Rapid Asymmetric Access to β-Hydroxysulfinic Acids and Allylsulfonic Acids by Chemoselective Reduction of β-Sultones

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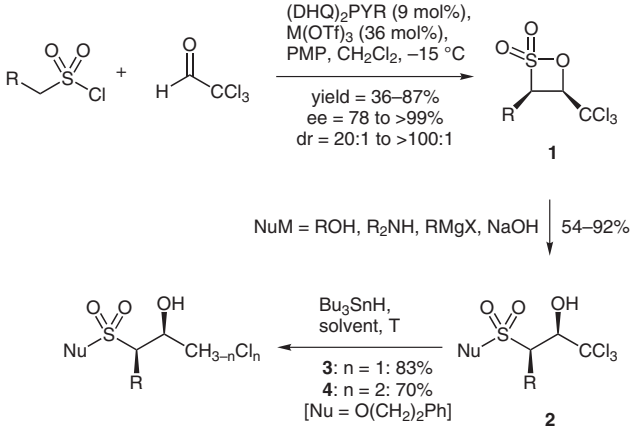
Abstract: The reduction of readily available optically active β-sultones bearing a β-trichloromethyl substituent proceeds chemoselectively at three different sites via C–Cl, C–O or S–O bond cleavage and allows for the formation of highly enantioenriched β-hydroxysulfinic acids and allylsulfonic acids.

Key words: reduction, sulfinic acid, sulfonic acid, sultine, sultone

Functionalized enantiopure molecules are attractive synthetic building blocks for the preparation of chemical libraries, if they are readily accessible and if reliable and generally applicable methods exist for their transformation into diverse compound classes using defined chemoselective reaction pathways occurring without racemization or epimerization.

As part of our program directed towards the development of catalytic asymmetric methodologies providing chiral sulfur containing building blocks, we have recently reported the first enantioselective synthesis of β-sultones **1**, the sulfonyl analogues of β-lactones.[1] A [2+2]-cyclocondensation of sulfonyl chlorides and electron-poor aldehydes such as chloral provides the strained four-membered rings in a highly enantio- and *syn*-selective process, which is catalyzed by a Lewis base–Lewis acid combination of the dimeric cinchona alkaloid derivative $(DHQ)_2PYR$ (dihydroquinine-2,5-diphenyl-4,6-pyrimidinediyl diether) and either $Bi(OTf)_3$ or $In(OTf)_3$ (Scheme 1). We demonstrated that enantioenriched β-sultones are attractive building blocks since regioselective nucleophilic ring opening with hydroxide, alcohol, amine or Grignard reagents provided almost enantio- and diastereomerically pure β-hydroxysulfonic acids, sulfonates, sulfonamides or sulfones **2** in a divergent manner. Moreover, a trichloromethyl group at the β-position could be utilized to introduce additional functionalities. Depending upon the reaction conditions, either mono or dichloro derivatives **3** and **4**, respectively, could be selectively formed by dechlorination.

In this letter we describe that β-sultones **1** can be chemoselectively reduced at three different reaction sites. In addition to partial dechlorination one can either reduce the cyclic sulfonic esters to provide β-hydroxysulfinic acids by S–O bond cleavage or generate allylsulfonic acids by C–O bond fission, in both cases taking advantage from the high ring strain of the four-membered heterocycle.



Scheme 1 Catalytic asymmetric synthesis of β-sultones **1** and further conversion into β-hydroxysulfonic acids, esters, amides or sulfones **2**

Sulfinic acid derivatives are of fundamental importance in asymmetric synthesis[2] and are very versatile synthetic intermediates.[3] Chiral sulfinate esters have, for example, been intensively used as the primary source for chiral sulfoxides.[4] Moreover, they have elicited interest in medicinal chemistry.[5] Homochiral β-hydroxysulfinic acids were recently reported by AstraZeneca as potent drug candidates for the treatment of reflux disease.[6]

