

# Synthesis of Functionalized 1,3-Butadienes *via* Pd-Catalyzed Cross-Couplings of Substituted Allenic Esters in Water at Room Temperature

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## 1. General Information:

### General Experimental Details

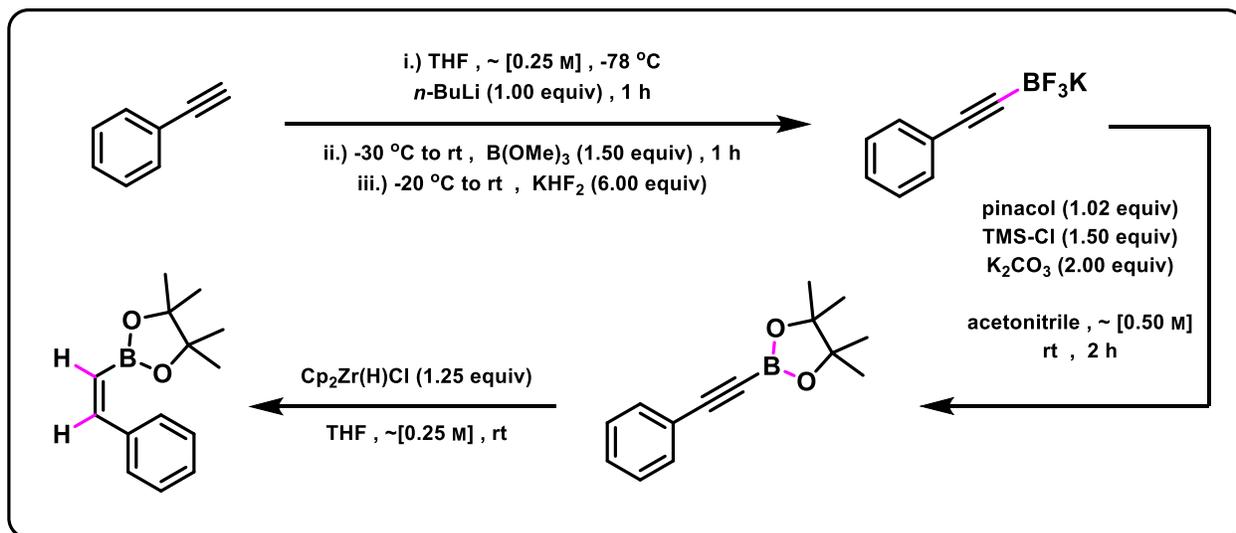
All manipulations were carried out under air unless otherwise noted. Silica gel TLC plates (standard grade, 230 – 400 mesh) were purchased from EMD Chemicals. Diethyl ether (Fisher), toluene (Aldrich), THF (Fisher) and DCM (Fisher) were purified using a solvent purifier system (SPS). Et<sub>3</sub>N (Fisher) was dried over activated 4 Å molecular sieves and stored on dried 4 Å sieves under argon. NMR solvents were purchased from Cambridge Isotopes Laboratories. CDCl<sub>3</sub> was dried over activated 4 Å molecular sieves and then stored over dried 4 Å sieves. Reaction vials (4 mL with green top polypropylene cap and PTFE septa) were purchased from Chemglass Life Sciences, and used as received without further drying. Reaction vials (4 mL black top) were purchased from VWR, and used as received without further drying. Reaction vials were also recycled and re-used. HPLC grade water was used to prepare surfactant solutions. TPGS-750-M was synthesized by a procedure published by this group,<sup>1</sup> and is also commercially available from Sigma-Aldrich. Ligands and catalysts were generously received from F. Hoffmann-La Roche AG and Johnson Matthey. All other reagents were purchased from Aldrich and Fischer and used as received. Melting points were determined using a MEL-TEMP II melting point apparatus with samples in Kimble Kimex 51 capillaries (1.5-1.8 x 90 mm). NMR spectra were recorded at 23 °C on Varian Unity INOVA (400, 500 and 600 MHz) spectrometers. Reported chemical shifts are referenced to residual solvent peaks. IR spectra were acquired on a FTIR Perkin Elmer Spectrum Two: UATR Two spectrometer using 1 cm<sup>-1</sup> resolution. High resolution mass analyses were obtained using a 5975C Mass Selective Detector, coupled with a 7890A Gas Chromatograph (Agilent Technologies). As capillary column a HP-5MS cross-linked 5% phenylmethylpolysiloxanediphenyl column (30 m x 0.250

mm, 0.25 micron, Agilent Technologies) was employed. Helium was used as carrier gas at a constant flow of 1 mL/min. Elemental analyses were performed at UCSB.

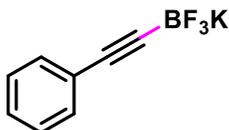
Unless otherwise noted, all reactions were performed under an atmosphere of argon. All commercially available reagents were used without further purification. A 2 wt % TPGS-750-M/H<sub>2</sub>O solution was prepared by dissolving 4 g TPGS-750-M in 196 g water (HPLC grade), followed by degassing with argon. TPGS-750-M was made as previously described,<sup>1</sup> and is available from Sigma-Aldrich (catalog #733857). Analytical thin layer chromatography (TLC) was performed using Silica Gel 60 F<sub>254</sub> plates (Merck, 0.25 mm thick). Developed chromatograms were analyzed by UV (lamp, 254 nm). Non-UV active compounds were developed using aqueous potassium permanganate (KMnO<sub>4</sub>), Vanillin/H<sub>2</sub>SO<sub>4</sub>, Ceric Ammonium Molybdenate (CAM stain), or Seebach's stain. Flash chromatography was performed in glass columns using Silica Flashed® P60 (SiliCycle, 40-63 µm). GCMS data was recorded on a 5975C Mass Selective Detector coupled with a 7890A Gas Chromatograph (Agilent Technologies). A capillary column (HP-5MS cross-linked 5% phenylmethylpolysiloxanediphenyl, 30 m x 0.250 mm, 0.25 micron, Agilent Technologies) was employed. Helium was used as carrier gas at a constant flow of 1 mL/min. <sup>1</sup>H and <sup>13</sup>C NMR were recorded at 22 °C on a Varian UNITY INOVA Avance at 400, 500, or 600 MHz. Chemical shifts in <sup>1</sup>H NMR spectra are reported in parts per million (ppm) on the δ scale from an internal standard of residual chloroform (7.26 ppm) or dichloromethane (5.30 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, sex = sextet, sep = septet, m = multiplet, br = broad w = weak), coupling constant in Hertz (Hz), and integration. Chemical shifts of <sup>13</sup>C NMR spectra are reported in ppm from the central peak of CDCl<sub>3</sub> (77.16 ppm) or the left peak of CD<sub>2</sub>Cl<sub>2</sub> (53.84 ppm) on the δ scale. IR data was collected on an FTIR Perkin Elmer Spectrum Two UATR Two spectrum using 1 cm<sup>-3</sup> resolution. Chiral HPLC data were collected using a Shimadzu SPD-m20a Prominence diode array detector. All unknown compounds were either made utilizing known procedures,<sup>2</sup> or prepared as shown below.

## 2. Synthetic Details

### 2.1 Synthesis of coupling partners



### Trifluoro(phenylethynyl)- $\lambda^4$ -borane, potassium salt<sup>3</sup>



To a solution of phenylacetylene (10.00 mmol, 1.00 equiv) in THF,  $\sim[0.25\text{ M}]$ , was added *n*-butyllithium (1.00 equiv) dropwise at  $-78\text{ }^\circ\text{C}$ , and the resulting solution was stirred for 1 h. The cold bath was then adjusted to  $-30\text{ }^\circ\text{C}$  and trimethylborate (1.50 equiv) was introduced dropwise, the solution was allowed to stir at this temperature for 1 h, then for an additional hour at room temperature. The reaction was then quenched, at  $0\text{ }^\circ\text{C}$  with vigorous stirring, by addition of an aqueous solution of  $\text{KHF}_2$ ,  $[5.0\text{ M}]$ , and further stirred for an additional 2-4 h (extra time stirring has no adverse effect) at rt (open flask). All solvent was removed *via* rotary evaporation (with aid of a heat gun if necessary), the resulting white residue was azeotroped with acetone to aid in removal of trace water (x 2-3). The RBF containing the

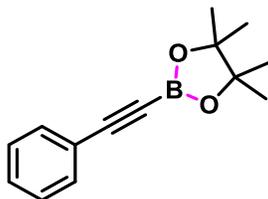
crude white residue was then filled  $\sim\frac{1}{2}$  full with acetone and heated with rotation on the roto-vap, without vacuum (just below the boiling point of acetone) for  $\sim$ 10-15 min (inorganic salts will remain suspended), and directly filtered 'hot' *via* vacuum filtration. This process was repeated on the RBF retaining the inorganic salts once more. The collected acetone washes were concentrated and once more heated and filtered to afford a white crystalline solid, which was triturated with pentanes (x2-3), and stored under high vacuum to afford the desired compound as a white crystalline solid, 1,202mg, 58%.

\*Note: Product  $-\text{BF}_3\text{K}$  salt is soluble in hot acetone, whereas excess  $\text{KHF}_2$  is not.

$^1\text{H}$  NMR: (500 MHz, acetone- $d_6$ )  $\delta$  7.38 – 7.29 (m, 2H), 7.27 – 7.17 (m, 3H)

$^{13}\text{C}$  NMR: (126 MHz, acetone)  $\delta$  132.1, 132.1, 128.8, 128.8, 127.3, 99.4

#### 4,4,5,5-Tetramethyl-2-(phenylethynyl)-1,3,2-dioxaborolane <sup>4</sup>



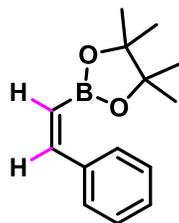
To a RBF, containing a Teflon coated stir bar, were dissolved the acetylinic- $\text{BF}_3\text{K}$  salt (1.90 mmol, 1.00 equiv),  $\text{K}_2\text{CO}_3$  (2.00 equiv) and pinacol (1.02 equiv) in acetonitrile at [0.50 M]. The resulting mixture was stirred at room temperature followed by the dropwise addition of TMS-Cl (1.50 equiv), upon complete addition the solution was further stirred for  $\sim$ 2-3 h. The reaction was then diluted with ether ( $\sim\frac{1}{2}$  the reaction volume), stirred for 5 min and allowed to settle. The salts were removed *via* filtration, and the crude organics removed *in vacuo*. The resulting crude residue was immediately purified *via* column chromatography on silica gel, eluting with 75% (EtOAc : hexanes), to afford the desired compound as a white solid, 268mg, 62%.

\*Note: Purification of boronate esters should be performed immediately after reaction work-up, and chromatography should take no longer than 10 min.

$^1\text{H}$  NMR: (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.56 – 7.47 (m, 2H), 7.38 – 7.29 (m, 3H), 1.32 (s, 12H)

$^{13}\text{C}$  NMR: (126 MHz,  $\text{CDCl}_3$ )  $\delta$  132.7, 132.3, 129.5, 128.9, 128.4, 128.4, 122.0, 84.6, 77.3, 24.9

**(Z)-4,4,5,5-Tetramethyl-2-styryl-1,3,2-dioxaborolane** <sup>5</sup>



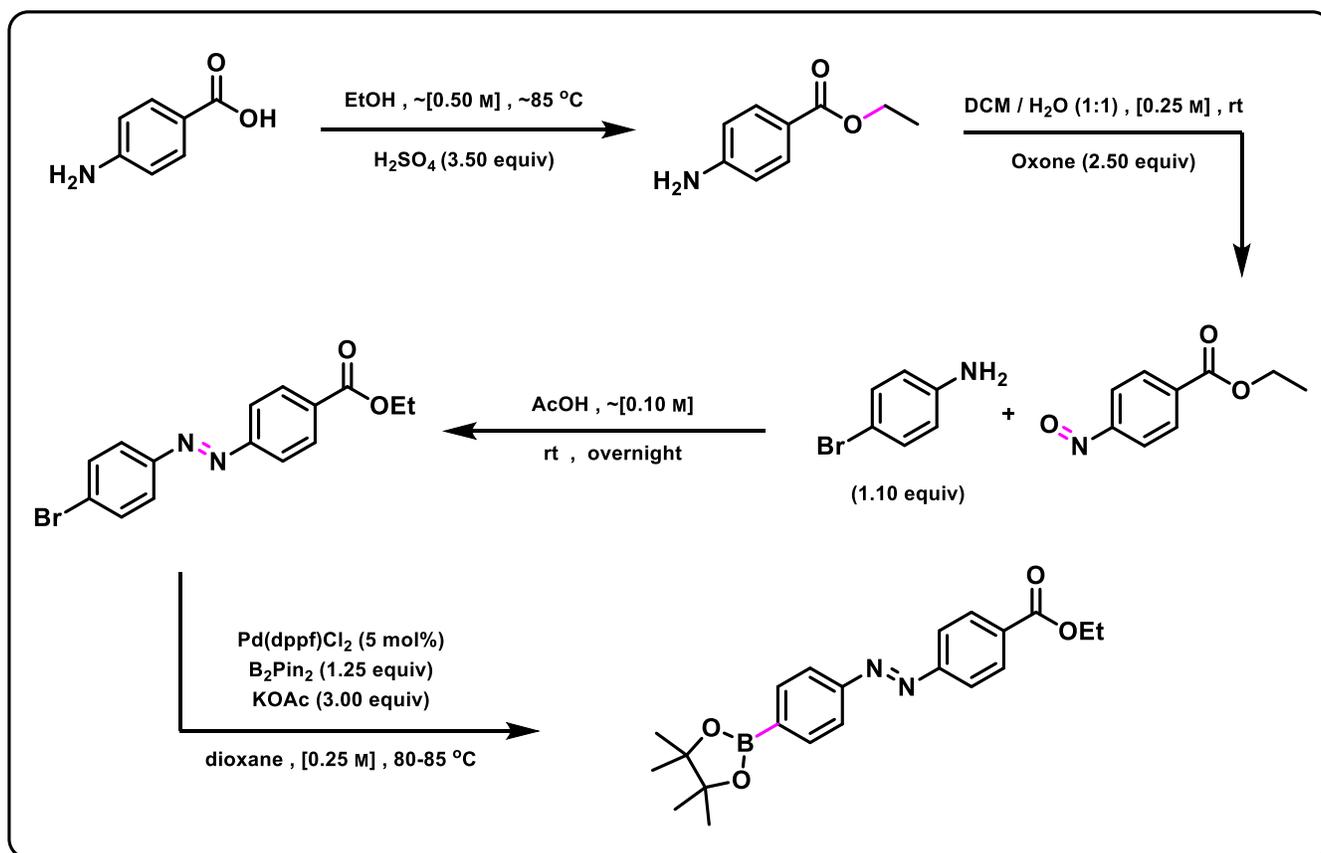
Schwartz's reagent (1.25 equiv) was weighed into a RBF containing a stir bar, the flask was placed under an argon atmosphere, to which was then added dry THF to arrive at a [0.50 M] mixture, all at rt. To this stirred suspension was added dropwise a solution of the acetylenic boronate pinacol ester (0.75 mmol, 1.00 equiv) in THF [0.50 M]. The reaction was stirred overnight at rt, producing a clear, green-yellow solution. Upon completion, as judged *via* TLC analysis, the reaction was quenched with water and transferred to a separatory funnel with ether. The aqueous phase was extracted (x 3) with ether and the collected organic layers were dried over anhydrous  $\text{Na}_2\text{SO}_4$ . The crude organic layers were then passed through a plug of silica with EtOAc to afford the desired compound as a pale yellow solid, without need for further purification, 144mg, 84%.

TLC:  $R_f$  = 0.68 (75% EtOAc : hexanes), UV,  $\text{I}_2$ ,  $\text{KMnO}_4$

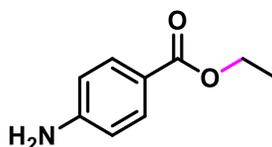
$^1\text{H}$  NMR: (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.57 – 7.49 (m, 2H), 7.32 – 7.25 (m, 4H), 5.60 (d,  $J$  = 14.9 Hz, 1H), 1.29 (s, 12H)

$^{13}\text{C}$  NMR: (126 MHz,  $\text{CDCl}_3$ )  $\delta$  148.3, 128.8, 128.1, 128.1, 103.9, 83.6, 24.9

IR: 2984, 2927, 2854, 1617, 1451, 1331, 1258, 1139  $\text{cm}^{-1}$



### Ethyl 4-aminobenzoate (Benzocaine)



To a stirred solution of 4-aminobenzoic acid (50.00 mmol, 1.00 equiv) in absolute ethanol, [0.50 M], was added dropwise concentrated sulfuric acid (3.50 equiv). The RBF was fitted with a jacketed water condenser and submerged in an oil bath, and the mixture was allowed to stir at reflux (bath set to  $\sim 85^\circ\text{C}$ ) overnight. Once the reaction was complete, *via* TLC analysis, the oil bath was removed and the RBF was allowed to cool to rt. Removal of the stir bar and concentration of the reaction mixture to  $\frac{1}{4}$  its volume *in vacuo* afforded a crude viscous material which was transferred to a large Erlenmeyer flask, containing a stir bar, with water and minimal ether. The flask was cooled in an ice bath and carefully

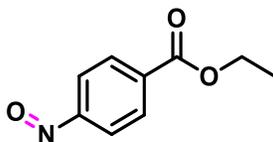
quenched with aqueous  $\text{Na}_2\text{CO}_3$ , with stirring, until a neutral pH was reached. The contents were then transferred to a separatory funnel and the aqueous phase was extracted with ether (x 3), the organic extracts were concentrated to 1/3 their volume and washed with  $\text{NaHCO}_3$  (x2-3) (to remove any trace carboxylic acid). The organic layer was dried over anhydrous  $\text{Na}_2\text{SO}_4$ , filtered and concentrated *in vacuo*, to afford the desired compound as clear/ faintly beige crystals, 6,772mg, 82%, without need for further purification.

\*Note: 3.50 equivalents of acid is required to deactivate the aniline moiety; use of fewer equivalents resulted in poor conversions, and catalytic amounts resulted in little to no reaction.

$^1\text{H}$  NMR: (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.06 – 7.65 (m, 2H), 6.67 – 6.60 (m, 2H), 4.32 (q,  $J = 7.1$  Hz, 2H), 4.03 (bs, 2H), 1.36 (t,  $J = 7.1$  Hz, 3H)

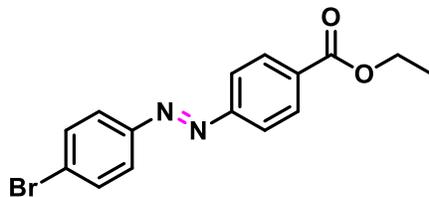
$^{13}\text{C}$  NMR: (126 MHz,  $\text{CDCl}_3$ )  $\delta$  166.9, 150.9, 131.7, 120.2, 113.9, 60.4, 14.6

### Ethyl 4-nitrosobenzoate <sup>6</sup>



To an Erlenmeyer flask (with good head space available), containing a Teflon coated stir bar, the starting aniline (15.00 mmol, 1.00 equiv) was dissolved in DCM,  $\sim$ [0.25 M], at rt with vigorous stirring. To the stirred mixture was slowly added, portion-wises an aqueous solution of Oxone<sup>®</sup> (2.50 equiv, [0.25 M]), and the reaction was allowed to proceed for 3 h to overnight, during which time a significant color change was observed. Upon complete consumption of aniline, *via* TLC analysis, the mixture was transferred to a separatory funnel. The aqueous phase was extracted with DCM (x2-3), concentrated to  $\frac{1}{2}$  its volume and then further washed with D.I. water (x 2-3). The organic layer was dried over anhydrous  $\text{Na}_2\text{SO}_4$ , filtered and concentrated to  $\sim$ 10% its initial volume. This material was directly used in the subsequent step without further manipulation.

### Ethyl (*E*)-4-((4-bromophenyl)diazenyl)benzoate



The nitroso ethyl ester above (15.00 mmol, 1.00 equiv), formed *in situ*, was taken up in glacial acetic acid to reach [0.10 M], followed by the addition of 4-bromoaniline (1.10 equiv). The reaction mixture was allowed to stir at rt overnight (~12 h). The reaction was diluted with water and transferred to an Erlenmeyer flask and *very slowly* neutralized with NaHCO<sub>3</sub>, with stirring. The aqueous layer was extracted with DCM (x2), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated *in vacuo*. The crude residue was subsequently purified *via* column chromatography on silica gel, eluting with 5 then 10% (ether : hexanes), to afford the desired compound as a free flowing vibrant deep tangerine solid, 1,942mg, 39%.

TLC:  $R_f = 0.54$  (20% ether : hexanes), UV, self stains on TLC plate

<sup>1</sup>H NMR: (500 MHz, CDCl<sub>3</sub>)  $\delta$  8.21 – 8.17 (m, 2H), 7.98 – 7.91 (m, 2H), 7.86 – 7.79 (m, 2H), 7.71 – 7.63 (m, 2H), 4.42 (q,  $J = 7.1$  Hz, 2H), 1.43 (t,  $J = 7.1$  Hz, 3H)

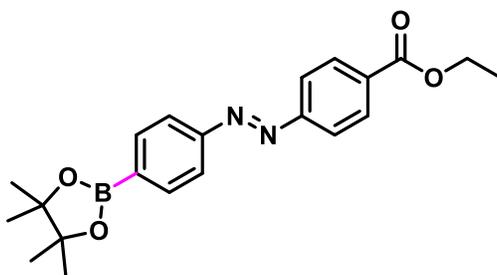
<sup>13</sup>C NMR: (126 MHz, CDCl<sub>3</sub>)  $\delta$  166.1, 155.0, 151.4, 132.6, 130.8, 126.4, 124.7, 122.8, 61.5, 14.5

IR: 2922, 2854, 1716, 1274, 1102 cm<sup>-1</sup>

HRMS: (ESI) calculated for [C<sub>15</sub>H<sub>13</sub>BrN<sub>2</sub>O<sub>2</sub>]: 333.0239 [M+H]<sup>+</sup>, found 333.0224

\*Predominately the *trans*-isomer

### Ethyl (*E*)-4-((4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)diazenyl)benzoate



A clean and dry RBF was taken into a glove-box and charged with Pd(dppf)Cl<sub>2</sub> (5 mol %), B<sub>2</sub>Pin<sub>2</sub> (1.25 equiv) and KOAc (3.00 equiv). Outside the glovebox dry dioxane was added to the flask (~0.25 M), with stirring, followed by the corresponding aryl bromide (2.00 mmol, 1.00 equiv). The flask was then fitted with a Vigreux air condenser and stirred at 80 °C for 2 h under argon. After cooling to rt, TLC analysis had indicated complete consumption of starting aryl bromide. The reaction flask was then transferred to a separatory funnel with ether and water, and the aqueous phase was extracted with ether (x 3). The combined organic extracts were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated *in vacuo*. The crude residue was directly purified *via* column chromatography on silica gel, eluting with 20% (ether : hexanes), to afford the desired compound as a free flowing deep orange/red solid, 514mg, 68%.

TLC:  $R_f = 0.33$  (20% ether : hexanes), UV, self stains on TLC plate

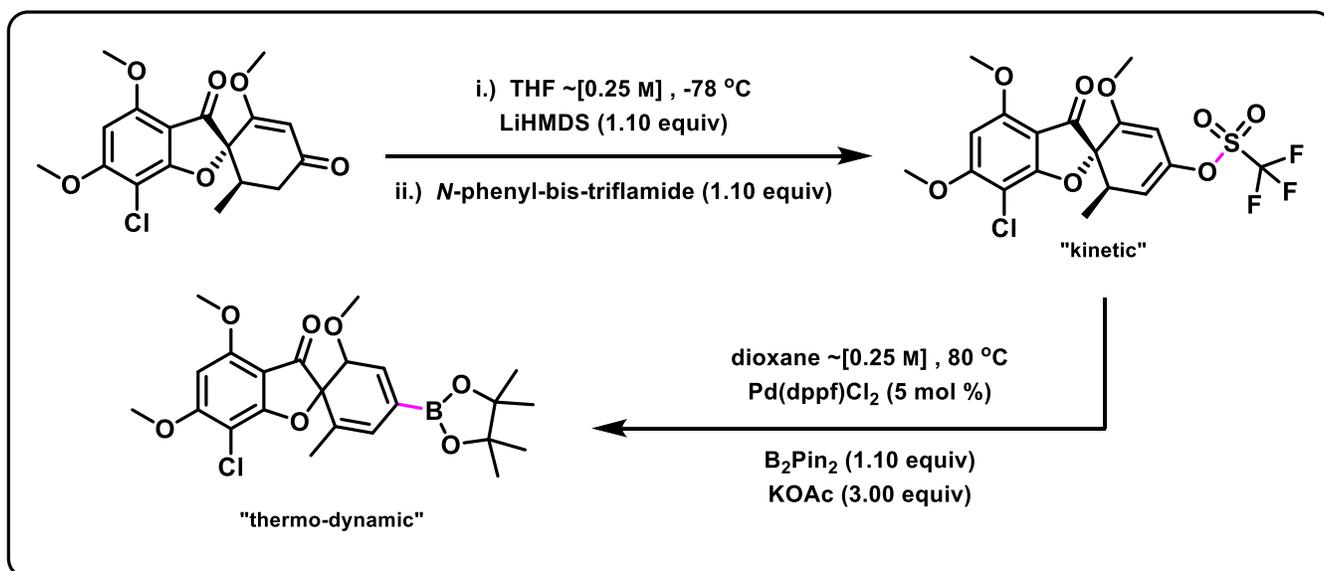
<sup>1</sup>H NMR: (500 MHz, CDCl<sub>3</sub>) δ 8.23 – 8.18 (m, 2H), 8.01 – 7.94 (m, 4H), 7.95 – 7.89 (m, 2H), 4.42 (q,  $J = 7.1$  Hz, 2H), 1.43 (t,  $J = 7.2$  Hz, 3H), 1.38 (s, 12H)

<sup>13</sup>C NMR: (126 MHz, CDCl<sub>3</sub>) δ 166.2, 155.3, 154.4, 135.8, 132.5, 130.7, 122.8, 122.4, 84.3, 61.4, 25.1, 14.5

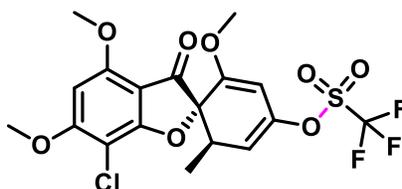
IR: 2984, 2922, 2849, 1721, 1357, 1269 cm<sup>-1</sup>

HRMS: (ESI) calculated for [C<sub>21</sub>H<sub>25</sub>BN<sub>2</sub>O<sub>4</sub>]: 381.1989 [M+H]<sup>+</sup>, found 381.1992

\*Predominately the *trans*-isomer



(2*S*,6'*R*)-7-Chloro-2',4,6-trimethoxy-6'-methyl-3-oxo-3*H*-spiro[benzofuran-2,1'-cyclohexane]-2',4'-dien-4'-yl trifluoromethanesulfonate <sup>2</sup>



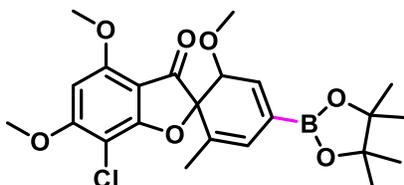
To a clean and dry RBF charged with a stir bar and containing the corresponding ketone (7.00 mmol, 1.00 equiv), in dry THF (~0.25 M) at -78 °C, was added LiHMDS (1.10 equiv) in one portion as a solid. Stirring was continued at this temperature for 2 h at which point *N*-phenyl-bis-triflamide (1.10 equiv) was introduced in one portion as a solid. The reaction mixture was allowed to warm to rt over the course of ~12 h at which point TLC analysis indicated completion. The reaction was then quenched with saturated ammonium chloride and extracted with ether (x3). The combined organic extracts were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated *in vacuo*. The crude residue was subsequently purified *via* column chromatography on silica gel, eluting with 50 then 60% (EtOAc : hexanes), to afford the desired compound as a white solid, 1,592mg, 47%.

TLC:  $R_f = 0.17$  (40% EtOAc : hexanes), UV, I<sub>2</sub>, Vanillin stain (purple that fades to olive green spot)

<sup>1</sup>H NMR: (500 MHz, CDCl<sub>3</sub>) δ 6.10 (s, 1H), 5.40 (dd, *J* = 4.0, 1.9 Hz, 1H), 5.19 (d, *J* = 1.9 Hz, 1H), 3.99 (s, 3H), 3.95 (s, 3H), 3.58 (s, 3H), 3.23 (qd, *J* = 7.3, 4.0 Hz, 1H), 1.13 (d, *J* = 7.3 Hz, 3H)

<sup>13</sup>C NMR: (126 MHz, CDCl<sub>3</sub>) δ 192.0, 191.9, 168.8, 164.4, 157.9, 157.9, 156.9, 143.9, 112.0, 117.4, 105.1, 105.1, 97.4, 95.6, 94.3, 90.2, 88.9, 58.8, 58.2, 58.2, 57.6, 57.0, 57.0, 56.5, 55.9, 55.8, 55.3, 54.7, 38.3, 37.2

**7-Chloro-4,6,6'-trimethoxy-2'-methyl-4'-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3H-spiro[benzofuran-2,1'-cyclohexane]-2',4'-dien-3-one**



To A clean and dry RBF was taken into a glove-box and charged with Pd(dppf)Cl<sub>2</sub> (5 mol %), B<sub>2</sub>Pin<sub>2</sub> (1.10 equiv) and KOAc (3.00 equiv). Outside the glovebox dry dioxane was added to the flask (~0.25 M), with stirring, followed by the corresponding vinyl triflate (3.00 mmol, 1.00 equiv). The flask was then fitted with a Vigreux air condenser and stirred at 80 °C for 2 h under argon. After cooling to rt, TLC analysis had indicated complete consumption of starting vinyl triflate. The reaction flask was then transferred to a separatory funnel with ether and water, and the aqueous phase was extracted with ether (x 3). The combined organic extracts were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated *in vacuo*. The crude residue was directly purified *via* column chromatography on silica gel, eluting with 50% (EtOAc : hexanes), to afford the desired compound as an off white solid, 374mg, 27%.

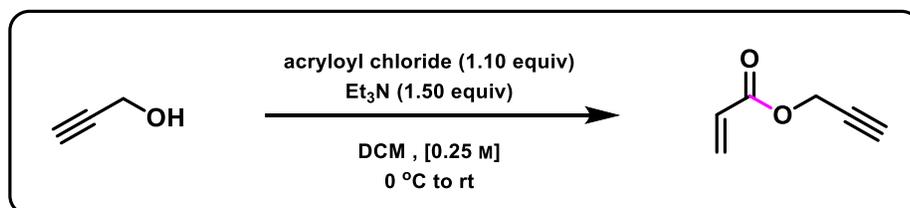
TLC: *R*<sub>f</sub> = 0.45 (50% EtOAc : hexanes), UV, I<sub>2</sub>

<sup>1</sup>H NMR: (500 MHz, CDCl<sub>3</sub>) δ 7.27 (s, 1H), 7.14 (s, 1H), 5.91 (s, 1H), 3.95 (s, 3H), 3.75 (s, 3H), 3.68-3.39 (s split, 1H), 3.40 (s, 3H), 2.13 (s, 3H), 1.37 (s, 12H)

$^{13}\text{C}$  NMR: (126 MHz,  $\text{CDCl}_3$ )  $\delta$  200.2, 162.1, 161.8, 140.7, 136.7, 133.4, 129.1, 129.1, 129.0, 113.5, 87.1, 83.9, 56.3, 56.0, 55.9, 24.9, 18.5

IR: 2974, 2927, 2849, 1607, 1581, 1367, 1274, 1128, 1097  $\text{cm}^{-1}$

HRMS: (ESI) calculated for  $[\text{C}_{23}\text{H}_{28}\text{BClO}_7]$ : 463.1699  $[\text{M}+\text{H}]^+$ , found 463.1712



### Prop-2-yn-1-yl acrylate (19)

To a solution of propargyl alcohol (20.00 mmol, 1.00 equiv) in DCM, [0.25 M], at 0 °C was added triethylamine (1.50 equiv), and the mixture was stirred ~5-10 min. Then, acryloyl chloride (1.10 equiv) was introduced dropwise (with a wide gauge vent-needle), and the reaction was allowed to slowly warm to rt (~2-12 h). Once TLC analysis had indicated full conversion the reaction was quenched with saturated  $\text{NaHCO}_3$ , and transferred to a separatory funnel with water and DCM. The organic phase was washed with 10% aqueous HCl (x3), then  $\text{NaHCO}_3$ , then D.I. water, dried over anhydrous  $\text{Na}_2\text{SO}_4$ , filtered and concentrated *in vacuo*. To the crude material were added a few crystals of MEHQ (radical inhibitor), and was of acceptable purity to use as such; clear light yellow oil, 1,705mg, 77%.

TLC:  $R_f$  = 0.21 (10% ether : hexanes), UV,  $\text{I}_2$

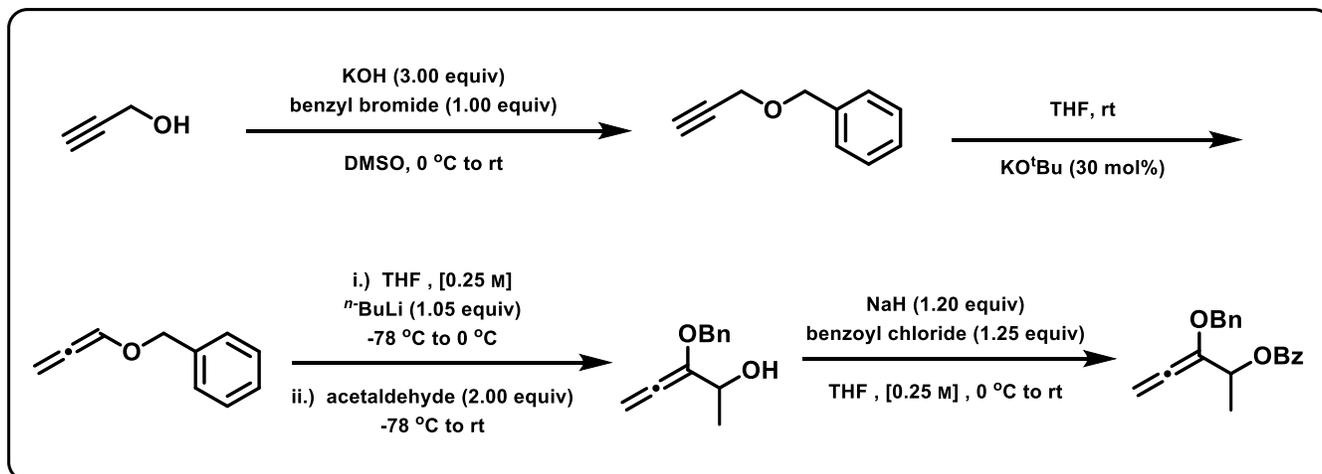
$^1\text{H}$  NMR: (500 MHz,  $\text{CDCl}_3$ )  $\delta$  6.46 (d,  $J$  = 17.5 Hz, 1H), 6.14 (ddd,  $J$  = 17.4, 10.5, 0.7 Hz, 1H), 5.88 (d,  $J$  = 10.5, Hz, 1H), 4.75 (d,  $J$  = 2.5 Hz, 2H), 2.48 (t,  $J$  = 2.5 Hz, 1H)

$^{13}\text{C}$  NMR: (126 MHz,  $\text{CDCl}_3$ )  $\delta$  165.4, 132.0, 127.7, 77.7, 75.1, 52.2

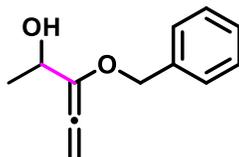
IR: 3285, 2126, 1726, 1409, 1170  $\text{cm}^{-1}$

## 2.2 Synthesis of allenic esters<sup>2,7</sup>

All allenic esters, and their intermediates, were prepared according to literature procedures. Only the allenolate shown below was unknown.



### 3-(Benzyloxy)penta-3,4-dien-2-ol



To a RBF charged with a magnetic stir bar and dry THF was added allenyl benzyl ether (20.00 mmol, 1.00 equiv, prepared according to known literature procedures, see reference section) and the resulting solution, ~[0.25 M], was cooled to -78 °C with stirring. Once at -78 °C, *n*-BuLi (~2.25 M in hexanes; 1.05 equiv) was added dropwise, and this mixture was then stirred for ~ 30-45 min at -78 °C and then ~30 min at rt. After this time, the solution was again brought to -78 °C and acetaldehyde (2.00 equiv) was added dropwise, as a concentrated solution in THF at 0 °C, the reaction mixture was covered with aluminum foil and allowed to stir overnight (~8-12 h). Once the reaction was complete *via* TLC analysis (see below) the reaction was quenched with saturated aqueous ammonium chloride, followed by transfer to a separatory funnel with water and diethyl ether. Extraction with ether (x 3) followed by drying of the organic extracts with anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtration, and subsequent concentration *via*

rotary evaporation provided the crude material which was then subjected to column chromatography on silica gel, eluting with 10 then 20% (ether : hexanes), to obtain the title compound as a clear colorless oil or as a light pale yellow viscous oil, 2,805mg, 74%.

