Studies Directed Toward the Total Synthesis of Azaspiracid: Stereoselective Construction of C_1-C_{12}, C_{13}-C_{19} and C_{21}-C_{25} Fragments.

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Electronic Supplementary Information

Alcohol 5: To a stirred solution of TBDPSCl (10.5 g, 10 mL, 38 mmol) and Et_3N (4.22 g, 5.8 mL, 41 mmol) in CH_2Cl_2 (300 mL) was added sequentially DMAP (459 mg, 3.75 mmol) and **4** (10.017 g, 10 mL, 111 mmol). After 17 h, the reaction was quenched with saturated aqueous NH_4Cl (250 mL). The solution was concentrated *in vacuo* to remove the CH_2Cl_2 and the aqueous layer was extracted with Et_2O (4 X 250 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 40% EtOAc / hexanes, to give **5** as a colorless oil (12.0 g, 36.5 mmol, 96%). IR (neat) 3346, 3069, 2933, 2858, 1109 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.64-7.70 (m, 4H), 7.36-7.47 (m, 6H), 3.66-3.72 (m, 4H), 2.08 (t, J = 4.7 Hz, OH), 1.63-1.72 (m, 4H), 1.06 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.8, 133.8, 129.9, 127.9, 64.2, 63.1, 30.1, 29.5, 27.1, 19.4; HRMS (ES+) calcd. for $C_{20}H_{29}O_2Si$ (M+H) 329.1931, found 329.1934.

Ester 6: To a stirred solution of **5** (2.06 g, 6.28 mmol) and powdered 4 Å molecular sieves (approx. 1 g) in CH_2Cl_2 (46.7 mL) at r.t. in a water bath was added sequentially TPAP (113 mg, 0.32 mmol) and NMO (1.10 g, 9.42 mmol). After 50 min, Ph_3PCHCO_2Me (2.61 g, 7.81 mmol) was added. The resulting solution was stirred for 40 min, diluted with 20% EtOAc / hexanes (25 mL), filtered through a small plug of silica gel (20% EtOAc / hexanes rinse), and concentrated *in vacuo*. The crude reaction was dissolved in CH_2Cl_2 (8 mL) and Ph_3PCHCO_2Me (2.12 g, 6.35 mmol) was added at r.t. After 16, the reaction was diluted with 20% EtOAc / hexanes (15 mL), filtered through a small plug of silica gel (20% EtOAc / hexanes rinse), concentrated in vacuo and purified chromatography over silica gel, eluting with 5-15% EtOAc / hexanes, to give **6** (1.61 g, 4.21 mmol, 78% over two steps) as a colorless oil: IR (neat) 2933, 2858, 1724, 1658, 1108 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 7.64-7.67 (m, 4H), 7.33-7.46 (m, 6H), 6.98 (dt, J = 6.8, 15.8, 1H), 5.83 (dt, J = 1.7, 15.8 Hz, 1H), 3.82 (s, 3H), 3.68 (t, J = 6.8 Hz, 2H), 2.29-2.37 (m, 2H), 1.62-1.75 (m, 2H), 1.07 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.3, 149.5, 135.8, 134.0, 129.8, 127.9, 121.3, 63.1, 51.6, 31.1, 28.9, 27.0, 19.4; HRMS (ES+) calcd. for $C_{23}H_{31}O_3Si$ (M+H) 383.2037, found 383.2033.

Aldehyde 7: To a stirred solution of **10** (820 mg, 2.15 mmol) in CH_2Cl_2 (38 mL) at -78°C was added DIBAL-H (5.2 mL, 5.2 mmol, 1M in CH_2Cl_2) was added dropwise over 20 min. After an additional 45 min, the reaction was warmed to 0°C. After 30 min, the reaction was quenched with aqueous sodium tartrate (50 mL, 10%). After 3 h, the solution was extracted with EtOAc (3 x 75 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* to give the allylic alcohol (760 mg, 2.14 mmol, 99%) as a colorless oil: IR (neat) 3332, 2931, 2857, 1108 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$)
δ 7.70 – 7.74 (m, 4H), 7.38-7.46 (m, 6H), 5.65-5.70 (m, 2H), 4.08 (d, J =4.3 Hz, 2H), 3.70-3.73 (m, 2H), 2.16-2.22 (m, 2H), 1.65-1.74 (m, 2H), 1.58 (bs, OH), 1.00 (s, 9H); ^{13}C

NMR (75 MHz, $CDCl_3$) δ 135.8, 134.2, 133.0, 129.8, 129.5, 127.9, 63.9, 63.4, 32.2, 28.7, 27.1, 19.5; HRMS (FAB+) calcd. for $C_{22}H_{30}O_2SiLi$ (M+Li) 361.2175, found 361.2178.

