

# The Tandem Intermolecular Hydroalkoxylation/ Claisen Rearrangement

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## General:

All reactions were carried out under an atmosphere of dry nitrogen unless otherwise specified. Anhydrous solvents were transferred via syringe to flame-dried glassware, which had been cooled under a stream of dry nitrogen. Anhydrous tetrahydrofuran (THF), and acetonitrile were dried using a mBraun solvent purification system. Triethylamine (over  $\text{CaH}_2$ ) and prenol alcohol were previously distilled before use. All other reagents were ordered from Sigma-Aldrich and used without any further purification, including anhydrous 1,4-dioxane.

Analytical thin layer chromatography (TLC) was performed using 250  $\mu\text{m}$  Silica Gel 60Å pre-coated plates (Whatman Inc.). Flash column chromatography was performed using 230-400 Mesh 60Å Silica Gel (Whatman Inc.). The eluents employed are reported as volume:volume percentages. Proton nuclear magnetic resonance ( $^1\text{H}$  NMR) spectra were recorded using Varian Unity Inova 500 MHz and Varian Mercury 300 MHz spectrometers. Chemical shift ( $\delta$ ) is reported in parts per million (ppm) downfield relative to tetramethylsilane (TMS, 0.0 ppm) or  $\text{CDCl}_3$  (7.26 ppm). Coupling constants ( $J$ ) are reported in Hz. Multiplicities are reported using the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad; Carbon-13 nuclear magnetic resonance ( $^{13}\text{C}$  NMR) spectra were recorded using Varian Unity Mercury 300 and 500 spectrometers at 75 MHz, and 125 MHz respectively. Chemical shift is reported in ppm relative to the carbon resonance of  $\text{CDCl}_3$  (77.23 ppm). Infrared spectra were obtained on a PerkinElmer Spectrum RX1 FTIR spectrometer at  $1.0\text{ cm}^{-1}$  resolution and are reported in wavenumbers. High resolution mass spectra (HRMS) were obtained by Mass Spectrometry Core Laboratory of University of Florida, and are reported as  $m/e$  (relative ratio). Accurate masses are reported for the molecular ion ( $\text{M}^+$ ) or a suitable fragment ion. All diastereoselectivities and regioselectivities for the reactions were observed in the spectrum of the crude reaction mixture on a Varian Unity Inova 500 MHz spectrometer.

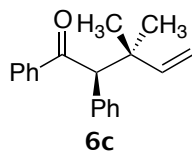
**General Procedure:** Note all gold and silver catalysts weighed in a glovebox under a dry argon atmosphere unless otherwise stated.

**Reflux conditions (Procedure A; Entries 2, 4, 5 from Table 1):** Although the catalyst systems varied in these experiments, the reactions conditions involve the same setup. An example procedure is as follows (entry 9): A test tube, with a septum on top, containing 1,3-bis(2,6-diisopropylphenyl-imidazol-2-ylidene)gold(I) chloride (6.2 mg, 0.01 mmol, 5 mol%), and silver tetrafluoroborate (1.9 mg, 0.01 mmol, 5 mol%) and stir bar, was taken from the glove box wrapped in aluminum foil and placed directly under dry nitrogen. A small portion of THF (0.2 mL) was added to the solid catalysts and the mixture was left to stir at room temperature for ten minutes, after which time a solution of the allylic alcohol (1.0 eq.) and the alkyne (3.0 eq.) in THF or 1,4-dioxane (0.8 mL) were added to the mixture all at once. The vessel was placed in an oil bath set to  $65^\circ\text{C}$  and left to stir for 18 h. After stirring for 18 h the reaction mixture was filtered through a short plug of silica with  $\text{CH}_2\text{Cl}_2$ , placed under vacuum to remove the solvents and purified by flash column chromatography.

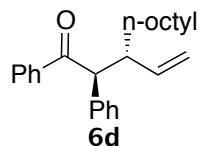
**Sealed Tube reactions (Procedure B; Entries 1, 4 from Table 1):** Although the catalyst systems varied in these experiments, the reactions were all setup under the same conditions. An example procedure is as follows (entry 8): A sealed tube, with a septum on top, containing 1,3-bis(2,6-diisopropylphenyl-imidazol-2-ylidene)gold(I) chloride (6.2 mg, 0.01 mmol, 5 mol%), and silver tetrafluoroborate (1.9 mg, 0.01 mmol, 5 mol%) and stir bar was taken from the glove box wrapped in aluminum foil and placed directly under dry nitrogen. A small portion of 1,4-dioxane (0.2 mL) was added to the solid catalysts and the mixture left to stir at room temperature for a ten minutes after which time a solution of the allylic alcohol (1 eq.) and the alkyne (3.0 eq.) in 1,4-dioxane (0.8 mL) were added to the mixture all at once. The septum was replaced (quickly) with a screw cap and the tube was placed at the appropriate temperature via an oil bath. The reaction was left to stir for 18 h. Filtered through a short plug of silica with CH<sub>2</sub>Cl<sub>2</sub>, placed under vacuum to remove the solvents and purified by flash column chromatography.

### Optimized Conditions:

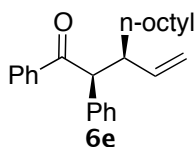
A pressure tube (screw cap) containing a stir bar was taken from the oven and placed directly into a glovebox. To this vessel was added 1,3-bis(2,6-diisopropylphenyl-imidazol-2-ylidene)gold(I) chloride (6.2 mg, 0.01 mmol, 5 mol%), and silver tetrafluoroborate (1.9 mg, 0.01 mmol, 5 mol%). The vessel was capped with a septum and then taken out of the glovebox where it was immediately placed under dry nitrogen atmosphere. 0.5 mL of THF was added to the tube and the mixture was left to stir ~10 mins to activate the complex. After this time a solution of alkyne (0.6 mmol in 0.5 mL of THF) was transferred to the tube, and the vessel was then placed in a 65 °C oil bath. 1.0 mL of a 0.2 M soln. of an allylic alcohol (in THF) was then added slowly over 12 hrs. via syringe pump (~0.8 mL/hr). After the addition was complete the solution was allowed to stir at this temperature for an additional 3 hrs. The tube is then sealed with a screwcap and placed in a 120 °C oil bath for 6 hrs. (**Note:** No problems occurred during this process, however, when sealed the reactions were placed behind a blast shield for added safety.) After cooling to room temperature the screwcap was removed and the solution was filtered over a plug of silica with EtOAc. The solution was then evaporated, the crude was characterized, and purified.



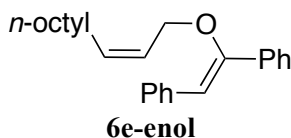
**3,3-dimethyl-1,2-diphenylpent-4-en-1-one (6c).** The following compound was made through various conditions, a representative reaction is shown here. The optimized conditions were employed with prenyl alcohol (**4b**) (1.0 mL of 0.2M soln., 0.2 mmol) diphenylacetylene (107 mg, 0.6 mmol, 3.0 eq.). Purified by flash column chromatography using a solvent gradient (0-20% CH<sub>2</sub>Cl<sub>2</sub>/hexanes) to yield the product as a clear colorless oil (43.5 mg, 83%). *R<sub>f</sub>* = 0.66 (20% EtOAc/hexanes). IR (neat) 3086, 3055, 2966, 2924, 1684, 1540, 1507, 1457, 1447 cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 7.87 (d, *J* = 7.5 Hz, 2H), 7.49-7.46 (m, 1H) 7.40-7.37 (m, 4H), 7.32-7.29 (m, 2H), 7.26-7.23 (m, 1H), 6.11 (dd, *J* = 17.5, 11.0, 1H), 4.95 (dd, *J* = 11.0, 1.0 Hz, 1H), 4.88 (dd, *J* = 17.5, 1.0 Hz, 1H), 4.59 (s, 1H), 1.17 (s, 3H), 1.14 (s, 3H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 200.2, 146.3, 138.7, 135.8, 132.7, 130.7, 128.7, 128.5, 128.3, 127.3, 112.2, 62.3, 50.0, 26.4, 24.9; HRMS (DART) Calcd for C<sub>19</sub>H<sub>21</sub>O (M+H)<sup>+</sup> 265.1587, found 265.1593.



***anti*-1,2-diphenyl-3-vinylundecan-1-one (6d)** The following compound was made with the optimized conditions with (*E*)-undec-2-en-1-ol<sup>1</sup> (**4c**) (1.0 mL of 0.2M soln., 0.2 mmol) and diphenylacetylene (110.0 mg, 0.62 mmol, 3.0 eq.). Purified by flash column chromatography using a solvent gradient (0-20% CH<sub>2</sub>Cl<sub>2</sub>/hexanes) to yield the product as a white solid (50.2 mg, 72%; major diastereomer, 5:1 *dr*): mp = 66-68°C *R*<sub>f</sub> = 0.36 (2% Et<sub>2</sub>O/pentanes). IR (neat) 3064, 3022, 2926, 2854, 2361, 2334, 1683, 1267, 913 cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 7.98 (d, *J* = 8.5 Hz, 2H), 7.51-7.46 (m, 1H), 7.42-7.38 (m, 2H), 7.29-7.22 (m, 4H), 7.17-7.13 (m, 1H), 5.38 (dt, *J* = 17.1, 10.3, Hz, 1H), 4.82 (dd, *J* = 10.3, 1.9 Hz, 1H), 4.76 (dd, *J* = 17.1, 1.9 Hz, 1H), 4.49 (d, *J* = 10.2 Hz, 1H), 3.06-2.98 (m, 1H), 1.43-1.51 (m, 1H), 1.22-1.28 (m, 15H), 0.85 (t, *J* = 7.0 Hz, 3H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 200.1, 139.8, 139.1, 137.8, 133.1, 129.3, 128.8, 128.7, 128.7, 127.1, 116.7, 58.6, 47.8, 33.9, 32.1, 29.7, 29.7, 29.5, 27.6, 22.9, 14.3; HRMS (DART) Calcd for C<sub>25</sub>H<sub>33</sub>O (M+H)<sup>+</sup> 349.2526, found 349.2547.



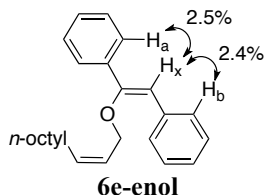
***syn*-1,2-diphenyl-3-vinylundecan-1-one (6e)** The following compound was made through various methods. A representative method is shown. Following the optimized conditions with (*Z*)-undec-2-en-1-ol<sup>2</sup> (**4d**) (1.0 mL of 0.2M soln., 0.2 mmol) and diphenylacetylene (107.0 mg, 0.6 mmol, 3.0 eq.). Purified by flash column chromatography using a solvent gradient (0-20% CH<sub>2</sub>Cl<sub>2</sub>/hexanes) to yield the product as a white solid (52.3 mg, 75%; major diastereomer, 11:1 *dr*): mp = 74-76°C; *R*<sub>f</sub> = 0.36 (40% CH<sub>2</sub>Cl<sub>2</sub>/hexanes). IR (neat) 3078, 3045, 2920, 2852, 1673, 1644, 1557, 1538, 1445 cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 7.96-7.92 (m, 2H), 7.50-7.45 (m, 1H), 7.42-7.35 (m, 3H), 7.32 – 7.27 (m, 3H), 7.23-7.18 (m, 1H), 5.62 (dddd, *J* = 17.2, 10.1, 8.7, 0.9 Hz, 1H), 5.07 (ddd, *J* = 17.2, 1.6, 0.9, 1H), 4.99 (dd, *J* = 10.3, 1.6 Hz, 1H), 4.54 (d, *J* = 10.2 Hz, 1H), 3.07–2.98 (m, 1H), 1.34-1.05 (m, 14H), 0.90-0.83 (m, 3H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 199.9, 140.6, 137.9, 137.7, 132.9, 129.3, 128.9, 128.7, 128.6, 127.3, 116.9, 58.3, 46.9, 32.0, 31.8, 29.7, 29.6, 29.4, 26.9, 22.8, 14.3; HRMS (DART) Calcd for C<sub>25</sub>H<sub>33</sub>O (M+H)<sup>+</sup> 349.2526, found 349.2530.



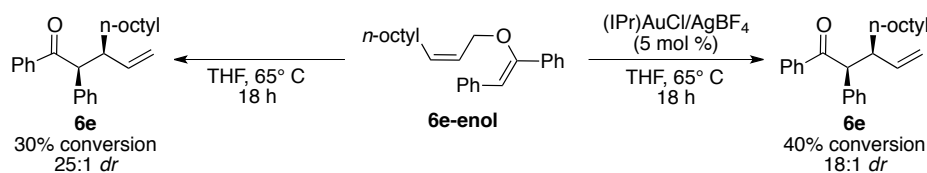
**((*Z*)-1-((*Z*)-undec-2-en-1-yloxy)ethene-1,2-diyl)dibenzene enol (6e-enol).** The following enol was obtained using the conditions discussed in Table 2, Entry 4. A pressure tube (screw cap) containing a stir bar was taken from the oven and placed directly into a glovebox. To this vessel was added 1,3-bis(2,6-diisopropylphenyl-imidazol-2-ylidene)gold(I) chloride (6.2 mg, 0.01 mmol, 5 mol%), and silver tetrafluoroborate (1.9 mg, 0.01 mmol, 5 mol%). The vessel was

capped with a septum and then taken out of the glovebox where it was immediately placed under dry nitrogen atmosphere. 0.5 mL of THF was added to the tube and the mixture was left to stir ~10 mins to activate the complex. After this time a solution of alkyne (107.0 mg, 0.6 mmol, 3.0 eq. in 0.5 mL of THF) was transferred to the tube, and the vessel was then placed in a 65 °C oil bath. (*Z*)-undec-2-en-1-ol<sup>1</sup> (**4d**) (1.0 mL of 0.2M soln., 0.2 mmol)) was then added slowly over 12 hrs. via syringe pump (~0.8 mL/hr). After the addition was complete the solution was allowed to stir at this temperature for an additional 6 hrs. After cooling the to room temperature the solution was filtered over a plug of silica with CH<sub>2</sub>Cl<sub>2</sub>. The solution was then evaporated, and the mixtures was purified by flash column chromatography using a solvent gradient (0-20% CH<sub>2</sub>Cl<sub>2</sub>/hexanes) to give the desired product **6e** (23.0 mg, 33%), and **6e-enol** (25.8 mg, 37%) as a clear, colorless oil. Characterization of the enol is as follows: *R<sub>f</sub>* = 0.70 (40% CH<sub>2</sub>Cl<sub>2</sub>/hexanes). IR (neat) 3057, 3022, 2925, 2855, 1634, 1600, 1492, 1448, 1199, 1058, 1026, 914 cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 7.77 (d, *J* = 7.5 Hz, 2H), 7.60 (d, *J* = 7.0 Hz, 2H), 7.42 (t, *J* = 7.0 Hz, 2H), 7.34-7.37 (m, 3H), 7.22 (t, *J* = 7.5 Hz, 1H) 6.14 (s, 1H), 5.69-5.74 (m, 1H), 5.57-5.63 (m, 1H), 4.38 (d, *J* = 6.5 Hz, 2H), 1.95 – 1.88 (m, 1H), 1.31-1.18 (m, 14H), 0.86 (t, *J* = 7.0, 3H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 155.3, 137.0, 136.3, 134.7, 128.9, 128.6, 128.5, 128.4, 126.8, 126.7, 125.0, 113.7, 66.2, 32.0, 29.7, 29.6, 29.5, 29.4, 27.7, 22.8, 14.3; HRMS (DART) Calcd for C<sub>25</sub>H<sub>33</sub>O (M+H)<sup>+</sup> 349.2526, found 349.2523.

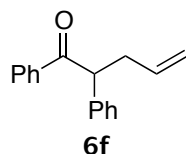
The *Z*-enol-configuration of **6e-enol** is established based on NOE DIFF experiments. The NOEs between vinyl-H (*s* = 6.14 ppm) and *ortho*-hydrogens (*d* = 7.77 (**H<sub>a</sub>**), 7.60 (**H<sub>b</sub>**) ppm) of the phenyl groups of **6e-enol** is clearly seen allowing for the elucidation of the *Z*-enol configuration.



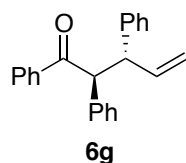
#### Scheme S1. Gold-catalyzed vs. Thermal Catalyzed Claisen Rearrangement



**6e-enol** was subjected to the reaction conditions reported above. The following experiments demonstrate that the Claisen Rearrangement (at least in the case of **6e-enol**) can be either a thermal or gold-catalyzed process. Conversions and diastereoselectivities were determined by <sup>1</sup>H NMR (500 MHz) of the crude material.

