Stereodivergent Approach to ß-Hydroxy α-Amino Acids from C_2-Symmetrical Alk-2-yne-1,4-diols

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Supporting Information

Experimental Procedures

General Considerations: Unless otherwise noted, reactions were carried out under an atmosphere of dry N_2. When necessary, solvents and reagents were dried prior to use. THF was distilled from Na/benzophenone ketyl and acetonitrile was distilled from P_2O_5 and stored over molecular sieves 3Å. Analytical thin layer chromatography (TLC) was performed on Alugram®Sil G/UV_{254} (Macherey-Nagel) silica gel plates. The crude products were purified by column chromatography on silica gel of 230-400 mesh (flash chromatography). Melting points are uncorrected. NMR spectra were recorded at 200 MHz, 300 MHz or 400 MHz for ^{1}H, at 50.3 MHz, 75.4 MHz or 100.6 MHz for ^{13}C and at 282.2 MHz for ^{19}F. Chemical shifts are given in ppm with respect to internal TMS. Infrared spectra were measured on a Perkin-Elmer 681 or on a Nicolet 510-FT on NaCl plates (neat) or in KBr; only the most significant absorptions, in cm^{-1}, are indicated. Microanalyses were performed by the Serveis Científico-Tècnics (Universitat de Barcelona). Optical rotations were measured on a Perkin-Elmer Polarimeter 241MC with a sodium lamp at 20 ± 2 ºC. HRMS (FAB^+) were obtained at the CACTI (Universidad de Vigo). Enantiomeric excesses were measured using a Shimadzu LC-6A high performance liquid chromatography (HPLC) with UV detection at 254 nm and Daicel Chiralcel OD-H (0.46 cm x 25 cm) column.

Enantiomerically enriched diols **1** have been previously obtained in our laboratory by asymmetric akynylation of aldehydes (**1a**[12]) or by reduction of the parent acetylenic diketones (**1c**[29], **1 d**[11]). Enantioenriched compound **1b** was commercially available (Lancaster, 98%e.e.). A sample of **1b** was also obtained by hydrolysis of its known, stereochemical enriched monobenzoate[12,30] (1% NaOH in MeOH, rt, 89%). Colorless solid, **mp:** 105–107 ºC (lit.[31] 107–108 ºC). $\mathbf{R_f}$ (CH_2Cl_2/MeOH 95:5): 0.32. **^{1}H NMR** ($CDCl_3$, 300 MHz): δ 0.99 (6H, d, J = 7.2 Hz, CH_3), 1.01 (6H, d, J = 7.2 Hz, CH_3), 1.84–1.92 (2H, m, C<u>H</u>(CH_3)$_2$), 2.40 (2H, bs, OH), 4.23 (2H, d, J = 5.6 Hz, C<u>H</u>OH). **^{13}C**

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NMR ($CDCl_3$, 75.4 MHz): δ 17.4 (CH_3), 18.1 (CH_3), 34.4 ($\underline{C}H(CH_2)_2$), 67.8 (CHOH), 85.3 (≡C). An analytical sample of **1b** was transformed into the corresponding Mosher diester derived from Mosher's (*R*)-acid. ^{19}F NMR analysis of the sample revealed a *syn*/*anti* ratio 95:5, >99 %e.e.

Propargylic diols **1a–c** (as a mixture of stereoisomers) were obtained by addition of dilithium acetylide to the corresponding aldehyde according to a reported protocol.[32] On the other hand, **1d** and its *meso* isomer were separated from commercial mixture of isomeric hex-3-yne-2,5-diols by temporal transformation into their dibromo derivatives as described in the literature.[33]

General procedure for reductions to *E* olefins: **preparation of (3*S*,4*E*,6*S*)-2,7-dimethyl-4-octene-3,6-diol (2b)**
A solution of 2,7-dimethyl-4-octyne-3,6-diol (**1b**, 160 mg, 0.94 mmol) in THF anhyd (2 mL) was added dropwise to a suspension of $LiAlH_4$ in THF anhyd (10 mL) at 0 ºC. After addition, the mixture was refluxed overnight. Then, EtOAc (2 mL) and sodium and potassium tartrate (2 mL, 1 M) were added cautiously. The aqueous layer was extracted with CH_2Cl_2 (15 mL) and the organic layer was dried over $MgSO_4$. The solvent was removed and the residue was purified by *flash* column chromatography using CH_2Cl_2/MeOH (98:2) to give diol **2b** (158 mg, 98%).

Compound 2b: Colorless solid, **mp**: 75-77 ºC. $\mathbf{R_f}$ (CH_2Cl_2/MeOH 95:5): 0.24. **^{1}H NMR** ($CDCl_3$, 300 MHz): δ 0.90 (6H, d, *J* = 6.6 Hz, CH_3), 0.94 (6H, d, *J* = 6.6 Hz, CH_3), 1.73 (2H, m, $C\underline{H}(CH_3)_2$), 1.82 (2H, bs, OH), 3.85 (2H, m, $C\underline{H}$-OH), 5.67 (2H, m, CH=). **^{13}C NMR** ($CDCl_3$, 75.4 MHz): δ 18.0 (CH_3), 18.2 (CH_3), 33.8 ($C\underline{H}(CH_3)_2$), 77.7 (CH-OH), 133.1 (CH=). **IR**: 3294, 2956, 1654, 1146. $\mathbf{[\alpha]_D}$ = +33.7 (*c* 1.02, $CHCl_3$). **HRMS** EI $(M-H_2O)^+$ calcd for $C_{10}H_{18}O$: 154.1358, found: 154.1361.

Partial reduction of diols **1a**, **1c** and **1d** (as a mixture of stereoisomers) afforded a mixture of chiral diols **2** and their *meso* stereoisomers **10.** Both stereoisomers were easily isolated by column chromatography. Diols **2a**,[34] **2c**,[35] **2d**,[33] **10a**,[34] **10c**,[35] and **10d**[33] have been previously described in the literature.

