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Benzoyloxymethyl *p*-Toluenethiosulfonate: a Crystalline, Stable Synthetic Equivalent for $^{+}CH_2S^{+}$

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Benzoyloxymethyl *p*-toluenethiosulfonate has been developed as a reagent for the one-pot preparation of α-sulfide disulfides and the corresponding symmetrical bissulfide disulfides. The reagent is effective for systems bearing terminal aryl groups.

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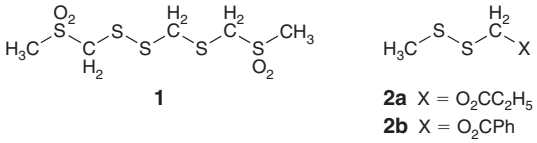
Introduction

Stemming from earlier reports[1,2] that dysoxysulfone **1** (Scheme 1) shows both antifungal and anticancer activity and our reports[3–5] that antifungal and antileukemic activity for structural relatives require the presence of a disulfide linkage, we have targeted disulfides for biological activity assessments. Related disulfides are now known to exhibit antimalarial activity as well.[6]

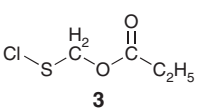
Like dysoxysulfone **1** itself, many of our synthetic targets have been α-substituted and unsymmetrical α,α′-disubstituted disulfides. A straightforward retrosynthetic analysis leads to the conclusion that a disulfide bearing a suitable leaving group on an α-carbon, such as **2**, would serve as a flexible intermediate from which an assortment of α-substituted disulfides might be accessed by means of simple substitution reactions.

Earlier work has shown that the α-ester disulfides **2a** and thus, probably, **2b** are suitable precursors for the synthesis of α-sulfone disulfides, i.e. X = O_2SR in **2**.[7,8] At this stage, only target methyl disulfides could be conveniently made. A previous report[8] described the successful preparation of the sulfenyl chloride ester **3** (Scheme 2), which is, to the best of our knowledge, the first synthetic equivalent for $^{+}CH_2S^{+}$.



1 **2a** X = $O_2CC_2H_5$; **2b** X = O_2CPh

Scheme 1.



3

Scheme 2.

Compound **3** has proved to be a useful platform from which to construct an assortment of α-sulfone disulfides.[8,9]

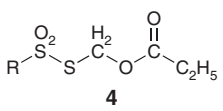
Treatment of **2a** with sulfuryl chloride/methylene chloride provides **3** as the major component in a mixture. Bulb-to-bulb distillation produces **3** which has been improved in purity but retains a persistent impurity. Furthermore, sulfenyl chlorides are often unstable so that prudent storage of unused **3** requires a freezer. This report describes the preparation of a new, stable synthetic equivalent for $^{+}CH_2S^{+}$. The new reagent has been applied to the one-pot conversion of mercaptans into α-sulfide disulfides.

Results and Discussion

In order to conserve electrophilicity at sulfenyl sulfur while introducing the possibility that a new reagent might be nicely crystalline, we elected to replace the sulfenyl chloride moiety in **3** with a thiosulfonate linkage. A pair of thiosulfonate propionates **4** (Scheme 3) were prepared and found to be persistent oils. Propionates were abandoned.

Because the yield of **2a** is quite low (15%), we had developed conditions[8] that afford the α-benzoate **2b** in better yield (see Scheme 4).

As part of the current study, a pair of methyl disulfides were treated with dibenzoyl peroxide in an attempt to obtain the



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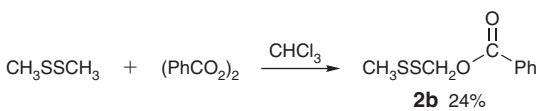
Scheme 3.



2b 24%

Scheme 4.

10.1071/CH04170 0004-9425/05/050362

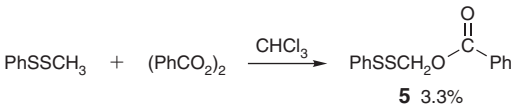
corresponding α-benzoate disulfides. In accord with our earlier report of the transition metal oxidation of phenyl methyl disulfide,[10] the α-benzoate was formed in very low yield (see Scheme 5). In contrast, benzyl methyl disulfide furnished benzaldehyde (see Scheme 6).

We turned, then, to work on the elaboration of a new thiosulfonate carboxylic acid ester. Prior to employing **2b** as a possible precursor for new reagent development, we confirmed that the benzoate group was comparable to propionate as a leaving group (see Scheme 7).

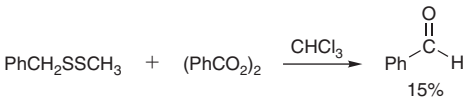
Thereafter, **2b** was smoothly transformed into the very nicely crystalline thiosulfonate benzoate **7** (see Scheme 8). Thiosulfonate carboxylic acid ester **7**, so produced, was isolated in excellent purity after simple recrystallization.

