Asymmetric Synthesis of α- and α,β-Substituted β-Alkoxycarbonyl Sulfonates

Dieter Enders,*^a Jean-Claude Adelbrecht,^a Wacharee Harnying^b

^a Institut für Organische Chemie, Rheinisch-Westfälische Technische Hochschule, Landoltweg 1, 52074 Aachen, Germany Fax +49(241)8092127; E-mail: Enders@rwth-aachen.de

^b Department of Chemistry, Faculty of Science, Khon Kaen University, Khon Kaen 40002, Thailand *Received 17 May 2005*

Abstract: An efficient asymmetric synthesis of substituted β alkoxycarbonyl sulfonates is described. Enantiopure α -substituted β -alkoxycarbonyl sulfonates can be obtained via α -alkylation of metalated sulfonates bearing 1,2:5,6-di-*O*-isopropylidene- α -D-allofuranose as the chiral auxiliary with alkyl bromoacetates. α , β -Disubstituted β -alkoxycarbonyl sulfonates were prepared starting from the corresponding enantiopure γ -nitro sulfonates by using TFA for the cleavage of the chiral auxiliary and causing a simultaneous Meyer reaction.

Key words: asymmetric synthesis, sulfonates, esters, alkylation, sugar auxiliary

Sulfonic acids and their derivatives represent important synthetic targets because they often exhibit interesting biological activities. β -Carboxy sulfonates and their amino substituted analogues represent a special class among which cysteic acid (CA, 2-amino-3-sulfopropionic acid) is probably the most prominent one. In organisms it is present in high concentrations in the plasma, urine and tissues.¹ However, the number of methods for the synthesis of this class of compounds in enantiomerically pure form is scarce.² In our ongoing research concerning the chemistry of sulfonates we have now developed a methodology for the asymmetric synthesis of substituted β -alkoxycarbonyl sulfonates.

The strategy used for the asymmetric synthesis of the title compounds is based on previous work undertaken in our group employing 1,2:5,6-di-*O*-isopropylidene- α -D-allo-furanose as the chiral auxiliary,³ which resulted in a highly efficient route towards a variety of different sulfonic acid derivatives.^{3–8} Therein we also reported an efficient asymmetric synthesis of α , β -disubstituted β -alkoxycarbonyl sulfonates from α , β -disubstituted γ -nitro sulfonates obtained by asymmetric Michael addition of chiral lithiated sulfonates to nitroalkenes.⁴

We now wish to describe a direct and efficient entry to α substituted β -alkoxycarbonyl sulfonates starting from enantiopure lithiated sulfonates obtained by metalation with *n*-butyllithium in THF and using bromoesters as electrophiles. At the beginning of our studies it was not clear which bromoester should be used and if different bromoesters would lead to significantly different results. With substrate **1a** in hand, a range of bromoesters was screened in order to identify optimum conditions in terms of yield and diastereoselectivity (Scheme 1). Typical reactions involved the addition of 1.5 equivalents of bromoester to the lithiated substrate at -95 °C. The results are collected in Table 1.



Scheme 1 Asymmetric α -alkylations of the sulfonate 1a with different bromoesters.

Table 1 α -Alkylations of the Chiral Sulfonate **1a** with DifferentBromoesters To Give the Sulfonates (*R*)-**2a**-c

(<i>R</i>)-2	R	Yield (%)	de (%) ^{a,b}
a	Me	80	84 (≥ 98)
b	<i>i</i> -Pr	76	80 (≥ 98)
c	<i>t</i> -Bu	74	75 (≥98)

^a Determined by ¹H NMR spectroscopy.

^b In brackets after recrystallization from EtOH.

As it was anticipated, the reactions proceeded smoothly, with both good yields and diastereomeric excesses of the desired products (*R*)-**2**. Recrystallization of the products from EtOH was amenable in all cases to furnish the diastereomerically pure sulfonates (de \ge 98%). It should be mentioned that the assignment of the configuration of the newly formed stereocenter to be *R* is based on results obtained from related reactions using unfunctionalized alkyl halides as electrophiles.³

From this screening, marginally higher yields were consistently obtained from reactions employing the methyl bromoacetate, indicating it as the electrophile of choice. Obviously and rather unexpected the asymmetric induction increases with a decreasing steric demand of the ester function. With optimum conditions determined, using the methyl bromoacetate as electrophile, the next step of our investigation centered on the extension to other chiral sul-

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fonate substrates **1a–d** (Scheme 2). The results of these reactions are collected in Table 2.

Whereas benzylic sulfonates **1a–c** show results consistent with our earlier trials, in which related electrophilic substitutions proceeded in high yields and with good diastereoselectivity, the allylic sulfonate **1d** gave product **2f** with a de value of only 40% and in a moderate yield. The major diastereomers (R)-**2a**,**d**,**e** could be easily obtained as pure stereoisomers with diastereomeric excesses superior to 98% by recrystallization from EtOH.

Racemization-free cleavage of the chiral auxiliary was carried out following procedures that have already been described.^{3,4} By refluxing the sulfonate (*R*)-**2a** in a MeOH–H₂O mixture containing a catalytic amount of Pd(OAc)₂ for four days followed by treatment with diazomethane, the desired methyl sulfonate (*R*)-**3a** was obtained in 94% yield (Scheme 3). Due to the fact that (*R*)-**2a** bears a methyl ester moiety it was found to be more effective to use MeOH as the solvent avoiding side products arising from transesterification.

As we have previously described, the cleavage of the chiral auxiliary of the γ -nitro sulfonates **4** with Pd(OAc)₂ led to either β -alkoxycarbonyl methyl sulfonates or γ -nitro methyl sulfonates in excellent diastereo- and enantiomeric excesses using different conditions.⁴ Since we could develop a less expensive method for the removal of



Scheme 2 Asymmetric α -alkylations of the sulfonates 1 with methyl bromoacetate.

Table 2 α -Alkylations of the Sulfonates 1a-d with Methyl Bromoacetate To Give the Sulfonates (R)-2a,d-f

1	(<i>R</i>)-2	\mathbb{R}^1	Yield (%)	de (%) ^{a,b}
a	a	C ~	80	84 (≥98)
b	d	t-Bu	75	80 (≥98)
c	e	MeO	78	80 (≥98)
d	f	Y Z	49	40

^a Determined by ¹H NMR spectroscopy.

^b In brackets after recrystallization from EtOH.



Scheme 3 Removal of the chiral auxiliary to give the methyl sulfonate (R)-3.

the chiral auxiliary, i.e. using trifluoro acetic acid (TFA) instead of $Pd(OAc)_2$,⁵ we investigated its applicability to the nitro sulfonates **4**.