To a stirred solution of the above alcohol (157.7 mg, 0.49 mmol) and powdered 4 Å molecular sieves (approx. 250 mg) in CH_2Cl_2 (3.6 mL) at r.t. in a water bath was sequentially added TPAP (7.8 mg, 0.022 mmol) and NMO (78.4 mg, 0.67 mmol). After 80 min, the solution was diluted with 20% EtOAc / hexanes (10 mL), filtered through a small plug of silica gel (20% EtOAc / hexanes rinse), and concentrated *in vacuo* give **7** (140.2 mg, 0.40 mmol, 89%) as a colorless oil: IR (neat) 2931, 2856, 1690 1107 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.47 (d, J = 7.9 Hz, 1H), 7.64-7.69 (m, 4H), 7.36-7.47 (m, 6H), 6.83 (dt, J = 6.7, 15.7 Hz, 1H), 6.12 (ddt, J = 1.5, 7.8, 15.7 Hz, 1H), 3.70 (t, J = 6.0, 2H), 2.43-2.50 (m, 2H), 1.71-1.80 (m, 2H), 1.06 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.3, 158.9, 135.8, 133.8, 133.3, 129.9, 127.9, 63.0, 30.9, 29.5, 27.1, 19.4; HRMS (ES+) calcd. for $C_{22}H_{29}O_2Si$ (M+H) 353.1937, found 353.1935.

Allylic alcohol 8: To a stirred solution of (1*S*, 2*S*)-*N*,*N'*-di-*p*-toluenesulfonyl-1,2-diphenyl-1,2-ethylenediamine (1.730 g, 3.32 mmol) in CH_2Cl_2 (24 mL) at 0°C was added BBr_3 (768.5 mg, 290 µL, 3.07 mmol) dropwise. After 15 min, the reaction was warmed to r.t. After 40 min, the solvent was removed *in vacuo* as described by Corey. The resultant yellow solid was dissolved in CH_2Cl_2 (20 mL) and the solvent was removed again *in vacuo*. The pale yellow solid was dissolved in CH_2Cl_2 (22 mL), cooled to 0°C, and a solution of $Ph_3SnCH_2CCH_3$ (1.118 g, 2.88 mmol) in CH_2Cl_2 (4 mL) was added dropwise over a period of 15 min. After an additional 3.5 h, the reaction was warmed to r.t. After 30 min, the reaction was cooled to -78°C and a precooled solution of **7** (591 mg, 1.68 mmol) in CH_2Cl_2 (2.5 mL) was added dropwise over a period of 10 min. After an additional 2 h, the reaction was quenched with a pH 7 aqueous buffer (50 mL) and extracted with CH_2Cl_2 (4 X 40 mL). The combined organic layers were was with saturated aqueous NaCl (100 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo*. The crude solid was dissolved in 25 % EtOAc / hexanes (30 mL) and cooled to 0°C to facilitate precipitation of the diamine auxiliary. After 30 min, the solid was filtered (25 % EtOAc / hexanes rinse) to yield pure (1*S*, 2*S*)-*N*,*N'*-di-*p*-toluenesulfonyl-1,2-diphenyl-1,2-ethylenediamine (1.680 g, 3.22 mmol 97%)as a white solid. The filtrate was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 5-16% EtOAc / hexanes, to give **8** (490 mg, 1.25 mmol, 74%) as a colorless oil. $[\alpha]_D^{23}$ -1.3° (c 1.05, $CHCl_3$); IR (neat) 3400, 3304, 2932, 2858, 1108 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.65-7.68 (m, 4H), 7.35-7.46 (m, 6H), 5.70 (dt, J = 6.7, 15.3 Hz, 1H), 5.51 (dd, J = 6.6, 15.3 Hz, 1H), 4.1-4.23 (m, 1H), 3.66 (t, J = 6.2 Hz, 2H), 2.39-2.43 (m, 2H), 2.12-2.19 (m, 2H), 2.03 (t, J = 2.5 Hz, 1H), 1.87 (d, J = 4.6 Hz, OH), 1.61-1.70 (m, 2H), 1.05 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.8, 134.2, 132.9, 131.2, 129.8, 127.8, 80.8,

