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SYNTHESIS OF β- AND γ-HYDROXY SULFONES BY REGIOSELECTIVE OPENING OF β,γ-EPOXY SULFONES

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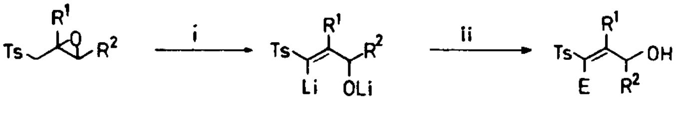
Summary: β,γ-Epoxy sulfones **1** derived from allylic sulfones react regioselectively with organomagnesium compounds in the presence or not of catalytic amounts of copper(I) bromide to afford β-hydroxy sulfones **2** or γ-tosylated allylic alcoholates **5** respectively. The Michael type addition of Grignard reagents to intermediates **5** in the presence of catalytic amount of copper(I) bromide yields γ-hydroxy sulfones **6**. The PCC oxidation of β- and γ-hydroxy sulfones give β- and γ-oxo sulfones **10** and **11** respectively. In the case of γ-oxo sulfones their treatment with DBU affords α-substituted, α, β- unsaturated carbonyl compounds.

INTRODUCTION

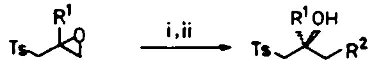
The great interest of β- and γ-hydroxy sulfones in organic synthesis is mainly based on their use as precursors of d^2 and d^3 reagents[1] through the corresponding metallation reaction.[2] Dianions of β-hydroxy sulfones[2,3] have been employed for the preparation of lactones[3a-c,f] and 2,5-disubstituted tetrahydrofurans.[3c] On the other hand β-hydroxy sulfones are useful in the synthesis of vinyl sulfones by a β-elimination reaction[4] and olefins by reductive elimination.[5] Mono or dianions of γ-alkoxy or γ-hydroxy sulfones[2,6] have been used in synthesis of cyclopropanes[6a], enones[6b], calcidiol lactone[6d] and desepoxyasperdiol.[6b,f] Recently,[7] we described the application of β,γ-epoxy sulfones[6b,c,8] in the synthesis of unsaturated γ-hydroxy sulfones by nucleophilic ring opening, followed by lithiation of the tosylated allylic alkoxide and reaction of the obtained dianion[9] with electrophilic reagents (Scheme 1) We report here the application of β,γ-epoxy sulfones in the synthesis of β- and γ-hydroxy sulfones by means of Grignard reagents.



Scheme 1. Reagents: i, 2 MeLi, ii, E^+.

RESULTS AND DISCUSSION

The treatment of β,γ-epoxy sulfones **1** [readily available by epoxidation with *m*-chloroperbenzoic acid (*m*-CPBA) of allylic sulfones[7,10]] with Grignard reagents in the presence of catalytic amounts of copper(I) bromide at room temperature affords regioselectively β-hydroxy sulfones **2** (Scheme 2 and Table 1)



1a, R^1=H
1b, R^1=Me

2

Scheme 2. Reagents: i, R^{2}MgX, CuBr (cat); ii, NH$_4$Cl.

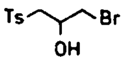
Table 1. Synthesis of β-hydroxy sulfones **2**.

		Product 2		
Epoxide 1	R^{2}MgX	no.	yield,[a] %	mp,[b] °C, or R_f[c]
1a	MeMgCl	**2a**	57	0.67[d]
1a	CH$_2$=CHMgBr[e]	**2b**	59	0.55
1a	CH$_2$=CHCH$_2$MgBr[e]	**2c**	56	0.63
1a	Bu^{n}MgBr	**2d**	74	0.78
1a	PhMgCl	**2e**	85	88-89
1b	MeMgCl	**2f**	67	0.61

[a] Isolated yield after column chromatography (silica gel , hexane/ether) based on the starting epoxide **1**. [b] From hexane/ether. [c] For oils; silica gel, hexane/ether:1/10. [d] Lit.[11] n_D 1.5355. [e] Stoichiometric amount of copper(I) bromide and two equivalents of Grignard reagent were used.

The regioselective opening of the epoxide takes place in short time (30 min.) and no competition with the eliminative ring fission to give the corresponding γ-tosylated allylic alcohols (see below) was observed, although the reaction was carried out in THF and at room temperature.[12] Therefore, we think that copper(I) bromide is the most efficient copper salt for this reaction. However, in the case of γ-substituted β,γ-epoxy sulfones, the elimination reaction was the only process observed.

When allyl- and vinyl-magnesium bromide were used a stoichiometric amount of copper(I) bromide has to be used in order to avoid the formation of the bromohydrin **3**. The halogenide-mediated epoxide opening was also observed with methylmagnesium iodide to yield a mixture of compounds **4** and **2a**.



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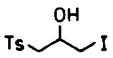

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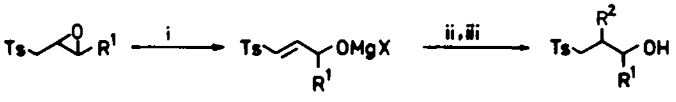
The treatment of β,γ-epoxy sulfones **1** with one equivalent of a Grignard reagent or sodium diethyl malonate leads to the corresponding γ-oxide α,β-unsaturated sulfones **5**. The subsequent *in situ* reaction of this intermediate with another equivalent of an organomagnesium compound[9] or sodium diethyl malonate in the presence of a catalytic amount of copper(I) bromide yields γ-hydroxy sulfones **6** (Scheme 3 and

Table 2).



