Reactions of 1,3-Dithiolane 1,3-Dioxides with Nucleophiles

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Reactions of benzenethiol with the 1,3-dithiolane 1,3-dioxides 3a-f gave the 1,4-dithiane 1-oxides 4-5, the \( \alpha,\beta \)-unsaturated sulfoxides 6-9, the ring-opening products 10-11 and various reduction products. Addition of benzenethiol, malononitrile, diethyl malonate or 2-mercapto-4,5-dihydrothiazole to the double bonds of the 2-alkenyl-1,3-dithiolane 1,3-dioxides 3g-h was performed with methylmagnesium chloride in methanol. Addition of methanol or an allyl group to the dioxide 3h occurred regioselectively to give the 1,3-dithiolane 1-oxide 19 or the 1,3-dithiolane 20.

Sulfoxides are versatile reagents in organic synthesis, being used as acyl nucleophile equivalents, in dehydroxylations to give alkenes, in the Pummerer rearrangement to give carbonyl compounds and in [2,3] sigmatropic rearrangements to give allylic alcohols. Sulfoxides are intrinsically chiral reagents and their use in asymmetric control is well documented. In contrast, there has been little work reported with disulfoxides, although compounds such as the trans-1,3-dithiolane 1,3-dioxides, which have \( C_2 \)-symmetry, are potential auxiliaries for enantioselective reactions. For example, Aggarwal and co-workers have shown both stereoselective addition reactions of \( \text{trans-1,3-dithiolane} \) with aromatic aldehydes and Diels-Alder reactions of \( \text{trans-2-methylene-1,3-benzodithiole} \) with dienes. Khair and his co-workers have demonstrated the use of \( C_2 \)-symmetric disulfoxides as chiral ligands in asymmetric Diels-Alder reactions. We report herein the addition and ring-expansion of 1,3-dithiolane 1,3-dioxides 3a-h in the presence of benzenethiol and other nucleophiles.

Results and Discussion

Preparation of Disulfoxides 3a-h.—Although 1,3-dithiolanes can be oxidized directly to their corresponding 1,3-dioxides by use of 2 equiv. of NaIO\(_4\), we carried out this transformation in two successive oxidation steps, as shown in Table 1. This method provided an ambiguous assignment of the stereostructures of the disulfoxides 3a-h. Oxidation of the 1,3-dithiolanes 1a-h with 1 equiv. of NaIO\(_4\) gave the corresponding monosulfoxides 2a-h in favour of the trans-isomers. The dithiolane 1d which had 2-methyl and 2-ethoxycarbonyl substituents afforded only the trans-isomer 2d, where the sulfinyl oxygen and ethoxycarbonyl group were on opposite faces of the molecule. In the \( ^1 \text{H} \) NMR spectra of compounds 2, the 2-H or 2-Me resonances of the trans-isomers usually occurred at lower field than those of the cis-isomers. The monosulfoxides 2a-h were then oxidized with 1 equiv. of \( m \)-chloroperbenzoic acid (m-CPBA)\(^*\) to give the corresponding disulfoxides 3a-h. The presence of \( C_2 \)-double bonds did not interfere with the oxidation process. Since the trans- and cis-isomers of 2b were both converted into the disulfoxide 3b, the product must have the trans-configuration. Similarly, the disulfoxides 3d-h must also have the trans-configuration. The disulfoxides 3a and 3c exist as a mixture of two isomers, where the cis-isomers have the two oxygen atoms and the methyl group on the same face to form a \( C_2 \)-symmetric molecule, as inferred by the coalescence of the C-4 and C-5 resonances. These results indicate that oxidation of the 1,3-dithiolane 1-oxides 2b and 2d-h occurred exclusively on the face opposite to the sulfinyl oxygen, whereas oxidation of the 1,3-dithiolane 1-oxides 2a and 2c were less selective, owing to the steric effect of the phenyl or the pentyl group.

Thermal Reactions of the Disulfoxides 3a-e in the Presence of Benzenethiol.—A methanolic solution of dioxide 3a and benzenethiol (1 equiv.) was heated at reflux to give the dithiane monoxide 4 in 72\%, as a mixture of the trans- and cis-isomers (86:14). The 2-H and C-2 resonances in the trans isomer of 4 appeared at low field (\( \delta \) 3.85 and 81.3). The C-5 resonance occurs at \( \delta \) 25.5 for the trans isomer, indicating an equatorial sulfinyl oxygen, whereas it resonates at \( \delta \) 16.1 for the cis isomer, indicating an axial configuration. Thermal ring expansion of the 2-methyl-1,3-dithiolane 1-oxide\(^10\) has been shown to involve an H-shift from the methyl group to the sulfinyl oxygen, accompanied by a concurrent ring opening to give an intermediate vinylthioethylsulfenic acid. The product 5,6-dihydro-1,4-dithiene is subsequently obtained by a ring-closure process presumably via the sulfur-stabilized carbonium ion intermediate. Accordingly, ring-expansion of the dioxide 3a to compound 4 was probably initiated by formation of the sulfenic acid intermediate A shown in Scheme 1. However, the intermediate A containing an electron deficient C=C double bond should act differently from the electrophilic vinyl sulfide species described above. The sulfenic acid A might undergo an intramolecular Michael addition\(^11\) to give a disulfoxide B, in which the less hindered sulf oxide group is selectively reduced.

