

Supporting Information

Rh(I)-Catalyzed Intramolecular [3+2] Cycloaddition Reactions of 1-Ene-, 1-Yne- and 1-Allene-Vinylcyclopropanes

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1. General

Air and moisture sensitive reactions were carried out in oven-dried glassware sealed with rubber septa under a positive pressure of dry argon. Similarly sensitive liquids and solutions were transferred via syringe. Reactions were stirred using Teflon-coated magnetic stir bars. Elevated temperatures were maintained using Thermostat-controlled silicone oil baths. Organic solutions were concentrated using a Büchi rotary evaporator with a desktop vacuum pump. Tetrahydrofuran, diethyl ether, and toluene were distilled from sodium and benzophenone prior to use. Dichloromethane was distilled from CaH₂ prior to use. Dichloroethane was distilled from P₂O₅ prior to use. Synthetic reagents were purchased from Acros, Aldrich, and Alfa Aesar and used without further purification, unless otherwise indicated. Analytical TLC was performed with 0.25 mm silica gel G plates with a 254 nm fluorescent indicator. The TLC plates were visualized by ultraviolet light and treatment with phosphomolybdic acid stain followed by gentle heating. Purification of products was accomplished by flash chromatography on silica gel and the purified compounds showed a single spot by analytical TLC.

NMR spectra were measured on Varian Mercury Plus 300 (¹H at 300 MHz, ¹³C at 75 MHz), Bruker ARX 400 (¹H at 400 MHz, ¹³C at 100 MHz), and Bruker AVANCE 600 (¹H at 600 MHz, ¹³C at 150 MHz) nuclear magnetic resonance spectrometers. Data for ¹H-NMR spectra are reported as follows: chemical shift (ppm, referenced to TMS; s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, dt = doublet of triplets, dm = doublet of multiplet, ddd = doublet of doublet of doublets, tdd = triplet of doublet of doublets, m = multiplet), coupling constant (Hz), and integration. Data for ¹³C-NMR are reported in terms of chemical shift (ppm) relative to residual solvent peak (CDCl₃: 77.0 ppm). 1D nOe experiments were conducted on a Bruker AVANCE 600 nuclear magnetic resonance spectrometer. Infrared spectra were recorded on Mettler-Toledo ReactIR iC10 system with an SiComp probe and are reported in wavenumbers (cm⁻¹). High-resolution mass spectra (HRMS) were recorded on a Bruker Apex IV FTMS mass spectrometer (ESI).

Abbreviations:

DCE = 1,2-dichloroethane

DCM = dichloromethane

DEAD = diethyl azodicarboxylate

DIBAL-H = diisobutylaluminum hydride

dppe = 1,2-bis(diphenylphosphino)ethane

dppb = 1,4-bis(diphenylphosphino)butane

dppp = 1,3-bis(diphenylphosphino)propane

EA = ethyl acetate

LDA = lithium diisopropylamide

PCC = pyridinium chlorochromate

PE = petroleum ether

TBAF = tetrabutylammonium fluoride

TBS = *tert*-butyldimethylsilyl

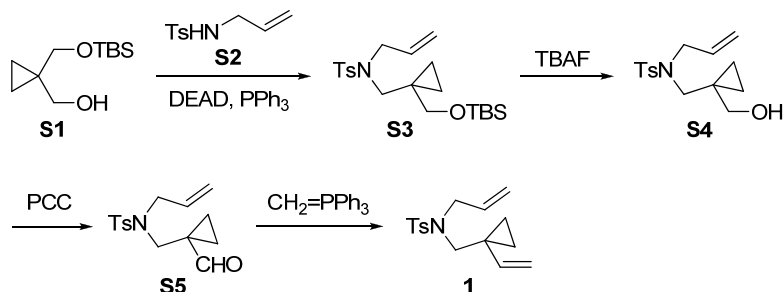
THF = tetrahydrofuran

TLC = thin layer chromatography

2. Experimental Procedures and Characterization Data

2.1 Synthesis of 1-Ene/Yne/Allene-VCP Substrates

1-Ene-VCP (**1**)



S1 to **S3**: To a stirred solution of alcohol **S1**¹ (705 mg, 3.26 mmol), tosylamide **S2** (1.11 g, 5.26 mmol), and PPh₃ (1.73 g, 6.60 mmol) in anhydrous THF (30 mL) was added DEAD (1.17 g, 6.72 mmol) at 0 °C. The mixture was then stirred for 45 h at room temperature. The mixture was concentrated and filtered through a pad of silica gel (eluted with PE/EA 10:1). The filtrate was concentrated and the crude product was purified by flash column chromatography on silica gel (eluted with PE/EA 20:1) to afford compound **S3** (1.13 g, 84%).

S3: Colorless oil. ¹H NMR (300 MHz, CDCl₃): δ 0.01 (s, 6H), 0.37-0.42 (m, 2H), 0.46-0.51 (m, 2H), 0.87 (s, 9H), 2.41 (s, 3H), 3.20 (s, 2H), 3.43 (s, 2H), 3.93 (d, *J* = 6.1 Hz, 2H), 5.08-5.17 (m, 2H), 5.58 (ddt, *J* = 10.3, 17.1, and 6.1 Hz, 1H), 7.28 (d, *J* = 8.0 Hz, 2H), 7.70 (d, *J* = 8.0 Hz, 2H). ¹³C NMR (75 MHz, CDCl₃): δ -5.4, 8.4, 18.2, 20.6, 21.5, 25.9, 50.4, 51.1, 65.2, 118.4, 127.2, 129.5, 133.2, 137.7, 142.9. IR (neat): ν 2935, 1646, 1609, 1356, 1155 cm⁻¹. HRMS (ESI) calcd for C₂₁H₃₅NNaO₃SSi (M+Na): 432.1999. Found: 432.1994.

S3 to **S4**: To silylether **S3** (1.13 g, 2.75 mmol) was added a 1.0 M solution of TBAF in THF (6 mL, 6 mmol). The resulting solution was stirred at room temperature for 14 h. Saturated aqueous NH₄Cl was added to quench the reaction, and the reaction mixture was extracted by ether. The combined organic layer was washed with water, dried over MgSO₄, and concentrated. The residue was filtered through a pad of silica gel (eluted with PE/EA 5:1) to afford crude alcohol **S4** (749 mg, 92%).

S4: Colorless oil. ¹H NMR (300 MHz, CDCl₃): δ 0.33-0.37 (m, 2H), 0.52-0.55 (m, 2H), 2.43 (s, 3H), 3.05 (m, 1H), 3.13 (s, 2H), 3.49 (d, *J* = 5.9 Hz, 2H), 4.00 (d, *J* = 6.9 Hz, 2H), 5.08-5.14 (m, 2H), 5.42-5.55 (m, 1H), 7.30 (d, *J* = 7.8 Hz, 2H), 7.71 (d, *J* = 7.8 Hz, 2H). ¹³C NMR (75 MHz, CDCl₃): δ 8.8, 20.8, 21.5, 50.4, 50.5, 66.0, 119.0, 127.0, 129.8, 132.6, 137.1, 143.5. IR (neat): ν 3542, 3009, 2935, 1646, 1605, 1341, 1162 cm⁻¹.

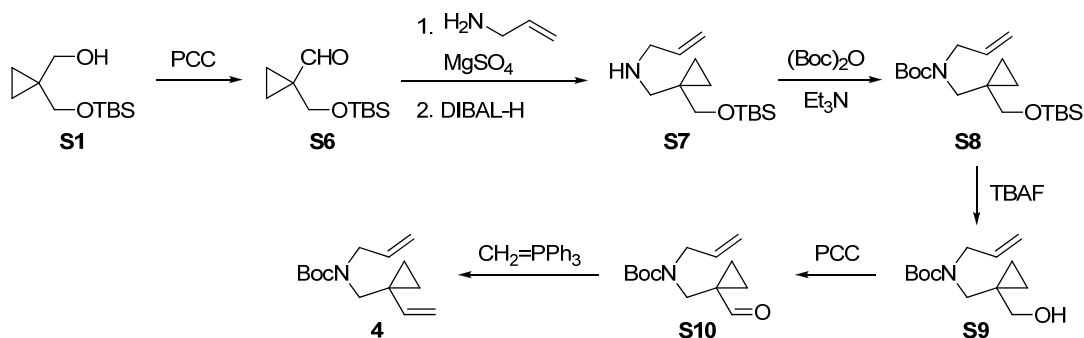
S4 to **1**: To a stirred solution of crude alcohol **S4** (749 mg, 2.53 mmol) in CH₂Cl₂ (20 mL) was added PCC (1.12 g, 5.21 mmol) at room temperature. The reaction mixture was stirred at room temperature for 14 h. Petroleum ether (20 mL) was added and the resulting mixture was filtered through a pad of silica gel. The filter cake was washed with PE/EA 4:1. The combined filtrate was concentrated and the crude aldehyde **S5** was used without further purification. To a suspension of methyltriphenylphosphonium bromide (1.84 g, 5.15 mmol) in THF (30 mL) at 0 °C was added *n*-BuLi (2.5 M in hexane, 2.2 mL, 5.5 mmol), and the resulting solution was stirred for 10 min. A solution of the above crude aldehyde **S5** in THF (10 mL) was added dropwise at 0 °C, and the resulting mixture was stirred for 2 h at room temperature. Water was added to quench the reaction, and the mixture was extracted with ether. The combined extract was washed with water and brine, dried over Na₂SO₄,

(1) Oh, C. H.; Hong, J. H. *Nucleosides, Nucleotides and Nucleic Acids* **2008**, *27*, 186.

and concentrated. The crude product was purified by flash column chromatography on silica gel (eluted with PE/EA 20:1) to afford 1-ene-VCP **1** (682 mg, 93%).

1: White solid, m.p. 30-31 °C. ¹H NMR (300 MHz, CDCl₃): δ 0.59-0.63 (m, 2H), 0.66-0.71 (m, 2H), 2.42 (s, 3H), 3.24 (s, 2H), 3.93 (d, *J* = 6.1 Hz, 2H), 4.88-4.97 (m, 2H), 5.08-5.15 (m, 2H), 5.52 (ddt, *J* = 10.1, 17.3, and 6.1 Hz, 1H), 5.89 (dd, *J* = 10.6 and 17.3 Hz, 1H), 7.28 (d, *J* = 7.9 Hz, 2H), 7.70 (d, *J* = 7.9 Hz, 2H). ¹³C NMR (75 MHz, CDCl₃): δ 13.0, 20.8, 21.5, 49.4, 52.8, 112.2, 118.3, 127.2, 129.5, 132.9, 137.5, 140.3, 143.0. IR (neat): ν 2998, 1650, 1605, 1348, 1152 cm⁻¹. HRMS (ESI) calcd for C₁₆H₂₁NNaO₂S (M+Na): 314.1185. Found: 314.1180.

1-Ene-VCP (**4**)



S1 to S6: To a stirred solution of alcohol **S1** (660 mg, 3.05 mmol) in CH₂Cl₂ (30 mL) was added PCC (1.32 g, 6.14 mmol). The reaction mixture was stirred at 25 °C for 4 h. The resulting solution was filtered through a pad of silica gel, and the filter cake was eluted with PE/EA 10:1. The combined filtrate was concentrated to afford the crude aldehyde **S6** (554 mg, 85%), which was used in the next step without further purification.

S6 to S8: Anhydrous MgSO₄ powder (1.77 g) was added to a solution of crude aldehyde **S6** (763 mg, 3.56 mmol) and allylamine (0.28 g, 4.9 mmol) in CH₂Cl₂ (26 mL) under room temperature. The reaction mixture was stirred for 18 h before it was filtered to remove insoluble MgSO₄. The filtrate was cooled to 0 °C under argon, and DIBAL-H solution (1M in hexanes, 8.5 mL, 8.5 mmol) was added dropwise. After stirred for 7 h at 0 °C, saturated aqueous solution of potassium sodium tartrate was added slowly to quench the reaction. The organic layer was separated and the aqueous phase was extracted with ether. The combined organic phase was dried over MgSO₄ and concentrated to afford the crude secondary amine **S7**. Chloroform (50 mL) was added to the crude amine **S7** and was distilled off to remove trace of water accompanied with **S7**. Dichloromethane (15 mL) was added, and to the resulting solution were added Et₃N (0.75 g, 7.4 mmol) and Boc₂O (1.03 g, 4.7 mmol). The reaction mixture was stirred at 25 °C for 36 h. After aqueous work-up and extraction with CH₂Cl₂, the combined organic phase was dried over MgSO₄ and concentrated. The residue was purified by flash column on silica gel (eluted with PE/EA 50:1 to 20:1) to afford the crude product **S8** as a colorless oil (541 mg, crude yield 43%).

S8 to S9: Following the procedure for the preparation of **S4** from **S3**, the above crude **S8** (541 mg, 1.52 mmol) was converted to alcohol **S9** (220 mg, 60%).

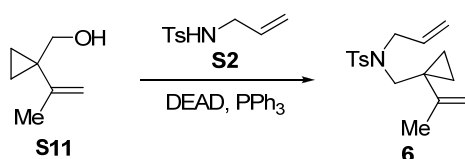
S9: Colorless oil. ¹H NMR (400 MHz, CDCl₃): δ 0.38-0.41 (m, 2H), 0.46-0.49 (m, 2H), 1.48 (s, 9H), 3.22 (s, 2H), 3.26 (dm, *J* = 5.7 Hz, 2H), 3.84 (dm, *J* = 3.6 Hz, 2H), 4.31 (br s, 1H), 5.07-5.14 (m, 2H), 5.76 (ddt, *J* = 10.6, 17.2, and 5.7 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 8.8, 21.8, 28.3, 50.3, 50.5, 66.4, 80.4, 116.5, 133.7, 157.1.

IR (neat): ν 3460, 2935, 1676, 1173 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{13}\text{H}_{23}\text{NNaO}_3$ (M+Na): 264.1570. Found: 264.1567.

S9 to 4: Following the procedure for the preparation of **1** from **S4**, alcohol **S9** (220 mg, 0.91 mmol) was converted to 1-ene-VCP **4** (178 mg, 81%).

4: Colorless oil. ^1H NMR (400 MHz, CDCl_3): δ 0.63-0.65 (m, 4H), 1.46 (s, 9H), 3.33-3.36 (m, 2H), 3.87-3.92 (m, 2H), 4.90-4.97 (m, 2H), 5.05-5.11 (m, 2H), 5.73 (ddt, $J = 10.5, 16.8,$ and 5.5 Hz, 1H), 5.79-5.84 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 12.4, 21.6, 28.3, 48.2, 48.6, 50.7, 51.2, 79.4, 111.7, 112.0, 115.6, 115.9, 134.0, 141.3, 155.7 (peak broadening and excess peaks are due to the rotamers of the amide bond). IR (neat): ν 2987, 1702, 1460, 1408 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{14}\text{H}_{23}\text{NNaO}_2$ (M+Na): 260.1621. Found: 260.1620.

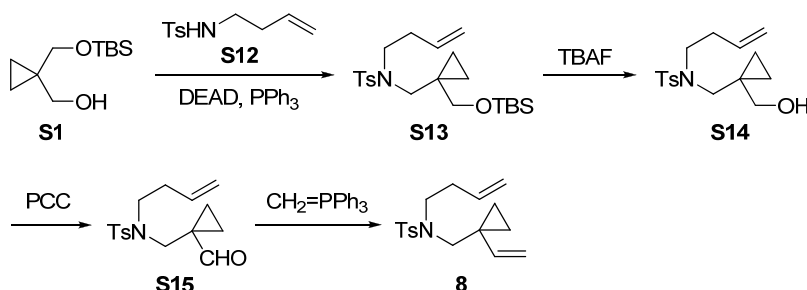
1-Ene-VCP (6)



To a stirred solution of alcohol **S11**² (88.2 mg, 0.79 mmol), tosylamide **S2** (252 mg, 1.19 mmol), and PPh_3 (420 mg, 1.60 mmol) in anhydrous THF (5 mL) was added DEAD (285 mg, 1.64 mmol) at 0 °C. The mixture was then stirred for 16 h at 25 °C. The reaction mixture was concentrated and filtered through a pad of silica gel (eluted with PE/EA 10:1). The filtrate was concentrated and the crude product was purified by flash column chromatography on silica gel (eluted with PE/EA 20:1) to afford 1-ene-VCP **6** (146 mg, 61%).

6: White solid, m.p. 40-42 °C. ^1H NMR (400 MHz, CDCl_3): δ 0.51 (dd, $J = 4.4$ and 6.2 Hz, 2H), 0.62 (dd, $J = 4.4$ and 6.2 Hz, 2H), 1.78 (s, 3H), 2.41 (s, 3H), 3.21 (s, 2H), 3.94 (dm, $J = 6.5$ Hz, 2H), 4.78 (m, 1H), 4.80 (m, 1H), 5.07-5.14 (m, 2H), 5.47 (ddt, $J = 10.2, 16.9,$ and 6.5 Hz, 1H), 7.27 (d, $J = 8.0$ Hz, 2H), 7.69 (d, $J = 8.0$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 11.2, 20.5, 21.5, 25.3, 49.2, 51.5, 113.1, 118.5, 127.3, 129.4, 132.9, 137.7, 143.0, 145.7. IR (neat): ν 3088, 2995, 1657, 1605, 1352, 1170 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{17}\text{H}_{23}\text{NNaO}_2\text{S}$ (M+Na): 328.1342. Found: 328.1339.

1-Ene-VCP (8)



S1 to S13: To a stirred solution of tosylamide **S12**³ (289 mg, 1.28 mmol), alcohol **S1** (276 mg, 1.28 mmol),

(2) Lervierend *Comptes Rendus des Seances de l'Academie des Sciences, Serie C: Sciences Chimiques* **1974**, 279, 755.

(3) Wang, Y.; Wang, J.; Su, J.; Huang, F.; Jiao, L.; Liang, Y.; Yang, D.; Zhang, S.; Wender, P. A.; Yu, Z.-X. *J. Am. Chem. Soc.* **2007**, 129, 10060.

and PPh_3 (679 mg, 2.59 mmol) in THF (15 mL) was added DEAD (484 mg, 2.78 mmol) at 0 °C. The mixture was then stirred for 45 h at room temperature. The mixture was concentrated and filtered through a pad of silica gel (eluted with PE/EA 10:1). The filtrate was concentrated and the crude product was purified by flash column chromatography on silica gel (eluted with PE/EA 20:1) to afford **S13** (221 mg, 41%).

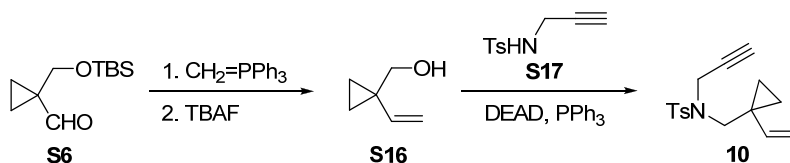
S13: Colorless oil. ^1H NMR (300 MHz, CDCl_3): δ 0.01 (s, 6H), 0.39-0.42 (m, 2H), 0.50-0.53 (m, 2H), 0.86 (s, 9H), 2.28-2.36 (m, 2H), 2.41 (s, 3H), 3.20 (s, 2H), 3.24-3.29 (m, 2H), 3.44 (s, 2H), 4.99-5.05 (m, 2H), 5.69 (ddt, $J = 10.3, 17.0,$ and 6.9 Hz, 1H), 7.28 (d, $J = 7.8$ Hz, 2H), 7.70 (d, $J = 7.8$ Hz, 2H). ^{13}C NMR (75 MHz, CDCl_3): δ -5.4, 8.5, 18.2, 20.9, 21.5, 25.9, 32.9, 48.2, 52.5, 65.0, 116.8, 127.2, 129.5, 134.8, 137.5, 142.9. IR (neat): ν 2942, 1650, 1598, 1158 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{37}\text{NNaO}_3\text{SSi}$ ($\text{M}+\text{Na}$): 446.2156. Found: 446.2147.

S13 to **S14**: Following the procedure for the preparation of **S4** from **S3**, silylether **S13** (200 mg, 0.47 mmol) was converted to crude alcohol **S14** (137 mg, 94%).

S14 to **8**: To a stirred solution of crude alcohol **S14** (136 mg, 0.44 mmol) in CH_2Cl_2 (8 mL) was added PCC (194 mg, 0.90 mmol) at room temperature. The reaction mixture was stirred at room temperature for 13 h. Petroleum ether (10 mL) was added and the resulting mixture was filtered through a pad of silica gel. The filter cake was washed with PE/EA 4:1. The combined filtrate was concentrated and the crude aldehyde **S15** was used without further purification. To a suspension of methyltriphenylphosphonium bromide (295 mg, 0.83 mmol) in THF (10 mL) at 0 °C was added *n*-BuLi (2.5 M in hexane, 0.35 mL, 0.87 mmol), and the resulting solution was stirred for 10 min. A solution of crude aldehyde **S15** in THF (5 mL) was added dropwise at 0 °C, and the resulting mixture was stirred for 3.5 h at room temperature. Water was added to quench the reaction, and the mixture was extracted with ether. The combined extract was washed with water and brine, dried over Na_2SO_4 , and concentrated. The crude product was purified by flash column chromatography on silica gel (eluted with PE/EA 20:1) to afford 1-ene-VCP **8** (116 mg, 86%).

8: Colorless oil. ^1H NMR (400 MHz, CDCl_3): δ 0.61-0.65 (m, 2H), 0.72-0.75 (m, 2H), 2.29-2.35 (m, 2H), 2.41 (s, 3H), 3.18-3.23 (m, 2H), 3.22 (s, 2H), 4.90-5.04 (m, 4H), 5.69 (ddt, $J = 10.5, 17.0,$ and 6.9 Hz, 1H), 5.87 (dd, $J = 10.5, 17.3$ Hz, 1H), 7.29 (d, $J = 7.9$ Hz, 2H), 7.68 (d, $J = 7.9$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 13.3, 21.0, 21.5, 32.9, 47.5, 54.7, 112.3, 116.7, 127.1, 129.6, 134.9, 137.0, 140.3, 143.0. IR (neat): ν 2939, 1639, 1605, 1348, 1170 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{17}\text{H}_{23}\text{NNaO}_2\text{S}$ ($\text{M}+\text{Na}$): 328.1342. Found: 328.1341.

1-Yne-VCP (10)



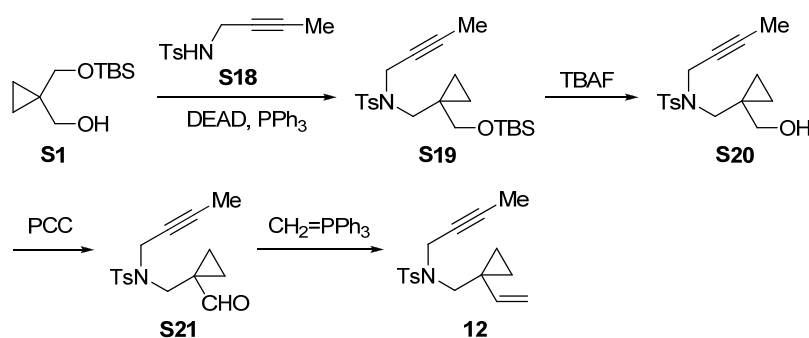
S6 to **S16**: To a suspension of methyltriphenylphosphonium bromide (10.71 g, 30.0 mmol) in THF (150 mL) at -10 °C was added *n*-BuLi (2.5 M in hexane, 12.0 mL, 30.0 mmol), and the resulting solution was stirred for 10 min. A solution of aldehyde **S6** (4.40 g, 20.5 mmol) in THF (20 mL) was added dropwise at 0 °C, and the resulting mixture was stirred for 5 min. Saturated aqueous NH_4Cl was added to quench the reaction, and the mixture was extracted with ether. The combined extract was washed with water and brine, dried over Na_2SO_4 , and concentrated. The crude product was purified by flash column chromatography on silica gel (eluted with PE). The product from the Wittig reaction was dissolved in THF (10 mL), and to this solution was added TBAF (1 M in THF, 30.8 mL, 30.8 mmol). The reaction mixture was stirred at room temperature for 14 h. Then saturated

aqueous NH_4Cl was added to quench the reaction, and the reaction mixture was extracted by ether. The combined organic layer was washed with water, dried over MgSO_4 , and concentrated. The residue was purified by flash column chromatography on silica gel (eluted with PE/EA 5:1) to afford crude alcohol **S16** (3.43 g, 43% purity, containing some inseparable byproduct TBSOH).

S16 to 10: Following the procedure for the preparation of **S3** from **S1**, the alcohol **S16** (110 mg, 1.17 mmol) and tosylamide **S17**⁴ (305 mg, 1.46 mmol) were converted to 1-yne-VCP **10** (136 mg, 40%).

10: Colorless oil. ^1H NMR (400 MHz, CDCl_3): δ 0.72 (s, 4H), 1.95 (t, $J = 2.4$ Hz, 1H), 2.42 (s, 3H), 3.23 (s, 2H), 4.24 (d, $J = 2.4$ Hz, 2H), 4.97 (dd, $J = 1.0$ and 10.8 Hz, 1H), 5.12 (dd, $J = 1.0$ and 17.4 Hz, 1H), 5.80 (dd, $J = 10.8$ and 17.4 Hz, 1H), 7.28 (d, $J = 7.9$ Hz, 2H), 7.72 (d, $J = 7.9$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 12.7, 19.5, 21.5, 35.5, 51.4, 74.2, 76.4, 112.4, 127.8, 129.3, 135.7, 139.9, 143.4. IR (neat): ν 3296, 3013, 2931, 2130, 1643, 1602, 1352, 1166 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{16}\text{H}_{19}\text{NNaO}_2\text{S}$ ($\text{M}+\text{Na}$): 312.1029. Found: 312.1029.

1-Yne-VCP (**12**)



S1 to S19: Following the procedure for the preparation of **S3** from **S1**, the alcohol **S1** (210 mg, 0.97 mmol) and tosylamide **S18**⁵ (243 mg, 1.09 mmol) were converted to compound **S19** (363 mg, 89%).

S19: Colorless oil. ^1H NMR (400 MHz, CDCl_3): δ 0.04 (s, 6H), 0.42-0.44 (m, 2H), 0.52-0.54 (m, 2H), 0.88 (s, 9H), 1.48 (t, $J = 2.4$ Hz, 3H), 2.41 (s, 3H), 3.15 (s, 2H), 3.52 (s, 2H), 4.19 (q, $J = 2.4$ Hz, 2H), 7.27 (d, $J = 8.0$ Hz, 2H), 7.72 (d, $J = 8.0$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ -5.5, 3.2, 7.9, 18.3, 19.7, 21.5, 25.9, 37.0, 50.3, 65.2, 71.8, 81.6, 128.0, 129.0, 136.2, 142.9. IR (neat): ν 2935, 2235, 1602, 1359, 1170 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{35}\text{NNaO}_3\text{SSi}$ ($\text{M}+\text{Na}$): 444.1999. Found: 444.1992.

S19 to S20: Following the procedure for the preparation of **S4** from **S3**, silylether **S19** (343 mg, 0.81 mmol) was converted to crude alcohol **S20** (258 mg, 100%), which was used in the next step without further purification.

S20 to 12: Following the procedure for the preparation of **1** from **S4**, crude alcohol **S20** (258 mg, 0.84 mmol) was converted to 1-yne-VCP **12** (238 mg, 87%).

