A New Method for the Dehydration of β-Hydroxy Sulfones: Synthesis of (*E,S*)-γ-Hydroxy-α,β-unsaturated Sulfones and (*S*)-ε-Hydroxy-(*E,E*)-α,γ-dienyl Sulfones

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Optically active (*E,S*)-γ-hydroxy-α,β-unsaturated sulfones and (*S*)-ε-hydroxy-(*E,E*)-α,γ-dienyl sulfones have been prepared in a one-pot dehydration procedure from β,γ-dihydroxy sulfones and δ,ε-dihydroxy allyl sulfones, respectively, *via* an elimination reaction of the corresponding cyclic sulfites or carbonates formed *in situ* by treatment with thionyl chloride or carbonyldiimidazole.

An γ-hydroxy-α,β-unsaturated sulfone has recently been utilized in stereocontrolled cycloadditions,[1] conjugate additions[2] and other reactions.[3] The synthesis of γ-hydroxy-α,β-unsaturated sulfones employing Knoevenagel condensation of aldehyde and substituted sulfinylmethyl phenyl sulfone in tandem with allylic sulfoxide–sulfenate rearrangement is known.[4] Dienyl phenyl sulfones which have two double bonds of different reactivity were selectively functionalized.[5] As the chiral γ-hydroxy-α,β-unsaturated sulfones and ε-hydroxy-α,γ-dienyl sulfones are useful synthons in organic transformations, we report here a convenient one-pot synthetic method for the preparation of optically active γ-hydroxy-α,β-unsaturated sulfones, **4a–b** and **8a–b**, and ε-hydroxy-α,γ-dienyl sulfones, **11a, b**, from dihydroxy sulfones and dihydroxy allyl sulfones, respectively. This one-pot procedure is based on the elimination reaction of the corresponding cyclic sulfites or cyclic carbonates formed *in situ* by treatment of dihydroxy sulfones or dihydroxy allyl sulfones with thionyl chloride or carbonyldiimidazole.

The enantioselective synthesis of optically active (*E*)-γ-hydroxy-α,β-unsaturated sulfones has been carried out (see Scheme 1). The (2*S*,3*S*)-dihydroxy sulfone **1a** was prepared† from (2*R*,3*S*)-2,3-*O*-isopropylidenedioxyoctanol[6] derived from 2-deoxy-D-ribose. On treatment of **1a** with thionyl chloride (1.2 equiv.) in the presence of triethylamine (5 equiv.) at room temperature for 3 h (Table 1, Method A), (*E,S*)-γ-hydroxy-α,β-unsaturated sulfone **4a**, $[\alpha]_D^{23}$ +43.7° (*c* 2.2, $CHCl_3$), m.p. 86–87 °C, was obtained directly as the only isolated product without formation of the *Z*-isomer, judged by ^1H NMR coupling constants (recorded in Hz) for vinyl protons of **4a**: δ_H 6.80 (dd, *J* 15.5 and 1.5, 1-H) and 7.24 (dd, *J* 15.5 and 3.5, 2-H). It is presumed that the cyclic sulfite **2a** is the intermediate in the above conversion.‡ Alternatively, reaction of **1a** with carbonyldiimidazole (2 equiv.) in dry dichloromethane at room temperature for 4 h gave the cyclic carbonate **3a**, which was stirred with silica gel in dichloromethane (Method B) to afford **4a** in 70% yield (Table 1). When **1a** was treated with $CO(Im)_2$ (4 equiv.) in dichloromethane for 12 h, **4a** was obtained directly in 78% yield after column chromatographic purification. On the other hand, the (2*R*,3*S*)-dihydroxy sulfone **5a** was prepared§ from (2*S*,3*S*)-2,3-*O*-isopropylidenedioxyoctanol[7] derived from L-tartaric acid. The (2*R*,3*S*)-dihydroxy sulfones **5a** and **5b** were also subjected to the elimination reactions to afford **8a** and **8b**,¶ which are summarized in Table 1 and Scheme 1.

Table 1 (*E,S*)-γ-Hydroxy-α,β-unsaturated sulfones and (*S*)-ε-hydroxy (*E,E*)-α,γ-dienyl sulfones

Entry	Substrate	Reaction conditions[a] (yield, %)	Product[b]
1	**1a**	A (65%), B (70%)	**4a**
2	**1b**	A (71%), B (81%)	**4b**
3	**5a**	A (72%), B (83%)	**8a**
4	**5b**	A (75%), B (78%)	**8b**
5	**9a**	B (75%)	**11a**
6	**9b**	B(74%)	**11b**

[a] A (Method A): $SOCl_2$ (1.2 equiv.), Et_3N (5 equiv.), CH_2Cl_2, room temp., 3 h. B (Method B): $CO(Im)_2$ (2 equiv.), CH_2Cl_2, room temp., 3 h and then SiO_2. [b] The specific rotations $[\alpha]_D^{25}$ values (given in units of 10^{-1} deg cm^2 g^{-1}): **4b**; +44.5 (*c* 3.62, $CHCl_3$), **8a**; +40.5 (*c* 2.1, $CHCl_3$), **8b**; +43.2 (*c* 4.7, $CHCl_3$), **11b**; −1.29 (*c* 0.16, CCl_4).

