Concise Asymmetric Synthesis of β-Hydroxy α-Amino Acids Using the Sulfinimine-Mediated Asymmetric Strecker Synthesis: Phenylserine and β-Hydroxyleucine

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β-Hydroxy α-amino acids are an important class of amino acids that are found in nature (threonine, serine, and β-hydroxy proline) and as constituents of more complex natural products. For example, β-hydroxy tyrosine and β-hydroxyphenylalanine derivatives are found in clinically important glycopeptide antibiotics, which include teicoplanin, ristocetin, actaplanin (A4696), and (A33512b).[1] β-Hydroxyleucine is found in lysobactin[2] and MeBmt in cyclosporin.[3] These densely functionalized amino acids are also useful building blocks for the asymmetric synthesis of β-lactams,[4] β-fluoro α-amino acids,[5] and sugars.[6] As a consequence of the essential role played by these amino acids in biological systems and their utility as synthetic building blocks, a number of useful strategies have been devised for their preparation.[7] Recent methods include Sharpless AE,[8] Sharpless AD,[9] electrophilic amination[10] and hydroxylation,[11] stereoselective hydrolysis of aziridine carboxylate esters,[12] aldol condensation[13] from oxazolidinone intermediates,[14] and others.[15]

As a continuation of our studies of the sulfinimine mediated asymmetric Strecker synthesis[5,16,17] and its application to the enantioselective synthesis of β-substituted α-amino acids, we describe a general route to β-hydroxy α-amino acids. The overall strategy is illustrated in Scheme 1 and involves the conversion of an enantiopure α-substituted aldehyde to an α-substituted sulfinimine. Addition of HCN affords the α-amino nitrile, which is hydrolyzed to the amino acid. This general approach has recently been employed in the asymmetric synthesis of β-fluoro α-amino acids[5] and (2*R*,3*S*)-alloisoleucine.[17] In these studies it was established that the sulfinyl group controlled the stereoselective addition of cyanide to the imine. However, there was no assurance that similar stereocontrol would be observed for β-hydroxy sulfinimines because of the better coordinating ability of oxygen. Herein we report concise asymmetric syntheses of all four stereoisomers of phenylserine and (2*R*,3*S*)-β-hydroxy leucine.

(*R*)-(−)- and (*S*)-(+)-2-[(*tert*-Butyldimethylsilyl)oxy]-2-phenylethanal (**1**) were prepared from commercially available mandelic acid in 80% yield using a literature procedure.[19] Treatment of these protected aldehydes with commercially available (*S*)-(+)- and (*R*)-(−)-*p*-toluenesulfinamide (**2**) in the presence of 6 equiv of $Ti(OEt)_4$ in CH_2Cl_2 for 2 h gave the corresponding sulfinimines **3** and **4** in 47−73% yield (Scheme 2).[20] The modest yields of **3** and **4** may reflect some deprotection of the TBDMS group during the course of the reaction, because yields generally exceed 80%.[20]

Next, the sulfinimines were treated with ethylaluminum cyanoisopropoxide [EtAl(O-*i*-Pr)CN], generated in situ by addition of 1.0 equiv of *i*-PrOH to 1.5 equiv of diethylaluminum cyanide (Et_2AlCN) (Scheme 3). If the sulfinyl group controls the stereoselectivity according to **TS-1** then *re* face addition of CN to sulfinimines (S_S,2*R*)-(+)-**3** and (S_S,2*S*)-(+)-**4** is predicted to give (S_S,2*R*,3*R*)-(+)-**5** and (S_S,2*R*,3*S*)-(+)-**6**, respectively, and was confirmed in the synthesis of phenylserine (2*S*,3*R*)-**7** and (2*S*,3*S*)-**8** of known absolute configurations. In a similar

