SUPPORTING INFORMATION

Chagosensine: A Riddle Wrapped in a Mystery Inside an Enigma

Marc Heinrich,[+] John J. Murphy,[+] Marina K. Ilg, Aurélien Letort, Jakub T. Flasz, Petra Philipps, and Alois Fürstner*

Max-Planck-Institut für Kohlenforschung, D-45470 Mülheim/Ruhr, Germany

Email: fuerstner@kofo.mpg.de

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General Experimental Methods

All reactions were carried out under Ar in flame-dried glassware unless water was used as solvent or it is otherwise noted. The following solvents and organic bases were purified by distillation over the drying agents indicated and were transferred under Ar: THF, Et_2O (Mg/anthracene); hexane, toluene (Na/K); Et_3N, diisopropylamine, diisopropylethylamine, 2,6-lutidine, HMPA, CH_2Cl_2, DMA, NMP (CaH_2); MeOH, EtOH, *i*-PrOH (Mg, stored over 3 Å MS). DMF, DMSO, 1,4-dioxane, MeCN and pyridine were dried by an adsorption solvent purification system based on molecular sieves. All other commercially available compounds (ABCR, Acros, Alfa Aesar, Aldrich, Fluka, STREM, TCI) were used as received unless otherwise noted. The following compounds were prepared according to the cited literature: methylenetriphenylphosphorane,[1] (*Z*)-((2-(benzyloxy)-1-(ethylthio)vinyl)oxy)trimethylsilane,[2] Me_2BBr,[3] MOMCl,[4] $PPh_3CH_2I_2$,[5] $Co(nmp)_2$,[6] $Pd(t\text{-}BuNC)_2Cl_2$,[7] (*S*)-4-benzyl-3-(2-(benzyloxy)acetyl)-oxazolidin-2-one,[8] diethyl allyl phosphate,[9] 4-O-tert-butyldimethylsilyl-2,3-O-isopropylidene-D-erythrose (*ent*-**30**),[10] tetrabutylammonium diphenylphosphinate,[11] diazomethane,[12] (−)-2,3-O-Isopropylidene-D-erythronolactone,[13] (*Z*)-6-((t-Dimethylsilyl)oxy)cyclohexadec-4-en-2-yn-1-ol.[14]

Thin phase chromatography (TLC) was performed on Macherey-Nagel precoated plates (POLYGRAM® SIL/UV254). Detection was achieved under UV light (254 nm) and by staining with either acidic *p*-anisaldehyde, cerium-ammonium-molybdenate or basic $KMnO_4$ solution.

Flash chromatography was performed with Merck silica gel 60 (40-63 µm pore size) using predistilled or HPLC-grade solvents. In some cases, fine Merck silica gel 60 (15-40 µm pore size) was necessary as indicated within the experimental procedures.

NMR-spectra were recorded on Bruker AV 300, AV 400, AV 500 or AVIII 600 spectrometers in the solvents indicated. Chemical shifts (δ) are reported in ppm relative to TMS; coupling constants (J) are given in Hz. Multiplets are indicated by the following abbreviations: s: singlet, d: doublet, t: triplet, q: quartet, p: pentet, h: hextet, hept: heptet, m: multiplet. The abbreviation br indicates a broad signal. ^{13}C spectra were recorded in [^1H]-decoupled manner and the values of the chemical shifts are rounded to one decimal point. Signal assignments were established using HSQC, HMBC, COSY, NOESY and other 2D experiments; numbering schemes as shown in the inserts. All spectra from 500 MHz and 600 MHz spectrometers were acquired by the NMR department under the guidance of Dr. Christophe Farès at the Max-Planck-Institut für Kohlenforschung.

IR spectra were recorded on Alpha Platinum ATR (Bruker) at ambient temperature, wavenumbers ($\tilde{\nu}$) are given in cm^{-1}.

Mass spectra were measured by the department for mass spectrometry at the Max-Planck-Institut für Kohlenforschung under the guidance of Prof. Wolfgang Schrader using the following devices: MS (EI):

Finnigan MAT 8200 (70 eV), ESI-MS: Bruker ESQ3000, accurate mass determinations: Bruker APEX III FT-MS (7 T magnet) or MAT 95 (Finnigan). The characteristic ion measured by high resolution mass spectrometry is given as the [M+Na$^+$]-adduct, unless otherwise noticed.

Optical rotations were measured with an A-Krüss Otronic Model P8000-t polarimeter at a wavelength of 589 nm. The values are given as specific optical rotation with exact temperature, concentration (c/(10 mg/mL)) and solvent.

LC-MS analyses were conducted on a Shimadzu LC-MS 2020 instrument (pumps LC-20AD, autosampler SIL-20AC, column oven CTO-20AC, diode array detector SPD-M20A, controller CBM-20A, ESI detector and software Labsolutions) with a ZORBAX Eclipse Plus column (C18 1.8 µm, 4.6 mm ID × 50 mm (Agilent)) or a YMC-ODS-A C18 column (S-5 µm, 120 Å, 4.6 mm ID × 150 mm). A binary gradient of MeCN or MeOH in water was used as eluent at a flow rate of 0.8 mL/min or 1.0 (4.6 mm ID). The oven temperature was kept at 35 °C and the detection wavelength at 250 nm. Conditions for each compound are specified below.

Supporting Crystallographic Data

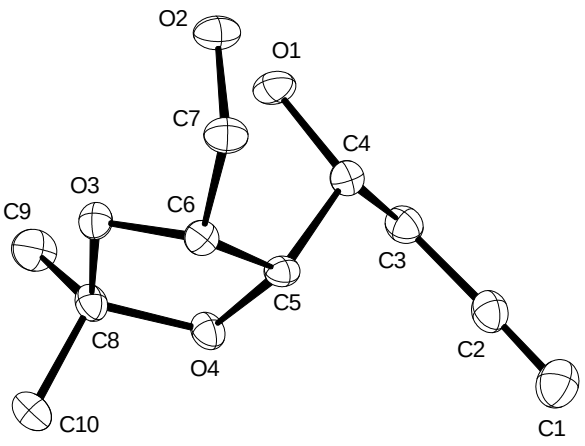


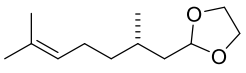
Figure S-1. Structure of *syn*-diol **39** in the solid state; hydrogen atoms have been omitted for clarity

X-ray Crystal Structure Analysis of *syn*-Diol 39: **CCDC 1983363.** C_{10} H_{16} O_4, Mr = 200.23 g · mol^{-1}, colourless, crystal size 0.380 × 0.200 × 0.180 mm^3, orthorhombic, space group $P2_12_12_1$, a = 7.8637(3) Å, b = 8.3178(3) Å, c = 16.4246(7) Å, α = 90°, β = 90°, γ = 90°, V = 1074.31(7) Å ^{3}, T = 100(2) K, Z = 4, D_{calc} = 1.238 g · cm^3, λ = 1.54178 Å, μ(Mo-Kα) = 0.791 mm^{-1}, Gaussian absorption correction (T_{min} = 0.82, T_{max} = 0.90), Bruker AXS Enraf-Nonius KappaCCD diffractometer, 5.386° < Θ < 72.139°, 33485 measured reflections, 2097 independent reflections, 2069 reflections with I > 2σ(I), R_{int} = 0.0299. The structure was solved by direct methods and refined by full-matrix least-squares against F^2 to R_1 = 0.0372 [I > 2σ(I)], wR^2 = 0.0893, 191 parameters. Three independent crystals were analyzed.

Synthesis of the Two Diastereomeric Northern Segments

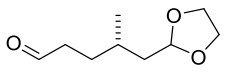
Fragment 6a

(*S*)-2-(2,6-Dimethylhept-5-en-1-yl)-1,3-dioxolane (S1). Triethylorthoformate (69 mL, 0.42 mol) and



ethylene glycol (117 mL, 2.09 mol) were added to a solution of CSA (1.62 g, 6.99 mmol) in CH_2Cl_2 (1.0 L). Neat (*S*)-citronellal (**11**) (25.2 mL, 139 mmol) was added dropwise *via* syringe over 10 min. The colourless solution was stirred at ambient temperature for 20 min before the reaction was quenched with sat. $NaHCO_3$ (300 mL). The aq. phase was separated and extracted with CH_2Cl_2 (3 × 200 mL). The combined organic phases were washed with brine (2 × 200 mL), dried over Na_2SO_4 and concentrated to a colourless liquid. This liquid can be purified by flash chromatography (hexane/*t*-butyl methyl ether 70:30) to give the title compound as a colourless liquid (27.1 g, 98%). More conveniently, the crude mixture was distilled under high vacuum, discarding the fore-run but collecting the fraction distilling between 66–69 °C at 1.6×10^{-2} mbar. The product **S1** was isolated as a colourless liquid in a slightly reduced yield (23.1 g, 84%). $[\alpha]_D^{20}$ = –4.3 (c = 1.15, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.10 (tq, *J* = 7.1, 2.2 Hz, 1H), 4.90 (dd, *J* = 5.2, 4.7 Hz, 1H), 4.02–3.91 (m, 2H), 3.89–3.80 (m, 2H), 2.08–1.88 (m, 2H), 1.76–1.62 (m, 5H), 1.60 (s, 3H), 1.54–1.44 (m, 1H), 1.44–1.32 (m, 1H), 1.28–1.13 (m, 1H), 0.95 (d, *J* = 6.5 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 131.2, 124.7, 103.8, 64.7, 64.6, 40.9, 37.5, 29.1, 25.7, 25.4, 19.8, 17.6 ppm. IR (film): $\tilde{\nu}$ = 2960, 2915, 2877, 1454, 1409, 1378, 1130, 1040, 945 cm^{-1}. MS (EI) *m/z* (%): 136 (10), 113 (28), 69 (20), 41 (35). HRMS (ESIpos) *m/z* calcd for $C_{12}H_{23}O_2$ [M+H$^+$]: 199.1693, found: 199.1692. The analytical and spectroscopic data are in agreement with those reported in the literature.[15]

(*S*)-5-(1,3-Dioxolan-2-yl)-4-methylpentanal (12). Sudan Red III (5-10 mg) was added to a solution of dioxolane **S1** (22.5 g, 114 mmol) in CH_2Cl_2 (500 mL). The solution was cooled to −78 °C before ozone



was bubbled (35-40 g/Nm^3, 420 min) through the mixture until a colour change from red/pink to pale yellow was observed. After purging with oxygen for 30 min, dimethyl sulfide (17 mL, 0.23 mol) was added and the mixture was allowed to reach ambient temperature over 12 h. The mixture was concentrated to give a yellow oil. After dissolving the residue in pentane (300 mL), the solution was washed with brine (3 × 200 mL). The combined brine washes were back-extracted with pentane (200 mL) and the combined pentane phases were dried over Na_2SO_4 and concentrated to a yellow oil. This residue was purified by flash chromatography (hexane/EtOAc 100:0 to 80:20) to yield the title compound as a colourless liquid (19 g, 97%). Alternatively, the crude product can be purified by distillation under high vacuum, collecting the fraction distilling between 72-75 °C at 6×10^{-2} mbar; in this case, the title compound was isolated as a colourless liquid in a deminished yield (10.3 g, 53 %). $[\alpha]_D^{20}$ = –5.9 (c = 1.36, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.77 (t, *J*

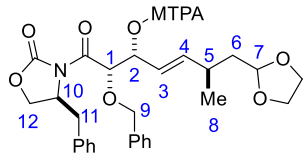
= 1.8 Hz, 1H), 4.89 (dd, *J* = 5.4, 4.6 Hz, 1H), 3.99–3.92 (m, 2H), 3.86–3.80 (m, 2H), 2.52–2.37 (m, 2H), 1.79–1.60 (m, 3H), 1.58–1.48 (m, 2H), 0.96 (d, *J* = 6.4 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 202.8, 103.6, 64.9, 64.8, 41.7, 40.7, 30.0, 29.1, 19.9 ppm. IR (film): $\tilde{\nu}$ = 2955, 2880, 2722, 1722, 1411, 1137, 1034, 948 cm^{-1}. MS (EI) *m/z* (%): 113 (3), 73 (100), 55 (6), 45 (20). HRMS (ESIpos) *m/z* calcd for $C_9H_{16}O_3Na$ [M+Na$^+$]: 195.0992, found: 195.0993. The analytical and spectroscopic data are in agreement with those reported in the literature.[16]

(*R*,*E*)-5-(1,3-Dioxolan-2-yl)-4-methylpent-2-enal (13). Diethyl allyl phosphate (12.7 mL, 71.3 mmol) was added to a solution of aldehyde **12** (10.2 g, 59.4 mmol) in THF (48 mL). $Pd(OAc)_2$ (530 mg, 2.36 mmol) and $NaHCO_3$ (6.00 g, 71.4 mmol) were introduced and the orange heterogeneous mixture was placed in a pre-heated oil bath at 86 °C. The mixture was stirred at reflux temperature under a stream of argon for 60 h, causing a gradual color change to pale green/brown. The mixture was allowed to cool and partitioned between *t*-butyl methyl ether (200 mL) and deionized water (100 mL). The aq. phase was separated and extracted *t*-butyl methyl ether (2 × 100 mL). The combined organic phases were washed with sat. NH_4Cl (100 mL) and brine (100 mL), dried over Na_2SO_4 and concentrated. The resulting orange oil was first purified by flash chromatography (hexane/*t*-butyl methyl ether 50:50) giving the product as a colourless liquid contaminated with the corresponding allyl enol ether. This material was further purified by Kugelrohr distillation, collecting the fraction that distilled between 80–90 °C at 2 × 10^{-2} mbar, to give the title compound as a pale-yellow pungent oil (5.87 g, 58%). $[\alpha]_D^{20}$ = –59.5 (c = 0.79, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.51 (d, *J* = 7.8 Hz, 1H), 6.80 (dd, *J* = 15.6, 7.6 Hz, 1H), 6.10 (ddd, *J* = 15.7, 7.8, 1.2 Hz, 1H), 4.87 (t, *J* = 4.8 Hz, 1H), 4.02–3.89 (m, 2H), 3.88–3.80 (m, 2H), 2.81–2.65 (m, 1H), 1.89–1.67 (m, 2H), 1.16 (d, *J* = 6.8 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 194.4, 163.2, 131.3, 102.9, 65.1, 65.0, 39.9, 33.2, 19.8 ppm. IR (film): $\tilde{\nu}$ = 2965, 2882, 1688, 1410, 1130, 1029, 977 cm^{-1}. MS (EI) *m/z* (%): 113 (3), 73 (100), 55 (3), 45 (15). HRMS (ESIpos) *m/z* calcd for $C_9H_{14}O_3Na$ [M+Na$^+$]: 193.0835, found: 193.0837.

Aldol S2. Et_3N (5.4 mL, 39 mmol) was added to a solution of (*S*)-4-benzyl-3-(2-(benzyloxy)acetyl)oxazolidin-2-one (9.68 g, 29.8 mmol) in CH_2Cl_2 (100 mL). The mixture was cooled to –78 °C before a solution of *n*-Bu_2BOTf (1 M solution in CH_2Cl_2, 30 mL, 30 mmol) was added at such a rate as to keep the internal temperature below –65 °C. The mixture was allowed to reach 0 °C over 1.25 h. At this point the mixture was re-cooled to –78 °C before a solution of enal **13** (4.22 g, 24.8 mmol) in CH_2Cl_2 (5 mL) was added at such a rate as to keep the internal temperature below −65 °C. The mixture was stirred at –78 °C for 20 min and allowed to reach 0 °C over 1.5 h. The reaction was quenched with methanol (140 mL) followed by pH 7 buffer (80 mL). Aq. hydrogen peroxide (35%,

40 mL) was added cautiously ensuring that the temperature remained below 10 °C. The mixture was stirred for an additional hour at 0 °C and the aq. phase was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic phases were washed with sat. $Na_2S_2O_3$ (200 mL, CAUTION: EXOTHERM!) and brine (100 mL), dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography (hexane/EtOAc 40:60) to give the *syn*-aldol adduct **S2** as a colourless syrup (9.84 g, 80%, dr = 12:1). $[\alpha]_D^{20}$ = +17.9 (c = 1.13, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.43–7.27 (m, 8H), 7.22–7.17 (m, 2H), 5.71 (ddd, *J* = 15.6, 7.4, 1.1 Hz, 1H), 5.56 (ddd, *J* = 15.5, 6.3, 1.0 Hz, 1H), 5.24 (d, *J* = 4.2 Hz, 1H), 4.84 (dd, *J* = 5.8, 4.4 Hz, 1H), 4.71 (d, *J* = 11.6 Hz, 1H), 4.66 – 4.57 (m, 2H), 4.37 (d, *J* = 5.4 Hz, 1H), 4.24–4.13 (m, 2H), 4.00–3.87 (m, 2H), 3.84–3.75 (m, 2H), 3.20 (dd, *J* = 13.4, 3.4 Hz, 1H), 2.66 (dd, *J* = 13.4, 9.7 Hz, 1H), 2.59 (s, 1H), 2.48–2.36 (m, 1H), 1.67 (ddd, *J* = 13.8, 7.8, 4.4 Hz, 1H), 1.58 (dt, *J* = 13.8, 6.2 Hz, 1H), 1.02 (d, *J* = 6.8 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.6, 153.4, 139.1, 137.1, 135.2, 129.5, 129.1, 128.7, 128.6, 128.4, 127.6, 126.6, 103.3, 80.2, 73.7, 73.5, 66.9, 64.8, 64.8, 55.7, 40.7, 37.9, 32.7, 20.7 ppm. IR (film): $\tilde{\nu}$ = 3467, 2957, 1776, 1707, 1389, 1210, 1110, 1028, 974 cm^{-1}. MS (EI) *m/z* (%): 1013.4 (30), 518.2 (100), 327.1 (2). HRMS (ESIpos) *m/z* calcd for $C_{28}H_{33}NO_7Na$ [M+Na$^+$]: 518.2149, found: 518.2154.

Mosher Ester Analysis of Alcohol S2. Et_3N (14 µL, 0.1 mmol) and DMAP (0.8 mg, 0.01 mmol) were added to a solution of alcohol **S2** (17 mg, 0.034 mmol) in CH_2Cl_2 (2 mL) followed by (*R*)-(–)-α-methoxy-α-trifluoromethyl-phenylacetyl chloride ((*R*)-MTPA-Cl) (7.6 µL, 0.04 mmol). The mixture was stirred at ambient temperature for 2 h, diluted with CH_2Cl_2 (2 mL) and sat. NH_4Cl (2 mL). The aq. phase was separated and extracted with CH_2Cl_2 (2 × 2 mL). The combined organic phases were dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography (hexane/EtOAc 70:30) to give the corresponding (*S*)-Mosher ester (*S*)-**S3** (19.1 mg, 79%) as a pale yellow oil. $[\alpha]_D^{20}$ = +6.7 (c = 1.91, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.59–7.53 (m, 2H), 7.41–7.25 (m, 11H), 7.19–7.13 (m, 2H), 5.87 (dd, *J* = 15.5, 7.8 Hz, 1H), 5.81 (dd, *J* = 8.2, 5.6 Hz, 1H), 5.61 (ddd, *J* = 15.5, 8.2, 1.0 Hz, 1H), 5.45 (d, *J* = 5.6 Hz, 1H), 4.76 (dd, *J* = 5.9, 4.3 Hz, 1H), 4.50 (d, *J* = 1.6 Hz, 2H), 4.49–4.39 (m, 1H), 4.23–4.08 (m, 2H), 3.93–3.86 (m, 2H), 3.79–3.70 (m, 2H), 3.53 (d, *J* = 1.2 Hz, 3H), 3.13 (dd, *J* = 13.4, 3.3 Hz, 1H), 2.54 (dd, *J* = 13.4, 9.8 Hz, 1H), 2.49–2.34 (m, 1H), 1.66–1.54 (m, 2H), 0.99(d, *J* = 6.8 Hz, 3H) ppm. IR (film): $\tilde{\nu}$ = 2957, 2878, 1779, 1749, 1709, 1454, 1390, 1246, 1169, 1109, 1019, 979, 699 cm^{-1}. MS (EI) *m/z* (%): 1445.5 (25), 734.3 (100), 478.2 (3), 375.6 (5). HRMS (ESIpos) *m/z* calcd for $C_{38}H_{40}NO_9F_3Na$ [M+Na$^+$]: 734.2547, found: 734.2548.



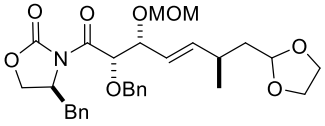
The corresponding Mosher ester (*R*)-**S3** (17.6 mg, 76%) was prepared analogously: $[\alpha]_D^{20}$ = +46.1 (c = 1.73, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.56–7.51 (m, 2H), 7.39– 7.27 (m, 11H), 7.21–7.14 (m, 2H), 5.82 (ddd, *J* = 7.6, 4.7, 0.8 Hz, 1H), 5.72 (ddd, *J* = 15.6, 7.8, 0.9 Hz, 1H), 5.55–5.47 (m, 1H), 5.44 (d,

J = 4.7 Hz, 1H), 4.76–4.63 (m, 2H), 4.57 (d, *J* = 11.8 Hz, 1H), 4.53–4.46 (m, 1H), 4.24 (dd, *J* = 9.0, 7.7 Hz, 1H), 4.15 (dd, *J* = 9.0, 2.5 Hz, 1H), 3.95–3.80 (m, 2H), 3.77–3.66 (m, 2H), 3.60 (d, *J* = 1.2 Hz, 3H), 3.18 (dd, *J* = 13.5, 3.4 Hz, 1H), 2.65 (dd, *J* = 13.5, 9.7 Hz, 1H), 2.44–2.28 (m, 1H), 1.68–1.46 (m, 2H), 0.95 (d, *J* = 6.8 Hz, 3H) ppm. IR (film): $\tilde{\nu}$ = 2957, 2878, 1779, 1749, 1709, 1454, 1390, 1246, 1169, 1109, 1019, 979, 699 cm^{-1}. MS (EI) *m/z* (%): 1445.5 (25), 734.3 (100), 478.2 (3), 375.6 (5). HRMS (ESIpos) *m/z* calcd for $C_{38}H_{40}NO_9F_3Na$ [M+Na^+]: 734.2547, found: 734.2549.

Table S-1. Mosher ester analysis for *syn*-aldol adduct **S2** according to Hoye and co-workers;[12] arbitrary numbering scheme as shown in the insert

Assignment	S2 [ppm]	(*S*)-S3 [ppm]	(*R*)-S3 [ppm]	Δ (δ (S–R)) [ppm]
1	5.24	5.45	5.44	+0.01
2	4.37	5.81	5.82	–0.01
3	5.56	5.61	5.51	+0.10
4	5.71	5.87	5.72	+0.15
5	2.41	2.42	2.36	+0.06
6	1.63	1.60	1.55	+0.05
7	4.84	4.76	4.68	+0.08
8	1.02	0.99	0.95	+0.04
9a	4.71	4.50	4.67	–0.12
9b	4.60	4.50	4.57	–0.07
10	4.63	4.45	4.49	–0.04
11a	3.20	3.13	3.18	–0.05
11b	2.66	2.54	2.65	–0.11
12a	4.18	4.16	4.24	–0.08
12b	4.18	4.12	4.15	–0.03

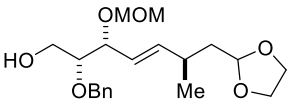
MOM-Ether 14. Tetrabutylammonium iodide (73 mg, 0.20 mmol) was added to a solution of alcohol **S2**



(9.78 g, 19.7 mmol) in CH_2Cl_2 (60 mL), whereupon the solution turned yellow. The solution was cooled to 0 °C before Hünig's base (24 mL, 0.14 mol) was added dropwise, causing the yellow colour to disappear. MOMCl (6.0 mL, 79 mmol) was added dropwise with vigorous stirring at such as rate as to keep the internal temperature ≤ +10 °C. Once the addition was complete, the mixture was allowed to reach ambient temperature and stirring was continued for 12 h. The reaction was quenched with sat. NH_4Cl (100 mL) and the phases were separated. The aq. phase was extracted with CH_2Cl_2 (3 × 100 mL) and the combined organic phases were washed with brine (100 mL), dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography (hexane/EtOAc 50:50) to give the title compound as a colourless syrup (10.7 g, quant.). $[\alpha]_D^{20}$ = –18.5 (c = 1.16, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.41–

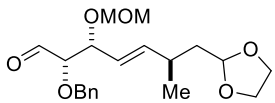
7.37 (m, 2H), 7.36–7.27 (m, 6H), 7.21–7.17 (m, 2H), 5.69 (dd, *J* = 15.5, 7.8 Hz, 1H), 5.51 (ddd, *J* = 15.6, 7.9, 1.0 Hz, 1H), 5.33 (d, *J* = 4.7 Hz, 1H), 4.82 (dd, *J* = 5.7, 4.6 Hz, 1H), 4.75 (d, *J* = 12.0 Hz, 1H), 4.66–4.53 (m, 4H), 4.41 (dd, *J* = 7.9, 4.6 Hz, 1H), 4.20–4.12 (m, 2H), 3.96–3.88 (m, 2H), 3.82–3.75 (m, 2H), 3.29 (s, 3H), 3.21 (dd, *J* = 13.4, 3.4 Hz, 1H), 2.69 (dd, *J* = 13.4, 9.6 Hz, 1H), 2.48–2.36 (m, 1H), 1.70–1.54 (m, 2H), 1.01 (d, *J* = 6.8 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.2, 153.3, 141.8, 137.6, 135.3, 129.6, 129.1, 128.5, 128.5, 128.1, 127.6, 123.9, 103.4, 94.0, 79.8, 77.2, 73.7, 66.8, 64.9, 64.8, 55.8, 55.6, 40.8, 37.8, 32.9, 20.8 ppm. IR (film): $\tilde{\nu}$ = 2954, 1779, 1709, 1389, 1210, 1105, 1032, 978 cm^{-1}. MS (EI) *m/z* (%): 1101.5 (30), 562.2 (100), 478.2 (8). HRMS (ESIpos) *m/z* calcd for $C_{30}H_{37}NO_8Na$ [M+Na$^+$]: 562.2411, found: 562.2416.

(2*R*,3*R*,6*R*,*E*)-2-(Benzyloxy)-7-(1,3-dioxolan-2-yl)-3-(methoxymethoxy)-6-methylhept-4-en-1-ol (S4).



Water (395 µL, 21.9 mmol) was added to a solution of oxazolidinone **14** (10.7 g, 19.8 mmol) in Et_2O (400 mL). The reaction was cooled to 0 °C before a solution of lithium borohydride (4 M in THF, 5.45 mL, 21.8 mmol) was added cautiously, causing evolution of hydrogen gas. After the addition was complete, stirring was continued at 0 °C for 50 min. The reaction was quenched with NaOH (1 M, 10 mL), the mixture was diluted with *t*-butyl methyl ether (100 mL) and stirred until clean phase separation was reached. The aq. phase was extracted with *t*-butyl methyl ether (3 × 100 mL). The combined organic phases were washed with brine (100 mL), dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography (*t*-butyl methyl ether) to give the title compound as a colourless syrup (6.42 g, 88%). $[\alpha]_D^{20}$ = –67.5 (c = 1.25, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32 (dd, *J* = 67.5, 11.9 Hz, 5H), 5.68 (ddd, *J* = 15.6, 7.7, 0.8 Hz, 1H), 5.41 (ddd, *J* = 15.6, 8.0, 1.1 Hz, 1H), 4.83 (dd, *J* = 5.6, 4.6 Hz, 1H), 4.79 (d, *J* = 11.7 Hz, 1H), 4.70 (d, *J* = 6.6 Hz, 1H), 4.65 (d, *J* = 11.7 Hz, 1H), 4.56 (d, *J* = 6.6 Hz, 1H), 4.20 (ddd, *J* = 8.1, 5.6, 0.9 Hz, 1H), 3.99–3.90 (m, 2H), 3.87–3.77 (m, 2H), 3.72 (ddd, *J* = 10.9, 7.1, 3.9 Hz, 1H), 3.64–3.51 (m, 2H), 3.37 (s, 3H), 2.54–2.37 (m, 1H), 2.26–2.12 (m, 1H), 1.80–1.56 (m, 2H), 1.04 (d, *J* = 6.9 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 141.1, 138.4, 128.5, 128.0, 127.8, 124.5, 103.4, 93.8, 81.3, 77.5, 73.4, 64.8 (2C), 62.1, 55.6, 40.7, 32.9, 20.8 ppm. IR (film): $\tilde{\nu}$ = 3489, 2955, 2885, 1454, 1406, 1098, 1028, 977 cm^{-1}. MS (EI) *m/z* (%): 755.4 (45), 389.2 (100), 305.2 (6). HRMS (ESIpos) *m/z* calcd for $C_{20}H_{30}O_6Na$ [M+Na$^+$]: 389.1935, found: 389.1933.

(2*S*,3*R*,6*R*,*E*)-2-(Benzyloxy)-7-(1,3-dioxolan-2-yl)-3-(methoxymethoxy)-6-methylhept-4-enal (15).

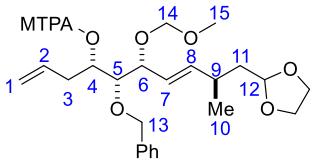


Sulfur trioxide pyridine complex (5.6 g, 35 mmol) was suspended in CH_2Cl_2 (100 mL) and the resulting mixture was cooled to –30 °C. After adding DMSO (11.2 mL, 158 mmol), a solution of alcohol **S4** (6.42 g, 17.5 mmol) and Hünig's base (12.2 mL, 70.0 mmol) in CH_2Cl_2 (50 mL) was added at –30 °C. The mixture was allowed to reach 0 °C over 2 h and the reaction was quenched with sat. NH_4Cl (50 mL). The aq. phase was

extracted with CH_2Cl_2 (3 × 100 mL), and the combined organic phases were washed with brine (100 mL), dried over Na_2SO_4 and concentrated. The resulting yellow oil was purified by flash chromatography (*t*-butyl methyl ether) to give the title compound as a colourless syrup (6.29 g, 98%, dr = 13:1). $[\alpha]_D^{20}$ = –145.0 (c = 1.33, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.72 (d, *J* = 1.6 Hz, 1H), 7.38–7.27 (m, 5H), 5.70 (ddd, *J* = 15.6, 7.6, 0.6 Hz, 1H), 5.52 (ddd, *J* = 15.6, 8.2, 1.0 Hz, 1H), 4.88–4.75 (m, 2H), 4.68 (d, *J* = 6.8 Hz, 1H), 4.63 (d, *J* = 12.2 Hz, 1H), 4.49 (d, *J* = 6.8 Hz, 1H), 4.42 (dd, *J* = 8.2, 3.6 Hz, 1H), 4.01–3.91 (m, 2H), 3.86–3.76 (m, 3H), 3.27 (s, 3H), 2.51–2.39 (m, 1H), 1.74–1.58 (m, 2H), 1.02 (d, *J* = 6.7 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 202.9, 142.1, 136.9, 128.5, 128.3, 128.2, 123.4, 103.3, 93.3, 85.4, 76.3, 73.5, 64.7, 64.6, 55.7, 40.5, 32.9, 20.6 ppm. IR (film): $\tilde{\nu}$ = 2954, 2887, 1733, 1149, 1096, 1027, 978 cm^{-1}. MS (EI) *m/z* (%): 751.4 (40), 419.2 (3), 387.2 (100). HRMS (ESIpos) *m/z* calcd for $C_{20}H_{28}O_6Na$ [M+Na$^+$]: 387.1778, found: 387.1779.

(4*S*,5*R*,6*R*,9*R*,*E*)-5-(Benzyloxy)-10-(1,3-dioxolan-2-yl)-6-(methoxymethoxy)-9-methyldeca-1,7-dien-4-ol (16). Magnesium bromide diethyl etherate (8.90 g, 34.5 mmol) was added to a solution of the aldehyde **15** (6.29 g, 17.3 mmol) in CH_2Cl_2 (100 mL) at 0 °C. The suspension became instantly yellow and was stirred at 0 °C for 1 h. Allyltrimethylsilane (5.5 mL, 35 mmol) was added in one portion and stirring continued at ambient temperature for 16 h before the reaction was quenched with sat. NH_4Cl (50 mL). The aq. phase was separated and extracted with CH_2Cl_2 (3 × 100 mL). The combined organic phases were washed with brine (100 mL), dried over Na_2SO_4 and concentrated to a yellow oil, which was purified by flash chromatography (*t*-butyl methyl ether) to give the title compound as a pale yellow syrup (6.47 g, 92%, dr = 14:1). $[\alpha]_D^{20}$ = –65.9 (c = 0.7, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37–7.27 (m, 5H), 5.85–5.68 (m, 2H), 5.42 (ddd, *J* = 15.6, 8.1, 1.1 Hz, 1H), 5.09–5.06 (m, 1H), 5.06–5.01 (m, 1H), 4.90 (d, *J* = 11.2 Hz, 1H), 4.83 (dd, *J* = 5.6, 4.6 Hz, 1H), 4.72 (d, *J* = 6.6 Hz, 1H), 4.63 (d, *J* = 11.3 Hz, 1H), 4.56 (d, *J* = 6.6 Hz, 1H), 4.30 (ddd, *J* = 8.1, 6.3, 0.8 Hz, 1H), 3.99–3.90 (m, 2H), 3.84–3.78 (m, 2H), 3.78–3.72 (m, 1H), 3.38–3.32 (m, 4H), 2.50–2.39 (m, 1H), 2.35 (dd, *J* = 7.0, 0.7 Hz, 1H), 2.33–2.27 (m, 2H), 1.75–1.60 (m, 2H), 1.05 (d, *J* = 6.8 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 141.3, 138.4, 135.0, 128.6, 128.3, 128.0, 125.2, 117.5, 103.5, 93.9, 82.7, 78.0, 77.4, 75.1, 70.6, 64.9 (2C), 55.8, 40.8, 39.0, 33.1, 20.9 ppm. IR (film): $\tilde{\nu}$ = 3477, 2929, 2886, 1454, 1401, 1212, 1097, 1028, 917 cm^{-1}. MS (EI) *m/z* (%): 835.5 (30), 629.3 (3), 429.2 (100), 345.2 (5). HRMS (ESIpos) *m/z* calcd for $C_{23}H_{34}O_6Na$ [M+Na$^+$]: 429.2248, found: 429.2247.

Mosher Ester Analysis of Alcohol 16. Et_3N (21 µL, 0.15 mmol) and DMAP (1 mg, 0.01 mmol) were added to a solution of alcohol **16** (21 mg, 0.051 mmol) in CH_2Cl_2 (2 mL), followed by (*R*)-(–)-α-methoxy-α-trifluoromethyl-phenylacetyl chloride ((*R*)-MTPA-Cl) (14.2 µL, 0.08 mmol). The mixture was stirred at ambient temperature for 2 h, diluted with CH_2Cl_2 (2 mL) and sat. NH_4Cl (2 mL). The aq. phase was separated and extracted with CH_2Cl_2 (2 × 2 mL). The combined organic phases were dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography (hexane/EtOAc 70:30) to give the corresponding (*S*)-Mosher ester (*S*)-**S5** (24.5 mg, 78%). $[\alpha]_D^{20}$ = –64.2 (c = 2.45, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.54 (d, *J* = 7.4 Hz, 2H), 7.39–7.24 (m, 8H), 5.68 (dddd, *J* = 16.8, 10.6, 7.8, 6.4 Hz, 1H), 5.56 (dd, *J* = 15.5, 7.8 Hz, 1H), 5.48–5.32 (m, 2H), 5.06 (d, *J* = 1.2 Hz, 1H), 5.02 (dd, *J* = 8.9, 1.8 Hz, 1H), 4.80 (dd, *J* = 5.6, 4.6 Hz, 1H), 4.74 (d, *J* = 11.6 Hz, 1H), 4.68 (d, *J* = 6.7 Hz, 1H), 4.62 (d, *J* = 11.6 Hz, 1H), 4.52 (d, *J* = 6.7 Hz, 1H), 4.19 (dd, *J* = 8.1, 5.3 Hz, 1H), 3.99–3.89 (m, 2H), 3.86–3.75 (m, 2H), 3.57 (t, *J* = 5.4 Hz, 1H), 3.51 (s, 3H), 3.34 (s, 3H), 2.62 (dddd, *J* = 13.3, 6.7, 3.4, 1.5 Hz, 1H), 2.53–2.33 (m, 2H), 1.74–1.55 (m, 2H), 0.99 (d, *J* = 6.8 Hz, 3H) ppm. IR (film): $\tilde{\nu}$ = 2953, 2888, 1746, 1453, 1250, 1169, 1122, 1026, 698 cm^{-1}. MS (EI) *m/z* (%): 1267.5 (20), 645.3 (100), 501.3 (2). HRMS (ESIpos) *m/z* calcd for $C_{33}H_{41}O_8F_3Na$ [M+Na$^+$]: 645.2646, found: 645.2645.

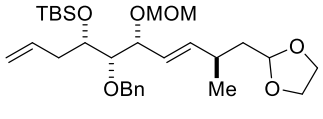


The corresponding ester (*R*)-**S5** (11.7 mg, 46%) was prepared analogously: $[\alpha]_D^{20}$ = –34.4 (c = 1.17, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61–7.55 (m, 2H), 7.40–7.23 (m, 8H), 5.73 (dddd, *J* = 16.9, 10.5, 7.5, 6.4 Hz, 1H), 5.50 (ddd, *J* = 15.5, 8.0, 0.7 Hz, 1H), 5.35–5.28 (m, 1H), 5.22 (ddd, *J* = 15.6, 8.3, 1.0 Hz, 1H), 5.12–5.10 (m, 1H), 5.07 (dd, *J* = 10.2, 1.7 Hz, 1H), 4.79 (dd, *J* = 5.7, 4.6 Hz, 1H), 4.69 (d, *J* = 11.7 Hz, 1H), 4.62 (d, *J* = 6.7 Hz, 1H), 4.53 (d, *J* = 11.7 Hz, 1H), 4.48 (d, *J* = 6.6 Hz, 1H), 4.07 (dd, *J* = 8.3, 5.7 Hz, 1H), 3.97–3.90 (m, 2H), 3.83–3.77 (m, 2H), 3.56–3.48 (m, 4H), 3.29 (s, 3H), 2.65 (dddd, *J* = 12.0, 6.6, 3.5, 1.5 Hz, 1H), 2.57–2.45 (m, 1H), 2.41–2.30 (m, 1H), 1.72–1.54 (m, 2H), 0.98 (d, *J* = 6.8 Hz, 3H) ppm. IR (film): $\tilde{\nu}$ = 2954, 2886, 1746, 1453, 1254, 1168, 1124, 1026, 920, 721, 698 cm^{-1}. MS (EI) *m/z* (%): 1267.5 (15), 1123.5 (3), 645.3 (100), 501.3 (4). HRMS (ESIpos) *m/z* calcd for $C_{33}H_{41}O_8F_3Na$ [M+Na$^+$]: 645.2646, found: 645.2647.

Table S-2. Mosher ester analysis for product **16** according to Hoye and co-workers;[12] arbitrary numbering scheme as shown in the insert

Assignment	16 [ppm]	(*S*)-S5 [ppm]	(*R*)-S5 [ppm]	Δ (δ (S–R)) [ppm]
1a	5.07	5.06	5.11	–0.05
1b	5.04	5.02	5.07	–0.05
2	5.79	5.68	5.73	–0.05
3a	2.36	2.62	2.65	–0.03
3b	2.30	2.42	2.50	–0.08
4	3.75	5.37	5.30	+0.07
5	3.35	3.57	3.53	+0.04
6	4.30	4.19	4.07	+0.12
7	5.43	5.37	5.22	+0.15
8	5.70	5.56	5.50	+0.06
9	2.44	2.42	2.35	+0.07
10	1.05	0.99	0.98	+0.01
11ab	1.66	1.63	1.61	+0.02
12	4.83	4.80	4.79	+0.01
13a	4.90	4.74	4.69	+0.05
13b	4.63	4.62	4.53	+0.09
14a	4.72	4.68	4.62	+0.06
14b	4.56	4.52	4.48	+0.04
15	3.33	3.34	3.29	+0.05

Compound S6. 2,6-Lutidine (3.7 mL, 32 mmol) and TBSOTf (5.44 mL, 23.7 mmol) were added to a solution of alcohol **16** (6.42 g, 15.8 mmol) in CH_2Cl_2 (100 mL) at 0 °C. The mixture was stirred at 0 °C for 2 h before the reaction was quenched with sat. NH_4Cl (50 mL). The aq. phase was separated and extracted with CH_2Cl_2 (2 × 100 mL). The combined organic phases were washed with brine (100 mL), dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography (hexane/EtOAc 80:20) to give the title compound as a colourless syrup (7.21 g, 88%). $[\alpha]_D^{20}$ = –68.4 (c = 1.02, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48–7.22 (m, 5H), 5.89–5.73 (m, 1H), 5.56 (dd, *J* = 15.6, 7.7 Hz, 1H), 5.43 (ddd, *J* = 15.6, 8.3, 0.9 Hz, 1H), 5.08–5.04 (m, 1H), 5.02 (d, *J* = 1.3 Hz, 1H), 4.81 (dd, *J* = 5.8, 4.5 Hz, 1H), 4.72–4.67 (m, 3H), 4.53 (d, *J* = 6.7 Hz, 1H), 4.24 (dd, *J* = 8.2, 4.3 Hz, 1H), 3.97–3.91 (m, 2H), 3.92–3.87 (m, 1H), 3.82–3.76 (m, 2H), 3.35 (s, 3H), 3.34–3.30 (m, 1H), 2.60–2.45 (m, 1H), 2.45–2.27 (m, 2H), 1.80–1.58 (m, 2H), 0.99 (d, *J* = 6.8 Hz, 3H), 0.89 (s, 9H), 0.02 (s, 3H), –0.01 (s, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 140.2, 138.9, 135.8, 128.4, 128.2, 127.6, 126.1, 117.0, 103.6, 93.6, 83.5, 76.4, 74.6, 72.6, 64.9, 64.8, 56.0, 40.8, 37.8, 33.1, 26.1, 20.8, 18.3, –4.2, –4.2 ppm. IR (film): $\tilde{\nu}$ = 2954, 2884, 1472,1255, 1147, 1098,



1028, 916, 835 cm^{-1}. MS (EI) *m/z* (%): 1063.6 (30), 543.3 (100), 459.3 (13), 351.2 (3). HRMS (ESIpos) *m/z* calcd for $C_{29}H_{48}O_6SiNa$ [M+Na$^+$]: 543.3112, found: 543.3111.

Alcohol 17. DDQ (233 mg, 1.00 mmol) was added in a single portion to a pre-heated solution of the benzyl ether **S6** (134 mg, 0.257 mmol) in a mixture of 1,2-dichloro-ethane (1.5 mL) and pH 7.4 buffer solution (1.5 mL) at 50 °C. The mixture was stirred at this temperature for 50 min before allowing the reaction to reach ambient temperature. The mixture was diluted with *t*-butyl methyl ether (20 mL) and the separated organic phase was washed with sat. $NaHCO_3$ (5 mL) and brine (5 mL). The organic phase was dried over Na_2SO_4 and concentrated, and the residue was purified by flash chromatography (hexane/EtOAc 70:30) to give the title compound as a colourless syrup (77.1 mg, 70%). $[\alpha]_D^{20}$ = –72.4 (c = 1.11, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.77 (ddt, *J* = 17.4, 10.2, 7.2 Hz, 1H), 5.64 (ddd, *J* = 15.6, 8.0, 0.7 Hz, 1H), 5.34 (ddd, *J* = 15.6, 8.5, 1.1 Hz, 1H), 5.13–5.04 (m, 2H), 4.83 (dd, *J* = 5.6, 4.7 Hz, 1H), 4.73 (d, *J* = 6.6 Hz, 1H), 4.56 (d, *J* = 6.7 Hz, 1H), 4.04 (dd, *J* = 8.3, 6.3 Hz, 1H), 3.97–3.92 (m, 2H), 3.85–3.79 (m, 3H), 3.47 (td, *J* = 6.4, 3.5 Hz, 1H), 3.38 (s, 3H), 2.57 (d, *J* = 6.4 Hz, 1H), 2.52–2.41 (m, 2H), 2.30–2.21 (m, 1H), 1.75–1.60 (m, 2H), 1.05 (d, *J* = 6.8 Hz, 3H), 0.91 (s, 9H), 0.10 (s, 3H), 0.09 (s, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 141.8, 134.2, 125.1, 117.7, 103.4, 93.4, 77.2, 77.0, 74.5, 71.6, 64.7 (2C), 55.5, 40.7, 38.5, 33.2, 25.9, 20.9, 18.1, –3.8, –4.4 ppm. IR (film): $\tilde{\nu}$ = 3494, 2954, 2929, 2885, 2857, 1472, 1408, 1361, 1253, 1147, 1094, 1030, 917, 836, 776 cm^{-1}. MS (EI) *m/z* (%): 883.5 (40), 453.3 (100), 369.2 (22), 237.1 (3). HRMS (ESIpos) *m/z* calcd for $C_{22}H_{42}O_6SiNa$ [M+Na$^+$]: 453.2643, found: 453.2645.

Alcohol 18. $Co(nmp)_2$ (355 mg, 0.628 mmol) was added to a solution of alcohol **17** (2.63 g, 6.12 mmol) in *i*-PrOH (61 mL). The solution was degassed by 3 freeze-pump-thaw cycles and back-filled with oxygen. After adding *t*-BuOOH (5 M in decane, 122 µL, 0.612 mmol), a balloon of oxygen was fitted to the flask which was placed in a pre-heated oil bath at 55 °C. The mixture turned green within 5 min of heating and stirring was continued for 16 h. After reaching ambient temperature, the mixture was concentrated to a green oil, which was purified by flash chromatography (hexane/EtOAc 20:80) to give the title product as a colourless syrup (1.89 g, 69% , dr ≥ 20:1). $[\alpha]_D^{20}$ = –19.7 (c = 1.04, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.74 (ddd, *J* = 15.7, 7.6, 1.1 Hz, 1H), 5.44 (ddd, *J* = 15.7, 6.7, 1.1 Hz, 1H), 4.84 (dd, *J* = 5.8, 4.6 Hz, 1H), 4.72 (d, *J* = 6.5 Hz, 1H), 4.66 (d, *J* = 6.5 Hz, 1H), 4.43–4.34 (m, 1H), 4.31 (q, *J* = 3.2 Hz, 1H), 4.27 (ddd, *J* = 7.7, 6.6, 0.9 Hz, 1H), 4.00–3.90 (m, 2H), 3.87–3.74 (m, 4H), 3.49 (dd, *J* = 11.6, 5.7 Hz, 1H), 3.39 (s, 3H), 2.43 (dddd, *J* = 14.4, 7.7, 6.7, 1.1 Hz, 1H), 2.07–1.97 (m, 1H), 1.94–1.88 (m, 2H), 1.71 (ddd, *J* = 13.7, 7.7, 4.6 Hz, 1H), 1.66–1.56 (m, 1H), 1.06 (d, *J* = 6.8 Hz, 3H), 0.91 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 140.0, 125.2, 103.5, 94.3, 86.5, 78.6, 75.4, 73.4, 64.9, 64.8, 64.7, 55.5, 40.8, 37.1, 33.1, 26.0, 20.9, 18.1, –3.9, –4.6 ppm. IR (film): $\tilde{\nu}$ = 3467, 2954, 2927, 2885,

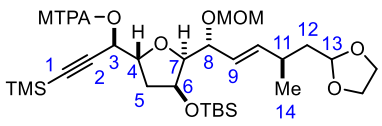
2856, 1472, 1361, 1255, 1131, 1035, 942, 836, 775 cm^{-1}. MS (EI) *m/z* (%): 915.5 (30), 469.3 (100), 385.2 (10). HRMS (ESIpos) *m/z* calcd for $C_{22}H_{42}O_7SiNa$ [M+Na^+]: 469.2592, found: 469.2597.

Aldehyde S7. Hünig's base (2.8 mL, 16 mmol) was added at –30 °C to a solution of alcohol **18** (1.13 g, 2.53 mmol) in CH_2Cl_2 (16 mL) and the resulting mixture was stirred for 5 min at this temperature. In a second flask a suspension of sulfur trioxide pyridine complex (1.26 g, 7.92 mmol) in CH_2Cl_2 (2.0 mL) was treated with DMSO (2.3 mL, 27 mmol) and the resulting mixture was stirred for 15 min at ambient temperature. This suspension was added to the alcohol solution at –30 °C, rinsing the flask with CH_2Cl_2 (5.0 mL). The mixture was allowed to slowly reach –20 °C over 1 h and stirring was continued for another 0.5 h at this temperature. The mixture was diluted with *t*-butyl methyl ether (20 mL) and the reaction was quenched with pH 7 phosphate buffer (50 mL). The aq. phase was separated and extracted with *t*-butyl methyl ether (3 × 50 mL). The combined organic phases were washed with brine (150 mL), dried over Na_2SO_4 and concentrated under reduced pressure to yield the crude aldehyde **S7** as a yellow oil which was used in the next step without further purification. An aliquot was purified for analytical purposes by flash chromatography (EtOAc/hexane 1:1). $[\alpha]_D^{20}$ = –0.4 (c = 0.79, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.74 (d, *J* = 2.5 Hz, 1H), 5.77 (ddd, *J* = 15.6, 7.6, 1.0 Hz, 1H), 5.44 (ddd, *J* = 15.7, 6.9, 1.1 Hz, 1H), 4.84 (dd, *J* = 5.7, 4.6 Hz, 1H), 4.73 (d, *J* = 6.5 Hz, 1H), 4.66 (d, *J* = 6.5 Hz, 1H), 4.54 (ddd, *J* = 9.6, 7.2, 2.5 Hz, 1H), 4.35–4.25 (m, 2H), 3.98–3.92 (m, 2H), 3.86 (dd, *J* = 7.6, 3.3 Hz, 1H), 3.83–3.78 (m, 2H), 3.39 (s, 3H), 2.50–2.37 (m, 1H), 2.18 (ddd, *J* = 13.0, 7.2, 2.3 Hz, 1H), 2.00 (ddd, *J* = 13.3, 9.4, 4.5 Hz, 1H), 1.71 (ddd, *J* = 13.9, 7.7, 4.6 Hz, 1H), 1.65–1.58 (m, 1H), 1.06 (d, *J* = 6.8 Hz, 3H), 0.91 (s, 9H), 0.10 (s, 3H), 0.08 (s, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 203.1, 140.6, 124.8, 103.5, 94.2, 87.5, 82.1, 74.9, 72.3, 64.9, 64.8, 55.6, 40.8, 37.2, 33.1, 25.9, 20.9, 18.1, −3.9, –4.6 ppm. IR (film) $\tilde{\nu}$ = 2956, 2928, 2884, 2858, 1733, 1472, 1258, 1128, 1097, 1028, 976, 939, 924, 833, 802, 775, 755, 733 cm^{-1}. MS (ESIpos) *m/z* (%): 467.2 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{22}H_{40}O_7SiNa$ [M+Na^+]: 467.2436, found: 467.2439.

Propargyl Alcohol 19. A Schlenk tube was charged with $Zn(OTf)_2$ (dried at 120 °C under high vacuum for 24 h, 2.25 mg, 6.18 mmol) and (–)-*N*-methylephedrine (dried azeotropically by distilling toluene off the compound (3 x), 1.18 g, 6.60 mmol). After the addition of toluene (6.0 mL), Hünig's base (1.2 mL, 6.9 mmol) was added and the resulting suspension was stirred for 2 h at ambient temperature before ethynyltrimethylsilane (0.91 mL, 6.3 mmol) was introduced. After stirring for another 1.5 h at ambient temperature, a solution of aldehyde **S7** (1.09 g, 2.45 mmol) in toluene (15.0 mL with rinses) was added in one portion to the milky suspension. After stirring for 18 h at ambient temperature, the reaction was quenched with sat. NH_4Cl (50 mL). The aq. phase was separated and extracted with *t*-butyl methyl ether (3 × 50 mL). The combined organic phases were dried over Na_2SO_4, filtered and

concentrated. The residue was purified by flash chromatography (hexane/ EtOAc 7:3) to provide the title compound as a yellow oil (0.96 g, 65% over 2 steps, dr = 10.7:1). $[\alpha]_D^{20}$ = –163 (c = 1.11, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.74 (ddd, *J* = 15.7, 7.6, 1.0 Hz, 1H), 5.43 (ddd, *J* = 15.7, 6.6, 1.2 Hz, 1H), 4.83 (dd, *J* = 5.8, 4.6 Hz, 1H), 4.70 (d, *J* = 6.6 Hz, 1H), 4.64 (d, *J* = 6.6 Hz, 1H), 4.36–4.22 (m, 4H), 3.983.91 (m, 2H), 3.85–3.79 (m, 2H), 3.76 (dd, *J* = 7.8, 3.3 Hz, 1H), 3.39 (s, 3H), 2.65 (br s, 1H), 2.42 (ddq, *J* = 7.0, 7.0, 7.0 Hz, 1H), 2.05 (ddd, *J* = 13.1, 6.1, 2.0 Hz, 1H), 1.91 (ddd, *J* = 13.2, 9.1, 4.5 Hz, 1H), 1.70 (ddd, *J* = 13.7, 7.7, 4.6 Hz, 1H), 1.60 (ddd, *J* = 13.1, 6.1, 6.1 Hz 1H), 1.05 (d, *J* = 6.8 Hz, 3H), 0.91 (s, 9H), 0.15 (s, 9H), 0.10 (s, 3H), 0.08 (s, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 138.9, 124.0, 102.7, 102.5, 93.2, 89.6, 85.7, 80.1, 74.1, 72.1, 65.0, 63.9, 63.8, 54.6, 39.8, 37.1, 32.1, 25.0, 19.9, 17.2, −1.1, −4.9, −5.6 ppm. IR (film) $\tilde{\nu}$ = 3432, 2956, 2929, 2886, 2858, 1472, 1408, 1361, 1251, 1129, 1099, 1036, 949, 841, 775 cm^{-1}. MS (ESIpos) *m/z* (%): 565.3 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{27}H_{50}O_7Si_2Na$ [M+Na$^+$]: 565.2987, found: 565.2987.

Mosher Ester Analysis of Propargyl Alcohol 19. Hünig's base (9.0 µL, 52 µmol) was added to a solution of alcohol **19** (10.9 mg, 17 µmol) in CH_2Cl_2 (0.35 mL) followed by (*R*)-(–)-α-methoxy-α-trifluoromethyl-phenylacetyl chloride ((*R*)-MTPA-Cl) (6.0 µL, 32 µmol). After stirring for 17 h at ambient temperature, the mixture was diluted with CH_2Cl_2 (3 mL) and the reaction was quenched with sat. $NaHCO_3$ (3 mL). The aq. phase was separated and extracted with CH_2Cl_2 (3 × 5 mL). The combined organic phases were dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography (hexane/*t*-butyl methyl ether 4:1) to give the corresponding (*S*)-Mosher ester (*S*)-**S8** (10 mg, 76%). $[\alpha]_D^{20}$ = –38.8 (c = 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.59–7.55 (m, 2H), 7.39 (tdd, *J* = 3.5, 2.3, 1.1 Hz, 3H), 5.72 (ddd, *J* = 15.8, 7.6, 1.1 Hz, 1H), 5.62 (d, *J* = 6.2 Hz, 1H), 5.43 (ddd, *J* = 15.6, 6.7, 1.1 Hz, 1H), 4.83 (dd, *J* = 5.8, 4.6 Hz, 1H), 4.64–4.59 (m, 2H), 4.41 (dt, *J* = 8.4, 6.5 Hz, 1H), 4.29 (ddd, *J* = 3.9, 3.3, 2.8 Hz, 1H), 4.21 (dd, *J* = 7.7, 6.6 Hz, 1H), 3.98–3.91 (m, 2H), 3.83–3.79 (m, 2H), 3.78 (dd, *J* = 7.5, 3.6 Hz, 1H), 3.57 (d, *J* = 1.1 Hz, 3H), 3.32 (s, 3H), 2.47–2.35 (m, 1H), 2.05–1.96 (m, 2H), 1.70 (ddd, *J* = 13.8, 7.7, 4.6 Hz, 1H), 1.60 (dt, *J* = 13.5, 5.9 Hz, 1H), 1.05 (d, *J* = 6.8 Hz, 3H), 0.89 (s, 9H), 0.17 (s, 9H), 0.06 (s, 3H), 0.06 (s, 3H) ppm. IR (film) $\tilde{\nu}$ = 2956, 2930, 2886, 2858, 1757, 1251, 1185, 1170, 1124, 1035, 844, 776 cm^{-1}. MS (ESIpos) *m/z* (%): 781.3 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{37}H_{57}O_9Si_2F_3Na$ [M+Na$^+$]: 781.3385, found: 781.3392.



The corresponding Mosher ester (*R*)-**S8** (13.7 mg, 92%) was prepared analogously: $[\alpha]_D^{20}$ = –26.0 (c = 1.3, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.58–7.52 (m, 2H), 7.42–7.35 (m, 3H), 5.73 (ddd, *J* = 15.7, 7.5, 1.0 Hz, 1H), 5.51–5.40 (m, 2H), 4.83 (dd, *J* = 5.8, 4.5 Hz, 1H), 4.63 (s, 2H), 4.47 (ddd, *J* = 8.8, 7.4, 6.4 Hz, 1H), 4.32 (dq, *J* = 4.6, 2.5 Hz, 1H), 4.26–4.19 (m, 1H), 4.00–3.90 (m, 2H), 3.86–3.77 (m, 3H), 3.65–3.57 (m, 3H), 3.31 (s, 3H), 2.48–2.36 (m, 1H), 2.11 (ddd, *J* = 13.1, 6.5, 2.4 Hz, 1H), 1.98 (ddd, *J* = 13.3,

8.9, 4.7 Hz, 1H), 1.70 (ddd, *J* = 13.8, 7.7, 4.6 Hz, 1H), 1.62 (dt, *J* = 13.6, 6.3, 5.8 Hz, 1H), 1.05 (d, *J* = 6.7 Hz, 3H), 0.90 (s, 9H), 0.14 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H) ppm. IR (film) $\tilde{\nu}$ = 2956, 2930, 2886, 2858, 1757, 1251, 1185, 1170, 1124, 1035, 844, 776 cm^{-1}. MS (ESIpos) *m/z* (%): 781.3 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{37}H_{57}O_9Si_2F_3Na$ [M+Na^+]: 781.3385, found: 781.3396.

Table S-3. Mosher ester analysis for product **19** according to Hoye and co-workers;[12] arbitrary numbering scheme as shown in the insert

Assignment	19 [ppm]	(*S*)-S8 [ppm]	(*R*)-S8 [ppm]	Δ (δ (S–R)) [ppm]
3	4.23	5.62	5.48	+0.19
4	4.31	4.41	4.47	–0.06
5a	2.04	2.02	2.11	–0.09
5b	1.92	1.99	1.98	+0.01
6	4.31	4.29	4.32	–0.03
7	3.76	3.78	3.81	–0.03
8	4.27	4.21	4.22	–0.01
9	5.43	5.43	5.44	–0.01
10	5.73	5.72	5.73	–0.02
11	2.42	2.41	2.42	+0.01
12a	1.70	1.70	1.70	0
12b	1.61	1.60	1.62	–0.02
13	4.83	4.83	4.83	0
14	1.05	1.05	1.05	0
TMS-Me	0.15	0.17	0.14	+0.03

Terminal Alkyne S9. K_2CO_3 (350 mg, 2.53 mmol) was added to a solution of TMS-alkyne **19** (890 mg, 1.64 mmol) in dry methanol (16 mL) at 0 °C. The suspension was allowed to warm to ambient temperature, while it was vigorously stirred for 2 h. The mixture was diluted with *t*-butyl methyl ether (20 mL) and the reaction was quenched with sat. NH_4Cl (5 mL). The organic phase was separated and the aq. phase was extracted with *t*-butyl methyl ether (2 × 20 mL). The combined organic phases were washed with brine (20 mL), dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography (hexane/EtOAc 60:40 to 40:60) to provide the title compund as a colourless syrup (698 mg, 85%, dr = 16:1). $[\alpha]_D^{20}$ = −20.7 (c = 2.26, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): *see Table S-4;* ^{13}C NMR (126 MHz, $CDCl_3$): *see Table S-4*. ^{29}Si NMR (99 MHz, $CDCl_3$) δ = 19.00 ppm. IR (film): $\tilde{\nu}$ = 3420, 3309, 2955, 292, 2885, 2857, 1472, 1361, 1254, 1127, 1099, 1063, 947, 835, 775 cm^{-1}. MS (EI) *m/z* (%): 963.5 (13), 493.3 (100). HRMS (ESIpos) *m/z* calcd for $C_{24}H_{42}O_7SiNa$ [M+Na^+]: 493.2592, found: 493.2594.

