

# **Structure and Thermal Reactivity of Some 2-Substituted 1,3-Oxathiolane S-Oxides**

R. Alan Aitken\*, Sarah Henderson and Alexandra M. Z. Slawin

*EaStCHEM School of Chemistry, University of St Andrews, St Andrews, UK*

\* Email: [raa@st-and.ac.uk](mailto:raa@st-and.ac.uk)

# Structure and Thermal Reactivity of Some 2-Substituted 1,3-Oxathiolane *S*-Oxides

Isomerisation of 2-benzylidene-1,3-dioxolane to 3-phenylbutyrolactone occurs readily under flash vacuum pyrolysis (FVP) conditions. 2-Diphenylmethyl-1,3-oxathiolane and 2-benzyl-1,3-oxathiolane have been prepared and the latter compound has been oxidised to the corresponding sulfoxide, whose structure and conformation is examined by  $^1\text{H}$  NMR, and to the sulfone whose X-ray structure is determined. 2-Benzylidene-1,3-oxathiolane is also prepared and the behaviour of the three *S*-oxidised oxathiolane derivatives upon FVP is examined. While extrusion of  $\text{SO}_n$  to give ethene and a carbonyl compound predominates in all three cases, the sulfoxide also gives bis(2-hydroxyethyl) disulfide, most likely formed via thiirane *S*-oxide and 1,2-oxathietane.

Keywords: 1,3-oxathiolane; pyrolysis; sulfoxide; sulfone; X-ray structure

## 1. Introduction

There has recently been increased interest in the use of gas-phase pyrolysis methods in the synthesis of heterocyclic compounds [1]. Some time ago, Oda and coworkers described the thermal conversion of 2-benzylidene-1,3-dioxolanes such as **1** and **2** (Scheme 1) into the corresponding 3-phenylbutyrolactones **3** and **4** [2]. However they used flow pyrolysis with the substrates introduced in benzene solution and carried through the furnace at atmospheric pressure by a stream of nitrogen gas. We were interested to re-examine this reaction under the more convenient and commonly used flash vacuum pyrolysis (FVP) conditions, and more importantly to try to extend it to the 1,3-oxathiolane analogues (Scheme 2) although we were of course aware of the possibility of  $\text{SO}$  or  $\text{SO}_2$  extrusion intervening in these processes.

## 2. Results and Discussion

The synthesis of **1** was first carried out using the reported methods (Scheme 3) [3,4] and

gave excellent yields of products which showed the expected NMR data although, due to the early date of the previous work, spectroscopic data was lacking for the intermediates in this pathway. Both  $\alpha$ -bromophenylacetaldehyde dimethyl acetal [3] and 2-( $\alpha$ -bromobenzyl-1,3-dioxolane [5] gave  $^1\text{H}$  NMR data in agreement with the previous reports, while their  $^{13}\text{C}$  NMR data were recorded for the first time, and for the target product **1** neither  $^1\text{H}$  nor  $^{13}\text{C}$  NMR data appear to have been previously reported. When compound **1** was subjected to flash vacuum pyrolysis in a conventional flow system at a pressure of  $10^{-2}$  Torr with an estimated contact time of 10 ms, complete reaction was observed with a furnace temperature of 600 °C to give as the main isolable product 2-phenylbutyrolactone **3**. Compound **3** showed  $^1\text{H}$  and  $^{13}\text{C}$  NMR data in good agreement with previous reports, [6] and the unexpectedly complex coupling pattern of the  $^1\text{H}$  NMR spectrum was in excellent agreement with a previous detailed analysis of its spectrum. [7] The product was obtained in 38% isolated yield which is double the yield obtained by Oda and co-workers [2] using benzene solution flow pyrolysis and encouraged us to examine the extension to sulfur analogues.

We first prepared the 2-diphenylmethyl-1,3-oxathiolane **5** from diphenylacetaldehyde (Scheme 4) and were able to fully characterise this previously unknown compound. The significant chemical shift differentiation of the two  $\text{CH}_2\text{O}$  protons ( $\delta$  4.39 vs. 3.87) pointed to a high degree of steric hindrance and we were unable to effect bromination of this compound under a range of conditions, so were unable to introduce the required exocyclic double bond.

Attention therefore turned to the 2-benzyl-1,3-oxathiolane series (Scheme 5). The oxathiolane **6** was readily prepared from phenylacetaldehyde dimethyl acetal and showed good agreement with the previously reported properties including  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra. [8,9] Oxidation using sodium periodate in aqueous methanol gave the

previously unknown *S*-oxide **7** in good yield while potassium permanganate oxidation in the presence of benzoic acid [10] gave the known *S,S*-dioxide **8** in low yield. This also had properties in agreement with the reported values [8]. Since there have been relatively few structural studies of simple *S*-oxidised 1,3-oxathiolanes, [11–13] we decided to examine the  $^1\text{H}$  NMR spectrum of sulfoxide **7** in detail and to determine the X-ray structure of the sulfone **8**.

At first sight the  $^1\text{H}$  NMR spectrum of **7** was unexpectedly complex (Figure 1, top) and this is attributed to the existence of *cis* and *trans*-isomers. Fortunately a detailed study by Pihlaja and co-workers [14] succeeded in analysing in detail the  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of a range of simple 1,3-oxathiolane *S*-oxides including the very similar example 2-(4-nitrophenyl)-1,3-oxathiolane *S*-oxide **11** (Figure 2). By comparing our spectra for **7** with the published values for **11** a remarkable degree of similarity was observed. In particular the marked difference between  $\delta_{\text{C}}$  for C-2 (100.1 vs. 110.8 for **11**, 100.2 vs. 110.4 for **7**) allowed us to unambiguously assign the isomer with the lower value as the *cis* and the higher as the *trans* by analogy. This then allowed assignment of each  $^1\text{H}$  NMR signal for **7** to either *cis* or *trans* isomers using an HSQC correlation (Figure 1, Table 1). Starting from the chemical shift assignments and coupling constants reported for **11** [14], these parameters were optimised using simulation to match the observed spectra for **7**. The final values are shown in Table 1 and the resulting simulated spectra for *cis* and *trans* isomers (Figure 1, middle and bottom) are in almost perfect agreement with experiment. The very high degree of similarity in the pattern of coupling constants between **7** and **11**, and particularly the high degree of difference between the values of  $J_{\text{H4a-H5s}}$  and  $J_{\text{H4s-H5a}}$  for the *trans* isomer as compared to the almost equal magnitude of these values for the *cis* isomer, leads us to the same conclusion as was reached for **11** [14]: that *trans*-**7** exists overwhelmingly as a single

half-chair conformation while *cis*-**7** is an almost equal mixture of two alternative half-chair conformations labelled A and B (Figure 3).