General procedure for reductions to *Z* olefins: **preparation of (3*S*,4*Z*,6*S*)-2,7-dimethyl-4-octene-3,6-diol (3b)**
$Pd/CaCO_3$ poisoned with lead (Lindlar catalyst, 5 wt.%, 66 mg) and quinoline (8 μL, 0.07 mmol) were added to a solution of 2,7-dimethyl-4-octyne-3,6-diol (**1b**, 160 mg, 0.94 mmol)* in EtOAc (10 mL). The mixture was shaken under hydrogen (1-2 atmospheres) until TLC showed complete conversion. The suspension was filtered through a short path

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[33] Hill, R. K.; Pendalwar, S. L.; Kielbasinski, K.; Baevsky, M.F.; Nugara, P. N. *Synthetic Commun.* **1990**, 1877–1884.
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of Celite® and the organic layer was washed with HCl (2N), a saturated solution of $NaHCO_3$, and dried over $MgSO_4$. The solvent was removed and the residue was purified by MPLC column chromatography using hexane/EtOAc (75:25) to give diol **3b** (157 mg, 97%).

Compound 3b: Colorless solid, **mp**: 69-71 ºC. $\mathbf{R_f}$ (CH_2Cl_2/MeOH 95:5): 0.39. **^{1}H NMR** ($CDCl_3$, 200 MHz): δ 0.91 (6H, d, *J* = 6.6 Hz, CH_3), 0.98 (6H, d, *J* = 6.6 Hz, CH_3), 1.71 (2H, m, C<u>H</u>(CH_3)$_2$), 1.85 (2H, bs, OH), 4.15 (2H, m, C<u>H</u>-OH), 5.56 (2H, m, CH=). **^{13}C NMR** ($CDCl_3$, 75.4 MHz): δ 18.0 (CH_3), 18.2 (CH_3), 34.1 (<u>C</u>H(CH_3)$_2$), 73.2 (CH-OH), 133.3 (CH=). **IR** (film): 3342, 2960, 1652, 1146. **$[\alpha]_D$** = +57.2 (*c* 1.01, $CHCl_3$). **HRMS** EI (M-H_2O)$^+$ calcd for $C_{10}H_{18}O$: 154.1358, found: 154.1363. **EA** calcd for $C_{10}H_{20}O_2$: C 69.72, H 11.70; found: C 69.64, H 11.80.

Partial hydrogenation of diols **1a**, **1c** and **1d** afforded a mixture of chiral diols **3** and their *meso* stereoisomers **11**. Both stereoisomers were easily isolated by column chromatography. Diols **3d**[33] and **11d**[33] have been previously described in the literature.

Compound 3c: Pale yellowish oil. $\mathbf{R_f}$ (hexane/EtOAc 65:35): 0.55. **^{1}H NMR** ($CDCl_3$, 300 MHz): δ 0.89 (6H, t, *J* = 6.6 Hz, C<u>H</u>$_3$CH$_2$), 1.30-1.52 (14H, m, CH_2), 1.95 (2H, bs, O<u>H</u>), 4.44 (2H, m, C<u>H</u>OH), 5.49 (2H, m, C<u>H</u>=). **^{13}C NMR** ($CDCl_3$, 75.4 MHz): δ 14.0 (<u>C</u>H$_3$(CH$_2$)$_4$CHOH), 22.5 (CH$_3$<u>C</u>H$_2$), 25.0 (CH$_3$CH$_2$<u>C</u>H$_2$), 31.7 (CH$_3$(CH$_2$)$_2$<u>C</u>H$_2$), 37.6 (CH$_3$(CH$_2$)$_3$<u>C</u>H$_2$), 68.3 (<u>C</u>HOH), 134.3 (=<u>C</u>) . **IR**: 3400, 2950, 1495. **HRMS** (EI), calcd for $C_{14}H_{28}O_2$ (M^+): 228.2089, found: 228.2088. **EA** calcd. for $C_{14}H_{28}O_2$: C 73.63, H 12.36; found: C 73.63, H 12.53.

Compound 11a: Colorless solid, **mp:** 105-108 ºC $\mathbf{R_f}$ (CH_2Cl_2/MeOH 95:5): 0.20. **^{1}H NMR** ($CDCl_3$, 300 MHz): δ 0.87-1.07 (4H, m, CH_2), 1.10-1.41 (8H, m, CH_2), 1.58-1.84 (8H, m, CH_2), 1.90-1,97 (2H, m, CH), 2.51 (2H, bs, OH), 4.09 (2H, m, C<u>H</u>OH), 5.50 (2H, m, CH=). **^{13}C NMR** ($CDCl_3$, 75.4 MHz): δ 25.8 (CH_2), 25.9 (CH_2), 26.3 (CH_2), 28.4 (CH_2), 43.8 (CH), 72.1 (<u>C</u>HOH), 132.8 (=<u>C</u>) . **IR**: 3363, 2910, 1490. **HRMS** (EI), calcd for $C_{16}H_{26}O$ (M^+-H_2O): 234.1984, found: 234.1989. **EA** calcd. for $C_{16}H_{28}O_2$: C 76.14, H 11.18; found: C 75.92, H 11.06.

Compound 11c: Pale yellowish oil. $\mathbf{R_f}$ (hexane/EtOAc 65:35): 0.19. **^{1}H NMR** ($CDCl_3$, 300 MHz): δ 0.88 (6H, t, *J* = 6.6 Hz, C<u>H</u>$_3$CH$_2$), 1.29-1.61 (14H, m, CH_2), 4.43 (2H, m, C<u>H</u>OH) 5.48 (2H, m, C<u>H</u>=). **^{13}C NMR** ($CDCl_3$, 75.4 MHz): δ 14.0 (<u>C</u>H$_3$(CH$_2$)$_4$CHOH), 22.7 (CH$_3$<u>C</u>H$_2$), 25.1 (CH$_3$CH$_2$<u>C</u>H$_2$), 31.8 (CH$_3$(CH$_2$)$_2$<u>C</u>H$_2$), 37.1 (CH$_3$(CH$_2$)$_3$<u>C</u>H$_2$), 67.3 (<u>C</u>HOH), 134.7 (=<u>C</u>) . **IR**: 3400, 2910, 1490. **HRMS** (EI), calcd for $C_{14}H_{28}O_2$ (M^+): 228.2089, found: 228.2085.