71.0, 70.9, 63.3, 32.1, 28.6, 27.8, 27.1, 19.4; HRMS (ES+) calcd. for $C_{25}H_{36}O_2NSi$ ($M+NH_4$) 410.2515, found 410.2518.

TES ether 9: To a stirred solution of **8** (205 mg, 0.52 mmol) in CH_2Cl_2 (8 mL) at -78°C was sequentially added 2,6-lutidine (83 mg, 90µL, 0.77 mmol) followed by TESOTf (164 mg, 140 µL, 0.62 mmol). After 25 min, the reaction was quenched with saturated aqueous NH_4Cl (25 mL) and extracted with EtOAc (4 X 25 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 1-5% EtOAc / hexanes, to give **18** (225 mg, 0.44 mmol, 85%) as a colorless oil. $[\alpha]_D^{23}$ +3.3° (c 0.95, $CHCl_3$); IR (neat) 3310, 2933, 2875, 1108 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.67-7.70 (m, 4H), 7.37-7.47 (m, 6H), 5.64 (dt, J = 6.5, 15.4 Hz, 1H), 5.48 (dd, J = 6.5, 15.4 Hz, 1H), 4.20 (q, J = 6.4 Hz, 1H), 3.69 (t, J = 6.3 Hz, 2H), 2.27-2.46 (m, 2H), 2.16 (q, J = 7.0 Hz, 2H), 1.94 (t, J = 2.4 Hz, 1H), 1.62-1.71 (m, 2H), 1.07 (s, 9H), 0.97 (t, J = 7.9 Hz, 9 H), 0.62 (q, J = 7.9 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.8, 134.3, 132.2, 131.4, 129.7, 127.8, 81.7, 72.2, 70.0, 63.5, 32.2, 28.9, 28.6, 27.1, 7.0, 5.1; HRMS (FAB+) calcd. for $C_{31}H_{46}O_2Si_2Li$ (M+Li) 513.3196, found 513.3198.

Acetylenic ketone 10: $CeCl_3 \bullet 7H_2O$ (512 mg, 1.37 mmol) was heated, with vigourous stirring, over a period of 4 h to 140°C in vacuo. After an additional 15 h at 140°C, the off-white solid was allowed to cool to r.t. An argon atmosphere was introduced followed by cool THF (5 mL) and the chalky solution was allowed to stir at r.t. After 3.5 h, the powdered solution was cooled to -78°C and *t*-BuLi (500 µL, 0.6 mmol, 1.2 M in pentane) was added until a color persisted. In a separate flask, a stirred solution of **9** (496 mg, 0.98 mmol) in THF (3.4 mL) was cooled to -78°C. A solution of n-BuLi (500 µL, 1.14 mmol, 2.29 M in hexanes) was added dropwise. After 35 min, the orange solution was warmed to -10°C. After 5 min, the solution was recooled to -78°C and added via cannula to the stirring $CeCl_3$ solution. An additional portion of THF (2 X 0.25 mL) was added in order to rinse the acetylene flask. After 20 min, a precooled solution of **12** (500 mg, 2.30 mmol) in THF (1.0 mL) was added to the organocerium solution. An additional portion of THF (2 X 0.25 mL) was added in order to the amide flask. After 1.1 h, the reaction was warmed to -30°C. After 10 min, the reaction was quenched with saturated aqueous NH_4Cl (10 mL), filtered through a plug of celite (EtOAc rinse) and concentrated *in vacuo*. The crude oil dissolved in EtOAc (100 mL), further diluted with saturated aqueous NH_4Cl (100 mL) and extracted with EtOAc (4 X 100 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 5-30% EtOAc / hexanes, to give **10** (435 mg, 0.620 mmol, 63%) as a colorless oil. $[\alpha]_D^{23}$ +2.7° (c 1.30, $CHCl_3$); IR (neat) 2933, 2876, 2213, 1677, 1108 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.91 (d, J = 7.8 Hz, 2H), 7.66 (m, 5H), 7.57 (t, J = 7.8 Hz, 2H),