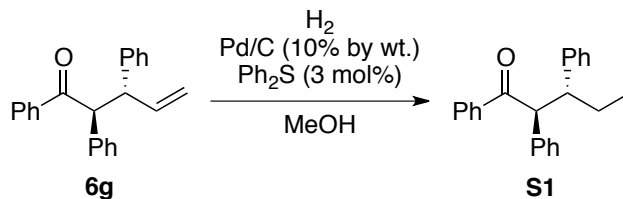


**1,2-diphenylpent-4-en-1-one (6f)** The following compound was made with the optimized conditions with allyl alcohol (1.0 mL of 0.2M soln., 0.2 mmol) and diphenylacetylene (107.0 mg, 0.6 mmol, 3.0 eq.). Purified by flash column chromatography using a solvent gradient (0-20% CH<sub>2</sub>Cl<sub>2</sub>/hexanes) to yield the product as a clear colorless oil (45.0 mg, 95%), that satisfactorily matched all previously reported data.<sup>3</sup>

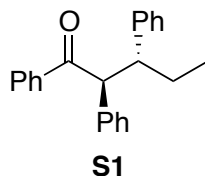


**anti-1,2,3-triphenylpent-4-en-1-one (6g)** The following compound was provided via Procedure A, with cinnamyl alcohol (40.0 mg, 0.3 mmol, 1.0 eq.), diphenylacetylene (160.0 mg, 0.9 mmol, 3.0 eq.), 1,3-bis(2,6-diisopropylphenyl-imidazol-2-ylidene)gold(I) chloride (9.3 mg, 0.015 mmol, 5 mol%), and silver tetrafluoroborate (3.0 mg, 0.015 mmol, 5 mol%) in 1.0 mL of THF. Purified by flash column chromatography using a solvent gradient (0-20% CH<sub>2</sub>Cl<sub>2</sub>/hexanes) to yield the product as a white solid (60 mg, 96%; major diastereomer; 5:1 *dr*). mp = 161-163 °C; *R<sub>f</sub>* = 0.15 (15% EtOAc/hexanes). IR (neat) 3065, 3027, 1673, 1595, 1447, 1267, 910 cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 7.98-7.95 (m, 2H), 7.51-7.46 (m, 1H), 7.42-7.37 (m, 2H), 7.31-7.29 (m, 4 H), 7.23-7.20 (m, 1H), 5.82 (ddd, *J* = 17.0, 10.2, 8.0 Hz, 1H), 5.10 (d, *J* = 11.5 Hz, 1H), 4.87 (ddd, *J* = 10.3, 1.6, 1.0 Hz, 1H), 4.75 (dt, *J* = 17.0, 1.6 Hz, 1H), 4.36 (dd, *J* = 11.5, 8.0 Hz, 1H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 198.8, 142.6, 139.6, 137.5, 137.3, 132.9, 129.4, 129.0, 128.7, 128.6, 128.5, 128.2, 127.6, 126.6, 116.6, 58.6, 53.2; HRMS (DART) Calcd for C<sub>23</sub>H<sub>21</sub>O (M+H)<sup>+</sup> 313.1587, found 313.1578

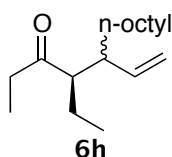
**Scheme S2.** Confirmation of Stereochemistry via synthesis  
of *anti*-1,2,3-triphenylpentan-1-one (erythro)



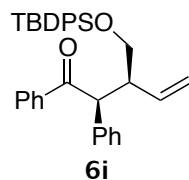
**Note<sup>4</sup>**  
mp of *anti* = 169-170 °C  
mp of *syn* = 91-92 °C



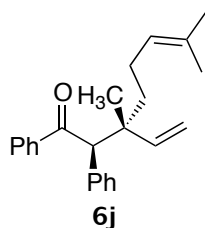
***anti*-1,2,3-triphenylpentan-1-one (S1)** The following compound was synthesized by the chemoselective reduction of *anti*-1,2,3-triphenylpent-4-en-1-one (**6g**) following a known procedure<sup>5</sup>. A flask containing a stir bar, *anti*-1,2,3-triphenylpent-4-en-1-one (**6g**, 60.0 mg, 0.19 mmol), Pd/C (6 mg, 10% by wt.), Ph<sub>2</sub>S (1.0 mg, 3 mol%) and 2 mL of MeOH was evacuated and backfilled 3 times with H<sub>2</sub> gas via a three way valve attached to a hydrogen balloon. The solution was allowed to mix at room temperature for 24 hrs. The solution was filtered through a plug of cealite with CH<sub>2</sub>Cl<sub>2</sub> and the solvent was evaporated. Purified by flash column chromatography using a solvent gradient (0-20% CH<sub>2</sub>Cl<sub>2</sub>/hexanes) to yield the product as a white solid (60 mg, quantitative, one observable diastereomer) which matched the well known melting point of the *anti*(erythro) product.<sup>4</sup> mp = 169-170°C; R<sub>f</sub> = 0.32 (40% CH<sub>2</sub>Cl<sub>2</sub>/hexanes). IR (neat) 3055, 3029, 2952, 2917, 2857, 1673, 1446, 1271 cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 7.78-7.71 (m, 2H), 7.49-7.44 (m, 1H), 7.41-7.36 (m, 1H), 7.35-7.30 (m, 2H), 7.30-7.26 (m, 4H), 7.24-7.19 (m, 2H), 7.11-7.08 (m, 1H), 4.91 (d, *J* = 10.9 Hz, 1H), 3.46 (td, *J* = 10.7, 4.3 Hz, 1H), 1.48-1.36 (m, 2H), 0.60 (t, *J* = 7.3 Hz, 3H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 199.6, 143.5, 138.1, 137.7, 132.7, 129.3, 129.2, 129.0, 128.5, 128.5, 128.5, 128.4, 128.4, 127.5, 126.34, 60.0, 50.5, 26.6, 11.9.; HRMS (DART) Calcd for C<sub>23</sub>H<sub>22</sub>O (M+H)<sup>+</sup> 315.1743, found 315.1735.



**4-ethyl-5-vinyltridecan-3-one (6h)** The following compound was made with the optimized conditions with (*E*)-undec-2-en-1-ol<sup>1</sup> (**4c**) (1.0 mL of 0.2M soln., 0.2 mmol) and 3-hexyne (70 μL, 0.6 mmol, 3.0 eq.). Purified by flash column chromatography using a solvent gradient (0-2% Et<sub>2</sub>O/pentanes) to yield the product as a clear colorless oil (45.5 mg, 90%; 1:1 mixture of diastereomers). R<sub>f</sub> = 0.95 (10% Et<sub>2</sub>O/pentanes). IR (neat) 2985, 2935, 1742, 1373, 1241, 1047 cm<sup>-1</sup>. <sup>1</sup>H NMR mixture of diastereomers (500 MHz, C<sub>6</sub>D<sub>6</sub>): δ 5.44-5.35 (m, 1H), 5.02 (dd, *J* = 10.5, 2.0 Hz, 2H), 4.98-4.93 (m, 1H), 2.45-2.37 (m, 3H), 2.30-3.26 (m, 1H), 1.57 (q, *J* = 7.0 Hz), 1.26-1.16 (m, 16 H), 1.02 (t, *J* = 7.5 Hz, 1H), 0.95 (d, *J* = 7.0 Hz, 2 H), 0.89-0.84 (m, 5H), 0.76 (t, *J* = 7.5 Hz). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 214.6, 140.3, 139.6, 116.7, 116.6, 58.2, 50.5, 46.8, 46.7, 44.2, 37.1, 33.1, 33.9, 32.0, 29.7, 29.7, 29.7, 29.5, 29.5, 27.5, 27.5, 23.2, 22.8, 17.2, 14.3, 14.2, 14.0, 12.1, 7.7, 1.2. HRMS (DART) Calcd for C<sub>17</sub>H<sub>33</sub>O (M+H)<sup>+</sup> 253.2526, found 253.2527.

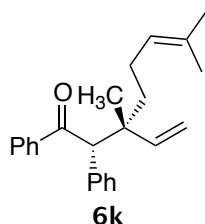


***syn*-3-(((*tert*-butyldiphenylsilyl)oxy)methyl)-1,2-diphenylpent-4-en-1-one (6i)** The following compound was with the optimized conditions optimized conditions with (*Z*)-4-(*tert*-butyldiphenylsilyloxy)-but-2-ene-1-ol (1.0 mL of 0.2M soln., 0.2 mmol) and diphenylacetylene (107.0 mg, 0.6 mmol, 3.0 eq.). Purified by flash column chromatography using a solvent gradient (0-1% Et<sub>2</sub>O/hexanes) to yield the product as a clear, colorless oil (70.0 mg, 70%; >25:1 *dr*): *R*<sub>f</sub> = 0.62 (20% Et<sub>2</sub>O/hexanes). IR (neat) 3071, 2958, 2857, 2822, 1683, 1447, 1109 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 8.05-7.94 (m, 2H), 7.61-7.55 (m, 2H), 7.53-7.17 (m, 14H), 6.03 (ddd, *J* = 17.2, 10.4, 8.2 Hz, 1H), 5.18-5.00 (m, 3H), 3.57 (dd, *J* = 10.0, 3.2 Hz, 1H), 3.48 (dd, *J* = 10.0, 4.1 Hz, 1H), 3.34-3.05 (m, 1H), 1.06 (s, 9H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 199.6, 164.6, 138.4, 137.2, 135.9, 135.7, 133.0, 129.8, 129.7, 129.5, 128.9, 128.8, 127.8, 127.7, 127.4, 117.5, 106.8, 64.8, 53.5, 49.2, 27.1, 19.6.

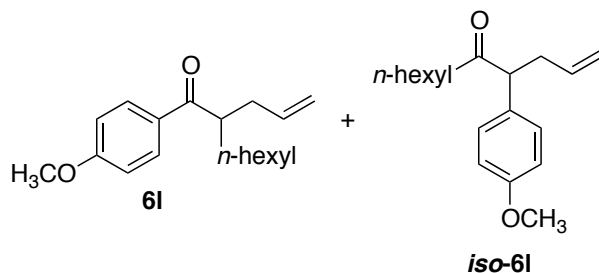


***anti*-3,7-dimethyl-1,2-diphenyl-3-vinyloct-6-en-1-one (6j)** The following compound was made using the optimized conditions with geraniol (1.0 mL of 0.2M soln., 0.2 mmol) and diphenylacetylene (108.0 mg, 0.6 mmol, 3.0 eq.). Purified by flash column chromatography using a solvent gradient (0-20% CH<sub>2</sub>Cl<sub>2</sub>/hexanes) to yield the product as a clear colorless oil (42.5 mg, 64%; major diastereomer; 5:1 *dr*). *R*<sub>f</sub> = 0.55 (40% CH<sub>2</sub>Cl<sub>2</sub>/hexanes). IR (neat) 3085, 3062, 3027, 2968, 2925, 1682, 1597, 1581, 1447, 1212, 1002, 915 cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 7.90-7.87 (m, 2H), 7.47-7.43 (m, 1H), 7.38-7.34 (m, 4H), 7.28-7.25 (m, 2H), 7.23-7.21 (m, 1H), 5.97 (ddd, *J* = 17.5, 10.8, 0.9 Hz, 1H), 5.06 (dd, *J* = 10.8, 1.2 Hz, 1H), 5.04-4.99 (m, 1H), 4.81 (dd, *J* = 17.5, 1.2 Hz, 1H), 4.64 (s, 1H), 1.97-1.80 (m, 2H), 1.70-1.42 (12H), 1.20 (s, 3H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 200.1, 144.4, 138.8, 135.4, 132.7, 131.4, 130.9, 128.7, 128.5, 128.2, 127.3, 124.9, 113.8, 61.8, 44.3, 38.4, 25.8, 23.2, 20.3, 17.7; HRMS (DART) Calcd for C<sub>24</sub>H<sub>29</sub>O (M+H)<sup>+</sup> 333.2213, found 333.2229.



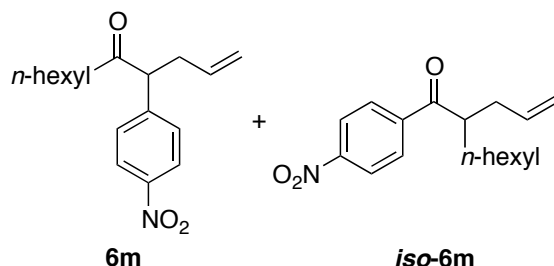


**syn-3,7-dimethyl-1,2-diphenyl-3-vinyloct-6-en-1-one (6k)** The following compound was made with the optimized conditions with nerol (1.0 mL of 0.2M soln., 0.2 mmol) and diphenylacetylene (108.0 mg, 0.6 mmol, 3.0 eq.). Purified by flash column chromatography using a solvent gradient (0-20% CH<sub>2</sub>Cl<sub>2</sub>/hexanes) to yield the product as a clear colorless oil (47.2 mg, 71%; major diastereomer; 8:1 *dr*).  $R_f$  = 0.56 (40% CH<sub>2</sub>Cl<sub>2</sub>/hexanes). IR (neat) 3063, 3020, 2969, 2924, 1684, 1447, 1215 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  7.91-7.85 (m, 2H), 7.49-7.41 (m, 1H), 7.40-7.33 (m, 4H), 7.31- 7.17 (m, 3H), 6.17 (dd,  $J$  = 17.6, 10.9 Hz, 1H), 5.06 (dd,  $J$  = 10.9, 1.4 Hz, 1H), 5.03-4.96 (m, 1H), 4.82 (dd,  $J$  = 17.6, 1.4 Hz, 1H), 4.66 (s, 1H), 1.93-1.78 (m, 1H), 1.62 (s, 3H), 1.61-1.38 (m, 6H), 1.14 (s, 3H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  200.2, 144.3, 138.8, 135.5, 132.7, 131.5, 131.0, 128.6, 128.5, 128.2, 127.4, 124.8, 114.2, 62.12, 44.5, 39.7, 25.9, 23.1, 20.3, 17.8. HRMS (DART) Calcd for C<sub>24</sub>H<sub>29</sub>O (M+H)<sup>+</sup> 333.2213, found 333.2207.



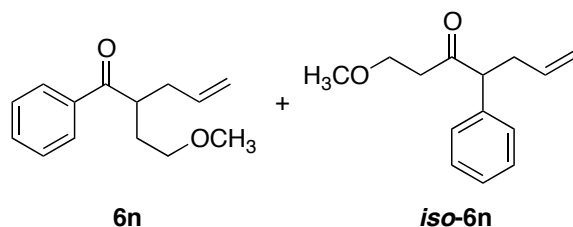
**2-allyl-1-(4-methoxyphenyl)octan-1-one (6l) and 4-(4-methoxyphenyl)undec-1-en-5-one (iso-6l)** The following mixture was made using the optimized conditions with allyl alcohol (1.0 mL of 0.2M soln., 0.2 mmol) and 1-(4-methoxyphenyl)-1-octyne<sup>8</sup> (129.8 mg, 0.6 mmol, 3.0 eq.) Purified by flash column chromatography using a solvent gradient (0-20% EtOAc/hexanes) to yield the inseparable mixture of products as a clear pale yellow oil (38.4 mg, 70%; 2:1 mixture of regioisomers aryl:alkyl ketone)  $R_f$  = 0.24 (40% CH<sub>2</sub>Cl<sub>2</sub>/hexanes). IR (neat) 3077, 2997, 2956, 2930, 1712, 1672, 1601, 1510, 1254, 1171, 1034 cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  7.94 (d,  $J$  = 8.9 Hz, 2H, major), 7.12 (d,  $J$  = 8.7 Hz, 2H, minor), 6.94 (d,  $J$  = 8.9 Hz, 2H, major), 6.85 (d,  $J$  = 8.7 Hz, 2H, minor), (ddd,  $J$  = 17.5, 10.5, 7.0 Hz 1H, major), 5.65 (ddd,  $J$  = 17.1, 10.2, 6.9 Hz, 1H, minor), 5.01 (dddd,  $J$  = 17.5, 3.5, 2.0, 1.5 Hz 1H, major), 4.99 (dddd,  $J$  = 17.5, 3.5, 2.0, 1.5 Hz 1H, minor), 4.97-4.91 (m, 4H, major and minor), 3.87 (s, 3H, major), 3.79 (s, 3H, minor), 3.64 (t,  $J$  = 7.5 Hz, 1H, minor), 3.44 (tt,  $J$  = 7.6, 5.8 Hz, 1H, major), 2.79-2.72 (m, 1H, minor), 2.53- 2.45 (m, 1H, major), 2.43-2.36 (m, 1H, minor), 2.36-2.31 (m, 2H, minor), 2.28-2.21 (m, 1H, major), 1.80-1.70 (m, 1H, major), 1.56-1.41 (m, 2H, major and minor), 1.29-1.09 (m, 18 H, major and minor), 0.88-0.79 (m, 6H, major and minor). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): 210.4, 202.5, 163.6, 136.3, 136.3, 130.8, 130.7, 129.5, 116.7, 116.6, 114.4, 114.0, 58.0, 55.7, 55.5, 45.7, 42.0, 36.8, 36.7, 32.4, 31.86, 31.71, 29.7, 28.9, 27.6, 23.9, 22.8, 22.7, 14.3, 14.2. HRMS (DART) Calcd for C<sub>18</sub>H<sub>27</sub>O<sub>2</sub> (M+H)<sup>+</sup> 275.2006, found 275.1996.





