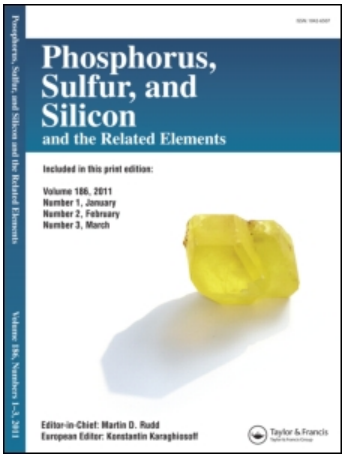


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

ORGANOSULFUR COMPOUNDS AS POTENTIAL FUNGICIDES: THE PREPARATION AND PROPERTIES OF SOME SUBSTITUTED BENZYL 2-HYDROXYETHYL OLIGOSULFIDES

Ezekiel T. Ayodele[a]; Harry R. Hudson[a]; Isaac A. O. Ojo[ab]; Max Pianka[a]
[a] School of Applied Chemistry, University of North London, London, United Kingdom [b] Obafemi Awolowo University, Nigeria

To cite this Article Ayodele, Ezekiel T. , Hudson, Harry R. , Ojo, Isaac A. O. and Pianka, Max(2000) 'ORGANOSULFUR COMPOUNDS AS POTENTIAL FUNGICIDES: THE PREPARATION AND PROPERTIES OF SOME SUBSTITUTED BENZYL 2-HYDROXYETHYL OLIGOSULFIDES', Phosphorus, Sulfur, and Silicon and the Related Elements, 159: 1, 123 — 142
To link to this Article: DOI: 10.1080/10426500008043656
URL: http://dx.doi.org/10.1080/10426500008043656

Phosphorus, Sulfur and Silicon, 2000, Vol. 159, pp. 123-142
Reprints available directly from the publisher
Photocopying permitted by license only

ORGANOSULFUR COMPOUNDS AS POTENTIAL FUNGICIDES: THE PREPARATION AND PROPERTIES OF SOME SUBSTITUTED BENZYL 2-HYDROXYETHYL OLIGOSULFIDES

EZEKIEL T. AYODELE, HARRY R. HUDSON*, ISAAC A.O. OJO† and MAX PIANKA

School of Applied Chemistry, University of North London, Holloway Road, London N7 8DB, United Kingdom

(Received August 24, 1999)

Compounds of the general type $ArCH_2S_nCH_2CH_2OH$ (n = 1 – 4, Ar = Ph, 2-MeC_6H_4, 4-MeC_6H_4, 4-ClC_6H_4, 4-$MeOC_6H_4$; n = 1 – 3, Ar = 2-ClC_6H_4; n = 2, Ar = 4-FC_6H_4; n = 3 or 4, Ar = 2-furyl) have been prepared as analogues of the trisulfide $PhCH_2SSSCH_2CH_2OH$ (an antimicrobial compound which occurs in the plant *Petiveria alliacea*) and their potential for application as agricultural fungicides has been examined. *In vitro* tests against *Fusarium culmorum*, *Fusarium oxysporum* and *Gauenomyceles graminis* showed that all compounds gave > 80% control of these organisms at 1000 ppm. Tests at 100 and 10 ppm showed varying levels of control but the activity did not depend significantly on the number of sulfur atoms present. Selected compounds were also shown to be active *in vivo* against *Erysiphe graminis* on barley seedlings, *Botrytis fabae* and *Uromyces viciae-fabae* on bean seedlings, *Podosphaera leucotricha* on apple seedlings, and *Phytophthora infestans* on potato leaf. The compounds were phytotoxic at concentrations greater than 0.33%.

Keywords: Organosulfur; fungicides; oligosulfides

INTRODUCTION

Organosulfur compounds of the general formula R-S_n-R′ are known to be of biological importance and many examples have been identified in plant extracts. For example, various symmetrical and unsymmetrical mono-, di-,

* Author for correspondence.
† Obafemi Awolowo University, Ile-Ife, Nigeria.

and tri-sulfides, in which R and/or R′ may be Me, Pr^n, allyl, or prop-1-enyl, etc. have been isolated from members of the onion family, including garlic (*Allium sativum L.*),[1] caucus (*Allium victorialis L.*),[2] and the leek.[3] Other polysulfides recognized as natural products include cystine trisulfide and glutathione trisulfide, which have been discussed with respect to the control of 5-aminolaevulinate synthetase activity in *Rhodopseudomonas spheroides*,[4] lenthionine (1,2,3,5,6-pentathiacycloheptane) which occurs in the edible mushroom, *Shiitake Lentihus edodes*,[5] and sporidesmin, an unusual cyclic trisulfide which is found in the fungus *Pithomyces chartarum*.[6] Also, the isolation, structural elucidation and synthesis[7,8] of an antimicrobial trisulfide (**1**) present in *Petiveria alliacea* (a tropical plant used broadly in popular medicine) have been reported, the active component being obtained from the chloroform-soluble fraction of the total water-alcohol extract of the stems and roots of the plant. The authors identified benzyl 2-hydroxyethyl trisulfide (**1**) by nmr and mass spectrometry, synthesised a range of analogues (both tri- and tetra-sulfides), and demonstrated their activity against a number of bacteria and fungal pathogens of medical significance.[7–9] Other unsymmetrical trisulfides have also been synthesised.[10]

$$PhCH_2SSSCH_2CH_2OH$$

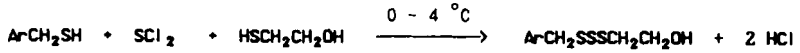
(1)

In this paper we describe the preparation and properties of a series of oligosulfides $ArCH_2S_nCH_2CH_2OH$ (n = 1, 2, 3 and **4**), some of which are known compounds and some of which are new, and we report their activity against pathogenic fungi of economic significance in agriculture.

RESULTS AND DISCUSSION

The reactions of mercaptoethanol and various substituted benzyl mercaptans with sulfur dichloride (Scheme 1) were carried out in order to obtain substituted benzyl 2-hydroxyethyl trisulfides (**2**). This method[8,9] had been used previously to prepare this type of compound, with separa-

tions carried out by preparative tlc, and we found it preferable to other procedures described in the literature. We also developed a suitable column chromatographic technique for the final work-up which gave pure products in good yields.



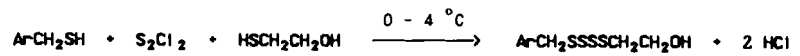
(2)

Ar = C_6H_5 (2a), 2-ClC_6H_4 (2b), 4-ClC_6H_4 (2c), 2-MeC_6H_4 (2d), 4-MeC_6H_4 (2e), 4-$MeOC_6H_4$ (2f), 2-furyl (2g)

SCHEME 1

As sulfur dichloride is sensitive to moisture, reactions were carried out in anhydrous ether and under inert conditions. It was also possible to separate small amounts of the symmetrical dibenzyl trisulfides, $ArCH_2SSSCH_2Ar$, which were formed as by-products by column chromatography, thereby giving the desired unsymmetrical trisulfides (**2**) virtually free from the symmetrical derivatives.

The reaction (Scheme 2) of sulfur monochloride with an equimolar mixture of mercaptoethanol and benzyl mercaptan (or substituted benzyl mercaptan) in dried absolute ether, under inert conditions and in the cold, was similarly used to prepare a series of unsymmetrical tetrasulfides (**3**).[8] These reactions were carried out under inert conditions because of the sensitivity of sulfur monochloride to atmospheric moisture, any contact with which causes decomposition to elemental sulfur.



