Supporting Information

Stereoselective Synthesis of the Cytotoxic Macrolide FD-891

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General features

NMR spectra were recorded at 500 MHz (^1H NMR) and 125 MHz (^{13}C NMR) in CDCl_3 solution at 25 °C. ^{13}C NMR signal multiplicities were determined with the DEPT pulse sequence. Mass spectra were run in the EI (70 eV) or the FAB (*m*-nitrobenzyl alcohol matrix) mode. IR data, which were measured as films on NaCl plates (oils) or as KBr pellets (solids), are given only when relevant functions ($\text{C}=\text{O}$, OH , etc.) are present. Optical rotations were measured at 25 °C. Reactions which required an inert atmosphere (all except those involving water or hydroxylic solvents in the reaction medium) were carried out under dry N_2 with flame-dried glassware. Commercial reagents were used as received. THF and Et_2O were freshly distilled from sodium-benzophenone ketyl. Dichloromethane was freshly distilled from CaH_2 . Tertiary amines were freshly distilled from KOH. Unless detailed otherwise, "work-up" means pouring the reaction mixture into brine, followed by extraction with the solvent indicated in parenthesis. If the reaction medium was acidic (basic), an additional washing with 5% aq NaHCO_3 (aq NH_4Cl) was performed. New washing with brine, drying over anhydrous MgSO_4 and elimination of the solvent under reduced pressure were followed by chromatography on a silica gel column (60-200 μm) with the indicated solvent. Where solutions were filtered through a Celite pad, the pad was additionally rinsed with the same solvent used, and the washing liquids incorporated to the main organic layer. Column chromatography was performed on silica gel (60-200 μ).

(Scheme and compound numbering corresponds to those of the paper)

Scheme 2

Experimental procedures and physical data

A solution of sultam **7** (3 g, ~11 mmol) in dry CH_2Cl_2 (45 mL) was cooled under N_2 to -5°C and treated with $n\text{Bu}_2\text{BOTf}$ (1M solution in CH_2Cl_2 , 12 mL, 12 mmol, ~1.1 eq). The mixture was then stirred for 5 min at this temperature, treated with N,N -diisopropyl ethylamine (2 mL, 12 mmol, ~1.2 eq), further stirred for 30 min. and cooled to -78°C . A solution of freshly prepared aldehyde **6** (4.5 g, ~14.3 mmol, 1.3 eq) in dry CH_2Cl_2 (15 mL) was then added dropwise. The reaction mixture was stirred at -78°C for 16 h, quenched by addition of a pH 7 buffer solution (35 mL) and stirred at room temperature for 30 min. Work-up (extraction with CH_2Cl_2) and column chromatography on silica gel (hexane-EtOAc, 90:10) afforded aldol **8** as a single diastereoisomer (6.03 g, 94% based on **7**): oil, $[\alpha]_D -51.7$ (c 3.3, CHCl_3); ^1H NMR (500 MHz) δ 7.70-7.65 (m, 4H), 7.45-7.35 (m, 6H), 4.24 (m, 1H), 3.95-3.85 (m, 3H), 3.60 (br s, 1H, OH), 3.52 (d, $J = 13.8$ Hz, 1H), 3.44 (d, $J = 13.8$ Hz, 1H), 3.18 (quintuplet, $J = 7$ Hz, 1H), 2.10-2.05 (m, 2H), 1.95-1.80 (m, 4H), 1.70 (m, 1H), 1.40-1.20 (m, 2H), 1.34 (d, $J = 7$ Hz, 3H), 1.18 (s, 3H), 1.07 (s, 9H), 0.97 (s, 3H); ^{13}C NMR (125 MHz) δ 176.1, 133.3, 133.2, 48.3, 47.7, 19.0 (C), 135.5 (x 2), 135.4 (x 2), 129.6 (x 2), 127.6 (x 4), 70.0, 64.9, 45.2, 44.6 (CH), 62.4, 53.0, 38.3, 36.3, 32.7, 26.4 (CH_2), 26.8 (x 3), 20.7, 19.8, 13.2 (CH_3); IR ν_{max} 3510 (br, OH), 1691 ($\text{C}=\text{O}$) cm^{-1} ; HR EIMS m/z (% rel.

int.) 526.2072 ($M^+ - tBu$, 1), 311 (14), 255 (100), 225 (91), 183 (74). Calcd. for $C_{32}H_{45}NO_5SSi-tBu$, $M = 526.2083$.

Aldol **8** (5.84 g, 10 mmol) was dissolved under N_2 in dry CH_2Cl_2 (50 mL) and treated at room temperature with N,N -diisopropyl ethylamine (10.4 mL, 60 mmol, 6 eq) and MOMCl (3 mL, 40 mmol, 4 eq). The reaction mixture was then stirred at reflux for 4 h. Work-up (extraction with CH_2Cl_2) and column chromatography on silica gel (hexane-EtOAc, 80:20) furnished **9** (5.7 g, 91%): amorphous solid, $[\alpha]_D -78.2$ (c 1, $CHCl_3$); 1H NMR (500 MHz) δ 7.70-7.65 (m, 4H), 7.45-7.35 (m, 6H), 4.66 (s, 2H), 4.02 (td, $J = 7.5$, 4 Hz, 1H), 3.88 (t, $J = 6.2$ Hz, 1H), 3.80 (br t, $J \sim 6.5$ Hz, 2H), 3.49 (d, $J = 13.8$ Hz, 1H), 3.42 (d, $J = 13.8$ Hz, 1H), 3.29 (overlapped quintuplet, 1H), 3.28 (s, 3H), 2.10-2.05 (m, 2H), 2.00-1.85 (m, 5H), 1.40-1.25 (m, 2H), 1.31 (d, $J = 7$ Hz, 3H), 1.16 (s, 3H), 1.07 (s, 9H), 0.96 (s, 3H); ^{13}C NMR (125 MHz) δ 174.0, 133.9, 133.8, 48.1, 47.6, 19.1 (C), 135.5 (x 2), 135.4 (x 2), 129.4 (x 2), 127.5 (x 4), 75.9, 64.9, 44.9, 44.5 (CH), 96.9, 60.6, 53.0, 38.3, 36.4, 32.7, 26.3 (CH_2), 55.8, 26.8 (x 3), 20.7, 19.8, 15.5 (CH_3); IR ν_{max} 1694 ($C=O$) cm^{-1} ; HR EIMS m/z (% rel. int.) 570.2363 ($M^+ - tBu$, 85), 508 (38), 448 (47), 255 (60), 213 (100), 183 (42), 135 (67). Calcd. for $C_{34}H_{49}NO_6SSi-tBu$, $M = 570.2346$.

$LiAlH_4$ (360 mg, 9.5 mmol, ~ 1.1 eq) was suspended under N_2 in dry Et_2O (100 mL) and cooled to 0 $^\circ C$. A solution of **9** (5.4 g, 8.6 mmol) in dry Et_2O (40 mL) was then added dropwise. The reaction mixture was stirred at 0 $^\circ C$ for 2 h and quenched by careful dropwise addition of satd aq NH_4Cl (5 mL), followed by stirring for 15 min. Filtration through Celite was followed by solvent removal under reduced pressure. Column chromatography on silica gel (hexane-EtOAc, 70:30) provided a mixture of alcohol **10** and sultam **7**. This mixture was triturated under pentane and filtered through glass wool to yield **10** (3.36 g, 94%) as an oil and N -depropionyl-**7** (1.48 g, 80% recovery) as a white solid, suitable for further synthetic use.

Alcohol **10**: oil, $[\alpha]_D +17.5$ (c 1.4, $CHCl_3$); 1H NMR (500 MHz) δ 7.70-7.65 (m, 4H), 7.45-7.35 (m, 6H), 4.67 (d, $J = 6.6$ Hz, 1H), 4.61 (d, $J = 6.6$ Hz, 1H), 3.99 (m, 1H), 3.77 (m, 2H), 3.62 (br t, $J \sim 9.5$ Hz, 1H), 3.52 (m, 1H), 3.37 (s, 3H), 2.80 (br s, 1H, OH), 1.95 (m, 1H), 1.80-1.70 (m, 2H), 1.07 (s, 9H), 0.83 (d, $J = 7$ Hz, 3H); ^{13}C NMR (125 MHz) δ 133.7 (x 2), 19.1 (C), 135.5 (x 4), 129.6 (x 2), 127.7 (x 4), 76.8, 38.5 (CH), 96.9, 65.2,

60.6, 34.3 (CH₂), 55.8, 26.8 (x 3), 11.2 (CH₃); IR $\nu_{\max}$ 3450 (br, OH) cm⁻¹; HR FABMS m/z 385.2208 (M⁺-CH₂OH). Calcd. for C₂₄H₃₆O₄Si-CH₂OH, M = 385.2199.

