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Supporting Information

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Total Synthesis of (−)-Amphidinolide E

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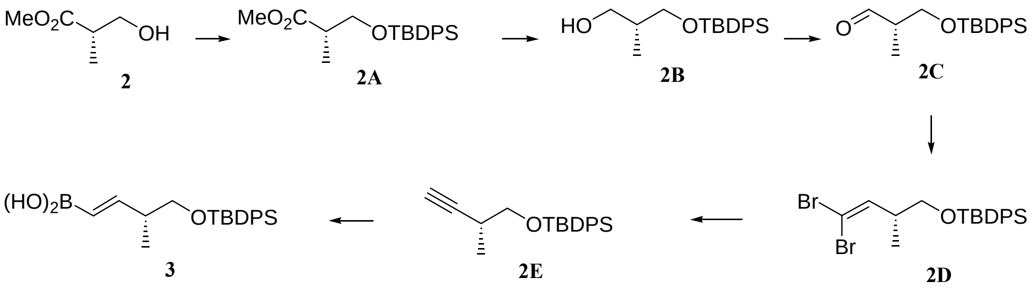
General Information

^{1}H- and ^{13}C-NMR spectra were obtained on Bruker DPX-300 (300 MHz), Bruker Avance-600 (600 MHz) and Varian / Oxford As-500 (500 MHz). Chemical shift values were recorded as parts per million relative to tetramethylsilane as an internal standard unless otherwise indicated, and coupling constants in Hertz. Mass spectra were recorded on a JEOL JMS 600W spectrometer using electron impact (EI) or chemical ionization (CI), and JEOL JMS AX505WA spectrometer using fast atom bombardment (FAB) method. Significant fragments are reported in the following fashion: *m*/*z* (relative intensity). MALDI-TOF spectrometric measurements were performed on Bruker Autoflex II LIFT-TOF/TOF mass spectrometer (dithranol matrix). Optical rotation data were obtained on a JASCO P-1030 automatic polarimeter.

The progress of reaction was checked on TLC plates (Merck 5554 Kiesel gel 60 F254), and the spots were visualized under 254 nm UV light and/or charring after dipping the TLC plate into vanillin solution (9.0 g of vanillin and 1.5 mL of concentrated sulfuric acid in 300 mL of methanol), $KMnO_4$ solution (3 g of $KMnO_4$, 20 g of K_2CO_3, and 5 mL of 5% NaOH solution in 300 mL of water), or phosphomolybdic acid solution (250 mg phosphomolybdic acid in 50 mL ethanol). Column chromatography was performed on silica gel (Merck 9385 Kiesel gel 60) using hexane-EtOAc (v/v). The solvents were simple distilled unless otherwise noted.

Unless otherwise specified, all reactions were conducted under a slight positive pressure of dry nitrogen. The usual work-up refers to washing the quenched reaction mixture with brine, drying the organic extracts over anhydrous $MgSO_4$ and evaporating under reduced pressure using a rotary evaporator.

All solvents used in reactions were dried under nitrogen atmosphere. THF was distilled from Na-benzophenone and CH_2Cl_2 was distilled from P_2O_5. Benzene was washed with conc. H_2SO_4, distilled from Na-benzophenone, and stored over 4 Å molecular sieves. Et_2O was distilled from LAH. CH_3CN was distilled from CaH_2 and stored over 4 Å molecular sieves. Pyridine and TEA was distilled over KOH and stored over 4 Å molecular sieves.



Boronic acid **3**

Imidazole (2.76 g, 40.6 mmol) and TBDPSCl (8.4 mL, 33 mmol) were added to a solution of methyl (*S*)-(+)-3-hydroxy-2-methylpropanoate (3 mL, 27 mmol) in CH_2Cl_2 (45 mL) at 0 °C. This mixture was stirred at r.t. for 1 h and the reaction was quenched by sat. NH_4Cl solution (20 mL). The reaction mixture was extracted with CH_2Cl_2 (20 mL), and the organic phase was washed with brine (20 mL), dried over $MgSO_4$, filtered, and concentrated. Purification of the residue by flash column chromatography (Hex-EtOAc, 15:1) provided ester **2A** (9.65 g, 100%). R_f 0.55 (Hex-EtOAc, 8:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 - 7.75 (m, 4 H), 7.41 - 7.50 (m, 6 H), 3.89, 3.80 (ABX, J_{AB}=9.8, J_{AX}=6.9, J_{BX}=5.9 Hz, 2 H), 3.73 (s, 3 H), 2.74 - 2.82 (m, 1 H), 1.22 (d, J=7.1 Hz, 3 H), 1.10 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 175.6, 135.8, 133.8, 133.7, 129.9, 127.9, 66.2, 51.8, 51.8, 42.6, 27.0, 19.5, 13.7. IR (neat): ν_{max} = 2943, 1739, 1589, 1466, 1389, 1254, 1199, 1107, 1026, 818, 702, 613, 505 cm^{-1}. MS *m/z* (CI, relative intensity): 355 (M^+-1, 1), 341 (2), 325 (6), 299 (28), 279 (100), 213 (2). HRMS (CI) calcd. for $C_{21}H_{27}O_3Si$ (M^+-1) 355.1729, found 355.1729. $[\alpha]^{27}_D$ +15.7 (*c* 1.00, $CHCl_3$).

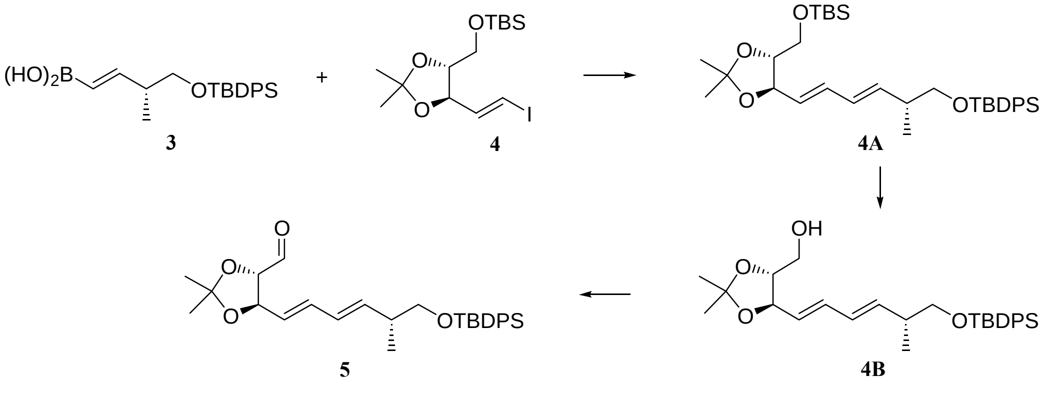
$LiBH_4$ (2.0 M in THF, 27 mL, 54mmol) was added to a solution of ester **2A** (9.65 g, 27.1 mmol) in Et_2O (270 mL) at 0 °C and the reaction mixture was allowed to warm to r.t. After 24 h, the reaction mixture was quenched by addition of sat. NH_4Cl solution (100 mL). The reaction mixture was extracted with Et_2O (100 mL × 2) and the organic phase was dried over $MgSO_4$, filtered, and concentrated. Purification of the residue by flash column chromatography (Hex-EtOAc, 4:1) gave alcohol **2B** (8.59 g, 97%). R_f 0.42 (Hex-EtOAc, 4:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 - 7.71 (m, 4 H), 7.35 - 7.44 (m, 6 H), 3.71, 3.60 (ABX, J_{AB}=10.0, J_{AX}=4. 7, J_{BX}= 7.6 Hz, 2 H), 3.63 -

3.68 (m, 2 H), 2.71 (dd, *J*=6.1, 4.9 Hz, 1 H), 1.94 - 2.02 (m, 1 H), 1.06 (s, 9 H), 0.83 (d, *J*=6.8 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 135.9, 135.9, 133.5, 133.5, 130.1, 128.1, 68.8, 67.7, 37.7, 27.2, 19.5, 13.5. IR (neat): ν_{max} = 3375, 3138, 3070, 3049, 2958, 1589, 1471, 1427, 1390, 1188, 1113, 939, 741 cm^{-1}. MS *m/z* (CI, relative intensity): 329 (M^++1, 100), 311 (9), 291 (3), 271 (18), 251 (49), 239 (5), 209 (7), 199 (16), 179 (11). HRMS (CI) calcd. for $C_{20}H_{29}O_2Si$ (M^++1) 329.1937, found 329.1938. $[\alpha]^{25}_{D}$ +3.9 (*c* 1.00, $CHCl_3$).

TEA (4.77 mL, 34.2 mmol) was added to a solution of alcohol **2B** (2.25 g, 6.84 mmol) in DMSO (14 mL) and CH_2Cl_2 (14 mL) at 0 °C. After the addition of SO_3·pyr complex (3.28 g, 20.5 mmol) the mixture was warmed to r.t. and stirred for 1 h. The reaction was quenched by sat. NH_4Cl solution (30 mL) and extracted with Et_2O (50 mL × 2). The organic phase was dried over $MgSO_4$, filtered, and concentrated. Flash column chromatography provided aldehyde **2C** (1.99 g, 90%). R_f 0.51 (Hex-EtOAc, 8:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.76 (d, *J*=1.7 Hz, 1 H), 7.65 (d, *J*=6.6 Hz, 4 H), 7.36 - 7.46 (m, 6 H), 3.90, 3.85 (ABX, J_{AB}=10.3, J_{AX}=4.9, J_{BX}=6.4 Hz, 2 H), 2.52 - 2.60 (m, 1 H), 1.10 (d, *J*=7.1 Hz, 3 H), 1.04 (s, 9 H), ^{13}C NMR (125 MHz, $CDCl_3$): δ 204.7, 135.8, 133.4, 130.1, 130.1, 128.0, 128.0, 64.4, 49.1, 27.0, 19.5, 10.6. IR (neat): ν_{max} = 3136, 3072, 2931, 2858, 2717, 1738, 1589, 1471, 1390, 1113, 823, 741 cm^{-1}. MS *m/z* (CI, relative intensity): 327 (M^++1, 4), 309 (6), 297 (2), 269 (75), 249 (100), 239 (7), 207 (23), 193 (13), 171 (19), 131 (14). HRMS (CI) calcd. for $C_{20}H_{27}O_2Si$ (M^++1) 327.1780, found 327.1782. $[\alpha]^{25}_{D}$ +11.4 (*c* 1.00, $CHCl_3$).

Corey-Fuchs reagent was prepared by the addition of a solution of CBr_4 (19.2 g, 57.9 mmol) in CH_2Cl_2 (13 mL) into a cold (0 °C) suspension of Zn powder (3.78 g, 57.9 mmol) and Ph_3P (15.2 g, 57.9 mmol) in CH_2Cl_2 (65 mL) followed by stirring for 20 min. A solution of aldehyde **2C** (6.30g, 19.3 mmol) in CH_2Cl_2 (13 mL) was added to the mixture and stirred at r.t. for 4 h and then it was poured into pentane (300 mL), filtered to remove the precipitate, and concentrated to give the dibromo olefin **2D**. This crude dibromo olefin **2D** was dissolved in THF (35 mL) and cooled to −78 °C. *n*-BuLi (2.5 M in Hex, 20 mL, 50 mmol) was added to the solution, and after 1 h the mixture was quenched by sat. $NaHCO_3$ solution (50 mL) and extracted with Et_2O (50 mL × 2). The ether extract was concentrated and the residue was purified by flash column chromatography (100% Hex) to give alkyne **2E** (5.61 g, 94% from aldehyde). R_f 0.32 (100% Hex). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 - 7.73 (m, 4 H), 7.39 - 7.47 (m, 6 H), 3.76, 3.57 (ABX, J_{AB}=9.7, J_{AX}=5.8, J_{BX}=7.7 Hz, 2 H), 2.65 - 2.73 (m, 1 H), 2.05 (d, *J*=2.4 Hz, 1 H), 1.26 (d, *J*=7.1 Hz, 3 H), 1.09 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 135.9, 135.9, 133.8, 133.8, 129.9, 127.9, 86.8, 69.3, 67.7, 29.1, 27.1, 19.6, 17.6. IR (neat): ν_{max} = 3309, 3070, 2935, 2858, 1635, 1469, 1427, 1388, 1257, 1110, 1014, 822, 741 cm^{-1}. MS *m/z* (CI, relative intensity): 323 (M^++1, 46), 305 (4), 283 (6), 269 (62), 265 (68), 245 (100), 227 (21), 203 (16), 171 (25), 137 (17). HRMS (CI) calcd. for $C_{21}H_{27}OSi$ (M^++1) 323.1831, found 323.1833. $[\alpha]^{25}_{D}$ +5.6 (*c* 1.00, $CHCl_3$).

$BHBr_2{\cdot}SMe_2$ soltuion (1 M in CH_2Cl_2, 10.4 mL, 10.4 mmol) was added to a solution of alkyne **2E** (2.80 g, 8.69 mmol) in CH_2Cl_2 (9 mL) at 0 °C. The mixture was stirred at r.t. for 2 h and cooled to 0 °C before being poured into water (15mL) and Et_2O (45 mL) at 0 °C. The mixture was stirred at r.t. for 30 min and the organic phase was washed with water (10 mL) and brine (10 mL), dried over $MgSO_4$, filtered, and concentrated. Flash column chromatography (Hex-EtOAc, 1:1) provided boronic acid **3** (2.49 g, 80%). R_f 0.45 (Hex-EtOAc, 1:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 - 7.70 (m, 4 H), 7.31 - 7.43 (m, 6 H), 6.95 (dd, *J*=17.9, 6.6 Hz, 1 H), 5.57 (d, *J*=17.6 Hz, 1 H), 3.64, 3.55 (ABX, J_{AB}=9.8, J_{AX}=6.1, J_{BX}=7.1 Hz, 2 H), 2.51 - 2.61 (m, 1 H), 1.08 (d, *J*=6.8 Hz, 3 H), 1.05 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.9, 135.9, 134.1, 134.1, 129.9, 127.9 68.2, 42.1, 27.2, 19.6, 16.1. IR (neat): ν_{max} = 3356, 3070, 2962, 1727, 1631, 1589, 1469, 1389, 1122, 999, 822, 741 cm^{-1}. $[\alpha]^{25}_{D}$ +5.8 (*c* 1.00, $CHCl_3$).



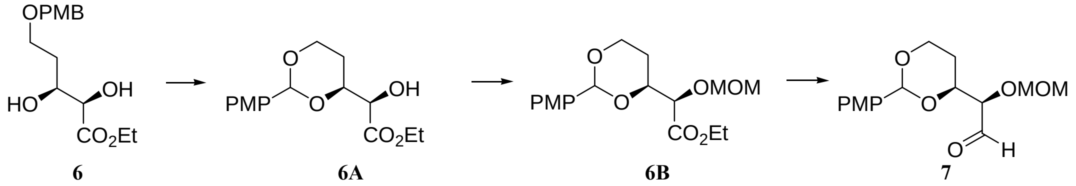
Aldehyde **5**

TlOEt (0.22 mL, 3.1 mmol) was added to a solution of boronic acid **3** (755 mg, 2.05 mmol), vinyl iodide **4** (744 mg, 1.86 mmol), and $Pd(Ph_3P)_4$ (214 mg, 0.185 mmol) in degassed THF (36 mL) and water (9 mL). After stirring for 2 h at r.t. the mixture was diluted with Hex-Et_2O (1:1, 200 mL) and filtered through a pad of silica. The organic phase was concentrated and purified by flash column chromatography (Hex-EtOAc, 15:1) to afford diene **4A** (1.09 g, 99%). R_f 0.65 (Hex-EtOAc, 8:1). ^{1}H NMR (500 MHz,

$CDCl_3$) δ 7.65 (d, *J*=7.8 Hz, 4 H), 7.33 - 7.44 (m, 6 H), 6.25 (dd, *J*=15.2, 10.3 Hz, 1 H), 6.05 (dd, *J*=15.4, 10.5 Hz, 1 H), 5.65 (dd, *J*=15.4, 7.3 Hz, 1 H), 5.56 (dd, *J*=15.3, 7.5 Hz, 1 H), 4.36 (t, *J*=7.5 Hz, 1 H), 3.68 - 3.78 (m, 3 H), 3.54, 3.49 (ABX, J_{AB}=9.8, J_{AX}=6.1, J_{BX}=6.6 Hz, 2 H), 2.39 - 2.48 (m, 1 H), 1.42 (d, *J*=7.6 Hz, 6 H), 1.04 (s, 9 H), 1.03 (d, *J*=7.1 Hz, 3 H), 0.89 (s, 9 H), 0.06 (d, *J*=1.7 Hz, 6 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.6, 135.9, 135.9, 134.4, 134.1, 134.1, 129.8, 129.2, 128.2, 127.8, 109.1, 81.7, 78.9, 68.6, 62.5, 39.6, 27.4, 27.2, 27.1, 26.1, 19.5, 18.6, 16.7. IR (neat): ν_{max} = 3070, 2954, 2931, 2858, 1658, 1589, 1469, 1427, 1377, 1254, 1111, 941, 837 cm^{-1}. MS *m/z* (CI, relative intensity): 595 (M^++1, 29), 579 (9), 565 (4), 537 (100), 521 (42), 479 (28), 459 (30), 405 (35), 327 (47), 281 (64), 251 (33), 209 (45). HRMS (CI) calcd. for $C_{35}H_{55}O_4Si_2$ (M^++1) 595.3639, found 595.3641. $[\alpha]^{26}_D$ +6.1 (*c* 0.70, $CHCl_3$).

