Stereocontrolled Syntheses of Novel Cyclic Sulfinates using *N*-Sulfinyl-*p*-toluenesulfonamide

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Chiral cyclic and bicyclic sulfinates (sultines) are formed with high stereoselection by the reaction of unsaturated alcohols with *N*-sulfinyl-*p*-toluenesulfonamide (TsNSO).

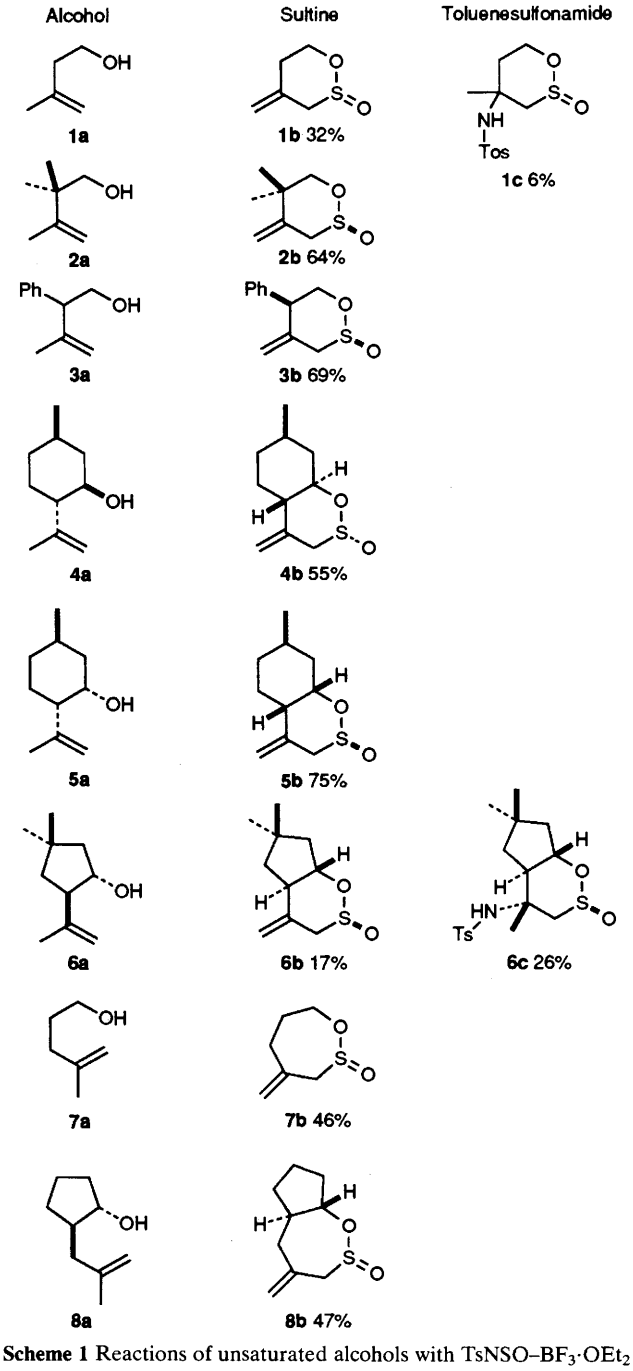
Cyclic sulfinates (sultines) are a fundamental heterocyclic system.[1] Although they have been long known,[2] there are few relatively general methods of synthesising sultines,[1,3,4] and those usually proceed without stereocontrol.[5] Sultines are versatile synthetic intermediates:[1] for example, they undergo ring-opening reactions, alkylation and oxidation at sulfur to give sultones,[6] and reductive desulfurisation. The stereogenic centre at sulfur is of potential value in asymmetric synthesis.