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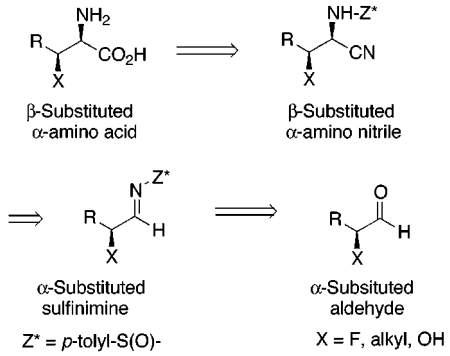
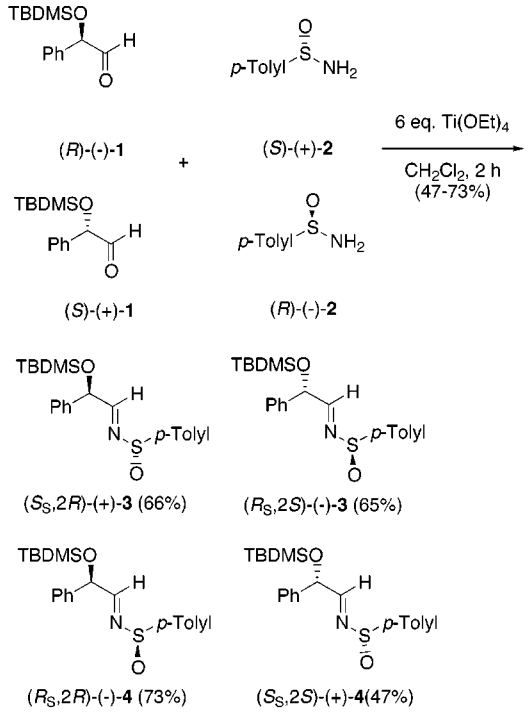
Scheme 1



Scheme 2



manner *Si* face addition to (R_S,2*R*)-(−)-**4** and (R_S,2*S*)-(−)-**3** gave (R_S,2*S*,3*R*)-(−)-**6** and (R_S,2*S*,3*S*)-(−)-**5**, respectively.

The diastereoselectivities for addition of EtAl(O-*i*-Pr)-CN to pseudoenantiomers (+)-**3**/(−)-**3** was 87% and 74% de, respectively, while for (+)-**4**/(−)-**4** the de was >96% (Scheme 3). These results suggest the operation of a double stereo-differentiation effect where the chirality of the resident hydroxyl moiety influences the asymmetric induction. In this context (+)-**4**/(−)-**4** would be considered a "matched pair", while (−)-**3**/(+)-**3** would be the "mismatched pair". However, the effect is weak, and the chirality of the sulfinyl group overrides any influence that the α-hydroxyl group may have and controls the asymmetric induction. It is interesting to note for chiral α-methyl and α-fluoro groups (Scheme 1) a double stereo-differentiation effect was not detected.[5,18] The fact that one is observed here may reflect the bulkiness of the TBDMS protecting group, because silyl ethers are generally considered to be weak Lewis bases.[21] The α-amino nitrile diastereoisomers were readily separated by chromatography or crystallization to give the yields

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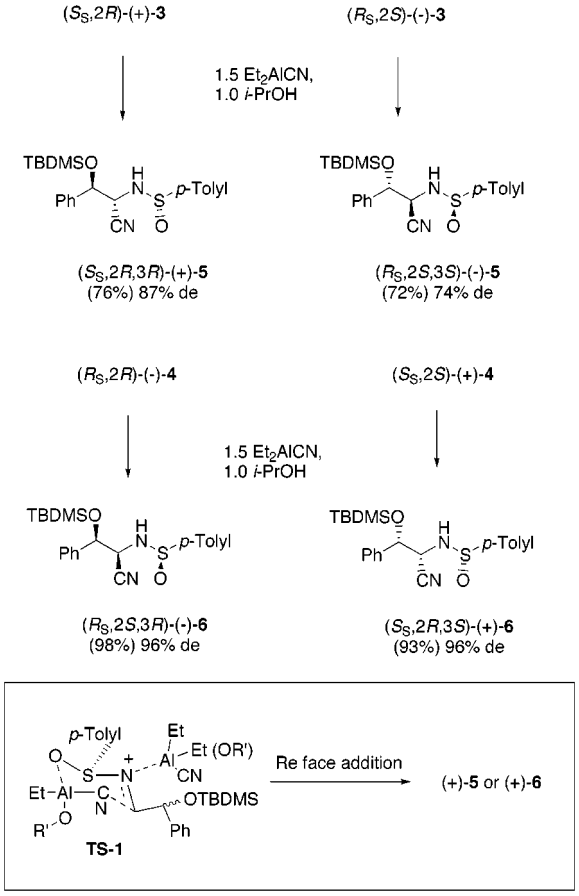
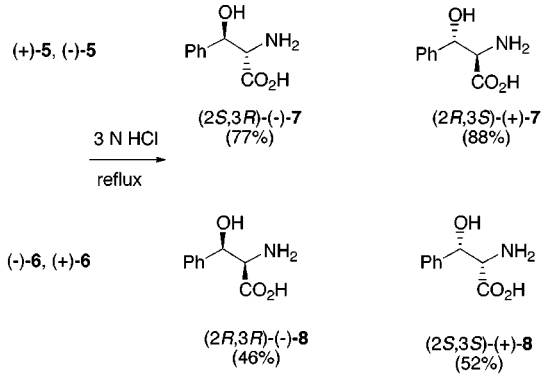
Scheme 3



