Supporting Information for:

Asymmetric Total Synthesis of (–)-Amphidinolide V through Effective Combinations of Catalytic Transformations

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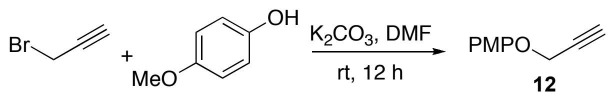
CONTENTS

General

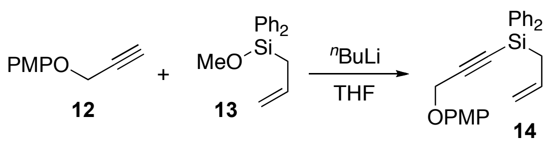
Unless otherwise stated, reactions were performed under a nitrogen atmosphere using freshly dried solvents. Tetrahydrofuran (THF) and diethyl ether (Et_2O) were dried by distillation from sodium and benzophenone. Methylene chloride (CH_2Cl_2), 1,2-dichloroethane (DCE), toluene (PhMe), triethylamine (Et_3N), acetonitrile (CH_3CN), dimethylformamide (DMF), and dimethylsulfoxide (DMSO), were dried by distillation from calcium hydride.[1] All reactions were monitored by thin-layer chromatography using Silicycle silica gel 60 Å F-254 pre-coated plates (0.25 mm) and were visualized by UV, *p*-anisaldehyde, or $KMnO_4$ staining. Flash column chromatography was performed using silica gel 60 Å (32–63 mesh) purchased from Sorbent Technologies. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance DRX-500 or Bruker AV-500 spectrometers. ^1H and ^{13}C chemical shifts are referenced to internal solvent resonances ($CHCl_3$ ^1H, $\delta = 7.26$; $CDCl_3$ ^{13}C, $\delta = 77.0$) and reported relative to $SiMe_4$; multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), qn (quintet), m (multiplet) and brs (broad signal). Coupling constants, *J*, are reported in Hertz. Electrospray ionization (ESI) mass spectra were recorded on a Micromass LCT equipped with a time-of-flight analyzer at the Mass Spectrometry Laboratory in the University of Illinois at Urbana-Champaign. Optical rotations were measured on a Jasco P-2000 polarimeter at the Illinois Institute of Technology using a 100 mm path-length cell at 589 nm.

EXPERIMENTAL DETAILS

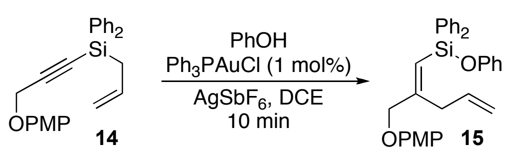
Synthesis of Silane 7



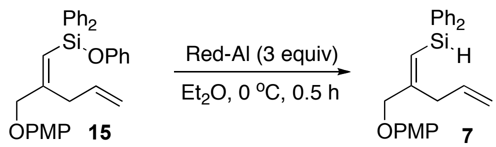
To a stirred suspension of 4-methoxyphenol (1.75 g, 14.1 mmol) and potassium carbonate (5.0 g, 36.2 mmol) in DMF (20 mL) was added propargyl bromide (1.9 mL, 16 mmol, 80% solution in toluene) and the reaction mixture was stirred for 12 h at rt. The reaction mixture was quenched with H_2O (200 mL) and extracted with Et_2O (3 x 50 mL). Combined extracts were washed with NaCl solution (10 wt.%, 2 x 50 mL), dried over $MgSO_4$, and solvent was removed under vacuum. The residue was purified by flash column chromatography (gradient elution 20:1 → 15:1 hexanes:EtOAc) to afford ether **12** (2.28 g, quantitative) as a yellow liquid. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 6.93 (d, J = 8.8 Hz, 2H), 6.85 (d, J = 8.8 Hz, 2H), 4.64 (d, J = 2.2 Hz, 2H), 3.77 (s, 3H), 2.51 (t, J = 2.4 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 154.5, 151.7, 116.1, 114.6, 78.9, 75.3, 56.6, 55.7. Both ^{1}H and ^{13}C NMR spectra are matched with reported.[2]



To a solution of propargyl ether **12** (4.60 g, 28.4 mmol) in 100 mL of THF was added ^{n}BuLi (11.4 mL, 2.5 M in hexanes, 28.4 mmol) at -78 °C. The resultant solution was warmed to 0 °C and stirred for 30 min. It was then cooled to -30 °C and silane **13**[3] (7.22 g, 28.4 mmol) was added. The reaction mixture was warmed to room temperature, stirred for 8 h, and quenched with saturated NH_4Cl solution. The reaction mixture was extracted with EtOAc (3 × 100 mL), combined extracts were dried over $MgSO_4$, and solvent was removed under vacuum. The residue was purified by flash column chromatography (gradient elution 100:1 → 50:1 hexanes:EtOAc) to afford alkynylsilane **14** (9.17 g, 84%) as a colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.64–7.57 (m, 4H), 7.44–7.39 (m, 2H), 7.39–7.33 (m, 4H), 7.00 (d, J = 9.0 Hz, 2H), 6.86 (d, J = 9.0 Hz, 2H), 5.86–5.75 (m, 1H), 4.98–4.87 (m, 2H), 4.77 (s, 2H), 3.79 (s, 3H), 2.16 (d, J = 7.7 Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 154.5, 151.7, 134.9, 133.1, 132.7, 129.9, 127.9, 116.7, 115.3, 114.5, 104.8, 87.5, 57.7, 55.7, 21.8; **HRMS** (ESI) calcd for $C_{25}H_{25}O_2Si$ $[M+H]^+$: 385.1624, found 385.1627.

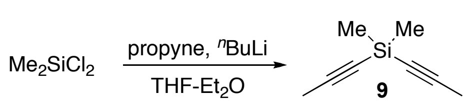


Anhydrous phenol was prepared by distillation from the benzene solution to remove the water/benzene azeotrope and the excess of benzene, followed by distillation of the residue under reduced pressure (bp = 85–86 °C / 20 mm). To a solution of alkynylsilane **14** (4.46 g, 11.6 mmol) and phenol (1.15 g, 12.18 mmol, 1.05 equiv) in 115 mL of DCE was added a pre-generated solution of $Ph_3PAuSbF_6$ (1 mol%), which was prepared by mixing stoichiometric amounts of Ph_3PAuCl (57.5 mg, 0.11 mmol) and $AgSbF_6$ (39.9 mg, 0.11 mmol) in DCE (1 mL) followed by filtration through a cotton plug to remove precipitated AgCl. The resultant brown solution was stirred at room temperature for 10 min and solvent was removed under reduced pressure. The crude product was purified by gravity column chromatography (gradient elution 100:1 → 35:1 hexanes:EtOAc) to afford vinyl silane **15** as a colorless oil (4.53 g, 82%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.74–7.67 (m, 4H), 7.48–7.35 (m, 6H), 7.17 (t, J = 7.9 Hz, 2H), 6.94 (t, J = 7.3 Hz, 1H), 6.91–6.82 (m, 6H), 6.26 (s, 1H), 5.53–5.41 (m, 1H), 4.94–4.85 (m, 2H), 4.53 (s, 2H), 3.80 (s, 3H), 3.00 (d, J = 6.8 Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 157.2, 154.9, 154.0, 152.6, 134.8, 134.6, 130.1, 129.3, 128.0, 121.4, 119.9, 118.4, 117.2, 116.0, 114.6, 71.8, 55.7, 38.4; **HRMS** (ESI) calcd for $C_{31}H_{31}O_3Si$ $[M+H]^+$: 479.2042, found 479.2062.



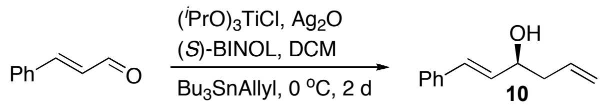
To a solution of phenoxysilane **15** (4.53 g, 9.46 mmol) in 100 mL of Et_2O was added Red-Al (8.6 mL, 65 wt.%, 3.3 M in PhMe) at 0 °C. The reaction mixture was stirred at 0 °C for 30 min and quenched by addition of Na_2SO_4•10 H_2O. The resultant mixture was stirred for additional 10 min and $MgSO_4$ was added. Formed suspension was stirred for 30 min, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (gradient elution 50:1 → 20:1 hexanes:EtOAc) to give silane **7** as a colorless oil (3.27 g, 89%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.60–7.53 (m, 4H), 7.44–7.32 (m, 6H), 6.92–6.81 (m, 4H), 6.11 (d, J = 5.5 Hz, 1H), 5.79–5.68 (m, 1H), 5.33 (d, J = 5.1 Hz, 1H), 5.09–4.99 (m, 2H), 4.53 (s, 2H), 3.79 (s, 3H), 3.09 (d, J = 7.0 Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 155.3, 154.0, 152.7, 135.3, 135.0, 134.1, 129.6, 128.0, 118.7, 117.0, 115.9, 114.6, 72.2, 55.7, 37.7; **HRMS** (ESI) calcd for $C_{25}H_{27}O_2$ Si $[M+H]^+$: 387.1780, found 387.1789.

Synthesis of Allylic Alcohol 6



Dichlorodimethylsilane was redistilled from CaH_2 prior to use. Propyne (bp = -23.2 °C) was condensed in the round bottom flask at -78 °C to the 6.5 mL volume (4.59 g, 114.5 mmol). Precooled to -78 °C THF-Et_2O mixture (1:1, V = 120 mL) was added to the reaction flask via cannula. Under vigorous stirring ^{n}BuLi (45.6 mL, 2.5 M in hexanes, 114 mmol) was slowly added to the resultant solution producing white precipitate of lithium acetylide. The reaction mixture was slowly warmed to 0 °C and stirred for 1 h. It was again cooled to -30 °C and dichlorodimethylsilane (4.67 mL, 5.0 g, 38.7 mmol) was added. The reaction mixture was warmed to rt and then refluxed for additional 5 h. After this time the reaction mixture was cooled to rt and quenched with saturated NH_4Cl solution. Layers were separated and the aqueous layer was extracted with Et_2O (2 × 10 mL). Combined organic extracts were dried over $MgSO_4$ and solvent was removed under vacuum (cold rotavapor bath). The crude material was purified by vacuum distillation (bp = 80 °C / 20 mm) to give silane **9** as a colorless oil (4.82 g, 91%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ

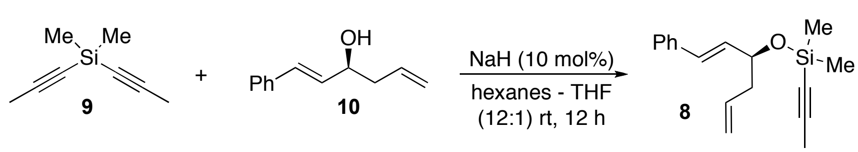
1.89 (s, 6H), 0.27 (s, 6H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 103.9, 81.0, 5.0, 0.6. Both ^{1}H and ^{13}C NMR spectra are matched with reported.[4]



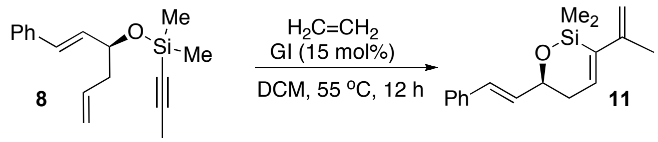
Alcohol **10** was prepared via modified reported method.[5] For the efficiency of overall procedure commercial Ag_2O has to be rigorously dried by heating at 140 °C in high vacuum (0.5 mm) for 2 days (time is not optimized). After that Ag_2O can be stored in the glovebox.

Preparation of the catalyst: Solution of (*i*-PrO)$_3$TiCl (1.5 mL, 1 M in hexanes, 1.5 mmol) was diluted with 30 mL of freshly redistilled CH_2Cl_2. To the resultant solution was added Ag_2O (173.8 mg, 0.75 mmol) and the reaction mixture was stirred for 7 h at room temperature under exclusion of light. After this time precipitate changed color from brown to grey. (*S*)-BINOL (430 mg, 1.5 mmol) was then added and the reaction mixture was stirred for 2 h producing orange-red solution. At this point TLC analysis indicated only small amount (< 5%) of free (*S*)-BINOL in the reaction mixture.

