Formal Total Synthesis of Oximidine II via a Suzuki-Type Cross-Coupling Macrocyclization Employing Potassium Organotrifluoroborates

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General Information. Proton NMR spectra were recorded on Bruker AMX (500 MHz) or Bruker DMX (500 MHz) spectrometers. Proton chemical shifts are reported in ppm (δ) relative to the solvent reference relative to TMS employed as the internal standard (CDCl_3 , δ 7.24 ppm; acetone- d_6 , δ 2.05 ppm). Data are reported as follows: chemical shift (multiplicity [singlet (s), doublet (d), triplet (t), quartet (q), and multiplet (m)], coupling constants [Hz], integration). Carbon NMR spectra were recorded on Bruker AMX (125 MHz) or Bruker DRX (125 MHz) spectrometers with complete proton decoupling. Carbon chemical shifts are reported in ppm (δ) relative to solvent resonance as the internal standard (CDCl_3 , δ 77.0; acetone- d_6 , δ 29.8 ppm, DMSO- d_6 , δ 39.5 ppm). NMR data were collected at 25 °C.

Infrared spectra were obtained on Perkin Elmer FT-IR 1600 spectrometer.

Melting points were recorded on a Thomas-Hoover capillary melting point apparatus and are not corrected.

Optical rotations were recorded on a Jasco Polarimeter at room temperature (path length 100 mm).

Mass spectra were obtained on Micromass autospec in Electrospray Ionization (EI) and Chemical Ionization (CI) modes using the OPUS software system. The method of ionization is given in parentheses.

All reactions were run using standard bench conditions. If moisture or oxygen sensitive reagents were used, the experiments were conducted using Schlenk techniques under a N_2 -atmosphere. THF, toluene and Et_2O were dried over Na/benzophenone and distilled, CH_2Cl_2 and NEt_3 was dried over CaH_2 and distilled prior to use. Other solvent were –if necessary- dried with 3 or 4 Å molecular sieves. All reagents were used as received from commercial sources. (2*R*,4*S*)-2-Phenyl-[1,3]dioxane-4-carbaldehyde **12** was prepared according to literature procedures.¹

Chromatographical purification was performed using either column chromatography (silica gel or alumina), or MPLC (Biotage®-system), or preparative rotating TLC ("Chromatotron", Harrison Research).

(Z)-1-Triisopropylsilyl-6-trimethylsilyl-hex-1,5-diyn-3-ene (16). 380 mg of $(\text{Ph}_3\text{P})_4\text{Pd}$ (0.3 mmol, 3 mol%) and 60 mg of CuI (0.3 mmol, 3 mol%) were suspended in 50 mL of Et_2O . 2.20 mL of *n*-BuNH₂ (22.0 mmol, 2.0 equiv), 1.74 mL of (Z)-1,2-dichloroethylene **15** (21.0 mmol, 1.9 equiv) and 2.55 mL of triisopropylsilylacetylene (11.0 mmol) was added and the reaction mixture was stirred at rt overnight. After evaporation of the solvent, the residue was taken up with petroleum ether and filtered through a silica/celite pad. Flash-chromatography (silica, petroleum ether 100%) yielded a colourless oil (2.48 g, 10.2 mmol, 93%). R_f (petroleum ether) = 0.77. ¹H NMR (500 MHz, CDCl_3): δ [ppm] = 1.07 (s, 3H), 1.09 (s, 18H), 5.89 (d, J = 7.5 Hz, 1H), 6.39 (d, J = 7.5 Hz, 1H). ¹³C NMR (125 MHz, CDCl_3): δ [ppm] = 11.3, 18.6, 100.1, 100.5, 112.4, 129.2.
*same as lit.*²

[1] (a) Isobe, M.; Ychikawa, Y.; Bai, D.-I.; Goto, T. *Tetrahedron Lett.* **1985**, 26, 5203; (b) Pawlak, J.; Nakanishi, K.; Iwashita, T.; Borowski, E. *J. Org. Chem.* **1987**, 52, 2896.

[2] Lu, Y.-F.; Harwig, C. W.; Fallis, A. G. *Can. J. Chem.* **1995**, 73, 2253.

To a suspension of 140 mg of $(\text{Ph}_3\text{P})_4\text{Pd}$ (0.12 mmol, 2.5 mol%), 25 mg of CuI (0.13 mmol, 2.5 mol%), 1.40 mL of trimethylsilylacetylene (9.9 mmol, 2.0 equiv) and 1.20 g of crude chloroene-yne (4.9 mmol) in 25 mL of Et_2O and 1.0 mL of $n\text{-BuNH}_2$ (10.0 mmol, 2.0 equiv) was added and the reaction mixture was stirred at rt overnight. After evaporation of the solvent, the residue was taken up with petroleum ether and filtered through a silica/Celite pad. Flash chromatography (silica, petroleum ether 100%) yielded a colourless oil (1.44 g, 4.7 mmol, 96%). R_f (petroleum ether) = 0.48. ^1H NMR (500 MHz, CDCl_3): δ [ppm] = 0.18 (s, 9H), 1.07 (s, 3H), 1.09 (s, 18H), 5.82 (d, J = 11.3 Hz, 1H), 5.84 (d, J = 11.3 Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3): δ [ppm] = -0.3, 11.2, 18.7, 100.0, 102.0, 103.0, 103.7, 120.0, 120.5.

same as lit.^[2]

(Z)-Hex-3-en-1,5-diynyl-triisopropyl-silane (18). 1.38 g **16** (4.5 mmol) was dissolved in 70 mL of benzene/methanol (1:1). 0.69 g of K_2CO_3 (5.0 mmol, 1.1 equiv) was added and the reaction mixture was stirred for 2 h at rt. Water (50 mL) was added and the aqueous phase was extracted with hexanes (3 x 50 mL). The organic phases were washed with brine, dried over anhydrous MgSO_4 and evaporated to leave a dark oil (1.01 g, 4.3 mmol, 96%). R_f (PE) = 0.66. ^1H NMR (500 MHz, CDCl_3): δ [ppm] = 1.07 (s, 3H), 1.08 (s, 18H), 3.30 (dd, J = 1.2, 0.7 Hz, 1H), 5.81 (dd, J = 11.0, 1.2 Hz, 1H), 5.91 (dd, J = 11.0, 0.7 Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3): δ [ppm] = 11.2, 18.7, 80.9, 84.8, 100.3, 103.4, 119.3, 122.0.

same as lit.^[2]

(Z)-(6-Bromo-hexa-3-en-1,5-diynyl)-triisopropyl-silane (17). 1.22 g of **16** (4.0 mmol, 1.0 equiv) was dissolved in 40 mL of acetone at 0 °C. 0.80 g of NBS (4.4 mmol, 1.1 equiv) and 0.14 g of AgNO_3 (0.8 mmol, 0.2 equiv) were added and the reaction mixture was stirred overnight while warming to rt. Water (50 mL) was added and the aqueous phase was extracted with hexanes (4 x 50 mL). The organic phases were washed with brine, dried over anhydrous MgSO_4 and evaporated to leave a slightly brown oil (1.24 g, 4.0 mmol, 99%), which was used without purification. R_f (petroleum ether) = 0.65. IR (neat):

$[\text{cm}^{-1}]$ = 2943, 2890, 2865, 2189, 2134, 1674, 1569, 1462, 1384, 1366, 1241, 1078, 996, 919, 883, 772, 743. ^1H NMR (500 MHz, CDCl_3): δ [ppm] = 1.08 (s, 3H), 1.10 (s, 18H), 5.78 (d, J = 10.8 Hz, 1H), 5.88 (d, J = 10.8 Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3): δ [ppm] = 11.2, 18.7, 57.5, 78.3, 100.3, 103.4, 119.8, 121.9. HRMS (CI): calcd. for $\text{C}_{15}\text{H}_{23}\text{BrSi}$ [M^+]: 310.0752; found: 310.0750.

(Z, Z)-(6-Bromo-hexa-3,5-dien-1-ynyl)-triisopropyl-silane (13). 5.2 mL of $\text{BH}_3\cdot\text{THF}$ (1M in THF, 5.2 mmol, 1.3 equiv) was added to 1.05 mL of cyclohexene (10.4 mmol, 2.6 equiv) at 0 °C and the mixture was stirred for 1.5 h, while a white suspension formed. The reaction mixture was diluted with 50 mL of pentane and 1.24 g of **17** (4.0 mmol) in 50 mL pentane was added. The suspension cleared within 5 min. After 30 min 0.2 mL of AcOH (16 mmol, 4.0 equiv) was added, the mixture was stirred for 15 min, and 1.93 mL of ethanolamine (32 mmol, 8.0 equiv) was added. After additional stirring for 10 min, the mixture was filtered through a silica pad with hexanes and the filtrate was evaporated to afford a dark oil (~1.1 g), which contained the product of ca. 90% purity (^1H -NMR). Chromatography (basic alumina, hexanes 100%) yielded a slightly coloured oil (0.71 g, 2.3 mmol, 57%, 2 steps). R_f (PE) = 0.66. IR (neat):

$[\text{cm}^{-1}]$ = 3081, 2943, 2891, 2865, 2137, 1627, 1604, 1549, 1462, 1383, 1366, 1296, 1241, 1079, 1016, 996, 980, 919, 883, 782, 735, 711. ^1H NMR (500 MHz, CDCl_3): δ [ppm] = 1.07 (s, 18H), 1.09 (s, 3H), 5.70 (ddd, J = 10.9, 1.4, 1.0 Hz, 1H), 6.35 (dt, J = 7.2, 1.3 Hz, 1H), 6.72 (td, J = 10.7, 1.0 Hz, 1H), 7.20 (ddd, J = 10.6, 7.2, 1.0 Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3): δ [ppm] = 11.2, 18.7, 100.0, 103.5, 112.0, 113.5, 129.9, 135.6. HRMS (CI): calcd. for $\text{C}_{15}\text{H}_{25}\text{BrSi}$ [M^+]: 312.0909; found: 312.0890.

