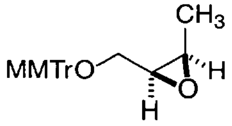
EXPERIMENTAL PROCEDURES

General. Flash chromatography was performed using silica gel 60 (230–400 mesh size). Analytical thin layer chromatography (TLC) was performed on glass-backed 0.25 mm thick silica gel plates precoated with 60 F-254. Spots were visualized under UV light and/or with staining with ethanolic *p*-anisaldehyde or ceric ammonium molybdate. All silica products were obtained from E. M. Science or Whatman. Optical rotations were obtained on a Perkin Elmer 241 polarimeter at 589 nm (sodium D line) using a 10 cm path length and a 1.0 mL volume. Concentration (*c*) is reported in g per 100 mL of the solvent specified. Infrared (FT-IR) spectra were recorded on a Galaxy 4020 and are reported in wavenumbers (cm^{-1}). Proton and carbon nuclear magnetic resonance (^1H NMR, ^{13}C NMR) spectra were measured on a Varian Gemini-300, Varian VXR-400, or Varian Inova-500 spectrometer. Proton NMR spectra were recorded in $CDCl_3$ or C_6D_6 solutions and are reported in parts per million (ppm) downfield (δ) from tetramethlysilane using residual chloroform (δ 7.26) or benzene (δ 7.20) as an internal reference. Proton NMR data are reported in the form: δ (multiplicity, coupling constants, number of protons). Carbon NMR spectra were recorded in $CDCl_3$ or C_6D_6 solutions and are reported in parts per million (ppm) downfield (δ) from tetramethlysilane (TMS) using residual chloroform ($CHCl_3$, δ 77.0) or benzene (δ 128.0) as an internal reference. Mass spectral data (MS, HRMS) data were recorded on a Kratos MS80 mass spectrometer by use of chemical ionization (CI), electron impact (EI), or fast atom bombardment (FAB). Combustion analyses were performed by Atlantic Microlab, Inc (Narcross, GA). All reagents and solvents were commercial grade and were used as received unless noted otherwise. Diethyl ether (Et_2O) and tetrahydrofuran (THF) were distilled under N_2 from sodium benzophenone ketyl immediately before use. *N,N*-diisopropylamine, *N,N*-diisopropylethylamine, methylene chloride (CH_2Cl_2), toluene, and triethylamine (Et_3N) were distilled from calcium hydride. Dimethylsulfoxide (DMSO), was distilled from calcium hydride and stored over 4A molecular sieves under argon. Dimethylformamide (DMF) was distilled from anhydrous $MgSO_4$ and stored under an atmosphere of argon. Oxalyl chloride was distilled from calcium hydride. Boron trifluoride diethyl etherate ($BF_3{\bullet}OEt_2$) was freshly distilled from calcium hydride and Et_2O under an atmosphere of argon. Hexanes and ethyl acetate (EtOAc) were distilled prior to use in chromatography. Copper(I) bromide-dimethyl sulfide (CuBr•DMS) was prepared from Cu_2Br_2.[1] All reactions were conducted in flame or oven-dried glassware under an atmosphere of argon unless otherwise noted. All non-volatile samples were pumped to constant weight at ambient temperature (0.2-0.1 mm Hg) following the removal of solvents *in vacuo*.



(2*S*,3*R*)-2,3-Epoxy-1-[(4-methoxyphenyl)diphenylmethoxy]butane (4)

Titanium(IV) isopropoxide (1.2 mL, 4.2 mmol) was added to a solution of crushed, flame dried 4A molecular sieves (3 g), (+)-diethyl tartrate (0.86 mL, 5.0 mmol), and CH_2Cl_2 (200 mL) at -20 °C. The reaction was stirred 10 min, and a solution of *cis*-but-2-en-1-ol (6.0 g, 83 mmol) and CH_2Cl_2 (5 mL) was added dropwise. After stirring the reaction 30 min at -20 °C, *tert*-butyl hydroperoxide (33 mL, 3.77 M in toluene) was added dropwise. The reaction was stirred 1 h, sealed with parafilm, and placed in a -20 °C freezer. After 25 h, the reaction was placed in a -20 °C bath under argon, and trimethyl phosphite (4.9 mL, 42 mmol) was added to the reaction over 1.6 h. The reaction was stirred 15 min. Triethylamine (23 mL, 170 mmol), dimethylaminopyridine (DMAP) (0.5 g), and 4-methoxytrityl choride (MMTrCl) (28 g, 92 mmol) were added. The reaction was warmed to 0 °C, stirred 6 h, and placed in a 0 °C freezer overnight. Thin layer chromatography indicated the reaction was not complete so additional MMTrCl (2 g, 6.6 mmol) was added. After stirring 3 h at 0 °C, MeOH (10 mL) was added. The reaction mixture was then filtered through a silica (40 g) and celite (25 g) pad using CH_2Cl_2. The filtrate was concentrated *in vacuo*. Hexanes (400 mL) were added to the resulting thick paste which was transferred to a fritted funnel. The filtrate was again concentrated *in vacuo*. Purification by flash column chromatography (800 g SiO_2, using a gradient elution of: hexanes to 30% EtOAc in hexanes) provided 24 g (80%) of **4** as a thick oil: R_f 0.48

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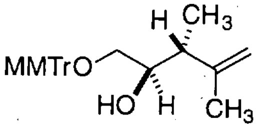
[1] Taylor, R.J.K.; Casey, G. In *Organocopper reagents: A Practical Approach*; Taylor, R.J.K., Ed.; Oxford University Press: Oxford, 1994, 38.

(40% EtOAc in hexanes); $[\alpha]_D^{23}$ +16.0 (*c* 3.95, $CHCl_3$); IR (neat) 3032, 2928, 1607, 1501, 1447, 1250, 1179, 1034 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.47 (m, 4H), 7.21–7.36 (m, 8H), 6.83 (m, 2H), 3.80 (s, 3H), 3.30 (A of ABX, J_{AB} = 9.94 Hz, J_{AX} = 5.37 Hz, 1H), 3.18 (m, 1H), 3.12 (B of ABX, J_{AB} = 9.8 Hz, J_{BX} = 4.8 Hz, 1H), 3.09 (m, 1H), 1.14 (d, *J* = 5.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.5, 144.4 144.2, 135.5, 130.3, 128.3, 127.8, 126.9, 113.1, 86.5, 61.9, 55.3, 55.2, 52.1, 13.4; MS (EI) *m/e* (relative intensity) 360 (20), 273 (100), 213 (25), 165 (20), 135 (18), 105 (37); HRMS *m/e* calcd for $C_{24}H_{24}O_3$ (M^+) 360.1725, found 360.1734.



(2*R*,3*R*)-1-[(4-Methoxyphenyl)diphenylmethoxy]-3,4-dimethylpent-4-en-2-ol (5)

Dibromoethane (3 drops) was added to a solution of 2-bromopropene (10 drops), flame-dried Mg turnings (3.1 g), and THF (30 mL). 2-Bromopropene (5.7 mL, 64.6 mmol) and THF (60 mL) were then simultaneously added via separate syringes maintaining a steady reflux. The reaction was stirred 1.5 h and cannulated into a -78 °C slurry of CuBr•DMS (6.6 g, 32.3 mmol) and THF (20 mL). The deep orange reaction was stirred 10 min, and a solution of epoxide **4** (7.76 g, 21.5 mmol), and THF (80 mL) was added. After 10 min, $BF_3{\bullet}OEt_2$ (2.5 mL, 14.4 mmol) was added dropwise. The reaction was warmed slowly to -20 °C over 2 h at which time it turned black. Saturated aqueous NH_4Cl (20 mL) was added, and the mixture was transferred to a separatory funnel with Et_2O. The organic layer was washed with H_2O (2 x 100 mL) and brine (150 mL). The aqueous layers were extracted with Et_2O (1 x 50 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash column chromatography (400 g SiO_2, using a gradient elution of: hexanes to 10% Et_2O in hexanes) provided 7.15 g (84%) of **5** as a thick clear colorless oil which crystallized upon storage in a -20 °C freezer. Mosher ester analysis[2] indicated 82% ee by ^1H NMR. Data for **5**: mp 94–97 °C; R_f 0.28 (20% Et_2O in hexanes); $[\alpha]_D^{23}$ -4.03 (*c*

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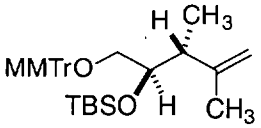
[2] Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* 1973, 95, 512–519

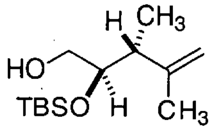
1.49, $CHCl_3$); IR (neat) 3584, 3061, 2965, 2930, 1607, 1510, 1447, 1250, 1090, 1036, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.47 (m, 4H), 7.21–7.36 (m, 8H), 6.84 (m, 2H), 4.82 (s, 1H), 4.79 (s, 1H), 3.80 (s, 3H), 3.60 (m, 1H), 3.32 (A of ABX, J_{AB} = 9.7 Hz, J_{AX} = 6.5 Hz, 1H), 3.05 (B of ABX, J_{AB} = 9.7 Hz, J_{BX} = 3.0 Hz, 1H), 2.40 (dq, J = 8.5, 6.8 Hz, 1H), 2.27 (d, J = 3.4 Hz, 1H), 1.68 (s, 3H), 0.83 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.5, 147.5, 144.5, 144.4, 135.6, 130.3, 128.4, 127.8, 126.9, 113.1, 86.3, 72.5, 65.5, 55.2, 44.4, 19.1, 15.6; MS (CI, CH_4) *m/e* (relative intensity) 402 (8), 325 (3), 273 (100), 213 (9), 143 (8); HRMS *m/e* calcd for $C_{27}H_{30}O_3$ (M^+) 402.2195, found 402.2197.