As is shown in Scheme 4, the cleavage of the auxiliary with simultaneous conversion of the primary nitro group to the corresponding ethyl esters (R,R)-5 in a Meyer reaction⁹ were accomplished in good yields upon treatment with TFA in refluxing EtOH for two days. On the other hand, the chiral auxiliary could be removed selectively by the combination of the addition of water and shorter reaction time. Thus, the γ -nitro isopropyl sulfonates (R,R)-6 were obtained in moderate to good yields by refluxing the γ -nitro sulfonates (R,R)-4 in an EtOH–H₂O solution containing 2% TFA for 15 hours and subsequent protection of the resulting sulfonic acids with triisopropylorthoformate in refluxing CH₂Cl₂.



Scheme 4 TFA cleavage of the chiral auxiliary of the γ -nitro sulfonates 4 to form either the β -ethoxycarbonyl methyl sulfonates 5 or the γ -nitro ispropyl sulfonates 6.

Under reaction conditions comparable to those using $Pd(OAc)_2$, TFA gave lower yields of the β -ethoxycarbonyl sulfonates (*R*,*R*)-**5a**,**b**. Whereas the γ -nitro sulfonates (*R*,*R*)-**6a**,**c** were obtained in higher yields, (*R*,*R*)-**6b** was isolated in slightly lower yield. However, using TFA instead of $Pd(OAc)_2$ seems to be a viable alternative for such transformations since the reactions proceed faster and give satisfactory yields.

The further synthetic transformation of β -alkoxycarbonyl sulfonates to the phamacologically interesting γ -hydroxy sulfonates,¹⁰ previously synthesized in our group by ring-

opening of enantio- and diastereomerically pure γ -sultones,⁷ was next investigated.

We found that the reduction of compound (R,R)-**5b** with BH₃·THF,¹¹ BH₃·SMe₂,¹² LiEt₃BH,¹³ or LiAlH₄ did not only proceed with the reduction of the ester group but also with a reductive cleavage of the methyl group to furnish the γ -hydroxy sulfonic acid. However, a chemoselective reduction of the ester group leaving the methyl sulfonate intact could be achieved by treatment with DIBAL-H at low temperature (Scheme 5). The desired α , β -substituted γ -hydroxy methyl sulfonate (R,R)-**7** was obtained in an excellent yield of 95% as well as diastereo- and enantiomeric excess (de, ee \geq 98%).

The ee value of (R,R)-7 was determined by HPLC analysis using a chiral stationary phase by comparison with its racemate and showed that this reaction proceeds without any detectable degree of racemization.



Scheme 5 Reduction of (R,R)-**5b** to give the γ -hydroxy methyl sulfonate (R,R)-**7**.

In summary, we have developed an efficient asymmetric access to benzylic α -substituted β -alkoxycarbonyl sulfonates in good yields as well as diastereo- and enantiomeric excesses via α -alkylation of lithiated chiral sulfonates with methyl bromoacetate. In addition, we have demonstrated an alternative removal of the chiral sugar auxiliary using TFA instead of Pd(OAc)₂ in the case of α , β -disubstituted γ -nitro sulfonates leading to either β -alkoxycarbonyl sulfonates or γ -nitro sulfonates in good yields. We have also shown that the enantioenriched title compounds are valuable substrates for the transformation to γ -hydroxy sulfonates. Additional transformations can be envisioned thus providing an array of useful bifunctional building blocks.

All moisture-sensitive reactions were carried out using standard Schlenk techniques unless stated otherwise. Solvents were dried and purified by conventional methods prior to use. THF was freshly distilled from sodium-lead alloy under Ar. Reagents of commercial quality were used from freshly opened containers or purified by common methods. n-BuLi (1.6 M in hexane) was purchased from Merck, Darmstadt. Preparative column chromatography was carried out on Merck silica gel 60, (particle size 0.040-0.063 mm, 230-240 mesh, flash). Analytical TLC was performed on silica gel 60 F₂₅₄ plates (Merck, Darmstadt). Optical rotation values were measured with a Perkin-Elmer P241 polarimeter. Microanalyses were obtained with a Vario EL element analyzer. Mass spectra were acquired with a Finnigan SSQ7000 (CI, 100 eV, EI 70 eV) spectrometer. HRMS data were recorded with a Finnigan MAT95 spectrometer. IR spectra were taken with a Perkin-Elmer FT/IR 1760 instrument. ¹H and ¹³C NMR spectra were recorded with Gemini 300 or Varian Inova 400 instruments and all measurements

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were performed with TMS as internal standard. Melting points were determined with a Tottoli melting point apparatus and are uncorrected.

Preparation of the Chiral Sulfonates 1; General Procedure 1 (GP 1)

To a solution of the corresponding sodium sulfonate (6 mmol) in DMF (30 mL) was added thionylchloride (2.1 mL) at 0 °C. Upon completion of the reaction after 4 h at r.t., ice-cold water and EtOAc were added to the reaction mixture. The organic phase was washed with water (5 ×) and dried over MgSO₄. After concentration under reduced pressure, the resulting sulfonyl chloride was diluted in EtOAc (40 mL) before pyridine (18 mmol) was added. 1,2:5,6-Di-isopropylidene- α -D-allofuranose (2 mmol) was added to the reaction mixture and then stirred for 24 h. The organic phase was washed with 1 M HCl (2 ×), followed by brine and dried over MgSO₄. Concentration under reduced pressure and chromatography (SiO₂, Et₂O–*n*-pentane) yielded the enatiopure sulfonate **1**. The data of the chiral sulfonates **1a,b** have been previously reported, see ref.^{3b}

Alkylation of Chiral Sulfonates with Bromoesters; General Procedure 2 (GP 2)

A solution of the enantiopure sulfonate **1** (1 equiv) in THF (20 mL/ mmol) was cooled down to -95 °C prior to the addition of *n*-BuLi (1.1 equiv of a 1.6 M solution in hexane). Upon completion of the addition the reaction mixture was stirred for 45 min at -95 °C before a solution of the bromoester (1.5 equiv) in THF (2 mL/mmol of electrophile) was added dropwise. The mixture was stirred for a further 1 h at -95 °C and left at -78 °C for 16 h. The reaction mixture was quenched with a pH 7 buffer solution (2 mL/mmol). After separation of the organic layer, the aqueous phase was extracted with EtOAc. The combined organic phases were washed with brine and dried over MgSO₄. Concentration under reduced pressure and purification by flash chromatography (SiO₂, EtOAc–*n*-pentane) afforded the sulfonate (*R*)-**2**.

