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β,γ-EPOXY SULFONES IN ORGANIC SYNTHESIS. PART 2:[†] PREPARATION OF β,γ-BIFUNCTIONALIZED SULFONES

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Abstract: Heteronucleophiles reagents react with β,γ-epoxy sulfones **1** at the γ-position in the presence of $Ti(OPr^i)_4$ or magnesium halides to afford regioselectively γ-functionalized β-hydroxy sulfones **2**. With soft nucleofiles such as sodium azide, triphenylphosphine, or sodium benzethiolate the reaction takes place in the absence of Lewis acids. In the case of basic reagents such as sodium methoxide or diethylamine the corresponding regioisomers, the β-functionalized γ-hydroxy sulfones **3** were exclusively obtained. The preparation of compounds **3** (R^2=H) was also carried out starting from 3-tosyl-2-propen-1-ol (**4**) by Michael addition of different heteronucleophiles.

The reactivity of β,γ-epoxy sulfones with nucleophilic reagents is based in two types of ring-opening: (a) α-proton abstraction and β-elimination to afford the corresponding allylic alcohol and (b) nucleophilic attack at the γ-position. The first reaction has been widely used in synthesis of cyclic[1] and acyclic[2] α,β-unsaturated carbonyl compounds, and γ-arylsulfonyl allylic alcohols.[3] The second process is the clasic nucleophilic opening of epoxides, which has been only carried out with organomagnesium compounds and copper(I) salts[2,4] to afford β-hydroxy sulfones. Following our studies on the reactivity of β,γ-epoxy sulfones[2,3f] we report here the ring-opening of these compounds by reaction with heteroatomic nucleophiles.

RESULTS AND DISCUSSION

The reaction of β,γ-epoxy sulfones **1** with different heteroatomic nucleophiles gave in general γ-functionalized β-hydroxy sulfones **2** resulting from the attack at the γ-position (Scheme 1 and Table 1). Thus, the ring-opening of epoxy sulfones **1** ocurred in the presence of $Ti(OPr^i)_4$[5] when isopropanol, ammonium thiocyanate, benzenethiol, ethylmagnesium bromide, iodine,[6] and trimethylsilyl cyanide were used

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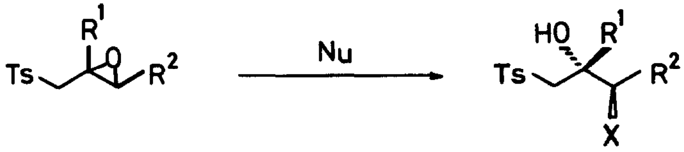
[†]For part 1 see reference 2.

as nucleophiles (Table 1, entries 2, 8-10, 11, 17, 21, and 23, respectively). No reaction was observed with other nucleophiles, such as carboxylic acids or ammonium carboxylates, ammonium chloride, and potassium cyanide in the presence of $Ti(OPr^i)_4$.[5] Magnesium halogenides[7] are the best reagents in order to obtain the corresponding halohydrins **2** (X=Cl, Br, I) under very mild reaction conditions (THF, room temperature; Table 1, entries 15, 16, and 18-20) acting both as Lewis acids and as a source of halogenide anions. Alternatively, $Ti(OPr^i)_4$ can be used when ethylmagnesium bromide or iodine[6] were used for the preparation of bromo or iodohydrins **2ah** or **2ai**.



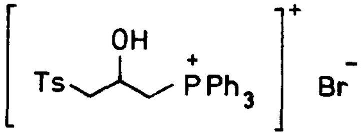
1a, $R^1=R^2=H$
1b, $R^1=Me$, $R^2=H$
1c, $R^1=H$, $R^2=Me$

2

X = OMe, OPr^i, NEt_2, N_3, SCN, SPh, Hal, PPh_3, CN.

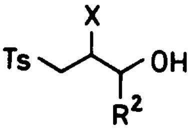
Scheme 1

In the case of soft nucleophiles such as sodium azide, triphenylphosphine,[8] and sodium benzenethiolate, the γ-ring-opening of epoxy sulfones **1** took place in the absence of $Ti(OPr^i)_4$ (Table 1, entries 6 and 7, 22, and 12-14, respectively). The corresponding phosphonium salt was isolated as its bromide **2aj** by treatment of the reaction mixture with concentrated hydrobromic acid.



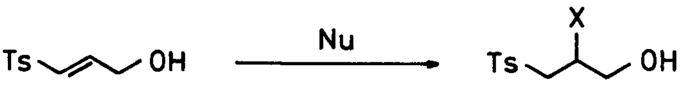
2aj

The regiochemistry of the process was in all cases the corresponding to the attack of the heteronucleophile at the γ-position of the β,γ-epoxy sulfone **1**, except in the reaction of sodium azide with compound **1a**, which afforded a 30% of compound **3ad**. The stereochemistry was studied in the reaction of *trans*-1-methyl-2-(tosylmethyl)oxirane (**1c**)[9] with different nucleophiles in the presence or not of $Ti(OPr^i)_4$ yielding compounds **2** as the corresponding *threo* stereoisomers (Table 1, entries 8, 14, and 19).



