Asymmetric Synthesis of (-)-Swainsonine

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SUPPORTING INFORMATION

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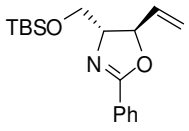
Section A: General Information

General methods and materials: Optical rotations were measured on a polarimeter in the solvent specified. ^{1}H NMR and ^{13}C NMR spectra were recorded on FT-NMR 125, or 500 MHz spectrometers. Chemical shifts values are reported in ppm relative to TMS or $CDCl_3$ as an internal standard and coupling constants in Hertz. IR spectra were measured on a FT-IR spectrometer. Mass spectral data were obtained high resolution mass spectrometer. Flash chromatography was executed using mixtures of ethyl acetate and hexane as eluants. Unless otherwise noted, all non-aqueous reactions were carried out under an argon atmosphere with commercial grade reagents and solvents. Tetrahydrofuran (THF) was distilled over sodium and benzophenone (indicator). Methylene chloride (CH_2Cl_2) was distilled from calcium hydride.

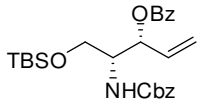
Section B: Experimental Procedures:



7

(4*R*, *trans*)-4,5-Dihydro-4-(*tert*-butyldimethylsilanyloxymethyl)-2-phenyloxazoline (7).

To a stirred solution of secondary allylic acetate (4.0 g, 10.6 mmol) and K_2CO_3 (4.4 g, 31.78 mmol) in CH_3CN (50 mL) was added $Pd(PPh_3)_4$ (612 mg, 0.53 mmol) under an argon atmosphere. The resulting mixture was heated under reflux for 24 h, whereupon it was allowed to cool rt and was filtered through a pad of silica, which was then evaporated under reduced pressure to give crude product. Purification by silica gel chromatography (ethyl acetate/hexane = 1/15) gave **7** (2.52 g, 75%); colorless oil; $[\alpha]_D^{25}$ +2.33 (c 1.0, $CHCl_3$); IR (neat) 2930, 2857, 1650, 1254, 1121 cm-1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.06 (s. 3H), 0.10 (s, 3H), 0.88 (s, 9H), 3.69-3.72 (dd, *J* = 6.5, 10.5 Hz, 1H), 3.94-3.97 (dd, *J* = 4.0, 10.5 Hz, 1H), 4.01-4.10 (ddd, *J* = 4.0, 6.5, 6.5 Hz, 1H), 5.03-5.06 (dddd, *J* = 1.0, 1.5, 6.5, 6.5 Hz, 1H), 5.23-5.25 (dt, *J* = 1.5, 10.5 Hz, 1H), 5.38-5.42 (dt, *J* = 1.5, 17.0 Hz, 1H), 5.95-6.01 (ddd, *J* = 6.5, 10.5, 17.0 Hz, 1H), 7.41-7.44 (ddd, *J* = 1.0, 1.5, 7.5 Hz, 2H), 7.48-7.51 (ddd, *J* = 1.5, 7.5, 7.5 Hz, 1H), 7.97-7.99 (ddd, *J* = 1.0, 1.5, 7.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ -5.1, 18.4, 26.0, 65.0, 74.4, 83.3, 116.6, 128.1, 128.0, 128.5, 131.6, 137.0, 164.1; HRMS m/e calcd for $C_{18}H_{27}NO_2Si$ (M+1) 318.1889, found 318.1895

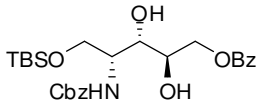


6

1(*R*)-[2-(*tert*-Butyldimethylsiloxy)-1(*R*)-[[*N*-phenylmethoxy)carbonyl]amino]ethyl]prop-2-enyl benzoate (6).

To a solution of oxazoline (**7**) (12 g, 37.80 mmol) in CH_2Cl_2 (75 mL) was added a solution of $NaHCO_3$ (6.35 g, 75.59 mmol) in water (75 mL), and the mixture was cooled in an ice bath. To this solution was added dropwise a solution of benzyl chloroformate (10.79 mL, 75.59 mmol). The mixture was stirred at rt for 8 h. The organic phase was separated, and the aqueous phase was extracted with CH_2Cl_2 (2×100 mL). The combined organic phase was washed with water, dried ($MgSO_4$), and concentrated in *vacuo*. Purification by silica gel chromatography (ethyl acetate/hexane = 1/8) gave **6** (17.40 g, 98 %) as a colorless oil; $[\alpha]_D^{25}$ +3.31 (c 1.0,

