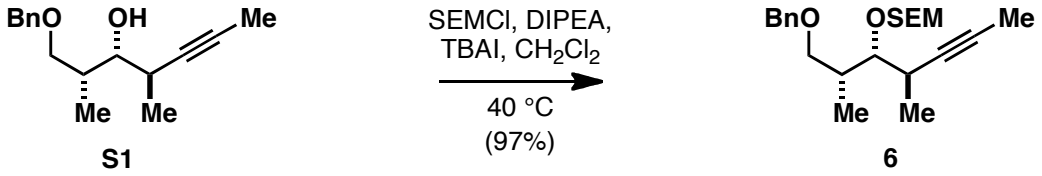
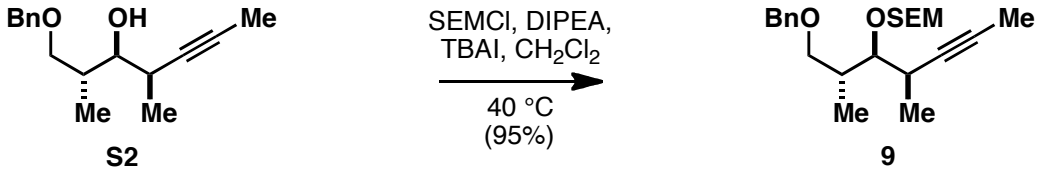
General. All reactions were conducted in flame-dried glassware under an argon atmosphere with dry solvents, unless otherwise noted. Anhydrous tetrahydrofuran (THF), dichloromethane (CH_2Cl_2), and toluene (PhMe) were obtained by passing HPLC grade solvents through activated alumina columns. Anhydrous diethyl ether (Et_2O) was obtained by distillation of HPLC grade diethyl ether over sodium and benzophenone. Anhydrous methanol (MeOH) was purchased from Aldrich. Chlorotriisopropoxy titanium(IV) was purchased from Aldrich as a 1 M solution in Hexanes. *n*-BuLi solutions were purchased from Aldrich and titrated monthly against *N*-benzylbenzamide. *c*-C_5H_9MgCl was purchased from Aldrich and titrated monthly using 1,10-phenatholine and *s*-butanol. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous materials, unless otherwise stated. Flash column chromatography was performed using Silicycle SiliaFlash P60 silica gel, 40-63 μm particle size. ^{1}H NMR data were recorded in $CDCl_3$ at 400 MHz on a Bruker AM-400 with calibration of spectra to residual $CHCl_3$ (7.26 ppm). ^{13}C data were recorded at 100 MHz on a Bruker AM-400 with calibration to the central line of $CDCl_3$ (77.16 ppm). Infrared spectra were recorded on a PerkinElmer SpectrumOne FT-IR instrument. All HRMS data was obtained from the University of Illinois Urbana-Champaign mass spectrometry lab. All compounds purified by chromatography were sufficiently pure for use in further experiments, unless indicated otherwise. Relative stereochemistry was defined using the *R**/*S** convention proposed by IUPAC. Brine refers to a saturated aqueous solution of NaCl.

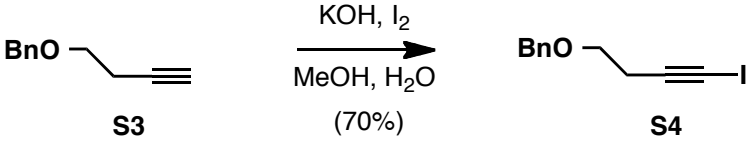
Experimental Data



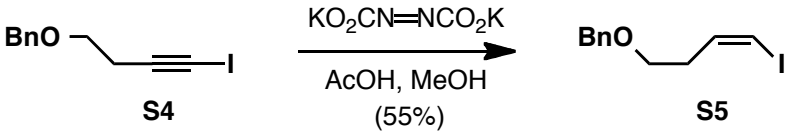
Synthesis of (6*R*,5*R*,4*R*)-7-(benzyloxy)-4,6-dimethyl-5-((2-trimethylsilyl)ethoxymethyloxy)-2-heptyn (6): The homopropargyl alcohol[1] (3.27 g, 13.27 mmol) was dissolved in CH_2Cl_2 (30 ml) under an argon atmosphere, *N*,*N*-Diisopropylethylamine, (DIPEA) (9.20 ml, 53.08 mmol), tetrabutyl ammoniumiodide, (TBAI) (4.90 g, 13.27 mmol), and SEMCl (6.60g, 39.81 mmol) were added and the reaction mixture was heated to 40 ˚C and stirred for 2 hr. The solution became orange and transparent in appearance. The reaction mixture was then cooled to room temperature and quenched with sat. aqueous NH_4Cl. Extraction of the aqueous layer 3X with Et_2O, drying of the organic phase with Na_2SO_4, filtration of the organic phase, concentration via rotary vaporization under vacuum, and column chromatography over silica (2% to 10% EtOAc in Hexanes) gave **6** as a clear oil (4.84 g, 97%). **Data for (6):** **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.32−7.31 (m, 4H), 7.28 (t, 1H, J = 4.0 Hz), 4.79 (app. dd, 2H, J_1 = 8.0 Hz, J_2 = 8.0 Hz), 4.50 (app. dd, 2H, J_1 = 8.0 Hz, J_2 = 12.0 Hz), 3.73−3.59 (m, 2H), 3.55-3.47 (m, 2H), 3.39 (dd, 1H, J_1 = 4.0 Hz, J_2 = 4.0 Hz), 2.74−2.63 (m, 1H), 2.16−2.07 (m, 1H), 1.77 (d, 3H, J = 4.0 Hz), 1.16 (d, 3H, J = 8.0 Hz), 0.99 (d, 3H, J = 8.0 Hz), 0.85 (m, 2H), 0.01 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 139.1, 129.0, 128.6, 128.2, 97.1, 83.2, 82.7, 77.1, 74.1, 73.0, 66.2, 36.3, 30.5, 18.7, 18.1, 12.0, 4.1, −1.1; IR (thin film, KBr) 2972, 2901, 1454, 1406, 1381, 1249, 1056, 859, 834, 752, 696 cm^{-1}; HRMS (ESI) *m*/*z* calc'd for $C_{22}H_{36}O_3SiNa$ 399.2331 found $C_{22}H_{36}O_3SiNa$ 399.2331; $[\alpha]_D^{20}$ = −5.14 ° (*c* = 0.55, $CHCl_3$).



Synthesis of (6*R*,5*S*,4*R*)-7-(benzyloxy)-4,6-dimethyl-5-((2-trimethylsilyl)ethoxymethyloxy)-2-heptyn (9): Performed as above in synthesis of **6**. **9** was a clear oil (2.00 g, 95%). **Data for (9): ^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.32−7.31 (m, 4H), 7.28 (t, 1H, J = 4.2 Hz), 4.76 (app. dd, 2H, J_1 = 8.0 Hz, J_2 = 8.0 Hz), 4.52 (d, 1H, J_1 = 2.0 Hz), 4.52 (d, 1H, J_1 = 2.0 Hz), 3.76−3.59 (m, 2H), 3.43−3.38 (m, 3H), 2.74−2.65 (m, 1H), 2.30−2.20, (m, 1H), 1.76 (d, 3H, J = 4.0 Hz), 1.18 (d, 3H, J = 8.1 Hz), 1.10 (d, 3H, J = 8.1 Hz), 0.85 (m, 2H), 0.02, (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 139.5, 129.5, 128.1, 127.2, 96.1, 84.0, 82.6, 73.5, 72.6, 66.7, 37.7, 29.2, 18.1, 18.0, 15.4, 4.0, −1.1; IR (thin film, KBr) 2970, 2900, 1465, 1406, 1375, 1251, 1056, 834, 752, 697 cm^{-1}; HRMS (ESI) *m*/*z* calc'd for $C_{22}H_{36}O_3SiNa$ 399.2331 found $C_{22}H_{36}O_3SiNa$ 399.2334; $[\alpha]_D^{20} = -13.00$ ° (c = 0.30, $CHCl_3$).

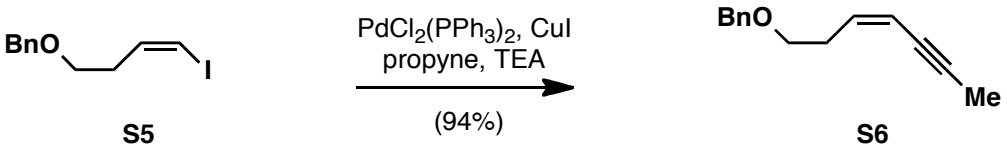


Synthesis of (((4-iodobut-3-yn-1-yl)oxy)methyl)benzene: The alkyne (prepared according the protocol of Marshall[2]) (0.40 g, 2.50 mmol) was dissolved in 2.5 ml of MeOH and cooled to 0 ˚C. 0.35 g (6.24 mmol) of KOH in 1 ml of H_2O was added. The resulting solution was stirred for 10 min then 0.40 g (3.75 mmol) of I_2 was added portion-wise over 3 min. The orange mixture turned white. After stirring for 1 h, 10 ml of H_2O was added. The aqueous phase was extracted 4X with hexane, concentrated, and passed through a short silica plug to give the crude iodide in 70% yield (0.50 g, 1.75 mmol) as a pink oil that was used without further purification in the next step.



S4 S5

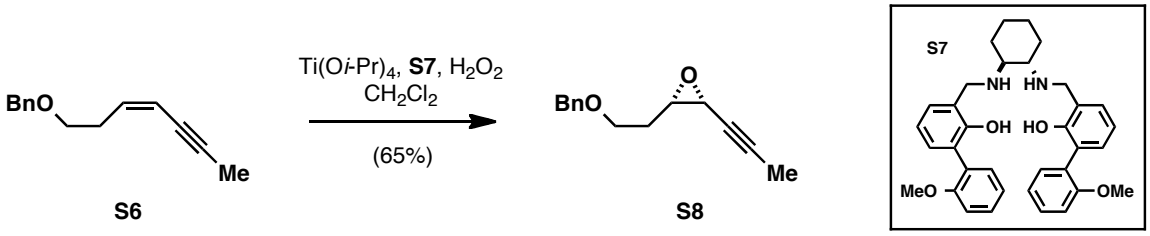
Synthesis of (*Z*)-(((4-iodobut-3-en-1-yl)oxy)methyl)benzene: 1,2-Diazenedicarboxamide (~5 g) was added to 50 ml of a stirred solution of 20% aqueous KOH. The resulting solution was stirred 1 h at rt, then filtered. The yellow solids were rinsed with MeOH, and the solvent was removed *in vacuo* overnight. The bright yellow dicarboxylate potassium salt (2.33g, 12.0 mmol) was stirred in 7 ml of MeOH at 0 ˚C in an open air atomosphere and the alkyne was added. 2.4 ml of acetic acid in 4 ml of MeOH was slowly added and the solution was stirred for 30 min. The solution changed from yellow to colorless and was quenched by dumping into a seperatory funnel with 100 ml of H_2O. The aqueous layer was extracted 3X with 30% Et_2O in Hexanes. The organic layers were dried with Na_2SO_4, filtered, and concentrated to give the pure product as a light yellow solid 55% (1.28 g). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38−7.27 (m, 5H), 6.34−6.27 (m, 2H), 4.55 (s, 2H), 3.56 (t, 2H, J = 4.0 Hz), 2.46 (dt, 2H, , J_1 = 4.1 Hz, J_2 = 6.2 Hz), **^{13}C NMR** (100 MHz, $CDCl_3$) δ 138.3, 138.4, 128.5, 127.7, 127.7, 84.1, 73.0, 68.2, 35.5; IR (thin film, KBr) 2857, 1453, 1360, 1282, 1260, 1216, 1098, 749, 695 cm^{-1}; δ HRMS (ESI) *m*/*z* calc'd for $C_{11}H_{13}ONaI$ 310.9909, found $C_{11}H_{13}ONaI$ 310.9911.



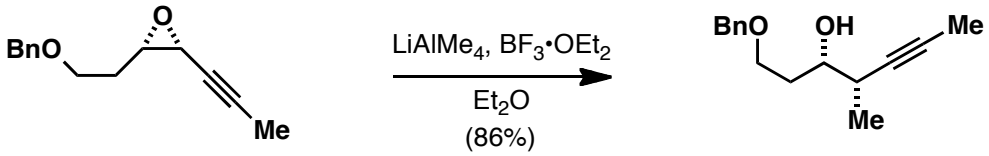
S5 S6

Synthesis of (*Z*)-((hept-3-en-5-yn-1-yloxy)methyl)benzene: 2.50 g (8.60 mmol) of the iodide was dissolved in TEA (15 ml) in a sealed tube. $PdCl_2(PPh_3)_2$ (0.263 g, 0.373 mmol) and CuI (0.257 g, 1.35 mmol) were quickly added and the tube flushed with argon. The mixture was cooled to −78 ˚C and propyne gas was bubbled into the reaction mixture via cannula. The yellow mixture turned orange then black and was allowed to warm to rt. After 1 h the reaction mixture was concentrated, 5 ml of EtOAc and 5 ml of H_2O were added and the aqueous phase extracted 2X with Et_2O. Drying of the organic phases with

Na_2SO_4, filtration, and concentration gave a crude oil that was subjected to chromatography over silica gel (2% to 5% EtOAc in Hexanes) to give the enyne as a light yellow oil (1.71 g, 94%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38−7.27 (m, 5H), 5.88 (dt, 1H, J_1 = 12.1 Hz, J_2 = 7.2 Hz), 5.51 (dq, 1H, J_1 = 12.2 Hz, J_2 = 1.6 Hz), 4.53 (s, 2H), 3.54 (t, 2H, J = 7.3 Hz), 2.63 (dt, 2H, J_1 = 7.2 Hz, J_2 = 7.2 Hz), 1.97 (d, 3H, J = 2.0 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 139.0, 138.8, 128.3, 127.9, 127.2, 111.1, 90.0, 76.4, 72.2, 69.6, 30.7, 23.1; IR (thin film, KBr) 2969, 2915, 1453, 1360, 1261, 1098, 1077, 734, 710 cm^{-1}; HRMS (ESI) *m/z* calc'd for $C_{14}H_{17}O$ 201.1279, found $C_{14}H_{17}O$ 201.1280.

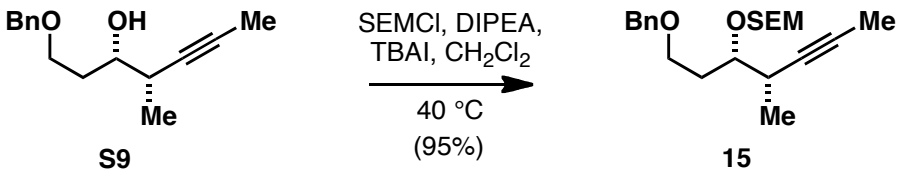


Synthesis of (2*S*,3*R*)-2-(2-(benzyloxy)ethyl)-3-(prop-1-yn-1-yl)oxirane: The Ti catalyst was prepared in situ as described.[3] The alkene (1.61 g, 8.04 mmol) dissolved in CH_2Cl_2 (20 ml) was added to the solution containing the catalyst (10 mol %). 5.75 ml of an aqueous solution of 30% H_2O_2 was added followed by 5 drops of H_2O. The reaction turned bright orange and was stirred for 6 h, after which time the reaction mixture was concentrated and chromatographed over silica (3% to 9% EtOAc in Hexanes) to give 1.13 g of the epoxide as a clear oil (65%). The *ee* was determined to be 90% by opening of the epoxide (next reaction in this document) and mosher analysis of the resultant alcohol. This epoxidation gave *ee's* in in the 98% range on a small scale; this higher *ee* is in accordance with literature values for this epoxidation reaction.[4] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38−7.27 (m, 5H), 4.55 (s, 2H), 3.71−3.66 (m, 2H), 3.44−3.42 (m, 1H), 3.20 (ddd, 1H, J_1 = 12.0 Hz, J_2 = 4.4 Hz, J_3 = 1.6 Hz), 2.09−1.92 (m, 1H), 1.85 (d, 3H, J = 2.4 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 138.2, 128.5, 127.1, 127.1, 82.4, 74.7, 73.8, 67.3, 56.1, 46.4, 30.3, 4.1; IR (thin film, KBr) 3395(b), 2987, 2919, 1718, 1453, 1365, 1273, 1096, 1074, 1026, 749, 713, 697 cm^{-1}; HRMS (ESI) *m/z* calc'd for $C_{14}H_{17}O_2$ 217.1227 found $C_{14}H_{17}O_2$ 201.1229; $[\alpha]_D^{20} = -1.81$ ° (*c* = 1.05, $CHCl_3$).



S8 **S9**

Synthesis of (3*S*,4*S*)-1-(benzyloxy)-4-methylhept-5-yn-3-ol: 5.30 ml (10.6 mmol) of a solution of $AlMe_3$ (2 M in PhMe) was added to 20 ml of Et_2O. The solution was cooled to −20 ˚C. MeLi (6.6 ml, 1.6 M in Et_2O) was added and the solution warmed to room temperature and stirred for 30 min, over which time a white precipitate formed in the solution. In a separate flask the epoxide (0.762 g, 3.52 mmol) was dissolved in 15 ml of CH_2Cl_2 and cooled to −78 ˚C. Freshly distilled BF_3•OEt_2 (1.0 g, 7.04 mmol) was added followed by dropwise addition of the ethereal $LiAlMe_4$ solution. The bright yellow solution was stirred at −78 ˚C for 40 min then 0.28 ml of MeOH and 0.98 ml of TEA were added. The mixture was warmed to −40 ˚C and stirred for 30 min, after which time the reaction was quenched by the addidion of 10 ml of 1 N HCl. The aqueous layer was extracted 3X with Et_2O. Combined organic phases were washed with saturated aqueous monobasic phosphate (NaH_2PO_4) solution that had been diluted 2X, then brine. The organic phases were then dried over Na_2SO_4, filtered, and concentrated. Column chromatography over silca gel with 12% EtOAc in Hexanes gave 0.703 g (86%) of the alcohol as a clear oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38−7.27 (m, 5H), 4.53 (s, 2H), 3.79−3.74 (m, 1H), 3.71−3.63 (m, 2H), 3.04 (d, 1H, J = 4.0 Hz), 2.54 (dqq, 1H, J_1 = 3.0 Hz, J_2 = 2.4 Hz, J_3 = 1.1 Hz), 2.02−1.96 (m, 1H), 1.87−1.81 (m, 1H), 1.79 (d, 3H, J = 2.5 Hz), 1.18 (d, 3H, J = 7.4 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 138.2, 129.1, 128.8, 128.2, 81.1, 78.2, 75.4, 74.1, 70.4, 34.2, 33.3, 17.1, 4.1; IR (thin film, KBr) 3092, 3025, 2975, 2966, 2920, 2855, 2850, 1496, 1451, 1250, 1210, 1176, 1178, 1101, 998, 801, 741, 610 cm^{-1}; HRMS (ESI) *m/z* calc'd for $C_{15}H_{20}O_2Na$ 255.1357 found $C_{15}H_{20}O_2Na$ 255.1361; $[\alpha]_D^{20} = -21.11$ ° (*c* = 0.68, $CHCl_3$).



Synthesis of (3*S*,4*S*)-1-(benzyloxy)-4-methyl-5-((2-trimethylsilyl)ethoxymethyloxy)-hept-5-yn (15): Performed as above in synthesis of **6**. **15** was a clear oil (2.02 g, 95%). **Data for (15): ^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38−7.27 (m, 5H), 4.72 (app. dd, 2H, J_1 = 20.0 Hz, J_2 = 7.6 Hz), 4.50 (s, 2H), 3.7 (app. dd, 1H, J_1 = 20.1 Hz, J_2 = 7.6 Hz), 3.63−3.56 (m, 4H), 2.83−2.74 (m, 1H), 1.96−1.87 (m, 2H), 1.78 (dd, 3H, J_1 = 1.2 Hz, J_2 = 2.4 Hz), 1.12 (dd, 3H, J_1 = 0.8 Hz, J_2 = 6.4 Hz), 0.93 (app. dd, 2H, J_1 = 8.2 Hz, J_2 = 8.2 Hz), 0.01 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 139.1, 129.4, 128.7, 128.0, 95.1, 81.5, 78.4, 77.3, 73.5, 67.8, 66.1, 32.3, 31.1, 18.2, 18.6, 4.2, −1.1; IR (thin film, KBr) 2953, 1722, 1248, 1099, 1055, 1025, 936, 858, 834, 749, 696 cm^{-1}; HRMS (ESI) *m*/*z* calc'd for $C_{15}H_{20}O_2Na$ 255.1357 found $C_{15}H_{20}O_2Na$ 255.1361; $[\alpha]_D^{20}$ = -34.13 ° (*c* = 0.58, $CHCl_3$).

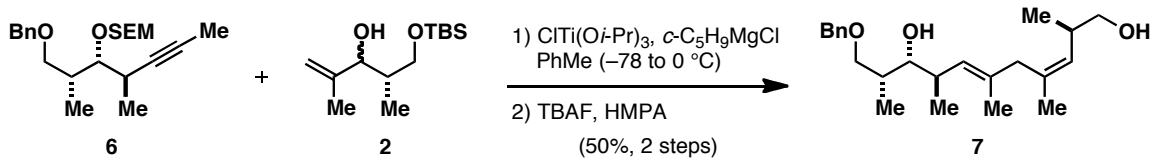
General Procedure: Titanium mediated coupling of alkynes and allylic alcohols

The alkyne (0.302 g, 0.802 mmol, 1 eq) was dissolved in 6.7 ml of PhMe and cooled to −78 ˚C. $ClTi(O\textit{i}\text{-}Pr)_3$ (1 M in Hexanes) was added dropwise (1.28 ml) followed by *c*-C_5H_9MgCl (2 M in Et_2O, 2.56 mmol). The light brown solution was warmed to −25 ˚C over the course of 30 min and stirred for an additional 45 min while the solution became dark brown. The solution was then recooled to −78 ˚C and the lithium alkoxide of the allylic alcohol[5] was added (1.5 eq, 1.20 mmol). This lithium alkoxide was formed by dissolving the allylic alcohol (0.293 g, 1.20 mmol) in 3 ml of Et_2O, cooling to −78 ˚C, adding *n*-BuLi (1.26 mmol, 2.45 M in Hexanes), and warming to room temperature over 20 min. The solution of lithium alkoxide was cooled to 0 ˚C and added slowly via cannula to the the dark-brown Titanium-alkyne complex at −78 ˚C, a slight redening of the dark brown solution is sometimes noted. The reaction was warmed to 0 ˚C over 7 h

and quenched by dumping into stirring, saturated NH_4Cl. The mixture was stirred until becoming white in color (~40 min) then passed through a short silica plug and concentrated to give an oil containing the product diene and allylic alcohol starting material. This oil was subjected to the following desilyation procedure, then purified via column chromatography over silica gel to give the pure, desilylated 1,4-diene products.

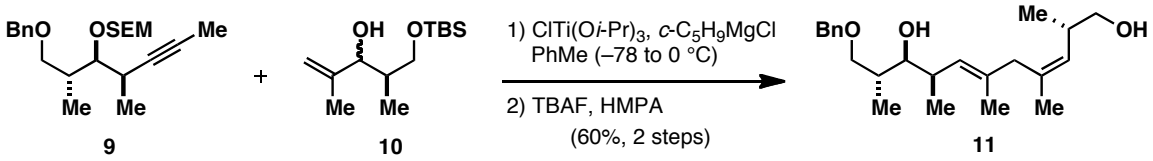
General Procedure: Desilylation of coupled 1,4-dienes

The crude diene (< 0.802 mmol) from the titanium-mediated coupling described above was dissolved in 4 ml of HMPA. Activated 4 Å molecular sieves (1.00 g) where added followed by 1.30 g of TBAF•$3H_2O$ and the reaction mixture was heated to 35 ˚C. After stirring for 4 h, an additional 0.200 g of TBAF•$3H_2O$ and molecular sieves (0.300 g) were added. The reaction was stirred until formation of the diol was complete by TLC then diluted with 10 ml of Et_2O. The mixture was then washed 1X with H_2O (5 ml). The organic phase was dried with Na_2SO_4, filtered, and concentrated *in vacuo*. The resulting crude oil was chromatographed over silica gel with 15% to 30% EtOAc in Hexanes to give the doubly desilylated 1,4-diene in yields of approximately 60%.

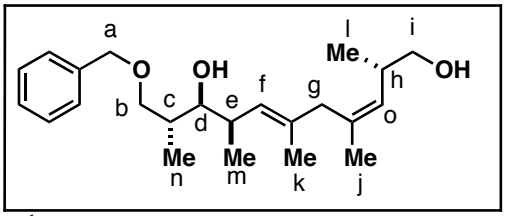


Synthesis of (2*R*,3*Z*,6*E*,8*R*,9*R*,10*R*)-11-(benzyloxy)-2,4,6,8,10-pentamethylundeca-3,6-diene-1,9-diol (7): 7 was prepared via Ti-mediated coupling followed by desilylation with TBAF as described above (see general procedures). **6** was used as a 9:1 mixture of diasteromers[1], this isomeric ratio is conserved during the synthesis of **7**. **7** was obtained as a clear oil in 50% over 2 steps. **Data for (7): ^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38−7.27 (m, 5H), 5.09 (d, 1H, J = 8.4), 5.06 (d, 1H, J = 8.4), 4.51 (s, 2H), 3.57−3.53 (m, 1H), 3.50−3.44 (m, 3H), 3.34−3.30 (m, 1H), 2.75 (d, 1H, J = 6.4 Hz), 2.75 (d, 1H,

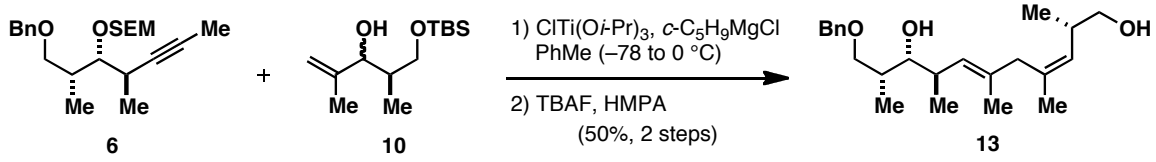
J = 6.4 Hz), 2.60−2.50 (m, 2H), 2.45 (dd, 1H, $J_1 = J_2$ = 6.8 Hz), 2.24 (bs, 1H), 1.98 (qd, 1H, J_1 = 3.6 Hz, J_2 = 2.0 Hz), 1.66 (d, 3H, , J_1 = 1.2 Hz), 1.61 (d, 3H, J_1 = 1.2 Hz), 0.96 (d, 3H, J = 7.2 Hz), 0.92 (d, 3H, J = 7.2 Hz), 0.88 (d, 3H, J = 7.2 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 138.8, 135.3, 134.6, 130.3, 128.9, 128.7, 127.9, 127.8, 76.7, 75.0, 73.6, 68.3, 42.3, 36.5, 35.9, 35.4, 24.1, 17.5, 17.4, 17.1, 10.2; IR (thin film, KBr) 3412, 2971, 2901, 1453, 1393, 1381, 1259, 1046, 801, 751, 697 cm^{-1}; HRMS (ESI) *m/z* calc'd for $C_{23}H_{36}O_3Na$ 383.2560 found $C_{23}H_{36}O_3Na$ 383.2562; $[\alpha]_D^{20}$ = −8.10 ° (*c* = 0.20, $CHCl_3$).



