Supporting Information

Asymmetric Synthesis of Dihydroindanes by Convergent Alkoxide-Directed Metallacycle-Mediated Bond Formation

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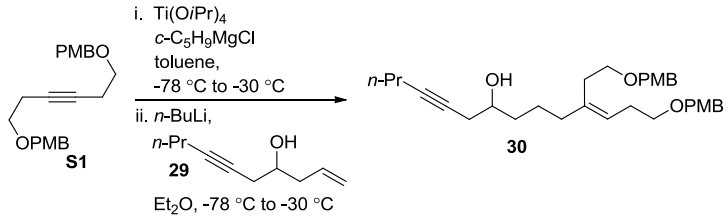
I. General Methods and Materials. All reactions were conducted in flame-dried glassware under a nitrogen atmosphere with dry solvents, unless otherwise noted. Dry diethyl ether, tetrahydrofuran, toluene and dichloromethane were obtained by passing inhibitor-free, HPLC grade solvents through activated alumina columns. Cyclopentylmagnesium chloride was purchased as a solution in Et_2O, and titrated on a monthly basis.[1] Titanium tetraisopropoxide was purified by distillation prior to use. All other commercially available reagents were used as received. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous materials, unless otherwise stated.

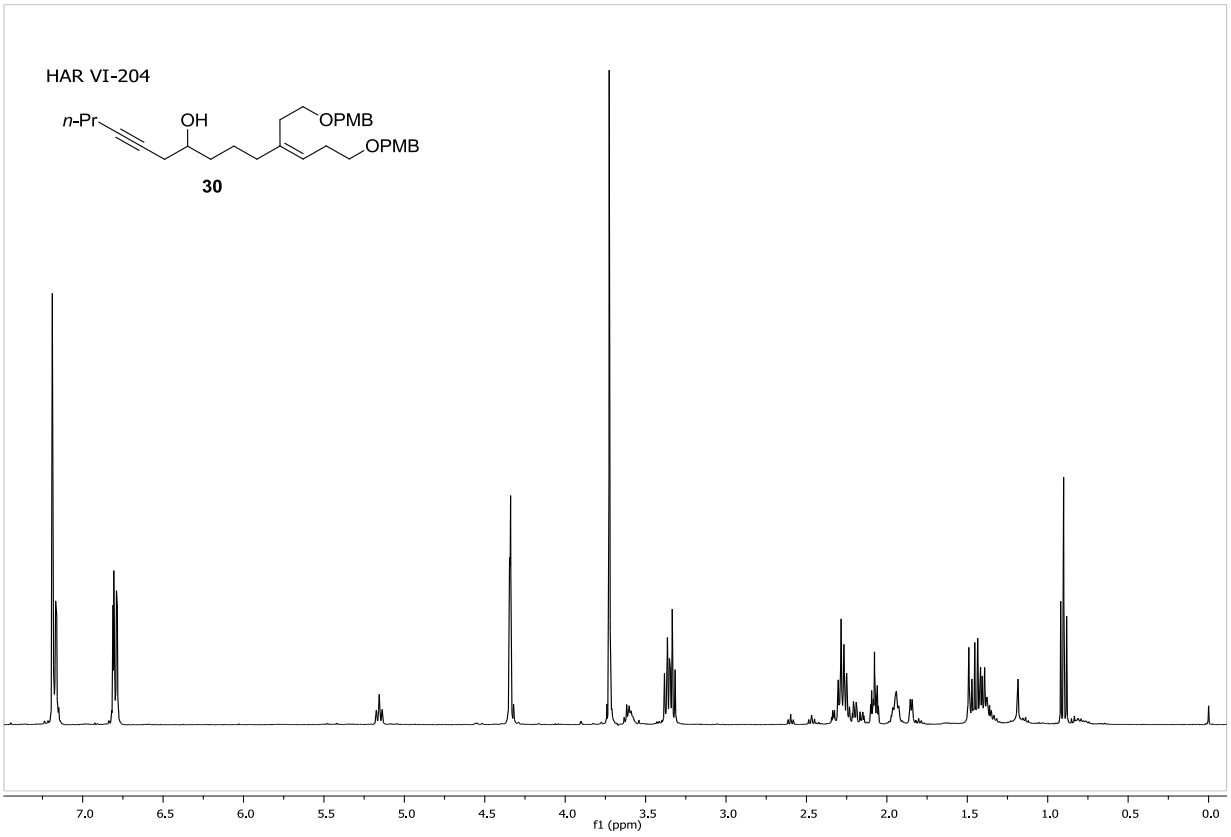
Reactions were monitored by thin-layer chromatography carried out on 250 μm E. Merck silica gel plates (60F-254) and visualized using UV light or appropriate stains, including *p*-anisaldehyde and potassium permanganate. Silica gel for flash column chromatography was purchased from Silicycle (P60, particle size 40-63 μm). ^{1}H NMR data were recorded at 400 MHz using a Bruker AVANCE-400 instrument. ^{1}H NMR chemical shifts are reported relative to residual $CHCl_3$ (7.26 ppm). ^{13}C NMR data were recorded at 100 MHz using a Bruker AVANCE-400 instrument. ^{13}C NMR chemical shifts were reported relative to the central peak of $CDCl_3$ (77.0 ppm). Infrared spectra were recorded using a Perkin Elmer Spectrum One FT-IR spectrometer. Low-resolution mass spectrometry was performed on a Waters Micromass® ZQTM instrument using electrospray ionization. Optical rotations were measured on Rudolph Research analytical Autopol IV Automatic polarimeter using a 0.5 mL capacity micro cell with a 10 cm path length. All compounds purified by chromatography were sufficiently pure for use in further experiments, unless indicated otherwise. Diastereoselectivity and regioselectivity are reported from analysis of the ^{1}H NMR of crude reaction mixtures. Characterization data for compounds **9-26** were previously reported. For compounds **9-18**, see: Ryan, J.; Micalizio, G. C. *J. Am. Chem. Soc.* **2006**, *128*, 2764-2765; for compounds **19-26**, see: Reichard, H. A.; Micalizio, G. C. *Angew. Chem. Int. Ed.* **2007**, *46*, 1440-1443.

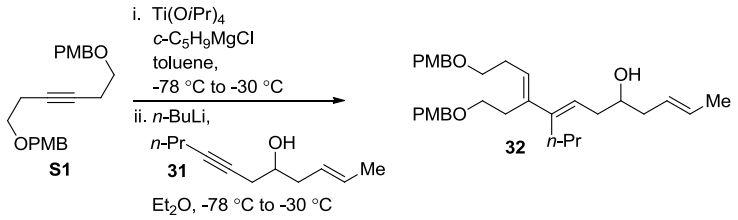
II. Alkene Substitution Screens (Manuscript Figure 6B):



(Z)-14-((4-methoxybenzyl)oxy)-11-(2-((4-methoxybenzyl)oxy)ethyl)tetradec-11-en-4-yn-7-ol (30):

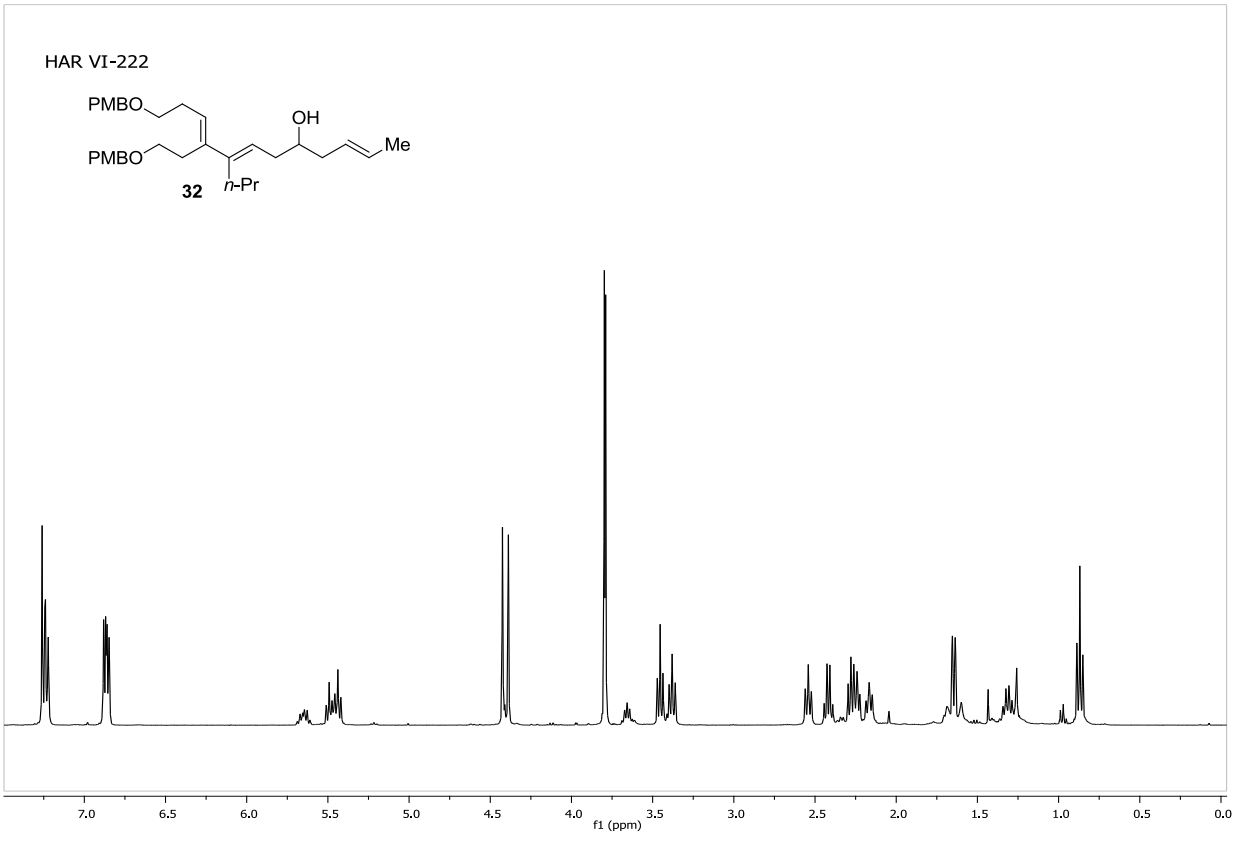
A 15-mL round-bottomed flask was charged with ($PMBOCH_2CH_2C)_2$ (**S1**, 0.106 g, 0.3 mmol, 3.3 equiv), toluene (3.0 mL), and Ti(O*i*Pr)$_4$ (0.088 mL, 0.085 g, 0.3 mmol, 3.3 equiv). The resulting solution was cooled to –78 °C (acetone/dry ice), and the Grignard solution (2M in Et_2O, 0.3 mL, 0.6 mmol, 6.6 equiv) was added dropwise. The flask was allowed to warm slowly to –30 °C over 30 minutes, and the same temperature was maintained for an additional 2h, at which point the resulting dark black solution was recooled to –78 °C. A separate 10-mL round-bottomed flask was charged with dec-1-en-6-yn-4-ol (**29**) (0.014 g, 0.09 mmol, 1.0 equiv) and diethyl ether (0.5 mL). The resulting solution was cooled to –78 °C, and a solution of *n*-BuLi (2.4 M in hexanes, 0.04 mL, 0.l mmol, 1.1 equiv) was added dropwise, and the solution was stirred for an additional 10 minutes at the same temperature. The solution of alkoxide thus prepared was added dropwise via syringe to the original solution of the prepared titanium-alkyne complex at –78 °C (an additional 0.5 mL of diethyl ether was used to rinse the flask), and the flask was allowed to warm to –30 °C, and stirred at the same temperature for 18h. The reaction was quenched by the addition of a saturated aqueous ammonium chloride solution (3 mL) and was vigorously stirred for 30 minutes. The aqueous layer was extracted with diethyl ether, and the combined organic extracts were dried over sodium sulfate. Analysis of the reaction mixture showed reduction of alkyne **S1** and coupling with the alkene portion of **29** to afford **30** as the predominant product (28 mg, 61%). The ^{1}H spectrum of **30** is shown below:

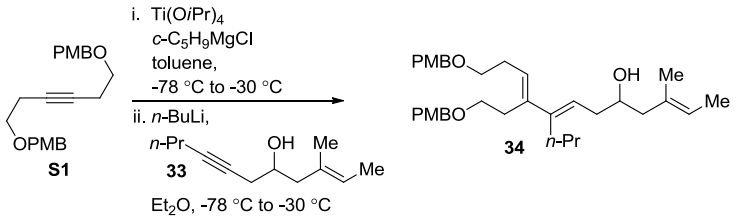




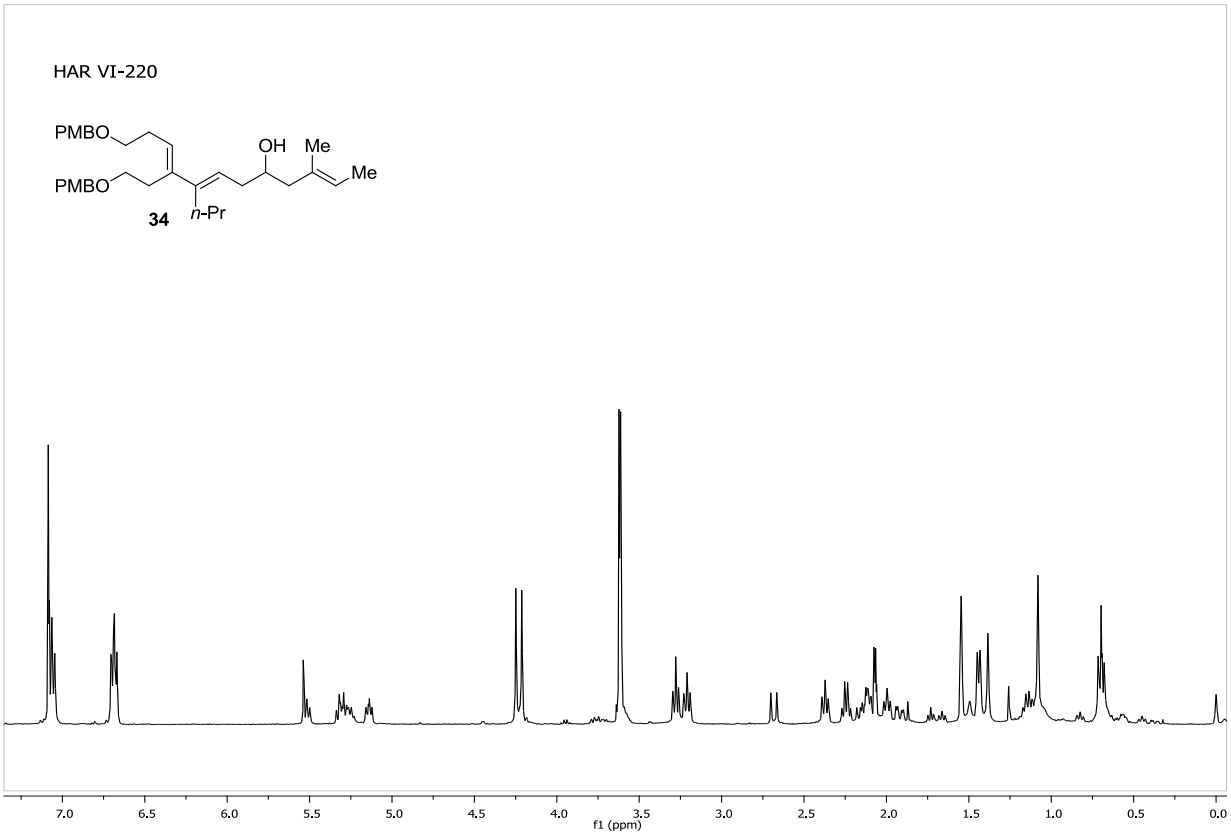
(2E,7E,9E)-12-((4-methoxybenzyl)oxy)-9-(2-((4-methoxybenzyl)oxy)ethyl)-8-propyldodeca-2,7,9-trien-5-ol (32): A 15-mL round-bottomed flask was charged with $(PMBOCH_2CH_2C)_2$ (0.106 g, 0.3 mmol, 3.3 equiv), toluene (3.0 mL), and Ti(O*i*Pr)$_4$ (0.088 mL, 0.085 g, 0.3 mmol, 3.3 equiv). The resulting solution was cooled to –78 °C (acetone/dry ice), and the Grignard solution (2M in Et_2O, 0.3 mL, 0.6 mmol, 6.6 equiv) was added dropwise. The flask was allowed to warm slowly to –30 °C over 30 minutes, and the same temperature was maintained for an additional 2h, at which point the resulting dark black solution was recooled to –78 °C. A separate 10-mL round-bottomed flask was charged with enyne **31** (0.016 g, 0.09 mmol, 1.0 equiv) and diethyl ether (0.5 mL). The resulting solution was cooled to –78

°C, and a solution of *n*-BuLi (2.4 M in hexanes, 0.04 mL, 0.l mmol, 1.1 equiv) was added dropwise, and the solution was stirred for an additional 10 minutes at the same temperature. The solution of alkoxide thus prepared was added dropwise via syringe to the original solution of the prepared titanium-alkyne complex at –78 °C (an additional 0.5 mL of diethyl ether was used to rinse the flask), and the flask was allowed to warm to –30 °C, and stirred at the same temperature for 18h. The reaction was quenched by the addition of a saturated aqueous ammonium chloride solution (3 mL) and was vigorously stirred for 30 minutes. The aqueous layer was extracted with diethyl ether, and the combined organic extracts were dried over sodium sulfate. Analysis of the reaction mixture showed reduction of alkyne **S1** and coupling with the alkyne portion of **31** to afford **32** as the predominant product (26 mg, 55%). The ^{1}H spectrum of **32** is shown below:



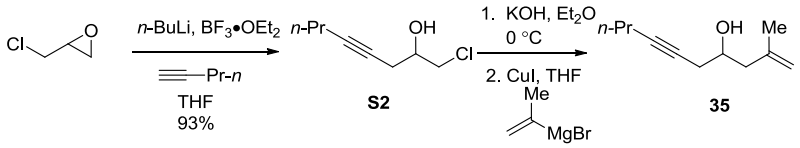


(2E,7E,9E)-12-((4-methoxybenzyl)oxy)-9-(2-((4-methoxybenzyl)oxy)ethyl)-3-methyl-8-propyldodeca-2,7,9-trien-5-ol (34): A 15-mL round-bottomed flask was charged with $(PMBOCH_2CH_2C)_2$ (0.106 g, 0.3 mmol, 3.3 equiv), toluene (3.0 mL), and $Ti(OiPr)_4$ (0.088 mL, 0.085 g, 0.3 mmol, 3.3 equiv). The resulting solution was cooled to –78 °C (acetone/dry ice), and the Grignard solution (2M in Et_2O, 0.3 mL, 0.6 mmol, 6.6 equiv) was added dropwise. The flask was allowed to warm slowly to –30 °C over 30 minutes, and the same temperature was maintained for an additional 2h, at which point the resulting dark black solution was recooled to –78 °C. A separate 10-mL round-bottomed flask was charged with enyne **33** (0.016 g, 0.09 mmol, 1.0 equiv) and diethyl ether (0.5 mL). The resulting solution was cooled to –78 °C, and a solution of *n*-BuLi (2.4 M in hexanes, 0.04 mL, 0.l mmol, 1.1 equiv) was added dropwise, and the solution was stirred for an additional 10 minutes at the same temperature. The solution of alkoxide thus prepared was added dropwise via syringe to the original solution of the prepared titanium-alkyne complex at –78 °C (an additional 0.5 mL of diethyl ether was used to rinse the flask), and the flask was allowed to warm to –30 °C, and stirred at the same temperature for 18h. The reaction was quenched by the addition of a saturated aqueous ammonium chloride solution (3 mL) and was vigorously stirred for 30 minutes. The aqueous layer was extracted with diethyl ether, and the combined organic extracts were dried over sodium sulfate. Analysis of the reaction mixture showed reduction of alkyne **S1** and coupling with the alkyne portion of **33** to afford **34** as the predominant product (26 mg, 55%). The ^1H spectrum of **34** is shown below:



The procedure for the synthesis of compound **36 is given in the section containing the general procedure for carbocycle synthesis.

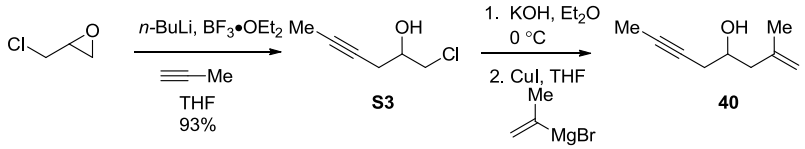
III. Preparation of Enyne and Alkyne Coupling Partners



2-methyldec-1-en-6-yn-4-ol (35). To a −78 °C solution of 1-pentyne (5.2 mL, 52.4 mmol) in THF (100 mL) was added *n*-BuLi (2.5 M in hexanes, 31.4 mmol) dropwise. The reaction mixture was allowed to stir at −78 °C for 30 min, then BF_3•OEt_2 (5.7 mL, 46.1 mmol) was added dropwise. The solution was stirred at −78 °C for an additional 30 min, and (+/-)-epichlorohydrin (1.7 mL, 20.9 mmol) was added dropwise via syringe. The reaction mixture was stirred for 30 min and quenched with sat $NaHCO_3$ at −78 °C. The resulting suspension was warmed to RT, and the aqueous layer was extracted with Et_2O. The combined

organic extracts were washed with brine and dried over $MgSO_4$. Concentration in vacuo afforded a crude oil, which was purified via flash chromatography, eluting with 95:5 to 80:20 hexanes: EtOAc, to provide 3.113 g (93%) of chlorohydrin **S2**.

To a 0 °C solution of chlorohydrin **S2** (400 mg, 2.50 mmol) in Et_2O (5.6 mL) was added freshly powdered KOH (0.7 g, 12.5 mmol). The reaction mixture was allowed to stir at the same temperature for 2h, at which point TLC analysis indicated complete consumption of **S2**. The suspension was decanted into a separatory funnel and washed with brine then dried over $MgSO_4$ and concentrated. The resulting slightly yellow oil was used without further purification. The intermediate epoxide was diluted with THF (13 mL). CuI (95 mg, 0.5 mmol) was added to the reaction mixture, and the resulting suspension was cooled to −78 °C. Isopropenylmagnesium bromide (0.5 M in THF, 3.7 mmol) was added dropwise via syringe, and the cooling bath was removed. After stirring at RT for 1 h, the reaction mixture was quenched with saturated aqueous NH_4Cl. The layers were separated, and the aqueous layer was extracted with Et_2O. The combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated in vacuo to give a crude oil, which was purified via flash chromatography, eluting with 95:5 to 80:20 hexanes: Et_2O, to provide 314 mg of enyne **7** (76%, 2 steps). Spectral data for **35**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.84-4.83 (m, 1H), 4.78-4.77 (m, 1H), 3.86-3.79 (m, 1H), 2.36-2.09 (m, 7H), 1.74 (s, 3H), 1.49 (sext, *J* = 7.1 Hz, 2H), 0.95 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.3, 112.3, 82.9, 76.0, 67.8, 44.7, 27.1, 22.4, 22.3, 20.7, 13.4; IR (thin film, NaCl): 3412, 2964, 2934, 2873, 1647, 1455, 1434, 1377, 1061 cm^{-1}; LRMS (EI, Na) calcd for $C_{11}H_{18}ONa$, expected: 189.1 *m/z* (M + Na), observed: 189.1 $(M + Na)^+$ *m/z*.



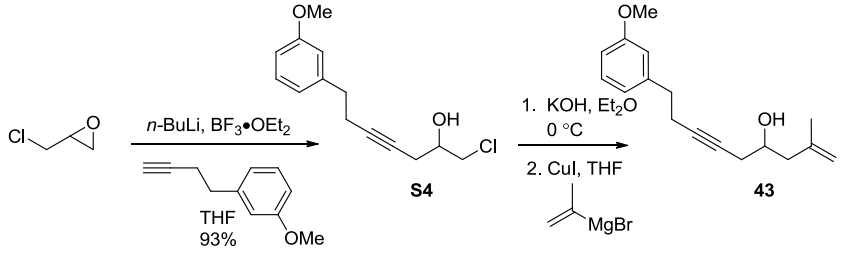
(+/-) 2-methyloct-1-en-6-yn-4-ol (40): A flame-dried 250-mL round-bottomed flask was charged with *n*-BuLi (2.4 M in hexanes, 28 mL, 66 mmol, 2.2 equiv) and THF (30 mL). The resulting solution was

cooled to −78 °C and saturated with a stream of propyne. After stirring for 20 min, the resulting suspension was treated with neat BF_3•OEt_2 (9.1 mL, 10.2 g, 72 mmol, 2.4 equiv) and was stirred for an additional 30 min at the same temperature. Epichlorohydrin (2.35 mL, 2.776 g, 30 mmol, 1.0 equiv) was added dropwise, and the solution was stirred for an additional 30 min, at which point it was quenched by the addition of saturated aqueous sodium bicarbonate. After warming to RT, the layers were separated, and the aqueous layer was extracted with diethyl ether. The combined organic extracts were washed with water and brine and dried over $MgSO_4$. Concentration in vacuo yielded a colorless oil, which was pushed through a short silica plug, eluting with 90:10 hexanes:EtOAc, to yield a volatile oil (**S3**, crude chlorohydrin) that was used without additional purification (2.1 g).

The crude chlorohydrin **S3** (2.1 g, 15.8 mmol, 1.0 equiv) was dissolved in diethyl ether (80 mL) in a 250-mL round-bottomed flask. The resulting solution was cooled to 0 °C, and freshly-powdered KOH (4.43 g, 79 mmol, 5.0 equiv) was added in small portions. The resulting suspension was stirred at 0 °C for 1.5 h, at which point TLC analysis indicated complete consumption of the chlorohydrin. The organic phase was decanted into a separatory funnel and was washed with saturated aqueous sodium bicarbonate and dried with Na_2SO_4. The ethereal extracts were concentrated in vacuo to approximately 5 mL, and the resulting crude epoxide was used as a solution without additional purification due to the volatility of the product. A yield of 100% was assumed for calculation of reagents in the following step.

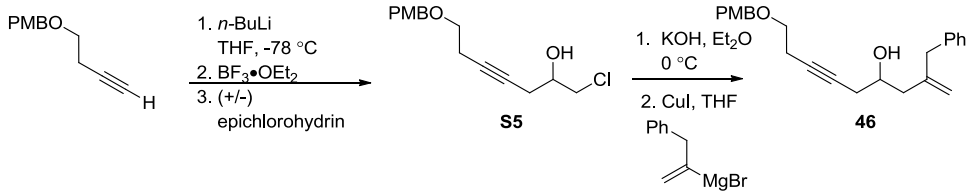
A flame-dried 250-mL round-bottomed flask was charged with THF (30 mL) and CuI (545 mg, 2.84 mmol, 0.2 equiv), and the resulting suspension was cooled to −40 °C. A solution of isopropenyl magnesium bromide (0.5 M in THF, 85 mL, 43 mmol, 3.0 equiv) was added dropwise via syringe, and after stirring for an additional 15 min at the same temperature, the ethereal solution of the crude epoxide was added dropwise via syringe. The resulting solution was allowed to warm to RT over 20 min, and TLC analysis indicated complete consumption of the intermediate epoxide. The reaction was quenched by the addition of saturated aqueous sodium bicarbonate, and the layers were separated. The aqueous layer was extracted with diethyl ether, and the combined organic extracts were washed with brine and

dried with $MgSO_4$. Concentration in vacuo yielded a crude oil, which was purified via flash chromatography, eluting with 90:10 pentane: Et_2O, and the fractions were carefully concentrated to give the title compound as a 2:1 solution of Et_2O to product due to product volatility (1.5 g product, 36% over 3 steps). Spectral data for **40**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.85 (s, 1H), 4.78 (d, *J* = 0.8 Hz, 1H), 3.86-3.80 (m, 1H), 2.39-2.25 (m, 3H), 2.18 (dd, *J* = 13.6, 8.4 Hz, 1H), 2.05 (br. s, 1H), 1.79 (t, *J* = 2.8 Hz, 3H), 1.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.3, 113.3, 78.2, 75.1, 67.7, 44.7, 27.1, 22.4, 3.5; IR (thin film, NaCl): 3406, 2920, 1647, 1440, 1376, 1271, 1060, 890, cm^{-1}; LRMS (EI, Na) calculated for $C_9H_{13}ONa$, expected: 161.1 *m/z* $(M+Na)^+$, observed: 161.2 *m/z* $(M+Na)^+$.



9-(3-methoxyphenyl)-2-methylnon-1-en-6-yn-4-ol (43): A 100-mL round-bottomed flask was charged with 1-(but-3-yn-1-yl)-3-methoxybenzene[1] (3.3 g, 20.6 mmol) and THF (41 mL) and the resulting solution was cooled to −78 °C. *n*-BuLi (2.4 M in hexanes, 12.4 mmol, 5.2 mL, 1.5 equiv) was added dropwise. The reaction mixture was allowed to stir at −78 °C for 30 min, then BF_3•OEt_2 (2.2 mL, 18.1 mmol, 2.2 equiv) was added dropwise. The solution was stirred at −78 °C for an additional 30 min, and a solution of epichlorohydrin (0.644 mL, 8.2 mmol, 1.0 equiv) in THF (5 mL) was added slowly via syringe. The reaction mixture was stirred for 1 h at the same temperature and was then quenched with saturated aqueous $NaHCO_3$ at −78 ^{o}C. The resulting suspension was warmed to RT, and the aqueous layer was extracted with Et_2O. The combined organic extracts were washed with brine and dried over anhydrous $MgSO_4$ then concentrated in vacuo. The resulting crude oil was purified via flash chromatography, eluting with 2-15% EtOAc-hexanes, to afford 977 mg (47%) of chlorohydrin **S4** as a colorless oil.

A 25-mL round-bottomed flask was charged with chlorohydrin **S4** (500 mg, 2.0 mmol, 1.0 equiv) and Et_2O (4.4 mL) and cooled to 0 °C. Freshly-powdered KOH (1.11 g, 19.8 mmol, 10.0 equiv) was added in small portions. The resulting suspension was allowed to stir at the same temperature for 1.5 h, at which point TLC analysis indicated complete consumption of the chlorohydrin. The suspension was decanted into a separatory funnel and washed with brine (2 x 20 mL) then dried over anhydrous $MgSO_4$, filtered, and concentrated. The resulting light yellow oil was diluted with THF (10 mL). CuI (75 mg, 0.4 mmol) was added to the reaction mixture, and it was cooled to −78 °C. Isopropenylmagnesium bromide (0.5 M in THF, 3.0 mmol) was added dropwise, and the cooling bath was removed, allowing the flask to warm to RT over 20 min, at which point TLC analysis indicated complete consumption of the intermediate epoxide. The reaction mixture was quenched with saturated aqueous NH_4Cl, and the aqueous layer was extracted with Et_2O. The combined organic extracts were washed with brine and dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The resulting crude oil was purified via flash chromatography, eluting with 10-15% EtOAc-hexanes, to afford enyne **43** (402 mg, 79%, 2 steps). Spectral data for **43**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (t, *J* = 7.6 Hz, 1H), 6.82-6.74 (m, 3H), 4.87-4.85 (m, 1H), 4.78-4.77 (m, 1H), 3.84-3.77 (m, 1H), 3.80 (s, 3H), 2.79 (t, *J* = 7.3 Hz, 2H), 2.51-2.13 (m, 6H), 1.91 (d, *J* = 4.0 Hz, 1H), 1.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 142.4, 142.3, 129.3, 120.8, 114.3, 113.4, 111.5, 82.3, 76.9, 67.7, 55.1, 44.7, 35.3, 27.1, 22.4, 20.8; IR (thin film, NaCl) 3368, 2930, 2835, 1644, 1489, 1453, 1259, 1080, 1055 cm^{-1}; LRMS (EI, Na) calcd for $C_{17}H_{23}O_2$, 259.2 *m/z* (M + H); observed, 259.2 $(M + H)^+$ *m/z*.



2-benzyl-9-((4-methoxybenzyl)oxy)non-1-en-6-yn-4-ol (46): A 100-mL round-bottomed flask was charged with 1-((but-3-yn-1-yloxy)methyl)-4-methoxybenzene[2] (4.0 g, 21.0 mmol, 2.0 equiv) and THF

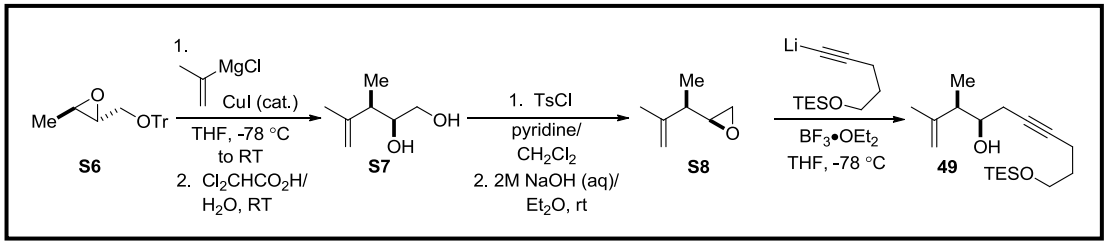
(20 mL), and the resulting solution was cooled to −78 °C. A solution of *n*-BuLi (2.4 M in hexanes, 6.6 mL, 15.75 mmol, 1.5 equiv) was added dropwise via syringe, and the reaction was stirred at the same temperature for 30 min. Neat BF_3•OEt_2 (2.93 mL, 3.28 g, 23.1 mmol, 2.2 equiv) was added, and the resulting suspension was stirred for an additional 30 min. (+/-)-Epichlorohydrin (0.820 mL, 0.973 g, 10.5 mmol, 1.0 equiv) was added dropwise via syringe, and after 10 min, TLC analysis indicated complete consumption of the chlorohydrin. The reaction was quenched by the addition of saturated aqueous sodium bicarbonate, and the resulting suspension was allowed to warm to RT. The layers were separated, and the aqueous layer was extracted with diethyl ether. The combined organic extracts were washed with brine, dried with $MgSO_4$, and concentrated in vacuo to afford a crude yellow oil, which was purified via flash chromatography, eluting with 95:5 hexanes:EtOAc, to afford 1-chloro-7-((4-methoxybenzyl)oxy)hept-4-yn-2-ol (**S5**) as a colorless oil (2.69 g, 90%).

A 100-mL round-bottomed flask was charged with chlorohydrin **S5** and diethyl ether (50 mL). The flask was cooled to 0 °C, and freshly-powdered KOH (2.69 g, 47.6 mmol, 5.0 equiv) was added in small portions. The resulting suspension was stirred at the same temperature for 1.5 h, at which point TLC analysis indicated complete consumption of the chlorohydrin. The organic phase was decanted into a separatory funnel and was washed with saturated aqueous sodium bicarbonate. The organic layer was dried with sodium sulfate and concentrated in vacuo to yield a light yellow oil, which was used without additional purification (2.34 g crude).

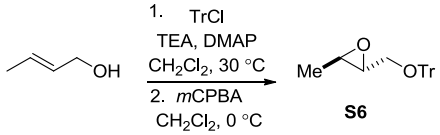
A 50-mL round bottomed flask with attached reflux condenser was charged with magnesium powder (0.197 g, 8.22 mmol, 3.0 equiv). After thermal activation of the magnesium powder, the flask was cooled to RT and purged with Ar. THF (15 mL) was added, followed by dibromoethane (0.1 mL). The resulting suspension was brought to reflux, and a solution of 2-(bromoallyl) benzene[3] (1.35 g, 6.85 mmol, 2.5 equiv) in THF (5 mL) was added dropwise to maintain reflux. After refluxing for 1.5 h, the flask was cooled to RT. A separate 100-mL flame-dried round-bottomed flask was charged with CuI (0.105 g, 0.551 mmol, 0.2 equiv) and THF (5 mL). The CuI suspension was cooled to −40 °C, and the

solution of Grignard reagent was added dropwise via syringe over 5 min. After stirring for 15 min at the same temperature, a solution of the intermediate epoxide (0.675 g, 2.74 mmol, 1.0 equiv) in THF (5 mL) was added dropwise via syringe. The reaction flask was warmed to RT for 30 min, at which point TLC analysis indicated complete consumption of the epoxide. The reaction was quenched by the addition of saturated aqueous ammonium chloride and was stirred vigorously for 10 min at RT. After separation of the layers, the aqueous layer was extracted with diethyl ether and the combined organic extracts were dried with $MgSO_4$. Concentration in vacuo gave a light yellow oil, which was purified via flash chromatography, eluting with 80:20 hexanes:EtOAc, to give the title compound as a colorless oil (0.680 g, 68%). Spectral data for **46**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.13 (m, 7H), 6.92 (d, *J* = 8.8 Hz, 2H), 4.99 (br. s, 1H), 4.93 (d, *J* = 1.6 Hz, 1H), 4.50 (s, 2H), 3.92-3.86 (m, 1H), 3.83 (s, 3H), 3.55 (t, *J* = 6.4 Hz, 2H), 3.41 (d, *J* = 3.2 Hz, 2H), 2.52-2.35 (m, 2H), 2.32 (ddd, *J* = 14.4, 4.4, 0.8, 1H), 2.19 (ddd, *J* = 14.4, 8.4, 0.8 Hz, 1H), 2.13 (br. s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.2, 145.5, 139.1, 130.1, 129.3, 129.0, 128.3, 126.2, 114.5, 113.8, 78.0, 77.2, 72.5, 68.3, 68.0, 55.2, 42.9, 42.3, 27.2, 20.1; IR (neat): 3425, 2906, 1644, 1613, 1512, 1453, 1216, 1173, 1087, 1033, 897, 821, 700; LRMS (EI, Na): Calculated for $C_{24}H_{28}O_3Na$; expected: 365.2 *m/z* $(M+Na)^+$; observed: 365.2 *m/z* $(M+Na)^+$.

Synthesis of (+/-)(3R,4R)-2,3-dimethyl-10-((triethylsilyl)oxy)dec-1-en-6-yn-4-ol (**49**):



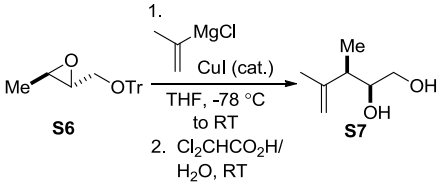
Preparation of compound **S6**:



A 100-mL round-bottomed flask was charged with crotyl alcohol (3.9 mL, 3.3 g, 45.7 mmol, 1.1 equiv) and CH_2Cl_2 (45 mL). Triethylamine (17.4 mL, 12.6 g, 125 mmol, 3.0 equiv), trityl chloride (11.6 g, 41.6

mmol, 1.0 equiv), and DMAP (1.0 g, 8.3 mmol, 0.2 equiv) were added sequentially, and the solution was heated to 30 °C for 3h, at which point TLC analysis indicated complete consumption of the trityl chloride. The flask was cooled to RT, and the resulting suspension was poured into a separatory funnel containing 1M HCl (100 mL). After separation of the layers, the aqueous layer was extracted with diethyl ether. The combined organic extracts were washed with saturated sodium bicarbonate and brine and dried with sodium sulfate. Concentration *in vacuo* afforded a white solid (10.3 g, 95%) that was used without additional purification.

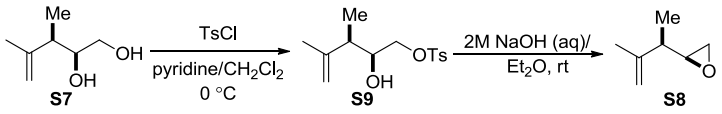
The crude tritylated product (10.3 g, 42 mmol) was dissolved in dichloromethane (50 mL) in a 250-mL round-bottomed flask. The resulting solution was cooled to 0 °C in an ice bath, and *m*CPBA (~70-75%, 12.9 g, 55 mmol, 1.3 equiv) was added all at once. The reaction was stirred for 5h at the same temperature, at which point TLC analysis indicated complete consumption of the alkene. The reaction was quenched by the addition of saturated sodium thiosulfate, and the resulting biphasic mixture was stirred for 10 min at RT. The layers were separated, and the organic layer was washed with 2M NaOH (3x 50 mL), saturated sodium bicarbonate, and brine and dried with sodium sulfate. Concentration *in vacuo* afforded **S6** (10.5 g), which was used without additional purification. The spectral data for **S6** matched those reported in the literature.[8]



(+/-) (2S,3R)-3,4-dimethylpent-4-ene-1,2-diol (S7): A 500-mL round-bottomed flask was charged with copper iodide (1.1 g, 5.77 mmol, 0.2 equiv) and THF (75 mL). The resulting suspension was cooled to −78 °C, and isopropenylmagnesium bromide (0.5 M in THF, 250 mL, 125 mmol, 4.2 equiv) was added via syringe. The flask was maintained at the same temperature for 30 min, and epoxide **S6** (10.0 g, 30.3 mmol, 1.0 equiv) was added as a solution in 25 mL of THF. The flask was immediately transferred to a 0

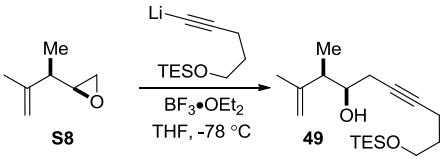
°C ice bath, and the darkening suspension was stirred at the same temperature for 2h. The flask was warmed to RT for an additional 30 min, at which point complete consumption of the epoxide was observed by TLC analysis. The flask was cooled to 0 °C, and the reaction was quenched by the addition of saturated ammonium chloride. The resulting biphasic mixture was stirred vigorously for 30 min at RT while a stream of air was bubbled into flask. The organic layer was separated, and the aqueous layer was extracted with diethyl ether. The combined organic extracts were washed with saturated sodium bicarbonate and brine and were dried with sodium sulfate. Concentration *in vacuo* yielded a light yellow oil, which was used without additional purification.

Water (25 mL) and dichloroacetic acid (9 mL) were added sequentially to the crude homoallylic alcohol in a 250-mL round-bottomed flask. The resulting suspension was stirred vigorously for 30 min at RT. TLC analysis indicated complete consumption of the trityl ether, and the flask was cooled to 0 °C. The pH of the suspension was adjusted to 10 by the addition of a 2M aqueous solution of sodium hydroxide. The resulting solution was extracted with diethyl ether, and the combined extracts were washed with saturated sodium bicarbonate and brine and were dried over sodium sulfate. Concentration *in vacuo* yielded white suspension, which was purified via column chromatography, eluting with 85:15 to 0:100 pentane:Et_2O, to give diol **S7** as a light yellow oil (2.4 g, 62% from epoxide **S6**). Spectral data for **S7**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.80-4.79 (m, 1H), 4.68-4.66 (m, 1H), 3.63 (dd, *J* = 7.2, 2.8 Hz, 1H), 3.48 (dd, *J* = 11.6, 8.4 Hz, 1H), 2.37 (br.s, 2H), 2.27-2.20 (m, 1H), 1.70 (dd, *J* = 1.6, 1.2 Hz, 3H), 1.10 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.1, 111.8, 73.8, 65.4, 44.1, 20.2, 15.0; IR (neat): 3368, 2966, 2933, 1645, 1439, 1376, 1047, 891; LRMS (EI, Na): calcd for $C_7H_{15}O_2$, 131.1 *m/z* (M + H); observed, 131.1 $(M + H)^+$ *m/z*.