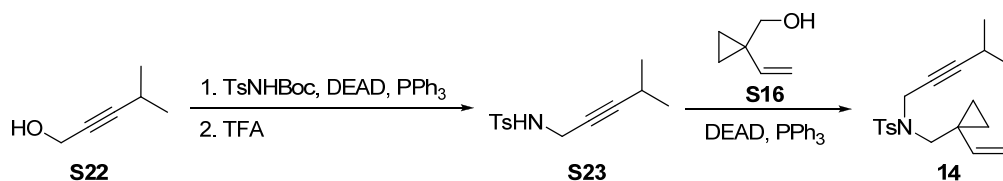
12: Colorless oil. ^1H NMR (400 MHz, CDCl_3): δ 0.71 (s, 4H), 1.48 (t, $J = 2.4$ Hz, 3H), 2.41 (s, 3H), 3.19 (s, 2H), 4.16 (q, $J = 2.4$ Hz, 2H), 4.96 (d, $J = 11.1$ Hz, 1H), 5.11 (d, $J = 17.2$ Hz, 1H), 5.81 (dd, $J = 11.1$ and 17.2 Hz, 1H), 7.28 (d, $J = 8.3$ Hz, 2H), 7.72 (d, $J = 8.3$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 3.2, 12.8, 19.7, 21.5, 36.1, 51.5, 71.6, 81.8, 112.3, 128.0, 129.1, 135.9, 140.1, 143.1. IR (neat): ν 3017, 2931, 2224, 1639, 1609, 1356,

(4) Dai, L.-Z.; Qi, M.-J.; Shi, Y.-L.; Liu, X.-G.; Shi, M. *Org. Lett.* **2007**, *9*, 3191.

(5) Zhang, Q.; Xu, W.; Lu, X. *J. Org. Chem.* **2005**, *70*, 1505.

1158 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{17}\text{H}_{21}\text{NNaO}_2\text{S}$ ($\text{M}+\text{Na}$): 326.1185. Found: 326.1183.

1-Yne-VCP (14)



S22 to S23: Following the procedure for the preparation of **S3** from **S1**, the propargyl alcohol **S22**⁶ (160 mg, 1.63 mmol) and TsNHBoc (413 mg, 1.52 mmol) were converted to *N*-Boc protected propargyl amide (587 mg, quantitative yield). The crude protected amide was dissolved in dry CH_2Cl_2 (7.5 mL) and was added trifluoroacetic acid (2.2 mL) at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for another 10 h. Saturated NaHCO_3 solution was added to quench the reaction, and the resulting mixture was extracted with CH_2Cl_2 . The combined extract was dried over MgSO_4 and concentrated. The crude product was purified by flash column chromatography on silica gel (eluted with PE/EA 20:1 to 3:1) to afford tosylamide **S23** (342 mg, 81%).

S23: White solid, m.p. 71-73 °C. ^1H NMR (400 MHz, CDCl_3): δ 0.96 (d, $J = 7.1$ Hz, 6H), 2.31 (triplet of heptet, $J = 2.1$ and 6.9 Hz, 1H), 2.43 (s, 3H), 3.81 (dd, $J = 2.1$ and 6.1 Hz, 2H), 4.73 (t, $J = 6.1$ Hz, 1H), 7.31 (d, $J = 8.0$ Hz, 2H), 7.78 (d, $J = 8.0$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 20.2, 21.5, 22.5, 33.3, 73.3, 90.7, 127.4, 129.6, 136.9, 143.5.

S23 to 14: Following the procedure for the preparation of **S3** from **S1**, the alcohol **S16** (104 mg, 1.06 mmol) and tosylamide **S23** (200 mg, 0.80 mmol) were converted to 1-yne-VCP **14** (137 mg, 52%).

14: Colorless oil. ^1H NMR (400 MHz, CDCl_3): δ 0.68-0.71 (m, 2H), 0.72-0.75 (m, 2H), 0.87 (d, $J = 6.6$ Hz, 6H), 2.22 (triplet of heptet, $J = 2.1$ and 7.1 Hz, 1H), 2.40 (s, 3H), 3.22 (s, 2H), 4.20 (d, $J = 2.1$ Hz, 2H), 4.96 (dd, $J = 1.0$ and 10.7 Hz, 1H), 5.13 (dd, $J = 1.0$ and 17.2 Hz, 1H), 5.82 (dd, $J = 10.7$ and 17.2 Hz, 1H), 7.27 (d, $J = 8.1$ Hz, 2H), 7.71 (d, $J = 8.1$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 12.7, 19.6, 20.1, 21.4, 22.5, 26.0, 51.3, 71.5, 92.2, 112.2, 127.8, 129.2, 136.1, 140.2, 143.0. IR (neat): ν 2976, 1646, 1602, 1449, 1348, 1162 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{19}\text{H}_{26}\text{NO}_2\text{S}$ ($\text{M}+\text{H}$): 332.1679. Found: 332.1679.

1-Yne-VCP (16)



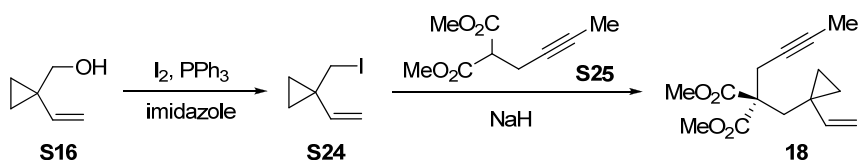
10 to 16: To a stirred solution of *i*- Pr_2NH (122 mg, 1.23 mmol) in THF (4 mL) at -78 °C was added *n*-BuLi (0.49 mL, 2.5 M in hexanes, 1.23 mmol) dropwise. After stirred for 30 min, a solution of 1-yne-VCP **10** (252 mg, 0.88 mmol) in THF (4 mL) was added. The reaction mixture was stirred at -78 °C for 1.5 h and then methyl chloroformate (132 mg, 1.40 mmol) was added. The resulting solution was further stirred for 4 h and then was

(6) Aoyagi, S.; Wang, T.-C.; Kibayashi, C. *J. Am. Chem. Soc.* **1993**, *115*, 11393.

allowed to warm to room temperature overnight. Water was added to quench the reaction, and the mixture was extracted with ether. The combined extract was washed with 1 M aqueous Na₂SO₄, dried over Na₂SO₄, and concentrated. The residue was purified by flash column chromatography on silica gel (eluted with PE/EA 10:1 to 5:1) to afford 1-yne-VCP **16** (40 mg, 13%) and the recovered starting compound **10** (125 mg, 50%).

16: Light-yellow oil. ¹H NMR (400 MHz, CDCl₃): δ 0.67-0.70 (m, 2H), 0.73-0.76 (m, 2H), 2.41 (s, 3H), 3.22 (s, 2H), 3.68 (s, 3H), 4.35 (s, 2H), 4.98 (dd, *J* = 0.9 and 10.7 Hz, 1H), 5.11 (dd, *J* = 0.9 and 17.7 Hz, 1H), 5.78 (dd, *J* = 10.7 and 17.7 Hz, 1H), 7.30 (d, *J* = 8.1 Hz, 2H), 7.71 (d, *J* = 8.1 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃): δ 12.9, 19.6, 21.5, 35.5, 52.0, 52.7, 77.2, 80.6, 112.8, 127.7, 129.6, 135.1, 139.6, 143.8, 152.9. IR (neat): ν 2928, 2256, 1724, 1650, 1602, 1356, 1263, 1166 cm⁻¹. HRMS (ESI) calcd for C₁₈H₂₁NO₄S (M+H): 348.1264. Found: 348.1262.

1-Yne-VCP (**18**)

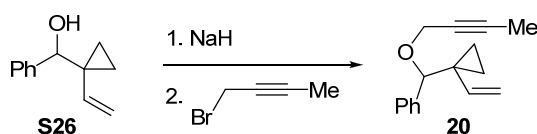


S16 to S24: To a stirred solution of alcohol **S16** (490 mg, 5.0 mmol), triphenylphosphine (1.57 g, 6.0 mmol), and imidazole (511 mg, 7.5 mmol) at 0 °C was added iodine (1.41 g, 5.0 mmol) in three portions. After 20 min, saturated aqueous Na₂S₂O₃ was added. The mixture was extracted with CH₂Cl₂, and the combined organic phase was dried over MgSO₄ and concentrated. The crude product was purified by flash column chromatography on silica gel (eluted with PE) to afford the iodide **S24** (255 mg, 25%).

S24 to 18: Diester **S25**⁷ (248 mg, 1.34 mmol) was added to a suspension of NaH (35 mg, 1.46 mmol) in THF (3 mL) at 0 °C. After stirred for 30 min, a solution of iodide **S24** (255 mg, 1.22 mmol) in THF (2 mL) was added. The reaction mixture was stirred at 50 °C for 31 h before saturated aqueous NH₄Cl was added. The mixture was extracted with ether, and the combined organic extract was washed with aqueous Na₂S₂O₃ to remove iodine. The organic phase was dried over MgSO₄ and concentrated. The crude product was purified by flash column chromatography on silica gel (eluted with PE/EA 50:1 to 20:1) to afford 1-yne-VCP **18** (140 mg, 39%).

18: Light-yellow oil. ¹H NMR (400 MHz, CDCl₃): δ 0.63 (s, 4H), 1.76 (t, *J* = 2.7 Hz, 3H), 2.25 (s, 2H), 2.93 (dd, *J* = 2.7 and 5.3 Hz, 2H), 3.69 (s, 6H), 4.81 (dd, *J* = 1.3 and 10.2 Hz, 1H), 4.84 (dd, *J* = 1.3 and 17.3 Hz, 1H), 5.95 (dd, *J* = 10.2 and 17.3 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 3.5, 13.1, 19.7, 23.2, 38.8, 52.4, 57.4, 74.0, 79.2, 112.0, 141.2, 170.9. IR (neat): ν 3009, 2957, 2268, 1743, 1646, 1441, 1211 cm⁻¹. HRMS (ESI) calcd for C₁₅H₂₀NaO₄ (M+Na): 287.1254. Found: 287.1252.

1-Yne-VCP (**20**)

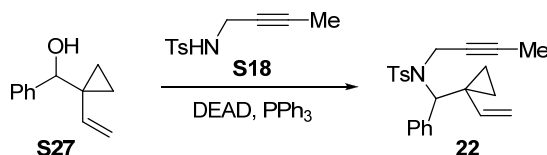


(7) Zhang, Q.; Xu, W.; Lu, X. *J. Org. Chem.* **2005**, *70*, 1505.

To a stirred solution of alcohol **S26**⁸ (104 mg, 0.60 mmol) in anhydrous DMSO (5 mL) was added NaH (29mg, 1.20 mmol) at 25 °C. After 1 h, 1-bromo-2-butyne (158 mg, 1.20 mmol) was added dropwise. The reaction mixture was stirred at 25 °C for 24 h, then water was added to quench the reaction. The mixture was extracted with dichloromethane, and the combined organic layer was dried over MgSO₄ and concentrated. The crude product was purified by flash column chromatography on silica gel (eluted with PE/EA 10:1) to afford 1-yne-VCP **20** (95 mg, 70%).

20: Colorless oil. ¹H NMR (400 MHz, CDCl₃): δ 0.66 (ddd, *J* = 4.0, 6.3, and 8.9 Hz, 1H), 0.70-0.77 (m, 2H), 0.81-0.86 (m, 1H), 1.85 (t, *J* = 2.2 Hz, 3H), 3.94 (dq, *J* = 15.5 and 2.2 Hz, 1H), 4.20 (dq, *J* = 15.5 and 2.2 Hz, 1H), 4.38 (s, 1H), 4.90-4.95 (m, 2H), 6.04 (dd, *J* = 10.6 and 16.9 Hz, 1H), 7.28-7.33 (m, 5H). ¹³C NMR (100 MHz, CDCl₃): δ 3.6, 10.5, 13.5, 26.7, 56.4, 75.2, 82.3, 83.4, 112.2, 127.6, 128.0, 129.4, 139.4, 139.7. IR (neat): ν 2931, 2253, 1609, 1460, 1069 cm⁻¹. HRMS (ESI) calcd for C₁₆H₁₈NaO (M+Na): 249.1250. Found: 249.1250.

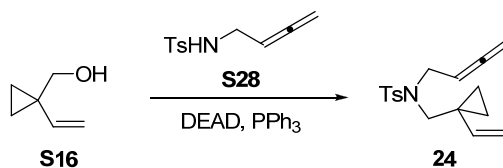
1-Yne-VCP (**22**)



S27 to **22**: Following the procedure for the preparation of **S3** from **S1**, the alcohol **S27** (45 mg, 0.26 mmol) and tosylamide **S18** (78 mg, 0.35 mmol) were converted to 1-yne-VCP **22** (31 mg, 31%).

22: Colorless oil. ¹H NMR (400 MHz, CDCl₃): δ 0.57-0.62 (m, 1H), 0.75-0.85 (m, 2H), 0.94-0.98 (m, 1H), 1.65 (t, *J* = 2.2 Hz, 3H), 2.39 (s, 3H), 4.02 (dq, *J* = 18.1 and 2.2 Hz, 1H), 4.22 (dq, *J* = 18.1 and 2.2 Hz, 1H), 4.87 (d, *J* = 10.6 Hz, 1H), 4.94 (d, *J* = 17.2 Hz, 1H), 4.99 (s, 1H), 5.96 (dd, *J* = 10.6 and 17.2 Hz, 1H), 7.16-7.22 (m, 5H), 7.65 (d, *J* = 8.4 Hz, 2H), 7.28-7.30 (m, 2H). ¹³C NMR (100 MHz, CDCl₃): δ 3.4, 12.5, 16.3, 21.4, 24.9, 35.5, 66.8, 75.2, 80.2, 112.1, 127.2, 127.7, 128.0, 128.3, 128.8, 137.9, 140.0, 142.8. IR (neat): ν 3091, 2931, 2246, 1639, 1605, 1345, 1158 cm⁻¹. HRMS (ESI) calcd for C₂₃H₂₅NNaO₂S (M+Na): 402.1498. Found: 402.1498.

1-Allene-VCP (**24**)



S16 to **24**: Following the procedure for the preparation of **S3** from **S1**, the alcohol **S16** (64 mg, 0.65 mmol) and tosylamide **S28**⁹ (137 mg, 0.61 mmol) were converted to 1-allene-VCP **24** (136 mg, 73%).

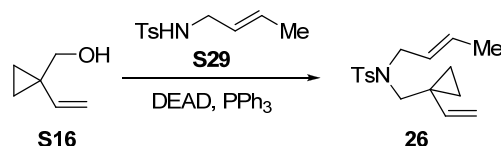
24: Colorless oil. ¹H NMR (400 MHz, CDCl₃): δ 0.62-0.66 (m, 2H), 0.68-0.72 (m, 2H), 2.42 (s, 3H), 3.29 (s, 2H), 4.00 (dt, *J* = 6.9 and 2.5 Hz, 2H), 4.67 (dt, *J* = 6.9 and 2.5 Hz, 2H), 4.78 (quintet, *J* = 6.9 Hz, 1H), 4.91 (d, *J* = 10.0 Hz, 1H), 4.97 (d, *J* = 17.0 Hz, 1H), 5.90 (dd, *J* = 10.0 and 17.0 Hz, 1H), 7.28 (d, *J* = 8.0 Hz, 2H), 7.70 (d, *J*

(8) Menningen, P.; Harcken, C.; Stecker, B.; Koerbe, S.; de Meijere, A.; Lopes, M. R.; Ollivier, J.; Salauen, J. *Synlett* **1999**, 10, 1534.

(9) Ohno, H.; Mizutani, T.; Kadoh, Y.; Aso, A.; Miyamura, K.; Fujii, N.; Tanaka, T. *J. Org. Chem.* **2007**, 72, 4378.

= 8.0 Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 12.9, 20.6, 21.5, 45.2, 52.3, 76.1, 85.6, 112.2, 127.2, 129.6, 137.7, 140.2, 143.1, 209.2. IR (neat): ν 3095, 3002, 2931, 1963, 1646, 1605, 1166 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{17}\text{H}_{21}\text{NNaO}_2\text{S}$ (M+Na): 326.1185. Found: 326.1185.

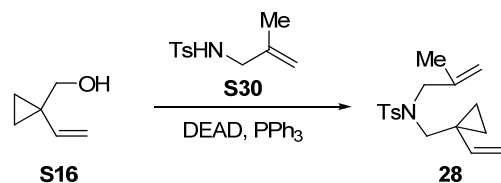
1-Ene-VCP (26)



S16 to 26: Following the procedure for the preparation of **S3** from **S1**, the alcohol **S16** (64 mg, 0.65 mmol) and tosylamide **S29**¹⁰ (137 mg, 0.61 mmol) were converted to 1-ene-VCP **26** (136 mg, 73%).

26: Colorless oil. ^1H NMR (400 MHz, CDCl_3): δ 0.59-0.62 (m, 2H), 0.67-0.70 (m, 2H), 1.60 (dd, $J = 1.4$ and 6.3 Hz, 3H), 2.42 (s, 3H), 3.22 (s, 2H), 3.86 (dm, $J = 6.6$ Hz, 2H), 4.88-4.95 (m, 2H), 5.14 (dtq, $J = 15.5$, 6.6, and 1.4 Hz, 1H), 5.55 (dq, $J = 15.5$ and 6.6 Hz, 1H), 5.90 (dd, $J = 10.9$ and 17.5 Hz, 1H), 7.28 (d, $J = 8.0$ Hz, 2H), 7.69 (d, $J = 8.0$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 13.0, 17.6, 20.9, 21.5, 48.8, 52.5, 112.1, 125.3, 127.3, 129.4, 129.9, 137.7, 140.4, 142.9. IR (neat): ν 2931, 1646, 1605, 1345, 1162 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{17}\text{H}_{23}\text{NNaO}_2\text{S}$ (M+Na): 328.1342. Found: 328.1342.

1-Ene-VCP (28)



S16 to 28: Following the procedure for the preparation of **S3** from **S1**, the alcohol **S16** and tosylamide **S30**¹¹ were converted to 1-ene-VCP **28**.

28: Colorless oil. ^1H NMR (400 MHz, CDCl_3): δ 0.55-0.58 (m, 2H), 0.61-0.64 (m, 2H), 1.64 (s, 3H), 2.42 (s, 3H), 3.23 (s, 2H), 3.83 (s, 2H), 4.78-4.86 (m, 4H), 5.78 (dd, $J = 10.7$ and 17.3 Hz, 1H), 7.28 (d, $J = 8.5$ Hz, 2H), 7.70 (d, $J = 8.5$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 13.2, 20.2, 21.0, 21.5, 53.0, 53.8, 112.1, 113.0, 127.3, 129.4, 137.7, 140.2, 140.4, 142.9. IR (neat): ν 2969, 1751, 1415, 1263 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{17}\text{H}_{24}\text{NO}_2\text{S}$ (M+H): 306.1522. Found: 306.1520.

(10) Fugami, K.; Oshima, K.; Utimoto, K. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 2050.

(11) Kataoka, T.; Yoshimatsu, M.; Noda, Y.; Sato, T.; Shimizu, H.; Hori, M. *J. Chem. Soc., Perkin Trans. 1* **1993**, 121.

2.2 Experimental Details for the Rh(I)-Catalyzed [3+2] Cycloaddition

Catalyst Screening for the [3+2] Reaction

1. $[\text{Rh}(\text{PPh}_3)_3]\text{OTf}$ as the catalyst: To a mixture of $\text{RhCl}(\text{PPh}_3)_3$ (5.2 mg, 5.6 μmol) and AgOTf (1.3 mg, 5.1 μmol) was added dry toluene (1 mL) and the resulting mixture was stirred under argon at room temperature for 10 minutes. The resulting suspension was used as catalyst solution.

2. $[\text{Rh}(\text{CO})_2]\text{SbF}_6$ as the catalyst: To a mixture of $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ (1.9 mg, 4.9 μmol) and AgSbF_6 (3.9 mg, 11 μmol) was added dry DCE (1 mL) and the resulting mixture was stirred under argon at room temperature for 10 minutes. The resulting suspension was used as catalyst solution.

3. $[\text{Rh}(\text{NBD})]\text{SbF}_6$ as the catalyst: To a mixture of $[\text{Rh}(\text{NBD})\text{Cl}]_2$ (2.0 mg, 4.3 μmol) and AgSbF_6 (3.5 mg, 10 μmol) was added dry DCE (1 mL) and the resulting mixture was stirred under argon at room temperature for 10 minutes. The resulting suspension was used as catalyst solution.

4. $[\text{Rh}(\text{dppe})]\text{SbF}_6$ as the catalyst: To a mixture of $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ (1.8 mg, 4.6 μmol) and AgSbF_6 (3.5 mg, 10 μmol) was added dry DCE (1 mL) and the resulting mixture was stirred under argon at room temperature for 10 minutes. Then dppe (4.3 mg, 11 μmol) was added and mixture was further stirred for 10 minutes. The resulting suspension was used as catalyst solution.

5. $[\text{Rh}(\text{dppb})]\text{SbF}_6$ as the catalyst: To a mixture of $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ (1.7 mg, 4.4 μmol) and AgSbF_6 (3.0 mg, 8.7 μmol) was added dry DCE (0.8 mL) and the resulting mixture was stirred under argon at room temperature for 10 minutes. Then dppb (4.8 mg, 11 μmol) was added and mixture was further stirred for 10 minutes. The resulting suspension was used as catalyst solution.

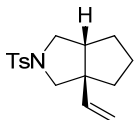
General Procedures for the [3+2] Cycloaddition

Preparation of the cationic Rh(I) catalyst solution: Anhydrous DCE (5.0 mL) was added to a mixture of $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ (9.9 mg, 25.4 μmol) and AgSbF_6 (21.0 mg, 61.1 μmol , 1.2 equiv. to Rh) under argon. The mixture was stirred at room temperature for 10 min. The resulting yellow suspension was left to stand until the formed AgCl precipitated. The supernatant was used in the [3+2] cycloaddition reactions as the catalyst precursor ($[\text{Rh}(\text{I})^+] = 10.2 \mu\text{mol/mL}$).

General procedure for the intramolecular [3+2] cycloaddition reaction: Under argon, the above $\text{Rh}(\text{I})^+$ solution (5 mL per mmol substrate, 5 mol %) was added to flame-dried reaction tube containing 1,3-bis(diphenylphosphino)propane (25 mg per mmol substrate, 6 mol %). The resulting light yellow solution was stirred at room temperature for 10 min, and then a solution of the 1-ene/yne/allene-VCP substrate in DCE (ca. 15 mL per mmol substrate) was added. The reaction tube was immersed into an oil bath (80 °C, unless otherwise indicated). When TLC indicated the disappearance of the starting material, the reaction mixture was cooled to room temperature and filtered through a thin pad of silica gel. The filter cake was washed with PE/EA 5:1, and the combined filtrate was concentrated. The crude product was purified by flash column chromatography on silica gel to afford the corresponding [3+2] cycloadduct.

Experimental Data for the [3+2] Cycloadducts

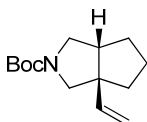
Cycloadduct (2)



Following the general procedure, 1-ene-VCP **1** (24.1 mg, 0.083 mmol) was converted to cycloadduct **2** (22.4 mg, 93%). Substrate concentration: 0.03 M, reaction time: 2 h.

2: Colorless oil. ^1H NMR (400 MHz, CDCl_3): δ 1.36-1.47 (m, 1H), 1.54-1.90 (m, 5H), 2.31 (heptet, $J = 4.1$ Hz, 1H), 2.44 (s, 3H), 2.97-3.02 (m, 2H), 3.10-3.19 (m, 2H), 4.88-4.94 (m, 2H), 5.80 (dd, $J = 10.5$ and 17.5 Hz, 1H), 7.33 (d, $J = 7.8$ Hz, 2H), 7.68 (d, $J = 7.8$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 21.5, 25.3, 32.4, 37.1, 48.6, 54.3, 56.1, 58.1, 111.5, 127.9, 129.5, 132.3, 143.2, 143.5. IR (neat): ν 2965, 1635, 1605, 1356, 1173 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{16}\text{H}_{21}\text{NNaO}_2\text{S}$ ($\text{M}+\text{Na}$): 314.1185. Found: 314.1183.

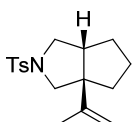
Cycloadduct (5)



Following the general procedure, 1-ene-VCP **4** (53.3 mg, 0.22 mmol) was converted to cycloadduct **5** (35.1 mg, 66%). Substrate concentration: 0.1 M, temperature: 80 $^\circ\text{C}$, reaction time: 13 h.

5: Colorless oil. ^1H NMR (400 MHz, CDCl_3): δ 1.46 (s, 9H), 1.51-1.55 (m, 1H), 1.69-1.93 (m, 5H), 2.35 (tt, $J = 4.9$ and 7.9 Hz, 1H), 3.13-3.20 (m, 1H), 3.25-3.34 (m, 1H), 3.38-3.59 (m, 2H), 5.00 (d, $J = 10.4$ Hz, 1H), 5.02 (d, $J = 17.7$ Hz, 1H), 5.90 (dd, $J = 10.4$ and 17.7 Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 20.5, 24.2, 30.8, 35.7, 48.0, 48.9, 51.3, 54.7, 54.9, 55.4, 79.0, 111.4, 143.4, 154.6. The redundant peaks are due to the rotamers of the amide moiety. IR (neat): ν 3091, 2969, 2879, 1702, 1404, 1181 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{14}\text{H}_{23}\text{NNaO}_2$ ($\text{M}+\text{Na}$): 260.1621. Found: 260.1618.

Cycloadduct (7)

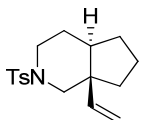


Following the general procedure, 1-ene-VCP **6** (23.5 mg, 0.077 mmol) was converted to cycloadduct **7** (12.4 mg, 53%). Substrate concentration: 0.03 M, temperature: 90 $^\circ\text{C}$, reaction time: 3.5 h. The reaction was also conducted under 0.2 M substrate concentration and 90 $^\circ\text{C}$ for 61 h. The reaction was messy and some unidentified byproducts were generated and can not be separated from the desired cycloadduct **7**.

7: Colorless oil. ^1H NMR (400 MHz, CDCl_3): δ 1.42-1.51 (m, 1H), 1.53-1.58 (m, 1H), 1.62-1.69 (m, 2H), 1.67 (s, 3H), 1.74-1.78 (m, 1H), 1.81-1.88 (m, 1H), 2.44 (s, 3H), 2.56 (m, 1H), 2.95 (d, $J = 9.8$ Hz, 1H), 3.03 (dd, $J = 3.5$ and 9.5 Hz, 1H), 3.14 (dd, $J = 7.9$ and 9.5 Hz, 1H), 3.19 (d, $J = 9.8$ Hz, 1H), 4.64 (s, 1H), 4.68 (m, 1H), 7.32

(d, $J = 8.4$ Hz, 2H), 7.68 (d, $J = 8.4$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 20.7, 21.5, 25.0, 33.1, 37.7, 45.5, 55.1, 58.3, 59.2, 109.3, 127.9, 129.5, 132.3, 143.4, 148.0. IR (neat): ν 2946, 1646, 1602, 1352, 1170 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{17}\text{H}_{23}\text{NNaO}_2\text{S}$ (M+Na): 328.1342. Found: 328.1341.

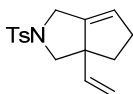
Cycloadduct (9)



Following the general procedure, 1-ene-VCP **8** (63.8 mg, 0.21 mmol) was converted to cycloadduct **9** (62.3 mg, 98%). Substrate concentration: 0.1 M, temperature: 80 °C, reaction time: 12 h.

9: White solid, m.p. 98-99 °C. ^1H NMR (400 MHz, CDCl_3): δ 1.12-1.95 (m, 2H), 1.25-1.32 (m, 1H), 1.58-1.79 (m, 6H), 2.05 (d, $J = 10.5$ Hz, 1H), 2.21 (dt, $J = 4.4$ and 11.4 Hz, 1H), 2.43 (s, 3H), 3.92 (dm, $J = 11.4$ Hz, 1H), 4.01 (d, $J = 10.5$ Hz, 1H), 5.20-5.24 (m, 2H), 6.02 (dd, $J = 11.0$ and 17.6 Hz, 1H), 7.31 (d, $J = 8.0$ Hz, 2H), 7.63 (d, $J = 8.0$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 20.8, 21.5, 25.1, 26.7, 33.9, 46.2, 46.9, 48.1, 56.9, 76.7, 77.0, 77.2, 77.3, 115.5, 127.5, 129.5, 133.7, 137.9, 143.1. IR (neat): ν 2931, 1602, 1345, 1170 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{17}\text{H}_{23}\text{NNaO}_2\text{S}$ (M+Na): 328.1342. Found: 328.1342.