**4-(4-nitrophenyl)undec-1-en-5-one (6m) and 2-allyl-1-(4-nitrophenyl)octan-1-one (iso-6m)**

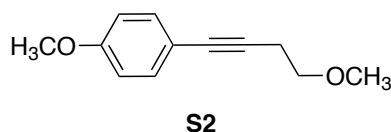
The following products were obtained using the optimized conditions with allyl alcohol (1.0 mL of 0.2M soln., 0.2 mmol) and 1-(4-nitrophenyl)-1-octyne<sup>7</sup> (138.2 mg, 0.6 mmol, 3.0 eq.) Purified by flash column chromatography using a solvent gradient (0-20% CH<sub>2</sub>Cl<sub>2</sub>/hexanes) to yield the product as a clear pale yellow oil (57.9 mg 99%; 8:1 mixture of regioisomers alkyl:aryl ketone). Analytical fractions of each were obtained; their characterization is as follows: **Alkyl Ketone (6m)**: R<sub>f</sub> = 0.27 (40% CH<sub>2</sub>Cl<sub>2</sub>/hexanes). IR (neat) 3079, 2956, 2930, 2858, 1716, 1606, 1521, 1346 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 8.18 (d, *J* = 8.7 Hz, 2H), 7.40 (d, *J* = 8.8 Hz, 2H), 5.61 (ddt, *J* = 17.1, 10.1, 6.9 Hz, 1H), 5.07-4.91 (m, 2H), 3.85 (t, *J* = 7.5 Hz, 1H), 2.81 (dtt, *J* = 14.2, 7.0, 1.3 Hz, 1H), 2.50-2.42 (m, 1H), 2.38 (dt, *J* = 7.1, 2.2 Hz, 2H), 1.57-1.41 (m, 2H), 1.28-1.09 (m, 8H), 0.82 (t, *J* = 6.9 Hz, 3H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 208.7, 147.4, 146.0, 134.8, 129.4, 124.2, 117.8, 58.4, 42.9, 36.9, 31.7, 28.8, 23.7, 22.6, 14.2. HRMS (DART) Calcd for C<sub>17</sub>H<sub>24</sub>NO<sub>3</sub> (M+H)<sup>+</sup> 290.1751, found 290.1745. **Aryl Ketone (iso-6m)**: R<sub>f</sub> = 0.29 (40% CH<sub>2</sub>Cl<sub>2</sub>/hexanes). IR (neat) 3075, 2929, 2857, 1689, 1526, 1346 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 8.32 (d, *J* = 8.9 Hz, 2H), 8.07 (d, *J* = 8.8 Hz, 2H), 5.72 (ddd, *J* = 17.1, 10.1, 7.1 Hz, 1H), 5.09-4.93 (m, 2H), 3.49 (tt, *J* = 7.5, 5.7 Hz, 1H), 2.58-2.45 (m, 1H), 2.34 – 2.22 (m, 1H), 1.85-1.67 (m, 2H), 1.33-1.11 (m, 8H), 0.91-0.78 (m, 3H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 202.6, 142.2, 135.4, 129.4, 124.2, 124.1, 117.4, 47.0, 36.4, 32.1, 31.8, 29.6, 27.5, 22.7, 14.2. HRMS (DART) Calcd for C<sub>17</sub>H<sub>24</sub>O (M+NH<sub>4</sub>)<sup>+</sup> 307.2016, found 307.2005.



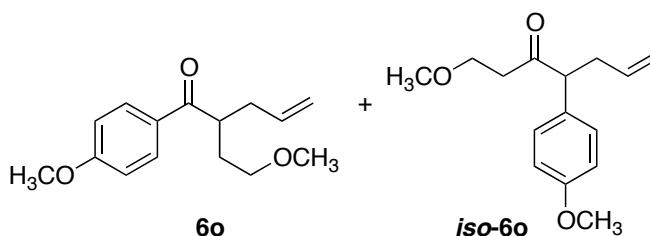
**2-(2-methoxyethyl)-1-phenylpent-4-en-1-one (6n) and 1-methoxy-4-phenylhept-6-en-3-one**

**(6n)** The following products were obtained using the optimized conditions with allyl alcohol (1.0 mL of 0.2M soln., 0.2 mmol) and 4-methoxy-1-phenyl-1-butyne<sup>10</sup>. Purified by flash column chromatography using a solvent gradient (0-20% EtOAc/hexanes) to yield the product as a clear colorless oil (34.5 mg, 79%; 3:1 mixture of regioisomers aryl:alkyl ketone). An analytical fraction of the aryl ketone was obtained; the characterization is as follows: *Aryl Ketone (6n)*:  $R_f$  = 0.65 (30% EtOAc/hexanes). IR (neat) 2928, 1671, 1601, 1508, 1396, 1247, 1171  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.00-7.95 (m, 2H), 7.59-7.53 (m, 1H), 7.49-7.45 (m, 2H), 5.73 (ddt,  $J$  = 17.1, 10.1, 7.0 Hz, 1H), 5.03 (dd,  $J$  = 17.0, 1.7 Hz, 1H), 4.97 (dd,  $J$  = 10.1, 1.7 Hz, 1H), 3.76-3.70 (m, 1H), 3.43-3.38 (m, 1H), 3.28 (ddd,  $J$  = 9.6, 7.6, 5.1 Hz, 1H), 3.22 (s, 3H), 2.55-2.47 (m, 1H), 2.31-2.23 (m, 1H), 2.07 (dddd,  $J$  = 13.9, 8.7, 6.2, 5.2 Hz, 1H), 1.81 (ddt,  $J$  = 14.0, 7.6, 5.3

Hz, 1H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  203.9, 137.7, 135.6, 133.1, 128.8, 128.5, 117.2, 70.5, 58.7, 42.7, 37.0, 32.1. HRMS (DART) Calcd for  $\text{C}_{14}\text{H}_{19}\text{O}_2$  ( $\text{M}+\text{H}$ ) $^+$  219.1380, found 219.1372. From a mixture of products the following NMR peaks were deduced as the alkyl ketone. **Alkyl Ketone (iso-6n)**:  $R_f$  = 0.65 (30% EtOAc/hexanes).  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.34-7.30 (m, 2H), 7.22-7.18 (m, 2H), 5.68-5.61 (ddd,  $J$  = 17.3, 10.1, 7.0 Hz, 1H), 5.05-4.92 (m, 2H), 3.59 (dt,  $J$  = 9.6, 6.6 Hz, 1H), 3.51 (dt,  $J$  = 9.6, 6.3 Hz, 1H), 3.25 (s, 3H), 2.81 (dt,  $J$  = 14.3, 7.2, 1.3 Hz, 1H), 2.68-2.56 (m, 2H), 2.47-2.39 (m, 1H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  208.1, 138.3, 135.9, 129.1, 128.6, 127.6, 116.8, 67.7, 59.3, 58.9, 42.0, 36.3.

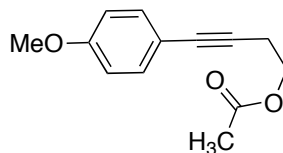


**1-methoxy-4-(4-methoxybut-1-yn-1-yl)benzene (S2)** The following compound was made through a related procedure for facile methylation of alcohols.<sup>11</sup> To a flask containing a stir bar and a mixture of MeI (0.31 mL, 5.0 mmol, 2.0 eq.), NaH (60% in mineral oil, 200 mg, 5.0 mmol, 2.0 eq.) and 3.0 mL of THF at room temperature was slowly and carefully added 4-(4-methoxyphenyl)-but-3-yn-1-ol<sup>10</sup> (neat, 440.0 mg, 2.5 mmol, 1.0 eq.). Minor bubbling occurred and the solution was placed in a 40°C oil bath for 1 hr. After this point the solution was cooled to r.t. and slowly quenched with 10 mL of deionized water. The solution was taken up in ether and washed with  $\text{NaHCO}_3$  and brine, dried over  $\text{NaSO}_4$ , and filtered. Purified by flash column chromatography using a solvent gradient (0-20% EtOAc/hexanes) to yield the product as a clear colorless oil (237.8 mg, 50%).  $R_f$  = 0.5 (20% EtOAc/hexanes). IR (neat) 3040, 2931, 2837, 1608, 1506, 1464, 1289, 1246, 1174, 1117  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.34 (d,  $J$  = 8.8 Hz, 2H), 6.81 (d,  $J$  = 8.8 Hz, 2H), 3.79 (s, 3H), 3.58 (t,  $J$  = 7.0 Hz, 2H), 3.41 (s, 3H), 2.67 (t,  $J$  = 7.0 Hz, 2H).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  159.3, 133.1, 115.9, 113.9, 85.2, 81.3, 71.1, 58.8, 55.3, 20.8. HRMS (DART) Calcd for  $\text{C}_{12}\text{H}_{15}\text{O}_2$  ( $\text{M}+\text{H}$ ) $^+$  191.1067, found 191.1073.



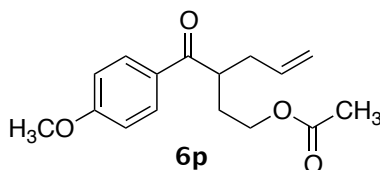
**2-(2-methoxyethyl)-1-(4-methoxyphenyl)pent-4-en-1-one (6o)** and **1-methoxy-4-(4-methoxyphenyl)hept-6-en-3-one (iso-6o)** The following products were obtained using the optimized conditions with allyl alcohol (1.0 mL of 0.2M soln., 0.2 mmol) and 1-methoxy-4-(4-methoxybut-1-yn-1-yl)benzene. Purified by flash column chromatography using a solvent gradient (0-20% EtOAc/hexanes) to yield the product as a white crystalline solid (43.2 mg, 87%; 9:1 mixture of regioisomers aryl:alkyl ketone). An analytical fraction of the aryl ketone **6o** was obtained; the characterization is as follows:  $R_f$  = 0.53 (50% Et<sub>2</sub>O/hexanes). IR (neat) 3064, 2925, 2874, 2822, 1682, 1447, 1117  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (500 MHz,  $\text{C}_6\text{D}_6$ ):  $\delta$  8.06 (d,  $J$  = 8.9 Hz, 2H), 6.68-6.63 (d,  $J$  = 8.8 Hz, 2H), 5.76 (ddd,  $J$  = 17.0, 10.2, 7.0 Hz, 1H), 5.02 (ddt,  $J$  = 17.0, 2.0, 1.5 Hz, 1H), 4.92 (ddt,  $J$  = 10.2, 2.0, 1.5 Hz, 1H), 3.74 (dddd,  $J$  = 8.6, 7.5, 6.1, 5.1 Hz, 1H), 3.24-3.12 (m, 5H), 2.99 (s, 3H), 2.63-2.55 (m, 1H), 2.27-2.19 (m, 1H), 2.20-2.12 (m, 1H), 1.78 (ddt,  $J$  = 14.0, 7.8, 5.2 Hz, 1H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  202.3, 163.7, 135.8, 130.8, 130.7, 117.0, 113.9,

70.5, 58.7, 55.7, 42.2, 37.1, 32.3. HRMS (DART) Calcd for  $C_{15}H_{21}O_3$  (M+H)<sup>+</sup> 249.1485, found 249.1489.



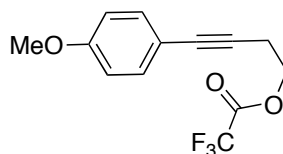
**S3**

**4-(4-methoxyphenyl)but-3-yn-1-yl acetate (S3)** The following compound was made via acetylation of the known alcohol 4-(4-methoxyphenyl)-but-3-yn-1-ol<sup>10</sup>. The procedure is as follows: To a solution of 4-(4-methoxyphenyl)-but-3-yn-1-ol<sup>10</sup> (358.0 mg, 2 mmol, 1.0 eq.), DMAP (12.0 mg, 0.1 mmol, 5 mol%) and pyridine (10 mL) submerged in an ice bath, was added acetic anhydride (0.4 mL, 4.2 mmol, 2.0 eq.). The solution was stirred for 2 hours then quenched with NaHCO<sub>3</sub> (10 mL), and diluted with EtOAc (30 mL). The organic phase was then washed with CuSO<sub>4</sub> (3x10mL). The organic phase was then dried over NaSO<sub>4</sub>, and filtered. Purified by flash column chromatography using a solvent gradient (0-20% EtOAc/hexanes) to yield the product as a clear colorless oil (100.0 mg, 23%).  $R_f$  = 0.44 (20% EtOAc/hexanes). IR (neat) 2960, 2838, 1737, 1606, 1509, 1442, 1234 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  7.33 (d,  $J$  = 8.9 Hz, 2H), 6.81 (d,  $J$  = 8.9 Hz, 2H), 4.24 (t,  $J$  = 7.0 Hz, 2H), 3.79 (s, 3H), 2.73 (t,  $J$  = 7.0 Hz, 2H), 2.09 (s, 3H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  171.0, 159.4, 133.1, 115.6, 114.0, 84.0, 81.9, 62.7, 55.4, 21.1, 20.1.



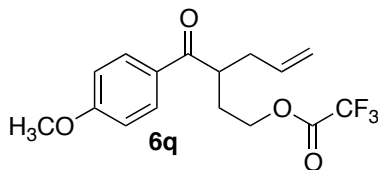
**6p**

**3-(4-methoxybenzoyl)hex-5-en-1-yl acetate (6p)** The following product was obtained using the optimized conditions with allyl alcohol (1.0 mL of 0.15 M soln., 0.15 mmol) and 4-(4-methoxyphenyl)but-3-yn-1-yl acetate (100 mg, 0.45 mmol, 3.0 eq.). Purified by flash column chromatography on florisil using a solvent gradient (0-20% EtOAc/hexanes) to yield the product as a clear oil (36.0 mg, 65% as an 8:1 mixture of regioisomers aryl:alkyl ketone). Data for the major isomer reported:  $R_f$  = 0.45 (20% EtOAc/hexanes). IR (neat) 3077, 2936, 2842, 1735, 1670, 1598, 1510, 1365, 1234, 1169, 1029 cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  7.94 (d,  $J$  = 8.8 Hz, 2H), 6.94 (d,  $J$  = 8.9 Hz, 2H), 5.72 (ddt,  $J$  = 17.0, 10.1, 7.1 Hz, 1H), 5.07-5.02 (m, 1H), 5.01 - 4.98 (m, 1H), 4.09 (dt,  $J$  = 11.3, 6.4 Hz, 1H), 4.01 (dt,  $J$  = 11.2, 6.5 Hz, 1H), 3.87 (s, 3H), 3.58 (dtd,  $J$  = 8.7, 6.7, 5.0 Hz, 1H), 2.53-2.45 (m, 1H), 2.30-2.22 (m, 1H), 2.21-2.11 (m, 1H), 1.93 (s, 3H), 1.86 (dtd,  $J$  = 11.4, 6.4, 4.8 Hz, 1H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  201.2, 171.1, 163.8, 135.3, 130.8, 130.1, 129.6, 117.4, 114.6, 114.1, 62.89, 55.70, 42.45, 37.19, 30.70, 21.04.

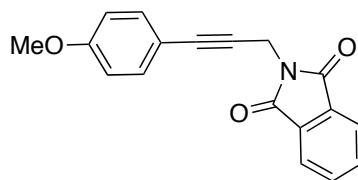


S4

**4-(4-methoxyphenyl)but-3-yn-1-yl 2,2,2-trifluoroacetate (S4)** To a solution of 4-(4-methoxyphenyl)-but-3-yn-1-ol<sup>10</sup> (358.0 mg, 2 mmol, 1.0 eq.), DMAP (12.0 mg, 0.1 mmol, 5 mol%) and pyridine (10 mL) submerged in an ice bath, was added acetic anhydride (0.4 mL, 4.2 mmol, 2.0 eq.). The solution was stirred for 2 hours then quenched with NaHCO<sub>3</sub> (10 mL), and diluted with EtOAc (30 mL). The organic phase was then washed with CuSO<sub>4</sub> (3x10mL). The organic phase was then dried over NaSO<sub>4</sub>, and filtered. Purified by flash column chromatography using a solvent gradient (0-20% EtOAc/hexanes) to yield the product as a clear colorless oil (100.0 mg, 23%). *R<sub>f</sub>* = 0.61 (20% EtOAc/hexanes). IR (neat) 2970, 2841, 1785, 1607, 1509, 1447, 1142 cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 7.33 (d, *J* = 8.6 Hz, 2H), 6.83 (d, *J* = 8.9 Hz, 1H), 4.52 (t, *J* = 6.9 Hz, 2H), 3.80 (s, 3H), 2.86 (t, *J* = 6.9 Hz, 2H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 159.7, 133.2, 116.6, 115.2, 114.1, 82.9, 82.1, 65.8, 55.4, 19.8. <sup>19</sup>F NMR (282 MHz, CDCl<sub>3</sub>): δ 75.39

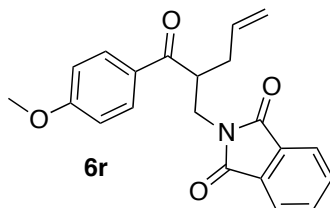


**3-(4-methoxybenzoyl)hex-5-en-1-yl 2,2,2-trifluoroacetate (6q)** The following product was obtained using the optimized conditions with allyl alcohol (1.0 mL of 0.16 M soln., 0.16 mmol) and 4-(4-methoxyphenyl)but-3-yn-1-yl 2,2,2-trifluoroacetate (130 mg, 0.48 mmol, 3.0 eq.). Purified by flash column chromatography on florisil using a solvent gradient (0-50% EtOAc/hexanes) to yield the product as a clear oil (26.0 mg, 50%; >25:1 mixture of regioisomers aryl:alkyl ketone). *R<sub>f</sub>* = 0.35 (20% EtOAc/hexanes). IR (neat) 2984, 1736, 1673, 1601, 1237, 1044 cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 8.04-7.93 (m, 2H), 6.97-6.92 (m, 2H), 5.74 (ddt, *J* = 17.1, 10.1, 7.1 Hz, 1H), 5.07-4.96 (m, 2H), 3.87 (s, 3H), 3.82-3.57 (m, 3H), 2.52 (dt, *J* = 14.0, 6.9 Hz, 1H), 2.27 (dt, *J* = 14.1, 7.1 Hz, 1H), 2.10-2.00 (m, 1H), 1.85-1.74 (m, 1H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 202.5, 163.8, 135.7, 130.9, 130.3, 124.5, 117.1, 114.6, 60.92, 55.70, 42.35, 37.04, 34.56, 29.05. <sup>19</sup>F NMR (282 MHz, CDCl<sub>3</sub>): δ 84.08.