(2*R*,3*R*)-2-(*tert*-Butyldimethylsilanyloxy)-1-[(4-methoxyphenyl)diphenylmethoxy]-3,4-dimethylpent-4-ene (**18**)

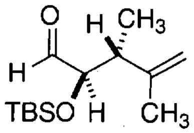
Alcohol **5** (3.55 g, 8.82 mmol), *tert*-butyldimethylsilyl chloride (1.6 g, 11 mmol), dimethylaminopyridine (DMAP) (54 mg, 0.44 mmol), and imidazole (1.2 g, 18 mmol) were stirred in DMF (15 mL) at ambient temperature 4 days. The reaction mixture was diluted with hexanes (50 mL) and extracted with saturated aqueous NH_4Cl (3 x 10 mL), H_2O (10 mL), and brine (15 mL). The combined aqueous layers were extracted with hexanes (3 x 15 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (150 g SiO_2, 5% EtOAc in hexanes) which provided 4.1 g (92%) of **18** as a thick oil: R_f 0.60 (20% EtOAc in hexanes); $[\alpha]_D^{24}$ +4.74 (*c* 1.02, $CHCl_3$); IR (neat) 3063, 2955, 2857, 1609, 1510, 1252, 1179, 1067, 1038, 833, 774, 704 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.47 (m, 4H), 7.35 (m, 2H), 7. 29 (m, 4H), 7.23 (m, 2H), 6.84 (m, 2H), 4.69 (s, 2H), 3.82 (s, 3H), 3.78 (m, 1H), 3.05 (d, J = 6.3 Hz, 2H), 2.57 (dq, J = 7.3, 4.0 Hz, 1H), 1.67 (s, 3H), 1.01 (d, J = 7.3 Hz, 3H), 0.87 (s, 9H), 0.04 (s, 3H), -0.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.4, 146.8, 144.8, 136.1, 130.4, 128.5, 127.6, 112.9, 111.9, 86.3, 74.6, 65.6, 55.2, 44.1, 25.9, 21.5, 18.0, 15.4, -4.3, -5.0; MS (CI, CH_4) *m/e* (relative intensity) 273 (100), 265 (50), 229 (10), 213 (30), 197 (30);

HRMS (FAB, Na) *m/e* calcd for $C_{33}H_{44}O_3SiNa$ (M^++Na^+) 539.2958, found 539.2956; Anal. calcd for $C_{33}H_{44}O_3Si$: C, 76.70; H, 8.58. Found: C, 76.98; H, 8.63.



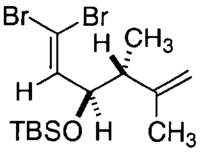
(2*R*,3*R*)-2-(*tert*-Butyldimethylsilanyloxy)-3,4-dimethylpent-4-en-1-ol (19)

2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (1.8 g, 7.7 mmol) was added to a solution of trityl ether **18** (1.02 g), *tert*-butyl alcohol (6 mL), aqueous pH = 7 buffer (6 mL), and CH_2Cl_2 (30 mL). The red reaction was stirred 18 h, quenched with saturated aqueous $NaHCO_3$ (10 mL), and transferred to a separatory funnel using CH_2Cl_2 (10 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ (15 mL), H_2O (15 mL), and brine (20 mL); dried over $MgSO_4$; filtered; and concentrated *in vacuo*. The residue was taken up in hexanes (20 mL). The organic layer was washed with $NaHCO_3$ (10 mL), H_2O (10 mL), and brine (15 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo* to provide an orange oil. Purification by flash column chromatography (50 g SiO_2, using a gradient elution of: hexanes to 10% EtOAc in hexanes) provided 373 mg (73%) of **19** as a clear colorless oil which could be further purified by Kugelrohr distillation (90 °C, 0.2 mm Hg). Data for **19**: R_f 0.55 (20% EtOAc in hexanes); $[\alpha]_D^{23}$ +2.93 (*c* 2.00, $CHCl_3$); IR (neat) 3426, 3073, 2957, 2930, 2859, 1642, 1462, 1256, 1065, 812, 755 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.80 (s, 1H), 4.77 (s, 1H), 3.77 (m, 1H), 3.54 (d, *J* = 4.8 Hz, 2H), 2.42 (dq, *J* = 6.9, 6.7 Hz, 1H), 1.65 (s, 3H), 1.70 (br s, 1H–OH), 1.04 (d, *J* = 6.9 Hz, 3H), 0.90 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.1, 111.7, 74.7, 64.0, 44.0, 25.8, 23.3, 21.4, 14.4, -4.5, -4.7; MS (CI, CH_4) *m/e* (relative intensity) 227 (1), 213 (4), 175 (11), 159 (8), 137 (7), 115 (10), 95 (11), 87 (37), 85 (80), 83 (100); HRMS *m/e* calcd for $C_{13}H_{27}OSi$ (M^+–OH) 227.1831, found 227.1829; Anal. calcd for $C_{13}H_{28}O_2Si$: C, 63.87; H, 11.55. Found: C, 63.57; H, 11.48.



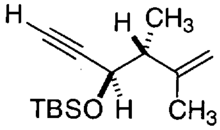
(2*R*,3*R*)-2-(*tert*-Butyldimethylsilanyloxy)-3,4-dimethylpent-4-enal (6)

Dimethylsulfoxide (0.46 mL, 6.55 mmol) was added dropwise to a solution of oxalyl chloride (0.29 mL, 3.3 mmol) and CH_2Cl_2 (8 mL) at -78 °C. After 20 min, a solution of alcohol **19** (400 mg, 1.6 mmol) and CH_2Cl_2 (4 mL) was added. The reaction stirred 30 min at -78 °C, and Et_3N (1.8 mL, 13 mmol) was added dropwise. The reaction was stirred 30 min at -78 °C, warmed to ambient temperature, and diluted with pentane (30 mL) and H_2O (10 mL). The organic layer was washed with H_2O (15 mL), saturated aqueous NH_4Cl (3 x 15 mL), and brine (20 mL); dried over Na_2SO_4; filtered; and concentrated *in vacuo*. Proton NMR and TLC indicated that alcohol **19** was cleanly converted to **6**, and it was used directly in the following reaction without further purification. Data for **6**: R_f 0.60 (20% EtOAc in hexanes); IR (neat) 3075, 2957, 2932, 2897, 2859, 1736, 1462, 1256, 1080, 839, 779 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.53 (d, *J* = 2.2 Hz, 1H), 4.80 (s, 1H), 4.78 (s, 1H), 3.9 (dd, *J* = 5.5, 2.2 Hz, 1H), 2.59 (dq, *J* = 7.0, 5.5 Hz, 1H), 1.74 s (3H), 1.09 (d, *J* = 7.0 Hz, 3H), 0.92 (s, 9H), 0.054 (s, 3H), 0.047 (s, 3H); MS (CI, CH_4) *m/e* (relative intensity) 241 (3), 213 (32), 185 (100), 155 (13), 115 (9), 83 (40), 73 (45), 75 (45); HRMS *m/e* calcd for $C_{12}H_{23}O_2Si$ (M^+–CH_3) 227.1467, found 227.1471.



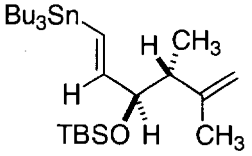
(3*R*,4*R*)-1,1-Dibromo-3-(*tert*-butyldimethylsilanyloxy)-4,5-dimethylhexa-1,5-diene (20)

Triphenylphosphine (2.6 g, 9.8 mmol) was added to a 0 °C solution of CBr_4 (1.6 g, 4.9 mmol), and CH_2Cl_2 (15 mL). The reaction stirred 10 min and was cooled to -78 °C. A solution of aldehyde **6** (398 mg, 1.64 mmol) in CH_2Cl_2 (5 mL) was added. After the reaction stirred 2 h at -78 °C, it was diluted with hexanes (30 mL) and water (5 mL). The organic layer was washed with H_2O (10 mL), saturated aqueous NH_4Cl (15 mL), and brine (20 mL); dried over $MgSO_4$; filtered through a plug of silica; and concentrated *in vacuo*. Purification by flash column chromatography (16 g SiO_2, using a gradient elution of: hexanes to 5% EtOAc in hexanes) provided 470 mg (72%, 2 steps) of **20** as a clear colorless oil: R_f 0.73 (20% EtOAc in hexanes); $[\alpha]_D^{23}$ -16.8 (*c* 1.64, $CHCl_3$); IR (neat) 3075, 2957, 2930, 2859, 1649, 1616, 1462, 1375, 1254, 1074, 839, 775 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.34 (d, *J* = 8.6 Hz, 1H), 4.79 (t, *J* = 1.6 Hz, 1H), 4.74 (s, 1H), 4.23 (dd, *J* = 8.6, 6.7 Hz, 1H), 2.3 (dq, *J* = 7.0, 6.7 Hz, 1H), 1.73 (s, 3H), 1.03 (d, *J* = 7.1 Hz, 3H), 0.87 (s, 9H), 0.07 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.2, 140.9, 112.4, 88.9, 76.1, 47.0, 25.7, 20.6, 18.0, 15.2, -4.4, -5.2; HRMS (FAB, Na) *m/e* calcd for $C_{10}H_{17}{}^{79}Br^{81}BrOSi$ ($M^+-C_4H_9$) 340.9395, found 340.9386.