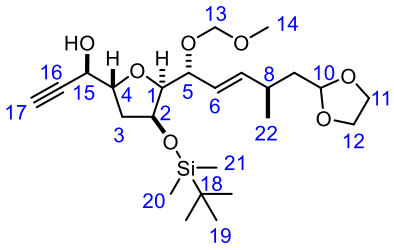
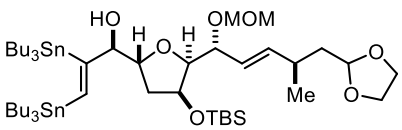


Table S-4. NMR data of terminal alkyne **S9**; arbitrary numbering scheme as shown in the insert

atom n°	^{1}H NMR (500 MHz, $CDCl_3$)					^{13}C NMR (126 MHz, $CDCl_3$)	
	δ [ppm]	m	*J* [Hz]	COSY	NOESY	δ [ppm]	HMBC
1	3.76	dd	7.8, 3.3	(2), 5	(3b)	86.6	3, (4), 5, 6
2	4.30	m	-	(1)	(21), (22), (19), (6)	73.0	(1), 3b, (5)
3a	2.06	ddd	13.1, 6.4, 2.0	3b, 4	4	37.9	(4)
3b	1.93	ddd	13.2, 8.9, 4.5	2, 3a, 4	(1), 15		
4	4.35	dt	8.9, 6.2	3ab, (15)	3a, 15-OH	80.9	3a, (15)
5	4.26	t	7.2	1, 6	7, 13ab, (14)	75.2	6, 7, 13ab
6	5.43	dd	15.7, 6.6	5, 7	(2), 8, (22)	125.0	5, 8
7	5.73	dd	15.7, 7.6	6, 8	5, (22)	140.0	5, 8, 9ab, 22
8	2.42	sept	7.0	9a, 7, 22	6, 22	33.1	6, 7, 10, 9ab
9a	1.70	ddd	14.0, 7.8, 4.6	9b, 8, (10)	9b	40.8	6, 7, 8
9b	1.60	dt	13.9, 6.2	9a, (10)	9a, 22		
10	4.83	dd	5.8, 4.6	(9ab)	(22)	103.5	11ab,12ab
11a	3.98–3.90	m	-	11b	11b, 12ab	64.9	12ab
11b	3.85–3.78	m	-	11a	11a, 12ab		
12a	3.98–3.90	m	-	12b	11ab, 12b	64.8	11ab
12b	3.85–3.78	m	-	12a	11ab, 12a		
13a	4.70	d	6.6	13b	5, 14	94.3	5, 8, 9ab, 14
13b	4.64	d	6.6	13a	2, 5, 14		
14	3.38	s	-	-	13ab, (5)	55.6	13ab
15	4.24	ddbr	6.2, -	4, (17)	(15-OH), 3b	65.3	3a(b), 17
16	-	-	-	-	-	82.1	4, (15), (15-OH), 17
17	2.42	d	2.1	15	-	73.8	-
18	-	-	-	-	-	18.1	19, 20 , 21
19	0.90	s	-	-	20, 21, (2)	26.0	-
20	0.09	s	-	-	19, (2)	–3.9	21
21	0.07	s	-	-	19, (2)	–4.6	20
22	1.05	d	6.8	8	(6), (7), 8, 9b, (10)	20.9	7, 8, 9ab
15-OH	2.92	ddbr	-, -	15	(4), (15)	-	-

Bis(alkenyl)stannane 6a. [(*t*BuNC)$_2$PdCl$_2$] (21 mg, 61 µmol) was added to a solution of alkyne **S9**

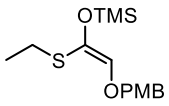


(284 mg, 0.603 mmol) in THF (2.0 mL) at ambient temperature. After dropwise addition of hexabutyldistannane (0.45 mL, 0.89 mmol) to the orange suspension, the mixture turned into a dark red solution, which colour intensity increased over time. After stirring for 20 h at ambient temperature, the mixture was concentrated under reduced pressure. The residual oil was purified by

flash chromatography ((hexane/NEt_3 99:1)/*t*-butyl methyl ether 9:1 to 8:1) to afford the title compound as a yellow-orange oil (588 mg, 93%). $[\alpha]_D^{20}$ = –8.1 (c = 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.81 (ddd, *J* = 1.2 Hz, J_{SnH} = 178.0, 63.6 Hz, 1H), 5.74 (ddd, *J* = 15.7, 7.6, 1.1 Hz, 1H), 5.43 (ddd, *J* = 15.7, 6.3, 1.1 Hz, 1H), 4.83 (dd, *J* = 5.8, 4.6 Hz, 1H), 4.69 (d, *J* = 6.5 Hz, 1H), 4.64 (d, *J* = 6.6 Hz, 1H), 4.29–4.23 (m, 2H), 4.13 (ddd, *J* = 9.2, 7.9, 6.0 Hz, 1H), 3.99–3.91 (m, 2H), 3.87–3.76 (m, 3H), 3.71 (dd, *J* = 8.1, 3.0 Hz, 1H), 3.38 (s, 3H), 2.82 (d, *J* = 2.0 Hz, 1H), 2.42 (ddt, *J* = 13.8, 6.3, 6.3 Hz, 1H), 1.82 (ddd, *J* = 13.1, 6.2, 1.7 Hz, 1H), 1.76–1.66 (m, 2H), 1.61 (ddd, *J* = 13.8, 6.6, 5.8 Hz, 1H), 1.55–1.38 (m, 12H), 1.31 (tt, *J* = 7.2, 7.2 Hz, 12H), 1.05 (d, *J* = 6.8 Hz, 3H), 0.99–0.82 (m, 39H), 0.06 (s, 6H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.1, 144.3, 139.5, 125.2, 103.5, 94.4, 87.8, 86.3, 80.4, 75.2, 73.4, 64.9, 64.8, 55.5, 40.8, 38.7, 33.1, 29.4, 29.3, 27.7, 27.5, 26.0, 20.9, 18.1, 13.8, 13.8, 11.5, 11.0, –3.8, –4.6 ppm. ^{119}Sn NMR (149 MHz, $CDCl_3$): δ = −59.2, –66.6 ppm. IR (film) $\tilde{\nu}$ = 3476, 2955, 2927, 2871, 2855, 1464, 1376, 1256, 1124, 1101, 1041, 951, 835, 775, 670 cm^{-1}. MS (ESIpos) *m/z* (%): 1073.5 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{48}H_{96}O_7SiSn_2Na$ [M+Na$^+$]: 1075.4860, found: 1075.4879.

Fragment 6b

Silyl Enol Ether 25. A solution of *n*-BuLi (1.6 M in THF, 4.2 mL, 6.7 mmol) was added dropwise to a solution of 2,2,6,6-tetramethylpiperidine (1.14 mL, 6.73 mmol) in THF (40 mL) at 0 °C. After removing the ice bath, the solution was stirred for 10 min at ambient temperature. After cooling the LiTMP solution to −105 °C, *S*-ethyl 2-((4-methoxybenzyl)oxy)ethanethioate (1.44 g, 5.99 mmol) was added dropwise. After stirring for 5 min, TMSCl (0.85 mL, 6.7 mmol) was added dropwise at the same temperature. After stirring for 30 min, the cold bath was removed and the mixture was concentrated under reduced pressure. The residue was diluted with hexane (20 mL) and filtered through a pad of dry Celite® under argon. After rinsing with hexane (2 × 10 mL), the combined filtrates were concentrated under reduced pressure. The residual yellow oil was used without further purification (1.71 g, 91%, *Z*/*E* = 9:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30–7.26 (m, 2H), 6.90–6.86 (m, 2H), 6.24 (s, 1H), 4.71 (s, 2H), 3.80 (s, 3H), 2.67 (q, *J* = 7.4 Hz, 2H), 1.23 (t, *J* = 7.4 Hz, 3H), 0.16 (s, 9H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 159.4, 136.9, 132.7, 129.4, 128.1, 113.8, 73.9, 55.3, 25.2, 15.0, 0.0 ppm. IR (film): $\tilde{\nu}$ = 2959, 2929, 1613, 1514, 1456, 1250, 1154, 1036, 870, 845 cm^{-1}. MS (ESIpos) *m/z* (%): 313 (100 (M+H)). HRMS (ESIpos): *m/z* calcd for $C_{15}H_{24}O_3SSiNa$ [M+Na$^+$]: 313.1288, found: 313.1288.



General Procedure for Mukaiyama Aldol Reaction. (*S*)-1-Methyl-2-(piperidinomethyl)-pyrrolidin (175 mol%) was added to a suspension of tin(II) triflate (150 mol%) in CH_2Cl_2 (0.09-0.20 M). After addition of dibutyltin diacetate (164 mol%) to the orange solution, the reaction was stirred for 30 min at ambient temperature. After cooling the light yellow solution to −65 °C, a solution of silyl enol ether

(150 mol%) in CH_2Cl_2 was added followed by a solution of aldehyde **13** (617 mg, 3.63 mmol) in CH_2Cl_2 (0.20 M). After stirring for 18 h at −65 °C, sat. $NaHCO_3$ (7.5 mL) was added to the cold mixture and the cold bath was removed. After reaching ambient temperature, the mixture was diluted with EtOAc (50 mL) and water (50 mL). The aq. phase was separated and extracted with EtOAc (2 × 50 mL). The combined organic phases were washed with brine (50 mL), dried over Na_2SO_4 and concentrated. The yellow residual oil was purified by flash chromatography (hexane/*t*-butyl methyl ether 2:3 to 1:1 to 3:7) to provide the title compounds.

Recovery of (*S*)-1-Methyl-2-(piperidinomethyl)-pyrrolidine (**26**): The aq. phase was treated with aq. solution of NaOH (10 w-%) until the solution reached pH = 14. After extracting the aq. phase with *t*-butyl methyl ether (3 × 50 mL) the combined organic phases were dried over Na_2SO_4 and concentrated. The residue was purified by Kugelrohr distillation, collecting the fraction that distilled between 115–125 °C at 12 mbar to give the diamine **26** as a colourless.

Aldol S10. According to General Procedure using (*Z*)-((2-(benzyloxy)-1-(ethylthio)vinyl)oxy)-trimethylsilane (*Z*/*E* = 78:22, 405 mg, 1.44 mmol) and aldehyde **13** in CH_2Cl_2 (0.09 M). Yellow oil (79 mg, 33%, >20:1 dr). $[\alpha]_D^{20}$ = +47.2 (c = 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.43–7.30 (m, 5H), 5.63 (ddd, *J* = 15.4, 7.5, 0.8 Hz, 1H), 5.52 (ddd, *J* = 15.5, 6.9, 0.8 Hz, 1H), 4.87–4.82 (m, 2H), 4.53 (d, *J* = 11.3 Hz, 1H), 4.33 (dd, *J* = 6.4, 5.0 Hz, 1H), 4.02 (d, *J* = 4.8 Hz, 1H), 3.95–3.89 (m, 2H), 3.83–3.76 (m, 2H), 2.87 (q, *J* = 7.3 Hz, 2H), 2.47–2.25 (m, 2H), 1.68 (ddd, *J* = 13.8, 8.1, 4.3 Hz, 1H), 1.59 (dt, *J* = 7.7, 6.1 Hz, 1H), 1.25 (t, *J* = 7.4 Hz, 3H), 1.02 (d, *J* = 6.8 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 201.7, 139.5, 136.9, 128.5, 128.2, 128.1, 125.5, 103.3, 87.4, 74.3, 73.7, 64.7, 64.7, 40.5, 32.8, 22.5, 20.6, 14.5 ppm. IR (film): $\tilde{\nu}$ = 3446, 2960, 2876, 1677, 1455, 1131, 1029, 973, 739, 701 cm^{-1}. MS (ESIpos) *m/z* (%): 403.2 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{20}H_{28}O_5SNa$ [M+Na$^+$]: 403.1550, found: 403.1554.

Mosher Ester Analysis of Alcohol S10. Hünig's base (9.6 µL, 55 µmol) was added to a solution of alcohol **S10** (7.5 mg, 20 µmol) in CH_2Cl_2 (0.3 mL) followed by (*S*)-(–)-α-methoxy-α-trifluoromethyl-phenylacetyl chloride ((*S*)-MTPA-Cl) (7.0 µL, 37 µmol). The mixture was stirred at ambient temperature for 17 h, diluted with CH_2Cl_2 (2 mL) and sat. NH_4Cl (2 mL). The aq. phase was separated and extracted with CH_2Cl_2 (2 × 2 mL). The combined organic phases were dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography (hexane/*t*-butyl methyl ether = 9:1) to give the corresponding (*R*)-Mosher ester (*R*)-**S11** (8.8 mg, 75%), which analyzed as follows: $[\alpha]_D^{20}$ = +50.0 (c = 0.88, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.53–7.48 (m, 2H), 7.39–7.29 (m, 8H), 5.77–5.69 (m, 2H), 5.48 (ddd, *J* = 15.6, 8.3, 1.0 Hz, 1H), 4.76 (dd, *J* = 6.3, 4.1 Hz, 1H), 4.70 (d, *J* = 11.3 Hz, 1H), 4.54 (d,

J = 11.3 Hz, 1H), 4.16 (d, *J* = 3.5 Hz, 1H), 3.94–3.89 (m, 2H), 3.78–3.73 (m, 2H), 3.50 (d, *J* = 0.9 Hz, 3H), 2.86 (dq, *J* = 13.4, 7.5 Hz, 1H), 2.79 (dq, *J* = 13.4, 7.4 Hz, 1H), 2.41 (dddd, *J* = 15.2, 8.0, 4.7, 1.2 Hz, 1H), 1.65 (ddd, *J* = 13.8, 8.5, 4.1 Hz, 1H), 1.56 (dt, *J* = 13.9, 6.3 Hz, 1H), 1.20 (t, *J* = 7.4 Hz, 3H), 0.98 (d, *J* = 6.7 Hz, 3H) ppm. IR (film): $\tilde{\nu}$ = 2958, 2876, 1751, 1678, 1453, 1270, 1247, 1169, 1124, 1082, 1017, 976, 765, 737, 720, 699 cm^{-1}. MS (ESIpos) *m/z* (%): 619.2 (100 (M+Na)). HRMS (ESI): *m/z* calcd for $C_{30}H_{35}O_7F_3SNa$ [$M+Na^+$]: 619.1948, found: 619.1955.

The corresponding Mosher ester (*S*)-**S11** (10.8 mg, 85%) was prepared analogously: $[\alpha]_D^{20}$ = −20.7 (c = 1.08, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.57–7.50 (m, 2H), 7.42–7.34 (m, 3H), 7.33–7.22 (m, 5H), 5.85 – 5.74 (m, 2H), 5.60 (ddd, *J* = 15.5, 8.6, 0.9 Hz, 1H), 4.74 (dd, *J* = 6.3, 4.1 Hz, 1H), 4.58 (d, *J* = 11.1 Hz, 1H), 4.42 (d, *J* = 11.1 Hz, 1H), 4.11 (d, *J* = 3.3 Hz, 1H), 3.93–3.85 (m, 2H), 3.75–3.67 (m, 2H), 3.54 (d, *J* = 1.3 Hz, 3H), 2.83 (dq, *J* = 13.4, 7.5 Hz, 1H), 2.76 (dq, *J* = 13.4, 7.4 Hz, 1H), 2.42 (hept, *J* = 7.2, 6.7, 6.4 Hz, 1H), 1.66 (ddd, *J* = 13.9, 8.5, 4.2 Hz, 1H), 1.57 (dt, *J* = 13.6, 6.5, 6.0 Hz, 1H), 1.20 (t, *J* = 7.4 Hz, 3H), 0.99 (d, *J* = 6.8 Hz, 3H) ppm. IR (film): $\tilde{\nu}$ = 2957, 2877, 1750, 1677, 1453, 1269, 1246, 1168, 1123, 1081, 1017, 976, 739, 718, 699 cm^{-1}. MS (ESIpos) *m/z* (%): 619.2 (100 (M+Na)). HRMS (ESI): *m/z* calcd for $C_{30}H_{35}O_7F_3SNa$ [$M+Na^+$]: 619.1948, found: 619.1954.

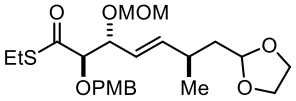
Table S-5. Mosher ester analysis for product **S10** according to Hoye and co-workers;[12] arbitrary numbering scheme as shown in the insert

Assignment	S10 [ppm]	(*S*)-S11 [ppm]	(*R*)-S11 [ppm]	Δ (δ(*S*–*R*)) [ppm]
2	4.02	4.11	4.16	−0.05
3	4.33	5.78	5.73	+0.05
4	5.53	5.60	5.48	+0.12
5	5.63	5.79	5.73	+0.06
6	2.41	2.42	2.41	+0.01
7a	1.67	1.66	1.65	+0.01
7b	1.59	1.57	1.56	+0.01
8	4.84	4.74	4.76	–0.02
9	1.02	0.99	0.98	+0.01
10a	4.84	4.58	4.70	−0.12
10b	4.53	4.42	4.54	−0.12

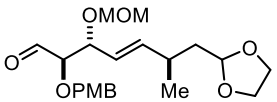
Aldol S12. According to General Procedure for Mukaiyama aldol using silyl enol ether **25** (1.70 g, 5.44 mmol) and aldehyde **13** in CH_2Cl_2 (0.20 M). Pale yellow oil (975 mg, 66%, >20:1 dr). Additionally, the diamine **26** was recovered as a colourless oil (551 g, 48%). $[\alpha]_D^{20}$ = +42.6 (c = 1.15, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.29 (m, 2H), 6.92–6.88 (m, 2H), 5.62 (ddd, *J* = 15.5, 7.5, 0.8 Hz, 1H), 5.50 (ddd, *J* = 15.5, 7.0,

0.8 Hz, 1H), 4.83 (dd, *J* = 6.0, 4.3 Hz, 1H), 4.77 (d, *J* = 11.0 Hz, 1H), 4.45 (d, *J* = 11.0 Hz, 1H), 4.30 (ddd, *J* = 7.0, 4.9, 0.9 Hz, 1H), 3.99 (d, *J* = 4.8 Hz, 1H), 3.96– 3.89 (m, 2H), 3.83–3.77 (m, 5H), 2.88 (d, *J* = 7.4 Hz, 1H), 2.85 (d, *J* = 7.4 Hz, 1H), 2.40 (hept, *J* = 6.9 Hz, 1H), 2.10 (br s, 1H), 1.67 (ddd, *J* = 13.8, 8.1, 4.3 Hz, 1H), 1.57 (dt, *J* = 13.8, 6.1 Hz, 1H), 1.25 (t, *J* = 7.4 Hz, 3H), 1.01 (d, *J* = 6.8 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 201.8, 159.6, 139.4, 129.9, 129.0, 125.6, 113.9, 103.3, 87.0, 73.9, 73.7, 64.7, 64.7, 55.3, 40.5, 32.8, 22.5, 20.6, 14.5 ppm. IR (film): $\tilde{\nu}$ = 3474, 2960, 2933, 2876, 1676, 1613, 1514, 1456, 1303, 1248, 1129, 1032, 973, 822 cm^{-1}. MS (ESIpos) *m/z* (%): 433.2 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{21}H_{30}O_6SNa$ [M+Na$^+$]: 433.1655, found: 433.1656.

MOM-Ether 20. Tetrabutylammonium iodide (17 mg, 46 µmol), MOMCl (1.4 mL, 18 mmol) and Hünig's base (5.5 mL, 32 mmol) were added to a solution of alcohol **S12** (1.90 g, 4.63 mmol) in CH_2Cl_2 (25 mL) at 0 °C. After stirring for 15 min at 0 °C, the ice bath was removed and the mixture was stirred for 17 h at ambient temperature. The reaction was quenched with sat. NH_4Cl (20 mL). The aq. phase was separated and extracted with *t*-butyl methyl ether (3 × 25 mL). The combined organic phases were washed with brine (50 mL), dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography (hexane/*t*-butyl methyl ether 4:1 to 7:3) to afford the title compound as a pale yellow oil (1.70 g, 81%). $[\alpha]_D^{20}$ = −35.3 (c = 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.29 (m, 2H), 6.91–6.85 (m, 2H), 5.60 (ddd, *J* = 15.6, 7.8, 0.6 Hz, 1H), 5.43 (ddd, *J* = 15.5, 8.4, 1.0 Hz, 1H), 4.81 (dd, *J* = 5.9, 4.4 Hz, 1H), 4.72 (d, *J* = 11.3 Hz, 1H), 4.66 (d, *J* = 6.7 Hz, 1H), 4.55 (d, *J* = 11.3 Hz, 1H), 4.51 (d, *J* = 6.7 Hz, 1H), 4.30 (dd, *J* = 8.3, 4.4 Hz, 1H), 4.05 (d, *J* = 4.4 Hz, 1H), 3.96–3.90 (m, 2H), 3.82–3.76 (m, 5H), 3.31 (s, 3H), 2.90–2.80 (m, 2H), 2.49–2.37 (m, 1H), 1.67 (ddd, *J* = 13.8, 8.1, 4.5 Hz, 1H), 1.62–1.55 (m, 1H), 1.23 (t, *J* = 7.4 Hz, 3H), 1.01 (d, *J* = 6.8 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 201.3, 159.3, 142.0, 129.6, 129.4, 123.5, 113.7, 103.3, 93.4, 86.2, 77.8, 73.4, 64.7, 64.7, 55.4, 55.3, 40.6, 33.0, 22.5, 20.7, 14.5 ppm. IR (film): $\tilde{\nu}$ = 2955, 2932, 2883, 1678, 1613, 1514, 1456, 1302, 1248, 1140, 1092, 1030, 974, 823 cm^{-1}. MS (ESIpos) *m/z* (%): 477.2 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{23}H_{34}O_7SNa$ [M+Na$^+$]: 477.1917, found: 477.1919.

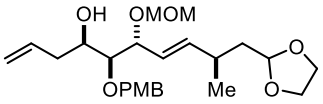


Aldehyde S13. Pd/C (10 wt.-%, 366 mg, 0.344 mmol, 10 mol%) and triethylsilane (1.8 mL, 11 mmol) were added to a solution of thioester **20** (1.70 g, 3.59 mmol) in CH_2Cl_2 (7.0 mL). After stirring for 2 h at ambient temperature, the reaction was filtered through a pad of Celite®, which was rinsed with CH_2Cl_2 (15 mL), and the combined filtrates were concentrated. Due to approximatly 72% conversion of thioester **20**, the residual yellow oil was dissolved in acetone (10 mL) and treated with Pd/C (10 wt.-%, 100 mg, 94.0 µmol, 2.6 mol%) and triethylsilane (0.60 mL, 3.8 mmol). After stirring for 2 h at ambient temperature, the reaction was filtered through a pad of Celite®, which was rinsed with CH_2Cl_2 (20 mL),



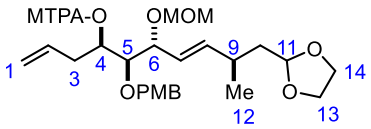
and the combined filtrates were concentrated. An analytical sample was purified by flash chromatography (hexane/*t*-butyl methyl ether 7:3) for characterization. The crude aldehyde was used without further purification in the next step. $[\alpha]_D^{20}$ = −27.1 (c = 1.19, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.60 (d, *J* = 2.3 Hz, 1H), 7.30–7.24 (m, 2H), 6.90–6.84 (m, 2H), 5.67 (ddd, *J* = 15.5, 7.8, 0.8 Hz, 1H), 5.42 (ddd, *J* = 15.6, 8.2, 1.0 Hz, 1H), 4.82 (dd, *J* = 5.7, 4.5 Hz, 1H), 4.68 (d, *J* = 6.7 Hz, 1H), 4.62 (d, *J* = 11.6 Hz, 1H), 4.58 (d, *J* = 11.6 Hz, 1H), 4.53 (d, *J* = 6.7 Hz, 1H), 4.34 (ddd, *J* = 8.0, 4.7, 0.7 Hz, 1H), 3.97–3.91 (m, 2H), 3.83–3.78 (m, 6H), 3.33 (s, 3H), 2.51–2.39 (m, 1H), 1.73–1.57 (m, 2H), 1.04 (d, *J* = 6.8 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 201.8, 159.5, 142.1, 129.7, 129.2, 123.6, 113.8, 103.3, 93.4, 84.8, 76.4, 72.5, 64.7 (2C), 55.5, 55.3, 40.6, 32.9, 20.7 ppm. IR (film): $\tilde{\nu}$ = 2954, 2886, 1734, 1613, 1514, 1464, 1303, 1249, 1149, 1097, 1031, 976, 822 cm^{-1}. MS (ESIpos) *m/z* (%): 417.2 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{21}H_{30}O_7Na$ [M+Na$^+$]: 417.1884, found: 417.1885.

Alcohol 21. Magnesium bromide diethyl etherate (2.30 g, 8.91 mmol) was added to crude aldehyde



S13 (1.42 g, 3.59 mmol) in CH_2Cl_2 (18 mL) at −30 °C. After stirring for 20 min, the yellow suspension was cooled to −78 °C and allyltributylstannane (1.3 mL, 4.2 mmol) was added dropwise. After stirring for 3.5 h and allowing the mixture to reach −35 °C, additional magnesium bromide diethyl etherate (500 mg, 1.93 mmol) was added due to unconsumed starting material. After stirring for additional 1.5 h at the same temperature, the reaction was quenched with sat. NH_4Cl (20 mL). The aq. phase was separated and extracted with *t*-butyl methyl ether (3 × 25 mL). The combined organic phases were washed with brine (50 mL), dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography (hexane/EtOAc 3:2) to afford the title compound as a yellow oil (753 mg, 49% over 2 steps, ≥ 20:1 dr, single diastereomer, ca. 80% conversion). $[\alpha]_D^{20}$ = −89.9 (c = 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.29–7.24 (m, 2H), 6.90–6.85 (m, 2H), 5.88–5.76 (m, 1H), 5.68 (ddd, *J* = 15.5, 7.8, 0.8 Hz, 1H), 5.44 (ddd, *J* = 15.5, 8.0, 1.0 Hz, 1H), 5.10–5.02 (m, 2H), 4.83 (dd, *J* = 5.7, 4.5 Hz, 1H), 4.74 (d, *J* = 11.0 Hz, 1H), 4.71 (d, *J* = 6.6 Hz, 1H), 4.55 (d, *J* = 6.5 Hz, 1H), 4.47 (d, *J* = 11.0 Hz, 1H), 4.28 (ddd, *J* = 8.0, 5.1, 0.8 Hz, 1H), 3.97–3.91 (m, 2H), 3.84–3.77 (m, 6H), 3.38 (s, 3H), 3.34 (dd, *J* = 5.1, 3.5 Hz, 1H), 2.77 (br s, 1H), 2.53–2.41 (m, 1H), 2.36–2.24 (m, 2H), 1.75–1.60 (m, 2H), 1.05 (d, *J* = 6.8 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 159.3, 141.4, 135.0, 130.2, 129.7, 125.0, 117.1, 113.8, 103.3, 93.4, 81.6, 76.6, 73.4, 70.2, 64.7, 64.7, 55.7, 55.3, 40.7, 38.1, 33.1, 20.8 ppm. IR (film): $\tilde{\nu}$ = 3514, 2953, 2886, 1613, 1514, 1464, 1401, 1302, 1248, 1151, 1097, 1031, 977, 917, 823 cm^{-1}. MS (ESIpos) *m/z* (%): 459.2 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{24}H_{36}O_7Na$ [M+Na$^+$]: 459.2353, found: 459.2352.

Mosher Ester Analysis of Alcohol 21. Hünig's base (6.5 µL, 37 µmol) was added to a solution of alcohol



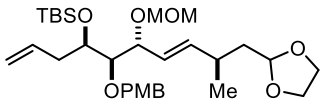
21 (6.0 mg, 14 µmol) in CH_2Cl_2 (0.2 mL) followed by (*S*)-(–)-α-methoxy-α-trifluoromethyl-phenylacetyl chloride ((*S*)-MTPA-Cl) (4.9 µL, 26 µmol). The mixture was stirred at ambient temperature for 17 h before it was diluted with CH_2Cl_2 (2 mL) and sat. NH_4Cl (2 mL). The aq. phase was separated and extracted with CH_2Cl_2 (2 × 2 mL). The combined organic phases were dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography (hexane/*t*-butyl methyl ether 7:3) to give the corresponding (*R*)-Mosher ester (*R*)-**S14** (8.9 mg, 99%), which analyzed as follows: $[\alpha]_D^{20}$ = −32.1 (c = 0.89, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.58–7.52 (m, 2H), 7.39–7.33 (m, 1H), 7.30–7.25 (m, 2H), 7.23–7.17 (m, 2H), 6.86–6.81 (m, 2H), 5.72–5.60 (m, 2H), 5.50 (ddd, *J* = 15.6, 8.3, 0.9 Hz, 1H), 5.28 (dt, *J* = 6.5, 5.1 Hz, 1H), 5.10–4.99 (m, 2H), 4.83 (dd, *J* = 5.7, 4.6 Hz, 1H), 4.74 (d, *J* = 11.1 Hz, 1H), 4.67 (d, *J* = 6.6 Hz, 1H), 4.51–4.44 (m, 2H), 4.13 (dd, *J* = 8.3, 4.8 Hz, 1H), 3.96–3.92 (m, 2H), 3.82–3.77 (m, 5H), 3.65 (dd, *J* = 5.7, 4.8 Hz, 1H), 3.51 (d, *J* = 1.1 Hz, 3H), 3.31 (s, 3H), 2.55–2.32 (m, 3H), 1.75–1.60 (m, 2H), 1.04 (d, *J* = 6.8 Hz, 3H) ppm. IR (film): $\tilde{\nu}$ = 2955, 2887, 1746, 1613, 1514, 1453, 1247, 1169, 1103, 1022, 920, 819, 721, 514 cm^{-1}. MS (ESIpos) *m/z* (%): 675.3 (100 (M+Na)). HRMS (ESI): *m/z* calcd for $C_{34}H_{43}O_9F_3Na$ [M+Na$^+$]: 675.2751, found: 675.2750.

The corresponding Mosher ester (*S*)-**S14** (6.7 mg, 75%) was prepared analogously: $[\alpha]_D^{20}$ = −41.6 (c = 1.08, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.59–7.55 (m, 2H), 7.39–7.32 (m, 3H), 7.17 (d, *J* = 8.7 Hz, 2H), 6.86–6.81 (m, 2H), 5.81–5.69 (m, 1H), 5.57 (dd, *J* = 15.6, 7.7 Hz, 1H), 5.44 (ddd, *J* = 15.6, 8.2, 0.8 Hz, 1H), 5.30 (dt, *J* = 6.9, 5.2 Hz, 1H), 5.14–5.06 (m, 2H), 4.82 (dd, *J* = 5.7, 4.5 Hz, 1H), 4.65 (d, *J* = 11.2 Hz, 1H), 4.61 (d, *J* = 6.6 Hz, 1H), 4.44–4.36 (m, 2H), 4.04 (dd, *J* = 8.2, 5.2 Hz, 1H), 3.97–3.90 (m, 2H), 3.83–3.76 (m, 5H), 3.59 (t, *J* = 5.1 Hz, 1H), 3.51 (d, *J* = 1.2 Hz, 3H), 3.29 (s, 3H), 2.54 (dddd, *J* = 9.4, 8.0, 4.1, 2.7 Hz, 1H), 2.50–2.40 (m, 2H), 1.73–1.59 (m, 2H), 1.01 (d, *J* = 6.8 Hz, 3H) ppm. IR (film): $\tilde{\nu}$ = 2954, 2888, 1746, 1613, 1514, 1452, 1248, 1168, 1122, 1082, 1025, 920, 820, 765, 720 cm^{-1}. MS (ESIpos) *m/z* (%): 675.3 (100 (M+Na)). HRMS (ESI): *m/z* calcd for $C_{34}H_{43}O_9F_3Na$ [M+Na$^+$]: 675.2751, found: 675.2747.

Table S-6. Mosher ester analysis for product **21** according to Hoye and co-workers;[12] arbitrary numbering scheme as shown in the insert

Assignment	21 [ppm]	(*S*)-S14 [ppm]	(*R*)-S14 [ppm]	Δ (*δ*(*S*–*R*)) [ppm]
1a	5.07	5.10	5.03	+0.07
1b	5.06	5.08	5.02	+0.06
2	5.82	5.74	5.65	+0.09
3a	2.31	2.54	2.48	+0.06
3b	2.29	2.45	2.38	+0.07
4	3.80	5.30	5.28	+0.02
5	3.34	3.59	3.65	−0.07
6	4.28	4.04	4.13	−0.09
7	5.44	5.44	5.50	−0.06
8	5.68	5.57	5.65	−0.08
9	2.47	2.45	2.48	–0.03
10a	1.70	1.68	1.71	−0.03
10b	1.63	1.61	1.63	−002
11	4.83	4.82	4.83	−0.01
12	1.05	1.01	1.04	−0.03

Compound S15. 2,6-Lutidine (0.27 mL, 2.3 mmol) and TBSOTf (0.39 mL, 1.7 mmol) were added to a solution of homoallylic alcohol **21** (500 mg, 1.15 mmol) in CH_2Cl_2 (4 mL) at 0 °C. After stirring for 1 h at the same temperature, the reaction was quenched with sat. NH_4Cl (5 mL). The aq. phase was separated and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic phases were dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography (hexane/*t*-butyl methyl ether 7:3) to afford the title compound as a colourless oil (527 mg, 84%). $[\alpha]_D^{20}$ = –75.0 (c = 0.98, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 7.30–7.27 (m, 2H), 6.89–6.83 (m, 2H), 5.80 (dddd, *J* = 15.8, 11.2, 7.9, 6.4 Hz, 1H), 5.66–5.54 (m, 2H), 5.06–4.98 (m, 2H), 4.84 (dd, *J* = 5.8, 4.4 Hz, 1H), 4.74 (d, *J* = 11.3 Hz, 1H), 4.68 (d, *J* = 6.6 Hz, 1H), 4.56 (d, *J* = 11.3 Hz, 1H), 4.49 (d, *J* = 6.6 Hz, 1H), 4.27–4.22 (m, 1H), 3.97–3.91 (m, 2H), 3.83–3.77 (m, 5H), 3.69 (ddd, *J* = 7.0, 6.1, 4.0 Hz, 1H), 3.54 (dd, *J* = 6.1, 2.6 Hz, 1H), 3.33 (s, 3H), 2.52–2.41 (m, 1H), 2.39–2.31 (m, 1H), 2.14 (dddt, *J* = 14.3, 7.7, 6.9, 0.9 Hz, 1H), 1.72 (ddd, *J* = 13.8, 8.1, 4.5 Hz, 1H), 1.63 (dt, *J* = 13.8, 6.0 Hz, 1H), 1.04 (d, *J* = 6.8 Hz, 3H), 0.87 (s, 9H), −0.01 (s, 3H), −0.05 (s, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): *δ* = 158.9, 141.4, 135.7, 131.4, 129.1, 125.0, 116.7, 113.5, 103.4, 92.7, 83.2, 76.2, 73.4, 72.5, 64.7, 64.7, 55.3, 55.3, 40.7, 38.1, 33.2, 25.9, 20.7, 18.1, −4.3, −4.5 ppm. IR (film): $\tilde{\nu}$ = 2953, 2929, 2884, 2857, 1613, 1514, 1463, 1248, 1148, 1094, 1031, 916, 831, 776 cm^{-1}.



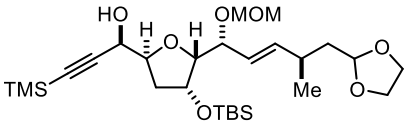
MS (ESIpos) *m/z* (%): 573.3 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{30}H_{50}O_7SiNa$ [M+Na$^+$]: 573.3218, found: 573.3219.

Alcohol 22. DDQ (680 mg, 3.00 mmol) was added to an emulsion of PMB-ether **S15** (550 mg, 0.999 mmol) in a 4:1 mixture of CH_2Cl_2 (8 mL) and pH 7.4 phosphate buffer (2 mL) at 0 °C. After stirring for 30 min at the same temperature, the reaction was quenched with a 3:1 mixture of sat. $NaHCO_3$ and sat. NaS_2O_3 (10 mL). The aq. phase was separated and extracted with *t*-butyl methyl ether (2 × 20 mL). The combined organic phases were washed with brine (50 mL), dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography (hexane/*t*-butyl methyl ether 4:1 to 7:3) to afford the title compound as a colourless oil (357 mg, 83%). $[\alpha]_D^{20}$ = –72.4 (c = 1.56, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.80 (ddt, *J* = 17.3, 10.2, 7.1 Hz, 1H), 5.61 (dd, *J* = 15.6, 7.6 Hz, 1H), 5.44 (ddd, *J* = 15.6, 8.3, 1.0 Hz, 1H), 5.14–5.04 (m, 2H), 4.85 (dd, *J* = 5.6, 4.6 Hz, 1H), 4.69 (d, *J* = 6.5 Hz, 1H), 4.51 (d, *J* = 6.5 Hz, 1H), 3.99–3.91 (m, 3H), 3.88–3.78 (m, 3H), 3.50 (td, *J* = 6.3, 3.8 Hz, 1H), 3.34 (s, 3H), 2.53–2.36 (m, 3H), 2.23 (dddt, *J* = 12.8, 6.9, 4.7, 0.7 Hz, 1H), 1.71 (ddd, *J* = 13.9, 8.1, 4.6 Hz, 1H), 1.64 (dt, *J* = 13.8, 5.9 Hz, 1H), 1.06 (d, *J* = 6.8 Hz, 3H), 0.91 (s, 9H), 0.12–0.09 (m, 6H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 141.5, 134.0, 125.2, 117.6, 103.4, 93.5, 77.2, 73.8, 71.1, 64.7 (2C), 55.6, 40.7, 39.0, 33.0, 25.9, 20.8, 18.1, −4.1, −4.6 ppm. IR (film): $\tilde{\nu}$ = 3507, 2953, 2929, 2885, 2857, 1472, 1407, 1361, 1252, 1150, 1094, 1067, 1030, 917, 835, 776 cm^{-1}. MS (ESIpos) *m/z* (%): 453.3 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{22}H_{42}O_6SiNa$ [M+Na$^+$]: 453.2643, found: 453.2640.

Alcohol 23. $Co(nmp)_2$ (46 mg, 81 µmol) was added to a solution of alcohol **22** (350 mg, 0.813 mmol) in *i*-PrOH (7.5 mL). The solution was degassed by 3 freeze-pump-thaw cycles and back-filled with oxygen. After adding *t*-BuOOH (5.5 M in decane, 14.8 µL, 0.81 µmol), a balloon of oxygen was fitted to the flask which was placed in a pre-heated oil bath at 55 °C. The mixture turned green within 5 min of heating and stirring was continued for 16 h. After reaching ambient temperature, the mixture was concentrated to a green oil, which was purified by flash chromatography (hexane/EtOAc 3:7) to give the title product as a colourless oil (249 mg, 69%, >20:1 dr, >20:1 r.r.). $[\alpha]_D^{20}$ = –21.3 (c = 1.43, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.68 (ddt, *J* = 15.6, 7.6, 0.8 Hz, 1H), 5.51 (ddt, *J* = 15.6, 7.6, 0.8 Hz, 1H), 4.88 (dd, *J* = 6.0, 4.3 Hz, 1H), 4.66 (dt, *J* = 6.3, 0.5 Hz, 1H), 4.60 (dd, *J* = 6.3, 0.6 Hz, 1H), 4.49 (ddd, *J* = 5.3, 4.5, 3.8 Hz, 1H), 4.27 (dddd, *J* = 7.9, 7.2, 5.5, 3.1 Hz, 1H), 4.17 (dd, *J* = 7.7, 5.7 Hz, 1H), 3.97–3.93 (m, 2H), 3.92 (dd, *J* = 5.7, 4.3 Hz, 1H), 3.83–3.79 (m, 2H), 3.66 (dd, *J* = 11.7, 3.1 Hz, 1H), 3.42 (dd, *J* = 11.7, 5.5 Hz, 1H), 3.33 (dd, *J* = 0.5, 0.4 Hz, 3H), 2.45 (hept, *J* = 6.9 Hz, 1H), 2.03 (br s, 1H), 1.91 (ddd, *J* = 12.8, 7.0, 3.7 Hz, 1H), 1.87 (ddd, *J* = 12.8, 7.9, 5.3 Hz, 1H), 1.72 (ddd, *J* = 13.7, 8.1, 4.3 Hz, 1H), 1.62 (dt, *J* = 13.8, 6.2 Hz, 1H), 1.06 (d, *J* = 6.8 Hz, 3H), 0.91 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H) ppm. ^{13}C NMR (126

MHz, $CDCl_3$): δ = 139.7, 126.2, 103.4, 94.4, 84.6, 78.1, 76.0, 72.5, 65.1, 64.7, 64.7, 55.6, 40.7, 36.7, 32.9, 25.8, 20.7, 18.0, −4.5, −4.9 ppm. ^{29}Si NMR (99 MHz, $CDCl_3$): δ = 19.3 ppm. IR (film): $\tilde{\nu}$ = 3456, 2952, 2929, 2885, 2857, 1472, 1407, 1361, 1254, 1140, 1099, 1034, 941, 835, 776, 667 cm^{-1}. MS (ESIpos) *m/z* (%): 469.3 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{22}H_{42}O_7SiNa$ [M+Na$^+$]: 469.2592, found: 469.2596.

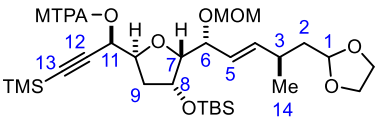
Propargyl Alcohol 24. Hünig's base (2.8 mL, 16 mmol) was added at to a solution of alcohol **23** (208 mg, 0.466 mmol) in CH_2Cl_2 (3.0 mL) –25 °C and the resulting mixture was stirred for 5 min at this temperature. In a second flask a suspension of sulfur trioxide pyridine complex (1.26 g, 7.92 mmol) in CH_2Cl_2 (1.0 mL) was treated with DMSO (0.33 mL, 4.6 mmol) and the resulting mixture was stirred for 15 min at ambient temperature. This suspension was added to the alcohol solution at –25 °C, rinsing the flask with CH_2Cl_2 (1.0 mL). The mixture was allowed to slowly reach −10 °C over 1.5 h. The mixture was diluted with *t*-butyl methyl ether (5 mL) and the reaction was quenched with pH 7 phosphate buffer (5 mL). The aq. phase was separated and extracted with *t*-butyl methyl ether (3 × 5 mL). The combined organic phases were washed with brine (15 mL), dried over Na_2SO_4 and concentrated under reduced pressure to yield the crude aldehyde as a yellow oil, which was used in the next step without further purification.



A Schlenk tube was charged with $Zn(OTf)_2$ (dried at 120 °C under high vacuum for 24 h, 924 mg, 2.54 mmol) and (–)-*N*-methylephedrine (dried azeotropically by distilling toluene off the compound (3 x), 510 mg, 2.85 mmol). After the addition of toluene (1.8 mL), Hünig's base (0.50 mL, 2.9 mmol) was introduced and the resulting suspension was stirred for 3 h at ambient temperature before ethynyltrimethylsilane (0.39 mL, 2.7 mmol) was added. After stirring for another 0.5 h at ambient temperature, a solution of crude aldehyde (207 mg, 0.465 mmol) in toluene (4.0 mL with rinses) was added in one portion to the milky suspension. After stirring for 15 h at ambient temperature, the reaction was quenched with sat. NH_4Cl (5 mL). The aq. phase was separated and extracted with *t*-butyl methyl ether (3 × 5 mL). The combined organic phases were dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography (hexane/EtOAc 7:3 to 3:2) to provide the title compound as a pale yellow oil (224 mg, 89% over 2 steps, dr = 19:1). $[\alpha]_D^{20}$ = –24.0 (c = 1.05, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.67 (ddd, *J* = 15.7, 7.7, 0.8 Hz, 1H), 5.51 (ddd, *J* = 15.7, 7.5, 1.0 Hz, 1H), 4.88 (dd, *J* = 5.9, 4.4 Hz, 1H), 4.66 (d, *J* = 6.3 Hz, 1H), 4.59 (d, *J* = 6.3 Hz, 1H), 4.57 (dt, *J* = 5.7, 4.4 Hz, 1H), 4.38 (d, *J* = 2.9 Hz, 1H), 4.32–4.26 (m, 1H), 4.17 (ddd, *J* = 7.5, 5.6, 0.8 Hz, 1H), 4.03 (dd, *J* = 5.6, 4.6 Hz, 1H), 3.97–3.91 (m, 2H), 3.85–3.80 (m, 2H), 3.33 (s, 3H), 2.57 (br s, 1H), 2.45 (hept, *J* = 6.9 Hz, 1H), 2.13 (ddd, *J* = 13.1, 7.4, 5.7 Hz, 1H), 1.96 (ddd, *J* = 12.9, 7.3, 4.0 Hz, 1H), 1.71 (ddd, *J* = 13.8, 8.2, 4.4 Hz, 1H), 1.63 (dt, *J* = 13.8, 6.0 Hz, 1H), 1.05 (d, *J* = 6.8 Hz, 3H), 0.91 (s, 9H), 0.16 (s, 9H), 0.09 (s, 3H),

0.08 (s, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 139.7, 126.1, 103.4, 103.2, 94.4, 90.8, 85.6, 80.3, 75.8, 72.2, 65.1, 64.7 (2C), 55.5, 40.7, 35.8, 33.0, 25.8, 20.7, 18.0, −0.2, −4.5, −4.9 ppm. ^{29}Si NMR (99 MHz, $CDCl_3$): δ = 19.3 ppm. IR (film): $\tilde{\nu}$ = 3436, 2955, 2929, 2887, 2858, 1472, 1408, 1361, 1251, 1140, 1099, 1036, 942, 839, 776, 761 cm^{-1}. MS (ESIpos) *m/z* (%): 565.3 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{27}H_{50}O_7Si_2Na$ [M+Na$^+$]: 565.2987, found: 565.2992.

Mosher Ester Analysis of Propargyl Alcohol 24. Hünig's base (12 µL, 69 µmol) was added to a solution of alcohol **24** (11.9 mg, 22 µmol) in CH_2Cl_2 (0.20 mL) followed by (*R*)-(−)-α-methoxy-α-trifluoromethyl-phenylacetyl chloride ((*R*)-MTPA-Cl) (7.8 µL, 42 µmol). After stirring for 17 h at ambient temperature, the mixture was diluted with CH_2Cl_2 (3 mL) and sat. $NaHCO_3$ (3 mL). The aq. phase was separated and extracted with CH_2Cl_2 (3 × 5 mL). The combined organic phases were dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography (hexane/*t*-butyl methyl ether 4:1) to give the corresponding (*S*)-Mosher ester (*S*)-**S16** (12.8 mg, 76%) as a colourless oil. $[\alpha]_D^{20}$ = −42.6 (c = 1.28, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.59–7.50 (m, 2H), 7.42–7.36 (m, 3H), 5.66–5.57 (m, 2H), 5.37 (ddd, *J* = 15.7, 7.8, 1.1 Hz, 1H), 4.84 (dd, *J* = 5.9, 4.4 Hz, 1H), 4.61 (d, *J* = 6.4 Hz, 1H), 4.51 (d, *J* = 6.4 Hz, 1H), 4.35 (ddd, *J* = 8.4, 5.7, 3.0 Hz, 1H), 4.26 (q, *J* = 6.0 Hz, 1H), 4.03 (ddd, *J* = 7.8, 4.6, 0.8 Hz, 1H), 3.98–3.90 (m, 2H), 3.85–3.78 (m, 2H), 3.61 (d, *J* = 1.3 Hz, 3H), 3.54 (dd, *J* = 5.6, 4.6 Hz, 1H), 3.30 (s, 3H), 2.48–2.36 (m, 1H), 2.12 (ddd, *J* = 12.4, 6.5, 5.6 Hz, 1H), 1.97 (ddd, *J* = 12.8, 8.0, 5.8 Hz, 1H), 1.70 (ddd, *J* = 13.8, 8.0, 4.4 Hz, 1H), 1.59 (dt, *J* = 13.8, 6.0 Hz, 1H), 1.04 (d, *J* = 6.8 Hz, 3H), 0.87 (s, 9H), 0.17 (s, 9H), 0.02 (s, 3H), 0.00 (s, 3H) ppm. IR (film) $\tilde{\nu}$ = 2954, 2930, 2887, 2858, 1759, 1452, 1251, 1170, 1123, 1072, 1036, 956, 844, 776, 764, 719, 699, 666 cm^{-1}. MS (ESIpos) *m/z* (%): 781.3 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{37}H_{57}O_9Si_2F_3Na$ [M+Na$^+$]: 781.3385, found: 781.3386.



The corresponding Mosher ester (*R*)-**S16** (8.6 mg, 52%) was prepared analogously: $[\alpha]_D^{20}$ = −17.2 (c = 0.86, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55–7.48 (m, 2H), 7.42–7.37 (m, 3H), 5.66 (dd, *J* = 15.6, 7.6 Hz, 1H), 5.56 (d, *J* = 2.8 Hz, 1H), 5.43 (ddd, *J* = 15.6, 7.9, 1.0 Hz, 1H), 4.85 (dd, *J* = 5.9, 4.4 Hz, 1H), 4.65 (d, *J* = 6.3 Hz, 1H), 4.56 (d, *J* = 6.3 Hz, 1H), 4.44–4.34 (m, 2H), 4.14 (dd, *J* = 7.8, 4.9 Hz, 1H), 3.98–3.91 (m, 3H), 3.84–3.77 (m, 2H), 3.52 (d, *J* = 1.2 Hz, 3H), 3.32 (s, 3H), 2.45 (hept, *J* = 7.1 Hz, 1H), 2.08 (dt, *J* = 12.6, 6.3 Hz, 1H), 1.99 (ddd, *J* = 13.0, 7.9, 5.4 Hz, 1H), 1.71 (ddd, *J* = 13.8, 8.0, 4.4 Hz, 1H), 1.60 (dt, *J* = 13.7, 6.1 Hz, 1H), 1.04 (d, *J* = 6.8 Hz, 3H), 0.87 (s, 9H), 0.15 (s, 9H), 0.00-–0.03 (m, 6H) ppm. IR (film) $\tilde{\nu}$ = 2955, 2931, 2887, 2858, 1759, 1453, 1252, 1171, 1147, 1124, 1071, 1037, 958, 922, 845, 777, 764, 722, 699 cm^{-1}. MS (ESIpos) *m/z* (%): 781.3 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{37}H_{57}O_9Si_2F_3Na$ [M+Na$^+$]: 781.3385, found: 781.3386.

Table S-7. Mosher ester analysis for product **24** according to Hoye and co-workers;[12] arbitrary numbering scheme as shown in the insert

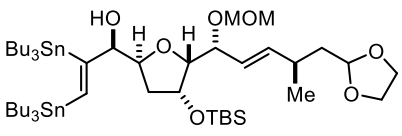
Assignment	24 [ppm]	(*S*)-S16 [ppm]	(*R*)-S16 [ppm]	Δ (*δ*(*S*–*R*)) [ppm]
1	4.88	4.84	4.85	−0.01
2a	1.71	1.70	1.71	−0.01
2b	1.63	1.59	1.60	−0.01
3	2.45	2.42	2.45	−0.03
4	5.67	5.61	5.66	–0.05
5	5.51	5.37	5.43	–0.06
6	4.17	4.03	4.14	–0.11
7	4.03	3.54	3.94	–0.40
8	4.57	4.26	4.39	–0.23
9a	2.13	2.12	2.08	+0.04
9b	1.96	1.97	1.99	−0.02
10	4.29	4.35	4.39	–0.04
11	4.38	5.61	5.56	+0.05
14	1.05	1.04	1.04	0
TMS-Me	0.16	0.17	0.15	+0.02

Terminal Alkyne S17. K_2CO_3 (80 mg, 0.58 mmol) was added to a solution of TMS-alkyne **24** (211 mg, 0.389 mmol) in methanol (4.5 mL) at 0 °C and the mixture was stirred for 1 h at the same temperature and for another 3 h at ambient temperature. After diluting the mixture with *t*-butyl methyl ether (5 mL), the reaction was quenched with sat. NH_4Cl (5 mL). The aq. phase was separated and extracted with *t*-butyl methyl ether (2 × 10 mL). The combined organic phases were dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography (hexane/EtOAc 3:2) to provide the title compound as a yellow oil (154 mg, 84%). $[\alpha]_D^{20}$ = –27.9 (c = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): *see Table S-8;* ^{13}C NMR (126 MHz, $CDCl_3$): *see Table S-8*. ^{29}Si NMR (99 MHz, $CDCl_3$) δ = 19.5 ppm. IR (film): $\tilde{\nu}$ = 3436, 3263, 2953, 2929, 2886, 2858, 1472, 1408, 1361, 1255, 1140, 1100, 1037, 950, 836, 777, 711, 668 cm^{-1}. MS (ESIpos) *m/z* (%): 493.3 (100 (M+Na)). HRMS (ESIpos) *m/z* calcd for $C_{24}H_{42}O_7SiNa$ [M+Na$^+$]: 493.2592, found: 493.2593.

Table S-8. NMR data of terminal alkyne **S17**; arbitrary numbering scheme as shown in the insert

atom n°	^{1}H NMR (500 MHz, $CDCl_3$)					^{13}C NMR (126 MHz, $CDCl_3$)	
	δ [ppm]	m	*J* [Hz]	COSY	NOESY	δ [ppm]	HMBC
1	4.03	dd	5.8, 4.5	2, 5	2, 3a, 6, 14	85.6	3ab, 5
2	4.56	ddd	5.7, 4.5, 3.8	1, 3ab	1, 3ab, 19, 20, 21	72.2	4
3a	2.15	ddd	13.0, 7.5, 5.7	2, 4, 3b	1, 2, 3b, 15	35.7	1
3b	1.97	dddd	13.0, 7.5, 3.8, 0.5	2, 3a, 4, 20, 21	(1), 15		
4	4.30	tdt	7.5, 3.1, 0.7	3ab, 15	3b, 6, 15	80.0	1, 2, 3a
5	4.17	ddd	5.8, 7.6, 0.6	1, 6	6, 7, 13ab, 14, 19, 20, 21	75.9	1, 6, 7, 13ab
6	5.51	ddt	15.6, 7.6. 0.8	5, 7	1, 4, 5, 8, 22	126.1	1, 7, 8
7	5.68	ddt	15.6, 7.6, 0.8	6, 8	5, 8, 9a, 22	139.8	5, 6, 8, 9b, 22
8	2.45	ddqd	8.3, 7.6, 6.9, 6.0	6, 7, 9ab, 10, 22	6, 7, 9b, 10, 22	33.0	6, 7, 9ab, 10, 22
9a	1.71	dddd	13.7, 8.3, 4.3, 0.6	8, 9b, 10	7, 22	40.7	7, 8, 10, 22
9b	1.62	dtd	13.7, 6.0, 0.6	8, 9a, 10	8, 22		
10	4.89	dd	6.0, 4.3	9ab	8, 11b, 12b, 22	103.4	8, 9
11a	3.98–3.90	m	-	11b	-	64.7	12ab
11b	3.86–3.78	m	-	11a	10		
12a	3.98–3.90	m	-	12b	-	64.7	11ab
12b	3.86–3.78	m	-	12a	10		
13a	4.66	dd	6.3, 0.6	13b	4, 14, 20, 21	94.4	5, 14
13b	4.59	dd	6.3, 0.6	13a	4, 14, 20, 21		
14	3.33	t	0.6	-	1, 5, 13ab	55.6	13ab
15	4.41	dddd	6.2, 3.1, 2.2, 0.5	4, 15-OH, 17	3a, 4, 15-OH	64.5	3a, 17
16	-	-	-	-	-	81.5	4, 15
17	2.40	d	2.2	15	-	74.0	3a, 15-OH
18	-	-	-	-	-	18.0	19, 20 , 21
19	0.91	s	-	-	2, 5, 20, 21	25.8	-
20	0.08	s	-	-	2, 3b, 5, 19, 13ab	–5.0	21
21	0.09	s	-	-	2, 3b, 5, 19, 13ab	–4.5	20
22	1.05	d	6.9	8	6, 7, 8, 9ab, 10	20.7	7, 8, 9ab
15-OH	2.62	d	6.2	15	15	-	-

Bis(alkenyl)stannane 6b. [(*t*BuNC)$_2$PdCl$_2$] (6.8 mg, 20 µmol) was added to a solution of alkyne **S17** (94.6 mg, 0.201 mmol) in THF (0.65 mL) at ambient temperature. After dropwise addition of hexabutyldistannane (0.15 mL, 0.30 mmol) to the orange suspension, the mixture turned into a dark red solution of increasing colour-intensity over time. After stirring for 20 h at ambient

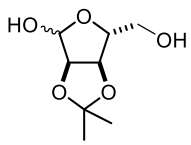


temperature, the mixture was concentrated. The residual oil was purified by flash chromatography ((hexane/NEt_3 99:1)/*t*-butyl methyl ether 9:1 to 8:1) to afford the title compound as a yellow-orange oil (166 mg, 78%). $[\alpha]_D^{20}$ = –13.8 (c = 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.89 (ddd, *J* = 2.1, J_{SnH} = 176.1, 66.2 Hz, 1H), 5.66 (dd, *J* = 15.6, 7.5 Hz, 1H), 5.52 (ddd, *J* = 15.6, 7.5, 0.9 Hz, 1H), 4.87 (dd, *J* = 5.8, 4.4 Hz, 1H), 4.66 (d, *J* = 6.3 Hz, 1H), 4.59 (d, *J* = 6.3 Hz, 1H), 4.52 (q, *J* = 2.3 Hz, 1H), 4.47– 4.42 (m, 1H), 4.27 (ddd, *J* = 8.3, 6.6, 3.0 Hz, 1H), 4.16 (dd, *J* = 7.5, 5.6 Hz, 1H), 3.99–3.90 (m, 3H), 3.84–3.78 (m, 2H), 3.33 (s, 3H), 2.45 (hept, *J* = 6.7 Hz, 1H), 2.25 (d, *J* = 2.2 Hz, 1H), 1.98 (ddd, *J* = 12.8, 8.4, 5.5 Hz, 1H), 1.72 (ddd, *J* = 13.8, 8.0, 4.4 Hz, 1H), 1.67–1.57 (m, 2H), 1.52–1.41 (m, 12H), 1.38–1.24 (m, 12H), 1.05 (d, *J* = 6.8 Hz, 3H), 0.94–0.85 (m, 39H), 0.07 (s, 3H), 0.06 (s, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.4, 140.8, 139.7, 126.2, 103.5, 94.3, 85.3, 81.1, 78.8, 76.2, 72.5, 64.7, 64.6, 55.5, 40.7, 33.7, 33.0, 29.2, 29.2, 27.5, 27.4, 25.9, 20.7, 18.0, 13.7, 13.7, 11.1, 10.9,–4.5, –5.0 ppm. ^{119}Sn NMR (149 MHz, $CDCl_3$): δ = –60.2, –64.1 ppm. IR (film) $\tilde{\nu}$ = 3437, 2955, 2926, 2872, 2855, 1463, 1376, 1254, 1144, 1101, 1038, 958, 836, 776, 666 cm^{-1}. MS (ESIpos) *m/z* (%): 1073.5 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{48}H_{96}O_7SiSn_2Na$ [M+Na$^+$]: 1075.4862, found: 1075.4877.

Synthesis of the Southern Segments

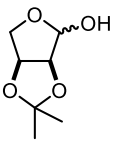
Diverted Approach by Ni-catalyzed Reductive Coupling with Isoprene

2,3-O-Isopropylidene-D-ribofuranose (27). Sulfuric acid (18 M, 0.24 mL, 4.3 mmol) was added



dropwise to a suspension of D-ribose (8.0 g, 53 mmol) in acetone. After stirring for 2.5 h, solid $NaHCO_3$ was added to the homogenous solution until a pH value of 7 was reached and the resulting mixture was stirred for 10 min. After filtration through cotton, the residue was concentrated and purified by flash chromatography (hexane/EtOAc 35:65) to afford the title compound as a colourless oil (7.98 g, 78%). $[\alpha]_D^{20}$ = −24.6 (c = 1.73, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.41 (s, 1H), 4.82 (dd, *J* = 5.9, 0.9 Hz, 1H), 4.57 (d, *J* = 6.0 Hz, 1H), 4.40 (t, *J* = 2.8 Hz, 1H), 3.74 (dd, *J* = 11.8, 2.2 Hz, 1H), 3.70 (dd, *J* = 11.9, 3.2 Hz, 1H), 1.48 (s, 3H), 1.32 (s, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 112.1, 102.9, 87.8, 86.8, 81.7, 63.6, 26.3, 24.7 ppm. IR (film): $\tilde{\nu}$ = 3371, 2942, 1376, 1211, 1160, 1067, 869 cm^{-1}. MS (EI) *m/z* (%): 175 (75), 157 (100), 115 (24), 101 (42), 97 (30), 85 (33), 69 (47), 68 (30), 59 (50), 57 (22), 43 (46). HRMS (ESIpos): *m/z* calcd for $C_8H_{14}O_5Na$ [M+Na$^+$]: 213.0733, found: 213.0734. The analytical and spectroscopic data are in agreement with those reported in the literature.[17]

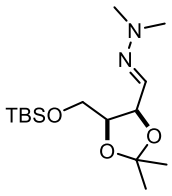
Lactol 28. $NaBH_4$ (3.4 g, 89.87 mmol) was added cautiously to a solution of **27** (4.3 g, 22.62 mmol) in



methanol (22 mL) at 4 °C. After stirring for 4 h at ambient temperature, acetic acid (6.73 mL, 89.87 mmol) was added dropwise and the mixture was stirred for 10 min until the excess borohydride had decomposed. Sodium periodate (5.3 g, 24.78) was added in

portions over 10 min and the reaction was then stirred for 1 h at ambient temperature. The resulting mixture was filtered through Celite®, which was rinsed with CH_2Cl_2 (200 mL). The aq. phase was separated and extracted with CH_2Cl_2 (3 × 200 mL). The combined organic phases were washed with brine and dried over Na_2SO_4, filtered and concentrated to give a colourless residue. The residue was purified by flash chromatography (hexane/EtOAc 1:1) to give the title compound as a colourless syrup (3.02 g, 83%, α/β = 9:1). $[\alpha]_D^{20}$ = +66 (c = 1.19, $CHCl_3$). Spectral data for α-**28:** ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.42 (d, *J* = 1.4 Hz, 1H), 4.84 (dd, *J* = 5.9, 3.5 Hz, 1H), 4.58 (d, *J* = 5.9 Hz, 1H), 4.11–4.00 (m, 2H), 2.69 (br s, 1H), 1.47 (d, *J* = 0.7 Hz, 3H), 1.32 (d, *J* = 0.8 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 112.3, 101.8, 85.1, 79.9, 72.0, 26.2, 24.7 ppm. Spectral and analytical data for β-**28**: ^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.99 (ddd, *J* = 11.5, 3.7, 0.7 Hz, 1H), 4.76 (ddd, *J* = 6.2, 3.8, 0.9 Hz, 1H), 4.49 (dd, *J* = 6.2, 3.6 Hz, 1H), 3.98 (dd, *J* = 11.0, 0.8 Hz, 1H), 3.88 (dd, *J* = 11.5, 1.5 Hz, 1H), 3.54 (dd, *J* = 11.0, 3.7 Hz, 1H), 1.54 (d, *J* = 0.7 Hz, 3H), 1.38 (d, *J* = 0.8 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 113.4, 97.4, 79.6, 78.2, 67.6, 26.0, 24.9 ppm. IR (film): $\tilde{\nu}$ = 3420, 2942, 1375, 1209, 1162, 1066, 987, 856 cm^{-1}. MS (EI) *m/z* (%): 145 (100), 99 (8), 85 (55), 71 (5), 59 (19), 43 (34). HRMS (ESIpos): *m/z* calcd for $C_7H_{12}O_4Na$ [M+Na$^+$]: 183.0628, found: 183.0629. The analytical and spectroscopic data are in agreement with those reported in the literature.[10]

Hydrazone 29. 1,1-Dimethylhydrazine (1.10 mL, 14.5 mmol) was added to a solution of the lactol **28** (1.96 g, 12.2 mmol) in anhydrous EtOH (23 mL). The mixture was stirred to reflux temperature for 2.5 h before it was cooled and concentrated to give the crude hydrazone as a pale yellow oil which was used directly in the next step.

