Preparation of Enantioenriched Alkylcarbastannatranes via Nucleophilic Inversion of Alkyl Mesylates for Use in Stereospecific Cross-Coupling Reactions

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Supporting Information:

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General reagent/analytical information

General reagent information:

BDH brand ethyl ether was purchased from VWR. EMD brand Omnisolv THF (unstabilized) was also purchased from VWR. These solvents were transferred to separate 20 L solvent-delivery kegs and vigorously purged with argon for 2 h. The solvents were further purified by passing them under argon pressure through two packed columns of neutral alumina. $Pd(dba)_2$ and JackiePhos were purchased from Strem. Acetonitrile (Sigma-Aldrich) was purged with argon prior to use. 5-Chloro-1-aza-5-stannabicyclo[3.3.3]undecane was purchased from Sigma-Aldrich, and purified through silica gel with 100% DCM prior to use. Reagents and solvents were used as received unless otherwise noted. Normal phase flash chromatography was performed using Silicycle silica gel (ultra pure grade). Reversed phase flash chromatography was performed using C18 silica gel, 17%C, 40-63 μm (Acros).

General analytical information:

All NMR spectra were obtained on a Bruker 300 (300 MHz for ^{1}H and 75 MHz for ^{13}C). All ^{1}H NMR experiments are reported in δ units, parts per million (ppm), and were measured relative to the signals for residual chloroform (7.26 ppm) unless otherwise noted. The following abbreviations are used to express the multiplicities: s = singlet; d = doublet; t = triplet; m = multiplet; brs = broad signal. Unless otherwise noted, all ^{13}C NMR spectra are reported in ppm relative to deuterochloroform (77.16 ppm), and were obtained with ^{1}H decoupling. All GC analyses were performed on a Shimadzu GC-2010 gas chromatograph with an FID detector using a 25 m x 0.20 mm capillary column with cross-linked methyl siloxane as the stationary phase. Chiral HPLC analyses were performed using a Shimadzu Prominence HPLC system with binary mobile phase pumps and UV-vis detector (LC-20AB, SPD-20A) using an OJ-RH (dimensions: 4.6 mm x 150 mm; particle size: 5 μm) chiral column (DAICEL CHEMICAL IND., LTD.), an IA (dimensions: 4.6 mm x 150 mm; particle size: 5 μm) chiral column (DAICEL CHEMICAL IND., LTD.), or an IC_3 (dimensions: 4.6mm x 250 mm; particle size 3 μm) chiral column (DAICEL CHEMICAL IND., LTD.).

General procedure information

Preparation of stannatrane-lithium solution:

To an empty 50 mL flame-dried one-neck RBF was added lithium granules (47.3 mg, 2.5 eq), stannatrane chloride (802 mg, 1.0 eq), and naphthalene (35 mg, 0.1 eq) under a strict argon atmosphere.[1] Without a stirbar, the RBF was sealed with a rubber stopper. THF (9 mL, 0.3 M) was injected through the rubber stopper, and the RBF was sonicated at 40-45 °C until lithium was almost completely consumed, confirmed by visual inspection (after 4-6 hours of heated sonication). The dark green/black opaque solution was then transferred under argon via cannula or argon flushed syringe to a sealed schlenk tube for storage at -20 °C. The stored solution decomposed at an approximate rate of 5-10% per day.

Preparation of additional stannatrane anion equivalents:

To a 50 mL flame-dried one-neck RBF sealed with a rubber stopper was added 1.0 eq stannatrane lithium solution and a magnetic stirbar under a strict argon atmosphere. The solution was cooled to 0 °C, and an appropriate amount of the necessary additive was added as a liquid or as a solid under positive argon pressure.[2] The mixture was stirred at 0 °C for one hour prior to use.

Preparation of 2° alkyl mesylate:

To a 200 mL RBF with magnetic stirbar was added the 2° alkyl alcohol (1.0 eq), triethylamine (2.0 eq), and dichloromethane (0.1 M). The RBF was sealed with a rubber stopper. At room temperature, methanesulfonyl chloride (1.31 mL, 1.1 eq) was added slowly over 5 minutes. The solution was allowed to stir at room temperature overnight. TLC stained with potassium permanganate was used to confirm reaction completion. The organic layer was washed with water, with saturated bicarbonate (x2), dried with sodium sulfate, and condensed. The resulting oil was then filtered through a large plug of silica using 100% DCM. Yield range is 70-95%. Mesylates were dried thoroughly, sealed under argon, and stored in the freezer.

General procedure A for the preparation of racemic alkylcarbastannatrane via carbastannatrane anion:

To a 50 mL flame dried one-neck RBF sealed with a rubber stopper was added 1.0 eq alkyl mesylate and a magnetic stirbar. The flask was evacuated and backfilled 3x with argon. THF (0.1 M) was added with stirring, followed by a slow addition of stannatrane anion (1.5 eq). The reaction was allowed to stir overnight. Water was added, and extracted with hexane 3 times. The organic layers were combined, dried with sodium sulfate, and condensed. The thick oil was purified with reversed phase column chromatography (100% acetonitrile to 15% DCM in acetonitrile). Fractions were monitored by reverse-phase HPLC with a c18 column or by reverse-phase TLC.

General procedure B for the preparation of enantioenriched alkylcarbastannatrane via carbastannatrane anion:

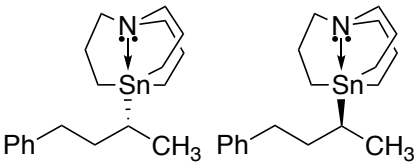
To a 50 mL flame dried one neck RBF sealed with a rubber stopper was added 1.0 eq alkyl mesylate and a magnetic stirbar. The flask was evacuated and backfilled 3x with argon. *n*-Hexane (0.1 M) was added with stirring, followed by a slow addition of stannatrane anion (1.5 eq). The reaction was allowed to stir overnight. Water was added, and extracted with hexane 3 times. The organic layers were combined, dried with sodium sulfate, and condensed. The thick oil was purified with reverse-phase column chromatography (100% acetonitrile to 15% DCM in acetonitrile). Fractions were monitored by reverse-phase HPLC with a c18 column or reverse-phase TLC.

General procedure C for arylation/acylation cross-coupling reactions with organic electrophiles:

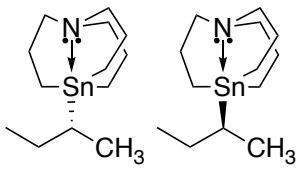
$Pd(dba)_2$ (5 mol %, 2.9 mg for 0.1 mmol scale), JackiePhos (10 mol %, 8 mg for 0.1 mmol scale), CuCl (2 equiv, 20 mg for 0.1 mmol scale) and KF (2 equiv, 11.6 mg for 0.1 mmol scale, NO KF for acylation reaction) were weighed out on the benchtop, and transferred to an oven-dried screwtop vial with stir bar. With stirring begun, the sealed vial was evacuated (50 mTorr) and backfilled three times with argon using a needle attached to a vacuum manifold. The tin reagent (1.2 equiv) and cross-coupling electrophile (1 equiv) was then added to the screw-top vial via microsyringe, followed by degassed CH_3CN (0.3 mL for 0.1 mmol scale). If the

electrophile or the tin reagent was a solid, it was weighed out on the benchtop alongside the other solids. The vial was then heated to 60 °C for 6-12 h. The reaction mixture was cooled to rt, diluted with ether or hexane, and washed sequentially with saturated aqueous KF and brine. The organics were combined and dried over Na_2SO_4. The solution was filtered and concentrated to provide the crude product. The crude product was purified by column chromatography.

Compound characterization data:

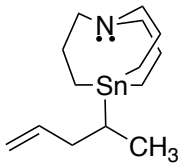


(R)*- and *(S)*-5-(4-Phenylbutan-2-yl)-1-aza-5-stannabicyclo[3.3.3]undecane.[3] *((R)*-6, *(S)*-6*). General procedure B was employed using stannatrane lithium (2.0 mmol, 6.7 mL) and the corresponding enantioenriched 4-phenylbutan-2-yl mesylate (1.7 mmol, 385 mg). A pale yellow oil (322 mg, 48%) was obtained after reversed phase column chromatography (100% acetonitrile). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.27 (m, 2H), 7.18 (m, 3H), 2.58 (m, 2H), 2.36 (t, 6H), 1.78 (m, 1H), 1.65 (m, 6H), 1.31 (m, 1H), 1.13 (d, J = 7.5 Hz, 3H), 0.79 (quart, J = 7.5 Hz, 1H), 0.67 (t, J = 6.5 Hz, 6H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 143.9, 128.6, 128.3, 125.5, 54.9, 39.0, 36.5, 24.2, 23.6, 18.6, 5.6 ppm. Enantiopurity of 96% was obtained via chiral resolution with an OJ-RH column, 85% B = (5% acetonitrile in methanol), 15% water, 1.2mL/min.

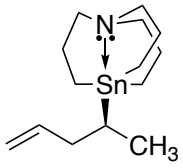


(R)*- and *(S)*-5-(*sec*-Butyl)-1-aza-5-stannabicyclo[3.3.3]undecane.[4] *((R)*-11, *(S)*-11*). General procedure B was employed using stannatrane lithium (2.2mmol, 7.3mL) and the corresponding enantioenriched *sec*-butyl mesylate (2.0 mmol, 300mg). A pale yellow oil (278mg, 45%) was

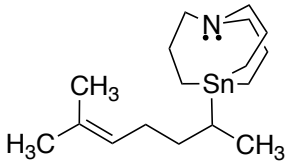
obtained after reversed phase chromatography (100% acetonitrile). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.35 (m, 6H), 1.64 (m, 6H), 1.46 (m, 2H), 1.05 (d, *J* = 7.5 Hz, 3H), 0.86 (t, *J* = 7.5 Hz, 3H), 0.66 (m, 1H), 0.63 (m, 6H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 55.0, 29.4, 26.7, 23.7, 18.5, 14.8, 5.7 ppm. Enantiopurity of 96% was obtained via cross-coupling with 4-bromoanisole and HPLC analysis of the resulting product.



5-(Pent-4-en-2-yl)-1-aza-5-stannabicyclo[3.3.3]undecane (12). General procedure A was employed using stannatrane lithium (10.1 mL, 3.01 mmol) and racemic pent-4-en-2-yl mesylate (412 mg, 2.51 mmol). A pale yellow oil was obtained (305 mg, 37% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 5.76 (m, 1H), 4.89 (m, 2H), 2.35 (m, 6H), 2.18 (m, 2H), 1.63 (m, 6H), 1.04 (d, J = 7.5Hz, 3H), 0.63 (m, 7H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 140.8, 113.7, 77.43, 54.9, 40.7, 23.6, 18.3, 5.66 ppm.

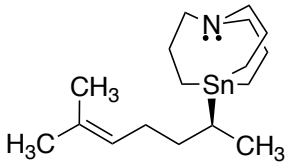


(*S*)-5-(Pent-4-en-2-yl)-1-aza-5-stannabicyclo[3.3.3]undecane ((*S*)-12). General procedure B was employed using stannatrane lithium (3.6 mL, 1.8 mmol) and (*S*)-pent-4-en-2-yl mesylate (197 mg, 1.2 mmol). A pale yellow oil was obtained (135 mg, 34% yield). Enantiopurity of 96% ee was assigned by cross-coupling with 4-bromobenzonitrile and HPLC analysis of the resulting product.

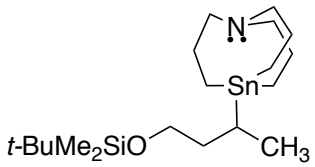


5-(6-Methyl-5-hepten-2-yl)-1-aza-5-stannabicyclo[3.3.3]undecane (13). General procedure A was employed using stannatrane lithium (9 mL, 2.73 mmol) and racemic 6-methyl-5-hepten-2-yl mesylate (375 mg, 1.82 mmol). A pale yellow oil was obtained (365 mg, 54% yield). ^{1}H NMR

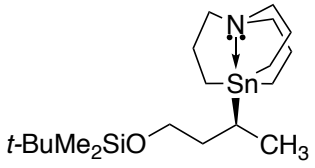
(300 MHz, $CDCl_3$) δ: 5.12 (m, 1H), 2.35 (m, 6H), 1.92 (m, 2H), 1.80-1.25 (m, 14H), 1.06 (d, *J* = 7.5 Hz, 3H), 0.65 (m, 7H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 130.6, 125.8, 54.9, 36.8, 28.6, 25.9, 24.1, 23.6, 18.6, 17.8, 5.5 ppm.



(S)-5-(6-Methyl-5-hepten-2-yl)-1-aza-5-stannabicyclo[3.3.3]undecane ((*S*)-13). General procedure B was employed using stannatrane lithium (9.5 mL, 2.90 mmol) and (*R*)-6-methyl-5-hepten-2-yl mesylate (400 mg, 1.93 mmol). A pale yellow oil was obtained (362 mg, 51% yield). Enantiopurity of 98.7% ee obtained by derivatization via cross-coupling with 4-bromo-2H-1,4-benzoxazin-3(4H)-one and resolution of the resulting product. Total % es from starting alcohol = 99.5% es.

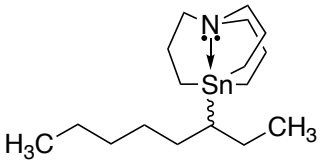


5-(4-((*tert*-Butyldimethylsilyl)oxy)butan-2-yl))-1-aza-5-stannabicyclo[3.3.3]undecane (14). General procedure A was employed using stannatrane lithium (6.95 mL, 2.78 mmol) and 4-((*tert*-Butyldimethylsilyl)oxy)butan-2-yl mesylate (522 mg, 1.85 mmol). A colorless oil was obtained (376 mg, 46% yield). ^1H NMR (300 MHz, $CDCl_3$) δ: 3.56 (m, 2H), 2.35 (m, 6H), 1.65 (m, 8H), 1.06 (d, J = 7.5Hz, 2H), 0.89 (s, 10H), 0.64 (m, 6H), 0.049 (s, 6H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 64.1, 54.9, 39.5, 26.3, 26.3, 26.2, 23.6, 19.6, 18.7, 18.6, 5.4, -4.8, -4.8 ppm.

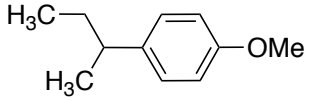


(*S*)-5-(4-((*tert*-Butyldimethylsilyl)oxy)butan-2-yl))-1-aza-5-stannabicyclo[3.3.3]undecane ((*S*)-14). General procedure B was employed using stannatrane lithium (7.4 mL, 0.74 mmol) and (*R*)-4-((*tert*-Butyldimethylsilyl)oxy)butan-2-yl mesylate (250 mg, 0.886 mmol). A colorless oil was obtained (151 mg, 46% yield). Enantiopurity of 94% ee obtained by cross-coupling with 2-

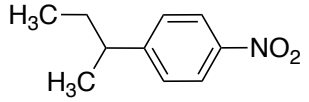
bromonaphthalene. Total % es from starting alcohol = 96% es.