1a, R^1=H
1c, R^1=Me

5

6

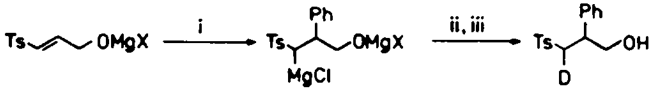
Scheme 3. Reagents: i, RMgX; ii, R^{2}MgX, CuBr; iii, NH$_4$Cl.

Table 2. Synthesis of γ-hydroxy sulfones **6**.

			Product **6**		
Epoxide	RM	R^{2}M	no.	yield,[a] %	mp,[b] °C, or R_f[c]
1a	MeMgCl	MeMgI	**6a**	56	0.39
1a	MeMgCl	CH_2=CHMgBr	**6b**	62	0.42
1a	MeMgCl	CH_2=CHCH$_2$MgBr	**6c**	74	0.47
1a	Bu^{n}MgBr	Bu^{n}MgBr	**6d**	50	0.61
1a	MeMgCl	PhMgCl	**6e**	62	132-133
1a	$(EtO_2C)_2CHNa$	$(EtO_2C)_2CHNa$	**6f**	70[d]	0.34[d]
1c	MeMgCl	MeMgI	**6g**[e]	63	0.47
1c	MeMgCl	CH_2=CHMgBr	**6h**[e]	69	97-98[f]
1c	MeMgCl	Bu^{n}MgBr	**6i**[e]	56	0.68
1c	MeMgCl	PhMgBr	**6j**[e]	66	122-123[g]

[a] Isolated yield after column chromatography (silica gel, hexane/ether) based on starting epoxide **1**. [b] From CCl_4. [c] For oils; silica gel, hexane/ether:1/10. [d] Compound **9** was isolated as a mixture of diastereoisomers (10/1, ^{13}C NMR). [e] Obtained as mixture of diastereoisomers ca. 1/1 (^{1}H NMR). [f] From hexane/dichloromethane. [g] Mixture of diastereoisomers 9/1 (^{13}C NMR).

The eliminative epoxide opening, which can be also carried out (see Table 2) with organolithium compounds,[7,9] gives the best results using methylmagnesium chloride. The second step yields in all cases optimal results in the presence of catalytic amounts of copper(I) bromide.[9] The dianion **7** resulting from the Michael type addition[13] of phenylmagnesium chloride to the alcoholate **5a** was characterized by deuterolysis with deuterium oxide, so compound **8** was isolated in 70 % yield (Scheme 4).



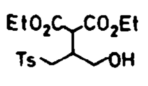
5a

7

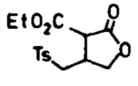
8

Scheme 4. Reagents: i, PhMgCl, CuBr; ii, D_2O; iii, NH$_4$Cl.

Compound **6f** resulting from the reaction of epoxide **1a** with sodium diethyl malonate, was transformed into the lactone **9** after purification by column chromatography on silica gel or on standing. Compound **9** was isolated as a mixture of diastereoisomers (table 2).



6f



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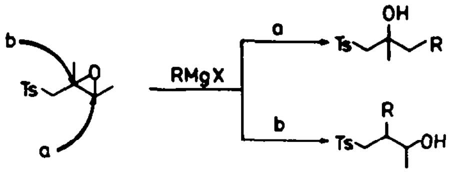
In conclusion, both strategies shown in Schemes 2 and 3 allow the regioselective opening of β, γ-epoxy sulfones to afford β- and γ-hydroxy sulfones (Scheme 5).



Scheme 5

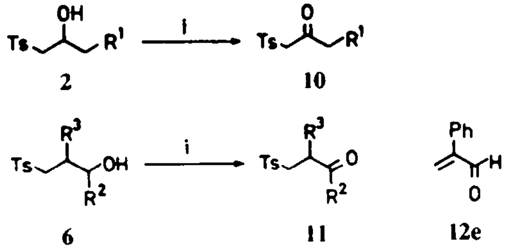
We have studied the oxidation of the obtained β- and γ-hydroxy sulfones in order to prepare the corresponding oxo sulfones.[14] The treatment of β- and γ-hydroxy sulfones **2** and **6** with two equivalents of pyridinium chlorochromate (PCC)[15] in anhydrous dichloromethane at room temperature led to β- and γ-keto sulfones **10** and **11** respectively (Scheme 6 and Table 3).

When the γ-hydroxy sulfone **6e** (R^2=H, R^3=Ph) was treated with PCC the aldehyde **12e**, resulting from

Table 3. Preparation of β- and γ-oxo sulfones **10** and **11**.

Hydroxy Sulfone	R^1	R^2	R^3	Reaction time (h)	Product no.	yield,[a] %	mp,[b] °C or R_f[c]
2d	Bu^n			4	**10d**	88	0.54
2e	Ph			3	**10e**	82	89-90[d]
6a		Me	H	3	**11a**	71	0.50
6d		Bu^n	H	3	**11d**	82	0.54
6e		Ph	H	4	**12e**[e]	76	0.80
6g		Me	Me	6	**11g**	82	0.62
6h		CH_2=CH	Me	6	**11h**	74	0.66
6i		Bu^n	Me	7	**11i**	90	0.72
6j		Ph	Me	6	**11j**	81	0.70

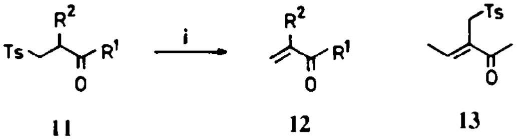
[a] Based on starting hydroxy sulfone. [b] From hexane/ether. [c] For oils, silica gel, ether/hexane:10/1. [d] Lit.[16]: mp 75-76 °C. [e] Lit.[17]: structure proposed according to MS-data.