Support for the presence of the thiosulfonate linkage in **7** was obtained by mass spectrometry (chemical ionization) which showed major ions as depicted in Scheme 9.

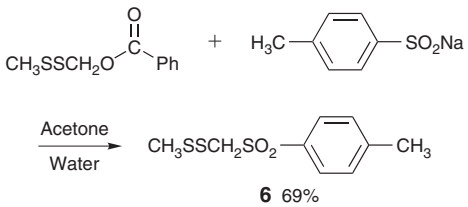
We have established a range of biological activity for α-sulfone disulfides[3–9,11–13] which includes pronounced antithrombotic activity.[11] In the search for new functionality, α-sulfide disulfides, which contain another moiety present in dysoxysulfone **1** (Scheme 1), were selected as synthetic targets to which the new reagent **7** (Scheme 8) might be applied.



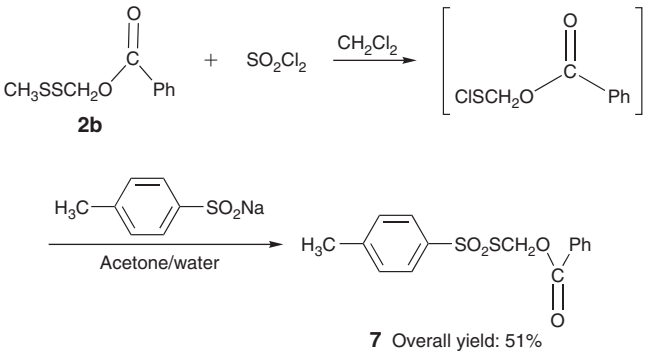
Scheme 5.



Scheme 6.



Scheme 7.



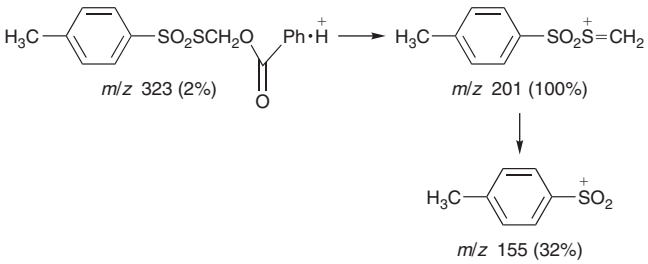
Scheme 8.

Scheme 10 presents the results of the first application of **7** to the one-pot preparation of the simple α-sulfide disulfide **8**.

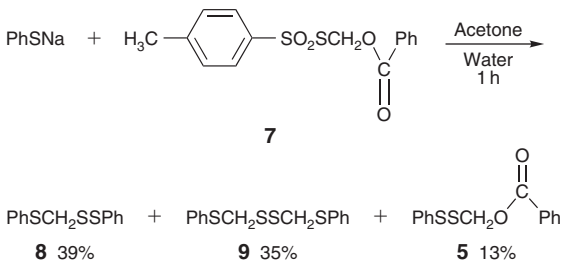
The unexpected formation of the bissulfide disulfide **9** might be rationalized by a phenyl mercaptide-catalyzed disproportionation reaction which converts **8** into **9**. In an attempt to enrich the product ratio to favour **8**, a second reaction was done. The second reaction, presented in Table 1, potentially disfavored the formation of **9** by significantly shortening the reaction time and diminishing the availability of SPh groups. Nonetheless, the relative yield of **9** was *increased*, albeit probably within experimental error, so that clean preparation of **8**, under these reaction conditions, is not possible. On the other hand, one-pot preparation of bissulfide disulfides like **9** is very economical. Such compounds will be of interest for biological testing.

In a brief examination of their chemistry, **8** and **9** were each subjected to oxidation with *m*-chloroperoxybenzoic acid as shown in Scheme 11.

Reactions between thiosulfonate benzoate **7** and a variety of mercaptide anions, both aryl and non-aryl, are summarized in Table 2. From the preparative standpoint, Table 2 results show that aryl mercaptide anions provide a richer array of useful products. The alkyl mercaptide anions did not furnish



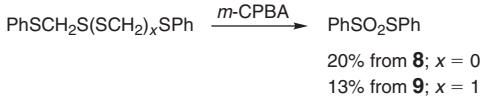
Scheme 9. Chemical ionization processes of **7** during mass spectrometry.



Scheme 10.