PPTS (138 mg, 0.549 mmol) was added to a solution of diene **4A** (1.09 g, 1.83 mmol) in EtOH (7 mL). The mixture was stirred for 12 h at r.t. and quenched by TEA (0.2 mL). Volatiles were removed under reduced pressure and the residue was purified by flash column chromatography (Hex-EtOAc, 4:1) to give alcohol **4B** (0.701 g, 80%). R_f 0.65 (Hex-EtOAc, 2:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (d, *J*=8.1 Hz, 4 H), 7.31 - 7.45 (m, 6 H), 6.28 (dd, *J*=15.2, 10.5 Hz, 1 H), 6.05 (dd, *J*=15.4, 10.5 Hz, 1 H), 5.68 (dd, *J*=15.2, 7.3 Hz, 1 H), 5.53 (dd, *J*=15.2, 7.8 Hz, 1 H), 4.35 (t, *J*=8.3 Hz, 1 H), 3.80 - 3.85 (m, 1 H), 3.78 (dt, *J*=8.4, 3.2 Hz, 1 H), 3.55 - 3.61 (m, 1 H), 3.46 - 3.55 (m, 2 H), 2.40 - 2.48 (m, 1 H), 1.88 (dd, *J*=8.3, 4.4 Hz, 1 H), 1.44 (d, *J*=3.7 Hz, 6 H), 1.04 (s, 9 H), 1.03 (d, *J*=6.8 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 139.1, 135.6, 135.2, 133.8, 129.6, 128.7, 127.6, 127.0, 109.1, 81.2, 77.9, 68.3, 60.7, 39.4, 27.1, 27.0, 26.9, 19.3, 16.4. IR (neat): ν_{max} = 3471, 3070, 2958, 2931, 2858, 1658, 1589, 1469, 1427, 1377, 1242, 1111, 991 cm^{-1}. MS *m/z* (CI, relative intensity): 479 (M^+-1, 20), 463 (93), 423 (39), 405 (100), 365 (31), 345 (51), 335 (21), 315 (31), 287 (24), 267 (33), 209 (95), 167 (37). HRMS (CI) calcd. for $C_{29}H_{39}O_4Si$ (M^+-1) 479.2617, found 479.2615. $[\alpha]^{26}_D$ +4.4 (*c* 0.55, $CHCl_3$).

TEA (0.29 mL, 2.1 mmol) was added to a solution of alcohol **4B** (200 mg, 0.416 mmol) in DMSO (1 mL) and CH_2Cl_2 (1 mL) at 0 °C. After the addition of SO_3·pyr complex (196 mg, 1.23 mmol), the mixture was warmed to r.t. and stirred for 1h. The reaction was quenched by sat. NH_4Cl solution (5 mL) and extracted with Et_2O (10 mL × 2). The organic phase was dried over $MgSO_4$, filtered, and concentrated. Flash column chromatography provided aldehyde **5** (119 mg, 60%). R_f 0.51 (Hex-EtOAc, 8:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.72 (d, *J*=2.0 Hz, 1 H), 7.58 - 7.68 (m, 4 H), 7.34 - 7.45 (m, 6 H), 6.29 (dd, *J*=15.2, 10.5 Hz, 1 H), 6.05 (dd, *J*=15.3, 10.4 Hz, 1 H), 5.71 (dd, *J*=15.4, 7.3 Hz, 1 H), 5.58 (dd, *J*=15.2, 7.3 Hz, 1 H), 4.51 (t, *J*=7.7 Hz, 1 H), 4.06 (dd, *J*=7.8, 2.0 Hz, 1 H), 3.47 - 3.56 (m, 2 H), 2.39 - 2.48 (m, 1 H), 1.50 (s, 3 H), 1.46 (s, 3 H), 1.05 (s, 9 H), 1.03 (d, *J*=6.9 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 199.7, 139.8, 135.6, 135.1, 133.8, 129.6, 128.3, 127.6, 125.8, 111.3, 84.7, 77.8, 68.3, 39.3, 26.9, 26.8, 26.2, 19.3, 16.3. IR (neat): ν_{max} = 3136, 3070, 2958, 2931, 2715, 1889, 1824, 1736, 1658, 1589, 1469, 1381, 1219, 1111, 991 cm^{-1}. MS *m*/*z* (CI, relative intensity): 479 (M^++1, 5), 463 (2), 421 (59), 401 (22), 379 (17), 363 (24), 343 (29), 301 (10), 269 (40), 223 (34), 165 (58), 135 (39), 101 (100). HRMS (CI) calcd. for $C_{29}H_{39}O_4Si$ (M^++1) 479.2617, found 479.2619. $[\alpha]^{27}_D$ +11.7 (*c* 0.60, $CHCl_3$).



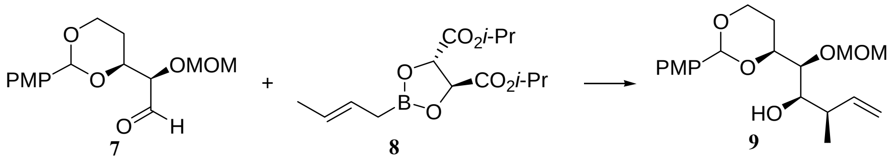
6 **6A** **6B** **7**

Adehyde **7**

Molecular sieves (3 Å, 4 g) were added to a solution of diol **6** (9.49 g, 31.8 mmol) in CH_2Cl_2 (636 mL) at 0 °C. The mixture was stirred at the same temperature for 30 min, followed by addition of DDQ (10.8 g, 47.7 mmol). After stirring for 3 h at 0 °C, the reaction mixture was filtered through a short path of silica. The filtrate was washed with sat. $NaHCO_3$ solution (100 mL × 2) and brine (50 mL), dried over $MgSO_4$, filtered, and concentrated. Purification of the residue by flash column chromatography (Hex-EtOAc, 4:1) yielded alcohol **6A** (8.69 g, 94%). R_f 0.25 (Hex-EtOAc, 2:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (d, *J*=8.8 Hz, 2 H), 6.87 (d, *J*=8.8 Hz, 2 H), 5.49 (s, 1 H), 4.22 - 4.35 (m, 4 H), 4.16 (dd, *J*=8.8, 2.4 Hz, 1 H), 3.99 (td, *J*=12.0, 2.2 Hz, 1 H), 3.80 (s, 3 H), 3.01 (d, *J*=8.8 Hz, 1 H), 2.30 (qd, *J*=12.6, 5.1 Hz, 1 H), 1.49 (d, *J*=13.4 Hz, 1 H), 1.30 (t, *J*=7.34 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 172.4, 160.1, 130.9, 127.4, 113.7, 101.1, 77.1, 73.4, 66.8, 62.0, 55.5, 26.5, 14.5. IR (neat): ν_{max} = 3502, 2972, 2933, 2854, 2708, 1745, 1614, 1518, 1302, 1246, 1030, 831 cm^{-1}. MS *m*/*z* (CI, relative intensity): 297 (M^++1, 100), 267 (2), 223 (3), 193 (30), 161 (61), 137 (38), 87 (7). HRMS (CI) calcd. for $C_{15}H_{21}O_6$ (M^++1) 297.1338, found 297.1337. $[\alpha]^{18}_D$ +32.9 (*c* 0.85, $CHCl_3$).

DMAP (4.28 g, 35.0 mmol) and DIPEA (19.9 ml, 115 mmol) were added to a solution of alcohol **6A** (11.3 g, 38.1 mmol) in CH_2Cl_2 (760 mL) at 0 °C. MOMCl (7.2 mL, 95 mmol) was slowly added to the mixture which was heated under reflux for 10 h then quenched by sat. NH_4Cl solution (500 mL). The aqueous phase was extracted with Et_2O (400 mL) and the combined organic phase was dried over $MgSO_4$, filtered, and concentrated. Flash column chromatography (Hex-EtOAc, 4:1) provided Ester **6B** (12.4 g, 95%). R_f 0.25 (Hex-EtOAc, 2:1). ^1H NMR (500 MHz, $CDCl_3$) δ 7.38 (d, J=8.8 Hz, 2 H), 6.86 (d, J=8.8 Hz, 2 H), 5.48 (s, 1 H), 4.75 (s, 2 H), 4.21 - 4.32 (m, 5 H), 3.97 (td, J=12.0, 2.5 Hz, 1 H), 3.78 (s, 3 H), 3.39 (s, 3 H), 2.13 (qd, J=12.7, 5.1 Hz, 1 H), 1.45 (br. d., J=11.7 Hz, 1 H), 1.29 (t, J=7.1 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.2, 160.1, 131.1, 127.6, 113.7, 101.5, 96.8, 77.9, 77.5, 66.7, 61.4, 56.3, 55.5, 26.7, 14.5. IR (neat): ν_{max} = 2964, 2935, 2898, 2840, 1747, 1616, 1587, 1518, 1466, 1250, 1109, 1032, 829 cm^{-1}. MS m/z (EI, relative intensity): 340 (M^+, 23), 309 (4), 295 (11), 278 (3), 262 (1), 221 (2), 193 (100), 152 (19), 135 (54), 121 (21), 109 (5). HRMS (EI) calcd. for $C_{17}H_{24}O_7$ (M^+) 340.1522, found 340.1524. $[\alpha]^{16}_D$ +40.8 (c 1.93, $CHCl_3$).

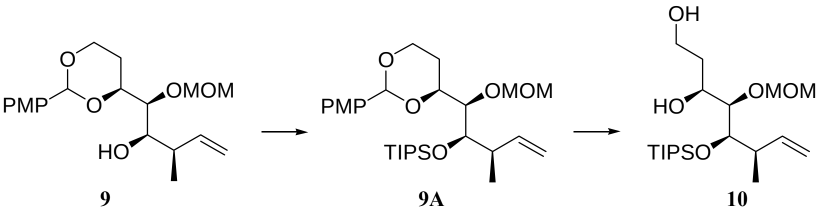
To a solution of ester **6B** (7.49 g, 22.0 mmol) in CH_2Cl_2 (110 mL) at –78 °C, DIBAL (1 M in Hex, 110 mL, 110 mmol) was added dropwise. After 2 h, MeOH was carefully added to the reaction mixture at −78 °C until it stopped foaming. The mixture was warmed up to r.t. and diluted with Et_2O (100 mL), washed with sat. NH_4Cl solution (50 mL) and sat. $NaHCO_3$ solution (50 mL). The organic phase was dried over $MgSO_4$, filtered and concentrated. Flash column chromatography (Hex-EtOAc, 2:1) provided aldehyde **7** (4.91 g, 75%) as white solid. R_f 0.23 (Hex-EtOAc, 1:1). ^1H NMR (500 MHz, $CDCl_3$) δ 9.80 (d, J=1.2 Hz, 1 H), 7.37 (d, J=8.8 Hz, 2 H), 6.87 (d, J=8.8 Hz, 2 H), 5.47 (s, 1 H), 4.80, 4.77 (ABq, J_{AB}=6.9 Hz, 2 H), 4.28 - 4.37 (m, 2 H), 4.08 (d, J=4.4 Hz, 1 H), 3.98 (td, J=12.0, 2.4 Hz, 1 H), 3.80 (s, 3 H), 3.43 (s, 3 H), 2.14 (qd, J=12.4, 5.1 Hz, 1 H), 1.54 (dd, J=13.5, 1.5 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 202.3, 160.2, 130.8, 127.6, 113.8, 101.7, 97.4, 83.1, 77.2, 66.8, 56.4, 55.5, 26.8. IR (neat): ν_{max} = 2958, 2868, 1736, 1614, 1587, 1516, 1464, 1362, 1302, 1250, 1153, 1105, 1034 cm^{-1}. MS m/z (EI, relative intensity): 296 (M^+, 32), 265 (6), 251 (5), 223 (3), 193 (100), 181 (5), 152 (6), 135 (79), 109 (15), 77 (12), 57 (9). HRMS (EI) calcd. for $C_{15}H_{20}O_6$ (M^+) 296.1260, found 296.1265. $[\alpha]^{23}_D$ +15.4 (c 1.25, $CHCl_3$).



7 **8** **9**

Homoallyl alcohol **9**

Powdered 4 Å molecular sieves (2 g) were poured into dry toluene (80 mL) and the mixture was cooled to −78 °C, followed by the addition of (***E***)-crotyllboronate **8** (11 g, 35 mmol). A solution of aldehyde **7** (6.99 g, 23.6 mmol) in dry toluene (100 mL) was added dropwise to the mixture and stirred for 36 h at −78 °C. 2 N NaOH (40 mL) was added to hydrolyze DIPT, and the two-phase mixture was warmed to 0 °C and stirred for 1 h before being filtered through a pad of Celite. The aqueous phase was extracted with Et_2O (30mL × 4). The combined organic phase was dried over K_2CO_3, filtered, and concentrated. Flash column chromatography (Hex-EtOAc, 3:1) provided homoallyl alcohol **9** (7.16 g, 86%, d.r. = 16:1) as white solid. R_f 0.45 (Hex-EtOAc, 1:1). ^1H NMR (500 MHz, $CDCl_3$) δ 7.40 (d, *J*=8.8 Hz, 2 H), 6.89 (d, *J*=8.6 Hz, 2 H), 5.86 (ddd, *J*=12.7, 10.2, 8.6 Hz, 1 H), 5.49 (s, 1 H), 5.16 (d, *J*=9.5 Hz, 1 H), 5.13 (d, *J*=2.4 Hz, 1 H), 4.93, 4.78 (ABq, , J_{AB}=6.7 Hz, 1 H), 4.30 (dd, *J*=11.5, 4.4 Hz, 1 H), 4.18 - 4.24 (m, 1 H), 3.96 (td, *J*=12.0, 2.5 Hz, 1 H), 3.81 (s, 3 H), 3.66 (dd, *J*=6.2, 3.1 Hz, 1 H), 3.47 - 3.53 (m, 1 H), 3.43 (s, 3 H), 2.48 - 2.57 (m, 1 H), 2.35 (d, *J*=5.6 Hz, 1 H), 1.96 (qd, *J*=12.3, 5.0 Hz, 1 H), 1.59 (dd, *J*=13.0, 1.2 Hz, 1 H), 1.10 (d, *J*=6.8 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.1, 140.9, 131.4, 127.5, 116.3, 113.8, 101.4, 98.6, 80.3, 79.0, 73.4, 66.9, 56.5, 55.5, 41.4, 27.4, 16.9. IR (neat): ν_{max} = 3435, 3080, 2925, 1614, 1589, 1518, 1464, 1373, 1304, 1250, 1173, 1144, 1101 cm^{-1}. MS *m/z* (CI, relative intensity): 353 (M^++1, 100), 321 (69), 297 (28), 265 (3), 245 (4), 193 (75), 181 (43), 155 (11), 137 (32), 99 (5), 87(5). HRMS (CI) calcd. for $C_{19}H_{29}O_6$ (M^++1) 353.1964, found 353.1966. $[\alpha]^{18}_D$ −5.6 (*c* 0.60, $CHCl_3$).