Scheme 6. Reagent: i, PCC.

the oxidation reaction followed by the *p*-toluenesulfinate elimination, was directly obtained.

The prepared γ-oxo sulfones **11** are interesting precursors of homoenolates[18] and they can be also transformed into α-substituted α,β-unsaturated carbonyl compounds.[19] Thus, compounds **12** have been obtained by treatment of sulfones **11** with one equivalent of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (2 hours) in THF (Scheme 7 and Table 4). This elimination reaction does not take place with other bases such as methanolic potassium hydroxide[19] or triethylamine.[15b]



Scheme 7. Reagent: i, DBU.

Table 4. Synthesis of α-substituted α,β-unsaturated carbonyl compounds.

γ-Oxo Sulfone	R^1	R^2	Product no.	Product yield,[a] %	Product mp,[b] °C or R_f[c]
11d	Bu^{n}	H	**12d**	30	--[d,e]
11h	$CH_2=CH$	Me	**13**	50[f]	124-125
11i	Bu^{n}	Me	**12i**	76	0.60[g]
11j	Ph	Me	**12j**	80	0.76[h]

[a] Based on compound **11**. Isolated crude product, pure by ^{1}H NMR. [b] From hexane/ether. [c] For oils; silica gel hexane/ether:1/10. [d] Decomposed on silica gel. [e] Lit.,[20] bp 45-47 °C/12 mm Hg. [f] Purified by column chromatography on silica gel (hexane/ether). [g] Lit.,[21] bp 53-54 °C/18 mm Hg. [h] Lit.,[22] only spectral data reported.

In the case of the vinyl derivative **11h** the expected elimination does not occur and only isomerization of the double bond was observed, compound **13** being exclusively obtained. This synthetic route allows the synthesis of α-substituted α,β-unsaturated compounds starting from β,γ-epoxy sulfones.

EXPERIMENTAL

General. Melting points were obtained with a Reichert thermovar apparatus. Column chromatography was done on Merck grade 60 silica gel (70-230 mesh) and TLC was carried out on Merck 60F-254 precoated silica gel on aluminium sheets (and visualization by UV). IR spectra were determined with a Pye Unicam SP3-200 spectrometer. ^1H NMR spectra were recorded on a Varian EM-360L and a Bruker AC-300 spectrometers. ^{13}C NMR spectra were obtained with a Bruker AC-300 spectrometer. All NMR spectra were made in carbon tetrachloride as solvent; chemical shifts are given in δ(ppm) relative to tetramethylsilane as an internal standard. Mass spectra were obtained with a Hewlett-Packard 5988A spectrometer at 70 eV. Microanalyses were performed by the Microanalyses Service of the University of Zaragoza. Organomagnesium compounds were prepared from the corresponding alkyl halide and magnesium chips in ether or were commercially available (Aldrich) in THF. Solvents were dried as usually. Epoxy sulfones were prepared as it has been previously described.[7]

Preparation of β-Hydroxy Sulfones 2. General Procedure. To a suspension of β,γ-epoxy sulfone **1** (0.5 mmol) and copper(I) bromide (5 mg) in THF (5 ml) was added the Grignard reagent (0.5 mmol) at 0°C. In the case of compounds **2b** and **2c** one equivalent of copper(I) bromide and two equivalents of the organomagnesium compound were used. After 30 min stirring at room temperature the mixture was hydrolyzed with water and 1N aqueous ammonium chloride solution and extracted with dichloromethane (10 ml). The organic layer was dried over anhydrous Na_2SO_4, and evaporated *in vacuo* (15 torr). The resulting residue was purified by column chromatography (hexane/ether) or by recrystallization to afford products **2**. Yields and melting points or R_f values are reported in Table 1. Spectral and analytical data follow.

1-Tosyl-2-butanol (2a)[11]: ν_{max} (film) 3500 (OH), 1300, and 1150 cm^{-1} (SO_2); δ_H (60 MHz) 0.9 (deform t, J=7Hz, 3H, CH_3CH_2), 1.35 (m, 2H, CH_2CH_3), 2.45 (s, 3H, CH_3Ar), 3.05 (d, J=6Hz, 2H, CH_2S), 3.30 (br s, 1H, OH), 3.9 (m, 1H, CHO), 7.25, and 7.8 (2d, J=8Hz, 4H, ArH); m/z 228 (M^+, 0.2 %), 210 (M^+-18, 0.7), 199 (27), 155 (57), 92 (52), 91 (100), 72 (28), and 65 (35).

1-Tosyl-4-penten-2-ol (2b): ν_{max} (film) 3500 (OH), 3070, 1640, 920 (CH=C), 1300, and 1140 cm^{-1} (SO_2); δ_H (60 MHz) 2.15 (t, J=6Hz, 2H, CH_2CH=), 2.35 (s, 3H, CH_3Ar), 3.0 (d, J=6Hz, 2H, CH_2S), 3.4 (d, J=3Hz, 1H, OH), 4.05 (m, 1H, CHO), 4.7-5.3 (m, 2H, CH_2=CH), 5.45-6.10 (m, 1H, CH=CH_2), 7.2, and 7.65 (2d, J=8Hz, 4H, ArH); m/z 240 (M^+, 0.5%), 222 (M^+-18, 0.2), 199 (67), 155 (96), 91 (100), and 65 (33); Anal. Calcd. for $C_{12}H_{16}O_3S$ C, 60.00; H, 6.67. Found: C, 59.6, H, 6.4.