Table 1. Reactions between phenyl mercaptide anions and 7 in aqueous acetone

Ratio of PhSNa to **7**	Reaction time [min]	Mole ratio **8** : **9**
2 : 1 (Scheme 10)	60	2.2 : 1
1 : 1	10	1.8 : 1

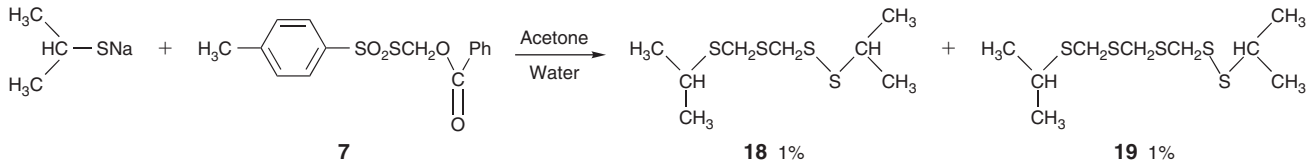


Scheme 11.

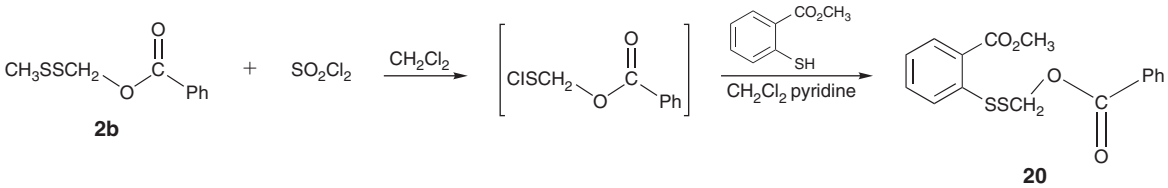
Table 2. Reactions between mercaptide anions and 7 in aqueous acetone
$RSNa + \mathbf{7} \rightarrow RSSCH_2OC(O)Ph + RSCH_2SSR + RSCH_2SSCH_2SR + RSSR$

R	Yields			
	$RSSCH_2OC(O)Ph$	$RSCH_2SSR$	$RSCH_2SSCH_2SR$	RSSR
Ph-	13% of **5**	39% of **8**	35% of **9**	[A]
p-Cl(C_6H_4)-	7% of **10**	40% of **11**	30% of **12**	[A]
o-$CH_3O_2C(C_6H_4)$-	0%	45% of **13**	25% of **14**	[A]
$CH_3CH_2CH_2$-	14% of **15**	0%	0%	–
$(CH_3)_2CH$-	11% of **16**	0%	0%	–
$PhCH_2$-	0%	6% of **17**	0%	59%[B]

[A] Typically, symmetrical aryl disulfides were recovered from product mixtures in approx. 15% yield. Air oxidation may account for some of that.
[B] GC-MS showed that starting benzyl thiol contained no detectable dibenzyl disulfide.



Scheme 12.



Scheme 13.

target α-sulfide disulfides upon reaction with **7**. From the standpoint of reaction pathways, the isopropyl mercaptide anion reaction provided a useful result. Nucleophilic attack by mercaptide anions on disulfides like **8** or **9** would produce α-sulfide mercaptide anions which are reasonable intermediates for these reactions. Such intermediates are known to extrude/add thioformaldehyde leading to a mixture of alternating carbon/sulfur frameworks.[2] Column chromatography of the product from the reaction between isopropyl mercaptide anions and **7** produced the benzoate disulfide **16** as shown in Table 2 and a pair of minor products as shown in Scheme 12.

Structural assignments for **18** and **19** rest upon ^{1}H NMR and mass spectra. The NMR spectra showed signals arising from non-equivalent isopropyl methyl protons (two doublets) and coincident isopropyl methine protons. The NMR spectrum of **18** showed a pair of non-equivalent methylene groups while the corresponding spectrum of **19** showed a trio of non-equivalent methylene groups. The mass spectra exhibited a common fragmentation pathway initiated by the loss of the disulfide moiety along with its isopropyl group, followed by sequential loss of thioformaldehyde units to produce the base peak at *m/z* 89 [$(CH_3)_2CHS{=}CH_2^+$].

To obtain support for our view that aryl mercaptide anions would transform **7** into an α-benzoate disulfide, thence into an α-sulfide disulfide and finally into a bissulfide disulfide, we chose to work with methyl *o*-mercaptobenzoate. The anion produced therefrom failed to furnish any benzoate disulfide upon reaction with **7** (entry 3, Table 2). However, the disulfide benzoate **2b** was smoothly transformed into the disulfide ester **20** as outlined in Scheme 13.