A single crystal X-ray diffraction study on the sulfone **8** gave a structure (Figure 4) showing an obvious "envelope" conformation with the ring oxygen out of the plane of the remaining four essentially coplanar ring atoms and a ring angle of only 94.2 ° at sulfur. As far as we are aware, there are only two previous X-ray structures of 1,3-oxathiolane *S,S*-dioxides: the carbohydrate-derived compounds **12** [15,16] and **13** [17]. These both show very similar envelope conformations and the bond lengths and angles within the ring are very similar to those observed for **8**. For the previous structures the envelope conformation was attributed to the conformationally constrained bicyclic nature of the compounds, but it is interesting to observe that **8**, although freed of any such constraints, still prefers to adopt such a conformation. The values for the C(2)–S and S–C(4) bond lengths as well as the C(2)–S–C(4) angle also agree well with those observed for the few unsaturated 1,3-oxathiole *S,S*-dioxides **14** [18,19] and **15** and **16** [20] to be crystallographically characterised although in all these cases the oxathiolane ring is planar.

To obtain a sulfur-containing system more closely analogous to **1**, we examined introduction of an exocyclic double bond at C-2. Attempted radical bromination of either **6** or **7** gave complex mixtures of products but the sulfone **8** was brominated in good yield to give the previously unknown compound **9** (Scheme 5). This proved to be rather unstable but was characterised spectroscopically and showed a distinctive AB pattern ( $\delta_{\text{H}}$  5.17, 4.71  $J = 9.6$  Hz) for the PhCHBr–CH(O)SO<sub>2</sub> function. There is some precedent for formation of 2-alkylidene-1,3-benzoxathiole *S,S*-dioxides in the study of griseofulvin analogues such as **15** [20,21] and chlorination / dehydrochlorination was successful in some cases. When a crude sample of **9** was treated with triethylamine in

diethyl ether at 0 °C, the resulting product gave spectra which were dramatically simplified as compared to all the earlier compounds **6–9** and consistent with the completely planar structure **10**. In particular there were two simple triplets for the ring CH<sub>2</sub> groups ( $\delta_{\text{H}}$  4.76, 3.36) and distinctive signals for PhCH= ( $\delta_{\text{H}}$  6.13;  $\delta_{\text{C}}$  103.6).

We now examined the pyrolysis behaviour of the sulfur heterocycles prepared under FVP conditions. Thermal extrusion of SO<sub>2</sub> from five-membered ring heterocycles is well known [22], but we are only aware of one report describing such extrusion from 1,3-oxathiolane 3,3-dioxides [23]. In this, 4,4-dimethyl-1,3-oxathiolane 3,3-dioxide was found to fragment cleanly into SO<sub>2</sub>, isobutene and formaldehyde. This allowed Gokel and coworkers to use the compound as a formyl anion equivalent [24], by deprotonation and alkylation with an alkyl halide, RX, at C-2 followed by thermal fragmentation to generate the corresponding aldehyde RCHO. However to our knowledge there have been no reports of thermal reactivity for 1,3-oxathiolane 3-oxides. When compound **7** was subjected to FVP, complete reaction was achieved at 500 °C and the products in the cold trap were readily identified as phenylacetaldehyde **17**, ethene and acetaldehyde. At the furnace exit there were several minor less volatile products. By lowering the reaction temperature to 450 °C, some starting material was obtained but the proportion of one minor product was increased allowing it to be isolated by preparative TLC and identified as bis(2-hydroxyethyl) disulfide **20**. At both 450 °C and at 400 °C the cold trap products were mainly phenylacetaldehyde **17**, ethene and acetaldehyde with increasing amounts of unreacted starting material recovered at the furnace exit. We propose that the unexpected disulfide product **20** is derived from thiirane *S*-oxide **18** (Scheme 6). Previous mechanistic studies have described formation of **20** from **18** in solution under acidic conditions [25,26] but under neutral gas-phase conditions a different explanation is required. We believe that ring expansion of **18** to give 1,2-

oxathietane **19** may be followed either by loss of sulfur and isomerisation, thus explaining the formation of acetaldehyde, or by homolysis of the O–S bond, dimerisation of the diradicals and hydrogen atom abstraction to give **20** as shown (Scheme 6).

The corresponding sulfone **8** showed a simpler pattern of behaviour with clean reaction upon FVP at 400 °C to give phenylacetaldehyde **17**, SO<sub>2</sub> and ethene as the only products (Scheme 7). This is entirely analogous to the behaviour of the 4,4-dimethyl compounds described by Gokel [23].

The unsaturated sulfone **10** was mainly unreacted at 400 °C but underwent complete reaction at 500 °C to give phenylacetic acid **22** as well as ethene and SO<sub>2</sub> (Scheme 8). Since the sample of **10** used contained some **8** there was also some phenylacetaldehyde present from its pyrolysis. We interpret the formation of **22** as involving the expected extrusion to form phenylketene **21** which is hydrolysed by adventitious moisture in the cold trap.

### 3. Conclusion

The previously reported thermal isomerisation of 2-benzylidene-1,3-dioxolane to 3-phenylbutyrolactone proceeds well under FVP conditions. An analogous process was not observed for *S*-oxidised sulfur analogues, which instead underwent SO<sub>n</sub> extrusion and fragmentation to give acyclic carbonyl products. A minor process observed for the cyclic sulfoxide **7** was formation of bis(2-hydroxyethyl) disulfide, apparently via thermal ring-expansion of thiirane *S*-oxide. Conformational analysis of **7** by <sup>1</sup>H NMR showed it to be remarkably similar to the 2-*p*-nitrophenyl analogue, while X-ray structure determination of **8** showed a similar envelope conformation to that observed in previous bicyclic examples.