(Z)-(1S,2S,4S)-1-(2-Phenyl-[1,3]dioxan-4-yl)-7-triisopropylsilanyl-hept-4-en-2,6-diyn-1-ol (19). 370 mg of Zn(OTf)₂ (1.0 mmol, 1.25 equiv) and 185 mg of (+)-NME (1.0 mmol, 1.25 equiv) were suspended in 5 mL of toluene at rt. 390 μ L of NEt₃ (3.0 mmol, 3.8 equiv) was added and the mixture was stirred for 2 h. 280 mg of **18** (1.2 mmol, 1.5 equiv) was added, the mixture was stirred for 15 min and 155 mg of **10** (0.8 mmol, 1.0 equiv) was added. After stirring for 2 h at rt, TLC showed complete conversion, and the mixture was extracted with saturated NH₄Cl·aq and Et₂O. The organic phases were washed with brine, dried over MgSO₄, filtered through a silica gel pad and evaporated. Purification via Chromatotron (hexanes:ethyl acetate 9:1 to 4:1) gave a clear oil (260 mg, 0.61 mmol, 77%). *R_f*(hexanes:ethyl acetate 2:1) = 0.65. [α]_D²⁰₅₈₉ +43.0 (*c* = 0.66, CHCl₃). IR (neat): [cm^{-1}] = 3038, 2942, 2890, 2864, 2138, 1464, 1394, 1362, 1306, 1240, 1214, 1128, 1098, 1074, 1018, 918, 883, 848, 750. ¹H NMR (500 MHz, CDCl₃): δ [ppm] = 1.10 (s, 21H), 1.77-1.83 (m, 1H), 1.87 (qd, *J* = 12.0, 5.1 Hz, 1H), 2.60 (brs, *J* = 6.1 Hz, 1H), 3.93-3.98 (m, 2H), 4.23 (ddd, *J* = 11.5, 5.0, 1.3 Hz, 1H), 4.53 (d, *J* = 6.9 Hz, 1H), 5.52 (s, 1H), 5.85 (dd, *J* = 11.0, 1.8 Hz, 1H), 5.89 (d, *J* = 11.0 Hz, 1H), 7.33-7.36 (m, 3H), 7.46-7.49 (m, 2H). ¹³C NMR (125 MHz, CDCl₃): δ [ppm] = 11.2, 18.6, 27.2, 66.3, 66.5, 79.6, 83.9, 93.2, 100.1, 101.3, 103.5, 119.1, 120.8, 126.1, 128.3, 129.0, 138.0. HRMS (EI): calc. for C₂₆H₃₆O₃SiNa [M+Na⁺]: 447.2331; found: 447.2342.

(Z)-(1S,2S,4S)-Triisopropyl-[7-methoxymethoxy-7-(2-phenyl-[1,3]dioxan-4-yl)-hept-3-en-1,5-diynyl]-silane (20). 1.70 g of **19** (4.0 mmol, 1.0 equiv) and 875 μ L of *i*-Pr₂NEt (5.0 mmol, 1.25 equiv) were dissolved in 60 mL of CH₂Cl₂ at 0 °C and 750 μ L of MOMCl (85%, 8.0 mmol, 2.0 equiv) were added dropwise. The mixture was stirred for 13 h at rt (TLC: low conversion), then a catalytic amount of DMAP (~ 30 mg) was added and the mixture was heated to reflux for 36 h. The mixture was extracted with saturated NH₄Cl·aq. and Et₂O, the organic phases were washed with brine, dried over MgSO₄ and evaporated. Purification via chromatography (silica gel, hexanes:ethyl acetate 9:1) afforded a clear oil (1.62 g, 3.46 mmol, 86%). *R_f*(hexanes:ethyl acetate 4:1) = 0.63. [α]_D²⁰₅₈₉ +43.0 (*c* = 0.69, CHCl₃). IR (neat): [cm^{-1}] = 3038, 2942, 2890, 2864, 2142, 1720, 1572, 1462, 1390, 1365, 1298, 1242, 1215, 1146, 1129, 1098, 1027, 918, 882, 751. ¹H NMR (500 MHz, CDCl₃): δ [ppm] = 1.07 (s, 3H), 1.10 (s, 18H), 1.81 (bd, *J* = 13.2 Hz, 1H), 1.89 (qd, *J* = 12.3, 5.0 Hz, 1H), 3.37 (s, 3H), 3.97 (dd, *J* = 11.8, 2.1 Hz, 1H), 4.06 (dd, *J* = 8.6, 2.2 Hz, 1H), 4.28 (dd, *J* = 11.2, 4.5 Hz, 1H), 4.61 (d, *J* = 5.8 Hz, 1H), 4.66 (d, *J* = 6.7 Hz, 1H), 4.93 (d, *J* = 6.7 Hz, 1H), 5.52 (s, 1H), 5.85 (dd, *J* = 11.1, 1.8 Hz, 1H), 5.89 (d, *J* = 11.1 Hz, 1H), 7.29-7.35 (m, 3H), 7.46-7.49 (m, 2H). ¹³C NMR (125 MHz, CDCl₃): δ [ppm] = 11.2, 18.6, 27.4, 55.6, 66.7, 69.3, 78.4, 84.6, 92.0, 94.4, 100.1, 101.0, 103.5, 119.0, 120.6, 126.1, 128.1, 128.7, 138.4. HRMS (EI): calc. for C₂₈H₄₀O₄NaSi [M+Na⁺]: 491.2594; found: 491.2598.

(Z,Z)-(1S,2S,4S)-Triisopropyl-[7-methoxymethoxy-7-(2-phenyl-[1,3]dioxan-4-yl)-hept-3,5-dien-1-ynyl]-silane (11). 622 mg of **20** (1.32 mmol, 1.0 equiv), 470 μ L of quinoline (4.0 mmol, 1.3 equiv) and 440 mg of Lindlar's catalyst (5 w/w% Pd on CaCO₃/Pb, 70 w/w%) were suspended in 50 mL of hexanes at rt. The mixture was degassed and purged with H₂ (4-5x) and then stirred at rt under H₂-pressure (balloon, 1 atm) for 21 h. The reaction mixture was filtered through Celite and evaporated. Purification via chromatography (silica gel, hexanes:ethyl acetate 40:1 to 10:1) yielded a clear oil (613 mg, 1.30 mmol, 98%). *R_f*(hexanes:ethyl acetate 4:1) = 0.57. [α]_D²⁰₅₈₉ -38.4 (*c* = 0.76, CHCl₃). IR (neat): [cm^{-1}] = 2942, 2889, 2864, 2138, 1764, 1642, 1631, 1596, 1462, 1426, 1366, 1310, 1241, 1212, 1141, 1099, 1028, 995, 916, 882, 847, 750. ¹H NMR (500 MHz, CDCl₃): δ [ppm] = 1.07 (s, 3H), 1.10 (s, 18H), 1.46 (dd, *J* = 13.3, 1.4 Hz, 1H), 1.84 (qd, *J* = 12.3, 5.0 Hz, 1H), 3.34 (s, 3H), 3.91-3.98 (m, 2H), 4.26 (dd, *J* = 11.3, 4.2 Hz, 1H), 4.61 (d, *J* = 6.7 Hz, 1H), 4.63 (d, *J* = 6.7 Hz, 1H), 4.61-4.64 (m, 1H), 5.52 (s, 1H), 5.52 (t, *J* = 10.3 Hz, 1H), 5.61 (d, *J* = 10.6 Hz, 1H), 6.80 (t, *J* = 10.9 Hz, 1H), 6.87 (t, *J* = 11.1 Hz, 1H), 7.29-7.35 (m, 3H),

7.46-7.49 (m, 2H). ^{13}C NMR (125 MHz, CDCl_3): δ [ppm] = 11.3, 18.7, 27.3, 55.4, 66.8, 73.1, 78.9, 94.0, 99.3, 101.1, 103.3, 112.4, 126.1, 128.1, 128.6, 129.3, 130.7, 135.0, 138.6. HRMS (EI): calc. for $\text{C}_{28}\text{H}_{42}\text{O}_4\text{NaSi}$ [$\text{M}+\text{Na}^+$]: 491.2750; found: 493.2760.

(Z,Z)-(3S,4S)-1-Benzylloxy-4-methoxymethoxy-10-triisopropylsilanyl-deca-5,7-dien-9-yn-3-ol (9). 2.5 mL of DIBALH (1M in CH_2Cl_2 , 2.5 mmol, 5 equiv) was added to 225 mg of **11** (0.48 mmol, 1.0 equiv) in 10 mL CH_2Cl_2 at -10°C , and the mixture was stirred for 1.5 h. Saturated Rochelle's salt solution was added and the mixture was extracted with ethyl acetate (4 x 50 mL). The organic phases were washed with brine, dried over MgSO_4 and evaporated. Purification via Chromatotron (hexanes:ethyl acetate 9:1 to 4:1) afforded a clear oil (155 mg, 0.33 mmol, 69%). R_f (hexanes:ethyl acetate 2:1) = 0.57. $[\alpha]_{589}^{20} +4.6$ ($c=1.57$, CHCl_3). IR (neat): $[\text{cm}^{-1}] = 3468, 2942, 2890, 2864, 2138, 1462, 1366, 1260, 1210, 1152, 1098, 1028, 962, 918, 883, 806, 749$. ^1H NMR (500 MHz, CDCl_3): δ [ppm] = 1.10 (s, 21H), 1.68-1.73 (m, 1H), 1.80-1.84 (m, 1H), 2.89 (d, $J=2.6$ Hz, 1H), 3.36 (s, 3H), 3.63-3.67 (m, 2H), 3.76-3.80 (m, 1H), 4.38 (dd, $J=9.2, 6.7$ Hz, 1H), 4.50 (s, 2H), 4.54 (d, $J=6.6$ Hz, 1H), 4.65 (d, $J=6.6$ Hz, 1H), 5.47 (t, $J=10.9$ Hz, 1H), 5.57 (d, $J=10.8$ Hz, 1H), 6.68 (t, $J=11.2$ Hz, 1H), 6.86 (t, $J=11.4$ Hz, 1H), 7.26-7.28 (m, 1H), 7.30-7.33 (m, 4H). ^{13}C NMR (125 MHz, CDCl_3): δ [ppm] = 11.3, 18.7, 32.7, 55.6, 67.7, 71.9, 73.2, 74.7, 93.8, 99.3, 103.3, 112.4, 127.6, 127.7, 128.4, 130.1, 130.9, 134.9, 138.2. HRMS (EI): calc. for $\text{C}_{28}\text{H}_{44}\text{O}_4\text{NaSi}$ [$\text{M}+\text{Na}^+$]: 495.2907; found: 495.2924.