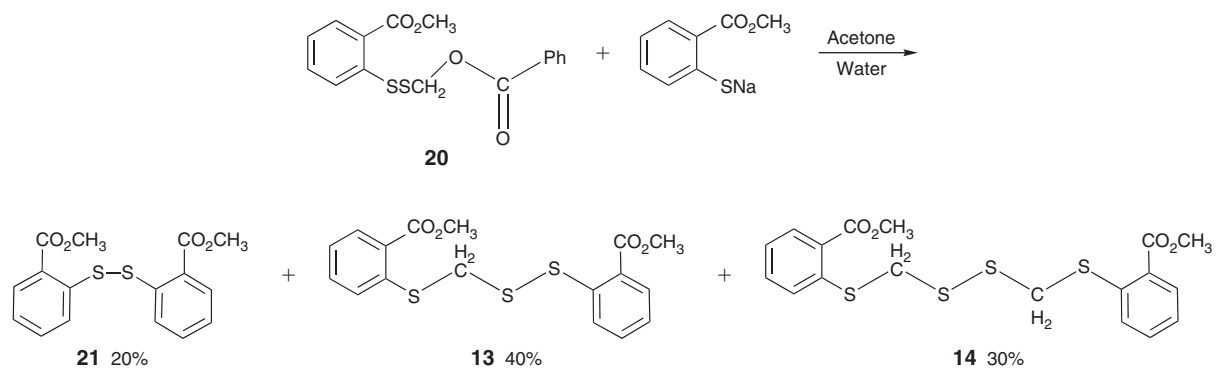
The disulfide diester **20** reacted with methyl *o*-mercaptobenzoate-derived anions to afford the expected mixture of products (see Scheme 14) in a result strongly reminiscent of the Table 2 results (entry 3).

Finally, reaction of the sulfide disulfide **13** with methyl *o*-mercaptobenzoate-derived anions produced virtually the same outcome as that shown in Scheme 14. A proposed mechanism for the reaction of aryl mercaptide anions with **7** is presented in Scheme 15.

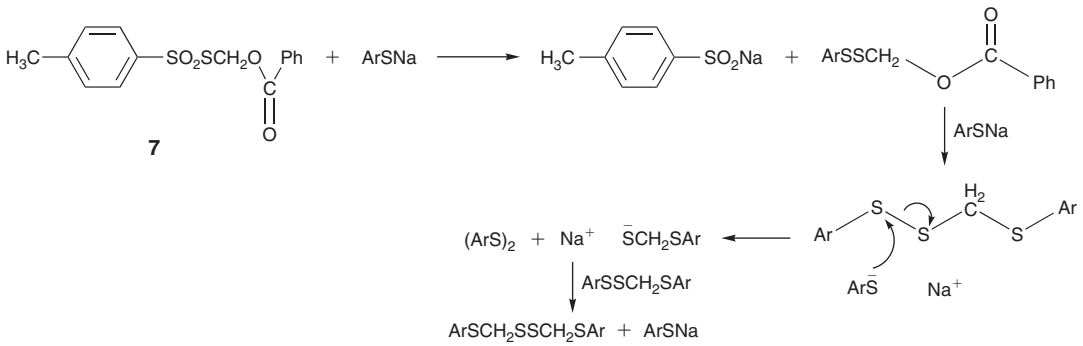
In conclusion, we have prepared and examined **7**, a new synthetic equivalent for $^+CH_2S^+$. With it, α-sulfide disulfides and bissulfide disulfides that bear terminal aryl groups are conveniently accessed.

Experimental

Infrared spectra were recorded on a Thermo Nicolet 2000 spectrometer. ^{1}H NMR (270 MHz) and ^{13}C NMR spectra were obtained on a JEOL JNM-GSX 270 Fourier-transform NMR system. Unless otherwise specified, all NMR spectra were obtained for compounds in deuterated chloroform using tetramethyl silane as an internal standard. Routine mass spectra (MS) were obtained on a Hewlett–Packard 5988A gas–liquid chromatography mass spectrometer (GLC-MS) system.[6] The CI(CH_4) spectrum for **7** was obtained on a Varian CP-3800 gas chromatograph equipped with a CP-8410 autoinjector and connected to a



Scheme 14.



Scheme 15.

Saturn 2000 mass-selective detector. Melting points were determined on a Gallenkamp MFB-595 capillary melting point apparatus and are uncorrected. Chloroform extracts were routinely dried over magnesium sulfate and filtered before solvent evaporation.

Reaction of Phenyl Methyl Disulfide with Dibenzoyl Peroxide

Phenyl methyl disulfide (1.0 g, 6.4 mmol) and dibenzoyl peroxide (2.2 g, 6.4 mmol) were added to chloroform (75 mL). The reaction mixture was refluxed for 24 h. Chloroform (75 mL) was added and the resultant mixture extracted with 2.5% w/v sodium hydroxide (2 × 125 mL aliquots). The solvent was evaporated and the residue chromatographed on silica gel employing 4 : 1 light petroleum/chloroform followed by 3 : 2 light petroleum/chloroform. The oily benzoate disulfide **5** was eluted (60 mg, 0.22 mmol, 3%). ν_{max} (neat)/cm^{-1} 1722. δ_H (270 MHz) 5.55 (2H, s, $SSCH_2O$), 7.22 (4H, m, ArH), 7.37 (2H, m, ArH), 7.54 (2H, m, ArH), 7.83 (2H, m, ArH). δ_C (68 MHz) 73.2, 127.4, 128.4, 128.7, 129.0, 129.3, 129.8, 133.4, 137.1, 165.8. *m/z* 276 (1%, $M^{+\bullet}$), 246 (4, $M^{+\bullet} - 30$), 105 (100). Note that the loss of 30 awu from the molecular ion is characteristic of C–O linked α-ester disulfides.[10]