A solution of alcohol **10** (3 g, 7.2 mmol) in dry CH₂Cl₂ (80 mL) was treated under N₂ at room temperature with Et₃N (3 mL, 21.6 mmol, 3 eq), DMAP (12 mg, 0.1 mmol) and TsCl (2.7 g, 14.2 mmol, 2 eq). The reaction mixture was then stirred for 16 h at room temperature and worked up (extraction with CH₂Cl₂). Column chromatography on silica gel (hexane to hexane-EtOAc, 80:20) afforded tosylate **11** (3.57 g, 87%): oil, [α]_D -7.2 (*c* 1.4, CHCl₃); ¹H NMR (500 MHz) δ 7.82 (d, *J* = 8 Hz, 2H), 7.70-7.65 (m, 4H), 7.45-7.35 (m, 6H), 7.32 (d, *J* = 8 Hz, 2H), 4.57 (d, *J* = 6.6 Hz, 1H), 4.51 (d, *J* = 6.6 Hz, 1H), 4.14 (dd, *J* = 9.3, 6.4 Hz, 1H), 3.96 (dd, *J* = 9.3, 7.3 Hz, 1H), 3.84 (br td, *J* = 6.4, 3.3 Hz, 1H), 3.73 (br t, *J* ~ 6 Hz, 2H), 3.26 (s, 3H), 2.44 (s, 3H), 2.10 (m, 1H), 1.70 (m, 2H), 1.08 (s, 9H), 0.92 (d, *J* = 7 Hz, 3H); ¹³C NMR (125 MHz) δ 144.5, 133.6 (x 2), 133.2, 19.0 (C), 135.4 (x 4), 129.7 (x 2), 129.6 (x 2), 127.7 (x 2), 127.6 (x 4), 75.4, 36.5 (CH), 96.6, 72.2, 60.4, 34.3 (CH₂), 55.4, 26.8 (x 3), 21.4, 11.2 (CH₃).

Tosylate **11** (3.42 g, ~6 mmol) and NaCN (882 mg, 18 mmol, 3 eq) were dissolved under N₂ in dry DMSO (60 mL) and stirred at 80 °C for 2 h. Work-up (extraction with Et₂O) and column chromatography on silica gel (hexane-EtOAc, 70:30) afforded nitrile **12** (2.48 g, 97%): dense oil, [α]_D -5.1 (*c* 1.5, CHCl₃); ¹H NMR (500 MHz) δ 7.75-7.70 (m, 4H), 7.50-7.40 (m, 6H), 4.67 (d, *J* = 6.6 Hz, 1H), 4.63 (d, *J* = 6.6 Hz, 1H), 3.85-3.80 (m, 3H), 3.36 (s, 3H), 2.51 (dd, *J* = 16.5, 5.5 Hz, 1H), 2.25 (dd, *J* = 16.5, 8.5 Hz, 1H), 2.19 (m, 1H), 1.75-1.65 (m, 2H), 1.11 (s, 9H), 1.07 (d, *J* = 7 Hz, 3H); ¹³C NMR (125 MHz) δ 133.4 (x 2), 119.1, 19.0 (C), 135.4 (x 4), 129.6 (x 2), 127.6 (x 4), 77.1, 34.2 (CH), 96.5, 60.4, 33.5, 20.4 (CH₂), 55.5, 26.7 (x 3), 14.2 (CH₃); IR $\nu_{\max}$ 2247 (C≡N) cm⁻¹; HR EIMS m/z (% rel. int.) 394.2169 (M⁺-OMe, 2), 368 (21), 336 (20), 306 (35), 246 (71), 213 (100), 200 (46), 183 (43), 91 (59). Calcd. for C₂₅H₃₅NO₃Si-OMe, M = 394.2202. Elemental analysis: C, 70.50; H, 8.41. Calcd. for C₂₅H₃₅NO₃Si: C, 70.55; H, 8.29.

A solution of nitrile **12** (703 mg, ~1.65 mmol) in dry THF (25 mL) was treated under N₂ at –78 °C with DIBAL (1M in hexane, 6.6 mL, 6.6 mmol, 4 eq). The reaction mixture was stirred for 15 min. at –78 °C, then for further 3 h at room temperature and quenched by careful addition of satd aq NH₄Cl (1 mL), followed by stirring for 15 min. Filtration through Celite was followed by solvent removal under reduced pressure. The crude aldehyde **4** (700 mg) was used as such in the later olefination step (page S-14). For analytical purposes, an aliquot was purified by means of column chromatography on silica gel (hexane-EtOAc, 80:20): oil, [α]_D –6.0 (*c* 0.8, CHCl₃); ¹H NMR (500 MHz) δ 9.75 (br s, 1H), 7.70–7.65 (m, 4H), 7.45–7.35 (m, 6H), 4.59 (s, 2H), 3.80–3.70 (m, 3H), 3.30 (s, 3H), 2.59 (dd, *J* = 16.2, 5 Hz, 1H), 2.41 (m, 1H), 2.20 (ddd, *J* = 16.2, 8.5, 2.5 Hz, 1H), 1.70 (m, 1H), 1.60 (m, 1H), 1.06 (s, 9H), 0.92 (d, *J* = 7 Hz, 3H); ¹³C NMR (125 MHz) δ 133.8 (x 2), 19.2 (C), 202.4, 135.6 (x 4), 129.6 (x 2), 127.7 (x 4), 78.0, 31.6 (CH), 96.4, 60.7, 46.6, 33.5 (CH₂), 55.7, 26.9 (x 3), 15.5 (CH₃); IR ν_{max} 1709 (C=O) cm^{–1}; HR FABMS *m/z* 367.2124 (M⁺–OMOM). Calcd. for C₂₅H₃₆O₄Si–OMOM, M = 367.2093.

Scheme 3

Experimental procedures and physical data

A solution of sultam **7** (3 g, 11 mmol) in dry CH_2Cl_2 (45 mL) was cooled under N_2 to $-5\text{ }^{\circ}\text{C}$ and treated with $n\text{Bu}_2\text{BOTf}$ (1M solution in CH_2Cl_2 , 12.1 mL, 12.1 mmol, 1.1 eq). The mixture was then stirred for 5 min at this temperature, treated with N,N -diisopropyl ethylamine (2.1 mL, 12.1 mmol, 1.1 eq), further stirred for 30 min. and cooled to $-78\text{ }^{\circ}\text{C}$. A solution of freshly prepared aldehyde **13** (2.33 g, ~ 14.2 mmol, 1.3 eq) in CH_2Cl_2 (15 mL) was then added dropwise. The reaction mixture was stirred at $-78\text{ }^{\circ}\text{C}$ for 16 h, quenched by addition of a pH

7 buffer solution (30 mL) and stirred at room temperature for 30 min. Work-up (extraction with CH₂Cl₂) and column chromatography on silica gel (hexane-EtOAc, 70:30) afforded aldol **14** as a single diastereoisomer (4.55 g, 95% based on **7**): oil, [α]_D –69 (*c* 1.9, CHCl₃); ¹H NMR (500 MHz) δ 7.35-7.25 (m, 5H), 4.51 (br s, 2H), 4.12 (m, 1H), 3.88 (t, *J* = 6.3 Hz, 1H), 3.70-3.60 (m, 2H), 3.50 (d, *J* = 13.8 Hz, 1H), 3.41 (d, *J* = 13.8 Hz, 1H), 3.40 (br s, 1H, OH), 3.13 (m, 1H), 2.10-2.05 (m, 2H), 1.95-1.80 (m, 3H), 1.80-1.70 (m, 2H), 1.40-1.30 (m, 1H), 1.30 (d, *J* = 7 Hz, 3H), 1.25 (m, 1H), 1.15 (s, 3H), 0.96 (s, 3H); ¹³C NMR (125 MHz) δ 176.3, 138.2, 48.3, 47.7 (C), 128.3 (x 2), 127.6 (x 2), 127.5, 69.8, 64.9, 44.9, 44.6 (CH), 73.1, 68.3, 53.1, 38.3, 33.9, 32.7, 26.4 (CH₂), 20.7, 19.8, 12.9 (CH₃); IR $\nu_{\max}$ 3410 (br, OH), 1692 (C=O) cm⁻¹; HR FABMS *m/z* 436.2160 (M+H⁺). Calcd. for C₂₃H₃₄NO₅S, M = 436.2158.

Aldol **14** (4.35 g, 10 mmol) was dissolved under N₂ in dry CH₂Cl₂ (100 mL) and treated at room temperature with 2,6-lutidine (1.75 mL, 15 mmol, 1.5 eq) and TBSOTf (2.75 mL, 12 mmol, 1.2 eq). The reaction mixture was then stirred at room temperature for 1 h. Work-up (extraction with CH₂Cl₂) and column chromatography on silica gel (hexane-EtOAc, 80:20) yielded **15** (4.84 g, 88%): white solid, mp 85-87 °C (from hexane-EtOAc); [α]_D –67.3 (*c* 2.2, CHCl₃); ¹H NMR (500 MHz) δ 7.35-7.25 (m, 5H), 4.50 (d, *J* = 12 Hz, 1H), 4.46 (d, *J* = 12 Hz, 1H), 4.14 (dt, *J* = 8.3, 5 Hz, 1H), 3.85 (t, *J* = 6.2 Hz, 1H), 3.65-3.55 (m, 2H), 3.49 (d, *J* = 13.8 Hz, 1H), 3.42 (d, *J* = 13.8 Hz, 1H), 3.14 (quintuplet, *J* ~ 7 Hz, 1H), 2.10-2.05 (m, 2H), 1.95-1.85 (m, 5H), 1.40-1.30 (m, 2H), 1.26 (d, *J* = 7 Hz, 3H), 1.15 (s, 3H), 0.97 (s, 3H), 0.88 (s, 9H), 0.06 (s, 6H); ¹³C NMR (125 MHz) δ 174.5, 138.8, 48.3, 47.7, 18.1 (C), 128.2 (x 2), 127.7 (x 2), 127.3, 70.3, 65.1, 46.3, 44.6 (CH), 72.8, 66.4, 53.1, 38.3, 36.0, 32.8, 26.4 (CH₂), 25.9 (x 3), 20.8, 19.8, 16.3, –4.4 (x 2) (CH₃); IR $\nu_{\max}$ 1693 (C=O) cm⁻¹. Elemental analysis: C, 63.50; H, 8.51. Calcd for C₂₉H₄₇NO₅SSi: C, 63.35; H, 8.62.