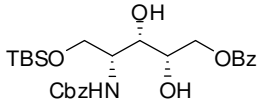
$CHCl_3$); IR (neat) : 3339, 2941, 1720, 1514, 1263, 1108 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 0.03 (s, 3H), 0.04 (s, 3H), 0.90 (s, 9H), 3.69 (dd, *J* = 5.5, 10.5 Hz, 1H), 3.82 (dd, *J* = 3.5, 10.5 Hz, 1H), 4.08 (ddd, *J* = 3.5, 5.5, 9.5 Hz, 1H), 5.06 (s, 2H), 5.15 (d, *J* = 9.5 Hz, 1H), 5.33 (d, *J* = 10.5 Hz, 1H), 5.44 (d, *J* = 17.0 Hz, 1H), 5.75 (t, *J* = 6.5, 6.5 Hz, 1H), 5.95 (ddd, *J* = 6.5, 10.5, 17.0 Hz, 1H), 7.25-7.29 (m, 5H), 7.44-7.47 (m, 2H), 7.57-7.60 (m, 1H), 8.05-8.07 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ -5.4, 18.4, 26.1, 55.8, 62.4, 67.1, 74.3, 119.4, 128.3, 128.3, 128.7, 128.7, 130.0, 130.3, 133.3, 133.7, 136.6, 156.4, 165.8; HRMS calcd for $C_{26}H_{35}NO_5Si$(M+1) 470.2363, Found 470.2359.



8c

(2*R*,3*S*,4*R*)-4-(benzyloxycarbonylamino)-5-(*tert*-butyldimethylsilyloxy)-2,3-dihydroxy-pentyl benzoate (8c)

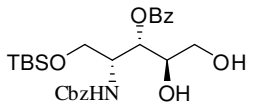
To a stirred solution of **6** (5 g, 10.65 mmol) in acetone (50 mL)/H_2O (5 mL) was added a *N*-methylmorpholine *N*-oxide (1.87 g, 15.97 mmol) and the solution of 2.5 wt.% OsO_4/water (6.67 mL, 0.019 mmol, 5 mol %) at 0^oC .The reaction mixture was allowed to stir at the same temperature for 15 h, at which time all staring material had been consumed as judged by TLC. The reaction mixture was poured into a solution of sat. aq Na_2SO_3 (100 mL). The solvent was evaporated under vacuum. The aqueous phase was extracted with CH_2Cl_2 (2×100 mL). The organic extract was washed with brine (100 mL), dried with $MgSO_4$, and evaporated in *vacuo*. Purification by silica gel chromatography (ethyl acetate/hexane = 1/3) gave **8c** (4.29 g, 80 %, dr> 9 : 1) as white solid; *Spectral data of the major isomer*: Mp 91~93^oC; $[\alpha]_D^{25}$ +31.60 (c 1.0, $CHCl_3$); IR (neat): 3434, 2944, 1703, 1520, 1274, 1085 cm^{-1}; ^1H NMR (500MHz, $CDCl_3$): δ 0.09 (s, 3H), 0.11 (s, 3H), 0.89 (s, 9H), 3.49 (d, *J* = 2.5 Hz, 1H), 3.70-3.79 (m, 1H), 3.78 (d, *J* = 4.5 Hz, 1H), 3.90 (dd, *J* = 1.0, 9.0 Hz, 1H), 3.96 (ddd, *J* = 3.5, 10.5, 14.0 Hz, 1H), 4.14 (dt, *J* = 4.0, 12.0 Hz, 1H), 4.55 (dd, *J* = 5.5, 12.0 Hz, 1H), 4.64 (dd, *J* = 2.5, 12.0 Hz, 1H), 5.16 (s, 2H), 5.41 (d, *J* = 9.0 Hz, 1H), 7.32-7.39 (m, 5H), 7.46 (d, *J* = 7.0 Hz, 2H), 7.59 (d, *J* = 7.0 Hz, 1H), 8.10 (d, *J* = 7.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ –5.4, 18.3, 26.0, 51.2, 66.2, 66.5, 67.6, 70.1, 73.3, 128.4, 128.5, 128.6, 128.8, 130.1, 130.2, 133.3, 136.4, 157.7, 167.5; HRMS calcd for $C_{26}H_{37}NO_7$ Si(M+1)504.2418, found 504.2418



8d

(2*S*,3*S*,4*R*)-4-(benzyloxycarbonylamino)-5-(*tert*-butyldimethylsilyloxy)-2,3-dihydroxy-pentyl benzoate (8d)

