Synthesis of the C9−C23 (C9'−C23') Fragment of the Dimeric Natural Product Rhizopodin

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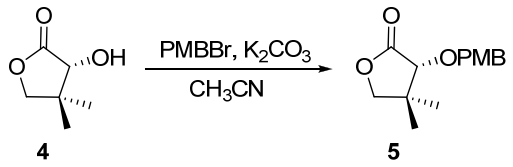
General Experimental

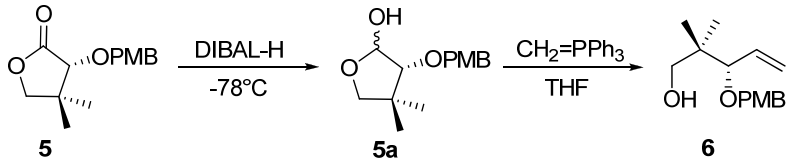
Commercially available reagents were used without further purification unless otherwise noted. All reactions were conducted in oven-dried (120 °C) or flame-dried glassware under a N_2 atmosphere, and at room temperature (20 to 25 °C) unless otherwise stated. All solvents were distilled prior to use: Tetrahydrofuran, diethyl ether and benzene were distilled from Na/benzophenone, dichloromethane, triethylamine, acetonitrile and diisopropylethylamine were distilled from CaH_2. Methanol was distilled under a N_2 atmosphere from Mg/I_2. All non-aqueous reactions were performed under an atmosphere of nitrogen or argon using oven-dried glassware and standard syringe in septa techniques. Evaporation and concentration under reduced pressure was performed at 50 - 500 mbar. ^1H NMR spectra were recorded in $CDCl_3$ (unless stated otherwise) on a Bruker Avance AV500 or DPX-300 at 500 MHz (125 MHz) or 300 MHz (75 MHz), respectively. Chemical shifts are reported as δ values (ppm) referenced to either a tetramethylsilane internal standard or the signals due to the solvent residual: $CDCl_3$, δ-H 7.268 ppm, δ-C 77.0 ppm. Data for ^1H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, brs = broad singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant (Hz), integration. Mass spectra were measured on ABI Q-star Elite. Optical rotations were measured on a Perkin-Elmer 351 polarimeter at 589 nm with a 100 mm path length cell at 20 °C (reported as follows: concentration (*c* in g/100mL), solvent). The reaction progress was checked on pre-coated TLC plates. TLC was carried out using pre-coated sheets (Qingdao silica gel 60-F250, 0.2 mm) which, after development, were visualized under UV light at 254 nm. Flash column chromatography was performed using the indicated solvents on E. Qingdao silica gel 60 (230 - 400 mesh ASTM). Yields refer to chromatographically purified compounds, unless otherwise stated.

Experimental procedures:

Detailed experimental procedures for compounds **5**, **5a**, **6**, **6a**, **7**-**10**, **10a**, **11**, **11a**, **12**, **14**-**19**, **19a**, **20**-**22**, **22a**, **23**-**25** and **3** were described as shown below.



To a solution of *D*-pantolactone (1.30 g, 10.0 mmol) in dry CH_3CN (30 mL) was added potassium carbonate (4.10 g, 30.0 mmol), followed by dropwise addition of 4-methoxybenzyl bromide (2.15 mL, 15.0 mmol) at room temperature. The reaction was heated at reflux for 6 h before it was cooled to room temperature. The solid was removed by passing through a pad of Celite and the filtrate was concentrated under reduced pressure. The residue was dissolved in ethyl acetate (50 mL) and washed with water (20 mL) and brine (20 mL); the organic phase was dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography (silica gel, hexanes: ethyl acetate, 4:1) to give lactone **5** (2.25 g, 90%) as turbid oil. $[\alpha]_D^{20}$ = +99.9 (*c* 2.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32 – 7.29 (m, 2H), 6.91 – 6.88 (m, 2H), 4.95 (d, *J* = 11.7 Hz, 1H), 4.69 (d, *J* = 11.7 Hz, 1H), 3.98 (d, *J* = 8.8 Hz, 1H), 3.85 (d, *J* = 8.8 Hz, 1H), 3.81 (s, 3H), 3.71 (s, 1H), 1.11 (s, 3H), 1.07 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 175.4, 159.5, 129.7, 129.3, 113.9, 80.1, 76.4, 72.0, 55.3, 40.2, 23.2, 19.2 ppm; HRMS (ESI) calculated for $C_{14}H_{18}O_4Na$ $[M+Na]^+$ 273.1103, found 273.1107.



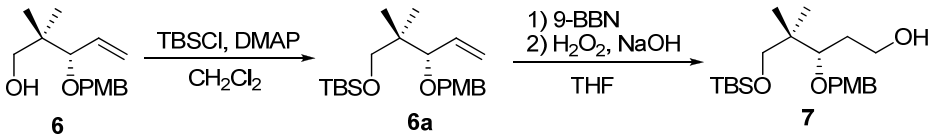
To a solution of **5** (2.0 g, 8.0 mmol) in THF (50 mL) at -78 °C, DIBAL-H (1 M in hexane, 12.0 mL, 12.0 mmol) was added over 10 minutes. After 3h, the reaction was quenched by slowly addition of MeOH (2.0 mL) at -78 °C. After saturated aqueous solution of

potassium sodium tartrate (20 mL) was added, the biphasic mixture was stirred vigorously at room temperature till both phases became clear. Layers were separated, the aqueous phase was extracted with ethyl acetate (20 mL x 3) and the combined organic layer was washed by water (20 mL) and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered and concentrated under reduce pressure. The residue was purified by silica gel chromatography to give **5a** as colorless oil (2.0 g, 99%). The product turned out to be an inseparable mixture of anomers in an approximate 1:1 ratio. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30 – 7.26 (m, 2H), 6.92 – 6.86 (m, 2H), 5.45 (dd, J = 9.7, 4.3 Hz, 1/2H), 5.36 – 5.34 (m, 1/2H), 4.64 (d, J = 11.6 Hz, 1/2H), 4.60 (d, J = 11.1 Hz, 1/2H), 4.56 (d, J = 11.1 Hz, 1/2H), 4.52 (d, J = 11.6 Hz, 1/2H), 4.09 (d, J = 9.8 Hz, 1/2H), 3.81 (s, 3/2H), 3.80 – 3.79 (m, 3/2H), 3.71 (d, J = 8.1 Hz, 1/2H), 3.67 – 5.65 (b, 1/2H), 3.62 (d, J = 8.4 Hz, 1/2H), 3.50 (d, J = 2.9 Hz, 1/2H), 3.45 (d, J = 4.3 Hz, 1/2H), 3.41 (d, J = 8.1 Hz, 1/2H), 1.11 (s, 3/2H), 1.11 (s, 3/2H), 1.19 (s, 3/2H), 1.06 (s, 3/2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): (reported as anomeric mixtures) δ 159.6, 159.2, 130.5, 129.6, 129.4, 129.1, 114.0, 113.8, 103.0, 97.5, 91.3, 85.1, 78.7, 74.1, 72.1, 55.3, 55.3, 42.0, 42.0, 25.8, 24.1, 20.4, 19.8 ppm; HRMS (ESI) calculated for $C_{14}H_{20}O_4Na$ $[M+Na]^+$ 275.1259, found 275.1262.

To a stirred suspension of methyl triphenylphosphonium iodide (6.40 g, 16.0 mmol) in THF (50 mL) at -78 °C, *n*-BuLi (4.5 mL, 11.3 mmol, 2.5 M in hexane) was added dropwise. The solution was stirred for 2h at -50 °C before addition of **5a** (1.20 g, 4.76 mmol) (pre-dissolved in 5 mL of THF) at -78 °C. The reaction mixture was allowed to warm to room temperature within 2h and stirred for additional 4h. The reaction was quenched with saturated aqueous NH_4Cl (3 mL) and diluted with ethyl acetate (150 mL). The organic phase was washed with water (20 mL) and brine (20 mL), then dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel chromatography to give alkene **6** as colorless oil (1.05 g, 88%). $[\alpha]_D^{20}$ = +44.0 (*c* 1.15, $CHCl_3$), (Literature [1]: $[\alpha]_D^{20}$ = +45.0 (*c* 1.04, $CHCl_3$)); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.27 – 7.22 (m, 2H), 6.90 – 6.86 (m, 2H), 5.80 (ddd, J = 17.2, 10.4, 8.3 Hz, 1H), 5.37 (dd,

[1] Blakemore, P. R.; Browder, C. C.; Hong, J.; Lincoln, C. M.; Nagornyy, P. A.; Robarge, L. A.; Wardrop, D. J.; White, J. D. *J. Org. Chem.* 2005, *70*, 5449-5460.

J = 10.4, 1.6 Hz, 1H), 5.24 (dd, *J* = 17.2, 1.2 Hz, 1H), 4.55 (d, *J* = 11.5 Hz, 1H), 4.23 (d, *J* = 11.5 Hz, 1H), 3.81 (s, 3H), 3.60 (d, *J* = 8.3 Hz, 1H), 3.52 (d, *J* = 10.9 Hz, 1H), 3.35 (d, *J* = 10.9 Hz, 1H), 0.88 (s, 3H), 0.88 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.2, 135.0, 130.1, 129.5, 119.7, 113.8, 87.8, 71.4, 70.0, 55.3, 38.5, 22.6, 19.8 ppm; HRMS (ESI) calculated for $C_{15}H_{22}O_3Na$ $[M+Na]^+$ 273.1467, found 273.1461.