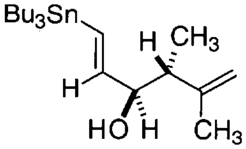
(3*R*,4*R*)-4-(*tert*-Butyldimethylsilanyloxy)-2,3-dimethylhex-1-en-5-yne (21)

n-Butyllithium (0.35 mL, 2.5 M in hexanes) was added to a -78 °C solution of **20** (150 mg, 0.377 mmol) and THF (2.5 mL). The reaction was stirred 1.5 h while warming to -50 °C. Saturated aqueous NH_4Cl (5 mL) was added, and the mixture was transferred to a separatory funnel using Et_2O (10 mL). The organic layer was washed with water (5 mL) and brine (10 mL); dried over $MgSO_4$; filtered; and concentrated *in vacuo*. Purification by flash column chromatography (8 g SiO_2, pentane) provided 65.5 mg (73%) of **21** as a clear colorless oil: R_f 0.55 (hexanes); $[\alpha]_D^{23}$ +44.4 (*c* 1.26, $CHCl_3$); IR (neat) 3312, 3077, 2957, 2932, 2859, 1649, 1462, 1252, 1098, 837, 777, 629 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.82 (s, 1H), 4.81 (s, 1H), 4.31 (dd, *J* = 6.7, 2.1 Hz, 1H), 2.39 (m, 2H), 1.73 (s, 3H), 1.12 (d, *J* = 7.0 Hz, 3H), 0.89 (s, 9H), 0.14 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.1, 112.1, 84.4, 73.1, 66.1, 47.7, 25.7, 20.7, 18.2, 14.8, -4.5, -5.3; MS (CI, CH_4) *m/e* (relative intensity) 238 (5), 223 (47), 181 (82), 169 (70), 139 (49), 113 (49), 85 (100), 75 (70); HRMS *m/e* calcd for $C_{14}H_{26}OSi$ (M^+) 238.1753, found 238.1748.



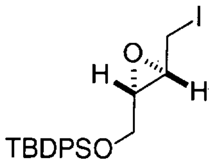
(1*E*,3*R*,4*R*)-3-(*tert*-Butyldimethylsilanyloxy)-4,5-dimethyl-1-(tributylstannanyl)hexa-1,5-diene (22)

Tributyltinhydride (0.10 mL, 0.38 mmol) was added to a solution of alkyne **21** (82 mg, 0.34 mmol), $PdCl_2(PPh_3)_2$ (4.8 mg, 6.7 μmol), and THF (1.7 mL). After 10 min, the reaction was concentrated *in vacuo*. Purification by flash column chromatography (10 g SiO_2, hexanes) provided 133 mg (73%) of **22** as a clear colorless oil: R_f 0.47 (hexanes); $[\alpha]_D^{26}$ +14.0 (*c* 0.865, $CHCl_3$); IR (neat) 2957, 2928, 2857, 1462, 1375, 1254, 1096, 1061, 835, 775 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.02 (d, *J* = 19.1 Hz, 1H), 5.85 (dd, *J* = 19.1, 6.3 Hz, 1H), 4.75 (s, 1H), 4.70 (s, 1H), 3.98 (apparent t, *J* = 6.3 Hz, 1H), 2.42 (apparent quintet, *J* = 6.8 Hz, 1H), 1.72 (s, 3H), 1.50 (m, 6H), 1.30 (m, 6H), 0.94 (d, *J* = 7.0 Hz, 3H), 0.89 (m, 15H), 0.88 (s, 9H), 0.03 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.0, 147.5, 128.2, 111.3, 79.6, 47.4, 29.1, 27.2, 25.9, 21.0, 18.3, 15.1, 13.7, 9.5, -4.1, -5.0; HRMS *m/e* calcd for $C_{22}H_{45}OSi^{116}Sn$ ($M^+–C_4H_9$) 469.2256, found 469.2251



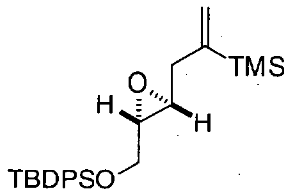
(1*E*,3*R*,4*R*)-4,5-Dimethyl-1-(tributylstannanyl)hexa-1,5-dien-3-ol (2)

Tetrabutylammonium fluoride (0.15 mL, 1.0 M in THF) was added to stannane **22** (63 mg, 0.12 mmol), and the reaction was stirred 3 h. Saturated aqueous NH_4Cl (0.1 mL) was added, and the mixture was placed directly on a column of silica gel (10 g). Purification by flash column chromatography using 5% EtOAc hexanes provided 31 mg (63%) of **2** as a clear yellow oil: R_f 0.62 (20% EtOAc in hexanes); IR (neat) 3443, 2959, 2926, 2872, 2855, 1645, 1456, 1375, 1094, 990, 889 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.20 (d, *J* = 18.8 Hz, 1H), 5.92 (dd, *J* = 19.0, 6.4 Hz, 1H), 4.91 (s, 1H), 4.86 (s, 1H), 3.84 (m, 1H), 2.24 (dq, *J* = 8.9, 7.0 Hz, 1H), 1.88 (s, 1H–OH), 1.73 (s, 3H), 1.49 (m, 6H), 1.31 (m, 6H), 0.97 (d, J = 7.0 Hz, 3H), 0.89 (m, 15H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.7, 147.2, 130.7, 113.0. 77.5, 47.6, 29.1, 27.2, 19.1, 15.6, 13.7, 9.5; MS (CI, CH_4) *m/e* (relative intensity) 359 (45), 357 (35), 355 (22), 289 (69), 265 (69), 207 (100), 199 (49), 177 (64), 169 (43), 119 (31), 107 (23), 91 (51); HRMS *m/e* calcd for $C_{16}H_{31}O^{116}Sn$ ($M^+-C_4H_9$) 355.1392, found 355.1397.



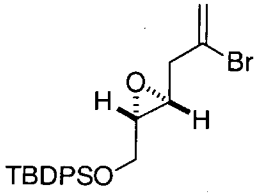
(2*S*,3*S*)-4-(*tert*-Butyldiphenylsilanyloxy)-2,3-epoxy-1-iodobutane (8)

Triphenylphosphine (2.62 g, 10.0 mmol) and imidazole (1.36 g, 20.0 mmol) were dissolved in CH_2Cl_2 (25 mL) at 0 °C. Iodine (2.54 g, 10.0 mmol) was added, and the resulting mixture was stirred 30 min. Alcohol **7** ($[\alpha]_D^{24}$ -13.0 (*c* 2.86, $CHCl_3$), 91% ee by Mosher Ester analysis)^2 (1.7 g, 5.0 mmol) was added, and the resulting mixture stirred 1 h. Aqueous sodium sulfite (10%, 20 mL) was added, and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2, and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash column chromatography (80g SiO_2 using a gradient elution of: hexanes to 5% EtOAc in hexanes) provided 2.1 g (91%) of **8** as a colorless oil R_f 0.44 (5% EtOAc in hexanes); $[\alpha]_D^{23}$ +1.74 (*c* 1.95, $CHCl_3$); IR (neat) 3071, 2959, 2930, 2859, 1472, 1427, 1113, 741, 702 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (m, 4H), 7.42 (m, 6H), 3.81 (A of ABX, J_{AB} = 12.0 Hz, J_{AX} = 4.3 Hz, 1H), 3.77 (B of ABX, J_{AB} = 12.0 Hz, J_{BX} = 3.4 Hz, 1H), 3.25 (A of ABX, J_{AB} = 9.7 Hz, J_{AX} = 6.4 Hz, 1H), 3.05 (B of ABX, J_{AB} = 9.7 Hz, J_{BX} = 5.8 Hz, 1H), 3.18 (ddd, J = 6.4, 5.8, 2.0 Hz, 1H), 3.02 (ddd, J = 4.3, 3.4, 2.0 Hz, 1H), 1.06 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.6, 135.5, 129.8, 127.8, 63.0, 62.0, 55.7, 26.7, 19.2, 4.1; MS (CI, CH_4) *m/e* (relative intensity) 395 (50), 365 (80), 309 (100), 267 (40), 199 (70), 181 (50), 128 (92), 91 (65); HRMS *m/e* calcd for $C_{16}H_{16}IO_2Si$ ($M^+-C_4H_9$) 394.9964, found 394.9979; Anal. calcd for $C_{20}H_{25}IO_2Si$: C, 53.10; H, 5.57. Found: C, 53.04; H, 5.58.



