

Supporting Information File 1

for

Carbohydrate-auxiliary assisted preparation of enantiopure 1,2-oxazine derivatives and aminopolyols

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§ Responsible for X-ray crystal structure determination

Experimental procedures and characterisation data

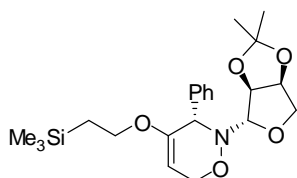
Methoxyallene [1], TMSE-allene [2], and benzyloxyallene [2] were prepared following literature procedures.

Preparation of 1,2-oxazines (3*S*)-3b and (3*R*)-3b

By a procedure similar to that for methoxyallene (Procedure 1), TMSE-allene (411 mg, 2.63 mmol) in THF (40 mL) was treated with *n*-BuLi (2.5 M in hexanes;

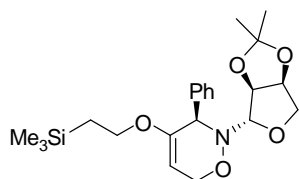
1.0 mL, 2.5 mmol) at $-40\text{ }^{\circ}\text{C}$, followed by slow addition of nitron **1a** (263 mg, 1.00 mmol) in dry THF (6 mL) at $-130\text{ }^{\circ}\text{C}$. The mixture was allowed to reach $-80\text{ }^{\circ}\text{C}$ within 2.5 h. After standard workup, crude products were isolated, by filtration through silica gel pad (hexane/ethyl acetate 6:1), as a yellow oil. Diastereomers were separated by an additional column (silica gel, hexane/ethyl acetate 9:1) to give (3*S*)-**3b** (133 mg, 32%, >95% purity) and (3*R*)-**3b** (78 mg, 19%) as colourless oils.

(3*S*,3*a'S*,4'*S*,6*a'**S*)-2-(2',2'-Dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4'-yl)-4-(2-trimethylsilyloxy)-3-phenyl-3,6-dihydro-2*H*-[1,2]oxazine ((3*S*)-**3b**):**



$[\alpha]_{\text{D}}^{22} = +107.2$ (c 1.03, CHCl_3); $^1\text{H NMR}$ (CDCl_3 , 700 MHz): $\delta = -0.15$ (s, 9H, SiMe_3), 0.79 (ddd, $J = 5.8, 8.7, 14.4$ Hz, 1H, CH_2Si), 0.85 (ddd, $J = 7.2, 9.0, 14.4$ Hz, 1H, CH_2Si), 1.31, 1.41 (2 s, 3H each, 2 Me), 3.68 (td, $J \approx 7.2, 9.2$ Hz, 1H, 4- OCH_2), 3.79 (dt, $J \approx 5.8, 9.2$ Hz, 1H, 4- OCH_2), 4.02 (d, $J = 9.6$ Hz, 1H, 6'-H), 4.24 (dd, $J = 3.5, 9.6$ Hz, 1H, 6'-H), 4.28 (dd_{br}, $J \approx 3.7, 13.7$ Hz, 1H, 6-H), 4.39 (s, 1 H, 4'-H), 4.60 (dt, $J \approx 2.0, 13.7$ Hz, 1H, 6-H), 4.80 (s_{br}, 1 H, 3-H), 4.82 (dt, $J \approx 1.6, 4.2$ Hz, 1H, 5-H), 4.86–4.89 (m, 2H, 3*a'*-H, 6*a'*-H), 7.26–7.31, 7.34–7.37 (2 m, 5H, Ph) ppm; $^{13}\text{C NMR}$ (CDCl_3 , 126 MHz): $\delta = -1.6$ (q, SiMe_3), 16.8 (t, CH_2Si), 24.6, 26.3 (2 q, 2 Me), 63.7 (d, C-3), 64.8 (t, 4- OCH_2 -), 67.4 (t, C-6), 76.6 (t, C-6'), 81.2, 84.3 (2 d, C-3*a'*, C-6*a'*), 92.2 (d, C-5), 94.8 (d, C-4'), 111.6 (s, C-2'), 127.8, 128.2, 129.9, 136.5 (3 d, s, Ph), 154.3 (s, C-4) ppm; IR (ATR): $\tilde{\nu} = 3065\text{--}2850$ (=C-H, C-H), 1730 (C=C), 1210, 1060 (C-O) cm^{-1} ; ESI-TOF (m/z): calcd. for $\text{C}_{22}\text{H}_{33}\text{NNaO}_5\text{Si}$ [$\text{M} + \text{Na}$]⁺: 442.2025; found: 442.2014.

(3*R*,3*a'S*,4'*S*,6*a'**S*)-2-(2',2'-Dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4'-yl)-4-(2-trimethylsilyloxy)-3-phenyl-3,6-dihydro-2*H*-[1,2]oxazine ((3*R*)-3b):**



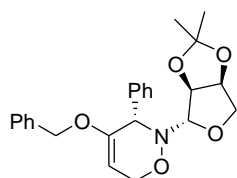
$[\alpha]_D^{22} = -55.7$ (*c* 1.25, CHCl_3); $^1\text{H NMR}$ (CDCl_3 , 500 MHz): $\delta = -0.13$ (s, 9H, SiMe_3), 0.79 (ddd, $J = 5.8, 8.9, 14.3$ Hz, 1H, CH_2Si), 0.85 (ddd, $J = 7.1, 9.2, 14.3$ Hz, 1H, CH_2Si), 1.33, 1.44 (2 s, 3H each, 2 Me), 3.68 (td, $J \approx 7.1, 9.2$ Hz, 1H, 4- OCH_2), 3.81 (td, $J \approx 5.8, 9.2$ Hz, 1H, 4- OCH_2), 3.89 (d, $J = 9.9$ Hz, 1H, 6'-H), 4.03 (dd, $J = 4.0, 9.9$ Hz, 1H, 6'-H), 4.39 (ddd, $J = 1.7, 3.1, 14.2$ Hz, 1H, 6-H), 4.44 (s, 1H, 3-H), 4.51 (ddd, $J = 1.3, 2.4, 14.2$ Hz, 1H, 6-H), 4.73 (s, 1H, 4'-H), 4.80 (dd, $J = 4.0, 6.1$ Hz, 1H, 6*a'*-H), 4.84 (t, $J \approx 3.0$ Hz, 1H, 5-H), 5.03 (d, $J = 6.1$ Hz, 1H, 3*a'*-H), 7.26–7.31, 7.36–7.39 (2 m, 5H, Ph) ppm; $^{13}\text{C NMR}$ (CDCl_3 , 126 MHz): $\delta = -1.5$ (q, SiMe_3), 16.9 (t, CH_2Si), 24.8, 26.3 (2 q, 2 Me), 63.7 (d, C-3), 64.6 (t, 4- OCH_2), 65.2 (t, C-6), 74.5 (t, C-6'), 81.1 (d, C-6*a'*), 81.6 (d, C-3*a'*), 91.8 (d, C-5), 96.4 (d, C-4'), 112.0 (s, C-2'), 127.6, 128.1, 129.1, 138.3 (3 d, s, Ph), 152.2 (s, C-4) ppm; IR (ATR): $\tilde{\nu} = 3060\text{--}2845$ (=C-H, C-H), 1730 (C=C), 1105, 1055 (C-O) cm^{-1} ; ESI-TOF (m/z): calcd. for $\text{C}_{22}\text{H}_{33}\text{NNaO}_5\text{Si}$ [$\text{M} + \text{Na}$] $^+$: 442.2025; found: 442.2010; Anal. calcd. for $\text{C}_{22}\text{H}_{33}\text{NO}_5\text{Si}$ (419.6): C 62.98, H 7.97, N 3.34; found: C 62.99, H 7.99, N 3.35.

Preparation of 1,2-oxazines (3*S*)-3c and (3*R*)-3c

By the procedure similar to that for methoxyallene (Procedure 1), benzyloxyallene (719 mg, 4.92 mmol) in THF (45 mL) was treated with *n*-BuLi (2.5 M in hexanes; 1.8 mL, 4.5 mmol) at -40 °C, followed by slow addition of nitrone **1a** (540 mg, 2.05 mmol) in dry THF (10 mL) at -130 °C. The mixture was allowed to reach -80 °C

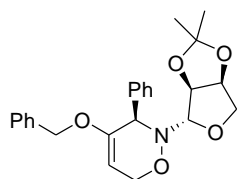
within 1.5 h. After standard workup, crude products were separated on a column (silica gel, hexane/ethyl acetate 6:1) to give enriched fractions of (3*S*)-**3c** (235 mg) and (3*R*)-**3c** (394 mg) as pale yellow oils. Each fraction was additionally chromatographed (silica gel, hexane/acetone 6:1, and 5:1, resp.) to give pure (3*S*)-**3c** (182 mg, 21%) and (3*R*)-**3c** (371 mg, 44%) as colourless oils.