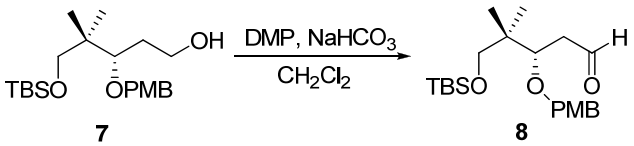
6 **6a** **7**

To a solution of **6** (0.10 g, 0.40 mmol) and Et_3N (0.16 g, 1.6 mmol) in dichloromethane (10 mL) at 0 °C, TBSCl (0.12 g, 0.8 mmol) was added in one portion, followed by a catalytic amount of DMAP (0.05 g). 3h later, saturated NH_4Cl (10 mL) was slowly added to quench the reaction. Layers were separated, and the aqueous layer was extracted with ethyl acetate (20 mL x 3). The combined organic layers were washed by water (20 mL) and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered and concentrated in *vacuo*. The residue was purified by silica gel chromatography to give **6a** as colorless oil (0.14 g, 95%). $[\alpha]_D^{20}$ = +12.6 (*c* 3.05, $CHCl_3$), (Literature [2]: $[\alpha]_D^{24}$ = +7.7 (*c* 1.5, CH_2Cl_2)); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30 (d, *J* = 8.5 Hz, 2H), 6.91 (d, *J* = 8.5 Hz, 2H), 5.88 – 5.81 (m, 1H), 5.33 (dd, *J* = 10.4, 1.7 Hz, 1H), 5.26 (m, 1H), 4.56 (d, *J* = 11.4 Hz, 1H), 4.28 (d, *J* = 11.4 Hz, 1H), 3.83 (s, 3H), 3.72 (d, *J* = 8.0 Hz, 1H), 3.52 (d, *J* = 9.3 Hz, 1H), 3.35 (d, *J* = 9.3 Hz, 1H), 0.95 (s, 9H), 0.94 (s, 3H), 0.88 (s, 3H), 0.08 (s, 6H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.0, 136.0, 131.5, 129.0, 118.1, 113.6, 84.1, 70.3, 69.3, 55.2, 39.6, 26.0, 21.1, 20.0, 18.2, -5.5, -5.5 ppm; HRMS (ESI) calculated for $C_{21}H_{36}SiO_3Na$ $[M+Na]^+$ 387.2331, found 387.2325.

To a solution of **6a** (0.11 g, 0.30 mmol) in THF (10 mL) at 0 °C, 9-BBN (0.5 M in THF, 2 mL) was dropwise added. The reaction was allowed to warm to room temperature. 4h later, NaOH (1 mL, 3 M) and H_2O_2 (1 mL, 30% in water) were added slowly. The resulting solution was refluxed for 1h. The mixture was diluted with ethyl acetate (50 mL) and water (5 mL). Layers were separated, and the aqueous layer was extracted with ethyl

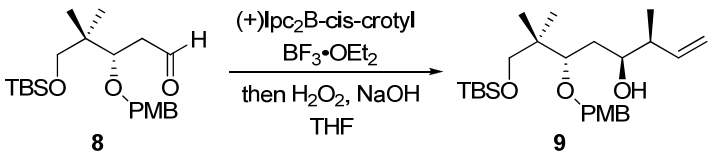
[2] Trost, B. M.; Yang, H.; Thiel, O. R.; Frontier, A. J.; Brindle, C. S. *J. Am. Chem. Soc.* **2007**, *129*, 2206-2207.

acetate (10 mL x 3). The combined organic layer was washed by water and brine (each 20 mL). The organic phase was dried over Na_2SO_4, concentrated in *vacuo*. The residue was purified by silica gel chromatography to give **7** as colorless oil (0.10 g, 86%). $[\alpha]_D^{20}$ = -6.4 (*c* 1.60, $CHCl_3$), (Literature [2]: $[\alpha]_D^{23}$ = -6.1 (c 1.5, CH_2Cl_2)); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29 (d, *J* = 8.5 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 4.62 (d, *J* = 10.8 Hz, 1H), 4.55 (d, *J* = 10.8 Hz, 1H), 3.80 (s, 3H), 3.77 (dd, *J* = 11.1, 5.3 Hz, 1H), 3.73 – 3.68 (m, 1H), 3.62 (dd, *J* = 9.5, 3.4 Hz, 1H), 3.56 (d, *J* = 9.6 Hz, 1H), 3.28 (d, *J* = 9.6 Hz, 1H), 1.78 – 1.70 (m, 2H), 0.93 (s, 9H), 0.91 (s, 3H), 0.88 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.2, 131.2, 129.3, 113.8, 81.0, 74.3, 69.7, 61.2, 55.2, 40.6, 33.3, 25.9, 21.6, 20.1, 18.3, -5.4, -5.5 ppm; HRMS (ESI) calculated for $C_{21}H_{38}SiO_4Na$ $[M+Na]^+$ 405.2437, found 405.2428.

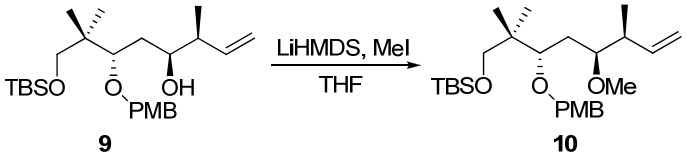


7 **8**

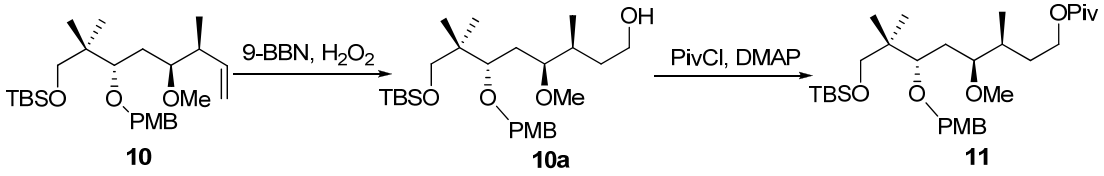
Alcohol **7** (0.50 g, 1.30 mmol) dissolved in CH_2Cl_2 (30 mL) was treated with Dess Martin periodinane (0.83 g, 2.0 mmol) and sodium bicarbonate (0.25 g, 3.0 mmol). 2 h later, the reaction mixture was filtered through a pad of silica gel and eluted with diethyl ether (20 mL). The filtrate was concentrated in *vacuo*. The residue was purified by silica gel chromatography to produce the aldehyde **8** (0.46 g, 92%) as an oil. $[\alpha]_D^{20}$ = +6.4 (*c* 1.7, $CHCl_3$), (Literature [2]: $[\alpha]_D^{25}$ +6.1 (*c* 1.8, CH_2Cl_2)); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.81 (t, *J* = 2.3 Hz, 1H), 7.23 (d, *J* = 8.8 Hz, 2H), 6.86 (d, *J* = 8.7 Hz, 2H), 4.52 (dd, *J* = 10.8, 12.8 Hz, 2H), 3.98 (t, *J* = 6.0 Hz, 1H), 3.81 (s, 3H), 3.53 (d, *J* = 9.8 Hz, 1H), 3.27 (d, *J* = 9.6 Hz, 1H), 2.64 (dd, *J* = 2.3, 6.0 Hz, 2H), 0.91 (s, 9H), 0.90 (s, 3H), 0.86 (s, 3H), 0.04 (S, 6H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.2, 159.1, 130.7, 129.1, 113.6, 77.5, 73.2, 69.2, 55.2, 45.5, 40.4, 25.8, 21.3, 20.1, 18.1, -5.5, -5.6 ppm. HRMS (ESI) calculated for $C_{21}H_{36}SiO_4Na$ $[M+Na]^+$ 403.2275, found 403.2280.



Potassium *tert*-butoxide (1.95 g, 16.8 mmol, pre-dried under high vacuum at 110 ^{o}C for 10 h) in THF (30mL) was cooled to -78 °C, *cis*-2-butene (1.88 g, 33.6 mmol) was introduced, followed by addition of *n*-BuLi (7.6 mL, 16.8 mmol, 2.2 M in hexanes). The resulting orange solution was stirred at -45 °C for 15 min and re-cooled to -78 °C before (+)-*B*-methoxydiisopinocampheylborane (6.40 g, 20.2 mmol) pre-dissolved in THF (25mL) was slowly added via cannula. 30 min later, BF_3•OEt_2 (2.8 mL, 21.8 mmol) was added and the reaction temperature was brought to -100 ^{o}C before aldehyde **8** (3.2 g, 8.4 mmol) pre-dissolved in THF (10 mL) was dropwise added. The reaction mixture was stirred for 6h at -78 °C and quenched by addition of a solution of NaOH (15 mL, 3 M) and H_2O_2 (6 mL, 30% in water). The mixture was refluxed for 2h and then cooled to room temperature. Volatiles were removed in *vacuo*, the aqueous residue was extracted with ethyl acetate (3 x 50 mL). The combined organic phase was washed with brine (50 mL), dried over Na_2SO_4, filtered and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography (hexanes: ethyl acetate, 9:1) to give alcohol **9** (2.86 g, 78%) as clear oil, d.r. > 97 : 3 (determined by ^{1}H NMR); $[\alpha]_D^{20}$ = -24.1 (*c* 1.85, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29 (d, *J* = 8.5 Hz, 2H), 6.89 (d, *J* = 8.5 Hz, 2H), 5.81 – 5.73 (m, 1H), 5.09 (d, *J* = 7.3 Hz, 1H), 5.06 (s, 1H), 4.62 (s, 2H), 3.80 (s, 3H), 3.73 (dd, *J* = 9.7, 2.1 Hz, 1H), 3.69 – 3.63 (m, 1H), 3.54 (d, *J* = 9.6 Hz, 1H), 3.29 (d, *J* = 9.6 Hz, 1H), 2.27 (m, 1H), 1.83 (d, *J* = 5.2 Hz, 1H), 1.66 – 1.59 (m, 1H), 1.48 – 1.55 (m, 1H), 1.04 (d, *J* = 6.8 Hz, 3H), 0.93 (s, 9H), 0.90 (s, 3H), 0.87 (s, 3H), 0.06 (s, 3H), 0.06 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.1, 141.0, 131.5, 129.3, 115.2, 113.8, 79.7, 74.2, 71.9, 69.8, 55.3, 44.3, 40.6, 34.6, 25.9, 21.7, 20.3, 18.3, 14.8, -5.4, -5.4 ppm; HRMS (ESI) calculated for $C_{25}H_{44}O_4SiNa$ $[M+Na]^+$ 459.2907, found 459.2925.