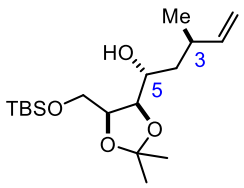


Imidazole (1.10 g, 16.2 mmol) and TBSCl (2.00 g, 13.3 mmol) were added to a solution of crude hydrazone in CH_2Cl_2 (45 mL) at 0 °C. The mixture was warmed to ambient temperature over 16 h and the reaction was quenched with sat. NH_4Cl (100 mL). The organic phase was separated and the aq. phase was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated to give a pale yellow residue. The residue was purified by flash chromatography (hexane/ EtOAc 4:1) to give the title compound as a colourless syrup. (3.5 g, 90%). $[\alpha]_D^{20}$ = +28.2 (c = 1.29, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.52 (d, *J* = 7.3 Hz, 1H), 4.74 (dd, *J* = 7.3, 6.7 Hz, 1H), 4.20 (ddd, *J* = 6.7, 5.8, 4.8 Hz, 1H), 3.73 (dd, *J* = 10.9, 5.8 Hz, 1H), 3.62 (dd, *J* = 11.0, 4.8 Hz, 1H), 2.81 (s, 6H), 1.48 (d, *J* = 0.7 Hz, 3H), 1.37 (s, 3H), 0.88 (s, 9H), 0.05 (s, 3H), 0.05 (s, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 130.6, 108.5, 78.4, 78.3, 62.3, 42.6, 27.6, 25.9, 25.2, 18.2, −5.3, −5.4 ppm. IR (film): $\tilde{\nu}$ = 2930, 2857, 1472, 1379, 1251, 1214, 1094, 1014, 837, 777 cm^{-1}. MS (EI) *m/z* (%): 655.4 (15), 570.4 (4), 431.2 (6), 339.2 (100), 259.2 (28). HRMS (ESIpos): *m/z* calcd for $C_{15}H_{32}N_2O_3SiNa$ [M+Na$^+$]: 339.2074, found: 339.2077. The analytical and spectroscopic data are in agreement with those reported in the literature.[10]

Aldehyde 30. Ozone was bubbled through a solution of hydrazone **29** (3.10 g, 9.79 mmol) and Sudan Red III (10 mg) in CH_2Cl_2 (100 mL) at −78 °C until the colour of the indicator had faded from red to yellow. Argon was bubbled through the mixture for 30 min at which point dimethylsulfide (3.62 mL, 49.0 mmol) was added and the mixture was allowed to reach ambient temperature over 4 h. The mixture was concentrated to a yellow residue. The residue was purified by flash chromatography (hexane/EtOAc 9:1) to give the title compound as a colourless liquid (1.87 g, 69%). Boiling Point: 75-80 °C at 1 × 10^{-3} mbar. $[\alpha]_D^{20}$ = −43.9 (c = 1.09, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.68 (d, *J* = 2.0 Hz, 1H), 4.47 (ddd, *J* = 7.9, 3.9, 2.8 Hz, 1H), 4.42 (dd, *J* = 7.9, 2.0 Hz, 1H), 3.78 (dd, *J* = 11.4, 3.9 Hz, 1H), 3.69 (dd, *J* = 11.4, 2.8 Hz, 1H), 1.57 (d, *J* = 0.8 Hz, 3H), 1.38 (d, *J* = 0.8 Hz, 3H), 0.88 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 200.2, 110.6, 80.8, 79.7, 60.5, 26.8, 25.7, 25.0, 18.2, −5.5, −5.7 ppm. IR (film): $\tilde{\nu}$ = 2931, 2858, 1732, 1381, 1254, 1214, 1146, 1091, 1015, 837, 778 cm^{-1}. MS (EI) *m/z* (%): 199 (5), 187 (3), 171 (6), 159 (32), 145 (3), 129 (70), 117 (100), 101 (32), 89 (30), 75 (100), 59 (19). HRMS (ESIpos): *m/z* calcd for $C_{13}H_{27}O_4Si$ [M+H$^+$]: 275.1673, found: 275.1677. The analytical and spectroscopic data are in agreement with those reported in the literature.[10]

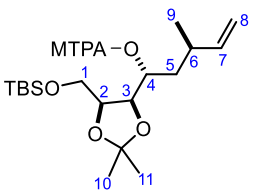
Phosphoramidite (*S,R,R*)-35. Phosphorus trichloride (0.14 mL, 1.62 mmol) was added to a solution of (*R*)-bis-1-(2-methoxyphenyl)ethylamine (462 mg, 1.62 mmol) and Et_3N (1.13 mL, 8.09 mmol) in THF (25 mL) at −78 °C. The mixture was allowed to reach ambient temperature and stirred for 4 h. (*S*)-BINOL (464 mg, 1.62 mmol) was then added in a single portion. The cloudy mixture was stirred for 16 h before it was filtered through Celite®, which was rinsed with EtOAc (50 mL). The combined filtrates were concentrated to give a pale yellow residue, which was purified by flash chromatography (hexane/EtOAc 9:1) to give the product as a white foam. The foam was triturated with cold *t*-butyl methyl ether to give the the title compound as a white solid (796 mg, 82%). $[\alpha]_D^{20}$ = +237.7 (c = 1.17, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.04–7.89 (m, 4H), 7.61–7.53 (m, 2H), 7.44–7.30 (m, 6H), 7.28–7.21 (m, 2H), 6.93 (td, *J* = 7.8, 1.7 Hz, 2H), 6.66 (td, *J* = 7.5, 1.1 Hz, 2H), 6.44–6.38 (m, 2H), 5.07–4.97 (m, 2H), 3.50 (s, 6H), 1.57 (s, 3 H), 1.56 (s, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 155.9, 150.7, 150.6, 150.1, 133.0, 132.9, 132.9, 132.2, 131.3, 130.4, 130.2, 129.4, 128.3, 128.1, 127.4, 127.4, 127.2, 127.2, 125.9, 125.7, 124.6, 124.4, 124.3, 124.2, 122.8, 122.4, 122.4, 121.7, 121.7, 119.4, 109.2 (2C), 54.6 (2C), 48.3, 48.2, 22.4, 22.2 ppm. ^{31}P NMR (162 MHz, $CDCl_3$): δ = 151.4 ppm. IR (film): $\tilde{\nu}$ = 3055, 2967, 2834, 1589, 1491, 1463, 1328, 1233, 1204, 1097, 1070, 1032, 948, 823, 749, 626 cm^{-1}. MS (EI) *m/z* (%): 901.4 (18), 745.5 (8), 600.2 (19), 504.4 (5), 387.1 (3), 286.2 (100), 241.2 (3). HRMS (ESIpos): *m/z* calcd for $C_{38}H_{35}NO_4P$ [M+H$^+$]: 600.2298, found: 600.2303.

Alcohol S18. To a solution of Ni(cod)$_2$ (100 mg, 0.36 mmol) in toluene (38 mL) was added



phosphoramidite (*S,R,R*)-**35** (222 mg, 0.37 mmol) and the resulting mixture was stirred for 10 min during which time the pale yellow solution became orange. To this mixture were added, sequentially and rapidly: isoprene (3.0 mL, 30 mmol), aldehyde **30** (1.94 g, 7.05 mmol) and triethylborane (1 M in hexane, 17 mL, 17 mmol). The resulting dark orange/red mixture was stirred at ambient temperature for 16 h. The reaction was quenched with sat. NH_4Cl (50 mL) and the mixture diluted with methyl *t*-butylether (50 mL). The aq. phase was separated and extracted with methyl *t*-butylether (2 × 50 mL). The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated to give a pale green/yellow oil. The diastereomeric mixture ((3*R*,5*R*)/(3*S*,5*S*)/(3*S*,5*R*) = 5.2:1:0.52) was purified by flash chromatography (toluene/methyl *t*-butylether 95:5) to give the title compound as a colourless oil (1.45 g, 60% (contaminated with 10% of the (3*S*,5*R*)-configured diastereomer (*ent*-**34**)). Spectral and analytical data for **S18**: $[\alpha]_D^{20}$ = +6.6 (c = 1.01, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.84 (ddd, *J* = 17.3, 10.3, 7.1 Hz, 1H), 5.01 (ddd, *J* = 17.2, 1.9, 1.3 Hz, 1H), 4.90 (ddd, *J* = 10.3, 1.9, 1.1 Hz, 1H), 4.22 (ddd, *J* = 10.1, 5.3, 3.4 Hz, 1H), 4.00 (dd, *J* = 8.9, 5.3 Hz, 1H), 3.93–3.86 (m, 1H), 3.85–3.83 (m, 1H), 3.82–3.76 (m, 1H), 3.58 (ddd, *J* = 10.3, 3.4, 0.7 Hz, 1H), 2.64–2.47 (m, 1H), 1.67–1.54 (m, 2H), 1.36 (s, 3H), 1.32 (s, 3H), 1.03 (d, *J* = 6.7 Hz, 3H), 0.91 (s, 9H), 0.13 (s, 3H), 0.12 (s, 3H) ppm.^{13}C NMR (101 MHz, $CDCl_3$): δ = 145.3, 111.8, 108.3, 81.2, 77.2, 66.7, 62.0, 40.7, 33.3, 28.1, 25.7, 25.4, 18.8, 18.2, −5.6, −5.7 ppm. IR (film): $\tilde{\nu}$ = 3489, 2933, 1471, 1370, 1255, 1219, 1082, 1004, 837, 780 cm^{-1}. MS (EI) *m/z* (%): 711.5 (4), 435.5 (3), 367.2 (100). HRMS (ESIpos): *m/z* calcd for $C_{18}H_{36}O_4SiNa$ [M+Na$^+$]: 367.2275, found: 367.2275.

Mosher Ester Analysis of Homoallyl Alcohol S18. Et_3N (13 µL, 0.091 mmol) and DMAP (0.4 mg, 0.003



mmol) were added to a solution of alcohol **S18** (10.5 mg, 0.031 mmol) in CH_2Cl_2 (1 mL) followed by (*R*)-(–)-α-methoxy-α-trifluoromethyl-phenylacetyl chloride ((*R*)-MTPA-Cl) (8.6 µL, 0.046 mmol). The resulting mixture was stirred at ambient temperature for 16 h. After quenching with sat. $NaHCO_3$ (3 mL), the aq. phase was separated and extracted with CH_2Cl_2 (3 × 5 mL). The combined organic phases were dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography (hexane/methyl *t*-butylether 95:5) to give the corresponding (*S*)-Mosher ester (*S*)-**S19** (10.2 mg, 60%). $[\alpha]_D^{20}$ = −15.4 (c = 1.02, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.60–7.53 (m, 2H), 7.43–7.36 (m, 3H), 5.72 (ddd, *J* = 17.4, 10.3, 7.4 Hz, 1H), 5.52 (ddd, *J* = 8.5, 5.3, 3.9 Hz, 1H), 4.98–4.93 (m, 1H), 4.93–4.90 (m, 1H), 4.19 (dd, *J* = 6.5, 5.3 Hz, 1H), 4.11–4.04 (m, 1H), 3.68 (dd, *J* = 11.1, 4.9 Hz, 1H), 3.58–3.52 (m, 4H), 2.24–2.14 (m, 1H), 1.87 (ddd, *J* = 14.3, 8.5, 5.6 Hz, 1H), 1.66 (ddd, *J* = 14.7, 9.0, 3.9 Hz, 1H), 1.36 (s, 3H), 1.29 (s, 3H), 1.04 (d, *J* = 6.6 Hz, 3H), 0.90 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H) ppm. IR (film): $\tilde{\nu}$ = 2932,

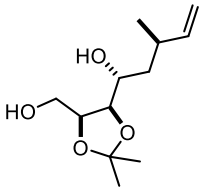
1749, 1463, 1380, 1254, 1169, 1104, 1019, 838, 778, 719 cm^{-1}. MS (EI) *m/z* (%): 1143.5 (40), 860.9 (5), 583.3 (100), 543.2 (8). HRMS (ESIpos): *m/z* calcd for $C_{28}H_{43}F_3O_6SiNa$ [M+Na^+]: 583.2673, found: 583.2674.

The corresponding Mosher ester (*R*)-**S19** (4.8 mg, 26%) was prepared analogously: $[\alpha]_D^{20}$ = +25.6 (c = 0.48, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.62–7.55 (m, 2H), 7.43–7.35 (m, 3H), 5.66 (ddd, *J* = 16.9, 10.5, 7.5 Hz, 1H), 5.49 (dt, *J* = 8.4, 4.0 Hz, 1H), 4.90–4.87 (m, 1H), 4.85 (d, *J* = 1.0 Hz, 1H), 4.29 (dd, *J* = 6.6, 4.2 Hz, 1H), 4.21–4.11 (m, 1H), 3.70 (dd, *J* = 11.0, 5.5 Hz, 1H), 3.62 (dd, *J* = 11.0, 6.1 Hz, 1H), 3.56 (s, 3H), 2.11– 1.99 (m, 1H), 1.85 (ddd, *J* = 14.5, 8.8, 5.6 Hz, 1H), 1.61–1.51 (m, 1H), 1.45 (s, 3H), 1.33 (s, 3H), 0.98 (d, *J* = 6.7 Hz, 3H), 0.89 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H) ppm. IR (film): $\tilde{\nu}$ = 2931, 1748, 1463, 1381, 1254, 1169, 1106, 1020, 837, 779, 719 cm^{-1}. MS (EI) *m/z* (%): 1143.5 (20), 860.4 (4), 583.3 (100), 543.2 (3). HRMS (ESIpos) *m/z* calcd for $C_{28}H_{43}F_3O_6SiNa$ [M+Na^+]: 583.2673, found: 583.2675.

Table S-9. Mosher ester analysis for product **S18** according to Hoye and co-workers;[12] arbitrary numbering scheme as shown in the insert

Assignment	S18	(*S*)-S19	(*R*)-S19	Δ (δ (S–R)) [ppm]
1a	3.89	3.68	3.70	-0.02
1b	3.84	3.56	3.62	-0.06
2	4.22	4.08	4.16	-0.08
3	4.00	4.19	4.29	-0.10
4	3.76	5.52	5.49	+0.03
5a	1.59	1.87	1.85	+0.02
5b	1.59	1.66	1.55	+0.11
6	2.55	2.19	2.05	+0.14
7	5.84	5.72	5.66	+0.06
8a	5.01	4.95	4.88	+0.07
8b	4.90	4.91	4.85	+0.06
9	1.03	1.04	0.98	+0.06
10	1.36	1.36	1.45	-0.09
11	1.32	1.29	1.33	-0.04

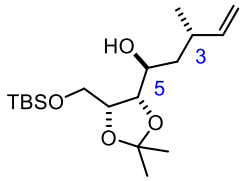
Diol 31. A solution of TBAF (1 M in THF, 4.4 mL, 4.4 mmol) was added dropwise to a solution of



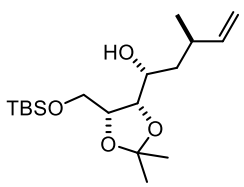
alcohol **S18** (1.45 g, 4.20 mmol, contaminated with 10% of the 1,3-*syn* diastereoisomers) in THF (20 mL) at 0 °C. The resulting mixture was stirred at 0 °C for 20 min before it was poured into a solution of sat. NH_4Cl. (50 mL) and diluted with EtOAc (50 mL). The organic phase was separated and the aq. layer was extracted with EtOAc (3 × 50 mL). The combined organic phases were washed with brine, dried over

Na_2SO_4, filtered and concentrated to a colourless residue. The residue was purified twice by flash chromatography (hexane/EtOAc 1:1) to yield the diol **31** (950 mg, 98%, contaminated with 10% of the 1,3-*syn* diastereoisomers). $[\alpha]_D^{20}$ = +2.9 (c = 1.05, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.84 (ddd, *J* = 17.2, 10.2, 7.9 Hz, 1H), 5.09 (dt, *J* = 17.3, 1.4 Hz, 1H), 4.97 (ddd, *J* = 10.2, 1.8, 0.8 Hz, 1H), 4.28 (ddd, *J* = 8.0, 5.2, 4.4 Hz, 1H), 3.98–3.85 (m, 2H), 3.83 (d, *J* = 7.9 Hz, 1H), 3.72 (dd, *J* = 11.4, 4.5 Hz, 1H), 2.95 (br s, 2H), 2.43 (dtd, *J* = 13.8, 6.9, 1.0 Hz, 1H), 1.83–1.73 (m, 1H), 1.55–1.45 (m, 1H), 1.42–1.39 (m, 3H), 1.34 (d, *J* = 0.7 Hz, 3H), 1.05 (d, *J* = 6.7 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 145.4, 113.3, 108.2, 80.1, 77.4, 69.1, 61.0, 41.0, 35.4, 28.0, 25.4, 20.1 ppm. IR (film): $\tilde{\nu}$ = 3458, 2954, 2929, 2857, 1740, 1461, 1440, 1388, 1253, 1128, 1080, 1004, 836, 777, 647 cm^{-1}. MS (EI) *m/z* (%): 215 (30), 141 (15), 137 (12), 131 (25), 123 (23), 119 (8), 113 (33), 109 (11), 99 (33), 95 (43), 91 (12), 85 (24), 83 (36), 81 (32), 79 (15), 74 (31), 73 (22), 59 (100), 43 (43), 41 (27). HRMS (ESIpos): *m/z* calcd for $C_{12}H_{22}O_4Na$ [M+Na$^+$]: 253.1410, found: 253.1413.

Alcohol 32. Phosphoramidite (*S,S,S*)-**35** (10.8 mg, 18.2 µmol) was added to a solution of $Ni(cod)_2$ (5.0 mg, 18 µmol) in toluene (1.9 mL) and the mixture was stirred for 10 min during which time the pale yellow solution became orange. To this mixture was added sequentially and rapidly: isoprene (0.15 mL, 1.5 mmol), aldehyde *ent*-**30** (100 mg, 0.364 mmol) and triethylborane (1 M in hexane, 0.88 mL, 0.88 mmol). The resulting dark orange/red mixture was stirred at ambient temperature for 16 h. The reaction was quenched with sat. NH_4Cl (50 mL) and methyl *t*-butylether (50 mL). The aq. phase was separated and extracted with methyl *t*-butylether (2 × 50 mL). The combined organic layers were washed with brine and dried over Na_2SO_4, filtered and concentrated to give a pale green/yellow oil. The diastereomeric mixture ((3*S,*5*S*)/(3*R,*5*R*)/(*3R,*5*S*) = 2:1:1) was purified by flash chromatography (toluene/methyl *t*-butylether 95:5) to give the (3*S,*5*S*)-**32** (37.5 mg, 30%), (3*R,*5*R*)-**33** (19 mg, 15%) and (*3R,*5*S*)-**34** (19 mg, 15%) a colourless oil. The spectral data are matching with **S18** (**32** = *ent*-**S18**). Analytical data for **32**: $[\alpha]_D^{20}$ = –5.8 (c = 1.01, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.84 (ddd, *J* = 17.3, 10.3, 7.1 Hz, 1H), 5.01 (ddd, *J* = 17.2, 1.9, 1.3 Hz, 1H), 4.90 (ddd, *J* = 10.3, 1.9, 1.1 Hz, 1H), 4.22 (ddd, *J* = 10.1, 5.3, 3.4 Hz, 1H), 4.00 (dd, *J* = 8.9, 5.3 Hz, 1H), 3.93–3.86 (m, 1H), 3.85–3.83 (m, 1H), 3.82–3.76 (m, 1H), 3.58 (ddd, *J* = 10.3, 3.4, 0.7 Hz, 1H), 2.64–2.47 (m, 1H), 1.67–1.54 (m, 2H), 1.36 (s, 3H), 1.32 (s, 3H), 1.03 (d, *J* = 6.7 Hz, 3H), 0.91 (s, 9H), 0.13 (s, 3H), 0.12 (s, 3H) ppm.^{13}C NMR (101 MHz, $CDCl_3$): δ = 145.3, 111.8, 108.3, 81.2, 77.2, 66.7, 62.0, 40.7, 33.3, 28.1, 25.7, 25.4, 18.8, 18.2, −5.6, −5.7 ppm. IR (film): $\tilde{\nu}$ = 3489, 2933, 1471, 1370, 1255, 1219, 1082, 1004, 837, 780 cm^{-1}. MS (EI) *m/z* (%): 711.5 (4), 435.5 (3), 367.2 (100). HRMS (ESIpos): *m/z* calcd for $C_{18}H_{36}O_4SiNa$ [M+Na$^+$]: 367.2275, found: 367.2275.



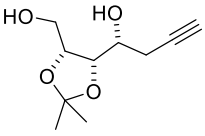
Spectral data for **33**: ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.78 (ddd, *J* = 17.4, 10.3, 7.3 Hz, 1H), 4.98 (dt, *J* =



17.2, 1.6 Hz, 1H), 4.91 (ddd, *J* = 10.3, 1.8, 1.0 Hz, 1H), 4.15 (td, *J* = 6.8, 4.3 Hz, 1H), 4.02 (dd, *J* = 6.5, 3.0 Hz, 1H), 3.94 (dd, *J* = 10.8, 7.1 Hz, 1H), 3.89 (dddd, *J* = 8.9, 5.7, 3.6, 2.2 Hz, 1H), 3.74 (dd, *J* = 10.7, 4.3 Hz, 1H), 2.76 (d, *J* = 5.7 Hz, 1H), 2.42 (tdd, *J* = 8.2, 6.6, 3.6 Hz, 1H), 1.76–1.62 (m, 2H), 1.47 (s, 3H), 1.36 (s, 3H), 1.02 (d, *J* = 6.7 Hz, 3H), 0.90 (s, 9H), 0.09 (s, 6H) ppm.

The α-Methylene-γ-lactone Route

Diol 39. Preparation of allenylmagnesium bromide:[18] A 250 mL 3-necked round-bottomed flask fitted



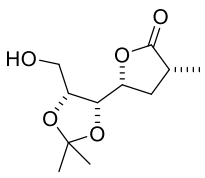
with a condenser, pressure equalizing dropping funnel and thermometer was charged with magnesium turnings (6.08 g, 250 mmol), ether (100 mL) and $HgCl_2$ (250 mg). The suspension was stirred for 30 min at ambient temperature before it was cooled to 0 °C. A small portion of a solution of propargyl bromide was added to initiate the reaction (2.28 mL). Once initiated (20 min, internal temperature reached 14 °C), the mixture was cooled to −20 °C and the remaining propargyl bromide (20 mL, 200 mmol, 80% soln.) was added dropwise over 30 min in order to maintain the temperature between −1 and +1 °C. After stirring for 45 min at 0 °C, the pale grey/green mixture was filtered through Celite® into to a graduated Schlenk tube and diluted to 200 mL with Et_2O. The clear pale yellow solution was titrated to be 0.745 M versus iodine (75% yield). The solution of allenylmagnesium bromide was stored at −20 °C for months without loss of activity.

The solution of allenyl Grignard reagent (185 mL, 0.745 M in Et_2O, 138 mmol) was added dropwise to a solution of (−)-2,3-O-isopropylidene-D-erythronolactone (19.9 g, 126 mmol) in THF (500 mL) at −78 °C, not letting the internal temperature rise above −70 °C. The colourless homogenous reaction was stirred at −78 °C for 1 h. The reaction was quenched with sat. NH_4Cl (100 mL, added in such a rate as to keep the temperature below −65 °C) and the mixture warmed to ambient temperature. Distilled water was added dropwise until a clear biphasic mixture was observed. The aq. phase was extracted with *t*-butyl methyl ether (3 × 500 mL) and the combined organic phases were washed with brine (200 mL), dried over Na_2SO_4 and concentrated to give the crude lactol **37** contaminated with small amounts of the corresponding allene as a colourless oil which was immediately used in the next step.

A solution of lactol **37** (25.0 g, 126 mmol) in THF (250 mL with rinses) was added dropwise to a solution of Dibal-H (90 mL, 51 mmol) in THF (250 mL, ***Caution***! Dissolution of Dibal-H is extremely exothermic) at −78 °C, not letting the temperature rise above −70 °C. The mixture was allowed to warm to 10 °C overnight before being cooled to 4 °C and the reaction was quenched cautiously with methanol (20 mL). This mixture was poured onto a 1:1 mixture of sat. Rochelle's (500 mL) and EtOAc (500 mL) and stirred overnight. The organic phase was separated and the aq. phase was extracted with EtOAc (3 × 200 mL). The combined organic phases were washed with brine (200 mL), dried over Na_2SO_4 and

concentrated to a colourless oil which solidified on standing. This solid represents a mixture of products (*syn*/*anti* = 95:5) and 4% of the corresponding allene. The crude solid was crystallized four times from boiling toluene (50 mL; 40 mL × 3) to give the title compound as colourless needles (25.1 g, 80% over 2 steps). The product is the pure *syn* diastereomer containing ≤ 0.2% allene by ^{1}H-NMR analysis. $[\alpha]_D^{20}$ = –24.2 (c = 1.12, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.35–4.22 (m, 2H), 3.94–3.79 (m, 3H), 3.11 (br d, *J* = 6.1 Hz, 1H), 2.68–2.60 (m, 1H), 2.59–2.45 (m, 2H), 2.05 (t, *J* = 2.7 Hz, 1H), 1.52 (s, 3H), 1.39 (s, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 108.5, 80.4, 77.1, 77.0, 70.6, 68.0, 60.9, 26.9, 24.8, 24.8 ppm. IR (film): $\tilde{\nu}$ = 3267, 3200, 2985, 2933, 2887, 1470, 1382, 1386, 1220, 1134, 1091, 1013, 841, 670 cm^{-1}. MS (EI) *m/z* (%): 185 (4), 131 (10), 103 (8), 85 (13), 73 (10), 67 (8), 59 (100), 55 (15), 43 (55), 39 (18). HRMS (ESIpos): *m/z* calcd for $C_{10}H_{16}O_4Na$ [M+Na$^+$]: 223.0941, found: 223.0942. Single crystals were grown by cooling the ethanol solution confirming absolute stereochemistry of **39** (see Figure S-1).

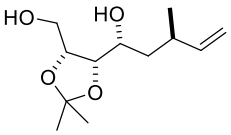
Lactone 43. A 100 mL autoclave was charged with $Pd(OAc)_2$ (7.4 mg, 0.033 mmol), PTSA·H_2O (125 mg, 0.66 mmol), diphenyl-(6-methyl-2-pyridyl)-phosphine (**45**) (273 mg, 0.98 mmol), BHT (724 mg, 3.29 mmol) and NMP (10 mL). The red mixture was stirred until a homogenous solution was obtained (around 10 min) before adding the diol **39** (6.58 g, 32.9 mmol). The autoclave was tightly closed and the mixture stirred under high-vacuum for 2 h. The autoclave was then pressurized with CO (60 bar) and the mixture was stirred at 45 °C for 16.5 h. The mixture was allowed to cool to ambient temperature before the autoclave was carefully vented. The mixture was filtered through a pad of Florisil® (100 g), which was rinsed with EtOAc (500 mL). The combined filtrates containing crude α,β-unsaturated ester **41** were concentrated.



The residue was diluted with EtOAc (250 mL) before adding Pd/C (10 wt.-%, 1.75 g, 1.64 mmol, 5 mol%). The flask was purged and back-filled with H_2 gas three times before the mixture was stirred for 1 h under balloon pressure of H_2. The catalyst was removed by filtration of the mixture through Celite®. The filtrate was concentrated to a pink oil, which was passed through silica (hexane/EtOAc 4:1) giving a mixture of lactone **43** and butenolide **42** (**43**/**42** = 0.45:1) as a colourless oil. The crude mixture was redissolved in EtOAc (150 mL) before adding Pd/C (10 wt.-%, 1.75 g, 1.64 mmol, 5 mol%). The flask was purged and back-filled with H_2 gas three times before the mixture was stirred for 16 h under balloon pressure of H_2. After filtration through Celite® and rinsing with EtOAc, the combined filtrates were concentrated to a colourless oil affording the title compound as a single isomer (6.94 g, 92% over 2 steps). $[\alpha]_D^{20}$ = –43.5 (c = 1.15, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.50 (ddd, *J* = 9.7, 6.5, 3.4 Hz, 1H), 4.35 (td, *J* = 6.5, 5.1 Hz, 1H), 4.15–4.09 (m, 1H), 3.93–3.78 (m, 2H), 2.73–2.60 (m, 1H), 2.46 (ddd, *J* = 12.5, 9.3, 6.5 Hz, 1H), 2.11–2.05 (m, 1H), 1.87 (ddd, *J* = 12.4, 11.1, 9.6 Hz, 1H), 1.47 (s, 3H), 1.38 (s, 3H), 1.29 (d, *J* = 7.1 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 179.1, 109.4, 77.6, 76.9, 75.4, 61.3,

34.7, 32.8, 26.9, 25.3, 15.2 ppm. IR (film): $\tilde{\nu}$ = 3457, 2983, 2937, 1765, 1456, 1381, 1215, 1167, 1035, 932, 856, 520 cm^{-1}. MS (EI) *m/z* (%): 215 (100), 199 (30), 181 (10), 155 (20), 137 (25), 131 (75), 109 (100), 99 (45), 85 (60), 81 (50), 59 (100), 43 (65). HRMS (ESIpos): *m/z* calcd for $C_{11}H_{18}O_5Na$ [M+Na^+]: 253.1046, found: 253.1046.

Diol 44. A solution of Dibal-H (1 M in CH_2Cl_2, 50 mL, 50 mmol) was added dropwise over 30 min to a

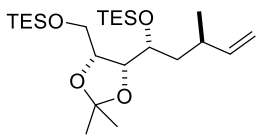


mechanically stirred solution of lactone **43** (5.52 g, 24.0 mmol) in CH_2Cl_2 (50 mL) at −78 °C. The resulting thick foamy mixture was mechanically agitated by a steel paddle at −78 °C for an additional 30 min. The reaction was quenched by sequential, and cautious, addition of *t*-butanol (15 mL) and water (15 mL). Silica gel (24 g) was added in one portion and the mixture was allowed to come to ambient temperature and stirred for 1 h until homogenous. The reaction slurry was filtered and the cake was washed with EtOAc (500 mL). The combined filtrates were dried over Na_2SO_4, filtered and concentrated to give the crude lactol as a colourless oil, which was used in the next step without further purification.

A solution of crude lactol in toluene (50 + 20 mL) was added dropwise to a suspension of methylene-triphenylphosphorane (13.25 g, 47.96 mmol) in toluene (100 mL) at −78 °C, ensuring that the internal temperature never rose above −70 °C. The mixture was allowed to warm to ambient temperature over 16 h during which time the yellow suspension became homogenous. The mixture was cooled to 4 °C and the reaction was cautiously quenched with sat. NH_4Cl (100 mL). The organic phase was separated, and the aq. phase was extracted with EtOAc (3 × 100 mL). The combined organic phases were washed with brine and dried over Na_2SO_4, filtered and concentrated to give a cloudy pale yellow residue. The residue was purified by flash chromatography (hexane/EtOAc 1:1) to give the title compound as a colourless oil which solidified on standing to a waxy solid (5.01 g, 91% over 2 steps). $[\alpha]_D^{20}$ = +9.4 (c = 2.23, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.75 (m, 1H), 4.98 (dd, *J* = 17.3, 1.6 Hz, 1H), 4.91 (dd, *J* = 10.3, 1.3 Hz, 1H), 4.22–4.15 (m, 1H), 4.04–3.99 (m, 1H), 3.82–3.68 (m, 3H), 2.83 (br s, 2H), 2.38 (hept, *J* = 6.8 Hz, 1H), 1.75–1.64 (m, 1H), 1.48 (s, 3H), 1.41–1.31 (m, 1H), 1.35 (s, 3H) 1.01 (dd, *J* = 6.7, 1.6 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 144.4, 112.7, 108.2, 79.1, 77.3, 67.0, 61.0, 41.3, 34.1, 27.2, 25.0, 19.3 ppm. IR (film): $\tilde{\nu}$ = 3406, 2935, 1640, 1372, 1215, 1038, 996, 862, 515 cm^{-1}. MS (EI) *m/z* (%): 483.3 (23), 253.1 (100), 231.1 (10). HRMS (ESIpos): *m/z* calcd for $C_{12}H_{22}O_4Na$ [M+Na^+]: 253.1410, found: 253.1411.

Completion of the Diverted Approach

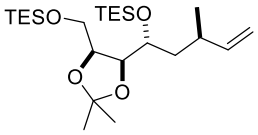
Compound S19. TESCl (3.7 mL, 22.04 mmol) and DMAP (100 mg, 0.82 mmol) were added to a solution



of diol **44** (1 g, 4.34 mmol) in pyridine (20 mL). The resulting cloudy mixture was stirred at ambient temperature for 16 h. The mixture was partitioned between water (50 mL) and methyl *t*-butylether (50 mL). The aq. phase was

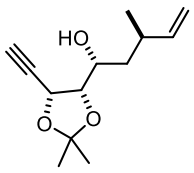
separated and extracted with methyl *t*-butylether (3 × 50 mL). The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated to a colourless residue. The residue was purified by flash chromatography (hexane/methyl *t*-butylether 95:5) to afford the title compound as a colourless oil (2.0 g, 100%). $[\alpha]_D^{20}$ = +25.8 (c = 1.08, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.77 (ddd, *J* = 17.3, 10.3, 7.1 Hz, 1H), 4.97 (dt, *J* = 17.2, 1.6 Hz, 1H), 4.90 (ddd, *J* = 10.3, 1.8, 1.1 Hz, 1H), 4.04 (q, *J* = 5.5 Hz, 1H), 4.01–3.96 (m, 1H), 3.92 (td, *J* = 7.7, 4.2 Hz, 1H), 3.72 (dd, *J* = 10.7, 5.6 Hz, 1H), 3.55 (dd, *J* = 10.7, 5.3 Hz, 1H), 2.49–2.36 (m, 1H), 1.51–1.45 (m, 2H), 1.43 (s, 3H), 1.32 (s, 3H), 1.02–0.93 (m, 21H), 0.70–0.57 (m, 12H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 144.9, 112.1, 107.8, 80.9, 78.1, 68.7, 62.1, 40.6, 33.2, 27.9, 25.4, 18.8, 7.0, 6.7, 5.5, 4.3 ppm. IR (film): $\tilde{\nu}$ = 2955, 2877, 1458, 1370, 1103, 1004, 911, 739 cm^{-1}. MS (EI) *m/z* (%): 939.6 (28), 573.3 (7), 481.3 (100), 345.2 (4). HRMS (ESIpos): *m/z* calcd for $C_{24}H_{50}O_4Si_2Na$ [M+Na$^+$]: 481.3140, found: 481.3138.

Compound S20. TESCl (3.46 mL, 20.6 mmol) and DMAP (100 mg, 0.82 mmol) were added to a solution



of diol **31** (950 g, 4.13 mmol) in pyridine (20 mL). The resulting cloudy mixture was stirred at ambient temperature for 16 h. The mixture was partitioned between water (50 mL) and methyl *t*-butylether (50 mL). The aq. phase was separated and extracted with methyl *t*-butylether (3 × 50 mL). The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated to a colourless residue. The residue was purified by flash chromatography (hexane/methyl *t*-butylether 95:5) to afford the title compound as a colourless oil (1.88 g, 99%, contaminated with 10% of the 1,3-*syn* diastereoisomers). $[\alpha]_D^{20}$ = −14.8 (c = 1.10, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.75 (ddd, *J* = 17.4, 10.3, 7.4 Hz, 1H), 4.98 (ddd, *J* = 17.2, 1.8, 1.2 Hz, 1H), 4.93 (ddd, *J* = 10.3, 1.8, 0.9 Hz, 1H), 4.18 (ddd, *J* = 7.6, 6.5, 4.2 Hz, 1H), 4.09 (dd, *J* = 6.5, 4.2 Hz, 1H), 4.03 (ddd, *J* = 7.0, 5.1, 4.0 Hz, 1H), 3.84 (dd, *J* = 10.9, 4.2 Hz, 1H), 3.68 (dd, *J* = 11.0, 7.6 Hz, 1H), 2.41–2.29 (m, 1H), 1.64 (dt, *J* = 13.7, 6.7 Hz, 1H), 1.46 (s, 3H), 1.44–1.39 (m, 1H), 1.33 (s, 3H), 1.00 (d, *J* = 6.8 Hz, 3H), 0.97 (t, *J* = 7.9 Hz, 18H), 0.65–0.59 (m, 12H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 144.6, 112.6, 107.9, 80.0, 78.6, 68.9, 62.9, 41.5, 33.9, 27.6, 25.3, 19.9, 6.9, 6.7, 5.3, 4.4 ppm. IR (film): $\tilde{\nu}$ = 2954, 2877, 1458, 1378, 1241, 1093, 1005, 910, 740 cm^{-1}. MS (EI) *m/z* (%): 939.6 (25), 545.3 (4), 481.3 (100), 383.3 (10), 327.2 (10). HRMS (ESIpos): *m/z* calcd for $C_{24}H_{50}O_4Si_2Na$ [M+Na$^+$]: 481.3140, found: 481.3141.

Alkyne 50a. Oxalyl chloride (1.9 mL, 22 mmol) was added dropwise to a solution of DMSO (3.0 mL,



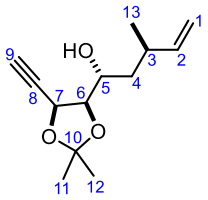
42 mmol) in CH_2Cl_2 (20 mL) at −78 °C at such a rate as to mainging the internal temperature below −65 °C. After 15 min of stirring at −78 °C, a solution of **S19** (2.02 g, 4.39 mmol) in CH_2Cl_2 (12 mL with rinses) was added dropwise, again ensuring that the internal temperature did not exceed −65 °C. Stirring was continued at −78 °C for 20 min before the temperature was raised to −35 °C over 30 min. Stirring was continued at this

temperature for 20 min before re-cooling the mixture to −78 °C. Hünig's base (11.5 mL, 66.0 mmol) was added dropwise, again ensuring the internal temperature did not exceed −65 °C. After stirring for 10 min at −78 °C, the mixture was allowed to reach 0 °C over 30 min and the reaction was quenched with sat. NH_4Cl (50 mL). The organic phase was separated and the aq. phase was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated to give the aldehyde **46** as a yellow oil, which was used without further purification (1.21 g, 81%, dr = 12.5:1).

Methanol (95 µL, 2.35 mmol) was added dropwise to a solution of KHMDS (467 mg, 2.33 mmol) in THF (2.5 mL) at 0 °C. The milky suspension was stirred for 20 min at the same temperature and then cooled to −78 °C, at which point a solution of dimethyl-(1-diazo-2-oxopropyl)-phosphonate (486 mg, 2.53 mmol) in THF (1.0 mL) was added dropwise. The yellow solution was stirred for 30 min at −78 °C before a solution of crude aldehyde **46** (247 mg, 0.72 mmol) in THF (2.0 mL with rinses) was added dropwise. The mixture was allowed to reach −50 °C over 10 min and then stirred for 1 h at −50 °C before the reaction was quenched with sat. NH_4Cl (20 mL). The resulting mixture was diluted with methyl *t*-butylether (20 mL). The aq. phase was separated and extracted with methyl *t*-butylether (3 × 30 mL). The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated to give the crude alkyne as a yellow oil, which was used without further purification.

A solution of TBAF trihydrate (341 mg, 1.08 mmol) in THF (1.1 mL) was added to a solution of crude alkyne in THF (5 mL) at 0 °C. After removing the ice bath, the mixture was stirred for 10 min at ambient temperature. The reaction was quenched with sat. NH_4Cl (20 mL) and the resulting mixture was diluted with methyl *t*-butylether (20 mL). The aq. phase was separated and extracted with methyl *t*-butylether (3 × 30 mL). The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated to a yellow residue, which was purified by flash chromatography (hexane/EtOAc 9:1) to afford the title compound as a colourless oil (131 mg, 81% over 2 steps). $[\alpha]_D^{20}$ = +54.5 (c = 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.82 (ddd, *J* = 17.4, 10.3, 7.1 Hz, 1H), 5.02 (dt, *J* = 17.3, 1.5 Hz, 1H), 4.93 (ddd, *J* = 10.3, 1.7, 1.0 Hz, 1H), 4.73 (dd, *J* = 5.8, 2.2 Hz, 1H), 4.05 (ddd, *J* = 9.9, 7.4, 2.6 Hz, 1H), 3.95 (dd, *J* = 7.4, 5.7 Hz, 1H), 2.55 (d, *J* = 2.2 Hz, 1H), 2.54–2.47 (m, 1H), 2.21 (s, 1H), 1.61–1.53 (m, 4H), 1.39–1.33 (m, 4H), 1.05 (d, *J* = 6.7 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 144.8, 112.4, 110.6, 81.1, 79.5, 76.1, 69.5, 66.9, 39.3, 33.6, 27.5, 25.9, 18.8 ppm. IR (film): $\tilde{\nu}$ = 3492, 3307, 2896, 2934, 1641, 1457, 1373, 1213, 1162, 1056, 913, 874, 664 cm^{-1}. MS (EI) *m/z* (%): 209 (11), 149 (3), 125 (10), 111 (6), 96 (27), 81 (24), 67 (31), 59 (76), 55 (62), 43 (100). HRMS (ESIpos): *m/z* calcd for $C_{13}H_{20}O_3Na$ [M+Na$^+$]: 247.1305, found: 247.1306.

Alkyne 50c. Oxalyl chloride (1.75 mL, 20.38 mmol) was added dropwise to a solution of DMSO (2.9 mL, 40.83 mmol) in CH_2Cl_2 (20 mL) at −78 °C, ensuring that the internal temperature did not exceed −65 °C. After 15 min at −78 °C, a solution of **S20** (1.87 g, 4.07 mmol) in CH_2Cl_2 (12 mL with rinses) was added dropwise, again ensuring that the internal temperature remained ≤ −65 °C. Stirring was continued at −78 °C for 20 min before raising the temperature to −35 °C over 30 min. Stirring was continued at this temperature for 20 min before re-cooling the mixture to −78 °C. Hünig's base (10.5 mL, 60.3 mmol) was added dropwise, again ensuring that the internal temperature did not exceed −65 °C. After 10 min at −78 °C, the mixture was allowed to reach 0 °C over 30 min and the reaction was quenched with sat. NH_4Cl (50 mL). The aq. phase was separated and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated to give the aldehyde **48** as a yellow oil, which was essentially pure and was used without further purification (1.07 g, 77%, dr = 3.8:1).



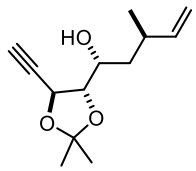
Methanol (400 µL, 9.87 mmol) was added dropwise to a solution of KHMDS (2 g, 9.98 mmol) in THF (10 mL) at 0 °C. The milky suspension was stirred for 20 min at the same temperature and then cooled to −78 °C. A solution of dimethyl-(1-diazo-2-oxopropyl)-phosphonate (2.00 g, 10.4 mmol) in THF (5 mL) was added dropwise at this temperature. The yellow solution was stirred for 30 min at −78 °C before a solution of crude aldehyde **48** (1.06 g, 3.1 mmol) in THF (9 mL with rinses) was added dropwise. The mixture was allowed to reach −50 °C over 10 min and stirring continued for 1 h. The reaction was quenched with sat. NH_4Cl (20 mL) and the mixture was diluted with methyl *t*-butylether (20 mL). The aq. phase was separated and extracted with methyl *t*-butylether (3 × 50 mL). The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated to give the crude alkyne as a yellow oil, which was used without further purification.

A solution of TBAF trihydrate (1.47 g, 4.65 mmol) in THF (4.7 mL) was added to a solution of the crude alkyne in THF (30 mL) at 0 °C. After removing the ice bath, the mixture was stirred for 10 min at ambient temperature. The reaction was quenched with sat. NH_4Cl (20 mL) and the mixture diluted with methyl *t*-butylether (30 mL). The aq. phase was separated and extracted with methyl *t*-butylether (3 × 30 mL). The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated to a yellow residue. The residue was purified by flash chromatography (hexane/EtOAc 9:1) to afford the title compound as a colourless oil (264 mg, 38% over 2 steps). $[\alpha]_D^{20}$ = −23.4 (c = 1.04, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): *see Table S-10*. ^{13}C NMR (101 MHz, $CDCl_3$): *see Table S-10*. IR (film): $\tilde{\nu}$ = 3479, 3298, 2986, 2937, 1640, 1457, 1373, 1227, 1162, 1068, 914, 866, 662 cm^{-1}. MS (EI) *m/z* (%): 471.3 (4), 356.2 (5), 247.1 (100), 215.1 (3). HRMS (ESIpos): *m/z* calcd for $C_{13}H_{20}O_3Na$ [M+Na$^+$]: 247.1305, found: 247.1305.

Table S-10. NMR data of alkyne **50c**; arbitrary numbering scheme as shown in the insert

atom n°	^{1}H NMR (400 MHz, $CDCl_3$)					^{13}C NMR (101 MHz, $CDCl_3$)	
	δ [ppm]	m	*J* [Hz]	COSY	NOESY	δ [ppm]	HMBC
1a	5.07	ddd	7.3, 1.8, 1.3	1b, 2	1b,13,3	112.7	3
1b	4.95	ddd	10.3, 1.8, 1.0	1a, 2	1a		
2	5.85	ddd	17.3, 10.3, 7.6	1ab, 3	4b, 13	145.3	1a, 3, 4ab, 13
3	2.48	m	-	2, 4ab, 13	1a, 5, 5-OH, 4ab, 13	34.7	1ab, 2, 4a, 13
4a	1.75	ddd	14.2, 8.0, 2.6	3, 4b	3, 5, 6, 13	40.8	3, 5-OH, 6, 13
4b	1.58	ddd	14.2, 9.9, 6.4	3, 4a, 5	2, 3, 5, 6, 13		
5	4.03	dddd	9.9, 8.4, 4.5, 2.6	4b, 5-OH, 6	3, 4ab, 5-OH, 13	70.1	6, 4b
6	3.91	dd	8.4, 5.8	7, 5	4ab, 5-OH, 7, 12	80.7	-
7	4.88	dd	5.8, 2.2	6, 9	5-OH, 6, 12	68.1	9
8	-	-	-	-	-	80.3	7, 6
9	2.62	d	2.2	7	-	76.1	7
10	-	-	-	-	-	110.7	7, 11, 12
11	1.52	q	0.5	12	12	27.5	12
12	1.35	q	0.5	11	6, 7, 11	25.9	11
13	1.06	d	6.7	3	1a, 2, 3, 4ab, 5	19.8	2, 3, 4ab
5-OH	2.18	dd	4.5, 0.6	5	3, 5, 6, 7	-	-

Alkyne 50b. IBX (2.43 g, 8.68 mmol) was added to a solution of diol **44** (1.00 g, 4.34 mmol) in DMSO

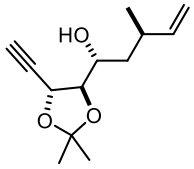


(8.7 mL). After stirring for 3.5 h, the reaction was quenched with water (40 mL). After stirring for 10 min, the resulting mixture was filtered through a small pad of Celite®, which was rinsed with methyl *t*-butylether (50 mL) and water (10 mL). From the filtrate, the aq. phase was separated and extracted with methyl *t*-butylether (3 × 50 mL). The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated to give the lactol **47** as a colourless oil, which was essentially pure and was used without further purification.

K_2CO_3 (1.8 g, 13 mmol) was added to a solution of crude lactol **47** in methanol (20 mL). The resulting suspension was heated to reflux and dimethyl-(1-diazo-2-oxopropyl)-phosphonate (2.5 g, 13 mmol) in methanol (8 mL) was added dropwise over 6 h. The red homogenous mixture was cooled in an ice bath and neutralized by cautious addition of HCl (1 M, 13 mL). The methanol was evaporated and the aq. solution was extracted with methyl *t*-butylether (3 × 50 mL). The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated to give a yellow residue. The residue was purified by flash chromatography (hexane/EtOAc 9:1) to afford the title compound as a colourless oil (247 mg, 25% over 2 steps). $[\alpha]_D^{20}$ = −14.4 (c = 1.20, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.78 (ddd,

J = 17.5, 10.2, 7.4 Hz, 1H), 5.02 (dt, *J* = 17.2, 1.4 Hz, 1H), 4.95 (dt, *J* = 10.3, 1.4 Hz, 1H), 4.55 (dd, *J* = 7.5, 2.1 Hz, 1H), 4.00 (dd, *J* = 7.5, 3.5 Hz, 1H), 3.70 (ddt, *J* = 9.4, 7.8, 4.0 Hz, 1H), 2.53 (d, *J* = 2.2 Hz, 1H), 2.49–2.37 (m, 1H), 1.95 (d, *J* = 8.0 Hz, 1H), 1.68 (ddd, *J* = 13.9, 9.3, 6.3 Hz, 1H), 1.49 (s, 3H), 1.46–1.39 (m, 4H), 1.05 (d, *J* = 6.7 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 144.3, 112.9, 110.7, 84.2, 80.9, 74.8, 68.1, 66.9, 40.8, 34.2, 26.7, 26.0, 19.4 ppm. IR (film): $\tilde{\nu}$ = 3474, 3301, 2988, 2934, 1641, 1457, 1375, 1213, 1162, 1056, 914, 875, 665 cm^{-1}. MS (EI) *m/z* (%): 209 (49), 149 (4), 125 (49), 111 (11), 96 (80), 81 (33), 67 (64), 59 (40), 55 (63), 43 (100). HRMS (ESIpos): *m/z* calcd for $C_{13}H_{20}O_3Na$ [M+Na$^+$]: 247.1305, found: 247.1307.

Alkyne 50d. IBX (4.52 g, 16.15 mmol) was added to a solution of diol **31** (1.86 g, 8.08 mmol) in DMSO



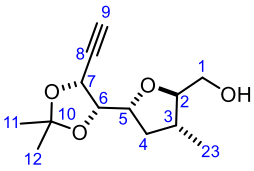
(16 mL). After stirring for 3.5 h, the reaction was quenched with water (80 mL). After stirring for 10 min, the resulting mixture was filtered through a small pad of Celite®, which was rinsed with methyl *t*-butylether (100 mL) and water (20 mL). From the filtrate, the aq. phase was separated and extracted with methyl *t*-butylether (3 × 100 mL). The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated to give the lactol **49** as a colourless oil, which was essentially pure and was used without further purification.

K_2CO_3 (4.46 g, 32.3 mmol) was added to a solution of crude lactol **49** in methanol (100 mL). The resulting suspension was stirred under reflux, while a solution of dimethyl-(1-diazo-2-oxopropyl)-phosphonate (4.63 g, 24.1 mmol) in methanol (20 mL) was added dropwise over 6 h. The red homogenous mixture was cooled in an ice bath and neutralized by cautious addition of HCl (1 M, 32.3 mL). The methanol was evaporated and the aq. solution was extracted with methyl *t*-butylether (3 × 100 mL). The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated to give a yellow residue. The residue was purified by flash chromatography (hexane/EtOAc 9:1) to afford the title compound as a colourless oil (511 mg, 28% over 2 steps). $[\alpha]_D^{20}$ = −24.3 (c = 1.02, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.79 (ddd, *J* = 17.3, 10.3, 7.7 Hz, 1H), 5.04 (ddd, *J* = 17.2, 1.7, 1.1 Hz, 1H), 4.96 (ddd, *J* = 10.3, 1.7, 0.9 Hz, 1H), 4.66 (dd, *J* = 7.2, 2.1 Hz, 1H), 4.10 (dd, *J* = 7.2, 3.4 Hz, 1H), 3.96 (ddd, *J* = 8.5, 4.8, 3.4 Hz, 1H), 2.54 (d, *J* = 2.1 Hz, 1H), 2.42 (dt, *J* = 14.3, 7.1 Hz, 1H), 2.15 (br s, 1H), 1.60–1.47 (m, 5H), 1.43 (s, 3H), 1.03 (d, *J* = 6.7 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 144.4, 113.1, 110.3, 84.0, 81.9, 74.5, 68.2, 65.0, 38.9, 34.7, 26.7, 25.8, 19.8 ppm. IR (film): $\tilde{\nu}$ = 3489, 3301, 2988, 2935, 1718, 1457, 1375, 1212, 1163, 1057, 914, 872, 669 cm^{-1}. MS (EI) *m/z* (%): 209 (87), 149 (4), 125 (17), 116 (7), 105 (17), 96 (27), 81 (49), 67 (100), 59 (13), 43 (43). HRMS (ESIpos): *m/z* calcd for $C_{13}H_{20}O_3Na$ [M+Na$^+$]: 247.1305, found: 247.1308.

General Procedure for Oxidative Mukaiyama Cyclization of Alkenes 50a-d. $Co(nmp)_2$ (10 mol%) was added to a solution of alkene **50a-d** (0.1 M, 100 mol%) in *i*-PrOH. The resulting homogenous solution

was degassed by 3 cycles of freeze-pump-thaw and back-filled with an atmosphere of oxygen. After adding *t*-BuOOH (5 M in decane, 10 mol%), a balloon of oxygen was fitted to the flask, which was placed in a pre-heated oil bath at 55 °C. The solution turned green within 5 min of heating and stirring was continued for 16 h. After cooling to ambient temperature, the mixture was concentrated to a green oil, which was purified by flash chromatography (hexane/EtOAc 1:1) to give the title compounds.

Compound 51a. According to General Procedure using alkene **50a** (854 mg, 3.81 mmol). Colourless oil

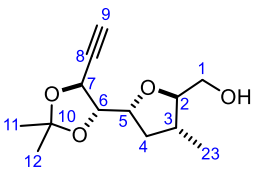


(589 mg, 64%). $[\alpha]_D^{20}$ = +37.6 (c = 1.03, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): *see Table S-11*. ^{13}C NMR (101 MHz, $CDCl_3$): *see Table S-11*. IR (film): $\tilde{\nu}$ = 3435, 3276, 2933, 2874, 1457, 1372, 1229, 1160, 1107, 1058, 864, 681 cm^{-1}. MS (EI) *m/z* (%): 225 (11), 165 (12), 151 (7), 121 (10), 115 (74), 95 (28), 95 (28), 79 (16), 71 (100), 67 (30), 55 (21), 43 (94). HRMS (ESIpos) *m/z* calcd for $C_{13}H_{20}O_4Na$ [M+Na$^+$]: 263.1254, found: 263.1254.

Table S-11. NMR data of THF **51a**; arbitrary numbering scheme as shown in the insert

atom n°	^{1}H NMR (400 MHz, $CDCl_3$)					^{13}C NMR (101 MHz, $CDCl_3$)	
	δ [ppm]	m	*J* [Hz]	COSY	NOESY	δ [ppm]	HMBC
1a	3.84	ddd	12.1, 2.8, 0.5	1-OH, 1b, 2	1-OH, 1b, 2, 11	62.1	-
1b	3.55	ddd	12.1, 3.8, 2.9	1-OH, 1a, 2	1-OH, 1a, 3, 23		
1-OH	1.99	br s	-	1ab	1ab	-	-
2	3.60	ddd	9.2, 3.8, 2.8	1ab, 3	1a, 3, 4b, 6, 23	86.3	4a, 23
3	2.28	ddp	11.1, 9.2, 6.6, 6.6	2, 4ab, 23	1b, 2, 5, 23	34.4	4ab, 23
4a	2.39	ddd	12.4, 6.6, 5.7	3, 4b, 5	4b, 5, 7, 23	37.6	23
4b	1.26	ddd	12.4, 11.1, 9.9	3, 4a, 5	2, 4a, 6, 7, 23		
5	4.30	ddd	9.9, 8.2, 5.7	4ab, 6	3, 4a, 7, 11	78.8	4b, 6
6	4.02	dd	8.2, 5.6	5, 7	2, 4b, 7, 11	81.4	4b
7	4.70	dd	5.6, 2.2	6, 9	4ab, 5, 6, 12	66.7	9
8	-	-	-	-	-	79.8	6, 7, 9
9	2.51	d	2.2	7	-	75.6	7
10	-	-	-	-	-	111.6	7, 11, 12
11	1.59	s	-	12	1a, 5, 12	27.7	12
12	1.40	s	-	11	6, 7, 11	26.3	11
23	1.06	d	6.6	3	1b, 2, 3, 4ab	16.2	4b

Compound 51b. According to General Procedure using alkene **50b** (235 mg, 1.05 mmol). Colourless oil



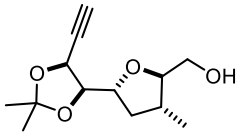
(165 mg, 65%). $[\alpha]_D^{20}$ = −35.7 (c = 1.03, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): *see Table S-12*. ^{13}C NMR (150 MHz, $CDCl_3$): *see Table S-12*. IR (film): $\tilde{\nu}$ = 3450, 3263, 2933, 2875, 1457, 1381, 1241, 1214, 1160, 1056, 870, 666 cm^{-1}. MS (EI) *m/z* (%): 225 (7), 165 (8), 151 (4), 121 (8), 115 (38), 96 (29), 95 (22), 79 (14), 71 (77),

67 (34), 55 (24), 43 (100). HRMS (ESIpos) *m/z* calcd for $C_{13}H_{20}O_4Na$ [M+Na$^+$]: 263.1254, found: 263.1255.

Table S-12. NMR data of THF **51b**; arbitrary numbering scheme as shown in the insert

atom n°	^{1}H NMR (600 MHz, $CDCl_3$)					^{13}C NMR (150 MHz, $CDCl_3$)	
	δ [ppm]	m	*J* [Hz]	COSY	NOESY	δ [ppm]	HMBC
1a	3.82	dd	12.0, 2.7	1b, 2	23	62.3	3
1b	3.53	dd	12.0, 4.1	1a, 2	3, 23		
2	3.60	ddd	9.3, 4.1, 2.7	1ab, 3	4b, 6, 11, 23	86.4	1a, 3, 4a, 23
3	2.22	ddp	11.2, 9.3, 6.7, 6.4	2, 4ab, 23	1b, 6, 23	34.6	1a, 4ab, 23
4a	2.17	m	-	3, 4b, 5, 6	4b, 6, 7, 23	37.1	3, 23
4b	1.61	m	-	3, 4a, 5, 6, 7	2, 4a, 6, 23		
5	4.04	m	-	4ab	11	78.4	4b, 7
6	4.05	m	-	4ab, 7	2, 3, 4ab, 12	84.3	4b, 5, 7
7	4.41	dd	7.4, 2.1	4b, 6, 9	4a, 11	66.9	9
8	-	-	-	-	-	80.8	6, 7, 9
9	2.55	d	2.1	7	-	74.9	7
10	-	-	-	-	-	111.0	11, 12
11	1.44	s	-	12	2, 5, 7	26.7	12
12	1.50	s	-	11	6	26.0	11
23	1.07	d	6.4	3	1ab, 2, 3, 4ab	15.9	4b
1-OH	1.77	br	-	-	-	-	-

Compound 51c. According to General Procedure using alkene **50c** (252 mg, 1.05 mmol). Colourless oil



(169 mg, 63%). $[\alpha]_D^{20}$ = −54.2 (c = 1.05, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.88 (dd, *J* = 5.8, 2.2 Hz, 1H), 4.24 (ddd, *J* = 9.3, 7.5, 5.8 Hz, 1H), 4.01 (dd, *J* = 7.5, 5.8 Hz, 1H), 3.72 (dd, *J* = 11.6, 2.8 Hz, 1H), 3.63–3.54 (m, 1H), 3.56–3.46 (m, 1H), 2.55 (d, *J* = 2.2 Hz, 1H), 2.38 (ddd, *J* = 12.6, 7.2, 5.8 Hz, 1H), 2.16 (ddt, *J* = 10.8, 8.6, 6.8 Hz, 1H), 1.99 (br s, 1H), 1.59 (ddd, *J* = 12.3, 10.8, 9.3 Hz, 1H), 1.53 (s, 3H), 1.35 (s, 3H), 1.08 (d, *J* = 6.6 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 110.5, 86.1, 80.3, 80.2, 77.6, 75.9, 68.4, 62.9, 38.8, 34.9, 27.4, 25.9, 16.6 ppm. IR (film): $\tilde{\nu}$ = 3450, 3281, 2934, 2875, 1457, 1372, 1229, 1163, 1075, 1043, 865, 663 cm^{-1}. MS (EI) *m/z* (%): 503.3 (55), 471.2 (5), 355.2 (3), 263.1 (100), 202.1 (3). HRMS (ESIpos) *m/z* calcd for $C_{13}H_{20}O_4Na$ [M+Na$^+$]: 263.1254, found: 263.1253.

Compound 51d. According to General Procedure using alkene **50d** (500 mg, 2.23 mmol). Colourless oil (312 mg, 58%). $[\alpha]_D^{20}$ = +12.4 (c = 1.04, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): *see Table S-13*. ^{13}C NMR (150 MHz, $CDCl_3$): *see Table S-13*. IR (film): $\tilde{\nu}$ = 3438, 3282, 2933, 2875, 1457, 1382, 1240, 1213, 1164, 1055, 869, 669 cm^{-1}. MS (EI) *m/z* (%): 225 (19), 165 (9), 151 (61), 121 (2), 115 (54), 109 (42), 97 (47), 91 (17), 81 (33), 69 (91), 57 (9), 43 (100). HRMS (ESIpos) *m/z* calcd for $C_{13}H_{20}O_4Na$ [M+Na^+]: 263.1254, found: 263.1255.

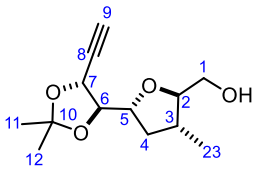


Table S-13. NMR data of THF **51d**; arbitrary numbering scheme as shown in the insert

atom n°	^{1}H NMR (400 MHz, $CDCl_3$)					^{13}C NMR (101 MHz, $CDCl_3$)	
	δ [ppm]	m	*J* [Hz]	COSY	NOESY	δ [ppm]	HMBC
1a	3.77	dd	11.8, 2.7	1b	3, 23	62.8	-
1b	3.53	dd	11.8, 4.9	1a, 2	3, 23		
2	3.60	ddd	9.1, 4.9, 2.7	1b, 3	3, 4b, 6, 7, 23	86.4	4a, 23
3	2.18	dddq	10.6, 9.1, 7.2, 6.4	2, 4b, 23	1ab, 2, 5, 23	34.8	1a, 4ab, 23
4a	2.23	ddd	11.8, 7.2, 5.9	4b, 5	4b, 5, 6, 7	37.2	6, 23
4b	1.61	ddd	11.8, 10.6, 9.5	3, 4a, 5	2, 4a, 6, 7, 23		
5	4.11	ddd	9.5, 5.9, 4.9	4ab, 6	3, 4a, 7, 11	78.1	4b, 7
6	4.18	dd	6.6, 4.9	5, 7	2, 4ab, 12	83.7	4b, 7
7	4.53	dd	6.6, 2.1	6, 9	2, 4ab, 5, 11	67.4	9
8	-	-	-	-	-	81.8	6, 7, 9
9	2.55	d	2.1	7	22	74.6	7
10	-	-	-	-	-	110.9	7, 11, 12
11	1.43	s	-	12	5, 7, 12	26.9	12
12	1.51	s	-	11	6, 9, 11	26.0	11
23	1.07	d	6.4	3	1ab, 2, 3, 4b	16.3	4b
1-OH	1.67	br	-	-	-	-	-

General Procedure for Hydroindation/Iodination of Alkynes 51a-d to give (*Z*)-Iodoalkenes 52a-d. A solution of Dibal-H (1 M in THF, 140 mol%) was added dropwise to a suspension of indium trichloride (0.3 M, 150 mol%) in THF at −78 °C. The reaction was stirred for 30 min at which point the solution had become homogenous. A solution of alkyne **51a-d** (0.5 M in THF, 100 mol%) was added dropwise at −78 °C, followed by a solution of triethylborane (1 M in THF,20 mol%) in THF. The reaction was initiated by slowly injecting 1 mL of air via syringe through the bottom of the solution. The mixture was stirred at the indicated temperature until the alkyne was fully consumed. Solid iodine (600 mol%) was added and the reaction was stirred at −78 °C until the alkenylindium species had been fully consumed. The reaction was quenched with $NaHCO_3$ (10 mL) and the resulting mixture was diluted with methyl

t-butylether (30 mL). The aq. phase was separated and extracted with methyl *t*-butylether (3 × 30 mL). The combined organic phases were washed with sat. $Na_2S_2O_3$, brine, dried over Na_2SO_4, filtered and concentrated to a yellow residue. The residue was purified by flash chromatography (hexane/EtOAc 7:3) to afford the title compounds.

(*Z*)-Iodoalkene 52a. According to General Procedure at −78 °C for 2.5 h using alkyne **51a** (569 mg, 2.37 mmol). Colourless oil (582 mg, 67%). $[\alpha]_D^{20}$ = −61.5 (c = 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.50 (dd, *J* = 7.7, 1.0 Hz, 1H), 6.35 (dd, *J* = 8.7, 7.7 Hz, 1H), 4.83 (ddd, *J* = 8.7, 6.3, 0.9 Hz, 1H), 4.16 (t, *J* = 6.6 Hz, 1H), 3.95 (ddd, *J* = 9.7, 6.9, 5.7 Hz, 1H), 3.81 (dd, *J* = 11.9, 2.7 Hz, 1H), 3.58 (ddd, *J* = 8.9, 3.9, 2.7 Hz, 1H), 3.51 (dd, *J* = 11.9, 4.0 Hz, 1H), 2.23–2.07 (m, 2H), 1.85 (br s, 1H), 1.51 (s, 3H), 1.44–1.33 (m, 4H), 1.05 (d, *J* = 6.3 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 137.2, 110.0, 86.2, 85.7, 81.0, 79.5, 77.1, 62.2, 37.8, 34.6, 27.8, 25.6, 16.1 ppm. IR (film): $\tilde{\nu}$ = 3495, 2931, 2873, 1456, 1379, 1250, 1215, 1161, 1088, 1055, 867, 590, 508 cm^{-1}. MS (EI) *m/z* (%): 759.1 (49), 580.0 (5), 483.0 (3), 391.0 (100), 338.0 (9). HRMS (ESIpos) *m/z* calcd for $C_{13}H_{21}IO_4Na$ [M+Na$^+$]: 391.0377, found: 391.0377. The analytical and spectroscopic data are in agreement with those reported in the literature.[19]

(*Z*)-Iodoalkene 52b. According to General Procedure at −40 °C for 36 h using alkyne **51b** (153 mg, 0.64 mmol). Colourless oil (216 mg, 92%). $[\alpha]_D^{20}$ = +22.9 (c = 0.56, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.61 (dd, *J* = 7.8, 0.8 Hz, 1H), 6.26 (dd, *J* = 8.5, 7.7 Hz, 1H), 4.59 (td, *J* = 8.3, 0.8 Hz, 1H), 4.10–4.04 (m, 1H), 3.86–3.75 (m, 2H), 3.61–3.56 (m, 1H), 3.53 (dd, *J* = 11.8, 4.0 Hz, 1H), 2.22 (dddd, *J* = 16.8, 12.6, 8.0, 6.2 Hz, 2H), 1.99 (br s, 1H), 1.47 (s, 3H), 1.45 (d, *J* = 0.7 Hz, 3H), 1.05 (d, *J* = 6.2 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 137.8, 110.1, 86.8, 86.2, 82.8, 79.6, 78.4, 62.3, 37.2, 34.7, 26.9, 26.8, 16.1 ppm. IR (film): $\tilde{\nu}$ = 3447, 2931, 2873, 1456, 1380, 1250, 1215, 1164, 1056, 873, 714 cm^{-1}. MS (EI) *m/z* (%): 759.1 (33), 631.2 (3), 572.1 (5), 467.0 (2), 391.0 (100), 338.0 (5). HRMS (ESIpos) *m/z* calcd for $C_{13}H_{21}IO_4Na$ [M+Na$^+$]: 391.0377, found: 391.0378.