## 4. Experimental Section

### 4.1 General

Melting points were determined on a Reichert hot-stage microscope and are uncorrected. NMR spectra were recorded for  $^1\text{H}$  at 300 or 400 MHz and for  $^{13}\text{C}$  at 75 or 100 MHz on Bruker instruments. Spectra were obtained for solutions in  $\text{CDCl}_3$  with  $\text{Me}_4\text{Si}$  as internal reference and coupling constants are given in Hz. Flash vacuum pyrolysis was conducted using a conventional flow system with the sample being volatilized from an electrically heated inlet tube through a horizontal quartz reactor tube (30 x 2.5 cm) heated externally by a laboratory tube furnace, and connected via a liquid nitrogen-cooled product collection trap to a rotary vacuum pump. The system was maintained at pressures in the range  $10^{-3}$ – $10^{-2}$  Torr corresponding to a contact time in the hot zone of 1–10 ms. Full details of the procedure are given in a recent publication [27]. CCDC 1570002 (**8**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via [www.ccdc.cam.ac.uk/data\\_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif).

### 4.2 Synthesis and Pyrolysis of 2-(Phenylmethylene)-1,3-dioxolane **1**

#### 4.2.1 $\alpha$ -Bromophenylacetaldehyde Dimethyl Acetal

To a solution of  $\beta$ -methoxystyrene [**5**] (21.7 g, 161 mmol) in  $\text{CH}_2\text{Cl}_2$  (100 mL) stirred at  $-50$  °C, a solution of bromine (8.3 mL, 25.8 g, 161 mmol) in  $\text{CH}_2\text{Cl}_2$  (30 mL) was added dropwise over 30 min. Sodium (3.84 g, 167 mmol) was dissolved in methanol (50 mL) to give a solution of sodium methoxide. To the cold reaction mixture, methanol (7.5 mL) was slowly added followed by the sodium methoxide solution. After 30 min, the resulting white suspension was added to water (200 mL) and the organic layer was



separated, washed with water (2 × 100 mL), dried and evaporated to give the title product (36.0 g, 98%) as a brown oil. <sup>1</sup>H NMR (300 MHz): 7.43–7.29 (5 H, m, Ph), 4.93 (1 H, d, *J* 6.9, CH(OMe)<sub>2</sub>), 4.74 (1 H, d, *J* 6.9, CHBr), 3.48, (3 H, s, OMe), 3.27 (3 H, s, OMe). <sup>13</sup>C NMR (100 MHz): 138.1 (C), 129.4 (CH), 128.51 (2CH), 128.47 (2CH), 105.9 (CH(OMe)<sub>2</sub>), 55.0 (OMe), 54.8 (OMe), 52.9 (CHBr).

#### 4.2.2 2-(*α*-Bromobenzyl)-1,3-dioxolane

A mixture of *α*-bromophenylacetaldehyde dimethyl acetal (10.0 g, 41 mmol), ethane-1,2-diol (3.62 g, 58 mmol) and *p*-toluenesulfonic acid (20 mg) was distilled in a bath held at 180 °C until evolution of methanol ceased. The residue was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (100 mL) and the solution was washed with aqueous sodium carbonate, dried and evaporated to give the title product (8.85 g, 89%) as a brown oil. <sup>1</sup>H NMR (400 MHz): 7.50–7.46 (2 H, m, Ph), 7.38–7.25 (3 H, m, Ph), 5.32 (1 H, d, *J* 4.4, OCHO), 4.91 (1 H, d, *J* 4.4, CHBr), 4.00–3.87 (4 H, m, CH<sub>2</sub>). <sup>13</sup>C NMR (100 MHz): 137.1 (C), 128.8 (2CH), 128.7 (CH), 128.4 (2CH), 104.6 (OCHO), 65.84 (CH<sub>2</sub>), 65.81 (CH<sub>2</sub>), 54.4 (CHBr).

#### 4.2.3 2-Benzylidene-1,3-dioxolane **1**

A solution of potassium *tert*-butoxide (0.22 g, 2.0 mmol) in *tert*-butanol (1.5 mL) was added to 2-(*α*-bromobenzyl)-1,3-dioxolane (0.50 g, 2.0 mmol) and the mixture was heated under reflux for 2 h. A vacuum was applied and once all the *tert*-butanol was removed the residue was extracted with diethyl ether (5 mL) which was washed with water, dried and evaporated to afford the product (0.35 g, 96%) as a pale yellow oil. <sup>1</sup>H NMR (400 MHz): 7.37 (2 H, d, *J* 8.0, Ph), 7.23 (2 H, t, *J* 8.0, Ph), 7.00 (1 H, t, *J* 8.0, Ph), 4.86 (1 H, s, PhCH=), 4.40 (2 H, t, *J* 7.2, CH<sub>2</sub>), 4.23 (2 H, t, *J* 7.2, CH<sub>2</sub>). <sup>13</sup>C NMR (100 MHz): 159.7 (OCO), 136.3 (C), 128.2 (3CH), 125.8 (2CH), 123.4 (CH), 74.7

(PhCH=), 67.0 (CH<sub>2</sub>), 64.8 (CH<sub>2</sub>).

#### 4.2.4 FVP of **1** to give 3-Phenylbutyrolactone **3**

FVP of 2-(phenylmethylene)-1,3-dioxolane (148 mg) at 600 °C and 10<sup>-2</sup> Torr gave at the furnace exit 3-phenylbutyrolactone **2** (56 mg, 38%). <sup>1</sup>H NMR (400 MHz): 7.38–7.25 (5 H, m, Ph), 4.43 (1 H, ddd, *J* 9.2, 8.4, 3.2, OCH<sub>2</sub>), 4.30 (1 H, ddd, 9.2, 9.2, 6.8, OCH<sub>2</sub>), 3.78 (1 H, dd, *J* 10.4, 9.2, PhCH-), 2.67, (1 H, dddd, *J* 12.4, 9.2, 6.8, 3.2, CH<sub>2</sub>), 2.40 (1 H, dddd, *J* 12.4, 10.4, 9.2, 8.4, CH<sub>2</sub>). <sup>13</sup>C NMR (100 MHz): 177.4 (CO), 136.6 (C), 128.7 (2CH), 127.8 (2CH), 127.5 (CH), 66.4 (CH<sub>2</sub>O), 45.3 (PhCH), 31.4 (CH<sub>2</sub>).