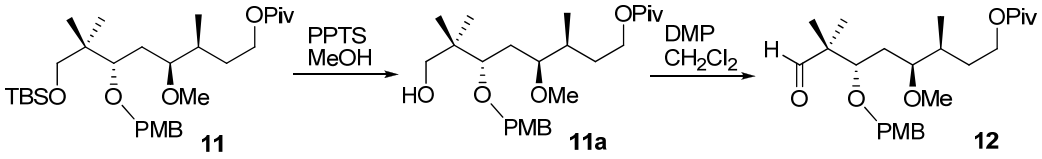
LiHMDS (4.1 mL, 1.0 M in THF, 4.10 mmol) was dropwise added to a solution of **9** (1.50 g, 3.44 mmol) in THF (30 mL) at -78 °C, followed by MeI (0.43 mL, 6.88 mmol). The reaction mixture was allowed to warm to room temperature and stirred for additional 2 h before being quenched with saturated aqueous solution of NH_4Cl (15 mL). Volatiles were removed in *vacuo*, the aqueous residue was extracted with ethyl acetate (3 x 20 mL). The combined organic layer was washed with brine (30 mL), dried over Na_2SO_4, filtered and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography (hexanes: ethyl acetate, 20:1) to give methyl ether **10** (1.38 g, 90%) as an oil. $[\alpha]_D^{20}$ = -37.6 (*c* 1.20, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28 (d, *J* = 8.5 Hz, 2H), 6.89 (d, *J* = 8.5 Hz, 2H), 5.84 (m, 1H), 5.06 (s, 1H), 5.03 (d, *J* = 6.0 Hz, 1H), 4.64 (d, *J* = 11.0 Hz, 1H), 4.52 (d, *J* = 11.0 Hz, 1H), 3.81 (s, 3H), 3.63 (dd, *J* = 7.9, 4.3 Hz, 1H), 3.54 (d, *J* = 9.5 Hz, 1H), 3.36 (s, 3H), 3.33 – 3.29 (m, 1H), 3.26 (d, *J* = 9.5 Hz, 1H), 2.60 (m, 1H), 1.53 – 1.46 (m, 1H), 1.01 (d, *J* = 6.9 Hz, 3H), 0.92 (s, 9H), 0.86 (s, 3H), 0.85 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.9, 140.3, 132.0, 128.8, 114.5, 113.7, 81.6, 79.8, 74.4, 69.6, 56.3, 55.3, 40.7, 39.2, 32.1, 25.9, 22.1, 19.8, 18.3, 15.4, -5.4, -5.5 ppm; HRMS (ESI) calculated for $C_{26}H_{46}O_4SiNa$ $[M+Na]^+$ 473.3063, found 473.3070.



9-BBN (10.0 mL, 5.00 mmol, 0.5 M in THF) was added to a cold solution (0 °C) of **10** (0.90 g, 2.00 mmol) in THF (25 mL) and the mixture was stirred at room temperature for 16 h. The reaction mixture was treated with NaOH (10 mL, 3 M in water) and H_2O_2 (8 mL, 30% in water) at room temperature for 3h. The biphasic mixture was separated and the aqueous layer was extracted with ethyl acetate (3 x 30 mL). The combined organic phase was washed with brine (30 mL), dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel chromatography to give the desired alcohol **10a** (0.82 g, 88%) as colorless oil. $[\alpha]_D^{20}$ = -26.9 (*c* 1.40, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.19 (d, *J* = 8.3 Hz, 2H), 6.80 (d, *J* = 8.4 Hz, 2H), 4.58 (d, *J* = 11.2 Hz, 1H), 4.41 (d, *J* = 11.1 Hz, 1H), 3.73, (s, 3H), 3.64 – 3.60 (m, 1H), 3.55 – 3.45 (m, 5H), 3.27 (s, 3H), 3.21 – 3.16

(m, 2H), 2.77 (brs, 1H), 1.98 (dd, J = 6.7, 3.2 Hz, 1H), 1.67 – 1.60 (m, 1H), 1.52 – 1.47 (m, 1H), 1.40 – 1.36 (m, 1H), 1.30 – 1.26 (m, 1H), 0.85 (s, 9H), 0.81 (d, J = 7.0 Hz, 3H), 0.79 (s, 3H), 0.78 (s, 3H), 0.03 (s, 3H), 0.03 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.0, 131.9, 128.8, 113.7, 82.5, 80.0, 74.5, 69.6, 62.1, 56.7, 55.3, 40.7, 34.9, 32.6, 31.2, 25.9, 22.1, 19.9, 18.3, 17.5, -5.4, -5.5 ppm; HRMS (ESI) calculated for $C_{26}H_{48}O_5SiNa$ $[M+Na]^+$ 491.3163, found 491.3156.

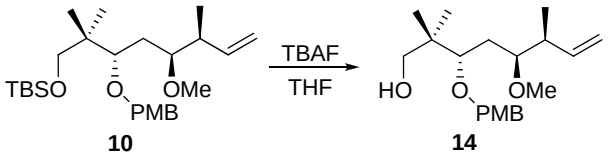
10a (0.47 g, 1.00 mmol) was dissolved in CH_2Cl_2 (15 mL) and treated with triethylamine (2.0 mL, 2.5 mmol), pivaloyl Chloride (1.5 mL, 1.2 mmol) and 4-DMAP (0.012 g, 0.1 mmol) at 0 °C. The resulting mixture was allowed to warm to room temperature and stirred for 16 h before it was quenched with saturated aqueous solution of NH_4Cl (10 mL). Layers were separated and the aqueous residue was extracted with CH_2Cl_2 (2 x 20 mL). The combined organic phases were washed with brine (15 mL), dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel chromatography to give the desired ester **11** (0.50 g, 90%) as colorless oil. $[\alpha]_D^{20}$ = -18.0 (c 0.17, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.19 (d, J = 8.4 Hz, 2H), 6.80 (d, J = 8.4 Hz, 2H), 4.56 (d, J = 11.1 Hz, 1H), 4.42 (d, J = 11.1 Hz, 1H), 4.10 – 3.98 (m, 2H), 3.72, (s, 3H), 3.57 – 3.52 (m, 1H), 3.46 (d, J = 9.5 Hz, 1H), 3.24 (s, 3H), 3.20 (d, J = 9.6 Hz, 1), 3.17 – 3.12 (m, 1H), 1.94 – 1.92 (m, 1H), 1.82 – 1.78 (m, 1H), 1.42 – 1.35 (m, 2H), 1.24 – 1.20 (m, 1H), 1.12 (s, 9H), 0.84 (s, 9H), 0.82 (d, J = 6.9 Hz, 3H), 0.80 (s, 3H), 0.78 (s, 3H), -0.03 (s, 3H), -0.04 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.6, 159.0, 131.9, 128.8, 113.7, 81.9, 80.1, 74.5, 69.7, 63.3, 56.5, 55.3, 40.7, 38.7, 31.3, 29.8, 27.3, 27.0, 25.9, 22.0, 20.0, 18.3, 15.8, -5.3, -5.5 ppm; HRMS (ESI) calculated for $C_{31}H_{56}O_6SiNa$ $[M+Na]^+$ 575.3738, found 575.3730.



