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Supporting Information

Molecular Editing and Assessment of the Cytotoxic Properties of Iejimalide and Progeny

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Evaluation of the Anti-Tumor Activity.

Monolayer proliferation assay: A modified propidium iodide assay was used to determine the cytotoxic activity of the compounds against human tumor cell lines. The test procedure has been described elsewhere.[1] The cell lines were established from patient-derived tumor xenografts passaged subcutaneously in nude mice, or were obtained from American Type Culture Collection, Rockville, MD, USA (PRXF 22RV1), or the National Cancer Institute, Bethesda, MD, USA (CXF HT29). Authenticity of all cell lines was proven by STR (short tandem repeat) analysis. All cells were grown at 37°C in a humidified atmosphere (95% air, 5% CO_2) in RPMI 1640 medium (PAA, Cölbe, Germany) supplemented with 10% fetal calf serum (PAA) and 0.1 mg·mL^{-1} gentamicin (PAA). Cell lines were incubated in 96 multi-well plates. Test compounds were added to the plates after one day at five concentrations in triplicate, and left for further four days. Inhibition of proliferation was determined by measuring the DNA content using an aqueous propidium iodide solution (7 µg·mL^{-1}). Fluorescence was measured using the Cytofluor 4000.

Colony formation assay: Effects of the test compounds on clonogenicity of tumor cells were investigated in a colony formation assay. Tumor xenografts were derived from patient tumors engrafted as a subcutaneously growing tumor in NMRI nu/nu mice obtained from Oncotest's breeding facility. Details of the test procedure have been described earlier.[1] Briefly, solid human tumor xenografts were removed from mice under sterile conditions, mechanically disaggregated and subsequently incubated with an enzyme cocktail consisting of collagenase type IV (41 U/mL), DNase I (125 U/mL), hyaluronidase type III (100 U/mL) and dispase II (1.0 U/mL) in RPMI 1640-Medium at 37°C for 45 minutes. Cells were passed through sieves of 200 μm and 50 μm mesh size and washed twice with sterile PBS-buffer. The percentage of viable cells was determined in a Neubauer-hemocytometer using trypan blue exclusion. The bottom layer consisted of 0.2 mL/well Iscove's Modified Dulbecco's Medium (IMDM, Invitrogen), supplemented with 20% (v/v) fetal calf serum (Sigma), 0.01% (w/v) gentamicin (Invitrogen) and 0.75% (w/v) agar (BD Biosciences). 1.5x10^4 to 4x10^4 cells were added to 0.2 mL of the same culture medium supplemented with 0.4% (w/v) agar and plated in 24-multiwell dishes onto the bottom layer. The test compounds were applied by continuous exposure (drug overlay) in 0.2 mL of culture medium. Every dish included six untreated control wells and drug-treated groups in triplicate at 6 concentrations. Cultures were incubated at 37°C and 7.5% CO_2 in a humidified atmosphere for 7–20 days and monitored closely for colony growth using an inverted microscope. Within this period, *in vitro* tumor growth led to the formation of colonies with a diameter of >50 µm. Colony counts were performed with an automatic image analysis system (OMNICON 3600, Biosys GmbH). 24 h prior to evaluation, vital colonies were stained with a sterile

[1] For a description of the assays, see: a) H. H. Fiebig, D. P. Berger, W. A. Dengler, E. Wallbrecher, B. R. Winterhalter in *Immunodeficient Mice in Oncology* (Eds.: D. P. Berger, H. H. Fiebig), *Contrib. Oncol.*, *Vol. 42*, Karger, Basel, **1992**, pp. 321-351; b) T. Roth, A. M. Burger, W. A. Dengler, H. Willmann, H. H. Fiebig, in *Relevance of Tumor Models for Anticancer Drug Development* (Eds.: H. H. Fiebig, A. M. Burger), *Contrib. Oncol.*, *Vol. 54*, Karger, Basel, **1999**, pp. 145-156; c) W. A. Dengler, J. Schulte, D. P. Berger, R. Mertelsmann, H. H. Fiebig, *Anti-Cancer Drugs* **1995**, *6*, 522-532; d) H. H. Fiebig, A. Maier, A. M. Burger, *Eur. J. Cancer* **2004**, 40, 802-820.

aqueous solution of 2-(4-iodophenyl)-3-(4-nitrophenyl)-5-phenyltetrazolium chloride (1 mg/mL, 100 μL/well).

***In vivo* evaluation in nude mice carrying tumor xenografts:** *In vivo* efficacy was determined in mice carrying human tumor xenografts. All experiments were conducted according to the guidelines of the German Animal Health and Welfare Act (Tierschutzgesetz). Animal health was examined at the day before tumor implantation and before randomization to ensure that only animals of good health were selected to enter testing procedures. The test procedure has been described elsewhere.[1] Briefly, tumor fragments of human tumor xenografts were implanted into the flanks of immune-deficient mice of NMRI nu/nu genetic background (Charles River, Sulzfeld, Germany). The fragments were obtained from tumors in serial passage, established either from direct implantation of patient material, or from injection of tumor cell lines obtained from National Cancer Institute, Bethesda, MD, USA. Tumor growth was assessed by serial calliper measurements of two perpendicular tumor diameters. Treatment was started when tumors were palpable and reached a median volume of ~100 mm^3, depending on tumor type. Each treatment group consisted of 4 mice. Animals with appropriate tumor volumes were randomly distributed into treatment and control groups (day 0). Tumor diameters and body weights were recorded twice weekly. For the evaluation of treatment efficacy, tumor volumes were calculated for each time point according to the formula (length x $width^2$)/2, and the median relative tumor volume was plotted the against time. Relative tumor volumes were calculated for each single tumor by dividing the tumor volume on day X by the initial tumor volume on day 0 at the time of randomization. A median body weight loss of >20% without recovery was considered not evaluable for anti-tumor efficacy. The U-Test by Mann-Whitney-Wilcoxon was used for the statistical analysis of the data based on median relative tumor volume parameters.

General: All reactions were carried out in flame-dried glassware under Ar. The solvents were purified by distillation over the drying agents indicated and were transferred under Ar: THF, Et_2O, 1,4-dioxane (Mg-anthracene), CH_2Cl_2 (P_4O_{10}), MeCN, Et_3N, pyridine, DMSO, EtOAc (CaH_2), MeOH (Mg), DMF (Desmodur®, dibutyltin dilaurate), hexane, toluene (Na/K). Flash chromatography: Merck silica gel 60 (230-400 mesh) or CombiFlash (Teledyne Isco). NMR: Spectra were recorded on a Bruker DPX 300, AV 400, or DMX 600 spectrometer in the solvents indicated; chemical shifts (δ) are given in ppm relative to TMS, coupling constants (*J*) in Hz. The solvent signals were used as references and the chemical shifts converted to the TMS scale ($CDCl_3$: $\delta_C \equiv 77.0$ ppm; residual $CHCl_3$ in $CDCl_3$: $\delta_H \equiv 7.24$ ppm; CD_2Cl_2: $\delta_C \equiv 53.8$ ppm; residual CH_2Cl_2 in CD_2Cl_2: $\delta_H \equiv 5.32$ ppm). IR: Magna IR750 (Nicolet) or spectrum One (Perkin Elmer) spectrometer, wavenumbers ($\tilde{\nu}$) in cm^{-1}. MS (EI): Finnigan MAT 8200 (70 eV), ESI-MS: ESQ3000 (Bruker), accurate mass determinations: Bruker APEX III FT-MS (7 T magnet) or MAT 95 (Finnigan). Melting points: Büchi melting point apparatus B-540 (corrected). Elemental analyses: H. Kolbe, Mülheim/Ruhr. Unless stated otherwise, commercially available compounds (Fluka, Lancaster, Aldrich) were used as received. The data of compound **8** and its precursors are contained in ref. 2.

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[2] A. Fürstner, C. Nevado, M. Waser, M. Tremblay, C. Chevrier, F. Teplý, C. Aïssa, E. Moulin, O. Müller, *J. Am. Chem. Soc*. **2007**, *129*, 9150-9161.

Building Blocks for the Phthalimide Route and the Biotinylated Analogue 24 (Scheme 3)

Alcohol S-1: A solution of $LiBHEt_3$ (1 M in THF, 55.2 mL, 55.2 mmol) was added dropwise at −78°C to a solution of ester **11** (5 g, 16.7 mmol)[3] in THF (167 mL). The cooling bath was removed and the mixture was slowly warmed to room temperature. The reaction was then cooled at 0°C and quenched with aq. sat. NH_4Cl (50 mL), the aqueous phase was extracted with EtOAc (3 × 10 mL), the combined organic layers were dried over $MgSO_4$, filtered and evaporated to give a crude colorless oil. Purification by flash chromatography, eluting with hexanes/EtOAc (1:1 → 0:1), afforded alcohol **S-1** as a white solid (4.5 g, quant.). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.74 (d, J = 15.1 Hz, 1H), 7.60–7.50 (m, 3H), 6.28 (s, 2H), 5.71 (s, 1H), 4.47 (d, J = 15.1 Hz, 1H), 4.00 (s, 2H), 3.91 (d, J = 15.1 Hz, 1H), 1.73 (s, 6H); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 170.2, 147.0, 139.7, 134.5, 134.2, 133.4, 131.6, 125.5, 125.1, 124.8, 121.7, 83.0, 69.4, 48.5, 15.8, 15.0; IR (film): $\tilde{\upsilon}$ = 3327, 2911, 2855, 1675, 1469, 1434, 1346, 1288, 1205, 1127, 1058, 1002, 919, 790, 746, 705 cm^{-1}; MS (EI): m/z (%): 273 (1, M^+), 255 (23), 222 (2), 196 (2), 182 (1), 163 (6), 150 (18), 133 (100), 106 (78), 91 (21), 77 (22); HRMS (ESI) m/z: calcd for $C_{16}H_{19}NO_3$ [M^+ +Na]: 296.12576, found: 296.12571.

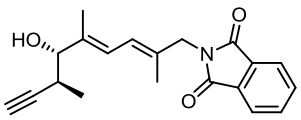
Aldehyde 12: MnO_2 (70 g, 824 mmol) was added to a solution of alcohol **S-1** (4.5 g, 16.48 mmol) in CH_2Cl_2 (200 mL) and the resulting suspension stirred for 18 h before it was filtered through a pad of Celite, which was carefully rinsed with CH_2Cl_2. Evaporation of the combined filtrates followed by purification of the residue by flash chromatography (hexanes/EtOAc, 6:1 → 4:1) gave aldehyde **12** as a white solid (3.4 g, 75%). Recrystallisation from CH_2Cl_2/hexanes at 0°C afforded colorless needles. M.p. = 150-152°C (CH_2Cl_2/hexanes); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 9.40 (s, 1H), 7.87–7.78 (m, 2H), 7.74–7.66 (m, 2H), 7.01 (d, J = 11.5 Hz, 1H), 6.44 (d, J = 11.5 Hz, 1H), 4.33 (s, 2H), 1.91 (s, 3H), 1.74 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 194.9, 167.9, 143.1, 142.5, 137.9, 134.2, 131.7, 123.4, 122.1, 45.0, 15.7, 9.4; IR (film): $\tilde{\upsilon}$ = 1771, 1708, 1674, 1633, 1467, 1420, 1385, 1332, 1228, 1177, 1088, 1009, 938, 911, 841, 793, 723, 711 cm^{-1}; MS (EI): m/z (%): 269 (1, M^+), 251 (3), 236 (2), 160 (9), 148 (3), 130 (7), 122 (19), 109 (100), 93 (5), 77 (14); HRMS (ESI) m/z: calcd for $C_{16}H_{15}NO_3$ [M^+ +Na]: 292.09448, found: 292.09441.

Compound 14: $Pd(OAc)_2$ (95.6 mg, 0.427 mmol) was dissolved in THF (70 mL) and the homogeneous brown solution was cooled to −78°C. PPh_3 (112 mg, 0.427 mmol) was added, followed by mesylate **13** (3.15 g, 10.26 mmol) and a solution of aldehyde **12** (2.3 g, 8.55 mmol) in THF (15 mL). A solution of $ZnEt_2$ (1.0 M in hexane, 25.7 mL, 25.7 mmol) was then slowly introduced. The resulting mixture was warmed to –20°C over a period of 1 h and stirring continued for 4 h at that temperature. The reaction was carefully quenched with sat. aq. NH_4Cl (50 mL) and H_2O (50 mL), the aqueous phase was extracted with EtOAc (3 × 50 mL), the combined organic layers were washed with

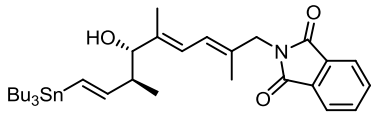
[3] See the accompanying paper in this issue: J. Gagnepain, E. Moulin, A. Fürstner, submitted.

brine (50 mL), dried over Na_2SO_4, filtered and evaporated, and the residue was purified by flash chromatography (hexanes/EtOAc, 20:1 → 10:1) to give alcohol **14** as a colorless oil (3.04 g, 74%). $[\alpha]_D^{20}$ = +40.6 (*c* = 2.3, CH_2Cl_2); ^{1}H NMR (CD_2Cl_2, 300 MHz): δ = 7.88–7.81 (m, 2H), 7.78–7.70 (m, 2H), 6.24 (s, 2H), 4.27 (s, 2H), 3.85 (dd, *J* = 6.8, 4.4 Hz, 1H), 2.74 (m, 1H), 2.28 (d, *J* = 4.4 Hz, 1H), 1.77 (s, 3H), 1.70 (s, 3H), 1.12 (d, *J* = 7.0 Hz, 3H), 1.02–1.08 (m, 21H); ^{13}C NMR (CD_2Cl_2, 75.5 MHz): δ = 168.5, 137.8, 134.3, 132.9, 132.5, 123.5, 122.9, 122.8, 110.2, 83.6, 80.8, 45.6, 33.2, 18.7, 18.2, 15.2, 12.3, 11.6; IR (film): $\tilde{\upsilon}$ = 3542, 2941, 2864, 2161, 1771, 1711, 1465, 1425, 1386, 1329, 1006, 939, 882, 724 cm^{-1}; MS (EI): *m*/*z* (%): 479 (0.3, M^+), 436 (1), 270 (100), 252 (10), 228 (1), 167 (12), 160 (35), 123 (38), 105 (13); HRMS (ESI) *m*/*z*: calcd for $C_{29}H_{41}NO_3Si$ [M^+ +Na]: 502.27493, found: 502. 27479.

Compound 15: A solution of TBAF (1 M in THF, 6.74 mL) was added to a solution of alcohol **14** (2.94 g, 6.13 mmol) in THF (30 mL) at 0°C. The resulting mixture was stirred at room temperature for 2 h before the reaction was quenched with H_2O (30 mL) and EtOAc (5 mL). The aqueous phase was extracted with EtOAc (2 × 5 mL), the combined organic layers were washed with brine (10 mL), dried over $MgSO_4$, filtered and evaporated, and the residue was purified by flash chromatography (hexanes/EtOAc, 10:1 → 4:1) to give alcohol **15** as a colorless oil (1.52 g, 77%). $[\alpha]_D^{20}$ = +42.1 (*c* = 1.0, CH_2Cl_2); ^{1}H NMR (CD_2Cl_2, 300 MHz): δ = 7.88–7.80 (m, 2H), 7.77–7.70 (m, 2H), 6.23 (s, 2H), 4.27 (s, 2H), 3.88 (dd, *J* = 7.1, 4.3 Hz, 1H), 2.67 (m, 1H), 2.33 (bs, 1H), 2.18 (d, *J* = 2.4 Hz, 1H), 1.77 (s, 3H), 1.69 (s, 3H), 1.09 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (CD_2Cl_2, 75.5 MHz): δ = 168.5, 137.7, 134.3, 133.2, 132.4, 123.5, 123.0, 122.6, 86.2, 80.9, 70.8, 45.5, 31.6, 17.8, 15.2, 12.1; IR (film): $\tilde{\upsilon}$ = 3466, 3286, 2934, 1770, 1705, 1387, 1329, 1006, 939, 911 cm^{-1}; MS (EI): *m*/*z* (%): 323 (0.4, M^+), 270 (78), 252 (11), 160 (100), 148 (12), 130 (21), 123 (69); HRMS (ESI) *m*/*z*: calcd for $C_{20}H_{21}NO_3$ [M^+ +Na]: 346.14139, found: 346. 14136.



Compound 16: *n*BuLi (1.6 M in hexane, 5.2 mL, 8.37 mmol) was added to a solution of $(Bu_3Sn)_2$ (4.85 g, 8.37 mmol) in THF (8 mL) at –78°C; once the addition was complete, the mixture was stirred at –40°C for 20 min. The resulting bright yellow solution was cooled to –78°C before CuCN (725.6 mg, 8.16 mmol) was introduced. The cooling bath was removed and stirring continued until all solid material had dissolved, affording a bright yellow homogeneous solution. After stirring for 1 h at room temperature, a solution of alkyne **15** (660 mg, 2.04 mmol) in THF (2 mL) was introduced and stirring continued for 10 min. The reaction was then quenched with MeOH (2 mL) and diluted with sat. aq. NH_4Cl (10 mL). Once all copper precipitates had dissolved, the blue aqueous phase was extracted with *tert*-butyl methyl ether (3 × 2 mL), the combined organic layers were dried over $MgSO_4$, filtered and evaporated, and the residue was purified by flash chromatography (hexanes/EtOAc, 1:0 → 6:1, containing 1% Et_3N) to give stannane **16** as a colorless oil (0.9 g, 72%, *E*/*Z* ≥ 16:1). $[\alpha]_D^{20}$ = +25.2 (*c* = 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.83–7.75 (m, 2H), 7.70–7.62 (m, 2H), 6.23 (d, *J* = 11.1 Hz, 1H), 6.11 (d, *J* = 11.1 Hz, 1H), 6.03 (d, *J* = 19.0 Hz, 1H), 5.78 (dd, *J* = 19.0, 7.6 Hz, 1H), 4.23 (s, 2H), 3.66 (d, *J* = 7.9 Hz, 1H), 2.29 (m, 1H), 1.97 (bs, 1H), 1.71 (s, 3H), 1.67 (s, 3H), 1.55–1.36 (m, 6H), 1.35–1.20 (m, 6H), 0.95–0.70 (m, 18H); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 168.0, 151.0, 138.0, 133.8, 131.9, 131.5, 130.8, 123.2, 123.1, 122.8, 80.7, 46.2, 45.2, 28.9, 27.1, 16.6, 15.0,



13.6, 11.8, 9.3; IR (film): $\tilde{\upsilon}$ = 3544, 2956, 2925, 2871, 1771, 1712, 1425, 1388, 1330, 1002, 940, 724 cm^{-1}; HRMS (ESI) *m*/*z*: calcd for $C_{32}H_{49}NO_3Sn$ [M^+ +Na]: 638.26326, found: 638.26266.

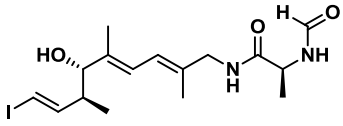
Compound 17: A solution of I_2 (362 mg, 1.42 mmol) in Et_2O (14 mL) was added to a solution of stannane **16** (860 mg, 1.36 mmol) in Et_2O (14 mL) at 0°C. The resulting brown mixture was stirred at room temperature for 30 min before the reaction was quenched with sat. aq. $Na_2S_2O_3$ (20 mL). The aqueous layer was extracted with EtOAc (3 × 4 mL), the combined organic phases were dried over $MgSO_4$, filtered and evaporated, and the crude material purified by flash chromatography (hexanes/EtOAc, 10:1 → 5:1, containing 1% Et_3N) to give iodide **17** as a white solid (551 mg, 90%). $[\alpha]_D^{20}$ = +25.6 (*c* = 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.85–7.79 (m, 2H), 7.72–7.66 (m, 2H), 6.48 (dd, *J* = 14.4, 8.2 Hz, 1H), 6.21 (dd, *J* = 11.0, 1.2 Hz, 1H), 6.11 (d, *J* = 11.0 Hz, 1H), 6.08 (dd, *J* = 14.4, 0.8 Hz, 1H), 4.25 (s, 2H), 3.74 (d, *J* = 8.0 Hz, 1H), 2.41–2.30 (m, 1H), 1.84 (bs, 1H), 1.74 (s, 3H), 1.66 (s, 3H), 0.86 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 168.1, 148.4, 137.8, 133.9, 132.3, 131.9, 123.3, 123.0, 122.8, 81.0, 75.9, 45.3, 44.4, 16.2, 15.1, 11.9; IR (film): $\tilde{\upsilon}$ = 3465, 2956, 2925, 1770, 1709, 1389, 1331, 1007, 941, 726 cm^{-1}; MS (EI): *m*/*z* (%): 270 (100), 252 (17), 181 (2), 160 (79), 123 (69), 105 (23); HRMS (ESI) *m*/*z*: calcd for $C_{20}H_{22}NO_3I$ [M^+ +Na]: 474.05337, found: 474.05366.

Compound 24: A solution of $MeNH_2$ in EtOH (33% *w*/*w*, 2 mL) was added to phthalimide **23** (12.6 mg, 0.0178 mmol) and the resulting mixture was heated in a microwave reactor at 60°C for 30 min. For work up, all volatile materials were evaporated under high vacuum and the residue taken up in aq. Na_2CO_3 (3 mL) and EtOAc (3 mL). The aqueous layer was extracted with EtOAc (3 × 1 mL), the combined organic phases were washed with brine (2 mL), dried ($MgSO_4$), filtered and evaporated to give the corresponding free amine **7** as a pale yellow oil. This material was immediately dissolved in DMF (0.5 mL) and treated with compound **25** (6.36 mg, 0.0178 mmol), HOBt (2.64 mg, 0.019 mmol) and EDC·HCl (5.1 mg, 0.0267 mmol). The resulting white suspension was stirred for 16 h to give a homogeneous bright yellow solution. The reaction was quenched with H_2O (2 mL), the aqueous layer was extracted with EtOAc (3 × 1 mL), the combined organic phases were washed with H_2O (3 × 2 mL) and brine (3 mL), dried ($MgSO_4$), filtered and evaporated. The residue was purified by flash chromatography (CH_2Cl_2/MeOH, 100:1 → 15:1) to give product **24** as a white solid (11 mg, 70%). $[\alpha]_D^{20}$ = +12.5 (*c* = 0.45, MeOH); ^{1}H NMR (600 MHz, CD_3OD): δ = 6.65 (dd, *J* = 10.4, 1.4 Hz, 1H), 6.50 (d, *J* = 15.7 Hz, 1H), 6.36 (d, *J* = 11.1 Hz, 1H), 6.21 (dd, *J* = 11.2, 1.1 Hz, 1H), 6.11 (dd, *J* = 14.9, 10.4 Hz, 1H), 5.98 (td, *J* = 15.4, 10.4 Hz, 1H), 5.64–5.59 (m, 1H), 5.57 (dd, *J* = 15.4, 8.9 Hz, 1H), 5.44–5.36 (m, 1H), 5.25–5.20 (m, 1H), 5.16 (d, *J* = 10.0 Hz, 1H), 5.12 (d, *J* = 9.4 Hz, 1H), 4.51 (dd, *J* = 7.8, 4.4 Hz, 2H), 4.33 (dd, *J* = 7.8, 4.4 Hz, 2H), 4.26 (dt, *J* = 10.0, 2.5 Hz, 2H), 3.84 (bs, 2H), 3.32–3.28 (m, 1H), 3.27 (s, 3H), 3.24–3.18 (m, 2H), 2.99 (s, 3H), 2.98–2.93 (m, 2H), 2.73 (d, *J* = 12.7 Hz, 2H), 2.66–2.54 (m, 2H), 2.27 (t, *J* = 7.5 Hz, 2H), 2.22 (t, *J* = 7.5 Hz, 2H), 1.83 (s, 3H), 1.83 (s, 3H),

1.82 (s, 3H), 1.80 (s, 3H), 1.79 (s, 3H), 1.78–1.30 (m, 20H), 1.09 (d, *J* = 6.7 Hz, 3H), 0.95 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (150 MHz, CD_3OD): δ= 176.6, 176.5, 169.6, 166.6, 147.6, 139.0, 137.8, 137.7, 135.1 134.9, 134.5, 134.3, 134.3, 133.5, 133.4, 132.7, 131.1, 129.7, 127.2, 127.2, 126.6, 121.9, 85.2, 81.7, 78.6, 72.2, 63.9, 62.1, 57.6, 57.5, 56.6, 48.1, 42.4, 41.6, 40.6, 39.7, 37.5, 37.3, 30.6, 30.3, 30.0, 28.1, 27.4, 27.3, 22.3, 21.4, 17.5, 15.6, 13.8, 12.7, 12.7; IR (film): $\tilde{\upsilon}$ = 2925, 2860, 1702, 1643, 1539, 1450, 1260, 1216, 1105, 988, 963 cm^{-1}; HRMS (ESI) *m*/*z*: calcd for $C_{53}H_{80}O_7N_4$ [M^+ +Na]: 939.56399, found: 939.56315.

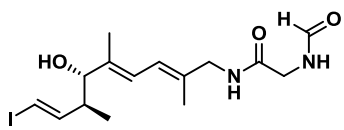
Building Blocks for the Preparation of Analogues Differing in the Amino Acid Terminus (Scheme 4)

Compound 27b: A Schlenk tube was charged under Ar with anhydrous Et_4NF (1.54 g, 10.3 mmol) and a solution of compound **26** (800 mg, 1.72 mmol)[3] in MeCN (17 mL). The reaction mixture for stirred for 16 h at 40°C before the solvent was evaporated. The residue was diluted with EtOAc (5mL), the organic layer was washed with sat. aq. Na_2CO_3 (5 mL), the aqueous phase was re-extracted with EtOAc (6 × 2 mL), the combined organic phases were washed with brine (5 mL), dried ($MgSO_4$), filtered and evaporated to give the crude amine as a colorless oil (519 mg).

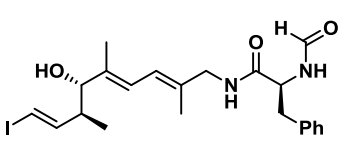


N-Formyl-L-alanine (112.4 mg, 0.96 mmol), HOBt (127 mg, 0.96 mmol), and *N*-methylmorpholine (176 μL, 1.6 mmol) were added to a solution of this amine (259 mg, 0.8 mmol) in CH_2Cl_2 (8 mL). The resulting mixture was cooled to 0°C before EDC·HCl (230 mg, 1.2 mmol) was added and stirring continued at room temperature for 16 h. The reaction was quenched with HCl (0.1 M, 8 mL), the aqueous phase was extracted with EtOAc (3 × 2 mL), the combined organic layers were dried over $MgSO_4$ and evaporated. Purification of the residue by flash chromatography (EtOAc/MeOH, 1:0 → 50:1) gave compound **27b** as a colorless oil (323 mg, 96%). $[\alpha]_D^{20}$ = +7.2 (*c* = 0.6, CH_2Cl_2); ^{1}H NMR (400 MHz, CD_2Cl_2): δ= 8.12 (s, 1H), 6.52 (dd, *J* = 14.5, 8.3 Hz, 1H), 6.35 (brs, 1H), 6.21–6.09 (m, 4H), 4.53–4.45 (m, 1H), 3.84 (brs, 2H), 3.77 (d, *J* = 7.9 Hz, 1H), 2.43–2.36 (m, 1H), 1.72 (s, 3H), 1.69 (s, 3H), 1.38 (d, *J* = 7.0 Hz, 3H), 0.88 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, CD_2Cl_2): δ= 171.9, 161.1, 149.2, 138.0, 135.0, 123.1, 121.3, 81.4, 76.0, 48.1, 47.2, 44.9, 18.6, 16.5, 15.1, 12.0; IR (film): $\tilde{\upsilon}$ = 3295, 2972, 2926, 2870, 1651, 1530, 1450, 1380, 1242, 1009 cm^{-1}; HRMS (ESI) *m*/*z*: calcd for $C_{16}H_{25}O_3N_2I$ [M^+ +Na]: 443.08021, found: 443.08020.

Compound 27a: Prepared analogously as a colorless oil (103 mg, 98%). $[\alpha]_D^{20}$ = +37.5 (*c* = 1.0, CH_2Cl_2); ^{1}H NMR (CD_2Cl_2, 300 MHz): δ= 8.18 (s, 1H), 6.98 (brs, 1H), 6.68 (brs, 1H), 6.55 (dd, *J* = 14.4, 8.2 Hz, 1H), 6.19–6.09 (m, 3H), 3.94 (d, *J* = 5.5 Hz, 2H), 3.86 (d, *J* = 5.8 Hz, 2H), 3.78 (d, *J* = 7.9 Hz, 1H), 2.43–2.36 (m, 1H), 1.73 (s, 3H), 1.70 (s, 3H), 0.89 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (CD_2Cl_2, 75 MHz): δ= 168.9, 162.1, 149.2, 138.3, 134.8, 123.1, 121.6, 81.3, 75.9, 47.3, 44.7, 42.1, 16.5, 15.1, 12.0; IR (film): $\tilde{\upsilon}$ = 3299, 2962, 2927, 2870, 1656, 1536, 1384, 1242, 1008, 948 cm^{-1}; HRMS (ESI) *m*/*z*: calcd for $C_{15}H_{23}O_3N_2I$ [M^+ +Na]: 429.06456, found: 429.06497.

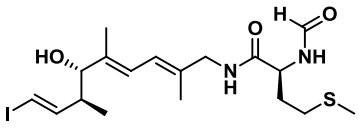


Compound 27c: Prepared analogously as a colorless oil (111 mg, 86%). $[\alpha]_D^{20}$ = +5.0 (*c* = 0.02, CH_2Cl_2);



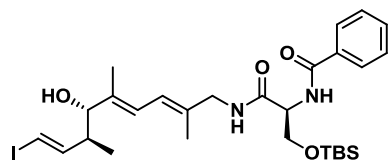
^{1}H NMR (400 MHz, CD_2Cl_2): δ = 8.10 (s, 1H), 7.32–7.17 (m, 5H), 6.54 (brdd, *J* = 14.5, 8.2 Hz, 2H), 6.17–6.05 (m, 4H), 4.75–4.69 (m, 1H), 3.85–3.71 (m, 3H), 3.13–3.03 (m, 2H), 2.44–2.35 (m, 1H), 1.69 (s, 3H), 1.64 (s, 3H), 0.89 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, CD_2Cl_2): δ = 170.7, 161.2, 149.2, 138.2, 137.0, 134.7, 129.7, 129.0, 127.4, 123.1, 121.8, 81.3, 75.9, 53.7, 47.4, 44.8, 38.7, 16.5, 15.1, 12.0; IR (film): $\tilde{\upsilon}$ = 3286, 2956, 2923, 2854, 1651, 1540, 1455, 1380, 1232, 1009 cm^{-1}; HRMS (ESI) *m*/*z*: calcd for $C_{22}H_{29}O_3N_2I$ [M^+ +Na]: 519.11151, found: 519.11163.