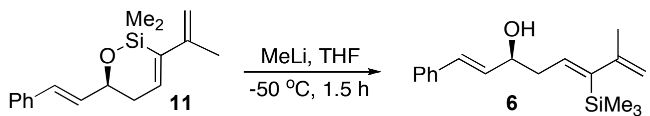
Asymmetric allyliation: The generated solution of catalyst was cooled to -15 °C and *trans*-cinnamaldehyde (945 µL, 7.5 mmol) and allyltributyltin (2.6 mL, 8.3 mmol) were added sequentially. The reaction mixture was warmed to 0 °C and kept at this temperature for 2 days without stirring. The reaction mixture was quenched with saturated $NaHCO_3$ solution and extracted with CH_2Cl_2 (2 x 20 mL). Combined organic extracts were dried over $MgSO_4$ and concentrated. The residue was purified by gravity column chromatography (gradient elution 15:1 → 5:1 hexanes:EtOAc) to afford alcohol **10** (1.24 g, 95%, >95% *ee*) as a colorless liquid. The enatiomeric excess of product was determined by derivatization with (–)-chloromenthoxydiphenylsilane according to the reported procedure.[6] **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.41–7.37 (m, 2H), 7.35–7.30 (m, 2H), 7.27–7.22 (m, 1H), 6.62 (d, *J* = 15.9 Hz, 1H), 6.25 (dd, *J* = 15.9 Hz, *J* = 6.4 Hz, 1H), 5.92–5.82 (m, 1H), 5.23–5.15 (m, 2H), 4.40–4.34 (m, 1H), 2.49–2.35 (m, 2H), 1.85–1.81 (m (OH), 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 136.6, 134.0, 131.6, 130.3, 128.5, 127.6, 126.5, 118.5, 71.7, 42.0. Both ^{1}H and ^{13}C NMR spectra are matched with reported.[7]



Silane **9** (2.35 g, 17.22 mmol) and alcohol **10** (1.50 g, 8.61 mmol) were dissolved in hexanes-THF mixture (12:1, 150 mL). Sodium hydride (20.6 mg, 0.86 mmol) was added, and the reaction mixture was stirred at room temperature overnight. The solvent was evaporated on rotavapor and excess of silane was distilled from residue in cold trap (-78 °C) under high vacuum (0.4 mm). The crude product was dissolved in hexanes (10 mL) and filtered through short layer of silicagel. The solvent was evaporated under vacuum to afford silyl ether **8** (2.24 g, 96%) as a pale yellow liquid. Product contained ~5% of inseparable symmetrical silaketal. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.41–7.37 (m, 2H), 7.34–7.29 (m, 2H), 7.26–7.21 (m, 1H), 6.56 (d, *J* = 15.9 Hz, 1H), 6.23 (dd, *J* = 15.9 Hz, *J* = 6.4 Hz, 1H), 5.92–5.81 (m, 1H), 5.14–5.06 (m, 2H), 4.53–4.47 (m, 1H), 2.49–2.35 (m, 2H), 1.89 (s, 3H), 0.28 (s, 3H), 0.25 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 137.0, 134.7, 131.9, 129.8, 128.5, 127.4, 126.5, 117.0, 103.6, 82.2, 73.9, 42.6, 4.8, 1.0, 0.8; **HRMS** (ESI) calcd for $C_{17}H_{22}OSiNa$ $[M+Na]^+$: 293.1338, found 293.1340.

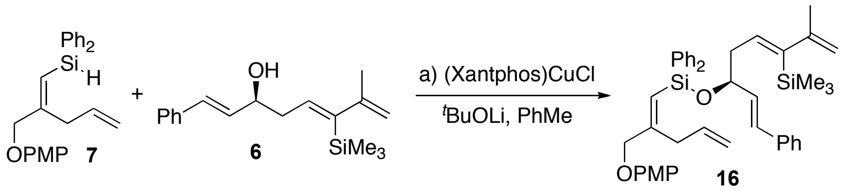


To a solution of silyl ether **8** (2.23 g, 8.25 mmol) in 825 mL of CH_2Cl_2 (0.01 M) was added Grubbs 1st generation catalyst $(PCy_3)_2Cl_2Ru{=}CHPh$ (1.02 g, 1.23 mmol, 15 mol%). Ethylene was then passed through the solution for 25 min followed by argon for 30 min to remove excess of ethylene. The reaction mixture was refluxed at 55 °C for 12 h and solvent was evaporated under reduced pressure. The residue was quickly purified by flash column chromatography (50:1 hexanes:EtOAc) to afford red-brown liquid. In order to remove ruthenium by-products generated during the reaction the crude material was dissolved in 10 mL of CH_2Cl_2 and 1 mL of DMSO was added.[8] Resultant solution was stirred at rt for 12 h and concentrated under reduced pressure. The residue was purified by gravity column chromatography (gradient elution 50:1 → 30:1 hexanes:EtOAc) to afford siloxene **11** (1.97 g, 88%) as a yellow liquid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.43–7.39 (m, 2H), 7.35–7.29 (m, 2H), 7.26–7.22 (m, 1H), 6.68–6.62 (m, 2H), 6.31 (dd, J = 15.8 Hz, J = 5.9 Hz, 1H), 4.99 (s, 1H), 4.83 (s, 1H), 4.60–4.55 (m, 1H), 2.51–2.37 (m, 2H), 1.91 (s, 3H), 0.40 (s, 3H), 0.38 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 144.5, 140.1, 139.7, 136.8, 131.6, 129.8, 128.4, 127.4, 126.5, 113.8, 71.3, 36.5, 20.8, 0.3, 0.1; **HRMS** (ESI) calcd for $C_{17}H_{23}OSi$ $[M+H]^+$: 271.1518, found 271.1503.



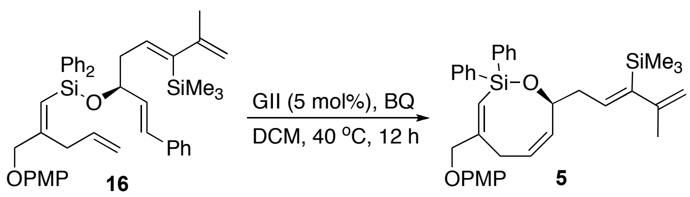
To a solution of siloxene **11** (976 mg, 3.61 mmol) in 35 mL of THF was added MeLi (2.7 mL, 1.6 M in Et_2O, 4.33 mmol, 1.2 equiv) at -50 °C and the reaction mixture was stirred at this temperature for 1.5 h. The reaction mixture was quenched cold with MeOH followed by saturated NH_4Cl solution and extracted with EtOAc (3 x 10 mL). Combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography (gradient elution 50:1 → 20:1 hexanes:EtOAc) to afford alcohol **6** (2.28 g, 80%) as a colorless liquid. $[\alpha]_D^{25} = -5.8°$ (0.08, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.42–7.37 (m, 2H), 7.35–7.30 (m, 2H), 7.27–7.22 (m, 1H), 6.61 (d, J = 16.0 Hz, 1H), 6.25 (dd, J = 16.0 Hz, J = 6.4 Hz, 1H), 6.04 (t, J = 7.4 Hz, 1H), 4.71–4.67 (m, 1H), 4.50–4.48 (m, 1H), 4.40–4.33 (m, 1H), 2.57–2.35 (m, 2H), 1.78 (s, 3H), 1.77–1.72 (brs, 1H), 0.19 (s, 9H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 151.0, 149.0, 137.1, 136.7, 131.7, 130.4, 128.6, 127.7, 126.5, 109.5, 72.6, 39.7, 24.7, 0.6; **HRMS** (ESI) calcd for $C_{18}H_{27}OSi$ $[M+H]^+$: 287.1831, found 287.1826.

Dehydrogenative Coupling and Synthesis of Epoxyaldehyde 3



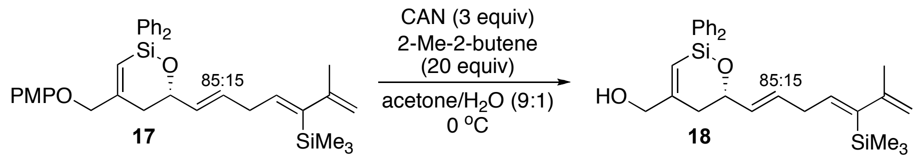
Preparation of the catalyst. (Xantphos)CuCl was prepared analogously to the reported procedure for synthesis of (Xantphos)CuI.[9] To a suspension of dry CuCl (108.9 mg, 1.1 mmol) in CH_2Cl_2 (10 mL) was added Xantphos (578.6 mg, 1.0 mmol) and resultant clear solution was stirred for 10 min. The solvent was removed under vacuum and the precipitated solid was triturated in dry and degassed acetonitrile (3 mL). The suspension was vigorously stirred for 4 h and filtered using Schlenk filter funnel under Ar atmosphere. The wet cake was washed with acetonitrile (3 x 5 mL) and dried under vacuum to afford an off-white powder (631.8 mg, 93%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.52 (d, J = 7.3 Hz, 2H), 7.45–7.37 (m, 8H), 7.32–7.25 (m, 4H), 7.24–7.18 (m, 8H), 7.08 (t, J = 7.7 Hz, 2H), 6.60–6.53 (m, 2H), 1.67 (s, 6H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 154.5 (t, J = 6.0 Hz), 133.7 (t, J = 7.9 Hz), 133.1, 131.4 (t, J = 17.6 Hz), 129.7, 128.5 (t, J = 5.1 Hz), 126.6, 124.7, 119.9 (t, J = 13.9 Hz), 35.7, 28.3. An Ar-C cannot be identified because of overlapping. Both ^{1}H and ^{13}C NMR spectra are matched with reported.[10]

Dehydrogenative coupling: To a solution of alcohol **6** (1.0 g, 3.49 mmol) and silane **7** (1.48 g, 3.84 mmol, 1.1 equiv) in 100 mL of toluene was added (Xantphos)CuCl (118.3 mg, 0.175 mmol, 5 mol%) and the reaction flask was placed in the preheated to 85 °C oil bath. Solution of *t*-BuOLi (195.6 mg, 2.44 mmol, 0.7 equiv) in 30 mL of toluene was slowly added to the reaction mixture via syringe pump over 5.5 h. After this time the reaction mixture was cooled to rt and quenched with saturated NH_4Cl solution. Layers were separated and water layer was extracted with EtOAc (3 x 10 mL). Combined organic extracts were dried over $MgSO_4$, concentrated under reduced pressure, and the residue was quickly purified by flash column chromatography to afford pale yellow oil. In order to remove unreacted silane **7**, it was converted to silanol[11] as follows: the crude product was dissolved in 15 mL of CH_3CN and $[RuCl_2(p\text{-cymene})]_2$ (21.4 mg, 0.035 mmol, 10 mol% relative to excess of silane used) was added followed by addition of 100 μL of H_2O. The reaction mixture was heated to 80 °C and stirred for 2 h. The reaction mixture was then cooled to rt and solvent was evaporated under vacuum. The residue was purified by gravity column chromatography (gradient elution 150:1 → 50:1 hexanes:EtOAc) to afford silyl ether **16** (2.27 g, 97%) as a colorless oil. $[\alpha]_D^{25}$ = –28.5° (0.97, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.66–7.61 (m, 4H), 7.43–7.31 (m, 6H), 7.30–7.25 (m, 2H), 7.24–7.19 (m, 3H), 6.86–6.79 (m, 4H), 6.29 (d, J = 15.9 Hz, 1H), 6.19 (d, J = 1.5 Hz, 1H), 6.13 (ddd, J = 15.9 Hz, J = 7.1 Hz, J = 1.3 Hz, 1H), 6.02 (dt, J = 7.3 Hz, J = 1.3 Hz, 1H), 5.56–5.47 (m, 1H), 4.92–4.84 (m, 2H), 4.66 (s, 1H), 4.49–4.41 (m, 4H), 3.78 (s, 3H), 2.97 (d, J = 7.0 Hz, 2H), 2.61–2.53 (m, 1H), 2.50–2.42 (m, 1H), 1.74 (s, 3H), 0.13 (d, J = 1.4 Hz, 9H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 155.8, 153.9, 152.7, 151.2, 147.0, 138.0, 136.9, 135.9, 135.7, 135.12, 135.05, 134.92, 132.0, 130.3, 129.79, 129.75, 128.4, 127.8, 127.4, 126.4, 120.1, 117.0, 115.9, 114.5, 109.3, 74.8, 72.0, 55.7, 40.3, 38.3, 24.7, 0.5; **HRMS** (ESI) calcd for $C_{43}H_{50}O_3Si_2Na$ $[M+Na]^+$: 693.3196, found 693.3188.

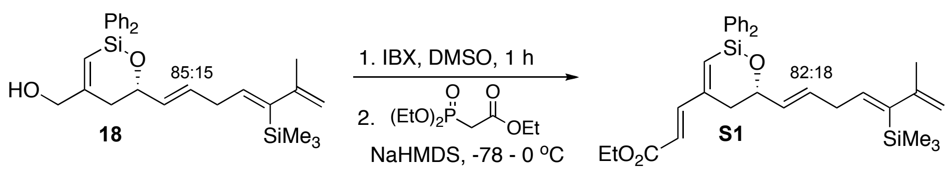


To a solution of vinyl silane **16** (1.59 g, 2.37 mmol) in CH_2Cl_2 (475 mL, 0.005 M) were added and Grubbs 2nd generation catalyst (SImes)$(PCy_3)Cl_2Ru$=CHPh (100.5 mg, 0.118 mmol, 5 mol%) and 1,4-benzoquinone (51.2 mg, 0.47 mmol, 20 mol%). The reaction mixture was refluxed at 40 °C for 12 h and then concentrated under reduced pressure. The residue was purified by gravity column chromatography (gradient elution 150:1 → 50:1 hexanes:EtOAc) to afford eight-membered siloxacycle **5** as a colorless oil (1.29 g, 96%). $[\alpha]_D^{25} = +10.2°$ (0.93, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.67–7.62 (m, 2H), 7.58–7.53 (m, 2H), 7.43–7.31 (m, 6H), 6.94–6.90 (m, 2H), 6.89–6.84 (m, 2H), 6.14 (s, 1H), 6.07 (t, J = 7.3 Hz, 1H), 5.90–5.83 (m, 1H), 5.51 (dd, J = 11.0 Hz, J = 4.8 Hz, 1H), 4.72–4.69 (m, 1H), 4.61–4.56 (m, 3H), 4.51 (d, J = 1.8 Hz, 1H), 3.80 (s, 3H), 3.61 (dd, J = 13.0 Hz, J = 8.4 Hz, 1H), 2.86 (dd, J = 13.0 Hz, J = 9.1 Hz, 1H), 2.62–2.55 (m, 1H), 2.50–2.43 (m, 1H), 1.79 (s, 3H), 0.16 (s, 9H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 157.6, 154.0, 152.7, 151.2, 147.0, 138.6, 136.1, 135.1, 134.6, 134.1, 130.6, 129.9, 129.6, 127.8, 127.6, 121.1, 116.0, 114.6, 109.3, 73.9, 71.7, 55.7, 40.0, 30.6, 24.7, 0.6; **HRMS** (ESI) calcd for $C_{35}H_{43}O_3Si_2$ $[M+H]^+$: 567.2751, found 567.2753.