(3)

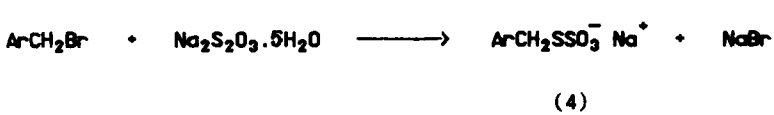
Ar = C_6H_5 (3a), 4-ClC_6H_4 (3b), 2-MeC_6H_4 (3c), 4-MeC_6H_4 (3d), 4-$MeOC_6H_4$ (3e), 2-furyl (3f)

SCHEME 2

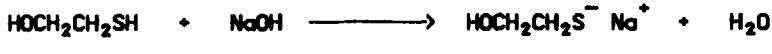
In addition to the desired product, a small amount of the symmetrical dibenzyl tetrasulfide, $ArCH_2SSSSCH_2Ar$, was also formed. As for the trisulfides, column chromatography on silica gel was used to separate this symmetrical by-product and any other impurities. The procedure used involved eluting first with petroleum ether (b.p. 40–60 °C), followed by mixtures of petroleum ether and dichloromethane in various proportions. Tlc was used to monitor the various eluants and the desired product was finally eluted with dichloromethane.

Other possible by-products in both the tri- and tetra-sulfide preparations (Schemes 1 and 2) are the symmetrical bis(2-hydroxyethyl) derivatives, $HOCH_2CH_2S_nCH_2CH_2OH$ (n = 3 or 4) but they were not detected and, if formed, were probably retained on the column.

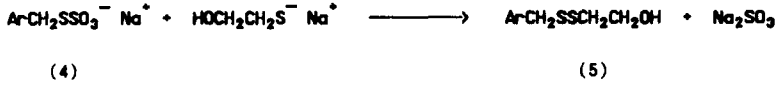
Using the reaction Schemes 3, 4, and 5 to prepare benzyl 2-hydroxyethyl disulfides (**5**) as described[11] we found that small amounts of the symmetrical disulfides, $ArCH_2SSCH_2Ar$, were also formed together with the desired products.[12] The symmetrical disulfides might result from a rearrangement reaction of the Bunte Salt (**4**) and it has also been suggested that the product (**5**) may undergo disproportionation to give the symmetrical disulfide.[13]



SCHEME 3

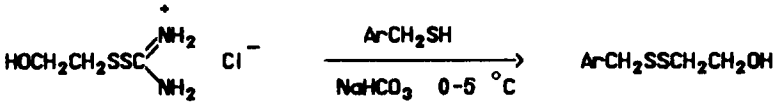


SCHEME 4



SCHEME 5

Using another method, however, apparently for the first time for making this type of compound, we were able to prepare pure unsymmetrical disulfides (**5**) without concomitant formation of the symmetrical products. This method involved the reaction of S-(2-hydroxyethylthio)isothiouronium chloride (**6**) with the benzyl mercaptans under alkaline conditions as shown (Scheme 6).



(**6**) (**5**)

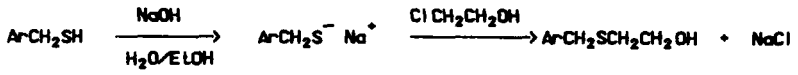
Ar = C_6H_5 (**5a**), 2-ClC_6H_4 (**5b**), 4-ClC_6H_4 (**5c**), 4-FC_6H_4 (**5d**), 2-MeC_6H_4 (**5e**), 4-MeC_6H_4 (**5f**), 4-$MeOC_6H_4$ (**5g**)

SCHEME 6

The complete absence of a molecular ion peak corresponding to the symmetrical benzyl disulfides, $ArCH_2SSCH_2Ar$, in the mass spectra of the products (**5**) indicated that these symmetrical disulfides had not been formed and that the benzyl 2-hydroxyethyl dusulfides (**5**) did not undergo disproportionation of the type reported by Hiskey *et al*[12] under our reaction conditions.

The various unsymmetrical benzyl 2-hydroxyethyl monosulfides prepared in this investigation were known; they were however prepared so that their fungicidal activity could be compared with that of the corresponding di-, tri-, and tetra-sulfides. In the preparation of unsymmetrical monosulfides (**7**), reaction of the benzyl sodium mercaptide with chloroethanol was used (Scheme 7),[14] and gave an almost quantitative yield of the various products.

The usual procedure was to dissolve the mercaptan and alkali in the minimum amount of water, followed by dilution with absolute ethanol and addition of the alkyl halide at such a rate that the reaction, which was exothermic, was kept under control. However, attention was paid to the fact that a mercaptan in alkaline medium may be oxidised to the disulfide and



(7)

Ar = C_6H_5 (7a), 2-ClC_6H_4 (7b), 4-ClC_6H_4, (7c), 2-MeC_6H_4 (7d), 4-MeC_6H_4 (7e), 4-$MeOC_6H_4$ (7f)

SCHEME 7

that the rate of oxidation depends on the length and manner of exposure to air. Therefore, in all the experiments involving the preparation of these monosulfides, inert conditions were used. Column chromatography was also utilized to remove any trace of impurity formed.

Products were characterized by elemental analysis, ^1H and ^{13}C NMR, and mass spectrometry (see Experimental).

Spectroscopy

NMR spectral data obtained for solutions of the various compounds in $CDCl_3$ are given in full in the experimental section. The ^1H spectra are relatively simple and are characterized in all cases by an aromatic multiplet, a singlet for the benzyl methylene protons, and two triplets for the methylene groups of the hydroxyethylthio group (Table I). In addition, individual singlets are observed for the aromatic methyl (δ_H 2.31 – 2.40) or methoxy substituent (δ_H 3.77 – 3.87) if present, together with a broader signal for the hydroxyl group in the range δ_H 2.13 – 3.06. A small, but systematic tendency for the ^1H chemical shift of all methylene protons to move downfield as the number of sulfur atoms increases from 1 – 4 makes it possible to detect, and in some cases to quantify, the different types of compound (mono-, di-, tri-, or tetra-sulfide) present in a reaction product. In the ^{13}C NMR spectra (Table II), a similar trend to lower field chemical shifts can be seen for the benzylic and SCH_2 carbon atoms as the number of sulfur atoms increases, the difference being most marked between the mono- and di-sulfides. The chemical shift of carbon adjacent to the hydroxyl group remains, however, fairly constant within the series (n = 1 – 4).

TABLE I Range of δ_H values/ppm for benzyl 2-hydroxyethyl oligosulfides $ArCH_2S_nCH_2CH_2OH$

	n = 1	*n = 2*	*n = 3*	*n = 4*
Ar	7.15 – 7.27	7.00 – 7.30	7.16 – 7.35	7.19 – 7.32 (m)
$ArC\underline{H}_2$	3.66 – 3.81	3.84 – 3.99	4.01 – 4.19	4.11 – 4.18 (s)
$SC\underline{H}_2CH_2$	2.55 – 2.68	2.48 – 2.54	2.88 – 2.98	3.05 – 3.07 (t)[a]
$CH_2C\underline{H}_2OH$	3.63 – 3.68	3.67 – 3.74	3.85 – 3.92	3.90 – 3.92 (t)[a]

a. $^3J_{HCCH}$ *ca.* 6 Hz

TABLE II Range of δ_C values/ppm for benzyl 2-hydroxyethyl oligosulfides $ArCH_2S_nCH_2CH_2OH$

	n = 1	*n = 2*	*n = 3*	*n = 4*
$Ar\underline{C}H_2$	34.4 – 35.4	40.9 – 43.3	41.4 – 43.0	42.8 – 43.4
$S\underline{C}H_2CH_2$	33.2 – 34.2	40.7 – 40.9	40.3 – 41.4	41.6 – 41.8
$CH_2\underline{C}H_2OH$	60.2 – 60.5	60.0 – 60.2	59.2 – 60.0	59.6 – 60.0

In the E.I. mass spectra (see experimental section), all compounds gave rise to molecular ion peaks, although these were generally of low intensity for tetrasulfides (**3**) (2–4%), trisulfides (**2**) (1-12%), and disulfides (**5**) (2–12%). For the monosulfides (**7**), molecular ions of higher relative intensity (10–47%) were observed. Weak ions corresponding to the loss of one or more sulfur atoms were detected for most compounds but the most abundant ions, frequently giving rise to the base peak, were the benzyl, $ArCH_2^+$ (or isomeric tropylium) ions, formed by cleavage of the $ArCH_2$-S bond. In addition, the hydroxyethyl group, $HOCH_2CH_2$, gave rise to a significant ion at *m/z* 45, which appeared with a relative intensity of 43 – 68% in compounds of all types (**2**, **3**, **5**, and **7**).