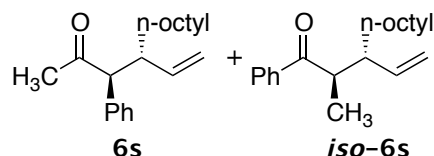
**S5**

**2-(3-(4-methoxyphenyl)prop-2-yn-1-yl)isoindoline-1,3-dione (S5)** The following compound was made via sonogashira coupling between N-propargylphthalimide<sup>12</sup> and 4-iodoanisole, the reaction is as follows: To a flask containing N-propargylphthalimide<sup>12</sup> (500 mg, 2.7 mmol, 1.0 eq.), 4-iodoanisole (631 mg, 2.7 mmol, 1.0 eq.), PPh<sub>3</sub>PdCl<sub>2</sub> (37.0 mg, 0.05 mmol, 2 mol%), CuI (20.0 mg, 4 mol%) and CH<sub>3</sub>CN (12 mL) under a N<sub>2</sub> atmosphere, was added Et<sub>3</sub>N (1.3 mL) at room temperature. The solution was stirred for 2 hours at room temperature then the volatiles were evaporated and the solid residue was triturated with EtOAc to give an light brown solid that was used without further purification (668.0 mg, 85%). *R<sub>f</sub>* = 0.71 (CH<sub>2</sub>Cl<sub>2</sub>). IR (neat) 2971, 2943, 1768, 1715, 1604, 1508, 1390, 1252 cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 7.89 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.73 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.35 (d, *J* = 8.8 Hz, 2H), 6.79 (d, *J* = 8.8 Hz, 2H), 4.66 (s, 2H), 3.78 (s, 3H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 167.40, 165.61, 165.55, 159.95, 134.43, 134.33, 133.62, 132.35, 123.73, 114.62, 114.03, 110.22, 83.09, 81.45, 55.47, 28.16.

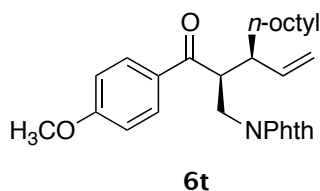


**6r**

**2-(2-(4-methoxybenzoyl)pent-4-en-1-yl)isoindoline-1,3-dione (6r)** The following product was obtained using the optimized conditions with allyl alcohol (1.0 mL of 0.12M soln., 0.12 mmol) and 2-(3-(4-methoxyphenyl)prop-2-yn-1-yl)isoindoline-1,3-dione (107 mg, 0.6 mmol, 3.0 eq.). Purified by flash column chromatography using a solvent gradient (20-100% CH<sub>2</sub>Cl<sub>2</sub>/hexanes) to yield the product as a clear oil (31.3 mg, 72%; >25:1 mixture of regioisomers aryl:alkyl ketone). *R<sub>f</sub>* = 0.41 (40% EtOAc/hexanes). IR (neat) 3076, 2935, 2842, 1711, 1671, 1598, 1511, 1172 cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 8.03-7.98 (m, 2H), 7.85-7.81 (m, 2H), 7.74-7.69 (m, 2H), 6.94-6.89 (m, 2H), 5.75 (ddt, *J* = 17.1, 10.2, 6.9 Hz, 1H), 5.05 (d, *J* = 17.3 Hz, 1H), 4.96 (d, *J* = 10.1 Hz, 1H), 4.15 (p, *J* = 6.8 Hz, 1H), 4.03 (dd, *J* = 13.5, 6.5 Hz, 1H), 3.94-3.87 (m, 1H), 3.85 (s, 3H), 2.64 (dt, *J* = 14.3, 7.0 Hz, 1H), 2.34 (dt, *J* = 14.0, 6.6 Hz, 1H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 199.2, 168.5, 163.9, 134.8, 134.2, 132.1, 131.0, 129.9, 123.5, 117.4, 114.1, 55.67, 44.09, 39.93, 34.68.



***anti*-3-phenyl-4-vinyldodecan-2-one (6s)** and ***anti*-2-methyl-1-phenyl-3-vinylundecan-1-one (iso-6s)** The following compounds were made with the optimized conditions with (*E*)-undec-2-en-1-ol<sup>1</sup> (1.0 mL of 0.2M soln., 0.2 mmol) and 1-phenyl-1-propyne (70 mg, 0.6 mmol, 3.0 eq.). Purified by flash column chromatography using a solvent gradient (0-20% CH<sub>2</sub>Cl<sub>2</sub>/hexanes) to yield the mixture of products as a clear colorless oil (45.0 mg, 78%; 4:1 mixture of regioisomers alkyl:aryl ketone; only one observable diastereomer for each regioisomer). Analytical fractions of each were obtained; their characterization is as follows: **Alkyl Ketone (6s)**: *R<sub>f</sub>* = 0.40 (40% CH<sub>2</sub>Cl<sub>2</sub>/hexanes). 2926, 2856, 1715, 1455, 1354, 1151 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.32-7.22 (m, 2H), 7.22-7.14 (m, 3H), 5.26 (ddd, *J* = 16.9, 10.4, 9.3 Hz, 1H), 4.82-4.72 (m, 2H), 3.59 (d, *J* = 10.2 Hz, 1H), 2.92-2.79 (m, 1H), 2.10 (s, 3H), 1.49-1.14 (m, 12H), 0.84 (t, *J* = 6.2 Hz, 3H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 208.3, 139.5, 137.5, 129.4, 128.7, 127.4, 116.7, 64.8, 46.1, 33.6, 32.1, 30.5, 29.8, 29.8, 29.5, 27.4, 22.9, 14.3. HRMS (DART) Calcd for C<sub>17</sub>H<sub>32</sub>O (*M*+H)<sup>+</sup> 287.2369, found 287.2362. **Aryl Ketone (iso-6s)**: *R<sub>f</sub>* = 0.42 (40% CH<sub>2</sub>Cl<sub>2</sub>/hexanes). IR (neat) 3067, 2927, 2855, 1684, 1458, 1355, 1214 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.97-7.92 (m, 2H), 7.60-7.53 (m, 1H), 7.51-7.44 (m, 2H), 5.51 (ddd, 17.0, 10.3, 9.6 Hz, 1H), 5.07 (dd, *J* = 10.3, 2.0 Hz, 1H), 4.95 (ddd, *J* = 17.0, 2.0, 0.7 Hz, 1H), 3.42 (q, *J* = 7.0 Hz, 1H), 2.52-2.39 (m, 1H), 1.33-1.15 (m, 14H), 1.11 (d, *J* = 6.9 Hz, 3H), 0.86 (t, *J* = 6.5 Hz, 3H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 204.6, 139.6, 137.6, 133.0, 128.8, 128.4, 116.9, 47.3, 44.7, 33.4, 32.1, 29.7, 29.5, 27.7, 22.9, 15.2, 14.3. HRMS (DART) Calcd for C<sub>20</sub>H<sub>31</sub>O (*M*+H)<sup>+</sup> 287.2369, found 287.2359.



***syn*-2-(4-methoxybenzoyl)-3-vinylundecylisoindoline-1,3-dione (6t)** The following products were obtained using the optimized conditions with (*Z*)-undec-2-en-1-ol (**4d**) (1.0 mL of 0.2M soln., 0.2 mmol) and 2-(3-(4-methoxyphenyl)prop-2-yn-1-yl)isoindoline-1,3-dione (180 mg, 0.6 mmol, 3.0 eq.). Purified by flash column chromatography using a solvent gradient (20-100% CH<sub>2</sub>Cl<sub>2</sub>/hexanes) to yield the product as a clear oil (56.0 mg, 59%, >25:1 *dr*; >25:1 mixture of regioisomers aryl:alkyl ketone). *R<sub>f</sub>* = 0.2 (80% CH<sub>2</sub>Cl<sub>2</sub>/hexanes). IR (neat) 3075, 2925, 2854, 1773, 1712, 1671, 1598, 1393, 1170 cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): 7.90-7.82 (m, 2H), 7.75 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.64 (dd, *J* = 5.5, 3.0 Hz, 2H), 6.83 (d, *J* = 8.9 Hz, 2H), 5.71 (ddd, *J* = 17.1, 10.2, 9.0 Hz, 1H), 5.17-4.74 (m, 2H), 4.28-4.05 (m, 2H), 3.87-3.75 (m, 4H), 2.50-2.36 (m, 1H), 1.55-1.44 (m, 1H), 1.36-1.02 (m, 10H), 0.86 (t, *J* = 7.1 Hz, 3H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 199.8, 168.4, 163.6, 138.9, 134.0, 132.1, 131.2, 130.8, 123.4, 117.0, 113.9, 55.6, 47.6, 45.8, 38.6, 32.0, 31.3, 29.7, 29.6, 29.5, 27.5, 22.9, 14.3.

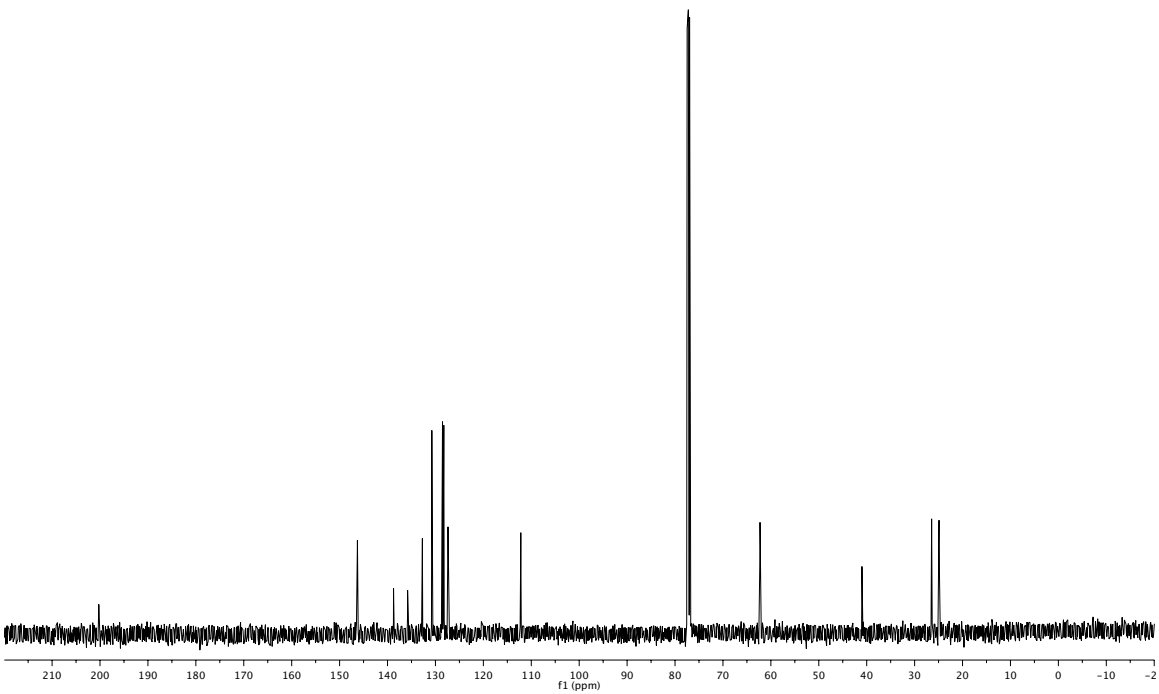
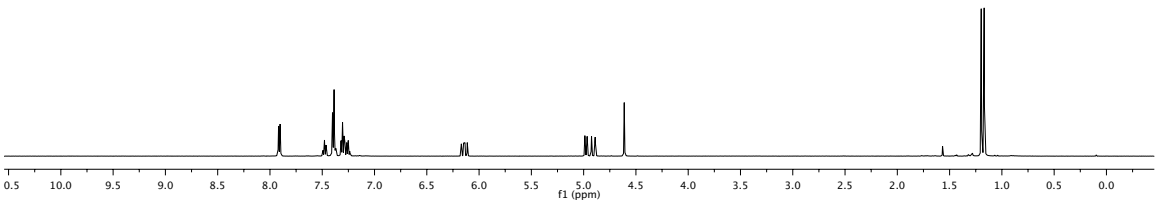
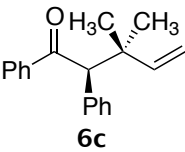
### Epimerization experiments (Eqs. 2):

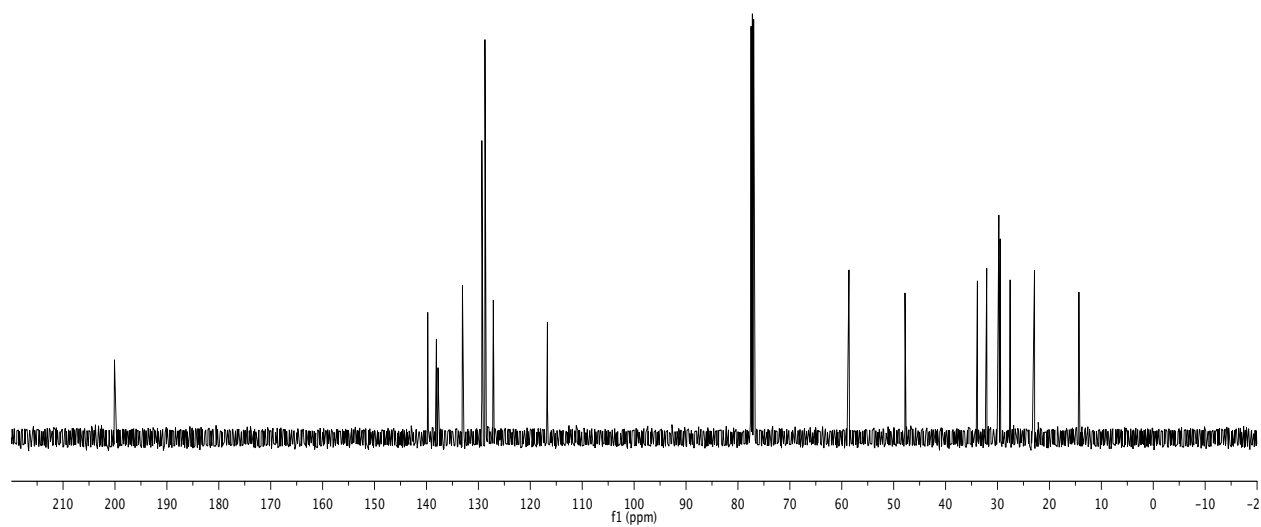
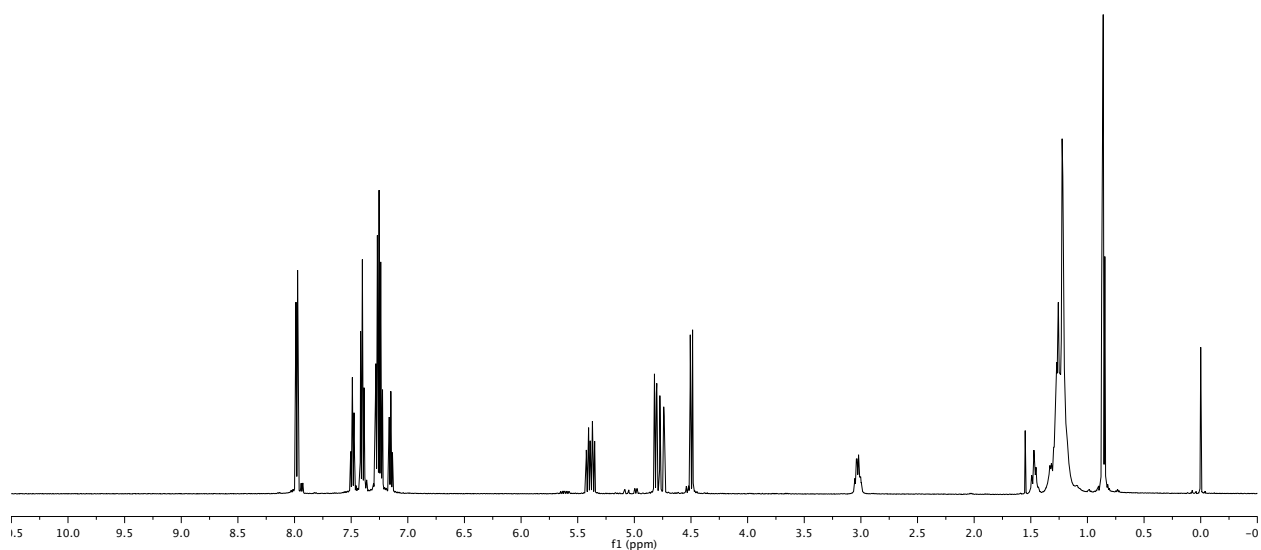
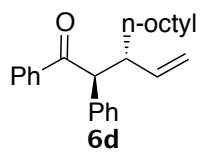
Single diastereomers of ketones **6d** and **6e** were obtained by careful separation via column chromatography. An example of these experiments is as follows: A pressure tube (screw cap) containing a stir bar was taken from the oven and placed directly into a glovebox. To this vessel was added 1,3-bis(2,6-diisopropylphenyl-imidazol-2-ylidene)gold(I) chloride (6.2 mg, 0.01 mmol, 5 mol%), and silver tetrafluoroborate (1.9 mg, 0.01 mmol, 5 mol%). The vessel was capped with a septum and then taken out of the glovebox where it was immediately placed under a dry nitrogen atmosphere. 0.5 mL of THF was added to the tube and the mixture was left to stir ~10 mins to activate the complex. After this time a solution of ketone **6d** or **6e** (0.2 mmol in 0.5 mL of THF) was transferred to the tube, and the vessel was then placed in a 65 °C oil bath and left to stir for 15 hrs. The tube was then sealed with a screwcap and placed in a 120 °C oil bath for 6 hrs (behind a safety shield). After cooling to room temperature the screwcap was removed and the solution was filtered over a plug of silica with EtOAc. The solution was then evaporated, and the crude was characterized by <sup>1</sup>H NMR (500 MHz) which showed exclusively the unaltered isomers **6d** and **6e** respectively.