11 (0.55 g, 1.00 mmol) was dissolved in methanol (20 mL), after pyridinium *p*-toluenesulfonate (0.013 g, 0.05 mmol) was added at 0 ^{o}C, the reaction mixture was stirred at room temperature and monitored with TLC. Upon the complete consumption of

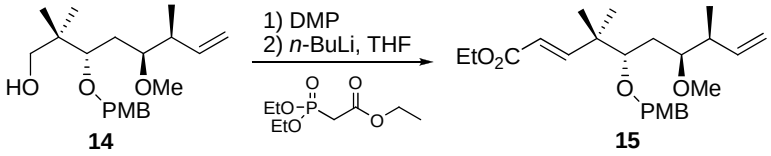
starting material, the reaction was quenched by addition of saturated aqueous solution of $NaHCO_3$ (10 mL). Volatiles were removed in *vacuo*, the aqueous residue was extracted with ethyl acetate (3 x 30 mL). The combined organic phases were washed with brine (15 mL), dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel chromatography to give alcohol **11a** (0.41 g, 93%) as colorless oil. $[\alpha]_D^{20}$ = -30.0 (*c* 0.25, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.18 (d, *J* = 8.4 Hz, 2H), 6.79 (d, *J* = 8.4 Hz, 2H), 4.52 (d, *J* = 10.9 Hz, 1H), 4.43 (d, *J* = 11.0 Hz, 1H), 4.05 – 4.01 (m, 2H), 3.71 (s, 3H), 3.47 – 3.44 (m, 2H), 3.28 – 3.26 (m, 1H), 3.24 (s, 3H), 3.17 – 3.15 (m, 1H), 2.82 (brs, 1H), 1.99 – 1.96 (m, 1H), 1.81 – 1.77 (m, 1H), 1.48 – 1.45 (m, 2H), 1.24 – 1.19 (m, 1H), 1.12 (s, 9H), 0.92 (s, 3H), 0.82 (s, 3H), 0.81 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.5, 159.2, 131.9, 129.0, 113.9, 83.2, 82.5, 74.6, 70.4, 63.1, 56.5, 55.2, 39.9, 38.7, 31.3, 30.7, 29.4, 27.2, 22.2, 21.5, 15.9 ppm; HRMS (ESI) calculated for $C_{25}H_{42}O_6Na$ $[M+Na]^+$ 461.2874, found 461.2865.

Alcohol **11a** (0.66 g, 1.50 mmol), dissolved in CH_2Cl_2 (30 mL), was treated with Dess Martin periodinane (1.24 g, 3.0 mmol) and sodium bicarbonate (0.42 g, 5.0 mmol). 2 h later, the reaction mixture was filtered through a pad of silica gel and eluted with diethyl ether (30 mL). The filtrate was concentrated in *vacuo* to provide the desired aldehyde **12** (0.56 g, 85%) as an oil, which is pure enough for next step reaction without further purification. $[\alpha]_D^{20}$ = -34.1 (*c* 1.70, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.62 (s, 1H), 7.23 (d, *J* = 8.4 Hz, 2H), 6.87 (d, *J* = 8.4 Hz, 2H), 4.53 (d, *J* = 10.9 Hz, 1H), 4.49 (d, *J* = 11.0 Hz, 1H), 4.15 – 4.05 (m, 2H), 3.82 – 3.77 (m, 1H), 3.79 (s, 3H), 3.32 (s, 3H), 3.30 – 3.24 (m, 1H), 2.12 – 2.05 (m, 1H), 1.90 – 1.81 (m, 1H), 1.50 – 1.40 (m, 2H), 1.31 – 1.25 (m, 1H), 1.20 (s, 9H), 1.11 (s, 3H), 1.06 (s, 3H), 0.88 (d, *J* = 6.9 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 205.9, 178.5, 159.3, 130.7, 129.1, 113.8, 81.4, 80.1, 74.4, 63.1, 56.4, 55.2, 51.2, 38.7, 31.5, 30.6, 29.4, 27.2, 19.2, 17.7, 15.8 ppm; HRMS (ESI) calculated for $C_{25}H_{40}O_6Na$ $[M+Na]^+$ 459.2723, found 459.2720.



10 **14**

TBAF (5.2 mL, 1.0 M in THF, 5.2 mmol) was added to a solution of **10** (1.20 g, 2.60 mmol) in THF (20 mL) at 0 °C. The reaction mixture was stirred at room temperature for 16 h and quenched by addition of saturated aqueous solution of NH_4Cl (15 mL). Volatiles were removed, and the aqueous solution was extracted with ethyl acetate (3 x 20 mL). The combined organic layer was washed with saturated aqueous solution of NH_4Cl (30 mL) and brine (30 mL), dried over Na_2SO_4, filtered and concentrated in *vacuo*. The residue was purified by silica gel flash chromatography (hexanes: ethyl acetate, 3:1) to give alcohol **14** (0.72 g, 80%) as an oil. $[\alpha]_D^{20}$ = -54.1 (*c* 0.80, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28 – 7.25 (m, 2H), 6.89 – 6.86 (m, 2H), 5.83 (ddd, *J* = 17.3, 10.6, 6.8 Hz, 1H), 5.10 – 5.01 (m, 2H), 4.59 (d, *J* = 10.9 Hz, 1H), 4.53 (d, *J* = 10.9 Hz, 1H), 3.80 (s, 3H), 3.61 – 3.49 (m, 2H), 3.36 (s, 3H), 3.35 – 3.27 (m, 2H), 2.66 – 2.62 (m, 1H), 1.58 – 1.55 (m, 2H), 1.01 (d, *J* = 6.9 Hz, 3H), 1.00 (s, 3H), 0.87 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.2, 139.5, 131.0, 129.1, 115.0, 113.9, 83.3, 82.1, 74.6, 70.5, 56.4, 55.3, 39.8, 38.4, 32.2, 22.4, 21.5, 15.3 ppm; HRMS (ESI) calculated for $C_{20}H_{32}O_4Na$ $[M+Na]^+$ 359.2198, found 359.2185.

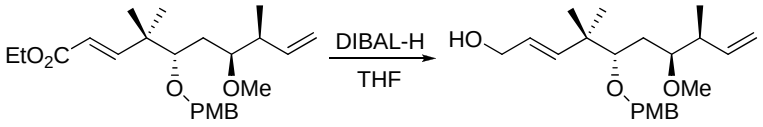


14 **15**

Alcohol **14** (0.55 g, 1.53 mmol) dissolved in CH_2Cl_2 (15 mL) was treated with Dess Martin periodinane (1.0 g, 2.40 mmol) and sodium bicarbonate (0.54 g, 6.4 mmol) at room temperature for 2 h. The reaction mixture was filtered through a pad of silica gel and eluted with diethyl ether (15 mL). The filtrate was concentrated in *vacuo* to produce the corresponding aldehyde, which was used in HWE reaction without further purification.

Triethylphosphonacetate (0.75 mL, 3.75 mmol) was dissolved in THF (15 mL), *n*-BuLi (0.85 mL, 1.9 mmol, 2.2 M in hexanes) was slowly added at -78 °C. The resulting

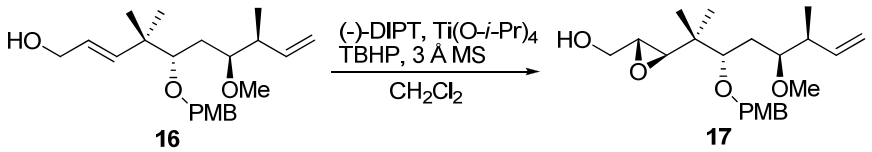
solution was stirred at -45 °C for 30 min and re-cooled to -78 °C, before the above aldehyde (pre-dissolved in 6 mL of THF) was added. The reaction mixture was allowed to warm to room temperature within 6h and quenched by addition of saturated aqueous solution of sodium bicarbonate (10 mL). Volatiles were removed in *vacuo*, the aqueous phase was extracted diethyl ether (3 x 15 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated in *vacuo*. The residue was purified by silica gel column chromatography (hexanes: ethyl acetate, 5:1) to provide **15** (0.57 g, 87%) as an oil. $[\alpha]_D^{20}$ = -28.8 (*c* 0.90, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.29 – 7.26 (m, 2H), 7.10 (d, *J* = 16.0 Hz, 1H), 6.90 – 6.86 (m, 2H),, 5.79 (d, *J* =15.9 Hz, 1H), 5.87 – 5.76 (m, 1H), 5.06 (s, 1H), 5.05 – 4.98 (m, 1H), 4.52 (q, *J* = 10.8 Hz, 1H), 4.19 (q, *J* = 7.0 Hz, 2H), 3.80 (s, 3H), 3.45 (dd, *J* = 7.4, 5.0 Hz, 1H), 3.34 (s, 3H), 3.32 - 3.26 (m, 1H), 2.63 – 2.57 (m, 1H), 1.49 – 1.40 (m, 1H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.09 (s, 6H), 0.98 (d, J = 7.0 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.0, 159.1, 156.1, 139.7, 131.0, 129.1, 118.8, 114.9, 113.7, 82.7, 81.1, 75.0, 60.2, 56.3, 55.3, 42.4, 38.5, 32.5, 23.4, 23.0, 15.3, 14.2 ppm; HRMS (ESI) calculated for $C_{24}H_{36}O_5Na$ $[M+Na]^+$ 427.2460, found 427.2460.



