

Oxidation of 3-Sulfanyl-alcohols with Sodium Metaperiodate: New Synthesis of Sultines

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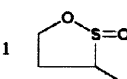
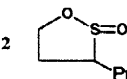
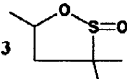
Abstract: A simple and highly efficient method for preparation of sultines by oxidation of 3-sulfanyl-alcohols with sodium metaperiodate is described.

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There are no reports available about sultines as natural products, except from Rochard's¹ work which showed the presence of the 3-propyl-1,2-oxathiolane-2-oxide in the yellow passion fruit. Nevertheless, many synthetic routes have been investigated from hydroxysulfoxydes upon reaction with SO_2Cl_2 ², sulfones³ and chloration of sulfanyl-alcohols⁴. In this latter case, Givens et al.^{4a} suggested that the sultines were formed via a disulfide intermediate. Their electrophilic cleavage was facilitated by neighboring nucleophilic species to give alkylsulfonates^{5a} or intramolecular cyclisations^{5b}.

We report herein a new synthetic route to sultines with sodium metaperiodate oxidation of 3-sulfanyl-alcohols. This synthesis first forms a disulfide compound which was isolated. The sultines can be obtained easily in a short time (4 hours) with good yields using excess of oxidizing agent (Table 1).

Table 1

3-sulfanyl-alcohols ^a (10 mmol)	NaIO_4 (mmol)	Reaction Time	Ratio of disulfides (%)	Ratio of sultines ^b (%)	Structure of sultines
$\text{CH}_3\text{-CH(SH)-CH}_2\text{-CH}_2\text{-OH}$	20	4h	0*	80*	 1
	10	30 min 24h	50 ^Δ 31 ^Δ	39 ^Δ 54 ^Δ	
	1.4	30 min 24h	89 ^Δ 84 ^Δ	0 ^Δ 3 ^Δ	
$\text{CH}_3\text{-CH(SH)-CH}_2\text{-CH}_2\text{-OH}$	20	4h	0*	98*	 2
	10	30 min 24h	36 ^Δ 22 ^Δ	64 ^Δ 76 ^Δ	
$\text{CH}_3\text{-C(CH}_3\text{)(SH)-CH}_2\text{-CH(CH}_3\text{)-OH}$	20	4h	0*	75*	 3
	10	30 min 24h	32 ^Δ 32 ^Δ	57 ^Δ 57 ^Δ	

^aThe 3-sulfanyl-alcohols were obtained as described in note 6. ^bMixture of 40/60 diastereomers cis/trans.

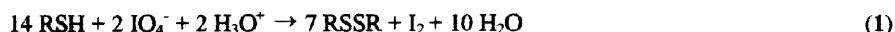
*Isolated yields. ^ΔRatio established by GC.

Sultines 2 and 3 have never been described. Attempts to synthesise 3 according to the method of King et al.^{4b}, by chloration of the 4-methyl-4-sulfanylpentan-2-ol in aqueous solution, were unsuccessful. The Table 1 shows that we are able to obtain either disulfide, sultine or a mixture of both depending of the amount of oxidizing agent.

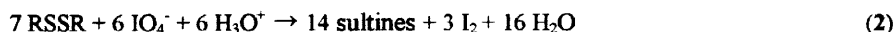
Together with the formation of disulfide and sultine, the presence of iodine was observed. This suggests a change in the oxidation number of iodine from +7 to 0. The presence of iodine is confirmed by sodium thiosulfate titration.

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We have established that 1/7 mol of NaIO₄ is necessary to oxidize one mole of 3-sulfanyl-alcohol in disulfide according to the equation (1):



Iodine is also involved in the formation of sultines by reaction with the disulfide but this reaction is very slow: only 3% were formed in 24 hours (Table 1). Further addition of 6/7 mol of NaIO₄ gave the sultines according to the equation (2):



Conclusion

The oxidation of 3-sulfanyl-alcohols with NaIO₄ represents a new suitable route to sultines. This method proceeds under very simple reaction conditions and can be performed with sodium metaperiodate, a cheap and safe oxidizing agent. A detailed mechanistic study of this oxidation reaction is in progress.