5-Benzylloxy-2,2-dimethyl-benzo[1,3]dioxin-4-one (23). 0.52 g of NaH (60% in mineral oil, 13 mmol, 1.3 equiv) was added to 1.94 g of 5-hydroxy-2,2-dimethyl-benzo[1,3]dioxin-4-one (**22**)^[3] (10.0 mmol, 1.0 equiv) in 25 mL of DMF at 0°C and the mixture was stirred for 0.5 h. The dark red solution was then treated with 1.8 mL of benzyl bromide (15 mmol, 1.5 equiv) and then stirred at rt overnight. Saturated aqueous NH_4Cl was added and the mixture was extracted with ethyl acetate (3 x 100 mL). The organic phases were washed with brine, dried over MgSO_4 and evaporated. The residue was dissolved in ethyl acetate and filtered through a silica gel pad. The filtrate was evaporated and recrystallized from $\text{Et}_2\text{O}/\text{EtOAc}$ (1:1) to yield fine, white crystals (2.72 g, 9.6 mmol, 96%). R_f (hexanes:ethyl acetate 2:1) = 0.41. mp ($\text{EtOAc}/\text{Et}_2\text{O}$) = $89-91^\circ\text{C}$. IR (neat): $[\text{cm}^{-1}] = 2996, 2942, 1736, 1607, 1585, 1498, 1481, 1453, 1388, 1378, 1331, 1259, 1239, 1204, 1150, 1093, 1075, 1038, 963, 921, 849, 803, 763, 737$. ^1H NMR (500 MHz, CDCl_3): δ [ppm] = 1.69 (s, 6H), 5.23 (s, 2H), 6.53 (d, $J=8.2$ Hz, 1H), 6.63 (d, $J=8.4$ Hz, 1H), 7.28 (t, $J=8.3$ Hz, 1H), 7.36 (t, $J=7.8$ Hz, 2H), 7.37 (t, $J=8.2$ Hz, 1H), 7.52 (d, $J=7.7$ Hz, 2H). ^{13}C NMR (125 MHz, CDCl_3): δ [ppm] = 25.6, 70.6, 103.8, 105.2, 107.1, 109.4, 126.6, 127.8, 128.6, 136.2, 136.2, 157.8, 158.0, 160.3. HRMS (CI): calcd. for $\text{C}_{17}\text{H}_{16}\text{O}_4$ [M^+]: 284.1049; found: 284.1039.

(Z,Z)-(3S,4S)-2-Benzylloxy-6-hydroxy-benzoic acid 3-(1-benzylloxy-4-methoxymethoxy-deca-5,7-dien-9-yn)-yl ester (21). 378 mg of **9** (0.8 mmol) was azeotroped with benzene at 40°C , then dissolved in 30 mL of THF at 0°C and treated with 0.96 mL of NaHMDS (1M in THF, 0.96 mmol, 1.2 equiv). The mixture was stirred for 1 h at 0°C . 342 mg of **11** (1.2 mmol, 1.5 equiv) in 5 mL of THF were added and the mixture was stirred at rt for 4 h. Saturated aqueous NH_4Cl (10 mL) was added and the mixture was extracted with EtOAc (3 x 50 mL). The organic phases were dried over MgSO_4 and evaporated. Purification via chromatography (Chromatotron, hexanes: EtOAc 6:1 to 4:1) afforded **21a** as a colourless oil (433 mg, 0.62 mmol, 77%). R_f (hexanes:ethyl acetate 4:1) = 0.54. $[\alpha]_{589}^{20} -19.3$ ($c=0.57$, CHCl_3). IR (neat): $[\text{cm}^{-1}] = 3631, 3372, 3032, 2942, 2890, 2864, 2139, 1732, 1652, 1608, 1581, 1497, 1454, 1366, 1298,$

^[3] Hadfield, A.; Schweitzer, H.; Trova, M. P.; Green, K. *Synth. Commun.* **1994**, 1025.

1256, 1228, 1174, 1154, 1072, 1030, 966, 918, 882, 811, 745. ¹H NMR (500 MHz, CDCl₃): δ [ppm] = 1.06 (s, 3H), 1.09 (s, 18H), 1.54-1.59 (m, 1H), 1.99-2.04 (m, 1H), 3.20 (s, 3H), 3.31-3.38 (m, 2H), 4.33 (d, *J* = 11.9 Hz, 1H), 4.38 (d, *J* = 11.9 Hz, 1H), 4.43 (d, *J* = 6.8 Hz, 1H), 4.51 (t, *J* = 7.0 Hz, 1H), 4.53 (d, *J* = 6.8 Hz, 1H), 4.98 (d, *J* = 11.0 Hz, 1H), 4.99 (d, *J* = 11.0 Hz, 1H), 5.39 (t, *J* = 9.0 Hz, 1H), 5.47-5.50 (m, 1H), 5.54 (d, *J* = 10.8 Hz, 1H), 6.45 (d, *J* = 8.3 Hz, 1H), 6.50 (t, *J* = 11.5 Hz, 1H), 6.60 (d, *J* = 8.4 Hz, 1H), 6.79 (t, *J* = 11.2 Hz, 1H), 7.18-7.35 (m, 10H), 7.43 (d, *J* = 7.1 Hz, 1H), 11.49 (s, 1H). ¹³C NMR (125 MHz, CDCl₃): δ [ppm] = 11.3, 18.6, 30.4, 55.4, 66.0, 71.0, 72.1, 73.1, 73.3, 93.8, 99.4, 103.2, 103.6, 110.3, 112.4, 127.5, 127.7, 128.0, 128.0, 128.0, 128.3, 128.4, 129.2, 131.0, 134.7, 135.0, 136.5, 138.2, 160.1, 163.7, 170.5. HRMS (EI): calcd. for C₄₂H₅₄O₇SiNa [M+ Na⁺]: 721.3537; found: 721.3545.

0.84 mL of TBAF (1M in THF, 0.84 mmol, 1.5 equiv) was added to 391 mg of the crude addition product (0.56 mmol) in 30 mL of THF at 0 °C and the mixture was stirred for 1 h at 0 °C. The mixture was filtered through a silica gel pad and evaporated. Purification via chromatography (Chromatotron, hexanes:EtOAc 6:1) yielded **21** as a colourless oil (229 mg, 0.42 mmol, 75%). *R_f* (hexanes:ethyl acetate 4:1) = 0.23. [α]_D²⁰₅₈₉ -7.8 (c=1.21, CHCl₃). IR (neat): [cm⁻¹] = 3285, 3063, 3032, 2931, 2888, 1732, 1656, 1652, 1607, 1581, 1496, 1455, 1373, 1298, 1257, 1228, 1176, 1153, 1090, 1072, 1029, 916, 845, 811, 746. ¹H NMR (500 MHz, CDCl₃): δ [ppm] = 1.60-1.60 (m, 1H), 1.90-1.93 (m, 1H), 3.21 (s, 3H), 3.29 (d, *J* = 2.1 Hz, 1H), 3.33-3.38 (m, 2H), 4.36 (d, *J* = 11.9 Hz, 1H), 4.38 (d, *J* = 11.9 Hz, 1H), 4.44 (d, *J* = 6.8 Hz, 1H), 4.50-4.54 (m, 1H), 4.51 (d, *J* = 6.8 Hz, 1H), 4.98 (d, *J* = 11.0 Hz, 1H), 4.99 (d, *J* = 11.0 Hz, 1H), 5.43 (t, *J* = 10.6 Hz, 1H), 5.47 (d, *J* = 10.8 Hz, 1H), 5.47-5.50 (m, 1H), 6.46 (d, *J* = 8.3 Hz, 1H), 6.59 (t, *J* = 11.5 Hz, 1H), 6.61 (d, *J* = 8.3 Hz, 1H), 6.76 (t, *J* = 11.3 Hz, 1H), 7.18-7.35 (m, 10H), 7.43 (d, *J* = 7.1 Hz, 1H), 11.48 (s, 1H). ¹³C NMR (125 MHz, CDCl₃): δ [ppm] = 30.2, 55.3, 65.9, 70.9, 72.0, 73.0, 73.2, 80.1, 84.8, 93.8, 103.2, 103.5, 110.2, 110.9, 127.5, 127.6, 128.0, 128.0, 128.2, 128.4, 129.7, 130.6, 135.0, 135.9, 136.4, 138.2, 160.0, 163.6, 170.4. HRMS (EI): calc. for C₃₃H₃₄O₇Na [M+Na⁺]: 565.2202; found: 565.2216.

(Z,Z)-(3S,4S)-2-Benzyloxy-6-trifluoromethanesulfonyloxy-benzoic acid 3-(1-benzyloxy-4-methoxymethoxy-deca-5,7-dien-9-yn)-yl ester (24). 250 mg of **21** (0.46 mmol) were dissolved in 5 mL of pyridine at 0 °C and 0.25 mL of Tf₂O (1.5 mmol, 3.0 equiv) was added. The mixture was stirred for 0.5 h at 0 °C and saturated NH₄Cl solution (10 mL) was added. The mixture was extracted with EtOAc (2 x 50 mL). The organic phases were washed with saturated CuSO₄ solution (2 x 100 mL) and brine, then dried over MgSO₄ and evaporated. Purification via chromatography (Chromatotron, hexanes:EtOAc 9:1) afforded the product as a clear oil (265 mg, 0.39 mmol, 85%). *R_f* (hexanes:ethyl acetate 4:1) = 0.25. [α]_D²⁰₅₈₉ +18.7 (c=0.90, CHCl₃). IR (neat): [cm⁻¹] = 3291, 3032, 2916, 1735, 1612, 1454, 1425, 1279, 1216, 1141, 1072, 1037, 952, 825, 751. ¹H NMR (500 MHz, CDCl₃): δ [ppm] = 1.93-1.99 (m, 1H), 2.01-2.05 (m, 1H), 3.26 (d, *J* = 2.1 Hz, 1H), 3.27 (s, 3H), 3.44-3.48 (m, 2H), 4.32 (d, *J* = 11.7 Hz, 1H), 4.41 (d, *J* = 11.7 Hz, 1H), 4.46 (d, *J* = 6.8 Hz, 1H), 4.52 (d, *J* = 6.8 Hz, 1H), 4.68 (dd, *J* = 9.6, 4.5 Hz, 1H), 5.08 (s, 2H), 5.40-5.46 (m, 2H), 5.50 (t, *J* = 9.3 Hz, 1H), 6.66 (quin, *J* = 10.5 Hz, 2H), 6.97 (d, *J* = 6.1 Hz, 1H), 6.98 (d, *J* = 6.0 Hz, 1H), 7.22-7.25 (m, 1H), 7.28-7.31 (m, 5H), 7.33-7.38 (m, 5H). ¹³C NMR (125 MHz, CDCl₃): δ [ppm] = 31.0, 55.5, 66.4, 71.1, 71.3, 73.0, 75.0, 80.2, 84.5, 93.7, 110.7, 112.3, 113.2, 118.1, 118.5 (q, ¹*J*_{CF} = 318 Hz), 127.4, 127.7, 127.7, 128.3, 128.5, 128.7, 129.7, 130.3, 131.6, 135.3, 136.0, 138.4, 146.9, 157.1, 162.8. ¹⁹F NMR (470 MHz, CDCl₃): δ [ppm] = -73.65 (s). HRMS (EI): calcd. for C₃₄H₃₃F₃O₉SiNa [M+ Na⁺]: 697.1695; found: 697.1663.