Scheme 4



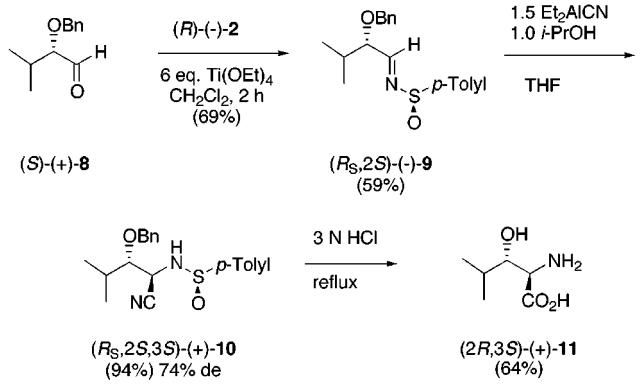
of the major pure diastereoisomers as indicated in Scheme 3.

Hydrolysis of the diastereomeric pure α-amino nitriles (+)-**5**/(−)-**5** and (−)-**6**/(+)-**6** was accomplished by refluxing with 3 N HCl for 4 h. Ion-exchange chromatography (Dowex-50) gave phenylserines **7** and **8** in 46−88% yield (Scheme 4). They were identified by comparison with literature, which indicated that they were >95% enantiomerically pure.[22]

(2*R*,3*S*)-3-Hydroxyleucine (**11**), a popular target,[2,8b,c,9d,23] was readily prepared as before from (*S*)-(+)-2-(benzyloxy)-3-methylbutanal (**8**) synthesized according to the method of Joullie et al. from L-valine (Scheme 5).[23] Thus addition

(22) These reaction conditions have been previously estabilished not to lead to racemization.[5,16,17] If epimerization of one to the stereocenters had occurred in the hydrolysis process the diastereoisomers would been detected by NMR.

Scheme 5



of EtAl(O-*i*-Pr)CN to sulfinimines (−)-**9** afforded the α-amino nitrile **10** in 94% yield and 74% de. Hydrolysis of the major diastereoisomer and isolation gave (2*R*,3*S*)-(+)-**11** in 64% isolated yield and >95% ee.

In summary, enantiopure α-hydroxy aldehydes are efficiently transformed, in good yield and high diastereoselectivity, to *β*-hydroxy α-amino acids via the sulfinimine-mediated asymmetric Strecker synthesis.

Experimental Section

General Procedure. Column chromatography was performed on silica gel, Merck grade 60 (230−400 mesh). Analytical and preparative thin-layer chromatography was performed on precoated silica gel plates (250 and 1000 μm) purchased from Analtech Inc. TLC plates were visualized with UV in an iodine chamber or with phosphomolybdic acid unless noted otherwise. THF was freshly distilled under nitrogen from a purple solution of sodium and benzophenone.

Unless stated otherwise, all reagents were purchased from commercial sources and used without additional purification. Dichloromethane was distilled over calcium hydride under an inert atmosphere. THF and ether were freshly distilled under nitrogen from a purple solution of sodium and benzophenone ketyl. (*S*)-(+)-2-[(*tert*-Butyldimethylsilyl)oxy]-2-phenylethanal (**1**) and (*R*)-(−)-2-[(*tert*-butyldimethylsilyl)oxy]-2-phenylethanal (**1**)[24] and (*S*)-(+)-2-(benzyloxy)-3-methylbutanal (**8**)[23] prepared as previously described.