**\*Note:** The reagent bottle of acetaldehyde (very low boiling point) was placed in an ice bath, fitted with a rubber septum, and the desired amount was transferred to a separate, pre-cooled (*via* ice bath) RBF (under argon) and dissolved in dry THF, ~[1.00 M]. This solution was transferred while cold to the reaction.

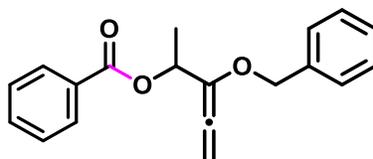
**\*Note:** The flash column should be packed and run with 1-2% Et<sub>3</sub>N to avoid acid-mediated decomposition of the cumulated enol ether.

TLC:  $R_f$  = 0.31 (20% ether : hexanes), UV, I<sub>2</sub>

<sup>1</sup>H NMR: (500 MHz, CDCl<sub>3</sub>) δ 7.40 – 7.27 (m, 5H), 5.55 (d,  $J$  = 2.1 Hz, 2H), 4.65 (s, 2H), 4.42 (m, 1H), 2.43 – 2.08 (bs, 1H), 1.34 (d,  $J$  = 6.5 Hz, 3H)

<sup>13</sup>C NMR: (126 MHz, CDCl<sub>3</sub>) δ 196.7, 137.4, 135.9, 128.5, 128.0, 127.7, 92.7, 70.9, 66.9, 20.5

### 3-(Benzyloxy)penta-3,4-dien-2-yl benzoate



To a slurry of NaH (1.20 equiv) in THF, at [0.25 M] global concentration, at 0 °C was added dropwise (with a vent needle) a concentrated solution of the corresponding allenol (5.786 mmol, 1.00 equiv) in THF. The mixture was stirred for 45-60 min and a concentrated solution of benzoyl chloride, in THF, was introduced slowly. The resulting mixture was allowed to stir, thus 0 °C to rt, overnight. The reaction was diluted with ether, at 0 °C, followed by slow dropwise addition of water, until no more gas evolved (to quench any residual NaH) and transferred to a separatory funnel. Extraction with ether (x 3) followed by drying of the organic extracts with anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtration, and subsequent

concentration *via* rotary evaporation provided the crude material which was then subjected to column chromatography on silica gel, eluting with 1 then 2 then 3% (ether : hexanes), to obtain the title compound as a clear colorless oil or as a light pale yellow viscous oil, 603mg, 35%.

**\*Note:** The flash column should be packed and run with 1-2% Et<sub>3</sub>N to avoid acid-mediated decomposition of the cumulated enol ether.

TLC:  $R_f = 0.42$  (10% ether : hexanes), UV, I<sub>2</sub>

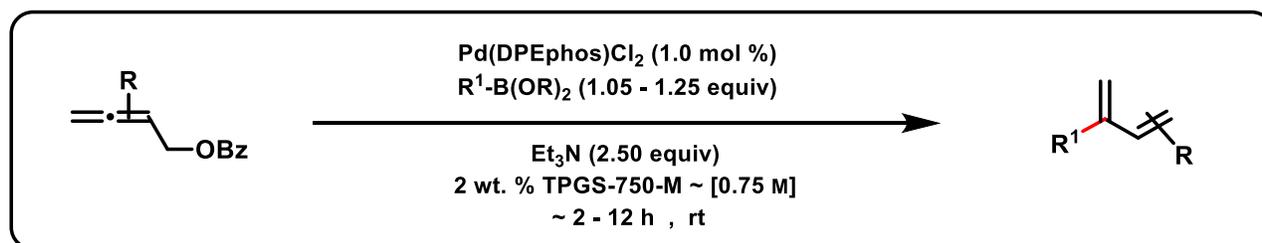
<sup>1</sup>H NMR: (500 MHz, CDCl<sub>3</sub>)  $\delta$  8.07 (m, 2H), 7.58 – 7.54 (m, 1H), 7.44 (m, 2H), 7.41 – 7.22 (m, 5H), 5.77 (m, 1H), 5.56 (m, 2H), 4.70 (s, 2H), 1.53 (d,  $J = 6.6$  Hz, 3H)

<sup>13</sup>C NMR: (126 MHz, CDCl<sub>3</sub>)  $\delta$  198.3, 166.0, 137.6, 133.0, 133.0, 130.7, 129.9, 128.4, 128.4, 127.8, 127.6, 92.5, 70.7, 69.8, 18.1

### 3. General Methods for Diene Synthesis

#### 3.1 General procedure 'A'

#### Suzuki-Miyaura and Sonogashira mediated $sp^2$ - $sp^2$ and $sp$ - $sp^2$ cross-couplings

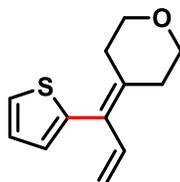


Into a screw cap vial was measured the desired allenic ester (1.00 equiv) followed by Pd(DPEphos)Cl<sub>2</sub> ( $\leq 1$  mol %). To this vial was then added a 2 wt % solution of TPGS-750-M in D.I. water to arrive at a  $\sim$ [0.75 M] solution and the reaction mixture was stirred with a strong vortex at rt. Then 'a few drops' of Et<sub>3</sub>N were added (to aid in reaction homogeneity, and possibly facilitating initial

reduction of the Pd(II) catalyst to the active Pd(0) species) followed by addition of the boron coupling partner (1.05 – 1.25 equiv) either dropwise for oils or in one portion for solids, followed by the remainder of Et<sub>3</sub>N (2.50 equivalents total) with rinsing any residue from the wall of the vial into solution. The reaction was capped and allowed to stir at rt for ~ 2–12 h. Upon complete consumption of allenic ester *via* TLC analysis (see below) a small amount of EtOAc was added to the reaction and gently stirred for ~ 5–10 min (milky pale yellow/orange solution will eventually become clear yellow/orange). This mixture was directly passed through a short plug of Celite on top of silica with ether and concentrated *via* rotary evaporation. Purification by column chromatography on silica gel afforded the desired product.

**\*Note:** The allenic ester is usually added first *via* glass pipette capillary action. This is due to the highly viscous nature of most of the allenic esters utilized in this research. Use of a microliter syringe was overly cumbersome, as well use of a disposable syringe/needle was impractical due to substantial, yet unavoidable, transfer losses of valuable material. However, reactions are typically unaffected by the order of addition as long as the boronate coupling partner is added last to help avoid potential protodeborylation.

#### 4-(1-(Thiophen-2-yl)allylidene)tetrahydro-2H-pyran (1)



Purification: column chromatography on silica gel eluting with 10% (ether : hexanes), clear colorless oil, (0.50 mmol scale) 83.3mg, 81%.

TLC:  $R_f = 0.29$  (10% ether : hexanes), UV, I<sub>2</sub>, vanillin stain (olive/ grey spot)

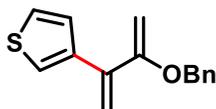
$^1\text{H}$  NMR: (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.30 (dd,  $J = 5.0, 1.0$  Hz, 1H), 7.02 (dd,  $J = 5.0, 3.5$  Hz, 1H), 6.93 (dd,  $J = 16.9, 10.6$  Hz, 1H), 6.76 (dd,  $J = 3.4, 1.0$  Hz, 1H), 5.15 (dd,  $J = 10.6, 1.4$  Hz, 1H), 4.88 (dd,  $J = 16.9, 1.3$  Hz, 1H), 3.80 – 3.74 (m, 2H), 3.64 (t,  $J = 5.5$  Hz, 2H), 2.64 – 2.57 (m, 2H), 2.24 (t,  $J = 5.5$  Hz, 2H)

$^{13}\text{C}$  NMR: (126 MHz,  $\text{CDCl}_3$ )  $\delta$  139.8, 139.5, 134.3, 127.3, 126.9, 125.3, 117.1, 99.2, 69.1, 68.7, 33.8, 31.3

IR: 3088, 2958, 2838, 1622, 1232, 1097, 692  $\text{cm}^{-1}$

HRMS: (ESI) calculated for  $[\text{C}_{12}\text{H}_{14}\text{OS}]$ : 207.0844  $[\text{M}+\text{H}]^+$ , found 207.0837

### 3-(3-(Benzyloxy)buta-1,3-dien-2-yl)thiophene (2)



Purification: column chromatography on silica gel eluting with 2% (ether : hexanes), white solid, (0.30 mmol scale) 64.4mg, 89%.

TLC:  $R_f = 0.69$  (30% ether : hexanes), UV,  $\text{I}_2$ , vanillin stain (deep blue/ grey spot)

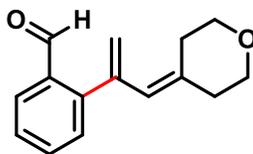
$^1\text{H}$  NMR: (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.48 – 7.38 (m, 4H), 7.38 – 7.27 (m, 3H), 7.23 – 7.13 (m, 1H), 5.74 (d,  $J = 1.8$  Hz, 1H), 5.37 (s, 1H), 4.93 (s, 2H), 4.41 (s, 2H)

$^{13}\text{C}$  NMR: (151 MHz,  $\text{CDCl}_3$ )  $\delta$  159.9, 140.8, 140.3, 137.2, 128.6, 128.2, 127.9, 127.5, 126.5, 126.2, 124.9, 123.2, 119.9, 115.0, 87.9, 69.8

IR: 3108, 3062, 2911, 1581, 1217, 1180, 697  $\text{cm}^{-1}$

HRMS: (ESI) calculated for  $[\text{C}_{15}\text{H}_{14}\text{OS}]$ : 243.0844  $[\text{M}+\text{H}]^+$ , found 243.0838

### 2-(3-(Tetrahydro-4H-pyran-4-ylidene)prop-1-en-2-yl)benzaldehyde (3)



Purification: column chromatography on silica gel eluting with 30% (ether : hexanes), clear colorless oil, (0.40 mmol scale) 80.4mg, 88%.

TLC:  $R_f$  = 0.35 (40% ether : hexanes), UV,  $I_2$ , vanillin stain (blue spot)

$^1\text{H}$  NMR: (500 MHz,  $\text{CDCl}_3$ )  $\delta$  (10.19, 9.87 – 9.80 (s, H)), (8.06 - 7.91 (m, 1H)), (7.67 - 7.53 (m, 1H)), (7.45 – 7.38 (m, 1H)), (7.33 - 7.6, (m, 1H)), 6.13 (s, 1H), 5.47 (s, 1H), 5.13 (d,  $J$  = 2.0 Hz, 1H), 3.80 – 3.67 (t,  $J$  = 5.5 Hz, 2H), 3.49 – 3.42 (t,  $J$  = 5.5 Hz, 2H), 2.28 (dt,  $J$  = 10.8, 2.9 Hz, 2H), 1.98 – 1.94 (dt,  $J$  = 10.8, 2.9 Hz, 2H)

$^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ ):  $\delta$  192.2, 146.4, 142.6, 139.7, 133.9, 133.8, 129.7, 128.0, 127.6, 125.7, 121.5, 69.4, 68.2, 37.9, 31.0

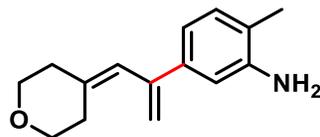
IR: 2958, 2849, 2745, 1690, 1596, 1097, 1009, 754  $\text{cm}^{-1}$

HRMS: (ESI) calculated for  $[\text{C}_{15}\text{H}_{16}\text{O}_2]$ : 251.1048  $[\text{M}+\text{Na}]^+$ , found 251.1051

-Note: Rotamers of *s-cis* and *s-trans* diene moieties observed with bulky, yet flexible or having the ability to coordinate, *-ortho* aromatic groups.

~ 4:1 ratio of restricted rotamers (see Spectra section)

#### **2-Methyl-5-(3-(tetrahydro-4H-pyran-4-ylidene)prop-1-en-2-yl)aniline (4)**



Purification: column chromatography on silica gel eluting with 40% (ether : hexanes), pale yellow solid, (0.40 mmol scale) 77.0mg, 84%.

TLC:  $R_f$  = 0.23 (50% ether : hexanes), UV,  $I_2$

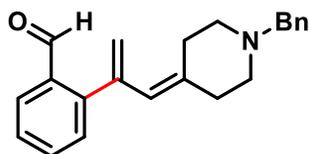
$^1\text{H}$  NMR: (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.00 (d,  $J$  = 8.0 Hz, 1H), 6.78 (dd,  $J$  = 7.75, 1.75 Hz, 1H), 6.73 (d,  $J$  = 2.0 Hz, 1H), 5.98 (d,  $J$  = 1.0 Hz, 1H), 5.46 (d,  $J$  = 1.5 Hz, 1H), 5.00 (t,  $J$  = 1.5 Hz, 1H), 3.79 – 3.76 (m, 2H), 3.62 (m, 4H), 2.36 (m, 4H), 2.17 (s, 3H)

$^{13}\text{C}$  NMR: (126 MHz,  $\text{CDCl}_3$ )  $\delta$  144.5, 144.4, 139.9, 138.9, 130.5, 124.1, 122.1, 117.2, 114.0, 113.2, 69.8, 69.1, 37.4, 31.3, 17.3

IR: 3452, 3363, 2963, 2854, 1565, 1092, 900  $\text{cm}^{-1}$

HRMS: (ESI) calculated for  $[\text{C}_{15}\text{H}_{19}\text{NO}]$ : 230.1545  $[\text{M}+\text{H}]^+$ , found 230.1553

### 2-(3-(1-Benzylpiperidin-4-ylidene)prop-1-en-2-yl)benzaldehyde (5)



Purification: column chromatography on silica gel eluting with 40% (ether : hexanes), off-yellow solid, (0.30 mmol scale) 68.8mg, 72%.

TLC:  $R_f$  = 0.26 (40% ether : hexanes), UV,  $\text{I}_2$ , Vanillin stain (orange/ tangerine spot)

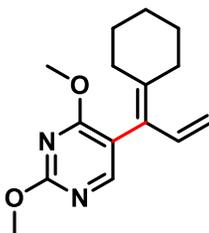
$^1\text{H}$  NMR: (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  10.17 (s, 1H), 7.88 (m, 1H), 7.56 – 7.26 (m, 7H), 7.23 – 7.19 (m, 1H), 6.06 (s, 1H), 5.43 (s, 1H), 5.08 (d,  $J$  = 2.0 Hz, 1H), 3.43 (s, 2H), 2.49 – 2.44 (t,  $J$  = 5.75 Hz, 2H), 2.29 – 2.26 (t,  $J$  = 5.50 Hz, 2H), 2.20 (t,  $J$  = 5.50 Hz, 2H), 1.95 (t,  $J$  = 5.50 Hz, 2H)

$^{13}\text{C}$  NMR: (126 MHz,  $\text{CDCl}_3$ )  $\delta$  192.4, 146.7, 143.0, 141.9, 138.6, 133.9, 133.7, 129.8, 129.1, 128.3, 127.8, 127.4, 127.1, 125.1, 121.2, 62.9, 55.2, 54.0, 37.1, 29.5

IR: 3031, 2932, 2797, 2750, 1690, 1596, 1269, 733  $\text{cm}^{-1}$

HRMS: (ESI) calculated for  $[\text{C}_{22}\text{H}_{23}\text{NO}]$ : 318.1858  $[\text{M}+\text{H}]^+$ , found 318.1856

### 4-(1-Cyclohexylideneallyl)-2,6-dimethoxypyrimidine (6)



Purification: column chromatography on silica gel loaded with minimal DCM and eluting with 10, then 20, then 30% (ether : hexanes), clear colorless oil, (0.50 mmol scale) 100.6mg, 77%.

TLC:  $R_f$  = 0.38 (20% ether : hexanes), UV,  $I_2$ , Vanillin stain (orange/ maroon spot)

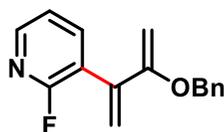
$^1\text{H}$  NMR: (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.86 (s, 1H), 6.96 (dd,  $J$  = 17.25, 10.75 Hz, 1H), 4.96 (dd,  $J$  = 10.75, 1.25 Hz, 1H), 4.53 (dd,  $J$  = 17.0, 1.50 Hz, 1H), 3.99 (s, 3H), 3.91 (s, 3H), 2.52 – 2.39 (m, 2H), 1.93 – 1.84 (m, 2H), 1.68 – 1.40 (m, 6H)

$^{13}\text{C}$  NMR: (126 MHz,  $\text{CDCl}_3$ )  $\delta$  169.2, 164.7, 159.1, 145.0, 133.9, 123.4, 114.5, 113.7, 54.8, 54.0, 33.4, 30.3, 28.3, 28.2, 26.8

IR: 2922, 2849, 1591, 1555, 1461, 1388  $\text{cm}^{-1}$

HRMS: (ESI) calculated for  $[\text{C}_{15}\text{H}_{20}\text{N}_2\text{O}_2]$ : 261.1603  $[\text{M}+\text{H}]^+$ , found 261.1600

### 3-(3-(Benzyloxy)buta-1,3-dien-2-yl)-2-fluoropyridine (7)



Purification: column chromatography on silica gel eluting with 5% (ether : hexanes), clear colorless oil, (0.30 mmol scale) 64.2mg, 84%.

TLC:  $R_f$  = 0.39 (30% ether : hexanes), UV,  $I_2$ , Vanillin stain (teal spot)

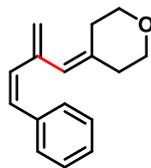
$^1\text{H}$  NMR: (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.30 – 8.07 (m, 1H), 7.70 (m, 1H), 7.55 – 7.29 (m, 5H), 7.22 – 7.13 (m, 1H), 6.01 (d,  $J$  = 1.0 Hz, 1H), 5.31 (s, 1H), 4.90 (s, 2H), 4.37 (d,  $J$  = 2.0 Hz, 1H), 4.06 (d,  $J$  = 3.0 Hz, 1H)

$^{13}\text{C}$  NMR: (126 MHz,  $\text{CDCl}_3$ )  $\delta$  161.8, 159.9, 158.5, 147.0, 146.9, 141.9, 141.8, 138.3, 138.3, 137.0, 128.6, 128.0, 127.5, 122.8, 122.6, 121.3, 121.2, 118.5, 118.5, 87.9, 70.0

IR: 3067, 3031, 2911, 2864, 1726, 1601, 1430, 1248, 1191, 697  $\text{cm}^{-1}$

HRMS: (ESI) calculated for  $[\text{C}_{16}\text{H}_{14}\text{FNO}]$ : 256.1138  $[\text{M}+\text{H}]^+$ , found 256.1142

**(Z)-4-(2-Methylene-4-phenylbut-3-en-1-ylidene)tetrahydro-2H-pyran (8)**



Purification: column chromatography on silica gel eluting with 12% (ether : hexanes), light golden solid, (0.347 mmol scale) 55.8mg, 71%.

TLC:  $R_f = 0.40$  (20% ether : hexanes), UV,  $I_2$

$^1\text{H}$  NMR: (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.43 – 7.05 (m, 5H), 6.47 (d,  $J = 12.0$  Hz, 1H), 6.26 (d,  $J = 12.0$  Hz, 1H), 5.64 (s, 1H), 5.19 (s, 1H), 5.03 (s, 1H), 3.58 (m, 4H), 2.51 – 2.47 (m, 2H), 2.07 – 2.04 (m, 2H)

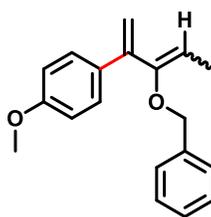
$^{13}\text{C}$  NMR: (126 MHz,  $\text{CDCl}_3$ )  $\delta$  142.2, 137.5, 137.1, 131.9, 130.2, 129.3, 127.8, 127.0, 124.3, 119.4, 69.2, 68.4, 37.3, 31.2

IR: 2953, 2927, 2849, 1716, 1456, 1232, 1102, 993, 697  $\text{cm}^{-1}$

HRMS: (ESI) calculated for  $[\text{C}_{16}\text{H}_{18}\text{O}]$ : 227.1436  $[\text{M}+\text{H}]^+$ , found 227.1427

Z:E ratio: >20:1; see spectral data section for NOESY analysis

**1-(3-(Benzyloxy)penta-1,3-dien-2-yl)-4-methoxybenzene (9)**



Purification: column chromatography on silica gel eluting with 1 CV hexanes then 1% (ether : hexanes), clear colorless oil, (0.40 mmol scale) 90.4mg, 81%.

TLC:  $R_f = 0.57$  (10% ether : hexanes), UV,  $I_2$ , Vanillin stain (maroon spot)

$^1\text{H}$  NMR: (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.50 – 7.29 (m, 7H), 7.00 – 6.87 (m, 2H), 5.44 – 5.36 (m, 1H), 5.29 – 5.24 (m, 1H), 4.67 (m, 1H), 3.85 – 3.82 (m, 3H), 1.69 – 1.62 (m, 3H)

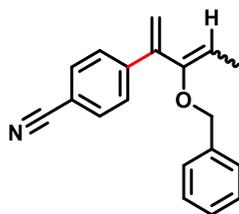
$^{13}\text{C}$  NMR: (126 MHz,  $\text{CDCl}_3$ )  $\delta$  159.4, 154.9, 144.9, 138.1, 132.4, 129.4, 128.4, 128.2, 127.9, 113.7, 113.5, 112.6, 71.8, 55.4, 11.2

IR: 2932, 2844, 1716, 1607, 1513, 1248, 1170, 1030  $\text{cm}^{-1}$

Z:E ratio  $\sim$  (9:1), determined via  $^1\text{H}$  NMR analysis of the methyl peaks  $\sim$  1.6 ppm

Major peak  $J = 7.0$  Hz, Minor peak  $J = 13.5$  Hz

#### 4-(3-(Benzyloxy)penta-1,3-dien-2-yl)benzonitrile (10)



Purification: column chromatography on silica gel eluting with 10 then 25% (ether : hexanes), clear colorless oil, (0.40 mmol scale) 86.7mg, 79%.

TLC:  $R_f = 0.26$  (10% ether : DCM), UV,  $\text{I}_2$ , Vanillin stain (spot)

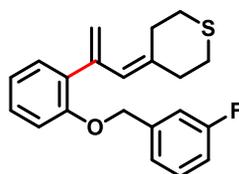
$^1\text{H}$  NMR: (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.69 – 7.43 (m, 4H), 7.42 – 7.21 (m, 5H), 5.56 (s, 1H), 5.38 – 5.33 (1, H), 5.11 – 4.99 (m, 1H), 4.64 (s, 2H), 1.72 – 1.66 (d  $J = 6.50$  Hz, 2H)

$^{13}\text{C}$  NMR: (126 MHz,  $\text{CDCl}_3$ )  $\delta$  153.7, 144.6, 144.3, 137.5, 132.3, 132.1, 128.9, 128.5, 128.1, 128.1, 127.3, 119.0, 116.7, 114.3, 111.5, 72.1, 11.3

IR: 3072, 2984, 2937, 2875, 2235, 1721, 1456, 1279, 1019, 697  $\text{cm}^{-1}$

Z:E ratio  $\sim$  (9:1), *via*  $^1\text{H}$ NMR analysis of the methyl peaks  $\sim$  1.6 ppm, Major  $J = 6.5$  Hz

#### 4-(2-(2-((3-Fluorobenzyl)oxy)phenyl)allylidene)tetrahydro-2H-thiopyran (11)



Purification: column chromatography on silica gel eluting with 1 CV hexanes then 2 then 5% (ether : hexanes), clear colorless oil, (0.40 mmol scale) 122.2mg, 90%.

TLC:  $R_f = 0.39$  (5% ether : hexanes), UV,  $I_2$ , Vanillin stain (vibrant fuchsia spot)

$^1\text{H NMR}$ : (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.36 – 7.14 (m, 5H), 7.03 – 6.88 (m, 3H), 6.08 (s, 1H), 5.34 (d,  $J = 2.0$  Hz, 1H), 5.25 (d,  $J = 1.5$  Hz, 1H), 5.07 (s, 2H), 2.69 (m, 2H), 2.52 – 2.45 (m, 6H)

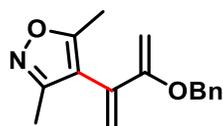
$^{13}\text{C NMR}$ : (126 MHz,  $\text{CDCl}_3$ )  $\delta$

IR: 2906, 2828, 1721, 1487, 1440, 1232, 749  $\text{cm}^{-1}$

HRMS: (ESI) calculated for  $[\text{C}_{21}\text{H}_{21}\text{FOS}]$ : 341.1375  $[\text{M}+\text{H}]^+$ , found 341.1364

-Note: Rotamers of *s-cis* and *s-trans* diene moieties observed with bulky, yet flexible, -*ortho* aromatic groups.

#### 4-(3-(Benzyloxy)buta-1,3-dien-2-yl)-3,5-dimethylisoxazole (12)



Purification: column chromatography on silica gel eluting with 20% (ether : hexanes), clear colorless oil, (0.30 mmol scale) 74.1mg, 97%.

TLC:  $R_f = 0.34$  (20% ether : hexanes), UV,  $I_2$ , Vanillin stain (tangerine spot)

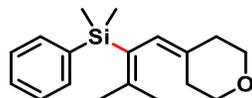
$^1\text{H NMR}$ : (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.44 – 7.36 (m, 4H), 7.36 – 7.31 (m, 1H), 6.01 (d,  $J = 2.0$  Hz, 1H), 5.12 (td,  $J = 1.8, 0.8$  Hz, 1H), 4.89 (s, 2H), 4.32 (t,  $J = 2.1$  Hz, 1H), 4.08 (d,  $J = 2.6$  Hz, 1H), 2.31 (s, 3H), 2.17 (s, 3H)

$^{13}\text{C NMR}$ : (126 MHz,  $\text{CDCl}_3$ )  $\delta$  166.3, 159.6, 158.1, 137.0, 133.5, 128.6, 128.0, 127.4, 118.4, 115.1, 87.7, 69.9, 11.4, 10.5

IR: 3031, 2932, 1581, 1331, 1258, 1097, 697  $\text{cm}^{-1}$

HRMS: (ESI) calculated for  $[\text{C}_{16}\text{H}_{17}\text{NO}_2]$ : 256.1338  $[\text{M}+\text{H}]^+$ , found 256.1344

**Dimethyl(3-methyl-1-(tetrahydro-4H-pyran-4-ylidene)but-2-en-2-yl)(phenyl)silane (13)**



Purification: column chromatography on silica gel eluting with 1 CV hexanes then 5% (ether : hexanes), clear colorless oil, (0.30 mmol scale) 64.1mg, 75%.

TLC:  $R_f = 0.24$  (5% ether : hexanes), UV,  $I_2$

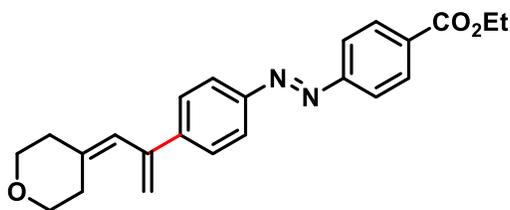
$^1\text{H NMR}$ : (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.55 – 7.49 (m, 2H), 7.33 (m, 3H), 5.70 (dd,  $J = 3.0, 1.5$  Hz, 1H), 3.69 – 3.66 (m, 2H), 3.58 (t,  $J = 5.5$  Hz, 2H), 2.27 – 2.23 (m, 2H), 2.07 (m, 2H), 1.71 (dd,  $J = 15.3, 1.6$  Hz, 6H), 0.37 (s, 6H)

$^{13}\text{C NMR}$ : (126 MHz,  $\text{CDCl}_3$ )  $\delta$  146.0, 140.3, 133.8, 133.4, 129.8, 128.7, 127.8, 126.2, 69.9, 68.5, 36.5, 30.8, 24.9, 23.3, -0.4

IR: 2958, 2838, 1607, 1430, 1232, 1102, 816  $\text{cm}^{-1}$

HRMS: (ESI) calculated for  $[\text{C}_{18}\text{H}_{26}\text{OSi}]$ : 287.1831  $[\text{M}+\text{H}]^+$ , found 287.1844

**Ethyl (E)-4-((4-(3-(tetrahydro-4H-pyran-4-ylidene)prop-1-en-2-yl)phenyl)diazenyl)benzoate (14)**



Purification: column chromatography on silica gel eluting with 20 then 40% (ether : hexanes), light orange solid, (0.30 mmol scale) 107.1mg, 94%.

TLC:  $R_f = 0.19$  (20% ether : hexanes), UV, material self stains on TLC plate

$^1\text{H NMR}$ : (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.22 – 8.18 (m, 2H), 7.96 – 7.90 (m, 4H), 7.60 – 7.56 (m, 2H), 6.06 (d,  $J = 1.8$  Hz, 1H), 5.65 (d,  $J = 1.6$  Hz, 1H), 5.20 (d,  $J = 1.5$  Hz, 1H), 4.42 (q,  $J = 7.1$  Hz, 2H), 3.82 – 3.78 (m, 2H), 3.64 (t,  $J = 5.5$  Hz, 2H), 2.41 (m, 2H), 2.35 – 2.32 (m, 2H), 1.43 (t,  $J = 7.1$  Hz, 3H)

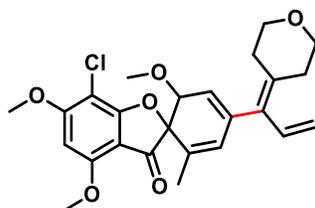
$^{13}\text{C}$  NMR: (126 MHz,  $\text{CDCl}_3$ )  $\delta$   $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  166.2, 155.3, 152.1, 144.4, 143.7, 140.1, 132.3, 130.7, 127.5, 123.4, 123.3, 122.7, 116.6, 69.7, 68.9, 61.4, 37.4, 31.4, 14.5

IR: 2983, 2953, 2838, 1710, 1269, 1097  $\text{cm}^{-1}$

HRMS: (ESI) calculated for  $[\text{C}_{23}\text{H}_{24}\text{N}_2\text{O}_3]$ : 399.1685  $[\text{M}+\text{Na}]^+$ , found 399.1702

\*Predominately *trans*-azo-isomer

**7-Chloro-4,6,6'-trimethoxy-2'-methyl-4'-(1-(tetrahydro-4*H*-pyran-4-ylidene)allyl)-3*H*-spiro[benzofuran-2,1'-cyclohexane]-2',4'-dien-3-one (15)**



Purification: column chromatography on silica gel eluting with 40 then 60% (EtOAc : hexanes), clear yellow crystal, (0.20 mmol scale) 67.4mg, 74%.

TLC:  $R_f$  = 0.19 (40% EtOAc : hexanes), UV,  $I_2$ , Vanillin stain (light purple spot)

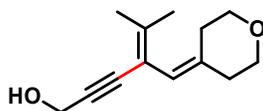
$^1\text{H}$  NMR: (600 MHz,  $\text{CDCl}_3$ )  $\delta$  14.31 (s, 1H), 6.97 (dd,  $J$  = 17.0, 10.6 Hz, 1H), 6.49 (d,  $J$  = 42.1 Hz, 2H), 5.93 (s, 1H), 5.13 (dd,  $J$  = 10.7, 1.9 Hz, 1H), 4.73 (dd,  $J$  = 17.0, 2.0 Hz, 1H), 3.96 (s, 3H), 3.80 (t,  $J$  = 5.5 Hz, 2H), 3.68 (s, 3H), 3.63 (t,  $J$  = 5.4 Hz, 2H), 3.44 (s, 3H), 2.61 (t,  $J$  = 5.5 Hz, 2H), 2.14 (m,  $J$  = 14.8 Hz, 5H)

$^{13}\text{C}$  NMR: (150 MHz,  $\text{CDCl}_3$ )  $\delta$  200.5, 162.2, 162.0, 161.9, 155.5, 140.4, 135.6, 134.5, 134.3, 134.2, 131.3, 124.0, 116.6, 109.8, 107.7, 69.2, 68.9, 56.4, 56.0, 55.8, 33.7, 30.8, 25.0, 19.0

IR: 2958, 2854, 1601, 1575, 1414, 1217, 1128, 1097  $\text{cm}^{-1}$

HRMS: (ESI) calculated for  $[\text{C}_{25}\text{H}_{27}\text{ClO}_6]$ : 481.1394  $[\text{M}+\text{Na}]^+$ , found 481.1400

**5-Methyl-4-((tetrahydro-4*H*-pyran-4-ylidene)methyl)hex-4-en-2-yn-1-ol (16)**



**Purification:** column chromatography on silica gel eluting with 60% (ether : hexanes), clear colorless oil, (0.30 mmol scale) 56.7mg, 92%.

TLC:  $R_f = 0.12$  (40% ether : hexanes), UV,  $I_2$ , Vanillin stain (deep purple spot)

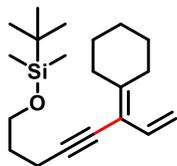
$^1\text{H NMR}$ : (500 MHz,  $\text{CDCl}_3$ )  $\delta$  5.81 – 5.63 (m, 1H), 4.41 (d,  $J = 2.8$  Hz, 2H), 3.73 – 3.69 (m, 2H), 3.66 (t,  $J = 5.5$  Hz, 2H), 2.41 – 2.37 (m, 2H), 2.28 – 2.25 (m, 2H), 1.98 (m, 4H), 1.74 (s, 3H)

$^{13}\text{C NMR}$ : (126 MHz,  $\text{CDCl}_3$ )  $\delta$  144.2, 138.0, 120.1, 113.5, 89.9, 85.6, 69.5, 68.5, 51.8, 36.9, 31.2, 23.3, 21.0

IR: 3392, 2911, 2854, 2209, 1367, 1092, 1019, 998  $\text{cm}^{-1}$

HRMS: (ESI) calculated for  $[\text{C}_{13}\text{H}_{18}\text{O}_2]$ : 206.1307  $[\text{M}+\text{H}]^+$ , found 206.1305

***t*-Butyl((6-cyclohexylideneoct-7-en-4-yn-1-yl)oxy)dimethylsilane (17)**



**Purification:** column chromatography on silica gel eluting with 100% pentanes, clear colorless oil, (0.30 mmol scale) 83.8mg, 88%.

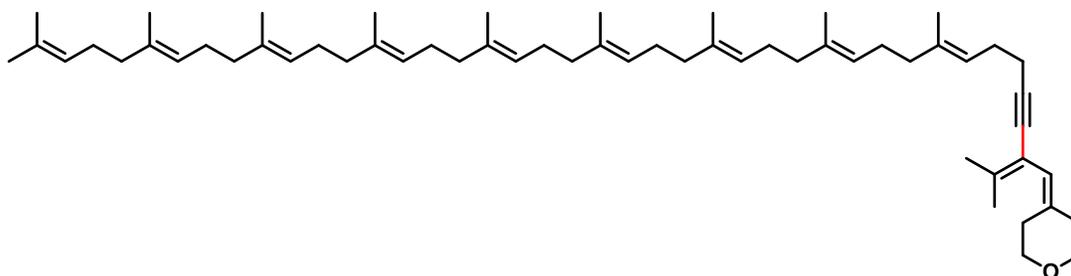
TLC:  $R_f = 0.66$  (10% ether : hexanes), UV,  $I_2$

$^1\text{H NMR}$ : (500 MHz,  $\text{CDCl}_3$ )  $\delta$  6.75 (dd,  $J = 16.7, 10.3$  Hz, 1H), 5.60 (dd,  $J = 16.8, 2.1$  Hz, 1H), 5.14 (dd,  $J = 10.4, 2.1$  Hz, 1H), 3.74 (t,  $J = 6.2$  Hz, 2H), 2.56 (t,  $J = 5.8$  Hz, 2H), 2.49 (t,  $J = 7.0$  Hz, 2H), 2.38 (t,  $J = 5.7$  Hz, 2H), 1.83 – 1.76 (m, 2H), 1.64 – 1.54 (m, 6H), 0.90 (s, 9H), 0.06 (s, 6H)

$^{13}\text{C NMR}$ : (126 MHz,  $\text{CDCl}_3$ )  $\delta$  149.9, 131.8, 115.4, 115.2, 94.5, 77.0, 62.0, 34.7, 32.3, 30.2, 28.1, 28.0, 26.8, 26.1, 18.5, 16.1, -5.2

IR: 2937, 2854, 2230, 1253, 832  $\text{cm}^{-1}$

**4-((7E,11E,15E,19E,23E,27E,31E,35E)-8,12,16,20,24,28,32,36,40-Nonamethyl-2-(propan-2-ylidene)hentetraconta-7,11,15,19,23,27,31,35,39-nonaen-3-yn-1-ylidene)tetrahydro-2H-pyran (18)**



**Purification:** column chromatography on silica gel eluting with 1 CV hexanes then 5% (ether : hexanes), clear/ light bronze oil, (0.30 mmol scale) 216.7mg, 90%.