(4R,2'S,4'S)-Acetic acid 4-hydroxy-4-(2'-phenyl-[1,3]dioxan-4'-yl)-but-2-ynyl ester (33). 9.3 g of Zn(OTf)₂ (25 mmol, 2.5 equiv) and 4.6 g of (+)-NME (25 mmol, 2.5 equiv) were suspended in 50 mL of toluene at rt. 6.5 mL of NEt₃ (50 mmol, 5.0 equiv) was added and the mixture was stirred for 2 h. 2.5 mL of propargyl acetate (**32**) (25 mmol, 2.5 equiv) was added, the mixture was stirred for 15 min and

1.90 g of **10**^[2] (9.9 mmol) was added. After stirring for 1.5 h at rt, TLC showed complete conversion, and the mixture was extracted with saturated NH₄Cl-aq and Et₂O. The organic phases were washed with brine, dried over MgSO₄, filtered through a silica gel pad and evaporated. Purification via chromatography (silica gel, hexanes:ethyl acetate 9:1 to 4:1) gave a clear oil (2.57 g, 8.8 mmol, 89%), which slowly solidified. *R_f* (hexanes:ethyl acetate 4:1) = 0.56. mp (CHCl₃) = 61-62 °C. $[\alpha]_{589}^{20} +12.0$ (c = 0.78, CHCl₃). IR (neat): $[\text{cm}^{-1}] = 3446, 2929, 2862, 1742, 1455, 1433, 1378, 1224, 1129, 1105, 1022, 920, 884, 847, 764, 700$. ¹H NMR (300 MHz, CDCl₃): δ [ppm] = 1.71 (dq, *J* = 13.3, 1.5 Hz, 1H), 1.87 (dq, *J* = 12.1, 5.2 Hz, 1H), 2.07 (s, 3H), 2.73 (d, *J* = 4.0 Hz, 1H), 3.91-4.03 (m, 2H), 4.31 (ddd, *J* = 11.5, 6.5, 1.1 Hz, 1H), 4.37-4.41 (m, 1H), 4.69 (s, 1H), 4.70 (s, 1H), 5.51 (s, 1H), 7.33-7.38 (m, 3H), 7.44-7.48 (m, 2H). ¹³C NMR (75 MHz, CDCl₃): δ [ppm] = 20.7 (q), 26.9 (t), 52.1 (t), 65.5 (d), 66.4 (t), 79.3 (d), 80.6 (s), 83.2 (s), 101.2 (d), 126.1 (d x2), 128.6 (d x2), 129.1 (d), 137.9 (s), 170.1 (s). HRMS (CI): calcd. for C₁₆H₁₈O₅ [M⁺]: 290.1154; found: 290.1143.

(4*R*,2'*S*,4'*S*)-Acetic acid 4-methoxymethoxy-4-(2'-phenyl-[1,3]dioxan-4'-yl)-but-2-ynyl ester (34). 1.70 g of **33** (5.9 mmol) in 15 mL of CH₂Cl₂ were treated with 1.1 mL of MOMCl (85%, 12 mmol, 2.0 equiv) and 1.75 mL of *i*-Pr₂NEt (10 mmol, 1.7 equiv) at 0 °C and stirred overnight. TLC indicated complete conversion and the mixture was extracted with saturated aq. NH₄Cl and CH₂Cl₂ (2 x 100 mL). The organic phases were dried over anhydrous MgSO₄ and evaporated. The resulting clear oil was used without further purification. *R_f* (hexanes:ethyl acetate 2:1) = 0.45. $[\alpha]_{589}^{20} +42.0$ (c = 1.46, CHCl₃). IR (neat): $[\text{cm}^{-1}] = 3035, 2936, 2889, 1748, 1636, 1452, 1435, 1398, 1377, 1361, 1314, 1272, 1223, 1150, 1129, 1101, 1069, 1026, 946, 918, 760, 715$. ¹H NMR (500 MHz, CDCl₃): δ [ppm] = 1.73 (d, *J* = 13.3 Hz, 1H), 1.94 (dq, *J* = 12.4, 5.0 Hz, 1H), 2.07 (s, 3H), 3.36 (s, 3H), 3.97 (dq, *J* = 12.0, 2.5 Hz, 1H), 4.03 (ddd, *J* = 11.5, 7.0, 2.5 Hz, 1H), 4.29 (dd, *J* = 11.7, 4.0 Hz, 1H), 4.49 (dt, *J* = 7.0, 1.6 Hz, 1H), 4.66 (d, *J* = 6.7 Hz, 1H), 4.73 (d, *J* = 1.6 Hz, 2H), 4.89 (d, *J* = 6.7 Hz, 1H), 5.52 (s, 1H), 7.30-7.33 (m, 3H), 7.46-7.48 (m, 2H). ¹³C NMR (75 MHz, CDCl₃): δ [ppm] = 20.7, 27.2, 52.1, 55.7, 66.6, 68.6, 78.1, 81.5, 82.0, 94.5, 101.1, 126.1, 128.1, 128.8, 138.3, 170.0. HRMS (EI): calc. for C₁₈H₂₂O₆Na [M+Na⁺]: 357.1314; found: 357.1319.

(4*R*,2'*S*,4'*S*)-4-Methoxymethoxy-4-(2'-phenyl-[1,3]dioxan-4'-yl)-but-2-yn-1-ol (35). 0.90 g of K₂CO₃ (6 mmol, 1.0 equiv) was added to 2.01 g of crude **34** (~5.9 mmol) in 15 mL of MeOH at 0 °C and the mixture was stirred for 0.5 h. The mixture was extracted with saturated aq. NH₄Cl and EtOAc (4 x 50 mL). The combined organic phases were washed with brine, dried over anhydrous MgSO₄ and evaporated to yield a clear oil (1.74 g, ~5.9 mmol ~99%), which was used without further purification. *R_f* (hexanes:ethyl acetate 2:1) = 0.25. $[\alpha]_{589}^{20} +50.8$ (c = 1.79, CHCl₃). IR (neat): $[\text{cm}^{-1}] = 3395, 2890, 1714, 1669, 1456, 1399, 1366, 1266, 1243, 1218, 1146, 1124, 1102, 1067, 1026, 918, 880, 764, 732$. ¹H NMR (500 MHz, CDCl₃): δ [ppm] = 1.74 (d, *J* = 13.2 Hz, 1H), 1.88 (brt, *J* = 5.3 Hz, 1H), 1.97 (dq, *J* = 12.5, 5.0 Hz, 1H), 3.37 (s, 3H), 3.97 (td, *J* = 10.7, 2.4 Hz, 1H), 4.01-4.07 (m, 1H), 4.26-4.34 (m, 3H), 4.51 (d, *J* = 6.7 Hz, 1H), 4.66 (d, *J* = 6.7 Hz, 1H), 4.90 (d, *J* = 6.7 Hz, 1H), 5.52 (s, 1H), 7.30-7.33 (m, 3H), 7.46-7.48 (m, 2H). ¹³C NMR (75 MHz, CDCl₃): δ [ppm] = 27.2, 51.0, 55.7, 66.6, 68.6, 78.2, 80.9, 85.8, 94.4, 101.1, 126.1, 128.1, 128.8, 138.3. HRMS (EI): calc. for C₁₆H₂₀O₅Na [M+Na⁺]: 315.1208; found: 315.1200.

(*Z*)-(4*R*,2'*S*,4'*S*)-4-Methoxymethoxy-4-(2'-phenyl-[1,3]dioxan-4'-yl)-but-2-en-1-ol (36). 1.74 g of **25** (5.9 mmol) and 0.12 mL of quinoline (1.0 mmol, 0.17 equiv) in 30 mL of MeOH at rt were degassed and purged with N₂ (repeated two times). 500 mg of Lindlar's catalyst (5 w/w% Pd on CaCO₃/Pb, 30 w/w%) were added and the suspension was degassed and purged with N₂ (three times), then with H₂ (three times). The mixture was stirred under H₂-atmosphere (balloon) for 24 h. The mixture was extracted

with aq. 15% KHSO_4 and Et_2O (3 x 100 mL), the organic phases were washed with brine, dried over anhydrous MgSO_4 and evaporated. The residue was subjected to chromatography (silica gel, hexanes:EtOAc 4:1) to yield a clear oil (1.42 g, 4.8 mmol, 81% over 3 steps). R_f (hexanes:ethyl acetate 1:1) = 0.29. $[\alpha]_{589}^{20}$ +37.9 (c = 2.07, CHCl_3). IR (neat): $[\text{cm}^{-1}]$ = 3430, 2928, 2863, 1453, 1399, 1367, 1244, 1216, 1140, 1367, 1244, 1028, 918, 759, 732. ^1H NMR (500 MHz, CDCl_3): δ [ppm] = 1.51 (brd, J = 11.9 Hz, 1H), 1.97 (qd, J = 12.4, 4.9 Hz, 1H), 2.11 (brs, 1H), 3.37 (s, 3H), 3.95 (t, J = 8.0 Hz, 1H), 4.01-4.04 (m, 1H), 4.07-4.10 (m, 1H), 4.18-4.22 (m, 1H), 4.28 (dd, J = 11.4, 4.9 Hz, 1H), 4.59-6.64 (m, 2H), 4.72 (d, J = 6.5 Hz, 1H), 5.49 (t, J = 10.3 Hz, 1H), 5.53 (s, 1H), 5.49 (dt, J = 10.4, 7.3 Hz, 1H), 7.30-7.36 (m, 3H), 7.46-7.47 (m, 2H). ^{13}C NMR (75 MHz, CDCl_3): δ [ppm] = 26.5, 55.4, 58.3, 66.8, 72.8, 78.6, 94.1, 101.2, 126.0, 127.9, 128.2, 128.8, 134.5, 138.3. HRMS (EI): calc. for $\text{C}_{16}\text{H}_{22}\text{O}_5\text{Na}$ [$\text{M}+\text{Na}^+$]: 317.1365; found: 357.1364.

(Z)-(4R,2'S,4'S)-4-Methoxymethoxy-4-(2'-phenyl-[1,3]dioxan-4'-yl)-but-2-enal (31). 855 mg of **36** (2.9 mmol) and 1.23 g of IBX (4.4 mmol, 1.5 equiv) in 15 mL of DMSO at rt were stirred for 1 h and then H_2O and Et_2O (100 mL each) were added. The organic phase was extracted with H_2O (5 x 150 mL), dried over anhydrous MgSO_4 and evaporated to yield a clear oil, which was used immediately for the next reaction (0.85 g, 2.8 mmol, 97%). R_f (hexanes:ethyl acetate 1:1) = 0.57. ^1H NMR (500 MHz, CDCl_3): δ [ppm] = 1.52 (d, J = 13.0 Hz, 1H), 1.95 (dq, J = 12.1, 5.0 Hz, 1H), 3.35 (s, 3H), 3.95 (td, J = 11.9, 2.0 Hz, 1H), 4.07-4.11 (m, 1H), 4.28 (dd, J = 11.3, 4.8 Hz, 1H), 4.68 (s, 2H), 5.03 (dd, J = 8.6, 5.5 Hz, 1H), 5.52 (s, 1H), 6.16 (dd, J = 11.4, 7.6 Hz, 1H), 6.52 (dd, J = 11.4, 9.0 Hz, 1H), 7.31-7.35 (m, 3H), 7.40-7.42 (m, 2H), 10.09 (d, J = 7.5 Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3): δ [ppm] = 26.5, 55.7, 66.6, 73.2, 78.2, 95.1, 101.3, 126.0, 128.1, 128.8, 132.9, 138.1, 146.0, 191.3.