3

When more basic reagents were used as nucleophiles the regioisomeric β-functionalized γ-hydroxy sulfones **3** were exclusively obtained. Sodium methoxide gave compound **3aa** and diethylamine compounds **3ac** and **3cc** (Table 1, entries 1 and 3-5) with or without Ti(OPr^i)$_4$. Products **3** should arise from the Michael addition of the nucleophile to the γ-tosylated allylic alcohol formed under the more basic reaction conditions by α-proton abstraction and β-elimination of the epoxy sulfone **1**. This fact was confirmed in the reaction of 3-tosyl-2-propen-1-ol **4** with different nucleophiles such as sodium methoxide, diethylamine, or sodium azide to afford products **3aa**, **3ac**, or **3ad**. Compounds **3ae** and **3af** were also prepared by reaction of allylic alcohol **4** with butylamine and sodium benzenethiolate, respectively (Scheme 2 and Table 2).



4 **3aa-af**

X = OMe, NEt$_2$, N$_3$, NHBu^n, SPh.

Scheme 2

β-Functionalized γ-hydroxy sulfones **3** are adequate precursors for α-functionalized α,β-unsaturated carbonyl compounds by oxidation of the alcohol function followed by *p*-toluenesulfinate elimination.[2,10] On the other hand, compound **3ad** could be a good precursor of 2-boc-amino-3-phenylsulfonyl-1-(2-tetrahydropyranyloxy)propane, used as building block for β,γ-unsaturated α-amino acids.[11]

From the results described in this paper we conclude that β,γ-epoxy sulfones are appropiate starting materials for the synthesis of β- and γ-functionalized γ- and β-hydroxy sulfones, respectively, by reaction with heteronucleophiles.

EXPERIMENTAL

General. For general information see ref. 2. All NMR spectra were recorded on a Bruker AC-300 spectrometer in CDCl$_3$ as solvent. ^{13}C NMR assignments were done on the basis of DEPT experiments.

Table 1. Nucleophilic Opening of β,γ-Epoxy Sulfones.

		Reaction conditions					Product		
Entry	Epoxide	Nu (equiv.)	$Ti(OPr^i)_4$(equiv.)	Solvent	T[a] (°C)	Time	no.	X	Yield,[a] %
1	**1a**	NaOMe (1.5)	0	MeOH	rt	5h	**3aa**	OMe	82
2	**1a**	Pr^iOH (exc.)	1.5	Pr^iOH	reflux	3d	**2ab**	OPr^i	52
3	**1a**	Et_2NH (exc.)	1.5	Et_2NH	rt	1d	**3ac**	NEt_2	60
4	**1a**	Et_2NH (exc.)	0	Et_2NH	reflux	1d	**3ac**	NEt_2	65
5	**1c**	Et_2NH (exc.)	0	Et_2NH	reflux	1d	**3cc**[b]	NEt_2	56
6	**1a**	NaN_3 (5)[c]	0	MeOH[d]	reflux	7h	**2ad**[e]	N_3	80
7	**1b**	NaN_3 (5)[c]	0	MeOH[d]	reflux	6h	**2bd**	N_3	56
8	**1a**	NH_4SCN (1.5)	1.5	THF	rt	15min	**2ae**	SCN	82
9	**1b**	NH_4SCN (1.5)	1.5	THF	rt	30min	**2be**	SCN	75
10	**1c**	NH_4SCN (1.5)	1.5	THF	rt	30min	**2ce**	SCN	80
11	**1a**	PhSH (1.5)	1.5	THF	reflux	1d	**2af**	SPh	86
12	**1a**	NaSPh (1.2)	0	THF	rt	10min	**2af**	SPh	89
13	**1b**	NaSPh (1.2)	0	THF	rt	15min	**2bf**	SPh	82
14	**1c**	NaSPh (1.2)	0	THF	rt	30min	**2cf**	SPh	91
15	**1a**	$MgCl_2$ (1.2)	0	THF	rt	20min	**2ag**	Cl	89
16	**1a**	$MgBr_2$ (1.2)	0	THF	rt	15min	**2ah**	Br	86

Table 1. cont.

17	**1a**	EtMgBr (1.2)	1.5	THF	rt	20min	**2ah**	Br	87
18	**1b**	$MgBr_2$ (1.2)	0	THF	rt	15min	**2bh**	Br	83
19	**1c**	$MgBr_2$ (1.2)	0	THF	rt	15min	**2ch**	Br	75
20	**1a**	MgI_2 (1.2)	0	THF	rt	20min	**2ai**	I	92
21	**1a**	I_2 (1.1)	1.1	CH_2Cl_2	rt	25min	**2ai**	I	93
22	**1a**	PPh_3 (1.0)	0	PhOH	60	4h	**2aj**[f]	PPh_3	74
23	**1a**	Me_3SiCN (3)	1.5	DME	reflux	1d	**2ak**	CN	60

[a] Isolated yield after column chromatography (silica gel), based on the starting epoxide **1**.

[b] *Erythro*/*threo* mixture 1/2.(^{1}H-NMR).

[c] Two equivalents of ammonium chloride were added.

[d] $MeOH/H_2O$: 8/1 (^{1}H-NMR).

[e] Compound **3ad** was also obtained. Regioisomers ratio **2ad**/**3ad** : 7/3.