Compound 27d: Prepared analogously as a colorless oil (115 mg, 92%). $[\alpha]_D^{20}$ = –10.0 (*c* = 0.02, CH_2Cl_2);



^{1}H NMR (400 MHz, CD_2Cl_2): δ = 8.15 (s, 1H), 6.75 (d, *J* = 7.7 Hz, 1H), 6.59 (t, *J* = 5.8 Hz, 1H), 6.55 (dd, *J* = 14.5, 8.2 Hz, 1H), 6.19–6.11 (m, 3H), 4.68–4.64 (m, 1H), 3.86 (d, *J* = 5.8 Hz, 2H), 3.79 (d, *J* = 7.9 Hz, 1H), 2.59–2.48 (m, 2H), 2.43–2.37 (m, 1H), 2.15–2.07 (m, 4H), 2.02–1.92 (m, 1H), 1.74 (s, 3H), 1.70 (s, 3H), 0.90 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, CD_2Cl_2): δ = 171.0, 161.4, 149.2, 138.2, 134.8, 123.1, 121.6, 81.4, 75.9, 51.3, 47.3, 44.8, 32.1, 30.5, 16.5, 15.4, 15.2, 12.1; IR (film): $\tilde{\upsilon}$ = 3286, 2962, 2916, 2865, 1651, 1532, 1441, 1383, 1236, 1008 cm^{-1}; HRMS (ESI) *m*/*z*: calcd for $C_{18}H_{29}O_3N_2IS$ [M^+ +Na]: 503.08358, found: 503.08353.

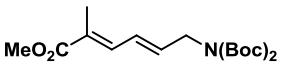
Compound 27e: Prepared analogously as a colorless oil (185 mg, 98%). $[\alpha]_D^{20}$ = +32.3 (*c* = 1.05, $CHCl_3$);



^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.83–7.76 (m, 2H), 7.55–7.37 (m, 3H), 7.20 (d, *J* = 5.8 Hz, 1H), 6.74 (bs, 1H), 6.50 (dd, *J* = 14.5, 8.3 Hz, 1H), 6.16–6.09 (m, 3H), 4.60–5.56 (m, 1H), 4.18 (dd, *J* = 9.7, 4.1 Hz, 1H), 4.14–4.04 (m, 2H), 3.76 (d, *J* = 8.0 Hz, 1H), 3.66 (dd, *J* = 9.6, 8.4 Hz, 1H), 2.45–2.30 (m, 1H), 1.74 (s, 3H), 1.68 (s, 3H), 0.90 (d, *J* = 6.5 Hz, 3H), 0.88 (s, 9H), 0.13 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.3, 167.2, 148.4, 137.4, 134.4, 133.6, 131.9, 128.6, 127.0, 123.1, 121.7, 81.1, 76.1, 62.7, 54.4, 47.2, 44.6, 25.8, 18.0, 16.2, 15.0, 11.8, –5.4, –5.6; IR (film): $\tilde{\upsilon}$ = 3305, 2954, 2928, 2857, 1639, 1535, 1485, 1253, 1110, 836, 778 cm^{-1}; HRMS (ESI) *m*/*z*: calcd for $C_{28}H_{43}O_4N_2ISi$ [M^+ +Na]: 649.19291, found: 649.19265.

Building Blocks for the C27-Desmethyl Analogue 40 (Scheme 5)

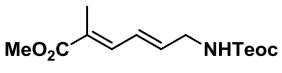
Methyl *N,N*-bis(*tert*-butoxycarbonyl)-6-amino-2-methyl-hex-2,4-dienoate (**32**)**:** A 50 mL Schlenk tube was charged with alkene **31** (1.45 g, 5.63 mmol),[4] bromide **30** (2 g, 11.27 mmol),[3] $Pd(OAc)_2$ (37.8 mg, 0.169 mmol), P(*o*–tol)$_3$ (102.75 mg, 0.338 mmol) and Et_3N (1.6 mL, 11.27 mmol). The resulting yellow suspension was stirred at 100°C whereby the mixture slowly became homogeneous. After 24 h, the reaction was quenched with NaOH (3 M, 10 mL) and extracted with *tert*-butyl methyl ether (3 × 10 mL), the combined extracts were washed with



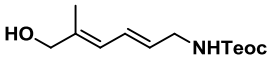
[4] R. D. Connell, T. Rein, B. Aakermark, P. Helquist, *J. Org. Chem.* **1988**, *53*, 3845-3849.

brine (50 mL), dried over $MgSO_4$, filtered and evaporated, and the residue was purified by flash chromatography (hexanes/EtOAc, 10:1) to give diene **32** (*E*/*Z* = 7:1) as a bright yellow oil (1.67 g, 87%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.11 (d, *J* = 11.3 Hz, 1H), 6.40 (dd, *J* = 14.2, 12.3 Hz, 1H), 5.99 (td, *J* = 15.2, 5.9 Hz, 1H), 4.24 (d, *J* = 5.9 Hz, 2H), 3.69 (s, 3H), 1.87 (s, 3H), 1.44 (s, 18H); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 168.7, 152.1, 137.4, 136.2, 127.1, 82.5, 51.7, 47.7, 28.0, 12.5; IR (neat): $\tilde{\upsilon}$ = 2980, 1748, 1708, 1434, 1366, 1341, 1222, 1136, 1101 cm^{-1}; MS (EI): *m*/*z* (%): 355 (M^+, 0.2), 299 (5), 284 (3), 243 (17), 199 (82), 125 (86), 57 (100); HRMS (ESI) *m*/*z*: calcd for $C_{18}H_{29}NO_6$ [M^+ +Na]: 378.18871, found: 378.18851.

Methyl *N*-(trimethylsilylethoxycarbonyl)-6-amino-2-methyl-hex-2,4-dienoate (**S-2**)**:** Trifluoroacetic acid (44 mL, 586 mmol) was added dropwise to a solution of compound **32** (5.2 g, 14.63 mmol) in CH_2Cl_2 (200 mL) at 0°C. The cooling bath was removed and stirring continued for 0.5 h. The solvents were evaporated and the resulting product was dried in high vacuum for 1 h. The residue was dissolved in CH_2Cl_2 (50 mL), Et_3N (14.2 mL, 102.2 mmol) and 4-nitrophenyl-2-trimethylsilylethyl-carbonate (5 g, 17.5 mmol) were added, and the resulting yellow solution was stirred for 24 h before the reaction was quenched with sat. aq. Na_2CO_3. The aqueous phase was extracted with CH_2Cl_2, the combined organic phases were washed with brine, dried over Na_2SO_4, filtered and evaporated, and the crude product was purified by flash chromatography (hexanes/acetone, 20:1 → 10:1, buffered with 1% Et_3N) to give compound **S-2** as a pale yellow oil (3.39 g, 76%). ^{1}H NMR (CD_2Cl_2, 400 MHz): δ = 7.15 (d, *J* = 11.3 Hz, 1H), 6.47 (ddt, *J* = 15.1, 11.3, 1.5 Hz, 1H), 6.04 (td, *J* = 15.1, 5.7 Hz, 1H), 4.91 (bs, 1H), 4.15 (t, *J* = 8.4 Hz, 2H), 3.89 (t, *J* = 5.6 Hz, 2H), 3.72 (s, 3H), 1.92 (s, 3H), 0.98 (t, *J* = 8.4 Hz, 2H), 0.04 (s, 9H); ^{13}C NMR (CD_2Cl_2, 100 MHz): δ = 168.9, 156.8, 138.0, 137.5, 127.6, 126.6, 63.4, 52.0, 43.0, 18.1, 12.8, −1.4; IR (neat): $\tilde{\upsilon}$ = 3352, 2952, 1694, 1644, 1521, 1435, 1246, 1224, 1104, 834 cm^{-1}; MS (ESI) *m*/*z*: 322.08 (M^+ +Na).

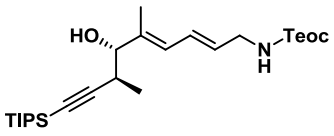


***N*-(Trimethylsilylethoxycarbonyl)-6-amino-2-methyl-hex-2,4-dien-1-ol** (**S-3**)**:** Dibal-H (16.2 mL, 1 M in hexane) was added dropwise to a solution of compound **S-2** (2.29 g, 7.35 mmol) in CH_2Cl_2 (50 mL) at −78°C. After stirring for 15 min at that temperature, the cooling bath was removed and the reaction was quenched with EtOAc (1 mL) and an aqueous solution of Rochelle salt (1 M, 20 mL). After stirring at room temperature for 2 h, the aqueous phase was extracted with EtOAc (2 × 5 mL), the combined organic phases were dried over $MgSO_4$ and evaporated, and the residue was purified by flash chromatography (hexanes/EtOAc, 4:1 → 2:1) to give **S-3** as a colorless oil (1.85 g, 92%). ^{1}H NMR (CD_2Cl_2, 400 MHz): δ = 6.41 (dd, *J* = 11.0, 15.0 Hz, 1H), 6.04 (d, *J* = 10.9 Hz, 1H), 5.66 (td, *J* = 15.0, 6.1 Hz, 1H), 4.87 (bs, 1H), 4.13 (t, *J* = 8.5 Hz, 2H), 4.02 (d, *J* = 5.5 Hz, 2H), 3.81 (t, *J* = 5.6 Hz, 2H), 2.00 (bs, 1H), 1.75 (s, 3H), 0.97 (t, *J* = 8.4 Hz, 2H), 0.04 (s, 9H); ^{13}C NMR (CD_2Cl_2, 75.5 MHz): δ = 156.9, 138.3, 129.7, 127.7, 123.6, 68.2, 63.3, 43.2, 18.0, 14.2, −1.4; IR (neat): $\tilde{\upsilon}$ = 3332, 2953, 1692, 1517, 1424, 1248, 1177, 1061, 954, 834 cm^{-1}; MS (EI): *m*/*z* (%): 271 (M^+, 0.2), 256 (0.2), 225 (2), 210 (2), 180 (4), 166 (10), 153 (3), 134 (7), 118 (30), 73 (100); HRMS (ESI) *m*/*z*: calcd for $C_{13}H_{25}NO_3Si$ [M^+ +Na]: 294.14959, found: 299.14992.

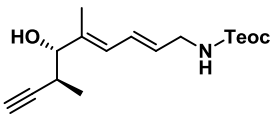


Compound S-4: MnO_2 (35 g, 409 mmol) was added to a solution of alcohol **S-3** (1.85 g, 6.82 mmol) in CH_2Cl_2 (60 mL) and the resulting suspension was stirred for 2 h. Insoluble residues were filtered off through a pad of Celite, which was carefully rinsed with CH_2Cl_2. The combined filtrates were evaporated to give the corresponding crude aldehyde **33** as a colorless oil, which was used immediately in the next step.

PPh_3 (70.7 mg, 0.27 mmol) was added to a solution of $Pd(OAc)_2$ (60.5 mg, 0.27 mmol) in THF (44 mL) at −78°C before compound **13** (2 g, 6.5 mmol) and a solution of the crude aldehyde in THF (10 mL) were added. A solution of $ZnEt_2$ (1.0 M in hexanes, 16.2 mL) was then slowly introduced and the resulting mixture stirred at that temperature for 30 min before it was warmed to –20°C over a period of 1 h. Stirring was continued overnight at –20°C before the reaction was carefully quenched with aq. sat. NH_4Cl (20 mL) and H_2O (20 mL). The resulting suspension was filtered, the aqueous phase extracted with EtOAc (2× 10 mL), the combined organic layers were dried over $MgSO_4$, filtered and evaporated, and the residue purified by flash chromatography (hexanes/EtOAc, 10:1) to give product **S-4** as a colorless oil (1.62 g, 50% over 2 steps). $[\alpha]_D^{20}$ = +50.5 (*c* = 0.8, CH_2Cl_2); ^{1}H NMR (CD_2Cl_2, 400 MHz): δ = 6.41 (ddt, *J* = 15.1, 10.9, 1.5 Hz, 1H), 6.05 (d, *J* = 10.9 Hz, 1H), 5.67 (dt, *J* = 15.1, 6.1 Hz, 1H), 4.76 (bs, 1H), 4.14 (t, *J* = 8.4 Hz, 2H), 3.84–3.78 (m, 3H), 2.74 (m, 1H), 2.28 (d, *J* = 4.6 Hz, 1H), 1.73 (s, 3H), 1.12 (d, *J* = 7.0 Hz, 3H), 1.08–1.04 (m, 21H), 0.98 (t, *J* = 8.4 Hz, 2H), 0.04 (s, 9H); ^{13}C NMR (CD_2Cl_2, 100 MHz): δ = 156.8, 137.6, 130.5, 127.4, 126.6, 110.1, 83.7, 80.5, 63.3, 43.2, 33.2, 18.8, 18.1, 18.1, 12.4, 11.6, −1.4; IR (neat): 3335, 2943, 2863, 2161, 1697, 1513, 1462, 1249, 1036, 858, 835 cm^{-1}; MS (ESI) *m*/*z* (MeOH): 502.34 (M^+ +Na); HRMS (ESI) *m*/*z*: calcd for $C_{26}H_{49}NO_3Si_2$ [M^+ +Na]: 502.31432, found: 502.31474.

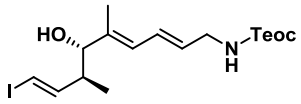


Compound 34: A solution of TBAF (1 M in THF, 2.19 mL) was added in 3 portions over 1 h to a solution of compound **S-4** (1.0 g, 2.09 mmol) in THF (40 mL) at 0°C. The mixture was stirred at that temperature for 30 minutes before the reaction was quenched with H_2O (10 mL). The aqueous phase was extracted with EtOAc (5 mL), the combined organic layers were washed with brine (10 mL), dried over $MgSO_4$, filtered and evaporated, and the residue was purified by flash chromatography (hexanes/EtOAc, 4:1 → 2:1) to give product **34** as a colorless oil (552 mg, 82%). $[\alpha]_D^{20}$ = +13.3 (*c* = 1.065, CH_2Cl_2); ^{1}H NMR (CD_2Cl_2, 300 MHz): δ = 6.41 (ddt, *J* = 15.1, 10.9, 1.4 Hz, 1H), 6.05 (d, *J* = 10.9 Hz, 1H), 5.70 (dt, *J* = 15.1, 6.0 Hz, 1H), 4.79 (bs, 1H), 4.14 (t, *J* = 8.4 Hz, 2H), 3.88–3.78 (m, 3H), 2.74 (dquint., *J* = 7.1, 2.4 Hz, 1H), 2.23 (bs, 1H), 2.18 (d, *J* = 2.4 Hz, 1H), 1.72 (s, 3H), 1.10 (d, *J* = 7.0 Hz, 3H), 0.97 (t, *J* = 8.4 Hz, 2H), 0.04 (s, 9H); ^{13}C NMR (CD_2Cl_2, 75.5 MHz): δ = 156.8, 137.4, 130.9, 127.2, 126.9, 86.1, 80.6, 70.9, 63.3, 43.1, 31.7, 18.0, 17.8, 12.1, −1.4; IR (neat): $\tilde{\upsilon}$ = 3309, 2953, 1694, 1517, 1452, 1248, 1058, 965, 858, 836 cm^{-1}; HRMS (ESI) *m*/*z*: calcd for $C_{17}H_{29}NO_3Si$ [M^+ +Na]: 346.18089, found: 346.18134.



Compound 36: *n*BuLi (1.6 M in hexane, 0.7 mL, 1.12 mmol) was added to a solution of $(Bu_3Sn)_2$ (0.65 g, 1.12 mmol) in THF (1 mL) at −78°C and the resulting mixture was stirred at −40°C for 20 min. The

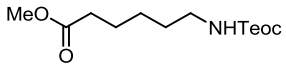
resulting bright yellow solution was cooled to −78°C before CuCN (99.6 mg, 1.12 mmol) was added as a solid. The cooling bath was removed and stirring was continued until all solid materials had dissolved to give a bright yellow homogeneous solution. The resulting lower-order cyanocuprate was stirred at room temperature for 1 h before a solution of alkyne **34** (90 mg, 0.28 mmol) in THF (2 mL) was introduced. After 10 min, the reaction was quenched with MeOH (2 mL) and diluted with a sat. aq. NH_4Cl (10 mL). After stirring at room temperature, the resulting blue aqueous phase was extracted with *tert*-butyl methyl ether (3 × 2 mL), the combined extracts were dried over $MgSO_4$, filtered and evaporated, and the residue was purified by flash chromatography (hexanes/EtOAc, 1:0 → 6:1, containing 1% Et_3N) to give alkenyl stannane **35** as a colorless oil (159 mg, 92%).

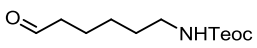


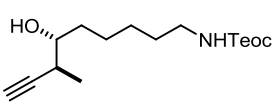
A solution of I_2 (69 mg, 0.271 mmol) in Et_2O (2.7 mL) was added at 0°C to a solution of stannane **35** (159 mg, 0.258 mmol) in CH_2Cl_2 (2.6 mL). The resulting brown mixture was stirred at room temperature for 10 min before the reaction was quenched with sat. aq. $Na_2S_2O_3$ (5 mL). The aqueous layer was extracted with EtOAc (3 × 2 mL), the combined organic phases were dried over $MgSO_4$, filtered and evaporated, and the residue was purified by flash chromatography (hexanes/EtOAc, 10:1 → 4:1, containing 1% Et_3N) to give iodide **36** as a colorless oil (110 mg, 95%). $[\alpha]_D^{20}$ = +20 (*c* = 1.0, CH_2Cl_2); ^{1}H NMR (CD_2Cl_2, 400 MHz): δ = 6.53 (dd, *J* = 14.5, 8.2 Hz, 1H), 6.40 (dd, *J* = 15.1, 10.9 Hz, 1H), 6.13 (d, *J* = 14.5 Hz, 1H), 5.99 (d, *J* = 10.8 Hz, 1H), 5.68 (dt, *J* = 15.1, 6.1 Hz, 1H), 4.80 (bs, 1H), 4.14 (t, *J* = 8.2 Hz, 2H), 3.82 (t, *J* = 5.7 Hz, 2H), 3.75 (d, *J* = 7.9 Hz, 1H), 2.74 (m, 1H), 1.86 (bs, 1H), 1.71 (s, 3H), 0.98 (t, *J* = 8.2 Hz, 2H), 0.90 (d, *J* = 6.9 Hz, 3H), 0.04 (s, 9H); ^{13}C NMR (CD_2Cl_2, 100 MHz): δ = 156.8, 149.0, 138.3, 130.7, 127.3, 126.8, 80.9, 76.0, 63.3, 44.8, 43.1, 18.0, 16.7, 12.1, −1.4; IR (neat): $\tilde{\upsilon}$ = 3353, 2955, 1698, 1521, 1249, 1060, 964, 859, 837 cm^{-1}; MS (EI): *m*/*z* (%): 451 (0.1, M^+), 436 (0.3), 270 (2), 242 (10), 181 (16), 169 (41), 152 (38), 73 (100); HRMS (ESI) *m*/*z*: calcd for $C_{17}H_{30}NO_3ISi$ [M^+ +Na]: 474.09319, found: 474.09348.

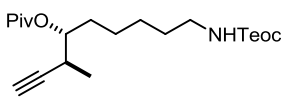
Building Blocks for the Preparation of Analogue 51 with the Flexible Spacer (Scheme 6)

Compound 42: Et_3N (4 mL, 28.5 mmol) and 4-nitrophenyl-2-trimethylsilylethyl carbonate (3.1 g, 10.9 mmol) were added to a solution of compound **41** (1.45 g, 7.98 mmol) in CH_2Cl_2 (50 mL) and the resulting yellow solution was stirred for 20 h. For work up, the mixture was extracted with aq. sat. Na_2CO_3 to remove the nitrophenol before it was washed with brine. The organic layer was dried over Na_2SO_4 and evaporated and the residue purified by flash chromatography (hexane/EtOAc, 4:1) to give compound **42** as a pale yellow oil (2.24 g, 96%). ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 4.69 (bs, 1H), 4.10 (t, *J* = 8.2 Hz, 2H), 3.62 (s, 3H), 3.11 (m, 2H), 2.29 (t, *J* = 7.4 Hz, 2H), 1.67-1.56 (m, 2H), 1.53-1.42 (m, 2H), 1.38-1.27 (m, 2H), 0.96 (t, *J* = 8.2 Hz, 2H), 0.03 (s, 9H); ^{13}C NMR (100 MHz, CD_2Cl_2): δ = 174.2, 157.0, 63.0, 51.6, 41.0, 34.2, 30.1, 26.6, 24.9, 18.1, –1.4; IR (film): $\tilde{\upsilon}$ = 3343, 2951, 1696, 1526, 1437, 1247, 1167, 1059, 945, 858, 834, 768 cm^{-1}; HRMS (ESI) *m*/*z*: calcd for $C_{13}H_{27}NO_4Si$ [M^+ +Na]: 312.16016, found: 312.16029; elemental analysis calcd (%) for $C_{13}H_{27}NO_4Si$: C 53.94, H 9.40; found: C 53.80, H 9.53.



Compound 43: Dibal-H (5.9 mL, 1 M in hexane) was slowly added to a solution of compound **42** (1.57  g, 5.4 mmol) in CH_2Cl_2 (45 mL) at –78°C and stirring was continued at this temperature for 1 h once the addition was complete. The reaction was then quenched with EtOAc (5 mL) followed by a sat. aq. solution of Rochelle salt (20 mL). After stirring for 1 h, the mixture was partitioned between EtOAc and brine, the combined organic layers were dried over Na_2SO_4 and evaporated, and the residue was purified by flash chromatography (hexane/EtOAc, 4:1) to give aldehyde **43** (1.01 g, 72%) along with recovered **42** (0.2 g). ^{1}H NMR (300 MHz, CD_2Cl_2): δ = 9.71 (s, 1H), 4.90 (bs, 1H), 4.09 (t, *J* = 7.9 Hz, 2H), 3.11 (m, 2H), 2.40 (t, *J* = 7.2 Hz, 2H), 1.67-1.55 (m, 2H), 1.54-1.40 (m, 2H), 1.40-1.25 (m, 2H), 0.94 (t, *J* = 7.9 Hz, 2H), 0.02 (s, 9H); ^{13}C NMR (75 MHz, CD_2Cl_2): δ = 202.7, 157.0, 62.9, 44.0, 40.9, 30.2, 26.6, 22.0, 18.0, –1.5; IR (film): $\tilde{\upsilon}$ = 3349, 2950, 1737, 1725, 1528, 1421, 1365, 1247, 1230, 1216, 1039, 857, 833, 769, 693 cm^{-1}; HRMS (ESI) *m*/*z*: calcd for $C_{12}H_{25}NO_3Si$ [M^+ +Na]: 282.14959, found: 282.14949; elemental analysis calcd (%) for $C_{12}H_{25}NO_3Si$: C 55.56, H 9.71; found: C 55.33, H 9.62.

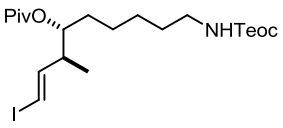
Compound 45: $Pd(OAc)_2$ (30 mg, 0.133 mmol) and PPh_3 (36 mg, 0.133 mmol) were successively  added to a solution of mesylate **44** (430 mg, 2.9 mmol)[5] in THF (16 mL) at –78°C. After stirring for 5 min, a solution of aldehyde **43** (500 mg, 1.927 mmol) in THF (3 mL) was introduced followed by the dropwise addition of $ZnEt_2$ (1.0 M in hexanes, 5.8 mL). After stirring for 30 min at –78°C, the solution was warmed to –20°C over a period of 1 h and stirred at this temperature for 18 h. The reaction was quenched with sat. aq. NH_4Cl, the aqueous phase was extracted with EtOAc, the combined extracts were washed with brine, dried over Na_2SO_4 and evaporated, and the residue was purified by flash chromatography (hexane/EtOAc, 10:1) to give compound **45** as a pale brown oil (333 mg, 55%, dr ≥ 10:1). $[\alpha]_D^{20}$ = –2.3 (*c* = 1.7, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.62 (bs, 1H), 4.09 (t, *J* = 8.2 Hz, 2H), 3.41 (m, 1H), 3.15 (m, 2H), 2.52 (m, 1H), 2.11 (d, *J* = 2.5 Hz, 1H), 1.85 (bs, 1H), 1.58-1.42 (m, 5H), 1.42-1.28 (m, 3H), 1.22 (d, *J* = 7.1 Hz, 3H), 0.95 (t, *J* = 8.2 Hz, 2H), 0.02 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.8, 85.2, 73.9, 70.9, 62.8, 40.8, 34.9, 32.9, 30.0, 26.6, 25.4, 17.8, 17.3, –1.5; IR (film): $\tilde{\upsilon}$ = 3311, 2937, 1692, 1526, 1248, 1137, 1042, 857, 834, 768, 693 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{16}H_{31}NO_3Si$ [M^+ +Na]: 336.19654, found: 336.19687.

Compound 46: DMAP (10 mg, 0.08 mmol) and pivaloyl chloride (0.5 mL, 4.06 mmol) were added to a  solution of compound **45** (298 mg, 0.95 mmol) in pyridine (5 mL) at 0°C. The mixture was stirred at ambient temperature for 20 h before it was partitioned between aq. sat. Na_2CO_3 and EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, and evaporated, and the residue was purified by flash chromatography (hexane/EtOAc, 10:1) to give product **46** as a colorless oil (317 mg, 84%, dr > 10:1). $[\alpha]_D^{20}$ = +9.4 (*c* = 1.7, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.84 (m, 1H), 4.60 (bs, 1H), 4.14 (t, *J* = 8.3 Hz, 2H), 3.14 (m, 2H), 2.69 (m, 1H), 2.05 (d, *J* = 2.4 Hz, 1H), 1.72-1.59 (m, 2H), 1.52-1.43 (m,

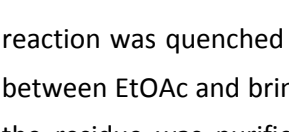
[5] J. A. Marshall, N. D. Adams, *J. Org. Chem.* **1998**, *63*, 3812-3813.

2H), 1.38-1.24 (m, 4H), 1.22 (s, 9H), 1.15 (d, *J* = 7.1 Hz, 3H), 0.97 (t, *J* = 8.3 Hz, 2H), 0.03 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ= 178.0, 156.8, 84.6, 74.4, 70.0, 62.8, 40.7, 38.9, 31.4, 30.1, 29.9, 27.2, 26.4, 25.1, 17.8, 16.6, –1.5; IR (film): $\tilde{\upsilon}$ = 3314, 2952, 1723, 1525, 1248, 1158, 1043, 858, 835, 693 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{21}H_{39}NO_4Si$ [M^+ +Na]: 420.25405, found: 420.25381.

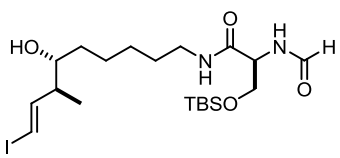
Compound S-5: A solution of compound **46** (218 mg, 0.548 mmol) in THF (5 mL) was added to a solution of $Cp_2Zr(H)Cl$ (210 mg, 0.81 mmol) in THF (5 mL) in the dark. The mixture was stirred for 45 min before it was cooled to 0°C and a solution of iodine (200 mg, 0.79 mmol) in THF (5 mL) was added. After 5 min the reaction was quenched with aq. sat. $Na_2S_2O_3$. After stirring for 10 min, the mixture was partitioned between EtOAc and brine, the combined organic layers were dried over Na_2SO_4 and evaporated, and the residue was purified by flash chromatography (hexane/EtOAc, 4:1) to give product **S-5** as a colorless syrup (197 mg, 69%, dr > 10:1). $[\alpha]_D^{20}$ = –7.3 (*c* = 1.25, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ= 6.40 (dd, *J* = 14.3, 8.6 Hz, 1H), 6.05 (d, *J* = 14.3 Hz, 1H), 4.77 (m, 1H), 4.61 (bs, 1H), 4.13 (t, *J* = 8.3 Hz, 2H), 3.12 (m, 2H), 2.39 (m, 1H), 1.56-1.38 (m, 4H), 1.36-1.22 (m, 4H), 1.19 (s, 9H), 1.09-0.92 (m, 5H), 0.02 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ= 177.9, 156.7, 147.3, 75.9, 75.1, 62.8, 44.6, 40.6, 38.9, 31.7, 29.9, 27.2, 26.4, 24.9, 17.7, 16.1, –1.5; IR (film): $\tilde{\upsilon}$ = 3352, 2970, 2951, 1725, 1365, 1230, 1217, 1158, 858, 835, 766, 693 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{21}H_{40}NO_4ISi$ [M^+ +Na]: 548.16636, found: 548.16594.



Compound 47: $LiHBEt_3$ (1 M in THF, 0.85 mL) was added dropwise to a solution of compound **S-5** (103 mg, 0.196 mmol) in THF (10 mL) at 0°C. After stirring for 2 h at this temperature, the reaction was quenched with aq. sat. NH_4Cl, and the mixture partitioned between EtOAc and brine. The combined organic layers were dried over Na_2SO_4 and evaporated, and the residue was purified by flash chromatography (hexane/EtOAc, 4:1) to give product **47** as a colorless oil (78 mg, 90%, dr > 10:1). $[\alpha]_D^{20}$ = –14 (*c* = 1.45, CH_2Cl_2); ^{1}H NMR (400 MHz, CD_2Cl_2): δ= 6.53 (dd, *J* = 14.5, 8.6 Hz, 1H), 6.09 (d, *J* = 14.5 Hz, 1H), 4.69 (bs, 1H), 4.11 (t, *J* = 8.2 Hz, 2H), 3.41 (m, 1H), 3.13 (m, 2H), 2.25 (m, 1H), 1.69 (bs, 1H), 1.53-1.41 (m, 4H), 1.41-1.26 (m, 4H), 1.03 (d, *J* = 6.9 Hz, 3H), 0.96 (t, *J* = 8.2 Hz, 2H), 0.04 (s, 9H); ^{13}C NMR (100 MHz, CD_2Cl_2): δ= 157.1, 148.7, 75.8, 74.6, 63.0, 47.0, 41.1, 34.9, 30.5, 26.9, 25.7, 18.1, 16.3, –1.4; IR (film): $\tilde{\upsilon}$ = 3336, 2932, 1692, 1522, 1248, 1058, 949, 857, 835, 693 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{16}H_{32}NO_3ISi$ [M^+ +Na]: 464.10884, found: 464.10893.



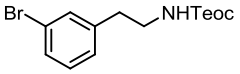
Compound 48: TBAF (1 M in THF, 0.8 mL) was added dropwise to a solution of compound **47** (76 mg, 0.17 mmol) in THF (3 mL) at 0°C. The mixture was stirred overnight at ambient temperature before an additional amount of TBAF (1 M in THF, 0.4 mL) was added and stirring continued for 16 h. The mixture was partitioned between EtOAc and aq. sat. Na_2CO_3, the combined organic layers were washed with brine, dried over Na_2SO_4, and evaporated. The resulting free amine was dissolved in CH_2Cl_2 (5 mL), O-TBS-N-formyl-L-serine (42 mg, 0.17 mmol),[3] HOBt (24 mg, 0.18 mmol), and N-methylmorpholine (0.055 mL, 0.5 mmol) were added, and the resulting solution was



cooled to 0°C before EDC·HCl (44 mg, 0.22 mmol) was introduced. The mixture was stirred for 20 h at ambient temperature before it was partitioned between EtOAc and brine. The combined organic layers were dried over Na_2SO_4 and evaporated, and the residue was purified by flash chromatography (hexane/EtOAc, 1:1) to give product **48** as a colorless syrup (66 mg, 74%, dr > 10:1). $[\alpha]_D^{20}$ = +4.6 (*c* = 1.05, CH_2Cl_2); ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 8.21 (s, 1H), 6.69 (d, *J* = 6.1 Hz, 1H), 6.53 (m, 2H), 6.08 (dd, *J* = 14.4, 0.8 Hz, 1H), 4.41 (m, 1H), 3.99 (dd, *J* = 9.7, 3.9 Hz, 1H), 3.62 (dd, *J* = 9.7, 7.5 Hz, 1H), 3.39 (m, 1H), 3.25 (m, 2H), 2.24 (m, 1H), 1.99 (bs, 1H), 1.55-1.28 (m, 8H), 1.03 (d, *J* = 6.9 Hz, 3H), 0.91 (s, 9H), 0.10 (s, 3H). 0.09 (s, 3H); ^{13}C NMR (100 MHz, CD_2Cl_2): δ = 169.8, 161.3, 148.7, 75.8, 74.6, 63.3, 53.5, 47.1, 39.8, 34.9, 29.8, 27.1, 26.0, 25.7, 18.4, 16.3, –5.3, –5.4; IR (film): $\tilde{\upsilon}$ = 3307, 2930, 2857, 1650, 1550, 1463, 1378, 1257, 1102, 990, 836, 778 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{20}H_{39}N_2O_4ISi$ +Na: 549.16160 [M^+ +Na], found: 549.16112.