Reaction of Benzyl Methyl Disulfide with Dibenzoyl Peroxide

Benzyl methyl disulfide was reacted with dibenzoyl peroxide and the products purified as described above for the reaction of phenyl methyl disulfide. Column fractions furnished benzaldehyde (90 mg, 0.85 mmol, 15%).

*Reaction of **2b** with the Sodium Salt of* p-*Toluenesulfinic Acid*

The disulfide benzoate **2b**[8] (0.5 g, 2.3 mmol) and the sodium salt of *p*-toluenesulfinic acid (0.5 g, 2.6 mmol) were added to 4 : 1 acetone/water (10 mL). The reaction mixture was heated at 50°C for 2 h. Chloroform (40 mL) was added and the resultant mixture extracted with water (25 mL). The solvent was evaporated and the residue chromatographed on silica gel employing 4 : 1 light petroleum/chloroform followed by 1 : 1 light petroleum/chloroform for elution. Chromatography furnished the α-sulfone disulfide **6** (0.40 g, 1.61 mmol, 70%) which was identical to previously obtained material[7] by ^{1}H and ^{13}C NMR spectra.

Preparation of Benzoyloxymethyl p-*Toluenethiosulfonate 7*

Procedure A

A solution of distilled sulfuryl chloride (0.626 g, 4.7 mmol) in dry methylene chloride (1 mL) was added to a solution of the disulfide benzoate **2b**[8] (1.0 g, 4.7 mmol) in dry methylene chloride (6 mL). The reaction mixture was refluxed for 0.5 h. The solvent was evaporated and dry methylene chloride (7 mL) added.

Procedure B

The sodium salt of *p*-toluenesulfinic acid (0.814 g, 4.6 mmol) was covered with 4 : 1 acetone/water (25 mL). The final methylene chloride solution from part A was added and the reaction mixture immersed in a constant temperature bath (50°C) for 4 h. The reaction mixture did not become homogeneous.

Chloroform (200 mL) was added and the resultant mixture washed with water (100 mL). The solvent was evaporated furnishing crude product (1.248 g). Crude product was recrystallized from methanol (16 mL) which gave the benzoate thiosulfonate **7** (0.571 g). A second crop of good purity **7** was obtained (0.199 g) from methanol (2 mL), mp 131–132°C (Found: C 56.1, H 4.2%. $C_{15}H_{14}O_4S_2$ requires C 55.9, H 4.4%). ν_{max} (KBr)/cm^{-1} 1726, 1329, 1142. δ_H (270 MHz) 2.34 (3H, s, $ArCH_3$), 5.83 (2H, s, OCH_2SS), 7.22 (2H, d, ArH), 7.35 (2H, t, ArH), 7.55 (1H, m, ArH), 7.70 (2H, d, *J* 8.1, ArH), 7.82 (2H, d, *J* 8.1, ArH). δ_C (68 MHz) 21.6, 67.8, 127.2, 128.3, 128.6, 129.85, 129.93, 133.7, 143.0, 145.0, 165.3. *m/z* CI(CH_4) 323 (2%, MH^+), 201 (100), 155 (32), 105 (54). A fragmentation pathway is proposed in Scheme 9.

Reaction of Mercaptide Anions with Benzoyloxymethyl p-*Toluenethiosulfonate 7*

A series of mercaptide anions were reacted with **7**. Results are summarized in Scheme 10 and Table 2. Details are provided for the reaction of *p*-chlorothiophenol (Table 2, entry 2).

Sodium metal (36 mg, 1.56 mmol) was dissolved in methanol (2 mL) and *p*-chlorothiophenol (226 mg, 1.56 mmol) added. The solvent was evaporated and the residue dried under vacuum. The residue was