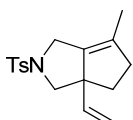
Cycloadduct (11)



Following the general procedure, 1-yne-VCP **10** (78.6 mg, 0.27 mmol) was converted to cycloadduct **11** (64.8 mg, 82%). Substrate concentration: 0.1 M, temperature: 80 °C, reaction time: 5 h.

11: White solid, m.p. 103-105 °C. ^1H NMR (400 MHz, CDCl_3): δ 1.71 (ddd, $J = 9.0$, 10.4, and 12.7 Hz, 1H), 1.92 (dd, $J = 6.6$ and 12.7 Hz, 1H), 2.40-2.46 (m, 1H), 2.43 (s, 3H), 2.58-2.67 (m, 1H), 2.83 (d, $J = 9.2$ Hz, 1H), 3.68 (d, $J = 9.2$ Hz, 1H), 3.76 (dm, $J = 13.6$ Hz, 1H), 3.83 (dm, $J = 13.6$ Hz, 1H), 4.88 (d, $J = 10.5$ Hz, 1H), 4.92 (d, $J = 17.4$ Hz, 1H), 5.51 (m, 1H), 5.71 (dd, $J = 10.5$ and 17.4 Hz, 1H), 7.31 (d, $J = 8.0$ Hz, 2H), 7.70 (d, $J = 8.0$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 21.5, 35.6, 36.3, 45.7, 58.0, 60.6, 112.5, 122.5, 127.4, 129.6, 134.4, 138.8, 143.2, 145.4. IR (neat): ν 2935, 1605, 1352, 1166 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{16}\text{H}_{19}\text{NNaO}_2\text{S}$ (M+Na): 312.1029. Found: 312.1027.

Cycloadduct (13)

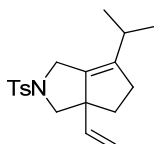


Following the general procedure, 1-yne-VCP **12** (33.2 mg, 0.10 mmol) was converted to cycloadduct **13** (25.8 mg, 78%). Substrate concentration: 0.04 M, temperature: 80 °C, reaction time: 23 h.

13: Colorless oil. ^1H NMR (400 MHz, CDCl_3): δ 1.62 (s, 3H), 1.72 (ddd, $J = 8.9$, 10.2, and 12.5 Hz, 1H), 1.89

(dd, $J = 6.6$ and 12.5 Hz, 1H), 2.23 (dd, $J = 8.9$ and 16.0 Hz, 1H), 2.43 (s, 3H), 2.64-2.72 (m, 1H), 2.83 (d, $J = 9.4$ Hz, 1H), 3.62 (d, $J = 9.4$ Hz, 1H), 3.69 (dm, $J = 12.7$ Hz, 1H), 3.77 (d, $J = 12.7$ Hz, 1H), 4.81-4.88 (m, 2H), 5.68 (dd, $J = 10.3$ and 17.1 Hz, 1H), 7.31 (d, $J = 7.9$ Hz, 2H), 7.71 (d, $J = 7.9$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 14.6, 21.5, 35.8, 40.3, 44.7, 58.1, 60.8, 111.9, 127.4, 129.5, 132.3, 134.7, 137.3, 139.5, 143.1. IR (neat): ν 2939, 1631, 1605, 1356, 1170 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{17}\text{H}_{21}\text{NNaO}_2\text{S}$ ($\text{M}+\text{Na}$): 326.1185. Found: 326.1184.

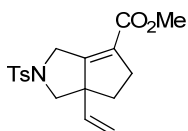
Cycloadduct (15)



Following the general procedure, 1-yne-VCP **14** (32.2 mg, 0.097 mmol) was converted to cycloadduct **15** (11.5 mg, 36%). Flash column chromatography also recovered 10.4 mg of compound **14** (32%). The yield of **15** was 53% based on the recovered starting material. Substrate concentration: 0.05 M, temperature: 80 °C, reaction time: 48 h.

15: Colorless oil. ^1H NMR (400 MHz, CDCl_3): δ 0.95 (d, $J = 7.0$ Hz, 3H), 0.98 (d, $J = 7.1$ Hz, 3H), 1.66 (dd, $J = 8.4$ and 12.4 Hz, 1H), 1.85 (dd, $J = 6.5$ and 12.4 Hz, 1H), 2.31 (dd, $J = 8.0$ and 15.0 Hz, 1H), 2.37-2.45 (m, 1H), 2.43 (s, 3H), 2.54-2.64 (m, 1H), 2.82 (d, $J = 9.3$ Hz, 1H), 3.60 (d, $J = 9.3$ Hz, 1H), 3.73 (ddm, $J = 4.0$ and 13.3 Hz, 1H), 3.86 (dd, $J = 1.6$ and 13.0 Hz, 1H), 4.82 (dd, $J = 1.0$ and 10.2 Hz, 1H), 4.86 (dd, $J = 1.0$ and 17.3 Hz, 1H), 5.66 (dd, $J = 10.2$ and 17.3 Hz, 1H), 7.30 (d, $J = 8.2$ Hz, 2H), 7.70 (d, $J = 8.2$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 21.16, 21.19, 21.5, 28.8, 35.2, 35.5, 45.0, 57.8, 60.8, 112.0, 127.4, 129.5, 134.7, 135.1, 139.4, 141.9, 143.2. IR (neat): ν 2924, 1602, 1468, 1348, 1166 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{19}\text{H}_{26}\text{NO}_2\text{S}$ ($\text{M}+\text{H}$): 332.1679. Found: 332.1678.

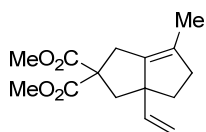
Cycloadduct (17)



Following the general procedure, 1-yne-VCP **16** (10.9 mg, 0.032 mmol) was converted to cycloadduct **17** (7.2 mg, 66%). Substrate concentration: 0.04 M, temperature: 80 °C, reaction time: 13.5 h.

17: Colorless oil. ^1H NMR (400 MHz, CDCl_3): δ 1.79 (ddd, $J = 8.9$, 10.5, and 12.8 Hz, 1H), 2.00 (dd, $J = 5.8$ and 12.8 Hz, 1H), 2.44 (s, 3H), 2.72 (dd, $J = 8.3$ and 15.8 Hz, 1H), 2.82 (d, $J = 9.5$ Hz, 1H), 2.82-2.91 (m, 1H), 3.73 (s, 3H), 3.73 (d, $J = 9.5$ Hz, 1H), 4.06 (ddd, $J = 1.7$, 4.0, and 16.8 Hz, 1H), 4.12 (dm, $J = 16.8$ Hz, 1H), 4.99 (d, $J = 10.8$ Hz, 1H), 5.00 (d, $J = 17.7$ Hz, 1H), 5.76 (dd, $J = 10.7$ and 17.7 Hz, 1H), 7.33 (d, $J = 8.5$ Hz, 2H), 7.72 (d, $J = 8.5$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 21.5, 34.8, 35.3, 46.9, 51.6, 57.2, 61.9, 113.9, 126.3, 127.5, 129.7, 134.0, 137.4, 143.6, 159.2, 164.6. IR (neat): ν 2961, 1720, 1643, 1602, 1352, 1166 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{18}\text{H}_{22}\text{NO}_4\text{S}$ ($\text{M}+\text{H}$): 348.1264. Found: 348.1263.

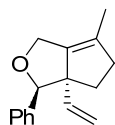
Cycloadduct (19)



Following the general procedure, 1-yne-VCP **18** (29.0 mg, 0.10 mmol) was converted to cycloadduct **19** (17.2 mg, 59%). Substrate concentration: 0.1 M, temperature: 80 °C, reaction time: 39 h. Initially, 5 mol % of [Rh(dppp)]SbF₆ was used as catalyst. After 23 h, another 5 mol % of [Rh(dppp)]SbF₆ was added to promote the reaction.

19: Colorless oil. ¹H NMR (400 MHz, CDCl₃): δ 1.67 (s, 3H), 1.79 (ddd, *J* = 8.4, 9.9, and 11.8 Hz, 1H), 1.90 (dd, *J* = 6.4 and 11.8 Hz, 1H), 2.14 (d, *J* = 13.1 Hz, 1H), 2.21 (dd, *J* = 8.4 and 15.2 Hz, 1H), 2.56 (d, *J* = 13.1 Hz, 1H), 2.59-2.67 (m, 1H), 2.73-2.84 (m, 2H), 3.700 (s, 3H), 3.704 (s, 3H), 4.87 (dd, *J* = 1.5 and 16.8 Hz, 1H), 4.88 (dd, *J* = 1.5 and 10.4 Hz, 1H), 5.79 (dd, *J* = 10.4 and 16.8 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 14.5, 31.5, 39.1, 39.9, 44.6, 52.7, 52.8, 61.8, 62.8, 111.0, 130.7, 141.4, 142.1, 172.3, 172.9. IR (neat): ν 2961, 2861, 1743, 1639, 1441, 1259 cm⁻¹. HRMS (ESI) calcd for C₁₅H₂₀NaO₄ (M+Na): 287.1254. Found: 287.1253.

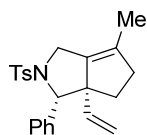
Cycloadduct (21)



Following the general procedure, 1-yne-VCP **20** (69.2 mg, 0.30 mmol) was converted to cycloadduct **21** (51.0 mg, 74%). Substrate concentration: 0.1 M, temperature: 80 °C, reaction time: 11.5 h.

21: Light-yellow oil. ¹H NMR (400 MHz, CDCl₃): δ 1.18 (dt, *J* = 12.8 and 9.3 Hz, 1H), 1.56 (dd, *J* = 7.1 and 12.8 Hz, 1H), 1.72 (s, 3H), 2.11 (dd, *J* = 8.9 and 15.5 Hz, 1H), 2.66 (m, 1H), 4.29 (dm, *J* = 12.1 Hz, 1H), 4.56 (d, *J* = 12.1 Hz, 1H), 4.98 (s, 1H), 5.09 (dd, *J* = 1.3 and 10.2 Hz, 1H), 5.17 (dd, *J* = 0.9 and 17.3 Hz, 1H), 6.12 (dd, *J* = 10.2 and 17.3 Hz, 1H), 7.07 (dm, *J* = 7.6 Hz, 2H), 7.21-7.25 (m, 1H), 7.29-7.33 (m, 2H). ¹³C NMR (100 MHz, CDCl₃): δ 14.8, 32.3, 41.2, 64.0, 67.0, 85.5, 111.2, 126.3, 126.9, 128.0, 131.7, 139.8, 142.4. IR (neat): ν 2931, 1639, 1605, 1460, 1024 cm⁻¹. HRMS (ESI) calcd for C₁₆H₁₈NaO (M+Na): 249.1250. Found: 249.1248.

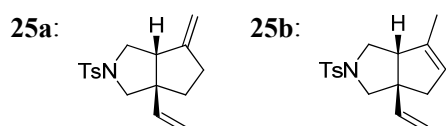
Cycloadduct (23)



Following the general procedure, 1-yne-VCP **22** (30.7 mg, 0.081 mmol) was converted to cycloadduct **23** (34.1 mg, quantitative yield). Substrate concentration: 0.04 M, temperature: 80 °C, reaction time: 5 h. ¹H NMR analysis of the crude product indicated a diastereomeric ratio of 6:1. The major diastereomer was obtained by recrystallization of the mixture in PE/EA mixed solvent, but the minor diastereomer could not be obtained in pure form.

23 (major diastereomer): Colorless crystals, m.p. 153-155 °C. ¹H NMR (400 MHz, CDCl₃): δ 1.59 (s, 3H), 1.74 (dd, *J* = 7.1 and 12.4 Hz, 1H), 1.81 (ddd, *J* = 8.4, 9.7, and 12.4 Hz, 1H), 2.14 (dd, *J* = 8.0 and 15.4 Hz, 1H), 2.43 (s, 3H), 2.51-2.56 (m, 1H), 3.97 (dm, *J* = 13.7 Hz, 1H), 4.16 (d, *J* = 13.7 Hz, 1H), 4.19 (s, 1H), 4.82 (dd, *J* = 1.8 and 17.2 Hz, 1H), 4.87 (dd, *J* = 1.8 and 10.2 Hz, 1H), 5.25 (dd, *J* = 10.2 and 17.2 Hz, 1H), 7.25-7.29 (m, 8H), 7.58 (d, *J* = 7.9 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃): δ 14.4, 21.5, 36.8, 39.5, 46.9, 66.1, 75.0, 112.4, 127.2, 127.6, 127.8, 129.3, 132.7, 134.2, 135.3, 137.5, 137.9, 143.2. IR (neat): ν 2939, 1602, 1354, 1166 cm⁻¹. HRMS (ESI) calcd for C₂₃H₂₆NO₂S (M+H): 380.1679. Found: 380.1682.

Cycloadducts (**25a** and **25b**)



Following the general procedure, 1-allene-VCP **24** (42.2 mg, 0.14 mmol) was converted to a mixture of cycloadducts **25a** and **25b** (20.3 mg, 48%). Substrate concentration: 0.05 M, temperature: 80 °C, reaction time: 13 h. ¹H NMR analysis of this product indicated that it was a mixture of *exo* and *endo* C=C bond isomers (**25a**: *exo* isomer, **25b**: *endo* isomer, **25a**:**25b** = 3.6:1).

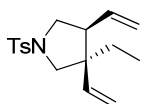
The [3+2] cycloaddition of substrate **24** was also conducted using [Rh(CO)₂Cl]₂ as the catalyst. Procedure: a solution of compound **24** (25.0 mg, 0.082 mmol) and [Rh(CO)₂Cl]₂ (1.2 mg, 3.1 μmol, 8 mol % Rh to the substrate) in dry toluene (1.8 mL, substrate concentration 0.4 M) was heated to 110 °C under argon. After 2 h, the reaction mixture was cooled to room temperature and concentrated. The residue was purified by flash column chromatography on silica gel (eluted with PE/EA 20:1 to 10:1) to afford a mixture of cycloadducts **25a** and **25b** (10.3 mg, 41%). ¹H NMR analysis indicated a **25a**:**25b** ratio of 10:1.

Pure **25b** could be obtained from acid-catalyzed isomerization of cycloadduct **25a**. To an NMR tube containing a solution of **25a** and **25b** (20.3 mg, ratio 3.6:1) in CDCl₃ (~0.5 mL) was added TsOH·H₂O (2.8 mg). The tube was heated to 40 °C for 43 h, and then 50 °C for 24 h. The solvent was evaporated and the residue was purified by flash column chromatography to afford pure cycloadduct **25b** (18.3 mg, 90%).

25a: Colorless oil. ¹H NMR (400 MHz, CDCl₃): δ 1.68 (dt, *J* = 13.0 and 7.7 Hz, 1H), 1.79 (dt, *J* = 13.0 and 7.7 Hz, 1H), 2.35-2.39 (m, 2H), 2.44 (s, 3H), 2.74-2.77 (m, 1H), 3.11 (d, *J* = 9.6 Hz, 1H), 3.18 (d, *J* = 9.6 Hz, 1H), 3.24 (dd, *J* = 4.0 and 9.7 Hz, 1H), 3.39 (dd, *J* = 8.4 and 9.7 Hz, 1H), 4.78 (q, *J* = 2.1 Hz, 1H), 4.87 (q, *J* = 2.1 Hz, 1H), 4.95 (d, *J* = 17.7 Hz, 1H), 4.97 (dd, *J* = 0.9 and 11.1 Hz, 1H), 5.79 (dd, *J* = 11.1 and 17.7 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.70 (d, *J* = 8.0 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃): δ 21.5, 29.7, 31.7, 34.3, 53.0, 53.7, 56.8, 108.0, 112.7, 127.8, 129.5, 133.0, 141.6, 143.4, 152.9. IR (neat): ν 2928, 1605, 1352, 1166 cm⁻¹. HRMS (ESI) calcd for C₁₇H₂₁NNaO₂S (M+Na): 326.1185. Found: 326.1185.

25b: Colorless oil. ¹H NMR (400 MHz, CDCl₃): δ 1.56 (s, 3H), 2.32 (dq, *J* = 16.6 and 2.6 Hz, 1H), 2.44 (s, 3H), 2.45 (m, 1H), 2.81 (dm, *J* = 7.6 Hz, 1H), 3.08 (d, *J* = 10.1 Hz, 1H), 3.16-3.25 (m, 3H), 4.89-4.94 (m, 2H), 5.21 (m, 1H), 5.88 (dd, *J* = 10.2 and 16.6 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.69 (d, *J* = 8.0 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃): δ 14.9, 21.5, 43.0, 50.1, 55.3, 58.1, 58.3, 111.9, 124.1, 127.8, 129.5, 132.8, 139.2, 142.4, 143.4. IR (neat): ν 2924, 1643, 1605, 1348, 1166 cm⁻¹. HRMS (ESI) calcd for C₁₇H₂₁NNaO₂S (M+Na): 326.1185. Found: 326.1185.

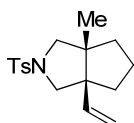
β -Hydride Elimination Byproduct (**27**)



Following the general procedure, 1-ene-VCP **26** (42.3 mg, 0.14 mmol) was converted to byproduct **27** (15.3 mg, 36%). Substrate concentration: 0.05 M, temperature: 80 °C, reaction time: 13 h. Flash column chromatography also recovered 6.6 mg of the substrate **26**. However, most of the starting material became unidentified inseparable high-polar complex mixture, which accounts for the mass balance.

27: Colorless oil. ^1H NMR (400 MHz, CDCl_3): δ 0.74 (t, $J = 7.5$ Hz, 3H), 1.21 (dq, $J = 13.7$ and 7.6 Hz, 1H), 1.58 (dq, $J = 13.7$ and 7.6 Hz, 1H), 2.31 (m, 1H), 2.45 (s, 3H), 3.02 (d, $J = 10.0$ Hz, 1H), 3.11 (t, $J = 10.0$ Hz, 1H), 3.49 (dd, $J = 7.6$ and 9.7 Hz, 1H), 3.52 (d, $J = 9.7$ Hz, 1H), 4.82 (d, $J = 17.5$ Hz, 1H), 5.00 (dm, $J = 17.0$ Hz, 1H), 5.07 (dd, $J = 1.7$ and 10.6 Hz, 1H), 5.08 (d, $J = 11.1$ Hz, 1H), 5.44 (dd, $J = 11.1$ and 17.3, 1H), 5.49 (ddd, $J = 10.6$ and 17.3 Hz, 1H), 7.34 (d, $J = 8.0$ Hz, 2H), 7.74 (d, $J = 8.0$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 9.3, 21.5, 29.8, 50.7, 51.1, 52.6, 54.5, 115.7, 118.3, 127.3, 129.6, 133.8, 134.6, 138.1, 143.3. IR (neat): ν 2939, 1643, 1602, 1352, 1166 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{17}\text{H}_{23}\text{NNaO}_2\text{S}$ ($\text{M}+\text{Na}$): 328.1342. Found: 328.1341.

Cycloadduct (**29**)

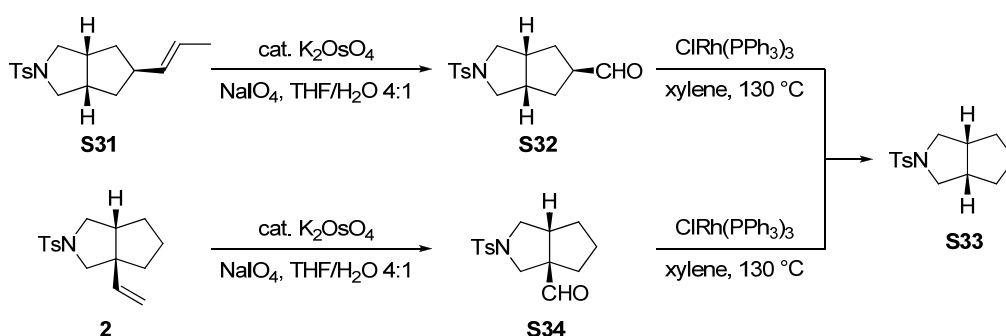


Following the general procedure, 1-ene-VCP **28** (40.7 mg, 0.13 mmol) was converted to cycloadduct **29** (11.7 mg, 29%). Substrate concentration: 0.05 M, temperature: 80 °C, reaction time: 24 h. Flash column chromatography also recovered substrate **28** (19.0 mg), so the yield of cycloadduct **29** was 54% brsm. However, the product contains minor amount of inseparable impurities (see page S52 for its ^1H and ^{13}C NMR spectra).

2.3 Stereochemical Determination

General. The stereochemistry of cycloadducts **2**, **7**, **9**, and **25** was determined by chemical derivation and then comparison with known compounds that have well-defined stereochemistry. The ring-fusion stereochemistry of cycloadducts **5** and **29** was deduced to be *cis* by analogy. The relative configuration of compounds **21**, **23**, and **27** was determined by 1D nOe analysis.

Chemical derivation of cycloadduct 2. A known compound **S31** was converted to aldehyde **S32** and then the formyl group was removed by Tsuji-Wilkinson decarbonylation reaction to afford the *cis*-fused bicyclic compound **S33**. On the other hand, the [3+2] cycloadduct **2** was converted to aldehyde **S34** and then decarbonylated using $\text{ClRh}(\text{PPh}_3)_3$ by following the same reaction sequence. Both routes gave the same decarbonylation product **S33**, indicating that the cycloadduct **2** has a *cis* ring-fusion.



S31 to S32: To a stirred mixture of bicyclic compound **S31**¹² (30 mg, 0.098 mmol) and $\text{K}_2\text{OsO}_4 \cdot 2\text{H}_2\text{O}$ (3.6 mg, 9.8 μmol) in $\text{THF}/\text{H}_2\text{O}$ (4:1, 5 mL) was added powdered NaIO_4 (64 mg, 0.30 mmol) in one portion. The reaction was stirred for 7.5 h under room temperature. Water (5 mL) and ether (10 mL) was added to quench the reaction, and the mixture was extracted with ether three times. The combined organic extract was combined, dried over Na_2SO_4 , and concentrated. The crude oil was purified by flash column chromatography on silica gel (eluted with PE/EA 10:1 to 4:1) to afford aldehyde **S32** (11 mg, 39%).

S32: Colorless oil. ^1H NMR (300 MHz, CDCl_3): δ 1.63-1.72 (m, 2H), 2.04-2.14 (m, 2H), 2.44 (s, 3H), 2.62-2.65 (m, 2H), 2.88-2.96 (m, 1H), 2.98-3.08 (m, 4H), 7.34 (d, $J = 7.8$ Hz, 2H), 7.68 (d, $J = 7.8$ Hz, 2H), 9.59 (d, $J = 1.9$ Hz, 1H). ^{13}C NMR (75.5 MHz, CDCl_3): δ 21.5, 32.9, 41.9, 52.0, 54.4, 128.0, 129.6, 131.7, 143.7, 202.7.

S32 to S33: A solution of aldehyde **S32** (11 mg, 0.037 mmol) and Wilkinson's catalyst $\text{RhCl}(\text{PPh}_3)_3$ (72 mg, 0.078 mmol) in xylene (4.5 mL) was bubbled dry argon for 2 min before it was immersed in an oil bath heated to 110°C . After 22 h, the reaction mixture was cooled to room temperature and filtered through a pad of silica gel. The filtrate was concentrated and the crude product was purified by flash column chromatography on silica gel (eluted with PE/EA 20:1) to afford the bicyclic compound **S33** (6.9 mg, 69%).

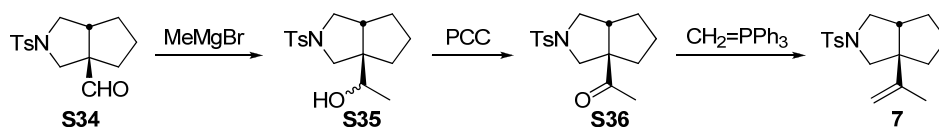
S33: Colorless oil. ^1H NMR (300 MHz, CDCl_3): δ 1.35-1.49 (m, 3H), 1.58-1.64 (m, 1H), 1.68-1.76 (m, 2H), 2.44 (s, 3H), 2.51-5.58 (m, 2H), 2.89 (dd, $J = 3.6$ and 9.7 Hz, 2H), 3.11 (dd, $J = 7.6$ and 9.3 Hz, 2H), 7.32 (d, $J = 8.0$ Hz, 2H), 7.68 (d, $J = 8.0$ Hz, 2H). ^{13}C NMR (75.5 MHz, CDCl_3): δ 21.5, 26.1, 32.7, 42.5, 54.5, 128.0, 129.5, 132.2, 143.4. HRMS (ESI) calcd for $\text{C}_{14}\text{H}_{19}\text{NNaO}_2\text{S}$ ($\text{M}+\text{Na}$): 388.1029. Found: 288.1028.

2 to S34: Following the procedure for the preparation of **S32** from **S31**, cycloadduct **2** (16 mg, 0.054 mmol) was converted to crude aldehyde **S34** (7.3 mg, 47%), which was used without further purification.

(12) Jiao, L.; Ye, S.; Yu, Z.-X. *J. Am. Chem. Soc.* **2008**, *130*, 7178.

S34 to S33: Following the procedure for the preparation of **S33** from **S32**, crude aldehyde **S34** (7.3 mg, 0.025 mmol) was converted to bicyclic compound **S33** (2.7 mg, 41%).

Determination of the stereostructure of cycloadduct 7. Aldehyde **S34** was converted to secondary alcohol **S35**, which was then oxidized to ketone **S36**. After treatment with methyldiene Wittig reagent, **S36** was converted to a bicyclic compound that is identical to cycloadduct **7** obtained from the [3+2] reaction. This confirmed the *cis* ring-fusion of the [3+2] cycloadduct **7**.

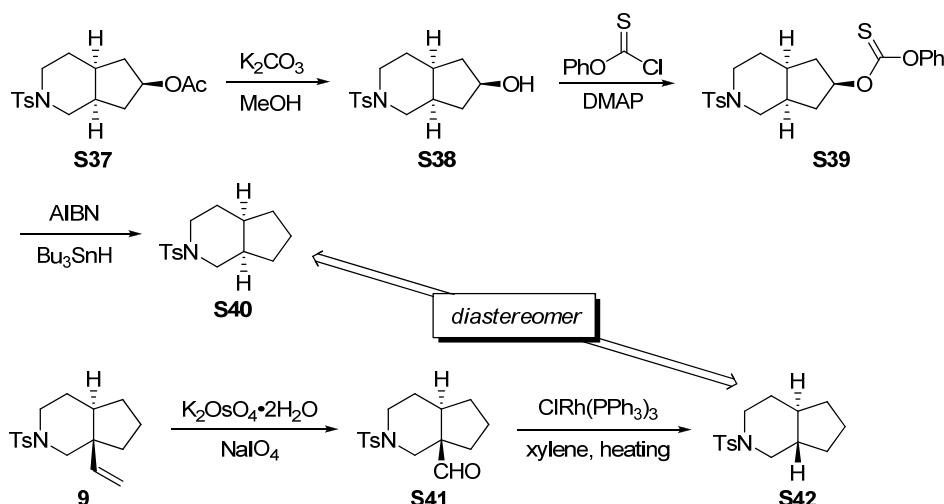


S34 to S35: To a solution of crude aldehyde **S34** (12 mg, 0.041 mmol) in THF (1 mL) was added MeMgBr (3 M in ether, 8 drops, excess amount) at 0 °C. After 10 min, saturated aqueous NH₄Cl was added, and the resulting mixture was extracted with ether. The combined organic extract was dried over MgSO₄ and concentrated. The crude product was directly subjected to PCC oxidation.

S35 to S36: Following the procedure for the preparation of **S5** from **S4**, crude alcohol **S35** was converted to bicyclic ketone **S36** (12 mg, 91% for 2 steps).

S36 to 7: Following the procedure for the preparation of **1** from **S5**, ketone **S36** (12 mg, 0.037 mmol) was converted to bicyclic cycloadduct **7** (7.1 mg, 62%).

Determination of the stereostructure of cycloadduct 9. Known compound **S37** was converted to a *cis*-fused aza-6,5-bicyclic compound **S38** in 3 steps. On the other hand, cycloadduct **9** was elaborated to aldehyde **S41** and then decarbonylated to afford a 6,5-ring compound **S42**. Compound **S42** is the stereoisomer of **S40**. Since **S40** is *cis*-fused, **S42** should be the *trans*-fused isomer. Thus, cycloadduct **9** is a *trans*-fused 6,5-bicyclic compound.