Commercial rhenium(VII) oxide was grounded to the fine powder in the glovebox prior to reaction. Eight-memebered cyclic siloxadiene **5** (1.5 g, 2.65 mmol) was dissolved in ether (17.6 mL, 0.15 M) inside of the glovebox and solution was cooled to -20 °C. Rhenium(VII) oxide (128.2 mg, 0.26 mmol, 10 mol%) was added and the reaction flask was sealed. The reaction flask was taken out of the glovebox and placed into an insulated box filled with ice. The reaction mixture was stirred at 0 °C for 16 h and quenched with Et_3N (0.5 mL). The solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography (gradient elution 50:1 → 15:1 hexanes:EtOAc) to yield six-membered siloxene **17** as a yellow oil (1.28 g, 85%). Siloxene **17** was obtained as inseparable mixture of double bond isomers (E/Z = 85:15). The major isomer is designated by (*), the minor isomer is denoted by (†). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.67–7.61 (m, 2H*, 2H†), 7.61–7.56 (m, 2H*, 2H†), 7.48–7.32 (m, 6H*, 6H†), 6.92–6.82 (m, 4H*, 4H†), 6.23 (s, 1H*, 1H†), 5.97 (t, J = 7.5 Hz, 1H*), 5.82–5.72 (m, 1H*, 1H†), 5.71–5.61 (m, 1H*, 2H†), 4.86 (s, 1H†), 4.70 (s, 1H*), 4.68–4.62 (m, 1H*, 1H†), 4.55–4.46 (m, 3H*, 2H†), 4.42 (s, 1H†), 3.79 (s, 3H*, 3H†), 2.93–2.87 (m, 2H*), 2.87–2.82 (m, 2H†), 2.45 (ddd, J = 17.2 Hz, J =10.1 Hz, J =1.2 Hz, 1H*, 1H†), 2.34 (dd, J =17.2 Hz, J =2.7 Hz, 1H*, 1H†), 1.79 (s, 3H*), 1.76 (s, 3H†), 0.18 (s, 9H*), 0.10 (s, 9H†); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 155.9, 154.0, 152.6, 151.0, 146.2, 139.4, 135.7†, 135.1, 134.9, 134.7, 134.5, 132.6, 132.2†, 130.1, 130.0, 129.9†, 129.5, 127.9, 127.8, 118.0, 115.9, 114.6, 110.3†, 109.4, 73.6, 72.4, 55.7, 36.7, 34.4, 32.7†, 24.7, 24.4†, 0.5, -1.5†; **HRMS** (ESI) calcd for $C_{35}H_{43}O_3Si_2$ $[M+H]^+$: 567.2751, found 567.2751.



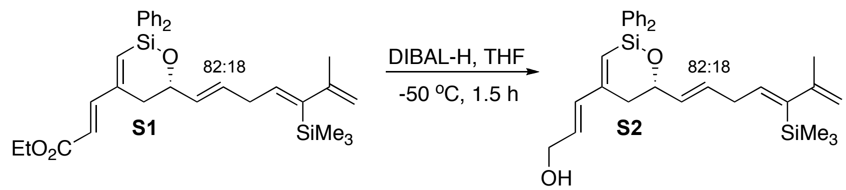
To a solution of siloxene **17** (1.0 g 1.76 mmol) in acetone-H_2O mixture (25 mL, 9:1) were added 2-methyl-2-butene (3.74 mL, 20 equiv) and CAN (2.9 g, 5.29 mmol, 3 equiv) sequentially at 0 °C. The reaction mixture was stirred for 20 min and quenched with Et_3N (3 mL). The solvent was evaporated under reduced pressure and the residue was dissolved in CH_2Cl_2 (15 mL). The solution was dried over $MgSO_4$ and concentrated under vacuum. Crude reaction mixture was purified by flash column chromatography (gradient elution 30:1 → 5:1 hexanes:EtOAc) to afford alcohol **18** (427 mg, 53%) as a yellow oil and recovered starting material (179 mg) which was resubjected to the reaction conditions (BORSM 64%). Alcohol **18** was obtained as inseparable mixture of double bond isomers formed during allylic transposition step. The major isomer is designated by (*), the minor isomer is denoted by (†).**^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.67–7.63 (m, 2H*, 2H†), 7.63–7.59 (m, 2H*, 2H†), 7.47–7.33 (m, 6H*, 6H†), 6.14 (d, J = 2.0 Hz, 1H*, 1H†), 5.96 (t, J = 7.5 Hz, 1H*), 5.82–5.71 (m, 1H*, 1H†), 5.69–5.59 (m, 1H*, 2H†), 4.86 (dd, J = 2.3 Hz, J = 1.4 Hz, 1H†), 4.69 (dd, J = 2.5 Hz, J = 1.4 Hz, 1H*), 4.65–4.58 (m, 1H*, 1H†), 4.50 (d, J = 1.8 Hz, 1H*), 4.41 (d, J = 1.5 Hz, 1H†), 4.13 (s, 2H*, 2H†), 2.92–2.87 (m, 2H*), 2.87–2.82 (m, 2H†), 2.36 (ddd, J =17.2 Hz, J =10.3 Hz, J = 2.1 Hz, 1H*, 1H†), 2.19 (dd, J =17.2 Hz, J =2.6 Hz, 1H*, 1H†), 1.78 (s, 3H*), 1.75 (s, 3H†), 1.74–1.66 (brs, 1H*, 1H†), 0.17 (s, 9H*), 0.09 (s, 9H†); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 160.1, 151.0, 146.2, 139.4, 135.7†, 135.3, 134.8, 134.7, 134.6, 132.6, 132.2†, 130.1, 130.0, 129.9†, 129.4, 127.9, 127.8, 114.3, 110.3†, 109.3, 72.5, 67.7, 36.8, 34.4, 32.6†, 24.7, 24.4†, 0.5, -1.5†; **HRMS** (ESI) calcd for $C_{28}H_{37}O_2Si_2$ $[M+H]^+$: 461.2332, found 461.2325.



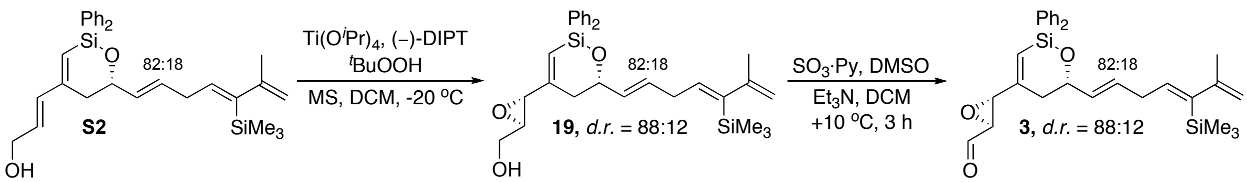
Oxidation: To a solution of alcohol **18** (2.09 g, 4.54 mmol) in 15 mL of DMSO was added IBX (2.54 g 9.08 mmol, 2 equiv) at rt and the reaction mixture was stirred for 1 h. After this time the reaction mixture was cooled to 0 °C and diluted with Et_2O (30 mL) and NaCl solution (10 wt.%, 50 mL). After separation of layers organic extract was washed with NaCl solution (10 wt.%, 3 x 10 mL) and combined aqueous phase was extracted with Et_2O (1 x 15 mL). Ether extracts were dried over $MgSO_4$ and concentrated under reduced pressure to give crude aldehyde as a colorless oil.

Olefination: To a solution of triethyl phosphonoacetate (1.82 mL, 9.08 mmol) in 25 mL of THF was added NaHMDS (1.67 g, 9.08 mmol) at 0 °C and the reaction mixture was stirred for 30 min. The reaction mixture was cooled to -78 °C and transferred to a cold (-78 °C) solution of crude aldehyde in 50 mL of THF via cannula. The reaction mixture was slowly warmed to 0 °C over 3 h and quenched with saturated NH_4Cl solution. The crude product was extracted with CH_2Cl_2 (3 x 20 mL), combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography (gradient elution

50:1 → 30:1 hexanes:EtOAc) to afford ester **S1** (1.9 g, 79%) as a pale yellow oil. Ester **S1** was obtained as inseparable mixture of double bond isomers formed during allylic transposition step. The major isomer is designated by (*), the minor isomer is denoted by (†). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.67–7.62 (m, 2H*, 2H†), 7.60–7.56 (m, 2H*, 2H†), 7.49–7.34 (m, 7H*, 7H†), 6.48 (s, 1H*, 1H†), 6.03–5.94 (m, 2H*, 1H†), 5.84–5.72 (m, 1H*, 1H†), 5.71–5.61 (m, 1H*, 2H†), 4.86 (dd, J = 2.2 Hz, J = 1.5 Hz, 1H†), 4.69 (dd, J = 2.5 Hz, J = 1.4 Hz, 1H*), 4.68–4.61 (m, 1H*, 1H†), 4.50 (d, J = 1.8 Hz, 1H*), 4.41 (d, J = 1.5 Hz, 1H†), 4.24 (q, J = 7.1 Hz, 2H*, 2H†), 2.93–2.88 (m, 2H*), 2.88–2.83 (m, 2H†), 2.57–2.46 (m, 2H*, 2H†), 1.79 (s, 3H*), 1.76 (s, 3H†), 1.31 (t, J = 7.2 Hz, 3H*, 3H†), 0.18 (s, 9H*), 0.09 (s, 9H†); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 166.9, 153.2, 151.0, 147.9. 146.4, 145.8†, 139.2, 135.6†, 134.9, 134.7, 134.2, 133.6, 132.5, 132.3, 131.9†, 130.5, 130.3, 130.2†, 129.8, 128.1, 127.9, 118.5, 110.3†, 109.4, 72.4, 60.5, 35.6, 34.4, 32.6†, 24.7, 24.4†, 14.3, 0.5, -1.5†; **HRMS** (ESI) calcd for $C_{32}H_{41}O_3Si_2$ $[M+H]^+$: 529.2594, found 529.2602.



To a solution of ester **S1** (1,9 g, 3.59 mmol) in 30 mL of THF was added DIBAL-H (9 mL, 1 M in toluene, 8.99 mmol, 2.5 equiv) at -78 °C. The reaction mixture was warmed to -50 °C and stirred at this temperature for 1.5 h. After this time the reaction mixture was quenched with MeOH followed by saturated solution of sodium potassium tartrate (20 mL). The reaction mixture was stirred at rt for 30 min and extracted with EtOAc (3 x 15 mL). Combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography (gradient elution 10:1 → 3:1 hexanes:EtOAc) to afford alcohol **S2** (1.59 g, 91%) as a colorless oil. Alcohol **S2** was obtained as inseparable mixture of double bond isomers formed during allylic transposition step. The major isomer is designated by (*), the minor isomer is denoted by (†). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.68–7.63 (m, 2H*, 2H†), 7.62–7.57 (m, 2H*, 2H†), 7.48–7.32 (m, 6H*, 6H†), 6.41 (d, J = 16.0 Hz, 1H*, 1H†), 6.05 (s, 1H*, 1H†), 6.02–5.93 (m, 2H*, 1H†), 5.82–5.62 (m, 2H*, 3H†), 4.86 (dd, J = 2.3 Hz, J = 1.4 Hz, 1H†), 4.69 (dd, J = 2.5 Hz, J = 1.4 Hz, 1H*), 4.66–4.59 (m, 1H*, 1H†), 4.50 (d, J = 1.8 Hz, 1H*), 4.41 (d, J = 1.5 Hz, 1H†), 4.31–4.21 (m, 2H*, 2H†), 2.93–2.87 (m, 2H*), 2.87–2.82 (m, 2H†), 2.55 (dd, J = 17.1 Hz, J = 2.8 Hz, 1H*, 1H†), 2.47 (ddd, J = 17.1 Hz, J = 10.0 Hz, J = 1.5 Hz, 1H*, 1H†), 1.79 (s, 3H*), 1.76 (s, 3H†), 1.49–1.43 (brs, 1H*, 1H†), 0.18 (s, 9H*), 0.09 (s, 9H†); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 154.7, 151.0, 146.2, 139.4, 135.8, 135.1, 134.9, 134.7, 134.5, 132.7, 132.3†, 130.2, 130.1, 130.0†, 129.5, 128.8, 128.0, 127.8, 123.4, 110.3†, 109.4, 72.6, 63.4, 36.0, 34.4, 32.7†, 24.7, 24.4†, 0.5, -1.5†; **HRMS** (ESI) calcd for $C_{30}H_{39}O_2Si_2$ $[M+H]^+$: 487.2489, found 487.2477.