15 **16**

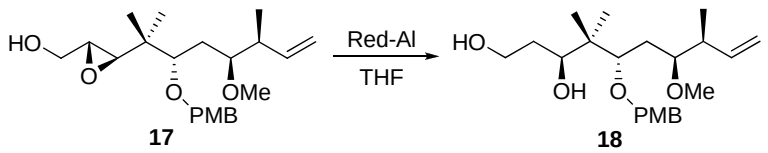
To a solution of ester **15** (0.50 g, 1.24 mmol) in THF (15 mL), DIBAL-H (3.6 mL, 3.6 mmol, 1.0 M in hexanes) was added at -78 °C. The reaction was stirred at -78 °C for 1h and slowly warmed to -30 °C. After being stirred -30 °C for 1h, the reaction was quenched with MeOH (2 mL) and diluted with saturated aqueous solution of Rochelle's salt (15 mL). The resulting reaction mixture was vigorously stirred for 6 h, then layers were separated and the aqueous phase was extracted with ethyl acetate (2 x 20 mL). The combined organic layer was washed with brine (15 mL), dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel column chromatography (hexanes : ethyl acetate, 2:1) to produce **16** (0.41 g, 92%) as an oil. $[\alpha]_D^{20}$ = -48.1 (*c* 1.23, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29 – 7.27 (m, 2H), 6.90 – 6.87 (m, 2H), 5.86 – 5.79 (m, 1H), 5.76 (d, *J* = 16.0 Hz, 1H), 5.63 – 5.28 (m, 1H), 5.06 – 5.04 (m, 1H), 5.02 (dd, *J* = 6.6, 5.2 Hz, 1H), 4.60 (d, *J* = 10.9 Hz, 1H), 4.51 (d, *J* = 10.9 Hz, 1H), 4.09 (d, *J*

= 5.8 Hz, 2H), 3.81 (s, 3H), 3.38 – 3.35 (m, 1H), 3.35 (s, 3H), 3.31 – 3.25 (m, 1H), 2.62 – 2.57 (m, 1H), 1.51 – 1.39 (m, 2H), 1.07 (s, 3H), 1.05 (s, 3H), 0.98 (d, J = 7.0 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.0, 140.2, 140.0, 131.4, 129.0, 126.4, 114.8, 113.8, 83.4, 81.6, 75.0, 64.0, 56.4, 55.3, 41.5, 38.8, 32.6, 24.4, 23.4, 15.4 ppm; HRMS (ESI) calculated for $C_{22}H_{34}O_4Na$ $[M+Na]^+$ 385.2355, found 385.2358.

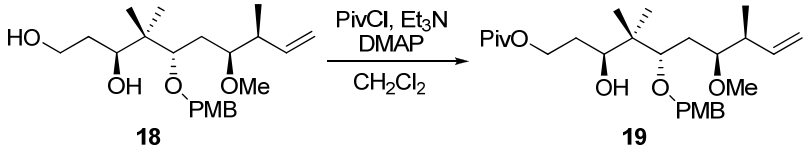


16 **17**

3Å molecular sieves (2.0 g, powder) was flame-dried at 0.5 mmHg for 6 h. After being cooled to room temperature, it was suspended in CH_2Cl_2 (10 mL) and cooled to -20 °C. (-)-diisopropyl tartrate (0.13 g, 0.55 mmol) was added, followed by addition of Ti(O-iPr)$_4$ (0.14 mL, 0.46 mmol) and TBHP (2.5 mL, 13.8 mmol, 5.5 M in decane,). The reaction mixture was aged for 30 min, before a solution of the allylic alcohol **16** (1.65 g, 4.56 mmol) dissolved in CH_2Cl_2 (10 mL) was dropwise added. The reaction mixture was stirred at -20 °C for 4 h. Water (10 mL) was added and the biphasic mixture was stirred for 1h before being filtered through a pad of celite. The filtrate was treated with an aqueous solution of NaOH saturated with NaCl (5 mL, 3 M) for 20 min at room temperature. Additional water (15 mL) was added, layers were separated and the aqueous phase was extracted with CH_2Cl_2 (2 x 10 mL). The combined organic phase was washed with brine (15 mL), dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified with silica gel chromatography to give epoxide **17** (1.50 g, 87%) as colorless oil, d.r. > 97 : 3. $[\alpha]_D^{20}$ = -35.5 (c 0.70, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28 – 7.26 (m, 2H), 6.90 – 6.87 (m, 2H), 5.88 – 5.79 (m, 1H), 5.09 – 5.01 (m, 2H), 4.61 (d, J = 11.0 Hz, 2H), 4.55 (d, J = 11.0 Hz, 2H), 3.82 (dd, J = 12.6, 2.6 Hz, 1H), 3.81 (s, 3H), 3.56 (dd, J = 12.5, 4.4 Hz, 1H), 3.49 (dd, J = 9.8, 2.0 Hz, 1H), 3.35 (s, 3H), 3.32 – 3.27 (m, 1H), 3.07 – 3.02 (m, 1H), 2.95 (d, J = 2.4 Hz, 1H), 2.64 – 2.61 (m, 1H), 1.59 – 1.47 (m, 2H), 0.99 (d, J = 6.9 Hz, 3H), 0.92 (s, 3H), 0.85 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.1, 139.7, 131.2, 128.8, 114.9, 113.8, 82.1, 81.3, 74.7, 62.1, 61.2, 56.3, 55.4, 55.3, 39.0, 38.6, 32.3, 20.3, 18.8, 15.4 ppm; HRMS (ESI) calculated for $C_{22}H_{34}O_5Na$ $[M+Na]^+$ 401.2304, found 401.2301.

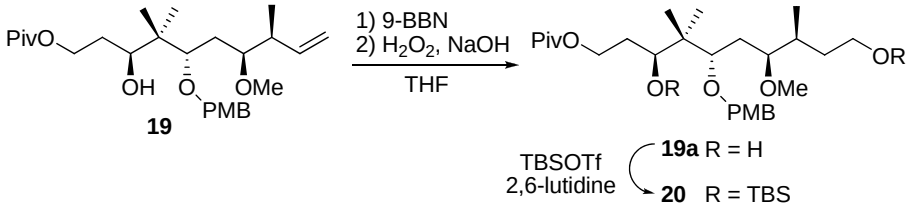


The epoxy alcohol **17** (0.50 g, 1.32 mmol) was dissolved in THF (8 mL) and treated with Red-Al (1.0 mL, 3.5 mmol, 3.5 M in toluene) at 0 °C for 2 days. Saturated aqueous solution of Rochelle's salt (5 mL) was added and the reaction mixture was vigorously stirred for 3 h. Volatiles were removed in *vacuo*. The aqueous phase was extracted with CH_2Cl_2 (2 x 10 mL). The combined organic phases were washed with brine (15 mL), dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel chromatography to give diol **18** (0.45 g, 90%) as colorless oil. $[\alpha]_D^{20}$ = -54.7 (*c* 0.80, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26 – 7.23 (m, 2H), 6.89 – 6.87 (m, 2H), 5.87 – 5.80 (m, 1H), 5.11 – 5.02 (m, 2H), 4.65 (d, *J* = 10.6 Hz, 1H), 4.52 (d, *J* = 10.6 Hz, 1H), 4.47 (s, 1H), 3.89 (d, *J* = 9.5 Hz, 1H), 3.85 – 3.78 (m, 4H), 3.55 (dd, *J* = 10.0, 1.4 Hz, 1H), 3.36 (s, 3H), 3.31 (ddd, *J* = 10.8, 4.5, 2.0 Hz, 1H), 2.70 – 2.62 (m, 1H), 1.71 – 1.63 (m, 2H), 1.59 – 1.51 (m, 2H), 1.11 (s, 3H), 1.02 (d, *J* = 7.0 Hz, 3H), 0.77 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.3, 139.4, 130.2, 129.1, 115.1, 113.9, 86.9, 81.5, 76.7, 75.5, 62.5, 56.3, 55.3, 41.1, 38.4, 32.8, 31.8, 23.0, 20.4, 15.4 ppm; HRMS (ESI) calculated for $C_{22}H_{36}O_5Na$ $[M+Na]^+$ 403.2460, found 403.2468.



To a solution of **18** (0.38 g, 1.00 mmol) in CH_2Cl_2 (15 mL), triethylamine (2.0 mL, 2.5 mmol), pivaloyl chloride (1.5 mL, 1.2 mmol) and 4-DMAP (0.012 g, 0.1 mmol) were added at 0 °C. The reaction solution was stirred for 4h at 0 °C and quenched with saturated aqueous solution of NH_4Cl (10 mL). Layers were separated and the aqueous residue was extracted with CH_2Cl_2 (2 x 10 mL). The combined organic phases were washed with brine (15 mL), dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel chromatography to give ester **19** (0.39 g, 85%) as colorless oil. $[\alpha]_D^{20}$ = -92.8 (*c* 1.45, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.25 – 7.23 (m, 2H), 6.89 – 6.86 (m, 2H), 5.83 (ddd, *J* = 17.3, 10.6, 6.8 Hz, 1H), 5.09 – 5.01 (m, 2H), 4.65 (d, *J* =

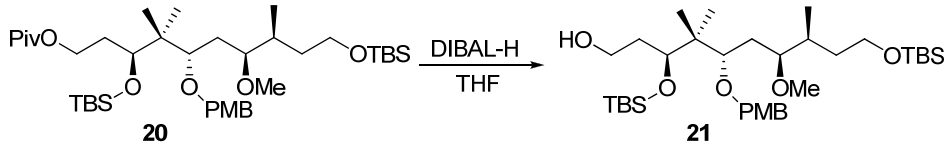
10.7 Hz, 1H), 4.54 (d, *J* = 10.7 Hz, 1H), 4.28 – 4.19 (m, 2H), 4.06 (s, 1H), 3.81 (s, 3H), 3.75 (d, *J* = 10.6 Hz, 1H), 3.55 (dd, *J* = 9.9, 1.6 Hz, 1H), 3.37 (s, 3H), 3.33 – 3.27 (m, 1H), 2.67 – 2.64 (m, 1H), 1.76 – 1.52 (m, 4H), 1.19 (s, 9H), 1.08 (s, 3H), 1.01 (d, *J* = 7.0 Hz, 3H), 0.78 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.4, 159.4, 139.5, 130.5, 129.0, 114.9, 114.0, 86.3, 81.6, 75.3, 71.9, 62.1, 56.3, 55.3, 41.1, 38.7, 38.6, 32.0, 31.0, 27.2, 22.8, 20.0, 15.3 ppm; HRMS (ESI) calculated for $C_{27}H_{44}O_6Na$ $[M+Na]^+$ 487.3036, found 487.3036.