S37 to S38: To a solution of compound **S37**¹³ (39 mg, 0.12 mmol) in MeOH (2.0 mL) was added powdered K₂CO₃ (17 mg, 0.13 mmol) in one batch under room temperature. The reaction mixture was stirred for 3.5 h, and

(13) Kavanagh, Y.; Chaney, C. M.; Muldoon, J.; Evans, P. J. *Org. Chem.* **2008**, *73*, 8601.

saturated aqueous NH_4Cl was added. The mixture was extracted with ether, and the combined organic extract was dried over MgSO_4 and concentrated. The crude product was purified by flash column chromatography on silica gel (eluted with PE/EA 3:1 to 1:1) to afford alcohol **S38** (37 mg, quantitative yield) as a colorless oil.

S38 to S39: To a stirred solution of alcohol **S38** (37 mg, 0.13 mmol) and DMAP (38 mg, 0.31 mmol) in dry CH_2Cl_2 (2 mL) was added phenyl chlorothioformate (42 mg, 0.24 mmol) dropwise under argon at room temperature. After 12 h, another portion of phenyl chlorothioformate (25 mg, 0.14 mmol) was added. After stirred for another 5 h, the reaction mixture was evaporated. The residue was purified by flash column chromatography on silica gel (eluted with PE/EA 5:1 to 1:1) to afford compound **S39** (37 mg, 74%) and recovered alcohol **S38** (6.2 mg).

S39 to S40: A solution of compound **S39** (23 mg, 0.053 mmol), $n\text{-Bu}_3\text{SnH}$ (35 mg, 0.12 mmol), and AIBN (2.4 mg, 0.015 mmol) in toluene (2 mL) was bubbled a stream of dry argon for 5 min. The reaction mixture was then heated to 75 °C in an oil bath and stirred for 2.5 h. After cooled to room temperature, the reaction mixture was concentrated and the residue was purified by flash column chromatography on silica gel (eluted with PE/EA 20:1 to 10:1) to afford **S40** (12 mg, 84%).

S40: Colorless oil. ^1H NMR (400 MHz, CDCl_3): δ 1.33-1.39 (m, 1H), 1.48-1.70 (m, 7H), 1.81-1.88 (m, 1H), 2.02-2.10 (m, 1H), 2.43 (s, 3H), 2.66 (ddd, $J = 3.5, 8.9,$ and 11.5 Hz, 1H), 2.86 (dd, $J = 4.4$ and 11.5 Hz, 1H), 3.01 (dd, $J = 6.2$ and 11.5 Hz, 1H), 3.18-3.23 (m, 1H), 7.32 (d, $J = 7.9$ Hz, 2H), 7.64 (d, $J = 7.9$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 21.4, 21.9, 26.4, 26.7, 29.3, 36.5, 38.3, 44.3, 46.8, 127.5, 129.4, 133.4, 143.1. HRMS (ESI) calcd for $\text{C}_{15}\text{H}_{22}\text{NO}_2\text{S}$ (M+H): 280.1366. Found: 280.1362.

9 to S41: Following the procedure for the preparation of **S32** from **S31**, cycloadduct **9** (60 mg, 0.20 mmol) was converted to aldehyde **S41** (15 mg, 25%).

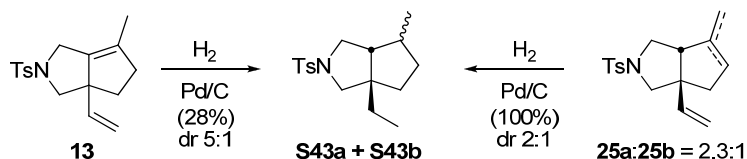
S41: White solid, m.p. 148-150 °C. ^1H NMR (400 MHz, CDCl_3): δ 1.16-1.28 (m, 1H), 1.33-1.42 (m, 1H), 1.64-1.78 (m, 5H), 1.80-1.90 (m, 2H), 2.16 (d, $J = 11.5$ Hz, 1H), 2.28 (dt, $J = 3.4$ and 11.5 Hz, 1H), 2.44 (s, 3H), 3.97 (dm, $J = 11.5$ Hz, 1H), 4.34 (dd, $J = 1.4$ and 11.5 Hz, 1H), 7.34 (d, $J = 8.0$ Hz, 2H), 7.66 (d, $J = 8.0$ Hz, 2H), 9.80 (d, $J = 1.7$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 21.1, 21.5, 25.6, 27.4, 29.9, 46.8, 47.6, 53.5, 55.4, 127.6, 129.7, 133.2, 143.7, 204.2. IR (neat): ν 2920, 1732, 1352, 1162 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{16}\text{H}_{22}\text{NO}_3\text{S}$ (M+H): 308.1315. Found: 308.1318.

S41 to S42: Following the procedure for the preparation of **S33** from **S32** (except that the reaction temperature was 130-140 °C), compound **S41** (15 mg, 0.048 mmol) was converted to bicyclic compound **S42** (3.2 mg, 25%).

S42: Colorless oil. ^1H NMR (400 MHz, CDCl_3): δ 0.84-0.94 (m, 1H), 0.99-1.08 (m, 1H), 1.09-1.18 (m, 1H), 1.32-1.43 (m, 2H), 1.59-1.67 (m, 2H), 1.69-1.78 (m, 2H), 1.86 (dm, $J = 12.9$ Hz, 1H), 1.98 (t, $J = 10.6$ Hz, 1H), 2.20 (dt, $J = 2.6$ and 11.9 Hz, 1H), 2.43 (s, 3H), 3.89 (dm, $J = 11.9$ Hz, 1H), 4.02 (ddd, $J = 1.3, 3.9,$ and 10.6 Hz, 1H), 7.32 (d, $J = 8.0$ Hz, 2H), 7.65 (d, $J = 8.0$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 21.5, 21.8, 27.7, 30.0, 30.3, 44.2, 44.8, 46.5, 51.8, 127.6, 129.5, 133.9, 143.1. HRMS (ESI) calcd for $\text{C}_{15}\text{H}_{22}\text{NO}_2\text{S}$ (M+H): 280.1366. Found: 280.1363.

Determination of the stereostructure of cycloadduct 25. Cycloadduct **13** was hydrogenated to give *cis*-fused bicyclic compounds **S43a** and **S43b** (dr 5:1). A mixture of cycloadducts **25a** and **25b** (ratio 2.3:1), obtained from the [3+2] reaction of 1-allene-VCP substrate **24**, was also hydrogenated under the same conditions. The hydrogenation product was a diastereomeric mixture (dr 2:1). These products matched **S43a** and **S43b** obtained

from the hydrogenation of compound **13**, indicating that cycloadducts **25a** and **25b** have a *cis* ring-fusion stereochemistry.



13 to **S43**: To a solution of **13** (6.9 mg, 0.023 mmol) in MeOH (1 mL) was added Pd/C (10% palladium on charcoal, 1.0 mg). The mixture was degassed in vacuum and hydrogen was run through for 2 min. The mixture was stirred at room temperature under an atmosphere of hydrogen for 12 h. The mixture was filtered through a thin pad of silica gel and the filter cake was washed with ether. The combined filtrate was concentrated and the residue was purified by flash column chromatography on silica gel (eluted with PE/EA 50:1 to 20:1) to give the hydrogenated product as a diastereomeric mixture of **S43a** and **S43b** (1.9 mg, 28%, dr 5:1).

25 to **S38**: Following the above procedure, a mixture of **25a** and **25b** (ratio 2.3:1, 21 mg, 0.10 mmol) was hydrogenated to afford a diastereomeric mixture of **S43a** and **S43b** (21 mg, quantitative yield, dr 2:1).

Determination of the stereostructures of compounds 21, 23, and 27 by 1D nOe experiments. See below for details.

The nOe correlation between the benzylic proton and the vinyl group in cycloadduct **21** indicates a *trans* relationship of the phenyl and the vinyl group (Figure S1).

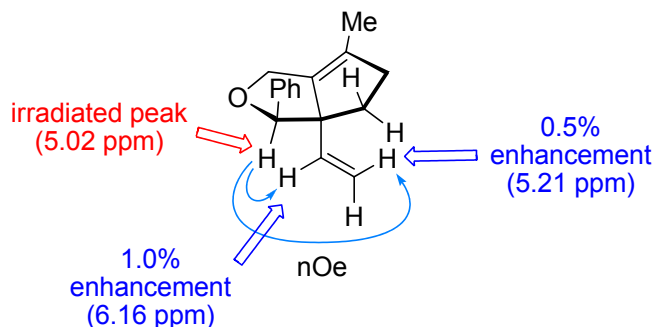


Figure S1. 1D nOe analysis of cycloadduct **21** (the 1D nOe spectrum is on page S43).

The protons on the cyclopentene moiety of cycloadduct **23** was assigned according to their coupling constants. By using the Karplus equation:¹⁴

$$J_{ab} = J^0 \cos^2 \phi - 0.28 \quad (0^\circ \leq \phi \leq 90^\circ)$$

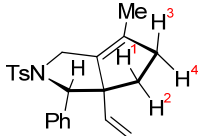
$$J_{ab} = J^{180} \cos^2 \phi - 0.28 \quad (90^\circ \leq \phi \leq 180^\circ)$$

we could calculate the coupling constants between H^1 , H^2 , H^3 , and H^4 ($J^0 = 8.5$ Hz and $J^{180} = 9.5$ Hz) on the basis of the MM2 optimized structure of **23** (Table S1). By comparing the calculated coupling constants and those measured by ^1H NMR, we could assign the chemical shifts for each proton (H^1 , H^2 , H^3 , and H^4). The 1D nOe experiment clearly demonstrated an nOe correlation between H^1 and the proton on the benzylic position,

(14) Williams, D. H.; Fleming, I. *Spectroscopic Methods in Organic Chemistry, Fifth Edition*; McGraw-Hill: Cambridge, 1995.

suggesting a *cis* relationship between the phenyl and vinyl group (Figure S2).

Table S1. ^1H NMR assignment of the cyclopentene moiety of cycloadduct **23**



H¹: 1.81 ppm, ddd, $J = 8.4, 9.7,$ and 12.4 Hz
H²: 1.74 ppm, dd, $J = 7.1$ and 12.4 Hz
H³: 2.14 ppm, dd, $J = 8.0$ and 15.4 Hz
H⁴: 2.54 ppm, m

MM2 optimized structure	calcd. coupling constant	measured coupling constant
$\phi_{\text{H}^1\text{-C-C-H}^3} = 32^\circ$	$J_{13} \sim 5.8$ Hz	8.4 Hz
$\phi_{\text{H}^1\text{-C-C-H}^4} = 156^\circ$	$J_{14} \sim 7.6$ Hz	9.7 Hz
$\phi_{\text{H}^2\text{-C-C-H}^3} = 86^\circ$	$J_{23} \sim 0$ Hz	0 Hz
$\phi_{\text{H}^2\text{-C-C-H}^4} = 37^\circ$	$J_{24} \sim 5.1$ Hz	7.1 Hz

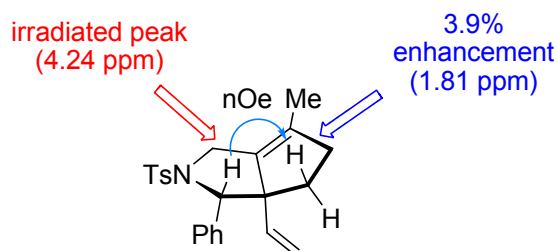


Figure S2. 1D nOe analysis of cycloadduct **23** (the 1D nOe spectrum is on page S45).

The nOe correlation between the allylic proton and the ethyl group in compound **27** indicates a *cis* relationship of the two vinyl groups (Figure S1).

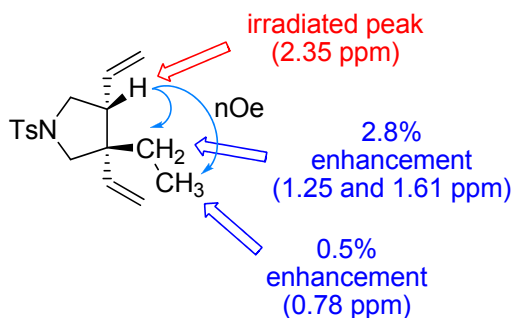
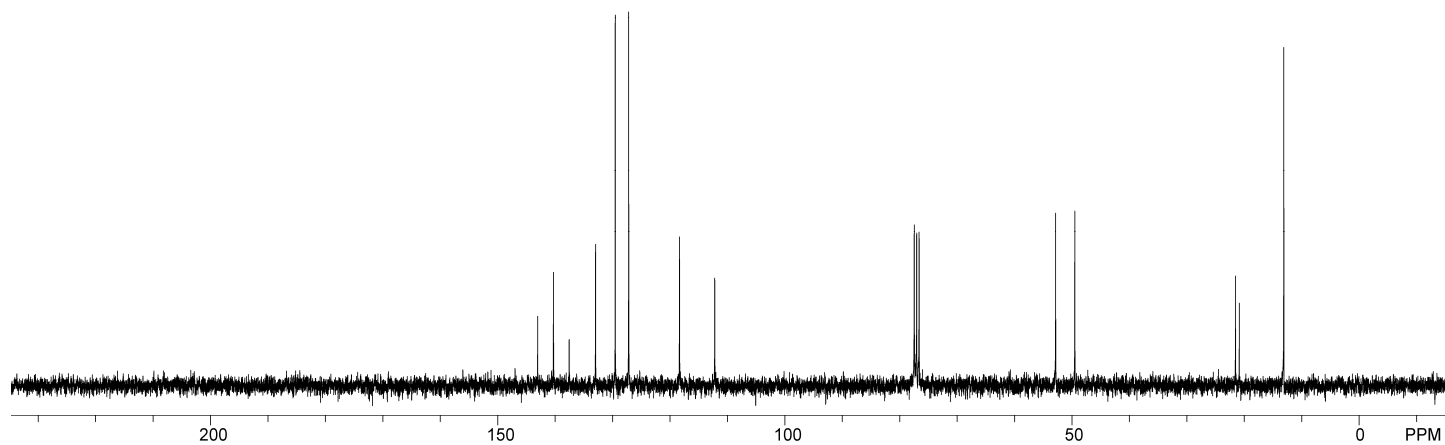
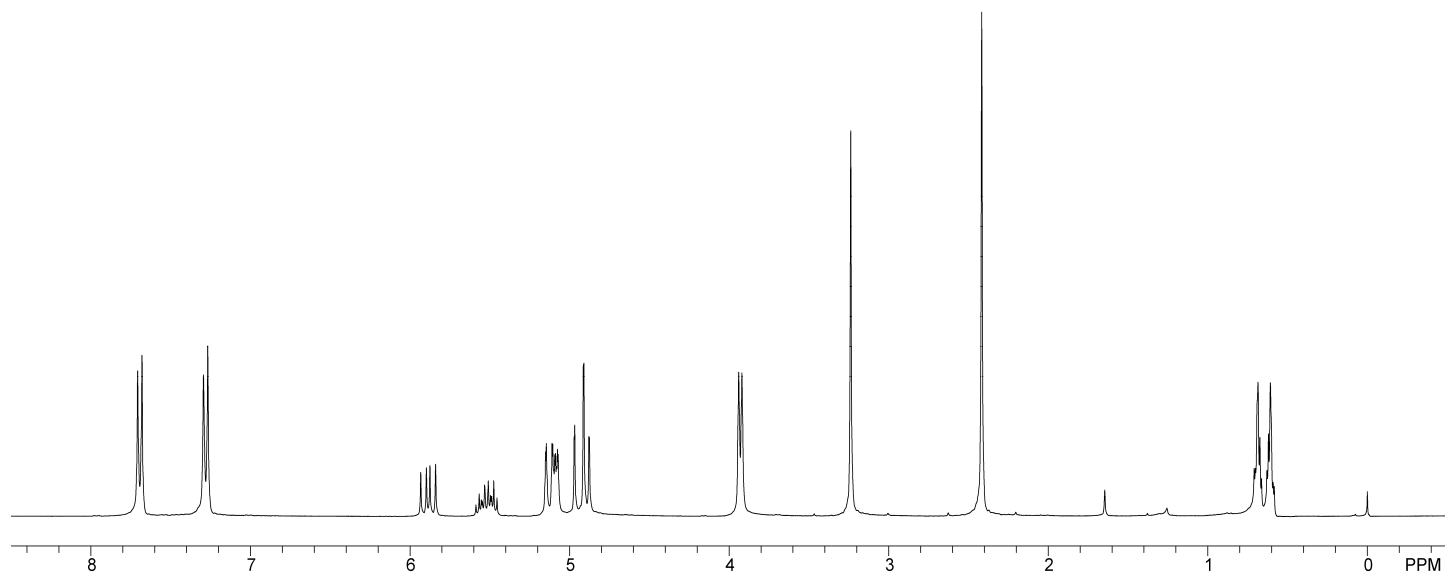
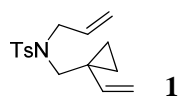
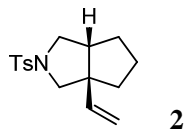


Figure S3. 1D nOe analysis of compound **27** (the 1D nOe spectrum is in page S50).

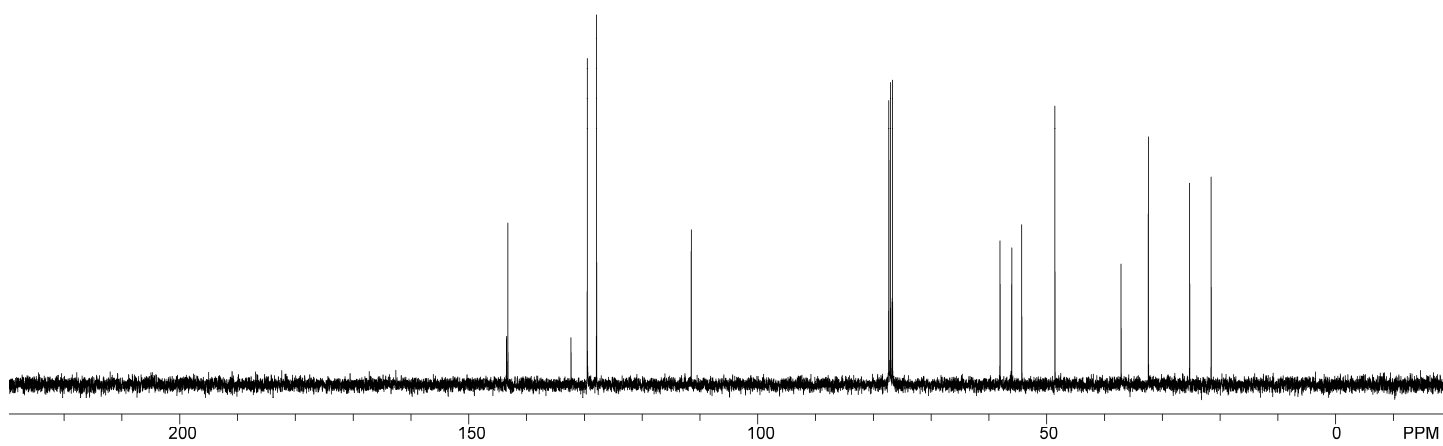
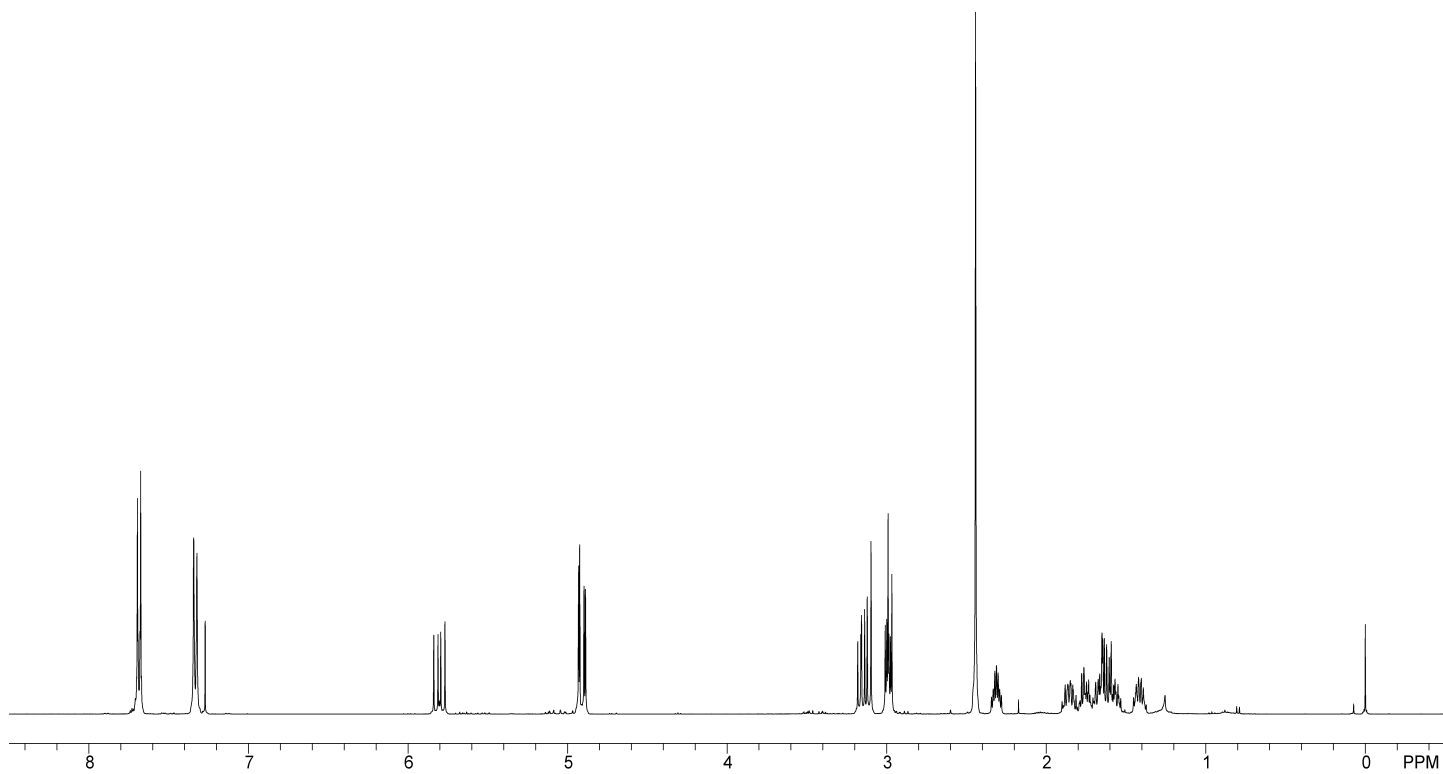
3. ^1H and ^{13}C -NMR Spectra for New Compounds

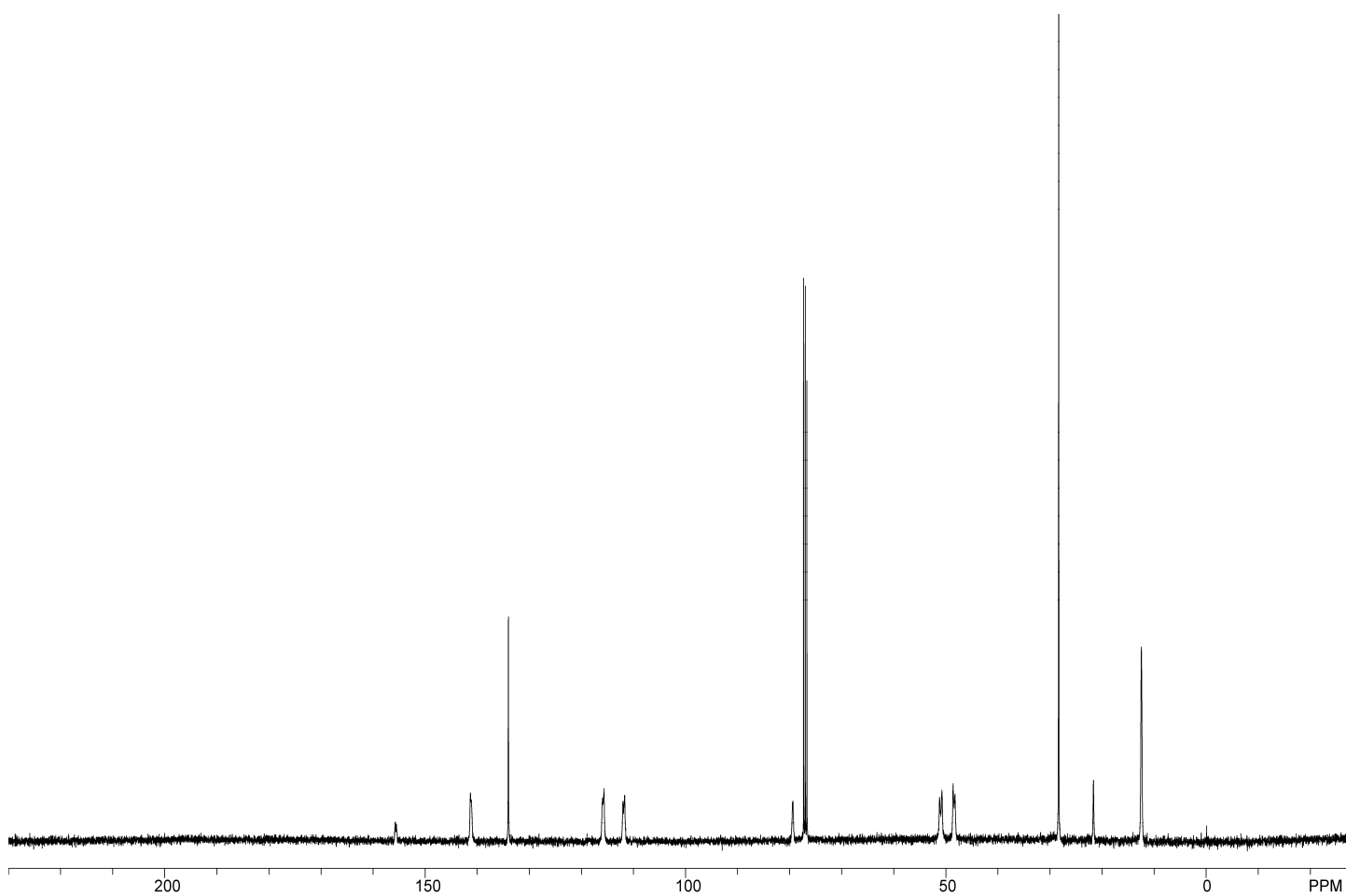
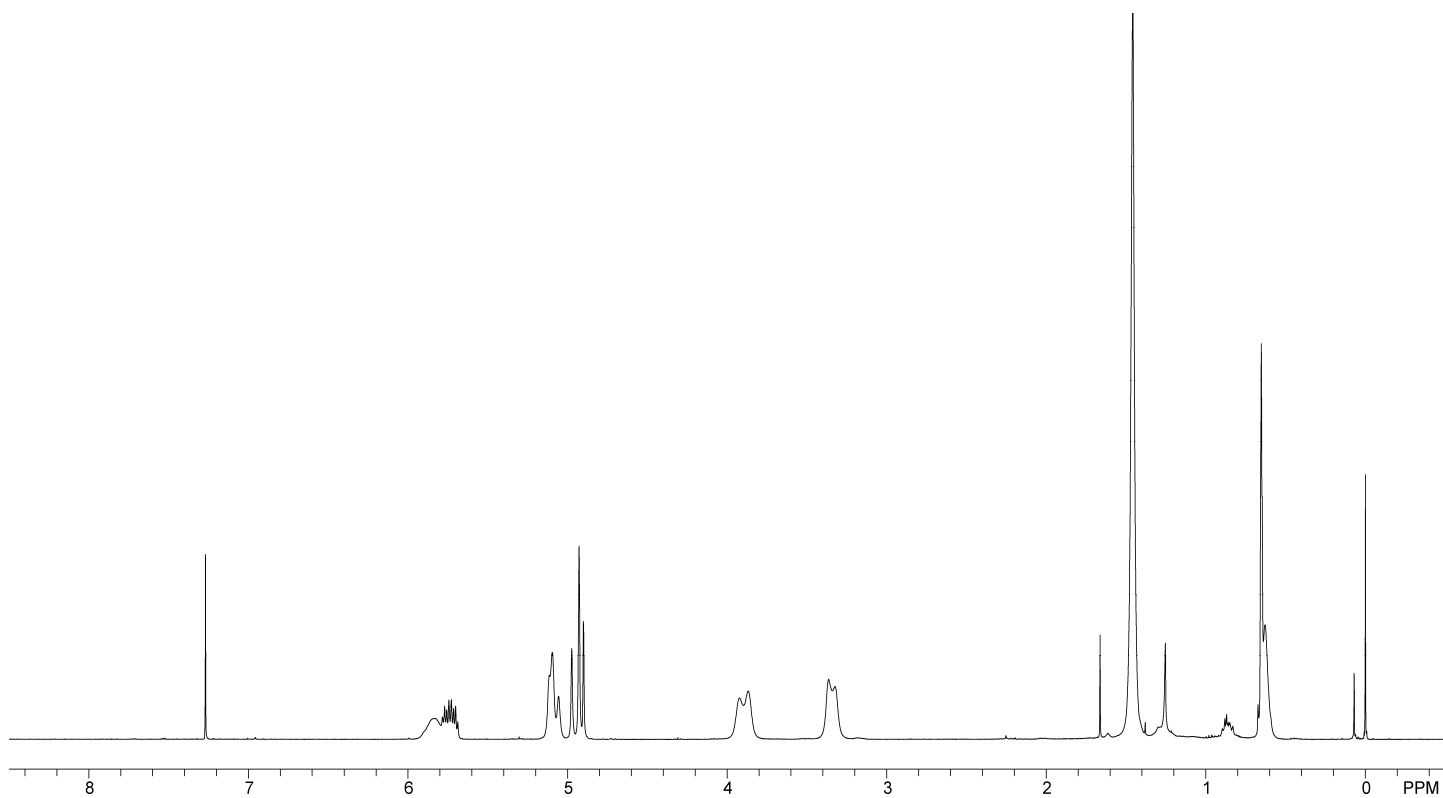
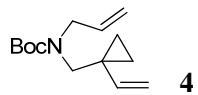
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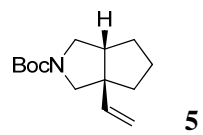