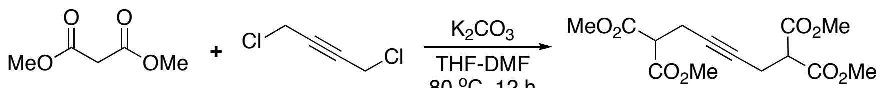


Epoxidation: To a suspension of activated molecular sieves (MS 4Å) in CH_2Cl_2 (750 mg in 8 mL) and (–)-D-DIPT (57.7 mg, 0.246 mmol, 15 mol%) was added Ti(*i*-PrO)$_4$ (48.5 μL, 0.164 mmol, 10 mol%) at 0 °C. The reaction mixture was cooled to -20 °C and solution of *t*-BuOOH (480 μL, 5.5 M in decane, 1.6 equiv) was added. The reaction mixture was stirred at -20 °C for 30 min and transferred to a cold (-20 °C) suspension of alcohol **S2** (800 mg, 1.64 mmol) and MS (750 mg) in 8.5 mL of CH_2Cl_2 via cannula. The reaction flask was sealed and the reaction mixture was kept at -20 °C in freezer for 12 h without stirring. After this time the reaction mixture was filtered through a pad of celite, quenched with $FeSO_4$ solution (30 wt.%), and extracted with EtOAc (3 x 20 mL). Combined organic extracts were concentrated under reduced pressure and the residue was purified by flash column chromatography (gradient elution 5:1 → 3:1 hexanes:EtOAc) to yield epoxyalcohol **19** (844 mg) as a mixture with (–)-D-DIPT. Epoxyalcohol **19** was obtained as inseparable mixture of double bond diastereomers and epimers at the allylic ether stereogenic center. The minor isomers are denoted by (†). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.66–7.61 (m, 2H), 7.61–7.56 (m, 2H), 7.48–7.33 (m, 6H), 6.31 (d, *J* = 1.8 Hz, 1H†), 6.25 (d, *J* = 1.8 Hz, 1H), 5.94 (t, *J* = 7.5 Hz, 1H), 5.81–5.69 (m, 1H), 5.68–5.56 (m, 1H), 4.85 (s, 1H†), 4.69 (s, 1H), 4.65–4.55 (m, 1H), 4.49 (d, *J* = 1.7 Hz, 1H), 4.41 (s, 1H†), 4.02–3.94 (m, 1H), 3.77–3.68 (m, 1H), 3.53 (d, *J* = 1.8 Hz, 1H†), 3.50 (d, *J* = 1.7 Hz, 1H), 3.19 (dt, *J* = 4.1 Hz, *J* = 2.1 Hz, 1H†), 3.10 (dt, *J* = 4.2 Hz, *J* = 2.3 Hz, 1H), 2.91–2.85 (m, 2H), 2.85–2.81 (m, 2H†), 2.35 (ddd, *J* = 17.4 Hz, *J* = 9.8 Hz, *J* = 2.0 Hz, 1H), 2.23 (ddd, *J* = 13.7 Hz, *J* = 12.0 Hz, *J* = 2.8 Hz, 1H†), 2.17 (dd, *J* = 17.4 Hz, *J* = 2.7 Hz, 1H), 1.83–1.76 (m, 4H), 1.75 (s, 3H†), 0.17 (s, 9H), 0.08 (s, 9H†); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 155.5, 151.0, 146.3, 145.8†, 139.3, 135.6†, 134.8, 134.6, 134.3, 132.4, 132.0†, 130.2, 130.1, 129.7, 129.5†, 128.0, 127.9, 122.3†, 119.9, 110.3†, 109.4, 72.7†, 72.6, 72.4†, 61.2, 59.1, 58.8†, 58.2, 57.8†, 35.1, 34.3, 34.0†, 32.6†, 24.7, 24.4†, 0.5, -1.5†; **HRMS** (ESI) calcd for $C_{30}H_{39}O_3Si_2$ $[M+H]^+$: 503.2438, found 503.2430.

Oxidation: To a solution of crude epoxyalcohol **19**, DMSO (2.3 mL, 32.9 mmol 20 equiv), and Et_3N (2.3 mL, 16.4 mmol, 10 equiv) in 7 mL of CH_2Cl_2 was added SO_3•Py (1.3 g, 8.22 mmol, 5 equiv) at 0 °C. The reaction mixture was warmed to 10 °C, stirred at this temperature for 3 h, and quenched with H_2O (15 mL). EtOAc (40 mL) was then added to the reaction mixture. After separation of layers organic extract was washed with NaCl solution (10 wt.%, 3 x 10 mL) and combined aqueous phase was extracted with EtOAc (1 x 10 mL). EtOAc extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography (gradient elution 10:1 → 3:1 hexanes:EtOAc) to yield epoxyaldehyde **3** (773 mg, 94%) as a pale yellow oil. Epoxyaldehyde **3** was obtained as inseparable mixture of double bond diastereomers and epimers at the allylic ether stereogenic center. The minor isomers are denoted by (†). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.12 (d, *J* = 6.1 Hz, 1H), 7.67–7.54 (m, 4H), 7.50–7.33 (m, 6H), 6.43 (s, 1H†), 6.37 (d, *J* = 1.8 Hz, 1H), 5.93 (t, *J* = 7.5 Hz, 1H), 5.83–5.70 (m, 1H), 5.67–5.56 (m, 1H), 4.85 (s, 1H†), 4.69 (s, 1H), 4.65–4.55 (m, 1H), 4.49 (s, 1H), 4.40 (s, 1H†), 3.77 (d, *J* = 1.5 Hz, 1H†), 3.73 (d, *J* = 1.3 Hz, 1H), 3.43 (dd, *J* = 6.1 Hz, *J* = 1.8 Hz, 1H†), 3.35 (dd, *J* = 6.1 Hz, *J* =

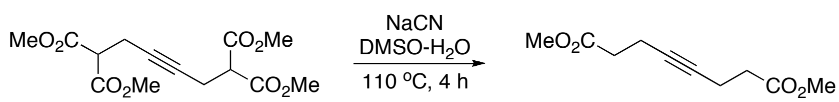
1.7 Hz, 1H), 2.92–2.85 (m, 2H), 2.85–2.81 (m, 2H†), 2.35 (ddd, J = 17.4 Hz, J = 9.8 Hz, J = 2.1 Hz, 1H), 2.19 (d, J = 5.8 Hz, 2H†), 2.11 (dd, J = 17.4 Hz, J = 2.7 Hz, 1H), 1.78 (s, 3H), 1.75 (s, 3H†), 0.17 (s, 9H), 0.09 (s, 9H†); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 197.0, 152.5, 151.0, 146.4, 139.1, 135.5†, 134.8, 134.6, 134.3, 133.7, 132.0, 131.6†, 130.44, 130.35, 130.0, 129.8†, 128.1, 128.0, 125.3†, 123.2, 110.3†, 109.4, 72.5, 72.3†, 59.5, 59.3†, 58.9, 58.5†, 34.6, 34.3, 33.6†, 32.6†, 24.7, 24.4†, 0.5, -1.5†; **HRMS** (ESI) calcd for $C_{30}H_{37}O_3Si_2$ $[M+H]^+$: 501.2281, found 501.2279.

Synthesis of Donor Aldehyde 4



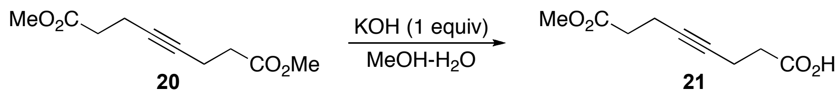
S3

To a solution of 1,4-dichloro-2-butyne (2.5 g, 2.0 mL, 20.3 mmol) and dimethyl malonate (23.2 mL, 203 mmol, 10 equiv) in THF-DMF mixture (150 mL 1:1) was added K_2CO_3 (14.0 g, 101.6 mmol, 5 equiv) and the reaction mixture was refluxed for 12 h. After this time the reaction mixture was cooled to rt, quenched with saturated NH_4Cl solution (100 mL), and diluted with H_2O (200 mL). After separation of layers organic extract was washed with NaCl solution (10 wt.%, 3 x 50 mL) and combined aqueous phase was extracted with EtOAc (2 x 20 mL). EtOAc extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Excess of malonate was distilled off under high vacuum and the residue was purified by flash column chromatography (gradient elution 5:1 → 3:1 hexanes:EtOAc) to yield tetraester **S3** (4.77 g, 75%) as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.75 (s, 12H), 3.45 (t, J = 7.7 Hz, 2H), 2.65 (d, J = 7.7 Hz, 4H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 168.3, 77.9, 52.7, 51.2, 18.8; **HRMS** (ESI) calcd for $C_{14}H_{19}O_8$ $[M+H]^+$: 315.1080, found 315.1068.

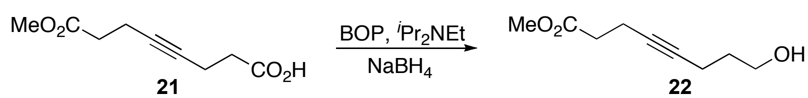


S3 **20**

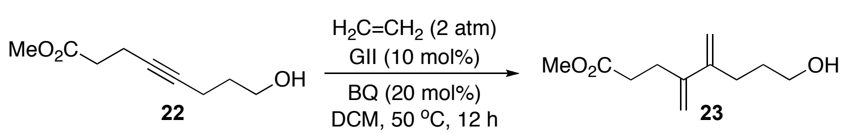
To a solution of tetraester **S3** (4.77 g, 15.2 mmol) in 130 mL of DMSO were added NaCN (1.86 g, 38.0 mmol, 2.5 equiv) and H_2O (820 μL, 45.6 mmol, 3 equiv) and the reaction flask was placed in the preheated to 110 °C oil bath. The reaction mixture was stirred at this temperature for 4 h and cooled to rt. The reaction mixture was quenched with saturated NH_4Cl solution (100 mL), diluted with H_2O (250 mL), and extracted with EtOAc (3 x 50 mL). Combined organic extracts were washed with NaCl solution (10 wt.%, 3 x 50 mL) and combined aqueous phase was extracted with EtOAc (2 x 15 mL). EtOAc extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by gravity column chromatography (gradient elution 15:1 → 3:1 hexanes:EtOAc) to yield diester **20** (1.69 g, 56%, white solid) and monodecarboxylated triester (1.42 g, 37%, off white solid). Triester was resubjected to the reaction conditions to yield additional 633 mg of the product. Combined yield is 2.32 g, 77%. Reaction can be performed without isolation of intermediate triester, however, yield of the product decreased to 64%. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.68 (s, 6H), 2.51–2.41 (m, 8H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 172.4, 79.0, 51.7, 33.7, 14.7; **HRMS** (ESI) calcd for $C_{10}H_{15}O_4$ $[M+H]^+$: 199.0970, found 199.0979.



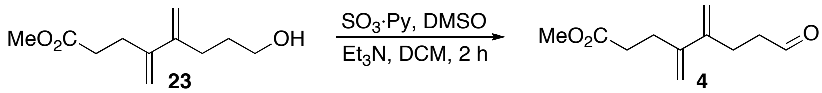
To a solution of diester **20** (1.64 g, 8.25 mmol) in MeOH-H_2O mixture (120 mL, 2:1) was added KOH (462.9 mg, 8.25 mmol, 1 equiv) at 0 °C and the reaction mixture was stirred at rt for 12 h. After this time MeOH was removed under vacuum and water layer was saturated with NaCl. The reaction mixture was extracted with EtOAc (5 x 30 mL) to separate unreacted starting material and potassium salt of monoacid **21** (organic phase) from potassium salt of diacid (aqueous phase). Combined organic extracts were acidified with 3 M HCl, dried over $MgSO_4$, and solvent was removed under reduced pressure. The residue was purified by flash column chromatography (gradient elution 10:1 → 1:5 hexanes:EtOAc) to afford monoacid **21** (819 mg, 54%, 70% BORSM, white solid) and recovered starting material (380.6 mg, 23%, off white solid) which was resubjected to the reaction conditions. The water solution of potassium salt of diacid was acidified with 3 M HCl end extracted with EtOAc (5 x 30 mL). Combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure to afford diacid (304,2 mg 22%) as a white powder which was recovered. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.69 (s, 3H), 2.58–2.41 (m, 8H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 177.7, 172.5, 79.2, 78.7, 51.7, 33.63, 33.58, 14.7, 14.4; **HRMS** (ESI) calcd for $C_9H_{12}O_4Na$ $[M+Na]^+$: 207.0633, found 207.0642.



To a solution of acid **21** (1.04 g, 5.67 mmol) and *i*-Pr_2NEt (1.18 mL, 6.8 mmol, 1.2 equiv) in 30 mL of THF was added (benzotriazol-1-yloxy)tris(dimethylamino)phosphonium hexafluorophosphate (BOP, 2.76 g, 6.23 mmol, 1.1 equiv) and the reaction mixture was stirred for 30 min. The reaction mixture was than cooled to 0 °C and $NaBH_4$ (536 mg, 14.16 mmol, 2.5 equiv) was added. After stirring at rt for 1 h the reaction mixture was quenched with saturated NH_4Cl and extracted with EtOAc (3 x 20 mL). Combined organic extracts were dried over $MgSO_4$ and solvent was removed under reduced pressure. The residue was purified by flash column chromatography (gradient elution 5:1 → 1:1 hexanes:EtOAc) to afford alcohol **22** (906 mg, 94%) as a colorless liquid. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.71–3.63 (m, 5H), 2.50–2.38 (m, 4H), 2.24–2.13 (m, 3H), 2.71–1.63 (m, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 172.6, 80.2, 78.6, 61.5, 51.6, 33.7, 31.4, 15.2, 14.6; **HRMS** (ESI) calcd for $C_9H_{15}O_3$ $[M+H]^+$: 171.1021, found 171.1018.

