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AN EASY PREPARATION OF SIMPLE SULTINES AND HYDROXYALKANESULFINATE SALTS

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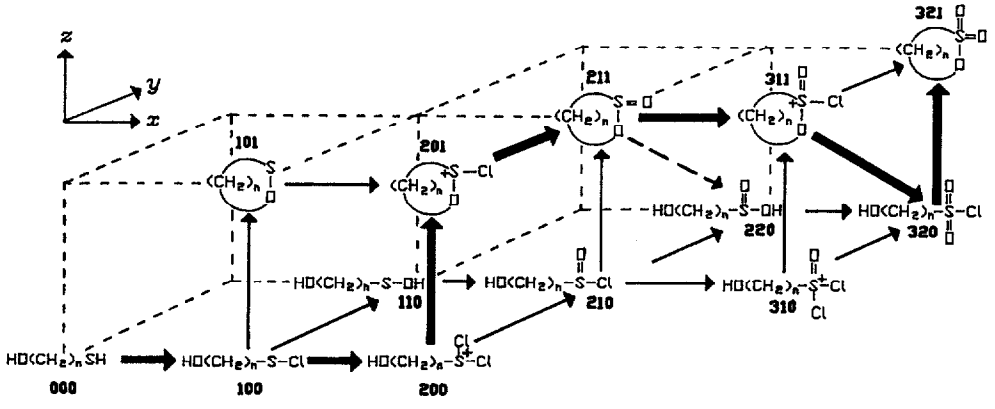
Summary: *In accord with mechanistic prediction a one-pot, two-stage, controlled chlorination–hydrolysis of $HO(CH_2)_nSH$ gave the sultine when n = 3 or 4, and the polymeric sulfinic ester when n = 5 or 6; alkaline hydrolysis of either product yielded the corresponding sodium ω-hydroxy-1-alkanesulfinate.*

Chlorination of α,ω-hydroxythiols (000) in water has recently been shown[1] to give ω-hydroxy-1-alkanesulfonyl chlorides (320), or, when *n* = 3 or 4, also the ω-chloro-1-alkanesulfonyl chloride, $Cℓ(CH_2)_nSO_2Cℓ$, and the sultone (321). We have previously proposed for the latter reaction the path shown by the heavy arrows in Scheme 1, in which the possible reactions are presented in a three-dimensional grid pattern[2].

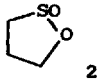
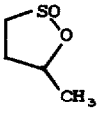
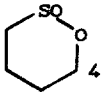
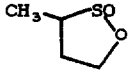
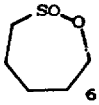
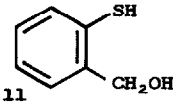
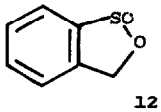
SCHEME 1



A prediction of this mechanism is that if the chlorination goes readily and in the same way in a non-polar medium, the addition of two equivalents of chlorine should give the acyclic dichlorosulfonium[3] ion (200), and when the cyclization 200 → 201 has a relatively high effective concentration, this would lead to 201, and this in turn with an equivalent of water should yield the sultine[5a] (211). This prediction has now been verified.

When carried out as a one-pot, two-step process (see General Procedure) the reaction gave good yields of five- and six-membered sultines as shown in Table 1.

TABLE 1. One-pot, Two-stage Chlorination of Hydroxythiols[a]

Thiol	Sultine[b]	Yield (%)[c]	Thiol	Sultine[b]	Yield (%)[c]
$HO(CH_2)_3SH$ 1	 2	90	$HOCHCH_2CH_2SH$ CH_3 7	 8	70[d]
$HO(CH_2)_4SH$ 3	 4	85	$HOCH_2CH_2CHSH$ 9 CH_3	 10	70[d]
$HO(CH_2)_5SH$ 5	 6	10[e]	 11	 12	80

[a] The thiols were obtained as described in note 6.