<u>General procedure for cyclization in one pot</u>: preparation of (*E*,4*S*,5*S*)-*trans*-4-(3-methyl-1-butenyl)-5-(1-methylethyl)-3-(4-methylphenyl)sulfonyl-2-oxazolidinone (6b)

p-Toluenesulfonyl isocyanate (148 μL, 0.98 mmol) was added to a solution of diol **2b** (67 mg, 0.39 mmol) in THF anhyd (1 mL) under N_2 at r.t. When the reaction is complete, the catalyst solution was added via *cannula*. This solution was prepared previously by adding

(^{i}PrO)$_3$P (24 μL, 0.10 mmol) to (dba)$_3$Pd$_2$·CHCl$_3$ (17 mg, 0.02 mmol) in THF anhyd (1 mL) and stirring at r.t. for 2 h until a yellow color was obtained. The reaction mixture was stirred at r.t. until TLC showed complete conversion. The solvent was removed and the residue was purified by *flash* column chromatography using hexane/EtOAc (80:20) to give oxazolidinone **6b** (117 mg, 85%).

Compound 6b: Colorless solid, **mp**: 77-79 ºC. $\mathbf{R_f}$ (hexane/EtOAc 80:20): 0.44. **^{1}H NMR** ($CDCl_3$, 300 MHz): δ 0.95-1.02 (12H, m, CH_3), 1.92 (1H, m, C<u>H</u>(CH_3)$_2$), 2.33 (1H, m, C<u>H</u>(CH_3)$_2$), 2.44 (3H, s, CH_3-Ar), 3.88 (1H, dd, *J* = 6.6, 3.6 Hz, CH-O), 4.59 (1H, dd, *J* = 8.7, 3.6 Hz, CHNTs), 5.27 (1H, ddd, *J* = 15.3, 8.7, 1.4 Hz, CH=), 5.84 (1H, dd, *J* = 15.3, 6.0 Hz, =C<u>H</u>-CH(CH_3)$_2$), 7.31 (2H, d, *J* = 8.3 Hz, CH(Ar)), 7.90 (2H, d, *J* = 8.3 Hz, CH(Ar)). **^{13}C NMR** ($CDCl_3$, 75.4 MHz): δ 16.6 (CH_3), 17.2 (CH_3), 21.6 (CH_3), 21.6 (CH_3-Ar), 30.5 (<u>C</u>H(CH_3)$_2$), 31.9 (<u>C</u>HCH_3)$_2$), 61.8 (CH-NTs), 85.1 (CH-O), 123.5 (CH=), 128.5 (CH(Ar)), 129.5 (CH(Ar)), 135.7 (C(Ar)-CH_3), 144.0 (=<u>C</u>H-CH(CH_3)$_2$), 145.2 (C(Ar)-SO_2)), 151.5 (C=O). **IR**: 1779, 1173. $\mathbf{[\alpha]_D}$ = -59.2 (*c* 2.7, $CHCl_3$). **EA** calcd for $C_{18}H_{25}NO_4S$: C 61.51, H 7.17, N 3.99; found: C 61.76, H 7.21, N 3.93.

Compound 6a: Colorless solid, **mp**: 92-94 ºC. $\mathbf{R_f}$ (hexane/EtOAc 80:20): 0.51. **^{1}H NMR** ($CDCl_3$, 300 MHz): δ 0.96-1.34 (10H, m, CH_2(cyclohexyl)), 1.61-1.83 (11H, m, C<u>H</u>-C<u>H</u>$_2$), 1.91-2.05 (1H, m, CH(cyclohexyl)), 2.44 (3H, s, CH_3), 3.88 (1H, dd, *J* = 6.3, 3.6 Hz, CH-O), 4.59 (1H, dd, *J* = 8.8, 3.6 Hz, CH-NTs), 5.27 (1H, ddd, *J* = 15.3, 8.8, 0.9 Hz, CH=), 5.82 (1H, dd, *J* = 15.3, 6.0 Hz, =CH(cyclohexyl)), 7.31 (2H, d, *J*=8.7, CH(Ar)), 7.89 (2H, d, *J*=8.7, CH(Ar)). **^{13}C NMR** ($CDCl_3$, 75.4 MHz): δ 21.6 (CH_3), 25.3 (CH_2), 25.4 (CH_2), 25.7 (CH_2), 25.7 (CH_2), 25.9 (CH_2), 26.0 (CH_2), 26.8 (CH_2), 27.5 (CH_2), 32.1 (CH_2), 39.9 (CH(cyclohexyl)), 41.4 (CH(cyclohexyl)), 61.8 (CH-NTs)), 84.4 (CH-O), 123.8 (CH=), 128.4 (CH(Ar)), 129.4 (CH(Ar)), 135.7 (C(Ar)-CH_3), 142.7 (=<u>C</u>H(cyclohexyl)), 145.1 (C(Ar)-SO_2), 151.4 (C=O). **IR**: 1782, 1175. **HRMS** (EI), calcd for $C_{24}H_{33}NO_4S$ (M+): 431.2130; found: 431.2141. **EA**: calcd for $C_{24}H_{33}NO_4S$: C 66.79, H 7.71, N 3.25; found: C 66.84, H 7.70, N 3.10.

Compound 6c: Colorless oil. $\mathbf{R_f}$ (hexane/EtOAc 90:10): 0.32. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 0.88-0.92 (6H, m, CH_3), 1.27-1.42 (12H, m, CH_2), 1.59-1.70 (2H, m, C<u>H</u>$_2$CH-O), 2.03-2.10 (2H, m, C<u>H</u>$_2$CH=), 2.44 (3H, s, CH_3), 4.10 (1H, ddd, *J* = 7.5, 5.5, 4.0 Hz, CHO), 4.44 (1H, dd, *J* = 8.9, 4.0 Hz, CH-NTs), 5.37 (1H, ddt, *J* = 15.3, 8.9, 1.5 Hz, CH=), 5.88 (1H, dt, *J* = 15.3, 6.7 Hz, =CHCH_2), 7.32 (2H, d, *J*=8.2, CH(Ar)), 7.89 (2H, d, *J*=8.2, CH(Ar)). **^{13}C NMR** ($CDCl_3$, 100.6 MHz): δ 13.9 (CH_3), 14.0 (CH_3), 21.7 (CH_2), 22.4 (CH_2), 22.5 (CH_2), 28.2 (CH_2), 23.9 (CH_2), 31.2 (CH_2), 31.3 (CH_2), 31.9 (CH_2), 33.7 (CH_2), 64.5 (CH-NTs), 80.7 (CH-O), 125.5 (CH=), 128.5 (CH(Ar)), 129.5 (CH(Ar)), 135.5 (C(Ar)-CH_3), 137.8 (=CHCH_2), 145.2 (C(Ar)-SO_2), 151.5 (C=O). **IR**: 1784, 1175. **HRMS** (FAB+), calcd for $C_{22}H_{34}NO_4S$ (M+1): 408.2209, found: 408.2190.