General Procedure for the Synthesis of Sulfinimines. (*S*S,2*S*)-(+)-*N*-[(*tert*-Butyldimethylsilyl)oxy]-2-phenylacetylidene-*p*-toluenesulfinamide (4). In an oven dried 100 mL single neck round-bottom flask equipped with a magnetic stir bar under argon was placed a solution of (*S*)-*tert*-butyldimethylsilyloxy phenylethanal (0.525 g, 2.1 mmol) in CH_2Cl_2 (10 mL). A solution of (*S*)-(+)-*p*-toluenesulfinamide (**2**) (0.355 g, 2.3 mmol) in CH_2Cl_2 (10 mL) and titanium tetraethoxide (2.6 mL, 6 equiv) was added, and the reaction mixture was stirred at room temperature for 2 h. After completion, monitored by TLC, the reaction mixture was cooled to 0 °C, quenched with ice-cold water (15 mL), filtered through Celite, and washed with EtOAc (3 × 25 mL). The combined organic phases were washed with brine (20 mL), dried ($MgSO_4$), and concentrated. Flash chromatography (hexane/EtOAc, 10:90) provided 0.38 g (47%) of (+)-**4** as an oil: $[\alpha]^{20}_D$ 147.4 (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ −0.09 (s, 3H), −0.06 (s, 3H), 0.85 (s, 9H), 2.4 (s, 3H), 5.4 (d, J = 5.9 Hz, 1H), 7.25−7.40 (m, 7H), 7.55 (d, J = 8 Hz, 2H), 8.05 (d, J = 5.9 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ −4.0, 18.8, 22.1, 26.4, 76.8, 125.2, 126.9, 128.9, 129.3, 130.4, 139.8, 142.1, 142.3, 166.7; IR 2932, 1620 cm^{-1}; HRMS calcd for $C_{21}H_{29}NO_2SSi$ (M + Na) 410.1586, found 410.1585.

(*R*S,2S)-(−)-*N*-[(*tert*-Butyldimethylsilyl)oxy]-2-phenylacetylidene]-*p*-toluenesulfinamide (3). Chromatography (hexane/EtOAc, 90:10) gave 0.255 g (65%) of (−)-**3** as a gel: $[\alpha]^{20}_D$ −184.3 (*c* 0.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0 (s, 3H), 0.15 (s, 3H), 0.9 (s, 9H), 2.4 (s, 3H), 5.47 (d, J = 5.5 Hz, 1H), 7.2−7.3 (m, 7H), 7.42 (d, J = 8.4 Hz, 2H), 8.1 (d, J = 5.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ −0.45, −0.4, 18.5, 22.0, 26.8, 77.0, 126.0, 127.0, 129.2, 130.1, 131.2, 139.2, 141.9, 142.4, 166.9; IR 1620 cm^{-1}; HRMS calcd for $C_{21}H_{29}NO_2SSi$ (M + Na) 410.1586, found 410.1586.

(*R*S,2*R*)-(−)-*N*-[(*tert*-Butyldimethylsilyl)oxy]-2-phenylacetylidene]-*p*-toluenesulfinamide (4). Chromatography (hexane/EtOAc, 90:10) afforded 0.285 g (73%) of (−)-**4** as an oil; $[\alpha]^{20}_D$ −173.8 (c 0.85, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ −0.1 (2s, 6H), 0.8 (s, 9H), 2.4 (s, 3H), 5.4 (d, J = 5.9 Hz, 1H), 7.3−7.5 (m, 7H), 7.55 (d, J = 6.6 Hz, 2H), 8.0 (d, J = 5.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ −4.0, 18.7, 21.9, 26.3, 76.7, 125.1, 126.8, 128.8, 129.2, 130.3, 139.7, 142.3, 166.7; IR: 1624 cm^{-1}. Anal. Calcd for $C_{21}H_{29}NO_2SSi$: C, 65.07; H, 7.54; N, 3.61. Found: C, 64.60; N, 7.67; N, 3.26.

(*S*S,2*R*)-(+)-*N*-[(*tert*-Butyldimethylsilyl)oxy]-2-phenylacetylidene]-*p*-toluenesulfinamide (3). Chromatography (hexane/Et0Ac, 90:10) provided 0.34 g (66%) of (+)-**3**: mp 60−61 °C; $[\alpha]^{20}_D$ 79.5 (*c* 4.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.67 (2s, 6H), 0.9 (s, 9H), 2.39 (s, 3H), 5.46 (d, J = 5.2 Hz, 1H), 7.21−7.39 (m, 7H), 7.42 (d, J = 8.1 Hz, 2H), 8.1 (d, J = 5.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ −4.3, −3.9, 1.6, 18.9, 22.1, 24.7, 29.3, 77.0, 125.3, 126.9, 128.7, 129.1, 130.4, 139.4, 1141.9, 142.3, 166.8. IR: 1623. Anal. Calcd for $C_{21}H_{29}NO_2SSi$: C, 65.07; H, 7.54; N, 3.61. Found: C, 65.01; H, 7.38; N, 3.58.