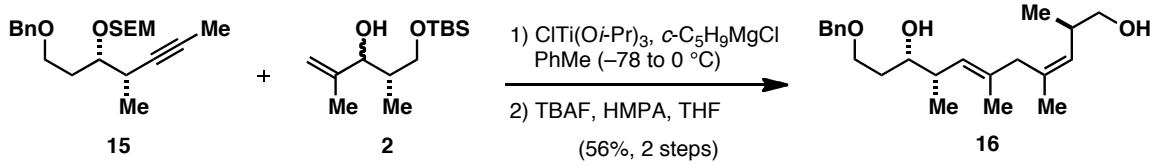
Synthesis of (2*S*,3*Z*,6*E*,8*R*,9*S*,10*R*)-11-(benzyloxy)-2,4,6,8,10-pentamethylundeca-3,6-diene-1,9-diol (11): 11 was prepared via Ti-mediated coupling followed by desilylation with TBAF as described above (see general procedures). **9** was used as a 23:1 mixture of diasteromers[1], this isomeric ratio is conserved during the synthesis of **11**. **11** was obtained as a clear oil in 60% yield over two steps. **Data for (11): ^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38−7.27 (m, 5H), 5.12(f) (d, 1H, J = 9.6 Hz), 5.04(o) (d, 1H, J = 9.6 Hz), 4.50(a) (app. dd, 2H, J_1 = 12.0 Hz, J_2 = 12.0 Hz), 3.60(b) (dd, 1H, J_1 = 12.0 Hz, J_2 = 4.0 Hz), 3.46(d) (bs, 1H), 3.45(i) (dd, 1H, J_1 = 8.0 Hz, J_2 = 5.6 Hz), 3.35−3.27(b,i) (m, 2H), 3.18(OH) (bs, 1H), 2.75(g) (d, 1H, J = 14.4 Hz), 2.67(g) (d, 1H, J = 14.4 Hz), 2.64−2.44(e,h) (m, 2H), 1.92−1.85(c) (m, 1H), 1.63(j) (d, 3H, , J_1 = 1.2 Hz), 1.51(k) (d, 3H, J_1 = 1.2 Hz), 1.01(m) (d, 3H, J = 7.2 Hz), 0.98(l) (d, 3H, J = 7.2 Hz), 0.91(n) (d, 3H, J = 7.2 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 138.7, 135.5, 135.3, 130.0, 129.4, 128.6, 127.9, 127.8, 76.5, 74.8, 73.5, 68.1, 42.7, 36.5, 35.7, 35.3, 24.3, 17.5, 17.4, 16.6, 10.1; IR (thin film, KBr) 3412, 2972, 2900, 1407, 1261, 1047, 753, 698 cm^{-1}; HRMS (ESI) *m/z* calc'd for $C_{23}H_{40}O_3Na$ 387.2875 found $C_{23}H_{40}O_3Na$ 387.2873; $[\alpha]_D^{20}$ = 0.88 ° (*c* = 0.80, $CHCl_3$).



[1]HNMR assignments **11**

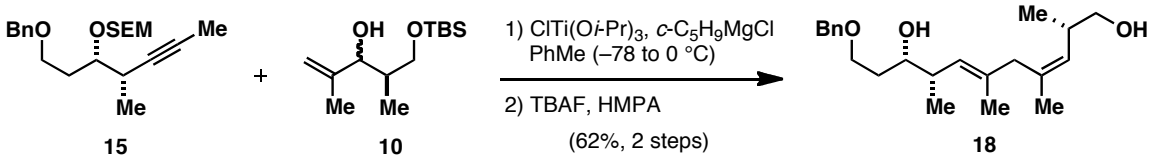


Synthesis of (2*S*,3*Z*,6*E*,8*R*,9*R*,10*R*)-11-(benzyloxy)-2,4,6,8,10-pentamethylundeca-3,6-diene-1,9-diol (13): 13 was prepared via Ti-mediated coupling followed by desilylation with TBAF as described above (see general procedures). **6** was used as a 9:1 mixture of diasteromers[1], this isomeric ratio is conserved during the synthesis of **13**. **13** was obtained as a clear oil in 50% over two steps. **Data for (13): ^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38-7.27 (m, 5H), 5.09 (d, 1H, J = 9.6 Hz), 5.03 (d, 1H, J = 9.6 Hz), 4.52 (s, 2H), 3.55 (dd, 1H, J_1 = 8.0 Hz, J_2 = 6.4 Hz), 3.48-3.42 (m, 3H), 3.32 (dd, 1H, J_1 = 8.0 Hz, J_2 = 8.0 Hz), 2.82-2.49 (m, 4H), 2.02-1.95 (m, 1H), 1.67 (d, 3H, J_1 = 1.2 Hz), 1.60 (d, 3H, J_1 = 1.2 Hz), 0.96 (d, 3H, J = 7.2 Hz), 0.93 (d, 3H, J = 7.2 Hz), 0.89 (d, 3H, J = 7.2 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 138.7, 135.5, 135.1, 130.0, 129.4, 128.6, 127.8 127.7, 76.5, 74.8, 73.5, 68.0, 42.7, 36.5, 35.7, 35.3, 24.3, 17.7, 17.4, 16.6, 10.1; (thin film, KBr) 3435, 2969, 2901, 1453, 1407, 1394, 1379, 1282, 1067, 1056, 879, 802, 751, 688, 665 cm^{-1}; HRMS (ESI) *m*/*z* calc'd for $C_{23}H_{36}O_3Na$ 383.2562, found $C_{23}H_{36}O_3Na$ 383.2565; $[\alpha]_D^{20}$ = 2.86 ° (*c* = 0.38, $CHCl_3$).

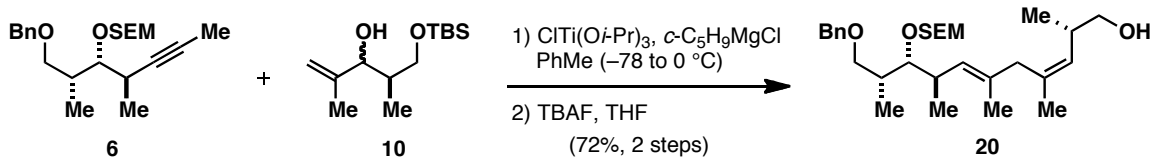


Synthesis of (2*R*,3*Z*,6*E*,8*S*,9*S*)-11-(benzyloxy)-2,4,6,8-tetramethylundeca-3,6-diene-1,9-diol (16): 16 was prepared via Ti-mediated coupling followed by desilylation with TBAF as described above (see general procedures). The *ee* of **15** used was only 90%, thus a minor diasteriomer was formed after coupling with the enantiomericly pure **2** resulting from cross-coupling with the minor enantiomer of **15**. **16** was obtained as a clear oil in 56% yield over two steps. **Data for (16): ^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38−7.27 (m, 5H), 5.01 (d, 1H, J = 9.2 Hz), 4.99 (d, 1H, J = 9.2 Hz), 4.51 (s, 2H),

3.73−3.60 (m, 2H), 3.55 (ddd, 1H, J_1 = 2.0 Hz, J_2 = 8.4 Hz, J_3 = 9.6 Hz), 3.44 (dd, 1H, J_1 = 6.0 Hz, J_2 = 12.0 Hz), 3.33 (dd, 1H, J_1 = 12.0 Hz, J_2 = 8.0 Hz), 2.75 (d, 1H, J = 3.9 Hz), 2.70 (d, 1H, J = 3.9 Hz), 2.63 (m, 1H), 2.49−2.40 (m, 1H), 1.85−1.77 (m, 1H), 1.74−1.60 (m, 1H), 1.64 (d, 3H, J_1 = 1.2 Hz), 1.57 (d, 3H, J_1 = 1.2 Hz), 1.00 (d, 3H, J = 7.2 Hz), 0.92 (d, 3H, J = 7.2 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 138.8, 135.9, 133.6, 129.8, 128.9, 128.8, 128.1, 128.0, 76.1, 73.7, 69.9, 68.2, 42.6, 39.3, 35.7, 34.4, 24.2, 17.5, 17.1, 16.7; IR (thin film, KBr) 3396, 2972, 2901, 1452, 1400, 1257, 802, 752, 696 cm^{-1}; HRMS (ESI) *m*/*z* calc'd for $C_{22}H_{34}O_3Na$ 369.2406 found $C_{23}H_{36}O_3Na$ 369.2409; $[\alpha]_D^{20}$ = −15.00 ° (*c* = 1.09, $CHCl_3$).



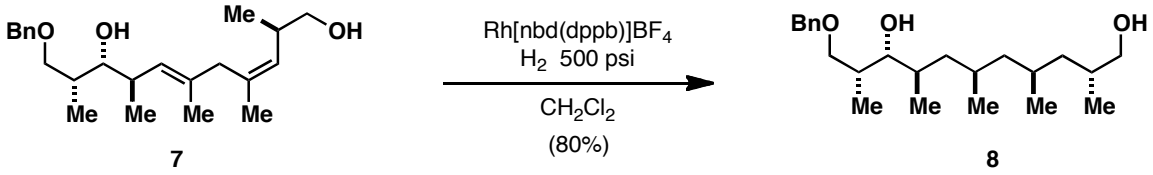
Synthesis of (2*S*,3*Z*,6*E*,8*S*,9*S*)-11-(benzyloxy)-2,4,6,8-tetramethylundeca-3,6-diene-1,9-diol (18): 18 was prepared via Ti-mediated coupling followed by desilylation with TBAF as described above (see general procedures). The *ee* of **15** used was only 90%, thus a minor diasteriomer was formed after coupling with the enantiomericly pure **10** resulting from cross-coupling with the minor enantiomer of **15**. **18** was obtained as a clear oil in 62% yield over two steps. **Data for (18): ^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38−7.27 (m, 5H), 5.02 (d, 1H, J = 9.2 Hz), 4.99 (d, 1H, J = 9.2 Hz), 4.51 (s, 2H), 3.73−3.68 (m, 1H), 3.65−3.59 (m, 1H), 3.55 (ddd, 1H, J_1 = 2.0 Hz, J_2 = 8.4 Hz, J_3 = 9.6 Hz), 3.43 (dd, 1H, J_1 = 6.0 Hz, J_2 = 12.0 Hz), 3.33 (dd, 1H, J_1 = 12.0 Hz, J_2 = 8.0 Hz), 2.79 (d, 1H, J = 12.0 Hz), 2.68 (d, 1H, J = 12.0 Hz), 2.66−2.57 (m, 1H), 2.49−2.40 (m, 1H), 1.85−1.78 (m,1H), 1.72−1.65 (m, 1H), 1.64 (d, 3H, J_1 = 1.2 Hz), 1.57 (d, 3H, J_1 = 1.2 Hz), 1.00 (d, 3H, J = 7.2 Hz), 0.92 (d, 3H, J = 7.2 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 138.3, 135.8, 133.5, 129.8, 128.9, 128.8, 128.0, 128.9, 76.0, 73.7, 69.9, 68.2, 42.7, 39.3, 35.8, 34.4, 24.2, 17.5, 17.2, 16.7; IR (thin film, KBr) 3377, 2958, 2924, 2868, 1455, 1374, 1075, 1028, 735, 697 cm^{-1}; HRMS (ESI) *m*/*z* calc'd for $C_{22}H_{34}O_3Na$ 369.2406 found $C_{22}H_{34}O_3Na$ 369.2407; $[\alpha]_D^{20}$ = 1.72 ° (*c* = 1.22, $CHCl_3$).



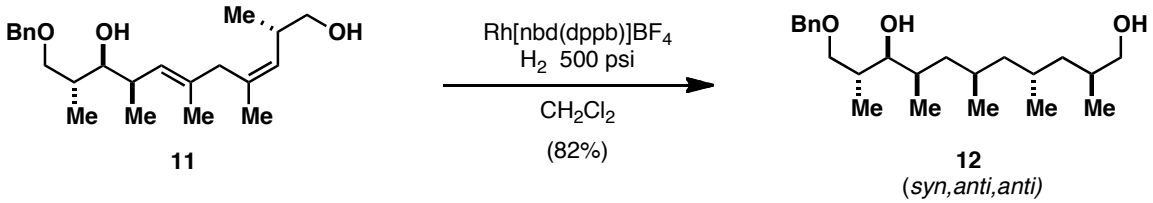
Synthesis of (2*S*,3*Z*,6*E*,8*R*,9*R*,10*R*)-11-(benzyloxy)-2,4,6,8,10-pentamethyl-9-((2-(trimethylsilyl)ethoxy)methoxy)undeca-3,6-dien-1-ol (20): 20 was prepared via Ti-mediated coupling as described above. The TBS group was then removed as follows. The crude coupling product was dissolved in 4 ml of THF. Activated 4 Å molecular sieves were then added. 1.30 g of TBAF•3H_2O was added and the mixture stirred for 6 h. Saturated NH_4Cl was then added and the aqueous layer was extracted with Et_2O (2X). The organic phases were dried over Na_2SO_4, filtered and concentrated. The crude oil was purified by column chromatography (5% to 10% EtOAc in Hexanes) to give the product as a clear oil in 72% yield (over two steps, Ti-coupling and desilylation). **Data for (20): ^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38−7.27 (m, 5H), 5.16 (d, 1H, *J* = 10.4 Hz), 5.00 (d, 1H, *J* = 10.4 Hz), 4.67 (s, 2H), 4.52 (d, 1H, *J* = 12.0 Hz), 4.44 (d, 1H, *J* = 12.0 Hz), 3.68−3.56 (m, 2H), 3.46−3.42 (m, 3H), 3.63−3.23 (m, 2H), 2.77 (d, 1H, *J* =14.4 Hz), 2.68 (d, 1H, *J* =14.4 Hz), 2.66−2.60 (m, 2H), 2.01−1.95 (m, 1H), 1.63 (d, 3H, *J* = 1.6), 1.52 (d, 3H, *J* = 1.6), 1.44 (m, 1H), 0.98 (d, 3H, *J* = 6.8), 0.95−0.90 (m, 9H), 0.01 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 138.8, 135.9, 132.5, 129.4, 129.0, 128.4, 127.7, 127.6, 96.5, 83.8, 73.6, 73.1, 68.1, 65.7, 42.4, 36.6, 35.9, 35.5, 23.8, 18.5, 18.2, 17.4, 16.2, 12.6, −1.3; IR (thin film, KBr) 3663, 3420, 2969, 2901, 1453, 1407, 1394, 1379, 1259, 1067, 1056, 879, 802, 751, 696, 665 cm^{-1}; HRMS (ESI) *m*/*z* calc'd for $C_{23}H_{36}O_3Na$ 383.2562 found $C_{23}H_{36}O_3Na$ 383.2565; $[\alpha]_D^{20}$ = 2.86 ° (*c* = 0.37, $CHCl_3$).

General Procedure: Hydrogenation of 1,4-dienes

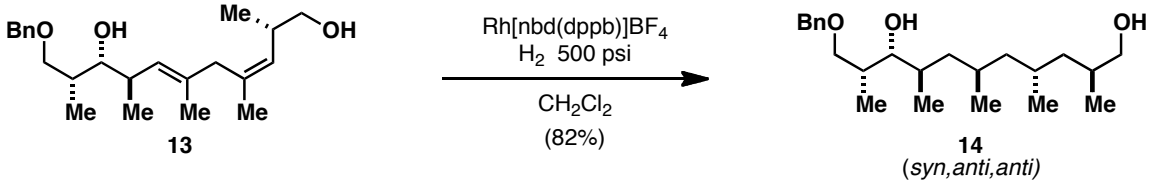
The diene (50 mg, 0.139 mmol) was dissolved in 1 ml of CH_2Cl_2. Rh[nbd(dppb)]BF_4 (30 mg, 30 mol %) was added. The glass reaction vial was placed inside of a reactor rated to 2000 psi and sealed tightly. The reactor was placed behind a blast shield and flushed with H_2 gas 5X. It was then pressurized to 500 psi with H_2. The reaction mixture was stirred for 3 h after which it was vented to release internal pressure. The reaction volume (1 ml) was diluted 1X wth hexanes and loaded onto a silica gel column. The reaction was then chromatagraphed with 10% to 30% EtOAc in Hexanes to give the hydrogenated, deoxypropionate products in 79% to 88% yields as clear oils.



Synthesis of (2*R*,4*S*,6*R*,8*R*,9*S*,10*R*)-11-(benzyloxy)-2,4,6,8,10-pentamethylundecane-1,9-diol (8): Synthesis of **8** was carried out as described above in the general procedure for the hydrogenation of 1,4-dienes. **8** was obtained as a clear oil in 80% yield. The stereochemistry of this product was assigned based on the established model for related directed hydrogenation reactions[6] and is based on minimization of $A^{1,3}$ strain in the transition state. Further stereochemical analysis of deoxypropionates based on ^{1}HNMR shifts can be found on page S52. **Data for (8): ^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38−7.27 (m, 5H), 4.51 (d, 1H, *J* = 4.4 Hz), 4.51 (d, 1H, *J* = 4.4 Hz), 3.54 (d, 2H, *J* = 4.8 Hz), 3.50−3.37 (m, 3H), 1.99−1.92 (m, 1H), 1.76−1.56 (m, 7H), 0.98−0.78 (m, 20H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 138.3, 128.5, 127.7, 127.7, 78.7, 75.8, 73.6, 69.5, 45.2, 42.0, 39.6, 35.1, 34.0, 33.4, 27.8, 27.4, 21.5, 20.9, 16.4, 16.2, 10.0; IR (thin film, KBr) 3419, 1454, 1378, 1074, 1028, 982, 734, 696 cm^{-1}; HRMS (ESI) *m*/*z* calc'd for $C_{23}H_{41}O_3$ 365.3056 found $C_{23}H_{41}O_3$ 365.3058; $[\alpha]_D^{20}$ = 25.00 ° (*c* = 0.80, $CHCl_3$).

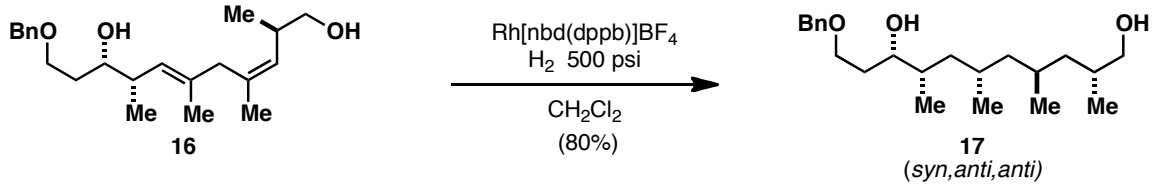


Synthesis of (2*S*,4*R*,6*R*,8*R*,9*S*,10*R*)-11-(benzyloxy)-2,4,6,8,10-pentamethylundecane-1,9-diol (12): Synthesis of **12** was carried out as described above in the general procedure for the hydrogenation of 1,4-dienes. **12** was obtained as a clear oil in 82% yield. **Data for (12): ^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38−7.27 (m, 5H), 4.53 (d, 1H, *J* = 3.2 Hz), 4.53 (d, 1H, *J* = 3.2 Hz), 3.60 (dd, 1H, J_1 = 8.0 Hz, J_2 = 4.0 Hz), 3.53−3.47 (m, 2H), 3.42−3.37 (m, 2H), 2.00−1.91 (m, 2H), 1.77−1.58 (m, 5H), 1.41−1.34 (m, 1H), 1.20−0.94 (m, 6H), 0.91 (d, 3H, *J* = 6.4 Hz), 0.87−0.80 (m, 12H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 137.9, 128.6, 127.9, 127.8, 78.6, 76.5, 73.7, 69.1, 45.7, 42.3, 41.7, 36.2, 33.3, 32.1, 27.3, 20.3, 19.4, 16.7, 13.8, 12.9; IR (thin film, KBr) 3421, 2958, 2913, 2870, 1456, 1379, 1074, 1028, 983, 734, 696 cm^{-1}; HRMS (ESI) *m*/*z* calc'd for $C_{23}H_{41}O_3$ 365.3056 found $C_{23}H_{41}O_3$ 365.3058; $[\alpha]_D^{20}$ = −14.20 ° (*c* = 0.51, $CHCl_3$).

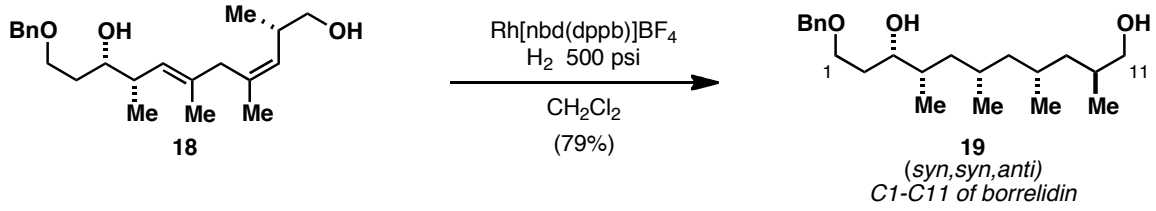


Synthesis of (2*S*,4*R*,6*R*,8*R*,9*R*,10*R*)-11-(benzyloxy)-2,4,6,8,10-pentamethylundecane-1,9-diol (14): Synthesis of **14** was carried out as described above in the general procedure for the hydrogenation of 1,4-dienes. **14** was obtained as a clear oil in 82% yield. **Data for (14): ^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38−7.27 (m, 5H), 4.51 (d, 1H, *J* = 3.2 Hz), 3.54 (d, 1H, *J* = 4.8 Hz), 3.54 (d, 1H, *J* = 4.8 Hz), 3.51−3.33 (m, 3H), 1.99−1.92 (m, 1H), 1.76−1.55 (m, 5H), 1.47−1.43 (m, 1H), 1.22−1.11 (m, 2H), 0.99−0.78 (m, 18H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 138.3, 128.6, 127.8, 127.7, 78.7, 75.8, 73.6, 69.0, 44.4, 42.1, 42.0, 35.2, 33.7, 33.3, 27.8, 27.4, 19.1, 16.8, 16.0, 10.0; IR (thin film, KBr) 3419, 2961, 2871, 1455, 1380, 1073, 1029, 735, 697 cm^{-1}; HRMS (ESI)

m/*z* calc'd for $C_{23}H_{41}O_3$ 365.3056 found $C_{23}H_{41}O_3$ 365.3051; $[\alpha]_D^{20}$ = 20.12 ° (*c* = 1.00, $CHCl_3$).

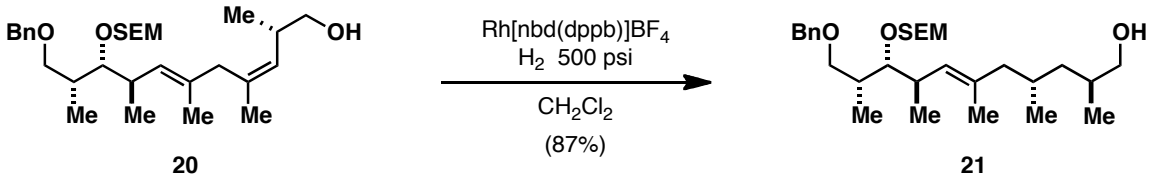


Synthesis of (2*R*,4*S*,6*S*,8*S*,9*S*)-11-(benzyloxy)-2,4,6,8-tetramethylundecane-1,9-diol (17): Synthesis of **17** was carried out as described above in the general procedure for the hydrogenation of 1,4-dienes. **17** was obtained as a clear oil in 80% yield. **Data for (17):** **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38−7.27 (m, 5H), 4.53 (s, 2H), 3.75−3.62 (m, 3H), 3.48−3.38 (m, 2H), 2.63 (bs, 1H), 1.86−1.55 (m, 5), 1.43−0.91 (m, 8H), 0.89 (d, 3H, *J* = 5.2 Hz), 0.87 (d, 3H, *J* = 5.2 Hz), 0.85 (d, 3H, *J* = 5.2 Hz), 0.84 (d, 3H, *J* = 5.2 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 138.1, 128.6, 127.9, 127.8, 74.4, 73.5, 70.0, 69.5, 45.8, 41.3, 40.0, 35.9, 34.1, 33.4, 27.5, 27.4, 21.0, 20.7, 16.3, 14.7; IR (thin film, KBr) 3380, 2954, 2919, 2870, 1456, 1378, 1095, 1029, 736, 698 cm^{-1}; HRMS (ESI) *m*/*z* calc'd for $C_{22}H_{38}O_3Na$ 373.2719 found $C_{22}H_{38}O_3Na$ 373.2716; $[\alpha]_D^{20}$ = −19.43 ° (*c* = 0.32, $CHCl_3$).



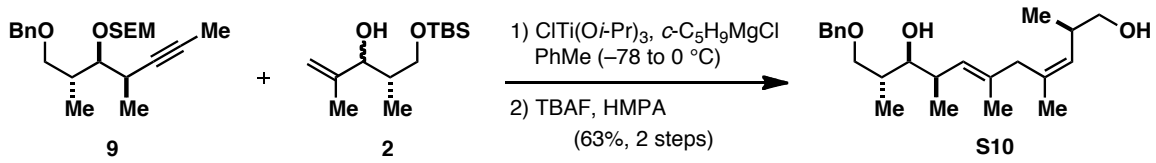
Synthesis of (2*S*,4*R*,6*S*,8*S*,9*S*)-11-(benzyloxy)-2,4,6,8-tetramethylundecane-1,9-diol (19): Synthesis of **19** was carried out as described above in the general procedure for the hydrogenation of 1,4-dienes. **19** was obtained as a clear oil in 79% **Data for (19): ^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38−7.27 (m, 5H), 4.53 (s, 2H), 3.76−3.52 (m, 3H), 3.49−3.38 (m, 2H), 2.63 (bs, 1H), 1.86−0.91 (m, 14H), 0.89 (d, 3H, *J* = 5.2 Hz), 0.88 (d, 3H, *J* = 5.2 Hz), 0.86 (d, 3H, *J* = 5.2 Hz), 0.85 (d, 3H, *J* = 5.2 Hz); **^{13}C NMR** (100

MHz, $CDCl_3$) δ 138.1, 128.6, 127.9, 127.8, 74.4, 73.5, 69.9, 69.4, 45.8, 41.3, 40.0, 35.9, 34.1, 33.4, 27.5, 27.4, 21.0, 20.6, 16.3, 14.7; IR (thin film, KBr) 3397, 2954, 2919, 2869, 1456, 1378, 1094, 1028, 735, 697 cm^{-1}; HRMS (ESI) *m/z* calc'd for $C_{22}H_{38}O_3Na$ 373.2719 found $C_{22}H_{38}O_3Na$ 373.2724; $[\alpha]_D^{20} = -2.50$ ° (*c* = 0.40, $CHCl_3$).

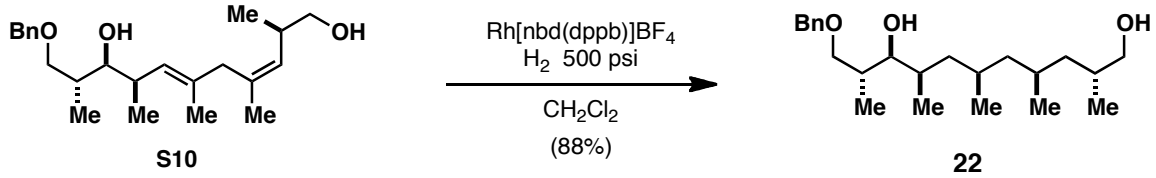


Synthesis of (2*S*,4*S*,8*R*,9*R*,10*R*,*E*)-11-(benzyloxy)-2,4,6,8,10-pentamethyl-9-((2-(trimethylsilyl)ethoxy)methoxy)undec-6-en-1-ol (21): Synthesis of **21** was carried out as described above in the general procedure for the hydrogenation of 1,4-dienes. **21** was obtained as a clear oil in 87% yield. **Data for (21): ^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38−7.27 (m, 5H), 5.09 (d, 1H, *J* = 12.0 Hz), 4.66 (d, 2H, *J* = 1.6 Hz), 4.52 (d, 1H, *J* = 12.0 Hz), 4.45 (d, 1H, *J* = 12.0 Hz), 3.64−3.59 (m, 2H), 3.52−3.36 (m, 4H), 3.30 (dd, 1H, J_1 = 12.0 Hz, J_2 = 6.8 Hz), 2.68−2.64 (m, 1H), 2.04−1.95 (m, 1H), 1.92 (dd, 1H, J_1 =12.0 Hz, J_2 = 6.0 Hz), 1.80 (dd, 1H, J_1 =12.0 Hz, J_2 = 8.0 Hz), 1.76−1.71 (m, 2H), 1.54 (s, 3H), 1.15−1.01 (m, 2H), 1.01−1.81 (m, 12H), 0.78 (d, 3H, *J* = 6.4 Hz), 0.00 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 138.78, 133.45, 129.48, 128.45, 127.76, 127.62, 96.47, 83.47, 73.66, 73.18, 69.18, 65.76, 48.93, 40.60, 36.52, 35.79, 33.31, 27.98, 19.17, 18.53, 18.23, 16.30, 16.16, 12.46, −1.25; IR (thin film, KBr) 3676, 2969, 2901, 1454, 1406, 1394, 1380, 1250, 1055, 1027, 861, 836, 697 cm^{-1}; HRMS (ESI) *m/z* calc'd for $C_{29}H_{52}O_4NaSi$ 515.3533 found $C_{29}H_{52}O_4NaSi$ 515.3531; $[\alpha]_D^{20}$ = 5.65 ° (*c* = 0.20, $CHCl_3$).

