Asymmetric Synthesis of 1,2-*anti*-Disubstituted Taurine Derivatives

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Received 12 February 2009

Abstract: An efficient asymmetric synthesis of *anti*-1,2-disubstituted taurine derivatives through nucleophilic addition of phenylmethanesulfonate to various *N*-acylimines in the presence of 1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose as a chiral auxiliary is described. The taurine derivatives were obtained in three steps with good overall yields (36–61%) and excellent enantiomeric excesses (83–98%). The diastereomeric excesses of 15–91% could be improved to 90–98% by column chromatography or recrystallization. The relative and absolute configurations of the products were determined by means of an X-ray crystal structure analysis.

Key words: taurine, asymmetric synthesis, sugar auxiliary, *N*-acylimines, α-amido sulfones, chiral auxiliary

Sulfonic acids and their derivatives are important biologically active constituents of mammals, marine algae, fish, and shellfish.[1] The best known are 2-aminoethanesulfonic acid (taurine) and related compounds such as 3-aminopropanesulfonic acid (homotaurine), 2-carbamimidamidoethanesulfonic acid (*N*-guanidinotaurine), cysteic acid, and 2-hydroxyethanesulfonic acid (isethionic acid) (Figure 1). Taurine is found in relatively high concentrations in the central nervous system, brain, heart, retina, and muscles, and is involved in various physiological processes such as brain development, neurotransmission, and immunomodulation.[2]

In view of the important physiological effects of these naturally occurring aminosulfonic acids, which can be regarded as sulfur analogues of amino acids, the development of new diastereo- and enantioselective methods for their synthesis is highly desirable.

Several reports have already been devoted to the synthesis of taurine derivatives. 1-Substituted taurines have been synthesized from olefins,[3] from β-amino secondary alcohols,[4] and from epoxides.[5] 2-Substituted taurines have been prepared from β-amino primary alcohols,[6] from aziridines,[7] and from 2-nitroalkanesulfonic acids.[8] 1,1-Disubstituted taurines are available from ketones through Corey–Chaykovsky epoxidation, episulfidation, and ammonia-induced ring cleavage, followed by oxidation with performic acid.[9] 1,2-Disubstituted taurines have been prepared from olefins[9,10] and from epoxides.[5] 2,2-Disubstituted taurines have been synthesized from aziridines,[11] from amino alcohols,[6f] and from ketones through the Strecker amino acid synthesis.[12]

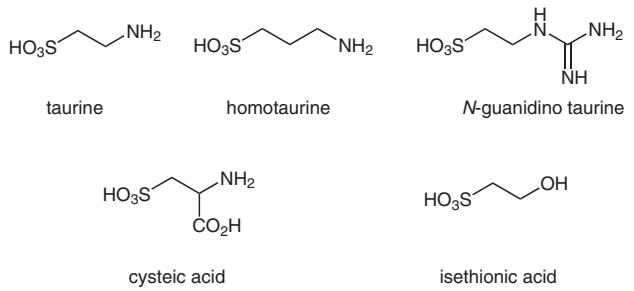


Figure 1 Taurine and related compounds

Our group has described an efficient asymmetric synthesis of 2-substituted and 1,2-disubstituted taurine derivatives through aza-Michael addition of the enantiopure hydrazines (2*S*)-2-(methoxymethyl)pyrrolidin-1-amine (SAMP) or (2*R*,3a*R*,6a*R*)-2-(methoxymethyl)hexahydrocyclopenta[*b*]pyrrol-1(2*H*)-amine (RAMBO) to α,β-unsaturated sulfonates in the presence of a Lewis acid catalyst.[13]

In our ongoing research on the asymmetric synthesis of sulfonic acid derivatives, we planned to gain access to 1,2-disubstituted taurine derivatives through nucleophilic addition to an *N*-acylimine of a chiral phenylmethanesulfonate bearing an enantiopure sugar auxiliary.

In previous communications and a full paper,[14] we reported on efficient asymmetric electrophilic α-substitution reactions of various alkyl halides and nitroalkenes with benzyl sulfonates bearing 1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose as a chiral auxiliary. In subsequent investigations, we extended this method by using allylic halides as electrophiles to give α,γ-substituted γ-sultones diastereo- and enantioselectively.[15] We also used this method in a highly efficient asymmetric synthesis of α,γ-substituted γ-amino sulfonates through diastereoselective ring-opening of the γ-sultones.[16]

Moreover, in our synthesis of various optically active α,γ-substituted sulfonates from the sultones,[17] we have shown that the ring-opening reaction of the γ-sultones proceeds by an S_N2 mechanism with inversion of configuration at the attacked γ-carbon. Very recently, the method has been extended to alkyl bromoacetates[18] and aldehydes[19] as electrophiles.

We now wish to describe a short three-step asymmetric synthesis of *anti*-configured 1,2-disubstituted taurine derivatives through addition of phenylmethanesulfonate to various *N*-acylimines using 1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose as a chiral auxiliary.

SYNTHESIS 2009, No. 10, pp 1683–1688
Advanced online publication: 14.04.2009
DOI: 10.1055/s-0029-1216643; Art ID: Z02409SS

Because of their high electrophilicity, *N*-acylimines are much more reactive than the corresponding *N*-alkyl and *N*-aryl analogues. *N*-Acylimines can be generated in situ from the corresponding α-amido sulfones **2**, which serve as stable precursors, by elimination with a suitable base. We used the benzyloxycarbonyl (Cbz) group as an activating *N*-acyl substituent to obtain the final 1,2-disubstituted taurine derivatives in a protected form that can easily be cleaved under mild conditions.