Removal of the Chiral Auxiliary To Give the α,β -Disubstituted β -Ethoxycarbonyl Methyl Sulfonates (*R*,*R*)-5; General Procedure 3 (GP 3)

A mixture of the γ -nitro sulfonate (*R*,*R*)-4 (1 mmol) in a solution of 2% TFA–EtOH (20 mL) was refluxed for 2 d. The resulting colorless solution was treated with an ethereal solution of diazomethane until the yellow color persisted. The solvent was evaporated under reduced pressure and the crude product was purified by flash column chromatography (SiO₂, Et₂O–*n*-pentane) to give the β-ethoxycarbonyl sulfonate (*R*,*R*)-**5**. The data of these compounds have been previously reported, see ref.^{4b}

Removal of the Chiral Auxiliary To Give the α , β -Disubstituted γ -Nitro Isopropyl Sulfonates (*R*,*R*)-6; General Procedure 4 (GP 4)

A mixture of the γ -nitro sulfonate (*R*,*R*)-4 (1 mmol) in a solution of 2% TFA–EtOH (18 mL) and H₂O (2 mL) was refluxed for 15 h. After removal of the solvent in vacuo, the crude sulfonic acid was dissolved in CH₂Cl₂ (10 mL) and triisopropylorthoformate (0.8 mL, 5 mmol) was added. The mixture was refluxed for 3 h. The solvent was evaporated under reduced pressure and the crude product was purified by flash column chromatography (SiO₂, Et₂O–*n*-pentane) to give the γ -nitro isopropyl sulfonates (*R*,*R*)-6.

Enantiopure Sulfonate 1c

According to GP 1, the crude product was purified by column chromatography (SiO₂; Et₂O–*n*-pentane, 1:2) to give **1c** as a colorless solid (1.51 g, 84%); mp 104 °C; $[\alpha]_D^{24}$ +53.8 (*c* = 1.0, CHCl₃).

IR (KBr): 3423, 2994, 2894, 1601, 1494, 1374, 1258, 1224, 1165, 1073, 1021, 884, 856, 831, 808, 696, 516 cm $^{-1}$.

¹H NMR (400 MHz, CDCl₃): δ = 1.41, 1.41, 1.51, 1.65 [4×s, 12 H, O₂C(CH₃)₂], 3.86 [s, 3 H, OCH₃], 3.90 [dd, *J* = 6.2, 8.7 Hz, 1 H, OCHHCH], 4.06 [dd, *J* = 6.9, 8.7 Hz, 1 H, OCHHCH], 4.20 [dd, *J* = 4.2, 8.4 Hz, 1 H, CH(OC)CH(OC)CH₂O], 4.32 [dt, *J* = 4.2, 6.4 Hz, 1 H, CH(OC)CH₂O], 4.46 [d, *J* = 14.0 Hz, 1 H, ArCH₂SO₃], 4.55 [d, *J* = 14.0 Hz, 1 H, ArCH₂SO₃], 4.68 [dd, *J* = 4.0, 4.7 Hz, 1 H, CH(OC)CH(OC)₂], 4.80 [dd, *J* = 4.7, 8.4 Hz, 1 H, CHOSO₂], 5.82 [d, *J* = 3.7 Hz, 1 H, CH(OC)₂], 6.96–7.38 (m, 4 H, ArH).

¹³C NMR (100 MHz, CDCl₃): $\delta = 25.2$, 26.3, 26.7, 26.8 [O₂C(*C*H₃)₂], 55.3 [OCH₃], 57.7 [ArCH₂SO₃], 65.3 [OCH₂CH], 74.8 [*C*H(OC)CH₂O], 76.7, 77.5, 77.9 [CHO], 103.9 [*C*H(OC)₂], 110.2, 113.8 [O₂C(CH₃)₂], 114.7, 116.6, 123.1, 129.9 [ArCH], 128.8 [ArC], 159.9 [ArCOCH₃].

MS (CI, 100 eV, methane): m/z (%) = 445 (35) [M⁺ + 1], 429 (55) [M⁺ - CH₃], 387 (33), 329 (11), 303 (10), 285 (15), 247 (5), 202 (16), 185 (37), 121 (88), 101 (100).

Anal. Calcd for $\rm C_{20}H_{28}O_9S$ (444.15): C, 54.04; H, 6.35. Found: C, 54.08; H, 6.22.

Enantiopure Sulfonate 1d

According to GP 1, the crude product was purified by column chromatography (SiO₂; Et₂O–*n*-pentane, 1:2) to give **1d** as a colorless solid (774 mg, 59%); mp 92 °C; $[\alpha]_D^{24}$ +51.1 (*c* = 1.0, CHCl₃).

IR (KBr): 2988, 2936, 2881, 1455, 1378, 1260, 1216, 1171, 1018, 891, 860, 837, 580 cm $^{-1}$.

¹H NMR (400 MHz, CDCl₃): $\delta = 1.30, 1.30, 1.41, 1.51 [4 \times s, 12 H, O_2C(CH_3)_2], 1.91 [s, 3 H, CH_2=CCH_3], 3.82 [d, <math>J = 14.0$ Hz, 1 H, CH₂SO₃], 3.86 [dd, J = 6.3, 8.8 Hz, 1 H, OCH₂CH], 3.91 [d, J = 14.2 Hz, 1 H, CH₂SO₃], 4.01 [dd, J = 6.9, 8.5 Hz, 1 H, OCH₂CH], 4.08 [dd, J = 4.1, 8.2 Hz, 1 H, CH(OC)CH(OC)CH₂O], 4.32 [dt, J = 4.1, 6.6 Hz, 1 H, CH(OC)CH₂O], 4.73 [dd, J = 3.6, 7.1 Hz, 1 H, CHOSO₂], 4.76 [br dd, J = 3.6, 4.7 Hz, 1 H, CH₂CH(CH₃)], 5.75 [d, J = 3.6 Hz, 1 H, CH(OC)₂].

¹³C NMR (100 MHz, CDCl₃): δ = 22.3 [CH₂=C(CH₃)], 25.1, 26.2, 26.4, 26.8 [O₂C(CH₃)₂], 59.6 [CH₂SO₃], 65.4 [OCH₂CH], 74.7 [CH(OC)CH₂O], 76.7, 77.1, 78.0 [CHO], 103.9 [CH(OC)₂], 110.1, 113.7 [O₂C(CH₃)₂], 121.1 [CH₂=C(CH₃)], 132.7 [CH₂=C(CH₃)].

MS (EI, 70 eV): m/z (%) = 363 (100) [M⁺ – CH₃], 305 (1), 245 (2), 167 (9), 127 (16), 113 (62), 101 (72), 55 (57).

HRMS: m/z [M⁺ – CH₃] calcd for C₁₆H₂₆O₈S: 363.1114; found: 363.1113.

β-Methoxycarbonyl Sulfonate (*R*)-2a

According to GP2, the sulfonate **1a** (0.615 g, 1.5 mmol) was deprotonated with *n*-BuLi (1.15 mL, 1.1 equiv) and reacted with methyl bromoacetate (240 µL, 1.5 equiv). Work up and flash chromatography (EtOAc–*n*-pentane, 1:3) yielded the sulfonate **2a** as a mixture of diastereomers (0.580 g, 80%); de = 84% (NMR). The major diastereomer (*R*)-**2a** was obtained as a colorless solid after recrystallization from EtOH; de ≥ 98% (NMR); mp 151 °C; $[\alpha]_D^{24}$ +91.5 (*c* = 1.0, CHCl₃).