[b] Characterized by comparison with authentic samples (in the cases of 2, 4, and 12), or by the reaction sequence sultine → hydroxysulfinate → hydroxysulfonyl chloride → acetoxysulfonpiperidide, following the pattern already described.[1]

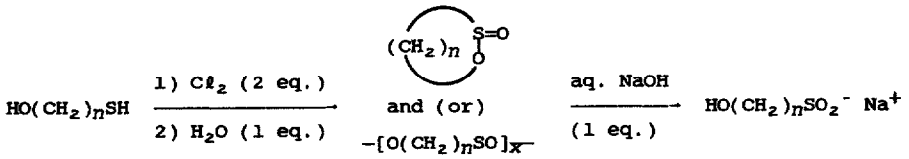
[c] Of distilled product.

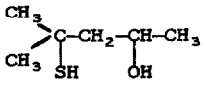
[d] Mixture of diastereomers.

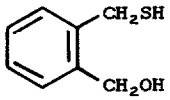
[e] The major product was an undistillable material, presumably $-[O(CH_2)_5SO]_x-$, see text.

The six-carbon thiol, $HO(CH_2)_6SH$, gave a product which showed only weak signals in the δ 3.8-4.2 range expected[5] for the sultine, but displayed strong approximate triplets at δ 3.7 and 2.7 appropriate to an acyclic sulfinic ester.[8] Alkaline hydrolysis of the crude product gave $HO(CH_2)_6SO_2^-\ Na^+$ (≥85%), as shown by: (a) the presence of only six strong peaks in the ^{13}C nmr spectrum,[9] and (b) formation of $HO(CH_2)_6SO_2C\ell$[1a] on brief treatment with $C\ell_2$. A polymeric ester structure for the chlorination-hydrolysis product, $-[O(CH_2)_6SO]_x-$, is consistent with these observations, and, in fact, is to be expected when the effective concentration of the cyclization 200 → 201 is less than the actual concentration of $RS^+C\ell_2$ and ROH groups, and hence coupling is favoured over cyclization.

The five-carbon thiol (5) gave a low yield of the sultine (Table 1); the crude product (mostly apparent polymer plus some sultine) with aqueous NaOH gave $HO(CH_2)_5SO_2^-Na^+$ (≥85%), which in turn with $C\ell_2$ yielded $HO(CH_2)_5SO_2C\ell$[1a]. Similar treatment of 8 and 10 (and, as is noted elsewhere[1b], 2 and 4) with aqueous NaOH yielded the hydroxysulfinates,[9] which on reaction with $C\ell_2$ gave the short-lived sulfonyl chlorides.[9]



13 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Hydroxythiols 13 and 14, however, gave no sign of any cyclic or polymeric sulfinic ester. We infer that the normal reaction does not go when 200 is so constituted that the loss of $SC\ell_2$ may lead to a relatively stable (*e.g.* tertiary or benzylic) cation.

These results provide not only strong support for the mechanism shown in Scheme 1, but also an especially convenient route to hydroxyalkanesulfinate salts and the simplest sultines.

General Procedure: A solution of chlorine (1.42 g, 20 mmol, as determined by iodimetric titration) was added dropwise to a stirred solution of the thiol (10 mmol) in $CH_2C\ell_2$ at -78°C. The reaction mixture was stirred for 5 min and then water (180 μL, 10 mmol) added from a microsyringe. The flask was removed from the cooling bath; the mixture was stirred as it came to room temperature (~10 min), and then dried with $MgSO_4$. Evaporation of the solvent and distillation of the crude product gave the sultine (211). Use of two equivalents of $SO_2C\ell_2$ instead of $C\ell_2$ gave, in our hands, similar or slightly poorer yields of the sultine.

The hydrolysis was carried out by stirring the crude chlorination–hydrolysis product with aqueous NaOH (0.34 M) for 1 h. The aqueous phase was washed with $CH_2C\ell_2$ and the water evaporated under reduced pressure to give the sodium hydroxyalkanesulfinate as a white solid.