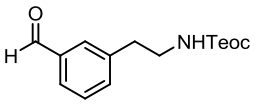
Building Blocks for the Preparation of Analogue 59 with an Aromatic Spacer (Scheme 7)

Compound 53: A solution of 3-bromophenylethylamine **52** (1.0 g, 5.0 mmol) in CH_2Cl_2 (29 mL) was



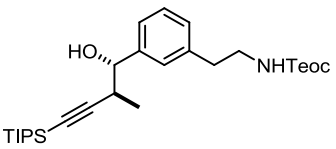
treated sequentially with Et_3N (702 µL, 5.0 mmol) and 4-nitrophenyl 2-(trimethylsilyl)ethyl carbonate (1.56 g, 5.5 mmol) and the resulting mixture was stirred for 20 h. This solution was then washed with sat. aq. Na_2CO_3 and brine, the organic layer was dried over $MgSO_4$ and evaporated, and the residue was purified by flash chromatography (0-12.5% EtOAc in hexanes) to give compound **53** as a colorless oil (1.49 g, 86%). ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.37 – 7.35 (m, 2H), 7.21 – 7.14 (m, 2H), 4.74 (brs, 1H), 4.11 (t, *J* = 8.4 Hz, 2H), 3.38 (td, *J* = 6.7, 6.7 Hz, 2H), 2.77 (t, *J* = 7.0 Hz, 2H), 0.95 (t, *J* = 8.4 Hz, 2H), 0.04 (s, 9H); ^{13}C NMR (100 MHz, CD_2Cl_2): δ = 156.8, 142.0, 132.2, 130.5, 129.8, 129.0, 122.7, 63.2, 42.2, 36.2, 18.0, –1.5; IR (film): $\tilde{\upsilon}$ = 3336, 2952, 1692, 1518, 1247, 1060, 857, 835, 777, 694 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{14}H_{22}O_2NSiBr$ [M^+ +Na]: 366.04955, found: 366.04981.

Compound 54: MeLi (2.0 M in Et_2O, 2.2 mL, 4.4 mmol) was added dropwise to a solution of

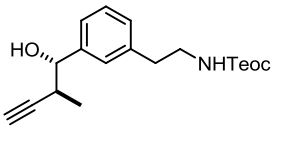


compound **53** (1.38 g, 4.0 mmol) in THF (150 mL) at –78°C. After stirring for 15 min, *t*BuLi (1.5 M in pentane, 2.94 mL, 4.4 mmol) was slowly introduced and stirring continued for another 15 min before dry DMF (776 µL, 10.0 mmol) was added. After 1h at –78°C, the mixture was allowed to reach room temperature over 30 min before the reaction was carefully quenched with sat. aq. NH_4Cl. The aqueous layer was extracted with EtOAc, the combined extracts were washed with brine, dried over $MgSO_4$ and evaporated, and the residue was purified by flash chromatography (0-33% EtOAc in hexanes) to give compound **54** as a colorless syrup (1.12 g, 95%). ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 9.99 (s, 1H), 7.73 – 7.71 (m, 2H), 7.50 – 7.48 (m, 2H), 4.72 (brs, 1H), 4.11 (t, *J* = 8.4 Hz, 2H), 3.43 (td, *J* = 6.5, 6.5 Hz, 2H), 2.89 (t, *J* = 7.0 Hz, 2H), 0.94 (t, *J* = 8.0 Hz, 2H), 0.03 (s, 9H); ^{13}C NMR (100 MHz, CD_2Cl_2): δ = 192.6, 156.8, 140.7, 137.2, 135.3, 130.0, 129.6, 128.3, 63.2, 42.2, 36.3, 18.0, –1.5; IR (film): $\tilde{\upsilon}$ = 3341, 2952, 1694, 1524, 1248, 1142, 1060, 859, 837, 693 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{15}H_{23}O_3NSi$ [M^+ +Na]: 316.13394, found: 316.13385.

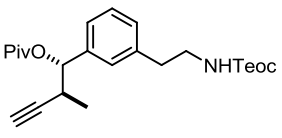
Compound S-6: $Pd(OAc)_2$ (33 mg, 0.15 mmol) and PPh_3 (38 mg, 0.15 mmol) were added to a solution of mesylate **13** (1.43 g, 4.7 mmol) in THF (29 mL) at –78°C. After stirring for 5 min, a solution of aldehyde **54** (861 mg, 2.9 mmol) in THF (10 mL) was introduced, followed by the dropwise addition of $ZnEt_2$ (1 M in hexane, 8.8 mL). After stirring for 30 min, the solution was warmed up to –20°C and stirring continued overnight at this temperature. The reaction was carefully quenched with aq. sat. NH_4Cl and allowed to reach ambient temperature, the aqueous phase was extracted with Et_2O, the combined extracts were washed with brine, dried over $MgSO_4$ and evaporated. Purification of the residue by flash chromatography (pentanes/Et_2O, 60:1 → 2:1) afforded a separable 1:1 mixture of compound **55** as a colorless oil (1.19 g, 80%). *anti*-**S-6** (561 mg)[6] analyzed as follows: $[\alpha]_D^{20}$ = –16.7 (*c* = 0.78, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.27 – 7.20 (m, 3H), 7.13 – 7.10 (m, 1H), 4.61 (brs, 1H), 4.45 (d, *J* = 6.9 Hz, 1H), 4.14 (t, *J* = 8.3 Hz, 2H), 3.42 (td, *J* = 6.4, 6.4 Hz, 2H), 2.85 – 2.80 (m, 1H), 2.80 (t, *J* = 7.1 Hz, 2H), 2.68 (brs, 1H), 1.11 (d, *J* = 7.0 Hz, 3H), 1.06 (s, 21H), 0.96 (t, *J* = 8.6 Hz, 2H), 0.03 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.8, 141.9, 139.0, 128.6, 128.4, 127.2, 125.1, 109.5, 84.4, 77.4, 63.1, 42.2, 36.9, 36.4, 18.8, 17.9, 17.8, 11.3, –1.3; IR (film): $\tilde{\upsilon}$ = 3352, 2943, 2891, 2865, 2162, 1697, 1519, 1463, 1250, 1060, 1039, 859, 837, 676 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{28}H_{49}O_3NSi_2$ [M^+ +Na]: 526.31432, found: 526.31487.



Compound *anti*-**55**: A solution of TBAF (1 M in THF, 890 µL) was added to a solution of compound *anti*-**S-6** (561 mg, 1.11 mmol) in THF (25 mL) at 0°C. After stirring for 1h, the reaction was quenched with sat. aq. $NaHCO_3$, the aqueous phase was extracted with EtOAc, and the combined organic layers were washed with brine, dried over $MgSO_4$ and evaporated. The residue was purified by flash chromatography (hexanes/EtOAc, 10:1 → 1:1) to yield product *anti*-**55** as a colorless oil (318 mg, 82%). $[\alpha]_D^{20}$ = +3.3 (*c* = 0.3, CH_2Cl_2); ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.30 – 7.20 (m, 3H), 7.13 – 7.10 (m, 1H), 4.79 (brs, 1H), 4.50 (d, *J* = 6.4 Hz, 1H), 4.11 – 4.06 (m, 2H), 3.37 (td, *J* = 6.6, 6.6 Hz, 2H), 2.80 – 2.73 (m, 4H), 2.22 (d, *J* = 2.4 Hz, 1H), 1.09 (t, *J* = 7.0 Hz, 3H), 0.94 (t, *J* = 8.2 Hz, 2H), 0.03 (s, 9H); ^{13}C NMR (100 MHz, CD_2Cl_2): δ = 156.9, 142.5, 139.4, 128.7, 128.6, 127.4, 125.0, 85.9, 77.3, 71.4, 63.1, 42.4, 36.5, 35.3, 18.0, 17.6, –1.4; IR (film): $\tilde{\upsilon}$ = 3422, 3311, 2953, 2896, 1699, 1519, 1250, 1057, 859, 837 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{19}H_{29}O_3NSi$ [M^+ +Na]: 370.18089, found: 370.18122.



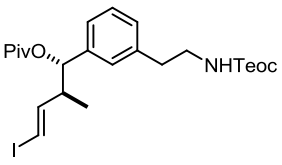
Compound S-7: Pivaloyl chloride (411 µL, 3.34 mmol) was added to a solution of compound *anti*-**55** (387 mg, 1.11 mmol) and DMAP (10 mg) in pyridine (4.6 mL) at 0°C. The mixture was stirred overnight at room temperature before the reaction was quenched with HCl (1 M). The aqueous phase was extracted with EtOAc, the combined organic layers were washed with sat. aq. $NaHCO_3$ and brine, dried over $MgSO_4$ and evaporated. Purification of the residue by flash chromatography (hexanes/EtOAc, 20:1 → 8:1) furnished product **S-7** as a yellow oil (298 mg, 62%). $[\alpha]_D^{20}$ = – 27.8 (*c* = 0.73, CH_2Cl_2); ^{1}H NMR (300 MHz, CD_2Cl_2): δ = 7.30 – 7.15 (m, 4H), 5.64 (d, *J* = 6.3 Hz, 1H), 4.81 (brs,



[6] The configuration of the alcohol was determined by Mosher ester analysis.

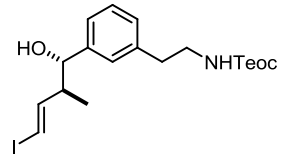
1H), 4.13 (t, *J* = 8.3 Hz, 2H), 3.40 (td, *J* = 6.6, 6.6 Hz, 2H), 2.96 – 2.90 (m, 1H), 2.81 (t, *J* = 7.0 Hz, 2H), 2.17 (d, *J* = 2.2 Hz, 1H), 1.25 (s, 9H), 1.13 (d, *J* = 7.0 Hz, 3H), 0.97 (t, *J* = 6.8 Hz, 2H), 0.05 (s, 9H); ^{13}C NMR (75 MHz, CD_2Cl_2): δ= 177.4, 156.9, 139.5, 139.3, 128.9, 128.8, 127.6, 125.2, 85.1, 77.3, 70.8, 63.1, 42.4, 39.2, 36.5, 32.9, 27.3, 18.1, 17.5, –1.4; IR (film): $\tilde{\upsilon}$ = 3311, 2956, 2901, 1723, 1523, 1479, 1279, 1250, 1152, 1059, 1034, 859, 838 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{24}H_{37}O_4NSi$ [M^+ +Na]: 454.23840, found: 454.23898.

Compound 56: A solution of compound **S-7** (298 mg, 0.69 mmol) in THF (4.6 mL) was added dropwise



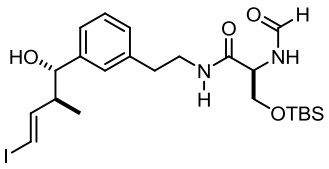
to a suspension of $Cp_2Zr(H)Cl$ (267 mg, 1.04 mmol) in THF (6.0 mL) in the dark. After stirring for 1 h, the mixture was cooled to 0°C before a solution of iodine (290 mg, 1.14 mmol) in THF (4.6 mL) was added dropwise until a pale yellow color persisted. After stirring for 5 min, the reaction was quenched with aq. sat. $Na_2S_2O_3$. The aqueous phase was extracted with EtOAc, the combined organic layers were washed with brine, dried over $MgSO_4$ and evaporated. The residue was purified by flash chromatography (hexanes/EtOAc, 10:1 → 6:1) to give product **56** as a pale yellow oil (260 mg, 67%). $[\alpha]_D^{20}$ = +7.9 (*c* = 0.11, CH_2Cl_2); ^{1}H NMR (400 MHz, CD_2Cl_2): δ= 7.30 – 7.26 (m, 1H), 7.14 – 7.09 (m, 3H), 6.47 (dd, *J* = 14.4, 8.7 Hz, 1H), 6.47 (dd, *J* = 14.4, 0.6 Hz, 1H), 5.47 (d, *J* = 7.4 Hz, 1H), 4.67 (brs, 1H), 4.11 (t, *J* = 8.3 Hz, 2H), 3.38 (td, *J* = 6.7, 6.7 Hz, 2H), 2.79 (t, *J* = 7.0 Hz, 2H), 2.68 – 2.62 (m, 1H), 1.20 (s, 9H), 0.97 – 0.91 (m, 5H), 0.04 (s, 9H); ^{13}C NMR (100 MHz, CD_2Cl_2): δ= 177.3, 156.8, 147.7, 139.9, 128.8, 128.8, 127.5, 125.2, 78.1, 76.6, 66.0, 47.1, 42.5, 39.1, 36.6, 27.3, 18.1, 16.3, 15.5, –1.4; IR (film): $\tilde{\upsilon}$ = 3336, 2955, 2902, 1723, 1521, 1279, 1250, 1152, 1059, 979, 946, 859, 837 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{24}H_{38}O_4NSiI$ [M^+ +Na]: 582.15071, found: 582.15090.

Compound S-8: A solution of $LiHBEt_3$ (1 M in hexanes, 1.60 mL) was added to a solution of compound



56 (255 mg, 0.46 mmol) in CH_2Cl_2 (26 mL) at 0°C. After stirring for 1 h, the reaction was quenched with EtOAc and sat. aq. NH_4Cl, the organic phase was washed with brine, dried over $MgSO_4$ and evaporated. The residue was purified by flash chromatography (hexanes/EtOAc, 10:1 → 3:1) to give product **S-8** as a colorless oil (176 mg, 81%). $[\alpha]_D^{20}$ = –59.4 (*c* = 1.7, CH_2Cl_2); ^{1}H NMR (400 MHz, CD_2Cl_2): δ= 7.30 – 7.26 (m, 1H), 7.16 – 7.12 (m, 3H), 6.57 (dd, *J* = 14.5, 8.4 Hz, 1H), 6.10 (dd, *J* = 14.5, 0.8 Hz, 1H), 4.68 (brs, 1H), 4.41 (d, *J* = 7.1 Hz, 1H), 4.11 (t, *J* = 8.4 Hz, 2H), 3.39 (td, *J* = 6.7, 6.7 Hz, 2H), 2.80 (t, *J* = 7.1 Hz, 2H), 2.56 – 2.47 (m, 1H), 0.95 (t, *J* = 8.3 Hz, 2H), 0.89 (d, *J* = 6.8 Hz, 3H), 0.03 (s, 9H); ^{13}C NMR (100 MHz, CD_2Cl_2): δ= 156.9, 148.7, 143.2, 139.6, 128.8, 128.6, 127.4, 125.1, 77.8, 76.4, 63.1, 48.8, 42.5, 36.6, 18.1, 16.3, –1.4; IR (film): $\tilde{\upsilon}$ = 3357, 2953, 2896, 1694, 1519, 1249, 1060, 949, 859, 837 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{19}H_{30}O_3NSiI$ [M^+ +Na]: 498.09319, found: 498.09377.

Compound 57: A solution of TBAF (1 M in THF, 517 µL) was slowly added to a solution of compound **S-8** (61.4 mg, 0.129 mmol) in THF (1.3 mL) at 0°C. The mixture was stirred overnight at room temperature before a second batch of TBAF (517 µL, 1 M in THF) was added. After additional 8 h, the

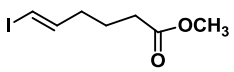


mixture was diluted with EtOAc and extracted with aq. sat. Na_2CO_3. The organic layers were washed with brine, dried over $MgSO_4$, and concentrated.

The resulting free amine was dissolved in CH_2Cl_2 (2.4 mL). O-TBS-N-formyl-L-serine (35.1 mg, 0.142 mmol), HOBt (19.2 mg, 0.142 mmol), and N-methylmorpholine (41.1 µL, 0.375 mmol) were successively added and the mixture was cooled to 0°C. EDC·HCl (32.2 mg, 0.168 mmol) was then introduced and stirring continued at room temperature for 20 h. The mixture was diluted with EtOAc and extracted with brine, the organic phase was dried over $MgSO_4$ and evaporated, and the residue was purified by flash chromatography (hexanes/EtOAc, 3:1 → 1:5) to give product **57** as a colorless oil (39 mg, 54%). $[\alpha]_D^{20}$ = –27.8 (*c* = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 8.11 (s, 1H), 7.28 – 7.24 (m, 1H), 7.13 – 7.10 (m, 3H), 6.58 (brdd, *J* = 14.4, 8.3 Hz, 2H), 6.44 (brs, 1H), 6.07 (dd, *J* = 14.4, 0.8 Hz, 1H), 4.41 – 4.35 (m, 2H), 4.00 (dd, *J* = 9.9, 3.8 Hz, 1H), 3.61 (dd, *J* = 9.9, 6.7 Hz, 1H), 3.53 – 3.49 (m, 1H), 3.45 – 3.41 (m, 1H), 2.80 (t, *J* = 6.9 Hz, 2H), 2.54 – 2.50 (m, 1H), 0.90 – 0.86 (m, 12H), 0.07 (s, 6H); ^{13}C NMR (100 MHz, CD_2Cl_2): δ = 169.6, 161.4, 148.8, 143.4, 139.3, 128.7, 128.3, 127.7, 125.3, 77.7, 76.2, 63.0, 53.6, 48.5, 41.2, 35.9, 25.9, 18.4, 16.3, –5.4, –5.5; IR (film): $\tilde{\upsilon}$ = 3309, 2954, 2928, 2857, 1647, 1533, 1383, 1253, 1107, 953, 835, 777, 707 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{23}H_{37}O_4N_2SiI$ [M^+ +Na]: 583.14596, found: 583.14548.

Building Blocks for the Preparation of Analogue 68 devoid of the Michael Acceptor Unit and the 1,4-Diene next to the Lactone Linkage (Scheme 9)

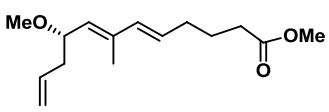
Methyl 6-iodohex-5-enoate (63): CuCN (45 mg, 0.5 mmol) was added to a solution of *t*BuPh$_2$SiLi in



THF (0.5 M, 1 mL, 0.5 mmol) at 0°C. After stirring for 20 min at this temperature, methyl hex-5-ynoate **62** (31.5 mg, 0.25 mmol) was added neat and stirring was continued for 15 min. MeOH (0.2 mL) was then added, followed by sat. aq. NH_4Cl (5 mL). The aqueous phase was extracted with *tert*-butyl methyl ether (2 mL), the combined organic layers were washed with brine (2 mL), dried ($MgSO_4$), filtered and evaporated.

A solution of ICl (76.2 mg, 0.469 mmol) in CH_2Cl_2 (5 mL) was added dropwise at 0°C to a solution of the crude alkenyl silane thus obtained in CH_2Cl_2 (2 mL). The reaction was quenched with sat. aq. $Na_2S_2O_3$ (2 mL), the aqueous phase was extracted with CH_2Cl_2 (2 mL), the combined organic phases were washed with brine (2 mL), dried ($MgSO_4$), filtered and evaporated, and the residue was purified by flash chromatography (pentane/Et_2O, 1:0 → 95:5) to give iodide **63** as a colorless oil (57 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.49 (dt, *J* = 14.4, 7.6 Hz, 1H), 6.06 (d, *J* = 14.4 Hz, 1H), 3.70 (s, 3H), 2.34 (t, *J* = 7.4 Hz, 2H), 2.12 (dt, *J* = 7.6, 7.4 Hz, 2H), 1.76 (quint., *J* = 7.3 Hz, 2H).

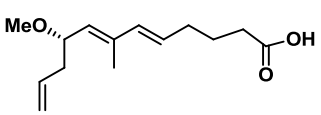
(*S*)-Methyl 9-methoxy-7-methyldodeca-5,7,11-trienoate (S-9): A 10 mL Schlenk tube was charged



with alkenyl stannane **64** (133 mg, 0.319 mmol),[3] alkenyl iodide **63** (76 mg, 0.29 mmol), [Ph_2PO_2][NBu_4] (160 mg, 0.348 mmol) and DMF (0.6 mL). The mixture was vigorously stirred while Pd(PPh_3)$_4$ (13.4 mg,

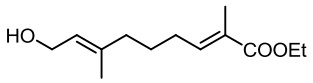
0.0116 mmol) and copper thiophene-2-carboxylate (CuTC, 66 mg, 0.348 mmol) were successively added, causing an immediate color change to black. After stirring for 10 min, the reaction was quenched at 0°C with H_2O (2 mL), and the resulting suspension was filtered through a pad of Celite, which was carefully rinsed with EtOAc (20 mL). The aqueous phase was extracted with EtOAc (2 × 1 mL), the combined organic layers were washed with H_2O (3 × 5 mL), brine (5 mL), dried over $MgSO_4$, filtered and evaporated, and the residue was purified by flash chromatography (hexanes/*tert*-butyl methyl ether, 1:0 → 9:1) to afford ester **S-9** as a colorless oil (48 mg, 66%). $[\alpha]_D^{20}$ = –29.6 (*c* = 1.2, CH_2Cl_2) ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 6.10 (d, *J* = 15.6 Hz, 1H), 5.85-5.70 (m, 1H), 5.68-5.60 (m, 1H), 5.22 (d, *J* = 9.1 Hz, 1H), 5.04-4.98 (m, 2H), 4.07-4.01 (m, 1H), 3.63 (s, 3H), 3.20 (s, 3H), 2.40-2.30 (m, 3H), 2.28-2.10 (m, 3H), 1.78-1.70 (m, 5H); ^{13}C NMR (100 MHz, CD_2Cl_2): δ = 174.5, 137.4, 135.7, 135.6, 131.4, 129.4, 117.1, 77.5, 56.3, 52.0, 40.8, 34.1, 32.9, 25.4, 13.6; IR (film): $\tilde{\upsilon}$ = 2933, 2818, 1737, 1641, 1436, 1242, 1193, 1152, 1092, 964, 914 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{15}H_{24}O_3$ [M^+ +Na]: 275.16177, found: 275.16147.

(*S*)-9-Methoxy-7-methyldodeca-5,7,11-trienoic acid (65): A solution of LiOH (3 M in H_2O, 0.38 mL, 1.14 mmol) was added to a solution of compound **S-9** (48 mg, 0.19 mmol) in MeOH/THF (1:1, 1 mL) and the resulting mixture was stirred for 24 h before it was acidified to pH ≈ 3 with 1 M aq. HCl (1.2 mL). The aqueous phase was extracted with *tert*-butyl methyl ether (3 × 2 mL), the combined extracts were dried over $MgSO_4$, filtered and evaporated, and the residue was purified by flash chromatography (hexanes/*tert*-butyl methyl ether, 9:1 → 1:1) to give acid **65** as a colorless oil (32 mg, 75%). $[\alpha]_D^{20}$ = –33.2 (*c* = 1.3, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.11 (d, *J* = 15.6, 1H), 5.78 (m, 1H), 5.64 (m, 1H), 5.25 (d, *J* = 9.0 Hz, 1H), 5.10-5.00 (m, 2H), 4.05 (m, 1H), 3.25 (s, 3H), 2.42-2.33 (m, 3H), 2.28-2.13 (m, 3H), 1.83-172 (m, 5H); ^{13}C NMR (100 MHz, CD_2Cl_2): δ = 179.1, 136.6, 135.3, 134.5, 130.6, 128.2, 116.8, 76.9, 55.9, 40.0, 33.3, 32.0, 24.4, 13.1; IR (film): $\tilde{\upsilon}$ = 3077, 2980, 2932, 1737, 1708, 1440, 1414, 1238, 1093, 965, 915 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{14}H_{22}O_3$-H: 237.14962 [M^--H]; found: 237.14930.



Building Blocks for the Preparation of Analogue 74 Devoid of the C5-C6 Double Bond (Scheme 10)

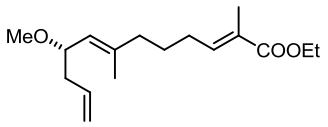
Compound 70. Hünig base (2.5 mL, 14.6 mmol) was added to a mixture of $(Et_2O)P(O)CH(Me)COOEt$ (2.8 mL, 12.86 mmol) and LiCl (500 mg, 11.79 mmol) in MeCN (60 mL) at 0°C and the resulting suspension was stirred at ambient temperature for 20 min before a solution of compound **69** (1.41 g, 9.9 mmol, containing 5% of the *Z*-isomer)[7] in MeCN (10 mL) was added dropwise at 0°C. After stirring overnight at ambient temperature, the mixture was partitioned between brine and EtOAc, the combined organic layers were dried over Na_2SO_4 and evaporated, and the residue was purified by flash chromatography (hexanes/EtOAc, 1:1) to give product **70** as a colorless syrup (1.906 g, 85%, containing 5% of



[7] R. M. Wilson, W. S. Jen, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2005**, *127*, 11616-11617.

inseparable (7*Z*)-isomer). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.72 (m, 1H), 5.38 (m, 1H), 4.19-4.08 (m, 4H), 2.16-2.08 (m, 2H), 2.01 (t, *J* = 7.6 Hz, 2H), 1.79 (s, 3H), 1.63 (s, 3H), 1.59-1.50 (m, 2H), 1.26 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.2, 141.8, 138.7, 127.9, 124.0, 60.3, 59.1, 39.1, 28.1, 26.4, 16.0, 14.2, 12.2; IR (film): $\tilde{\upsilon}$ = 3420, 2923, 1706, 1647, 1445, 1367, 1255, 1174, 1122, 1080, 1001, 774 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{13}H_{22}O_3$ [M^+ +Na]: 249.14612, found: 249.14626.

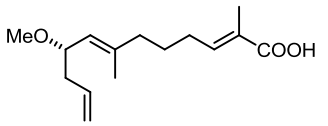
Compound 71: MnO_2 (1.5 g, 17 mmol) was added to a solution of compound **70** (163 mg, 0.72 mmol) in CH_2Cl_2 (15 mL) and the resulting mixture was stirred for 15 h before it was filtered through a pad of Celite. The filtrate was evaporated and the resulting aldehyde was directly used in the next step (148 mg, 92%).



Allylmagnesium bromide (1 M in Et_2O, 1.25 mL) was added over 30 min to a solution of (–)-Ipc_2BOMe (410 mg, 1.29 mmol) in Et_2O (1 mL) at 0°C. Stirring was continued for 30 min at 0°C and for 1 h at ambient temperature. The resulting salts were filtered off under Ar through a pad of Celite and the filtrate was cooled to –78°C before a solution of the crude aldehyde (148 mg, 0.66 mmol) in Et_2O (1 mL) was added dropwise over the course of 30 min. After stirring at –78°C for 2 h, the mixture was allowed to reach ambient temperature before the reaction was quenched with a mixture of H_2O_2 (0.5 mL, 30% *w*/*w*) and NaOH (3 M, 1.2 mL). The resulting mixture was stirred at reflux temperature for 1h and at ambient temperature for another 14 h before it was partitioned between EtOAc and brine. The combined organic layers were dried over Na_2SO_4 and evaporated, and the residue was purified by flash chromatography (hexanes/EtOAc, 4:1) to give the corresponding homoallylic alcohol which was contaminated with by-products derived from the IPC-borane reagent.

This material was added to a mixture of Meerwein salt (130 mg, 0.875 mmol) and proton sponge (217 mg, 1 mmol) in CH_2Cl_2 (5 mL) at 0°C. The cooling bath was removed and the mixture allowed to stir at ambient temperature for 3 h. After filtration through a pad of Celite, a standard extractive work up followed by purification of the residue by flash chromatography (hexanes/EtOAc, 10:1) afforded compound **71** as a colorless oil (50 mg, 27% over 2 steps, containing 5% of the corresponding (7*Z*)-isomer). Isomerically pure *E*-**71** was obtained by preparative HPLC, which analyzed as follows: $[\alpha]_D^{20}$ = –8.7 (*c* = 0.45, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.74 (m, 1H), 5.77 (m, 1H), 5.09-4.96 (m, 3H), 4.17 (q, *J* = 7.0 Hz, 2H), 3.93 (m, 1H), 3.23 (s, 3H), 2.34 (m, 1H), 2.24-2.00 (m, 5H), 1.81 (s, 3H), 1.66 (d, *J* = 1.2 Hz, 3H), 1.62-1.52 (m, 2H), 1.28 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.2, 141.7, 139.1, 134.7, 128.0, 125.8, 116.6, 76.9, 60.3, 55.6, 40.1, 39.2, 28.1, 26.6, 16.6, 14.2, 12.3; IR (film): $\tilde{\upsilon}$ = 2980, 2934, 1709, 1648, 1446, 1367, 1257, 1174, 1094, 913, 774 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{17}H_{28}O_3$ [M^+ +Na]: 303.19306, found: 303.19332.

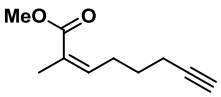
Compound 72: LiOH (1 M in H_2O, 0.5 mL) was added to a solution of ester **71** (22 mg, 0.078 mmol) in a mixture of MeOH (0.4 mL) and THF (0.4 mL) and the resulting solution was stirred for 20 h. For work up, the mixture was acidified with HCl (0.5 M) until a pH of ca. 2 was reached, the aqueous phase was extracted with EtOAc, the combined extracts were dried over Na_2SO_4 and evaporated. Acid **72** could be used in the next step without further purification (19 mg, 97%). $[\alpha]_D^{20}$ = –17.3 (*c* = 0.55, CH_2Cl_2); ^{1}H NMR (300



MHz, CD_2Cl_2): δ= 6.91 (m, 1H), 5.78 (m, 1H), 5.10-4.96 (m, 3H), 3.94 (m, 1H), 3.21 (s, 3H), 2.33 (m, 1H), 2.26-2.02 (m, 5H), 1.83 (s, 3H), 1.67 (s, 3H), 1.65-1.54 (m, 2H); ^{13}C NMR (75 MHz, CD_2Cl_2): δ= 173.5, 145.3, 139.5, 135.5, 127.5, 126.4, 116.6, 77.2, 55.7, 40.5, 39.6, 28.7, 26.9, 16.7, 12.2; IR (film): $\tilde{\upsilon}$ = 2931, 1684, 1641, 1421, 1284, 1092, 961, 913 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{15}H_{24}O_3$ [M^+ +Na]: 275.16176, found: 275.16191.

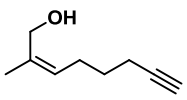
Building Blocks for the C17-Desmethoxy Analogue 81 (Scheme 11)

(2*Z*)-Methyl 2-methyloct-2-en-7-ynoate (76): Pyridine·SO_3 (3.65 g, 23 mmol) was added at 0°C to a solution of hex-5-yn-1-ol (**75**) (0.5 g, 5.1 mmol), Et_3N (3.2 mL, 23 mmol) and DMSO (2 mL, 23 mmol) in CH_2Cl_2 (20 mL), and the resulting mixture was stirred at room temperature for 30 min. The reaction was quenched with H_2O (20 mL), the aqueous phase was extracted with CH_2Cl_2 (2 × 3 mL), the combined organic layers were washed with brine (10 mL), dried with Na_2SO_4, filtered and carefully evaporated to give crude hex-5-yn-1-al (339 mg, 3.53 mmol) as a colorless oil.