dissolved in acetone (7 mL) and a solution of the benzoate thiosulfonate **7** (250 mg, 0.78 mmol) in acetone (5 mL) was added. The reaction mixture was stirred at ambient temperature for 1 h. Water (10 mL) was added and the resultant mixture extracted with chloroform (100 mL). The solvent was evaporated and the residue was chromatographed on silica gel employing light petroleum followed by 1 : 9 methylene chloride/light petroleum for elution. Di-*p*-chlorophenyl disulfide (33 mg, 0.12 mmol, 15%) was obtained. Further elution gave the sulfide disulfide **11** (104 mg, 0.31 mmol, 40%), mp 99–101°C (Found: C 47.0, H 3.4%. $C_{13}H_{10}Cl_2S_3$ requires C 46.8, H 3.0%). ν_{max} (KBr)/cm^{-1} 1474. δ_H (270 MHz) 4.09 (2H, s, SCH_2SS), 7.27 (8H, m, ArH). δ_C (68 MHz, $CDCl_3$, Me_4Si) 43.9, 129.25, 129.34, 129.6, 132.3 (shoulder observed), 133.5, 133.8, 135.1. *m/z* 334 (2.2%, $M^{+\bullet}+2$), 332 (2.8, $M^{+\bullet}$), 159 (36), 157 (100). Futher elution gave the oily bissulfide disulfide **12** (44 mg, 0.12 mmol, 30%). ν_{max} (film)/cm^{-1} 1475, 1398. δ_H (270 MHz) 4.18 (4H, s, SCH_2SS), 7.29 (4H, d, ArH), 7.36 (4H, d, ArH). δ_C (68 MHz) 41.2, 129.4, 131.9, 132.7, 133.6. *m/z* 159 (38%), 157 (100). Later fractions gave the disulfide benzoate **10** (18 mg, 0.058 mmol, 7%). ν_{max} (neat)/cm^{-1} 3062, 1727. δ_H (270 MHz) 5.53 (2H, s, OCH_2SS), 7.12 (2H, d, ArH), 7.36 (2H, t, ArH), 7.45 (3H, m, ArH), 7.78 (2H, d, ArH). δ_C (68 MHz) 73.2, 128.4, 129.1, 129.2, 129.7, 130.1, 133.5, 135.8, 165.7. *m/z* 312 (0.4%, $M^{+\bullet}+2$), 310 (1.1, $M^{+\bullet}$), 282 (1),[10] 280 (2.5, $M^{+\bullet}-30$), 159 (3), 157 (8), 105 (100).

The sodium salt of thiophenol was treated with **7** as described above for *p*-chlorothiophenol. Crude product was chromatographed on silica gel employing light petroleum then 1 : 9 methylene chloride/light petroleum and 1 : 1 methylene chloride/light petroleum for elution. Elution furnished the sulfide disulfide **8** (160 mg, 0.61 mmol, 39%), mp 51.9–52.3°C (Found: C 59.1, H 4.6%. $C_{13}H_{12}S_3$ requires C 59.0, H 4.6%). ν_{max} (KBr)/cm^{-1} 1435. δ_H (270 MHz) 4.16 (2H, s, SCH_2SS), 7.27 (10H, m, ArH). δ_C (68 MHz) 43.5, 127.2, 127.4, 128.1, 129.1, 130.7, 134.1, 136.6. *m/z* 264 (3.8%, $M^{+\bullet}$), 123 (100). Further elution gave the oily bissulfide disulfide **9** (85 mg, 0.274 mmol, 35%). ν_{max} (neat)/cm^{-1} 1581, 1479. δ_H (270 MHz) 4.23 (4H, s, SCH_2SS), 7.31 (10H, m, ArH). δ_C (68 MHz, $CDCl_3$, Me_4Si) 45.1, 127.3, 129.2, 130.4, 134.4. *m/z* 310 (2.8%, $M^{+\bullet}$), 123 (100). Further elution furnished the oily disulfide ester **5** (71 mg, 0.257 mmol, 17%) which was identical to previously isolated material by IR and ^{1}H, and ^{13}C NMR spectroscopy. The properties of **5** are described under above.

The sodium salt of methyl *o*-mercaptobenzoate was treated with **7** as described above for *p*-chlorothiophenol. Crude product was chromatographed on silica gel employing 4 : 1 light petroleum/chloroform, followed by 7 : 3 light petroleum/chloroform and 1 : 1 light petroleum/chloroform for elution. Elution afforded di-*o*-carbomethoxyphenyl disulfide (52 mg, 0.16 mmol, 20%). Further elution gave the sulfide disulfide **13** (133 mg, 0.35 mmol, 45%), mp 108–109°C. ν_{max} (KBr)/cm^{-1} 1708. δ_H (270 MHz) 3.88 (3H, s, CO_2CH_3), 3.92 (3H, s, CO_2CH_3), 4.19 (2H, s, SCH_2SS), 7.25 (2H, d, ArH), 7.52 (2H, m, ArH), 7.99 (2H, t, ArH), 8.06 (2H, t, ArH). δ_C (68 MHz) 40.7, 52.3, 52.4, 125.1, 125.6, 125.9, 126.6, 127.2, 128.4, 131.48, 131.55, 132.7, 132.9, 138.7, 140.9, 166.7, 166.8. *m/z* 181 (100%). Additional elution furnished the bissulfide disulfide **14** (42 mg, 0.097 mmol, 25%), mp 88–89°C. ν_{max} (KBr)/cm^{-1} 1710. δ_H (270 MHz) 3.88 (6H, s, CO_2CH_3), 4.32 (4H, s, SCH_2SS), 7.21 (2H, t, ArH), 7.50 (4H, m, ArH), 7.97 (2H, d, ArH). δ_C (68 MHz) 42.5, 52.3, 125.0, 126.6, 128.1, 131.4, 132.7, 139.1, 166.8. *m/z* 181 (100%).