Fungicidal Activity

The results of *in vitro* screening against *Fusarium culmorum*, *Fusarium oxysporum*, and *Gauenomyceles graminis* are shown in Tables III – VI, from which it can be seen that all compounds gave 80 – 100% control of these organisms at 1000 ppm. At lower concentrations (100 and 10 ppm)

there was generally a decrease in activity but the level of control varied only slightly with changes in the number of sulfur atoms present. The effect of benzene ring substituents was not strongly marked but the most active compound overall appeared to be 4-fluorobenzyl 2-hydroxyethyl disulfide (**5d**). It is noteworthy that several compounds gave comparable results to those obtained with phenylmercury acetate when tested against the same fungi (Table VII).

TABLE III Fungicidal activity *in vitro* of benzyl 2-hydroxyethyl trisulfides (**2**)[a]

Cpd. no.	*Ar*	*(1)*[b]			*(2)*[b]			*(3)*[b]		
		10	*100*	*1000*	*10*	*100*	*1000*	*10*	*100*	*1000/ppm*
2a	Ph	1	2	4	1	2	4	1	2	4
2b	2-ClC_6H_4	2	2	4	2	3	4	2	3	4
2e	4-MeC_6H_4	2	3	4	2	2	4	2	3	4
2f	4-$MeOC_6H_4$	2	3	4	2	3	4	2	3	4

[a] % control: 0 = 0–10; 1 = 11–20; 2 = 21–49; 3 = 50–79; 4 = 80–100.
[b] (1) *Fusarium culmorum*; (2) *Fusarium oxysporum*; (3) *Gauenomyceles graminis*.

TABLE IV Fungicidal activity *in vitro* of benzyl and furfuryl 2-hydroxyethyl tetrasulfides (**3**)[a]

Cpd. no.	*Ar*	*(1)*[b]			*(2)*[b]			*(3)*[b]		
		10	*100*	*1000*	*10*	*100*	*1000*	*10*	*100*	*1000/ppm*
3a	Ph	2	2	4	2	3	4	2	2	4
3b	4-ClC_6H_4	2	3	4	2	3	4	1	2	4
3c	2-MeC_6H_4	1	3	4	1	3	4	1	3	4
3d	4-MeC_6H_4	1	2	4	1	2	4	1	3	4
3e	4-$MeOC_6H_4$	1	2	4	1	3	4	1	2	4
3f	2-furyl	1	2	4	1	2	4	1	2	4

[a] % control: 0 = 0–10; 1 = 11–20; 2 = 21–49; 3 = 50–79; 4 = 80–100.
[b] (1) *Fusarium culmorum*; (2) *Fusarium oxysporum*; (3) *Gauenomyceles graminis*.

TABLE V Fungicidal activity *in vitro* of benzyl 2-hydroxyethyl disulfides (**5**)[a]

Cpd. no.	*Ar*	*(1)*[b]			*(2)*[b]			*(3)*[b]		
		10	*100*	*1000*	*10*	*100*	*1000*	*10*	*100*	*1000/ppm*
5a	Ph	0	3	4	1	3	4	2	3	4
5b	2-ClC_6H_4	0	3	4	2	3	4	2	4	4
5d	4-FC_6H_4	2	3	4	2	3	4	3	4	4
5e	2-MeC_6H_4	1	3	4	1	3	4	2	4	4
5g	4-$MeOC_6H_4$	1	3	4	2	3	4	2	4	4

[a] % control: 0 = 0–10; 1 = 11–20; 2 = 21–49; 3 = 50–79; 4 = 80–100.
[b] (1) *Fusarium culmorum*; (2) *Fusarium oxysporum*; (3) *Gauenomyceles graminis*.

TABLE VI Fungicidal activity *in vitro* of benzyl 2-hydroxyethyl monosulfides (**7**)[a]

Cpd. no.	*Ar*	*(1)*[b]			*(2)*[b]			*(3)*[b]		
		10	*100*	*1000*	*10*	*100*	*1000*	*10*	*100*	*1000/ppm*
7a	Ph	2	3	4	1	2	4	1	2	4
7b	2-ClC_6H_4	2	2	4	1	2	4	0	4	4
7c	4-ClC_6H_4	2	3	4	0	1	4	1	2	4
7d	2-MeC_6H_4	2	3	4	1	2	4	0	1	4
7f	4-$MeOC_6H_4$	2	3	4	1	2	4	1	2	4

[a] % control: 0 = 0–10; 1 = 11–20; 2 = 21–49; 3 = 50–79; 4 = 80–100.
[b] (1) *Fusarium culmorum*; (2) *Fusarium oxysporum*; (3) *Gauenomyceles graminis*.

TABLE VII Fungicidal activity *in vitro* of reference fungicides[a]

Fungicide[b]	*(1)*[c]			*(2)*[c]			*(3)*[c]		
	10	*100*	*1000*	*10*	*100*	*1000*	*10*	*100*	*1000/ppm*
guazatine/ imazalil	3	3	4	3	3	4	3	3	4
PhHgOAc	2	3	4	2	3	4	2	3	4

[a] % control: 0 = 0–10; 1 = 11–20; 2 = 21–49; 3 = 50–79; 4 = 80–100.
[b] Commercial formulations.
[c] (1) *Fusarium culmorum*; (2) *Fusarium oxysporum*; (3) *Gauenomyceles graminis*.

Glasshouse screening *in vivo* showed selected compounds to be active at a concentration of 0.33% against *Erisyphe graminis* on barley seedlings, *Podosphaera leucotricha* on apple seedlings, and *Uromyces viciae-fabae* or *Botrytis fabae* on bean seedlings but at higher concentrations all compounds were phytotoxic, causing leaf damage. Activity against *Phytophthora infestans* was demonstrated in potato leaf disc tests for certain compounds.[15] Overall, 4-fluorobenzyl 2-hydroxyethyl disulfide (**5d**) gave the greatest spectrum of disease control, reducing infection in all host-pathogen systems examined. Greatest disease control was observed against barley powdery mildew (*ca.* 65% after 10 days), chocolate spot on broad bean (*ca.* 40% after 8 days) and blight on potato (> 50% after 4 days).

4-Methoxybenzyl 2-hydroxyethyl disulfide (**5g**) gave best control of apple powdery mildew (*ca.* 80% after 17 days), while 4-methoxybenzyl 2-hydroxyethyl monosulfide (**7f**) gave best control of bean rust (*ca.* 70% after 19 days) and also provided > 50% control of potato blight. 4-Methoxybenzyl 2-hydroxyethyl trisulfide (**2f**) and 2-chlorobenzyl 2-hydroxyethyl disulfide (**5b**) also showed *in vivo* activity against certain organisms, but not against *Botrytis fabae* or *Phytophthora infestans*.

EXPERIMENTAL

Starting Materials, Solvents and Reagents

Most reagents were supplied by Aldrich Chemical Company or Lancaster Synthesis and were used directly. Sulfur monochloride, b.p. 138–139 °C, was purified by distillation over sulfur. Sulfur dichloride was purified by distillation, b.p. 58–60 °C. Diethyl ether and petroleum ether (b.p. 40–60 °C) were dried over sodium wire, and dichloromethane over molecular sieves. Silica gel for column chromatography was obtained from Merck.

S-(2-Hydroxyethylthio)isothiouronium chloride (**6**) was prepared as described,[16] m.p. 105–106 °C (lit. 106–107 °C) (Found: C, 19.07; H, 4.82; N, 14.93; S, 33.89. Calc. for $C_3H_9ClN_2OS_2$: C, 19.09; H, 4.82; N, 14.86; S, 33.93%).

Analytical methods

Carbon, hydrogen, nitrogen and sulfur were determined on a Carlo Erba 1106 Elemental Analyser. Melting points were recorded on a Gallenkamp apparatus with mercury in glass thermometer and are uncorrected.

Spectroscopy

Nmr spectra were recorded in $CDCl_3$ on a Bruker AM250 FT spectrometer operating at 250.13 MHz or 62.89 MHz for ^1H and ^{13}C nmr spectra, respectively, with TMS as internal standard. EI mass spectra were obtained on a Kratos Profile spectrometer operating at 70 eV.