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*Oxidant, NaIO\(_4\) (1 equiv.). Oxidant \( m \)-CPBA (1 equiv.). The cis-isomer of 3a (or 3c) had the two oxygen atoms and the methyl group on the same face.
observed for compound 8. The stereochemical outcome was in agreement with a concerted H-shift as shown in C.

Treatment of the dithiolane dioxide 3d with benzenethiol in refluxing methanol gave the thiol 10 and the corresponding phenyl disulfide 11. These products were characterised by characteristic methyl doublets in the $^1$H NMR spectra. The reaction sequence was presumably initiated by direct attack of benzenethiol on one of the sulfide groups to give the intermediate anion D, stabilized by the other adjacent ester and the other sulfide group.

2-Propyl-1,3-dithiolane 1,3-dioxide 3e was heated to 110 °C in a sealed tube in the presence of benzenethiol to give the partially reduced product 2e. Partial deoxygenation of the disulfide 3f gave the monosulfoxide 2f on treatment with lithium ethanethiolate (1 equiv.) and complete deoxygenation gave the dithiolane 1f on treatment with lithium dimethylcuprate (2 equiv.). These results were consistent with a previous report on the reduction of vinyl sulfoxides with EtMgBr-CuI.12

**Addition to the C=C Double Bond of the Disulfoxides 3g and 3h.** Allyl sulfoxides are known to undergo [2,3] sigmatropic rearrangements to form intermediates, which can be reduced with benzenethiol to give allyl alcohols.14 However, it was noted that benzenethiol adds to the C=C double bond of 2-styryl-1,3-dithiolane 1,3-dioxide 3g in MeOH upon mediation with a Grignard reagent to give the disulfide 12 in 91% yield. Use of malonitrile as the nucleophile gave the addition product 13 as a diastereomeric mixture (67:33). Similar reactions of 2-prop-1-enyl-1,3-dithiolane 1,3-dioxide 3h with the nucleophiles benzenethiol, malononitrile, diethyl malonate and 2-mercaptop-4,5-dihydrothiazole in the presence of MeMgCl gave the addition products 14, 15, 16 and 17 respectively. In one case, addition of malononitrile to the disulfide 3h was mediated by Al$_2$O$_3$.15

Alternatively, reduction of the sulfenic acid A to the thiol B, followed by an intramolecular Michael addition would lead to the same product. The 1,3-dithiolane 1,3-dioxide 3h, generated from 4,4-dimethylycloclohex-2-ene, underwent a similar ring expansion to afford the 1,4-dithiane 1-oxide 14. Since the ring-junction protons (1-H and 6-H) in compound 5 showed a small coupling constant (3.2 Hz), this bicyclic compound was determined to have a cis fused ring-junction and the resonance of C=4 at $\delta$ 21.7 was taken to indicate an equatorial sulfinyl oxygen.5 The reaction of 2-methyl-2-pentyl-1,3-dithiolane 1,3-dioxide 3c under similar conditions gave the α,β-unsaturated sulfoxides 6 and 8 accompanied by a significant amount of the disulfide 7. This reaction was considered to involve the sulfenic acid intermediates generated from deprotonation of either the methyl or the pentyl group, similar to that shown in Scheme 1. Subsequent disproportionation of these sulfenic acid intermediates with benzenethiol would lead to the observed products. From the distribution of products, ($6 + 7$):$8 = 7:1$, deprotonation of the methyl group appeared to be the more favoured process. In order to promote the ring closure of compounds 6 and 8, the reaction temperature was raised to 110 °C for a prolonged period. However, such conditions yielded mainly the disulfides 7 and 9, but no cyclization product.