General procedure for oxidation reactions

A solution of NaIO₄ (20 mmol) in water (40 ml) was added to a solution of 3-sulfanyl-alcohol (10 mmol) in acetonitrile (20 ml) at room temperature. The mixture was stirred for 4 hours and then extracted with Et₂O (3 x 20 ml). The combined organic solutions were washed with a solution of sodium thiosulphate (0.1M) and dried over Na₂SO₄. The sultines were obtained as a yellow oil with a purity up to 95%, after evaporation of the solvent under reduced pressure. No further purification is required. The sultines were identified by FTIR, GC/MS and multinuclear NMR spectroscopy⁷.

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6. The 3-sulfanyl-alcohols were prepared via the reaction of thioacetic acid with crotonaldehyde, *trans*-2-hexenal and mesityl oxide. Reduction with LiAlH₄ gave 3-sulfanylbutan-1-ol, 3-sulfanylhexas-1-ol and 4-methyl-4-sulfanylpentan-2-ol in 65% yield after purification.
7. Spectroscopic data for the selected compounds are given below. ¹H and ¹³C{¹H} NMR were run on Bruker AC-200 spectrometer with CDCl₃ as solvent. COSY 2D NMR experiments were used for the assignments of signals.
3-methyl-1,2-oxathiolane-2-oxide: IR: 1121 cm⁻¹. *Cis isomer:* ¹H NMR: δ(ppm) 4.88-4.73 (m, 1H), 4.46-4.25 (m, 1H), 3.19-2.96 (m, 1H), 2.39-2.19 (m, 2H), 1.41 (d, 3H, J=6.5 Hz); ¹³C{¹H} NMR: δ 75.3 (C-5), 62.7 (C-3), 29.7 (C-4), 11.1 (CH₃); MS (70eV): 39 (34), 41 (84), 42 (18), 43 (15), 48 (13), 50 (26), 55 (M⁺, 100), 56 (23), 78 (59), 90 (7), 120 (36), 121 (1), 122 (1). *Trans isomer:* ¹H NMR: δ(ppm) 4.88-4.73 (m, 2H), 4.58-4.25 (m, 1H), 3.46-3.27 (m, 1H), 2.86-2.62 (m, 1H), 1.99-1.83 (m, 1H), 1.23 (d, 3H, J=7.5 Hz); ¹³C{¹H} NMR: δ 74.7 (C-5), 66.6 (C-3), 30.1 (C-4), 13.1 (CH₃); MS (70eV): 39 (32), 41 (76), 42 (16), 43 (15), 48 (12), 50 (23), 55 (M⁺, 100), 56 (22), 78 (54), 90 (6), 120 (37), 121(<1), 122 (<1).
3, 3-dimethyl, 5-methyl-1, 2-oxathiolane-2-oxide: IR: 1117 cm⁻¹. *Cis isomer:* ¹H-NMR: δ(ppm) 4.90-4.70 (m, 1H), 2.42-1.95 (m, 2H), 1.54 (d, 3H, J=6.2 Hz), 1.39 (s, 3H), 1.25 (s, 3H); ¹³C{¹H} NMR: δ 86.7 (C-5), 43.3 (C-4), 23.5 (C-5), 21.4 (C-3), 20.5 (C-3); MS (70eV): 41 (70), 42 (7), 43 (71), 55 (89), 56 (28), 69 (55), 83 (M⁺, 100), 92 (43), 104 (14), 133 (8), 148 (3). *Trans isomer:* ¹H-NMR: δ(ppm) 5.31-5.09 (m, 1H), 2.42-1.95 (m, 2H), 1.44 (d, 3H, J=6.4 Hz), 1.36 (s, 3H), 1.35 (s, 3H); ¹³C{¹H} NMR: δ 84.1 (C-5), 44.3 (C-4), 24.3 (C-5), 21.2 (C-3), 20.1 (C-3); MS (70eV): 41 (70), 42 (7), 43 (91), 55 (M⁺, 100), 56 (32), 69 (48), 83 (99), 92 (60), 104 (17), 133 (<1), 148 (2).