[f] Isolated as the corresponding phosphonium bromide after treatment of the reaction mixture with conc. hydrobromic acid.

Table 2. Michael Addition of Heteronucleophiles to 3-Tosyl-2-propen-1-ol(**4**).

	Reaction conditions				Product		
Entry	Nu (equiv.)	Solvent	T^a(°C)	Time	no.	X	Yield,^{a}%
1	NaOMe (1.5)	MeOH	rt	4h	**3aa**	OMe	96
2	Et_2NH (exc.)	Et_2NH	reflux	20h	**3ac**	NEt_2	84
3	NaN_3 (2.5)	MeOH	reflux	1d	**3ad**	N_3	80
4	Bu^nNH_2(exc.)	Bu^nNH_2	reflux	6h	**3ae**	$NHBu^n$	91
5	NaSPh (2.5)	THF	rt	3h	**3af**	SPh	70

[a] Isolated yield after column chromatography (silica gel), based on the starting compound **4**.

Nucleophilic Opening of β,γ-Epoxy Sulfones. General Procedure.

a) By means of $Ti(OPr^i)_4$. A solution of the epoxide **1** (0.5 mmol), nucleophile (see Table 1) and titanium(IV) isopropoxide (0.45 ml, 1.5 mmol) in the corresponding solvent (*ca.* 5ml) was stirred under argon at the temperature and for the time shown in Table 1. The resulting mixture was hydrolyzed with a 9% aqueous sulfuric acid solution and extracted with ether (2x10 ml). The organic layer was washed with water, dried over anhydrous Na_2SO_4 and evaporated in vacuo (15 torr). The resulting residue was purified by column chromatography on silica gel (hexane/ether) or/and by recrystallization to afford products **2**.

b) Without $Ti(OPr^i)_4$. The solution of the epoxide **1** (0.5 mmol) and nucleophile[12] in the appropiate solvent (*ca.* 5 ml) was stirred under argon[13] in the conditions shown in Table 1. The reaction mixture was hydrolyzed with water and worked up as above[14] to yield products **2** or/and **3**.

2-Methoxy-3-tosyl-1-propanol (**3aa**): mp 240-241°C (dec., hexane/CH_2Cl_2); ν_{max} ($CDCl_3$) 3490 (OH), 1300, and 1140 cm^{-1} (SO_2); δ_H 2.43 (s, 3H, CH_3Ar), 2.92 (br s, 1H, OH), 3.26 (s, 3H, CH_3O), 3.37 (d, J=5.5Hz, 2H, CH_2O), 3.56 (dd, J=11.6, 4.0Hz, 1H, 1xCH_2S), 3.69-3.82 (m, 2H, CHO and 1xCH_2S), 7.34, and 7.79 (2d, J=8.1Hz, 4H, ArH); δ_C 21.36 (CH_3Ar), 57.06 (CH_3O), 57.40 (CH_2S), 62.28 (CH_2O), 75.99 (CHO), 127.82, 129.59, 136.81, and 144.53 (ArC); *m/z* 213 (M^+-31, 24%), 156 (14), 155 (95), 149 (19), 92 (20), 91 (100), 89 (12), 65 (21), and 59 (23). Anal. Calcd. for $C_{11}H_{16}O_4S$:C,54.08; H,6.60. Found C, 53.75, H, 6.51.

1-Isopropoxy-3-tosyl-2-propanol (**2ab**): R_f 0.6 (hexane/ether:1/10); ν_{max} (film) 3450 (OH), 1250, and 1125 cm^{-1} (SO_2); δ_H 1.09, 1.12 (2d, J=5.6Hz, 6H, 2xCH_3CH), 2.45 (s,3H,CH_3Ar), 3.15 (br s, 1H, OH), 3.30 (d, J=7.5Hz, 1H, 1xCH_2S), 3.31 (d, J=4.0Hz, 1H, 1xCH_2S), 3.45 (d, J=5.1Hz, 2H, CH_2O), 3.56 (m, J=6.1Hz, $CHCH_3$), 4.23 (m, 1H, $CHCH_2$), 7.37, and 7.81 (2d, J=8.1Hz, 4H, ArH); δ_C 21.58, 21.87, 21.90 (3xCH_3), 59.67 (CH_2S), 65.65 (CH_2O), 70.33, 72.34 (2xCHO), 128.00, 129.92, 136.50, and 144.92 (ArC); *m/z* 254 (M^+-18, 1.6%), 199 (19), 157 (12), 156 (23), 155 (43), 92 (71), 91 (100), 89 (16), 65 (45), 63 (17), 49 (16), 43 (37), and 41 (13).