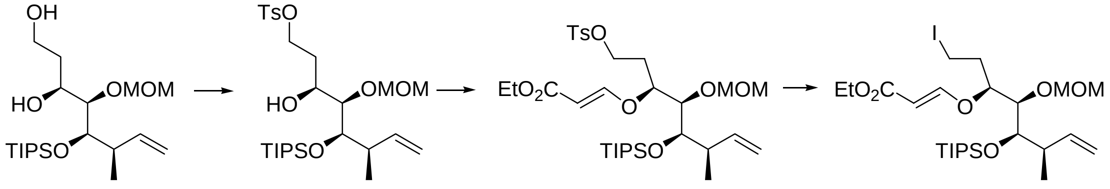


Diol **10**

Collidine (3.40 mL, 25.6 mmol) was added to a solution of homoallyl alcohol **9** (4.50 g, 12.8 mmol) in CH_2Cl_2 (25 mL). After cooling to 0 °C, TIPSOTf (4.20 mL, 15.6 mmol) was added dropwise and the resulting mixture was warmed up to r.t. The reaction was completed within 2 h and quenched by sat. NH_4Cl solution (10 mL). The Organic phase was washed with brine and dried over $MgSO_4$, filtered and concentrated. Flash column chromatography (Hex-EtOAc, 6:1) provided TIPS ether **9A** (6.43 g, 99%). R_f 0.55 (Hex-EtOAc, 4:1). ^1H NMR (500 MHz, $CDCl_3$) δ 7.41 (d, *J*=8.8 Hz, 2 H), 6.88

(d, *J*=8.8 Hz, 2 H), 6.02 (ddd, *J*=17.5, 10.3, 7.6 Hz, 1 H), 5.45 (s, 1 H), 5.06 (d, *J*=17.4 Hz, 1 H), 5.00 (d, *J*=10.3 Hz, 1 H), 4.77, 4.75 (ABq, J_{AB}=7.0 Hz, 2 H), 4.24 (dd, *J*=11.4, 3.8 Hz, 1 H), 4.10 - 4.15 (m, 2 H), 3.90 (td, *J*=12.5, 2.2 Hz, 1 H), 3.81 (s, 3 H), 3.61 (t, *J*=5.5 Hz, 1 H), 3.39 (s, 3 H), 2.65 - 2.73 (m, 1 H), 2.08 (qd, *J*=12.5, 4.9 Hz, 1 H), 1.61 (dd, *J*=13.3, 1.3 Hz, 1 H), 1.17 (d, *J*=7.1 Hz, 3 H), 1.12 (s, 21 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.0, 141.7, 131.7, 127.5, 114.3, 113.6, 101.3, 98.6, 82.1, 77.4, 76.8, 67.1, 56.1, 55.5, 41.2, 28.5, 18.6, 18.5, 17.9, 13.4. IR (neat): ν_{max} = 3074, 2943, 2893, 2866, 1616, 1518, 1464, 1250, 1171, 1103, 1038, 916, 827 cm^{-1}. MS *m*/*z* (CI, relative intensity): 509 (M^++1, 35), 477 (83), 465 (20), 431 (3), 373 (11), 329 (100), 311 (19), 297 (8), 267 (7), 241 (45), 181 (46). HRMS (CI) calcd. for $C_{28}H_{49}O_6Si$ (M^++1) 509.3298, found 509.3296. $[\alpha]^{16}_D$ +11.2 (*c* 0.89, $CHCl_3$).

CAN (17.0 g, 31.0 mmol) was added to a solution of TIPS ether **9A** (5.18 g, 10.2 mmol) in CH_3CN (500 mL) and water (55 mL) at 0 °C. The reaction mixture was stirred for 2 h at the same temperature and quenched by sat. $NaHCO_3$ solution (100 mL). TEA (5 mL) was added to prevent acetal formation and the mixture was diluted with Et_2O (500 mL). The organic phase was washed with brine (100mL), dried over Na_2SO_4, filtered and concentrated. Flash column chromatography (Hex-EtOAc, 4:1) provided diol **10** (3.68 g, 92%). R_f 0.21 (Hex-EtOAc, 2:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.02 (ddd, *J*=17.5, 10.3, 7.6 Hz, 1 H), 5.04 - 5.10 (m, 2 H), 4.78, 4.72 (ABq, J_{AB}=6.9 Hz, 2 H), 4.05 (dd, *J*=5.5, 3.5 Hz, 1 H), 3.98 - 4.03 (m, 1 H), 3.78 - 3.86 (m, 2 H), 3.42 (s, 3 H), 2.84 (d, *J*=5.9 Hz, 1 H), 2.67 (dd, *J*=6.8, 4.2 Hz, 1 H), 2.58 - 2.63 (m, 1 H), 1.75 - 1.88 (m, 2 H), 1.14 (d, *J*=7.1 Hz, 3 H), 1.10 (s, 21 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 141.3, 115.1, 98.4, 83.8, 76.5, 70.5, 61.9, 56.2, 41.1, 36.6, 18.5, 17.9, 13.4. IR (neat): ν_{max} = 3419, 3076, 2945, 2893, 2868, 1639, 1464, 1385, 1254, 1213, 1151, 1099, 1038 cm^{-1}. MS *m*/*z* (CI, relative intensity): 391 (M^++1, 12), 371 (4), 359 (100), 341 (2), 315 (9), 285 (19), 273 (7), 241 (16), 229 (12), 185 (38), 155 (37). HRMS (CI) calcd. for $C_{20}H_{43}O_5Si$ (M^++1) 391.2880, found 391.2881. $[\alpha]^{16}_D$ +29.2 (*c* 1.11, $CHCl_3$).



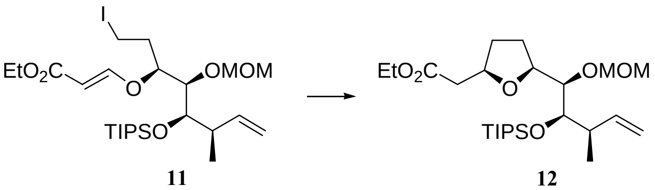
10 **10A** **10B** **11**

Iodide **11**

A solution of diol **10** (8.65g, 22.1 mmol) and TEA (6.20 mL, 44.4 mmol) in CH_2Cl_2 (200 mL) was treated with *p*-toluenesulfonyl chloride (5.06 g, 26.6 mmol). The mixture was stirred at 0 °C for 6 h, and then the reaction was quenched by sat. NH_4Cl solution (100 mL). The reaction mixture was extracted with Et_2O (50 mL × 2), dried over $MgSO_4$, filtered, concentrated and purified by flash column chromatography (Hex-EtOAc, 6:1) to give tosylate **10A** (12.0 g, 99%). R_f 0.22 (Hex-EtOAc, 8:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, *J*=8.3 Hz, 2 H), 7.33 (d, *J*=8.3 Hz, 2 H), 5.96 (ddd, *J*=17.5, 10.3, 7.5 Hz, 1 H), 5.04 (d, *J*=12.5 Hz, 1 H), 5.02 (d, *J*=5.4 Hz, 1 H), 4.74, 4.65 (ABq, J_{AB}=6.9 Hz, 2 H), 4.15 - 4.25 (m, 2 H), 4.02 (dd, *J*=5.9, 3.4 Hz, 1 H), 3.77 - 3.85 (m, 1 H), 3.36 (s, 3 H), 3.31 (dd, *J*=5.9, 3.4 Hz, 1 H), 2.52 - 2.59 (m, 1 H), 2.44 (s, 3 H), 2.34 (d, *J*=7.1 Hz, 1 H), 1.90 - 1.97 (m, 1 H), 1.79 - 1.86 (m, 1 H), 1.11 (d, *J*=6.8 Hz, 3 H), 1.08 (s, 21 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 144.8, 141.0, 133.6, 130.0, 128.1, 115.2, 98.4, 83.2, 76.4, 68.1, 66.1, 56.2, 41.1, 34.4, 21.8, 18.5, 18.4, 17.5, 13.3. IR (neat): ν_{max} = 3543, 3070, 2945, 2893, 2868, 2725, 1638, 1599, 1464, 1362, 1176, 1038, 918, 814, 663 cm^{-1}. MS *m*/*z* (FAB, relative intensity): 545 (M^++1, 14), 513 (53), 469 (16), 439 (6), 285 (80), 241 (50), 229 (29), 157 (69), 137 (100), 99 (62), 45 (82). HRMS (FAB) calcd. for $C_{27}H_{49}O_7SSi$ (M^++1) 545.2968, found 545.2953. $[\alpha]^{19}_D$ +9.4 (*c* 3.60, $CHCl_3$).

Ethyl propiolate (2.60 mL, 25.6 mmol) and N-methylmorpholine (0.56 mL, 5.1 mmol) were added to a solution of tosylate **10A** (9.30 g, 17.1 mmol) in CH_2Cl_2 (17 mL). The reaction mixture was stirred for 12 h and concentrated under reduced pressure. The residue was purified by flash column chromatography (Hex-EtOAc, 8:1) to give β-alkoxyacrylate **10B** (10.57 g, 96%). R_f 0.44 (Hex-EtOAc, 8:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, *J*=8.3 Hz, 2 H), 7.32 - 7.36 (m, 3 H), 5.89 (ddd, *J*=17.6, 10.0, 8.1 Hz, 1 H), 5.17 (d, *J*=12.2 Hz, 1 H), 5.04 (d, *J*=17.4 Hz, 1 H), 5.00 (d, *J*=10.3 Hz, 1 H), 4.63, 4.56 (ABq, J_{AB}=6.9 Hz, 2 H), 4.20 - 4.25 (m, 1 H), 4.17 (q, *J*=7.1 Hz, 2 H), 4.10 - 4.15 (m, 1 H), 3.94 - 4.01 (m, 2 H), 3.50 (t, *J*=6.0 Hz, 1 H), 3.31 (s, 3 H), 2.50 - 2.57 (m, 1 H), 2.44 (s, 3 H), 2.33 - 2.41 (m, 1 H), 1.79 - 1.88 (m, 1 H), 1.29 (t, *J*=7.2 Hz, 3 H), 1.11 (d, *J*=6.8 Hz, 3 H), 1.07 (s, 21 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.0, 163.3, 145.1, 140.5, 133.0, 130.1, 128.1, 115.7, 98.7, 97.6, 82.1, 80.7, 76.6, 66.5, 60.0, 56.1, 40.8, 30.9, 21.9, 18.5, 18.5, 14.6, 13.3. IR (neat): ν_{max} = 3080, 2945, 2868, 1711, 1639, 1599, 1464, 1367, 1284, 1178, 1132, 1099, 1039, 964 cm^{-1}. MS *m*/*z* (FAB, relative intensity): 643 (M^++1, 7), 611 (7), 599 (3), 511 (2), 465 (11), 439 (13), 383 (15), 311 (13), 285 (79), 241 (74), 157 (100). HRMS (FAB) calcd. for $C_{32}H_{55}O_9SSi$ (M^++1) 643.3336, found 643.3328. $[\alpha]^{19}_D$ –3.4 (*c* 3.95, $CHCl_3$).

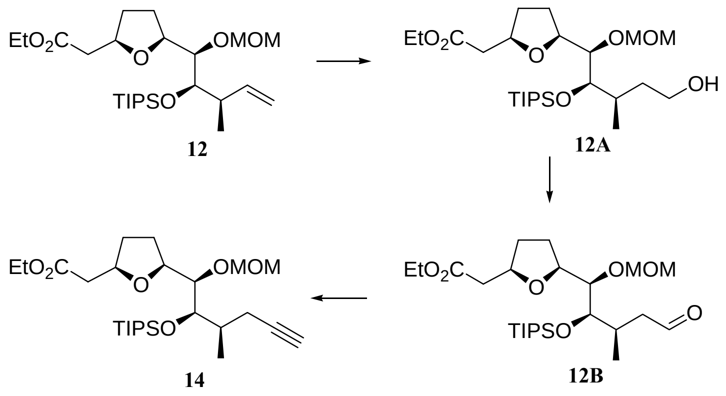
NaI (3.92 g, 26.2 mmol) was added to a solution of β-alkoxyacrylate **10B** (8.41 g, 13.1 mmol) in acetone (260 mL) and the mixture was heated under reflux for 3 h. The reaction was quenched by water (50 mL) and extracted with Et_2O (100 mL × 2). The combined organic phase was dried over $MgSO_4$, concentrated, and purified by flash column chromatography (Hex-EtOAc, 11:1) to give iodide **11** (7.31 g, 93%). R_f 0.44 (Hex-EtOAc, 8:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (d, J=12.2 Hz, 1 H), 5.94 (ddd, J=17.5, 10.1, 7.6 Hz, 1 H), 5.29 (d, J=12.2 Hz, 1 H), 5.11 (d, J=17.4 Hz, 1 H), 5.08 (d, J=10.5 Hz, 1 H), 4.69, 4.60 (ABq, J_{AB}=7.1 Hz, 2 H), 4.20 - 4.25 (m, 1 H), 4.16 (q, J=7.0 Hz, 2 H), 4.02 (dd, J=5.9, 3.7 Hz, 1 H), 3.56 (t, J=5.9 Hz, 1 H), 3.37 (s, 3 H), 3.21 - 3.25 (m, 1 H), 3.08 - 3.14 (m, 1 H), 2.56 - 2.63 (m, 1 H), 2.40 - 2.48 (m, 1 H), 2.05 - 2.13 (m, 1 H), 1.28 (t, J=7.1 Hz, 3 H), 1.15 (d, J=7.1 Hz, 3 H), 1.11 (s, 21 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.2, 162.6, 139.8, 114.6, 97.7, 96.8, 83.7, 80.4, 75.6, 59.0, 55.3, 40.1, 34.2, 17.6, 17.5, 17.0, 13.7, 12.4. IR (neat): ν_{max} = 3076, 2945, 2897, 2868, 1712, 1643, 1463, 1369, 1282, 1132, 1039, 918, 831 cm^{-1}. MS m/z (FAB, relative intensity): 599 (M^++1, 8), 567 (15), 555 (5), 537 (2), 499 (1), 395 (32), 311 (21), 241 (92), 229 (22), 197 (17), 157 (100), 115 (71). HRMS (FAB) calcd. for $C_{25}H_{48}O_6SiI$ (M^++1) 599.2265, found 599.2265. $[\alpha]^{24}_D$ –4.5 (c 9.40, $CHCl_3$).



11 **12**

Ester **12**

TTMSS (3.30 mL, 10.7 mmol) was added to a solution of iodide **11** (4.92 g, 8.23 mmol) in toluene at −20 °C, followed by the addition of Et_3B (1M in toluene, 12.3 mL, 12.3 mmol). After 1 h, the reaction mixture was quickly filtered through a pad of silica. The silica pad was rinsed with Et_2O (150 mL). The combined organic phase was concentrated and purified by flash column chromatography (Hex-EtOAc, 25:1) to give ester **12** (3.58 g, 92%). R_f 0.42 (Hex-EtOAc, 8:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.98 (ddd, J=17.5, 10.1, 7.8 Hz, 1 H), 5.01 (d, J=17.4 Hz, 1 H), 4.97 (d, J=10.3 Hz, 1 H), 4.73, 4.72 (ABq, J_{AB}=6.9 Hz, 2 H), 4.23 (tt, J=6.7 Hz, 1 H), 4.09 - 4.15 (m, 3 H), 3.98 (t, J=4.8 Hz, 1 H), 3.47 (t, J=5.5 Hz, 1 H), 3.38 (s, 3 H), 2.63, 2.43 (ABX, J_{AB}=15.0 Hz, J_{AX}=6.7 Hz, J_{BX}=6.7 Hz, 2 H), 2.55 - 2.60 (m, 1 H), 1.99 - 2.07 (m, 1 H), 1.90 - 1.99 (m, 2 H), 1.57 - 1.65 (m, 1 H), 1.25 (t, J=7.2 Hz, 3 H), 1.08 - 1.13 (m, 24 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.7, 141.8, 114.3, 98.1, 82.9, 79.2, 77.0, 75.4, 60.6, 56.1, 41.3, 41.3, 31.7, 28.0, 18.6, 18.5, 18.5, 18.2, 14.4, 13.4. IR (neat): ν_{max} = 3074, 2945, 2868, 1738, 1639, 1464, 1383, 1192, 1151, 1099, 1038, 916, 679 cm^{-1}. MS *m*/*z* (CI, relative intensity): 473 (M$^+$+1, 5), 455 (1), 441 (100), 411 (20), 397 (20), 367 (12), 299 (8), 267 (42), 237 (57), 219 (10), 157 (79), 131 (5). HRMS (CI) calcd. for $C_{25}H_{49}O_6Si$ (M$^+$+1) 473.3298, found 473.3294. [α]$^{17}_D$ +10.0 (*c* 0.57, $CHCl_3$).