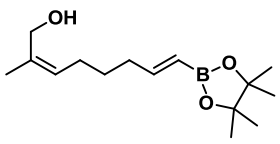
In a separate Schlenk tube a solution of KHMDS in toluene (7.1 mL, 3.56 mmol) was added at –78°C to a solution of $(CF_3CH_2O)_2P(O)CH(Me)CO_2Me$ (1.24 g, 3.71 mmol) and 18-crown-6 (740 mg, 2.82 mmol) in THF (10 mL). After 30 min, a solution of the crude hex-5-yn-1-al in THF (5 mL) was introduced and stirring continued at −78°C for 1 h. The reaction was quenched with sat. aq. NH_4Cl (20 mL), the resulting mixture was allowed to stand at room temperature and the aqueous phase was extracted with Et_2O (3 × 5 mL). The combined organic layers were washed with H_2O (20 mL) and brine (20 mL), dried over Na_2SO_4, and evaporated. Purification of the residue by flash chromatography (hexanes/EtOAc, 30:1) afforded ester **76** as a colorless oil (566 mg, 66% over 2 steps). ^{1}H NMR (CD_2Cl_2, 300 MHz): δ= 5.90 (qt, *J* = 1.3, 7.5 Hz, 1H), 3.69 (s, 3H), 2.51 (dt, *J* = 1.1, 7.6 Hz, 2H), 2.18 (dt, *J* = 2.7, 7.2 Hz, 2H), 1.96 (t, *J* = 2.6 Hz, 1H), 1.86 (q, *J* = 1.3 Hz, 3H), 1.61 (quint., *J* = 7.3 Hz, 2H); ^{13}C NMR (CD_2Cl_2, 75.5 MHz): δ= 168.5, 141.9, 128.2, 84.5, 68.6, 51.4, 29.0, 28.7, 20.8, 18.4; IR (film): $\tilde{\upsilon}$ = 2951, 1714, 1647, 1455, 1434, 1367, 1240, 1194, 1124 cm^{-1}; MS (EI): *m*/*z* (%): 166 (0.4, M^+), 165 (3), 151 (3), 138 (28), 127 (75), 107 (100), 95 (73), 91 (61), 79 (65); HRMS (CI, *i*–butane) calcd for $C_{10}H_{15}O_2$ [M^+ +H]: 167.10721, found: 167.10725.

(2*Z*)-2-Methyloct-2-en-7-yn-1-ol (**S-10**): A solution of Dibal–H in hexane (1 M, 5.9 mL, 5.92 mmol) was slowly added to a solution of ester **76** (493 mg, 2.96 mmol) in CH_2Cl_2 (30 mL) at −78°C. The resulting mixture was stirred 30 min at −78°C before it was quenched with EtOAc (5 mL). The cooling bath was removed and a sat. aq. solution of Rochelle salt was added (20 mL). The mixture was stirred at room temperature until a clean separation of the phases was reached. The aqueous layer was extracted with Et_2O (3 × 5 mL), the combined organic phases were dried over Na_2SO_4, filtered and evaporated to yield alcohol **S-10** as a colorless oil (409 mg). The crude product was used in the next step without further purification. ^{1}H NMR (CD_2Cl_2, 300 MHz): δ= 5.25 (tt, *J* = 0.8, 7.5 Hz, 1H), 4.10 (m, 2H), 2.17 (dt, *J* = 2.6, 7.1 Hz, 4H),

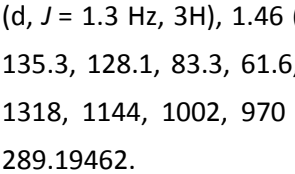


1.99 (t, *J* = 2.6 Hz, 1H), 1.77 (q, *J* = 1.1 Hz, 3H), 1.69 (bs, 1H), 1.55 (quint., *J* = 7.1 Hz, 2H); ^{13}C NMR (CD_2Cl_2, 75.5 MHz): δ = 136.2, 127.2, 84.7, 68.7, 61.5, 28.9, 26.6, 21.4, 17.9; IR (film): $\tilde{\upsilon}$ = 3300, 2937, 2862, 1433, 1378, 1247, 1002 cm^{-1}; MS (EI): *m*/*z* (%): 137 (1.6), 123 (19), 109 (21), 105 (35), 95 (34), 91 (38), 81 (62), 79 (80), 71 (38), 67 (54), 43 (100); HRMS (CI, *i*-butane) calcd for $C_9H_{15}O$ [M^+ +H]: 139.11229, found: 139.11226.

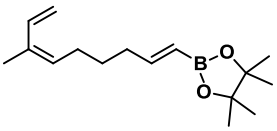
(2*Z*,7*E*)-2-Methyl-8-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)octa-2,7-dien-1-ol (**77**): To a solution of **S-10** (300 mg, 2.17 mmol) in THF (4 mL) was added pinacol borane (1 mL, 6.52 mmol) and 9–BBN (52.6 mg, 0.217 mmol). The mixture was stirred for 12 h before the reaction was quenched with sat. aq. NH_4Cl (10 mL). The aqueous phase was extracted with *tert*-butyl methyl ether (3 × 3 mL), the combined extracts were dried over $MgSO_4$, filtered and evaporated to give a crude colorless oil. Purification by flash chromatography (hexanes/acetone, 10:1) afforded alcohol **77** as a colorless oil (459 mg, 79%). ^{1}H NMR (CD_2Cl_2, 400 MHz): δ = 6.52 (td, *J* = 17.9, 6.5 Hz, 1H), 5.38 (td, *J* = 17.9, 1.6 Hz, 1H), 5.27 (d, *J* = 7.5 Hz, 1H), 4.08 (s, 2H), 2.18–2.10 (m, 2H), 2.05 (dt, *J* = 7.5 Hz, 2H), 1.77 (d, *J* = 1.3 Hz, 3H), 1.46 (quint., *J* = 7.4 Hz, 2H), 1.23 (s, 12H); ^{13}C NMR (CD_2Cl_2, 100 MHz): δ = 154.4, 135.3, 128.1, 83.3, 61.6, 35.6, 29.0, 27.3, 24.9, 21.3; IR (film): $\tilde{\upsilon}$ = 3435, 2977, 2928, 1638, 1362, 1318, 1144, 1002, 970 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{15}H_{27}O_3B$ [M^+ +Na]: 289.19455, found: 289.19462.



(2*Z*,7*E*)-2-Methyl-8-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)octa-2,7-dien-1-ol (**S-11**): Dess-Martin periodinane (804 mg, 1.89 mmol) was added in one portion to a solution of alcohol **77** (459 mg, 1.72 mmol) in CH_2Cl_2 (9 mL) at 0°C. After stirring for 1 h at room temperature, the mixture was diluted with pentanes before it was filtered through a pad of Celite. The filtrate was evaporated to give a crude white solid, which was purified by flash chromatography (hexanes/acetone, 10:1) to give aldehyde **S-11** as a colorless oil (352 mg, 78%). ^{1}H NMR (CD_2Cl_2, 300 MHz): δ = 10.10 (s, 1H), 6.56 (td, *J* = 17.9, 6.5 Hz, 1H), 6.54–6.46 (m, 1H), 5.41 (td, *J* = 17.9, 1.5 Hz, 1H), 2.56 (q, *J* = 7.6 Hz, 2H), 2.20 (dt, *J* = 7.0 Hz, 2H), 1.74 (d, *J* = 1.2 Hz, 3H), 1.61 (quint., *J* = 7.5 Hz, 2H), 1.23 (s, 12H); ^{13}C NMR (CD_2Cl_2, 75.5 MHz): δ = 191.3, 153.5, 149.3, 136.6, 83.3, 35.4, 28.6, 26.5, 25.0, 16.5; MS (EI): *m*/*z* (%): 264 (11, M^+), 249 (8), 235 (3), 221 (9), 206 (16), 181 (22), 164 (73), 149 (48), 136 (29), 120 (50), 101 (61), 93 (39), 83 (69), 41 (100); IR (film): $\tilde{\upsilon}$ = 2978, 2928, 1677, 1638, 1362, 1321, 1144, 996, 970 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{15}H_{25}BO_3$ [M^+ +Na]: 287.17944, found: 287.17884.



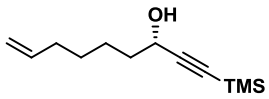
(3*Z*,8*E*)-3-Methyl-9-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)nona-1,2,7-triene (**78**): *n*BuLi (1.6 M in hexanes, 0.9 mL, 1.46 mmol) was added dropwise to a suspension of methyltriphenylphosphonium bromide (569 mg, 1.6 mmol) in THF (3 mL) at −78°C. The resulting mixture was allowed to reach ambient temperature. After stirring for 30 min, the orange solution was cooled again to −78°C before a solution of aldehyde **77** (352 mg, 1.33 mmol) in THF (3 mL) was slowly added. The mixture



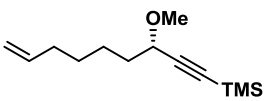
was warmed to ambient temperature over the course of 1 h before the reaction was quenched with sat. aq. NH_4Cl (5 mL) and H_2O (5 mL). The aqueous phase was extracted with Et_2O (2 × 5 mL), the combined extracts were dried over $MgSO_4$ and evaporated. Purification of the residue by flash chromatography (pentane/Et_2O, 95:5) afforded diene **78** as a colorless oil (209 mg, 60%). ^{1}H NMR (CD_2Cl_2, 300 MHz): δ = 6.77 (ddd, *J* = 0.75, 10.9, 17.3 Hz, 1H), 6.57 (td, *J* = 6.4, 17.7 Hz, 1H), 5.43–5.34 (m, 2H), 5.18 (d, *J* = 17.3 Hz, 1H), 5.07 (td, *J* = 1.5, 10.9 Hz, 1H), 2.11–2.21 (m, 4H), 1.80 (q, *J* = 1.1 Hz, 3H), 1.49 (quint., *J* = 7.5 Hz, 2H), 1.23 (s, 12H); ^{13}C NMR (CD_2Cl_2, 75 MHz): δ = 154.4, 134.1, 132.9, 131.3, 113.4, 83.3, 35.7, 28.9, 27.2, 24.9, 19.8; IR (film): $\tilde{\upsilon}$ = 2983, 2930, 1650, 1472, 1331, 1130, 1109, 851 cm^{-1}; MS (EI): *m*/*z* (%): 262 (28, M^+), 247 (16), 233 (6), 220 (3), 205 (14), 194 (5), 162 (33), 147 (22), 134 (93), 119 (30), 94 (63), 84 (84), 79 (100); HRMS (ESI): *m*/*z*: calcd for $C_{16}H_{27}BO_2$ [M^+ +Na]: 285.19963, found: 287.19984.

Building Blocks for the Preparation of Analogue 90 Devoid of the Trisubstituted Alkene at C13–C14 (Scheme 12)

(*S*)-1-(Trimethylsilyl)non-8-en-1-yn-3-ol (**S-12**): A Schlenk tube was charged with ketone **82** (0.66 g, 3.17 mmol)[8] and degassed *iso*-propanol (10 mL). The resulting solution was purged with Ar for 0.5 h before the ruthenium complex **91** was added as a solid (0.114 g, 0.19 mmol). The resulting mixture was stirred for 12 h and evaporated, and the residue purified by flash chromatography (pentanes/Et_2O, 100:1 → 20:1) to give alcohol **S-12** as a colorless oil (648 mg, 97%, *ee* = 98% determined by chiral GC). $[\alpha]_D^{20}$ = +2 (*c* = 1.0, CH_2Cl_2); ^{1}H NMR (CD_2Cl_2, 300 MHz): δ = 5.88–5.72 (m, 1H), 5.05–4.90 (m, 2H), 4.34 (t, *J* = 6.4 Hz, 1H), 2.06 (q, *J* = 6.4 Hz, 2H), 1.91 (bs, 1H), 1.75–1.60 (m, 2H), 1.55–1.35 (m, 4H), 0.16 (s, 9H); ^{13}C NMR (CD_2Cl_2, 75.5 MHz): δ = 138.7, 114.4, 106.9, 89.3, 62.8, 37.5, 33.6, 28.4, 24.6, –0.2; IR (film): $\tilde{\upsilon}$ = 3337, 2989, 2870, 1641, 1392, 1250, 1142, 839 cm^{-1}; MS (EI): *m*/*z* (%): 210 (0.2), 195 (7), 177 (6), 167 (6), 153 (6), 127 (43), 118 (9), 105 (11), 99 (54), 92 (14), 75 (100); HRMS (ESI): *m*/*z*: calcd for $C_{12}H_{22}OSi$ [M^+ +Na]: 233.13308, found: 233.13321.



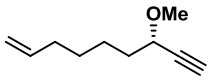
(*S*)-(3-Methoxynon-8-en-1-ynyl)trimethylsilane (**83**): *n*BuLi (1.6 M in hexane, 1.9 mL, 3.08 mmol) was added dropwise to a solution of alcohol **S-12** (648 mg, 3.08 mmol) in THF (11 mL) at –78°C. The resulting mixture was stirred for 10 min at –78°C before MeI (1.5 mL, 24.6 mmol) was introduced. The temperature was then raised to –25°C before DMSO (0.75 mL) was slowly added to give a white suspension. After stirring for 1h at that temperature, the cooling bath was removed and stirring continued at room temperature for 12h. The reaction was quenched with ice water and aq. sat. NH_4Cl (1:1, 10 mL), the aqueous phase was extracted with Et_2O (2 × 5 mL), the combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, filtered and evaporated to give product **S-13** as a colorless oil (690 mg, quant.). $[\alpha]_D^{20}$ = –32.4 (*c* = 1.25, CH_2Cl_2); ^{1}H NMR (CD_2Cl_2, 300 MHz): δ = 5.81–5.65 (m, 1H), 4.97–4.80 (m, 2H),



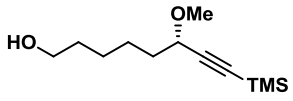
[8] J. Ackroyd, M. Karpf, A. S. Dreiding, *Helv. Chim. Acta* **1985**, 68, 338-344.

3.81 (t, *J* = 6.5 Hz, 1H), 3.26 (s, 3H), 2.05–1.90 (m, 2H), 1.65–1.50 (m, 2H), 1.40–1.35 (m, 4H), 0.08 (s, 9H); ^{13}C NMR (CD_2Cl_2, 75.5 MHz): δ = 139.4, 114.5, 105.3, 90.6, 71.9, 56.4, 35.7, 34.0, 29.0, 25.1, 0.0; IR (film): $\tilde{\upsilon}$ = 2930, 1641, 1464, 1333, 1250, 1105, 840 cm^{-1}; MS (EI): *m*/*z* (%): 224 (M^+, 0.6), 209 (8), 195 (2), 181 (5), 167 (3), 141 (100), 113 (32), 89 (16), 73 (18); HRMS (ESI): *m*/*z*: calcd for $C_{13}H_{24}OSi$ [M^+ +Na]: 247.14886, found: 247.14870.

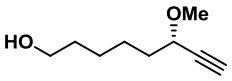
(*S*)-7-Methoxynon-1-en-8-yne (**S-13**): A solution of TBAF (1 M in THF, 1 mL, 1 mmol) was slowly added to a solution of alkene **S-13** (187 mg, 0.83 mmol) in THF (8 mL) at 0°C. The resulting mixture was stirred for 30 min at 0°C before the reaction was quenched with H_2O (10 mL). The aqueous layer was extracted with Et_2O (3 × 5 mL), the combinated organic phases were washed with brine (10 mL), dried over Na_2SO_4, filtered and evaporated to give a crude pale yellow oil, which was purified by flash chromatography (hexanes/Et_2O, 2:1 → 1:1) to give compound **83** as a colorless oil (110 mg, 87%). $[\alpha]_D^{20}$ = –24.9 (*c* = 0.48, CH_2Cl_2); IR (film): $\tilde{\upsilon}$ = 2928, 2859, 1641, 1464, 1336, 1104 cm^{-1}; ^{1}H NMR (CD_2Cl_2, 300 MHz): δ = 5.81–5.65 (m, 1H), 4.95–4.80 (m, 2H), 3.83 (td, *J* = 6.5, 2.1 Hz, 1H), 2.27 (s, 3H), 2.38 (d, *J* = 2.1 Hz, 1H), 1.92–2.20 (M, 2H), 1.65–1.55 (m, 2H), 1.43–1.25 (m, 4H); ^{13}C NMR (CD_2Cl_2, 75.5 MHz): δ = 139.3, 114.5, 83.2, 73.8, 71.3, 56.5, 35.8, 34.0, 29.0, 25.0; MS (EI): *m*/*z* (%): 152 (M^+, 0.04), 137 (1), 105 (8), 91 (14), 84 (4), 79, (14), 69 (100); HRMS (CI, *i*–butane) calcd for $C_{10}H_{16}O$ [M^+ +H]: 153.12794, found: 153.12794. Attempts at selective hydroboration of this product at the alkyne site with pinacol borane under a variety of conditions led to hardly tractable product mixtures, cf. Text.

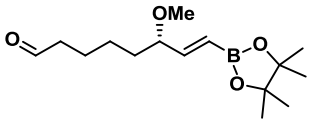


(*S*)-6-Methoxy-8-(trimethylsilyl)oct-7-yn-1-ol (**S-14**): To a solution of alkene **83** (640 mg, 2.85 mmol) in 1,4-dioxane/water (19/5 mL) were sequentially added 2,6-lutidine (0.65 mL, 5.71 mmol), OsO_4 (0.715 mL, 0.057 mmol, 2.5% *w*/*w* in *t*BuOH) and $NaIO_4$ (2.44 g, 11.42 mmol). The resulting heterogeneous mixture was vigorously stirred for 1.5 h before it was diluted with water. The aqueous phase was extracted with Et_2O (3 × 10 mL), the combined organic layers were washed with HCl (1 M, 2 × 10 mL), aq. $Na_2S_2O_3$ (10% *w*/*w*, 10 mL) and brine (10 mL), dried over $MgSO_4$, and carefully evaporated to give a pink oil (914 mg).

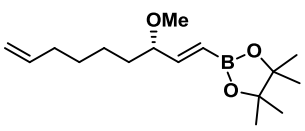


This crude aldehyde was dissolved in MeOH (20 mL) and treated with $NaBH_4$ (130 mg, 3.42 mmol) at 0°C. After 30 min, the mixture was diluted with sat. aq. $NaHCO_3$ (10 mL) and extracted with *tert*-butyl methyl ether (3 × 5 mL). The combined extracts were washed with brine (10 mL), dried over $MgSO_4$, and carefully evaporated, and the residue was purified by flash chromatography (hexanes/Et_2O, 1:1) to give alcohol **S-14** as a colorless oil (453 mg, 70% over both steps). $[\alpha]_D^{20}$ = –24.2 (*c* = 1.29, CH_2Cl_2); ^{1}H NMR (CD_2Cl_2, 400 MHz): δ = 3.90 (t, *J* = 6.6 Hz, 1H), 3.57 (t, *J* = 6.6 Hz, 2H), 3.34 (s, 3H), 1.73–1.30 (m, 8H), 0.16 (s, 9H); ^{13}C NMR (CD_2Cl_2, 100 MHz): δ = 105.2, 90.6, 71.9, 63.0, 56.4, 35.8, 33.1, 25.9, 25.4, 0.0; MS (EI): *m*/*z* (%): 228 (M^+, 0.06), 213 (4), 141 (100), 113 (31), 83 (10), 73 (15); IR (film): $\tilde{\upsilon}$ = 3355, 2936, 2862, 2168, 1464, 1333, 1249, 1087, 1006, 838, 759 cm^{-1}; HRMS (CI, *i*-butane) calcd for $C_{12}H_{25}O_2Si$+H: 229.16238, found: 229.16211.

(*S*)-6-Methoxyoct-7-yn-1-ol (**84**): A solution of TBAF (1 M in THF, 1.9 mL, 1.9 mmol) was added  dropwise to a solution of alcohol **S-14** (427 mg, 1.87 mmol) in THF (7 mL) at 0°C. The resulting mixture was stirred for 30 min at 0°C before the reaction was quenched with H_2O (10 mL). The mixture was extracted with Et_2O (3 × 5 mL), the combinated extracts were washed with brine (10 mL), dried over Na_2SO_4, filtered and evaporated, and the residue was purified by flash chromatography (hexanes/Et_2O, 2:1 → 1:1) to give compound **84** as a colorless oil (247 mg, 85%). $[\alpha]_D^{20}$ = –32.1 (*c* = 1.0, CH_2Cl_2); ^{1}H NMR (CD_2Cl_2, 400 MHz): δ = 3.93 (dt, *J* = 6.5, 2.0 Hz, 1H), 3.58 (t, *J* = 6.6 Hz, 2H), 3.37 (s, 3H), 2.48 (d, *J* = 2.0 Hz, 1H), 1.78–1.30 (m, 9H); ^{13}C NMR (CD_2Cl_2, 100 MHz): δ = 83.2, 73.8, 71.3, 62.9, 56.5, 35.8, 33.1, 25.8, 25.3; IR (film): $\tilde{\upsilon}$ = 3291, 2935, 2862, 1463, 1335, 1081, 1055, 998 cm^{-1}; MS (EI): *m*/*z* (%): 156 (M^+, 0.01), 125 (1), 111 (2), 97 (5), 84 (25), 69 (100); HRMS (CI, *i*–butane) calcd for $C_9H_{16}O_2$ [M^+ +Na]: 157.12286, found: 157.12300.

(*S*,*E*)-6-Methoxy-8-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)oct-7-enal (**S-15**): Pinacol borane  (0.5 mL, 3.16 mmol) and 9–BBN (38 mg, 0.158 mmol) were added to a solution of alkyne **84** (247 mg, 1.58 mmol) in THF (3 mL), and the resulting mixture was stirred for 12 h before the reaction was quenched with sat. aq. NH_4Cl (4 mL). The aqueous phase was extracted with *tert*-butyl methyl ether (3 × 3 mL), the combined extracts were dried over $MgSO_4$, filtered and evaporated, and the residue was purified by flash chromatography (pentane/Et_2O, 1:1) to give alcohol **85** contaminated with boron impurities.

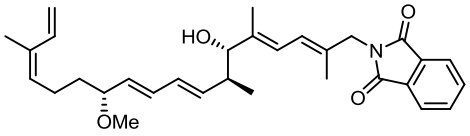
Dess–Martin periodinane (1 g, 2.45 mmol) was added to a solution of this compound (464 mg) in CH_2Cl_2 (10 mL) at 0°C. The mixture was stirred for 3 h at room temperature before the reaction was quenched with a mixture of sat. aq. $NaHCO_3$, sat. aq. $Na_2S_2O_3$ and H_2O (1:1:1, 10 mL). The resulting mixture was vigorously stirred for 30 min, the aqueous phase was extracted with CH_2Cl_2 (5 mL), the combined organic layers were washed with brine, dried with Na_2SO_4, filtered and evaporated. The residue was purified by flash chromatography (hexanes/acetone, 15:1 → 10:1) to give aldehyde **S-15** as a colorless oil (273 mg, 61% over 2 steps). $[\alpha]_D^{20}$ = –51.5 (*c* = 1.4, CH_2Cl_2); ^{1}H NMR (CD_2Cl_2, 400 MHz): δ = 9.70 (t, *J* = 1.7 Hz, 1H), 6.32 (dd, *J* = 18.1, 6.7 Hz, 1H), 5.52 (dd, *J* = 18.1, 1.1 Hz, 1H), 3.54 (qd, *J* = 6.7, 1.0 Hz, 1H), 3.22 (s, 3H), 2.38 (dt, *J* = 7.3, 1.8 Hz, 2H), 1.65–1.26 (m, 6H), 1.23 (s, 12H); ^{13}C NMR (CD_2Cl_2, 100 MHz): δ = 202.8, 153.3, 83.7, 83.6, 56.7, 44.2, 35.1, 25.2, 25.0, 25.0, 22.4; IR (film): $\tilde{\upsilon}$ = 2979, 2935, 2822, 1724, 1640, 1462, 1390, 1361, 1322, 1271, 1214, 1143, 1107; 1087; 1000; 969; 848 cm^{-1}; MS (EI): *m*/*z* (%): 282 (M^+,0.3), 267 (0.8), 197 (100), 182 (3), 167 (3), 141 (7), 138 (9); HRMS (ESI): *m*/*z*: calcd for $C_{15}H_{27}O_4B$ [M^+ +Na]: 305.18946, found: 305.18956.

(*S*,*E*)-2-(3-Methoxynona-1,8-dienyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**86**)**:** Prepared as  described for compound **83**; colorless oil (90 mg, 67%). $[\alpha]_D^{20}$ = –15.5 (*c* = 1, CH_2Cl_2); ^{1}H NMR (CD_2Cl_2, 400 MHz): δ = 6.35 (dd, *J* = 18.1, 6.7 Hz, 1H), 5.87–5.75 (m, 1H), 5.53 (dd, *J* = 18.1, 1.0 Hz, 1H), 5.30–4.89 (m, 2H), 3.55 (dt, *J* = 6.7, 0.9 Hz, 1H), 3.23 (s, 3H), 2.05 (q, *J* = 6.1 Hz, 2H), 1.57–1.29 (m, 6H), 1.25 (s, 12H); ^{13}C NMR (CD_2Cl_2, 100 MHz): δ = 153.6, 139.5, 114.3, 83.9, 83.5, 56.7, 35.2, 34.1, 29.3, 25.2; IR (film): $\tilde{\upsilon}$ = 2978, 2932, 2859, 1641, 1464, 1362, 1333, 1145, 1105, 998, 970, 849 cm^{-1};

MS (EI): *m*/*z* (%): 280 (M^+, 2), 265 (5), 197 (100), 180 (2), 165 (3), 141 (5), 112 (7); HRMS (ESI): *m*/*z*: calcd for $C_{16}H_{29}O_3B$ [M^+ +Na]: 303.21019, found: 303.21042.

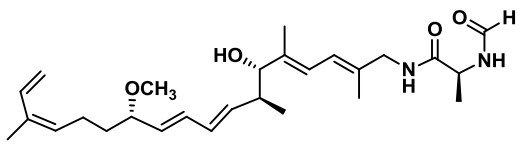
Stille Coupling Reactions

Compound 19: A Schlenk tube was charged with stannane **18** (222 mg, 0.486 mmol),[3] alkenyl iodide

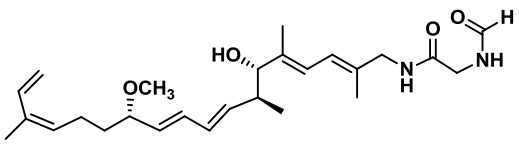


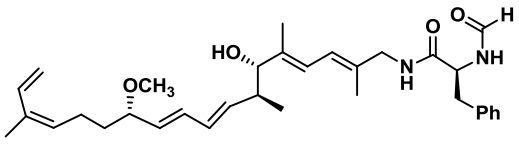
17 (200 mg, 0.442 mmol), $[Ph_2PO_2][NBu_4]$ (244 mg, 0.53 mmol) and DMF (0.9 mL). The resulting homogeneous mixture was vigorously stirred and $Pd(PPh_3)_4$ (20 mg, 0.017 mmol) and copper thiophene-2-carboxylate (CuTC, 101 mg, 0.53 mmol) were added. The mixture instantaneously turned dark and after 10 min the reaction was quenched at 0°C with H_2O (2 mL). The resulting suspension was filtered through a pad of Celite, which was carefully washed with EtOAc (50 mL). The aqueous phase was extracted with EtOAc (2 × 2 mL), the combined organic layers were washed with water (3 × 10 mL) and brine (10 mL) before they were dried over $MgSO_4$, filtered and evaporated. The residue was purified by flash chromatography (hexanes/EtOAc, 8:1 → 4:1, containing 1% Et_3N), furnishing compound **19** as a colorless oil (163 mg, 75%). $[\alpha]_D^{20}$ = +28.5 (*c* = 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.85–7.80 (m, 2H), 7.72–7.67 (m, 2H), 6.72 (dd, *J* = 16.8, 10.9 Hz, 1H), 6.24 (dd, *J* = 11.1, 1.1 Hz, 1H), 6.16–6.09 (m, 3H), 5.59 (dd, *J* = 14.1, 8.3 Hz, 1H), 5.42 (dd, *J* = 14.2, 8.1 Hz, 1H), 5.32 (t, *J* = 7.6 Hz, 1H), 5.15 (d, *J* = 17.3 Hz, 1H), 5.03 (d, *J* = 10.8 Hz, 1H), 4.26 (s, 2H), 3.71 (d, *J* = 8.3 Hz, 1H), 3.49 (q, *J* = 7.0 Hz, 1H), 3.20 (s, 3H), 2.41–2.30 (m, 1H), 2.26–2.12 (m, 2H), 1.77 (d, *J* = 0.8 Hz, 3H), 1.75 (s, 3H), 1.70 (s, 3H), 1.68–1.57 (m, 1H), 1.53–1.45 (m, 1H), 0.87 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 168.2, 138.2, 136.4, 134.0, 133.7, 132.7, 132.7, 132.4, 132.0, 131.1, 130.4, 123.3, 123.1, 113.3, 81.8, 81.2, 56.1, 45.3, 41.1, 35.5, 23.2, 19.7, 17.0, 15.1, 11.8; IR (film): $\tilde{\upsilon}$ = 3469, 2927, 1771, 1709, 1388, 1424, 1387, 1330, 1088, 990, 939, 906, 725, 712 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{31}H_{39}NO_4$ [M^+ +Na]: 512.27687, found: 512.27713.

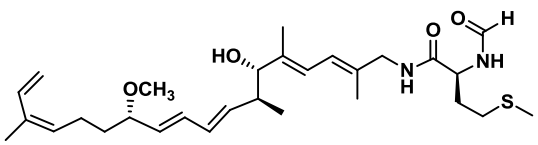
Compound S-16b: Prepared analogously as a colorless oil (286 mg, 88%). $[\alpha]_D^{20}$ = +2.5 (*c* = 0.1, $CHCl_3$);



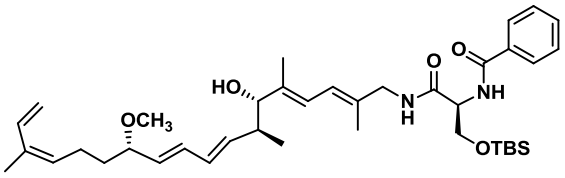
^{1}H NMR (C_6D_6, 400 MHz): δ = 7.72 (s, 1H), 6.90 (dd, *J* = 17.3, 10.8 Hz, 1H), 6.41 (brt, *J* = 5.9 Hz, 1H), 6.33 (brd, *J* = 7.6 Hz, 1H), 6.25–6.08 (m, 4H), 5.75 (dd, *J* = 14.6, 7.8 Hz, 1H), 5.45 (dd, *J* = 14.6, 7.8 Hz, 1H), 5.36 (t, *J* = 7.5 Hz, 1H), 5.18 (d, *J* = 17.3 Hz, 1H), 5.05 (d, *J* = 10.8 Hz, 1H), 4.53–4.46 (m, 1H), 3.78 (dd, *J* = 15.5, 5.7 Hz, 1H), 3.74–3.69 (m, 2H), 3.51–3.46 (td, *J* = 7.5, 5.5 Hz, 1H), 3.16 (s, 3H), 2.41–2.23 (m, 3H), 1.80 (s, 3H), 1.76 (s, 3H), 1.64–1.50 (m, 2H), 1.62 (s, 3H), 1.19 (d, *J* = 6.9 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (C_6D_6, 100 MHz): δ = 171.9, 160.8, 138.7, 137.0, 134.2, 133.1, 132.9, 131.0, 130.9, 128.3, 122.8, 121.5, 113.5, 82.0, 81.5, 56.1, 47.7, 47.0, 41.2, 36.3, 23.7, 20.0, 18.6, 17.2, 14.9, 12.1; IR (film): $\tilde{\upsilon}$ = 3300, 2972, 2927, 2870, 1652, 1533, 1446, 1380, 1239, 1097, 991 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{27}H_{42}O_4N_2$ [M^+ +Na]: 481.30368, found: 481.30400.