9-BBN (12.0 mL, 0.5 M in THF, 6.00 mmol) was added to a cold (0 °C) solution of **19** (1.20 g, 2.58 mmol) in THF (25 mL). The reaction was stirred for 16 h at room temperature, and then treated with a solution of NaOH (10 mL, 3 M) and H_2O_2 (8 mL, 30% aqueous solution) for 3h. Solvent was removed and the aqueous residue was extracted with ethyl acetate (2 x 30 mL). The combined organic phase was washed with brine (15 mL), dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel chromatography to give diol **19a** (1.07 g, 86%) as colorless oil. $[\alpha]_D^{20}$ = -56.0 (*c* 3.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.25 – 7.22 (m, 2H), 6.89 – 6.86 (m, 2H), 4.67 (d, *J* = 10.8 Hz, 1H), 4.52 (d, *J* = 10.8 Hz, 1H), 4.28 – 4.21 (m, 2H), 4.01 (s, 1H), 3.80 (s, 3H), 3.76 (d, *J* = 10.6 Hz, 1H), 3.73 – 3.69 (m, 1H), 3.62 – 3.58 (m, 1H), 3.56 (dd, *J* = 9.5, 1.7 Hz, 1H), 3.37 (s, 3H), 3.28 (dt, *J* = 10.7, 2.5 Hz, 1H), 2.15 – 2.10 (m, 1H), 1.73 – 1.64 (m, 3H), 1.62 – 1.58 (m, 1H), 1.37 – 1.31 (m, 1H), 1.19 (s, 9H), 1.08 (s, 3H), 0.90 (d, *J* = 7.0 Hz, 3H), 0.80 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.4, 159.3, 130.3, 128.9, 113.8, 86.1, 82.2, 75.3, 72.0, 62.0, 61.7, 56.5, 55.2, 41.1, 38.6, 34.2, 31.7, 31.0, 30.8, 27.1, 22.5, 19.9, 17.3 ppm; HRMS (ESI) calculated for $C_{27}H_{46}O_7Na$ $[M+Na]^+$ 505.3141, found 505.3126.

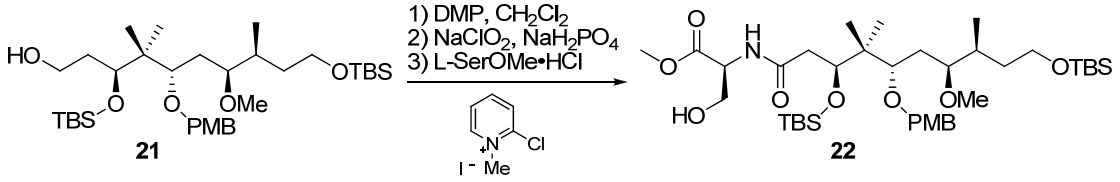
Diol **19a** (0.30 g, 0.62 mmol) was dissolved in CH_2Cl_2 (10 mL), 2,6-lutidine (0.22 mL, 1.86 mmol) and TBSOTf (0.27 mL, 1.24 mmol) were added sequentially at -78 °C. The reaction mixture was stirred for 6h at -50 °C before being quenched with saturated

aqueous solution of NH_4Cl (10 mL). Layers were separated and the aqueous phase was extracted with CH_2Cl_2 (2 x 10 mL). The combined organic phases were washed with brine (15 mL), dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel chromatography to give **20** (0.38 g, 88%) as colorless oil. $[\alpha]_D^{20}$ = -36.8 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28 – 7.26 (m, 2H), 6.89 – 6.86 (m, 2H), 4.61 (d, *J* = 10.9 Hz, 1H), 4.53 (d, *J* = 10.9 Hz, 1H), 4.28 – 4.23 (m, 1H), 4.08 – 4.00 (m, 1H), 3.81 (s, 3H), 3.73 – 3.65 (m, 2H), 3.65 – 3.60 (m, 1H), 3.60 – 3.55 (m, 1H), 3.31 (s, 3H), 3.27 – 3.22 (m, 1H), 2.09 – 1.93 (m, 2H), 1.82 – 1.65 (m, 2H), 1.50 – 1.38 (m, 2H), 1.20 (s, 9H), 1.18 – 1.12 (m, 1H), 0.96 (s, 3H), 0.93 (s, 9H), 0.90 (s, 9H), 0.89 (s, 3H), 0.87 (d, *J* = 7.2 Hz, 3H), 0.09 (s, 3H), 0.07 (s, 3H), 0.05 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.4, 159.0, 131.8, 128.6, 113.8, 82.3, 81.2, 74.6, 74.2, 62.1, 61.6, 56.4, 55.3, 44.2, 38.7, 33.8, 31.8, 31.8, 30.5, 27.3, 26.2, 26.0, 20.7, 19.9, 18.5, 18.3, 15.9, -3.7, -3.7, -5.3, -5.3 ppm; HRMS (ESI) calculated for $C_{39}H_{74}O_7Si_2Na$ $[M+Na]^+$ 733.4871, found 733.4853.



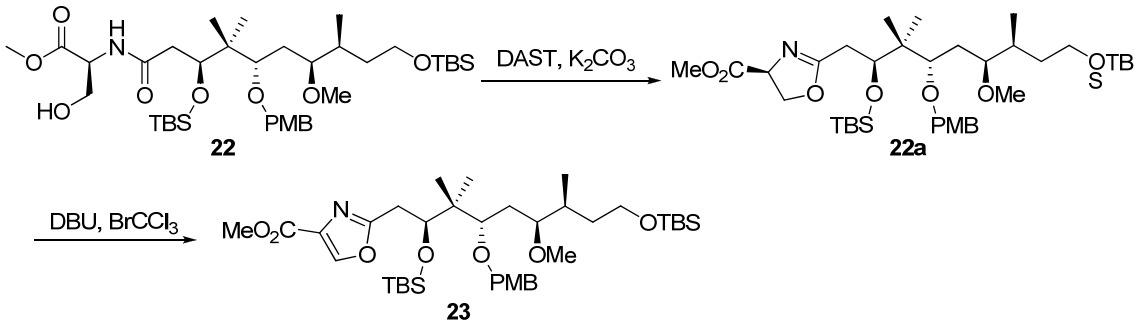
Compound **20** (1.30 g, 1.83 mmol), dissolved in CH_2Cl_2 (30 mL), was treated with DIBAL-H (4.5 mL, 4.5 mmol, 1.0 M in hexanes) at -78 °C. 1h later, the reaction mixture was allowed to warm to -30 °C and stirred for another 1h, then it was quenched with MeOH (3 mL) and saturated aqueous solution of Rochelle's salt (20 mL). The biphasic mixture was vigorously stirred for 5 h. Layers were separated, the aqueous phase was extracted with CH_2Cl_2 (2 x 20 mL). The combined organic phase was dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel column chromatography (hexanes: ethyl acetate, 3:1) to provide **21** (1.04 g, 90%) as an oil. $[\alpha]_D^{20}$ = -38.5 (*c* 0.70, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29 – 7.26 (m, 2H), 6.90 – 6.86 (m, 2H), 4.64 (d, *J* = 11.0 Hz, 1H), 4.51 (d, *J* = 11.0 Hz, 1H), 3.81 (s, 3H), 3.80 – 3.75 (m, 1H), 3.73 – 3.70 (m, 1H), 3.70 – 3.58 (m, 3H), 3.53 – 3.47 (m, 1H), 3.31 (s, 3H), 3.22 – 3.16 (m, 1H), 2.09 – 2.04 (m, 1H), 1.92 – 1.86 (m, 1H), 1.77 – 1.70 (m, 1H), 1.64 – 1.55 (m, 1H), 1.50 – 1.39 (m, 2H), 1.19 – 1.12 (m, 1H), 1.00 (s, 3H), 0.92 (s, 9H), 0.90 (s, 12H), 0.86 (d, *J* = 6.9 Hz, 3H), 0.11 (s, 3H), 0.09 (s, 3H), 0.06 (s, 6H) ppm; ^{13}C NMR

(125 MHz, $CDCl_3$): δ 159.1, 131.7, 128.8, 113.8, 83.1, 81.7, 75.0, 74.2, 61.4, 60.2, 56.6, 55.3, 44.2, 36.0, 33.5, 31.7, 30.3, 26.2, 26.0, 20.4, 19.3, 18.4, 18.3, 15.8, -3.6, -3.9, -5.3, -5.4 ppm; HRMS (ESI) calculated for $C_{34}H_{66}O_6Si_2Na$ $[M+Na]^+$ 649.4296, found 649.4285.