A 16% nuclear Overhauser enhancement of the vinyl proton ($\delta$ 6.18) in the sulfoxide 8 was observed by irradiation of the adjacent methyl group ($\delta$ 1.83), indicating the Z-configuration for compound 8. Due to the deshielding effect of the sulfoxide group, the vinyl proton on the β-carbon of E-isomer usually resonates at lower field (about $\delta$ 6.4) than that of the Z-isomer.13 The configuration of 9 was assigned as $Z$, due to the vinyl resonance at $\delta$ 6.12 which was close to the value

Two possible mechanisms were considered to account for the observed additions (Scheme 2). Path a evoked direct addition of the nucleophile to the C=C double bond; the intermediate might be stabilised by coordination to the sulfinyl oxygen as shown in E. Path b involved a primary isomerisation of compound 3g (or 3h) to the conjugated disulfide F, which then underwent a Michael-type reaction16 with the nucleophile to give the observed product. Path a seemed less likely since the addition of EtSH to 2-methyl-2-styryl-1,3-dithiolane 1,3-dioxide 3f, containing no hydrogen atom at C-2 failed (Table 2, entry 7). We thought the addition performed in MeOD would afford doubly deuteriated products G via path b. To our surprise, the monodeuteriated addition product [7H]-12 was obtained from

![Scheme 1 Reagents and conditions: PhSH, MeOH, 70 °C, 36 h (72%)](image-url)
occurred at 6.5.94 and 5.99, respectively, whereas the minor diastereoisomers (a) with chloromagnesium acetate in MeOH gave 2-(2-methoxy-

spectrum, the vinyl resonances of the major 2-isomers supported our assumption, the addition of the conjugated disulfoxide has been measured to have a 

exchange of the C,-D, even in the presence of aqueous NH4Cl. From literature, the acidity of 2-H in 1,3-dithiane 1,3-dioxide has been described previously.4 J Values are given in Hz.

Table 2 Reactions of 1,3-dithiolane 1,3-dioxides 3a-h

<table>
<thead>
<tr>
<th>Entry</th>
<th>Disulfoxide</th>
<th>Reaction conditions</th>
<th>Products (yield, %; ratio of isomers)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3a</td>
<td>PhSH, MeOH, 70 °C, 36 h</td>
<td>4 (72; 86:14)</td>
</tr>
<tr>
<td>2</td>
<td>3b</td>
<td>PhSH, MeOH, 70 °C, 22 h</td>
<td>5 (73)</td>
</tr>
<tr>
<td>3</td>
<td>3c</td>
<td>PhSH, MeOH, 70 °C, 40 h</td>
<td>6 (10) + 7 (10) + 8 (3)</td>
</tr>
<tr>
<td>4</td>
<td>3d</td>
<td>PhSH, MeOH, 110 °C (sealed), 12 h</td>
<td>7 (22) + 9 (10)</td>
</tr>
<tr>
<td>5</td>
<td>3d</td>
<td>PhSH, MeOH, 70 °C, 3 h</td>
<td>10 (14; 80:20) + 11 (41:67:33)</td>
</tr>
<tr>
<td>6</td>
<td>3e</td>
<td>PhSH, MeOH, 110 °C (sealed), 18 h</td>
<td>2e (27) + 3e (50)</td>
</tr>
<tr>
<td>7</td>
<td>3f</td>
<td>EtSH, BuLi, THF, room temp., 4 h</td>
<td>2f (43)</td>
</tr>
<tr>
<td>8</td>
<td>3f</td>
<td>Me,CuLi, Et,O, THF, 0 °C, 5 h</td>
<td>3f (36)</td>
</tr>
<tr>
<td>9</td>
<td>3g</td>
<td>PhSH, MeMgCl, MeOH, room temp., 24 h</td>
<td>12 (91; 50:50)</td>
</tr>
<tr>
<td>10</td>
<td>3g</td>
<td>PhSH, MeMgCl, MeOD, room temp., 24 h</td>
<td>13 (42; 67:33)</td>
</tr>
<tr>
<td>11</td>
<td>3h</td>
<td>CH2(CN)2, MeMgCl, MeOH, room temp., 19 h</td>
<td>14 (98; 57:43)</td>
</tr>
<tr>
<td>12</td>
<td>3h</td>
<td>PhSH, MeMgCl, MeOH, room temp., 24 h</td>
<td>15 (46; 67:33)</td>
</tr>
<tr>
<td>13</td>
<td>3h</td>
<td>CH2(CN)2, MeMgCl, MeOD, room temp., 1 h</td>
<td>16 (28; 56:44)</td>
</tr>
<tr>
<td>14</td>
<td>3h</td>
<td>CH2(CN)2, Al2O3, room temp., 72 h</td>
<td>17 (46; 71:29)</td>
</tr>
<tr>
<td>15</td>
<td>3h</td>
<td>CH2(CN)2, PhSH, MeMgCl, MeOH, room temp., 1 h</td>
<td>18 (83; 100:0)</td>
</tr>
<tr>
<td>16</td>
<td>3h</td>
<td>PhSH, MeMgCl, MeOD, room temp., 1 h</td>
<td>19 (55; 33:33:17:17)</td>
</tr>
<tr>
<td>17</td>
<td>3h</td>
<td>Me2CO,H, MeMgCl, MeOH, room temp., 1 h</td>
<td>20 (53)</td>
</tr>
<tr>
<td>18</td>
<td>3h</td>
<td>PhSH, MeMgCl, MeOH, room temp., 1 h</td>
<td>20 (53)</td>
</tr>
<tr>
<td>19</td>
<td>3h</td>
<td>PhSH, MeMgCl, MeOD, room temp., 1 h</td>
<td>20 (53)</td>
</tr>
<tr>
<td>20</td>
<td>3h</td>
<td>CH2=CHCH2SiMe3, (CF3CO)2O, THF, room temp., 12 h</td>
<td>20 (53)</td>
</tr>
</tbody>
</table>