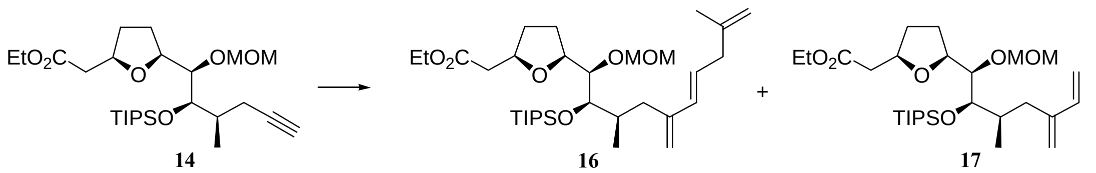
Alkyne **14**

A solution of 2-methyl-2-butene (1.90 mL, 18.0 mmol) in THF (5 mL) was cooled to 0 °C and borane-THF complex (1 M in Hexane, 8.80 mL, 8.80 mmol) was added. After 1 h at 0 °C the disiamylborane solution was added via cannular to ester **12** (2.10g, 4.44 mmol) in THF (2 mL) at 0 °C over 15 min. The resulting solution was stirred at 0 °C for 3 h and poured into water (37 mL). Sodium perborate tetrahydrate (1.35 g, 8.77 mmol,) was then added and the white suspension was stirred vigorously for 1 h at r.t. The mixture was extracted with Et_2O (20 mL × 3), dried over Na_2SO_4, filtered, and concentrated. Flash column chromatography (Hex-EtOAc, 2:1) provided alcohol **12A** (2.00 g, 92%). R_f 0.18 (Hex-EtOAc, 4:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.74, 4.68 (ABq, J_{AB}=6.9 Hz, 2 H), 4.29 (tt, *J*=6.6 Hz, 1 H), 4.25 (td, *J*=7.5, 3.2 Hz, 1 H), 4.10 - 4.17 (m, 2 H), 3.96 (dd, *J*=5.1, 3.2 Hz, 1 H), 3.68 - 3.75 (m, 1 H), 3.54 - 3.61 (m, 1 H), 3.45 (dd, *J*=5.1, 2.9 Hz, 1 H), 3.39 (s, 3 H), 2.67, 2.46 (ABX, J_{AB}=15.4, J_{AX}=6.9, J_{BX}=6.6 Hz, 2 H), 2.31 (t, *J*=5.3 Hz, 1 H), 2.01 - 2.11 (m, 2 H), 1.90 - 1.98 (m, 3 H), 1.59 - 1.68 (m, 1 H), 1.31 - 1.40 (m, 1 H), 1.25 (t, *J*=7.1 Hz, 3 H), 1.09 (s, 21 H), 1.03 (d, *J*=6.8 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.7, 98.0, 82.1, 77.3, 77.0, 75.9, 61.4, 60.6, 56.1, 40.8, 35.2, 31.5, 31.2, 28.6, 19.1, 18.5, 14.4, 13.2. IR (neat): ν_{max} = 3454, 2945, 2891, 2868, 1738, 1464, 1383, 1300, 1196, 1151, 1039, 883, 679 cm^{-1}. MS *m*/*z* (FAB, relative intensity): 491 (M$^+$+1, 1), 460 (2), 447 (1), 415 (3), 385 (3), 307

(24), 289 (14), 255 (9), 154 (100), 136 (69), 107 (22), 85 (18). HRMS (FAB) calcd. for $C_{25}H_{51}O_7Si$ (M^++1) 491.3404, found 491.3398. $[\alpha]^{19}_D$ +8.1 (*c* 3.05, $CHCl_3$).

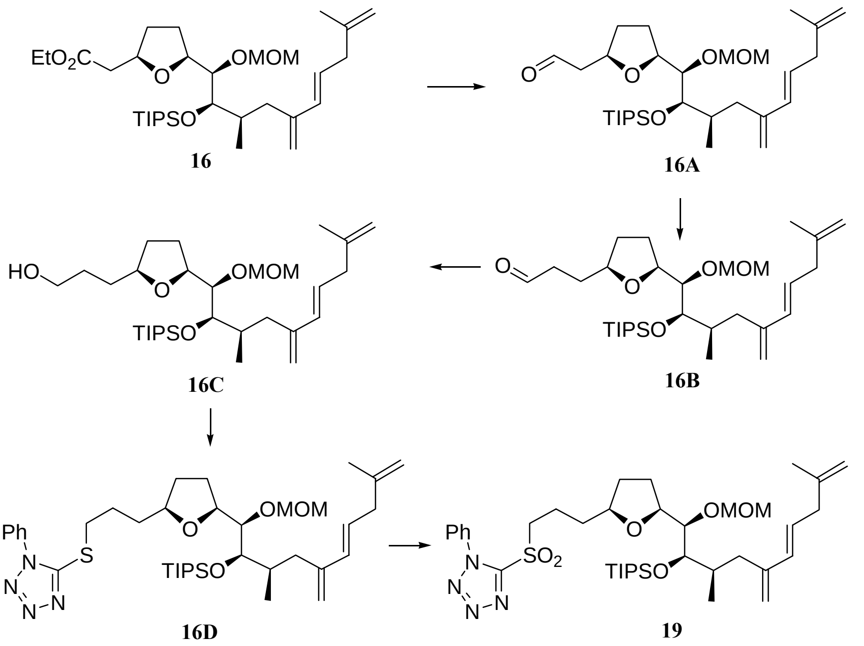
Dess-Martin periodinane (2.12 g, 5.00mmol) was added to a solution of alcohol **12A** (1.23 g, 2.51 mmol) and pyridine (0.81 mL, 10 mmol) in CH_2Cl_2 (25 mL) at 0 °C. The reaction mixture was warmed up to r.t. and stirred for 3 h and then quenched by sat. $Na_2S_2O_3$ (10 mL) solution. The organic phase was washed with sat. $NaHCO_3$ solution (10 mL) and brine (10mL), dried over $MgSO_4$, filtered, and concentrated. Flash column chromatography (Hex-EtOAc, 8:1) provided aldehyde **12B** (1.16 g, 95%). R_f 0.45 (Hex-EtOAc, 4:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.71 (d, *J*=2.4 Hz, 1 H), 4.72, 4.69 (ABq, J_{AB}=6.9 Hz, 2 H), 4.20 - 4.29 (m, 2 H), 4.08 - 4.16 (m, 2 H), 3.94 (t, *J*=4.4 Hz, 1 H), 3.47 (t, *J*=3.7 Hz, 1 H), 3.39 (s, 3 H), 2.87 (dd, *J*=16.6, 3.4 Hz, 1 H), 2.64, 2.45 (ABX, J_{AB}=15.4, J_{AX}=6.9, J_{AB}=6.5 Hz, 2 H), 2.54 - 2.61 (m, 1 H), 2.14 (ddd, *J*=16.7, 9.5, 3.2 Hz, 1 H), 2.00 - 2.08 (m, 1 H), 1.88 - 2.00 (m, 2 H), 1.59 - 1.68 (m, 1 H), 1.25 (t, *J*=7.2 Hz, 3 H), 1.09 (s, 21 H), 1.05 (d, *J*=7.1 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 204.0, 171.6, 97.9, 82.3, 77.0, 76.7, 75.9, 60.6, 56.1, 47.5, 40.9, 31.3, 30.1, 28.5, 19.4, 18.4, 18.4, 14.4, 13.1. IR (neat): ν_{max} = 2945, 2893, 2868, 2715, 1732, 1464, 1383, 1300, 1194, 1151, 1039, 883, 679 cm^{-1}. MS *m/z* (CI, relative intensity): 489 (M^++1, 2), 457 (30), 427 (67), 413 (42), 383 (21), 283 (39), 265 (23), 253 (100), 235 (16), 157 (38), 111 (8), 59 (2). HRMS (CI) calcd. for $C_{25}H_{49}O_7Si$ (M^++1) 489.3248, found 489.3241. $[\alpha]^{19}_D$ –8.0 (*c* 1.23, $CHCl_3$).

To a solution of aldehyde **12B** (268 mg, 0.548 mmol) and Cs_2CO_3 (536 mg, 1.64 mmol) in EtOH (7.2 mL) at 0 °C, dimethyl 1-diazo-2-oxopropylphosphonate **13** (263 mg, 1.37 mmol) in EtOH (2.4 mL) was added slowly. The reaction mixture was stirred for 1 h at r.t. and diluted with Et_2O (15 mL) and quenched by sat. NH_4Cl solution (5 mL). The mixture was extracted with Et_2O (10 mL× 2), washed with brine (10 mL) and dried over Na_2SO_4. After filtration and evaporation, flash column chromatography (Hex-EtOAc, 10:1) provided alkyne **14** (252 mg, 95%). R_f 0.54 (Hex-EtOAc, 8:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.72, 4.70 (ABq, *J*=6.6 Hz, 2 H), 4.26 (tt, *J*=6.7 Hz, 1 H), 4.09 - 4.20 (m, 3 H), 3.91 (dd, *J*=6.2, 4.3 Hz, 1 H), 3.53 (t, *J*=4.5 Hz, 1 H), 3.39 (s, 3 H), 2.66, 2.45 (ABX, J_{AB}=15.2, J_{AX}=6.6, J_{BX}=6.9 Hz, 2H), 2.52 (m, 1 H), 2.09 - 2.16 (m, 1 H), 2.01 - 2.10 (m, 2 H), 1.91 - 1.99 (m, 3 H), 1.58 - 1.67 (m, 1 H), 1.25 (t, *J*=7.1 Hz, 3 H), 1.15 (d, *J*=6.6 Hz, 3 H), 1.06 - 1.11 (m, 21 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.6, 97.7, 84.4, 82.7, 78.5, 76.2, 75.7, 69.3, 60.6, 56.0, 41.2, 36.3, 31.4, 28.3, 22.7, 18.5, 17.1, 14.4, 13.3. IR (neat): ν_{max} = 3311, 2945, 2891, 2868, 1738, 1464, 1385, 1300, 1190, 1151, 1038, 883, 679 cm^{-1}. MS *m/z* (CI, relative intensity): 483 (M$^+$-1, 2), 453 (61), 441 (31), 423 (8), 409 (15), 391 (4), 343 (4), 279 (40), 249 (100), 157 (31), 145 (6), 111 (2). HRMS (CI) calcd. for $C_{26}H_{47}O_6Si$ (M$^+$-1) 483.3142, found 483.3145. $[\alpha]^{24}_{D}$ +17.8 (*c* 0.58, $CHCl_3$).



Triene **16**

Grubbs' 2nd generation catalyst (25 mg, 0.030 mmol) was added to a solution of alkyne **14** (143 mg, 0.295 mmol) in CH_2Cl_2 (1.5 mL) and the mixture was stirred under ethylene atmosphere. The reaction was monitored by TLC, which was completed within 3 h at r.t. After removal of the ethylene balloon, 2-methyl-1,4-pentadiene (**15**, 0.35 mL, 3.0 mmol) was added to the mixture and the reaction vial was sealed, and heated to 40 ^{o}C. Another portion of 2-methyl-1,4-pentadiene (0.35 mL, 3.0 mmol) was added 4 h later to the mixture and the reaction mixture was further stirred for 20 h. Volatiles were removed under reduced pressure and the residue was purified by flash column chromatography (benzene-EtOAc, 100:1) to give triene **16** (102 mg, 65%) along with diene **17** (29.0 mg, 19%). R_f 0.56 (Pentane-Et_2O, 4:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.06 (d, *J*=15.9 Hz, 1 H), 5.74 (dt, *J*=15.9, 7.1 Hz, 1 H), 4.98 (d, *J*=1.7 Hz, 1 H), 4.87 (s, 1 H), 4.74 (s, 3 H), 4.71 (s, 1 H), 4.25 (tt, *J*=6.6 Hz, 1 H), 4.08 - 4.17 (m, 3 H), 3.89 (dd, *J*=6.4, 4.4 Hz, 1 H), 3.58 (dd, *J*=5.9, 4.2 Hz, 1 H), 3.40 (s, 3 H), 2.78 (br. d., *J*=6.8 Hz, 2 H), 2.75 (br. s., 1 H), 2.65, 2.44 (ABX, J_{AB}=15.0, J_{AX}=6.5, J_{BX}=7.0 Hz, 2 H), 1.97 - 2.10 (m, 3 H), 1.91 - 1.97 (m, 1 H), 1.86 (dd, *J*=11.3, 11.1 Hz, 1 H), 1.72 (s, 3 H), 1.60 - 1.67 (m, 1 H), 1.26 (t, *J*=7.1 Hz, 3 H), 1.08 - 1.15 (m, 21 H), 0.95 (d, *J*=6.6 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.5, 145.1, 144.7, 133.8, 128.0, 115.5, 110.9, 97.8, 83.0, 79.4, 77.7, 75.4, 60.5, 55.9, 41.6, 41.3, 36.5, 35.3, 31.5, 28.1, 22.6, 18.6, 18.5, 16.5, 14.4, 13.3. IR (neat): ν_{max} = 3076, 2945, 2891, 2868, 1738, 1651, 1604, 1464, 1383, 1298, 1186, 1151, 1038, 885, 679 cm^{-1}. MS *m/z* (CI, relative intensity): 565 (M$^+$-1, 2), 535 (13), 523 (30), 491 (10), 479 (2), 361 (100), 331 (45), 299 (5), 187 (28), 175 (15), 157 (76), 131 (5). HRMS (CI) calcd. for $C_{32}H_{57}O_6Si$ (M$^+$-1) 565.3924, found 565.3924. $[\alpha]^{20}_{D}$ +3.6 (*c* 1.12, $CHCl_3$).



Sulfone **19**

To a solution of triene **16** (276 mg, 0.471 mmol) in THF (2.5 mL) at –78 °C, DIBAL (1 M in toluene, 1.40 mL, 1.40 mmol) was added dropwise. After 1 h, MeOH was carefully added to the reaction mixture at −78 °C until it stopped foaming. The mixture was warmed up to r.t. and diluted with Et_2O (100 mL), and washed with sat. NH_4Cl solution (50 mL) and sat. $NaHCO_3$ solution (50 mL), dried over $MgSO_4$, filtered and concentrated. Flash column chromatography (Hex-EtOAc, 4:1) provided aldehyde **16A** (236 mg, 96%). R_f 0.27 (Hex-EtOAc, 2:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.80 (t, *J*=2.2 Hz, 1 H), 6.06 (d, *J*=15.9 Hz, 1 H), 5.72 (dt, *J*=14.7, 7.6 Hz, 1 H), 4.97 (d, *J*=1.7 Hz, 1 H), 4.86 (s, 1 H), 4.75, 4.69 (ABq, J_{AB}=6.9 Hz, 2H), 4.73 (s, 1 H), 4.70 (s, 1 H), 4.29 (tt, *J*=6.4 Hz, 1 H), 4.13 (dt, *J*= 5.9 Hz, 1 H), 3.89 (dd, *J*=6.2, 4.5 Hz, 1 H), 3.58 (dd, *J*=5.4 Hz, 1 H), 3.38 (s, 3 H), 2.77 (br. d., *J*=4.6 Hz, 2 H), 2.74 (br. s., 1 H), 2.68, 2.56 (ABXY, J_{AB}=16.1, J_{AX}=7.1 J_{AY}=2.5, J_{BX}=5.4 J_{BY}=2.0 Hz, 2 H), 1.91 - 2.12 (m, 4 H), 1.85 (dd, *J*=13.4, 11.0 Hz, 1 H), 1.71 (s, 3 H), 1.57 - 1.64 (m, 1 H), 1.11 (s, 21 H), 0.94 (d, *J*=6.8 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 201.9, 145.1, 144.8, 133.9, 128.1, 115.7, 111.0, 97.8, 82.9, 79.4, 77.6, 74.2, 56.1, 49.8, 41.6, 36.5, 35.3, 31.8, 28.2, 22.7, 18.6, 18.5, 16.6, 13.3. IR (neat): ν_{max} = 3076, 2945, 2893, 2868, 2725, 2360, 1728, 1651, 1604, 1464, 1385, 1215, 1151, 1039, 883, 679 cm^{-1}. MS *m/z* (CI, relative intensity): 523 (M^++1, 3), 505 (2), 491 (19), 479 (33), 447 (16), 429 (6), 373 (4), 331 (8), 317 (100), 287 (37), 161 (42). HRMS (CI) calcd. for $C_{30}H_{55}O_5Si$ (M^++1) 523.3819, found 523.3828. $[\alpha]^{20}_D$ +3.2 (*c* 0.78, $CHCl_3$).