General Procedure for the Addition of Et_2AlCN/*i*-PrOH to the Sulfinimines. (*S*S,2*R*,3*S*)-(+)-*N*-(*p*-Toluenesulfinyl)-2-amino-[(*tert*-butyl-dimethylsilyl)oxy]-3-phenylpropionitrile (6). In an oven dried two neck 100 mL round-bottom flask fitted with a magnetic stir bar and an argon balloon was placed a solution of (+)-**4** (0.31 g, 0.8 mmol) in THF (15 mL), and the mixture was cooled to −78 °C. In a separate one neck round-bottom flask equipped with a magnetic stir bar under argon, was placed a solution of diethyl aluminum cyanide (1.2 mL, 1.2 mmol) in THF (10 mL). The reaction mixture was cooled to 0 °C, and *i*-PrOH (0.08 mL) was added via syringe, stirred at this temperature for 10−15 min, and then cannulated to the sulfinimine solution at −78 °C. The reaction mixture was allowed to warm to room temperature, stirred for 8 h, cooled to −78 °C, and quenched with a saturated NH_4Cl solution (10 mL). The solution was filtered through Celite and washed with EtOAc (2 × 15 mL), and the combined organic phases were washed with brine (15 mL), dried ($MgSO_4$), and concentrated. Flash chromatography (hexane/EtOAc, 85:15) afforded 0.34 g (93% of major diastereoisomer) of (+)-**6** as an oil: $[\alpha]^{20}_D$ 66.6 (*c* 0.45 $CHCl_3$); ^{1}H NMR ($CHCl_3$) δ −1.5 (s, 3H), 0.2 (s, 3H), 1.0 (s, 9H), 2.4 (s, 3H), 4.1 (dd, J = 9.1 & 3.3 Hz, 1H), 5.0 (d, J = 3.3 Hz, 1H), 5.05 (d, J = 9.2 Hz, 1H), 7.3−7.4 (m, 7H), 7.57 (d, J = 8 Hz, 2H); ^{13}C NMR ($CHCl_3$) δ −5.1, −4.7, 17.9, 21.1, 25.6, 50.9, 76.8, 116.1, 125.9, 126.4, 128.4, 128.7, 129.8, 138.4, 139.7, 141.9; IR: 3443−2584, 2249 cm^{-1}; HRMS calcd for $C_{22}H_{30}N_2O_2SSi$ (M + Na) 437.1694, found 437.1695.

(*S*S,2*S*,3*R*)-(−)-*N*-(*p*-Toluenesulfinyl)-2-amino-[(*tert*-butyldimethyl-silyl)oxy]-3-phenylpropionitrile (6). Chromatography (hexane/EtoAc, 85:15) provided 0.210 g (100% of major diastereoisomer) of (−)-**6** in 96% de as an oil: $[\alpha]^{20}_D$ −72.32 (*c* 0.43, $CHCl_3$); IR 2247 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ −0.1 (s, 3H), 0.19 (s, 3H), 0.95 (s, 9H), 2.4 (s, 3 H), 4.1 (d, J = 3.3 & 9.2 Hz, 1 H), 5.0 (d, J = 3.3 Hz, 1H), 5.0 (d, J = 9.2 Hz, 1H), 7.25−7.39 (m, 7 H), 7.58 (d, J = 8 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ −4.3, −3.9, 18.8, 21.9, 26.4, 51.9, 77.6, 117.0, 126.7, 127.3, 129.2, 129.6, 130.7, 139.3, 140.4, 142.9. Anal. Calcd for $C_{22}H_{30}N_2O_2SSi$: C, 63.73; H, 7.29; N, 6.76. Found: C, 63.42; H, 7.40; N, 6.42.