**TLC:**  $R_f = 0.26$  (5% ether : hexanes), UV,  $I_2$

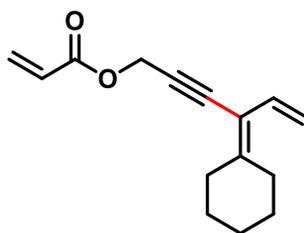
$^1\text{H NMR}$ : (500 MHz,  $\text{CDCl}_3$ )  $\delta$  5.76 (s, 1H), 5.20 (m, 1H), 5.14 – 5.09 (m, 8H), 3.72 (t,  $J = 5.5$  Hz, 2H), 3.67 (t,  $J = 5.5$  Hz, 2H), 2.50 – 2.44 (m, 2H), 2.36 (t,  $J = 7.3$  Hz, 2H), 2.29 – 2.22 (m, 4H), 2.07 (m, 18H), 2.00 – 1.97 (m, 17H), 1.74 (s, 3H), 1.68 (s, 3H), 1.60 (m, 27H)

$^{13}\text{C NMR}$ : (126 MHz,  $\text{CDCl}_3$ )  $\delta$  141.9, 137.4, 136.5, 135.2, 135.1, 135.1, 135.1, 135.1, 135.0, 135.0, 131.4, 124.6, 124.4, 124.4, 124.4, 124.4, 124.3, 123.1, 120.7, 114.4, 92.7, 80.5, 69.7, 68.7, 39.9, 39.9, 39.9, 37.1, 31.2, 27.9, 26.9, 26.9, 26.9, 26.8, 26.8, 25.8, 23.2, 20.9, 20.2, 17.8, 16.3, 16.2, 16.2, 16.2

**IR:** 2958, 2916, 2844, 1664, 1440, 1383, 1102, 848  $\text{cm}^{-1}$

**HRMS:** (ESI) calculated for  $[\text{C}_{58}\text{H}_{90}\text{O}]$ : 825.6890  $[\text{M}+\text{Na}]^+$ , found 825.6909

**4-Cyclohexylidenehex-5-en-2-yn-1-yl acrylate (21)**



Purification: column chromatography on silica gel eluting with 1 CV hexanes then 5% (ether : hexanes), clear/ light bronze oil, (0.50 mmol scale) 83.0mg, 72%.

TLC:  $R_f$  = 0.45 (10% ether : hexanes), UV,  $I_2$ , Vanillin stain (deep purple spot)

$^1\text{H}$  NMR: (500 MHz,  $\text{CDCl}_3$ )  $\delta$  6.71 (dd,  $J$  = 16.8, 10.4 Hz, 1H), 6.46 (dd,  $J$  = 17.3, 1.4 Hz, 1H), 6.16 (dd,  $J$  = 17.3, 10.5 Hz, 1H), 5.87 (dd,  $J$  = 10.4, 1.4 Hz, 1H), 5.60 (dd,  $J$  = 16.9, 1.9 Hz, 1H), 5.17 (dd,  $J$  = 10.4, 1.9 Hz, 1H), 4.99 (s, 2H), 2.55 (t,  $J$  = 5.9 Hz, 2H), 2.39 (m, 2H), 1.66 – 1.57 (m, 6H)

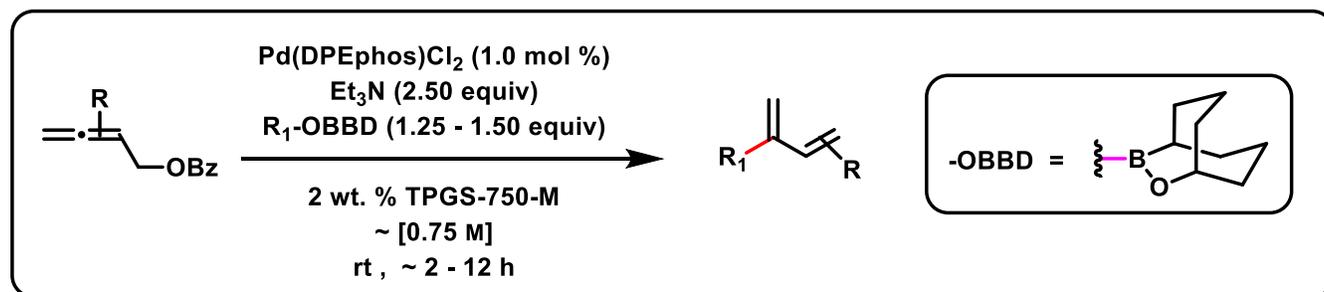
$^{13}\text{C}$  NMR: (126 MHz,  $\text{CDCl}_3$ )  $\delta$  165.6, 152.8, 131.6, 131.0, 128.1, 115.9, 114.2, 87.6, 83.5, 53.3, 34.8, 30.3, 28.1, 28.0, 26.7

IR: 2927, 2854, 2225, 1731, 1404, 1165  $\text{cm}^{-1}$

HRMS: (ESI) calculated for  $[\text{C}_{15}\text{H}_{18}\text{O}_2]$ : 231.1385  $[\text{M}+\text{H}]^+$ , found 231.1375

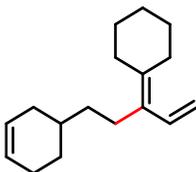
## 3.2 General procedure 'B'

### OBBD derivative-mediated $\text{sp}^2$ - $\text{sp}^3$ cross-couplings



Reactions utilizing  $-\text{OBBD}$  derivatives were performed analogously as described for general procedure 'A.'

#### 4-(3-Cyclohexylidenepent-4-en-1-yl)cyclohex-1-ene (22)



Purification: column chromatography on silica gel eluting with 100%, clear colorless oil, (0.30 mmol scale) 37.4mg, 54% (volatile compound).

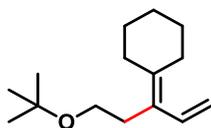
$^1\text{H}$  NMR: (500 MHz,  $\text{CDCl}_3$ )  $\delta$  6.82 (dd,  $J = 17.5, J = 11$  Hz, 1H), 5.67 (m, 2H), 5.17 (dd,  $J = 17, J = 1.5$  Hz, 1H), 4.99 (dd,  $J = 11$  Hz,  $J = 1$  Hz, 1H), 2.37-2.21 (m, 6H), 2.19-2.11 (m, 1H), 2.09-2.01 (m, 2H), 1.84-1.65 (m, 2H), 1.62-1.50 (m, 7H), 1.35-1.19 (m, 3H)

$^{13}\text{C}$  NMR: (126 MHz,  $\text{CDCl}_3$ )  $\delta$  140.2, 134.3, 128.9, 127.2, 126.8, 111.3, 36.7, 34.3, 32.1, 31.7, 30.3, 29.1, 28.7, 28.5, 27.1, 25.5, 25.1

IR: 3082, 3025, 2920, 2851, 1624, 1446, 1352, 1263, 1232, 984, 908, 890, 733, 652  $\text{cm}^{-1}$

HRMS: (EI) calculated for  $[\text{C}_{17}\text{H}_{26}]$ : 230.2035  $[\text{M}]^+$ , found 230.2035

**(5-(*t*-Butoxy)pent-1-en-3-ylidene)cyclohexane (23)**



Purification: column chromatography on silica gel eluting with 100%, clear colorless oil, (0.30 mmol scale) 42.7mg, 64% (volatile compound).

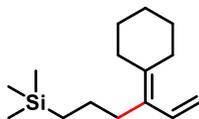
$^1\text{H}$  NMR: (500 MHz,  $\text{CDCl}_3$ )  $\delta$  6.83 (dd,  $J = 17, J = 11$  Hz, 1H), 5.23 (d,  $J = 17.5$  Hz, 1H) 5.00 (d,  $J = 11.5$  Hz, 1H), 3.30 (t,  $J = 8$  Hz, 2H), 2.54 (t,  $J = 8$  Hz, 2H), 2.36- 2.21 (m, 4H), 1.65-1.48 (m, 6H), 1.18 (s, 9H)

$^{13}\text{C}$  NMR: (126 MHz,  $\text{CDCl}_3$ )  $\delta$  142.3, 134.4, 124.9, 111.6, 72.8, 61.1, 31.9, 30.4, 29.3, 28.8, 28.5, 27.7, 27.1

IR: 3093, 2973, 2925, 1726, 1627, 1445, 1361, 1272, 1195, 1072, 907, 892, 733, 711  $\text{cm}^{-1}$

HRMS: (EI) calculated for  $[\text{C}_{15}\text{H}_{26}\text{O}]$ : 222.1984  $[\text{M}]^+$ , found 222.1988

**(4-Cyclohexylidenehex-5-en-1-yl)trimethylsilane (24)**



Purification: column chromatography on silica gel eluting with 100% hexanes, clear colorless oil, (0.30 mmol scale) 46.1mg, 65% (volatile compound).

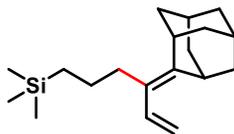
$^1\text{H}$  NMR: (500 MHz,  $\text{CDCl}_3$ )  $\delta$  6.82 (dd,  $J = 17.5$ ,  $J = 11$  Hz, 1H), 5.16 (dd,  $J = 17.5$  Hz,  $J = 1.5$  Hz, 1H), 5.00 (dd,  $J = 11.5$  Hz,  $J = 1.5$  Hz, 1H), 2.34 (t,  $J = 6$  Hz, 2H), 2.28-2.21 (m, 4H), 1.61-1.52 (m, 6H), 1.40-1.31 (m, 2H), 0.57-0.50 (m, 2H), -0.03 (s, 9H)

$^{13}\text{C}$  NMR: (126 MHz,  $\text{CDCl}_3$ )  $\delta$  140.4, 134.5, 128.9, 111.4, 31.8, 31.7, 30.3, 28.7, 28.5, 27.2, 24.2, 17.5, -1.5

IR: 2925, 2854, 1625, 1247, 860, 833, 734  $\text{cm}^{-1}$

HRMS: (EI) calculated for  $[\text{C}_{15}\text{H}_{28}\text{Si}]$ : 236.1960  $[\text{M}]^{+\bullet}$ , found 236.1957

**(4-((1r,3r,5R,7S)-Adamantan-2-ylidene)hex-5-en-1-yl)trimethylsilane (25)**



Purification: column chromatography on silica gel eluting with 100% hexanes, clear colorless oil, (0.30 mmol scale) 75.3mg, 87%.

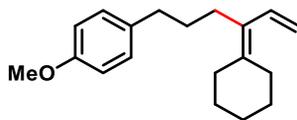
$^1\text{H}$  NMR: (500 MHz,  $\text{CDCl}_3$ )  $\delta$  6.81 (dd,  $J = 17.5$ ,  $J = 11$  Hz, 1H), 5.17 (dd,  $J = 17$  Hz,  $J = 1.5$  Hz, 1H), 4.97 (dd,  $J = 11$  Hz,  $J = 1.5$  Hz, 1H), 3.16 (s, 1H), 2.91 (s, 1H), 2.26 (m, 2H), 1.99-1.80 (m, 8H), 1.79-1.67 (m, 4H), 1.40-1.31 (m, 2H), 0.58-0.50 (m, 2H), -0.02 (s, 9H)

$^{13}\text{C}$  NMR: (126 MHz,  $\text{CDCl}_3$ )  $\delta$  147.9, 134.1, 125.7, 111.1, 39.5, 39.4, 37.3, 34.1, 32.7, 31.4, 28.3, 24.3, 17.5, -1.5

IR: 3083, 2951, 2907, 1627, 1476, 1246, 1107, 988, 888, 850, 832, 755, 739, 690  $\text{cm}^{-1}$

HRMS: (EI) calculated for [C<sub>19</sub>H<sub>32</sub>Si]: 288.2273 [M]<sup>+</sup>, found 288.2271

**1-(4-Cyclohexylidenehex-5-en-1-yl)-4-methoxybenzene (26)**



Purification: column chromatography on silica gel eluting with 0 – 2% (ether : hexanes), clear colorless oil, (0.30 mmol scale) 76.2mg, 94%.

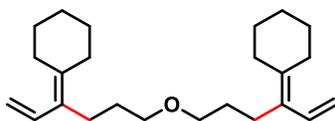
<sup>1</sup>H NMR: (500 MHz, CDCl<sub>3</sub>) δ 7.12 (d, *J* = 8.4 Hz, 2H), 6.85 (d, *J* = 11.4 Hz, 2H), 6.82 (dd, *J* = 17.4 Hz, *J* = 10.8 Hz, 1H), 5.08 (d, *J* = 16.2 Hz, 1H) 4.97 (d, *J* = 10.8 Hz, 1H), 3.80 (s, 3H), 2.60 (t, *J* = 7.8 Hz, 2H), 2.34 (t, *J* = 6 Hz, 2H), 2.30 (m, 2H), 2.22 (t, *J* = 6 Hz, 2H), 1.69-1.65 (m, 2H), 1.64-1.50 (m, 6H)

<sup>13</sup>C NMR: (126 MHz, CDCl<sub>3</sub>) δ 157.8, 140.5, 134.8, 134.3, 129.4, 128.5, 113.8, 111.4, 55.4, 35.4, 31.7, 31.5, 30.3, 28.7, 28.5, 27.2, 27.1

IR: 3088, 2923, 2859, 1721, 1612, 1511, 1451, 1270, 1243, 1175, 1038, 891, 826, 806, 712 cm<sup>-1</sup>

HRMS: (EI) calculated for [C<sub>19</sub>H<sub>26</sub>O]: 270.1984 [M]<sup>+</sup>, found 270.1982

**(Oxybis(hex-1-en-6-yl-3-ylidene))dicyclohexane (27)**



Purification: column chromatography on silica gel eluting with 100% hexanes, clear colorless oil, (0.30 mmol scale) 44.2mg, 43%.

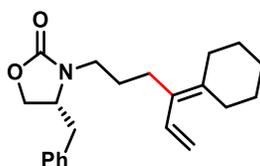
$^1\text{H}$  NMR: (500 MHz,  $\text{CDCl}_3$ )  $\delta$  6.82 (dd,  $J = 17.5$  Hz,  $J = 11$  Hz, 2H), 5.20 (dd,  $J = 17$  Hz,  $J = 1$  Hz, 2H), 4.99 (dd,  $J = 11$  Hz,  $J = 1.5$  Hz, 2H), 3.41 (t,  $J = 6.5$  Hz, 4H), 2.37- 2.31 (m, 8H), 2.29 2.24 (m, 4H), 1.67-1.61 (m, 4H), 1.60-1.50 (m, 12H)

$^{13}\text{C}$  NMR: (126 MHz,  $\text{CDCl}_3$ )  $\delta$  140.7, 134.2, 128.2, 111.6, 70.8, 31.7, 30.4, 29.8, 28.7, 28.5, 27.1, 24.0

IR: 3093, 2924, 2852, 2251, 1624, 1447, 1115, 985, 906, 852, 731, 649  $\text{cm}^{-1}$

HRMS: (EI) calculated for  $[\text{C}_{24}\text{H}_{38}\text{O}]$ : 342.2923  $[\text{M}]^+$ , found 342.2911

**(*R*)-4-Benzyl-3-(4-cyclohexylidenehex-5-en-1-yl)oxazolidin-2-one (28)**



Purification: column chromatography on silica gel eluting with 0-10-20-25% (ethyl acetate : hexanes), clear colorless oil, (0.30 mmol scale) 95.1mg, 93%.

Note: Product can co-eluted with the borabicyclodecanol formed during transmetallation.

TLC:  $R_f = 0.30$  (20% EtOAc : hexanes), UV,  $I_2$ , vanillin stain

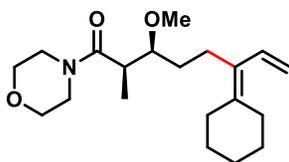
$^1\text{H}$  NMR: (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.28-7.03 (m, 5H), 6.73 (dd,  $J = 17.4$  Hz,  $J = 10.8$  Hz, 1H), 5.05 (d,  $J = 17.4$  Hz 1H), 4.93 (d,  $J = 10.8$  Hz, 1H), 4.30 (br, s, 1H), 4.11-4.02 (m, 1H), 3.98-3.88 (m, 2H), 3.50-3.42 (m, 1H), 3.06-2.96 (m, 2H), 2.63-2.53 (m, 1H), 2.31-2.10 (m, 6H), 1.85-1.69 (m, 4H), 1.66-1.29 (m, 16H)

$^{13}\text{C}$  NMR: (126 MHz,  $\text{CDCl}_3$ )  $\delta$  158.1, 141.0, 135.7, 134.1, 129.0, 129.0, 127.4, 127.3, 111.6, 71.0, 66.8, 56.0, 42.2, 38.6, 32.1, 31.7, 30.3, 29.0, 28.4, 27.1, 26.9, 26.3, 24.5, 22.1

IR: 3092, 3029, 2922, 2854, 1746, 1450, 1412, 1386, 1340, 1300, 1251, 732, 700  $\text{cm}^{-1}$

HRMS: (ESI) calculated for  $[\text{C}_{22}\text{H}_{29}\text{NO}_2\text{Na}]^+$ : 362.2091  $[\text{M}+\text{Na}]^+$ , found 362.2094

**(2*R*,3*S*)-6-Cyclohexylidene-3-methoxy-2-methyl-1-morpholinoct-7-en-1-one (29)**



Purification: column chromatography on silica gel eluting with 50% (ethyl acetate : hexanes), clear colorless oil, (0.30 mmol scale) 78.1mg, 77%.

TLC:  $R_f = 0.10$  (20% EtOAc : hexanes), UV,  $I_2$ , vanillin stain

$^1\text{H}$  NMR: (500 MHz,  $\text{CDCl}_3$ )  $\delta$  6.79 (dd,  $J = 17.5$  Hz,  $J = 11$  Hz, 1H), 5.16 (dd,  $J = 17.5$  Hz,  $J = 1$  Hz, 1H), 4.98 (dd,  $J = 11$  Hz,  $J = 1$  Hz, 1H), 3.70-3.50 (m, 8H), 3.44 (s, 3H), 3.41 (dt,  $J = 7$  Hz,  $J = 2$  Hz, 1H), 2.85 (p,  $J = 7$  Hz, 1H), 2.36-2.17 (m, 6H), 1.70-1.39 (m, 12H), 1.21 (d,  $J = 7$  Hz, 3H)

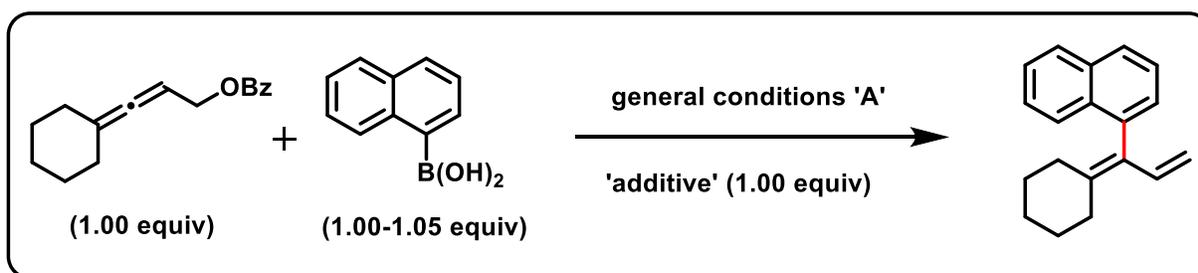
$^{13}\text{C}$  NMR: (126 MHz,  $\text{CDCl}_3$ )  $\delta$  173.6, 140.6, 134.2, 128.3, 111.5, 83.8, 71.1, 67.1, 67.0, 58.6, 46.4, 42.2, 39.6, 31.6, 30.3, 28.7, 28.5, 27.1, 26.4, 22.2, 15.2

IR: 3092, 2966, 2923, 2853, 2254, 1638, 1430, 1227, 1115, 1098, 1069, 1032, 894, 731  $\text{cm}^{-1}$

HRMS: (ESI) calculated for  $[\text{C}_{20}\text{H}_{33}\text{NO}_3\text{Na}]^+$ : 358.2353  $[\text{M}+\text{Na}]^+$ , found 358.2350

### 3.3 General procedure 'C'

#### Robustness screen

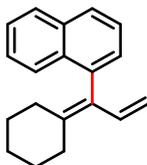


$\text{Pd}(\text{DPEphos})\text{Cl}_2$  (1-2 mg) was added to a microwave vial fitted with a spin vane, septum, and argon needle, followed by 0.4 mL of a 2 wt % solution of TPGS-750-M, and the mixture was stirred vigorously until homogeneous.  $\text{Et}_3\text{N}$  (0.05 mL) was added via syringe and the mixture was left stirring while the other reagents were weighed out. Naphthylboronic acid (51.6-54.2 mg, 0.300-0.315 mmol,

1.00-1.05 equiv) was added as a solid, followed immediately by 0.30 mmol (1.00 equiv) of the appropriate additive and then, quickly, 0.3 mmol of the allenolate. The reaction was left to stir for ca. 30 min (reaction followed by TLC), and once complete, the mixture was diluted with EtOAc and the entire contents of the reaction vessel were filtered through a short plug of silica gel. Volatiles were removed under reduced pressure to afford a crude mixture of product and additive, which was purified by flash chromatography on silica gel, eluting with 0-100% (EtOAc : hexanes), isolating both the desired product and additive. Yields obtained of product and recovered additive, after removal of trace volatiles on high-vacuum, were used then as a measure of the functional group tolerance of the reaction with respect to functionality in the additive.

\*\*\* All additives were commercially available and the recovered compounds displayed identical spectrographic properties ( $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR).

### 1-(1-Cyclohexylideneallyl)naphthalene (30)



Purification: column chromatography on silica gel (extra 1-2 inches of  $\text{SiO}_2$ ) eluting with 100% hexanes, clear colorless oil, (0.30 mmol scale) 83 - 94%.

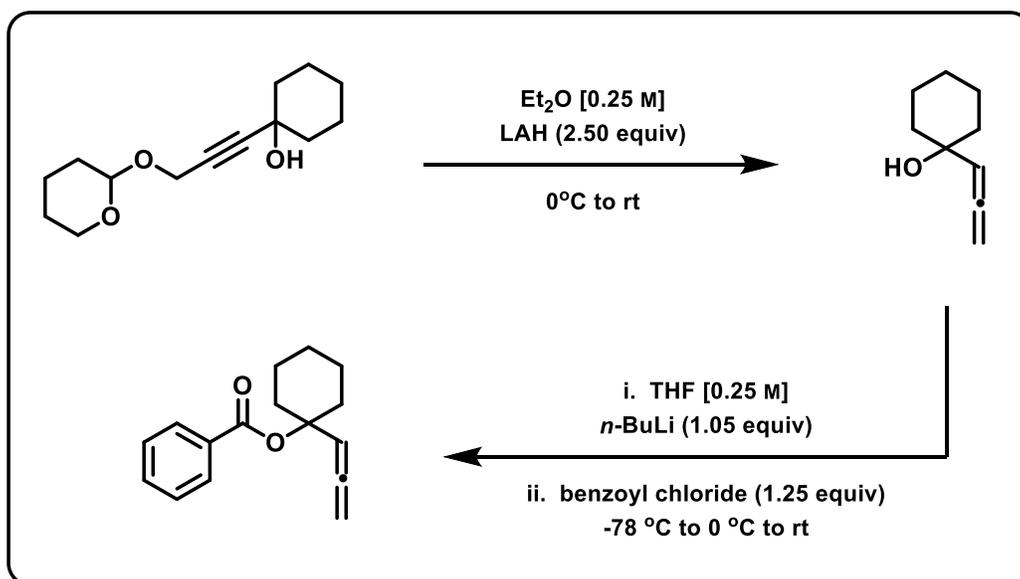
TLC:  $R_f = 0.60$  (100% hexanes), UV,  $\text{I}_2$

$^1\text{H}$  NMR: (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.90 – 7.85 (m, 1H), 7.84 – 7.77 (m, 2H), 7.53 – 7.39 (m, 3H), 7.20 (ddd,  $J = 17.1, 8.7, 4.2$  Hz, 2H), 4.97 (dd,  $J = 10.7, 1.7$  Hz, 1H), 4.36 (dd,  $J = 17.1, 1.7$  Hz, 1H), 2.84 – 2.46 (m, 2H), 1.88 – 1.72 (m, 4H), 1.60 (tt,  $J = 14.2, 7.0$  Hz, 2H), 1.45 – 1.35 (m, 2H)

$^{13}\text{C}$  NMR: (126 MHz,  $\text{CDCl}_3$ )  $\delta$  142.9, 138.3, 134.7, 133.8, 132.6, 130.5, 128.2, 127.4, 126.9, 126.2, 125.8, 125.7, 125.6, 115.6, 33.5, 30.3, 28.6, 28.4, 27.0

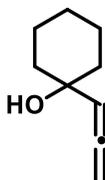
HRMS: ( $\text{EI}^+$ ) calculated for  $[\text{C}_{19}\text{H}_{20}]$ : 248.1565  $[\text{M}]^+$ , found 248.1563

#### 4. Scale-Up Example<sup>2</sup>



\*\*\*Prepared according to known literature procedures.<sup>2</sup>

#### 1-(Propa-1,2-dien-1-yl)cyclohexan-1-ol



Purification: column chromatography on silica gel eluting with 20 then 30% (ether : hexanes), viscous clear colorless oil, (10.50 mmol scale) 978mg, 67%.

TLC:  $R_f$  = 0.31 (30% ether : hexanes), UV, I<sub>2</sub>, Vanillin stain (grey/ lavender spot)

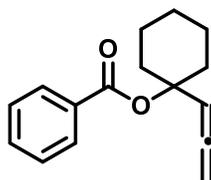
$^1\text{H}$  NMR: (500 MHz,  $\text{CDCl}_3$ )  $\delta$  5.29 (t,  $J = 6.7$  Hz, 1H), 4.87 (dd,  $J = 6.8, 2.5$  Hz, 2H), 1.68 – 1.59 (m, 7H), 1.47 (m, 3H), 1.34 (m,  $J = 5.2$  Hz, 1H)

$^{13}\text{C}$  NMR: (126 MHz,  $\text{CDCl}_3$ )  $\delta$  206.4, 99.5, 78.3, 70.6, 38.4, 25.6, 22.7

IR: 3356, 2930, 2855, 1957, 1450, 1053, 1036, 954, 843  $\text{cm}^{-1}$

HRMS: (ESI) calculated for  $[\text{C}_9\text{H}_{14}\text{O}]$ : 139.1123  $[\text{M}+\text{H}]^+$ , found 139.1118

### 1-(Propa-1,2-dien-1-yl)cyclohexyl benzoate



Purification: column chromatography on silica gel eluting with 1 CV hexanes, then 1 then 3% (ether : hexanes), viscous clear colorless oil, (6.23 mmol scale) 1,177mg, 78%.

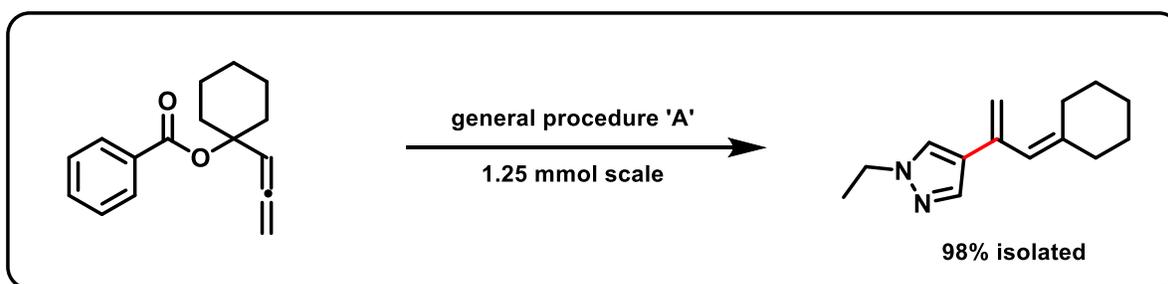
TLC:  $R_f = 0.47$  (7% ether : hexanes), UV,  $\text{I}_2$ , Vanillin stain (deep grey/ purple spot)

$^1\text{H}$  NMR: (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.03 (m, 2H), 7.56 – 7.52 (m, 1H), 7.43 (t,  $J = 7.8$  Hz, 2H), 5.78 (t,  $J = 6.7$  Hz, 1H), 4.88 (d,  $J = 6.7$  Hz, 2H), 2.33 (d,  $J = 12.2$  Hz, 2H), 1.78 (m, 2H), 1.65 – 1.57 (m, 5H), 1.40 – 1.33 (m, 1H)

$^{13}\text{C}$  NMR: (151 MHz,  $\text{CDCl}_3$ )  $\delta$  207.9, 165.4, 132.7, 131.8, 129.6, 128.4, 96.0, 81.4, 78.0, 35.6, 25.5, 22.4

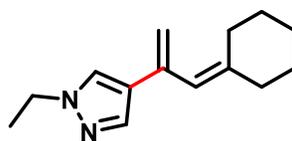
IR: 2936, 2866, 1951, 1712, 1450, 1275, 1240, 1106, 1036, 715  $\text{cm}^{-1}$

HRMS: (ESI) calculated for  $[\text{C}_{16}\text{H}_{18}\text{O}_2]$ : 265.1205  $[\text{M}+\text{Na}]^+$ , found 265.1197



\*\*\*Prepared according to general procedure 'A' above.

#### 4-(3-Cyclohexylideneprop-1-en-2-yl)-1-ethyl-1H-pyrazole



Purification: column chromatography on silica gel eluting with 30 then 40% (ether:hexanes), faintly yellow clear oil, (1.25 mmol scale) 266 mg, 98%.

TLC:  $R_f = 0.17$  (25% ether:hexanes), UV,  $I_2$ , Vanillin stain (deep crimson spot)

$^1\text{H NMR}$ : (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.55 (s, 1H), 7.34 (s, 1H), 5.81 (d,  $J = 2.3$  Hz, 1H), 5.35 (d,  $J = 2$  Hz, 1H), 4.80 (t,  $J = 1.7$  Hz, 1H), 4.11 (q,  $J = 7.3$  Hz, 2H), 2.29 – 2.26 (m, 2H), 2.21 – 2.18 (m, 2H), 1.63 – 1.55 (m, 4H), 1.46 (t,  $J = 7.3$  Hz, 5H)

$^{13}\text{C NMR}$ : (151 MHz,  $\text{CDCl}_3$ )  $\delta$  144.4, 136.8, 136.1, 125.9, 123.7, 121.2, 110.2, 47.1, 37.5, 30.1, 28.9, 28.2, 26.8, 15.6

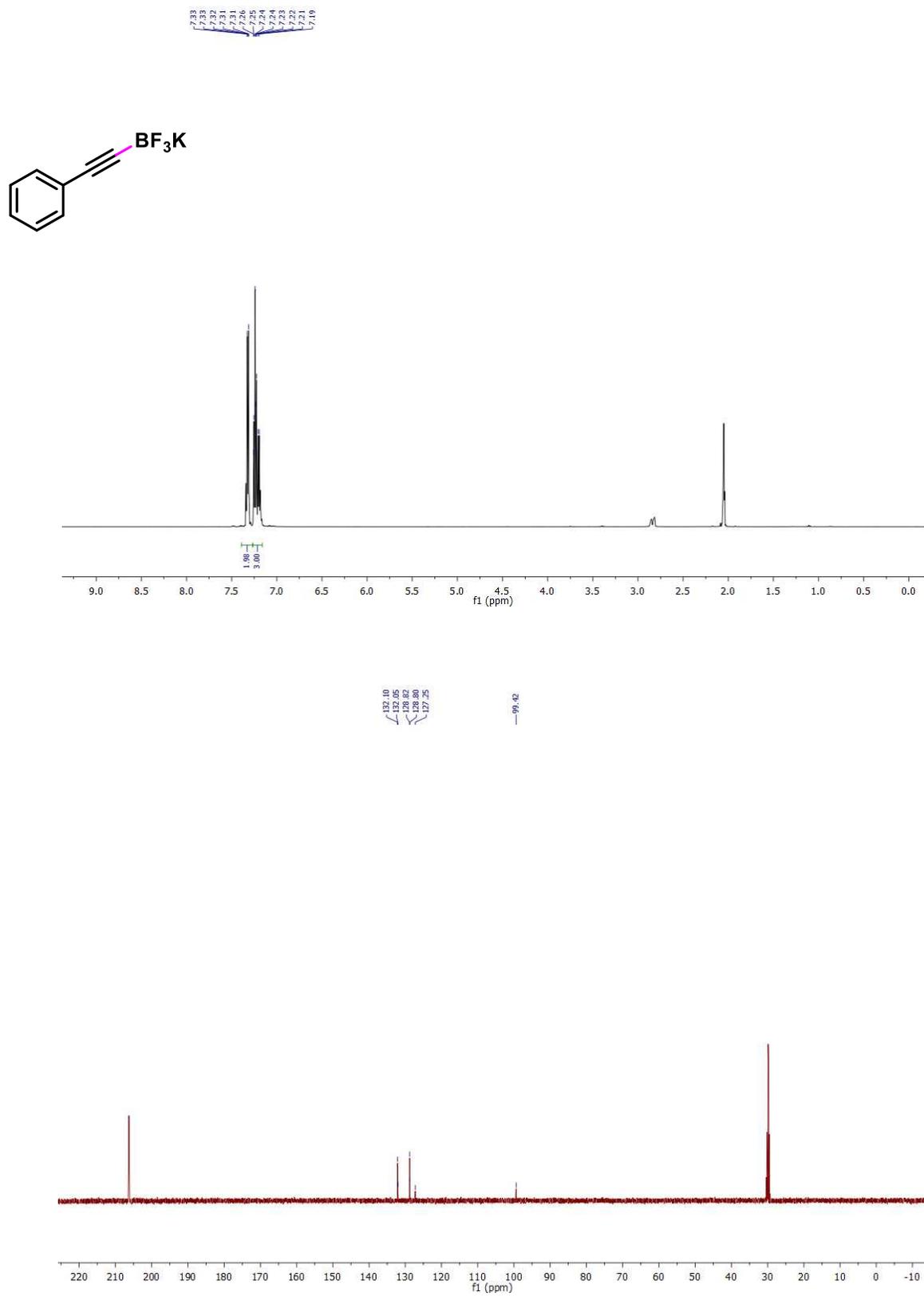
IR: 2989, 2925, 2855, 1613, 1444, 1053, 1036, 995, 849  $\text{cm}^{-1}$

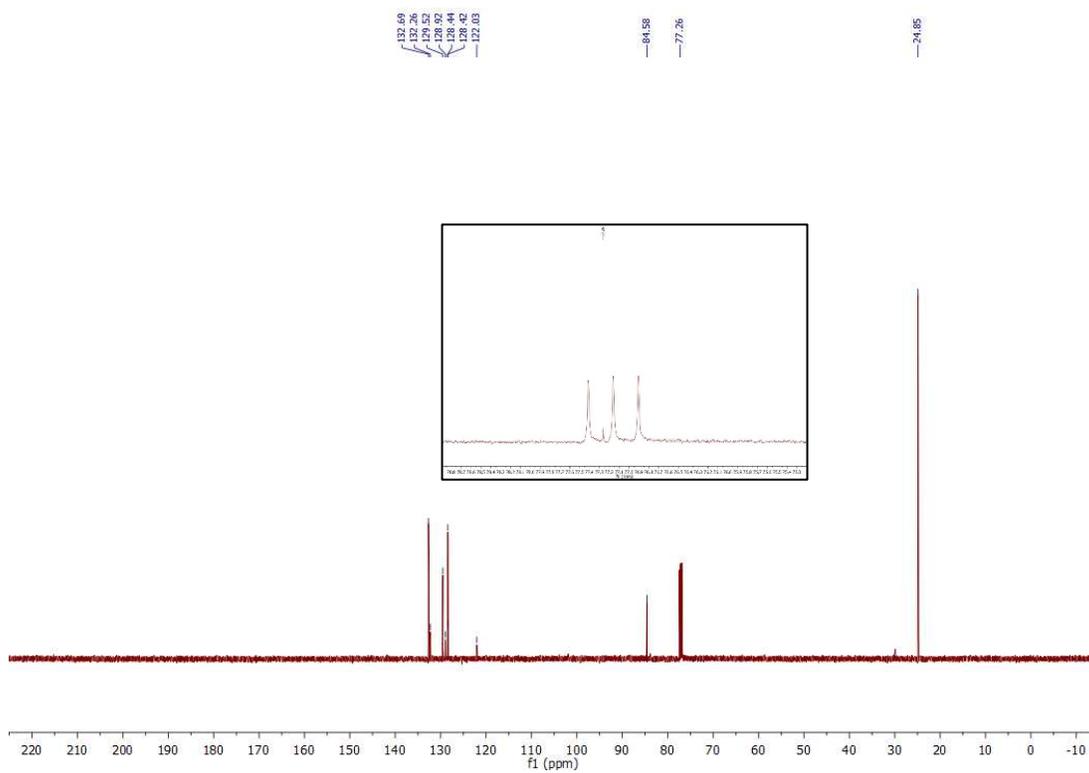
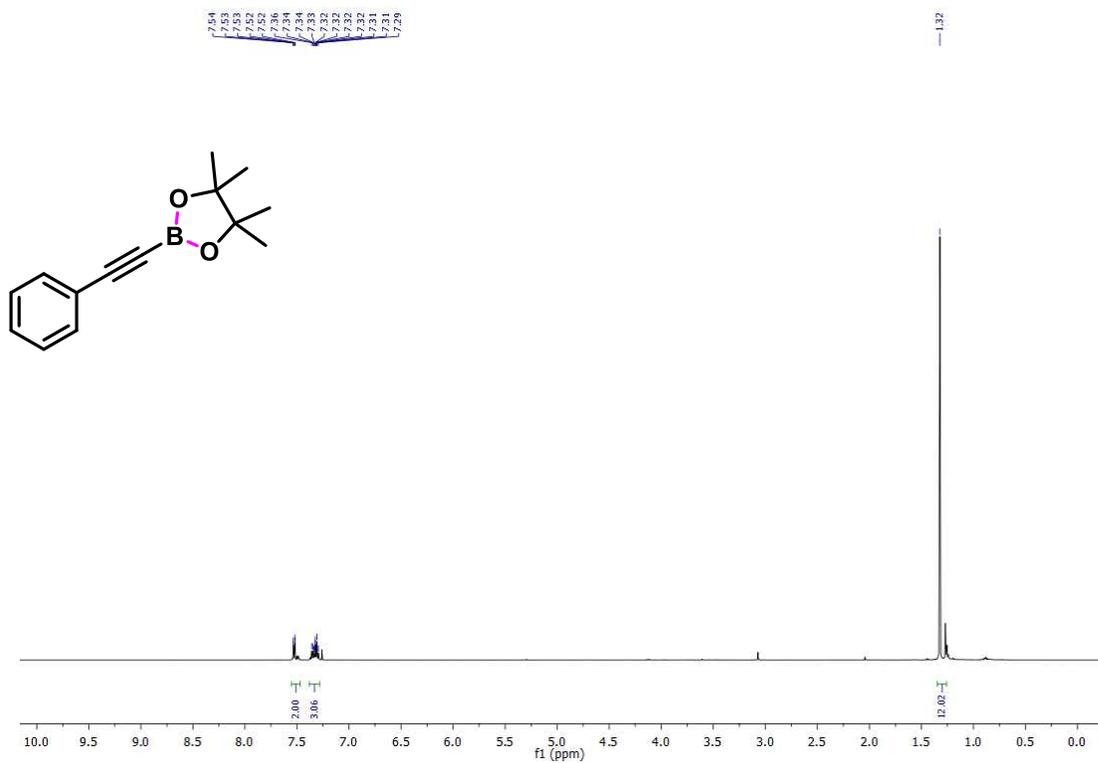
HRMS: (ESI) calculated for  $[\text{C}_{14}\text{H}_{20}\text{N}_2]$ : 217.1705  $[\text{M}+\text{H}]^+$ , found 217.1711