We report here a new, versatile and stereoselective route to sultines. We have discovered that a variety of unsaturated alcohols react with TsNSO–BF_3·OEt_2 to give sultines (see Scheme 1). The general procedure† is described for **2b**. TsNSO[7] (0.81 g, 3.5 mmol) was dissolved in benzene (20 ml) and cooled to 10 °C. 2,2,3-Trimethylbut-3-en-1-ol (0.31 g, 2.0 mmol) was added, followed by BF_3·OEt_2 (0.12 ml, 1.0 mmol). The yellow solution was stirred for 2 h prior to addition of water (10 ml). Extraction (CH_2Cl_2) and chromatography (silica; 9 : 1, 40–60 °C light petroleum ethyl acetate as eluant) afforded sultine **2b** (64%) as a pale-yellow oil.

Both six- and seven-membered monocyclic sultines can be prepared. Entries 4, 5, 6 and 8 show that bicyclic sultines, which may possess either *cis*- or *trans*-fusion at the ring junction, may also be prepared from suitably substituted cycloalkanols. In all the examples studied, the only sultines isolated contained an exocyclic alkene moiety. The reactions proceeded stereoselectively: ring-junction stereochemistry, (entries 4, 5, 6 and 8) is determined by the configuration of the alcohol. In every case the S=O linkage was found to adopt an axial orientation, attributable to dipole minimisation.[8] X-Ray determinations‡ of single crystals of **4b** and **5b** confirmed the relative configurations at the four chiral centres, the S=O unit being axial. An X-ray determination‡ on a single crystal of **6c** (Fig. 1) established the *anti*-relation of the toluenesulfonamide and S=O linkages.

The chemical shifts of the α-methylene hydrogen atoms in the ^1H NMR spectra of each of the sultines are also consistent with the designated configurations and conformations.

Bicyclic sultines can also be prepared in one step. Thus, when 3,7-dimethyloct-6-enal (citronellal) was added to a solution of TsNSO (1.5 equiv.) in benzene at 6 °C followed by



Scheme 1 Reactions of unsaturated alcohols with TsNSO–BF_3·OEt_2

† New compounds gave satisfactory elemental analyses and exhibited spectroscopic data (IR, ^1H NMR, and ^{13}C NMR) in agreement with their structures.

‡ *Crystal data* for **4b**: $C_{10}H_{16}O_2S$, M = 200.30, monoclinic, space group $P2_1$ (C^2_2, No. 4), a = 10.420(10), b = 4.756(7), c = 10.989(7) Å, β = 104.49°(7) U = 527.3(10) Å^3, Z = 2, D_c = 1.284 g cm^{-3}, Mo-Kα radiation ($\bar{\lambda}$ = 0.71069 Å), μ(Mo-Kα) = 2.62 cm^{-1}, F(000) = 215.98. 504 Independent reflections with $|F|/\sigma(|F|) > 3.0$ were used in the analysis. Final R = 0.0761.

Crystal data for **5b**: $C_{10}H_{16}O_2S$, M = 200.3, monoclinic, space group $P2_1$ (C^2_2, No. 4), a = 5.278(6), b = 8.712(11), c = 11.672(20) Å, β = 104.79°(11) U = 518.9(12) Å^3, Z = 2, D_c = 1.282 g cm^{-3}, Mo-Kα radiation ($\bar{\lambda}$ = 0.71069 Å), μ(Mo-Kα) = 2.66 cm^{-1}, F(000) = 215.98. 492 Independent reflections with $|F|/\sigma(|F|) > 3.0$ were used in the analysis. Final R = 0.0377.

Crystal data for **6c**: $C_{17}H_{25}NO_4S_2$, M = 371.5, triclinic, space group $P\bar{1}$ (C^1_i, No. 2), a = 6.384(8), b = 6.217(8), c = 24.987(23) Å, α = 90.07(9), β = 91.44(9), γ = 110.60(10)°, U = 927.9(19) Å^3, Z = 2, D_c = 1.228 g cm^{-3}, Mo-Kα radiation ($\bar{\lambda}$ = 0.71069 Å), μ(Mo-Kα) = 2.94 cm^{-1}, F(000) = 395.95. 1600 Independent reflections with $|F|/\sigma(|F|) > 3.0$ were used in the analysis. Final R = 0.0768.