(3*S*,3*a'S*,4'*S*,6*a'**S*)-4-Benzoyloxy-2-(2',2'-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4'-yl)-3-phenyl-3,6-dihydro-2*H*-[1,2]oxazine ((3*S*)-**3c**):**



$[\alpha]_{\text{D}}^{22} = +109.8$ (*c* 1.40, CHCl_3); $^1\text{H NMR}$ (CDCl_3 , 700 MHz): $\delta = 1.31, 1.41$ (2 s, 3H each, 2 Me), 4.03 (d, $J = 9.6$ Hz, 1H, 6'-H), 4.23-4.27 (m, 2H, 6'-H, 6-H), 4.44 (s, 1H, 4'-H), 4.59 (dt, $J \approx 2.0, 13.8$ Hz, 1H, 6-H), 4.70, 4.77 (2 d, $J = 12.3$ Hz, 2H, Bn), 4.87–4.89 (m, 2H, 3*a'*-H, 6*a'*-H), 4.90 (dt, $J \approx 1.6, 4.3$ Hz, 1H, 5-H), 4.91 (s_{br}, 1H, 3-H), 7.00–7.02, 7.20–7.25, 7.29–7.34, 7.40–7.42 (4 m, 10H, 2 Ph) ppm; $^{13}\text{C NMR}$ (CDCl_3 , 175 MHz): $\delta = 24.6, 26.3$ (2 q, 2 Me), 63.6 (d, C-3), 67.2 (t, C-6), 69.0 (t, Bn), 76.6 (t, C-6'), 81.2, 84.3 (2 d, C-3*a'*, C-6*a'*), 93.6 (d, C-5), 94.8 (d, C-4'), 111.7 (s, C-2'), 126.5, 127.4, 128.0, 128.2*, 129.8, 136.4, 136.9 (5 d, 2 s, 2 Ph), 153.7 (s, C-4) ppm, *higher intensity; IR (ATR): $\tilde{\nu} = 3090\text{--}2850$ (=C-H, C-H), 1675 (C=C), 1202, 1090, 1070, 1055 (C-O) cm^{-1} ; ESI-TOF (m/z): calcd. for $\text{C}_{24}\text{H}_{27}\text{NNaO}_5$ [$\text{M} + \text{Na}$]⁺: 432.1787; found: 432.1792. Anal. calcd. for $\text{C}_{24}\text{H}_{27}\text{NO}_5$ (409.5): C 70.40, H 6.65, N 3.42; found: C 68.70, H 6.58, N 3.44.

(3*R*,3*a'S*,4'*S*,6*a'**S*)-4-Benzoyloxy-2-(2',2'-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4'-yl)-3-phenyl-3,6-dihydro-2*H*-[1,2]oxazine ((3*R*)-3c):**



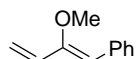
$[\alpha]_D^{22} = -51.3$ (c 1.57, CHCl_3); $^1\text{H NMR}$ (CDCl_3 , 500 MHz): $\delta = 1.35$, 1.46 (2 s, 3H each, 2 Me), 3.91 (d, $J = 9.9$ Hz, 1H, 6'-H), 4.05 (dd, $J = 4.0$, 9.9 Hz, 1H, 6'-H), 4.40 (ddd, $J = 1.7$, 3.3, 14.3 Hz, 1H, 6-H), 4.53 (ddd, $J = 1.7$, 2.4, 14.3 Hz, 1H, 6-H), 4.57 (s, 1H, 3-H), 4.72 (d, $J = 12.1$ Hz, 1H, Bn), 4.76 (s, 1H, 4'-H), 4.80 (d, $J = 12.1$ Hz, 1H, Bn), 4.82 (dd, $J = 4.0$, 6.1 Hz, 1H, 6*a'*-H), 4.96 (t, $J \approx 3.0$ Hz, 1H, 5-H), 5.05 (d, $J = 6.1$ Hz, 1H, 3*a'*-H), 7.06–7.08, 7.22–7.35, 7.41–7.44 (3 m, 10H, 2 Ph) ppm; $^{13}\text{C NMR}$ (CDCl_3 , 126 MHz): $\delta = 24.8$, 26.3 (2 q, 2 Me), 63.6 (d, C-3), 65.1 (t, C-6), 69.0 (t, Bn), 74.5 (t, C-6'), 81.0 (d, C-6*a'*), 81.6 (d, C-3*a'*), 93.2 (d, C-5), 96.5 (d, C-4'), 112.0 (s, C-2'), 126.7, 127.6, 127.7, 128.2, 128.3, 129.0 136.7 138.2 (6 d, 2 s, 2 Ph), 152.0 (s, C-4) ppm; IR (ATR): $\tilde{\nu} = 3090\text{--}2845$ (=C-H, C-H), 1675 (C=C), 1220, 1205, 1090 (C-O) cm^{-1} ; ESI-TOF (m/z): calcd. for $\text{C}_{24}\text{H}_{27}\text{NNaO}_5$ [$\text{M} + \text{Na}$] $^+$: 432.1787; found: 432.1766. Anal. calcd. for $\text{C}_{24}\text{H}_{27}\text{NO}_5$ (409.5): C 70.40, H 6.65, N 3.42; found: C 70.41, H 6.63, N 3.41.

Isolation of by-products 4 and 5

Compounds **4** (8 mg, 1%) and **5** (38 mg, 3%) were isolated as colourless oils from the reaction of lithiated methoxyallene (2.4 equiv.) generated from methoxyallene (640 mg, 0.77 mL, 9.13 mmol) and *n*-BuLi (2.5 M in hexanes; 3.5 mL, 8.75 mmol) with nitrone **1a** (960 mg, 3.65 mmol) at -78 °C, after standard workup (see Procedure 1) and additional purification on column. Diene **4** undergoes fast

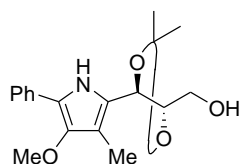
decomposition either during purification on silica or storage. Major products (3*S*)-**3a** (303 mg) and (3*R*)-**3a** (92 mg) were isolated in 25% and 8% yield, respectively.

(Z)-2-Methoxy-1-phenylbuta-1,3-diene (4) [3,4]:



CC (silica gel, hexane/dichloromethane 7:3). ^1H NMR (CDCl_3 , 500 MHz): δ = 3.77 (s, 3 H, OMe), 5.22 (dt, $J \approx 2.1, 11.0$ Hz, 1 H, 4-H), 5.75 (dd, $J = 2.1, 17.1$ Hz, 1 H, 4-H), 5.84 (s, 1 H, 1-H), 6.63 (dd, $J = 11.0, 17.1$ Hz, 1 H, 3-H), 7.17–7.24, 7.29–7.34 (2 m, 5 H, Ph) ppm; ^{13}C NMR (CDCl_3 , 126 MHz): δ = 54.8 (q, OMe), 103.9 (d, C-1), 116.0 (t, C-4), 125.8, 128.1, 129.4, 136.6 (3 d, s, Ph), 129.6 (d, C-3), 154.0 (s, C-2) ppm.

(4'*S*,5'*S*)-2-(2',2'-Dimethyl-5'-hydroxymethyl-[1,3]dioxolan-4'-yl)-4-methoxy-3-methyl-5-phenyl-1*H*-pyrrole (5):



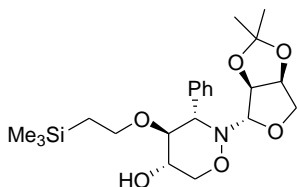
CC (silica gel, hexane/ethyl acetate 4:1). $[\alpha]_{\text{D}}^{22} = -43.1$ (c 0.80, CHCl_3); ^1H NMR (CDCl_3 , 500 MHz): δ = 1.49, 1.62 (2 s, 3H each, 2 Me), 2.08 (s, 3H, 3-Me), 2.11 (dd, $J \approx 4.0, 8.1$ Hz, 1H, OH), 3.45 (ddd, $J = 3.8, 8.1, 12.1$ Hz, 1H, 5'- CH_2 -), 3.61 (dt, $J = 4.0, 12.1$ Hz, 1H, 5'- CH_2 -), 3.72 (s, 3H, OMe), 4.33 (dt, $J = 3.8, 7.3$ Hz, 1H, 5'-H), 5.37 (d, $J = 7.3$ Hz, 1H, 4'-H), 7.15–7.19, 7.34–7.38, 7.60–7.64 (3 m, 5H, Ph), 8.98 (s_{br}, 1 H, NH) ppm; ^{13}C NMR (CDCl_3 , 126 MHz): δ = 7.6 (q, 3-Me), 24.3, 27.1 (2 q, 2 Me), 61.3 (q, OMe), 62.2 (t, 5'- CH_2 -), 71.7 (d, C-4'), 77.5 (d, C-5'), 107.8 (s, C-2'), 112.4, 119.3, 119.4 (3 s, C-2, C-3, C-5), 123.9, 125.5, 128.7, 131.9 (3 d, s, Ph), 143.9 (s, C-4) ppm; IR (ATR): $\tilde{\nu} = 3470\text{--}3340$ (O-H, N-H), $3080\text{--}2830$ (=C-H, C-H),

1210, 1035 (C-O) cm^{-1} ; ESI-TOF (m/z): calcd. for $\text{C}_{18}\text{H}_{23}\text{NNaO}_4$ [$\text{M} + \text{Na}$] $^+$: 340.1525; found: 340.1566; Anal. calcd. for $\text{C}_{18}\text{H}_{23}\text{NO}_4$ (317.4): C 68.17, H 7.30, N 4.41; found: C 68.19, H 7.39, N 4.37.

Hydroxylation of (3S)-3b

Following the general Procedure 2, compound (3S)-3b (289 mg, 0.69 mmol) in THF (40 mL) was treated with a solution of $\text{BF}_3 \cdot \text{THF}$ (1 M in THF, 3.6 mL, 3.6 mmol). After oxidative workup, the crude mixture was chromatographed (silica gel, hexane/ethyl acetate 2:1) to yield compounds **8** (106 mg, 35%, first eluted) as colourless crystals and **9** (175 mg, 58%) as a colourless oil.