Synthesis of *(−)-vittatalactone*

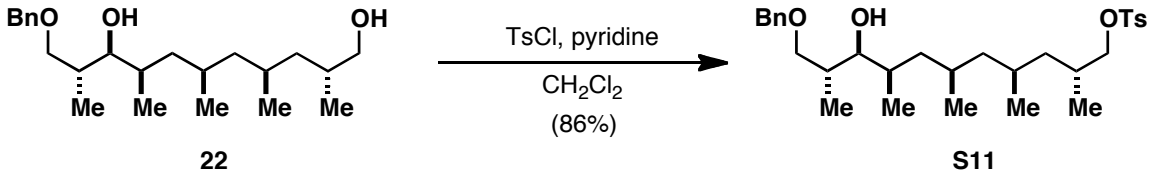


Synthesis of (2*R*,3*Z*,6*E*,8*R*,9*S*,10*R*)-11-(benzyloxy)-2,4,6,8,10-pentamethylundeca-3,6-diene-1,9-diol: Ti-mediated coupling of **9** and **2** and desilylation of the resultant 1,4-diene was carried out as described in the general procedures. The product 1,4-diene was obtained as a clear oil in 63% yield. The preparation of **9** is described at the beginning of this SI document. Preparation of **2** was carried out as previously reported.[5] **Data: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38−7.27 (m, 5H), 5.10 (d, 1H, J = 9.6 Hz), 5.00 (d, 1H, J = 9.6 Hz), 4.50 (app. dd, 2H, J_1 = 24.0 Hz, J_2 = 12.0 Hz), 3.60 (dd, 1H, J_1 = 12.0 Hz, J_2 = 4.0 Hz), 3.46−3.42 (m, 2H), 3.35−3.27 (m, 2H), 2.72 (app. dd, 2H, J_1 = 24.0 Hz, J_2 = 14.0 Hz), 2.66−2.59 (m, 1H), 2.52−2.44 (m, 1H), 1.92−1.84 (m, 2H), 1.63 (d, 3H, J = 1.2 Hz), 1.50 (d, 3H, J = 1.2 Hz), 1.02 (d, 3H, J = 7.2 Hz), 0.99 (d, 3H, J = 7.2 Hz), 0.93 (d, 3H, J = 7.2 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 137.9, 135.8, 132.0, 129.7, 129.5, 128.6, 127.9, 127.8, 80.2, 74.3, 73.7, 68.1, 42.5, 36.5, 35.9, 35.6, 24.0, 17.4, 16.2, 15.7, 15.2; IR (thin film, KBr) 3415, 2962, 2925, 1453, 1375, 1260, 1075, 1027, 802, 735, 697, 668 cm^{-1}; HRMS (ESI) *m*/*z* calc'd for $C_{23}H_{36}O_3Na$ 387.2562 found $C_{23}H_{36}O_3Na$ 383.2567; $[\alpha]_D^{20}$ = −4.55 ° (*c* = 0.55, $CHCl_3$).



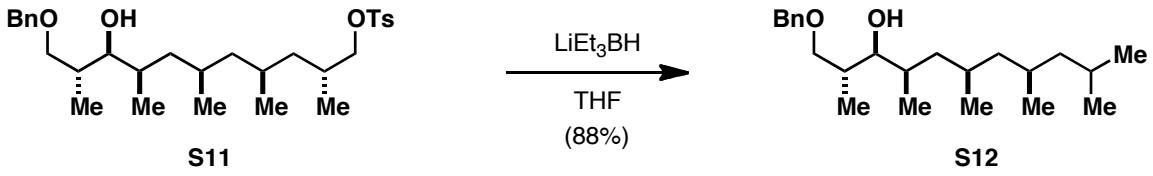
Synthesis of (2*R*,4*S*,6*R*,8*R*,9*S*,10*R*)-11-(benzyloxy)-2,4,6,8,10-pentamethylundecane-1,9-diol (22): The synthesis of **22** was carried out as described in the general procedure for the hydrogenation of 1,4-dienes. **22** was obtained as a clear oil in 88% yield. **Data**

for (22): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.27 (m, 5H), 4.51 (d, 1H, J = 3.2 Hz), 3.60 (dd, 1H, J_1 = 4.8 Hz, J_2 = 5.3 Hz), 3.53−3.38 (m, 4H), 2.01−1.91 (m, 1H), 1.77−1.56 (m, 6H), 1.48−1.39 (m, 2H), 1.28−0.92 (m, 6H), 0.92−0.81 (m, 13H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 137.8, 128.6, 127.9, 127.1, 78.2, 76.5, 73.6, 69.1, 46.2, 41.5, 40.9, 36.2, 33.8, 32.8, 27.3, 27.1, 20.6, 20.4, 16.3, 13.7, 13.1; IR (thin film, KBr) 3663, 2971, 2901, 1406, 1394, 1382, 1250, 1056, 1066, 829 cm^{-1}; HRMS (ESI) *m*/*z* calc'd for $C_{23}H_{41}O_3$ 365.3056 found $C_{23}H_{41}O_3$ 365.3054; $[\alpha]_D^{20}$ = −7.30 ° (*c* = 0.41, $CHCl_3$).



22 S11

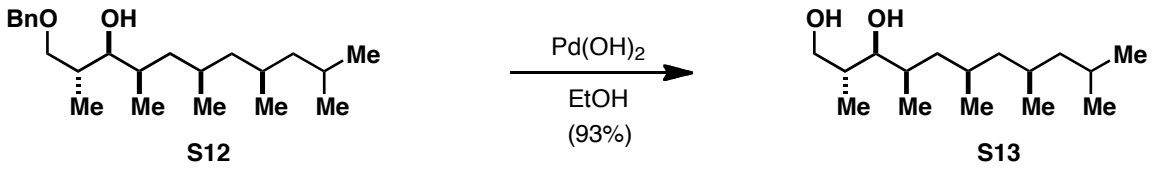
Synthesis of (2*R*,4*S*,6*R*,8*R*,9*S*,10*R*)-11-(benzyloxy)-9-hydroxy-2,4,6,8,10-pentamethylundecyl 4-methylbenzenesulfonate: The diol **22** (50 mg, 0.137 mmol) was dissolved in dry pyridine (0.50 ml) and cooled to 0 °C. 79 mg (0.414 mmol) of TsCl in 0.15 ml of dry CH_2Cl_2 was added via syrige. The solution turned bright yellow and was stirred at 0 °C until complete by TLC (1 h). The reaction was then diluted with 10 ml of Et_2O and washed with 1 N HCl, saturated $NaHCO_3$, and brine. The organic phase was separated and dried over Na_2SO_4. The Na_2SO_4 was filtered off and the organic phase concentrated to give the crude tosylate (60 mg, 86%) as a light yellow oil, which was used without further purification in the next step.



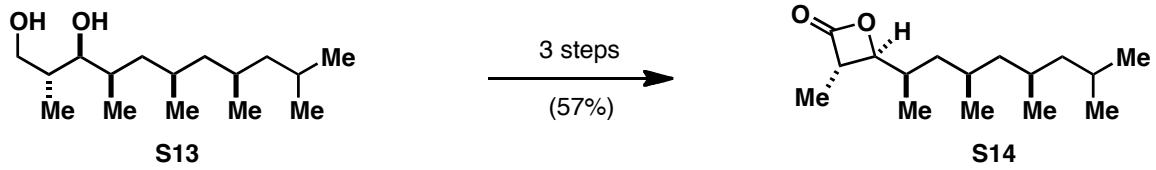
S11 S12

The crude tosylate from the previous step was dried by azeotropic removal of water with PhMe. The tosylate (60 mg, 0.116 mmol) was dissolved in 0.10 ml of dry THF and cooled to 0 °C. 0.30 ml of $LiEt_3BH$ (1 M in THF) was added dropwise. The reaction

was stirred at 0 °C for 30 min then diluted with 2 ml of H_2O and 10 ml of Et_2O. The aqueous phase was extracted 2X with Et_2O and the combined organic phases were dried over Na_2SO_4. The Na_2SO_4 was filtered off and the organic phase concentrated to give a crude oil which was purified over silica gel (2% to 10% EtOAc in Hexanes) to give the alcohol as a clear oil (36 mg, 88%). **Data: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38−7.27 (m, 5H), 4.53 (d, 1H, J = 3.2 Hz), 3.60 (dd, 1H, J_1 = 12.0 Hz, J_2 = 4.4 Hz), 3.50 (dd, 1H, J_1 = 8.0 Hz, J_2 = 8.0 Hz), 3.38 (dd, 1H, J_1 = 8.0 Hz, J_2 = 2.0 Hz), 3.30 (bs, 1H), 2.02−1.91 (m, 1H), 1.74-1.53 (m, H), 1.37−1.26 (m, 1H), 1.16−0.9 (m, 5H), 0.89−0.82 (m, 18H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 137.9, 128.6, 127.9, 127.8, 78.9, 76.4, 73.7, 48.1, 44.8, 42.7, 36.2, 32.2, 27.7, 27.3, 25.3, 23.3, 22.7, 20.2, 19.7, 13.8, 12.8; IR (thin film, KBr) 2987, 2901, 1406, 1393, 1382, 1250, 1229, 1065, 1056, 891 cm^{-1}; HRMS (ESI) *m/z* calc'd for $C_{23}H_{41}O_2$ 349.3107 found $C_{23}H_{41}O_3$ 349.3112; $[\alpha]_D^{20}$ = −1.58 ° (*c* = 0.20, $CHCl_3$).



The diol[7,8] was formed by dissolving the benzyl alcohol (30 mg, 0.086 mmol) in 1 ml of EtOH and adding 60 mg of $Pd(OH)_2$ on carbon (20% Pd). H_2 was bubbled through the reaction mixture for 45 min at which time the reaction was complete by TLC. The reaction was passed through a pipette plug, concentrated, then purified via silica gel chromatography (10% to 30% EtOAc in Hexanes) to give the product diol as a clear oil (21 mg, 93%). The analylitcal data for the diol was consistent with previous literature reports of this diol.[7,8]



S13 S14

Synthesis of *(−)-vittatalactone*: *(−)-vittatalactone* was prepared from the diol intermediate as described in the literature.[7] Analytical data for intermediates in this sequence were in accordance with the literature.[7]

Step 1: The diol (8.0 mg, 0.031 mmol) was dissolved in 4 ml of CH_2Cl_2. 1.5 ml of saturated aqueous $NaHCO_3$ was added. 5 mg of NaBr was added and the mixture cooled to 0 °C. TEMPO radical (5 mg) was added and the mixture stirred for 5 min. 20 mg of 12 % aqueous NaOCl was added and the mixture stirred for 20 min after which time the reaction appeared complete by TLC analysis. The reaction was then quenched with 4 ml of saturated aqueous $Na_2S_2O_4$. The aqueous layer was extracted 2X with EtOAc and the combined organic layers were dried over Na_2SO_4. The solution was filtered and concentrated to give a pink oil that was used immediately in the next step.

Step 2: A stock solution of the oxidant was prepared on the same scale and in the same fashion as previously reported.[7] This solution was added to the neat aldehyde (formed in Step 1) and the mixture stirred for 3 h at which time the reaction was complete by TLC. The reaction was diluted with 10 ml of water and extracted with EtOAc 2X. The organic phases were dried over Na_2SO_4, filtered, and concentrated. The crude oil was purified via silica gel chromatography (19% EtOAc, 1% AcOH in Hexanes to 40% EtOAc, 1% AcOH in Hexanes) to give the product carboxylic acid as an off white solid (7.0 mg, 82% over two steps).

Step 3: The carboxylic acid (formed in Step 2) (6.0 mg, 0.022 mmol) was dissolved in 0.10 ml of pyridine. TsCl (10 mg, 0.052 mmol) was added and the reaction stirred for 16 h at room temperature. The mixture was then diluted with 5 ml of Et_2O and 5 ml of water. The aqueous phase was extracted 2X with Et_2O. The combined organic phases were washed with saturated aqueous NaH_2PO_4 that had been diluted 2X with water. The organic phases were then dried over Na_2SO_4, filtered and concentrated. Column chromatography over silica gel (3% to 10% EtOAc in Hexanes) gave *(−)-vittatalactone* as a clear oil (4.1 mg, 72%). **Data for *(−)-vittatalactone*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.87 (dd, 1H, J_1 = 8.0 Hz, J_2 = 4.0 Hz), 3.25 (qd, 1H, J_1 = 7.5 Hz, J_2 = 4.1 Hz),

1.91−1.82 (m, 1H), 1.68−1.61 (m, 1H), 1.60−1.58 (m, 1H), 1.58−1.52 (m, 1H), 1.40 (d, 3H, J = 7.5 Hz), 1.24−1.20 (m, 1H), 1.24−1.05 (m, 4 H), 1.02 (d, 3H, J = 6.5 Hz), 0.91−0.83 (m, 7H), 0.84 (d, 6H, J = 6.5 Hz); **^{13}C NMR** (100 MHz, 77.15 ppm, $CDCl_3$) δ 172.22, 83.93, 49.07, 46.17, 45.32, 39.98, 34.97, 27.82, 27.47, 25.36, 24.07, 21.96, 21.19, 20.93, 15.95, 13.06; IR (thin film, KBr) 2959, 2901, 1824, 1456, 1382, 1250, 1119, 1065, 983, 862 cm^{-1}; HRMS (ESI) m/z calc'd for $C_{16}H_{30}O_2Na$ 277.2144 found $C_{16}H_{30}O_2Na$ 277.2144; $[\alpha]_D^{20}$ = −2.8 ° (c = 1.01, $CHCl_3$).

Table S1: ^{1}H NMR shifts for vittatalactone

Pfaltz[8]		Micalizio
#	**δ_H (m, *J* (Hz))**	**δ_H (m, *J* (Hz))**
1	3.87 (dd, 4, 8.2)	3.87 (dd, 4.0, 8.1)
2	3.24 (dq, 4.1, 7.5)	3.25 (dq, 4.1, 7.5)
3	1.87 (m)	1.91-1.82 (m)
4	1.72-1.48 (m)	1.68-1.52 (m)
5	1.39 (d, 7.5)	1.40 (d, 7.5)
6	1.27-0.96 (m)	1.24-1.20 (m)
7	1.24-1.05 (m)	1.24-1.05 (m)
8	1.02 (d, 6.6)	1.02 (d, 6.5)
9	0.94-0.81 (m)	0.91-.83 (m)
10	0.90 (d, 6.1)	--
11	0.88 (d, 6.1)	--
12	0.84 (d, 6.5)	0.84 (d, 6.5)

Table S2: ^{13}C NMR shifts for vittatalactone

	Pfaltz[8]	Breit[7]	Micalizio
#	**δ_C**	**δ_C**	**δ_C**
1	172.3	172.2	172.22
2	83.99	83.9	83.93
3	49.13	49.0	49.07
4	46.24	46.1	46.17
5	45.39	45.3	45.32
6	40.05	39.9	39.98
7	35.03	34.9	34.97
8	27.89	27.8	27.82
9	27.54	27.4	27.47
10	25.43	25.3	25.36
11	24.13	24.0	24.07
12	22.03	21.9	21.96
13	21.26	21.1	21.19
14	20.99	20.9	20.93
15	16.02	15.9	15.95
16	13.33	13.0	13.06

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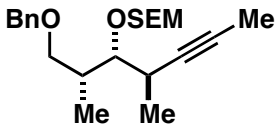

6

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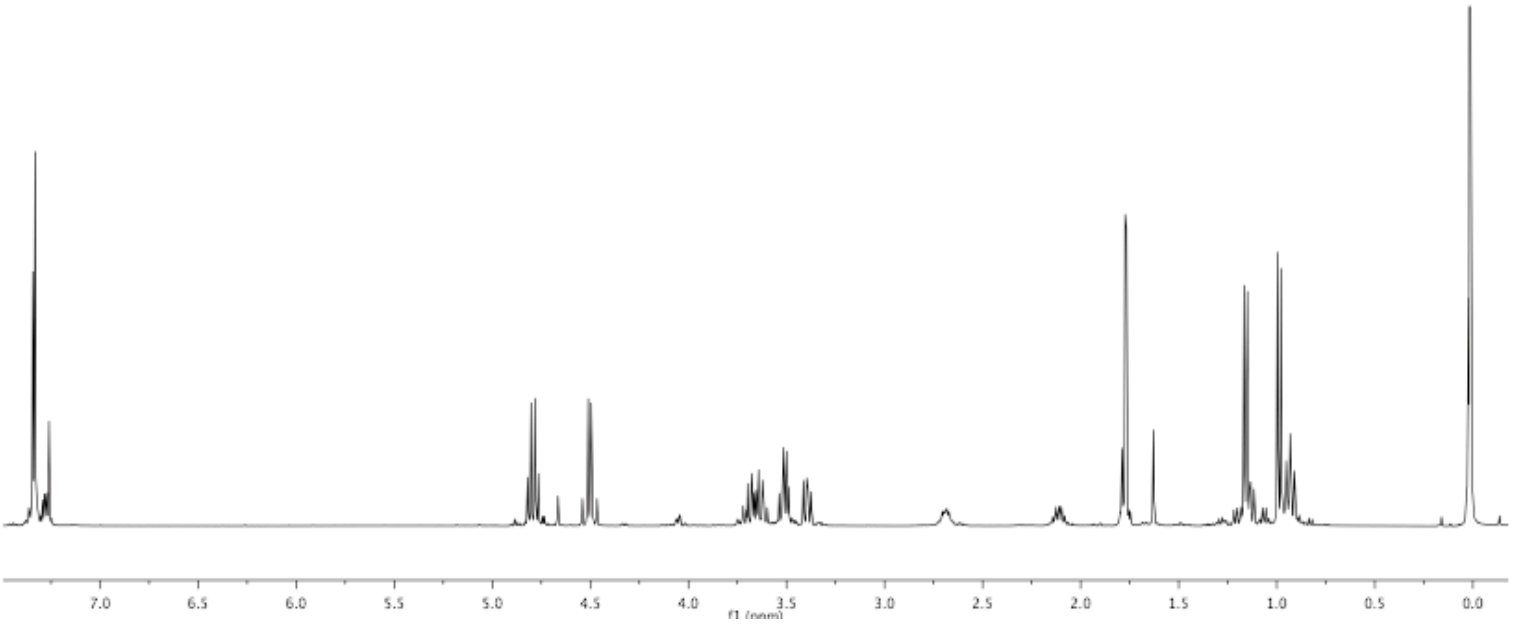
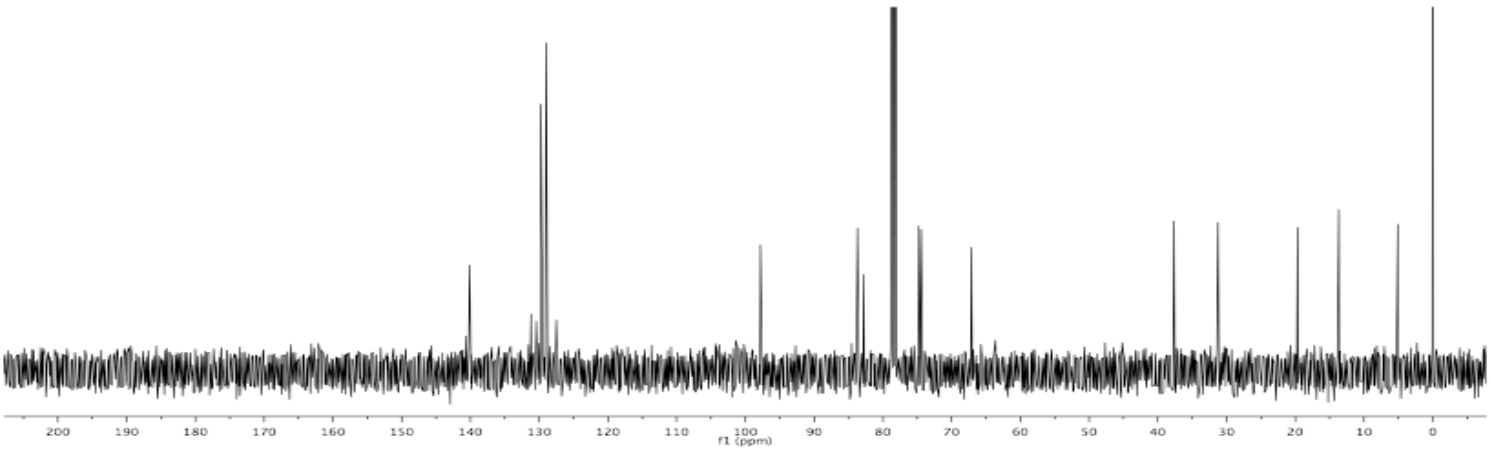
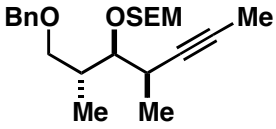




^{1}H (400 MHz, $CDCl_3$) and ^{13}C (100 MHz, $CDCl_3$)



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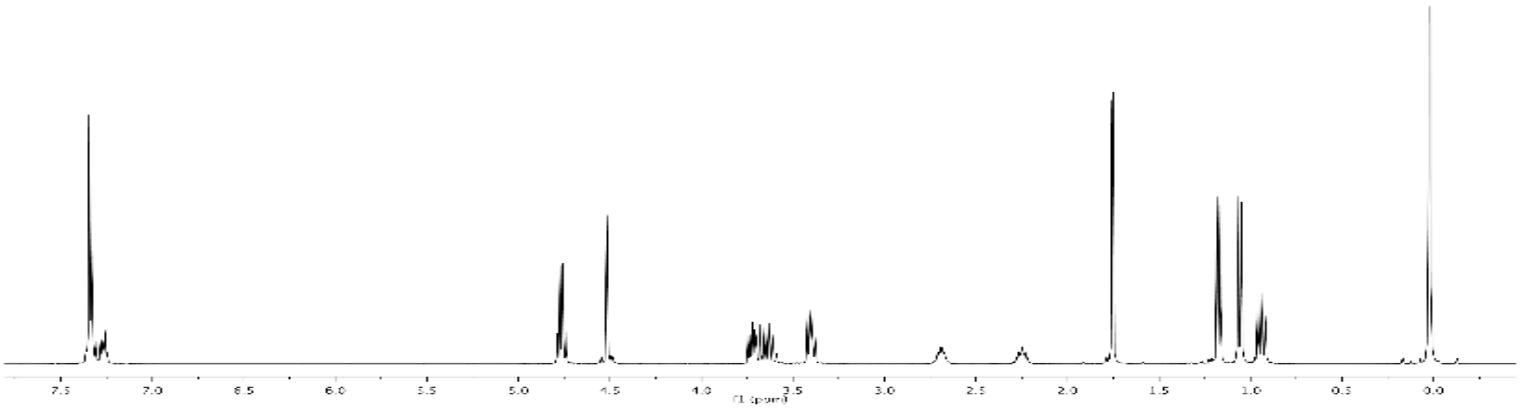
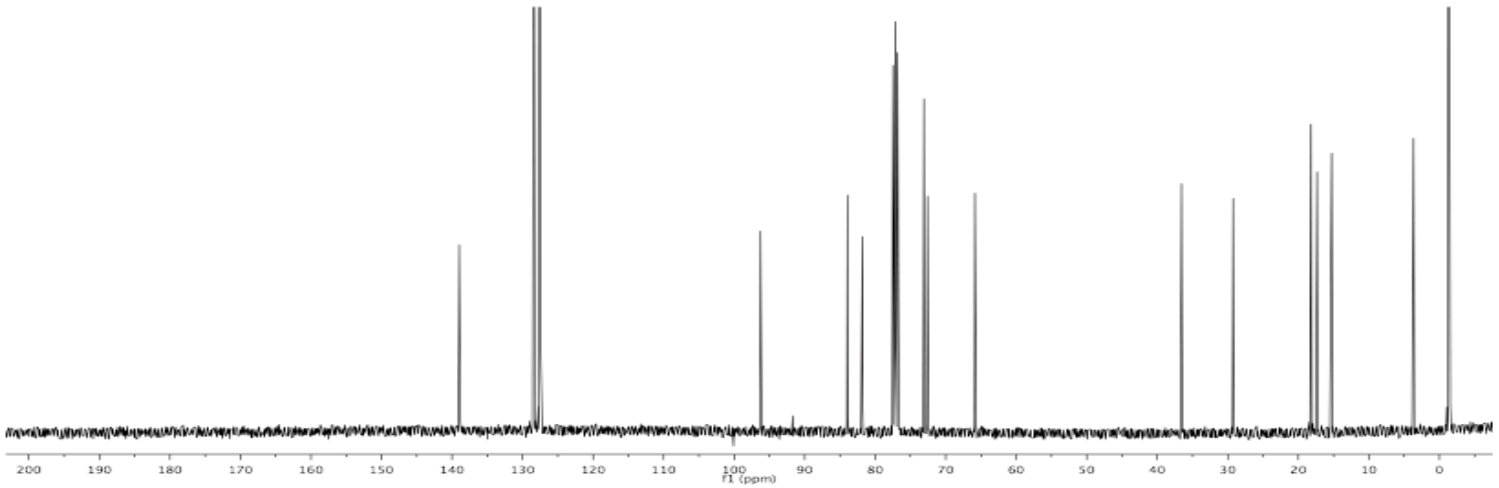
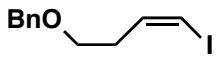
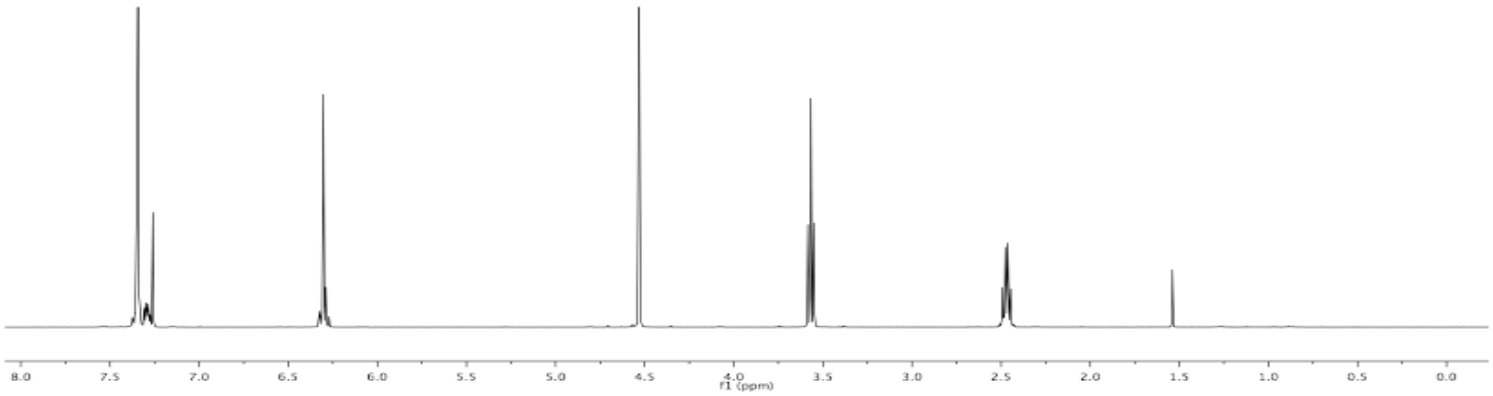


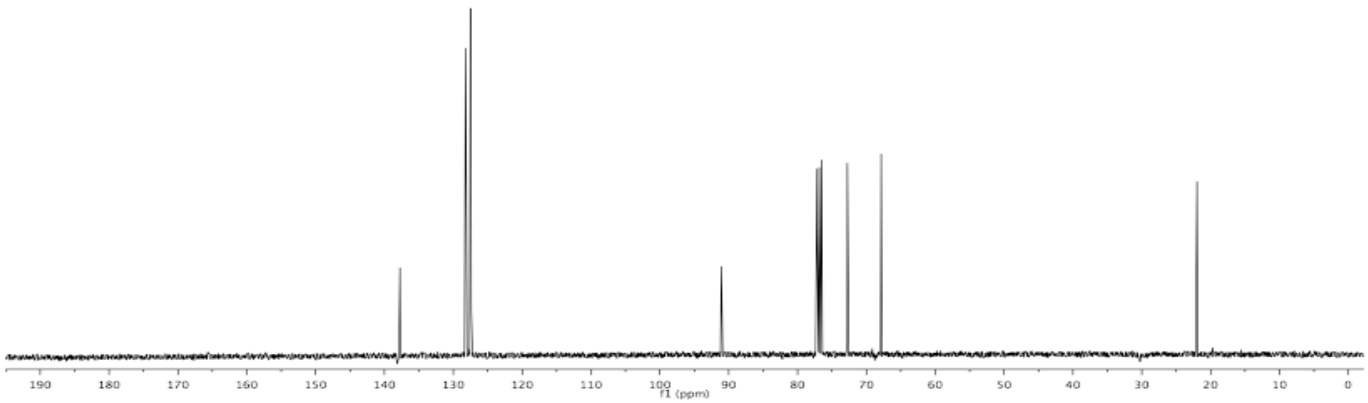


^{1}H (400 MHz, $CDCl_3$) and ^{13}C (100 MHz, $CDCl_3$)