A solution of **21** (0.21 g, 0.34 mmol) in CH_2Cl_2 (15 mL) was treated with Dess Martin periodinane (0.29 g, 0.68 mmol) and sodium bicarbonate (0.14 g, 1.72 mmol) at room temperature. 2 h later, the reaction mixture was filtered through a pad of silica gel and eluted with diethyl ether (15 mL). The combined filtrate was concentrated in *vacuo*. The residue was dissolved in *tert*-butanol (10 mL) and 2,3-dimethyl-but-2-ene (5 mL) at 0 °C, and treated with a solution of $NaClO_2$ (0.15 g, 1.73 mmol) and NaH_2PO_4 (0.20 g) in water (5 mL). On completion of the reaction, monitored by TLC, it was diluted with ethyl acetate-H_2O (50 mL: 15 mL). Layers were separated and the aqueous phase was extracted with ethyl acetate (2 x 20 mL). The combined organic layers were dried over Na_2SO_4 concentrated in *vacuo* to produce the corresponding carboxylic acid, which was unstable and used in the next step reaction without further purification. Thus, the crude carboxylic acid was dissolved in CH_2Cl_2 (15 mL) and cooled to 0 ^oC, after DIPEA (3 mL, 16.3 mmol), *L*-SerOMe•HCl (0.26 g, 1.70 mmol) and Mukaiyama reagent (0.22 g, 0.85 mmol) were added, the reaction mixture was allowed to warm to room temperature and stirred for 16 h. Saturated sodium bicarbonate (15 mL) was added to quench the reaction, layers were separated and the aqueous phase was extracted with CH_2Cl_2 (2 x 20 mL). The combined organic phases were washed with brine (20 mL), dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel chromatography to give amide **22** (0.22 g, 86%) as colorless oil. $[\alpha]_D^{20}$ = -24.8 (*c* 0.80, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 7.29 – 7.26 (m, 2H), 6.89 – 6.86 (m, 2H), 6.65 (d, *J* = 7.2 Hz, 1H), 4.62 – 4.60 (m, 1H), 4.61 (d, *J* = 10.9 Hz, 1H), 4.51 (d, *J* = 10.9 Hz, 1H), 4.09 (dd, *J* = 6.2, 3.6 Hz, 1H), 3.94 – 3.91 (m, 1H), 3.88 (d, *J* = 3.6 Hz, 1H), 3.80 (s, 3H), 3.77 (s, 3H), 3.72 – 3.66 (m, 1H), 3.64 – 3.58 (m, 1H), 3.52 (dd, *J* = 8.3, 3.0 Hz, 1H), 3.31 (s, 3H), 3.26 – 3.21 (m, 1H), 2.76 (dd, *J* = 15.4, 3.5 Hz, 1H), 2.31 (dd, *J* = 15.4, 6.3 Hz, 1H), 2.09

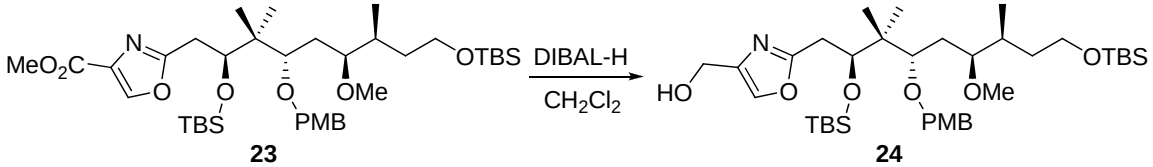
– 2.03 (m, 1H), 1.79 – 1.74 (m, 1H), 1.57 – 1.48 (m, 2H), 1.21 – 1.14 (m, 1H), 0.97 (s, 3H), 0.93 (s, 3H), 0.91 (s, 9H), 0.89 (s, 9H), 0.87 (d, J = 6.9 Hz, 3H), 0.10 (s, 3H), 0.05 (s, 9H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 172.3, 170.1, 159.0, 131.6, 128.8, 113.8, 82.6, 82.0, 74.8, 74.7, 63.5, 61.5, 56.5, 55.3, 54.8, 52.4, 44.2, 40.7, 33.6, 32.1, 30.3, 26.1, 26.0, 21.2 ,20.6, 18.3, 15.8, -4.0, -4.6, -5.3, -5.4 ppm; HRMS (ESI) calculated for $C_{38}H_{71}NO_9Si_2Na$ $[M+Na]^+$ 764.4565, found 764.4555.



Amide **22** (0.23 g, 0.31 mmol) was dissolved in CH_2Cl_2 (15 mL) and treated with DAST (62 μL, 0.46 mmol, 95% purity) at -78 °C. The reaction mixture was stirred for 1h. After K_2CO_3 (0.11 g, 0.76 mmol) was added, the reaction was allowed to warm to room temperature and stirred for 2h before it was poured into saturated aqueous solution of $NaHCO_3$ (10 mL) and extracted with ethyl acetate (2 x 50 mL). The combined organic phases were washed with brine (20 mL), dried over Na_2SO_4 and concentrated in *vacuo*. A small portion of the oxazoline intermediate **22a** was purified for characterization purposes by passing through a small silica gel column (eluting with hexanes / ethyl acetate 2 : 1). $[\alpha]_D^{20}$ = -2.5 (c 0.70, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29 – 7.26 (m, 2H), 6.89 – 6.86 (m, 2H), 4.77 – 4.71 (m, 1H), 4.60 (d, J = 10.9 Hz, 1H), 4.50 (d, J = 10.9 Hz, 1H), 4.49 (dd, J = 9.3, 7.7 Hz, 1H), 4.43 (dd, J = 10.7, 8.7 Hz, 1H), 4.13 – 4.08 (m, 1H), 3.80 (s, 3H), 3.78 (s, 3H), 3.72 – 3.67 (m, 1H), 3.64 – 3.60 (m, 1H), 3.58 (dd, J = 9.1, 3.1 Hz, 1H), 3.30 (s, 3H), 3.29 – 3.25 (m, 1H), 2.82 (dd, J = 15.7, 4.1 Hz, 1H), 2.43 (dd, J = 15.7, 6.2 Hz, 1H), 2.08 – 2.04 (m, 1H), 1.79 – 1.74 (m, 1H), 1.50 – 1.46 (m, 2H), 1.22 – 1.15 (m, 1H), 0.96 (s, 3H), 0.90 – 0.87 (m, 21H), 0.86 (d, J = 7.0 Hz, 3H), 0.07 (s, 3H), 0.06 (s, 6H), 0.02 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.6, 169.2, 158.9, 131.7, 128.6, 113.7, 81.9, 80.9, 74.6, 74.3, 69.0, 68.2, 61.6, 56.2, 55.2, 52.4, 44.5,

33.8, 33.1, 31.5, 30.3, 26.0, 25.9, 20.7, 19.7, 18.3, 15.8, -4.1, -4.4, -5.3, -5.4 ppm; HRMS (ESI) calculated for $C_{38}H_{69}NO_8Si_2Na$ $[M+Na]^+$ 746.4459, found 746.4443.

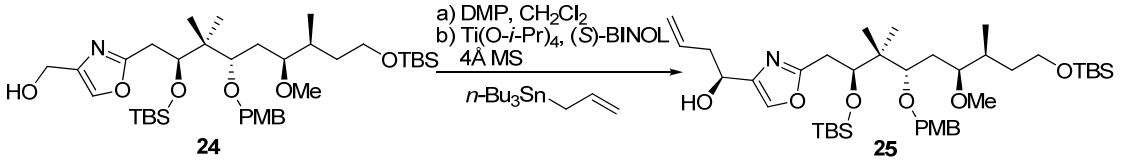
The above crude oxazoline was dissolved in CH_2Cl_2 (15 mL) and cooled to 0 °C. DBU (0.14 mL, 0.93 mmol) was added, followed by $BrCCl_3$ (0.12 mL, 1.24 mmol). The resulting reaction mixture was stirred for 20 h at room temperature. Saturated aqueous solution of NH_4Cl (15 mL) was added to quench the reaction. Layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 x 25 mL). The combined organic phases were washed with brine (15 mL), dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel chromatography (hexanes : ethyl acetate, 4 : 1) to give oxazole **23** as colorless oil (0.17 g, 75%). $[\alpha]_D^{20}$ = -37.3 (*c* 0.90, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.14 (s, 1H), 7.29 – 7.26 (m, 2H), 6.89 – 6.86 (m, 2H), 4.61 (d, *J* = 11.0 Hz, 1H), 4.52 (d, *J* = 11.0 Hz, 1H), 4.18 (dd, *J* = 7.9, 3.3 Hz, 1H), 3.91 (s, 3H), 3.81 (s, 3H), 3.72 – 3.66 (m, 1H), 3.66 – 3.59 (m, 1H), 3.56 (d, *J* = 8.1 Hz, 1H), 3.28 (s, 3H), 3.26 – 3.23 (m, 1H), 3.20 (dd, *J* = 15.6, 3.3 Hz, 1H), 2.97 (dd, *J* = 15.6, 8.0 Hz, 1H), 2.11 – 2.04 (m, 1H), 1.81 – 1.74 (m, 1H), 1.59 – 1.47 (m, 2H), 1.22 – 1.15 (m, 1H), 0.97 (s, 3H), 0.95 (s, 3H), 0.90 (s, 9H), 0.87 (d, *J* = 7.0 Hz, 3H), 0.85 (s, 9H), 0.06 (s, 6H), 0.02 (s, 3H), -0.34 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.6, 161.7, 159.0, 143.6, 133.4, 131.6, 128.6, 113.7, 82.1, 81.5, 75.7, 74.7, 61.2, 56.3, 55.3, 51.9, 44.3, 33.6, 32.8, 31.7, 30.1, 26.0, 25.9, 21.2, 20.3, 18.3, 18.2, 15.9, -4.3, -4.7, -5.3, -5.4 ppm; HRMS (ESI) calculated for $C_{38}H_{67}NO_8Si_2Na$ $[M+Na]^+$ 744.4303, found 744.4298.