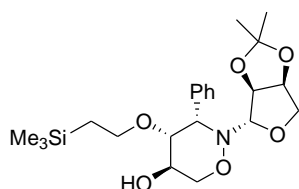
(3S,4S,5S,3'aS,4'S,6'aS)-2-(2',2'-Dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4'-yl)-4-(2-trimethylsilyloxy)-3-phenyl-[1,2]oxazinan-5-ol (**8**):



mp 121-125 °C; $[\alpha]_{\text{D}}^{22} = +131.8$ (c 1.35, CHCl_3); ^1H NMR (CDCl_3 , 500 MHz): $\delta = -0.22$ (s, 9H, SiMe_3), 0.50 (ddd, $J = 5.4, 11.7, 13.5$ Hz, 1H, CH_2Si), 0.69 (ddd, $J = 5.5, 11.9, 13.5$ Hz, 1H, CH_2Si), 1.29, 1.35 (2 s, 3H each, 2 Me), 2.36 (d_{br} , $J = 3.8$ Hz, 1H, OH), 2.72 (ddd, $J = 5.4, 9.5, 11.9$ Hz, 1H, 4-OCH₂), 3.11 (ddd, $J = 5.5, 9.5, 11.7$ Hz, 1H, 4-OCH₂), 3.47 (dd_{br} , $J \approx 8.2, 9.4$ Hz, 1H, 4-H), 3.63–3.71 (m, 2H, 5-H, 6-H), 3.92 (d, $J = 9.4$ Hz, 1H, 3-H), 3.94 (d, $J = 9.4$ Hz, 1H, 6'-H), 4.08 (dd_{br} , $J \approx 4.0, 9.5$ Hz, 1H, 6-H), 4.19 (dd, $J = 4.4, 9.4$ Hz, 1H, 6'-H), 4.46 (s, 1H, 4'-H), 4.81 (dd, $J = 4.4, 6.1$ Hz, 1H, 6a'-H), 4.87 (d, $J = 6.1$ Hz, 1H, 3a'-H), 7.26–7.34, 7.37–7.42 (2 m, 5H, Ph) ppm; ^{13}C NMR (CDCl_3 , 126 MHz): $\delta = -1.7$ (q, SiMe_3), 18.7 (t, CH_2Si), 24.5,

26.3 (2 q, 2 Me), 67.9 (d, C-3), 69.8 (t, 4-OCH₂-), 70.6 (d, C-5), 71.4 (t, C-6), 77.4 (t, C-6'), 81.4 (d, C-6a'), 84.5 (d, C-3a'), 85.6 (d, C-4), 94.9 (d, C-4'), 111.7 (s, C-2'), 128.3, 128.7*, 137.1 (2 d, s, Ph) ppm, *higher intensity; IR (ATR): $\tilde{\nu}$ = 3400 (O-H), 3035–2870 (=C-H, C-H), 1050 (C-O) cm⁻¹; ESI-TOF (*m/z*): calcd. for C₂₂H₃₅NNaO₆Si [M + Na]⁺: 460.2131; found: 460.2149; Anal. calcd. for C₂₂H₃₅NO₆Si (437.6): C 60.38, H 8.06, N 3.20; found: C 60.57, H 8.10, N 3.21.

(3*S*,4*R*,5*R*,3'*aS*,4'*S*,6'*aS*)-2-(2',2'-Dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4'-yl)-4-(2-trimethylsilyloxy)-3-phenyl-[1,2]oxazinan-5-ol (9):



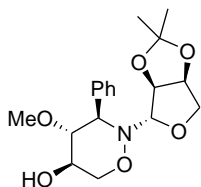
$[\alpha]_D^{22} = +122.6$ (c 1.12, CHCl₃); ¹H NMR (CDCl₃, 500 MHz): δ = -0.11 (s, 9H, SiMe₃), 0.67 (ddd, *J* = 4.9, 10.9, 13.8 Hz, 1H, CH₂Si), 0.76 (ddd, *J* = 6.3, 11.4, 13.8 Hz, 1H, CH₂Si), 1.29, 1.36 (2 s, 3H each, 2 Me), 2.30 (s_{br}, 1H, OH), 2.95 (ddd, *J* = 4.9, 9.5, 11.4 Hz, 1H, 4-OCH₂), 3.27 (m_c, 1H, 4-H), 3.31 (ddd, *J* = 6.3, 9.5, 10.9 Hz, 1H, 4-OCH₂), 3.70 (s_{br}, 1H, 5-H), 3.82 (d, *J* = 12.1 Hz, 1H, 6-H), 3.95 (d, *J* = 9.4 Hz, 1H, 6'-H), 4.21 (dd, *J* = 4.6, 9.4 Hz, 1H, 6'-H), 4.40 (dd, *J* = 1.2, 12.1 Hz, 1H, 6-H), 4.44 (d, *J* = 2.4 Hz, 1H, 3-H), 4.64 (s, 1H, 4'-H), 4.82 (t_{br}, *J* ≈ 5.2 Hz, 1H, 6a'-H), 4.96 (d, *J* = 6.1 Hz, 1H, 3a'-H), 7.24–7.31, 7.43–7.46 (2 m, 5H, Ph) ppm; ¹³C NMR (CDCl₃, 126 MHz): δ = -1.5 (q, SiMe₃), 18.3 (t, CH₂Si), 24.6, 26.3 (2 q, 2 Me), 62.8 (d, C-3), 66.4 (d, C-5), 69.1 (t, 4-OCH₂-), 71.1 (t, C-6), 77.6 (t, C-6'), 78.2 (d, C-4), 81.2 (d, C-6a'), 84.6 (d, C-3a'), 95.7 (d, C-4'), 111.6 (s, C-2'), 127.8, 128.1, 129.5, 136.6 (3 d, s, Ph) ppm; IR (ATR): $\tilde{\nu}$ = 3450 (O-H), 3065–2845 (=C-H, C-H), 1090, 1065 (C-O) cm⁻¹; ESI-TOF (*m/z*): calcd. for C₂₂H₃₅NNaO₆Si [M + Na]⁺: 460.2131; found: 460.2128;

Anal. calcd. for C₂₂H₃₅NO₆Si (437.6): C 60.38, H 8.06, N 3.20; found: C 60.36, H 8.09, N 3.25.

Hydroxylation of (3*R*)-3a

By the procedure similar to that for (3*S*)-3a (Procedure 2), compound (3*R*)-3a (810 mg, 2.43 mmol) in THF (60 mL) was treated with a solution of BF₃·THF (1 M in THF, 9.8 mL, 9.8 mmol). After standard oxidative workup, the crude mixture was chromatographed (silica gel, hexane/ethyl acetate 1:1) to yield an enriched fraction of **10** (186 mg, first eluted) and pure **11** (568 mg, 66%). Additional chromatography purification of **10** (silica gel, dichloromethane/acetone 9:1) yielded an analytically pure sample (109 mg, 13%). Both alcohols were isolated as colourless oils.

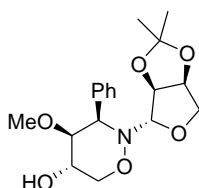
(3*R*,4*R*,5*R*,3*a'**S*,4'*S*,6*a'**S*)-2-(2',2'-Dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4'-yl)-4-methoxy-3-phenyl-[1,2]oxazinan-5-ol (**10**):



$[\alpha]_D^{22} = -79.4$ (*c* 1.08, CHCl₃); ¹H NMR (CDCl₃, 500 MHz): $\delta = 1.29, 1.32$ (2 s, 3H each, 2 Me), 2.70 (d, *J* = 2.1 Hz, 1H, OH), 2.89 (s, 3H, OMe), 3.37 (t, *J* \approx 8.8 Hz, 1H, 4-H), 3.64 (d, *J* = 9.1 Hz, 1H, 3-H), 3.63-3.69 (m_{br}, 1H, 5-H), 3.79 (t, *J* \approx 10.9 Hz, 1H, 6-H), 3.88 (d, *J* = 9.6 Hz, 1H, 6'-H), 4.04 (dd, *J* = 5.7, 11.2 Hz, 1H, 6-H), 4.17 (dd, *J* = 4.3, 9.6 Hz, 1H, 6'-H), 4.45 (s, 1H, 4'-H), 4.75 (dd, *J* = 4.3, 6.1 Hz, 1H, 6a'-H), 4.99 (d, *J* = 6.1 Hz, 1H, 3a'-H), 7.27–7.37, 7.41–7.45 (2 m, 5H, Ph) ppm; ¹³C NMR (CDCl₃, 126 MHz): $\delta = 24.7, 26.3$ (2 q, 2 Me), 60.8 (q, OMe), 69.6 (d, C-3), 70.6* (t, C-6, and d, C-5), 75.5 (t, C-6'), 78.8 (d, C-3a'), 81.2 (d, C-6a'), 87.8 (d, C-4), 96.5 (d, C-4'),

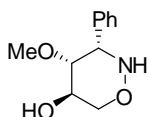
111.9 (s, C-2'), 128.5, 129.0*, 136.8 (2 d, s, Ph) ppm, *higher intensity; IR (ATR): $\tilde{\nu}$ = 3455 (O-H), 3035–2835 (=C-H, C-H), 1105, 1055 (C-O) cm^{-1} ; Anal. calcd. for $\text{C}_{18}\text{H}_{25}\text{NO}_6$ (351.4): C 61.52, H 7.17, N 3.99; found: C 61.53, H 7.19, N 3.79.

(3*R*,4*S*,5*S*,3*a'S*,4'*S*,6*a'**S*)-2-(2',2'-Dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4'-yl)-4-methoxy-3-phenyl-[1,2]oxazinan-5-ol (11):**



$[\alpha]_{\text{D}}^{22} = +4.4$ (*c* 0.97, CHCl_3); $^1\text{H NMR}$ (CDCl_3 , 500 MHz): δ = 1.30, 1.34 (2 s, 3H each, 2 Me), 2.32 (d, J = 5.4 Hz, 1H, OH), 3.14 (s, 3H, OMe), 3.30 (t_{br}, J \approx 4.1 Hz, 1H, 4-H), 3.77 (dd, J = 4.5, 11.9 Hz, 1H, 6-H), 3.81 (d, J = 9.7 Hz, 1H, 6'-H), 3.89 (m_c, 1H, 5-H), 4.08 (dd, J = 4.3, 9.7 Hz, 1H, 6'-H), 4.28 (d, J = 3.5 Hz, 1H, 3-H), 4.38 (dd, J = 2.8, 11.9 Hz, 1H, 6-H), 4.67 (s, 1H, 4'-H), 4.76 (dd, J = 4.3, 6.1 Hz, 1H, 6*a'*-H), 4.98 (d, J = 6.1 Hz, 1H, 3*a'*-H), 7.26–7.33, 7.44–7.48 (2 m, 5H, Ph) ppm; $^{13}\text{C NMR}$ (CDCl_3 , 126 MHz): δ = 24.7, 26.3 (2 q, 2 Me), 58.7 (q, OMe), 64.4 (d, C-3), 65.3 (d, C-5), 70.7 (t, C-6), 75.3 (t, C-6'), 80.6 (d, C-3*a'*), 81.1 (d, C-6*a'*), 81.3 (d, C-4), 97.8 (d, C-4'), 111.8 (s, C-2'), 127.7, 128.1, 129.2, 137.1 (3 d, s, Ph) ppm; IR (ATR): $\tilde{\nu}$ = 3440 (O-H), 3090–2830 (=C-H, C-H), 1095, 1050 (C-O) cm^{-1} ; ESI-TOF (m/z): calcd. for $\text{C}_{18}\text{H}_{25}\text{NNaO}_6$ [$\text{M} + \text{Na}$]⁺: 374.1580; found: 374.1577; Anal. calcd. for $\text{C}_{18}\text{H}_{25}\text{NO}_6$ (351.4): C 61.52, H 7.17, N 3.99; found: C 61.47, H 7.15, N 3.88.