2-Diethylamino-3-tosyl-1-propanol (**3ac**): R_f 0.4 (hexane/ether:1/10); ν_{max} (film) 3400 (OH), 1300, and 1140 cm^{-1} (SO_2); δ_H 0.9 (t, *J*=7.1Hz, 6H, 2xCH_3CH_2), 2.13, 2.17, 2.44, 2.48 (4q, *J*=7.0Hz, 4H, 2xCH_2N), 2.38 (s, 3H, CH_3Ar), 2.70-2.85 (m with dd at 2.81, *J*=14.0, 9.0Hz, 2H, CHN and 1xCH_2S), 3.16 (dd, *J*=14.0, 1.7Hz, 1H, 1xCH_2S), 3.27-3.57 (m, 2H, 1xCH_2O and OH), 3.57 (d, *J*=5.0Hz, 1H, 1xCH_2O), 7.30, and 7.72 (2d, *J*=8.2Hz, 4H, ArH); δ_C 13.99 (CH_3CH_2), 21.56 (CH_3Ar), 43.22 (CH_2N), 53.27 (CHN), 55.53 (CH_2S), 61.14 (CH_2O), 127.85, 130.02, 136.39, and 144.95 (ArC); *m/z* 285 (M^+, 0.2%), 254 (56), 116 (18), 114 (100), 100 (21), 99 (100), 92 (12), 91 (78), 86 (18), 84 (66), 72 (28), 71 (93), 70 (56), 65 (55), 58 (31), 57 (20), 56 (93), 44 (24), 43 (14), and 42 (55).

(threo/erythro)-*3-Diethylamino-4-tosyl-2-butanol* (**3cc**): R_f 0.5 (hexane/ether:1/10); ν_{max} (film) 3450 (OH), 1300, and 1140 cm^{-1} (SO_2); δ_H 0.96, 1.07 (2t, *J*=7.1Hz, 6H, 2xCH_3CH_2), 1.14, 1.28 (2d, *J*=6.0Hz, 3H, CH_3CH), 2.20-2.60 (m with s at 2.45, 8H, 2xCH_2CH_3, OH, and CH_3Ar), 2.84-3.75 (6m, 4H, CH_2S, CHN, and CHO), 7.36, and 7.80 (2d, *J*=8.1Hz, 4H, ArH); δ_C 14.40 (CH_3CH_2), 18.76 (CH_3CO), 21.53 (CH_3Ar), 44.21 (CH_2N), 53.52 (CHN), 60.39 (CH_2S), 66.24 (CHO), 127.65, 129.84, 136.92, and 144.82 (ArC); *m/z* 299 (M^+, 0.4%), 255 (15), 254 (100), 114 (34), 99 (21), 91 (14), and 84 (10).

3-Azido-1-tosyl-2-propanol (**2ad**) and *2-azido-3-tosyl-1-propanol* (**3ad**): R_f 0.5 (hexane/ether:1/10); ν_{max} (film) 3500 (OH), 2100 (N_3), 1290, and 1140 cm^{-1} (SO_2); δ_H (for **2ad**) 2.45 (s, 3H, CH_3), 3.20-3.43 (m, 5H, CH_2S, CH_2N, and OH), 4.32 (m, 1H, CHO), 7.37, and 7.80 (2d, *J*=8.1Hz, 4H, ArH); δ_C (for **2ad**) 21.53 (CH_3), 55.23 (CH_2N), 59.48 (CH_2S), 65.58 (CHO), 127.82, 130.07, 135.92, and 145.35 (ArC); *m/z* 199 (M^+-56, 19%), 155 (43), 92 (30), 91 (100), 89 (12), 65 (38), 63 (12), 44 (11), and 43 (18).

3-Azido-2-methyl-1-tosyl-2-propanol (**2bd**): R_f 0.5 (hexane/ether:1/5); ν_{max} (film) 3500 (OH), 2110 (N_3), 1300, and 1150 cm^{-1} (SO_2); δ_H 1.45 (s, 3H, CH_3CO), 2.45 (s, 3H, CH_3Ar), 3.26, 3.40 (2d, *J*=14.2Hz, 2H, CH_2S), 3.39, 3.48 (2d, *J*=12.4Hz, 2H, CH_2N), 3.87 (br s, 1H, OH), 7.37, and 7.80 (2d, *J*=8.1Hz, 4H, ArH); δ_C 21.43 (CH_3Ar), 25.31 (CH_3CO), 59.57 (CH_2S), 62.22 (CH_2N), 72.18 (CO), 127.43, 129.90, 137.57, and 145.07 (ArC); *m/z* 213 (M^+-56, 66%), 157 (10), 155 (60), 139 (14), 105 (12), 92 (15), 91 (100), 89 (14), 77 (12), 65 (39), and 43 (23).

(2-Hydroxy-3-tosyl)propyl thiocyanate (**2ae**)[15]: R_f 0.45 (hexane/ether:1/10); ν_{max} (film) 3440 (OH), 2140 (SCN), 1290, and 1135 cm^{-1} (SO_2); δ_H 2.44 (s, 3H, CH_3), 3.02 (dd, *J*=13.5, 7.0Hz, 1H, 1xCH_2SCN), 3.18 (dd, *J*=13.5, 4.0Hz, 1H, 1xCH_2S), 3.38-3.43 (m, 2H, CH_2SO_2), 4.10 (br s, 1H, OH), 4.48 (m, 1H, CHO), 7.37, and 7.80 (2d, *J*=8.0Hz, 4H, ArH); δ_C 21.48 (CH_3), 39.47 (CH_2SCN), 60.09 (CH_2SO_2), 65.12 (CHO), 112.24 (SCN), 127.78, 130.06, 135.72, and 145.42 (ArC); *m/z* 271 (M^+, 0.5%), 199 (14), 155 (47), 139 (17), 92 (21), 91 (100), 89 (18), 77 (10), 73 (23), 72 (16), 65 (41), 63 (17), 46 (15), and 45 (28).