* Ratio of isomers was not determined. ** Starting material 3h was recovered.

the reaction of the disulfoxide 3g with benzenethiolate ion in MeOD. Similarly, the monodeuterated product [3H]-14 or [3H]-15 was also obtained from the reaction of the sulfoxide 3h with either benzenethiol or malononitrile with the Grignard MeMgCl in MeOD. Since there was no deuterium atom incorporated at C-2 in the final product, we assumed a rapid exchange of the C2-D, even in the presence of aqueous NH4Cl. From literature, the acidity of 2-H in 1,3-dithiane 1,3-dioxide has been measured to have a pK4 value of 25.5. To support our assumption, the addition of the conjugated disulfoxide 18 with PhSMgCl in MeOD, followed by work-up with aqueous NH4Cl, gave the adduct 14 containing no deuterium atom.

Treatment of 2-prop-1-enyl-1,3-dithiolane 1,3-dioxide 3h with chloromagnesium acetate in MeOH gave 2-(2-methoxy-propyliden)-1,3-dithiolane 1-oxide 19 as a mixture of four diastereoisomers (a:b:c:d = 33:33:17:17). In the 1H NMR spectrum, the vinyl resonances of the major Z-isomers (a+b) occurred at δ 5.94 and 5.99, respectively, whereas the minor E-isomers (c and d) resonated at lower field (δ 6.40 and 6.44 respectively). The reaction presumably proceeded with an intermediate α,β-unsaturated dithiolanium ion H (Scheme 3) derived from a Pummerer rearrangement similar to that proposed for the reactions of sulfoxides with Grignard reagents or allyltrimethylsilane.7 Efficient trapping with methanol of the intermediate H, which presumably adopts the favourable trans-conformation at C(1')-C(2), leads to the formation of the Z-isomers. Similarly, the reaction of the dioxide 3h with allyltrimethylsilane in the presence of trifluoroacetic anhydride, gave the diallylated product 20. In both reactions, the nucleophile added selectively at the γ-carbon (C-2') of the α,β-unsaturated dithiolanium intermediate. The second allyl group was introduced by a subsequent Michael-type reaction to give the intermediate I, which then underwent isomerisation to furnish the final product 20.

**Experimental**

General information concerning instrumentation and materials has been described previously.8 J Values are given in Hz.

![Scheme 2](image)

Scheme 2 Reagents and conditions: PhSH, MeMgCl, MeOD, room temp. 24 h. Path a: direct addition. Path b: i, isomerisation; ii, Michael addition; iii, work-up with aq. NH4Cl.

![Scheme 3](image)

Scheme 3 Reagents and conditions: MeCO,H, MeMgCl, MeOH, room temp., 1 h, giving 19 (55%), or CH2=CHCH2SiMe3, (CF3CO)2O, THF, room temp., 12 h, giving 20 (53%).
1,3-Dithiolanes 1a–h were prepared from the corresponding carbonyl compounds by literature methods.\textsuperscript{19}