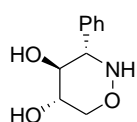
(3*S*,4*R*,5*R*)-4-Methoxy-3-phenyl-[1,2]oxazinan-5-ol (13):



By a procedure similar to that for **6** (Procedure 3), 1,2-oxazine **7** (255 mg, 0.72 mmol) was dissolved in 1N HCl in MeOH (8 mL) and heated at 40 °C for 4 h (TLC monitoring, hexane/AcOEt 1:2, potassium permanganate stain). After workup and purification on a column (silica gel, dichloromethane/methanol 40:1) compound **13** (127 mg, 83%) was isolated as a colourless solid.

mp 112-113 °C; $[\alpha]_D^{22} = +47.9$ (*c* 1.00, CHCl₃); ¹H NMR (CDCl₃, 500 MHz): $\delta = 3.19$ (s, 3H, OMe), 3.40 (t_{br}, *J* = 1.5 Hz, 1H, 4-H), 3.87 (ddd_{br}, *J* = 12.1, 2.1, 0.9 Hz, 1H, 6-H), 3.89 (dd, *J* = 3.7, 2.2 Hz, 1H, 5-H), 4.25 (dd, *J* = 12.1, 1.1 Hz, 1H, 6-H), 4.58 (d, *J* = 2.0 Hz, 1H, 3-H), 7.27–7.36 (m, 5H, Ph) ppm; ¹³C NMR (CDCl₃, 126 MHz): $\delta = 59.0$ (q, OMe), 60.3 (d, C-3), 65.2 (d, C-5), 71.2 (t, C-6), 78.2 (d, C-4), 127.5, 127.6, 128.3, 137.3 (3d, s, Ph) ppm; IR (ATR): $\tilde{\nu} = 3390\text{--}3220$ (O-H, N-H), 3060–2830 (=C-H, C-H), 1090 (C-O) cm⁻¹; ESI-TOF (*m/z*): calcd. for C₁₁H₁₃NO₃ [M + H]⁺: 210.1130; found: 210.1128; Anal. calcd. for C₁₁H₁₅NO₃ (209.2): C 63.14, H 7.23, N 6.69; found: C 63.15, H 7.13, N 6.72.

(3S,4S,5S)-3-Phenyl-[1,2]oxazine-4,5-diol (14**):**



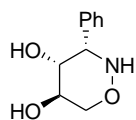
To a solution of 1,2-oxazine **8** (100 mg, 0.23 mmol) in EtOH (8.0 mL) acidic ion exchange resin DOWEX-50 (1.26 g; washed several times with EtOH before usage) was added. The suspension was vigorously stirred at 50 °C for 10 d, and then decanted. The resin was washed with three portions of ammonia in methanol solution (7 N, ca. 5.0 mL each) and the organics combined. After evaporation of the solvents, compound **14** (35 mg, 78%) was isolated as a colourless solid.

mp 153-154 °C; $[\alpha]_D^{22} = +33.8$ (*c* 1.05, CH₃OH); ¹H NMR (CD₃OD, 500 MHz, 50 °C): $\delta = 3.60\text{--}3.69$ (m, 3H, 4-H, 5-H, 6-H), 3.85 (d, *J* = 9.2 Hz, 1H, 3-H), 4.02–4.08 (m, 1H, 6-H), 7.27–7.31, 7.32–7.36, 7.38–7.41 (3 m, 5H, Ph) ppm; ¹³C NMR (CD₃OD, 126 MHz, 50 °C): $\delta = 69.2$ (d, C-3), 72.6 (d, C-5), 74.3 (t, C-6), 77.1 (d, C-4), 129.2, 129.5, 129.9, 137.6 (3 d, s, Ph) ppm; IR (neat): $\tilde{\nu} = 3460, 3150$ (O-H, N-H), 3085–2885 (=C-H, C-H), 1030 (C-O) cm⁻¹; ESI-TOF (*m/z*): calcd. for C₁₀H₁₃NNaO₃ [*M* + Na]⁺: 218.0793; found: 218.0843; Anal. calcd. for C₁₀H₁₃NO₃ (195.2): C 61.53, H 6.71, N 7.18; found: C 61.45, H 6.67, N 7.13.

Synthesis of **14** by demethylation of **12**

To a solution of 1,2-oxazine **12** (59 mg, 0.28 mmol) in CH₂Cl₂ (4.4 mL) a solution of BBr₃ (1 M in CH₂Cl₂, 0.85 mL, 0.85 mmol) was slowly added at –78 °C and stirred for 1 h, and then at room temperature overnight. The mixture was diluted with MeOH (3 mL) and the solvents were removed. The crude mixture was flash chromatographed (silica gel, dichloromethane/methanol 20:1) to give an enriched fraction of **14** (33 mg). Additional purification on a column (silica gel, dichloromethane/methanol 25:1) furnished **14** (10 mg, 18%) as a colourless solid.

(3*S*,4*R*,5*R*)-3-Phenyl-[1,2]oxazine-4,5-diol (**15**):

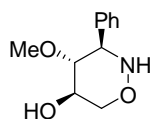


Following the general Procedure 3, compound **9** (160 mg, 0.37 mmol) in 1 N HCl in MeOH (10 mL) was heated overnight at 40 °C. The crude product was purified on a column (silica gel, dichloromethane/methanol 30:1) to give *N*-unsubstituted 1,2-oxazine derivative (89 mg, 82%) as a colourless oil. $[\alpha]_D^{22} = 25.7$ (*c* 0.68, CHCl₃); ¹H

NMR (CDCl₃, 500 MHz): δ = -0.12 (s, 9H, SiMe₃), 0.68 (ddd, J = 5.6, 10.5, 13.8 Hz, 1H, CH₂Si), 0.74 (ddd, J = 6.3, 10.7, 13.8 Hz, 1H, CH₂Si), 3.07 (ddd, J = 5.6, 9.7, 10.6 Hz, 1H, 4-OCH₂), 3.40 (ddd, J = 6.3, 9.7, 10.5 Hz, 1H, 4-OCH₂), 3.43 (m_c, 1H, 4-H), 3.81 (m_c, 1H, 5-H), 3.86 (d_{br}, J \approx 12.4 Hz, 1H, 6-H), 4.23 (dd, J = 1.2, 12.4 Hz, 1H, 6-H), 4.58 (d, J = 1.9 Hz, 1H, 3-H), 7.24–7.30 (m, 5H, Ph) ppm; ¹³C NMR (CDCl₃, 126 MHz): δ = -1.5 (q, SiMe₃), 18.4 (t, CH₂Si), 60.1 (d, C-3), 66.0 (d, C-5), 68.7 (t, 4-OCH₂), 71.4 (t, C-6), 76.1 (d, C-4), 127.40, 127.44, 128.1, 137.6 (3 d, s, Ph) ppm; IR (ATR): $\tilde{\nu}$ = 3485–3230 (O-H, N-H), 3090–2850 (=C-H, C-H), 1245, 1085 (C-O) cm⁻¹; ESI-TOF (m/z): calcd. for C₁₅H₂₅NO₃Si [M + Na]⁺: 318.1501; found: 318.1504. To a solution of this partially deprotected 1,2-oxazine (80 mg, 0.27 mmol) in EtOH (7.0 mL), acidic ion exchange resin DOWEX-50 (533 mg; washed several times with EtOH before usage) was added. The suspension was vigorously stirred at 50 °C for 4 d, and then decanted. The resin was washed with three portions of ammonia in methanol solution (7 N, ca. 4.0 mL each) and the organics were combined. After evaporation of the solvents compound **15** (49 mg, 92%) was isolated as a colourless solid.

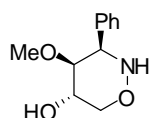
mp 190-192 °C; $[\alpha]_D^{22}$ = +65.6 (c 1.26, CH₃OH); ¹H NMR (CD₃OD, 500 MHz): δ = 3.70 (dt, J \approx 1.7, 3.7 Hz, 1H, 5-H), 3.74 (m_c, 1H, 4-H), 3.89 (ddd_{br}, J \approx 0.9, 1.7, 12.5 Hz, 1H, 6-H), 4.25 (dd, J = 1.5, 12.5 Hz, 1H, 6-H), 4.57 (d, J = 1.6 Hz, 1H, 3-H), 7.24–7.27, 7.30–7.35 (2 m, 5H, Ph) ppm; ¹³C NMR (CD₃OD, 126 MHz): δ = 61.7 (d, C-3), 69.3 (d, C-5), 69.5 (d, C-4), 71.3 (t, C-6), 128.3, 128.7, 129.2, 139.6 (3 d, s, Ph) ppm; IR (neat): $\tilde{\nu}$ = 3480, 3170 (O-H, N-H), 3065–2850 (=C-H, C-H), 1070, 1005 (C-O) cm⁻¹; ESI-TOF (m/z): calcd. for C₁₀H₁₃NNaO₃ [M + Na]⁺: 218.0793; found: 218.0787; Anal. calcd. for C₁₀H₁₃NO₃ (195.2): C 61.53, H 6.71, N 7.18; found: C 61.57, H 6.69, N 7.18.