Compound S-16a: Prepared analogously as a colorless oil (20 mg, 61%). ^{1}H NMR (400 MHz, CD_2Cl_2):  δ = 8.20 (s, 1H), 6.77 (ddd, *J* = 17.3, 10.8, 0.8 Hz, 2H), 6.48 (t, *J* = 5.5 Hz, 1H), 6.19–6.12 (m, 4H), 5.64 (dd, *J* = 12.3, 8.1 Hz, 1H), 5.43 (dd, *J* = 14.3, 7.8 Hz, 1H), 5.38 (t, *J* = 7.6 Hz, 1H), 5.19 (dd, *J* = 17.4, 0.9 Hz, 1H), 5.07 (dt, *J* = 10.8, 1.6 Hz, 1H), 3.94 (d, *J* = 5.4 Hz, 2H), 3.86 (d, *J* = 5.9 Hz, 2H), 3.74 (d, *J* = 8.2 Hz, 1H), 3.53 (dt, *J* = 7.4, 6.2 Hz, 1H), 3.21 (s, 3H), 2.43–2.32 (m, 1H), 2.27–2.14 (m, 2H), 2.09 (bs, 1H), 1.81 (d, *J* = 1.1 Hz, 3H), 1.73 (s, 3H), 1.72 (s, 3H), 1.69–1.58 (m, 1H), 1.54–1.44 (m, 1H), 0.87 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (CD_2Cl_2, 100 MHz): δ = 168.7, 161.9, 138.6, 137.0, 134.5, 134.1, 133.1, 133.0, 132.8, 131.3, 131.0, 123.1, 121.8, 113.5, 82.1, 81.6, 56.3, 47.3, 42.1, 41.5, 36.0, 23.6, 19.9, 17.3, 15.1, 12.0; HRMS (ESI): *m*/*z*: calcd for $C_{26}H_{40}O_4N_2$ [M^+ +Na]: 467.28802, found: 467.28844.

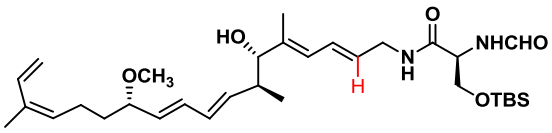
Compound S-16c: Prepared analogously as a colorless oil (39 mg, 73%). $[\alpha]_D^{20}$ = +9.4 (*c* = 1.0, $CHCl_3$);  ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 8.12 (s, 1H), 7.32–7.18 (m, 4H), 6.78 (ddd, *J* = 17.4, 10.8, 0.8 Hz, 1H), 6.45 (brd, *J* = 7.9 Hz, 1H), 6.20–6.03 (m, 5H), 5.66–5.61 (m, 1H), 5.48–5.42 (m, 1H), 5.38 (t, *J* = 7.6 Hz, 1H), 5.19 (dd, *J* = 17.4, 0.8 Hz, 1H), 5.07 (dt, *J* = 10.8, 1.6 Hz, 1H), 4.73–4.67 (m, 1H), 3.82 (dd, *J* = 15.3, 5.9 Hz, 1H), 3.77–3.73 (m, 2H), 3.52 (dt, *J* = 7.4, 6.1 Hz, 1H), 3.21 (s, 3H), 3.07 (dd, *J* = 7.0, 3.6 Hz, 2H), 2.40–2.34 (m, 1H), 2.24–2.15 (m, 2H), 1.81 (d, *J* = 1.1 Hz, 3H), 1.70 (s, 3H), 1.64 (s, 6H), 1.65–1.59 (m, 1H), 1.53–1.44 (m, 1H), 0.89 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, CD_2Cl_2): δ = 170.6, 161.1, 138.6, 137.0, 136.9, 134.3, 134.2, 133.2, 133.0, 132.8, 131.4, 131.0, 129.7 (x 2), 129.0 (x 2), 127.4, 123.1, 122.0, 113.5, 82.1, 81.6, 56.3, 47.4, 41.5, 41.5, 38.6, 36.0, 23.6, 19.9, 17.3, 15.1, 11.9; IR (film): $\tilde{\upsilon}$ = 3300, 2925, 2850, 1661, 1534, 1455, 1379, 1089, 993, 700 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{33}H_{46}O_4N_2$ [M^+ +Na]: 557.33498, found: 557.33485.

Compound S-16d: Prepared analogously as a colorless oil (38 mg, 71%). $[\alpha]_D^{20}$ = +6.5 (*c* = 1.0, $CHCl_3$);  ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 8.17 (s, 1H), 6.78 (ddd, *J* = 17.3, 10.8, 0.8 Hz, 1H), 6.61 (brd, *J* = 7.8Hz, 1H), 6.45 (brs, 1H), 6.20–6.13 (m, 4H), 5.67–5.62 (m, 1H), 5.45–5.43 (m, 1H), 5.38 (t, *J* = 7.6 Hz, 1H), 5.19 (dd, *J* = 17.3, 0.9 Hz, 1H), 5.07 (dt, *J* = 10.8, 1.6 Hz, 1H), 4.65 (dt, *J* = 7.4, 7.2 Hz, 1H), 3.86 (d, *J* = 5.9 Hz, 2H), 3.75 (d, *J* = 8.1 Hz, 1H), 3.53 (dt, *J* = 7.3, 6.1 Hz, 1H), 3.21 (s, 3H), 2.60–2.49 (m, 2H), 2.41–2.35 (m, 1H), 2.24–2.14 (m, 2H), 2.10 (s, 3H), 2.03–1.92 (m, 2H), 1.81 (d, *J* = 1.1 Hz, 3H), 1.74 (s, 3H), 1.73 (m, 3H), 1.65–1.59 (m, 1H), 1.53–1.45 (m, 1H), 0.90 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, CD_2Cl_2): δ = 170.9, 161.3, 138.6, 137.0, 134.4, 134.2, 133.2, 133.0, 132.8, 131.4, 131.0, 123.1, 121.8, 113.5, 82.1, 81.6, 56.3, 51.3, 47.3, 41.5, 36.0, 32.1, 30.5, 23.6, 19.9, 17.3, 15.4, 15.2, 12.0; IR (film): $\tilde{\upsilon}$ = 3275, 2925, 2850, 1660, 1534, 1451, 1380, 1092, 993 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{29}H_{46}O_4N_2S$ [M^+ +Na]: 541.30705, found: 541.30715.

Compound S-16e: Prepared analogously as a colorless oil (378 mg, 74%). $[\alpha]_D^{20}$ = +39.1 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, CD_2Cl_2): δ= 7.82–7.78 (m, 2H), 7.50 (t, *J* = 7.3 Hz, 1H), 7.45–7.39 (m, 2H), 7.20 (d, *J* = 5.9 Hz, 1H), 6.74 (ddd, *J* = 17.4, 10.8, 0.7 Hz, 1H), 6.20–6.09 (m, 4H), 5.60 (dd, *J* = 14.2, 8.2 Hz, 1H), 5.44 (dd, *J* = 14.2, 8.0 Hz, 1H), 5.33 (t, *J* = 7.5 Hz, 1H), 5.16 (d, *J* = 17.3 Hz, 1H), 5.05 (d, *J* = 10.8 Hz, 1H), 4.60–4.50 (m, 1H), 4.19 (dd, *J* = 9.7, 4.1 Hz, 1H), 4.00–3.84 (m, 2H), 3.73 (d, *J* = 8.4 Hz, 1H), 3.65 (dd, *J* = 9.6, 8.6 Hz, 1H), 3.51 (q, *J* = 7.3 Hz, 1H), 3.22 (s, 3H), 2.44–2.32 (m, 1H), 2.27–2.10 (m, 2H), 1.79 (d, *J* = 1.0 Hz, 3H), 1.74 (s, 3H), 1.71 (s, 3H), 1.66–1.59 (m, 1H), 1.55–1.43 (m, 1H), 0.88 (d, *J* = 6.1 Hz, 3H), 0.88 (s, 9H), 0.13 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ= 170.3, 167.2, 137.8, 136.3, 133.9, 133.7, 133.7, 132.9, 132.7, 132.3, 131.9, 131.3, 130.4, 128.6, 127.1, 123.1, 121.9, 113.3, 81.9, 81.2, 62.7, 56.2, 54.4, 47.3, 41.2, 35.5, 25.8, 23.2, 19.7, 18.1, 17.0, 15.0, 11.7, –5.4, –5.6; IR (film): $\tilde{\upsilon}$ = 3336, 2931, 2858, 1648, 1513, 1483, 1362, 1264, 1102, 993, 837 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{39}H_{60}O_5N_2Si$ [M^+ +Na]: 687.41681, found: 687.41637.

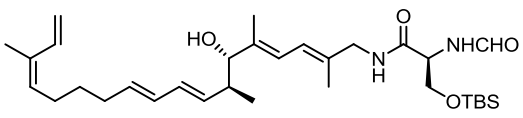


Compound S-17: Prepared analogously from iodide **37** (30 mg, 0.055 mmol) and stannane **18** (25.6 mg, 0.061 mmol) as a colorless oil (29 mg, 92%). $[\alpha]_D^{20}$ = +27.4 (*c* = 1.0, CH_2Cl_2); ^{1}H NMR (CD_2Cl_2, 400 MHz): δ= 8.22 (s, 1H), 6.77 (dd, *J* = 17.4, 10.8 Hz, 1H), 6.61 (bs, 1H), 6.55 (bs, 1H), 6.43 (dd, *J* = 15.1, 11.0 Hz, 1H), 6.21–6.11 (m, 2H), 5.98 (d, *J* = 10.9 Hz, 1H), 5.69–5.58 (m, 2H), 5.49–5.41 (m, 2H), 5.38 (t, *J* = 7.5 Hz, 1H), 5.19 (d, *J* = 17.3 Hz, 1H), 5.07 (d, *J* = 10.8 Hz, 1H), 4.46–4.39 (m, 1H), 4.02 (dd, *J* = 9.8, 4.0 Hz, 1H), 3.99–3.85 (m, 2H), 3.70 (d, *J* = 7.9 Hz, 1H), 3.61 (dd, *J* = 9.7, 7.6 Hz, 1H), 3.61 (q, *J* = 6.9 Hz, 1H), 3.20 (s, 3H), 2.37 (m, 1H), 2.28–2.12 (m, 2H), 1.89 (bs, 1H), 1.80 (s, 3H), 1.73 (s, 3H), 1.68–1.42 (m, 2H), 0.92–0.84 (m, 11H), 0.10 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (CD_2Cl_2, 100 MHz): δ= 169.6, 161.2, 139.2, 136.7, 134.1, 133.2, 133.0, 132.7, 131.4, 131.0, 129.0, 128.5, 126.6, 113.4, 81.6, 81.5, 63.1, 56.3, 53.4, 41.8, 41.5, 36.0, 25.9, 23.6, 19.9, 18.4, 17.2, 12.0, –5.4, –5.5; IR (film): $\tilde{\upsilon}$ = 3287, 2929, 2857, 1652, 1543, 1465, 1379, 1257, 1104, 838, 780 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{32}H_{54}N_2O_5Si$ [M^+ +Na]: 597.36942, found: 597.36915.



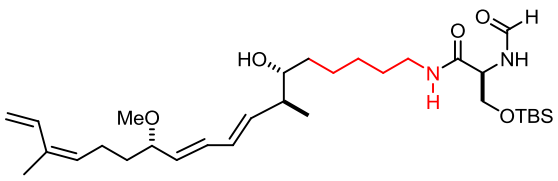
Suzuki Coupling Reactions

Compound 79: $Pd(dppf)Cl_2$ (7.9 mg, 0.0108 mmol) and $Ba(OH)_2(H_2O)_8$ (34 mg, 0.108 mmol) were added to a solution of alcohol **27** (R^1 = H, R^2 = CH_2OTBS, 40 mg, 0.072 mmol) and boronate **78** (22.9 mg, 0.087 mmol) in DMF (0.25 mL). The mixture was vigorously stirred for 1 h before it was diluted with ice water (2 mL). The aqueous phase was extracted with EtOAc (3 × 2 mL), the combined organic layers were washed with brine (5 mL), dried over $MgSO_4$ and evaporated to give a crude brown solid. Purification



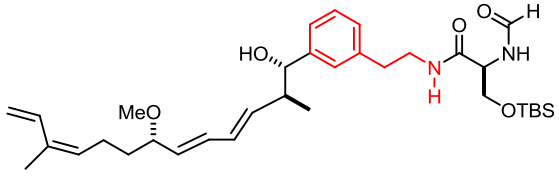
by flash chromatography (hexanes/acetone, 3:1) furnished compound **79** as a colorless syrup (23.7 mg, 59%). $[\alpha]_D^{20}$ = +20.4 (*c* = 1.0, CH_2Cl_2). ^{1}H NMR (CD_2Cl_2, 400 MHz): δ = 8.22 (s, 1H), 6.77 (dd, *J* = 1.0, 17.1 Hz, 1H), 6.50–6.65 (m, 2H), 5.99–6.15 (m, 2H), 5.64 (td, *J* = 7.1, 14.6 Hz, 1H), 5.48 (dd, *J* = 8.3, 14.9 Hz, 1H), 5.40 (t, *J* = 7.7 Hz, 1H), 5.19 (d, *J* = 17.1 Hz, 1H), 5.06 (td *J* = 1.5, 10.8 Hz, 1H), 4.44 (dt, *J* = 4.0, 7.3 Hz, 1H), 4.04 (dd, *J* = 4.0, 9.8 Hz, 1H), 3.80–3.95 (m, 2H), 3.71 (d, *J* = 8.3 Hz, 1H), 3.58–3.66 (m, 1H), 2.34 (m, 1H), 2.17 (q, *J* = 7.3 Hz, 2H), 2.08 (q, *J* = 7.1 Hz, 2H), 1.81 (s, 3H), 1.80 (s, 3H), 1.74 (s, 3H), 1.72 (s, 3H), 1.46 (q, *J* = 7.3 Hz, 2H), 0.89 (s, 9H), 0.88 (d, *J* = 4.6 Hz, 3H), 0.10 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (CD_2Cl_2, 100 MHz): δ = 169.8, 161.2, 138.6, 134.3, 134.1, 133.8, 132.8, 132.5, 131.3, 130.7, 123.0, 122.2, 113.4, 82.1, 63.1, 53.4, 47.5, 41.6, 32.5, 29.8, 27.2, 26.0, 25.0, 19.9, 18.4, 17.4, 15.1, 11.9, –5.4, –5.5; IR (film): $\tilde{\upsilon}$ = 3298, 2928, 2857, 1651, 1540, 1463, 1380, 1257, 1111, 988, 837 cm^{-1}; MS (EI): *m*/*z* (%): 501 (9, M^+ – *t*Bu), 369 (100), 351 (23), 341 (47), 311 (8), 237 (45), 230 (13), 209 (16), 202 (28), 189 (24), 174 (21), 171 (16), 140 (67), 123 (46), 109 (26), 95 (49), 84 (84), 79 (100); HRMS (ESI): *m*/*z*: calcd for $C_{32}H_{54}O_4Si$ [M^+ +Na]: 581.37451, found: 581.37422.

Compound S-18: Prepared analogously as a colorless oil (40 mg, 68%). $[\alpha]_D^{20}$ = +27 (*c* = 0.1, CH_2Cl_2);



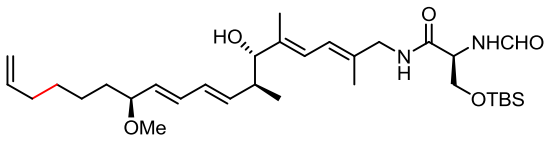
^{1}H NMR (600 MHz, CD_2Cl_2): δ = 8.21 (s, 1H), 6.78 (ddd, *J* = 17.3, 10.8, 0.8 Hz, 1H), 6.53 (brs, 1H), 6.39 (brs, 1H), 6.19-6.08 (m, 2H), 5.64 (dd, *J* = 14.6, 8.3 Hz, 1H), 5.44 (dd, *J* = 14.6, 9.9 Hz, 1H), 5.38 (t, *J* = 8.5 Hz, 1H), 5.19 (dd, *J* = 17.4, 1.5 Hz, 1H), 5.07 (dt, *J* = 10.8, 1.6 Hz, 1H), 4.38 (td, *J* = 7.6, 3.9 Hz, 1H), 4.01 (dd, *J* = 9.8, 3.9 Hz, 1H), 3.59 (dd, *J* = 9.8, 7.7 Hz, 1H), 3.52 (m, 1H), 3.40-3.38 (m, 1H), 3.28-3.25 (m, 2H), 3.21 (s, 3H), 2.24-2.19 (m, 3H), 1.81 (d, *J* = 1.1 Hz, 3H), 1.60-1.59 (m, 2H), 1.54-1.47 (m, 4H), 1.37-1.35 (m, 4H), 1.03 (d, *J* = 6.9 Hz, 3H), 0.91 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (150 MHz, CD_2Cl_2): δ = 170.1, 161.5, 136.8, 134.5, 133.4, 133.3, 133.3, 131.5, 131.4, 113.8, 82.0, 75.6, 63.6, 56.6, 53.8, 43.9, 40.2, 36.4, 35.1, 30.3, 27.6, 26.3, 26.1, 24.0, 20.2, 18.8, 17.2, –5.0, –5.1; IR (film): $\tilde{\upsilon}$ = 3297, 2929, 2857, 1648, 1543, 1463, 1379, 1252, 1100, 989, 939, 900, 835, 777 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{31}H_{56}N_2O_5Si$ [M^+ +Na]: 587.3852, found: 587.3851.

Compound S-19: Prepared analogously as a colorless oil (31.9 mg, 95%). $[\alpha]_D^{20}$ = –13.0 (*c* = 1.0, CH_2Cl_2); ^{1}H NMR (300 MHz, CD_2Cl_2, 25°C): δ = 8.16 (s, 1H), 7.30 – 7.25 (m, 1H), 7.17 – 7.10 (m, 3H), 6.78 (dd, *J* = 10.9, 6.5 Hz, 1H), 6.50 (brd, *J* = 6.8 Hz, 1H), 6.37 (brt, *J* = 5.0 Hz, 1H), 6.20 – 6.14 (m, 2H), 5.73 – 5.66 (m, 1H), 5.50 – 5.42 (m, 1H), 5.42 – 5.36 (m, 1H), 5.19 (d, *J* = 17.3 Hz, 1H), 5.07 (d, *J* = 10.8 Hz, 1H), 4.39 – 4.33 (m, 2H), 4.01 (dd, *J* = 9.9, 3.8 Hz, 1H), 3.62 – 3.47 (m, 4H), 3.22 (s, 3H), 2.80 (t, *J* = 7.0 Hz, 2H), 2.55 – 2.47 (m, 2H), 2.25 – 2.17 (m, 2H), 1.81 (d, *J* = 0.9 Hz, 3H), 1.68 – 1.45 (m, 2H), 0.89 – 0.86 (m, 12H), 0.07 (s, 6H); ^{13}C NMR (75 MHz, CD_2Cl_2, 25°C): δ = 169.6, 161.3, 143.7, 139.2, 136.7, 134.2, 133.2, 133.0, 132.8, 131.5, 131.0, 128.7, 128.2, 127.7, 125.6, 113.5, 81.6, 78.5, 63.0, 56.3, 53.5, 45.4, 41.2, 36.0, 25.9, 23.6, 19.9, 18.4,



17.1, –5.4, –5.5; IR (film): $\tilde{\upsilon}$ = 3298, 2919, 2857, 1651, 1536, 1463, 1381, 1255, 1102, 990, 837, 779, 708 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{34}H_{54}O_5N_2Si$ [M^+ +Na]: 621.36942, found: 621.36898.

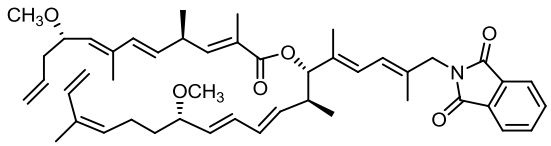
Compound 87: Prepared analogously as a colorless oil (27.4 mg, 65%). $[\alpha]_D^{20}$ = +5.2 (*c* = 0.75, CH_2Cl_2);



^{1}H NMR (CD_2Cl_2, 400 MHz): δ = 8.23 (s, 1H), 6.65–6.59 (m, 2H), 6.21–6.12 (m, 3H), 5.88–5.75 (m, 1H), 5.68–5.59 (m, 1H), 5.49–5.41 (m, 1H), 4.99 (ddd, *J* = 17.1, 3.6, 1.6 Hz, 1H), 4.92 (dt, *J* = 10.2, 1.1 Hz, 1H), 4.46–4.40 (m, 1H), 4.05 (dd, *J* = 9.8, 3.8 Hz, 1H), 3.96–3.82 (m, 2H), 3.74 (d, *J* = 7.1 Hz, 1H), 3.62 (dd, *J* = 9.8, 7.7 Hz, 1H), 3.52 (q, *J* = 6.5 Hz, 1H), 3.21 (s, 3H), 2.38 (m, 1H), 2.04 (q, *J* = 6.7 Hz, 1H), 1.75 (s, 3H), 1.73 (s, 3H), 1.57–1.29 (m, 6H), 0.90 (d, *J* = 2.6 Hz, 3H), 0.89 (s, 9H), 0.11 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (CD_2Cl_2, 100 MHz): δ = 163.8, 161.2, 139.5, 138.5, 136.8, 134.5, 133.6, 132.5, 131.5, 123.1, 122.2, 114.3, 82.4, 82.1, 63.1, 56.2, 53.4, 47.5, 41.5, 35.9, 34.1, 29.3, 25.9, 25.2, 18.4, 17.3, 15.1, 11.9, –5.4, –5.5; IR (film): $\tilde{\upsilon}$ = 3291, 2927, 2852, 1653, 1538, 1461, 1382, 1255, 1108, 987, 839 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{32}H_{56}N_2O_5Si$ [M^+ +Na]: 599.38507, found: 599.38640.

Esterification Reactions

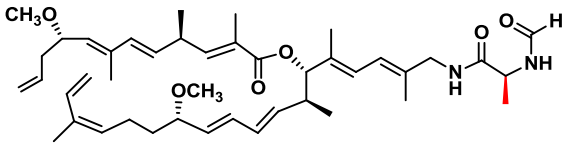
Compound 21: EDC·HCl (113 mg, 0.59 mmol) was added at 0°C to a solution of acid **20** (112 mg, 0.425 mmol)[3] and 4–pyrrolidinylpyridine (10 mg, 0.065 mmol) in CH_2Cl_2 (2 mL). The cooling bath was removed and the homogeneous solution stirred at room temperature for 10 min. The full consumption of **20** was checked by TLC (hexanes/EtOAc, 4:1) and the formation of a less polar spot corresponding to the activated acid derivative was observed (if necessary, more EDC·HCl was added to obtain a full conversion). At this stage, a solution of alcohol **19** (160 mg, 0.327 mmol) in CH_2Cl_2 (1 mL) was added before the solvent was removed by passing a gentle stream of argon over the mixture. The resulting viscous residue was slowly stirred for 18 h before the mixture was taken up in the minimum amount of $CHCl_3$ and purified by flash chromatography (hexanes/EtOAc, 8:1 → 4:1) to give ester **21** as a white solid (177 mg, 75%).



$[\alpha]_D^{20}$ = +12.0 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (CD_2Cl_2, 400 MHz): δ = 7.87–7.82 (m, 2H), 7.76–7.71 (m, 2H), 6.77 (dd, *J* = 17.3, 10.8 Hz, 1H), 6.57 (dd, *J* = 9.7, 1.5 Hz, 1H), 6.23 (s, 2H), 6.14–6.04 (m, 3H), 5.84–5.72 (m, 1H), 5.64–5.54 (m, 2H), 5.44–5.34 (m, 2H), 5.25 (d, *J* = 8.9 Hz, 1H), 5.18 (d, *J* = 17.3 Hz, 1H), 5.10–4.98 (m, 4H), 4.27 (s, 2H), 4.10–3.98 (m, 1H), 3.49 (q, *J* = 6.9 Hz, 1H), 3.30–3.21 (m, 1H), 3.20 (s, 3H), 3.16 (s, 3H), 2.61 (m, 1H), 2.40–2.30 (m, 1H), 2.26–2.12 (m, 3H), 1.83 (d, *J* = 1.3 Hz, 3H), 1.80 (s, 3H), 1.77 (s, 6H), 1.73 (s, 3H), 1.66–1.56 (m, 1H), 1.52–1.42 (m, 1H), 1.13 (d, *J* = 6.7 Hz, 3H), 0.96 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (CD_2Cl_2, 100 MHz): δ = 168.4, 167.4, 145.1, 136.8, 136.2, 135.3, 135.2, 134.4, 134.1, 133.7, 133.5, 133.1, 133.0, 132.7, 132.5, 132.0, 131.9, 131.0, 130.7, 127.2, 124.2, 123.5, 122.6, 116.8, 113.4, 82.9, 81.6, 77.1, 56.1, 56.0, 45.5, 40.4, 39.9, 36.7, 36.0, 23.6, 20.5, 19.9, 17.0, 15.3, 13.2, 12.9, 12.6; IR (film): $\tilde{\upsilon}$ = 2972, 2929, 1772, 1717, 1388, 1330, 1099, 990

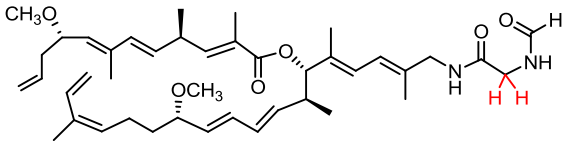
cm^{-1}; MS (EI): *m*/*z* (%): 735 (1, M^+), 694 (2), 516 (11), 440 (4), 281 (10), 247 (29), 215 (55), 137 (100), 107 (67); HRMS (ESI): *m*/*z*: calcd for $C_{47}H_{61}NO_6$ [M^+ +Na]: 758.43884, found: 758.43910.

Compound 28b: Prepared analogously as a white solid (311 mg, 71%). $[\alpha]_D^{20}$ = +14.0 (*c* = 1.0, $CHCl_3$);



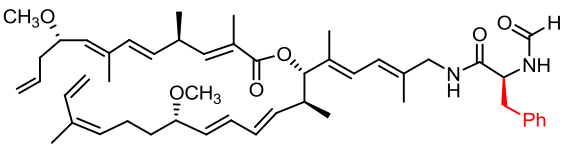
^{1}H NMR (C_6D_6, 400 MHz): δ = 7.65 (s, 1H), 6.94 (m, 2H), 6.49 (d, *J* = 10.8 Hz, 1H), 6.17–6.06 (m, 4H), 5.94 (ddt, *J* = 17.1, 10.1, 7.0 Hz, 1H), 5.78–5.63 (m, 3H), 5.54–5.45 (m, 3H), 5.37–5.40 (m, 2H), 5.23 (d, *J* = 17.5 Hz, 1H), 5.17–5.07 (m, 3H), 4.40–4.35 (m, 1H), 4.00 (dt, *J* = 8.9, 6.4 Hz, 1H), 3.76–3.66 (m, 2H), 3.49 (td, *J* = 7.6, 5.5 Hz, 1H), 3.22–3.17 (m, 1H), 3.19 (s, 3H), 3.15 (s, 3H), 2.66–2.61 (m, 1H), 2.54–2.47 (m, 1H), 2.39–2.30 (m, 3H), 1.94 (d, *J* = 1.3 Hz, 3H), 1.84 (s, 3H), 1.80 (s, 3H), 1.62 (d, *J* = 1.3 Hz, 3H), 1.56 (s, 3H), 1.35–1.29 (m, 2H), 1.15 (d, *J* = 7.0 Hz, 3H), 1.03 (d, *J* = 7.0 Hz, 3H), 0.96 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (C_6D_6, 100 MHz): δ = 160.3, 144.9, 136.0, 135.6, 135.0, 134.2, 134.0, 133.1, 132.9, 131.4, 131.0, 131.0, 130.9, 127.4, 116.9, 113.5, 81.4, 77.2, 56.0, 55.9, 47.6, 47.6, 40.6, 40.0, 35.2, 23.7, 20.5, 20.0, 18.5, 17.1, 14.9, 13.1, 12.8, 12.8, 12.6; IR (film): $\tilde{\upsilon}$ = 3296, 2972, 2931, 1660, 1532, 1451, 1378, 1231, 1098, 991, 968 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{43}H_{64}O_6N_2$ [M^+ +Na]: 727.46566, found: 727.46508.

Compound 28a: Prepared analogously as a colorless oil (16 mg, 61%). $[\alpha]_D^{20}$ = +20.0 (*c* = 1.0, CH_2Cl_2);



^{1}H NMR (CD_2Cl_2, 300 MHz): δ = 8.22 (s, 1H), 6.76 (dd, *J* = 17.3, 10.8 Hz, 1H), 6.57 (dd, *J* = 9.8, 1.6 Hz, 1H), 6.51 (brs, 1H), 6.25–6.05 (m, 6H), 5.77 (ddt, *J* = 17.2, 10.2, 7.0 Hz, 1H), 5.59 (dd, *J* = 15.5, 7.0 Hz, 2H), 5.43–5.36 (m, 2H), 5.24 (d, *J* = 9.5 Hz, 1H), 5.18 (d, *J* = 17.4 Hz, 1H), 5.08–4.95 (m, 4H), 4.04 (td, *J* = 9.0, 6.4 Hz, 1H), 3.94 (d, *J* = 5.4 Hz, 2H), 3.87 (d, *J* = 5.7 Hz, 2H), 3.53–3.45 (m, 1H), 3.30–3.21 (m, 1H), 3.20 (s, 3H), 3.17 (s, 3H), 2.68–2.56 (m, 1H), 2.40–2.28 (m, 1H), 2.25–2.16 (m, 3H), 1.83 (d, *J* = 1.3 Hz, 3H), 1.80 (d, *J* = 1.0 Hz, 3H), 1.77 (d, *J* = 1.1 Hz, 3H), 1.75 (s, 3H), 1.73 (s, 3H), 1.66–1.43 (m, 2H), 1.13 (d, *J* = 6.8 Hz, 3H), 0.96 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (CD_2Cl_2, 75 MHz): δ = 168.4, 167.5, 161.6, 145.2, 136.8, 136.2, 135.3, 135.1, 135.0, 134.1, 133.7, 133.1, 133.0, 132.7, 131.9, 131.9, 131.0, 130.7, 127.2, 124.1, 121.5, 116.8, 113.5, 83.0, 81.6, 77.2, 56.1, 56.0, 47.3, 42.1, 40.4, 39.9, 36.6, 36.0, 23.6, 20.5, 19.9, 17.0, 15.2, 13.2, 12.8, 12.6; IR (film): $\tilde{\upsilon}$ = 3316, 2962, 2928, 1694, 1663, 1542, 1448, 1383, 1260, 1097, 1016, 988, 800 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{42}H_{62}O_6N_2$ [M^+ +Na]: 713.45001, found: 713.45081.