A solution of compound **15** (4.5 g, 8.2 mmol) in dry CH₂Cl₂ (80 mL) was treated under N₂ at –78 °C with DIBAL (1M in hexane, 16.4 mL, 16.4 mmol, 2 eq). The reaction mixture was stirred for 1 h at –78 °C and quenched by careful addition of satd aq NH₄Cl (4 mL), followed by stirring for 15 min. Filtration through Celite and solvent removal under reduced pressure gave a mixture of the expected aldehyde and sultam **7**. This mixture was triturated under pentane and filtered through glass wool to yield, after solvent removal, the crude oily

aldehyde (~2.5 g, ~7.4 mmol), sufficiently pure for synthetic purposes, and N-depropionyl-**7** (1.41 g, ~80% recovery) as a white solid, suitable for further synthetic use. The crude aldehyde was used as such in the following step.

A solution of sultam *ent*-**7** (2.2 g, 8 mmol) in dry CH₂Cl₂ (35 mL) was cooled under N₂ to –5 °C and treated with *n*Bu₂BOTf (1M solution in CH₂Cl₂, 9 mL, 9 mmol). The mixture was then stirred for 5 min at this temperature, treated with N,N-diisopropyl ethylamine (1.6 mL, 9 mmol), further stirred for 30 min. and cooled to –78 °C. A solution of the crude aldehyde from above in CH₂Cl₂ (10 mL) was then added dropwise. The reaction mixture was stirred at –78 °C for 16 h, quenched by addition of a pH 7 buffer solution (25 mL) and stirred at room temperature for 30 min. Work-up (extraction with CH₂Cl₂) and column chromatography on silica gel (hexane-EtOAc, 85:15) afforded aldol **16** as a single diastereoisomer (3.98 g, 80% overall, based on **15**): white solid, mp 100-102 °C (from hexane-EtOAc); [α]_D +45 (*c* 3.1, CHCl₃); ¹H NMR (500 MHz) δ 7.35-7.25 (m, 5H), 4.50 (d, *J* = 12 Hz, 1H), 4.46 (d, *J* = 12 Hz, 1H), 4.28 (td, *J* = 6.8, 1.5 Hz, 1H), 3.90 (dt, *J* = 9.3, 2.5 Hz, 1H), 3.86 (t, *J* = 6.2 Hz, 1H), 3.80 (d, *J* = 2 Hz, 1H, OH), 3.55-3.45 (m, 3H), 3.41 (d, *J* = 13.8 Hz, 1H), 3.21 (qd, *J* = 7, 2.5 Hz, 1H), 2.10-2.05 (m, 2H), 1.95-1.85 (m, 5H), 1.62 (m, 1H), 1.40-1.30 (m, 2H), 1.23 (d, *J* = 7 Hz, 3H), 1.15 (s, 3H), 0.97 (s, 3H), 0.88 (s, 9H), 0.83 (d, *J* = 7 Hz, 3H), 0.09 (s, 3H), 0.07 (s, 3H); ¹³C NMR (125 MHz) δ 176.9, 138.6, 48.3, 47.7, 18.0 (C), 128.2 (x 2), 127.5 (x 2), 127.3, 71.5, 69.8, 64.9, 44.5, 41.5, 39.5 (CH), 72.8, 67.3, 53.0, 38.3, 34.6, 32.7, 26.4 (CH₂), 25.9 (x 3), 20.7, 19.8, 11.3, 10.0, –4.6, –4.7 (CH₃); IR $\nu_{\max}$ 3510 (br, OH), 1673 (C=O) cm^{–1}; HR EIMS *m/z* (% rel. int.) 550.2684 (M⁺–*t*Bu, 3), 532 (4), 300 (6), 91 (100). Calcd. for C₃₂H₅₃NO₆SSi–*t*Bu, M = 550.2653. Elemental analysis: C, 63.39; H, 8.60. Calcd for C₃₂H₅₃NO₆SSi: C, 63.22; H, 8.79.

Aldol **16** (3.40 g, 5.6 mmol) was dissolved under N₂ in dry CH₂Cl₂ (60 mL) and treated at room temperature with 2,6-lutidine (980 μ L, 8.4 mmol, 1.5 eq) and TBSOTf (1.6 mL, 7 mmol, 1.25 eq). The reaction mixture was then stirred at reflux for 1 h. Work-up (extraction with CH₂Cl₂) and column chromatography on silica gel (hexane-EtOAc, 80:20) yielded **17** (~4 g) partially contaminated with by-products. An aliquot was carefully purified for analytical purposes: oil, [α]_D +42.3 (*c* 3.2, CHCl₃); ¹H NMR (500 MHz) δ 7.35-7.25 (m, 5H), 4.51 (br s, 2H), 4.29 (t, *J* = 4.4 Hz, 1H), 3.81 (br t, *J* ~ 6.2 Hz, 1H), 3.68 (dt, *J* = 8.8, 4.5 Hz, 1H), 3.59 (br t, *J* ~ 7.5 Hz, 2H), 3.48 (d, *J* = 13.8 Hz, 1H), 3.40 (d, *J* = 13.8 Hz, 1H), 3.20 (qd, *J* = 7, 4.5 Hz, 1H), 2.10-2.05 (m, 2H), 1.95-1.80 (m, 5H), 1.75 (m, 1H), 1.40-1.30 (m, 2H), 1.24 (d, *J* = 7 Hz, 3H), 1.15 (s, 3H), 0.97 (s, 3H), 0.96 (d, *J* = 7 Hz, 3H), 0.90 (s, 9H), 0.88 (s, 9H), 0.10 (s, 3H), 0.09 (s, 3H), 0.08 (s, 3H), 0.06 (s, 3H); ¹³C NMR (125 MHz) δ 175.3, 138.8, 48.3, 47.7, 18.3, 18.2 (C), 128.3 (x 2), 127.6 (x 2), 127.3, 70.8, 70.7, 65.1, 45.8, 44.6, 42.1 (CH), 72.8, 66.6, 53.1, 38.3, 34.9, 32.8, 26.4 (CH₂), 26.0 (x 6), 20.7, 19.8, 15.8, 11.3, –4.2, –4.3, –4.4 (x 2) (CH₃); IR $\nu_{\max}$ 1696 (C=O) cm^{–1}; HR EIMS *m/z* (% rel. int.) 706.3949 (M⁺–Me, 3), 664 (99), 414 (29), 328 (32), 91 (100). Calcd. for C₃₈H₆₇NO₆SSi₂–Me, M = 706.3993.

Compound **17** from above (4 g) was dissolved in 3:1 THF/H₂O (60 mL), cooled to 0 °C and treated with 30% H₂O₂ (7.5 mL, ~66 mmol) and LiOH monohydrate (925 mg, 22 mmol). The mixture was then stirred at room temperature for 36 h. After this, an 1.6M aqueous solution of Na₂S₂O₃ (50 mL) was added, followed by stirring for 15 min. Most of the THF was then removed by evaporation under reduced pressure, and the remaining aqueous layer was extracted three times with CH₂Cl₂. The organic layer was then dried over anhyd. MgSO₄, and evaporated under reduced pressure to yield a mixture of crude **18** and *ent*-**7**. This mixture was triturated under hexane and filtered through glass wool to yield, after solvent removal, the crude oily acid (~2.5 g) and N-depropionyl-*ent*-**7** (725 mg, ~60% recovery) as a white solid, suitable for further synthetic use. The crude acid was used as such in the following step. An aliquot was carefully purified for analytical purposes: oil, $[\alpha]_D +5.8$ (*c* 1.2, CHCl₃); ¹H NMR (500 MHz) δ 7.35-7.25 (m, 5H), 4.50 (d, *J* = 12 Hz, 1H), 4.48 (d, *J* = 12 Hz, 1H), 4.29 (dd, *J* = 6.6, 2.4 Hz, 1H), 3.96 (m, 1H), 3.50 (m, 2H), 2.69 (qd, *J* = 7, 2.5 Hz, 1H), 1.95-1.85 (m, 2H), 1.70 (m, 1H), 1.15 (d, *J* = 7 Hz, 3H), 0.90 (d, 3H, overlapped), 0.89 (s, 9H), 0.87 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H), 0.01 (s, 3H) (COOH proton not detected); ¹³C NMR (125 MHz) δ 181.3, 138.5, 18.3 (x 2) (C), 128.3 (x 2), 127.6 (x 2), 127.5, 73.9, 70.6, 43.8, 42.4 (CH), 73.1, 67.0, 35.8 (CH₂), 26.0 (x 6), 10.4, 10.1, -3.6, -4.0, -4.1, -4.2 (CH₃); IR $\nu_{\max}$ 3500-3200 (br, OH), 1704 (C=O) cm⁻¹; HR FABMS *m/z* 525.3391 (M+H⁺). Calcd. for C₂₈H₅₃O₅Si₂, M = 525.3432.