(2-Hydroxy-2-methyl-3-tosyl)propyl thiocyanate (**2be**):[15] R_f 0.4 (hexane/ether:1/10); ν_{max} (film) 3480 (OH), 2140 (SCN), 1300, and 1150 cm^{-1} (SO_2); δ_H 1.52 (s, 3H, CH_3CO), 2.46 (s, 3H, CH_3Ar), 2.60 (s, 2H, CH_2SCN), 3.04, 3.51 (2d, *J*=14.1Hz, 2H, CH_2SO_2), 3.40 (br s, 1H, OH), 7.37, and 7.79 (2d, *J*=8.0Hz, 4H, ArH); δ_C 21.33, 21.57 (2xCH_3), 51.97, 52.88 (2xCH_2), 63.68 (CO), 112.75 (SCN), 127.96, 129.93, 136.86, and 145.05 (ArC); *m/z* 270 (M^+-15, 0.1%), 213 (46), 155 (51), 139 (16), 105 (14), 92 (19), 91 (100), 89 (20), 87 (38), 77 (12), 65 (53), 63 (16), 59 (12), 53 (11), 46 (13), 45 (24), and 43 (21).

(threo)-*(2-Hydroxy-1-methyl-3-tosyl)propyl thiocyanate* (**2ce**):[15] R_f 0.3 (hexane/ether:1/10); ν_{max} (film) 3520 (OH), 2130 (SCN), 1290, and 1130 cm^{-1} (SO_2); δ_H 1.49 (d, *J*=6.9Hz, 3H, CH_3CH), 2.47 (s, 3H, CH_3Ar), 3.34 (d, *J*=5.6Hz, 2H, CH_2S), 3.45 (m, 1H, CHSCN), 3.58 (br s, 1H, OH), 4.37 (m, 1H, CHO), 7.41, and 7.82 (2d, *J*=8.0Hz, 4H, ArH); δ_C 16.03 (CH_3CH), 21.84 (CH_3Ar), 48.52 (CHSCN), 53.39 (CH_2SO_2), 68.67 (CHO), 110.74 (SCN), 127.78, 130.07, 135.65, and 145.42 (ArC); *m/z* 286 (M^++1, 1%), 285 (M^+, 4), 199 (81), 157 (11), 156 (11), 155 (97), 139 (15), 112 (10), 92 (23), 91 (100), 89 (15), 87 (19), 65 (40), and 59 (12).

1-Phenylthio-3-tosyl-2-propanol (**2af**): mp 111-112°C (hexane/CH_2Cl_2); ν_{max} ($CHCl_3$) 3500(OH), 1300, and 1150 cm^{-1} (SO_2); δ_H 2.33 (s, 3H, CH_3), 2.88 (dd, *J*=14.0, 6.6Hz, 1H, 1xCH_2SPh), 2.99 (dd, *J*=14.0, 6.0Hz, 1H, 1xCH_2SPh), 3.19 (dd, J=14.4, 8.6Hz, 1H, 1xCH_2SO_2), 3.31 (br s, 1H, OH), 3.41 (dd, J=14.4, 2.6Hz, 1H, 1xCH_2SO_2), 4.04 (m, 1H, CHO), 7.10-7.25 (m with d at 7.21, J=8.2Hz, 7H, Ph and 2x*p*-TolH), and 7.64 (d, J=8.2Hz, 2H, *p*-TolH); δ_C 21.47 (CH_3), 39.91 (CH_2SPh), 60.56 (CH_2SO_2), 65.05 (CHO), 126.73, 127.80, 128.90, 128.92, 130.19, 134.17, 135.87, and 144.89 (ArC); *m/z* 322 (M^+, 9%), 155 (21), 149 (90), 124 (16), 123 (45), 116 (11), 109 (15), 92 (10), 91 (100), 89 (13), 79 (13), 77 (31), and 65 (57). Anal. Calcd. for $C_{16}H_{18}O_3S_2$: C, 59.60; H, 5.63. Found: C, 60.04; H, 5.67.

1-Phenylthio-2-methyl-3-tosyl-2-propanol (**2bf**): R_f 0.5 (hexane/ether:1/10); ν_{max} (film) 3480 (OH), 1300, and 1140 cm^{-1} (SO_2); δ_H 1.48 (s, 3H, CH_3CO), 2.39 (s, 3H, CH_3Ar), 3.29 (d, J=3.8Hz, 2H, CH_2SPh), 3.37, 3.50 (2d, J=14.3Hz, 2H, CH_2SO_2), 3.86 (s, 1H, OH), 7.15-7.36 (m with d at 7.28, J=8.2Hz, Ph and 2x*p*-TolH), and 7.73 (d, J=8.2Hz, 2H, 2x*p*-TolH); δ_C 21.35 (CH_3Ar), 26.82 (CH_3CO), 45.70 (CH_2SPh), 63.29 (CH_2SO_2), 72.38 (CO), 126.18, 127.34, 128.76, 129.43, 129.69, 135.99, 137.59, and 144.68 (ArC); *m/z* 338 (M^++2, 1%), 337 (M^++1, 1), 336 (M^+, 7), 213 (84), 163 (17), 155 (77), 139 (10), 125 (10), 124 (100), 123 (36), 91 (84), 77 (19), and 65 (26).