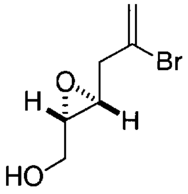
(4*S*,5*S*)-6-(*tert*-Butyldiphenylsilanyloxy)-4,5-epoxy-2-trimethylsilylhex-1-ene (10)

1,2-Dibromoethane (0.45 mL, 5.0 mmol) was added to magnesium turnings (1.7 g, 72 mmol) in THF (20 mL). (1-Bromovinyl)trimethylsilane (3.2 g, 18 mmol) in THF (5 mL) was added dropwise while maintaining reflux. The reaction was heated to reflux for 30 min then cooled to ambient temperature. The Grignard reagent was cannulated into a mixture of iodide **8** (4.10 g, 9.0 mmol), copper(I) iodide (171 mg, 0.9 mmol), HMPA (6.3 mL, 36 mmol), and THF (8.0 mL) at -25 °C. The reaction was stirred 1 h, quenched with saturated aqueous NH_4Cl, and diluted with ether (150 mL). The organic layer was separated, and the aqueous layer was extracted with ether. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash column chromatography (80 g SiO_2 using a gradient elution of: hexanes to 5% EtOAc in hexanes) provided 3.46 g (91%) of **10** as a clear colorless oil: R_f 0.51 (5% EtOAc in hexanes); $[\alpha]_D^{23}$ -7.85 (*c* 1.35, $CHCl_3$); IR (neat) 3071, 3052, 2957, 2895, 2859, 1588, 1472, 1427, 1248, 1113, 839, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.69–7.67 (m, 4H), 7.43–7.36 (m, 6H), 5.71 (ddd, *J* = 3.0, 1.5, 1.5 Hz, 1H), 5.43 (d, *J* = 3.0 Hz, 1H) 3.80 (A of ABX, J_{AB} = 11.9 Hz, J_{AX} = 4.4 Hz, 1H), 3.76 (B of ABX, J_{AB} = 11.9 Hz, J_{BX} = 3.6 Hz, 1H), 2.97–2.90 (m, 2H), 2.44 (A of ABX, J_{AB} = 15.2 Hz, J_{AX} = 5.8 Hz, 1H), 2.27 (B of ABX, J_{AB} = 15.2 Hz, J_{BX} = 5.8 Hz, 1H), 1.05 (s, 9H), 0.10 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.8, 135.6, 133.3, 129.7, 127.7, 126.4, 63.9, 58.7, 55.6, 37.9, 26.7, 19.2, -1.8; MS (EI) *m/e* (relative intensity) 367 (15), 293 (12), 271 (65), 241 (35), 217 (50), 195 (65), 163 (55), 135 (62), 91 (70), 73 (100); HRMS *m/e* calcd for $C_{21}H_{27}O_2Si_2$ (M^+–C_4H_9) 367.1549, found 367.1557; Anal. calcd for $C_{25}H_{36}O_2Si_2$: C, 70.70; H, 8.54. Found: C, 70.54; H, 8.51.



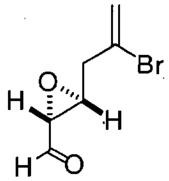
(4*S*,5*S*)-2-Bromo-6-(*tert*-butyldiphenylsilanyloxy)-4,5-epoxyhex-1-ene (11)

A solution of bromine (0.49 mL, 9.5 mmol) and CH_2Cl_2 (10 mL) was added to a solution of alkene **10** (3.1 g, 7.3 mmol) and CH_2Cl_2 (10 mL) at -78 °C. After 10 min, a solution of sodium sulfite (0.55 g, 4.4 mmol) and methanol (10 mL) was added. The resulting mixture stirred 10 min, and aqueous sodium sulfite (10%, 10 mL) was added. The organic layer was separated, and the aqueous layer was extracted with hexanes. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo.* The residue was dissolved in methanol (20 mL) and cooled to 0 °C. Sodium methoxide (11.7 mL, 1.0 M in methanol) was added. After 2 h, water (30 mL) and hexanes (30 mL) were added. The organic layer was separated, and the aqueous layer was extracted with hexanes. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo.* Purification by flash column chromatography (65 g SiO_2 using a gradient elution of: hexanes to 5% EtOAc in hexanes) provided 2.65 g (85%) of **11** as a clear colorless oil: R_f 0.49 (5% EtOAc in hexanes); $[\alpha]_D^{23}$ -3.03 (*c* 1.06, $CHCl_3$); IR (neat) 3071, 3050, 2930, 2855, 1632, 1472, 1427, 1111, 909 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.70–7.66 (m, 4H), 7.44–7.37 (m, 6H), 5.72 (s, 1H), 5.53 (d, J = 1.9 Hz, 1H), 3.84 (A of ABX, J_{AB} = 11.8 Hz, J_{AX} = 4.5 Hz, 1H), 3.78 (B of ABX, J_{AB} = 11.8 Hz, J_{BX} = 3.4 Hz, 1H), 3.08 (ddd, J = 6.0, 6.0, 2.1 Hz, 1H), 3.01 (ddd, J = 4.5, 3.6, 2.1 Hz, 1H), 2.75 (A of ABX, J_{AB} = 15.2 Hz, J_{AX} = 6.0 Hz, 1H), 2.58 (B of ABX, J_{AB} = 15.2 Hz, J_{BX} = 5.6 Hz, 1H), 1.05 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.6, 133.3, 129.8, 128.4, 127.7, 118.9, 63.6, 58.3, 54.0, 43.8, 26.8, 19.2; MS (CI, CH_4) *m/e* (relative intensity) 373 (14), 293 (39), 263 (78), 253 (47), 241 (77), 225 (84), 199 (100), 183 (80), 163 (86), 139 (88), 115 (47), 91 (78); HRMS *m/e* calcd for $C_{18}H_{18}BrO_2Si$ (M^+–C_4H_9) 373.0259, found 373.0260; Anal. calcd for $C_{22}H_{27}BrO_2Si$: C, 61.25; H, 6.31; Br 18.52. Found: C, 61.48; H, 6.31; Br 18.33.



(2*S*,3*S*)-5-Bromo-2,3-epoxyhex-5-en-1-ol (23)

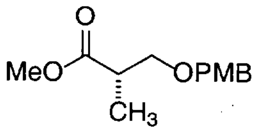
Tetrabutylammonium fluoride (14 mL, 1.0 M in THF) was added to bromide **11** (5.0 g, 11.6 mmol), and the reaction was stirred 30 min. The mixture was placed directly on a column of silica gel (250 g). Purification by flash column chromatography using a gradient elution of: 40% Et_2O in hexanes to 90% Et_2O in hexanes provided 2.1 g (93%) of **23** as a clear yellow oil: R_f 0.20 (20% EtOAc in hexanes); $[\alpha]_D^{23}$ +14 (*c* 0.40, $CHCl_3$); IR (neat) 3404, 2998, 2920, 1632, 1415, 1150, 1010, 897 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.73 (d, *J* = 1.1 Hz, 1H), 5.55 (d, *J* = 1.1 Hz, 1H), 3.96 (A of ABX, J_{AB} = 12.7 Hz, J_{AX} = 4.1 Hz, 1H), 3.69 (B of ABX, J_{AB} = 12.7 Hz, J_{BX} = 2.5 Hz, 1H), 3.21 (m, 1H), 3.05 (m, 1H), 2.77 (A of ABX, J_{AB} = 15.3 Hz, J_{AX} = 6.0 Hz, 1H), 2.65 (B of ABX, J_{AB} = 15.3 Hz, J_{BX} = 5.3 Hz, 1H), 1.90 (br s, 1H–OH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 128.1, 119.2, 61.2, 58.3, 53.7, 43.6; MS (CI, CH_4) *m/e* (relative intensity) 191 (1), 182 (3), 163 (50), 161 (35), 135 (10), 121 (10), 84 (100); HRMS *m/e* calcd for C_5H_6BrO (M^+–CH_2OH) 160.9602, found 160.9634; Anal. calcd for $C_6H_9O_2Br$: C, 37.33; H, 4.70; Br, 41.39. Found: C, 37.55; H, 4.90; Br, 41.10.



(2*S*,3*S*)-5-Bromo-2,3-epoxyhex-5-enal (12)

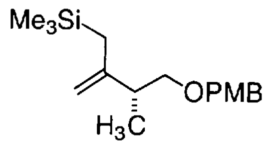
Alcohol **23** (270 mg, 1.39 mmol) was dissolved in CH_2Cl_2 (5.0 mL). Sodium bicarbonate (1.18 g, 14.0 mmol) and Dess-Martin periodinane (1.20 g, 2.80 mmol) were added. After 1.5 h, the mixture was placed directly on a column of silica gel (25 g). Purification by flash column chromatography using a gradient elution of: 5% EtOAc in hexanes to 15% EtOAc in hexanes provided 200 mg

(75%) of **12** as a light yellow oil: R$_f$ 0.30 (30% EtOAc in hexanes); $[\alpha]_D^{23}$ +33.4 (*c* 1.00, CHCl$_3$); IR (neat) 2999, 2917, 2836, 2733, 1730, 1632, 1415, 1146, 1018, 901 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 9.06 (d, *J* = 6.2 Hz, 1H), 5.77 (d, *J* = 0.8 Hz, 1H), 5.60 (d, *J* = 1.9 Hz, 1H), 3.49 (m, 1H), 3.28 (dd, *J* = 6.2, 1.6 Hz, 1H), 2.83 (A of ABX, J_{AB} = 15.3 Hz, J_{AX} = 6.1 Hz, 1H), 2.76 (B of ABX, J_{AB} = 15.3 Hz, J_{BX} = 4.9 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 197.2, 126.7, 120.1, 58.6, 54.7, 43.0; MS (CI, CH$_4$) m/e (relative intensity) 161 (5), 151 (3), 135 (7), 121 (10), 88 (45), 86 (87), 84 (100) 83 (48); HRMS m/e calcd for C$_5$H$_6$BrO (M$^+$–CHO) 160.9602, found 160.9606.



