1 Hz) (Found: C, 52.8; H, 7.45. C₇H₁₂O₂S requires C, 52.5; H, 7.55%).

(d) Diethyl bromomalonate (7e) (90 g, 0.38 mol) and dimethyl sulphide (117 g, 1.88 mol) gave diethyl (methylthio)malonate (6e)²⁰ (65 g, 83%), b.p. 60 °C at 0.3 mmHg (lit.,^{20a} 155 °C at 14 mmHg) (Found: C, 46.3; H, 6.65. Calc. for C₈H₁₄O₄S: C, 46.6; H, 6.85%).



SCHEME 4

(31.4 g, 0.5 mol) in Me₂SO (35 g) gave ethyl γ -(methylthio)crotonate (6c) (13 g, 83%), b.p. 62 °C at 0.8 mmHg, λ_{\max} 210 and 267 nm (ϵ 12 800 and 2 027), δ 6.87 (1 H, dt, *J* 15 and 7.4 Hz), 5.83 (1 H, dt, *J* 15 and 1.1 Hz), 4.20 (2 H, q, *J* 7.2 Hz), 3.18 (2 H, dd, *J* 7.4 and 1.1 Hz), 2.01 (3 H, s), and 1.28 (3 H, t, *J* 7.2 Hz) (Found: C, 52.45; H, 7.55. C₇H₁₂O₂S requires C, 52.5; H, 7.55%).

Unsymmetrical Sulphides from the Corresponding Organic Halides and Dimethyl or Diethyl Sulphide. General Procedure.—A mixture of the organic halide and an excess of dimethyl or diethyl sulphide was heated for 12–96 h at 60 °C in a pressure vessel. Trialkylsulphonium bromide crystallized from the mixture and was filtered off and washed with acetone–ether (1:1). Distillation of the residue from the combined filtrates furnished the pure unsymmetrical sulphide (Table 2).

(a) Ethyl bromoacetate (7b) (76.3 g, 0.46 mol) and dimethyl sulphide (170 g, 2.74 mol) gave ethyl (methylthio)acetate (6b)¹⁸ (54.8 g, 89%).

(e) Ethyl bromoacetate (7b) (10 g, 60 mmol) and diethyl sulphide (27 g, 300 mmol) gave ethyl (ethylthio)acetate (6f) (8.5 g, 95%), b.p. 86 °C at 20 mmHg (lit.,²¹ 98–103 °C at 35 mmHg), δ 4.19 (2 H, q, *J* 7.1 Hz), 3.22 (2 H, s), 2.68 (2 H, q, *J* 7.2 Hz), 1.27 (3 H, t, *J* 7.1 Hz), and 1.26 (3 H, t, *J* 7.2 Hz) (Found: C, 48.5; H, 8.2. Calc. for C₆H₁₂O₂S: C, 48.65; H, 8.2%).

Methyl Benzyl Sulphide (6g).—A mixture of benzyl bromide (7f) (17 g, 0.1 mol), dimethyl sulphide (37 g, 0.5 mol), and Me₂SO (20 g) was heated for 24 h at 60 °C in a pressure vessel. The resultant trimethylsulphonium bromide^{2a} was filtered off and the filtrate worked up as before. Distillation of the residue from the filtrate gave the pure sulphide (6g) (13.7 g, 100%), b.p. 101 °C at 23 mmHg (lit.,²² 100 °C at 13 mmHg), δ 7.23 (5 H, s), 3.60 (2 H, s), and 1.90 (3 H, s) (Found: C, 69.55; H, 7.3. Calc. for C₈H₁₆S: C, 69.55; H, 7.3%).

Methyl Phenacyl Sulphide (6d).—A mixture of phenacyl bromide (7g) (5 g, 25 mmol), dimethyl sulphide (7.8 g, 125 mmol), and Me₂SO (10 g) was heated for 12 h at 60 °C in a pressure vessel, then worked up and distilled as above to yield the sulphide (6d) (2.6 g, 63%), b.p. 85 °C at 0.2

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¹⁹ A. F. Ferris, *J. Org. Chem.*, 1955, **20**, 780.