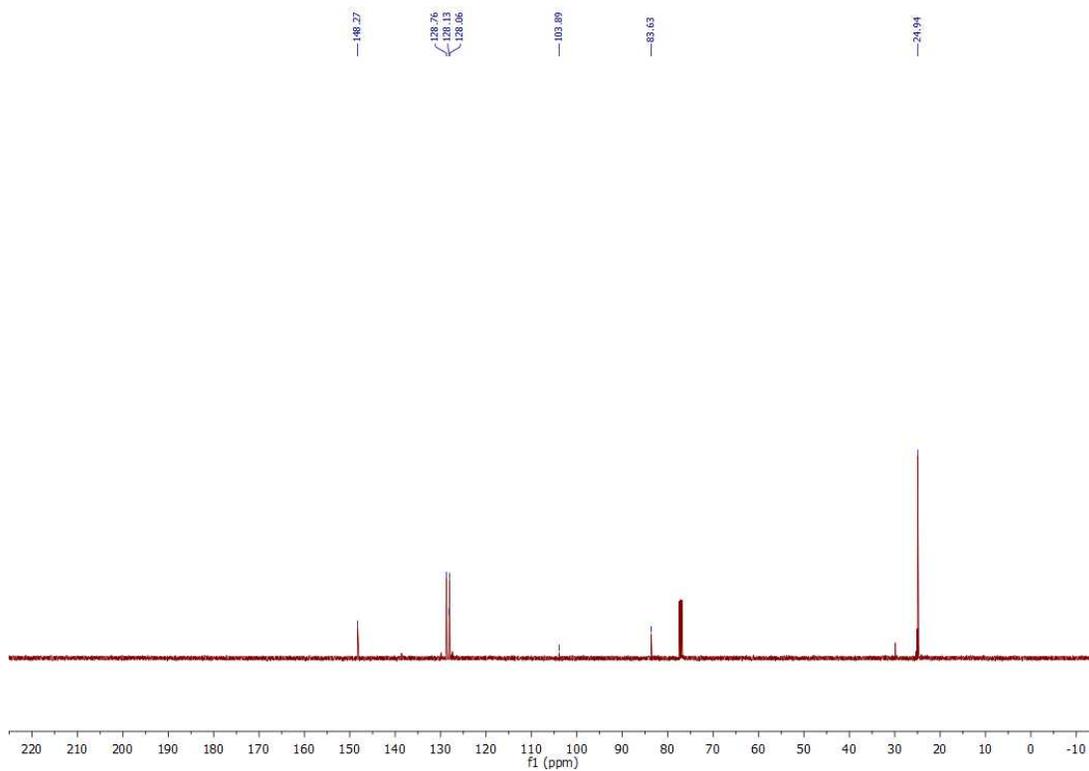
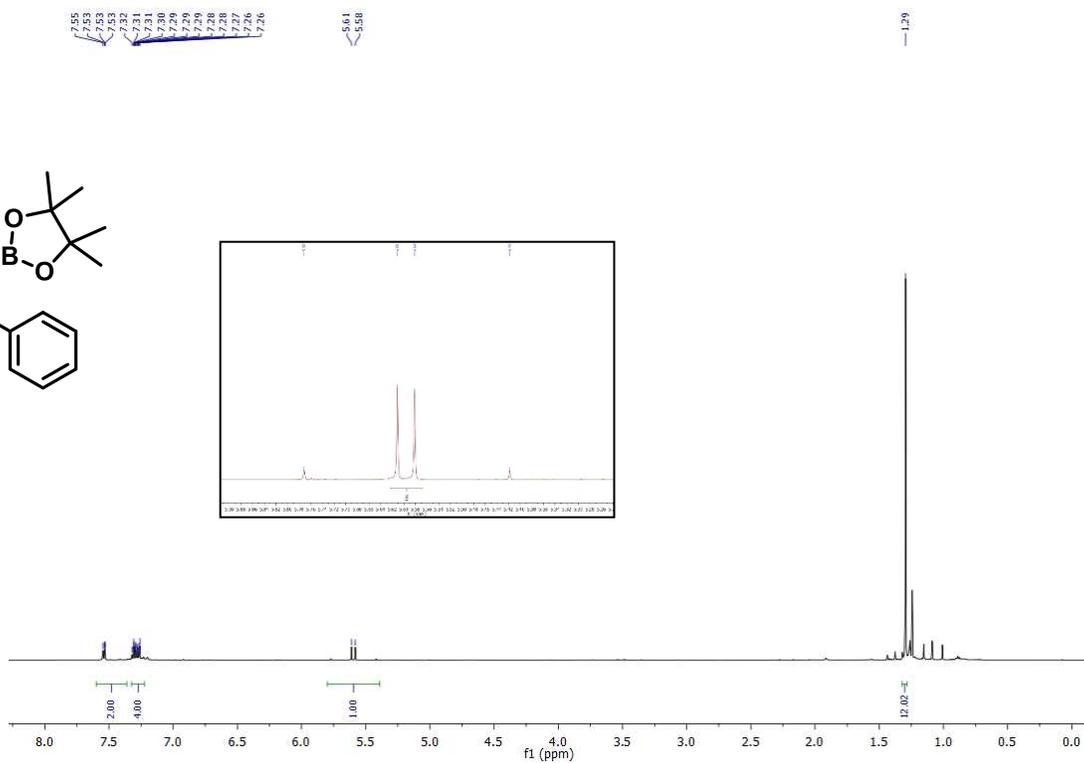
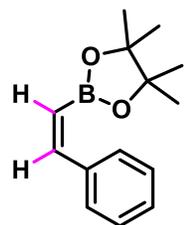
## 5. References

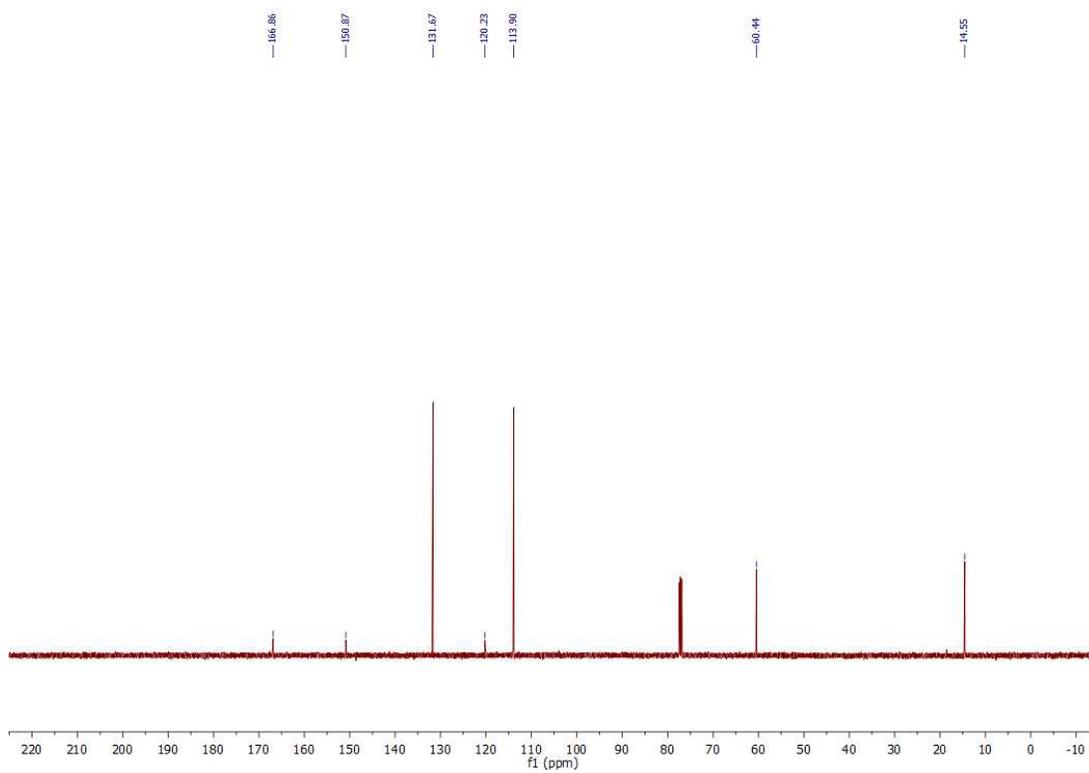
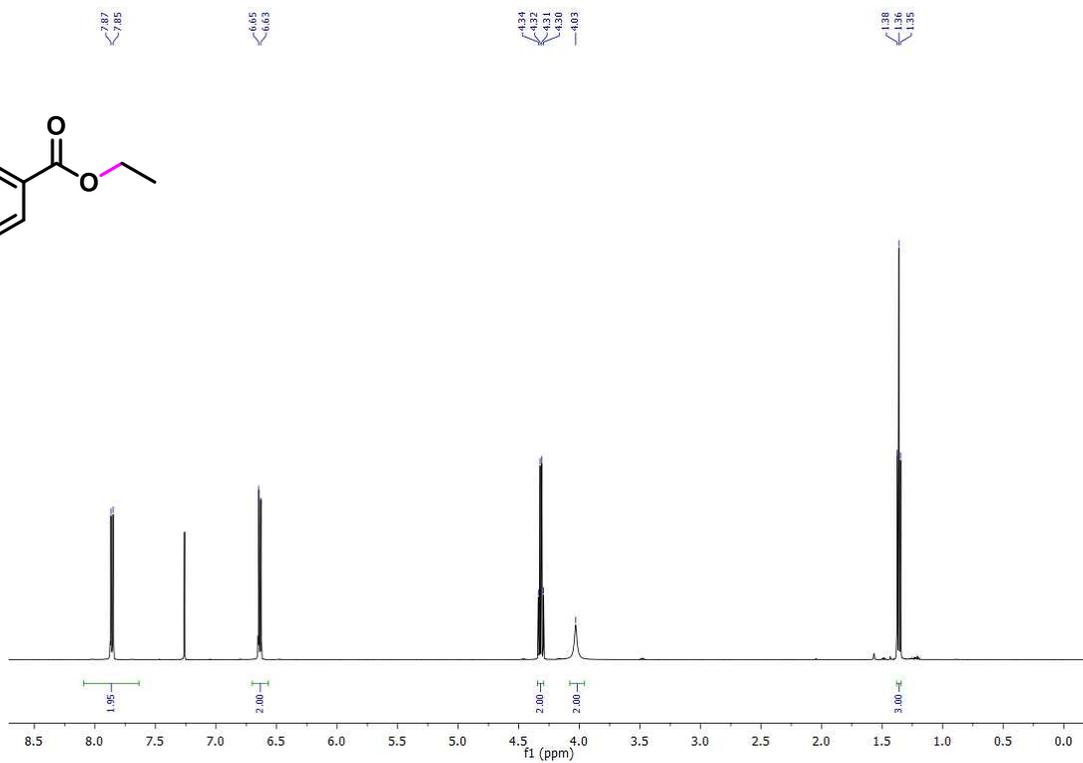
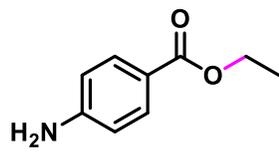
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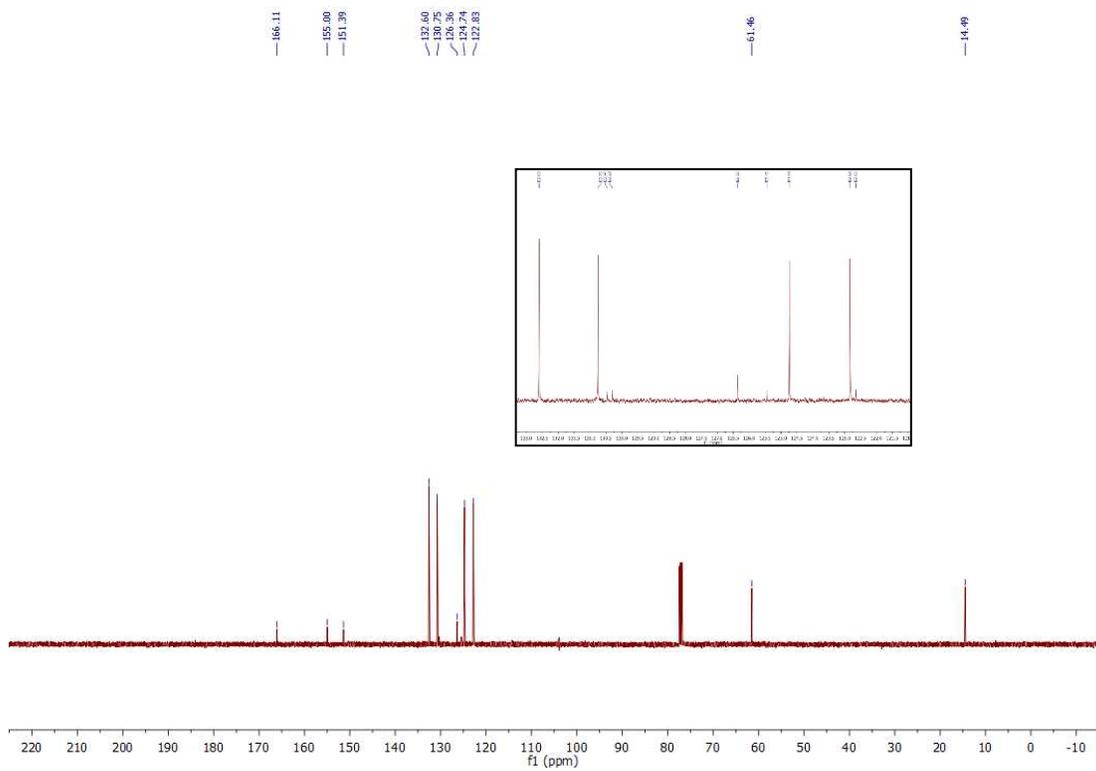
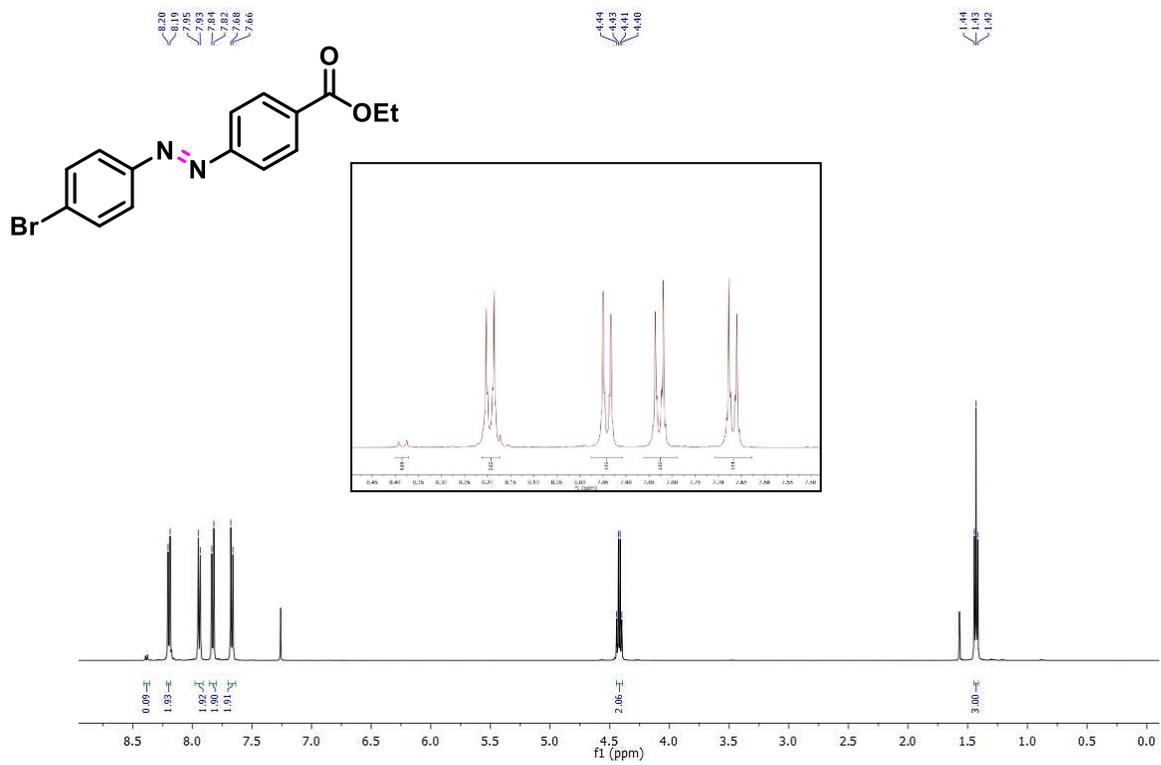
## 6. NMR Spectra

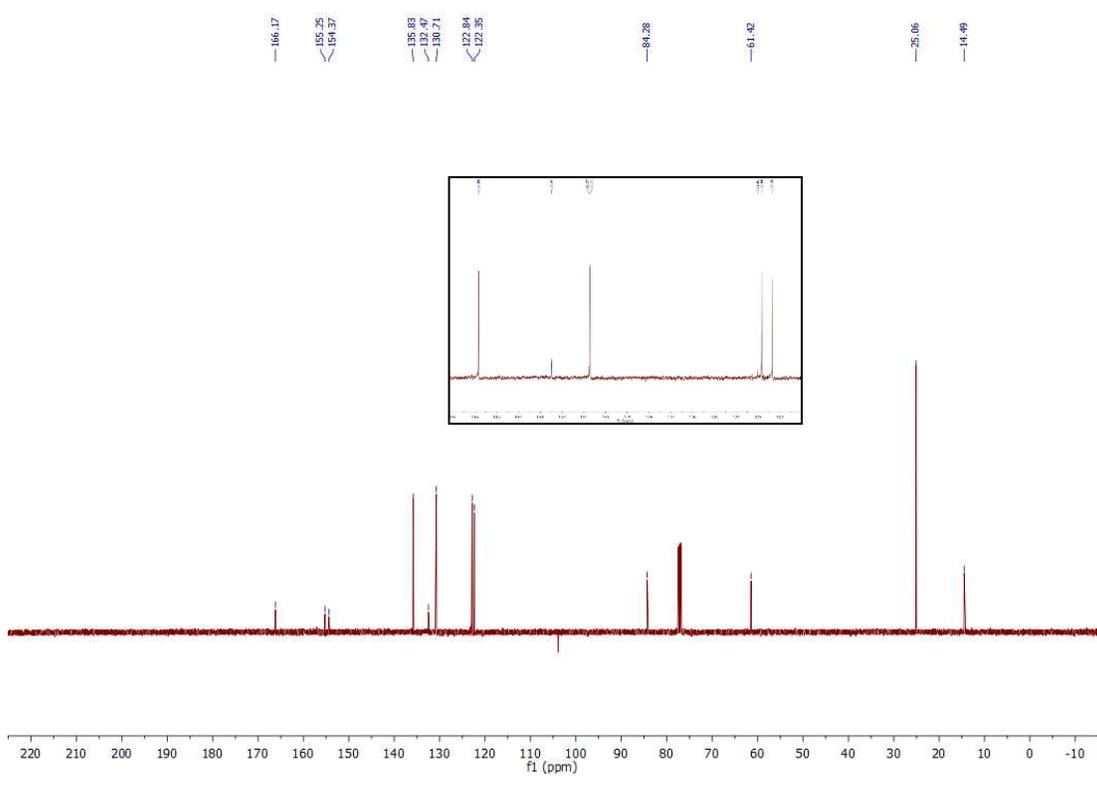
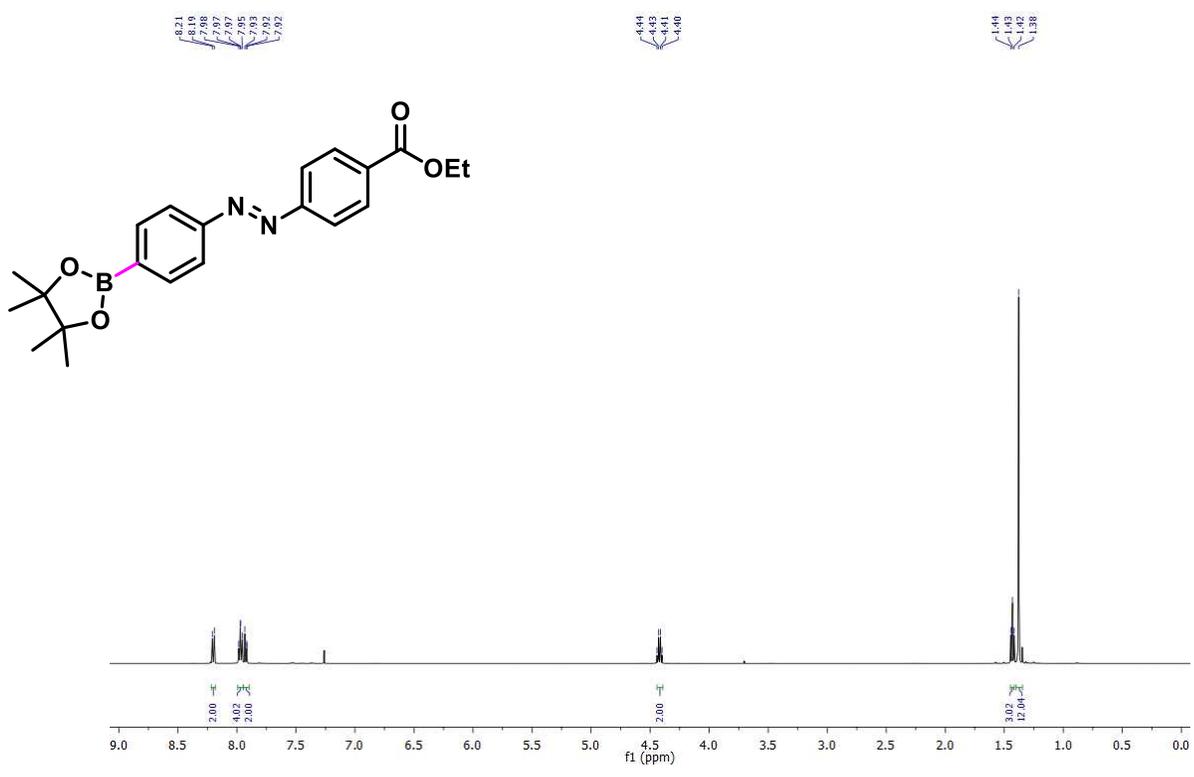


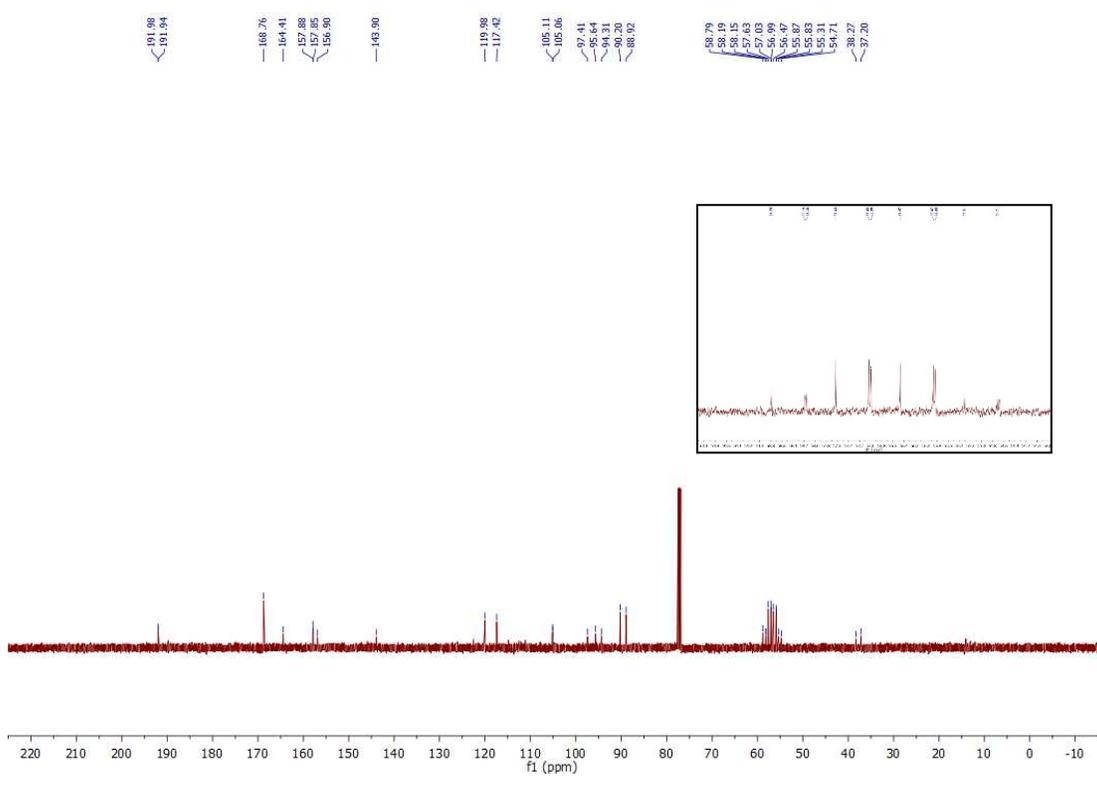
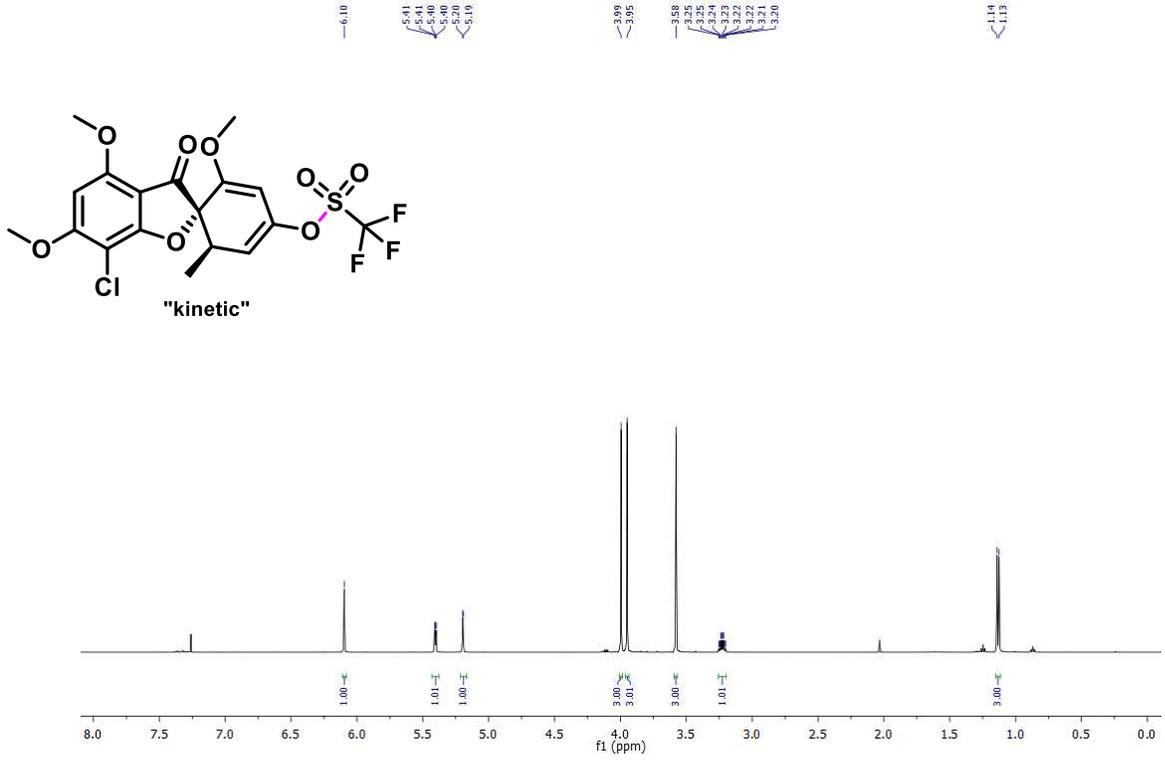


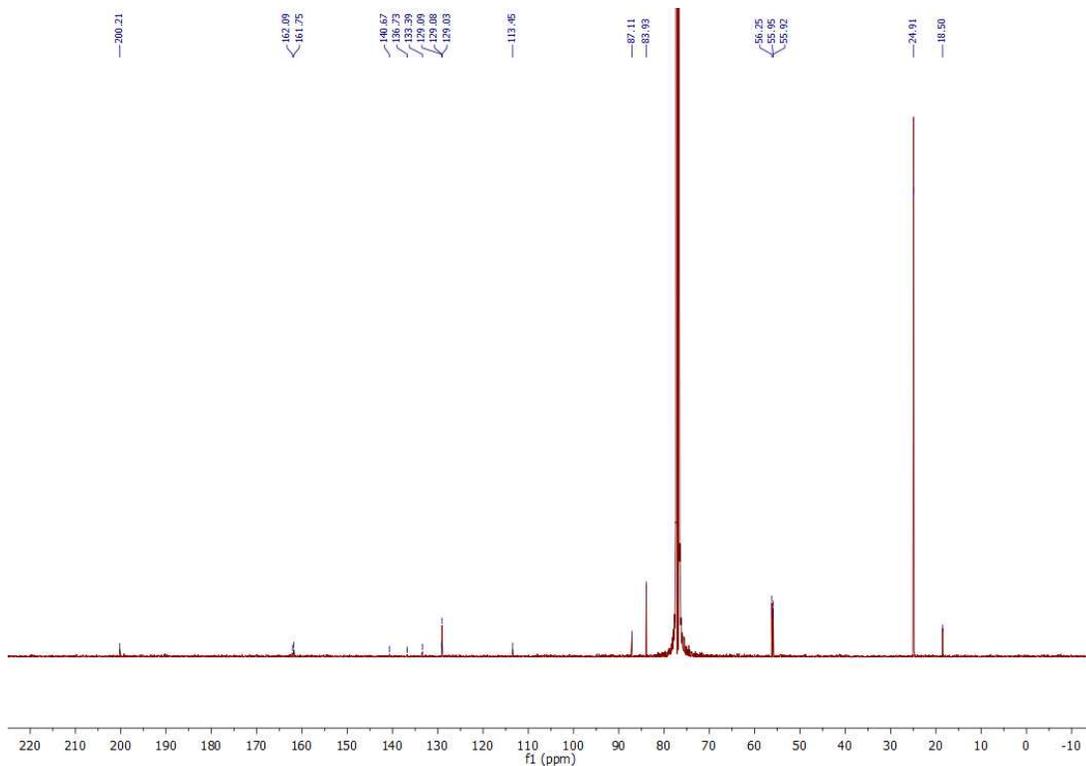
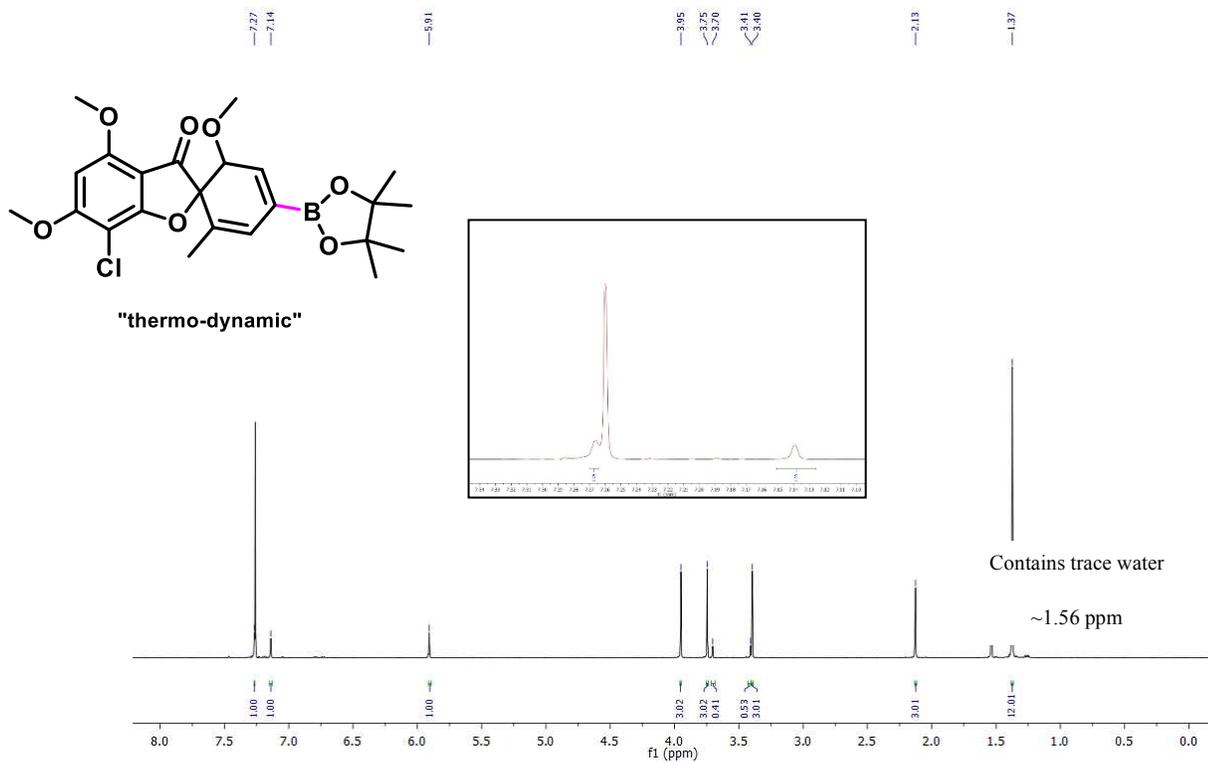