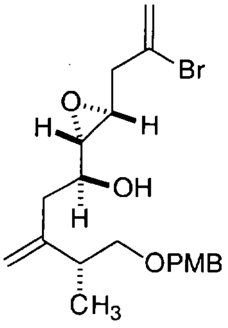
(*S*)-3-(4-methoxybenzyloxy)-2-methylpropionic acid methyl ester (24)

(*S*)-Methyl 3-hydroxy-2-methylpropionate (1.18 g, 10.0 mmol), 4-methoxybenzyl-2,2,2-trichloroacetimidate (3.67 g, 13.0 mmol), camphorsulfonic acid (232 mg, 1.0 mmol), and CH$_2$Cl$_2$ (20 mL) stirred at ambient temperature for 12 h and quenched with water. The combined organic layers were dried over MgSO$_4$, filtered, and concentrated *in vacuo*. Purification by flash column chromatography (60 g SiO$_2$, using a gradient elution of: hexanes to 5% EtOAc in hexanes) provided 2.08 g (88%) of ester **24** as a colorless oil: R$_f$ 0.44 (5% EtOAc in hexanes); $[\alpha]_D^{23}$ +9.1 (*c* 1.00, CHCl$_3$); IR (neat) 2951, 1736, 1613, 1512, 1248 cm^{-1}; 1H NMR (300 MHz, CDCl$_3$) δ 7.21 (d, *J* = 8.4 Hz, 2H), 6.85 (d, *J* = 8.4 Hz, 2H), 4.43 (s, 2H), 3.76 (s, 3H), 3.66 (s, 3H), 3.61 (A of ABX, J_{AB} = 9.2 Hz, J_{AX} = 7.5 Hz, 1H), 3.12 (B of ABX, J_{AB} = 9.2 Hz, J_{BX} = 6.0 Hz, 1H), 2.75 (ddq, *J* = 7.5, 6.0, 6.9 Hz, 1H), 1.15 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 175.1, 159.0, 130.0, 129.0, 113.5, 72.5, 71.4, 55.0, 51.5, 40.0, 13.8; MS (CI, CH$_4$) *m/e* (relative intensity) 238 (10), 150 (10), 137 (100), 121 (75); HRMS *m/e* calcd for C$_{13}$H$_{18}$O$_4$ (M$^+$) 238.1205, found 238.1203; Anal. calcd for C$_{13}$H$_{18}$O$_4$: C, 65.53; H, 7.61. Found: C, 65.38; H, 7.52.

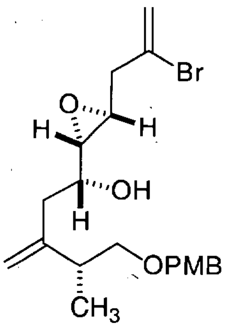


(*R*)-4-(4'-Methoxybenzyloxy)-3-methyl-2-(trimethylsilylmethyl)-1-butene (13)

Cerium (III) chloride heptahydrate (7.44 g, 20.0 mmol) was stirred at 150 °C under 0.3 mm Hg for 7 h. The dry cerium chloride was cooled to ambient temperature, and THF (20 mL) was added. The suspension stirred at ambient temperature for 12 h then was cooled to -78 °C. Trimethylsilylmethylmagnesium chloride (20 mL, 1.0 M in ether) was added. After 30 min, ester **24** (1.2 g, 5.0 mmol) was added. The reaction was warmed to ambient temperature and stirred 4 h. The reaction was then cooled to 0 °C, diluted with ether (40 mL), and quenched with saturated aqueous NH_4Cl. The organic layer was separated, and the aqueous layer was extracted with ether. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was diluted with CH_2Cl_2 (50 mL) and silica gel (5 g). The suspension was stirred for 39 h and filtered. The filtrate was concentrated, and the residue was purified by flash column chromatography (45 g SiO_2, using a gradient elution of: hexanes to 5% EtOAc in hexanes) to provide 1.04 g (70%) of **13** as a thick clear colorless oil: R_f 0.44 (5% EtOAc in hexanes); $[\alpha]_D^{23}$ +8.29 (*c* 1.40, $CHCl_3$); IR (neat) 3077, 2957, 2857, 1615, 1514, 1248, 1036, 853 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, J = 8.6 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 4.61 (s, 1H), 4.59 (s, 1H), 4.46 (A of AB, J_{AB} = 11.6 Hz, 1H), 4.43 (B of AB, J_{AB} = 11.6 Hz, 1H), 3.81 (s, 3H), 3.49 (A of ABX, J_{AB} = 9.1 Hz, J_{AX} = 8.3 Hz, 1H), 3.20 (B of ABX, J_{AB} = 9.1 Hz, J_{BX} = 5.1 Hz, 1H), 2.24 (m, 1H), 1.56 (A of AB, J_{AB} = 13.8 Hz, 1H), 1.51 (B of AB, J_{AB} = 13.8 Hz, 1H), 1.08 (d, J = 6.7 Hz, 3H), 0.01 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 149.8, 130.8, 129.1, 113.7, 106.5, 76.7, 74.8, 72.6, 55.2, 41.0, 26.6, 17.1, -1.3; MS (CI, CH_4) *m/e* (relative intensity) 291 (3), 209 (53), 171 (29), 156 (50), 121 (100) 73 (68); HRMS *m/e* calcd for $C_{17}H_{27}O_2Si$ (M^+–H) 291.1780, found 291.1787; Anal. calcd for $C_{17}H_{28}O_2Si$: C, 69.81; H, 9.65. Found: C, 69.68; H, 9.69.



14a

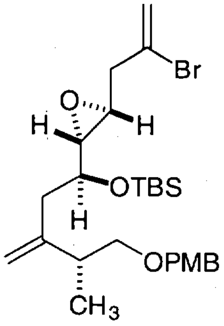


14b

(2*R*,5*S*,6*S*,7*S*)-9-Bromo-6,7-epoxy-1-(4-methoxybenzyloxy)-2-methyl-3-methylene-dec-9-en-5-ol (14a)

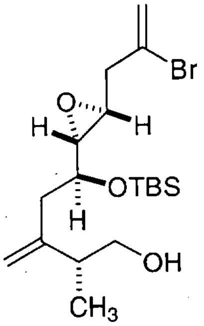
Aldehyde **12** (96 mg, 0.50 mmol) and allylsilane **13** (175 mg, 0.60 mmol) were dissolved in CH_2Cl_2 (5.0 mL) and cooled to -78 °C. Boron trifluoride diethyl etherate (0.076 mL, 0.60 mmol) was added. The reaction was stirred 2 h at -78 °C, and aqueous saturated $NaCO_3$ (10 mL) was added. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 x 5 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash column chromatography (15 g SiO_2, using a gradient elution of: 5% EtOAc in hexanes to 30% EtOAc in hexanes) provided 91 mg (44%) of alcohol **14a** and 34 mg (16%) **14b** as colorless oils. Data for **14a**: R_f 0.25 (30% EtOAc in hexanes); $[\alpha]_D^{23}$ -6.29 (*c* 1.34, $CHCl_3$); IR (neat) 3449, 2961, 2932, 2907, 2859, 1632, 1613, 1512, 1246, 1034, 895, 820 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, J = 8.6 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 5.74 (d, J = 1.3 Hz, 1H), 5.54 (d, J = 1.6 Hz, 1H), 4.98 (s, 2H), 4.43 (s, 2H), 3.81 (s, 3H), 3.80 (m, 1H), 3.41 (A of ABX, J_{AB} = 9.1 Hz, J_{AX} = 7.6 Hz, 1H), 3.35 (B of ABX, J_{AB} = 9.1 Hz, J_{BX} = 6.1 Hz, 1H), 3.22 (td, J = 5.6, 2.1 Hz, 1H), 2.87 (dd, J = 4.3, 2.1 Hz, 1H), 2.72 (A of ABX, J_{AB} = 15.6 Hz, J_{AX} = 6.0 Hz, 1H), 2.66 (B of ABX, J_{AB} = 15.6 Hz, J_{BX} = 5.0 Hz, 1H), 2.58 (br s, 1H–OH), 2.52 (q, J = 6.9 Hz, 1H), 2.45 (A of ABX, J_{AB} = 14.3 Hz, J_{AX} = 9.4 Hz, 1H), 2.24 (B of ABX, J_{AB} = 14.3 Hz, J_{BX} = 3.5 Hz, 1H), 1.06 (d, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 148.3, 130.3, 129.3, 128.4, 118.9, 113.8, 112.7, 74.6, 72.8, 68.7, 60.5, 55.3, 53.9, 43.8, 40.1, 39.7, 17.2; MS (CI, CH_4) *m/e* (relative intensity) 410 (0.3), 203 (10), 137 (41), 122 (46), 121 (100), 82 (21); HRMS *m/e* calcd for

$C_{20}H_{27}BrO_4$ (M^+) 410.1093, found 410.1087; Anal. calcd for $C_{20}H_{27}BrO_4$: C, 58.40; H, 6.62; Br, 19.43. Found: C, 58.12; H, 6.59; Br, 19.41



(2*R*,5*S*,6*S*,7*S*)-9-Bromo-5-(*tert*-butyldimethylsilanyloxy)-6,7-epoxy-1-(4-methoxybenzyloxy)-2-methyl-3-methylene-dec-9-ene (25)