7.36-7.45 (m, 6H), 5.64 (dt, J = 6.7, 15.2 Hz, 1H), 5.44 (dd, J = 6.4, 15.2 Hz, 1H), 4.23 (q, 6.4 Hz, 1H), 3.66 (t, J = 6.2 Hz, 2H), 3.41 (t, J = 7.3 Hz, 2H), 3.00 (t, J = 7.3 Hz, 2H), 2.43-2.57 (m, 2H), 2.13 (q, J = 7.0 Hz, 2H), 1.59-1.68 (m, 2H), 1.05 (s, 9H), 0.94 (t, J = 7.9 Hz, 9H), 0.59 (q, J = 7.9 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 182.5, 138.9, 135.8, 134.23, 134.16, 132.2, 131.7, 129.8, 129.7, 128.3, 127.8, 94.0, 81.3, 71.5, 63.4, 50.5, 38.3, 32.1, 29.5, 28.6, 27.1, 19.4, 7.0, 5.0; HRMS (FAB+) calcd. for $C_{40}H_{54}O_5SSi_2Li$ (M+Li) 709.3391, found 709.3403.

Weinreb amide 12: To a stirred solution of 3-(benzenesulphonyl)propionyl chloride (978 mg, 4.20 mmol) in CH_2Cl_2 (20 mL) at -10°C was sequentially added *N,O*-dimethylhyroxylamine hydrochloride (448 mg, 4.60 mmol) and Et_3N (1.01g, 1.4 mL, 10.0 mmol). After 15 min, the reaction was allowed to warm to r.t. After 14 h, the solution was quenched with saturated aqueous NH_4Cl (50 mL) and extracted with CH_2Cl_2 (3 X 100 mL). The dried ($MgSO_4$) extracted was concentrated *in vacuo* and purified by chromatography over a short plug of silica gel, eluting with 75% EtOAc / hexanes, to give **12** (680 mg, 3.13 mmol, 75%) as a pale yellow solid: IR (neat) 3606, 3063, 2974, 2934, 1662, 145, 1307, 1087 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91-7.94 (m, 2H), 7.66-7.69 (m, 1H), 7.55-7.64 (m, 2H), 3.68 (s, 3H), 3.43 (dt, J = 7.6, 9.4, 2H), 3.13 (s, 3H), 2.93 (t, J = 7.6 Hz, 2H) ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.4, 139.1, 134.1, 129.5, 128.2, 61.6, 51.5, 32.5, 25.5; HRMS (ES+) calcd. for $C_{11}H_{16}NO_4S$ (M+H) 258.0800, found 258.0801.

***Cis* Alkene:** To a stirred solution of **10** (83 mg, 0.118 mmol) in hexanes (4.4 mL) was added sequentially quinoline (21.9 mg, 20 µL, 0.169 mmol) and Lindlar's catalyst (15.2 mg). The solution was placed under an atmosphere of H_2 and allowed to stir. During the course of the reaction an additional portion of quinoline (15 µL) and Lindlar's catalyst (28 mg) were added. After the reaction was judged to be complete by ^{1}H NMR, an atmosphere of argon was reintroduced and the solution was filtered through a small plug of Celite (EtOAc rinse). The filtrate was concentrated *in vacuo* and purified over silica gel, eluting with 5-20% EtOAc/hexanes, to give the *cis*-alkene (47.3 mg, 0.067 mmol, 57%) as a pale yellow oil. $[\alpha]_D^{23}$ -3.9° (c 1.00, $CHCl_3$); IR (neat) 3068, 2953, 2934, 2875, 1693, 1618, 1089 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 (dd, J = 1.6, 7.3 H, 2H), 7.64-7.68 (m, 5H), 7.56 (dd, J = 6.4, 7.9, 2H), 7.35-7.45 (m, 6H), 6.24 (dt, J = 6.8, 11.5 Hz, 1H), 6.12 (d, J = 11.5 Hz, 1H), 5.55 (dt, J = 6.4, 15.4, 1H), 5.37 (dd, J = 6.6, 15.4 Hz, 1H), 4.13 (q, J = 6.0 Hz, 1H), 3.65 (t, J = 6.4 Hz, 2H), 3.40 (t, J = 7.1 Hz, 2H), 2.97 (t, J = 8.7 Hz, 2H), 2.73 (dt, J = 1.0, 5.6 Hz, 2H), 2.09 (q, J = 7.4 Hz, 2H), 1.59-1.66 (m, 2H), 1.04 (s, 9H), 0.92 (t, J = 5.5 Hz, 6H), 0.55 (q, J = 5.5 Hz, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.9, 147.2, 139.2, 135.7, 134.2, 134.1, 133.0, 130.9, 129.8, 129.6,