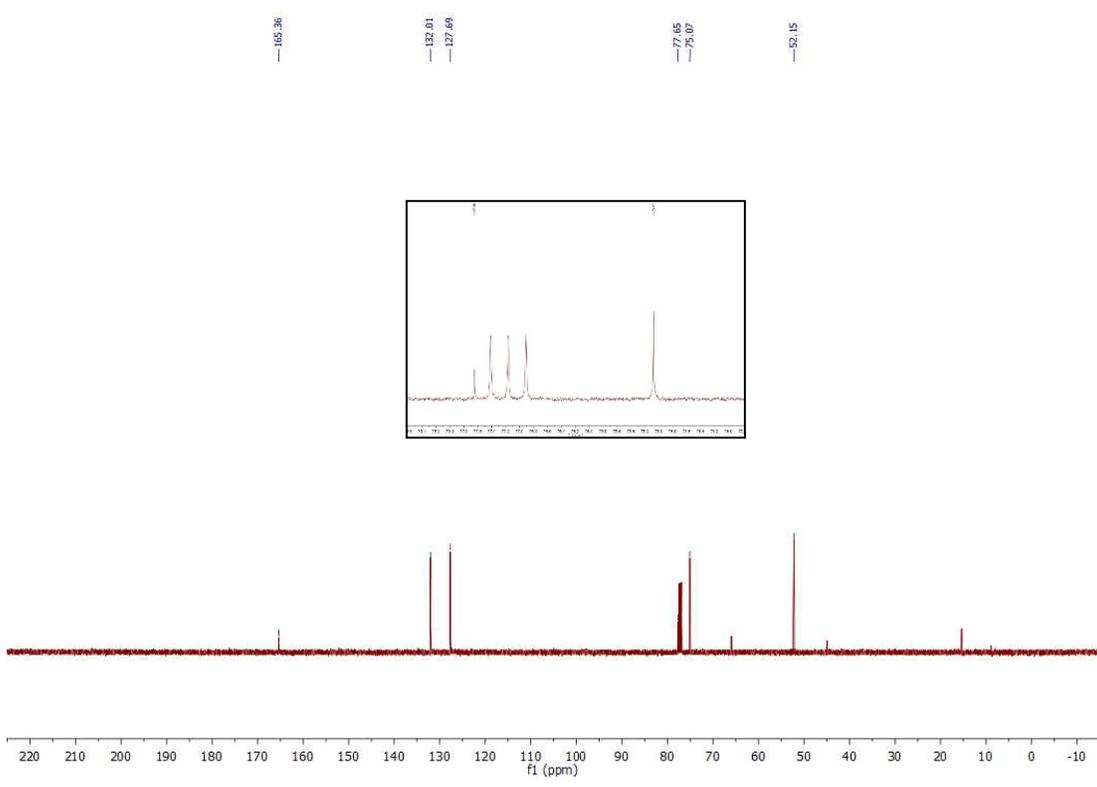
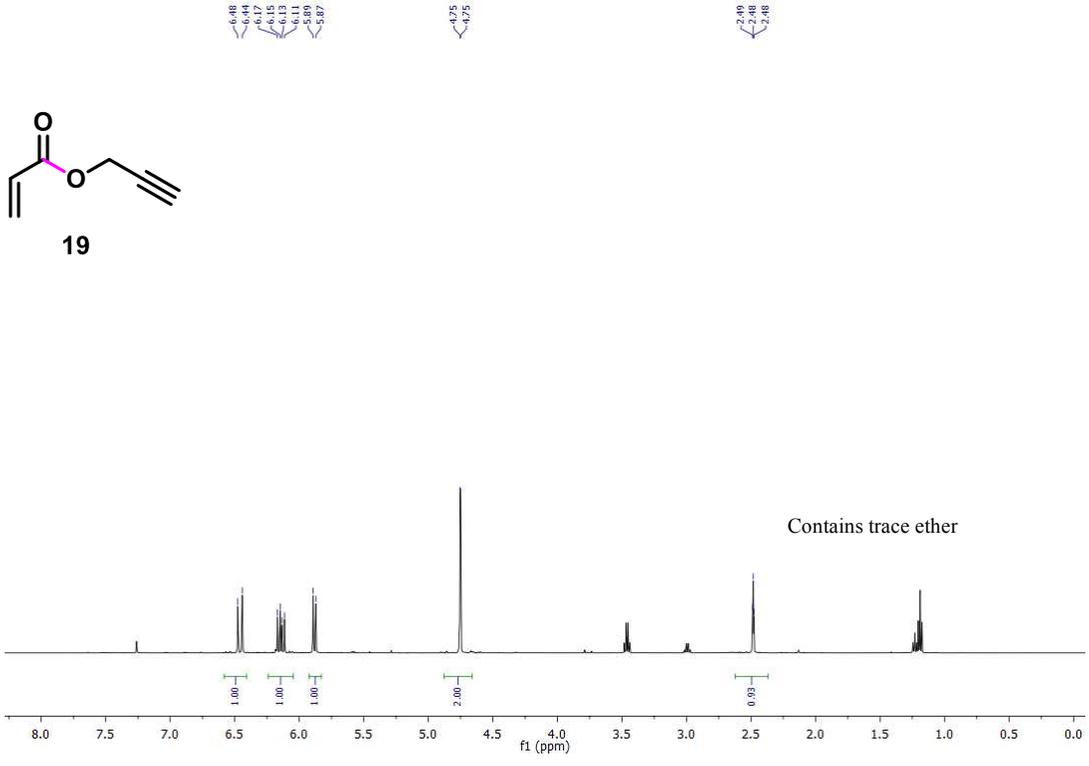


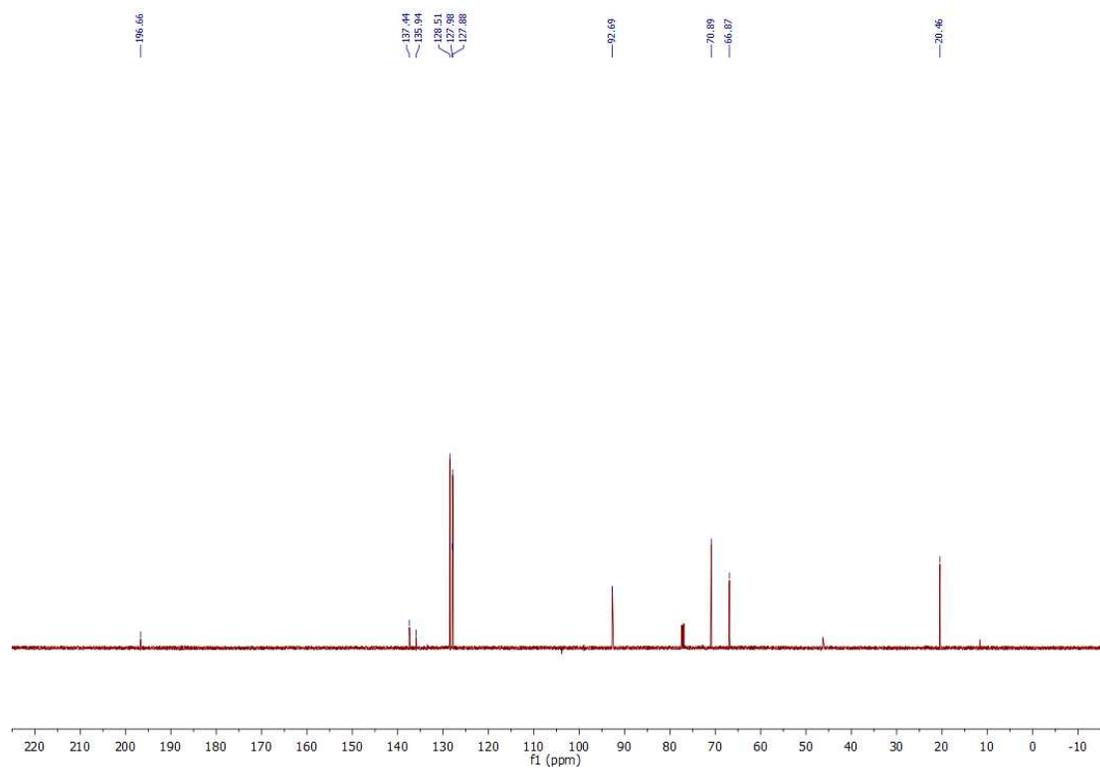
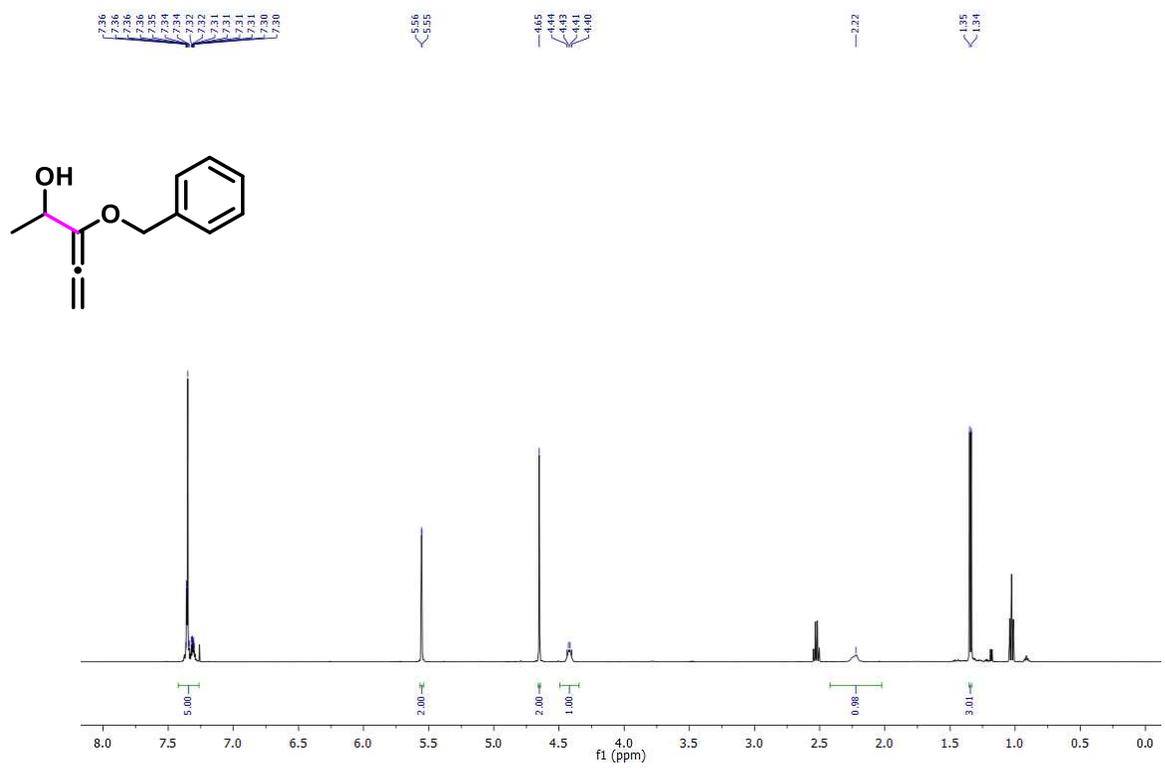






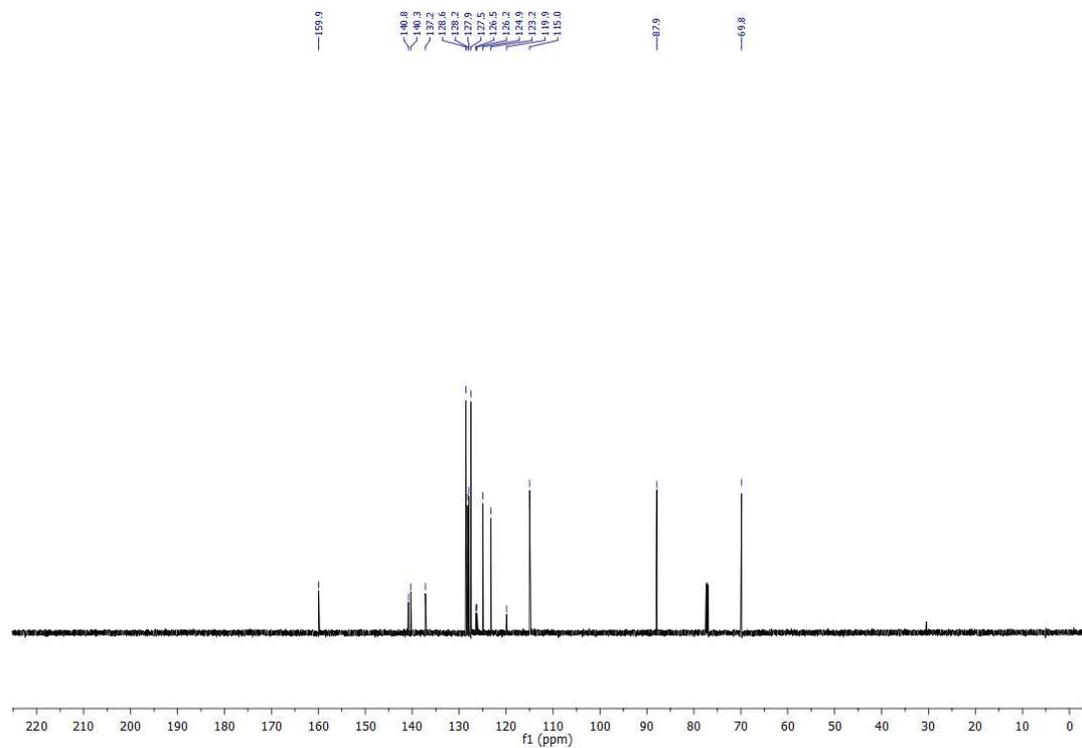
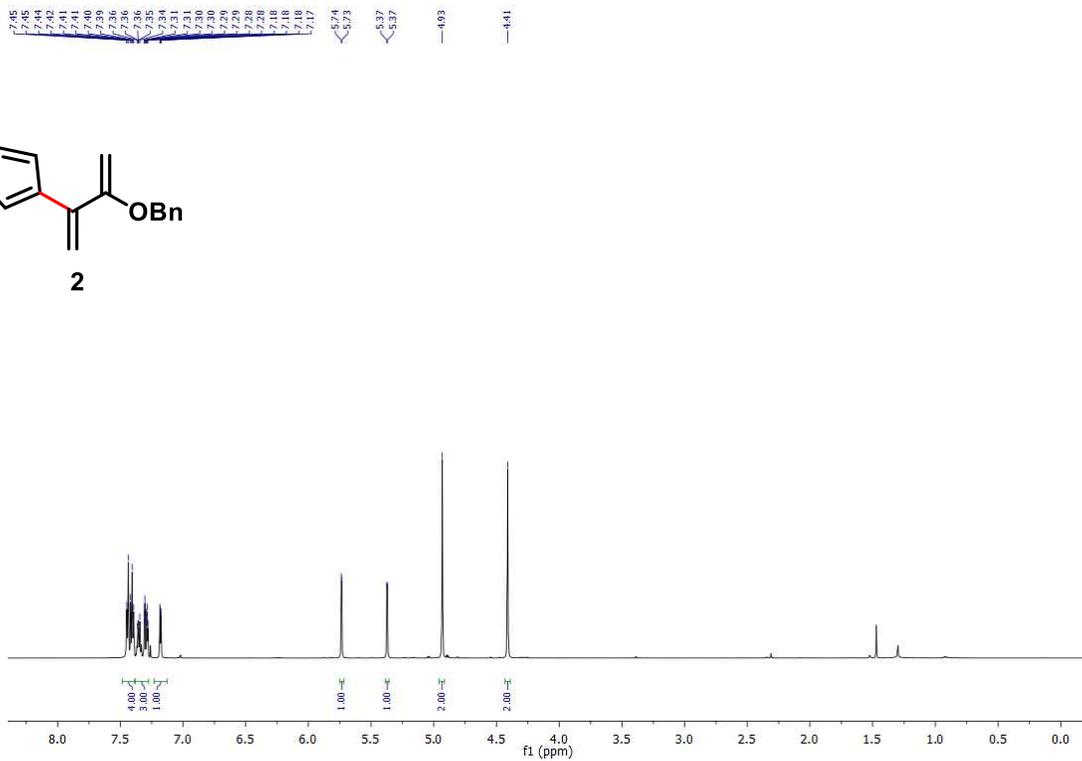
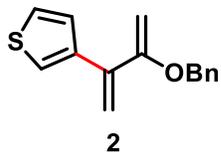


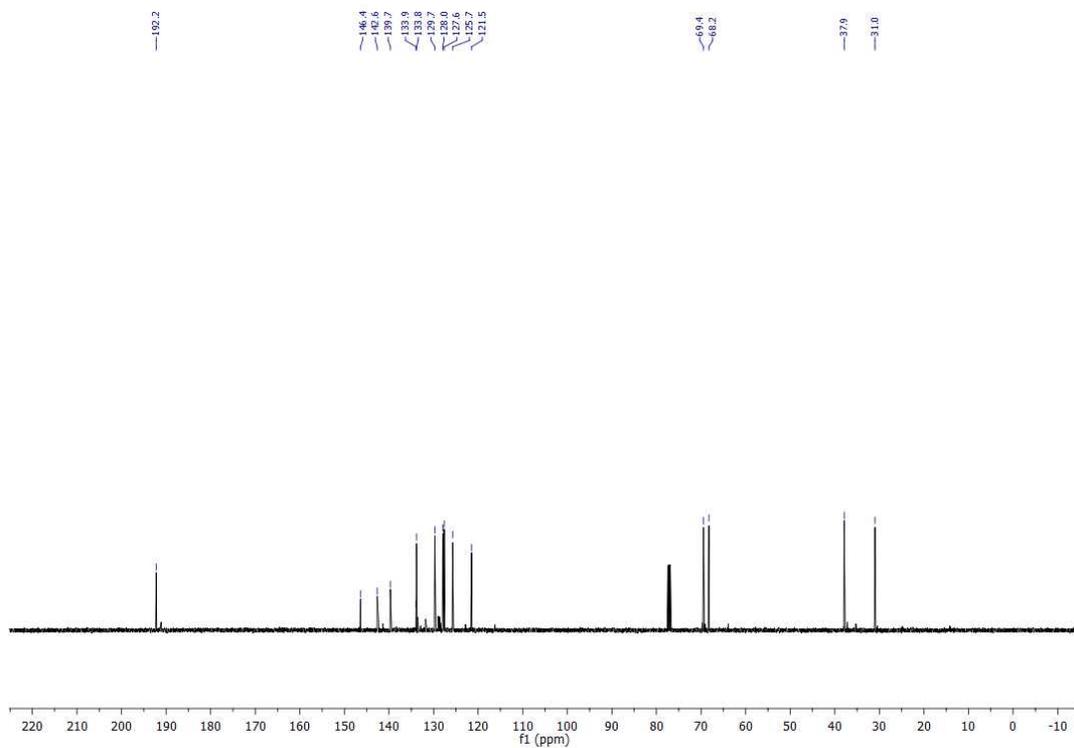
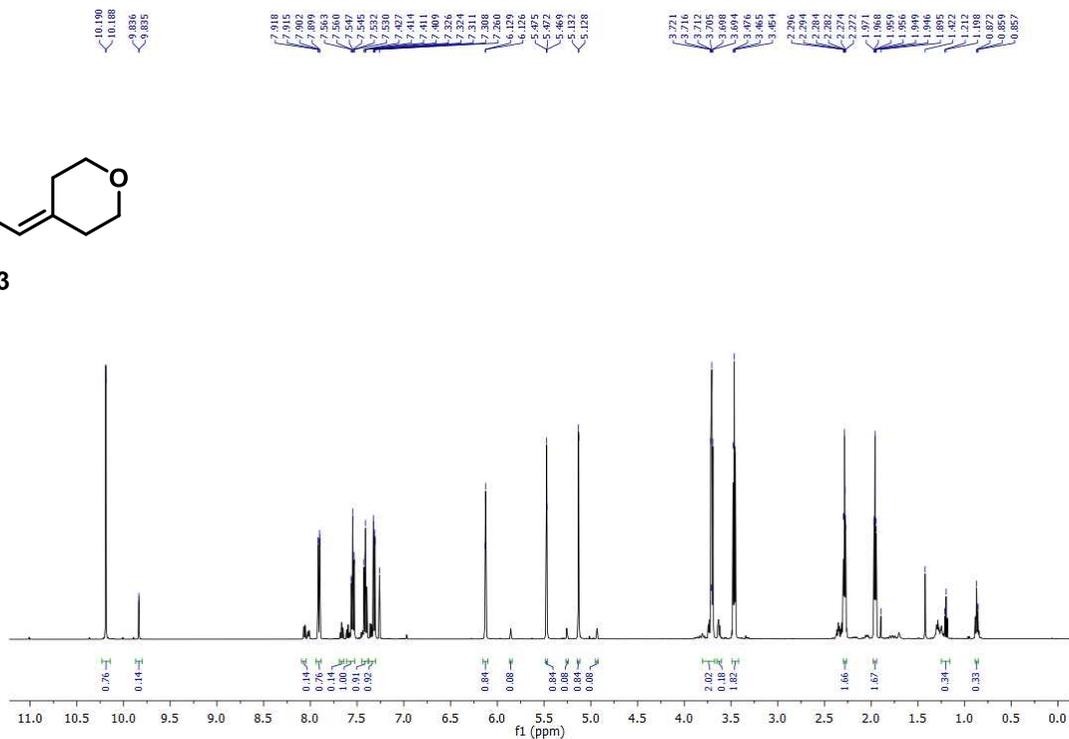
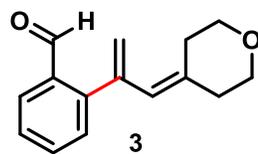


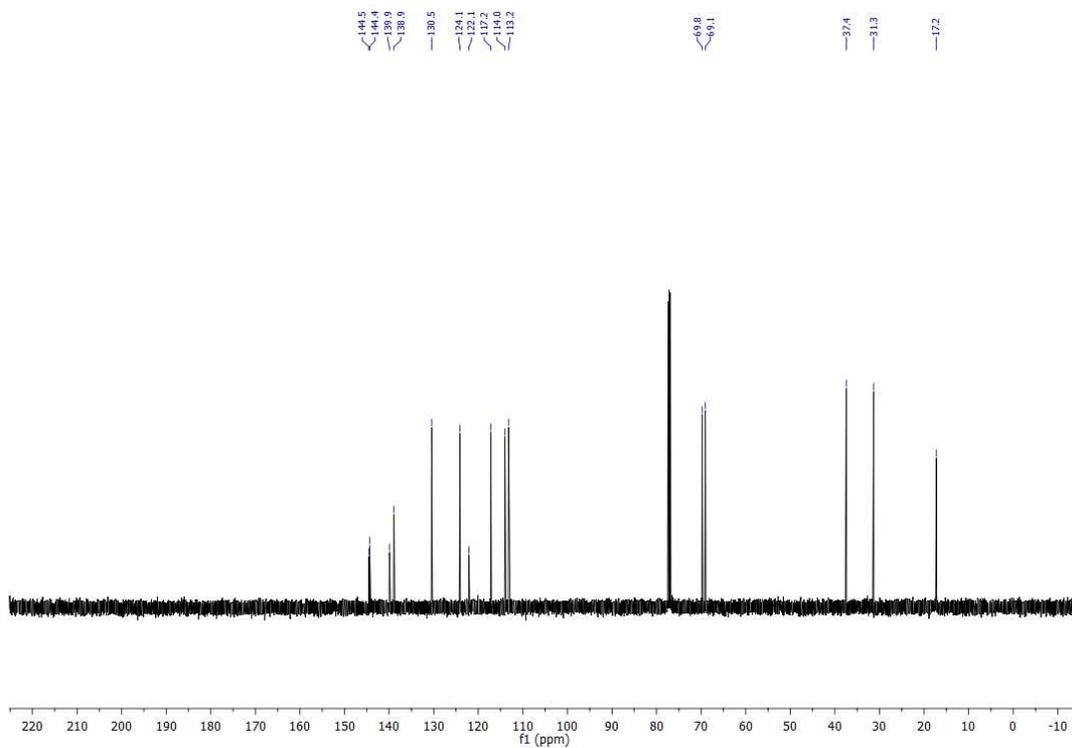
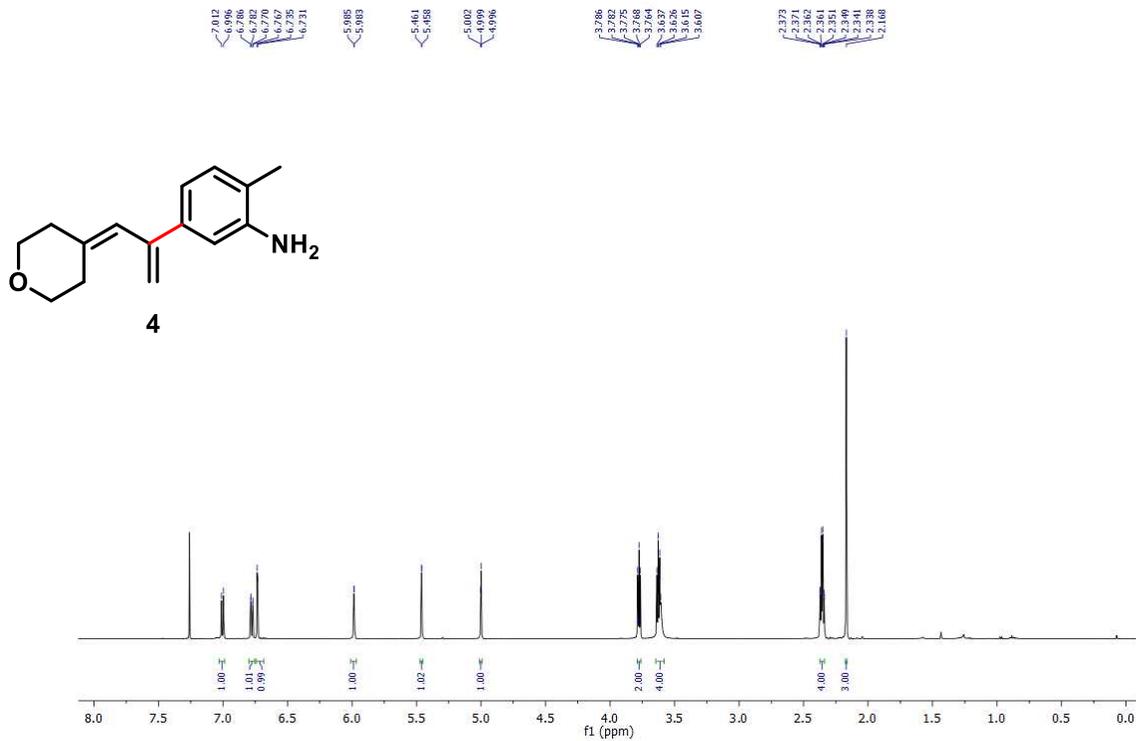


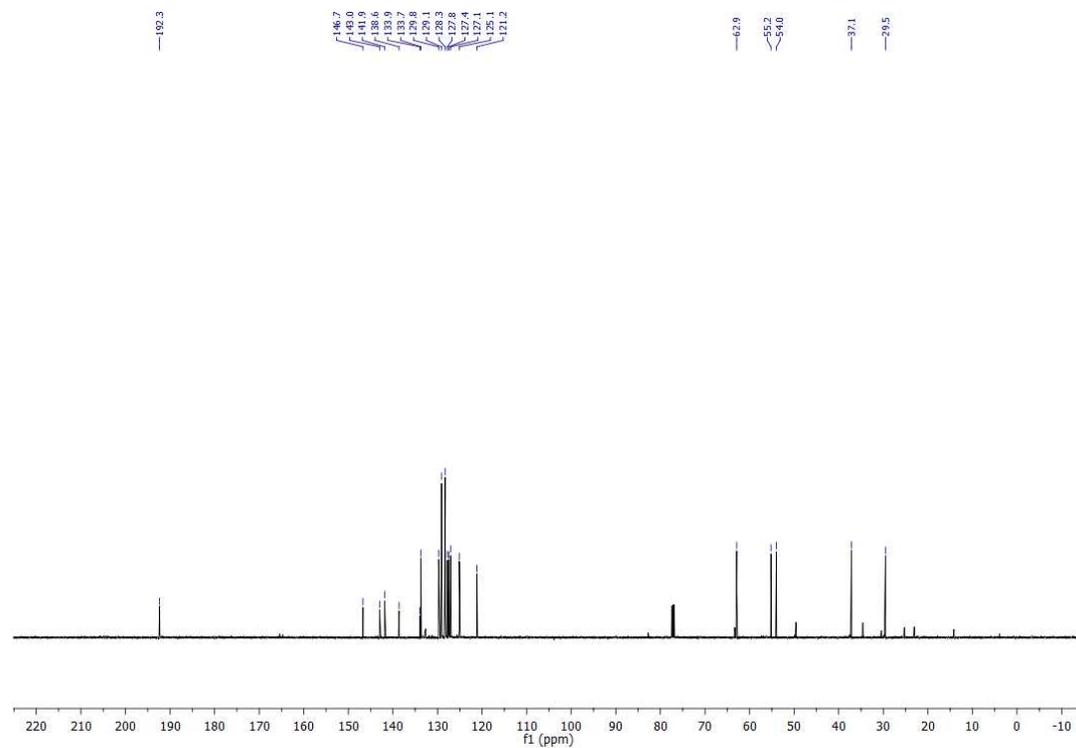
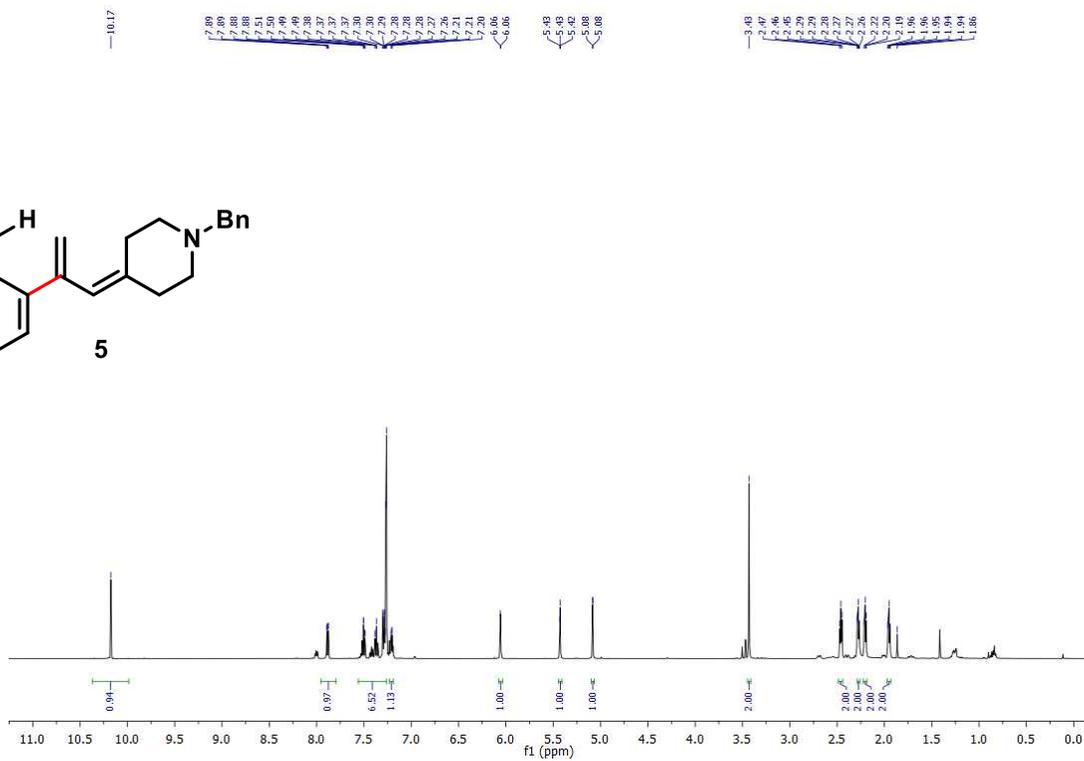
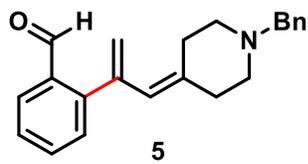


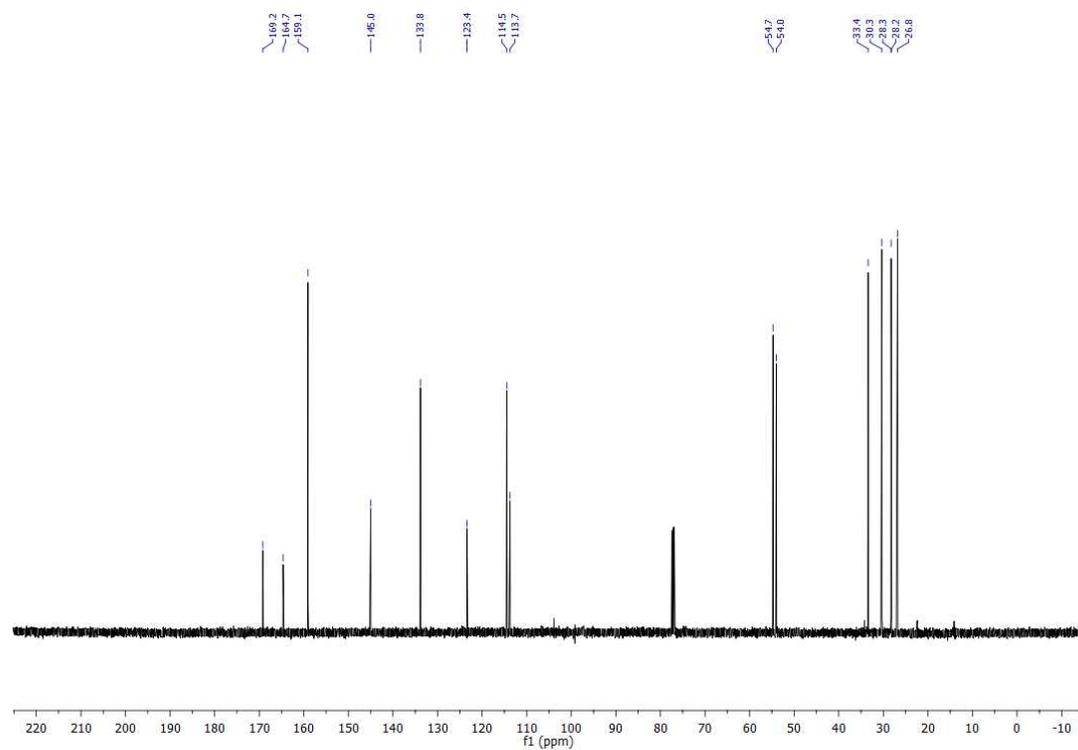
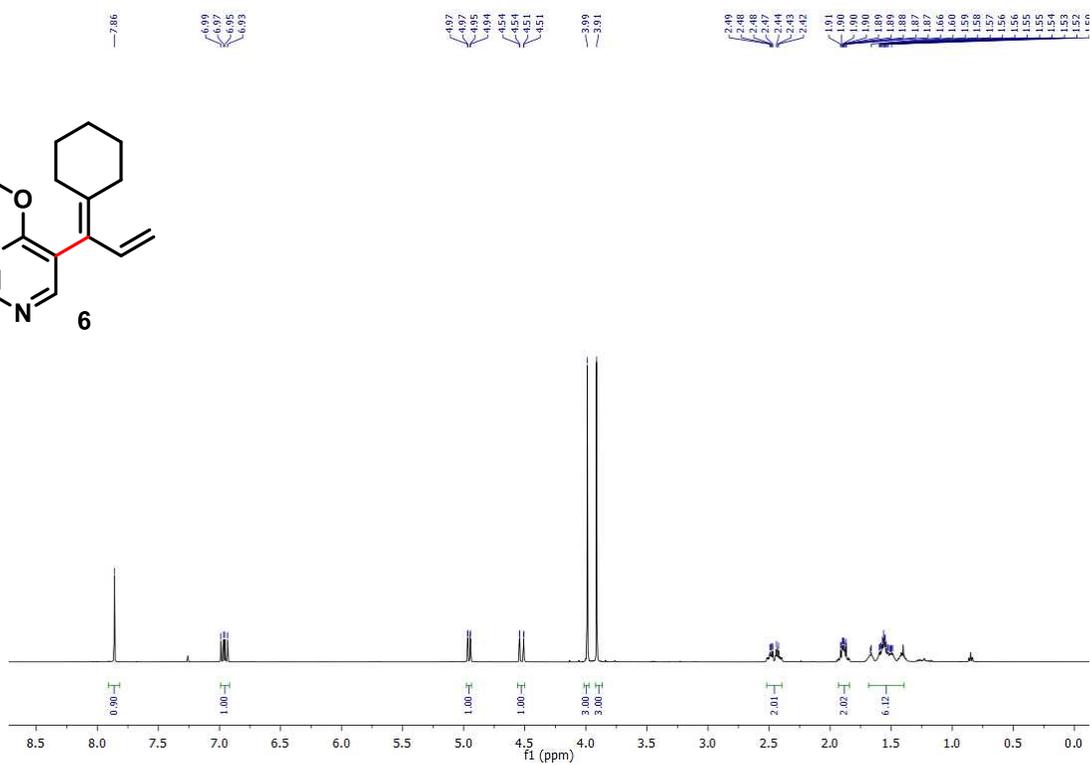
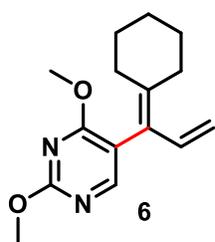