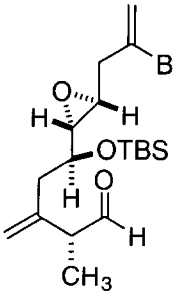
tert-Butyldimethylsilyl trifluoromethanesulfonate (TBSOTf) (77 mL, 0.34 mmol) was added to a solution of alcohol **14a** (68.9 mg, 0.168 mmol), *N*,*N*-diisopropylethylamine (0.15 mL, 0.84 mmol), and CH_2Cl_2 (0.75 mL). The reaction was stirred 2.5 h and diluted with CH_2Cl_2 (5 mL) and saturated aqueous NH_4Cl (3 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 2 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash column chromatography (16 g SiO_2 using 5% EtOAc in hexanes) provided 65 mg (74%) of **25** as a clear colorless oil: R_f 0.47 (20% EtOAc in hexanes); $[\alpha]_D^{23}$ -2.20 (*c* 1.09, $CHCl_3$); IR (neat) 3079, 2955, 2930, 2857, 1632, 1613, 1512, 1248, 1103, 835, 777 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, J = 8.6 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 5.72 (d, J = 1.6 Hz, 1H), 5.52 (d, J = 1.6 Hz, 1H), 4.91 (s, 1H), 4.90 (s, 1H), 4.44 (A of AB, J_{AB} = 11.8 Hz, 1H), 4.42 (B of AB, J_{AB} = 11.8 Hz, 1H), 3.82 (m, 1H), 3.80 (s, 3H), 3.46 (A of ABX, J_{AB} = 9.1 Hz, J_{AX} = 7.9 Hz, 1H), 3.26 (B of ABX, J_{AB} = 9.1 Hz, J_{BX} = 5.6 Hz, 1H), 3.15 (m, 1H), 2.81 (dd, J = 4.0, 2.0 Hz, 1H), 2.67 (A of ABX, J_{AB} = 15.4 Hz, J_{AX} = 6.6 Hz, 1H), 2.61 (B of ABX, J_{AB} = 15.4 Hz, J_{BX} = 4.2 Hz, 1H), 2.45 (q, J = 6.7 Hz, 1H), 2.36 (A of ABX, J_{AB} = 14.2 Hz, J_{AX} = 6.6 Hz, 1H), 2.29 (B of ABX, J_{AB} = 14.2 Hz, J_{BX} = 5.5 Hz, 1H), 1.10 (d, J = 6.7 Hz, 3H), 0.87 (s, 9H), 0.04 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 147.5, 130.7, 129, 1, 128.7, 118.8, 113.8, 112.3, 74.5, 72.7, 69.5, 60.5, 55.3, 53.7, 43.9, 41.3, 39.4, 25.8, 18.1, 16.9, -4.4, -4.8; MS (CI, CH_4) *m/e* (relative intensity) 467 (1), 343 (2), 228 (7), 197 (21), 135 (18), 122 (61), 121 (100); HRMS *m/e* calcd for $C_{22}H_{32}BrO_4Si$ ($M^+-C_4H_9$) 467.1254, found 467.1270; Anal. calcd for $C_{26}H_{41}BrO_4Si$: C, 59.42; H, 7.86; Br, 15.20. Found: C, 59.67; H, 7.90; Br, 15.26.



(2*R*,5*S*,6*S*,7*S*)-9-Bromo-5-(*tert*-butyldimethylsilanyloxy)-6,7-epoxy-2-methyl-3-methylene-dec-9-en-1-ol (26)

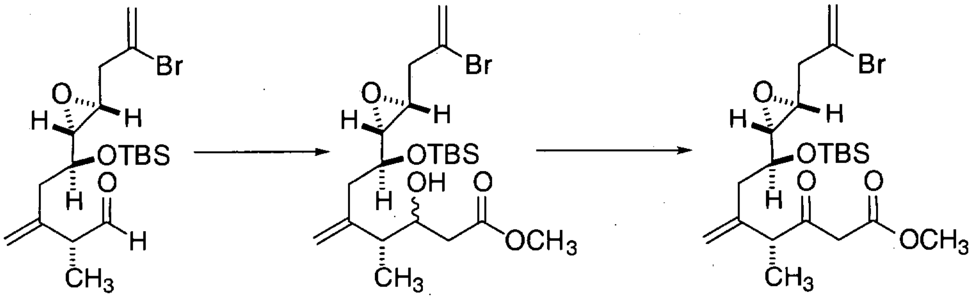
2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (52 mg, 0.228 mmol) was added to a solution of **25** (60 mg), *tert*-butyl alcohol (0.4 mL), aqueous pH = 7 buffer (0.4 mL), and CH_2Cl_2 (2 mL). After the red solution stirred 1.5 h, it was diluted with CH_2Cl_2 (10 mL), and saturated aqueous $NaHCO_3$ (10 mL) was added. The aqueous layer was extracted with CH_2Cl_2 (3 x 5 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ (15 mL), H_2O (15 mL), and brine (20 mL); dried over Na_2SO_4; filtered; and concentrated *in vacuo*. Purification by flash column chromatography (16 g SiO_2, using a gradient elution of: 10% EtOAc in hexanes to 50% EtOAc in hexanes) provided 45 mg (96%) of **26** as a clear colorless oil: R_f 0.23 (20% EtOAc in hexanes); $[\alpha]_D^{23}$ +18.2 (*c* 0.665, $CHCl_3$); IR (neat) 3451, 2955, 2930, 2857, 1632, 1472, 1254, 1107, 837, 777 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.72 (d, *J* = 1.8 Hz, 1H), 5.53 (d, *J* = 1.9 Hz, 1H), 5.05 (d, *J* = 1.1 Hz, 1H), 4.99 (s, 1H), 3.73 (dt, *J* = 6.2, 5.2 Hz, 1H), 3.56 (m, 2H), 3.13 (m, 1H), 2.84 (dd, *J* = 5.2, 2.1 Hz, 1H), 2.68 (d of A of ABX, J_{AB} = 15.4 Hz, J_{AX} = 6.4 Hz, *J* = 0.8 Hz, 1H), 2.64 (d of B of ABX, J_{AB} = 15.4 Hz, J_{BX} = 4.5 Hz, *J* = 0.8 Hz, 1H), 2.40 (d of A of ABX, J_{AB} = 14.1 Hz, J_{AX} = 6.3 Hz, *J* = 1.0 Hz, 1H), 2.37 (m, 1H), 2.34 (d of B of ABX, J_{AB} = 14.1 Hz,

J_{BX} = 6.1 Hz, J = 1.0 Hz, 1H), 1.84 (s, 1H–OH), 1.06 (d, J = 6.8 Hz, 3H), 0.88 (s, 9H), 0.07 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.8, 128.4, 119.0, 113.4, 70.3, 66.2, 60.6, 54.6, 43.8, 41.9, 41.8, 25.8, 18.1, 16.5, -4.4, -4.7; MS (CI, CH_4) *m/e* (relative intensity) 389 (1), 330 (4), 305 (40), 249 (30), 225 (60), 197 (40), 157 (50), 115 (77), 75 (100); HRMS (FAB, Na) *m/e* calcd for $C_{18}H_{33}BrO_3SiNa$ (M^++Na^+) 427.1281, found 427.1282.



(2*R*,5*S*,6*S*,7*S*)-9-Bromo-5-(*tert*-butyldimethylsilanyloxy)-6,7-epoxy-2-methyl-3-methylene-dec-9-enal (15)

Alcohol **26** (40 mg, 0.10 mmol) was dissolved in CH_2Cl_2 (5.0 mL). Sodium bicarbonate (84 mg, 1.0 mmol) and Dess-Martin periodinane (85 mg, 0.20 mmol) were added. The reaction was stirred 1.5 h, and the mixture was placed directly on a column of silica gel (10 g). Purification by flash column chromatography using 15% EtOAc in hexanes provided 35 mg (90%) of **15** as a colorless oil: R_f 0.48 (20% EtOAc in hexanes); $[\alpha]_D^{23}$ +24 (*c* 1.5, $CHCl_3$); IR (neat) 2930, 2857, 1723, 1632, 1462, 1254, 1096, 837, 777 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.48 (d, J = 1.9 Hz, 1H), 5.72 (d, J = 1.0 Hz, 1H), 5.53 (d, J = 1.6 Hz, 1H), 5.18 (s, 1H), 5.02 (s, 1H), 3.77 (q, J = 5.4 Hz, 1H), 3.13 (m, 2H), 2.81 (dd, J = 4.6, 2.2 Hz, 1H), 2.69 (A of ABX, J_{AB} = 15.5 Hz, J_{AX} = 6.9 Hz, 1H), 2.63 (B of ABX, J_{AB} = 15.5 Hz, J_{BX} = 4.3 Hz, 1H), 2.38 (m, 2H), 1.24 (d, J = 7.0 Hz, 3H), 0.87 (s, 9H), 0.06 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.2, 141.7, 128.3, 119.0, 116.4, 69.8, 60.1, 54.3, 52.6, 43.8, 41.6, 25.8, 18.1, 12.8, -4.4, -4.9; MS (CI, CH_4) *m/e* (relative intensity) 403 (10), 401 (9), 347(12), 305 (40), 249 (35), 225 (58), 197 (53), 155 (63), 105 (100), 75 (95); HRMS *m/e* calcd for $C_{18}H_{31}BrO_3Si$ (M^+) 402.1226, found 402.1242.