Crude acid **18** from above (2.5 g) was dissolved under N₂ in dry CH₂Cl₂ (100 mL), cooled to 0 °C and treated with 1,1'-carbonyldiimidazole (1 g, ~6.5 mmol). After stirring the reaction mixture for 30 min. at 0 °C, *N,O*-dimethylhydroxylamine chlorhydrate (1.32 g, 13.5 mmol) was added, and the stirring was continued for 16 h at room temperature. Work-up (extraction with CH₂Cl₂) and column chromatography on silica gel (hexane-EtOAc, 80:20) furnished Weinreb amide **19** (2.07 g, 65% overall yield from **16**): oil, $[\alpha]_D +14.3$ (*c* 2.2, CHCl₃); ¹H NMR (500 MHz) δ 7.35-7.25 (m, 5H), 4.49 (s, 2H), 4.10 (t, *J* = 5.3 Hz, 1H), 3.67 (overlapped m, 1H), 3.66 (s, 3H), 3.52 (br t, *J* = 7 Hz, 2H), 3.14 (s, 3H), 3.00 (m, 1H), 1.90 (m, 2H), 1.70 (m, 1H), 1.11 (d, *J* = 7 Hz, 3H), 0.93 (d, *J* = 7 Hz, 3H), 0.89 (s, 9H), 0.87 (s, 9H), 0.05 (s, 9H), 0.04 (s, 3H); ¹³C NMR (125 MHz) δ 176.5 (br), 138.5, 18.2, 18.1 (C), 128.2 (x 2), 127.6 (x 2), 127.4, 73.3, 70.6, 44.8, 38.0 (CH), 72.9, 66.7, 35.2 (CH₂), 61.0,

32.3 (br), 26.0 (x 6), 13.6, 11.5, -3.9, -4.0 (x 2), -4.5 (CH₃); IR $\nu_{\max}$ 1735 (C=O) cm⁻¹; HR FABMS m/z 568.3830 (M+H⁺). Calcd. for C₃₀H₅₈NO₅Si₂, M = 568.3854.

A solution of Weinreb amide **19** (2 g, ~3.5 mmol) in dry THF (35 mL) was cooled under N₂ at -20 °C and treated dropwise with MeMgBr (3M en Et₂O, 4.2 mL, 12.6 mmol, 3.6 eq). The reaction mixture was then stirred at -20 °C for 15 min., then for 1 h at 0 °C and worked up (extraction with CH₂Cl₂). Column chromatography on silica gel (hexane-EtOAc, 85:15) afforded ketone **20** (1.43 g, 78%): oil, [α]_D +18.3 (*c* 1.5, CHCl₃); ¹H NMR (500 MHz) δ 7.35-7.25 (m, 5H), 4.50 (d, *J* = 12 Hz, 1H), 4.48 (d, *J* = 12 Hz, 1H), 4.26 (dd, *J* = 6.5, 2.5 Hz, 1H), 3.91 (distorted q, *J* ~ 5 Hz, 1H), 3.50 (m, 2H), 2.62 (qd, *J* = 7, 2.5 Hz, 1H), 2.15 (s, 3H), 1.87 (q, *J* ~ 6.5 Hz, 2H), 1.68 (m, 1H), 1.10 (d, *J* = 7 Hz, 3H), 0.89 (s, 9H), 0.88 (d, 3H, overlapped), 0.86 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H), 0.05 (s, 3H), 0.02 (s, 3H); ¹³C NMR (125 MHz) δ 210.8, 138.5, 18.3, 18.2 (C), 128.4 (x 2), 127.7 (x 2), 127.5, 72.8, 70.7, 50.2, 44.0 (CH), 73.1, 67.0, 35.8 (CH₂), 28.7, 26.0 (x 6), 10.8, 10.5, -3.6, -4.0, -4.1 (x 2) (CH₃); IR $\nu_{\max}$ 1714 (C=O) cm⁻¹; HR EIMS m/z (% rel. int.) 465.2795 (M⁺-*t*Bu, 1), 319 (14), 279 (41), 173 (66), 131 (32), 91 (100). Calcd. for C₂₉H₅₄O₄Si₂-*t*Bu, 465.2856.

Ketone **20** (1.41 g, 2.7 mmol) was dissolved under N₂ at -78 °C in dry CH₂Cl₂ (25 mL) and treated with Me₂AlCl (1M in hexane, 10.8 mL, 10.8 mmol, 4 eq). The reaction mixture was stirred for 5 min. at -78 °C, then cooled to -90 °C and treated dropwise with *n*Bu₃SnH (1.1 mL, 4.1 mmol, ~1.5 eq). After stirring for 1 h at -90 °C, the cooling bath was removed, satd aq NaHCO₃ (10 mL) was added and the mixture was further stirred at room temperature for 30 min. Work-up (extraction with CH₂Cl₂) provided a 92:8 mixture of diastereoisomeric alcohols (1.29 g, 91%), which was carefully purified by means of flash column chromatography on silica gel (hexane-EtOAc, 95:5) to yield pure **21** (1.16 g): oil, [α]_D -7.1 (*c* 1.1, CHCl₃); ¹H NMR (500 MHz) δ 7.35-7.25 (m, 5H), 4.50 (d, *J* = 12 Hz, 1H), 4.49 (d, *J* = 12 Hz, 1H), 3.95 (dd, *J* = 5.5, 1.5 Hz, 1H), 3.82 (m, 2H), 3.53 (t, *J* = 7 Hz, 2H), 2.20 (br s, 1H, OH), 1.95-1.80 (m, 3H), 1.62 (m, 1H), 1.16 (d, *J* = 6.5 Hz, 3H), 0.97 (d, *J* = 7 Hz, 3H), 0.95 (d, *J* = 7 Hz, 3H), 0.92 (s, 9H), 0.90 (s, 9H), 0.08 (br s, 12H); ¹³C NMR (125 MHz) δ 138.4, 18.3, 18.2 (C), 128.4 (x 2), 127.7 (x 2), 127.5, 76.4, 71.7, 71.3, 44.1, 41.5 (CH), 73.1, 66.7, 35.5 (CH₂), 26.0 (x 3), 25.9 (x 3), 21.0, 10.9, 8.6, -3.4, -3.8, -4.0, -4.5 (CH₃); IR $\nu_{\max}$ 3460 (br, OH) cm⁻¹; HR FABMS m/z 525.3780 (M+H⁺). Calcd. for C₂₉H₅₇O₄Si₂, 525.3795.

A solution of alcohol **21** (1.05 g, 2 mmol) in dry CHCl_3 (90 mL) was treated under N_2 at room temperature with proton sponge[®] (8.6 g, 40 mmol, 20 eq) and MeOTf (2.25 mL, 20 mmol, 10 eq). The reaction mixture was then stirred at reflux for 16 h and quenched by addition of satd aq ammonia (6 mL), followed by stirring for further 30 min. at room temperature. Work-up (extraction with CH_2Cl_2) and column chromatography on silica gel (hexane-EtOAc, 95:5) gave **22** (916 mg, 85%): oil, $[\alpha]_{\text{D}} +3.9$ (c 1.4, CHCl_3); ^1H NMR (500 MHz) δ 7.35-7.25 (m, 5H), 4.50 (d, $J = 12$ Hz, 1H), 4.48 (d, $J = 12$ Hz, 1H), 3.85-3.80 (m, 2H), 3.52 (t, $J = 7$ Hz, 2H), 3.29 (s, 3H), 3.17 (quintuplet, $J \sim 6$ Hz, 1H), 1.90 (m, 2H), 1.70 (sext, $J \sim 7$ Hz, 1H), 1.65 (m, 1H), 1.12 (d, $J = 7$ Hz, 3H), 0.93 (d, $J = 7$ Hz, 3H), 0.89 (s, 9H), 0.88 (s, 9H), 0.86 (d, $J = 7$ Hz, 3H), 0.07 (s, 3H), 0.06 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (125 MHz) δ 138.6, 18.5, 18.3 (C), 128.4 (x 2), 127.7 (x 2), 127.5, 79.7, 73.0, 70.9, 44.4, 41.4 (CH), 73.1, 66.9, 35.5 (CH_2), 56.4, 26.1 (x 3), 26.0 (x 3), 16.5, 11.2, 10.5, -3.4, -3.7, -3.9, -4.0 (CH_3); HR FABMS m/z 481.3159 ($\text{M}^+ - t\text{Bu}$). Calcd. for $\text{C}_{30}\text{H}_{58}\text{O}_4\text{Si}_2 - t\text{Bu}$, $M = 481.3169$.

Degussa-type 20% palladium hydroxide on carbon (150 mg) was suspended in EtOH (20 mL) and stirred at room temperature under H_2 for 10 min. A solution of compound **22** (835 mg, ~ 1.55 mmol) in EtOH (20 mL) was then added via syringe. The reaction mixture was stirred at room temperature and ambient pressure until consumption of the starting material (ca. 3 h, TLC monitoring). Filtration through Celite was followed by solvent removal under reduced pressure and column chromatography on silica gel (hexane-EtOAc, 90:10) to yield primary alcohol **23** (681 mg, 98%): oil, $[\alpha]_{\text{D}} -2.3$ (c 1.2, CHCl_3); ^1H NMR (500 MHz) δ 3.90-3.80 (m, 3H), 3.72 (m, 1H), 3.29 (s, 3H), 3.17 (quintuplet, $J \sim 6$ Hz, 1H), 2.40 (br s, 1H, OH), 1.95-1.80 (m, 3H), 1.67 (m, 1H), 1.10 (d, $J = 7$ Hz, 3H), 0.93 (d, $J = 7$ Hz, 3H), 0.92 (d, $J = 7$ Hz, 3H), 0.90 (s, 9H), 0.89 (s, 9H), 0.10 (s, 3H), 0.09 (s, 3H), 0.08 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (125 MHz) δ 18.5, 18.2 (C), 80.1, 72.5, 71.9, 44.2, 40.6 (CH), 59.8, 36.9 (CH_2), 56.3, 26.1 (x 3), 26.0 (x 3), 15.9, 11.7, 11.2, -3.3, -3.8, -4.1, -4.2 (CH_3); IR ν_{max} 3460 (br, OH) cm^{-1} ; HR EIMS m/z (% rel. int.) 391.2696 ($\text{M}^+ - t\text{Bu}$, 1), 231 (24), 229 (14), 189 (19), 131 (38), 89 (31), 75 (27), 73 (40). Calcd. for $\text{C}_{23}\text{H}_{52}\text{O}_4\text{Si}_2 - t\text{Bu}$, 391.2700.