The sodium salt of propane-1-thiol was treated with **7** as described above for *p*-chlorothiophenol. Crude product was chromatographed on silica gel employing light petroleum, 9 : 1 light petroleum/methylene chloride, 1 : 1 light petroleum/methylene chloride and methylene chloride. Elution gave the liquid disulfide ester **15** (26 mg, 0.11 mmol, 14%). ν_{max} (neat)/cm^{-1} 1724. δ_H (270 MHz) 0.91 (3H, t, CH_3),1.68 (2H, sextet, CH_2), 2.75 (2H, t, CH_2), 5.50 (2H, s, $SSCH_2O$), 7.46 (2H, t, ArH), 7.58 (1H, t, ArH), 8.06 (2H, d, ArH). δ_C (68 MHz) 13.0, 22.4, 41.8, 76.6, 128.6, 129.6, 129.9, 133.4, 165.9. *m/z* 242 (0.5%, $M^{+\bullet}$), 212 (6, $M^{+\bullet}-30$),[10] 105 (100).

The sodium salt of 2-mercaptopropane was treated with **7** as described above for *p*-chlorothiophenol. Crude product was chromatographed on silica gel employing light petroleum, 9 : 1 light petroleum/chloroform, 4 : 1 light petroleum/chloroform, and 1 : 1 light petroleum/chloroform.

Column elution furnished the oily bissulfide disulfide **18** (1.3 mg, 0.0053 mmol, 1.4%). δ_H (270 MHz) 1.27 (6H, d, CH_3), 1.31 (6H, d, CH_3), 3.11 (2H, septet, CH), 3.84 (2H, s, SCH_2S), 3.97 (2H, s, SCH_2SS). *m/z* 242 (2.1%, $M^{+\bullet}$), 167 (12, $M^{+\bullet}-(CH_3)_2CHS$), 135 (26, $M^{+\bullet}-(CH_3)_2CHSS$), 89 (100, $M^{+\bullet}-(CH_3)_2CHSSCH_2S$). Further elution gave the oily trissulfide disulfide **19** (1.0 mg, 0.0034 mmol, 1.3%). δ_H (270 MHz) 1.27 (6H, d, CH_3), 1.31 (6H, d, CH_3), 3.11 (2H, sept, CH), 3.79 (2H, s, SCH_2S), 3.94 (2H, s, SCH_2S), 3.98 (2H, s, SCH_2SS). *m/z* 181 (34%, $M^{+\bullet}-(CH_3)_2CHSS$), 135 (7, $M^{+\bullet}-(CH_3)_2CHSSCH_2S$), 89 (100, $M^{+\bullet}-(CH_3)_2CHSSCH_2SCH_2S$). Further elution furnished the disulfide ester **16** (20 mg, 0.082 mmol, 11%). ν_{max} (neat)/cm^{-1} 1724. δ_H (270 MHz) 1.30 [6H, d, $C(CH_3)_2$], 3.08 (1H, septet, CH) 5.47 (2H, s, OCH_2SS), 7.45 (2H, t, ArH), 7.58 (1H, t, ArH), 8.04 (2H, d, ArH). δ_C (68 MHz) 22.6, 41.6, 74.7, 128.6, 129.6, 129.9, 133.4, 165.9. *m/z* 242 (0.6%, $M^{+\bullet}$), 212 (7, $M^{+\bullet}-30$),[10] 105 (100).

The sodium salt of benzyl thiol was treated with **7** as described above for *p*-chlorothiophenol. Crude product was chromatographed on silica gel employing light petroleum and 9 : 1 light petroleum/chloroform. Elution gave dibenzyl disulfide (112.9 mg, 0.46 mmol, 59%). Further elution afforded the sulfide disulfide **17** (12.6 mg, 0.043 mmol, 6%). δ_H (270 MHz) 3.29 (2H, s, CH_2), 3.77 (2H, s, CH_2), 3.95 (2H, s, CH_2), 7.28 (10H, m, ArH). δ_C (68 MHz) 35.2, 40.9, 43.7, 127.3, 127.6, 128.6, 129.1, 129.4, 137.2, 137.4. *m/z* 137 (43%), 91 (100).