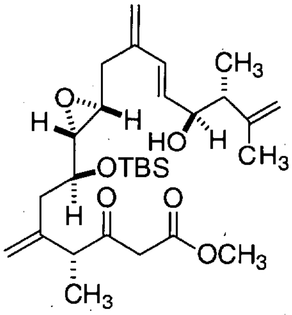


15 **27** **3**

(4*R*,7*S*,8*S*,9*S*)-11-Bromo-7-(*tert*-butyldimethylsilanyloxy)-8,9-epoxy-4-methyl-5-methylene-3-oxo-dodec-11-enoic acid methyl ester (3)

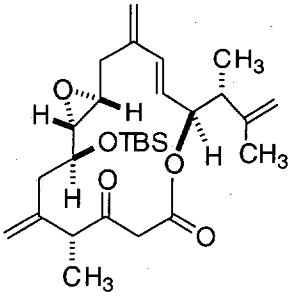
n-Butyllithium (0.12 mL, 2.5 M in hexanes) was added to diisopropylamine (0.60 mL, 0.30 mmol) in THF (0.6 mL) at -78°C. After 10 min, methyl acetate (0.5 M in THF, 0.50 mL, 0.25 mmol) was added. The resulting reaction was stirred 15 min, and aldehyde **15** (30 mg, 0.075 mmol) was added. After an additional 10 min, The reaction was quenched with saturated aqueous NH_4Cl, and diluted with ether. The organic layer was separated, and the aqueous layer was extracted with ether. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo* which provided 35 mg (99%) of **27** as a 2:1 mixture of alcohols as a clear colorless oil: Characteristic data for the mixture: R_f 0.11 (20% EtOAc in hexanes); IR (neat) 3320 cm^{-1}; HRMS *m/e* calcd for $C_{20}H_{34}{}^{81}BrO_4Si$ (M^+–OCH_3) 447.1405, found 447.1389

The mixture of alcohols **27** (35 mg, 0.075 mmol) was dissolved in CH_2Cl_2 (5.0 mL). Sodium bicarbonate (84 mg, 1.0 mmol) and Dess-Martin periodinane (64 mg, 0.15 mmol) were added. After 1 h, the mixture was placed directly on a column of silica gel (10 g). Purification by flash column chromatography using 15% EtOAc in hexanes provided 23 mg (66%) of ketone **3** as a light yellow oil: R_f 0.34 (15% EtOAc in hexanes); $[\alpha]_D^{23}$ -19 (*c* 1.0, $CHCl_3$); IR (neat) 2857, 1750, 1715, 1634, 1468, 1254, 1119, 837, 777 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.71 (s, 1H), 5.52 (d, *J* = 1.7 Hz, 1H), 5.13 (s, 1H), 5.03 (s, 1H), 3.77 (m, 1H), 3.71 (s, 3H), 3.52 (A of AB, J_{AB} = 15.8 Hz, 1H), 3.50 (B of AB, J_{AB} = 15.8 Hz, 1H), 3.37 (q, *J* = 6.9 Hz, 1H), 3.13 (m, 1H), 2.80 (dd, *J* = 4.8, 1.9 Hz, 1H), 2.68 (A of ABX, J_{AB} = 15.4 Hz, J_{AX} = 6.5 Hz, 1H), 2.62 (B of ABX, J_{AB} = 15.4 Hz, J_{BX} = 4.0 Hz, 1H), 2.34 (d, *J* = 5.7 Hz, 2H), 1.25 (d, *J* = 6.9 Hz, 3H), 0.86 (s, 9H), 0.06 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.0, 167.7, 143.1, 128.4, 119.0, 116.2, 69.7, 60.2, 54.3, 53.3, 52.3, 46.3, 43.8, 41.1, 25.7, 18.1, 15.1, -4.4, -4.8; MS (CI, CH_4) *m/e* (relative intensity) 419 (6), 417 (5), 367 (3), 305 (8), 269 (5), 225 (13), 101 (26), 75 (100); HRMS *m/e* calcd for $C_{17}H_{26}BrO_5SiBr$ (M^+–C_4H_9) 417.0733, found 417.0751; Anal. calcd for $C_{21}H_{35}O_5BrSi$: C, 53.05; H, 7.42; Br, 16.80. Found: C, 53.33; H, 7.45 Br, 16.89.



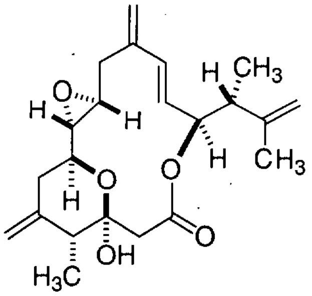
(4*R*,7*S*,8*S*,9*S*,12*E*,14*S*,15*R*)-7-(*tert*-Butyldimethylsilanyloxy)-5,11-dimethylene-8,9-epoxy-14-hydroxy-3-oxo-4,15,16-trimethylheptadeca-12,16-dienoic acid methyl ester (16)

Bromide **3** (38 mg, 0.080 mmol), stannane **2** (31 mg, 0.080 mmol), and tris(dibenzylideneacetone)-dipalladium(0)-chloroform adduct (9.0 mg, 0.017 mmol) in CH_2Cl_2 (1.0 mL) stirred for 20 h at ambient temperature. The mixture was placed directly on a silica gel column (10 g). Purification by flash column chromatography using a gradient elution of: 5% EtOAc in hexanes to 30% EtOAc in hexanes provided 31 mg (81%) of **16** as a thick clear colorless oil: R_f 0.40 (30% EtOAc in hexanes); $[\alpha]_D^{23}$ -25 (*c* 0.34, $CHCl_3$); IR (neat) 3505, 3077, 2955, 2857, 1748, 1715, 1645, 1456, 1255, 1086, 837 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.34 (d, *J* = 15.8 Hz, 1H), 6.34 (dd, *J* = 15.8, 7.3 Hz, 1H), 5.14 (s, 2H), 5.13 (s, 1H), 5.03 (s, 1H), 4.92 (s, 1H), 4.88 (s, 1H), 3.94 (ddd, *J* = 8.0, 8.0, 2.0 Hz, 1H), 3.73 (m, 1H), 3.72 (s, 3H), 3.53 (A of AB, J_{AB} = 15.8 Hz, 1H), 3.51 (B of AB, J_{AB} = 15.8 Hz, 1H), 3.37 (q, *J* = 6.8 Hz, 1H), 3.04 (m, 1H), 2.73 (dd, *J* = 5.0, 2.0 Hz, 1H), 2.48 (A of ABX, J_{AB} = 15.4 Hz, J_{AX} = 6.9 Hz, 1H), 2.40 (B of ABX, J_{AB} = 15.4 Hz, J_{BX} = 4.2 Hz, 1H), 2.32 (m, 2H), 2.27 (m, 1H), 1.96 (d, *J* = 2.2 Hz, 1H–OH), 1.74 (s, 3H), 1.24 (d, *J* = 6.8 Hz, 3H), 0.97 (d, *J* = 7.0 Hz, 3H), 0.86 (s, 9H), 0.05 (s, 3H), 0.3 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.1, 167.8, 146.9, 143.2, 141.4, 134.0, 130.5, 117.6, 116.1, 113.5, 74.4, 70.1, 60.5, 55.3, 53.3, 52.3, 48.2, 46.3, 41.2, 34.5, 25.8, 18.8, 18.1, 15.7, 15.1, -4.4, -4.8; MS (CI, CH_4) *m/e* (relative intensity); HRMS *m/e* calcd for $C_{29}H_{48}O_6SiNa$ (M^++Na) 543.3118, found 543.3119



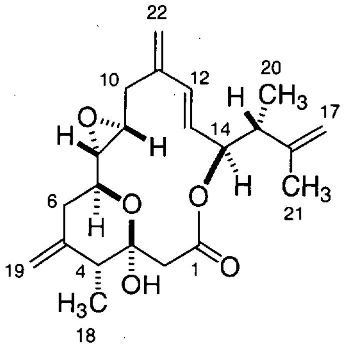
(5*R*,8*S*,9*S*,10*S*,13*E*,15*S*)-8-(*tert*-Butyldimethylsilanyloxy)-[(1*R*)-1,2-dimethylallyl]-9,10-epoxy-5-methyl-6,12-dimethylene-4-oxacyclopentadec-13-ene-2,4-dione (17)

Ester **16** (43 mg, 0.081 mmol) was dissolved in toluene (40 mL) and heated to reflux (oil bath temperature, 120-130 °C) in a culture tube sealed with a teflon coated cap for 1.5 h. The reaction was concentrated, and purified by flash column chromatography (5% EtOAc in hexanes) to give macrolide **17** (23 mg, 72%) as a colorless oil: R_f 0.41 (15% EtOAc in hexanes); $[\alpha]_D^{23}$ -42 (*c* 0.27, $CHCl_3$); IR (neat) 3082, 2953, 2857, 1746, 1715, 1462, 1250, 1126, 965, 837 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.36 (d, *J* = 15.9 Hz, 1H), 5.51 (dd, *J* = 15.8, 9.1 Hz, 1H), 5.22 (dd, *J* = 15.4, 9.1 Hz, 1H), 5.20 (s, 2H), 5.11 (s, 1H), 5.08 (s, 1H), 4.78 (s, 1H), 4.75 (s, 1H), 4.00 (td, *J* = 5.6, 2.2 Hz, 1H), 3.51 (A of AB, J_{AB} = 14.1 Hz, 1H), 3.32 (B of AB, J_{AB} = 14.1 Hz, 1H), 3.32 (m, 1H), 2.85 (s, 1H), 2.85 (m, 1H), 2.79 (s, 1H), 2.50 (dq, *J* = 15.4, 6.9 Hz, 1H), 2.20 (m, 1H) 2.06 (d, *J* = 5.5 Hz, 2H), 1.69 (s, 3H), 1.22 (d, *J* = 7.0 Hz, 3H), 0.96 (d, *J* = 7.1 Hz, 3H), 0.83 (s, 9H), 0.03 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.4, 165.1, 145.6, 143.2, 140.4, 137.3, 125.7, 121.1, 115.5, 112.7, 78.7, 68.2, 62.7, 54.6, 53.4, 46.7, 44.7, 40.1, 34.7, 25.7, 19.6, 18.2, 15.4, 14.9, -4.7, -4.9; MS (EI) *m/e* (relative intensity) 488 (20), 431 (67), 387 (30), 339 (25), 283 (100), 239 (60), 197 (75), 133 (40), 91 (40); HRMS *m/e* calcd for $C_{28}H_{44}O_5Si$ (M^+) 488.2958, found 488.2973.