Compound 6d: Colorless solid, **mp**: 99-103 ºC. $\mathbf{R_f}$ (CH_2Cl_2/MeOH): 0.81. **^{1}H NMR** ($CDCl_3$, 300 MHz): δ 1.40 (3H, d, *J* = 6 Hz, CH_3), 1.75 (3H, dd, *J* = 6.6, 1.8 Hz, C<u>H</u>$_3$-CH=), 2.45 (3H, s, CH_3-Ar), 4.25 (1H, m, CH-O), 4.36 (1H, m, CH-NTs), 5.35 (1H, m, CH=), 5.90 (1H, m, =C<u>H</u>CH_3), 7.35 (2H, d, *J*=8.1, CH(Ar)), 7.91 (2H, d, *J*=8.1, CH(Ar)). **^{13}C NMR** ($CDCl_3$, 75.4 MHz): δ 14.9 (<u>C</u>H_3-CH=), 17.5 (<u>C</u>H_3-CHO), 21.5 (CH_3-Ar), 63.8

(CH-O), 75.3 (CH-NTs), 122.6 (CH=), 128.3 (CH(Ar)), 129.4 (CH(Ar)), 132.5 (=CHCH$_3$), 135.2 (C(Ar)-CH$_3$), 145.2 (C(Ar)-SO$_2$), 151.2 (C=O). **HRMS** (FAB+) calcd for $C_{14}H_{18}NO_4S$ (M+1): 296.0957, found 296.0943. **EA** calcd for $C_{14}H_{17}NO_4S$: C 56.93, H 5.80, N 4.74; found: C 56.74, H 5.67, N 4.63.

General procedure for cyclization in two steps: preparation of (*E*,4*R*,5*S*)-*trans*-4-(3-methyl-1-butenyl)-5-(1-methylethyl)-3-(4-methylphenyl)sulfonyl-2-oxazolidinone (7b)

p-Toluenesulfonyl isocyanate (252 μL, 1.65 mmol) was added to a solution of diol **3b** (104 mg, 0.60 mmol) in THF anhyd (1 mL) at r.t. When the reaction is complete (~1 h), the solvent was removed and the residue was filtrated through a pad of silica gel using CH_2Cl_2/MeOH (98:2) to give impure dicarbamate **5b** (342 mg, 100%) which was used without further purification. An analytical sample of **5b** showed the following physical and spectroscopical data: colorless solid, **mp**: 174-175ºC. **R$_f$** (CH_2Cl_2/MeOH 98:2): 0.27. **^{1}H NMR** ($CDCl_3$, 300 MHz): δ 0.64 (6H, d, *J* = 6.9 Hz, CH_3), 0.70 (6H, d, *J* = 6.6 Hz, CH_3), 1.68 (2H, m, C<u>H</u>(CH_3)$_2$), 2.42 (6H, s, CH_3-Ar), 4.93 (2H, bs, NH), 5.22 (2H, m, CH-O), 5.37 (2H, m, CH=), 7.27-7.30 (4H, m, CH(Ar)), 7.81 (2H, d, *J* = 8.1 Hz, CH(Ar)), 7.86 (2H, d, *J* = 8.1 Hz, CH(Ar)). **^{13}C NMR** ($CDCl_3$, 75.4 MHz): δ 17.4 (CH_3), 17.6 (CH_3), 21.5 (CH_3-Ar), 32.0 (<u>C</u>H(CH_3)$_2$), 76.6 (CH-O), 128.2 (CH=), 129.4 (CH(Ar)), 129.5 (CH(Ar)), 135.8 (C(Ar)), 144.6 (C(Ar)-SO$_2$), 149.9 (C=O). **IR**: 3350, 1746, 1162. **[α]$_D$** = +36.5 (*c* 1.05, $CHCl_3$). **HRMS** (FAB+), calcd for $C_{26}H_{35}N_2O_8S_2$ (M+1): 567.1834, found: 567.1809. **EA** calcd for $C_{26}H_{34}N_2O_8S_2$: C 55.11, H 6.05, N 4.94; found: C 55.39, H 5.95, N 5.15. A catalyst solution was prepared by adding (^{i}PrO)$_3$P (111 μL, 0.45 mmol) to (dba)$_3$Pd$_2$·$CHCl_3$ (77 mg, 0.075 mmol) in CH_3CN anhyd (1.3 mL) and stirring at r.t. until a yellow color was observed. This solution was added via *cannula* to dicarbamate **5b** (342 mg, 0.60 mmol) in CH_3CN anhyd (1 mL). The reaction mixture was stirred at r.t. until TLC showed complete conversion. The solvent was removed and the residue was purified by MPLC column chromatography using hexane/EtOAc (90:10) to give oxazolidinone **7b** (147 mg, 70%).