(*R*S,2*S*,3*S*))-(−)-*N*-(*p*-Toluenesulfinyl]-2-amino-[(*tert*-butyldimethyl-silyl)oxy]-3-phenylpropionitrile (5). Chromatography (hexane/EtOAc, 85:15) gave 0.14 g (72% of major diastereoisomer) of (−)-**5** as a gel: $[\alpha]^{20}_D$ −11.4 (*c* 0.57, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ −0.1 (s, 3H), 0.1 (s, 3H), 0.9 (s, 9H), 2.4 (s, 3H), 4.2 (m, 1H), 4.5 (d, J = 9.2 Hz, 1H), 4.99 (d, J = 5.1 Hz, 1H); 7.26−7.5 (m, 9H); ^{13}C NMR ($CDCl_3$) δ −5.3, −5.0, 17.9, 21.3, 25.5, 49.4, 74.7, 116.8, 125.9, 127.3, 128.5, 128.9, 129.8, 137.6, 139.4, 142.2; IR: 3588−3090, 2245 cm^{-1}; HRMS calcd for $C_{22}H_{30}N_2O_2SSi$ (M + Na) 437.1694, found 437.1694.

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(S_S,2*R*,3*R*)-(+)-*N*-(*p*-Toluenesulfinyl]-2-amino-[(*tert*-butyldimethyl-silyl)oxy]-3-phenylpropionitrile (5). Chromatography (hexane/EtOAc, 85:15) provided 0.22 g (76% of major diastereoisomer) of (+)-**5** in as an oil: $[\alpha]^{20}_D$ 189.6 (*c* 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ −0.10 (s, 3H), 0.6 (s, 3H), 0.87 (s, 9H), 2,43 (s, 3H), 4.21 (dd, *J* = 5.1 & 9 Hz, 1H), 4.5 (d, *J* = 9 Hz, 1H), 4.98 (d, *J* = 5.1 Hz, 1H), 7.33−7.54 (m, 9H); ^{13}C NMR ($CDCl_3$) δ −4.4, −4.1, 18.7, 22.1, 26.3, 50.0, 75.4, 117.5, 126.8, 128.0, 129.3, 129.7, 130.6, 138.2, 140.1, 143.0. IR: 3600−3000, 2247. Anal. Calcd for $C_{22}H_{30}N_2O_2SSi$: C, 63.73; H, 7.29; N, 6.76. Found: C, 63.71; H, 7.22; N, 6.68.

General Procedure for the Synthesis of Phenylserines. (2*S*,3*S*)-(+)-Phenylserine (8). In a single neck 25 mL round-bottom flask was placed (+)-**6** (0.08 g, 0.2 mmol) in 3 N HCl (10 mL), and the solution was refluxed for 4 h. The reaction mixture was cooled to room temperature and loaded in a DOWEX-50 ion-exchange resin column, and the column was eluted with distilled water (70 mL) until the pH became neutral. At this time the column was eluted with 10% NH_4OH (150 mL), and the eluant was concentrated to afford 0.018 g (52%) of (+)-**8**: mp 172−174 °C (dec) [lit.[25a] 175 °C (dec)]; $[\alpha]^{20}_D$ 60.7 (*c* 0.4, 6 N HCl), [lit.[25b] $[\alpha]^{20}_D$ 66.0 (1.07 5 N HCl)]; ^{1}H NMR (D_2O) δ 4.1 (d, *J* = 5.5 Hz, 1H), 4.87 (d, *J* = 5.5 Hz, 1H), 7.4 (m, 5H).

(2*R*,3*R*)-(−)-Phenylserine (8): 0.022 g (46%); mp 174 °C (dec) $[\alpha]^{20}_D$ −63.2 (c 0.65, 6 N HCl); [lit.[25b] $[\alpha]^{20}_D$ −66.0 (*c* 1.07, 5 N HCl)]; ^{1}H NMR (D_2O) δ 4.09 (d, *J* = 5.5 Hz, 1H); 4.87 (d, *J* = 5.5 Hz, 1H); 7.4−7.5 (m, 5H). Other spectral properties are in agreement with literature values.