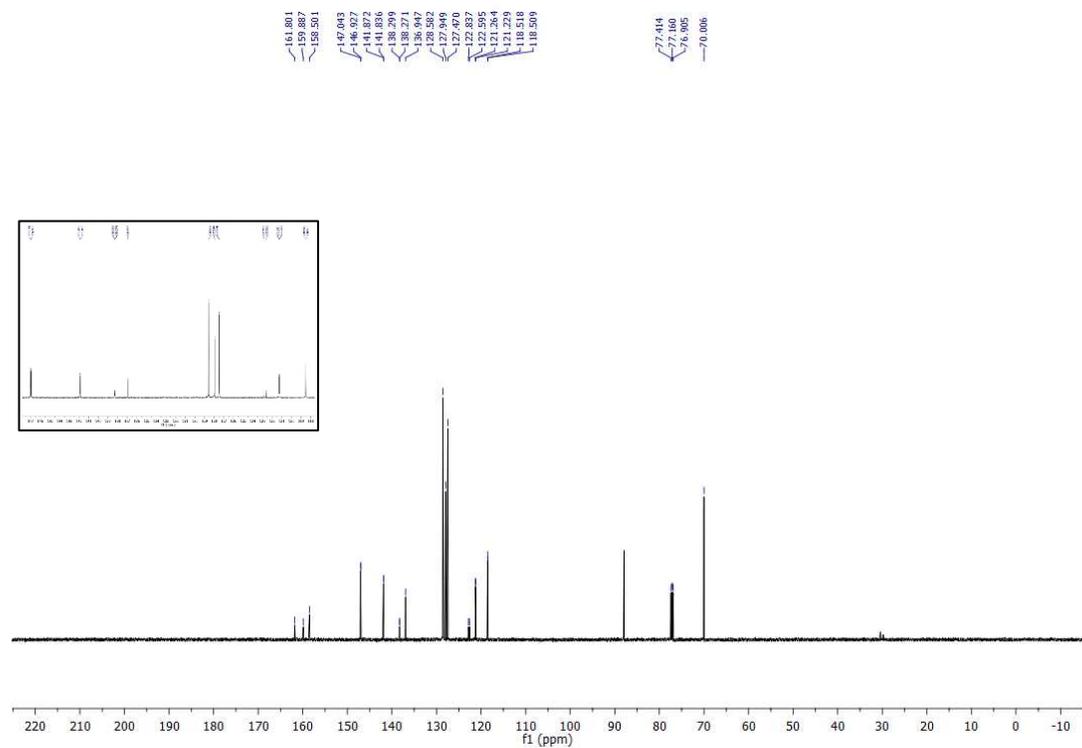
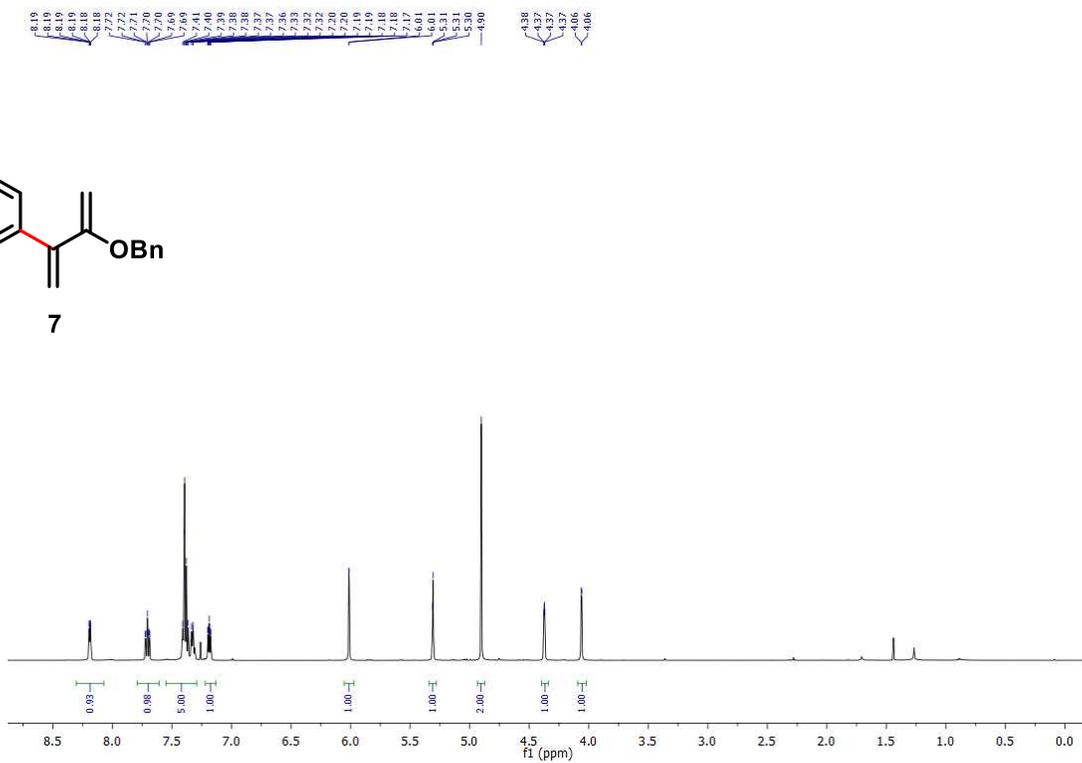
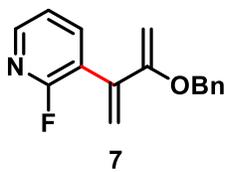




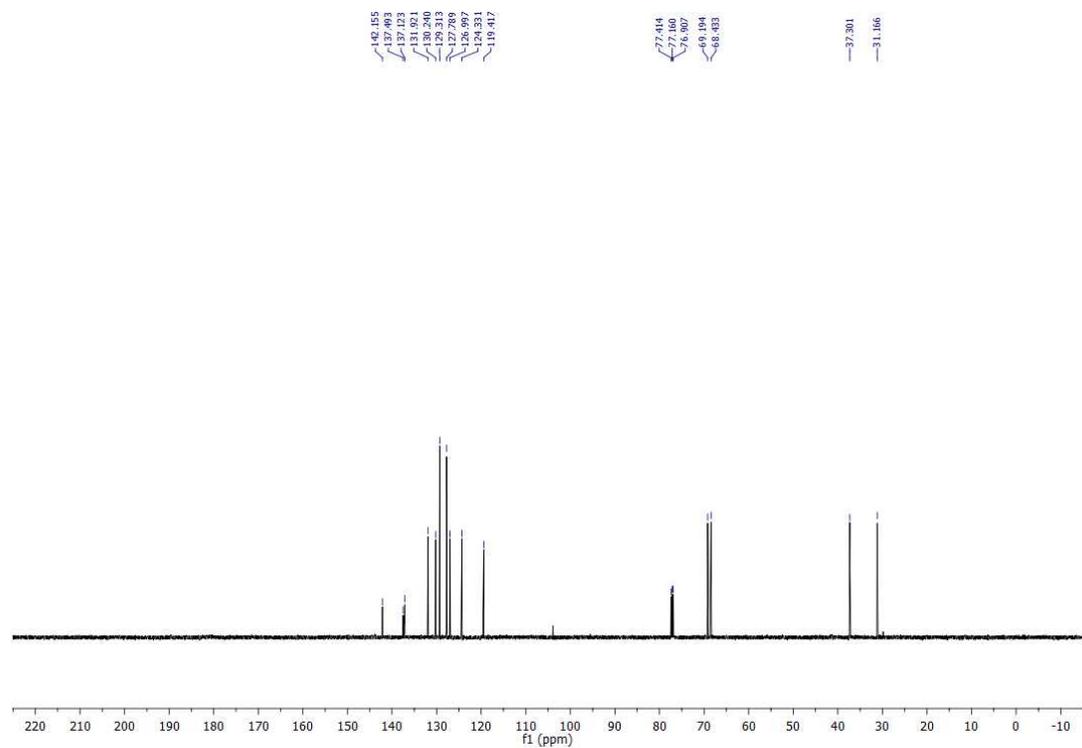
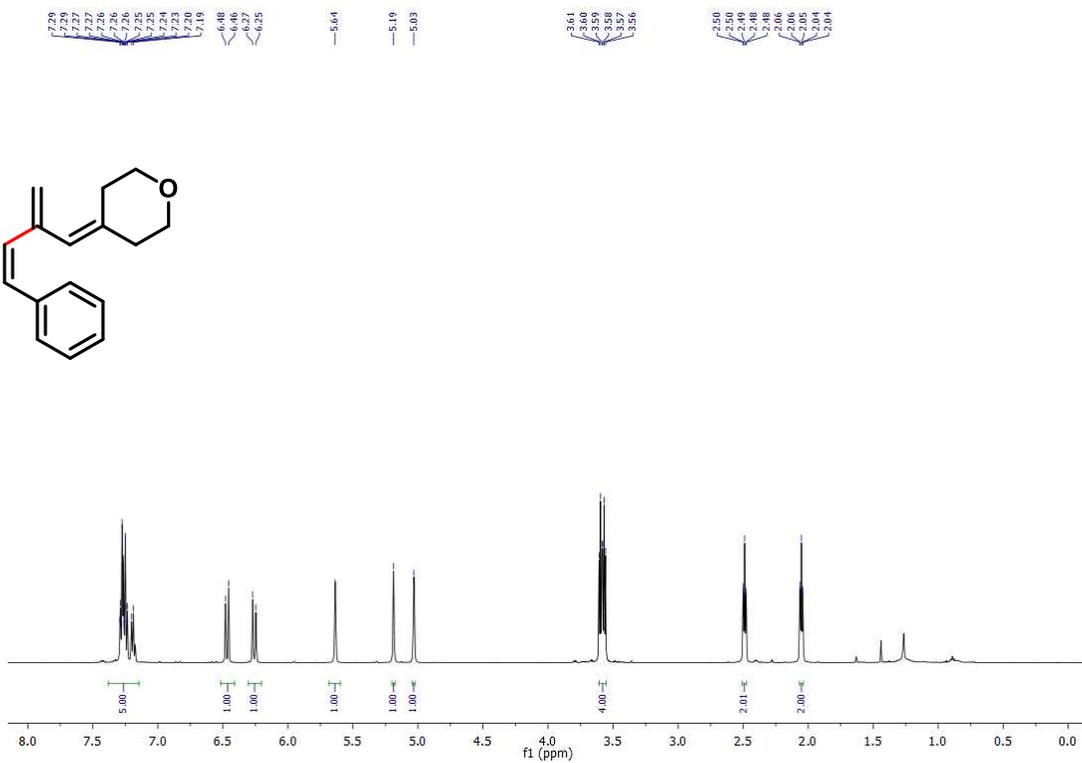
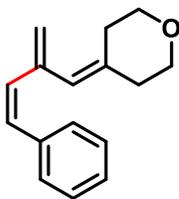


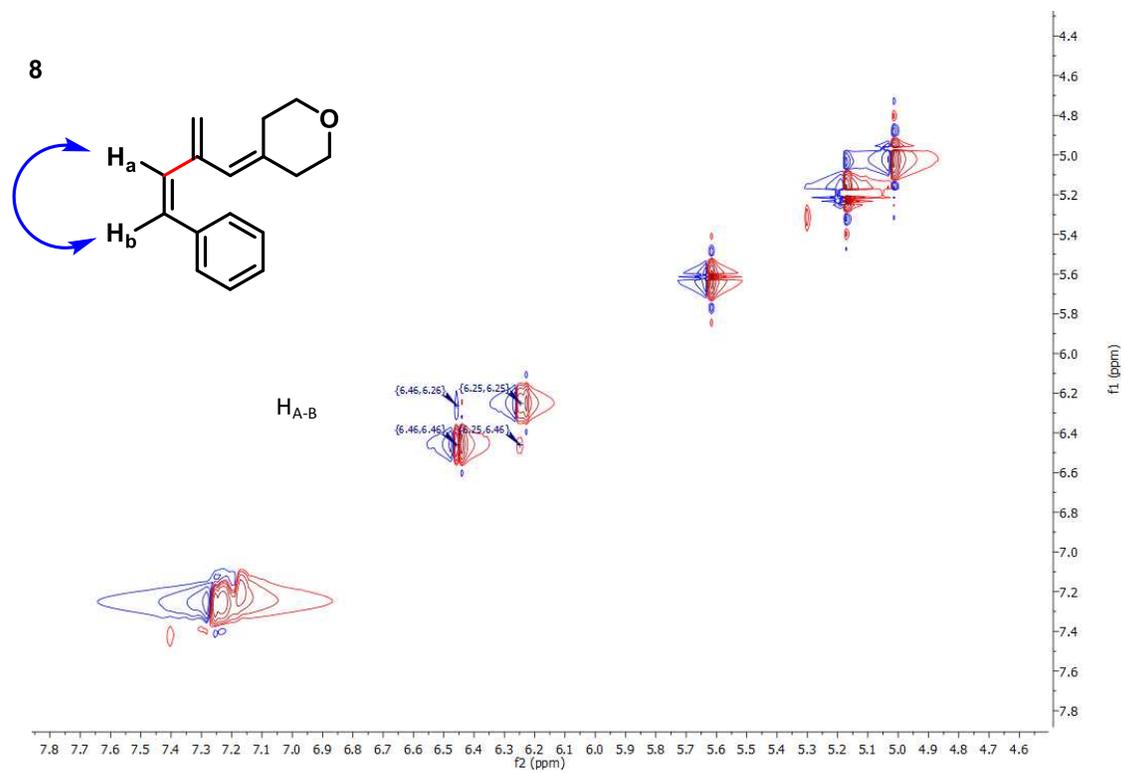
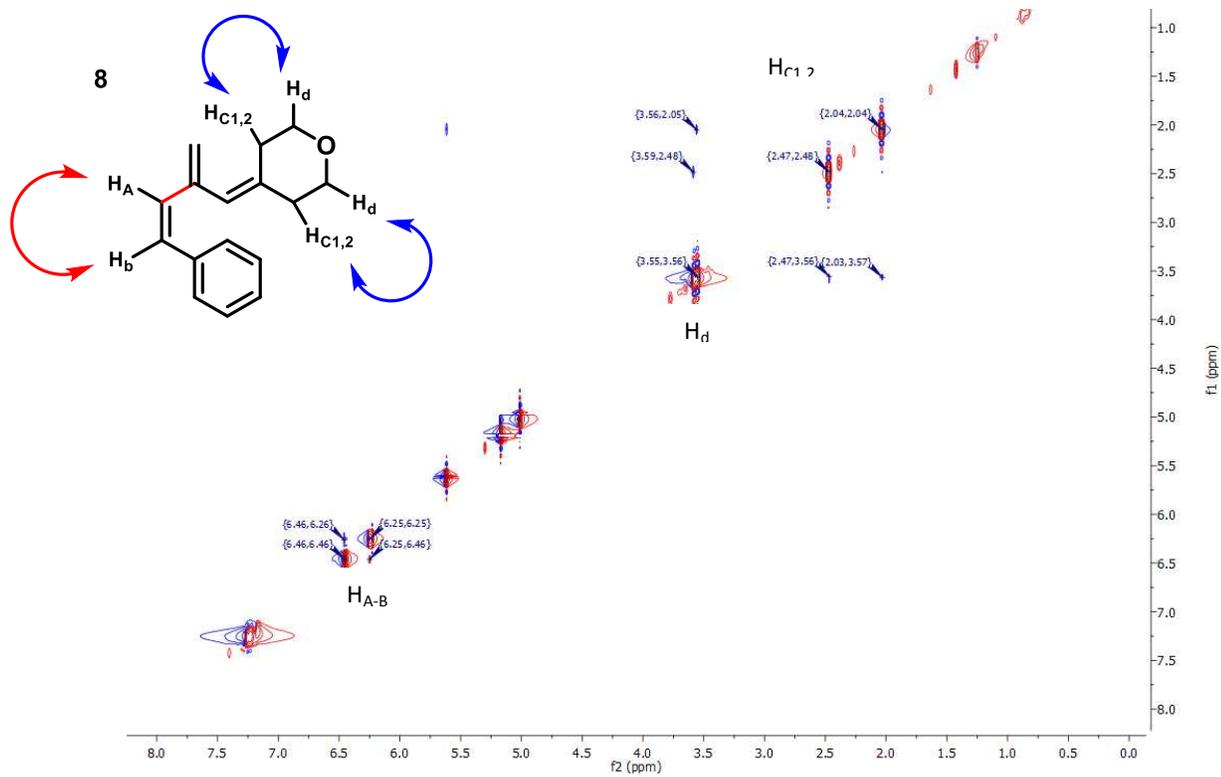


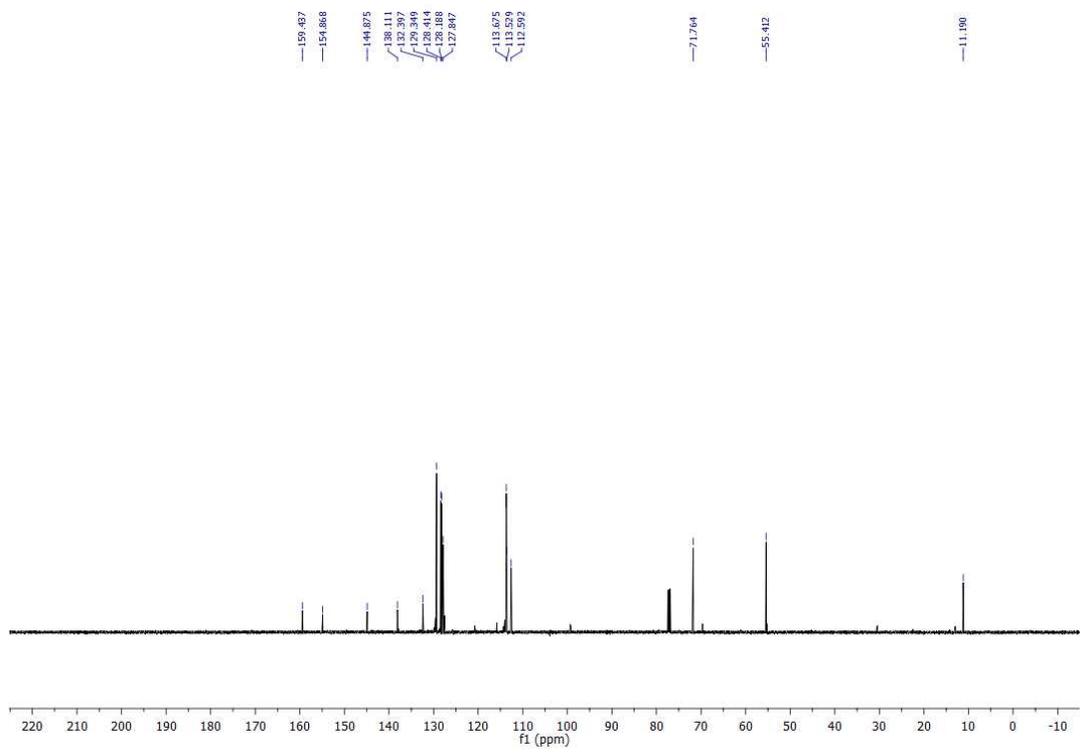
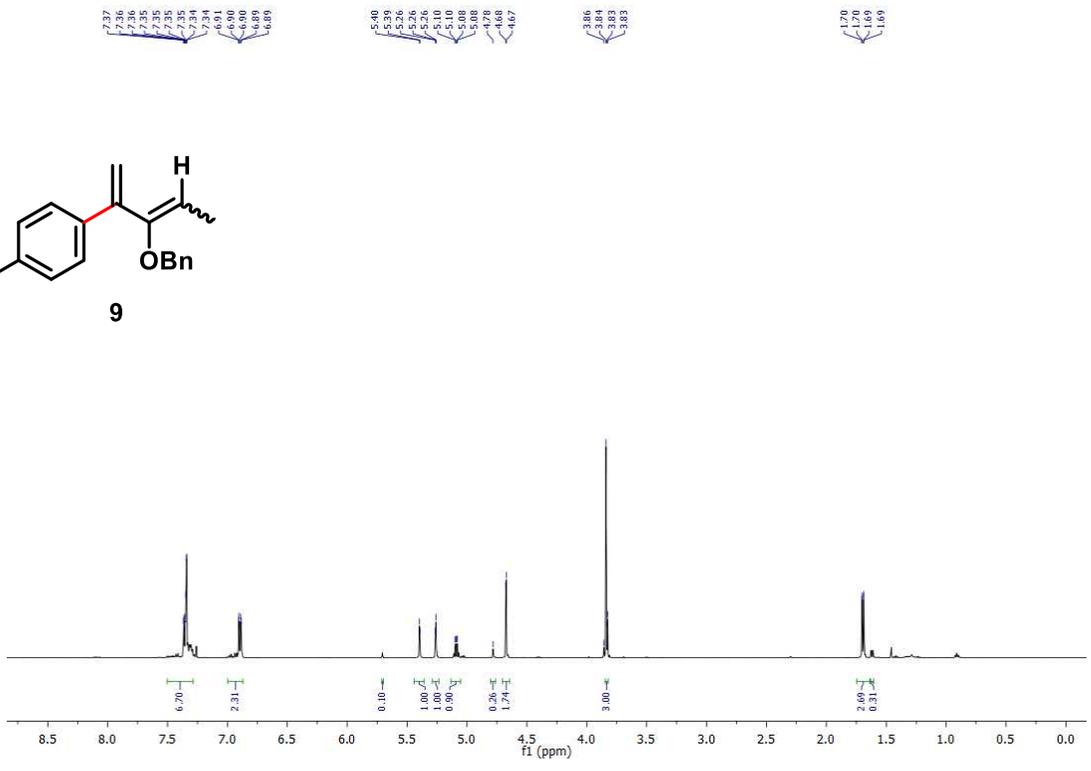
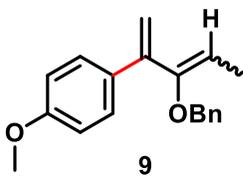


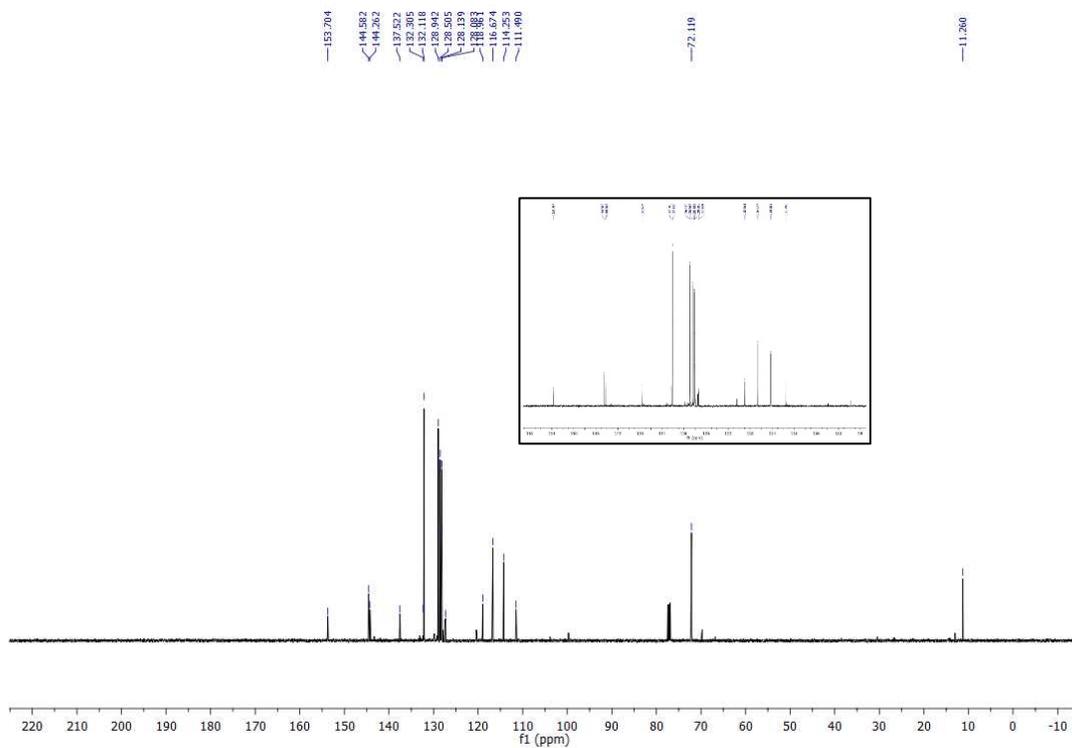
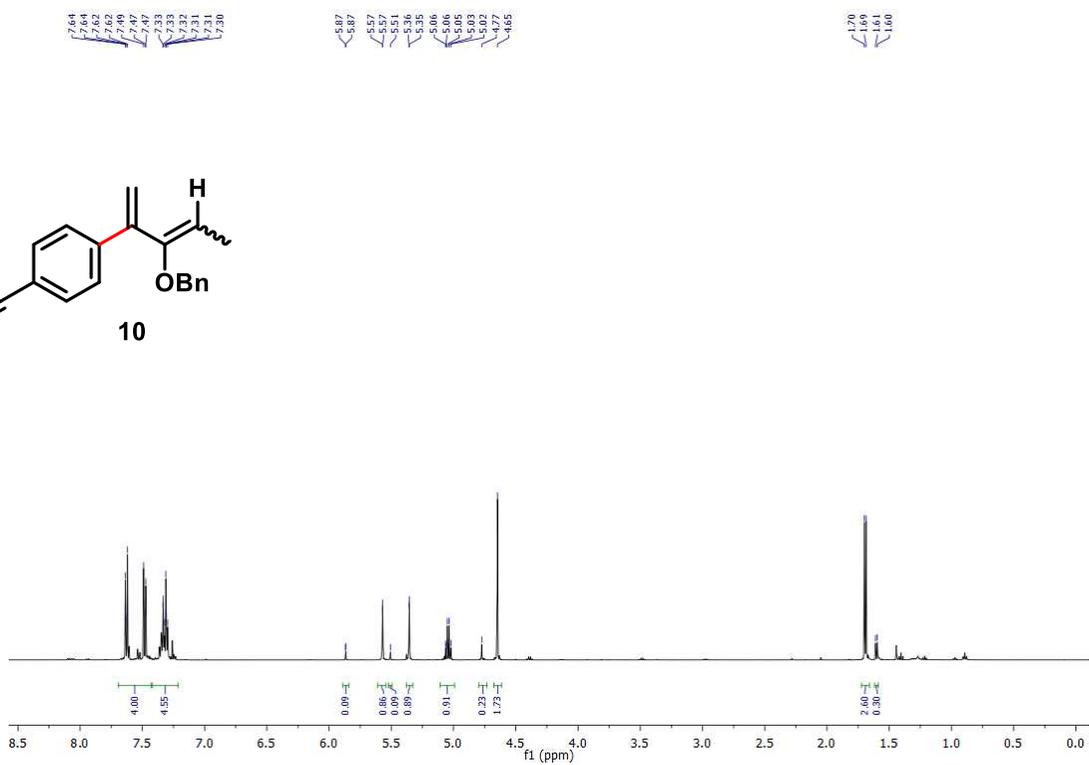
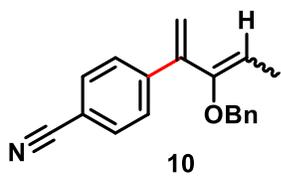


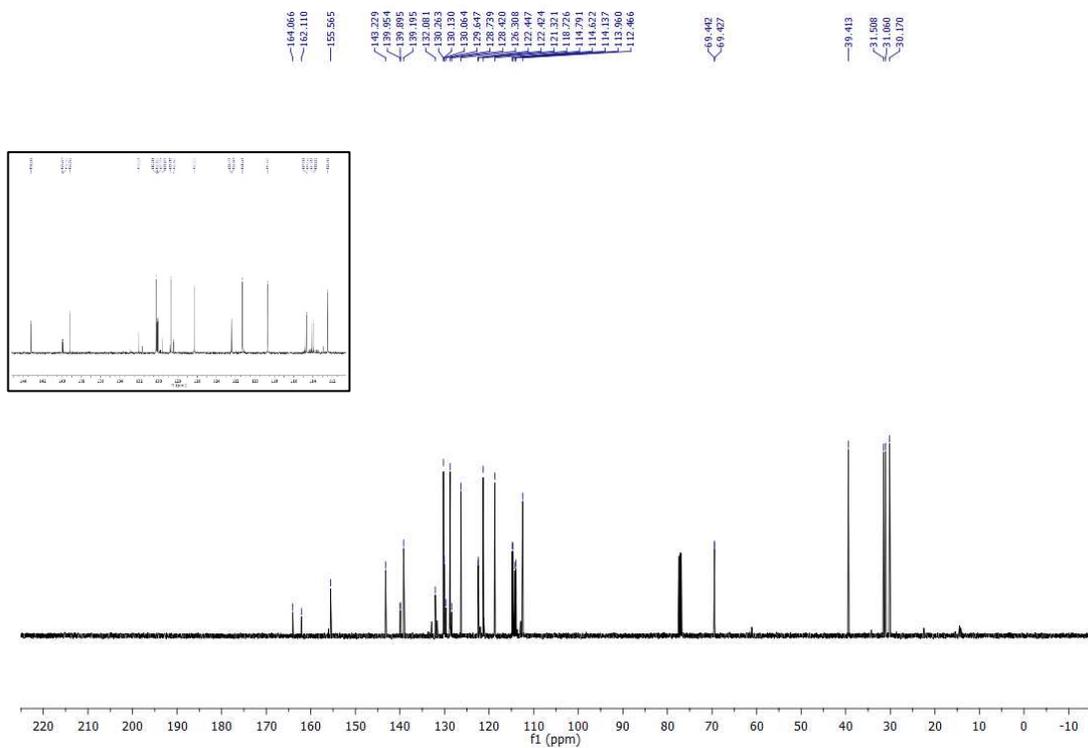
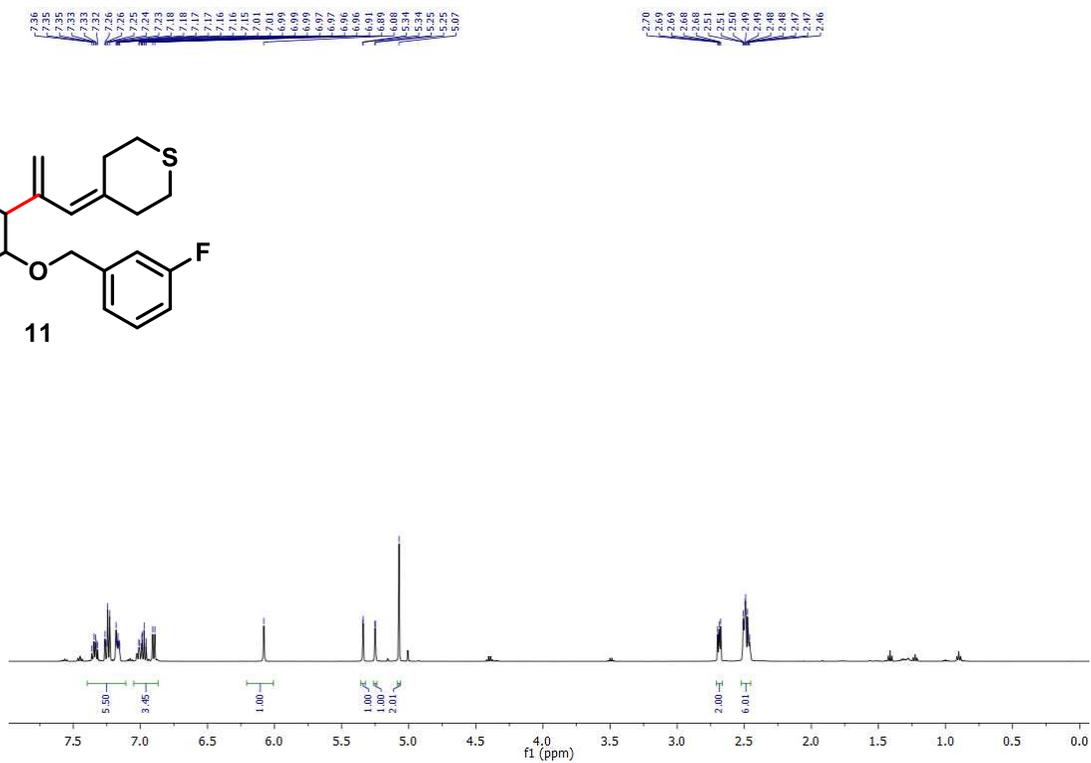
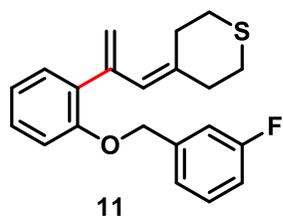
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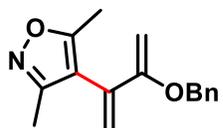




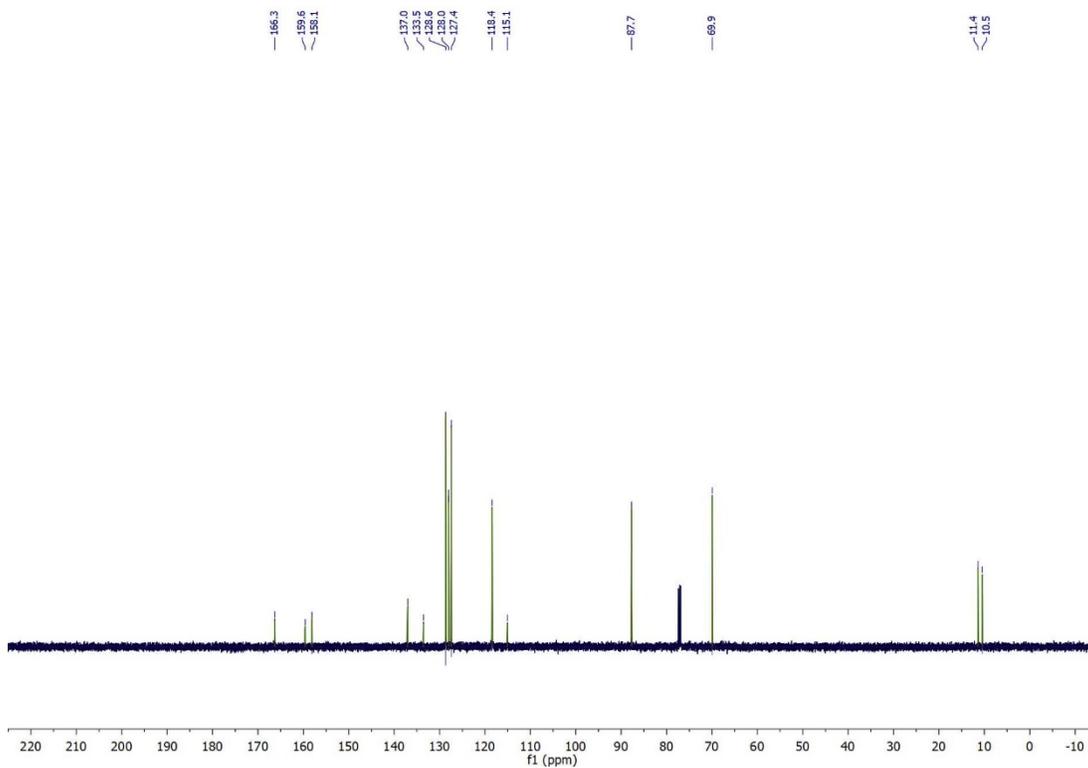
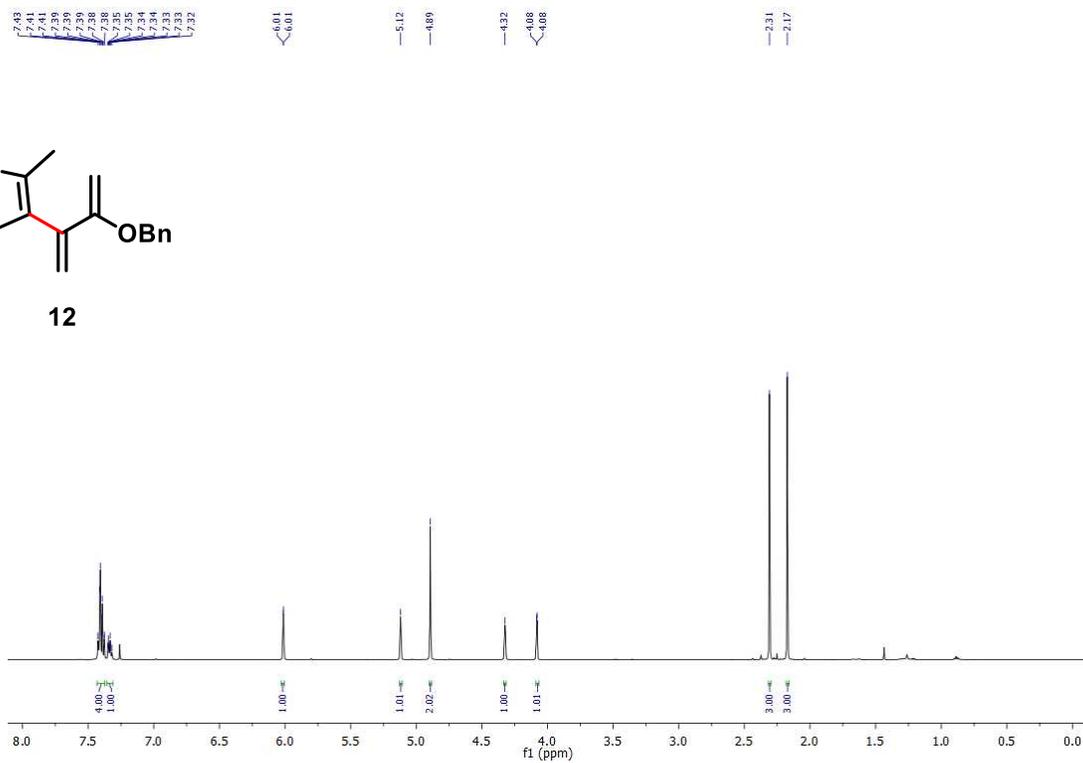