Preparation of Unsymmetrical Trisulfides (2)

4-Methylbenzyl 2-hydroxyethyl trisulfide (**2e**). Twice distilled sulfur dichloride (3.19 g, 0.031 mol) in absolute ether (20ml) was added to a mixture of 2-hydroxyethyl mercaptan (2.65 g, 0.031 mol) and 4-methylbenzyl mercaptan (4.70 g, 0.034 mol) and the reaction mixture was maintained between 0–4 °C with an ice-salt bath. After the addition of sulfur dichloride, the reaction mixture was allowed to reach room temperature and the stirring was continued for an additional 24 h. The mixture was diluted with dichloromethane (500 ml), a 10-fold dilution, and extracted with 3 portions of water (3 × 100 ml). The organic layer was removed and dried with anhydrous magnesium sulfate, and the solvent was removed by rotary evaporation to give a light yellow clear oil which was subjected to chromatography on a silica gel column with light petroleum ether (b.p. 40–60 °C) as the first eluting solvent. This solvent was able to remove the symmetrical trisulfide, di-(4-methylbenzyl) trisulfide which is the major impurity. The column was then eluted with petroleum ether/dichloromethane (4:1) until no spot due to the symmetrical compound was observed in the tlc. Finally the desired compound was eluted with dichloromethane, followed by the total removal of solvent by rotary evaporation. Total removal of solvent was carried out under reduced pressure by collecting the material in a flask fitted for shaking. This gave *4-methylbenzyl 2-hydroxyethyl trisulfide* (**2e**) (2.3 g, 38%) as a clear yellow oil; tlc (2:1 ether/DCM on silica) gave a single spot with R_f 0.62; (Found: C, 48.83; H, 5.78; S, 39.00. $C_{10}H_{14}OS_3$ requires: C: 48.73; H, 5.74; S, 39.03%); $\delta_H(CDCl_3)$ 2.31 (CH_3, s, 3H), 2.64 (OH, s, 1H), 2.93 (SCH_2CH_2OH, t, 2H, $^3J_{HCCH} = 6$ Hz), 3.86 ($HOCH_2CH_2S$, t, 2H, $^3J_{HCCH} = 6$ Hz), 4.04 ($ArCH_2$, s, 2H), 7.17 (Ar -H, m, 4H); δ_C ($CDCl_3$) 21.12 (CH_3), 41.29 (SCH_2CH_2), 42.86 ($ArCH_2S$), 59.68 ($HOCH_2$), 127.03 (ArC-1) 129.27 (ArC-2, 6), 133.13 (ArC-3, 5), 137.34 (ArC-4); MS: m/z (%) 246 (M^+, 2), 214 (2), 181 (7), 137 (10), 105 (100), 45 (65).

A similar procedure to the above was used to prepare the following.

2-Chlorobenzyl 2-hydroxyethyl trisulfide (**2b**) (3.62 g, 36.7%), a clear light yellow oil; tlc (2:1 ether/DCM on silica) gave a single spot, R_f 0.59; (Found: C, 40.40; H, 4.20; S, 36.20. $C_9H_{11}ClOS_3$ requires: C, 40.51; H, 4.16; S, 36.02%); δ_H ($CDCl_3$) 2.41 (OH, s, 1H), 2.97 (SCH_2CH_2OH, t, 2H, $^3J_{HCCH}$ = 6Hz), 3.91 ($HOCH_2CH_2S$, t, 2H, $^3J_{HCCH}$ = 6 Hz), 4.19 (Ar-CH_2, s, 2H), 7.23 – 7.33 (Ar-H, m, 2H), 7.33 (Ar-H, m, 2H); δ_C ($CDCl_3$) 40.58 (SCH_2CH_2), 41.46 (Ar-CH_2), 59.56 ($HOCH_2$), 128.89 (ArC-1), 126.68 (ArC-3), 127.1 (ArC-5), 129.80 (ArC-6), 131.70 (ArC-2), 133.96 (ArC-4); MS: m/z (%) 266 (M^+, 2), 234 (2), 201 (1), 157 (3), 125 (17), 45 (59).

2-Methylbenzyl 2-hydroxyethyl trisulfide (**2d**), a light yellow clear oil; tlc (2:1 ether/DCM on silica) gave a single spot, R_f 0.52; (Found: C, 48.76; H, 5.72; S, 38.80. $C_{10}H_{14}OS_3$ requires: C, 48.73; H, 5.74; S, 39.03%); δ_H ($CDCl_3$) 2.38 (CH_3, s, 3H), 2.41 (OH, s, 1H), 2.94 (SCH_2CH_2OH, t, 2H, $^3J_{HCCH}$ = 6Hz), 3.87 ($HOCH_2CH_2S$, t, 2H, $^3J_{HCCH}$ = 6Hz), 4.11 (Ar-CH_2, s, 2H), 7.16 (Ar-H, m, 4H); δ_C ($CDCl_3$) 22.29 (CH_3), 41.38 (SCH_2CH_2), 42.98 (Ar-CH_2), 60.04 ($HOCH_2$), 127.16 (ArC-1), 128.84 (ArC-2), 129.38 (ArC-6), 133.24 (ArC-3), 133.8 (ArC-5), 137.39 (ArC-4); MS: m/z (%), 246 (M^+, 2), 214 (3), 181 (3), 137 (3), 105 (100), 45 (62).

Benzyl 2-hydroxyethyl trisulfide (**2a**)[8] (2.87 g, 26.9%), a light yellow clear oil; tlc (2:1 ether/DCM on silica) gave a single spot, R_f 0.86; (Found: C, 46.33; H, 5.24; S, 41.50. Calc. for $C_9H_{12}OS_3$: C, 46.51; H, 5.21, S, 41.51%); δ_H ($CDCl_3$) 2.57 (OH, s, 1H), 2.92 (SCH_2CH_2OH, t, 2H $^3J_{HCCH}$ = 6 Hz), 3.85 ($HOCH_2CH_2S$, t, 2H, $^3J_{HCCH}$ = 6 Hz), 4.07 (Ar-CH_2, s, 2H), 7.03 (Ar-H, m, 5H); δ_C ($CDCl_3$) 41.28 (SCH_2CH_2), 42.97 (Ar- CH_2S), 59.61 ($HOCH_2$), 127.62 (ArC-2), 128.61 (ArC-3,5), 129.40 (ArC-2,6), 136.24 (ArC-4); MS: m/z (%), 232 (M^+, 3), 200 (4), 167 (14), 124 (23), 91 (100), 45 (68).

4-Chlorobenzyl 2-hydroxyethyl trisulfide (**2c**) (3.25 g, 33%), a light yellow clear oil; tlc (2: 1 ether/DCM on silica) gave a single spot, R_f 0.65; (Found : C, 40.27; H, 4.29; S, 36.36. $C_9H_{11}ClOS_3$ requires: C, 40.51; H, 4.16; S, 36.02%); δ_H ($CDCl_3$) 2.40 (OH, s, 1H), 2.97 (SCH_2CH_2OH, t, 2H, $^3J_{HCCH}$ = 6 Hz), 3.89 ($HOCH_2CH_2S$, t, 2H, $^3J_{HCCH}$ = 6 Hz), 4.04 ($ArCH_2$, s, 2H), 7.28 (Ar-H, m, 4H); δ_C ($CDCl_3$) 40.31 (SCH_2CH_2), 41.39 (Ar-CH_2S), 59.52 ($HOCH_2$), 126.59 (ArC-1), 129.78 (ArC-3,5), 131.65 (ArC-2,6), 133.84 (ArC-4); MS: m/z (%) 266 (M^+, 2), 234 (1), 201 (2), 157 (1), 125 (23), 45 (62).