According to the procedure described above for the **8c**, **6** was converted to the **8d (**0.45 g, 8.4 %, dr> 9:1) as a colorless oil; $[\alpha]_D^{25}$ -10.58 (c1.0, $CHCl_3$); IR (neat): 3432, 2944, 2862, 1713, 1517, 1271, 1108, 840, 777, 710 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 0.04 (S, 6H), 0.85 (s, 9H), 3.08 (d, *J* = 5.0 Hz, 1H), 3.36-3.38 (m, 1H), 3.80-3.81 (m, 2H), 3.90-3.91 (m, 1H), 3.99 (ddd, *J* = 5.0, 10.0, 10.0 Hz, 2H), 4.44-4.50 (m, 2H), 5.07-5.13 (m, 2H), 5.35 (d, *J* = 8.0 Hz, 1H), 7.30-7.35 (m, 5H), 7.43 (t, *J* = 7.5 Hz, 2H), 7.56 (d, *J* = 7.5 Hz, 1H), 8.03 (d, *J* = 7.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ -5.4, 18.4, 26.0, 53.5, 64.2, 66.0, 67.3, 70.5, 71.3, 128.4, 128.5, 128.6, 128.8, 130., 130.0, 133.4, 136.5, 156.9, 167.1; HRMS calcd for $C_{26}H_{37}NO_7$ Si(M+1)504.2418**,** found 504.2415

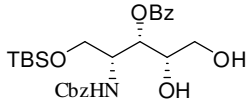


8a

(2*R*,3*S*,4*R*)-2-(benzyloxycarbonylamino)-1-(*tert*-butyldimethylsilyloxy)-4,5-dihydroxypentan-3-yl benzoate (8a)

To a stirred solution of **6** (162 mg, 0.35 mmol) in acetone (3 mL)/H_2O (0.3 mL) was added a *N*-methylmorpholine *N*-oxide (0.12 g, 0.52 mmol) and the solution of 2.5 wt. % OsO_4/water (0.43 mL, 0.04 mmol,

10 mol %) at 0°C .The reaction mixture was allowed to stir at the same temperature for 10 h, at which time all staring material had been consumed as judged by TLC. The reaction mixture was poured into a solution of 15% $Na_2S_2O_3$ (3 mL), extracted with CH_2Cl_2 (5 mL × 2). The organic extract was washed with brine (5 mL), dried with $MgSO_4$ and evaporated *in vacuo*. Purification by silica gel chromatography (ethyl acetate/hexane = 1/3) gave **8a** (156 mg, 90%, dr> 9 : 1) as a colorless oil; *Spectral data of the major isomer*: $[\alpha]_D^{25}$ +31.60 (c1.0, $CHCl_3$) IR (neat): 3434, 2944, 1703, 1520, 1274, 1085 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ -0.08 (s, 3H), -0.05 (s, 3H), 0.80 (s, 9H), 2.41 (dd, *J* = 4.5, 9 Hz, 1H), 3.56-3.60 (ddd, *J* = 5.0, 5.5, 7.0 Hz, 1H), 3.69(ddd, *J* = 2.5, 9.5, 12.0 Hz, 1H), 3.76 (ddd, *J* = 6.0, 11.0, 17.0 Hz, 2H), 3.81 (dddd, *J* = 3.0, 5.5, 5.5, 8.5 Hz, 1H), 4.30 (d, *J* = 5.5 Hz, 1H), 4.34-4.36 (m, 1H), 5.15-5.27 (m, 2H), 5.26 (d, *J* = 9.5 Hz, 1H), 5.32 (dd, *J* = 1.5, 9.5 Hz, 1H), 7.37-7.41 (m, 5H), 7.46 (t, *J* = 7.5 Hz, 2H), 7.60 (t, *J* = 7.5 Hz, 1H), 7.81 (dd, *J* = 1.5, 7.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ -5.5, -5.4, 18.4, 25.9, 26.1, 52.2, 63.2, 63.3, 67.9, 70.2, 73.2, 128.5, 128.7, 128.8, 128.9, 129.6, 130.1, 133.7, 136.2, 158.0, 166.18; HRMS calcd for $C_{26}H_{37}NO_7Si$(M+1)504.2418, found 504.2422



8b

(2*R*,3*S*,4*S*)-2-(benzyloxycarbonylamino)-1-(*tert*-butyldimethylsilyloxy)-4,5-dihydroxypentan-3-yl benzoate (8b)