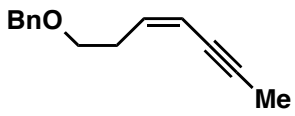


S5

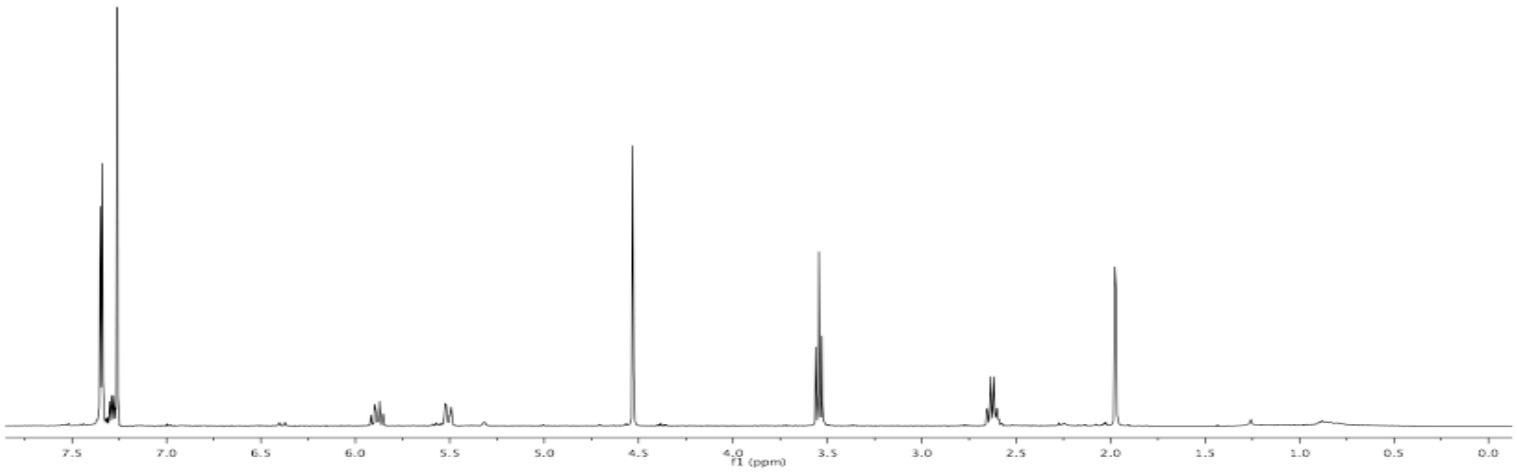


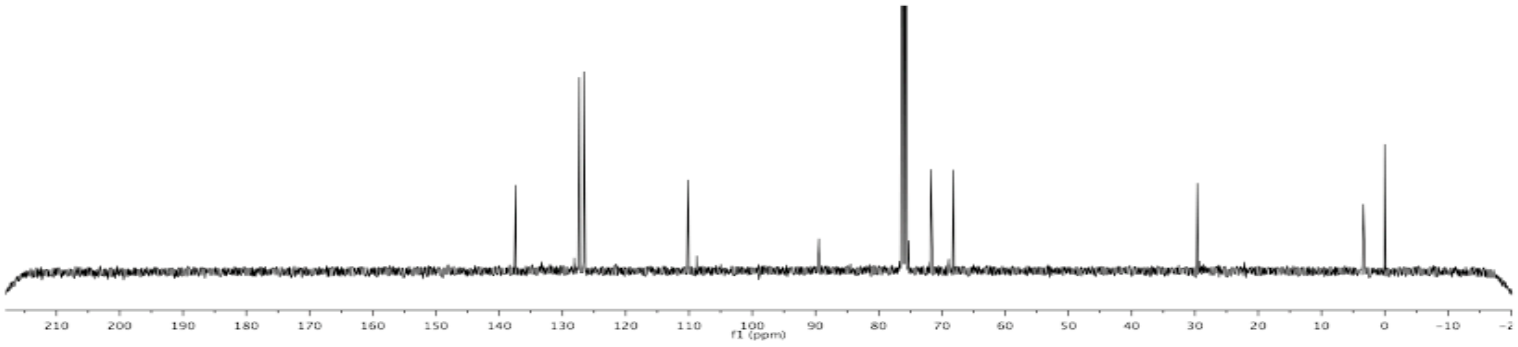


^{1}H (400 MHz, $CDCl_3$) and ^{13}C (100 MHz, $CDCl_3$)

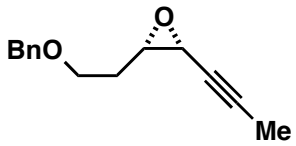


S6

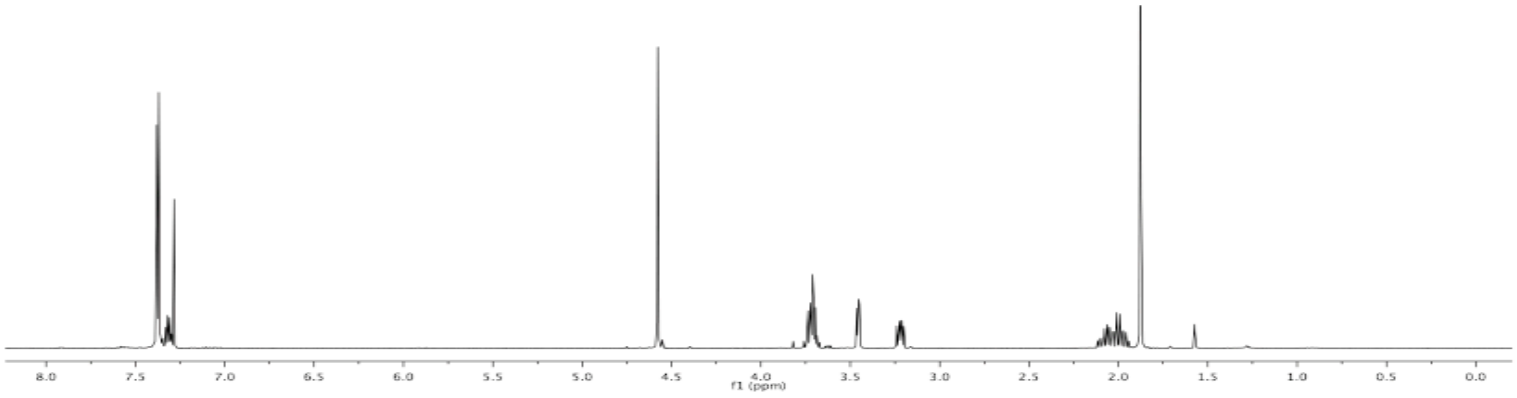


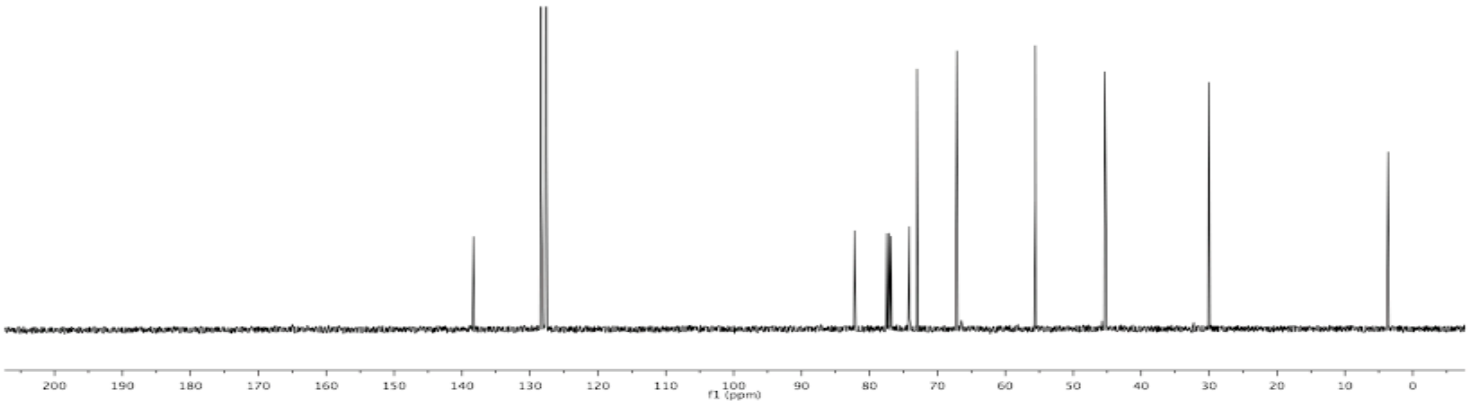


^{1}H (400 MHz, $CDCl_3$) and ^{13}C (100 MHz, $CDCl_3$)

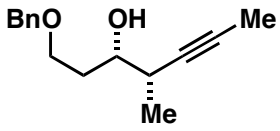


S8

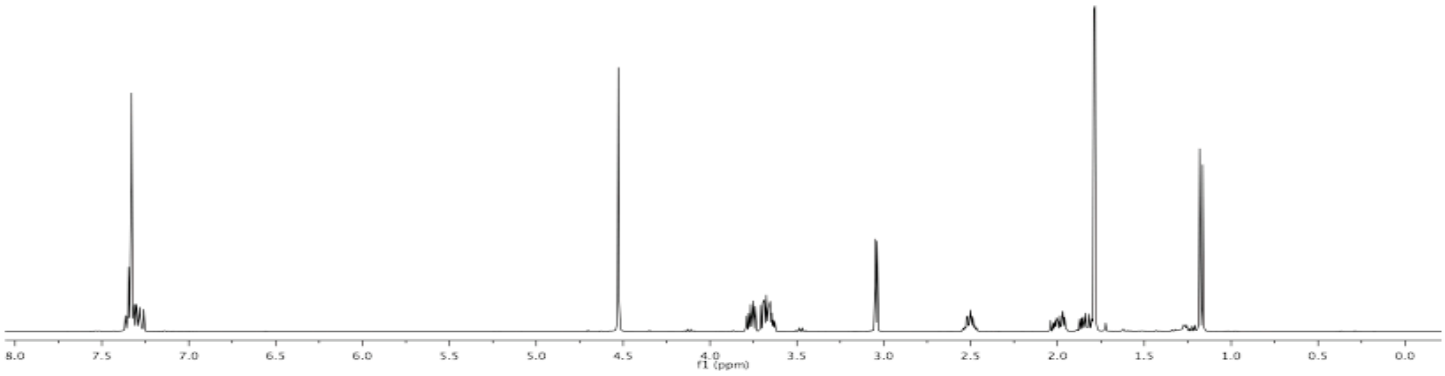


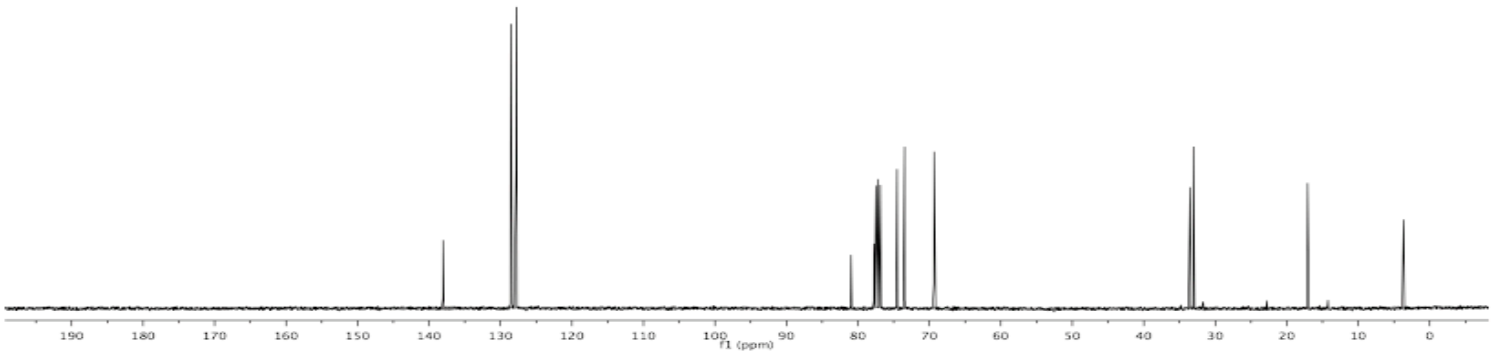


^{1}H (400 MHz, $CDCl_3$) and ^{13}C (100 MHz, $CDCl_3$)

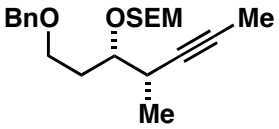


S9



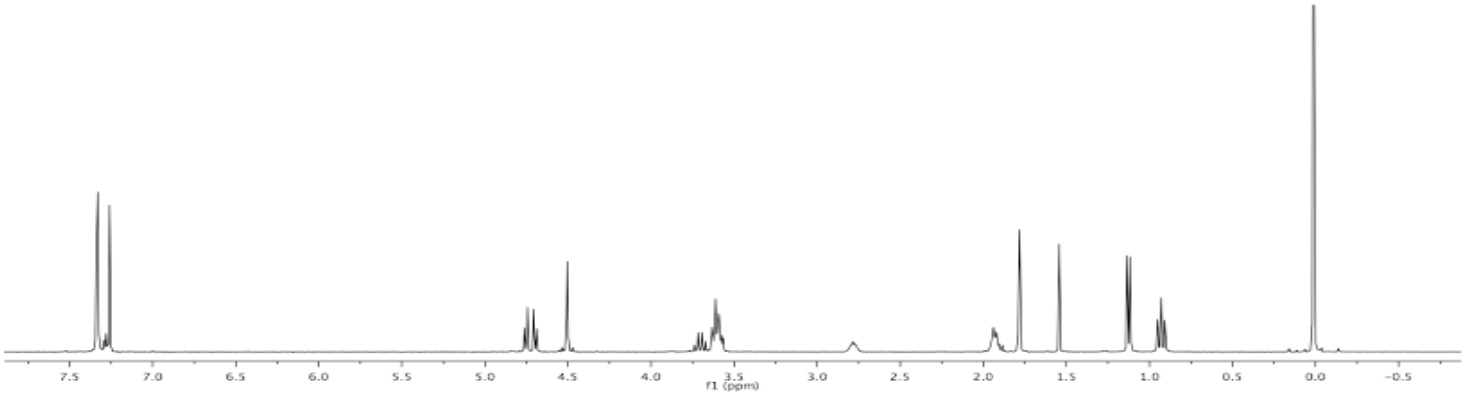


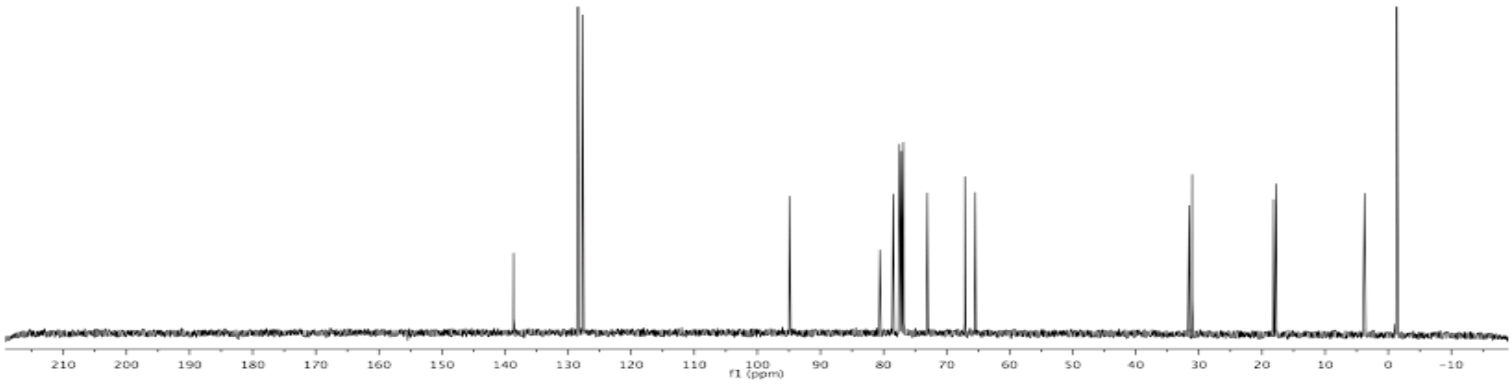
^{1}H (400 MHz, $CDCl_3$) and ^{13}C (100 MHz, $CDCl_3$)



15

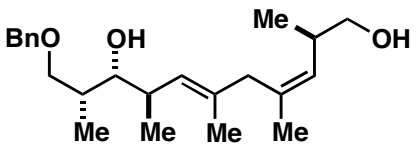
e.r. = 10:1



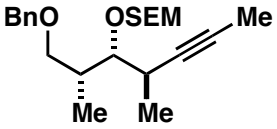


^{1}H (400 MHz, $CDCl_3$) and ^{13}C (100 MHz, $CDCl_3$)

generated from the isomeric mixture of alkynes

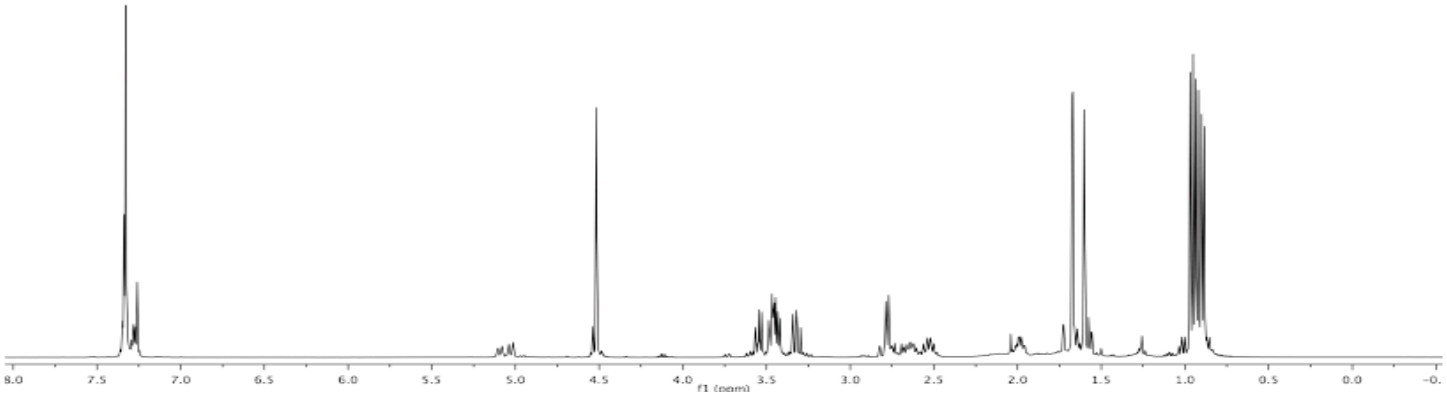


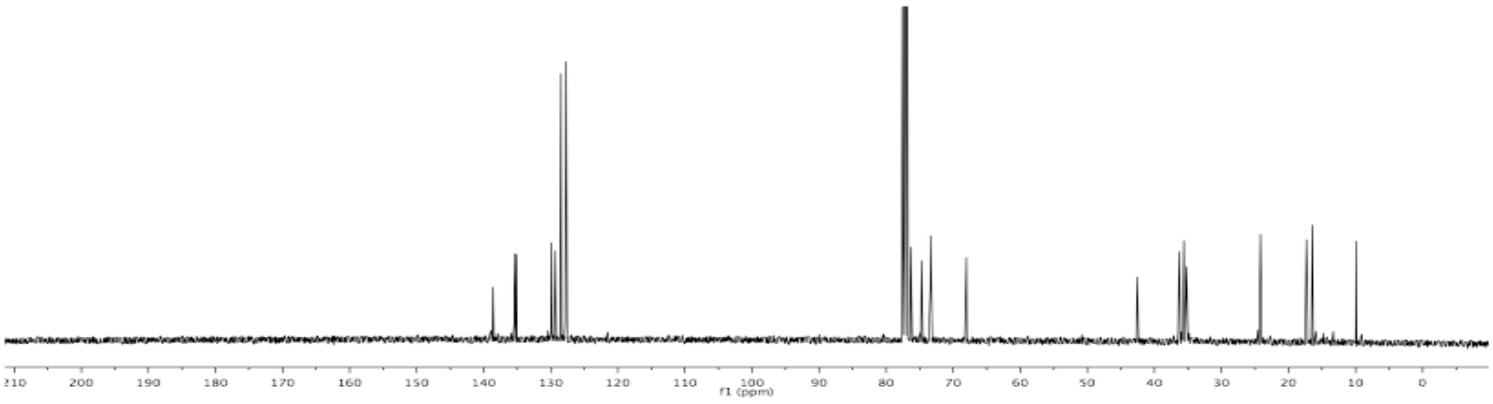
7



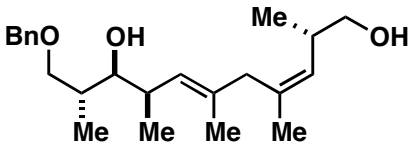
6

d.r. = 9:1



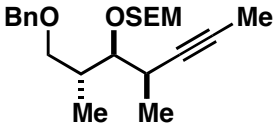


^{1}H (400 MHz, $CDCl_3$) and ^{13}C (100 MHz, $CDCl_3$)



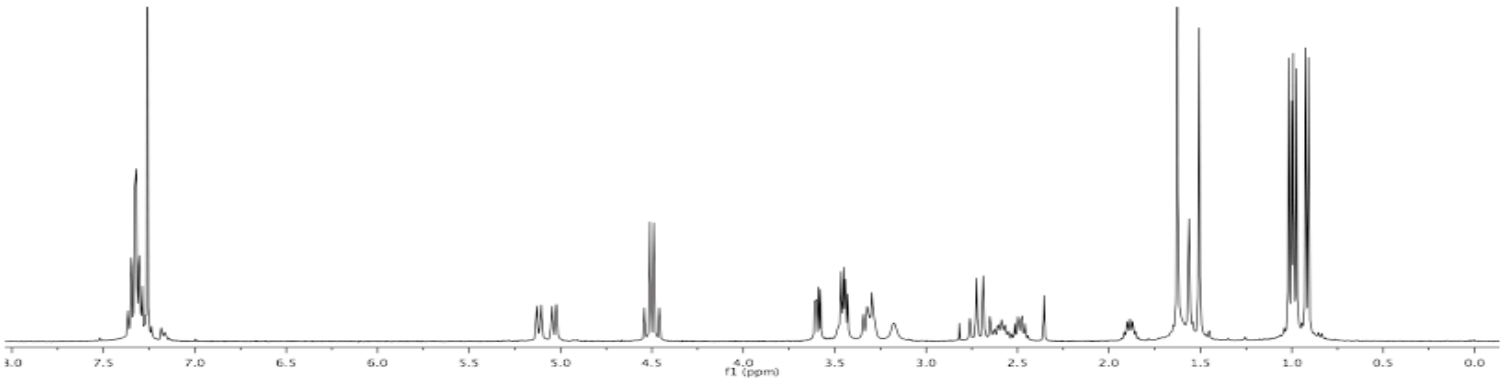
11

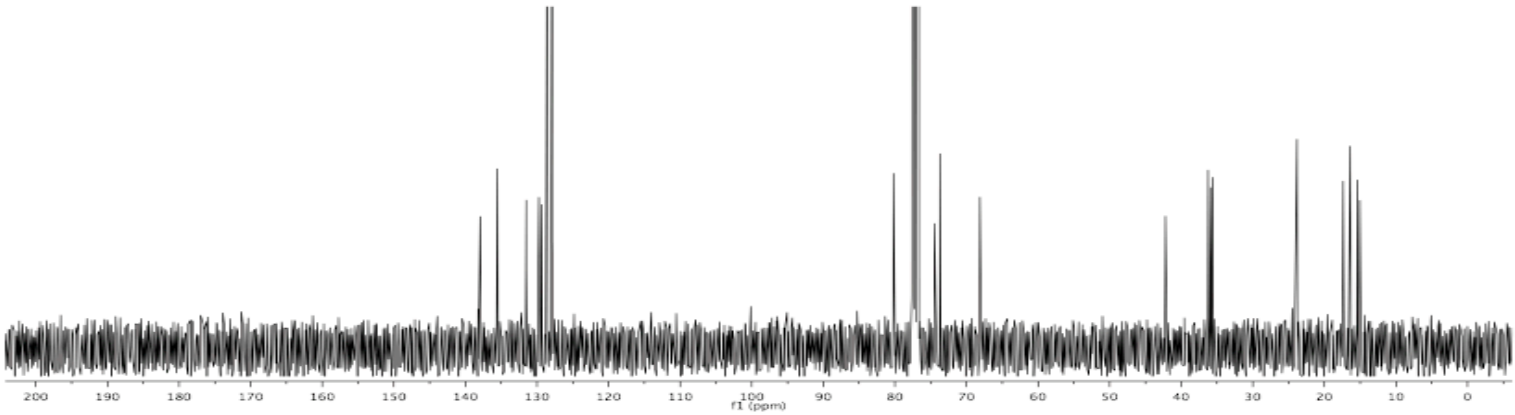
generated from the isomeric mixture of alkynes



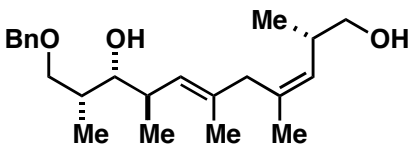
9

d.r. = 23:1



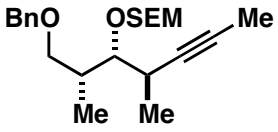


^{1}H (400 MHz, $CDCl_3$) and ^{13}C (100 MHz, $CDCl_3$)



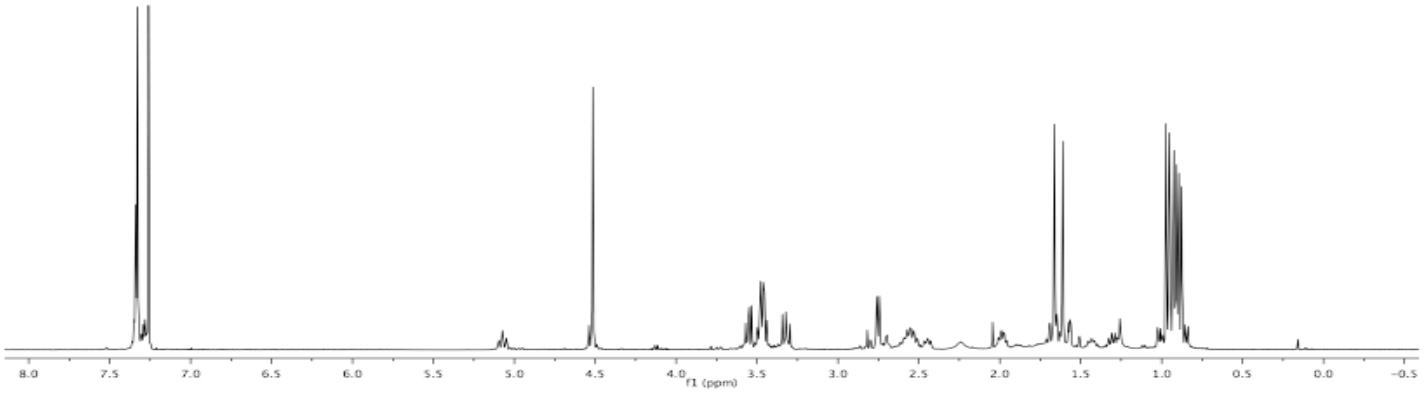
13

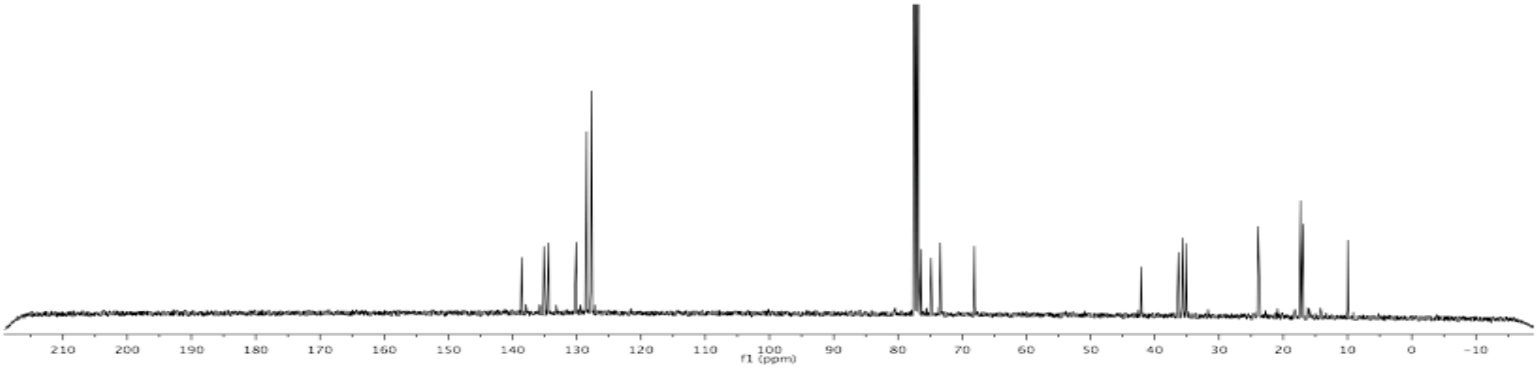
generated from the isomeric mixture of alkynes