First, we investigated the reaction between α-amido sulfone **2a** and the enantiopure sulfonate **1** (Figure 2). One equivalent of sulfonate **1** was deprotonated with one equivalent of butyllithium at –100 °C and then treated with 0.5 equivalents of α-amido sulfone **2a** at –100 °C for 2 h and then overnight at –78 °C. After aqueous workup, the 1,2-disubstituted taurine derivative **3a** was obtained in very good yield (82%). In this method, 0.5 equivalents of the enantiopure sulfonate **1** are regenerated in the elimination step that forms the corresponding acylimine from **2a**, and can be separated and recovered by flash column chromatography.

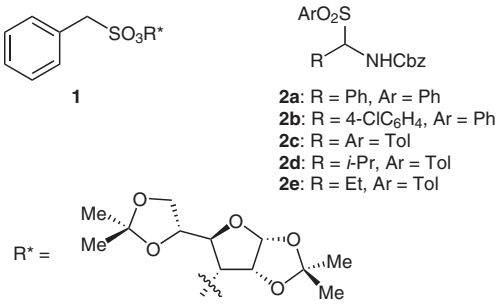
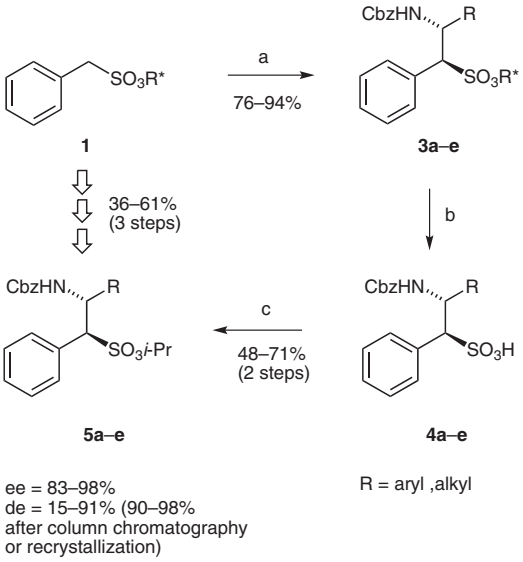


Figure 2 Enantiopure sulfonate **1** and α-amido sulfones **2a–e**

Cleavage of the chiral auxiliary was accomplished by treatment with trifluoroacetic acid in refluxing ethanol. Subsequent treatment of the resulting sulfonic acid **4a** with triisopropyl orthoformate in dichloromethane gave the final protected 1,2-disubstituted taurine derivative **5a** in good overall yield (58%, three steps) and high stereoselectivities [ee = 97%; de = 66% (98% after recrystallization)] (Scheme 1).

We then applied these conditions to various α-amido sulfones **2**. Thus, the enantiopure sulfonate **1** was deprotonated with butyllithium in tetrahydrofuran at –100 °C, the α-amido sulfone was added at –100 °C, and the mixture was kept for 2 h at –100 °C and then overnight at –78 °C to give the final 1,2-disubstituted taurine derivative **5a–e** in good overall yields and high stereoselectivities. The results are summarized in Table 1.

A single crystal X-ray structure analysis carried out on compound **5d** provided unambiguous proof of the structure (Figure 3).[20] The configuration of the stereogenic center at the α-position is *S* and that at the β-position is *R*. Therefore, on the assumption that the reaction mechanism is uniform, all the 1,2-disubstituted taurine derivatives **5a–e** are expected to have a (1*S*,2*R*)-configuration.



Scheme 1 Synthesis of the protected 1,2-disubstituted taurine derivatives **5a–e** from the enantiopure sulfonate **1**. *Reagents and conditions*: (a) BuLi (1.0 equiv), THF, –100 °C, 1 h, then α-amido sulfone **2a–e** (0.5 equiv), –100 °C, 2 h, then –78 °C, overnight; (b) 2% TFA in EtOH, reflux; (c) $(i\text{-PrO})_3CH$, CH_2Cl_2, rt.

Table 1 Asymmetric Syntheses of Protected Taurine Derivatives **5a–e**

Product	R	Yield (%)[a]	de (%)[b]	ee (%)[b]
5a	Ph	58	66 (98)[c]	97
5b	4-ClC_6H_4	36	35 (98)[d]	93
5c	4-Tol	61	37 (90)[d]	98
5d	*i*-Pr	49	91 (98)[d]	98
5e	Et	46	15	83

[a] Overall yield of the three-step synthesis.
[b] Determined by HPLC on a chiral stationary phase.
[c] The value in parentheses is after recrystallization.
[d] The values in parentheses is after flash column chromatography.

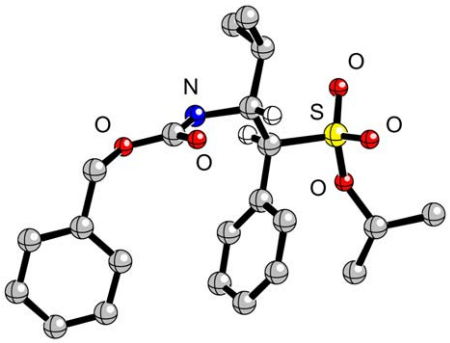


Figure 3 X-ray crystal structure of **5d**

In summary, we have developed an efficient three-step asymmetric synthesis of protected 1,2-disubstituted taurine derivatives starting from the sulfonate **1**. The resulting *anti*-configured β-amino sulfonates **5a–e** were

obtained in moderate-to-good overall yields (36–61%) and good-to-excellent stereoselectivities [ee = 83–98%, de = 15–91% (90–98% after column chromatography or recrystallization)]. The relative and absolute configuration of the compounds was determined by X-ray crystal structure analysis on a typical example.