1-Tosyl-5-hexen-2-ol (2c): ν_{max} (film) 3500 (OH), 3060, 1630, 910 (CH=C), 1300, and 1140 cm^{-1} (SO_2); δ_H (60 MHz) 1.5 (m, 2H, CH_2CHO), 2.15 (m, 2H, CH_2CH=), 2.3 (s, 3H, CH_3Ar), 3.05 (d, J=6Hz, 2H, CH_2S), 3.4 (d, J=4Hz, 1H, OH) 3.9 (m, 1H, CHO), 4.6-5.1 (m, 2H, CH_2=CH), 5.2-5.9 (m, 1H, CH=CH_2), 7.2, and 7.6 (2d, J=8Hz, 4H, ArH); m/z 236 (M^+-18, 3%), 199 (41), 155 (65), 139 (27), 92 (37), 91 (100), 81 (32), 80 (50), 79 (24), and 65 (33); Anal. Calcd. for $C_{13}H_{18}O_3S$: C, 61.42; H, 7.09. Found: C, 61.1; H, 7.2.

1-Tosyl-2-heptanol (2d): ν_{max} (film) 3500 (OH), 1300, and 1140 cm^{-1} (SO_2); δ_H (60 MHz) 0.8 (deform t, J=7Hz, 3H, CH_3CH_2), 1.25 [m, 8H, $(CH_2)_4CH_3$], 2.35 (s, 3H, CH_3Ar), 3.0 (d, J=6Hz, 2H, CH_2S), 3.3 (d, J=3Hz, 1H, OH), 3.9 (m, 1H, CHO), 7.25, and 7.7 (2d, J=8Hz, 4H, ArH); m/z 20 (M^+, 0.7%), 252 (M^+-18, 2), 199 (46), 157 (20), 155 (67), 92 (40), 91 (100), 65 (32), and 55 (32).

1-Phenyl-3-tosyl-2-propanol (2e): ν_{max} (Nujol) 3500 (OH), 1290, and 1150 cm^{-1} (SO_2); δ_H (60 MHz, $CDCl_3$) 2.45 (s, 3H, CH_3Ar), 2.8 (2d, J=6Hz, 2H, CH_2Ph), 3.1 (d, J=6Hz, 2H, CH_2S), 3.25 (br s, 1H, OH), 4.35 (m, 1H, CHO), 7.2-7.5 (m, 7H, Ph and 2x*p*-TolH), and 7.75 (d, J=8Hz, 2x*p*-TolH); m/z 272 (M^+-18, 3%), 155 (37), 117 (64), 92 (47), 91 (100), and 65 (26). Anal. Calcd. for $C_{16}H_{18}O_3S$: C, 66.18; H, 6.25. Found: C, 66.3; H, 6.1.

2-Methyl-1-tosyl-2-butanol (2f): ν_{max} (film) 3500 (OH), 1300, and 1140 cm^{-1} (SO_2); δ_H (60 MHz) 0.85 (t, J=7Hz, 3H, CH_3CH_2), 1.25 (s, 3H, CH_3CO), 1.55 (q, J=7Hz, 2H, CH_2CH_3), 2.35 (s, 3H, CH_3Ar), 3.05 (s, 2H, CH_2S), 3.4 (br s, 1H, OH), 7.15, and 7.6 (2d, J=8Hz, 4H, ArH); m/z 242 (M^+, 0.2%), 213 (100), 155 (46), and 91 (33). Anal. Calcd. for $C_{12}H_{18}O_3S$: C, 59.50; H, 7.44. Found: C, 59.1; H, 7.1.

Preparation of γ-Hydroxy Sulfones 6, 8 and Compound 9. General Procedure. To a solution of epoxy sulfone **1** (0.5 mmol) in THF (5 ml) was added a solution of the corresponding Grignard reagent[*] (0.5 mmol, see Table 2) at 0°C. After 30 min stirring at room temperature, the resulting solution was added to a suspension of copper(I) bromide (5 mg) and the corresponding organomagnesium compound[*] (0.75 mmol). After 1 d stirring[**] the reaction mixture was quenched with water and 1N aqueous ammonium chloride solution and extracted with dichloromethane. The organic phase was dried over anhydrous Na_2SO_4 and evaporated *in vacuo* (15 torr). The resulting crude product was purified by column chromatography (hexane/ether) or by recrystallization to afford products **6**. Yields and physical data are reported in Table 2. Spectral and analytical data follow.

2-Methyl-3-tosyl-1-propanol (6a): ν_{max} (film) 3500 (OH), 1290, and 1140 cm^{-1} (SO_2); δ_H (60 MHz, $CDCl_3$) 1.0 (d, J=7Hz, 3H, CH_3CH), 1.7 (m, 1H, $CHCH_3$), 2.45 (s, 3H, CH_3Ar), 2.9 (br s, 1H, OH), 3.1-3.6 (m, 4H, CH_2O and CH_2S), 7.35, and 7.75 (2d, J=8Hz, 4H, ArH); *m/z* 228 (M^+, 5%), 186 (24), 157 (69), 156 (56), 139 (33), 92 (100), 91 (65), and 65 (30). Anal. Calcd. for $C_{11}H_{16}O_3S$: C, 57.90; H, 7.02. Found C, 57.2; H, 6.8.