(*Z*)-Iodoalkene 52c. According to General Procedure at −40 °C for 36 h using alkyne **51c** (156 mg, 0.65 mmol). Colourless oil (188 mg, 79%). $[\alpha]_D^{20}$ = +75.1 (c = 1.27, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.50 (dd, *J* = 7.8, 1.1 Hz, 1H), 6.34 (t, *J* = 7.9 Hz, 1H), 4.91 (ddd, *J* = 7.9, 6.5, 1.2 Hz, 1H), 4.26 (t, *J* = 6.5 Hz, 1H), 3.99–3.91 (m, 1H), 3.69 (dd, *J* = 11.6, 2.8 Hz, 1H), 3.58 (ddd, *J* = 8.7, 5.6, 2.8 Hz, 1H), 3.46 (dd, *J* = 11.6, 5.6 Hz, 1H), 2.19 (ddd, *J* = 12.0, 7.2, 5.9 Hz, 1H), 2.12–2.02 (m, 1H), 1.89 (br s, 1H), 1.57 (ddd, *J* = 12.0, 10.8, 9.3 Hz, 1H), 1.48 (s, 3H), 1.40 (s, 3H), 1.05 (d, *J* = 6.5 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 137.7, 109.2, 86.0, 84.9, 80.2, 80.1, 76.7, 63.3, 38.4, 35.1, 27.5, 25.2, 16.4 ppm. IR (film): $\tilde{\nu}$ = 3457, 2931, 2873, 1455, 1380,

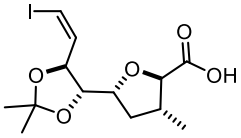
1245, 1214, 1162, 1049, 870, 513 cm^{-1}. MS (EI) *m/z* (%): 759.1 (23), 659.3 (2), 572.1 (4), 467.0 (2), 391.0 (100). HRMS (ESIpos) *m/z* calcd for $C_{13}H_{21}IO_4Na$ [M+Na^+]: 391.0377, found: 391.0378.

(*Z*)-Iodoalkene 52d. According to General Procedure at −78 °C for 2.5 h using alkyne **51d** (292 mg, 1.22 mmol). Colourless oil (394 mg, 88%). $[\alpha]_D^{20}$ = −42.6 (c = 0.57, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.56 (dd, *J* = 7.8, 0.9 Hz, 1H), 6.33–6.24 (m, 1H), 4.53 (td, *J* = 8.2, 0.9 Hz, 1H), 4.12 (ddd, *J* = 9.9, 5.7, 4.2 Hz, 1H), 3.93 (dd, *J* = 8.1, 4.3 Hz, 1H), 3.78–3.69 (m, 1H), 3.71–3.62 (m, 1H), 3.53 (dd, *J* = 11.4, 5.6 Hz, 1H), 2.26 (ddd, *J* = 11.6, 7.1, 5.7 Hz, 1H), 2.17 (ddt, *J* = 11.1, 9.0, 6.6 Hz, 1H), 1.95 (br s, 1H), 1.69–1.60 (m, 1H), 1.46 (s, 2H), 1.44 (s, 3H), 1.08 (d, *J* = 6.5 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 138.3, 110.0, 86.2, 86.0, 81.6, 80.7, 78.0, 63.1, 36.6, 34.9, 26.9, 26.9, 16.3 ppm. IR (film): $\tilde{\nu}$ = 3440, 2932, 2873, 1456, 1380, 1282, 1239, 1166, 1045, 840, 713 cm^{-1}. MS (EI) *m/z* (%): 759.1 (39), 633.2 (2), 572.1 (4), 489.0 (2), 391.0 (100), 311.0 (2). HRMS (ESIpos) *m/z* calcd for $C_{13}H_{21}IO_4Na$ [M+Na^+]: 391.0377, found: 391.0375.

General Procedure for Oxidation of Alkenyl Iodides 52a-d to Carboxylic Acids S21a-d. Water (1000 mol%), bis-(acetoxy)iodobenzene (220 mol%) and TEMPO (30 mol%) were added to a solution of alkenyl iodide **52a-d** (0.2 M, 100 mol%) in MeCN. The pale orange solution was stirred for 19 h at ambient temperature. The reaction was quenched with aq. NaOH (5% w/w, 100 mL) and the separated aq. phase was washed with *t*-butyl methyl ether (2 × 50 mL). The aq. solution was acidified with HCl (2 M) until pH 3 was reached and pH 3.5 phosphate buffer solution (50 mL) was added. The aq. 3-4 pH solution was extracted with EtOAc (2 × 200 mL). The combined organic phases were washed with a 1:1 mixture of pH 5 phosphate buffer and brine (200 mL). After drying over Na_2SO_4 and filtration, the solution was concentrated under reduced pressure to afford the title compounds, which were used in the next step without further purification.

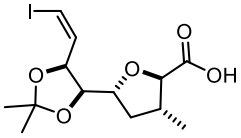
Carboxylic Acid S21a. According to general Procedure using alkenyl iodide **52a** (566 mg, 1.54 mmol). Yellow oil (542 mg, 80%). $[\alpha]_D^{20}$ = –65.4 (c = 1.10, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.54 (dd, *J* = 7.7, 1.0 Hz, 1H), 6.45 (t, *J* = 7.9 Hz, 1H), 4.88 (ddd, *J* = 7.8, 6.5, 1.0 Hz, 1H), 4.22 (dd, *J* = 6.6, 5.6 Hz, 1H), 4.12 (dt, *J* = 9.9, 5.7 Hz, 1H), 4.04 (d, *J* = 8.6 Hz, 1H), 2.44–2.31 (m, 1H), 2.17 (ddd, *J* = 12.7, 7.2, 5.8 Hz, 1H), 1.59–1.46 (m, 4H), 1.42 (s, 3H), 1.26 (d, *J* = 6.6 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 174.9, 137.6, 110.1, 85.8, 83.1, 79.8, 79.7, 79.1, 39.8, 37.5, 27.6, 25.6, 17.6 ppm. IR (film) $\tilde{\nu}$ = 2982, 2933, 1728, 1739, 1285, 1245, 1216, 1055, 866 cm^{-1}. MS (EI) *m/z* (%): 809.0 (5), 787.0 (23), 659.1 (3), 593.0 (2), 405.0 (100), 277.1 (9). HRMS (ESIpos): *m/z* calcd for $C_{13}H_{19}IO_5Na$ [M+Na^+]: 405.0169, found: 405.0170.

Carboxylic Acid S21b. According to general Procedure using alkenyl iodide **52b** (92 mg, 0.25 mmol).



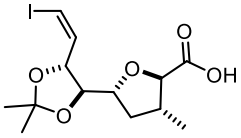
Yellow oil (96 mg, 88%). $[\alpha]_D^{20}$ = +33.2 (c = 0.81, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.60 (dd, *J* = 7.8, 0.9 Hz, 1H), 6.28 (t, *J* = 8.1 Hz, 1H), 4.71 (td, *J* = 8.3, 0.9 Hz, 1H), 4.27 (ddd, *J* = 10.1, 5.8, 4.3 Hz, 1H), 4.05 (d, *J* = 9.3 Hz, 1H), 3.76 (dd, *J* = 8.3, 4.3 Hz, 1H), 2.40 (ddq, *J* = 10.8, 9.2, 6.6 Hz, 1H), 2.26 (ddd, *J* = 12.5, 7.0, 5.8 Hz, 1H), 1.64 (dt, *J* = 12.3, 10.5 Hz, 1H), 1.46 (s, 3H), 1.45 (s, 3H), 1.28 (d, *J* = 6.5 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.5, 137.6, 110.3, 86.6, 82.9, 81.4, 79.5, 79.0, 39.8, 37.0, 27.0, 26.6, 17.0 ppm. IR (film) $\tilde{\nu}$ = 2984, 2933, 1728, 1373, 1285, 1245, 1216, 1056, 872, 715 cm^{-1}. MS (EI) *m/z* (%): 809.0 (5), 787.0 (23), 659.1 (3), 593.0 (2), 405.0 (100), 277.1 (9). HRMS (ESIneg): *m/z* calcd for $C_{13}H_{18}IO_5$: 381.0204 $[M-H]^-$, found: 381.0207.

Carboxylic Acid S21c. According to general Procedure using alkenyl iodide **52c** (174 mg, 0.47 mmol).



Yellow oil (185 mg, 89%). $[\alpha]_D^{20}$ = +116.7 (c = 1.01, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.56 (dd, *J* = 7.8, 1.2 Hz, 1H), 6.39 (t, *J* = 7.9 Hz, 1H), 4.94 (ddd, *J* = 7.9, 6.6, 1.2 Hz, 1H), 4.34 (t, *J* = 6.3 Hz, 1H), 4.14 (dt, *J* = 9.5, 5.8 Hz, 1H), 4.03 (d, *J* = 9.0 Hz, 1H), 2.38 (ddp, *J* = 10.6, 9.0, 6.6 Hz, 1H), 2.23 (ddd, *J* = 12.6, 7.2, 5.7 Hz, 1H), 1.65 (ddd, *J* = 12.3, 10.6, 9.5 Hz, 1H), 1.49 (s, 3H), 1.41 (s, 3H), 1.28 (d, *J* = 6.6 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 174.2, 137.5, 109.4, 85.4, 82.6, 79.9, 79.1, 78.8, 39.5, 37.7, 27.3, 25.0, 17.5 ppm. IR (film) $\tilde{\nu}$ = 2983, 2933, 1723, 1380, 1285, 1245, 1214, 1163, 1098, 1054, 867, 715 cm^{-1}. MS (EI) *m/z* (%): 665.3 (3), 637.3 (4), 609.2 (8), 564.3 (2), 539.5 (2), 477.0 (12), 427.0 (4), 397.0 (3), 381.0 (100), 353.2 (3). HRMS (ESIneg): *m/z* calcd for $C_{13}H_{18}IO_5$ $[M-H]^-$: 381.0204, found: 381.0207.

Carboxylic Acid S21d. According to general Procedure using alkenyl iodide **52d** (380 mg, 1.03 mmol).

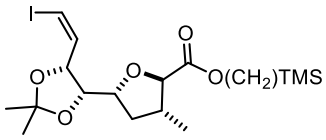


Yellow oil (421 mg, 93%). $[\alpha]_D^{20}$ = −0.8 (c = 0.62, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.58 (d, *J* = 7.8 Hz, 1H), 6.29 (t, *J* = 8.0 Hz, 1H), 4.51 (t, *J* = 8.2 Hz, 1H), 4.32 (ddd, *J* = 9.7, 5.6, 4.0 Hz, 1H), 4.09 (d, *J* = 9.2 Hz, 1H), 3.97 (dd, *J* = 8.3, 4.0 Hz, 1H), 2.52–2.31 (m, 2H), 1.82–1.69 (m, 1H), 1.46 (s, 3H), 1.44 (s, 3H), 1.32 (d, *J* = 6.4 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.4, 137.8, 110.3, 86.3, 82.6, 80.8, 80.7, 79.7, 39.5, 36.2, 26.9, 26.8, 17.2 ppm. IR (film) $\tilde{\nu}$ = 2983, 2930, 1729, 1456, 1380, 1282, 1238, 1218, 1167, 1097, 1061, 873, 716 cm^{-1}. MS (EI) *m/z* (%): 787.0 (23), 659.1 (35), 531.2 (10), 405.0 (100), 277.1 (78). HRMS (ESIneg): *m/z* calcd for $C_{13}H_{18}IO_5$ $[M-H]^-$: 381.0204, found: 381.0207.

General Procedure for the Protection of Carboxylic Acids S21a-d to give the Southern Fragments 7a-d. DMAP (30 mol%), N-(3-dimethylaminopropyl)-N-ethylcarbodiimide hydrochloride (150 mol%) and 2-(trimethylsilyl)-ethanol (260 mol%) were added to a solution of crude carboxylic acid **S21a-d** (0.2 M, 100 mol%) in CH_2Cl_2. After stirring for 4 h at ambient temperature, the mixture was diluted with EtOAc

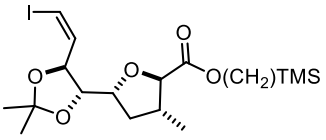
(10 mL) and the reaction was quenched with water (10 mL). The aq. phase was separated and extracted with EtOAc (3 × 10 mL). The combined organic phases were washed with brine (30 mL), dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography (hexane/*t*-butyl methyl ether 95:5) to yield the southern fragments **7a-d**.

Compound 7a. According to general Procedure using carboxylic acid **S21a** (528 mg, 1.38 mmol).



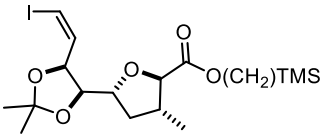
Colourless oil (523 mg, 78%). $[\alpha]_D^{20}$ = –77 (c = 1.17, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.53–6.43 (m, 2H), 4.89–4.83 (m, 1H), 4.25–4.09 (m, 4H), 4.04–3.98 (m, 1H), 2.35 (dddt, *J* = 14.1, 9.6, 7.5, 6.7 Hz, 1H), 2.11 (ddd, *J* = 11.9, 7.4, 5.8 Hz, 1H), 1.51 (s, 3H), 1.45–1.36 (m, 4H), 1.20 (d, *J* = 6.7 Hz, 3H), 1.04–0.96 (m, 2H), 0.04 (s, 9H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 172.9, 137.5, 109.9, 85.5, 83.8, 79.9, 79.8, 78.7, 63.1, 39.4, 37.0, 27.4, 25.5, 18.2, 17.4, −1.5 ppm. IR (film) $\tilde{\nu}$ = 2956, 2897, 1747, 1456, 1379, 1250, 1214, 1175, 1131, 1086, 1058, 860, 837 cm^{-1}. MS (EI) *m/z* (%): 987.2 (28), 875.1 (2), 659.3 (2), 581.1 (1), 505.1 (100). HRMS (ESIpos): *m/z* calcd for $C_{18}H_{31}IO_5SiNa$ [M+Na$^+$]: 505.0877, found: 505.0878.

Compound 7b. According to General Procedure using carboxylic acid **S21b** (145 mg, 0.223 mmol).



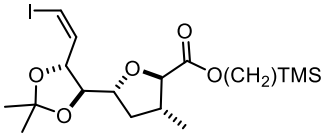
Colourless oil (154 mg, 84%). $[\alpha]_D^{20}$ = +23.8 (c = 0.56, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.61 (dd, *J* = 7.7, 0.8 Hz, 1H), 6.26 (dd, *J* = 8.4, 7.8 Hz, 1H), 4.62 (td, *J* = 8.2, 0.8 Hz, 1H), 4.31 (dt, *J* = 9.7, 5.9 Hz, 1H), 4.27–4.17 (m, 2H), 4.02 (d, *J* = 8.0 Hz, 1H), 3.82 (dd, *J* = 8.0, 5.9 Hz, 1H), 2.42 (dddt, *J* = 13.4, 9.9, 7.7, 6.6 Hz, 1H), 2.24 (ddd, *J* = 12.2, 7.3, 5.9 Hz, 1H), 1.46 (s, 3H), 1.44–1.34 (m, 4H), 1.20 (d, *J* =6.7 Hz, 3H), 1.05–0.98 (m, 2H), 0.05 (s, 9H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.8, 137.8, 110.2, 86.8, 83.7, 82.4, 79.8, 79.6, 63.1, 39.6, 36.7, 26.9, 26.8, 17.8, 17.4, −1.5 ppm. IR (film) $\tilde{\nu}$ = 2957, 2896, 1748, 1456, 1380, 1250, 1215, 1174, 1130, 1059, 860, 838 cm^{-1}. MS (EI) *m/z* (%): 987.2 (23), 859.3 (4), 743.1 (4), 649.2 (1), 505.1 (100). HRMS (ESIpos): *m/z* calcd for $C_{18}H_{31}IO_5SiNa$ [M+Na$^+$]: 505.0877, found: 505.0879.

Compound 7c. According to General Procedure using carboxylic acid **S21c** (171 mg, 0.45 mmol).



Colourless oil (167 mg, 77%). $[\alpha]_D^{20}$ = +92.2 (c = 1.07, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.53 (dd, *J* = 7.8, 1.1 Hz, 1H), 6.39 (t, *J* = 7.8 Hz, 1H), 4.92 (ddd, *J* = 8.0, 6.8, 1.1 Hz, 1H), 4.39 (dd, *J* = 6.7, 5.2 Hz, 1H), 4.26–4.14 (m, 3H), 4.00 (d, *J* = 7.7 Hz, 1H), 2.43–2.30 (m, 1H), 2.13 (ddd, *J* = 12.2, 7.6, 6.0 Hz, 1H), 1.58 (dt, *J* = 12.2, 9.4, 1H), 1.49 (s, 3H), 1.43–1.38 (m, 3H), 1.21 (d, *J* = 6.6 Hz, 3H), 1.05–0.96 (m, 2H) 0.04 (s, 9H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.9, 137.2, 109.0, 85.6, 83.3, 79.7, 79.0, 78.6, 63.1, 39.4, 36.5, 27.2, 25.0, 18.2, 17.4, −1.5 ppm. IR (film) $\tilde{\nu}$ = 2955, 2896, 1747, 1456, 1380, 1250, 1215, 1176, 1099, 1058, 861, 838 cm^{-1}. MS (EI) *m/z* (%): 987.2 (31), 903.1 (2), 743.1 (5), 623.2 (2), 505.1 (100). HRMS (ESIpos): *m/z* calcd for $C_{18}H_{31}IO_5SiNa$ [M+Na$^+$]: 505.0877, found: 505.0875.

Compound 7d. According to general Procedure using carboxylic acid **S21d** (421 mg, 1.10 mmol).

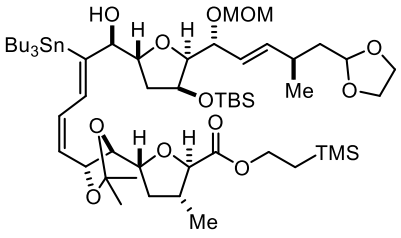


Colourless oil (317 mg, 60%). $[\alpha]_D^{20}$ = −22.4 (c = 1.01, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.55 (dd, *J* = 7.8, 0.9 Hz, 1H), 6.28 (t, *J* = 8.0 Hz, 1H), 4.41 (td, *J* = 8.3, 0.9 Hz, 1H), 4.33 (ddd, *J* = 9.4, 6.0, 2.8 Hz, 1H), 4.27–4.20 (m, 2H), 4.12–4.05 (m, 2H), 2.50–2.36 (m, 1H), 2.27 (ddd, *J* = 11.9, 7.5, 6.0 Hz, 1H), 1.75 (dt, *J* = 11.9, 9.7 Hz, 1H), 1.46 (d, *J* = 0.7 Hz, 3H), 1.43 (s, 3H), 1.25 (d, *J* = 6.6 Hz, 3H), 1.05–0.98 (m, 2H), 0.04 (s, 9H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.8, 137.9, 110.3, 86.0, 83.3, 80.5, 80.4, 79.0, 63.2, 39.4, 34.3, 26.9, 26.8, 17.8, 17.5, −1.5 ppm. IR (film) $\tilde{\nu}$ = 2956, 2896, 1747, 1456, 1380, 1250, 1176, 1097, 1063, 860, 838, 697 cm^{-1}. MS (EI) *m/z* (%): 987.2 (35), 903.1 (2), 743.1 (5), 623.2 (3), 505.1 (100). HRMS (ESIpos): *m/z* calcd for $C_{18}H_{31}IO_5SiNa$ [M+Na$^+$]: 505.0877, found: 505.0880.

The Macrocyclic "Library" and End-Game

General Procedure for the Site-Selective Stille Reaction. A suspension comprising the northern fragment **6a-b** (0.08 M, 100 mol%), (*t*-$Bu_3P)_2Pd$ (20 mol%), tetrabutylammonium diphenylphosphinate (130 mol%), lithium chloride (300 mol%) and the southern fragment **7a-d** (150 mol%) in degassed *N*-methyl-2-pyrrolidone was placed in a preheated oil bath at 50 °C. After stirring for 14 h at 50 °C, the brown mixture was cooled to ambient temperature and the reaction was quenched with pH 7 phosphate buffer (20 mL). The aq. phase was separated and extracted with *t*-butyl methyl ether (3 × 30 mL). The combined organic phases were washed with brine (2 × 50 mL), dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography ((hexane/NEt_3=99:1)/*t*-butyl methyl ether = 9:1 to 4:1 to 3:1 to 3:2 to 1:1 to 1:2) to afford the dienylstannanes **53**.

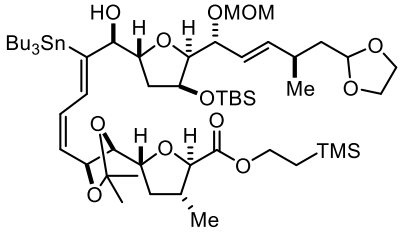
Dienylstannane 53aa. According to General Procedure using northern fragment **6a** (204 mg, 0.194 mmol), (*t*-$Bu_3P)_2Pd$ (15 mol%) and southern fragment **7a**.



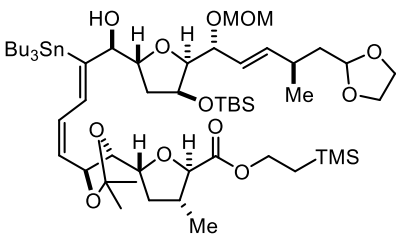
Pale yellow oil (109 mg, 50%). $[\alpha]_D^{20}$ = –11.5 (c = 1.04, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.00 (dd, J_{SnH} = 109.2 Hz, *J* = 11.1, 1H), 6.18 (t, *J* = 11.5, 10.8 Hz, 1H), 5.74 (ddd, *J* = 15.7, 7.6, 1.0 Hz, 1H), 5.62 (t, *J* = 10.9, 10.1 Hz, 1H), 5.43 (ddd, *J* = 15.6, 6.3, 1.1 Hz, 1H), 5.12 (dd, *J* = 10.0, 6.3 Hz, 1H), 4.83 (dd, *J* = 5.8, 4.6 Hz, 1H), 4.69 (d, *J* = 6.5 Hz, 1H), 4.64 (d, *J* = 6.5 Hz, 1H), 4.29–4.17 (m, 5H), 4.14–4.06 (m, 2H), 4.02–3.91 (m, 4H), 3.85–3.77 (m, 2H), 3.70 (dd, *J* = 8.2, 2.9 Hz, 1H), 3.38 (s, 3H), 2.89 (brs, 1H), 2.43 (dp, *J* = 13.8, 6.8 Hz, 1H), 2.32 (dp, *J* = 13.7, 9.1, 6.6, 6.1 Hz, 1H), 2.07 (ddd, *J* = 12.7, 7.4, 5.7 Hz, 1H), 1.78 (ddd, *J* = 13.2, 6.2, 1.5 Hz, 1H), 1.70 (dddd, *J* = 13.7, 7.6, 4.4 Hz, 1H), 1.65–1.57 (m, 2H), 1.53 (s, 3H), 1.51–1.42 (m, 6H), 1.41 (s, 3H), 1.35–1.26 (m, 7H), 1.17 (d, *J* = 6.6 Hz, 3H), 1.05 (d, *J* = 6.8 Hz, 3H), 1.02–0.96 (m, 8H), 0.92–0.83 (m, 18H), 0.06 (s, 6H), 0.04 (s, 9H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.0, 154.7, 139.7, 134.8, 132.7, 127.6, 125.0, 109.7, 103.5,

94.4, 86.2, 84.5, 83.9, 81.2, 80.8, 79.2, 75.2, 73.4, 72.6, 64.9, 64.8, 63.2, 55.5, 40.8, 39.6, 38.8, 37.2, 33.1, 29.2, 27.9, 27.5, 26.0, 25.8, 20.9, 18.3, 18.1, 17.5, 13.8, 11.7, –1.4, –3.8, –4.6 ppm. ^{119}Sn NMR (149 MHz, $CDCl_3$): δ = –50.8 ppm. IR (film) $\tilde{\nu}$ = 3482, 2955, 2928, 2857, 1749, 1731, 1463, 1378, 1251, 1215, 1178, 1127, 1099, 1048, 945, 860, 836, 776 cm^{-1}. MS (ESIpos) *m/z* (%): 1139.6 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{54}H_{100}O_{12}Si_2SnNa$ [M+Na$^+$]: 1139.5667, found: 1139.5679.

Dienylstannane 53ba. According to General Procedure using northern fragment **6a** (58.6 mg, 0.056 mmol) and southern fragment **7b**. Pale yellow oil (25.5 mg, 41%). $[\alpha]_D^{20}$ = –44.3 (c = 1.28, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.13 (dd, *J* = 11.4, J_{SnH} = 112.0 Hz, 1H), 6.20 (td, *J* = 11.2, 1.0 Hz, 1H), 5.74 (ddd, *J* = 15.7, 7.5, 1.0 Hz, 1H), 5.49–5.37 (m, 2H), 4.92–4.80 (m, 2H), 4.69 (d, *J* = 6.5 Hz, 1H), 4.63 (d, *J* = 6.5 Hz, 1H), 4.32–4.07 (m, 6H), 4.01–3.87 (m, 3H), 3.88–3.76 (m, 2H), 3.76 (dd, *J* = 8.0, 3.0 Hz, 1H), 3.63 (dd, *J* = 8.4, 4.9 Hz, 1H), 3.37 (s, 3H), 2.85 (d, *J* = 2.2 Hz, 1H), 2.41 (h, *J* = 7.0 Hz, 1H), 2.37–2.24 (m, 1H), 2.10–1.98 (m, 1H), 1.87–1.69 (m, 2H), 1.73–1.65 (m, 1H), 1.66–1.58 (m, 1H), 1.51–1.41 (m, 13H), 1.36–1.24 (m, 6H), 1.16 (d, *J* = 6.6 Hz, 3H), 1.05 (d, *J* = 6.8 Hz, 3H), 1.03–0.94 (m, 8H), 0.92–0.84 (m, 18H), 0.07–0.03 (m, 15H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.5, 155.0, 139.5, 134.7, 133.8, 127.7, 125.0, 109.5, 103.3, 94.2, 86.0, 83.6, 83.3, 82.4, 80.5, 78.8, 75.1, 73.3 (2C), 64.7, 64.7, 63.0, 55.3, 40.7, 39.6, 38.3, 36.7, 32.9, 29.0, 27.3, 27.2, 26.8, 25.8, 20.7, 17.9, 17.3, 17.3, 13.6, 11.5, −1.5, −4.0, −4.8 ppm. ^{119}Sn NMR (149 MHz, $CDCl_3$): δ = –51.6 ppm. IR (film) $\tilde{\nu}$ = 3475, 2955, 2928, 1748, 1462, 1378, 1251, 1215, 1174, 1129, 1051, 939, 836, 776, 694 cm^{-1}. MS (ESIpos) *m/z* (%): 1139.6 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{54}H_{100}O_{12}Si_2SnNa$ [M+Na$^+$]: 1139.5668, found: 1139.5678.



Dienylstannane 53ca. According to General Procedure using northern fragment **6a** (70 mg, 0.067 mmol) and southern fragment **7c**. Pale yellow oil (34.3 mg, 46%). $[\alpha]_D^{20}$ = +21.6 (c = 0.45, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.04 (dd, *J* = 11.4, J_{SnH} = 111.9 Hz, 1H), 6.16 (td, *J* = 11.2, 1.3 Hz, 1H), 5.74 (ddd, *J* = 15.7, 7.6, 1.1 Hz, 1H), 5.56–5.39 (m, 2H), 5.19 (ddd, *J* = 8.5, 7.0, 1.2 Hz, 1H), 4.83 (dd, *J* = 5.8, 4.6 Hz, 1H), 4.70 (d, *J* = 6.6 Hz, 1H), 4.64 (d, *J* = 6.6 Hz, 1H), 4.39 (dd, *J* = 7.1, 4.2 Hz, 1H), 4.31–4.24 (m, 2H), 4.23–4.12 (m, 4H), 4.07–3.91 (m, 4H), 3.88–3.78 (m, 2H), 3.72 (dd, *J* = 8.0, 3.0 Hz, 1H), 3.38 (s, 3H), 2.80 (d, *J* = 2.5 Hz, 1H), 2.50–2.39 (m, 1H), 2.34 (dq, *J* = 9.5, 7.5 Hz, 1H), 2.11 (ddd, *J* = 12.2, 7.5, 6.1 Hz, 1H), 1.82 (ddd, *J* = 13.1, 6.2, 1.6 Hz, 1H), 1.74–1.66 (m, 2H), 1.65–1.59 (m, 2H), 1.50 (s, 3H), 1.50–1.42 (m, 6H), 1.40 (s, 3H), 1.35–1.26 (m, 6H), 1.21 (d, *J* = 6.7 Hz, 3H), 1.06 (d, *J* = 6.9 Hz, 3H), 1.04–0.92 (m, 8H), 0.91–0.85 (m, 18H), 0.08 (s, 3H), 0.08 (s, 3H), 0.04 (s, 9H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.8, 154.3, 139.4, 134.9, 132.6, 127.0, 125.0, 108.5, 103.4, 94.3, 86.1, 83.1 (2C), 80.6, 79.5, 79.2, 75.1, 73.2, 72.7, 64.7,



64.7, 63.0, 55.3, 40.7, 39.6, 38.5, 35.8, 33.0, 29.0, 27.3, 27.1, 25.9, 25.0, 20.8, 18.0, 17.9, 17.5, 13.6, 11.4, −1.5, −3.8, −4.8 ppm. ^{119}Sn NMR (149 MHz, $CDCl_3$): δ = –51.4 ppm. IR (film) $\tilde{\nu}$ = 3475, 2955, 2928, 1749, 1463, 1379, 1251, 1215, 1174, 1100, 1038, 938, 837, 776 cm^{-1}. MS (ESIpos) *m/z* (%): 1139.6 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{54}H_{100}O_{12}Si_2SnNa$ [M+Na$^+$]: 1139.5668, found: 1139.5685.

Dienylstannane 53da. According to General Procedure using northern fragment **6a** (61 mg, 58 µmol) and southern fragment **7d**. Yellow oil (33.4 mg, 50%). $[\alpha]_D^{20}$ = +1.9 (c = 0.94, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.99 (dd, *J* = 11.1, J_{SnH} = 109.9 Hz, 1H), 6.19 (td, *J* = 11.2, 1.0 Hz, 1H), 5.73 (ddd, *J* = 15.7, 7.6, 1.1 Hz, 1H), 5.51–5.38 (m, 2H), 4.83 (dd, *J* = 5.8, 4.6 Hz, 1H), 4.74–4.67 (m, 2H), 4.63 (d, *J* = 6.5 Hz, 1H), 4.31–4.17 (m, 5H), 4.10 (td, *J* = 8.8, 6.5 Hz, 1H), 4.05–3.88 (m, 5H), 3.84–3.79 (m, 2H), 3.70 (dd, *J* = 8.1, 3.0 Hz, 1H), 3.37 (s, 3H), 2.86 (br s, 1H), 2.46–2.33 (m, 2H), 2.12 (ddd, *J* = 11.9, 7.4, 5.9 Hz, 1H), 1.78 (ddd, *J* = 13.1, 6.2, 1.6 Hz, 1H), 1.73–1.66 (m, 2H), 1.64–1.56 (m, 2H), 1.51–1.41 (m, 12H), 1.33–1.26 (m, 6H), 1.21 (d, *J* = 6.7 Hz, 3H), 1.05 (d, *J* = 6.8 Hz, 3H), 1.03–0.94 (m, 8H), 0.90–0.84 (m, 18H), 0.08–0.00 (m, 15H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.7, 154.8, 139.5, 135.2, 133.5, 128.4, 125.0, 109.5, 103.4, 94.2, 86.0, 84.5, 83.2, 81.8, 80.6, 79.2, 75.0, 73.9, 73.2, 64.7, 64.7, 63.2, 55.3, 40.6, 39.3, 38.6, 35.1, 32.9, 29.0, 27.3, 27.2, 27.0, 25.8, 20.8, 17.9, 17.8, 17.4, 13.6, 11.6, −1.5, −3.9, −4.8 ppm. ^{119}Sn NMR (149 MHz, $CDCl_3$): δ = −51.7 ppm. IR (film) $\tilde{\nu}$ = 2956, 2929, 1743, 1462, 1378, 1251, 1215, 1174, 1100, 1042, 943, 861, 836 cm^{-1}. MS (ESIpos) *m/z* (%): 1139.6 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{54}H_{100}O_{12}Si_2SnNa$ [M+Na$^+$]: 1139.5668, found: 1139.5685.

Dienylstannane 53ab. According to General Procedure using northern fragment **6b** (80 mg, 0.076 mmol) and southern fragment **7a**. Yellow oil (45.3 mg, 53%). $[\alpha]_D^{20}$ = −5.3 (c = 1.05, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.15 (dtd, *J* = 11.5, 1.4, J_{SnH} = 113.0 Hz, 1H), 6.14 (td, *J* = 11.3, 1.0 Hz, 1H), 5.65 (dd, *J* = 16.1, 7.7 Hz, 1H), 5.57 (t, *J* = 10.4 Hz, 1H), 5.50 (ddd, *J* = 15.6, 7.6, 0.9 Hz, 1H), 5.15 (ddd, *J* = 9.8, 6.5, 1.0 Hz, 1H), 4.87 (dd, *J* = 5.8, 4.4 Hz, 1H), 4.65 (d, *J* = 6.3 Hz, 1H), 4.61–4.56 (m, 2H), 4.44 (dt, *J* = 5.5, 4.2 Hz, 1H), 4.26–4.17 (m, 4H), 4.15 (dd, *J* = 7.8, 5.5 Hz, 1H), 4.09 (t, *J* = 6.8 Hz, 1H), 4.00 (d, *J* = 7.5 Hz, 1H), 3.98–3.91 (m, 3H), 3.84–3.77 (m, 2H), 3.33 (s, 3H), 2.45 (hept, *J* = 6.7 Hz, 1H), 2.38–2.25 (m, 2H), 2.06 (ddd, *J* = 12.2, 7.5, 5.8 Hz, 1H), 1.93 (ddd, *J* = 12.6, 8.4, 5.4 Hz, 1H), 1.71 (ddd, *J* = 13.8, 8.0, 4.5 Hz, 1H), 1.66–1.55 (m, 2H), 1.52 (s, 3H), 1.50–1.41 (m, 6H), 1.39 (s, 3H), 1.35–1.20 (m, 7H), 1.16 (d, *J* = 6.7 Hz, 3H), 1.05 (d, *J* = 6.8 Hz, 3H), 1.04–0.93 (m, 8H), 0.90 (s, 9H), 0.88 (t, *J* = 7.3 Hz, 9H), 0.07 (s, 3H), 0.05 (s, 3H), 0.04 (s, 9H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.0, 152.8, 140.1, 132.8, 132.1, 127.1, 126.2, 109.6, 103.6, 94.5, 85.5, 83.8, 81.3, 80.9, 79.3, 77.2, 76.3, 72.8, 72.6, 64.9, 64.8, 63.2, 55.7, 40.9, 39.6, 37.3,

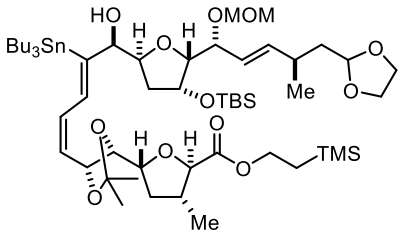
34.2, 33.2, 29.2, 27.9, 27.4, 26.0, 25.7, 20.9, 18.4, 18.2, 17.5, 13.8, 11.4, −1.4, −4.3, −4.8 ppm. ^{119}Sn NMR (149 MHz, $CDCl_3$): δ = –53.2 ppm. IR (film) $\tilde{\nu}$ = 3461, 2955, 2929, 1749, 1462, 1378, 1251, 1215, 1130, 1042, 958, 864, 836, 777 cm^{-1}. MS (ESIpos) *m/z* (%): 1139.6 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{54}H_{100}O_{12}Si_2SnNa$ [M+Na$^+$]: 1139.5668, found: 1139.5685.

Dienylstannane 53bb. According to General Procedure using northern fragment **6b** (97 mg, 92 µmol) and southern fragment **7b**. Pale yellow oil (47.4 mg, 46%). $[\alpha]_D^{20}$ = −23.2 (c = 1.75, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33 (dtd, *J* = 11.5, 1.4, J_{SnH} = 114.6 Hz, 1H), 6.26–6.14 (m, 1H), 5.70–5.59 (m, 1H), 5.51 (ddd, *J* = 15.6, 7.7, 0.9 Hz, 1H), 5.42 (dd, *J* = 10.9, 9.1 Hz, 1H), 4.96–4.83 (m, 2H), 4.65 (d, *J* = 6.3 Hz, 1H), 4.61 (q, *J* = 1.6 Hz, 1H), 4.58 (d, *J* = 6.3 Hz, 1H), 4.50–4.42 (m, 1H), 4.27–4.12 (m, 5H), 4.03–3.97 (m, 2H), 3.95–3.89 (m, 2H), 3.86–3.78 (m, 2H), 3.65 (dd, *J* = 8.4, 5.4 Hz, 1H), 3.33 (m, 3H), 2.55 (br s, 1H), 2.44 (p, *J* = 7.0 Hz, 1H), 2.40–2.27 (m, 1H), 2.10–1.96 (m, 2H), 1.71 (ddd, *J* = 13.8, 8.0, 4.4 Hz, 1H), 1.65–1.56 (m, 2H), 1.50–1.39 (m, 13H), 1.33–1.26 (m, 6H), 1.16 (d, *J* = 6.6 Hz, 3H), 1.05 (d, *J* = 6.8 Hz, 3H), 1.03–0.93 (m, 8H), 0.90–0.85 (m, 18H), 0.07 (s, 3H), 0.06 (s, 3H), 0.04 (s, 9H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.0, 152.9, 139.8, 134.4, 131.8, 127.1, 126.1, 109.5, 103.4, 94.2, 85.2, 83.5, 83.2, 80.5, 79.4, 76.7, 76.2, 73.3, 72.5, 64.7, 64.6, 63.2, 55.4, 40.8, 39.6, 36.7, 34.2, 33.0, 29.0, 27.3, 27.2, 26.8, 25.9, 20.7, 18.0, 17.8, 17.4, 13.6, 10.9, −1.5, −4.4, −5.0 ppm. ^{119}Sn NMR (149 MHz, $CDCl_3$): δ = –53.2 ppm. IR (film) $\tilde{\nu}$ = 3517, 2954, 2928, 2856, 1747, 1462, 1378, 1251, 1215, 1173, 1128, 1088, 1039, 958, 836, 776, 666 cm^{-1}. MS (ESIpos) *m/z* (%): 1139.6 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{54}H_{100}O_{12}Si_2SnNa$ [M+Na$^+$]: 1139.5668, found: 1139.5679.

Dienylstannane 53cb. According to General Procedure using northern fragment **6b** (81 mg, 0.076 mmol) and southern fragment **7c**. Yellow oil (26.9 mg, 32%). $[\alpha]_D^{20}$ = +19.8 (c = 1.03, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.21 (dd, *J* = 11.4 Hz, J_{SnH} = 114.7, 1H), 6.13 (td, *J* = 11.3, 1.2 Hz, 1H), 5.66 (dd, *J* = 15.6, 7.5 Hz, 1H), 5.52 (dd, *J* = 13.9, 7.0 Hz, 1H), 5.48 (t, *J* = 10.4 Hz, 1H), 5.23 (td, *J* = 8.3, 6.9, 0.6 Hz, 1H), 4.87 (dd, *J* = 5.8, 4.4 Hz, 1H), 4.68–4.56 (m, 3H), 4.44 (td, *J* = 4.9, 3.2 Hz, 1H), 4.38 (dd, *J* = 7.0, 4.4 Hz, 1H), 4.27–4.09 (m, 5H), 4.01–3.84 (m, 4H), 3.88–3.72 (m, 2H), 3.33 (s, 3H), 2.45 (p, *J* = 7.1 Hz, 1H), 2.38–2.27 (m, 2H), 2.15–2.02 (m, 1H), 1.96 (td, *J* = 8.1, 4.2 Hz, 1H), 1.71 (ddd, *J* = 13.7, 8.0, 4.4 Hz, 1H), 1.66–1.53 (m, 3H), 1.50 (s, 3H), 1.48–1.35 (m, 9H), 1.34–1.24 (m, 6H), 1.20 (d, *J* = 6.6 Hz, 3H), 1.05 (d, *J* = 6.8 Hz, 3H), 1.03–0.92 (m, 8H), 0.91–0.84 (m, 18H), 0.09–0.00 (m, 15H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.9, 151.9, 139.8, 133.2, 131.9, 126.3, 126.2, 108.4, 103.4, 94.3, 85.4, 83.1, 80.5, 79.6, 79.0, 76.4, 76.1, 72.9, 72.5, 64.7, 64.7, 63.0, 55.5, 40.8, 39.5, 36.0, 34.0, 33.0, 29.0, 27.3, 27.2, 25.9, 25.0, 20.7, 18.0, 18.0, 17.4,

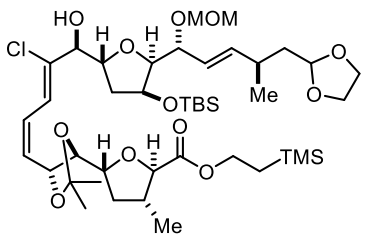
13.6, 11.0, −1.5, −4.4, −5.0 ppm. ^{119}Sn NMR (149 MHz, $CDCl_3$): δ = –53.2 ppm. IR (film) $\tilde{\nu}$ = 3483, 2955, 2930, 1747, 1463, 1379, 1252, 1212, 1100, 1039, 950, 862, 837, 776 cm^{-1}. MS (ESIpos) *m/z* (%): 1139.6 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{54}H_{100}O_{12}Si_2SnNa$ [M+Na$^+$]: 1139.5668, found: 1139.5688.

Dienylstannane 53db. According to General Procedure using northern fragment **6b** (93 mg, 89 µmol) and southern fragment **7d**. Orange oil (69 mg, 70%). $[\alpha]_D^{20}$ = +10.9 (c = 1.32, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.10 (dd, *J* = 11.3, J_{SnH} = 115.3 Hz, 1H), 6.21–6.11 (m, 1H), 5.65 (dd, *J* = 15.6, 7.6 Hz, 1H), 5.51 (ddd, *J* = 15.6, 7.6, 0.9 Hz, 1H), 5.43 (dd, *J* = 10.6, 9.1 Hz, 1H), 4.87 (dd, *J* = 5.8, 4.4 Hz, 1H), 4.69–4.62 (m, 2H), 4.62–4.53 (m, 2H), 4.46–4.41 (m, 1H), 4.26–4.18 (m, 4H), 4.15 (t, *J* = 8.1, 7.0 Hz, 1H), 4.01 (d, *J* = 8.4 Hz, 1H), 3.98 (dd, *J* = 8.7, 5.4 Hz, 1H), 3.95–3.88 (m, 3H), 3.86–3.77 (m, 2H), 3.33 (s, 3H), 2.46 (dq, *J* = 14.2, 7.1 Hz, 1H), 2.41–2.30 (m, 2H), 2.14 (ddd, *J* = 11.9, 7.5, 6.1 Hz, 1H), 1.91 (ddd, *J* = 12.8, 8.8, 5.1 Hz, 1H), 1.80–1.68 (m, 2H), 1.66–1.58 (m, 2H), 1.50–1.38 (m, 12H), 1.35–1.26 (m, 6H), 1.23 (d, *J* = 6.6 Hz, 3H), 1.05 (d, *J* = 6.8 Hz, 3H), 1.03–0.93 (m, 8H), 0.91–0.85 (m, 18H), 0.07 (s, 6H), 0.04 (s, 9H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.7, 153.3, 139.8, 133.7, 132.5, 127.4, 126.3, 109.5, 103.5, 94.5, 85.4, 83.1, 81.7, 80.8, 79.0, 77.5, 76.1, 74.3, 72.5, 64.7, 64.6, 63.1, 55.5, 40.7, 39.4, 34.6, 34.4, 33.0, 29.1, 27.3, 27.2, 26.9, 25.9, 20.8, 18.0, 17.8, 17.4, 13.6, 11.4, −1.5, −4.3, −5.0 ppm. ^{119}Sn NMR (149 MHz, $CDCl_3$): δ = –53.9 ppm. IR (film) $\tilde{\nu}$ = 3482, 2955, 2928, 2856, 1746, 1462, 1378, 1251, 1214, 1174, 1141, 1099, 1059, 1040, 955, 860, 837, 776, 695 cm^{-1}. MS (ESIpos) *m/z* (%): 1139.6 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{54}H_{100}O_{12}Si_2SnNa$ [M+Na$^+$]: 1139.5668, found: 1139.5676.



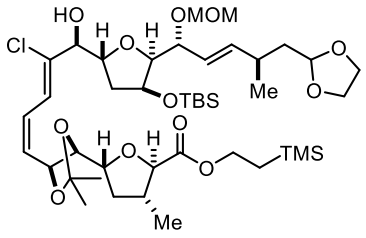
General Procedure for Chloro-Destannylation to give Chlorodienes S22. 2,6-Lutidine (630 mol%) and copper(II) chloride (600 mol%) were added to a solution of dienylstannane **53** (0.05 M, 100 mol%) in THF. The resulting purple suspension was stirred for 20 h at ambient temperature, during which time the colour of the mixture gradually turned brown. After filtration through a short plug of silica, which was rinsed with *t*-butyl methyl ether (25 mL), the combined filtrates were concentrated under reduced pressure. The residue was purified by flash chromatography (EtOAc/hexane 2:3 to 1:1 to 3:2) to afford the title compounds.

Chlorodiene S22aa. According to General Procedure using dienylstannane **53aa** (174 mg, 0.156 mmol). Colourless oil (105 mg, 78%). $[\alpha]_D^{20}$ = −28.3 (c = 0.90, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.70 (d, *J* = 11.0 Hz, 1H), 6.57 (td, *J* = 11.0, 1.0 Hz, 1H), 5.82 (t, *J* = 10.3 Hz, 1H), 5.75 (ddd, *J* = 15.7, 7.6, 1.1 Hz, 1H), 5.43 (ddd, *J* = 15.7, 6.3, 1.1 Hz, 1H), 5.00 (dd, *J* = 9.7, 6.4 Hz, 1H), 4.83 (dd, *J* = 5.7, 4.6 Hz, 1H), 4.70 (d, *J* = 6.5 Hz, 1H), 4.63 (d, *J* = 6.5 Hz, 1H), 4.47

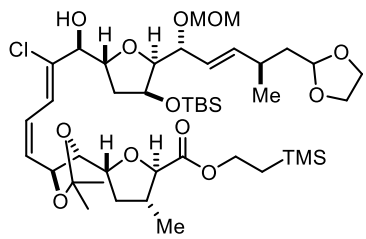


(dt, *J* = 9.5, 5.9 Hz, 1H), 4.32–4.13 (m, 5H), 4.09 (t, *J* = 6.3 Hz, 1H), 4.05 (t, *J* = 4.9, 1.8 Hz, 1H), 4.01 (d, *J* = 7.5 Hz, 1H), 3.98 – 3.91 (m, 2H), 3.84–3.78 (m, 2H), 3.74 (dd, *J* = 8.1, 3.0 Hz, 1H), 3.37 (s, 3H), 3.06 (br s, 1H), 2.48–2.29 (m, 2H), 2.06 (ddd, *J* = 12.6, 7.4, 5.7 Hz, 1H), 1.97 (ddd, *J* = 13.1, 6.0, 1.6 Hz, 1H), 1.81 (ddd, *J* = 13.3, 9.6, 4.2 Hz, 1H), 1.70 (ddd, *J* = 13.7, 7.7, 4.6 Hz, 1H), 1.61 (dt, *J* = 13.8, 6.2 Hz, 1H), 1.52 (s, 3H), 1.40 (s, 3H), 1.34–1.27 (m, 1H), 1.18 (d, *J* = 6.6 Hz, 3H), 1.05 (d, *J* = 6.8 Hz, 3H), 1.03–0.97 (m, 2H), 0.90 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H), 0.04 (s, 9H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.1, 139.8, 136.9, 130.2, 126.6, 124.9, 121.0, 109.9, 103.5, 94.5, 86.9, 83.9, 80.7, 79.3, 79.0, 78.1, 75.2, 73.2, 73.1, 64.9, 64.8, 63.2, 55.6, 40.8, 39.5, 38.6, 37.1, 33.1, 27.8, 26.0, 25.8, 20.9, 18.4, 18.1, 17.5, –1.4, –3.8, –4.6 ppm. IR (film) $\tilde{\nu}$ = 3447, 2955, 2931, 2859, 1730, 1463, 1379, 1252, 1214, 1132, 1102, 1045, 941, 861, 838, 776 cm^{-1}. MS (ESIpos) *m/z* (%): 883.4 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{42}H_{73}O_{12}Si_2ClNa$ [M+Na$^+$]: 883.4221, found: 883.4231.

Chlorodiene S22ba. According to General Procedure using dienylstannane **53ba** (31.7 mg, 0.028 mmol). Colourless oil (19.5 mg, 89%). $[\alpha]_D^{20}$ = −24.6 (c = 0.975, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.90 (d, *J* = 10.9 Hz, 1H), 6.58 (td, *J* = 11.0, 1.2 Hz, 1H), 5.74 (ddd, *J* = 15.6, 7.5, 1.1 Hz, 1H), 5.60 (ddd, *J* = 11.1, 8.5, 1.1 Hz, 1H), 5.45 (ddd, *J* = 15.6, 6.3, 1.1 Hz, 1H), 4.91 (td, *J* = 8.5, 1.2 Hz, 1H), 4.83 (dd, *J* = 5.8, 4.5 Hz, 1H), 4.71–4.62 (m, 2H), 4.52 (ddd, *J* = 9.3, 6.3, 4.6 Hz, 1H), 4.32 (dd, *J* = 3.4, 1.7 Hz, 1H), 4.28–4.09 (m, 5H), 4.01–3.89 (m, 3H), 3.86–3.77 (m, 3H), 3.62 (dd, *J* = 8.5, 3.5 Hz, 1H), 3.36 (s, 3H), 3.31 (br d, *J* = 5.3 Hz, 1H), 2.43 (dq, *J* = 14.1, 7.0 Hz, 1H), 2.36–2.25 (m, 1H), 2.12–1.93 (m, 3H), 1.70 (ddd, *J* = 13.8, 7.7, 4.6 Hz, 1H), 1.65–1.55 (m, 2H), 1.43 (d, *J* = 3.5 Hz, 6H), 1.19 (d, *J* = 6.6 Hz, 3H), 1.05 (d, *J* = 6.8 Hz, 3H), 1.01 (dd, *J* = 9.0, 8.0 Hz, 2H), 0.90 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H), 0.05 (s, 9H). ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.1, 139.2, 137.2, 130.3, 127.2, 125.1, 120.7, 109.4, 103.4, 94.3, 86.6, 83.5, 82.2, 78.7, 77.7, 77.0, 75.2, 73.8, 73.1, 64.7, 64.7, 63.1, 55.4, 40.7, 39.7, 38.0, 36.6, 32.9, 27.2, 26.6, 25.9, 20.7, 18.0, 17.4, 17.4, -1.5, -4.0, -4.7 ppm. IR (film) $\tilde{\nu}$ = 3471, 2955, 2929, 2859, 1742, 1461, 1380, 1251, 1215, 1172, 1128, 1090, 1034, 939, 834, 806, 774, 696 cm^{-1}. MS (ESIpos) *m/z* (%): 883.4 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{42}H_{73}O_{12}Si_2ClNa$ [M+Na$^+$]: 883.4221, found: 883.4216.

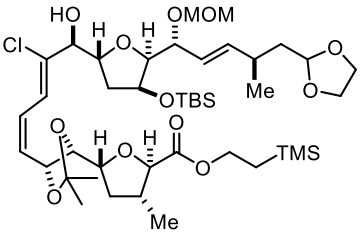


Chlorodiene S22ca. According to General Procedure using dienylstannane **53ca** (34 mg, 0.031 mmol). Colourless oil (23.4 mg, 89%). $[\alpha]_D^{20}$ = +28.4 (c = 1.17, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.78 (d, *J* = 11.0 Hz, 1H), 6.56 (td, *J* = 11.1, 1.3 Hz, 1H), 5.81–5.64 (m, 2H), 5.44 (ddd, *J* = 15.7, 6.3, 1.1 Hz, 1H), 5.07 (ddd, *J* = 8.4, 6.8, 1.3 Hz, 1H), 4.83 (dd, *J* = 5.7, 4.5 Hz, 1H), 4.69 (d, *J* = 6.6 Hz, 1H), 4.64 (d, *J* = 6.6 Hz, 1H), 4.50 (dt, *J* = 9.5, 5.7 Hz, 1H), 4.34–4.24 (m, 3H), 4.23–4.18 (m, 2H), 4.15 (dt, *J* = 9.1, 5.7 Hz, 1H), 4.05 (d, *J* = 5.0 Hz, 1H), 3.98 (d, *J* = 7.6 Hz, 1H),



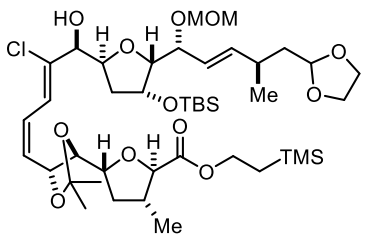
3.97–3.90 (m, 2H), 3.87–3.79 (m, 2H), 3.75 (dd, *J* = 8.0, 3.1 Hz, 1H), 3.36 (s, 3H), 3.03 (s, 1H), 2.48–2.30 (m, 2H), 2.17 (ddd, *J* = 12.2, 7.5, 5.9 Hz, 1H), 1.99 (ddd, *J* = 12.9, 6.1, 1.7 Hz, 1H), 1.90 (ddd, *J* = 13.2, 9.6, 4.2 Hz, 1H), 1.70 (ddd, *J* = 13.7, 7.7, 4.6 Hz, 1H), 1.65–1.54 (m, 1H), 1.49 (s, 3H), 1.39 (s, 3H), 1.34–1.28 (m, 1H), 1.21 (d, *J* = 6.6 Hz, 3H), 1.05 (d, *J* = 6.8 Hz, 3H), 1.03–0.98 (m, 2H), 0.90 (s, 9H), 0.10 (s, 3H), 0.08 (s, 3H), 0.04 (s, 9H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): *δ* = 173.0, 139.4, 136.5, 129.4, 126.4, 124.8, 120.9, 108.8, 103.4, 94.3, 86.8, 83.3, 79.8, 78.9, 78.8, 77.4, 75.1, 73.6, 73.0, 64.7, 64.7, 63.1, 55.4, 40.7, 39.4, 38.4, 36.8, 32.9, 27.3, 25.8, 25.1, 20.8, 18.2, 18.0, 17.4, −1.5, −4.0, −4.8 ppm. IR (film) $\tilde{\nu}$ = 3434, 2955, 2928, 2859, 1732, 1462, 1380, 1251, 1214, 1132, 1099, 1039, 949, 860, 837, 776, 696 cm^{-1}. MS (ESIpos) *m/z* (%): 883.4 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{42}H_{73}O_{12}Si_2ClNa$ [M+Na$^+$]: 883.4221, found: 883.4218.

Chlorodiene S22da. According to General Procedure using dienylstannane **53da** (50 mg, 49 µmol).



Colourless oil (24.4 mg, 63%). $[\alpha]_D^{20}$ = −12.1 (c = 1.04, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 6.80 (d, *J* = 10.9 Hz, 1H), 6.54 (td, *J* = 11.0, 1.2 Hz, 1H), 5.73 (ddd, *J* = 15.6, 7.6, 1.1 Hz, 1H), 5.63 (ddd, *J* = 11.1, 8.4, 1.0 Hz, 1H), 5.43 (ddd, *J* = 15.7, 6.4, 1.1 Hz, 1H), 4.82 (dd, *J* = 5.8, 4.5 Hz, 1H), 4.72–4.59 (m, 3H), 4.48 (dt, *J* = 9.6, 6.0 Hz, 1H), 4.32–4.12 (m, 5H), 4.06 (d, *J* = 5.9 Hz, 1H), 4.00 (d, *J* = 7.9 Hz, 1H), 3.97–3.91 (m, 2H), 3.86 (dd, *J* = 7.8, 5.4 Hz, 1H), 3.83–3.77 (m, 2H), 3.73 (dd, *J* = 8.0, 3.1 Hz, 1H), 3.36 (s, 3H), 3.14 (s, 1H), 2.47–2.31 (m, 2H), 2.21 (ddd, *J* = 12.7, 7.4, 5.8 Hz, 1H), 1.96 (ddd, *J* = 13.0, 6.1, 1.8 Hz, 1H), 1.81 (ddd, *J* = 13.2, 9.5, 4.3 Hz, 1H), 1.69 (ddd, *J* = 13.6, 7.7, 4.5 Hz, 1H), 1.64–1.54 (m, 2H), 1.43 (s, 3H), 1.42 (s, 3H), 1.21 (d, *J* = 6.6 Hz, 3H), 1.04 (d, *J* = 6.8 Hz, 3H), 1.03–0.97 (m, 2H), 0.89 (s, 9H), 0.08 (s, 3H), 0.06 (s, 3H), 0.03 (s, 9H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): *δ* = 172.9, 139.4, 136.5, 131.2, 126.9, 124.9, 121.8, 109.8, 103.4, 94.2, 86.6, 83.2, 82.4, 80.1, 79.1, 77.9, 75.8, 75.1, 73.0, 64.7, 64.7, 63.2, 55.4, 40.7, 39.2, 38.3, 36.7, 32.9, 27.1, 27.0, 25.8, 20.7, 18.2, 18.0, 17.4, −1.5, −4.0, −4.8 ppm. IR (film) $\tilde{\nu}$ = 3472, 2955, 2930, 2887, 1736, 1461, 1406, 1380, 1251, 1215, 1174, 1132, 1100, 1045, 943, 859, 836, 775 cm^{-1}. MS (ESIpos) *m/z* (%): 883.4 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{42}H_{73}O_{12}Si_2ClNa$ [M+Na$^+$]: 883.4221, found: 883.4224.

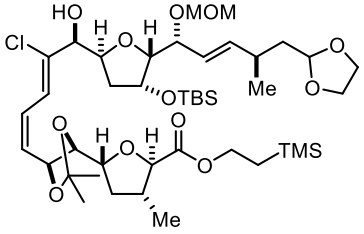
Chlorodiene S22ab. According to General Procedure using dienylstannane **53ab** (45.3 mg, 41 µmol).



Colourless oil (34.4 mg, 98%). $[\alpha]_D^{20}$ = −0.5 (c = 1.02, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 6.75 (dt, *J* = 11.1, 1.2 Hz, 1H), 6.54 (td, *J* = 11.1, 1.1 Hz, 1H), 5.77 (t, *J* = 10.4 Hz, 1H), 5.73–5.62 (m, 1H), 5.50 (ddd, *J* = 15.6, 7.5, 0.9 Hz, 1H), 5.02 (ddd, *J* = 9.6, 6.4, 1.1 Hz, 1H), 4.88 (dd, *J* = 5.9, 4.4 Hz, 1H), 4.65 (d, *J* = 6.3 Hz, 1H), 4.59 (d, *J* = 6.2 Hz, 1H), 4.57–4.43 (m, 3H), 4.28–4.11 (m, 4H), 4.10 (t, *J* = 6.4 Hz, 1H), 4.01 (d, *J* = 7.4 Hz, 1H), 3.99–3.89 (m, 3H), 3.86–3.77 (m, 2H), 3.33 (s, 3H), 2.67 (d, *J* = 3.6 Hz, 1H), 2.45 (hept, *J* = 6.8 Hz, 1H), 2.41–2.27 (m, 1H), 2.04

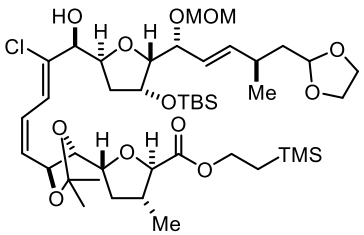
(ddd, *J* = 12.0, 7.4, 5.7 Hz, 1H), 1.93 (ddd, *J* = 13.2, 8.3, 5.3 Hz, 1H), 1.72 (dddd, *J* = 12.4, 7.9, 6.7, 3.9 Hz, 2H), 1.62 (dt, *J* = 13.8, 6.1 Hz, 1H), 1.52 (s, 3H), 1.40 (s, 3H), 1.31–1.20 (m, 1H), 1.17 (d, *J* = 6.7 Hz, 3H), 1.05 (d, *J* = 6.8 Hz, 3H), 1.05–0.95 (m, 2H), 0.90 (s, 9H), 0.07 (s, 3H), 0.07 (s, 3H), 0.04 (s, 9H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.1, 140.0, 135.5, 129.9, 126.3, 126.2, 119.2, 109.9, 103.6, 94.6, 85.7, 83.9, 80.9, 79.1, 78.9, 76.0, 74.8, 73.3, 72.5, 64.9, 64.8, 63.3, 55.7, 40.8, 39.4, 37.1, 34.3, 33.2, 27.8, 26.0, 25.8, 20.9, 18.5, 18.2, 17.5, −1.4, −4.3, −4.7 ppm. IR (film) $\tilde{\nu}$ = 3445, 2955, 2931, 2892, 1746, 1732, 1461, 1379, 1251, 1215, 1129, 1099, 1041, 939, 861, 837, 776 cm^{-1}. MS (ESIpos) *m/z* (%): 883.4 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{42}H_{73}O_{12}Si_2ClNa$ [M+Na$^+$]: 883.4221, found: 883.4220.

Chlorodiene S22bb. According to General Procedure using dienylstannane **53bb** (34.7 mg, 31 µmol).