Compound 7b: colorless solid, **mp**: 136-138ºC. **R$_f$** (hexane/EtOAc 80:20): 0.58. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 0.81 (3H, d, *J* = 6.4 Hz, CH_3), 0.96 (3H, d, *J* = 6.4 Hz, CH_3), 1.00 (3H, d, *J* = 6.4 Hz, CH_3), 1.03 (3H, d, *J* = 6.4 Hz, CH_3), 1.77 (1H, m, C<u>H</u>(CH_3)$_2$), 2.31 (1H, m, C<u>H</u>(CH_3)$_2$), 2.43 (3H, s, CH_3-Ar), 4.10 (1H, dd, *J* = 10.4, 6.1 Hz, CH-O), 4.81 (1H, dd, *J* = 10.0, 6.1 Hz, CH-NTs), 5.10 (1H, dd, *J* = 15.4, 10.0 Hz, CH=), 5.92 (1H, dd, *J* = 15.4, 6.2 Hz, =C<u>H</u>-CH(CH_3)$_2$), 7.29 (2H, d, *J* = 8.2 Hz, CH(Ar)), 7.90 (2H, d, *J* = 8.2 Hz, CH(Ar)). **^{13}C NMR** ($CDCl_3$, 100.6 MHz): δ 16.8 (CH_3), 19.3 (CH_3), 21.5 (CH_3), 21.6 (CH_3), 21.7 (CH_3-Ar), 27.6 (<u>C</u>H(CH_3)$_2$), 30.8 (<u>C</u>H(CH_3)$_2$), 63.5 (CH-NTs), 84.7 (CH-O), 117.9 (CH=), 128.9 (CH(Ar)), 129.3 (CH(Ar)), 135.6 (C(Ar)), 145.2 (C(Ar)-SO$_2$)), 146.3 (=<u>C</u>H(CH_3)$_2$)), 151.6 (C=O). **IR**: 1787, 1167. **[α]$_D$** = +79.1 (*c* 0.82, $CHCl_3$). **HRMS** (FAB+), calcd for $C_{18}H_{26}NO_4S$ (M+1): 352.1583, found: 352.1571. **EA** calcd for $C_{18}H_{25}NO_4S$: C 61.51, H 7.17, N 3.99; found: C 61.46, H 7.09, N 3.81.

Compound 7a: Colorless solid, **mp**: 120-122 ºC. **R$_f$** (hexane/EtOAc 80:20): 0.51. **^{1}H NMR** ($CDCl_3$, 300 MHz): δ 0.94-1.37 (10H, m, CH_2(cyclohexyl)), 1.45-1.81 (10H, m, CH_2(cyclohexyl)), 1.88-2.06 (2H, m, CH(cyclohexyl)), 2.43 (3H, s, CH_3), 4.17 (1H, dd, *J*

= 10.8, 6.2 Hz, CH-O), 4.79 (1H, dd, *J* = 9.9, 6.2 Hz, CH-NTs), 5.08 (1H, ddd, *J* = 15.3, 9.9, 0.9 Hz, CH=), 5.86 (1H, dd, *J* = 15.3, 6.3 Hz, =C<u>H</u>-CH(cyclohexyl)), 7.29 (2H, d, *J* = 8.4 Hz, CH(Ar)), 7.90 (2H, d, *J* = 8.4 Hz, CH(Ar)). **^{13}C NMR** ($CDCl_3$, 75.4 MHz): δ 21.6 (CH_3), 24.8 (CH_2), 24.9 (CH_2), 25.7 (CH_2), 25.7 (CH_2), 25.9 (CH_2), 26.0 (CH_2), 27.0 (CH_2), 29.1 (CH_2), 32.1 (CH_2), 32.3 (CH_2), 36.7 (<u>C</u>H(cyclohexyl)), 40.2 (<u>C</u>H(cyclohexyl)), 63.5 (CH-NTs), 83.1 (CH-O), 118.5 (CH=), 128.9 (CH(Ar)), 129.3 (CH(Ar)), 135.6 (C(Ar)-CH_3), 144.9 (=CH(cyclohexyl)), 145.1 (C(Ar)-SO_2), 151.6 (C=O). **IR**: 1782, 1175. **HRMS** (FAB+), calcd for $C_{24}H_{34}NO_4S$ (M+1): 432.2209, found: 432.2217. **EA**: calcd for $C_{24}H_{33}NO_4S$: C 66.79, H 7.71, N 3.25; found: C 66.63, H 7.87, N 3.08.

Compound 7c: Colorless solid, **mp**: 44-46 ºC. **R_f** (hexane/EtOAc 90:10): 0.32. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 0.87-0.92 (6H, m, CH_3), 1.26-1.44 (12H, m, CH_2), 1.55-1.64 (2H, m, C<u>H</u>$_2$CHO), 1.96-2.14 (2H, m, C<u>H</u>$_2$CH=), 2.44 (3H, s, CH_3), 4.55 (1H, m, CH-O), 4.80 (1H, dd, *J* = 9.7, 6.7 Hz, CH-NTs), 5.13 (1H, ddt, *J* = 15.2, 9.7, 1.4 Hz, CH=), 5.88 (1H, dt, *J* = 15.2, 6.4 Hz, =C<u>H</u>-CH_2), 7.28 (2H, d, *J* = 8.3 Hz, CH(Ar)), 7.89 (2H, d, *J* = 8.3 Hz, CH(Ar)). **^{13}C NMR** ($CDCl_3$, 100.61 MHz): δ 13.8 (CH_3), 14.0 (CH_3), 21.6 (CH_2), 22.3 (CH_2), 22.4 (CH_2), 24.7 (CH_2), 28.1 (CH_2), 29.4 (CH_2), 31.3 (CH_2), 31.3 (CH_2), 32.0 (CH_2), 63.7 (CH-NTs), 79.4 (CH-O), 121.3 (CH=), 128.9 (CH(Ar)), 129.3 (CH(Ar)), 135.5 (C(Ar)-CH_3), 139.6 (=$CHCH_2$), 145.1 (C(Ar)-SO_2), 151.6 (C=O). **IR**: 1784, 1175. **HRMS** (FAB+), calcd for $C_{22}H_{33}NO_4S$ (M+1): 408.2209; found: 408.2227. **EA**: calcd for $C_{22}H_{33}NO_4S$: C 64.83, H 8.16, N 3.44; found: C 65.02, H 7.98, N 3.32.