All solvents were dried by conventional methods. Starting materials and reagents were purchased from commercial suppliers and used without further purification. THF was freshly distilled from Na/Pb alloy under argon. Preparative column chromatography: Merck silica gel 60, particle size 0.040–0.063 mm (230–240 mesh, flash). Analytical TLC: silica gel 60, F254 plates (Merck, Darmstadt). Optical rotation values were measured on a PerkinElmer P241 polarimeter. IR spectra were recorded on a PerkinElmer 1760 FT-IR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on a Gemini 300 or a Varian Inova 400, and all measurements were performed with tetramethylsilane as the internal standard. Mass spectra were acquired on a Finnigan SSQ 7000 spectrometer (EI: 70 eV). Microanalyses were obtained with a Vario EL element analyzer.

1,2-Disubstituted Taurine Derivatives 3a–e; General Procedure

The enantiopure sulfonate **1** (1.0 equiv) was dissolved in anhyd THF (20 mL) and the solution was cooled to –100 °C. After 20 min, BuLi (1.0 equiv) was added dropwise. The solution was stirred for 1 h, after which the α-amido sulfone **2** (0.5 equiv) was added. The mixture was stirred for 2 h at –100 °C, and then at –78 °C to r.t. overnight. The mixture was quenched with H_2O (5 mL) and evaporated to dryness. The crude product was purified by flash column chromatography (silica gel, Et_2O–pentane 1:1) to yield the sulfonate esters **3a**–**e**.

1,2:5,6-Di-*O*-isopropylidene-α-d-allofuranos-3-yl (1*S*, 2*R*)-2-[(Benzyloxycarbonyl)amino]-1,2-diphenylethanesulfonate (3a)

According to the general procedure, the sulfonate **1** (400 mg, 0.97 mmol) was deprotonated with a 1.6 M solution of BuLi in hexane (0.60 mL) and allowed to react with α-amido sulfone **2a** (185 mg, 0.49 mmol). Workup and flash column chromatography gave **3a** as a colourless solid; yield: 262 mg (82%); mp 123 °C.

IR (KBr): 3350, 2987, 2937, 2361, 1718, 1522, 1455, 1373, 1244, 1168, 1121, 1025, 922, 878, 834, 756, 699, 606, 512 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30 (s, 3 H, CH_3), 1.33 (s, 3 H, CH_3), 1.46 (s, 3 H, CH_3), 1.57 (s, 3 H, CH_3), 3.77 (dd, *J* = 7.1, 9.0 Hz, 1 H, C*H*HOC), 3.97 (dd, *J* = 7.3, 9.0 Hz, 1 H, CH*H*OC), 4.03 (d, *J* = 5.7 Hz, 1 H, $SO_3CHCHCHCH_2O$), 4.18 [br s, 1 H, $SO_3CHCHOC(CH_3)_2$], 4.30 (br s, 1 H, $SO_3CHCHCHO$), 4.76 (dd, *J* = 4.6, 8.5 Hz, 1 H, $PhCHSO_3CH$), 4.81 (br s, 1 H, $PhCHSO_3$), 5.06 [d, *J* = 12.3 Hz, 1 H, C(O)CH*H*Ph], 5.10 [d, *J* = 12.2 Hz, 1H, C(O)C*H*HPh], 5.48 (br s, 1 H, NH), 5.66 [d, *J* = 3.7 Hz, 1 H, $SO_3CHCHCH(O)_2$], 5.90 (dd, *J* = 4.3, 9.6 Hz, 1 H, PhC*H*NH), 7.10–7.20 (m, 15 H, Ph*H*).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.2 (CH_3), 26.4 (CH_3), 26.7 (CH_3), 26.8 (CH_3), 55.1 (Ph*C*HNH), 65.2 (*C*H_2OC), 67.2 (O*C*H_2Ph), 72.1 (Ph*C*HSO_3), 74.5 (CHO), 76.8 (CHO), 77.7 (CHO), 103.6 [*C*H(OC)$_2$], 110.1 [(O)$_2$*C*(CH$_3$)$_2$], 113.6 [(O)$_2$*C*(CH$_3$)$_2$], 127.0, 128.0, 128.3, 128.4, 128.8, 129.4, 130.3 (CH_{arom}), 136.1, 138.3 (C_{arom}), 155.1 (NH*C*O).

MS (EI, 70 eV): *m/z* (%) = 638 (12), 286 (6), 240 (68), 196 (43), 180 (5), 113 (5), 101 (10), 91 (100), 56 (6).

Anal. Calcd for $C_{34}H_{39}NO_{10}S$: C, 62.47; H, 6.01; N, 2.14. Found: C, 62.39; H, 6.26; N, 2.17.

1,2:5,6-Di-*O*-isopropylidene-α-d-allofuranos-3-yl (1*S*, 2*R*)-2-[(Benzyloxycarbonyl)amino]-2-(4-chlorophenyl)-1-phenylethanesulfonate (3b)

According to the general procedure, the sulfonate **1** (928 mg, 2.24 mmol) was deprotonated with a 1.6 M solution of BuLi in hexane (1.40 mL) and allowed to react with α-amido sulfone **2b** (465 mg, 1.12 mmol). Workup and flash column chromatography gave **3b** as a colourless solid; yield: 581 mg (76%); mp 135 °C.