IR (KBr): 3439, 2949, 1729, 1456, 1371, 1344, 1241, 1214, 1169, 1114, 1049, 1016, 975, 877, 837, 697 $\rm cm^{-1}.$

¹H NMR (400 MHz, CDCl₃): $\delta = 1.27, 1.29, 1.38, 1.49 [4 \times s, 12 H, O_2C(CH_3)_2], 3.16 [dd, <math>J = 10.7, 16.5 Hz, 1 H, CH_2CO_2CH_3], 3.47 [dd, J = 4.1, 16.5 Hz, 1 H, CH_2CO_2CH_3], 3.53 [s, 3 H, OCH_3], 3.79 [dd, J = 6.3, 8.5 Hz, 1 H, OCH_2CH], 3.95 [dd, J = 6.6, 8.5 Hz, 1 H, OCH_2CH], 4.06 [dd, J = 4.7, 8.5 Hz, 1 H, CH(OC)CH(OC)CH_2O], 4.19 [dt, J = 4.7, 6.3 Hz, 1 H, CH(OC)CH_2O], 4.39 [br dd, J = 3.9, 4.7 Hz, 1 H, CH(OC)CH(OC)_2], 4.62 [dd, J = 4.7, 8.5 Hz, 1 H, CHOSO_2], 4.85 [dd, J = 3.9, 10.4 Hz, 1 H, ArCHSO_3], 5.67 [d, J = 4.7, 8.5 Hz, 1 H, CHOSO_2], 4.85 [dd, J = 3.9, 10.4 Hz, 1 H, ArCHSO_3], 5.67 [d, J = 4.7, 8.5 Hz, 1 H, CHOSO_2], 4.85 [dd, J = 3.9, 10.4 Hz, 1 H, ArCHSO_3], 5.67 [d, J = 4.7, 8.5 Hz, 1 H, CHOSO_2], 4.85 [dd, J = 3.9, 10.4 Hz, 1 H, ArCHSO_3], 5.67 [d, J = 4.7, 8.5 Hz, 1 H, CHOSO_2], 4.85 [dd, J = 3.9, 10.4 Hz, 1 H, ArCHSO_3], 5.67 [d, J = 4.7, 8.5 Hz, 1 H, CHOSO_2], 4.85 [dd, J = 3.9, 10.4 Hz, 1 H, ArCHSO_3], 5.67 [d, J = 4.7, 8.5 Hz, 1 H, CHOSO_3], 5.67 [d, J = 4.7, 8.5 Hz, 1$

3.8 Hz, 1 H, CH(OC)₂], 7.30–7.33 (m, 3 H, ArH), 7.42–7.46 (m, 2 H, ArH).

¹³C NMR (100 MHz, CDCl₃): $\delta = 25.4$, 26.3, 26.7, 26.8 [O₂C(CH₃)₂], 35.4 [CH₂CO₂CH₃], 52.4 [OCH₃], 64.1 [ArCHSO₃], 65.7 [OCH₂CH], 74.9 [CH(OC)CH₂O], 77.1 [CH(OC)CH(OC)CH₂O], 77.6 [CH(OC)CH(OC)₂], 77.9 [CHOSO₂], 103.9 [CH(OC)₂], 110.2, 113.8 [(O)₂C(CH₃)₂], 128.9, 129.5, 129.7 (ArCH), 131.0 (ArC), 169.5 (C=O).

MS (EI, 70 eV): m/z (%) = 471 (53) [M⁺ – CH₃], 397 (6), 163 (39), 121 (100), 113 (46), 101 (55), 59 (11).

Anal. Calcd for $C_{22}H_{30}O_{10}S$ (486.54): C, 54.31; H, 6.22. Found: C, 53.96; H, 5.90.

β-Isopropoxycarbonyl Sulfonate (R)-2b

According to GP2, the sulfonate **1b** (0.205 g, 0.5 mmol) was deprotonated with *n*-BuLi (0.35 mL, 1.1 equiv) and reacted with isopropyl bromoacetate (100 µL, 1.5 equiv). Work up and flash chromatography (EtOAc–*n*-pentane, 1:3) yielded the sulfonate **2b** as a mixture of diastereomers (0.190 g, 76%); de = 80% (NMR). The major diastereomer (*R*)-**2b** was obtained as a colorless solid after recrystallization from EtOH; de \geq 98% (NMR); mp 148 °C; [α]_D²⁴ +80.1 (*c* = 1.0, CHCl₃).

IR (KBr): 3439, 2984, 2936, 1729, 1456, 1370, 1335, 1262, 1232, 1162, 1111, 1045, 1014, 875, 844, 826, 808, 695 $\rm cm^{-1}.$

¹H NMR (400 MHz, CDCl₃): δ = 1.12 [d, J = 5.2 Hz, 3 H, CH(CH₃)₂], 1.16 [d, J = 5.2 Hz, 3 H, CH(CH₃)₂], 1.40, 1.43, 1.51, 1.63 [4 × s, 12 H, O₂C(CH₃)₂], 3.26 [dd, J = 11.1, 16.1 Hz, 1 H, CH₂CO₂CH(CH₃)₂], 3.53 [dd, J = 4.2, 16.1 Hz, 1 H, CH₂CO₂CH(CH₃)₂], 3.92 [dd, J = 6.4, 8.7 Hz, 1 H, OCH₂CH], 4.10 [dd, J = 6.7, 8.7 Hz, 1 H, OCH₂CH], 4.18 [dd, J = 4.5, 8.4 Hz, 1 H, CH(OC)CH(OC)CH₂O], 4.19 [dt, J = 4.5, 6.4 Hz, 1 H, CH(OC)CH₂O], 4.51 [br t, J = 3.9 Hz, 1 H, CH(OC)CH(OC)₂], 4.72 [dd, J = 4.7, 8.5 Hz, 1 H, CHOSO₂], 4.91–4.98 [m, 2 H, ArCHSO₃, CH(CH₃)₂], 5.79 [d, J = 3.8 Hz, 1 H, CH(OC)₂], 7.42–7.45 (m, 3 H, ArH), 7.55–7.58 (m, 2 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 21.6, 21.7 [CH(CH₃)₂] 25.4, 26.4, 26.7, 26.8 [(O)₂C(CH₃)₂], 35.7 (CH₂CO₂CH₃), 64.3 (ArCHSO₃), 65.7 [OCH₂CH], 68.9 [CH(CH₃)₂], 74.9 [CH(OC)CH₂O], 77.3 [CH(OC)CH(OC)CH₂O], 77.7 [CH(OC)CH(OC)₂], 77.9 (CHOSO₂), 103.9 [CH(OC)₂], 110.2, 113.7 [O₂C(CH₃)₂], 128.7, 129.4, 129.8 (ArCH), 131.0 (ArC), 168.4 (C=O).