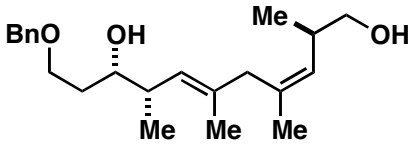
6

d.r. = 9:1



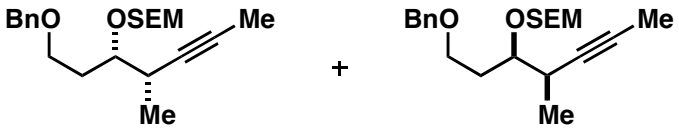


^{1}H (400 MHz, $CDCl_3$) and ^{13}C (100 MHz, $CDCl_3$)

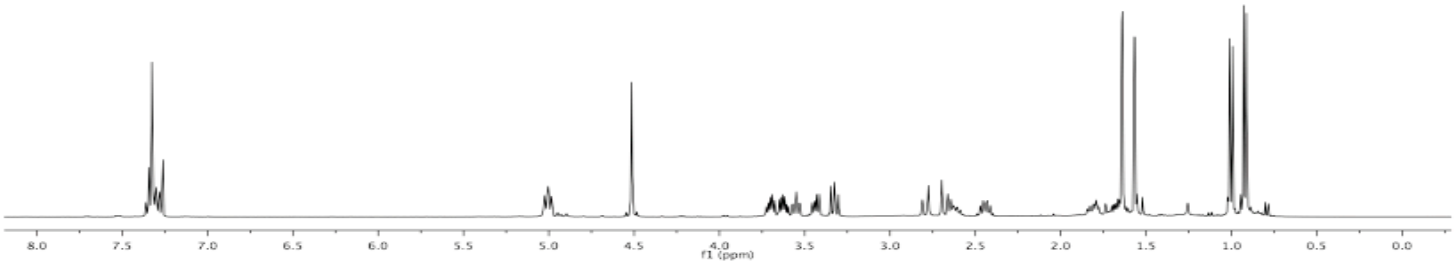


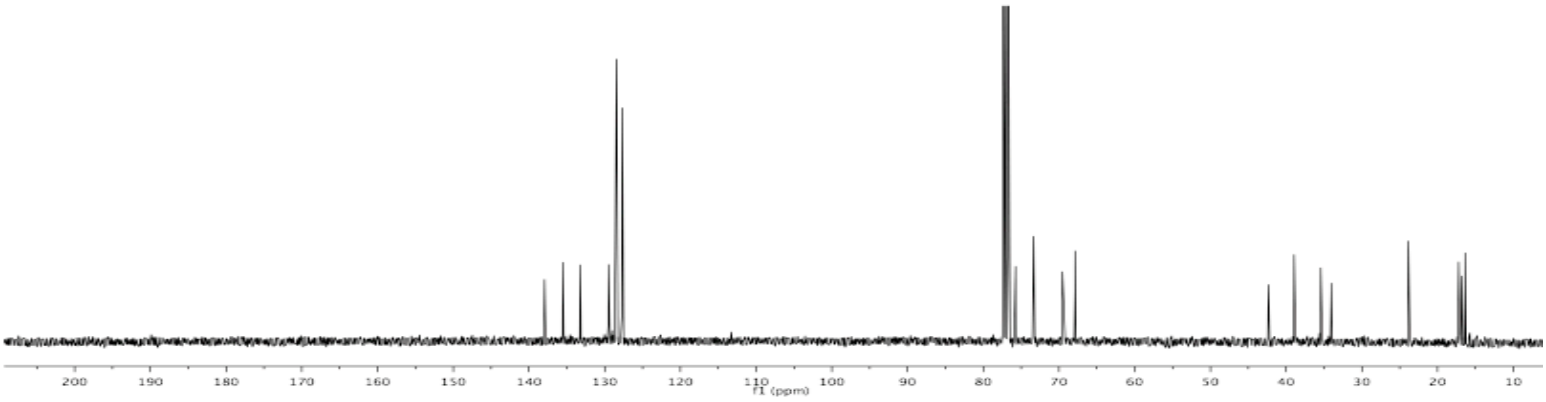
16

generated from the enantiomeric mixture of alkynes



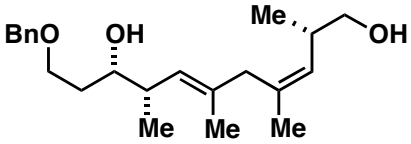
10 : 1



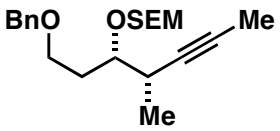


^{1}H (400 MHz, $CDCl_3$) and ^{13}C (100 MHz, $CDCl_3$)

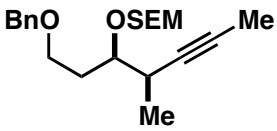
generated from the enantiomeric mixture of alkynes



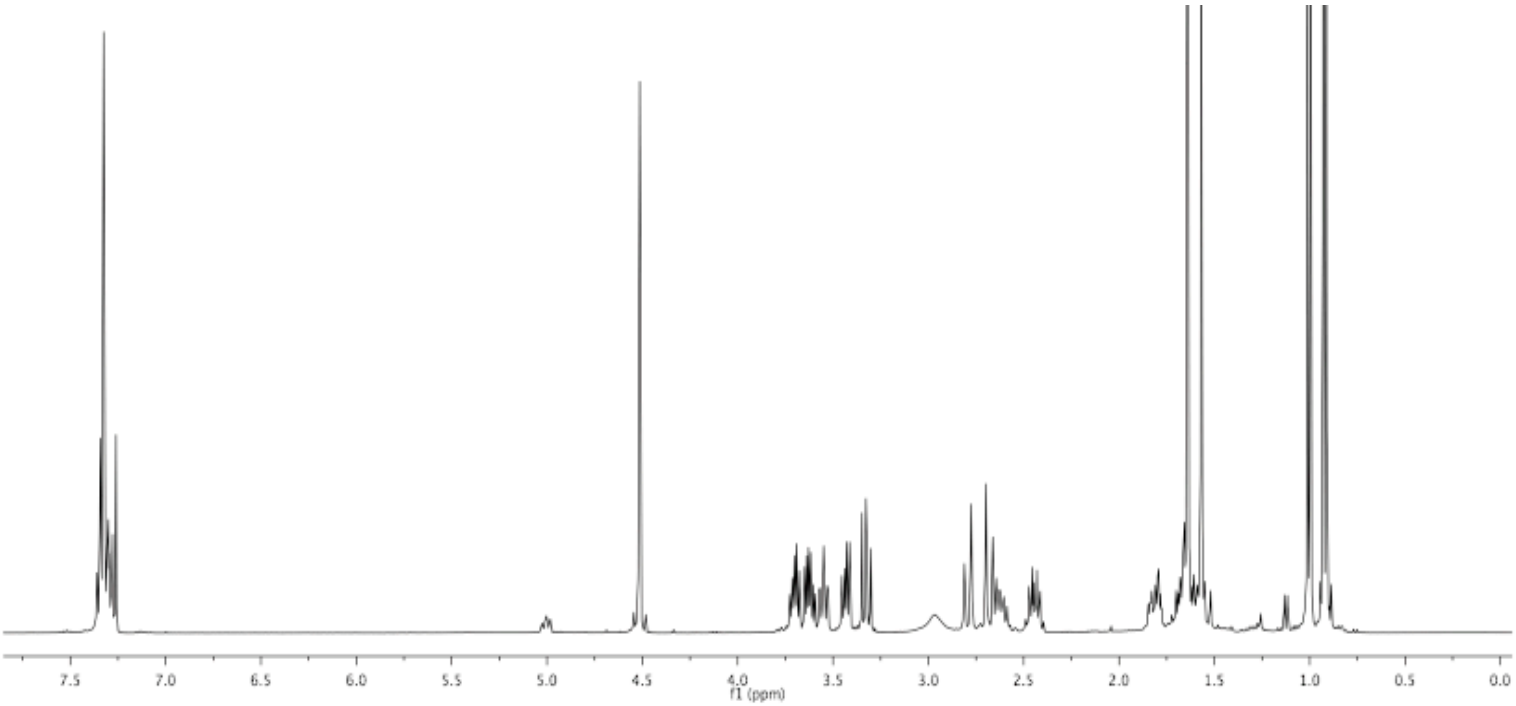
18

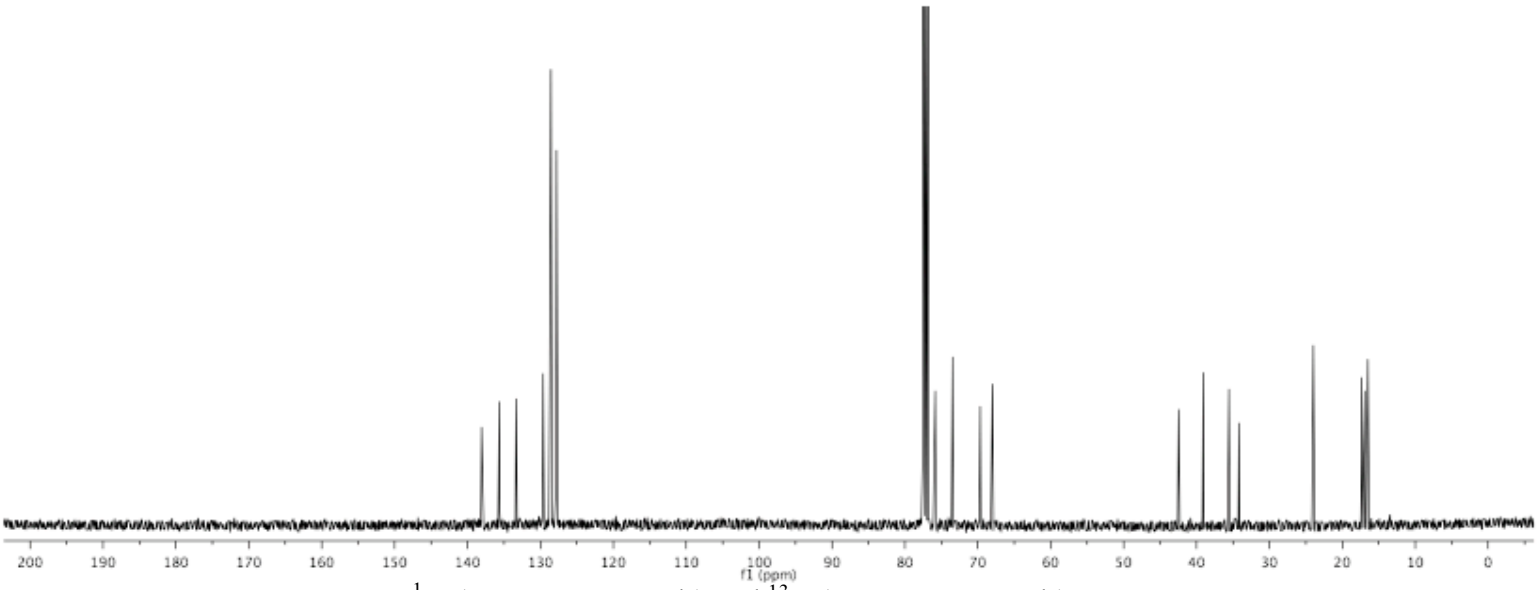


+

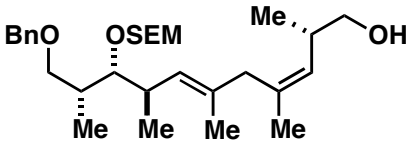


10 : 1



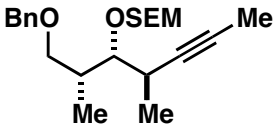


^{1}H (400 MHz, $CDCl_3$) and ^{13}C (100 MHz, $CDCl_3$)



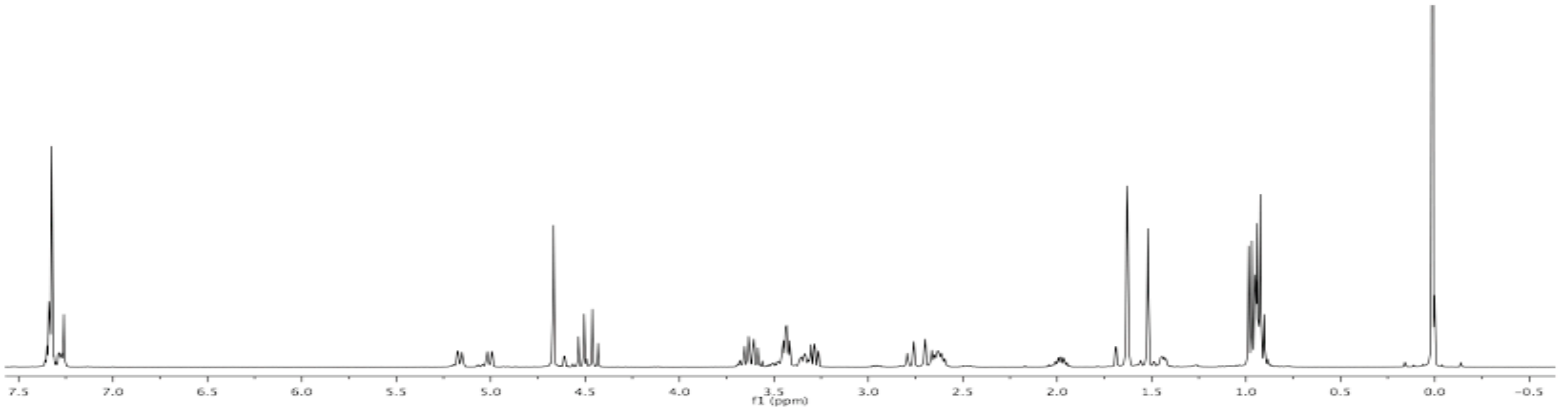
20

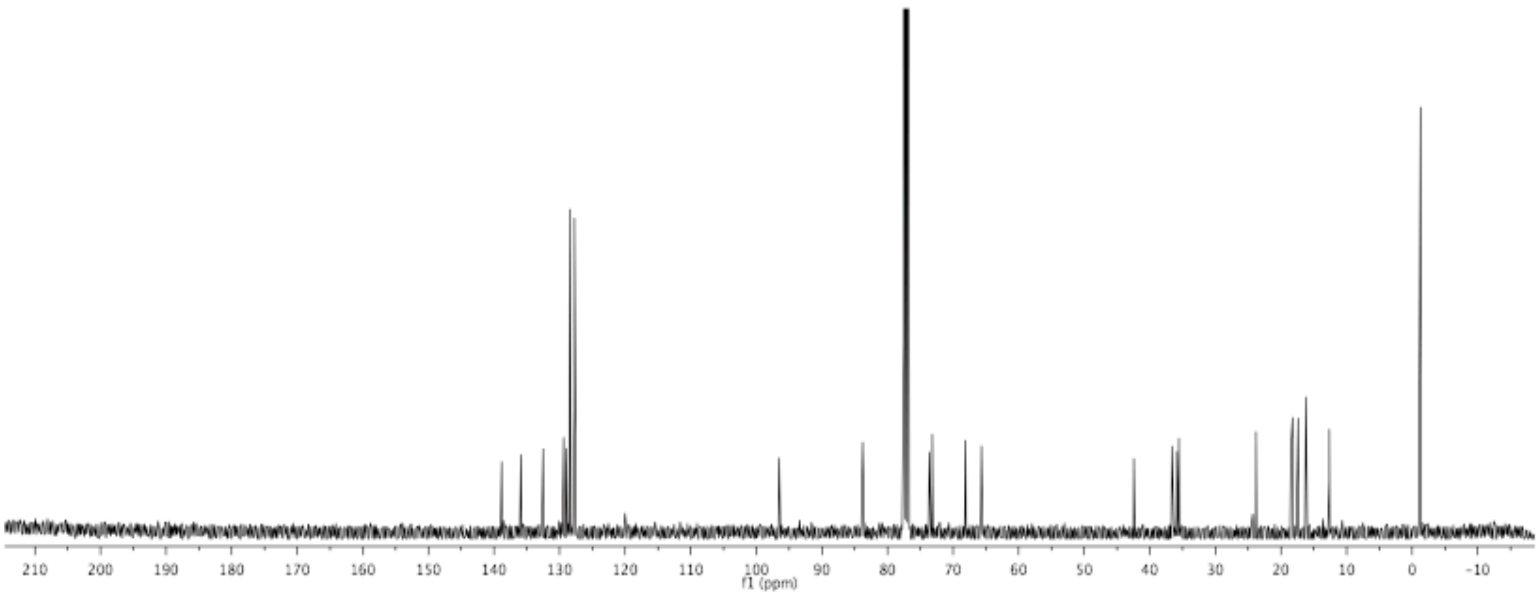
generated from the isomeric mixture of alkynes



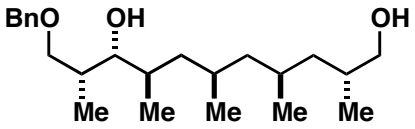
6

d.r. = 9:1



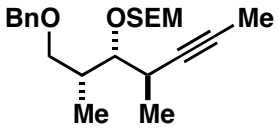


^{1}H (400 MHz, $CDCl_3$) and ^{13}C (100 MHz, $CDCl_3$)



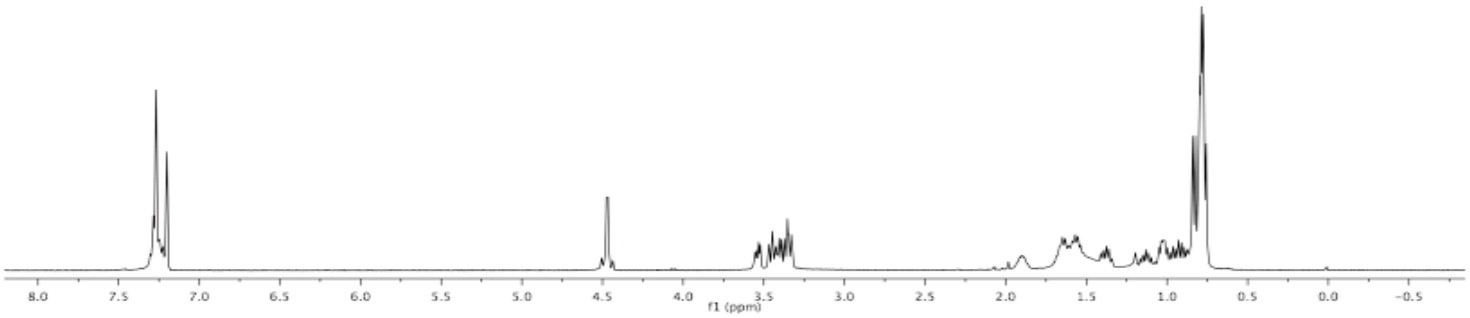
8

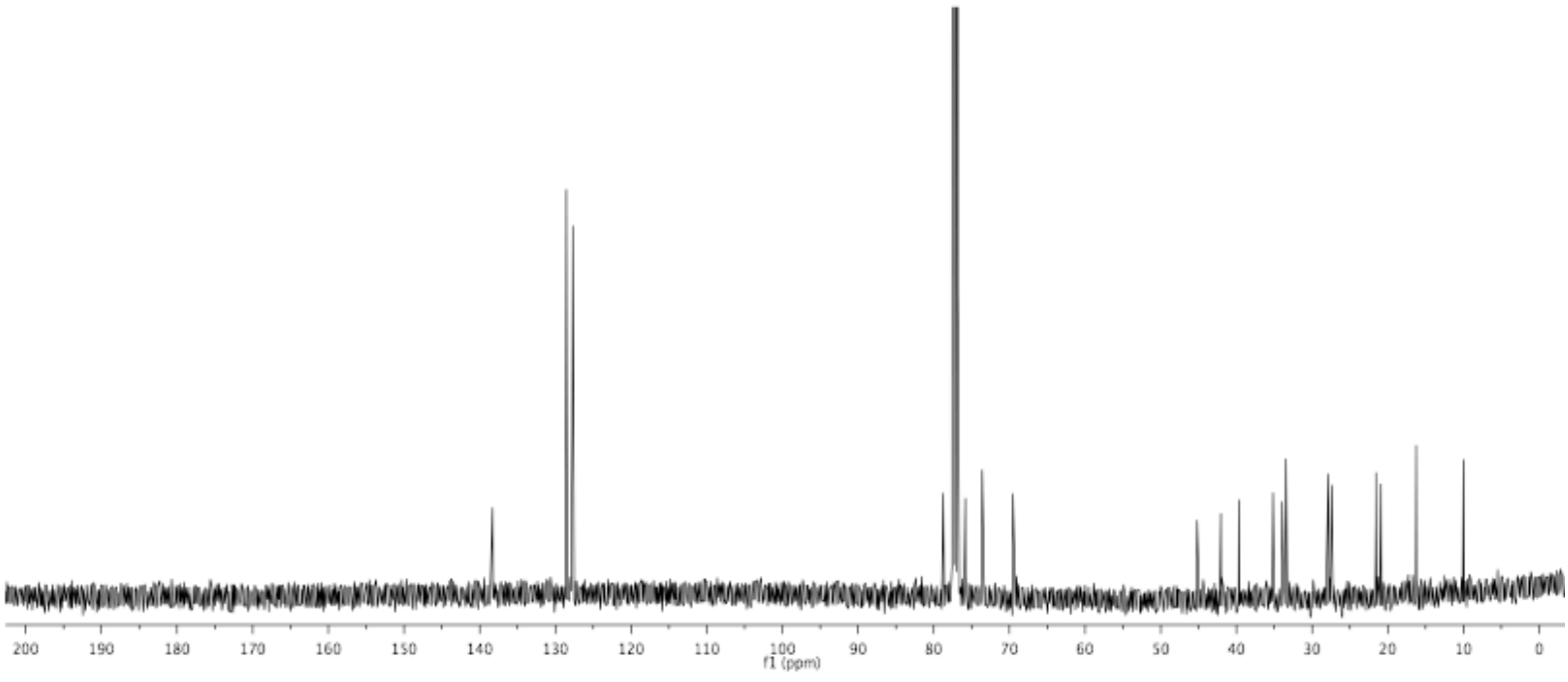
generated from the isomeric mixture of alkynes



6

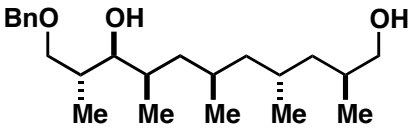
d.r. = 9:1



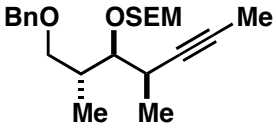


^{1}H (400 MHz, $CDCl_3$) and ^{13}C (100 MHz, $CDCl_3$)

generated from the isomeric mixture of alkynes

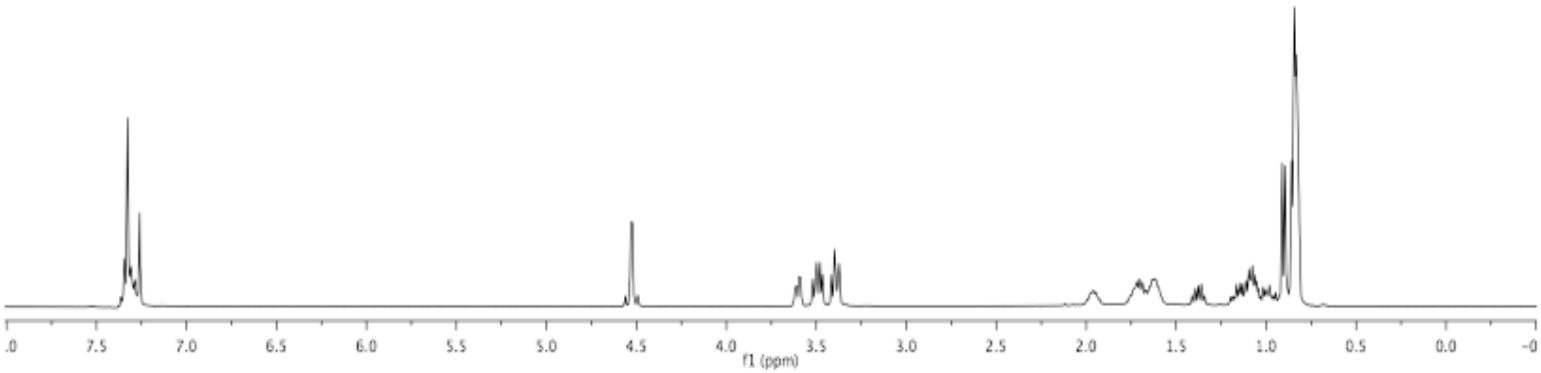


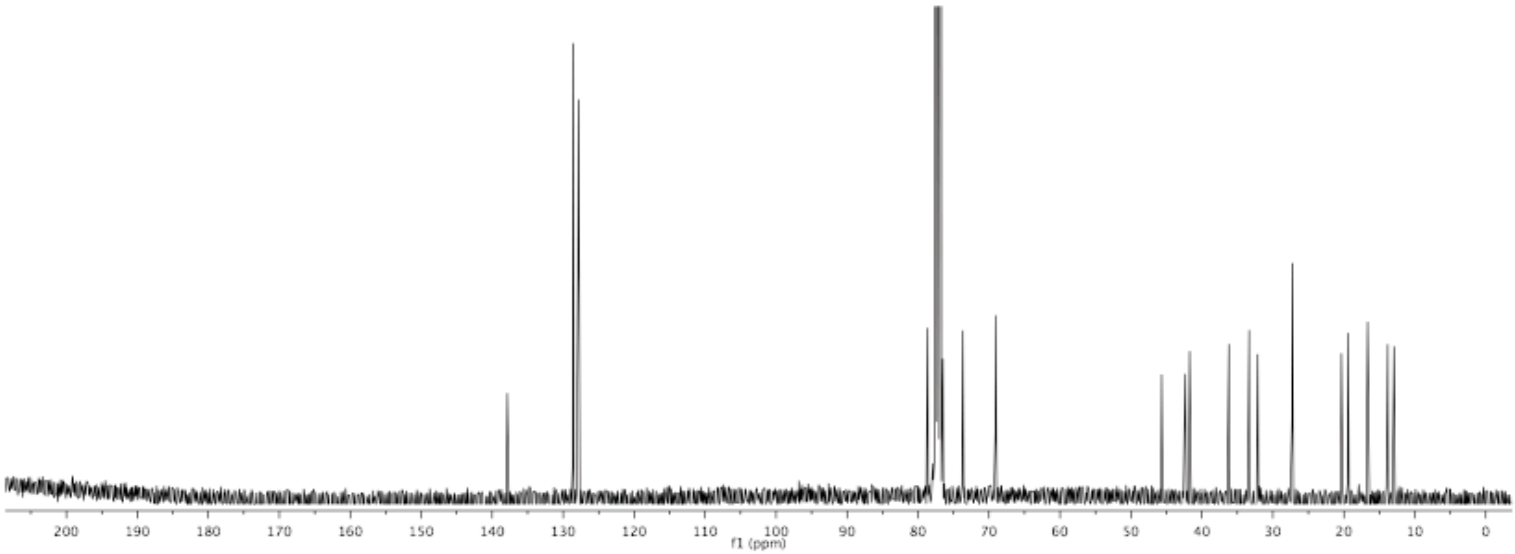
12
(*syn,anti,anti)*



9

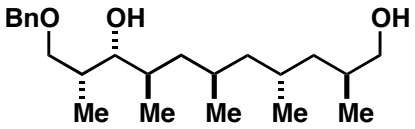
d.r. = 23:1



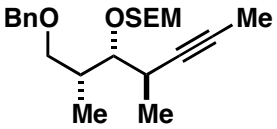


^{1}H (400 MHz, $CDCl_3$) and ^{13}C (100 MHz, $CDCl_3$)

generated from the isomeric mixture of alkynes

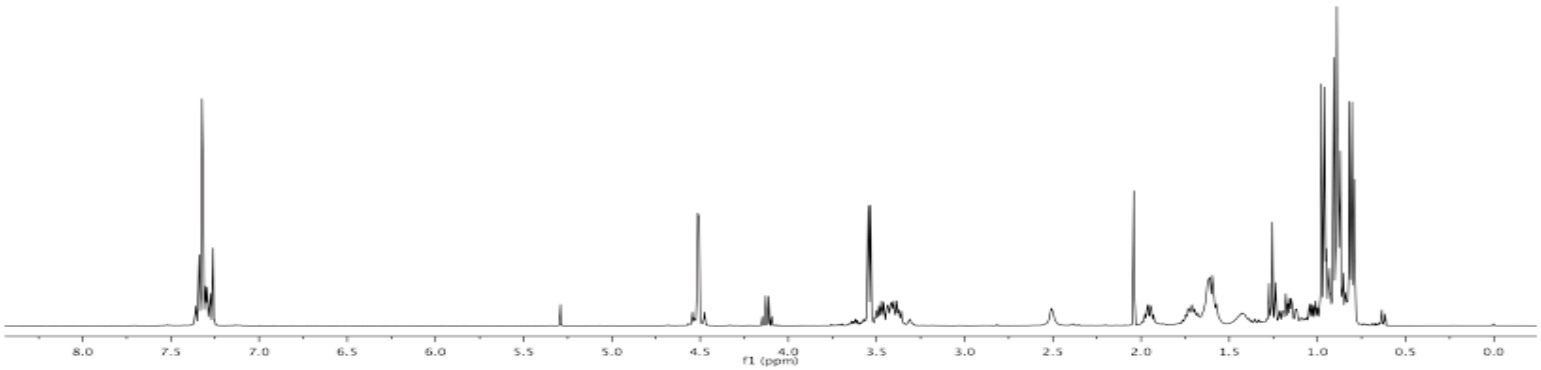


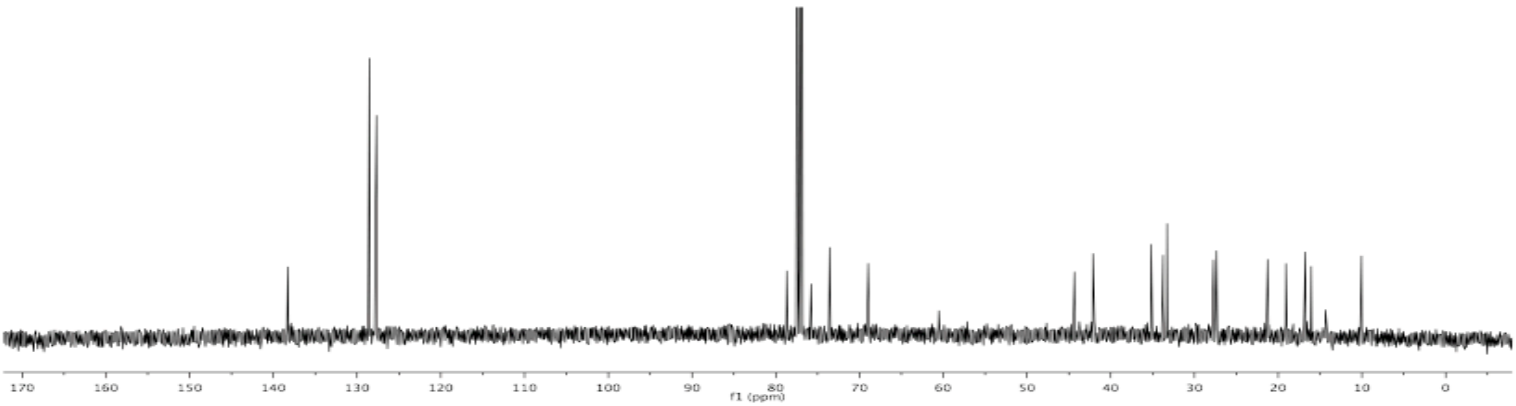
14
(*syn,anti,anti)*



6

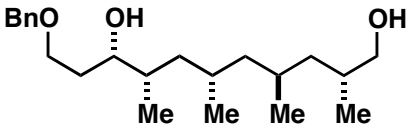
d.r. = 9:1



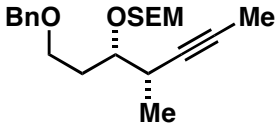


^{1}H (400 MHz, $CDCl_3$) (contains CH_2Cl_2 and EtOAc) and ^{13}C (100 MHz, $CDCl_3$) (contains EtOAc)