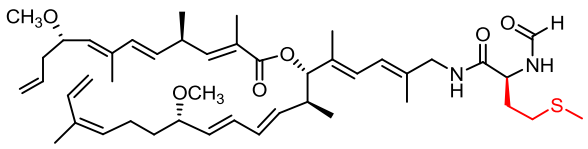
Compound 28c: Prepared analogously as a colorless oil (42 mg, 75%). $[\alpha]_D^{20}$ = +34.5 (*c* = 1.0, $CHCl_3$);



^{1}H NMR (CD_2Cl_2, 400 MHz): δ = 8.13 (s, 1H), 7.31–7.20 (m, 5H), 6.77 (dd, *J* = 17.3, 10.8 Hz, 1H), 6.57 (dd, *J* = 9.8, 1.4 Hz, 1H), 6.51 (brd, *J* = 4.8 Hz, 1H), 6.22–6.04 (m, 5H), 5.87 (brm, 1H), 5.77 (ddt, *J* = 17.2, 10.2, 7.0 Hz, 1H), 5.59 (dd, *J* = 15.5, 6.9 Hz, 2H), 5.44–5.35 (m, 2H), 5.24 (d, *J* = 8.9 Hz, 1H), 5.19 (d, *J* = 17.3 Hz, 1H), 5.08–4.99 (m, 4H), 4.67 (td, *J* = 7.2, 7.2 Hz, 1H), 4.08–4.01 (m, 1H), 3.82 (dd,

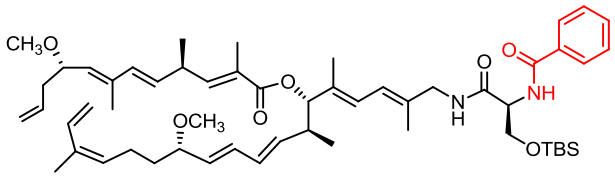
J = 15.4, 6.0 Hz, 1H), 3.73 (dd, *J* = 15.1, 5.7 Hz, 1H), 3.52–3.47 (m, 1H), 3.29–3.21 (m, 1H), 3.20 (s, 3H), 3.19–3.17 (brs, 3H), 3.08 (d, *J* = 7.0 Hz, 2H), 2.65–2.55 (m, 1H), 2.37–2.30 (m, 1H), 2.23–2.16 (m, 3H), 1.83 (d, *J* = 1.4 Hz, 3H), 1.80 (d, *J* = 1.0 Hz, 3H), 1.76 (d, *J* = 1.1 Hz, 3H), 1.72 (s, 3H), 1.63 (s, 3H), 1.51–1.43 (m, 2H), 1.13 (d, *J* = 6.8 Hz, 3H), 0.96 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (CD_2Cl_2, 100 MHz): δ = 170.4, 167.5, 161.0, 145.1, 136.9, 136.8, 136.2, 135.2, 135.2, 135.0, 134.1, 133.7, 133.1, 133.0, 132.7, 132.0, 131.9, 131.0, 130.7, 129.7, 129.0, 127.4, 127.2, 124.2, 121.7, 116.8, 113.4, 83.0, 81.6, 77.2, 56.2, 56.0, 53.7, 47.4, 40.4, 39.9, 38.6, 36.6, 36.0, 23.6, 20.5, 19.9, 17.0, 15.2, 13.2, 12.8, 12.6; IR (film): $\tilde{\upsilon}$ = 3291, 2925, 2855, 1651, 1496, 1443, 1380, 1261, 1238, 1095, 990, 966, 801, 736, 699 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{49}H_{68}O_6N_2$ [M^+ +Na]: 803.49696, found: 803.49703.

Compound 28d: Prepared analogously as a colorless oil (46 mg, 82%). $[\alpha]_D^{20}$ = +29.5 (*c* = 1.0, $CHCl_3$);



^{1}H NMR (CD_2Cl_2, 400 MHz): δ = 8.18 (s, 1H), 6.77 (ddd, *J* = 17.3, 10.8, 0.8 Hz, 1H), 6.57 (dd, *J* = 9.8, 1.4 Hz, 1H), 6.51 (brm, 1H), 6.28–6.22 (m, 2H), 6.19–6.06 (m, 4H), 5.78 (ddt, *J* = 17.1, 10.2, 7.0 Hz, 1H), 5.59 (dd, *J* = 15.5, 6.9 Hz, 2H), 5.42–5.35 (m, 2H), 5.24 (d, *J* = 8.9 Hz, 1H), 5.19 (dd, *J* = 17.4, 1.1 Hz, 1H), 5.09–4.96 (m, 4H), 4.62 (td, *J* = 7.4, 6.8 Hz, 1H), 4.04 (td, *J* = 9.0, 6.4 Hz, 1H), 3.86 (d, *J* = 5.7 Hz, 2H), 3.52–3.47 (m, 1H), 3.29–3.22 (m, 1H), 3.20 (s, 3H), 3.20–3.17 (brs, 3H), 2.65–2.48 (m, 3H), 2.38–2.31 (m, 1H), 2.24–2.14 (m, 4H), 2.10 (s, 3H), 2.00–1.93 (m, 1H), 1.83 (d, *J* = 1.4 Hz, 3H), 1.80 (d, *J* = 1.0 Hz, 3H), 1.77 (d, *J* = 1.1 Hz, 3H), 1.75 (s, 3H), 1.73 (s, 3H), 1.63–1.59 (m, 1H), 1.51–1.43 (m, 1H), 1.13 (d, *J* = 6.8 Hz, 3H), 0.96 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (CD_2Cl_2, 100 MHz): δ = 170.7, 167.5, 161.1, 145.1, 136.8, 136.2, 135.2, 135.2, 135.0, 134.1, 133.7, 133.1, 133.0, 132.9, 132.0, 131.9, 131.0, 130.7, 127.2, 124.2, 121.5, 116.8, 113.4, 83.0, 81.6, 77.2, 56.1, 56.0, 51.3, 47.3, 40.4, 39.9, 36.6, 36.0, 32.0, 30.5, 23.6, 20.5, 19.9, 17.0, 15.4, 15.2, 13.2, 12.8, 12.6; IR (film): $\tilde{\upsilon}$ = 3275, 2967, 2925, 1706, 1655, 1539, 1448, 1378, 1216, 1097, 988, 966 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{45}H_{68}O_6N_2S$ [M^+ +Na]: 787.46903, found: 787.46891.

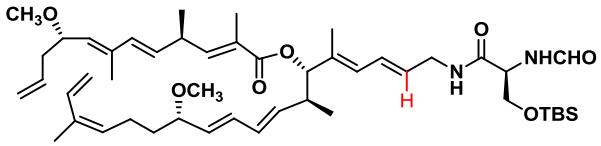
Compound 28e: Prepared analogously as a colorless oil (419 mg, 79%). $[\alpha]_D^{20}$ = +35.7 (*c* = 0.4, $CHCl_3$);



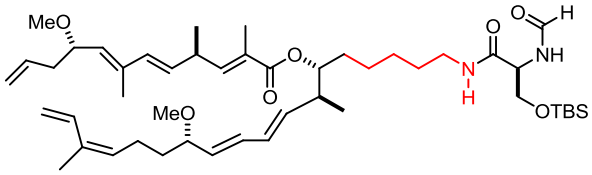
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.82–7.78 (m, 2H), 7.50 (t, *J* = 7.3 Hz, 1H), 7.45–7.39 (m, 2H), 7.19 (d, *J* = 5.8 Hz, 1H), 6.78–6.68 (m, 2H), 6.54 (dd, *J* = 9.7, 1.3 Hz, 1H), 6.24–6.18 (m, 1H), 6.15–6.00 (m, 4H), 5.84–5.69 (m, 1H), 5.59–5.45 (m, 2H), 5.39–5.29 (m, 3H), 5.24 (d, *J* = 9.0 Hz, 1H), 5.16 (d, *J* = 17.0 Hz, 1H), 5.09–4.90 (m, 4H), 4.58–4.51 (m, 1H), 4.19 (dd, *J* = 9.6, 4.0 Hz, 1H), 4.06–3.82 (m, 2H), 3.68–3.60 (m, 1H), 3.50–3.43 (m, 1H), 3.22 (s, 3H), 3.22–3.18 (m, 1H), 3.17 (s, 3H), 2.52–2.63 (m, 1H), 2.39–2.29 (m, 1H), 2.27–2.10 (m, 3H), 1.81 (d, *J* = 1.2 Hz, 3H), 1.79 (s, 3H), 1.74 (d, *J* = 1.0 Hz, 3H), 1.73 (s, 3H), 1.71 (s, 3H), 1.68–1.58 (m, 1H), 1.53–1.42 (m, 1H), 1.10 (d, *J* = 6.8 Hz, 3H), 0.93 (d, *J* = 7.0 Hz, 3H), 0.87 (s, 9H), 0.13 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.2, 167.2, 144.9, 136.4, 135.9, 134.6, 134.4, 133.7, 133.7, 133.4, 132.9, 132.7, 132.3, 132.1, 131.9, 131.5, 131.4, 130.4, 130.2, 128.6, 127.1, 126.7, 124.3, 121.8, 116.9, 113.3, 82.7, 81.3, 76.9, 62.7, 56.0, 54.4, 47.3, 40.0, 39.6, 36.3, 35.6, 25.8,

23.2, 20.3, 19.7, 18.0, 16.8, 15.1, 13.1, 12.6, 12.5, –5.4, –5.6; IR (film): $\tilde{\upsilon}$ = 2927, 2857, 1710, 1638, 1535, 1450, 1254, 1099, 989, 836, 778 cm^{-1}; HRMS (ESI): *m/z*: calcd for $C_{55}H_{82}O_7N_2Si$ [M^+ +Na]: 933.57844, found: 933.57835.

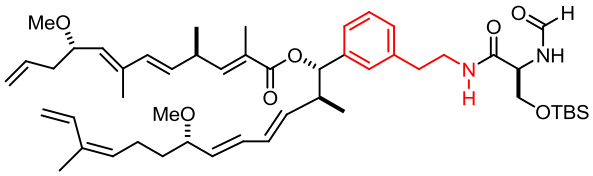
Compound 38: Prepared analogously from **53** as a colorless oil (34 mg, 83%). $[\alpha]_D^{20}$ = +34.4 (*c* = 1.0, CH_2Cl_2); ^1H NMR (CD_2Cl_2, 400 MHz): δ = 8.22 (s, 1H), 6.76 (dd, *J* = 17.3, 10.8 Hz, 1H), 6.58–6.53 (m, 2H), 6.49 (bs, 1H), 6.40 (dd, *J* = 15.1, 11.0 Hz, 1H), 6.15–6.00 (m, 3H), 5.85–5.53 (m, 4H), 5.43–5.33 (m, 2H), 5.25 (d, *J* = 9.1 Hz, 1H), 5.18 (d, *J* = 17.3 Hz, 1H), 5.10–4.98 (m, 3H), 4.95 (d, *J* = 8.4 Hz, 1H), 4.45–4.38 (m, 1H), 4.08–4.00 (m, 2H), 3.99–3.84 (m, 2H), 3.60 (dd, *J* = 9.6, 7.6 Hz, 1H), 3.48 (q, *J* = 7.0 Hz, 1H), 3.22–3.30 (m, 1H), 3.20 (s, 3H), 3.16 (s, 3H), 2.60 (sext., *J* = 7.5 Hz, 1H), 2.38–2.29 (m, 1H), 2.12–2.26 (m, 3H), 1.82 (d, *J* = 1.3 Hz, 3H), 1.80 (d, *J* = 1.0 Hz, 3H), 1.77 (d, *J* = 1.1 Hz, 3H), 1.75 (s, 3H), 1.68–1.42 (m, 2H), 1.12 (d, *J* = 6.8 Hz, 3H), 0.94 (d, *J* = 6.8 Hz, 3H), 0.88 (s, 9H), 0.10 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (CD_2Cl_2, 100 MHz): δ = 169.6, 167.4, 161.1, 145.2, 136.8, 136.1, 135.6, 135.1, 134.1, 133.7, 133.1, 133.0, 132.8, 132.0, 131.9, 131.0, 130.7, 129.8, 128.2, 127.9, 127.1, 116.8, 113.4, 82.7, 81.6, 77.1, 63.1, 56.1, 56.0, 53.4, 41.7, 40.4, 39.8, 36.7, 36.0, 25.9, 23.6, 20.5, 19.9, 18.4, 16.9, 13.2, 12.8, 12.6, –5.4, –5.5; IR (film): $\tilde{\upsilon}$ = 3296, 2927, 1709, 1696, 1656, 1539, 1458, 1385, 1256, 1101, 963, 839 cm^{-1}; HRMS (ESI): *m/z*: calcd for $C_{48}H_{76}N_2O_7Si$ [M^+ +Na]: 843.53202, found: 843.53140.



Compound 50: Prepared analogously as a colorless oil using DCC as the coupling agent (33 mg, 74%). $[\alpha]_D^{20}$ = –2.0 (*c* = 0.35, CH_2Cl_2); ^1H NMR (400 MHz, CD_2Cl_2): δ = 8.21 (s, 1H), 6.77 (dd, *J* = 17.2, 10.8 Hz, 1H), 6.57 (d, *J* = 9.8, 1.4 Hz, 1H), 6.53 (brs, 1H), 6.40 (brs, 1H), 6.18-6.05 (m, 3H), 5.78 (ddt, *J* = 17.1, 10.2, 7.0 Hz, 1H), 5.62 (dd, *J* = 14.2, 8.0 Hz, 1H), 5.61 (dd, *J* = 15.7, 7.0 Hz, 1H), 5.45-5.36 (m, 2H), 5.26 (d, *J* = 9.0 Hz, 1H), 5.18 (dd, *J* = 17.3, 0.8 Hz, 1H), 5.08-4.99 (m, 3H), 4.88 (dt, *J* = 8.5, 4.5 Hz, 1H), 4.38 (td, *J* = 7.0, 3.9 Hz, 1H), 4.07-4.00 (m, 2H), 3.60 (dd, *J* = 9.8, 7.5 Hz, 1H), 3.52 (m, 1H), 3.31-3.15 (m, 3H), 3.25 (s, 3H), 3.21 (s, 3H), 2.50-2.45 (m, 1H), 2.38-2.31 (m, 1H), 2.24-2.17 (m, 2H), 1.85 (d, *J* = 1.4 Hz, 3H), 1.81 (s, 3H), 1.78 (d, *J* = 1.1 Hz, 3H), 1.53-1.46 (m, 5H), 1.36-1.23 (m, 4H), 1.15 (d, *J* = 6.8 Hz, 3H), 1.02 (d, *J* = 6.8 Hz, 3H), 0.91 (s, 9H), –0.02 (s, 3H), –0.03 (s, 3H); ^{13}C NMR (75 MHz, CD_2Cl_2): δ = 169.7, 168.3, 161.1, 145.0, 136.9, 135.6, 135.2, 134.2, 133.8, 133.0, 133.0, 132.8, 132.0, 131.9, 131.0, 130.9, 127.3, 116.8, 113.5, 81.6, 77.2, 63.3, 56.2, 56.1, 53.4, 41.2, 40.4, 39.8, 36.8, 36.0, 34.3, 31.9, 29.8, 27.0, 26.0, 25.6, 23.6, 20.6, 20.6, 19.9, 18.4, 16.7, 13.2, 12.8, –5.4, –5.5; IR (film): $\tilde{\upsilon}$ = 3300, 2928, 2285, 1706, 1650, 1539, 1463, 1379, 1257, 1098, 990, 965, 911, 837, 814, 778 cm^{-1}; HRMS (ESI): *m/z*: calcd for $C_{47}H_{78}N_2O_7Si$ [M^+ +Na]: 833.5474, found: 833.5470.

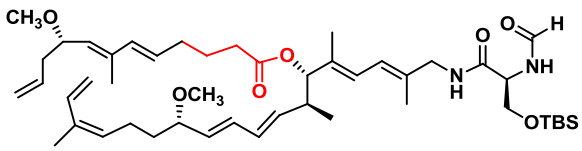


Compound 58: Prepared analogously as a colorless oil using DCC as the coupling agent (23.6 mg, 52%). $[\alpha]_D^{20}$ = – 4.5 (*c* = 1.0, CH_2Cl_2); ^1H NMR (400 MHz, CD_2Cl_2): δ = 8.15 (s, 1H), 7.30 – 7.26 (m, 1H),



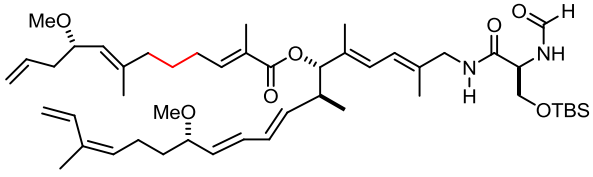
7.20 – 7.17 (m, 1H), 7.13 – 7.11 (m, 2H), 6.76 (dd, *J* = 17.3, 10.8 Hz, 1H), 6.68 (brd, *J* = 7.0 Hz, 1H), 6.60 (dd, *J* = 9.8, 1.4 Hz, 1H), 6.39 (brt, *J* = 5.6 Hz, 1H), 6.17 – 6.06 (m, 3H), 5.77 (ddt, *J* = 17.2, 10.2, 6.9 Hz, 1H), 5.66 – 5.56 (m, 2H), 5.49 – 5.34 (m, 3H), 5.25 (d, *J* = 9.0 Hz, 1H), 5.18 (d, *J* = 17.3 Hz, 1H), 5.07 – 5.04 (m, 3H), 4.42 – 4.37 (m, 1H), 4.08 – 4.00 (m, 2H), 3.66 – 3.58 (m, 2H), 3.50 (td, *J* = 7.3, 6.2 Hz, 1H), 3.34 – 3.21 (m, 2H), 3.19 (s, 3H), 3.17 (s, 3H), 2.82 – 2.71 (m, 3H), 2.37 – 2.30 (m, 1H), 2.23 – 2.15 (m, 3H), 1.85 (d, *J* = 1.3 Hz, 3H), 1.79 (d, *J* = 0.9 Hz, 3H), 1.76 (d, *J* = 1.1 Hz, 3H), 1.66 – 1.57 (m, 1H), 1.51 – 1.44 (m, 1H), 1.12 (d, *J* = 6.8 Hz, 3H), 0.92 – 0.83 (m, 12H), 0.08 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (100 MHz, CD_2Cl_2): δ = 169.7, 167.7, 161.3, 145.7, 140.3, 139.2, 136.8, 135.8, 135.2, 134.1, 133.8, 133.0, 132.9, 132.0, 131.8, 131.1, 131.0, 129.0, 128.6, 127.0, 125.3, 116.8, 113.5, 81.6, 80.0, 77.2, 63.2, 56.2, 56.0, 54.2, 53.4, 43.1, 41.0, 40.4, 36.7, 36.1, 36.0, 26.0, 25.9, 23.6, 20.5, 19.9, 18.5, 16.9, 13.2, 12.7, –5.3, –5.4; IR (film): $\tilde{\upsilon}$ = 2931, 2855, 1711, 1652, 1375, 1256, 1216, 1102, 991, 837 cm^{-1}; MS (ESI): *m*/*z*: calcd for $C_{50}H_{76}O_7N_2Si$ [M^+ +Na]: 867, found: 867.

Compound 67: Prepared analogously from acid **65** (19 mg, 0.085 mmol) and alcohol **66** (50 mg, 0.085mmol)[3] as a colorless oil (36 mg, 54%). $[\alpha]_D^{20}$ = +25.9 (*c* = 0.6, CH_2Cl_2); ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 8.23 (s, 1H), 6.77 (dd, *J* = 17.3, 10.9 Hz, 1H), 6.50 (m, 2H), 6.22 (d, *J* = 11.2 Hz, 1H), 6.17–6.03 (m, 4H), 5.78 (m, 1H), 5.68–5.53 (m, 2H), 5.45–5.35 (m, 2H), 5.25-5.15 (m, 2H), 5.10–4.98



(m, 4H), 4.44 (m, 1H), 4.05 (m, 2H), 3.96–3.80 (m, 2H), 3.62 (dd, *J* = 9.8, 7.6 Hz, 1H), 3.50 (m, 1H), 3.20 (s, 3H), 3.19 (s, 3H), 2.55 (m, 1H), 2.40–2.30 (m, 1H), 2.30–2.16 (m, 5H), 2.11 (m, 2H), 1.81 (d, *J* = 1.1 Hz, 3H), 1.77 (d, *J* = 1.1 Hz, 3H), 1.75 (s, 3H), 1.73 (s, 3H), 1.72–1.65 (m, 2H), 1.63 (m, 1H), 1.49 (m, 1H), 0.93 (d, *J* = 6.9 Hz, 3H), 0.89 (s, 9H), 0.11 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (75 MHz, CD_2Cl_2): δ = 172.7, 169.8, 161.2, 137.0, 136.4, 135.5, 135.4, 135.3, 134.8, 134.2, 133.0 (2x), 132.9, 131.1, 131.0, 130.7, 129.0, 124.6, 121.8, 116.7, 113.5, 82.8, 81.6, 77.2, 63.1, 56.2, 56.0, 53.7, 47.5, 40.5, 39.9, 36.1, 34.4, 32.6, 25.9, 25.3, 23.6, 19.9, 18.4, 17.1, 15.2, 13.3, 12.7, –5.4, –5.5; IR (film): $\tilde{\upsilon}$ = 3301, 2928, 2857, 1733, 1651, 1538, 1463, 1380, 1257, 1099, 990, 965, 837, 779 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{47}H_{76}N_2O_7Si$ [M^+ +Na]: 831.53140, found: 831.53110.

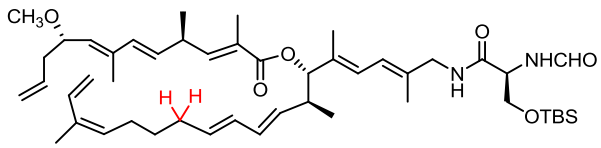
Compound 73: Prepared analogously as a colorless oil using DCC as the coupling agent (10 mg, 89%).



$[\alpha]_D^{20}$ = +4 (*c* = 0.01, CH_2Cl_2); ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 8.23 (s, 1H), 6.80-6.71 (m, 2H), 6.56-6.46 (m, 2H), 6.23 (d, *J* = 11.4 Hz, 1H), 6.18-6.04 (m, 3H), 5.84-5.71 (m, 1H), 5.60 (m, 1H), 5.43-5.33 (m, 2H), 5.18 (dd, *J* = 17.3, 1.5 Hz, 1H), 5.09-4.96 (m, 5H), 4.42 (m, 1H), 4.05 (m, 1H), 3.96-3.80 (m, 3H), 3.62 (dd, *J* = 9.7, 7.7 Hz, 1H), 3.49 (dd, *J* = 14.1, 6.8 Hz, 1H), 3.20 (s, 3H), 3.17 (s, 3H), 2.61 (m, 1H), 2.36-2.27 (m, 1H), 2.27-2.09 (m, 5H), 2.06 (t, *J* = 7.5 Hz, 2H), 1.80 (d, *J* = 1.1 Hz, 3H), 1.79 (d, *J* = 1.1 Hz, 3H), 1.74 (s, 6H), 1.66 (d, *J* = 1.3 Hz, 3H),

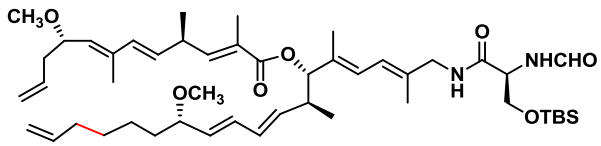
1.60-1.44 (m, 4H), 0.96 (d, *J* = 6.8 Hz, 3H), 0.88 (s, 9H), 0.10 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (75 MHz, CD_2Cl_2): δ= 169.8, 167.3, 161.2, 142.3, 139.5, 136.3, 135.5, 135.3, 135.0, 134.1, 133.1, 133.0, 132.7, 131.0, 130.6, 128.4, 126.4, 124.2, 121.9, 116.5, 113.4, 82.9, 81.6, 77.2, 63.1, 56.1, 55.7, 53.4, 47.4, 40.5, 39.9, 39.6, 36.1, 28.4, 27.2, 25.9, 23.6, 19.9, 18.4, 17.0, 16.7, 15.2, 12.8, 12.5, –5.4, –5.5; IR (film): $\tilde{\upsilon}$ = 3310, 2928, 2858, 1651, 1536, 1463, 1384, 1254, 1101, 990, 910, 837, 779 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{48}H_{78}N_2O_7Si$ [M^+ +Na]: 845.54705, found: 845.54630.

Compound 80: Prepared analogously as a colorless oil (27 mg, 86%). $[\alpha]_D^{20}$ = +21.7 (*c* = 1.0, CH_2Cl_2).



^{1}H NMR (CD_2Cl_2, 400 MHz): δ= 8.22 (s, 1H), 6.76 (dd, *J* = 17.3, 10.8 Hz, 1H), 6.59–6.47 (m, 3H), 6.22 (d, *J* = 11.3 Hz, 1H), 6.13 (d, *J* = 11.1 Hz, 1H), 6.11–5.95 (m, 3H), 5.85–5.72 (m, 1H), 5.64–5.54 (m, 2H), 5.46 (dd, *J* = 14.4, 8.2 Hz, 1H), 5.38 (t, *J* = 7.6 Hz, 1H), 5.25 (d, *J* = 9.1 Hz, 1H), 5.18 (d, *J* = 16.5 Hz, 1H), 5.09–4.98 (m, 4H), 4.45–4.39 (m, 1H), 4.08–4.02 (m, 2H), 3.95–3.80 (m, 2H), 3.61 (t, *J* = 8.7 Hz, 1H), 3.30–3.22 (m, 1H), 3.20 (s, 1H), 2.58 (m, 1H), 2.58 (quint., *J* = 7.0 Hz, 1H), 2.15 (q, *J* = 7.7 Hz, 2H), 2.06 (q, *J* = 7.3 Hz, 2H), 1.83 (d, *J* = 1.3 Hz, 3H), 1.80 (d, *J* = 1.0 Hz, 3H), 1.77 (d, *J* = 1.1 Hz, 3H), 1.74 (s, 6H), 1.44 (quint., *J* = 7.5 Hz, 2H), 1.13 (d, *J* = 6.7 Hz, 3H), 0.94 (d, *J* = 6.9 Hz, 3H), 0.88 (s, 9H), 0.1 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (CD_2Cl_2, 100 MHz): δ= 169.8, 167.5, 161.2, 145.1, 136.8, 135.1, 134.1, 133.7, 133.5, 133.2, 132.8, 131.9, 131.9, 131.5, 131.3, 130.9, 127.2, 124.1, 121.9, 116.8, 113.4, 83.1, 77.1, 63.1, 56.0, 53.4, 47.4, 40.4, 39.8, 36.6, 32.5, 29.9, 27.2, 25.9, 20.5, 19.9, 17.2, 15.2, 13.2, 12.6, –5.4, –5.5; IR (film): $\tilde{\upsilon}$ = 2927, 1651, 1551, 1450, 1385, 1259, 1104, 987, 839 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{48}H_{76}N_2O_6Si$ [M^+ +Na]: 827.53649, found: 827.53682.

Compound 88: Prepared analogously as a colorless oil (22.7 mg, 58%). $[\alpha]_D^{20}$ = +22.7 (*c* = 1.0, CH_2Cl_2);



^{1}H NMR (CD_2Cl_2, 300 MHz): δ= 8.23 (s, 1H), 6.60–6.45 (m, 3H), 6.24 (d, *J* = 11.3 Hz, 1H), 6.18–6.03 (m, 4H), 5.90–5.70 (m, 2H), 5.64–5.54 (m, 2H), 5.44–5.34 (m, 1H), 5.25 (d, *J* = 9.0 Hz, 1H), 5.10–4.88 (m, 5H), 4.42 (td, *J* = 6.9, 4.0 Hz, 1H), 4.09–4.01 (m, 2H), 3.97–3.78 (m, 2H), 3.61 (dd, *J* = 9.8, 7.7 Hz, 1H), 3.54–3.44 (m, 2H), 3.20 (s, 3H), 3.17 (s, 3H), 2.62 (m, 1H), 2.34 (m, 1H), 2.20 (quint., *J* = 6.8 Hz, 1H), 2.09–1.98 (m, 1H), 1.83 (d, *J* =1.2 Hz, 3H), 1.76 (d, *J* = 1.0 Hz, 3H), 1.74 (s, 6H), 1.57–1.24 (m, 6H), 1.13 (d, *J* = 6.8 Hz, 3H), 0.95 (d, *J* = 6.8 Hz, 3H), 0.88 (s, 9H), 0.10 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (CD_2Cl_2, 75.5 MHz): δ= 169.8, 167.4, 161.1, 145.1, 139.5, 136.8, 136.1, 135.3, 135.2, 135.0, 133.7, 133.1, 132.8, 132.0, 131.9, 130.7, 127.2, 124.3, 121.8, 116.8, 114.3, 83.0, 82.4, 77.1, 63.1, 56.1, 56.0, 47.4, 40.4, 39.9, 36.7, 35.9, 34.1, 29.3, 25.9, 25.2, 20.5, 18.4, 17.0, 15.2, 13.2, 12.8, 12.6, –5.4, –5.5; IR (film): $\tilde{\upsilon}$ = 2931, 2853, 1651, 1535, 1466, 1387, 1256, 1102, 991, 840 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{48}H_{78}N_2O_7Si$ [M^+ +Na]: 845.54705, found: 845.54683.

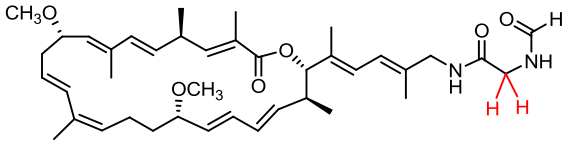
Ring Closing Alkene Metathesis Reactions

Macrocycle 23. Complex **22** (12.9 mg, 0.0152 mmol, 10 mol%) was added to a solution of ester **21** (110 mg, 0.152 mmol) in toluene (152 mL). The resulting mixture was stirred at 50°C for 4 h before the reaction was quenched with ethyl vinyl ether (ca 1 g). After stirring for 30 min at room temperature, the mixture was concentrated and the residue purified by flash chromatography (hexanes/EtOAc, 10:1 → 5:1, containing 1% Et_3N) to give macrocycle **23** as a white solid (86 mg, 77%). $[\alpha]_D^{20}$ = –12.5 (*c* = 0.47, CH_2Cl_2); ^{1}H NMR (CD_2Cl_2, 400 MHz): δ = 7.87–7.81 (m, 2H), 7.77–7.71 (m, 2H), 6.56 (dd, *J* = 10.3, 1.4 Hz, 1H), 6.46 (d, *J* = 15.6 Hz, 1H), 6.28 (d, *J* = 11.1 Hz, 1H), 6.22 (dd, *J* = 11.1, 1.2 Hz, 1H), 6.03 (dd, *J* = 14.5, 10.4 Hz, 1H), 5.96 (dd, *J* = 14.5, 10.4 Hz, 1H), 5.89 (d, *J* = 15.4 Hz, 1H), 5.56–5.33 (m, 4H), 5.20–5.13 (m, 1H), 5.09 (d, *J* = 10.1 Hz, 1H), 5.08 (d, *J* = 9.4 Hz, 1H), 4.27 (s, 2H), 4.11 (dt, *J* = 9.6, 2.7 Hz, 1H), 3.29–3.21 (m, 1H), 3.20 (s, 3H), 3.19–3.11 (m, 1H), 2.94 (s, 3H), 2.67–2.47 (m, 3H), 2.35–2.23 (m, 1H), 1.91–1.81 (m, 1H), 1.78 (s, 3H), 1.77 (s, 3H), 1.76 (s, 6H), 1.74 (d, *J* = 0.9 Hz, 3H), 1.65–1.52 (m, 1H), 1.34–1.24 (m, 1H), 1.03 (d, *J* = 6.7 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (CD_2Cl_2, 100 MHz): δ = 168.4, 167.5, 145.6, 137.1, 136.2, 134.6, 134.4, 133.9, 133.8, 133.7, 133.3, 132.5, 132.4, 132.0, 131.2, 131.2, 129.7, 128.8, 125.9, 125.4, 125.3, 123.5, 122.5, 83.1, 79.8, 77.0, 56.4, 55.8, 45.5, 41.0, 40.9, 38.3, 35.2, 23.2, 21.5, 20.8, 16.8, 15.3, 13.1, 12.2, 12.1; IR (film): $\tilde{\upsilon}$ = 2972, 2927, 1773, 1717, 1428, 1387, 1331, 1258, 1216, 1106, 990, 965, 726 cm^{-1}; MS (EI): *m*/*z* (%): 707 (4, M^+), 675 (4), 485 (4), 452 (4), 438 (4), 406 (4), 281 (13), 237 (77), 206 (100), 191 (20), 173 (20), 159 (34), 145 (27), 131 (22), 123 (17), 111 (20), 98 (25); HRMS (ESI): *m*/*z*: calcd for $C_{45}H_{57}NO_6$ [M^+ +Na]: 730.40824, found: 730. 40781.