Compound 7d: Colorless solid, **mp**: 72-74 ºC. **R_f** (CH_2Cl_2/MeOH): 0.81. **^{1}H NMR** ($CDCl_3$, 300 MHz): δ 1.24 (3H, d, *J* = 6.3 Hz, CH_3), 1.76 (3H, dd, *J* = 6.9, 2.1 Hz, C<u>H</u>$_3$-CH=), 2.45 (3H, s, CH_3-Ar), 4.25 (1H, m, CH-O), 4.77 (1H, m, CH-NTs), 5.17 (1H, m, CH=), 5.89 (1H, m, =C<u>H</u>CH_3), 7.35 (2H, d, *J* = 8.1 Hz, CH(Ar)), 7.91 (2H, d, *J* = 8.1 Hz, CH(Ar)). **^{13}C NMR** ($CDCl_3$, 75.4 MHz): δ 15.0 (<u>C</u>H_3-CHO), 17.5 (<u>C</u>H_3-CH=), 21.5 (CH_3-Ar), 65.9 (CH-O), 76.9 (CHN-Ts), 126.4 (CH=), 128.3 (CH(Ar)), 129.5 (CH(Ar)), 134.2 (=<u>C</u>HCH_3), 135.4 (<u>C</u>(Ar)-CH_3), 145.2 (C(Ar)-SO_2), 151.2 (C=O). **HRMS** (FAB+), calcd for $C_{14}H_{18}NO_4S$ (M+1): 296.0957; found: 296.0964.

<u>General procedure for oxidation of *trans*-oxazolidinones</u>: (4*R*,5*S*)-5-(1-methylethyl)-3-(4-methylphenyl)sulfonyl-2-oxazolidinone-4-carboxylic acid (12b)

Ozone was bubbled through a solution of oxazolidinone **6b** (81 mg, 0.23 mmol) in CH_2Cl_2 anhyd (8 mL) at –78 ºC until TLC showed complete conversion. Then, nitrogen was bubbled through the blue solution for a few minutes before adding Me_2S (~50 μL) and stirring at r.t. for 90 min. Then, the solution was diluted with CH_2Cl_2 (10 mL) and a phosphate buffer (pH=7, 4 mL). The aqueous layer was washed with CH_2Cl_2 (3x10 mL). The combined organic layer was dried over $MgSO_4$ anhyd. Removal of solvent afforded crude (4*R*,5*S*)-5-(1-methylethyl)-3-(4-methylphenyl)sulfonyl-2-oxazolidinone-4-carbaldehyde (72 mg, 99%): Colorless solid. **R_f** (hexane/EtOAc 65:35): 0.65. **^{1}H NMR** ($CDCl_3$, 300 MHz): δ 0.90 (6H, d, *J* = 6.9 Hz, CH_3), 1.91 (1H, m, C<u>H</u>$(CH_3)_2$), 2.47 (3H, s, CH_3-Ar), 4.26 (1H, dd, *J* = 5.7, 5.4 Hz, CH-O), 4.46 (1H, dd, *J* = 5.4, 1.8 Hz, CH-NTs), 7.39 (2H, d, *J* = 8.4 Hz, CH(Ar)), 7.96 (2H, d, *J* = 8.4 Hz, CH(Ar)), 9.79 (1H, d, *J* = 1.8 Hz, CHO). **^{13}C NMR** ($CDCl_3$, 75.4 MHz): δ 16.1 (CH_3), 16.5 (CH_3), 21.7 (CH_3-Ar), 32.3

($\underline{C}H(CH_3)_2$), 64.8 (CH-NTs), 78.8 (CH-O), 128.6 (CH(Ar)), 130.0 (CH(Ar)), 133.8 (C(Ar)), 146.4 (C(Ar)-SO_2), 150.9 (C=O), 195.3 (CHO). The above crude mixture was dissolved in CH_3CN (1.3 mL). An aqueous solution of NaH_2PO_4 (24 mg in 0.9 mL) and H_2O_2 (33% p/v, 0.25 mL) was added and the mixture was cooled to 0-4 ºC. Then, an aqueous $NaClO_2$ solution (45 mg, 0.9 mL) was added and the green homogenous solution was stirred at r.t. until starting material was consumed. The reaction mixture was quenched by addition of an aqueous solution of $NaHSO_3$ (50 mg, 1 mL). The mixture was stirred for 30 min and then acidified with HCl 2 N. CH_2Cl_2 (5 mL) was added and the aqueous layer was extracted with CH_2Cl_2 (5 mL). The organic layer was dried over $MgSO_4$ anhyd, and the solvent was removed. The crude residue dissolved in EtOAc and washed with 2 eq. of $NaHCO_3$ in H_2O (0.5 mL). The aqueous layer was acidified and then extracted with Et_2O and CH_2Cl_2. The combined organic layer was dried over $MgSO_4$ anhyd and the solvent was removed to give oxazolidinone **12b** (71 mg, 94%).

Compound 12b: Colorless solid, **mp**: 106-108 ºC. $\mathbf{R_f}$ (hexane/EtOAc 65:35): 0.20. **^{1}H NMR** ($CDCl_3$, 300 MHz): δ 0.97 (3H, d, *J* = 6.6 Hz, CH_3), 0.99 (3H, d, *J* = 6.6 Hz, CH_3) 2.00 (1H, m, $C\underline{H}(CH_3)_2$), 2.45 (3H, s, CH_3-Ar), 4.31 (1H, dd, *J* = 5.9, 4.2 Hz, CH-O), 4.70 (1H, d, *J* = 4.2 Hz, CH-NTs), 7.35 (2H, d, *J* = 8.3 Hz, CH(Ar)), 7.99 (2H, d, *J* = 8.3 Hz, CH(Ar)). **^{13}C NMR** ($CDCl_3$, 75.4 MHz): δ 16.2 (CH_3), 16.7 (CH_3), 21.7 (CH_3-Ar), 32.7 ($\underline{C}H(CH_3)_2$), 59.4 (CH-NTs), 81.8 (CH-O), 129.0 (CH(Ar)), 129.6 (CH(Ar)), 134.0 (C(Ar)), 146.0 (C(Ar)-SO_2), 151.0 (C=O), 172.9 (CO_2H). **IR**: 1787, 1173. **$[\alpha]_D$ =** +16.3 (*c* 1.35, $CHCl_3$). **HRMS** (EI^+) calcd for $C_{14}H_{17}NO_6S$: 327.0777, found: 327.0772.