²⁰ (a) H. Brintzinger and M. Langheck, *Chem. Ber.*, 1953, **86**, 557; (b) H. Wittmann, D. Sobhi, and F. A. Petio, *Z. Naturforsch.*, 1976, **31b**, 850.

²¹ H. L. Yale, E. J. Pribye, W. Braker, J. Bernstein, and W. A. Lott, *J. Amer. Chem. Soc.*, 1950, **72**, 3716.

²² J. Drabowicz and M. Mikolajczyk, *Synthesis*, 1976, 527.

mmHg (lit.,²³ 102—104 °C at 2 mmHg), δ 8.08—7.21 (5 H, m), 3.73 (2 H, s), and 2.11 (3 H, s) (Found: C, 65.45; H, 6.05. Calc. for $C_9H_{10}OS$: C, 65.05; H, 6.1%).

Bis(methylthio)methane (8).—Dibromomethane (15 g, 86 mmol) and dimethyl sulphide (64.25 g, 1.03 mol) were heated for 24 h at 120 °C in a pressure vessel. The mixture was worked up and distilled as before to yield the thioacetal (8) (6.11 g, 65%), b.p. 149—150 °C at 760 mmHg (lit.,²⁴ 148—150 °C at 760 mmHg), δ 3.61 (2 H, s) and 2.13 (6 H, s).*

Diethyl (Methylthiomethyl)malonate (9).—Diethyl (methylthio)malonate (6e) (3 g, 14.6 mmol), methyl iodide (6.2 g, 43.7 mmol), and sodium hydrogen carbonate (3 g, 35.7 mmol) in Me_2SO (14 g) were stirred for 24 h at 20 °C. The mixture was then added to water (100 ml) and the aqueous mixture was repeatedly extracted with ether. The combined extracts were dried (Na_2SO_4) and evaporated. Chromatographic separation of the residue on silica gel furnished the sulphide (9) (1.63 g, 51%), b.p. 90 °C at 0.7 mmHg, δ 4.25 (4 H, q, J 7.1 Hz), 2.18 (3 H, s), 1.68 (3 H, s), and 1.28 (3 H, t, J 7.1 Hz) (Found: C, 49.15; H, 7.3. $C_9H_{16}O_4S$ requires C, 49.1; H, 7.3%).

Diethyl Bis(methylthio)malonate (10).—Diethyl (methylthio)malonate (6e) (3 g, 14.6 mmol) and sodium hydrogen carbonate (3 g, 35.7 mmol) in Me_2SO (15 g) were stirred for 6 h at 85 °C. The mixture was worked up and chromatographed as above to yield the bis-sulphide (10)^{3a,15} (2.38 g, 65%), b.p. 85 °C at 0.2 mmHg, δ 4.28 (4 H, q, J 7.1 Hz), 2.08 (6 H, s), and 1.29 (6 H, t, J 7.1 Hz) (Found: C, 43.0; H, 6.3. Calc. for $C_9H_{16}O_4S_2$: C, 42.85; H, 6.4%).

Symmetrical Sulphides from the Corresponding Unsymmetrical Methyl Sulphides and Organic Halides. General Procedure.—A mixture of the unsymmetrical sulphide and organic halide was heated for 1—10 days at 20—120 °C (Table 3). The products were isolated by distillation or crystallization.

(a) Dimethyl α -(bromomethyl)fumarate (7a) (4.8 g, 20 mmol) and dimethyl α -(methylthiomethyl)fumarate (6a) (4 g, 20 mmol) gave after chromatographic separation [silica gel; ether-petroleum (1:1)] *di*-(2,3-bismethoxycarbonylprop-2-enyl) sulphide (5a) (4.47 g, 66%), b.p. 120 °C (air-bath temperature) at 10^{-5} mmHg, λ_{max} 222 nm (ϵ 15 460), δ 6.71 (2 H, s), 3.99 (4 H, s), 3.82 (6 H, s), and 3.76 (6 H, s) (Found: C, 48.6; H, 5.25%; M^+ , 346.0715. $C_{14}H_{18}O_6S$ requires C, 48.6; H, 5.25%; M , 346.0722).