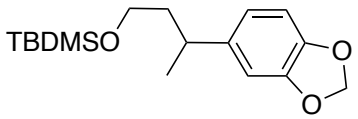
5-(Oct-3-yl)-1-aza-5-stannabicyclo[3.3.3]undecane (15). General procedure A was employed using stannatrane lithium (13.5 mL, 4.11 mmol) and racemic 3-octyl mesylate (521 mg, 2.5 mmol). A pale yellow oil was obtained (478 mg, 51% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.35 (m, 6H), 1.63 (m, 6H), 1.53- 1.15 (m, 10H), 0.83 (m, 6H), 0.63 (m, 7H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 55.0, 33.9, 33.2, 29.8, 26.2, 23.7, 23.0, 14.6, 14.4, 6.8 ppm.



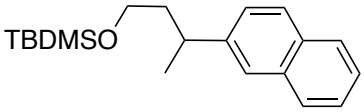
***(S)*-1-(*sec*-Butyl)-4-methoxybenzene.[3] (16a).** General procedure C was employed using *(S)*-5-(*sec*-butyl)-1-aza-5-stannabicyclo[3.3.3]undecane and 1-bromo-4-methoxybenzene on a 0.1 mmol scale. A pale yellow oil (12.2 mg, 88%) was obtained after column chromatography (0-10% ethyl acetate in hexanes) ^{1}HNMR (300 MHz, CDCl3): δ 7.11 (d, *J* = 8.5, 2H), 6.86 (d, *J* = 8.5 Hz, 2H), 3.80 (s, 3H), 2.56 (m, 1H), 1.58 (m, 2H), 1.23 (d, *J* = 7 Hz, 3H), 0.83 (t, *J* = 7.0 Hz, 3H) ppm. ^{13}CNMR (125 MHz, CDCl3): δ 157.9, 140.0, 128.0, 113.8, 55.4, 41.0, 31.5, 22.2, 12.4 ppm.



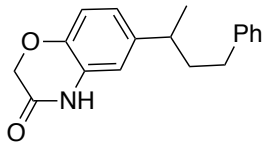
***(S)*-1-(*sec*-Butyl)-4-nitrobenzene.[3] (16b).** General procedure C was employed using *(S)*-5-(*sec*-butyl)-1-aza-5-stannabicyclo[3.3.3]undecane and 1-bromo-4-nitrobenzene on a 0.1 mmol scale. A yellow oil (13.7 mg, 90%) was obtained after column chromatography (0-5% diethyl ether in hexanes. H NMR (500 MHz, CDCl3): δ 8.15 (d, *J* = 9 Hz, 2H), 7.33 (d, *J* = 8.5 Hz, 2H), 2.73 (M, 1H), 1.63 (m, 2H), 1.27 (d, *J* = 7 Hz, 3H), 0.83 (t, *J* = 7.5 Hz, 3H) ppm. C NMR (75 MHz, CDCl3): δ 155.7, 146.5, 128.1, 123.8, 42.0, 31.1, 21.7, 12.3 ppm.



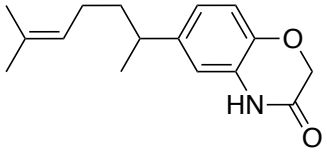
1-(4-((*tert*-Butyldimethylsilyl)oxy)butan-2-yl)-3,4-(methylenedioxy)benzene (16c). General procedure C was employed using 5-(4-((*tert*-butyldimethylsilyl)oxy)butan-2-yl)-1-aza-5-stannabicyclo[3.3.3]undecane and 1-bromo-3,4-(methylenedioxy)benzene on a 0.04 mmol scale. A white crystalline solid was obtained (9 mg, 71% yield) after column chromatography (50% DCM in hexane). The enantioenriched product was formed using (*S*)-5-(4-((*tert*-butyldimethylsilyl)oxy)butan-2-yl))-1-aza-5-stannabicyclo[3.3.3]undecane on a 0.1 mmol scale. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 6.68 (m, 3H), 5.92 (s, 2H), 3.50 (m, 2H), 2.81 (m, 1H), 1.73 (q, *J* = 6.6 Hz, 2H), 1.20 (d, *J* = 8.4 Hz, 3H), 0.88 (s, 9H), 0.00 (s, 6H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 147.7, 145.7, 141.5, 120.1, 108.2, 107.4, 100.9, 61.3, 41.5, 36.1, 26.1, 22.7, 18.4, -5.1 ppm.



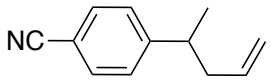
2-(4-((*tert*-Butyldimethylsilyl)oxy)butan-2-yl)naphthalene (16d). General procedure C was employed using 5-(4-((*tert*-butyldimethylsilyl)oxy)butan-2-yl)-1-aza-5-stannabicyclo[3.3.3] undecane and 2-bromonaphthalene on a 0.04 mmol scale. A white crystalline solid was obtained (9.5 mg, 73% yield) after column chromatography 10% to 50% DCM in hexane. The enantioenriched product was formed using (*S*)-5(4((*tert*-butyldimethylsilyl)oxy)butan-2-yl))-1-aza-5-stannabicyclo[3.3.3]undecane on a 0.1 mmol scale. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.80 (m, 3H), 7.62 (s, 1H), 7.35 (m, 3H), 3.53 (m, 2H), 3.07 (m, 1H), 1.89 (q, *J* = 6.9 Hz, 2H), 1.34 (d, *J* = 6.9 Hz, 3H), 0.89 (s, 9H), 0.00 (s, 6H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 144.8, 133.8, 132.3, 128.1, 127.7, 127.6, 126.0, 125.9, 125.4, 125.2, 61.4, 41.2, 36.4, 26.1, 22.5, 18.4, -5.2 ppm.



6-(4-Phenylbutan-2-yl)-2H-1,4-benzoxazin-3(4H)-one (16e). General procedure C was employed using 1-(4-phenylbutan-2-yl)-5-aza-1-stanna-bicyclo[3.3.3]undecane and 4-bromo-2H-1,4-benzoxazin-3(4H)-one on a 0.1 mmol scale (18.5 mg, 78%). A pale yellow solid was obtained after column chromatography (5% to 30% ethyl acetate in DCM). The enantioenriched product was obtained using (*S*)-5-(4-phenylbutan-2-yl)-1-aza-5-stannabicyclo[3.3.3]undecane. ^{1}H NMR (300 MHz, CD_2Cl_2) δ: 8.71, (s, 1H), 7.25, (m, 2H), 7.14, (m, 3H), 6.91, (d, J = 8.3 Hz, 1H), 6.82, (dd J_1 = 8.25 Hz, J_2 = 2.01 Hz, 1H), 6.66, (d, J = 2.01, 1H), 4.59, (s, 2H), 2.66, (m, 1H), 2.50, (m, 2H), 1.87, (m, 2H), 1.23, (d, J = 6.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 166.4, 142.9, 142.6, 142.2, 128.7, 128.6, 126.6, 126.0, 122.9, 116.8, 114.9, 67.8, 40.4, 39.3, 34.2, 22.6.

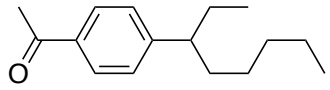


6-(6-Methyl-5-hepten-2-yl)-2H-1,4-benzoxazin-3(4H)-one (16f). General procedure C was employed using 5-(6-methyl-5-hepten-2-yl)-1-aza-5-stannabicyclo[3.3.3]undecane and 4-bromo-2H-1,4-benzoxazin-3(4H)-one on a 0.1 mmol scale. A white crystalline solid was obtained (19.5 mg, 90% yield) after column chromatography (0% to 25% ethyl acetate in DCM). The enantioenriched product was obtained using (*S*)-5-(6-methyl-5-hepten-2-yl)-1-aza-5-stannabicyclo[3.3.3]undecane. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.25 (s, 1H), 6.89 (d, J = 8.4 Hz, 1H), 6.79 (d, J = 6.3 Hz, 1H), 6.60 (d, J = 2.0 Hz, 1H), 5.07 (m, 1H), 4.60 (s, 2H), 2.63 (m, 1H), 1.86 (m, 2H), 1.57 (t, J = 7.5 Hz, 2H), 1.52 (s, 3H), 1.19 (d, J = 6.9 Hz, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 166.1, 142.8, 141.8, 131.8, 126.0, 124.4, 122.8, 116.7, 114.5, 67.5, 39.0, 38.5, 26.1, 25.9, 22.6, 17.8 ppm.

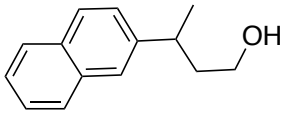


4-(Pent-4-en-2-yl)-benzonitrile (16g). General procedure C was employed using 5-(pent-4-en-2-yl)-1-aza-5-stannabicyclo[3.3.3]undecane and 4-bromobenzonitrile on a 0.1 mmol scale. A

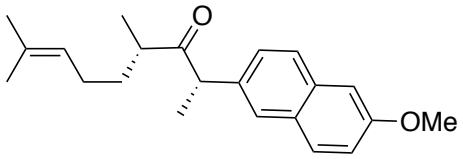
colorless oil was obtained (12.6 mg, 87% yield) after column chromatography (10% to 30% DCM in hexanes). The enantioenriched product was obtained using (*S*)-5-(pent-4-en-2-yl)-1-aza-5-stannabicyclo[3.3.3]undecane. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.58 (d, *J* = 8.3 Hz, 2H), 7.28 (d, *J* = 8.3 Hz, 2H), 5.64 (m, 1H), 4.98 (m, 2H), 2.80 (m, 1H), 2.30 (m, 2H), 1.25 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 152.6, 136.1, 132.3, 128.0, 119.2, 116.9, 109.9, 42.3, 40.1, 21.3.



3-Octylacetophenone (16h). General procedure C was employed using 5-(oct-3-yl)-1-aza-5-stannabicyclo[3.3.3]undecane and 4-bromoacetophenone on a 0.1mmol scale (16.6 mg, 85%). A pale yellow oil was obtained after column chromatography (30% DCM in hexane). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.87 (d, *J* = 8.1 Hz, 2H), 7.23 (d, *J* = 9 Hz, 2H), 2.59 (s, 3H), 2.47 (m, 1H), 1.60 (m, 4H), 1.20 (m, 6H), 0.82 (t, J = 6.8 Hz, 3H), 0.76 (t, J = 7.4 Hz, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 198.1, 152.3, 135.3, 128.6, 128.1, 48.1, 36.4, 32.0, 29.7, 27.4, 26.7, 22.7 ppm.



3-(2-Naphthyl)-butan-1-ol (16i). General procedure C was employed using (*S*)-3-(5-aza-1-stanna-bicyclo[3.3.3]undecan-1-yl)butan-1-ol and 2-bromonaphthalene on a 0.1 mmol scale (14.3 mg, 84%). A pale yellow oil was obtained after column chromatography (0 to 50% ethyl acetate in DCM). The enantioenriched product was obtained using (*S*)-3-(5-aza-1-stanna-bicyclo[3.3.3]undecan-1-yl)butan-1-ol. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.8, (m, 3H), 7.64, (d, *J* = 1.1, 1H), 7.42, (m, 3H), 3.59, (m, 2H), 3.07, (m, 1H), 1.95, (q, *J* = 6.7 Hz, 2H), 1.36, (d, *J* = 6.9 Hz, 3H), 1.26, (brs, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 144.3, 133.7, 132.4, 128.3, 127.74, 127.67, 126.1, 125.7, 125.38, 125.36, 61.4, 41.0, 36.7, 22.6.

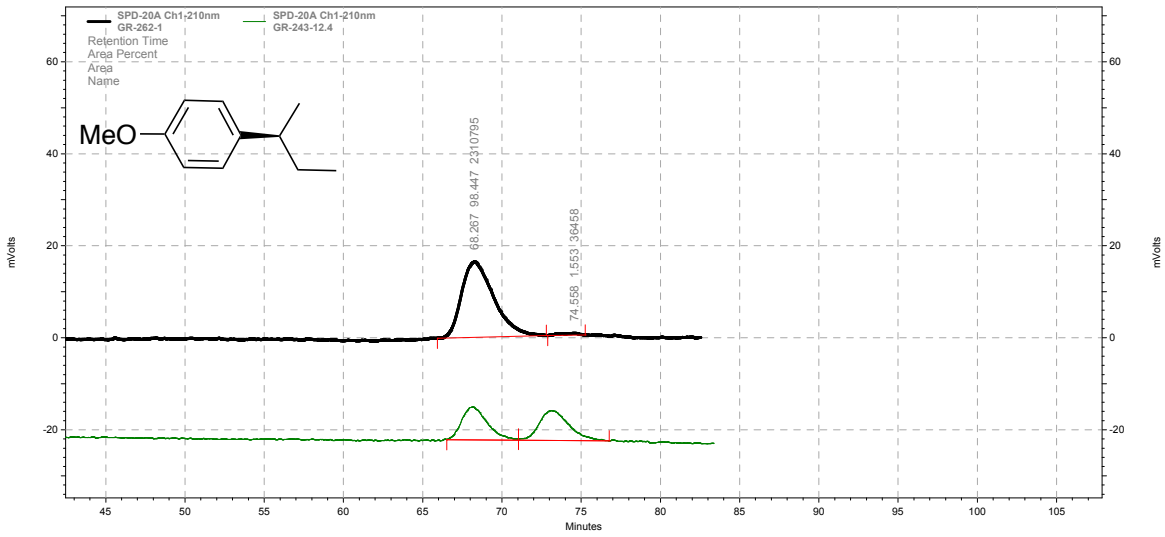


(2*S*,4*R*)-2-(6-Methoxynaphthalen-2-yl)-4,8dimethylnon-7-en-3-one (16j). General procedure C was employed using (S)-5-(6-methyl-5-hepten-2-yl)-1-aza-5-stannabicyclo[3.3.3]undecane and *S*-phenyl (*S*)-2-(6-methoxynaphthalen-2-yl)propanethioate on a 0.1 mmol scale (17 mg, 62%). A colorless oil was obtained after column chromatography (0% to 25% ethyl acetate in hexane). The mixture of diastereomers was obtained using racemic 5-(6-methyl-5-hepten-2-yl)-1-aza-5-stannabicyclo[3.3.3]undecane on a 0.1 mmol scale. ^{1}H NMR (300 MHz, CD_2Cl_2) δ: 7.72, (m, 2H), 7.62, (d, *J* = 1.5 Hz, 1H), 7.35, (m, 1H), 7.14, (m, 2H), 4.73, (m, 1H), 4.03, (q, *J* = 6.9 Hz, 1H), 3.90, (s, 3H), 2.65, (m, 1H), 1.59, (m, 4H), 1.47, (s, 3H), 1.43, (d, *J* = 6.9 Hz, 3H), 1.33, (s, 3H), 1.18, (m, 1H), 1.06, (d, *J* = 7.05 Hz, 3H). ^{13}C NMR (75 MHz, CD_2Cl_2) δ: 214.2, 158.1, 136.0, 132.0, 129.5, 127.6, 127.2, 127.1, 124.1, 119.3, 105.9, 55.6, 51.7, 44.6, 33.0, 25.8, 25.6, 18.1, 17.6, 17.5.