Compound 12a: Colorless solid, **mp:** 93-96 ºC. $\mathbf{R_f}$ (CH_2Cl_2/MeOH 9:1): 0.28. **^{1}H NMR** ($CDCl_3$/CD_3OD, 300 MHz): δ 1.0-1.34 (6H, m, cyclohexyl), 1.66-1.86 (5H, m, cyclohexyl), 2.46 (3H, s, CH_3-Ar), 4.28 (1H, dd, *J* = 5.7, 3.9 Hz, CH-O), 4.74 (1H, d, *J* = 3.9 Hz, CH-NTs), 7.35 (2H, d, *J* = 8.4 Hz, CH(Ar)), 7.99 (2H, d, *J* = 8.4 Hz, CH(Ar)). **^{13}C NMR** ($CDCl_3$/CD_3OD, 75.4 MHz): δ 21.7 (CH_3-Ar), 25.0 (CH_2), 25.2 (CH_2), 25.6 (CH_2), 26.3 (CH_2), 27.0 (CH_2), 41.9 (CH), 60.4 (CH-NTs), 82.2 (CH-O), 128.6 (CH(Ar)), 129.3 (CH(Ar)), 134.3 (C(Ar)), 145.6 (C(Ar)-SO_2), 151.5 (C=O), 172.2 (CO_2H). **IR:** 1787, 1173. **HRMS** (EI), calcd for $C_{17}H_{21}NO_6S$ (M+): 367.1089, found: 367.1075. **EA** calcd. for $C_{17}H_{21}NO_6S$: C 55.57, H 5.76, N 3.81; found: C 55.40, H 6.00, N 3.87.

Compound 12c: Colorless solid, **mp**: 77-8 ºC. $\mathbf{R_f}$ (hexane/EtOAc 65:35): 0.32. **^{1}H NMR** ($CDCl_3$/CD_3OD, 400 MHz): δ 0.87 (3H, t, *J* = 6.4 Hz, CH_3), 1.26-1.29 (6H, m, CH_2), 1.75 (2H, m, $C\underline{H}_2$-CHO), 2.44 (3H, s, CH_3-Ar), 4.53 (1H, dt, *J* = 6.2, 4.4 Hz, CH-O), 4.60 (1H, d, *J* = 4.4 Hz, CH-NTs), 7.35 (2H, d, *J* = 8.4 Hz), 7.98 (2H, d, *J* = 8.4 Hz). **^{13}C NMR** ($CDCl_3$/CD_3OD, 100.6 MHz): δ 13.8 (CH_3), 21.7 (CH_3-Ar), 22.3 (CH_2), 23.5 (CH_2), 31.1 (CH_2), 35.0 (CH_2), 62.0 (CH-NTs), 77.8 (CH-O), 129.0 (CH(Ar)), 129.6 (CH(Ar)), 134.0 (C(Ar)), 146.0 (C(Ar)-SO_2), 151.0 (C=O), 172.9 (CO_2H). **IR**: 1791, 1173. **HRMS** (FAB+), calcd for $C_{16}H_{22}NO_6S$ (M+1): 356.1168; found: 356.1163. **EA** calcd. for $C_{16}H_{21}NO_6S$: C 54.07, H 5.96, N 3.94; found: C 54.00, H 6.20, N 3.73.

Compound 12d: Colorless solid. **mp**: 170-171 ºC. $\mathbf{R_f}$ (hexane/EtOAc 80:20): 0.07; (CH_2Cl_2/MeOH 9:1): 0.30. **^{1}H NMR** ($CDCl_3$/CD_3OD, 400 MHz): δ 1.53 (3H, d, *J* = 6.4 Hz, CH_3), 2.45 (3H, s, CH_3-Ar), 4.54 (1H, d, *J* = 4.8 Hz, CH-NTs), 4.62 (1H, dq, *J* = 7.3,

4.8 Hz, CH-O), 7.35 (2H, d, *J* = 8.4 Hz, CH(Ar)), 8.00 (2H, d, *J* = 8.4 Hz, CH(Ar)). **^{13}C NMR** ($CDCl_3/CD_3OD$, 100.6 MHz): δ 20.8 (CH_3), 21.7 (CH_3-Ar), 63.4 (CH-NTs), 74.5 (CH-O), 129.1 (CH(Ar)), 129.5 (CH(Ar)), 134.1 (C(Ar)), 145.8 (C(Ar)-SO_2), 151.0 (C=O), 169.9 (CO_2H). **IR**: 1789, 1173. **HRMS** (FAB+), calcd for $C_{12}H_{14}NO_6S$ (M+1): 300.0542; found: 300.0530. **EA** calcd. for $C_{12}H_{13}NO_6S$: C 48.16, H 4.38, N 4.68; found: C 48.33, H 4.54, N 4.40.

General procedure for oxidation of *cis*-oxazolidinones: (4*S*,5*S*)-5-(1-methylethyl)-3-(4-methylphenyl)sulfonyl-2-oxazolidinone-4-carboxylic acid (13b)