MS (EI, 70 eV): m/z (%) = 499 (91) [M⁺ – CH₃], 397 (19), 245 (8), 191 (32), 149 (56), 133 (25), 113 (82), 101 (100), 91 (30), 59 (15). Anal. Calcd for C₂₄H₃₄O₁₀S (514.59): C, 56.02; H, 6.66. Found: C, 55.68; H, 6.71.

β-tert-Butoxycarbonyl Sulfonate (R)-2c

According to GP2, the sulfonate **1a** (0.294 g, 0.5 mmol) was deprotonated with *n*-BuLi (0.35 mL, 1.1 equiv) and reacted with *tert*-butyl bromoacetate (160 µL, 1.5 equiv). Work up and flash chromatography (EtOAc–*n*-pentane, 1:3) yielded the sulfonate **2c** as a mixture of diastereomers (0.284 g, 74%); de = 75% (NMR). The major diastereomer (*R*)-**2c** was obtained as a colorless solid after recrystallization from EtOH; de \geq 98% (NMR); mp 156 °C; [α]_D²³ +75.16 (*c* = 2.4, CHCl₃).

IR (KBr): 3429, 2940, 2936, 1711, 1460, 1367, 1338, 1262, 1223, 1176, 1145, 1076, 1016, 888, 840, 697, 571, 505 $\rm cm^{-1}.$

¹H NMR (400 MHz, CDCl₃): $\delta = 1.19 [s, 9 H, C(CH_3)_3]$, 1.28, 1.31, 1.39, 1.51 [4 × s, 12 H, O₂C(CH₃)₂], 3.09 [dd, J = 11.3, 15.9 Hz, 1 H, CH₂CO₂C(CH₃)₃], 3.37 [dd, J = 4.4, 15.9 Hz, 1 H, CH₂CO₂C(CH₃)₃], 3.80 [dd, J = 6.9, 8.8 Hz, 1 H, OCH₂CH], 3.97 [dd, J = 6.3, 8.5 Hz, 1 H, OCH₂CH], 4.05 [dd, J = 4.4, 8.2 Hz, 1 H, CH(OC)CH(OC)CH₂O], 4.18 [dt, J = 4.7, 6.6 Hz, 1 H,

 $CH(OC)CH_2O$], 4.38 [dd, J = 3.9, 4.6 Hz, 1 H, $CH(OC)CH(OC)_2$], 4.59 [dd, J = 4.7, 8.5 Hz, 1 H, $CHOSO_2$], 4.77 [dd, J = 4.1, 11.2 Hz, 1 H, ArCHSO₃], 5.67 [d, J = 3.8 Hz, 1 H, $CH(OC)_2$], 7.30–7.32 (m, 3 H, ArH), 7.42–7.45 (m, 2 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 25.3, 26.3, 26.7, 26.7 [O₂C(CH₃)₂], 27.8 [CO₂C(CH₃)₃], 36.4 [CH₂CO₂C(CH₃)₃], 64.4 (ArCHSO₃), 65.7 [OCH₂CH], 74.9 [CH(OC)CH₂O], 77.1 [CH(OC)CH(OC)CH₂O], 77.7 [CH(OC)CH(OC)₂], 77.9 (CHOSO₂), 81.7 [C(CH₃)₃], 103.9 [CH(OC)₂], 110.2, 113.7 [O₂C(CH₃)₂], 128.7, 129.4, 129.9 (ArCH), 131.1 (ArC), 168.0 (C=O).

MS (EI, 70 eV): m/z (%) = 513 (100) [M⁺ – CH₃], 397 (23), 149 (82), 129 (17), 113 (62), 101 (83).

HRMS: m/z [M⁺ – CH₃] calcd for C₂₅H₃₆O₁₀S: 513.1795; found: 513.1795.

β-Methoxycarbonyl Sulfonate (*R*)-2d

According to GP2, the sulfonate **1b** (0.294 g, 0.5 mmol) was deprotonated with *n*-BuLi (0.35 mL, 1.1 equiv) and reacted with methyl bromoacetate (80 µL, 1.5 equiv). Work up and flash chromatography (EtOAc–*n*-pentane, 1:3) yielded the sulfonate **2d** as a mixture of diastereomers (0.235 g, 75%); de $\ge 80\%$ (NMR). The major diastereomer (*R*)-**2d** was obtained as a colorless solid after recrystallization from EtOH; de $\ge 98\%$ (NMR); mp 120 °C; $[\alpha]_{\rm D}^{24}$ +79.7 (*c* = 1.1, CHCl₃).

IR (KBr): 3457, 2976, 2950, 2899, 1737, 1372, 1235, 1162, 1117, 1048, 1017, 994, 878, 837, 606 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): $\delta = 1.34$ [s, 9 H, C(CH₃)₃], 1.38, 1.40, 1.48, 1.60 [4 × s, 12 H, O₂C(CH₃)₂], 3.25 [dd, J = 10.4, 16.8 Hz, 1 H, CH₂CO₂CH₃], 3.91 [dd, J = 4.1, 16.8 Hz, 1 H, CH₂CO₂CH₃], 3.91 [dd, J = 6.5, 8.5 Hz, 1 H, OCH₂CH], 4.08 [dd, J = 6.6, 8.5 Hz, 1 H, OCH₂CH], 4.17 [dd, J = 4.4, 8.5 Hz, 1 H, CH(OC)CH(OC)CH₂O], 4.31 [dt, J = 4.4, 6.6 Hz, 1 H, CH(OC)CH₂O)CH₂O], 4.31 [dt, J = 4.4, 6.6 Hz, 1 H, CH(OC)CH₂O)CH₂O], 4.46 [br t, J = 4.2 Hz, 1 H, CH(OC)CH(OC)₂], 4.72 [dd, J = 4.9, 8.5 Hz, 1 H, CHOSO₂], 4.93 [dd, J = 4.1, 10.4 Hz, 1 H, ArCHSO₃], 5.78 [d, J = 3.9 Hz, 1 H, CH(OC)₂], 7.40–7.47 (m, 4 H, ArH).

¹³C NMR (100 MHz, CDCl₃): $\delta = 25.4$, 26.4, 26.8, 26.8 [O₂C(CH₃)₂], 31.4 [C(CH₃)₃], 34.8 [C(CH₃)₃], 35.4 [CH₂CO₂CH₃], 52.4 (OCH₃), 63.8 (ArCHSO₃), 65.6 (OCH₂CH), 74.9 [CH(OC)CH₂O], 76.8 [CH(OC)CH(OC)CH₂O], 77.6 [CH(OC)CH(OC)₂], 77.8 (CHOSO₂), 103.9 [CH(OC)₂], 110.2, 113.8 [(O)₂C(CH₃)₂], 125.8 (ArCH), 127.8 (ArC), 129.3 (ArCH), 152.6 (ArC), 169.7 (C=O).