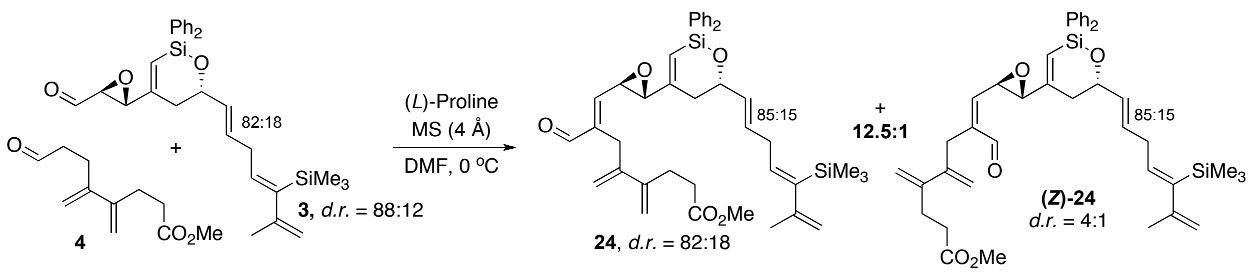


Alcohol **22** (1.12 g, 6.56 mmol) was dissolved in 80 mL of CH_2Cl_2 in 500 mL Schlenk tube and Grubbs 2nd generation catalyst (SImes)(PCy_3)Cl_2Ru=CHPh (556.6 mg, 0.656 mmol, 10 mol%) and 1,4-benzoquinone (141.7 mg, 1.31 mmol, 20 mol%) were added. Ethylene gas was then passed through the solution for 15 min and additional 2 atm (30 psi) of ethylene were introduced. Schlenk tube was sealed and placed in the preheated to 50 °C oil bath. After stirring at 50 °C for 12 h the reaction mixture was cooled to rt and concentrated under reduced pressure. The residue was purified by flash column chromatography (gradient elution 10:1 → 2:1 hexanes:EtOAc) to give alcohol **23** as a green liquid (992 mg, 76%) and its aldehyde (126.3 mg, 10%, green liquid). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 5.11 (s, 1H), 5.10 (s, 1H), 4.99 (s, 1H), 4.97 (s, 1H), 3.68–3.63 (m, 5H), 2.58 (dd, J = 9.0 Hz, J = 6.3 Hz, 2H), 2.47 (dd, J = 9.0 Hz, J = 6.3 Hz, 2H), 2.33 (dt, J = 7.6 Hz, J = 0.9 Hz, 2H), 1.74–1.67 (m, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 173.7, 146.4, 145.7, 112.5, 112.3, 62.5, 51.6, 33.3, 31.4, 30.3, 29.3; **HRMS** (ESI) calcd for $C_{11}H_{19}O_3$ $[M+H]^+$: 199.1334, found 199.1341.



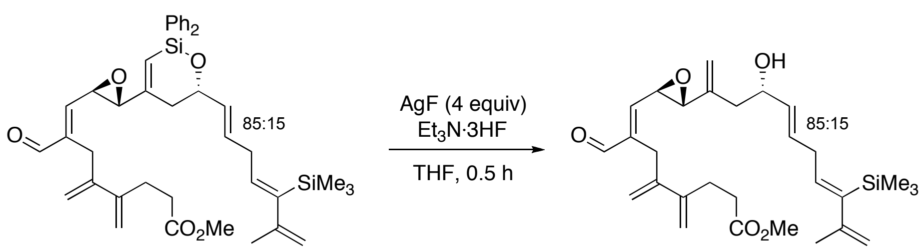
To a solution of alcohol **23** (271 mg, 1.37 mmol), DMSO (1.0 mL, 13.7 mmol 10 equiv), and Et_3N (1.9 mL, 13.7 mmol, 10 equiv) in 10 mL of CH_2Cl_2 was added solution of SO_3•Py (1.09 g, 6.83 mmol, 5 equiv) in 1 mL of DMSO at 0 °C. The reaction mixture was slowly warmed to rt over 2 h and quenched with H_2O (10 mL). EtOAc (40 mL) was then added to the reaction mixture, and after separation of layers organic extract was washed with NaCl solution (10 wt.%, 3 x 10 mL). The combined aqueous phase was extracted with EtOAc (1 x 10 mL), organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography (gradient elution 15:1 → 10:1 hexanes:EtOAc) to afford aldehyde **4** (212 mg, 79%) as a colorless liquid. **^{1}H NMR** (500 MHz, $CDCl_3$): 9.75 (s, 1H), 5.11 (s, 1H), 5.07 (s, 1H), 5.00–4.97 (m, 2H), 3.64 (s, 3H), δ 2.60–2.53 (m, 6H), 2.47–2.41 (m, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 201.7, 173.4, 145.2, 145.0, 112.9, 112.7, 51.5, 42.6, 33.1, 29.1, 26.3; **HRMS** (ESI) calcd for $C_{11}H_{16}O_3Na$ $[M+Na]^+$: 219.0997, found 219.0999.

Cross-Aldol Condensation and Final Elaboration



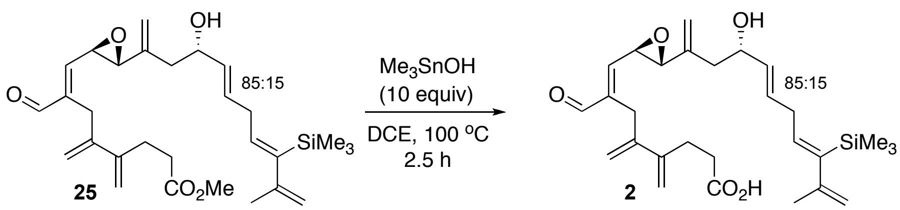
To a solution of acceptor aldehyde **3** (681 mg, 1.36 mmol) in 680 μL of DMF (2 M) were added activated molecular sieves (MS, 4Å, 680 mg) and L-proline (156.6 mg, 1.36 mmol) and the reaction mixture was cooled to 0 °C. Under vigorous stirring solution of acceptor aldehyde (400 mg, 2.04 mmol) in DMF (2 mL, 1.0 M) was added to the reaction mixture over 24 h at 0 °C via syringe pump. After completed addition the reaction mixture was stirred for additional 3 h and resultant orange-red suspension was diluted with EtOAc and filtered through a pad of celite. Collected filtrate was washed with NaCl solution (10 wt.%, 3 x 15 mL) and combined aqueous phase was extracted with EtOAc (1 x 10 mL). Combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by gravity column chromatography (gradient elution 25:1 → 10:1 hexanes:EtOAc) to afford epoxyaldehyde **24** (554 mg, 60%, colorless oil) and its (Z)-isomer (54,5 mg, 6%, colorless oil). Epoxyaldehyde **24** was isolated as inseparable mixture of double bond diastereomers and epimers at the allylic ether stereogenic center. The minor isomers are denoted by (†). For ***(E)*-24**: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.47 (s, 1H), 9.46 (s, 1H†), 7.67–7.54 (m, 4H), 7.48–7.32 (m, 6H), 6.34 (d, J = 1.8 Hz, 1H†), 6.29–6.23 (m, 2H), 5.93 (t, J = 7.5 Hz, 1H), 5.82–5.69 (m, 1H), 5.68–5.56 (m, 1H), 5.15–5.11 (m, 2H), 4.99 (s, 1H), 4.97 (s, 1H†), 4.84 (s, 1H†), 4.83 (s, 1H†), 4.81 (s, 1H), 4.78 (s, 1H†), 4.68 (d, J = 2.4 Hz, J = 1.3 Hz, 1H), 4.64–4.54 (m, 1H), 4.48 (d, J = 1.54 Hz, 1H), 4.40 (s, 1H†), 3.66–3.59 (m, 4H), 3.55 (d, J = 1.5 Hz, 1H†), 3.51 (d, J = 1.5 Hz, 1H), 3.41 (d, J = 16.1 Hz, 1H), 3.25 (d, J = 16.1 Hz, 1H), 2.91–2.85 (m, 2H), 2.85–2.81 (m, 2H†), 2.58–2.52 (m, 2H), 2.43–2.38 (m, 2H), 2.33 (ddd, J = 17.4 Hz, J = 9.9 Hz, J = 2.2 Hz, 1H), 2.15 (dd, J = 17.4 Hz, J = 2.7 Hz, 1H), 1.77 (s, 3H), 1.74 (s, 3H†), 0.16 (s, 9H), 0.08 (s, 9H†); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 192.6, 173.3, 154.2, 151.0, 150.2, 146.4, 145.7, 144.2, 143.5, 139.2, 134.8, 134.6, 134.0, 132.2, 130.4, 130.3, 129.8, 128.0, 127.9, 123.3†, 121.0, 113.2, 112.9, 110.3†, 109.4, 72.5, 62.7, 55.4, 54.2†, 51.5, 35.1, 34.3, 33.9†, 33.1, 32.6†, 29.4, 28.2, 24.7, 24.4†, 0.5, -1.5†; **HRMS** (ESI) calcd for $C_{41}H_{51}O_5Si_2$ $[M+H]^+$: 679.3275, found 679.3266.

For ***(Z)*-24**: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.2 (s, 1H), 7.66–7.54 (m, 4H), 7.48–7.33 (m, 6H), 6.35 (s, 1H†), 6.28 (d, J = 1.8 Hz, 1H), 5.98 (d, J = 8.5 Hz, 1H), 5.93 (t, J = 7.6 Hz, 1H), 5.83–5.70 (m, 1H), 5.69–5.56 (m, 1H), 5.30 (s, 1H), 5.04–4.95 (m, 3H), 4.84 (s, 1H†), 4.68 (s, 1H), 4.66–4.55 (m, 1H), 4.48 (s, 1H), 4.40 (s, 1H†), 4.17 (dd, J = 8.4 Hz, J = 1.3 Hz, 1H†), 4.06 (dd, J = 8.4 Hz, J = 1.4 Hz, 1H), 3.67 (s, 3H), 3.66 (s, 3H†), 3.45 (d, J = 1.5 Hz, 1H†), 3.41 (d, J = 1.1 Hz, 1H), 3.29–3.18 (m, 2H), 2.93–2.85 (m, 2H), 2.85–2.80 (m, 2H†), 2.62–2.56 (m, 2H), 2.52–2.45 (m, 2H), 2.38 (ddd, J = 17.4 Hz, J = 9.9 Hz, J = 1.9 Hz, 1H), 2.26–2.22 (m, 2H†), 2.18 (dd, J = 17.4 Hz, J = 2.6 Hz, 1H), 1.77 (s, 3H), 1.74 (s, 3H†), 0.16 (s, 9H), 0.08 (s, 9H†); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 189.7, 173.4, 154.3, 151.0, 146.4, 144.5, 143.6, 143.2, 142.7, 139.2, 134.8, 134.6, 134.0, 132.2, 131.8, 130.3, 130.2, 129.8, 128.0, 127.9, 123.3†, 121.0, 115.7, 113.7, 110.3†, 109.4, 72.5, 63.0, 53.9, 51.6, 35.2, 34.3, 33.7, 33.2, 32.6†, 29.7†, 28.9, 24.7, 24.4†, 0.5, -1.5†.

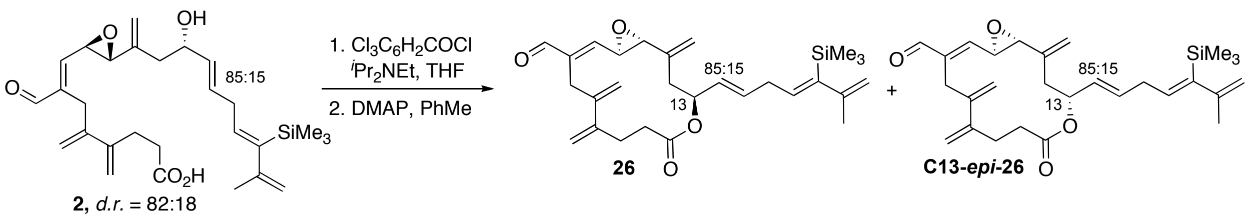


24, *d.r.* = 82:18 **25**, *d.r.* = 82:18

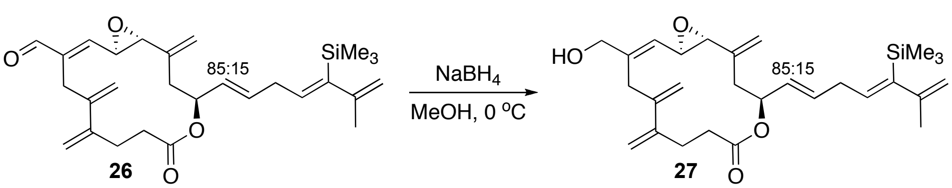
To a solution of silyl ether **24** (277 mg, 0.41 mmol) in 15 mL of THF were added Et_3N•3HF (332 μL, 2.05 mmol, 5 equiv) and AgF (207 mg, 1.63 mmol, 4 equiv) and the reaction mixture was stirred for 30 min under exclusion of light. The reaction mixture was quenched with saturated $NaHCO_3$ solution and extracted with EtOAc (3 x 10 mL). Combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography (gradient elution 10:1 → 2:1 hexanes:EtOAc) to afford alcohol **25** (157.2 mg, 77%) as a colorless oil. Diastereomers of **25** were partially separable at this stage and after gravity column chromatography (gradient elution 5:1 → 2:1 hexanes:EtOAc) were isolated 2 fractions: diastereomeric mixture (101.2 mg) and clean alcohol **25** as inseparable mixture of double bond isomers formed during allylic transposition step. The major isomer is designated by (*), the minor isomer is denoted by (†). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.46 (s, 1H*, 1H†), 6.25 (d, J = 8.5 Hz, 1H*, 1H†), 5.90 (t, J = 7.5 Hz, 1H*), 5.71–5.58 (m, 1H*, 2H†), 5.53–5.42 (m, 1H*, 1H†), 5.30 (s, 1H*, 1H†), 5.15 (s, 2H*, 2H†), 5.12 (s, 1H*, 1H†), 5.00 (s, 1H*, 1H†), 4.83 (dd, J = 2.2 Hz, J = 1.5 Hz, 1H†), 4.80 (s, 1H*, 1H†), 4.67 (dd, J = 2.4 Hz, J = 1.3 Hz, 1H*), 4.46 (d, J = 1.8 Hz, 1H*), 4.38 (d, J = 1.5 Hz, 1H†), 4.21–4.13 (m, 1H*, 1H†), 3.65 (s, 3H*, 3H†), 3.61 (dd, J = 8.5 Hz, J = 2.0 Hz, 1H*, 1H†), 3.49 (d, J = 1.8 Hz, 1H*, 1H†), 3.39 (d, J = 16.1 Hz, 1H*, 1H†), 3.25 (d, J = 16.1 Hz, 1H*, 1H†), 2.88–2.82 (m, 2H*), 2.82–2.78 (m, 2H†), 2.62–2.55 (m, 2H*, 2H†), 2.46 (dd, J = 8.7 Hz, J = 6.4 Hz, 2H*, 2H†), 2.29–2.22 (m, 1H*, 1H†), 2.22–2.08 (m, 2H*, 2H†), 1.76 (s, 3H*), 1.73 (s, 3H†), 0.15 (s, 9H*), 0.06 (s, 9H†); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 192.7, 173.5, 150.9, 150.5, 146.6, 145.6, 144.1, 143.2, 140.6, 139.0, 135.4†, 132.8, 132.4†, 130.6†, 130.1, 116.8, 113.0, 112.8, 110.3†, 109.4, 71.7, 61.7, 55.6, 51.6, 39.9, 34.3, 33.1, 32.6†, 29.3, 28.1, 24.6, 24.4†, 0.5, -1.5†; **HRMS** (ESI) calcd for $C_{29}H_{43}O_5Si$ $[M+H]^+$: 499.2880, found 499.2884.