(Z)-(1S,2S,4S)-4-(5,5-Dibromo-1-methoxymethoxy-penta-2,4-dienyl)-2-phenyl-[1,3]dioxane (37). A solution of 3.85 g of CBr_4 (11.6 mmol, 4 equiv) in 80 mL of CH_2Cl_2 at 0 °C was treated with 6.08 g of PPh_3 (23.2 mmol, 8 equiv). After 5 min 8.0 mL of NEt_3 (61 mmol, 20 equiv) was added and after an additional 5 min, 0.85 g of crude **31** (~2.8 mmol) in 20 mL of CH_2Cl_2 was added. The reaction mixture was stirred for 0.75 h and then poured into 900 mL of hexanes. The whitish precipitate was filtered off through a silica gel pad and washed with Et_2O (300 mL). The filtrate was evaporated and the residue was purified by chromatography (Chromatotron, hexanes 100% to hexanes:EtOAc 9:1) to yield a clear oil (1.10 g, 2.45 mmol, 84% over 2 steps). R_f (hexanes:ethyl acetate 6:1) = 0.78. $[\alpha]_{589}^{20}$ -7.7 (c = 0.54, CHCl_3). IR (neat): $[\text{cm}^{-1}]$ = 2856, 1716, 1558, 1637, 1600, 1456, 1374, 1218, 1172, 1108, 1068, 1027, 918, 880, 846, 817, 772. ^1H NMR (500 MHz, CDCl_3): δ [ppm] = 1.48 (dq, J = 13.2, 1.4 Hz, 1H), 1.86 (dq, J = 12.0, 4.8 Hz, 1H), 3.34 (s, 3H), 3.94-4.01 (m, 2H), 4.28 (dd, J = 11.3, 4.8 Hz, 1H), 4.53 (dd, J = 9.2, 6.3 Hz, 1H), 4.64 (s, 2H), 5.52 (s, 1H), 5.58 (m, 1H), 6.17 (td, J = 11.0, 1.0 Hz, 1H), 7.32-7.36 (m, 4H), 7.46-7.48 (m, 2H). ^{13}C NMR (125 MHz, CDCl_3): δ [ppm] = 26.9, 55.5, 66.7, 73.9, 78.6, 94.4, 95.0, 101.1, 126.0, 128.1, 128.7, 129.8, 130.4, 132.3, 138.4. HRMS (EI): calc. for $\text{C}_{17}\text{H}_{20}\text{Br}_2\text{O}_4\text{Na}$ [$\text{M}+\text{Na}^+$]: 468.9626; found: 468.9649.

(Z,Z)-(1S,2S,4S)-4-(5-Bromo-1-methoxymethoxy-penta-2,4-dienyl)-2-phenyl-[1,3]dioxane (38). 1.10 g of **37** (2.45 mmol), and 57 mg of $\text{Pd}(\text{PPh}_3)_4$ (0.049 mmol, 2 mol%) in 35 mL of benzene were degassed and purged with Ar. 690 μL of $n\text{-Bu}_3\text{SnH}$ (2.48 mmol, 1.01 equiv) were added and the mixture was stirred at rt overnight. The solvent was evaporated and the reaction mixture was purified by chromatography (Chromatotron, hexanes 100% to hexanes:EtOAc 6:1) to yield a clear oil that crystallized on standing (800 mg, 2.15 mmol, 88%). R_f (hexanes:ethyl acetate 4:1) = 0.56. $[\alpha]_{589}^{20}$ -30.0 (c = 1.63, CHCl_3). mp (CHCl_3) = 75-76 °C. IR (neat): $[\text{cm}^{-1}]$ = 2929, 2848, 1365, 1292, 1218, 1139, 1098, 1027, 771. ^1H NMR (500 MHz, CDCl_3): δ [ppm] = 1.45 (d, J = 12.8 Hz, 1H), 1.84 (dq, J = 12.4, 4.7 Hz, 1H), 3.34

(s, 3H), 3.91-3.98 (m, 2H), 4.26 (dd, $J = 11.2, 4.6$ Hz, 1H), 4.57 (dd, $J = 9.4, 6.9$ Hz, 1H), 4.59 (d, $J = 6.7$ Hz, 1H), 4.62 (d, $J = 6.7$ Hz, 1H), 5.52 (s, 1H), 5.58 (t, $J = 10.3$ Hz, 1H), 6.32 (d, $J = 7.3$ Hz, 1H), 6.63 (t, $J = 10.9$ Hz, 1H), 7.01 (dd, $J = 10.6, 7.4$ Hz, 1H), 7.30-7.34 (m, 3H), 7.46-7.48 (m, 2H). ^{13}C NMR (125 MHz, CDCl_3): δ [ppm] = 27.1, 55.4, 66.7, 73.5, 78.7, 94.0, 101.1, 111.9, 126.1, 127.5, 128.1, 128.7, 129.1, 130.1, 138.5. HRMS (EI): calc. for $\text{C}_{17}\text{H}_{21}\text{BrO}_4\text{Na}$ [$\text{M}+\text{Na}^+$]: 391.0521; found: 391.0530.

(Z,Z)-(3S,4S)-1-Benzoyloxy-8-bromo-4-methoxymethoxy-octa-5,7-dien-3-ol (29). 0.800 g of **38** (2.15 mmol) in 25 mL of CH_2Cl_2 was treated with 10.8 mL of DIBALH (1M in toluene, 10.8 mmol, 5.0 equiv) at 0 °C and stirred for 10 min. The mixture was quenched with EtOAc and EtOH and the mixture was filtered through a silica gel pad. The solvent was evaporated and the residue was purified by chromatography (Chromatotron, hexanes:EtOAc 4:1 to 2:1) to yield a clear oil (601 mg, 1.61 mmol, 75%). R_f (hexanes:ethyl acetate 2:1) = 0.21. $[\alpha]_D^{20} +31.7$ ($c = 1.51$, CHCl_3). IR (neat): $[\text{cm}^{-1}] = 3461, 3084, 3029, 2928, 2888, 1718, 1637, 1601, 1570, 1496, 1453, 1406, 1364, 1276, 1207, 1151, 1098, 1028, 919, 811, 737, 714$. ^1H NMR (500 MHz, CDCl_3): δ [ppm] = 1.68-1.72 (m, 1H), 1.79-1.82 (m, 1H), 2.91 (d, $J = 3.1$ Hz, 1H), 3.36 (s, 3H), 3.63-3.68 (m, 2H), 3.77-3.82 (m, 1H), 4.33 (dd, $J = 9.6, 6.8$ Hz, 1H), 4.57 (dd, $J = 9.4, 6.9$ Hz, 1H), 4.49 (s, 2H), 4.63 (d, $J = 6.7$ Hz, 1H), 5.53 (t, $J = 10.0$ Hz, 1H), 6.26 (dt, $J = 7.2, 1.3$ Hz, 1H), 6.60 (t, $J = 10.9$ Hz, 1H), 6.92 (dd, $J = 10.7, 7.2$ Hz, 1H), 7.26-7.32 (m, 5H). ^{13}C NMR (125 MHz, CDCl_3): δ [ppm] = 32.5, 55.6, 67.7, 71.9, 73.3, 75.0, 93.7, 111.9, 127.3, 127.7, 127.7, 128.4, 129.3, 130.9, 138.1. HRMS (EI): calc. for $\text{C}_{17}\text{H}_{23}\text{BrO}_4\text{Na}$ [$\text{M}+\text{Na}^+$]: 393.0677; found: 393.0689.

2,2-Dimethyl-5-trimethylsilanylethynyl-benzo[1,3]dioxin-4-one (39). 1.63 g of **10**^[3] (5.0 mmol), 1.41 mL of trimethylsilylacetylene (10.0 mmol, 2.0 equiv), 40 mg of CuI (0.2 mmol, 4 mol%), 231 mg of $\text{Pd}(\text{PPh}_3)_4$ (0.2 mmol, 4 mol%) and 1.75 mL of *i*-Pr₂NEt (10.0 mmol, 2.0 equiv) in 50 mL of CH_2Cl_2 were degassed and purged with N_2 and the mixture was stirred for 24 h. The reaction mixture was extracted with saturated aq. $\text{NH}_4\text{Cl}/\text{Et}_2\text{O}$ (3 x 50 mL), the organic phases were washed with brine, dried over MgSO_4 and evaporated. The residue was purified by chromatography (Chromatotron, hexanes:EtOAc 19:1) to yield a clear oil (1.35 g, 4.9 mmol, 98%), which solidified upon standing. R_f (hexanes:ethyl acetate 4:1) = 0.61. mp (hexanes/EtOAc) = 60-61 °C. IR (neat): $[\text{cm}^{-1}] = 2994, 2959, 2900, 2155, 1748, 1670, 1592, 1578, 1472, 1438, 1389, 1378, 1319, 1286, 1272, 1250, 1228, 1207, 1073, 1045, 967, 924, 846, 808, 775, 760, 732$. ^1H NMR (500 MHz, CDCl_3): δ [ppm] = 0.27 (s, 9H), 1.69 (s, 6H), 6.88 (d, $J = 8.2$ Hz, 1H), 7.25 (d, $J = 8.0$ Hz, 1H), 7.40 (t, $J = 8.0$ Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3): δ [ppm] = -0.3, 25.7, 102.3, 102.5, 105.6, 114.4, 117.5, 125.1, 129.2, 134.7, 156.5, 158.6. HRMS (CI): calcd. for $\text{C}_{15}\text{H}_{18}\text{O}_3\text{Si}$ [M^+]: 274.1025; found: 274.1034.