We found that exposure of *syn*-configured α,β-disubstituted β-sultones **1** to $LiAlH_4$ in Et_2O at ambient temperature provides β-hydroxysulfinic acids **5** within a few minutes in good yield and without epimerization (Table 1).[7]

To evade overreduction to the corresponding thiol, a large excess of the hydride source and extended reaction times had to be avoided. The free acids were obtained by purification with an ion-exchange resin. Although sulfinic acids have been reported to be unstable even in the absence of oxygen due to disproportionation, the here reported β-hydroxysulfinic acids **5** are remarkably stable and do not have to be stored as a salt. After several months at –18 °C under N_2 the material was basically unchanged.

The reduction conditions were also compatible with a 2-chloroethyl substituent at the α-position. Sulfinic acid **5d** could either be isolated after acidic workup or cyclized to

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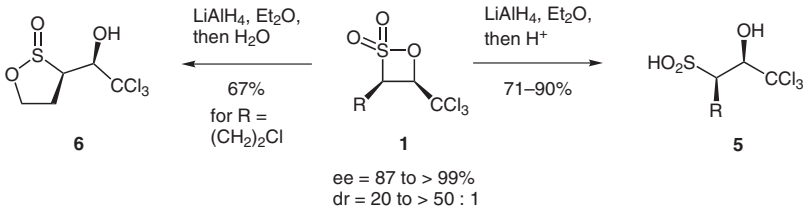
Table 1 Chemoselective Reduction of β-Sultones **1** with $LiAlH_4$



Entry	5	R	Yield (%)[a]	dr[b]
1	**5a**	Me	73	20:1
2	**5b**	Et	90	>50:1
3	**5c**	*n*-Pr	77	>50:1
4	**5d**	$(CH_2)_2Cl$	71	>50:1
5	**5e**	Bn	86	>50:1

[a] Isolated yield.
[b] Determined by ^1H NMR.

γ-sultine **6** by quenching with water. To our knowledge this is the first reported example for the formation of a γ-sultine by nucleophilic displacement of a halide with a sulfinate oxygen.[8] γ-Sultines were recently reported as a new class of flavor compounds. 3-Propyl-γ-sultine was, for example, identified in the extracts of the yellow passion fruit as enantiomerically pure epimeric mixture with respect to the configuration at S.[9] In our case a 2.9:1 diastereomeric mixture was formed, which was separable by column chromatography. In the major epimer the S=O bond adopts the axial position as determined by X-ray crystal structure analysis (Figure 1).[10,11] The five-membered ring adopts a distorted envelope conformation in the solid state and the hydroxyl units form intermolecular rather than intramolecular hydrogen bonds with the sulfinyl moieties.[12]

If the reduction of β-sultones **1** was performed under hydrogenation conditions using a catalytic amount of Pd/C (2 mol%) in EtOH [$p(H_2)$ = 1 atm], dichloroallylsulfonic acids **7** were obtained without significant racemization of the remaining stereocenter (Table 2). Only few enantioselective methods for the synthesis of α-substituted sulfonic acids have been reported so far,[13] although enantiomerically pure sulfonic acid derivatives often display interesting biological activities.[14] While chloroethyl-substituted acid **7d** was formed in 80% yield (entry 4), all the other examples proceeded in high yield. Further dechlorination, hydrogenation or isomerization of the generated C=C double bond were much slower under the described reaction conditions than the initial reaction.