128.2, 127.8, 126.4, 72.5, 63.5, 50.9, 38.6, 36.5, 32.3, 28.6, 27.1, 19.4, 7.0, 5.1; HRMS (FAB+) calcd. for $C_{40}H_{56}O_5SSi_2Li$ (M+Li) 711.3547, found 711.3561.

Fragment A: To a solution of the above *cis*-alkene (13.0 mg, 0.018 mmol) in MeOH (0.8 mL) and CH_2Cl_2 (0.4 mL) was added a solution of Et_3N•HF (240 µL Et_3N, 50 µL 48% aqueous HF, 1.4 mL MeOH) in three portions over 1 h. After the consumption of starting material was observed by thin layer chromatography (TLC), the solution was treated with PPTS (260 mg, 1.03 mmol). After 30 min, the reaction was neutralized with $NaHCO_3$ (solid), filtered, concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10-30% Et_2O / hexanes, to give **A** (7.0 mg, 3.13 mmol, 64%) as a pale yellow solid: $[\alpha]_D^{23}$ +20.7° (c 0.70, $CHCl_3$); IR (neat) 2929, 2856, 1107 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.91 (d, J = 7.3 Hz, 2H), 7.64-7.68 (m, 5H), 7.57 (dd, J = 6.5, 7.7 Hz, 2H), 7.35-7.45 (m, 6H), 6.02 (dt, J = 4.2, 10.0 Hz, 1H), 5.67 (dt, J = 6.6 Hz, 15.4 Hz), 5.54 (d, J = 10.0 Hz, 1H), 5.44 (dd, J = 6.5 Hz, 15.4 Hz, 1H), 4.19 (q, J = 6.6 Hz, 1H), 3.66 (t, J = 6.4 Hz, 2H), 3.19 (s, 3H), 3.00-3.25 (m, 2H), 2.11-2.27 (m, 3H), 1.87-1.97 (m, 3H), 1.57-1.70 (m, 2H), 1.05 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.1, 135.8, 134.1, 133.9, 133.1, 129.9, 129.8, 129.7, 129.5, 128.3, 127.8, 127.4, 97.2, 69.4, 63.4, 52.2, 48.8, 32.0, 30.5, 29.4, 28.8, 27.0, 19.4; HRMS (FAB+) calcd. for $C_{35}H_{44}NO_5SSiLi$ (M+Li) 611.2839, found 611.2842.

Aldehyde 14: To a stirred solution of 1-trimethysiloxy-1,3-butadiene (**13**) (2.84 g, 3.5 mL, 20 mmol) in CH_2Cl_2 (100 mL) was added sequentially 2-methoxy-1,3-dioxolane (2.07 g, 1.9 mL, 20 mmol) and freshly dried $ZnCl_2$ (321 mg, 2.4 mmol) at r.t. After 24 h, the reaction was quenched with saturated aqueous $NaHCO_3$ (100 mL) and extracted with CH_2Cl_2 (3 x 150 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by *via* factional distillation (1 mm, 94-96°C), to give **14** (1.744 g, 12.3 mmol, 61%) as a colorless oil. IR (neat) 2958, 2890, 1687, 1134 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.50 (d, J = 7.8 Hz,1H), 6.84 (dt, J = 6.9,15.8 Hz, 1H), 6.20 (dd 7.9, 15.8 Hz 1H), 5.02 (t, J = 4.3 Hz, 1H), 3.75-4.08 (m, 4H), 2.68-2.73 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.9, 151.5, 135.7, 102.4, 65.3, 37.3; HRMS (ES+) calcd. for $C_7H_{10}NaO_3$ (M+Na) 165.0522, found 165.0519.