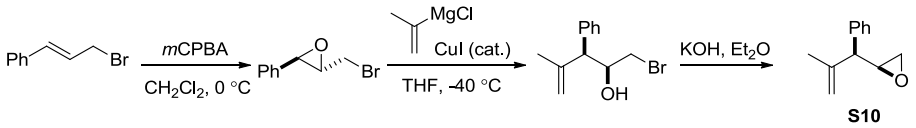


(S)-2-((R)-3-methylbut-3-en-2-yl)oxirane (S7): A 500-mL round-bottomed flask was charged with diol **S7** (2.3 g, 17.7 mmol, 1.0 equiv) and CH_2Cl_2 (250 mL), and the resulting suspension was cooled to 0 °C in an ice bath. Triethylamine (12.3 mL, 8.9 g, 89 mmol, 5.0 equiv), tosyl chloride (4.4 g, 23.0 mmol, 1.3 equiv), and DMAP (50 mg) were added. The reaction was stirred for 3h at the same temperature and was then poured into a separatory funnel containing 1M HCl (100 mL). The layers were separated, and the organic layer was washed with saturated sodium bicarbonate and brine and dried over sodium sulfate. The solvent was removed *in vacuo*, and the resulting crude oil was purified via flash chromatography, eluting with 95:5 to 75:25 hexanes:EtOAc, to afford the intermediate monotosylate as a light yellow oil (2.7g, 54%). Spectral data for tosylate **S9**: Spectral data for **S9**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 2H), 4.76-4.75 (m, 1H), 4.71-4.70 (m, 1H), 4.07 (dd, *J* = 10.0, 6.8 Hz, 1H), 3.89 (dd, *J* = 10.4, 7.2 Hz, 1H), 3.76 (dt, *J* = 7.6, 3.2 Hz, 1H), 2.44 (s, 3H), 2.23-2.19 (m, 1H), 2.12 (br s, 1H), 1.64 (s, 3H), 1.06 (2, 3H) ; ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.1, 145.0, 132.7, 129.9, 127.9, 112.5, 72.8, 70.9, 43.5, 21.6, 19.9, 14.8; IR (neat): 3539, 3074, 2968, 1654, 1598, 1451, 1354, 1172, 1095, 958, 812, 665; LRMS (EI, Na): calcd for $C_{14}H_{20}O_4SNa$, 307.1 *m/z* (M + Na); observed, 307.2 $(M + Na)^+$ *m/z*.

A 200-mL round-bottomed flask was charged with tosylate **S9** (2.5 g, 8.8 mmol, 1.0 equiv) and diethyl ether (45 mL). An aqueous solution of NaOH (2M, 22 mL, 44 mmol, 5.0 equiv) was added to the ethereal solution, and the resulting biphasic mixture was stirred vigorously at room temperature for 12h. The layers were separated, and the aqueous layer was extracted with diethyl ether. The combined organic extracts were washed with saturated sodium bicarbonate and brine and dried over sodium sulfate. The resulting solution of epoxide **S8** was concentrated to approximately 3mL, and the concentration of the title compound was determined via ^{1}H NMR analysis. The epoxide was used without additional purification as a solution in diethyl ether due to its volatility.



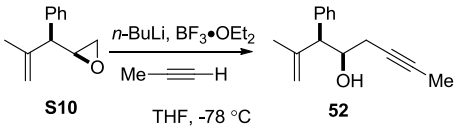
(+/-) (3R,4R)-2,3-dimethyl-10-((triethylsilyl)oxy)dec-1-en-6-yn-4-ol (49): A 50-mL round-bottomed flask was charged with triethyl(pent-4-yn-1-yloxy)silane [9] (1.23 g, 6.7 mmol, 2.5 equiv) and dry THF (15 mL). The flask was cooled to −78 °C in an acetone/dry ice bath, and a solution of nBuLi (2.4 M in hexanes, 1.67 mL, 4.0 mmol, 1.5 equiv) was added dropwise. The resulting light yellow solution was stirred for 30 min at the same temperature, and BF_3•OEt_2 (0.75 mL, 0.83 g, 5.9 mmol, 2.2 equiv) was added dropwise. After stirring for an additional 30 minutes at −78 °C, a solution of epoxide **S8** in diethyl ether (300 mg epoxide by mass, 2.68 mmol, 1.0 equiv) was added all at once. After an additional 1h at −78 °C, TLC analysis indicated complete consumption of the starting epoxide, and the reaction was quenched by the addition of an aqueous solution of saturated sodium bicarbonate. The flask was warmed to RT, and the layers were then separated. The aqueous layer was extracted with diethyl ether. The combined organic extracts were washed with saturated aqueous sodium bicarbonate and brine and dried over magnesium sulfate. The solvent was removed *in vacuo*, and the resulting crude oil was purified via flash chromatography, eluting with 97:3 to 90:10 hexanes:Et_2O, to afford the title compound as a colorless oil (0.5 g, 63% over 2 steps from tosylate **S9**). Spectral data for **49**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.81-4.80 (m, 1H), 4.78-4.77 (m, 1H), 3.68 (t, J = 6.4 Hz, 2H), 3.65-3.60 (m, 1H), 2.41-2.24 (m, 5H), 1.73-1.67 (m, 6H), 1.10 (d, J = 7.2 Hz, 3H), 0.96 (t, J = 8.0 Hz, 9H), 0.59 (q, J = 8.0 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.6, 111.8, 82.7, 77.2, 71.6, 61.4, 45.8, 32.1, 25.5, 20.4, 15.2, 14.4, 6.7, 4.4; LRMS (EI, Na): calcd for $C_{18}H_{35}O_2Si$, 311.2 *m/z* (M + H); observed, 311.0 $(M + H)^+$ *m/z*.



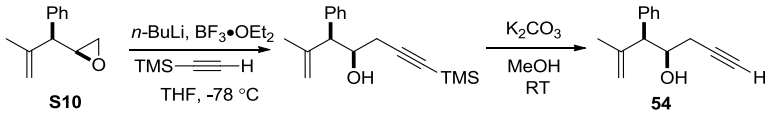
**Epoxidation of cinnamyl bromide was performed according to the literature procedure.[4]

(+/-)-(*S*)-2-((*S*)-2-methyl-1-phenylallyl)oxirane (S10): A 500-mL round-bottomed flask equipped with magnetic stir bar was charged with CuI (0.880 g, 4.6 mmol, 0.2 equiv) and THF (50 mL). The resulting suspension was cooled to −40 °C, and isopropenylmagnesium bromide (0.5 M in THF, 115 mL, 57.5 mmol, 2.5 equiv) was added via syringe over 5 min. After 15 minutes a solution of (+/-)-(2*S*,3*R*)-2-(bromomethyl)-3-phenyloxirane (4.9 g, 23 mmol, 1.0 equiv) in THF (20 mL) was added via syringe over 5 minutes. The reaction flask was allowed to warm to RT over 30 min, and the resulting black suspension was quenched by the addition of saturated aqueous ammonium chloride. The resulting biphasic mixture was stirred vigorously at RT for 30 min, and the layers were separated. The aqueous layer was extracted with diethyl ether, and the combined organic extracts were washed with ammonium chloride, water and brine and dried with $MgSO_4$. Concentration in vacuo yielded the intermediate bromohydrin, which was used without additional purification (5.9 g).

A 250-mL round-bottomed flask equipped with magnetic stir bar was charged with the crude bromohydrin (5.9 g, 23.0 mmol, 1.0 equiv) and diethyl ether (120 mL). The resulting solution was cooled to 0 °C in an ice bath, and freshly powered KOH (6.45 g, 115 mmol, 5.0 equiv) was added in small portions over 5 min. The resulting light yellow suspension was stirred at the same temperature for 2h, at which point TLC analysis indicated complete consumption of the starting material. The organic phase was decanted into a separatory funnel, and the remaining solid was extracted with diethyl ether. The combined organic extracts were washed with saturated aqueous $NaHCO_3$ and dried with Na_2SO_4. Concentration in vacuo yielded a light yellow oil, which was purified via flash chromatography, eluting with 95:5 hexanes:EtOAc, to give the title compound as a colorless oil (2.4 g, 60% over two steps). Spectral Data for **S10**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.20 (m, 5H), 5.22 – 4.81 (m, 2H), 3.29 (ddd, *J* = 6.7, 3.9, 2.7 Hz, 1H), 3.01 (d, *J* = 6.9 Hz, 1H), 2.82 (dd, *J* = 4.9, 3.9 Hz, 1H), 2.44 (dd, *J* = 5.0, 2.7 Hz, 1H), 1.64 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.0, 139.4, 128.4, 128.4, 126.9, 112.5, 55.1, 54.3, 46.7, 22.2; IR (neat): 2973, 1647, 1493, 1452, 1375, 1261, 1032, 945, 896, 753, 699; Satisfactory mass spectral data for the epoxide could not be obtained.

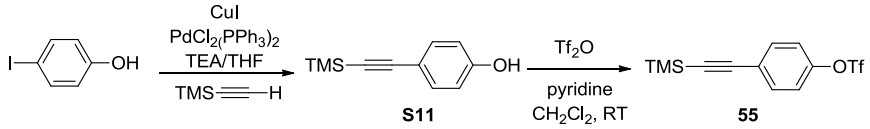


(+/-) (3*S*,4*R*)-2-methyl-3-phenyloct-1-en-6-yn-4-ol (52): Prepared according to the procedure for the preparation of **49** using **S10** (0.500 g) and propyne (excess). The crude material was purified via flash chromatography, eluting with 95:5 to 90:10 hexanes:EtOAc. The title compound was obtained as a colorless oil (0.550 g, 89% yield). Spectral data for **52**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.23 (m, 5H), 5.04 (d, *J* = 1.6 Hz, 1H), 4.91 (d, *J* = 1.5 Hz, 1H), 4.34 (ddd, *J* = 12.1, 7.3, 4.3 Hz, 1H), 3.49 (d, *J* = 8.3 Hz, 1H), 2.55-2.32 (m, 2H), 1.89 (br. s, 1H), 1.85 (t, *J* = 2.4 Hz, 3H), 1.58 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.4, 139.4, 128.8, 128.3, 126.8, 112.5, 78.3, 75.3, 69.9, 58.1, 25.7, 21.4, 3.5; IR (neat): 3444, 2918, 1644, 1599, 1493, 1451, 1374, 1271, 1070, 893, 750, 698; LRMS (EI, Na) calcd for $C_{15}H_{19}O$, 215.1 *m/z* (M + H); observed, 215.1 *m/z* $(M + H)^+$.



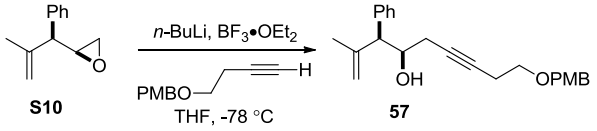
(3*S*,4*R*)-2-methyl-3-phenylhept-1-en-6-yn-4-ol (54): A 50-mL round-bottomed flask was charged with trimethylsilylacetylene (1.01 mL, 0.705 g, 7.18 mmol, 2.5 equiv) and THF (10 mL). The reaction flask was cooled to −78 °C, and a solution of *n*-BuLi (2.4 M, 1.8 mL, 4.31 mmol, 1.5 equiv) was added dropwise. The resulting solution was stirred at the same temperature for 30 min, and neat BF_3•OEt_2 (0.8 mL, 0.9 g, 6.3 mmol, 2.2 equiv) was added via syringe. After stirring for an additional 30 min at −78°C, a solution of **S10** (0.500 g, 2.87 mmol, 1.0 equiv) in THF (3 mL) was added dropwise via syringe. TLC analysis indicated complete consumption of **S10** after 15 minutes of additional stirring. The reaction was quenched by the addition of saturated aqueous sodium bicarbonate, and the layers were separated. The aqueous layer was extracted with diethyl ether, and the combined organic extracts were washed with brine, dried with $MgSO_4$, and concentrated in vacuo to give the crude enyne, which was used without additional purification (0.735 g).

A 25-mL round-bottomed flask was charged with the crude TMS-protected enyne (0.700 g, 2.57 mmol, 1.0 equiv), MeOH (5.0 mL), and K_2CO_3 (0.080 g). The resulting suspension was stirred at RT for 30 min, at which point TLC analysis indicated complete consumption of the starting material. Concentration *in vacuo* and purification of the resulting crude oil via a short plug of silica gel, eluting with 80:20 hexanes:EtOAc, gave **54** as a colorless oil (0.505 g, 98%). Spectral data for **54**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46-7.33 (m, 5H), 5.13 (t, *J* = 0.8 Hz, 1H), 5.01 (t, *J* = 1.2 Hz, 1H), 4.44-4.40 (m, 1H), 3.56 (d, *J* = 8.4 Hz, 1H), 2.66 (ddd, *J* = 16.8, 4.4, 2.4 Hz, 1H), 2.52 (ddd, *J* = 16.8, 6.4, 2.4 Hz, 1H), 2.19 (t, *J* = 2.8 Hz, 1H), 1.98 (br. s, 1H), 1.74 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.2, 139.0, 128.8, 128.4, 126.9, 112.6, 80.9, 70.8, 69.6, 57.9, 25.2, 21.4; IR (neat): 3294, 2914, 1644, 1493, 1451, 1374, 1072, 895, 750, 699; LRMS (EI, Na) calcd for $C_{14}H_{17}O$; expected: 201.1 $(M + H)^+$ *m/z*; observed: 201.2 $(M + H)^+$ *m/z*.



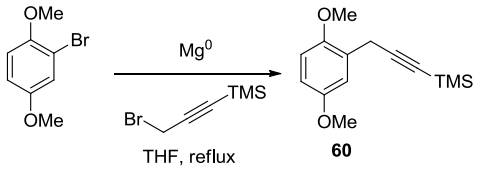
4-((trimethylsilyl)ethynyl)phenyl trifluoromethanesulfonate (55): A 250-mL round-bottomed flask was charged with 4-iodophenol (5g, 22.7 mmol, 1.0 equiv) and flushed with Ar. THF (100 mL), $PdCl_2(PPh_3)_2$ (0.520 g, 0.74 mmol, 0.033 equiv), CuI (0.170 g, 0.893 mmol, 0.04 equiv), and TEA (5.0 mL) were added, and the resulting solution was cooled to 0 °C. Trimethylsilylacetylene (3.4 mL, 2.39 g, 24.3 mmol, 1.07 equiv) was added dropwise via syringe over 5 min, and the flask was allowed to warm to RT and was stirred overnight. The reaction was filtered through a pad of Celite, concentrated, and dry loaded onto a column of SiO_2. Elution with 90:10 hexanes:EtOAc afforded **S11** as a red oil (3.45 g, 73%), whose spectral propertied matched those reported in the literature.[5] **55**: A 100-mL round-bottomed flask was charged with **S11** (2.5 g, 12.0 mmol, 1.0 equiv) and CH_2Cl_2 (15 mL). The resulting solution was cooled to 0 °C, and pyridine (1.94 mL, 1.9 g, 24.0 mmol, 2.0 equiv) was added dropwise via syringe. A solution of Tf_2O (4.06 g, 14.4 mmol, 1.2 equiv) in CH_2Cl_2 (5 mL) was added dropwise via

syringe, and the flask was allowed to warm to RT. After stirring at RT for 1h, TLC analysis indicated complete consumption of the phenol. The reaction was diluted with Et_2O, washed with 1M HCl, saturated aqueous $NaHCO_3$, water, and brine. The organic layer was dried with $MgSO_4$ and concentrated in vacuo to afford a crude oil, which was purified via flash chromatography, eluting with 100:0 to 90:10 hexanes:EtOAc, to give **55** as a light yellow oil (3.1 g, 76%). Spectral data for **55**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.8 Hz, 2H), 7.21 (d, *J* = 8.8 Hz, 2H), 0.26 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.0, 133.8, 123.9, 121.3, 120.3, 102.8, 97.7, -0.3; IR (neat): 2957, 2176, 1498, 1248, 1217, 1047, 837, 758; LRMS (EI, Na): calculated for $C_{11}H_{13}NaSi$, expected: 196.1 (M+Na-OTf), found: 196.1.

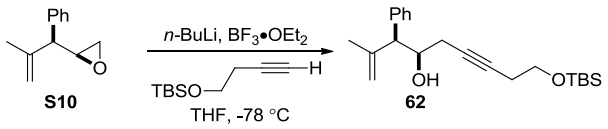


(+/-) (3*S*,4*R*)-9-((4-methoxybenzyl)oxy)-2-methyl-3-phenylnon-1-en-6-yn-4-ol (57): A 50-mL round-bottomed flask was charged with 1-((but-3-yn-1-yloxy)methyl)-4-methoxybenzene[2] (0.650 g, 3.42 mmol, 1.7 equiv) and THF (10 mL). The resulting solution was cooled to −78°C, and BuLi (2.5 M in hexanes, 1.2 mL, 2.99 mmol, 1.5 equiv) was added dropwise. After 30 min, BF_3•OEt_2 (0.490 mL, 0.565 g, 3.98 mmol, 2.0 equiv) was added. After an additional 30 minutes of stirring at the same temperature, a solution of **S10** (0.350 g, 1.99 mmol, 1.0 equiv) in THF (5 mL) was added dropwise. After 15 min, TLC analysis indicated complete consumption of the epoxide, and the reaction was quenched by the addition of saturated aqueous $NaHCO_3$. The resulting suspension was warmed to RT and stirred for 30 min at RT. The layers were separated, and the aqueous layer was extracted with diethyl ether. The combined organic extracts were washed with brine and dried with $MgSO_4$. After concentration in vacuo, the resulting crude oil was purified via flash chromatography, eluting with 80:20 to 70:30 hexanes:EtOAc, to afford the title compound as a colorless oil (0.580 g, 80%). Characterization data for **57**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.17 (m, 7H), 6.82 (d, *J* = 8.7 Hz, 2H), 5.14 – 4.91 (m, 1H), 4.93 – 4.79 (m, 1H), 4.44 (s, 2H), 4.25 – 4.21 (m, 1H), 3.75 (s, 3H), 3.51 (t, *J* = 6.9 Hz, 2H), 3.38 (d, *J* = 8.3 Hz, 1H), 2.50-2.29 (m, 4H), 1.82 (br.

s, 1H), 1.58 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.2, 145.5, 139.4, 130.1, 129.3, 128.9, 128.4, 126.8, 113.8, 112.6, 79.9, 77.4, 72.6, 69.9, 68.4, 58.1, 55.2, 25.8, 21.4, 20.2; IR (neat): 3340, 2968, 1611, 1513, 1393, 1250, 1066, 703; LRMS (EI, Na) Calculated for $C_{24}H_{28}O_3Na$; expected: 387.2 *m/z* $(M + Na)^+$; observed, 387.3 *m/z* $(M + Na)^+$.

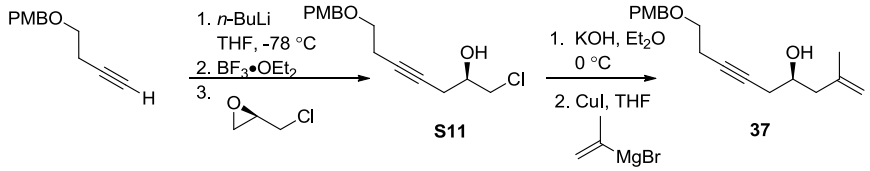


(3-(2,5-dimethoxyphenyl)prop-1-yn-1-yl)trimethylsilane (60): A 50-mL 3-neck round-bottomed flask was charged with magnesium powder (0.196 g, 8.17 mmol, 1.2 equiv) and fitted with a reflux condenser. The magnesium turnings were activated thermally in vacuo, and THF (10 mL) was then added to the cooled flask. Dibromoethane (0.075 mL) was added, and the suspension was brought to reflux. A solution of the aryl bromide (1.3 g, 6.81 mmol, 1.0 equiv) in THF (5 mL) was added dropwise over 5 min to maintain reflux. The suspension was heated at reflux for 1h and was then cooled to RT. 3-bromo-1-trimethylsilylpropyne was added dropwise via syringe, and the suspension was heated to reflux for an additional 5h. After cooling to RT, the reaction was quenched with 1M HCl. The layers were separated, and the aqueous layer was extracted with diethyl ether. The combined organic extracts were washed with saturated aqueous $NaHCO_3$ and dried with $MgSO_4$. Concentration in vacuo yielded a crude oil, which was purified via flash chromatography, eluting with 100:0 to 98:2 hexanes:EtOAc, to give the title compound as a colorless oil mixed with a minor amount of 1,4-dimethoxybenzene. The yield of the title compound was 1.12 g (75%). Characterization data for **60**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (br. s, 1H), 6.76 (s, 1H), 6.75 (s, 1H), 3.80 (s, 3H), 3.78 (s. 3H), 3.62 (s, 1H), 3.62 (s, 1H), 0.23 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.6, 150.9, 125.8, 114.9, 112.0, 110.8, 104.2, 87.2, 55.8, 55.5, 20.6, 0.1; IR (neat): 2957, 2176, 1498, 1248, 1217, 1047, 837, 758; LRMS (EI, Na) calculated for $C_{14}H_{21}O_2Si$; expected: 249.2 *m/z* $(M + H)^+$; observed, 249.1 *m/z* $(M + H)^+$.



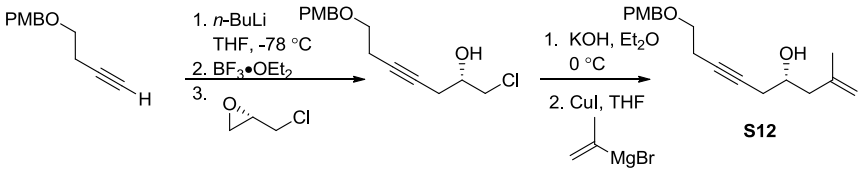
(+/-) (3*S*,4*R*)-9-((tert-butyldimethylsilyl)oxy)-2-methyl-3-phenylnon-1-en-6-yn-4-ol (62): Prepared according to the procedure for the synthesis of **57** using (but-3-yn-1-yloxy)(tert-butyl)dimethylsilane[6] (1.36 g) and **S10** (0.570 g). The crude material was purified via flash chromatography, eluting with 95:5 to 90:10 Hexanes: EtOAc, to give the title compound as a colorless oil (0.890 g, 74 % yield). Spectral data for **62**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29-7.17 (m, 5H), 4.96 (s, 1H), 4.84 (t, *J* = 1.6 Hz, 1H), 4.25-4.19 (m, 1H), 3.68 (t, *J* = 6.8 Hz, 2H), 3.37 (d, *J* = 8.4 Hz, 1H), 2.49-2.28 (m, 4H), 1.82 (d, *J* = 4.4 Hz, 1H), 1.58 (s, 3H), 0.85 (s, 9H), 0.03 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.4, 139.4, 128.9, 128.4, 126.8, 112.6, 80.0, 77.4, 69.9, 62.2, 58.1, 25.9, 25.8, 23.2, 21.4, 18.3, -5.3; IR (neat): 2957, 2176, 1498, 1248, 1217, 1047, 837, 758; IR (neat): 3305, 2960, 1495, 1424, 1209, 1137, 1049, 886, 829, 730, 702; LRMS (EI, Na) calculated for $C_{22}H_{35}O_2Si$; expected: 359.2 *m/z* $(M + H)^+$; observed, 359.3 *m/z* $(M + H)^+$.

Preparation of enantioenriched enyne coupling partners:

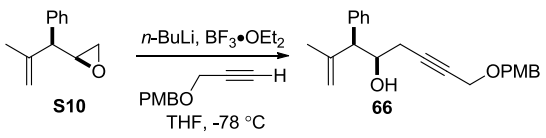


(*S*)-9-((4-methoxybenzyl)oxy)-2-methylnon-1-en-6-yn-4-ol (37): **S11** was prepared according to the procedure described for **S4** using (*R*)-epichlorohydrin (0.490 g), yielding **S11** in 87% yield (1.3 g). **37** was prepared according to the procedure for the synthesis of **43** (yield = 1.0 g, 80% over 2 steps from **S11**). Spectral data for **37**: $[\alpha]_D^{26.1}$ = +24.3 (*c* = 0.97, $CHCl_3$) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.8 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 4.87-4.86 (m, 1H), 4.80-4.79 (m, 1H), 4.48 (s, 2H), 3.89-3.82 (m, 1H), 3.80 (s, 3H), 3.54 (t, *J* = 6.8 Hz, 2H), 2.50-2.18 (m, 6H), 2.07 (br s, 1H), 1.76 (s, 3H); ^{13}C NMR (100

MHz, $CDCl_3$) δ 159.2, 142.3, 130.1, 129.3, 113.8, 113.4, 79.8, 72.6, 68.3, 67.7, 55.2, 44.8, 27.2, 22.4, 20.2; IR (thin film, NaCl) 3391, 2912, 2861, 1612, 1513, 1247, 1091, 1035 cm^{-1}; LRMS (EI, Na) calcd for $C_{18}H_{25}O_3$, 289.2 *m/z* (M + H); observed, 289.2 $(M + H)^+$ *m/z*. **37** was determined to possess an enantioenrichment of 92%. Enantioenrichment for **37** was determined through the preparation of the corresponding Mosher's ester.



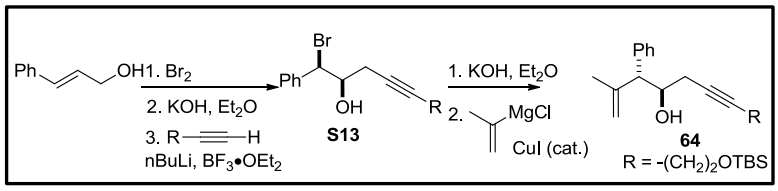
(*R*)-9-((4-methoxybenzyl)oxy)-2-methylnon-1-en-6-yn-4-ol (S12): The chlorohydrin was prepared according to the procedure described for **S4** using (*S*)-epichlorohydrin (0.550 g). **S12** was prepared according to the procedure for the synthesis of **37** (yield = 1.04 g, 63% from (*S*)-epichlorohydrin). Spectral data for **S12**: $[\alpha]_D^{25.4} = -21.0$ (*c* = 1.1, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.8 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 4.87-4.86 (m, 1H), 4.80-4.79 (m, 1H), 4.48 (s, 2H), 3.89-3.82 (m, 1H), 3.80 (s, 3H), 3.54 (t, *J* = 6.8 Hz, 2H), 2.50-2.18 (m, 6H), 2.07 (br s, 1H), 1.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 142.3, 130.1, 129.3, 113.8, 113.4, 79.8, 72.6, 68.3, 67.7, 55.2, 44.8, 27.2, 22.4, 20.2; IR (thin film, NaCl) 3391, 2912, 2861, 1612, 1513, 1247, 1091, 1035 cm^{-1}; LRMS (EI, Na) calcd for $C_{18}H_{25}O_3$, 289.2 *m/z* (M + H); observed, 289.2 $(M + H)^+$ *m/z*.. **S12** was determined to possess an enantioenrichment of $\geq$ 95%. Enantioenrichment for **S12** was determined through the preparation of the corresponding Mosher's ester.

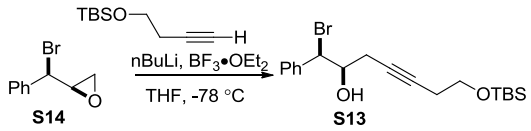


(+/-) (3*S*,4*R*)-8-((4-methoxybenzyl)oxy)-2-methyl-3-phenyloct-1-en-6-yn-4-ol (66): The general procedure for epoxide opening was followed using **S10** (0.500 g) and 1-methoxy-4-((prop-2-yn-1-

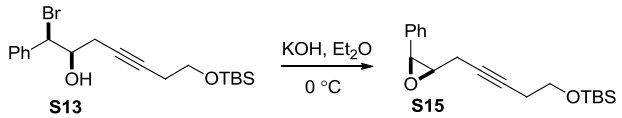
yloxy)methyl)benzene[7] (1.19 g). **66** was obtained as a colorless oil in 67% yield (0.730 g). Characterization data for **66**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28-7.13 (m, 7H), 6.80 (d, *J* = 8.8 Hz, 2H), 4.94 (d, *J* = 0.4 Hz, 1H), 4.83 (d, *J* = 1.6 Hz, 1H), 4.46 (s, 2H), 4.25 (ddd, *J* = 11.2, 6.4, 4.4 Hz, 1H), 4.09 (t, *J* = 2.0 Hz, 2H), 3.71 (s, 3H), 3.37 (d, *J* = 8.4 Hz, 1H), 2.54 (ddt, *J* = 16.8, 4.0, 2.4 Hz, 1H), 2.39 (ddt, *J* = 16.8, 6.4, 2.0 Hz, 1H), 1.90 (br. s, 1H), 1.56 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.3, 145.3, 139.1, 129.7, 129.5, 128.8, 128.5, 127.0, 113.8, 112.7, 83.3, 78.7, 71.0, 69.9, 58.1, 57.3, 55.2, 25.8, 21.5; IR (neat): 3425, 2911, 1611, 1512, 1217, 1173, 1065, 1031, 895, 819, 699; LRMS (EI, Na): calculated for $C_{23}H_{27}O_3$; expected: 351.2; observed: 351.2 $(M+H)^+$ *m/z*.

Preparation of *Anti*- Coupling Partner **64**:

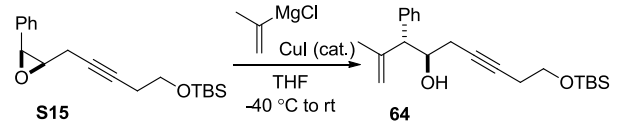




(1R,2R)-1-bromo-7-((tert-butyldimethylsilyl)oxy)-1-phenylhept-4-yn-2-ol (S13): The general procedure for epoxide opening was followed using **S14** (0.920 g, 4.3 mmol, 1.0 equiv) [10] and (but-3-yn-1-yloxy)(tert-butyl)dimethylsilane (1.75 g, 9.44 mmol, 2.5 equiv). The title compound was isolated as a colorless oil (1.15 g, 67%). Characterization data for **S13**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46-7.29 (m, 5H), 5.17 (d, *J* = 7.1 Hz, 1H), 4.04 (dq, *J* = 10.7, 5.3 Hz, 1H), 3.71 (t, *J* = 7.0 Hz, 2H), 2.64 (d, *J* = 5.2 Hz, 1H), 2.48-2.37 (m, 3H), 2.25-2.18 (m, 1H), 0.90 (s, 9H), 0.08 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.85, 128.81, 128.77, 128.10, 80.74, 75.73, 73.50, 62.07, 61.19, 25.88, 24.79, 23.19, 18.32, -5.27, -5.28; IR (neat): 3442, 2953, 1471, 1255, 1099, 835, 776, 697; LRMS (EI, Na) expected: 397.1 *m/z* $(M + H)^+$; observed, 397.2 *m/z* $(M + H)^+$.



tert-butyldimethyl((5-((2R,3S)-3-phenyloxiran-2-yl)pent-3-yn-1-yl)oxy)silane (S15): A 25-mL round-bottomed flask was charged with **S13** (0.800 g, 2.0 mmol, 1.0 equiv) and diethyl ether (12 mL). The resulting solution was cooled to 0 °C, and freshly-powdered KOH (1.12 g, 20 mmol, 10 equiv) was added in small portions. After stirring the resulting suspension for 3h at the same temperature, TLC analysis indicated complete consumption of the starting material. The organic phase was decanted into a separatory funnel, and the remaining solid was washed with ether. The combined organic extracts were washed with saturated aqueous $NaHCO_3$ and dried with Na_2SO_4. Concentration in vacuo afforded a crude oil, which was purified via flash chromatography, eluting with 90:10 hexanes:Et_2O, to give the title compound as a colorless oil (0.330 g, 52%). Characterization data for **S15**:^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.28 (m, 5H), 4.12 (d, *J* = 4.1 Hz, 1H), 3.67 (t, *J* = 7.1 Hz, 2H), 3.39 (ddd, *J* = 6.5, 5.6, 4.1 Hz, 1H), 2.37-2.29 (m, 3H), 2.05-1.98 (m, 1H), 0.89 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 134.63, 128.13, 127.77, 126.49, 79.08, 76.00, 62.08, 57.47, 57.29, 25.88, 23.13, 18.32, 18.07, -5.28; IR (neat): 2928, 1471, 1255, 1101, 835, 776, 699, 662; LRMS (EI, Na) expected: 317.2 *m/z* $(M + H)^+$; observed, 317.2 *m/z* $(M + H)^+$.

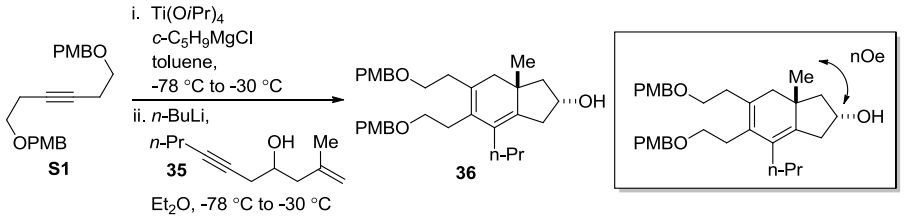


(3R,4R)-9-((tert-butyldimethylsilyl)oxy)-2-methyl-3-phenylnon-1-en-6-yn-4-ol (64): The general procedure for epoxide opening with isopropenyl Grignard reagents was followed using **S15** (0.330 g, 1.55 mmol, 1.0 equiv). The title compound was isolated as a light yellow oil (0.250 g, 62%). Spectral data for **64**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.16 (m, 5H), 5.12 (s, 1H), 5.01 (t, *J* = 4.0 Hz, 1H), 4.19 (ddd, *J* = 10.0, 6.7, 3.5 Hz, 1H), 3.71 (t, *J* = 7.2 Hz, 2H), 3.36 (d, *J* = 9.8 Hz, 1H), 2.43-2.26 (m, 3H), 2.14-2.00 (m, 1H), 1.70 (s, 3H), 0.90 (s, 9H), 0.07 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.57, 139.96, 128.53,

128.23, 126.95, 111.93, 80.04, 70.22, 62.23, 58.83, 25.89, 25.31, 23.25, 21.80, 18.33, -5.28; IR (neat): 3443, 2953, 1644, 1471, 1253, 1098, 834, 775; LRMS (EI, Na) expected: 359.2 *m/z* $(M + H)^+$; observed, 359.3 *m/z* $(M + H)^+$.

IV. General Method for Titanium-Mediated Coupling Reactions and Representative Stereochemical Assignment:

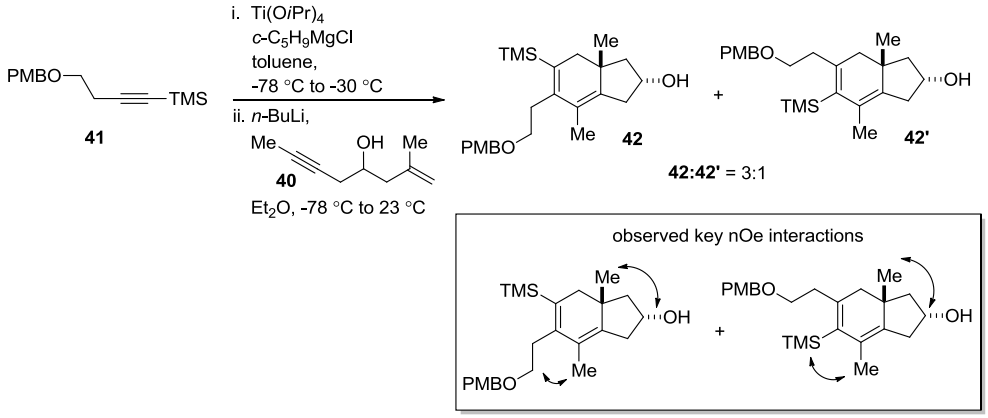
The following general procedure was followed for all carbocycle syntheses in Tables 1 and 2. For subsequent entries: final reaction temperatures, masses/yields of the obtained products, and information about diastereo- and regio-selectivity are given. Yields are for individual experiments and may differ from those reported in the manuscript tables, which are averages of at least two experiments.



5,6-bis(2-(4-methoxybenzyloxy)ethyl)-3a-methyl-7-propyl-2,3,3a,4-tetrahydro-1*H*-inden-2-ol (36). To a solution of alkyne **S1** (106 mg, 0.3 mmol) in toluene (3.0 mL) was added Ti(O*i*-Pr)$_4$ (0.088 mL, 0.3 mmol) in a dropwise manner via a dry gas-tight syringe, followed by cooling to −78 ^{o}C. To the clear, colorless solution was added *c*-C_5H_9MgCl (1.18 M in diethyl ether, 0.6 mmol), in a dropwise manner via gas-tight syringe. The resulting yellow-brown solution was then slowly warmed to −30 ^{o}C over 30 min, stirred for 1 h, then cooled to −78 ^{o}C to afford a black solution. To a separate −78 ^{o}C solution of enyne **35** (15 mg, 0.09 mmol) in Et_2O (0.5 mL) was added *n*-BuLi (2.4 M in hexanes, 0.099 mmol) in a dropwise manner via gas-tight syringe. The resulting solution was removed from the cold bath and allowed to stir for 20 minutes, followed by dropwise transfer via cannula into the original −78 ^{o}C black titanium solution (with 0.5 mL Et_2O to rinse the cannula). The reaction vessel was then slowly warmed to −30 ^{o}C, stirred for 12 h, and warmed to 0 ^{o}C for 3h then quenched with sat. NH_4Cl (5 mL). The resulting aqueous layer

was extracted with Et_2O. The combined organic extracts were then washed with saturated aqueous $NaHCO_3$ and brine and dried over anhydrous $MgSO_4$. The resulting crude material was purified via flash chromatography, eluting with 90:10 to 40:60 EtOAc-hexanes, to provide 39 mg (83%) of carbocycle **36** (diastereomeric ratio $\geq$ 20:1). **Spectral Data for 36**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.8 Hz, 4H), 6.86 (d, *J* = 8.8 Hz, 4H), 4.49-4.48 (m, 1H), 4.38 (s, 2H), 4.35 (s, 2H), 3.79 (s, 6H), 3.46 (t, *J* = 7.8 Hz, 2H), 3.34-3.28 (m, 2H), 2.81 (dd, *J* = 17.7, 7.8 Hz, 1H), 2.72-2.64 (m, 1H), 2.59-2.52 (m, 1H), 2.39-2.26 (m, 3H), 2.15-1.93 (m, 5H), 1.48-1.43 (m, 2H), 1.33-1.20 (m, 2H), 0.87 (t, *J* = 7.3 Hz, 3H), 0.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 159.0, 140.9, 130.8, 130.6, 129.3, 129.2, 128.9, 128.9, 128.2, 113.7, 72.6, 72.5, 72.0, 70.1, 68.6, 55.3, 50.8, 43.1, 39.6, 38.4, 34.4, 31.7, 29.7, 28.2, 22.5, 21.7, 14.0; IR (thin film, NaCl) 3435, 2955, 2929, 2857, 1612, 1513, 1463, 1302, 1248, 1173, 1092, 1035 cm^{-1}; LRMS (EI, Na) calcd for $C_{33}H_{44}NaO_5$, 543.3 (M + Na); observed, 543.4 (M + Na)$^+$ *m/z*.

Representative Spectral Analysis of Stereo- and Regioselectivity

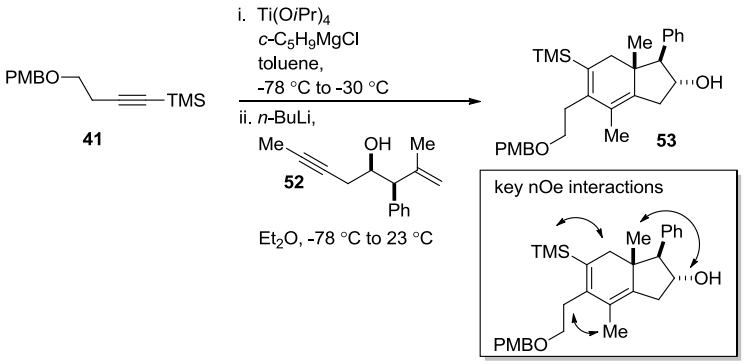


(+/-)-(2*S*,3a*S*)-6-(2-((4-methoxybenzyl)oxy)ethyl)-3a,7-dimethyl-5-(trimethylsilyl)-2,3,3a,4-tetrahydro-1H-inden-2-ol (42): Prepared according to the general procedure for titanium-mediated coupling reactions using 0.021 g (0.15 mmol, 1.0 equiv) of enyne **40** and 0.130 g (0.495 mmol, 3.3 equiv) of alkyne **41** and warming to a final temperature of 23 °C for 16h. The desired carbocycle was formed as a 3:1 inseparable mixture of regioisomers and with diastereomeric ratio: >20:1. The crude material was

purified via flash chromatography, eluting with 85:15 to 80:20 hexanes:EtOAc. The title compound was isolated as a colorless oil (mixture of regioisomers, combined yield: 46 mg, 75%).

Although not shown here, in cases where inseparable mixtures of regioisomers were isolated, it was found that stirring the carbocycles in a 1:1 mixture of 1M HCl and THF for 24h led to selective protodesilylation of the major regioisomers (through a stabilized allylic carbocationic intermediate not accessible from the minor regioisomers) and generally allowed for the protodesilylated products to be isolated as single isomers. See the procedure for the synthesis of **S21 for a more detailed procedure.