The salt was chlorinated by addition of $C\ell_2$ (1 eq.) in $CH_2C\ell_2$ with stirring at room temperature. Immediate filtration to remove the NaCℓ, and evaporation of the solvent under reduced pressure gave the hydroxyalkanesulfonyl chloride (320).

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REFERENCES AND NOTES

1(a). J.F. King, M.R. Webster, N. Chiba, J.K. Allen, K.J.M. Parker, R. Rathore, and S. Skonieczny, *Phosphorus Sulfur,* **31**, 161 (1987). (b) J.F. King and R. Rathore, *Phosphorus Sulfur,* **33**, 165 (1987).

2. In this Scheme the starting material is placed at the origin and successive reactions of the same kind as progressive movements along a particular axis, *i.e.* each chlorination leads to the species one unit further along the *x*-axis, each hydrolysis one along the *y*-axis, and each cyclization to the species one up the *z*-axis. The numerical structure designations are simply the *x*, *y*, and *z* coordinates written in compressed form.

3. The product of chlorination of the sulfenyl chloride, for example, is written as the dichlorosulfonium ion (**200**); this and the other sulfonium ion structures in Scheme 1 are used merely as a convenient notation and not to draw a distinction between sulfonium salt and sulfurane ($HO(CH_2)_nSCl_3$), or other possible structures.[4]

4. *Cf.* G.E. Wilson, Jr. *Tetrahedron,* **38**, 2597 (1982).

5. (a) Previous work on the synthesis of sultines has been well-summarized: N.K. Sharma, F. de Reinach-Hirtzbach, and T. Durst, *Can. J. Chem.* **54**, 3012 (1976); (b) G.W. Buchanan, N.K. Sharma, F. de Reinach-Hirtzbach, and T. Durst, *Can, J. Chem.* **55**, 44 (1977).

6. Thiol sources: (a) the 4-, 5-, and 6-carbon straight chain α,ω-hydroxythiols, from alkaline hydrolysis of the thiuronium salts[1a]; (b) **1**, **11**, and **14** from lithium aluminum hydride reduction of, respectively, the corresponding carboxylic acids or thiophthalic anhydride; (c) **7**, **9**, and **13** from addition of thioacetic acid to the α,β-unsaturated carbonyl compound[7] (*e.g.* methyl vinyl ketone for **7**), followed by $NaBH_4$ reduction and subsequent treatment with aqueous NaOH.

7. M.W. Bullock, J.A. Brockman, Jr., E.L. Patterson, J.V. Pearce, M.H. von Saltza, F. Sanders, and E.L.R. Stokstad, *J. Am. Chem. Soc.* **76**, 1828 (1954).

8. R.V. Norton and I.B. Douglass, *Org. Mag. Res.* **6**, 89 (1974).

9. ^{13}Cmr spectra of the (previously unreported) sodium hydroxyalkanesulfinate salts (in D_2O) and hydroxyalkanesulfonyl chlorides (in $CDCl_3$): (a) $HO(CH_2)_5SO_2^-\ Na^+$, δ 24.2, 27.2, 33.7, 63.3, 64.1; (b) $HO(CH_2)_6SO_2^-\ Na^+$, δ 24.3, 27.4, 30.5, 33.7, 63.3, 64.3; (c) $HOCH(CH_3)CH_2CH_2SO_2^-\ Na^+$, δ 21.6,30.0, 56.6, 66.7; (d) $HOCH_2CH_2CH(CH_3)SO_2^-\ Na^+$, δ 12.7, 33.5, 60.3, 62.0; (e) $HOCH(CH_3)CH_2CH_2SO_2Cl$, 23.7, 33.1, 62.5, 65.4; (f) $HOCH_2CH_2CH(CH_3)SO_2Cl$, 15.2, 33.8, 58.7, 68.7.

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