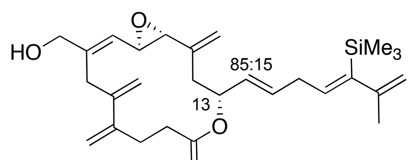
In a Schlenk tube (2 mL) Me_3SnOH (181 mg, 1.0 mmol, 10 equiv) was added to a solution of methyl ester **25** (50 mg, 0.1 mmol) in 400 μL of DCE. Schlenk tube was sealed and placed in the preheated to 100 °C oil bath. The reaction mixture was stirred at this temperature for 2.5 h and cooled to rt. The resultant yellow suspension was concentrated under reduced pressure and the residue was purified by flash column chromatography (gradient elution 4:1 → 1:3 hexanes:EtOAc) to afford seco-acid **2** (48.5 mg, quantitative) as a colorless oil. Seco-acid **2** was isolated as inseparable mixture of double bond isomers formed during allylic transposition step. The major isomer is designated by (*), the minor isomer is denoted by (†). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.46 (s, 1H*, 1H†), 6.25 (d, J = 8.5 Hz, 1H*, 1H†), 5.90 (t, J = 7.6 Hz, 1H*), 5.71–5.58 (m, 1H*, 2H†), 5.53–5.42 (m, 1H*, 1H†), 5.31 (s, 1H*, 1H†), 5.17 (s, 1H*, 1H†), 5.15 (s, 1H*, 1H†), 5.13 (s, 1H*, 1H†), 5.03 (s, 1H*, 1H†), 4.83 (dd, J = 2.6 Hz, J = 1.5 Hz, 1H†), 4.81 (s, 1H*, 1H†), 4.67 (dd, J = 2.6 Hz, J = 1.5 Hz, 1H*), 4.47 (d, J = 1.8 Hz, 1H*), 4.39 (d, J = 1.5 Hz, 1H†), 4.23–4.16 (m, 1H*, 1H†), 3.64 (dd, J = 8.5 Hz, J = 2.0 Hz, 1H*, 1H†), 3.49 (d, J = 1.5 Hz, 1H*, 1H†), 3.38 (d, J = 16.1 Hz, 1H*, 1H†), 3.27 (d, J = 16.1 Hz, 1H*, 1H†), 2.89–2.83 (m, 2H*), 2.83–2.78 (m, 2H†), 2.63–2.56 (m, 2H*, 2H†), 2.53–2.46 (m, 2H*, 2H†), 2.29–2.18 (m, 2H*, 2H†), 1.76 (s, 3H*), 1.73 (s, 3H†), 0.15 (s, 9H*), 0.07 (s, 9H†); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 192.8, 178.0, 150.9, 150.5, 146.6, 145.5, 144.2, 143.2, 140.4, 138.9, 135.3†, 132.6, 132.1†, 130.9†, 130.4, 117.1, 113.3, 112.9, 110.3†, 109.4, 71.8, 61.8, 55.4, 39.8, 34.3, 33.1, 32.6†, 29.0, 28.1, 24.6, 24.4†, 0.5, -1.5†; **HRMS** (ESI) calcd for $C_{28}H_{41}O_5Si$ $[M+H]^+$: 485.2723, found 485.2727.



To a solution of seco-acid **2** (199 mg, 0.41 mmol) in 3 mL of THF were added *i*-Pr_2NEt (572 μL, 3.28 mmol, 8 equiv) and $Cl_3C_6H_2COCl$ (256 μL, 1.64 mmol, 4 equiv) and the reaction mixture was stirred at rt for 2 h. After this time pale yellow solution was added dropwice to a solution of DMAP (501.6 mg, 4.1 mmol, 10 equiv) in 205 mL of toluene (0.002 M) producing a white precipitate. The reaction mixture was stirred for 8 h and concentrated under reduced pressure. The residue was purified by flash column chromatography (gradient elution 5:1 → 3:1 hexanes:EtOAc) to afford mixture of epimeric macrolactones (118.0 mg, 61%) and dimeric macrolide (23 mg, 6%). Macrolactones were separated by gravity column chromatography (gradient elution 15:1 → 5:1 hexanes:EtOAc) to give **26** (96.3 mg, 50%, colorless oil) and ***C13-epi-26*** (21,4 mg 11%, colorless oil). Macrolactone **26** was isolated as inseparable mixture of double bond isomers formed during allylic transposition step. The major isomer is designated by (*), the minor isomer is denoted by (†). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.46 (s, 1H*, 1H†), 6.12 (d, *J* = 8.6 Hz, 1H*, 1H†), 5.88 (t, *J* = 7.6 Hz, 1H*), 5.77–5.67 (m, 1H*, 1H†), 5.58 (t, *J* = 7.0 Hz, 1H†), 5.41–5.34 (m, 1H*, 1H†), 5.32–5.25 (m, 2H*, 2H†), 5.13–5.07 (m, 3H*, 3H†), 5.00–4.96 (m, 2H*, 2H†), 4.83 (dd, *J* = 2.4 Hz, *J* = 1.3 Hz, 1H†), 4.67 (dd, *J* = 2.4 Hz, *J* = 1.3 Hz, 1H*), 4.46 (d, *J* = 1.5 Hz, 1H*), 4.37 (d, *J* = 1.5 Hz, 1H†), 3.65–3.58 (m, 2H*, 2H†), 3.40 (d, *J* = 1.5 Hz, 1H*, 1H†), 3.12 (d, *J* = 15.0 Hz, 1H*, 1H†), 2.88–2.76 (m, 3H*, 3H†), 2.54–2.40 (m, 3H*, 3H†), 2.36 (dd, *J* = 14.6 Hz, *J* = 9.1 Hz, 1H*, 1H†), 2.22–2.13 (m, 1H*, 1H†), 1.76 (s, 3H*), 1.72 (s, 3H†), 0.14 (s, 9H*), 0.07 (s, 9H†); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 193.0, 172.5, 150.9, 150.0, 147.0, 146.0, 145.3, 144.3, 140.5, 138.4, 134.9†, 132.9†, 132.5, 128.5, 128.1†, 115.8, 115.1, 114.3, 110.3†, 109.4, 75.0, 61.5, 57.0, 38.0, 34.2, 33.4, 32.5†, 29.5, 28.8, 24.6, 24.3†, 0.4, -1.5†; **HRMS** (ESI) calcd for $C_{28}H_{39}O_4Si$ $[M+H]^+$: 467.2618, found 467.2624.

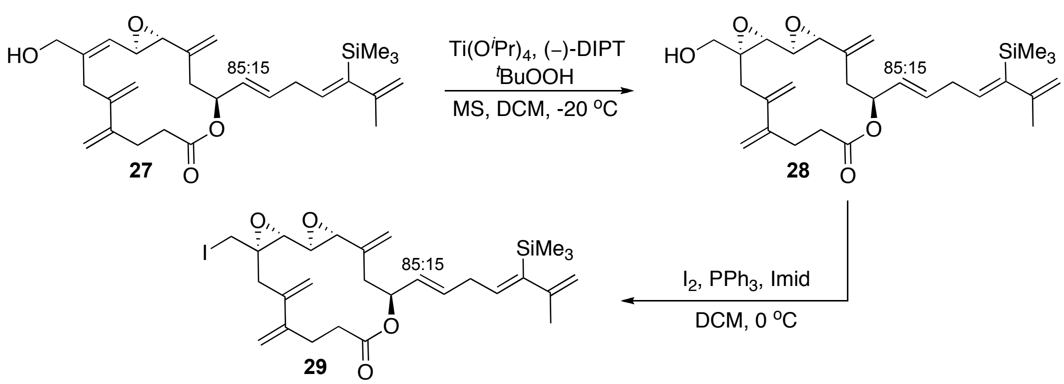


To a solution of aldehyde **26** (135 mg, 0.24 mmol) in 5 mL of MeOH was added $NaBH_4$ (11 mg, 0.24 mmol, 1 equiv) at 0 °C and the reaction mixture was stirred for 2 min. The reaction mixture was quenched with saturated NH_4Cl solution and extracted with EtOAc (3 x 10 mL). Combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography (gradient elution 5:1 → 3:1 hexanes:EtOAc) to afford alcohol **27** (124.0 mg 91%) as a colorless oil. Alcohol **27** was isolated as inseparable mixture of double bond isomers formed during allylic transposition step. The major isomer is designated by (*), the minor isomer is denoted by (†). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.89 (t, *J* = 7.5 Hz, 1H*), 5.79–5.67 (m, 1H*, 1H†), 5.60 (t, *J* = 7.0 Hz, 1H†), 5.47–5.34 (m, 1H*, 1H†), 5.31 (d, *J* = 8.7 Hz, 1H*, 1H†), 5.29–5.20 (m, 2H*, 2H†), 5.16 (s, 1H*, 1H†), 5.08 (s, 1H*, 1H†), 5.03 (s, 1H*, 1H†), 4.99 (s, 1H*, 1H†), 4.87 (s, 1H*, 1H†), 4.83 (dd, J = 2.2 Hz, J = 1.5 Hz, 1H†), 4.68 (dd, J = 2.4 Hz, J = 1.3 Hz, 1H*), 4.47 (d, J = 1.8 Hz, 1H*), 4.38 (d, J = 1.5 Hz, 1H†), 4.11–4.01 (m, 2H*, 2H†), 3.46–3.37 (m, 2H*, 2H†), 3.25 (d, J = 1.8 Hz, 1H*, 1H†), 2.97 (d, J = 15.0 Hz, 1H*, 1H†), 2.88–2.83 (m, 2H*), 2.83–2.78 (m, 2H†), 2.61–2.47 (m, 3H*, 3H†), 2.43–2.34 (m, 2H*, 2H†), 2.31 (dd, J = 14.4 Hz, J = 9.4 Hz, 1H*, 1H†), 1.76 (s, 3H*), 1.72 (s, 3H†), 1.70–1.54 (brs, 1H*, 1H†), 0.14 (s, 9H*), 0.07 (s, 9H†); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 172.1, 150.9, 147.4, 146.9, 145.8, 144.0, 141.3, 138.5, 135.0†, 132.7†, 132.3, 128.6, 128.2†, 123.8, 115.1, 114.4, 113.0, 110.3†, 109.4, 75.7, 65.9, 61.3, 58.4, 38.0, 34.17, 34.14, 33.5, 32.6†, 29.7, 24.6, 24.3†, 0.4, -1.5†; **HRMS** (ESI) calcd for $C_{28}H_{41}O_4Si$ $[M+H]^+$: 469.2774, found 469.2768.



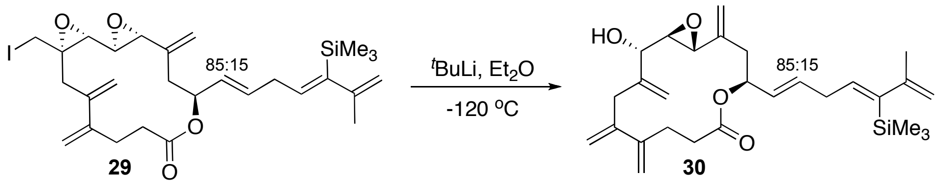
C13-*epi*-27

Alcohol **C13-*epi*-27** was obtained by reduction of aldehyde **C13-*epi*-26** with $NaBH_4$ as it described for **26**. Alcohol **C13-*epi*-27** was isolated as inseparable mixture of double bond isomers formed during allylic transposition step. The major isomer is designated by (*), the minor isomer is denoted by (†). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.90 (t, J = 7.5 Hz, 1H*), 5.82–5.71 (m, 1H*, 1H†), 5.60 (t, J = 7.0 Hz, 1H†), 5.47–5.38 (m, 2H*, 2H†), 5.38–5.30 (m, 1H*, 1H†), 5.29–5.23 (m, 2H*, 2H†), 5.22 (s, 1H*, 1H†), 5.05 (s, 1H*, 1H†), 5.03 (s, 1H*, 1H†), 4.83 (s, 1H*, 2H†), 4.68 (dd, J = 2.6 Hz, J = 1.5 Hz, 1H*), 4.48 (d, J = 1.5 Hz, 1H*), 4.38 (d, J = 1.5 Hz, 1H†), 4.07–3.92 (m, 3H*, 3H†), 3.60 (d, J = 14.9 Hz, 1H*, 1H†), 3.32 (d, J = 1.8 Hz, 1H*, 1H†), 2.99 (d, J = 14.9 Hz, 1H*, 1H†), 2.89–2.83 (m, 2H*), 2.83–2.79 (m, 2H†), 2.52–2.30 (m, 3H*, 3H†), 2.26–2.15 (m, 2H*, 2H†), 2.09 (ddd, J = 14.9 Hz, J = 11.2 Hz, J = 1.2 Hz, 1H*, 1H†), 1.77 (s, 3H*), 1.73 (s, 3H†), 1.56–1.36 (brs, 1H*, 1H†), 0.15 (s, 9H*), 0.08 (s, 9H†); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 172.0, 150.9, 147.5, 147.0, 145.8, 143.0, 141.4, 138.5, 134.9†, 132.9†, 132.5, 128.7, 128.3†, 123.9, 118.7, 116.6, 114.0, 110.4†, 109.4, 75.8, 65.5, 62.2, 53.6, 34.8, 34.6, 34.2, 32.6†, 32.1, 31.5, 24.7, 24.4†, 0.5, -1.5†; **HRMS** (ESI) calcd for $C_{28}H_{41}O_4Si$ $[M+H]^+$: 469.2774, found 469.2767.