According to the procedure described above for the **8a**, **6** was converted to the **8b** (15 mg, 8.7 %, dr> 9 : 1) as a colorless oil; $[\alpha]_D^{25}$ -20.52 (c1.0,$CHCl_3$); IR (neat): 3853, 3742, 3435, 2928, 2858, 1713, 1515 ,1462, 1269, 1108, 840, 708cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 0.06 (s, 6H), 0.90 (s, 9H), 2.37-2.40 (m, 1H), 2.87 (d, *J* = 6.5 Hz, 1H), 3.64 (ddd, *J* = 5.5, 10.5, 10.5 Hz, 2H), 3.73 (ddd, *J* = 6.0, 10.5, 10.5 Hz, 2H), 3.90 (dd, *J* = 3.0, 10.5 Hz, 1H), 4.03 (dddd, *J* = 3.0, 6.0, 6.0, 6.0 Hz, 1H), 4.27-35 (m, 1H), 5.00-5.08 (m, 2H), 5.19 (d, *J* = 9.5 Hz, 1H), 5.45 (dd, *J* = 3.5, 6.0 Hz, 1H), 7.22-7.31 (m, 5H), 7.47 (t, *J* = 7.5 Hz, 2H), 7.60 (dt, *J* = 2.5, 7.5 Hz, 1H), 8.07 (d, *J* = 7.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ -5.4, 18.4, 26.0, 53.1, 63.0, 636, 67.3, 71.4, 73.4, 128.3, 128.4, 128.7, 128.8, 129.5, 130.2, 133.8, 136.4, 156.5, 167.1; HRMS calcd for $C_{26}H_{37}NO_7Si$ (M+1)504.2418**,** found 504.2420.

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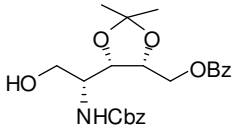


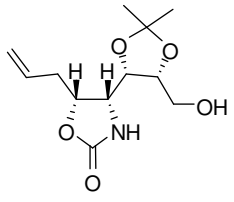
5

((4*R*,5*S*)-5-((*R*)-1-(benzyloxycarbonylamino)-2-hydroxyethyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl benzoate (5)

To a solution of **8c** (4.5 g, 8.93 mmol) in acetone (45 mL) was added 2,2-dimethoxypropane (8.86 mL, 71.48 mmol) and a catalytic amount of pyridinium *p*-toluensulfonate (0.17 g, 0.89 mmol). The resulting solution was stirred at 40°C for 5 h, After the reaction was complete as determined by TLC and the mixture was concentrated and purified by column chromatography (ethyl acetate/hexane = 1/8) to afford the compound (3.84 g, 79%) as a colorless oil. The product was directly used in the next step. Analytical sample: $[\alpha]_D^{25}$ -14.68 (c1.0,$CHCl_3$); IR (neat): 3745, 3445, 2942, 1723, 1504, 1266, 1105 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 0.08 (s, 6H), 0.91 (s, 9H), 1.38 (s, 3H), 1.52 (s, 3H), 3.56 (t, *J* = 9 Hz, 1H), 3.73 (dd, *J* = 4.0, 9.0 Hz, 1H), 4.01-4.05 (m, 1H), 4.47 (d, *J* = 6.5 Hz, 2H), 4.53 (ddd, *J* = 6.5, 6.5, 6.5 Hz, 1H), 4.59 (dd, *J* = 1.0, 6.5 Hz, 1H), 5.06-5.5.14 (m, 3H), 7.30-7.36 (m, 5H), 7.43-7.46 (m, 2H), 7.55-7.59 (m, 1H), 8.07-8.09 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ -5.3, -5.1, 18.5, 24.9, 26.1, 27.5, 50.9, 63.3, 64.0, 67.2, 73.9, 75.4, 108.8, 128.4, 128.4, 128.6, 128.8, 130.4, 130.2, 133.2, 136.62, 155.8, 166.4; HRMS calcd for $C_{29}H_{41}NO_7Si$(M+1)544.2731, found 544.2729.

To a solution of above compound (11.72 g, 21.55 mmol) in THF (220 mL) were added pyridine(72 mL) and 70%HF-Pyr. complex (21.55 mL) at 0°C. After 10 min, the solution was allowed to warm to room temperature. The mixture was stirred for 5 h and quenched with saturated $NaHCO_3$ solution (80 mL) and the solution stirred for 1h. The resulting mixture was diluted with Et_2O (300 mL). The organic phase was successively washed with saturated aqueous $NaHCO_3$ (150 mL), sat. aq. $CuSO_4$ (300 mL) and brine (150 mL), dried over anhydrous