**General Procedure for Oxidation of the Dithiolanes 1a–h to the Disulfides 3a–h via the Monosulfides 2a–h.** A solution of 2-methyl-2-phenyl-1,3-dithiolane 1a (1.26 g, 6.1 mmol) in MeOH (70 cm\(^3\)) was stirred with aqueous NaI\(\text{O}_4\) (1.3 g, 6.1 mmol) in 15 cm\(^3\) of water at 0°C for 12 h. The yellow solid was filtered off and the filtrate was concentrated and then extracted with EtOAc (3 × 30 cm\(^3\)). The extracts were combined, washed with brine (3 × 30 cm\(^3\)), dried (Na\(\text{SO}_4\)) and filtered. The filtrate was concentrated and chromatographed on silica gel with EtOAc-hexane (1:1) to give the monosulfide 2a (0.85 g, 66%) as a mixture of the trans- and cis-isomers (84:16). The monosulfide 2a in CH\(_2\)Cl\(_2\) (40 cm\(^3\)) was treated with a solution of m-CPBA (0.68 g, 4 mmol) in CH\(_2\)Cl\(_2\) (10 cm\(^3\)) at 0°C for 2 h. The white solid was filtered off and the filtrate was washed with aqueous Na\(\text{SO}_4\) (20%), dried (Na\(\text{SO}_4\)) and concentrated. The residue was chromatographed on silica gel with EtOAc to give the disulfide 3a (0.58 g, 64%) as a white solid. This was obtained as a mixture of the trans- and cis-isomers (75:25), when the cis-sulfides were also cis to the methyl group.

2-Methyl-2-phenyl-1,3-dithiolane 1a. A mixture of trans- and cis-isomers (66%; 84:16); \(\delta\) (CDCl\(_3\)) 1.13 (s, 3 H), 1.95 (3 H, t, J\textsubscript{7} = 7.1), 2.68-3.02 (4 H, m), 2.79 (1 H), 3.14-3.86 (4 H, m), 6.24 (1 H, d, J = 16)/6.53 (1 H, d, J = 16)/6.88 (1 H, d, J = 15.6)/6.85 (d, J = 7.6) and 7.29-7.46 (4 H, d, J = 15.6), m/z (M', 75%) and 199 (42) and 140 (100); \(\delta\) (CDCl\(_3\)) 1.35 (s), 2.70 (1 H), 2.85-3.02 (4 H, m), 3.05-3.21 (1 H, m), 3.33-3.49 (2 H, m), 3.80-3.94 (1 H, m), 5.37 (1 H, d, J = 10.0)/5.88 (1 H, d, J = 10.0)/5.98 (1 H, d, J = 10.0) and \(\delta\) (CDCl\(_3\)) 20.3 (q), 29.1 (q), 31.35 (s), 31.65 (t), 32.7 (t), 43.3 (t), 54.8 (t), 76.4 (s), 119.5 (d) and 144.0 (d) (Found: M\(^+\) = 216.0634. Calc. for C\(_9\)H\(_{10}\)O\(_2\): M, 216.0624). Minor isomer: methyl ether, m.p. 90-91°C; HPLC (EtOAc) \(t\) = 7.9 min; \(\delta\) (Me\(\text{CN}\))/cm\(^{-1}\) 1054; m/z (M', 75%), 199 (42) and 140 (100); \(\delta\) (CDCl\(_3\)) 1.03 (3 H, s), 1.04 (3 H, s), 1.64-2.05 (4 H, m), 2.38-2.62 (2 H, m), 2.85-3.02 (4 H, m), 3.05-3.21 (1 H, m), 3.33-3.49 (2 H, m), 3.80-3.94 (1 H, m), 5.37 (1 H, d, J = 10.0)/5.88 (1 H, d, J = 10.0)/5.98 (1 H, d, J = 10.0) and \(\delta\) (CDCl\(_3\)) 20.3 (q), 29.1 (q), 31.35 (s), 31.65 (t), 32.7 (t), 43.3 (t), 54.8 (t), 76.4 (s), 119.5 (d) and 144.0 (d) (Found: M\(^+\) = 216.0624. Calc. for C\(_{10}\)H\(_{11}\)O\(_2\): M, 216.0642).


8,8-Dimethyl-2,5-dithiacycloc[4.4.0]dec-9-ene 2-oxide 5.—Thermolysis of the disulfide 3b by a procedure similar to that of 3a described above gave 73% yield of the bicycle 5 as a white solid, m.p. 108–109°C; m/z 216 (M+, 99%) and 107 (100); δ(CDC13) 1.08 (s, Me), 1.11 (s, Me), 1.74 (br d, J 13.4, 7.8 Hz), 2.04 (dd, J 13.4 and 13.7, 7.8 Hz), 2.83 (dd, J 4.1 and 4.1, 1-H), 3.02–3.18 (m, 3-H and 4-H), 3.39 (dd, J 13.4 and 3.2, 6-H), 3.47 (dd, J 5.2 and 3.2, 10-H), 3.60 (dd, J 9.2 and 4.3, 5-H), 5.82 (d, J 10.0, 9-H) and 6.01 (dd, J 10.0 and 5.2, 10-H); δ(CDC13) 21.7 (t, C-4), 74.8 (t, Me), 100.8 (d, C-7), 129.3 (d-C-6), 52.9 (t-C-3), 63.3 (d-C-1), 120.8 (d-C-9) and 143.0 (d-C-10) (Found: M+, 216.0645. Calc. for C11H18O2S: M+, 216.0642).