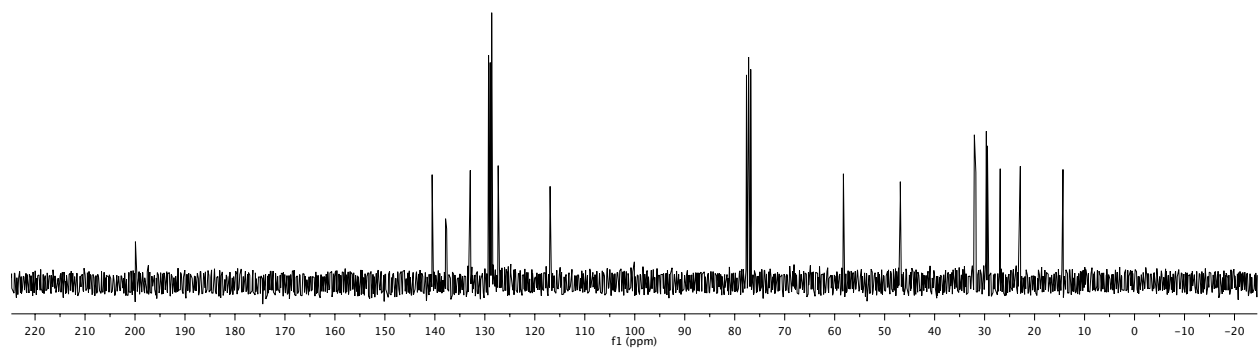
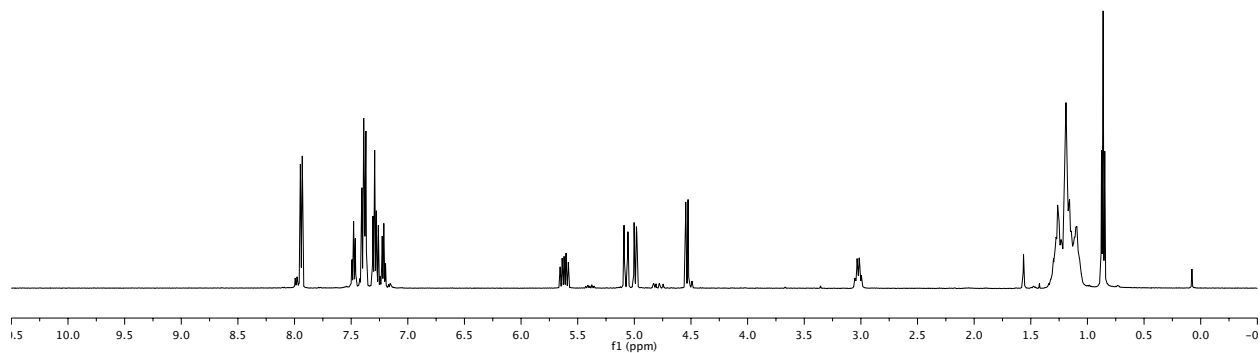
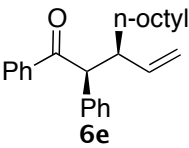
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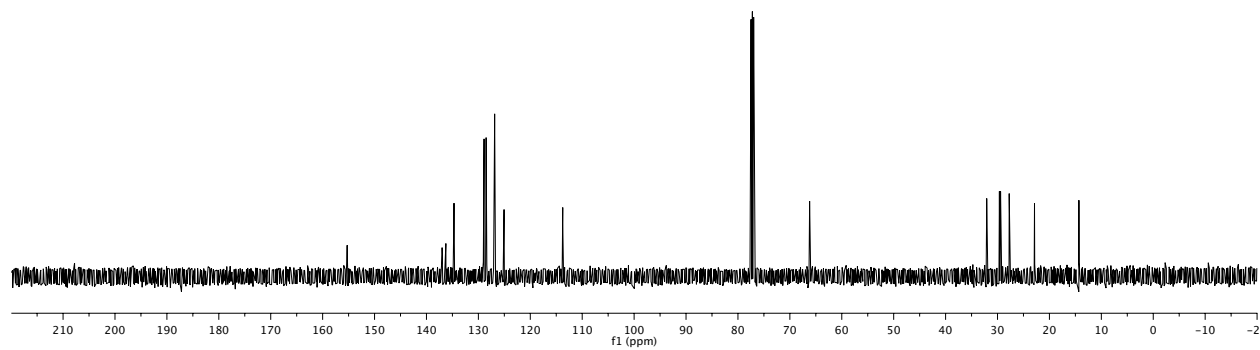
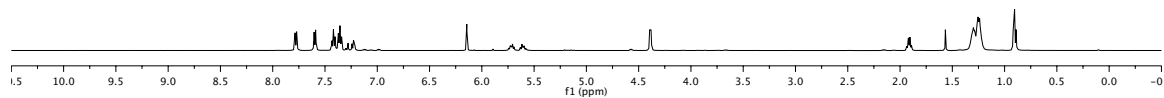
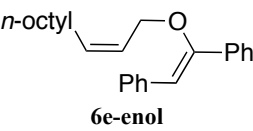
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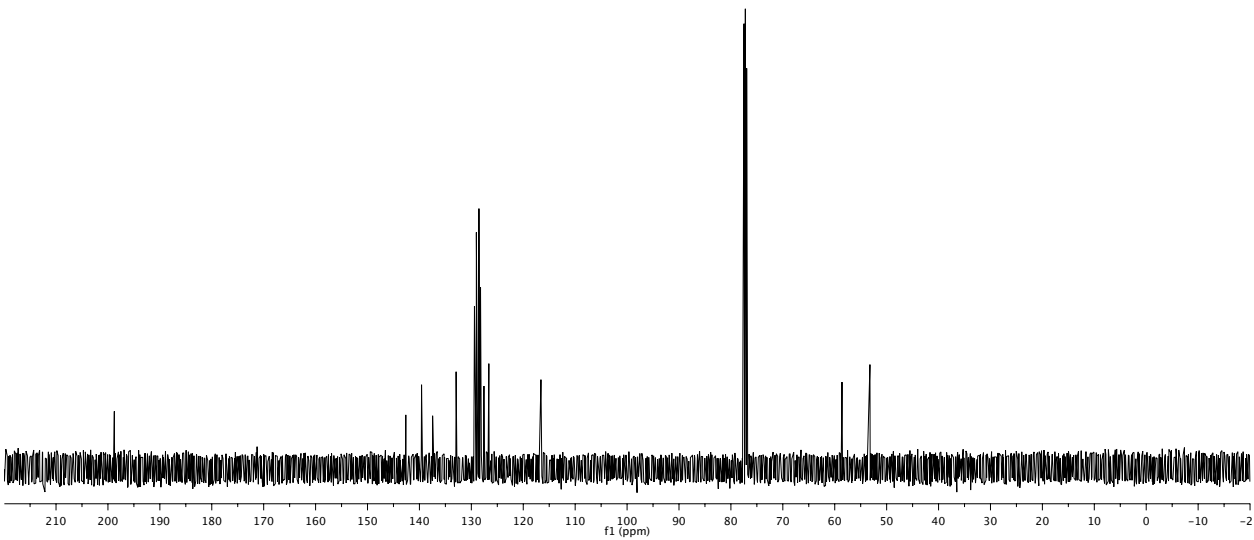
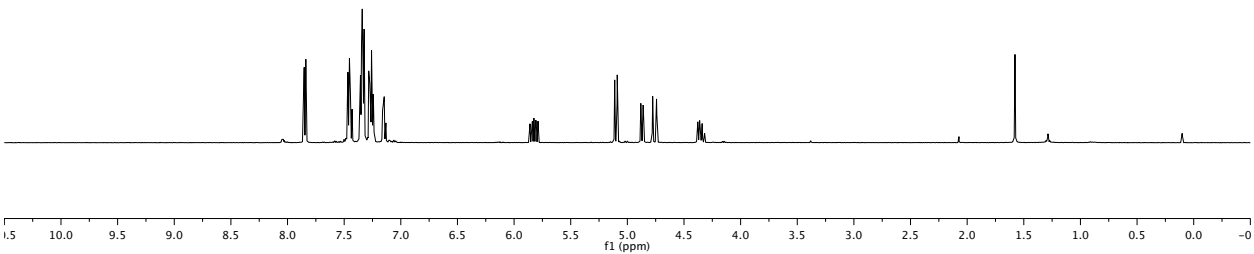
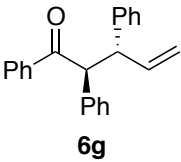


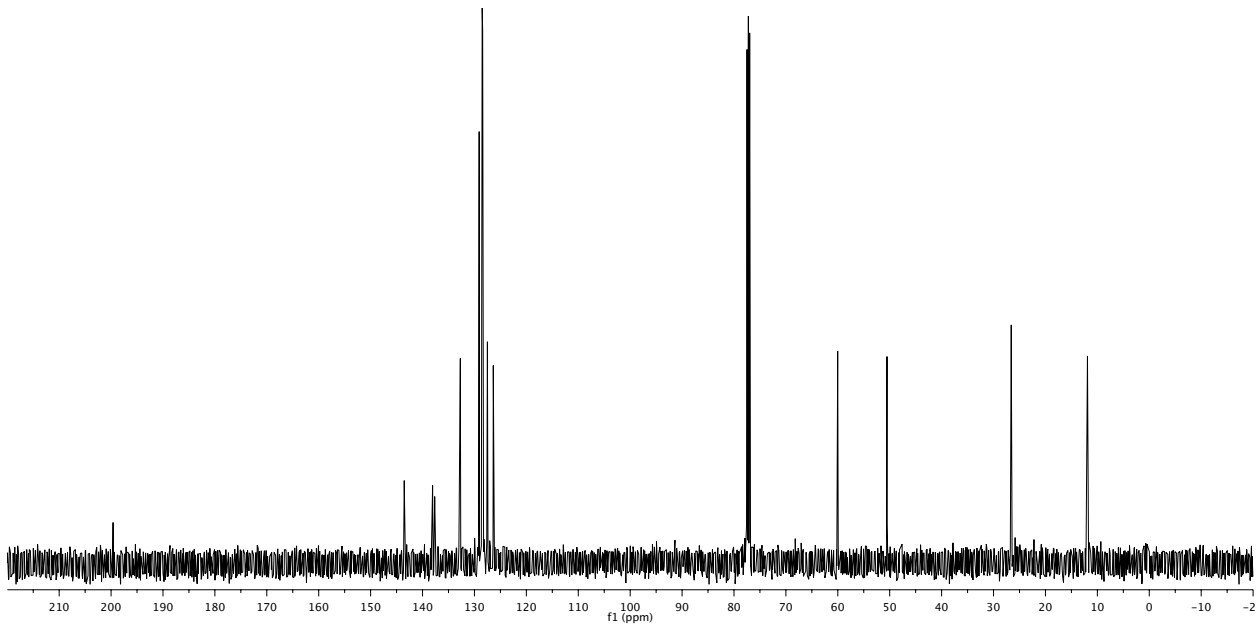
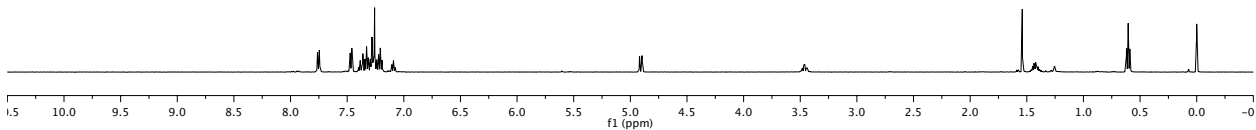
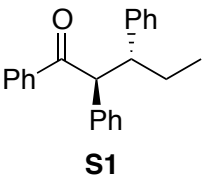


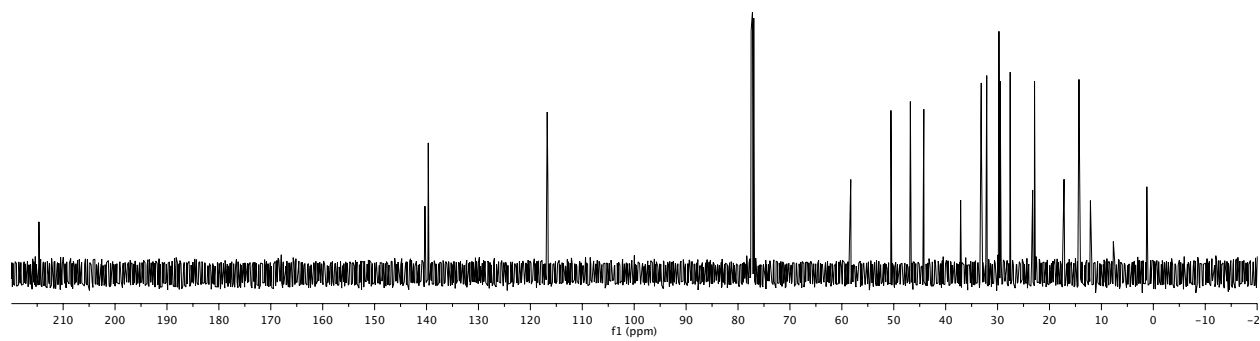
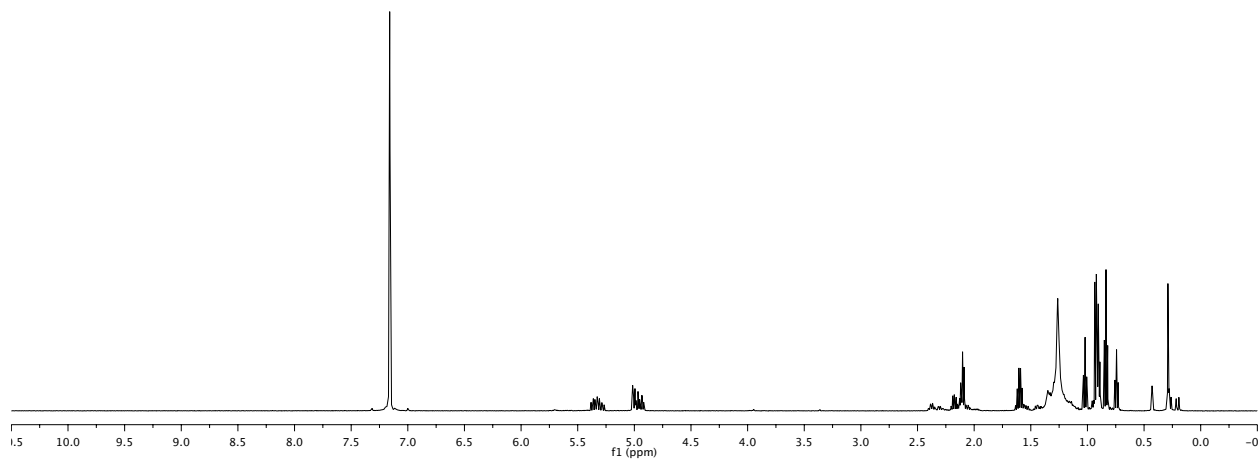
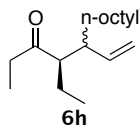