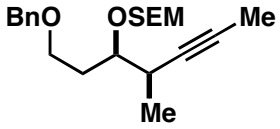
generated from the enantiomeric mixture of alkynes



17
(*syn,anti,anti)*



+



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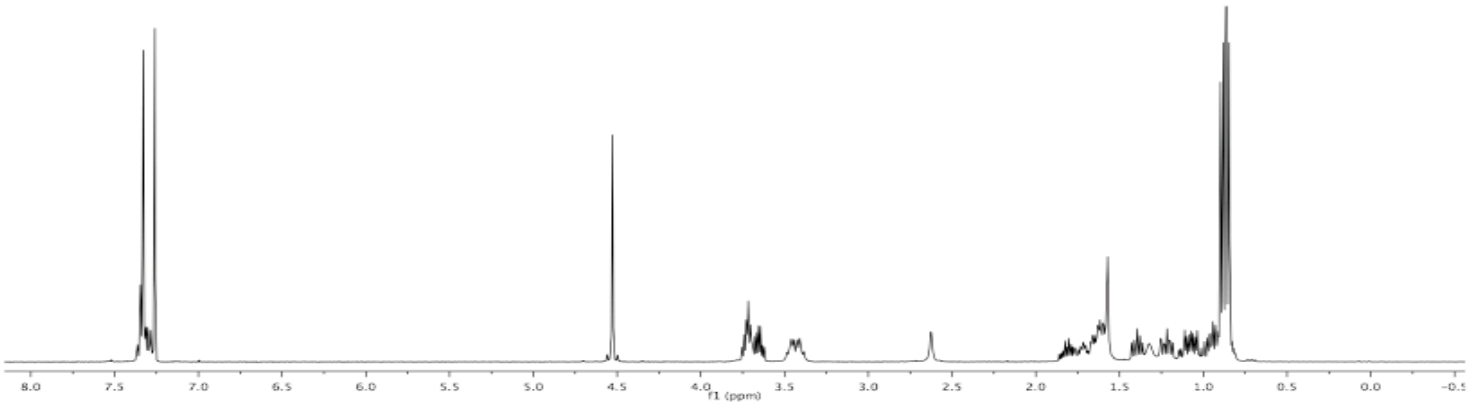

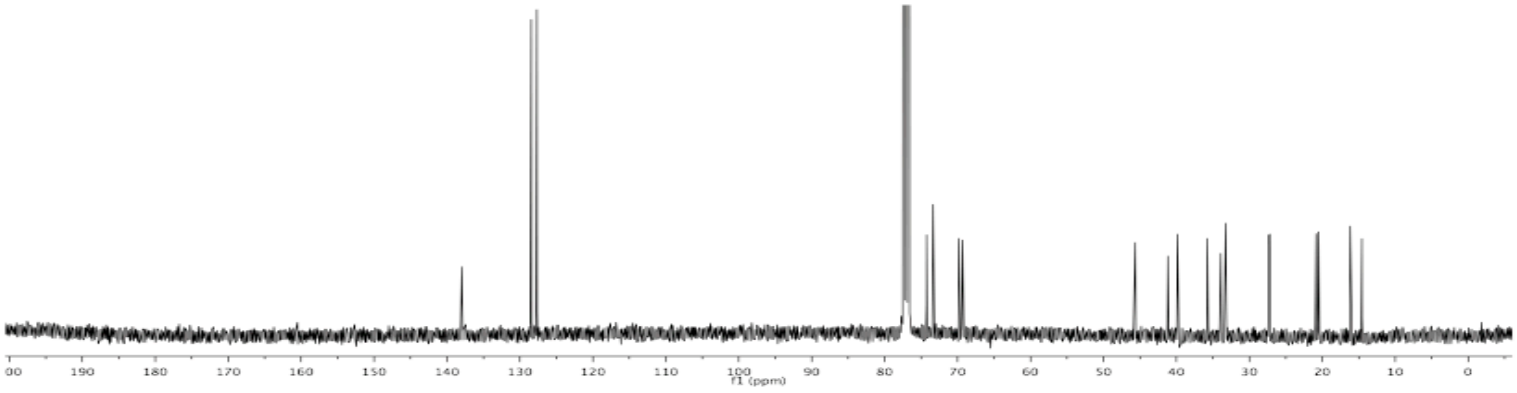

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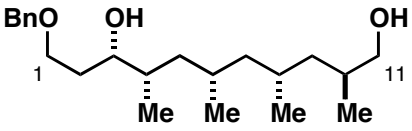
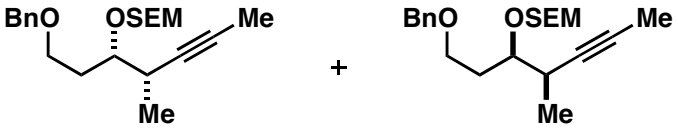


19
(*syn,syn,anti)*
C1-C11 of borrelidin

generated from the enantiomeric mixture of alkynes



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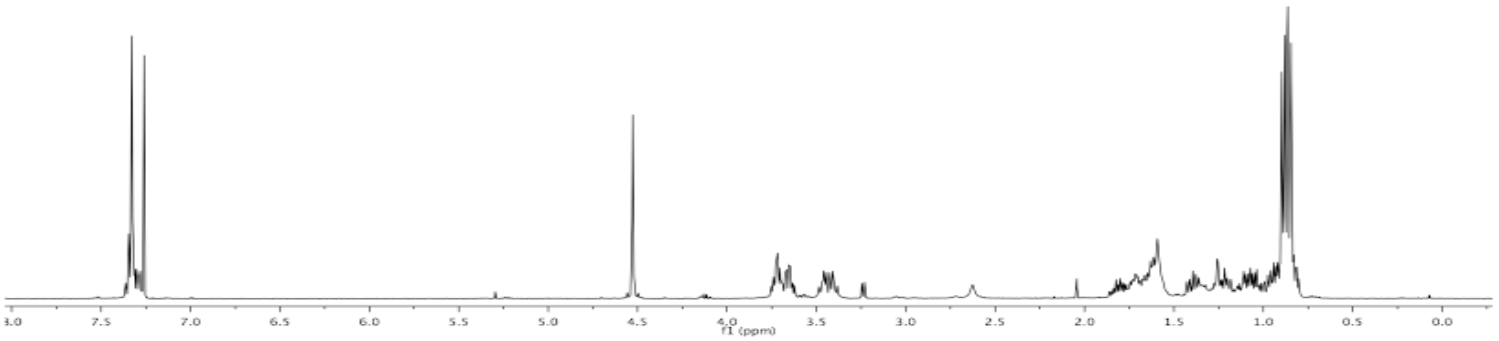
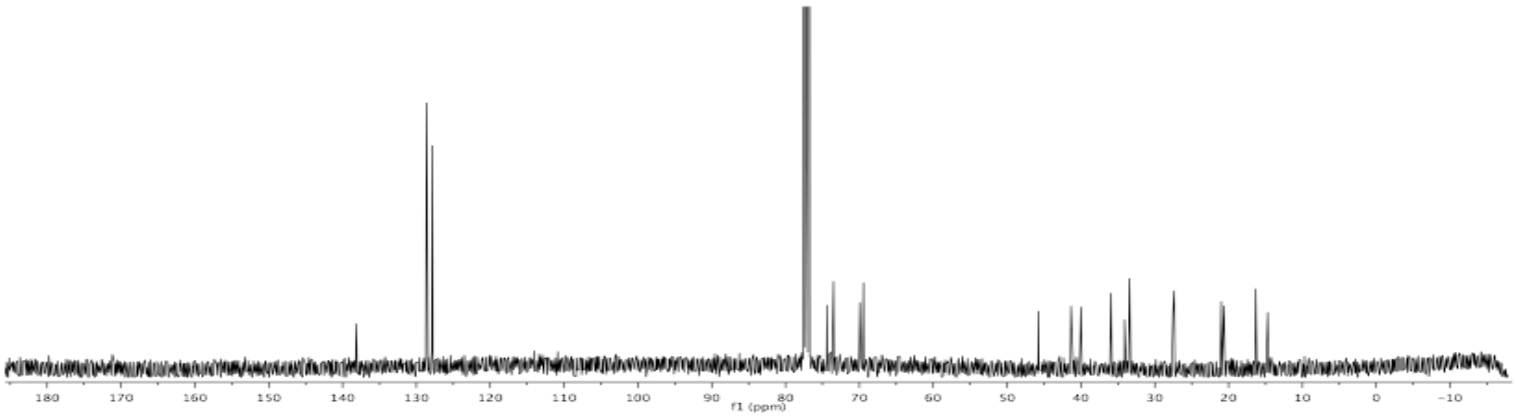
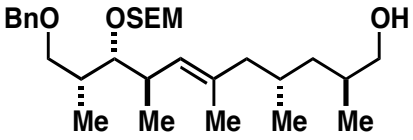


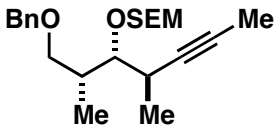


^{1}H (400 MHz, $CDCl_3$) and ^{13}C (100 MHz, $CDCl_3$)



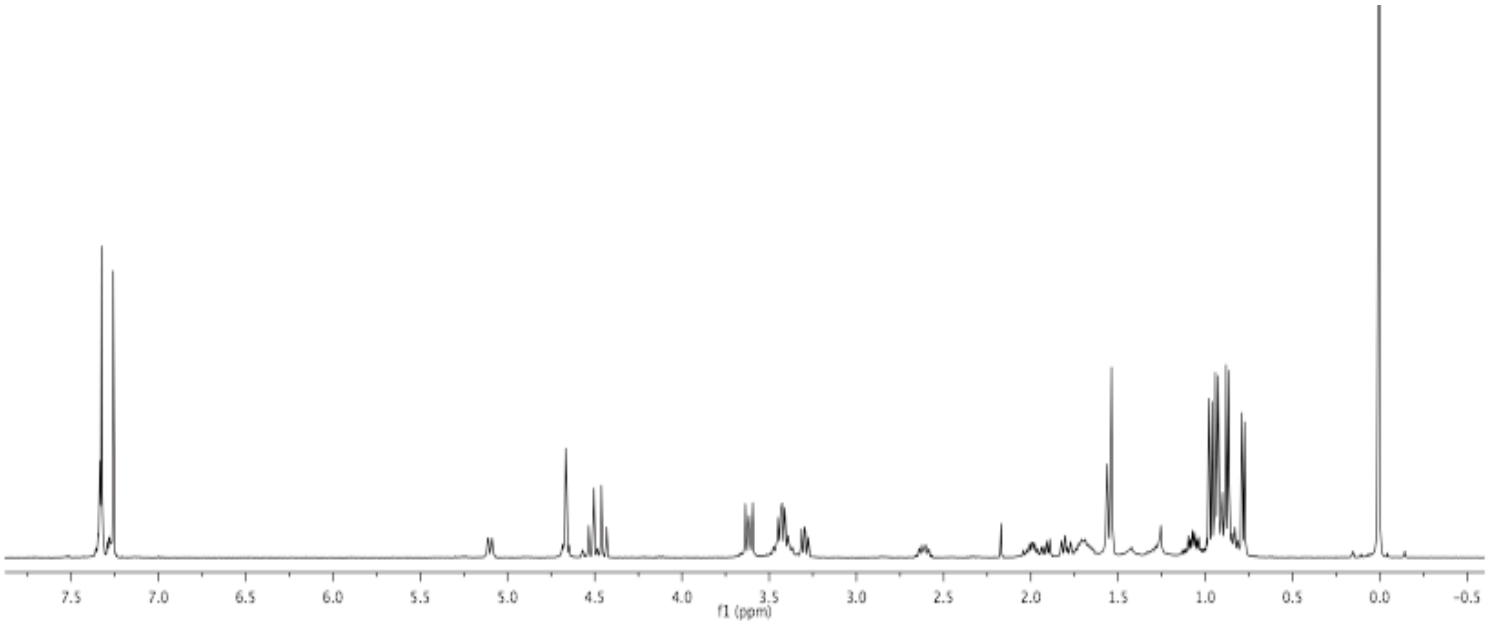
21

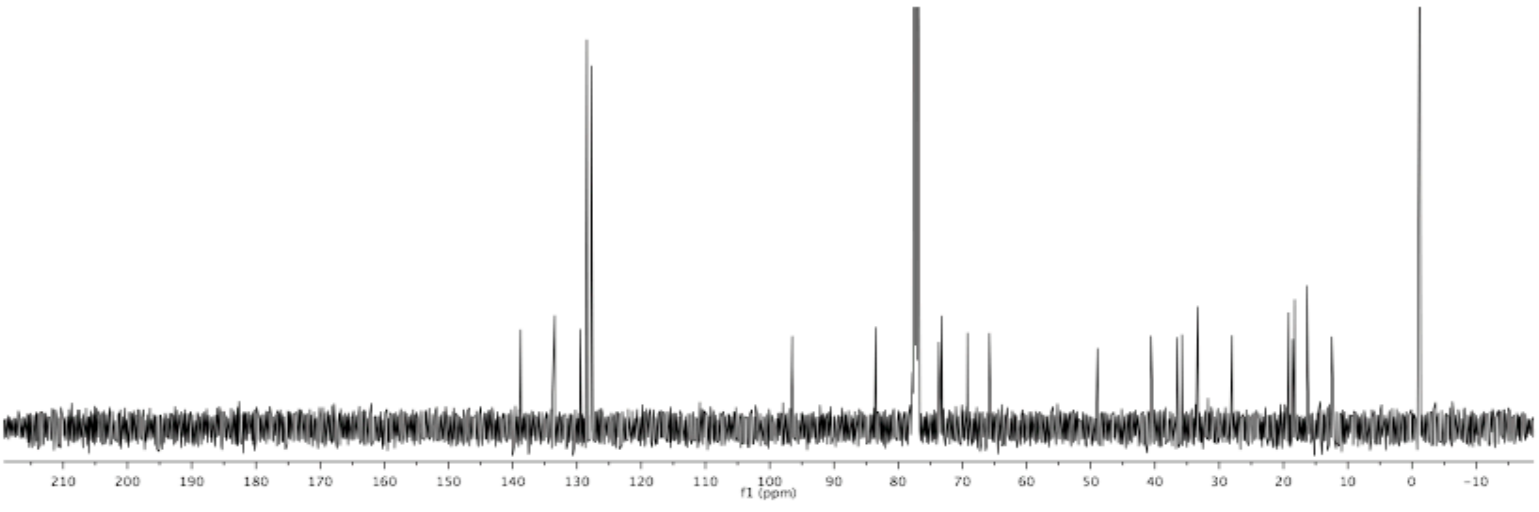
generated from the isomeric mixture of alkynes



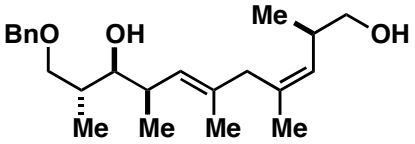
6

d.r. = 9:1



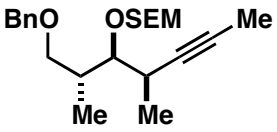


^{1}H (400 MHz, $CDCl_3$) and ^{13}C (100 MHz, $CDCl_3$)



S10

generated from the isomeric mixture of alkynes



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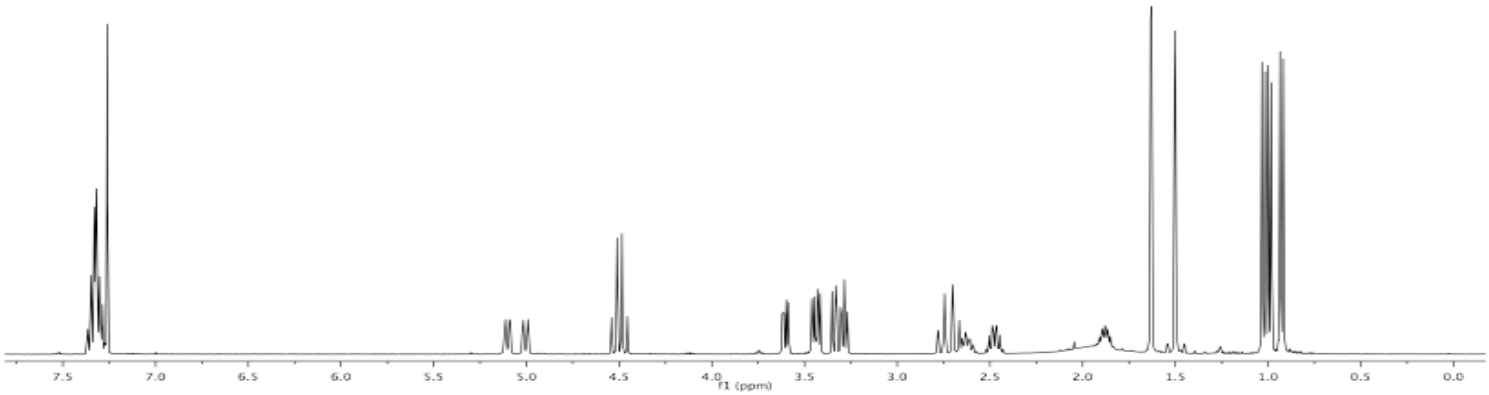
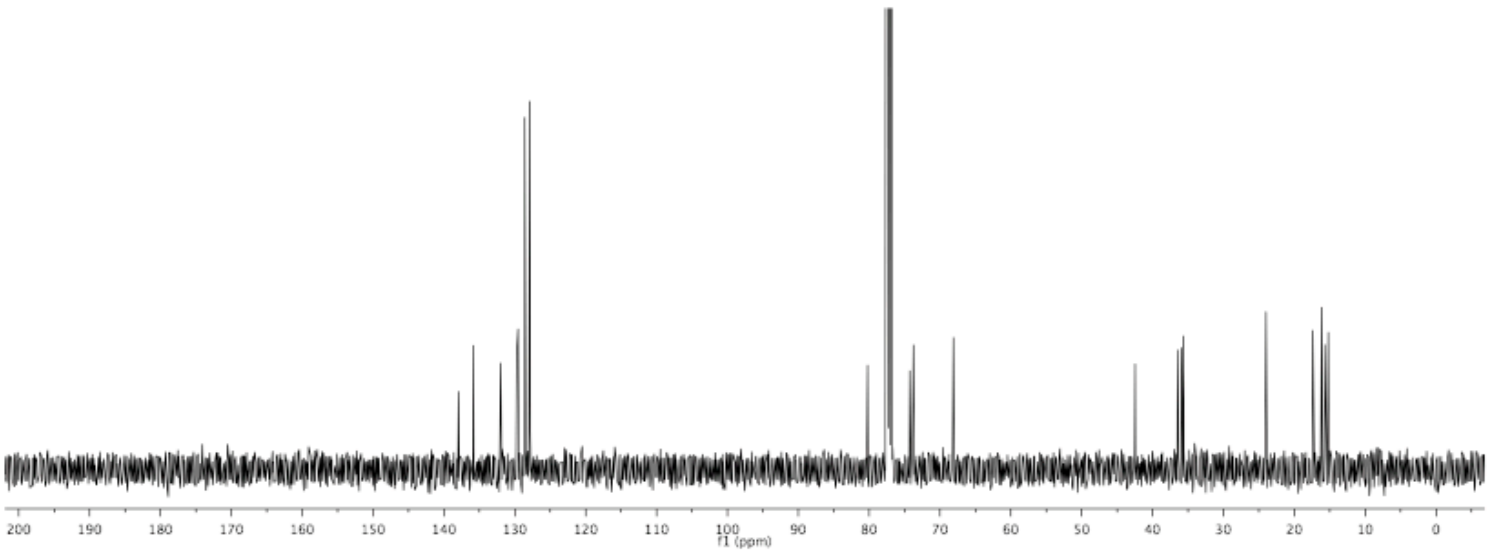
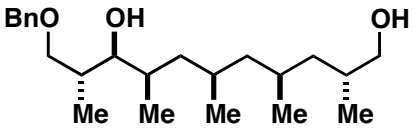


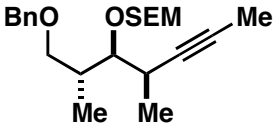


^{1}H (400 MHz, $CDCl_3$) and ^{13}C (100 MHz, $CDCl_3$)



22

generated from the isomeric mixture of alkynes



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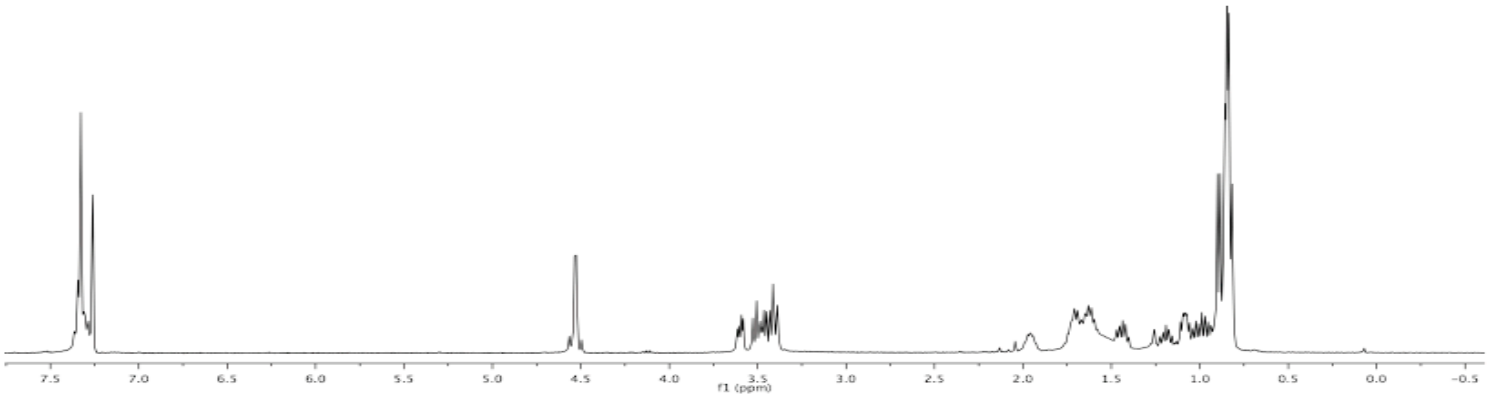
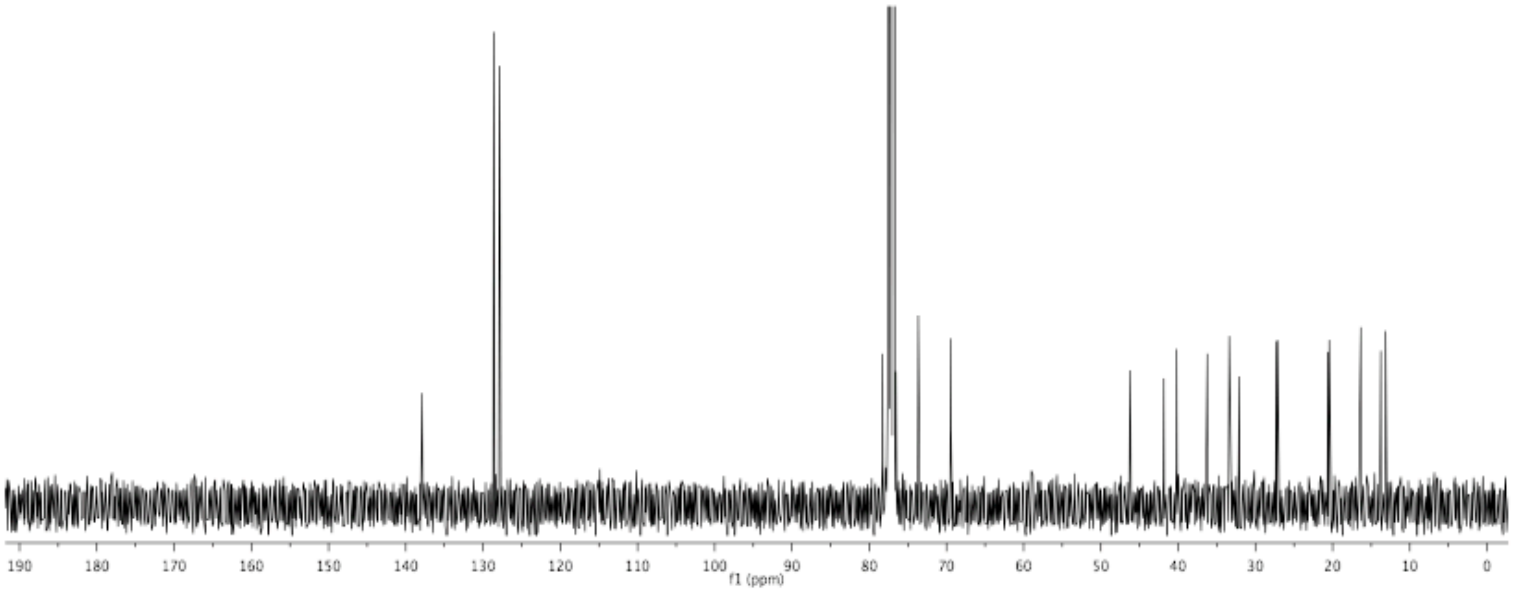
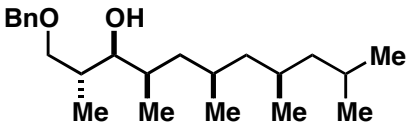
d.r. = 23:1