Two mechanistic scenarios might account for the product formation which are depicted in Scheme 2: the reaction could either proceed by oxidative addition of Pd(0) to the trichloromethyl group followed by β-elimination (path A) or alternatively oxidative addition might involve the four-membered ring system providing an oxypalladacycle intermediate (path B). In both cases Pd(II) would be formed

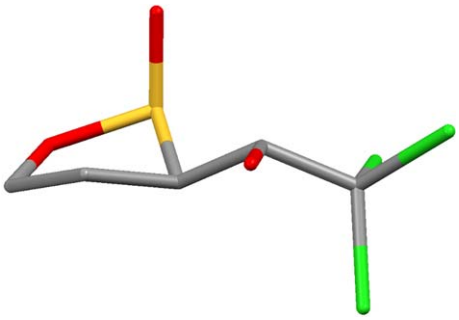
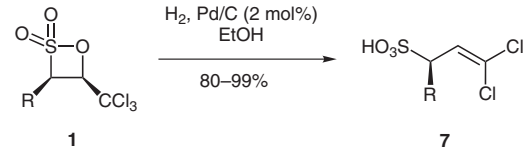


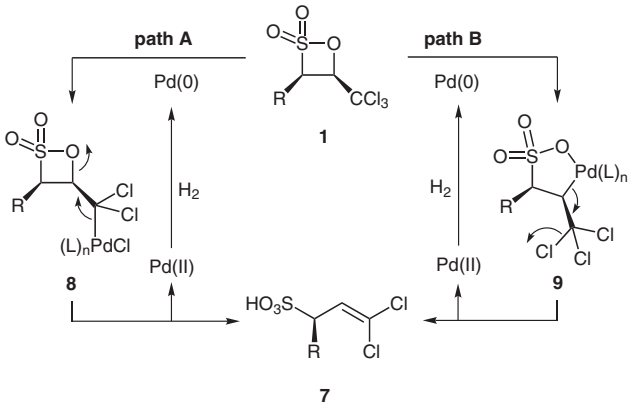
Figure 1 X-ray crystal structure of the major γ-sultine isomer **6** with an axial S=O group

Table 2 Chemoselective Hydrogenation of β-Sultones **1**[7]

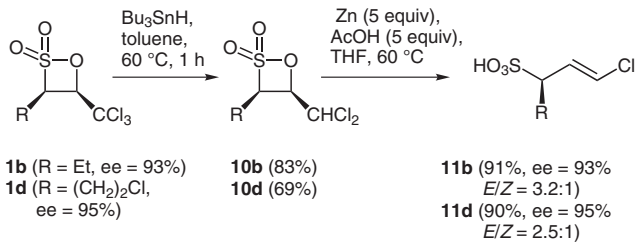


Entry	7	R	Yield (%)[a]	1: ee (%)[b]	7: ee (%)[b]
1	**7a**	Me	97	87	85
2	**7b**	Et	97	>99	>99
3	**7c**	*n*-Pr	95	89	86
4	**7d**	$(CH_2)_2Cl$	80	94	94
5	**7e**	Bn	88	99	99
6	**7f**	$(CH_2)_2O$-*p*-$MeOC_6H_4$	99	>99	>99

[a] Isolated yield.
[b] Determined by chiral column HPLC (Daicel OD-H) after esterification with TMS-diazomethane.



Scheme 2 Mechanistic alternatives for the formation of dichloroallylsulfonic acids **7**



1b (R = Et, ee = 93%)
1d (R = $(CH_2)_2Cl$, ee = 95%)

10b (83%)
10d (69%)

11b (91%, ee = 93% *E*/*Z* = 3.2:1)
11d (90%, ee = 95% *E*/*Z* = 2.5:1)

Scheme 3 Formation of monochloroallylsulfonic acid **11**

which is then reduced with H_2 to regenerate Pd(0). HCl generated during this process protonates the corresponding Pd-sulfonate intermediates. At this point we cannot exclude one of these two mechanisms.

Monochloroallylsulfonic acids **11** were not available by hydrogenation of the dichloromethyl-substituted β-sultones **10**, which were prepared from **1** by selective partial dechlorination with Bu_3SnH (Scheme 3), due to overreduction of the generated C=C double bond. However, treatment of **10** with Zn and HOAc in THF at 60 °C furnished **11** without racemization of the remaining stereocenter as a mixture of the *E*- and *Z*-isomer (2.5–3.2:1).[7]

In conclusion, we have shown that the reduction of optically active β-sultones bearing a trichloromethyl group at the β-position can proceed chemoselectively at three different sites and without significant racemization or epimerization. In addition to the dechlorination with Bu_3SnH, β-hydroxysulfinic acids[15] and allylsulfonic acids[16] are now readily available in highly enantioenriched form by a direct operationally simple synthetic approach. These compounds would be difficult to access by alternative routes.