#### 4.3 Synthesis of 2-(diphenylmethyl)-1,3-oxathiolane **5**

A solution of diphenylacetaldehyde (2.19 g, 11.2 mmol), 2-mercaptoethanol (0.87 g, 11.1 mmol) and *p*-toluenesulfonic acid (0.02 g, 0.1 mmol) in toluene (35 mL) was heated under reflux under Dean-Stark azeotropic distillation conditions. After heating for 3 h the solution was cooled to room temperature and most of the solvent removed under reduced pressure. The resulting solid was filtered off to give the product (1.24 g, 43%) as a white solid, mp 75–78 °C. HRMS (ESI) *m/z* calcd for C<sub>16</sub>H<sub>16</sub>OSNa: 279.0820, found: 279.0809 [M + Na]. <sup>1</sup>H NMR (300 MHz): 7.34–7.21 (10 H, m, Ph), 5.83 (1 H, d, *J* 9.0, OCHS), 4.39 (1 H, m, OCH<sub>2</sub>), 4.25 (1 H, d, *J* 9.0, Ph<sub>2</sub>CH), 3.87 (1 H, m, OCH<sub>2</sub>) and 2.98 (2 H, m, SCH<sub>2</sub>). <sup>13</sup>C NMR (75 MHz): 141.76 (C), 141.74 (C), 128.5 (2CH), 128.4 (2CH), 128.32 (2CH), 128.28 (2CH), 127.0 (CH), 126.7 (CH), 89.5 (OCS), 72.1 (CH<sub>2</sub>O), 58.0 (CH<sub>2</sub>S), 32.8 (Ph<sub>2</sub>CH).

#### 4.4 Synthesis of 2-benzyl-1,3-oxathiolane and its S-oxides

##### 4.4.1 Synthesis of 2-benzyl-1,3-oxathiolane 6

Phenylacetaldehyde dimethyl acetal (5.8 g, 34.9 mmol), 2-mercaptoethanol (3.9 g, 3.5 mL, 49.9 mmol) and *p*-toluenesulfonic acid (0.01 g) were heated to 100 °C. Once the methanol produced had boiled off, the residual oil was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (15 mL) and the solution was washed with water, dried and evaporated to afford the product (5.64 g, 90%) as a brown oil. <sup>1</sup>H NMR (400 MHz): 7.32–7.22 (5 H, m, Ph), 5.28 (1 H, t, *J* 6.2, OCHS), 4.35 (1 H, m, OCH<sub>2</sub>), 3.79 (1 H, m, OCH<sub>2</sub>), 3.23 (1 H, m, SCH<sub>2</sub>), 3.02 (3 H, m, SCH<sub>2</sub> and CH<sub>2</sub>Ph). <sup>13</sup>C NMR (100 MHz) 137.4 (C), 129.1 (2CH), 128.3 (2CH), 126.7 (CH), 87.3 (OCHS), 71.4 (CH<sub>2</sub>O), 42.9 (PhCH<sub>2</sub>), 32.7 (CH<sub>2</sub>S). The NMR data reported agree with the literature values [8,9]

##### 4.4.2 Synthesis of 2-benzyl-1,3-oxathiolane 3-oxide 7

To a stirred solution of 2-benzyl-1,3-oxathiolane (1.00 g, 5.6 mmol) in methanol (10 mL) a solution of sodium metaperiodate (1.24 g, 5.8 mmol) in water (5 mL) was added dropwise. The reaction mixture was stirred overnight then filtered and the filtrate extracted with CH<sub>2</sub>Cl<sub>2</sub> (20 mL) which was dried and evaporated to yield the product (0.81 g, 74%) as an orange oil. HRMS (ESI) *m/z* calcd for C<sub>10</sub>H<sub>12</sub>SO<sub>2</sub>Na: 219.0456, found: 219.0444 [M + Na].  $\nu_{\max}/\text{cm}^{-1}$  1213, 1055, 1030 (S=O), 747, 540. *m/z* (ESI) 219.04 (M + Na, 100%).

*Trans diastereomer* <sup>1</sup>H NMR (400 MHz): 7.33–7.24 (5 H, m, Ph), 4.68 (1 H, dd, *J* 6.4, 5.6, OCHS), 4.54 (1 H, m, OCH<sub>2</sub>), 4.30 (1 H, m, OCH<sub>2</sub>), 3.38–3.22 (2 H, m, PhCH<sub>2</sub>), 2.99–2.90 (1 H, m, SCH<sub>2</sub>), 2.46 (1 H, m, SCH<sub>2</sub>). <sup>13</sup>C NMR (100 MHz): 135.3 (C), 128.6 (2CH), 128.5 (2CH), 127.1 (CH), 110.4 (OCS), 68.9 (CH<sub>2</sub>O), 52.5 (CH<sub>2</sub>S), 36.7 (PhCH<sub>2</sub>).

*Cis diastereomer*  $^1\text{H}$  NMR (400 MHz): 7.33–7.24 (5 H, m, Ph), 4.64 (1 H, m, OCH<sub>2</sub>), 4.41 (1 H, dd,  $J$  6.8, 6.0, OCHS), 3.87 (1 H, m, OCH<sub>2</sub>), 3.38–3.22 (3 H, m, PhCH<sub>2</sub> and SCH<sub>2</sub>), 2.99–2.90 (1 H, m, SCH<sub>2</sub>);  $^{13}\text{C}$  NMR (100 MHz) 135.9 (C), 129.4 (2CH), 129.3 (2CH), 127.0 (CH), 100.2 (OCS), 67.8 (CH<sub>2</sub>O), 54.2 (CH<sub>2</sub>S), 32.8 (PhCH<sub>2</sub>).