2-(Tosylmethyl)-3-buten-1-ol (6b): ν_{max} (film) 3500 (OH), 3070, 1640 (CH=C), 1280, and 1140 cm^{-1} (SO_2); δ_H (60 MHz, $CDCl_3$) 2.35 (s, 3H, CH_3Ar), 2.65 (m, 1H, $CHCH_2O$), 3.05 (br s, 1H, OH), 3.1, 3.2 (2d, J=6Hz, 2H, CH_2S), 3.5 (m, 2H, CH_2O), 4.7-5.15 (m, 2H, CH_2=CH), 5.2-5.95 (m, 1H, CH=CH_2), 7.2, and 7.7 (2d, J=8Hz, 4H, ArH); *m/z* 240 (M^+, 0.2 %), 212 (M^+-18, 0.5), 210 (28), 156 (48), 140 (22), 139 (21), 92 (100), 91 (57), and 65 (31).

2-(Tosylmethyl)-4-penten-1-ol (6c): ν_{max} (film) 3500 (OH), 3070, 1630 (CH=C), 1300, and 1140 cm^{-1} (SO_2); δ_H (60 MHz) 1.25 (m, 1H, CHCO), 2.15 (deform t, J=6Hz, 2H, CH_2CH=), 2.4 (s, 3H, CH_3Ar), 2.75-3.4 (m with br s at 3.0, 3H, CH_2S and OH), 3.55 (m, 2H, CH_2O), 4.7-5.2 (m, 2H, CH_2=CH), 5.2-5.95 (m, 1H, CH=CH_2), 7.2, and 7.7 (2d, J=8Hz, 4H, ArH); *m/z* 236 (M^+-18, 2%), 213 (20), 157 (100), 139 (54), 92 (45), 91 (63), 80 (33), and 65 (36). Anal. Calcd. for $C_{13}H_{18}O_3S$: C, 61.39; H, 7.13. Found C, 61.0, H, 6.9.

2-(Tosylmethyl)-1-hexanol (6d): ν_{max} (film) 3480 (OH), 1290, and 1140 cm^{-1} (SO_2); δ_H (60 MHz) 0.85 (deform t, 3H, CH_3CH_2), 1.25 [m, 7H, $(CH_2)_3CH_3$ and $CHCH_2$], 2.4 (s, 3H, CH_3Ar), 2.95 (m, 2H, CH_2O), 3.3 (d, J=6Hz, 2H, CH_2S), 4.1 (br s, 1H, OH), 7.3, and 7.75 (2d, J=8Hz, 4H, ArH); *m/z* 270 (M^+, 0.3 %), 157 (100), 156 (37), 155 (21), 139 (30), 92 (66), 91 (69), and 65 (25). Anal. Calcd. for $C_{14}H_{22}O_3S$: C, 62.19; H, 8.2. Found: C, 61.5; H, 8.5.

2-Phenyl-2-tosyl-1-propanol (6e): ν_{max} (Nujol) 3480 (OH), 1270, and 1130 cm^{-1} (SO_2); δ_H (60 MHz, $CDCl_3$) 2.25 (br s, 1H, OH), 2.4 (s, 3H, CH_3Ar), 3.3 (m, 1H, CHPh), 3.45 (d, J=6Hz, 2H, CH_2S), 3.8 (m, 2H, CH_2O), 6.9-7.4 (m with s at 7.1, 7H, Ph, and 2x*p*-TolH), and 7.6 (d, J=8Hz, 2H, 2x*p*-TolH); *m/z* 290 (M^+, 0.5%), 105 (28), 104 (100), and 91 (59). Anal. Calcd. for $C_{16}H_{18}O_3S$: C, 66.21; H, 6.21. Found: C, 66.4; H, 6.4.

Ethyl 2-(ethoxycarbonyl)-3-(tosylmethyl)-4-hydroxybutanoate (6f): ν_{max} (film) 3500 (OH), 1730 (C=O), 1300, and 1150 cm^{-1} (SO_2); δ_H (60 MHz, $CDCl_3$) 1.3 (t, J=7Hz, 6H, 2xCH_3CH_2), 1.8-2.1 (m, 1H, $CHCH_2$), 2.45 (s, 3H, CH_3Ar), 3.1-3.6 (m, 4H, CH_2S and CH_2OH), 3.9-4.4 (m, with q at 4.15, J=7Hz, 6H, 2xCH_2OC, CHCO, and OH), 7.35, and 7.8 (2d, J=8Hz, 4H, ArH).

(threo/erythro)-**3-Methyl-4-tosyl-2-butanol (6g)**: ν_{max} (film) 3500 (OH), 1290, and 1145 cm^{-1} (SO_2); δ_H (300 MHz, $CDCl_3$) 1.01, 1.07 (2d, J=7Hz, CH_3CH), 1.08, 1.18 (2d, J=6.5Hz, 3H. CH_3CO), 2.05, 2.2 (2m, 1H, $CHCH_2$), 2.45 (s, 3H, CH_3Ar), 2.70 (br s, 1H, OH), 2.85-2.94 (m, 1H, CH_2S), 3.34-3.46 (m, 1H, CH_2S), 3.59, 3.92 (2m, 1H, CHO), 7.38, and 7.81 (2d, J=8Hz, 4H, ArH); δ_C (75 MHz, $CDCl_3$) 14.23, 16.44 (CH_3CH), 18.56, 20.31 (CH_3CO), 21.37 (CH_3Ar), 34.61, 35.86 ($CHCH_2$), 58.58 (CH_2S), 69.06, 70.44 (CO), 127.42, 127.56, 128.94, 129.71, 136.72, and 144.43 (ArC); *m/z* 242 (M^+, 4%), 224 (M^+-18, 6), 201 (34), 200 (32), 183 (70), 182 (22), 158 (56), 157 (34), 156 (66), 139 (20), 92 (100), 91 (56), 65 (29), and 45 (37).