4-Methoxybenzyl 2-hydroxyethyl trisulfide (**2f**)[8](4.02 g, 35%), a light yellow clear oil; tlc (2:1 ether/DCM on silica) gave a single spot, R_f 0.57; (Found: C, 45.82, H, 5.36; S, 36.80. Calc. for $C_{10}H_{14}O_2S_3$: C, 45.76; H, 5.39; S, 36.65%); δ_H ($CDCl_3$) 2.40 (OH, s, 1H), 2.88 (SCH_2CH_2OH, t, 2H, $^3J_{HCCH} = 6$ Hz), 3.92 ($HOCH_2CH_2S$, t, 2H, $^3J_{HCCH} = 6$ Hz), 4.01 (Ar-CH_2, s, 2H), 7.35 (Ar-H, m, 4H); δ_C ($CDCl_3$) 41.32 (SCH_2CH_2), 42.96 ($ArCH_2$), 55.11 (CH_3O), 59.16 ($HOCH_2$), 114.19 (ArC-1), 129.54 (ArC-3,5), 132.78 (ArC-2,6), 158.89 (ArC-4); MS: m/z (%), 262(M^+, 2), 197 (4), 186 (3), 153 (2), 121 (29), 45 (53).

2-Furfuryl 2-hydroxyethyl trisulfide (**2g**)[8] (3.22 g, 34%), a yellow oil (which turned dark on exposure to light after about 24h); tlc (3:1 ether/DCM on silica) gave a single spot, R_f 0.46; (Found: C, 38.17; H, 4.78; S, 43.40. Calc. for $C_7H_{10}O_2S_3$: C, 38.71; H, 4.54; S, 43.26%); δ_H ($CDCl_3$) 2.52 (OH, s, 1H), 2.98 (SCH_2CH_2OH), t, 2H $^3J_{HCCH} = 7$ Hz), 3.90 ($HOCH_2CH_2S$, t, 2H $^3J_{HCCH} = 7$ Hz), 4.09 (Ar-CH_2, s, 2H), 6.33 (Ar-H, m, 2H), 7.40 (Ar-H, m, 1H), δ_C ($CDCl_3$) 35.32 (SCH_2CH_2), 41.69 (Ar-CH_2), 59.62 ($HOCH_2$), 109.50 (Furyl C-3), 110.66 (Furyl C-4), 142.43 (Furyl C-5) 149.20 (Furyl C-2); MS: m/z (%), 222 (M^+, 2); 186 (1), 157 (1), 118 (1), 81 (100), 45 (49).

Preparation of Unsymmetrical Tetrasulfides (3)

2-Methylbenzyl 2-hydroxyethyl tetrasulfide (**3c**). Twice distilled sulfur monochloride (2.48 ml, 0.031 mol) in absolute ether was added to a stirred mixture of 2-methylbenzyl mercaptan (4.59 ml, 0.034 mol) and 2-mercaptoethanol (2.38 ml, 0.034 mol) in ether (25 ml), and the reaction mixture was maintained between 0–4 °C with an ice-salt bath. After the addition of sulfur monochloride, the mixture was allowed to reach room temperature and the stirring was continued for an additional 4 h. The reaction mixture was worked up as described for the preparation of 4-methylbenzyl 2-hydroxyethyl trisulfide above to give *2-methylbenzyl 2-hydroxyethyl tetrasulfide* (5.58 g, 53%) as a deep yellow clear oil; tlc (2:1 ether/DCM on silica) gave a single spot, R_f 0.59; (Found: C, 43.20; H, 5.14; S, 45.80. $C_{10}H_{14}OS_4$ requires: C, 43.17; H, 5.07; S, 46.00%); δ_H($CDCl_3$) 2.21 (OH, s, 1H), 2.40 (CH_3, s, 3H), 3.06 (SCH_2CH_2OH, t, 2H, $^3J_{HCCH} = 6$ Hz), 3.91 ($HOCH_2S$, t, 2H, $^3J_{HCCH} = 6$ Hz), 4.18 (Ar-CH_2, s, 2H), 7.18 (Ar-H, m, 4H); δ_C ($CDCl_3$) 19.53 (CH_3), 41.76 (SCH_2CH_2), 42.83 (Ar-CH_2), 60.04 ($HOCH_2$), 126.14 (ArC-1), 128.31 (ArC-3), 127.9 (ArC-5), 130.85

(ArC-2), 130.2 (ArC-6), 137.06 (ArC-4); MS: m/z (%) 278 (M^+, 2), 214 (9), 186 (2), 137 (4), 105 (100), 45 (60).

A similar procedure to the above was used to prepare the following.

Benzyl 2-hydroxyethyl tetrasulfide (**3a**)[8] (5.28 g, 37%), a deep yellow oil; tlc (2:1 ether/DCM on silica) gave a single spot, R_f 0.64; (Found: C, 40.71, H, 4.54; S, 48.60. Calc. for $C_9H_{12}OS_4$: C, 40.74; H, 4.58; S. 48.56%); δ_H ($CDCl_3$) 2.30 (OH, s, 1H), 3.05 (SCH_2CH_2OH, t, 2H, $^3J_{HCCH} = 6$ Hz), 3.90 ($HOCH_2CH_2S$, t, 2H, $^3J_{HCCH} = 6$ Hz), 4.15 (Ar-CH_2, s, 2H), 7.62 (Ar-H, m, 5H); δ_C ($CDCl_3$) 41.65 (SCH_2CH_2), 43.31 (Ar- CH_2S), 59.80 ($HOCH_2$), 127.67 (ArC-1), 128.67 (ArC-3, 5), 129.43 (ArC-2,6), 135.99 (ArC-4); MS: m/z (%), 264 (M^+, 2), 200 (11), 167 (3), 123 (5), 91(100), 45(13).

4-Methoxybenzyl 2-hydroxyethyl tetrasulfide (**3e**) (4.49 g, 48%), a deep yellow oil; tlc (2:1 ether/DCM on silica) gave a single spot, R_f 0.53; (Found: C, 40.83; H, 4.78; S, 43.30. $C_{10}H_{14}O_2S_4$ requires: C, 40.82; H, 4.80; S, 43.50%); δ_H ($CDCl_3$) 2.61 (OH, s, 1H); 3.05 (SCH_2CH_2OH, t, 2H, $^3J_{HCCH} = 6$ Hz), 3.77 (CH_3O, s, 3H), 3.92 ($HOCH_2CH_2S$, t, 2H, $^3J_{HCCH} = 6$ Hz); δ_C ($CDCl_3$) 41.62 (SCH_2CH_2), 43.07 (Ar-CH_2S), 55.23 (CH_3O), 59.79 ($HOCH_2$), 114.50 (ArC-1), 130.63 (ArC-3,5), 131.30 (ArC-2,6), 159.06 (ArC-1); MS: m/z (%), 294 (M^+, 2), 230 (8), 198 (5), 153 (5), 129 (100), 45 (62).

4-Chlorobenzyl 2-hydroxyethyl tetrasulfide (**3b**) (5.24 g, 40%), a deep yellow oil; tlc (2:1 ether/DCM on silica) gave a single spot, R_f 0.61; (Found: C, 36.23; H, 3.69; S, 42.79. $C_9H_{11}ClOS_4$ requires; C, 36.19, H, 3.79; S, 42.85%); δ_H 2.13 (OH, s, 1H), 3.07 (SCH_2CH_2OH, t, 2H, $^3J_{HCCH} = 6$ Hz), 3.92 ($HOCH_2CH_2S$, t, 2H, $^3J_{HCCH} = 6$ Hz), 4.11 (Ar-CH_2S, s, 2H), 7.29 (Ar-H, m, 4H); δ_C ($CDCl_3$) 41.71 (SCH_2CH_2), 43.39 ($ArCH_2$), 59.60 ($HOCH_2$), 126.47 (ArC-1), 128.51 (ArC-3,5), 130.76 (ArC-2,6), 134.63 (ArC-4); MS: m/z (%), 298 (M^+, 3), 266 (8), 234 (3), 201 (5), 157 (4), 121 (100), 45 (59).