#### 4.4.3 Synthesis of 2-benzyl-1,3-oxathiolane 3,3-dioxide **8**

2-benzyl-1,3-oxathiolane (1.00 g, 5.6 mmol), benzoic acid (0.68 g, 5.6 mmol) and benzyltriethylammonium chloride (0.21 g, 0.94 mmol) were stirred in CH<sub>2</sub>Cl<sub>2</sub> (30 mL). A solution of potassium permanganate (2.00 g, 12.7 mmol) in water (50 mL) was added and the mixture was stirred vigorously overnight. Sodium metabisulfite was added until the reaction mixture turned colourless and the suspension was filtered through celite. The CH<sub>2</sub>Cl<sub>2</sub> layer was separated and the aqueous layer extracted with CH<sub>2</sub>Cl<sub>2</sub> (30 mL). The combined organic phase was washed with aqueous hydrazine dihydrochloride, aqueous sodium hydroxide and then dried and evaporated to yield the product (0.36 g, 31%) as colourless crystals, mp 98–99.5 °C, (lit. [8] 95–96.5 °C). HRMS (ESI)  $m/z$  calcd for C<sub>10</sub>H<sub>12</sub>SO<sub>3</sub>Na: 235.0405, found: 235.0398 [M + Na].  $^1\text{H}$  NMR (400 MHz): 7.36–7.28 (5 H, m, Ph), 4.53 (1 H, ddd,  $J$  10.4, 6.0, 4.0, OCH<sub>2</sub>), 4.30 (1 H, dd,  $J$  8.4, 4.4, OCHS), 4.13 (1 H, ddd,  $J$  10.4, 9.6, 7.2, OCH<sub>2</sub>), 3.27–3.21 (3 H, m, PhCH<sub>2</sub> and SCH<sub>2</sub>), 3.05 (1 H, dd,  $J$  14.8, 8.4, SCH<sub>2</sub>).  $^{13}\text{C}$  NMR (100MHz): 134.6 (C), 129.3 (2CH), 128.7 (2CH), 127.3 (CH), 91.7 (OCHS), 64.6 (CH<sub>2</sub>O), 48.9 (CH<sub>2</sub>S), 34.1 (PhCH<sub>2</sub>).  $m/z$  (ESI) 235.04 (M + Na, 100%). The NMR data reported are in agreement with those in literature [8].

#### 4.4.4 X-ray structure determination of 2-benzyl-1,3-oxathiolane 3,3-dioxide **8**

Data were collected on a Rigaku Saturn 724 diffractometer using graphite

monochromated Mo-K $\alpha$  radiation,  $\lambda = 0.71075 \text{ \AA}$ . Crystal data for C<sub>10</sub>H<sub>12</sub>O<sub>3</sub>S,  $M = 212.26$ , colourless platelet  $0.20 \times 0.10 \times 0.010 \text{ mm}$ . Monoclinic, space group  $P2_1/n$ ,  $a = 12.535(5)$ ,  $b = 5.7368(16)$ ,  $c = 15.205(5) \text{ \AA}$ ,  $\beta = 112.539(7)^\circ$ ,  $V = 1009.9(6) \text{ \AA}^3$ ,  $Z = 4$ ,  $D_c = 1.396 \text{ g/cm}^3$ ,  $T = 125 \text{ K}$ ,  $R = 0.0344$ ,  $R_w = 0.0780$  for 1387 data with  $I > 2\sigma(I)$  and 127 parameters.

#### 4.5 Preparation of 2-benzylidene-1,3-oxathiolane 3,3-dioxide

##### 4.5.1 Synthesis of 2-( $\alpha$ -bromobenzyl)-1,3-oxathiolane 3,3-dioxide **9**

A solution of 2-benzyl-1,3-oxathiolane 3,3-dioxide (0.10 g, 0.47 mmol), *N*-bromosuccinimide (0.08g, 0.47 mmol) and AIBN (0.008 g) in CH<sub>2</sub>Cl<sub>2</sub> (5 mL) was heated under reflux. After 4 hours the reaction mixture was filtered, washed with water, dried and evaporated to yield the product (0.10 g, 72%) as an unstable white solid which still contained some starting material and succinimide but was used without further purification for the next step. HRMS (ESI)  $m/z$  calcd for C<sub>10</sub>H<sub>11</sub>O<sub>3</sub><sup>79</sup>BrSNa: 312.9510 and C<sub>10</sub>H<sub>11</sub>O<sub>3</sub><sup>81</sup>BrSNa: 314.9490, found 312.9499 [<sup>79</sup>Br-M + Na] and 314.9477 [<sup>81</sup>Br-M + Na].  $\nu_{\text{max}}/\text{cm}^{-1}$  1314 (S=O), 1117 (S=O), 1076 (C-O), 1055 (C-O), 754 (C-S), 692 (C-Br). <sup>1</sup>H NMR (400 MHz): 7.51–7.26 (5 H, m, Ph), 5.17 (1 H, d,  $J$  9.6, OCHS), 4.71 (1 H, d,  $J$  9.6, PhCHBr), 4.66–4.61 (1 H, m, OCH<sub>2</sub>), 4.30–4.23 (1 H, m, OCH<sub>2</sub>), 3.35–3.31 (2 H, m, SO<sub>2</sub>CH<sub>2</sub>). <sup>13</sup>C NMR (100 MHz): 134.5 (C), 130.0 (CH), 129.0 (2CH), 128.6 (2CH), 92.7 (OCHS), 64.1 (CH<sub>2</sub>O), 50.6 (CH<sub>2</sub>S), 47.8 (PhCHBr).  $m/z$  (ESI) 314.95 (<sup>81</sup>Br-M + Na, 100%), 312.95 (<sup>79</sup>Br-M + Na, 98%).