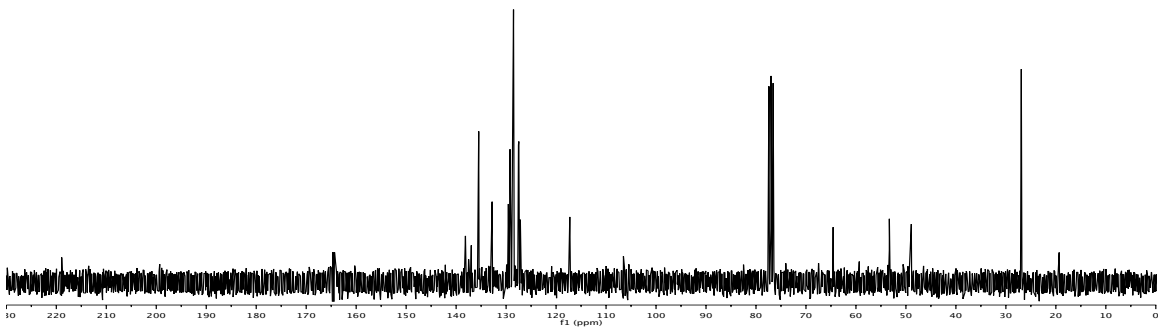
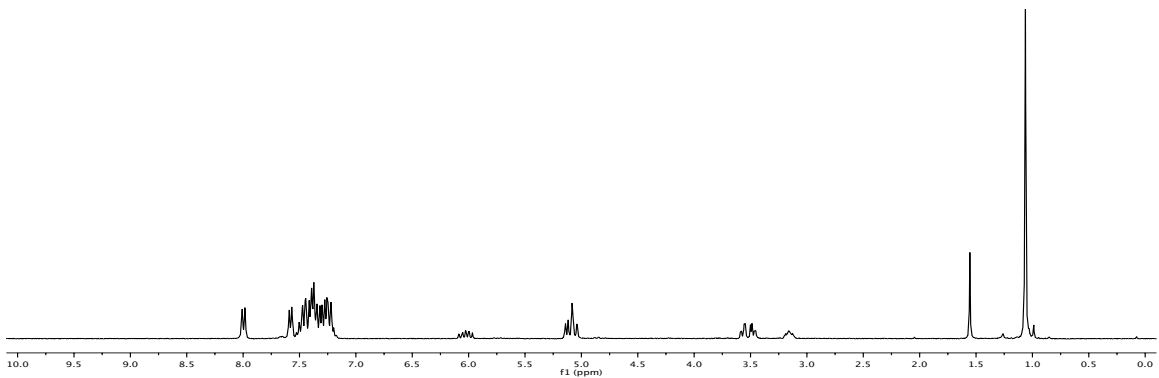
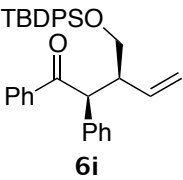


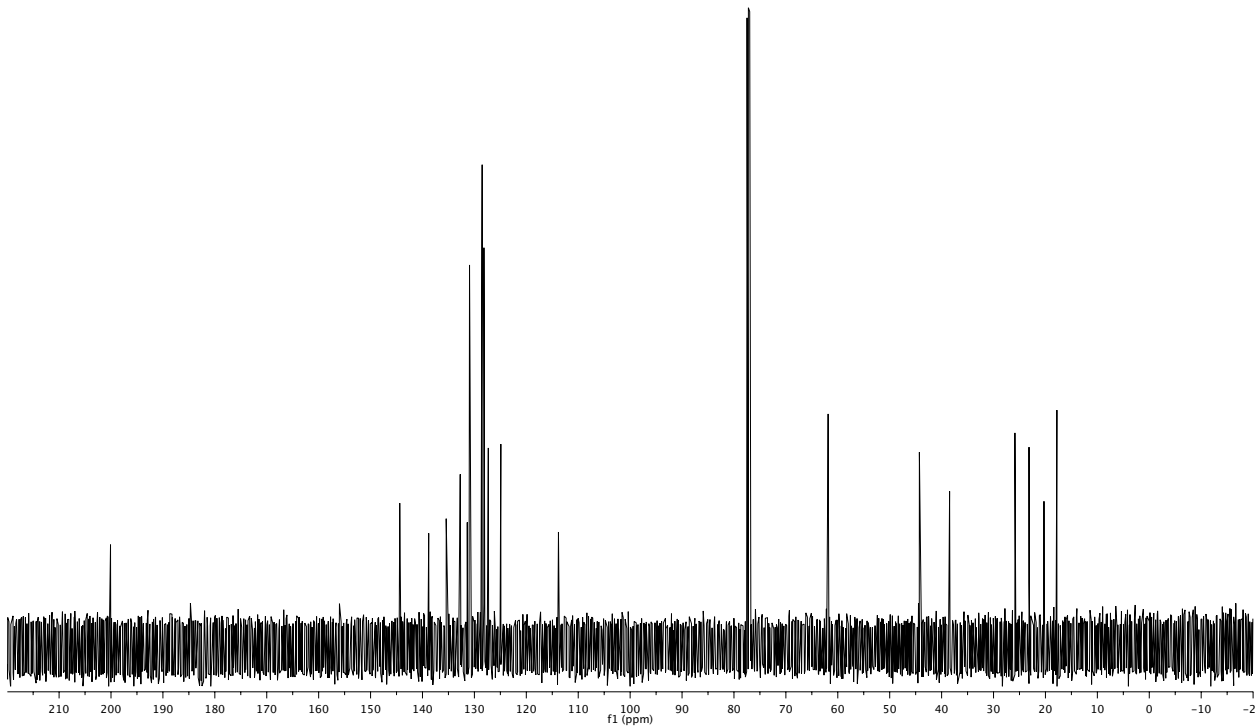
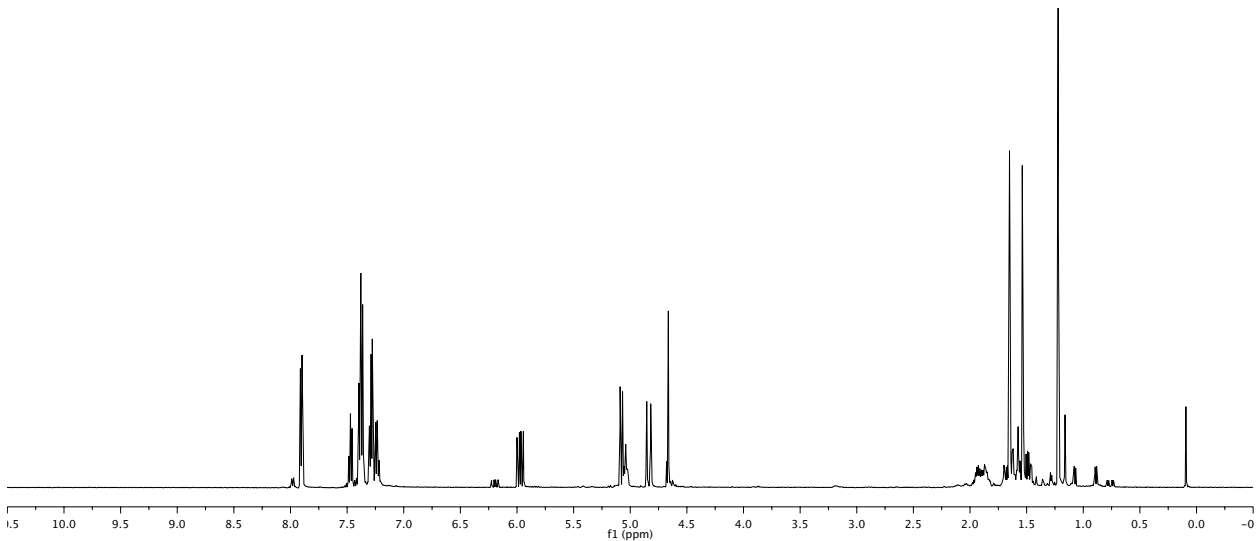
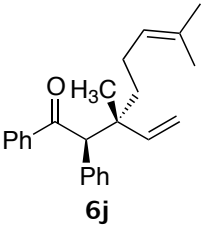


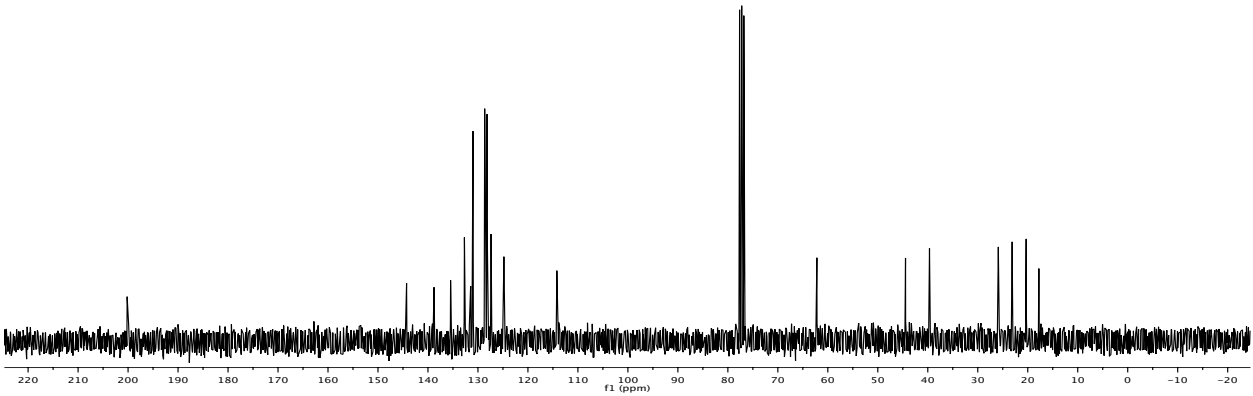
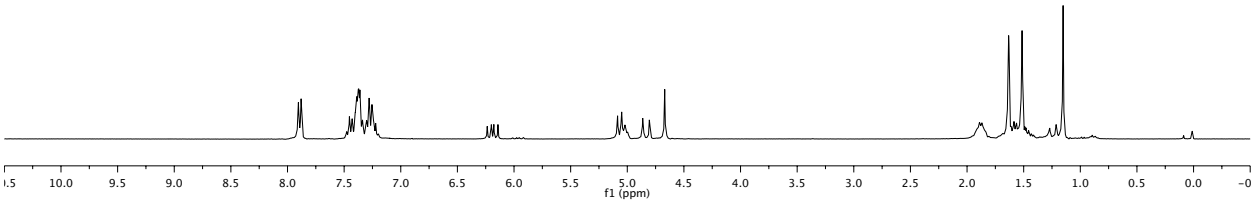
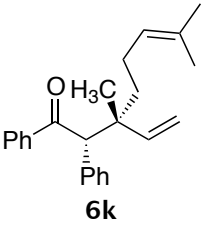


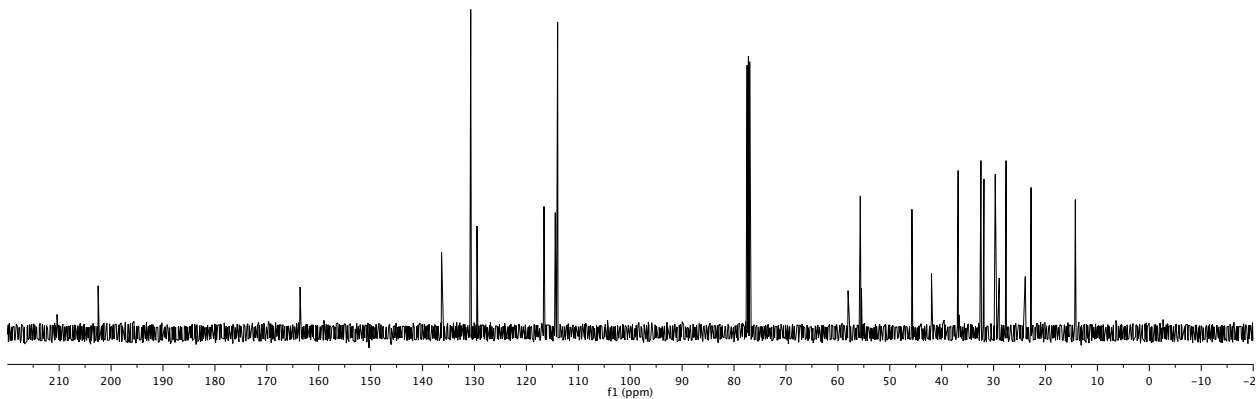
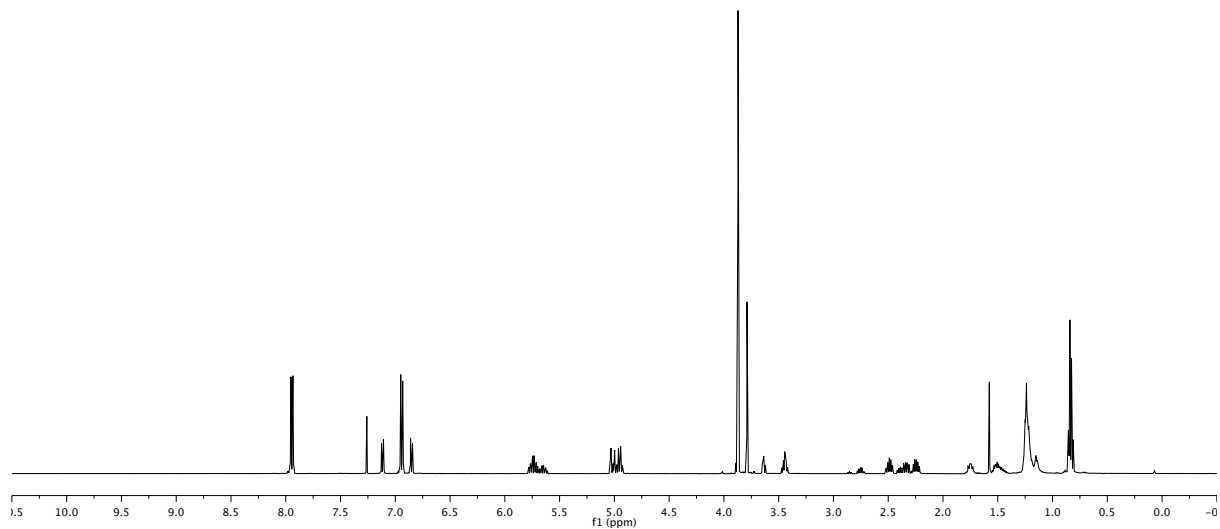
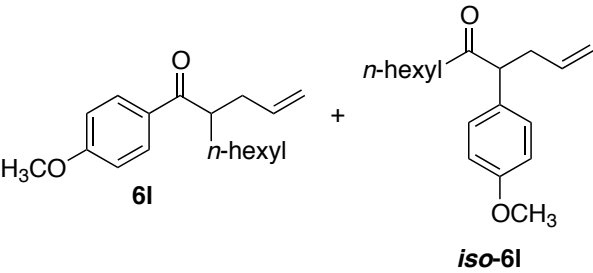


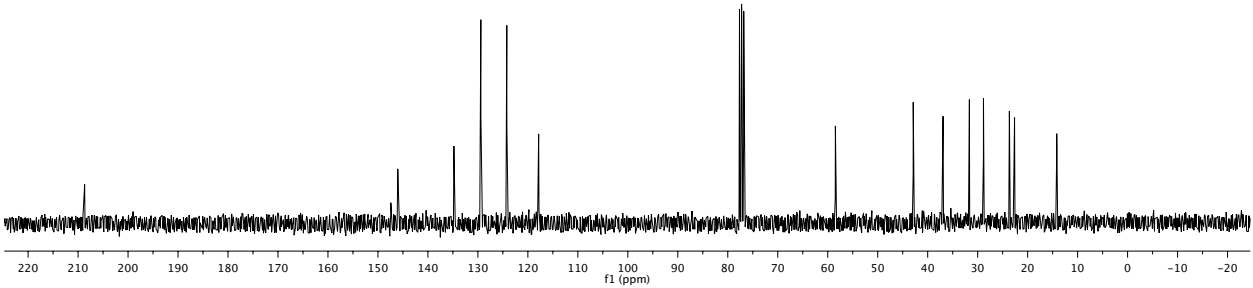
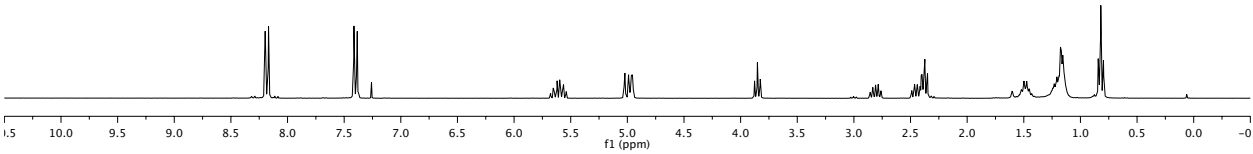
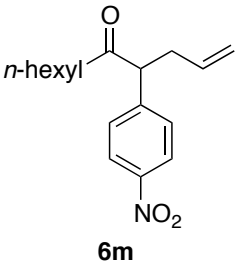


