# Efficient Synthetic Methodology for 1,3-Dithiolane 1-Oxides *via* Singlet Oxidation of 1,3-Dithiolanes<sup>†</sup>

## Bipin Pandey,\* Smita Y. Bal, Uday R. Khire and Ashok T. Rao National Chemical Laboratory, Pune 411 008, India

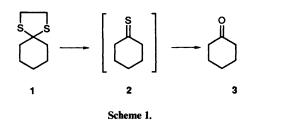
Singlet oxidation of 1,3-dithiolanes furnishes synthetically useful yields of 1,3-dithiolane 1-oxides. However, 2-ethyl-2-phenyl-1,3-dithiolane **13** gave 2-ethyl-4-hydroxy-2-phenyl-1,3-dithiolane **19** as a major product.

1,3-Dithiolane constitutes an important functional group in organic chemistry, but, its photochemistry remains underexplored. Broadly speaking, photolysis of 1,3-dithiolanes, in the absence of oxygen, leads to product(s) derived from initial C-S bond cleavage.<sup>1,2</sup> Thus, Berchtold *et al.*<sup>2</sup> have rationalized the formation of various photolysis products from dithiolane 1 via thioketone 2 (Scheme 1). Recently, Takahashi et al.<sup>3</sup> have reported a unique and efficient photodethioketalization of 1,3-dithiolanes in the presence of triplet sensitizers and molecular oxygen, but without suggesting any mechanism. For example, photolysis of 1 and benzophenone in an oxygen atmosphere is shown to give ketone 3 (65%).<sup>3</sup> Since singlet oxidation of thicketones, e.g. 2, are known to yield ketones, e.g.  $3^{4,5}$  we were curious as to whether  ${}^{1}O_{2}$ , generated by the interaction of either triplet sensitizer<sup>6</sup> or photochemically derived thicketone<sup>5</sup> with molecular oxygen, accomplishes dethioketalization.

Also, our recent interest in hydroperoxide-type intermediates e.g. 22 (Scheme 3),<sup>7</sup> which could also be obtained by singlet oxidation of dithiolanes, prompted us to examine the reaction of  ${}^{1}O_{2}$  with 1,3-dithiolanes. As a result, this communication describes a synthetically useful methodology for the preparation of 1,3-dithiolane 1-oxides under neutral and mild conditions and concludes that  ${}^{1}O_{2}$  is certainly not the species involved during Takahashi dethioketalization.<sup>3</sup>

#### **Results and Discussion**

The various 1,3-dithiolanes (1, 4, 11-13) and 1,3-dithianes (7, 8, 14) were prepared according to the literature procedure<sup>8</sup> and singlet oxidation was carried out, in MeOH, as per the standard procedure, with slight modification (for details see Experimental



section). Normally >90% of dithiolane or dithiane was consumed during singlet oxidation, although the reaction was fast in the early stages of irradiation. Identical products were obtained with either Rose Bengal or Methylene Blue as sensitizers, ensuring the involvement of  ${}^{1}O_{2}$ . Although many variations in experimental conditions are possible as far as duration of irradiation, degree of O<sub>2</sub>-saturation/agitation, solvent variation, and concentration of substrate and photosensitizer are concerned, the above reaction conditions furnished synthetically useful yields of 1,3-dithiolane 1-oxides and 1.3-dithiane 1-oxides as shown in Scheme 2.1 The stereoselectivity of oxygenation was governed by steric factors. Thus, the major stereoisomers of compounds 16 and 17 contained oxygen 'syn' to the alkyl group, which could be easily ascertained by <sup>1</sup>H NMR. Interestingly, no di-S-oxides or sulphone was observed during singlet oxidation,<sup>9</sup> and, surprisingly, no dethioketalization occurred either! Subsequently we have examined the validity of 65% yield of 3 from 1 under reported experimental conditions with a 200 W lamp.<sup>3</sup> However, we faced problems in reproducing these results; with repeated trials, a maximum of only 10% dethioketalized product 3 could be observed by GLC.§

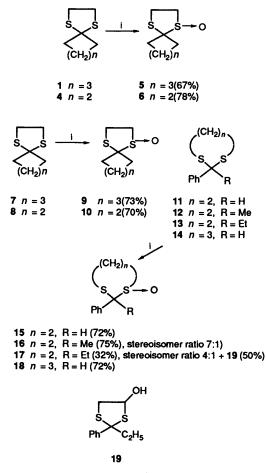
Another unusual observation was the isolation of the OH insertion product 19 (50%),‡ besides the 1,3-dithiolane 1-oxide 17 (32%) during the singlet oxidation of 2-ethyl-2-phenyl-1,3-dithiolane 13. However, such insertion products could not be observed with other substrates, even after repeated trials.