(3*R*,4*R*,5*R*)-4-Methoxy-3-phenyl-[1,2]oxazinan-5-ol (*ent*-12):



Following the Procedure 4 compound **10** (60 mg, 0.17 mmol) was dissolved in 1 N HCl in MeOH (2 mL). Standard workup and purification on a column (silica gel, dichloromethane/methanol 40:1) furnished *ent*-**12** (30 mg, 84%) as a colourless solid. mp 110-112 °C; $[\alpha]_D^{22} = -61.5$ (*c* 1.18, CHCl₃); The spectroscopic data correspond with those of compound **12**. Anal. calcd. for C₁₁H₁₅NO₃ (209.2): C 63.14, H 7.23, N 6.69; found: C 63.12, H 7.24, N 6.61.

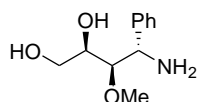
(3*R*,4*S*,5*S*)-4-Methoxy-3-phenyl-[1,2]oxazinan-5-ol (*ent*-13):



Following the Procedure 4 compound **11** (289 mg, 0.82 mmol) was dissolved in methanolic HCl (1 N, 9.5 mL). Standard workup and purification on a column (silica gel, dichloromethane/methanol 40:1) yielded *ent*-**13** (159 mg, 92%) as a colourless solid.

mp 110-113 °C; $[\alpha]_D^{22} = -48.8$ (*c* 1.10, CHCl₃); The spectroscopic data correspond with those of compound **13**. Anal. calcd. for C₁₁H₁₅NO₃ (209.2): C 63.14, H 7.23, N 6.69; found: C 63.17, H 7.32, N 6.54.

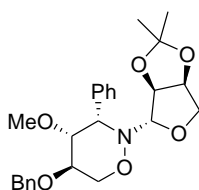
(2*R*,3*R*,4*S*)-4-Amino-3-methoxy-4-phenylbutane-1,2-diol (17**):**



Following the Procedure 4 compound **13** (76 mg, 0.36 mmol) in THF (4 mL) was reacted with SmI_2 (ca. 0.1 M solution in THF, 11 mL, ~1.1 mmol). After workup and filtration through a short silica gel pad (dichloromethane/methanol 15:1), compound **17** (73 mg, 95%) was isolated as a colourless oil.

$[\alpha]_{\text{D}}^{22} = +17.1$ (c 1.12, MeOH); $^1\text{H NMR}$ ($\text{CDCl}_3/\text{CD}_3\text{OD}$ 20:1, 500 MHz): $\delta = 3.31$ (s, 3H, OMe), 3.58 (t_{br}, $J \approx 3.3$ Hz, 1H, 3-H), 3.62 (dd, $J = 4.8, 11.5$ Hz, 1H, 1-H), 3.69 (dd, $J = 5.6, 11.5$ Hz, 1H, 1-H), 3.88 (td, $J \approx 2.8, 5.2$ Hz, 1H, 2-H), 4.57 (d, $J = 3.7$ Hz, 1H, 4-H), 7.30–7.39, 7.46–7.49 (2 m, 5H, Ph) ppm; $^{13}\text{C NMR}$ ($\text{CDCl}_3/\text{CD}_3\text{OD}$ 20:1, 126 MHz): $\delta = 56.1$ (d, C-4), 61.5 (q, OMe), 62.0 (t, C-1), 71.6 (d, C-2), 82.2 (d, C-3), 127.1, 128.8, 129.1, 136.7 (3 d, s, Ph) ppm; IR (ATR): $\tilde{\nu} = 3530\text{--}3245$ (O-H, N-H), 3035–2855 (=C-H, C-H), 1080 (C-O) cm^{-1} ; ESI-TOF (m/z): calcd. for $\text{C}_{11}\text{H}_{18}\text{NO}_3$ $[\text{M} + \text{H}]^+$: 212.1287; found: 212.1282.

(3*S*,4*R*,5*R*,3*a'S*,4'*S*,6*a'**S*)-5-Benzyloxy-2-(2',2'-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4'-yl)-4-methoxy-3-phenyl-[1,2]oxazine (18):**



A solution of **7** (261 mg, 0.74 mmol) in DMF (3 mL) was added to NaH (60% in mineral oil; 46 mg, 1.04 mmol) at 0 °C. Benzyl bromide (160 mg, 0.89 mmol) was added and the solution was stirred at room temperature overnight. Then H_2O (6 mL) was added, the aqueous layer was extracted with Et_2O (3 × 25 mL), and the combined organics dried with MgSO_4 . After filtration, the solvent was removed in

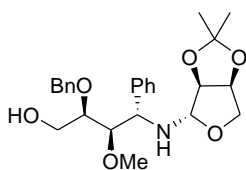
vacuo. The crude product was purified by column chromatography (silica gel, hexane/ethyl acetate, 5:1) to give compound **18** as a colourless oil (278 mg, 85%).

$[\alpha]_D^{22} = +111.3$ (c 0.83, CHCl_3); $^1\text{H NMR}$ (CDCl_3 , 500 MHz): $\delta = 1.29, 1.36$ (2 s, 3H each, 2 Me), 3.08 (s, 3H, OMe), 3.27 (m_c, 1H, 4-H), 3.48 (m_c, 1H, 5-H), 3.94 (d, $J = 9.3$ Hz, 1H, 6'-H), 4.00 (d_{br}, $J \approx 12.6$ Hz, 1H, 6-H), 4.23 (dd, $J = 1.6, 12.6$ Hz, 1H, 6-H), 4.31 (dd, $J = 4.6, 9.3$ Hz, 1H, 6'-H), 4.54 (d, $J = 2.1$ Hz, 1H, 3-H), 4.62 (d, $J = 12.3$ Hz, 1H, Bn), 4.63 (s, 1H, 4'-H), 4.69 (d, $J = 12.3$ Hz, 1H, Bn), 4.81 (t_{br}, $J \approx 5.2$ Hz, 1H, 6a'-H), 4.96 (d, $J = 6.1$ Hz, 1H, 3a'-H), 7.24–7.33, 7.35–7.41, 7.45–7.48 (3 m, 10H, 2 Ph) ppm; $^{13}\text{C NMR}$ (CDCl_3 , 126 MHz): $\delta = 24.5, 26.3$ (2 q, 2 Me), 59.1 (q, OMe), 63.2 (d, C-3), 68.0 (t, C-6), 70.8 (t, Bn), 71.6 (d, C-5), 77.6 (t, C-6'), 78.8 (d, C-4), 81.4 (d, C-6a'), 84.6 (d, C-3a'), 95.6 (d, C-4'), 111.4 (s, C-2'), 127.5, 127.7, 127.8, 128.2, 128.5, 129.6, 137.0, 138.2 (6 d, 2 s, 2 Ph) ppm; IR (ATR): $\tilde{\nu} = 3090$ – 2825 (=C-H, C-H), 1105, 1090, 1065, 1055 (C-O) cm^{-1} ; ESI-TOF (m/z): calcd. for $\text{C}_{25}\text{H}_{31}\text{NNaO}_6$ $[\text{M} + \text{Na}]^+$: 464.2044; found: 464.2054; Anal. calcd. for $\text{C}_{25}\text{H}_{31}\text{NO}_6$ (441.5): C 68.01, H 7.08, N 3.17; found: C 68.23, H 7.24, N 2.99.

Reaction of 1,2-oxazine **18** with Sml_2

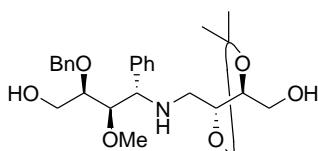
Following the general Procedure 4, compound **18** (105 mg, 0.24 mmol) in THF (3 mL) was added to Sml_2 solution (ca. 0.1 M in THF, 10 mL, ~1.0 mmol) and stirred overnight. After standard workup, the crude mixture was purified on column (silica gel, dichloromethane/methanol 40:1 gradient to 10:1) to give unconsumed **18** (5 mg, 5%), an enriched fractions of **19** (40 mg), and diol **20** (18 mg, 17%). Additional purification of the second fraction (silica gel, hexane/ethyl acetate 1:2) yielded compound **20** (19 mg, 18%). All compounds were isolated as colourless oils.

(2R,3R,3a'S,4S,4'S,6a'S)-2-Benzoyloxy-4-(2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-ylamino)-3-methoxy-4-phenylbutan-1-ol (19):



$[\alpha]_D^{22} = +66.8$ (*c* 1.06, CHCl_3); $^1\text{H NMR}$ (CDCl_3 , 500 MHz): $\delta = 1.27, 1.38$ (2 s, 3H each, 2 Me), 3.29 (s, 3H, OMe), 3.49 (dd, $J = 3.1, 5.5$ Hz, 1H, 3-H), 3.62 (dt, $J \approx 4.2, 5.5$ Hz, 1H, 2-H), 3.73 (dd, $J = 3.7, 12.1$ Hz, 1H, 1-H), 3.78 (dd, $J = 4.5, 12.1$ Hz, 1H, 1-H), 3.95 (d, $J = 10.6$ Hz, 1H, 6'-H), 4.00 (dd, $J = 3.6, 10.6$ Hz, 1H, 6'-H), 4.17 (d, $J = 3.1$ Hz, 1H, 4-H), 4.43 (d, $J = 6.0$ Hz, 1H, 3a'-H), 4.47 (s, 1H, 4'-H), 4.58, 4.67 (2 d, $J = 11.7$ Hz, 2H, Bn), 4.81 (dd, $J = 3.6, 6.0$ Hz, 1H, 6a'-H), 7.27–7.36 (m, 10H, 2 Ph) ppm; $^{13}\text{C NMR}$ (CDCl_3 , 126 MHz): $\delta = 24.6, 26.1$ (2 q, 2 Me), 56.4 (d, C-4), 60.1 (t, C-1), 60.2 (q, OMe), 71.4 (t, C-6'), 72.2 (t, Bn), 78.1 (d, C-2), 80.7 (d, C-6a'), 85.4 (d, C-3), 85.8 (d, C-3a'), 91.7 (d, C-4'), 112.2 (s, C-2'), 127.5, 127.67, 127.73, 127.8, 128.4, 128.7, 138.3, 140.5 (6 d, 2 s, 2 Ph) ppm; IR (ATR): $\tilde{\nu} = 3455\text{--}3345$ (O-H, N-H), 3090–2830 (=C-H, C-H), 1095, 1060 (C-O) cm^{-1} ; ESI-TOF (m/z): calcd. for $\text{C}_{25}\text{H}_{34}\text{NO}_6$ [$\text{M} + \text{H}$] $^+$: 444.2381; found: 444.2372.