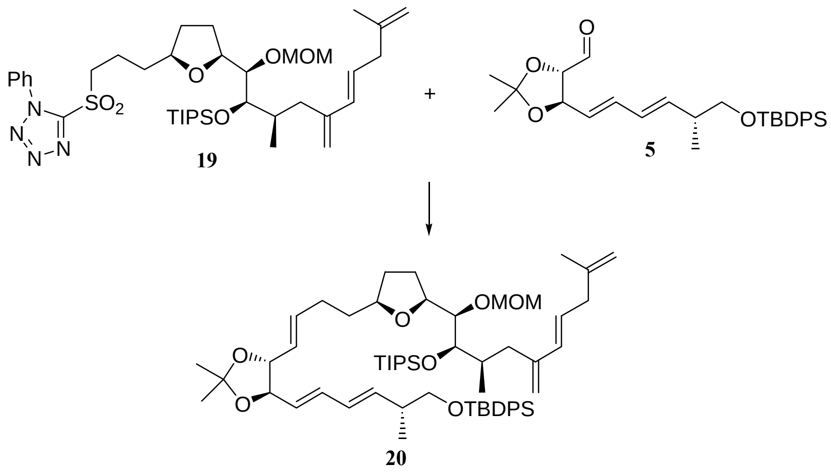
Potassium *t*-butoxide (116 mg, 1.04 mmol) was added to a solution of (methoxymethyl)triphenylphosphonium chloride (387 mg, 1.13 mmol) in THF (5 mL) at 0 °C. The resulting red solution was stirred for 10 min at the same temperature, followed by dropwise addition of a solution of aldehyde **16A** (236 mg, 0.451 mmol) in THF (3 mL). The reaction mixture was stirred for 30 min at 0 °C and warmed up to r.t. then further stirred for 30 min. Sat. $NaHCO_3$ solution (5 mL) was added to quench the reaction and the two phase mixture was extracted with Et_2O (20 mL × 2). The organic phase was dried over $MgSO_4$, filtered and concentrated. The crude enol ether was dissolved in THF (10 mL) and water (1 mL) then cooled to 0 °C. Mercury acetate (430 mg, 1.35 mmol) was added to the solution in one portion and the mixture was stirred for 30 min at 0 °C then quenched by sat. KI solution (10 mL). The two phase mixture was extracted with Et_2O (20 mL × 2) and the organic phase was washed with sat. KI solution (10 mL × 3), dried over $MgSO_4$, filtered and concentrated. Flash column chromatography (Hex-EtOAc, 4:1) provided aldehyde **16B** (189 mg, 78%). R_f 0.25 (Hex-EtOAc, 4:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.78 (s, 1 H), 6.06 (d, *J*=15.7 Hz, 1 H), 5.73 (dt, *J*=15.3, 7.3 Hz, 1 H), 4.97 (s, 1 H), 4.87 (s, 1 H), 4.73 (s, 1 H), 4.75, 4.71 (ABq, J_{AB}=6.9 Hz, 2 H), 4.70 (s, 1 H), 4.06 (dt, *J*=6.8 Hz, 1 H), 3.88 (dd, *J*=6.4, 4.2 Hz, 1 H), 3.80 - 3.86 (m, 1 H), 3.57 (dd, *J*=5.9, 4.4 Hz, 1 H), 3.39 (s, 3 H), 2.77 (br. d., *J*=6.8 Hz, 3 H), 2.44 - 2.62 (m, 2 H), 1.91 - 2.03 (m, 3 H), 1.83 - 1.90 (m, 3 H), 1.75 - 1.83 (m, 1 H), 1.71 (s, 3 H), 1.50 - 1.57 (m, 1 H), 1.11 (s, 21 H), 0.95 (d, *J*=6.8 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 202.7, 145.1, 133.8, 128.1, 115.7, 111.0, 97.9, 83.3, 79.3, 78.0, 77.9, 56.0, 41.6, 41.0, 36.5, 35.2, 31.5, 28.4, 28.2, 22.7, 18.6, 18.6, 16.6, 13.3. IR (neat): ν_{max} = 3076, 2945, 2893, 2868, 2725, 2360, 1728, 1651, 1604, 1464, 1385, 1215, 1151, 1039, 883, 679 cm^{-1}. $[\alpha]^{20}_{D}$ –1.0 (*c* 0.54, $CHCl_3$).

Sodium borohydride (27.0 mg, 0.714 mmol) was added to a solution of aldehyde **16B** (189 mg, 0.352 mmol) in MeOH (3.5 mL) at 0 °C. The reaction mixture was warmed up to r.t. and stirred for 30 min. The reaction was quenched by sat. NH_4Cl solution (2 mL) and extracted with Et_2O (10 mL × 2), dried over $MgSO_4$, filtered and concentrated. Flash column chromatography (Hex-EtOAc, 2:1) provided alcohol **16C** (175 mg, 92%). R_f 0.21 (Hex-EtOAc,2:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.06 (d, *J*=15.8 Hz, 1 H), 5.73 (dt, *J*=15.8, 7.0 Hz, 1 H), 4.97 (d, *J*=1.8 Hz, 1 H), 4.87 (s, 1 H), 4.75 (s, 2 H), 4.73 (s, 1 H), 4.70 (s, 1 H), 4.08 (q, *J*=7.0 Hz, 1 H), 3.89 (dd, *J*=6.6, 4.0 Hz, 1 H), 3.80 - 3.86 (m, 1 H), 3.61 - 3.69 (m, 2 H), 3.59 (dd, *J*=6.2, 4.0 Hz, 1 H), 3.39 (s, 3 H), 2.77 (br. d., *J*=7.0 Hz, 3 H), 2.48 (br. s., 1 H), 1.97 - 2.05 (m, 2 H), 1.88 - 1.96

(m, 2 H), 1.82 - 1.88 (m, 1 H), 1.71 (s, 3 H), 1.63 - 1.69 (m, 3 H), 1.56 - 1.62 (m, 1 H), 1.48 - 1.56 (m, 1 H), 1.11 (s, 21 H), 0.95 (d, *J*=6.6 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 145.1, 144.8, 133.8, 128.1, 115.6, 111.0, 98.1, 83.6, 79.4, 79.3, 78.0, 63.1, 56.0, 41.6, 36.5, 35.2, 32.9, 31.8, 30.2, 28.1, 22.7, 18.6, 18.6, 16.6, 13.3, 13.3. IR (neat): ν_{max} = 3435, 3076, 2943, 2868, 1651, 1604, 1464, 1385, 1244, 1217, 1149, 1097, 1034, 968, 883, 679 cm^{-1}. $[\alpha]^{21}_{D}$ –7.0 (*c* 0.39, $CHCl_3$).

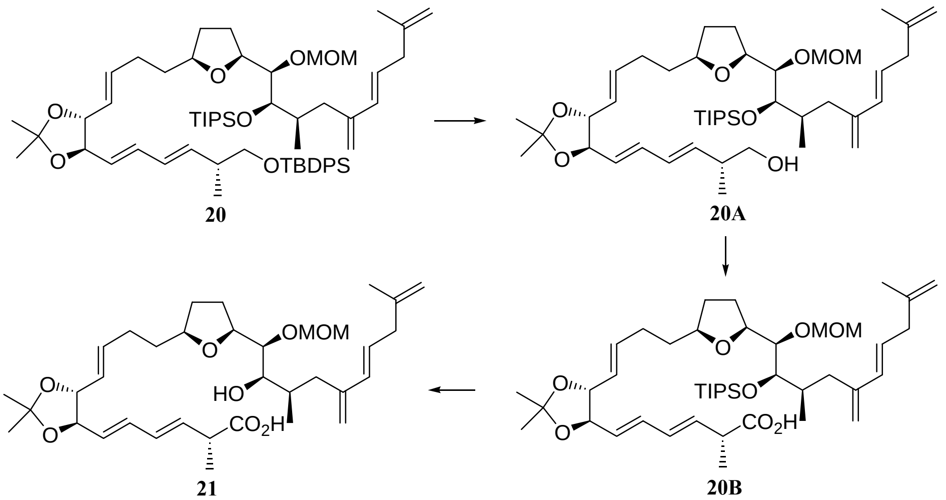
Ph_3P (239 mg, 0.913 mmol), 1-phenyl-1*H*-tetrazole-5-thiol (**18**, 163 mg, 0.913 mmol) and DIAD (0.19 mL, 0.96 mmol) were added to a solution of alcohol **16C** (164 mg, 0.304 mmol) in THF at 0 °C. After stirring for 10 min at r.t., the solvent was removed under reduced pressure and the residue was purified by flash column chromatography (Hex-EtOAc, 10:1) to afford sulfide **16D** (200 mg, 94%). R_f 0.52 (Hex-EtOAc, 4:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 - 7.59 (m, 5 H), 6.05 (d, *J*=15.8 Hz, 1 H), 5.72 (dt, *J*=15.8, 7.0 Hz, 1 H), 4.96 (d, *J*=1.8 Hz, 1 H), 4.86 (s, 1 H), 4.73 (s, 3 H), 4.69 (s, 1 H), 4.05 (q, *J*=6.8 Hz, 1 H), 3.87 (dd, *J*=6.6, 4.0 Hz, 1 H), 3.79 - 3.85 (m, 1 H), 3.57 (dd, *J*=6.2, 4.0 Hz, 1 H), 3.43 (t, *J*=7.3 Hz, 2 H), 3.38 (s, 3 H), 2.76 (d, *J*=8.4 Hz, 3 H), 1.87 - 2.03 (m, 6 H), 1.80 - 1.87 (m, 1 H), 1.70 (s, 3 H), 1.64 - 1.69 (m, 2 H), 1.48 - 1.54 (m, 1 H), 1.10 (s, 18 H), 1.09 (s, 3 H), 0.94 (d, *J*=7.0 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 154.7, 145.1, 144.8, 134.0, 133.8, 130.3, 130.0, 128.1, 124.1, 115.6, 111.0, 97.8, 83.2, 79.3, 78.4, 77.8, 56.0, 41.6, 36.6, 35.3, 34.9, 33.6, 31.6, 28.1, 26.2, 22.7, 18.6, 18.5, 16.6, 13.3. IR (neat): ν_{max} = 3074, 2943, 2866, 2729, 1649, 1599, 1500, 1462, 1387, 1277, 1244, 1149, cm^{-1}. MS *m*/*z* (FAB, relative intensity): 699 (M^++1, 0.7), 683 (1), 667 (1), 655 (1), 475 (4), 363 (5), 289 (73), 227 (14), 157 (57), 115 (87), 45 (100). HRMS (FAB) calcd. for $C_{38}H_{63}N_4O_4SSi$ (M^++1) 699.4339, found 699.4319. $[\alpha]^{21}_{D}$ +1.7 (*c* 0.34, $CHCl_3$).

A solution of sulfide **16D** (200 mg, 0.286 mmol) in EtOH (3 mL) at 0 °C was treated with ammonium molybdate tetrahydrate (70.4 mg, 0.0572 mmol) in H_2O_2 (30 % in water, 0.25 mL, 2.8 mmol). The resultant suspension was stirred at r.t. for 12 h, added water (5 mL) and extracted with Et_2O (20 mL × 2). The combined organic extracts were washed with sat. $NaHCO_3$ solution (10 mL), dried over $MgSO_4$, filtered, and concentrated. Flash column chromatography (Hex-EtOAc, 8:1) provided sulfone **19** (166 mg, 79%). R_f 0.52 (Hex-EtOAc, 4:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 - 7.71 (m, 2 H), 7.57 - 7.64 (m, 3 H), 6.05 (d, *J*=15.9 Hz, 1 H), 5.73 (dt, *J*=15.9, 7.1 Hz,1 H), 4.96 (d, *J*=1.7 Hz, 1 H), 4.86 (s, 1 H), 4.74, 4.70 (ABq, J_{AB}= 6.6 Hz, 2 H) 4.73 (s, 1 H), 4.69 (s, 1 H), 4.07 (q, *J*=6.9 Hz, 1 H), 3.88 (dd, *J*=6.6, 4.2 Hz, 1 H), 3.81 - 3.85 (m, 1 H), 3.82 (t, *J*=7.9 Hz, 2 H), 3.58 (dd, *J*=5.6, 4.4 Hz, 1 H), 3.38 (s, 3 H), 2.76 (d, *J*=8.6 Hz, 3 H), 1.89 - 2.12 (m, 6 H), 1.84 (dd, *J*=13.3, 11.1 Hz, 1 H), 1.71 (s, 3 H), 1.67 - 1.76 (m, 2 H), 1.50 - 1.57 (m, 1 H), 1.11 (s, 18 H), 1.10 (s, 3 H), 0.94 (d, *J*=6.8 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 153.7, 145.1, 144.8, 133.9, 133.3, 131.6, 129.9, 128.0, 125.3, 115.6, 111.0, 97.9, 83.2, 79.3, 78.2, 77.8, 56.2, 56.0, 41.6, 36.5, 35.2, 34.2, 31.5, 28.1, 22.7, 19.6, 18.6, 18.6, 16.6, 13.3. IR (neat): ν_{max} = 3076, 2945, 2868, 1644, 1597, 1498, 1482, 1342, 1153, 1099, 1039, 966, 885, 687 cm^{-1}. MS *m/z* (CI, relative intensity): 731 (M^++1, 1), 715 (2), 699 (3), 586 (1), 525 (9), 497 (7), 467 (3), 396 (3), 321 (9), 223 (8), 195 (38), 147 (59), 119 (98), 94 (100). HRMS (CI) calcd. for $C_{38}H_{63}N_4O_6SSi$ (M^++1) 731.4237, found 731.4245. $[\alpha]^{21}_{D}$ −2.1 (*c* 1.07, $CHCl_3$).