(2*R*,3*S*)-(+)-Phenylserine (7): 0.027 g (88%); mp 182−184 °C (lit. [26a] 183−186 °C); $[\alpha]^{20}_D$ 48.7 (*c* 2.5, 6 N HCl) [lit.[27] $[\alpha]^{20}_D$ 50.2 (*c* 2, 6 N HCl)]; $[\alpha]^{20}_D$ 30.6 (*c* 0.7, H_2O) [lit.[27] $[\alpha]^{20}_D$ 30.2 (*c* 0.62 H_2O]; ^{1}H NMR (D_2O) δ 4.15 (d, *J* = 5.86 Hz, 1H); 4.86 (d, *J* = 5.87 Hz, 1H); 7.41−7.44 (m, 5H). Other spectral properties are in agreement with literature values.

(2*S*,3*R*)-(−)-Phenylserine (7): 0.08 g (77%); mp 184 °C (dec) (lit.[25a] 184−86 °C) (dec); $[\alpha]^{20}_D$ −48.2 (*c* 2.2, 6 N HCl) [lit.[27] $[\alpha]^{20}_D$ −50.2 (*c* 2, 6 N HCl); $[\alpha]^{20}_D$ −32.8 (*c* 0.10, H_2O) [lit.[27] $[\alpha]^{20}_D$ −31.5 (*c* 0.1 H_2O]; ^{1}H NMR (D_2O) δ 4.18 (d, *J* = 5.86 Hz, 1 H), 4.88 (d, *J* = 5.86 Hz, 1H), 7.35−7.45 (m, 5 H). Other spectral properties are in agreement with literature values.

(R_S,2*S*)-(−)-*N*-[(O-benzyloxy)-isovelarylidene]-*p*-toluenesulfinamide (9). Chromatography (hexane/EtoAc, 90:10) gave 0.39 g (59%) of (−)-**9** as an oil: $[\alpha]^{20}_D$ −304 (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.82 (d, *J* = 6.97 Hz, 3H), 0.92 (d, *J* = 6.97 Hz, 3H), 2.0 (m, 1H), 2.4 (s, 3H), 3.8 (t, *J* = 6.2 Hz, 1H), 4.4 & 4.6 (d, *J* = 11.63 Hz, 1 H), 7.2−7.4 (m, 7H), 7.6 (d, *J* = 6.6 Hz, 2H), 8.16 (d, *J* = 5.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 18.7, 18.9, 22.0, 32.6, 72.7, 85.4, 125.0, 128.5, 128.6, 129.0, 130.5, 138.4, 142.4, 167.5; IR: 1624 cm^{-1}; HRMS calcd for $C_{19}H_{23}NO_2S$ (M + H) 330.1479, found 330.1520.

(RS,2*S*,3*S*)-(+)-(*N*-*p*-Toluenesulfinyl)-2-amino-(*O*-benzyloxy)-3-isovelaronitrile (10). Chromatography (hexane/EtOAc, 80:20) gave 0.21 g (94%) of (+)-**10** in 74% de as an oil: $[\alpha]^{20}_D$ 18.9 (*c* 0.38, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.97 (d, *J* = 6.6 Hz, 3H), 1.1 (d, *J* = 6.6 Hz, 3H), 2.0 (m, 1H), 2.45 (s, 3H), 3.37 (dd, *J* = 2.2 & 8.8 Hz, 1H), 4.2 (dd, *J* = 1.8 & 7.3 Hz, 1H), 4.7 & 4.9 (d, *J* = 10.6 Hz, 1H), 5.15 (d, *J* = 7.7 Hz, 1H), 7.2−7.4 (m, 7H), 7.6 (d, *J* = 6.6 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 18.0, 18.6, 20.9, 29.7, 41.8, 74.7, 84.7, 118.8, 125.5, 127.9, 128.0, 129.5, 136.8, 139.4, 141.7; IR 3150, 2245, 1595 cm^{-1}; HRMS calcd for $C_{20}H_{24}N_2O_2S$ (M + Na) 379.1455, found 379.1456.

(2*R*,3*S*)-(+)-3-Hydroxyleucine (11): mp 212−213 °C (lit.[2] 213−14 °C); $[\alpha]^{20}_D$ 2.7 (*c* 0.8, H_2O); $[\alpha]^{20}_D$ 3.5 (*c* 1, H_2O). It has spectral properties identical with literature values.[2]

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Supporting Information Available: ^{1}H, ^{13}C, and IR spectra for compounds (−)-**3**, (+)-**4**, (−)-**5**, (+)-**6**, (−)-**9**, and (+)-**10**. This material is available free of charge via the Internet at http://pubs.acs.org.

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