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[*] In the case of compound **6f** sodium diethyl malonate, generated from diethyl malonate and sodium hydride in THF, was used.

[**] In the case of compound **8**, the reaction was quenched with D_2O (200 μl) and stirred for 1 hour.

(threo/erythro)-**3-(Tosylmethyl)-4-penten-2-ol (6h)**: ν_{max} (Nujol) 3500 (OH), 3050, 1630 (CH=C), 1300, and 1140 cm^{-1} (SO_2); δ_H (60 MHz, $CDCl_3$) 1.05, 1.15 (2d, *J*=6Hz, 3H, CH_3CO), 1.8 (m, 1H, CHC=), 2.35 (br s, 1H, OH), 2.45 (s, 3H, CH_3Ar), 3.05-3.45 (m, 2H, CH_2S), 3.5-4.3 (m, 1H, CHO), 4.85-5.25 (m, 2H, CH_2=CH), 5.35-6.05 (m, 1H, CH=CH_2), 7.35, and 7.8 (2d, *J*=8Hz, 4H, ArH); *m/z* 239 (M^+-15, 0.2%), 156 (56), 140 (22), 92 (100), 91 (48), 65 (26), and 45 (31).

(threo/erythro)-**3-(Tosylmethyl)-2-hexanol (6i)**: ν_{max} (film) 3500 (OH), 1300, and 1140 cm^{-1} (SO_2); δ_H (60 MHz) 0.7-1.5 [m, 12H, CH_3CH, CH_3CH_2, and $(CH_2)_3$], 1.9 (m, 1H, $CHCH_2$), 2.35 (s, 3H, CH_3Ar), 2.65-3.55 (m, 3H, CH_2S and OH), 3.9 (m, 1H, CHO), 7.2, and 7.65 (2d, *J*=8Hz, 4H, ArH); *m/z* 269 (M^+-15, 0.5%), 200 (40), 157 (68), 156 (100), 139 (21), 92 (96), 91 (51), 65 (24), and 45 (40).

(threo/erythro)-**3-Phenyl-4-tosyl-2-butanol (6j)**: ν_{max} ($CDCl_3$) 3500 (OH), 1270, and 1130 cm^{-1} (SO_2); for the major diastereoisomer δ_H (300 MHz, $CDCl_3$) 0.96 (d, *J*=7Hz, 3H, CH_3CH), 2.00 (br s, 1H, OH), 2.33 (s, 3H, CH_3Ar), 3.22 (m, 1H, CHPh), 3.40, 3.45 (2dd, *J*=12, 6Hz, 2H, CH_2S), 4.18 (m, 1H, CHO), 6.87-7.20 (m, 7H, Ph and 2x*p*-TolH), and 7.60 (d, *J*=8Hz, 2x*p*-TolH); for the major diastereoisomer δ_C (75 MHz, $CDCl_3$) 20.71 (CH_3CO), 21.48 (CH_3Ar), 46.88 (CHPh), 58.30 (CHO), 68.99 (CH_2S), 126.92, 127.75, 128.27, 128.89, 129.60, 136.60, 137.57, and 144.35 (ArC); *m/z* 304 (M^+, 5%), 105 (29), 104 (100), 91 (29), 65 (38), and 45 (20).

3-Deuterio-2-phenyl-3-tosyl-1-propanol (8): δ_H (300 MHz, $CDCl_3$) 2.10 (br s, 1H, OH), 2.41 (s, 3H, CH_3Ar), 3.41 (m, 2H, CHPh and CHS), 3.80 (dd, *J*=11.5, 5 Hz, 1H, CH_2O), 3.93 (dd, *J*=11.5, 5 Hz, 1H, CH_2O), 7.08-7.30 (m, 7H, Ph and 2x*p*-TolH), 7.68 (d, *J*=8Hz, 2H, 2x*p*-TolH); δ_C (75 MHz, $CDCl_3$) 21.54 (CH_3Ar), 42.8 (CHPh), 58.04 (t, *J*=22.9Hz, CD), 65.81 (CH_2O), 127.27, 127.65, 127.87, 128.76, 129.76, 136.45, 139.65, and 144.56 (ArC); *m/z* 291 (M^+, 2%), 261 (20), 106 (24), 105 (100), 104 (49), 92 (25), 91 (47) and 65 (20).

(cis/trans)-**2-(Ethoxycarbonyl)-3-(tosylmethyl)-γ-butyrolactone (9)**: ν_{max} (film) 1780, 1730 (C=O), 1300, and 1150 cm^{-1} (SO_2); for the major diastereoisomer δ_H (300 MHz, $CDCl_3$) 1.30 (t, *J*=7Hz, CH_3CH_2), 2.47 (s, 3H, CH_3Ar), 3.25-3.52 (m, 4H, CH_2S, $CHCH_2S$, and CHC=O), 4.13, 4.63 (2dd, *J*=7.5, 9.5Hz, 2H, OCH_2CH), 4.24 (q, *J*=7Hz, 2H, OCH_2CH_3), 7.38, and 7.7 (2d, *J*=8Hz, 4H, ArH); for the major diastereoisomer δ_C (75 MHz, $CDCl_3$) 13.84 (CH_3CH_2), 21.51 (CH_3Ar), 34.28 (CH_2CH_3), 50.80 ($CHCH_2$), 57.27 ($CHCO_2$), 62.40 (OCH_2CH), 70.29 (CH_2S), 127.87, 130.09, 135.22, 145.48 (ArC), 166.14 (CO_2CH_2CH), 170.28 ($CO_2CH_2CH_3$); *m/z* 326 (M^+, 11%), 281 (21), 171 (32), 170 (29), 157 (38), 155 (47), 144 (21), 143 (54), 139 (53), 92 (21), 91 (100), and 65 (35). Anal. Calcd. for $C_{15}H_{18}O_6S$: C, 55.21; H, 5.52. Found: C, 55.0; H, 5.8.