MS (CI, 100 eV, methane): m/z (%) = 543 (0.1) [M⁺ + 1], 542 (0.3) [M⁺], 527 (10) [MH⁺ - CH₃], 421 (12), 219 (100), 203 (12), 177 (14), 101 (10).

Anal. Calcd for $C_{26}H_{38}O_{10}S$ (542.22): C, 57.55; H, 7.07. Found: C, 57.59; H, 7.35.

β-Methoxycarbonyl Sulfonate (*R*)-2e

According to GP2, the sulfonate **1c** (0.222 g, 0.5 mmol) was deprotonated with *n*-BuLi (0.35 mL, 1.1 equiv) and reacted with methyl bromoacetate (80 µL, 1.5 equiv). Work up and flash chromatography (EtOAc–*n*-pentane, 1:3) yielded the sulfonate **2e** as a mixture of diastereomers (0.201 g, 78%); de = 80% (NMR). The major diastereomer (*R*)-**2e** was obtained as a colorless solid after recrystallization from EtOH; de \geq 98% (NMR); mp 108 °C; [α]_D²⁴ +81.8 (*c* = 1.2, CHCl₃).

IR (KBr): 3439, 2985, 2950, 1729, 1598, 1493, 1441, 1374, 1323, 1261, 1238, 1214, 1166, 1114, 1049, 1014, 877, 832, 694, 546 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ = 1.38, 1.41, 1.49, 1.60 [4 × s, 12 H, O₂C(CH₃)₂], 3.25 [dd, *J* = 10.7, 16.7 Hz, 1 H, CH₂CO₂CH₃], 3.55 [dd, J = 4.1, 16.7 Hz, 1 H, $CH_2CO_2CH_3$], 3.65 [s, 3 H, CO_2CH_3], 3.87 [s, 3 H, ArOCH₃], 4.08 [dd, J = 6.6, 8.5 Hz, 1 H, OCH₂CH], 4.16 (dd, J = 4.7, 8.5 Hz, 1 H, OCH₂CH), 4.30 [dd, J = 4.4, 8.5 Hz, 1 H, $CH(OC)CH(OC)CH_2O$], 4.19 [dt, J = 4.4, 6.3 Hz, 1 H, $CH(OC)CH_2O$], 4.52 [br t, J = 4.1 Hz, 1 H, $CH(OC)CH(OC)_2$], 4.72 (dd, J = 4.9, 8.5 Hz, 1 H, CHOSO₂), 4.93 (dd, J = 4.1, 10.7 Hz, 1 H, ArCHSO₃), 5.78 [d, J = 3.9 Hz, 1 H, $CH(OC)_2$], 6.85 (dd, J = 2.4, 8.2 Hz, 1 H, ArH), 6.97 (br t, J = 2.4 Hz, 1 H, ArH), 7.13 (d, J = 8.0 Hz, 1 H, ArH), 7.30 (br s, 1 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 25.4, 26.4, 26.7, 26.8 [O₂C(CH₃)₂], 35.4 (CH₂CO₂CH₃), 52.4 (CO₂CH₃), 55.4 (ArOCH₃), 64.1 (ArCHSO₃), 65.7 (OCH₂CH), 74.9 [CH(OC)CH₂O], 76.8 [CH(OC)CH(OC)CH₂O], 77.7 [CH(OC)CH(OC)₂], 78.0 (CHOSO₂), 103.9 [CH(OC)₂], 110.2, 113.8 [O₂C(CH₃)₂], 114.9, 115.6, 121.9, 132.4 (ArCH), 129.8 (ArC), 159.9 (ArCOCH₃), 169.5 (C=O).

MS (CI, 100 eV, methane): m/z (%) = 517 (2) [M⁺ + 1], 516 (14) [M⁺], 501 (34) [M⁺ - CH₃], 459 (22), 429 (7), 375 (36), 274 (11), 203 (42), 193 (100), 151 (35), 101 (69).

Anal. Calcd for $C_{23}H_{32}O_{11}S$ (516.56): C, 53.48; H, 6.24. Found: C, 53.53; H, 6.39.

β-Methoxycarbonyl Sulfonate (R)-2f

According to GP2, the sulfonate **1d** (0.189 g, 0.5 mmol) was deprotonated with *n*-BuLi (0.35 mL, 1.1 equiv) and reacted with methyl bromoacetate (80 μ L, 1.5 equiv). Work up and flash chromatography (EtOAc–*n*-pentane, 1:3) yielded the sulfonate **2f** as a mixture of diastereomers (0.110 g, 49%); de = 40% (NMR).

IR (KBr): 2990, 2901, 1727, 1651, 1442, 1370, 1252, 1163, 1114, 1017, 929, 879, 842, 607 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): $\delta = 1.37$ [s, 6 H, O₂C(CH₃)₂], 1.45, 1.56 [2 × s, 6 H, O₂C(CH₃)₂], 1.98 [s, 3 H, CH₂=CCH₃], 2.99 [dd, J = 10.6, 16.6 Hz, CHHCO₂CH₃ (minor)], 3.00 [dd, J = 11.1, 16.3 Hz, CHHCO₂CH₃ (major)], 3.25 [dd, J = 4.2, 16.6 Hz, CHHCO₂CH₃ (major)], 3.29 [dd, J = 3.7, 16.3 Hz, CHHCO₂CH₃ (major)], 3.70 (s, 3 H, CO₂CH₃), 3.91 (m, 1 H, OCHHCHO], 4.10 [m, 2 H, OCHHCHO, CH(OC)CH(OC)CH₂O], 4.31 [m, 2 H, CH(OC)CH₂O, CH(OC)CH(OC)₂], 4.80 [m, 2 H, CHOSO₂, CHSO₃], 5.22 [m, 1 H, CH₂=CH(CH₃) (minor)], 5.28 [br s, 1 H, CH₂=CH(CH₃) (major)], 5.49 [d, J = 3.7 Hz, 1 H, CH(OC)₂ (minor)], 5.82 [d, J = 3.5 Hz, 1 H, CH(OC)₂ (major)].

¹³C NMR (75 MHz, CDCl₃, major isomer): δ = 22.0 [CH₂=C(CH₃)], 25.1, 26.2, 26.6, 26.7 [O₂C(CH₃)₂], 34.0 (CH₂CO₂CH₃), 52.2 (CO₂CH₃), 64.4 (CHSO₃), 65.7 [OCH₂CH], 74.9 [CH(OC)CH₂O], 76.7, 77.2, 77.6 [CHO], 104.0 [CH(OC)₂], 110.2, 113.7 [O₂C(CH₃)₂], 119.8 [CH₂=C(CH₃)], 136.1 [CH₂=C(CH₃)], 169.9 (C=O).

MS (EI, 70 eV): m/z (%) = 435 (82) [M⁺ – CH₃], 361 (8), 167 (7), 127 (100), 113 (34), 101 (52), 85 (41), 59 (11).