The tentative mechanism for this complex oxygenation process is shown in Scheme 3. Presumably, the formation of dithiolane S-oxides and OH insertion products both could be rationalized via the hydroperoxide 22, which could be formed either via a step-wise electron transfer process through a tight

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<sup>&</sup>lt;sup>‡</sup> All 1,3-dithiolane 1-oxides were characterized by satisfactory IR, <sup>1</sup>H NMR and mass spectroscopy. A characteristic feature of the S-oxides was a strong absorption at v 1050 cm<sup>-1</sup> in the IR and complex multiplets between 2.6 and 4.0 in the <sup>1</sup>H NMR for the methylenes in the dithiolane skeleton. Wherever possible, authentic sample of dithiolane S-oxides were prepared by known methods.<sup>7,15</sup> and superimposability of IR spectra was confirmed. Selected spectral data for both isomers of 19 are as follows: v<sub>max</sub>(film): 3400br/cm<sup>-1</sup>;  $\delta_{H}(CDCl_3)$  0.75–1.00 (3 H, m), 2.3 (3 H, q), 3.0–3.5 (2 H, m), 5.8 (1 H, br s, D<sub>2</sub>O exchangeable), 7.2–7.4 (3 H, m) and 7.5–7.7 (2 H, m);  $\delta_{C}(CDCl_3)$  11.14 and 12.19 (q), 38.59 and 39.29 (t), 47.09 and 47.62 (t), 86.35 and 86.59 (d), 126.91, 127.60, 127.78, 127.90 and 128.19 (aromatic); m/z: 226 (M<sup>+</sup>, 5%), 197 (40) and 121 (100).

<sup>§</sup> Some other side products could be observed by GLC.



Scheme 2. Reagents and conditions: i, <sup>1</sup>O<sub>2</sub>, MeOH.

ion-pair 21 or via a concerted process.<sup>10,11</sup> Based on a detailed study by Foote *et al.*<sup>12</sup> 22 could also be represented as the thiadioxirane 28 or H-bonded 29. The reduction of 22/29 by 20 could result in the formation of S-oxides, *i.e.* 25. On the other hand, Pummerer rearrangement<sup>13</sup> of 22 via concerted intermediate 26 or stepwise intermediate 27 could lead to 24, which on further reduction with 20 could furnish OH insertion product 23.<sup>14</sup> The proposed mechanism explains the need for polar protic solvent (MeOH) and rationalizes the usually fast oxidation in the early stages of oxidation.

In summary, 1,3-dithiolane 1-oxides constitute important synthetic intermediates and the present unprecedented, efficient singlet oxidation methodology under neutral and mild conditions should complement conventional oxidizing methods.<sup>†</sup>

### Experimental

General Procedure for the Preparation of 1,3-Dithiolane (or Dithiane) 1-Oxides.—The solution of 1,3-dithiolane (or dithiane)  $(2-4 \times 10^{-2} \text{ mol dm}^{-3})$  in MeOH (25 ml), with photosensitizer (either Rose Bengal or Methylene Blue)  $(1-2 \times 10^{-5} \text{ mol dm}^{-3})$  was saturated with oxygen for 20–30 min. The solution was irradiated in a Pyrex vessel with a 200 W Hanovia lamp for 4–5 h, under continuous oxygen agitation. The ambient temperature was maintained  $(\pm 2 \text{ °C})$  by continuous water circulation. The progress of the reaction was monitored by either GLC or <sup>1</sup>H NMR. Removal of solvent and purification of the residue by column chromatography on silica [elution, hexane–acetone (5:1)] furnished 1,3-dithiolane (or dithiane) 1-oxides. In the case of 1,3-dithiolane 13, along with 1,3-dithiolane 1-oxide 17, an OH insertion product 19 was also observed.

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<sup>†</sup> In the *m*-chloroperbenzoic acid procedure,<sup>13</sup> more than 50% of dithiolane remains unchanged and under exhaustive conditions, *i.e.* warming up and longer duration of reaction, side products are formed.