##### 4.5.2 Preparation of 2-benzylidene-1,3-oxathiolane 3,3-dioxide **10**

A solution of 2-( $\alpha$ -bromobenzyl)-1,3-oxathiolane 3,3-dioxide (0.24 g, 0.82 mmol) in diethyl ether (5 mL) was stirred at 0 °C. Triethylamine (0.12 g, 1.20 mmol) was added

slowly and the reaction mixture left to stir for 1 h. Addition of CH<sub>2</sub>Cl<sub>2</sub> (10 mL) gave a clear solution which washed with water (2 × 10 mL), dried and evaporated to yield the product. This was then recrystallized from hexane/diethyl ether (3:1) to obtain the pure product (22.5 mg, 13 %) as colourless crystals. <sup>1</sup>H NMR (400 MHz): 7.60-7.29 (5 H, m, Ph), 6.13 (1 H, s, PhCH=), 4.76 (2 H, t, *J* 6.6, OCH<sub>2</sub>), 3.35 (2 H, t, *J* 6.6, SO<sub>2</sub>CH<sub>2</sub>). <sup>13</sup>C NMR (100 MHz) (obtained from a mixture containing **8**): 147.4 (OCS), 131.9 (C), 129.2 (2CH), 128.6 (2CH), 128.4 (CH), 103.6 (PhCH=), 65.9 (CH<sub>2</sub>O), 46.4 (CH<sub>2</sub>S).

#### 4.6 *Flash vacuum pyrolysis of 1,3-oxathiolane S-oxides*

##### 4.6.1 *Flash vacuum pyrolysis of 2-benzyl-1,3-oxathiolane 3-oxide 7*

FVP of **7** (49.5 mg) at 500 °C gave, in the cold trap, a mixture of phenylacetaldehyde **17** <sup>1</sup>H NMR (300 MHz): 9.75 (1 H, t, *J* 2.4, CHO), 7.42–7.22 (5 H, m, ArH), 3.70 (2 H, d, *J* 2.4, CH<sub>2</sub>) (agrees with lit. [28]); ethene <sup>1</sup>H NMR (300 MHz): 5.40 (s); and acetaldehyde <sup>1</sup>H NMR (400 MHz): 9.79 (1 H, q, *J* 2.8, CHO), 2.20 (3 H, d, *J* 2.8). At the furnace exit there was a small amount of material consisting of bis(2-hydroxyethyl) disulfide **20** and other unidentified components.

FVP of **7** (103 mg) at 450 °C gave, in the cold trap, a mixture of phenylacetaldehyde, ethene and acetaldehyde as described above. At the furnace exit there was an oil consisting of unchanged **7**, bis(2-hydroxyethyl) disulfide and other unidentified components. Preparative TLC (SiO<sub>2</sub>, EtOAc) yielded bis(2-hydroxyethyl) disulfide **20** <sup>1</sup>H NMR (400 MHz): 3.92 (2 H, t, *J* 5.8, CH<sub>2</sub>OH), 2.89 (2 H, t, *J* 5.8, SCH<sub>2</sub>), 1.25 (1H, br s, -OH). <sup>13</sup>C NMR (100 MHz): 60.3 (CH<sub>2</sub>O), 41.2 (CH<sub>2</sub>S) (agrees with lit. [29]).

##### 4.6.2 *Flash vacuum pyrolysis of 2-benzyl-1,3-oxathiolane 3,3-dioxide 8*

FVP of **8** (38.1 mg) at 400 °C gave, in the cold trap, a mixture of phenylacetaldehyde,

$^1\text{H}$  NMR as above;  $^{13}\text{C}$  NMR (100 MHz) 199.5 (CO), 129.6 (2CH), 129.0 (2CH), 127.4 (CH), 50.6 ( $\text{CH}_2$ ) (agrees with lit. [28]) and ethene  $^1\text{H}$  NMR as above.

#### 4.6.3 Flash vacuum pyrolysis of 2-benzylidene-1,3-oxathiolane 3,3-dioxide **10**

FVP of **10** (46.8 mg, containing some **8**) at 500 °C gave, in the cold trap, a mixture of phenylacetaldehyde **17**,  $^1\text{H}$  NMR as above, ethene,  $^1\text{H}$  NMR as above, and phenylacetic acid **22**  $^1\text{H}$  NMR (400 MHz) 7.40–7.22 (5 H, m, ArH), 3.72 (2 H, s,  $\text{CH}_2$ );  $^{13}\text{C}$  NMR (100 MHz) 178.5 (CO), 134.5 (C), 129.3 (2CH), 128.6 (2CH), 127.3 (CH), 40.8 ( $\text{CH}_2$ ) (agrees with lit. [30]).

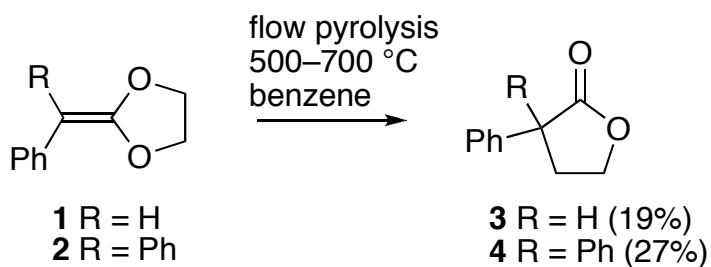
- [1] Aitken RA, Boubalouta Y. Recent advances in the synthesis of heterocyclic compounds using flash vacuum pyrolysis. *Adv Heterocycl Chem.* 2015;115:93–150.
- [2] Oda M, Morimoto K, Thanh NC, Ohta R, Kuroda S. Thermal rearrangement of phenyl-substituted ketene ethylene acetals. *Heterocycles.* 2003;60:1673–1680.
- [3] Baldwin JE, Walker LE. Syntheses of Phenylketene Acetals via  $\alpha$ -Bromophenylacetaldehyde Acetals. *J Org Chem.* 1966;31:3985–3989.
- [4] McElvain SM, Curry MJ. Ketene acetals XIX. 2-Methylene-1,3-dioxolanes and 1,3-dioxanes. *J Am Chem Soc.* 1948;70:3781–3786.
- [5] Blattner K, Schank K. Zum Mechanismus einer  $\alpha$ -Bromoacetal/Ester-Umlagerung. *Leibigs Ann Chem.* 1977;1109–1115.
- [6] Rück-Braun K, Möller C. Novel Intramolecular Cyclocarbonylations Involving  $\pi$ -Alkene-Hydridoiron Intermediates: From  $[\eta^5\text{-C}_5\text{H}_5(\text{CO})_2\text{Fe}]$ -Substituted (*Z*)-Enals to  $\alpha,\beta$ -Butenolides and  $\gamma$ -Butyrolactones. *Chem Eur J.* 1999;5:1038–1044.
- [7] Karlsson S, Hallberg A, Gronowitz, S. Hydrozirconation of (*E*)-3-methoxy-1-phenyl-1-propene and (*E*)-3-phenyl-2-propanol. *J Organomet Chem.* 1991;403:133–144.
- [8] Gokel GW, Gerdes HM, Dishong DM. Sulfur heterocycles 3. Heterogeneous, phase-transfer, and acid-catalyzed potassium permanganate oxidation of sulfides