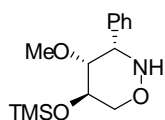
(2R,3R,4S,4'R,5'S)-2-Benzoyloxy-4-[(5-hydroxymethyl-2,2-dimethyl-[1,3]dioxolan-4-ylmethyl)amino]-3-methoxy-4-phenylbutan-1-ol (20):



$[\alpha]_D^{22} = +38.5$ (*c* 1.07, CHCl_3); $^1\text{H NMR}$ (CDCl_3 , 500 MHz): $\delta = 1.34, 1.43$ (2 s, 3H each, 2 Me), 2.49 (dd, $J = 5.8, 12.2$ Hz, 1H, N- CH_2), 2.58 (dd, $J = 4.6, 12.2$ Hz, 1H, N- CH_2), 3.37 (s, 3H, OMe), 3.45 (dd_{br}, $J \approx 4.1, 8.2$ Hz, 1H, 2-H), 3.47–3.52 (m, 2H, 3-

H, 5'-CH₂), 3.61 (dd, $J = 5.2, 12.1$ Hz, 1H, 5'-CH₂), 3.72–3.79 (m, 2H, 1-H), 3.97 (d, $J = 4.6$ Hz, 1H, 4-H), 4.17 (dt, $J \approx 4.9, 6.7$ Hz, 1H, 5'-H), 4.26 (td, $J \approx 4.8, 5.8$ Hz, 1H, 4'-H), 4.49, 4.68 (2 d, $J = 11.8$ Hz, 2H, Bn), 7.27–7.36 (m, 10H, 2 Ph) ppm; ¹³C NMR (CDCl₃, 126 MHz): $\delta = 25.0, 27.4$ (2 q, 2 Me), 46.1 (t, N-CH₂), 59.7 (t, C-1), 60.49 (t, 5'-CH₂), 60.53 (q, OMe), 61.83 (d, C-4), 71.8 (t, Bn), 75.8 (d, C-4'), 77.32 (d, C-2), 77.34 (d, C-5'), 85.7 (d, C-3), 108.2 (s, C-2'), 127.70, 127.71, 127.74, 127.76, 128.4, 128.7, 138.3, 140.2 (6 d, 2 s, 2 Ph) ppm; IR (ATR): $\tilde{\nu} = 3465\text{--}3300$ (O-H, N-H), 3090–2825 (=C-H, C-H), 1090, 1050 (C-O) cm⁻¹; ESI-TOF (m/z): calcd. for C₂₅H₃₆NO₆ [M + H]⁺: 446.2543; found: 446.2564.

(3*S*,4*R*,5*R*)-4-Methoxy-3-phenyl-5-trimethylsilyloxy-[1,2]oxazinane (21):

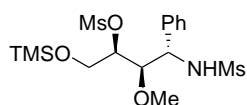


To a solution of 1,2-oxazine **13** (70 mg, 0.33 mmol) in dry CH₂Cl₂ (1.5 mL) were added dropwise at 0 °C imidazole (36 mg, 0.52 mmol), DMAP (2 mg, 5 mol%) and TMSCl (63 μ L, 54 mg, 0.50 mmol) in CH₂Cl₂ (3 mL). The reaction mixture was allowed to reach room temperature and stirred overnight. Then CH₂Cl₂ (2 mL) was added followed by H₂O (2 mL), and the layers were separated. The aqueous layer was extracted with three portions of CH₂Cl₂ (5 mL each), the combined organics were washed with brine, dried over Na₂SO₄, and then filtered, and the solvents were removed under reduced pressure. Purification by column chromatography (silica gel, hexane/ethyl acetate 2:1) yielded **21** (85 mg, 90%) as a colourless oil.

$[\alpha]_D^{22} = -13.8$ (c 1.35, THF); ¹H NMR (CDCl₃, 400 MHz): $\delta = 0.20$ (s, 9H, SiMe₃), 3.22 (s, 3H, OMe), 3.25 (m_c, 1H, 4-H), 3.78 (dt_{br}, $J \approx 1.4, 12.3$ Hz, 1H, 6-H), 3.87 (dt, $J \approx 1.7, 3.5$ Hz, 1H, 5-H), 4.16 (dd, $J = 1.4, 12.3$ Hz, 1H, 6-H), 4.63 (d, $J = 1.6$ Hz, 1H, 3-

$[\alpha]_D^{22} = +36.9$ (*c* 1.24, CHCl_3); $^1\text{H NMR}$ (CDCl_3 , 500 MHz): $\delta = 0.12, 0.14$ (2 s, 9H each, 2 SiMe_3), 2.56 (s, 3H, NMs), 3.26 (s, 3H, OMe), 3.43 (dd, $J = 3.1, 5.9$ Hz, 1H, 3-H), 3.66 (dd, $J = 3.0, 10.3$ Hz, 1H, 1-H), 3.79–3.85 (m, 2H, 1-H, 2-H), 4.72 (dd, $J = 3.1, 8.3$ Hz, 1H, 4-H), 5.41 (d, $J = 8.3$ Hz, 1H, NH), 7.29–7.40 (m, 5H, Ph) ppm; $^{13}\text{C NMR}$ (CDCl_3 , 126 MHz): $\delta = -0.5, 0.3$, (2 q, 2 SiMe_3), 42.0 (q, NMs), 57.1 (d, C-4), 61.2 (q, OMe), 64.1 (t, C-1), 73.9 (d, C-2), 85.4 (d, C-3), 127.0, 127.9, 128.8, 140.2 (3 d, s, Ph) ppm; IR (ATR): $\tilde{\nu} = 3290$ (N-H), 3065–2830 (=C-H, C-H), 1320 (S=O), 1250, 1150, 1085 (C-O) cm^{-1} ; ESI-TOF (m/z): calcd. for $\text{C}_{18}\text{H}_{35}\text{NNaO}_5\text{SSi}_2$ $[\text{M} + \text{Na}]^+$: 456.1672; found: 456.1678.

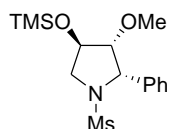
(2R,3R,4S)-2-O-Methylsulfonyl-4-methylsulfonylamino-3-methoxy-4-phenyl-1-O-trimethylsilylbutan-1,2-diol (24):



$[\alpha]_D^{22} = +28.8$ (*c* 1.25, CHCl_3); $^1\text{H NMR}$ (CDCl_3 , 500 MHz): $\delta = 0.19$ (s, 9H, SiMe_3), 2.58 (s, 3H, NMs), 3.07 (s, 3H, OMs), 3.17 (s, 3H, OMe), 3.67 (dd, $J = 1.7, 7.7$ Hz, 1H, 3-H), 4.02 (dd, $J = 2.1, 12.7$ Hz, 1H, 1-H), 4.16 (dd, $J = 4.4, 12.7$ Hz, 1H, 1-H), 4.71 (dd, $J = 1.7, 10.1$ Hz, 1H, 4-H), 4.77 (ddd, $J = 2.1, 4.4, 7.7$ Hz, 1H, 2-H), 5.61 (d, $J = 10.1$ Hz, 1H, NH), 7.32–7.43 (m, 5H, Ph) ppm; $^{13}\text{C NMR}$ (CDCl_3 , 126 MHz): $\delta = -0.6$ (q, SiMe_3), 38.1 (q, OMs), 42.0 (q, NMs), 56.5 (d, C-4), 61.6 (q, OMe), 61.7 (t, C-1), 83.9 (d, C-3), 84.2 (d, C-2), 126.6, 128.3, 129.1, 139.0 (3 d, s, Ph) ppm; IR (ATR): $\tilde{\nu} = 3285$ (N-H), 3060–2840 (=C-H, C-H), 1320 (S=O), 1175, 1155 (C-O) cm^{-1} ; ESI-TOF (m/z): calcd. for $\text{C}_{16}\text{H}_{29}\text{NNaO}_7\text{S}_2\text{Si}$ $[\text{M} + \text{Na}]^+$: 462.1052; found: 462.1052.

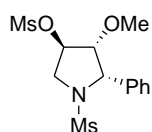
(2S,3R,4R)-3-Methoxy-4-trimethylsilyloxy-1-methylsulfonyl-2-phenylpyrrolidine

(25):



$[\alpha]_D^{22} = +98.5$ (*c* 0.41, CHCl_3); $^1\text{H NMR}$ (CDCl_3 , 500 MHz): $\delta = 0.19$ (s, 9H, SiMe_3), 2.75 (s, 3H, NMs), 2.95 (s, 3H, OMe), 3.55 (dt, $J \approx 1.4$, 11.9 Hz, 1H, 5-H), 3.65 (ddd, $J = 0.9$, 2.5, 5.1 Hz, 1H, 3-H), 3.78 (dd, $J = 3.4$, 11.9 Hz, 1H, 5-H), 4.24 (m_c , 1H, 4-H), 4.90 (d, $J = 5.1$ Hz, 1H, 2-H), 7.25–7.29, 7.31–7.39 (2 m, 5H, Ph) ppm; $^{13}\text{C NMR}$ (CDCl_3 , 126 MHz): $\delta = -0.1$ (q, SiMe_3), 36.4 (q, NMs), 55.3 (t, C-5), 58.9 (q, OMe), 65.7 (d, C-2), 73.4 (d, C-4), 88.6 (d, C-3), 127.5, 128.0, 128.1, 136.8 (3 d, s, Ph) ppm; IR (ATR): $\tilde{\nu} = 3065$ – 2830 (=C-H, C-H), 1340 (S=O), 1155, 1110, 1020 (C-O) cm^{-1} ; ESI-TOF (m/z): calcd. for $\text{C}_{15}\text{H}_{25}\text{NNaO}_4\text{SSi}$ $[\text{M} + \text{Na}]^+$: 366.1171; found: 366.1171.