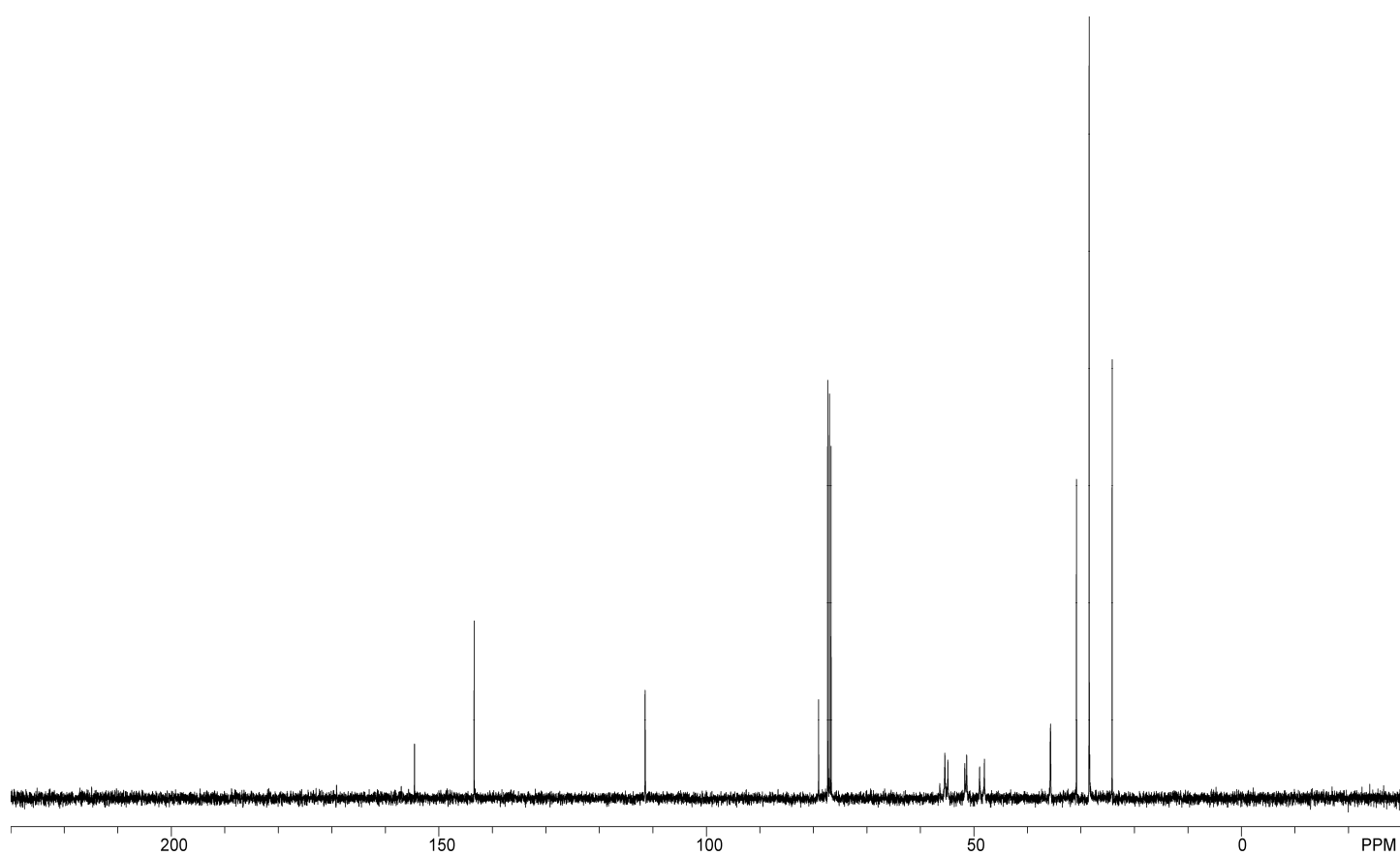
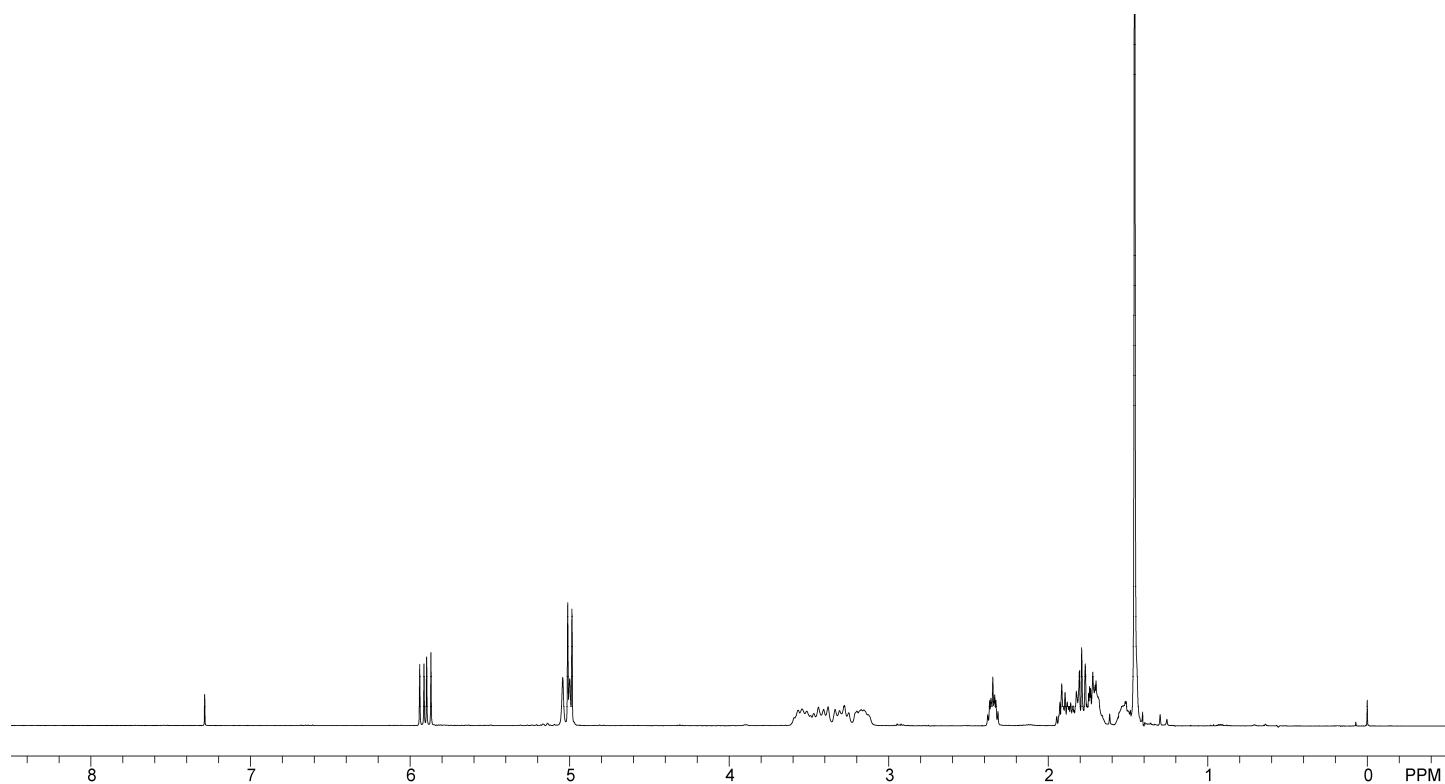
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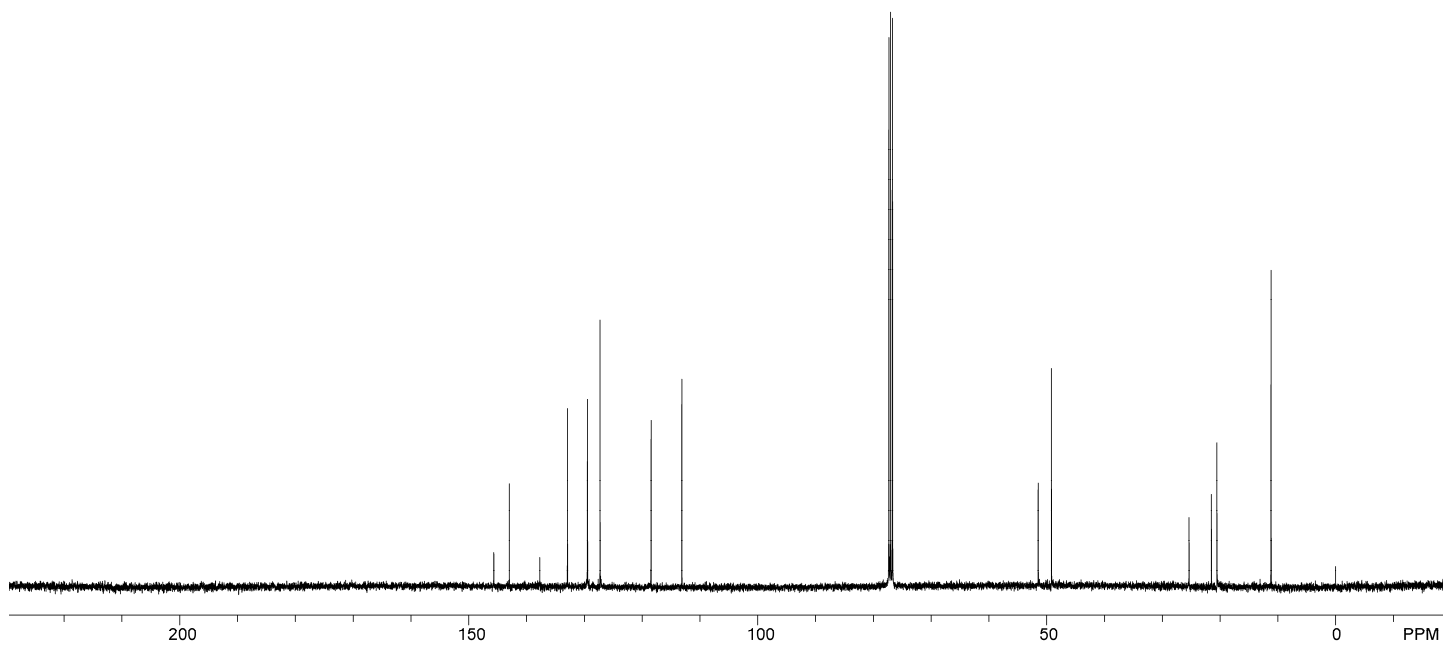
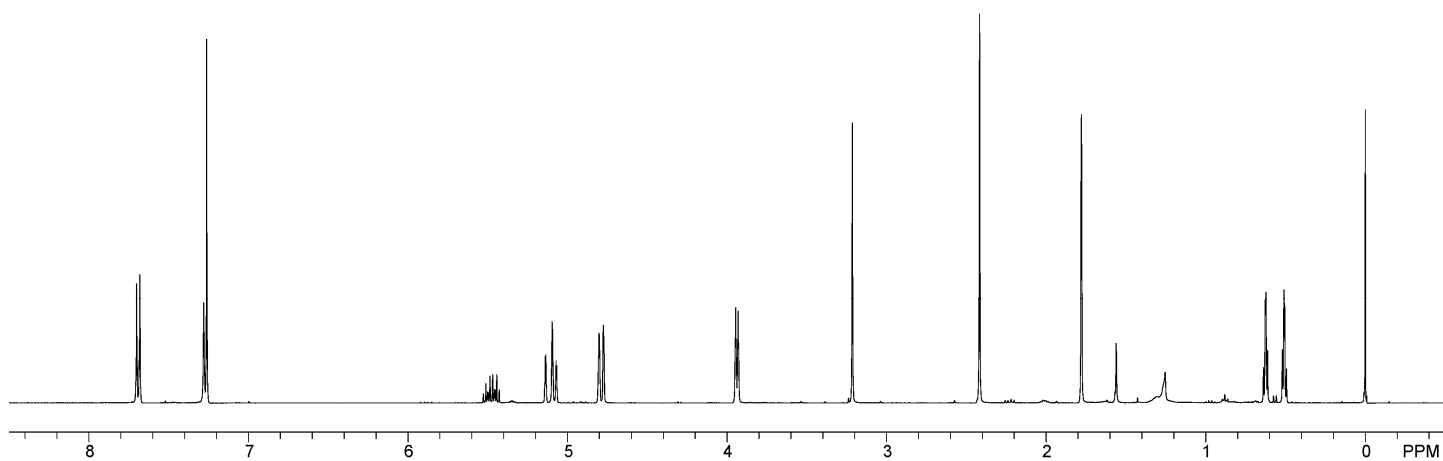
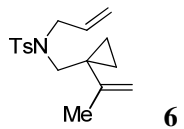


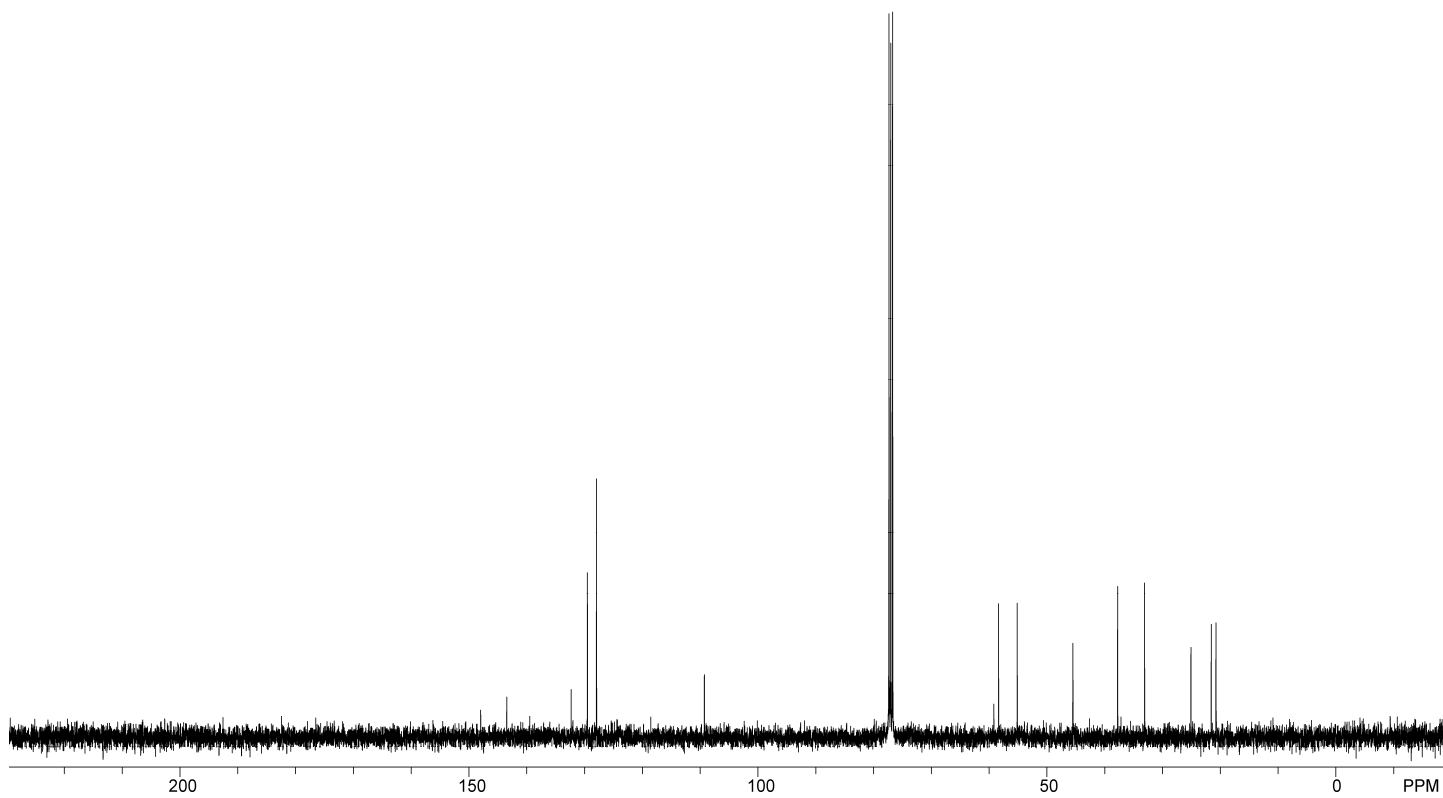
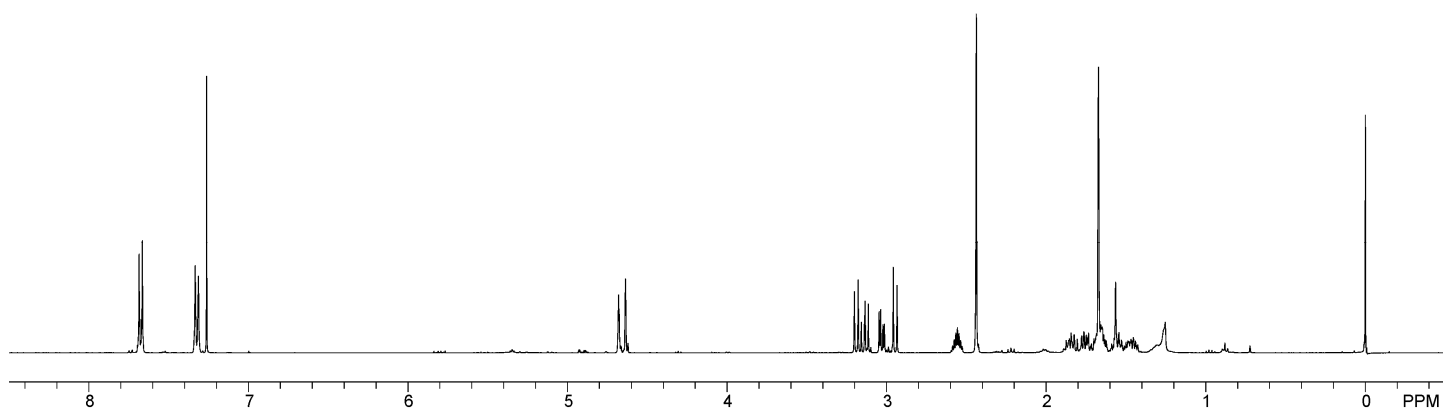
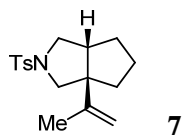


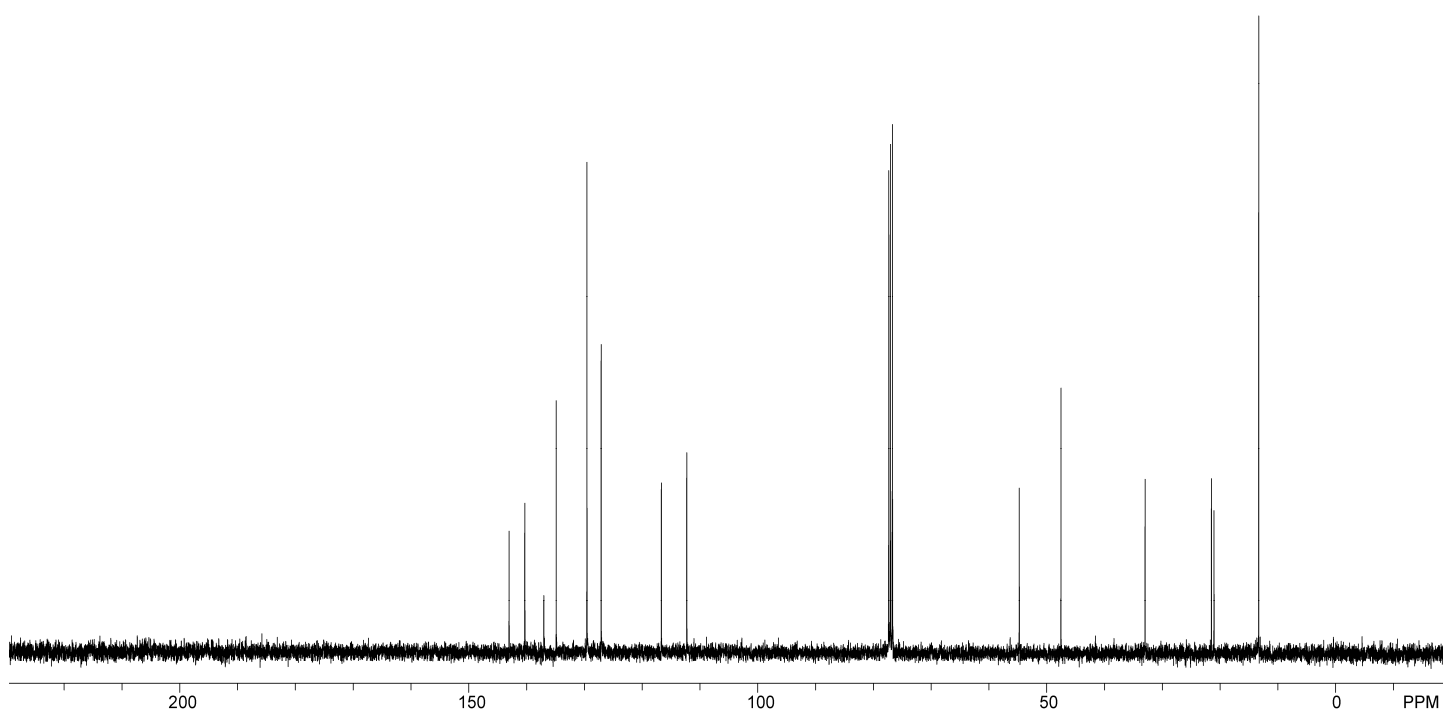
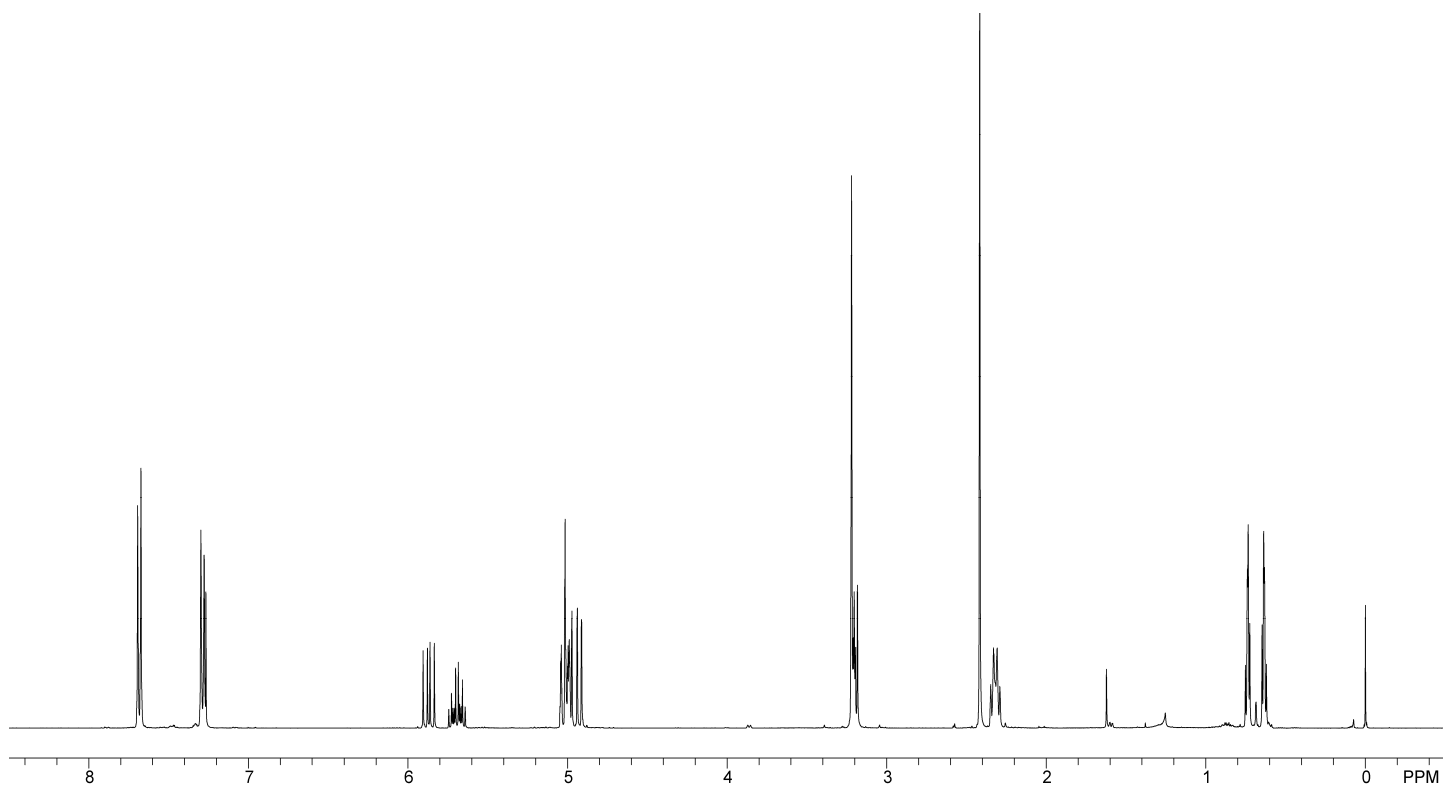
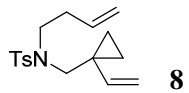