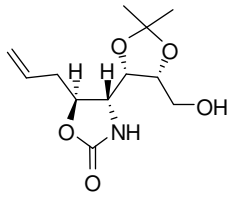
Na_2SO_4, filtered, and concentrated. The residue was purified by flash chromatography (ethyl acetate/hexane = 1/2) to afford alcohol **5** (9.16 g, 99%) as a colorless oil: $[\alpha]_D^{25}$ -21.28 (c1.0, $CHCl_3$); IR (neat): 3439, 2934, 1716, 1509, 1456, 1272, 1218, 1074, 709 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 1.39 (s, 3H), 1.54 (s, 3H), 2.24-2.25 (m, 1H), 3.72-3.81 (m, 2H), 4.04-4.07 (m, 1H), 4.45-4.57 (m, 4H), 5.08-5.17 (m, 2H), 5.29-5.30 (m, 1H), 7.31-7.37 (m, 5H), 7.44-7.47 (m, 2H), 7.56-7.60 (m, 1H), 8.07-8.09 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 24.9, 27.3, 51.5, 63.8, 64.7, 67.5, 75.3, 75.5, 109.16, 128.4, 128.5, 128.6, 128.8, 130.0, 133.4, 136.4, 156.5, 166.5; HRMS calcd for $C_{23}H_{27}NO_7$ (M+1) 430.1866, found 430.1862.



9

(4*S*,5*S*)-5-allyl-4-((4*S*,5*R*)-5-(hydroxymethyl)-2,2-dimethyl-1,3-dioxolan-4-yl)oxazolidin-2-one (9)

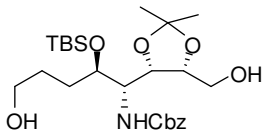
To a solution of **4** (60 mg, 0.13 mmol) in THF (13 mL) at 0°C was treated with NaH (60% dispersion in oil, 15 mg, 0.38 mmol, 3.0 equiv) in several portions over 15 min. After 2 h, the reaction mixture was quenched by the addition of saturated aqueous $NaHCO_3$ (20 mL) and the aqueous layer was extracted with EtOAc (4×50 mL). The combined organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. Purification by silica gel chromatography (ethyl acetate/hexane =2:1) provided **9** (32 mg, 96%) as a white waxy material; IR (neat): 3745, 2924, 1739, 1541, 1375, 1217, 1040 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 1.40 (s, 3H), 1.54 (s, 3H), 2.24-2.31 (m, 1H), 2.53 (dddd, *J* = 1.5, 5.5, 7.5, 15.0 Hz, 1H), 2.75(dddd, *J* = 1.5, 5.7, 8.6, 15.0 Hz, 1H), 3.69-3.70 (m, 1H), 3.93 (dd, *J* = 2.7, 7.7 Hz, 1H), 3.95 (dd, *J* = 4.7, 12.5 Hz 1H), 4.26 (ddd, *J* = 2.4, 4.7, 7.1 Hz, 1H), 4.30 (dd, *J* = 2.7, 7.2 Hz, 1H), 4.74(ddd, *J* = 5.5, 8.0, 8.5 Hz, 1H,), 5.18 (ddd, *J* = 1.5, 1.5, 10.5 Hz, 1H), 5.21 (ddd, *J* = 1.5, 1.5, 17.0 Hz, 1H), 5.89 (dddd, *J*=5.7, 7.5, 10.5, 17.0 Hz, 1H), 5.93 (amide proton, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 25.0, 26.8, 34.5, 55.2, 60.1, 74.8, 76.4, 78.4, 109.2, 118.5, 133.3, 159.1; HRMS calcd for $C_{12}H_{19}NO_5$ (M+1) 258.1341**,** found 258.1343.



9'

(4*S*,5*R*)-5-allyl-4-((4*S*,5*R*)-5-(hydroxymethyl)-2,2-dimethyl-1,3-dioxolan-4-yl)oxazolidin-2-one (9')

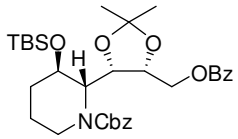
According to the procedure described above for the **9**, **4** was converted to the **9'** as a white solid; ^1H NMR (500 MHz, $CDCl_3$): δ 1.39 (s, 3H), 1.53 (s, 3H), 2.19-2.57 (m, 2H), 3.65 (t, *J* = 3.5 Hz, 1H), 3.72 (dd, *J* = 2.0, 12.5 Hz, 1H), 3.98 (dd, *J* = 4.5, 12.5 Hz, 1H), 4.06(dd, *J* = 3.5, 7.0 Hz, 1H), 4.27 (ddd, *J* = 2.5, 4.5, 7.0 Hz, 1H), 4.51(td, *J* = 4.5, 6.0 Hz, 1H), 5.22 (dddd, *J* = 1.5, 1.5, 1.5, 10.5 Hz, 1H), 5.24 (ddd, *J* = 1.5, 1.5, 17.0 Hz, 1H), 5.80-5.86 (m, 1H), 5.94 (amide proton, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 25.1, 26.9, 39.0, 56.8, 59.8, 76.2, 76.8, 78.6, 109.2, 119.8, 131.6, 158.9; HRMS calcd for $C_{12}H_{19}NO_5$ (M+1)258.1341, found 258.1341.