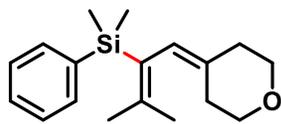




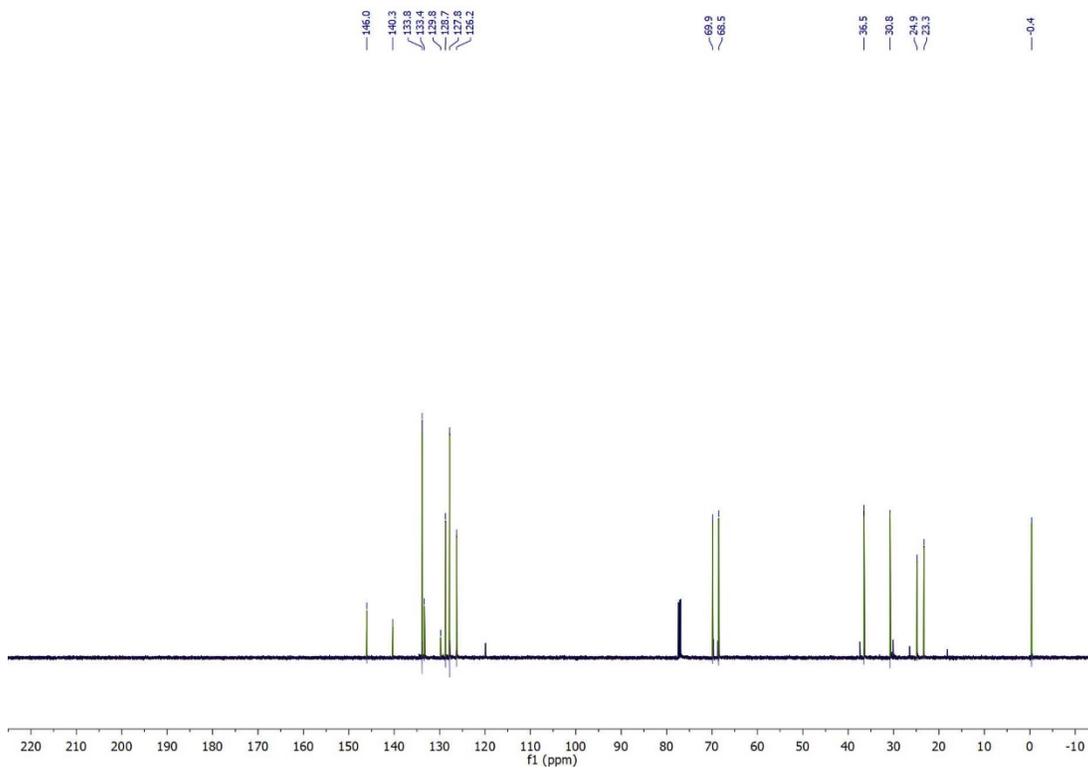
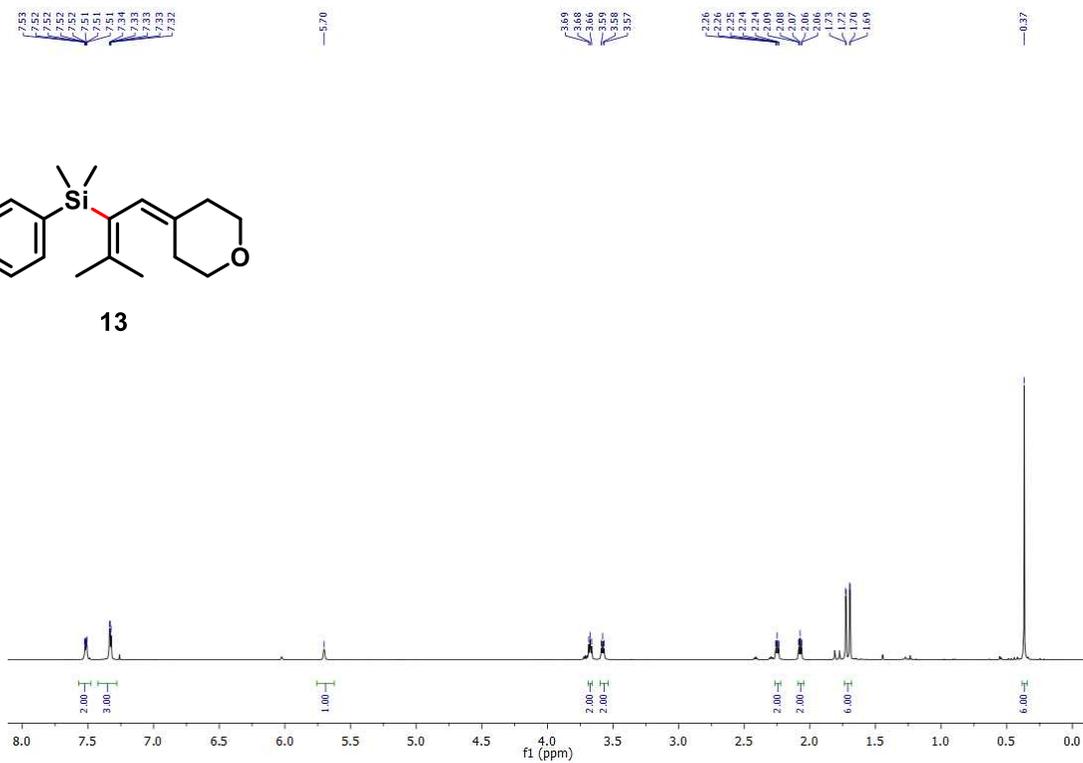


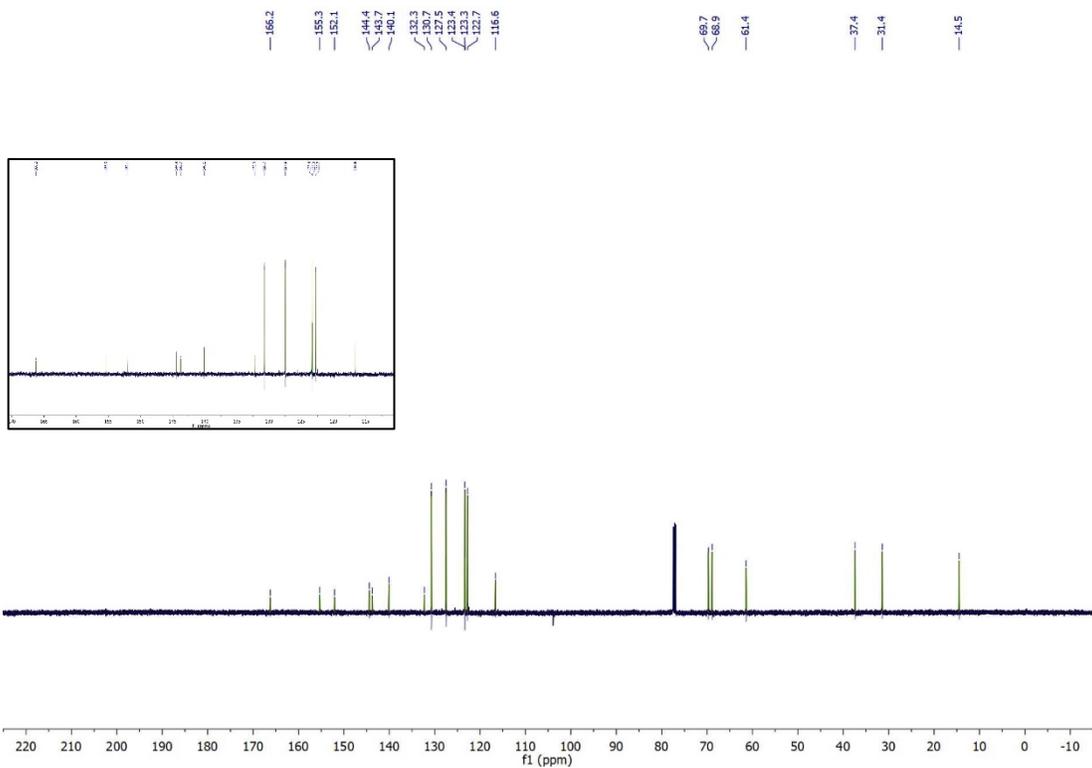
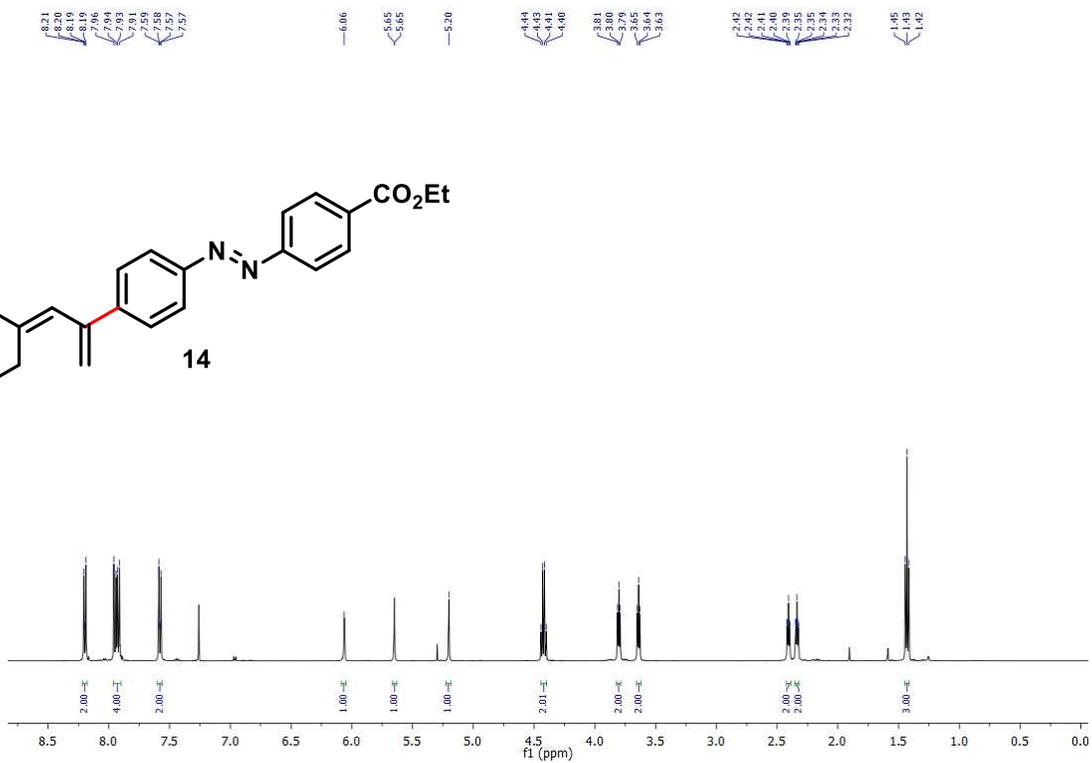
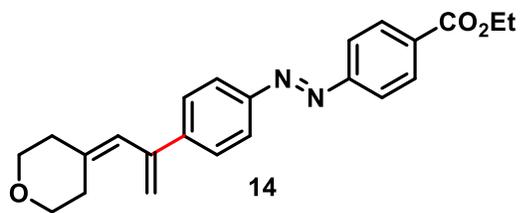
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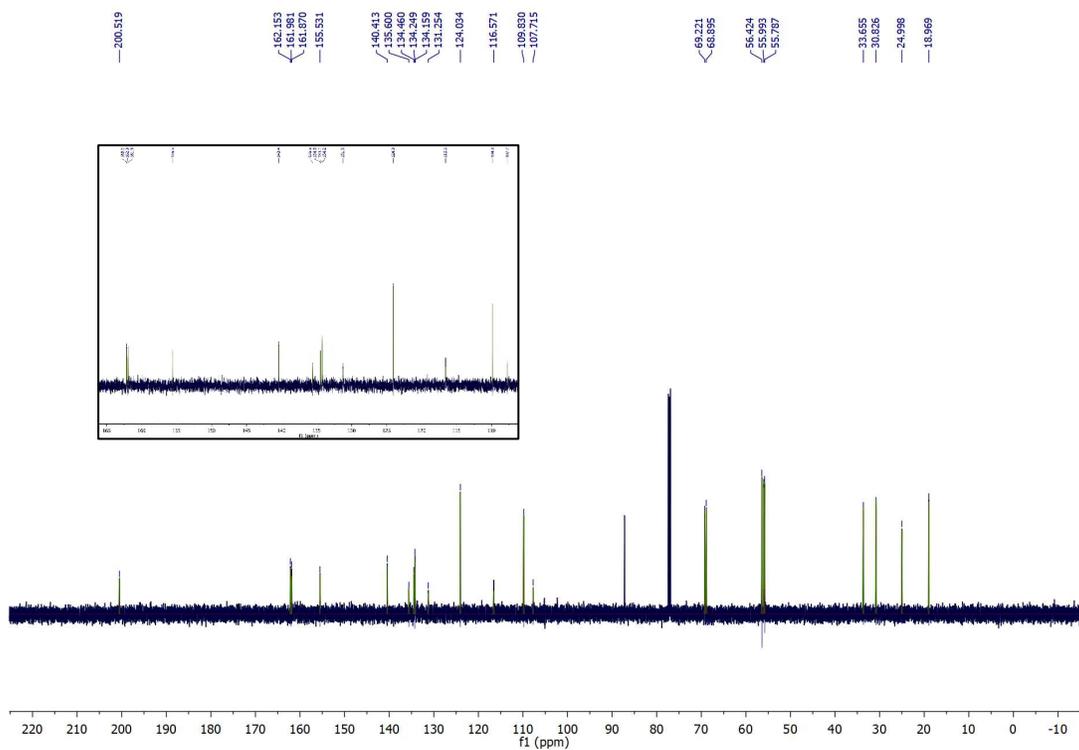
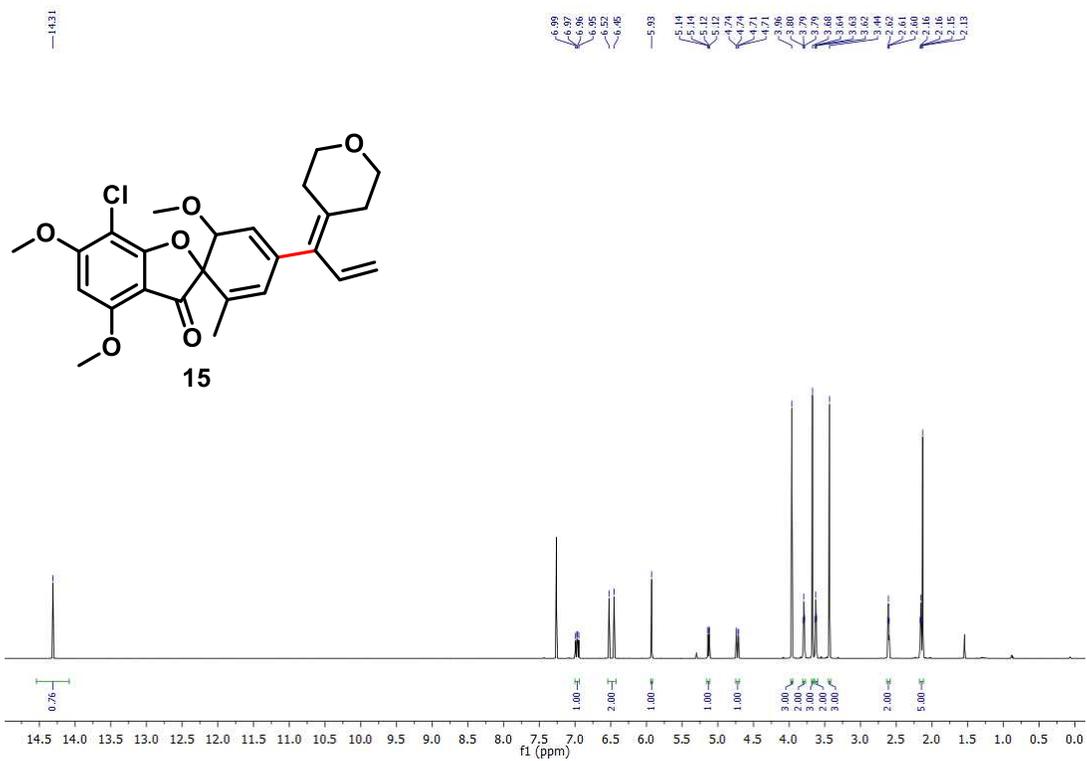


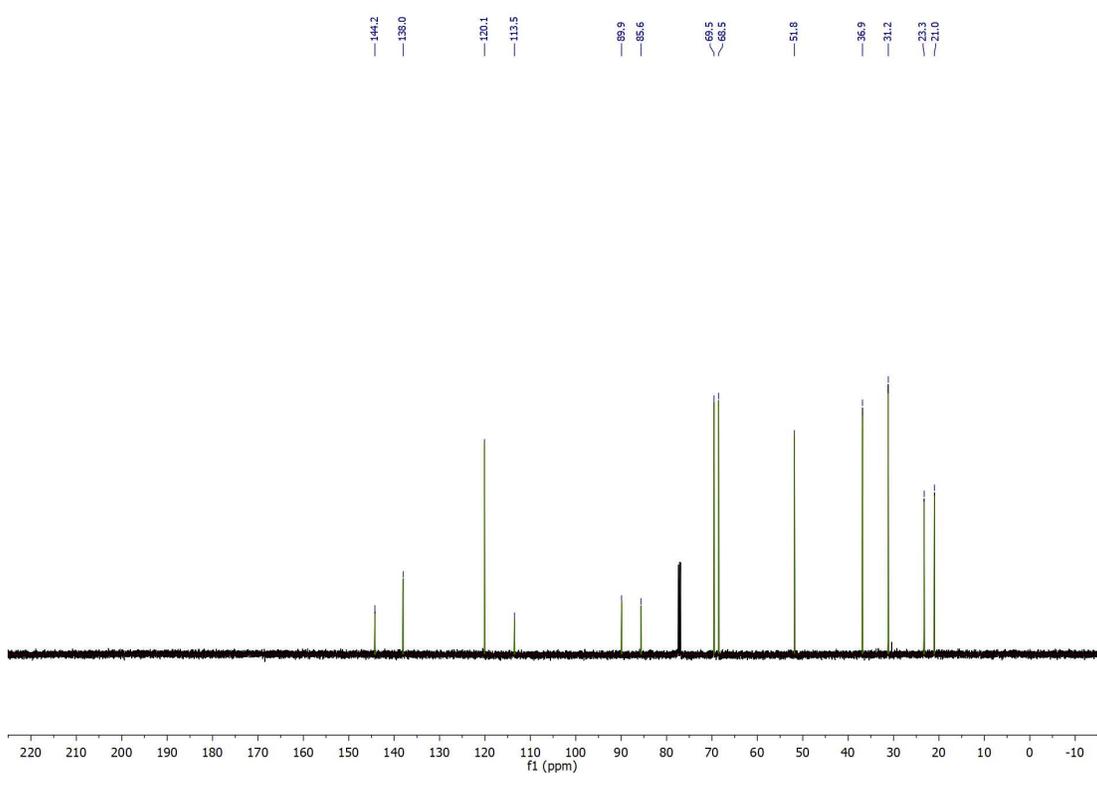
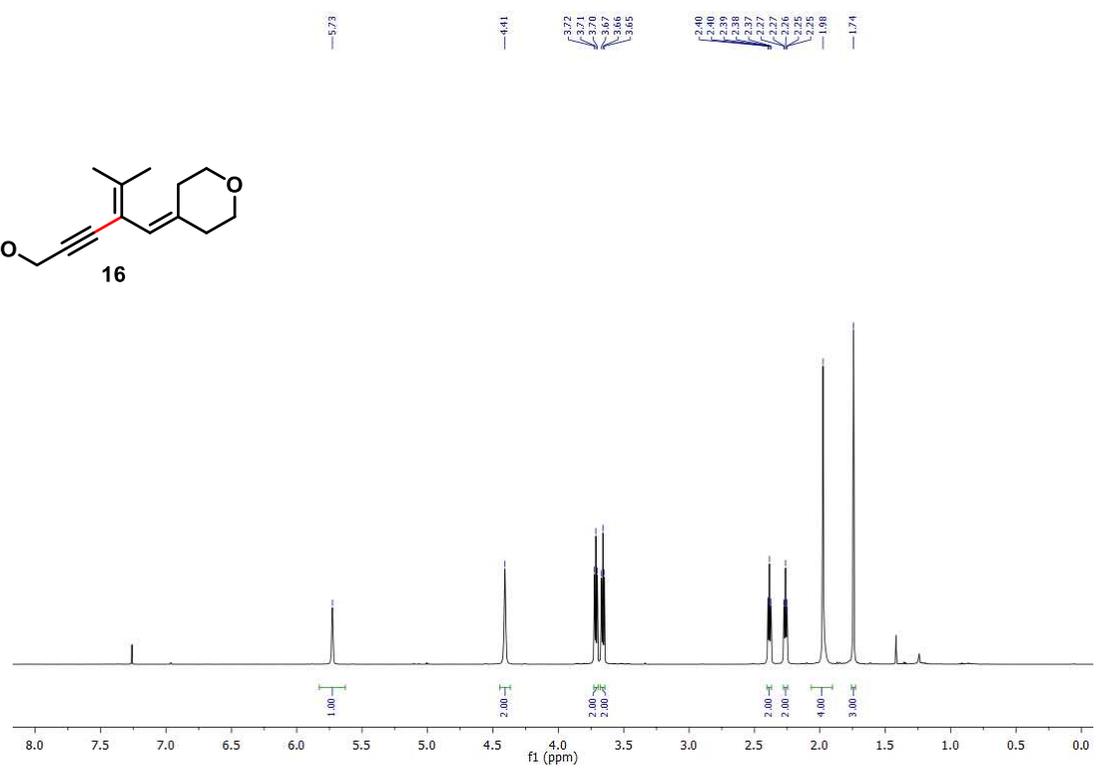
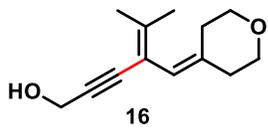


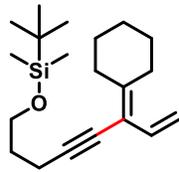
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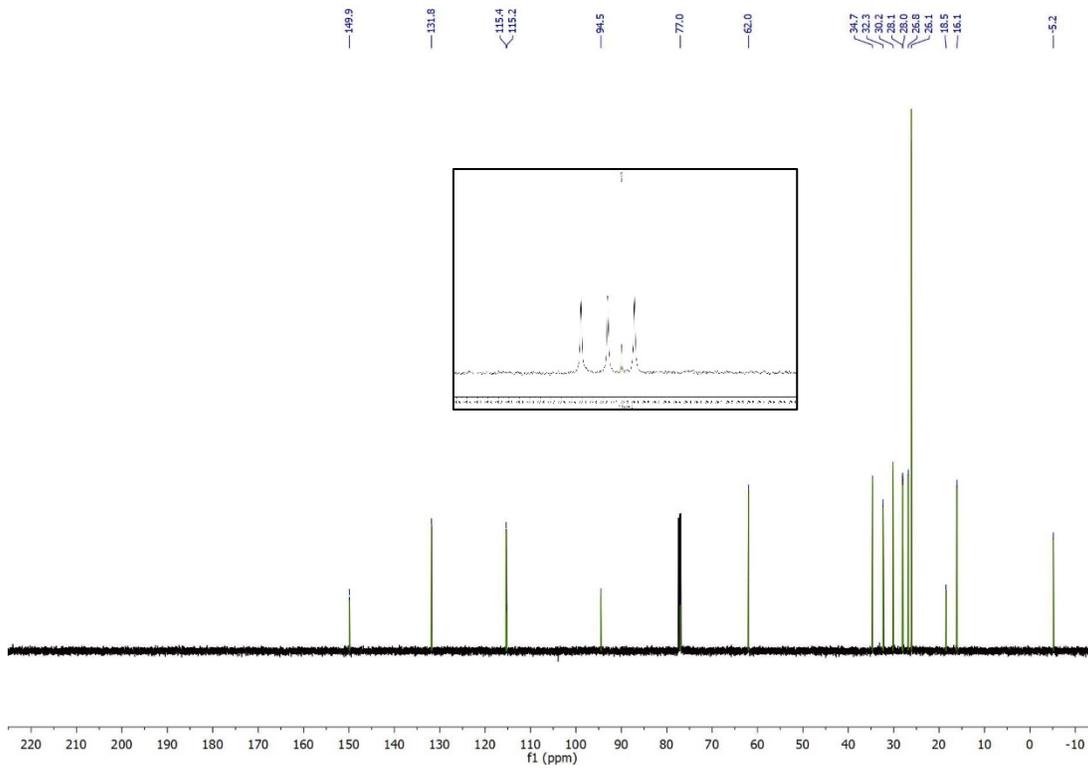
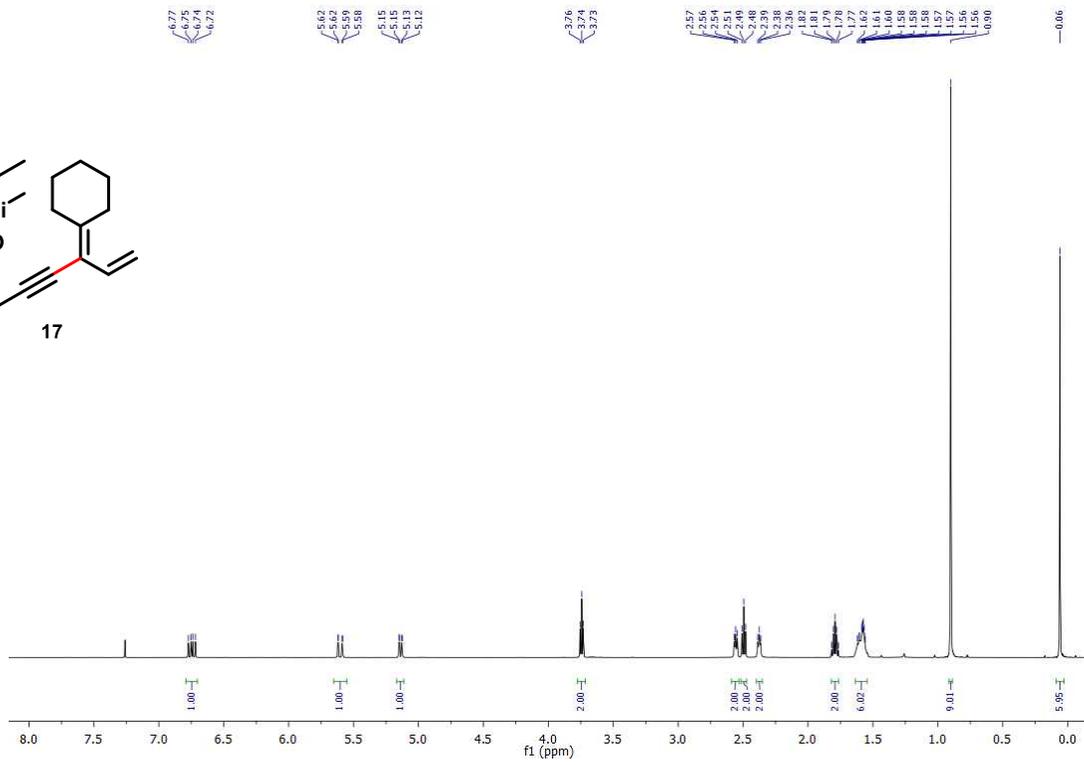


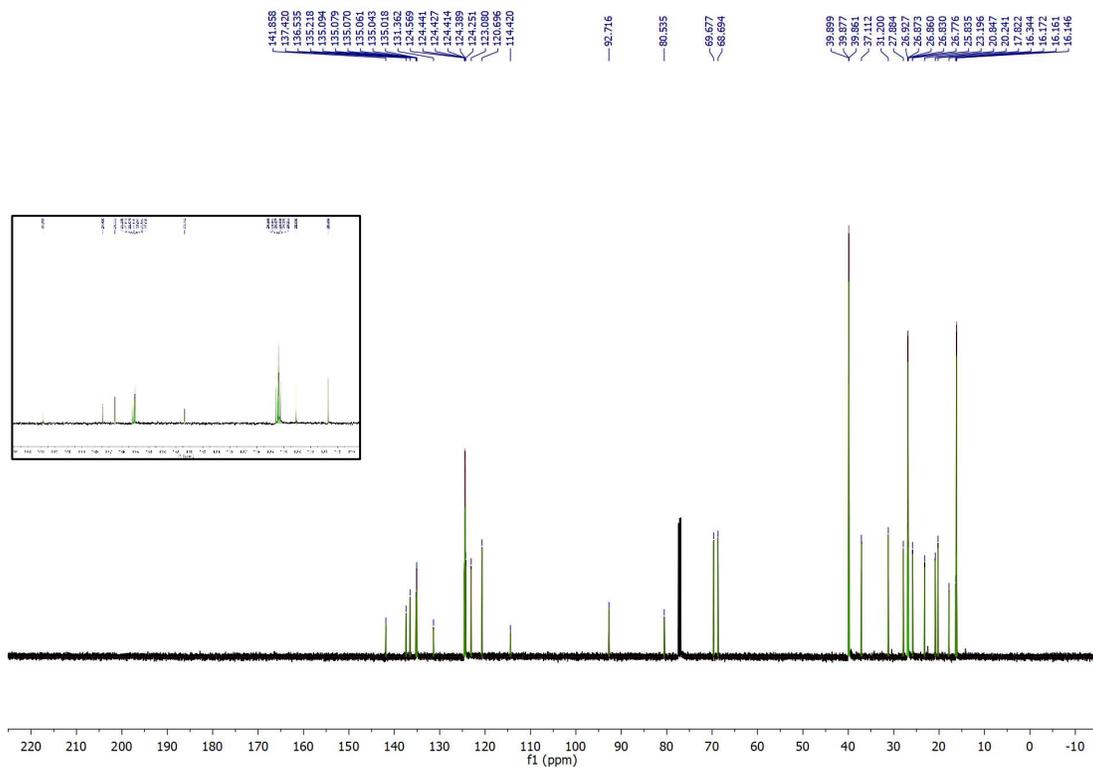
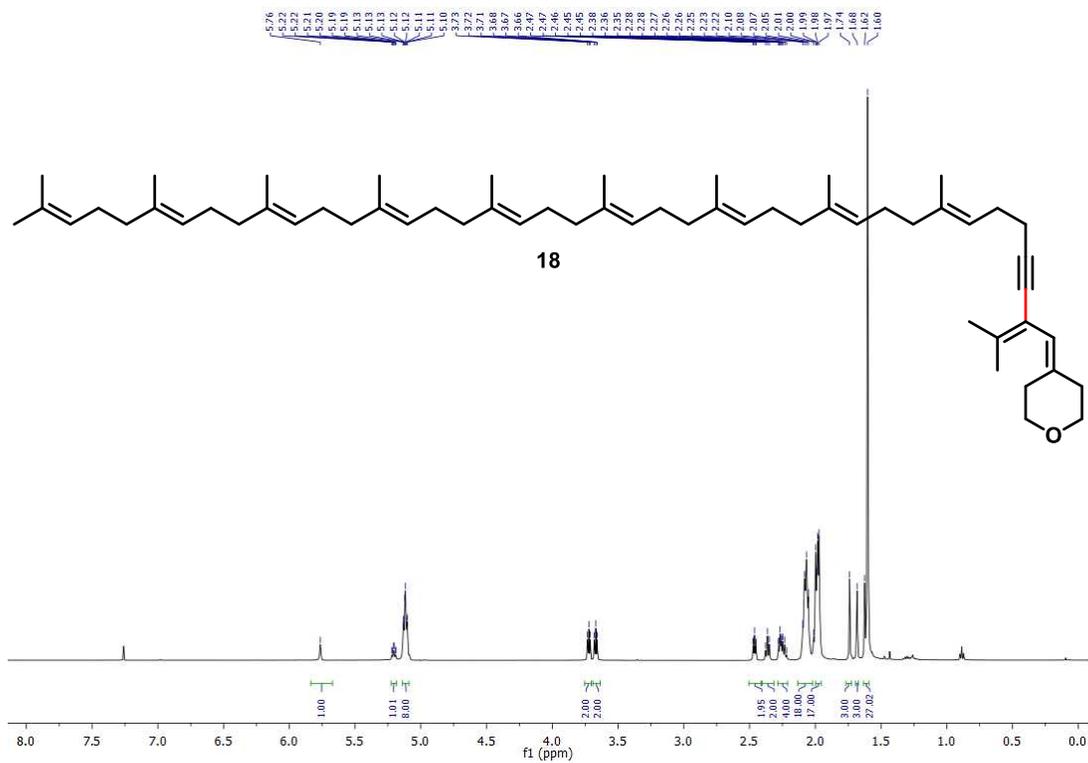


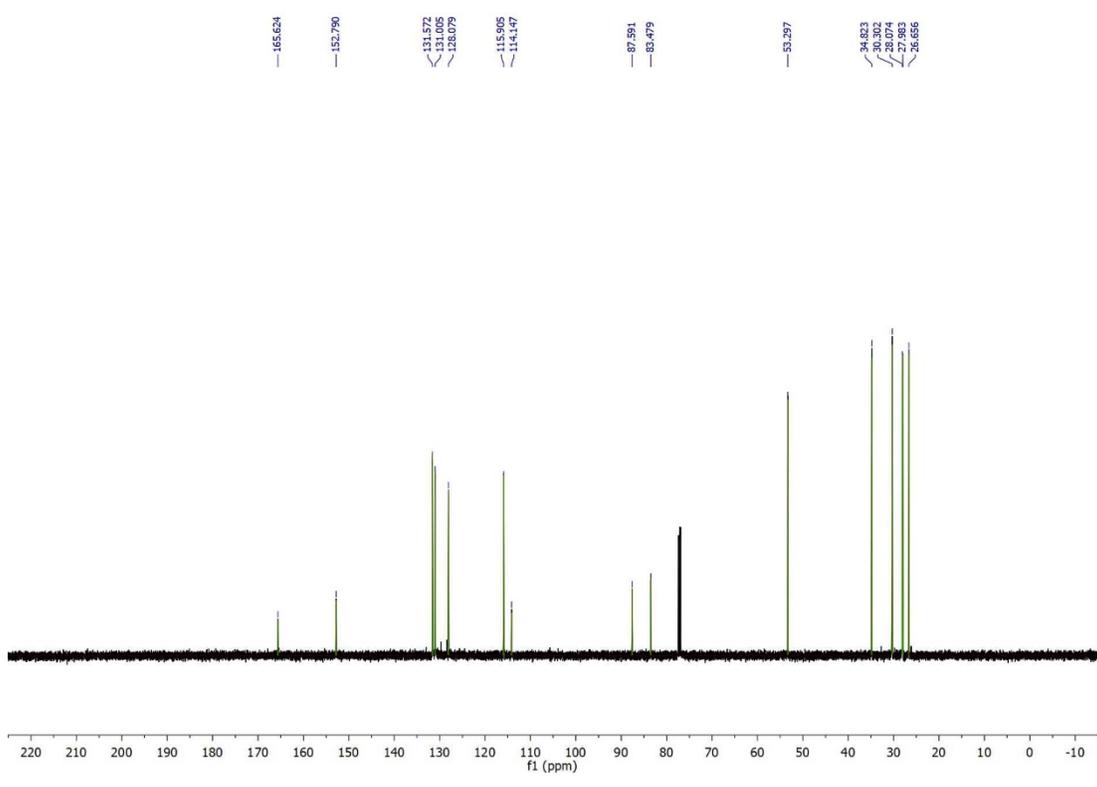
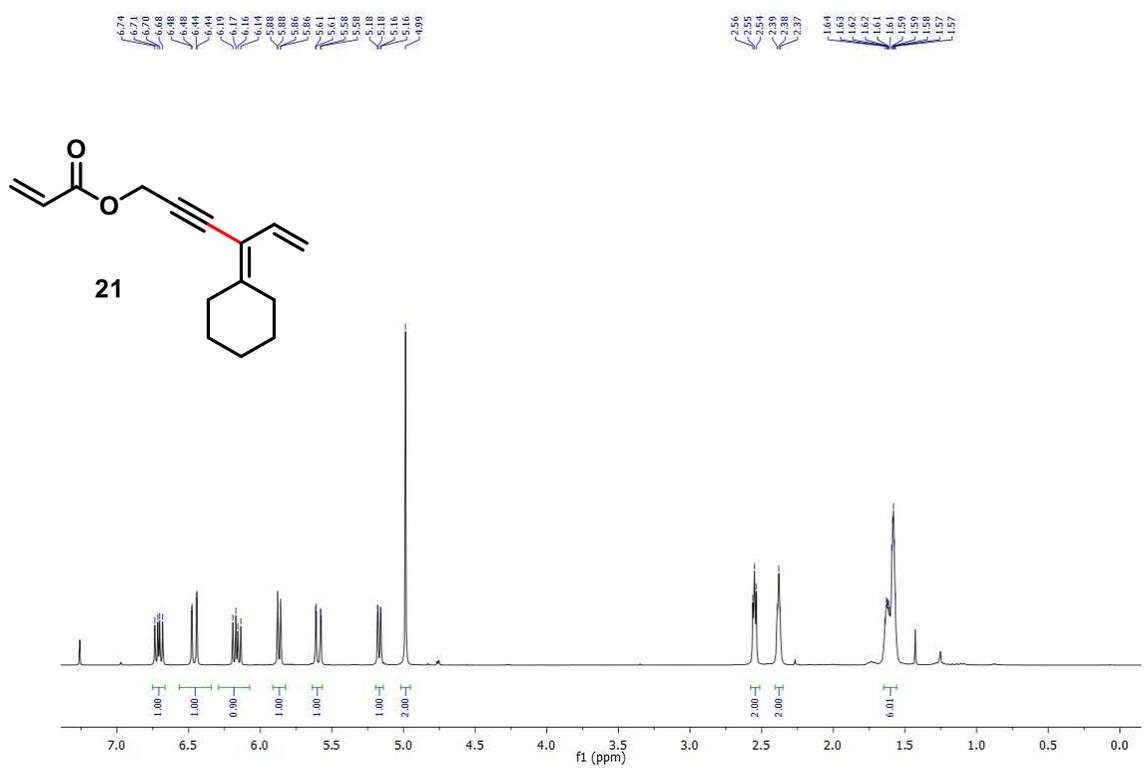