Synthesis of β- and γ-Oxo Sulfones 10 and 11, and 12e. General Procedure. To a solution of β- or γ-hydroxy sulfone (0.5 mmol) in dry dichloromethane (5ml) was added pyridinium chlorochromate (215 mg, 1 mmol). The resulting suspension was stirred at room temperature (see Table 3) and then filtered off through a short silica gel column. The filtrate was evaporated *in vacuo* (15 torr) to give compound **10**, **11** or **12e**. Yields and melting points or R_f values are reported in Table 3. Spectral and analytical data follow.

1-Tosyl-2-heptanone (10d): ν_{max} (film) 1710 (C=O), 1310, and 1150 cm^{-1} (SO_2); δ_H (60 MHz) 0.85 (deform t, *J*=7Hz, 3H, CH_3CH_2), 1.25 [m, 6H, $(CH_2)_3CH_3$], 2.35 (s, 3H, CH_3Ar), 2.26 (deform t, *J*=7Hz, 2H, CH_2CO), 3.9 (s, 2H, CH_2S), 7.2, and 7.6 (2d, *J*=8Hz, 4H, ArH); *m/z* 268 (M^+, 1%), 155 (45), 148 (21), 139 (51), 112 (24), 99 (29), 91 (100), 71 (22), and 65 (39). Anal. Calcd. for $C_{14}H_{20}O_3S$: C, 62.69; H, 7.46. Found: C, 62.1; H, 7.3.

3-Phenyl-1-tosyl-2-propanone[16] **(10e)**: ν_{max} (Nujol) 1710 (C=O), 1305, 1290, and 1140 cm^{-1} (SO_2); δ_H (60 MHz, $CDCl_3$) 2.4 (s, 3H, CH_3Ar), 3.95 (s, 2H, CH_2Ph), 4.05 (s, 2H, CH_2S), 7.0-7.4 (m, 7H, Ph and 2x*p*-TolH), and 7.7 (d, *J*=8Hz, 2x*p*-TolH); *m/z* 288 (M^+, 14%), 155 (31), 133 (55), 91 (100), and 65 (36).

2-Methyl-2-tosylpropanal (11a): ν_{max} (film) 1715 (C=O), 1310, and 1150 cm^{-1} (SO_2); δ_H (60 MHz) 1.25 (d, *J*=8Hz, 3H, CH_3CH), 2.4 (s, 3H, CH_3Ar), 2.6-3.7 (m, 3H, CH_2S and $CHCH_3$), 7.3, 7.7 (2d, *J*=8Hz, 4H, ArH), and 9.55 (s, 1H, CHO); *m/z* 226 (M^+, 5%), 156 (27), 150 (23), 139 (21), 119 (25), 92 (78), 91 (91), 89 (20), 65 (50), and 43 (100).

2-(Tosylmethyl)-hexanal (11d): ν_{max} (film) 1710 (C=O), 1300, and 1140 cm^{-1} (SO_2); δ_H (60 MHz) 0.8 (deform t, *J*=7Hz, CH_3CH_2), 1.3 [m, 6H, $(CH_2)_3CH_3$], 2.4 (s, 3H, CH_3Ar), 2.5-3.3 (m, 3H, CH_2S and CHO), 7.25, 7.7 (2d, *J*=8Hz, 4H, ArH), and 9.45 (s, 1H, CHO); *m/z* 268 (M^+, 0.2%), 226 (20), 139 (55), 91 (36), 85 (100), 64 (24), 57 (61), and 55 (29). Anal. Calcd. for $C_{14}H_{20}O_3S$: C, 62.69; H, 7.46. Found: C, 62.5; H, 7.7.

2-Phenyl-2-propenal[17] **(12e)**: ν_{max} (film) 1665 cm^{-1} (C=O); δ_H (60 MHz, CDCl$_3$) 6.05, 6.5 (2s, 2H, CH$_2$), 7.1-7.8 (m, 5H, Ph), and 9.8 (s, 1H, CHO); *m/z* 132 (M^+, 3%), 105 (100), 91 (57), 77 (48), 65 (37), and 51 (21).

3-Methyl-4-tosyl-2-butanone (11g): ν_{max} (film) 1705 (C=O), 1300, and 1140 cm^{-1} (SO$_2$); δ_H (60 MHz) 1.2 (d, *J*=7Hz, 3H, C*H*$_3$CH), 2.15 (s, 3H, CH$_3$CO), 2.45 (s, 3H, C*H*$_3$Ar), 2.6-3.8 (m, 3H, CH$_2$S and CHCO), 7.25, and 7.7 (2d, *J*=8Hz, 4H, ArH); *m/z* 240 (M^+, 1%), 150 (25), 92 (27), 91 (54), 65 (41), and 43 (100).