S5

Benzyl (1*S*,2*R*)-2-(*tert*-butyldimethylsilyloxy)-5-hydroxy-1-((4*S*,5*R*)-5-(hydroxymethyl)-2,2-dimethyl-1,3-dioxolan-4-yl)pentylcarbamate

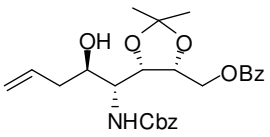
To a solution of **3** (72 mg, 0.3 mmol) in MeOH (11 mL) was added 2N NaOH (1.22 mL, 7.32 mmol) and the resulting mixture was stirred at room temperature. The reaction was monitored by TLC. Upon reaction completion (ca. 1 h), the solvent was evaporated under vacuum and the resulting residue was treated with aqueous saturated $NaHCO_3$ (6 mL) and AcOEt (6 mL). A standard extractive workup followed by column chromatography (ethyl acetate/hexane = 1/1) gave the diol (82 mg, 85%) as a colorless syrup: **Rotamer**: ^{1}H NMR (500 MHz, $CDCl_3$): δ -0.08 (s, 3×0.15H), -0.02(s, 3×0.15H), 0.09 (s, 3×0.85H), 0.13 (s, 3×0.85H), 0.85 (s, 9×0.15H), 0.90 (s, 9×0.85H), 1.25 (s, 3×0.15H), 1.35 (s, 3H), 1.40-1.47 (m, 3.55H), 1.45 (s, 3×0.85H), 1.48-1.60 (m, 2H), 1.64-1.71 (m, 1H), 2.21-2.27 (m, 1H), 3.49-3.66 (m, 4H), 3.72-3.80 (m, 1H), 3.95-3.98 (td, *J* = 3.0, 9.0 Hz, 1H), 4.15-4.24 (ddd, *J* = 6.5, 6.5, 6.5 Hz, 1H), 4.39-4.43 (dd, *J* = 2.5, 6.5 Hz, 1H), 5.05-5.19 (m, 2H), 5.26-5.28 (d, *J* = 9.0 Hz, 1H), 7.31-7.40 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$): δ -4.4, -4.2, 18.2, 25.3, 26.1, 27.7, 29.4, 51.9, 61.9, 63.1, 67.3, 73.5, 74.0, 78.0, 108.7, 128.3, 128.4, 128.8, 136.6, 156.5; HRMS calcd for $C_{25}H_{43}NO_7Si$ (M+1)498.2887, found 498.2890.



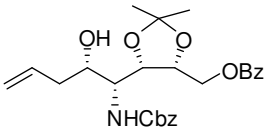
11

(2*S*,3*R*)-Benzyl 2-((4*S*,5*R*)-5-(benzoyloxymethyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-3-(*tert*-butyldimethylsilyloxy)piperidine-1-carboxylate(11)

Spectral data of **11**: $[\alpha]_D^{25}$ +33.03 (c1.0, $CHCl_3$); IR (neat): 3745, 2932, 1704, 1452, 1264, 1074 cm^{-1}; **Rotamer**: ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.03 (s, 3×0.6H), 0.06 (s, 3×.06H), 0.08 (s, 3×0.4H), 0.11 (s, 3×0.4H), 0.85 (s, 9×0.6H), 0.88 (s, 9×0.4H), 1.28 (s, 3×0.4H), 1.38 (s, 3×0.6H), 1.48 (s, 3×0.6H), 1.51 (s, 3×0.4H), 1.70- 1.89 (m, 2H), 1.96-2.09 (m, 2H), 2.98-3.04 (td, *J* = 2.0, 13.5 Hz, 0.6H), 3.17-3.23 (td, *J* = 1.0, 13.5 Hz, 0.4H), 3.85 (br, 0.6H), 3.92(br, 0.4H), 4.09-4.12(m, 0.4H), 4.24-4.27 (m, 1H), 4.40-4.44 (m, 0.6H), 4.45-4.46 (m, 3H), 4.53-4.56 (m, 0.6H), 4.62-4.64 (m, 0.4H), 5.02-5.04 (d, *J* = 12.5 Hz, 0.6H), 5.11-5.14 (d, *J* = 12.5 Hz, 0.4H), 5.20-5.22 (d, *J* = 12.5 Hz, 0.4H), 5.28-5.30 (d, *J* = 12.5 Hz, 0.6H), 7.25-7.46 (m, 7H), 7.54-7.57 (m, 1H), 8.08-8.12 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ -4.8, -4.4, 18.1, 25.8, 28.1, 28.4, 39.4, 56.9, 64.2, 66.1, 67.0, 73.4, 75.0, 109.0, 127.5, 127.9, 128.6, 130.0, 133.4, 137.4, 156.7, 166.7; HRMS calcd for $C_{32}H_{45}NO_7Si$ (M+1) 584.3044, found 584.3041.