IR (KBr): 3373, 2988, 2932, 1720, 1528, 1497, 1455, 1375, 1244, 1168, 1022, 877, 832, 758, 698, 517 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.29 (s, 3 H, CH_3), 1.36 (s, 3 H, CH_3), 1.45 (s, 3 H, CH_3), 1.56 (s, 3 H, CH_3), 3.78 (dd, *J* = 7.3, 8.5 Hz, 1 H, C*H*HOC), 3.94–4.02 (m, 2 H, CH*H*OC, $SO_3CHCHCHCH_2O$), 4.16 [dd, *J* = 4.0, 6.0 Hz, 1 H, $SO_3CHCHOC(CH_3)_2$], 4.25–4.31 (m, 1 H, $SO_3CHCHCHO$), 4.71–4.79 (m, 2 H, $PhCHSO_3CH$, $PhCHSO_3$), 5.09 [s, 2 H, C(O)CH_2Ph], 5.61 (d, *J* = 9.3 Hz, 1 H, NH), 5.65 [d, *J* = 3.7 Hz, 1 H, $SO_3CHCHCH(O)_2$], 5.79 (dd, *J* = 4.7, 9.2 Hz, 1 H, PhC*H*NH), 7.06–7.42 (m, 14 H, PhH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.1 (CH_3), 26.2 (CH_3), 26.6 (CH_3), 26.7 (CH_3), 54.9 (Ph*C*HNH), 65.1 (*C*H_2OC), 67.3 (O*C*H_2Ph), 71.8 (Ph*C*HSO_3), 74.6 (CHO), 76.8 (CHO), 77.6 (CHO), 77.7 (CHO), 103.6 [*C*H(OC)$_2$], 110.2 [(O)$_2$*C*(CH$_3$)$_2$], 113.6 [(O)$_2$*C*(CH$_3$)$_2$], 128.1, 128.2, 128.5, 128.6, 129.0, 129.7, 130.2 (CH_{arom}), 134.0, 136.0, 136.9 (C_{arom}), 155.1 (NH*C*O).

MS (EI, 70 eV): *m/z* (%) = 672 (5), 274 (59), 230 (26), 214 (11), 179 (14), 166 (19), 127 (6), 108 (9), 91 (100), 65 (5).

Anal. Calcd for $C_{34}H_{38}NO_{10}SCl$: C, 59.34; H, 5.57; N, 2.04. Found: C, 59.44; H, 5.83; N, 1.90.

1,2:5,6-Di-*O*-isopropylidene-α-d-allofuranos-3-yl (1*S*, 2*R*)-2-[(Benzyloxycarbonyl)amino]-1-phenyl-2-(4-tolyl)ethanesulfonate (3c)

According to the general procedure, the sulfonate **1** (900 mg, 2.17 mmol) was deprotonated with a 1.6 M solution of BuLi in hexane (1.36 mL) and allowed to react with α-amido sulfone **2c** (445 mg, 1.09 mmol). Workup and flash column chromatography gave **3c** as a colourless solid; yield: 685 mg (94%); mp 84 °C.

IR (KBr): 3852, 3742, 3620, 3364, 2986, 2361, 2340, 2329, 1720, 1522, 1459, 1373, 1243, 1168, 1024, 836, 739, 698, 601, 518 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30 (s, 3 H, CH_3), 1.34 (s, 3 H, CH_3), 1.46 (s, 3 H, CH_3), 1.56 (s, 3 H, CH_3), 2.32 (s, 3 H, PhCH_3), 3.77 (dd, *J* = 7.2, 9.0 Hz, 1 H, C*H*HOC), 3.97 (dd *J* = 7.4, 9.0 Hz, 1 H, CH*H*OC), 4.04 (d, *J* = 4.9 Hz, 1 H, $SO_3CHCHCHCH_2O$), 4.17 [br s, 1 H, $SO_3CHCHOC(CH_3)_2$], 4.29 (br s, 1 H, $SO_3CHCHCHO$), 4.73 (dd, *J* = 4.9, 8.7 Hz, 1 H, $PhCHSO_3CH$), 4.80 (br s, 1 H, $PhCHSO_3$), 5.05 [d, *J* = 12.3 Hz, 1 H, C(O)CH*H*Ph], 5.09 [d, *J* = 12.2 Hz, 1 H, C(O)CH*H*Ph], 5.47 (br s, 1 H, NH), 5.66 [d, *J* = 3.7 Hz, 1 H, $SO_3CHCHCH(O)_2$], 5.85 (dd, *J* = 4.4, 9.7 Hz, 1 H, PhC*H*NH), 6.99–7.40 (m, 14 H, PhH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.2 (Ph*C*H_3), 25.3 (CH_3), 26.4 (CH_3), 26.7 (CH_3), 26.8 (CH_3), 55.0 (CH_3Ph*C*HNH), 65.1 (*C*H_2OC), 67.1 (O*C*H_2Ph), 72.1 (Ph*C*HSO_3), 74.4 (CHO), 76.7 (CHO), 77.6 (CHO), 103.6 [*C*H(OC)$_2$], 110.1 [(O)$_2$*C*(CH$_3$)$_2$], 113.6 [(O)$_2$*C*(CH$_3$)$_2$], 126.6, 127.8, 128.1, 128.4, 128.7, 129.1, 130.0 (CH_{arom}), 135.3, 136.1, 137.8 (C_{arom}), 155.1 (NH*C*O).

MS (EI, 70 eV): *m/z* (%) = 652 (5), 544 (5), 300 (5), 254 (71), 236 (13), 210 (44), 193 (7), 146 (55), 107 (9), 101 (23), 91 (100), 55 (16).