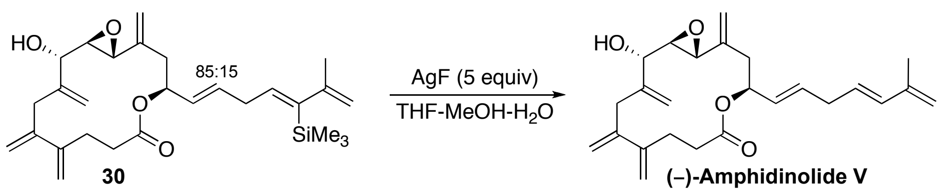


Epoxidation: To a suspension of activated molecular sieves (MS 4Å) in CH_2Cl_2 (100 mg in 6 mL) and (–)-D-DIPT (21.0 mg, 0.090 mmol) was added Ti(i-PrO)$_4$ (17.6 μL, 0.060 mmol) at 0 °C. The reaction mixture was cooled to -20 °C and solution of t-BuOOH (174 μL, 5.5 M in decane, 0.96 mmol) was added. The reaction mixture was stirred at -20 °C for 30 min and 2 mL of resultant suspension was added to a cold (-20 °C) suspension of alcohol **27** (70 mg, 0.149 mmol) and MS (100 mg) in 1 mL of CH_2Cl_2 via syringe. The reaction flask was sealed and the reaction mixture was kept at -20 °C in freezer for 12 h without stirring. After this time the reaction mixture was filtered through a pad of celite. The filtrate was concentrated under reduced pressure and the residue was purified by flash column chromatography (gradient elution 10:1 → 2:1 hexanes:EtOAc) to yield diepoxide **28** (74 mg) as inseparable mixture with (–)-D-DIPT. Diepoxide **28** was obtained as inseparable mixture of double bond isomers formed during allylic transposition step. The major isomer is designated by (*), the minor isomer is denoted by (†). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.88 (t, *J* = 7.6 Hz, 1H*), 5.76–5.65 (m, 1H*, 1H†), 5.58 (t, *J* = 7.0 Hz, 1H†), 5.42–5.32 (m, 1H*, 1H†), 5.28–5.21 (m, 2H*, 2H†), 5.17 (s, 1H*, 1H†), 5.10 (s, 1H*, 1H†), 5.04 (s, 1H*, 1H†), 4.99 (s, 1H*, 1H†), 4.95 (s, 1H*, 1H†), 4.83 (s, 1H†), 4.67 (dd, *J* = 2.4 Hz, *J* = 1.3 Hz, 1H*), 4.46 (d, *J* = 1.1 Hz, 1H*), 4.37 (d, *J* = 1.5 Hz, 1H†), 3.83 (dd, *J* = 12.7 Hz, *J* = 2.3 Hz, 1H*, 1H†), 3.72 (dd, *J* = 12.7 Hz, *J* = 8.4 Hz, 1H*, 1H†), 3.39 (d, *J* = 1.8 Hz, 1H*, 1H†), 3.02 (d, *J* = 6.8 Hz, 1H*, 1H†), 2.91–2.81 (m, 4H*, 2H†), 2.81–2.77 (m, 2H†), 2.73–2.64 (m, 1H*, 1H†), 2.56–2.48 (m, 1H*, 1H†), 2.48–2.34 (m, 4H*, 4H†), 2.30 (dd, *J* = 14.7 Hz, *J* = 8.9 Hz, 1H*, 1H†), 1.87–1.80 (brs, 1H*, 1H†), 1.76 (s, 3H*), 1.71 (s, 3H†), 0.14 (s, 9H*), 0.07 (s, 9H†); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 172.1, 150.9, 147.7, 147.0, 143.3, 139.7, 138.5, 134.9†, 132.8†, 132.4, 128.6, 128.2†, 117.2, 114.7, 113.6, 110.3†, 109.4, 73.1, 63.4, 62.6, 59.6, 58.3, 57.4, 37.4, 34.6, 34.2, 33.6, 32.5†, 29.6, 24.6, 24.3†, 0.4, -1.5†; **HRMS** (ESI) calcd for $C_{28}H_{41}O_5Si$ $[M+H]^+$: 485.2723, found 485.2715.

Iodination: To a solution of crude epoxyalcohol **28** in 7 mL of CH_2Cl_2 were added PPh_3 (156.3 mg, 0.60 mmol, 4 equiv) and imidazole (71 mg, 1.04 mmol, 7 equiv) and the reaction mixture was cooled to 0 °C. Iodine (151.3 mg, 0.60 mmol, 4 equiv) was then added and the reaction mixture was warmed to rt and stirred under exclusion of light for 1.5 h. The reaction mixture was concentrated under reduced pressure and the residue was purified by flash column chromatography (gradient elution 20:1 → 10:1 hexanes:EtOAc) to yield iododiepoxide **29** (75.8 mg, 85% over 2 steps) as a colorless oil. Iododiepoxide **29** was obtained as inseparable mixture of double bond isomers formed during allylic transposition step. The major isomer is designated by (*), the minor isomer is denoted by (†). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.88 (t, *J* = 7.5 Hz, 1H*), 5.76–5.64 (m, 1H*, 1H†), 5.59 (t, *J* = 7.0 Hz, 1H†), 5.45–5.32 (m, 1H*, 1H†), 5.31–5.23 (m, 2H*, 2H†), 5.22 (s, 1H*, 1H†), 5.10 (s, 2H*, 2H†), 5.03 (s, 1H*, 1H†), 4.97 (s, 1H*, 1H†), 4.83 (s, 1H†), 4.68 (s, 1H*), 4.47 (d, *J* = 1.8 Hz, 1H*), 4.37 (d, *J* = 1.1 Hz, 1H†), 3.57 (d, *J* = 10.4 Hz, 1H*, 1H†), 3.40 (d, *J* = 1.8 Hz, 1H*, 1H†), 3.19–3.11 (m, 2H*, 2H†), 2.99 (d, *J* = 5.8 Hz, 1H*, 1H†), 2.89–2.77 (m, 3H*, 3H†), 2.72–2.63 (m, 1H*, 1H†), 2.57–2.50 (m, 1H*, 1H†), 2.46–2.33 (m, 4H*, 4H†), 2.29 (dd, *J* = 14.7 Hz, *J* = 7.9 Hz, 1H*, 1H†), 1.76 (s, 3H*), 1.72 (s, 3H†), 0.14 (s, 9H*), 0.07 (s, 9H†); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 172.0, 151.0, 147.4, 147.0, 143.3, 139.4, 138.5, 134.9†, 132.8†, 132.4, 128.5, 128.1†, 117.7, 115.1, 113.8, 110.3†, 109.4, 73.3, 66.4, 61.0, 58.2, 57.5, 36.9, 35.6, 34.2, 33.6, 32.5†, 29.9, 24.7, 24.4†, 11.9, 0.5, -1.5†; **HRMS** (ESI) calcd for $C_{28}H_{40}O_4SiI$ $[M+H]^+$: 595.1741, found 595.1749.



To a solution of epoxyiodide **29** (36 mg, 0.061 mmol) in 30 mL of Et_2O (0.002 M) was added *t*-BuLi (71 μL, 1.7 M in pentane, 0.12 mmol, 2 equiv) at -120 °C (Trapp mixture: THF/Et_2O/pentane = 4:1:1) and the reaction mixture was stirred for 2 min. The reaction mixture was quenched cold with MeOH followed by saturated NH_4Cl solution at 0 °C and extracted with EtOAc (3 x 10 mL). Combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography (gradient elution 10:1 → 3:1 hexanes:EtOAc) to afford alcohol **30** (22.7 mg 80%) as a colorless oil and recovered starting material (3.5 mg). Alcohol **30** was obtained as inseparable mixture of double bond isomers formed during allylic transposition step. The major isomer is designated by (*), the minor isomer is denoted by (†). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.88 (t, *J* = 7.6 Hz, 1H*), 5.77–5.65 (m, 1H*, 1H†), 5.59 (t, *J* = 7.0 Hz, 1H†), 5.47 (s, 1H*, 1H†), 5.45–5.34 (m, 2H*, 2H†), 5.23 (s, 1H*, 1H†), 5.19 (s, 1H*, 1H†), 5.16 (s, 1H*, 1H†), 5.13 (s, 1H*, 1H†), 5.10 (s, 1H*, 1H†), 5.08 (s, 1H*, 1H†), 4.92 (s, 1H*, 1H†), 4.83 (s, 1H†), 4.67 (dd, *J* = 2.2 Hz, *J* = 1.5 Hz, 1H*), 4.47 (d, *J* = 1.5 Hz, 1H*), 4.37 (d, *J* = 1.5 Hz, 1H†), 4.04–3.98 (m, 1H*, 1H†), 3.46 (d, *J* = 1.2 Hz, 1H*, 1H†), 3.25 (d, *J* = 16.2 Hz, 1H*, 1H†), 3.10 (d, *J* = 16.2 Hz, 1H*, 1H†), 2.88–2.77 (m, 3H*, 3H†), 2.76–2.69 (m, 1H*, 1H†), 2.67–2.58 (m, 1H*, 1H†), 2.50–2.34 (m, 4H*, 4H†), 2.22 (d, *J* = 5.5 Hz, 1H*, 1H† (OH)), 1.76 (s, 3H*), 1.72 (s, 3H†), 0.17 (s, 9H*), 0.07 (s, 9H†); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 171.9, 150.9, 146.9, 144.9, 144.6, 142.1, 140.7, 138.6, 135.0†, 132.9†, 132.6, 127.7, 127.3†, 115.2, 114.86, 114.82, 114.0, 110.3†, 109.4, 74.4, 71.4, 63.2, 58.0, 39.2, 39.1, 34.2, 33.7, 32.5†, 30.5, 24.7, 24.4†, 0.5, -1.5†; **HRMS** (ESI) calcd for $C_{28}H_{41}O_4Si$ $[M+H]^+$: 469.2774, found 469.2777.



To a solution of vinyl silane **30** (18 mg, 0.038 mmol) in 900 μL of THF-MeOH-H_2O mixture (10:9:1) was added AgF (24.4 mg, 0.19 mmol, 5 equiv) and the reaction mixture was stirred at rt for 3 h under exclusion of light. After this time TLC analysis indicated ~80% conversion. The reaction mixture was quenched saturated $NaHCO_3$ solution and extracted with EtOAc (3 x 5 mL). Combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by gravity column chromatography (gradient elution 7:1 → 5:1 hexanes:EtOAc) to give Amphidinolide V (9.5 mg, 62%) as a colorless oil and recovered starting material (~1 mg). $[\alpha]_D^{25} = -12.6°$ (0.8, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.12 (d, *J* = 15.6 Hz, 1H), 5.77–5.67 (m, 1H), 5.59 (dt, *J* = 15.6 Hz, *J* = 6.7 Hz, 1H), 5.47 (s, 1H), 5.46–5.39 (m, 2H), 5.23 (s, 1H), 5.19 (s, 1H), 5.16 (s, 1H), 5.13 (s, 1H), 5.10 (s, 1H), 5.08 (s, 1H), 4.93 (s, 1H), 4.89 (s, 2H), 4.03–3.97 (m, 1H), 3.46 (d, *J* = 1.2 Hz, 1H), 3.25 (d, *J* = 16.2 Hz, 1H), 3.10 (d, *J* = 16.2 Hz, 1H), 2.86–2.78 (m, 3H), 2.77–2.70 (m, 1H), 2.67–2.59 (m, 1H), 2.51–2.35 (m, 4H), 2.30–2.21 (brs, 1H), 1.83 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 171.9, 144.9, 144.6, 142.1, 141.8, 140.7, 134.1, 132.0, 128.0, 127.4, 115.13, 115.08, 114.8 (2x), 114.0, 74.3, 71.4, 63.3, 57.9, 39.13, 39.07, 35.1, 33.7, 30.5, 18.6; **HRMS** (ESI) calcd for $C_{25}H_{33}O_4$ $[M+H]^+$: 397.2379, found 397.2377.