Data for crystallographic analyses were measured $3.5 < 2\theta < 40°$ ($3.5 < 2\theta < 45°$ for **4b**) on a Nicolet R3 diffractometer by the ω scan method. Structures were solved by direct methods and refined by blocked cascade least-squares methods. Complex scattering factors were taken from the program package SHELXTL as implemented on the Data General DG30 computer. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Instructions for Authors, Issue No. 1.

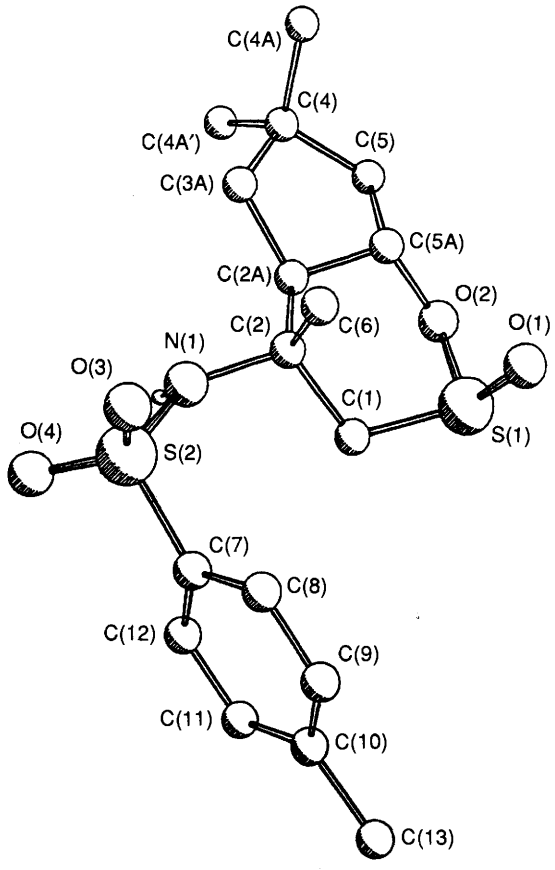


Fig. 1 Crystal structure of **6c**

addition of $BF_3{\cdot}OEt_2$ (0.5 equiv.), and the mixture stirred 3 h at 5 °C, **4b** (40%), m.p. 98.5–100 °C, was isolated from the mixture by column chromatography (silica gel, light petroleum–ethyl acetate 9 : 1). This result is consistent with an initial oxo–ene reaction leading to the framework of isopulegol **4a**,[9] followed by a second and mechanistically discrete process by which the sultine ring is formed.

The mechanistic pathways involved are currently under investigation. The higher yield obtained from the *gem*-dimethyl alcohol **2a**, as compared with **1a**, is attributable to the Thorpe–Ingold effect.[10] *N*-Sulfinyl compounds of the form R–N=S=O and the related *N*-sulfinylsulfonamides are well known as dienophiles in [4 + 2] cycloadditions.[11] A possible pathway is a hetero-ene reaction across the N=S linkage of TsNSO and the allylic moiety of the alcohol, leading to formation of a carbon–sulfur bond; subsequent ring closure involving S–O bond formation, followed by elimination of $TsNH_2$ from the sulfur atom would then give the sultine. However, in this study, two eliminations of $TsNH_2$ at carbon have been observed: the sulfonamides **1c** and **6c** were isolated and separately treated with $BF_3{\cdot}OEt_2$ in CH_2Cl_2 (2 equiv., 20 °C, 16 h) to give, respectively, the sultines **1b** and **6b**. In the formation of sultines from the unsaturated alcohols, further investigation could reveal whether eliminations of the type **1b** to give **1c** are involved, and if so whether such eliminations provide the exclusive pathway to sultines, or whether other routes are also involved.

A notable feature of the reactions herein described is the suppression of the more usual formal imino–ene reaction[12] of TsNSO. The reaction of various unsaturated alcohols with $TsNSO{-}BF_3{\cdot}OEt_2$ provides a new route to sultines the scope and synthetic potential of which are being examined.

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