A solution of alcohol **23** (675 mg, ~1.5 mmol) and 1-phenyl-1*H*-tetrazole-5-thiol (535 mg, 3 mmol, 2 eq) in dry THF (30 mL) was cooled to 0 °C under N₂ and treated sequentially with *n*Bu₃P (935 μL, ~3.75 mmol, 2.5 eq) and DIAD (740 μL, ~3.75 mmol, 2.5 eq). After stirring for 90 min. at 0 °C, the reaction was quenched by addition of H₂O (1 mL) and then stirred vigorously for 2 min. Work-up (extraction with EtOAc) and column chromatography on silica gel (hexane-EtOAc, 95:5 to 90:10) provided the intermediate sulfide **i** (835 mg, 91%) as a colourless oil: [α]_D +1.6 (*c* 1.4, CHCl₃); ¹H NMR (500 MHz) δ 7.60-7.50 (m, 5H), 3.88 (dd, *J* = 5.5, 2 Hz, 1H), 3.80 (distorted q, *J* ~ 5.5 Hz, 1H), 3.50-3.40 (m, 2H), 3.27 (s, 3H), 3.16 (quintuplet, *J* ~ 6.5 Hz, 1H), 2.19 (m, 1H), 2.00 (m, 1H), 1.80 (distorted sext, *J* ~ 6 Hz, 1H), 1.63 (quint d, *J* = 6.5, 2 Hz, 1H), 1.11 (d, *J* = 6.5 Hz, 3H), 0.93 (d, *J* = 7 Hz, 3H), 0.92 (d, *J* = 7 Hz, 3H), 0.89 (s, 9H), 0.88 (s, 9H), 0.09 (s, 6H), 0.08 (s, 6H); ¹³C NMR (125 MHz) δ 154.3, 133.9, 18.5, 18.3 (C), 130.0, 129.7 (x 2), 123.8 (x 2), 79.7, 72.5, 72.2, 44.0, 41.4 (CH), 34.8, 28.8 (CH₂), 56.4, 26.1 (x 3), 26.0 (x 3), 16.3, 11.7, 10.8, -3.3, -3.8, -4.1 (x 2) (CH₃); HR EIMS *m/z* (% rel. int.) 551.2907 (M⁺-*t*Bu, 19), 445 (16), 349 (40), 171 (100). Calcd. for C₃₀H₅₆N₄O₃SSi₂-*t*Bu, 551.2907.

A solution of the sulfide from above (835 mg, 1.37 mmol) in EtOH (40 mL) was treated at 0 °C with Mo₇O₂₄(NH₄)₆·4H₂O (495 mg, ~0.4 mmol, ~0.3 eq) and 30% aq H₂O₂ (1.55 mL, 13.7 mmol, 10 eq). After stirring at room temperature for 16 h, the reaction mixture was poured into a saturated aqueous solution of sodium tiosulphate, stirred for 5 min. and extracted with EtOAc. The combined organic phases were washed with brine, dried over MgSO₄ and filtered. Solvent removal in vacuo and column chromatography of the residue on silica gel (hexane-EtOAc, 7:3) afforded sulphone **5** (755 mg, 86%) as a dense oil, which solidifies in the freezer: [α]_D +5.7 (*c* 1.5, CHCl₃); ¹H NMR (500 MHz) δ 7.75-7.60 (m, 5H), 3.90-3.80 (m, 4H), 3.26 (s, 3H), 3.16 (quintuplet, *J* ~ 6 Hz, 1H), 2.35 (m, 1H), 2.18 (m, 1H), 1.75 (m, 1H), 1.65 (m, 1H), 1.12 (d, *J* = 6.5 Hz, 3H), 0.94 (d, *J* = 7 Hz, 3H), 0.91 (d, *J* = 7 Hz, 3H), 0.90 (s, 9H), 0.89 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H), 0.09 (s, 3H), 0.08 (s, 3H); ¹³C NMR (125 MHz) δ 153.6, 133.2, 18.4, 18.2 (C), 131.4, 129.7 (x 2), 125.1 (x 2), 79.7, 72.1, 71.2, 44.0, 41.2 (CH), 52.0, 27.2 (CH₂), 56.3, 26.1 (x 3), 26.0 (x 3), 15.7, 12.6, 11.4, -3.3, -4.0, -4.3 (x 2) (CH₃); HR EIMS *m/z* (% rel. int.) 583.2786 (M⁺-*t*Bu, 3), 381 (50), 171 (100). Calcd. for C₃₀H₅₆N₄O₅SSi₂-*t*Bu, 583.2805. Elemental analysis: C, 56.33; H, 8.98. Calcd for C₃₀H₅₆N₄O₅SSi₂: C, 56.21; H, 8.81.

Scheme 4

Experimental procedures and physical data

A solution of NaHMDS (1M in THF, 2.2 mL, 2.2 mmol, 2 eq) was added at -78°C under N_2 to a mixture of sulphone **5** (705 mg, 1.1 mmol) and aldehyde **4** (crude, as obtained from DIBAL reduction of **12**, 700 mg, ~ 1.65 mmol, 1.5 eq) in DME-HMPA (9:1, 16 mL). The resulting mixture was stirred for 2 h at the same temperature, and then worked up (extraction with CH_2Cl_2). Column chromatography of the residue on silica gel (hexanes-EtOAc, 85:15) gave rise to olefin **24** (660 mg, 75% based on recovered **5**), as a single isomer ($> 95\%$ *E*), as well as 35 mg (5%) of unreacted **5**: oil, $[\alpha]_{\text{D}} -4.2$ (c 0.8, CHCl_3); ^1H NMR (500 MHz) δ 7.70-7.65 (m, 4H), 7.45-7.35 (m, 6H), 5.45 (m, 2H), 4.63 (d, $J = 6.8$ Hz, 1H), 4.61 (d, $J = 6.8$ Hz, 1H), 3.83 (br d, $J = 5.9$ Hz, 1H), 3.76 (m, 3H), 3.68 (br quintuplet, $J = 4.0$ Hz, 1H), 3.32 (s, 3H), 3.31 (s, 3H), 3.15 (br quintuplet, $J = 6.4$ Hz, 1H), 2.35-2.20 (m, 3H), 1.85-1.60 (m, 6H), 1.14 (d, $J = 6.0$ Hz, 3H), 1.07 (s, 9H), 0.95 (d, $J = 6.8$ Hz, 3H), 0.91 (s, 18H), 0.88 (d, $J = 6.2$ Hz, 3H), 0.87 (d, $J = 6.2$ Hz, 3H), 0.09 (s, 3H), 0.08 (s, 6H), 0.06 (s, 3H); ^{13}C NMR (125 MHz) δ 134.0 (x 2), 19.2, 18.5, 18.3 (C), 135.6 (x 4), 131.5, 129.6 (x 2), 127.6 (x 5), 79.9, 78.6, 72.8, 72.7, 43.1, 41.3, 37.0 (CH), 96.5, 60.9, 38.9, 35.6, 34.1 (CH_2), 56.4, 55.5, 26.9 (x 3), 26.1 (x 3), 26.0 (x 3), 16.5, 14.7, 10.6, 10.5, -3.2 , -3.4 , -4.0 , -4.1 (CH_3); HR EIMS m/z (% rel. int.) 785.5017 ($\text{M}^+ - t\text{Bu}$, 1), 317 (14), 271 (42), 232 (18), 231 (100), 213 (17), 199 (9), 89 (10), 73 (18). Calcd. for $\text{C}_{48}\text{H}_{86}\text{O}_6\text{Si}_3 - t\text{Bu}$, $M = 785.5028$. Elemental analysis: C, 68.50; H, 10.39. Calcd for $\text{C}_{48}\text{H}_{86}\text{O}_6\text{Si}_3$: C, 68.35; H, 10.28.