23 **24**

Oxazole **23** (0.40 g, 0.55 mmol) was dissolved in CH_2Cl_2 (20 mL) and treated with DIBAL-H (1.7 mL, 1.7 mmol, 1.0 M in hexanes) at -78 °C. 1h later, the reaction was slowly warmed to -30 °C and quenched with *tert*-Butanol (2 mL) and saturated solution of Rochelle's salt (20 mL). Layers were separated and the aqueous phase was extracted with CH_2Cl_2 (2 x 40 mL). The combined organic layers were dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel column chromatography

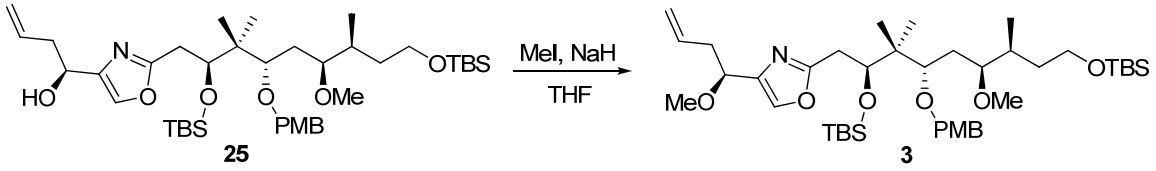
(hexanes : ethyl acetate, 2 : 1) to provide **24** (0.28 g, 73%) as an oil. $[\alpha]_D^{20}$ = -36.6 (*c* 1.40, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.47 (s, 1H), 7.30 – 7.27 (m, 2H), 6.90 – 6.87 (m, 2H), 4.62 (d, *J* = 10.8 Hz, 1H), 4.55 (s, 2H), 4.53 (d, *J* = 10.8 Hz, 1H), 4.18 (dd, *J* = 7.8, 3.1 Hz, 1H), 3.81 (s, 3H), 3.73 – 3.67 (m, 1H), 3.66 – 3.61 (m, 1H), 3.58 (dd, *J* = 8.9, 2.9 Hz, 1H), 3.29 (s, 3H), 3.29 – 3.24 (m, 1H), 3.13 (dd, *J* = 15.6, 3.0 Hz, 1H), 2.85 (dd, *J* = 15.6, 7.8 Hz, 1H), 2.09 – 2.04 (m, 1H), 1.82 – 1.75 (m, 1H), 1.55 – 1.51 (m, 2H), 1.25 – 1.16 (m, 1H), 0.98 (s, 3H), 0.95 (s, 3H), 0.91 (s, 9H), 0.88 (d, *J* = 7.0 Hz, 3H), 0.86 (s, 9H), 0.06 (s, 6H), 0.02 (s, 3H), -0.32 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.1, 159.0, 140.4, 134.3, 131.7, 128.6, 113.7, 82.1, 81.4, 75.8, 74.7, 61.7, 56.9, 56.3, 55.3, 44.3, 33.7, 32.8, 31.5, 30.3, 26.0, 26.0, 20.9, 20.1, 18.3, 18.3, 15.9, -4.4, -4.7, -5.3, -5.4 ppm; HRMS (ESI) calculated for $C_{37}H_{67}NO_7Si_2Na$ $[M+Na]^+$ 716.4354, found 716.4370.



A solution of **24** (0.52 g, 0.75 mmol) in CH_2Cl_2 (20 mL) was treated with Dess-Martin periodinane (0.64 g, 1.50 mmol) and sodium bicarbonate (0.14 g, 1.72 mmol). 2 h later, the reaction was filtered through a pad of silica gel and eluted with diethyl ether (20 mL). The filtrate was concentrated in *vacuo* to produce the corresponding aldehyde, which was used in next step of reaction without further purification.

4Å molecular sieves (1.3 g, pre-dried under high vacuum for 8 h) was suspended in CH_2Cl_2 (20 mL), after (*S*)-BINOL (0.04 g, 0.15 mmol) and Ti(*i*-PrO)$_4$ (45 μL, 0.15 mmol) was added at room temperature, the orange suspension was heated at reflux for 1h and then cooled to room temperature. The above aldehyde, pre-dissolved in CH_2Cl_2 (5 mL), was added *via* cannula. 10 min later, the reaction mixture was cooled to -78 °C before allyltributylstannane (0.36 mL, 1.2 mmol) was added slowly. The reaction was then kept at -20 °C for 60 h. After saturated aqueous solution of $NaHCO_3$ (20 mL) was added to quench the reaction, it was diluted with CH_2Cl_2 (20 mL) and further stirred at room temperature for 2 h. Molecular sieves were removed by filtration through a pad of Celite. The filtrate was separated and the aqueous phase was extracted with CH_2Cl_2 (2 x 25 mL).

The combined organic phases were washed with brine (20 mL), dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel chromatography to give **25** (0.36 g, 65% over 2 steps, 78% brsm) as colorless oil, d.r. > 97 : 3 (determined by ^{1}H NMR); $[\alpha]_D^{20}$ = -41.3 (*c* 2.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.44 (s, 1H), 7.30 – 7.27 (m, 2H), 6.89 – 6.87 (m, 2H), 5.85 (m, 1H), 5.22 – 5.13 (m, 2H), 4.70 – 4.67 (m, 1H), 4.62 (d, *J* = 10.9 Hz, 1H), 4.53 (d, *J* = 10.9 Hz, 1H), 4.20 (dd, *J* = 7.9, 3.0 Hz, 1H), 3.81 (s, 3H), 3.73 – 3.66 (m, 1H), 3.65 – 3.59 (m, 2H), 3.30 (s, 3H), 3.30 – 3.26 (m, 1H), 3.11 (dd, *J* = 15.7, 3.0 Hz, 1H), 2.85 (dd, *J* = 15.7, 7.9 Hz, 1H), 2.67 – 2.61 (m, 1H), 2.56 – 2.51 (m, 1H), 2.47 (d, *J* = 5.1 Hz, 1H), 2.12 – 2.03 (m, 1H), 1.83 – 1.75 (m, 1H), 1.57 – 1.49 (m, 2H), 1.27 – 1.16 (m, 1H), 0.97 (s, 3H), 0.94 (s, 3H), 0.91 (s, 9H), 0.88 (d, *J* = 7.0 Hz, 3H), 0.86 (s, 9H), 0.06 (s, 6H), 0.02 (s, 3H), -0.32 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.8, 159.0, 143.2, 134.1, 133.6, 131.7, 128.6, 118.3, 113.7, 82.1, 81.3, 75.8, 74.7, 66.6, 61.7, 56.3, 55.3, 44.2, 40.9, 33.7, 32.8, 31.5, 30.3, 26.0, 26.0, 20.8, 20.0, 18.3, 15.9, -4.4, -4.6, -5.2, -5.3 ppm; HRMS (ESI) calculated for $C_{40}H_{71}NO_7Si_2Na$ $[M+Na]^+$ 756.4667, found 756.4678.



Allylic alcohol **25** (0.22 g, 0.30 mmol) was dissolved in THF (20 mL) and treated with NaH (18 mg, 0.45 mmol, 60% dispersion in mineral oil) at 0 °C. 1 h later, MeI (58 μL, 0.90 mmol) was added via syringe. The reaction mixture was allowed to warm to room temperature and stirred for 2 h before carefully quenched with saturated aqueous solution of NH_4Cl (10 mL). Volatiles were removed in *vacuo*, the aqueous residue was extracted with ethyl acetate (2 x 25 mL). The combined organic phases were washed with brine (20 mL), dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel chromatography to give the desired compound **3** (0.21 g, 93%) as colorless oil. $[\alpha]_D^{20}$ = -48.5 (*c* 2.23, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.46 (s, 1H), 7.30 – 7.27 (m, 2H), 6.89 – 6.87 (m, 2H), 5.87 – 5.78 (m, 1H), 5.14 – 5.03 (m, 2H), 4.63 (d, *J* = 10.9 Hz, 1H), 4.54 (d, *J* = 10.9 Hz, 1H), 4.24 – 4.19 (m, 2H), 3.80 (s, 3H), 3.72 – 3.68 (m, 1H), 3.66 – 3.60 (m, 2H), 3.34 (s, 3H), 3.31 (s, 3H), 3.30 – 3.26 (m, 1H), 3.12 (dd, *J* = 15.7, 2.9 Hz,

1H), 2.89 (dd, *J* = 15.7, 8.0 Hz, 1H), 2.58 (t, *J* = 6.6 Hz, 2H), 2.11 – 2.05 (m, 1H), 1.83 – 1.76 (m, 1H), 1.58 – 1.55 (m, 2H), 1.24 – 1.18 (m, 1H), 0.95 (s, 3H), 0.94 (s, 3H), 0.91 (s, 9H), 0.89 (d, *J* = 7.0 Hz, 3H), 0.86 (s, 9H), 0.06 (s, 6H), 0.01 (s, 3H), -0.31 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.8, 159.0, 140.9, 134.8, 134.4, 131.7, 128.6, 117.0, 113.7, 82.1, 81.4, 76.4, 75.7, 74.7, 61.6, 56.8, 56.3, 55.2, 44.2, 39.0, 33.7, 32.9, 31.6, 30.3, 26.1, 26.0, 20.9, 20.1, 18.3, 18.3, 15.9, -4.5, -4.6, -5.3, -5.3 ppm; HRMS (ESI) calculated for $C_{41}H_{74}NO_7Si_2$ $[M+H]^+$ 748.5004, found 748.4992.

** The end **