Anal. Calcd for $C_{35}H_{41}NO_{10}S$: C, 62.95; H, 6.19; N, 2.10. Found: C, 62.79; H, 6.22; N, 2.21.

1,2:5,6-Di-*O*-isopropylidene-α-d-allofuranos-3-yl (1*S*, 2*R*)-2-[(Benzyloxycarbonyl)amino]-3-methyl-1-phenylbutane-1-sulfonate (3d)

According to the general procedure, the sulfonate **1** (1030 mg, 2.49 mmol) was deprotonated with a 1.6 M solution of BuLi in hexane (1.55 mL) and allowed to react with α-amido sulfone **2d** (449 mg, 1.24 mmol). Workup and flash column chromatography gave **3d** as a colourless solid; yield: 615 mg, (80%); mp 151 °C.

IR (KBr): 3361, 3034, 2979, 1712, 1533, 1457, 1362, 1246, 1169, 1115, 1018, 872, 840, 741, 700, 597, 462 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.89 [d, *J* = 6.7 Hz, 3 H, PhCH-CHCH(CH_3)CH_3], 1.05 [d, *J* = 6.6 Hz, 3 H, PhCH-CHC*H*(CH$_3$)CH_3], 1.26 (s, 3 H, CH_3), 1.36 (s, 3 H, CH_3), 1.47 (s, 3 H, CH_3), 1.52 (s, 3 H, CH_3), 1.85 [sept, *J* = 6.6 Hz, 1 H, PhCH-CHC*H*(CH$_3$)$_2$], 3.87 (dd, *J* = 6.1, 8.6 Hz, 1 H, C*H*HOC), 3.97–4.03 [m, 2 H, CH*H*OC, SO_3CHC*H*CHCH(O)$_2$], 4.10 (dd, *J* = 4.0, 8.7 Hz, 1 H, SO_3CHC*H*CHCH$_2$), 4.29–4.33 (m, 1 H, SO_3CHCHC*H*CH$_2$), 4.56–4.65 (m, 2 H, PhC*H*CHNH, PhCHC*H*NH), 4.67 [dd, *J* = 4.6, 8.7 Hz, 1 H, PhCHSO$_3$C*H*], 4.99 [s, 2 H, C(O)CH*H*Ph], 5.61 (d, *J* = 3.7 Hz, 1 H, SO_3CHCHC*H*(O)$_2$], 7.21–7.52 (m, 10 H, Ph*H*).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.5 [CH(*C*H$_3$)CH$_3$)], 20.3 [CH(CH$_3$)*C*H$_3$)], 25.3 (CH_3), 26.4 (CH_3), 26.7 (CH_3), 26.8 (CH_3), 31.2 [*C*H(CH$_3$)CH$_3$)], 55.9 (Ph*C*HNH), 65.1 (*C*H$_2$OC), 66.9 (O*C*H$_2$Ph), 68.8 (Ph*C*HSO$_3$), 74.4 (CHO), 77.6 (CHO), 77.7 (CHO), 103.4 [*C*H(OC)$_2$], 110.1 [(O)$_2$*C*(CH$_3$)$_2$], 113.5 [(O)$_2$*C*(CH$_3$)$_2$], 127.9, 128.0, 128.4, 128.9, 129.3, 130.0 (C_{arom}), 130.3 (CH_{arom}), 136.4 (C_{arom}), 155.7 (NH*C*O).

MS (EI, 70 eV): *m/z* (%) = 604 (7), 206 (35), 162 (52), 113 (5), 101 (15), 91 (100).

Anal. Calcd for $C_{31}H_{41}NO_{10}S$: C, 60.08; H, 6.67; N, 2.26. Found: C, 60.23; H, 6.59; N, 2.27.

1,2:5,6-Di-*O*-isopropylidene-α-d-allofuranos-3-yl (1*S*, 2*R*)-2-[(Benzyloxycarbonyl)amino]-1-phenylbutane-1-sulfonate (3e)

According to the general procedure, the sulfonate **1** (915 mg, 2.21 mmol) was deprotonated with a 1.6 M solution of BuLi in hexane (1.38 mL) and allowed to react with α-amido sulfone **2e** (385 mg, 1.11 mmol). Workup and flash column chromatography gave **3e** as a colourless solid; yield: 517 mg (77%); mp 132 °C.

IR (KBr): 3854, 3744, 3673, 3648, 3398, 2982, 2362, 2342, 2330, 1717, 1647, 1534, 1458, 1377, 1237, 1168, 1021, 930, 843, 742, 699, 599, 514, 464 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.91 (t, *J* = 7.3 Hz, 3 H, CH_3CH$_2$), 1.33 (s, 3 H, CH_3), 1.35 (s, 3 H, CH_3), 1.42 (s, 3 H, CH_3), 1.44–1.49 (m, 1 H, CH$_3$CH_2), 1.52 (s, 3 H, CH_3), 1.70–1.76 (m, 1 H, CH$_3$CH_2), 3.68 (dd, *J* = 6.9, 8.6 Hz, 1 H, C*H*HOC), 3.90 (dd, *J* = 6.7, 8.6 Hz, 1 H, C*H*HOC), 4.02 (dd, *J* = 4.4, 8.5 Hz, 1 H, SO_3CHC*H*CHCH$_2$O), 4.10–4.14 (m, 1 H, SO_3CHCHC*H*CH$_2$O), 4.32–4.40 (m, 1 H, PhCHC*H*NH), 4.64–4.69 (m, 2 H, PhC*H*CHNH, SO_3C*H*CHCHCH$_2$O), 4.78 (dd, *J* = 4.3, 5.0 Hz, 1 H, SO_3CHC*H*CHO$_2$), 5.11 [d, *J* = 12.2 Hz, 1 H, C(O)CH*H*Ph], 5.15 [d, *J* = 12.2 Hz, 1 H, C(O)C*H*HPh], 5.38 (d, *J* = 8.9 Hz, 1 H, NH), 5.76 [d, *J* = 3.7 Hz, 1 H, SO_3CHCHC*H*(O)$_2$], 7.29–7.45 (m, 10 H, Ph*H*).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 10.3 (*C*H$_3$CH$_2$), 25.5 (CH_3), 25.6 (CH$_3$*C*H$_2$), 26.2 (CH_3), 26.7 (CH_3), 54.4 (PhCH*C*HNH), 65.5 (*C*H$_2$OC), 66.8 (O*C*H$_2$Ph), 70.2 (Ph*C*HSO$_3$), 74.8 (CHO), 78.0 (CHO), 103.8 [*C*H(OC)$_2$], 110.2 [(O)$_2$*C*(CH$_3$)$_2$], 113.7 [(O)$_2$*C*(CH$_3$)$_2$], 127.9, 128.0, 128.4, 128.8, 129.2, 129.8 (CH_{arom}), 131.0 (C_{arom}), 136.5 (C_{arom}), 155.7 (NH*C*O).