A solution of olefin **24** (655 mg, 0.77 mmol) in 10% NaOH/MeOH (30 mL) was stirred at reflux for 4 h. Work-up (extraction with CH₂Cl₂) and column chromatography of the residue on silicagel (hexanes-EtOAc, 7:3) afforded alcohol **25** (418 mg, 89%): oil, $[\alpha]_D -25.8$ (*c* 0.7, CHCl₃); ¹H NMR (500 MHz) δ 5.44 (m, 2H), 4.70 (d, *J* = 6.8 Hz, 1H), 4.66 (d, *J* = 6.8 Hz, 1H), 3.85-3.70 (m, 4H), 3.65 (br quintuplet, *J* = 4.4 Hz, 1H), 3.42 (s, 3H), 3.31 (s, 3H), 3.14 (quintuplet, *J* = 6.4 Hz, 1H), 2.40 (br s, 1H, OH), 2.35-2.20 (m, 3H), 1.85-1.60 (m, 6H), 1.13 (d, *J* = 6.0 Hz, 3H), 0.93 (d, *J* = 6.8 Hz, 3H), 0.90 (s, 18H), 0.88 (overlapped d, 3H), 0.85 (d, *J* = 7.0 Hz, 3H), 0.07 (s, 9H), 0.05 (s, 3H); ¹³C NMR (125 MHz) δ 18.5, 18.3 (C), 131.1, 127.9, 80.3, 79.9, 72.8, 72.7, 43.1, 41.2, 37.2 (CH), 96.9, 60.1, 38.8, 35.3, 33.5 (CH₂), 56.4, 55.9, 26.1 (x 3), 26.0 (x 3), 16.4, 15.0, 10.6, 10.5, -3.3, -3.4, -4.0, -4.1 (CH₃); IR $\nu_{\max}$ 3440 (br, OH) cm⁻¹; HR FABMS *m/z* 605.4640 (M+H⁺). Calcd. for C₃₂H₆₉O₆Si₂, M = 605.4633. Elemental analysis: C, 63.60; H, 11.47. Calcd for C₃₂H₆₈O₆Si₂: C, 63.52; H, 11.33.

A solution of alcohol **25** (411 mg, 0.68 mmol) and 1-phenyl-1*H*-tetrazole-5-thiol (303 mg, 1.7 mmol, 2.5 eq) in dry THF (10 mL) was cooled to 0 °C under N₂ and treated sequentially with Ph₃P (446 mg, 1.7 mmol, 2.5 eq) and DIAD (335 μ L, 1.7 mmol, 2.5 eq). After stirring for 1 h at room temperature, the reaction was quenched by addition of H₂O (1 mL) and then stirred vigorously for 2 min. Work-up (extraction with CH₂Cl₂) and column chromatography on silica gel (hexanes-EtOAc, 85:15) provided the intermediate sulfide **ii** (484 mg, 93%) as a colourless oil: $[\alpha]_D -9.4$ (*c* 1.1, CHCl₃); ¹H NMR (500 MHz) δ 7.60-7.50 (m, 5H), 5.43 (m, 2H), 4.66 (d, *J* = 7.0 Hz, 1H), 4.64 (d, *J* = 7.0 Hz, 1H), 3.80 (d, *J* = 5.9 Hz, 1H), 3.74 (br q, *J* = 5.7 Hz, 1H), 3.60-3.50 (m, 2H), 3.44 (m, 1H), 3.39 (s, 3H), 3.30 (s, 3H), 3.13 (quintuplet, *J* = 6.4 Hz, 1H), 2.30-2.20 (m, 3H), 2.00 (m, 2H), 1.85-1.60 (m, 4H), 1.12 (d, *J* = 6.2 Hz, 3H), 0.92 (d, *J* = 7.0 Hz, 3H), 0.89 (s, 21H, overlapping a methyl doublet), 0.84 (d, *J* = 7.0 Hz, 3H), 0.06 (s, 9H), 0.04 (s, 3H); ¹³C NMR (125 MHz) δ 154.3, 133.8, 18.5, 18.2 (C), 130.9, 130.0, 129.7 (x 2), 128.0, 123.8 (x 2), 80.6, 79.8, 72.7, 72.6, 43.1, 41.2, 36.8 (CH), 96.6, 38.8, 35.3, 30.8, 30.2 (CH₂), 56.4, 55.8, 26.1 (x 3), 26.0 (x 3), 16.4, 14.8, 10.6, 10.5, -3.3, -3.4, -4.0, -4.1 (CH₃); HR EIMS *m/z* (% rel. int.) 707.4053 (M⁺-*t*Bu, 3), 476 (13), 473 (10), 341 (10), 317 (11), 271 (26), 232 (14), 231 (78), 89 (14), 73 (26). Calcd. for C₃₉H₇₂N₄O₅Si₂S-*t*Bu, M = 707.4058.

A solution of the sulfide from above (484 mg, ~0.63 mmol) in EtOH (20 mL) was treated at 0 °C with Mo₇O₂₄(NH₄)₆·4H₂O (200 mg, ~0.16 mmol, ~0.25 eq) and 30% aq H₂O₂ (725 μ L, 6.4 mmol, ~10 eq). After

stirring overnight for 16 h, the reaction was poured into a saturated aqueous solution of sodium tiosulphate, stirred for 5 min. and extracted with EtOAc. The organic phase was washed with brine, dried over MgSO₄ and filtered. Solvent removal in vacuo and column chromatography of the residue on silica gel (hexanes-EtOAc, 7:3) furnished sulphone **3** (479 mg, 95%) as a colourless oil: $[\alpha]_D -8.4$ (*c* 1.6, CHCl₃); ¹H NMR (500 MHz) δ 7.70 (m, 2H), 7.65-7.60 (m, 3H), 5.44 (m, 2H), 4.65 (m, 2H), 3.94 (ddd, *J* = 14.8, 10.3, 5.7 Hz, 1H), 3.85-3.77 (m, 2H), 3.75 (br q, *J* = 5.5 Hz, 1H), 3.57 (m, 1H), 3.40 (s, 3H), 3.31 (s, 3H), 3.14 (quintuplet, *J* = 6.6 Hz, 1H), 2.30-2.20 (m, 3H), 2.20-2.05 (m, 2H), 1.85-1.65 (m, 3H), 1.64 (qt, *J* = 7.0, 1.7 Hz, 1H), 1.13 (d, *J* = 6.2 Hz, 3H), 0.93 (d, *J* = 7.0 Hz, 3H), 0.92 (d, *J* = 6.6 Hz, 3H), 0.89 (s, 18H), 0.85 (d, *J* = 7.0 Hz, 3H), 0.07 (s, 3H), 0.06 (s, 6H), 0.05 (s, 3H); ¹³C NMR (125 MHz) δ 153.5, 133.1, 18.5, 18.2 (C), 131.4, 130.4, 129.7 (x 2), 128.5, 125.1 (x 2), 80.1, 79.8, 72.7, 72.6, 43.2, 41.2, 37.1 (CH), 96.8, 53.4, 38.8, 35.2, 24.1 (CH₂), 56.4, 55.9, 26.1 (x 3), 26.0 (x 3), 16.4, 14.9, 10.7, 10.5, -3.2, -3.4, -4.0, -4.1 (CH₃); HR EIMS *m/z* (% rel. int.) 739.3972 (M⁺-*t*Bu, 1), 505 (10), 271 (24), 232 (15), 231 (80). Calcd. for C₃₉H₇₂N₄O₇SSi₂-*t*Bu, M = 739.3956. Elemental analysis: C, 58.61; H, 9.17. Calcd for C₃₉H₇₂N₄O₇SSi₂: C, 58.75; H, 9.10.

Scheme 5

Experimental procedures and physical data

A solution of olefin **iii**¹ (830 mg, 1.5 mmol) in *tert*-BuOH (15 mL) was added dropwise to an ice-cooled solution of AD-mix-β² (2.1 g) in H₂O (15 mL). The reaction mixture was stirred at 0 °C for 24 h, quenched by

addition of solid Na_2SO_3 (2.3 g) and further stirred at room temperature for 45 min. Work-up (extraction with EtOAc) and column chromatography on silicagel (hexane-EtOAc 70:30 to 50:50) provided an intermediate 1,2-diol (545 mg, 62%, as a mixture of diastereomers) which was used for the next reaction. In addition, 192 mg of unreacted olefin **iii** were recovered. Yield of diol was thus 81%, based on consumed starting product. **Note of caution: more extended reaction times give rise to yield decrease, due to attack to the other olefinic bonds. Dihydroxylation with the standard OsO_4/NMO procedure proceeds nonselectively and gives low yields.**³

The diol from above (530 mg, ~ 0.9 mmol) was dissolved in CH_2Cl_2 (20 mL) and added to a suspension of NaIO_4 supported on silica gel⁴ (1.8 g) in CH_2Cl_2 (20 mL). The reaction mixture was stirred at room temperature until consumption of the starting material (ca. 30 min, TLC monitoring; if necessary, more oxidizing reagent may be added). After filtration and solvent removal under reduced pressure, crude aldehyde **2** (~ 500 mg) was obtained with sufficient purity for the next olefination step: ^1H NMR (500 MHz) δ 9.77 (t, $J = 1.5$ Hz, 1H), 7.08 (s, 1H), 5.52 (d, $J = 9$ Hz, 1H), 4.20 (q, $J = 7$ Hz, 2H), 4.02 (distorted q, $J \sim 5$ Hz, 1H), 3.62 (t, $J = 4$ Hz, 1H), 3.01 (dd, $J = 6, 2$ Hz, 1H), 2.90 (dd, $J = 3, 2$ Hz, 1H), 2.70-2.60 (m, 2H), 2.53 (m, 1H), 1.98 (s, 3H), 1.85 (s, 3H), 1.29 (t, $J = 7$ Hz, 3H), 1.04 (d, $J = 7$ Hz, 3H), 0.88 (s, 9H), 0.87 (s, 9H), 0.12 (s, 3H), 0.07 (s, 3H), 0.04 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (125 MHz) δ 168.9, 132.1, 126.0, 18.2, 18.0 (C), 200.1, 142.4, 137.7, 73.3, 68.8, 58.0, 57.2, 37.6 (CH), 60.6, 48.3 (CH_2), 25.9 (x 3), 25.8 (x 3), 16.6, 15.6, 14.3, 14.0, -4.2 , -4.5 , -4.9 , -5.2 (CH_3).