Spectroscopic Data for (–)-Amphidinolide V

Comparison of spectroscopic data of synthetic material with the reported[12] for (–)-Amphidinolide V ($CDCl_3$, data for synthetic material referenced to 7.26 (^{1}H NMR) and 77.0 (^{13}C NMR)):

^{1}H NMR data (δ (ppm), multiplicity, *J* (Hz), #H)		**^{13}C NMR data (δ, ppm)**	
Reported	**Synthetic**	**Reported**	**Synthetic**
6.12 (d, 15.6, 1H)	6.12 (d, 15.6, 1H)	171.9	171.9
5.77–5.67 (m, 1H)	5.77–5.67 (m, 1H)	145.0	144.9
5.60 (dt, 15.6, 6.7, 1H)	5.59 (dt, 15.6, 6.7, 1H)	144.6	144.6
5.46 (s, 1H)	5.47 (s, 1H)	142.1	142.1
5.45–5.43 (m, 1H)	5.46–5.39 (m, 2H)	141.9	141.8
5.43–5.40 (m, 1H)		140.8	140.7
5.24 (s, 1H)	5.23 (s, 1H)	134.1	134.1
5.19 (s, 1H)	5.19 (s, 1H)	132.0	132.0
5.16 (s, 1H)	5.16 (s, 1H)	128.1	128.0
5.13 (s, 1H)	5.13 (s, 1H)	127.5	127.4
5.10 (s, 1H)	5.10 (s, 1H)	115.1	115.13
5.08 (s, 1H)	5.08 (s, 1H)	115.1	115.08
4.93 (s, 1H)	4.93 (s, 1H)	114.9	114.8 (2x)
4.89 (s, 2H)	4.89 (s, 2H)	114.8	
4.00 (dd, 5.8, 5.4, 1H)	4.03–3.97 (m, 1H)	114.0	114.0
3.46 (brs, 1H)	3.46 (d, 1.2, 1H)	74.3	74.3
3.25 (d, 16.4, 1H)	3.25 (d, 16.2, 1H)	71.4	71.4
3.11 (d, 16.4, 1H)	3.10 (d, 16.2, 1H)	63.3	63.3
2.85–2.82 (m, 2H)	2.86–2.78 (m, 3H)	58.0	57.9
2.82–2.79 (m, 1H)		39.2	39.13
2.77–2.70 (m, 1H)	2.77–2.70 (m, 1H)	39.1	39.07
2.67–2.50 (m, 1H)	2.67–2.59 (m, 1H)	35.1	35.1
2.47–2.43 (m, 2H)	2.51–2.35 (m, 4H)	33.7	33.7
2.41–2.39 (m, 2H)		30.5	30.5
2.12 (d, 5.4, 1H, OH)	2.30–2.21 (brs, 1H)	18.6	18.6
1.83 (s, 3H)	1.83 (s, 3H)		

(–)-Amphidinolide V
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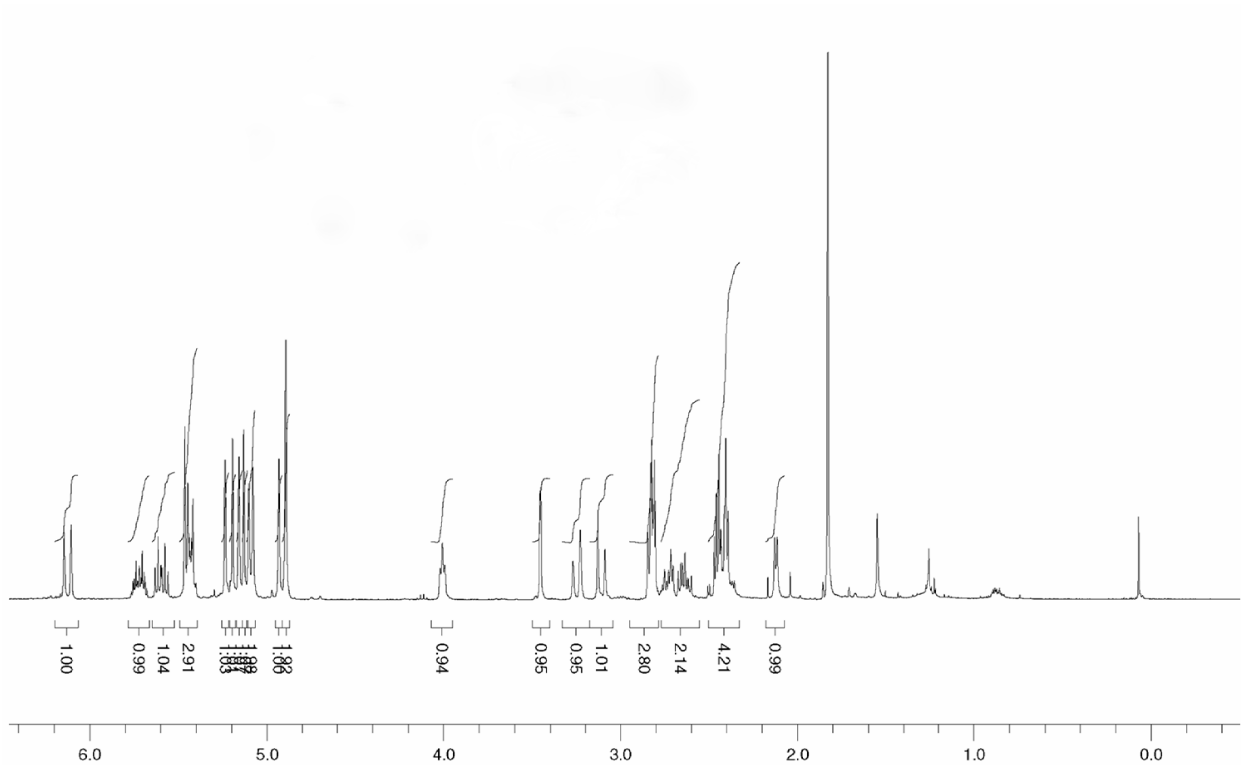
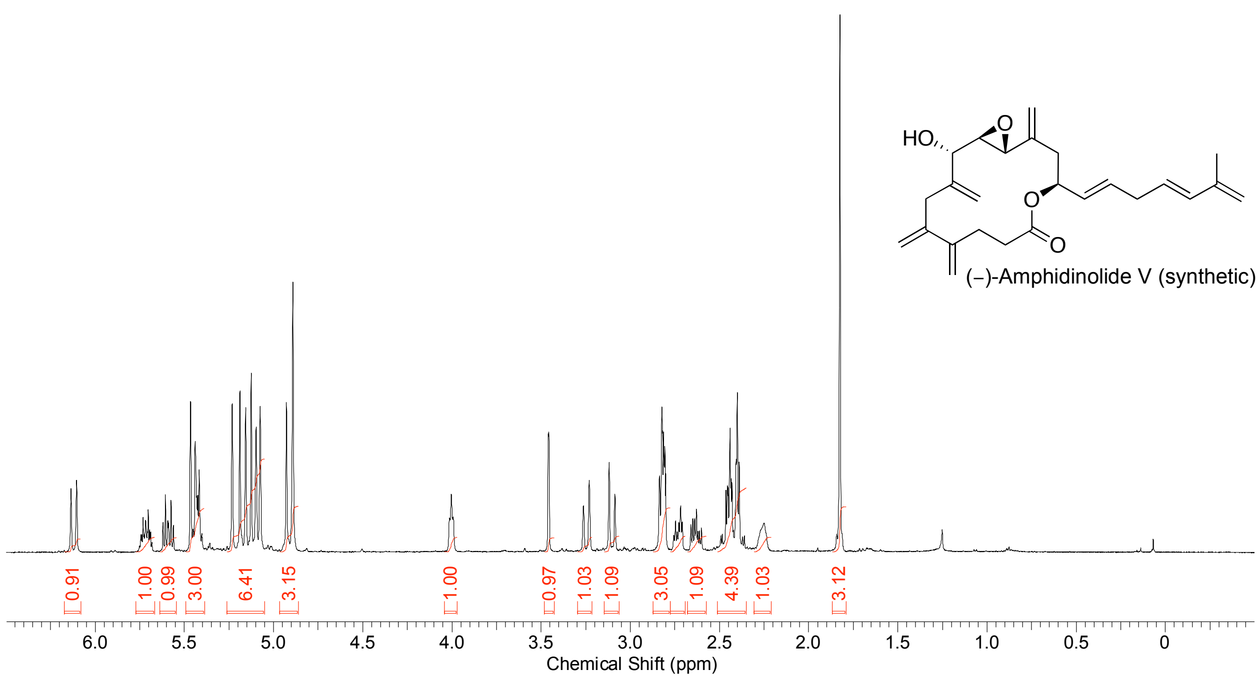
Fürstner, A.; Larionov, O.; Flügge, S. *Angew. Chem., Int. Ed.* **2007**, *46*, 5545–5548

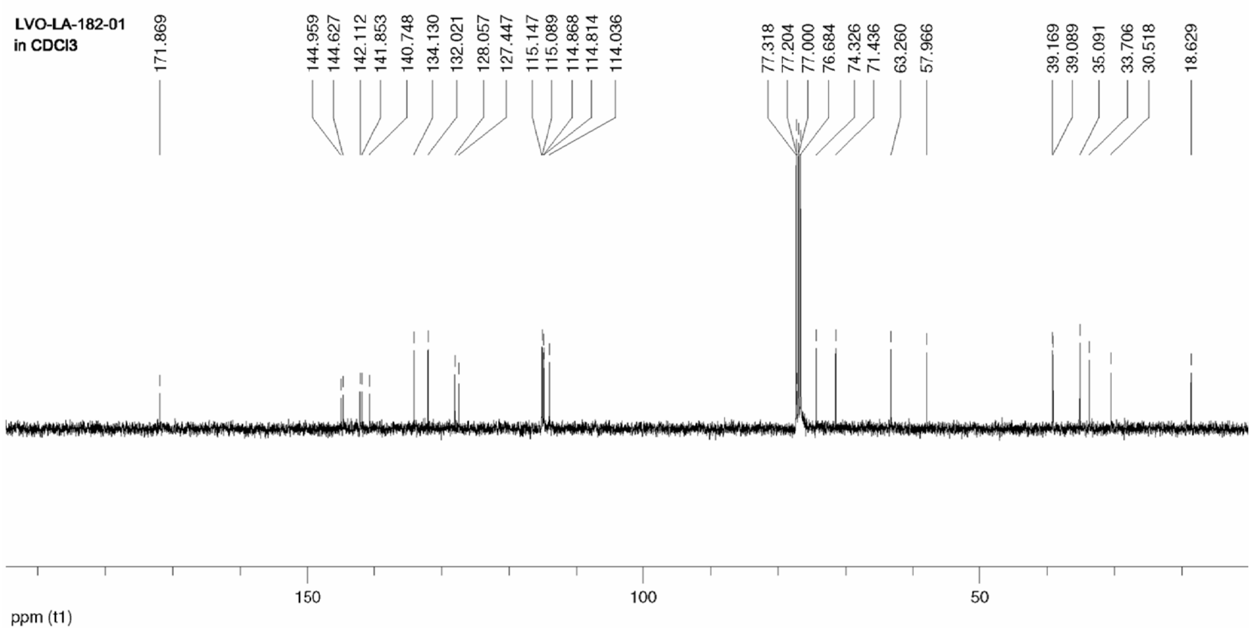


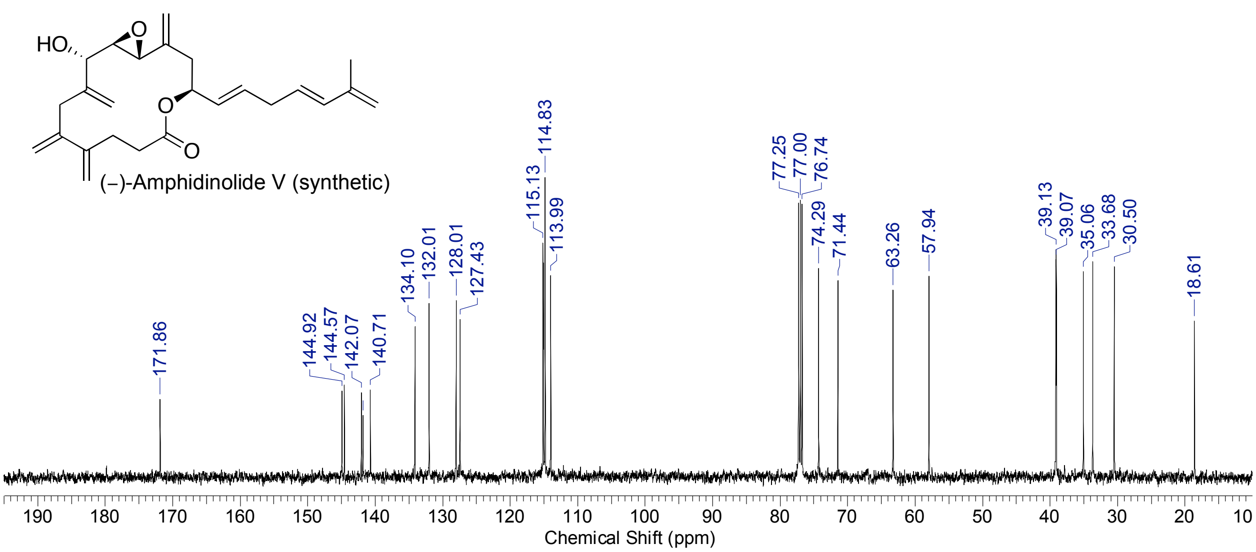


(–)-Amphidinolide V

Spectrum reproduced from:

Fürstner, A.; Larionov, O.; Flügge, S. *Angew. Chem., Int. Ed.* **2007**, *46*, 5545–5548





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