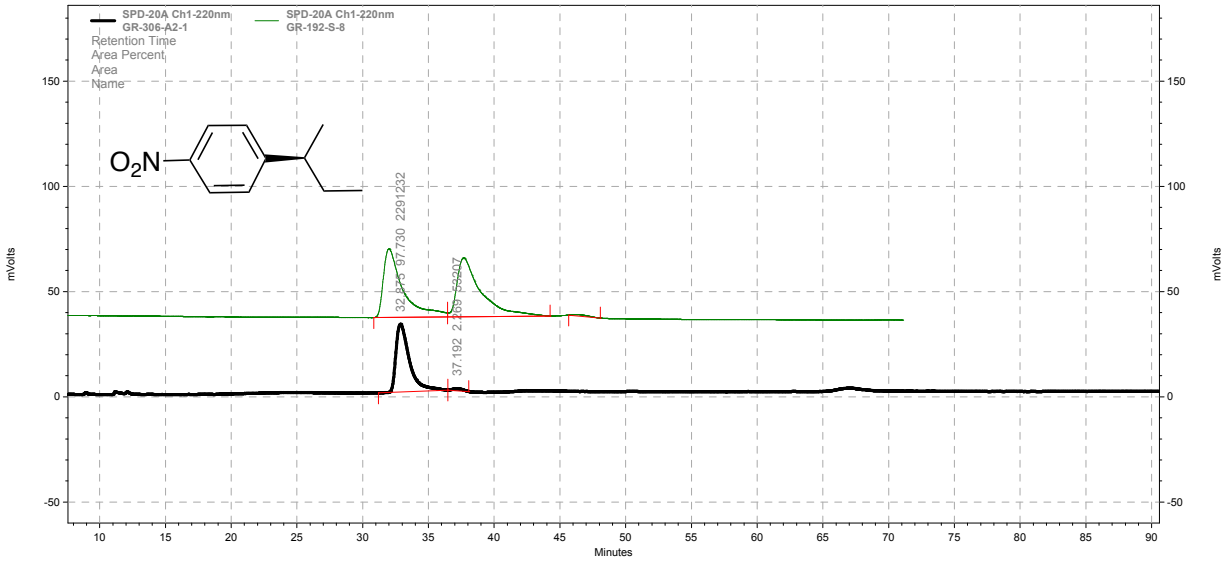
References

1. Wang, D. Y.; Wang, C.; Uchiyama, M. *J. Am. Chem. Soc.* **2015**, *137*, 10488-10491.
2. Hibino, J.-I.; Matsubara, S.; Morizawa, Y.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1984,** *25*, 2151-2154.
3. Li, L.; Wang, C. Y.; Huang, R.; Biscoe, M. R. *Nat. Chem.* **2013,** *5*, 607-612.
4. Wang, C.-Y.; Ralph, G.; Derosa, J.; Biscoe, M. R. *Angew. Chem. Int. Ed.* **2017,** *56*, 856-860.

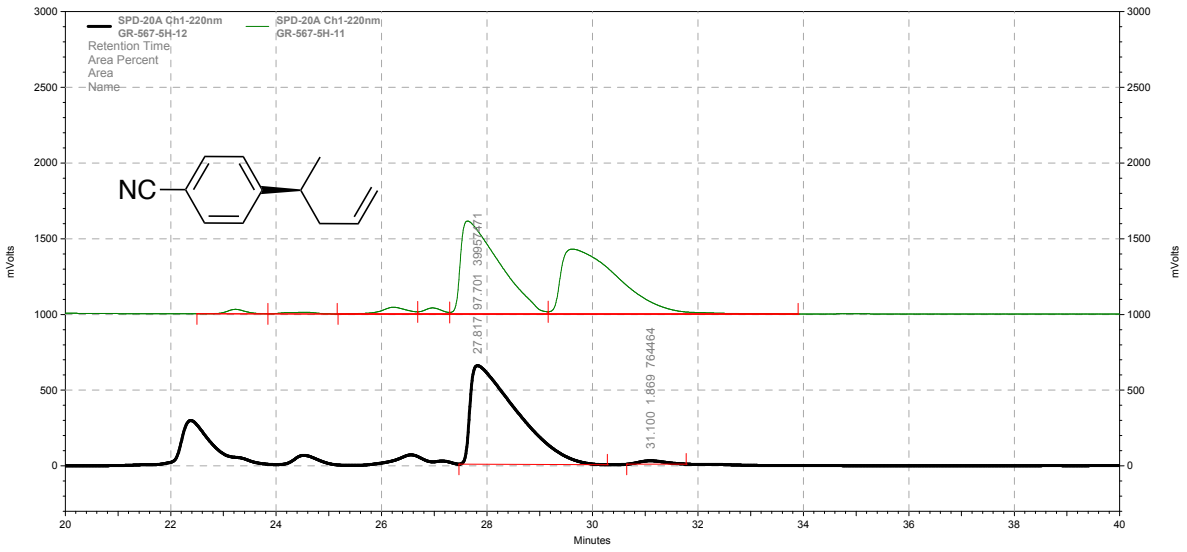
Chiral HPLC data



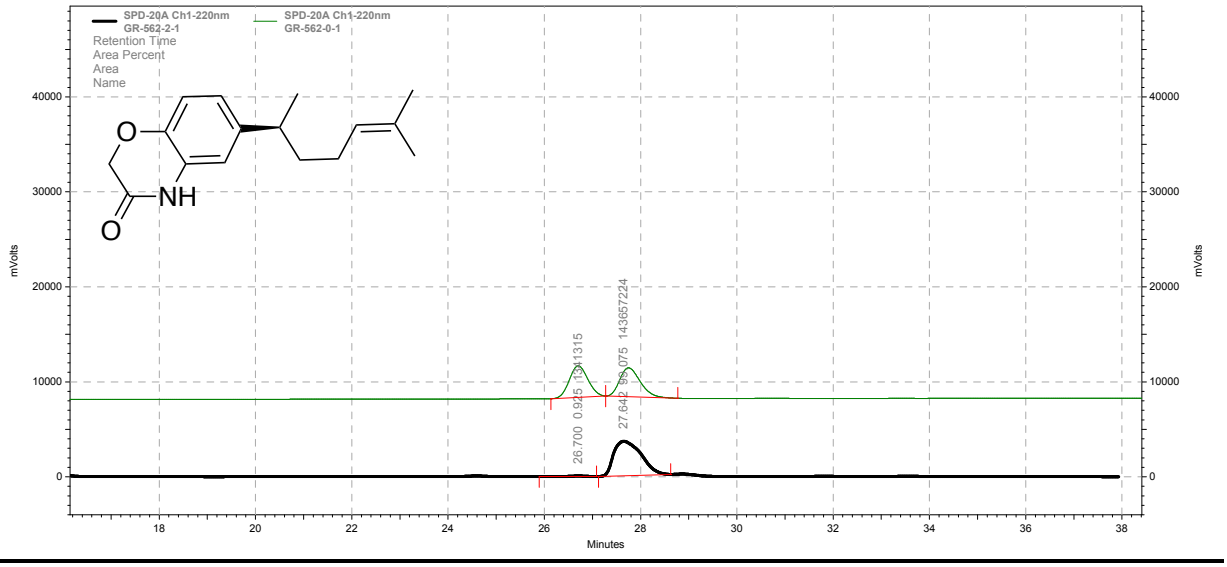
Column	IA, 250 x 4.6
Mobile phase	57% = (5% acetonitrile in methanol), 43% water
Flow	1.3 mL/min
Wavelength	220nm
Result	96% e.e. (99% e.s.)



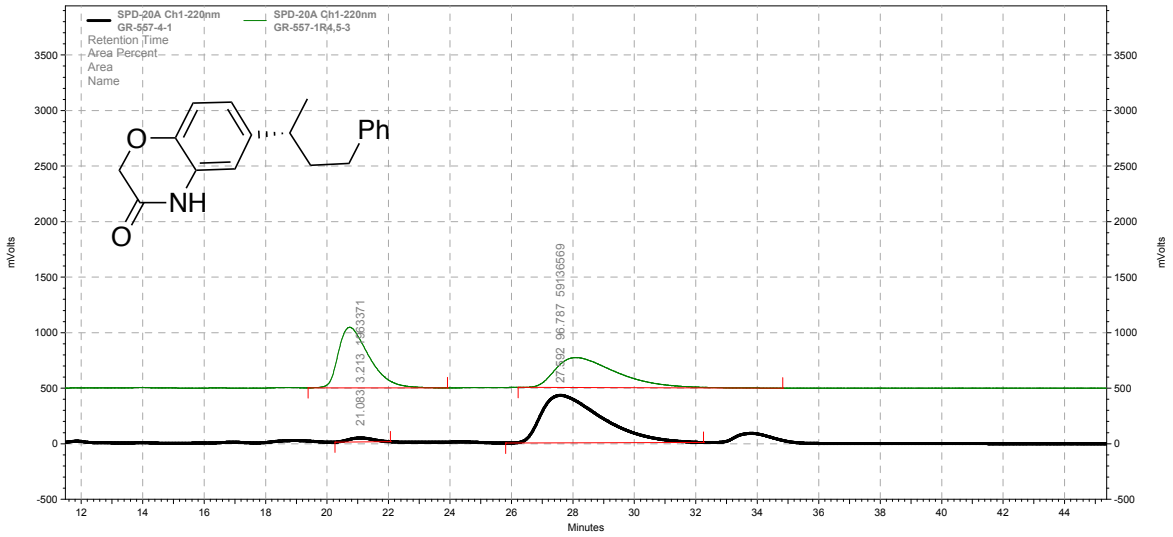
Column	IA, 250 x 4.6
Mobile phase	70% = (5% acetonitrile in methanol), 30% (0.1% phosphoric acid)
Flow	1.0 mL/min
Wavelength	220nm
Result	96% e.e. (98% e.s.)



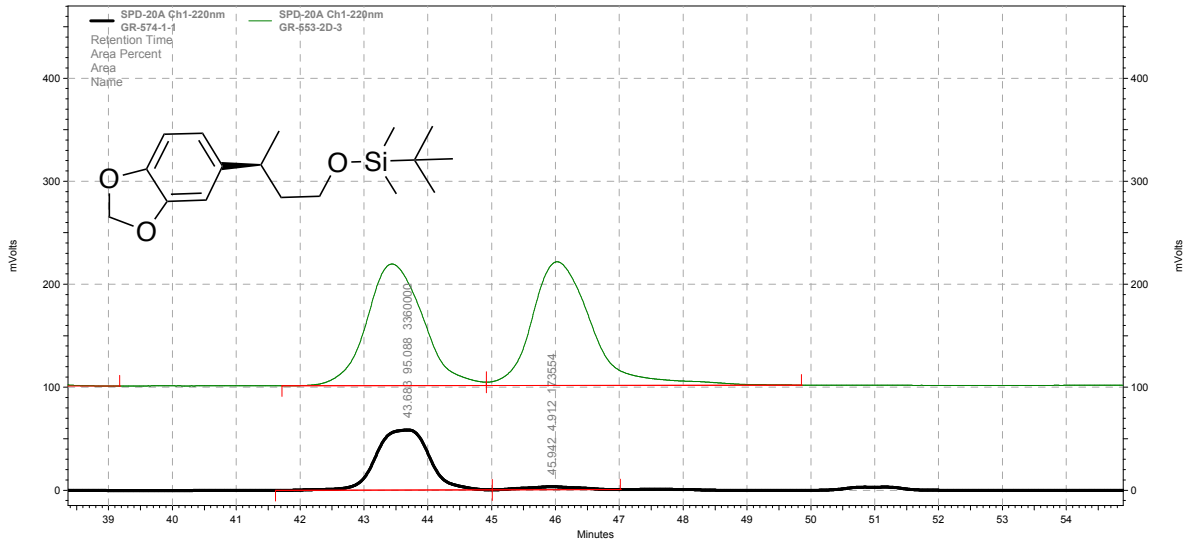
Column	IA, 250 x 4.6
Mobile phase	70% = 99.9% hexane, 0.1% isopropanol
Flow	0.6 mL/min
Wavelength	220nm
Result	96% e.e. (96% e.s.)



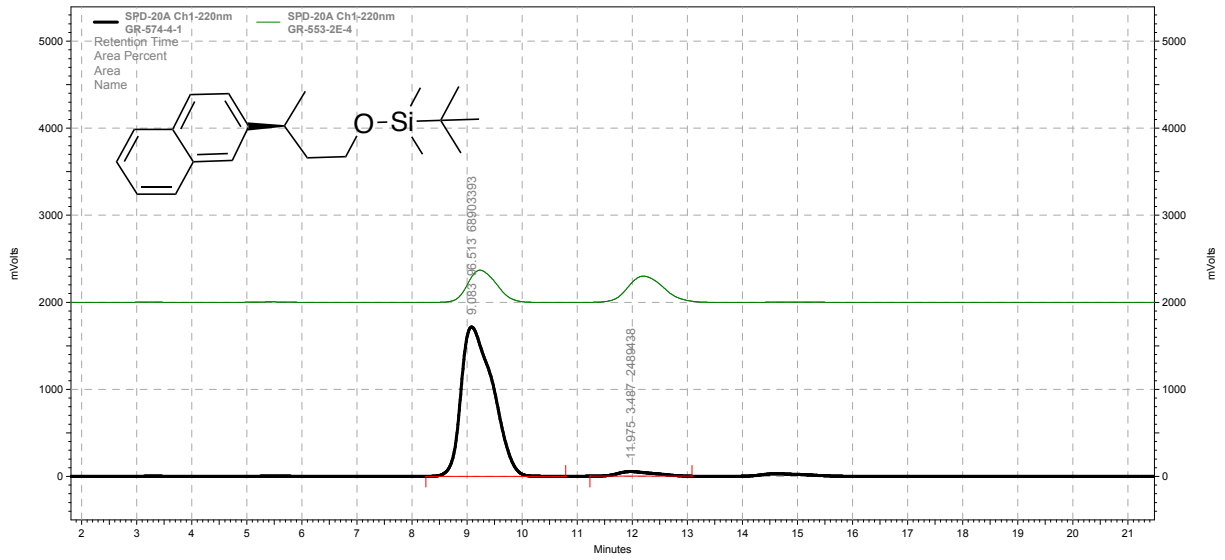
Column	IA, 250 x 4.6
Mobile phase	95% hexane, 5 % isopropanol
Flow	0.3 mL/min
Wavelength	220nm
Result	98% e.e. (99% e.s.)