Anal. Calcd for $C_{19}H_{30}O_{10}S$ (450.51): C, 50.66; H, 6.71. Found: C, 50.66; H, 6.85.

Methyl (*R*)-3-Methoxysulfonyl-3-phenylpropionate [(*R*)-3a]

The sulfonate (*R*)-**2a** (0.560 g, 1.15 mmol) was dissolved in a solution of MeOH–H₂O (18:2 mL). To the solution was added Pd(OAc)₂ (15 mol%) and the mixture was refluxed for 4 d. The palladium residues were removed by filtration and the filter cake was washed with MeOH. The filtrate was treated with an ethereal solution of diazomethane until the yellow color persisted. The solvent was evaporated under reduced pressure and the crude product was purified by flash column chromatography (SiO₂; Et₂O–*n*-pentane, 1:3) to give the methyl sulfonate (*R*)-**3a** as a colorless solid (0.279 g, 94%); ee \geq 98% [based on the de value of (*R*)-**2a**]; mp 95 °C; [α]_D²⁵ +13.85 (*c* = 1.2, CHCl₃).

IR (KBr): 2966, 1728, 1602, 1496, 1454, 1354, 1243, 1156, 1087, 986, 824, 795, 773, 743, 700, 569 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 3.15 (dd, *J* = 8.9, 16.8 Hz, 1 H, CHHCO₂CH₃), 3.41 (dd, *J* = 5.4, 16.8 Hz, 1 H, CHHCO₂CH₃), 3.63 (s, 3 H, OCH₃), 3.69 (s, 3 H, OCH₃), 4.83 (dd, *J* = 5.4, 8.9 Hz, 1 H, CH₂CHSO₃CH₃), 7.36–7.48 (m, 5 H, ArH).

¹³C NMR (75 MHz, CDCl₃): δ = 35.3 (CH₂), 52.3 (OCH₃), 57.3 (OCH₃), 62.4 (CHSO₃), 129.0, 129.4, 129.5 (ArCH), 131.6 (ArC), 169.8 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 258 (8) [M⁺], 163 (31), 121 (100), 104 (9), 91 (6), 77 (5), 59 (6).

Anal. Calcd for $C_{11}H_{14}O_5S$ (258.30): C, 51.15; H, 5.46. Found: C, 50.62; H, 5.52.

Isopropyl (1*R*,2*R*)-2-Nitromethyl-1-phenylpentane Sulfonate [(*R*,*R*)-6a]

According to GP 4, the sulfonate (*R*,*R*)-4a (500 mg, 1.0 mmol) was refluxed in a solution of 2% TFA–EtOH (18 mL) and H₂O (2 mL) for 15 h. After removal of the solvent in vacuo, a solution of the crude sulfonic acid and triisopropylorthoformate (0.8 mL, 5 mmol) in CH₂Cl₂ (10 mL) was refluxed for 3 h. The crude product was purified by column chromatography (SiO₂; Et₂O–*n*-pentane, 15:85) to give (*R*,*R*)-6a as a colorless solid (234 mg, 75%); mp 44 °C; de \geq 98% (¹H NMR); ee \geq 98% [based on the de value of the sulfonate (*R*,*R*)-4a]; [α]_D²³ +13.3 (*c* = 1.0, CHCl₃).

IR (KBr): 3036, 2970, 2937, 2876, 1552, 1455, 1386, 1355, 1325, 1224, 1161, 1089, 909, 736, 701, 632, 555 $\rm cm^{-1}.$

¹H NMR (400 MHz, CDCl₃): $\delta = 0.82$ (t, J = 7.3 Hz, 3 H, CH₂CH₃), 1.04 (d, J = 6.3 Hz, 3 H, OCH(CH₃)CH₃), 1.20 (m, 1 H, CHCHHCH₂CH₃), 1.20–1.39 (m, 2 H, CH₂CH₃), 1.30 (d, J = 6.0Hz, 3 H, OCH(CH₃)CH₃), 1.60 (m, 1 H, CHCHHCH₂CH₃), 3.10 (m, 1 H, CHCH₂NO₂), 4.49 (d, J = 8.0 Hz, 1 H, ArCHSO₃), 4.62 (dd, J = 6.3, 14.0 Hz, 1 H, CHHNO₂), 4.67 [sept, J = 6.3 Hz, 1 H, CH(CH₃)₂], 4.78 (dd, J = 5.5, 14.0 Hz, 1 H, CHHNO₂), 7.39–7.46 (m, 5 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 13.7 (CH₂CH₃), 19.2 (CH₂CH₃), 22.2, 23.4 [CH(CH₃)₂], 30.3 (CH₂CH₂CH₃), 38.4 (CHCH₂NO₂), 68.1 (CHSO₃), 76.9 (CH₂NO₂), 79.0 (SO₃CH), 128.8, 129.2, 129.7 (ArCH), 131.0 (ArC).

MS (CI, 100 eV, methane): *m*/*z* (%) = 330 (1) [M⁺ + 1], 316 (2), 288 (11), 206 (100), 159 (22), 117 (2), 91 (1).

Anal. Calcd for $C_{15}H_{23}NO_5S$ (329.41): C, 54.69; H, 7.04; N, 4.25. Found: C, 54.90; H, 7.13; N, 4.24.

Isopropyl (1*R*,2*R*)-2-Nitromethyl-3-methyl-1-phenylbutane Sulfonate [(*R*,*R*)-6b]

According to GP 4, the sulfonate (*R*,*R*)-**4b** (530 mg, 1.0 mmol) was refluxed in a solution of 2% TFA–EtOH (18 mL) and H₂O (2 mL) for 15 h. After removal of the solvent in vacuo, a solution of the crude sulfonic acid and triisopropylorthoformate (0.8 mL, 5 mmol) in CH₂Cl₂ (10 mL) was refluxed for 3 h. The crude product was purified by column chromatography (SiO₂; Et₂O–*n*-pentane, 1:4) to give (*R*,*R*)-**6b** as a colorless solid (141 mg, 43%); mp 101 °C; de \geq 98% (¹H NMR); ee \geq 98% [based on the de value of the sulfonate (*R*,*R*)-**4b**]; [α]_D²⁴ +33.7 (*c* = 1.1, CHCl₃).

IR (KBr): 3066, 2965, 1565, 1499, 1460, 1427, 1386, 1349, 1333, 1167, 1091, 916, 707, 601 $\rm cm^{-1}$.

¹H NMR (300 MHz, CDCl₃): $\delta = 0.65$ [d, J = 6.9 Hz, 3 H, CH(CH₃)₂], 0.95 [d, J = 6.9 Hz, 3 H, CH(CH₃)₂], 1.02 [d, J = 6.4 Hz, 3 H, SO₃CH(CH₃)₂], 1.28 [d, J = 6.2 Hz, 3 H, SO₃CH(CH₃)₂], 1.81 (m, 1 H, CHCH(CH₃)₂], 3.33 (m, 1 H, CHCH₂NO₂), 4.29 (d, J = 9.9

Hz, 1 H, ArCHSO₃), 4.54–4.68 [m, 2 H, SO₃C*H*(CH₃)₂, C*H*HNO₂], 5.03 (dd, *J* = 5.0, 14.8 Hz, 1 H, CH*H*NO₂), 7.39–7.49 (m, 5 H, ArH).