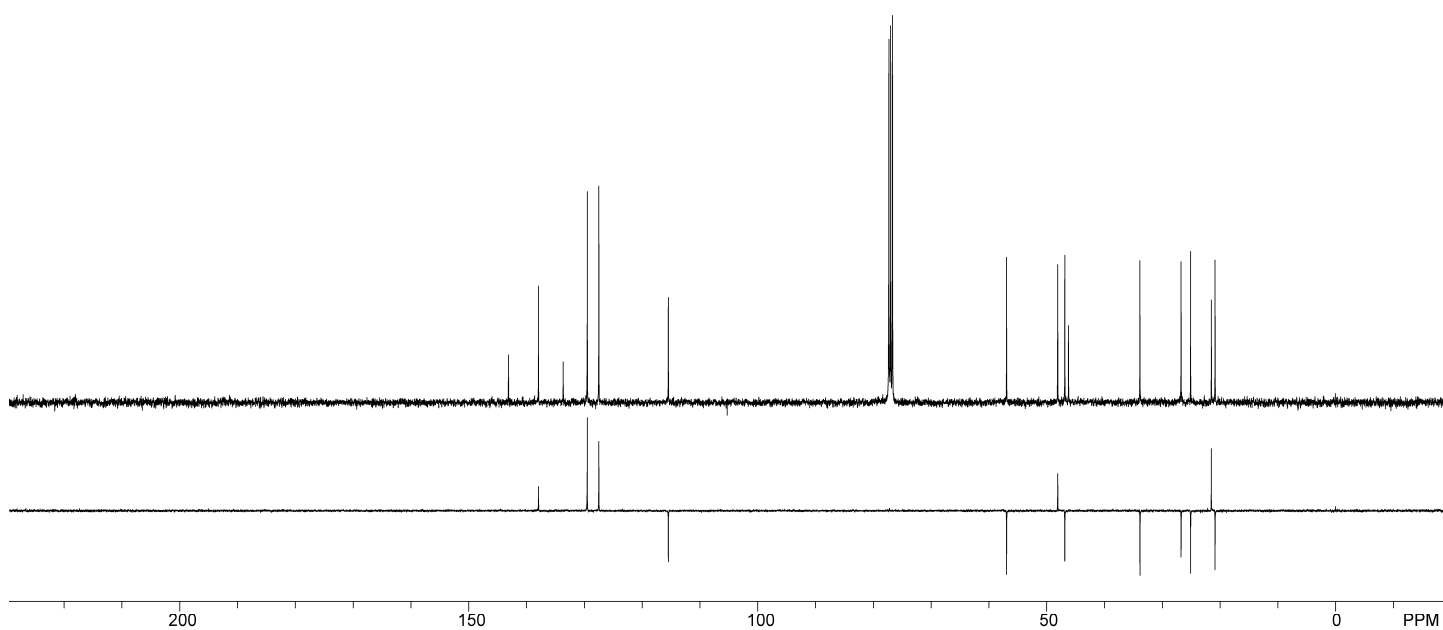
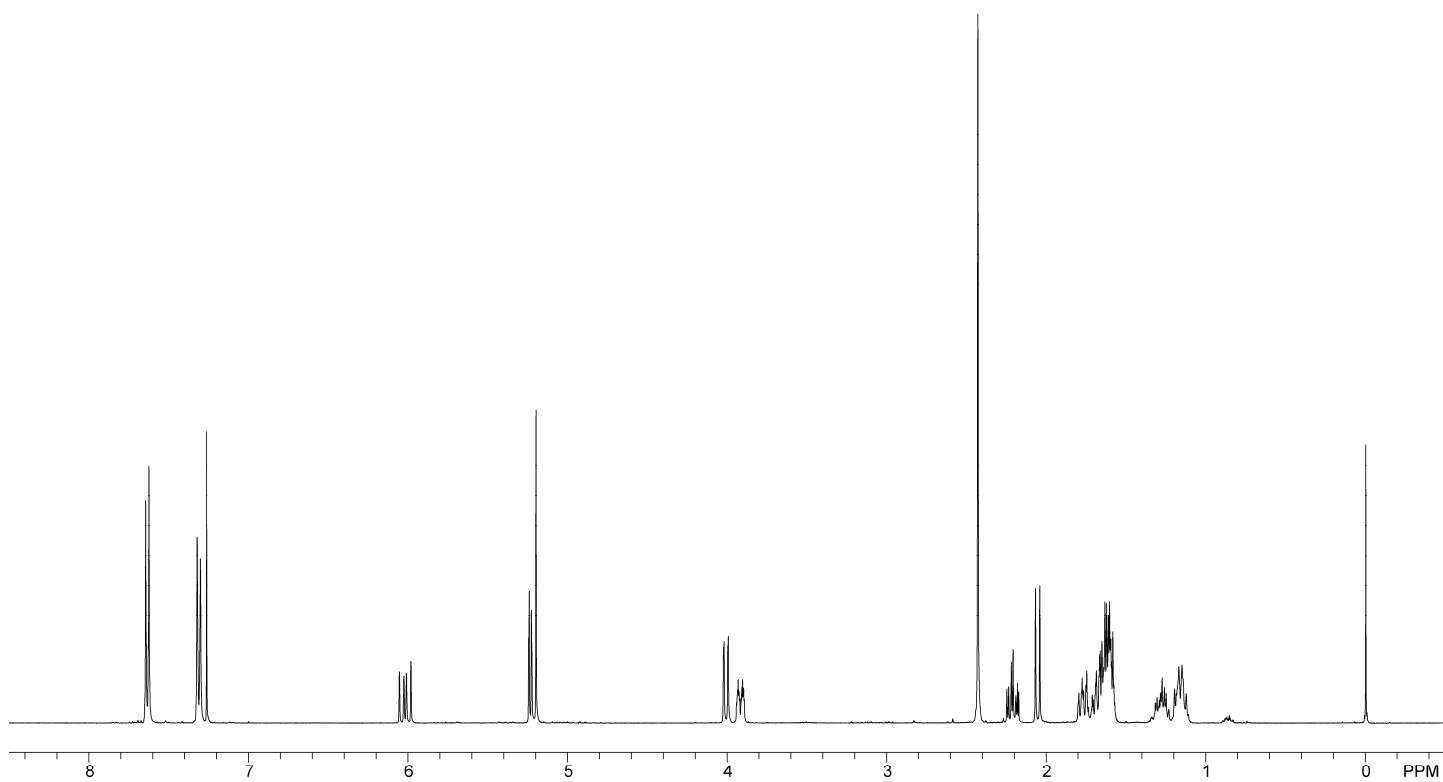
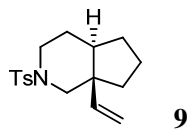
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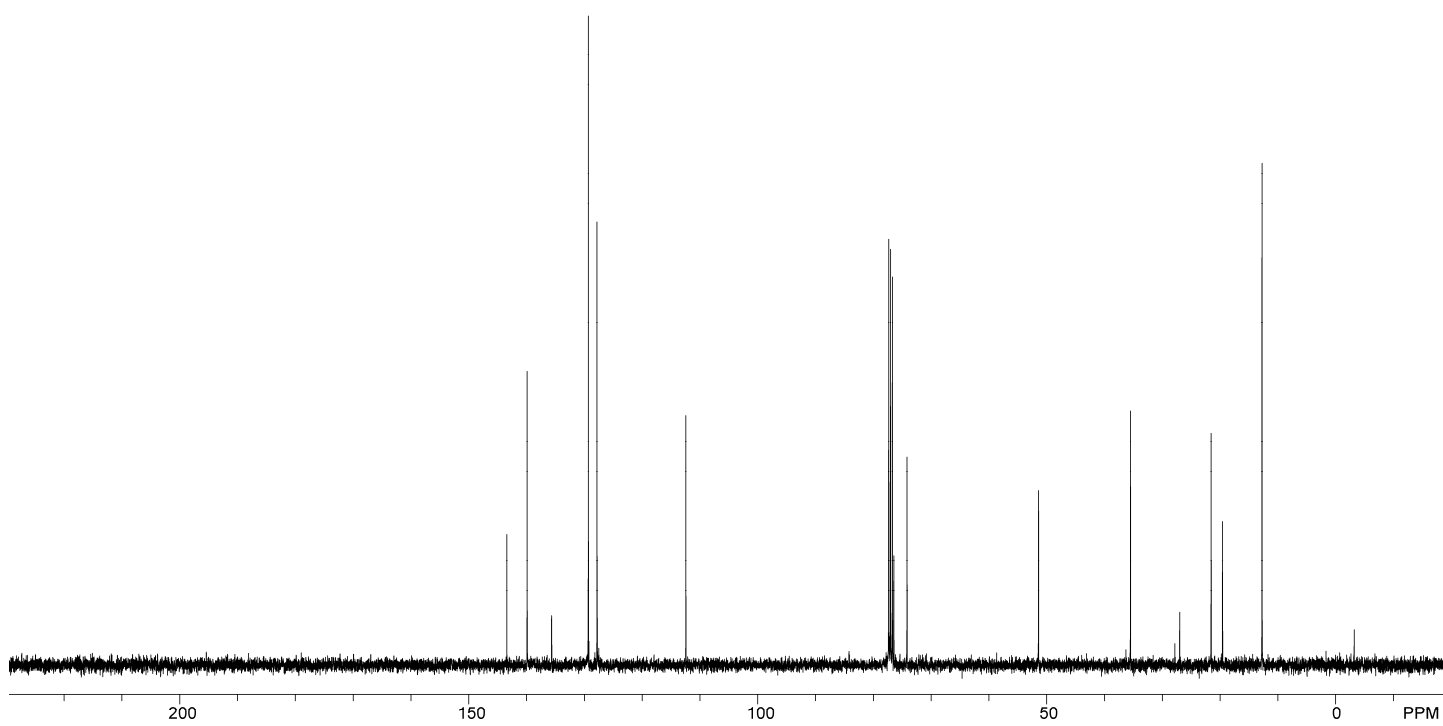
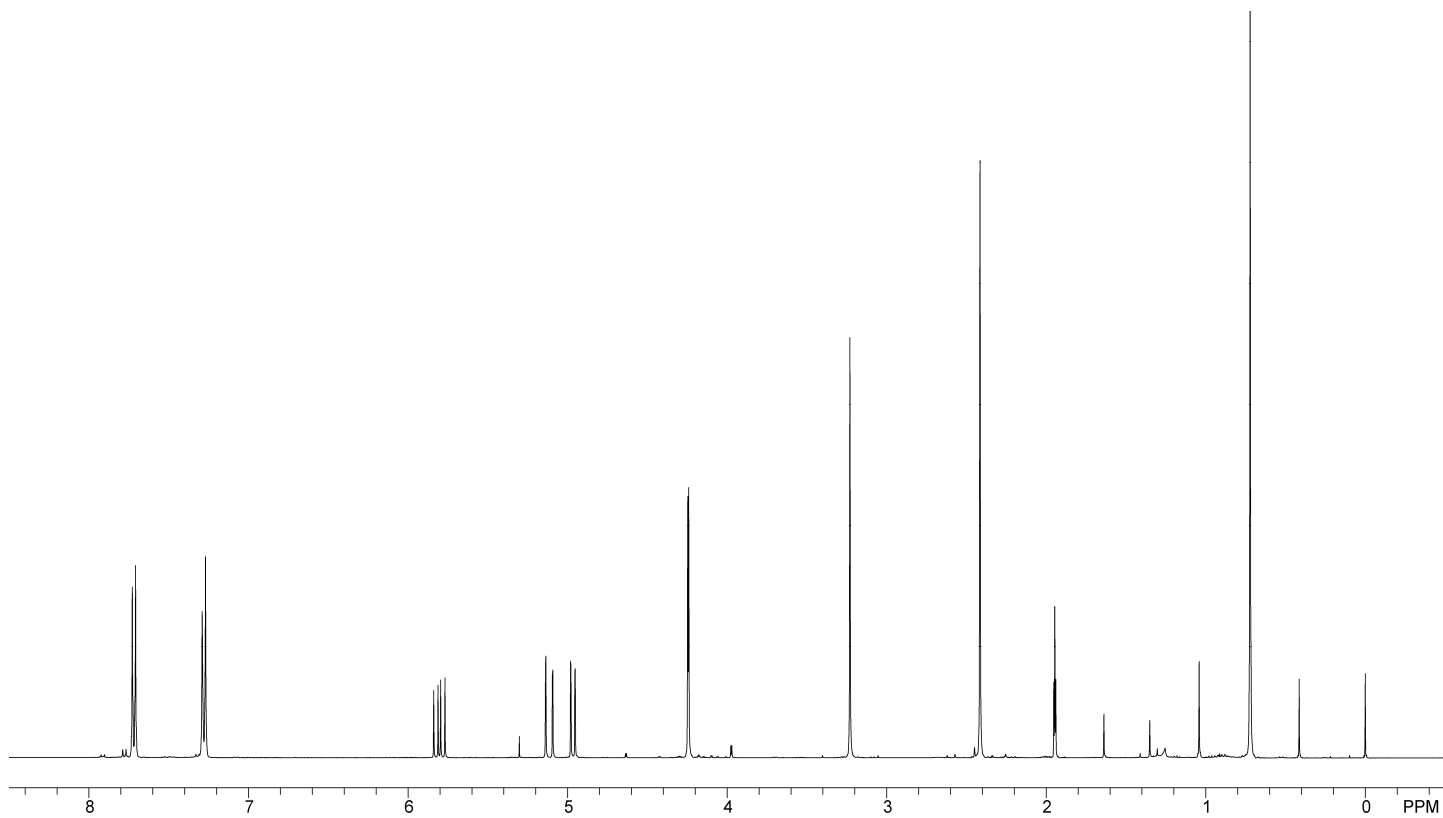
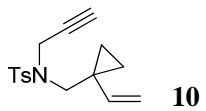


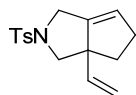






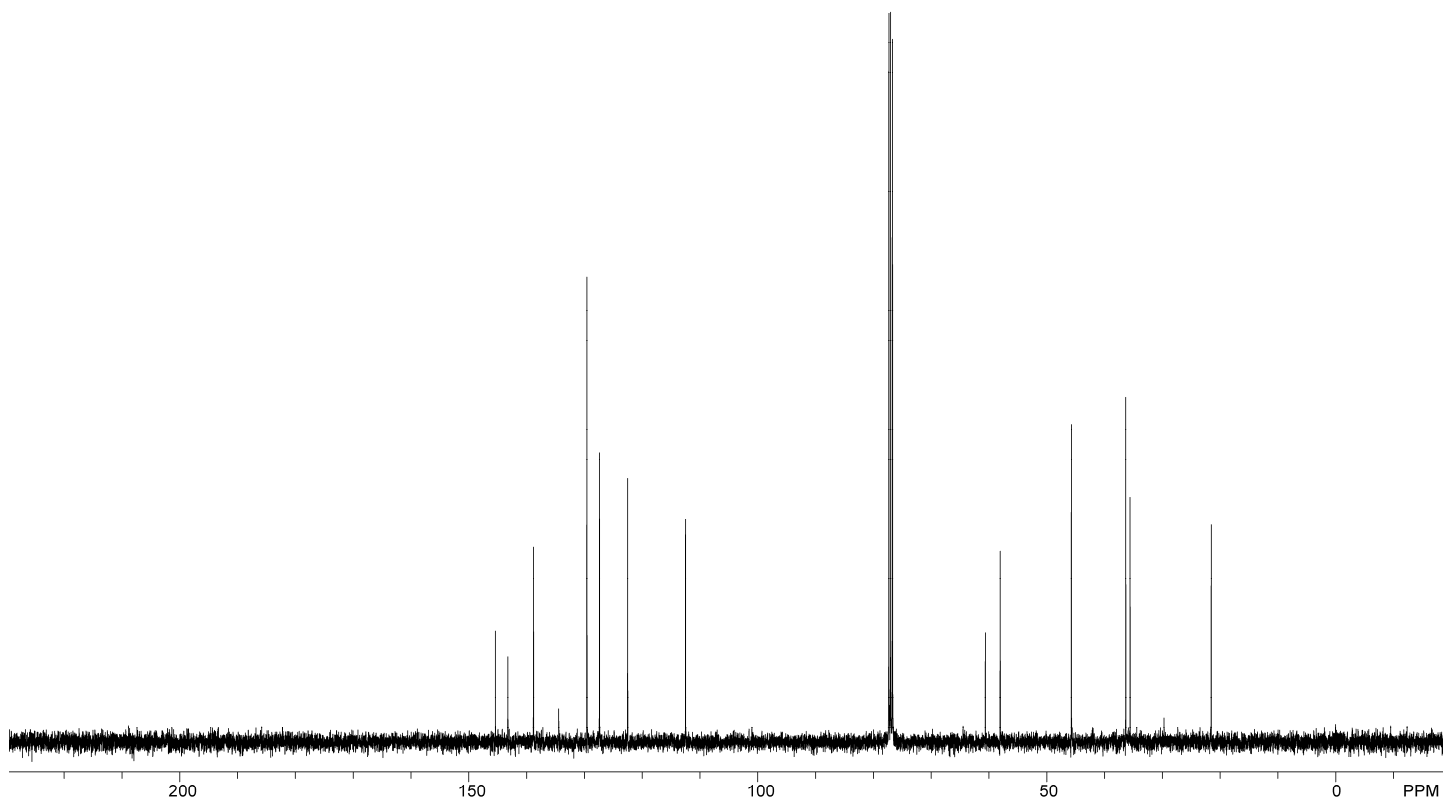
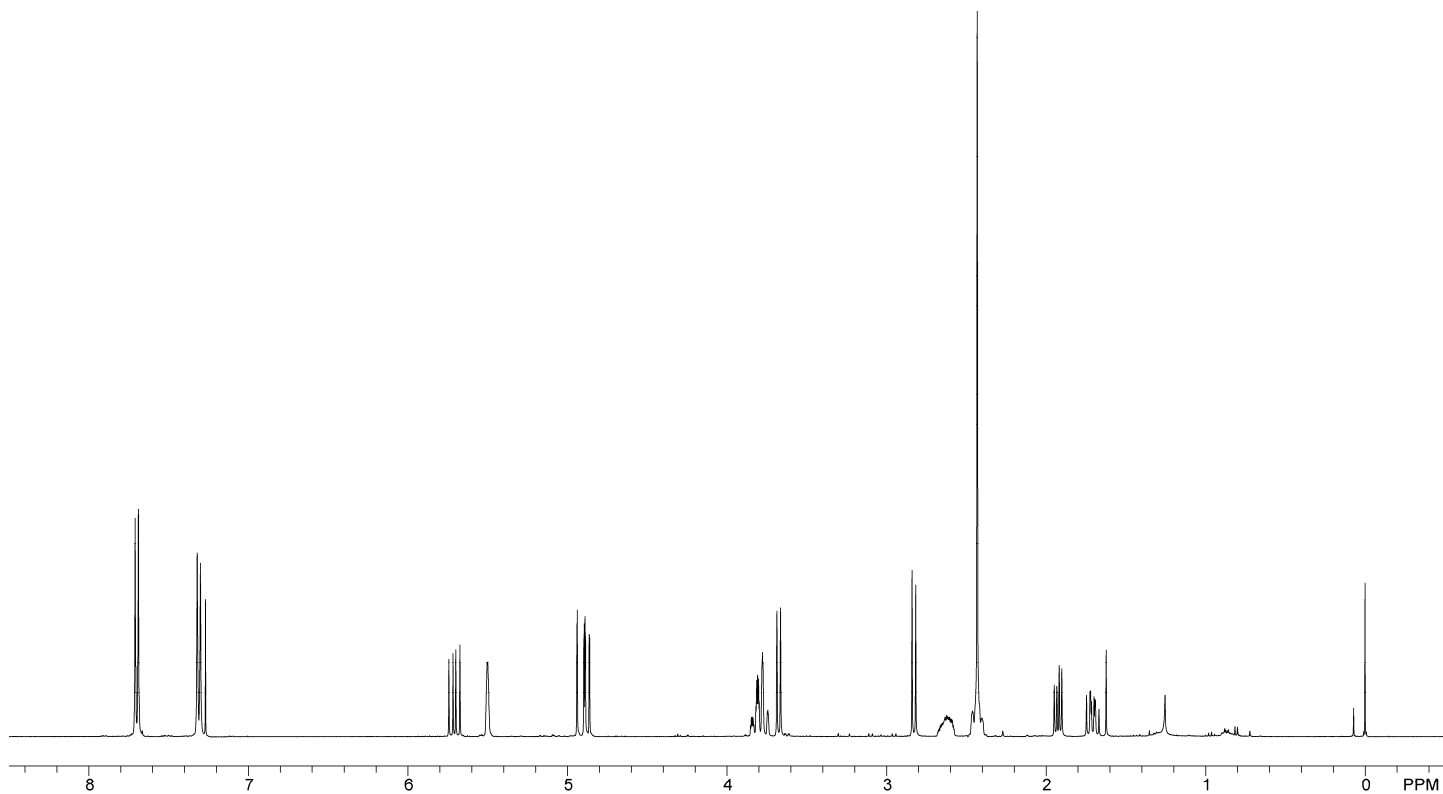