Colourless oil (26.2 mg, 98%). $[\alpha]_D^{20}$ = −13.4 (c = 1.31, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.96 (d, *J* = 11.0 Hz, 1H), 6.58 (td, *J* = 11.0, 1.1 Hz, 1H), 5.67 (ddd, *J* = 15.6, 7.7, 0.7 Hz, 1H), 5.61–5.48 (m, 2H), 4.98 (td, *J* = 8.7, 1.1 Hz, 1H), 4.88 (dd, *J* = 6.0, 4.4 Hz, 1H), 4.66 (d, *J* = 6.3 Hz, 1H), 4.62–4.54 (m, 2H), 4.54–4.48 (m, 2H), 4.26–4.15 (m, 3H), 4.11–4.03 (m, 2H), 4.01 (d, *J* = 8.0 Hz, 1H), 3.97–3.90 (m, 2H), 3.86–3.76 (m, 2H), 3.61 (dd, *J* = 8.6, 3.2 Hz, 1H), 3.33 (s, 3H), 3.30 (d, *J* = 3.6 Hz, 1H), 2.45 (hept, *J* = 6.9 Hz, 1H), 2.39–2.26 (m, 1H), 2.11–1.99 (m, *J* = 13.0, 7.3, 5.7 Hz, 2H), 1.77–1.69 (m, 2H), 1.67–1.56 (m, 2H), 1.46–1.42 (m, 6H), 1.21 (d, *J* = 6.6 Hz, 3H), 1.05 (d, *J* = 6.8 Hz, 3H), 1.03–0.97 (m, 2H), 0.90 (s, 9H), 0.07 (s, 6H), 0.05 (s, 9H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.7, 139.7, 136.8, 129.9, 127.1, 126.1, 119.0, 109.4, 103.4, 94.2, 85.1, 83.4, 81.8, 78.5, 77.4, 76.1, 75.2, 73.8, 72.5, 64.7, 64.6, 63.4, 55.4, 40.7, 39.6, 36.6, 33.9, 33.0, 27.2, 26.6, 25.9, 20.8, 18.0, 17.8, 17.4, −1.5, −4.5, −4.9 ppm. IR (film) $\tilde{\nu}$ = 3493, 2955, 2929, 2859, 1742, 1461, 1379, 1251, 1215, 1174, 1128, 1089, 1041, 943, 860, 837, 776, 696 cm^{-1}. MS (ESIpos) *m/z* (%): 883.4 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{42}H_{73}O_{12}Si_2ClNa$ [M+Na$^+$]: 883.4221, found: 883.4227.

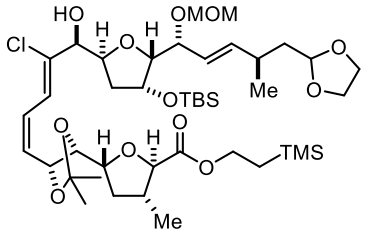
Chlorodiene S22cb. According to General Procedure using dienylstannane **53cb** (38 mg, 34 µmol).



Yellow oil (31.3 mg, 96%). $[\alpha]_D^{20}$ = +45.3 (c = 1.76, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.81 (dt, *J* = 11.0, 1.3 Hz, 1H), 6.54 (td, *J* = 11.1, 1.3 Hz, 1H), 5.73–5.61 (m, 2H), 5.52 (ddd, *J* = 15.6, 7.4, 0.9 Hz, 1H), 5.09 (ddd, *J* = 8.4, 6.7, 1.3 Hz, 1H), 4.88 (dd, *J* = 5.9, 4.3 Hz, 1H), 4.66 (d, *J* = 6.3 Hz, 1H), 4.60 (d, *J* = 6.3 Hz, 1H), 4.55 (ddd, *J* = 8.2, 6.8, 3.3 Hz, 1H), 4.51–4.45 (m, 2H), 4.28 (dd, *J* = 6.7, 5.7 Hz, 1H), 4.25–4.09 (m, 4H), 4.01–3.91 (m, 4H), 3.86–3.77 (m, 2H), 3.33 (s, 3H), 2.74 (d, *J* = 3.1 Hz, 1H), 2.51–2.40 (m, 1H), 2.40–2.29 (m, 1H), 2.17 (ddd, *J* = 12.2, 7.5, 5.9 Hz, 1H), 1.97 (ddd, *J* = 13.3, 8.2, 5.4 Hz, 1H), 1.77–1.68 (m, 2H), 1.66–1.54 (m, 2H), 1.49 (s, 3H), 1.39 (s, 3H), 1.21 (d, *J* = 6.6 Hz, 3H), 1.06 (d, *J* = 6.8 Hz, 3H), 1.02–0.97 (m, 2H), 0.90 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H), 0.03 (s, 9H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.0, 139.7, 135.1, 129.2, 126.2 (2C), 119.2,

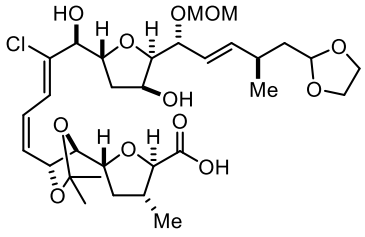
108.8, 103.5, 94.5, 85.6, 83.3, 80.0, 78.7, 78.6, 75.9, 74.6, 73.8, 72.4, 64.7, 64.7, 63.2, 55.6, 40.7, 39.3, 36.9, 33.9, 33.0, 27.4, 25.9, 25.2, 20.8, 18.1, 18.0, 17.4, −1.5, −4.4, −4.9 ppm. IR (film) $\tilde{\nu}$ = 3493, 2955, 2929, 2859, 1742, 1461, 1379, 1251, 1215, 1174, 1128, 1089, 1041, 943, 860, 837, 776, 696 cm^{-1}. MS (ESIpos) *m/z* (%): 883.4 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{42}H_{73}O_{12}Si_2ClNa$ [M+Na^+]: 883.4221, found: 883.4227.

Chlorodiene S22db. According to General Procedure using dienylstannane **53db** (59 mg, 53 µmol).



Colourless oil (44.6 mg, 98%). $[\alpha]_D^{20}$ = +13.5 (c = 1.24, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.79 (dt, *J* = 11.0, 1.1 Hz, 1H), 6.52 (td, *J* = 11.1, 1.2 Hz, 1H), 5.72–5.56 (m, 2H), 5.50 (ddd, *J* = 15.6, 7.6, 1.0 Hz, 1H), 4.87 (dd, *J* = 5.9, 4.3 Hz, 1H), 4.67–4.57 (m, 3H), 4.52–4.44 (m, 2H), 4.42–4.37 (m, 1H), 4.24–4.12 (m, 4H), 3.97 (d, *J* = 8.1 Hz, 1H), 3.95–3.88 (m, 3H), 3.86 (dd, *J* = 8.1, 5.0 Hz, 1H), 3.84–3.76 (m, 2H), 3.32 (s, 3H), 2.77 (d, *J* = 3.6 Hz, 1H), 2.43 (h, *J* = 7.4, 6.9 Hz, 1H), 2.35 (dtt, *J* = 14.0, 9.0, 6.7 Hz, 1H), 2.21 (ddd, *J* = 12.0, 7.5, 5.9 Hz, 1H), 1.96 (ddd, *J* = 13.3, 8.3, 5.2 Hz, 1H), 1.81 (ddd, *J* = 12.9, 6.6, 3.2 Hz, 1H), 1.70 (ddd, *J* = 13.9, 8.2, 4.5 Hz, 1H), 1.66–1.56 (m, 2H), 1.42 (s, 3H), 1.41 (s, 3H), 1.21 (d, *J* = 6.6 Hz, 3H), 1.04 (d, *J* = 6.8 Hz, 3H), 1.02–0.96 (m, 2H), 0.89 (s, 9H), 0.07 (s, 3H), 0.07 (s, 3H), 0.03 (s, 9H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.9, 139.7, 135.6, 130.5, 126.7, 126.3, 120.4, 109.7, 103.4, 94.5, 85.2, 83.1, 82.2, 79.9, 78.5, 75.9, 75.7, 75.2, 72.4, 64.7, 64.6, 63.2, 55.5, 40.7, 39.3, 36.3, 34.8, 33.0, 27.1, 26.9, 25.8, 20.8, 18.0, 17.9, 17.4, −1.5, −4.4, −4.9 ppm. IR (film) $\tilde{\nu}$ = 3442, 2954, 2930, 2886, 1733, 1461, 1380, 1251, 1214, 1173, 1098, 1061, 1038, 973, 940, 859, 836, 775, 697 cm^{-1}. MS (ESIpos) *m/z* (%): 883.4 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{42}H_{73}O_{12}Si_2ClNa$ [M+Na^+]: 883.4221, found: 883.4224.

***Seco*-Acid S23.** A solution of TBAF trihydrate (29 mg, 93 µmol) in THF (0.15 mL) was added dropwise at



0 °C to a solution of compound **S22aa** (10 mg, 12 µmol) in THF (0.05 mL). After stirring for 17 h at 0°C, the mixture was slowly warmed to ambient temperature, before it was diluted with EtOAc (5 mL) and sat. NH_4Cl (5 mL). The aq. phase was separated and extracted with EtOAc (2 × 5 mL). The combined organic phases were washed with a 1:3 mixture of sat. NH_4Cl and brine (10 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash chromatography (EtOAc/AcOH 99:1) to afford the title compound as a colourless oil (6.0 mg, 80%). $[\alpha]_D^{20}$ = –34.8 (c = 0.60, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.74 (d, *J* = 11.0 Hz, 1H), 6.58 (td, *J* = 11.0, 1.1 Hz, 1H), 5.94 (dd, *J* = 15.7, 6.7 Hz, 1H), 5.73 (ddd, *J* = 10.5, 9.6, 1.0 Hz, 1H), 5.40 (ddd, *J* = 15.7, 8.8, 1.3 Hz, 1H), 5.02 (dd, *J* = 9.4, 5.7 Hz, 1H), 4.85 (t, *J* = 4.8 Hz, 1H), 4.73 (d, *J* = 6.6 Hz, 1H), 4.60 (d, *J* = 6.5 Hz, 1H), 4.52 (dt, *J* = 9.5, 5.9 Hz, 1H), 4.37–4.27 (m, 2H), 4.19–4.08 (m, 2H), 4.07 (d, *J* = 5.7 Hz, 1H), 4.01 (d, *J* = 8.9 Hz, 1H), 4.01–3.90 (m, 2H), 3.90 (dd,

J = 7.2, 3.1 Hz, 1H), 3.87–3.76 (m, 2H), 3.37 (s, 3H), 2.50 (ddq, *J* = 14.2, 7.6, 7.0 Hz, 1H), 2.43–2.26 (m, 1H), 2.17 – 2.00 (m, 2H), 1.93 (ddd, *J* = 13.6, 9.6, 4.8 Hz, 1H), 1.79 (dt, *J* = 14.0, 5.1 Hz, 1H), 1.67 (ddd, *J* = 14.0, 8.5, 4.6 Hz, 1H), 1.52 (s, 3H), 1.45–1.38 (m, 4H), 1.25 (d, *J* = 6.6 Hz, 3H), 1.09 (d, *J* = 6.8 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 174.1, 142.3, 137.2, 129.8, 126.7, 123.8, 120.8, 109.9, 103.5, 93.6, 85.2, 83.2, 80.5, 79.7, 79.3, 77.8, 77.0, 73.3, 72.8, 64.9, 64.8, 55.6, 41.0, 39.6, 38.0, 37.5, 32.1, 27.7, 25.6, 19.8, 17.6 ppm. IR (film) $\tilde{\nu}$ = 3448, 2958, 2928, 1733, 1380, 1259, 1215, 1100, 1031, 869 cm^{-1}. MS (ESIneg) *m/z* (%): 645.3 (100 (M+Na)). HRMS (ESIneg): *m/z* calcd for $C_{31}H_{46}O_{12}Cl$ $[M-H]^-$: 645.2683, found: 645.2687.

Macrocycle 9. $NaHCO_3$ (217 mg, 2.58 mmol) was added to a suspension of 2-bromo-1-ethyl-pyridinium tetrafluoroborate (74 mg, 0.27 mmol) and *seco*-acid **S23** (5.5 mg, 8.5 µmol) in 1,2-dichloroethane (17 mL) in a sealed tube. The tube was placed in a pre-heated oil bath at 80 °C and the mixture was stirred for 22 h. The light purple suspension was cooled to ambient temperature before the reaction was quenched with pH 7 phosphate buffer (10 mL). The aq. phase was separated and extracted with EtOAc (2 × 15 mL). The combined organic phases were washed with brine (30 mL), dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography (hexane/EtOAc/AcOH 1:1:0 to 1:2:0 to 100:0:0 to 99:0:1) to provide the title compound as a colourless oil (1.6 mg, 30%); a second fraction contained recovered starting material **S23** (3.1 mg, 56%) [Conditions for LC-MS: ZORBAX Eclipse Plus C-18, 1.8 µm, 50 × 4.6 mm, MeCN/H_2O = 70:30, v = 0.8 mL/min, λ = 250 nm, 35 °C, 181 bar, t(carboxylate) = 1.0 min, t(**S23**) = 1.1 min, t(**9**) = 11.6 min]. $[\alpha]_D^{20}$ = –83.3 (c = 0.15, $CHCl_3$). λ_{max} (MeCN) = 249 nm. ^{1}H NMR (600 MHz, $CDCl_3$): *see Table S-14;* ^{13}C NMR (150 MHz, $CDCl_3$): *see Table S-14*. IR (film): $\tilde{\nu}$ = 3455, 2959, 2923, 1747, 1651, 1456, 1379, 1365, 1260, 1215, 1149, 1096, 1030, 870, 847, 800 cm^{-1}. MS (ESIpos) *m/z* (%): 651.3 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{31}H_{45}O_{11}ClNa$: 651.2542, found: 651.2548.

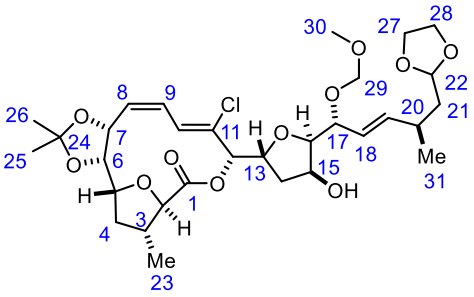


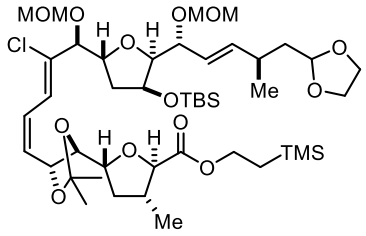
Table S-14. NMR data of 13-membered lactone **9**; numbering scheme as shown in the insert

atom n°	^{1}H NMR (500 MHz, $CDCl_3$)					^{13}C NMR (126 MHz, $CDCl_3$)	
	δ [ppm]	**m**	***J*** [Hz]	**COSY**	**NOESY**	**δ** [ppm]	**HMBC**
1	-	-	-	-	-	170.5	2
2	4.04	d	5.4	3, 4a	(4a), 23	82.7	4, 23
3	2.78	m	-	2, (4a), 4b, 23	5, 4a, 23	32.3	23
4a	1.93	ddd	11.4, 7.4, 4.2	(2), 3, 4b, 5	3, 5, 4b	39.0	23
4b	1.52	td	11.5, 10.3	3, 4a, 5	4a, (23)		
5	3.31	dd	11.7, 4,2	4ab, (6)	4a, 6, 10	75.8	2, 7
6	4.06	d	5.5	7, (5), (8)	5, 7	77.4	7
7	4.75	dd	7.2, 5.4	(4), 7, 8	6, 8, 26	76.6	8, (9)
8	5.61	ddd	11.8, 7.1, 0.9	7,9, (10)	7, 9	125.2	7, 9
9	6.67	dd	11.8, 11.2	8, 10	8, 10	130.7	7
10	7.78	dt	11.2, 0.8	(8), 9, (12)	9, 13, 5, (25)	124.9	(8), 12
11	-	-	-	-	-	131.6	9, 10, 12
12	5.09	d	7.3	13, (10)	13	81.4	(10), (13)
13	4.57	ddd	9.6, 7.3, 6.2	12, 14a, 14b	10, 12, 14b	78.4	12
14a	2.14	ddd	13.2, 9.4, 4.6	13, 14b, (15)	12, 14b, 15	37.3	12, (16)
14b	2.08	ddd	13.2, 6.3, 1.7	13, 14a, 15	13, 14a, (15)		
15	4.38	m	-	16, 15-OH	16, 14a, (15-OH), (14b)	72.8	14b
16	3.94	dd	6.4, 3.3	15, 17	15, 17, 18	84.6	(14b), (17)
17	4.34	dd	8.8, 6.2	16, 18, (19)	16, 19, 29	76.8	19, 29ab
18	5.48	ddd	15.7, 8.8, 1.2	17, 19	16, 31, (20)	124.4	(20)
19	5.87	dd	15.7, 7.0	18, (17)	17, (20)	141.9	17, 20
20	2.49	tq	8.1, 6.9	19, 21b, 31	(18), 19, 31	32.4	31
21a	1.75	dt	13.9, 5.3	22, 21b	20	41.0	(22), 31
21b	1.67	ddd	13.9, 8.4, 4.5	20, 21a, (22)	32		
22	4.84	dd	5.1, 4.5	21a, 21b	28a, 29a	103.5	28b, 29b
23	1.13	d	6.9	3, (4a)	2, 3	18.8	2
24	-	-	-	-	-	109.7	6, 24, 25
25	1.67	s	-	26, (6)	(2), 26	25.8	26
26	1.40	s	-	25	7, 8	26.0	25
27a	3.98–3.92	m	-	27b, 28ab	28a, 28b	64.9	-
27b	3.86–3.78	m	-	27a, 28ab	28a, 28b		
28a	3.98–3.92	m	-	27ab, 28b	27a, 27b	64.8	-
28b	3.86–3.78	m	-	27ab, 28a	27a, 27b		
29a	4.74	d	6.6	29b	(17), 29b, (30)	93.7	30, (17)
29b	4.63	d	6.6	(17), 29a	(17), 29a, 30		
30	3.39	s	-	-	29b	55.8	29a, 29b
31	1.08	d	6.8	20	20, (21a), (21b)	20.1	20

15-OH	3.18	d	4.2	15	15	-	-

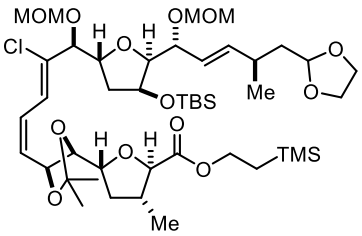
General Procedure for MOM-Protection of Chlorodienes S22. Hünig's base (2600 mol%), tetrabutylammonium iodide (25 mol%) and MOMCl (1500 mol%) were added to a solution of chlorodiene **S22** (0.01 M, 100 mol%) in 1,2-dichloroethane. The dark orange mixture was stirred for 16 h at 50 °C. After reaching ambient temperature, the mixture was diluted with *t*-butyl methyl ether (10 mL) and sat. $NaHCO_3$ (15 mL). The aq. phase was separated and extracted with *t*-butyl methyl ether (2 × 30 mL). The combined organic phases were washed with brine (40 mL), dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography (hexane/EtOAc 7:3 to 3:2 to 1:1 to 1:2) to afford the title compounds.

MOM-Ether S24aa. According to General Procedure using chlorodiene **S22aa** (103 mg, 0.12 mmol).



Colourless oil (99.5 mg, 92%). $[\alpha]_D^{20}$ = –50.8 (c = 0.75, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.65–6.52 (m, 2H), 5.84 (t, *J* = 9.9 Hz, 1H), 5.74 (ddd, *J* = 15.6, 7.6, 1.1 Hz, 1H), 5.47 (ddd, *J* = 15.7, 6.1, 1.0 Hz, 1H), 4.99 (dd, *J* = 9.8, 6.3 Hz, 1H), 4.83 (dd, *J* = 5.9, 4.5 Hz, 1H), 4.73–4.61 (m, 4H), 4.53 (dt, *J* = 9.8, 6.4 Hz, 1H), 4.27–4.07 (m, 7H), 4.01 (d, *J* = 7.5 Hz, 1H), 3.98–3.90 (m, 2H), 3.86-3.77 (m, 2H), 3.72 (dd, *J* = 8.0, 3.0 Hz, 1H), 3.41 (s, 3H), 3.37 (s, 3H), 2.47–2.28 (m, 2H), 2.04 (ddd, *J* = 12.7, 7.4, 5.6 Hz, 1H), 1.92 (ddd, *J* = 13.0, 6.0, 1.6 Hz, 1H), 1.74-1.64 (m, 2H), 1.64–1.56 (m, 1H), 1.52 (s, 3H), 1.41 (s, 3H), 1.35–1.29 (m, 1H), 1.17 (d, *J* = 6.6 Hz, 3H), 1.05 (d, *J* = 6.8 Hz, 3H), 1.03–0.98 (m, 2H), 0.89 (s, 9H), 0.07 (s, 3H), 0.07 (s, 3H), 0.04 (s, 9H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.1, 139.1, 134.9, 130.8, 126.3, 125.4, 123.0, 110.0, 103.5, 95.0, 94.1, 86.8, 83.9, 82.1, 80.8, 79.1, 78.8, 75.6, 73.1, 72.8, 64.9, 64.8, 63.3, 55.7, 55.5, 40.8, 39.5, 38.3, 37.0, 33.1, 27.8, 26.0, 25.8, 21.0, 18.4, 18.1, 17.6, –1.4, –3.8, –4.6 ppm. IR (film): $\tilde{\nu}$ = 2954, 2929, 2894, 1748, 1458, 1379, 1251, 1216, 1137, 1101, 1047, 919, 862, 836 cm^{-1}. MS (ESIpos) *m/z* (%): 927.4 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{44}H_{77}O_{13}ClSi_2Na$ [M+Na$^+$]: 927.4483, found: 927.4493.

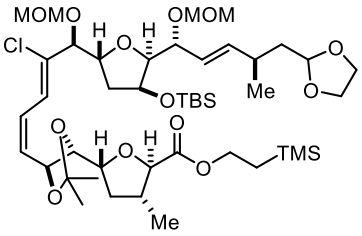
MOM-Ether S24ba. According to General Procedure using chlorodiene **S22ba** (19.5 mg, 23 µmol).



Colourless oil (18.4 mg, 87%). $[\alpha]_D^{20}$ = –67.2 (c = 0.92, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.83–6.75 (m, 1H), 6.58 (td, *J* = 11.0, 1.2 Hz, 1H), 5.74 (ddd, *J* = 15.7, 7.5, 1.1 Hz, 1H), 5.61 (ddd, *J* = 11.2, 8.5, 1.1 Hz, 1H), 5.46 (ddd, *J* = 15.7, 6.3, 1.1 Hz, 1H), 4.88–4.79 (m, 2H), 4.73–4.61 (m, 4H), 4.53 (dt, *J* = 9.7, 6.4 Hz, 1H), 4.28–4.09 (m, 6H), 4.02–3.88 (m, 3H), 3.86–3.76 (m, 3H), 3.65 (dd, *J* = 8.4, 3.8 Hz, 1H), 3.41 (s, 3H), 3.36 (s, 3H), 2.42 (dq, *J* = 14.1, 7.0 Hz, 1H), 2.37–2.25 (m, 1H), 2.06 (ddd, *J* = 12.1, 7.5, 6.3 Hz, 1H), 1.89 (ddd, *J* = 12.8, 6.1, 1.7 Hz, 1H), 1.80 (ddd,

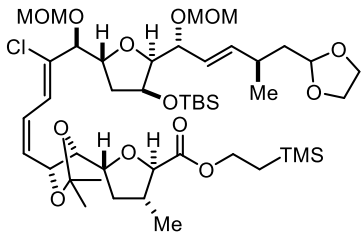
J = 13.1, 9.7, 4.1 Hz, 1H), 1.70 (ddd, *J* = 13.8, 7.6, 4.6 Hz, 1H), 1.64–1.55 (m, 2H), 1.44 (s, 6H), 1.18 (d, *J* = 6.6 Hz, 3H), 1.06–0.99 (m, 5H), 0.89 (s, 9H), 0.08–0.04 (m, 15H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.5, 138.9, 134.9, 130.9, 127.0, 125.4, 123.4, 109.7, 103.4, 94.7, 93.9, 86.5, 83.7, 82.7, 81.6, 78.6, 78.0, 75.6, 73.8, 72.8, 64.7, 64.6, 63.1, 55.5, 55.3, 40.7, 39.6, 37.9, 36.6, 32.9, 27.2, 26.7, 25.8, 20.7, 18.0, 17.4, 17.3, −1.5, −4.0, −4.7 ppm. IR (film): $\tilde{\nu}$ = 2954, 2930, 2894, 1743, 1462, 1380, 1251, 1215, 1173, 1129, 1089, 1053, 1047, 919, 837, 775, 694 cm^{-1}. MS (ESIpos) *m/z* (%): 927.4 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{44}H_{77}O_{13}ClSi_2Na$ [M+Na$^+$]: 927.4483, found: 927.4484.

MOM-Ether S24ca. According to General Procedure using chlorodiene **S22ca** (23 mg, 27 µmol).



Colourless oil (20 mg, 80%). $[\alpha]_D^{20}$ = –0.2 (c = 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.68 (dd, *J* = 11.0, 1.0 Hz, 1H), 6.55 (td, *J* = 11.1, 1.3 Hz, 1H), 5.80–5.67 (m, 2H), 5.47 (ddd, *J* = 15.7, 6.1, 1.1 Hz, 1H), 5.05 (ddd, *J* = 8.4, 6.8, 1.3 Hz, 1H), 4.83 (dd, *J* = 5.9, 4.5 Hz, 1H), 4.72–4.62 (m, 4H), 4.53 (dt, *J* = 9.8, 6.4 Hz, 1H), 4.30–4.07 (m, 7H), 4.01−3.89 (m, 3H), 3.87–3.77 (m, 2H), 3.72 (dd, *J* = 8.0, 2.9 Hz, 1H), 3.41 (s, 3H), 3.36 (s, 3H), 2.47–2.30 (m, 2H), 2.17 (ddd, *J* = 12.3, 7.5, 5.9 Hz, 1H), 1.93 (ddd, *J* = 13.0, 6.1, 1.6 Hz, 1H), 1.76–1.66 (m, 2H), 1.64–1.55 (m, 2H), 1.49 (s, 3H), 1.40 (s, 3H), 1.21 (d, *J* = 6.6 Hz, 3H), 1.05 (d, *J* = 6.8 Hz, 3H), 1.03–0.97 (m, 2H), 0.89 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H), 0.04 (s, 9H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.9, 138.8, 134.2, 129.8, 126.2, 125.3, 123.4, 108.9, 103.4, 94.8, 93.8, 86.6, 83.4, 81.7, 79.9, 78.9, 78.6, 75.5, 73.6, 72.7, 64.7, 64.7, 63.1, 55.5, 55.4, 40.7, 39.4, 38.0, 36.8, 32.9, 27.3, 25.8, 25.1, 20.8, 18.3, 18.0, 17.4, −1.5, −3.9, −4.8 ppm. IR (film): $\tilde{\nu}$ = 2955, 2930, 2894, 1747, 1462, 1380, 1251, 1215, 1153, 1100, 1037, 919, 836, 775 cm^{-1}. MS (ESIpos) *m/z* (%): 927.4 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{44}H_{77}O_{13}ClSi_2Na$ [M+Na$^+$]: 927.4483, found: 927.4491.

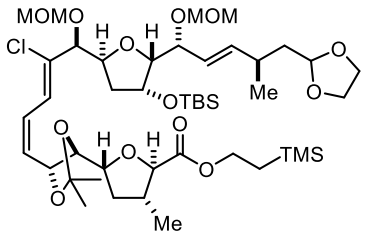
MOM-Ether S24da. According to General Procedure using chlorodiene **S22da** (24 mg, 28 µmol). Yellow



oil (20.5 mg, 81%). $[\alpha]_D^{20}$ = –31.7 (c = 1.09, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.70 (dd, *J* = 10.9, 1.0 Hz, 1H), 6.54 (td, *J* = 11.0, 1.2 Hz, 1H), 5.74 (ddd, *J* = 15.7, 7.6, 1.1 Hz, 1H), 5.66 (ddd, *J* = 11.1, 8.2, 1.0 Hz, 1H), 5.46 (ddd, *J* = 15.6, 6.1, 1.1 Hz, 1H), 4.82 (dd, *J* = 5.9, 4.5 Hz, 1H), 4.70 (d, *J* = 6.5 Hz, 1H), 4.65 (d, *J* = 6.5 Hz, 1H), 4.63–4.58 (m, 3H), 4.52 (ddd, *J* = 9.8, 7.4, 5.9 Hz, 1H), 4.20 (m, 5H), 4.08 (d, *J* = 7.4 Hz, 1H), 4.02 (d, *J* = 7.6 Hz, 1H), 3.98–3.89 (m, 3H), 3.83–3.78 (m, 2H), 3.71 (dd, *J* = 8.0, 3.0 Hz, 1H), 3.38 (s, 3H), 3.36 (s, 3H), 2.47–2.34 (m, 2H), 2.18 (ddd, *J* = 12.0, 7.4, 5.9 Hz, 1H), 1.95–1.88 (m, 1H), 1.74–1.55 (m, 4H), 1.43 (s, 6H), 1.22 (d, *J* = 6.7 Hz, 3H), 1.04 (d, *J* = 6.8 Hz, 3H), 1.02–0.96 (m, 2H), 0.88 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H), 0.04 (s, 9H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.8, 138.8, 134.3, 131.7, 126.5, 125.3, 124.0, 110.0, 103.4, 94.8, 93.7, 86.6, 83.1, 82.2, 81.9, 79.8, 78.6, 75.5, 75.5, 72.6, 64.7, 64.6, 63.1, 55.4, 55.4, 40.7, 39.3,

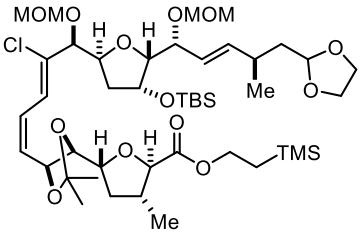
38.1, 35.8, 32.9, 27.2, 27.0, 25.8, 20.8, 18.2, 18.0, 17.4, −1.5, −4.0, −4.8 ppm. IR (film): $\tilde{\nu}$ = 2955, 2930, 2886, 1744, 1463, 1371, 1252, 1214, 1153, 1137, 1100, 1050, 1035, 977, 938, 919, 859, 837, 775 cm^{-1}. MS (ESIpos) *m/z* (%): 927.4 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{44}H_{77}O_{13}ClSi_2Na$ [M+Na$^+$]: 927.4483, found: 927.4487.

MOM-Ether S24ab. According to General Procedure using chlorodiene **S22ab** (34 mg, 40 µmol). Yellow



oil (31 mg, 86%). $[\alpha]_D^{20}$ = −43 (c = 1.57, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 6.64 (d, *J* = 11.0 Hz, 1H), 6.54 (td, *J* = 11.0, 1.1 Hz, 1H), 5.77 (ddd, *J* = 10.7, 9.7, 0.9 Hz, 1H), 5.65 (dd, *J* = 15.6, 7.7 Hz, 1H), 5.43 (ddd, *J* = 15.5, 8.0, 1.0 Hz, 1H), 4.98 (ddd, *J* = 9.6, 6.3, 1.2 Hz, 1H), 4.85 (dd, *J* = 5.9, 4.4 Hz, 1H), 4.66–4.57 (m, 4H), 4.49 (dt, *J* = 5.2, 3.8 Hz, 1H), 4.43 (td, *J* = 7.2, 4.2 Hz, 1H), 4.34 (d, *J* = 4.1 Hz, 1H), 4.25–4.08 (m, 5H), 4.01 (d, *J* = 7.4 Hz, 1H), 3.97–3.91 (m, 2H), 3.86 (dd, *J* = 6.4, 4.2 Hz, 1H), 3.83–3.78 (m, 2H), 3.36 (s, 3H), 3.32 (s, 3H), 2.48–2.29 (m, 2H), 2.12–1.99 (m, 2H), 1.87 (ddd, *J* = 12.8, 7.3, 3.6 Hz, 1H), 1.70 (ddd, *J* = 13.8, 8.0, 4.4 Hz, 1H), 1.59 (dt, *J* = 13.8, 6.2 Hz, 1H), 1.52 (s, 3H), 1.40 (s, 3H), 1.25 (dt, *J* = 12.1, 9.5 Hz, 1H), 1.17 (d, *J* = 6.7 Hz, 3H), 1.05–0.96 (m, 5H), 0.90 (s, 9H), 0.08 (s, 3H), 0.08 (s, 3H), 0.04 (s, 9H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): *δ* = 172.9, 140.0, 134.9, 130.0, 126.3, 126.2, 121.1, 109.8, 103.4, 94.5, 94.4, 84.6, 83.7, 80.8, 79.9, 79.0, 78.0, 76.2, 73.1, 72.2, 64.7, 64.6, 63.1, 55.8, 55.6, 40.6, 39.3, 36.9, 35.5, 33.0, 27.7, 25.9, 25.6, 20.7, 18.3, 18.1, 17.4, −1.5, −4.4, −4.9 ppm. IR (film): $\tilde{\nu}$ = 2953, 2930, 2889, 2858, 1747, 1731, 1462, 1379, 1252, 1214, 1142, 1036, 937, 863, 837, 777 cm^{-1}. MS (ESIpos) *m/z* (%): 927.4 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{44}H_{77}O_{13}ClSi_2Na$ [M+Na$^+$]: 927.4483, found: 927.4482.

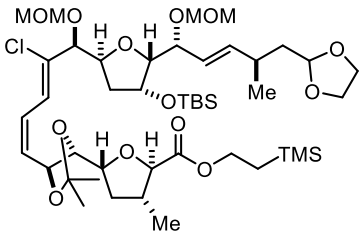
MOM-Ether S24bb. According to General Procedure using chlorodiene **S22bb** (26.2 mg, 0.030 mmol).



Colourless oil (20.9 mg, 74%). $[\alpha]_D^{20}$ = –52.9 (c = 1.05, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 6.80 (d, *J* = 11.0 Hz, 1H), 6.58 (td, *J* = 11.0, 1.1 Hz, 1H), 5.70–5.54 (m, 2H), 5.42 (ddd, *J* = 15.5, 8.0, 1.0 Hz, 1H), 4.85 (dd, *J* = 6.0, 4.4 Hz, 1H), 4.80 (td, *J* = 8.5, 1.1 Hz, 1H), 4.68–4.62 (m, 3H), 4.58 (d, *J* = 6.3 Hz, 1H), 4.53–4.43 (m, 2H), 4.39 (d, *J* = 4.3 Hz, 1H), 4.30–4.10 (m, 4H), 3.98 (d, *J* = 8.4 Hz, 1H), 3.96–3.91 (m, 2H), 3.88 (dd, *J* = 6.4, 4.3 Hz, 1H), 3.84–3.77 (m, 2H), 3.67 (dd, *J* = 8.3, 4.4 Hz, 1H), 3.37 (s, 3H), 3.32 (s, 3H), 2.45–2.29 (m, 2H), 2.18–2.03 (m, 2H), 1.89 (ddd, *J* = 12.9, 7.3, 3.6 Hz, 1H), 1.70 (ddd, *J* = 13.8, 8.0, 4.4 Hz, 1H), 1.63–1.58 (m, 1H), 1.56–1.47 (m, 1H), 1.44 (s, 6H), 1.18 (d, *J* = 6.7 Hz, 3H), 1.06–0.99 (m, 5H), 0.90 (s, 9H), 0.08 (s, 3H), 0.08 (s, 3H), 0.05 (s, 9H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): *δ* = 172.4, 139.8, 135.1, 130.2, 127.3, 126.4, 121.4, 109.6, 103.3, 94.4, 94.4, 84.6, 83.7, 83.0, 79.9, 78.4, 77.6, 76.2, 73.8, 72.2, 64.6, 64.6, 62.9, 55.6, 55.4, 40.6, 39.6, 36.6, 35.5, 33.0, 27.1, 26.6, 25.8, 20.7, 18.0, 17.4, 17.3, −1.6, −4.4, −5.0 ppm. IR (film): $\tilde{\nu}$ = 2954, 2930, 2889, 1746, 1462, 1380, 1251, 1215, 1172, 1129, 1088, 1055, 1036, 939, 860, 836, 775 cm^{-1}. MS

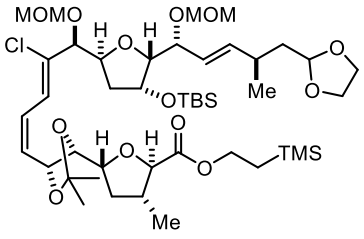
(ESIpos) *m/z* (%): 927.4 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{44}H_{77}O_{13}ClSi_2Na$ [M+Na$^+$]: 927.4483, found: 927.4483.

MOM-Ether S24cb. According to General Procedure using chlorodiene **S22cb** (28 mg, 33 µmol).



Colourless oil (24.2 mg, 81%). $[\alpha]_D^{20}$ = +0.6 (c = 1.36, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.74 (dd, *J* = 11.0, 1.1 Hz, 1H), 6.56 (td, *J* = 11.1, 1.3 Hz, 1H), 5.75–5.62 (m, 2H), 5.45 (ddd, *J* = 15.6, 8.0, 1.0 Hz, 1H), 5.05 (ddd, *J* = 8.3, 6.7, 1.3 Hz, 1H), 4.86 (dd, *J* = 6.0, 4.4 Hz, 1H), 4.68–4.57 (m, 4H), 4.52–4.44 (m, 2H), 4.38 (d, *J* = 3.5 Hz, 1H), 4.27–4.10 (m, 5H), 3.99–3.91 (m, 3H), 3.89 (dd, *J* = 6.3, 4.2 Hz, 1H), 3.83–3.77 (m, 2H), 3.36 (s, 3H), 3.33 (s, 3H), 2.48–2.30 (m, 2H), 2.22–2.08 (m, 2H), 1.85 (ddd, *J* = 12.8, 7.3, 3.7 Hz, 1H), 1.71 (ddd, *J* = 13.8, 7.9, 4.4 Hz, 1H), 1.65–1.52 (m, 2H), 1.49 (s, 3H), 1.40 (s, 3H), 1.20 (d, *J* = 6.6 Hz, 3H), 1.04 (d, *J* = 6.8 Hz, 3H), 1.02–0.97 (m, 2H), 0.90 (s, 9H), 0.08 (s, 6H), 0.04 (s, 9H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.9, 139.8, 134.4, 128.9, 126.5, 126.4, 121.2, 108.8, 103.4, 94.7, 94.4, 84.7, 83.4, 80.0, 79.7, 78.7, 78.1, 76.2, 73.8, 72.3, 64.7, 64.6, 63.1, 55.7, 55.6, 40.6, 39.3, 37.1, 34.9, 33.0, 27.5, 25.9, 25.2, 20.7, 18.3, 18.1, 17.4, −1.5, −4.4, −4.9 ppm. IR (film): $\tilde{\nu}$ = 2954, 2930, 2891, 2858, 1746, 1733, 1463, 1380, 1252, 1215, 1144, 1100, 1066, 1036, 957, 942, 925, 860, 837, 776 cm^{-1}. MS (ESIpos) *m/z* (%): 927.4 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{44}H_{77}O_{13}ClSi_2Na$ [M+Na$^+$]: 927.4483, found: 927.4495.

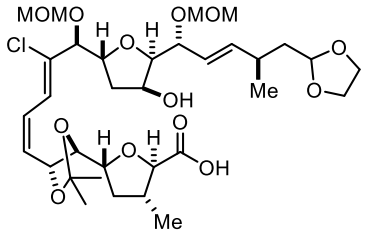
MOM-Ether S24db. According to General Procedure using chlorodiene **S22db** (45 mg, 52 µmol).



Colourless oil (36 mg, 77%). $[\alpha]_D^{20}$ = −27.6 (c = 1.01, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.73 (dt, *J* = 11.0, 1.0 Hz, 1H), 6.53 (td, *J* = 11.0, 1.2 Hz, 1H), 5.70–5.58 (m, 2H), 5.42 (ddd, *J* = 15.6, 8.0, 1.1 Hz, 1H), 4.85 (dd, *J* = 6.0, 4.3 Hz, 1H), 4.67–4.51 (m, 5H), 4.48 (dt, *J* = 5.0, 3.6 Hz, 1H), 4.43 (td, *J* = 7.3, 4.3 Hz, 1H), 4.31 (d, *J* = 4.3 Hz, 1H), 4.25–4.12 (m, 3H), 4.16–4.08 (m, 1H), 4.01 (d, *J* = 7.8 Hz, 1H), 3.97–3.89 (m, 3H), 3.84 (dd, *J* = 6.6, 4.1 Hz, 1H), 3.84–3.75 (m, 2H), 3.35 (s, 3H), 3.32 (s, 3H), 2.47–2.32 (m, 2H), 2.21–2.06 (m, 2H), 1.90 (ddd, *J* = 12.9, 7.1, 3.3 Hz, 1H), 1.74–1.63 (m, 2H), 1.58 (dt, *J* = 13.8, 6.2 Hz, 1H), 1.44–1.39 (m, 6H), 1.22 (d, *J* = 6.6 Hz, 3H), 1.05–0.96 (m, 5H), 0.90 (s, 9H), 0.08 (s, 3H), 0.08 (s, 3H), 0.03 (s, 9H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.7, 139.8, 134.5, 130.8, 126.8, 126.5, 122.3, 109.8, 103.4, 94.5, 94.3, 84.6, 83.2, 82.1, 79.9, 79.6, 77.9, 76.2, 75.4, 72.3, 64.7, 64.6, 63.1, 55.7, 55.6, 40.6, 39.3, 35.7, 35.5, 33.0, 27.2, 26.9, 25.9, 20.8, 18.1, 18.0, 17.4, −1.5, −4.4, −4.9 ppm. IR (film): $\tilde{\nu}$ = 2954, 2931, 2891, 1748, 1462, 1371, 1251, 1213, 1144, 1098, 1065, 1035, 937, 861, 837, 776 cm^{-1}. MS (ESIpos) *m/z* (%): 927.4 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{44}H_{77}O_{13}ClSi_2Na$ [M+Na$^+$]: 927.4483, found: 927.4488.

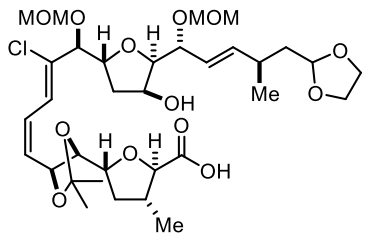
General Procedure for Liberating the *Seco*-Acids 8. A solution of TBAF (1 M in THF, 500 mol%) was added dropwise to a solution of compounds **S24** (0.15 M, 100 mol%) in THF at 0 °C. After stirring for 2 h at 0 °C, the ice bath was removed and stirring was continued for 2.5 h at ambient temperature. The mixture was diluted with NaOH (0.1 M, 5 mL) and *t*-butyl methyl ether (10 mL). The ethereal phase was extracted with NaOH (0.1 M, 3 mL). The combined aq. phases were washed with *t*-butyl methyl ether (20 mL) and carefully acidified with HCl (1 M, 1 mL) until a visible cloudiness was persistent in the solution (pH = 4). The solution was extracted with EtOAc (3 × 10 mL). The combined organic phases were washed with a 3:1 mixture of brine and pH 4 phosphate buffer (15 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The *seco*-acids were used in the next step without further purification.

***Seco*-Acid 8aa**. According to General Procedure using ester **S24aa** (99 mg, 0.11 mmol). Colourless oil



(75.5 mg, 99%). $[\alpha]_D^{20}$ = –65.6 (c = 0.91, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.63 (d, *J* = 11.0 Hz, 1H), 6.55 (td, *J* = 10.8, 1.1 Hz, 1H), 5.85 (dd, *J* = 15.6, 7.0 Hz, 1H), 5.75 (t, *J* = 10.2 Hz, 1H), 5.47 (ddd, *J* = 15.6, 8.6, 1.2 Hz, 1H), 4.99 (dd, *J* = 9.6, 5.7 Hz, 1H), 4.83 (t, *J* = 4.9 Hz, 1H), 4.69 (d, *J* = 6.6 Hz, 1H), 4.66–4.52 (m, 4H), 4.34-4.28 (m, 2H), 4.18–4.07 (m, 3H), 4.02 (d, *J* = 8.5 Hz, 1H), 3.97–3.90 (m, 2H), 3.86–3.77 (m, 3H), 3.40 (s, 3H), 3.36 (s, 3H), 3.30 (brs, 1H), 2.52–2.40 (m, 1H), 2.40–2.29 (m, 1H), 2.13–2.04 (m, 1H), 2.00 (ddd, *J* = 13.3, 6.4, 1.4 Hz, 1H), 1.80 (ddd, *J* = 13.7, 9.4, 4.8 Hz, 1H), 1.75–1.61 (m, 2H), 1.51 (s, 3H), 1.42–1.33 (m, 4H), 1.22 (d, *J* = 6.6 Hz, 3H), 1.06 (d, *J* = 6.8 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): *δ* = 174.5, 141.5, 135.1, 130.4, 126.4, 124.4, 122.8, 110.0, 103.4, 94.1, 93.8, 84.5, 83.1, 81.7, 80.7, 79.3, 78.9, 76.8, 73.2, 72.8, 64.9, 64.8, 55.7, 55.6, 40.9, 39.6, 37.8, 37.3, 32.4, 27.7, 25.6, 20.1, 17.7 ppm. IR (film): $\tilde{\nu}$ = 3477, 2957, 2932, 2894, 1735, 1380, 1250, 1216, 1151, 1101, 1032, 918, 869 cm^{-1}. MS (ESIpos) *m/z* (%): 713.3 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{33}H_{51}O_{13}ClNa$ [M+Na$^+$]: 713.2910, found: 713.2917.

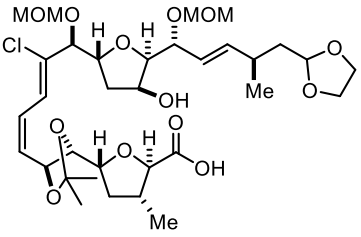
***Seco*-Acid 8ba**. According to General Procedure using ester **S24ba** (18.4 mg, 0.11 mmol). Colourless oil



(14.0 mg, 99%). $[\alpha]_D^{20}$ = –111.9 (c = 0.70, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 6.79 (dd, *J* = 11.0, 1.0 Hz, 1H), 6.56 (td, *J* = 11.0, 1.2 Hz, 1H), 5.86 (ddd, *J* = 15.7, 7.1, 0.8 Hz, 1H), 5.63 (ddd, *J* = 11.1, 8.6, 1.1 Hz, 1H), 5.50 (ddd, *J* = 15.7, 8.2, 1.3 Hz, 1H), 4.94 (td, *J* = 8.5, 1.2 Hz, 1H), 4.88 (dd, *J* = 5.3, 4.5 Hz, 1H), 4.71 (d, *J* = 6.5 Hz, 1H), 4.69–4.61 (m, 3H), 4.55 (dt, *J* = 9.1, 6.6 Hz, 1H), 4.32 (td, *J* = 6.6, 2.1 Hz, 2H), 4.20 (d, *J* = 6.6 Hz, 1H), 4.13–4.05 (m, 1H), 4.03 (d, *J* = 8.6 Hz, 1H), 3.98–3.89 (m, 3H), 3.87–3.78 (m, 2H), 3.62 (dd, *J* = 8.6, 2.8 Hz, 1H), 3.41 (s, 3H), 3.37 (s, 3H), 2.46 (dtd, *J* = 8.2, 6.9, 3.5 Hz, 1H), 2.39–2.28 (m, 1H), 2.11 (ddd, *J* = 13.7, 7.1, 4.7 Hz, 1H), 2.00 (ddd, *J* = 13.2, 6.6, 1.6 Hz, 1H), 1.89 (ddd, *J* = 13.5, 9.1, 4.9 Hz, 1H), 1.74–1.63 (m, 3H),

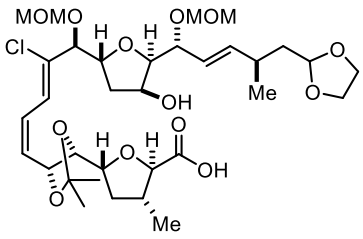
1.47−1.40 (m, 6H), 1.23 (d, *J* = 6.6 Hz, 3H), 1.06 (d, *J* = 6.8 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.6, 140.9, 134.7, 131.1, 126.8, 124.5, 123.7, 109.5, 103.3, 94.1, 93.6, 84.0, 83.4, 81.9, 81.1, 78.8, 77.2, 76.6, 73.7, 72.6, 64.7, 64.6, 55.7, 55.5, 40.7, 39.7, 37.4, 36.7, 32.2, 27.2, 26.6, 20.1, 17.2 ppm. IR (film): $\tilde{\nu}$ = 3485, 2957, 2929, 2894, 1742, 1457, 1380, 1258, 1215, 1129, 1091, 1032, 918, 877, 799 cm^{-1}. MS (ESIneg) *m/z* (%): 689.3 (100 (M−H)). HRMS (ESIneg): *m/z* calcd for $C_{33}H_{50}O_{13}Cl$ [M−H]$^-$: 689.2945, found: 689.2948.

***Seco*-Acid 8ca**. According to General Procedure using ester **S24ca** (20 mg, 0.022 mmol). Colourless oil



(15.3 mg, 99%). $[\alpha]_D^{20}$ = –40.6 (c = 0.76, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.64 (d, *J* = 11.0 Hz, 1H), 6.56 (td, *J* = 10.9, 1.3 Hz, 1H), 5.85 (dd, *J* = 15.7, 7.0 Hz, 1H), 5.66 (dd, *J* = 10.9, 8.6 Hz, 1H), 5.49 (ddd, *J* = 15.7, 8.4, 1.2 Hz, 1H), 5.08 (ddd, *J* = 8.3, 6.6, 1.3 Hz, 1H), 4.85 (t, *J* = 4.9 Hz, 1H), 4.70 (d, *J* = 6.5 Hz, 1H), 4.67–4.61 (m, 3H), 4.54 (dt, *J* = 9.2, 6.4 Hz, 1H), 4.34–4.28 (m, 2H), 4.24–4.18 (m, 1H), 4.13 (d, *J* = 6.4 Hz, 1H), 4.06 (dt, *J* = 9.6, 6.1 Hz, 1H), 3.99–3.92 (m, 3H), 3.87 (dd, *J* = 6.4, 3.3 Hz, 1H), 3.84–3.79 (m, 2H), 3.41 (s, 3H), 3.37 (s, 3H), 2.53–2.42 (m, 1H), 2.42–2.32 (m, 1H), 2.27 (dt, *J* = 12.5, 6.3 Hz, 1H), 2.01 (ddd, *J* = 13.3, 6.4, 1.6 Hz, 1H), 1.89–1.81 (m, 1H), 1.79–1.55 (m, 3H), 1.50 (s, 3H), 1.39 (s, 3H), 1.28–1.25 (m, 3H), 1.07 (d, *J* = 6.8 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.0, 141.1, 134.8, 130.7, 125.6, 124.4, 123.3, 109.3, 103.3, 94.0, 93.7, 84.4, 82.7, 81.0, 80.0, 78.9, 78.9, 76.6, 74.2, 72.6, 64.7, 64.7, 55.6, 55.5, 40.8, 39.4, 38.1, 37.5, 32.2, 27.5, 25.1, 20.0, 17.6 ppm. IR (film): $\tilde{\nu}$ = 3472, 2957, 2932, 2894, 1734, 1457, 1381, 1214, 1151, 1100, 1033, 975, 918, 870, 802 cm^{-1}. MS (ESIneg) *m/z* (%): 689.3 (100 (M−H)). HRMS (ESIneg): *m/z* calcd for $C_{33}H_{50}O_{13}Cl$ [M−H]$^-$: 689.2945, found: 689.2934.

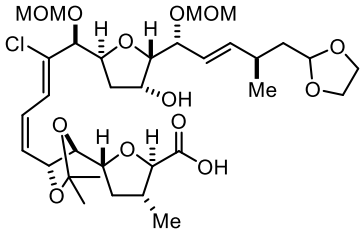
***Seco*-Acid 8da**. According to General Procedure using ester **S24da** (20 mg, 0.022 mmol). Colourless oil



(14.5 mg, 95%). $[\alpha]_D^{20}$ = –54.3 (c = 1.38, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.76 (dd, *J* = 11.0, 1.1 Hz, 1H), 6.53 (td, *J* = 11.1, 1.1 Hz, 1H), 5.91 (dd, *J* = 15.8, 6.6 Hz, 1H), 5.64 (ddd, *J* = 11.0, 8.7, 1.1 Hz, 1H), 5.44 (ddd, *J* = 15.7, 8.8, 1.4 Hz, 1H), 4.84 (t, *J* = 4.8 Hz, 1H), 4.73–4.59 (m, 5H), 4.45 (ddt, *J* = 10.2, 7.4, 5.1 Hz, 1H), 4.37–4.27 (m, 2H), 4.16 (dt, *J* = 9.4, 5.9 Hz, 1H), 4.10 (d, *J* = 7.3 Hz, 1H), 3.99–3.92 (m, 3H), 3.89 (dd, *J* = 6.8, 3.0 Hz, 1H), 3.85–3.79 (m, 2H), 3.75 (dd, *J* = 7.9, 6.4 Hz, 1H), 3.42 (s, 3H), 3.37 (s, 3H), 2.52–2.39 (m, 2H), 2.33 (ddd, *J* = 12.5, 7.2, 5.6 Hz, 1H), 1.99 (dd, *J* = 12.9, 5.8 Hz, 1H), 1.89 (ddd, *J* = 13.5, 10.3, 4.6 Hz, 1H), 1.78 (dt, *J* = 14.0, 5.2 Hz, 1H), 1.67 (ddd, *J* = 13.7, 8.4, 4.6 Hz, 1H), 1.57 (dt, *J* = 11.9, 9.7 Hz, 1H), 1.44 (s, 3H), 1.42 (s, 3H), 1.22 (d, *J* = 6.6 Hz, 3H), 1.07 (d, *J* = 6.8 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 174.1, 141.6, 133.9, 131.6, 126.2, 124.0, 122.8, 109.9, 103.3, 93.9, 93.6, 84.4, 83.4, 82.3, 81.6, 80.8, 79.8, 76.8, 76.8, 72.8, 64.7, 64.6, 55.6, 55.5, 40.8, 39.2, 37.8, 37.2, 31.9, 27.0, 27.0, 19.6, 17.7 ppm. IR (film): $\tilde{\nu}$ = 3449, 2957,

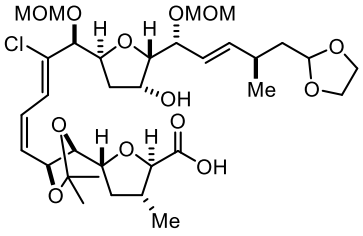
2933, 2895, 1740, 1381, 1214, 1152, 1100, 1033, 980, 918, 875 cm^{-1}. MS (ESIneg) *m/z* (%): 689.3 (100 (M−H)). HRMS (ESIneg): *m/z* calcd for $C_{33}H_{50}O_{13}Cl$ $[M-H]^-$: 689.2945, found: 689.2951.

***Seco*-Acid 8ab**. According to General Procedure using ester **S24ab** (31 mg, 0.034 mmol). Colourless oil



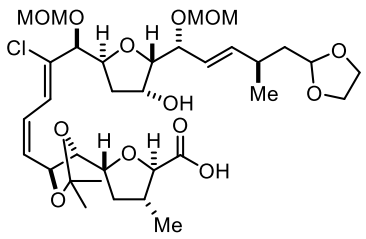
(23.7 mg, 99%). $[\alpha]_D^{20}$ = –68.4 (c = 0.95, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 6.65 (d, *J* = 11.1 Hz, 1H), 6.56 (td, *J* = 11.0, 1.2 Hz, 1H), 5.71 (ddd, *J* = 15.6, 7.6, 1.0 Hz, 1H), 5.70 (ddd, *J* = 11.0, 9.2, 1.0 Hz, 1H), 5.45 (ddd, *J* = 15.5, 7.3, 1.1 Hz, 1H), 5.00 (ddd, *J* = 9.3, 5.7, 1.0 Hz, 1H), 4.84 (dd, *J* = 5.7, 4.6 Hz, 1H), 4.66 (d, *J* = 6.2 Hz, 1H), 4.63 (d, *J* = 6.7 Hz, 1H), 4.61 (d, *J* = 6.1 Hz, 1H), 4.59 (d, *J* = 6.7 Hz, 1H), 4.57 (ddd, *J* = 9.3, 6.3, 4.5 Hz, 1H), 4.49 (dd, *J* = 4.8, 2.9 Hz, 1H), 4.38 (d, *J* = 4.5 Hz, 1H), 4.23 (td, *J* = 7.1, 1.0 Hz, 1H), 4.16–4.11 (m, 1H), 4.15–4.10 (m, 1H), 4.02 (d, *J* = 8.8 Hz, 1H), 3.98–3.92 (m, 2H), 3.86–3.77 (m, 2H), 3.77 (dd, *J* = 7.0, 2.9 Hz, 1H), 3.39 (s, 3H), 3.36 (s, 3H), 2.44 (hept, *J* = 7.0 Hz, 1H), 2.39–2.31 (m, 1H), 2.09 (m, 1H), 2.08 (ddd, *J* = 13.2, 9.2, 4.3 Hz, 1H), 1.99 (ddd, *J* = 13.2, 6.3, 1.1 Hz, 1H), 1.69 (ddd, *J* = 13.9, 7.9, 4.6 Hz, 1H), 1.62 (dt, *J* = 13.9, 6.1 Hz, 1H), 1.53 (s, 3H), 1.41 (s, 3H), 1.39–1.34 (m, 1H), 1.24 (d, *J* = 6.6 Hz, 3H), 1.04 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$): δ = 173.4, 140.3, 135.4, 129.7, 126.2, 125.4, 121.2, 109.9, 103.3, 94.9, 94.4, 84.4, 82.8, 80.7, 79.8, 79.3, 78.3, 77.0, 73.3, 72.5, 64.7 (2C), 55.8, 55.8, 40.6, 39.5, 37.3, 35.5, 32.8, 27.7, 25.5, 20.7, 17.4 ppm. IR (film): $\tilde{\nu}$ = 3484, 2929, 1735, 1379, 1215, 1144, 1100, 1051, 1029, 868 cm^{-1}. MS (ESIneg) *m/z* (%): 689.3 (100 (M−H)). HRMS (ESIneg): *m/z* calcd for $C_{33}H_{50}O_{13}Cl$ $[M-H]^-$: 689.2945, found: 689.2949.

***Seco*-Acid 8bb**. According to General Procedure using ester **S24bb** (20.9 mg, 0.023 mmol). Colourless



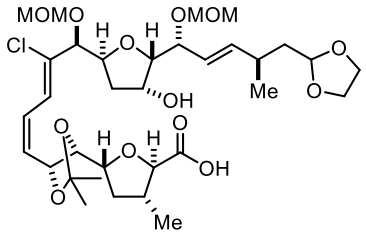
oil (16 mg, 99%). $[\alpha]_D^{20}$ = –116.6 (c = 0.80, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.78 (d, *J* = 11.0 Hz, 1H), 6.56 (td, *J* = 11.1, 1.0 Hz, 1H), 5.72 (ddd, *J* = 15.5, 7.6, 0.9 Hz, 1H), 5.61 (ddd, *J* = 11.0, 8.7, 1.0 Hz, 1H), 5.44 (ddd, *J* = 15.5, 7.5, 1.1 Hz, 1H), 4.98–4.89 (m, 1H), 4.84 (dd, *J* = 5.7, 4.6 Hz, 1H), 4.69–4.62 (m, 2H), 4.60 (d, *J* = 6.2 Hz, 1H), 4.57 (d, *J* = 6.6 Hz, 1H), 4.56–4.46 (m, 2H), 4.39 (d, *J* = 4.6 Hz, 1H), 4.29–4.20 (m, 1H), 4.11–4.00 (m, 2H), 3.98–3.90 (m, 2H), 3.89–3.77 (m, 3H), 3.67–3.58 (m, 1H), 3.38 (s, 3H), 3.36 (s, 3H), 2.48–2.34 (m, 2H), 2.21–2.03 (m, 3H), 1.73–1.61 (m, 3H), 1.47–1.42 (m, 6H), 1.23 (d, *J* = 6.7 Hz, 3H), 1.03 (d, *J* = 6.7 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.5, 140.6, 134.6, 130.8, 127.0, 125.3, 123.1, 109.5, 103.3, 94.8, 94.2, 84.1, 83.4, 81.5, 79.8, 79.2, 77.0, 76.9, 73.7, 72.5, 64.7, 64.7, 55.8, 55.7, 40.6, 39.2, 36.6, 35.8, 32.7, 27.2, 26.6, 20.6, 17.8 ppm. IR (film): $\tilde{\nu}$ = 3320, 2961, 2933, 2878, 1739, 1461, 1380, 1214, 1128, 1089, 1054, 1028, 879 cm^{-1}. MS (ESIneg) *m/z* (%): 689.3 (100 (M−H)). HRMS (ESIneg): *m/z* calcd for $C_{33}H_{50}O_{13}Cl$ $[M-H]^-$: 689.2945, found: 689.2951.

***Seco*-Acid 8cb**. According to General Procedure using ester **S24cb** (24 mg, 27 µmol). Colourless oil



(17.9 mg, 98%). $[\alpha]_D^{20}$ = –52.7 (c = 0.82, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.64 (d, *J* = 11.0 Hz, 1H), 6.55 (td, *J* = 11.0, 1.4 Hz, 1H), 5.72 (ddd, *J* = 15.5, 7.6, 0.9 Hz, 1H), 5.63 (dd, *J* = 11.0, 8.8 Hz, 1H), 5.46 (ddd, *J* = 15.5, 7.2, 1.1 Hz, 1H), 5.07 (ddd, *J* = 8.4, 6.7, 1.4 Hz, 1H), 4.88–4.82 (m, 1H), 4.69–4.61 (m, 3H), 4.57 (d, *J* = 6.7 Hz, 1H), 4.54–4.48 (m, 2H), 4.35 (d, *J* = 4.9 Hz, 1H), 4.30–4.21 (m, 2H), 4.06 (dt, *J* = 9.5, 5.8 Hz, 1H), 3.99–3.92 (m, 3H), 3.85–3.77 (m, 3H), 3.40 (s, 3H), 3.36 (s, 3H), 2.46–2.32 (m, 3H), 2.23 (ddd, *J* = 12.5, 7.3, 5.7 Hz, 1H), 2.15–2.03 (m, 2H), 1.75–1.56 (m, 2H), 1.51 (s, 3H), 1.39 (s, 3H), 1.24 (d, *J* = 7.0 Hz, 3H), 1.04 (d, *J* = 6.8 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.7, 140.2, 134.8, 130.5, 125.7, 125.3, 122.6, 109.3, 103.3, 94.8, 94.1, 84.1, 82.8, 80.0, 79.8, 78.7, 77.0, 74.2, 72.8, 64.7, 55.7, 55.7, 40.6, 39.3, 37.7, 36.0, 32.8, 29.7, 27.5, 25.2, 20.7, 17.6 ppm. IR (film): $\tilde{\nu}$ = 3466, 2926, 1731, 1457, 1380, 1214, 1149, 1100, 1028, 976, 922, 870 cm^{-1}. MS (ESIneg) *m/z* (%): 689.3 (100 (M−H)). HRMS (ESIneg): *m/z* calcd for $C_{33}H_{50}O_{13}Cl$ $[M-H]^-$: 689.2945, found: 689.2950.