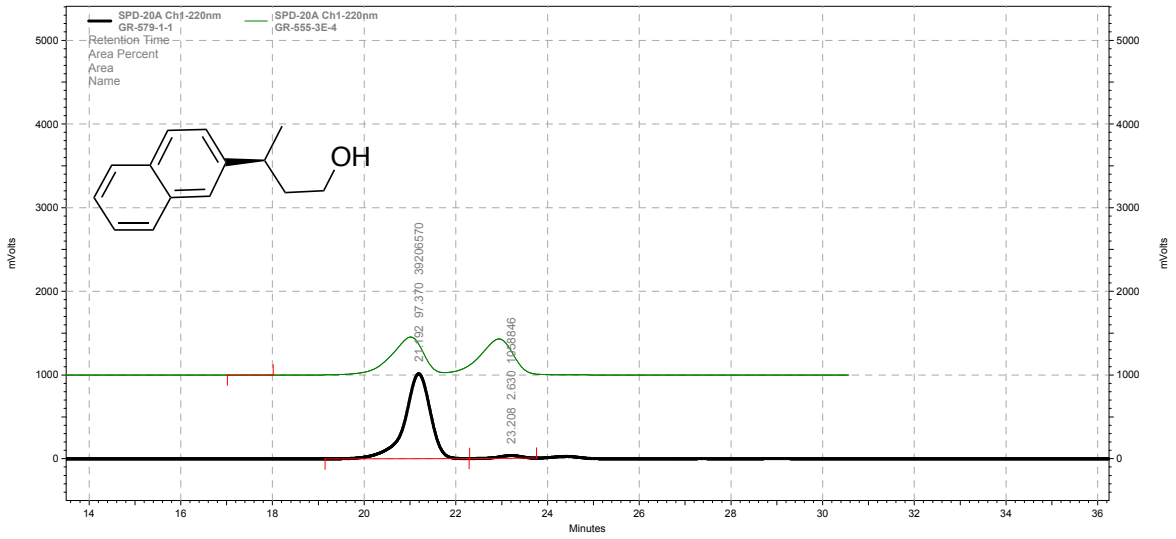
Column	IA, 250 x 4.6
Mobile phase	60% = (5% acetonitrile in methanol), 30% water
Flow	1.2 mL/min
Wavelength	220nm
Result	94% e.e. (96% e.s.)



Column	OJ-RH, 150 x 4.6
Mobile phase	40% acetonitrile in water for 10min, gradient to 60% acetonitrile in water at 50min
Flow	1.0 mL/min
Wavelength	220nm
Result	90% e.e. (92% e.s.)



Column	OJ-RH, 150 x 4.6
Mobile phase	70% acetonitrile, 30% water
Flow	1.2 mL/min
Wavelength	220nm
Result	94% e.e. (96% e.s.)



Column	IA, 250 x 4.6
Mobile phase	35% acetonitrile, 65% water
Flow	1.4 mL/min
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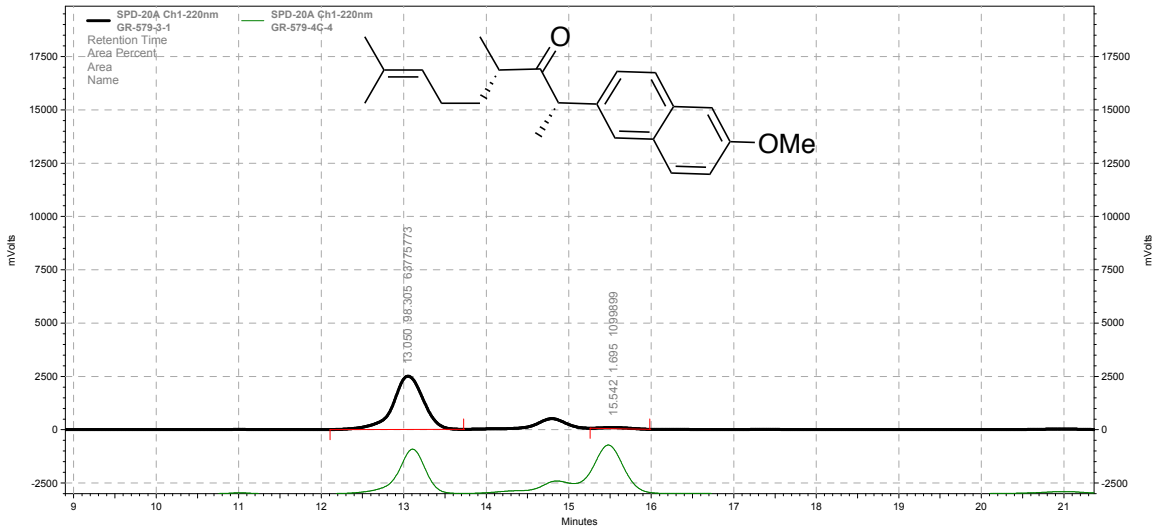
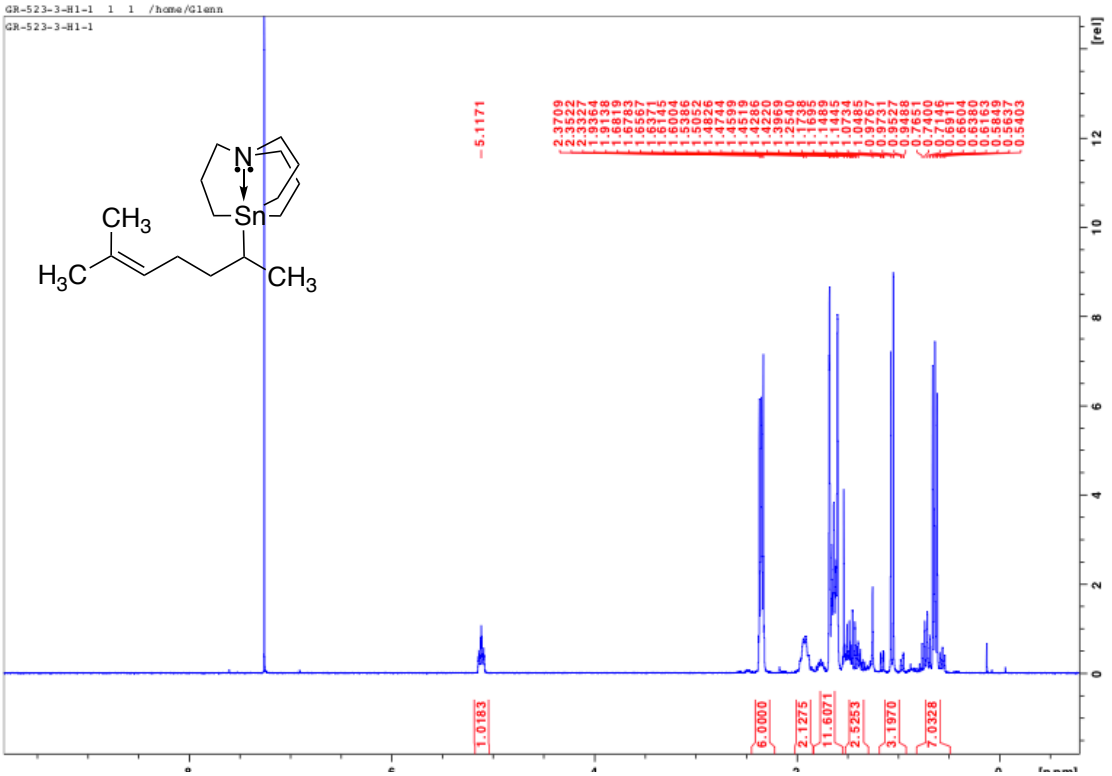
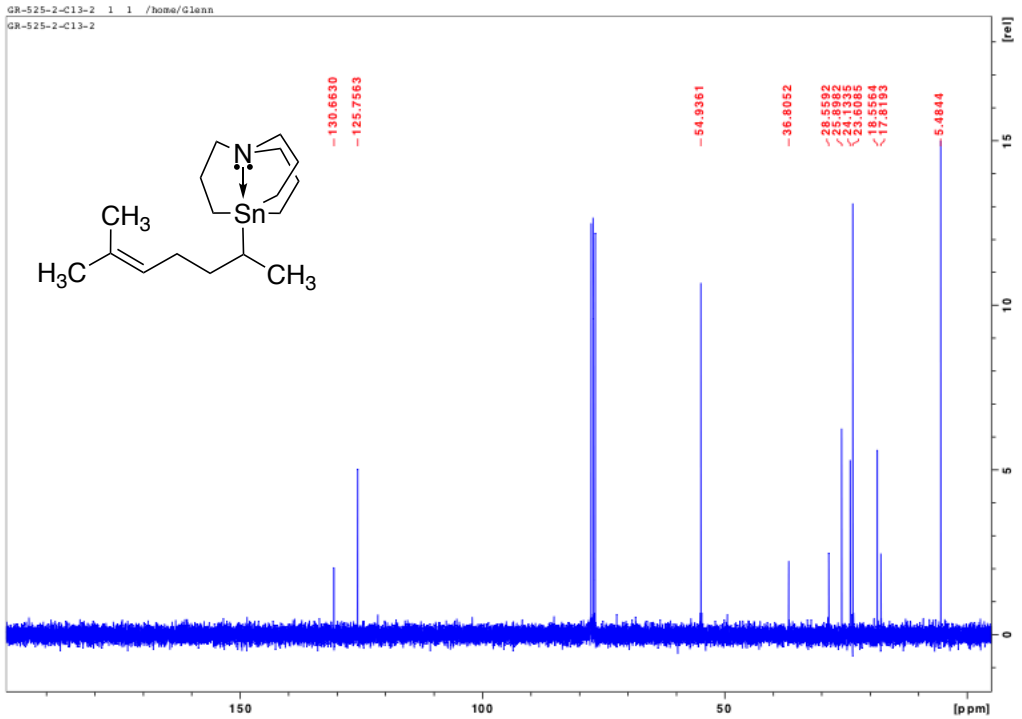
Result	94% e.e. (96% e.s.)

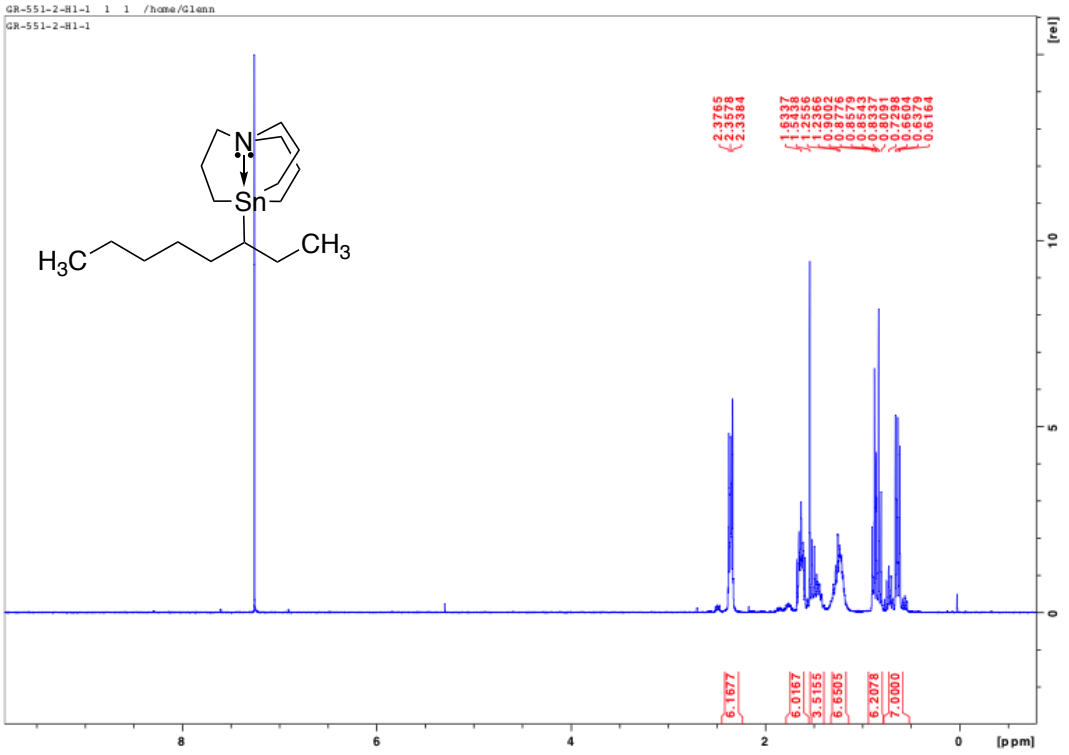


Column	IA, 250 x 4.6
Mobile phase	60% acetonitrile, 20% water
Flow	1.0 mL/min
Wavelength	220nm
Result	58:1 d.r.