Alcohol 15: To a stirred solution of **14** (11.0 g, 77.5 mmol) in Et_2O (300 mL) at -78°C was added DIBAL-H (105 mL, 105 mmol, 1.0 M in CH_2Cl_2) dropwise over a period of 30 min. After an additional 15 min, the reaction was warmed to r.t. After 1.5 h, the reaction was quenched with aqueous potassium tartrate (400 mL, 10%). After 16 h, the solution was extracted with EtOAc (3 x 250 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* to give **15** (8.46 g, 58.8 mmol, 76%) as a colorless oil. IR (neat)

3418, 2888, 1398, 1139 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.67-5.85 (m, 2H), 4.91 (t, J = 4.8 Hz, 1H), 4.11-4.15 (t, J = 4.7 Hz, 2H), 3.84-4.01 (m, 4H), 2.45 (dd, J = 4.7, 4.8, 2H), 1.43 (bs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 132.9, 126.1, 103.8, 65.2, 63.7, 37.2; HRMS (ES+) calcd. for $C_7H_{12}NaO_3$ (M+Na) 167.0679, found 167.0676.

Iodide 16: To a stirred solution of PPh_3 (6.236 g, 23.8 mmol) and imidazole (1.803 g, 26.5 mmol) in Et_2O (110 mL) and MeCN (37 mL) at 0°C was added I_2 (6.013 g, 23.7 mmol) in two portions. After 25 min, a solution of **15** (1.15 g, 7.99 mmol) in Et_2O (15 mL) and MeCN (6 mL) was added *via* cannula to the stirred solution. An additional amount of in Et_2O (6 mL) and MeCN (2 mL)was added to rinse the alcohol flask. After 30 min at 0°C, the reaction was poured into 15% Et_2O / hexanes (400 mL), filtered and concentrated *in vacuo* and purified over a small plug of silica gel, eluting with 20% Et_2O / petroleum ether, to give **16** (1.85 g, 7.28 mmol, 91%) as a yellow oil. IR (neat) 2952, 2883, 1397, 1138 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.87 (dt, J = 7.3, 15.3 Hz, 1H), 5.72 (dt, J = 6.9, 15.3 Hz, 1H), 4.87-4.91 (m, 1H), 3.83-4.00 (m, 6H) 2.41 (m, 2H), ^{13}C NMR (75 MHz, $CDCl_3$) δ 131.5, 128.2, 103.5, 65.2, 37.0, 6.1.

Adduct 18: To a stirred solution of NaHMDS (36 mL, 36 mmol, 1.0 M in THF) in THF (65 mL) at 78°C was added dropwise a solution of **17** (7.996 g, 34.3 mmol) in THF (40 mL) over 30 mL. An additional amount of THF (2 X 5 mL) was added to rinse the oxazolidinone flask. After an additional 20 min, iodide **16** (12.60 g, 49.6 mmol) was added via cannula. An additional amount of THF (2 X 10 mL) was added to rinse the iodide flask. After 1.75 h, the reaction was quenched with saturated aqueous NH_4Cl (100 mL) and allowed to warm to r.t. The solution was concentrated *in vacuo* to remove the THF and the aqueous layer was extracted with EtOAc (4 X 125 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10-40% EtOAc / hexanes, to give **18** (12.22 g, 34.0 mmol, 99%) as a colorless oil. $[\alpha]_D^{23}$ -26.1° (c 1.07, $CHCl_3$); IR (neat) 3028, 2975, 2886, 1782, 1698 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20-7.37 (m, 5H), 5.53-5.59 (m, 2H), 4.68 (t, J = 4.8 Hz, 1H), 4.64-4.68 (m, 1H), 4.13-3.19 (m, 2H), 3.78-3.97 (m, 5H), 3.26-3.32 (m, 1H), 2.69 (dd, J = 9.9, 13.3 Hz, 1H), 2.40-2.50 (m, 1H), 2.38 (t, J = 3.3 Hz, 2H), 2.19-2.24 (m, 1H), 1.17 (d, J = 6.8, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.7, 153.3, 135.6, 130.6, 129.60, 129.58, 129.1, 127.5, 126.7, 104.1, 66.2, 65.1, 55.5, 38.2, 37.6, 37.1, 16.6; HRMS (ES+) calcd. for $C_{20}H_{25}NO_5$ ($M+H^+$) 360.1805, found 360.1814.