 ^{13}C NMR (75 MHz, CDCl₃): δ = 16.0, 20.6 [CH(CH₃)₂], 22.2, 23.4 [SO₃CH(CH₃)₂], 28.1 [CH(CH₃)₂], 42.9 (CHCH₂NO₂), 68.8 (CHSO₃), 73.4 (CH₂NO₂), 79.1 (SO₃CH), 129.0, 129.3, 129.7 (ArCH), 132.3 (ArC).

MS (CI, 100 eV, methane): m/z (%) = 330 (24) [M⁺ + 1], 316 (2), 288 (48), 206 (100), 159 (14), 117 (2), 91 (2).

Anal. Calcd for $C_{15}H_{23}NO_5S$ (329.41): C, 54.69; H, 7.04; N, 4.25. Found: C, 54.63; H, 7.15; N, 4.34.

Isopropyl (1*R*,2*R*)-2-Nitromethyl-1-phenylbutane Sulfonate [(*R*,*R*)-6c]

According to GP 4, the sulfonate (*R*,*R*)-4c (510 mg, 1.0 mmol) was refluxed in a solution of 2% TFA–EtOH (18 mL) and H₂O (2 mL) for 15 h. After removal of the solvent in vacuo, a solution of the crude sulfonic acid and triisopropylorthoformate (0.8 mL, 5 mmol) in CH₂Cl₂ (10 mL) was refluxed for 3 h. The crude product was purified by column chromatography (SiO₂; Et₂O–*n*-pentane, 1:9) to give (*R*,*R*)-6c as a colorless viscous liquid (262 mg, 84%); de \geq 98% (¹H NMR); ee \geq 98% [based on the de value of the sulfonate (*R*,*R*)-4c]; [α]_D²² +29.5 (*c* = 1.0, CHCl₃).

IR (film): 2980, 2940, 2882, 1555, 1497, 1459, 1354, 1170, 1093, 912, 755, 704, 605 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): $\delta = 0.88$ (t, J = 7.4 Hz, 3 H, CH₂CH₃), 1.03 [d, J = 6.2 Hz, 3 H, OCH(CH₃)CH₃], 1.23 (m, 1 H, CHCHHCH₃), 1.29 [d, J = 6.2 Hz, 3 H, OCH(CH₃)CH₃], 1.67 (dqd, J = 3.7, 7.4, 14.6 Hz, 1 H, CHCHHCH₃), 3.08 (m, 1 H, CHCH₂NO₂), 4.47 (d, J = 8.7 Hz, 1 H, ArCHSO₃), 4.66 [sept, J = 6.2 Hz, 1 H, CH(CH₃)₂], 4.72 (dd, J = 5.9, 14.1 Hz, 1 H, CHHNO₂), 4.80 (dd, J = 6.2, 14.1 Hz, 1 H, CHHNO₂), 7.38–7.48 (m, 5 H, ArH).

¹³C NMR (75 MHz, CDCl₃): δ = 10.1 (CH₂CH₃), 21.4 (CH₂CH₃), 22.2, 23.4 [CH(CH₃)₂], 39.8 (CHCH₂NO₂), 68.1 (CHSO₃), 75.0 (CH₂NO₂), 79.3 (SO₃CH), 129.1, 129.4, 129.9 (ArCH), 131.4 (ArC).

MS (CI, 100 eV, methane): m/z (%) = 316 (1) [M⁺ + 1], 302 (3), 274 (18), 220 (2), 192 (100), 145 (18), 91 (1).

Anal. Calcd for $C_{14}H_{21}NO_5S$ (315.39): C, 53.32; H, 6.71; N, 4.44. Found: C, 53.06; H, 6.74; N, 4.71.

Methyl (1*R*,2*R*)-2-Hydroxymethyl-3-methyl-1-phenylbutane Sulfonate [(*R*,*R*)-7]

To a solution of the ester (*R*,*R*)-**5b** (77 mg, 0.25 mmol) in anhyd CH₂Cl₂ (2.5 mL) was added a solution of DIBAL in CH₂Cl₂ (1 M, 0.65 mL) dropwise at -78 °C under Ar. The reaction mixture was stirred at -78 °C for 30 min, then stirring was continued at -20 °C for 3 h. The mixture was quenched with a large excess of MeOH and a few drops of methanolic HCl (2 N). After removal of MeOH in vacuo, the solid was triturated with CH₂Cl₂ for 30 min. The mixture was filtered and washed with CH₂Cl₂. The solvent was evaporated under reduced pressure and the crude product was purified by flash column chromatography (SiO₂; Et₂O-*n*-pentane, 3:7) to give the product (*R*,*R*)-7 as a colorless viscous liquid (63 mg, 95%); $d \ge 98\%$ (NMR and HPLC); $ee \ge 98\%$ (HPLC, Chiralpak AD; *n*-heptane-*i*-PrOH, 95:5); $[a]_D^{22} + 39.0$ (*c* = 1.6, CHCl₃).

IR (CHCl₃): 3397, 2961, 1537, 1497, 1456, 1349, 1163, 1041, 990, 823, 758, 704, 594 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): $\delta = 0.80$ [d, J = 7.0 Hz, 3 H, CH(CH_{3})₂], 0.96 [d, J = 7.0 Hz, 3 H, CH(CH_{3})₂], 1.52 (m, 1 H, CHCH(CH₃)₂], 2.33 (m, 1 H, CHCH₂OH), 2.62 (br s, 1 H, OH), 3.45 (s, 3 H, SO₃CH₃), 3.98 (dd, J = 3.0, 13.1 Hz, 1 H, CHHOH), 4.15 (dd, J = 3.5, 13.1 Hz, 1 H, CHHOH), 4.63 (d, J = 11.1 Hz, 1 H, ArCHSO₃), 7.39–7.49 (m, 5 H, ArH).

¹³C NMR (75 MHz, CDCl₃): δ = 16.8, 21.8 [CH(CH₃)₂], 27.8 [CH(CH₃)₂], 46.9 (CHCH₂OH), 57.5 (SO₃CH₃), 60.0 (CHCH₂OH), 68.1 (CHSO₃), 129.0, 129.1, 129.7 (ArCH), 132.7 (ArC).

MS (CI, 100 eV, methane): m/z (%) = 273 (1) [M⁺ + 1], 177 (17), 159 (100), 147 (8), 137 (9), 119 (5), 105 (5), 91 (3), 75 (14).

Anal. Calcd for $C_{13}H_{20}O_4S$ (272.36): C, 57.33; H, 7.40. Found: C, 57.07; H, 7.19.

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