4-Methylbenzyl 2-hydroxyethyl tetrasulfide (**3d**) (4.65 g, 44%), a deep yellow oil; tlc (2:1 ether/DCM on silica) gave a single spot R_f 0.61; (Found: C, 43.28; H, 4.98; S, 45.76. $C_{10}H_{14}OS_4$ requires: C, 43.17; H, 5.07; S, 46.00%); δ_H ($CDCl_3$) 2.33 (CH_3, s, 3H) 3.05 (SCH_2CH_2OH, t, 2H, $^3J_{HCCH} = 6$ Hz), 3.90 ($HOCH_2CH_2S$, t, 2H, $^3J_{HCCH} = 6$ Hz), 4.12 (Ar-CH_2S, s, 2H), 7.19 (Ar-H, m, 4H); δ_C ($CDCl_3$) 19.29 (CH_3), 41.70 (SCH_2CH_2), 42.79 (Ar-CH_2S), 59.99 ($HOCH_2$),

126.09 (ArC-1), 128.20 (ArC-3,5), 130.69 (ArC-2,6), 136.94 (ArC-4); MS: m/z (%), 278 (M^+, 2); 214 (11), 186 (3) 137 (5), 105 (100), 45 (49).

2-Furfuryl 2-hydroxyethyl tetrasulfide (**3f**) (3.68 g, 31%), a deep yellow oil (which turned dark on exposure to light after 24 h); tlc (3:1 ether/DCM on silica) gave a single spot, R_f 0.42; (Found; C, 32.96; H, 3.86; S, 50.29. $C_7H_{10}O_2S_4$ requires: C, 33.08; H, 3.97; S, 50.36%); δ_H ($CDCl_3$) 2.57 (OH, s, 1H), 2.99 (SCH_2CH_2OH, t, 2H $^3J_{HCCH} = 7$ Hz), 2.92 ($HOCH_2CH_2S$, t, 2H $^3J_{HCCH} = 7$ Hz), 4.11 ($ArCH_2$, s, 2H), 6.39 (Ar-H, m, 2H), 7.47 (Ar-H, m, 1H); δ_C ($CDCl_3$) 35.38 (SCH_2CH_2), 41.83 ($ArCH_2$), 60.01 ($HOCH_2$), 109.65 (Furyl C-3), 111.02 (Furyl C-4), 143.02 (Furyl C-5), 149.57 (Furyl C-2); MS: m/z (%), 254 (M^+, 4), 222 (5), 190 (9), 158 (3), 113 (6), 81 (100), 45 (47).

Preparation of Unsymmetrical Disulfides (5)

2-Chlorobenzyl 2-hydroxyethyl disulfide (**5b**). To a solution of 2-chlorobenzyl mercaptan (6.05 ml, 0.046 mol) and 2-hydroxyethylthioisothiouronium chloride (9.40 g, 0.049 mol) in methanol (100 ml) was added a solution of sodium hydrogen carbonate (6.00 g, 0.071 mol) in water (100 ml) with vigorous stirring in an ice/salt bath. Stirring was continued for 2 h after which an oil separated out. The mixture was worked up as described earlier on to give *2-chlorobenzyl 2-hydroxyethyl disulfide* (**5b**) (6.58 g, 61%) as a clear light yellow oil; tlc (2: 1 ether/DCM on silica) gave a single spot R_f 0.63; (Found: C, 46.43; H, 4.87; S, 28.00. $C_9H_{11}ClOS_2$ requires: C, 46.05; H, 4.73; S, 27.26%); δ_H ($CDCl_3$) 2.54 (SCH_2CH_2OH, t, 2H, $^3J_{HCCH} = 6$ Hz), 2.80 (OH, s, 1H), 3.71 ($HOCH_2CH_2S$, t, 2H, $^3J_{HCCH} = 6$ Hz), 3.99 ($ArCH_2S$, s, 2H), 7.17 (Ar-H, m, 4H); δ_C ($CDCl_3$) 40.78 (SCH_2CH_2), 40.93 (Ar-CH_2S), 60.06($HOCH_2$), 129.71 (ArC-2), 133.91 (ArC-5), 126.70 (ArC-1), 131.41 (ArC-6), 134.03 (ArC-3), 134.73 (ArC-4); MS; m/z (%), 234 (M^+, 5), 202 (1), 157 (3), 125 (100), 45 (53).

A similar procedure to the above was used to prepare the following.

4-Methoxybenzyl 2-hydroxyethyl disulfide (**5g**) (6.2 g, 58 %), a white crystalline solid; tlc (2: 1 ether/DCM on silica) gave a single spot, R_f0.57; (Found: C, 52.13; H, 6.15; S, 27.42; $C_{10}H_{14}O_2O_2$ requires: C, 52.16; H, 6.13; S, 27.83%); m.p. 89–91 °C; δ_H ($CDCl_3$) 2.47 (OH, s, 1H), 2.54 (SCH_2CH_2OH, t, 2H, $^3J_{HCCH} = 6$Hz), 3.74 ($HOCH_2CH_2S$, t, 2H, $^3J_{HCCH}$= 6 Hz), 3.77 (CH_3O, s, 3H), 3.85 (Ar-CH_2S, s, 2H), 6.86 – 7.21

(Ar-H, m, 4H); δ_C ($CDCl_3$) 40.79 (SCH_2CH_2), 42.74 (Ar-CH_2S), 55.21 (CH_3O), 60.15 ($HOCH_2$), 113.85 (ArC-1), 129.21 (ArC-3,5), 130.41 (ArC-2,6), 188.99 (ArC-4); MS: m/z (%), 230 (M^+, 2), 198 (1) 158 (3), 121 (100), 45 (46).

2-Methylbenzyl 2-hydroxyethyl disulfide (**5e**)[8,9](6.47 g, 65%), a clear light yellow oil; tlc (2: 1 ether/DCM on silica) gave a single spot, R_f 0.62; (Found: C, 56.14; H, 6.59; S, 29.89. Calc. for $C_{10}H_{14}OS_2$: C, 56.04; H, 6.60; S, 29.89%), δ_H ($CDCl_3$) 2.38 (CH_3, s, 3H), 2.48 (SCH_2CH_2, t, 2H, $^3J_{HCCH}$ = 6 Hz); 2.49 (OH, s, 1H), 3.67 ($HOCH_2CH_2S$, t, 2H, $^3J_{HCCH}$ = 6 Hz), 3.91 (Ar-CH_2, s, 2H), 7.15 (Ar-H, m, 4H); δ_C ($CDCl_3$) 19.21 (CH_3) 40.79 (SCH_2CH_2), 41.42 ($ArCH_2$), 60.03 ($HOCH_2$), 125.91 (ArC-1), 127.79 (ArC-2), 130.49 (ArC-6), 134.67 (ArC-3), 134.12 (ArC-5), 136.68 (ArC-4); MS: m/z (%), 214 (M^+, 4), 182 (2), 137 (6), 105 (100), 45 (48).

Benzyl 2-hydroxyethyl disulfide (**5a**)[8,9] (5.86 g, 63%), a clear light yellow oil; tlc (2: 1 ether/DCM on silica) gave a single spot, R_f 0.70; (Found: C, 54.04; H, 5.97; S, 32.20. Calc. for $C_9H_{12}OS_2$: C, 53.99; H, 6.04; S, 31.97%); δ_H ($CDCl_3$) 2.34 (OH, s, 1H), 2.49 (SCH_2CH_2OH, t, 2H, $^3J_{HCCH}$ = 6 Hz), 3.68 ($HOCH_2CH_2$, t, 2H, $^3J_{HCCH}$ = 6 Hz), 3.88 (Ar-CH_2, s, 2H), 7.30 (Ar-H, m, 5H); δ_C ($CDCl_3$) 40.74 (SCH_2CH_2) 43.30 ($ArCH_2$) 60.13 ($HOCH_2$), 127.53 (ArC-1), 128.77 (ArC- 3,5), 129.29 (ArC-3,6), 137.14 (ArC-4); MS: m/z (%), 200 (M^+, 8), 168 (2), 153 (1), 123 (2), 91 (100), 45 (56).