¹ Murga, J.; García-Fortanet, J.; Carda, M.; Marco, J. A. *Synlett* **2004**, 2830-2832.

² Sharpless, K. B.; Amberg, W.; Bennani, Y. L.; Crispino, G. A.; Hartung, J.; Jeong, K.-S.; Kwong, H.-L.; Morikawa, K.; Wang, Z.-M.; Xu, D.; Zhang, X.-L. *J. Org. Chem.* **1992**, 57, 2768-2771.

³ Andrus, M. B.; Lepore, S. D.; Sclafani, J. A. *Tetrahedron Lett.* **1997**, 38, 4043-4046.

⁴ Zhong, Y.-L.; Shing, T. K. M. *J. Org. Chem.* **1997**, 62, 2622-2624.

A solution of NaHMDS (1M in THF, 960 μL , 0.96 mmol, 1.6 eq) was added at -78 $^\circ\text{C}$ under N_2 to a mixture of sulphone **3** (478 mg, 0.6 mmol) and aldehyde **2** (crude, 500 mg, ~ 0.9 mmol, 1.5 eq) in DME-HMPA (9:1, 10 mL). The resulting mixture was stirred for 3 h at the same temperature and then worked up (extraction with EtOAc). Column chromatography of the residue on silica gel (hexanes-EtOAc, 85:15) gave rise to olefin **26** (405 mg, 60%) as a 1:1 *E/Z* mixture, which was used in the next step.

A solution of compound **26** (225 mg, 0.20 mmol) and *N,N*-diisopropyl ethylamine (1.5 mL) in dry CH_2Cl_2 (15 mL) was cooled to $-78\text{ }^\circ\text{C}$ and treated with freshly prepared Me_2BBr ($\sim 1.76\text{ M}$ solution in CH_2Cl_2 , 455 μL , 0.8 mmol, 4 eq, added in two portions within 1 h). The reaction mixture was stirred at $-78\text{ }^\circ\text{C}$ for 1 h and quenched with satd aq NaHCO_3 solution/THF (1:2, 40 mL). The resulting mixture was vigorously stirred at room temperature for 5 min., then worked up (extraction with EtOAc). Column chromatography on silica gel (hexanes-EtOAc, 9:1) afforded compound **27** (208 mg, 96%) as a 1:1 *E/Z* mixture. This material was carefully rechromatographed on flash silica gel (hexanes-EtOAc, 95:5) to yield **Z-27** (100 mg) and **E-27** (105 mg).

E-27: oil; $[\alpha]_{\text{D}} +5.0$ (c 1.1, CHCl_3); ^1H NMR (500 MHz) δ 7.11 (s, 1H), 5.66-5.40 (m, 5H), 4.21 (q, $J = 7.0\text{ Hz}$, 2H), 3.81 (dd, $J = 6.0, 1.5\text{ Hz}$, 1H), 3.76 (m, 1H), 3.61 (t, $J = 4.2\text{ Hz}$, 1H), 3.57-3.46 (m, 2H), 3.31 (s, 3H), 3.14 (quintuplet, $J = 6.6\text{ Hz}$, 1H), 2.96 (dd, $J = 5.1, 1.8\text{ Hz}$, 1H), 2.89 (dd, $J = 3.7, 2.2\text{ Hz}$, 1H), 2.69 (m, 1H), 2.35-2.05 (br m, 8H), 2.08 (br s, 3H), 1.86 (br s, 3H), 1.75 (sext, $J = 6.4\text{ Hz}$, 1H), 1.70-1.55 (m, 2H), 1.31 (t, $J = 7.1\text{ Hz}$, 3H), 1.13 (d, $J = 6.1\text{ Hz}$, 3H), 1.07 (d, $J = 7.0\text{ Hz}$, 3H), 0.93 (d, $J = 6.8\text{ Hz}$, 3H), 0.90 (br s, 36H), 0.89 (overlapped d, 3H), 0.85 (d, $J = 7.1\text{ Hz}$, 3H), 0.09 (s, 3H), 0.08 (s, 3H), 0.07 (s, 6H), 0.06 (s, 3H), 0.05 (s, 6H), 0.03 (s, 3H) (hydroxyl signal not detected); ^{13}C NMR (125 MHz) δ 169.1, 131.9, 125.8, 18.5, 18.3, 18.2, 18.1 (C), 142.6, 138.1, 131.1, 129.8, 129.3, 127.9, 79.9, 73.6, 73.5, 72.9, 72.8, 72.7, 58.6, 56.9, 43.1, 41.3, 38.1, 37.6 (CH), 60.6, 38.9, 38.3, 38.1, 36.8 (CH_2), 56.4, 26.1 (x 3), 26.0 (x 3), 25.9 (x 3), 25.8 (x 3), 16.6, 16.5, 15.6, 14.3, 14.0, 13.7, 10.6, 10.5, -3.2 , -3.4 , -4.0 , -4.1 , -4.1 , -4.5 , -4.8 , -4.9 (CH_3); IR ν_{max} 3530 (br OH), 1708 (C=O) cm^{-1} ; FAB MS: no peak in the vicinity of the molecular ion could be detected. Elemental analysis: C, 65.65; H, 10.99. Calcd for $\text{C}_{59}\text{H}_{116}\text{O}_9\text{Si}_4$: C, 65.50; H, 10.81.

Z-27: oil; $[\alpha]_{\text{D}} +5.6$ (c 0.5, CHCl_3); ^1H NMR (500 MHz) δ 7.11 (s, 1H), 5.65-5.35 (m, 5H), 4.21 (q, $J = 7.1\text{ Hz}$, 2H), 3.81 (dd, $J = 6.0, 1.5\text{ Hz}$, 1H), 3.76 (dt, $J = 5.9, 5.2\text{ Hz}$, 1H), 3.60 (t, $J = 4.3\text{ Hz}$, 1H), 3.58-3.50 (m, 2H), 3.31 (s, 3H), 3.14 (quint, $J = 6.6\text{ Hz}$, 1H), 2.97 (dd, $J = 5.3, 2.4\text{ Hz}$, 1H), 2.90 (dd, $J = 3.9, 2.4\text{ Hz}$, 1H), 2.70 (m, 1H), 2.36 (m, 1H), 2.33-2.12 (m, 7H), 2.01 (br s, 3H), 1.86 (br s, 3H), 1.75 (sext, $J = 6.4\text{ Hz}$, 1H), 1.68-1.56 (m, 2H), 1.31 (t, $J = 7.1\text{ Hz}$, 3H), 1.13 (d, $J = 6.1\text{ Hz}$, 3H), 1.07 (d, $J = 6.8\text{ Hz}$, 3H), 0.93 (d, $J = 6.8\text{ Hz}$, 3H), 0.91 (overlapped d, 3H), 0.90 (br s, 36H), 0.85 (d, $J = 7.1\text{ Hz}$, 3H), 0.11 (s, 3H), 0.07 (s, 12H), 0.06 (s, 3H), 0.05 (s, 3H), 0.03 (s, 3H) (hydroxyl signal not detected); ^{13}C NMR (125 MHz) δ 169.1, 131.9, 125.9, 18.5, 18.3, 18.2, 18.1 (C), 142.7, 138.1, 131.1, 128.4, 128.0, 127.9, 79.9, 73.8, 73.7, 72.8, 72.8, 72.8, 58.7, 57.1, 43.1, 41.3, 38.1, 37.6 (CH), 60.6, 38.9, 36.9, 32.9, 32.8 (CH_2), 56.4, 26.1 (x 3), 26.0 (x 3), 25.9 (x 3), 25.8 (x 3), 16.6, 16.5, 16.0,

14.3, 14.0, 13.6, 10.6, 10.5, -3.2, -3.4, -3.9, -4.1, -4.1, -4.5, -4.7, -4.9 (CH₃); IR $\nu_{\max}$ 3500 (br OH), 1708 (C=O) cm⁻¹; FAB MS: no peak in the vicinity of the molecular ion could be detected. Elemental analysis: C, 65.39; H, 10.67. Calcd for C₅₉H₁₁₆O₉Si₄: C, 65.50; H, 10.81.

A solution of hydroxy ester *E-27* (54 mg, 0.05 mmol) in dry THF (2 mL) was treated under N₂ at room temperature with TMSOK (65 mg, 0.50 mmol, 10 eq). After stirring at room temperature for 10 hours, the reaction was quenched with citric acid (0.5M en H₂O, 1 mL) and vigorously stirred for 20 min. Work-up (extraction with EtOAc, 3 x 10 mL) and solvent removal in vacuo provided a crude *seco*-acid which was used without further purification in the following macrolactonization step.