anti- 4



syn- 4'

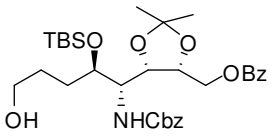
((4R,5S)-5-((1R,2R)-1-(benzyloxycarbonylamino)-2-hydroxypent-4-enyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl benzoate (4)

To a solution of **5** (1.18 g, 2.76 mmol) in anhydrous dichloromethane (28 mL) was added Dess-Martin periodinane (1.5 g, 3.59 mmol) at 0°C. The resulting mixture was stirred at rt and monitored by TLC. Upon reaction completion (ca. 1 h) the reaction was diluted with Et_2O (30 mL) and quenched with aqueous saturated $NaHCO_3$ (30 mL) and $Na_2S_2O_3$ (3.4 g, 13.79 mmol). After 1.5 h of stirring the combined organic phases were dried with $MgSO_4$ and evaporated in *vacuo*. The residue was directly used in the next step. A solution of $TiCl_4$ (4.14 mL, 4.14 mmol; 1.0 M in toluene) was added to a solution of above the product in dry CH_2Cl_2 over 20 min at –78 °C. This yellow solution was stirred for another 30 min at –78 °C and added to a solution of allyltrimethylsilane (0.48 mL, 3.03 mmol) dropwise over 30 min at –78 °C. The mixture was stirred at -78°C until complete conversion was observed by TLC (ca. 10 h). The reaction was diluted with AcOEt (40 mL) and

quenched with aqueous saturated NH_4Cl (100 mL). The combined organic phases were dried with $MgSO_4$, evaporated in *vacuo* and the product was purified by column chromatography (ethyl acetate/hexane = 1:3) to yield *anti*-**4** and *syn*-**4'**(1.07 g, 83%, dr>15:1) as a colorless oil. [α]25 D+1.99 (c1.0, $CHCl_3$); IR (neat): 3745, 3439, 2932, 1716, 1512, 1272, 1070 cm^{-1};**Rotamer**: ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.38 (s, 3H), 1.52 (s, 3H), 2.16-2.22(m, 1H), 2.26 (ddd, *J* = 7.0, 7.5, 8.0 Hz, 1H), 2.41-2.46 (m, 1H), 3.65-3.71 (m, 1H), 3.92 (t, *J* = 8.0 Hz, 1H), 4.40-4.46 (m, 2H), 4.54 (ddd, *J* = 4.5, 7.0, 7.0 Hz, 1H), 4.72 (dd, *J* = 6.5, 7.5 Hz, 1H), 5.06-5.17 (m, 4H), 5.28 (t, *J* = 9.0 Hz, 1H), 5.85 (dddd, *J* = 6.0, 6.0, 9.5, 15.5 Hz, 1H), 7.27-7.38 (m, 5H), 7.39-7.49 (m, 2H), 7.52-7.60 (m, 1H), 8.02-8.12 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 24.9, 27.3, 38.7, 53.3, 63.9, 67.4, 72.3, 74.3, 75.7, 109.0, 119.2, 128.3, 128.4, 128.4, 128.6, 128.6, 128.8, 128.8, 128.9, 129.9, 133.3, 134.5, 136.5, 156.2, 166.4; HRMS calcd for $C_{26}H_{31}NO_7$ (M+1)470.2179, found 470.2181.

Comment [U2]: Multi, range needed

Comment [U3]: Multi, range needed



3

((4R,5S)-5-((5S,6R)-6-(3-hydroxypropyl)-8,8,9,9-tetramethyl-3-oxo-1-phenyl-2,7-dioxa-4-aza-8-siladecan-5-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl benzoate (3)