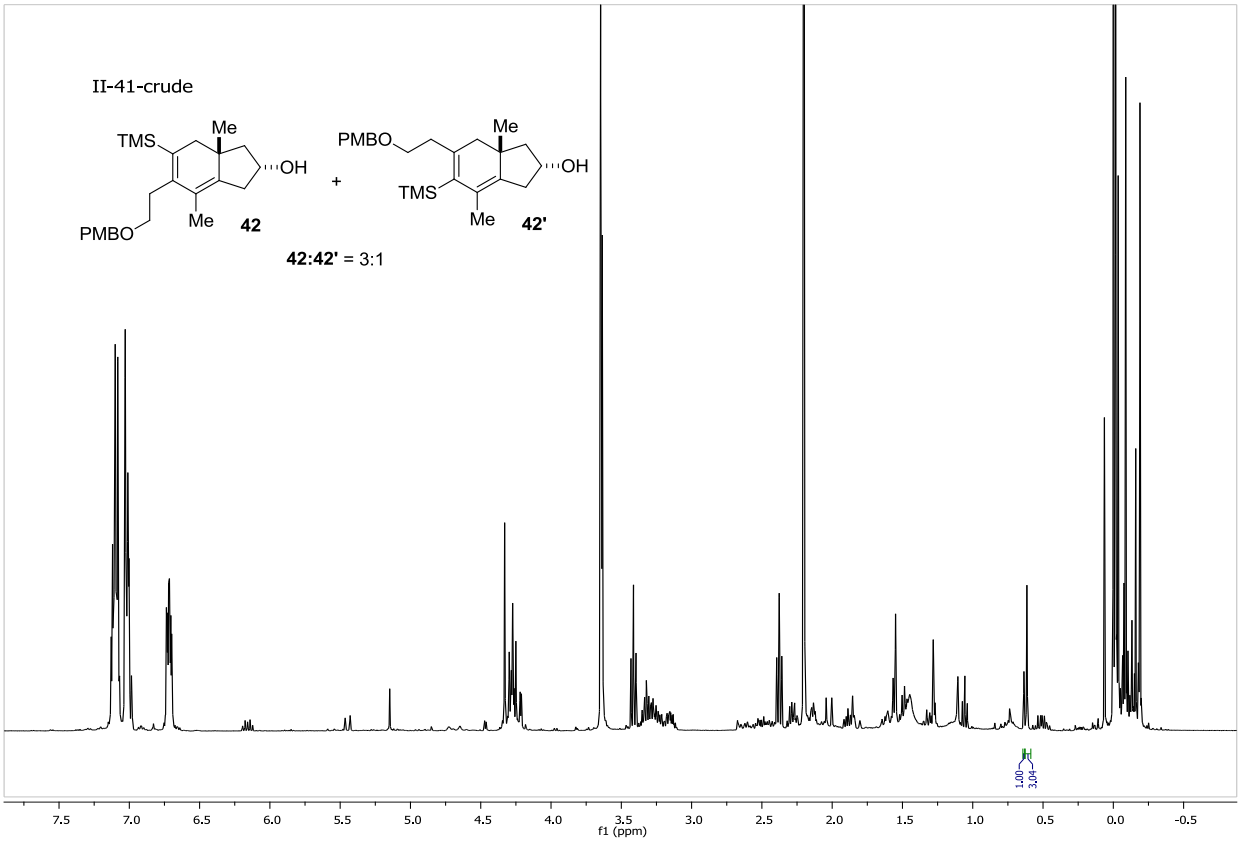
Spectral Data for **42** and **42'** (inseparable mixture of regioisomers): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.4 Hz, 2H), 7.23 (d, *J* = 2H), 6.85 (d, *J* = 8.4 Hz, 2H), 6.84 (d, *J* =8.8 Hz, 2H), 4.48-4.40 (m, 1H), 4.48-4.40 (m, 1H), 4.44 (s, 2H), 4.41 (s, 2H), 3.78 (s, 3H), 3.78 (s, 3H), 3.52-3.24 (m, 2H), 3.52-3.24 (m, 2H), 2.79-2.50 (m, 3H), 2.79-2.50 (m, 3H), 2.76 (dd, *J* = 18.0, 7.2 Hz, 1H), 2.31-1.93 (m, 3H), 2.15 (d, *J* = 16.0 Hz, 1H), 2.01-1.93 (m, 2H), 1.95 (d, *J* = 16.0 Hz, 1H), 1.78 (br. s, 1H), 1.72 (br. s, 1H), 1.69 (s, 3H), 1.68 (s, 3H), 1.43 (dd, *J* = 12.4, 8.4 Hz, 1H), 1.41 (dd, *J* = 10.8, 8.0 Hz, 1H), 0.76 (s, 3H), 0.74 (s, 3H), 0.19 (s, 9H), 0.11(s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 159.1, 144.5, 144.2, 142.6, 138.3, 133.7, 129.2, 129.2, 129.1, 128.6, 127.1, 124.3, 113.7, 113.7, 72.6, 72.6, 71.9, 71.9, 69.0, 55.2, 51.0, 50.7, 44.8, 41.3, 39.1, 38.8, 38.5, 38.1, 32.9, 21.0, 21.0, 19.1, 15.3, 2.7, 0.1; IR (neat): 3379, 2949, 1612, 1512, 1245, 1088, 1035, 833, 755; LRMS (EI, Na): calculated for $C_{24}H_{37}O_5Si$, expected: 401.2 $(M+H)^+$, observed: 401.2 $(M+H)^+$.

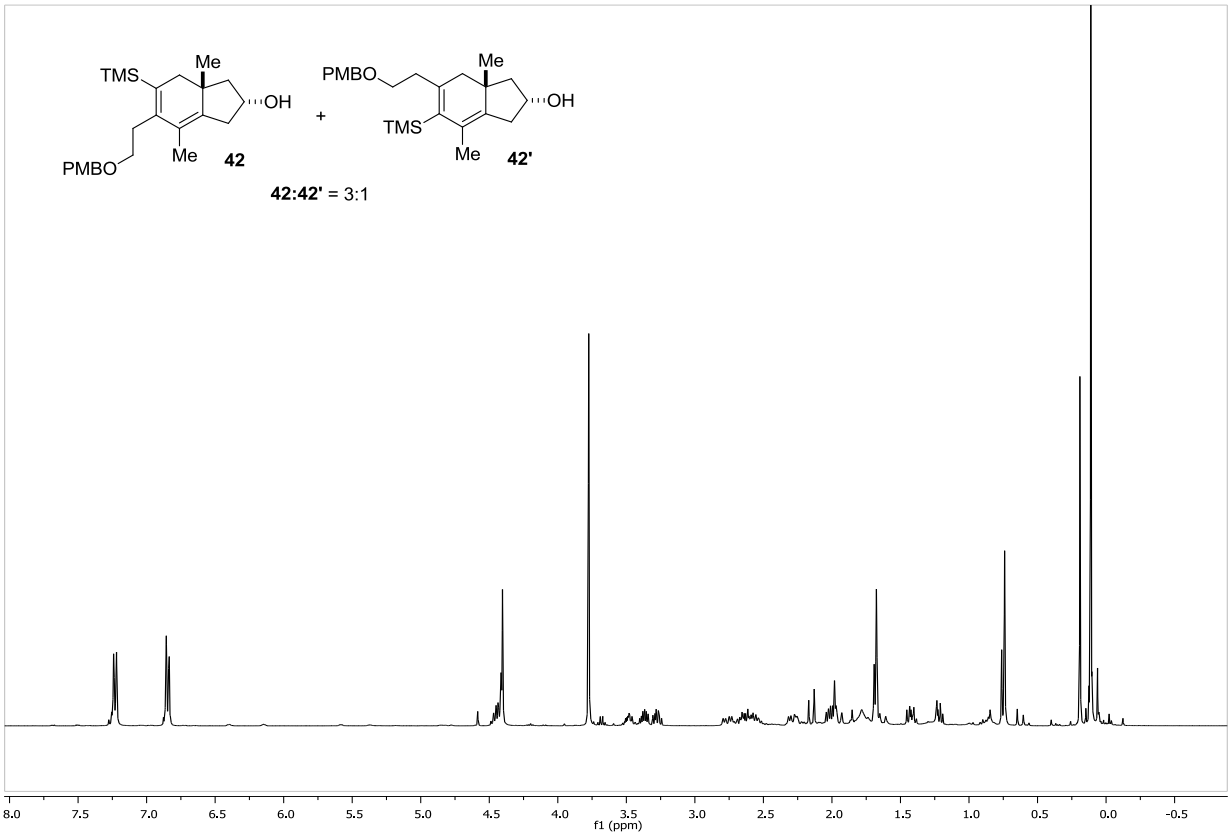


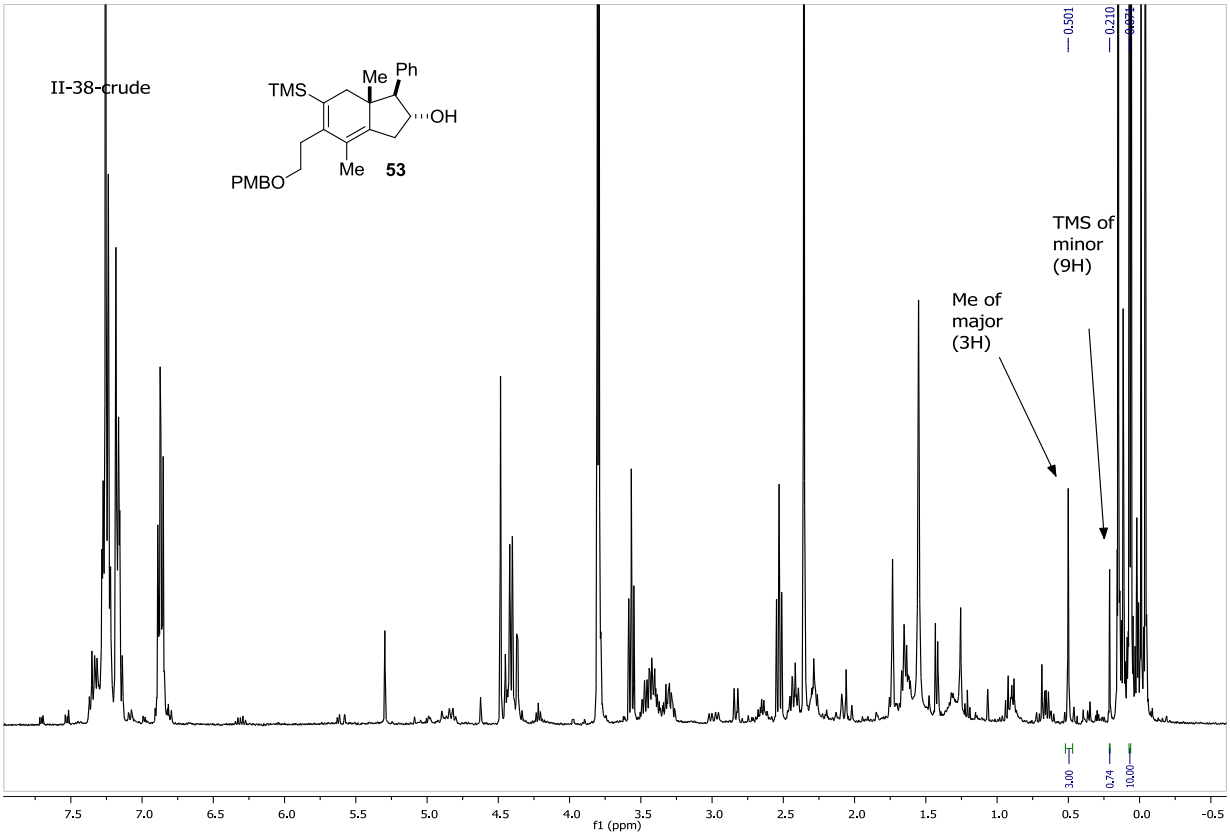
(+/-)-(2*R*,3*R*,3a*R*)-6-(2-((4-methoxybenzyl)oxy)ethyl)-3a,7-dimethyl-3-phenyl-5-(trimethylsilyl)-2,3,3a,4-tetrahydro-1H-inden-2-ol (53): Prepared according to the general procedure for titanium-mediated coupling reactions using 0.032 g (0.150 mmol, 1.0 equiv) of enyne **52** and 0.130 g (0.495 mmol, 3.3 equiv) of alkyne **41** and warming to a final temperature of 23 °C for 16h. The desired carbocycle was formed as a separable 13:1 mixture of regioisomers, each with a diastereomeric ratio: >20:1. The title compound was isolated as a colorless oil (single isomer, yield: 0.045 g, 64%). Spectral Data for **53**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.21 (m, 7H), 6.86 (d, *J* = 8.8 Hz, 2H), 4.81 (dd, *J* = 18.8, 8.4 Hz, 1H), 4.41 (s, 2H), 3.79 (s, 3H), 3.43-3.26 (m, 2H), 2.97 (dd, *J* = 18.0, 8.0 Hz, 1H), 2.82 (d, *J* = 10.4 Hz, 1H), 2.70-2.57 (m, 2H), 2.42 (dd, *J* = 18.4, 8.4 Hz, 1H), 2.10 (d, *J* = 15.6 Hz, 1H), 2.03 (d, *J* = 16.0 Hz, 1H), 1.73 (s, 3H), 0.49 (s, 3H), 0.07 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 142.9, 142.8, 137.8, 130.6, 129.4, 129.2, 128.9, 128.4, 126.8, 125.1, 113.7, 73.1, 72.6, 70.5, 65.6, 55.3, 43.0, 40.4, 36.6, 32.9, 15.9, 15.1, 0.1; IR (neat): 3342, 2954, 1612, 1512, 1246, 1084, 1017, 830, 733, 702; LRMS (EI, Na): calculated for $C_{30}H_{41}O_3Si$, expected: 477.3 $(M+H)^+$, observed: 477.3 $(M+H)^+$.

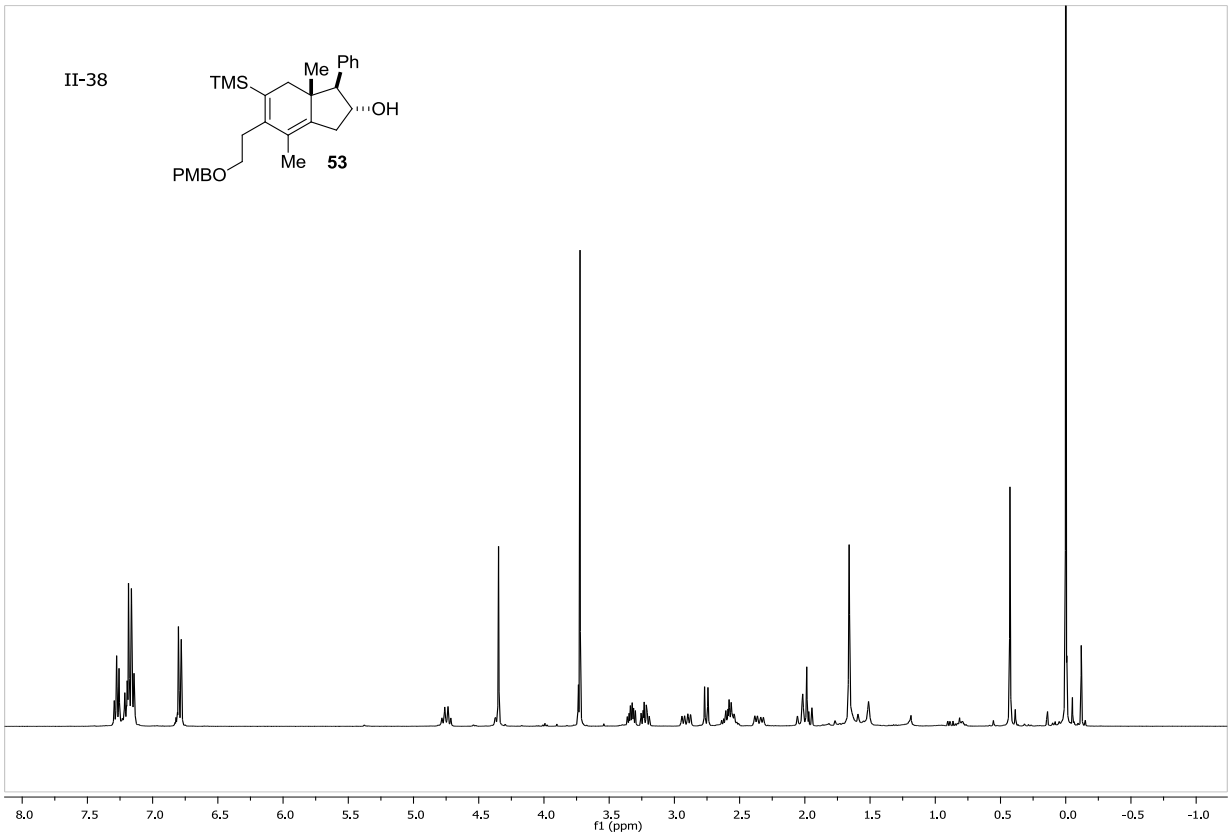
**Representative procedure for determination of diastereoselectivity and regioselectivity:

Diastereoselectivity and regioselectivity were determined by analysis of the ^{1}H NMR spectra of the crude material. COSY and NOESY analysis supported the assignments of the major stereoisomers indicated. Representative crude NMR spectra for compounds **42/42'** (3:1 regioisomeric ratio) and **53** (12:1 regioisomeric ratio) are shown below.

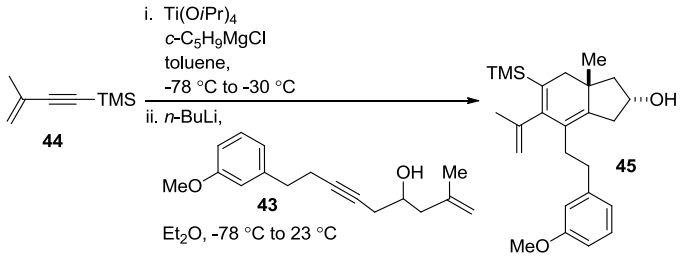

II-41-crude
TMS
Me
OH
PMBO
Me
42
+
PMBO
Me
OH
TMS
Me
42'
42:42' = 3:1
1.00
3.04
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


TMS
Me
OH
PMBO
Me
42
+
PMBO
Me
OH
TMS
Me
42'
42:42' = 3:1
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

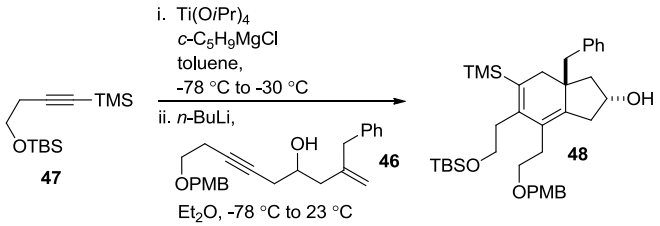

II-38-crude
TMS
Me
Ph
OH
PMBO
Me
53
TMS of minor (9H)
Me of major (3H)
0.501
0.210
3.00
0.74
10.00
f1 (ppm)


II-38
TMS
Me
Ph
OH
PMBO
Me
53
f1 (ppm)

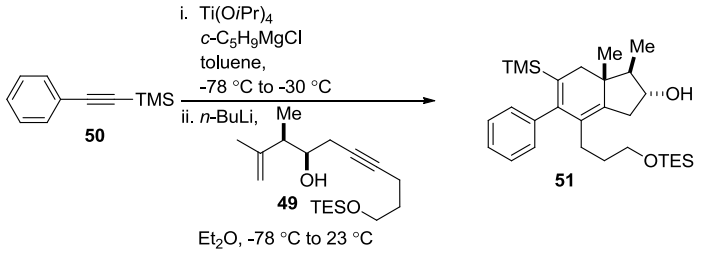
V. Carbocycle Synthesis: Procedures and Characterization Data



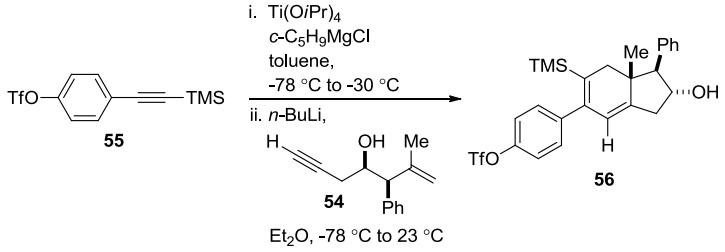
(+/-) 7-(3-methoxyphenethyl)-3a-methyl-6-(prop-1-en-2-yl)-5-(trimethylsilyl)-2,3,3a,4-tetrahydro-1*H*-inden-2-ol (45): Prepared according to the general procedure for titanium-mediated coupling reactions using 0.023 g (0.09 mmol, 1.0 equiv) of enyne **43** and 0.041 g (0.3 mmol, 3.3 equiv) of alkyne **44** and warming to a final temperature of 23 °C for 16h. The title compound was formed as a separable 4:1 mixture of regioisomers and with diastereomeric ratio $\geq$ 20:1. The crude material was purified via flash chromatography, eluting with 80:20 hexanes:EtOAc. The title compound was isolated as a colorless oil (single isomer: 0.019 g, 53% yield). ^{1}H and ^{13}C NMR spectra showed evidence of hindered rotation around the isopropenyl group: ^{1}H NMR spectrum: broad Me singlet at 1.80 ppm, broad vinyl signals at 5.05 and 4.85 ppm; ^{13}C spectrum: suppressed signal for vinyl carbons at 146.2 and 128.2 ppm, suppressed Me peak at 40.6 ppm, and three singlets for the TMS group at 0.3 ppm)[11]. Spectral data for **45**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (t, *J* = 7.8 Hz, 1H), 6.75-6.68 (m, 3H), 5.05-5.04 (m, 1H), 4.86-4.85 (m, 1H) 4.45-4.38 (s, 3H), 2.73 (dd, *J* = 17.9, 7.6 Hz, 1H), 2.66-2.59 (m, 1H), 2.52-2.45 (m, 1H), 2.28-2.22 (m, 3H), 2.07-2.00 (m, 3H), 1.80 (br s, 3H), 1.40 (dd, *J* = 12.4, 8.3 Hz, 1H), 1.26 (br s, 1H), 0.83 (s, 3H) 0.11 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 146.2, 144.1, 129.1, 128.2, 121.2, 115.6, 114.7, 110.7, 77.3, 71.8, 55.1, 51.1, 40.6, 39.5, 38.2, 35.9, 32.1, 24.5, 20.8, 0.3 (three coincident resonances- hindered rotation of TMS group); IR (thin film, NaCl) 3401, 2950, 1638, 1602, 1246, 1151, 1094, 1057 cm^{-1}; LRMS (EI, Na) calcd for $C_{25}H_{37}O_2Si$, 397.3 *m/z* (M + H); observed, 397.3 $(M + H)^+$ *m/z.*



(2*S*,3a*S*)-3a-benzyl-6-(2-((tert-butyldimethylsilyl)oxy)ethyl)-7-(2-((4-methoxybenzyl)oxy)ethyl)-5-(trimethylsilyl)-2,3,3a,4-tetrahydro-1H-inden-2-ol (48): Prepared according to the general procedure for titanium-mediated coupling reactions using 0.072 g (0.2 mmol, 1.0 equiv) of enyne **46** and 0.170 g (0.65 mmol, 3.3 equiv) of alkyne **47** and warming to a final temperature of 23 °C for 16h. The title compound was formed as a separable 5:1 mixture of regioisomers and with diastereomeric ratio $\geq$ 20:1. The crude material was purified via flash chromatography, eluting with 85:15 hexanes:EtOAc. The title compound was isolated as a colorless oil (single isomer, 0.068 g, 55% yield). Spectral data for **48**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25-7.17 (m, 5H), 7.04 (dd, *J* = 8.0, 1.6 Hz, 2H), 6.85 (d, *J* = 8.8 Hz, 2H), 4.45 (d, *J* = 12.0 Hz, 1H), 4.39 (d, *J* = 12.0 Hz, 1H), 4.06 (p, *J* = 5.2 Hz, 1H), 3.79 (s, 3H), 3.67-3.30 (m, 4H), 2.70 (d, *J* = 12.8 Hz, 1H), 2.69-2.14 (m, 7H), 2.26 (d, *J* = 13.2 Hz, 1H), 1.99 (dd, *J* = 16.8, 2.0 Hz, 1H), 1.39 (dd, *J* = 13.2, 5.2 Hz, 1H), 1.02 (br. s, 1H), 0.89 (s, 9H), 0.19 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.1, 145.8, 142.9, 139.3, 132.2, 130.3, 130.2, 129.2, 127.8, 127.1, 125.9, 113.7, 72.5, 71.9, 68.7, 63.9, 55.2, 46.9, 43.7, 40.3, 39.7, 38.9, 36.4, 30.1, 26.0, 18.4, 0.6, -5.2, -5.3; IR (neat): 3411, 2951, 2855, 1612, 1512, 1248, 1087, 909, 885, 731, 702; LRMS (EI, Na): calculated for $C_{37}H_{56}O_4Si_2Na$; expected: 643.4; observed: 643.4 $(M+Na)^+$.

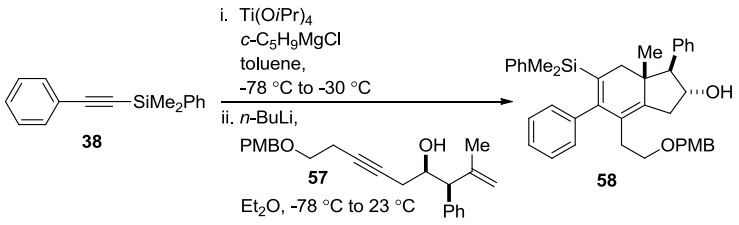


(+/-) (2R,3R,3aR)-3,3a-dimethyl-6-phenyl-7-(3-((triethylsilyl)oxy)propyl)-5-(trimethylsilyl)-2,3,3a,4-tetrahydro-1H-inden-2-ol (51): Prepared according to the general procedure for titanium-mediated coupling reactions using 0.060 g (0.189 mmol, 1.0 equiv) of enyne **49** and 0.109 g (0.625 mmol, 3.3 equiv) of alkyne **50** and warming to a final temperature of 23 °C for 16h. Carbocycle formation occurred with 3:1 regioisomeric ratio and $\geq$ 20:1 diastereomeric ratio. The crude material was purified via flash chromatography, eluting with 95:5 hexanes:EtOAc. The title compound was isolated as a colorless oil (mixture of regioisomers: 0.060 g, 63% yield). Spectral data for **51**: *major isomer:* ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53-7.26 (m, 5H), 4.18 (q, *J* = 8.8 Hz, 1H), 3.49 (t, *J* = 7.2 Hz, 2H), 3.09 (dd, *J* = 18.8, 8.4 Hz, 1H), 2.50 (d, *J* = 15.6 Hz, 1H), 2.44 (d, *J* = 8.0 Hz, 4.0 Hz, 1H), 2.18 (d, *J* = 15.2 Hz, 1H), 2.10-1.38 (m, 6H), 1.25 (d, *J* = 6.8 Hz, 3H), 1.08 (t, *J* = 7.6 Hz, 9H), 0.98 (s, 3H), 0.69 (q, *J* = 8.0 Hz, 6H), 0.09 (s, 9H), *minor isomer*: 7.53-7.26 (m, 5H), 4.18 (q, *J* = 8.8 Hz, 1H), 3.83-3.76 (m, 2H), 3.11 (dd, *J* = 17.6, 8.0 Hz, 1H), 2.57 (d, *J* = 16.8 Hz, 1H), 2.44 (d, *J* = 8.0 Hz, 4.0 Hz, 1H), 2.27 (d, *J* = 16.8 Hz, 1H), 2.10-1.38 (m, 6H), 1.23 (d, *J* = 6.8 Hz, 3H), 1.14 (t, *J* = 8.0 Hz, 9H), 1.02 (s, 3H), 0.79 (q, *J* = 8.0 Hz, 6H), 0.00 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$), *mixture of isomers*: δ 149.5, 147.9, 145.7, 143.3, 142.3, 137.8, 133.3, 130.6, 129.0, 127.7, 127.4, 127.1, 126.5, 77.2, 77.1, 62.8, 62.7, 54.0, 53.7, 46.7, 39.9, 26.7, 32.0, 29.0, 25.7, 15.4, 15.0, 11.2, 4.4, 1.6, -0.8; IR (neat): 3376, 2954, 2876, 1489, 1247, 1097, 1015, 911, 837, 742; LRMS (EI, Na): calcd for $C_{29}H_{49}O_2Si_2$, 485.3 *m/z* (M +H); observed, 485.3 $(M+H)^+$ *m/z.*



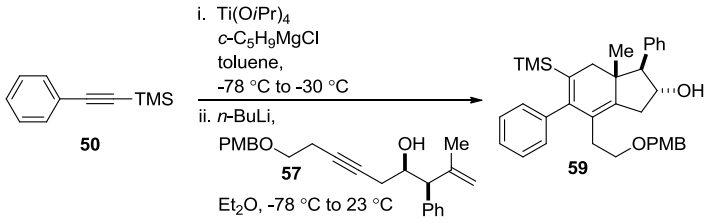
(+/-)-4-((1*R*,2*R*,7a*R*)-2-hydroxy-7a-methyl-1-phenyl-6-(trimethylsilyl)-2,3,7,7a-tetrahydro-1H-inden-5-yl)phenyl trifluoromethanesulfonate (56): Prepared according to the general procedure for titanium-mediated coupling reactions using 0.100 g (0.500 mmol, 1.0 equiv) of enyne **54** and 0.561 g (1.65 mmol, 3.3 equiv) of alkyne **55** and warming to a final temperature of 23 °C for 16h. Carbocycle

formation occurred with ≥ 20:1 regioisomeric and diastereomeric ratio. The crude material was purified via flash chromatography, eluting with 85:15 hexanes:EtOAc. The title compound was isolated as a colorless oil (single isomer, yield: 0.140 g, 52%). Spectral Data for **56**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46-7.26 (m, 9H), 5.83 (t, *J* = 2.2 Hz, 1H), 4.93 (dd, *J* = 18.3, 8.4 Hz, 1H), 3.14 (ddd, *J* = 18.8, 8.6, 1.5 Hz, 1H), 2.98 (d, *J* = 10.0 Hz, 1H), 2.56 (dd, *J* = 18.8, 8.1 Hz, 1H), 2.39 (d, *J* = 16.0 Hz, 1H), 2.29 (d, *J* = 16.0 Hz, 1H), 1.81 (br. s, 1H), 0.75 (s, 3H), -0.20 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.5, 148.5, 144.8, 144.3, 137.5, 130.8, 130.1, 128.9, 128.5, 127.1, 120.8, 120.8, 117.2, 72.9, 65.2, 42.9, 40.5, 36.8, 16.1, -0.9; IR (neat): 3342, 2957, 1601, 1495, 1424, 1248, 1209, 1138, 1017, 884, 834, 751, 699; LRMS (EI): calculated for $C_{26}H_{29}F_3O_4SSiNa$, expected: 545.2 $(M+Na)^+$, observed: 545.4 $(M+Na)^+$.

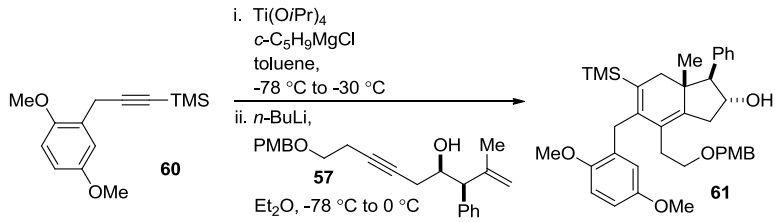


(+/-)-(2*R*,3*R*,3a*R*)-5-(dimethyl(phenyl)silyl)-7-(2-((4-methoxybenzyl)oxy)ethyl)-3a-methyl-3,6-diphenyl-2,3,3a,4-tetrahydro-1H-inden-2-ol (58): Prepared according to the general procedure for titanium-mediated coupling using 0.066 g (0.18 mmol,1.0 equiv) of enyne **57** and 0.142 g (0.6 mmol, 3.3 equiv) of alkyne **38** and warming to a final temperature of 23 °C for 16h. Carbocycle formation occurred with ≥ 20:1 regioisomeric and diastereomeric ratio. The crude material was purified via flash chromatography, eluting with 90:10 to 70:30 hexanes:EtOAc. The title compound was obtained as a colorless oil (single isomer: 0.062 g, 57 % yield). Spectral data for **58**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24-6.85 (m, 19H), 4.86 (dd, *J* = 18.5, 8.4 Hz, 1H), 4.24 (d, *J* = 12.0 Hz, 1H), 4.19 (d, *J* = 12.0 Hz, 1H), 3.80 (s, 3H), 3.22-3.05 (m, 3H), 2.87 (d, *J* = 10.2 Hz, 1H), 2.52 (dd, *J* = 18.7, 8.2 Hz, 1H), 2.31-2.05 (m, 4H), 1.72 (br. s, 1H), 0.62 (s, 3H), -0.10 (s, 3H), -0.23 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.0, 149.3, 145.4, 141.5, 139.6, 137.5, 133.6, 130.8, 129.0, 128.8, 128.8, 128.6, 128.4, 128.4, 127.6, 127.4, 126.9, 126.8, 126.2, 113.7, 72.9, 72.1, 68.5, 65.4, 55.3, 43.4, 40.4, 36.4, 30.1, 16.1, -1.9, -2.3; IR (neat):

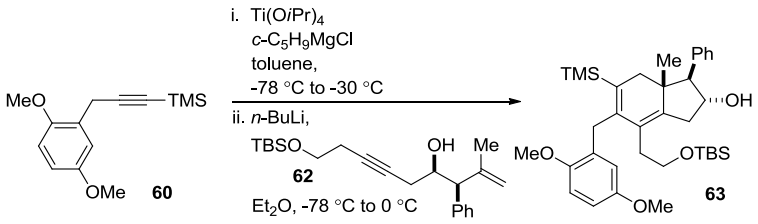
3375, 2959, 1668, 1610, 1512, 1248, 1077, 1032, 820, 730, 700; LRMS (EI, Na): calcd for $C_{34}H_{39}O_3Si$, 523.3 *m/z* (M -Ph); observed, 523.2 $(M - Ph)^+$ *m/z.*



(+/-) (2*R*,3*R*,3a*R*)-7-(2-((4-methoxybenzyl)oxy)ethyl)-3a-methyl-3,6-diphenyl-5-(trimethylsilyl)-2,3,3a,4-tetrahydro-1H-inden-2-ol (59): Prepared according to the general procedure for titanium-mediated coupling reactions using 0.200 g (0.546 mmol, 1.0 equiv) of enyne **57** and 0.314 g (1.8 mmol, 3.3 equiv) of alkyne **50** and warming to a final temperature of 23 °C for 16h. Carbocycle formation occurred with 17:1 regioisomeric ratio and $\geq$ 20:1 diastereomeric ratio. The crude material was purified via flash chromatography, eluting with 80:20 hexanes:EtOAc. The title compound was isolated as a colorless oil (single isomer: 0.168 g, 57% yield). Spectral data for **59**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.21 (m, 9H), 7.15 (d, *J* = 8.0 Hz, 2H), 6.86 (d, *J* = 8.0 Hz, 2H), 6.76 (d, *J* = 9.1 Hz, 1H), 4.87 (q, *J* = 8.0 Hz, 1H), 4.25 (d, *J* = 12.0 Hz, 1H), 4.21 (d, *J* = 12.0 Hz, 1H), 3.81 (s, 3H), 3.24-3.01 (m, 3H), 2.92 (d, *J* = 8.0 Hz, 1H), 2.53 (dd, *J* = 16.0 Hz, 8.0 Hz, 1H), 2.32-2.09 (m, 4H), 1.77 (br. s, 1H), 0.70 (s, 3H), -0.35 (2, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.0, 147.7, 144.7, 141.9, 137.7, 130.8, 130.7, 129.0, 128.6, 128.4, 127.6, 126.9, 126.7, 126.1, 114.0, 113.7, 73.0, 72.1, 68.5, 65.6, 65.0, 55.3, 43.4, 40.0, 36.3, 30.1, 16.0, -1.0; IR (neat): 3376, 2957, 1672, 1610, 1512, 1246, 1075, 834, 702; LRMS (EI, Na): calcd for $C_{32}H_{33}O_3$, 465.3 *m/z* (M -TMS); observed, 465.3 $(M - TMS)^+$ *m/z.*

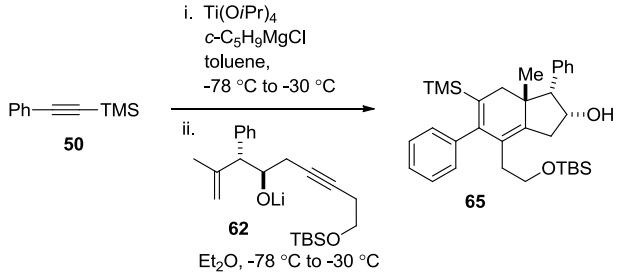


(+/-) (2*R*,3*R*,3a*R*)-6-(2,5-dimethoxybenzyl)-7-(2-((4-methoxybenzyl)oxy)ethyl)-3a-methyl-3-phenyl-5-(trimethylsilyl)-2,3,3a,4-tetrahydro-1H-inden-2-ol (61): Prepared according to the general procedure for titanium-mediated coupling reactions using 0.2 g (0.546 mmol, 1.0 equiv) of enyne **57** and 0.448 g (1.81 mmol, 3.3 equiv) of alkyne **60** and warming to a final temperature of 0 °C for 16h. Carbocycle formation occurred with ≥ 20:1 regioisomeric and diastereomeric ratio. The crude material was purified via flash chromatography, eluting with 85:15 to 75:25 hexanes:EtOAc. The title compound was obtained as a colorless oil. (single isomer: 0.194 g, 58% yield). Spectral data for **61**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.23 (m, 7H), 6.88 (d, *J* = 8.7 Hz, 2H), 6.76 (d, *J* = 8.8 Hz, 1H), 6.71 – 6.61 (m, 2H), 4.82 (q, *J* = 8.7 Hz, 1H), 4.37 (d, *J* = 12.0 Hz, 1H), 4.36 (d, *J* = 12.0 Hz, 1H), 3.81 (s, 6H), 3.74 (dd, *J* = 17.2, 2.4 Hz, 1H), 3.66 (s, 3H), 3.53 (d, *J* = 17.0 Hz, 1H), 3.38-3.26 (m, 2H), 3.03 (dd, *J* = 18.5, 8.4 Hz, 1H), 2.88 (d, *J* = 10.2 Hz, 1H), 2.47 (dd, *J* = 18.5, 8.2 Hz, 1H), 2.31-2.15 (m, 4H), 1.71 (br. s, 1H), 0.71 (s, 3H), 0.05 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.0, 153.5, 151.0, 145.2, 143.2, 137.8, 131.1, 130.9, 130.4, 129.0, 128.9, 128.4, 126.9, 126.9, 114.6, 113.7, 111.4, 110.9, 72.9, 72.3, 69.1, 65.8, 55.9, 55.5, 55.3, 43.1, 40.6, 36.4, 31.2, 29.7, 15.9, 0.1; IR (neat): 3376, 2957, 1672, 1610, 1512, 1246, 1075, 834, 702; LRMS (EI, Na) calculated for $C_{35}H_{39}O_5$, expected: 539.3 *m/z* $(M - TMS)^+$ observed, 539.3 *m/z* $(M - TMS)^+$.



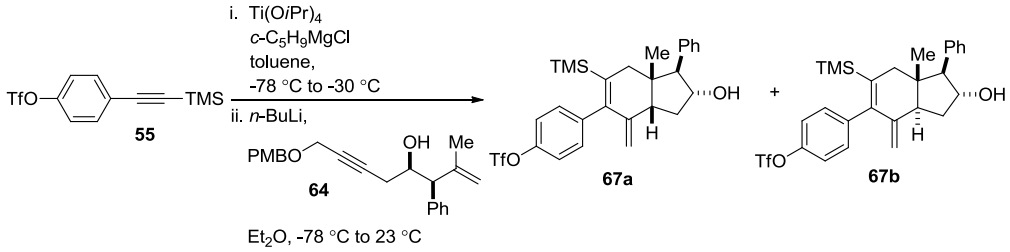
(+/-)-(2*R*,3*R*,3a*R*)-7-(2-((tert-butyldimethylsilyl)oxy)ethyl)-6-(2,5-dimethoxybenzyl)-3a-methyl-3-phenyl-5-(trimethylsilyl)-2,3,3a,4-tetrahydro-1H-inden-2-ol (63): Prepared according to the general procedure for titanium-mediated coupling reactions using 0.066 g (0.18 mmol, 1.0 equiv) of enyne **62** and 0.149 g (0.6 mmol, 3.3 equiv) of alkyne **60** and warming to a final temperature of 0 °C for 16h. Carbocycle formation occurred with ≥ 20:1 regioisomeric and diastereomeric ratio. The crude material

was purified via flash chromatography, eluting with 90:10 hexanes:EtOAc. The title compound was isolated as a colorless oil (single isomer, yield = 0.062 g, 54%). Spectral data for **63**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.25 (m, 5H), 6.75 (d, *J* = 8.0 Hz, 1H), 6.67 (dd, *J* = 8.0, 4.0 Hz, 1H), 6.61 (d, *J* = 4 Hz, 1H), 4.84 (dd, *J* = 18.6, 8.5 Hz, 1H), 3.81 (s, 3H), 3.80-3.68 (m, 1H), 3.66 (s, 3H), 3.56-3.45 (m, 3H), 3.05 (dd, *J* = 18.4, 8.4 Hz, 1H), 2.90 (d, *J* = 10.3 Hz, 1H), 2.50 (dd, *J* = 18.5, 8.3 Hz, 1H), 2.29-2.09 (m, 4H), 1.67 (br. s, 1H), 0.89 (s, 9H), 0.72 (s, 3H), 0.05 (s, 9H), 0.03 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.5, 151.1, 145.0, 143.5, 137.8, 130.8, 130.6, 128.9, 128.4, 127.3, 126.9, 114.6, 111.4, 110.8, 72.9, 65.8, 62.5, 55.9, 55.5, 43.1, 40.6, 36.6, 32.7, 31.3, 26.0, 18.3, 15.9, 1.0, 0.1, -5.4, -5.4; IR (neat): 3375, 2953, 1663, 1497, 1250, 1220, 1048, 834, 735, 701; LRMS (EI, Na): calcd for $C_{36}H_{55}O_4Si_2$, 606.4 *m/z* (M + H); observed, 606.4 $(M + H)^+$ *m/z*.