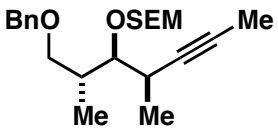


^{1}H (400 MHz, $CDCl_3$) and ^{13}C (100 MHz, $CDCl_3$)



S12

generated from the isomeric mixture of alkynes



9

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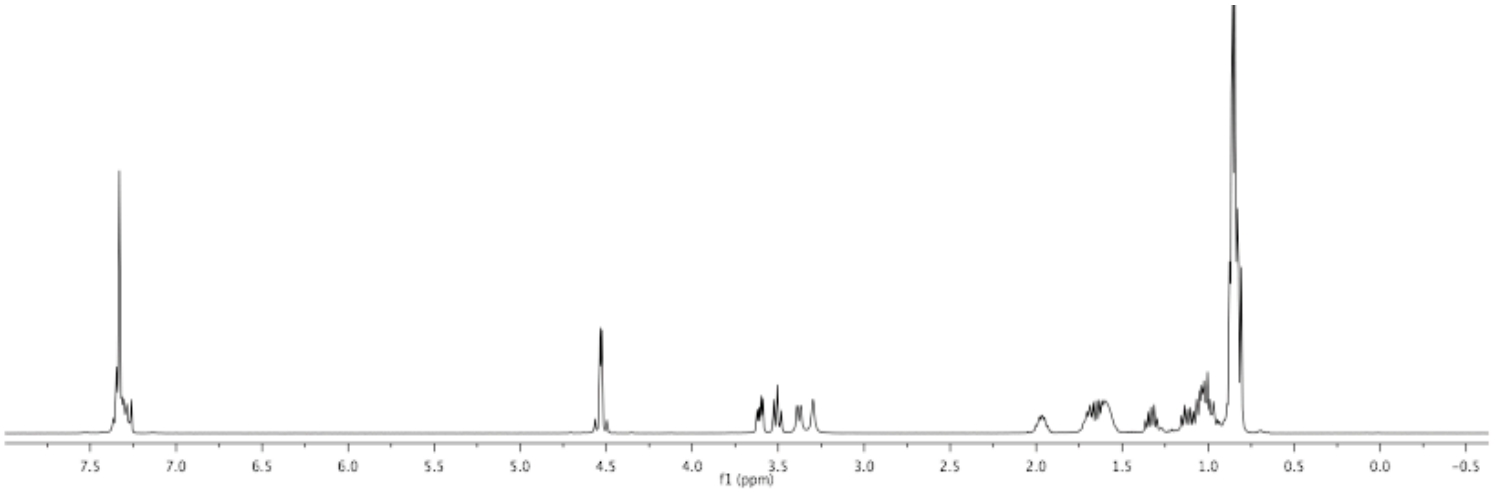
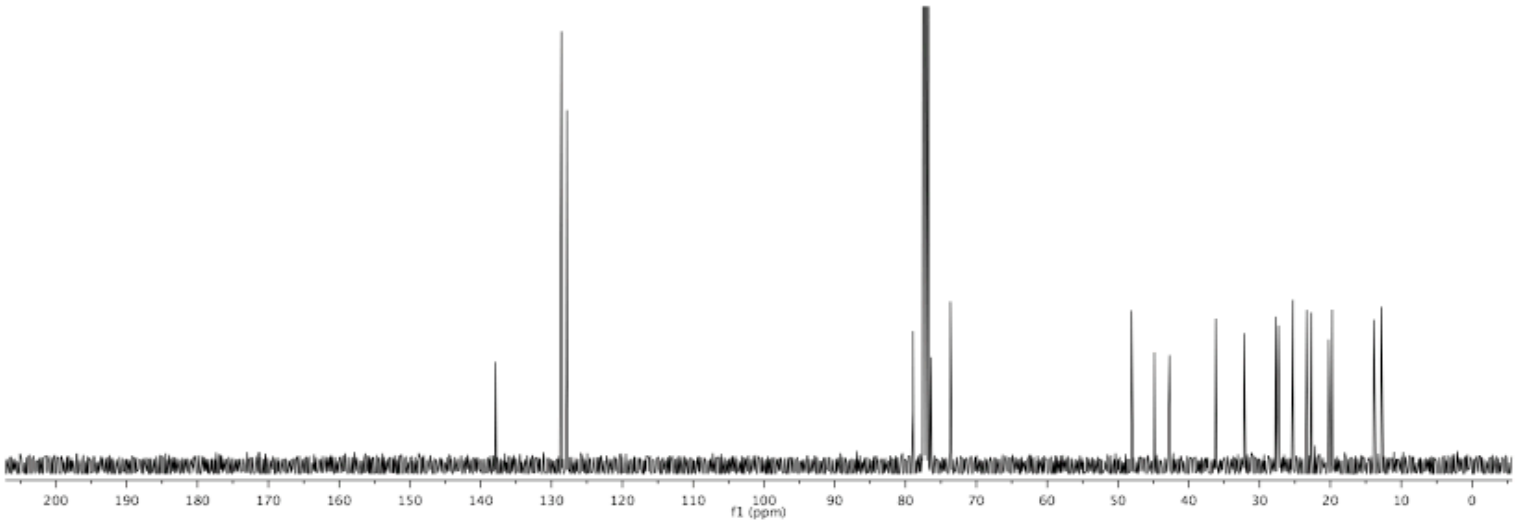
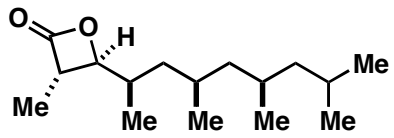
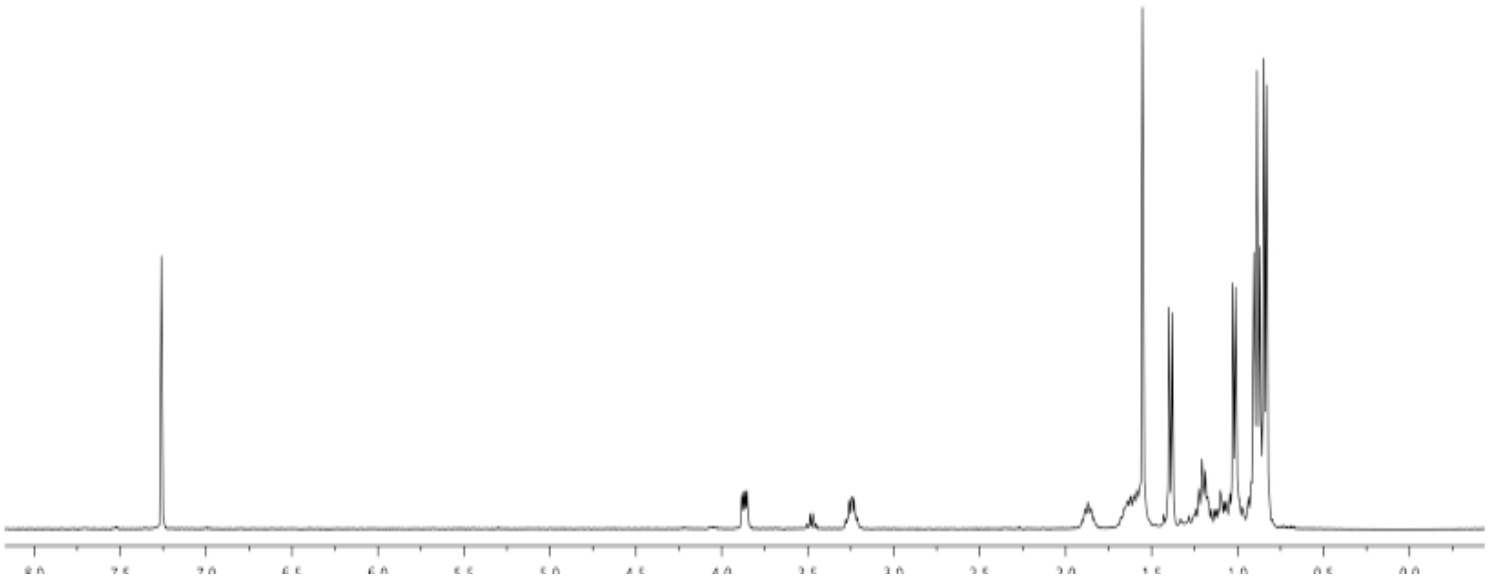


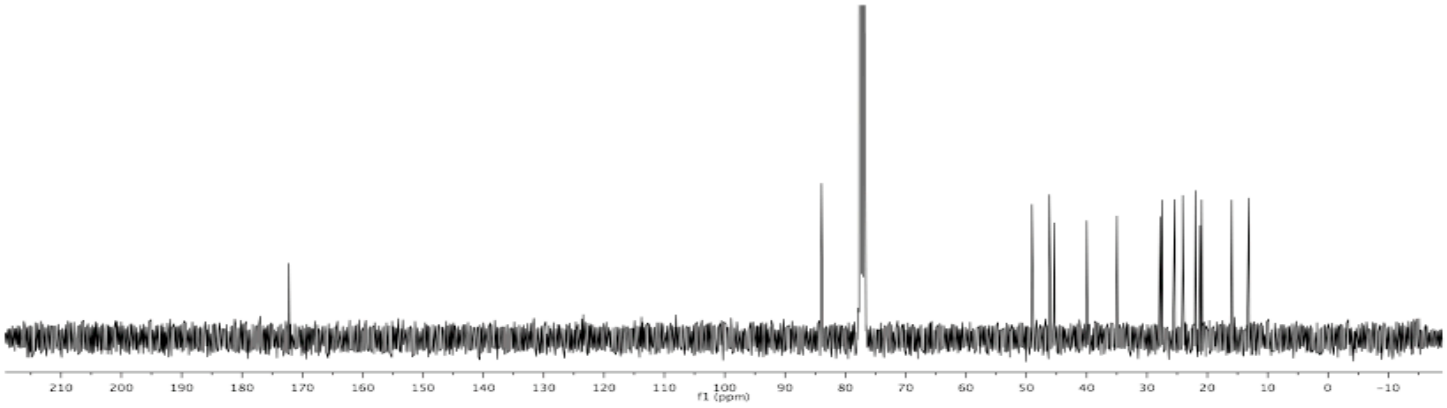


^{1}H (400 MHz, $CDCl_3$) and ^{13}C (100 MHz, $CDCl_3$)



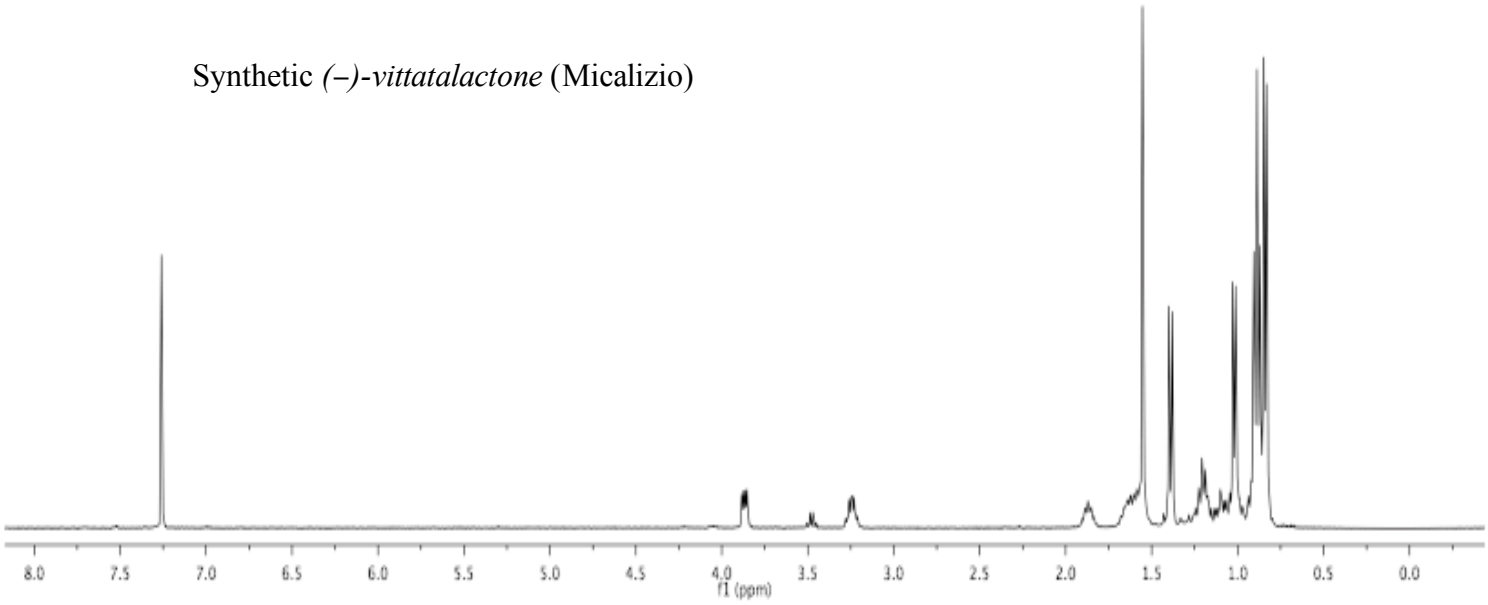
(–)-vittatalactone



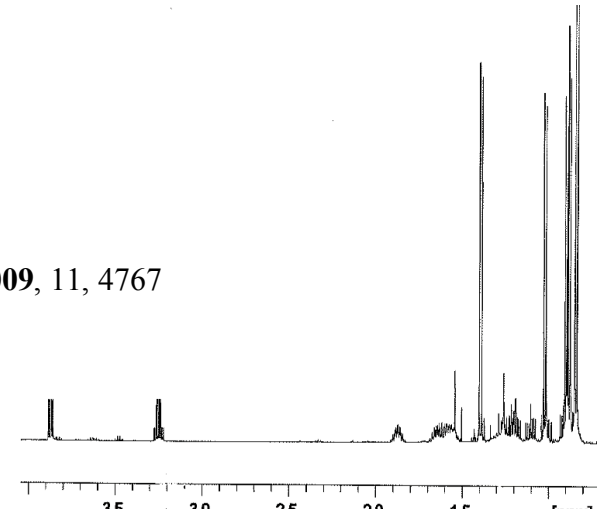


^{1}H (400 MHz, $CDCl_3$, EtOAc trace) and ^{13}C (100 MHz, $CDCl_3$)

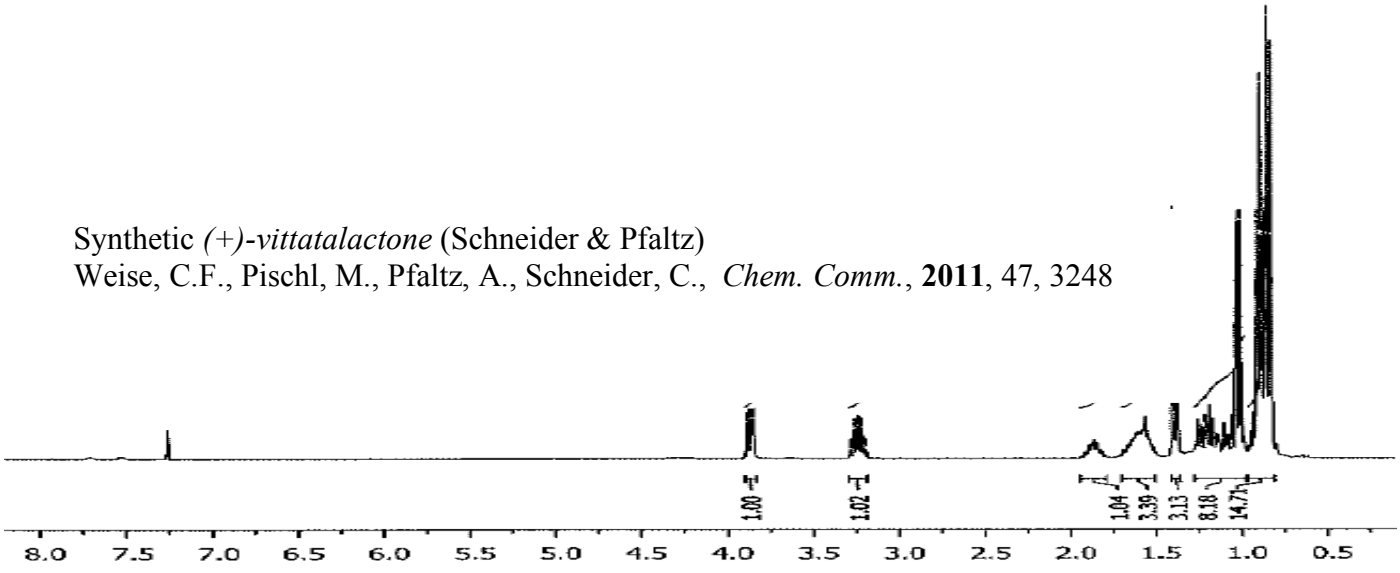
Synthetic *(–)-vittatalactone* (Micalizio)



Synthetic *(–)-vittatalactone* (Breit)
Schmidt, Y.; Breit, B. *Org. Lett.* **2009**, 11, 4767

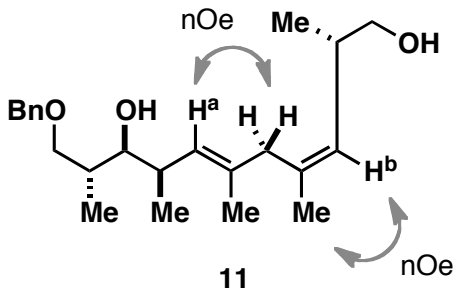


Synthetic *(+)-vittatalactone* (Schneider & Pfaltz)
Weise, C.F., Pischl, M., Pfaltz, A., Schneider, C., *Chem. Comm.*, **2011**, 47, 3248



Assignment of Alkene Geometry of Representative (*Z*,*E*)-1,4-dienes: Products of Ti-mediated Allylic Alcohol-Alkyne Coupling Reaction

A sample of **11** was irradiated at proton 5.04 ppm (H^b) (**Fig. 2.2**). Correlation to the adjacent allylic methyl group was observed as expected for the *Z* stereoisomer with respect to this alkene. The bis-allylic, methylenic, protons at 2.67-2.75 ppm were irradiated (**Fig. 2.3**) and correlation was observed to only H^a and not H^b as expected for the stereoisomer in **Fig 2.1**. Also, see the section following immediately for another example of stereochemical proof. See SETION I for proton assignments for **11.**



11

Fig. 2.1 nOe correlations

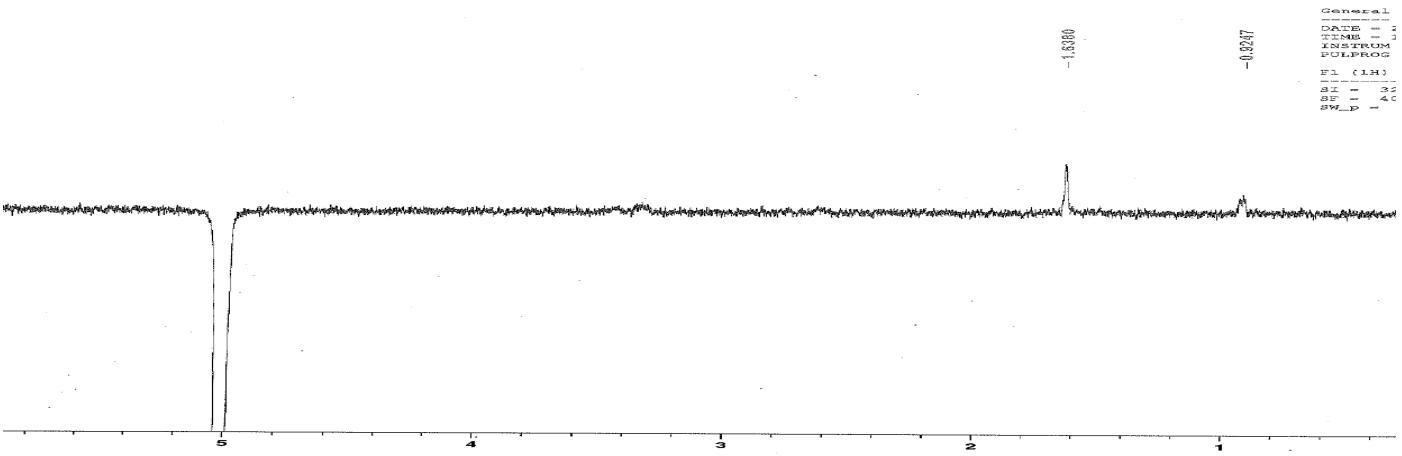


Fig. 2.2

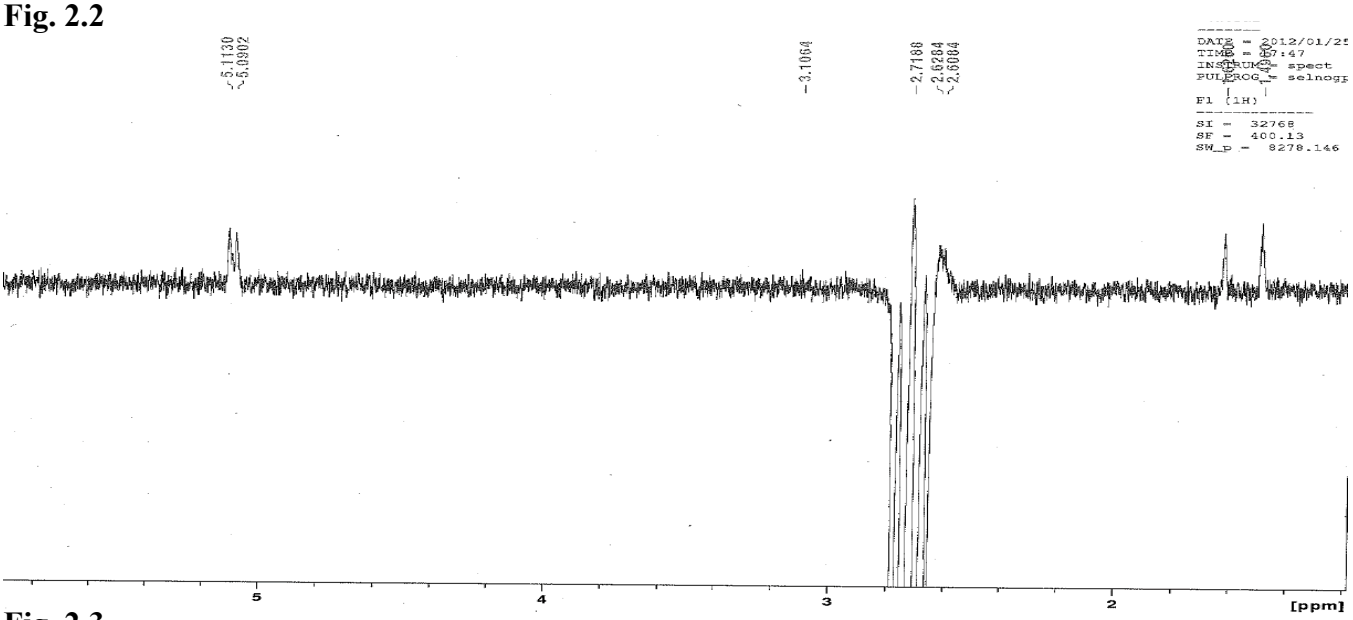


Fig. 2.3

Regarding the d.r. for the Ti-mediated Coupling Reaction: Analysis of the Crude Reaction Mixture

While NMR spectra of the 1,4-dienes did not clearly indicate a minor olefinic isomer, nOe experiments were carried out on a crude reaction mixture (**Fig. 2.4** – pg S51) of the protected derivative of **S10** (**Fig. 2.5**; containing unreacted allylic alcohol and a trace of reduced alkyne) to search for the potential presence of a minor alkene isomer derived from the Ti-mediated coupling reaction. Due to the large difference in chemical shift between the two allylic methyl groups, we targeted individual irradiation of each to probe for the presence of a minor isomer. Irradiation of H^b showed enhancement of H^a (methine) and H^c (methylenic protons), **Fig. 2.6** (see enhancements from 2.5-2.8 ppm). Irradiation of H^d showed enhancement of methylenic protons H^c (**Fig. 2.7**), without substantial enhancements of an allylic methine proton ($H^{e'}$; expected in the same vicinity as the major product's allylic methines – 2.5-2.8 ppm).

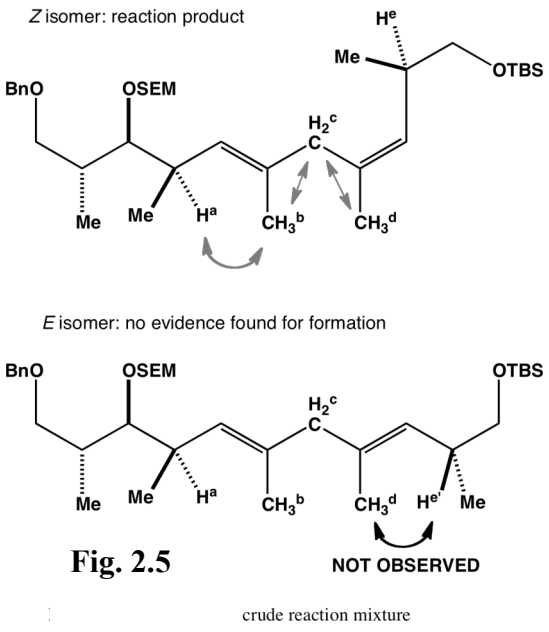


Fig. 2.5

There is a small irregularity visible adjacent to the methylene enhancement at the baseline in **Fig. 2.7** (2.75 ppm) that may indicate the presence of a minor stereoisomer ($H^d/H^{e'}$ enhancement). In the spectrum of the crude material (**Fig. 2.4** inset), a minor peak that could correspond to an additional allylic methyl peak can be seen at 1.69 ppm (the major is at 1.67 ppm). During irradiation of the major peak at 1.67, the minor peak at 1.69 is also irradiated. If the perturbation in the baseline of the nOe spectrum in the region of 2.75 ppm is due to the irradiation of this minor allylic methyl group, and subsequent enhancement of an allylic methine in the minor product, we conclude that the peak at 1.69 may represent a minor alkene isomer of the 1,4-diene product (an *E,E*-isomer). If this is the case, integration reveals that the selectivity for this reaction is at least 20:1.

That said, we note that the alkyne starting material employed for this coupling reaction was nearly a 20:1 mixture of stereoisomers (resulting from the stereoselective propargylation reaction employed to generate it, see: *J. Am. Chem. Soc.* **2005**, *127*, 3694). This ratio also corresponds to that observed for the major/minor allylic methyl peaks discussed (1.67 vs. 1.69 ppm).