A solution of **4** (89.8 mg, 0.19 mmol) in 2 mL of CH_2Cl_2 at 0 °C was treated with 2,6-lutidine (0.04 mL, 0.38 mmol, 2 equiv) and TBDMSOTf (0.06 mL, 0.28 mmol, 1.5 equiv), and the solution was stirred at 0°C for 3 h. The reaction mixture was quenched with the addition of saturated aqueous $NaHCO_3$ and extracted with EtOAc (3×10 mL). The combined organic layer was dried (Na_2SO_4) and concentrated under reduced pressure. Purification by Flash silica gel chromatography (ethyl acetate/hexane = 8:1) afforded the compound (0.11 g, 98%) as a colorless oil: [α]25 D -2.56 (c1.0,$CHCl_3$); IR (neat): 3741, 3443, 2940, 1723, 1505, 1269, 1216, 1072 cm^{-1};**Rotamer**: ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.04-0.05 (m, 6H), 0.87 (s, 9H), 1.33 (s, 0.8×3H), 1.35 (s, 0.2×3 H), 1.47 (s, 0.8×3H), 1.50 (s, 0.2×3H), 2.26-2.37 (ddd, *J* = 6.0, 7.0, 12.0 Hz, 2H), 3.67-3.71 (m, 0.2H), 3.74-3.77 (ddd, *J* = 5.5, 6.0, 6.0 Hz, 0.8H), 3.79-3.84 (m, 0.2H), 3.91-3.94 (dd, *J* = 7.5, 9.0 Hz, 0.8H), 4.38 (dd, *J* = 6.0, 12.0 Hz, 1H), 4.41 (d, *J* = 7.0 Hz, 1H), 4.47 (dd, *J* = 6.5, 12.0 Hz, 1H), 4.54-4.56(m, 0.2H), 4.59-4.60 (d, *J* = 7.0 Hz, 0.8H), 5.01 (d, *J* = 12.5 Hz, 1H), 5.02 (dd, *J* = 3.5, 10.0 Hz, 1H), 5.05 (dd, *J* = 5.5, 17.0 Hz, 1H), 5.13(d, *J* = 12.5 Hz, 1H), 5.18 (d, *J* = 9.5Hz, 0.8H), 5.25 (d, *J* = 9.5Hz, 0.2H), 5.85 (dddd, *J* = 7.0, 7.0, 10.0, 17.0 Hz, 1H,), 7.25-7.33 (m, 5H), 7.39-7.42 (m, 2H), 7.51-7.54 (m,1H), 7.99-8.05 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ -4.9, -3.8, 18.3, 25.0, 26.1, 27.3, 31.1, 38.8, 52.6, 64.1, 67.2, 73.2, 73.6, 75.7, 108.8, 117.9, 128.3, 128.3, 128.4, 128.5, 128.7, 129.0, 130.1, 130.1, 130.3, 133.2, 134.3, 136.8, 155.8, 166.4; HRMS calcd for $C_{32}H_{45}NO_7Si$ (M+1)584.3044, found 584.3049.

To a solution of borane/dimethylsulfide (1.86 mL, 19.63 mmol) of THF at -78°C was added 3.8 g (6.54 mmol) of the above compound in THF (65 mL). The resulting solution was stirred at ambient temperature for 16 h, recooled to 0°C and aqueous 1 M $NaHCO_3$ (79 mL) was added to that, which followed immediately by careful addition of 30% H_2O_2 (11 mL). The mixture was stirred vigorously for 3 h at ambient temperature and partitioned with Et_2O. The aqueous phase was extracted with Et_2O (3×80 mL). The organic extracts were combined, washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. The crude product was purified by chromatography (ethyl acetate/hexane = 1:2) to give **3** (2.8 g, 71%): [α]25 D +3.84 (c1.0, $CHCl_3$); IR (neat): 3444, 2940, 2861, 1720, 1508, 1460, 1266, 1216, 1068, 837, 707 cm^{-1} ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.08 (s, 6H), 0.90 (s, 9H), 1.35 (s, 3H), 1.50 (s, 3H), 1.56-1.70 (m, 3H), 1.74-1.82 (m, 1H), 3.49-3.52 (m, 1H), 3.63-3.67 (m, 1H), 3.75-3.78 (m, 1H), 3.90-3.94 (t, *J* = 9.0 Hz, 1H), 4.41-4.42 (d, *J* = 6.0 Hz, 2H), 4.50-4.54 (td, *J* = 6.0, 7.5 Hz, 1H), 4.66-4.67 (d, *J* = 7.5 Hz, 1H), 5.03-5.05 (d, *J* = 12.5 Hz, 1H), 5.14-5.16 (d, *J* = 12.5 Hz, 1H), 5.19-5.21 (d, *J* = 10.0 Hz, 1H), 7.27-7.36 (m, 5H), 7.42-7.45 (m, 2H), 7.54-7.57 (m, 1H), 8.04-8.08 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ -4.8, -3.9, 18.3, 24.8, 26.1, 26.8, 27.3, 29.2, 51.7, 63.1, 64.2, 67.4, 72.7, 73.7, 75.7, 108.8, 128.4, 128.4, 128.6, 128.8, 130.0, 130.2, 133.2, 136.7, 156.1, 166.4; HRMS calcd for $C_{32}H_{47}NO_8Si$ (M+1)602.3149, found 602.3152.