Acknowledgment

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(7) **General Procedure for β-Hydroxysulfinic Acids 5**: To a stirred solution of the corresponding β-sultone **1** in Et_2O (10 mL/mmol) a solution of $LiAlH_4$ (1 M in THF, 0.5 equiv) in Et_2O (2.5 mL/mmol **1**) was added dropwise at r.t. After 10 min the reaction mixture was quenched with ice and HCl (1 M, 1 mL/mmol **1**). Et_2O was removed in a stream of N_2 and the remaining aqueous solution was filtrated over Amberlite IR-120 (acidic form). The resin was washed with H_2O until the eluate was no longer acidic. Concentration in vacuo yielded the corresponding sulfinic acids **5**. For **1d** and **1e** the quenched, acidified reaction mixture was not purified by ion-exchange resin, but extracted with $CHCl_3$ (4 ×). In the case of **1d** quenching the reaction mixture with H_2O followed by extraction with $CHCl_3$ yielded the corresponding γ-sultine **6**.
General Procedure for γ,γ-Dichloroallylsulfonic Acids 7: The corresponding β-sultone **1** was dissolved in EtOH (1 mL/5 mg **1**) and Pd (10% on activated charcoal, 0.02 equiv) was added. The suspension was stirred for 21 h under a positive pressure (1 atm) of H_2. The reaction mixture was then filtrated over Celite, repeatedly washed with EtOH and the filtrate was concentrated in vacuo. H_2O (1 mL/5 mg) was added to the dark oily residue and the solids were removed by filtration. Concentration of the colorless filtrate yielded the corresponding sulfonic acids **7**.
General Procedure for γ-Monochloroallylsulfonic Acids 11: To a stirred solution of the corresponding β-sultone **10** in THF (1 mL/7 mg) AcOH (5 equiv) was added, followed by Zn dust (5 equiv). The flask was subsequently closed and stirring was continued at 60 °C for 12 h. The reaction mixture was filtrated over Celite and the filter cake was washed with EtOH. The filtrate was concentrated in vacuo and the residue was dissolved in H_2O. To remove unreacted sultone the aqueous layer was washed with MTBE (2 × 25 mL). To remove Zn salts the aqueous layer was subsequently filtrated over Amberlite IR-120 (acidic form) and the resin was washed with H_2O until the eluate was no longer acidic. Concentration in vacuo yielded the corresponding monochloroallylsulfonic acids **11**.

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(9) (a) Yolka, S.; Dunach, E.; Loiseau, M.; Lizzani-Cuvelier, L.; Fellous, R.; Rochard, S.; Schippa, C.; George, G. *Flavour Frag. J.* **2002**, *17*, 425. (b) A biosynthesis has been proposed which proceeds via oxidation of 3-mercaptohexan-1-ol, which is mainly responsible for the flavor of the yellow passion fruit and which has also been detected to considerably contribute to the bouquet of Sauvignon blanc wines (see ref. 9a).

(10) For a previous X-ray crystal structure analysis of a γ-sultine, see ref. 8c.

(11) Inconsistency exists in literature with regard to the relative stability of γ-sultines possessing either an axial or equatorial S=O entity. While isomerization of axial S=O into equatorial S=O on storage at room temperature for several weeks has been reported (ref. 8b), isomerization to an axial S=O with I_2 has been described later: lka, S.; Fellous, R.; Lizzani-Cuvelier, L.; Loiseau, M. *Tetrahedron Lett.* **1999**, *40*, 3159.