(2S,3R,4R)-3-Methoxy-2-phenyl-4-methylsulfonyloxy-1-methylsulfonyl-pyrrolidine (26):

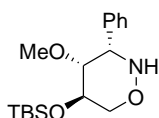


$[\alpha]_D^{22} = +57.1$ (*c* 1.03, CHCl_3); $^1\text{H NMR}$ (CDCl_3 , 500 MHz): $\delta = 2.66$ (s, 3H, NMs), 3.06 (s, 3H, OMe), 3.14 (s, 3H, OMs), 3.89 (dd, $J = 3.8$, 12.9 Hz, 1H, 2-H), 4.07–4.11 (m, 2H, 2-H, 4-H), 5.06 (d, $J = 5.5$ Hz, 1H, 5-H), 5.12 (dt, $J \approx 2.3$, 4.3 Hz, 1H, 3-H), 7.30–7.39 (m, 5H, Ph) ppm; $^{13}\text{C NMR}$ (CDCl_3 , 126 MHz): $\delta = 39.1$ (q, OMs), 40.1 (q, NMs), 51.6 (t, C-2), 59.1 (q, OMe), 65.0 (d, C-5), 79.6 (d, C-3), 85.6 (d, C-4), 128.26, 128.29, 128.4, 135.1 (3 d, s, Ph) ppm; IR (ATR): $\tilde{\nu} = 3020$ – 2840 (=C-H, C-H), 1325

(S=O), 1175, 1145 (C-O) cm^{-1} ; ESI-TOF (m/z): calcd. for $\text{C}_{13}\text{H}_{19}\text{NNaO}_6\text{S}_2$ [$\text{M} + \text{Na}$] $^+$: 372.0551; found: 372.0552; Anal. calcd. for $\text{C}_{13}\text{H}_{19}\text{NO}_6\text{S}_2$ (349.4): C 44.68, H 5.48, N 4.01; found: C 44.70, H 5.56, N 4.11.

(3*S*,4*R*,5*R*)-5-(*tert*-Butyldimethylsilyloxy)-4-methoxy-3-phenyl-[1,2]oxazinane

(27):

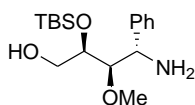


By a similar procedure to that for TMSCl, to 1,2-oxazine **13** (713 mg, 3.41 mmol) in dry CH_2Cl_2 (25 mL) were added dropwise at 0 °C imidazole (525 mg, 7.71 mmol), DMAP (21 mg, 0.17 mmol, 5 mol %) and TBSCl (1.035 g, 6.87 mmol) in CH_2Cl_2 (10 mL). The reaction mixture was stirred for five days at room temperature. After workup and purification through a column (silica gel, hexane/ethyl acetate 3:1) compound **27** (995 mg, 90%) was isolated as a colourless oil.

$[\alpha]_{\text{D}}^{22} = +4.0$ (c 0.92, CHCl_3); ^1H NMR (CDCl_3 , 500 MHz): $\delta = 0.136, 0.140$ (2 s, 3H each, SiMe_2), 0.96 (s, 9H, Si^tBu), 3.21 (s, 3H, OMe), 3.25 (m_c, 1H, 4-H), 3.78 (dt, $J \approx 1.5, 12.3$ Hz, 1H, 6-H), 3.88 (dt, $J \approx 1.7, 3.5$ Hz, 1H, 5-H), 4.13 (dd, $J = 1.4, 12.3$ Hz, 1H, 6-H), 4.64 (d, $J = 1.8$ Hz, 1H, 3-H), 7.25–7.33 (m, 5H, Ph) ppm; ^{13}C NMR (CDCl_3 , 126 MHz): $\delta = -4.9, -4.7$ (2 q, SiMe_2), 18.1, 25.8 (s, q, Si^tBu), 58.9 (q, OMe), 60.0 (d, C-3), 65.6 (d, C-5), 71.3 (t, C-6), 78.9 (d, C-4), 127.4, 127.5, 128.2, 138.1 (3 d, s, Ph) ppm; IR (ATR): $\tilde{\nu} = 3290$ (N-H), 3065–2825 (=C-H, C-H), 1255, 1120, 1095 (C-O) cm^{-1} ; ESI-TOF (m/z): calcd. for $\text{C}_{17}\text{H}_{30}\text{NO}_3\text{Si}$ [$\text{M} + \text{H}$] $^+$: 324.1995; found: 324.2010.

(2*R*,3*R*,4*S*)-4-Amino-2-*O*-(*tert*-butyldimethylsilyl)-3-methoxy-4-phenyl-butane-

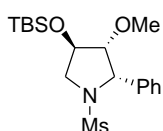
1,2-diol (28):



Following the general Procedure 4, compound **27** (500 mg, 1.54 mmol) in THF (25 mL) was added to a solution of SmI_2 (ca. 0.1 M in THF, 57 mL, ~5.7 mmol). After workup and filtration through a short silica gel pad (dichloromethane/methanol 15:1), compound **28** (463 mg, 92%) was isolated as a colourless oil.

$[\alpha]_{\text{D}}^{22} = +27.0$ (c 0.97, CHCl_3); $^1\text{H NMR}$ (CDCl_3 , 400 MHz): $\delta = 0.07$, 0.12 (2 s, 3H each, SiMe_2), 0.92 (s, 9H, Si^tBu), 3.27 (s, 3H, OMe), 3.37 (dd, $J = 0.9$, 5.6 Hz, 1H, 3-H), 3.57 (dd, $J = 4.4$, 12.3 Hz, 1H, 1-H), 3.83 (dd, $J = 1.5$, 12.3 Hz, 1H, 1-H), 3.91 (ddd, $J = 1.5$, 4.4, 5.6 Hz, 1H, 2-H), 4.46 (s_{br} , 1H, 4-H), 7.25–7.30, 7.32–7.41 (2 m, 5H, Ph) ppm; $^{13}\text{C NMR}$ (CDCl_3 , 126 MHz): $\delta = -4.9$, -4.6 (2 q, SiMe_2), 18.1, 25.9 (s, q, Si^tBu), 52.1 (d, C-4), 59.7 (q, OMe), 61.2 (t, C-1), 70.6 (d, C-2), 87.0 (d, C-3), 126.2, 127.1, 128.6, 145.4 (3 d, s, Ph) ppm; IR (ATR): $\tilde{\nu} = 3460\text{--}3250$ (O-H, N-H), 3065–2855 (=C-H, C-H), 1255, 1130, 1090 (C-O) cm^{-1} ; ESI-TOF (m/z): calcd. for $\text{C}_{17}\text{H}_{32}\text{NO}_3\text{Si}$ [$\text{M} + \text{H}$] $^+$: 326.2146; found: 326.2137.

(2*S*,3*R*,4*R*)-4-(*tert*-Butyldimethylsilyloxy)-3-methoxy-1-methylsulfonyl-2-phenylpyrrolidine (29):

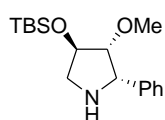


To a solution of amino alcohol **28** (86 mg, 0.26 mmol) in CH_2Cl_2 (4 mL), triethylamine (147 μL , 105 mg, 1.04 mmol) followed by methanesulfonyl chloride (41 μL , 61 mg, 0.53 mmol) were added at 0 °C. After stirring at room temperature overnight, H_2O (8

mL) was added. The two layers were separated, and the aqueous layer was extracted with a few portions of CH₂Cl₂, the combined extracts were dried with MgSO₄, and the solvents were removed in vacuo. The crude mixture was purified by column chromatography (silica gel, hexane/EtOAc, 4:1) to furnish compound **29** as a colourless oil (56 mg, 55 %).

$[\alpha]_D^{22} = +88.1$ (*c* 1.19, CHCl₃); ¹H NMR (CDCl₃, 500 MHz): $\delta = 0.14, 0.15$ (2 s, 3H each, SiMe₂), 0.93 (s, 9H, Si^tBu), 2.75 (s, 3H, NMs), 2.96 (s, 3H, OMe), 3.63 (dd_{br}, *J* \approx 1.1, 11.8 Hz, 1H, 5-H), 3.63 (dd, *J* = 2.4, 5.0 Hz, 1H, 3-H), 3.78 (dd, *J* = 3.5, 11.8 Hz, 1H, 5-H), 4.26–4.27 (m, 1H, 4-H), 4.90 (d, *J* = 5.0 Hz, 1H, 2-H), 7.25–7.39 (m, 5H, Ph) ppm; ¹³C NMR (CDCl₃, 126 MHz): $\delta = -4.8^*$ (q, SiMe₂), 18.1, 25.7 (s, q, Si^tBu), 36.9 (q, NMs), 55.3 (t, C-5), 58.9 (q, OMe), 65.7 (d, C-2), 73.8 (d, C-4), 88.8 (d, C-3), 127.6, 128.0, 128.2, 136.7 (3 d, s, Ph) ppm, *double intensity; IR (ATR): $\tilde{\nu} = 3065\text{--}2830$ (=C-H, C-H), 1345 (S=O), 1160, 1120, 1020 (C-O) cm⁻¹; ESI-TOF (*m/z*): calcd. for C₁₈H₃₁NNaO₄SSi [M + Na]⁺: 408.1635; found: 408.1611.