(+/-) (2R,3S,3aR)-7-(2-((tert-butyldimethylsilyl)oxy)ethyl)-3a-methyl-3,6-diphenyl-5-(trimethylsilyl)-2,3,3a,4-tetrahydro-1H-inden-2-ol (65): Prepared according to the general procedure for titanium-mediated coupling reactions using 0.050 g (0.139 mmol, 1.0 equiv) of enyne **62** and 0.080 g (0.46 mmol, 3.3 equiv) of alkyne **50** and warming to a final temperature of −30 °C for 16h. Product formation occurred as a largely intractable mixture of products, with the major product isolated from the reaction mixture being the isomer shown (yield: 0.016 g, 22%, isolated as a single diastereomer). Diastereoselectivity and regioselectivity could not be determined from the crude ^{1}H spectrum. The crude material was purified via flash chromatography, eluting with 95:5 hexanes:Et_2O, to afford the title compound as a light yellow oil. Spectral data for **65**: ^{1}H NMR (400 MHz, $CDCl_3$) δ) 7.40-7.10 (m, 5H), 4.91-4.83 (m, 1H), 3.39-3.29 (m, 2H), 3.26 (d, *J* = 6.8 Hz, 1H), 3.11 (dd, *J* = 18.8, 8.4 Hz, 1H), 2.63 (dd,

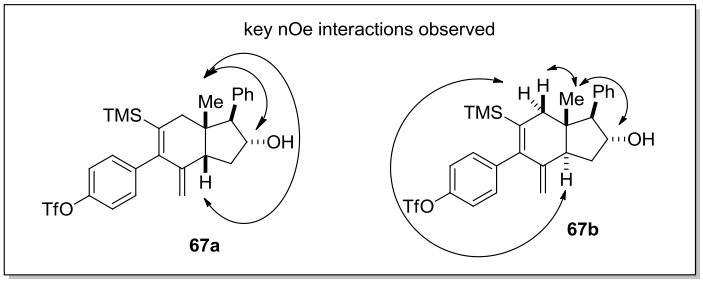
J = 18.8, 8.0 Hz, 1H), 2.27-2.04 (m, 2H), 2.14 (d, *J* = 16.4 Hz, 1H), 1.77 (d, *J* = 16.0 Hz, 1H), 1.60 (br. s, 1H), 1.21 (s, 3H), 0.83 (s, 9H), -0.08 (s, 3H), -0.10 (s, 3H), -0.38 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.6, 145.4, 142.2, 137.6, 131.8, 130.9, 128.4, 127.7, 126.8, 126.7, 126.4, 77.2, 73.5, 62.5, 62.1, 43.6, 38.3, 36.5, 33.8, 26.0, 23.3, 18.4, -0.9, -5.2, -5.3; IR (neat): 3335, 2953, 2856, 1600, 1471, 1247, 1087, 908, 831, 731, 701; LRMS (EI, Na): calcd for $C_{33}H_{49}O_2Si_2$, 533.3 *m/z* (M +H); observed, 533.3 $(M+H)^+$ *m/z*.



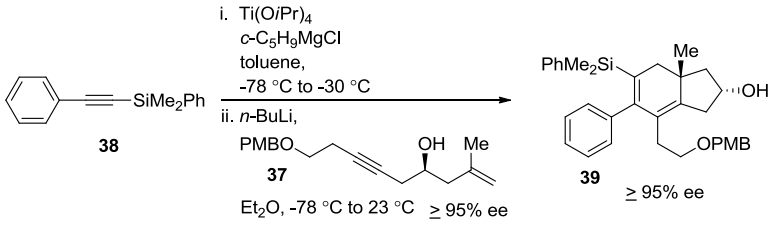
4-((1*S*,2*R*,3a*S*,7a*S*)-2-hydroxy-7a-methyl-4-methylene-1-phenyl-6-(trimethylsilyl)-2,3,3a,4,7,7a-hexahydro-1H-inden-5-yl)phenyl trifluoromethanesulfonate (67a) and 4-((1*S*,2*R*,3a*R*,7a*S*)-2-hydroxy-7a-methyl-4-methylene-1-phenyl-6-(trimethylsilyl)-2,3,3a,4,7,7a-hexahydro-1H-inden-5-yl)phenyl trifluoromethanesulfonate (67b): Prepared according to the general procedure for titanium-mediated coupling using 0.100 g (0.262 mmol, 1.0 equiv) of enyne **64** and 0.295 g (0.866 mmol, 3.3 equiv) of alkyne **55** and warming to a final temperature of 23 °C for 16h. A separable mixture of the *syn*- and *anti*-hydroindanes was obtained, each as a colorless oil. Carbocycle formation occurred with 10:1 regioisomeric ratio and ≥ 20:1 diastereomeric ratio at C16 and C18 but with a 1:1 diastereomeric ratio of separable *cis* and *trans* hydroindanes. The crude material was purified via flash chromatography, eluting with 90:10 hexanes:EtOAc. The hydroindanes were each isolated as 10:1 regioisomeric mixtures (yield of **67a**: 0.042 g, 30%, yield of **67b**: 0.048 g, 34%). In addition to the nOe interactions indicated below, the relative *cis* and *trans*- assignments were supported by the upfield shift of the *trans*- methyl group[12] (0.50 vs 0.87 ppm). Spectral data for **67a** (*cis*-hydroindane): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67-7.44 (m, 9H), 5.28 (s, 1H), 4.99 (ddd, *J* = 12.8, 7.6, 5.2 Hz, 1H), 4.67 (s, 1H), 3.12 (d, *J* = 5.2 Hz, 1H), 2.97 (dd, *J* = 11.6, 7.6 Hz, 1H), 2.93 (d, *J* = 17.2 Hz, 1H), 2.81 (ddd, *J* = 14.8, 12.8, 7.2 Hz, 1H), 2.44 (d, *J* = 17.6

Hz, 1H), 2.18 (ddd, J = 20.4, 11.6, 7.6 Hz, 1H), 1.86 (br. s, 1H), 0.87 (s, 3H), 0.09 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.5, 146.3, 143.0, 141.7, 138.8, 132.0, 129.0, 128.2, 126.5, 120.6, 115.8, 113.8, 78.0, 65.1, 49.5, 43.5, 41.7, 40.6, 23.6, -0.6; IR (neat): 3411, 2957, 1601, 1496, 1423, 1248, 1209, 1137, 883, 830, 702; LRMS: calculated for $C_{27}H_{32}F_3O_4SSi$, expected: 537.2 $(M+H)^+$, observed: 537.2 $(M+H)^+$.

Spectral Data for **67b** (*trans*-hydroindane): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42-7.08 (m, 9H), 4.90 (ddd, J = 9.6, 7.6, 2.0 Hz, 1H), 4.90 (br. s, 1H), 4.33 (dd, J = 1.2, 0.8 Hz, 1H), 2.96-2.89 (m, 1H), 2.90 (d, J = 7.6 Hz, 1H), 2.41 (d, J = 17.6 Hz, 1H), 2.26 (ddd, J = 14.0, 11.6, 9.2 Hz, 1H), 2.12 (d, J = 17.6 Hz, 1H), 1.95 (ddd, J = 10.0, 8.0, 2.0 Hz, 1H), 1.81 (br. s, 1H), 0.50 (s, 3H), -0.29 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.6, 147.7, 146.1, 142.7, 138.4, 132.3, 132.0, 128.6, 128.4, 126.8, 120.7, 120.3, 117.2, 112.4, 75.5, 67.8, 49.4, 45.1, 44.2, 34.4, 13.4, -0.89; IR (neat): 3410, 3294, 2960, 1600, 1495, 1425, 1248, 1210, 1160, 1050, 888, 831, 733; LRMS: calculated for $C_{27}H_{32}F_3O_4SSi$, expected: 537.2 $(M+H)^+$, observed: 537.2 $(M+H)^+$.

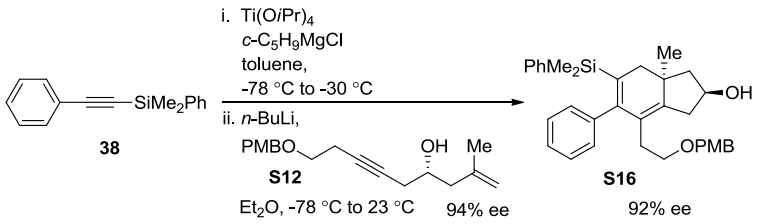


VI. Enantiospecific Carbocycle Synthesis



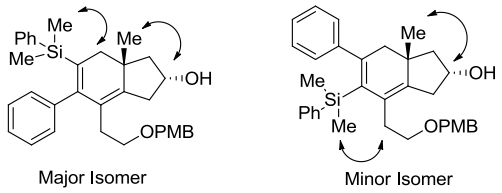
(2*S*,3a*S*)-5-(dimethyl(phenyl)silyl)-7-(2-((4-methoxybenzyl)oxy)ethyl)-3a-methyl-6-phenyl-2,3,3a,4-tetrahydro-1H-inden-2-ol (39). Prepared according to the general procedure for titanium-mediated

coupling using 0.150 g (0.520 mmol, 1.0 equiv) of enyne **37** and 0.407 g (1.72 mmol, 3.3 equiv) of alkyne **38** and warming to RT for 16h. The title compound was formed as a separable 2:1 mixture of regioisomers (combined 0.200 g, 74% yield). The resulting crude material was purified by silica gel chromatography, eluting with 90:10 hexanes:EtOAc, to provide carbocycle **39** as a colorless oil. Spectral data for major regioisomer: $[\alpha]_D^{24.8}$ = −46.1 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.36 (m, 2H), 7.31-7.27 (m, 4H), 7.21-7.20 (m, 2H), 7.13 (d, *J* = 8.8 Hz, 2H), 6.99-6.95 (m, 2H), 6.84 (d, *J* = 8.8 Hz, 2H), 4.49-4.43 (m, 1H), 4.22 (s, 2H), 3.80 (s, 3H), 3.18-3.05 (m, 2H), 2.79 (dd, *J* = 17.4, 6.6 Hz, 1H), 2.45 (dd, *J* = 17.7, 5.6 Hz, 1H), 2.31-2.14 (m, 3H), 2.07-1.98 (m, 2H), 1.87 (br s, 1H), 1.52 (dd, *J* = 12.6, 6.8 Hz, 1H), 0.87 (s, 3H) −0.06 (s, 3H), −0.15 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.0, 148.9, 146.9, 141.9, 139.7, 133.7, 130.6, 129.5, 129.0, 128.4, 127.6, 127.5, 126.7, 125.7, 113.7, 72.1, 72.0, 55.3, 50.9, 41.4, 39.3, 38.5, 30.1, 21.4, −1.9, −2.4; IR (thin film, NaCl) 3369, 2951, 1612, 1512, 1427, 1247, 1087 cm^{-1}; LRMS (EI, Na) calcd for $C_{34}H_{40}NaO_3Si$, 547.3 *m/z* (M + Na); observed, 547.3 (M + Na)$^+$ *m/z*. Minor Regioisomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.10 (m, 12H), 6.84 (d, *J* = 8.0 Hz, 2H), 4.49-4.43 (m, 1H), 4.38 (d, *J* = 12.0 Hz, 1H), 4.26 (d, *J* = 12.0 Hz, 1H), 3.77 (s, 3H), 3.25-3.22 (m, 2H), 2.64 (dd, *J* = 16.4, 6.0 Hz, 1H), 2.49 (dd, *J* = 15.6, 4.0 Hz, 1H), 2.44-2.36 (m, 3H), 2.36-2.26 (m, 1H), 2.01 (dd, *J* = 11.2, 5.2 Hz, 1H), 1.67 (dd, *J* = 17.2, 4.8 Hz, 1H), 1.63 (br. s, 1H), 1.17 (s, 3H) −0.13 (s, 3H), −0.31 (s, 3H).



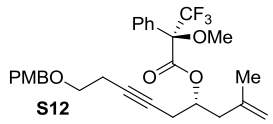
(2*R*,3a*R*)-5-(dimethyl(phenyl)silyl)-7-(2-((4-methoxybenzyl)oxy)ethyl)-3a-methyl-6-phenyl-2,3,3a,4-tetrahydro-1H-inden-2-ol (S16): prepared according to the procedure for the synthesis of **39** using 0.150 g (0.520 mmol, 1.0 equiv) of enyne **S12** and 0.407 g (1.72 mmol, 3.3 equiv) of alkyne **38** and warming to a final temperature of 23 °C for 16h. The title compound was formed as a separable 2:1 mixture of

regioisomers (combined 0.185 g, 69% yield). Optical rotation for **S16**: $[\alpha]_D^{26.2}$ = +43.2 (*c* = 0.6, $CHCl_3$); Analysis of the corresponding Mosher's esters of the starting enynes and the isolated carbocycles showed efficient retention of stereochemical purity through the titanium-mediated coupling reaction: Key interactions observed in 2D NOESY experiment for assignment of regioisomeric identity:



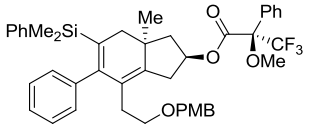
Crude ^1H NMR spectra obtained in Mosher's ester analysis of starting enynes and hydroindane products are given below:

II-211-Mosher Crude



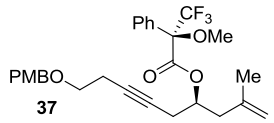
S12

II-219-Mosher Crude



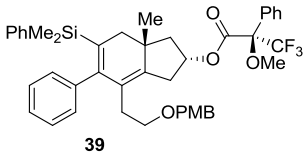
S16

II-214-Mosher Crude



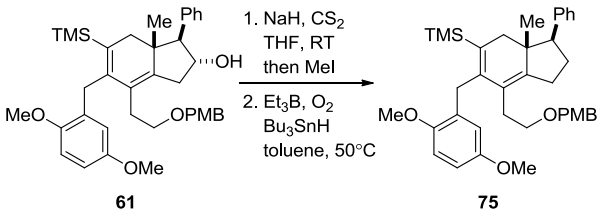
37

II-221-Mosher Crude



39

VII. Derivatization Studies (Figure 9):

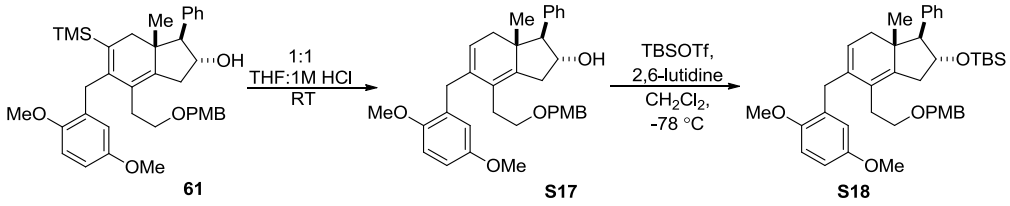


61 **75**

(+/-) ((3*R*,3a*R*)-6-(2,5-dimethoxybenzyl)-7-(2-((4-methoxybenzyl)oxy)ethyl)-3a-methyl-3-phenyl-2,3,3a,4-tetrahydro-1H-inden-5-yl)trimethylsilane (75): A 4-mL scintillation vial equipped with magnetic stir bar was charged with **61** (0.068 g, 0.111 mmol, 1.0 equiv) and THF (3.0 mL). The resulting solution was cooled to 0 °C, and NaH (60% in oil, 8.9 mg, 0.222 mmol, 2.0 equiv) was added. The solution was stirred for 30 min. at the same temperature, and carbon disulfide (0.135 mL, 0.169 g, 2.22 mmol, 20 equiv) was added. The solution was warmed to RT and stirred for 30 min, at which point MeI (0.200 mL, 0.456 g, 3.2 mmol, 25 equiv) was added, and the solution was stirred at RT for an additional 30 min. The reaction was quenched by the addition of saturated aqueous $NaHCO_3$. The solution was diluted with water and was extracted with diethyl ether. The combined organic extracts were washed with brine and dried with sodium sulfate. After concentration in vacuo, the resulting crude oil was pushed through a quick plug of SiO_2 , eluting with 100:0 to 90:10 hexanes: EtOAc, to afford the crude xanthate as an off-white solid, which was used without additional purification (0.077 g).

The crude xanthante (0.033 g, 0.047 mmol, 1.0 equiv) was dissolved in toluene (2.5 mL) in a 4-mL scintillation vial. Tributyltin hydride (0.126 mL, 0.137 g, 0.47 mmol, 10.0 equiv) was added, and the resulting solution was heated to 50 °C under Ar in an oil bath. Triethylborane (1 M in hexane, 0.020 mL, 0.020 mmol, 0.70 equiv) was added, and the tubing was removed, leaving the open needle, which allowed for air to enter the vial slowly. After 30 min, a single drop of water was added, and the reaction was stirred for an additional 30 min, at which point the reaction was judged to be complete by TLC analysis. The vial was cooled to RT and the solution was concentrated in vacuo to yield a crude yellow oil, which was purified via flash chromatography, eluting with 100:0 to 90:10 hexanes:EtOAc, to afford the desired

product as a colorless oil (0.022 g, 79%). Spectral Data for **75**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.21 (m, 7H), 6.88 (d, *J* = 8.7 Hz, 2H), 6.76 (d, *J* = 9.1 Hz, 1H), 6.73 – 6.63 (m, 2H), 4.39 (d, *J* = 12.0, 1H), 4.35 (d, *J* = 12.0, 1H), 3.81 (s, 6H), 3.75 (dd, *J* = 17.1, 1.9 Hz, 1H), 3.66 (s, 3H), 3.55 (d, *J* = 17.1 Hz, 1H), 3.39 – 3.23 (m, 2H), 2.93 (dd, *J* = 13.0, 6.2 Hz, 1H), 2.65 – 2.43 (m, 2H), 2.36-2.13 (m, 5H), 2.02 – 1.91 (m, 1H), 0.67 (s, 3H), 0.06 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.00, 153.49, 151.06, 150.06, 143.38, 140.66, 130.96, 130.63, 130.40, 128.93, 128.45, 127.87, 126.24, 126.11, 114.51, 113.70, 111.51, 110.88, 72.19, 69.29, 57.87, 55.90, 55.55, 55.26, 43.57, 40.71, 31.11, 29.60, 27.24, 26.77, 14.74, 0.08; IR (neat): 2928, 1611, 1498, 1247, 1223, 1096, 1033, 835; LRMS (EI, Na) calculated for $C_{35}H_{39}O_4$ expected: 523.3 *m/z* $(M - TMS)^+$; observed, 523.3 *m/z* $(M - TMS)^+$.

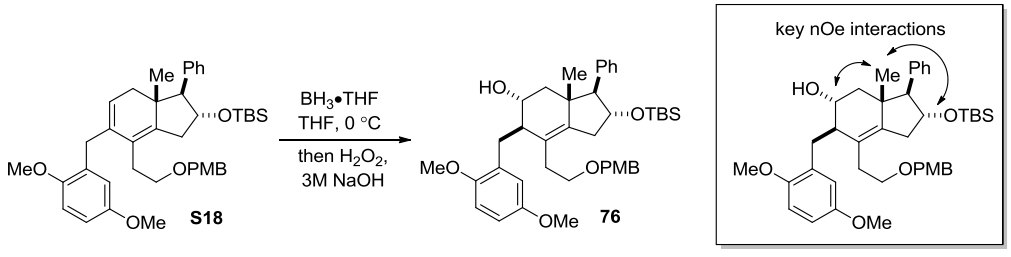


(+/-) *tert*-butyl(((2*R*,3*R*,3a*R*)-6-(2,5-dimethoxybenzyl)-7-(2-((4-methoxybenzyl)oxy)ethyl)-3a-methyl-3-phenyl-2,3,3a,4-tetrahydro-1H-inden-2-yl)oxy)dimethylsilane (S18): A 10-mL round-bottomed flask equipped with magnetic stir bar was charged with **61** (0.066 g, 0.1 mmol, 1.0 equiv), THF (2 mL), and 1M HCl (2 mL). The resulting solution was stirred vigorously for 16h at RT. After dilution with diethyl ether, the organic phase was washed with saturated aqueous $NaHCO_3$ and dried with $MgSO_4$. Concentration in vacuo yielded a light yellow oil, which was used without additional purification (**S17**, 0.059 g). The crude diene (0.059 g, 0.1 mmol, 1.0 equiv) was dissolved in dry CH_2Cl_2 in a 4-mL scintillation vial. The resulting solution was cooled to −78°C, and 2,6-lutidine (0.023 mL, 0.021 g, 0.2 mmol, 2.0 equiv) and TBSOTf (0.032 g, 0.12 mmol, 1.2 equiv) were added successively. After stirring for 15 min, the reaction was judged to be complete by TLC analysis and was quenched by the addition of MeOH (0.050 mL). After warming to RT, the solution was loaded directly only a column of SiO_2, and

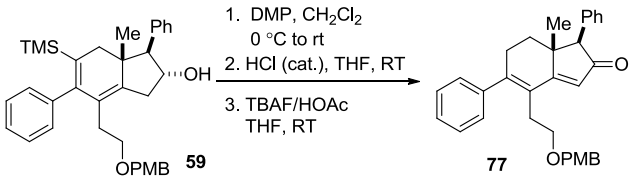
the desired product was obtained by eluting with 100:0 to 95:5 hexanes: EtOAc, yielding a colorless oil (0.050 g, 71% from **61**).

Spectral data for **S17**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29-7.15 (m, 7H), 6.83 (d, *J* = 8.8 Hz, 2H), 6.71-6.62 (m, 3H), 5.23 (dd, *J* = 6.0, 2.8 Hz, 1H), 4.76 (q, *J* = 8.4 Hz,1H), 4.36 (s, 2H), 3.74 (s, 3H), 3.70 (s, 3H), 3.63 (s, 3H), 3.54 (d, *J* = 15.6 Hz, 1H), 3.31-3.21 (m, 2H), 3.23 (d, *J* = 16.4 Hz, 1H), 2.99 (dd, *J* = 18.4, 8.4 Hz, 1H), 2.85 (d, *J* = 10.4 Hz, 1H), 2.43-2.23 (m, 5H), 1.88 (dd, *J* = 16.4, 6.8 Hz, 1H), 0.67 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.0, 153.4, 151.3, 143.2, 137.7, 135.4, 130.7, 130.0, 129.0, 128.8, 128.2, 126.8, 125.4, 121.2, 115.6, 113.7, 111.3, 111.1, 72.8, 72.3, 68.9, 65.3, 55.9, 55.5, 55.2, 43.9, 36.7, 36.1, 32.4, 29.6, 16.7; IR (neat): 3443, 2925, 1721, 1609, 1499, 1463, 1248, 1178, 1076, 821, 735, 707; LRMS (EI, Na): calculated for $C_{35}H_{40}O_5Na$, expected: 563.3 $(M+Na)^+$, observed: 563.3 $(M+Na)^+$.

Spectral data for **S18**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31-7.18 (m, 7H), 6.89 (d, *J* = 8.7 Hz, 2H), 6.77 (d, *J* = 9.6 Hz, 1H), 6.70 (m, 2H), 5.30 (d, *J* = 5.6 Hz, 1H), 4.75 (dd, *J* = 18.0, 8.1 Hz, 1H), 4.43 (s, 2H), 3.81 (s, 3H), 3.77 (s, 3H), 3.71 (s, 3H), 3.61 (d, *J* = 17.1 Hz, 1H), 3.43-3.37 (m, 2H), 3.29 (d, *J* = 16.4 Hz, 1H), 3.04 – 2.89 (m, 2H), 2.45-2.26 (m, 4H), 1.89 (dd, *J* = 16.3, 6.6 Hz, 1H), 0.79 (s, 3H), 0.74 (s, 9H), -0.00 (s, 3H), -0.18 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.03, 153.47, 151.33, 144.15, 138.53, 135.20, 130.81, 130.23, 129.32, 128.96, 127.65, 126.33, 124.84, 121.37, 115.58, 113.74, 111.33, 111.14, 74.00, 72.33, 68.97, 65.72, 55.94, 55.56, 55.22, 43.19, 37.30, 36.70, 32.46, 29.68, 25.66, 17.85, 17.03, -4.47, -4.95; IR (neat): 2928, 2854, 1711, 1607, 1498, 1249, 1223, 1099, 1044, 835, 776, 661. LRMS (EI, Na) calculated for $C_{41}H_{55}O_5Si$ expected: 655.4 *m/z* $(M + H)^+$; observed, 655.3 *m/z* $(M + H)^+$.



(+/-)(2*R*,3*R*,3a*R*,5*R*,6*R*)-2-((tert-butyldimethylsilyl)oxy)-6-(2,5-dimethoxybenzyl)-7-(2-((4-methoxybenzyl)oxy)ethyl)-3a-methyl-3-phenyl-2,3,3a,4,5,6-hexahydro-1H-inden-5-ol (76): A 4-mL scintillation vial equipped with magnetic stir bar was charged with **S18** (0.045 g, 0.064 mmol, 1.0 equiv). After purging thoroughly with Ar, THF (2.0 mL) was added, and the resulting solution was cooled to 0 °C. BH_3•THF (1.0 M in THF, 0.190 mL, 0.190 mmol, 3.0 equiv) was added dropwise via syringe, and the solution was allowed to stir at the same temperature for 1h. Additional borane (0.190 mL, 3.0 equiv) was added, and after an additional 1h of stirring, a final addition of 0.120 mL (2.0 equiv) was added. After stirring at 0 °C for a final 30 min, the reaction was quenched by the slow addition of a pre-mixed 1:1 solution of 30 % H_2O_2(aq): 3M NaOH (aq) (0.6 mL). The solution was allowed to warm slowly to room temperature over 20 min and was then stirred at RT for 1h. The solution was diluted with diethyl ether, and the organic phase was washed with saturated aqueous $NaHCO_3$, water, and brine, and was dried with sodium sulfate. Concentration in vacuo yielded a crude oil, which was purified via flash chromatography, eluting with 95:5 to 90:10 hexanes:EtOAc, to yield the desired product as a colorless oil (0.035 g, 76%). ^{1}H NMR analysis of the crude material showed a 10:1 diastereomeric ratio. Spectral data for **76**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.21 (m, 7H), 6.88 (d, *J* = 8.7 Hz, 2H), 6.76 (d, *J* = 9.1 Hz, 1H), 6.73 – 6.63 (m, 2H), 4.78 (td, *J* = 9.1, 6.0 Hz, 1H), 4.48 (s, 2H), 3.81 (m, 1H), 3.80 (s, 3H), 3.76 (s, 3H), 3.72 (s, 3H), 3.65-3.50 (m, 2H), 3.25 – 3.11 (m, 1H), 2.90 (dd, *J* = 17.3, 8.5 Hz, 1H), 2.69 (d, *J* = 9.6 Hz, 1H), 2.58-2.34 (m, 5H), 1.95 (br. s, 1H), 1.58 (dd, *J* = 12.1, 4.4 Hz, 1H), 1.48 (dd, *J* = 12.0, 8.0 Hz, 1H), 0.73 (s, 9H), 0.67 (s, 3H), -0.02 (s, 3H), -0.21 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.08, 153.48, 151.67, 142.52, 138.08, 130.53, 129.77, 129.50, 129.13, 127.61, 126.38, 126.26, 116.72, 113.78, 111.60, 111.32, 73.83, 72.57, 69.93, 68.01, 65.57, 55.86, 55.61, 55.21, 47.69, 44.75, 42.20, 37.27, 32.82, 31.16, 25.68, 21.76, 17.87, -4.56, -4.92; IR (neat): 3411, 2928, 1611, 1498, 1463, 1248, 1096, 1033, 835, 775; LRMS (EI, Na) calculated for $C_{41}H_{56}O_6SiNa$ expected: 695.4 *m/z* $(M + Na)^+$; observed, 695.5 *m/z* $(M + Na)^+$.



(1*R*,7a*R*)-4-(2-((4-methoxybenzyl)oxy)ethyl)-7a-methyl-1,5-diphenyl-7,7a-dihydro-1H-inden-2(6H)-one (77): A 25-mL round-bottomed flask was charged with **59** (0.097 g, 0.179 mmol, 1.0 equiv) and CH_2Cl_2 (6.0 mL). The resulting solution was cooled to 0 °C in an ice bath, and DMP (0.114 g, 0.269 mmol, 1.5 equiv) was added. The resulting suspension was stirred at the same temperature for 1h and was then warmed to RT for 30 min, at which point TLC analysis indicated complete consumption of the starting material. The suspension was diluted with diethyl ether (10 mL), and saturated aqueous $NaHCO_3$ (2 mL) and saturated aqueous $Na_2S_2O_3$ (2 mL) were added. The mixture was stirred vigourously for 15 min, and the layers were separated. The aqueous layer was extracted with diethyl ether and the combined organic extracts were washed with saturated aqueous $NaHCO_3$, water, and brine and were then dried with Na_2SO_4. Concentration in vacuo yielded a colorless crude oil, which was used without additional purification (0.85 mg). The crude ketone was dissolved in THF (4.0 mL), and 1M HCl (0.2 mL) was added dropwise. The mixture was stirred vigorously at RT for 30 min and was then quenched by the addition of 2 drops of saturated aqueous sodium bicarbonate. The mixture was pushed through a short plug of SiO_2, eluting with diethyl ether. Concentration in vacuo yielded a crude yellow dienone, which purified via flash chromatography, eluting with 70:30 hexanes:EtOAc, to give a yellow oil (intermediate allylsilane), which was a 1:1 mixture of diastereomers (0.068 g, 70% over two steps).

The intermediate allylsilane (0.059 g, 0.110 mmol, 1.0 equiv) was dissolved in THF (3.0 mL) in a dry 4-dram scintillation vial, and the resulting solution was cooled to 0 °C. In a separate 4-mL scintillation vial, a solution of TBAF (1.0 M in THF, 1.0 mL) was buffered with HOAc (0.060 mL, 0.063 g, 1.05 mmol). To the dienone solution was added the solution of buffered TBAF (0.22 mL, 0.22 mmol, 2.0 equiv), and the resulting yellow solution was stirred at 0 °C for 1h and was then warmed to RT for 30 min. The solution was then diluted with diethyl ether and was washed with saturated aqueous sodium

bicarbonate (3x), water and brine and dried with $MgSO_4$. Concentration in vacuo yielded the clean desilylated dienone (0.045 g, 88%). Spectral data for **77**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.17 (m, 12H), 6.87 (d, *J* = 8.7 Hz, 2H), 6.13 (s, 1H), 4.34 (d, *J* = 11.6 Hz, 1H), 4.31 (d, *J* = 11.6 Hz, 1H), 3.81 (s, 3H), 3.59 (s, 1H), 3.47-3.43 (m, 2H), 2.61-2.57 (m, 4H), 2.13-2.06 (m, 1H), 2.01-1.94 (m, 1H), 0.80 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 207.1, 176.6, 159.0, 148.2, 141.4, 135.8, 130.3, 130.0, 129.0, 128.4, 128.2, 127.5, 127.4, 126.9, 126.4, 122.4, 113.7, 72.3, 68.5, 66.4, 55.2, 45.2, 33.7, 31.7, 30.0, 22.8; IR (neat): 2925, 1689, 1595, 1247, 1170, 1088, 1033, 821, 700; LRMS (EI, Na) calculated for $C_{32}H_{33}O_3$ expected: 465.2 *m/z* $(M+H)^+$; observed, 465.5 *m/z* $(M+H)^+$.

VIII. References

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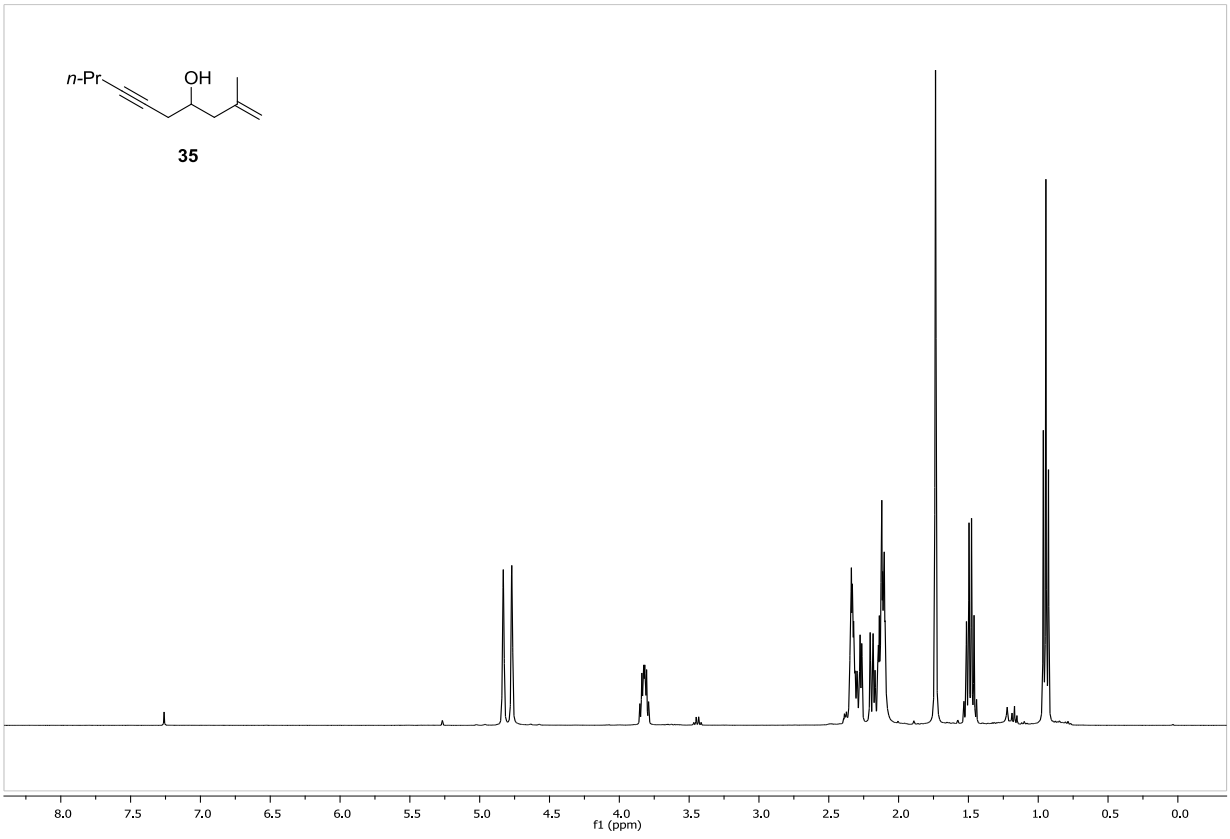
IX. ^{1}H and ^{13}C NMR Spectra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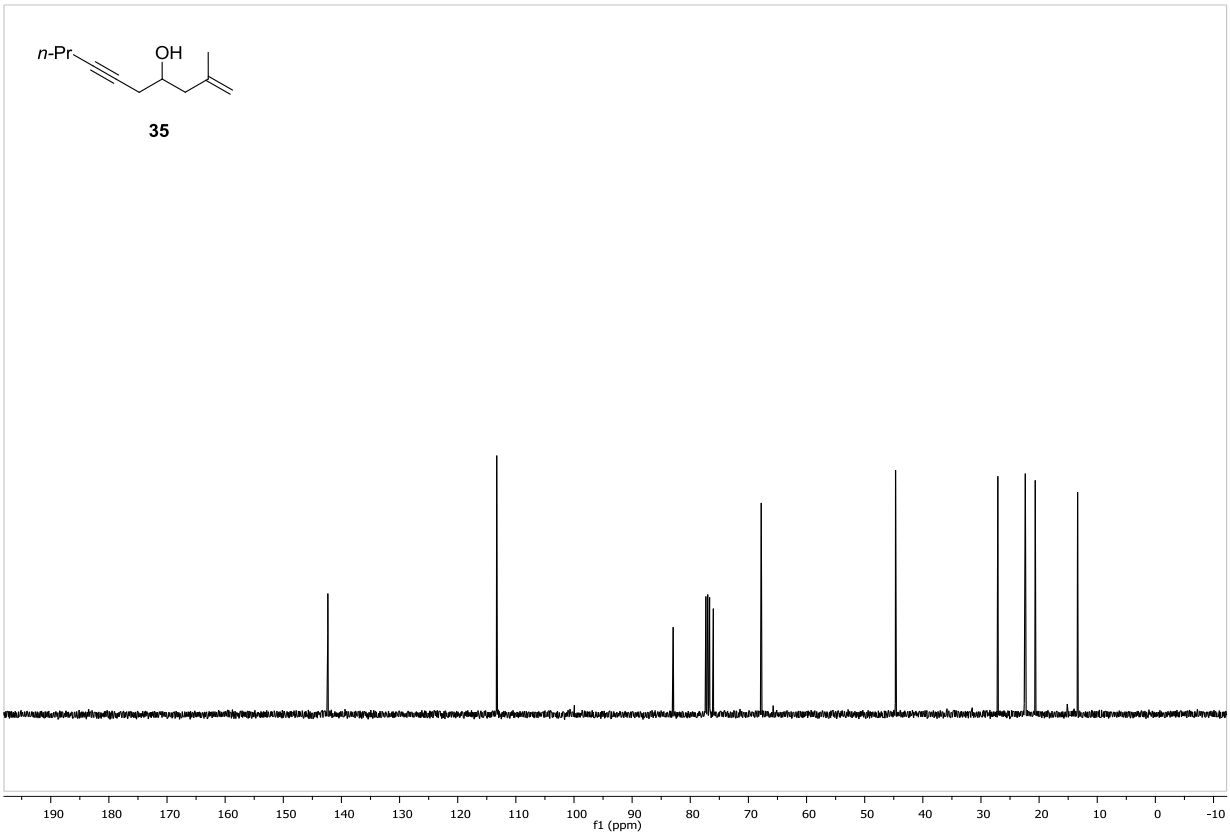
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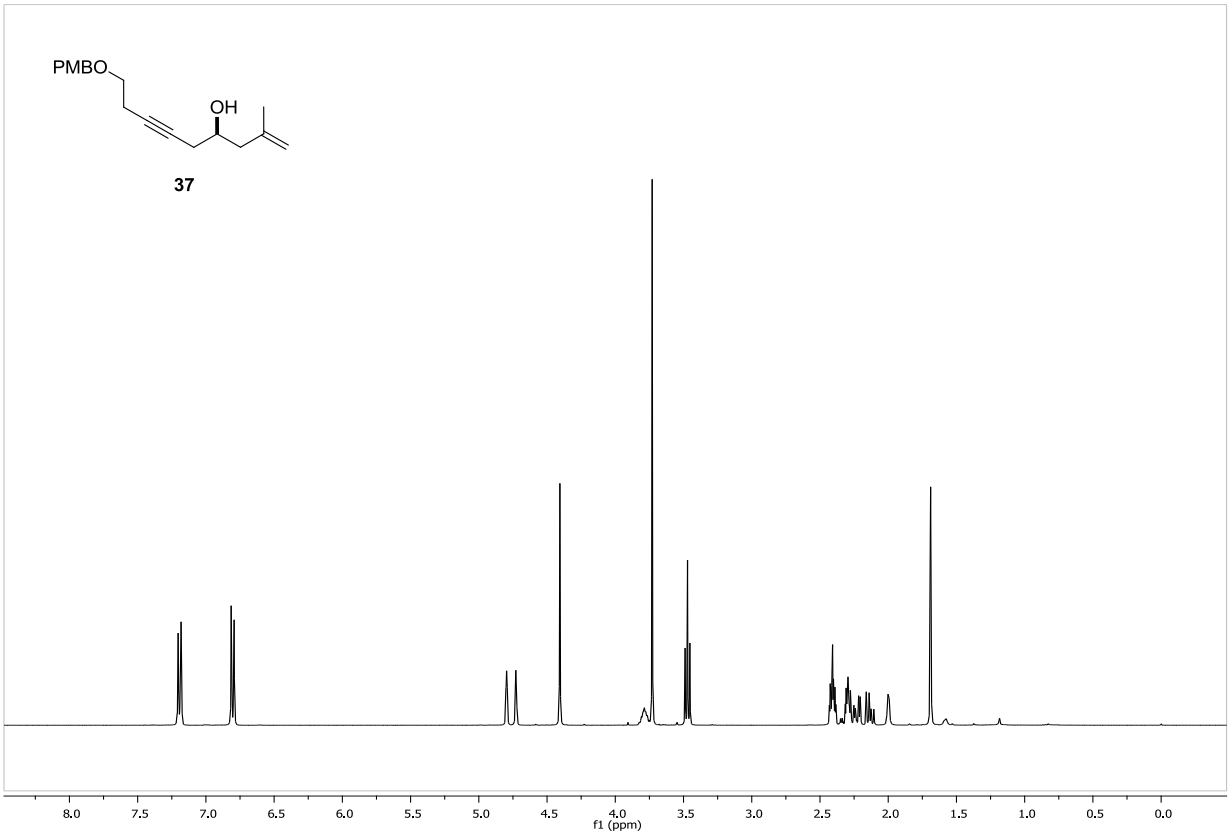
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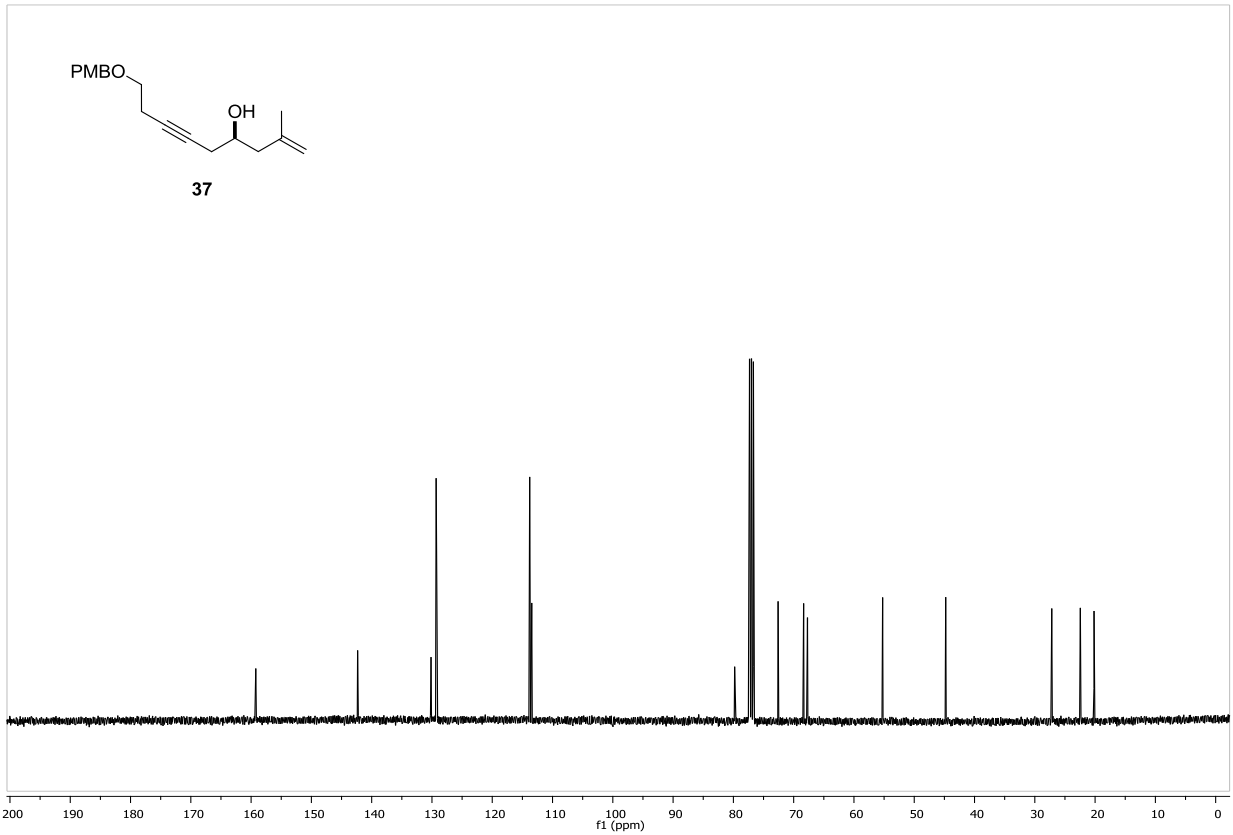
f1 (ppm)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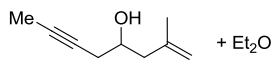
II-263