(12) Each unit cell contains two independent molecules with the same configuration, but with slightly different conformations. The second conformer not depicted in Figure 1 shows a stronger distortion of the envelope resembling a half-chair conformation. Supplementary crystallographic data have been deposited with the Cambridge Crystallographic Data Centre as deposition 676601. This material is available free of charge via the Internet at http://www.ccdc.cam.ac.uk/products/csd/request/.

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(15) Analytical data for sulfinic acids **5**: **5a**: ^{1}H NMR (300 MHz, D_2O): δ = 4.66 (d, *J* = 1.6 Hz, 1 H, C*H*OH), 3.19 (dq, *J* = 1.6, 7.2 Hz, 1 H, CHS), 1.36 (dd, *J* = 7.2 Hz, 3 H, Me). ^{13}C NMR (75 MHz, D_2O): δ = 101.8 (CCl_3), 76.9 (*C*HCCl$_3$), 61.6 (CSO_2H), 6.3 (Me). IR (ATR): 2970, 2497, 1454, 1365, 1216 cm^{-1}. $[\alpha]_D^{23.6}$ +37.68 ± 0.12 (*c* = 1.25, H_2O; sample with ee = 87%). **5b**: ^{1}H NMR (300 MHz, D_2O): δ = 4.57 (d, *J* = 1.3 Hz, 1 H, C*H*OH), 2.91 (ddd, *J* = 1.3, 4.4, 9.3 Hz, 1 H, CHS), 2.00 (tdd, *J* = 3.4, 7.8, 15.6 Hz, 1 H, CH*H*CHS), 1.60 (tdd, *J* = 7.5, 9.3, 15.6 Hz, 1 H, CH*H*CHS), 0.96 (dd, *J* = 7.5, 7.8 Hz, 3 H, Me). ^{13}C NMR (75 MHz, D_2O): δ = 102.2 (CCl_3), 75.8 (*C*HCCl$_3$), 67.1 (CSO_2H), 16.6 (*C*H$_2$CH$_3$), 11.9 (Me). IR (ATR): 3356, 2970, 1365, 1228 cm^{-1}. $[\alpha]_D^{27.9}$ +53.18 ± 0.12 (*c* = 0.6, H_2O; sample with ee >99%). **5c**: ^{1}H NMR (300 MHz, D_2O): δ = 4.72 (m, 1 H, C*H*OH), 2.94–3.06 (m, 1 H, CHS), 1.94–2.14 (m, 1 H, CH*H*CHS), 1.41–1.81 (m, 3 H, CH*H*CHS, C*H*$_2$CH$_3$), 0.83–1.01 (m, 3 H, Me). ^{13}C NMR (75 MHz, D_2O): δ = 102.4 (CCl_3), 76.1 (*C*HCCl$_3$), 65.5 (CSO_2H), 25.1 (*C*H$_2$Et), 20.8 (CH$_2$*C*H$_2$CH$_3$), 13.4 (Me). IR (ATR): 3402, 1352, 1139 cm^{-1}. $[\alpha]_D^{24.0}$ +30.32 ± 0.93 (*c* = 0.55, H_2O; sample with ee = 85%). **5d**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.02 (m, 1 H, C*H*OH), 2.74–3.82 (m, 2 H, C*H*HCl, CHS), 2.54–3.61 (m, 1 H, CH*H*Cl), 2.74–2.86 (m, 1 H, C*H*HCHS), 2.28–2.41 (m, 1 H, CH*H*CHS). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 101.5 (CCl_3), 77.2 (*C*HCCl$_3$), 61.7 (CSO_2H), 42.2 (CH_2Cl), 26.0 (*C*H$_2$CHS). IR (ATR): 3386, 2923, 1111 cm^{-1}. $[\alpha]_D^{22.0}$ +31.93 ± 0.49 (*c* = 1.00, $CHCl_3$; sample with ee = 96%). **5e**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.25–7.35 (m, 5 H, CH_{Ph}), 5.23 (br, 2 H, OH, SO_2H), 5.15 (m, 1 H, C*H*OH), 2.60–3.78 (m, 2 H, C*H*HPh, CHS), 3.12 (dd, *J* = 11.5, 15.3 Hz, 1 H, CH*H*Ph). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 129.2 (2 × C_{Ph}), 128.8 (2 × C_{Ph}), 128.7 ($C_{Ph,q}$), 127.2 (C_{Ph}), 101.8 (CCl_3), 76.0 (*C*HCCl$_3$), 65.5 (CSO_2H), 29.7 (*C*H$_2$Ph). IR (ATR): 3383, 1496, 1454, 1106 cm^{-1}. $[\alpha]_D^{21.5}$ +41.51 ± 0.44 (*c* = 1.15, $CHCl_3$; sample with ee = 99%). γ-Sultine **6**: HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_5H_7O_3SCl_3$: 251.9176; found: 251.9175. Anal. Calcd for $C_5H_7Cl_3O_3S$: C, 23.69; H, 2.78. Found: C, 23.90; H, 2.88. (2*S*)-**6**: R_f 0.39 (EtOAc–cyclohexane, 1:1); mp 123.5–124.4 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.88 (ddd, *J* = 4.0, 8.7, 12.8 Hz, 1 H, C*H*HO), 4.70 (m, 1 H, C*H*OH), 4.48–4.57 (m, 1 H, CH*H*O), 3.76 (d, *J* = 4.4 Hz, 1 H, OH), 3.72 (ddd, *J* = 4.4, 8.4, 10.6 Hz, 1 H, CHS), 2.76–2.90 (m, 1 H, CH$_2$C*H*HCH), 2.39–2.49 (m, 1 H, CH$_2$CH*H*CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 101.4 (CCl_3), 78.6 (Cl$_3$*C*CHO), 76.0 (CH$_2$*C*H$_2$O), 68.5 (CHS), 24.1 (CH$_2$*C*H$_2$CH). IR (ATR): 3292, 1082, 1075 cm^{-1}. $[\alpha]_D^{23.9}$ –92.33 ± 0.21 (*c* = 1.05, $CHCl_3$; sample with ee = 96%). (2*R*)-**6**: R_f: 0.50 (EtOAc–cyclohexane, 1:1); mp 108.1–110.0 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.89 (dt, *J* = 7.2, 8.4 Hz, 1 H, C*H*HO), 4.70–4.78 (m, 1 H, CH*H*O), 4.58 (m, 1 H, C*H*OH), 3.78–3.85 (m, 1 H, CHS), 3.38 (br, 1 H, OH), 2.52–2.73 (m, 2 H, CH$_2$C*H*$_2$CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 102.0 (CCl_3), 78.1 (Cl$_3$*C*CHO), 77.2 (CHS), 75.7 (CH$_2$*C*H$_2$O), 24.6 (CH$_2$*C*H$_2$CH). IR (ATR): 3289, 1088, 1051 cm^{-1}. $[\alpha]_D^{23.6}$ +4.24 ± 1.1 (*c* = 0.20, $CHCl_3$; sample with ee = 96%).