5-Ethynyl-2,2-dimethyl-benzo[1,3]dioxin-4-one (40). 206 mg of **39** (0.75 mmol) in 5 mL of THF is treated with 1.0 mL of TBAF (1M in THF, 1.0 mmol, 1.3 equiv) at 0 °C. The mixture is stirred for 15 min, then diluted with 50 mL of hexanes and filtered through a silica gel pad. The filtrate is evaporated to provide the product as an off-white solid (150 mg, 0.74 mmol, 99%), which decomposes slowly upon standing. R_f (hexanes:ethyl acetate 6:1) = 0.41. mp (hexanes/EtOAc) = 81-82 °C. IR (neat): $[\text{cm}^{-1}] = 3255, 2999, 2104, 1742, 1593, 1579, 1474, 1438, 1390, 1379, 1318, 1284, 1253, 1206, 1168, 1145, 1075, 1045, 1016, 964, 920, 848, 808, 773$. ^1H NMR (300 MHz, CDCl_3): δ [ppm] = 1.69 (s, 6H), 3.49 (s, 1H), 6.93 (dd, $J = 8.3, 1.0$ Hz, 1H), 7.28 (dd, $J = 7.7, 1.0$ Hz, 1H), 7.44 (t, $J = 7.8$ Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3): δ [ppm] = 25.6, 81.1, 84.1, 105.3, 114.5, 118.0, 124.0, 129.6, 135.0, 156.5, 158.7. HRMS (CI): calcd. for $\text{C}_{12}\text{H}_{10}\text{O}_3$ [M^+]: 202.0630; found: 202.0637.

Potassium (*E*)-2-(2,2-dimethyl-4-oxo-4*H*-benzo[1,3]dioxin-5-yl) vinyltrifluoroborate (41). 9.3 mL of 2,5-dimethylhexa-2,4-diene (65 mmol, 6 equiv) in 80 mL of THF was treated with 30 mL of BH₃·THF (1M in THF, 30 mmol, 2.5 equiv) at 0 °C. The mixture was stirred for 2 h, then 2.40 g of **40** (11.9 mmol) in 20 mL of THF was added and the mixture was stirred for 1 h. 4 mL of H₂O was added carefully and after 90 min 9 mL of CH₂O (37% in H₂O) was added. The mixture was stirred overnight, extracted with brine/EtOAc (3 x 150 mL) and the organic phases were evaporated. The residue was dissolved in 40 mL of acetone and 9.4 g of KHF₂ (120 mmol, 10 equiv) in 15 mL of H₂O was added. The mixture was stirred overnight, evaporated and the residue was extracted with hot acetone (3 x 30 mL) and MeCN (50 mL). The organic phases were evaporated and the residue was dissolved in acetone. After addition of Et₂O, a precipitate formed which was filtered off and dried. The product was obtained in two charges as a white or off-white solid (2.47 g, 8.0 mmol, 66%). mp (acetone/Et₂O) = 207-209 °C (dec.). ¹H NMR (500 MHz, acetone-*d*₆): δ [ppm] = 1.71 (s, 6H), 6.37 (dq, *J*_{H-H} = 18.2 Hz, *J*_{H-F} = 3.8 Hz, 1H), 6.86 (d, *J* = 7.7 Hz, 1H), 7.36 (d, *J* = 7.8 Hz, 1H), 7.52 (t, *J* = 8.0 Hz, 1H), 7.61 (d, *J* = 18.2 Hz, 1H). ¹³C NMR (125 MHz, acetone-*d*₆): δ [ppm] = 25.2, 105.2, 110.9, 114.9, 121.6, 132.7 (q, *J*_{C-B} = 4.4 Hz), 135.5, 142.3, 146.4, 156.9, 160.4. ¹¹B NMR (300 MHz, acetone-*d*₆): δ [ppm] = 3.6 (brs). ¹⁹F NMR (470 MHz, acetone-*d*₆): δ [ppm] = -142.0 (s).

(1*E*,3*Z*,5*Z*)-(7*S*,8*S*)-5-(10-Benzyloxy-8-hydroxy-7-methoxymethoxy-deca-1,3,5-trienyl)-2,2-dimethyl-benzo[1,3]dioxin-4-one (42). 112 mg of **29** (0.30 mmol), 124 mg of **41** (0.4 mmol, 1.3 equiv), 390 mg of Cs₂CO₃ (1.2 mmol, 4 equiv) and 35 mg of Pd(PPh₃)₄ (0.03 mmol, 10 mol%) in 11 mL of THF/H₂O (10:1) was degassed and purged with N₂ (three times). The mixture was heated to reflux for 4 h, then cooled and extracted with saturated aq. NH₄Cl/EtOAc (3 x 50 mL). The organic phases were dried over MgSO₄ and evaporated. The residue was purified by chromatography (Chromatotron, hexanes:EtOAc 4:1 to 2:1) to yield a clear oil (138 mg, 0.28 mmol, 93%). *R*_f(hexanes:ethyl acetate 2:1) = 0.15. [α]_D²⁰₅₈₉ +6.9 (c=0.51, CHCl₃). IR (neat): [cm⁻¹] = 2923, 2889, 1730, 1674, 1578, 1555, 1473, 1456, 1390, 1379, 1319, 1270, 1210, 1147, 1098, 1080, 1042, 966, 922, 770, 732. ¹H NMR (500 MHz, CDCl₃): δ [ppm] = 1.69 (s, 6H), 1.72-1.75 (m, 1H), 1.80-1.84 (m, 1H), 2.92 (d, *J* = 1.9 Hz, 1H), 3.37 (s, 3H), 3.61-3.69 (m, 2H), 3.78-3.82 (m, 1H), 4.45 (dd, *J* = 9.7, 6.9 Hz, 1H), 4.50 (s, 2H), 4.56 (d, *J* = 6.6 Hz, 1H), 4.67 (d, *J* = 6.6 Hz, 1H), 5.42 (t, *J* = 10.4 Hz, 1H), 6.34 (t, *J* = 11.0 Hz, 1H), 6.38 (t, *J* = 11.0 Hz, 1H), 6.82-6.85 (m, 2H), 7.22 (dd, *J* = 15.4, 10.9 Hz, 1H), 7.23-7.26 (m, 1H), 7.30-7.34 (m, 5H), 7.43 (t, *J* = 8.0 Hz, 1H), 7.74 (d, *J* = 15.4 Hz, 1H). ¹³C NMR (125 MHz, CDCl₃): δ [ppm] = 26.0, 32.7, 55.6, 67.7, 72.0, 73.2, 74.6, 93.9, 105.2, 110.8, 116.4, 121.0, 125.3, 127.5, 127.6, 127.7, 128.4, 128.7, 132.2, 132.3, 135.1, 138.3, 141.5, 157.0, 160.3. HRMS (EI): calc. for C₂₉H₃₄O₇Na [M+Na⁺]: 517.2202; found: 517.2182.

(9*Z*,12*E*)-(7*S*,8*S*)-7-(2-Benzyloxyethyl)-4-hydroxy-8-methoxymethoxy-11-methylene-8,11-dihydro-7*H*-6-oxa-benzocyclodecen-5-one (44). 46.7 mg of **29** (0.126 mmol) was azeotroped with benzene. 46.8 mg of **41** (0.15 mmol, 1.2 equiv) was added and the mixture was azeotroped with benzene once more. The mixture was then dissolved in 2 mL of DMF and cooled to 0 °C. 150 μL of NaHMDS (1M in THF, 0.15 mmol, 1.2 equiv) was added and the mixture was stirred for 1 h. 3 mL of H₂O was added carefully and the mixture was diluted with THF (30 mL). 17 mg of Pd(PPh₃)₄ (0.015 mmol, 10 mol%) and 195 mg of Cs₂CO₃ (0.6 mmol, 4 equiv) were added and the mixture was degassed and purged with N₂. It was then heated to reflux for 2 d and extracted with saturated aqueous NH₄Cl and Et₂O (3 x 50 mL). The organic phases were dried over MgSO₄ and purified via Chromatotron (hexanes:ethyl acetate 9:1 to 4:1) to give the product as a pale oil (4.3 mg, 0.01 mmol, 7%). *R*_f (hexanes:ethyl acetate 4:1) = 0.36. ¹H NMR (500 MHz, CDCl₃): δ [ppm] = 1.97-2.03 (m, 1H), 2.31-2.37 (m, 1H), 3.29 (s, 3H), 3.60-3.65 (m, 2H), 4.36 (dd, *J* = 9.9, 3.4 Hz, 1H), 4.48 (d, *J* = 6.6 Hz, 1H), 4.52 (s, 2H), 4.54 (d, *J* = 6.6 Hz, 1H), 4.99 (s,

1H), 5.16 (s, 1H), 5.32 (d, $J = 10.0$ Hz, 1H), 5.71 (t, $J = 10.6$ Hz, 1H), 6.13 (d, $J = 16.0$ Hz, 1H), 6.60 (d, $J = 11.4$ Hz, 1H), 6.68 (d, $J = 7.3$ Hz, 1H), 6.90 (d, $J = 8.3$ Hz, 1H), 7.14 (d, $J = 16.0$ Hz, 1H), 7.23-7.25 (m, 2H), 7.29-7.36 (m, 4H) 10.54 (s, 1H). ^{13}C NMR (125 MHz, CDCl_3): δ [ppm] = 29.7, 55.6, 67.1, 72.5, 73.2, 75.4, 94.1, 115.4, 116.6, 118.7, 127.5, 127.8, 128.3, 129.4, 131.5, 134.2, 134.7, 137.8, 138.4, 142.5, 142.8, 161.9, 170.5. HRMS (EI): calc. for $\text{C}_{26}\text{H}_{28}\text{O}_6\text{Na}$ [$\text{M}+\text{Na}^+$]: 459.1784; found: 459.1763.

2,2-Dimethyl-5-triisopropylsilanylethynyl-benzo[1,3]dioxin-4-one (30). 0.98 g of **10**^[4] (3.0 mmol), 1.04 mL of triisopropylsilylacetylene (4.5 mmol, 1.5 equiv), 29 mg of CuI (0.15 mmol, 5 mol%), 173 mg of $\text{Pd}(\text{PPh}_3)_4$ (0.15 mmol, 5 mol%) and 0.79 mL of *i*-Pr₂NEt (4.5 mmol, 1.5 equiv) in 200 mL of THF were degassed and purged with N₂ and the mixture was stirred for 20 h. The reaction mixture was extracted with saturated aq. $\text{NH}_4\text{Cl}/\text{Et}_2\text{O}$ (3 x 50 mL). The organic phases were washed with brine, dried over MgSO_4 and evaporated. The residue was purified by chromatography (Chromatotron, hexanes 100% to hexanes:EtOAc 19:1) to yield a clear oil (1.04 g, 2.9 mmol, 97%), which solidified upon standing. R_f (hexanes:ethyl acetate 6:1) = 0.64. mp (hexanes/EtOAc) = 46-48 °C. IR (neat): $[\text{cm}^{-1}] = 2942, 2891, 2864, 2158, 1752, 1592, 1579, 1472, 1389, 1378, 1318, 1287, 1271, 1251, 1224, 1208, 1073, 1044, 923, 883, 808, 705$. ^1H NMR (500 MHz, CDCl_3): δ [ppm] = 1.14 (s, 21H), 1.68 (s, 6H), 6.88 (d, $J = 8.2$ Hz, 1H), 7.26 (d, $J = 7.7$ Hz, 1H), 7.40 (t, $J = 8.0$ Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3): δ [ppm] = 11.4, 18.6, 25.8, 99.6, 103.9, 105.5, 114.3, 117.2, 125.5, 129.6, 134.6, 156.5, 158.4.