(b) Ethyl bromoacetate (7b) (2.5 g, 15 mmol) and ethyl (methylthio)acetate (6b) (2 g, 15 mmol) gave bis(ethoxycarbonylmethyl) sulphide (5b) (2.4 g, 76%), b.p. 120 °C at 0.7 mmHg (lit.,²⁵ 130—131 °C at 8 mmHg), δ 4.18 (4 H, q, J 7.1 Hz), 3.37 (4 H, s), and 1.27 (6 H, t, J 7.1 Hz), m/e 206 (M^+) (Found: C, 46.7; H, 6.9. Calc. for $C_8H_{14}O_4S$: C, 46.6; H, 6.85%).

(c) Ethyl γ -bromocrotonate (7c) (3.7 g, 20 mmol) and ethyl γ -(methylthio)crotonate (6c) (3 g, 20 mmol) gave *bis*-(3-ethoxycarbonylprop-2-enyl) sulphide (5c) (2.1 g, 43%), b.p. 95 °C (air-bath temperature) at 10^{-5} mmHg, λ_{max} 212 nm (ϵ 21 895), δ 6.86 (2 H, dt, J 15.7 and 7.3 Hz), 5.85 (2 H, dt, J 15.7 and 1.2 Hz), 4.21 (4 H, q, J 7.1 Hz), 3.19 (4 H, dd, J 7.3 and 1.2 Hz), and 1.30 (6 H, t, J 7.1 Hz) (Found: C, 55.7; H, 7.0%; M^+ , 258.0948. $C_{12}H_{18}O_4S$ requires C, 55.8; H, 7.05%; M , 258.0926).

* Although the 1H n.m.r. spectrum suggested that the thioacetal (8) was pure, the compound did not give satisfactory analytical data.

²³ L. M. Long, *J. Amer. Chem. Soc.*, 1946, **68**, 2159.

(d) Ethyl α -(bromomethyl)acrylate (7d)¹⁹ (2.4 g, 13 mmol) and ethyl α -(methylthiomethyl)acrylate (6d) (2 g, 13 mmol) gave *bis*-(2-ethoxycarbonylprop-2-enyl) sulphide (5d) (1.62 g, 48%), b.p. 110 °C (air-bath temperature) at 10^{-5} mmHg, λ_{max} 209 nm (ϵ 10 231), δ 6.22 (2 H, d, J 1.2 Hz), 5.67 (2 H, overlapping dt, J 1.2 and 1.1 Hz), 4.25 (4 H, q, J 7.1 Hz), 3.35 (4 H, d, J 1.1 Hz), and 1.31 (6 H, t, J 7.1 Hz), m/e 258 (M^+) (Found: C, 56.1; H, 7.0. $C_{12}H_{18}O_4S$ requires C, 55.8; H, 7.05%).

(e) Benzyl bromide (7f) (0.86 g, 5 mmol) and methyl benzyl sulphide (6g) (1.04 g, 7.5 mmol) gave after preparative t.l.c. [silica gel GF₂₅₄; ether-petroleum (1:4)] dibenzyl sulphide (5e) (1.0 g, 80%), m.p. 48 °C (from petroleum) (lit.,²² 48—50 °C), δ 7.24 (10 H, s) and 3.56 (4 H, s) (Found: C, 78.05; H, 6.55; S, 14.9. Calc. for $C_{14}H_{14}S$: C, 78.5; H, 6.6; S, 14.95%).

(f) Phenacyl bromide (7g) (0.5 g, 3 mmol) and methyl phenacyl sulphide (6h) (0.6 g, 3 mmol) gave after chromatography [silica gel, ether-petroleum (4:1)] diphenacyl sulphide (5f)^{16c} (0.5 g, 61%), m.p. 74 °C (from dichloromethane) (lit.,^{16c} 76—77 °C), λ_{max} 206 and 246 nm (ϵ 20 514 and 20 117), δ 8.04—7.20 (10 H, m) and 3.95 (4 H, s) (Found: C, 70.5; H, 5.3%; M^+ , 270.0694. Calc. for $C_{16}H_{14}O_2S$: C, 71.1; H, 5.2%; M , 270.0714).