3-(Tosylmethyl)-4-penten-2-one (11h): ν_{max} (film) 1710 (C=O), 1300, and 1140 cm^{-1} (SO$_2$); δ_H (60 MHz) 2.15 (s, 3H, CH$_3$CO), 2.45 (s, 3H, C*H*$_3$Ar), 2.8-3.2 (m, 1H, CH$_2$S), 3.45-3.9 (m, 2H, CHO and CH$_2$S), 5.0-6.0 (m, 3H, CH$_2$=CH), 7.3, and 7.7 (2d, *J*=8Hz, 4H, ArH); *m/z* 224 (M^+-C$_2$H$_4$, 1%), 92 (34), 91 (46), and 43 (100).

3-(Tosylmethyl)-2-heptanone (11i): ν_{max} (film) 1710 (C=O), 1300, and 1140 cm^{-1} (SO$_2$); δ_H (60 MHz) 0.8 (deform t, *J*=7Hz, 3H, C*H*$_3$CH$_2$), 1.2 [m, 6H, (C*H*$_2$)$_3$CH$_3$], 2.1 (s, 3H, CH$_3$CO), 2.4 (s, 3H, C*H*$_3$Ar), 2.8-3.9 (m, 3H, CHCO and CH$_2$S), 7.25, and 7.7 (2d, *J*=8Hz, 4H, ArH); *m/z* 282 (M^+, 0.2%), 150 (54), 119 (35), 92 (36), 91 (66), 71 (56), 65 (45), 55 (25) and 43 (100). Anal. Calcd. for $C_{15}H_{22}O_3S$: C, 63.83; H, 7.80. Found: C, 63.4; H, 7.7.

3-Phenyl-4-tosyl-2-butanone (11j): ν_{max} (film) 1710 (C=O), 1300, and 1150 cm^{-1} (SO$_2$); δ_H (60 MHz) 2.0 (s, 3H, CH$_3$CO), 2.35 (s, 3H, C*H*$_3$Ar), 3.05 (m, 1H, CH$_2$S), 3.8-4.4 (m, 2H, CHCO and CH$_2$S), 6.85-7.4 (m, 7H, Ph and 2x*p*-TolH), and 7.6 (d, *J*=8Hz, 2H, 2x*p*-TolH; *m/z* 302 (M^+, 0.3%), 163 (32), 105 (24), 104 (100), 91 (57), 65 (24), and 43 (89).

Preparation of α,β-Unsaturated Carbonyl Compounds 12, and Compound 13. General Procedure. A solution of γ-oxo sulfone **11** (0.4 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (93 μl, 0.6 mmol) in THF (4 ml) was stirred at room temperature for 2 hours. To the reaction mixture was added dichloromethane (20 ml) and washed with a 1N aqueous solution of ammoniun chloride. The organic layer was dried over anhydrous Na$_2$SO$_4$ and evaporated *in vacuo* (15 torr) to afford pure compounds **12**. In the case of compound **13** the crude product was purified by column chromatography on silica gel. Yields and melting points or R_f values are reported in Table 4, spectral and analytical data follow.

2-Methylenehexanal[20] **(12d)**: ν_{max} (film) 1630 cm^{-1} (C=O); δ_H (60 MHz) 0.8 (deform t, 3H, CH$_3$), 1.0-2.0 [m, 6H, (C*H*$_2$)$_3$CH$_3$], 5.85, 6.1 (2s, 2H, CH$_2$=C), and 9.5 (s, 1H, CHO).

(Z)-**3-(Tosylmethyl)-3-penten-2-one (13)**: ν_{max} (film) 1660 (C=O), 1300, and 1140 cm^{-1} (SO$_2$); δ_H (60 MHz, CDCl$_3$) 2.0 (d, *J*=7Hz, 3H, C*H*$_3$CH), 2.2 (s, 3H, CH$_3$CO), 2.45 (s, 3H, C*H*$_3$Ar), 4.25 (s, 2H, CH$_2$S), 7.05 (q, *J*=7Hz, 1H, C*H*CH$_3$), 7.25, and 7.7 (2d, *J*=8Hz, 4H, ArH); *m/z* 252 (M^+, 4%), 97 (99), 92 (21), 91 (53), 65 (41), and 43 (100). Anal. Calcd. for $C_{13}H_{16}O_3S$: C, 61.90; H, 6.35. Found: C, 61.3; H, 6.5.

3-Methylene-2-heptanone[21] **(12i)**: ν_{max} (film) 3080, 1620 (CH=C), and 1660 cm^{-1} (C=O); δ_H (60 MHz) 0.9 (deform t, 3H, CH$_3$), 1.3 [m, 6H, (C*H*$_2$)$_3$CH$_3$], 2.25 (s, 3H, CH$_3$CO), 5.7, and 5.9 (2s, 2H, CH$_2$=C); *m/z* 126 (M^+, 32%), 98 (47), 91 (100), 69 (20), and 56 (49).

3-Phenyl-3-buten-2-one (12j): ν_{max} (film) 3050, 3020, 1600, 1490, 770, 700 (CH=C), and 1680 cm^{-1} (C=O); δ_H (60 MHz, CDCl$_3$) 2.3 (s, 3H, CH$_3$), 5.75, 6.0 (2s, 2H, CH$_2$=C), and 7.2 (s, 5H, Ph)[22]; *m/z* 146 (M^+, 24%), 105 (100), 104 (30), 103 (74), 91 (30), 77 (62), and 43 (52).[22]

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