Ozone was bubbled through a solution of oxazolidinone **7b** (147 mg, 0.42 mmol) in CH_2Cl_2 anhyd (12 mL) at –78 ºC until TLC showed complete conversion. Then, nitrogen was bubbled through the blue solution for a few minutes before adding Me_2S (~50 μL) and stirring at r.t. for 90 min. The solution was diluted with CH_2Cl_2 (10 mL) and a phosphate buffer (pH=7, 5 mL) was added. The aqueous layer was washed with CH_2Cl_2 (3x10 mL). The combined organic layer was dried over $MgSO_4$ anhyd. Removal of solvent afforded crude (4*S*,5*S*)-5-(1-methylethyl)-3-(4-methylphenyl)sulfonyl-2-oxazolidinone-4-carbaldehyde (130 mg, 100%): Colorless solid. **R_f** (hexane/EtOAc 80:20): 0.13. **^{1}H NMR** ($CDCl_3$, 300 MHz): δ 1.02 (3H, d, *J* = 6.6 Hz, CH_3), 1.04 (3H, d, *J* = 6.6 Hz, CH_3), 1.89 (1H, m, C<u>H</u>(CH_3)$_2$), 2.47 (3H, s, CH_3-Ar), 4.39 (1H, dd, *J* = 8.6, 8.1 Hz, CH-O), 4.88 (1H, dd, *J* = 8.1, 2.5 Hz, CH-NTs), 7.38 (2H, d, *J* = 8.7 Hz, CH(Ar)), 7.93 (2H, d, *J* = 8.7 Hz, CH(Ar)), 9.78 (1H, d, *J* = 2.5 Hz, CHO). **^{13}C NMR** ($CDCl_3$, 75.4 MHz): δ 18.1 (CH_3), 18.5 (CH_3), 21.7 (CH_3-Ar), 28.7 (<u>C</u>H(CH_3)$_2$), 65.3 (CH-NTs), 82.8 (CH-O), 128.9 (CH(Ar)), 129.8 (CH(Ar)), 134.1 (C(Ar)), 146.2 (C(Ar)-SO_2), 150.89 (C=O), 194.9 (CHO). The above crude mixture was dissolved in CH_3CN (1.5 mL). An aqueous solution of NaH_2PO_4 (124 mg in 0.9 mL) and H_2O_2 (33% p/v, 0.3 mL) was added and the mixture was cooled to 0-4 ºC. Then, an aqueous $NaClO_2$ solution (62 mg, 0.9 mL) was added and the green homogenous solution was stirred at r.t. until starting material was consumed. The reaction mixture was quenched by addition of an aqueous solution of $NaHSO_3$ (65 mg, 0.8 mL). The mixture was stirred for 30 min and then acidified with HCl 2 N. CH_2Cl_2 (5 mL) was added and the aqueous layer was extracted with CH_2Cl_2 (5 mL). The organic layer was dried over $MgSO_4$ anhyd, and the solvent was removed. The crude residue did not need further purification and oxazolidinone **13b** (136 mg, 99%) was obtained.

Compound 13b: Colorless solid, **mp**: 188-192 ºC. **R_f** (hexane/EtOAc 65:35): 0.28. **^{1}H NMR** ($CDCl_3/CD_3OD$, 300 MHz): δ 1.02 (3H, d, *J* = 6.6 Hz, CH_3), 1.04 (3H, d, *J* = 6.6 Hz, CH_3) 1.89 (1H, m, C<u>H</u>(CH_3)$_2$), 2.44 (3H, s, CH_3-Ar), 4.26 (1H, dd, *J* = 9.9, 7.3 Hz, CH-O), 4.91 (1H, d, *J* = 7.3 Hz, CH-NTs), 7.34 (2H, d, *J* = 8.1 Hz, CH(Ar)), 7.94 (2H, d, *J* = 8.1 Hz, CH(Ar)). **^{13}C NMR** ($CDCl_3/CD_3OD$, 75.4 MHz): δ 18.2 (CH_3), 18.9 (CH_3), 21.6 (CH_3-Ar), 28.9 (<u>C</u>H(CH_3)$_2$), 61.4 (CH-NTs), 82.5 (CH-O), 128.8 (CH(Ar)), 129.4 (CH(Ar)), 134.2 (C(Ar)), 145.6 (C(Ar)-SO_2), 151.3 (C=O), 168.7 (CO_2H). **IR**: 1791, 1727, 1175. **$[\alpha]_D$ =** -18.7 (*c* 1.7, MeOH). **HRMS** (FAB+), calcd for $C_{14}H_{18}NO_6S$ (M+1): 328.0855, found: 328.0842. **EA** calcd for $C_{14}H_{17}NO_6S$: C 51.37, H 5.23, N 4.28; found: C 51.30, H 5.40, N 3.99.

Compound 13c: Colorless solid, **mp**: 192-194 ºC. **R_f** (hexane/EtOAc 65:35): 0.36. **^{1}H**

NMR ($CDCl_3/CD_3OD$, 300 MHz): δ 0.87 (3H, t, *J* = 6.4 Hz, CH_3), 1.26-1.31 (6H, m, CH_2), 1.67 (2H, m, C<u>H</u>$_2$-CHO), 2.45 (3H, s, CH_3-Ar), 4.06 (bs, COOH), 4.71 (1H, dt, *J* = 8.7, 4.2 Hz, CH-O), 4.92 (1H, d, *J* = 8.7 Hz, CH-NTs), 7.35 (2H, d, *J* = 8.3 Hz), 7.96 (2H, d, *J* = 8.3 Hz). **^{13}C NMR** ($CDCl_3/CD_3OD$, 75.4 MHz): δ 13.5 (CH_3), 21.3 (CH_3-Ar), 22.0 (CH_2), 24.9 (CH_2), 29.8 (CH_2), 30.9 (CH_2), 61.2 (CH-NTs), 76.7 (CH-O), 128.8 (CH(Ar)), 129.2 (CH(Ar)), 134.0 (C(Ar)), 145.6 (C(Ar)-SO_2), 151.4 (C=O), 168.4 (CO_2H). **IR**: 1792, 1727, 1175. **HRMS** (FAB+), calcd for $C_{16}H_{22}NO_6S$ (M+1): 356.1168; found: 356.1159.

Compound 13d: Colorless solid, **mp**: 197-199 ºC. **R_f**: (CH_2Cl_2/MeOH 9:1): 0.32. **^{1}H NMR** ($CDCl_3/CD_3OD$, 300 MHz): δ 1.43 (3H, d, *J* = 6.4 Hz, CH_3), 2.45 (3H, s, CH_3-Ar), 4.89 (1H, part A of ABX_3 system, *J* = 8.4 Hz, CH-NTs), 4.93 (1H, part B of ABX_3 system *J* = 8.4, 6.4 Hz, C<u>H</u>-O), 7.35 (2H, d, *J* = 8.3 Hz, CH(Ar)), 7.98 (2H, d, *J* = 8.3 Hz, CH(Ar)). **^{13}C NMR** ($CDCl_3/CD_3OD$, 75.4 MHz): δ 15.7 (CH_3), 21.6 (CH_3-Ar), 61.5 (CH-NTs), 72.7 (CH-O), 129.0 (CH(Ar)), 129.4 (CH(Ar)), 134.2 (C(Ar)), 145.7 (C(Ar)-SO_2), 151.2 (C=O), 168.5 (CO_2H). **IR**: 1790, 1171. **EA** calcd. for $C_{12}H_{13}NO_6S$: C 48.16, H 4.38, N 4.68; found: C 48.16, H 4.63, N 4.61.