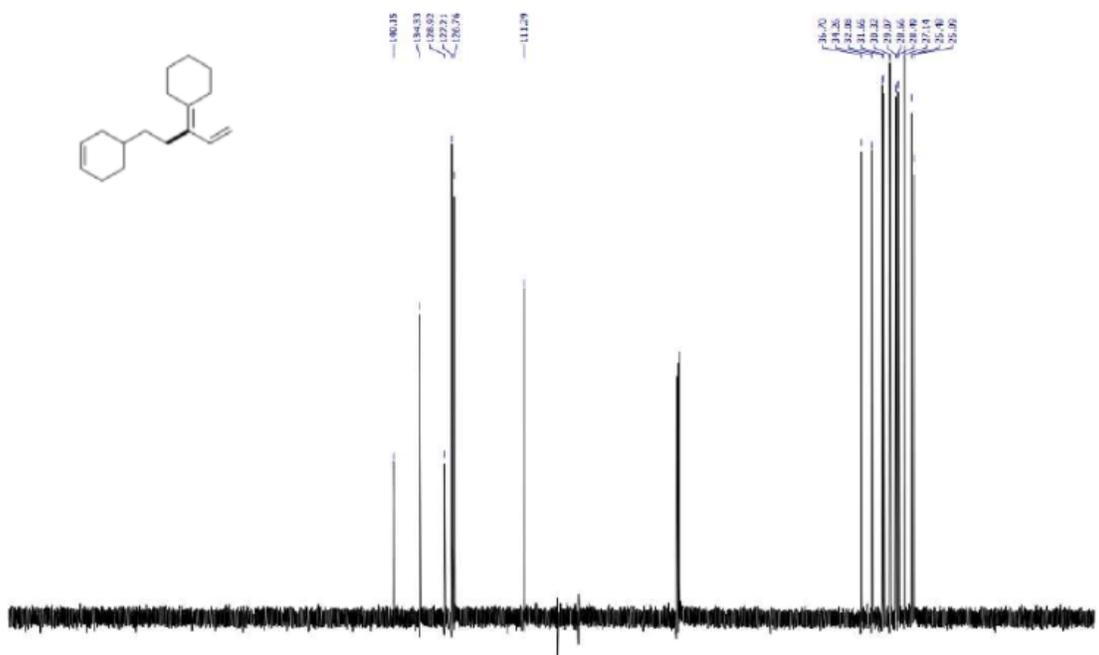
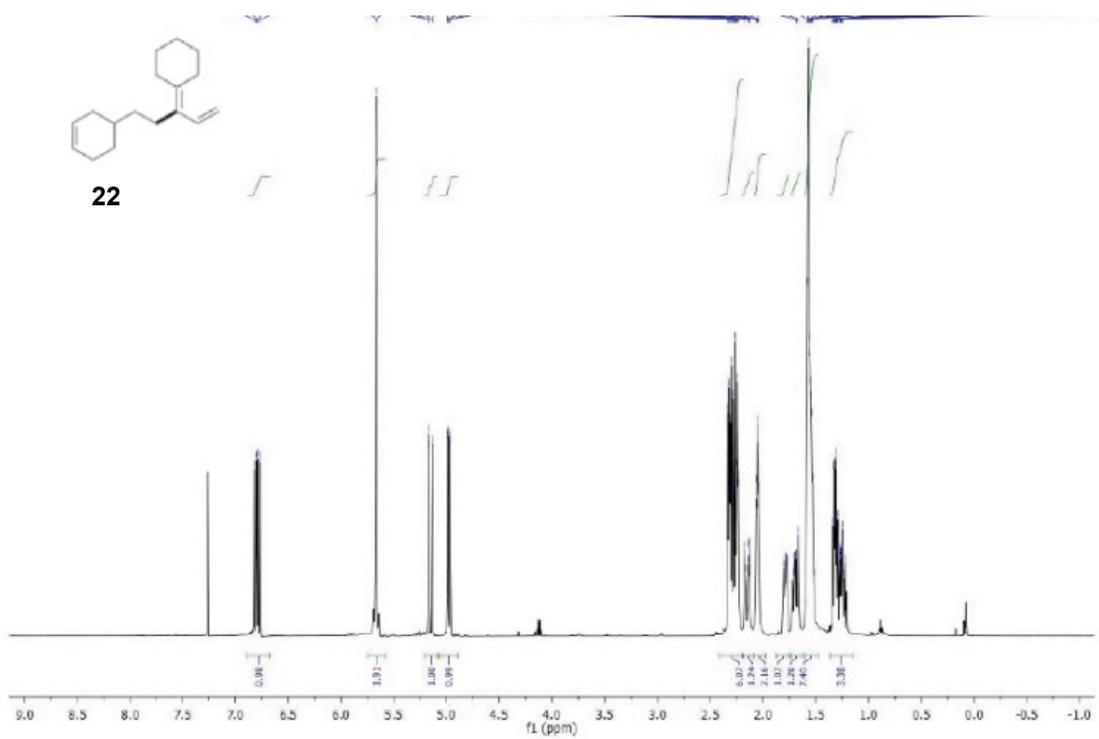


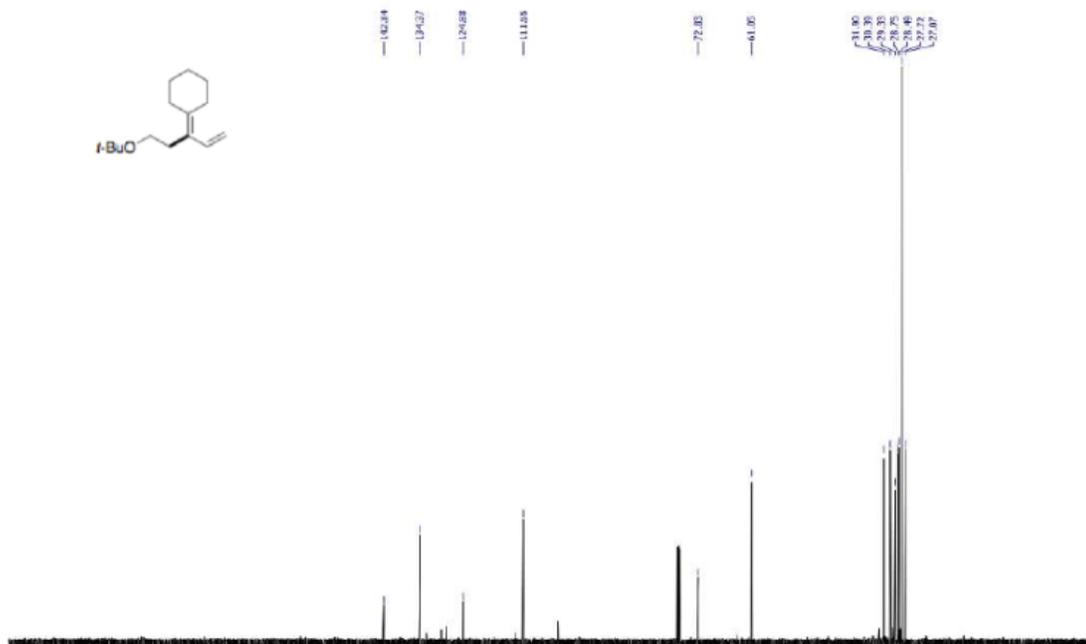
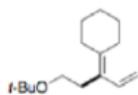
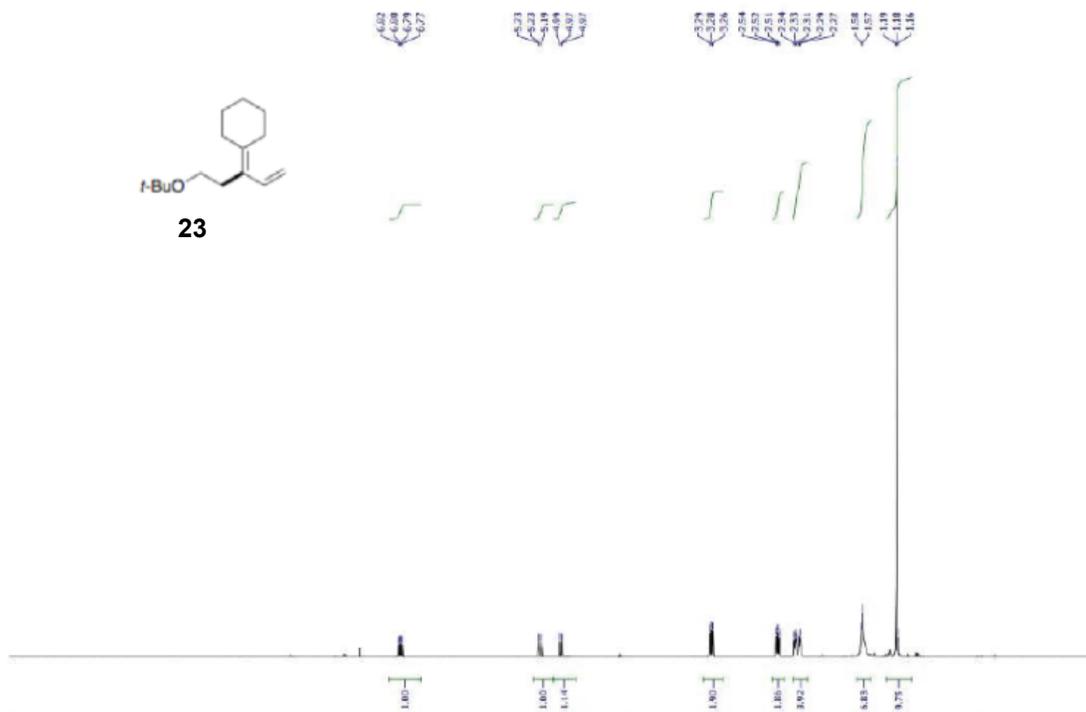
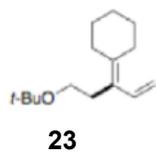
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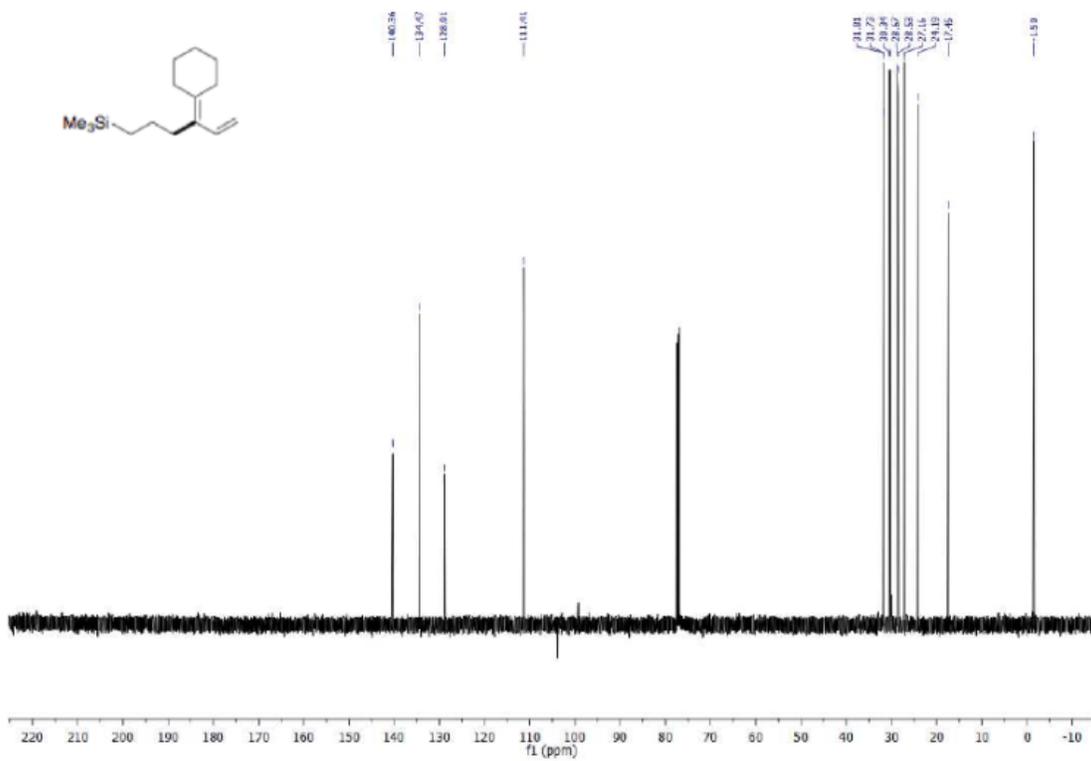
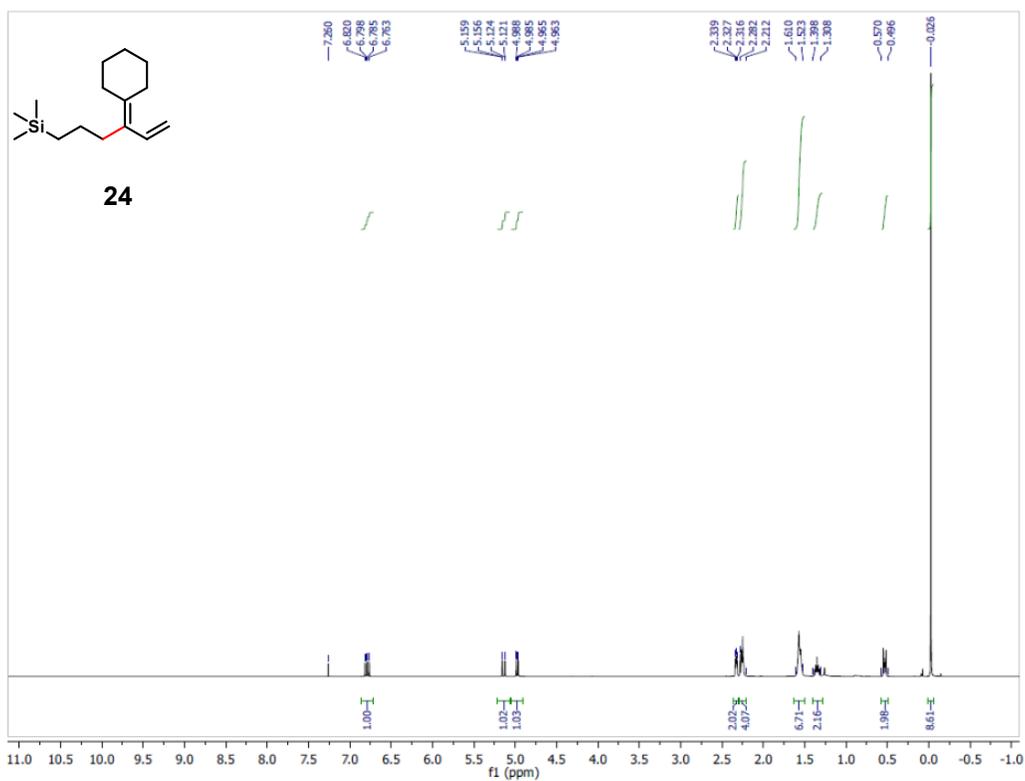


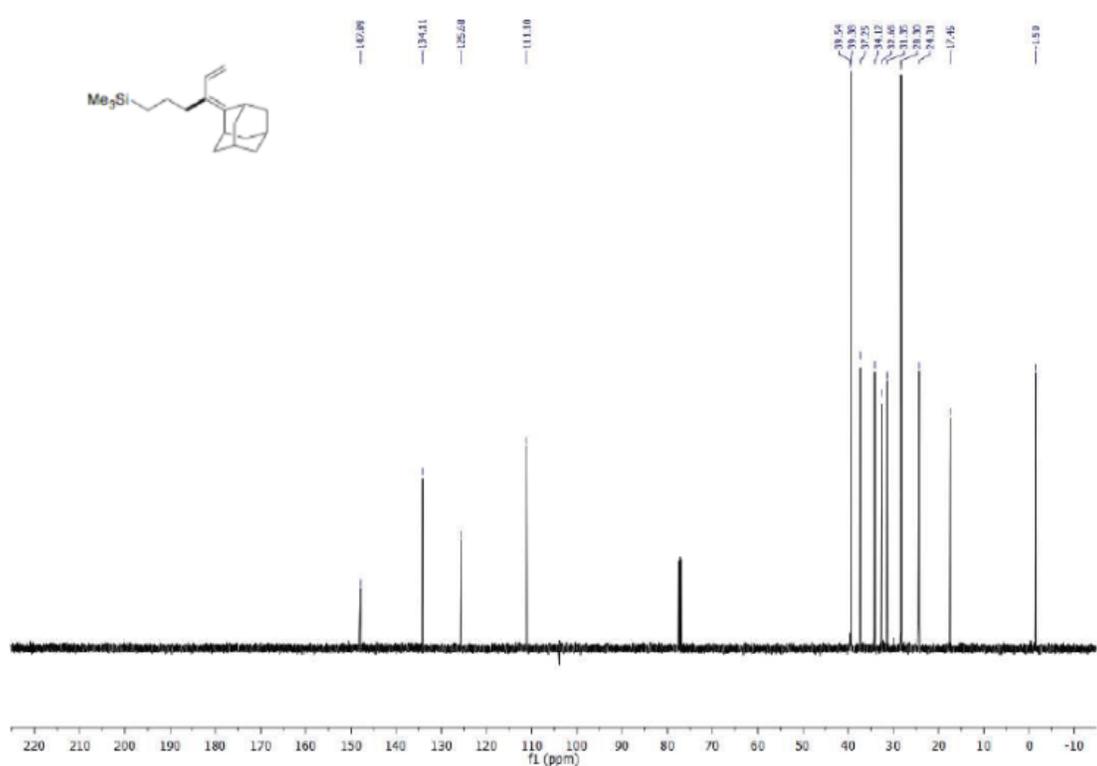
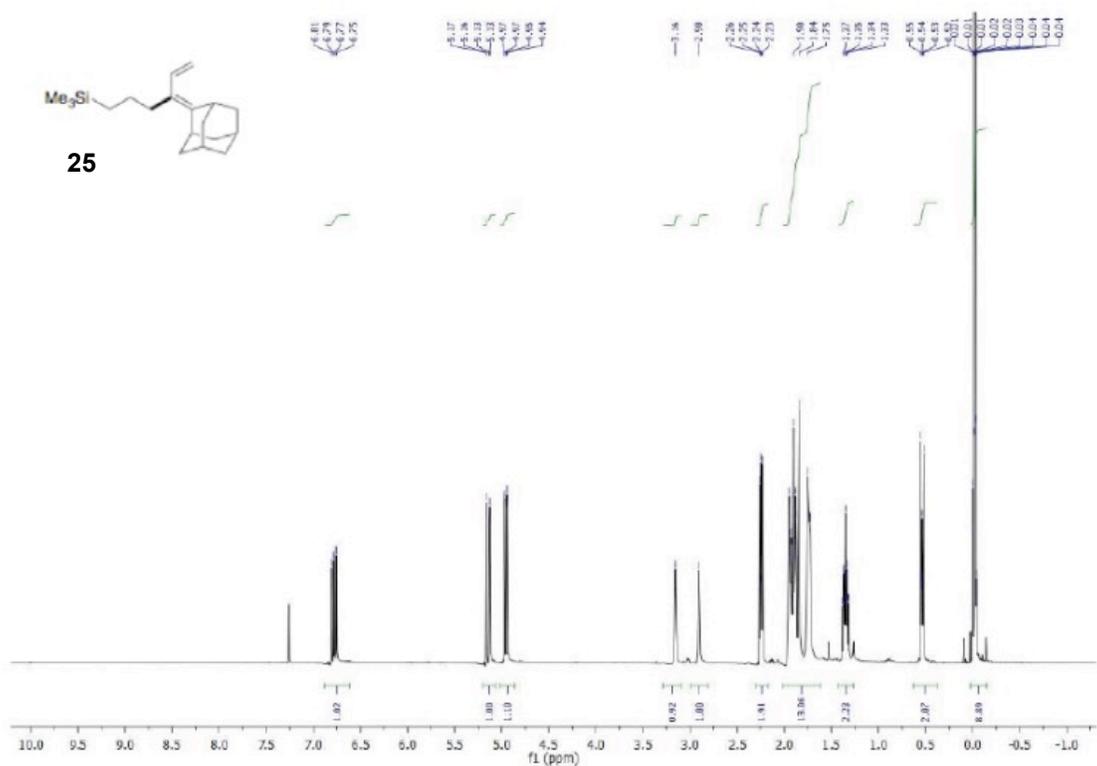




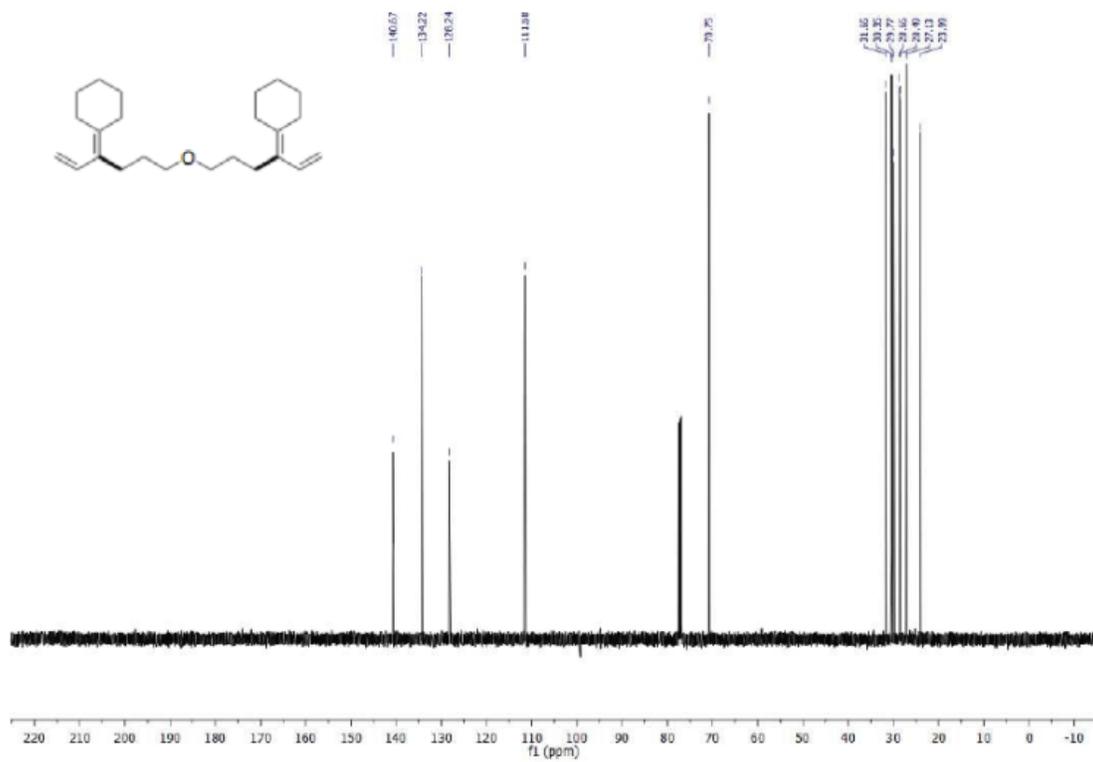
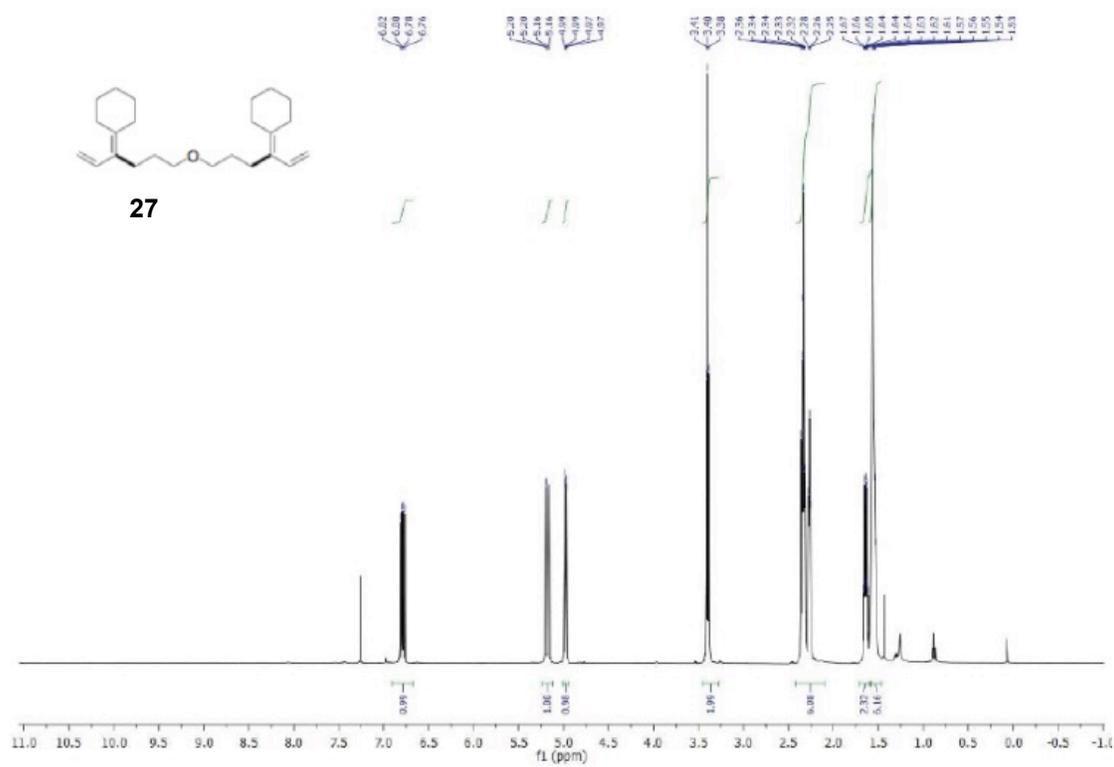


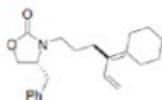
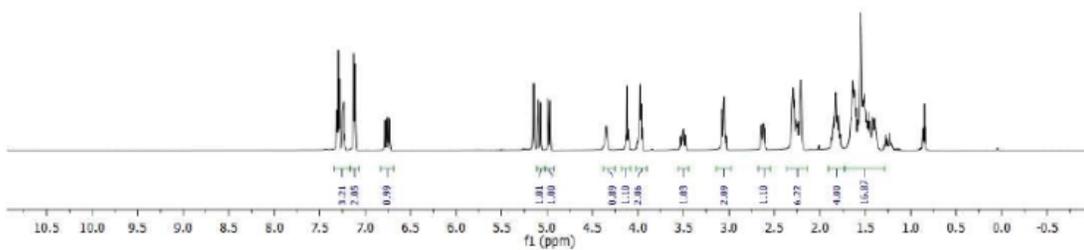
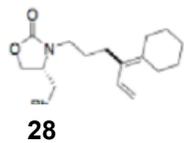




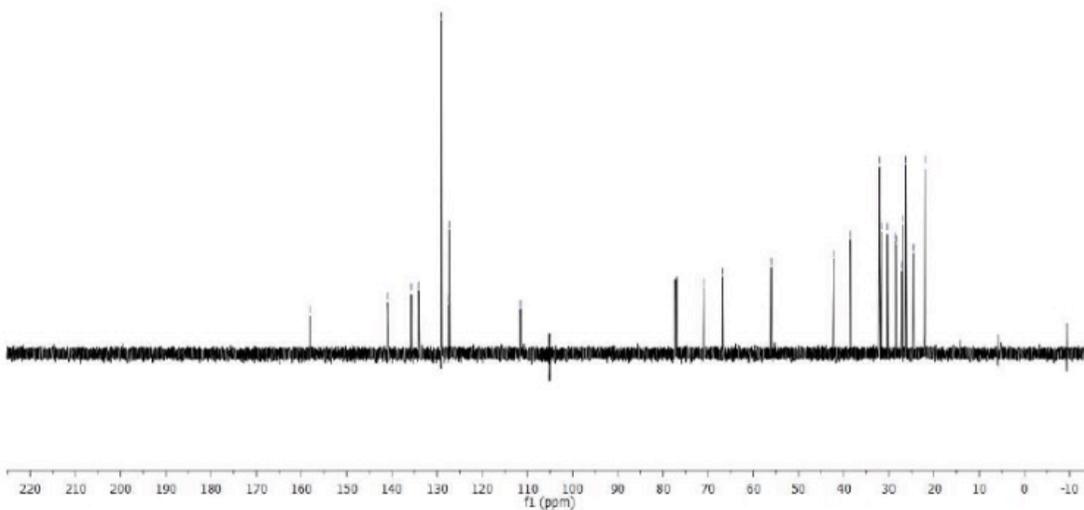


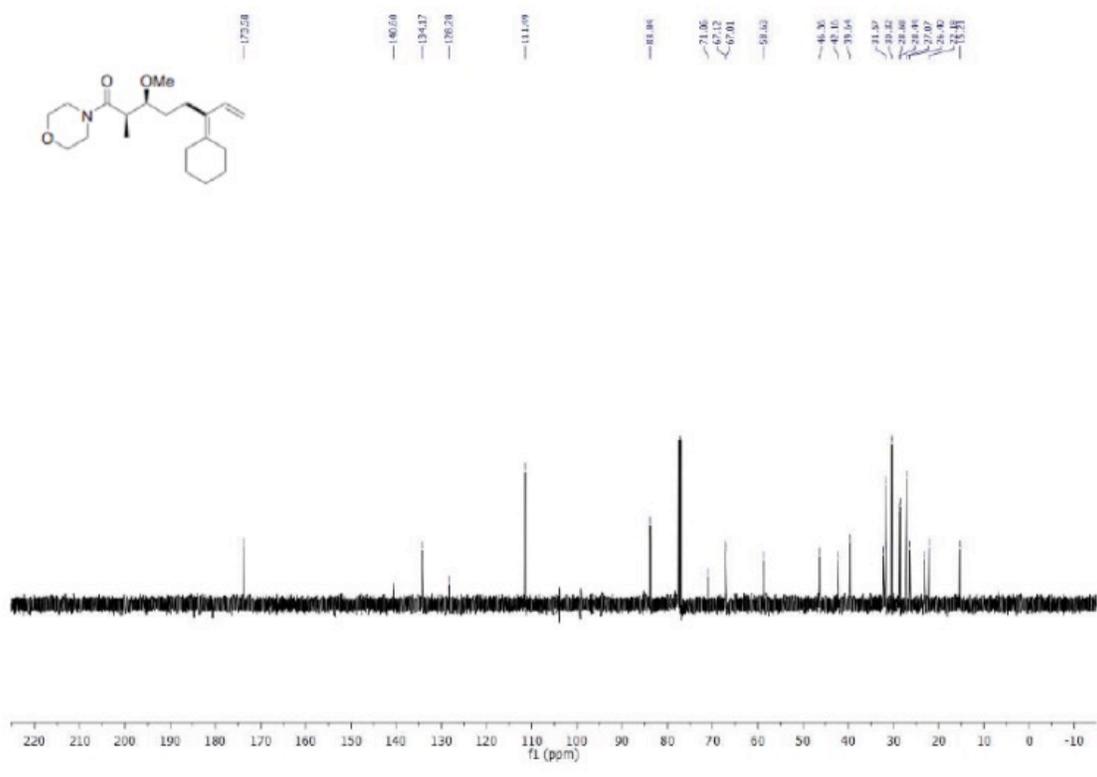
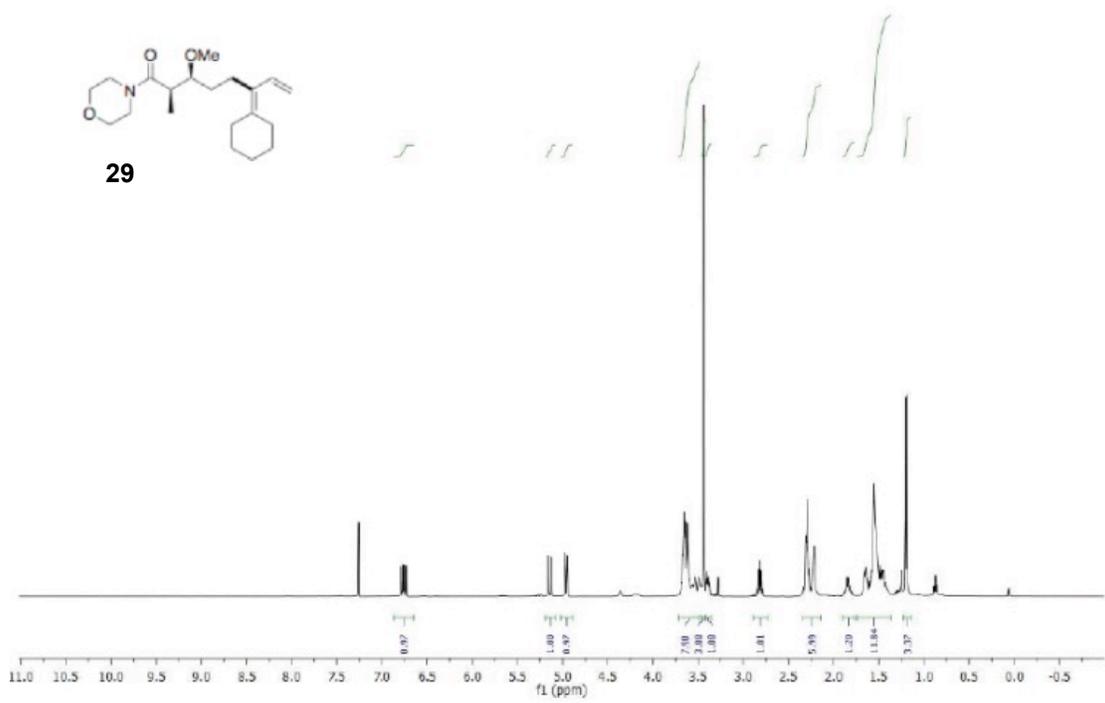


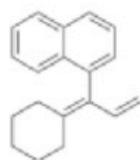




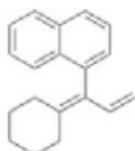
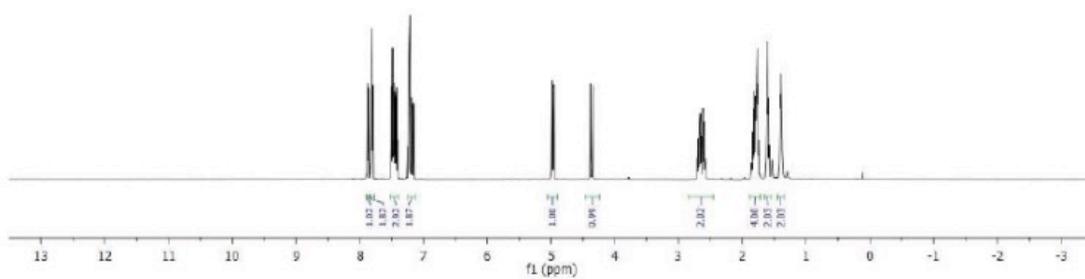
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30



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