4-Chlorobenzyl 2-hydroxyethyl disulfide (**5c**) (6.95 g, 64%), a clear light yellow oil; tlc (2: 1 ether/DCM on silica) gave a single spot, R_f 0.59; (Found : C, 46.13; H, 4.67; S, 29.10. $C_9H_{11}ClO_2S_2$ requires: C, 46.05; H, 4.73; S, 27.31%); δ_H($CDCl_3$) 2.36 (OH, s, 1H), 2.86 (SCH_2CH_2OH, t, 2H, $^3J_{HCCH}$ = 6 Hz), 3.73 ($HOCH_2CH_2S$, t, 2H, $^3J_{HCCH}$ = 6 Hz), 3.84 (Ar-CH_2, s, 2H), 7.27 (Ar-H, m, 4H); δ_C ($CDCl_3$) 40.91 (SCH_2CH_2), 42.58 (Ar-CH_2), 60.16 ($HOCH_2$), 128.69 (ArC-1), 130.58 (ArC-3,5), 133.37 (ArC-2,6), 135 (ArC-4); MS: m/z (%), 234 (M^+, 2); 202 (1), 167 (1), 157 (2), 152 (100), 45 (43).

4-Methylbenzyl 2-hydroxyethyl disulfide (**5f**)[8,9](5.98 g, 60%), a clear light yellow oil; tlc (2: 1 ether/DCM on silica) gave a single spot, R_f 0.59; (Found : C, 56.11; H, 6.68; S, 29.84. Calc. for $C_{10}H_{14}OS_2$: C 56.04; H, 6.60; S, 29.89); δ_H ($CDCl_3$) 2.31 (CH_3, s, 3H), 2.49 (OH, s, 1H) 2.53 (SCH_2CH_2OH, t, 2H, $^3J_{HCCH}$ = 6 Hz), 3.69 ($HOCH_2CH_2S$, t, 2H, $^3J_{HCCH}$ = 6 Hz); 3.84 (Ar-CH_2, s, 2H), 7.17 (Ar-H, m, 4H); δ_C ($CDCl_3$), 21.12 (CH_3), 40.76 (SCH_2CH_2), 43.17 ($ArCH_2S$), 60.13($HOCH_2$), 129.14

(ArC-1), 129.22 (ArC-3,5), 133.99 (ArC-2,6), 137.21 (ArC-4); MS: m/z (%), 214 (M^+, 5), 182 (3), 137 (8), 105 (100).

4-Fluorobenzyl 2-hydroxyethyl disulfide (**5d**)[8,9](6.59 g, 65%), a yellow oil; tlc (3:1 ether/DCM on silica) gave a single spot, R_f 0.59; (Found: C, 49.49; H, 5.04; S, 29.10. Calc. for $C_9H_{11}FOS_2$: C, 49.55; H, 5.08; S, 29.33%); δ_H ($CDCl_3$) 2.41 (OH, s, 1H), 2.54 (SCH_2CH_2OH, t, 2H $^3J_{HCCH} = 6$ Hz), 3.73 ($HOCH_2CH_2S$, t, 2H, $^3J_{HCCH} = 6$ Hz), 3.86 ($ArCH_2S$, s, 2H), 6.96 – 7.00 (Ar-H, m, 2H), 7.03 – 7.31 (Ar-H, m, 2H); δ_C ($CDCl_3$) 40.83 (SCH_2CH_2), 42.50 ($ArCH_2S$); 60.13 ($HOCH_2$), 115.63 (ArC-1), 130.94 (ArC-3,5), 133.01 (ArC-2,6), 160.26 (ArC-4); MS: m/z (%) 218 (M^+, 9), 186 (2), 141 (4), 139 (1), 121 (1), 109 (100), 45 (56).

Preparation of Unsymmetrical Monosulfides (7)

2-Chlorobenzyl 2-hydroxyethyl monosulfide (**7b**).[14] 2-Chlorobenzyl mercaptan (11.7 ml, 0.090 mol) was added to a solution of sodium hydroxide (3.60 g, 0.090 mol) in water (10 ml) diluted with ethanol (100 ml). No attempt was made to isolate the mercaptide. 2-Chloroethanol (6.04 ml, 0.090 mol) was added to the above mixture with cooling in an ice-salt bath and vigorous stirring. The mixture was heated under reflux for 4 h and allowed to cool. It was then diluted with water and the crude product separated out as an oil. The oil was washed with water in order to remove any remaining sodium chloride and extracted with dichloromethane. The dichloromethane layer was extracted with three portions of water (3 × 100 ml) and dried over magnesium sulfate, followed by the removal of solvent by rotary evaporation under reduced pressure. Similar chromatographic method as described above was used to give 2-chlorobenzyl 2-hydroxyethyl monosulfide[16] (12.4 g, 68%) as a yellow oil; tlc (3:1 ether/DCM on silica) gave a single spot, R_f 0.72; (Found: C, 53.36; H, 5.53; S, 15.90. Calc. for $C_9H_{11}ClOS$: C, 53.33; H, 5.49; S, 15.79%); δ_H ($CDCl_3$) 2.64 (SCH_2CH_2OH, t, 2H, $^3J_{HCCH} = 6$ Hz), 3.06 (OH, s, 1H), 3.68 ($HOCH_2CH_2S$, t, 2H, $^3J_{HCCH} = 6$ Hz), 3.81 ($ArCH_2$, s, 2H), 7.17 – 7.32 (Ar-H, m, 4H); δ_C ($CDCl_3$) 33.25 (SCH_2CH_2), 34.39 ($ArCH_2S$), 60.53 ($HOCH_2$), 126.85 (ArC-1), 129.71 (ArC-2), 130.73 (ArC-6), 133.81 (ArC-3), 133.2 (ArC-5), 135.84 (ArC-4); MS: m/z (%), 202 (M^+, 10), 157 (9), 125 (100), 45 (61).

A similar procedure to the above was used to prepare the following.

2-Methylbenzyl 2-hydroxyethyl monosulfide (**7d**)[14] (9.0 g, 62%), a yellow oil; tlc (3:1 ether/DCM on silica) gave a single spot, R_f0.68; (Found: C, 65.80; H, 7.70; S, 17.80. Calc. for $C_{10}H_{14}OS$: C, 65.80; H, 7.67; S, 17.59%); δ_C ($CDCl_3$) 2.38 (CH_3, s, 3H), 2.61 (OH, s, 1H), 2.68 (SCH_2CH_2OH, t, 2H, $^3J_{HCCH}$ = 6 Hz), 3.66 ($HOCH_2CH_2S$, t, 2H, $^3J_{HCCH}$ = 6 Hz), 3.71 (Ar-CH_2, s, 2H), 7.15 (Ar-H, m, 4H); δ_C ($CDCl_3$) 19.13 (CH_3), 33.81 (SCH_2CH_2), 34.54 ($ArCH_2S$), 60.44 ($HOCH_2$), 125.86 (ArC-1), 127.44 (ArC-2), 129.63 (ArC-6), 135.63 (ArC-3), 135.0 (ArC-5) 136.63 (ArC-4); MS: m/z (%) 182 (M^+, 49), 137 (6), 105 (100), 45 (48).

4-Methoxybenzyl 2-hydroxyethyl monosulfide (**7f**)[14] (13.3 g, 67%), a yellow oil; tlc (3:1 ether/DCM on silica) gave a single spot, R_f 0.69; (Found: C, 60.84; H, 7.11; S, 15.90. Calc. for $C_{10}H_{14}OS$: C, 60.58; H, 7.12; S, 16.14); δ_H ($CDCl_3$) 2.58 (OH, s, 2H), 2.60 (SCH_2CH_2OH, t, 2H, $^3J_{HCCH}$ = 6 Hz), 3.67 ($HOCH_2CH_2S$, t, 2H, $^3J_{HCCH}$ = 6 Hz), 3.78 (CH_3O, s, 3H), 3.87 (Ar-CH_2, s, 2H), 6.82 – 7.20 (Ar-H, m, 4H); δ_C ($CDCl_3$) 34.19 (SCH_2CH_2), 35.10 (Ar-CH_2S), 55.25 (CH_3O), 60.26 ($HOCH_2$), 113.98 (ArC-1), 129.92 (ArC-3,5), 135.33 (ArC-2,6), 158.69 (ArC-4); MS: m/z (%), 198 (M^+, 30), 153 (3), 121 (100), 45 (47).