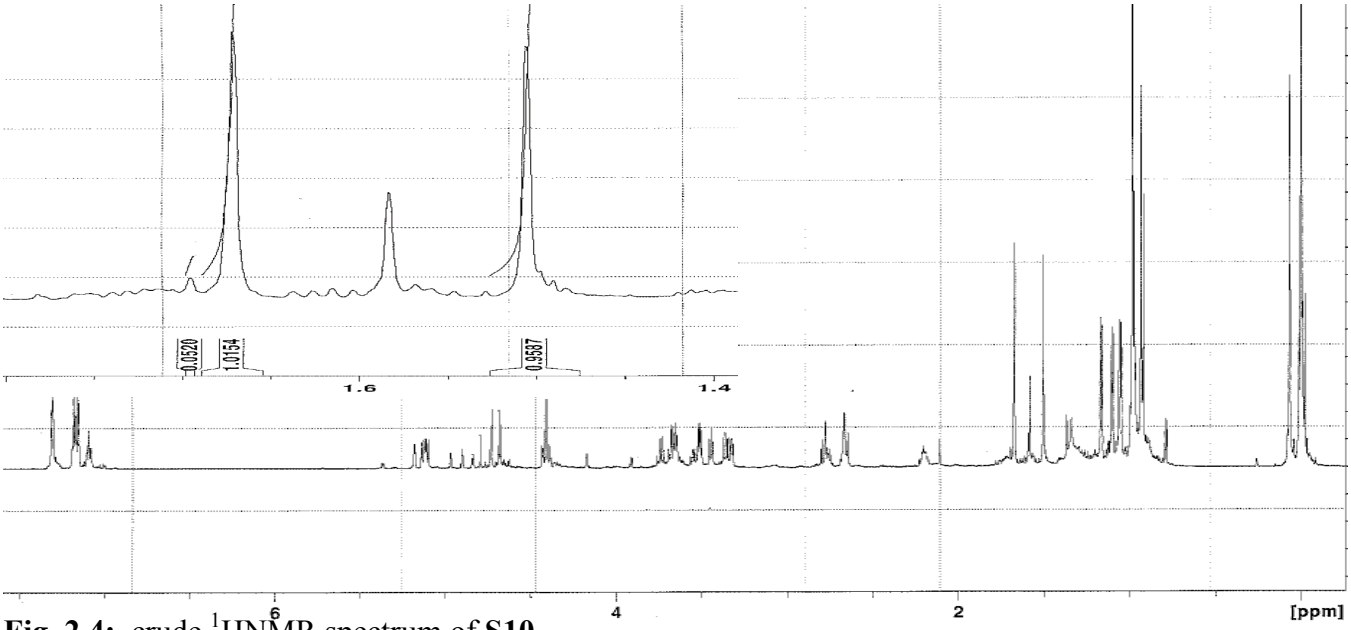


Fig. 2.4: crude ^{1}HNMR spectrum of **S10**

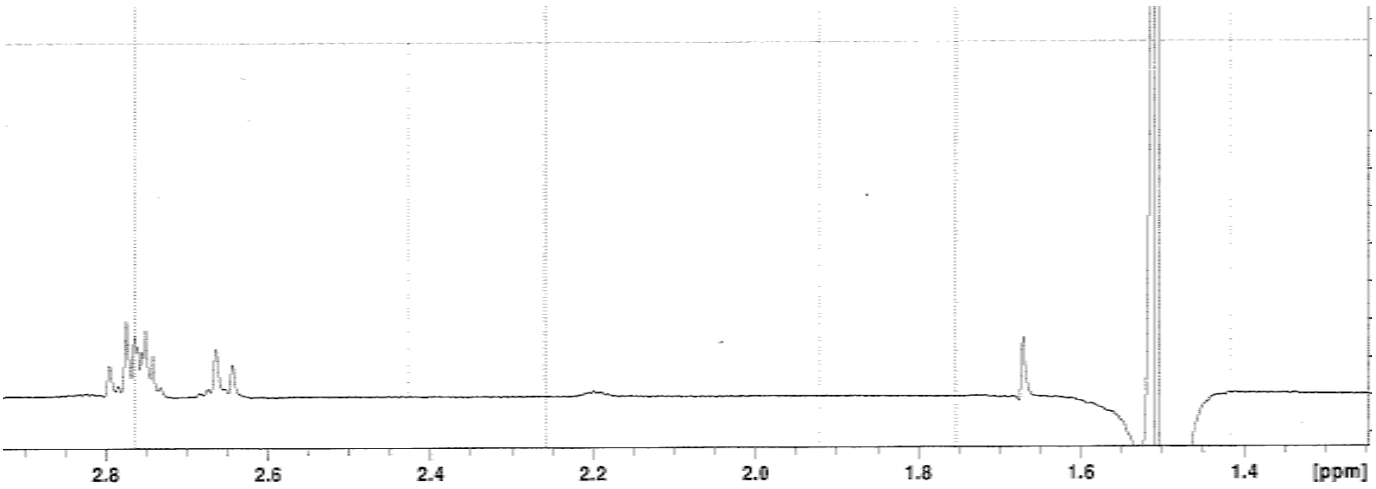


Fig. 2.6

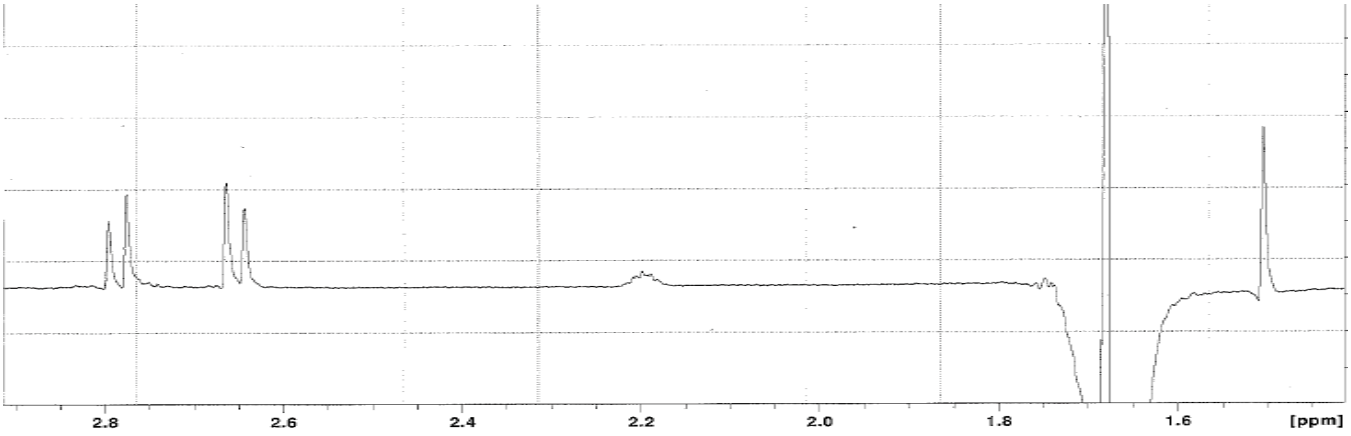
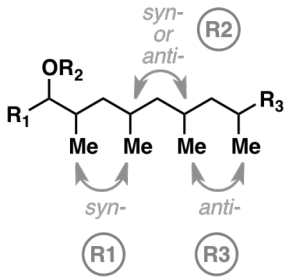
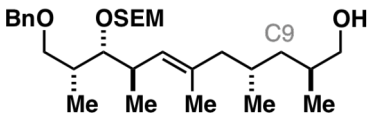


Fig. 2.7

Application of Breit's Method[2] for the Direct Assignment of the Relative Configurations of Deoxypropionates



As outlined in **Figure 2B** of our manuscript, the Ti-mediated coupling/directed hydrogenation can be used to deliver a range of deoxypropionate tetrads having a *syn* relationship between the first pair of methyl groups (R1 for "relationship 1"), a *syn* or *anti* relationship between the 2nd and 3rd methyl groups (R2), and an *anti* relationship between the 3rd and 4th methyl groups of the tetrad (R3).



21

To confirm that the relationship between the 3rd and 4th methyl groups (termed "R3" above) was *anti*, we applied Breit's analysis to compound **21**. This example was selected due to the simplicity of the ^{1}H NMR spectrum that relates to the presence of only a single deoxypropionate diad.

At 1.09 ppm the ^{1}HNMR signal corresponding to the methylenic protons at C9 of **21** (see **Fig. 2.8**) is observed. This signal integrates to 2-H and is made up of two dd within 0.01 ppm of each other, corresponding to a Δδ of 0.01ppm. According to Breit's empirical tool, this small Δδ is consistent with an *anti* relationship between the flanking methyl groups. This assignment is in full agreement with that anticipated based on the well established selectivity of hydroxyl-directed hydrogenation reactions of such homoallylic systems.[1]

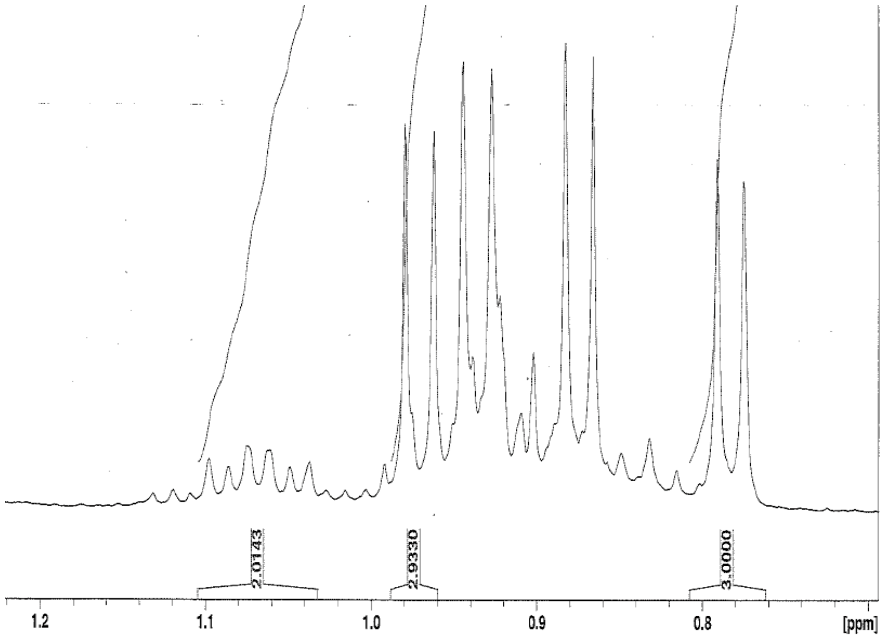
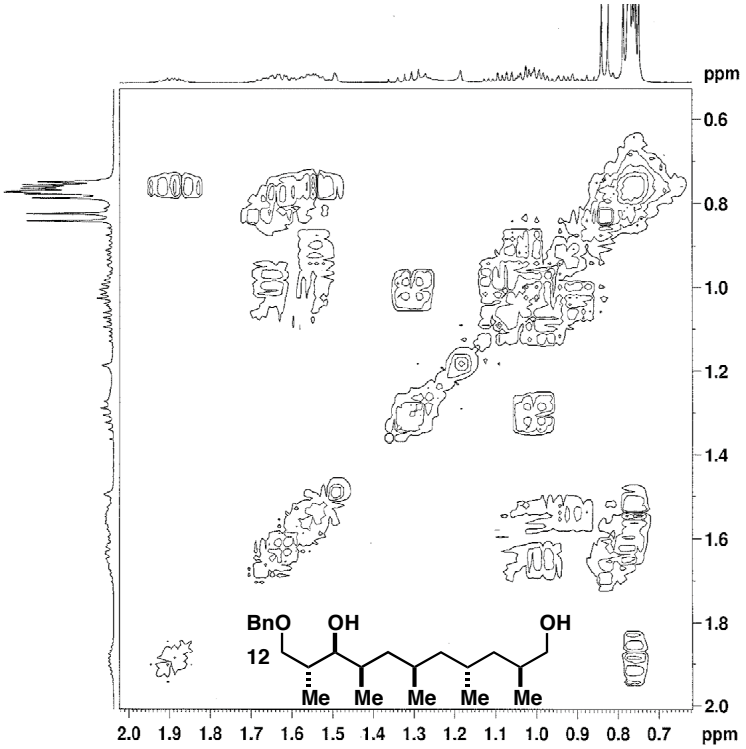


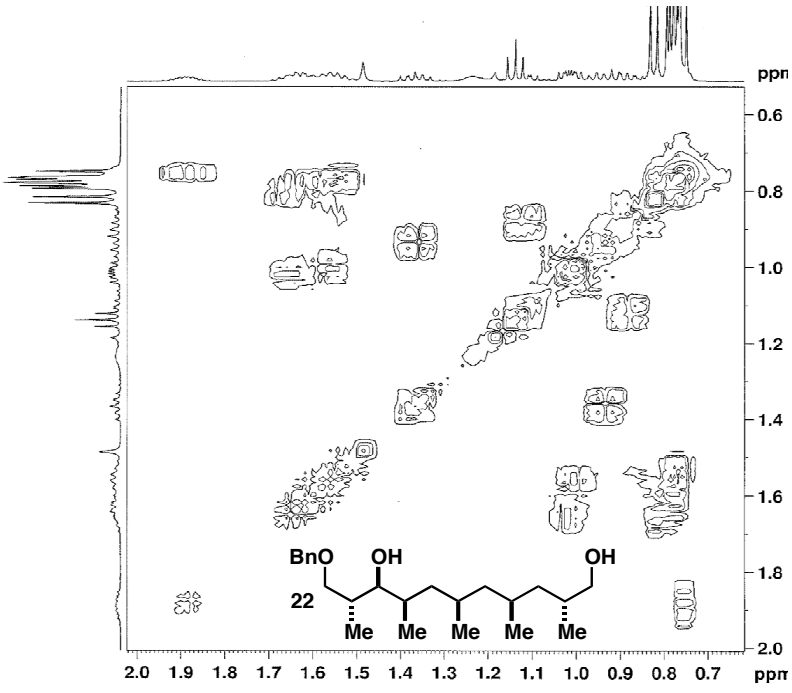
Fig. 2.8 Characteristic region of ^{1}HNMR spectrum of **21**

Following from the conclusion that the directed hydrogenation of the (*Z*)-alkene proceeds to deliver the *anti*-product, application of Breit's empirical tool can be employed to assign the stereochemistry of the



complex deoxypropionate tetrads prepared. For example, in deoxypropionate isomer **12** there exists only one *syn* relationship. In the COSY NMR spectrum of **12**, only one pair of diastereotopic methylene protons having a large Δδ is evident [(R1)(1.00 and 1.32 ppm; Δδ = 0.32)]. Based on Breit's method, this value is indicative of a *syn* relationship of the flanking methyl groups and these signals correspond to the methylene (R1). The multiplet from 1.05-0.95 ppm corresponds to the (R2) and (R3) methylenes. They do not have high Δδ's as seen in this COSY, suggesting that the assignment of the remaining stereochemical relationships in the deoxypropionate are *anti* – an assignment that is consistent with the selectivity pattern secured for the directed hydrogenation, and the absolute stereochemistry of each coupling partner.

Comparison of this analysis of **12** to the following analysis of the closely related diastereomer **22** in which R2 is *syn* will serve to further validate these claims when both examples are considered together.



In contrast to the spectral characteristics of the *syn-anti-anti*-isomer **12,** COSY spectrum of the *syn-syn-anti*-isomer **22** indicates substantial differences in the diastereotopic nature of the deoxypropionate methylenes. Here, two methylenes have diastereotopic protons that have relatively large Δδ values. 1) methylene-(R1) – 0.90/1.35 (Δδ = 0.45), and 2) methylene-(R2) 0.88/1.14 (Δδ = 0.26). The diastereotopic nature of the protons is consistent with the assignment that they are part of *syn*-deoxypropionate motifs. In contrast, the diastereotopic protons on methylene (R3) appear together at 0.98 ppm. The relatively small Δδ associated with these protons is consistent with

the assignment that this methylene is part of an *anti*-deoxypropionate motif. In general, these combined spectral characteristics are typical of deoxypropionate structures that contain 1 *anti* + 2 *syn* deoxypropionate motifs.

On the Selectivity of the *Rh-catalyzed, Directed, Double-hydrogenation*

In the *double-hydrogenation* of the 1,4-dienes discussed in this manuscript, two new stereocenters are formed, and the possibility of generating four diastereomeric products exists. For the given diene **S10** in **Fig. 1** (below) the four hypothetical products are illustrated as **22**, **b**, **c**, and **d**. Products **b** and **c** would arise if one of the alkenes of the 1,4-diene is hydrogenated on the opposite face to that expected from hydroxyl-direction [colors in these structures represent expected (Blue) and unexpected (Red) stereochemical outcomes for each hydrogenation]. Isomer **d** is expected to be the least likely, as it results from two known unfavorable hydrogenation reactions.[1]

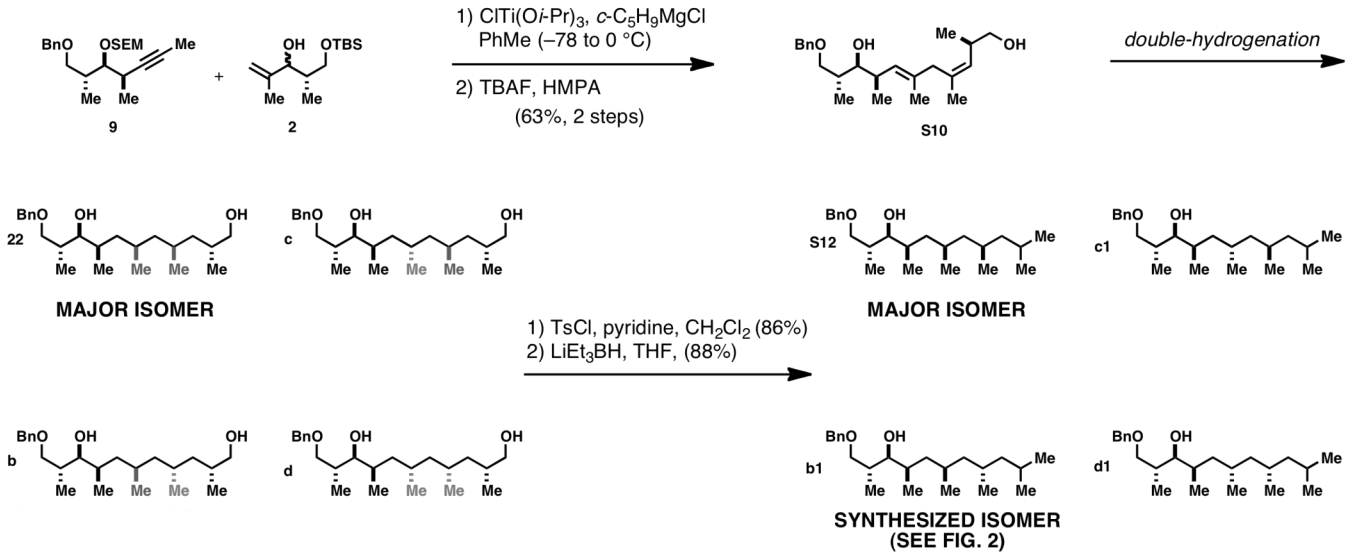


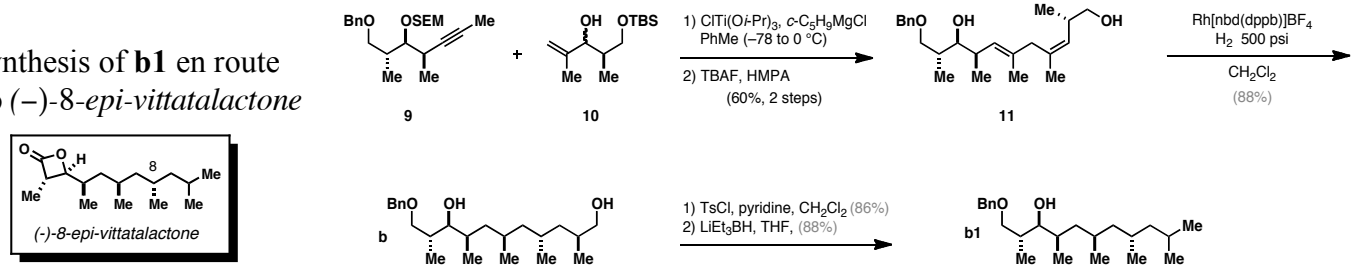
Fig. 1 analysis of synthesis of **S12**

Without authentic samples of isomers **b-d**, it is not possible to assess the ^{1}H NMR of the crude products of hydrogenation to determine the precise diastereoselectivity of the hydrogenation reaction. That said, through purposeful synthesis of isomer **b1**, and comparison to the major isomer **S12** (above), we confirm that the directed hydrogenation process proceeds with exquisite levels of selectivity (as previously reported with isolated alkenes; ≥ 20:1).[1]

Compound **b1** was synthesized as described in **Fig. 2** of page S55. Having obtained ^{13}C NMR data for compound **b1**, synthesized as described, we find a substantial difference in chemical shifts for

b1 and **S12** (isomers that differ only in the relative stereochemistry of C8) – see **Fig. 3** on page S55. Given that the Rf's of the deoxypropionates prepared in these studies were identical, we conclude that simple flash column chromatography would not result in an enhancement of dr. As such, the lack of **b1** in the sample of **S12** (and vice versa), provides support for the expected high selectivity of the directed hydrogenation reaction.

Fig. 2 synthesis of **b1** en route to (–)-8-*epi*-vittatalactone



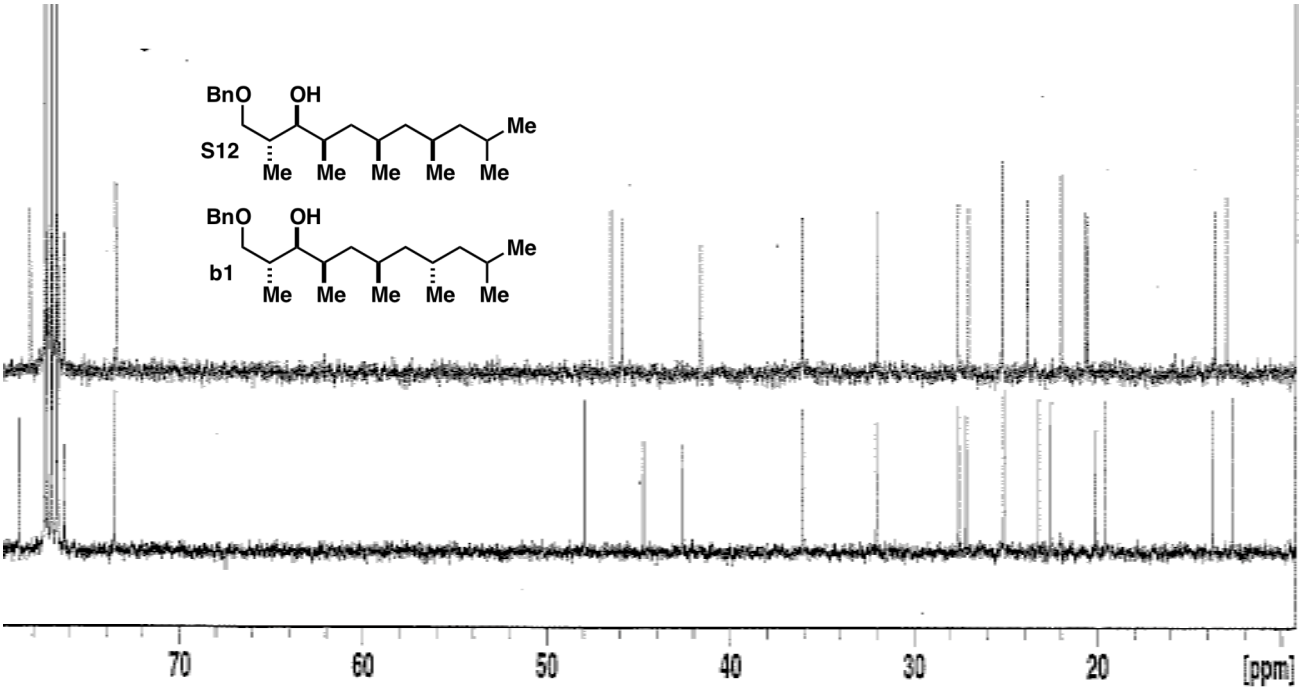


Fig. 3 ^{13}CNMR spectra of **b1** and **S12** superimposed.

The preceding constitutes an example of two deoxypropionate epimers, showing how the difference of one stereocenter greatly alters the shifts of many of the peaks in the ^{13}CNMR spectrum. Data presented in Figures **4** and **5** (page S56) serve to illustrate that significant changes in the ^{13}C spectra also surface when the deoxypropionates are isomeric at two stereocenters. The comparisons of the ^{13}CNMR spectrums of these compounds display the great effect that stereochemical changes have on the ^{13}C chemical shifts.

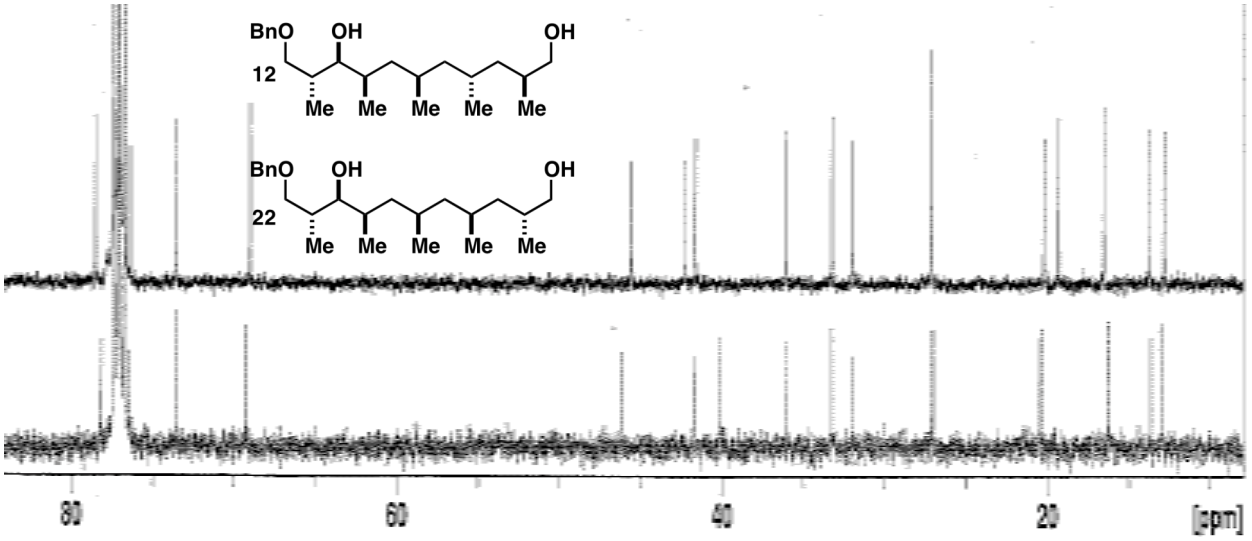


Fig. 4 ^{13}CNMR spectra of **12** and **22** superimposed.

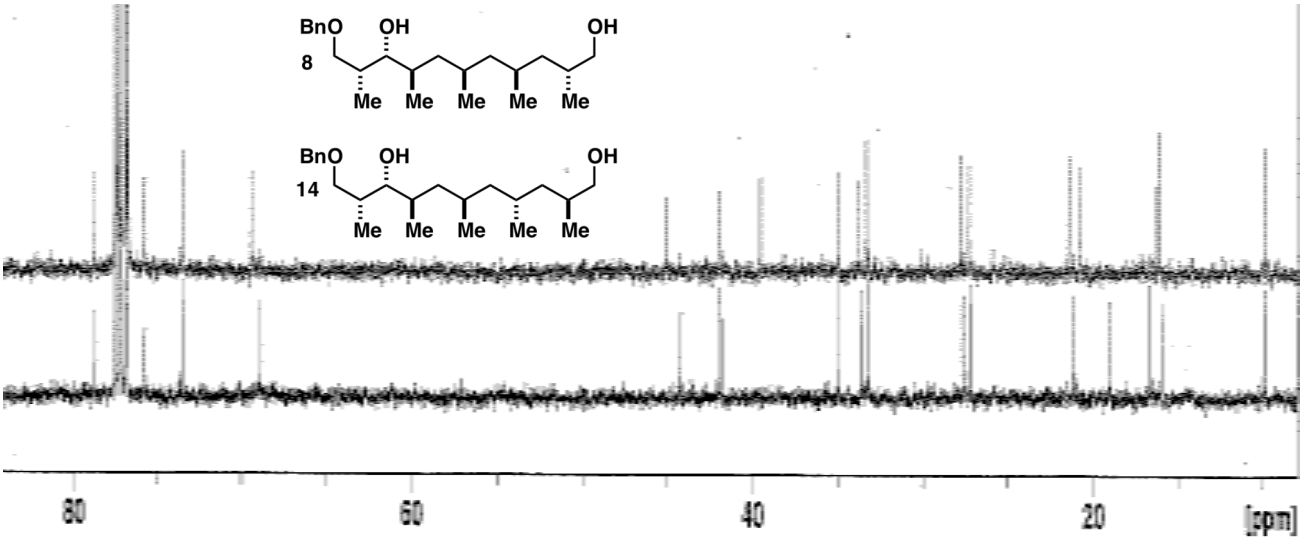


Fig. 5 ^{13}CNMR spectra of **8** and **14** superimposed.

Given the substantial differences in chemical shifts seen within these series, and the lack of evidence for minor isomers present in each sample, we conclude that the directed hydrogenation reactions performed proceed with the expected high levels of stereoselectivity previously reported for isolated trisubstituted alkenes.

Reduction of Catalyst Loading for Rh-directed Hydrogenation

Compound **22** was synthesized just as previously described in the experimental section of this SI except 10 mol % of Rh catalyst was used. The yield of **22** was 84% and full reduction of the diene starting material was observed.

References For SECTION III

(1) Evans, D. A.; Morrissey, M. M.; Dow, R. L. *Tet. Lett*. **1985**, *26*, 6005.
(2) Schmidt, Y.; Breit, B. *Org. Lett*. **2010**, 2218.