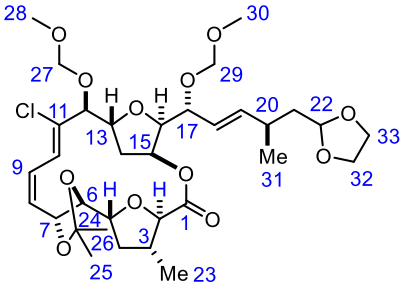
***Seco*-Acid 8db**. According to General Procedure using ester **S24db** (36 mg, 40 µmol). Colourless oil



(27.4 mg, 99%). $[\alpha]_D^{20}$ = –70.5 (c = 0.98, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.72 (d, *J* = 11.0 Hz, 1H), 6.54 (td, *J* = 11.0, 1.2 Hz, 1H), 5.70 (ddd, *J* = 15.6, 7.6, 0.9 Hz, 1H), 5.63 (ddd, *J* = 11.1, 8.6, 1.1 Hz, 1H), 5.45 (ddd, *J* = 15.5, 7.3, 1.1 Hz, 1H), 4.84 (dd, *J* = 5.7, 4.5 Hz, 1H), 4.69–4.59 (m, 4H), 4.57 (d, *J* = 6.8 Hz, 1H), 4.54–4.46 (m, 2H), 4.35 (d, *J* = 4.6 Hz, 1H), 4.24 (t, *J* = 6.6 Hz, 1H), 4.15 (dt, *J* = 9.6, 5.6 Hz, 1H), 4.00 (d, *J* = 8.2 Hz, 1H), 3.97–3.92 (m, 2H), 3.86–3.79 (m, 3H), 3.78 (dd, *J* = 6.9, 3.0 Hz, 1H), 3.39 (s, 3H), 3.37 (s, 3H), 2.50–2.37 (m, 2H), 2.27 (ddd, *J* = 12.4, 7.2, 5.6 Hz, 1H), 2.16–2.01 (m, 2H), 1.69 (ddd, *J* = 13.8, 7.9, 4.6 Hz, 1H), 1.67–1.55 (m, 2H), 1.43 (s, 3H), 1.42 (s, 3H), 1.24 (d, *J* = 6.5 Hz, 3H), 1.03 (d, *J* = 6.8 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 174.3, 140.2, 134.5, 131.2, 126.5, 125.4, 122.5, 109.9, 103.3, 94.9, 93.9, 84.2, 82.9, 82.1, 80.5, 79.8, 78.7, 76.9, 76.1, 72.6, 64.7, 64.7, 55.8, 55.6, 40.6, 39.2, 37.2, 35.7, 32.7, 27.1, 27.0, 20.7, 17.8 ppm. IR (film): $\tilde{\nu}$ = 3470, 2933, 2890, 1736, 1455, 1372, 1215, 1148, 1098, 1054, 1028, 976, 921, 876, 760 cm^{-1}. MS (ESIneg) *m/z* (%): 689.3 (100 (M−H)). HRMS (ESIneg): *m/z* calcd for $C_{33}H_{50}O_{13}Cl$ $[M-H]^-$: 689.2945, found: 689.2949

General Procedure for Yamaguchi Macrolactonization of *Seco*-Acids 8 to give Macrolactones 10. Hünig's base (650 mol%) and 2,4,6-trichlorobenzoyl chloride (450 mol%) were added to a solution of *seco*-acid **8** (0.1 M, 100 mol%) in THF at 0 °C. After stirring for 2 h at this temperature, the solvent was removed under reduced pressure and the residue was redissolved in toluene to make a 0.005 M solution. The resulting solution of the mixed Yamaguchi anhydride was added via syringe pump over a period of 20 h to a solution of DMAP (0.01 M, 2500 mol%) in toluene at 110 °C. Once the addition was complete, stirring was continued for additional 2 h at the same temperature. The mixture was cooled to ambient temperature and the reaction was quenched with sat. NH_4Cl (100 mL). The aq. phase was separated and extracted with EtOAc (3 × 100 mL). The combined organic phases were washed with brine (150 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash chromatography (EtOAc/hexane 3:2 to 4:1 to 9:1) to provide the title compounds.

Macrolactone 10aa. According to General Procedure using *seco*-acid **8aa** (30 mg, 43 µmol). Colourless oil (12 mg, 40%). %). Additional fractions contained an epimerized macrolactone **S25** (1.8 mg, 6%) and the cyclic head-to-tail dimer **S26aa** (3.9 mg, 13%) [Conditions for LC-MS: ZORBAX Eclipse Plus C-18, 1.8 µm, 50 × 4.6 mm, MeCN/H_2O = 70:30, v = 0.8 mL/min, λ = 250 nm, 35 °C, 158 bar, t(**S25**) = 2.7 min, t(**10aa**) = 3.4 min, t (**S26aa**) = 16.0 min].



Analytical and spectral data of macrolactone **10aa**: $[\alpha]_D^{20}$ = –25.9 (c = 0.80, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$, 2 main conformers, ratio 1:0.8, major conformer): *see Table S-15*. ^{13}C NMR (150 MHz, $CDCl_3$, 2 main conformers, ratio 1:0.8, major conformer): *see Table S-15*. ^{1}H NMR (600 MHz, $CDCl_3$, minor conformer): *see Table S-16*. ^{13}C NMR (150 MHz, $CDCl_3$, minor conformer): *see Table S-16*. IR (film): $\tilde{\nu}$ = 2958, 2933, 2892, 1741, 1454, 1381, 1256, 1213, 1151, 1099, 1031, 960 cm^{-1}. MS (ESIpos) *m/z* (%): 695.3 (100 (M+Na)) *see Figures S-2 – S-4.* HRMS (ESIpos): *m/z* calcd for $C_{33}H_{49}O_{12}ClNa$: 695.2805, found: 695.2811.

Table S-15. NMR data of the major conformer of macrolactone **10aa**; numbering scheme as shown in the insert

atom n°	^{1}H NMR (600 MHz, $CDCl_3$)						^{13}C NMR (151 MHz, $CDCl_3$)	
	δ [ppm]	m	*J* [Hz]	COSY	NOESY	ROESY	δ [ppm]	HMBC
1	-	-	-	-	-		170.1	2, 15, (3)
2	3.90	d	9.2	3	2*	23	80.3	3, 23
3	2.81	ddp	12.2, 9,2, 6.5	2, 23, (4b)	3*	-	37.6	2, 4ab, 23
4a	2.17	ddd	11.8, 6.3, 5.1	4b, 5, (3)	4a*	-	37.0	6, 23
4b	1.59	m	-	4a, 5	4b*	23		
5	4.15	m	-	4b, (4a), (6)	5*	-	81.4	4b, 7

6	4.68	m	-	(5), 7	6*	-	77.9	4b, 5, 7, 8
7	5.19	m	-	6, 8	7*	-	75.3	5, 8
8	5.92–5.86	m	-	7, 9, 10	8*	-	130.8	7, 9, 10
9	6.61–6.55	m	-	8	9*	-	123.4	7
10	6.59	m	-	8	10*	-	122.9	8, 12
11	-	-	-	-	-		133.9	9, 10, 13
12	4.49	d	4.9	13	12*	-	78.3	14ab, 27ab
13	4.56	m	-	12	13*	-	81.1	12, 14ab
14a 14b	2.50–2.42	m	-	13, 15	14a* 14b*	-	32.2	12, 16
15	4.95	q	8.7	14ab, 16	15*	-	76.2	13,
16	4.05	dd	7.9, 1.3	15	16*	-	80.7	(15), (14)
17	4.19	m	-	18	-	-	75.2	15, 19, 13, 29ab
18	5.58	dd	15.6, 8.6	17, 19, 20	18*	-	125.5	17, 19, 20
19	5.63	dd	15.6, 7.3	18, 20	19*	-	141.3	17, 18, 20, 21ab
20	2.45	p	7.4	19, 31, (21ab)	20*	-	33.1	18, 19, 21ab, 22, 31
21a 21b	1.70 1.16	m m	- -	(20), 21b, 22 21a, 22	21a*b* 21a*b*	-	40.9	19, 20, 22, 31
22	4.83	dd	5.9, 4.4	21ab	22*	-	103.6	28b, 29b
23	1.11	d	6.5	3	23*	(2), (4b)	16.8	2, 4b
24	-	-	-	-	-	-	107.9	6, 25, 26
25	1.48	s	-	26	25*	-	27.2	-
26	1.38	s	-	25	26*	-	24.8	-
27a 27b	4.66 4.59	d d	6.5 6.6	27b 27a	27a* 27b*	- -	95.1	12, 28
28	3.38	s	-	-	-	-	56.1	27ab
29a 29b	4.72 4.67	d d	6.6 6.7	29b 29a	29ba* 29ab*	- -	93.8	17, 30
30	3.42	s	-	-	-	-	55.5	29ab
31	1.04	d	6.8	20	31*	-	20.8	20, 21ab
32a 32b	3.96–3.91 3.83–3.78	m m	-	-	-	-	64.8	33ab
33a 33b	3.96–3.91 3.83–3.78	m m	-	-	-	-	64.9	32ab

NOESY displays fast exchange with minor conformer (*).

Table S-16. NMR data of the minor conformer of macrolactone **10aa;** numbering scheme as shown in the insert

atom n°	^{1}H NMR (600 MHz, $CDCl_3$)						^{13}C NMR (151 MHz, $CDCl_3$)	
	δ [ppm]	m	*J* [Hz]	COSY	NOESY	ROESY	δ [ppm]	HMBC
1	-	-	-	-	-		170.8	3
2	4.09	d	7.0	3	2*	23	87.4	(3), 4a, 23
3	2.58	dddq	9.7, 7.6, 7.0, 6.7	2, (4b), 23	3*	-	35.5	2, 4ab, 23
4a	2.33	ddd	12.8, 7.6, 6.0	4b, 5	4a*	-	39.4	(5), 6, 23
4b	1.93	dt	12.2, 9.9	4a, 5	4b*	23		
5	4.48	dd	9.8, 6.0	4ab	5*	-	77.8	2, 4b, 6
6	4.18	m	-	7	6*	-	80.0	4b, 5
7	4.91	ddd	7.2, 5.5, 1.7	6, 8	7*	-	75.7	6, 9
8	5.70	dd	11.0, 7.4	7, 9	8*	-	134.3	6, (10)
9	6.34	td	11.3, 1.6	8, 10	9*, 10, 12	-	124.3	7
10	6.63	d	11.7	9	9, 10*	-	122.8	6, 8
11	-	-	-	-	-		134.1	6, 9, 10, 13
12	4.18	m	-	13	12*	-	81.6	(10), 27ab
13	3.92	m	-	10, 12, 14b	13*	-	84.6	12
14a	1.82	td	12.8, 3.3	13, 14b, 15	14a*	-	38.1	-
14b	1.70	m	-	14a	14b*			
15	5.30	td	3.5, 1.0	16	15*	-	75.0	(14b), (2)
16	4.20	m	-	15	16*	-	84.3	12, (15), 17
17	4.18	m	-	7	17*	-	75.5	16, 18, 19, 29a
18	5.27	dd	15.5, 7.5	17, 19	18*, 19, 19*	-	124.2	20
19	5.60	dd	15.4, 8.2	18, 20	19*	-	141.7	20, 21ab, 31
20	2.38	p	7.1	19, 31, (21ab)	20*	-	33.3	18, 19, 21ab, 22, 31
21a 21b	1.60	m	-	22	21a*b*	-	40.6	19, 20, 22, 31
22	4.77	dd	5.6, 4.6	21ab	22*	-	103.4	20, 32ab, 33ab
23	1.16	d	6.7	3	23*	(2), (4b)	17.8	4b
24	-	-	-	-	-	-	108.4	7, 25, 26
25	1.57	s	-	26	25*	-	28.1	-
26	1.38	s	-	25	26*	-	26.2	-
27a	4.72	d	6.5	27b	27a*	-	95.4	12, 28
27b	4.69	d	6.6	-	27b*	-		
28	3.38	s	-	-	-	-	56.0	27ab
29a	4.72	d	6.6	29b, 29b*	29ba*	-	93.5	16, 17, 30

29b	4.55	d	6.6	29a	29ab*	-		
30	3.44	s	-	-	-	-	56.3	29ab
31	0.97	d	6.8	20	31*	-	21.3	20, 21ab
32a	3.96–3.91	m	-	-	-	-	64.9	33ab
32b	3.83–3.78	m						
33a	3.96–3.91	m	-	-	-	-	64.9	32ab
33b	3.83–3.78	m						

NOESY displays fast exchange with major conformer (*).

The cyclic monomer **10aa** and the head-to-tail dilactone (lactide) **S26** could be unambiguously distinguished by MS-MS fragmentation experiments, see below

Figure S-2. MS (ESIpos) analysis of macrocycle **10aa** *m/z* = 695.3 $[M+Na]^+$, *m/z* = 1367.6 $[2M+Na]^+$.

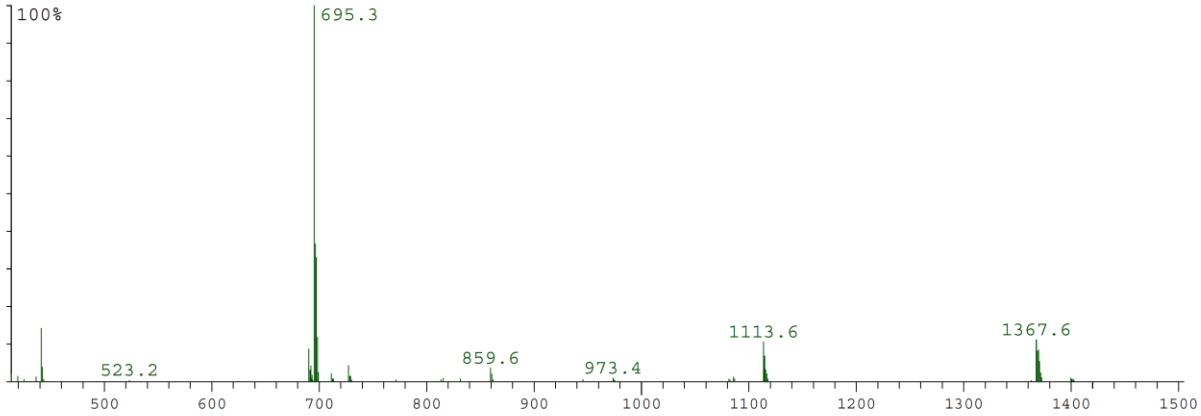


Figure S-3. MS-MS-Fragmentation of macrolactone **10aa** with *m/z* = 695.3 $[M+Na]^+$ as the precursor with increasing normalized collision energy (NCE).

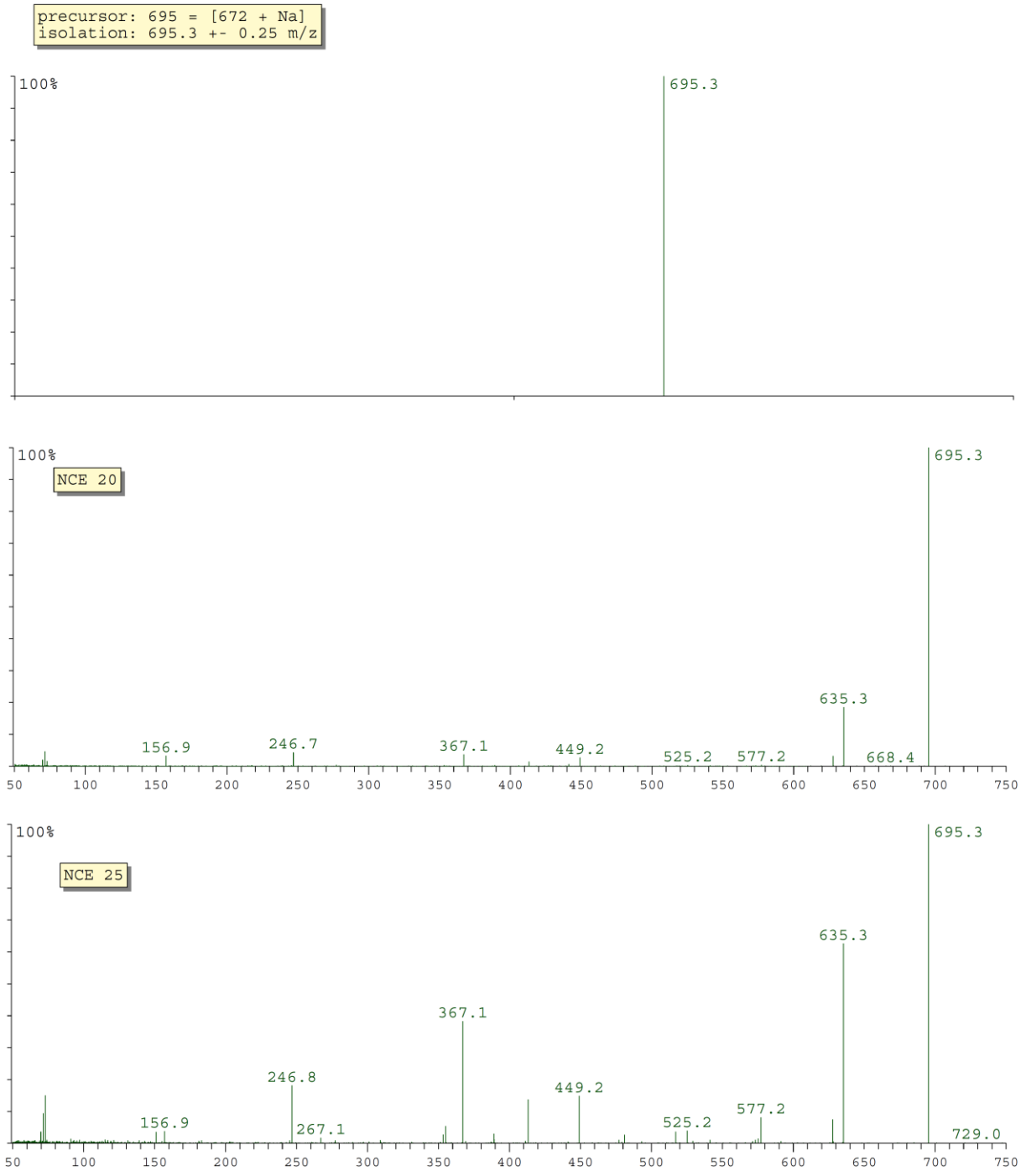
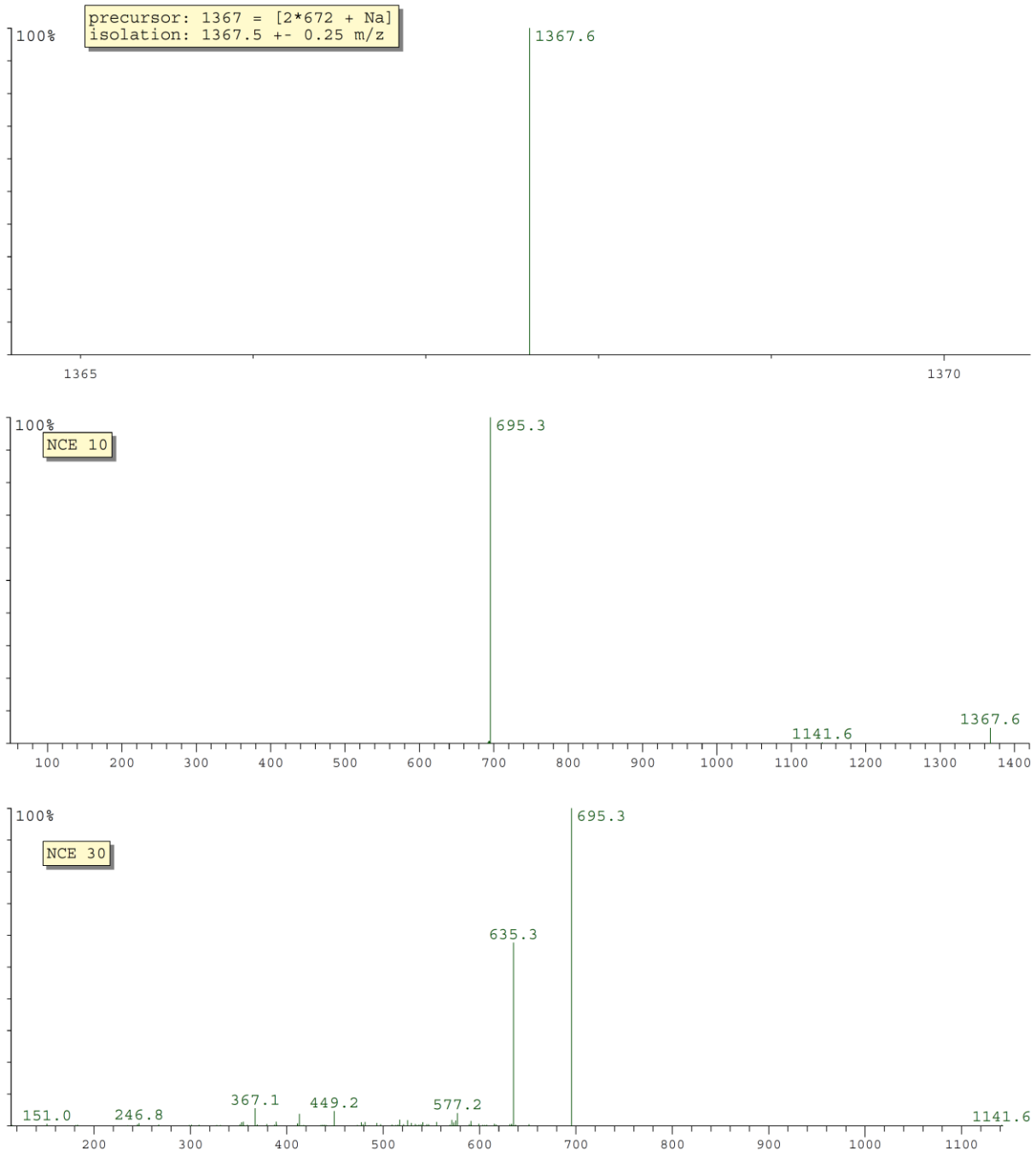
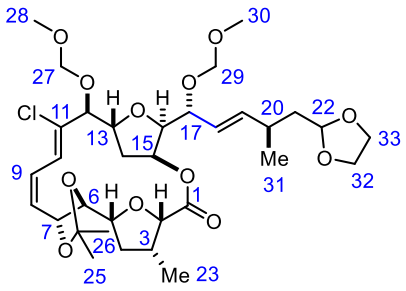


Figure S-4. MS-MS-Fragmentation of macrolactone **10aa** with *m/z* = 1367.6 $[2M+Na]^+$ as the precursor with increasing normalized collision energy (NCE).



After isolation of *m/z* = 1367.6 for the MS-MS-fragmentation analysis, a small NCE of 10 induces immediate fragmentation of the dimeric adduct [2M+Na] to the monomeric characteristic ion [M+Na]. Increasing the NCE to 30, the fragmentation pattern also matches with MS-MS-fragmentation analysis of [M+Na] in Figure S-3. These results clearly indicate that **10aa** is the monomeric species, although a dimeric adduct was observed in the ESI-MS experiment (see Figure S-2).

Analytical and spectral data of the C-2 epimeric macrolactone **S25** $[\alpha]_D^{20}$ = –7.6 (c = 0.17, $CHCl_3$).

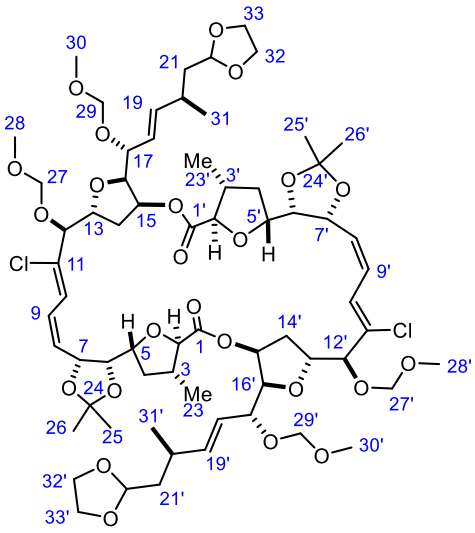


^{1}H NMR (500 MHz, $CDCl_3$,): *see Table S-17;* ^{13}C NMR (126 MHz, $CDCl_3$,): *see Table S-17;* IR (film): $\tilde{\nu}$ = 2957, 2926, 2854, 1732, 1666, 1458, 1379, 1260, 1216, 1152, 1098, 1031, 867, 800 cm^{-1}. MS (ESIpos) *m/z* (%): 695.3 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{33}H_{49}O_{12}ClNa$: 695.2805, found: 695.2809.

Table S-17. NMR data of epimerized macrolactone **S25**; numbering scheme as shown in the insert

atom n°	**^{1}H NMR** (500 MHz, $CDCl_3$)					**^{13}C NMR** (126 MHz, $CDCl_3$)	
	δ [ppm]	**m**	***J*** [Hz]	**COSY**	**NOESY**	**δ** [ppm]	**HMBC**
1	-	-	-	-	-	170.7	-
2	4.40	d	9.0	3	3, 5, 7	80.3	23
3	2.59–2.46	m	-	2, 6	2/6, 4a, 5, 23	39.6	23
4a	1.89	ddd	12.2, 5.6, 4.8	4b, (5)	3, 4b, 5, (7)	36.1	23
4b	1.02–0.98	m	-	3, 4a, 5	2/6, 4a		
5	4.06	ddd	13.2, 8.2, 4.7	2/6, 4b	2/6, 4a, 25, (3)	82.6	(7)
6	4.41	dd	8.0, 5.8	5, 7	3, 5, 7, 10	82.4	-
7	5.18	td	5.9, 2.4	2/6, 8	2/6, 8, 10, 24	75.8	(9)
8	5.86	ddd	10.9, 5.9, 1.0	7, 9	7, 9	129.9	-
9	6.44	td	10.9, 2.4	8, 10	8	125.4	-
10	6.78	dd	10.9, 1.0	9	6, 7, 13, (28/30)	124.5	-
11	-	-	-	-	-	134.1	12
12	4.19	d	9.5	13	14a, (28/30)	81.4	27ab
13	4.04	ddd	12.0, 9.6, 2.5	12, 14a	2/6, 10	83.8	(12)
14a	1.79	ddd	12.4, 11.6, 3.6	13, (15)	12, 14b, 15, 16	40.0	-
14b	1.70–1.64	m	-	14a	14a, 15		
15	5.78	t	3.7	16	14a, (14b), 16	74.5	-
16	4.21	m	-	15	14a, 15, 18, 19, 29ab, 28/30	84.3	(17)
17	4.23	m	-	18	15, 29ab	75.1	29ab
18	5.28	dd	15.5, 6.5	17, 19	16, 20	124.0	(20)
19	5.69	dd	15.5, 7.9	18, (20)	16, (31)	142.0	31
20	2.40	hept	7.0	19, 31	18, 31	33.2	31
21a	1.67	ddd	13.6, 7.8, 4.6	21b, 22	21b, 31	40.8	22
21b	1.58	m	-	21a, 22	21a, 31		
22	4.83	dd	5.7, 4.6	(21ab)	21b, (31), 32a, 33a	103.6	(21ab)
23	0.93	d	7.0	3	3, (14b)	14.5	-
24	-	-	-	-	-	108.9	25, 26
25	1.58	s	-	-	5, 26	28.8	-
26	1.47	s	-	-	7, 25	26.3	-

27a 27b	4.75 4.73	d d	6.7 6.7	27b 27a	12, 28 12, 28	95.5	28
28	3.39	s	-	-	27ab	56.0	27ab
29a 29b	4.70 4.68	d d	6.5 6.5	29b 29a	30 30	94.4	17, 30
30	3.39	s	-	-	29ab	55.4	29ab
31	1.00	d	6.8	20	(18), (19), 20, 21ab	20.5	-
32a 32b	3.96–3.89 3.85–3.78	m m	-	-	-	64.8	33ab
33a 33b	3.96–3.91 3.83–3.78	m m	-	-	-	64.8	32ab



Analytical and spectral data of lactide **S26aa.** $[\alpha]_D^{20}$ = –47.7 (c = 0.39, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$, major conformer): *see Table S-18*. ^{13}C NMR (151 MHz, $CDCl_3$, major conformer, broad signals indicate time-averaged chemical shift): *see Table S-18.* IR (film): $\tilde{\nu}$ = 2956, 2927, 2855, 1740, 1462, 1379, 1259, 1214, 1150, 1099, 1029, 835 cm^{-1}. MS (ESIpos) *m/z* (%): 1367.6 (100 (M+Na)) *see Figure S-5 – S-7;* HRMS (ESIpos): *m/z* calcd for $C_{66}H_{98}O_{24}Cl_2Na$: 1367.5717, found: 1367.5728.

Table S-18. NMR data of cyclic dimer **S26aa**; numbering scheme as shown in the insert

atom n°	^{1}H NMR (600 MHz, $CDCl_3$)					^{13}C NMR (151 MHz, $CDCl_3$)	
	δ [ppm]	m	*J* [Hz]	COSY	NOESY	δ [ppm]	HMBC
1/1’	-	-	-	-	-	171.6	-
2/2’	4.07	d	6.2	3	(23)	83.0	23
3/3’	2.22	m	-	2, (4ab), 23	(4b)	39.6	23
4a/4a’ 4b/4b’	1.96 1.17	ddd m	13.4, 7.6, 5.8 -	3, 4b, 5 (3), 4a, 5	- (3)	37.0	2, 23
5/5’	4.14	m	-	4ab	-	79.3	2, (4b), (7)
6/6’	4.12	m	-	7	(25)	81.3	(4b)
7/7’	4.89	ddd	8.6, 6.0, 0.9	6	10, (25)	74.1	9
8/8’	5.66	ddd	11.4, 8.6, 0.9	7, 9	9	129.7	(6)
9/9’	6.50	td	11.3, 0.9	8, 10	8, (10)	125.8	(7)
10/10’	6.98	d	11.2	9	7	122.5	-
11/11’	-	-	-	-	-	134.1	9
12/12’	4.13	m	-	-	(26)	81.6	27ab
13/13’	4.16	m	-	14ab	-	80.8	(12)

14a/14a’ 14b/14b’	2.13 1.91	ddd dd	14.2, 9.7, 4.1 14.2, 5.6	13, 14b, 15 13, 14a	14b 14a	36.8	-
15/15’	5.33	dd	4.2, 3.1	14a, 16	(16)	75.0	14b, 16
16/16’	3.98	dd	8.5, 2.9	15, 17	(15), (18)	83.6	17
17/17‘	4.18	ddd	8.6, 7.5, 0.9	16, 18	16, (29ab)	75.7	16, 18, 19, 29ab
18/18‘	5.26	ddd	15.5, 7.5, 0.9	17, 19	(31)	124.1	17, 20
19/19’	5.64	ddd	15.5, 8.2, 0.6	18, 20	(31)	141.4	17, 20, 21ab, 31
20/20‘	2.38	hept	7.0	19, 21ab, 31	22, 31	33.2	18, 19, 21ab, 22, 31
21a/21a‘ 21b/21b’	1.65 1.59	ddd ddd	13.8, 8.1, 4.6 13.8, 6.2, 5.7	20, 21b, 22 20, 21a, 22	(31) (31)	40.7	19, (20), 22, 31
22/22‘	4.78	dd	5.6, 4.6	21ab	20, 31, 32a, 33a	103.5	21ab, 32ab, 33ab
23/23’	1.18	d	6.8	3	2	19.7	(2)
24/24’	-	-	-	-	-	110.0	25, 26
25/25’	1.54	s	-	-	(26)	27.8	-
26/26‘	1.39	s	-	-	(25)	25.4	-
27a/27a’ 27b/27b’	4.67 4.66	d d	6.7 6.7	- -	(12) (12)	94.5	12, 28
28/28’	3.43	s	-	-	27ab	55.8	27ab
29a/29a’ 29b/29b‘	4.65 4.64	d d	6.5 6.5	29b 29a	30 30	94.4	17, 30
30/30‘	3.36	s	-	-	29ab	55.5	29ab
31/31‘	0.99	d	6.8	20	(18), (19), 20, 22	21.0	19, (20), 21ab
32a/32a‘ 32b/32b‘	3.96–3.90 3.84–3.79	m m	-	32b, 33b 32a, 33a	-	64.8	33ab
33a/33a‘ 33b/33b‘	3.96–3.90 3.84–3.79	m m	-	32b, 33b 32a, 33a	-	64.8	32ab

Figure S-5: MS (ESIpos) analysis of lactide **S26aa**. *m/z* = 1367.6 $[M+Na]^+$, *m/z* = 695.3 $[M+2Na]^{2+}$.

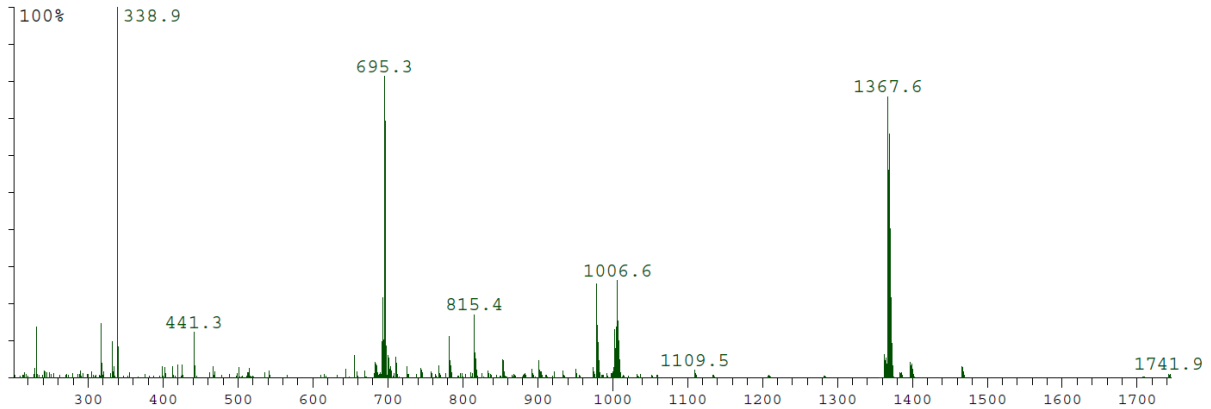


Figure S-6. MS-MS-Fragmentation of lactide **S26aa** with *m/z* = 1367.6 $[M+Na]^+$ with increasing normalized collision energy (NCE).

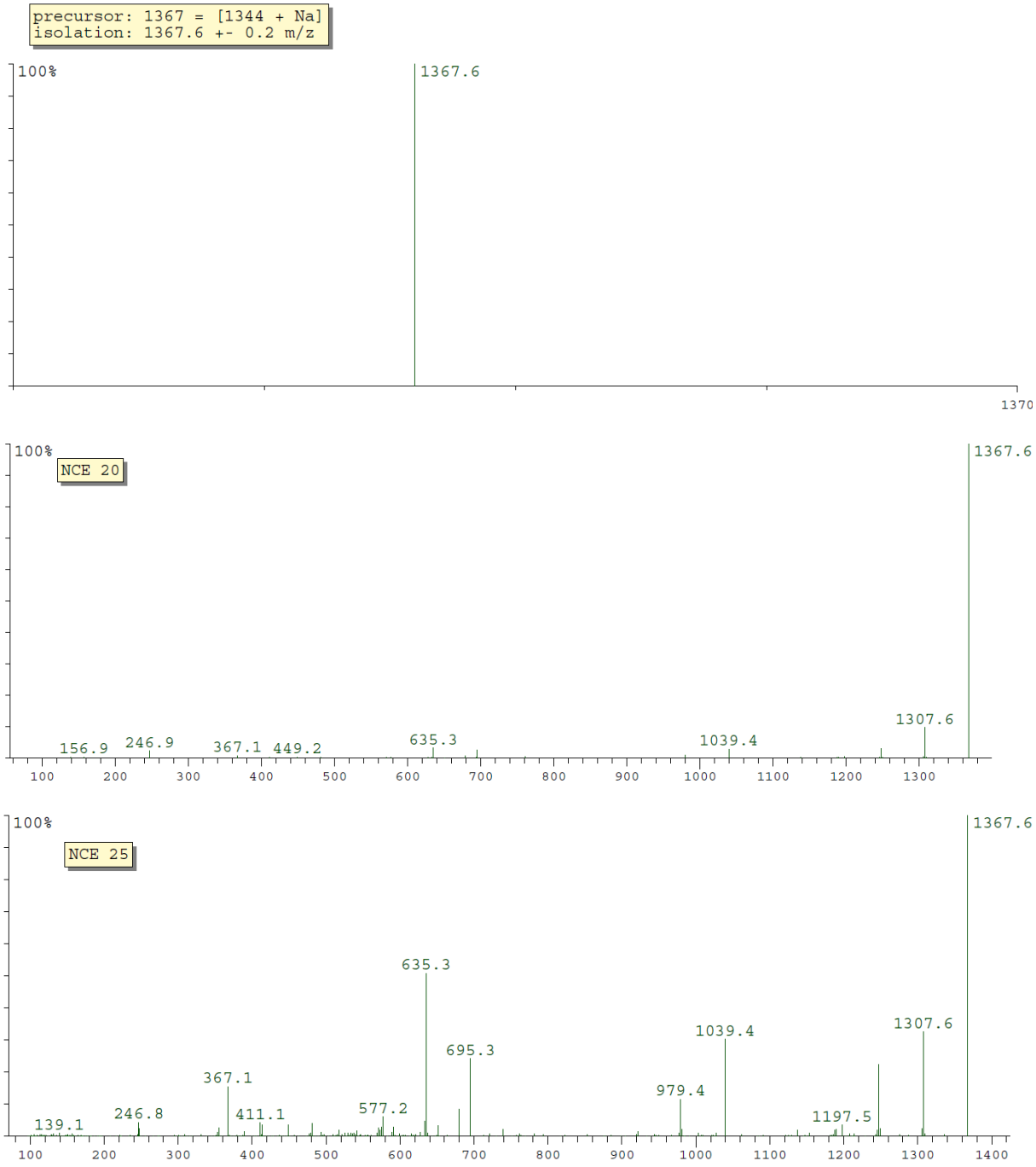
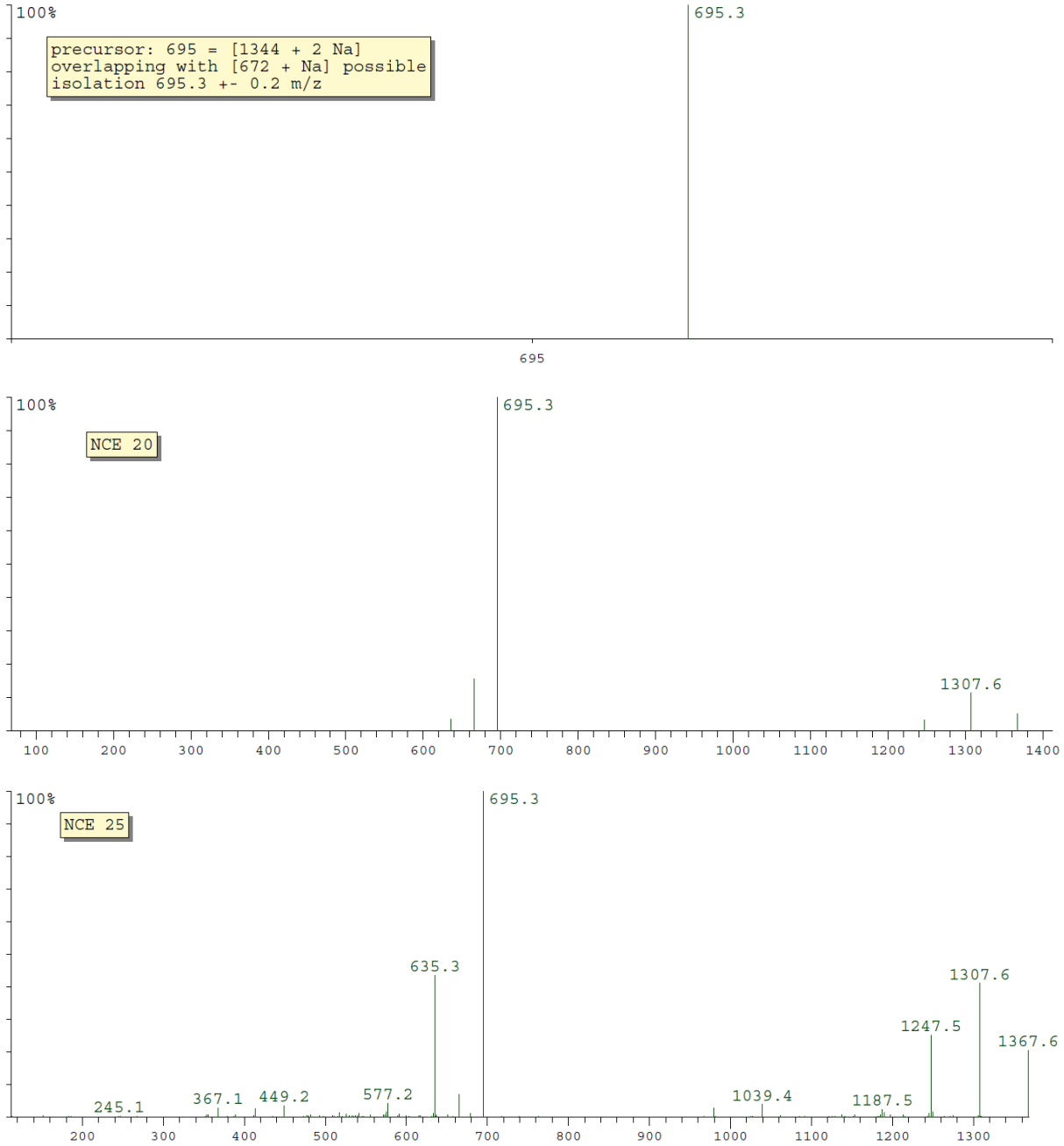
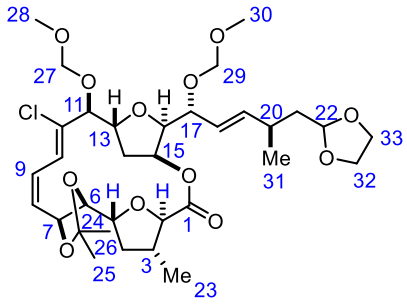


Figure S-7. MS-MS-Fragmentation of lactide **S26aa** with *m/z* = 695.3 $[M+2Na]^{2+}$ with increasing normalized collision energy (NCE).



After isolation of *m/z* = 695.3 for the MS-MS-fragmentation analysis, a NCE of 20 induces fragmentation with higher mass *m/z* = 1307.6 in the area of $[M+Na]^+$. Increasing the NCE to 30, the fragmentation pattern at higher molecular weight *m/z* > 1000 shows the characteristic ion $[M+Na]^+$ of **S26aa** and its fragmentation products from MS-MS-fragmentation analysis in Figure S-6. These results clearly indicate that **S26aa** is the lactide, although a double charged adduct $[M+2Na]^{2+}$ was observed in the ESI-MS experiment (see Figure S-5).

Macrolactone 10ba. According to General Procedure using *seco*-acid **8ba** (13.7 mg, 20.3 µmol).



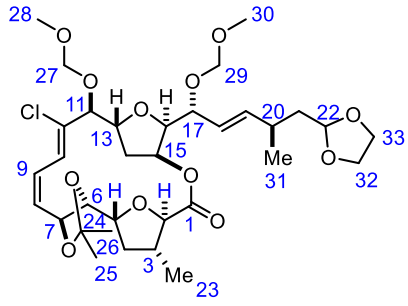
Colourless solid (8.3 mg, 61%). $[\alpha]_D^{20}$ = +0.8 (c = 0.83, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): *see Table S-19*. ^{13}C NMR (150 MHz, $CDCl_3$): *see Table S-19*. IR (film): $\tilde{\nu}$ = 2958, 2929, 2892, 1745, 1456, 1371, 1256, 1214, 1152, 1128, 1096, 1063, 1032, 972, 921 cm^{-1}. MS (ESIpos) *m/z* (%): 695.3 (100 (M+Na)); HRMS (ESIpos): *m/z* calcd for $C_{33}H_{49}O_{12}ClNa$ [M+Na$^+$]: 695.2805, found: 695.2805.

Table S-19. NMR data of the macrolactone **10ba**; numbering scheme as shown in the insert

atom n°	^{1}H NMR (600 MHz, $CDCl_3$)					^{13}C NMR (151 MHz, $CDCl_3$)	
	δ [ppm]	m	*J* [Hz]	COSY	NOESY	δ [ppm]	HMBC
1	-	-	-	-	-	170.9	3, 15
2	3.91	d	9.0	3	3, 4b, 22, 23	85.8	3, 4a, 23
3	2.64	ddp	11.4, 9.0, 6.6	2, 4ab, 23	2, 4a, 5, 23	37.7	2, 4ab, 23
4a	2.18	ddd	12.0, 6.6, 5.6	3, 5, 4b	3, 5, 4b, 6	36.7	5, 23
4b	1.89	td	11.8, 10.4	3, 5, 4a	2, 4a, 6, 23		
5	4.16	ddd	10.4, 5.5, 1.5	4ab	3, 4a, 6, 7, 10, 13	78.0	2, 4b, 6, 7
6	3.68	dd	8.2, 1.4	7	4ab, 5, 7, 8, 21	80.4	4b, 5, 7, 8
7	5.09	ddd	8.3, 7.3, 1.6	8, 6	5, 6, 8, 10, 22	74.7	6, 8, 9
8	5.75	ddd	11.1, 7.4, 0.8	9, 7	6, 7, 9	133.7	6, 10
9	6.46	td	10.7, 1.6	10, 8	8	125.4	7
10	6.37	dt	10.4, 0.8	9	5, 7, 12, 13, 14a	121.4	8, 12
11	-	-	-	-	-	136.1	9, 10, 12
12	4.20	d	8.0	13	10, 14b, 27ab, 28	78.8	10, 13, 14b, 27ab
13	4.43	ddd	11.5, 7.9, 3.3	12, 14ab	5, 13, 14a	80.8	12, 14b, 15
14a	2.14	ddd	12.7, 3.3, 1.3	13, 14b	10, 13, 14b, 15	38.4	12
14b	1.77	ddd	12.7, 11.9, 2.9	13, 14a, 15	12, 14a, 15, 16		
15	5.48	td	3.0, 0.9	14b, 16	14ab, 16, 18	76.2	2, 14a, 16, 17
16	4.14	m	-	15	14b, 15, 18, 19, 30	82.8	14a, 15, 17, 18
17	4.13	m	-	18	19, 29ab	75.3	15, 16, 18, 19, 29ab
18	5.25	ddd	15.5, 7.1, 0.9	17, 19	15, 16, 20, 31	123.5	17, 20
19	5.55	dd	15.4, 8.1	18, 20	16, 17, 20, 21a, 31	142.1	17, 20, 21ab, 31
20	2.40	m	-	19, 21ab, 31	18, 19, 22, 31	33.1	18, 19, 21ab, 22, 31
21a	1.64	ddd	13.9, 8.0, 4.6	20, 21b, 22	19, 31	40.6	19, 20, 22, 31
21b	1.59	dt	13.8, 6.0	20, 21a, 22	31		
22	4.79	dd	5.6, 4.6	21ab	20, 31, 32b, 33b	103.3	20, 21ab, 32ab, 33ab
23	1.17	d	6.6	3	2, 3, 4b	15.8	2, 4b

24	-	-	-	-	-	109.4	25, 26
25	1.43	s	-	-	6	27.1	26
26	1.39	s	-	-	2, 7	26.1	25
27a	5.05	d	6.9	27b	12, 28	97.5	12, 28
27b	4.74	d	6.8	27a	12, 28		
28	3.49	s	-	-	12, 27ab	56.6	27ab
29a	4.69	d	6.7	29b	17, 30	93.2	17, 30
29b	4.60	d	6.7	29a	17, 30		
30	3.37	s	-	-	16, 27b, 29ab	55.1	29ab
31	0.98	d	6.8	20	18, 19, 20, 21ab, 22	21.0	19, 20, 21ab
32a 32b	3.96–3.90 3.84–3.78	AA'm BB'm	-	-	-	64.7	22, 33ab
33a 33b	3.96–3.90 3.84–3.78	AA'm BB'm	-	-	-	64.7	22, 32ab

Macrolactone 10ca. According to General Procedure using *seco*-acid **8ca** (15.3 mg, 22.1 µmol).



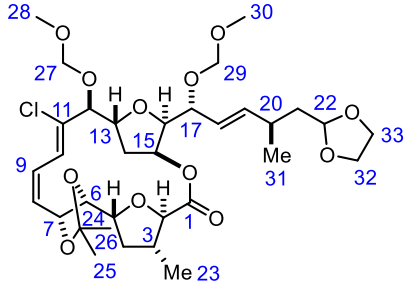
Colorless oil (2.1 mg, 14%). $[\alpha]_D^{20}$ = −24.8 (c = 0.21, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$, major rotamer): *see Table S-20*. ^{13}C NMR (151 MHz, $CDCl_3$, major rotamer): *see Table S-20*. IR (film): $\tilde{\nu}$ = 2958, 2929, 2854, 1739, 1651, 1458, 1380, 1221, 1152, 1100, 1032, 973, 920, 875 cm^{-1}. MS (ESIpos) *m/z* (%): 695.3 (100 (M+Na)); HRMS (ESIpos): *m/z* calcd for $C_{33}H_{49}O_{12}ClNa$ [M+Na$^+$]: 695.2805, found: 695.2810.

Table S-20. NMR data of the macrolactone **10ca**; numbering scheme as shown in the insert

atom n°	**^{1}H NMR** (600 MHz, $CDCl_3$)					**^{13}C NMR** (151 MHz, $CDCl_3$)	
	δ [ppm]	**m**	***J*** [Hz]	**COSY**	**NOESY**	**δ** [ppm]	**HMBC**
1	-	-	-	-	-	170.1	2, 3
2	4.05	d	5.2	3	3, 15, 23	87.1	3, 23
3	2.56	m	-	2, 23	2, 4b, 23	35.7	4ab, 23
4a 4b	2.54 1.73	m td	- 11.8, 10.4	4b, 5 4a, 5	4b, 5, 23 3, 4a, 6, 23	39.1	2, 3, 6, 23
5	4.26	qd	7.7, 2.5	4ab, 6	4a, 8, 10, 25	78.6	2, 3, 4b, 6, 7
6	3.94	m	-	5, 7	4b, 7, 23, 26	82.5	4ab, 7, 8, 9, 23
7	4.86	ddd	6.4, 5.1, 1.3	6, 8	6, 8, 10, 26	76.7	5, 6, 8, 9
8	5.61	ddd	11.4, 7.1, 1.0	7, 9	5, 7, 9, 25	126.4	-
9	6.53	td	11.4, 1.2	8, 10	8	126.7	7
10	7.22	br	-	9	5, 7, 12, 13, 25	124.3	8, 9, 12
11	-	-	-	-	-	134.6	9, 12

12	4.23	d	6.8	13	10, 14a, 27ab, 28	80.3	27ab
13	4.07	m	-	12, 14ab	10, 14b	83.8	12
14a	1.92	m	-	13, 14b, 15	12, 15	36.9	-
14b	1.87	m	-	13, 14a, 15	13		
15	5.32	m	-	14ab	2, 14a, 16, 17	75.3	2, 16
16	4.20	d	4.6	-	15, 18	82.9	17
17	4.19	d	5.7	18	15, 18, 19, 29ab, 30	74.6	16, 18, 19, 29ab
18	5.30	d br	-	17, 19	16, 17, 20, 31	124.0	20
19	5.62	dd	15.6, 8.1	18, 20	17, 20, 21a, 31, 21a, 22	141.7	17, 20, 21ab, 31
20	2.39	m	-	19, 21ab, 31	18, 19, 22, 21b, 31	33.1	18, 19, 21ab, 22, 31
21a	1.67–1.58	m	-	20, 21b, 22	19, 22, 31	40.5	19, 20, 22, 31
21b	1.67–1.58	m	-	20, 21a, 22	20, 31		
22	4.78	dd	5.7, 4.5	21ab	20, 31, 32b, 33b	103.3	19, 20, 21a, 31, 32b, 33b
23	1.14	d	6.5	3	2, 3, 4ab, 6	18.9	2, 3, 4ab
24	-	-	-	-	-	108.1	6, 7, 25, 26
25	1.53	s	-	-	5, 8, 10, 26	28.2	26
26	1.37	s	-	-	6, 7, 25	25.7	25
27a	4.72	d	6.7	27b	12, 28	95.1	12, 28
27b	4.67	d	6.8	27a	12, 28		
28	3.38	s	-	-	12, 27ab	55.7	27ab
29a	4.71	d	6.6	29b	17, 19, 30	93.2	17, 30
29b	4.60	d	6.6	29a	17, 30		
30	3.40	s	-	-	17, 29ab	55.1	17, 29ab
31	0.98	d	6.8	20	18, 19, 20, 21ab, 22	20.9	19, 20, 21ab
32a	3.97–3.90	AA'm	-	-	-	64.7	22, 33ab
32b	3.84–3.78	BB'm					
33a	3.97–3.90	AA'm	-	-	-	64.7	22, 32ab
33b	3.84–3.78	BB'm					

Macrolactone 10da. According to General Procedure using *seco*-acid **8da** (13.5 mg, 19.5 µmol).



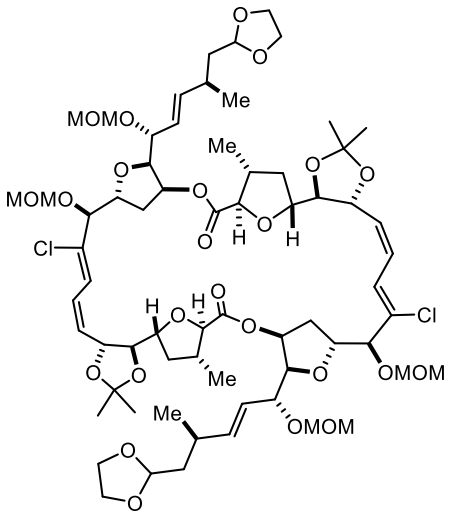
Lactone **10da** (1.5 mg, 11%) as a colourless oil and lactide **S26da** (1.2 mg, 9%) as a yellow oil. Analytical and spectral data for lactone **10da**: $[\alpha]_D^{20}$ = +46.7 (c = 0.15, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): *see Table S-21*. ^{13}C NMR (151 MHz, $CDCl_3$): *see Table S-21*. IR (film): $\tilde{\nu}$ = 2918, 2850, 1742, 1252, 1153, 1141, 1098, 1068, 1029 cm^{-1}. MS (ESIpos) *m/z* (%): 695.3 (100 (M+Na)); HRMS (ESIpos): *m/z* calcd for $C_{33}H_{49}O_{12}ClNa$ [M+Na$^+$]: 695.2805, found: 695.2801.

Table S-21. NMR data of the macrolactone **10da**; numbering scheme as shown in the insert

atom n°	^{1}H NMR (600 MHz, $CDCl_3$)					^{13}C NMR (151 MHz, $CDCl_3$)	
	δ [ppm]	m	*J* [Hz]	COSY	NOESY	δ [ppm]	HMBC
1	-	-	-	-	-	170.4	3
2	3.99	d	5.3	3	3, 23	85.9	3, 4a, 23
3	2.61	ddqd	7.3, 7.1, 6.9, 5.3	2, 4ab, 23	2, 4a, 23	35.7	4ab, 23
4a	2.43	ddd	12.5, 7.3, 7.1	3, 4b, 5	3, 4b, 5	39.8	2, 3, 6, 23
4b	1.75	ddd	12.5, 8.8, 7.1	3, 4a, 5	4a, 5, 23		
5	4.04	ddd	8.8, 7.1, 4.5	4ab, 6	4ab, 6, 7, 10	80.1	2, 4b, 6, 7
6	3.81	dd	8.6, 4.5	5, 7	5, 8, 21	81.3	4b, 7
7	4.60	ddd	8.6, 8.5, 1.4	6, 8	5, 10, 22	76.8	5, 6, 9
8	5.67	ddd	11.0 ,8.5, 1,1	7, 9	6, 9	132.	6, 10
9	6.45	td	11.0, 1.4	8, 10	8	125.8	7, 10
10	6.64	dd	11.0, 1.1	9	5, 7, 13	122.1	8, 9, 12
11	-	-	-	-	-	134.5	9, 10, 12
12	4.14	dt	9.2, 0.9	13	14a, 27ab	81.8	10, 13, 27ab
13	4.08	ddd	12.0, 9.2, 3.1	12, 14a	10, 14b	83.0	12, 15
14a	1.82	ddd	13.0, 12.0, 3.1	13, 14b, 15	12, 14b, 15, 16, 17	38.2	12
14b	1.73	ddd	13.0, 3.1, 1.2	14a	13, 14a, 15		
15	5.41	ddd	3.3, 3,1, 1.2	14a, 16	14ab, 16, 17, 18	75.2	14b
16	4.18	d	3.30	15	14a, 15, 18, 19, 29ab, 30	84.1	17, 18
17	4.19	d	5.9	18	14a, 15, 18, 19, 29ab, 30	75.6	16, 18, 19, 29a
18	5.25	dddd	15.4, 5.9, 2.3, 1.1	17, 19	15, 16, 17, 20	123.7	20
19	5.60	dd	15.4, 8.0	18, 20	16, 17, 31	141.9	17, 20, 21ab, 31
20	2.38	dqdd	8.0, 6.8, 5.9, 4.5	19, 21ab, 31	18, 21b, 31	33.0	18, 19, 21ab, 22, 31
21a	1.63	dd	13.8, 4.5	20, 21b, 22	31	40.6	19, 20, 22, 31
21b	1.59	dt	13.8, 5.9	20, 21a, 22	20, 31		
22	4.78	dd	5.9, 4.5	21ab	21ab	103.2	20, 21ab, 32ab, 33ab
23	1.14	d	6.9	3	2, 3, 4b	17.8	4b
24	-	-	-	-	-	110.0	25, 26
25	1.44	s	-	-	6	27.0	26
26	1.44	s	-	-	7	26.9	25
27a	4.71	dd	6.7, 0.9	-	12, 28	95.2	12, 28
27b	4.70	dd	6.7, 0.9	-	12, 28		
28	3.37	s	-	-	27ab	55.8	27ab

29a	4.73	d	6.7	29b	16, 17, 30	93.6	17, 30
29b	4.69	d	6.7	29a	16, 17, 30		
30	3.43	s	-	-	16, 17, 29ab	55.3	29ab
31	0.96	d	6.8	20	19, 20, 21ab	20.9	19, 20, 21ab
32a 32b	3.96–3.90 3.84–3.78	AA‘ m BB‘ m	-	-	-	64.7	33ab
33a 33b	3.96–3.90 3.84–3.78	AA‘ m BB‘ m	-	-	-	64.7	32ab

Analytical and spectral data for lactide **S26da**. $[\alpha]_D^{20}$ = +12.5 (c = 0.12, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$):



δ = 6.73 (d, *J* = 10.8 Hz, 1H), 6.57 (td, *J* = 11.0, 1.0 Hz, 1H), 5.64–5.57 (m, 2H), 5.27 (ddd, *J* = 15.5, 8.3, 1.0 Hz, 1H), 5.23 (td, *J* = 3.3, 2.4, 0.5 Hz, 1H), 4.78 (dd, *J* = 5.6, 4.5 Hz, 1H), 4.69–4.60 (m, 4H), 4.48 (td, *J* = 8.8, 1.0 Hz, 1H), 4.40–4.31 (m, 2H), 4.15 (td, *J* = 8.2, 0.8 Hz, 1H), 4.11 (ddd, *J* = 9.1, 6.1, 4.5 Hz, 1H), 3.99 (d, *J* = 8.0 Hz, 1H), 3.96–3.88 (m, 4H), 3.84–3.77 (m, 2H), 3.40 (s, 3H), 3.36 (s, 3H), 2.41–2.28 (m, 2H), 2.16–2.08 (m, 1H), 2.11–2.05 (m, 1H), 2.04–1.97 (m, 1H), 1.72 (dt, *J* = 12.1, 9.5 Hz, 1H), 1.68–1.55 (m, 2H), 1.44 (s, 3H), 1.43 (s, 3H), 1.26 (d, *J* = 7.3 Hz, 3H), 0.94 (d, *J* = 6.8 Hz, 3H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$): δ = 171.1, 141.6, 134.4, 130.4, 127.3, 124.0, 121.4, 109.9, 103.3, 94.9, 93.8, 83.1, 82.6, 81.8, 80.0, 80.0, 79.3, 76.0, 75.2, 74.9, 64.7, 64.7, 55.8, 55.2, 40.5, 39.4, 35.5, 34.7, 33.1, 27.1, 26.9, 20.9, 18.0 ppm. IR (film): $\tilde{\nu}$ = 2957, 2920, 2851, 1738, 1465, 1372, 1252, 1215, 1054, 843, 795 cm^{-1}. MS (ESIpos) *m/z* (%): 1367.3 (100 (M+Na)); HRMS (ESIpos): *m/z* calcd for $C_{66}H_{98}O_{24}Cl_2Na$ [M+Na$^+$]: 1367.5717, found: 1367.5717.

Macrolactone 10ab. According to General Procedure using *seco*-acid **8ab** (23.7 mg, 34.. µmol). Pale yellow oil (7.8 mg, 34%). $[\alpha]_D^{20}$ = −38.8 (c = 0.17, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): *see Table S-22*. ^{13}C NMR (151 MHz, $CDCl_3$): *see Table S-22*. IR (film): $\tilde{\nu}$ = 2926, 1741, 1726, 1260, 1217, 1163, 1095, 1028, 801 cm^{-1}. MS (ESIpos) *m/z* (%): 695.3 (100 (M+Na)); HRMS (ESIpos): *m/z* calcd for $C_{33}H_{49}O_{12}ClNa$ [M+Na$^+$]: 695.2805, found: 695.2802.

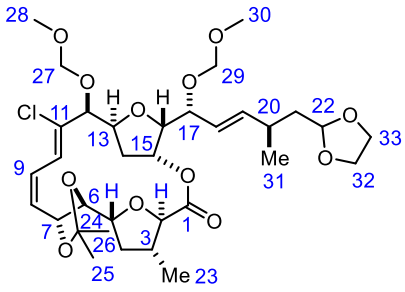


Table S-22. NMR data of the macrolactone **10ab**; numbering scheme as shown in the insert

atom n°	^{1}H NMR (600 MHz, $CDCl_3$)					^{13}C NMR (151 MHz, $CDCl_3$)	
	δ [ppm]	m	*J* [Hz]	COSY	NOESY	δ [ppm]	HMBC
1	-	-	-	-	-	171.2	2, 3
2	3.98	d	6.4	3	3, 4b, 23, 25	84.2	3, 4a, 23
3	2.64	ddqd	8.4, 7.3, 6.8, 6.4	2, 4ab, 23	2, 4a, 5, 23	36.3	2, 4a, 23
4a	2.00	dt	12.3, 7.3	3, 4b, 5	3, 4b, 5	37.4	2, 6, 23
4b	1.40	ddd	12.3, 8.9, 8.4	3, 4a, 5	2, 4a, 6, 23		
5	3.88	ddd	8.9, 7.3, 4.4	4ab, 6	3, 4a, 6, 8, 10, 13, 25	78.2	2, 4b, 6, 7
6	4.06	dd	6.5, 4.4	5, 7	5, 4b, 7, 8, 26	80.9	4b, 7
7	4.89	ddd	6.5, 4.6, 1.5	6, 8	6, 8, 26	76.8	5, 6, 9
8	5.41	ddd	11.9, 4.6, 1,2	7, 9	5, 6, 7	124.3	7
9	6.46	ddd	11.9, 10.4, 1.5	8, 10	-	126.3	7
10	7.38	dt	10.4, 1.2	9	5, 12, 13, 25	124.4	8
11	-	-	-	-	-	133.7	9, 10
12	4.83	dd	3.2, 1.2	13	10, 13, 27ab, 28	73.4	10, 27ab
13	4.19	ddd	12.2, 3.2, 0.3	12, 14ab	5, 10, 12, 14b, 25	83.9	12
14a	2.03	ddd	13.2, 12.2, 3.1	13, 14b, 15	14b, 15, 16	33.3	12
14b	1.72	ddd	13.2, 2.4, 0.5	13, 14a	13, 14a, 15, 17		
15	5.48	dd	3.5, 3,1	14a, 16	14ab, 16, 17, 30	75.4	13, 14b, 16
16	3.99	dd	3.5, 9.3	15, 17	14a, 15, 18	82.4	17
17	4.19	ddd	9.3, 7.8, 0.5	16, 18	14b, 15, 18, 19, 25, 29ab	74.2	16, 19, 29ab
18	5.36	ddd	15.5, 7.8, 1.1	17, 19	16, 17, 20, 31	126.4	16, 20
19	5.62	ddd	15.5, 7.7, 0.8	18, 20	17, 20, 21a, 31	140.8	17, 20, 21ab, 31
20	2.45	ddqd	8.0, 7.7, 6.8, 6.1	19, 21ab, 31	18, 19, 21b, 31	32.8	18, 19, 21ab, 22, 31
21a	1.71	ddd	13.8, 8.0, 4.5	20, 21b, 22	19, 22, 31	40.7	19, 20, 22, 31
21b	1.62	dt	13.8, 6.1	20, 21a, 22	20, 22, 31		
22	4.85	dd	6.1, 4.5	21ab	21ab, 31, 32ab, 33ab	103.4	20, 21ab, 32ab, 33ab
23	1.14	d	6.9	3	2, 3, 4b	17.8	4b
24	-	-	-	-	-	109.6	6, 25, 26
25	1.66	s	-	-	3, 5, 10, 13, 17, 26	26.5	26
26	1.42	s	-	-	6, 7, 25	25.3	25
27a	4.74	d	6.5	-	12, 28	95.6	12, 28
27b	4.69	d	6.5	-	12, 28		
28	3.40	s	-	-	12, 27ab	55.6	27ab
29a	4.66	d	6.6	29b	17, 30	93.5	17, 30
29b	4.43	d	6.6	29a	17, 30		

30	3.23	s	-	-	15, 17, 23, 32a, 33a, 29ab	55.5	29ab
31	1.06	d	6.8	20	18, 19, 20, 21ab, 22	20.8	19, 20, 21ab
32a 32b	3.97–3.92 3.85–3.78	m m	-	-	-	64.7	33ab
33a 33b	3.97–3.92 3.85–3.78	m m	-	-	-	64.7	32ab

Macrolactone 10bb. According to General Procedure using *seco*-acid **8bb** (15.6 mg, 23.1 µmol). Colourless oil (11.2 mg, 72%). $[\alpha]_D^{20}$ = −136.9 (c = 1.12, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) *see Table S-23*. ^{13}C NMR (151 MHz, $CDCl_3$) *see Table S-23.* IR (film): $\tilde{\nu}$ = 2985, 2960, 2931, 2879, 1737, 1456, 1380, 1214, 1181, 1151, 1125, 1079, 1051, 972, 923, 884 cm^{-1}. MS (ESIpos) *m/z* (%): 1367 (100 (2M+Na)); HRMS (ESIpos): *m/z* calcd for $C_{33}H_{49}O_{12}ClNa$ [M+Na$^+$]: 695.2805, found: 695.2805.