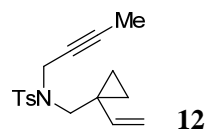




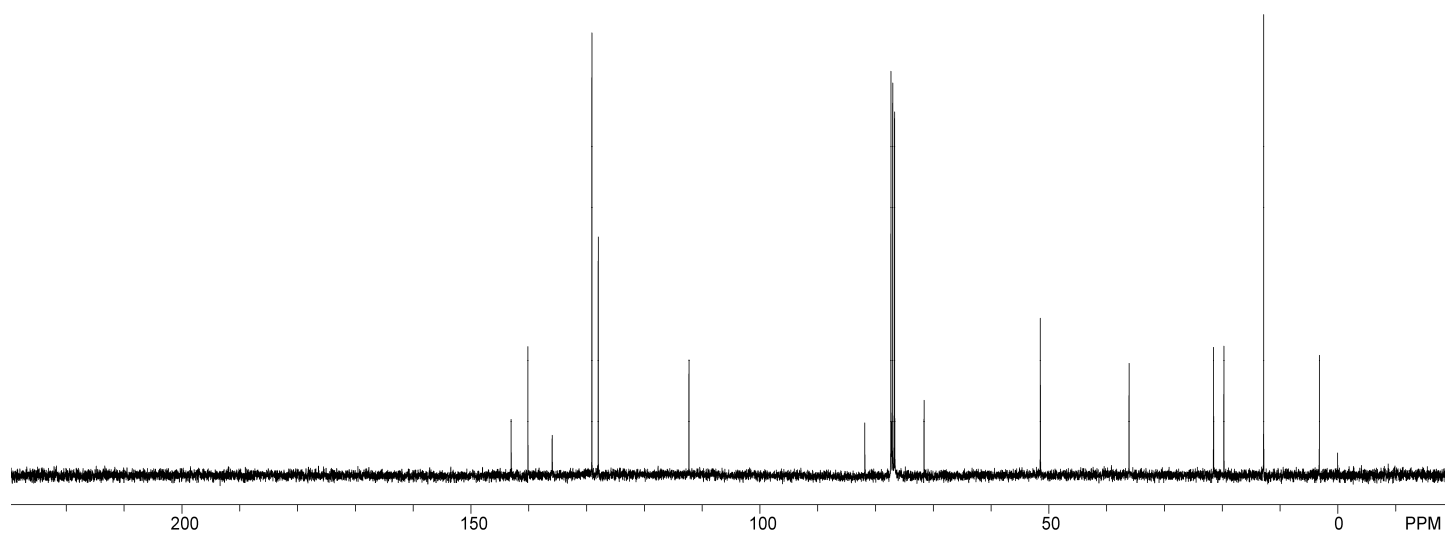
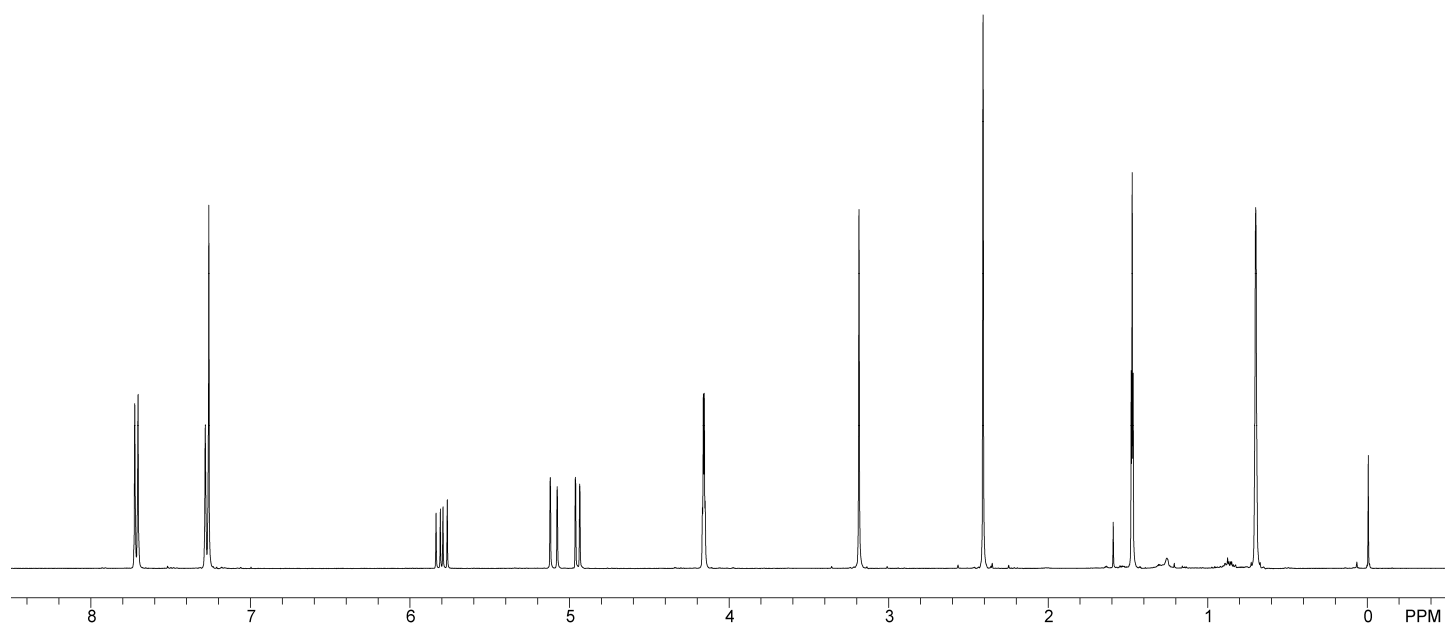
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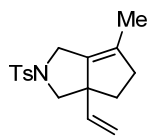
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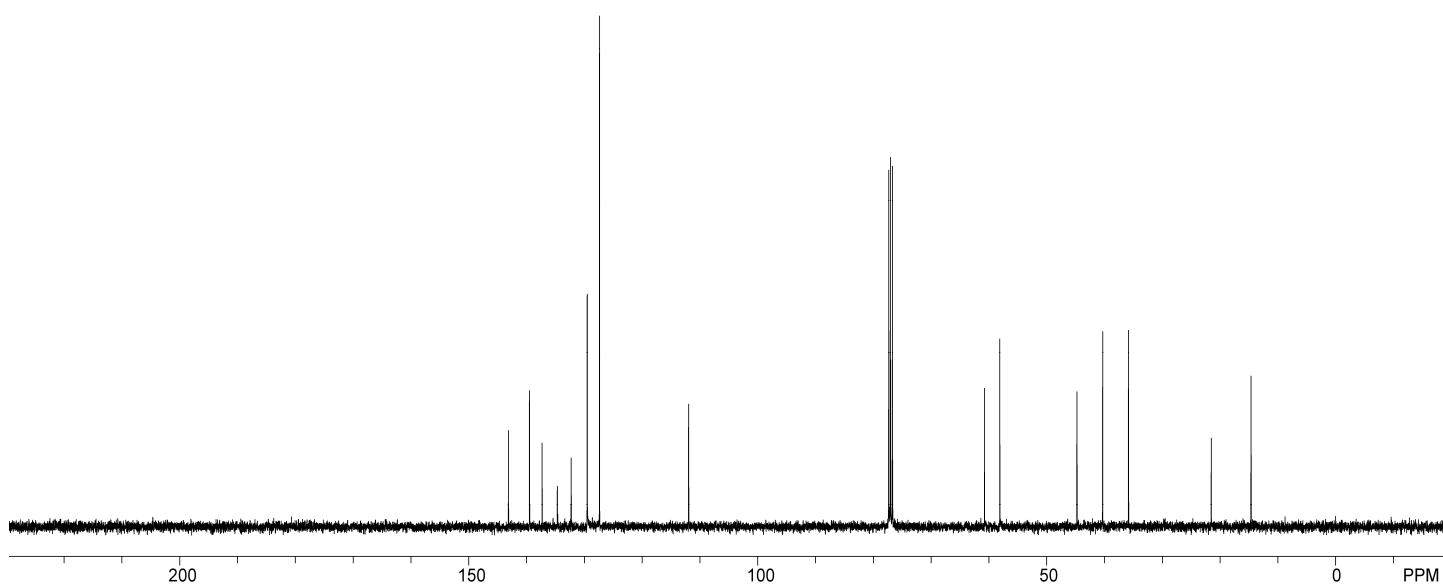
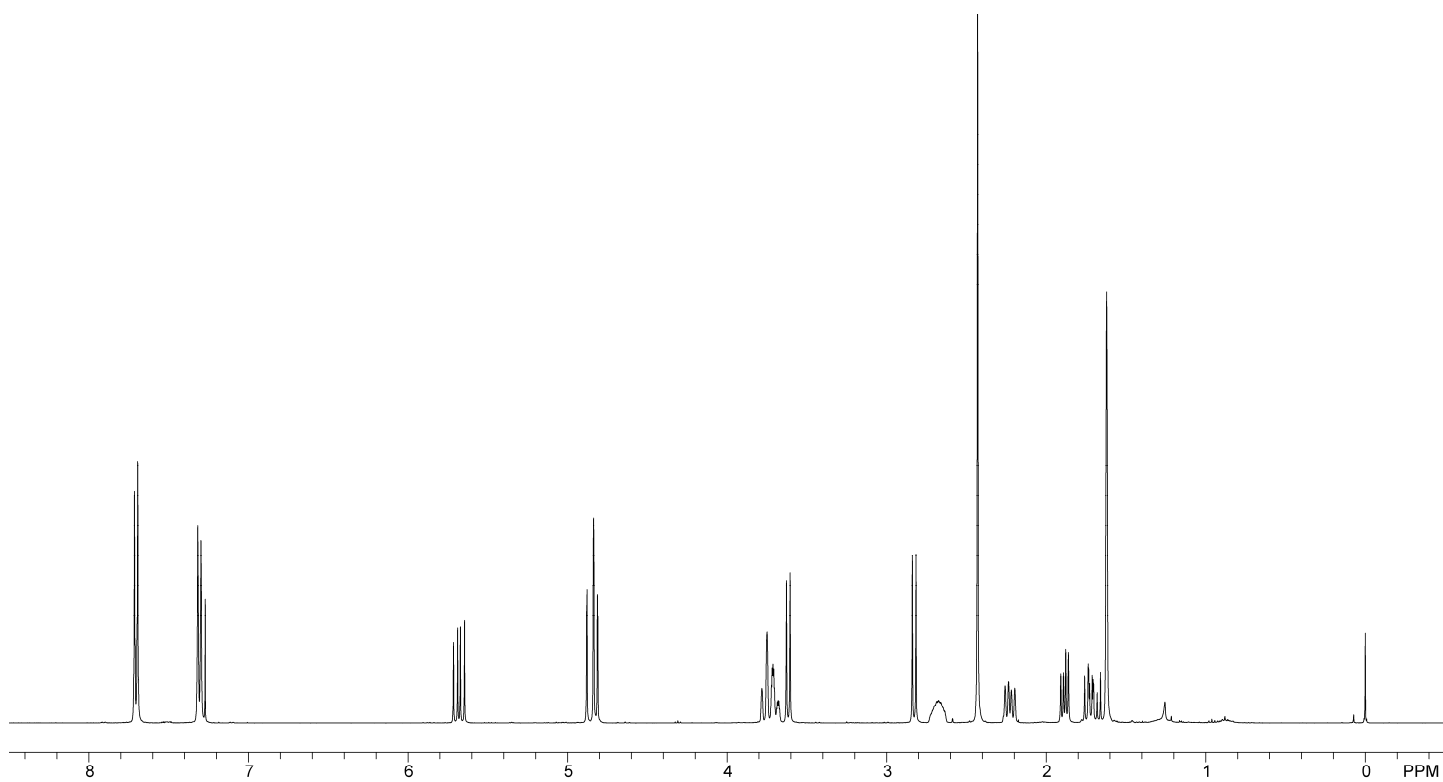
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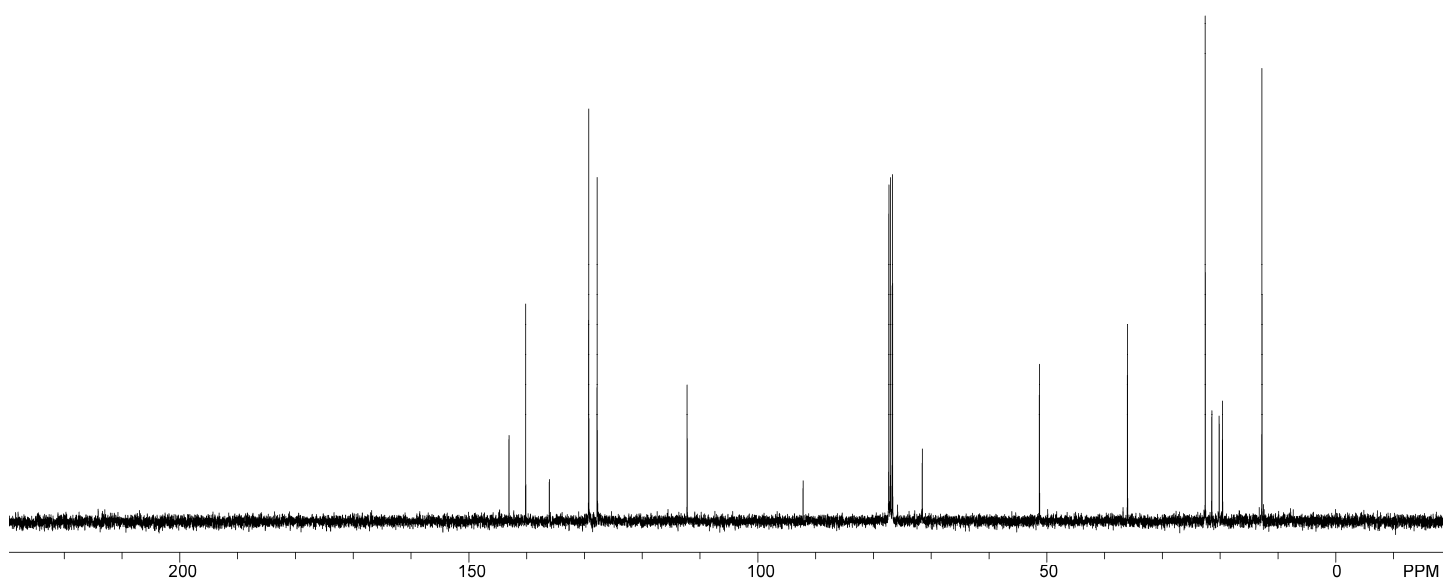
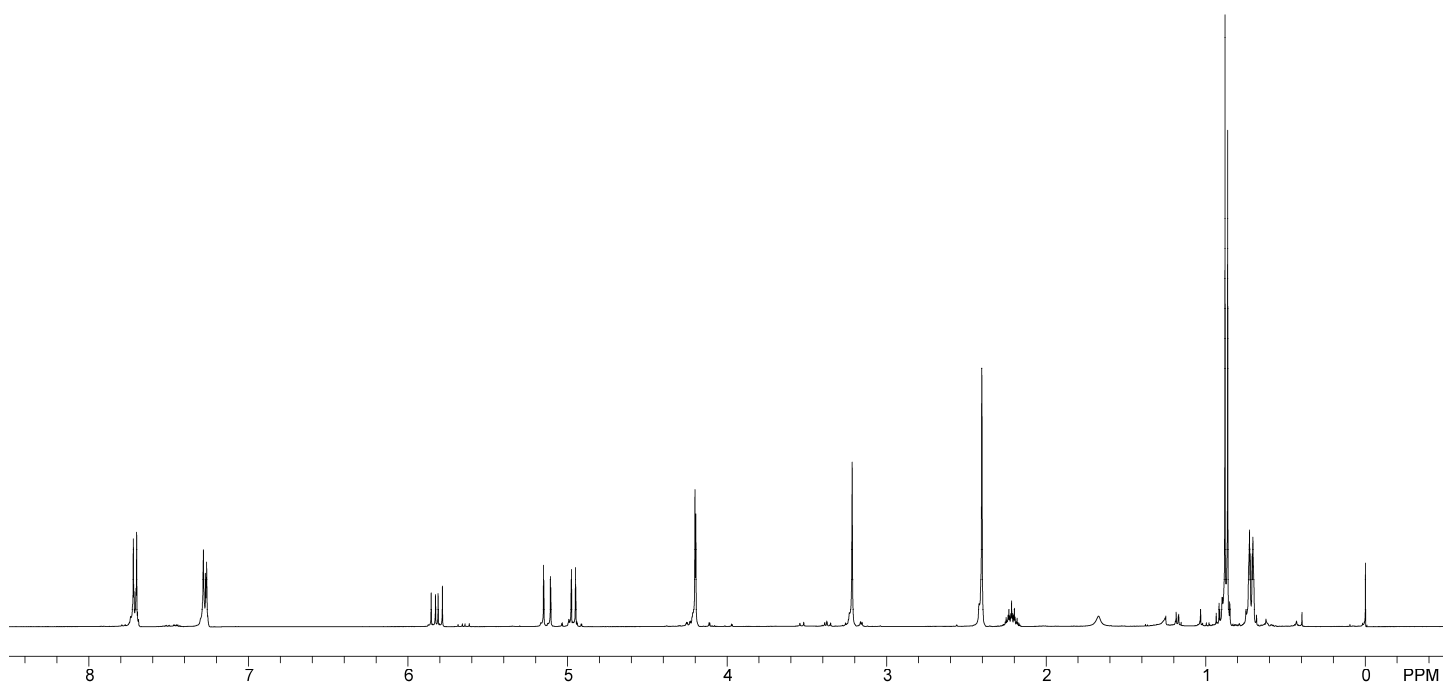
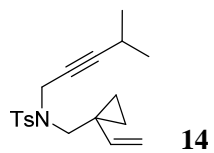


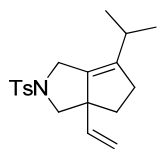


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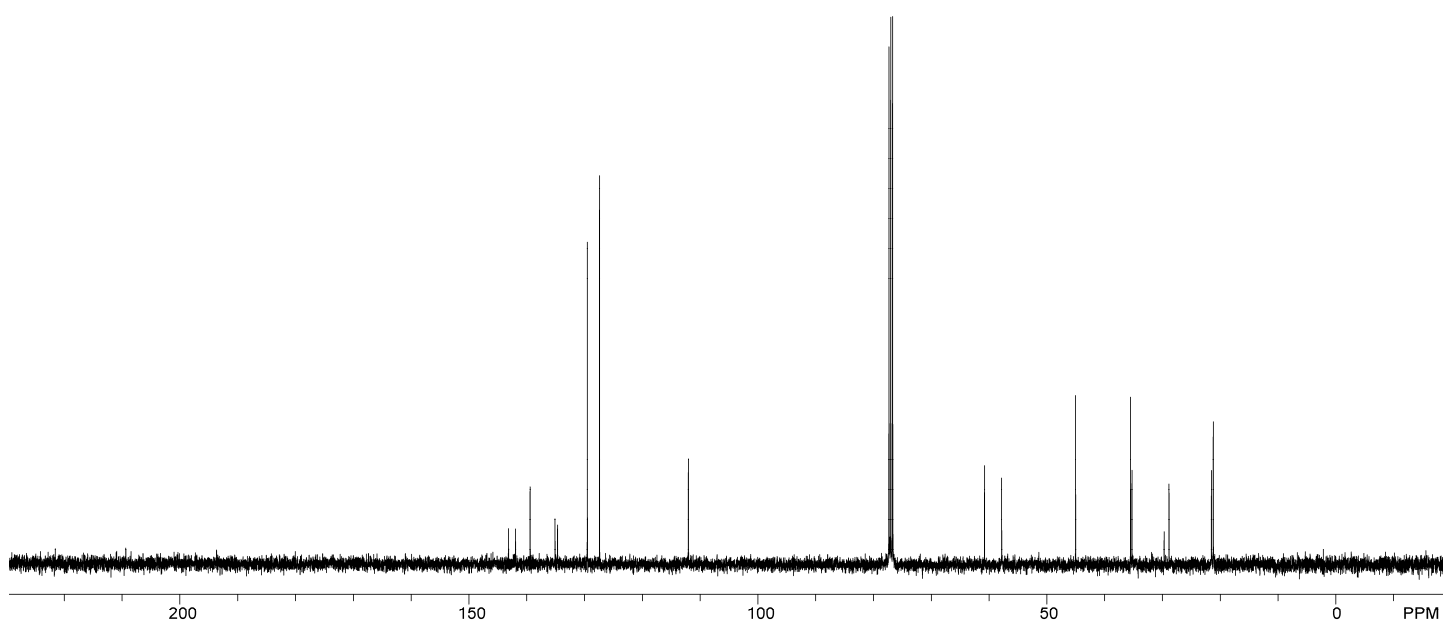
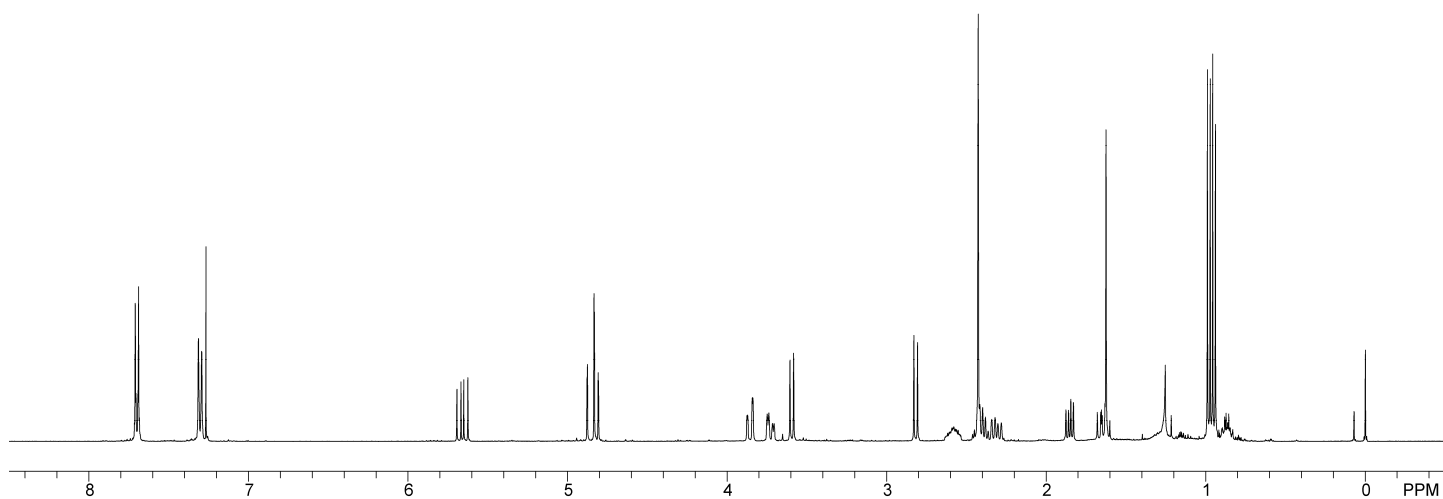


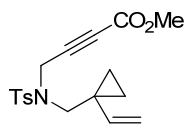




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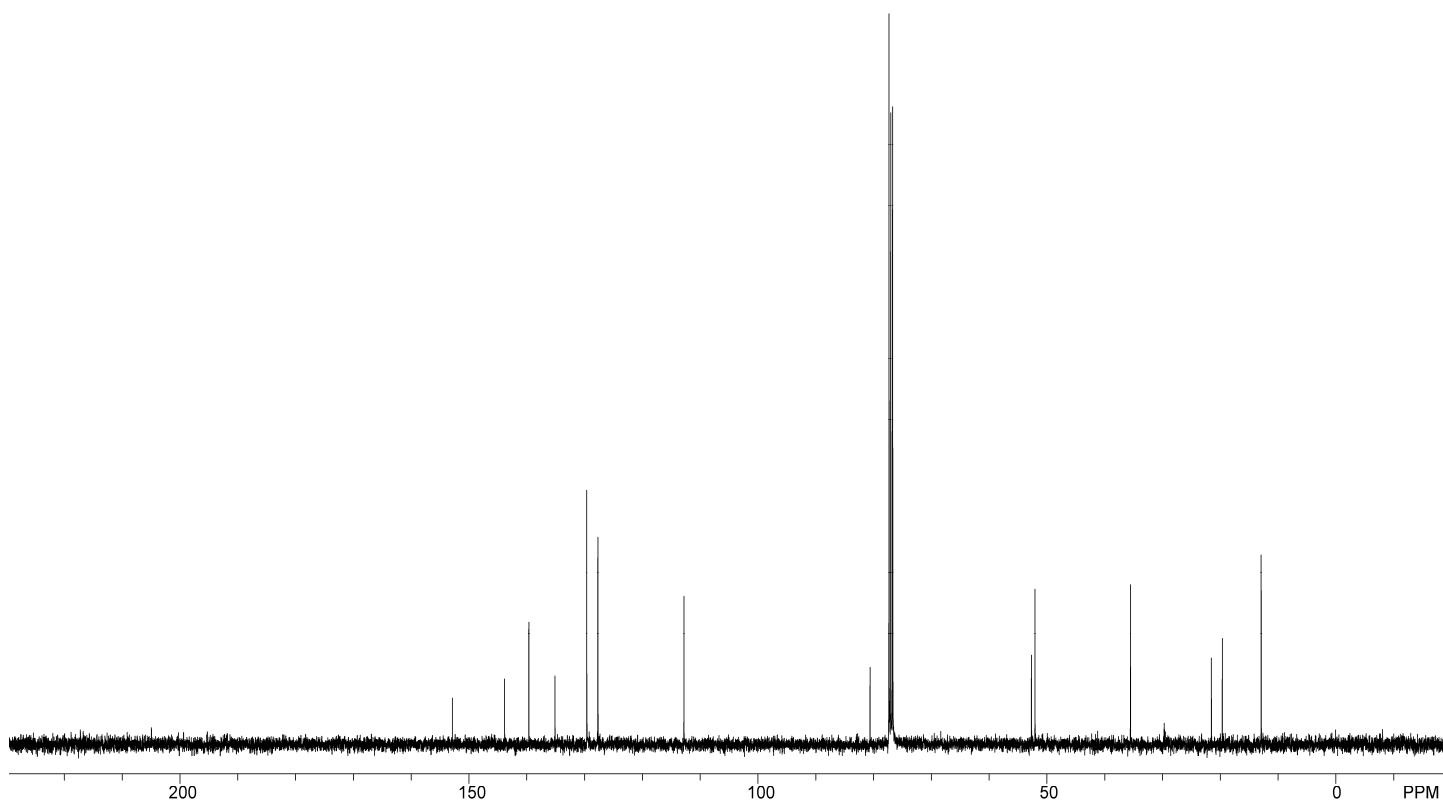
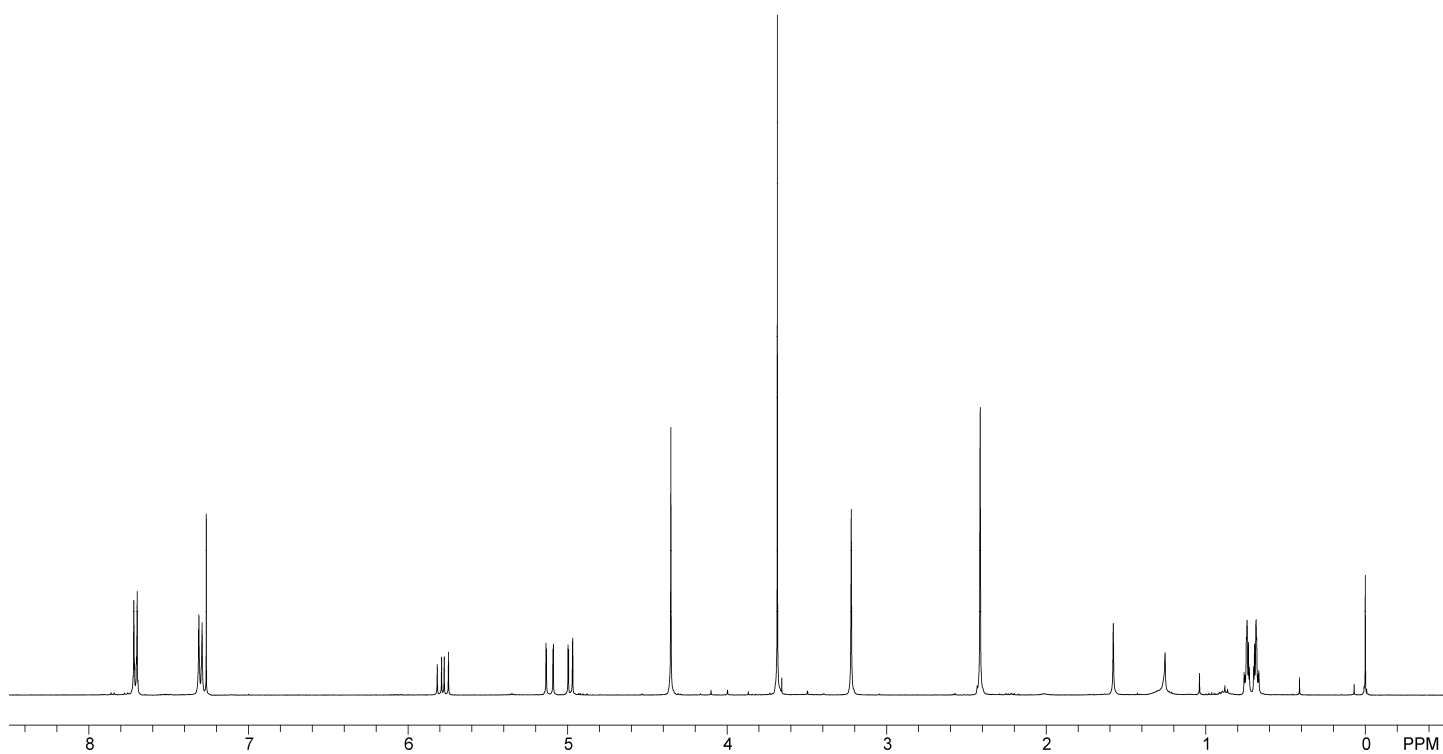
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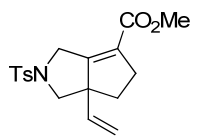