^{1}H and ^{13}C NMR Spectra



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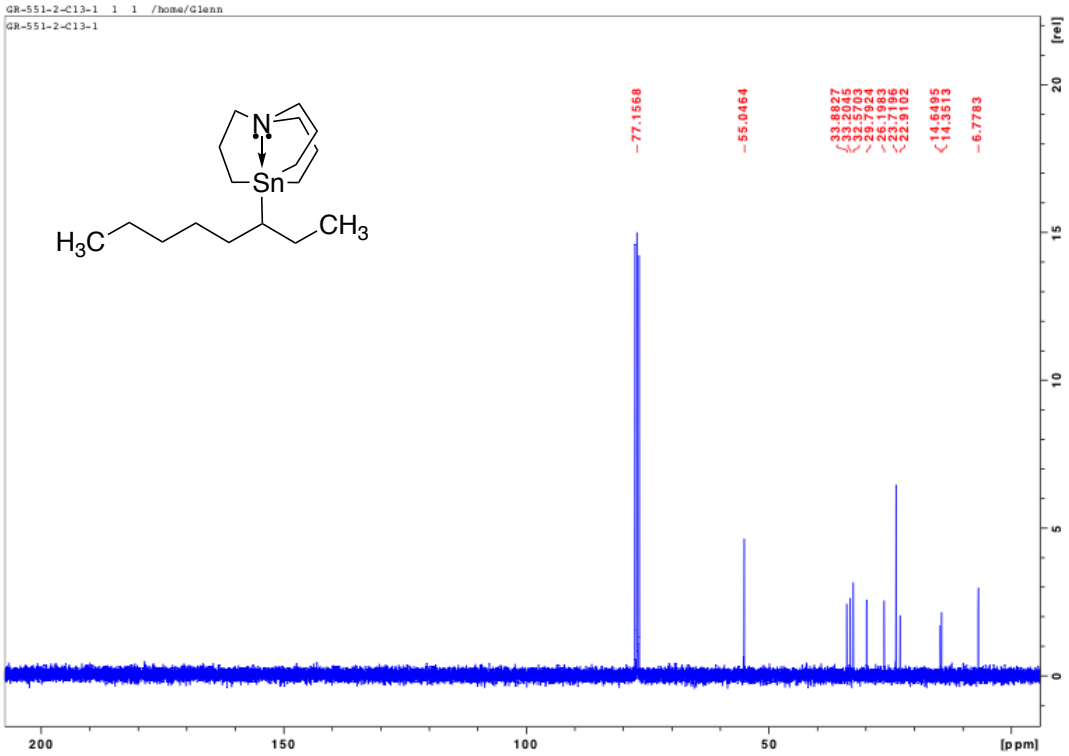
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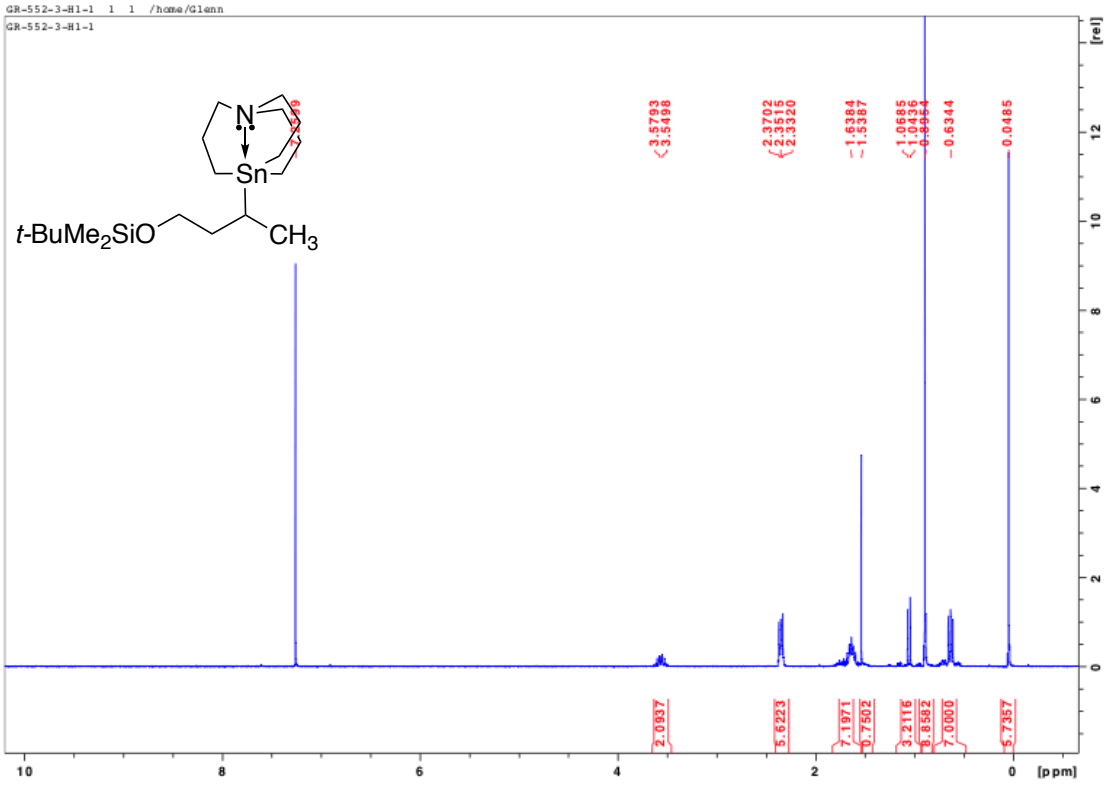
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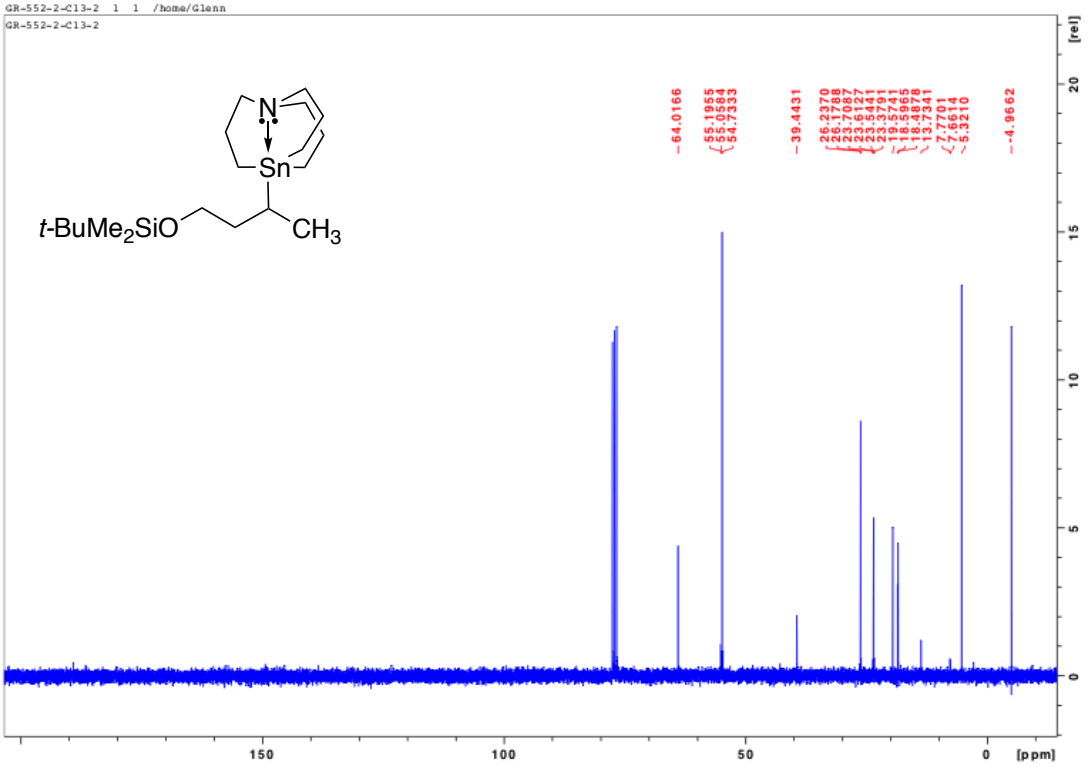
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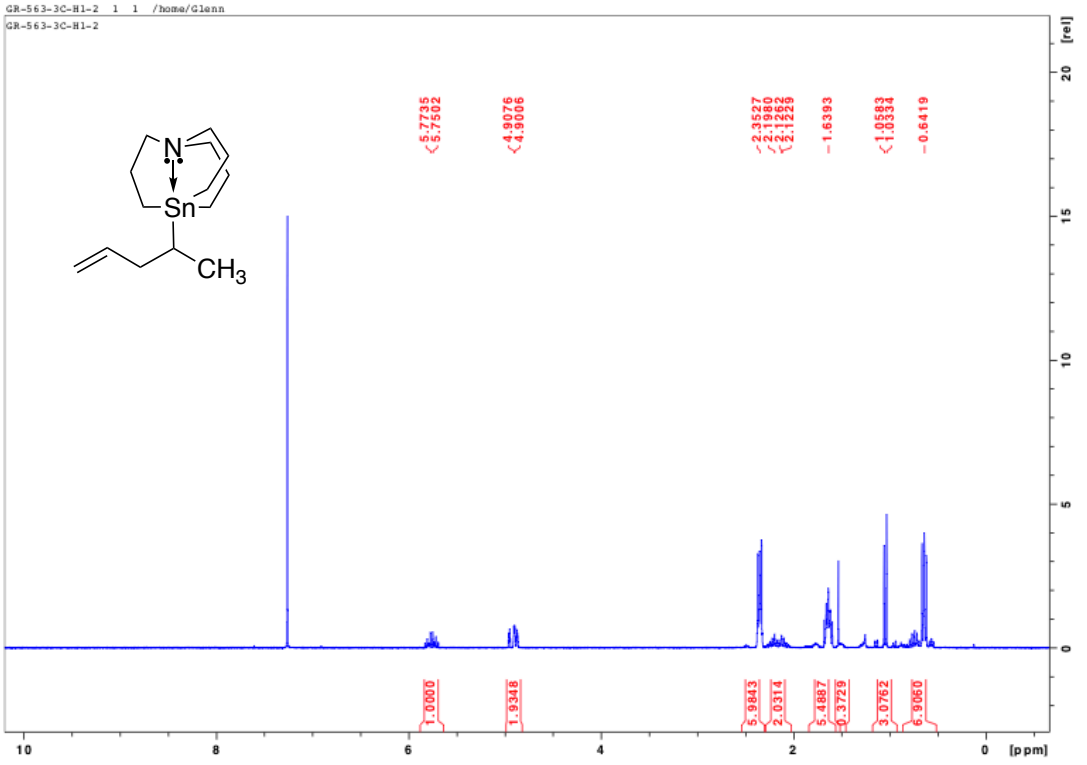
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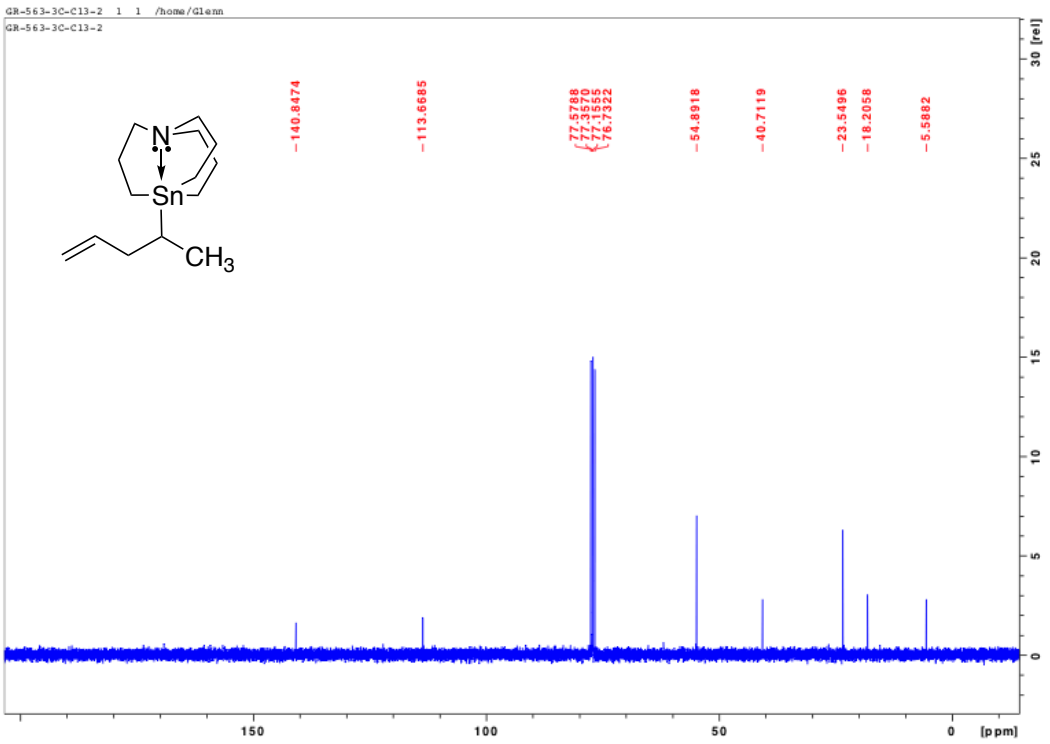
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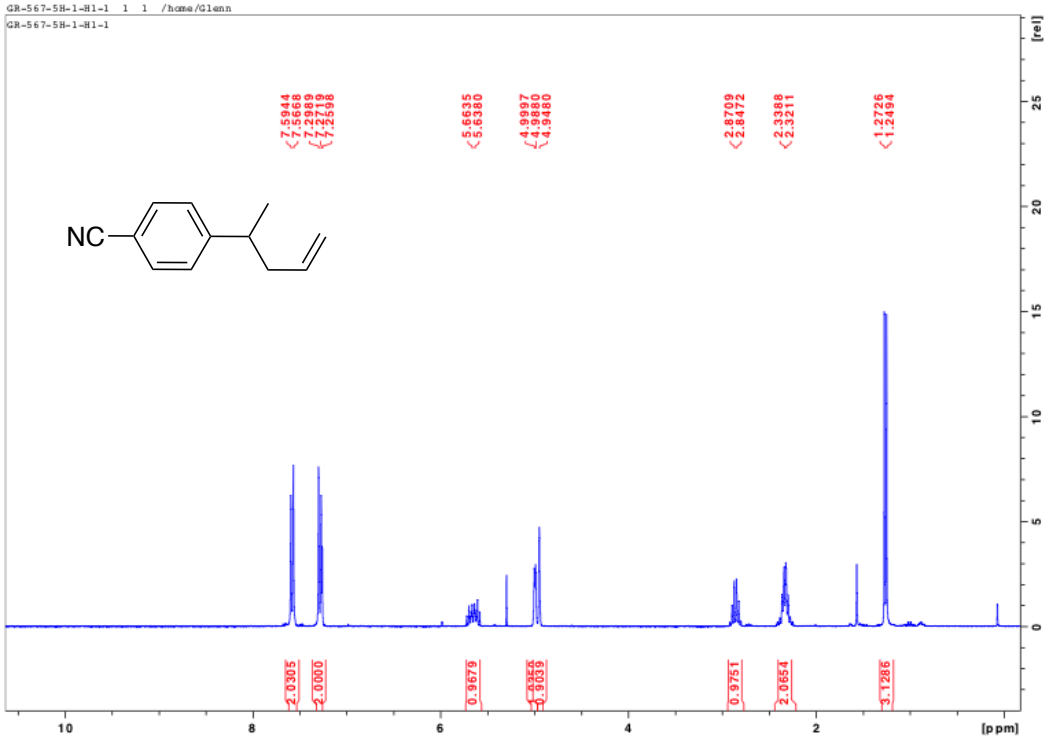