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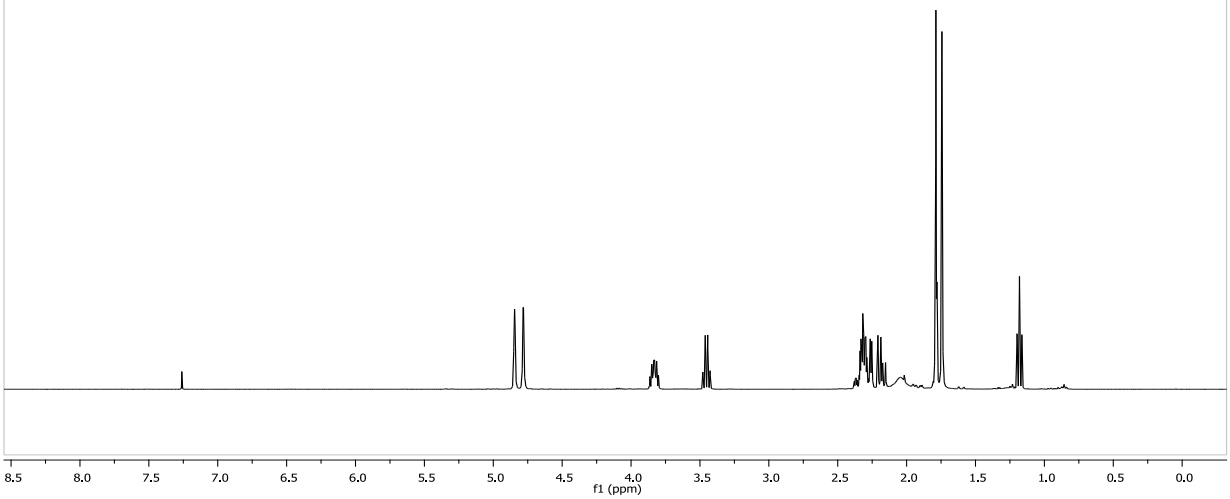
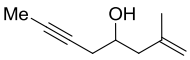


II-263



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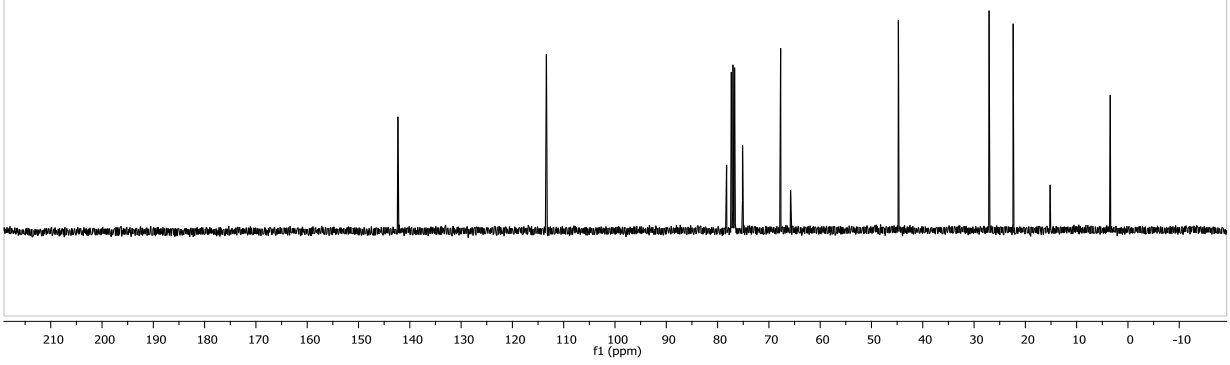

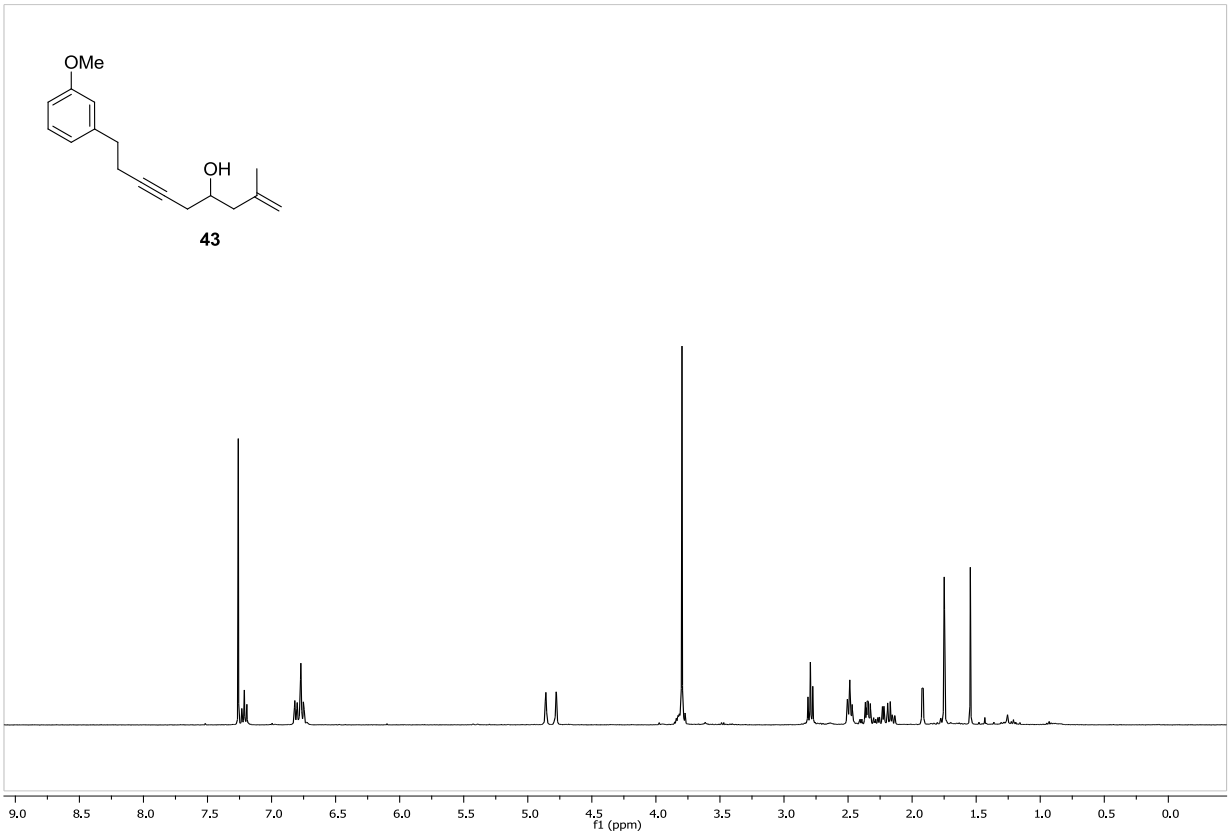
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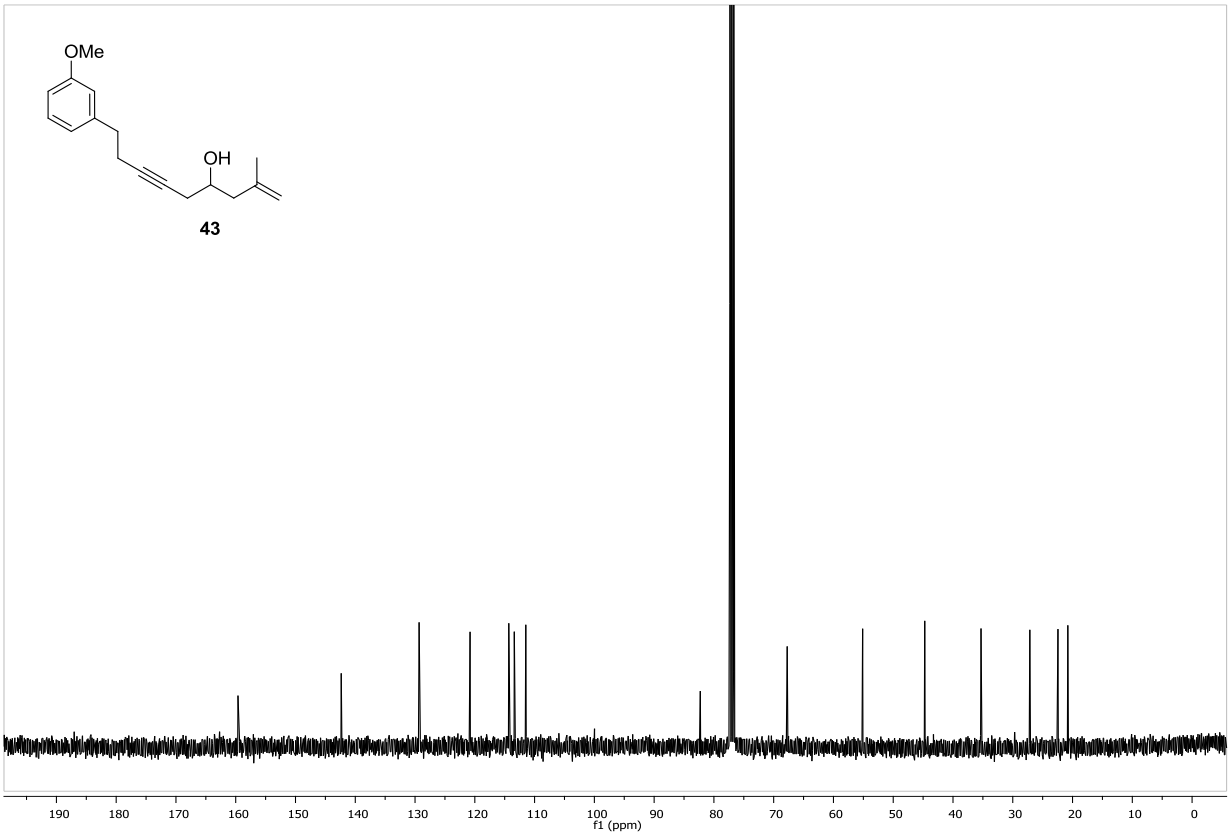
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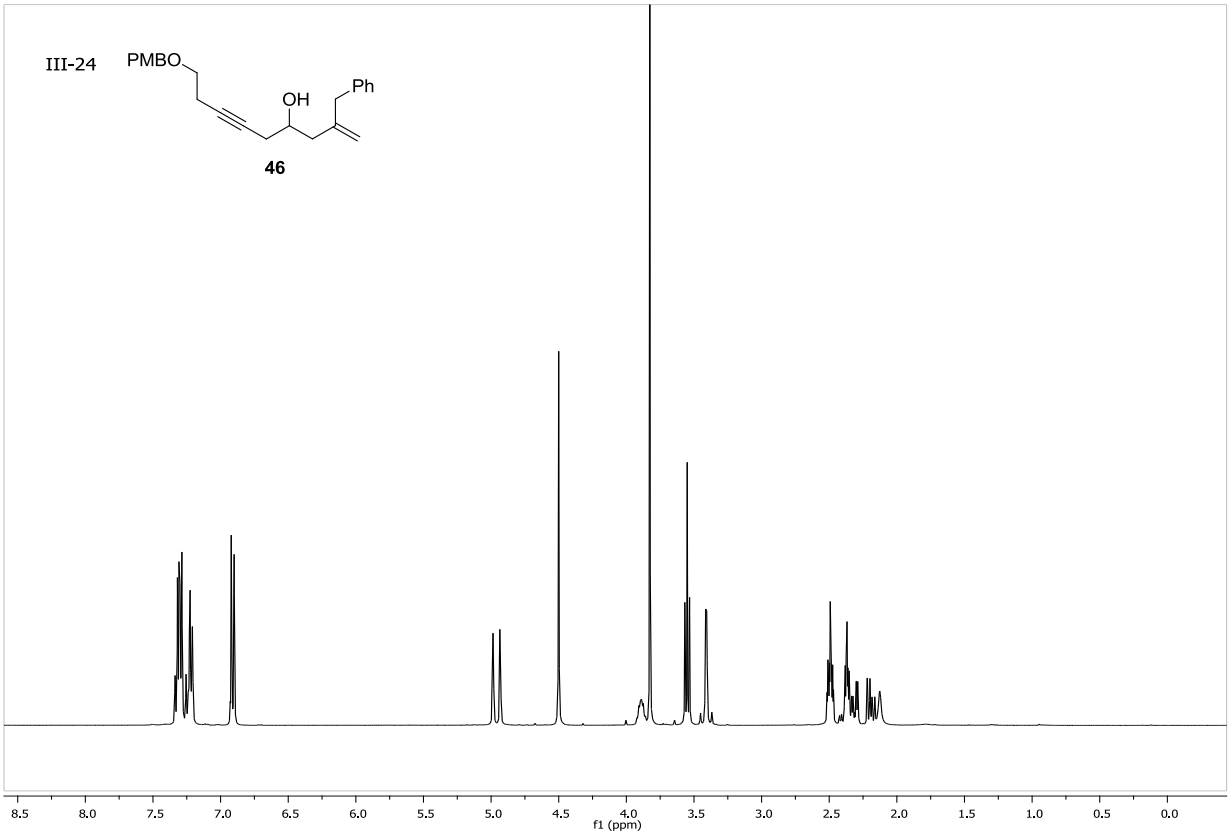
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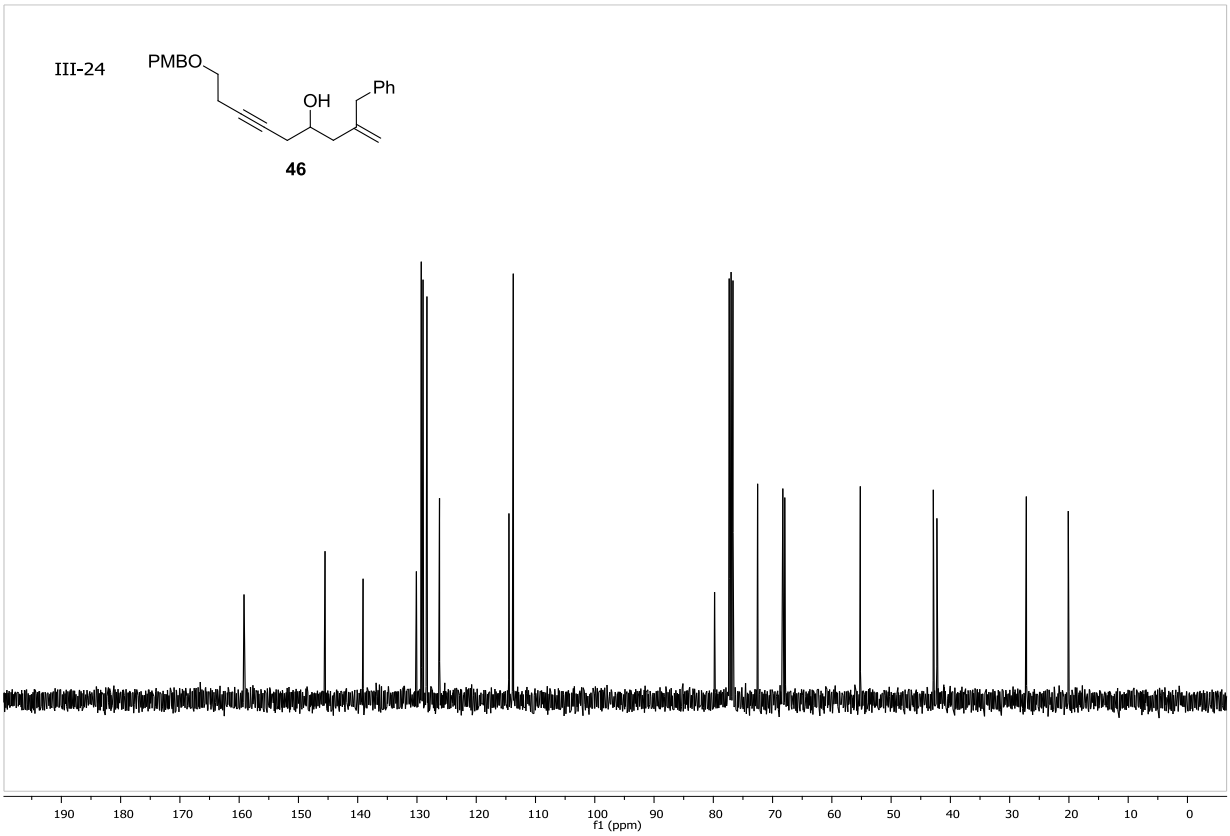
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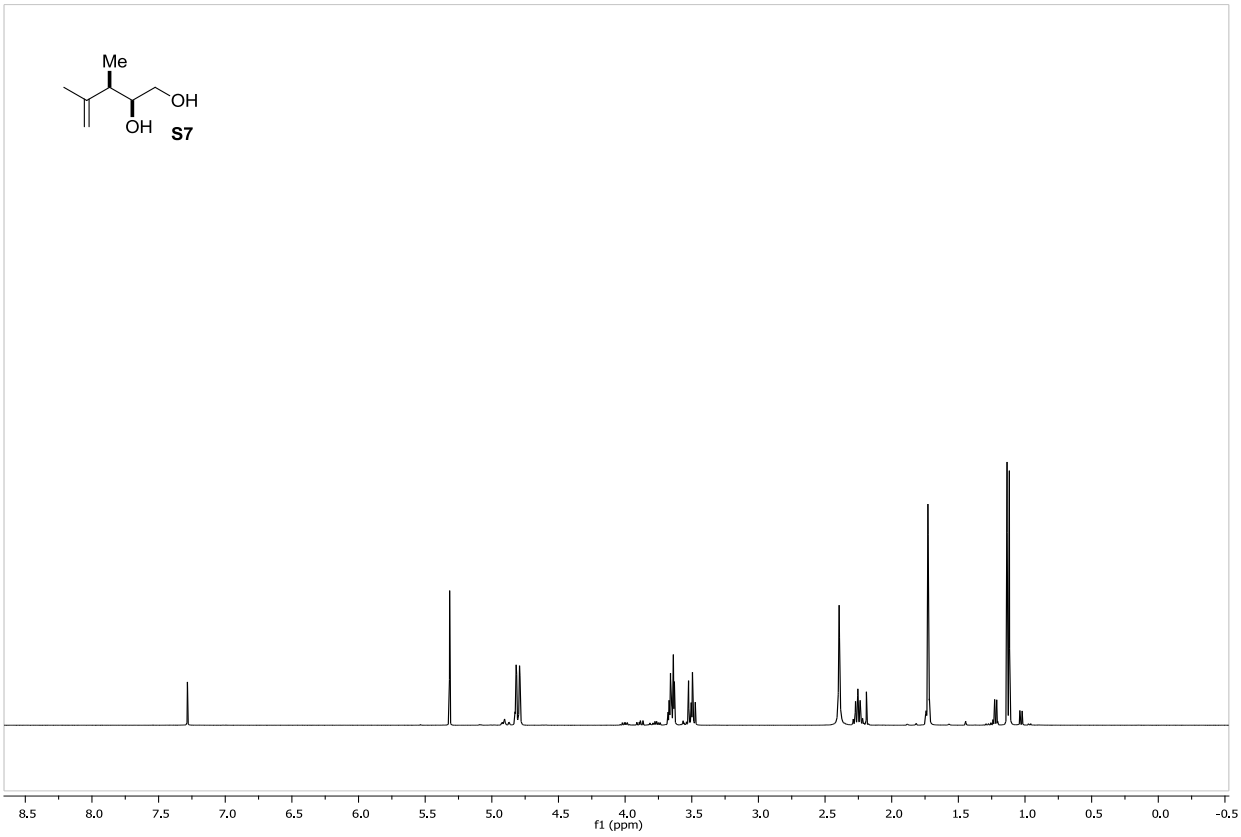
f1 (ppm)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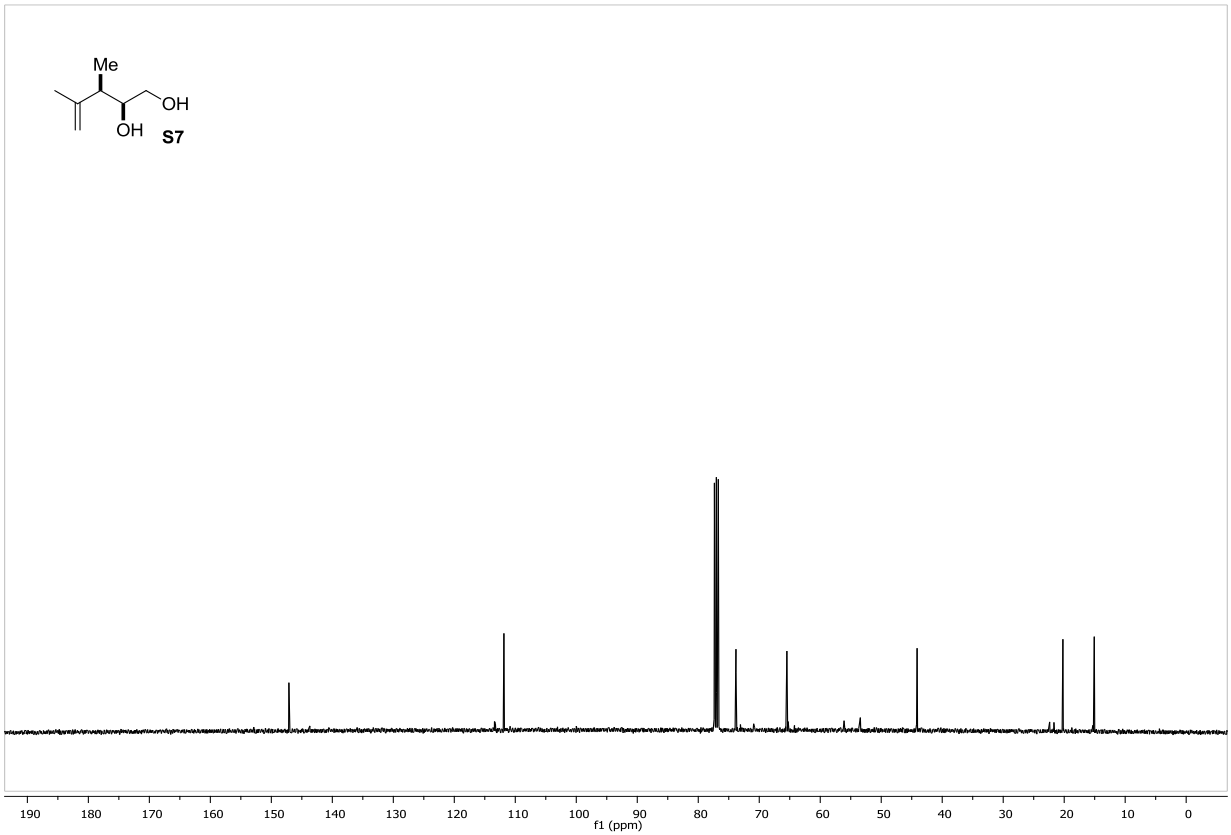
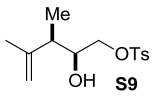
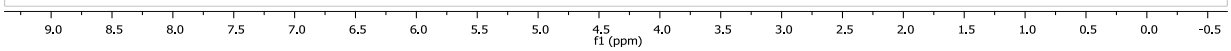
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