(16) Analytical data for sulfonic acids **7** and **11**: **7a**: ^{1}H NMR (300 MHz, D_2O): δ = 5.83 (d, *J* = 10.1 Hz, 1 H, CH=CCl$_2$), 3.78–3.88 (m, 1 H, CHS), 1.26 (d, *J* = 6.9 Hz, 3 H, Me). ^{13}C NMR (75 MHz, D_2O): δ = 126.0 (*C*=C), 123.8 (C=*C*), 56.6 (CSO_3H), 14.8 (Me). IR (ATR): 2941, 1621, 1141, 1007 cm^{-1}. HRMS (ESI): *m*/*z* [M – H]$^-$ calcd for $C_4H_6O_3SCl_2$: 202.9332; found: 202.9343. $[\alpha]_D^{22.9}$ –75.46 ± 0.42 (*c* = 1.30, H_2O; sample with ee = 85%). **7b**: ^{1}H NMR (300 MHz, D_2O): δ = 5.77 (d, *J* = 10.4 Hz, 1 H, C*H*=CCl$_2$), 3.57–3.67 (m, 1 H, CHS), 1.79–1.95 (m, 1 H, CH*H*CHS), 1.41–1.57 (m, 1 H, C*H*HCHS), 0.79 (t, *J* = 7.3 Hz, 3 H, Me). ^{13}C NMR (75 MHz, D_2O): δ = 125.1 (*C*=C), 124.9 (C=*C*), 63.1 (CSO_3H), 23.1 (*C*H$_2$CHS), 10.2 (Me). IR (ATR): 3412, 1663, 1621, 1178, 1039 cm^{-1}. HRMS (ESI): *m*/*z* [M – H]$^-$ calcd for $C_5H_8O_3SCl_2$: 216.9498; found: 216.9495. $[\alpha]_D^{28.0}$ –87.32 ± 0.10 (*c* = 0.95, H_2O; sample with ee >99%). **7c**: ^{1}H NMR (300 MHz, D_2O): δ = 5.77 (d, *J* = 10.4 Hz, 1 H, CH=CCl$_2$), 3.66–3.77 (m, 1 H, CHS), 1.70–1.85 (m, 1 H, CH*H*CHS), 1.42–1.59 (m, 1 H, C*H*HCHS), 1.07–1.36 (m, 2 H, C*H*$_2$CH$_3$), 0.75 (t, *J* = 7.3 Hz, 3 H, Me). ^{13}C NMR (75 MHz, D_2O): δ = 125.4 (*C*=C), 124.7 (C=*C*), 61.3 (CSO_3H), 31.5 (*C*H$_2$CHS), 19.1 (*C*H$_2$CH$_3$), 12.8 (Me). IR (ATR): 2958, 1622, 1198, 1080 cm^{-1}. HRMS (ESI): *m*/*z* [M – H]$^-$ calcd for $C_6H_{10}O_3SCl_2$: 230.9655; found: 230.9654. $[\alpha]_D^{26.4}$ –79.53 ±