A solution of above mentioned *seco*-acid in dry CH₂Cl₂ (8 mL) was treated sequentially under N₂ at room temperature with N,N-diisopropyl ethylamine (70 μ L, 0.40 mmol, 8 eq), DMAP (12 mg, 0.1 mmol, 2 eq) and 2,4,6-trichlorobenzoyl chloride (32 μ L, 0.20 mmol, 4 eq). After stirring at room temperature for 1 h, the reaction mixture was poured into a saturated aqueous NH₄Cl solution and worked up (extraction with CH₂Cl₂, 3 x 15 mL). Column chromatography on silica gel (hexanes-EtOAc, 9:1) gave macrolactone *E-28* (26 mg, 50% overall yield for the two steps) as a colourless oil: [α]_D +11.8 (c 0.8, CHCl₃); ¹H NMR (500 MHz) δ 7.19 (s, 1H), 5.69 (d, *J* = 9.7 Hz, 1H), 5.60-5.45 (m, 4H), 3.81 (dd, *J* = 5.9, 1.3 Hz, 1H), 3.76 (br q, *J* = 6.0 Hz, 1H), 3.59 (t, *J* = 4.2 Hz, 1H), 3.55-3.45 (m, 2H), 3.31 (s, 3H), 3.14 (quintuplet, *J* = 6.6 Hz, 1H), 2.95 (dd, *J* = 5.1, 1.8 Hz, 1H), 2.88 (dd, *J* = 3.9, 2.0 Hz, 1H), 2.72 (m, 1H), 2.35-2.10 (m, 8H), 2.08 (br s, 3H), 1.90 (br s, 3H), 1.75 (sext, *J* = 6.4 Hz, 1H), 1.70-1.55 (m, 2H), 1.14 (d, *J* = 6.2 Hz, 3H), 1.08 (d, *J* = 6.8 Hz, 3H), 0.93 (d, *J* = 6.8 Hz, 3H), 0.89 (overlapped d, 3H), 0.89 (br s, 36H), 0.85 (d, *J* = 7.0 Hz, 3H), 0.09 (s, 3H), 0.08 (s, 3H), 0.07 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H), 0.02 (s, 3H); ¹³C NMR (125 MHz) δ 165.4, 131.7, 125.1, 18.5, 18.3, 18.2, 18.1 (C), 146.6, 141.0, 131.1, 129.9, 129.2, 127.9, 79.9, 73.6, 73.5, 72.8, 72.7, 72.7, 58.9, 57.0, 43.1, 41.3, 38.1, 37.6 (CH), 38.9, 38.3, 38.1, 36.8 (CH₂), 56.4, 26.1 (x 3), 26.0 (x 3), 25.9 (x 3), 25.8 (x 3), 16.5, 16.4, 15.1, 14.0, 13.7, 10.6, 10.5, -3.2, -3.4, -3.9, -4.1 (x 2), -4.4, -4.7, -4.8 (CH₃); IR $\nu_{\max}$, 1768 (C=O) cm⁻¹; FAB MS: no peak in the vicinity of the molecular ion could be detected. Elemental analysis: C, 66.29; H, 10.77. Calcd for C₅₇H₁₁₀O₈Si₄: C, 66.09; H, 10.70.

A solution of macrolactone *E-28* (20 mg, ~0.02 mmol) in dry DMF (200 μ L) was treated under N_2 at room temperature with TASf (55 mg, 0.2 mmol, 10 eq). After stirring at room temperature for 4 d, the reaction was directly poured into silica gel and eluted with EtOAc to afford lactone *E-1* (3.5 mg, 32%): oil; 1H NMR (500 MHz) δ 7.30 (br. s, 1H), 5.76 (ddd, J = 15.0, 10.0, 5.0 Hz, 1H), 5.65-5.55 (m, 3H), 5.49 (d, J = 10.8 Hz, 1H), 5.12 (br s, 2H, OH), 4.84 (dt, J = 9.6, 3.4 Hz, 1H), 4.14 (br s, 1H), 3.97 (br s, 1H, OH), 3.87 (app d, J = 8.1 Hz, 1H), 3.81 (d, J = 9.4 Hz, 1H), 3.60 (m, 2H), 3.34 (s, 3H), 3.24 (dd, J = 4.5, 2.5 Hz, 1H), 3.15 (br s, 1H), 3.11 (ddd, J = 10.6, 7.2, 3.7 Hz, 1H), 2.85 (br s, 1H, OH), 2.60-2.40 (m, 3H), 2.40-2.15 (m, 4H), 2.09 (s, 3H), 2.02 (s, 3H), 2.00-1.75 (br m, 3H), 1.60-1.55 (m, 1H), 1.19 (d, J = 6.2 Hz, 3H), 1.14 (d, J = 7.1 Hz, 3H), 0.92 (d, J = 7.1 Hz, 3H), 0.90 (d, J = 6.8 Hz, 3H), 0.79 (d, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz) δ 168.8, 135.8, 124.7 (C), 144.0, 141.6, 130.2, 129.4, 129.3, 128.1, 82.7, 78.4, 76.5, 73.2, 71.0, 70.9, 56.0, 55.0, 39.7 (x 2), 36.0, 34.6 (CH), 38.2, 36.8, 35.9, 34.4 (CH_2), 55.9, 16.5, 16.4, 16.3, 15.6, 13.7, 11.6, 4.9 (CH_3). NMR spectra identical to those of a natural sample.

Hydroxy ester *Z-27* (70 mg, ~0.065 mmol) was subjected to the saponification/macrolactonization protocol used for the conversion of *E-27* into *E-28*. This provided macrolactone *Z-28* (36 mg, 54% overall yield for the two steps) as a colourless oil: $[\alpha]_D +15.4$ (c 1.30, $CHCl_3$); 1H NMR (500 MHz) δ 7.19 (s, 1H), 5.69 (d, J = 9.7 Hz, 1H), 5.60-5.40 (m, 4H), 3.81 (d, J = 6.0 Hz, 1H), 3.76 (br q, J = 5.5 Hz, 1H), 3.60-3.50 (m, 3H), 3.31 (s, 3H), 3.14 (quintuplet, J = 6.4 Hz, 1H), 2.96 (br d, J = 5.0 Hz, 1H), 2.90 (dd, J = 3.7, 1.7 Hz, 1H), 2.73 (m, 1H), 2.40-2.35 (m, 1H), 2.34-2.10 (m, 7H), 2.08 (br s, 3H), 1.90 (br s, 3H), 1.75 (sext, J = 6.2 Hz, 1H), 1.70-1.50 (m, 2H), 1.13 (d, J = 6.0 Hz, 3H), 1.08 (d, J = 6.8 Hz, 3H), 0.93 (d, J = 6.8 Hz, 3H), 0.91 (d overlapped, 3H), 0.90 (br s, 36H), 0.85 (d, J = 7.1 Hz, 3H), 0.10 (s, 3H), 0.08 (s, 3H), 0.07 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (125 MHz) δ 165.4, 131.7, 125.1, 18.5, 18.3, 18.2, 18.1 (C), 146.6, 141.0, 131.1, 128.4, 128.0 (x 2), 79.9, 73.8, 73.7, 72.8 (x 2), 72.6, 59.0, 57.1, 43.1, 41.3, 38.2, 37.6 (CH), 38.9, 36.9, 32.9, 32.8 (CH_2), 56.4, 26.1 (x 3), 26.0 (x 3), 25.9 (x 3), 25.9 (x 3), 16.5, 16.4, 15.1, 14.0, 13.6, 10.6, 10.5, -3.2, -3.4, -3.9, -4.1 (x 2),

−4.5, −4.7, −4.8 (CH₃); IR ν_{max} 1769 (C=O) cm^{−1}; FAB MS: no peak in the vicinity of the molecular ion could be detected. Elemental analysis: C, 65.98; H, 10.57. Calcd for C₅₇H₁₁₀O₈Si₄: C, 66.09; H, 10.70.

Macrolactone **Z-28** (10 mg, ~0.01 mmol) was subjected to deprotection under the same conditions as for the conversion of *E-28* into *E-1* to afford macrolactone **Z-1** (2 mg, 36%): oil; [α]_D +65.9 (*c* 0.15, MeOH); ¹H NMR (500 MHz) δ 7.15 (s, 1H), 5.70-5.50 (m, 4H), 5.47 (d, *J* = 11.0 Hz, 1H), 5.04 (ddd, *J* = 13.1, 5.6, 2.5 Hz, 1H), 4.11 (br s, 1H), 4.00 (s, 1H, OH), 3.88 (br d, *J* = 8.2 Hz, 1H), 3.82 (d, *J* = 9.3 Hz, 1H), 3.65 (q, *J* = 6.0 Hz, 1H), 3.60 (qd, *J* = 6.0, 2.5 Hz, 1H), 3.35 (s, 3H), 3.19 (br s, 1H), 3.14 (dd, *J* = 6.0, 2.2 Hz, 1H), 3.05 (m, 1H), 2.91 (br s, 1H, OH), 2.60-2.45 (m, 4H), 2.30-2.15 (m, 3H), 2.07 (s, 3H), 2.00 (s, 3H), 1.95 (m, 1H), 1.90-1.80 (m, 2H), 1.75 (br s, 1H, OH), 1.19 (d, *J* = 6.2 Hz, 3H), 1.17 (d, *J* = 7.2 Hz, 3H), 0.96 (d, *J* = 6.8 Hz, 3H), 0.93 (d, *J* = 7.1 Hz, 3H), 0.79 (d, *J* = 7.0 Hz, 3H) (two hydroxyl signals not detected); ¹³C NMR (125 MHz) δ 169.3, 135.1, 124.1 (C), 143.7, 141.3, 130.3, 129.6, 129.5, 125.5, 82.5, 78.2, 76.8, 73.1, 71.9, 70.4, 56.9, 56.2, 39.6 (x 2), 47.0, 36.1 (CH), 36.8, 36.0, 31.5, 30.6 (CH₂), 56.0, 17.0, 16.4, 15.4, 15.4, 13.7, 11.4, 5.0 (CH₃). HR FAB MS *m/z* 591.3879 (M+H⁺). Calcd for C₃₃H₅₅O₈, M = 591.3896.