(2S,3R,4R)-4-(tert-Butyldimethylsilyloxy)-3-methoxy-2-phenylpyrrolidine (30):



To a solution of freshly prepared, crude amino alcohol **28** (350 mg, 1.07 mmol) in CH₂Cl₂ (20 mL), were added triethylamine (166 μ L, 121 mg, 1.21 mmol), CBr₄ (414 mg, 1.25 mmol), and PPh₃ (328 mg, 1.25 mmol) at 0 °C. The resulting mixture was stirred overnight at room temperature and quenched with aqueous NaOH soln. (1 N, ca. 20 mL). The layers were separated, the aqueous layer was extracted with a few portions of Et₂O, and the organics were combined, dried over MgSO₄ and filtered, and the solvents were removed under reduced pressure. The crude mixture

was filtered through a short silica gel pad to give enriched **30** (210 mg), with the triphenylphosphine oxide as the main impurity. Additional column chromatography (silica gel, diethylether) furnished **30** (110 mg, 33%) as a colourless oil.

$[\alpha]_D^{22} = +29.7$ (c 1.11, CHCl_3); $^1\text{H NMR}$ (CDCl_3 , 500 MHz): $\delta = 0.11, 0.13$ (2 s, 3H each, SiMe_2), 0.92 (s, 9H, Si^tBu), 2.83 (dd, $J = 3.0, 11.6$ Hz, 1H, 5-H), 3.09 (s, 3H, OMe), 3.47 (dd, $J = 5.5, 11.6$ Hz, 1H, 5-H), 3.58 (dd, $J = 1.2, 4.1$ Hz, 1H, 3-H), 4.31 (ddd, $J = 1.2, 3.0, 5.5$ Hz, 1H, 4-H), 4.34 (d, $J = 4.1$ Hz, 1H, 2-H), 7.22–7.26, 7.30–7.34, 7.38–7.41 (3 m, 5H, Ph) ppm; $^{13}\text{C NMR}$ (CDCl_3 , 126 MHz): $\delta = -4.73, -4.68$ (2 q, SiMe_2), 18.0, 25.8 (s, q, Si^tBu), 54.4 (t, C-5), 57.9 (q, OMe), 64.3 (d, C-2), 76.4 (d, C-4), 89.7 (d, C-3), 126.8, 127.8, 127.9, 138.9 (3 d, s, Ph) ppm; IR (ATR): $\tilde{\nu} = 3315$ (N-H), 3090–2825 (=C-H, C-H), 1105 (C-O) cm^{-1} ; ESI-TOF (m/z): calcd. for $\text{C}_{17}\text{H}_{30}\text{NO}_2\text{Si}$ [$\text{M} + \text{H}$] $^+$: 308.2040; found: 308.2055.

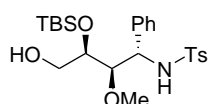
Synthesis of pyrrolidine derivative **30** by demesylation of **29**

To a solution of mesylated pyrrolidine **29** (50 mg, 0.13 mmol) in THF (8 mL), a freshly prepared solution of LDA [by treatment of diisopropylamine (1.0 equiv.) with BuLi (1.0 equiv.) at -78 °C in THF and stirring for 30 min] was added (0.70 mmol added in three portions, ~ 0.23 mmol each every 4 h) at room temperature and stirred for 16 h. The reaction mixture was quenched with sat. NH_4Cl solution followed by the addition of EtOAc. The two layers were separated, and the aqueous layer was extracted with CH_2Cl_2 . The combined organics were dried over MgSO_4 , filtered and concentrated. Compound **30** (5 mg, 13%) was isolated by chromatography (silica gel, dichloromethane/methanol 30:1) as a light orange oil.

Attempted cyclisation of **28** with *p*TsCl

To a solution of freshly prepared unpurified amino alcohol **28** (501 mg, 1.54 mmol) in dry CH₂Cl₂ (35 mL), triethylamine (1.24 mL, 893 mg, 8.82 mmol) followed by *p*TsCl (656 mg, 3.44 mmol) was slowly added at 0 °C, and stirred at room temperature overnight. Then the reaction was quenched with H₂O, the resulting solution was extracted with a few portions of CH₂Cl₂, the combined organics were dried over Na₂SO₄ and filtered, and the solvents were removed. The crude mixture was chromatographed on silica (hexane/ethyl acetate 3:1 gradient to 1:1) to furnish an inseparable ~1:1 mixture of *N,O*-tosylated compounds (136 mg, 14%, first eluted fraction, see Results and Discussion part) and ~4:1 mixture of tosylamides (301 mg, 41%). The latter fraction was additionally purified (silica gel, hexane/ethyl acetate 3:1) to yield analytically pure **31** (177 mg, 24%) as a colourless solid.

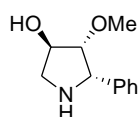
(2*R*,3*R*,4*S*)-2-(*tert*-Butyldimethylsilyl)-3-methoxy-4-phenyl-4-(*p*-toluenesulfonylamino)butan-1-ol (**31**):



mp 124-126 °C; $[\alpha]_D^{22} = +22.5$ (*c* 0.98, CHCl₃); ¹H NMR (CDCl₃, 500 MHz): δ = 0.07, 0.08 (2 s, 3H each, SiMe₂), 0.89 (s, 9H, Si^{*t*}Bu), 2.00 (dd_{br}, *J* ≈ 3.1, 8.8 Hz, 1H, OH), 2.29 (s, 3H, Me), 3.07 (s, 3H, OMe), 3.36 (dd, *J* = 1.5, 7.6 Hz, 1H, 3-H), 3.65 (dt_{br}, *J* ≈ 2.5, 12.0 Hz, 1H, 1-H), 3.77 (ddd_{br}, *J* = 3.3, 8.8, 12.0 Hz, 1H, 1-H), 3.81 (dt, *J* ≈ 3.3, 7.6 Hz, 1H, 2-H), 4.63 (dd_{br}, *J* ≈ 1.5, 9.5 Hz, 1H, 4-H), 5.55 (d, *J* = 9.5 Hz, 1H, NH), 7.01 (d, *J* = 8.2 Hz, 2H, Ts), 7.03–7.11 (m, 5H, Ph), 7.46 (d, *J* = 8.2 Hz, 2H, Ts) ppm; ¹³C NMR (CDCl₃, 126 MHz): δ = -4.8, -4.6 (2 q, SiMe₂), 18.0 (s, Si^{*t*}Bu), 21.3 (q, Me), 25.8 (q, Si^{*t*}Bu), 56.6 (d, C-4), 61.3 (q, OMe), 63.7 (t, C-1), 73.3 (d, C-2), 86.1 (d, C-3),

126.5, 126.9, 127.0 128.1, 129.1, 137.7, 139.4, 142.9 (5 d, 3 s, Ph, Ts) ppm; IR (ATR): $\tilde{\nu}$ = 3580-3175 (O-H, N-H), 3035–2825 (=C-H, C-H), 1335 (S=O), 1155, 1090, 1050 (C-O) cm^{-1} ; ESI-TOF (m/z): calcd. for $\text{C}_{24}\text{H}_{37}\text{NNaO}_5\text{SSi}$ [$\text{M} + \text{Na}$] $^+$: 502.2054; found: 502.2041. Anal. calcd. for $\text{C}_{24}\text{H}_{37}\text{NO}_5\text{SSi}$ (479.7): C 60.09, H 7.77, N 2.92; found: C 60.09, H 7.79, N 2.93.

(3R,4R,5S)-4-Methoxy-5-phenylpyrrolidin-3-ol (32**):**



Pyrrolidine **30** (51 mg, 0.16 mmol) was dissolved in 1 N HCl in MeOH (8 mL) and stirred at room temperature for three days. The reaction mixture was quenched with excess solid NaHCO_3 , the inorganics were filtered off and the solvents removed to dryness. The crude mixture was chromatographed on silica gel (dichloromethane/methanol 9:1) to give **32** (23 mg, 72%) as colourless crystals.

mp 192-195 °C; $[\alpha]_{\text{D}}^{22} = +48.3$ (c 0.88, CH_3OH); ^1H NMR (CD_3OD , 500 MHz): δ = 3.29 (d_{br} , $J \approx 12.5$ Hz, 1H, 2-H), 3.32 (s, 3H, OMe), 3.75 (dd , $J = 4.8, 12.5$ Hz, 1H, 2-H), 3.93 (dd_{br} , $J \approx 0.9, 3.2$ Hz, 1H, 4-H), 4.60 (dt_{br} , $J \approx 0.9, 4.8$ Hz, 1H, 3-H), 4.85 (d, $J = 3.2$ Hz, 1H, 5-H), 7.41–7.48, 7.51–7.54 (2 m, 5H, Ph) ppm; ^{13}C NMR (CDCl_3 , 126 MHz): δ = 53.0 (t, C-2), 58.5 (q, OMe), 65.4 (d, C-5), 72.5 (d, C-3), 87.4 (d, C-4), 129.7, 129.9, 130.3, 132.3 (3 d, s, Ph) ppm; IR (neat): $\tilde{\nu}$ = 3400–3250 (O-H, N-H), 3100–2805 (=C-H, C-H), 1100 (C-O) cm^{-1} ; ESI-TOF (m/z): calcd. for $\text{C}_{11}\text{H}_{16}\text{NO}_2$ [$\text{M} + \text{H}$] $^+$: 194.1181; found: 194.1153.

References

1. Pérez, M.; Canoa, P.; Gómez, G.; Teijeira, M.; Fall, Y. *Synthesis* **2005**, 411–414.
doi:10.1055/s-2004-834946
2. Helms, M.; Schade, W.; Pulz, R.; Watanabe, T.; Al-Harrasi, A.; Fišera, L.; Hlobilová, I.; Zahn, G.; Reissig, H.-U. *Eur. J. Org. Chem.* **2005**, 1003–1019.
doi:10.1002/ejoc.200400627
3. Krijnen, E. S.; Zuilhof, H.; Lodder, G. *J. Org. Chem.* **1994**, *59*, 8139–8150.
doi:10.1021/jo00105a035
4. Kucerovy, A.; Neuenschwander, K.; Meinreb, S. M. *Synthetic Commun.* **1983**, *13*, 875–879. doi:10.1080/00397918308059540