- to sulfones and a survey of their carbon-13 nuclear magnetic resonance spectra. *J Org Chem.* 1980;45:3634–3639.
- [9] Streinz L, Koutek B, Saman D. An effective synthesis of 1,3-oxathiolanes. *Collect Czech Chem Commun.* 1997;62:665–671.
- [10] Aitken RA, Mesher STE, Ross FC, Ryan BM. Effect of added benzoic acid on the phase-transfer catalysed permanganate oxidation of organosulfur compounds. *Synthesis.* 1997;787–791.
- [11] Aitken RA, Hill L. 1,3-Dioxoles and 1,3-oxathioles. *Compr Heterocycl Chem II.* 1996;3:525–567.
- [12] Aitken RA, Power LA. 1,3-Dioxoles and 1,3-oxathioles. *Compr Heterocycl Chem III.* 2008;4:841–891.
- [13] Aitken RA, Power LA. Recent advances in the chemistry of 1,3-dioxoles and 1,3-oxathioles: an update. *Adv Heterocycl Chem.* 2013;108:163–193.
- [14] Pihlaja K, Sinkkonen J, Stájer G. 3-Oxo-1,3-oxathiolanes - synthesis and stereochemistry. *Magn Reson Chem.* 2008;46:244–249.
- [15] Skelton BW, Stick RV, Tilbrook DMG, White AH, Williams SJ. Investigations into the chemistry of some 1,6-epithio and 1,6-episeleno  $\beta$ -D-glucopyranoses. *Aust J Chem.* 2000;53:389–397.
- [16] Budesinsky M, Polakova J, Hamernikova M, Cisarova I, Trnka T, Cerny M. 1,6-Anhydro-1-thio- $\beta$ -D-glucopyranose (Thiolevoglucosan) and the corresponding sulfoxides and sulfone. *Collect Czech Chem Commun.* 2006;71:311–336.
- [17] Sivapriya K, Hariharaputran S, Suhas VL, Chandra N, Chandrasekaran S. Conformationally locked thiosugars as potent  $\alpha$ -mannosidase inhibitors: synthesis, biochemical and docking studies. *Bioorg Med Chem.* 2007;15:5659–5665.
- [18] Block E, Aslam M, Iyer R, Hutchinson J.  $\alpha$ -Haloalkanesulfonyl bromides in organic synthesis 3.  $\alpha$ -Alkylidene ketones and 1,3-oxathiole 3,3-dioxides from trimethylsilyl enol ethers. *J Org Chem.* 1984;49:3664–3666.
- [19] Block E, Aslam M, Eswarakrishnan V, Gebreyes K, Hutchinson J, Iyer R, Lafitte J-A, Wall A.  $\alpha$ -Haloalkanesulfonyl bromides in organic synthesis 5. Versatile reagents for the synthesis of conjugated polyenes, enones, and 1,3-oxathiol 1,1-dioxides. *J Am Chem Soc.* 1986;108:4568–4580.

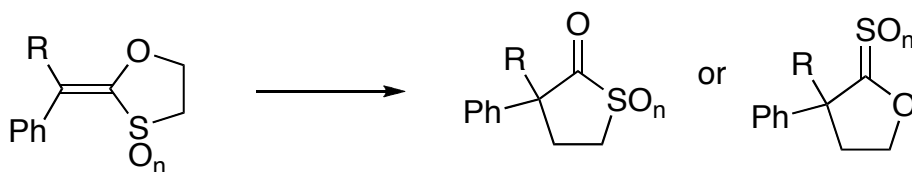


- [20] Friedrich M, Meichle W, Bernhard H, Rihs G, Otto H-H. Sulfogriseofulvin derivatives. Synthesis by [4+2] cycloaddition, structure, properties, crystal structure analysis, and antifungal activity of spiro[1,3-benzoxathiole-2,1'-cyclohex-2'-en]-4'-one 3,3-dioxides. Arch Pharm (Weinheim Ger). 1996;329:361–370.
- [21] Meichle W, Otto H-H. Darstellung und Dehydratisierung von 2-( $\alpha$ -Alkyl)- oder ( $\alpha$ -Aryl)-substituierten Hydroxymethyl-5-methoxy-1,3-benzoxathiol-3,3-dioxiden. Arch Pharm (Weinheim Ger). 1989;322:263–270.
- [22] Aitken RA, Gosney I, Cadogan JIG. Extrusion of SO<sub>2</sub> from heterocyclic compounds, part 2: five-membered rings. Prog Heterocycl Chem. 1993;5:1–33.
- [23] Gokel GW, Gerdes HM, Miles DE, Hufnal JM, Zerby GA. Sulfur heterocycles 1. Use of 4,4-dimethyl-1,3-oxathiolane 3,3-dioxide as a carbonyl anion equivalent. Tetrahedron Lett. 1979;20:3375–3378. only previous oxathiolane diox pyrrol
- [24] Aitken RA, Thomas AW. Heterocyclic acyl and formyl anion equivalents. Adv Heterocycl Chem. 2001;79:89–114.
- [25] Kondo K, Negishi A, Ojima I. Acid-catalyzed ring opening reactions of episulfoxides. J Am Chem Soc. 1972;94:5786–5793.
- [26] Saleh A, Tillett JG. The acid-catalysed hydrolysis of episulfoxides. J Chem Soc Perkin Trans 2. 1981;132–139.
- [27] Aitken RA, Horsburgh CER. Flash vacuum pyrolysis of *o*-phenylene sulfite: formation and purification of cyclopentadienone dimer. In: Afonso CAM, Candeias NR, Simao DP, Trindade AF, Coelho JAS, Tan B, Franzén R, editors. Comprehensive organic chemistry experiments for the laboratory classroom. Cambridge: RSC; 2017, p. 690–693.
- [28] Zhang L, Zha Z, Wang Z. An Efficient Electrochemical Method for the Paired Synthesis of Carbonyl Compounds and Homoallylic Alcohols in a Simple Home-Made Cell. Synlett. 2010:1915–1918.
- [29] Christoforou A, Nicolaou G, Elemen Y. N-Phenyltriazolinedione as an efficient, selective, and reusable reagent for the oxidation of thiols to disulfides. Tetrahedron Lett. 2006;47:9211–9213.
- [30] León T, Correa A, Martín R. Ni-Catalyzed direct carboxylation of benzyl halides with CO<sub>2</sub>. J Am Chem Soc. 2013;135:1221–1224.