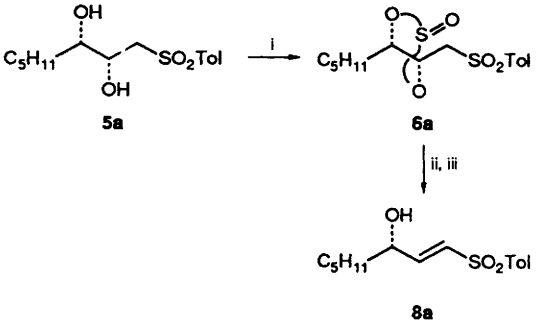
Dehydrations of β-hydroxy sulfones to prepare α,β-unsaturated sulfones are normally carried out by first acetylating the hydroxy group and then effecting elimination with sodium hydroxide.[8] Therefore, the present method is a mild and one-pot dehydration of β-hydroxy sulfones. The cyclic sulfites or carbonates formed *in situ* by treating β,γ-dihydroxy sulfones

† Compound **1a** was prepared from (2*R*,3*S*)-2,3-*O*-isopropylidenedioxyoctanol: i, PhSSPh, Bu_3P, benzene, room temp., 4 h (74%); ii, Dowex 50 WX 8 resin, MeOH, room temp., 12 h (90%); iii, MCPBA, MeOH, 0 °C, room temp., 12 h (78%).

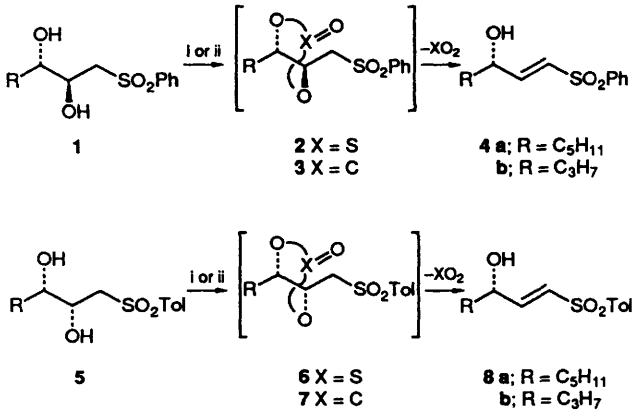
‡ As indirect evidence, treatment of the compound **1a** with thionyl chloride (1.2 equiv.) in the presence of triethylamine (2 equiv.) at room temp. for 30 min provided the cyclic sulfite **2a**: δ_H(80 MHz; $CDCl_3$) 0.89 (3 H, t), 1.07–1.97 (8 H, m), 3.48 (1 H, dd, *J* 12 and 6), 3.92 (1 H, dd, *J* 16 and 8), 4.94–5.41 (2 H, m), 7.64 (3 H, m) and 8.00 (2 H, m), after column chromatographic separation (EtOAc–hexanes 1 : 1, R_f 0.68, 0.72), which was treated with LDA (3 equiv.) in THF at −30 °C for 30 min to afford compound **4a** (75%).

§ Compound **5a** was prepared: i, Ph_3P, I_2, imidazole, toluene, 80 °C, 3 h (82%); ii, *p*-$TolSO_2Na$, DMF, 100 °C, 3 h (72%); iii, Dowex 50 WX 8 resin, MeOH, 40 °C, 5 h (86%).

¶ The cyclic sulfite **6a** was easily converted into the cyclic sulfate, which upon treatment with triethylamine (1.1 equiv.) in CH_2Cl_2 at room temp. for 2 h followed by acidic work-up with 20% H_2SO_4 afforded compound **8a** by the following reaction sequence: i, $SOCl_2$, CCl_4, reflux, 3 h (95%); ii, $NaIO_4$, $RuCl_3 \cdot H_2O$ (cat), CCl_4, room temp., 1 h; iii, Et_3N, CH_2Cl_2, room temp., 2 h then 20% H_2SO_4 work-up (75% overall).