Coupling of Ethyl (Methylthio)acetate (6b) and Ethyl γ -Bromocrotonate (7c).—A mixture of the sulphide (6b) (14 g, 0.104 mol) and the bromo-ester (7c) (40 g, 0.208 mol) was heated for 3 h at 150 °C while a stream of pure nitrogen was blown into the flask. G.l.c. (10% SE 30 on Chromosorb WAW-DMCS) showed that the resulting mixture comprised ethyl γ -(ethoxycarbonylmethylthio)crotonate (21) (55%), bis(ethoxycarbonylmethyl) sulphide (5b) (15%), and bis(3-ethoxycarbonylprop-2-enyl) sulphide (5c) (12%). Distillation of the mixture through a 50-cm Teflon spinning-band column furnished the pure sulphides (5b) (3.5 g, 16%), b.p. 78 °C at 10^{-2} mmHg; (21) (11.6 g, 48%), b.p. 110 °C at 10^{-2} mmHg, δ 6.83 (1 H, overlapping dt, J 15.4 and 7.5 Hz), 5.87 (1 H, dt, J 15.4 and 1.0 Hz), 4.18 (4 H, br q, J 7.1 Hz), 3.35 (2 H, dd, J 7.5 and 1.0 Hz), 3.12 (2 H, s), and 1.27 (6 H, t, J 7.1 Hz) (Found: C, 51.6; H, 6.85; S, 14.0%; M^+ , 232.0759. $C_{10}H_{16}O_4S$ requires C, 51.7; H, 6.95; S, 13.8%; M , 232.0769); and (5c) (3.5 g, 13%), b.p. 130 °C at 10^{-2} mmHg.

Coupling of Methyl Benzyl Sulphide (6g) and Ethyl Bromoacetate (7b).—The sulphide (6g) (6.9 g, 50 mmol) and the bromo-ester (7b) (4.8 g, 29 mmol) were heated for 5 h at 130 °C. Separation of 500 mg of the resulting mixture (8.76 g) by preparative t.l.c. [silica gel GF₂₅₄; ether-petroleum (1:14)] yielded dibenzyl sulphide (5e) (133 mg, 27%), ethyl (benzylthio)acetate (22) (189 mg, 38%), b.p. 115 °C (air-bath temperature) at 0.5 mmHg (lit.,²⁵ 183—184 °C at 50 mmHg), δ 7.27 (5 H, s), 4.16 (2 H, q, J 7.2 Hz), 3.81 (2 H, s), 3.04 (2 H, s), and 1.26 (3 H, t, J 7.2 Hz) (Found: C, 62.65; H, 6.7; S, 15.65. Calc. for $C_{11}H_{14}O_2S$: C, 62.85; H, 6.7; S, 15.2%).

Bis(methoxycarbonylmethyl) Sulphide (23).—A mixture of methyl bromoacetate (15 g, 0.1 mol) and dimethyl sulphide (9.1 g, 0.15 mol) was heated for 96 h at 60 °C in a pressure vessel. The resulting trimethylsulphonium bromide (15.4 g, 100%) was filtered off and washed with acetone-ether (1:1), and the residue from the combined filtrates was distilled through a Vigreux column to yield the sulphide

²⁴ D. Welti and D. Whittaker, *J. Chem. Soc.*, 1962, 4372.

²⁵ A. Chauveau and R. Mathis-Noel, *Ann. Fac. Sci. Univ. Toulouse, Sci. Math. Sci. Phys.*, 1961, **25**, 111.

(23) (8.32 g, 96%), b.p. 91 °C at 2 mmHg (lit.,²⁶ 135 °C at 21 mmHg), δ 3.74 (6 H, s) and 3.40 (4 H, s) (Found: C, 40.35; H, 5.55%; M^+ , 178.0315. Calc. for $C_6H_{10}O_4S$: C, 40.45; H, 5.7%; M , 178.0300).

²⁶ H. L. Morrill, G. W. Steahly, and F. B. Zienty, *J. Org. Chem.*, 1961, **26**, 4103.

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