Benzyl 2-hydroxyethyl monosulfide (**7a**)[14] (7.4 g, 59%), a yellow oil; tlc (3:1 ether/DCM on silica) gave a single spot, R_f 0.73. (Found: C, 64.17; H, 7.20; S, 18.80. Calc. for $C_9H_{12}OS$: C, 64.26; H, 7.21; S, 19.02); δ_H ($CDCl_3$) 2.55 (SCH_2CH_2OH, t, 2H, $^3J_{HCCH}$ = 6 Hz), 2.88 (OH, s, 1H), 3.63 ($HOCH_2CH_2S$, t, 2H $^3J_{HCCH}$ = 6 Hz), 3.67 ($ArCH_2$, s, 2H), 7.27 (ArH, m, 5H); δ_C ($CDCl_3$) 33.78 (SCH_2CH_2), 35.28 (Ar-CH_2S), 60.22 ($HOCH_2$) 128.57 (ArC-1), 129.24 (ArC-3,5), 130.11 (ArC-2,6), 131.47 (ArC-4); MS: m/z (%), 168 (M^+, 27) 123 (22), 91 (100), 45 (54).

4-Chlorobenzyl 2-hydroxyethyl monosulfide (**7c**)[14] (13.2 g, 7.3%), a yellow oil; tlc (3:1 ether/DCM on silica) gave a single spot, R_f0.69; (Found: C, 53.29; H. 5.46; S, 15.84. Calc for $C_9H_{11}ClOS$: C, 53.33; H, 5.49; S, 15.79%). δ_H ($CDCl_3$) 2.66 (SCH_2CH_2OH, t, 2H, $^3J_{HCCH}$ = 6 Hz), 3.04 (OH, s, 1H), 3.69 ($HOCH_2CH_2S$, t, 2H, $^3J_{HCCH}$ = 6 Hz), 3.79 (Ar-CH_2, s, 2H), 7.29 (Ar-H, m, 4H); δ_C ($CDCl_3$) 33.46 (SCH_2CH_2), 34.75 (Ar-CH_2S), 60.42 ($HOCH_2$), 128.68 (ArC-1), 129.38 (ArC-3,5), 132.13 (ArC-2,6), 134.89 (ArC-4); MS: m/z (%), 202 (M^+, 12), 157 (9), 125 (100), 45 (50).

4-Methylbenzyl 2-hydroxyethyl monosulfide (**7e**)[14] (7.35 g, 60%), a yellow oil, tlc (3:1 ether/DCM on silica) gave a single spot, R_f0.70; (Found: C, 65.78; H, 7.74; S, 17.63. Calc. for $C_{10}H_{14}OS$: C, 65.80; H, 7.67; S,

17.59%); δ_H ($CDCl_3$) 2.31 (CH_3, s, 3H), 2.89 (OH, s, 1H), 2.61 (SCH_2CH_2OH, t, 2H, $^3J_{HCCH} = 6$ Hz), 3.64 ($HOCH_2CH_2S$, t, 2H, $^3J_{HCCH} = 6$ Hz), 3.66 (Ar-CH_2, s, 2H), 7.16 (Ar-H, m, 4H); δ_C ($CDCl_3$) 21.06 (CH_3), 34.19 (SCH_2CH_2), 35.41 ($ArCH_2S$), 60.24 ($HOCH_2$), 128.72 (ArC-1), 129.25 (ArC-3,5), 134.94 (ArC-2,6), 136.77 (ArC-4); MS: m/z (%) 182 (M^+, 42), 137 (5), 105 (100), 45 (54).

Biological Screening

(a) In vitro activity

Fungicidal tests *in vitro* were carried out by standard techniques in Saboround Dextrose Agar (SDA) as nutrient. For *Fusarium culmorum, Fusarium oxysporum* and *Gauenomyceles graminis*, sample concentrations of 1000 ppm, 100 ppm and 10 ppm were used. A control solution containing SDA (13g) in water (200 ml) was prepared. Also, solutions containing (a) guazatine-imazalil, and (b) phenylmercury acetate at various concentrations of active ingredient (1000 ppm, 100 ppm, 10 ppm) were prepared as standards. The solutions were poured into Petri dishes and allowed to cool. Each plate was then inoculated with a 5 mm agar plug containing actively growing fungus. All plates were kept in a sterilized incubator, maintained at 25°C. The growth diameter of fungal spore was measured every three days until there was complete growth on the control dish, i.e. until all the surface of the plate was covered with fungal spore (approximate diameter, 86 cm).

(b) In vivo activity

Assessments of *in vivo* activity were carried out by standard techniques at the Scottish Agricultural College. Glasshouse tests involved the post-inoculation treatment of seedlings with 0.1–0.33% solutions of test compounds in acetone/water (1:5). The extent of leaf infection was assessed after 6–10 days growth (for *Erisyphe graminis* and *Botrytis fabae*) or 13–19 days growth (for *Podosphaera leucotricha* and *Uromyces viciae-fabae*). Activity against *Phytophthora infestans* was determined using potato leaf discs which were floated on 0.33% solutions of the test compounds in distilled water. A droplet containing a suspension of sporangiospores was placed on the leaf disc, and the Petri dishes were placed in a controlled environment room for 4 days. Leaf discs were then examined for blight infection.

Acknowledgements

We are grateful to the Overseas Development Administration of the UK for the provision of a scholarship and the authorities of Ladoke Akintola University, Ogbomoso, for a period of study leave (for ETA). We thank British Technology Group Ltd. for financial support, Dr. Paul Matewele (University of North London) for assitance with *in vitro* screening, and Dr. Dale Walters of the Scottish Agricultural College for carrying out glasshouse tests and potato leaf disc tests *in vivo*. Thanks are also due to Professor A. E. Akingbohungbe and Dr. Julius Olaifa for their support and advice and Dr. Richard A'Court (BTG) for many helpful discussions.

References

1. D. M. Oaks, H. Hartmann and K. P. Dimick, *Anal. Chem.*, **36**, 1560 (1964).
2. H. Nishimura, K. Fujiwara, J. Mizutani and Y. Obata, *J. Agr. Food Chem.*, **19**, 1971 (1971).
3. L. Schreyen, P. Dirinck, F. Van Wassenhove and N. Schamp, *J. Agr. Food Chem.*, **24**, 336 (1976).
4. J. D. Sandy, R. C. Davis and A. Neuberger, *Biochem J.*, **150**, 245 (1975).
5. K. Morita and S. Kobayashi, *Tetrahedron Lett.*, 573 (1966).
6. R. Hodges and J. S. Shannon, *Aust. J. Chem.* **19**, 1059 (1966).
7. C. Von Szczepanski, J. Heindl, E. Schröder, H.-J. Kessler and U. Redmann (to Schering A.-G.), *Ger. Offen.* 2, 114, 653 (1972).
8. C. Von Szczepanski, P. Zgorzelak and G. A. Hoyer, *Arzneim-Forsch.*, **22**, 1975 (1972); *Chem. Abstr.* **78**, 55353h (1973).
9. C. Von Szczepanski, J. Heindl, G. A. Hoyer and E. Schröder, *Eur. J. Med. Chem. – Chim. Ther.*, **12**, 279–84 (1977): *Chem. Abstr.*, **87**, 134208d (1977).
10. A. W. Mott and G. Barany, *Synthesis*, 657 (1984).
11. M. E. Alonso and H. Aragona, *Org. Synth.*, Coll. Vol., **6**, 235 (1988).
12. E. T. Ayodele, H. R. Hudson, I. A. O. Ojo and M. Pianka, unpublished.
13. R.G. Hiskey, F. I. Carroll, R. M. Babb, J. O. Bledsoe, R.T. Puckett and B. W. Roberts, *J. Org. Chem.*, **26**, 1152 – 56 (1961).
14. R. Kuhn and O. Dann, *Chem. Ber.*, **73**, 1092–4 (1940).
15. E. T. Ayodele, Ph.D. thesis, University of North London, 1994.
16. K. Sirakawa, O. Aki, T. Tsujikawa and T. Tsuda, *Chem. Pharm. Bull.*, **18**, 235–42 (1970).