MS (EI, 70 eV): *m/z* (%) = 605 (3), 590 (29), 547 (6), 414 (8), 356 (7), 320 (6), 282 (13), 238 (7), 192 (53), 148 (55), 113 (6), 101 (16), 91 (100).

Anal. Calcd for $C_{30}H_{39}NO_{10}S$: C, 59.49; H, 6.49; N, 2.31. Found: C, 59.73; H, 6.58; N, 2.52.

Isopropyl Sulfonates 5a–e; General Procedure

The taurine derivative **3** was dissolved in a solution of TFA in EtOH. The solution was refluxed for 16 h and then evaporated to dryness. The resulting oil was dissolved in CH_2Cl_2, (*i*-PrO)$_3$CH was added dropwise and the mixture was stirred at r.t.. The solvent was removed in vacuo and the crude product was purified by flash column chromatography (SiO_2, Et_2O-pentane 1:1) to yield the final products **5a-e**.

Isopropyl (1*S*, 2*R*)-2-[(Benzyloxycarbonyl)amino]-1,2-diphenylethanesulfonate (5a)

According to the general procedure, the sulfonic acid ester **3a** (271 mg, 0.42 mmol) was refluxed in EtOH (10 mL) containing TFA (0.2 mL) for 17 h. The resulting oil was dissolved in CH_2Cl_2 (10 mL) and (*i*-PrO)$_3$CH (1.0 mL, 4.5 mmol) was added dropwise. The mixture was stirred at r.t. for 4 h. Workup and flash column chromatography gave **5a** as a colourless solid; yield: 133 mg (71%); de = 66% (HPLC, Daicel Chiralpak IA, heptane–*i*-PrOH, 7:3) (de ≥ 98% after recrystallization from *i*-PrOH); ee = 97% (HPLC, Daicel Chiralpak IA, heptane–EtOH, 7:3); mp 121 °C; $[\alpha]_D^{25}$ +13.8 (*c* 1.0, $CHCl_3$).

IR (KBr): 3341, 3064, 3036, 2932, 1698, 1542, 1456, 1343, 1282, 1251, 1166, 1091, 1026 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.08 [d, *J* = 6.0 Hz, 3 H, SO_3CH(CH$_3$)CH_3], 1.26 [d, *J* = 6.0 Hz, 3 H, SO_3CH(CH_3)CH$_3$], 4.57 (br s, 1 H, PhC*H*SO$_3$), 4.76 [sept, *J* = 6.2, 1 H, (CH$_3$)$_2$C*H*O$_3$S], 5.05 [d, *J* = 12.3 Hz, 1 H, C(O)OCH*H*Ph], 5.09 [d, *J* = 12.3 Hz, 1 H, C(O)OC*H*HPh], 5.47 (br s, 1 H, N*H*), 5.78 (dd, *J* = 4.4, 9.5 Hz, 1 H, PhC*H*NH), 7.08–7.39 (m, 15 H, Ph*H*).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.7 (CH_3), 23.3 (CH_3), 55.2 (Ph*C*HNH), 67.2 (CH_2), 71.8 (Ph*C*HSO$_3$), 78.6 [SO_3CH(CH$_3$)$_2$], 126.9, 128.1, 128.4, 128.5, 128.8, 129.3, 130.2 (CH_{arom}), 136.1, 138.8 (C_{arom}), 155.1 (NH*C*O).

MS (EI, 70 eV): *m/z* (%) = 240 (32), 196 (26), 180 (6), 91 (100).

Anal. Calcd for $C_{25}H_{27}NO_5S$: C, 66.20; H, 6.00; N, 3.09. Found: C, 66.39; H, 6.34; N, 2.88.

Isopropyl (1*S*, 2*R*)-2-[(Benzyloxycarbonyl)amino]-2-(4-chlorophenyl)-1-phenylethanesulfonate (5b)

According to the general procedure, the sulfonic acid ester **3b** (360 mg, 0.52 mmol) was refluxed in EtOH (20 mL) containing TFA (0.2 mL) for 3 d. The resulting oil was dissolved in CH_2Cl_2 (10 mL) and (*i*-PrO)$_3$CH (1.4 mL, 6.3 mmol) was added dropwise. The mixture was stirred at r.t. for 20 h. Workup and flash column chromatography gave **3b** as a colourless solid; yield: 122 mg (48%); de = 35% (HPLC, Daicel Chiralpak IA, heptane–EtOH 3:1) (de ≥ 98% after flash column chromatography); ee = 93% (HPLC, Daicel Chiralpak IA, heptane–EtOH, 3:1); mp 132 °C; $[\alpha]_D^{25}$ +4.9 (*c* 1.1, $CHCl_3$).