(threo)-*3-Phenylthio-1-tosyl-2-butanol* (**2cf**): mp 86-87°C(hexane/ether); ν_{max} ($CDCl_3$) 3500 (OH), 1290, and 1130 cm^{-1} (SO_2); δ_H 1.17 (d, J=7.0Hz, 3H, CH_3CH), 2.34 (s, 3H, CH_3Ar), 3.22 (m, 1H, CHSPh), 3.30 (dd, J=14.4, 8.9Hz, 1H, 1xCH_2S), 3.40 (d, J=2.6Hz, 1H, OH), 3.52 (dd, J=14.4, 2.3Hz, 1H, 1xCH_2S), 4.06 (m, 1H, CHO), 7.14-7.40 (m with d at 7.22, J=8.1Hz,7H,Ph and 2x*p*-TolH), and 7.65 (d, J=8.1Hz, 2H, *p*-TolH); δ_C 15.40 (CH_3CS), 21.49 (CH_3Ar), 48.17 (CHS), 59.78 (CH_2S), 67.93 (CHO), 127.53, 127.86, 128.88, 129.86, 132.71, 135.93, and 144.88 (ArC); *m/z* 338 (M^++2, 1%), 337 (M^++1, 1), 336 (M^+, 6), 163 (31), 155 (13), 138 (15), 137 (100), 135 (17), 109 (23), 91 (39), and 65 (18). Anal. Calcd. for $C_{17}H_{20}O_3S_2$: C, 60.68; H, 5.99. Found: C, 60.31; H, 5.87.

3-Chloro-1-tosyl-2-propanol (**2ag**): mp 69-70°C (hexane/ether); ν_{max} ($CDCl_3$) 3480 (OH), 1290, and 1135 cm^{-1} (SO_2); δ_H 2.37 (s, 3H, CH_3), 3.20-3.31 (m, 2H, CH_2S), 3.53 (d, J=4.9Hz, 2H, CH_2Cl), 3.80 (br s, 1H, OH), 4.30 (m, 1H, CHO), 7.29, and 7.73 (2d, J=7.8Hz, 4H, ArH); δ_C 21.51 (CH_3), 47.56 (CH_2Cl), 59.51 (CH_2S), 66.10 (CHO), 127.85, 130.00, 135.99, and 145.25 (ArC); *m/z* 250 (M^++2, 1%), 248 (M^+, 2), 199 (42), 157 (10), 155 (81), 139 (11), 92 (71), 91 (100), 89 (10), and 65 (24). Anal. Calcd. for $C_{10}H_{13}ClO_3S$: C, 48.30; H, 5.27. Found: C, 48.56; H, 5.48.

3-Bromo-1-tosyl-2-propanol (**2ah**): mp 67-68°C (hexane/ether); ν_{max} ($CDCl_3$) 3450 (OH), 1300, and 1140 cm^{-1} (SO_2); δ_H 2.44 (s, 3H, CH_3), 3.30-3.55 (m, 5H, CH_2S, CH_2Br, and OH), 4.35 (m, 1H, CHO), 7.37, 7.81 (2d, J=8.0Hz, 4H,ArH); δ_C 21.49 (CH_3), 36.6 (CH_2Br), 60.29 (CH_2S), 65.55 (CHO), 127.81, 129.95, 135.95, and 145.18 (ArC); *m/z* 294 (M^++2, 1%), 292 (M^+, 1), 199 (31), 155 (39), 139 (21), 105 (13), 92 (73), 91 (100), 89 (18), 77 (12), 65 (53), 57 (10), and 43 (17). Anal. Calcd. for $C_{10}H_{13}BrO_3S$: C, 40.96; H, 4.44. Found: C, 41.36; H, 4.57.

3-Bromo-2-methyl-1-tosyl-2-propanol (**2bh**): R_f 0.45 (hexane/ether:1/5); ν_{max} (film) 3460 (OH), 1300, and 1140 cm^{-1} (SO_2); δ_H 1.48 (s, 3H, CH_3CO), 2.37 (s, 3H, CH_3Ar), 3.22, 3.45 (2d, J=14.3Hz, 2H, CH_2S), 3.49, 3.55 (2d, J=10.0Hz, 2H, CH_2Br), 3.77 (br s, 1H, OH), 7.29, and 7.73 (2d, J=8.1Hz, 4H, ArH); δ_C 21.51 (CH_3Ar), 26.09 (CH_3CO), 41.43 (CH_2Br), 62.43 (CH_2S), 71.27 (CO), 127.55, 129.94, 137.56, and 145.08 (ArC); *m/z* 308 (M^++2, 0.7%), 306 (M^+, 0.8), 214 (11), 213 (100), 155 (46), 139 (10), 105 (10), 92 (11), 91 (42), and 65 (17).