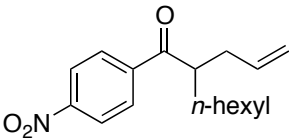




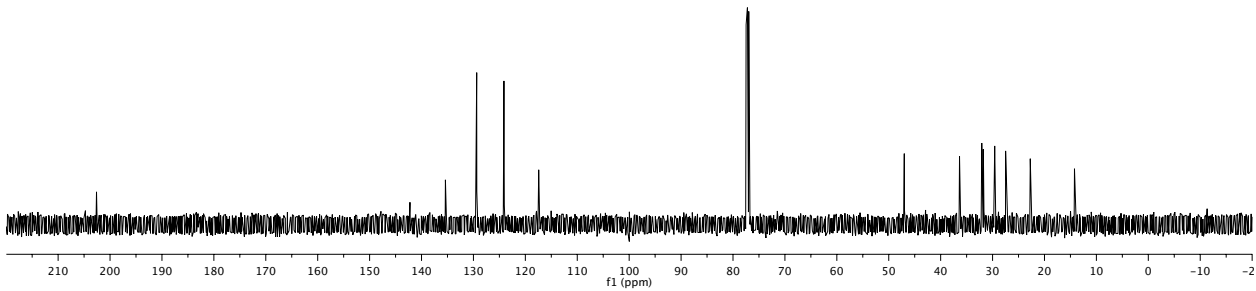
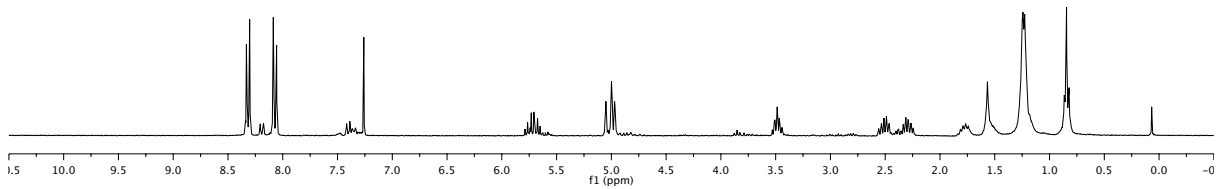


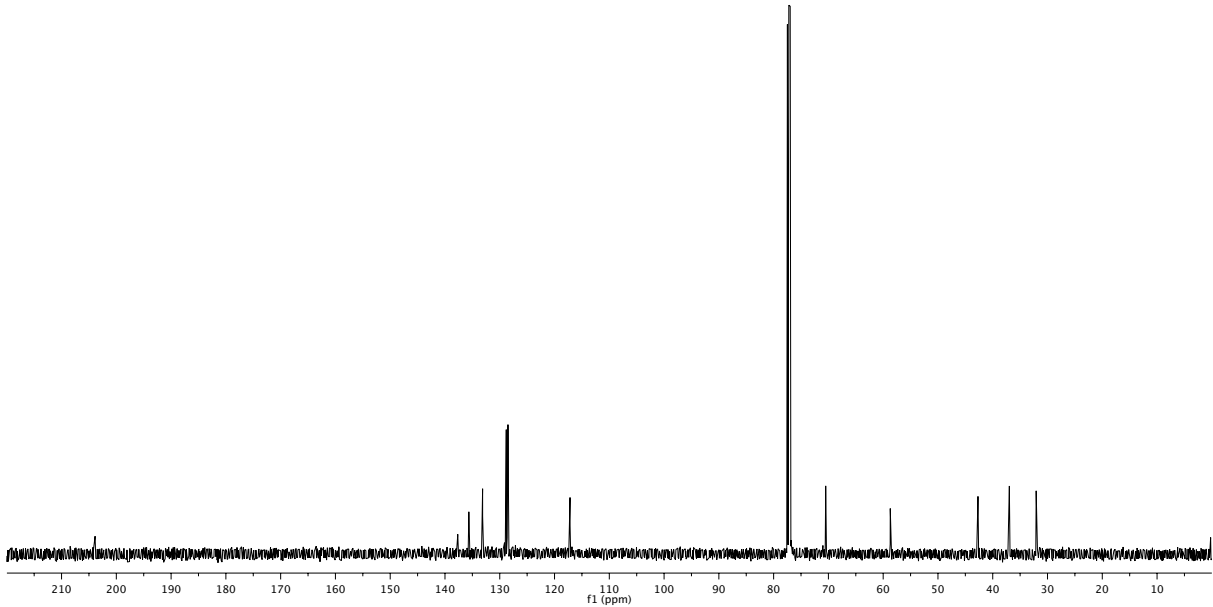
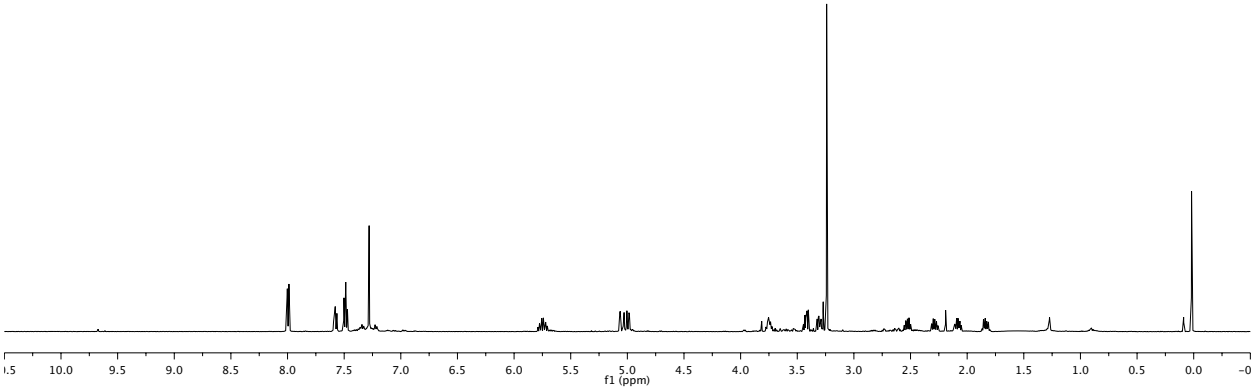
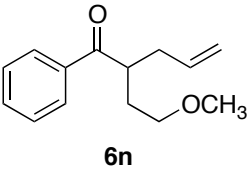




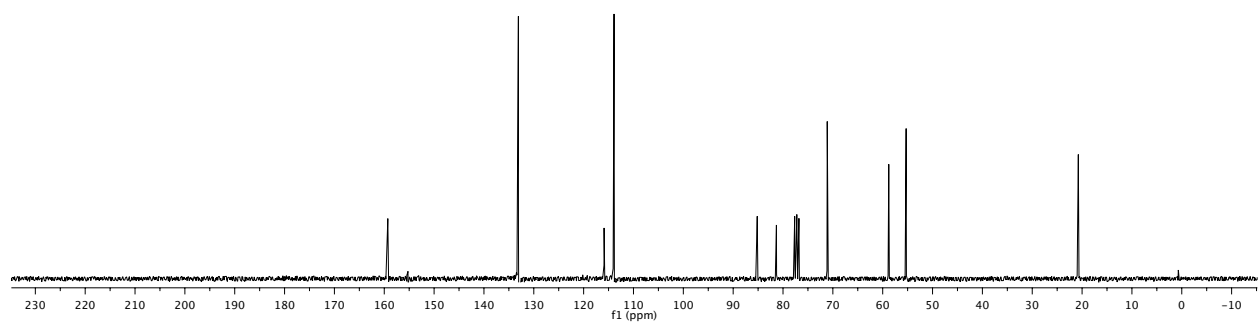
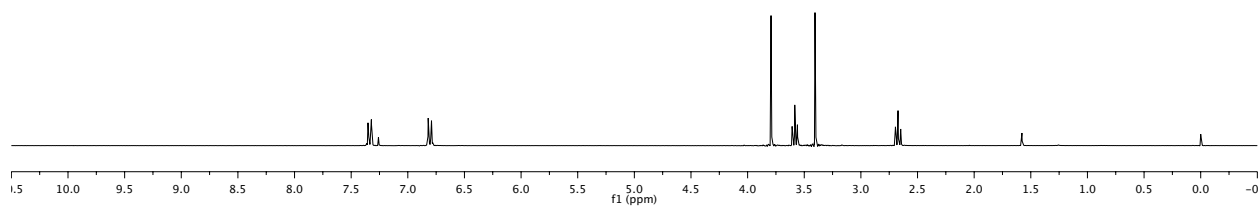
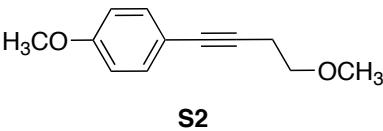


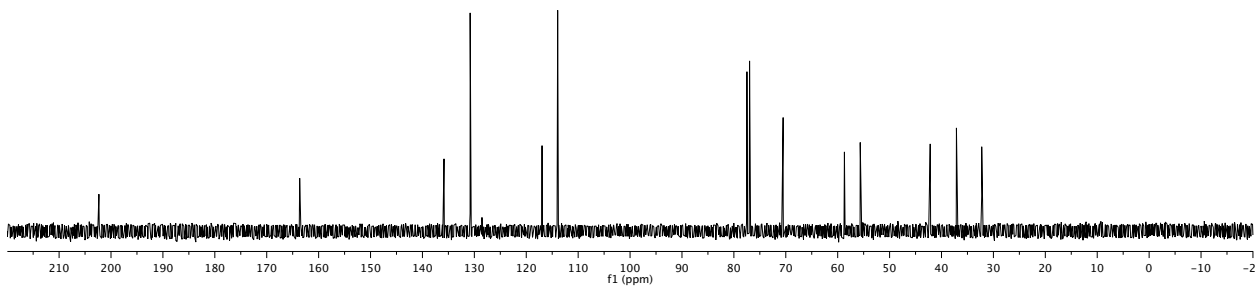
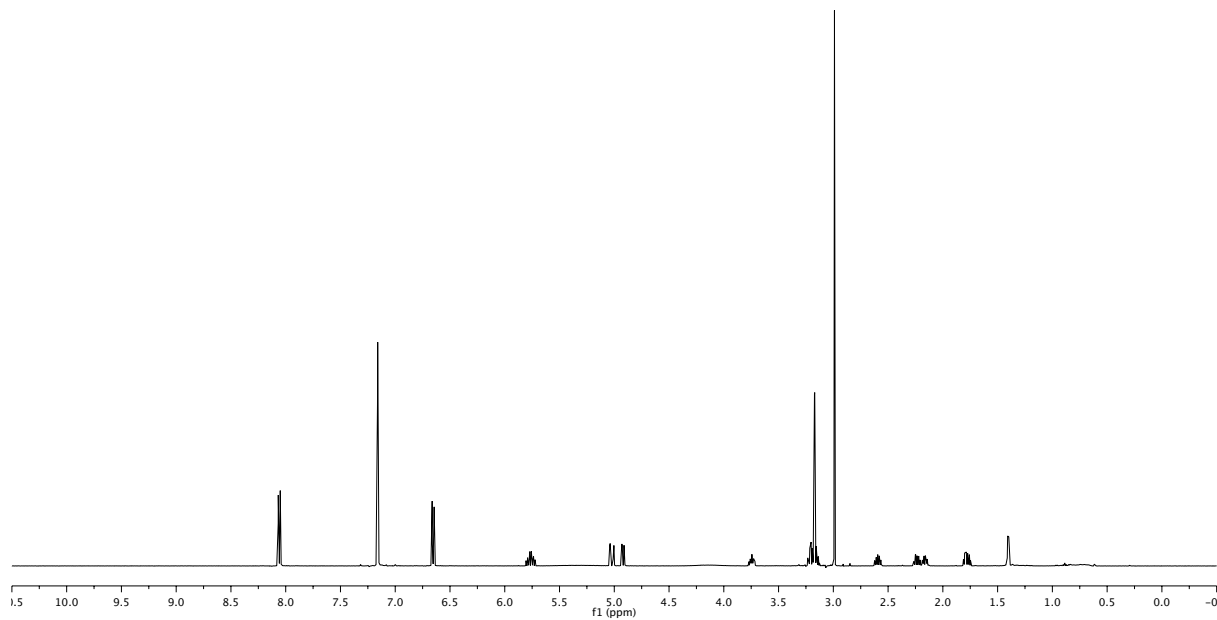
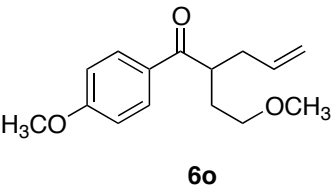
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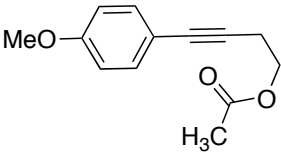




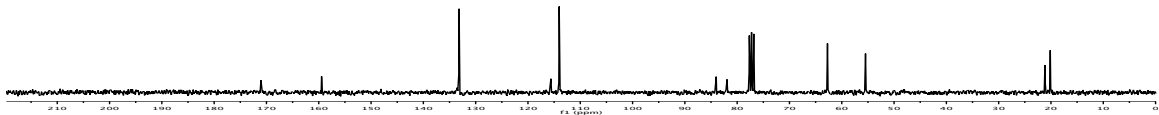
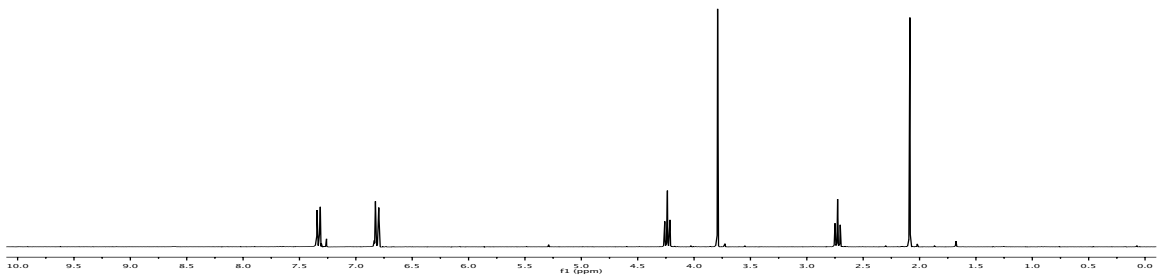


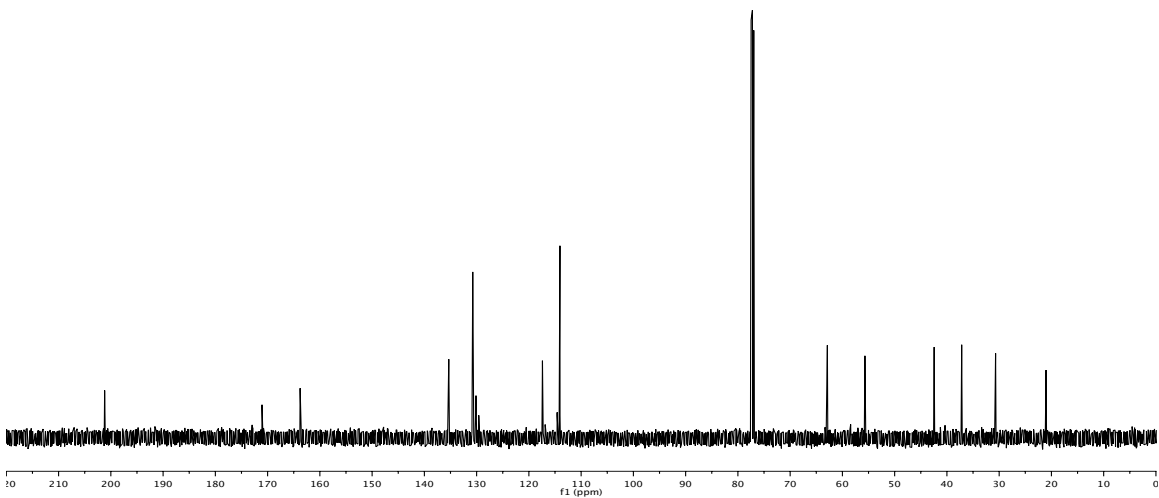
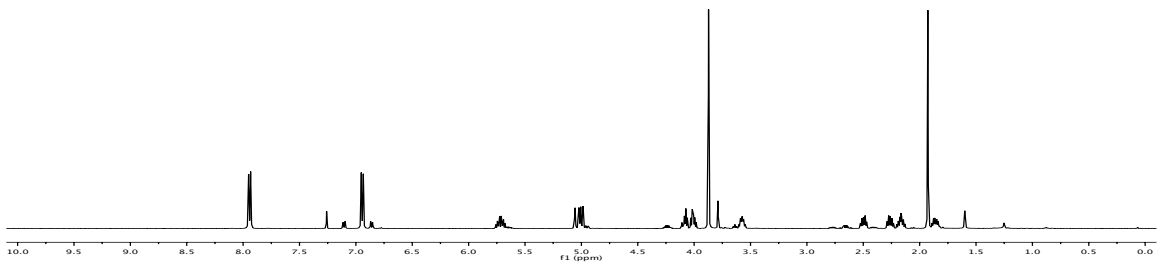
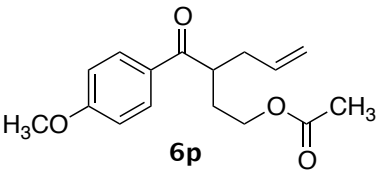