Hept-1-en-2-yl-2-Mercaptoethyl Sulfoxide 6, Hept-1-en-2-yl-2-Phenylthioethyl Sulfoxide 7, Hept-2-en-2-yl-2-Mercaptoethyl Sulfoxide 8 and Hept-2-en-2-yl-2-Phenylthioethyl Sulfoxide 9.—Compounds 6–9 were obtained by thermolysis of the disulfide 3e at 70°C or 110°C (Table 2) by a procedure similar to that of 3a described above. 6: Oil, TLC (hexane-ETOAc: 1: Rf, 0.34; vmax(neat)/cm−1 1622 and 1048; m/z 206 (M+, 9%), 129 (48) and 61 (100); δ(CDC13) 0.88 (t, J 6.7, 3 Me), 1.27–1.36 (4 H, m), 1.61–1.68 (2 H, m), 2.00–2.32 (2 H, m), 2.69–3.02 (4 H, m), 5.64 (1 H, d, J 18) and 5.83 (1 H, d, J 18); δ(CDC13) 13.9 (q), 17.1 (t), 22.3 (t), 27.6 (t), 31.2 (t), 54.9 (t), 116.3 (t) and 152.0 (s) (Found: M+, 206.0792. Calc. for C12H18OS: M+, 206.0799). 7: Oil, TLC (hexane-ETOAc: 1: Rf, 0.54; vmax(neat)/cm−1 1623, 1434, 1052 and 740; m/z (20 eV) 315 (M+ + 1, 99%), 168 (61) and 141 (100); δ(CDC13) 0.90 (t, J 6.5, Me), 1.25–1.35 (4 H, m), 1.90–2.00 (2 H, m), 2.81–3.13 (4 H, m), 3.62 (1 H, s), 5.79 (1 H, s), 7.22–7.37 (3 H, m) and 7.50–7.60 (2 H, m); δ(CDC13) 13.9 (q), 23.0 (t), 27.5 (t), 35.1 (t), 43.3 (t), 58.2 (t), 73.0 (t), 129.1 (d-C-5), 136.6 (s) and 151.8 (s) (Found: M+, 314.0815. Calc. for C13H19OS: M+, 314.0834). 8: Oil, TLC (hexane-ETOAc: 1: Rf, 0.28; vmax(neat)/cm−1 1650 and 1048; m/z 206 (M+, 10%) and 103 (100); δ(CDC13) 0.89 (3 H, t, J 6.9), 1.24–1.48 (4 H, m), 1.83 (3 H, s), 2.13–2.25 (2 H, m), 2.72–2.96 (4 H, m) and 6.18 (1 H, t, J 7.5); δ(CDC13) 9.2 (q), 13.8 (q), 17.5 (t), 22.3 (t), 27.8 (t), 30.8 (t), 54.6 (t), 135.2 (d) and 136.9 (s) (Found: M+, 206.0793). 9: Oil, TLC (30% EtOAc-hexane: 3:7); Rf, 0.26; vmax(neat)/cm−1 1574 and 1048; m/z (20 eV) 315 (M+ + 1, 16%), 169 (69) and 151 (100); δ(CDC13) 0.90 (3 H, t, J 7.1), 1.25–1.42 (4 H, m), 1.77 (3 H, s), 2.12–2.19 (2 H, m), 2.88–3.05 (4 H, m), 6.12 (1 H, t, J 7.3), 7.22–7.36 (3 H, m) and 7.50–7.55 (2 H, m); δ(CDC13) 9.2 (q), 13.8 (q), 22.3 (t), 27.7 (t), 30.5 (t), 49.5 (t), 127.3 (d), 128.0 (d, C-2), 129.1 (d, C-2), 135.2 (d) and 136.6 (2 C) (Found: M+, 314.0836. Calc. for C13H18O3S: M+, 314.0832).