(threo)-*3-Bromo-1-tosyl-2-butanol* (**2ch**): mp 75-76°C (hexane/ether); ν_{max} ($CDCl_3$) 3460 (OH), 1300, and 1140 cm^{-1} (SO_2); δ_H 1.65 (d, J=7.0Hz, 3H, CH_3CH), 2.45 (s,3H, CH_3Ar), 3.33 (dd, J=14.4, 8.8Hz, 1H, 1xCH_2S), 3.50 (dd, J=14.4, 1.7Hz, 1H, 1xCH_2S), 3.64 (d, J=3.8Hz, 1H, OH), 4.16 (m, 2H, CHO and CHBr), 7.38, and 7.82 (2d, J=8.1Hz, 4H, ArH); δ_C 21.00 (CH_3CH), 21.49 (CH_3Ar), 52.15 (CHBr), 59.62 (CH_2), 70.16 (CHO), 127.83, 129.93, 135.98, and 145.12 (ArC); *m/z* 308 (M^++2, 0.3%), 306 (M^+, 0.4), 200 (10), 199 (97), 157 (12), 156 (10), 155 (99), 139 (16), 107 (13), 105 (11), 92 (41), 91 (100), 89 (15), 65 (45), 63 (14), and 43 (15). Anal. Calcd. for $C_{11}H_{15}BrO_3S$: C, 43.01; H, 4.92. Found: C, 43.00; H, 5.10.

3-Iodo-1-tosyl-2-propanol (**2ai**): mp 115-116°C (hexane/CH_2Cl_2); ν_{max} ($CDCl_3$) 3480 (OH), 1300, and 1140 cm^{-1} (SO_2); δ_H 2.45 (s, 3H, CH_3), 3.28-3.42 (m, 5H, CH_2I, CH_2S, and OH), 4.09 (m, 1H, CHO), 7.38, and 7.81 (2d, J=8.0Hz, 4H, ArH); δ_C 11.31 (CH_2I), 21.53 (CH_3), 61.75 (CH_2S), 65.34 (CHO), 127.82, 129.96, 135.92, and 145.17 (ArC); *m/z* 340(M^+, 0.2%), 213 (49), 195 (26), 167 (16), 155 (53), 141 (11), 139 (86), 92 (19), 91 (100), 65 (32), and 63 (11). Anal. Calcd. for $C_{11}H_{15}IO_3S$: C, 35.31; H, 3.85. Found: C, 36.00; H, 3.80.

[(2-Hydroxy-3-tosyl)propyl]triphenylphosphonium bromide (**2aj**): mp 127-128°C (hexane/CH_2Cl_2); ν_{max} (Nujol) 3450 (OH), 1275, and 1130 cm^{-1} (SO_2); δ_H 2.39 (s, 3H, CH_3), 3.76 (dt, J_{gem}=14.1Hz, J_{P-H}=4.0Hz, 1H, 1xCH_2P), 3.92 (dd, J=14.1, 13.4Hz, 1H, CH_2S), 4.18 (dd, J=14.1, 8.2Hz, 1H, CH_2S), 4.50-4.70 (m, 2H, CHO and 1xCH_2P), 7.29 (d, J=8.0Hz, 2H, 2x*p*-TolH), 7.60-7.85 (m,18H,3xPh, 2x*p*-TolH, and OH); δ_P 58.99; δ_C 21.55 (CH_3), 30.60 (d, J=53.0Hz,CH_2P), 61.52 (d, J=14.9Hz, CH_2S), 61.83 (d, J=4.7Hz, CHO), 118.32 (d, J=86.3Hz, C_i, Ph), 127.73, 129.92, 136.09, 144.98 (*p*-TolC), 130.19 (d, J=12.7Hz, C_m, Ph), 133.96 (d, J=10.3Hz, C_o, Ph), and 134.90 (d, J=3.0Hz, C_p, Ph); *m/z* 386 (M^+-169, 5%), 278 (36), 277 (94), 201 (15), 199 (18), 183 (19), 155 (45), 152 (12), 139 (11), 132 (10), 92 (15), 91 (100), 89 (10), 77 (27), 65 (27), and 51 (18). Anal. Calcd. for $C_{28}H_{28}BrO_3PS$: C, 60.54; H, 5.08. Found: C, 59.98; H, 5.08.

2-Hydroxy-3-tosylbutanenitrile (**2ak**): mp 100-101°C (hexane/ether); ν_{max} (Nujol) 3400 (OH), 2240 (CN), 1275, and 1135 cm^{-1} (SO_2); δ_H 2.47 (s,3H, CH_3), 2.64 (dd, J=16.9, 5.9Hz, 1H, 1xCH_2CN), 2.72 (dd, J=16.9, 5.6Hz, 1H, 1xCH_2CN), 3.31 (dd, J=14.1, 3.4Hz, 1H, 1xCH_2S), 3.39 (dd, J=14.1, 8.3Hz, 1H, 1xCH_2S), 3.88 (br s, 1H, OH), 4.48 (m, 1H, CHO), 7.40, and 7.81 (2d, J=8.2Hz, 4H, ArH); δ_C 21.63 (CH_3), 25.36 (CH_2CN), 60.68 (CH_2S), 62.50 (CHO), 116.18 (CN), 127.94, 130.27, 135.69, and 145.75 (ArC); *m/z* 239 (M^+, 3%), 172 (10), 155 (46), 92 (42), 91 (100), 86 (11), 84 (21), and 65 (23). Anal. Calcd. for $C_{11}H_{13}NO_3S$: C, 55.21; H, 5.48; N, 5.85. Found: C, 54.91; H, 5.40; N, 5.81.