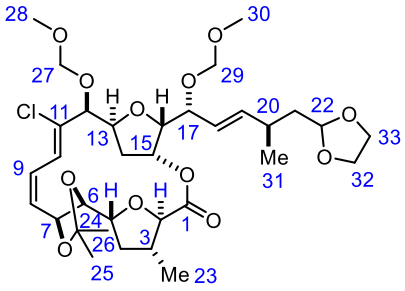
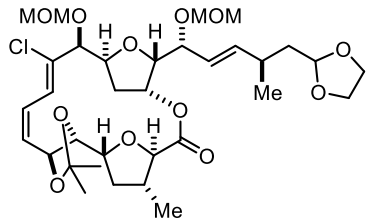


Table S-23. NMR data of the macrolactone **10bb**; numbering scheme as shown in the insert

atom n°	^{1}H NMR (600 MHz, $CDCl_3$)					^{13}C NMR (151 MHz, $CDCl_3$)	
	δ [ppm]	m	*J* [Hz]	COSY	NOESY	δ [ppm]	HMBC
1	-	-	-	-	-	170.6	2, 3, 15, 23
2	4.13	d	2.4	3	3, 23, 30	84.6	4ab, 23
3	2.74	dqdd	8.4, 7.1, 4.5, 2.3	4a, 23	2, 4a, 23	33.4	4ab, 23
4a 4b	2.38 1.75	dt ddd	12.3, 8.5 12.3, 7.5, 4.4	3, 4b, 5 4a, 5	3, 4b, 5 4a, 6, 23	35.5	2, 5, 23
5	3.75	ddd	8.7, 7.5, 1.6	4ab	4a, 6, 7, 9, 10	75.7	2, 4ab, 6, 7
6	3.62	dd	8.8, 1.6	7	4b, 5, 7, 8, 21	80.4	4ab, 5, 7, 8
7	4.95	td	9.0, 1.0	6, 8	5, 6, 9, 10, 22	73.2	6, 8, 9, 10
8	5.54	dd	9.7, 9.0	7, 9	6, 9, 10	130.5	6, 10
9	6.48	td	9.7, 0.9	8, 10	5, 7, 8, 12, 13, 14b	127.6	7
10	6.46	dd	9.7, 1.5	9	5, 7, 8, 12, 13, 14b	121.0	8, 12
11	-	-	-	-	-	136.1	8, 9, 12
12	4.74	d	2.1	13	9, 10, 13	73.5	10, 13, 14a, 27ab
13	4.51	ddd	11.9, 3.7, 2.7	12, 14ab	9, 10, 12, 14b, 15, 17	81.3	12, 14ab, 15
14a 14b	2.13 1.73	ddd ddd	13.4, 11.9, 3.1 13.8, 8.1, 4.5	13, 14b, 15 13, 14a	14b, 15, 16 9, 10, 13, 14ab, 15	32.4	12
15	5.39	t	3.2	14a, 16	13, 14ab, 16, 17, 29a, 30	75.3	14b, 16, 17
16	4.00	dd	8.9, 3.2	15, 17	14a, 15, 28	82.6	14b, 17, 18
17	4.26	ddd	8.6, 7.8, 0.7	16, 18	13, 15, 19, 29ab, 30	74.0	16, 18, 19, 29ab

18	5.38	ddd	15.5, 7.9, 1.1	17, 19	20, 22, 29a, 30, 31	126.1	16, 17, 20
19	5.74	ddd	15.6, 7.7, 0.7	18, 20	17, 20, 21a, 22, 29a, 31	141.2	17, 20, 21ab, 31
20	2.47	ddqd	8.6, 7.7, 6.8, 5.9	19, 21ab, 31	18, 19, 22, 31	32.9	18, 19, 21ab, 22, 31
21a 21b	1.73 1.64	dd dt	13.4, 13.7 13.8, 5.9	20, 21b, 22 20, 21a, 22	19, 22, 31 22, 31	40.6	19, 20, 22, 31
22	4.86	dd	5.9, 4.4	21ab	18, 19, 20, 21ab, 32b, 33b	103.4	20, 21ab, 32ab, 33ab
23	1.13	d	7.1	3	2, 3, 4b, 25	19.4	2, 3, 4ab
24	-	-	-	-	-	108.9	25, 26
25	1.44	s	-	-	6	27.2	26
26	1.44	s	-	-	7, 23	26.4	25
27a	4.82	d	6.6	27b	28	96.9	12, 28
27b	4.75	d	6.6	27a	28		
28	3.44	s	-	-	16, 27ab	56.0	27ab
29a	4.71	d	6.8	29b	15, 17, 18, 19, 30	93.2	17, 30
29b	4.44	d	6.8	29a	17, 30		
30	3.25	s	-	-	2, 15, 17, 18, 29ab	55.5	29ab
31	1.07	d	6.8	20	18, 19, 20, 21ab, 22	21.0	19, 20, 21ab
32a 32b	3.97–3.92 3.86–3.78	AA‘ m BB‘ m	-	-	- 22	64.7	33ab
33a 33b	3.97–3.92 3.86–3.78	AA‘ m BB‘ m	-	-	- 22	64.7	32ab

Macrolactone 10cb. According to General Procedure using *seco*-acid **8cb** (19 mg, 27.5 µmol). Pale yellow oil (9.4 mg, 51%). $[\alpha]_D^{20}$ = −117.3 (c = 0.94, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.43 (td, *J* = 10.8, 1.4 Hz, 1H), 6.37–6.31 (m, 1H), 5.74 (ddd, *J* = 15.6, 7.7, 0.7 Hz, 1H), 5.49 (dd, *J* = 10.9, 9.5 Hz, 1H), 5.41–5.32 (m, 2H), 5.02 (ddd, *J* = 9.5, 5.9, 1.3 Hz, 1H), 4.86 (dd, *J* = 5.8, 4.5 Hz, 1H), 4.81 (d, *J* = 3.5 Hz, 1H), 4.74–4.65 (m, 3H), 4.41 (d, *J* = 6.8 Hz, 1H), 4.24 (dd, *J* = 9.0, 7.9 Hz, 1H), 4.11 (dt, *J* = 11.9, 3.5 Hz, 1H), 4.04 (dd, *J* = 8.1, 5.9 Hz, 1H), 4.01–3.90 (m, 3H), 3.88–3.79 (m, 4H), 3.39 (s, 3H), 3.23 (s, 3H), 2.68 (ddt, *J* = 11.6, 8.8, 6.6 Hz, 1H), 2.46 (p, *J* = 7.0 Hz, 1H), 2.33–2.25 (m, 1H), 2.01 (td, *J* = 12.5, 2.7 Hz, 1H), 1.79–1.69 (m, 2H), 1.67–1.57 (m, 1H), 1.57–1.52 (m, 1H), 1.50 (s, 3H), 1.38 (s, 3H), 1.08 (d, *J* = 1.9 Hz, 3H), 1.06 (d, *J* = 2.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.2, 141.2, 134.8, 130.6, 126.2, 125.1, 121.3, 109.0, 103.4, 95.5, 93.0, 84.0, 83.5, 82.8, 81.4, 77.6, 75.6, 74.7, 73.7, 72.9, 64.7(2), 55.5, 55.4, 40.6, 39.4, 35.2, 32.9, 32.3, 28.1, 25.7, 20.9, 16.0. IR (film): $\tilde{\nu}$ = 2956, 2927, 2889, 1745, 1456, 1380, 1371, 1213, 1149, 1081, 1031, 919,



866, 808, 755 cm^{-1}. MS (ESIpos) *m/z* (%): 695.3 (100 (M+Na)); HRMS (ESIpos): *m/z* calcd for $C_{33}H_{49}O_{12}ClNa$ [M+Na^+]: 695.2805, found: 695.2805. The macrolactone **10cb** decomposed upon storage under an argon atmosphere in the freezer.

Macrolactone 10db. According to General Procedure using *seco*-acid **8db** (27.6 mg, 40 µmol). Pale yellow oil (15.1 mg, 56%). $[\alpha]_D^{20}$ = −154.4 (c = 0.39, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): *see Table S-24.* ^{13}C NMR (151 MHz, $CDCl_3$): *see Table S-24*. IR (film): $\tilde{\nu}$ = 2935, 2887, 1744, 1198, 1156, 1091, 1029 cm^{-1}. MS (ESIpos) *m/z* (%): 695.3 (100 (M+Na)); HRMS (ESIpos): *m/z* calcd for $C_{33}H_{49}O_{12}ClNa$ [M+Na^+]: 695.2805, found: 695.2812.

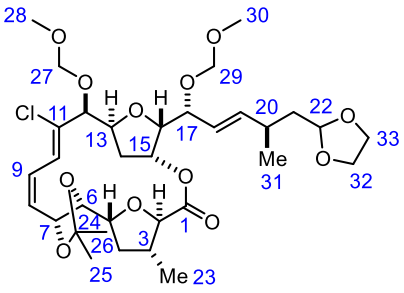


Table S-24. NMR data of the macrolactone **10db**; numbering scheme as shown in the insert

atom n°	^{1}H NMR (600 MHz, $CDCl_3$)					^{13}C NMR (151 MHz, $CDCl_3$)	
	δ [ppm]	m	*J* [Hz]	COSY	NOESY	δ [ppm]	HMBC
1	-	-	-	-	-	171.1	2, 3, 15
2	4.01	d	6.4	3	23	84.7	2, 4a. 23
3	2.84	ddqd	10.7, 7.1, 6.8, 6.4	2, 4ab, 23	4a, 5, 23	34.0	2, 4ab, 23
4a	2.40	ddd	11.8, 7.1, 4.3	3, 4b, 5	3, 4b, 5	39.6	6, 23
4b	1.41	dt	11.8, 10.7	3, 4a, 5	4a, 23		
5	3.92	dd	10.7, 4.3	4ab	3, 4a, 7, 25	83.0	2, 4b, 7
6	3.81	d	4.1	7	7, 8	83.3	4b, 5
7	4.77	dd	8.9, 4.1	6, 8	5, 6, 10	79.1	5, 9
8	5.74	ddd	10.5, 8.9, 0,9	7, 9, 10	6, 9, 26	134.9	6, 10
9	6.36	td	10.5, 1.3	8, 10	8	124.8	7
10	6.43	d	10.5	8, 9	7, 12, 14b	121.8	8, 12
11	-	-	-	-	-	135.7	9, 10, 12
12	4.58	s			10, 27ab	78.4	10, 13, 27ab
13	4.55	dd	11.6, 3.5	14ab	14b	80.2	12
14a	2.25	ddd	13.3, 11.6, 2.9	13, 14b, 15	14b, 15	34.2	12
14b	1.99	ddd	13.3, 3.5, 1.0	13, 14a	10, 13, 14a		
15	5.63	dd	3.3, 2,9	14a, 16	14a, 16	76.3	14b, 16, 17
16	3.97	dd	3.3, 8.3	15, 17	15, 18	81.1	14b, 17, 18
17	4.18	dd	8.3, 8.0	16, 18	19, 29a	73.8	16, 18, 19, 29ab
18	5.35	ddd	15.6, 8.0, 1.1	17, 19	16, 20	125.8	16, 20
19	5.67	ddd	15.6, 7.7, 0.7	18, 20	17, 31	141.5	17, 20, 21ab, 31
20	2.46	ddqd	8.1, 7.7, 6.8, 6.0	19, 21ab, 31	18, 31	32.9	18, 19, 21ab, 22, 31
21a	1.71	ddd	13.8, 8.1, 4.4	20, 21b, 22		40.6	19, 20, 22, 31
21b	1.63	ddd	13.8, 6.0, 5.9	20, 21a, 22	31		

22	4.84	dd	5.9, 4.4	21ab	32b, 33b	103.4	20, 21ab, 32ab, 33ab
23	1.13	d	6.8	3	2, 3, 4b	17.8	2, 3, 4b
24	-	-	-	-	-	110.9	6, 7, 25, 26
25	1.39	s	-	-	5	28.0	26
26	1.44	s	-	-	8	27.5	25
27a	4.86	d	6.4	27b	12, 28	97.3	12, 28
27b	4.80	d	6.4	27a	12, 28		
28	3.43	s	-	-	27ab	56.1	27ab
29a	4.71	d	6.8	29b	17	93.0	17, 30
29b	4.42	d	6.8	29a	30		
30	3.24	s	-	-	29b	55.6	29ab
31	1.06	d	6.8	20	19, 20, 21b	20.9	19, 20, 21ab
32a	3.97–3.92	AA′ m	-	-	-	64.7	33ab
32b	3.85–3.78	BB′ m			22		
33a	3.97–3.92	AA′ m	-	-	-	64.7	32ab
33b	3.85–3.78	BB′ m			22		

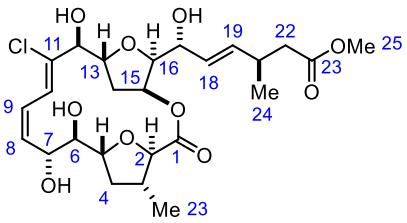
Endgame: General Procedure for the Global Deprotection, Pinnick Oxidation and Final Esterification.

A solution of Me_2BBr (0.5 M in CH_2Cl_2, 2000 mol%) was added dropwise to a solution of macrolactone **10** (0.01 M, 100 mol%) in CH_2Cl_2 at –78 °C. After stirring for 30 min at –78 °C, the yellow mixture was poured into a solution of pH 7 phosphate buffer (0.15 ml), rinsing the flask with CH_2Cl_2 (1.5 mL). The emulsion was concentrated under reduced pressure to yield the crude aldehyde, which was used in the next step without further purification.

The residue was dissolved into a 1:1 solution of THF and *t*-BuOH (0.01 M) before 2-methyl-2-butene (1000 equiv.) was introduced. A solution of sodium chlorite (8 equiv.) and sodium dihydrogen phosphate (9.60 equiv.) in water (900 equiv.) was added at 0 °C with a glass pipette. After stirring for 30 min at 0 °C the reaction was quenched with sodium thiosulfate pentahydrate (13 equiv.). After removing the ice bath, the mixture was stirred for 5 min before adding sodium sulfate in small portions until the organic phase was dried. The mixture was diluted with CH_2Cl_2 (2 mL), filtered through a short pad of Na_2SO_4, which was rinsed with CH_2Cl_2 (15 mL in total). The combined filtrates were evaporated under reduced pressure at ambient temperature and the resulting crude carboxylic acid was used in the next step without further purification.

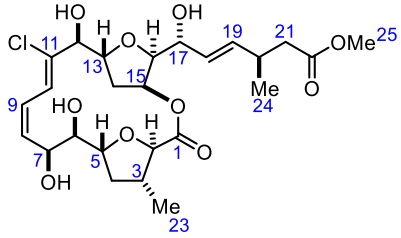
A freshly prepared solution of diazomethane in diethyl ether (ca. 0.1 mL) was added dropwise to a solution of the crude carboxylic acid in CH_2Cl_2 (0.02 M) at ambient temperature until a yellow colour persisted. After stirring for 5 min, the reaction was quenched with drops of formic acid until the yellow colour had dissipated. After concentrating the mixture under reduced pressure at ambient temperature, the residue was purified by preparative HPLC.

Macrocycle 2aa. According to General Procedure using compound **10aa** (2.5 mg, 3.7 µmol). Colourless



amorphous solid (0.4 mg, 20% over 3 steps). [Conditions for LC-MS: YMC-ODS-A C18, 5 µm, 150 × 4.6 mm, MeOH/H_2O = 40:60, v = 1.0 mL/min, λ = 250 nm, 35 °C, 153 bar, t(aldehyde) = 10.6 min, t(**1aa**) = 8.6 min, t(**2aa**) = 25.2 min]. $[\alpha]_D^{20}$ = +32.5 (c = 0.04, $CHCl_3$). ^{1}H NMR (600 MHz, CD_3OD/[D_5]-pyridine 1:1 (v/v), referenced on CD_2HOD): *see Table S-25;* ^{13}C NMR (151 MHz, CD_3OD/[D_5]-pyridine 1:1 (v/v), referenced on CD_2HOD): *see Table S-25*. IR (film): $\tilde{\nu}$ = 3386, 2958, 2922, 2852, 1736, 1455, 1259, 1095, 1063, 1039, 1010, 970, 876, 799, 758 cm^{-1}. MS (ESIpos) *m/z* (%): 553.2 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{25}H_{35}O_{10}ClNa$ [M+Na$^+$]: 553.1811, found: 553.1809.

Macrocycle 2ba. According to General Procedure using compound **10ba** (4.7 mg, 7.0 µmol) and



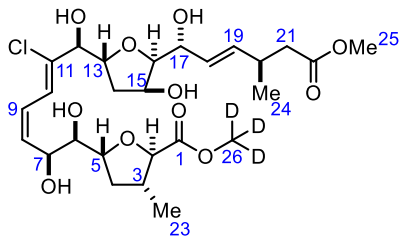
purification by preparative HPLC (YMC-ODS-A C18, 5 µm, 150 × 20 mm, MeCN/H_2O = 30:70, v = 20 mL/min, λ = 250 nm, 35 °C, 93 bar, t(**2ba**) = 5.58 min). Colourless amorphous solid (2.0 mg, 54% over 3 steps). [Conditions for LC-MS: YMC-ODS-A C18, 5 µm, 150 × 4.6 mm, MeCN/H_2O = 30:70, v = 0.8 mL/min, λ = 250 nm, 35 °C, 77 bar, t(aldehyde) = 5.67 min, t(**1ba**) = 2.67 min, t(**2aa**) = 6.94 min]. λ_{max}(MeCN) = 252 nm, λ_{max}(MeOH) = 249 nm.

The analytical data of this compound were extracted from spectra of the complex mixture formed upon solvolysis (cf. main text) using various 2D NMR techniques: ^{1}H NMR (600 MHz, CD_3OD/[D_5]-pyridine 1:1 (v/v), referenced on CD_2HOD): *δ* = 7.20–7.17 (m, 1H, H-10), 6.42 (ddd, *J* = 11.6, 10.5, 1.2 Hz, 1H, H-9), 5.73 (ddd, *J* = 15.5, 7.3, 1.0 Hz, 1H, H-19), 5.71 (dd, *J* = 11.4, 7.6 Hz, 1H, H-8), 5.53 (ddd, *J* = 15.5, 7.1, 1.2 Hz, 1H, H-18), 5.39 (td, *J* = 3.1, 1.2 Hz, 1H, H-15), 4.82–4.75 (m, 1H, H-7), 4.46 (ddd, *J* = 11.6, 6.8, 3.3 Hz, 1H, H-13), 4.42 (ddd, *J* = 8.3, 7.1, 1.0 Hz, 1H, H-17), 4.33 (d, *J* = 6.9 Hz, 1H, H-12), 4.10 (dd, *J* = 8.7, 3.4 Hz, 1H, H-16), 4.09–4.05 (m, 1H, H-5), 3.99 (d, *J* = 9.0 Hz, 1H, H-2), 3.51 (s, 3H, H-25), 3.45 (dd, *J* = 7.2, 2.7 Hz, 1H, H-6), 2.58 (tdq, *J* = 7.3, 7.1 6.9 Hz, 1H, H-20), 2.42 (ddp, *J* = 11.2, 9.0, 7.0 Hz, 1H, H-3), 2.24 (ddd, *J* = 15.2, 7.3, 5.8 Hz, 1H, H-21), 2.18 (ddd, *J* = 15.0, 7.2, 5.1 Hz, 1H, H-21), 2.04–1.94 (m, 2H, H-14, H-4), 1.89 (t, *J* = 10.8, 1H, H-4), 1.79 (td, *J* = 12.2, 3.0 Hz, 1H, H-14), 0.96 (d, *J* = 6.6 Hz, 3H, H-23), 0.90 (dd, *J* = 6.8, 1.0 Hz, 3H, H-24) ppm. MS (ESIneg) *m/z* (%): 529.2 (100 (M−H)). HRMS (ESIneg): *m/z* calcd for $C_{25}H_{35}O_{10}Cl$ [M−H]$^-$: 529.1846, found: 529.1852.

Table S-25. NMR data of macrocycle **2aa**; numbering scheme as shown in the insert

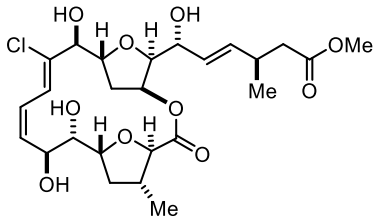
atom n°	^{1}H NMR (600 MHz, CD_3OD/[D_5]-pyridine 1:1 (v/v), referenced on CD_2HOD)					^{13}C NMR (151 MHz, CD_3OD/[D_5]-pyridine 1:1)	
	δ [ppm]	**m**	***J*** [Hz]	**COSY**	**NOESY**	**δ** [ppm]	**HMBC**
1	-	-	-	-	-	171.3	-
2	4.09	d	4.2	(3)	(3), 23	87.1	23
3	2.53	m	-	2, (4ab)	(2), 4a, 23	36.4	(4ab), 23
4a	2.22	ddd	12.3, 7.5, 7.5	(3), 4b, (5)	3, 4b, 5	38.9	23
4b	1.35	ddd	12.3, 8.4, 6.0	4a, 5	4b, 6, 23		
5	3.77	ddd	8.4, 7.5, 6.5	4ab, 6,	4a, (6), 7, (10), (13)	81.7	(4b), (7)
6	4.02	d	6.5	5	4b, 5, 7	81.8	-
7	4.66	d	8.8	8	(4b), 5, 6, (8), 10	71.5	(6), 9
8	6.07	ddd	11.3, 8.8, 0.9	7, 9	(7), 9	137.2	(6), (7), 9, 10
9	6.35	ddd	11.2, 11.2, 1.1	8, 10	8	123.6	7
10	6.93	dd	10.9, 0.9	9	(5), 7, 13	123.2	(8), (12)
11	-	-	-	-	-	137.1	9, 10, 12
12	4.32	d	9.0	13	14a	79.5	(10), (13)
13	4.28	ddd	11.5, 9.1, 3.1	12, 14a, (14b)	(4a), (5), 10, 14b	85.5	12, (14a), (15)
14a	1.73	ddd	12.6, 11.4, 3.1	13, 14b, (15)	(12), (15), (16)	39.0	-
14b	1.67	ddd	12.8, 3.0, 0.6	(13), 14a	(5), (13), (15)		
15	5.40	m	-	(14a), 16	(14ab), 16	76.4	(14b)
16	4.20	dd	8.7, 3.7	(15), 17	15, (18)	86.9	(14b), 17
17	4.54	dd	8.7, 6.8	16, 18	(18), 19, (20)	72.1	(16), (18), 19
18	5.55	ddd	15.5, 6.8, 1.1	17, 19	(16), 17, 20, (24)	128.9	(17)
19	5.81	dd	15.5, 7.3, 1.1	18, (20)	17, (24)	138.0	17, (20), 21ab, 24
20	2.54	m	-	(19), 21ab, 24	(18), (19), 24	34.0	(18), 19, 21ab, 24
21a	2.18	dd	15.1, 7.5	20	(19), 20, 24	41.8	24
21b	2.15	dd	15.1, 6.9				
22	-	-	-	-	-	173.2	21ab, 25
23	0.83	d	7.0	3	2, 3	19.5	(2), (3), (4)
24	0.85	d	6.8	20	20, (18), (19)	20.4	21ab
25	3.46	s	-	-	-	51.8	-

Analytical and spectral data for [**D_3]-methyl ester 55ba.** [Conditions for LC-MS: YMC-ODS-A C18, 5 µm, 150 × 4.6 mm, MeCN/H_2O = 30:70, v = 1.0 mL/min, λ = 250 nm, 35 °C, 86 bar, t(**2ba**) = 8.50 min, t(**55ba**) = 7.42 min]. $[\alpha]_D^{20}$ = −8.5 (c = 0.20, $CHCl_3$). λ_{max}(MeCN) = 247 nm. ^{1}H NMR (600 MHz, CD_3OD/[D_5]-pyridine 1:1 (v/v), referenced on CD_2HOD): *δ* = 7.21–7.14 (m, 1H, H-10), 6.50 (td, *J* = 11.1, 1.2 Hz, 1H, H-9), 5.90 (ddd, *J* = 15.6, 7.1, 1.4 Hz, 1H, H-19), 5.83–5.77 (m, 2H, H-18, H-8), 4.80 (ddd, *J* = 7.4, 6.6, 1.3 Hz, 1H, H-7), 4.77



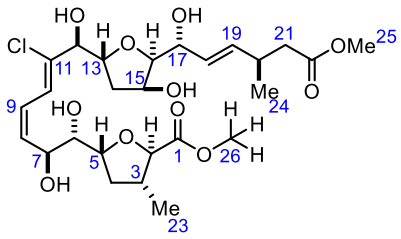
(dt, *J* = 9.4, 5.3 Hz, 1H, H-13), 4.65 (dddd, *J* = 6.6, 5.3, 1.4, 0.7 Hz, 1H, H-17), 4.39 (t, *J* = 3.7 Hz, 1H, H-15), 4.35 (d, *J* = 6.6 Hz, 1H, H-12), 4.23 (ddd, *J* = 9.8, 5.9, 2.7 Hz, 1H, H-5), 4.01 (d, *J* = 8.9 Hz, 1H, H-2), 3.87 (dd, *J* = 7.7, 3.0 Hz, 1H, H-16), 3.50 (s, 3H, H-25), 3.45 (dd, *J* = 7.2, 2.7 Hz, 1H, H-6), 2.60 (hept, *J* = 6.9 Hz, 1H, H-20), 2.25 (dd, *J* = 15.0, 7.2 Hz, 1H, H-21), 2.20–2.11 (m, 3H, H-21, H-14, H-3), 2.05 (ddd, *J* = 13.1, 6.5, 1.0 Hz, 1H, H-14), 1.98 (ddd, *J* = 11.9, 7.2, 5.9 Hz, 1H, H-4), 1.77 (ddd, *J* = 11.9, 10.7, 9.8 Hz, 1H, H-4), 1.03 (d, *J* = 6.5 Hz, 3H, H-23), 0.90 (d, *J* = 6.8 Hz, 3H, H-24). ^{13}C NMR (600 MHz, CD_3OD/[D_5]-pyridine 1:1 (v/v), referenced on CD_2HOD): *δ* = 174.3 (C1), 173.6 (C22), 137.7 (C11), 136.4 (C8), 136.3 (C19), 129.9 (C18), 125.6 (C9), 123.8 (C10), 87.8 (C16), 84.4 (C2), 81.0 (C5), 80.7 (C13), 79.2 (C12), 76.3 (C6), 73.2 (C15), 72.2 (C17), 70.7 (C7), 51.7 (C25), 42.0 (C21), 40.7 (C3), 39.5 (C14), 37.6 (C4), 34.3 (C20), 20.5 (C24), 17.5 (C23). IR (film): $\tilde{\nu}$ = 3403, 2971, 1739, 1558, 1222, 1088, 813, 769 cm^{-1}. MS (ESIpos) *m/z* (%): 588.2 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{26}H_{36}O_{11}ClD_3Na$ [M+Na$^+$]: 588.2261, found: 588.2256.

Macrocycle 2ca. According to General Procedure using compound **10ca** (2.1 mg, 3.1 µmol) and



purification by preparative HPLC (YMC-ODS-A C18, 5 µm, 150 × 20 mm, MeCN/H_2O = 30:70, v = 20 mL/min, λ = 250 nm, 35 °C, 95 bar, t(**2ca**) = 5.57 min). Colourless amorphous solid (0.3 mg, 18% over 3 steps). [Conditions for LC-MS: YMC-ODS-A C18, 5 µm, 150 × 4.6 mm, MeOH/H_2O = 50:50, v = 0.8 mL/min, λ = 250 nm, 35 °C, 120 bar, t(aldehyde) = 6.06 min, t(**1ca**) = 3.31 min, t(**2ca**) = 10.74 min; YMC-ODS-A C18, 5 µm, 150 × 4.6 mm, MeCN/H_2O = 30:70, v = 1.0 mL/min, λ = 250 nm, 35 °C, 86 bar, t(**2ca**) = 6.77 min (λ_{max}(MeCN) = 249 nm; λ_{max}(MeOH) = 249 nm), t(**55ca**) = 6.21 min].

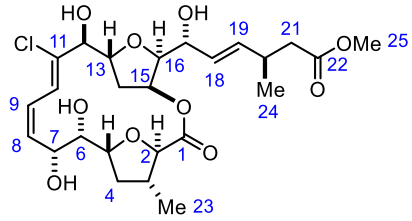
Analytical and spectral data for **methyl ester 55ca**. $[\alpha]_D^{20}$ = 10.0 (c = 0.03, $CHCl_3$). ^{1}H NMR (600 MHz,



CD_3OD/[D_5]-pyridine 1:1 (v/v), referenced on CD_2HOD, decomposition of **2ca** by exposure to methanol): *δ* = 7.19–7.16 (m, 1H, H-10), 6.53 (td, *J* = 11.0, 1.2 Hz, 1H, H-9), 5.97–5.88 (m, 2H, H-19, H-8), 5.79 (ddd, *J* = 15.6, 5.3, 1.1 Hz, 1H, H-18), 4.80 (ddd, *J* = 9.1, 4.7, 1.3 Hz, 1H, H-7), 4.76 (dt, *J* = 9.3, 6.6, 6.5 Hz, 1H, H-13), 4.65–4.62 (m, 1H, H-17), 4.36 (t, *J* = 3.7 Hz, 1H, H-15), 4.33 (d, *J* = 6.5 Hz, 1H, H-12), 4.29 (dt, *J* = 9.4, 5.7 Hz, 1H, H-5), 3.97 (d, *J* = 8.1 Hz, 1H, H-2), 3.95 – 3.93 (m, 1H, H-6), 3.84 (dd, *J* = 7.7, 3.0 Hz, 1H, H-16), 3.59 (s, 3H, H-26), 3.51 (s, 3H, H-25), 2.64–2.56 (m, 1H, H-20), 2.25 (dd, *J* = 15.0, 7.2 Hz, 1H, H-21''), 2.22–2.15 (m, 3H, H-21', H-4'', H-3), 2.10 (td, *J* = 9.1, 4.7 Hz, 1H, H-14'), 2.04 (ddd, *J* = 13.2, 6.5, 1.1 Hz, 1H, H-14''), 1.68 (dt, *J* = 11.8, 9.7 Hz, 1H, H-4'), 1.02 (d, *J* = 6.4 Hz, 3H, H-23), 0.91 (d, *J* = 6.8 Hz, 3H, H-24) ppm. ^{13}C NMR (600 MHz, CD_3OD/[D_5]-pyridine 1:1 (v/v), referenced on CD_2HOD, decomposition by exposure to methanol): *δ* = 173.3 (C1), 172.6 (C22), 136.2 (C11), 135.4 (C8), 135.2 (C19), 128.8 (C18),

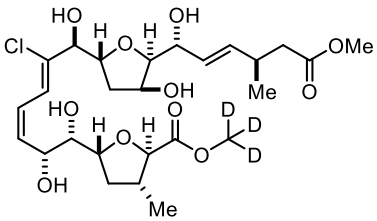
124.3 (C9), 122.8 (C10), 86.7 (C16), 83.0 (C2), 80.8 (C5), 79.6 (C13), 78.1 (C12), 76.6 (C6), 72.1 (C15), 71.1 (C17), 69.3 (C7), 51.2 (C26), 50.7 (C25), 40.9 (C21), 39.6 (C3), 38.5 (C14), 36.5 (C4), 33.2 (C20), 19.4 (C24), 16.9 (C23) ppm. IR (film): $\tilde{\nu}$ = 3410, 3375, 2922, 1736, 1571, 1438, 1289, 1219, 979, 807 cm^{-1}. MS (ESIpos) *m/z* (%): 585.2 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{26}H_{39}O_{11}ClNa$ [M+Na^+]: 585.2073, found: 585.2074.

Macrocycle 2da. According to General Procedure using compound **10da** (1.5 mg, 3.1 µmol) and purification by preparative HPLC (YMC-ODS-A C18, 5 µm, 150 × 20 mm, MeCN/H_2O = 30:70, v = 20 mL/min, λ = 250 nm, 35 °C, 95 bar, t(**2da**) = 6.60 min). Colourless amorphous solid (0.3 mg, 26% over 3 steps). [Conditions for LC-MS: YMC-ODS-A C18, 5 µm, 150 × 4.6 mm, MeOH/H_2O = 50:50, v = 0.8 mL/min, λ = 250 nm, 35 °C, 120 bar, t(aldehyde) = 7.79 min, t(**1da**) = 4.10 min, t(**2da**) = 15.67 min]. λ_{max}(MeCN) = 248 nm, λ_{max}(MeOH) = 246 nm.

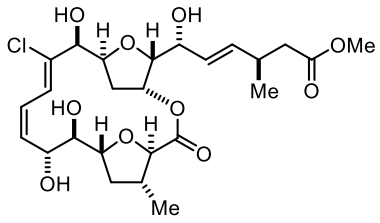


The analytical data of this compound were extracted from spectra of the complex mixture formed upon solvolysis (cf. main text) using various 2D NMR techniques. ^{1}H NMR (600 MHz, CD_3OD/[D_5]-pyridine 1:1 (v/v), referenced on CD_2HOD, opening of macrolactone over time): *δ* = 6.76 (d, *J* = 10.9 Hz, 1H, H-10), 6.30 (t, *J* = 11.1 Hz, 1H, H-9), 5.83 (dd, *J* = 15.7, 7.4 Hz, 1H, H-19), 5.60 (ddd, *J* = 11.6, 8.6, 1.0 Hz, 1H, H-8), 5.53 (ddd, *J* = 15.7, 8.7, 7.3 Hz, 1H, H-18), 5.42 (t, *J* = 3.4 Hz, 1H, H-15), 4.47 (t, *J* = 7.6 Hz, 1H, H-17), 4.29 (d, *J* = 8.7 Hz, 1H, H-12), 4.22–4.16 (m, 3H, H-16, H-13, H-7), 3.77 (d, *J* = 7.0 Hz, 1H, H-2), 3.71 (dd, *J* = 9.7, 1.6 Hz, 1H, H-6), 3.52 (s, 3H, H-25), 3.46 (dd, *J* = 8.5, 4.3 Hz, 1H, H-5), 2.58–2.52 (m, 1H, H-20), 2.21–2.16 (m, 4H, H-21, H-14, H-3), 2.01–1.97 (m, 1H, H-4), 1.87–1.83 (m, 1H, H-14), 1.42–1.38 (m, 1H, H-4), 0.92 (d, *J* = 6.6 Hz, 3H, H-23), 0.90 (d, *J* = 6.8 Hz, 3H, H-24).

Analytical and spectral data for [**D_3]-methyl ester 55da**. [YMC-ODS-A C18, 5 µm, 150 × 4.6 mm, MeCN/H_2O = 30:70, v = 1.0 mL/min, λ = 250 nm, 35 °C, 99 bar, t(**2da**) = 8.42 min, t(**55da**) = 5.77 min]. λ_{max}(MeCN) = 247 nm. ^{1}H NMR (600 MHz, CD_3OD/[D_5]-pyridine 1:1 (v/v), referenced on CD_2HOD): *δ* = 7.11 (d, *J* = 11.0 Hz, 1H), 6.47 (td, *J* = 11.1, 1.2 Hz, 1H), 5.94–5.86 (m, 2H), 5.78 (ddd, *J* = 15.6, 5.3, 1.2 Hz, 1H), 4.76–4.69 (m, 2H), 4.64–4.58 (m, 1H), 4.32 (d, *J* = 5.0 Hz, 1H), 4.21 (d, *J* = 6.1 Hz, 1H), 4.00 (d, *J* = 8.4 Hz, 1H), 3.77–3.71 (m, 2H), 3.51 (s, 3H), 3.46 (ddd, *J* = 8.5, 4.8, 3.5 Hz, 1H), 2.61 (hept, *J* = 7.5 Hz, 1H), 2.26 (dd, *J* = 15.0, 7.3 Hz, 1H), 2.20–2.15 (m, 2H), 2.13–2.08 (m, 1H), 2.03–1.96 (m, 1H), 1.92 (ddd, *J* = 13.5, 9.6, 4.5 Hz, 1H), 1.70 (dt, *J* = 12.1, 10.2 Hz, 1H), 1.04 (d, *J* = 6.6 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 3H). MS (ESIpos) *m/z* (%): 588.2 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{26}H_{36}O_{11}ClD_3Na$ [M+Na^+]: 588.2261, found:588.2260.

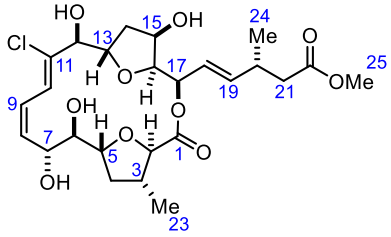


Macrocycle 2ab. According to General Procedure using compound **10ab** (7.8 mg, 12 µmol) and



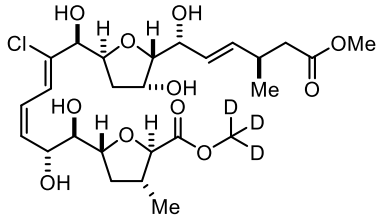
purification by preparative HPLC (YMC-ODS-A C18, 5 µm, 150 × 20 mm, MeCN/H_2O = 30:70, v = 20 mL/min, λ = 250 nm, 35 °C, 95 bar, t(**54ab**) = 5.44 min, t(**2ab**) = 7.52 min) affording the title compound (1.7 mg, 28%) and 18-membered macrolactone **54ab** (1.0 mg, 16%) as colourless amorphous solids. [Conditions for LC-MS: YMC-ODS-A C18, 5 µm, 150 × 4.6 mm, MeCN/H_2O = 30:70, v = 0.8 mL/min, λ = 250 nm, 35 °C, 99 bar, t(aldehyde) = 7.69 min, t(**1ab**) = 2.27 min, t(**351a**) = 9.72 min; YMC-ODS-A C18, 5 µm, 150 × 4.6 mm, MeCN/H_2O = 30:70, v = 1.0 mL/min, λ = 250 nm, 35 °C, 105 bar, t(**55ab**) = 6.27 min t(**54ab**) = 6.76 min, t(**2ab**) = 9.77 min].

Analytical and spectral data for 18-membered **macrolactone 54ab:** $[\alpha]_D^{20}$ = −4.1 (c = 0.17, $CHCl_3$).



λ_{max}(MeCN) = 248 nm. ^{1}H NMR (600 MHz, CD_3OD/[D_5]-pyridine 1:1 (v/v), referenced on CD_2HOD): *see Table S-26;* ^{13}C NMR (151 MHz, CD_3OD/[D_5]-pyridine 1:1 (v/v), referenced on CD_2HOD): *see Table S-26*. IR (film): $\tilde{\nu}$ = 3422, 2961, 2924, 2856, 1728, 1606, 1400, 1260, 1087, 1020, 798 cm^{-1}. MS (ESIpos) *m/z* (%): 553.2 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{25}H_{35}O_{10}ClNa$ [M+Na$^+$]: 553.1811, found: 553.1812.

Analytical and spectral data for [**D_3]-methyl ester 55ab**. λ_{max}(MeCN) = 245 nm. ^{1}H NMR (600 MHz,

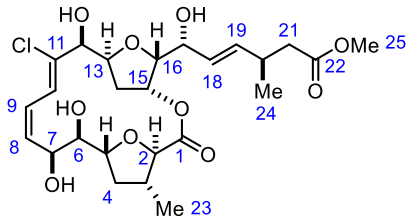


CD_3OD/[D_5]-pyridine 1:1 (v/v), referenced on CD_2HOD): δ = 7.21–7.19 (m, 1H), 6.54–6.49 (m, 1H), 5.97–5.92 (m, 1H), 5.78–5.75 (m, 2H), 4.85–4.81 (m, 1H), 4.81–4.79 (m, 1H), 4.74 (ddd, *J* = 10.9, 9.2, 4.6 Hz, 1H), 4.60–4.52 (m, 2H), 4.51–4.45 (m, 1H), 4.00 (d, *J* = 8.7 Hz, 1H), 3.87 (td, *J* = 6.8, 3.1 Hz, 1H), 3.61–3.57 (m, 1H), 3.50 (s, 3H), 2.59 (ddd, *J* = 14.7, 11.7, 6.6 Hz, 1H), 2.26–2.20 (m, 3H), 2.16–2.11 (m, 1H), 2.03–1.97 (m, 2H), 1.67 (dt, *J* = 12.1, 10.4 Hz, 1H), 1.01 (d, *J* = 6.6 Hz, 3H), 0.89 (d, *J* = 6.8 Hz, 3H).

Table S-26. NMR data of expanded macrolactone **54ab**; numbering scheme as shown in the insert

atom n°	^{1}H NMR (600 MHz, $CD_3OD/[D_5]$-pyridine 1:1 (v/v), referenced on CD_2HOD)					^{13}C NMR (151 MHz, $CD_3OD/[D_5]$-pyridine 1:1)	
	δ [ppm]	**m**	***J*** [Hz]	**COSY**	**NOESY**	**δ** [ppm]	**HMBC**
1	-	-	-	-	-	172.7	17
2	4.09	d	8.1	3	23	86.5	23
3	2.38	dddq	10.4, 8.1, 7.0, 6.6	2, 4ab, 23	23	39.5	2, 23
4a	2.00	ddd	12.1, 7.0, 5.7	3, 4b, 5	4b, 5, 6	38.7	23
4b	1.80	dt	11.8, 10.4	3, 4a, 5	4a, 6		
5	4.41	ddd	10.2, 5.6, 1.4	4ab	4a, 6	81.6	2, 4b
6	3.73	dd	2.3, 1.4	7	4ab, 5, 7, 8	73.7	-
7	4.81	ddd	5.5, 2.3, 1.8	6, 8	6, 8, 10	77.6	9
8	5.61	ddd	11.8, 5.5	7, 9	6, 7, 9	134.0	-
9	6.55	ddd	11.7, 11.1, 1.7	8, 10	8	125.2	-
10	7.76	d	11.0	9	7, 12	124.8	12
11	-	-	-	-	-	137.3	9, 10
12	4.18	d	7.6	13	10, 13, 14a, 16	78.2	10, 14ab
13	4.60	td	7.6, 6.0	12, 14ab	12, 14b	78.6	12, 14a
14a	2.37	dt	13.9, 6.1	13, 14b, 15	12, 14b, 15, 16	39.9	-
14b	2.20	ddd	13.9, 8.0, 1.2	13, 14a	13, 14a		
15	4.41	dd	6.1, 1.4	14a, 16	14a, 16, 17	73.6	14b
16	3.71	dd	3.3, 1.4	15	12, 14a, 15, 17	84.5	13, 14b
17	5.80	dt	7.0, 1.4	18	15, 16, 19	74.4	16, 18, 19
18	6.04	ddd	15.8, 6.9, 1.3	17, 19	-	125.5	17, 20
19	5.73	ddd	15.8, 7.1, 1.1	18, 20	17	139.4	17, 20. 21ab, 24
20	2.48	heptd	7.1, 1.2	19, 21ab, 24	21ab, 24	34.2	18, 19, 21ab, 24
21a	2.13	dd	15.1, 7.2	20	24	41.7	19, 20, 24
21b	2.06	dd	15.1, 7.3	20	20, 24		
22	-	-	-	-	-	173.4	21ab, 25
23	1.03	d	6.6	3	2, 3	17.9	2, 3
24	0.79	d	6.8	20	19, 20, 21ab	19.9	19, 20, 21ab
25	3.47	s	-	-	-	51.7	-
4xOH	5.08	br	-	-	-	-	-

Macrocycle 2bb. According to General Procedure using compound **10bb** (10.0 mg, 14.8 µmol) and purification by preparative HPLC (YMC-ODS-A C18, 5 µm, 150 × 20 mm, MeCN/H_2O = 25:75, v = 20 mL/min, λ = 250 nm, 35 °C, 100 bar, t(**54ab**) = 8.80 min, t(**2bb**) = 11.92 min)) affording the title compound **2bb** (2.0 mg, 25%) and 18-membered macrolactone **54bb** (2.2 mg, 28%) as colourless amorphous solids. [Conditions for LC-MS: YMC-ODS-A C18, 5 µm, 150 × 4.6 mm, MeCN/H_2O = 30:70, v = 0.8 mL/min, λ = 250 nm, 35 °C, 87 bar, t(aldehyde) = 6.46 min, t(**1bb**) = 3.12 min, t(**2bb**) = 7.61 min, t(**54bb**) = 5.75 min; YMC-ODS-A C18, 5 µm, 150 × 4.6 mm, MeCN/H_2O = 30:70, v = 1.0 mL/min, λ = 250 nm, 35 °C, 99 bar, t(**54bb**) = 5.86 min, t(**2bb**) = 7.67 min, t(**55bb**) = 7.69 min]. Analytical and spectral data for **2bb:** λ_{max}(MeCN) = 248 nm.



The analytical data of this compound were extracted from spectra of the complex mixture formed upon solvolysis (cf. main text) using various 2D NMR techniques. ^{1}H NMR (600 MHz, CD_3OD/[D_5]-pyridine 1:1 (v/v), referenced on CD_2HOD, decomposition of title compound to 18-membered ring **54bb** and open D_3-methyl ester **55bb** over time): *δ* = 6.61 (dt, *J* = 10.1, 1.4 Hz, 1H, H-10), 6.43–6.38 (m, 1H, H-9), 5.87–5.82 (m, 2H, H-19, H-18), 5.57–5.53 (m, 2H, H-15, H-8), 4.86 (d, *J* = 1.4 Hz, 1H, H-12), 4.74 (dd, *J* = 10.2, 9.0 Hz, 1H, H-7), 4.53–4.48 (m, 2H, H- 17, H-13), 4.07 (dd, *J* = 9.5, 3.4 Hz, 1H, H-16), 4.00 (d, *J* = 7.0 Hz, 1H, H-2), 3.86 (ddd, *J* = 9.4, 6.4, 1.0 Hz, 1H, H-5), 3.51 (s, 3H, H-25), 3.39 (dd, *J* = 9.3, 1.0 Hz, 1H, H-6), 2.70–2.62 (m, 2H, H-20, H-3), 2.28 (dd, *J* = 15.0, 6.8 Hz, 1H, H-21), 2.26–2.22 (m, 1H, H-14), 2.18 (dd, *J* = 15.0, 7.6 Hz, 1H, H-21), 2.00–1.97 (m, 2H, H-4), 1.88–1.82 (m, 1H, H-14), 0.93 (d, *J* = 6.8 Hz, 3H, H-24), 0.90 (d, *J* = 6.7 Hz, 3H, H-23). ^{13}C NMR (600 MHz, CD_3OD/[D_5]-pyridine 1:1 (v/v), referenced on CD_2HOD, signals and asignment by 2D-spectra): *δ* = 173.4 (22), 172.7 (1), 138.3 (11), 135.7 (19), 134.3 (8), 131.5 (18), 126.1 (9), 121.5 (10), 85.5 (16), 85.4 (2), 80.5 (5), 76.9 (15), 76.6 (17), 75.2 (6), 70.1 (7), 70.0 (12), 69.5 (13), 51.4 (25), 41.8 (21), 37.3 (4), 35.1 (3), 33.9 (20), 32.4 (14), 20.2 (24), 17.3 (23) ppm. MS (ESIpos) *m/z* (%): 553.2 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{25}H_{35}O_{10}ClNa$ [M+Na$^+$]: 553.1811, found:553.1809.

Analytical and spectral data for 18-membered **macrolactone 54bb:** $[\alpha]_D^{20}$ = −6.4 (c = 0.22, CH_2Cl_2). λ_{max}(MeCN) = 246 nm. ^{1}H NMR (600 MHz, CD_3OD/[D_5]-pyridine 1:1 (v/v), referenced on CD_2HOD): *see Table S-27;* ^{13}C NMR (151 MHz, CD_3OD/[D_5]-pyridine 1:1 (v/v), referenced on CD_2HOD): *see Table S-27*. IR (film): $\tilde{\nu}$ = 3413, 2964, 2927, 1726, 1262, 1084, 1059, 797 cm^{-1}. MS (ESIpos) *m/z* (%): 553.2 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{25}H_{35}O_{10}ClNa$ [M+Na$^+$]: 553.1811, found: 553.1810.

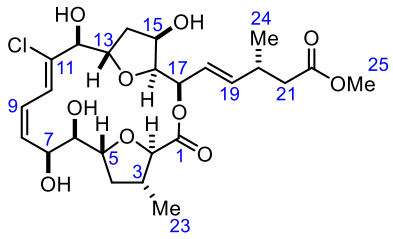
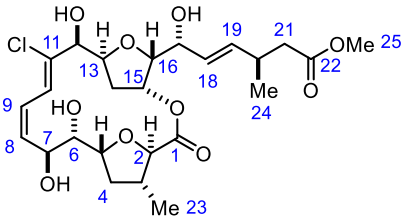


Table S-27. NMR data of expanded macrolactone **54bb**; numbering scheme as shown in the insert

atom n°	^{1}H NMR (600 MHz, CD_3OD/[D_5]-pyridine 1:1 (v/v), referenced on CD_2HOD)					^{13}C NMR (151 MHz, CD_3OD/[D_5]-pyridine 1:1)	
	δ [ppm]	**m**	***J*** [Hz]	**COSY**	**NOESY**	**δ** [ppm]	**HMBC**
1	-	-	-	-	-	172.8	17
2	4.13	d	9.6	3	23	86.5	23
3	2.43	m	-	2, 4, 23	4, 5, 23	40.5	2, 23
4a 4b	1.93-1.99 1.93-1.99	m	-	3, 5	3, 5, 6, 23	37.7	23
5	4.20	dd	9.7, 6.5	4	3, 4, 6	80.8	-
6	3.41	d	9.2	7	4, 5, 7, 8	75.4	5, 7
7	4.89	t	9.7	6, 8	6, 8, 10	70.3	6, 9
8	5.54	ddd	11.0, 10.1, 1.0	7, 9	6, 7	135.2	-
9	6.57	td	11.1, 0.8	8, 10	-	126.8	7
10	6.79	dd	11.0, 1.0	9	7, 12	123.4	8
11	-	-	-	-	-	140.0	10
12	4.09	d	9.5	13	10, 14a, 16	77.4	10, 14ab
13	4.51	ddd	9.5, 8.0, 5.0	12, 14ab	14b	76.9	12, 15
14a 14b	2.37 2.22	ddd dd	14.1, 6.2, 5.1 14.3, 8.1	13, 14b, 15 13, 14a	12, 14b, 15 13, 14a	40.3	-
15	4.43	dd	6.1, 3.1	14a, 16	14a, 16, 17	73.6	14b
16	3.71	dd	3.1, 1.4	15	12, 15, 17	84.3	13, 14a, 15
17	5.88	dt	6.9, 1.2	18	15, 16, 19	74.3	16, 18, 19
18	6.05	ddd	15.7, 6.9, 1.3	17, 19	20, 24	125.5	16, 17, 20
19	5.71	ddd	15.5, 7.0, 1.1	18, 20	17, 20, 24	139.2	17, 20, 21ab, 24
20	2.43	hept	7.0	19, 21ab, 24	18, 19, 24	34.1	18, 19, 21ab, 24
21a 21b	2.10 2.02	dd dd	15.0, 7.1 15.1, 7.4	20, 21b 20, 21a	24 24	41.6	19, 20, 24
22	-	-	-	-	-	173.4	21ab, 25
23	1.05	d	6.5	3	2, 3, 4	16.5	2
24	0.76	d	6.8	20	18, 19, 20, 21ab	19.8	19, 20, 21ab
25	3.46	s	-	-	-	51.8	-
4xOH	5.07	s	-	-	-	-	-

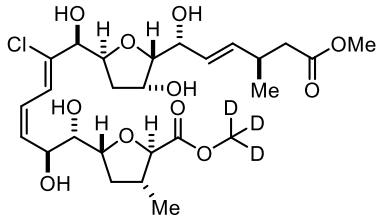
Macrocycle 2cb. According to General Procedure using compound **10cb** (2.0 mg, 3.0 µmol) and purification by preparative HPLC (YMC-ODS-A C18, 5 µm, 150 × 20 mm, MeCN/H_2O = 25:75, v = 20 mL/min, λ = 250 nm, 35 °C, 93 bar, t(**2cb**) = 8.29 min). Colourless amorphous solid (0.3 mg, 19% over 3 steps). [Conditions for LC-MS: YMC-ODS-A C18, 5 µm, 150 × 4.6 mm, MeCN/H_2O = 30:70, v = 0.8 mL/min,



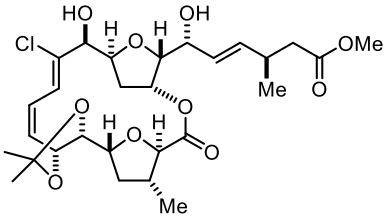
λ = 250 nm, 35 °C, 92 bar, t(aldehyde) = 4.95 min, t(**1cb**) = 2.33 min; YMC-ODS-A C18, 5 µm, 150 × 4.6 mm, MeCN/H_2O = 30:70, v = 1.0 mL/min, λ = 250 nm, 35 °C, 96 bar, t(**54cb**) = 3.48 min, t(**2cb**) = 5.70 min, t(**55cb**) = 6.76 min]. Analytical and spectral data for **2cb:** λ_{max}(MeCN) = 247 nm.

The analytical data of this compound were extracted from spectra of the complex mixture formed upon solvolysis (cf. main text) using various 2D NMR techniques. ^{1}H NMR (600 MHz, CD_3OD/[D_5]-pyridine 1:1 (v/v), referenced on CD_2HOD, mixture of **2cb** and 18-membered macrolactone **54cb**,decomposition of both compounds to open D_3-methyl ester **55cb**): *δ* = 6.66–6.62 (m, 1H, H-10), 6.47–6.42 (m, 1H, H-9), 6.01–5.96 (m, 1H, H-8), 5.85 (dd, *J* = 15.5, 5.9 Hz, 1H, H-19), 5.82 (dd, *J* = 15.6, 4.8 Hz, 1H, H-18), 5.53 (t, *J* = 3.2 Hz, 1H, H-15), 4.91 (dd, *J* = 10.1, 1.4 Hz, 1H, H-7), 4.86 (d, *J* = 10.7 Hz, 1H, H-12), 4.56 (dt, *J* = 11.9, 3.1 Hz, 1H, H-13), 4.52 (dd, *J* = 9.3, 4.8 Hz, 1H, H-17), 4.07 (dd, *J* = 9.3, 3.4 Hz, 1H, H-16), 4.01 (d, *J* = 4.9 Hz, 1H, H-2), 3.86 (dd, *J* = 9.8, 1.8 Hz, 1H, H-6), 3.66 (dt, *J* = 9.7, 7.3 Hz, 1H, H-5), 3.51 (s, 3H, H-25), 2.65 (hept, *J* = 7.4 Hz, 1H, H-20), 2.64–2.56 (m, 2H, H-14, H-3), 2.47 (dt, *J* = 12.6, 7.2 Hz, 1H, H-4), 2.27 (dd, *J* = 15.0, 6.9 Hz, 1H, H-21), 2.17 (dd, *J* = 15.0, 7.7 Hz, 1H, H-21), 1.82 (dd, *J* = 13.1, 3.5 Hz, 1H, H-14), 1.63 (dt, *J* = 12.6, 7.4 Hz, 1H, H-4), 0.93 (d, *J* = 6.7 Hz, 3H, H-24), 0.87 (d, *J* = 6.9 Hz, 3H, H-23). MS (ESIpos) *m/z* (%): 553.2 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{25}H_{35}O_{10}ClNa$ [M+Na$^+$]: 553.1811, found:553.1811.

Analytical and spectral data for [**D_3]-methyl ester 55cb**. λ_{max}(MeCN) = 246 nm. ^{1}H NMR (600 MHz, CD_3OD/[D_5]-pyridine 1:1 (v/v), referenced on CD_2HOD): *δ* = 7.25 (dt, *J* = 10.9, 1.1 Hz, 1H), 6.54 (td, *J* = 11.0, 1.2 Hz, 1H), 5.94 (ddd, *J* = 11.1, 8.8, 1.1 Hz, 1H), 5.78–5.75 (m, 2H), 4.80–4.75 (m, 2H), 4.61 (t, *J* = 3.8 Hz, 1H), 4.59 (d, *J* = 4.3 Hz, 1H), 4.58–4.55 (m, 1H), 4.40 (dt, *J* = 9.7, 5.4 Hz, 1H), 4.00–3.97 (m, 2H), 3.90 (dd, *J* = 7.2, 3.1 Hz, 1H), 3.51 (s, 3H), 2.63–2.56 (m, 2H), 2.27–2.21 (m, 1H), 2.22–2.14 (m, 2H), 2.17–2.11 (m, 2H), 1.73 (dt, *J* = 12.0, 10.1 Hz, 1H), 1.01 (d, *J* = 6.6 Hz, 3H), 0.89 (d, *J* = 6.8 Hz, 3H). MS (ESIpos) *m/z* (%): 588.2 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{26}H_{36}O_{11}ClD_3Na$ [M+Na$^+$]: 588.2261, found:588.2260.



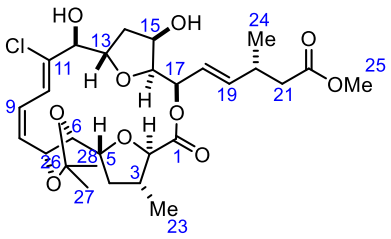
Acetonide S27. According to General Procedure using compound **10db** (3.2 mg, 4.8 µmol) and purification by preparative HPLC (YMC-ODS-A C18, 5 µm, 150 × 20 mm, MeCN/H_2O = 50:50, v = 20 mL/min, λ = 250 nm, 35 °C, 77 bar, t(**S28**) = 6.71 min, t(**S27**) = 13.41 min) affording the 16-membered ring **S27** (1.0 mg, 37%) and 18-membered macrolactone **S28** (0.5 mg, 18%) as colourless amorphous solids.



[Conditions for LC-MS: YMC-ODS-A C18, 5 µm, 150 × 4.6 mm, MeCN/H_2O = 50:50, v = 0.8 mL/min, λ = 250 nm, 35 °C, 53 bar, t(aldehyde) = 13.29 min, t(carboxylic acid) = 7.85 min, t(**S27**) = 15.86 min,

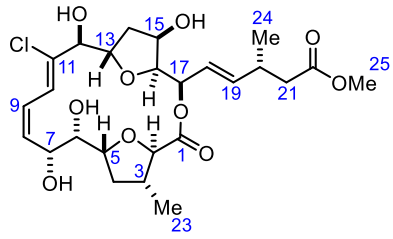
t(**S28**) = 10.18 min; YMC-ODS-A C18, 5 µm, 150 × 4.6 mm, MeCN/H_2O = 50:50, v = 1.0 mL/min, λ = 250 nm, 35 °C, 86 bar, t(**S27**) = 8.66 min, t(**S28**) = 18.33 min].

Analytical and spectral data for 18-membered **acetonide S28:** $[\alpha]_D^{20}$ = +12.0 (c = 0.05, $CHCl_3$).



λ_{max}(MeCN) = 248 nm. ^{1}H NMR (600 MHz, CD_3OD/[D_5]-pyridine 1:1 (v/v), referenced on CD_2HOD, ring extension of 16-membered to 18-membered ring): *see Table S-28;* ^{13}C NMR (151 MHz, CD_3OD/[D_5]-pyridine 1:1 (v/v), referenced on CD_2HOD): *see Table S-28*. IR (film): $\tilde{\nu}$ = 3468, 2960, 2931, 1727, 1608, 1454, 1379, 1259, 1171, 1059, 1015, 873, 798, 760 cm^{-1}. MS (ESIpos) *m/z* (%): 593.2 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{28}H_{39}O_{10}ClNa$ [M+Na$^+$]: 593.2124, found: 593.2125.

Expanded Macrolactone 54db. According to General Procedure using compound **10db** (3.2 mg, 4.8 µmol), dimethylborobromide (0.38 mL, 40 equiv.) and purification by preparative HPLC (YMC-ODS-A C18, 5 µm, 150 × 20 mm, MeCN/H_2O = 25:75, v = 20 mL/min, λ = 250 nm, 35 °C, 90 bar, t(**54db**) = 9.67 min) affording the 18-membered macrolactone (0.6 mg, 24%), the acetonide-protected macrolactone **S27** (0.4 mg, 15%) and its 18-membered analogue **S28** (0.2 mg, 7%) as colourless amorphous solids. [Conditions for LC-MS: YMC-ODS-A C18, 5 µm, 150 × 4.6 mm, MeCN/H_2O = 30:70, v = 1.0 mL/min, λ = 250 nm, 35 °C, 97 bar, t(**54db**) = 13.27 min]. Analytical and spectral data for **54db:** $[\alpha]_D^{20}$ = +10.0 (c = 0.06, $CHCl_3$). λ_{max}(MeCN) = 248 nm. ^{1}H NMR (600 MHz, CD_3OD/[D_5]-pyridine 1:1 (v/v), referenced on CD_2HOD): *see Table S-29;* ^{13}C NMR (151 MHz, CD_3OD/[D_5]-pyridine 1:1 (v/v), referenced on CD_2HOD): *see Table S-29*. IR (film): $\tilde{\nu}$ = 3430, 2951, 2922, 2850, 1731, 1261, 1059, 1018, 795 cm^{-1}. MS (ESIpos) m/z (%): 553.2 (100 (M+Na)). HRMS (ESIpos): m/z calcd for $C_{25}H_{35}O_{10}ClNa$ [M+Na$^+$]: 553.1811, found: 553.1811.