Olefin **20**

LiHMDS (1 M in THF, 0.50 mL, 0.50 mmol) was added dropwise to a solution of sulfone **19** (245 mg, 0.335 mmol) in THF (1.7 mL) at −78 °C. The resulting yellow solution was stirred at −40 °C for 1 h, and then cooled to −78 °C. Aldehyde **5** (240 mg, 5.01 mmol) in DMF (5.1 mL) and DMPU (1.7 mL) was added slowly to the lithiated sulfone solution and the reaction mixture was allowed to warm slowly to r.t. and stirred for 12 h. The reaction mixture was partitioned between water (10 mL) and Et_2O (10 mL), and the aqueous phase was extracted with Et_2O (20 mL × 2). The combined organic phase was washed with brine (10 mL), dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash column chromatography (Hex-EtOAc, 8:1) to give olefin **20** (244 mg, 74%, *E*:*Z* = 10:1). R_f 0.55 (Hex-EtOAc, 4:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 - 7.67 (m, 4 H), 7.34 - 7.43 (m, 6 H), 6.24 (dd, *J*=15.3, 10.4 Hz, 1 H), 6.05 (d, *J*=16.6 Hz, 1 H), 6.01 - 6.06 (m, 1 H), 5.69 - 5.83 (m, 2 H), 5.64 (dd, *J*=15.4, 7.1 Hz, 1 H), 5.50 (dd, *J*=15.2, 6.8 Hz, 1 H), 5.41 (dd, *J*=15.4, 7.3 Hz, 1 H), 4.97 (d, J=1.7 Hz, 1 H), 4.86 (s, 1 H), 4.74 (s, 2 H), 4.73 (s, 1 H), 4.69 (s, 1 H), 4.01 - 4.11 (m, 3 H), 3.87 (dd, J=6.5, 4.0 Hz, 1 H), 3.72 - 3.81 (m, 1 H), 3.57 (dd, J=6.6, 3.9 Hz, 1 H), 3.54, 3.49 (ABX, J_{AB}=9.8, J_{AX}=6.4, J_{BX}=6.6 Hz, 2 H), 3.38 (s, 3 H), 2.76 (d, J=8.3 Hz, 3 H), 2.39 - 2.48 (m, 1 H), 2.11 - 2.20 (m, 1 H), 2.03 - 2.11 (m, 1 H), 1.94 - 2.02 (m, 2 H), 1.81 - 1.92 (m, 3 H), 1.71 (s, 3 H), 1.60 - 1.68 (m, 1 H), 1.45 - 1.54 (m, 2 H), 1.43 (s, 3 H), 1.43 (s, 3 H), 1.11 (s, 18 H), 1.10 (s, 3 H), 1.04 (s, 9 H), 1.03 (d, J=6.9 Hz, 3 H), 0.94 (d, J=6.6 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 145.1, 144.8, 138.6, 136.5, 135.9, 135.8, 134.5, 134.1, 134.1, 133.8, 129.8, 129.2, 128.1, 127.8, 126.9, 126.0, 115.6, 111.0, 108.8, 97.8, 83.3, 82.6, 82.0, 79.3, 78.6, 77.9, 68.6, 55.9, 41.7, 39.5, 36.6, 35.5, 35.3, 31.6, 29.3, 28.2, 27.3, 27.1, 22.6, 19.5, 18.6, 18.6, 16.6, 16.5, 13.3. IR (neat): ν_{max} = 3072, 2933, 2866, 1651, 1603, 1464, 1429, 1238, 1111, 1051, 989, 885, 702 cm^{-1}. MALDI-TOF MS: 1005 (M^++Na). HRMS (FAB) calcd. for $C_{60}H_{94}O_7Si_2Na$ (M^++Na) 1005.6436, found 1005.6472. $[\alpha]^{25}_{D}$ +3.0 (*c* 0.35, $CHCl_3$).

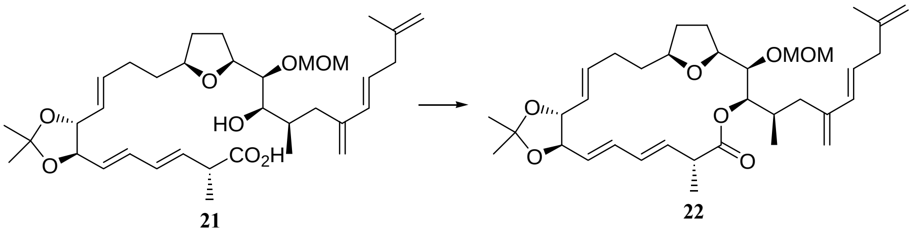


Seco acid **21**

Sodium hydroxide solution (15%, 1 mL) was added to a solution of olefin **20** (185 mg, 0.188 mmol) in DMPU (10 mL) at r.t. and the resulting mixture was stirred vigorously for 2 h. The reaction was diluted with Et_2O (20 mL) and quenched by sat. NH_4Cl solution (10 mL). The aqueous phase was extracted with Et_2O (10 mL × 2) and the combined organic phase was washed with brine (10 mL), dried over $MgSO_4$, filtered, and concentrated. Flash column chromatography (Hex-EtOAc, 4:1) provided alcohol **20A** (123 mg, 88%). R_f 0.22 (Hex-EtOAc, 4:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.27 (dd, J=15.2, 10.3 Hz, 1 H), 6.13 (dd, J=15.2, 10.5 Hz, 1 H), 6.05 (d, J=15.9 Hz, 1 H), 5.68 - 5.85 (m, 2 H), 5.60 (dd, J=15.2, 7.8 Hz, 1 H), 5.55 (dd, J=17.5, 7.3 Hz, 1 H), 5.41 (dd, *J*=15.4, 7.3 Hz, 1 H), 4.97 (s, 1 H), 4.87 (s, 1 H), 4.75 (s, 2 H), 4.73 (s, 1 H), 4.70 (s, 1 H), 4.01 - 4.11 (m, 3 H), 3.85 - 3.91 (m, 1 H), 3.74 - 3.82 (m, 1 H), 3.57 (dd, *J*=6.4, 3.9 Hz, 1 H), 3.48 - 3.55 (m, 1 H), 3.41 - 3.47 (m, 1 H), 3.39 (s, 3 H), 2.77 (d, *J*=6.8 Hz, 2 H), 2.75 (br. s., 1 H), 2.36 - 2.46 (m, 1 H), 2.06 - 2.20 (m, 2 H), 1.95 - 2.04 (m, 2 H), 1.83 - 1.93 (m, 3 H), 1.71 (s, 3 H), 1.61 - 1.68 (m, 1 H), 1.46 - 1.56 (m, 2 H), 1.43 (s, 6 H), 1.11 (s, 18 H), 1.10 (br. s., 3 H), 1.02 (d, *J*=6.6 Hz, 3 H), 0.95 (d, *J*=6.6 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 145.1, 144.8, 137.8, 136.6, 134.0, 133.8, 130.4, 128.1, 127.7, 125.9, 115.6, 111.0, 108.9, 97.8, 83.3, 82.5, 81.9, 79.3, 78.5, 77.9, 67.5, 56.0, 41.6, 39.9, 36.6, 35.4, 35.3, 31.5, 29.4, 28.2, 27.3, 27.2, 22.6, 18.6, 18.6, 16.5, 16.5, 13.3. IR (neat): ν_{max} = 3448, 3093, 3078, 2943, 2868, 1649, 1604, 1462, 1377, 1238, 1153, 1038, 991, 885, 679, 511 cm^{-1}. MALDI-TOF MS: 767 (M^++Na). HRMS (FAB) calcd. for $C_{44}H_{76}O_7Si_1Na$ (M^++Na) 767.5258, found 767.5253. $[\alpha]^{25}_D$ +5.8 (*c* 0.58, $CHCl_3$).

IBX (88.0 mg, 0.314 mmol) was dissolved in DMSO (1 mL). Upon stirring at r.t. for 20 min, the opaque solution turned to clear. To the solution, alcohol **20A** (77.7 mg, 0.104 mmol) in THF (1 mL) was added dropwise. After 3 hr stirring, the reaction was quenched by sat. $Na_2S_2O_3$ solution (3 mL) and extracted with Et_2O (10 mL × 2). The organic phase was washed with sat. $NaHCO_3$ solution (5 mL × 2) and brine (5 mL), dried over $MgSO_4$, filtered, and concentrated. This crude aldehyde was directly dissolved in *t*-BuOH (3.3 mL) and 2-methyl-2-butene (3.3 mL). After cooling to 0 °C, $NaClO_2$ (59.0 mg, 0.522 mmol) and NaH_2PO_4 (50.0 mg, 0.626 mmol) in water (3.3mL) was added to the solution. The reaction mixture was stirred vigorously for 5 h at r.t. , diluted with EtOAc (30 mL), and quenched by water (10 mL). The aqueous phase was extracted with EtOAc (10 mL × 2) and the combined organic phase was washed with brine (10 mL), dried over $MgSO_4$, filtered, and concentrated. Flash column chromatography ($CHCl_3$-MeOH, 30:1) provided acid **20B** (70.4 mg, 89%). R_f 0.43 ($CHCl_3$-MeOH, 10:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.27 (dd, *J*=15.2, 10.5 Hz, 1 H), 6.15 (dd, *J*=15.2, 10.5 Hz, 1 H), 6.05 (d, *J*=15.7 Hz, 1 H), 5.69 - 5.81 (m, 3 H), 5.58 (dd, *J*=15.2, 7.1 Hz, 1 H), 5.40 (dd, *J*=15.4, 7.3 Hz, 1 H), 4.97 (d, *J*=1.5 Hz, 1 H), 4.87 (s, 1 H), 4.76, 4.74 (ABq, J_{AB}=6.9 Hz, 2 H), 4.73 (s, 1 H), 4.69 (s, 1 H), 4.01 - 4.11 (m, 3 H), 3.86 (dd, *J*=6.5, 4.0 Hz, 1 H), 3.75 - 3.81 (m, 1 H), 3.57 (dd, *J*=6.5, 4.0 Hz, 1 H), 3.39 (s, 3 H), 3.16 - 3.23 (m, 1 H), 2.76 (d, *J*=6.8 Hz, 3 H), 2.12 - 2.21 (m, 1 H), 2.02 - 2.11 (m, 1 H), 1.94 - 2.01 (m, 2 H), 1.81 - 1.93 (m, 3 H), 1.71 (s, 3 H), 1.59 - 1.68 (m, 1 H), 1.46 - 1.53 (m, 2 H), 1.43 (s, 3 H), 1.42 (s, 3 H), 1.30 (d, *J*=6.8 Hz, 3 H), 1.10 (s, 18 H), 1.10 (s, 3 H), 0.94 (d, *J*=6.6 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 179.4, 145.1, 144.8, 136.8, 133.8, 133.3, 133.0, 130.9, 128.9, 128.1, 125.8, 115.6, 111.0, 109.0, 97.8, 83.4, 82.6, 81.7, 79.3, 78.6, 77.8, 55.9, 42.7, 41.6, 36.6, 35.5, 35.3, 31.5, 29.3, 28.1, 27.3, 27.2, 22.6, 18.6, 18.6, 17.2, 16.5, 13.3. IR (neat): ν_{max} = 3076, 2941, 2868, 1736, 1711, 1653, 1604, 1462, 1390, 1371, 1151, 1036, 989, 885, 806, 679 cm^{-1}. MALDI-TOF MS: 781 (M$^+$+Na). HRMS (FAB) calcd. for $C_{44}H_{74}O_8Si_1Na$ (M$^+$+Na) 781.5051, found 781.5059. $[\alpha]^{25}_D$ –16.3 (*c* 0.25, $CHCl_3$).

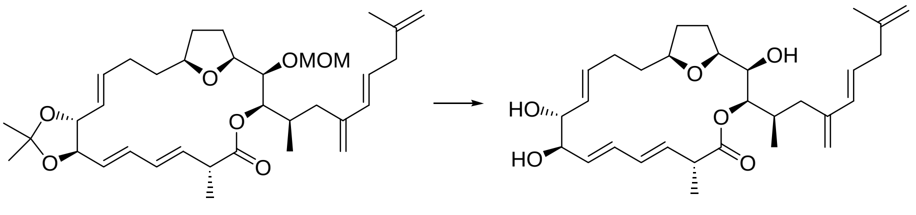
TBAF (1 M in THF, 0.28 mL, 0.28 mmol) was added dropwise to a solution of acid **20B** (70.4 mg, 0.0927 mmol) in THF (3 mL). After 1 h, another portion of TBAF (1 M in THF, 0.10 mL, 0.10 mmol) was added to the brown reaction mixture and the mixture was stirred for 1 h before the addition of the last portion of TBAF (1 M in THF, 0.10 mL, 0.10 mmol). The reaction was finished within 1 h and filtered through a short path of silica being rinsed with Hex-EtOAc-AcOH (1:1:0.01, 100 mL). After concentration, the residue was purified by flash column chromatography ($CHCl_3$-MeOH, 30:1) to afford the *seco* acid **21** (52.6 mg, 94%). R_f 0.35 ($CHCl_3$-MeOH, 10:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.12 - 6.24 (m, 2 H), 6.06 (d, *J*=15.7 Hz, 1 H), 5.66 - 5.79 (m, 3 H), 5.56 (dd, *J*=14.6, 7.5 Hz, 1 H), 5.39 (dd, *J*=15.3, 7.7 Hz, 1 H), 5.01 (d, *J*=6.8 Hz, 1 H), 4.98 (d, *J*=1.5 Hz, 1 H), 4.87 (s, 1 H), 4.72 (s, 1 H), 4.69 (d, *J*=6.6 Hz, 1 H), 4.69 (s, 1 H), 3.94 - 4.07 (m, 3 H), 3.65 - 3.72 (m, 1 H), 3.62 (d, *J*=7.6 Hz, 1 H), 3.36 (s, 3 H), 3.21 (d, *J*=9.0 Hz, 1 H), 3.11 - 3.19 (m, 1 H), 2.89 - 2.95 (m, 1 H), 2.71 - 2.80 (m, 2 H), 2.14 - 2.22 (m, 1 H), 2.03 - 2.13 (m, 1 H), 1.83 - 1.95 (m, 3 H), 1.73 - 1.82 (m, 2 H), 1.70 (s, 3 H), 1.46 - 1.54 (m, 2 H), 1.42 (s, 6 H), 1.37 - 1.45 (m, 1 H), 1.27 (d, *J*=7.1 Hz, 3 H), 0.84 (d, *J*=6.6 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 177.7, 145.2, 145.0, 137.3, 134.3, 134.1, 134.0, 131.2, 128.7, 128.3, 126.3, 116.0, 111.2, 109.3, 97.5, 82.6, 82.5, 80.8, 79.3, 79.0, 77.1, 56.6, 43.5, 41.7, 36.3, 35.1, 34.8, 30.4, 29.4, 28.5, 27.5, 27.4, 22.9, 17.5, 16.0. IR (neat): ν_{max} = 3454, 3076, 2981, 2933, 1732, 1651, 1604, 1456, 1379, 1223, 1153, 1097, 1028, 991, 887, 731, 584 cm^{-1}. MALDI-TOF MS: 625 (M$^+$+Na). HRMS (FAB) calcd. for $C_{35}H_{54}O_8Na$ (M$^+$+Na) 625.3716, found 625.3731. $[\alpha]^{25}_D$ –73.8 (*c* 0.97, $CHCl_3$).