*Oxidations of **8** and **9** with* m-*Chloroperoxybenzoic Acid*

Each compound was oxidized following the procedure outlined for the sulfide disulfide **8**. The sulfide disulfide **8** (100 mg, 0.38 mmol) and *m*-chloroperoxybenzoic acid (50%, 328 mg) were dissolved in chloroform (10 mL), and the reaction mixture was stirred at ambient temperature for 7 days. Chloroform (100 mL) was added and the resultant mixture extracted with 2.5% w/v sodium hydroxide (2 × 100 mL portions). The solvent was evaporated and the residue chromatographed on silica gel employing light petroleum and 1 : 1 light petroleum/methylene chloride. Phenyl benzenethiosulfonate (19 mg, 0.076 mmol, 20%) was eluted.

Oxidation of **9** furnished phenyl benzenethiosulfonate (13%).

In each case, the phenyl benzenethiosulfonate was identical with freshly prepared authentic material (compare *m*-chloroperbenzoic acid oxidation of diphenyl disulfide) by IR, ^{1}H, and ^{13}C NMR spectra.

*Preparation of Disulfide Diester **20***

Procedure A

The disulfide benzoate **2b** (1.0 g) was converted into a solution of the ester sulfenyl chloride as described in Procedure A above for the preparation of **7**.

Procedure B

The solution from Procedure A was added to a solution of methyl 2-mercaptobenzoate (785 mg, 4.67 mmol) in methylene chloride (3 mL). Dry pyridine (0.8 mL) was added and the reaction stirred at ambient temperature, overnight. Chloroform (100 mL) was added and the resultant mixture extracted with 2.5% hydrochloric acid (100 mL). The solvent was evaporated affording crude **20** which was chromatographed on silica gel employing 1 : 1 light petroleum/chloroform for elution. Clean disulfide diester **20** (1.153 g, 3.45 mmol, 74%), mp 57–59°C. ν_{max} (KBr)/cm^{-1} 1716, 1699. δ_H (270 MHz) 3.93 (3H, s, OCH_3), 5.52 (2H, s, OCH_2SS), 7.13 (1H, t, ArH), 7.35 (3H, m, ArH), 7.53 (1H, t, ArH), 7.85 (2H, d, ArH), 7.96 (1H, d, ArH), 8.12 (1H, d, ArH). δ_C (68 MHz) 52.4, 73.1, 125.4, 126.2, 127.1, 128.4, 129.2, 129.9, 131.3, 132.7, 133.4, 141.5, 165.7, 166.9. *m/z* 334 (0.8%, $M^{+\bullet}$), 304 (3, $M^{+\bullet}-30$),[10] 105 (100) was obtained.

*Reaction of Disulfide Diester **20** with the Sodium Salt of Methyl 2-Mercaptobenzoate*

Sodium metal (36 mg, 1.56 mmol) was dissolved in methanol (2 mL) and methyl 2-mercaptobenzoate (262 mg, 1.56 mmol) added. The solvent

was evaporated and the residue dried under vacuum. The residue was dissolved in acetone (15 mL) and a solution of the disulfide diester **20** (521 mg, 1.56 mmol) in acetone (3 mL) was added. The reaction mixture was stirred at ambient temperature for 1 h.

Water (10 mL) was added and the resultant mixture extracted with chloroform (100 mL). The solvent was evaporated and the residue was chromatographed on silica gel employing 7 : 3 light petroleum/chloroform and 1 : 1 light petroleum/chloroform for elution. Elution gave the simple symmetrical disulfide **21** (104 mg, 0.311 mmol, 20%). Further elution furnished the sulfide disulfide **13** (237 mg, 0.62 mmol, 40%) which was identical to described previously material (see above description of the reaction of mercaptide anions with **7**) by ^{1}H NMR, ^{13}C NMR, and IR spectroscopy. Further elution gave the bissulfide disulfide **14** (101 mg, 0.24 mmol, 30%) which was identical to described previously material (see above) by ^{1}H NMR, ^{13}C NMR, and IR spectroscopy.

*Reaction of Sulfide Disulfide **13** with the Sodium Salt of Methyl 2-Mercaptobenzoate*

The sodium salt of methyl 2-mercaptobenzoate, prepared from methyl 2-mercaptobenzoate (131 mg, 0.78 mmol), was reacted with the sulfide disulfide **13** (296 mg, 0.78 mmol) as in the preceding procedure and the crude product chromatographed on silica gel. Elution with 7 : 3 light petroleum/chloroform followed by 1 : 1 light petroleum/chloroform gave symmetrical disulfide **21** (55 mg, 0.16 mmol, 21%) followed by unchanged disulfide **13** (113 mg, 38%) and then bissulfide disulfide **14** (53 mg, 0.124 mmol, 32%).

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