Expanded Macrolactone 54aa. A solution of macrocycle **2aa** (0.4 mg, 0.8 µmol) in toluene (2.5 mL) was heated under reflux. After stirring for 268 h, the solution was cooled to ambient temperature, concentrated and purification by preparative HPLC (YMC-ODS-A C18, 5 µm, 150 × 20 mm, MeCN/H_2O = 25:75, v = 20 mL/min, λ = 250 nm, 35 °C, 90 bar, t(**2aa**) = 8.34 min t(**54aa**) = 8.92 min) affording the title compound (0.3 mg, 75%) as a courless amorphous solid. [Conditions for LC-MS: YMC-ODS-A C18, 5 µm, 150 × 4.6 mm, MeCN/H_2O = 25:75, v = 1.0 mL/min, λ = 250 nm, 35 °C, 102 bar, t(**2aa**) = 10.66 min, t(**54aa**) = 11.39 min]. $[\alpha]_D^{20}$ = +230 (c = 0.03, CH_2Cl_2). λ_{max}(MeCN) = 245 nm. ^{1}H NMR (600 MHz,

$CD_3OD/[D_5]$-pyridine 1:1 (v/v), referenced on CD_2HOD): *see Table S-30;* ^{13}C NMR (151 MHz, $CD_3OD/[D_5]$-pyridine 1:1 (v/v), referenced on CD_2HOD): *see Table S-30*. IR (film): $\tilde{\nu}$ = 3477, 3366, 3318, 2959, 2923, 2856, 1729, 1462, 1286, 1121, 1074, 1034, 796 cm^{-1}. MS (ESIpos) m/z (%): 553.2 (100 (M+Na)). HRMS (ESIpos): m/z calcd for $C_{25}H_{35}O_{10}ClNa$ [M+Na^+]: 553.1811, found: 553.1816.

Table S-28. NMR data of 18-membered acetonide **S28**; numbering scheme as shown in the insert

atom n°	**^{1}H NMR** (600 MHz, $CD_3OD/[D_5]$-pyridine 1:1 (v/v), referenced on CD_2HOD)					**^{13}C NMR** (151 MHz, $CD_3OD/[D_5]$-pyridine 1:1)	
	δ [ppm]	**m**	***J*** [Hz]	**COSY**	**NOESY**	**δ** [ppm]	**HMBC**
1	-	-	-	-	-	172.8	3, 17
2	3.99	d	6.7	3	3, 23	85.7	3, 4a, 5, 23
3	2.50	dh	8.7, 6.8	2, 4ab, 23	2, 4a, 5, 23	39.3	2, 4b, 23
4a	2.28	ddd	11.9, 7.3, 5.8	3, 4b, 5	3, 4b, 5	38.6	2, 3, 6, 23
4b	1.41	dt	11.9, 9.2	3, 4a, 5	3, 5, 6, 23		
5	4.09	ddd	9.4, 6.5, 5.7	4ab, 6	3, 4a, 6, 7, 10	81.8	2, 4b, 6, 7
6	3.72	dd	8.1, 6.5	5, 7	4b, 5, 7, 8, 27	83.1	4b, 7
7	4.71	ddd	9.3, 8.0, 1.0	6, 8	5, 6, 8, 10, 28	78.4	5, 9
8	5.64	ddd	11.0, 9.4, 1.2	7, 9	6, 7, 9	132.2	6, 10
9	6.56	td	11.0, 1.0	8, 10	8, 10	127.6	7
10	7.29	d	10.4	9	5, 7, 9, 13	123.4	8
11	-	-	-	-	-	137.6	9, 10, 12, 13
12	4.29	d	3.7	13	13, 14a	79.0	10, 14ab
13	4.79	ddd	9.4, 7.1, 3.7	12, 14ab	10, 12, 14b	82.0	14a
14a	2.31	ddd	13.4, 9.4, 5.3	13, 14b, 15	12, 14b, 15, 16	38.8	-
14b	2.16	ddd	13.4, 7.1, 1.7	13, 14a	13, 14a, 15		
15	4.43	ddd	5.2, 3.4, 1.7	14a, 16	14ab, 16, 17	73.0	14b, 17
16	3.87	dd	3.5, 1.9	15, 17	14a, 15, 17	85.6	18
17	5.77	dt	6.8, 1.6	16, 18	15, 16	75.1	16, 18, 19
18	6.09	ddd	15.7, 6.6, 1.3	17, 19	20, 24	125.5	16, 17, 20
19	5.79	ddd	15.6, 7.0, 1.3	18, 20	20, 24	139.0	17, 21ab, 24
20	2.55	heptd	6.5, 1.2	19, 21ab, 24	18, 19, 24	34.2	18, 19, 21ab, 24
21a	2.20	dd	15.1, 7.4	20, 21b	24	41.7	19, 20, 24
21b	2.13	dd	15.2, 7.1	20, 21a	24		
22	-	-	-	-	-	173.4	20, 21ab, 25
23	1.03	d	6.7	3	2, 3, 4b	18.7	2, 3, 4b
24	0.84	d	6.8	20	18, 19, 20, 21ab	20.0	19, 20, 21ab
25	3.49	s	-	-	-	51.8	-
26	-	-	-	-	-	110.3	27, 28
27	1.31	s	-	-	6, 28	27.6	28
28	1.20	s	-	-	7, 27	27.4	27

Table S-29. NMR data of 18-membered macrolactone **54db**; numbering scheme as shown in the insert

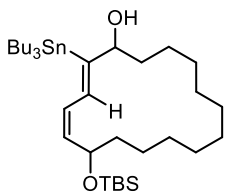
atom n°	^{1}H NMR (600 MHz, CD_3OD/[D_5]-pyridine 1:1 (v/v), referenced on CD_2HOD)				^{13}C NMR (151 MHz, CD_3OD/[D_5]-pyridine 1:1)	
	δ [ppm]	**m**	***J*** [Hz]	**COSY**	**δ** [ppm]	**HMBC**
1	-	-	-	-	172.6	17
2	4.09	d	5.9	3	86.1	4a, 23
3	2.51	ddqd	7.9, 7.5, 6.8, 5.9	2, 4ab, 23	38.8	2, 23
4a	2.37	ddd	12.1, 7.5, 6.3	3, 4b, 5	38.0	6, 23
4b	1.65	ddd	12.1, 8.9, 7.9	3, 4a, 5		
5	4.38	dt	8.9, 6.2	4ab, 6	82.7	2, 4b, 6, 7
6	3.87	t	6.2	5, 7	76.9	4b, 7
7	4.66	td	6.6, 1.4	6, 8	74.7	6, 9
8	5.83	ddd	11.7, 6.7, 1.1	7, 9	135.0	6, 7
9	6.57	ddd	11.6, 11.2, 1.4	8, 10	125.4	7
10	7.57	dd	10.9, 1.0	9	124.5	8, 12
11	-	-	-	-	137.2	9, 10, 13
12	4.22	d	6.5	13	78.8	10, 14ab
13	4.63	q	7.0	14ab	79.9	12, 14a
14a	2.34	ddd	13.7, 7.0, 5.4	13, 15	39.9	12
14b	2.22	ddd	13.7, 7.7, 1.6	13		
15	4.44	ddd	5.4, 3.5, 1.5	14a, 16	73.3	14b
16	3.80	dd	3.5, 1.7	15	84.8	13, 14b
17	5.77	dt	7.0, 1.4	18	74.8	18, 19
18	6.01	ddd	15.8, 7.1, 1.3	17, 19	125.4	17, 20
19	5.73	ddd	15.8, 7.1, 1.1	18, 20	139.4	17, 20, 21ab, 24
20	2.49	m	-	19, 21ab, 24	34.2	18, 21ab, 24
21a	2.15	dd	15.1, 7.3	20	41.7	19, 20, 24
21b	2.07	dd	15.1, 7.2	20		
22	-	-	-	-	173.4	20, 21ab, 25
23	1.06	d	6.8	3	19.2	2, 4b
24	0.79	d	6.8	20	20.0	19, 20, 21ab
25	3.47	s	-	-	51.7	-
4xOH	5.08	s	-	-	-	-

Table S-30. NMR data of 18-membered macrolactone **54aa**; numbering scheme as shown in the insert

atom n°	^{1}H NMR (600 MHz, CD_3OD/[D_5]-pyridine 1:1 (v/v), referenced on CD_2HOD)				^{13}C NMR (151 MHz, CD_3OD/[D_5]-pyridine 1:1)	
	δ [ppm]	**m**	***J*** [Hz]	**COSY**	**δ** [ppm]	**HMBC**
1	-	-	-	-	172.9	3, 17
2	4.00	d	6.4	3	86.7	4a, 23
3	2.46	m	-	2, 4ab, 23	39.3	2, 4a, 23
4a	2.16–2.21	m	-	3, 4b, 5	37.9	3, 23
4b	1.75	dt	12.0, 8.8	3, 4a, 5		
5	4.31	ddd	9.1, 6.3, 2.8	4ab, 6	83.0	2, 4b, 6
6	3.99	dd	2.8, 1.3	5, 7	78.5	-
7	4.92	dt	9.2, 1.3	6, 8	72.4	-
8	6.07	t	10.3	7, 9	134.1	7
9	6.49	td	11.2, 0.9	8, 10	124.4	7
10	7.35	d	11.3	9	121.1	-
11	-	-	-	-	137.2	9, 12
12	4.18	d	2.0	13	77.5	13
13	4.69	td	7.7, 1.7	14ab	77.3	-
14a	2.62	ddd	13.2, 7.8, 4.9	13, 14b, 15	38.3	-
14b	2.09	dd	13.2, 7.3	13, 14a		
15	4.44	dd	4.9, 2.8	14a, 16	73.4	14b
16	4.17	dd	9.0, 2.8	15, 17	86.5	13, 14b, 17
17	5.76	dd	9.1, 5.8	16	75.3	16, 18, 19
18	5.73	ddd	15.6, 5.6, 1.1	19	125.5	19, 20
19	5.82	ddd	15.5, 7.1, 0.9	18, 20	138.6	20, 21ab, 24
20	2.58	ddp	8.0, 7.5, 6.8	19, 21ab, 24	34.2	18, 19, 21ab, 24
21a	2.20	dd	15.2, 7.5	20	41.8	20, 24
21b	2.18	dd	15.1, 8.0	20		
22	-	-	-	-	173.4	20, 21ab, 25
23	0.97	d	6.7	3	18.8	2
24	0.87	d	6.7	20	19.9	19, 20, 21ab
25	3.49	s	-	-	51.7	-
4xOH	5.08	s	-	-	-	-

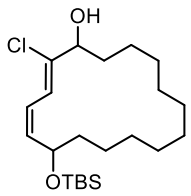
Synthesis of a Reference Compound

(2*Z*,4*Z*)-6-((*t*-Dimethylsilyl)oxy)-2-(tristannyl)cyclohexadeca-2,4-dien-1-ol (S37). A solution of Bu_3SnH (5.5 µL, 20 µmol) in CH_2Cl_2 (0.1 mL) was added dropwise over 90 min *via* syringe pump to a solution of (*Z*)-6-((t-dimethylsilyl)oxy)cyclohexadec-4-en-2-yn-1-ol (7.1 mg, 19 µmol) and $[Cp^*RuCl]_4$ (1.0 mg, 3.7 µmol, 19 mol%) in CH_2Cl_2 (0.1 mL). All volatiles were evaporated and the residue was purified by flash



chromatography (hexane/*t*-butyl methyl ether 19:1) to afford the title compound as a pale yellow oil (10 mg, 79%, *Z*/*E* > 20:1, α/β > 95:5). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.84 (d, *J* = 11.4 Hz, J_{SnH} = 115 Hz, 1H), 5.93 (dt, *J* = 11.2, 1,2 Hz, 1H), 5.42 (ddd, *J* = 11.2, 8.6, 1,1 Hz, 1H), 4.62 (q, *J* = 7.0 Hz, 1H), 4.24 (ddd, *J* = 9.6, 4.7, 2.9 Hz, 1H), 1.54–1.38 (m, 12H), 1.36–1.25 (m, 20H), 1.03–0.96 (m, 5H), 0.91–0.86 (m, 10H), 0.88 (s, 9H), 0.05 (s, 3H), 0.03 (s, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): *δ* = 155.4, 137.3, 135.1, 127.2, 81.1, 68.5, 37.23, 37.18, 29.4, 27.6, 27.5, 27.4, 27.2, 27.0, 26.6, 26.3, 26.1, 25.3, 24.3, 18.4, 13.9, 11.7, −4.0, −4.5 ppm. ^{119}Sn NMR (150 MHz, $CDCl_3$): *δ* = –53.5 ppm. IR (film): $\tilde{\nu}$ = 3481, 2954, 2926, 2855, 1462, 1251, 1071, 1005, 836, 775, 676 cm^{-1}. MS (EI) *m/z* (%): 599 (13), 597 (12), 468 (14), 467 (57), 466 (25), 265 (45), 464 (19), 463 (25), 365 (47), 364 (19), 363 (35), 362 (14), 361 (19), 281 (11), 251 (16), 249 (13), 218 (18), 217 (100), 195 (12), 193 (11), 179 (12), 177 (17), 175 (12), 135 (35), 121 (34), 107 (12), 95 (16), 93 (21), 91 (12), 81 (16), 79 (16), 75 (24), 73 (13), 67 (17). HRMS (ESIneg): *m/z* calcd for $C_{34}H_{67}O_2SiSn$ [M−H]$^-$: 655.3937, found: 655.3946.

(*Z*,*Z*)-Chlorodiene 59. A solution of dienylstannane **S37** (9.7 mg, 15 µmol) in THF (0.2 mL) was added

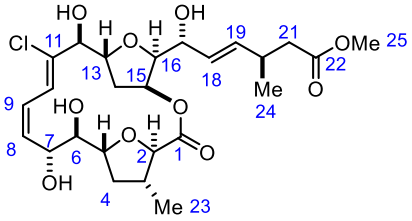


to a suspension of copper(II) chloride (5.0 mg, 37 µmol) in THF (0.15 mL). The resulting mixture was stirred at ambient temperature for 24 h. The mixture was diluted with *t*-butyl methyl ether (2.5 mL) and the reaction was quenched with sat. $NaHCO_3$ (3 mL). The aq. phase was extracted with *t*-butyl methyl ether (3 × 4 mL). The combined organic phases were washed with brine (5 mL), dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography (hexane/*t*-butyl methyl ether 15:1 to 10:1) to afford the title compound (4.0 mg, 67%) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 6.41 (dd, *J* = 11.0, 0.9 Hz, 1H), 6.30 (td, *J* = 11.0, 1.3 Hz, 1H), 5.64 (ddd, *J* = 11.0, 8.4, 0.9 Hz, 1H), 4.49 (dddd, *J* = 8.3, 7.2, 5.6, 1.3 Hz, 1H), 4.33 (dd, *J* = 10.2, 4.6 Hz, 1H), 1.93–1.78 (m, 2H), 1.71–1.65 (m, 1H), 1.53–1.49 (m, 1H), 1.45–1.40 (m, 1H), 1.38–1.30 (m, 11H), 1.23–1.07 (m, 4H), 0.88 (s, 9H), 0.05 (s, 3H), 0.03 (s, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): *δ* = 140.6, 137.4, 122.0, 121,1, 75.4, 69.2, 37.1, 34.7, 27.6, 27.5, 27.1, 26.9, 26.3, 26.0, 25.9, 25.2, 24.2, 18.3, –4.1, –4.6 ppm. IR (film): $\tilde{\nu}$ = 3368, 2927, 2856, 1727, 1461, 1360, 1251, 1074, 835, 775, 734, 663, 584 cm^{-1}. MS (ESIpos) *m/z* (%): 423.2 (100 (M+Na)). HRMS (ESIpos): *m/z* calcd for $C_{22}H_{41}O_2ClSiNa$ [M+Na$^+$]: 423.2457, found: 423.2453.

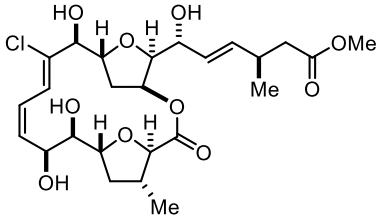
NMR Comparison

^{1}H-NMR Data

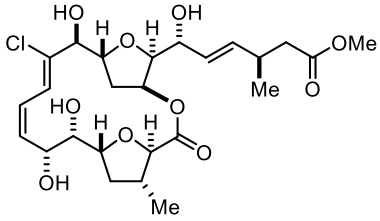
Table S-31. Comparison of ^{1}H-NMR shifts of **2xa**-series with methyl ester of chagosensine.[20]



2aa



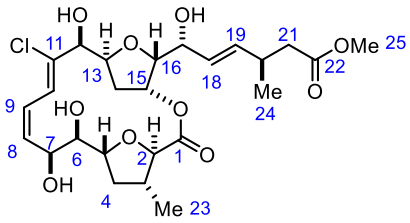
2ba



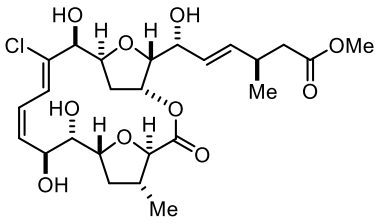
2da

atom n°	methyl ester of chagosensine	**2aa**	**2ba**	**2da**
2	4.38	4.09	3.99	3.77
3	2.38	2.53	2.42	2.19
4a	2.14	2.22	1.99	2.00
4b	1.96	1.35	1.89	1.40
5	4.19	3.77	4.07	3.46
6	4.03	4.02	3.45	3.71
7	4.31	4.66	4.78	4.19
8	5.93	6.07	5.71	5.60
9	6.17	6.35	6.42	6.30
10	6.42	6.93	7.19	6.76
12	4.42	4.32	4.33	4.29
13	4.15	4.28	4.46	4.19
14a	2.14	1.73	2.00	2.19
14b	1.58	1.67	1.79	1.85
15	5.08	5.40	5.39	5.42
16	4.20	4.20	4.10	4.19
17	4.52	4.54	4.42	4.47
18	5.52	5.55	5.53	5.53
19	5.71	5.81	5.73	5.83
20	2.75	2.54	2.58	2.56
21a	2.45	2.18	2.24	2.19
21b	2.33	2.15	2.18	2.19
23	0.98	0.83	0.96	0.92
24	1.08	0.85	0.90	0.90
25	3.67	3.46	3.51	3.52

Table S-32. Comparison of ^{1}H-NMR shifts of **2xb**-series with methyl ester of chagosensine.[20]



2bb

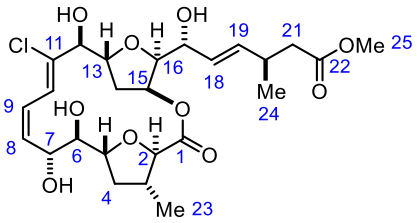


2cb

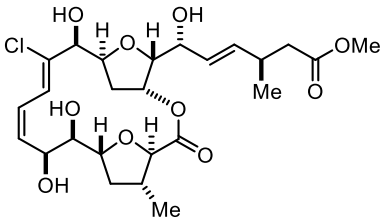
atom n°	methyl ester of chagosensine	**2bb**	**2cb**
2	4.38	4.00	4.01
3	2.38	2.66	2.60
4a	2.14	1.99	2.47
4b	1.96	1.98	1.63
5	4.19	3.86	3.66
6	4.03	4.39	3.86
7	4.31	4.74	4.91
8	5.93	5.56	5.99
9	6.17	6.41	6.45
10	6.42	6.61	6.65
12	4.42	4.86	4.86
13	4.15	4.50	4.56
14a	2.14	2.24	2.60
14b	1.58	1.86	1.82
15	5.08	5.55	5.53
16	4.20	4.07	4.07
17	4.52	4.50	4.52
18	5.52	5.84	5.82
19	5.71	5.84	5.85
20	2.75	2.66	2.65
21a	2.45	2.28	2.27
21b	2.33	2.18	2.17
23	0.98	0.90	0.87
24	1.08	0.93	0.93
25	3.67	3.51	3.51

^{13}C-NMR Data

Table S-33. Comparison of ^{13}C-NMR shifts of **2aa** and **2bb** with methyl esters of chagosensine.[20] Color code: $\Delta\delta \leq$ 0.5 ppm; 0.5 < $\Delta\delta$ < 1.0 ppm; $\Delta\delta \geq$ 1.0 ppm



2aa



2bb

atom n°	methyl ester of chagosensine	**2aa**	**Δδ**	**2bb**	**Δδ**
1	170.5	171.3	–0.8	172.7	–2.2
2	**80.8**	**87.1**	**–6.3**	**85.4**	**–4.6**
3	36.6	36.4	0.2	35.1	1.5
4	38.0	38.9	–0.9	37.3	0.7
5	**72.4**	**81.7**	**–9.3**	**80.5**	**–8.1**
6	75.5	81.8	–6.3	75.2	0.3
7	72.0	71.5	0.5	70.1	1.9
8	133.6	137.2	–3.6	134.3	–0.7
9	128.2	123.6	4.6	126.1	2.1
10	126.9	123.2	3.7	121.5	5.4
11	136.2	137.1	–0.9	138.3	–2.1
12	**61.3**	**79.5**	**–18.2**	**70.0**	**–8.7**
13	**70.7**	**85.5**	**–14.8**	**69.5**	1.2
14	32.9	39.0	–6.1	32.4	0.5
15	72.7	76.4	–3.7	76.9	–4.2
16	81.8	86.9	–5.1	85.5	–3.7
17	**67.2**	**72.1**	**–4.9**	**76.6**	**–9.4**
18	128.5	128.9	–0.4	131.5	–3.0
19	133.4	138.0	–4.6	135.7	–2.3
20	31.2	34.0	–2.8	33.9	–2.7
21	40.2	41.8	–1.6	41.8	–1.6
22	172	173.2	–1.2	173.4	–1.4
23	14.8	19.5	–4.7	17.3	–2.5
24	19.5	20.4	–0.9	20.2	–0.7
25	51.2	51.8	–0.6	51.4	–0.2

Coupling Pattern within the THF Rings & Comparison with Reference Compounds

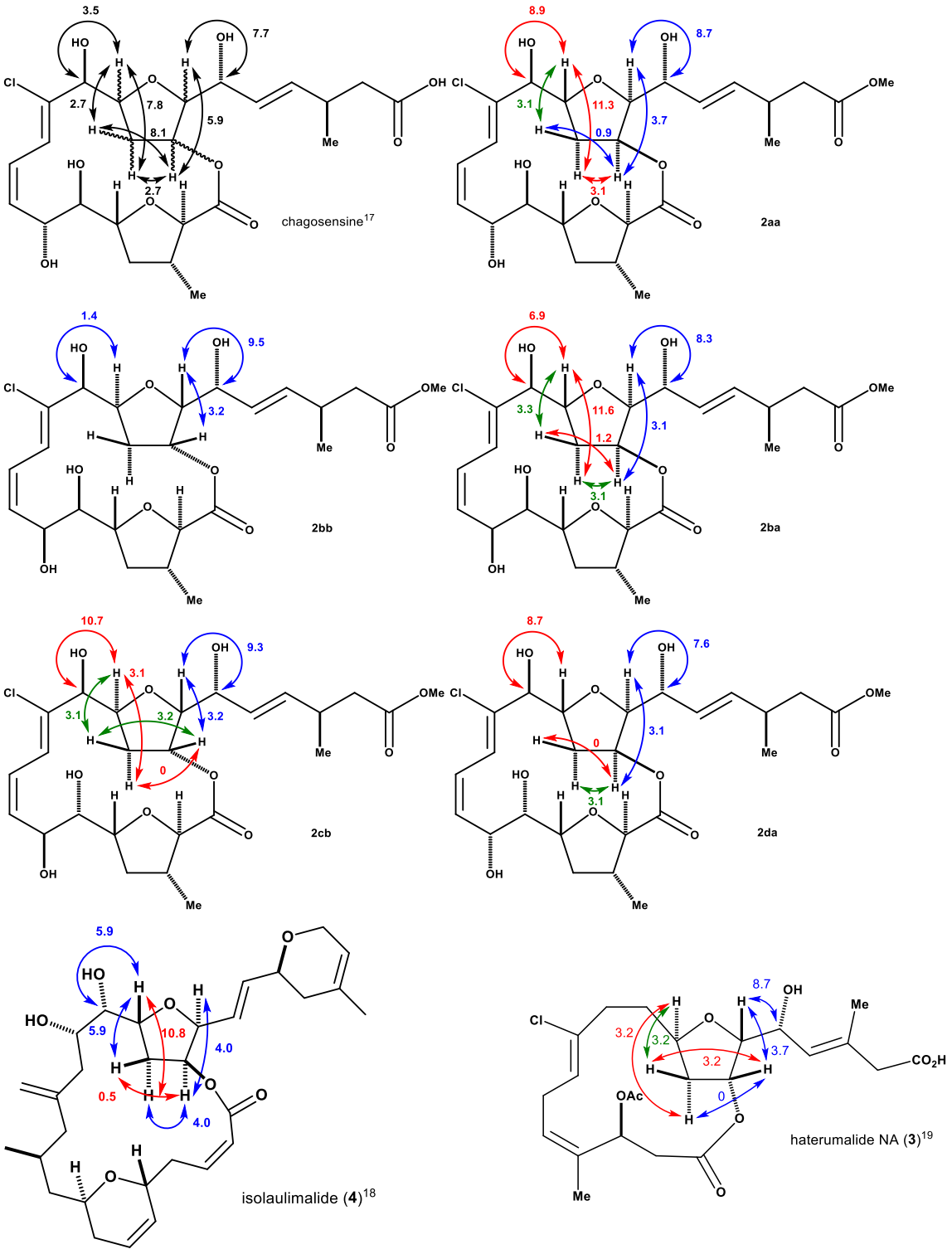


Figure S-8. Comparison of the *J*-Couplings of the northern THF-ring. Color code: ***J*** **≤ 1.0 Hz**; **1.0 < Δ*J*** **< 3.0 Hz**; **Δ*J*** **≥ 3.0 Hz**.[20-22]

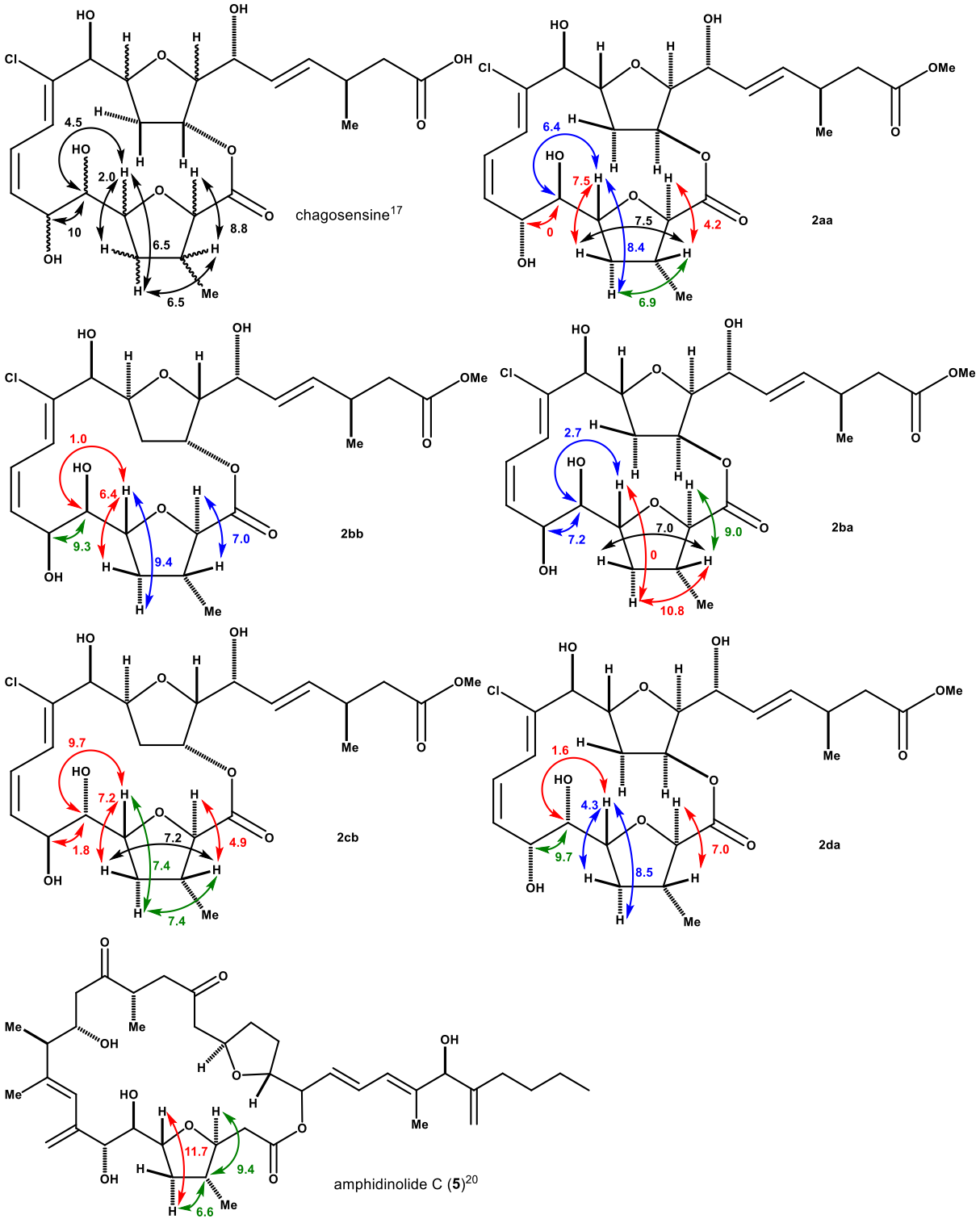


Figure S-9. Comparison of the *J*-Couplings of the southern part. Color code: $J \leq 1.0$ Hz; $1.0 < \Delta J < 3.0$ Hz; $\Delta J \geq 3.0$ Hz.[20, 23]

NOESY Cross Peaks along the Macrocyclic Framework

Comparison of chagosensine with methyl ester **2aa** and **2bb** and the stable macrocycles **10ba**, **10da** and **10ab**, **10bb**, **10bd**.

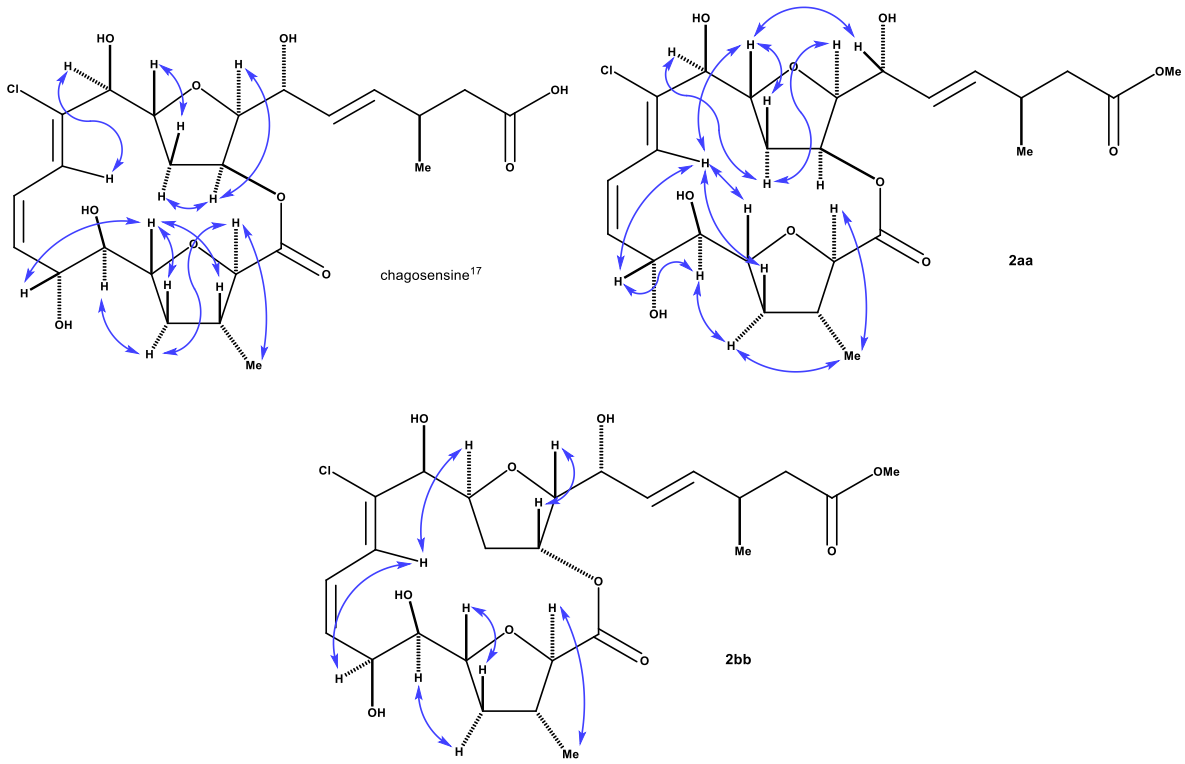


Figure S-10. Comparison of observed correlations in the isolated natural product reported by the isolation team with NOESY correlations of methyl esters **2aa** and **2bb**.[20]

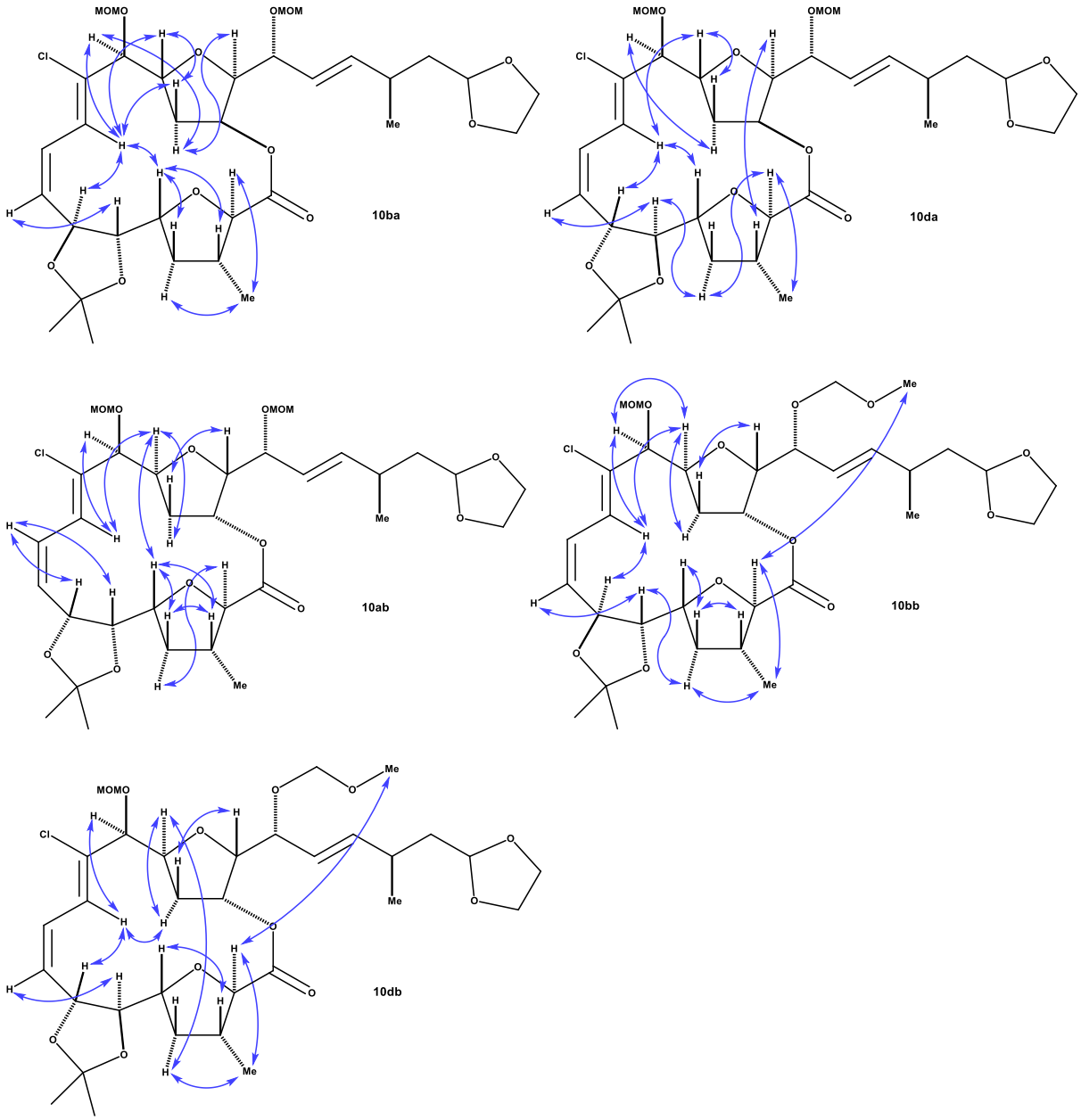
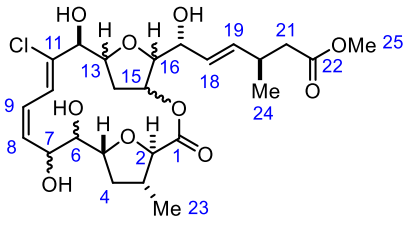


Figure S-11. NOe correlations of stable macrolactones **10ba**, **10da**, **10ab**, **10bb**, **10db**, which were subject to solvolysis and/or ring expansion upon global protection.

Detailed Analysis of ^{1}H-NMR Data

Comparison of methyl ester of chagosensine as reported in the literature with synthetic methyl esters **2aa**, **2ba**, **2da**, **2bb**, **2cb**.[20]



atom number	**methyl ester of chagosensine (reference signal missing)**	**2aa (CD_2HOD as reference)**
2	4.38 (d, $J_{(2-3)}$ = 8.8 Hz, 1H)	4.09 (d, $J_{(2-3)}$ = 4.2 Hz, 1H)
3	2.38 (m, 1 H)	2.53 (m, 2H)
4a	2.14 (dt, $J_{(4a-4b)}$ = 11.8, $J_{(4a-3)}$ = $J_{(4a-5)}$ = 6.5 Hz, 1H)	2.22 (dt, $J_{(4a-4b)}$ = 12.3, $J_{(4a-3)}$ = $J_{(4a-5)}$ = 7.5 Hz, 1H)
4b	1.96 (m, 1 H)	1.35 (ddd, $J_{(4b-4a)}$ = 12.3, $J_{(4b-5)}$ = 8.4, $J_{(4b-3)}$ = 6.0 Hz, 1H)
5	4.19 (ddd, $J_{(5-4a)}$ = 6.5, $J_{(5-6)}$ = 4.5, $J_{(5-4b)}$ = 2.0 Hz, 1H)	3.77 (dt, $J_{(5-4b)}$ = 8.4, $J_{(5-4a)}$ = 7.5, $J_{(5-6)}$ = 6.0 Hr, 1H)
6	4.03 (dd, $J_{(6-7)}$ = 10.0, $J_{(6-5)}$ = 4.5 Hz, 1H)	4.02 (d, $J_{(6-5)}$ = 6.4 Hz, 1H)
7	4.31 (dd, $J_{(7-6)}$ = 10,0, $J_{(7-8)}$ = 8,1 Hz, 1H)	4.66 (d, $J_{(7-8)}$ = 8.7 Hz, 1H)
8	5.93 (dd, $J_{(8-9)}$ = 10.9, $J_{(8-7)}$ = 8.1 Hz, 1H)	6.07 (ddd, $J_{(8-9)}$ = 11.3, $J_{(8-7)}$ = 8.8, $J_{(8-10)}$ = 0.9 Hz, 1H)
9	6.17 (dd, $J_{(9-8)}$ = 10.9, $J_{(9-10)}$ = 7.7 Hz, 1H)	6.35 (td, $J_{(9-8)}$ = $J_{(9-10)}$ = 11.2, $J_{(9-7)}$ = 1.2 Hz, 1H)
10	6.42 (d, $J_{(10-9)}$ = 7.7 Hz, 1H)	6.93 (dd, $J_{(10-9)}$ = 10.9, $J_{(10-8)}$ = 0.9 Hz, 1H)
12	4.42 (d, $J_{(12-13)}$ = 3.5 Hz, 1H)	4.32 (d, $J_{(12-13)}$ = 9.0 Hz, 1H)
13	4.15 (ddd, $J_{(13-14b)}$ = 7.8, $J_{(13-12)}$ = 3.5, $J_{(13-14a)}$ = 2.7 Hz, 1H)	4.28 (ddd, $J_{(13-14a)}$ = 11.3 , $J_{(13-12)}$ = 9.0, $J_{(13-14b)}$ = 3.1 Hz, 1H)
14a	2.14 (dt, $J_{(14a-14b)}$ = 12.3, $J_{(14a-13)}$ = $J_{(14a-15)}$ = 2.7 Hz, 1H)	1.73 (ddd, $J_{(14a-14b)}$ = 12.7, $J_{(14a-13)}$ = 11.3, $J_{(14a-15)}$ = 3.1 Hz, 1H)
14b	1.58 (m, 1 H)	1.67 (ddd, $J_{(14b-14a)}$ = 12.8, $J_{(14b-13)}$ = 3.1, $J_{(14b-15)}$ = 0.6 Hz, 1H)
15*	5.08 (ddd, $J_{(15-14b)}$ = 8.1, $J_{(15-16)}$ = 5.9, $J_{(15-14a)}$ = 2.9 Hz, 1H)	5.40 (m, 1H)
16	4.20 (dd, $J_{(16-17)}$ = 7.7, $J_{(16-15)}$ = 5.9 Hz, 1H)	4.20 (dd, $J_{(16-17)}$ = 8.7, $J_{(16-15)}$ = 3.7 Hz, 1H)
17	4.52 (dd, $J_{(17-16)}$ = 7.7, $J_{(17-18)}$ = 6.1 Hz, 1H)	4.54 (dd, $J_{(17-16)}$ = 8.7, $J_{(17-18)}$ = 6.8 Hz, 1H)
18	5.52 (dd, $J_{(18-19)}$ = 15.0, $J_{(18-17)}$ = 6.1 Hz, 1H)	5.55 (ddd, $J_{(18-19)}$ = 15.5, $J_{(18-17)}$ = 6.8, $J_{(18-20)}$ = 1.2 Hz, 1H)
19	5.71 (dd, $J_{(19-18)}$) = 15.0, $J_{(19-20)}$ = 7.8 Hz, 1H)	5.60 (ddd, $J_{(19-18)}$) = 15.5, $J_{(19-20)}$ = 7.3, $J_{(19-17)}$ = 1.1 Hz, 1H)
20	2.75 (m, 1H)	2.54 (m, 2H)
21a	2.33 (dd, $J_{(21a-21b)}$ = 16, $J_{(21a-20)}$ = 5 Hz, 1H)	2.18 (dd, $J_{(21a-21b)}$ = 15.1, $J_{(21a-20)}$ = 7.5 Hz, 1H)
21b	2.45 (dd, $J_{(21b-21a)}$ = 16, $J_{(21b-20)}$ = 10 Hz, 1H)	2.15 (dd, $J_{(21b-21a)}$ = 15.1, $J_{(21b-20)}$ = 6.9 Hz, 1H)
23	0.98 (d, $J_{(23-3)}$ = 6.6 Hz, 3H)	0.83 (d, $J_{(23-3)}$ = 6.9 Hz, 3H)
24	1.08 (d, $J_{(24-20)}$ = 6.5 Hz, 3H)	0.85 (d, $J_{(24-20)}$ = 6.8 Hz, 3H)
25	3.67 (s, 3H)	3.46 (s, 3H)

atom number	**methyl ester of chagosensine (reference signal missing)**	**2ba (CD_2HOD as reference)**
2	4.38 (d, $J_{(2-3)}$ = 8.8 Hz, 1H)	3.99 (d, $J_{(2-3)}$ = 9.0 Hz, 1H)
3	2.38 (m, 1 H)	2.42 (ddp, $J_{(3-4b)}$ = 11.2, $J_{(2-3)}$ = 9.0, $J_{(3-4a)}$ = $J_{(3-23)}$ = 7.0 Hz, 1H)
4a	2.14 (dt, $J_{(4a-4b)}$ = 11.8, $J_{(4a-3)}$ = $J_{(4a-5)}$ = 6.5 Hz, 1H)	1.99 (m, 2H)
4b	1.96 (m, 1 H)	1.89 (ddd, $J_{(4b-4a)}$ = $J_{(4b-3)}$ = 10.8, 1H)
5	4.19 (ddd, $J_{(5-4a)}$ = 6.5, $J_{(5-6)}$ = 4.5, $J_{(5-4b)}$ = 2.0 Hz, 1H)	4.09-4.05 (m, 1H)
6	4.03 (dd, $J_{(6-7)}$ = 10.0, $J_{(6-5)}$ = 4.5 Hz, 1H)	4.45 (dd, $J_{(6-7)}$ = 7.2, $J_{(6-5)}$ = 2.7 Hz, 1H)
7	4.31 (dd, $J_{(7-6)}$ = 10,0, $J_{(7-8)}$ = 8,1 Hz, 1H)	4.82-4.75 (m, 1H)
8	5.93 (dd, $J_{(8-9)}$ = 10.9, $J_{(8-7)}$ = 8.1 Hz, 1H)	5.71 (dd, $J_{(8-9)}$ = 11.4, $J_{(8-7)}$ = 7.6 Hz, 1H)
9	6.17 (dd, $J_{(9-8)}$ = 10.9, $J_{(9-10)}$ = 7.7 Hz, 1H)	6.42 (ddd, $J_{(9-8)}$ = 11.5, $J_{(9-10)}$ = 10.5 Hz, $J_{(9-7)}$ = 1.2 Hz, 1H)
10*	6.42 (d, $J_{(10-9)}$ = 7.7 Hz, 1H)	7.17-7.20 (m, 1H)
12	4.42 (d, $J_{(12-13)}$ = 3.5 Hz, 1H)	4.33 (d, $J_{(12-13)}$ = 6.9 Hz, 1H)
13	4.15 (ddd, $J_{(13-14b)}$ = 7.8, $J_{(13-12)}$ = 3.5, $J_{(13-14a)}$ = 2.7 Hz, 1H)	4.46 (ddd, $J_{(13-14a)}$ = 11.6 , $J_{(13-12)}$ = 6.8, $J_{(13-14b)}$ = 3.3 Hz, 1H)
14a	2.14 (dt, $J_{(14a-14b)}$ = 12.3, $J_{(14a-13)}$ = $J_{(14a-15)}$ = 2.7 Hz, 1H)	2.04-1.94 (m, 2H)
14b	1.58 (m, 1 H)	1.79 (td, $J_{(14b-14a)}$ = $J_{(14b-13)}$ = 12.2, $J_{(14b-15)}$ = 3.0 Hz, 1H)
15*	5.08 (ddd, $J_{(15-14b)}$ = 8.1, $J_{(15-16)}$ = 5.9, $J_{(15-14a)}$ = 2.9 Hz, 1H)	5.39 (td, $J_{(15-14a)}$ = $J_{(15-16)}$ = 3.1, $J_{(15-14b)}$ = 1.2 Hz, 1H)
16	4.20 (dd, $J_{(16-17)}$ = 7.7, $J_{(16-15)}$ = 5.9 Hz, 1H)	4.10 (dd, $J_{(16-17)}$ = 8.7, $J_{(16-15)}$ = 3.4 Hz, 1H)
17	4.52 (dd, $J_{(17-16)}$ = 7.7, $J_{(17-18)}$ = 6.1 Hz, 1H)	4.42 (ddd, $J_{(17-16)}$ = 8.3, $J_{(17-18)}$ = 7.1, $J_{(17-18)}$ = 1.0 Hz, 1H)
18	5.52 (dd, $J_{(18-19)}$ = 15.0, $J_{(18-17)}$ = 6.1 Hz, 1H)	5.53 (ddd, $J_{(18-19)}$ = 15.5, $J_{(18-17)}$ = 7.1, $J_{(18-20)}$ = 1.2 Hz, 1H)
19	5.71 (dd, $J_{(19-18)}$) = 15.0, $J_{(19-20)}$ = 7.8 Hz, 1H)	5.73 (ddd, $J_{(19-18)}$) = 15.5, $J_{(19-20)}$ = 7.3, $J_{(19-17)}$ = 1.0 Hz, 1H)
20	2.75 (m, 1H)	2.58 (tdq, $J_{(20-19)}$ = $J_{(20-21a)}$ = 7.3, $J_{(20-21a)}$ = 7.1, $J_{(20-24)}$ = 6.9 Hz, 1H)
21a	2.33 (dd, $J_{(21a-21b)}$ = 16, $J_{(21a-20)}$ = 5 Hz, 1H)	2.24 (dd, $J_{(21a-21b)}$ = 15.2, $J_{(21a-20)}$ = 7.3 Hz, 1H)
21b	2.45 (dd, $J_{(21b-21a)}$ = 16, $J_{(21b-20)}$ = 10 Hz, 1H)	2.18 (dd, $J_{(21b-21a)}$ = 15.2, $J_{(21b-20)}$ = 7.1 Hz, 1H)
23	0.98 (d, $J_{(23-3)}$ = 6.6 Hz, 3H)	0.96 (d, $J_{(23-3)}$ = 6.6 Hz, 3H)
24	1.08 (d, $J_{(24-20)}$ = 6.5 Hz, 3H)	0.90 (d, $J_{(24-20)}$ = 6.8 Hz, 3H)
25	3.67 (s, 3H)	3.51 (s, 3H)

atom number	**methyl ester of chagosensine (reference signal missing)**	**2da (CD_2HOD as reference)**
2	4.38 (d, $J_{(2-3)}$ = 8.8 Hz, 1H)	3.77 (d, $J_{(2-3)}$ = 7.0 Hz, 1H)
3	2.38 (m, 1 H)	2.21-2.16 (m, 4H)
4a	2.14 (dt, $J_{(4a-4b)}$ = 11.8, $J_{(4a-3)}$ = $J_{(4a-5)}$ = 6.5 Hz, 1H)	2.01-1.97 (m, 1H)
4b	1.96 (m, 1 H)	1.42-1.38 (m, 1H)
5	4.19 (ddd, $J_{(5-4a)}$ = 6.5, $J_{(5-6)}$ = 4.5, $J_{(5-4b)}$ = 2.0 Hz, 1H)	3.46 (dd, J = 8.5, J = 4.3, 1H)
6	4.03 (dd, $J_{(6-7)}$ = 10.0, $J_{(6-5)}$ = 4.5 Hz, 1H)	3.71 (dd, J = 9.7, J = 1.6 Hz, 1H)
7	4.31 (dd, $J_{(7-6)}$ = 10,0, $J_{(7-8)}$ = 8,1 Hz, 1H)	4.22-4.16 (m, 3H)
8	5.93 (dd, $J_{(8-9)}$ = 10.9, $J_{(8-7)}$ = 8.1 Hz, 1H)	5.60 (ddd, $J_{(8-9)}$ = 11.6, $J_{(8-7)}$ = 8.6, $J_{(8-10)}$ = 1.0 Hz, 1H)
9	6.17 (dd, $J_{(9-8)}$ = 10.9, $J_{(9-10)}$ = 7.7 Hz, 1H)	6.35 (t, $J_{(9-8)}$ = $J_{(9-10)}$ = 11.1, 1H)
10	6.42 (d, $J_{(10-9)}$ = 7.7 Hz, 1H)	6.76 (d, $J_{(10-9)}$ = 10.9 Hz, 1H)
12	4.42 (d, $J_{(12-13)}$ = 3.5 Hz, 1H)	4.29 (d, $J_{(12-13)}$ = 8.7 Hz, 1H)
13	4.15 (ddd, $J_{(13-14b)}$ = 7.8, $J_{(13-12)}$ = 3.5, $J_{(13-14a)}$ = 2.7 Hz, 1H)	4.22-4.16 (m, 3H)
14a	2.14 (dt, $J_{(14a-14b)}$ = 12.3, $J_{(14a-13)}$ = $J_{(14a-15)}$ = 2.7 Hz, 1H)	2.21-2.16 (m, 4H)
14b	1.58 (m, 1 H)	1.87-1.83 (m, 1H)
15	5.08 (ddd, $J_{(15-14b)}$ = 8.1, $J_{(15-16)}$ = 5.9, $J_{(15-14a)}$ = 2.9 Hz, 1H)	5.42 (t, $J_{(15-14a)}$ = $J_{(15-16)}$ = 3.1, 1H)
16	4.20 (dd, $J_{(16-17)}$ = 7.7, $J_{(16-15)}$ = 5.9 Hz, 1H)	4.22-4.16 (m, 3H)
17	4.52 (dd, $J_{(17-16)}$ = 7.7, $J_{(17-18)}$ = 6.1 Hz, 1H)	4.47 (t, $J_{(17-16)}$ = $J_{(17-18)}$ = 7.6 Hz, 1H)
18	5.52 (dd, $J_{(18-19)}$ = 15.0, $J_{(18-17)}$ = 6.1 Hz, 1H)	5.54 (ddd, $J_{(18-19)}$ = 15.7, $J_{(18-17)}$ = 7.3, $J_{(18-20)}$ = 1.3 Hz, 1H)
19	5.71 (dd, $J_{(19-18)}$) = 15.0, $J_{(19-20)}$ = 7.8 Hz, 1H)	5.83 (dd, $J_{(19-18)}$ = 15.7, $J_{(19-20)}$ = 7.4, $J_{(19-17)}$ = 1.0 Hz, 1H)
20	2.75 (m, 1H)	2.58-2.50 (m, 2H)
21a	2.33 (dd, $J_{(21a-21b)}$ = 16, $J_{(21a-20)}$ = 5 Hz, 1H)	2.21-2.16 (m, 4H)
21b	2.45 (dd, $J_{(21b-21a)}$ = 16, $J_{(21b-20)}$ = 10 Hz, 1H)	2.21-2.16 (m, 4H)
23	0.98 (d, $J_{(23-3)}$ = 6.6 Hz, 3H)	0.92 (d, $J_{(23-3)}$ = 6.6 Hz, 3H)
24	1.08 (d, $J_{(24-20)}$ = 6.5 Hz, 3H)	0.90 (d, $J_{(24-20)}$ = 6.8 Hz, 3H)
25	3.67 (s, 3H)	3.52 (s, 3H)

atom number	**methyl ester of chagosensine (reference signal missing)**	**2bb (CD_2HOD as reference)**
2	4.38 (d, $J_{(2-3)}$ = 8.8 Hz, 1H)	4.00 (d, $J_{(2-3)}$ = 7.0 Hz, 1H)
3	2.38 (m, 1 H)	2.70-2.62 (m, 2H)
4a	2.14 (dt, $J_{(4a-4b)}$ = 11.8, $J_{(4a-3)}$ = $J_{(4a-5)}$ = 6.5 Hz, 1H)	2.00-1.97 (m, 2H)
4b	1.96 (m, 1 H)	2.00-1.97 (m, 2H)
5	4.19 (ddd, $J_{(5-4a)}$ = 6.5, $J_{(5-6)}$ = 4.5, $J_{(5-4b)}$ = 2.0 Hz, 1H)	3.86 (ddd, $J_{(5-4)}$ = 9.4, $J_{(5-4)}$ = 6.4, $J_{(5-6)}$ = 1.0 Hz, 1H)
6	4.03 (dd, $J_{(6-7)}$ = 10.0, $J_{(6-5)}$ = 4.5 Hz, 1H)	3.39 (dd, $J_{(6-7)}$ = 9.3, $J_{(6-5)}$ = 1.0 Hz, 1H)
7	4.31 (dd, $J_{(7-6)}$ = 10,0, $J_{(7-8)}$ = 8,1 Hz, 1H)	4.74 (dd, $J_{(7-8)}$ = 10.2, $J_{(7-6)}$ = 9.0 Hz, 1H)
8	5.93 (dd, $J_{(8-9)}$ = 10.9, $J_{(8-7)}$ = 8.1 Hz, 1H)	5.57-5.53 (m, 2H)
9	6.17 (dd, $J_{(9-8)}$ = 10.9, $J_{(9-10)}$ = 7.7 Hz, 1H)	6.43-6.38 (m, 1H)
10	6.42 (d, $J_{(10-9)}$ = 7.7 Hz, 1H)	6.61 (dt, $J_{(10-9)}$ = 10.1, $J_{(10-8)}$ = $J_{(10-12)}$ = 1.4 Hz, 1H)
12	4.42 (d, $J_{(12-13)}$ = 3.5 Hz, 1H)	4.86 (d, $J_{(12-10)}$ = 1.4 Hz, 1H)
13	4.15 (ddd, $J_{(13-14b)}$ = 7.8, $J_{(13-12)}$ = 3.5, $J_{(13-14a)}$ = 2.7 Hz, 1H)	4.53-4.48 (m, 2H)
14a	2.14 (dt, $J_{(14a-14b)}$ = 12.3, $J_{(14a-13)}$ = $J_{(14a-15)}$ = 2.7 Hz, 1H)	2.26-2.22 (m, 1H)
14b	1.58 (m, 1 H)	1.88-1.82 (m, 1H)
15	5.08 (ddd, $J_{(15-14b)}$ = 8.1, $J_{(15-16)}$ = 5.9, $J_{(15-14a)}$ = 2.9 Hz, 1H)	5.57-5.53 (m, 2H)
16	4.20 (dd, $J_{(16-17)}$ = 7.7, $J_{(16-15)}$ = 5.9 Hz, 1H)	4.07 (dd, $J_{(16-17)}$ = 9.5, $J_{(16-15)}$ = 3.2 Hz, 1H)
17	4.52 (dd, $J_{(17-16)}$ = 7.7, $J_{(17-18)}$ = 6.1 Hz, 1H)	4.53-4.48 (m, 1H)
18	5.52 (dd, $J_{(18-19)}$ = 15.0, $J_{(18-17)}$ = 6.1 Hz, 1H)	5.87-5.82 (m, 1H)
19	5.71 (dd, $J_{(19-18}$) = 15.0, $J_{(19-20)}$ = 7.8 Hz, 1H)	5.87-5.82 (m, 1H)
20	2.75 (m, 1H)	2.70-2.62 (m, 2H)
21a	2.33 (dd, $J_{(21a-21b)}$ = 16, $J_{(21a-20)}$ = 5 Hz, 1H)	2.28 (dd, $J_{(21a-21b)}$ = 15.0, $J_{(21a-20)}$ = 7.7 Hz, 1H)
21b	2.45 (dd, $J_{(21b-21a)}$ = 16, $J_{(21b-20)}$ = 10 Hz, 1H)	2.18 (dd, $J_{(21b-21a)}$ = 15.0, $J_{(21b-20)}$ = 6.9 Hz, 1H)
23	0.98 (d, $J_{(23-3)}$ = 6.6 Hz, 3H)	0.90 (d, $J_{(23-3)}$ = 6.7 Hz, 3H)
24	1.08 (d, $J_{(24-20)}$ = 6.5 Hz, 3H)	0.93 (d, $J_{(24-20)}$ = 6.7 Hz, 3H)
25	3.67 (s, 3H)	3.51 (s, 3H)

atom number	**methyl ester of chagosensine (reference signal missing)**	**2cb (CD_2HOD as reference)**
2	4.38 (d, $J_{(2-3)}$ = 8.8 Hz, 1H)	4.01 (d, $J_{(2-3)}$ = 4.9 Hz, 1H)
3	2.38 (m, 1 H)	2.64-2.56 (m, 2H)
4a	2.14 (dt, $J_{(4a-4b)}$ = 11.8, $J_{(4a-3)}$ = $J_{(4a-5)}$ = 6.5 Hz, 1H)	2.47 (dt, $J_{(4a-4b)}$ = 12.6, $J_{(4a-3)}$ = $J_{(4a-5)}$ = 7.2 Hz, 1H)
4b	1.96 (m, 1 H)	1.63 (dt, $J_{(4b-4a)}$ = 12.6, $J_{(4b-3)}$ = $J_{(4b-5)}$ = 7.4 Hz, 1H)
5	4.19 (ddd, $J_{(5-4a)}$ = 6.5, $J_{(5-6)}$ = 4.5, $J_{(5-4b)}$ = 2.0 Hz, 1H)	3.66 (dt, $J_{(5-6)}$ = 9.7, $J_{(5-4a)}$ = $J_{(5-4b)}$ = 7.3 Hz, 1H)
6	4.03 (dd, $J_{(6-7)}$ = 10.0, $J_{(6-5)}$ = 4.5 Hz, 1H)	3.86 (dd, $J_{(6-5)}$ = 9.8, $J_{(6-7)}$ = 1.8 Hz, 1H)
7	4.31 (dd, $J_{(7-6)}$ = 10,0, $J_{(7-8)}$ = 8,1 Hz, 1H)	4.91 (dd, $J_{(7-8)}$ = 10.1, $J_{(7-6)}$ = 1.4 Hz, 1H)
8	5.93 (dd, $J_{(8-9)}$ = 10.9, $J_{(8-7)}$ = 8.1 Hz, 1H)	6.01-5.96 (m, 1H)
9	6.17 (dd, $J_{(9-8)}$ = 10.9, $J_{(9-10)}$ = 7.7 Hz, 1H)	6.47-6.42 (m, 1H)
10	6.42 (d, $J_{(10-9)}$ = 7.7 Hz, 1H)	6.66-6.62 (m, 1H)
12	4.42 (d, $J_{(12-13)}$ = 3.5 Hz, 1H)	4.86 (d, $J_{(12-13)}$ = 10.7 Hz, 1H)
13	4.15 (ddd, $J_{(13-14b)}$ = 7.8, $J_{(13-12)}$ = 3.5, $J_{(13-14a)}$ = 2.7 Hz, 1H)	4.86 (dt, $J_{(13-12)}$ = 11.9, $J_{(13-14a)}$ = $J_{(13-14b)}$ = 3.1 Hz, 1H)
14a	2.14 (dt, $J_{(14a-14b)}$ = 12.3, $J_{(14a-13)}$ = $J_{(14a-15)}$ = 2.7 Hz, 1H)	2.64-2.56 (m, 2H)
14b	1.58 (m, 1 H)	1.82 (dd, $J_{(14b-14a)}$ = 13.1, $J_{(14-13)}$ = 3.5 Hz, 1H)
15	5.08 (ddd, $J_{(15-14b)}$ = 8.1, $J_{(15-16)}$ = 5.9, $J_{(15-14a)}$ = 2.9 Hz, 1H)	5.53 (t, $J_{(15-14a)}$ = $J_{(15-16)}$ = 3.2 Hz, 1H)
16	4.20 (dd, $J_{(16-17)}$ = 7.7, $J_{(16-15)}$ = 5.9 Hz, 1H)	4.07 (dd, $J_{(16-17)}$ = 9.3, $J_{(16-15)}$ = 3.4 Hz, 1H)
17	4.52 (dd, $J_{(17-16)}$ = 7.7, $J_{(17-18)}$ = 6.1 Hz, 1H)	4.52 (dd, $J_{(17-16)}$ = 9.3, $J_{(17-18)}$ = 4.8 Hz, 1H)
18	5.52 (dd, $J_{(18-19)}$ = 15.0, $J_{(18-17)}$ = 6.1 Hz, 1H)	5.82 (dd, $J_{(18-19)}$ = 15.6, $J_{(18-17)}$ = 4.8 Hz, 1H)
19	5.71 (dd, $J_{(19-18}$) = 15.0, $J_{(19-20)}$ = 7.8 Hz, 1H)	5.85 (dd, $J_{(19-18)}$ = 15.6, $J_{(19-20)}$ = 5.9 Hz, 1H)
20	2.75 (m, 1H)	2.65 (hept, $J_{(20-19)}$ = $J_{(20-21)}$ = $J_{(20-24)}$ = 7.4 Hz, 1H)
21a	2.33 (dd, $J_{(21a-21b)}$ = 16, $J_{(21a-20)}$ = 5 Hz, 1H)	2.27 (dd, $J_{(21a-21b)}$ = 15.0, $J_{(21a-20)}$ = 6.9 Hz, 1H)
21b	2.45 (dd, $J_{(21b-21a)}$ = 16, $J_{(21b-20)}$ = 10 Hz, 1H)	2.17 (dd, $J_{(21b-21a)}$ = 15.0, $J_{(21b-20)}$ = 7.7 Hz, 1H)
23	0.98 (d, $J_{(23-3)}$ = 6.6 Hz, 3H)	0.87 (d, $J_{(23-3)}$ = 6.9 Hz, 3H)
24	1.08 (d, $J_{(24-20)}$ = 6.5 Hz, 3H)	0.93 (d, $J_{(24-20)}$ = 6.7 Hz, 3H)
25	3.67 (s, 3H)	3.51 (s, 3H)

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