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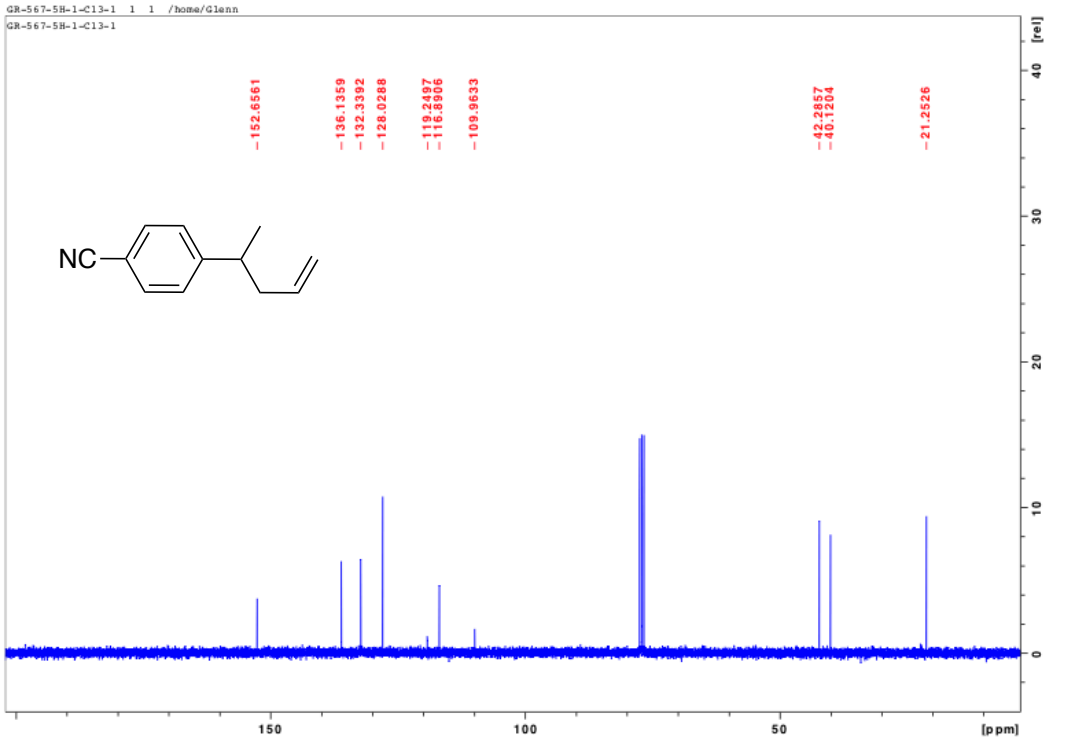
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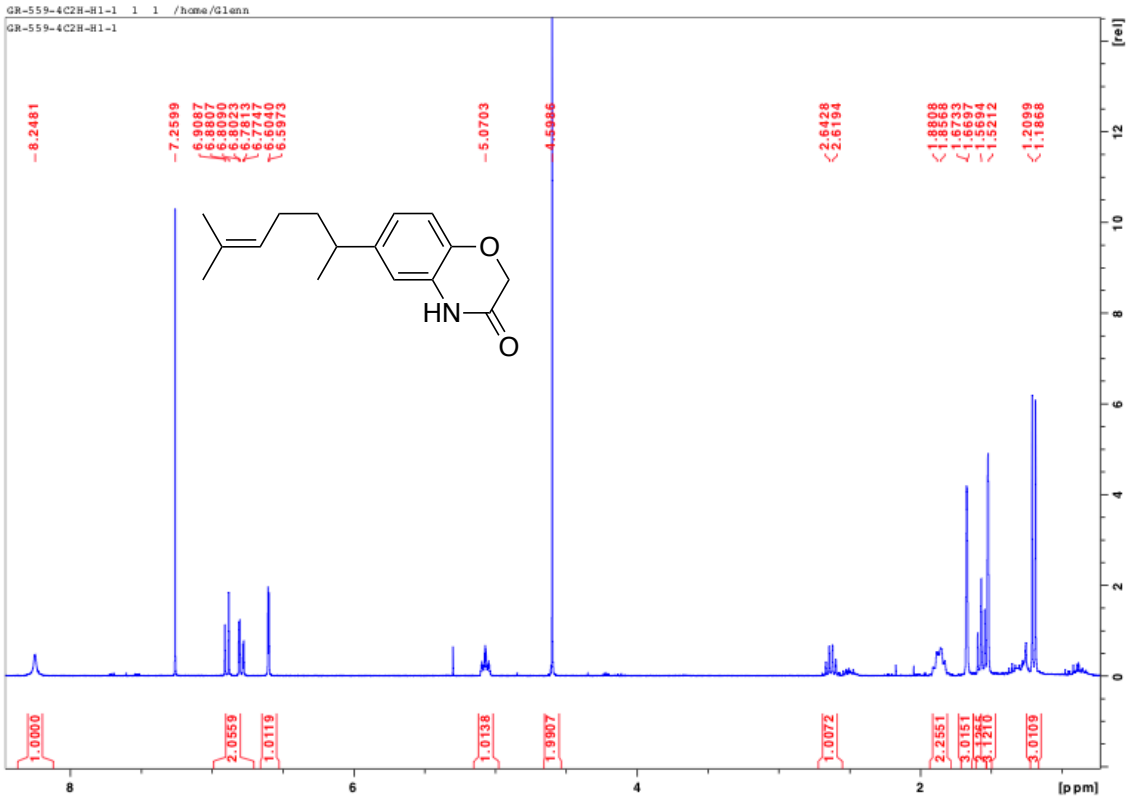
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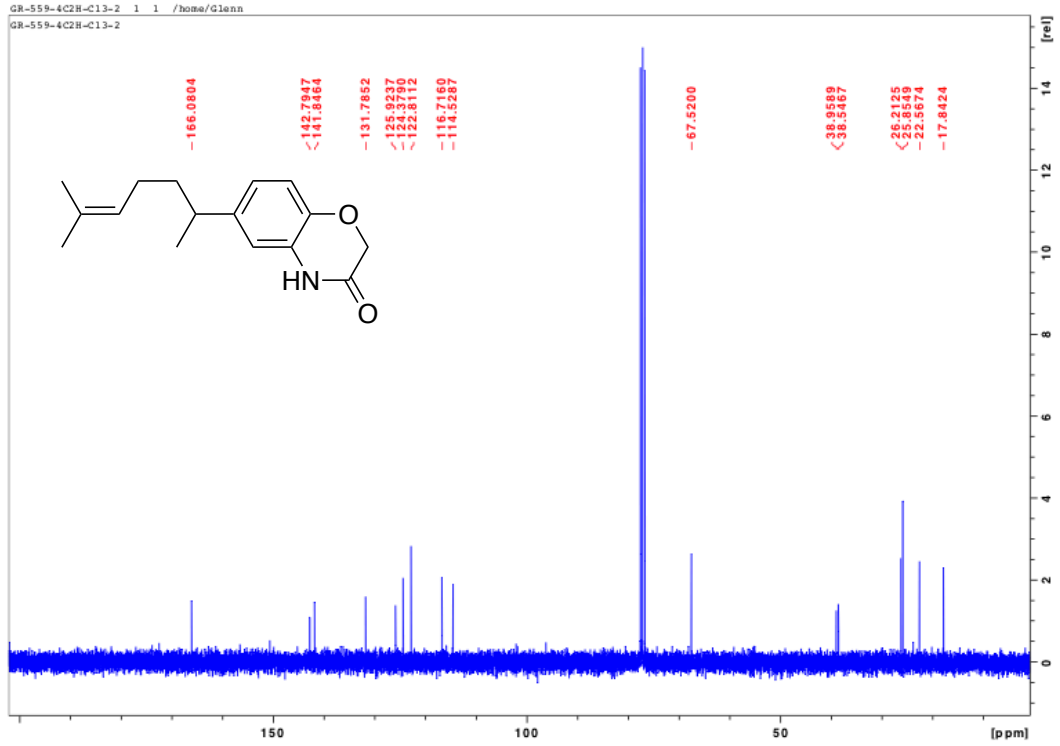
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50
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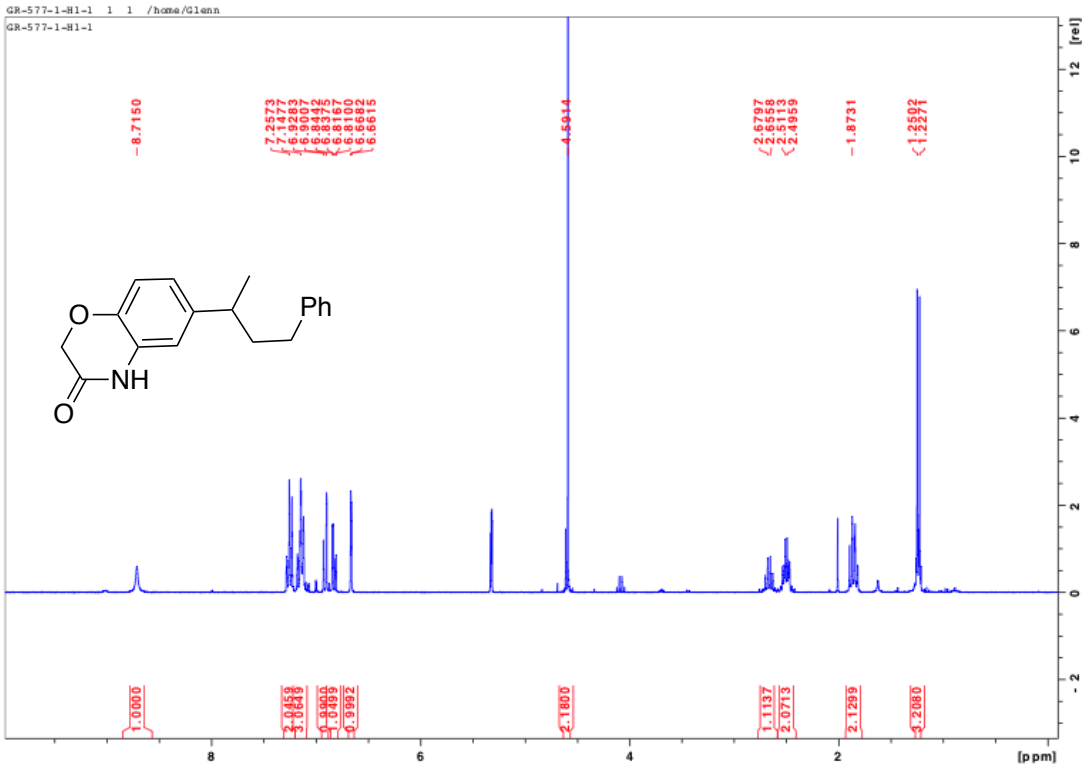
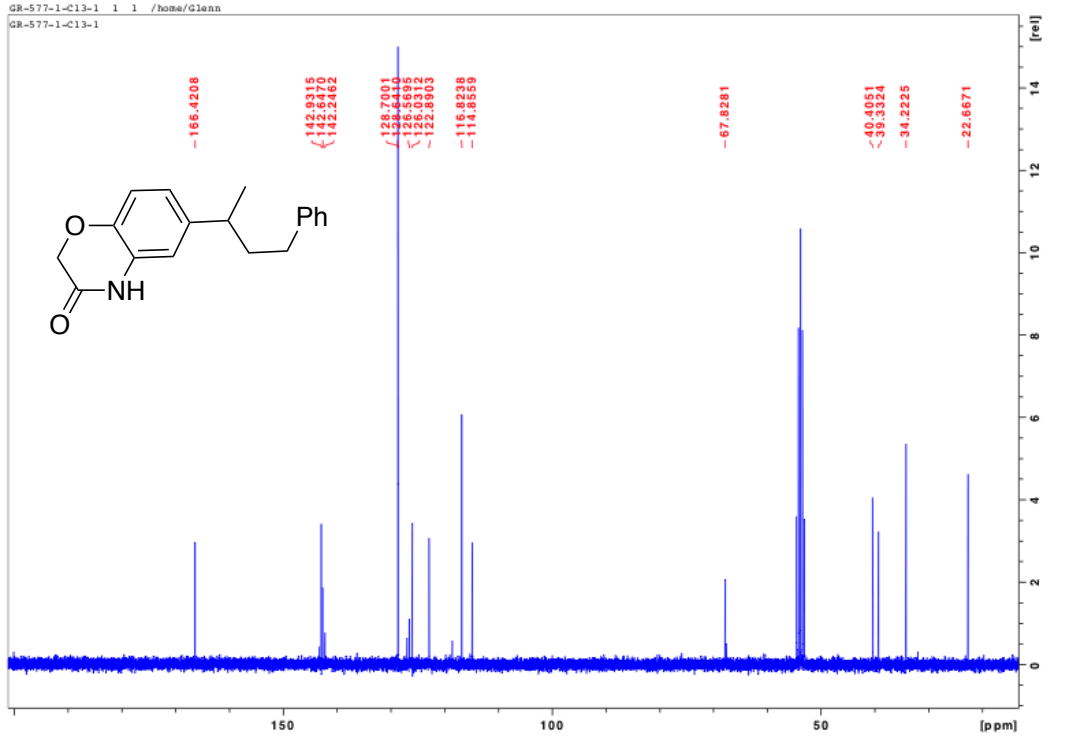
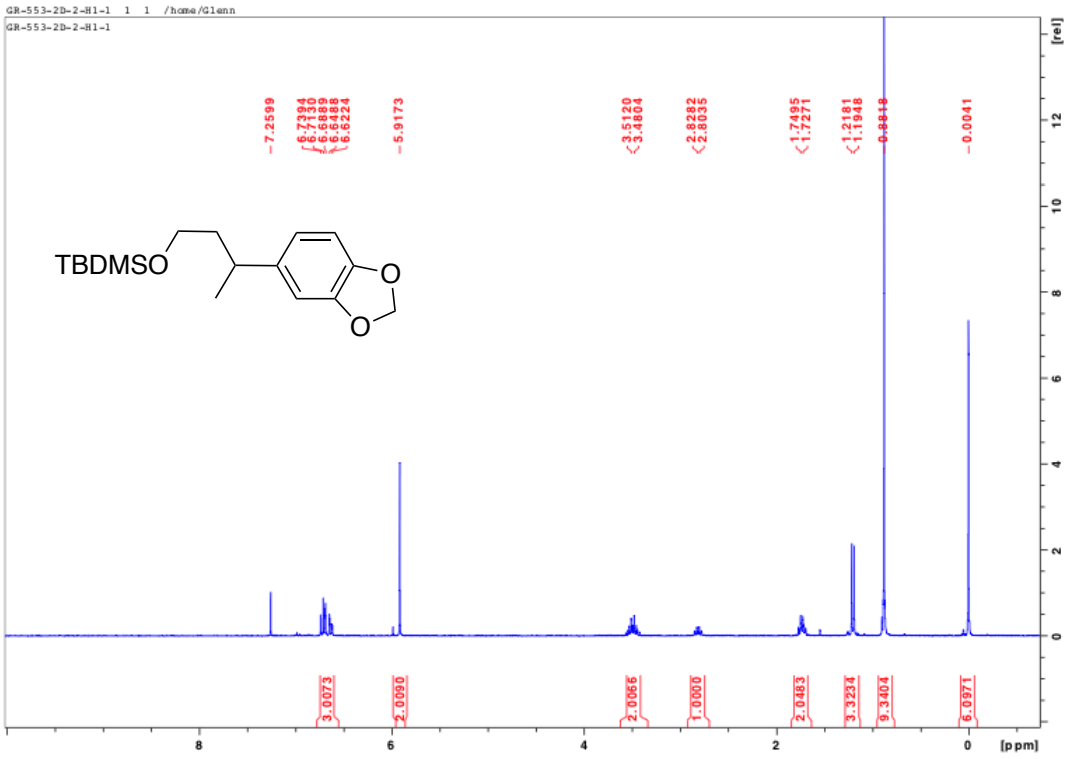
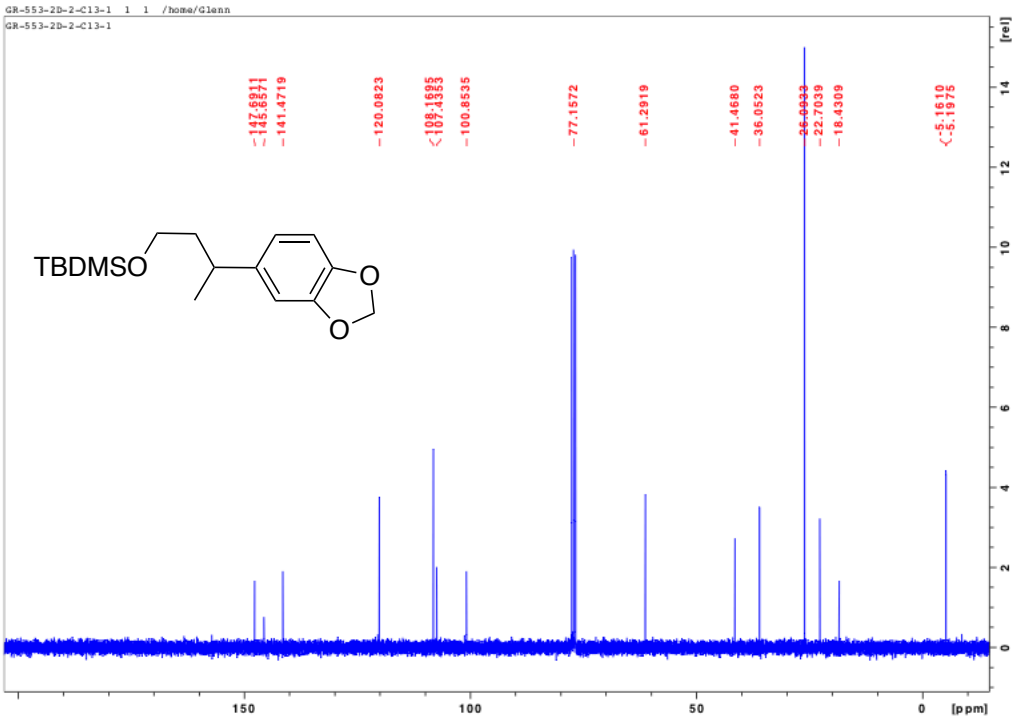
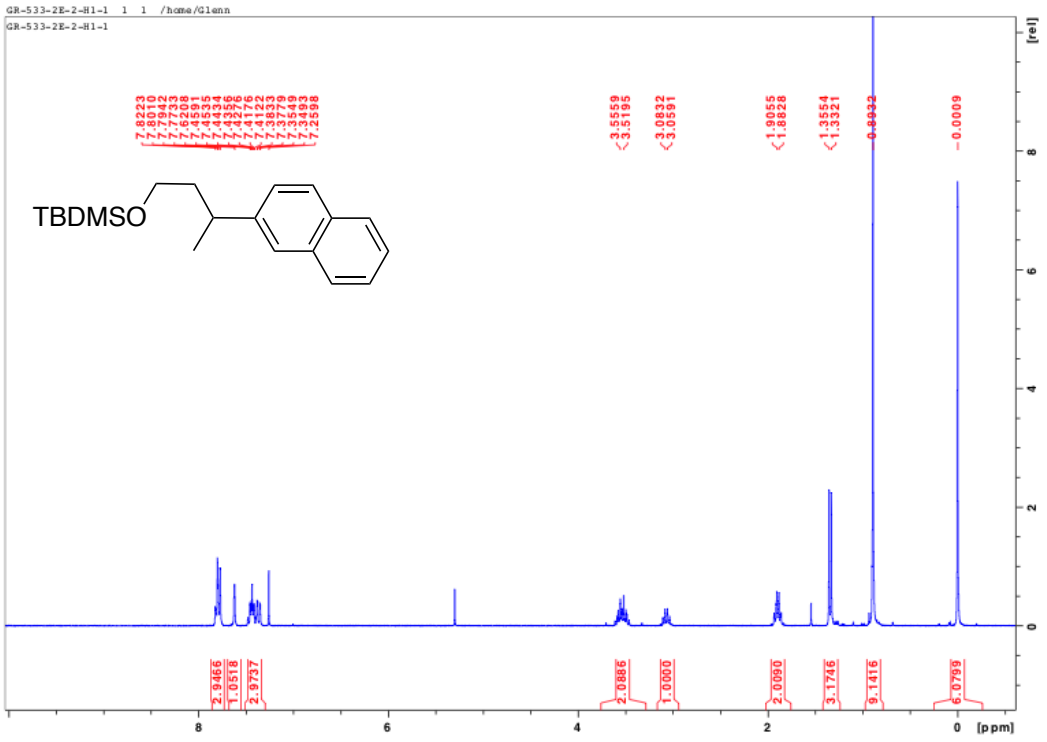
[rel]