21 **22**

Lactone **22**

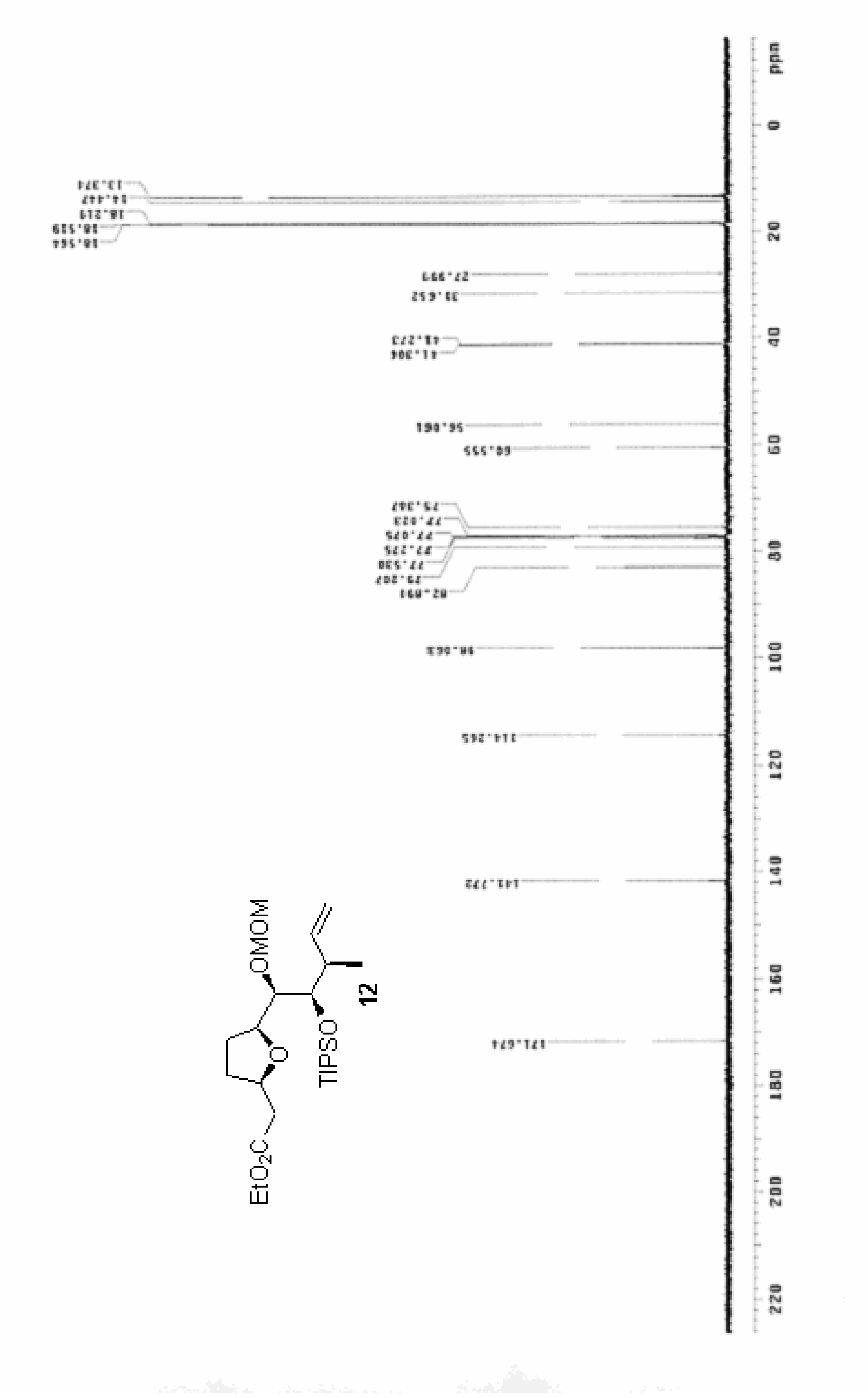
Ethoxyacetylene (40% in Hex, 0.030 mL, 0.13 mmol) was added to a solution of the *seco* acid **21** (52.6 mg, 0.0873 mmol) and [RuCl$_2$(*p*-cymene)]$_2$ (1.0 mg, 0.0016 mmol) in toluene (8 mL) at 0 ^{o}C. The mixture was warmed to r.t. and stirred for 30 min. The dark red solution was filtered through a pad of silica gel, and silica gel was washed with dry Et$_2$O (50 mL) under N$_2$ atmosphere. The filtrate was concentrated under reduced pressure. The crude ethoxyvinyl ester was dissolved in toluene (3 mL) and added to a solution of CSA (2.0 mg, 0.0087 mmol) in toluene (14 mL). The reaction mixture was heated to 50 ^{o}C for 2 h, filtered through a pad of silica gel, and concentrated. The residue was purified by flash column chromatography (Hex-EtOAc, 10:1) to afford lactone **22** (22.5 mg, 44%). R_f 0.45 (Hex-EtOAc, 4:1). ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.30 (dd, *J*=14.9, 10.8 Hz, 1 H), 6.19 (dd, *J*=14.9, 10.8 Hz, 1 H), 6.04 (d, *J*=15.7 Hz, 1 H), 5.68 - 5.76 (m, 2 H), 5.55 (dd, *J*=14.7, 9.3 Hz, 2 H), 5.31 (ddd, *J*=15.2, 8.6, 1.5 Hz, 1 H), 5.12 (d, *J*=7.1 Hz, 1 H), 4.98 (s, 1 H), 4.87 (s, 1 H), 4.73 (s, 1 H), 4.70 (s, 1 H), 4.67 (d, *J*=6.8 Hz, 1 H), 4.64 (dd, *J*=10.3, 1.2 Hz, 1 H), 4.02 (t, *J*=8.5 Hz, 1 H), 3.98 (t, *J*=8.5 Hz, 1 H), 3.72 (dd, *J*=8.9, 1.3 Hz, 1 H), 3.52 (td, *J*=9.3, 6.4 Hz, 1 H), 3.36 (s, 3 H), 3.24 - 3.32 (m, 2 H), 2.77 (d, *J*=7.1 Hz, 2 H), 2.30 - 2.39 (m, 3 H), 1.86 - 1.98 (m, 2 H), 1.82 (dd, *J*=14.3, 11.9 Hz, 1 H), 1.71 (s, 3 H), 1.62 - 1.70 (m, 1 H), 1.46 - 1.54 (m, 2 H), 1.43 (s, 3 H), 1.43 (s, 3 H), 1.26 - 1.32 (m, 1 H), 1.24 (d, *J*=6.6 Hz, 3 H), 1.11 - 1.19 (m, 1 H), 0.91 (d, *J*=6.6 Hz, 3 H). ^{13}C NMR (75 MHz, CDCl$_3$): δ 174.5, 144.5, 144.1, 138.5, 135.8, 135.4, 133.3, 131.3, 127.9, 127.7, 125.4, 115.7, 110.8, 109.0, 97.2, 83.0, 82.3, 80.7, 79.2, 78.0, 77.7, 77.2, 56.3, 44.0, 41.3, 35.8, 32.1, 31.6, 28.8, 27.7, 27.1, 27.1, 22.5, 17.1, 14.7. IR (neat): ν_{max} = 3443, 3063, 3078, 2981, 2929, 1732, 1653, 1604, 1454, 1377, 1238, 1171, 1090, 1030, 991, 885, 758, 580 cm^{-1}. MALDI-TOF MS: 607 (M$^+$+Na). HRMS (FAB) calcd. for $C_{35}H_{52}O_7Na$ (M$^+$+Na) 607.3611, found 607.3627. $[\alpha]^{25}_{D}$ –178.7 (*c* 0.46, CHCl$_3$).



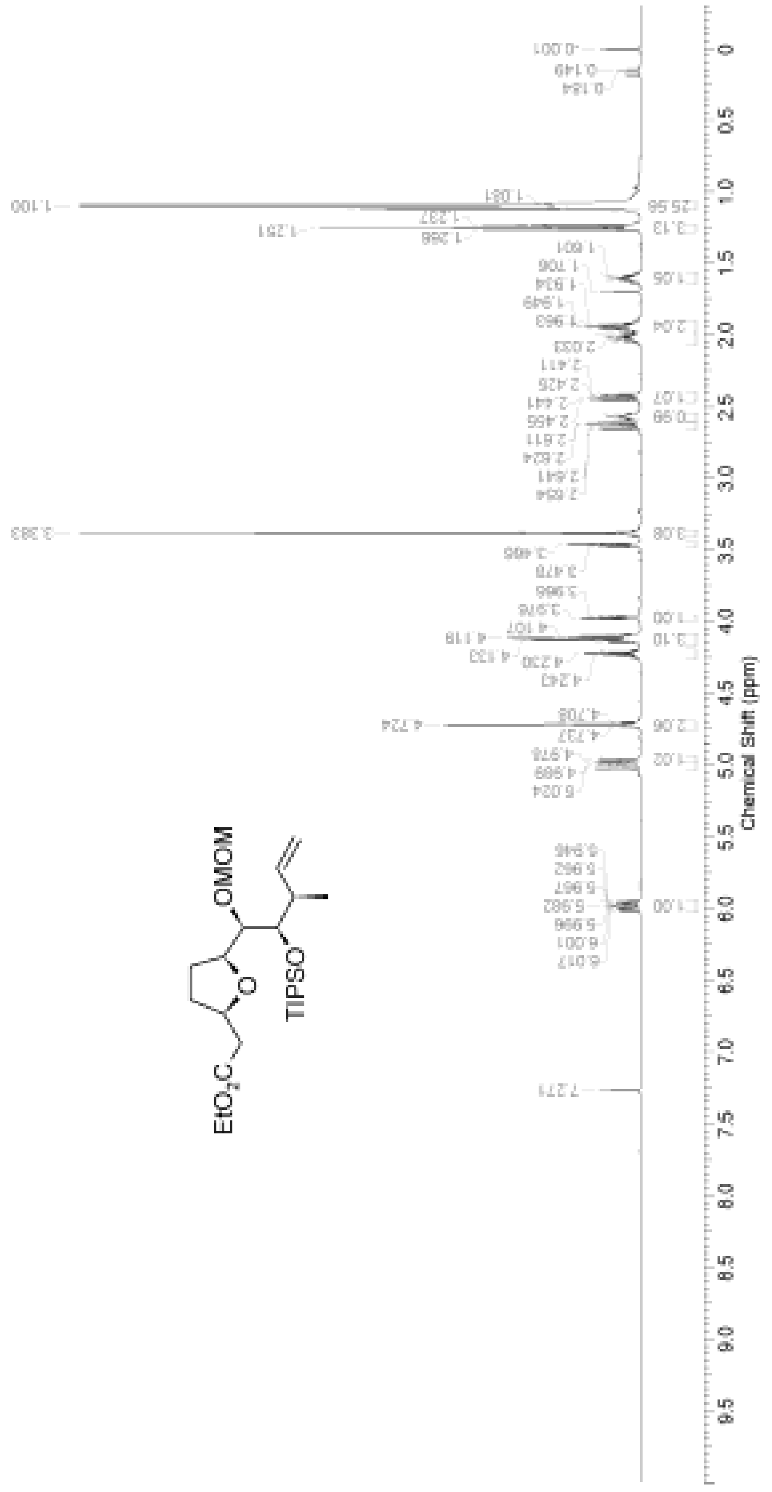
22 **1**

Amphidinolide E (**1**)

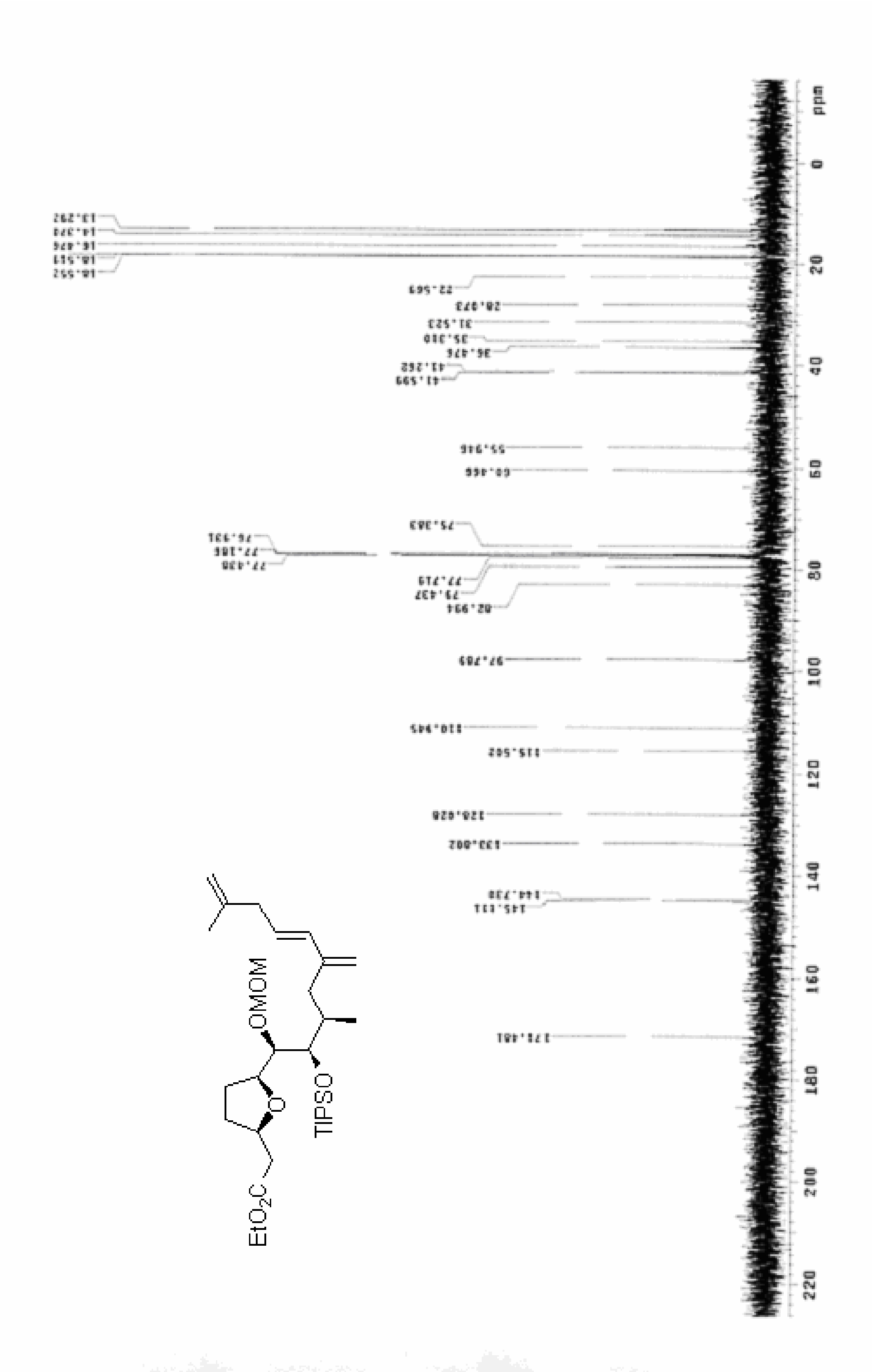
Hydrochloric acid solution (4 N, 0.3 mL) was added dropwise to a solution of lactone **22** (22.5 mg, 0.0385 mmol) in MeOH (3.6 mL). After 1 h, MeOH (0.5 mL) and 4 N HCl solution (0.2 mL) was added to the mixture. After 2 h, MeOH (0.5 mL) and 4 N HCl solution (0.1 mL) was added to the mixture. After 1 h, the mixture was diluted with Et_2O (10 mL) and carefully quenched by sat. $NaHCO_3$ solution (5 mL). The aqueous phase was extracted with EtOAc (10 mL × 3), and the combined organic phase was dried over $MgSO_4$, filtered, and concentrated. The residue was purified by column chromatography ($CHCl_3$-MeOH, 100:1) to afford amphidinolide E (**1**, 14.8 mg, 77%). R_f 0.25 ($CHCl_3$-MeOH, 20:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.23 (dd, *J*=14.7, 10.7 Hz,1 H), 6.15 (dd, *J*=14.8, 10.8 Hz, 1 H), 6.05 (d, *J*=15.7 Hz, 1 H), 5.69 (dt, *J*=15.7, 6.9 Hz, 1 H), 5.62 - 5.66 (m, 1 H), 5.62 (dd, *J*=14.5, 9.7 Hz, 1 H), 5.53 (dd, *J*=14.9, 9.1 Hz, 1 H), 5.27 (dd, *J*=15.3, 8.4 Hz, 1 H), 4.98 (s, 1 H), 4.87 (s, 1 H), 4.75 (s, 1 H), 4.71 (s, 1 H), 4.66 (d, *J*=9.6 Hz, 1 H), 3.94 (t, *J*=8.5 Hz, 1 H), 3.88 (t, *J*=8.9 Hz, 1 H), 3.71 (d, *J*=7.5 Hz, 1 H), 3.56 (dt, *J*=7.2 Hz, 1 H), 3.38 - 3.44 (m, 1 H), 3.23 - 3.29 (m, 1 H), 2.73 - 2.83 (m, 2 H), 2.40 (dd, *J*=13.6, 2.1 Hz,1 H), 2.23 - 2.33 (m, 2 H), 1.84 - 1.92 (m, 1 H), 1.75 - 1.82 (m, 2 H), 1.72 (s, 3 H), 1.57 - 1.64 (m, 1 H), 1.43 - 1.50 (m, 1 H), 1.36 - 1.43 (m, 1 H), 1.28 - 1.35 (m, 2 H), 1.25 (d, *J*=6.7 Hz, 3 H), 0.92 (d, *J*=6.7 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 174.4, 144.7, 144.0, 135.1, 134.9, 134.1, 133.3, 131.4, 131.4, 129.4, 127.9, 115.7, 110.7, 79.9, 78.3, 78.1, 77.6, 77.2, 73.2, 44.1, 41.3, 36.1, 32.6, 32.3, 29.9, 29.0, 27.1, 22.5, 17.5, 15.4. IR (neat): ν_{max} = 3417, 3076, 2925, 2854, 2731, 1865, 1732, 1668, 1606, 1456, 1377, 1319, 1248, 1169, 1088, 1047, 991, 889 cm^{-1}. MS *m/z* (CI, relative intensity): 501 (M^++1, 18), 483 (100), 465 (93), 449 (21), 401 (18), 345 (18), 291 (22), 257 (12), 179 (22), 121 (12), 109 (13), 71 (10), 57 (12). HRMS (CI) calcd. for $C_{30}H_{45}O_6$ (M^++1) 501.3216, found 501.3213. $[\alpha]^{30}_D$ –131.1 (*c* 0.21, $CHCl_3$).