IR (KBr): 2250, 3064, 2934, 2863, 1699, 1537, 1457, 1339, 1249, 1163, 1089, 1017, 915, 836, 739, 700, 585, 535 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.06 [d, *J* = 6.2 Hz, 3 H, SO_3CH(CH$_3$)CH_3], 1.26 [d, *J* = 6.2 Hz, 3 H, SO_3CH(CH_3)CH$_3$], 4.50 (d, *J* = 4.2 Hz, 1 H, PhC*H*SO$_3$), 4.74 [sept, *J* = 6.2, 1 H, (CH$_3$)$_2$C*H*O$_3$S], 5.04 [d, *J* = 12.2 Hz, 1 H, C(O)OCH*H*Ph], 5.08 [d, *J* = 12.4 Hz, 1 H, C(O)OC*H*HPh], 5.53 (br s, 1 H, N*H*), 5.69 (dd, *J* = 4.6, 9.0 Hz, 1 H, PhC*H*NH), 7.03–7.42 (m, 14 H, Ph*H*).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.5 (CH_3), 23.3 (CH_3), 55.0 (Ph*C*HNH), 67.2 (CH_2), 71.5 (Ph*C*HSO$_3$), 78.8 [SO_3CH(CH$_3$)$_2$], 128.1, 128.2, 128.5, 128.6, 128.7, 128.9, 129.3, 129.5, 130.1 (CH_{arom}), 134.0, 136.0, 137.3 (C_{arom}), 155.2 (NH*C*O).

MS (EI, 70 eV): *m/z* (%) = 274 (40), 230 (21), 226 (8), 91 (100), 65 (8).

Anal. Calcd for $C_{25}H_{26}NO_5SCl$: C, 61.53; H, 5.37; N, 2.87. Found: C, 61.40; H, 5.33; N, 2.96.

Isopropyl (1*S*, 2*R*)-2-[(Benzyloxycarbonyl)amino]-1-phenyl-2-(4-tolyl)ethanesulfonate (5c)

According to the general procedure, the sulfonic acid ester **3c** (771 mg, 1.16 mmol) was refluxed in EtOH (28 mL) containing TFA (0.56 mL) for 15 h. The resulting oil was dissolved in CH_2Cl_2 (28 mL) and (*i*-PrO)$_3$CH (2.8 mL, 12.6 mmol) was added dropwise. The mixture was stirred at r.t. for 4 h. Workup and flash column chromatography gave **5c** as a colourless solid; yield: 352 mg (65%); de = 37% (HPLC, Daicel Chiralpak IA, heptane–EtOH, 9:1) (de = 90% after flash column chromatography); ee = 98% (HPLC, Daicel Chiralpak IA, heptane–EtOH, 9:1); mp 119 °C; $[\alpha]_D^{25}$ +5.6 (*c* 1.2, $CHCl_3$).

IR (KBr): 3388, 3333, 3032, 2977, 2934, 1728, 1691, 1530, 1455, 1344, 1247, 1165, 1090, 1020, 913, 815, 739, 697, 595, 533 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.06 [d, *J* = 6.1 Hz, 3 H, $SO_3CH(CH_3)CH_3$], 1.25 [d, *J* = 6.1 Hz, 3 H, $SO_3CH(CH_3)CH_3$], 2.31 (s, 3 H, PhC*H*$_3$), 4.53 (br s, 1 H, PhC*H*SO_3), 4.73 [sept, *J* = 6.2, 1 H, $(CH_3)_2CHO_3S$], 5.02 [d, *J* = 12.4 Hz, 1 H, C(O)OCH*H*Ph], 5.06 [d, *J* = 12.3 Hz, 1 H, C(O)OC*H*HPh], 5.49 (br s, 1 H, N*H*), 5.73 (dd, *J* = 4.6, 9.6 Hz, 1 H, PhC*H*NH), 6.97–7.38 (m, 14 H, Ph*H*).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.3 (Ph*C*H$_3$), 22.7 (CH_3), 23.3 (CH_3), 55.1 (*C*HNH), 67.1 (CH_2), 71.9 (Ph*C*HSO_3), 78.5 [$SO_3CH(CH_3)_2$], 126.9, 128.0, 128.4, 128.7, 129.1, 129.2, 130.2 (CH_{arom}), 135.7, 136.2, 137.8 (C_{arom}), 155.1 (NH*C*O).

MS (EI, 70 eV): *m/z* (%) = 254 (54), 210 (48), 91 (100), 65 (5).

Anal. Calcd for $C_{26}H_{29}NO_5S$: C, 66.79; H, 6.25; N, 3.00. Found: C, 66.74; H, 6.65; N, 3.05.

Isopropyl (1*S*, 2*R*)-2-[(Benzyloxycarbonyl)amino]-3-methyl-1-phenylbutane-1-sulfonate (5d)

According to the general procedure, the sulfonic acid ester **3d** (404 mg, 0.65 mmol) was refluxed in EtOH (23 mL) containing TFA (0.46 mL) for 16 h. The resulting oil was dissolved in CH_2Cl_2 (24 mL) and (*i*-PrO)$_3$CH (2.3 mL, 10.4 mmol) was added dropwise. The mixture was stirred at r.t. for 22 h. Workup and flash column chromatography gave **5d** as a colourless solid; yield: 166 mg (61%); de = 91% (HPLC, Daicel Chiralpak IA, heptane–*i*-PrOH, 9:1) (de ≥ 98% after flash column chromatography); ee = 98% (HPLC, Daicel Chiralpak IA, heptane–*i*-PrOH, 9:1); mp 118 °C; $[\alpha]_D^{25}$ +67.6 (*c* 1.0, $CHCl_3$).