Me
OH
OH
S7
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

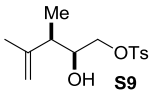
SNGIII-268



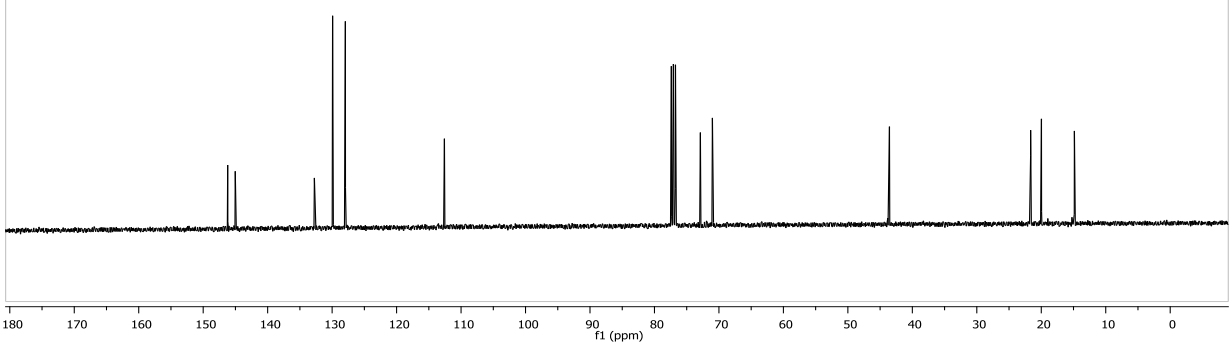
S9



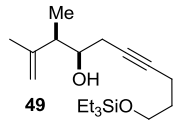
SNGIII-268



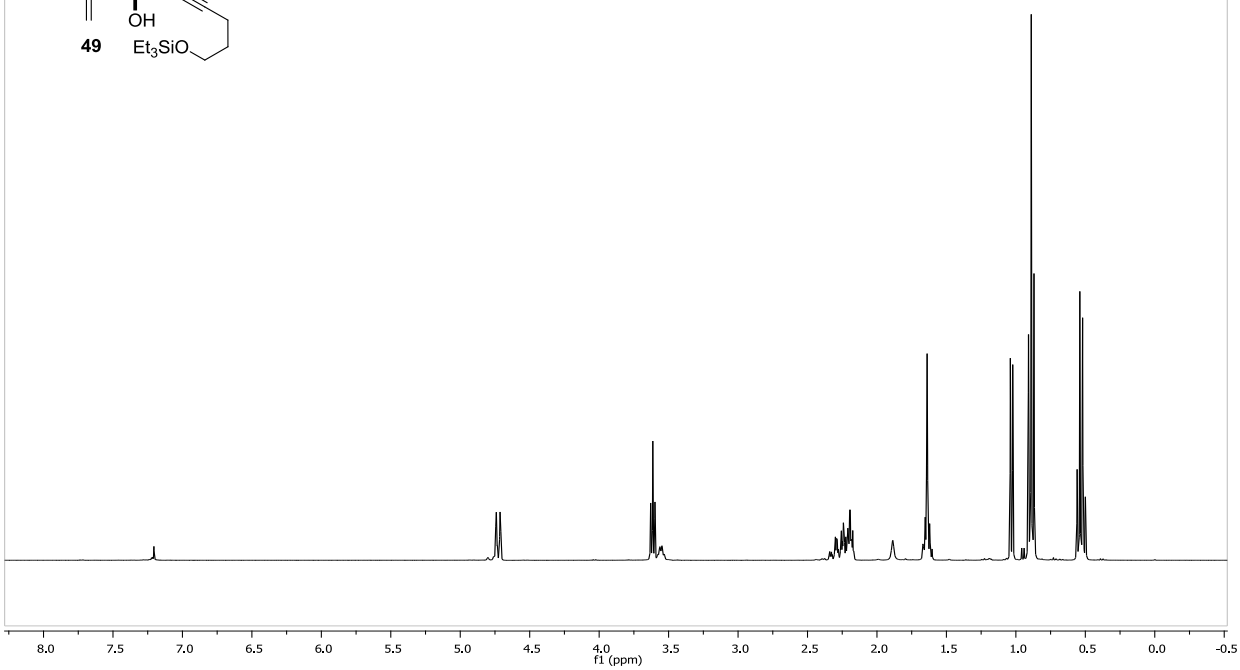
S9



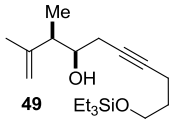
SNGIII-269



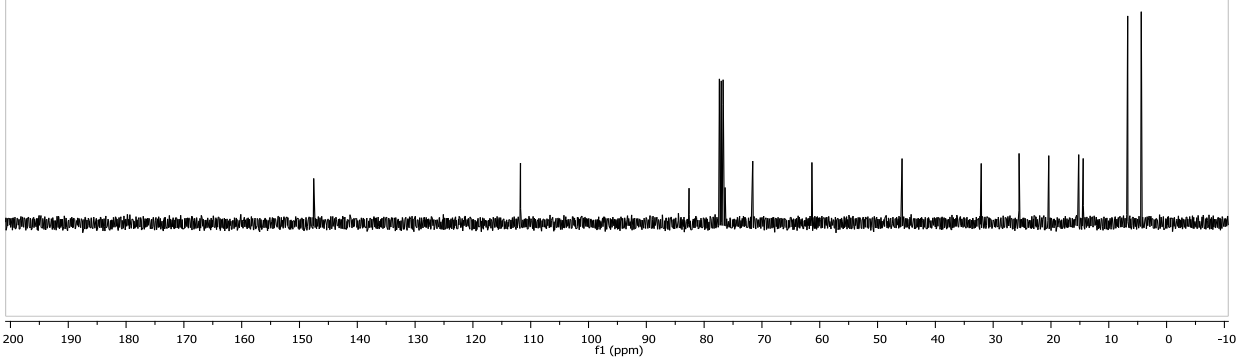
49

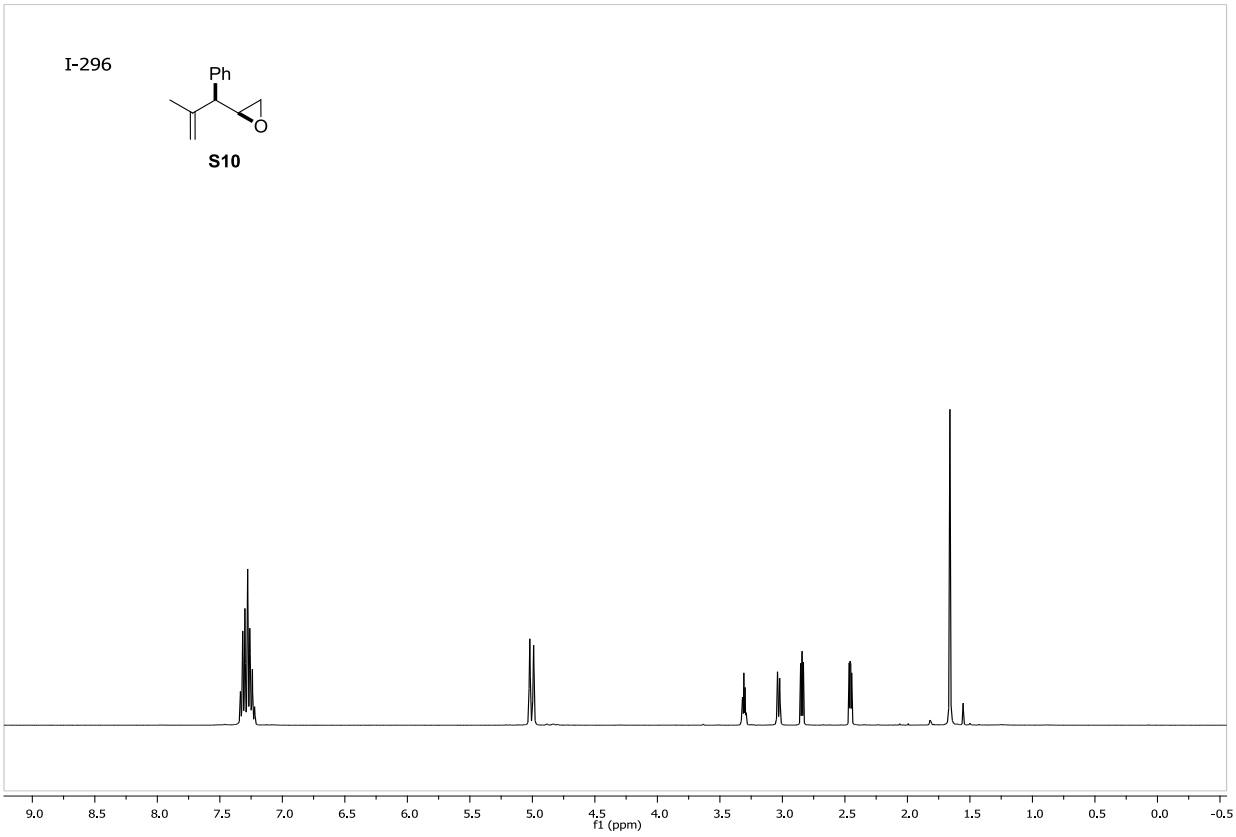


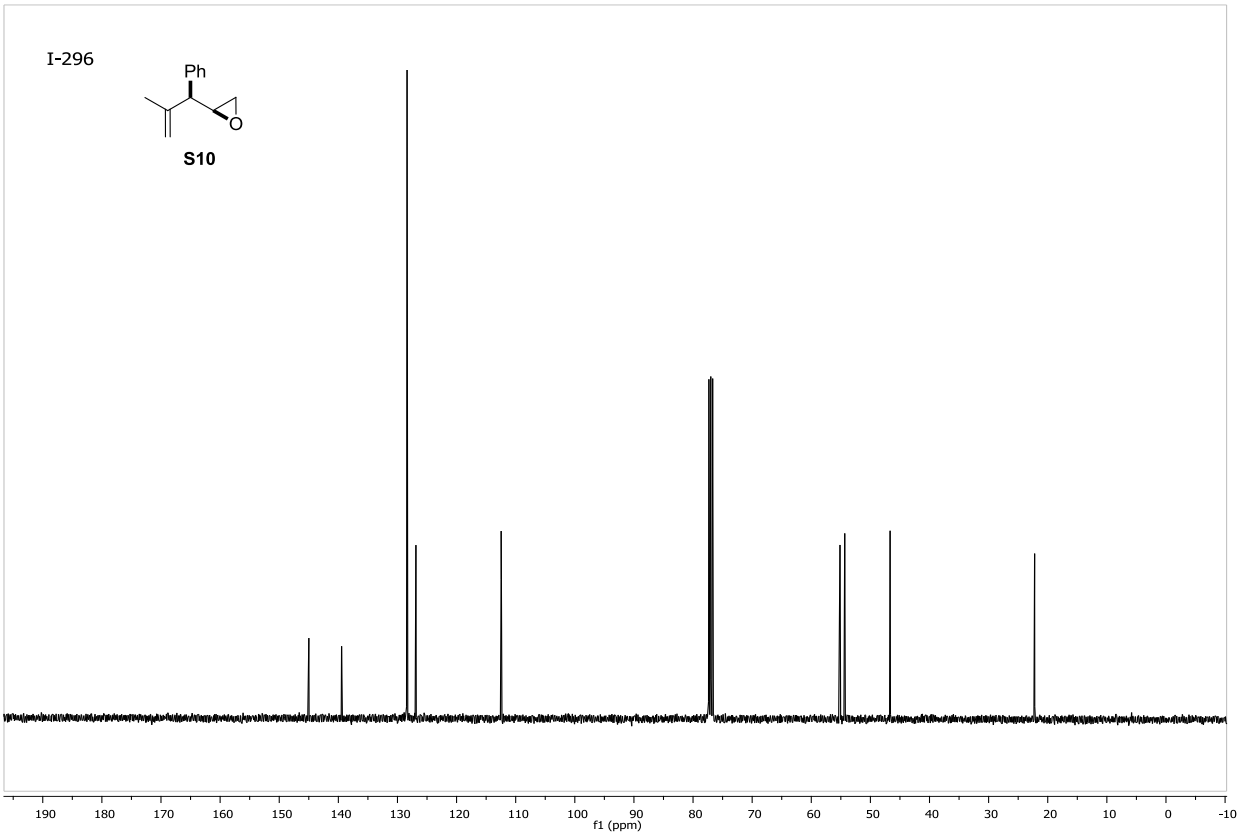
SNGIII-269



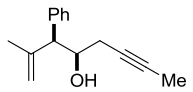
49



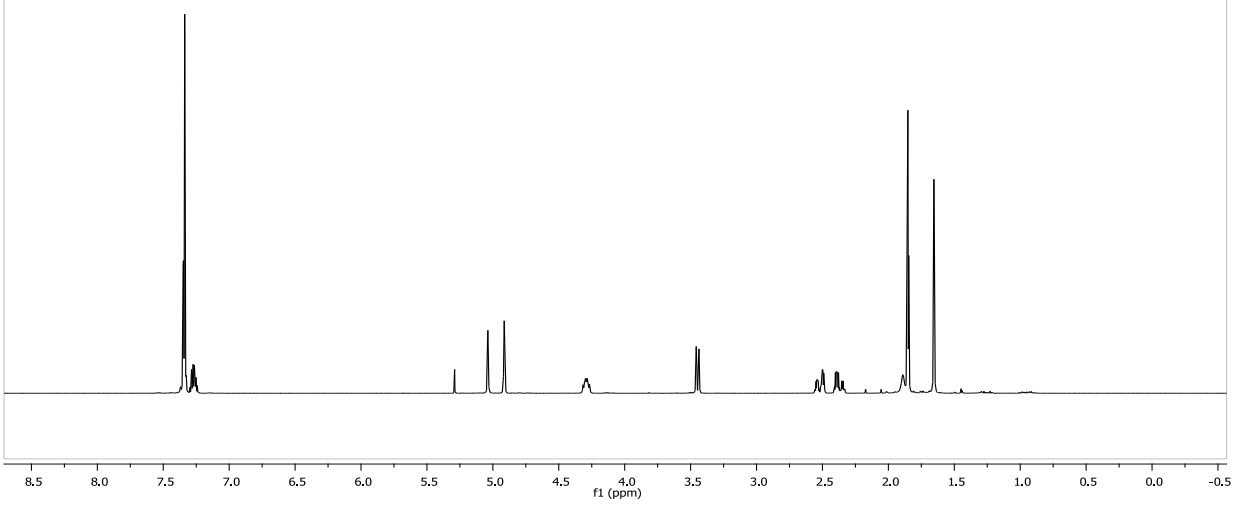

I-296
Ph
O
S10
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


I-296
Ph
O
S10
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

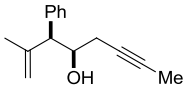
II-242



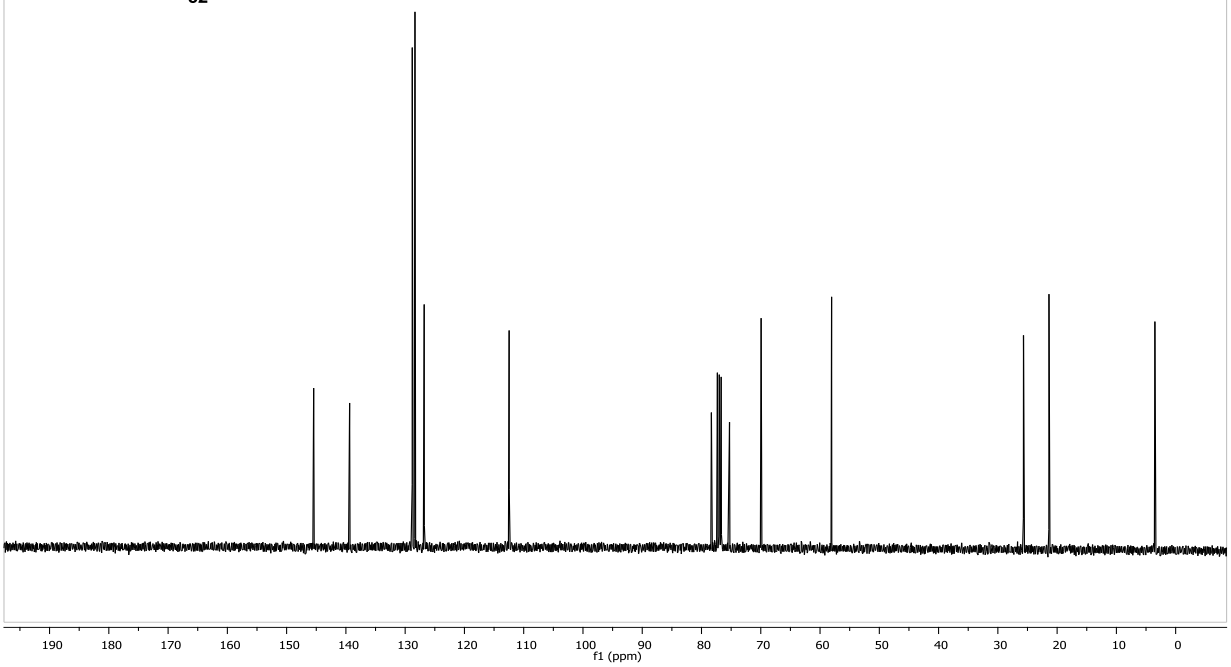
52



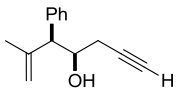
II-242



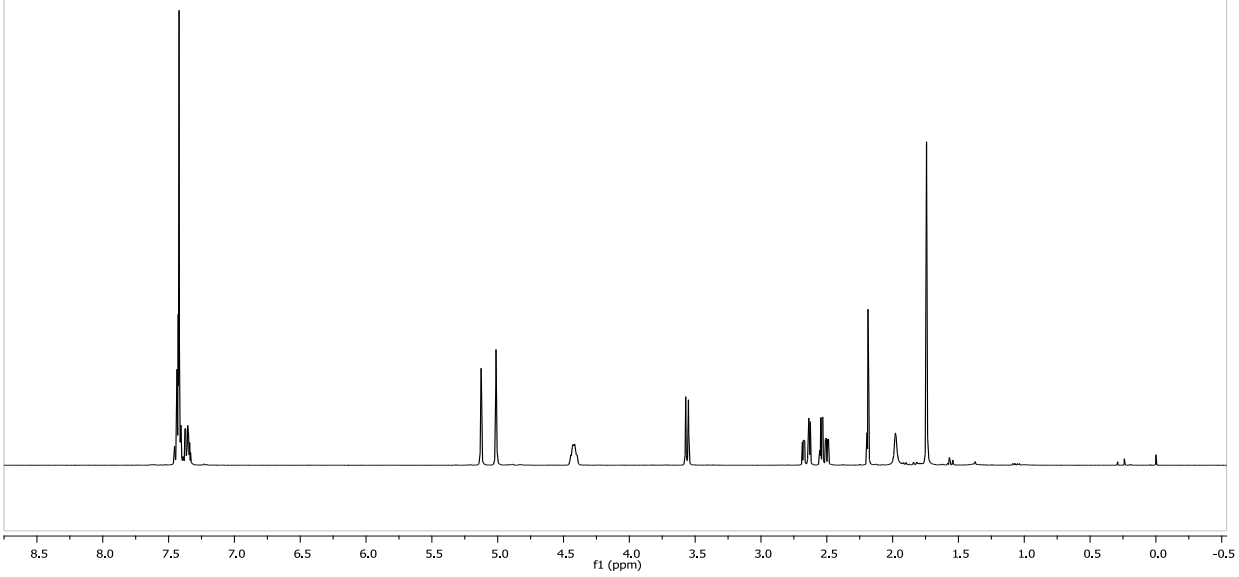
52



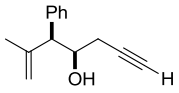
II-206



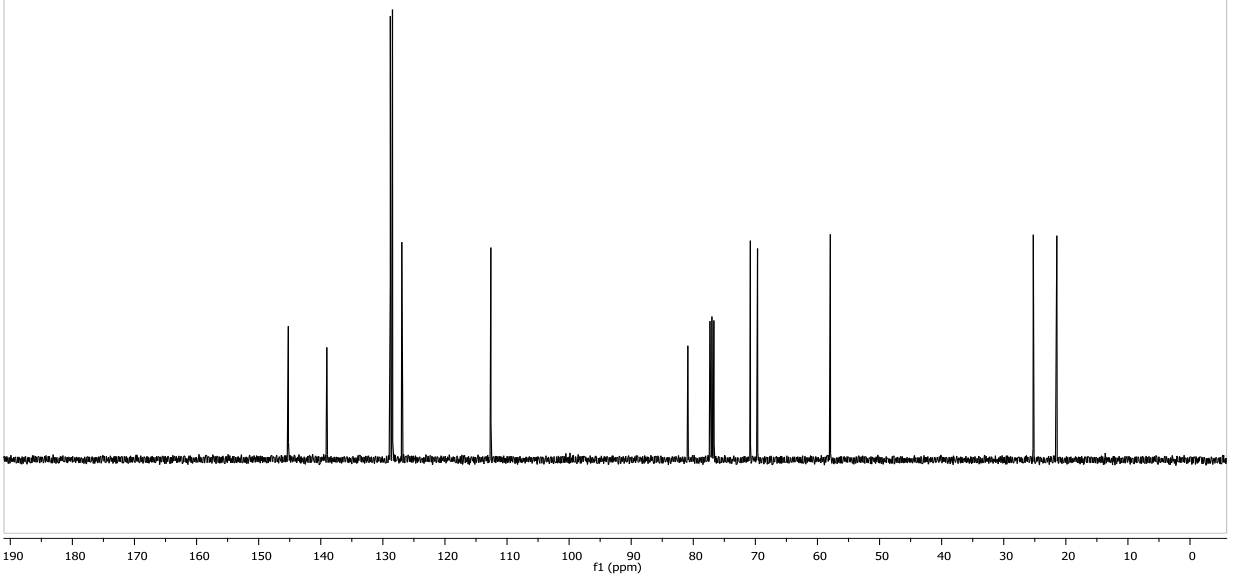
54



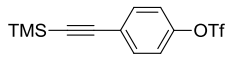
II-206



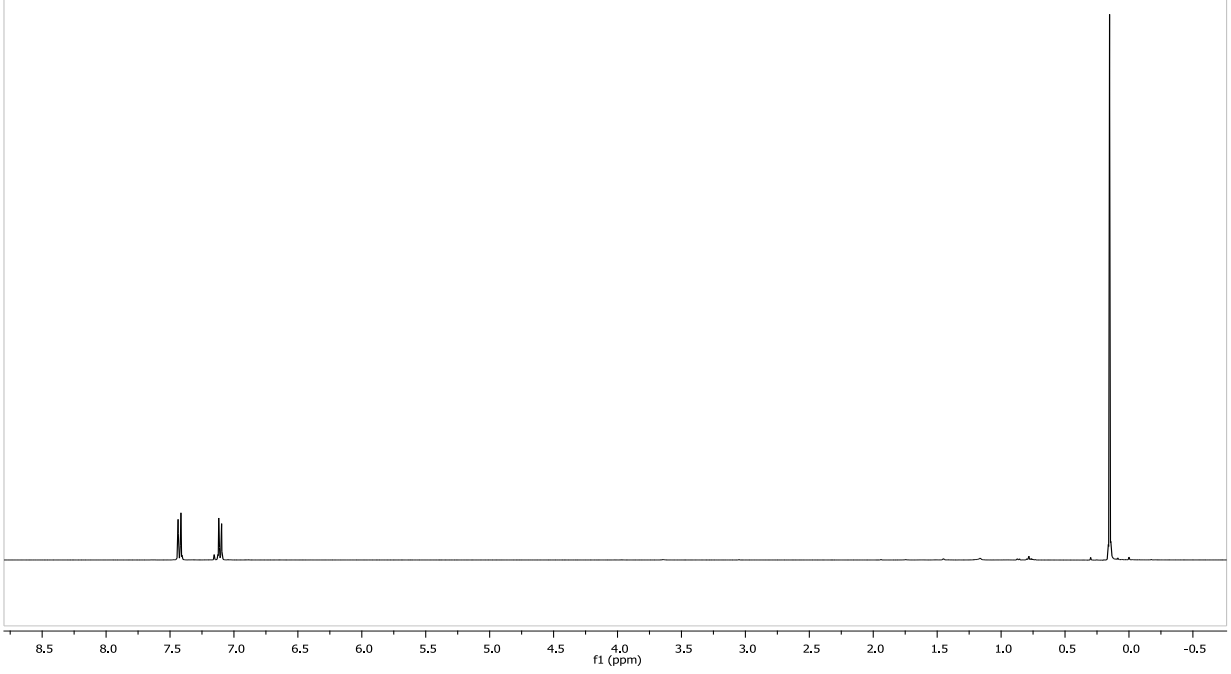
54



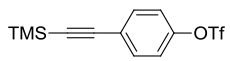
II-247



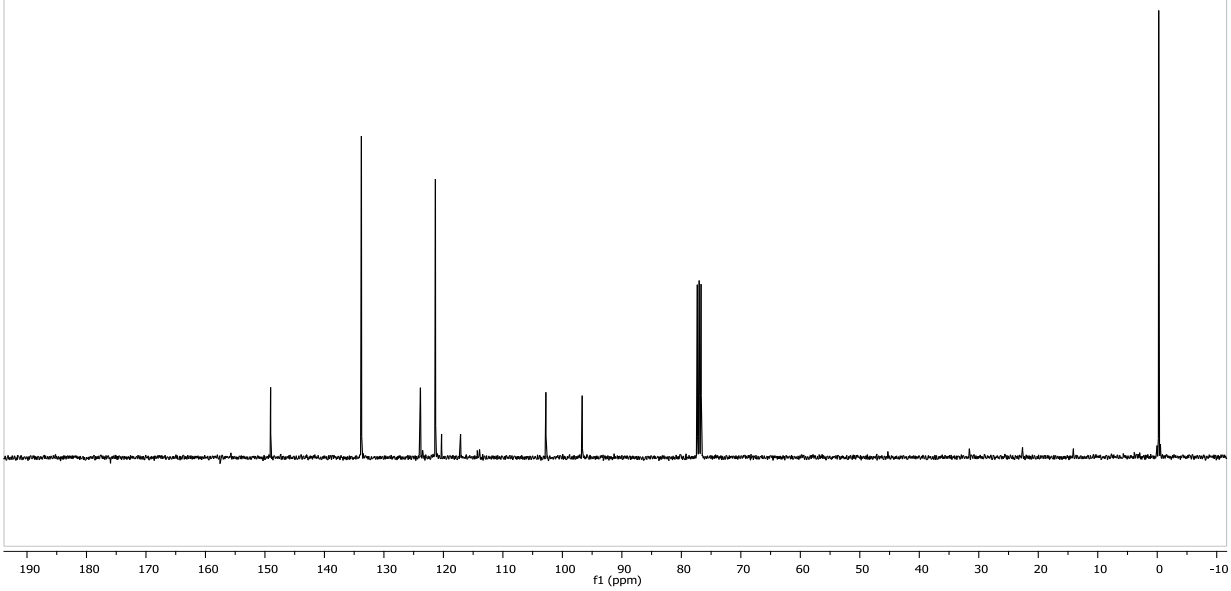
55

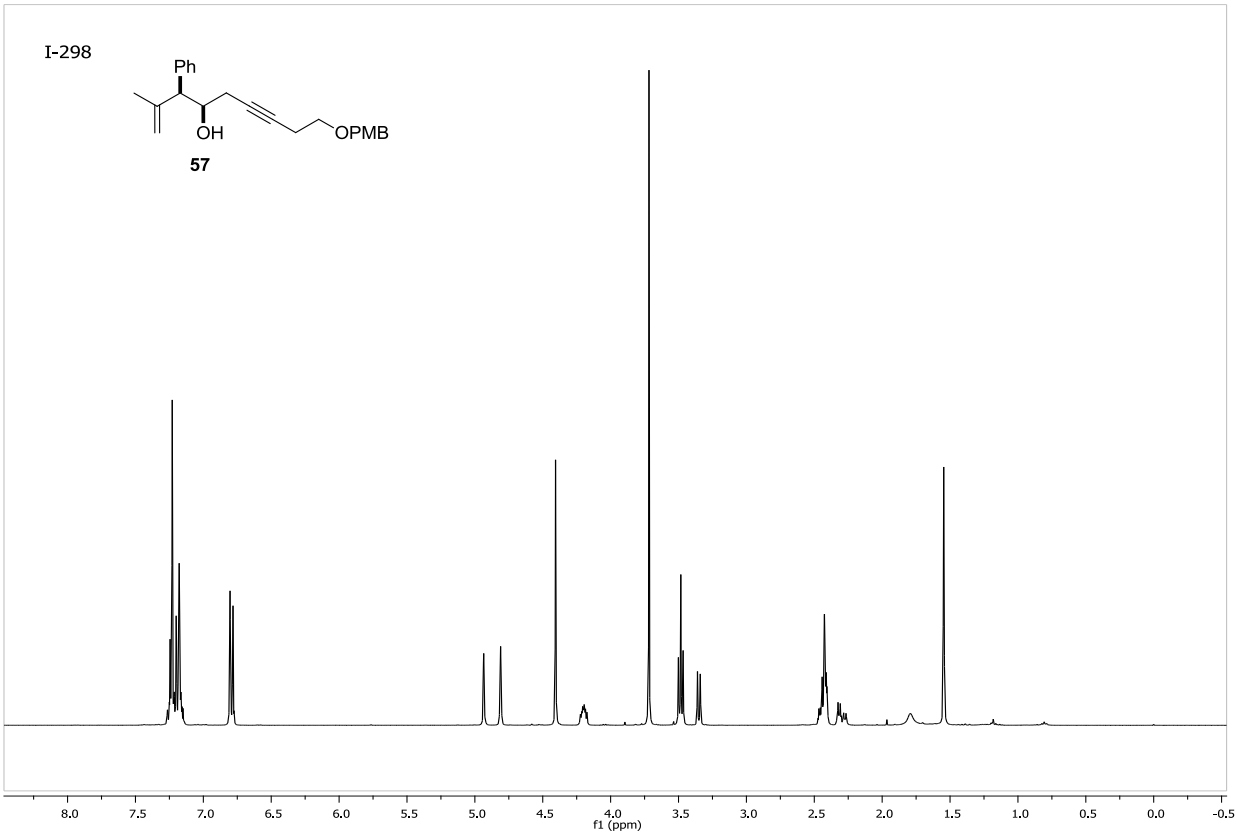


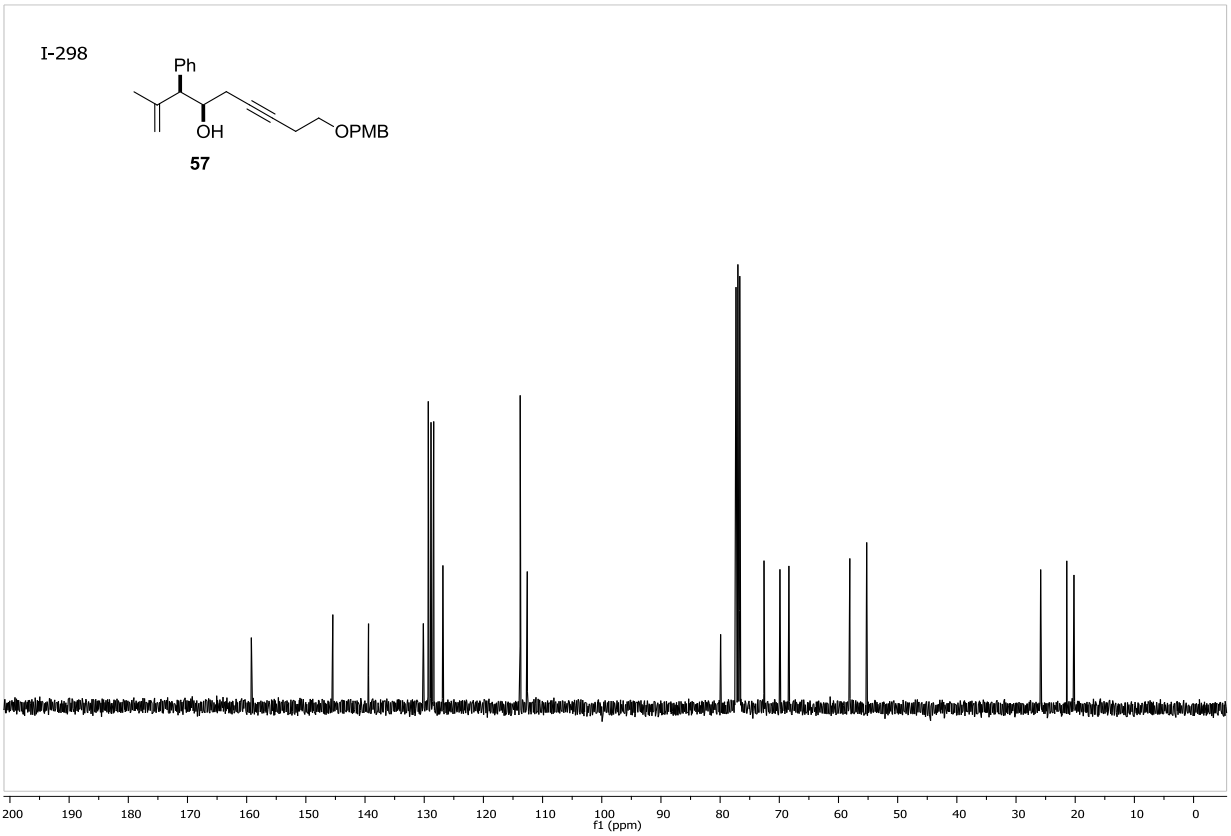
II-247



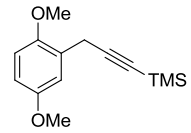
55




I-298
Ph
OH
OPMB
57
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

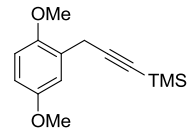

I-298
Ph
OH
OPMB
57
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

II-42

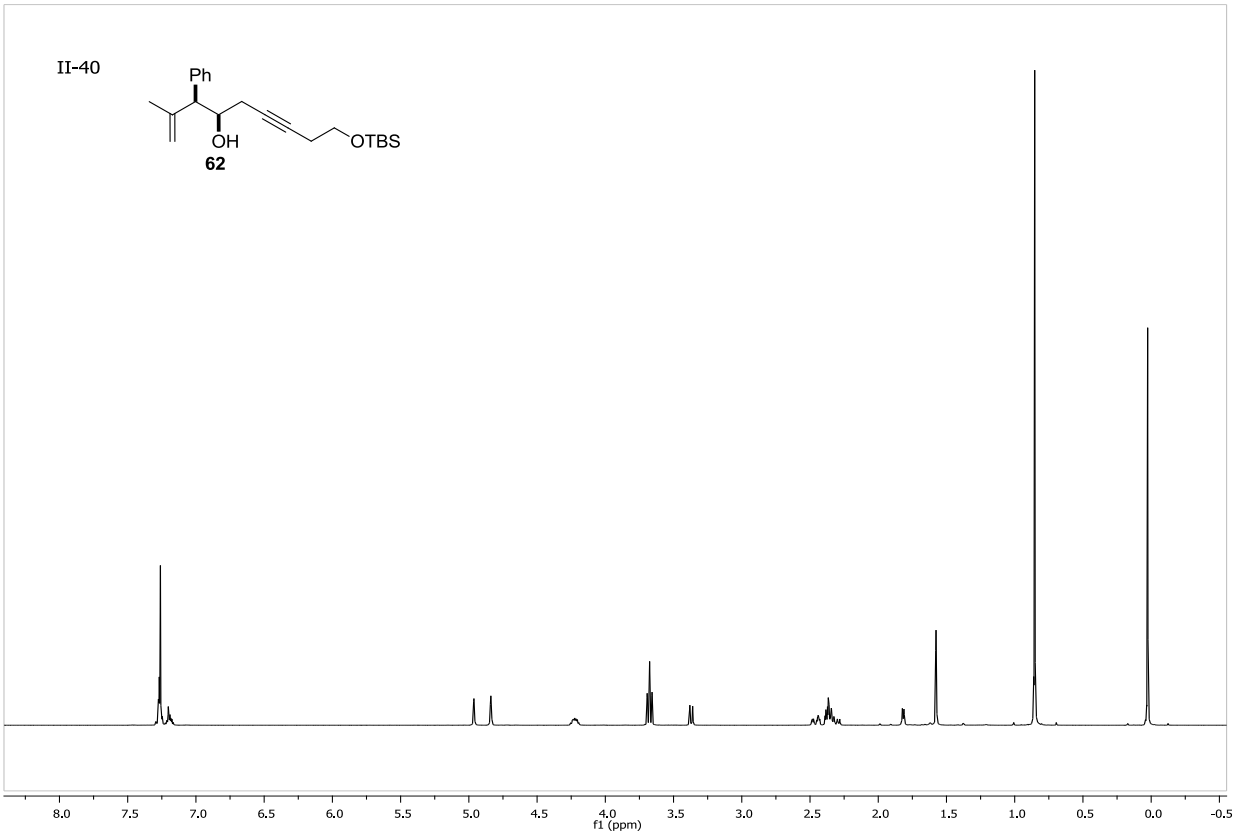


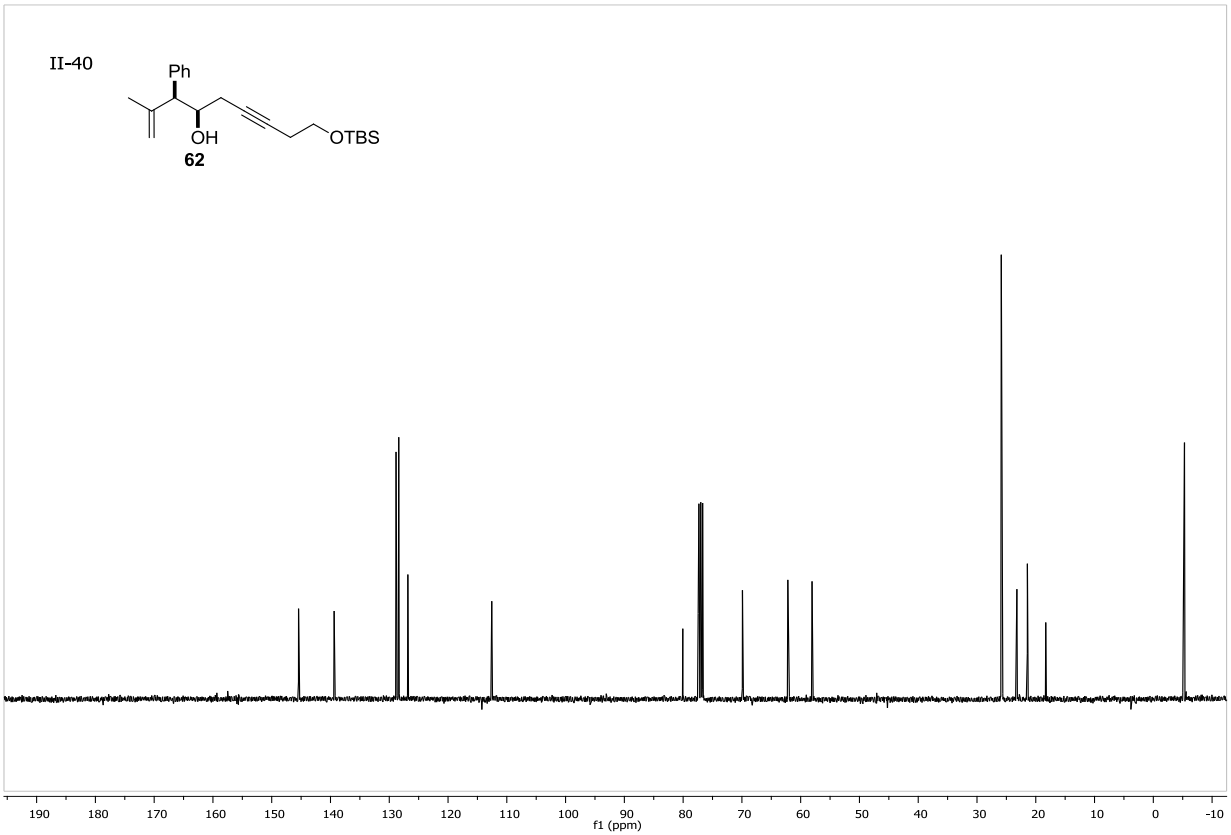
60

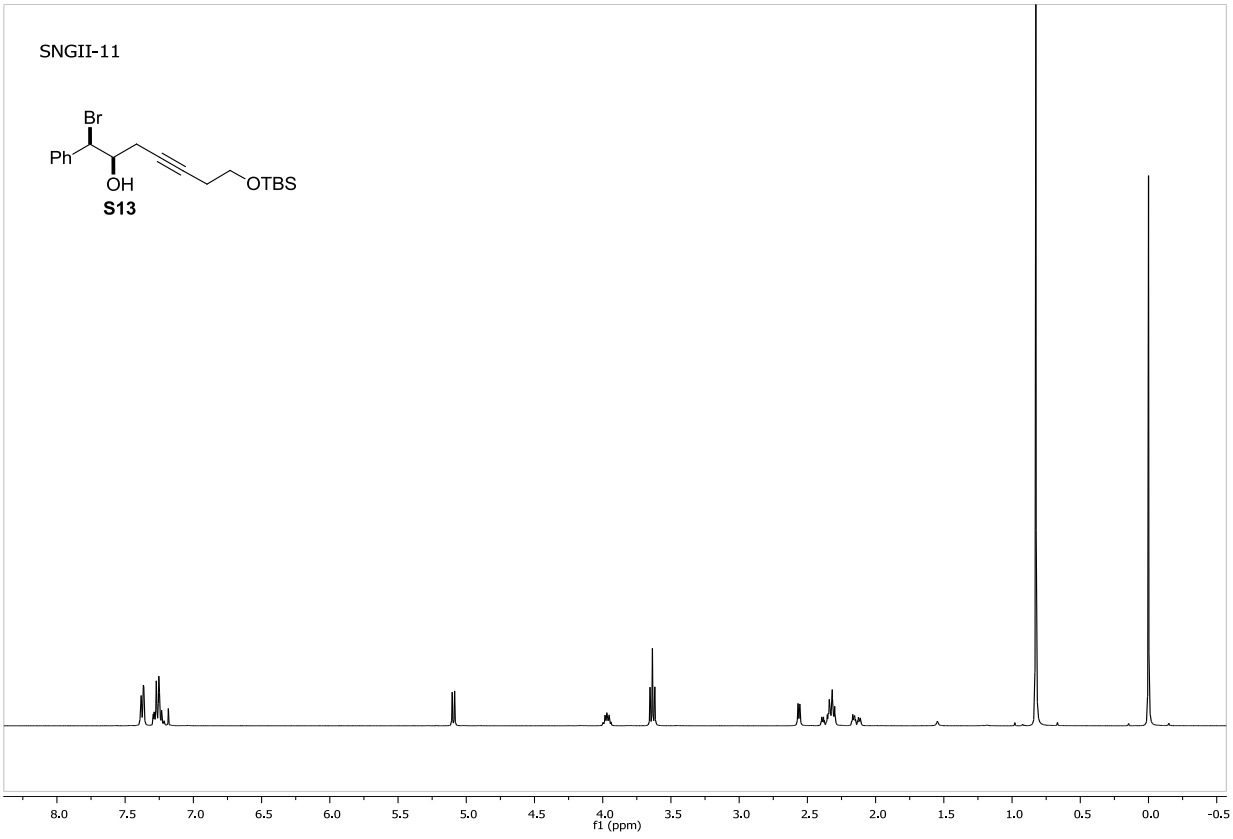
II-42

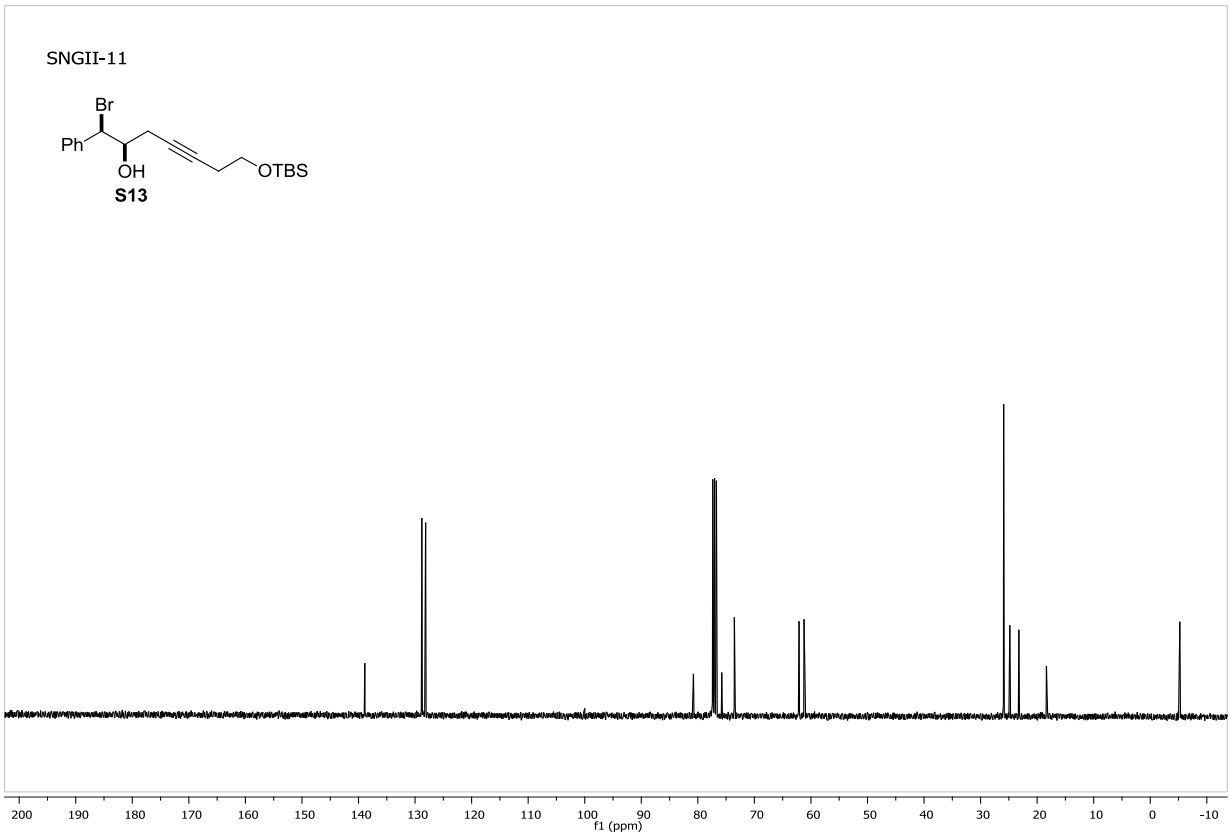


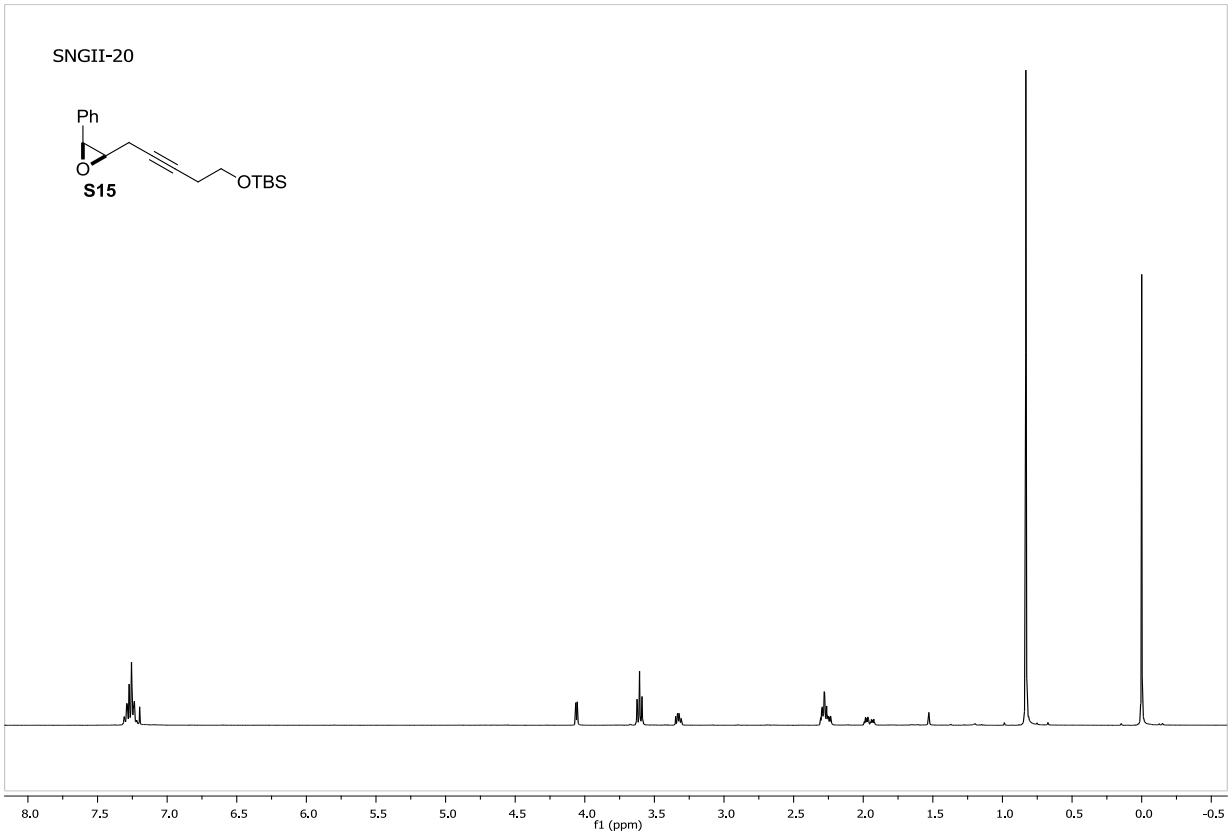
60

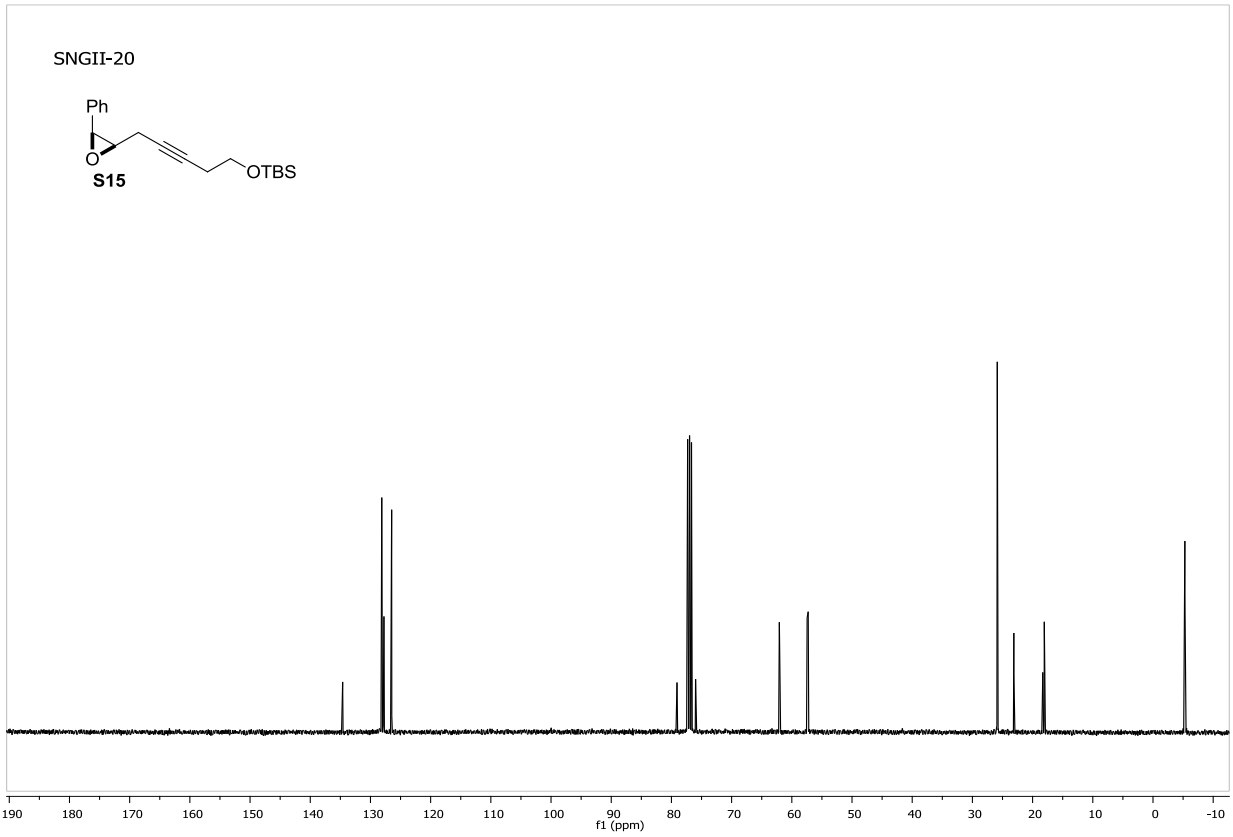

II-40
Ph
OH
OTBS
62
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


II-40
Ph
OH
OTBS
62
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

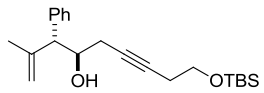

SNGII-11
Br
Ph
OH
OTBS
S13
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


SNGII-11
Br
Ph
OH
OTBS
S13
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


SNGII-20
Ph
O
OTBS
S15
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

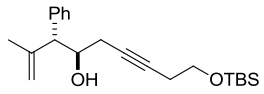

SNGII-20
Ph
O
OTBS
S15
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

SNGII-13

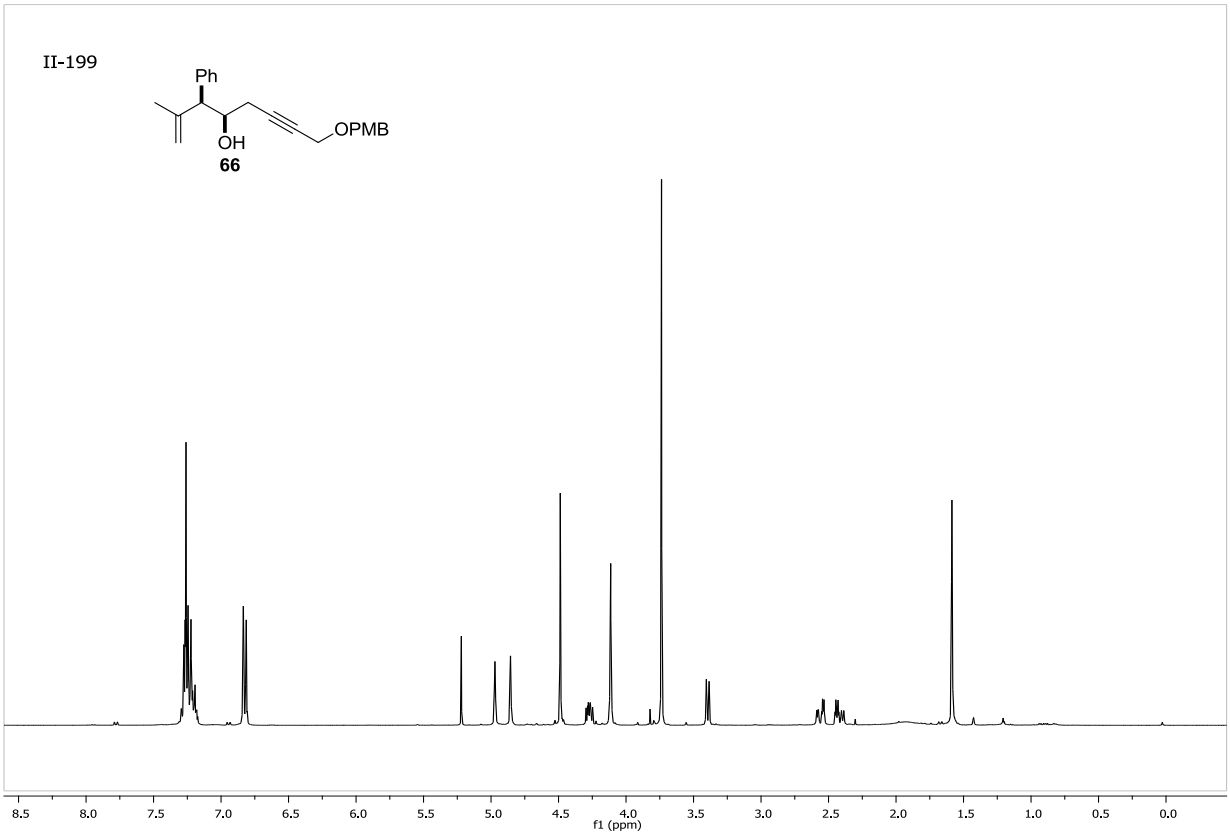


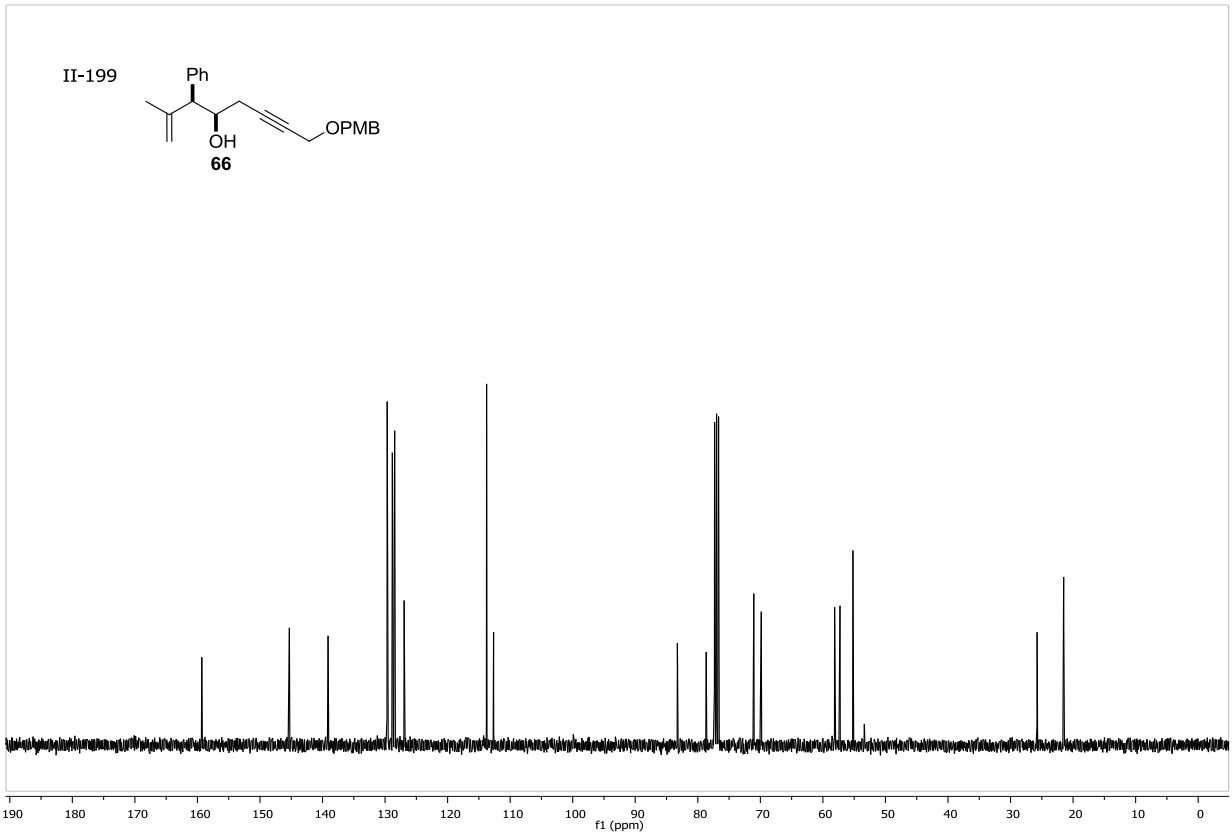
64

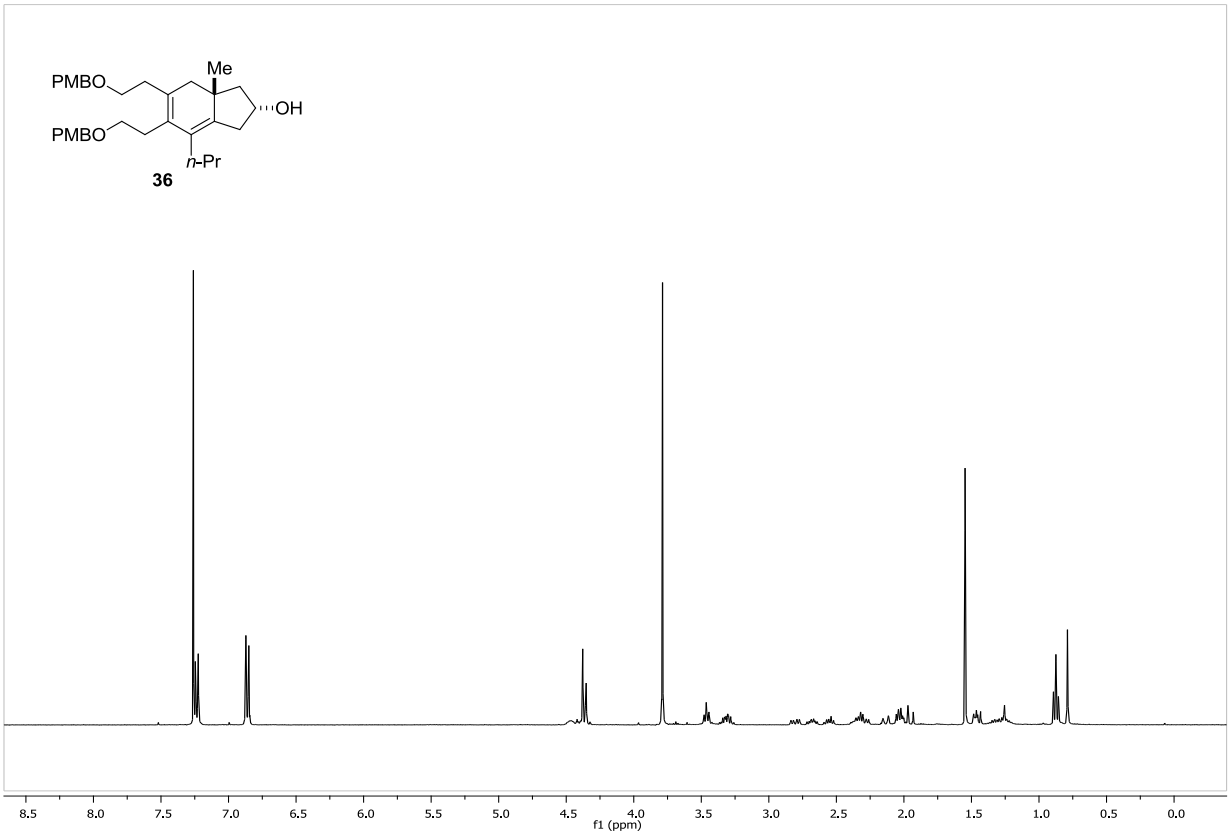