Benzyl Ester 20: To a stirred solution of BnOH (710.6 mg, 680 µL, 6.57 mmol) in THF (10 mL) at 0°C was added *n*-BuLi (2.0 mL, 5 mmol, 2.5 M in hexanes). After 10 min, a

precooled solution of **18** (1.188 g, 3.31 mmol) in THF (5 mL) was added via cannula. An additional portion of THF (2 X 1 mL) was added to rinse the auxiliary flask. After 30 min, the reaction was quenched with saturated aqueous NH_4Cl (50 mL) and allowed to warm to r.t. The solution was concentrated *in vacuo* to remove the THF and the aqueous layer was extracted with EtOAc (4 X 75 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10-80% EtOAc / hexanes, to give sequentially **20** (866 mg, 2.99 mmol, 90%) as a colorless oil and recovered (R)-(+)-4-benzyl-2-oxazolidinone (500 mg, 2.82 mmol, 85%) as a white solid. $[\alpha]_D^{23}$ +3.0° (c 2.70, $CHCl_3$); IR (neat) 2950, 2884, 1727, 1137 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.30-7.40 (m, 5H), 5.46-5.50 (m, 2H), 5.11 (s, 2H), 4.83 (t, J = 4.8 Hz, 1H), 3.81-3.99 (m, 5H), 2.50-2.59 (m, 1H), 2.33-2.44 (m, 2H), 2.15-2.22 (m, 1H), 1.16 (d, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.2, 136.4, 130.8, 128.7, 128.32, 128.30, 126.4, 104.1, 66.3, 65.1, 39.7, 37.6, 36.9, 16.7; HRMS (FAB+) calcd. for $C_{17}H_{21}O_4$ (M-H) 289.1440, found 289.1418.

Lactone 19: To a stirred solution of **20** (810 mg, 2.79 mmol) in t-BuOH (24.6 mL) and H_2O (24.6 mL) at O°C was added sequentially solid $NaHCO_3$ (1.736 g, 20.7 mmol) and AD mix α*(6.306 g). After 1.5 h, the reaction was warmed to r.t. After 4 h, the reaction was quenched with solid $Na_2S_2O_5$ until effervescence ceased. After an additional 10 min, the reaction was diluted with saturated aqueous NaCl (100 mL) and extracted with EtOAc (3 X 150 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 30-80% EtOAc / hexanes, to give **19** (465.5 mg, 2.16 mmol, 77%, 10:1 d.s.) as a white solid. Recrystallization from EtOAc / hexanes at 0°C provided **19** (410 mg, 1.90 mmol, 68%, > 20:1 d.s.) as a white solid. $[\alpha]_D^{23}$ +13.4 (c 1.54 , $CHCl_3$); IR (neat) 3450, 2921, 1761, 1119 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.11 (t, J = 4.5 Hz, 1H), 4.28-4.35 (m, 1H), 3.86-4.00 (m, 5H), 2.99 (d, J = 3.8 Hz, OH), 2.60-2.75 (m, 1H), 2.34-2.41 (m, 1H), 1.79-1.99 (m, 4H), 1.27 (d, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.4, 102.7, 80.8, 69.1, 65.3, 65.0, 36.5, 35.6, 32.3, 15.3; HRMS (ES+) calcd. for $C_{10}H_{17}O_5$ ($M+H^+$) 217.1070, found 217.1072.

Methoxy acetal 21: To a stirred solution of **19** (270 mg, 1.24 mmol) in MeOH (50 mL) was added *p*-TsOH•H_2O (776 mg, 4.0 mmol) at r.t. After 20 h, the reaction was quenched with solid $NaHCO_3$ until effervesce ceased. The solution was concentrated *in vacuo* to remove the MeOH. The resulting white solid was dissolved EtOAc (75 mL) and NaCl (75 mL) and the layers separated. The aqueous layer was extracted with EtOAc (3 X 75 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 30-60% EtOAc / hexanes, to give