(Z,Z)-(3S,4S)-2-Hydroxy-6-[(triisopropylsilanyl)-ethynyl] benzoic acid 3-(1-benzyloxy-8-bromo-4-methoxymethoxy-octa-5,7-dienyl) ester (47). 262 mg of **29** (0.7 mmol) and 301 mg of **30** (0.84 mmol, 1.2 equiv) were azeotroped with benzene at 30 °C, then dissolved in 6 mL of THF at -20 °C and treated with 1.05 mL of NaHMDS (1M in THF, 1.05 mmol, 1.5 equiv). The mixture was stirred for 5 h while it was warming slowly to 0 °C. Saturated aqueous NH_4Cl (10 mL) was added and the mixture was extracted with EtOAc (3 x 50 mL). The organic phases were dried over MgSO_4 and evaporated to leave a yellow oil, which was used directly without further purification. An analytical sample was purified by chromatography (Chromatotron, hexanes:EtOAc 15:1). R_f (hexanes:ethyl acetate 6:1) = 0.42. $[\alpha]_{589}^{20} +11.5$ ($c=1.33$, CHCl_3). IR (neat): $[\text{cm}^{-1}] = 3367, 3030, 2942, 2890, 2863, 2143, 1739, 1666, 1594, 1572, 1496, 1447, 1369, 1296, 1250, 1208, 1167, 1153, 1132, 1099, 1066, 1016, 919, 883, 814, 735$. ^1H NMR (500 MHz, CDCl_3): δ [ppm] = 1.13 (s, 21H), 1.96-2.00 (m, 2H), 3.20 (s, 3H), 3.50-3.56 (m, 2H), 4.39 (d, $J = 11.8$ Hz, 1H), 4.46 (d, $J = 11.8$ Hz, 1H), 4.48 (d, $J = 6.9$ Hz, 1H), 4.56 (d, $J = 6.9$ Hz, 1H), 4.66 (t, $J = 8.7$ Hz, 1H), 5.52 (t, $J = 10.2$ Hz, 1H), 5.61-5.64 (m, 1H), 6.27 (d, $J = 7.2$ Hz, 1H), 6.63 (t, $J = 10.8$ Hz, 1H), 6.91 (dd, $J = 11.4, 8.5$ Hz, 1H), 6.93 (d, $J = 8.7$ Hz, 1H), 7.13 (d, $J = 7.4$ Hz, 1H), 7.22-7.32 (m, 6H), 11.31 (s, 1H). ^{13}C NMR (125 MHz, CDCl_3): δ [ppm] = 11.6, 18.8, 30.6, 55.4, 66.1, 72.5, 73.3, 73.7, 93.4, 97.1, 107.0, 112.3, 112.3, 118.4, 124.7, 127.2, 127.6, 127.8, 128.3, 128.3, 129.6, 130.2, 133.7, 138.0, 162.2, 169.2. HRMS (EI): calcd. for $\text{C}_{35}\text{H}_{47}\text{BrO}_6\text{SiNa}$ [$\text{M}+\text{Na}^+$]: 693.2223; found: 693.2240.

(Z,Z)-(3S,4S)-2-Ethynyl-6-hydroxy benzoic acid 3-(1-benzyloxy-8-bromo-4-methoxymethoxy-octa-5,7-dienyl) ester (48). Crude **47** (~0.7 mmol) was dissolved in 10 mL of THF and treated with 2.0 mL of TBAF (1M in THF, 2.0 mmol, 2.8 equiv) at 0 °C. The mixture was stirred for 1.5 h, then extracted with saturated aq. $\text{NH}_4\text{Cl}/\text{EtOAc}$ (3 x 50 mL). The organic phases were dried over MgSO_4 and evaporated. The residue was purified by chromatography (Chromatotron, hexanes:EtOAc 9:1) to yield a clear oil (355 mg, 0.69 mmol, 98% over two steps). R_f (hexanes:ethyl acetate 6:1) = 0.33. $[\alpha]_{589}^{20} -5.3$ ($c=0.83$, CHCl_3). IR (neat): $[\text{cm}^{-1}] = 3284, 2890, 1741, 1665, 1597, 1571, 1448, 1293, 1245, 1209,$

^[4] Fürstner, A.; Konetzki, I. *Tetrahedron* **1996**, 52, 15071.

1097, 1028, 919, 814. ¹H NMR (500 MHz, CDCl₃): δ [ppm] = 1.97-2.09 (m, 2H), 3.23 (s, 1H), 3.25 (s, 3H), 3.55-3.61 (m, 2H), 4.44 (d, *J* = 11.8 Hz, 1H), 4.46 (d, *J* = 11.8 Hz, 1H), 4.53 (d, *J* = 6.8 Hz, 1H), 4.59 (d, *J* = 6.8 Hz, 1H), 4.70 (t, *J* = 8.2 Hz, 1H), 5.53-5.62 (m, 2H), 6.25 (d, *J* = 7.1 Hz, 1H), 6.62 (t, *J* = 10.9 Hz, 1H), 6.91 (dd, *J* = 10.4, 7.4 Hz, 1H), 6.98 (d, *J* = 8.2 Hz, 1H), 7.10 (d, *J* = 7.4 Hz, 1H), 7.22-7.31 (m, 5H), 7.33 (t, *J* = 7.9 Hz, 1H), 11.23 (s, 1H). ¹³C NMR (125 MHz, CDCl₃): δ [ppm] = 30.4, 55.6, 66.1, 72.4, 73.2, 74.4, 82.4, 83.0, 93.8, 112.4, 113.1, 118.9, 123.3, 127.1, 127.2, 127.6, 127.8, 128.3, 129.7, 129.7, 134.0, 138.1, 162.2, 169.2. HRMS (EI): calc. for C₂₆H₂₇BrO₆Na [M+Na⁺]: 537.0889; found: 573.0896.

(Z,Z)-(3S,4S)-2-(*tert*-Butyl-dimethyl-silanyloxy)-6-ethynyl benzoic acid 3-(1-benzyloxy-8-bromo-4-methoxymethoxy-octa-5,7-dienyl) ester (28). 355 mg of **48** (0.69 mmol) was dissolved in 4 mL of DMF at 0 °C. 102 mg of imidazole (1.5 mmol, 2 equiv) and 18 mg of DMAP (0.15 mmol, 0.2 equiv) were added followed by 345 μL of TBDMSOTf (1.5 mmol, 2 equiv) and the mixture was stirred overnight while warming to rt. The crude reaction mixture was subjected to chromatography (2 x Chromatotron, first with hexanes 100% to hexanes:EtOAc 9:1 and then with hexanes:EtOAc 19:1) to yield a clear oil (341 mg, 0.54 mmol, 79%). *R_f* (hexanes:ethyl acetate 2:1) = 0.69. [α]_D²⁰₅₈₉ +13.8 (c = 0.66, CHCl₃). IR (neat): [cm⁻¹] = 3286, 3030, 2953, 2929, 2887, 2858, 1735, 1572, 1460, 1407, 1362, 1290, 1257, 1151, 1111, 1062, 1028, 919, 834, 784, 736. ¹H NMR (500 MHz, CDCl₃): δ [ppm] = 0.21 (s, 3H), 0.22 (s, 3H), 0.97 (s, 9H), 2.07-2.09 (m, 1H), 2.15-2.18 (m, 1H), 3.28 (s, 3H), 3.35 (s, 1H), 3.65-3.71 (m, 2H), 4.47 (d, *J* = 11.9 Hz, 1H), 4.52 (d, *J* = 6.8 Hz, 1H), 4.53 (d, *J* = 11.9 Hz, 1H), 4.56 (d, *J* = 6.9 Hz, 1H), 4.68 (dd, *J* = 9.1, 4.6 Hz, 1H), 5.31-5.33 (m, 1H), 5.67 (t, *J* = 10.1 Hz, 1H), 6.16 (d, *J* = 7.1 Hz, 1H), 6.55 (t, *J* = 11.0 Hz, 1H), 6.84 (d, *J* = 8.2 Hz, 1H), 6.91 (dd, *J* = 10.4, 7.4 Hz, 1H), 7.08 (d, *J* = 7.5 Hz, 1H), 7.17 (t, *J* = 8.0 Hz, 1H), 7.26-7.33 (m, 5H). ¹³C NMR (125 MHz, CDCl₃): δ [ppm] = -4.3, -4.1, 18.4, 25.8, 30.7, 55.6, 66.9, 71.6, 73.1, 74.3, 80.8, 81.0, 93.7, 111.6, 120.3, 120.8, 125.5, 125.7, 127.5, 127.6, 127.8, 128.4, 128.9, 130.0, 130.5, 138.4, 152.5, 166.2. HRMS (EI): calcd. for C₃₂H₄₁BrO₆SiNa [M+ Na⁺]: 651.1753; found: 651.1735.