Michael addition of nucleophiles to 3-tosyl-2-propen-1-ol (4). General procedure. A solution of compound **4** (106 mg, 0.5 mmol) and the nucleophile (see Table 2) in the corresponding solvent (5 ml) was stirred at the temperature indicated in Table 2. The reaction mixture was treated with water and extracted with ether (2x10 ml). The organic layer was dried (Na_2SO_4) and concentrated in vacuo (15 and 0.1 torr) to give crude products **3**, which were purified by column chromatography (silica gel, hexane/ether) or/and by recrystallization.

2-Azido-3-tosyl-1-propanol (**3ad**): R_f 0.5 (hexane/ether: 1/10); ν_{max} (film) 3500 (OH), 2140 (N_3), 1290, and 1130 cm^{-1} (SO_2); δ_H 2.46 (s, 3, CH_3), 3.02 (s, 1H, OH), 3.25 (dd, J=14.6, 7.8Hz, 1H, 1xCH_2S), 3.37 (dd, J=14.6, 4.4, 1H, 1xCH_2S), 3.73, 3.74 (2d, J=5Hz, 2H, CH_2O), 3.96 (m, 1H, CHN), 7.37, and 7.80 (2d, J=8.1Hz, 4H, ArH); δ_C 21.61 (CH_3), 56.62 (CH_2S), 57.94 (CHN), 64.10 (CH_2O), 127.94, 130.04, 136.24, and 145.16 (ArC); *m/z* 227 (M^+-28, 0.3%), 212 (M^+-43, 2), 156 (10), 155 (25), 139 (36), 133 (40), 132 (16), 105 (24), 92 (28), 91 (100), 89 (10), 77 (10), and 65 (30).

2-Butylamino-3-tosyl-1-propanol (**3ae**): mp 73-74°C (hexane/ether); ν_{max} ($CDCl_3$) 3500 (OH), 1300, and 1145 cm^{-1} (SO_2); δ_H 0.81 (t, J=7.0Hz, 3H, CH_3CH_2), 1.27 (m, 4H, $CH_2CH_2CH_3$), 2.36 (s, 3H, CH_3Ar), 2.44 (t, J=6.6Hz, 2H, CH_2N), 2.59 (br s, 2H, NH and OH), 3.08 (m, 1H, CHN), 3.14 (m, 2H, CH_2S), 3.37, 3.60 (2dd, J=11.1, 4.1Hz, 2H, CH_2O), 7.28, and 7.71 (2d, J=8.0Hz, 4H, ArH); δ_C 13.73 (CH_3CH_2), 20.13 (CH_2CH_3), 21.42 (CH_3Ar), 31.94 (CH_2CH_2N), 46.27 (CH_2N), 54.26 (CHN), 57.41 (CH_2S), 63.32 (CH_2O), 127.65, 129.84, 136.4, and 144.78 (ArC); *m/z* 255 (M^+-30, 15%), 254 (100), 155 (15), 139 (25), 114 (18), 91 (93), 89 (13), 84 (18), 65 (36), 57 (19), and 56 (48). Anal. Calcd. for $C_{14}H_{23}NO_3S$: C, 58.92; H, 8.12; N, 4.91. Found: C, 59.29; H, 8.02; N, 4.85.

2-Phenylthio-3-tosyl-1-propanol (**3af**): R_f 0.45 (hexane/ether: 1/10); ν_{max} (film) 3500 (OH), 1300, and 1140 cm^{-1} (SO_2); δ_H 2.42 (s, 4H, CH_3 and OH), 3.30 (dd, J=14.1, 3.5Hz, 1H, 1xCH_2SO_2), 3.54 (dd, J=14.1, 8.5Hz, 1H, 1xCH_2SO_2), 3.63 (m, 1H, CHS), 3.84 (m, 2H, CH_2O), 7.20-7.32 (m, 7H, Ph and 2x*p*-TolH), and 7.72 (d, J=8.2Hz, 2H, 2x*p*-TolH); δ_C 21.55 (CH_3), 45.13 (CHS), 57.16 (CH_2S), 62.82 (CH_2O), 127.89, 128.02, 129.20, 129.94, 131.87, 132.66, 135.97, and 144.99 (ArC); *m/z* 324 (M^++2, 1%), 323

(M^++1, 2), 322 (M^+, 12), 167 (24), 166 (35), 155 (18), 149 (22), 137 (11), 136 (62), 135 (52), 122 (100), 110 (14), 109 (27), 91 (64), 77 (13), and 65 (33).

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12. Sodium thiophenolate was prepared from thiophenol and sodium methoxide, and magnesium iodide from magnesium and iodine in THF.
13. Except when sodium azide, diethylamine, and triphenylphosphine were used as nucleophiles.
14. In the case of the reaction with triphenylphosphine (Table 1, entry 22) 48% hydrobromic acid (1 mmol) was added and after 1 h stirring the reaction mixture was diluted with water.
15. Decomposed on standing.