SNGII-13

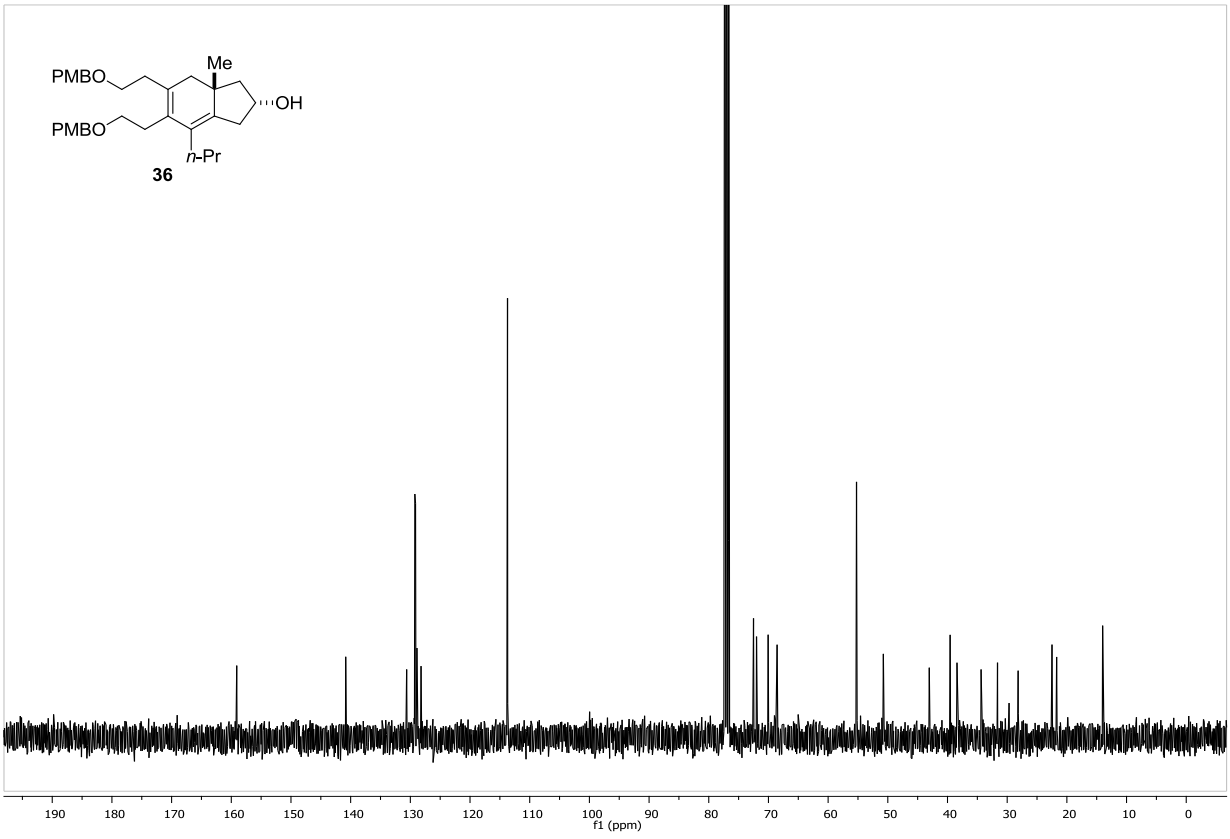


64

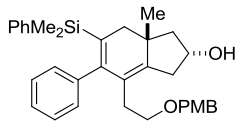

II-199
Ph
OH
OPMB
66
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


II-199
Ph
OH
OPMB
66
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


Me
PMBO
OH
PMBO
n-Pr
36
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

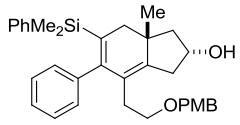

Me
PMBO
OH
PMBO
n-Pr
36
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

II-216


Me
PhMe2Si
OH
OPMB

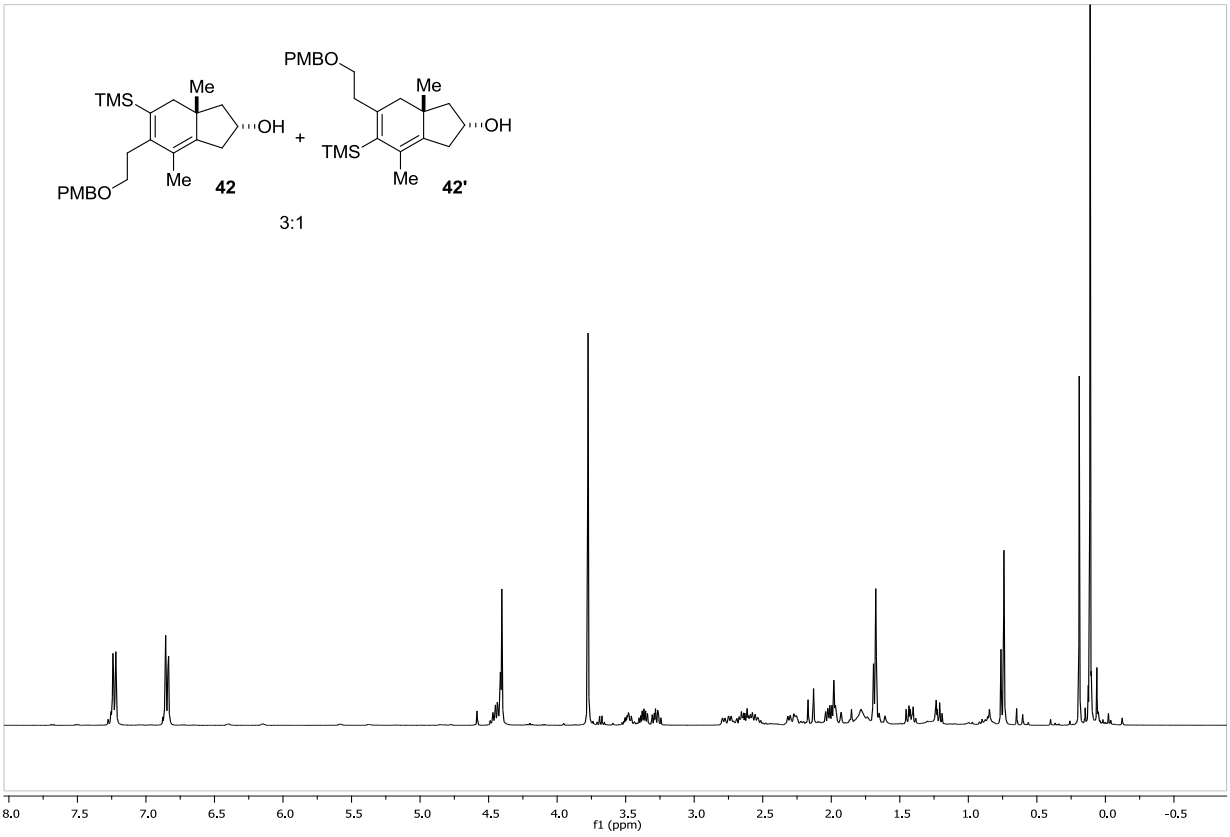
39

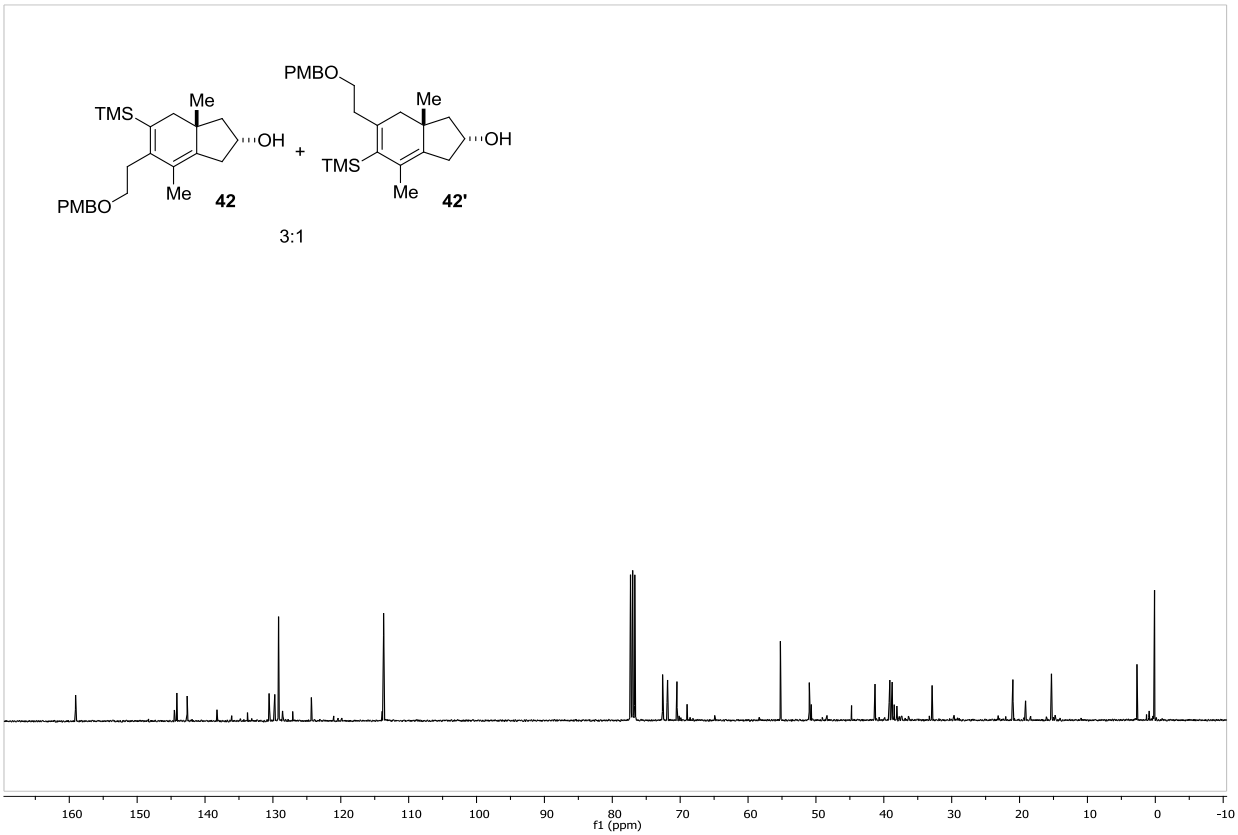
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

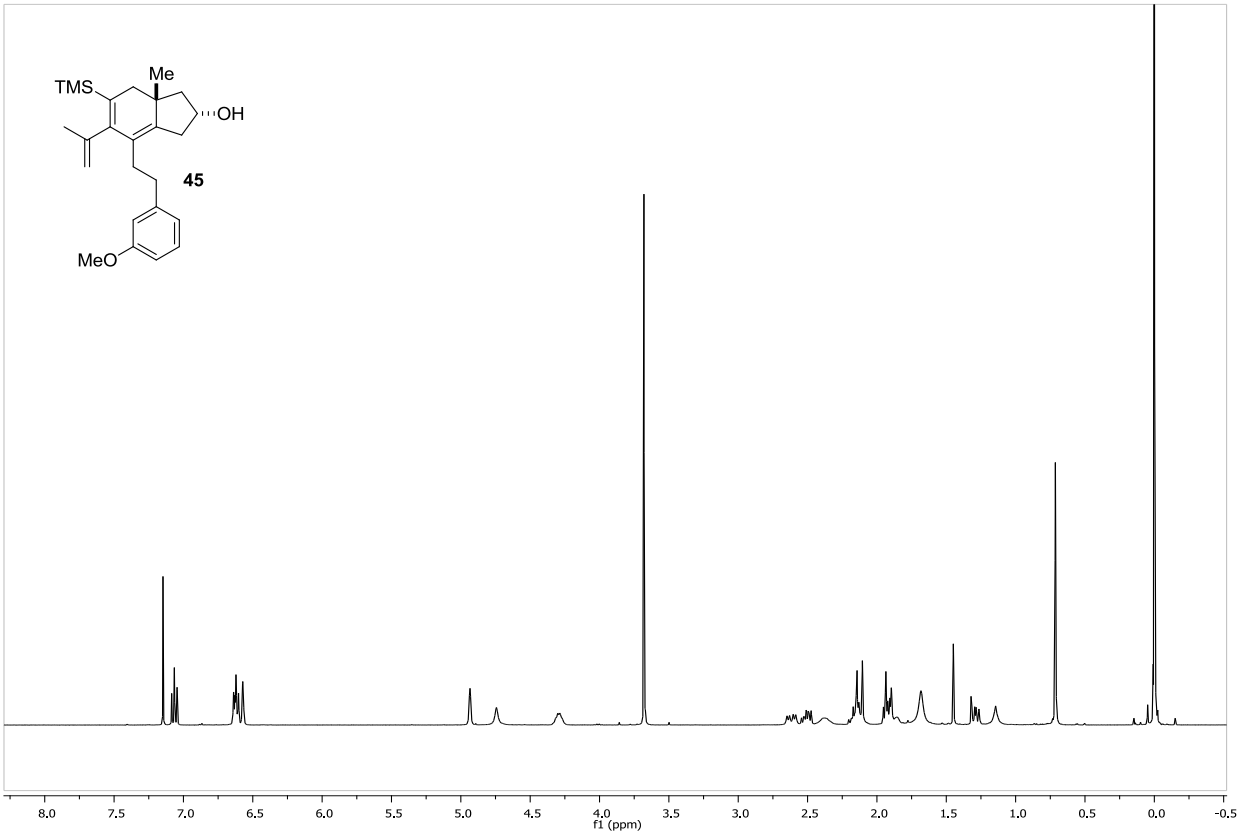

Me
PhMe2Si
OH
OPMB

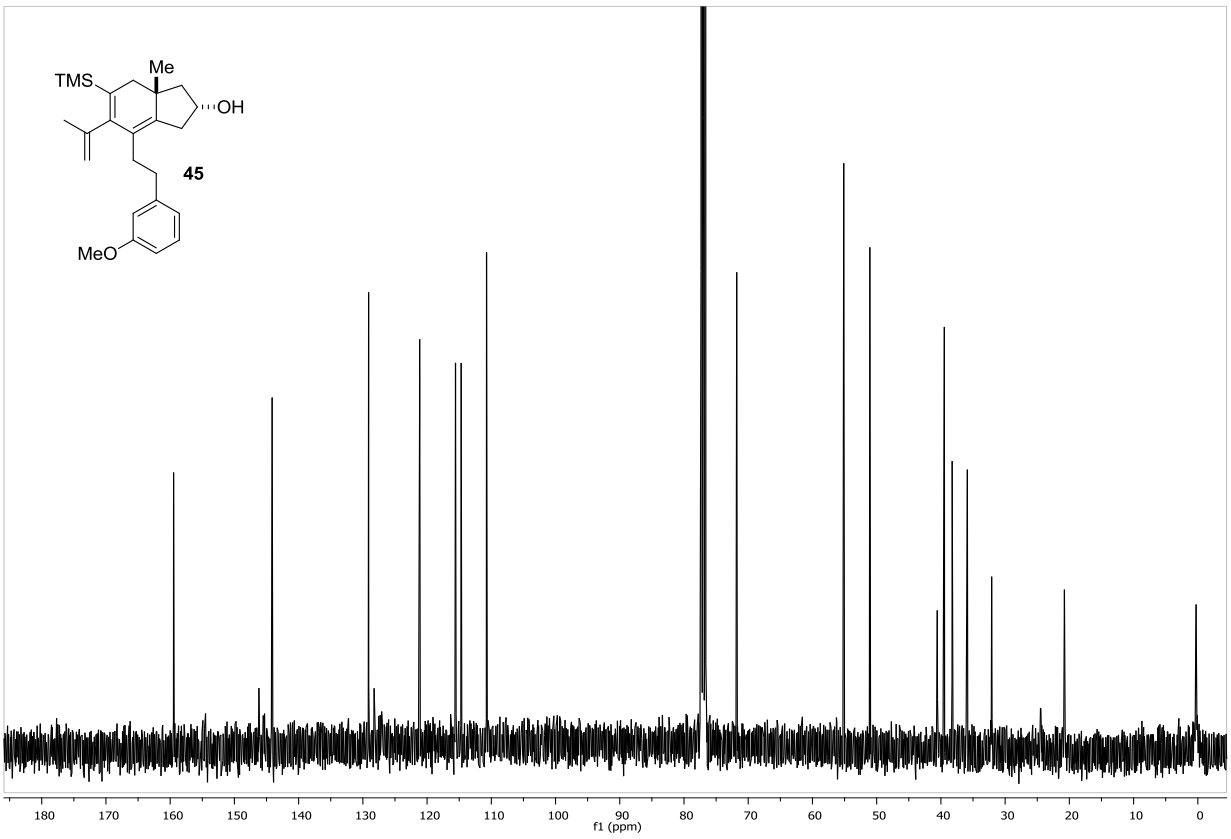
39

190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

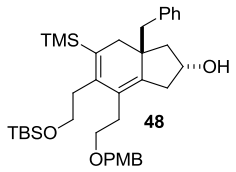

PMBO
Me
TMS
OH
+
TMS
Me
OH
PMBO
Me
42
42'
3:1
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

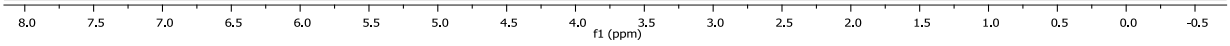

PMBO
Me
TMS
OH
+
TMS
Me
OH
PMBO
Me
42
42'
3:1
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


TMS
Me
OH
45
MeO
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

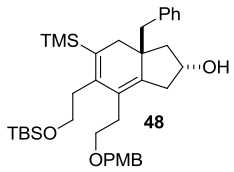

TMS
Me
OH
45
MeO
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

III-32

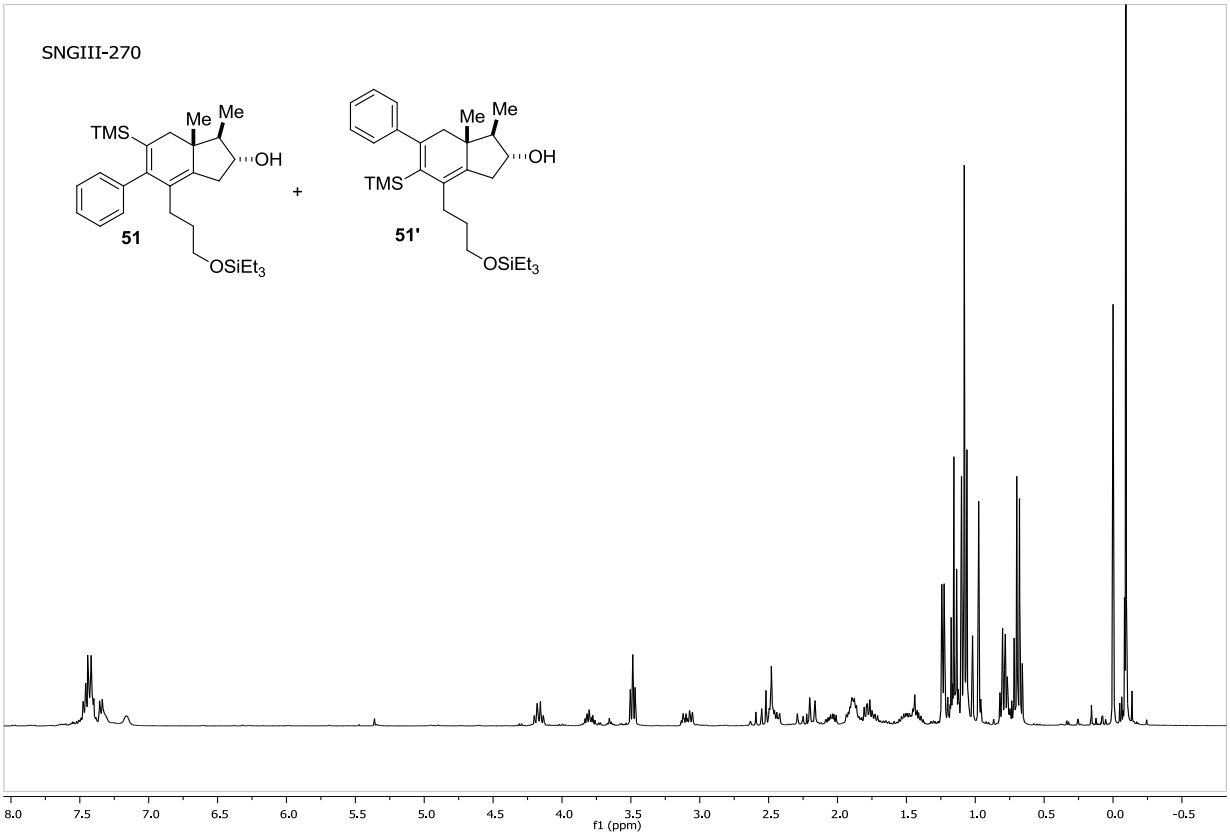

Ph
TMS
OH
TBSO
48
OPMB

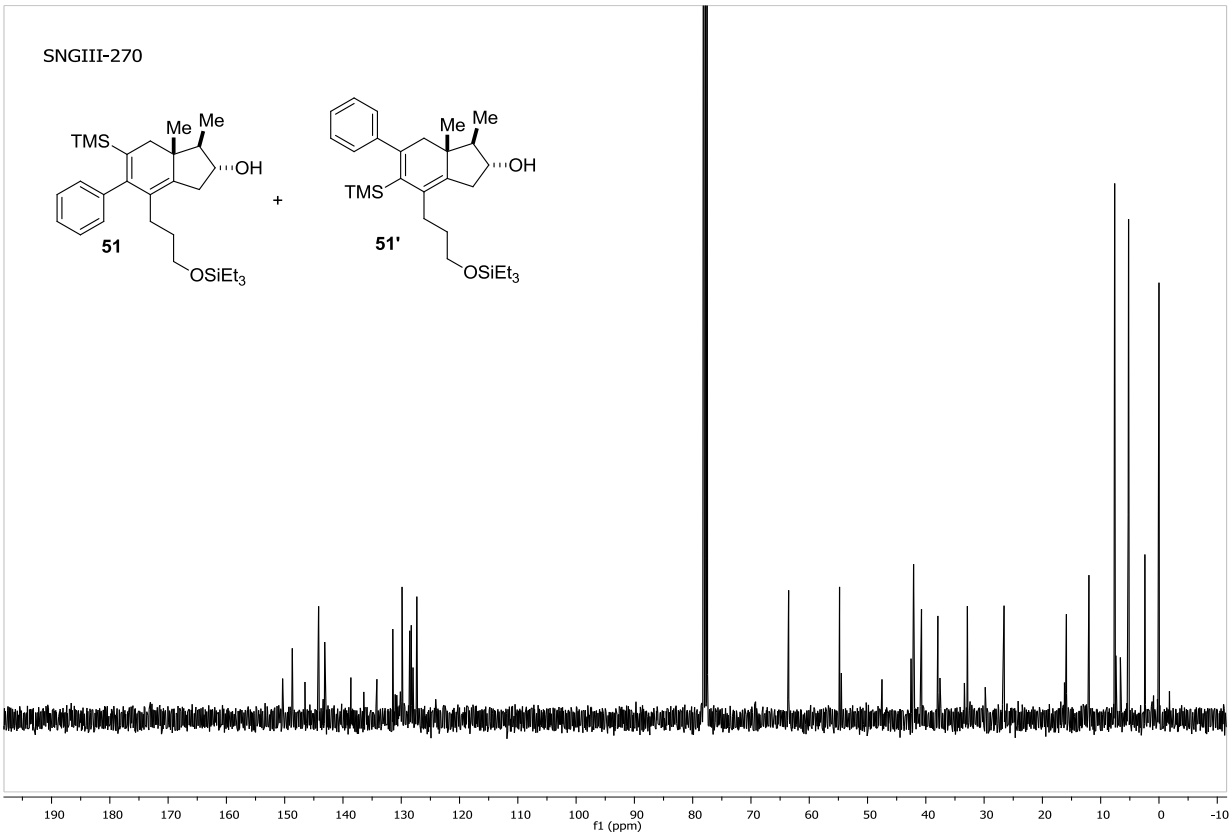

8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

III-32

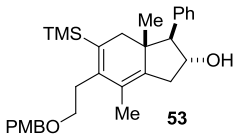

Ph
TMS
OH
TBSO
48
OPMB

190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


SNGIII-270
TMS
Me
Me
OH
51
+
TMS
Me
Me
OH
51'
OSiEt3
OSiEt3
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

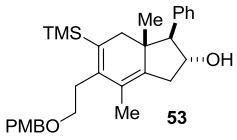

SNGIII-270
TMS
Me
Me
OH
51
+
TMS
Me
Me
OH
51'
OSiEt3
OSiEt3
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

III-38



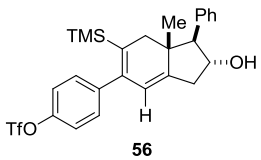
53

SNGIII-38



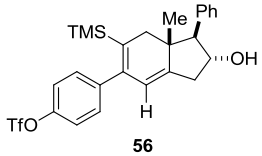
53

II-223



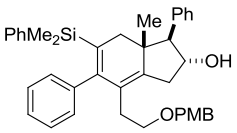
56

II-223

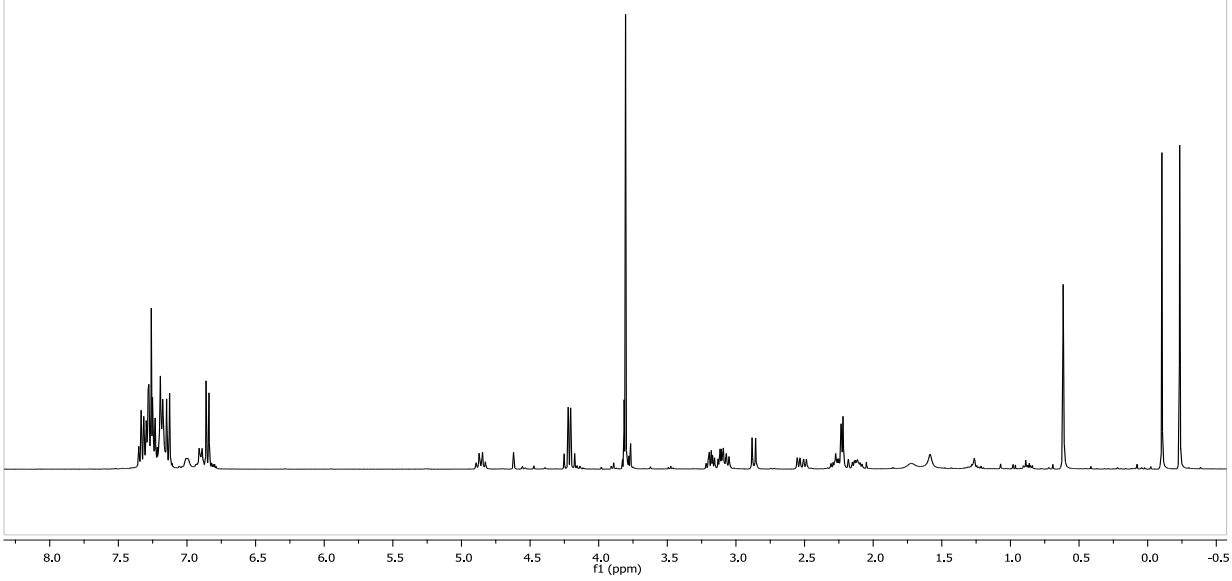


56

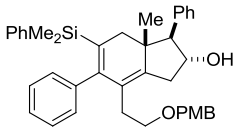
II-27



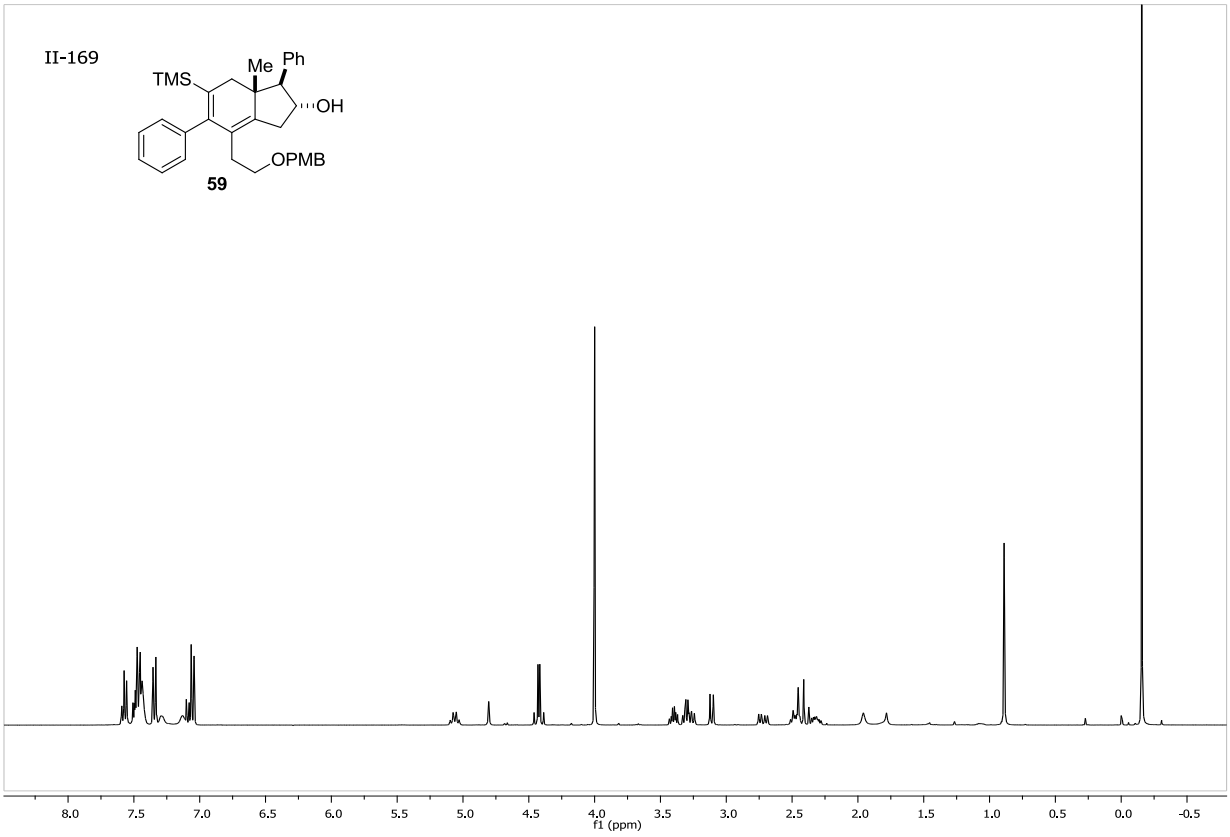
58

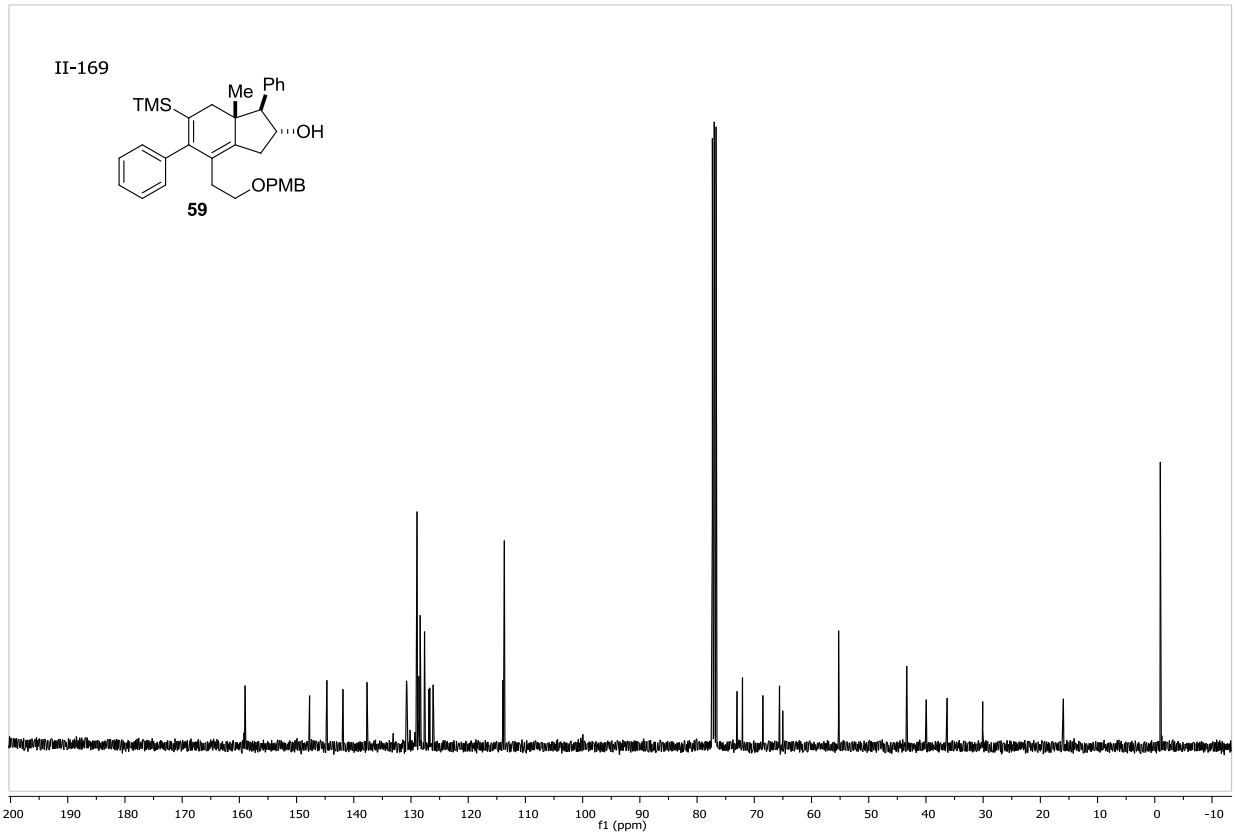


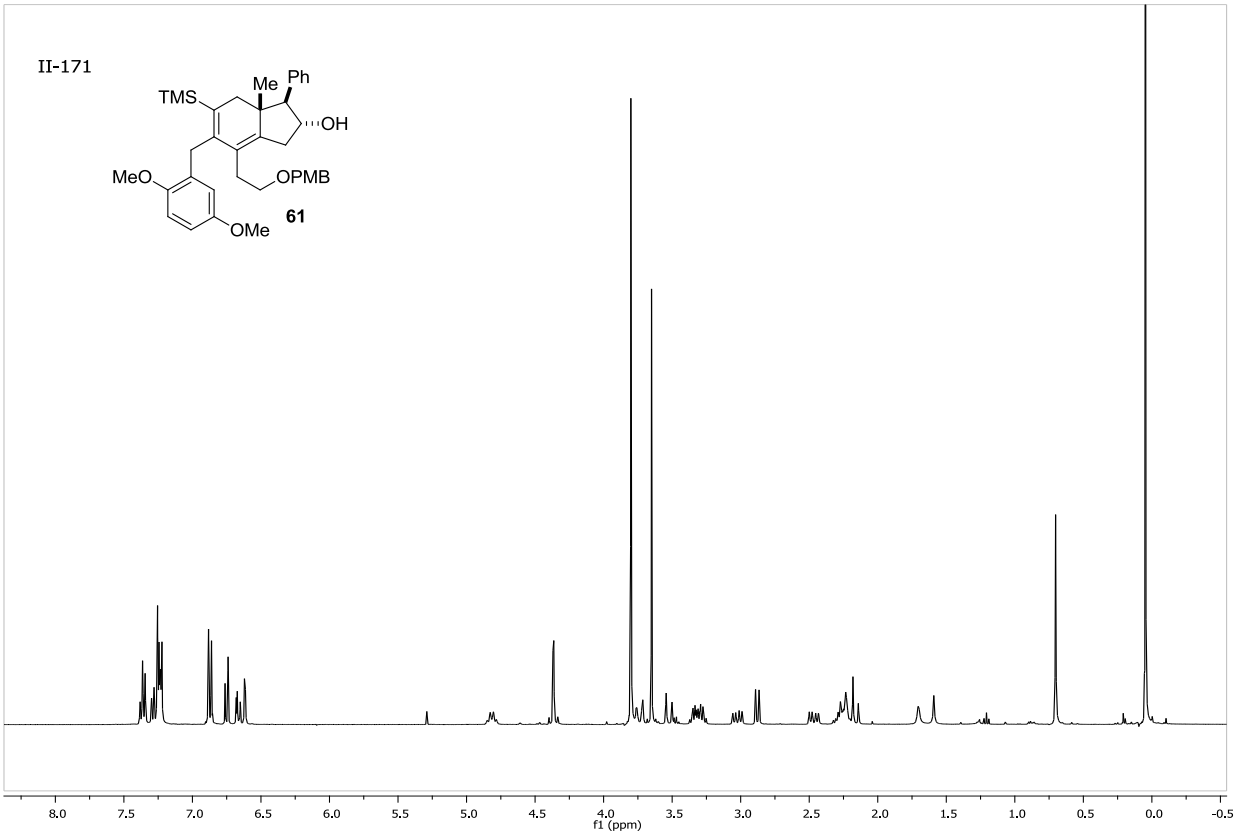
II-45

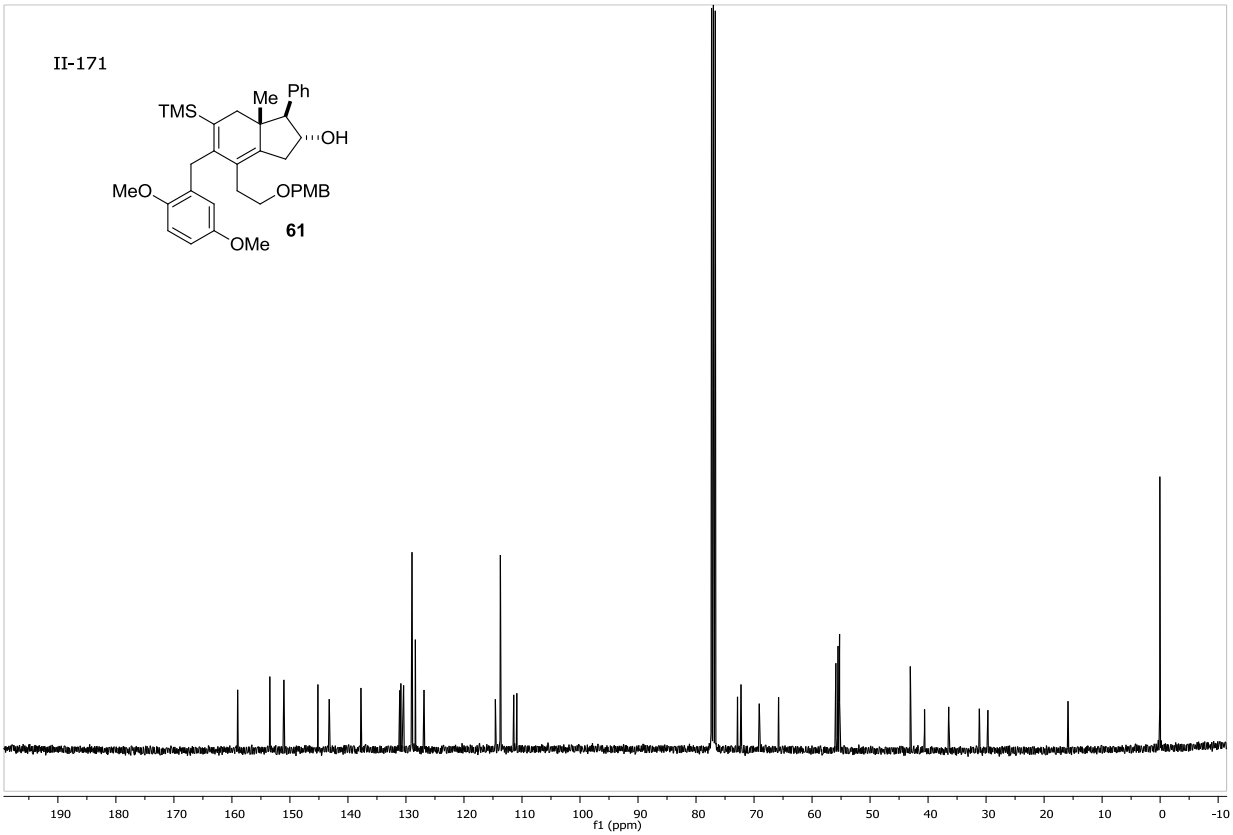


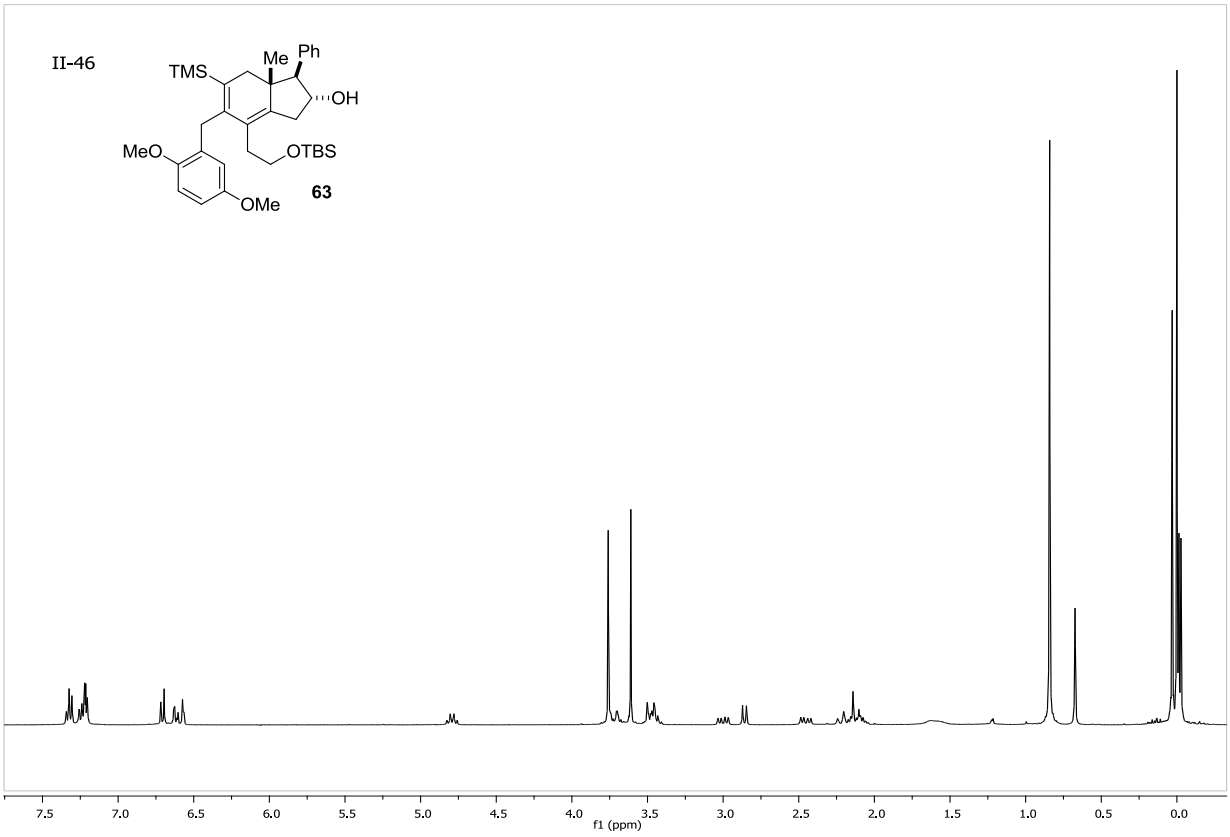
58

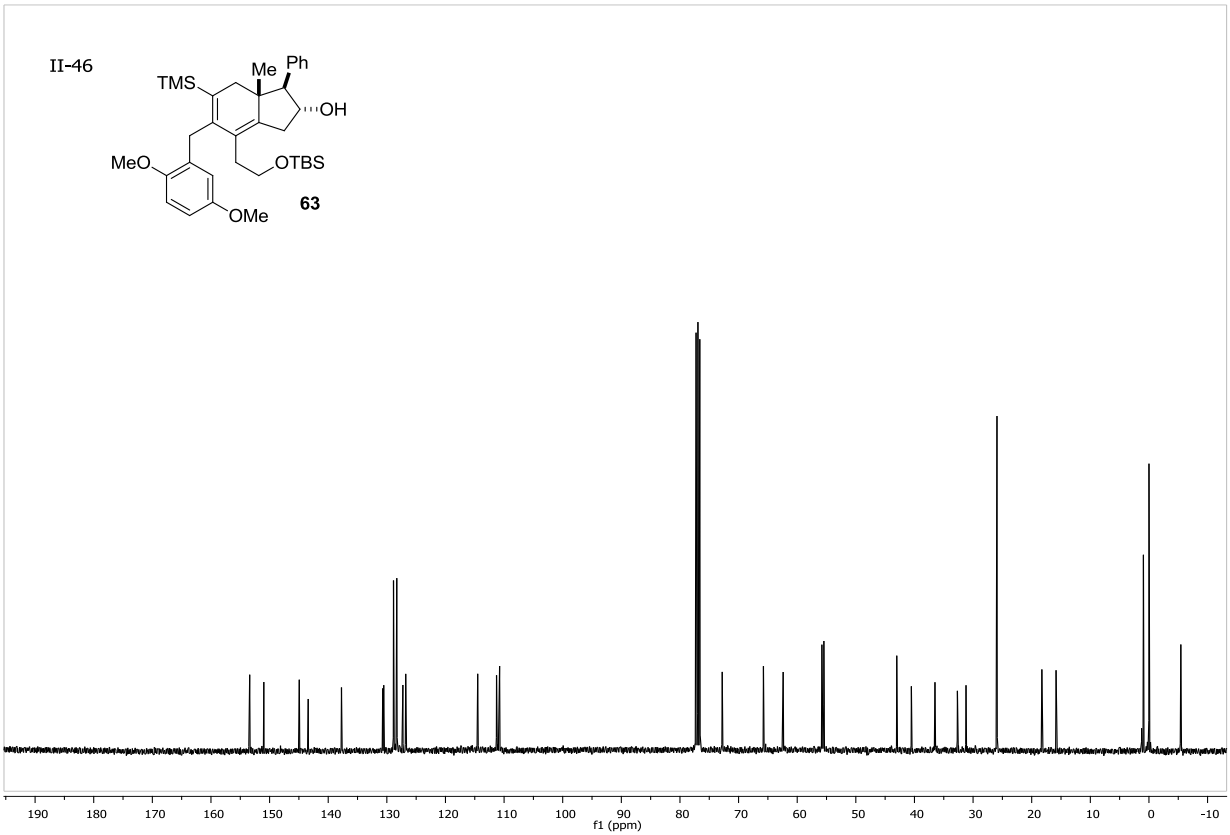

II-169
TMS
Me
Ph
OH
OPMB
59
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