1-Ethoxycarbonyl-2-Mercaptoethyl Sulfoxide 10 and 1-Ethoxycarbonyl-2-Phenylthioethyl Sulfoxide 11.—Thermolysis of the disulfide 3d by a procedure similar to that described for compound 3a, gave the monosulfides 10 (14%) and 11 (41%). Either compound 10 or 11 existed as a mixture of diastereoisomers. 10, a mixture of two isomers (80:20); oil, TLC (EtOAc) Rf 0.34; vmax(neat)/cm−1 1723 and 1020; m/z 211 (M+ + 1, 11%) and 150 (100); δ(CDC13) 1.32 (t, J 7.2, Me), 1.58 (d, J 7.3, Me major), 1.53 (d, J 7.3, minor), 2.92–3.12 (4 H, m), 3.62 (1 H, q, J 7.3) and 3.78 (q, J 7.3) and 4.25 (q, J 7.2, Me).
OCH3)/4.26 (d, J 7.2), δ(CDCl3) 10.9 (q), 14.1 (q), 17.9 (t), 55.0 (t, major)/52.6 (t, minor), 60.5 (d)/59.2 (d), 62.1 (t, OCH3) and 168.6 (s) (Found: M+, 210.0270. Calc. for C9H12O3S2: M, 210.0384). II, a mixture of two isomers (67:33): oil, TLC (EtOAc): Rf 0.53; v_max (neat)/cm⁻¹: 1723, 1049 and 1045; m/z: 319 (M* + 1, 76%), 168 (100); δ(CDCl3) 1.28 (t, J 7.0, Me major)/1.32 (t, J 7.0, Me minor), 1.52 (d, J 7.3, Me)/1.59 (d, J 7.3, Me), 3.02-3.25 (4 H, m), 3.56 (q, J 7.3) (4.15-4.30 (2 H, m), OCH3), 7.21-7.37 (3 H, m) and 7.47-7.56 (2 H, m); δ(CDCl3) 10.7 (q, Me major)/10.8 (q), 14.1 (q), 30.8 (t)/31.2 (t), 50.1 (t)/50.3 (t), 60.45 (d), 62.0 (t), 127.1 (s), 127.4 (d), 128.1 (d), 129 (d, 2 C) and 168.5 (s) (Found: M*, 318.0442. Calc. for C13H13O4S3: M, 318.0418).

2-(2-Phenyl-1-phenylthioethyl)-1,3-dithiolane 1,3-Dioxide 12.—To a solution of benzenethiol (0.1 cm³, 1 mmol) in MeOH (2 cm³) was added dropwise a solution of MeMgl (0.8 cm³, 1.25 mol dm⁻³, diethyl ether). The mixture was stirred for 20 min, after which a solution of the disulfide (3a, 228 mg, 1 mmol) in THF (2 cm³) was added to it. The mixture was stirred at room temperature for a further 24 h to complete the addition (TLC analysis). Saturated aqueous NH₄Cl (1 cm³) was then added to the mixture and MeOH and THF removed by rotary evaporation. The residue was extracted with EtOAc (3 x 30 cm³) and the combined extracts were dried (Na₂SO₄) and filtered. The filtrate was concentrated and the residue chromatographed on silica gel to give the title compound 15 (34 mg, 28%) (Found: M+, 296.9986. Calc. for C9H12O2S2: M, 296.9968). Minor isomer: oil, HPLC (EtOAc-acetone: 1:1): t 11.4 min; v_max (neat)/cm⁻¹: 2965, 1577, 1434, 1087, 1030 (s, =O), 750 and 692; δ(CDCl3) 1.24 (t, J 7.1, Me), 1.71-1.79, 1.90-2.02 (2 H, m), 3.38 (t, J 9.1 and 3.1, 1'H, 3.54-3.94 (5 H, m) and 7.54-7.60 (5 H, m); δ(CDCl3) 11.2 (q), 26.6 (t), 47.0 (d), 50.4 (t), 52.3 (t), 98.6 (d), 128.5 (d), 129.2 (d) and 131.8 (s) and 134.1 (d, 2 C) (Found: M*, 288.0302. Calc. for C13H12O2S3: M, 288.0312).

2-[1-(Dicyanomethyl)propyl]-1,3-dithiolane 1,3-Dioxide 15.—Method A: Addition of the dithiolane dioxide (c, 28%) with malononitrile by a procedure similar to that described for compound 12 gave the title compound 15 (46%) containing two diastereoisomers (67:33). Method B: Neutral alumina (6 g) was activated by heating at 140 °C for 2 h, cooled and added to a solution of malononitrile (33 mg, 0.5 mmol) in THF (1 cm³). The mixture was stirred for 0.5 h after which a solution of the dithiolane dioxide (89 mg, 0.5 mmol) in THF (1 cm³) was added to it and the whole stirred for 72 h under an atmosphere of argon. After removal of the THF, the residue was extracted with EtOAc (2 x 10 cm³). The combined extracts were washed with brine, dried (Na₂SO₄) and filtered. The filtrate was concentrated and the residue chromatographed on silica gel by elution with EtOAc to give the title compound 15 (34 mg, 28%) as a mixture of two isomers (56:44); colourless solid, m.p. 125-127 °C; TLC (EtOAc): Rf 0.25; v_max (KBr)/cm⁻¹: 2971, 2168 (CN), 1628, 1094 and 1026; m/z: 244 (M*+, 4%) and 108 (100); δ(CDCl3) 1.19-1.21 (t, J 7.4, Me), 2.05-2.19 (2 H, m), 2.81-2.92 (1 H, m, 1'H), 3.67-3.90 (5 H, m), 4.49 (d, J 5.8, CH(NMe)₂) major)/4.99 (d, J 3.0, minor) (Found: M*, 244.0341. Calc. for C13H12N2O2S3: M, 244.0399). When the reaction was conducted in MeOD, [¹H]-H-15 was obtained, accompanied by recovery of the starting material 3a; m/z: 245 (M*+, 1%) and 108 (100); δ(CDCl3) 2.28-2.30 (1 H, m, 1'-H), 3.74-3.95 (5 H, m), 4.54 (d, J 5.9, CH(NMe)₂) major) and 5.07 (d, J 3.0, minor) (Found: M*, 245.0401. Calc. for C13H11N2O2S3: M, 245.0402).