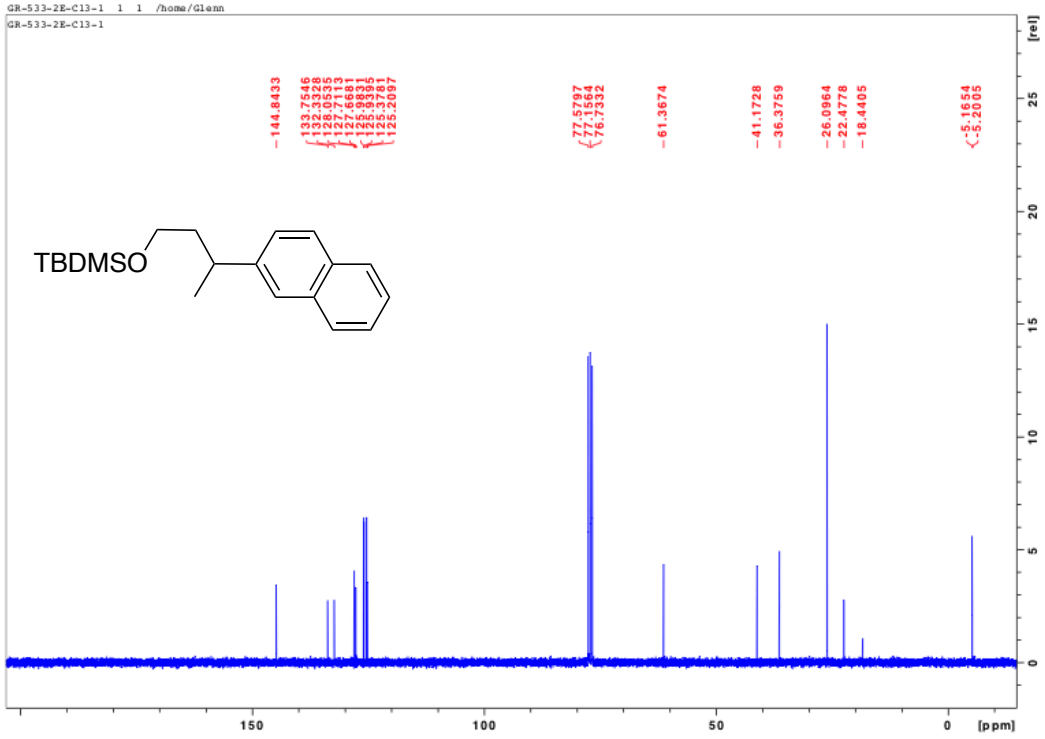

GR-577-1-H1-1 1 1 /home/Glenn
GR-577-1-H1-1
8.7150
7.2573
7.1477
6.9283
6.9007
6.8442
6.8315
6.8167
6.8100
6.6682
6.6615
4.5914
2.6797
2.6558
2.5113
2.4959
1.8731
1.2502
1.2271
O
NH
O
Ph
1.0000
2.0458
3.0849
0.9000
1.0499
0.9992
2.1800
1.1137
2.0713
2.1299
3.2080
8
6
4
2
[ppm]
[rel]

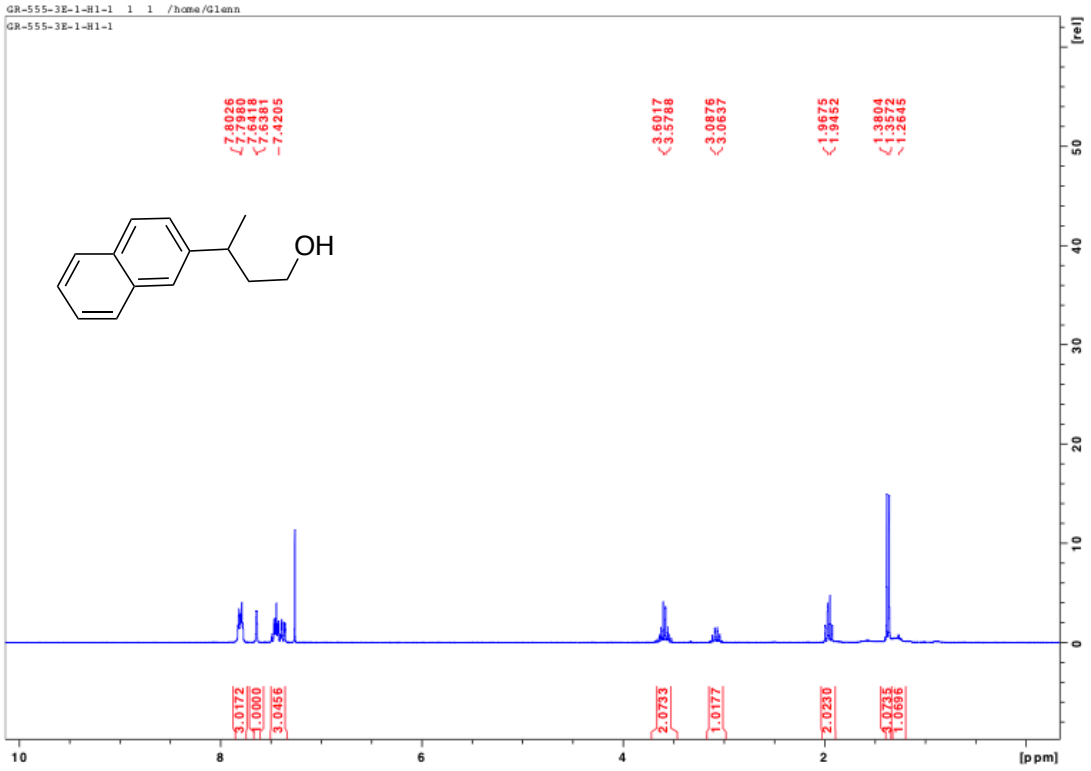

GR-577-1-C13-1 1 1 /home/Glenn
GR-577-1-C13-1
166.4208
142.9315
142.7700
142.2462
128.7001
128.6410
126.5995
126.0312
122.8903
116.8238
114.8559
67.8281
40.4051
39.3324
34.2225
22.6671
O
NH
O
Ph
150
100
50
[ppm]
[rel]

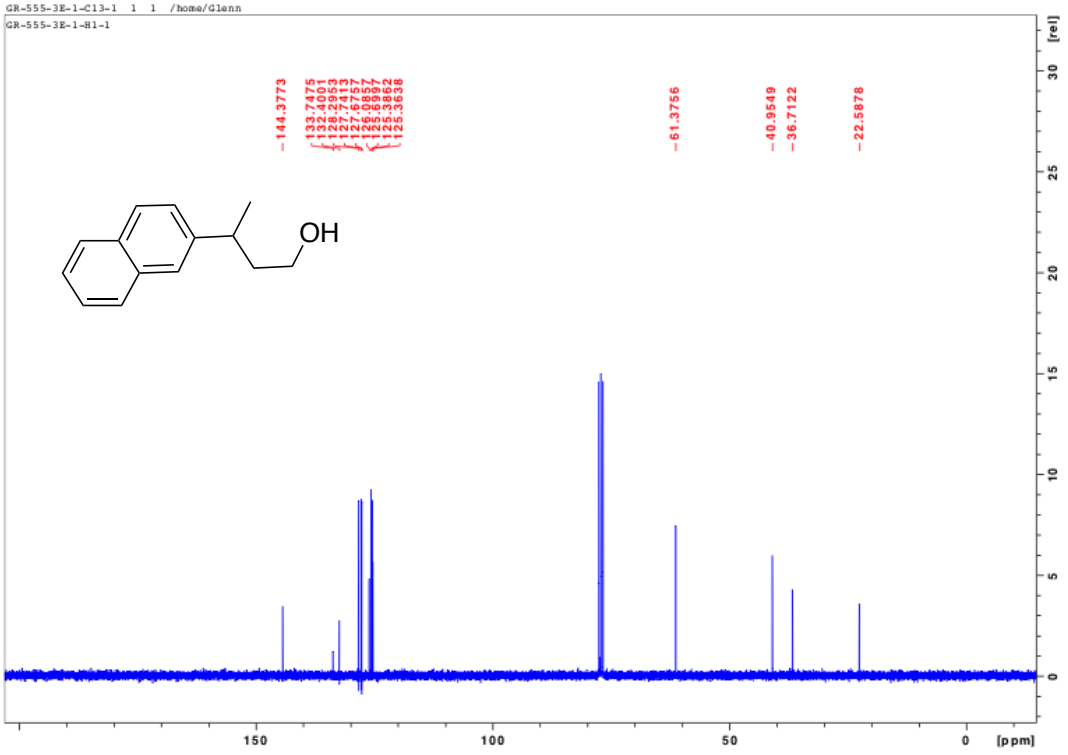

GR-553-2D-2-H1-1 1 1 /home/Glenn
GR-553-2D-2-H1-1
7.2599
6.7394
6.7130
6.6889
6.6488
6.6224
5.9173
3.5120
3.4804
2.8282
2.8035
1.7495
1.7271
1.2181
1.1948
0.8818
0.0041
TBDMSO
O
O
3.0073
2.0090
2.0066
1.0000
2.0483
3.3234
9.3404
6.0971
8
6
4
2
0
[ppm]
[rel]