Compound 29b: A solution of the ruthenium complex **22** (37.3 mg, 0.044 mmol, 0.1 equiv) in toluene (3 mL) was added to a solution of ester **28b** (311 mg, 0.44 mmol) in toluene (350 mL). The resulting brown mixture was stirred at 50°C for 4 h under a continuous flow of Ar. The reaction was quenched with ethyl vinyl ether (0.42 mL, 4.4 mmol), stirred for 30 min at room temperature, and concentrated to a volume of ca. 5 mL. This solution was absorbed on silica which was added on top of a silica gel column and the product eluted with hexanes/EtOAc (4:1 → 1:1, containing 1% Et_3N) to give macrocycle **29b** as a white solid (219 mg, 74%). $[\alpha]_D^{20}$ = –7.8 (*c* = 0.09, CH_2Cl_2); ^{1}H NMR (600 MHz, CD_2Cl_2): δ = 8.16 (s, 1H), 6.56 (dd, *J* = 10.2, 1.5 Hz, 1H), 6.46 (d, *J* = 15.6 Hz, 1H), 6.28 (dd, *J* = 10.9, 1.1 Hz, 1H), 6.24 (brd, *J* = 6.2 Hz, 1H), 6.12 (dd, *J* = 11.3, 1.5 Hz, 1H), 6.07 (brt, *J* = 6.2 Hz, 1H), 6.04 (dd, *J* = 14.8, 10.5 Hz, 1H), 5.96 (dd, *J* = 15.2, 10.5 Hz, 1H), 5.88 (d, *J* = 15.5 Hz, 1H), 5.51 (ddd, *J* = 15.2, 10.4, 4.7 Hz, 1H), 5.47 (dd, *J* = 15.5, 8.9 Hz, 1H), 5.37 (dd, *J* = 15.0, 8.4 Hz, 1H), 5.35 (dd, *J* = 14.7, 9.5 Hz, 1H), 5.17 (dd, *J* = 10.7, 5.7 Hz, 1H), 5.09 (d, *J* = 10.0 Hz, 1H), 5.07 (d, *J* = 9.3 Hz, 1H), 4.49 (qdd, *J* = 7.1, 7.1, 0.7 Hz, 1H), 4.11 (td, *J* = 9.8, 2.8 Hz, 1H), 3.88 (dd, *J* = 15.5, 6.1 Hz, 1H), 3.84 (dd, *J* = 15.4, 6.0 Hz, 1H), 3.27–3.23 (m, 1H), 3.20 (s, 3H), 3.16–3.12 (m, 1H), 2.93 (s, 3H), 2.63 (brd, *J* = 13.7 Hz, 1H),

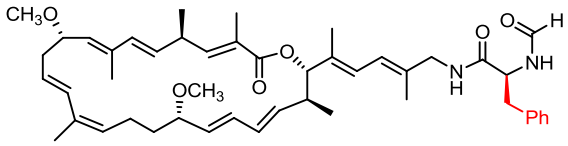
2.57–2.51 (m, 2H), 2.28 (dt, *J* = 13.6, 10.3 Hz, 1H), 1.88–1.84 (m, 1H), 1.77 (s, 3H), 1.76 (d, *J* = 1.5 Hz, 3H), 1.76 (d, *J* = 1.5 Hz, 3H), 1.74 (s, 3H), 1.73 (d, *J* = 1.1 Hz, 3H), 1.60–1.55 (m, 1H), 1.39 (d, *J* = 7.0 Hz, 3H), 1.31–1.25 (m, 1H), 1.03 (d, *J* = 6.7 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (150 MHz, CD_2Cl_2): δ = 171.8, 167.5, 161.0, 145.6, 137.1, 136.1, 135.8, 134.2, 133.8, 133.7, 133.3, 132.3, 132.0, 131.2, 129.7, 128.8, 125.9, 125.4, 125.3, 121.1, 83.2, 79.8, 77.0, 56.5, 55.9, 48.1, 47.1, 41.0, 40.9, 38.3, 35.3, 23.2, 21.5, 20.8, 18.6, 16.8, 15.1, 14.2, 13.1, 12.1, 12.1; IR (film): $\tilde{\upsilon}$ = 2967, 1734, 1714, 1456, 1373, 1360, 1226, 1216, 1117 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{41}H_{60}O_6N_2$ [M^+ +Na]: 699.43436, found: 699.43469.

Compound 29a: Prepared analogously as a colorless oil (7 mg, 75%). $[\alpha]_D^{20}$ = –3.0 (*c* = 0.22, CH_2Cl_2);



^{1}H NMR (600 MHz, CD_2Cl_2): δ = 8.23 (s, 1H), 6.57 (dd, *J* = 10.2, 1.5 Hz, 1H), 6.46 (d, *J* = 15.1 Hz, 1H), 6.34 (brs, 1H), 6.28 (dd, *J* = 11.1, 1.2 Hz, 1H), 6.13 (dd, *J* = 11.2, 1.4 Hz, 1H), 6.04 (dd, *J* = 14.8, 10.4 Hz, 1H), 5.97 (dd, *J* = 15.2, 10.6 Hz, 1H), 5.95 (brt, *J* = 5.5 Hz, 1H), 5.87 (d, *J* = 15.4 Hz, 1H), 5.51 (ddd, *J* = 15.4, 10.5, 4.9 Hz, 1H), 5.48 (dd, *J* = 15.5, 8.9 Hz, 1H), 5.37 (dd, *J* = 14.9, 8.5 Hz, 1H), 5.36 (dd, *J* = 14.7, 9.6 Hz, 1H), 5.17 (dd, *J* = 10.3, 5.7 Hz, 1H), 5.08 (d, *J* = 9.9 Hz, 1H), 5.06 (d, *J* = 9.4 Hz, 1H), 4.11 (td, *J* = 9.9, 2.6 Hz, 1H), 3.94 (d, *J* = 5.9 Hz, 2H), 3.88 (d, *J* = 5.6 Hz, 2H), 3.28–3.23 (m, 1H), 3.20 (s, 3H), 3.18–3.11 (m, 1H), 2.93 (s, 3H), 2.63 (brd, *J* = 13.7 Hz, 1H), 2.56–2.49 (m, 2H), 2.29 (dt, *J* = 13.7, 10.2 Hz, 1H), 1.88–1.85 (m, 1H), 1.78 (d, *J* = 0.9 Hz, 3H), 1.76 (s, 3H), 1.76 (s, 3H), 1.75 (s, 3H), 1.73 (d, *J* = 1.2 Hz, 3H), 1.60–1.56 (m, 1H), 1.31–1.26 (m, 1H), 1.03 (d, *J* = 6.6 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (150 MHz, CD_2Cl_2): δ = 168.2, 167.5, 161.5, 145.6, 137.1, 136.1, 135.6, 134.3, 133.7, 133.7, 133.3, 132.3, 132.3, 132.0, 131.2, 129.7, 128.7, 125.8, 125.3, 121.4, 83.1, 79.8, 76.9, 56.4, 55.8, 47.2, 42.0, 41.0, 40.8, 38.2, 35.2, 23.1, 21.4, 20.7, 16.7, 15.1, 13.1, 12.1, 12.0; IR (film): $\tilde{\upsilon}$ = 3301, 2962, 2921, 2865, 1704, 1668, 1648, 1539, 1451, 1385, 1256, 1213, 1102, 991, 963 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{40}H_{58}O_6N_2$ [M^+ +Na]: 685.41870, found: 685.41873.

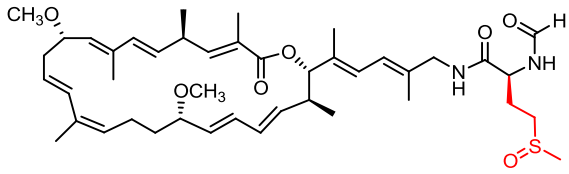
Compound 29c: Prepared analogously as a colorless oil (26 mg, 84%). $[\alpha]_D^{20}$ = –4.2 (*c* = 0.19, CH_2Cl_2);



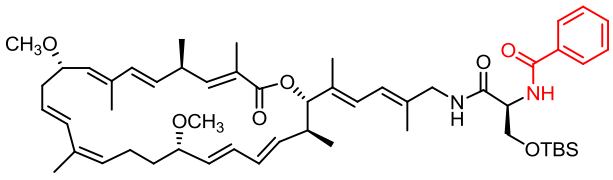
^{1}H NMR (600 MHz, CD_2Cl_2): δ = 8.13 (s, 1H), 7.32–7.28 (m, 2H), 7.25–7.21 (m, 3H), 6.57 (dd, *J* = 10.3, 1.5 Hz, 1H), 6.46 (d, *J* = 15.8 Hz, 1H), 6.30 (brd, *J* = 8.1 Hz, 1H), 6.24 (d, *J* = 11.1 Hz, 1H), 6.07 (dd, *J* = 11.3, 1.4 Hz, 1H), 6.04 (dd, *J* = 14.7, 10.4 Hz, 1H), 5.97 (dd, *J* = 15.3, 10.5 Hz, 1H), 5.90 (brt, *J* = 5.6 Hz, 1H), 5.89 (d, *J* = 15.4 Hz, 1H), 5.52 (ddd, *J* = 15.2, 10.3, 4.7 Hz, 1H), 5.48 (dd, *J* = 15.4, 9.0 Hz, 1H), 5.38 (dd, *J* = 15.0, 8.1 Hz, 1H), 5.36 (dd, *J* = 14.7, 9.4 Hz, 1H), 5.18 (dd, *J* = 10.8, 5.8 Hz, 1H), 5.08 (brd, *J* = 10.1 Hz, 2H), 4.68 (td, *J* = 7.1, 7.0 Hz, 1H), 4.11 (td, *J* = 9.7, 2.7 Hz, 1H), 3.81 (dd, *J* = 15.6, 6.1 Hz, 1H), 3.75 (dd, *J* = 15.3, 5.9 Hz, 1H), 3.28–3.22 (m, 1H), 3.20 (s, 3H), 3.19–3.12 (m, 1H), 3.08 (dd, *J* = 6.9, 2.1 Hz, 2H), 2.94 (s, 3H), 2.63 (brd, *J* = 13.4 Hz, 1H), 2.56–2.50 (m, 2H), 2.29 (dt, *J* = 13.7, 10.3 Hz, 1H), 1.89–1.85 (m, 1H), 1.77 (s, 3H), 1.76 (d, *J* = 1.4 Hz, 3H), 1.75 (s, 3H), 1.74 (d, *J* = 1.1 Hz, 3H), 1.65 (s, 3H), 1.60–1.55 (m, 1H), 1.33–1.27 (m, 1H), 1.04 (d, *J* = 6.8 Hz, 3H), 0.91 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (150 MHz, CD_2Cl_2): δ = 170.4, 167.5, 161.0, 145.6, 137.1, 136.9, 136.1, 135.6, 134.3, 133.8, 133.7,

133.3, 132.3, 132.3, 132.0, 131.2, 129.7, 129.6, 129.0, 128.8, 127.4, 125.9, 125.4, 125.3, 121.6, 83.2, 79.8, 77.0, 56.5, 55.9, 53.7, 47.3, 41.0, 40.9, 38.5, 38.3, 35.3, 23.2, 21.5, 20.8, 16.8, 15.2, 13.1, 12.1, 12.1; IR (film): $\tilde{\upsilon}$ = 3270, 2921, 1714, 1668, 1651, 1532, 1453, 1385, 1259, 1213, 1097, 991, 963 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{47}H_{64}O_6N_2$ [M^+ +Na]: 775.46566, found: 775.46686.

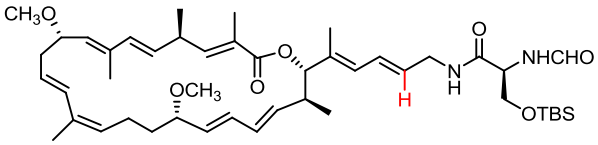
Compound 29d: Prepared analogously using 100 mol% of complex **22**, which was added in four equal portions to the reaction mixture over the course of 5 h. Brown oil (16 mg, 46%). $[\alpha]_D^{20}$ = –15.0 (*c* = 0.04, CH_2Cl_2); ^{1}H NMR (CD_2Cl_2, 600 MHz): δ = 8.21 (s, 1H), 7.39 (brd, *J* = 7.4 Hz, 0.5H), 7.17 (brd, *J* = 7.0 Hz, 0.5H), 7.00 (brt, *J* = 6.1 Hz, 0.5H), 6.93 (brt, *J* = 6.1 Hz, 0.5H), 6.56 (dd, *J* = 10.3, 1.5 Hz, 1H), 6.46 (d, *J* = 15.9 Hz, 1H), 6.28 (d, *J* = 11.4 Hz, 1H), 6.14 (ddd, *J* = 11.2, 5.2, 1.3 Hz, 1H), 6.04 (dd, *J* = 14.8, 10.4 Hz, 1H), 5.96 (dd, *J* = 15.1, 10.4 Hz, 1H), 5.88 (d, *J* = 15.5 Hz, 1H), 5.51 (ddd, *J* = 15.0, 10.3, 4.7 Hz, 1H), 5.47 (dd, *J* = 15.5, 8.8 Hz, 1H), 5.40–5.32 (m, 2H), 5.17 (dd, *J* = 10.8, 5.8 Hz, 1H), 5.09 (d, *J* = 10.2 Hz, 1H), 5.06 (d, *J* = 9.6 Hz, 1H), 4.75–4.69 (m, 1H), 4.11 (td, *J* = 9.8, 2.7 Hz, 1H), 3.86 (d, *J* = 6.0 Hz, 2H), 3.26–3.23 (m, 1H), 3.20 (s, 3H), 3.16–3.12 (m, 1H), 2.97–2.90 (m, 1H), 2.93 (s, 3H), 2.82–2.74 (m, 1H), 2.63 (brd + s, 2.5H), 2.57 (s, 1.5H), 2.56–2.45 (m, 2.5H), 2.37–2.21 (m, 2.5H), 1.88–1.84 (m, 1H), 1.78 (s, 3H), 1.76 (s, 3H), 1.76 (d, *J* = 1.4 Hz, 3H), 1.75 (s, 3H), 1.73 (d, *J* = 1.1 Hz, 3H), 1.59–1.55 (m, 1H), 1.32–1.26 (m, 1H), 1.03 (d, *J* = 6.8 Hz, 3H), 0.91 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (CD_2Cl_2, 150 MHz): δ = 170.3, 167.5, 161.7, 161.4, 145.6, 137.1, 136.2, 133.8, 133.7, 133.3, 132.3, 132.0, 131.2, 129.7, 128.8, 125.9, 125.5, 125.3, 121.4, 121.2, 83.2, 79.8, 77.0, 56.5, 55.8, 50.9, 50.6, 50.2, 41.0, 40.9, 38.8, 38.3, 37.8, 23.2, 21.5, 20.8, 16.8, 15.3, 13.1, 12.1, 12.0; HRMS (ESI): *m*/*z*: calcd for $C_{43}H_{64}O_7N_2S$ [M^+ +Na]: 775.43265, found: 775.43329.



Compound 29e: Prepared analogously as a white solid (350 mg, 86%). $[\alpha]_D^{20}$ = –7 (*c* = 0.15, CH_2Cl_2); ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.81 (m, 2H), 7.54 (m, 1H), 7.46 (m, 2H), 7.14 (d, *J* = 5.7 Hz, 1H), 6.63 (m, 1H), 6.57 (d, *J* = 10.2 Hz, 1H), 6.46 (d, *J* = 15.5 Hz, 1H), 6.28 (d, *J* = 11.4 Hz, 1H), 6.16 (d, *J* = 11.4 Hz, 1H), 6.09-5.85 (m, 3H), 5.56-5.43 (m, 2H), 5.42-5.34 (m, 2H), 5.18 (m, 1H), 5.08 (m, 2H), 4.54 (m, 1H), 4.20-4.05 (m, 2H), 4.00-3.82 (m, 2H), 3.71 (m, 1H), 3.29-3.21 (m, 1H), 3.20 (s, 3H), 3.18-3.10 (m, 1H), 2.95 (s, 3H), 2.67-2.47 (m, 3H), 2.30 (m, 1H), 1.87 (m, 1H), 1.77 (bs, 12H), 1.75 (s, 3H), 1.67-1.51 (m, 1H), 1.33-1.24 (m, 1H), 1.03 (d, *J* = 6.7 Hz, 3H), 0.90 (m, 12H), 0.14 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (100 MHz, CD_2Cl_2): δ = 170.4, 167.5, 167.2, 145.6, 137.1, 135.9, 134.3, 134.2, 134.1, 133.8, 133.7, 133.3, 132.4, 132.3, 132.1 (2x), 132.0, 131.2, 129.8, 128.9, 128.8, 127.3, 125.5, 125.4, 121.6, 83.3, 79.8, 77.0, 63.2, 56.5, 55.9, 55.0, 47.4, 41.0 (2x), 38.3, 35.3, 25.9, 23.2, 21.5, 20.8, 18.4, 16.8, 15.2, 13.1, 12.1, 12.0, –5.4, –5.5; IR (film): $\tilde{\upsilon}$ = 3298, 2925, 2856, 1711, 1640, 1535, 1463, 1258, 1215, 1100, 988, 963, 836, 778, 692 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{53}H_{78}N_2O_7Si$ [M^+ +Na]: 905.54705, found: 905.54773.

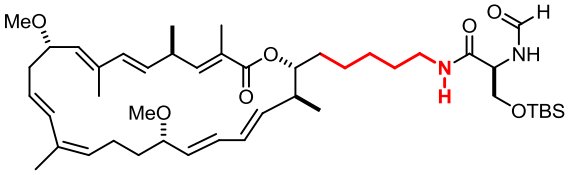


Macrocycle 39: Prepared analogously as a colorless oil (20.5 mg, 63%). $[\alpha]_D^{20}$ = –2.0 (*c* = 0.19, CH_2Cl_2);



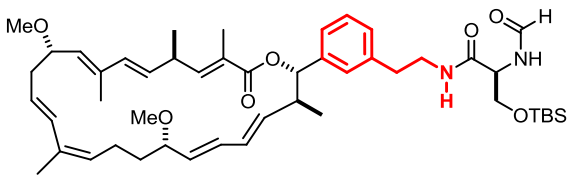
^{1}H NMR (CD_2Cl_2, 600 MHz): δ = 8.22 (s, 1H), 6.57 (dd, *J* = 10.4, 1.5 Hz, 1H), 6.56–6.48 (m, 1H), 6.46 (d, *J* = 15.5 Hz, 1H), 6.28 (d, *J* = 11.6 Hz, 1H), 6.15 (d, *J* = 15.7 Hz, 1H), 6.41 (ddt, *J* = 15.1, 10.9, 1.3 Hz, 1H), 6.08 (d, *J* = 11.0 Hz, 1H), 6.03 (dd, *J* = 14.0, 10.5 Hz, 1H), 5.96 (dd, *J* = 15.1, 10.5 Hz, 1H), 5.88 (d, *J* = 15.4 Hz, 1H), 5.69 (dt, *J* = 15.0, 6.4 Hz, 1H), 5.52 (ddd, *J* = 15.5, 10.2, 4.3 Hz, 1H), 5.47 (dd, *J* = 15.4, 9.1 Hz, 1H), 5.37 (dd, *J* = 15.0, 8.1 Hz, 1H), 5.34 (dd, *J* = 14.8, 9.3 Hz, 1H), 5.17 (dd, *J* = 10.6, 5.6 Hz, 1H), 5.07 (d, *J* = 9.4 Hz, 1H), 5.04 (d, *J* = 10.1 Hz, 1H), 4.40 (td, *J* = 7.0, 3.8 Hz, 1H), 4.11 (td, *J* = 9.8, 2.8 Hz, 1H), 4.03 (dd, *J* = 9.7, 3.9 Hz, 1H), 3.95–3.99 (m, 2H), 3.59 (dd, *J* = 9.7, 7.6 Hz, 1H), 3.27–3.22 (m, 1H), 3.20 (s, 3H), 3.19–3.14 (m, 1H), 2.93 (s, 3H), 2.62 (d, *J* = 13.6 Hz, 1H), 2.58–2.49 (m, 1H), 2.29 (dt, *J* = 13.6, 10.2 Hz, 1H), 1.91–1.86 (m, 1H), 1.78 (s, 3H), 1.76 (s, 3H), 1.75 (d, *J* = 2.5 Hz, 3H), 1.73 (d, *J* = 1.0 Hz, 3H), 1.63–1.59 (m, 1H), 1.30–1.28 (m, 1H), 1.03 (d, *J* = 6.8 Hz, 3H), 0.90 (d, *J* = 6.6 Hz, 3H) 0.88 (s, 9H), 0.09 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (CD_2Cl_2, 150 MHz): δ = 169.6, 167.5, 161.1, 145.7, 137.1, 136.0, 134.9, 133.8, 133.3, 132.4, 132.3, 132.0, 131.3, 130.2, 129.7, 129.0, 128.8, 128.1, 125.8, 125.3, 82.7, 79.8, 77.0, 63.0, 56.4, 55.9, 53.4, 41.7, 41.0, 40.9, 38.3, 35.2, 25.9, 23.2, 21.5, 20.8, 18.3, 16.7, 13.1, 12.2, 12.0, –5.4, –5.5; IR (film): $\tilde{\upsilon}$ = 3298, 2924, 1707, 1694, 1652, 1452, 1387, 1106, 963, 838 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{46}H_{72}N_2O_7Si$ [M^+ +Na]: 815.50010, found: 815.50075.

Compound S-20. Prepared analogously as a colorless oil (8.7 mg, 55%). $[\alpha]_D^{20}$ = +7.0 (*c* = 0.14, CH_2Cl_2);



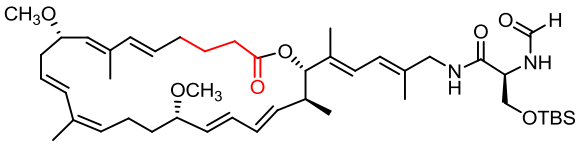
^{1}H NMR (400 MHz, CD_2Cl_2): δ = 8.22 (s, 1H), 6.58 (dd, *J* = 10.3, 1.5 Hz, 1H), 6.57 (brs, 1H), 6.45 (d, *J* = 15.4 Hz, 1H), 6.40 (brs, 1H), 5.98-5.93 (m, 2H), 5.88 (d, *J* = 15.4 Hz, 1H), 5.56-5.47 (m, 1H), 5.50 (dd, *J* = 15.8, 8.8 Hz, 1H), 5.38-5.34 (m, 2H), 5.17 (dd, *J* = 10.9, 5.9 Hz, 1H), 5.08 (d, *J* = 9.5 Hz, 1H), 4.78 (td, *J* = 9.0, 2.9 Hz, 1H), 4.40-4.36 (m, 1H), 4.12 (ddd, *J* = 10.1, 9.5, 2.8 Hz, 1H), 4.02 (dd, *J* = 9.8, 3.8 Hz, 1H), 3.60 (dd, *J* = 9.8, 7.6 Hz, 1H), 3.30-3.16 (m, 4H), 3.23 (s, 3H), 2.94 (s, 3H), 2.66-2.51 (m, 2H), 2.35-2.24 (m, 2H), 1.86-1.79 (m, 1H), 1.78 (s, 3H), 1.75 (d, *J* = 1.5 Hz, 3H), 1.74 (d, *J* = 1.1 Hz, 3H), 1.52-1.22 (m, 10H), 1.06 (d, *J* = 6.7 Hz, 3H), 1.01 (d, *J* = 6.7 Hz, 3H), 0.91 (s, 9H), 0.11 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (75 MHz, CD_2Cl_2): δ = 168.6, 167.3, 160.0, 144.4, 136.0, 135.5, 132.6, 132.3, 132.3, 131.5, 131.3, 131.0, 129.6, 128.7, 127.7, 124.9, 124.3, 78.8, 76.0, 76.0, 62.1, 55.3, 54.8, 52.3, 42.3, 39.9, 38.7, 37.2, 34.2, 31.4, 28.7, 25.9, 24.9, 24.1, 22.1, 20.6, 19.6, 17.3, 16.2, 12.1, 11.0, –6.5, –6.6; IR (film): $\tilde{\upsilon}$ = 3313, 2928, 2858, 1650, 1546, 1463, 1379, 1258, 1218, 1104, 990, 964, 837, 811, 779, 745 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{45}H_{74}N_2O_7Si$ [M^+ +Na]: 805.5151, found: 805.5158.

Compound S-21: Prepared analogously as a pale brown oil (5.4 mg, 70%). $[\alpha]_D^{20}$ = – 52.0 (*c* = 0.18, CH_2Cl_2); ^{1}H NMR (600 MHz, CD_2Cl_2): δ = 8.16 (s, 1H), 7.33 – 7.26 (m, 2H), 7.19 – 7.15 (m, 2H), 6.69 (brd, *J* = 6.5 Hz, 1H), 6.57 (dd, *J* = 10.4, 1.4 Hz, 1H), 6.47 (d, *J* = 15.7 Hz, 1H), 6.43 (brs, 1H), 6.14 (dd,

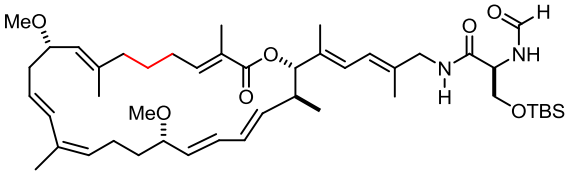


J = 15.0, 10.4 Hz, 1H), 6.03 (dd, *J* = 15.3, 10.5 Hz, 1H), 5.91 (d, *J* = 15.4 Hz, 1H), 5.56 – 5.41 (m, 5H), 5.20 – 5.18 (m, 1H), 5.09 (d, *J* = 9.4 Hz, 1H), 4.40 – 4.38 (m, 1H), 4.12 (td, *J* = 9.7, 2.7 Hz, 1H), 4.05 (dd, *J* = 9.8, 3.7 Hz, 1H), 3.66 – 3.58 (m, 2H), 3.34 – 3.25 (m, 2H), 3.20 (s, 3H), 3.20 – 3.13 (m, 1H), 2.98 (s, 3H), 2.83 – 2.76 (m, 2H), 2.69 – 2.61 (m, 2H), 2.52 – 2.49 (m, 1H), 2.34 – 2.28 (m, 1H), 1.92 – 1.88 (m, 1H), 1.81 (s, 3H), 1.77 (s, 3H), 1.74 (s, 3H), 1.62 – 1.57 (m, 1H), 1.32 – 1.28 (m, 1H), 1.02 (d, *J* = 6.7 Hz, 3H), 0.86 (s, 9H), 0.84 (d, *J* = 6.8 Hz, 3H), 0.07 (s, 6H); ^{13}C NMR (150 MHz, CD_2Cl_2): δ = 169.6, 167.7, 161.3, 146.0, 139.9, 139.4, 137.1, 136.0, 133.8, 133.8, 133.2, 132.3, 132.3, 131.8, 131.3, 129.6, 129.1, 128.9, 128.8, 125.7, 125.3, 79.9, 79.6, 76.9, 63.1, 55.8, 54.2, 53.3, 44.7, 41.0, 40.9, 38.3, 36.0, 35.2, 25.9, 23.2, 21.4, 20.7, 18.4, 16.7, 13.1, 12.2, –5.4, –5.5; IR (film): $\tilde{\upsilon}$ = 2931, 2850, 1737, 1681, 1534, 1451, 1373, 1226, 1216, 1105 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{48}H_{72}O_7N_2Si$ [M^+ +Na]: 839.50010, found: 839.50006.

Compound S-22: Prepared analogously from ester **67** (36 mg, 0.044 mmol) as a pale brown oil (29 mg, 85%). $[\alpha]_D^{20}$ = −19 (*c* = 0.1, CH_2Cl_2); ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 8.24 (s, 1H), 6.53−6.50 (brs, 2H), 6.40 (d, *J* = 15.5 Hz, 1H), 6.26 (d, *J* = 11.3 Hz, 1H), 6.15 (d, *J* = 11.3 Hz, 1H), 6.10−5.98 (m, 2H), 5.92 (d, *J* = 15.6 Hz, 1H), 5.62−5.51 (m, 2H), 5.50−5.40 (m, 2H), 5.23 (dd, *J* = 9.1, 7.0, 1H), 5.08 (d, *J* = 9.3 Hz, 1H), 5.04 (d, *J* = 9.9, Hz, 1H), 4.43 (m, 1H), 4.13 (ddd, *J* = 9.6, 9.6, 3.2 Hz, 1H), 4.06 (dd, *J* = 9.6, 3.9 Hz, 1H), 3.96−3.82 (m, 2H), 3.63 (dd, *J* = 9.6, 7.7 Hz, 1H), 3.35−3.29 (m, 1H), 3.23 (s, 3H), 3.25-3.19 (m, 1H), 3.14 (s, 3H), 2.63−2.52 (m, 2H), 2.48−2.38 (m, 1H), 2.32−2.20 (m, 3H), 2.05−1.93 (m, 2H), 1.78 (s, 3H), 1.76 (s, 3H), 1.74 (s, 3H), 1.73 (s, 3H), 1.66−1.60 (m, 2H), 1.34−1.26 (m, 2H), 0.90 (s, 9H), 0.90 (d, *J* = 6.7 Hz, 3H), 0.09 (s, 6H); ^{13}C NMR (75 MHz, CD_2Cl_2): δ = 173.1, 169.8, 161.2, 137.0, 136.4, 135.8, 135.1, 134.5, 133.8, 133.3, 132.2, 131.3, 130.8, 129.9, 129.1, 129.0, 125.5, 125.4, 121.8, 83.2, 80.2, 77.3, 63.1, 56.5, 56.1, 53.5, 47.4, 40.5, 40.0, 35.9, 35.1, 33.4, 26.3, 26.0, 23.3, 20.8, 18.4, 17.5, 15.3, 13.5, 12.2, −5.4, −5.5; IR (film): $\tilde{\upsilon}$ = 3308, 2929, 2858, 1732, 1656, 1537, 1462, 1377, 1257, 1103, 989, 965, 838 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{45}H_{72}N_2O_7Si$ [M^+ +Na]: 803.5007, found: 803.5000.