2-[1-(Dicyanomethyl)propyl]-1,3-dithiolane 1,3-Dioxide 15.—Method A: Addition of the dithiolane dioxide (c, 28%) with diethyl malonate by a procedure similar to that described for compound 12 gave the title compound 15 (46%) containing two diastereoisomers (71:29). Liquid, TLC (MeOH-EtOAc: 1:9): Rf 0.4, v_max (neat)/cm⁻¹: 2975, 1722 (s, C=O), 1231, 1093 and 1032; m/z: 339 (M* + 1, 2.2%) and 108 (100); δ(CDCl3) 1.02 (t, J 7.3, Me major)/0.5 (t, J 7.3, Me minor), 1.27-1.37 (6 H, m), 1.54-1.74 (2 H, m), 2.85-2.94 (1 H, m), 3.50-3.98 (7 H, m) and 4.19-4.39 (3 H, m) (Found: M*, 338.0855. Calc. for C13H13N2O2S2: M, 338.0858).

2-[1-(4,5-Dihydro-1,3-thiazol-2-ylthio)propyl]-1,3-dithiolane 1,3-Dioxide 17.—Addition reaction of the dithiolane dioxide (c, 28%) with 2-mercaptop-4,5-dihydrotiazole by a procedure similar to that described for compound 12 gave the title compound 17 (83%). Liquid, TLC (MeOH-EtOAc: 1:9): Rf 0.1, v_max (neat)/cm⁻¹: 1625 and 1030; m/z: 297 (M*+, 1%) and 119 (100); δ(CDCl3) 1.03 (t, J 7.2, Me), 1.82-1.94 (1 H, m), 2.02-2.15 (1 H, m), 3.35-3.49 (2 H, m), 3.60-3.99 (6 H, m) and 4.11-4.22 (2 H, m); δ(CDCl3) 10.2 (q), 25.7 (d), 28.0 (t), 51.2 (t) and 53.0 (t), 53.4 (t), 53.6 (t), 94.9 (d, C-2) and 199.4 (s) (Found: M*, 296.9968. Calc. for C13H12N2O2S3: M, 296.9986).
2-propyliden-1,3-dithiolane 20 was oxidized with NaIO₄ (1 equiv.) to give the 2-propyliden-1,3-dithiolane 1-oxide 18a (59%) as a mixture of E- and Z-isomers (79:21); pale yellow oil, TLC (EtOAc-hexane, 1:1) Rₓ 0.13; νmax(neat)/cm⁻¹ 2965, 1676, 1397, 1171 and 1045; m/z 162 (M⁺, 47%) and 145 (100); δ(CDCl₃) 1.06 (t, J 7.5, Me), 2.12–2.27 (2 H, m), 2.57–2.78, 3.40–3.64, 3.98–4.12 (4 H, m) and 6.46 (t, J 7.1, 1'-H E-isomer)/6.09 (t, J 7.8, 1'-H Z-isomer); δ(CDCl₃) 12.4 (q), 26.5 (t), 50.1 (t), 50.4 (t), 155.7 (d) (Found: M', 178.0122). Further oxidation of the monosulfoxide 18a with m-CPBA (1 equiv.) gave 42% yield of the dioxide 19: oil, νmax(neat)/cm⁻¹ 2973, 1607, 1459, 1327 and 1092; m/z 178 (M⁺, 11%) and 156.7 (d) (Found: M', 156.7109). 

The residue chromatographed on silica gel by elution with EtOAc-hexane (2:1) to give the title compound 21; pale yellow oil, δ(CDCl₃) 12.5 (q), 26.5 (t), 50.1 (t), 50.4 (t), 155.7 (d) and 156.7 (d) (Found: M⁺, 178.0115. Calc. for C₆H₁₂O₂S₂: M⁺, 178.0122).

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References


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