IR (KBr): 3386, 2870, 2877, 1724, 1537, 1500, 1458, 1384, 1347, 1304, 1250, 1168, 1093, 1051, 990, 905, 746, 699, 627, 602, 549 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.90 [d, *J* = 6.7 Hz, 3 H, $CHCH(CH_3)CH_3$], 1.06 [d, *J* = 6.7 Hz, 3 H, $CHCH(CH_3)CH_3$], 1.06 [d, *J* = 6.2 Hz, 3 H, $SO_3CH(CH_3)CH_3$], 1.32 [d, *J* = 6.2 Hz, 3 H, $SO_3CH(CH_3)CH_3$], 1.90–1.97 [m, 1 H, $CHCH(CH_3)_2$], 4.37 (d, *J* = 5.1 Hz, 1 H, PhC*H*SO_3), 4.49–4.62 [m, 1 H, PhCHC*H*NH], 4.74 [sept, *J* = 6.2 Hz, 1 H, $SO_3CH(CH_3)_2$], 5.05 [s, 2 H, C(O)OCH_2Ph], 7.22–7.47 (m, 10 H, Ph*H*).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.2 [PhCHCH(*C*H$_3$)CH$_3$], 20.4 [PhCHCH(CH$_3$)*C*H$_3$], 22.6 (CH_3), 23.5 (CH_3), 31.1 [PhCH*C*H(CH$_3$)$_2$], 55.9 (Ph*C*HNH), 66.8 (CH_2), 68.5 (Ph*C*HSO_3), 78.4 [$SO_3CH(CH_3)_2$], 127.9, 128.0, 128.4, 128.8, 129.0, 130.0 (CH_{arom}), 130.8, 136.4 (C_{arom}), 155.8 (NH*C*O).

MS (EI, 70 eV): *m/z* (%) = 290 (8), 209 (5), 206 (26), 162 (32), 91 (100), 65 (5).

Anal. Calcd for $C_{22}H_{29}NO_5S$: C, 62.98; H, 6.97; N, 3.34. Found: C, 63.05; H, 6.97; N, 3.19.

Isopropyl (1*S*, 2*R*)-2-[(Benzyloxycarbonyl)amino]-1-phenylbutane 1-sulfonate (5e)

According to the general procedure, the sulfonic acid ester **3e** (488 mg, 0.81 mmol) was refluxed in EtOH (12 mL) containing TFA (0.3 mL) for 16 h. The resulting oil was dissolved in CH_2Cl_2 (10 mL) and (*i*-PrO)$_3$CH (1.8 mL, 8.1 mmol) was added dropwise. The mixture was stirred at r.t. for 23 h. Workup and flash column chromatography gave **5e** as a colourless solid; yield: 198 mg (60%); de = 15% (HPLC, Daicel Chiralpak IA, heptane–EtOH, 9:1); ee = 83% (HPLC, Daicel Chiralpak IA, heptane–EtOH, 9:1); mp 97 °C.

IR (KBr): 3382, 3063, 3038, 2977, 2873, 1709, 1533, 1457, 1343, 1285, 1235, 1165, 1085, 977, 908, 755, 698, 638, 594, 526, 469 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.91 (t, *J* = 7.4 Hz, 3 H, C*H*$_3$CH$_2$), 1.07 [d, *J* = 6.2 Hz, 3 H, $SO_3CH(CH_3)CH_3$], 1.25 [d, *J* = 6.2 Hz, 3 H, $CHCH(CH_3)CH_3$], 1.78–1.94 (m, 2 H, CH_3CH_2), 4.26–4.33 (m, 1 H, PhCHC*H*NH), 4.52 (d, *J* = 7.0 Hz, 1 H, Ph*C*HSO_3), 4.69 [sept, *J* = 6.2 Hz, 1 H, $SO_3CH(CH_3)_2$], 5.05–5.17 [m, 3 H, C(O)OCH_2Ph, NH], 7.30–7.48 (m, 10 H, Ph*H*).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 10.3 [*C*H$_3$CH$_2$], 22.5 (CH_3), 23.5 (CH_3), 25.3 (CH_3CH_2), 54.4 (PhCH*C*HNH), 66.8 (CH_2), 69.9 (Ph*C*HSO_3), 78.5 [$SO_3CH(CH_3)_2$], 127.4, 128.1, 128.4, 128.7, 129.0, 130.9 (CH_{arom}), 130.7, 136.5 (C_{arom}), 155.7 (NH*C*O).

MS (EI, 70 eV): *m/z* (%) = 405 (5), 192 (73), 181 (25), 148 (84), 117 (7), 107 (9), 91 (100), 65 (13).

Anal. Calcd for $C_{21}H_{27}NO_5S$: C, 62.20; H, 6.71; N, 3.45. Found: C, 61.76; H, 6.53; N, 3.41.

Acknowledgment

This work was supported by the Fonds der Chemischen Industrie. We thank BASF AG and Bayer AG for the donation of chemicals.

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(20) CCDC 713539 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from www.ccdc.cam.ac.uk/data_request/cif or by contacting the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK: fax: +44(1223)336033.