Potassium (2E,5Z,7Z)-(3S,4S)-2-{2-[3-(1-Benzyloxy-8-bromo-4-methoxymethoxy-octa-5,7-dienyl)]-3-hydroxy-phenyl}-vinyltrifluoroborate (27). 3.15 mL of 2,5-dimethylhexa-2,4-diene (22 mmol) in 17 mL of THF was treated with 5 mL of BH₃·SMe₂ (2M in toluene, 10 mmol) at 0 °C. The mixture was stirred for 3 h to give a clear, ~0.4M solution of *i*-PP₂BH. 215 mg of **28** (0.34 mmol) in 3 mL of THF was stirred at rt and 1.3 mL of *i*-PP₂BH (0.4M in THF, 0.52 mmol, 0.6 equiv) was added. The reaction was monitored by TLC and after disappearance of the starting material (0.5 h), 0.5 mL of H₂O was added carefully at 0 °C. After an additional 1.5 h, 2.5 mL of CH₂O (37% in H₂O) was added. The mixture was stirred overnight, extracted with brine/EtOAc (3 x 50 mL) and the organic phases were evaporated. The residue was dissolved in 15 mL of acetone/MeCN (2:1) and 0.53 g of KHF₂ (6.8 mmol, 20 equiv) in 5 mL of H₂O was added. The mixture was stirred for 4 h at rt, evaporated and the residue was extracted with hot acetone (3 x 20 mL) and MeCN (20 mL). The organic phases were evaporated and the residue was dried in vacuo at 50 °C overnight to yield the slightly impure product as a pale wax (249 mg, >99%). ¹H NMR (500 MHz, acetone-*d*₆): δ [ppm] = 2.00-2.09 (m, 2H), 3.24 (s, 3H), 3.64-3.70 (m, 2H), 4.50 (s, *J* = 2H), 4.61 (m, 2H), 4.82 (dd, *J* = 9.4, 6.8 Hz, 1H), 5.48-5.53 (m, 1H), 5.75 (t, *J* = 10.4 Hz, 1H), 6.16 (dq, *J*_{H-H} = 17.9 Hz, *J*_{H-F} = 3.6 Hz, 1H), 6.46 (d, *J* = 7.0 Hz, 1H), 6.58 (t, *J* = 10.9 Hz, 1H), 6.73 (d, *J* = 8.0 Hz, 1H), 7.04 (d, *J* = 7.6 Hz, 1H), 7.11 (d, *J* = 8.0 Hz, 1H), 7.17 (t, *J* = 17.9 Hz, 1H), 7.21 (dd, *J* = 10.8, 7.5 Hz, 1H), 7.22-7.26 (m, 2H), 7.27-7.31 (m, 2H), 7.33-7.36 (m, 2H), 10.5 (brs, 1H). ¹³C NMR (125 MHz, acetone-*d*₆): δ [ppm] = 31.3, 55.7, 67.2, 73.4, 73.9, 74.4, 95.0, 112.3, 114.7, 116.1, 118.7, 128.0, 128.5, 128.8, 129.0, 129.4, 132.2, 132.9, 134.1, 139.9, 144.6, 159.2, 170.4. ¹⁹F NMR (470 MHz, acetone-*d*₆): δ [ppm] = -142.0 (s).

(9Z,11Z,13E)-(7S,8S)-7-(2-Benzyloxy-ethyl)-4-(hydroxy)-8-methoxymethoxy-7,8-dihydro-6-oxa-benzocyclododecen-5-one (49). 114 mg of **27** (0.156 mmol) was dissolved in 170 mL

of THF/H₂O (10:1), 390 mg of Cs₂CO₃ (0.65 mmol, 5 equiv) and 20 mg of Pd(PPh₃)₄ (0.017 mmol, 10 mol%) were added, the mixture was degassed and purged with N₂ and then heated to reflux for 20 h. After cooling to rt, the mixture was extracted with saturated NH₄Cl/EtOAc (3 x 100 mL), the organic phases were dried over MgSO₄ and purified by chromatography (Chromatotron, hexanes:EtOAc 4:1) to yield a clear oil (28.5 mg, 0.065 mmol, 42% over 2 steps). *R_f* (hexanes:ethyl acetate 2:1) = 0.37. [α]_D²⁰₅₈₉ -137.7 (c=0.57, CHCl₃). IR (neat): [cm⁻¹] = 3315, 3011, 2925, 1730, 1662, 1604, 1575, 1495, 1463, 1423, 1363, 1326, 1294, 1247, 1216, 1155, 1098, 1056, 1029, 1000, 955, 918, 852, 804, 764, 738. ¹H NMR (500 MHz, CDCl₃): δ [ppm] = 2.11-2.18 (m, 2H), 3.22 (s, 3H), 3.35 (s, 1H), 3.63-3.68 (m, 2H), 4.48 (d, *J* = 6.6 Hz, 1H), 4.55 (s, 2H), 4.55 (d, *J* = 6.6 Hz, 1H), 4.65 (dd, *J* = 10.3, 3.7 Hz, 1H), 5.45-5.48 (m, 1H), 5.64 (t, *J* = 10.2 Hz, 1H), 5.87 (dd, *J* = 10.1, 3.7 Hz, 1H), 6.19 (dd, *J* = 11.8, 3.2 Hz, 1H), 6.31 (t, *J* = 10.8 Hz, 1H), 6.71-6.76 (m, 3H), 6.78 (d, *J* = 8.2 Hz, 1H), 7.19 (t, *J* = 8.0 Hz, 1H), 7.26-7.31 (m, 1H), 7.32-7.35 (m, 4H). ¹³C NMR (125 MHz, DMSO-*d*₆): δ [ppm] = 27.6, 54.7, 65.7, 67.9, 72.1, 73.3, 92.4, 114.2, 118.6, 121.8, 126.8, 127.3, 127.5, 127.8, 128.2, 129.5, 130.0, 130.2, 131.8, 132.2, 137.4, 138.5, 153.9, 168.0. (Note: In other solvents (CDCl₃, C₆D₆ or acetone-*d*₆), many signals broaden at rt.) HRMS (EI): calc. for C₂₆H₂₈O₆Na [M+Na⁺]: 459.1784; found: 459.1776.

(9Z,11Z,13E)-(7S,8S)-7-(2-Benzyloxy-ethyl)-4-(*tert*-butyl-dimethyl-silanyloxy)-8-methoxymethoxy-7,8-dihydro-6-oxa-benzocyclododecen-5-one (50). 8.1 mg of **49** (0.019 mmol) in 0.7 mL of DMF were treated at rt with 30 mg of TBDMSCl (0.19 mmol, 10 equiv) and 13 mg of imidazole (0.19 mmol, 10 equiv). The mixture was stirred for 16 h. The mixture was then extracted with saturated NH₄Cl solution and Et₂O (4 x 20 mL), the organic phases were dried over MgSO₄ and evaporated. Purification via chromatography (silica gel, hexanes:EtOAc 19:1) gave the product as a clear oil (9.0 mg, 0.016 mmol, 86%). *R_f*(hexanes:ethyl acetate 4:1) = 0.56. [α]_D²⁰₅₈₉ -105.3 (c=0.66, CHCl₃). IR (neat): [cm⁻¹] = 2928, 2858, 1730, 1670, 1637, 1571, 1555, 1462, 1364, 1292, 1254, 1152, 1102, 1062, 1031, 1000, 955, 918, 840, 807, 775, 732. ¹H NMR (500 MHz, CDCl₃): δ [ppm] = 0.18 (s, 3H), 0.19 (s, 3H), 0.96 (s, 9H), 2.05-2.11 (m, 1H), 2.16-2.23 (m, 1H), 3.33 (s, 3H), 3.65-3.82 (m, 2H), 3.84-3.88 (m, 1H), 4.49-4.55 (m, 4H), 4.60 (dd, *J* = 10.7, 2.6 Hz, 1H), 5.39-5.42 (m, 1H), 5.65 (t, *J* = 11.2 Hz, 1H), 5.86 (dd, *J* = 11.0, 3.9 Hz, 1H), 6.18 (dd, *J* = 11.9, 3.9 Hz, 1H), 6.33 (t, *J* = 11.1 Hz, 1H), 6.62 (d, *J* = 16.0 Hz, 1H), 6.73 (d, *J* = 8.1 Hz, 1H), 6.77 (d, *J* = 7.6 Hz, 1H), 6.99 (dd, *J* = 16.0, 11.4 Hz, 1H), 7.15 (t, *J* = 8.0 Hz, 1H), 7.25-7.28 (m, 1H), 7.30-7.35 (m, 4H). ¹³C NMR (125 MHz, CDCl₃): δ [ppm] = -4.2, -4.1, 18.4, 26.0, 29.2, 55.4, 67.8, 68.8, 77.8, 75.3, 93.2, 118.0, 121.3, 126.4, 126.9, 127.2, 127.5, 127.5, 128.3, 129.3, 130.0, 131.0, 132.1, 132.2, 137.9, 138.5, 152.3, 168.2. HRMS (EI): calc. for C₃₂H₄₂O₆SiNa [M+Na⁺]: 573.2648; found: 573.2632.

(9Z,11Z,13E)-(7S,8S)- 4-(*tert*-Butyl-dimethyl-silanyloxy)-7-(2-hydroxy-ethyl)-8-methoxymethoxy-7,8-dihydro-6-oxa-benzocyclododecen-5-one (6). 18.6 mg of **50** (0.033 mmol) was dissolved in 2 mL of CH₂Cl₂/buffer-solution pH = 7 and 150 mg of DDQ (0.66 mmol, 20 equiv) were added. The mixture was stirred at rt overnight, then heated to reflux for 6 h and stirred at rt again overnight. The mixture was then extracted with saturated aqueous NaHCO₃ and CH₂Cl₂ (4 x 25 mL). The organic phases were dried over MgSO₄ and evaporated. Chromatographic purification (silica gel hexanes:EtOAc 6:1 to 3:1) yielded a clear oil (11.6 mg, 0.025 mmol, 77%). *R_f*(hexanes:ethyl acetate 4:1) = 0.16. [α]_D²⁰₅₈₉ -153.2 (c=0.65, CHCl₃). IR (neat): [cm⁻¹] = 3434, 2931, 2858, 1828, 1769, 1730, 1633, 1572, 1463, 1454, 1257, 1152, 1101, 1047, 949, 913, 839, 807, 786, 740. ¹H NMR (500 MHz, CDCl₃): δ [ppm] = 0.20 (s, 3H), 0.21 (s, 3H), 0.97 (s, 9H), 2.04-2.08 (m, 1H), 2.20 (bt, *J* = 5.8 Hz, 1H), 2.22-2.26 (m, 1H), 3.36 (s, 3H), 3.80-3.83 (m, 1H), 3.84-3.88 (m, 1H), 4.53 (d, *J* = 6.5 Hz, 1H), 4.57 (d, *J* = 6.5 Hz, 1H), 4.65 (dd, *J* = 10.7, 2.9 Hz, 1H), 5.44-5.48 (m, 1H), 5.72 (t, *J* = 11.3 Hz, 1H), 5.86 (dd, *J* = 11.1, 4.1 Hz, 1H), 6.20 (dd, *J* = 11.9, 4.1 Hz, 1H), 6.34 (t, *J* = 11.4 Hz, 1H), 6.64 (d, *J* = 16.0 Hz, 1H), 6.73 (d, *J* = 8.1 Hz, 1H), 6.78 (d, *J* = 7.7 Hz, 1H), 6.98

(dd, $J = 16.0, 11.4$ Hz, 1H), 7.15 (t, $J = 8.0$ Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3): δ [ppm] = -4.2, 18.4, 25.8, 32.0, 55.6, 60.2, 68.7, 76.4, 93.3, 117.9, 121.3, 126.3, 126.6, 127.2, 129.4, 130.0, 131.0, 132.4, 132.7, 138.1, 152.3, 168.2. HRMS (EI): calc. for $\text{C}_{25}\text{H}_{36}\text{O}_6\text{NaSi}$ [$\text{M}+\text{Na}^+$]: 483.2179; found: 483.2184.

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Integration curve

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