0.14 (*c* = 1.20, H_2O; sample with ee = 86%). **7d**: ^{1}H NMR (300 MHz, D_2O): δ = 5.83 (d, *J* = 10.4 Hz, 1 H, CH=CCl_2), 3.99 (td, *J* = 3.7, 10.4 Hz, 1 H, CHS), 3.64 (td, *J* = 5.4, 10.9 Hz, 1 H, C*H*HCl), 3.37–3.38 (m, 1 H, CH*H*Cl), 2.23–2.36 (m, 1 H, CH*H*CHS), 1.96–2.28 (m, 1 H, C*H*HCHS). ^{13}C NMR (75 MHz, D_2O): δ = 126.0 (*C*=C), 124.0 (C=*C*), 59.0 (CSO_3H), 41.7 (CH_2Cl), 32.5 (*C*H_2CHS). IR (ATR): 2539, 1621, 1193, 1060 cm^{-1}. HRMS (ESI): *m*/*z* [M – H]$^-$ calcd for $C_5H_7O_3SCl_3$: 250.9109; found: 250.9109. $[\alpha]_D^{28.5}$ –134.18 ± 0.07 (*c* = 1.37, MeOH; sample with ee = 94%). **7e**: ^{1}H NMR (300 MHz, D_2O): δ = 7.20–7.35 (m, 5 H, CH_{Ph}), 5.94 (d, *J* = 10.3 Hz, 1 H, CH=CCl_2), 4.09 (m, 1 H, CHS), 3.37 (dd, *J* = 3.1, 13.7 Hz, 1 H, CH*H*Ph), 2.82 (m, 1 H, C*H*HPh). ^{13}C NMR (75 MHz, D_2O): δ = 139.7 ($C_{Ph,q}$), 131.7 (2 × C_{Ph}), 131.1 (2 × C_{Ph}), 129.3, 127.9, 127.2 (C=*C*), 65.5 (CSO_3H), 38.5 (*C*H_2Ph). IR (ATR): 3029, 1621, 1216, 1154, 1038 cm^{-1}. HRMS (ESI): *m*/*z* [M – H]$^-$ calcd for $C_{10}H_{10}O_3SCl_2$: 278.9655; found: 278.9654. $[\alpha]_D^{23.8}$ –75.97 ± 0.13 (*c* = 0.95, MeOH; sample with ee = 99%). **7f**: ^{1}H NMR (300 MHz, D_2O): δ = 6.75–6.85 (m, 4 H, CH_{Ph}), 5.84 (d, *J* = 10.6 Hz, 1 H, CH=CCl_2), 3.90–4.05 (m, 2 H, CHS, CH_2OAr), 3.75–3.87 (m, 1 H, CH_2C_{ring}), 3.63 (s, 3 H, OMe), 2.23–2.39 (m, 1 H, C*H*$_2$CHS), 1.81–1.97 (m, 1 H, C*H*$_2$CHS). ^{13}C NMR (75 MHz, D_2O): δ = 153.2 (C_{Ph}), 151.9 (C_{Ph}), 125.2 (*C*=C), 124.4 (C=*C*), 116.4 (2 × CH_{Ph}), 114.8 (2 × CH_{Ph}), 65.9 (CH_2O), 58.9 (CSO_3H), 55.7 (OMe), 29.5 (*C*H_2CHS). IR (ATR): 3422, 1621, 1509, 1216, 1167, 1032 cm^{-1}. HRMS (ESI): *m*/*z* [M – H]$^-$ calcd for $C_{12}H_{14}O_5SCl_2$: 338.9866; found: 338.9866. $[\alpha]_D^{20.3}$ –80.63 ± 0.26 (*c* = 0.55, MeOH; sample with ee >99%). **11b**: ^{1}H NMR (300 MHz, D_2O; *E*-isomer): δ = 6.34 (d, *J* = 13.4 Hz, 1 H, CH=C*H*Cl), 5.81 (dd, *J* = 10.3, 13.4 Hz, 1 H, C*H*=CHCl), 3.38 (dt, *J* = 3.7, 10.3 Hz, 1 H, CHS), 1.88–2.04 (m, 1 H, CH*H*CHS), 1.50–1.66 (m, 1 H, C*H*HCHS), 0.86 (t, *J* = 7.5 Hz, 3 H, Me). ^{1}H NMR (300 MHz, D_2O; *Z*-isomer): δ = 6.45 (d, *J* = 7.2 Hz, 1 H, CH=C*H*Cl), 5.74 (dd, *J* = 7.2, 10.3 Hz, 1 H, C*H*=CHCl), 3.95 (dt, *J* = 3.2, 10.3 Hz, 1 H, CHS), 1.88–2.04 (m, 1 H, CH*H*CHS), 1.50–1.66 (m, 1 H, C*H*HCHS), 0.87 (t, *J* = 7.5 Hz, 3 H, Me). ^{13}C NMR (75 MHz, D_2O; *E*-isomer): δ = 127.9 (*C*=C), 123.0 (C=*C*), 64.1 (CSO_3H), 22.7 (*C*H_2CHS), 10.6 (Me). ^{13}C NMR (75 MHz, D_2O; *Z*-isomer): δ = 126.3 (*C*=C), 123.6 (C=*C*), 60.5 (CSO_3H), 23.2 (*C*H_2CHS), 10.4 (Me). IR (ATR): 2973, 1694, 1115 cm^{-1}. HRMS (ESI): *m*/*z* [M – H]$^-$ calcd for $C_5H_9O_3SCl$: 182.9888; found: 182.9889.