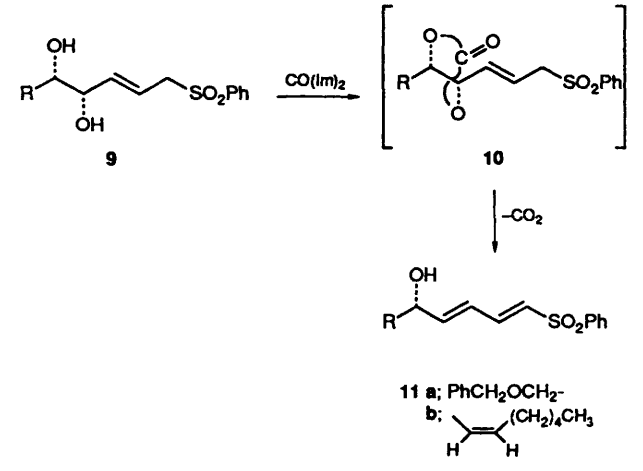
5a **6a** **8a**



Scheme 1 *Reagents and conditions:* i, Method A: $SOCl_2$, Et_3N; ii, Method B: $CO(Im)_2$ then SiO_2

with thionyl chloride or carbonyldiimidazole are suitable leaving groups for these β-elimination reactions.

This elimination method was extended to dihydroxy allyl sulfones **9a** and **9b** prepared from 4-*O*-benzyl-2,3-isopropylidene-L-threose[9] (Scheme 2). Treatment of dihydroxy allyl sulfone **9a*** with carbonyldiimidazole (2 equiv.) in dry dichloromethane at room temperature for 3 h gave the cyclic carbonate, which without separation was stirred with silica gel in dichloromethane for 6 h (Method B) to afford the dienyl sulfone **11a**, $[\alpha]_D^{25}$ +7.27 (*c* 1.1, CCl_4) with the (*E*,*E*)-isomer as the only isolated product, checked by ^1H NMR; δ_H(500 MHz; $CDCl_3$), 3.57 (1 H, dd, *J* 9.5 and 3.5), 3.79 (1 H, dd, *J* 9.5 and 7.0), 4.47 (1 H, m), 4.56 (2 H, s), 6.18 (1 H, dd, *J* 15.5 and 5.0), 6.37 (1 H, d, *J* 15.5), 6.42 (1 H, dd, *J* 14 and 11), 7.25 (1 H, m) and 7.30–7.88 (10 H, m). The other method (Method A) was not applicable to prepare the dienyl sulfone **11a**, in our hands. The results are summarized in Table 1 and Scheme 2.



Scheme 2

The functionalization and use of these unsaturated sulfones in the synthesis of natural products is currently in progress.

Typical Procedures.—Method A. To a stirred solution of the dihydroxy sulfone **1a** (286 mg, 1.00 mmol) in dry CH_2Cl_2 (10 ml) at 0 °C was added Et_3N (505 mg, 5 equiv.), followed by $SOCl_2$ (143 mg, 1.2 equiv.). The reaction mixture was warmed to room temperature and stirred for 3 h and then concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel using EtOAc–hexanes (1:1) as the eluent to afford compound **4a** (174 mg, 65%), m.p. 86–87 °C (Found: C, 62.75; H, 7.7; S, 11.7. $C_{14}H_{20}SO_3$ requires C, 62.65; H, 7.51; S, 11.94%); ν_{max}($CHCl_3$)/cm^{-1} 3400 (OH), 1640 (CH=CH), 1300 (SO_2) and 1150 (SO_2); δ_H(80 MHz; $CDCl_3$), 1.06 (3 H, t, 8-Me), 1.25–1.95 [8 H, br m, $(CH_2)_4$], 4.52 (1 H, m, 3-H), 6.80 (1 H, dd, *J* 15.5 and 1.5, 1-H), 7.24 (1 H, dd, *J* 15.5 and 3.5, 2-H) and 7.78–8.15 (5 H, m, Ph); *m*/*z* 268 (M^+) and 250 ($M^+ - 18$).

Method B. To a stirred solution of the diol **9a** (362 mg, 1.00 mmol) in dry CH_2Cl_2 (10 cm^3) at room temperature was added carbonyldiimidazole (320 mg, 2.00 mmol). The reaction mixture was stirred for 3 h and then silica gel (4.0 g) was added to it and stirring continued for 6 h. The mixture was then filtered and the filtrate was concentrated under reduced pressure and the crude product purified by column chromatography (EtOAc–hexanes, 1:1, R_f 0.62) to afford compound **11a** (258 mg, 75%) (Found: C, 66.3; H, 5.95; S, 9.3. $C_{19}H_{20}O_4S$ requires C, 66.25; H, 5.85; S, 9.31%); ν_{max}(neat)/cm^{-1} 3400 (OH), 1640 (conjugated diene), 1300 (SO_2) and 1140 (SO_2); *m*/*z* 344 (M^+) and 326 ($M^+ - 18$).

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* Compound **9a** was prepared from 4-*O*-benzyl-2,3-isopropylidene-L-threose[9]: i, Ph_3P=$CHCO_2Et$, toluene, reflux, 3 h (82%); ii, DIBAH (2 equiv.), CH_2Cl_2, −78 °C, 3 h (90%); iii, PBr_3, ether, 0 °C, 2 h (73%); iv, $NaSO_2Ph$, DMF, room temp., 4 h (93%); v, Dowex 50 WX 8 resin, MeOH, room temp., 6 h (91%).

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