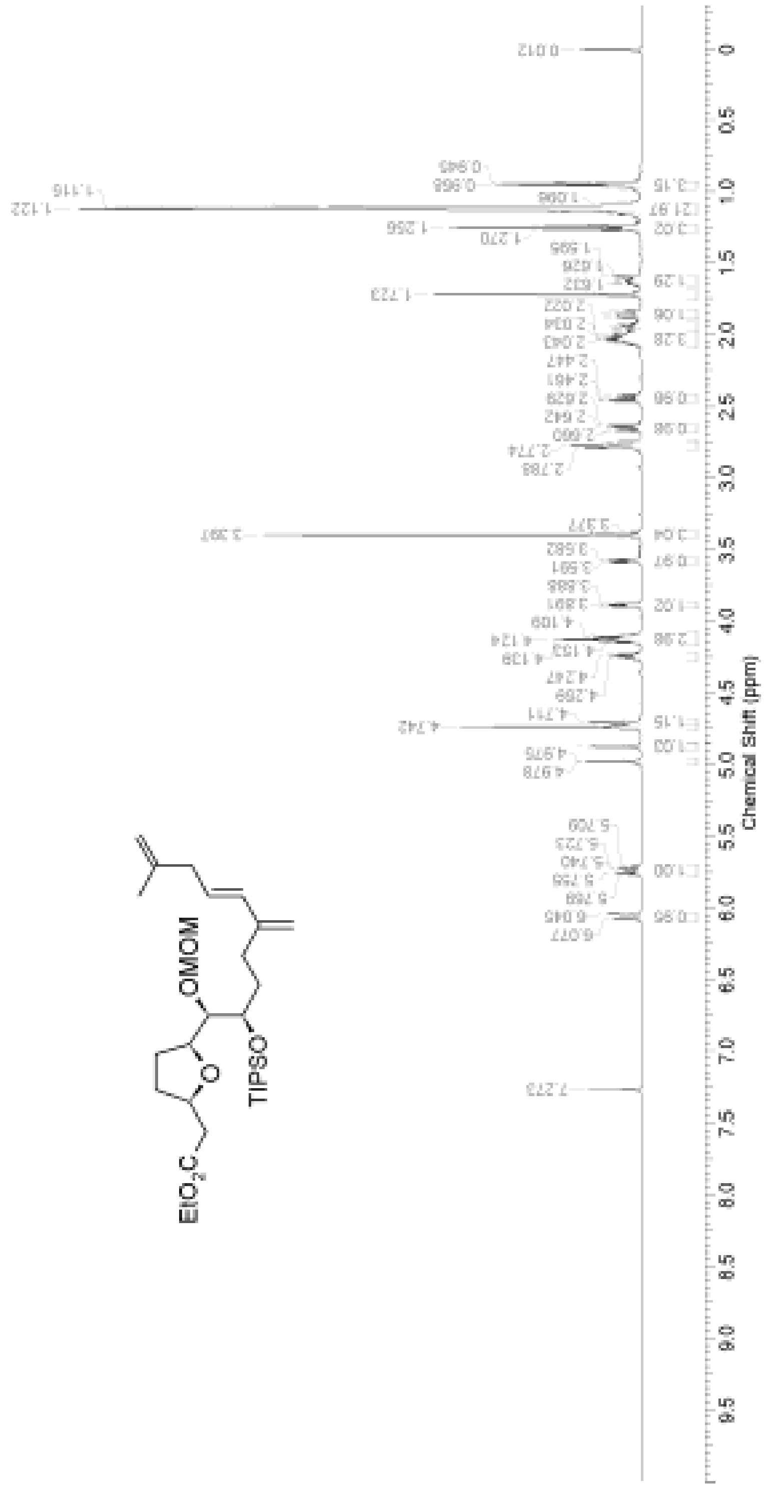
^{13}C-NMR (125 MHz, CDCl$_3$) of **12**



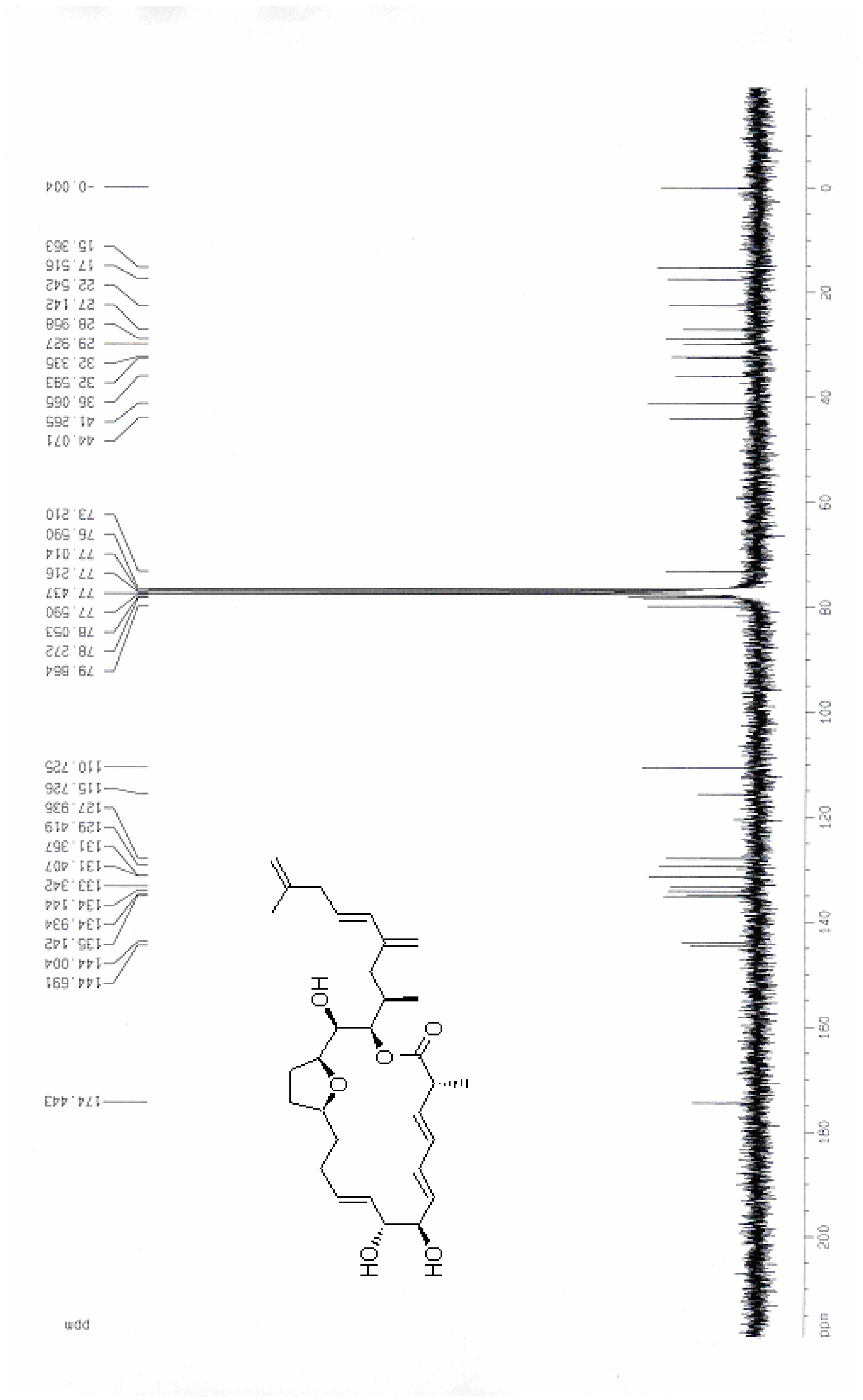
^{1}H-NMR (500 MHz, CDCl$_3$) of **12**



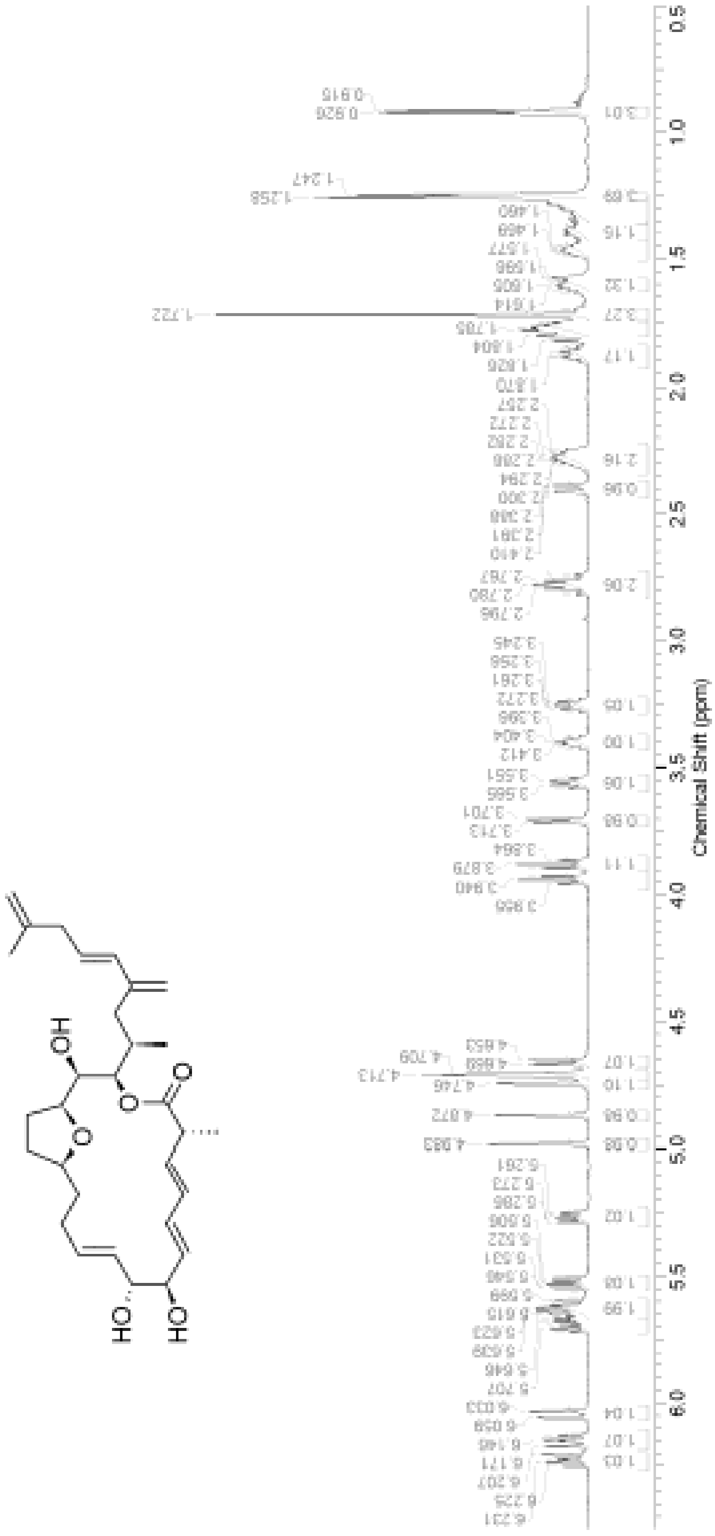
^{13}C-NMR (125 MHz, CDCl$_3$) of **16**



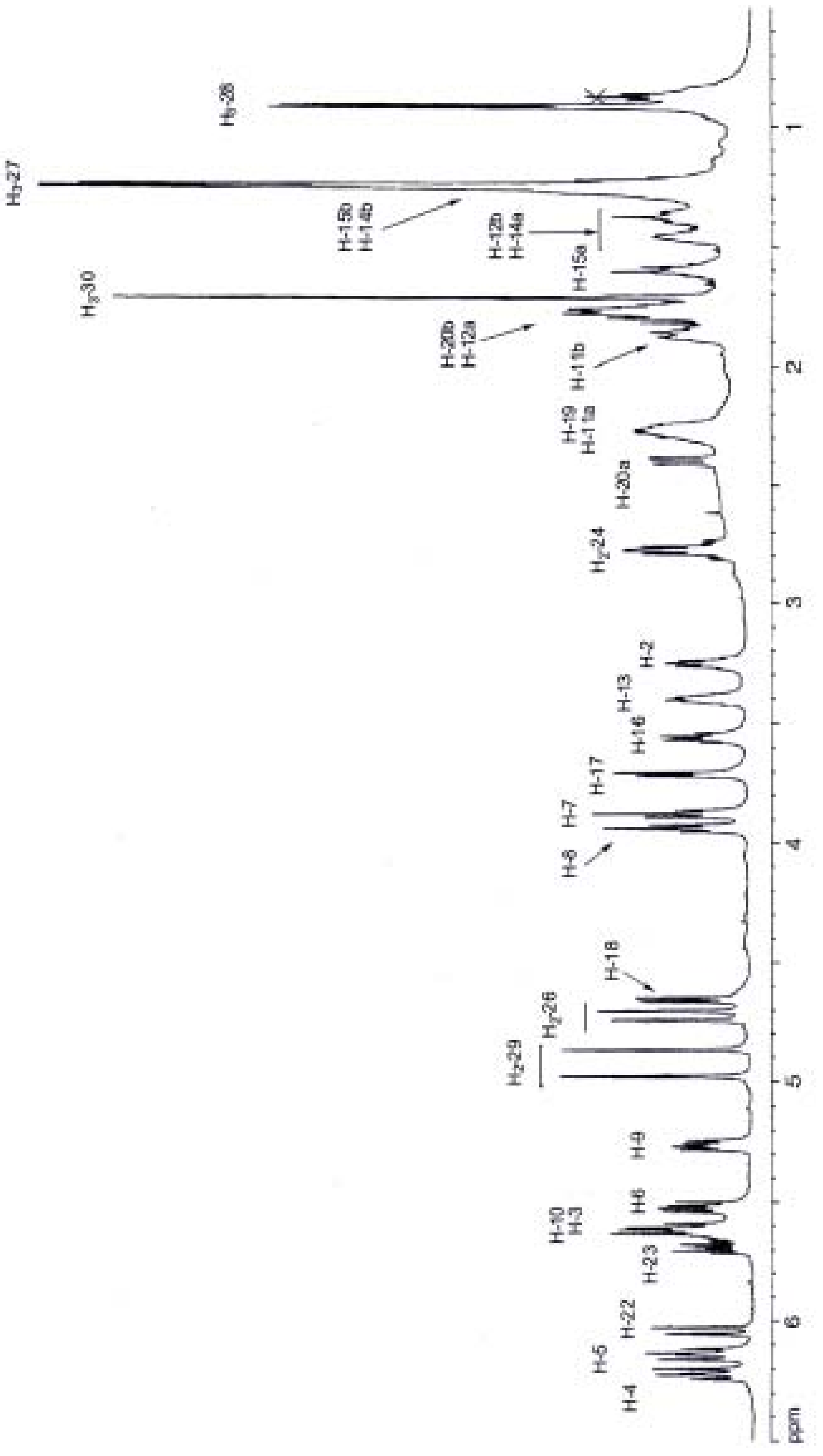
^{1}H-NMR (500 MHz, CDCl3) of **16**



^{13}C-NMR (75 MHz, $CDCl_3$) of the synthetic sample of amphidinolide E (**1**)



^{1}H-NMR (600 MHz, CDCl$_3$) of the synthetic sample of amphidinolide E (**1**)



^{1}H-NMR (600 MHz, CDCl$_3$) of the natural sample of amphidinolide E (**1**)[1]

Comparison of ^{13}C NMR data for synthetic and natural samples of amphidinolide E (**1**)

Natural sample ($CDCl_3$)[1]	Synthetic sample ($CDCl_3$)
δ	
174.4	174.4
144.7	144.7
144.0	144.0
135.1	135.1
134.9	134.9
134.2	134.1
133.3	133.3
131.4	131.4
131.4	131.4
129.4	129.4
127.9	127.9
115.7	115.7
110.7	110.7
79.9	79.9
78.3	78.3
78.0	78.1
77.6	77.6
76.7	76.6
73.2	73.2
44.1	44.1
41.3	41.3
36.1	36.1
32.6	32.6
32.3	32.3
29.9	29.9
29.0	29.0
27.1	27.1
22.5	22.5
17.5	17.5
15.4	15.4