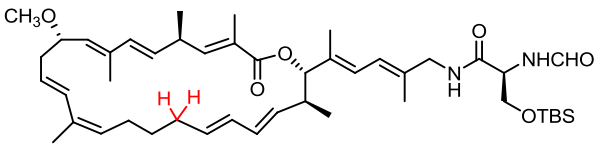


Compound S-23: Prepared analogously as a colorless oil (7.0 mg, 66%). $[\alpha]_D^{20}$ = +30 (*c* = 0.1, CH_2Cl_2); ^{1}H NMR (600 MHz, CD_2Cl_2): δ = 8.23 (s, 1H), 6.71 (t, *J* = 7.5 Hz, 1H), 6.53 (brd, *J* = 5.7 Hz, 1H), 6.48 (t, *J* = 5.6 Hz, 1H), 6.37 (d, *J* = 15.5 Hz, 1H), 6.24 (d, *J* = 11.4 Hz, 1H), 6.16-6.05 (m, 3H), 5.60-5.56 (m, 1H), 5.55 (dd, *J* = 15.3, 8.5 Hz, 1H), 5.43 (dd, *J* = 14.7, 7.1 Hz, 1H), 5.23 (t, *J* = 7.8 Hz, 1H), 5.04 (d, *J* = 8.4 Hz, 1H), 4.94 (dd, *J* = 9.2, 1.2 Hz, 1H), 4.44-4.41 (m, 1H), 4.06 (dd, *J* = 9.8, 4.0 Hz, 1H), 4.00 (ddd, *J* = 8.8, 8.7, 4.3 Hz, 1H), 3.94-3.82 (m, 2H), 3.62 (dd, *J* = 9.8, 7.6 Hz, 1H), 3.48 (d, *J* = 6.5 Hz, 1H), 3.22 (s, 3H), 3.17 (s, 3H), 2.63-2.56 (m, 1H), 2.53-2.49 (m, 1H), 2.27-2.22 (m, 1H), 2.21-2.17 (m, 1H), 2.12-2.08 (m, 3H), 2.07-2.00 (m, 1H), 1.98 (t, *J* = 7.5 Hz, 2H), 1.77 (s, 3H), 1.76 (s, 3H), 1.74 (s, 3H), 1.63 (d, *J* = 1.2 Hz, 3H), 1.63-1.59 (m, 2H), 1.53-1.42 (m, 2H), 0.97 (d, *J* = 6.9 Hz, 3H), 0.88 (s, 9H), 0.10 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 169.8,

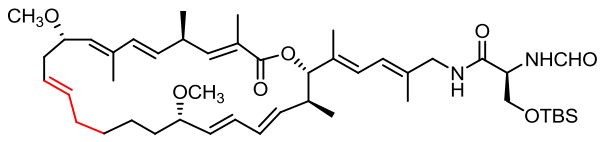


167.3, 161.1, 142.1, 139.5, 135.7, 135.3, 135.0, 132.8, 132.8, 132.4, 131.0, 129.7, 129.0, 128.5, 126.6, 126.1, 124.1, 121.9, 82.7, 80.7, 77.2, 63.1, 56.3, 55.7, 47.4, 40.6, 40.1, 39.6, 35.7, 28.1, 26.9, 25.9, 23.0, 20.7, 18.4, 17.2, 16.6, 15.2, 12.7, 12.4, 1.1, –5.4, –5.5; IR (film): $\tilde{\upsilon}$ = 3297, 2929, 2857, 1653, 1531, 1463, 1384, 1259, 1096, 1019, 964, 837, 800 cm^{-1}; HRMS (ESI): *m/z*: calcd for $C_{46}H_{74}N_2O_7Si$ [M^+ +Na]: 817.5157, found: 817.5158.

Macrocycle S-24: Prepared analogously from ester **80** (5 mg, 0.0062 mmol) as a colorless syrup (3.6 mg, 75%). $[\alpha]_D^{20}$ = –8 (*c* = 0.12, CH_2Cl_2). ^{1}H NMR (CD_2Cl_2, 600 MHz): δ = 8.23 (s, 1H), 6.57–6.48 (m, 3H), 6.33 (d, *J* = 15.5 Hz, 1H), 6.28 (d, *J* = 11.0 Hz, 1H), 6.14 (d, *J* = 11.3 Hz, 1H), 6.06 (d, *J* = 15.5 Hz, 1H), 6.04 (dd, *J* = 14.9, 10.4 Hz, 1H), 5.96 (dd, *J* = 14.9, 10.3 Hz, 1H), 5.63 (td, *J* = 15.5, 7.3 Hz, 1H), 5.57–5.51 (m, 2H), 5.51 (dd, *J* = 15.5, 8.5 Hz, 1H), 5.18 (d, *J* = 9.2 Hz, 1H), 4.94 (dd, *J* = 10.0, 1.6 Hz, 1H), 4.45–4.40 (m, 1H), 4.16–4.11 (m, 1H), 3.95–3.81 (m, 2H), 3.64–3.59 (m, 1H), 3.22 (s, 3H), 2.57–2.50 (m, 1H), 2.48–2.36 (m, 2H), 2.12–1.98 (m, 4H), 1.78 (d, *J* = 1.4 Hz, 3H), 1.77 (d, *J* = 1.0 Hz, 3H), 1.76 (s, 6H), 1.74 (s, 6H), 1.40–1.30 (m, 2H), 1.06 (d, *J* = 6.7 Hz, 3H), 0.90–0.87 (m, 12H), 0.1 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (CD_2Cl_2, 150 MHz): δ = 169.8, 167.6, 161.2, 145.2, 136.8, 135.5, 134.8, 134.0, 134.0, 133.2, 132.4, 132.0, 131.9, 131.6, 130.7, 129.8, 129.2, 126.4, 125.3, 125.2, 121.9, 85.6, 76.6, 63.1, 56.0, 47.4, 40.2, 39.9, 37.8, 32.2, 30.0, 26.9, 25.9, 21.2, 20.7, 18.4, 17.3, 15.2, 15.2, 13.2, 12.3, –5.4, –5.5; IR (film): $\tilde{\upsilon}$ = 2930, 2857, 1653, 1541, 1255, 1217, 1111, 965, 838 cm^{-1}; HRMS (ESI): *m/z*: calcd for $C_{46}H_{72}O_6N_2Si$ [M^+ +Na]: 799.51519, found: 799.51159.

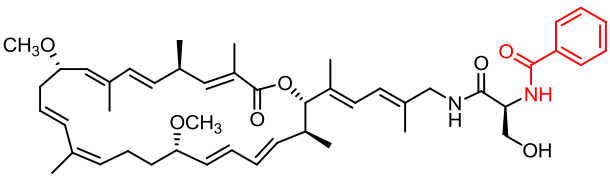


Macrocycle 89: Prepared analogosly as a colorless oil (6.8 mg, 64%, *E*/*Z* = 2:1). Further purification by HPLC afforded pure *E*-**89** (1.6 mg). $[\alpha]_D^{20}$ = –47 (*c* = 0.42, CH_2Cl_2); ^{1}H NMR (CD_2Cl_2, 600 MHz): δ = 8.23 (s, 1H), 6.59 (dd, *J* = 10.0, 1.5 Hz, 1H), 6.53 (d, *J* = 6.5 Hz, 1H), 6.50 (t, *J* = 6.0 Hz, 1H), 6.27 (d, *J* = 11.2 Hz, 1H), 6.16–6.05 (m, 4H), 5.72 (dd, *J* = 14.8, 6.9 Hz, 1H), 5.52 (dd, *J* = 15.5, 8.3, 1H), 5.47-5.39 (m, 2H), 5.21-5.14 (m, 2H), 4.92 (d, *J* = 9.8 Hz, 1H), 4.41 (td, *J* = 7.4, 3.8 Hz, 1H), 4.05 (dd, *J* = 9.8, 3.8 Hz, 1H), 3.97 (td, *J* = 9.6, 3.7 Hz, 1H), 3.93 (dd, *J* = 15.2, 6.2 Hz, 1H), 3.83 (dd, *J* = 15.2, 5.5 Hz, 1H), 3.60 (dd, *J* = 9.8, 7.7 Hz, 1H), 3.54 (q, *J* = 6.5 Hz, 1H), 3.28-3.21 (m, 1H), 3.20 (s, 3H), 3.19 (s, 3H), 2.66-2.59 (m, 1H), 2.44-2.38 (m, 1H), 2.19-2.09 (m, 1H), 1.93 (q, *J* = 6.5 Hz, 2H), 1.85 (d, *J* = 1.4 Hz, 3H), 1.75 (s, 3H), 1.74 (s, 3H), 1.73 (d, *J* = 1.1 Hz, 3H), 1.49-1.43 (m, 1H), 1.42-1.36 (m, 1H), 1.40-1.28 (m, 4H), 1.10 (d, *J* = 6.8 Hz, 3H), 0.94 (d, *J* = 6.8 Hz, 3H), 0.87 (s, 9H), 0.10 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (CD_2Cl_2, 150 MHz): δ = 169.7, 167.6, 161.1, 145.6, 137.4, 135.9, 135.5, 134.8, 133.9, 133.3, 133.0, 132.0, 131.9, 131.8, 129.8, 126.4, 125.4, 125.1, 121.7, 84.2, 80.8, 77.2, 63.0, 56.3, 55.8, 47.3, 39.1, 38.1, 37.6, 34.6, 31.9, 28.2, 25.8, 23.8, 21.3, 18.3, 15.9, 15.2, 13.2, 12.4, 12.0, 1.09, –5.5, –5.6; IR (film): $\tilde{\upsilon}$ = 2921, 2872, 1660, 1442, 1392, 1110, 989, 820 cm^{-1}; HRMS (ESI): *m/z*: calcd for $C_{46}H_{74}N_2O_7Si$ [M^+ +Na]: 817.51575, found: 817.51522.



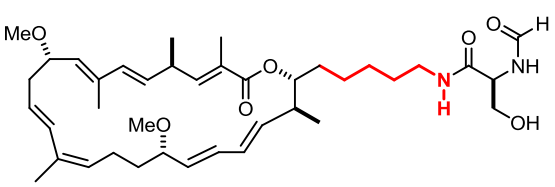
Final Deprotections

Compound 9: A solution of TBAF (1 M in THF, 0.41 mL) was added dropwise to a solution of macrocycle **29e** (350 mg, 0.4 mmol) in THF (4.1 mL) at 0°C. After stirring for 15 min, the mixture was absorped on silica and the product purified by flash chromatography (hexanes/EtOAc, 1:1 → 0:1) to give compound **9** as a white solid (301 mg, 99%). $[\alpha]_D^{20}$ = +4 (*c* = 0.16, CH_2Cl_2); ^{1}H NMR (600 MHz, CD_2Cl_2): δ = 7.82 (m, 2H), 7.55 (m, 1H), 7.47 (m, 2H), 7.27 (d, *J* = 6.6 Hz, 1H), 6.92 (t, *J* = 5.6 Hz, 1H), 6.57 (m, 1H), 6.45 (d, *J* = 15.2 Hz, 1H), 6.27 (d, *J* = 10.9 Hz, 1H), 6.13 (m, 1H), 6.06-5.94 (m, 2H), 5.89 (d, *J* = 15.2 Hz, 1H), 5.55-5.45 (m, 2H), 5.40-5.34 (m, 2H), 5.18 (m, 1H), 5.08 (m, 2H), 4.60 (m, 1H), 4.23 (m, 1H), 4.11 (dt, *J* = 9.9, 2.2 Hz, 1H), 3.95-3.83 (m, 2H), 3.74 (m, 1H), 3.27 (m, 1H), 3.21 (s, 3H), 3.20 (m, 1H), 3.15 (m, 1H), 2.95 (s, 3H), 2.63 (m, 1H), 2.55-2.47 (m, 2H), 2.29 (m, 1H), 1.88 (m, 1H), 1.77 (s, 3H), 1.76 (s, 3H), 1.75 (s, 3H), 1.74 (s, 3H), 1.70 (s, 3H), 1.61-1.54 (m, 1H), 1.33-1.25 (m, 1H), 1.04 (d, *J* = 6.8 Hz, 3H), 0.90 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 171.3, 168.2, 167.5, 145.6, 137.1, 136.1, 135.6, 134.2, 133.8, 133.7, 133.7, 133.3, 132.4 (2x), 132.3, 132.1, 131.2, 129.8, 129.0, 128.8, 127.5, 126.0, 125.4, 125.3, 121.0, 83.1, 80.0, 77.1, 63.1, 56.5, 55.9, 55.4, 47.0, 41.0, 40.8, 38.2, 35.3, 23.2, 21.5, 20.8, 16.8, 15.2, 13.2, 12.1, 12.0; IR (film): $\tilde{\upsilon}$ = 3333, 2925, 1710, 1643, 1529, 1448, 1257, 1216, 1104, 989, 964, 744, 712 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{47}H_{64}N_2O_7$ [M^+ +Na]: 791.46057, found: 791.46082.



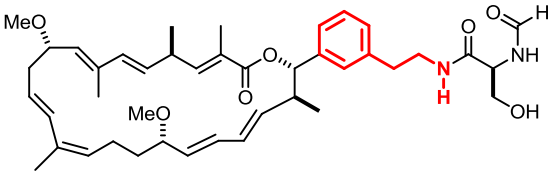
Compound 40: Prepared analogously as a colorless oil (17 mg, 97%). $[\alpha]_D^{20}$ = –10.0 (*c* = 0.15, CH_2Cl_2); ^{1}H NMR (CD_2Cl_2, 600 MHz): δ = 8.26 (s, 1H), 6.87 (bs, 2H), 6.78 (bs, 1H), 6.56 (d, *J* = 10.2 Hz, 1H), 6.43 (t, *J* = 15.8Hz, 1H), 6.39 (d, *J* = 10.7 Hz, 1H), 6.15-5.95 (m, 3H), 5.88 (d, *J* = 15.4 Hz, 1H), 5.67 (dt, *J* = 14.9, 6.1 Hz, 1H), 5.54–5.44 (m, 2H), 5.39-5.33 (m, 1H), 5.19–5.14 (m, 1H), 5.07 (d, *J* = 9.7 Hz, 1H), 5.02 (d, *J* = 10.1 Hz, 1H), 4.47 (bs, 1H), 4.13–4.03 (m, 2H), 3.94–3.89 (m, 2H), 3.63 (dd, *J* = 11.4, 5.1 Hz, 1H), 3.28–3.24 (m, 1H), 3.20 (s, 3H), 3.18–3.13 (m, 1H), 2.94 (s, 3H), 2.61 (d, *J* = 13.1, 5.1 Hz, 1H), 2.58–2.46 (m, 2H), 2.28 (dt, *J* = 13.7, 10.3 Hz, 1H), 1.90–1.84 (m, 1H), 1.77 (s, 3H), 1.75 (s, 6H), 1.72 (s, 3H), 1.60–1.55 (m, 1H), 1.33–1.28 (m, 1H), 1.03 (d, *J* = 6.6 Hz, 3H), 0.90 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (CD_2Cl_2, 150 MHz): δ = 170.4, 167.5, 161.9, 145.7, 137.1, 136.0, 134.9, 133.7, 133.3, 132.3, 132.3, 132.0, 131.2, 130.0, 129.8, 129.0, 128.8, 127.7, 126.0, 125.3, 82.7, 79.9, 77.0, 62.8, 56.4, 56.0, 53.1, 41.6, 40.9, 40.7, 38.2, 35.3, 23.2, 21.5, 20.7, 16.7, 13.1, 12.3, 12.1; IR (film): $\tilde{\upsilon}$ = 3331, 2926, 2850, 1712, 1656, 1545, 1448, 1388, 1259, 1097 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{40}H_{58}N_2O_7$ [M^+ +Na]: 701.41362, found: 701.41357.

Compound 51: Prepared analogously as a colorless oil (8.4 mg, 66%). $[\alpha]_D^{20}$ = –11.0 (*c* = 0.1, CH_2Cl_2); ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 8.27 (s, 1H), 6.79 (brs, 1H), 6.59 (brs, 1H), 6.51 (dd, *J* = 10.0, 1.2 Hz, 1H),



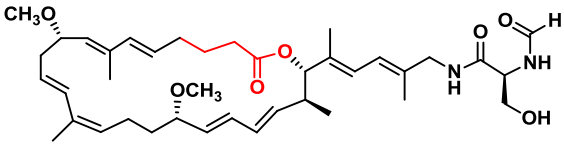
6.46 (d, *J* = 15.5 Hz, 1H), 6.00-5.90 (m, 2H), 5.87 (d, *J* = 15.4 Hz, 1H), 5.55 (m, 2H), 5.38-5.33 (m, 2H), 5.16 (dd, *J* = 11.0, 5.6 Hz, 1H), 5.07 (d, *J* = 9.4 Hz, 1H), 4.79 (td, *J* = 9.2, 2.7 Hz, 1H), 4.46-4.42 (m, 1H), 4.11 (ddd, *J* = 10.1, 9.6, 2.6 Hz, 1H), 4.06 (ddd, *J* = 11.1, 4.1, 3.5 Hz, 1H), 3.65-3.58 (m, 1H), 3.29-3.15 (m, 4H), 3.21 (s, 3H), 2.93 (s, 3H), 2.66-2.51 (m, 2H), 2.34-2.23 (m, 2H), 1.87-1.79 (m, 1H), 1.77 (s, 3H), 1.75 (s, 3H), 1.74 (s, 3H), 1.61-1.27 (m, 10H), 1.06 (d, *J* = 6.7 Hz, 3H), 1.01 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, CD_2Cl_2): δ= 170.6, 168.7, 161.8, 145.7, 137.1, 136.5, 133.7, 133.5, 133.4, 132.6, 132.4, 132.0, 130.8, 129.8, 128.8, 125.9, 125.4, 79.9, 77.1, 77.1, 63.0, 56.4, 55.9, 52.9, 43.6, 41.0, 39.7, 38.3, 35.3, 32.4, 29.6, 26.3, 25.2, 23.2, 21.7, 20.8, 17.3, 13.2, 12.1; IR (film): $\tilde{\upsilon}$ = 3324, 2928, 1649, 1545, 1450, 1381, 1259, 1218, 1103, 990, 964, 745 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{39}H_{60}N_2O_7$ [M^+ +Na]: 691.4296, found: 691.4293.

Compound 59: Prepared analogously as a colorless oil (4 mg, 80%). $[\alpha]_D^{20}$ = – 97.8 (*c* = 0.23, CH_2Cl_2);



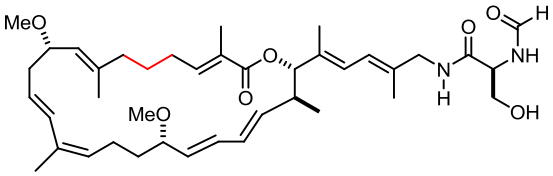
^{1}H NMR (600 MHz, CD_2Cl_2): δ= 8.12 (s, 1H), 7.32 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.26 (d, *J* = 7.8 Hz, 1H), 7.18 (brs, 1H), 7.16 (d, *J* = 7.4 Hz, 1H), 6.85 (brd, *J* = 7.4 Hz, 1H), 6.58 (dd, *J* = 10.2, 1.2 Hz, 1H), 6.53 (brs, 1H), 6.46 (d, *J* = 15.6 Hz, 1H), 6.15 (dd, *J* = 15.3, 10.5 Hz, 1H), 6.04 (dd, *J* = 15.3, 10.5 Hz, 1H), 5.93 (d, *J* = 15.6 Hz, 1H), 5.56 – 5.52 (m, 1H), 5.52 – 5.42 (m, 4H), 5.20 (dd, *J* = 9.7, 6.4 Hz, 1H), 5.09 (d, *J* = 9.0 Hz, 1H), 4.42 – 4.40 (m, 1H), 4.11 (td, *J* = 9.8, 2.6 Hz, 1H), 4.05 (ddd, *J* = 11.4, 3.9, 3.9 Hz, 1H), 3.67 – 3.62 (m, 1H), 3.57 – 3.54 (m, 1H), 3.34 – 3.30 (m, 2H), 3.21 (s, 3H), 3.20 – 3.16 (m, 1H), 3.05 (dd, *J* = 7.6, 4.6 Hz, 1H), 3.00 (s, 3H), 2.83 – 2.81 (m, 2H), 2.70 – 2.65 (m, 1H), 2.61 (d, *J* = 13.5 Hz, 1H), 2.51 – 2.44 (m, 1H), 2.32 (dt, *J* = 13.7, 10.0 Hz, 1H), 1.95 – 1.90 (m, 1H), 1.82 (d, *J* = 1.8 Hz, 3H), 1.78 (d, *J* = 1.8 Hz, 3H), 1.73 (d, *J* = 1.2 Hz, 3H), 1.61 – 1.57 (m, 1H), 1.34 – 1.26 (m, 1H), 1.02 (d, *J* = 7.2 Hz, 3H), 0.85 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (150 MHz, CD_2Cl_2): δ= 170.6, 168.1, 161.7, 146.2, 139.8, 139.3, 137.1, 135.9, 133.8, 133.8, 133.2, 132.3, 132.3, 131.7, 131.3, 129.6, 129.4, 129.2, 128.8, 128.8, 125.8, 125.3, 125.3, 80.1, 80.1, 76.9, 62.8, 56.4, 55.8, 52.7, 44.3, 40.9, 40.8, 38.2, 35.4, 35.2, 23.2, 21.3, 20.7, 16.6, 13.1, 12.2; IR (film): $\tilde{\upsilon}$ = 3301, 2962, 2926, 2870, 1709, 1651, 1532, 1453, 1385, 1259, 1213, 1103, 1064, 991, 963, 799 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{42}H_{58}O_7N_2$ [M^+ +Na]: 725.41362, found: 725.41450.

Compound 68: Prepared analogously as a pale brown oil (23 mg, 93%). $[\alpha]_D^{20}$ = −1.0 (*c* = 0.4, CH_2Cl_2);



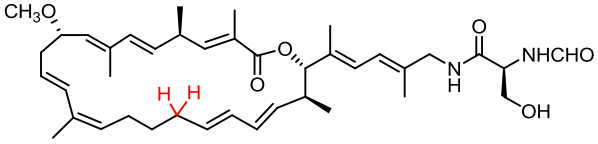
^{1}H NMR (400 MHz, CD_2Cl_2): δ= 8.26 (s, 1H), 6.76 (d, *J* = 6.6 Hz, 1H), 6.70 (t, *J* = 5.5 Hz, 1H), 6.40 (d, *J* = 15.6 Hz, 1H), 6.26 (d, *J* = 11.4 Hz, 1H), 6.12 (d, *J* = 11.4, 1H), 6.10−5.98 (m, 2H), 5.91 (d, *J* = 15.6 Hz, 1H), 5.62−5.40 (m, 4H), 5.23 (dd, *J* = 9.3, 7.2 Hz, 1H), 5.07 (d, *J* = 11.4 Hz, 1H), 5.04 (d, *J* = 9.9 Hz, 1H), 4.50−4.46 (m, 1H), 4.16−4.10 (m, 2H), 3.99−3.82 (m, 2H), 3.65 (ddd, *J* = 11.3, 8.5, 5.0 Hz, 1H), 3.34−3.29 (m, 1H), 3.27−3.18 (m, 1H), 3.23 (s, 3H), 3.13 (s, 3H), 3.12−3.10 (m, 1H), 2.63−2.52 (m, 2H), 2.48−2.38 (m, 1H), 2.31−2.21 (m, 3H), 2.05−1.92 (m, 3H), 1.78 (s, 3H), 1.75 (brs, 6H), 1.72 (s, 3H), 1.34−1.23 (m, 1H), 0.90 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, CD_2Cl_2): δ= 173.1, 170.7, 161.9, 137.0, 136.4, 135.5, 135.0, 134.5, 133.8, 133.3, 132.2, 131.2, 130.8, 129.9, 129.1, 129.0, 125.4, 125.2, 121.1,

83.2, 80.2, 77.3, 62.8, 56.5, 56.1, 53.0, 47.1, 40.5, 39.9, 35.8, 35.0, 33.4, 26.2, 23.3, 20.7, 17.5, 15.2, 13.4, 12.3; IR (film): $\tilde{\upsilon}$ = 3301, 2927, 1727, 1656, 1535, 1449, 1378, 1197, 1146, 1102, 990, 965, 866 cm^{-1}; HRMS (ESI): *m/z*: calcd for $C_{39}H_{58}N_2O_6$ [M^+ +Na]: 689.4139, found: 689.4136.



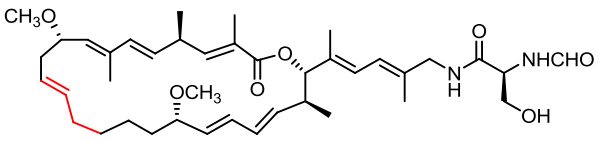
Compound 74: Prepared analogously as a colorless oil (0.8 mg, 65%). $[\alpha]_D^{20}$ = -2.0 (*c* = 0.2, CH_2Cl_2); ^{1}H NMR (600 MHz, CD_2Cl_2): δ = 8.25 (s, 1H), 6.74-6.71 (m, 2H), 6.64 (m, 1H), 6.36 (d, *J* = 15.5 Hz, 1H), 6.22 (d, *J* = 11.3 Hz, 1H), 6.17-6.06 (m, 3H), 5.59 (dd, *J* = 15.0, 8.0 Hz, 1H), 5.58-5.53 (m, 1H), 5.42 (dd, *J* = 15.0, 7.5 Hz, 1H), 5.24 (t, *J* = 7.7 Hz, 1H), 5.06 (d, *J* = 7.5 Hz, 1H), 4.91 (dd, *J* = 9.2, 0.8 Hz, 1H), 4.48-4.46 (m, 1H), 4.12 (m, 1H), 4.00 (ddd, *J* = 9.0, 8.9, 4.3 Hz, 1H), 3.92-3.84 (m, 2H), 3.65-3.61 (m, 1H), 3.48 (c, *J* = 6.7 Hz, 1H), 3.23 (s, 3H), 3.18 (s, 3H), 2.64-2.59 (m, 1H), 2.54-2.50 (m, 1H), 2.25-2.20 (m, 1H), 2.17-2.09 (m, 3H), 2.05-1.95 (m, 3H), 1.77 (s, 6H), 1.77 (s, 3H), 1.73 (s, 3H), 1.63 (d, *J* = 1.1 Hz, 3H), 1.66-1.53 (m, 2H), 1.49-1.41 (m, 2H), 1.00 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 170.6, 167.3, 161.8, 142.1, 139.7, 135.5, 135.1, 135.0, 132.7, 132.7, 132.7, 130.9, 129.8, 129.0, 128.5, 126.4, 125.9, 123.5, 121.4, 82.3, 81.0, 77.3, 62.8, 56.2, 55.8, 53.0, 47.2, 40.6, 39.7, 39.5, 35.8, 28.2, 27.0, 23.2, 20.6, 18.4, 17.1, 16.6, 15.1, 13.0, 12.5; IR (film): $\tilde{\upsilon}$ = 3318, 2927, 2857, 1650, 1535, 1447, 1383, 1258, 1182, 1094, 991, 964, 868, 802, 737 cm^{-1}; HRMS (ESI): *m/z*: calcd for $C_{40}H_{60}N_2O_7$ [M^+ +Na]: 703.4297, found: 703.4293.

Compound 81: Prepared analogously as a colorless oil (2.9 mg, 95%). $[\alpha]_D^{20}$ = –2 (*c* = 0.3, CH_2Cl_2); ^{1}H



NMR (CD_2Cl_2, 600 MHz): δ = 8.25 (s, 1H), 6.71 (bs, 1H), 6.64 (bs, 1H), 6.57 (td, *J* = 10.0, 1.6 Hz, 1H), 6.33 (d, *J* = 15.9 Hz, 1H), 6.26 (d, *J* = 11.1 Hz, 1H), 6.13 (d, *J* = 11.5 Hz, 1H), 6.05 (d, *J* = 14.9 Hz, 1H), 6.03–5.94 (m, 1H), 5.61 (td, *J* = 15.0, 7.3 Hz, 1H), 5.58–5.50 (m, 2H), 5.17 (d, *J* = 9.3 Hz, 1H), 4.95 (dd, *J* = 9.5, 1.8 Hz, 1H), 4.50–4.40 (m, 1H), 4.16–4.10 (m, 3H), 3.94–3.80 (m, 3H), 3.67–3.60 (m, 2H), 3.22 (s, 3H), 2.57–2.51 (m, 1H), 2.44–2.40 (m, 2H), 2.10–2.00 (m, 4H), 1.78 (d, *J* = 1.3 Hz, 3H), 1.77 (s, 3H), 1.75 (s, 6H), 1.74 (s, 3H), 1.40–1.30 (m, 2H), 1.07 (d, *J* = 6.7 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (CD_2Cl_2, 150 MHz): δ = 170.7, 167.6, 161.9, 145.2, 137.0, 135.3, 134.9, 133.9, 133.2, 132.4, 132.0, 131.5, 130.7, 129.9, 129.3, 125.2, 124.9, 121.3, 83.5, 76.7, 62.8, 56.0, 52.9, 47.1, 40.1, 39.9, 37.6, 32.2, 29.9, 21.2, 20.7, 17.4, 15.2, 13.2, 12.3, 12.3; HRMS (ESI): *m/z*: calcd for $C_{40}H_{58}N_2O_6$: 685.41881, found: 685.42481.

Compound 90: Prepared analogously as a colorless oil (1 mg, 73%). $[\alpha]_D^{20}$ = –85 (*c* = 0.07, CH_2Cl_2); ^{1}H



NMR (CD_2Cl_2, 600 MHz): δ = 8.25 (s, 1H), 6.91 (bs, 1H), 6.77 (bs, 1H), 6.60 (d, *J* = 10.0, Hz, 1H), 6.27 (d, *J* = 11.3, Hz, 1H), 6.16–6.05 (m, 4H), 5.72 (dd, *J* = 14.6, 6.9 Hz, 1H), 5.53 (dd, *J* = 15.5, 8.1 Hz, 1H), 5.47–5.39 (m, 2H), 5.16 (dd, *J* = 9.9 Hz, 1H), 4.94 (d, *J* = 9.4 Hz, 1H), 4.51–4.46 (m, 1H), 4.09 (d, *J* = 11.2 Hz, 1H), 3.98 (td, *J* = 9.6, 3.7 Hz, 1H), 3.87 (d, *J* = 5.9 Hz, 1H), 3.70–3.62 (m, 1H), 3.54 (dd,

J = 13.1, 6.7 Hz, 1H), 3.28–3.21 (m, 1H), 3.20 (s, 3H), 3.19 (s, 3H), 2.63 (m, 1H), 2.44–2.38 (m, 1H), 2.16–2.09 (m, 1H), 1.96–1.90 (m, 2H), 1.84 (d, *J* = 1.0 Hz, 3H), 1.75 (s, 6H), 1.73 (s, 3H), 1.50–1.40 (m, 6H), 1.11 (d, *J* = 6.7 Hz, 3H), 0.96 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (CD_2Cl_2, 150 MHz): δ = 170.6, 167.6, 161.9, 145.6, 137.4, 135.8, 135.4, 134.7, 133.9, 133.0, 132.0, 131.8, 129.9, 126.6, 125.4, 124.9, 121.1, 84.1, 80.9, 77.3, 62.8, 56.3, 55.8, 47.1, 46.3, 39.1, 38.2, 37.5, 34.6, 32.0, 28.3, 27.1, 23.9, 21.3, 16.1, 15.2, 13.3, 12.5, 12.2, 8.7; IR (film): $\tilde{\upsilon}$ = 3309, 2924, 2854, 1656, 1535, 1453, 1385, 1258, 1077, 1017, 993, 799 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{40}H_{60}N_2O_7Si$ [M^+ +Na]: 703.42927, found: 703.42995.