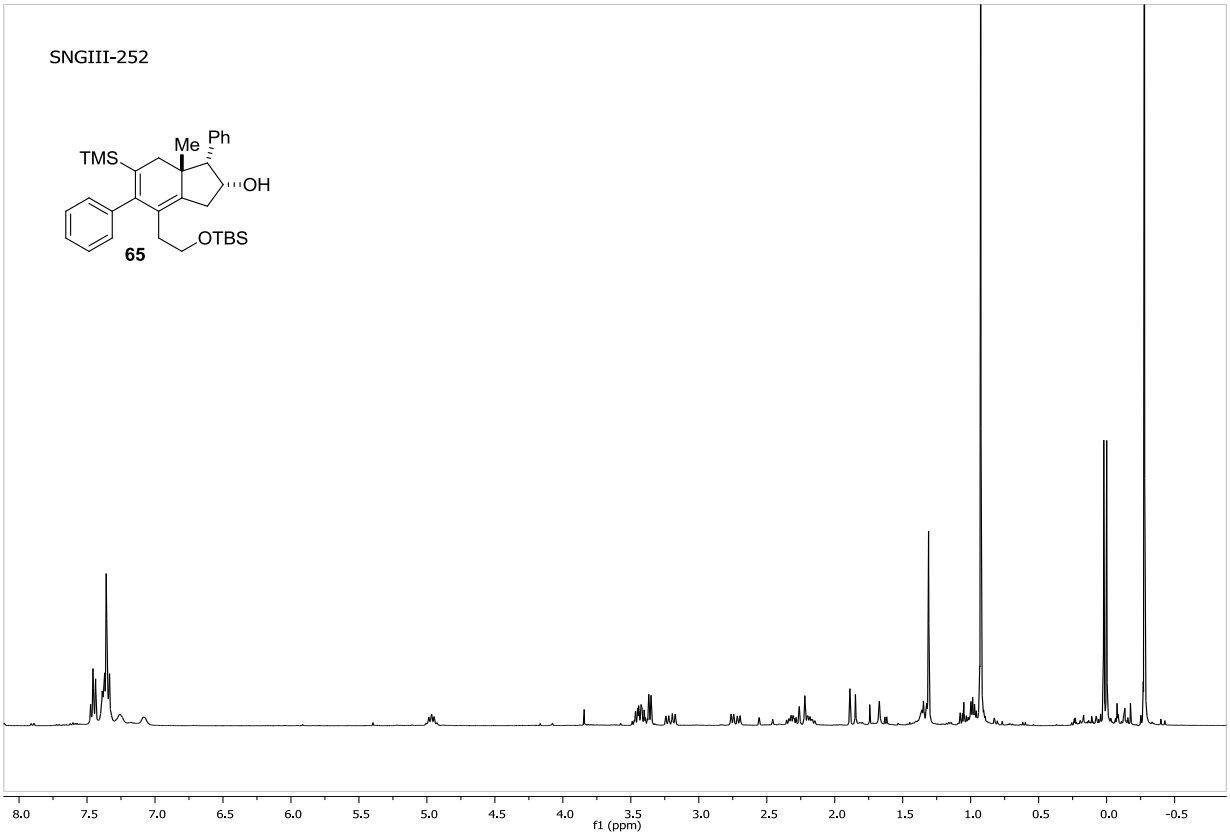

II-169
TMS
Me
Ph
OH
OPMB
59
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

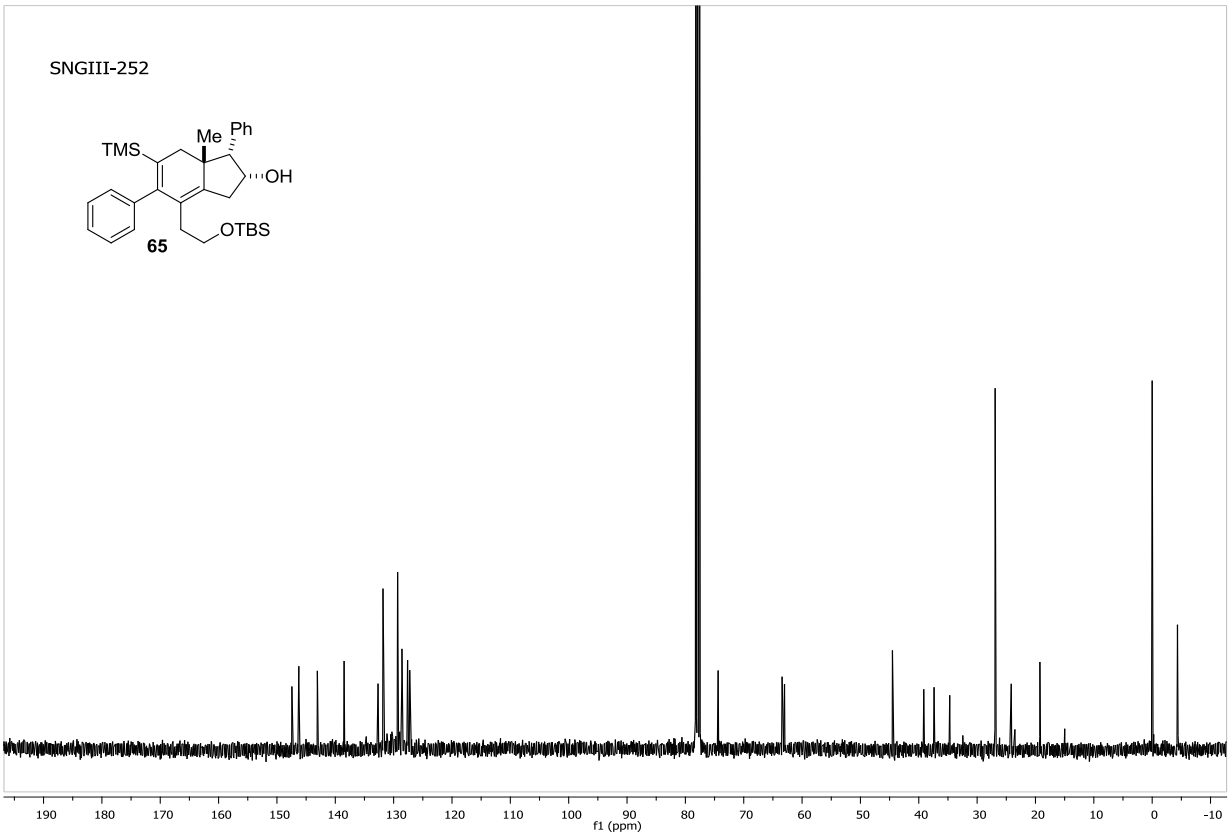

II-171
TMS
Me
Ph
OH
MeO
OPMB
OMe
61
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


II-171
TMS
Me
Ph
OH
MeO
OPMB
OMe
61
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

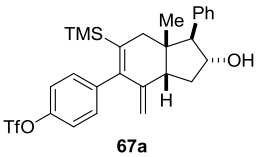

II-46
TMS
Me
Ph
OH
MeO
OTBS
OMe
63
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


II-46
TMS
Me
Ph
OH
MeO
OTBS
OMe
63
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


SNGIII-252
TMS
Me
Ph
OH
OTBS
65
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

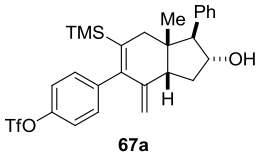

SNGIII-252
TMS
Me
Ph
OH
OTBS
65
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

II-217

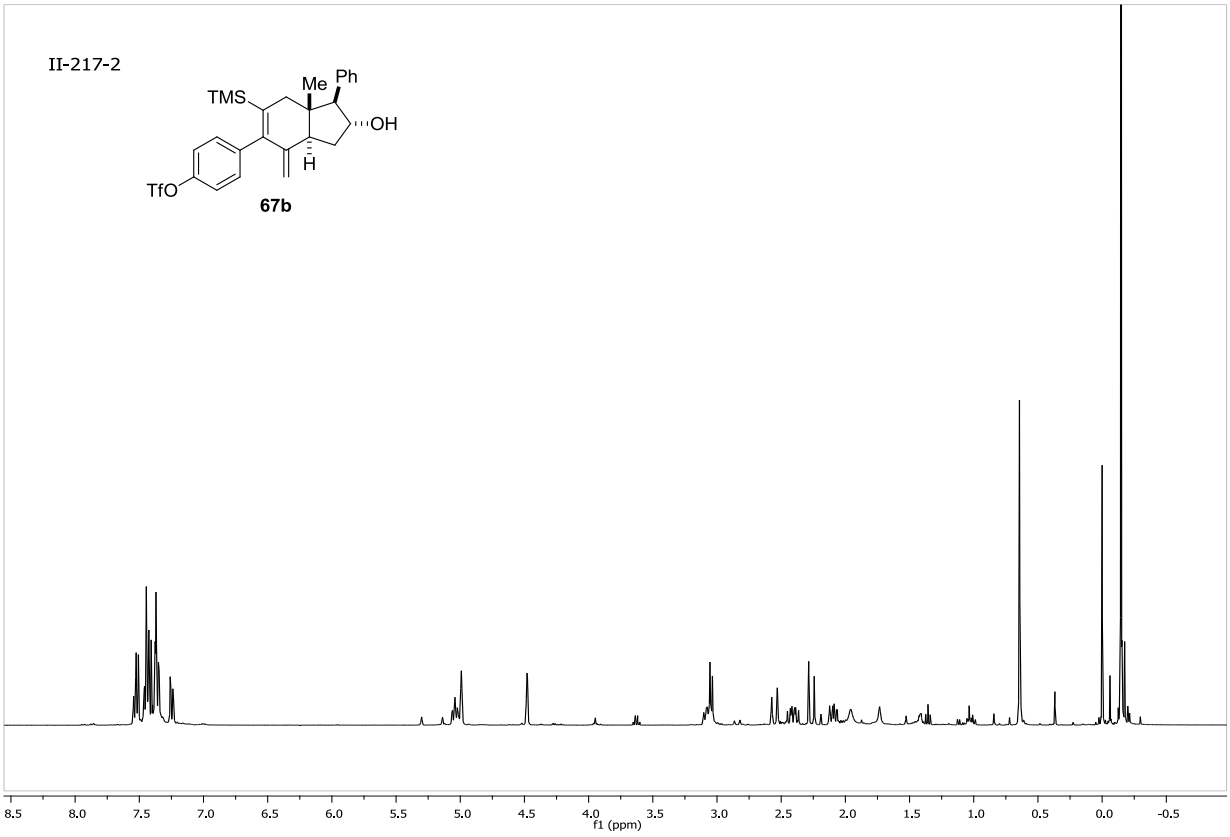


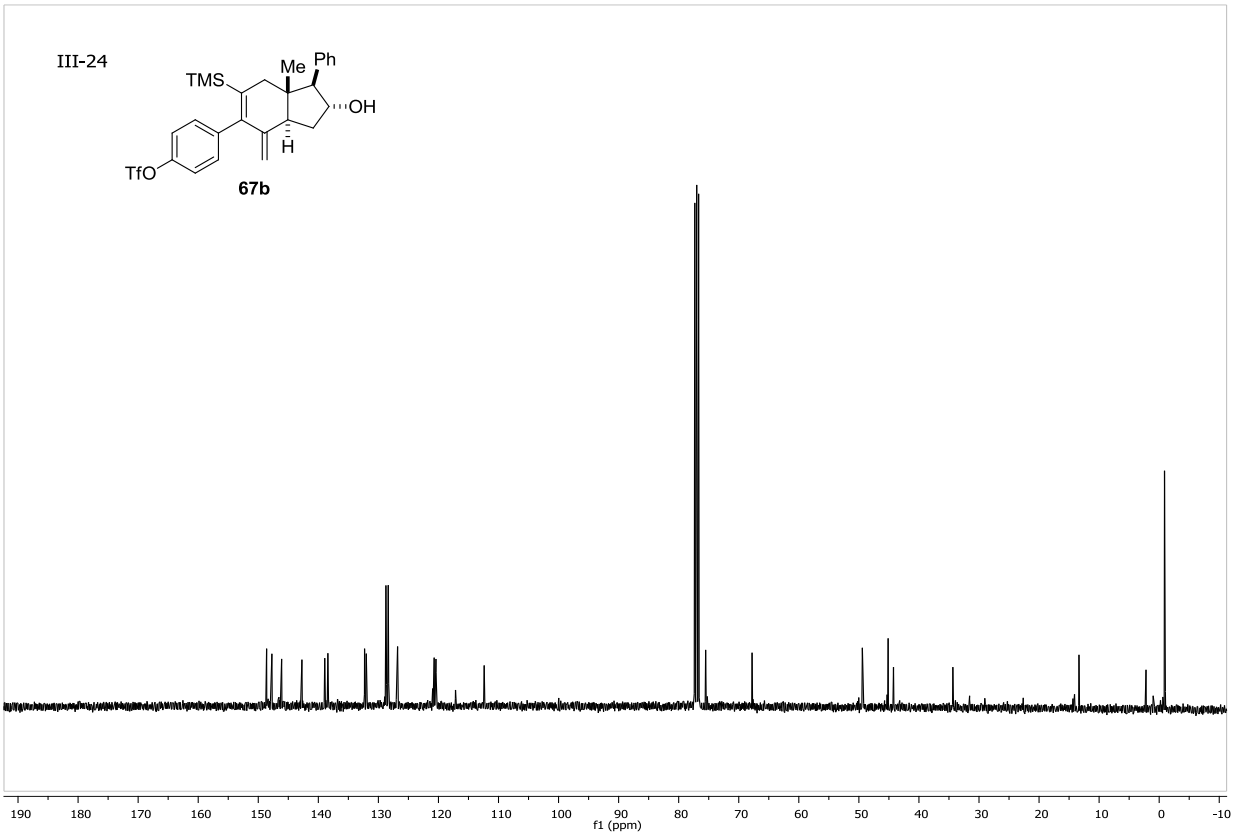
67a

III-24

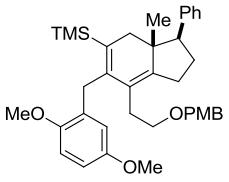


67a


II-217-2
Me
Ph
TMS
OH
H
TfO
67b
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

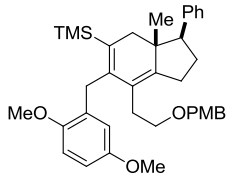

III-24
Me
Ph
TMS
OH
H
TfO
67b
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

II-176

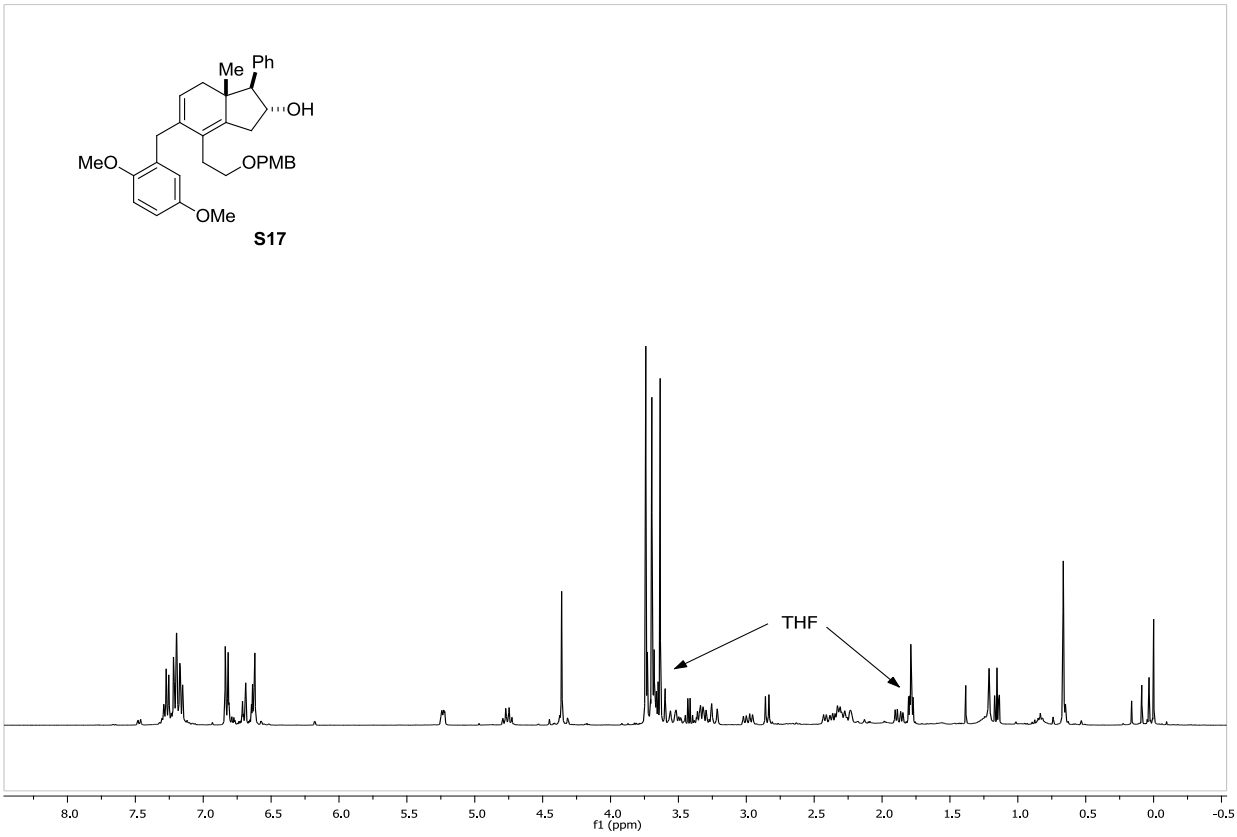


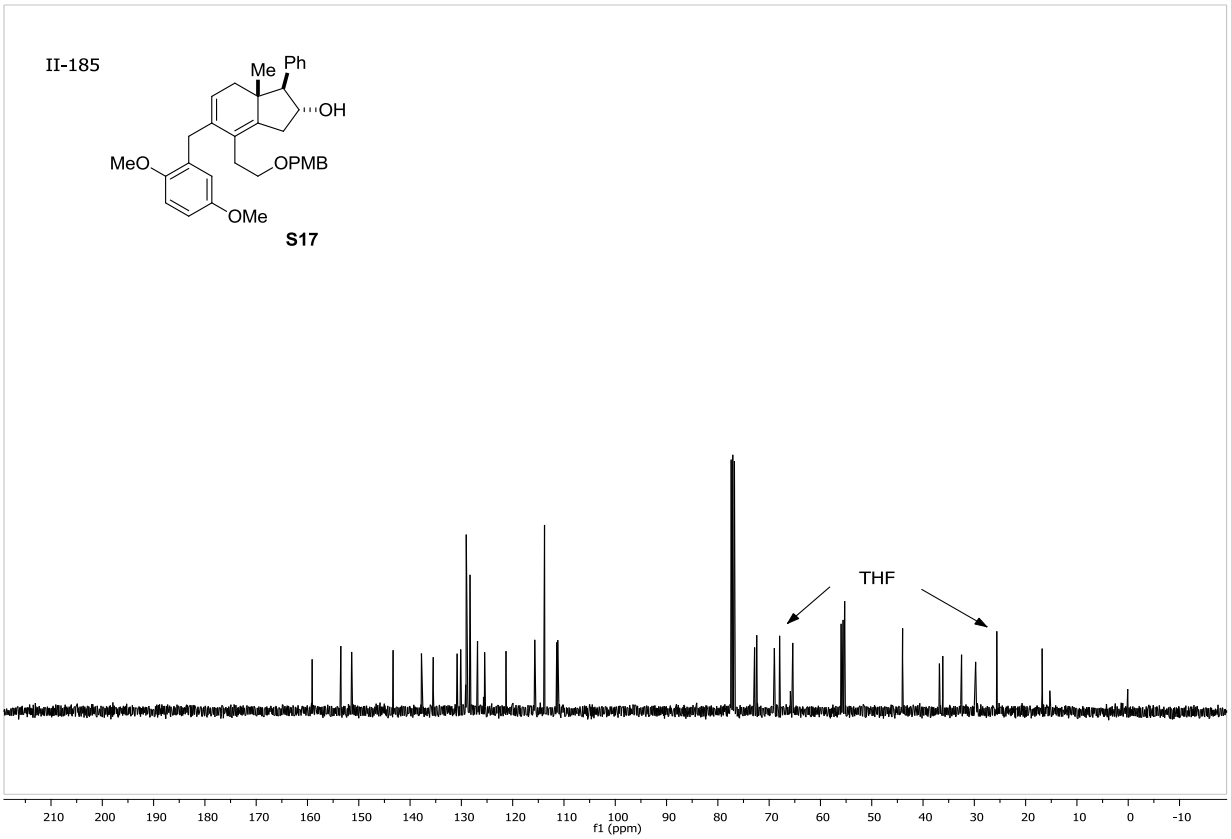
75

II-176

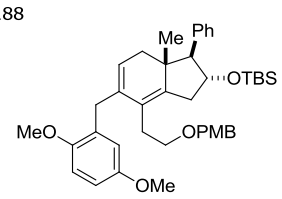


75

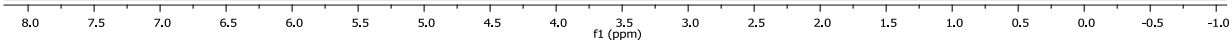

Me
Ph
OH
MeO
OPMB
OMe
S17
THF
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


II-185
Me
Ph
OH
MeO
OPMB
OMe
S17
THF
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

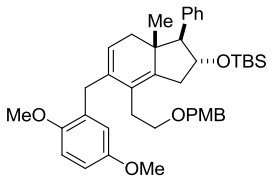
II-188



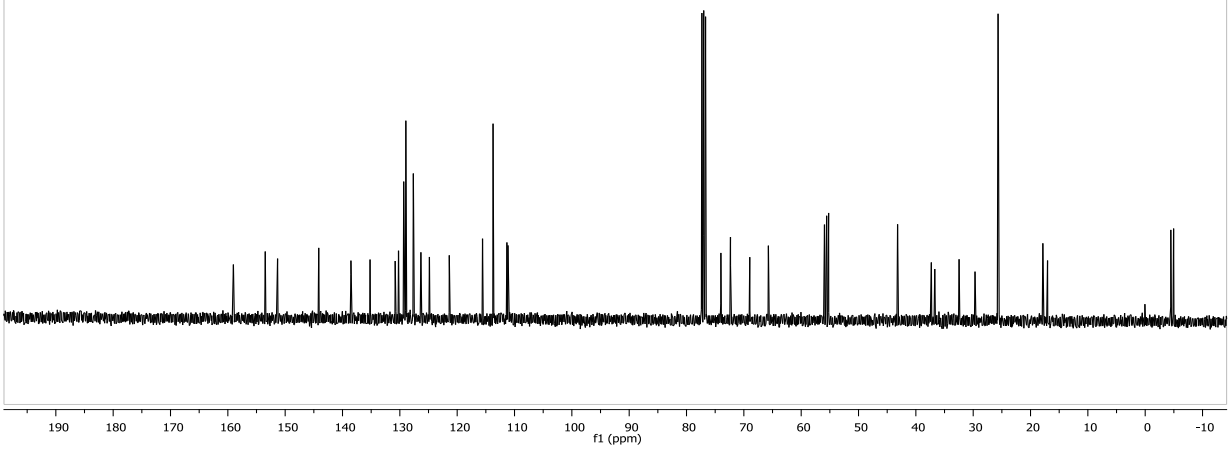
S18

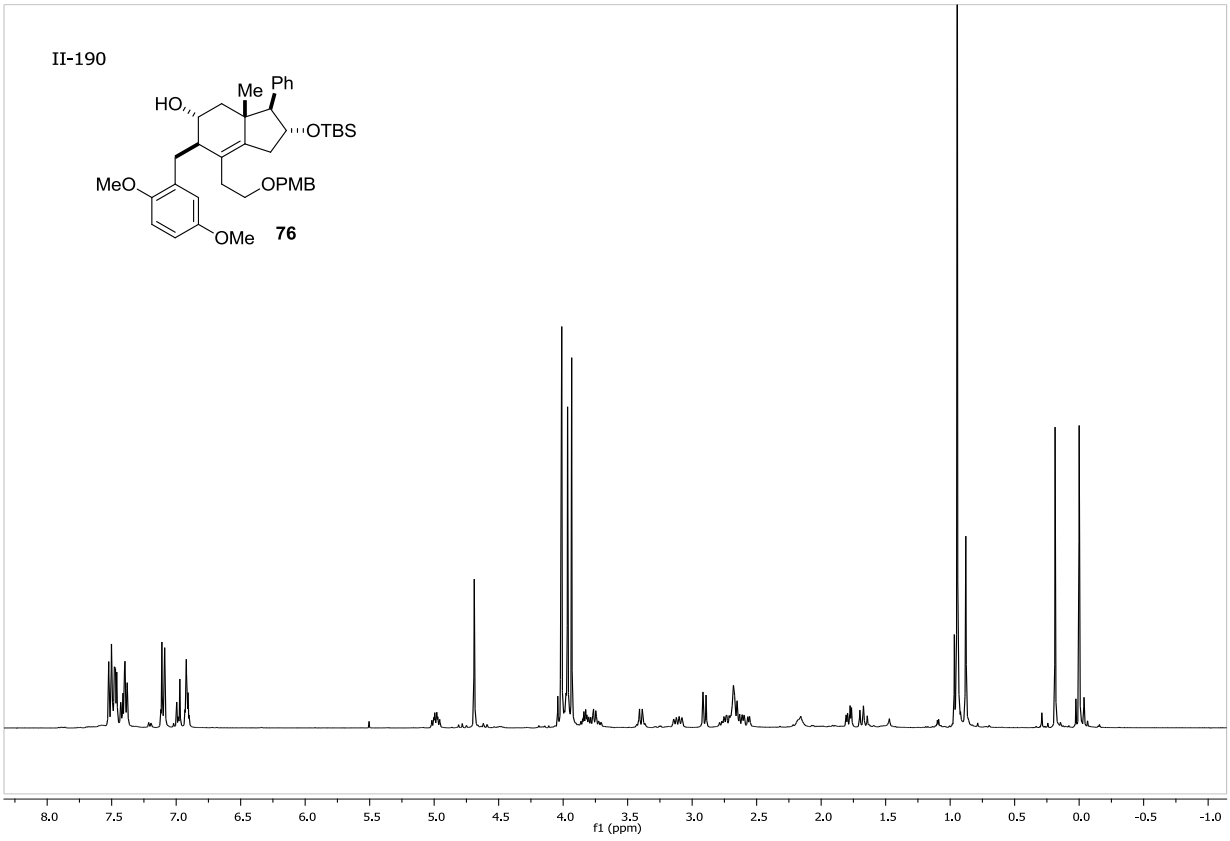


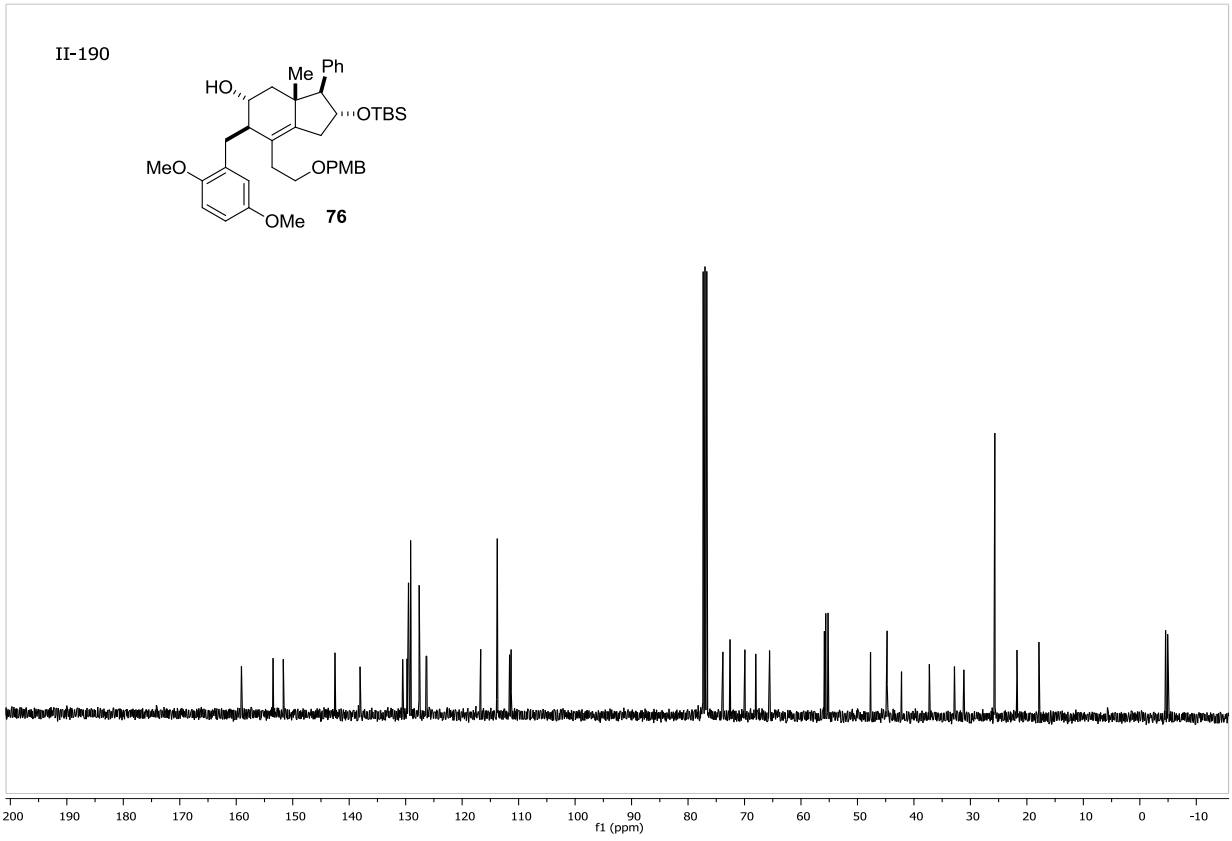
II-188

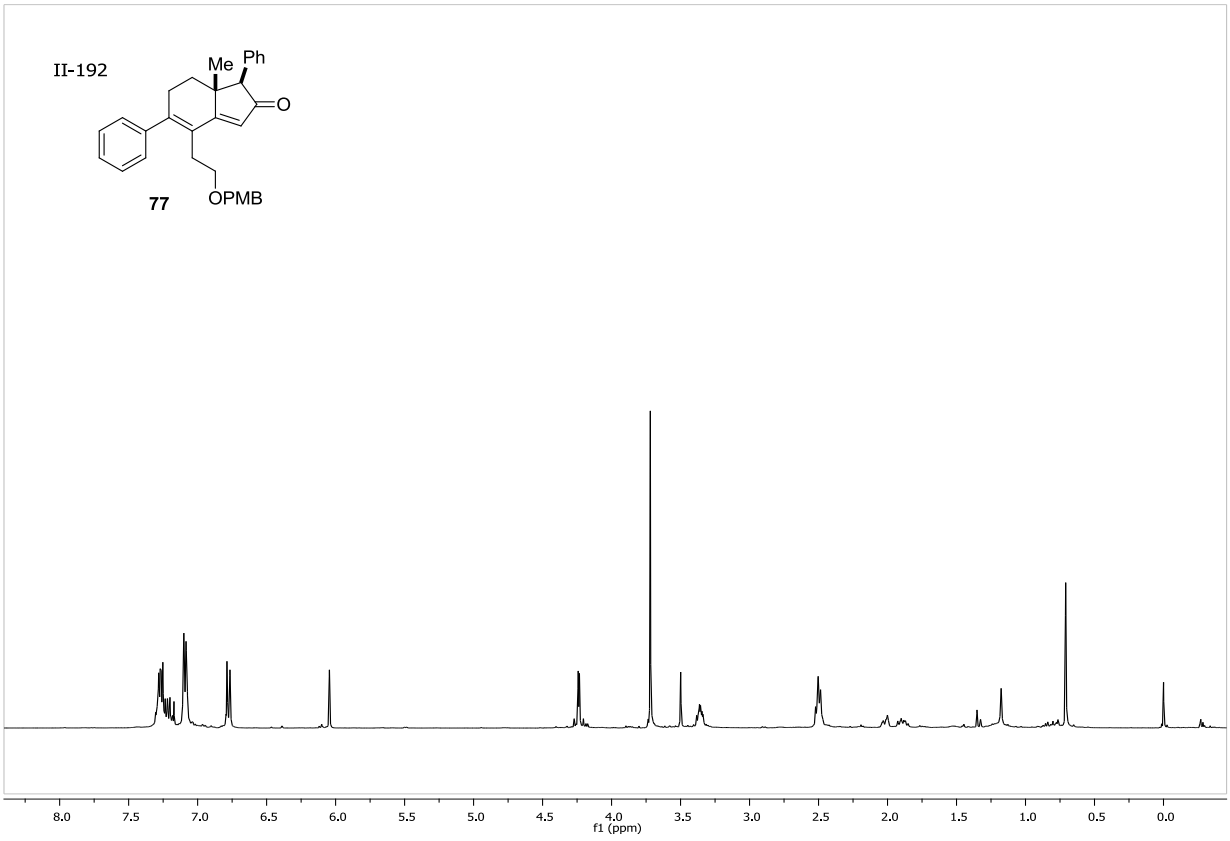


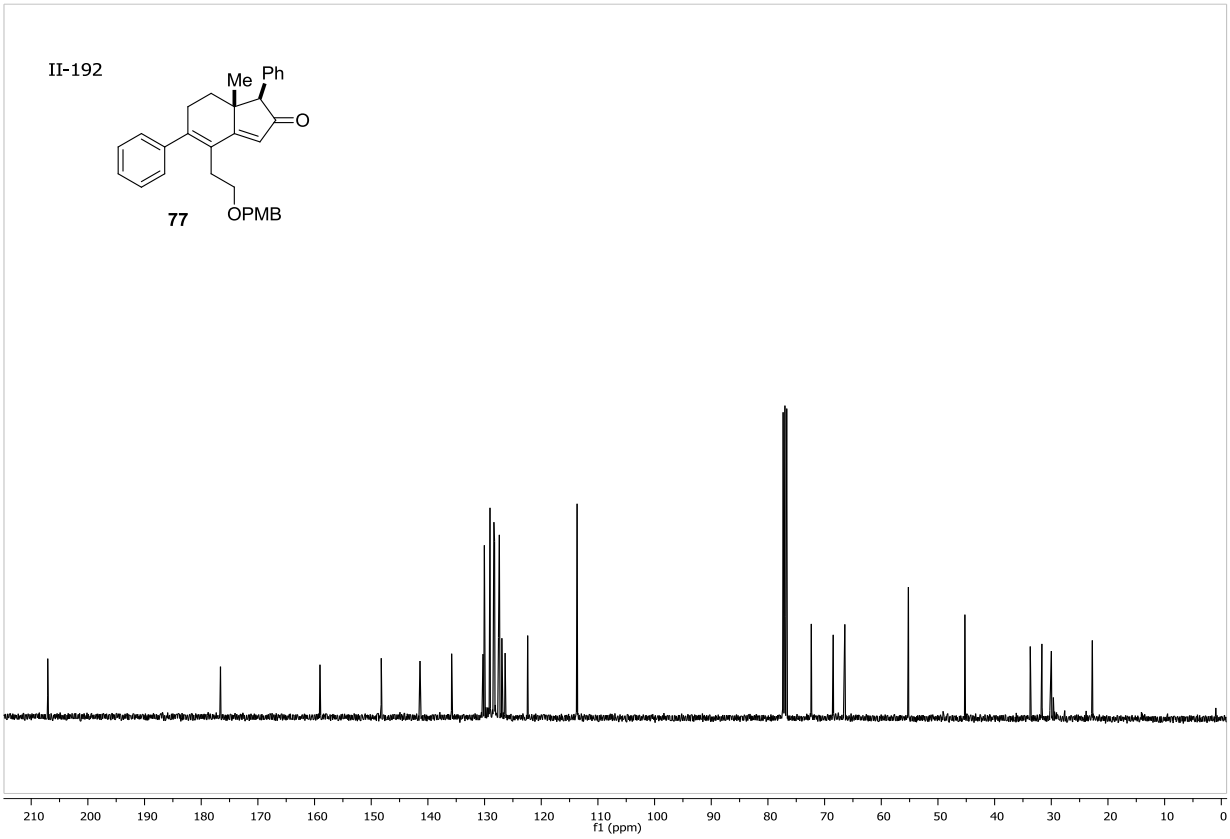
S18




II-190
HO
Me
Ph
OTBS
MeO
OPMB
OMe
76
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


II-190
HO
Me
Ph
OTBS
MeO
OPMB
OMe
76
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


II-192
Me
Ph
O
OPMB
77
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


II-192
Me
Ph
O
OPMB
77
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)