sequentially **B** (15 mg, 0.08 mmol, 7%) as a colorless oil, **21a** (22 mg, 0.10 mmol, 8%) as a colorless oil, **21** (106 mg, 0.49 mmol, 40%) as a colorless oil and **22** (106 mg, 0.49 mmol, 40%) as a colorless oil. Resubmission twice of compounds **21a** and **22** to the above reaction conditions yielded **21** (177 mg, 0.82 mmol, 66%). $[\alpha]_D^{23}$ -69.4° (c 1.28 $CHCl_3$); IR (neat) 3452, 2950, 1734, 1438, 1105 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.11 (t, J = 4.7 Hz, 1H), 4.25 (bs, 1H), 3.89-3.94 (M, 1H), 3.69 (s, 3H), 3.34 (s, 3H), 2.66-2.73 (m, 1H), 2.08-2.19 (m, 3H), 1.70-1.79 (m, 1H), 1.24 (d, J = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.6, 104.0, 78.5, 72.8, 55.6, 52.2, 43.8, 37.2, 32.4, 17.5; HRMS (FAB+) calcd. for $C_{10}H_{19}O_5$ $(M+H^+)$ 219.1232, found 219.1227.

Fragment B: To a stirred solution of **21** (169.1 mg, 0.782 mmol) in MeCN (20 mL) was added imidazole (2.022 g, 29.7 mmol) and heated to reflux. An additional portion of imidazole was added during the course of the reaction (960 mg, 14.1 mmol). After 6.5 h, the reaction allowed to cool to r.t. and quenched with saturated aqueous NH_4Cl (50 mL). . The solution was concentrated *in vacuo* to remove the MeCN and the aqueous layer was extracted with EtOAc (4 X 75 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over a short plug of silica gel, eluting with 66% EtOAc / hexanes, to give **B** (140 mg, 0.761 mmol, 97%) as a colorless oil. $[\alpha]_D^{23}$ -56.2° (c 0.89, $CHCl_3$); IR (neat) 2934, 2361, 1738, 1096 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.15 (dd, J = 1.9, 5.4 Hz, 1H), 5.03-5.09 (d of d of d, J = 1.6, 5.3, 7.4 Hz, 1H), 4.34-4.27 (m, 1H), 3.36 (s, 3H), 2.66-2.70 (m, 1H), 2.36-2.42 (d of d of d, J = 1.9, 7.4, 14.7 Hz, 1H), 2.19-2.29 (m, 2H), 1.79-1.89 (m, 1H), 1.24 (d, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.9, 104.0, 81.1, 72.1, 55.4, 42.7, 31.5, 30.1, 16.0; HRMS (FAB+) calcd. for $C_9H_{15}O_4$ $(M+H^+)$ 187.0970, found 187.0954.

Fragment C: To a stirred solution of the known alcohol **25**[1] (264 mg, 1.2 mmol) in CH_2Cl_2 (8.6 mL) at 0°C was added sequentially Et_3N (182 mg, 250 µL, 3.41 mmol), DMAP (14.6 mg, 0.12 mmol) and TESCl (226 mg, 252 µL, 1.50 mmol). After 5 min, the solution was warmed to r.t. After 30 min, the reaction was quenched with saturated aqueous NH_4Cl (25 mL) and extracted with EtOAc (3 x 35 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 2-10% EtOAc / hexanes, to give **C** (345 mg, 1.03 mmol, 86%) as a colorless oil: $[\alpha]_D^{23}$ +12.0° (c 1.13 , $CHCl_3$); IR (neat) 2952, 2933, 2907, 2874, 1456, 1095 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.13 (d, J = 3.7 Hz, 1H), 3.51 (dd, J = 4.8, 9.8 Hz, 1H), 3.30 (dd, J = 7.0, 9.8 Hz, 1H), 2.83-2.93 (m, 4H), 1.96-2.14 (m, 2H), 1.59-1.89 (m, 4H), 1.09 (d, J = 6.9 Hz, 3H), 0.95 (t, J = 7.7 Hz, 9 H), 0.91 (d, J = 6.3 Hz, 3H), 0.58 (q, J = 7.7 Hz,

6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 68.0, 55.6, 38.3, 36.2, 33.5, 31.5, 31.0, 26.7, 17.8, 7.0, 4.6; HRMS (ES+) calcd. for $C_{16}H_{35}OS_2Si$ ($M+H^+$) 335.1898, found 335.1891.

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