(–)-Amphidinolide P (1)

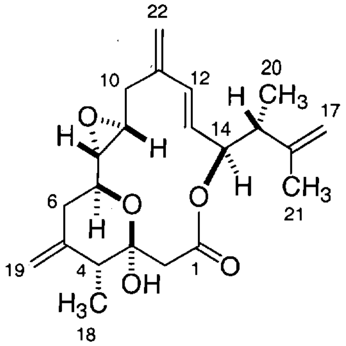
Acetic acid (0.29 mL, 5.0 mmol) was added to tetrabutylammonium fluoride (6.0 mL, 1.0 M in THF). A portion (0.3 mL) of the solution was added to ketoester **17** (5.0 mg, 0.010 mmol). After the reaction stirred 1 h at 65 °C, saturated aqueous NH_4Cl (0.10 mL) was added. The mixture was placed directly on a column of silica gel (5 g). Purification by flash column chromatography (gradient elution of 5% EtOAc in hexanes to 15% EtOAc in hexanes) gave amphidinolide P (**1**) (2.9 mg, 78%) as a white solid: R_f 0.39 (15% EtOAc in hexanes); $[\alpha]_D^{23}$ -30 (*c* 0.09, MeOH); IR (neat) 3488, 3081, 2930, 1713, 1643, 1439, 1188, 972, 897 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.24 (d, *J* = 16.3 Hz, 1H), 5.64 (dd, *J* = 16.2, 7.6 Hz, 1H), 5.34 (dd, *J* =9.0, 7.8 Hz, 1H), 4.98 (br s, 1H), 4.94 (br s, 1H), 4.92 (br s, 1H), 4.86 (br s, 1H), 4.85 (br s, 1H), 4.81 (br s, 1H), 4.27 (d, *J* = 2.0 Hz, 1H), 3.51 (ddd, *J* = 11.6, 8.4, 2.6 Hz, 1H), 2.72 (d, *J* = 13.8 Hz, 1H), 2.66 (dd, *J* = 8.4, 1.8 Hz, 1H), 2.56 (dd, *J* = 12.8, 2.6 Hz, 1H), 2.52 (br d, *J* = 9.5 Hz, 1H), 2.47 (dq, *J* = 9.2, 7.1 Hz, 1H), 2.41 (d, *J* = 11.9 Hz, 1H), 2.31 (d, *J* = 12.1 Hz, 1H), 2.21 (dd, *J* = 13.6, 9.7 Hz, 1H), 2.15 (t, *J* = 12.6, 11.8 Hz, 1H), 1.99 (br q, *J* = 6.5 Hz, 1H), 1.71 (s, 3H), 0.96 (d, *J* = 6.6 Hz, 3H), 0.95 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, CDCl3) _ 172.4, 146.5, 143.7, 142.2, 133.6, 129.1, 118.2, 112.3, 110.0, 99.2, 78.5, 73.5, 62.8, 58.3, 45.2, 45.02, 45.01, 39.4, 36.3, 19.5, 16.1, 11.8; MS (EI) m/e (relative intensity) 374 (10), 305 (15), 287 (33) 263 (34), 219 (20), 159 (35), 133 (59), 105 (100); HRMS m/e calcd for C22H30O5 (M+) 374.2093, found 374.2088.



Amphidinolide P

Amphidinolide P: Proton Data

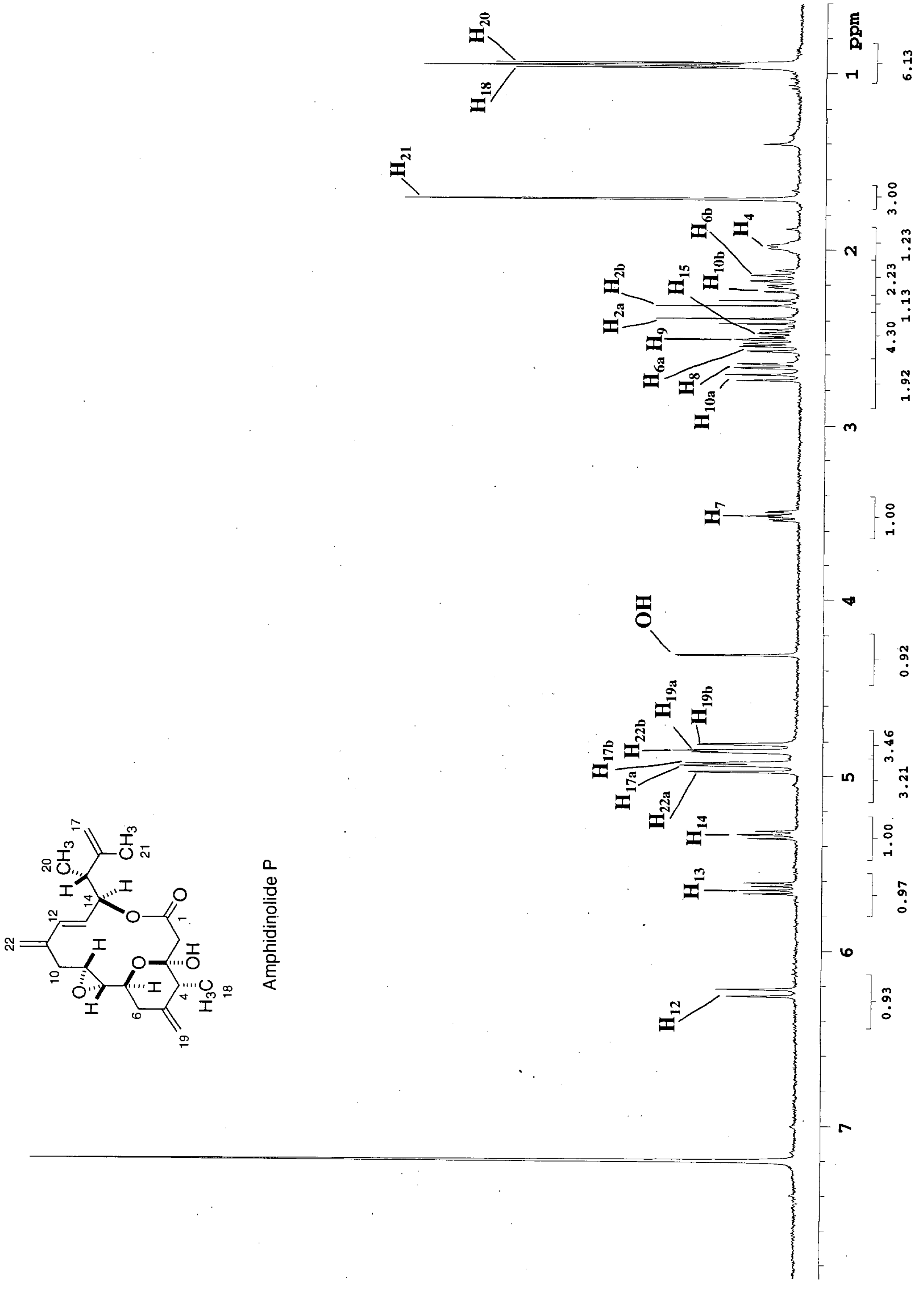
Position	Natural			Synthetic		
	δ	multi.	Coupling (Hz)	δ	multi.	Coupling (Hz)
12	6.24	d	16.2	6.24	d	16.3
13	5.64	dd	16.2, 7.5	5.64	dd	16.2,7.6
14	5.34	dd	9.3, 7.5	5.34	dd	9.0, 7.8
22(a)	4.98	br s		4.98	br s	
17(a)	4.93	br s		4.94	br s	
17(b)	4.92	br s		4.92	br s	
19(a)	4.86	br s		4.86	br s	
22(b)	4.85	br s		4.85	br s	
19(b)	4.81	br s		4.81	br s	
3–OH	4.31	d	1.5	4.27	d	2.0
7	3.51	ddd	11.7, 8.3, 2.5	3.51	ddd	11.6, 8.4, 2.6
10(a)	2.72	d	13.9	2.72	d	13.8
8	2.66	dd	8.3,1.4	2.66	dd	8.4,1.8
6(a)	2.56	dd	12.7, 2.5	2.56	dd	12.8, 2.6
9	2.52	d	9.5, 1.4	2.52	br d	9.5
15	2.47	qd	9.3, 7.3	2.47	dq	9.2, 7.1
2(a)	2.41	d	12.0	2.41	d	11.9
2(b)	2.31	d	12.0	2.31	d	12.1
10(b)	2.21	dd	13.9, 9.5	2.21	dd	13.6, 9.7
6(b)	2.14	t	12.7, 11.7	2.15	t	12.6, 11.8
4	1.99	br q	6.9	1.99	br q	6.5
21	1.71	s		1.71	s	
18	0.96	d	6.9	0.96	d	6.6
20	0.95	d	7.3	0.95	d	7.0



Amphidinolide P

Amphidinolide P: Carbon Data

Carbon #	**Natural (δ)**	**Synthetic (δ)**
1	172.4	172.4
16	146.5	146.5
5	143.7	143.7
11	142.3	142.2
12	133.6	133.6
13	129.1	129.1
22	118.1	118.2
17	112.3	112.3
19	110.0	110.0
3	99.2	99.2
14	78.5	78.5
7	73.5	73.5
8	62.8	62.8
9	58.2	58.3
4	45.2	45.2
15	45.04	45.02
2	45.01	45.01
6	39.4	39.4
10	36.4	36.3
21	19.5	19.5
18	16.1	16.1
20	11.8	11.8


Amphidinolide P