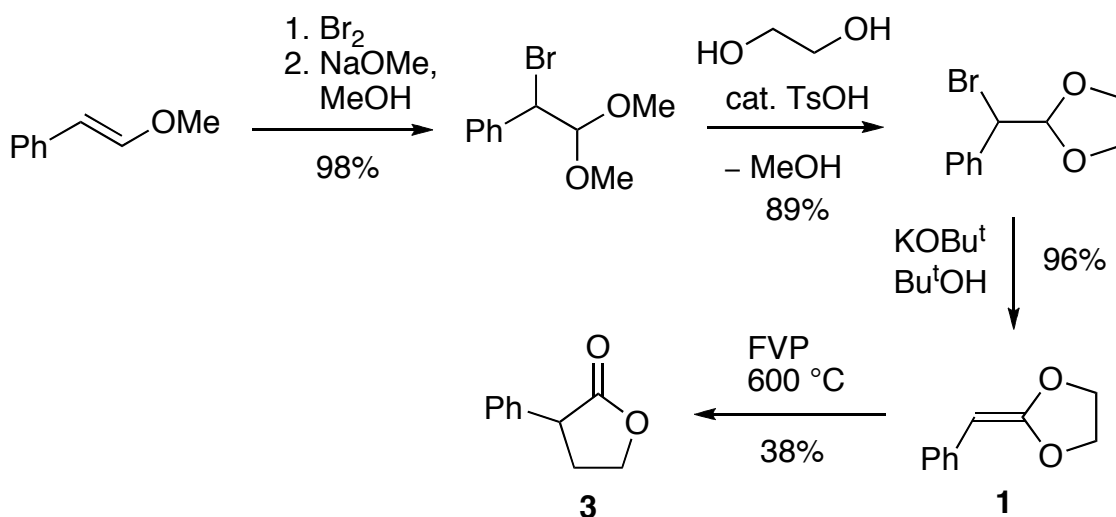
## Schemes and Figures



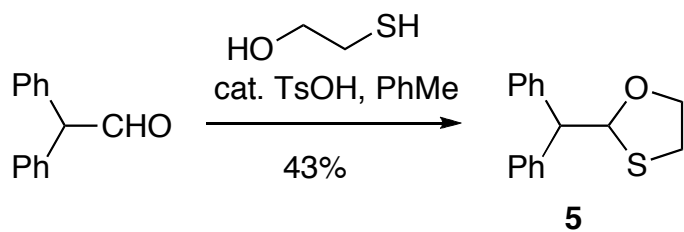
Scheme 1. Thermal conversion of 2-benzylidene-1,3-dioxolanes into 2-phenylbutyrolactones [2].



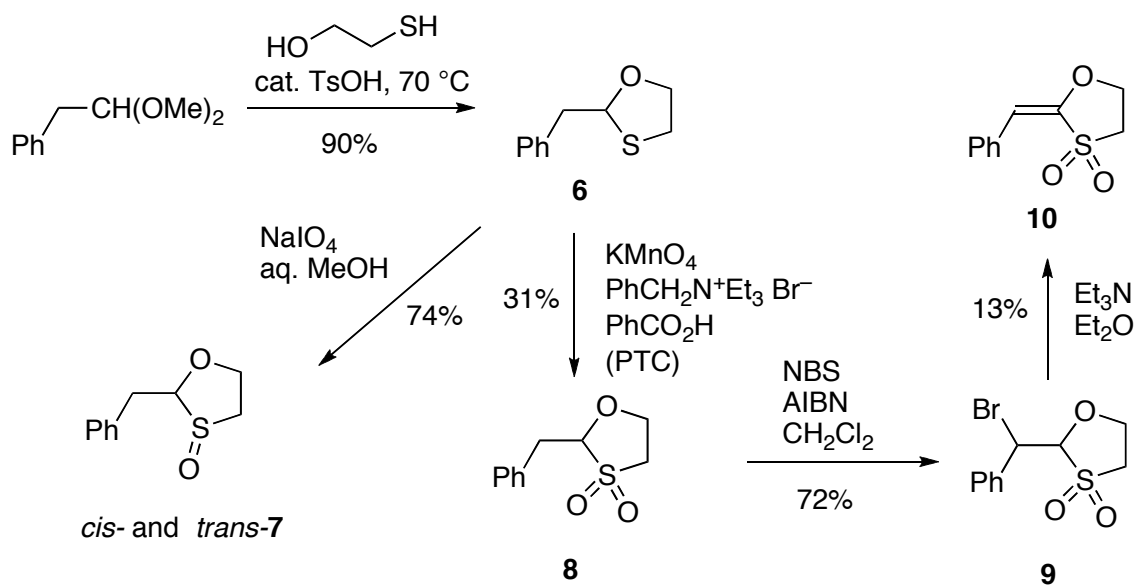
Scheme 2. Possible thermal rearrangement of 1,3-oxathiolane systems.



Scheme 3. Synthesis and thermal rearrangement of 1 to give 3.



Scheme 4. Synthesis of 2-diphenylmethyl-1,3-oxathiolane **5**.



Scheme 5. Synthesis of 2-benzyl-1,3-oxathiolane derivatives **6–10**.