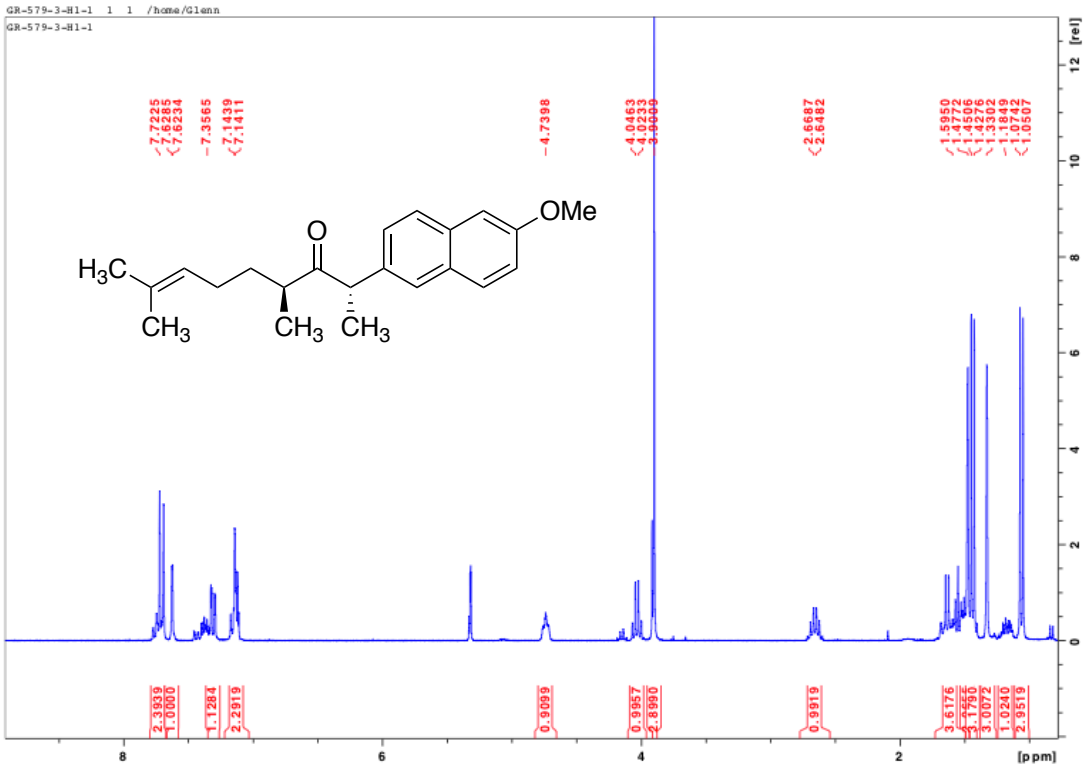

GR-553-2D-2-C13-1 1 1 /home/Glenn
GR-553-2D-2-C13-1
147.6911
145.8571
141.4719
120.0823
108.1695
107.4353
100.8535
77.1572
61.2919
41.4680
36.0523
26.0933
22.7039
18.4309
-5.1610
-5.1975
TBDMSO
O
O
150
100
50
0
[ppm]
[rel]

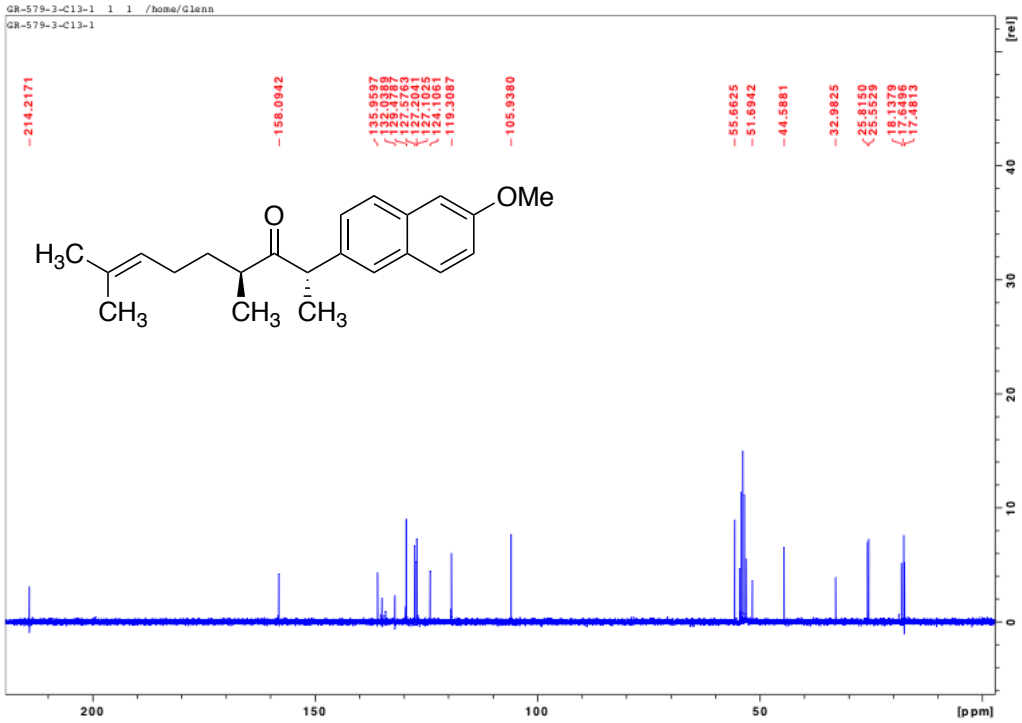

GR-533-2E-2-H1-1 1 1 /home/Glenn
GR-533-2E-2-H1-1
TBDMSO
[rel]
[ppm]

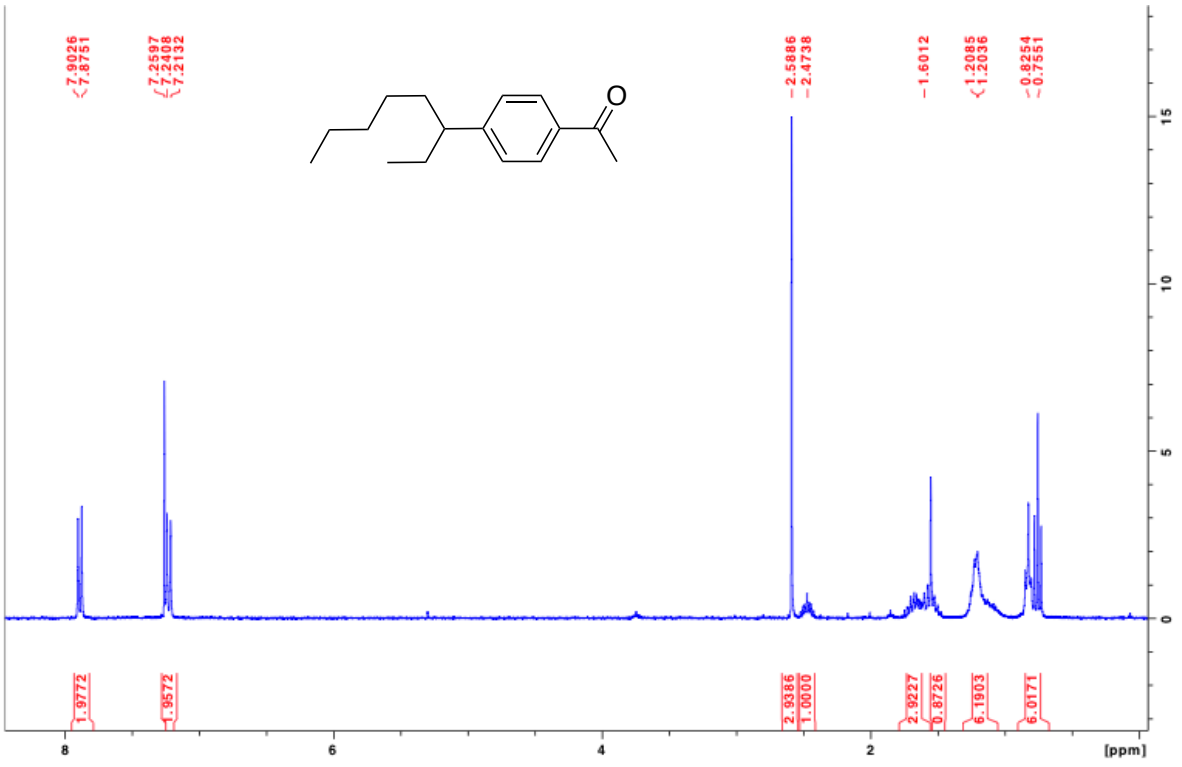

GR-533-2E-C13-1 1 1 /home/Glenn
GR-533-2E-C13-1
TBDMSO
[rel]
[ppm]

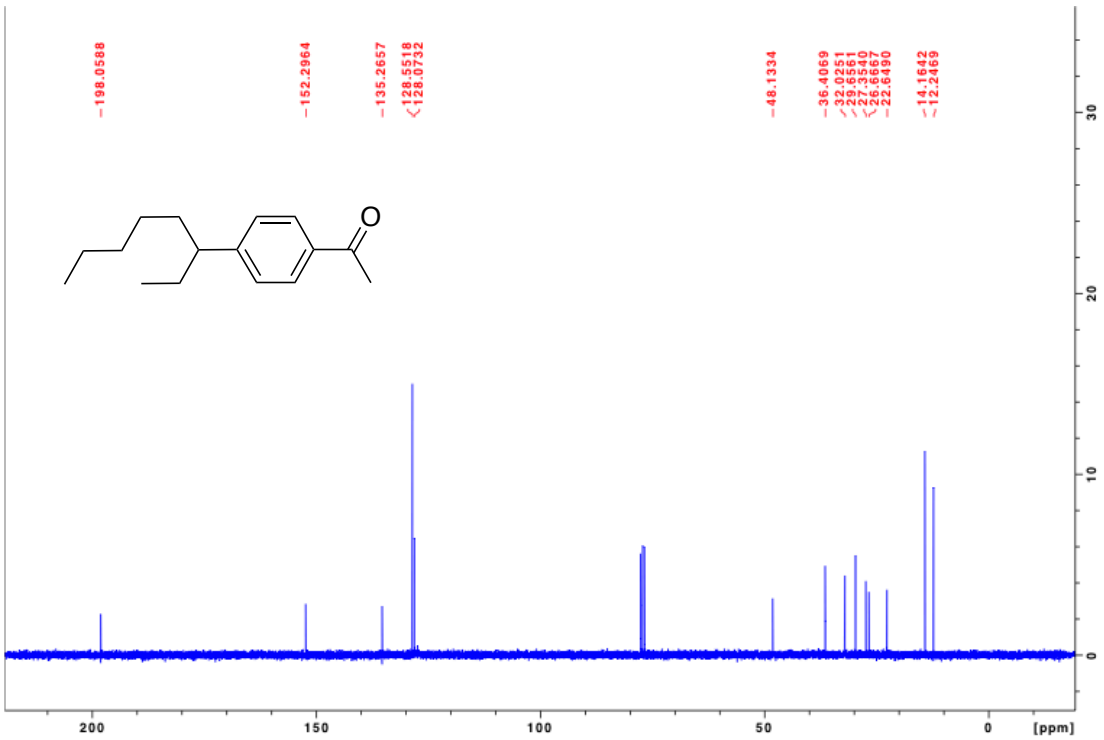

GR-555-3E-1-H1-1 1 1 /home/Glenn
GR-555-3E-1-H1-1
7.8026
7.7960
7.6418
7.6381
7.4205
3.6017
3.5788
3.0876
3.0637
1.9675
1.9452
1.3804
1.3572
1.2645
OH
3.0172
1.0000
3.0456
2.0733
1.0177
2.0230
1.0735
1.0696
[rel]
[ppm]


GR-555-3E-1-C13-1 1 1 /home/Glenn
GR-555-3E-1-H1-1
144.3773
133.7475
132.4001
128.2913
127.7413
127.6757
126.0857
125.6987
125.4892
123.3638
61.3756
40.9549
36.7122
22.5878
OH
[rel]
[ppm]


GR-579-3-H1-1 1 1 /home/Glenn
GR-579-3-H1-1
7.7225
7.6285
7.6234
7.3565
7.1439
7.1411
4.7398
4.0463
4.0233
3.9999
2.6687
2.6482
1.5950
1.4772
1.4596
1.4276
1.3302
1.1849
1.1742
1.0507
O
OMe
H3C
CH3
CH3
CH3
2.3939
1.0000
1.1284
2.2919
0.9099
0.9957
2.8990
0.9919
3.6176
3.0072
1.0240
2.9519
8
6
4
2
[ppm]
[rel]


GR-579-3-C13-1 1 1 /home/Glenn
GR-579-3-C13-1
214.2171
158.0942
135.9587
132.0787
129.4787
127.5763
127.2041
127.1025
124.1061
119.3087
105.9380
55.6625
51.6942
44.5881
32.9825
25.8159
25.5529
18.1379
17.4486
17.4813
O
OMe
H3C
CH3
CH3
CH3
200
150
100
50
[ppm]
[rel]


7.9026
7.8751
7.2597
7.2408
7.2132
2.5886
2.4738
1.6012
1.2085
1.2036
0.8254
0.7551
1.9772
1.9572
2.9386
1.0000
2.9227
0.8726
6.1903
6.0171
8
6
4
2
[ppm]
O


198.0588
152.2964
135.2657
128.5518
128.0732
48.1334
36.4069
32.0251
29.6561
27.3540
26.6667
22.6490
14.1642
12.2469
200
150
100
50
0
[ppm]
O