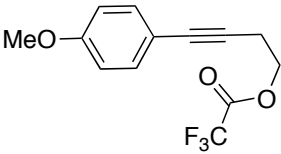




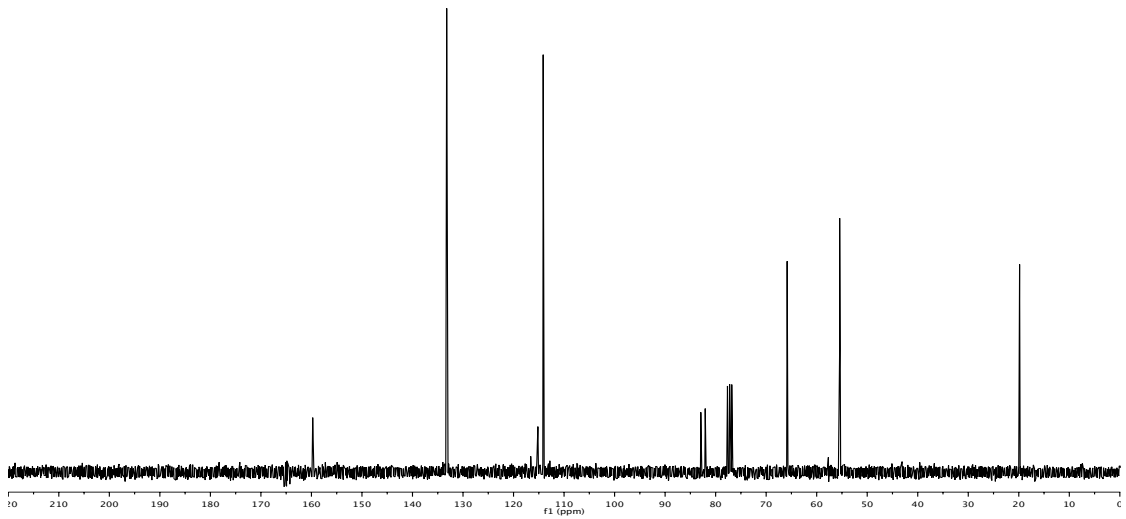
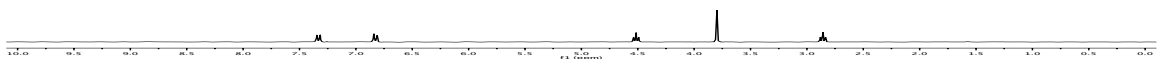
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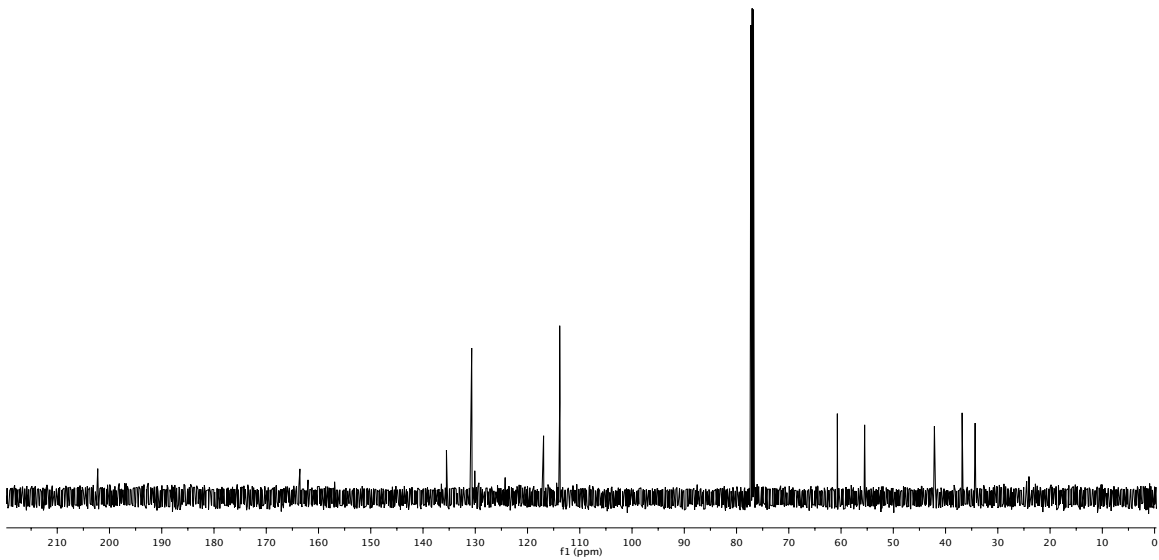
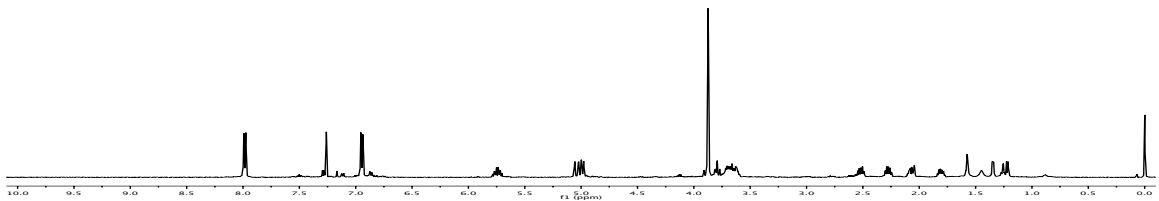
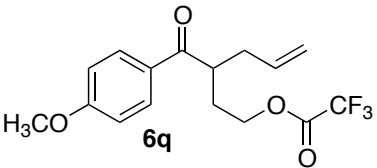


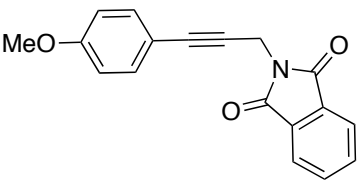




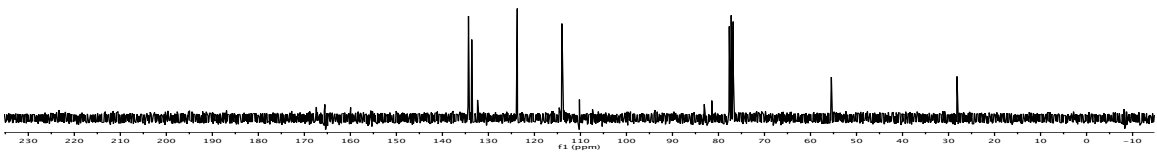
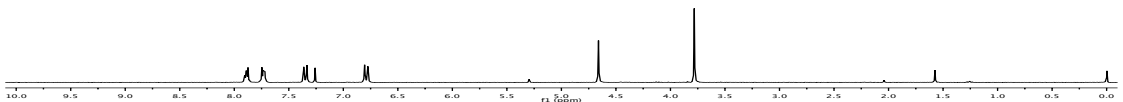
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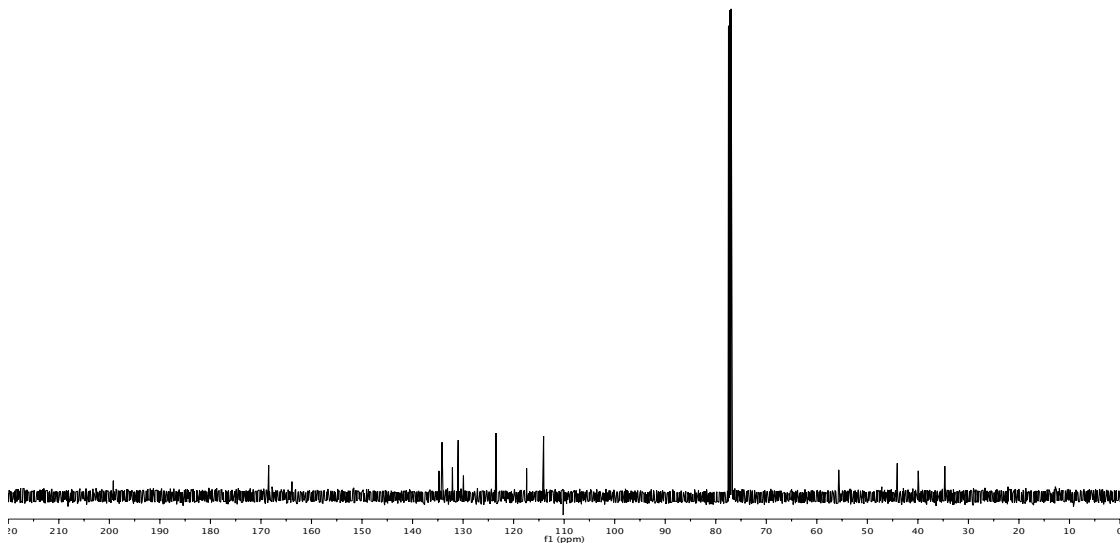
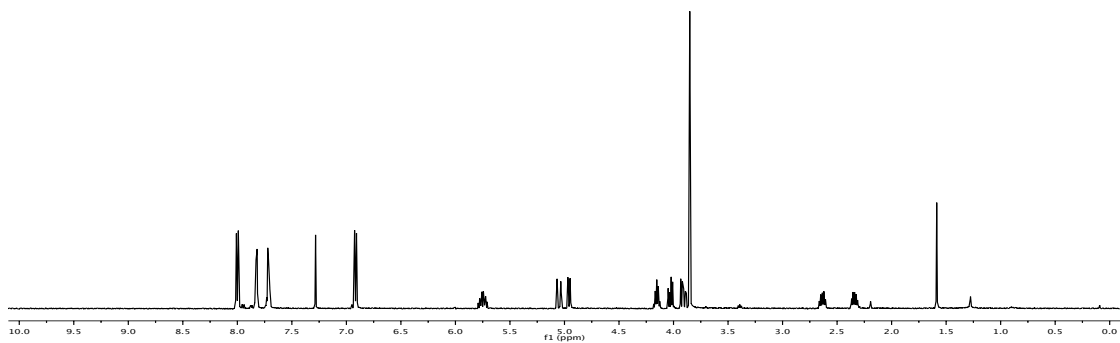
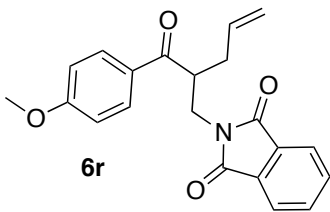


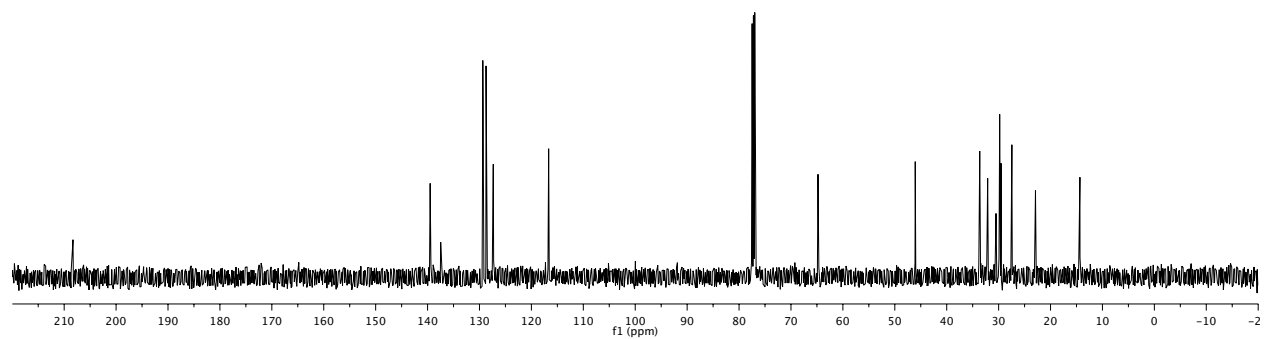
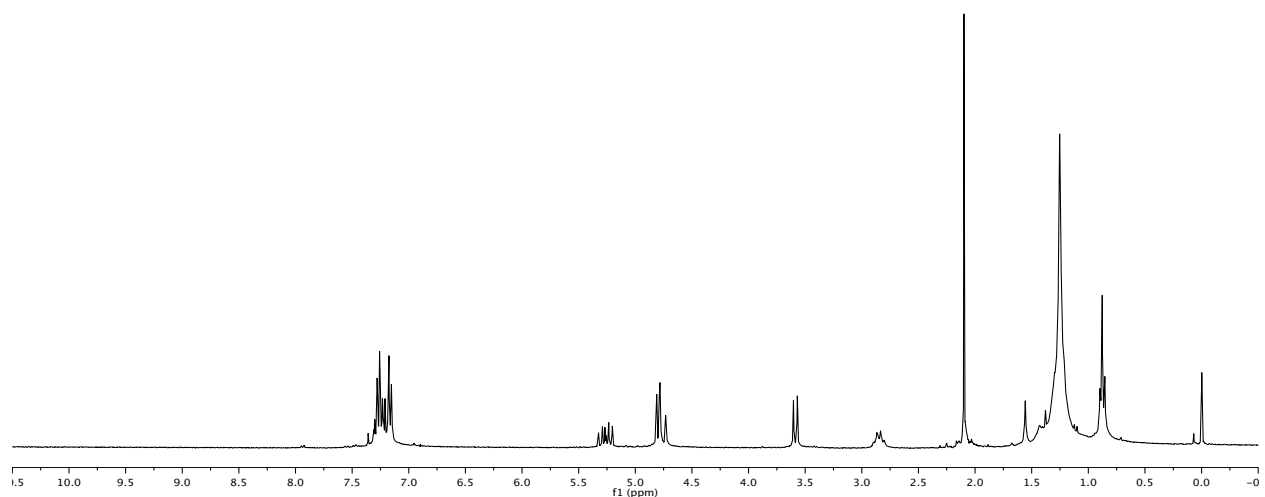
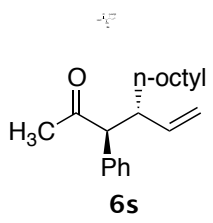


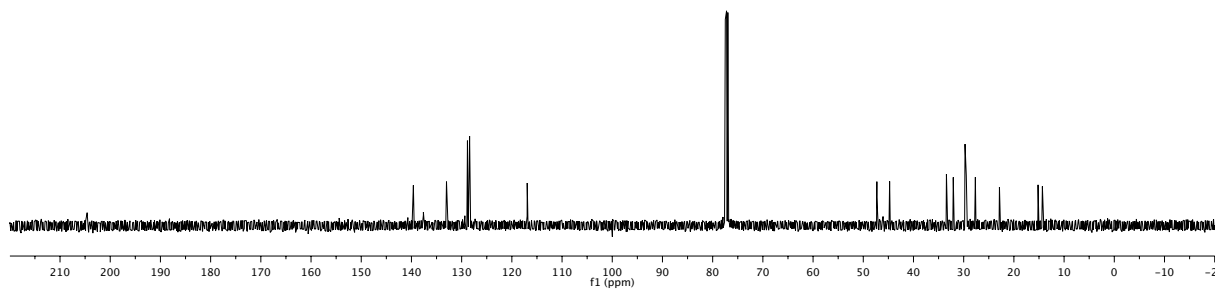
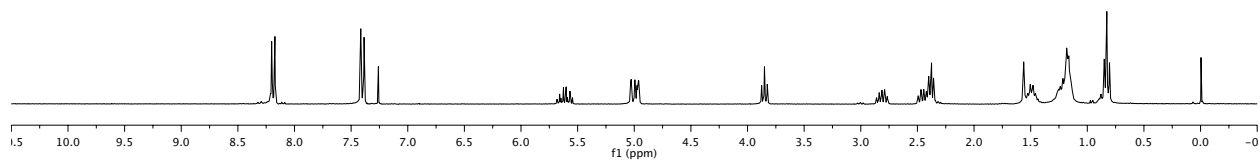
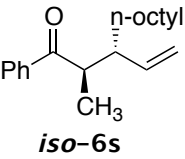
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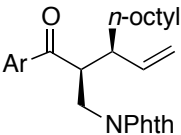












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