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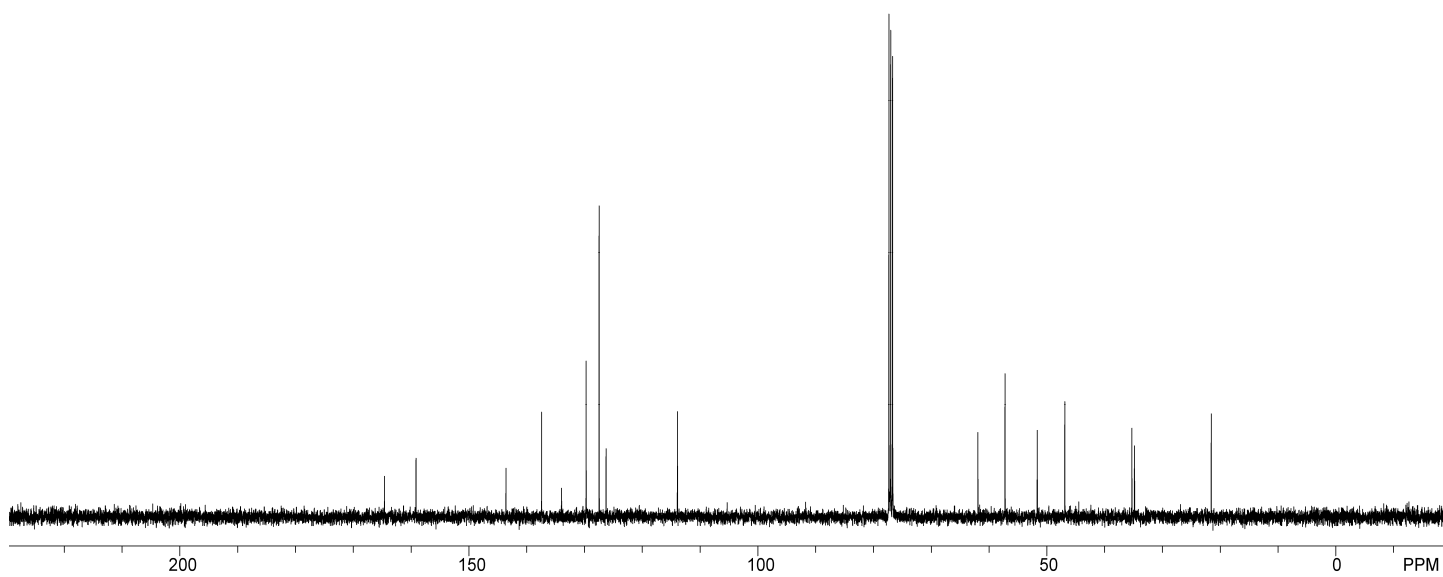
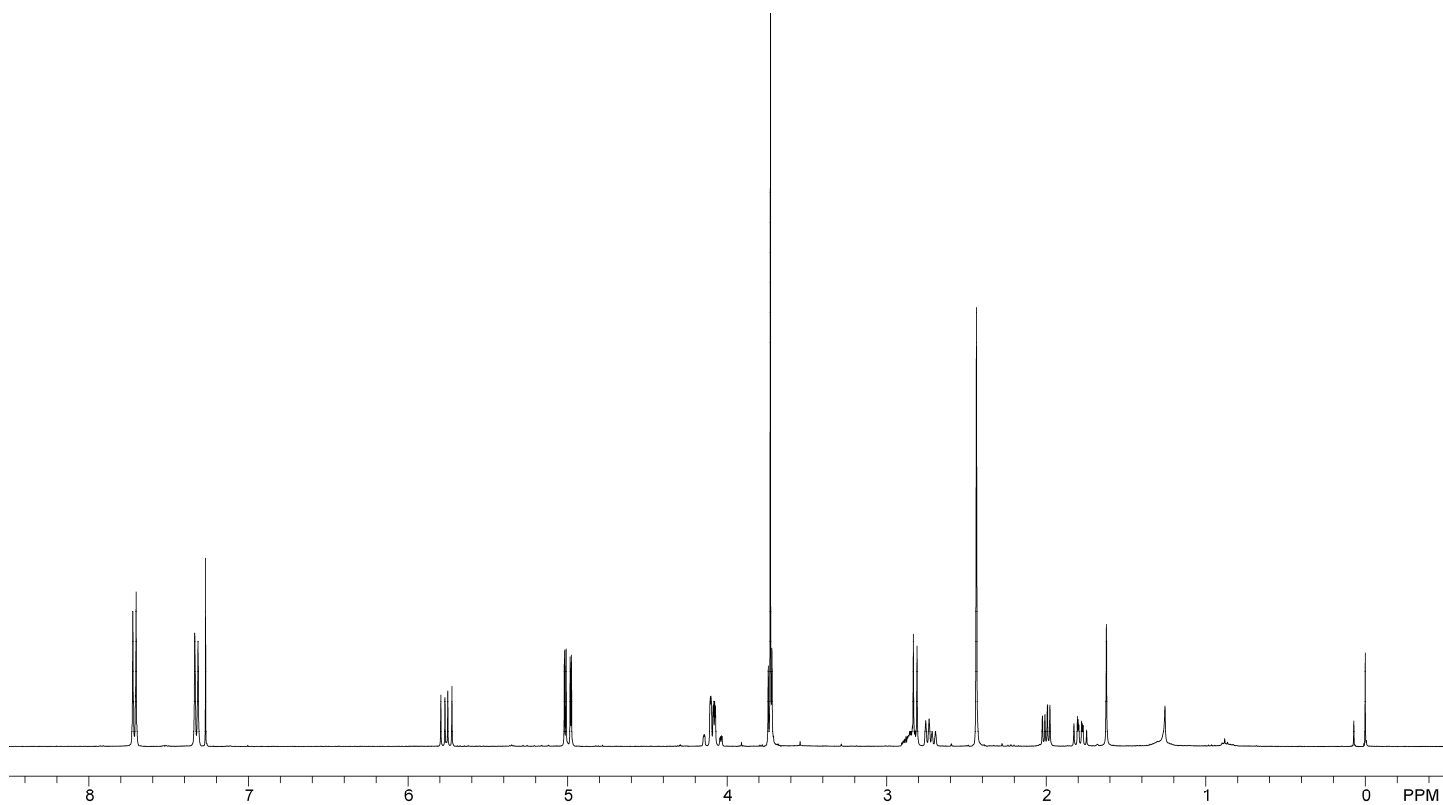
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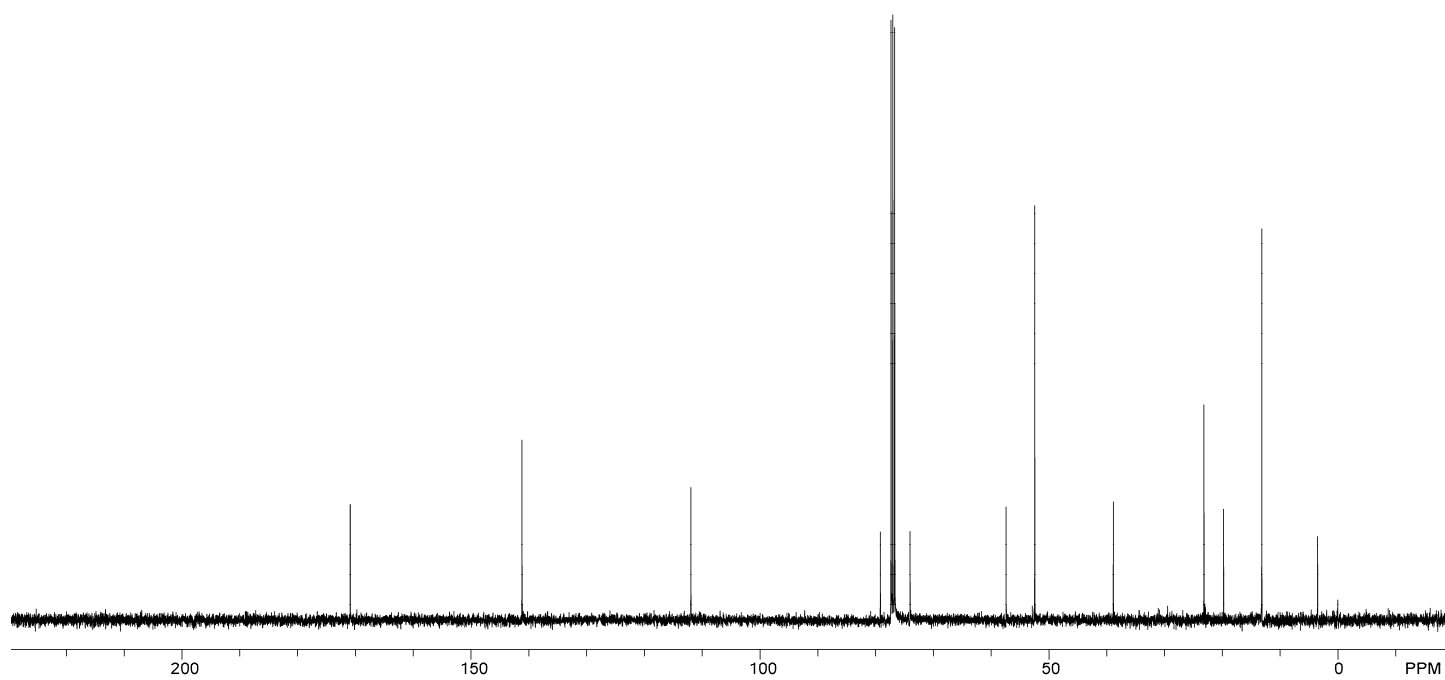
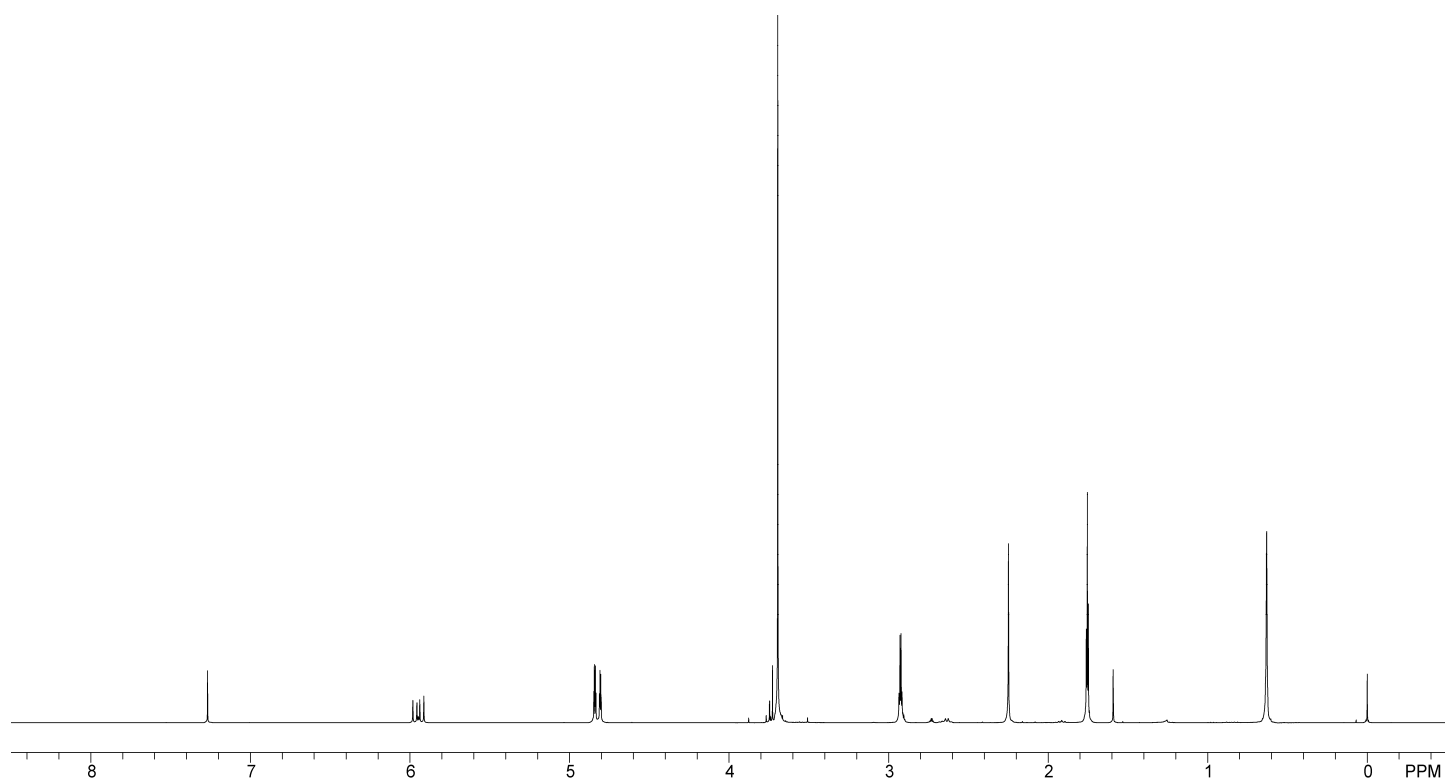
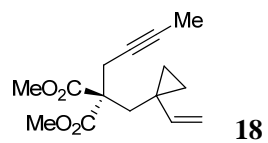


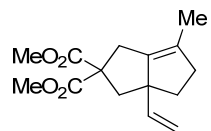


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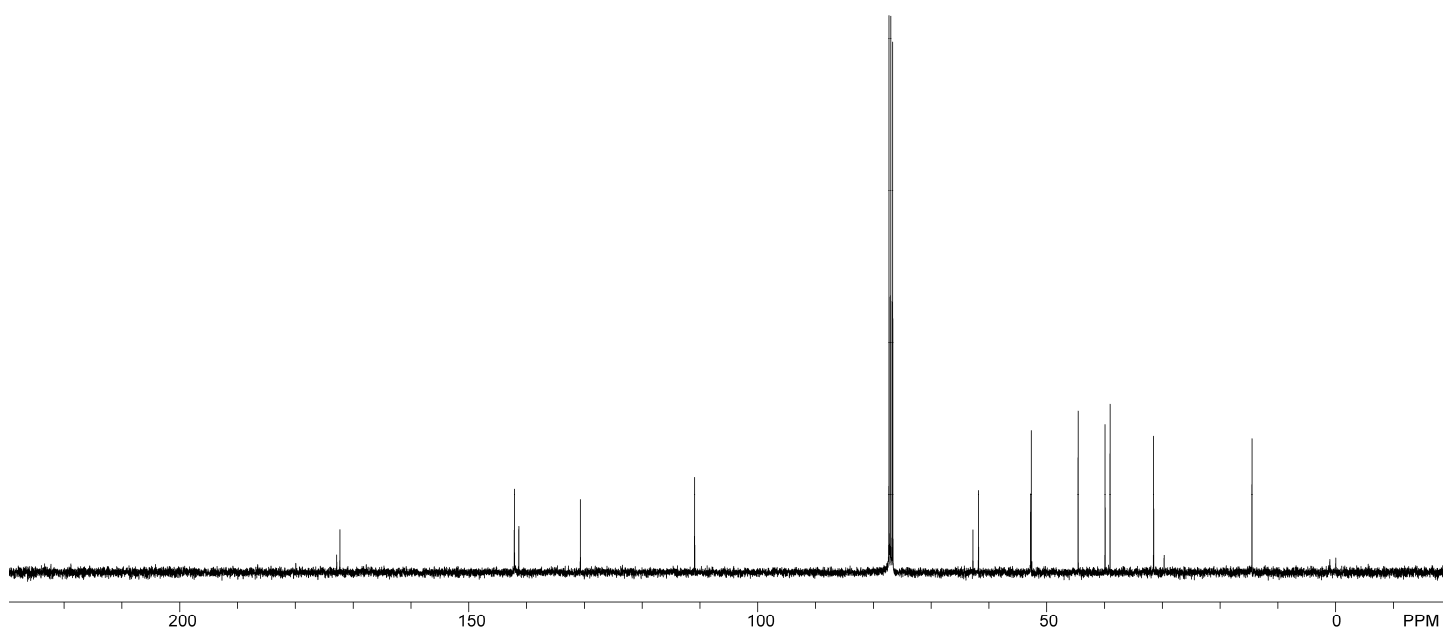
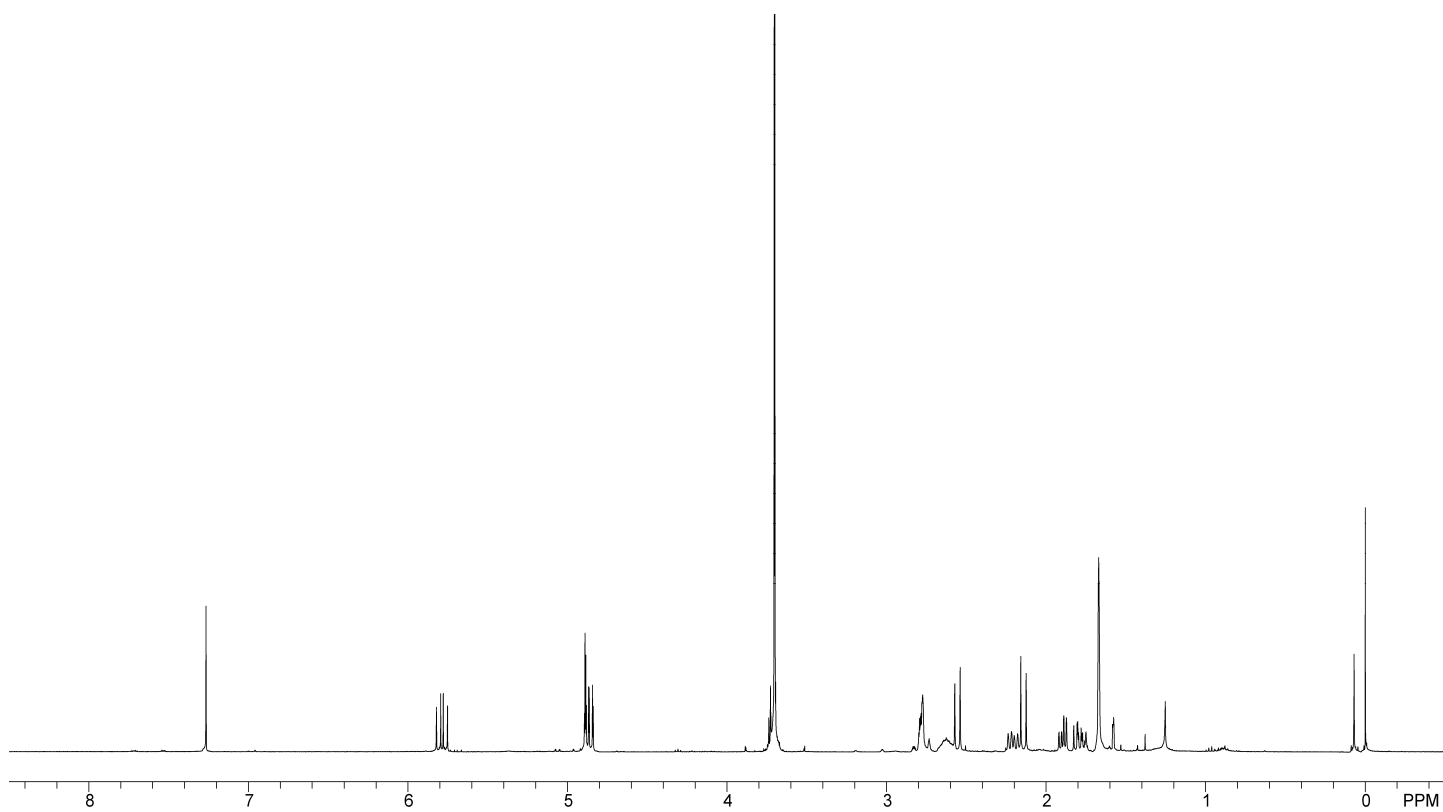


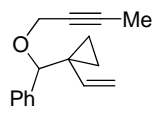




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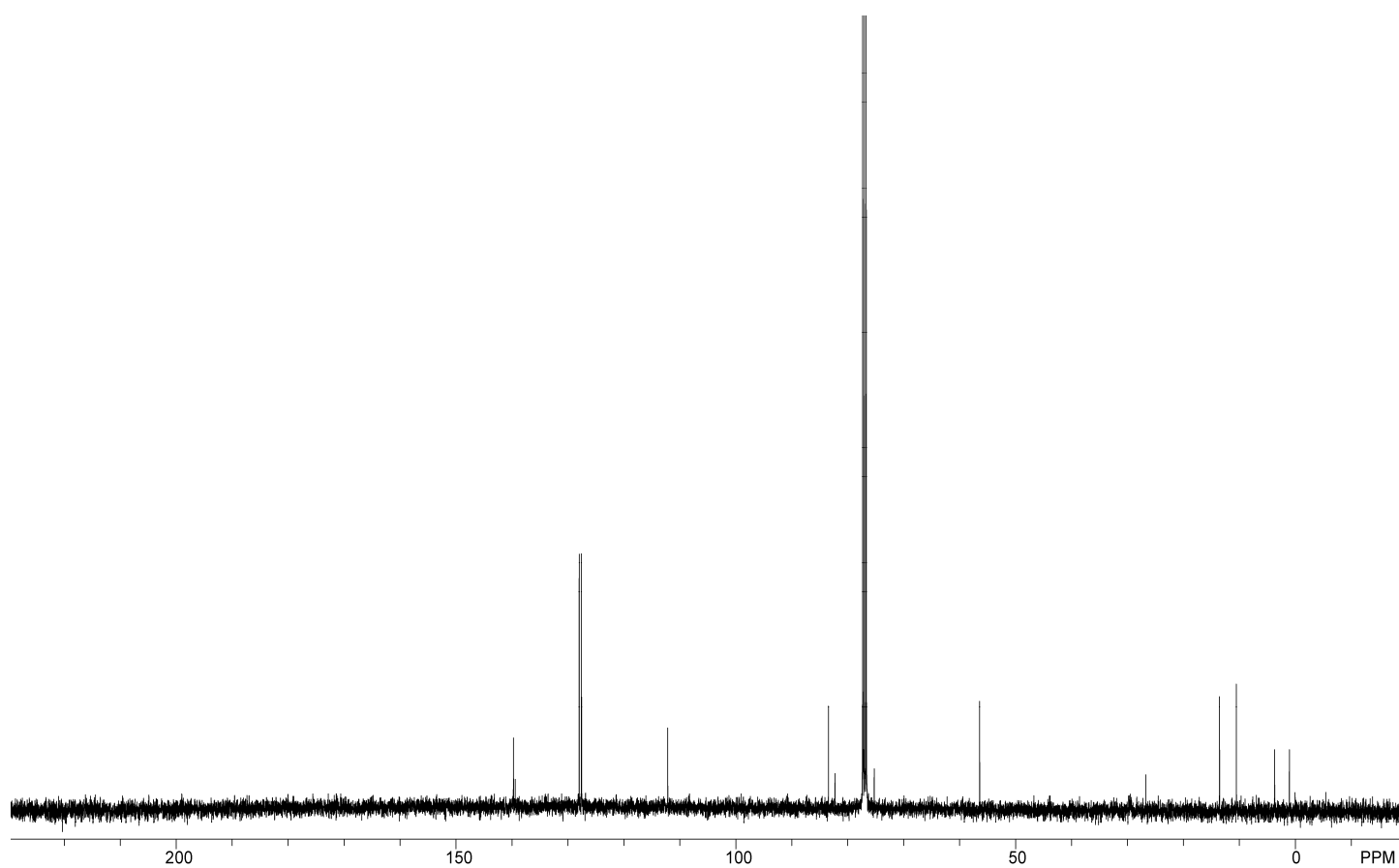
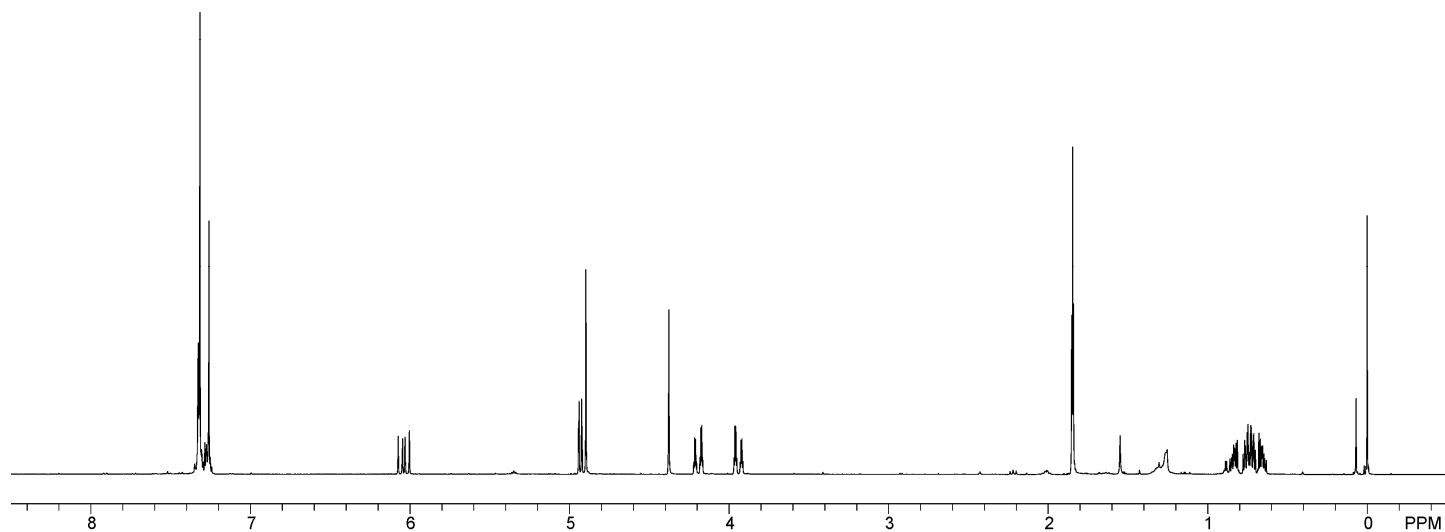
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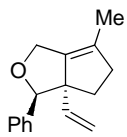




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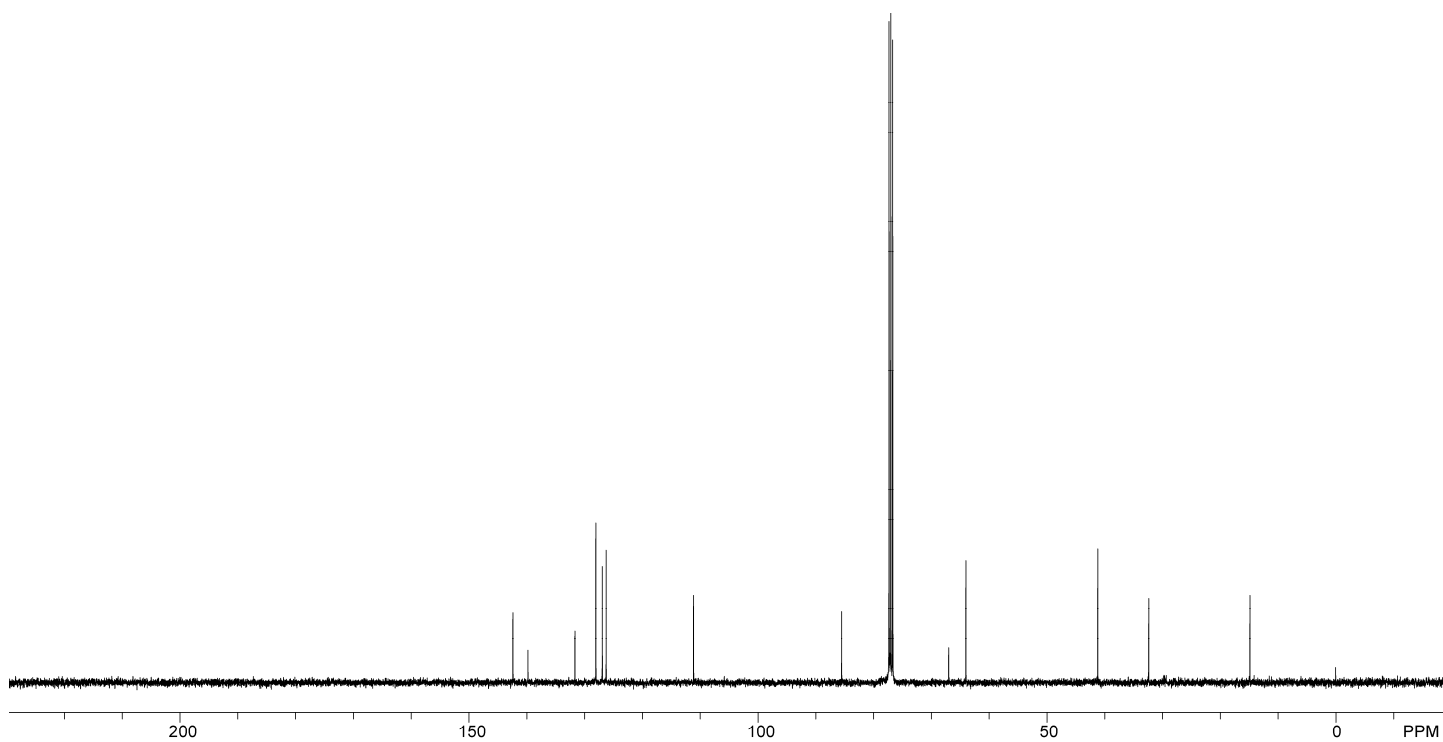
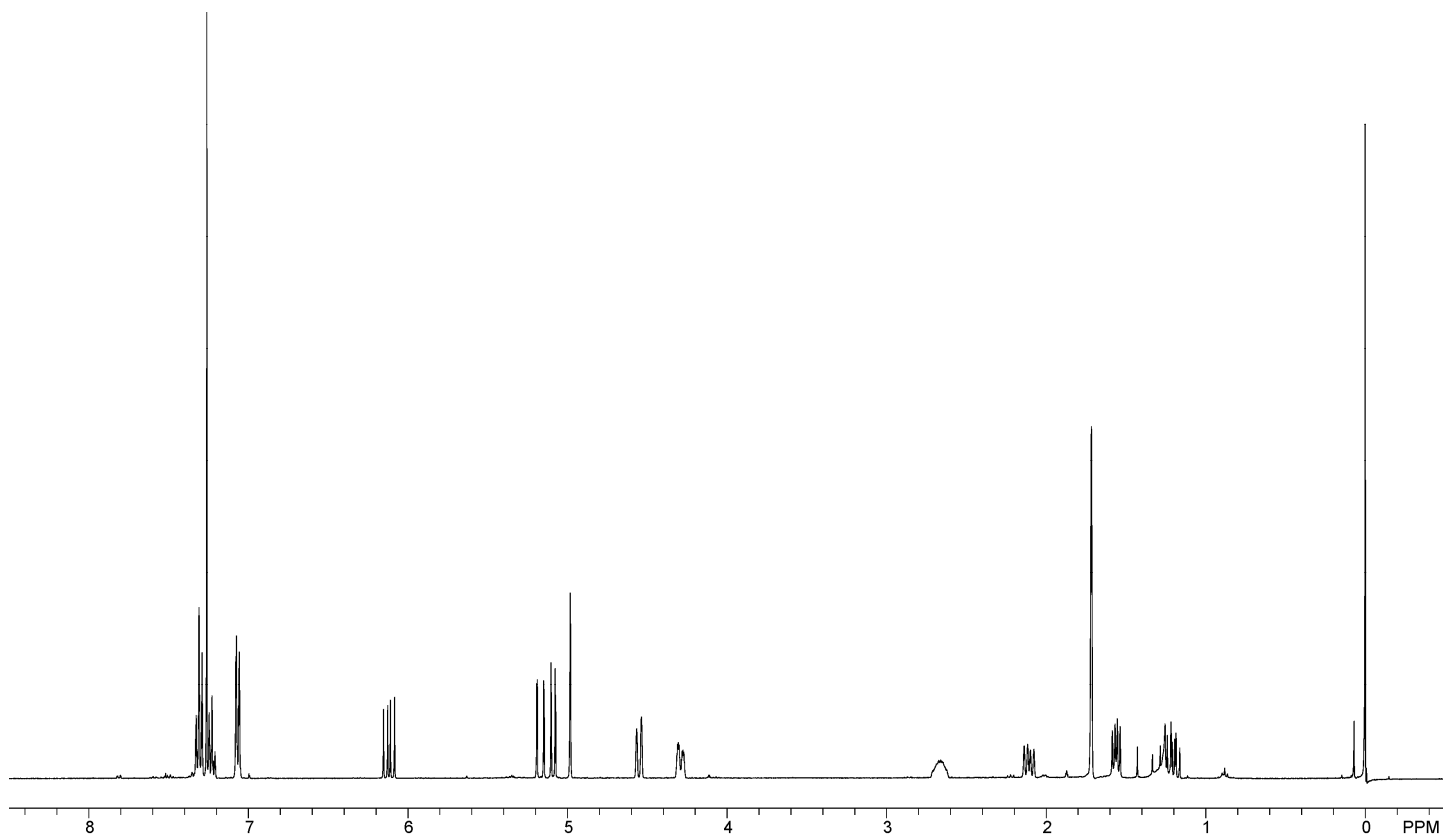
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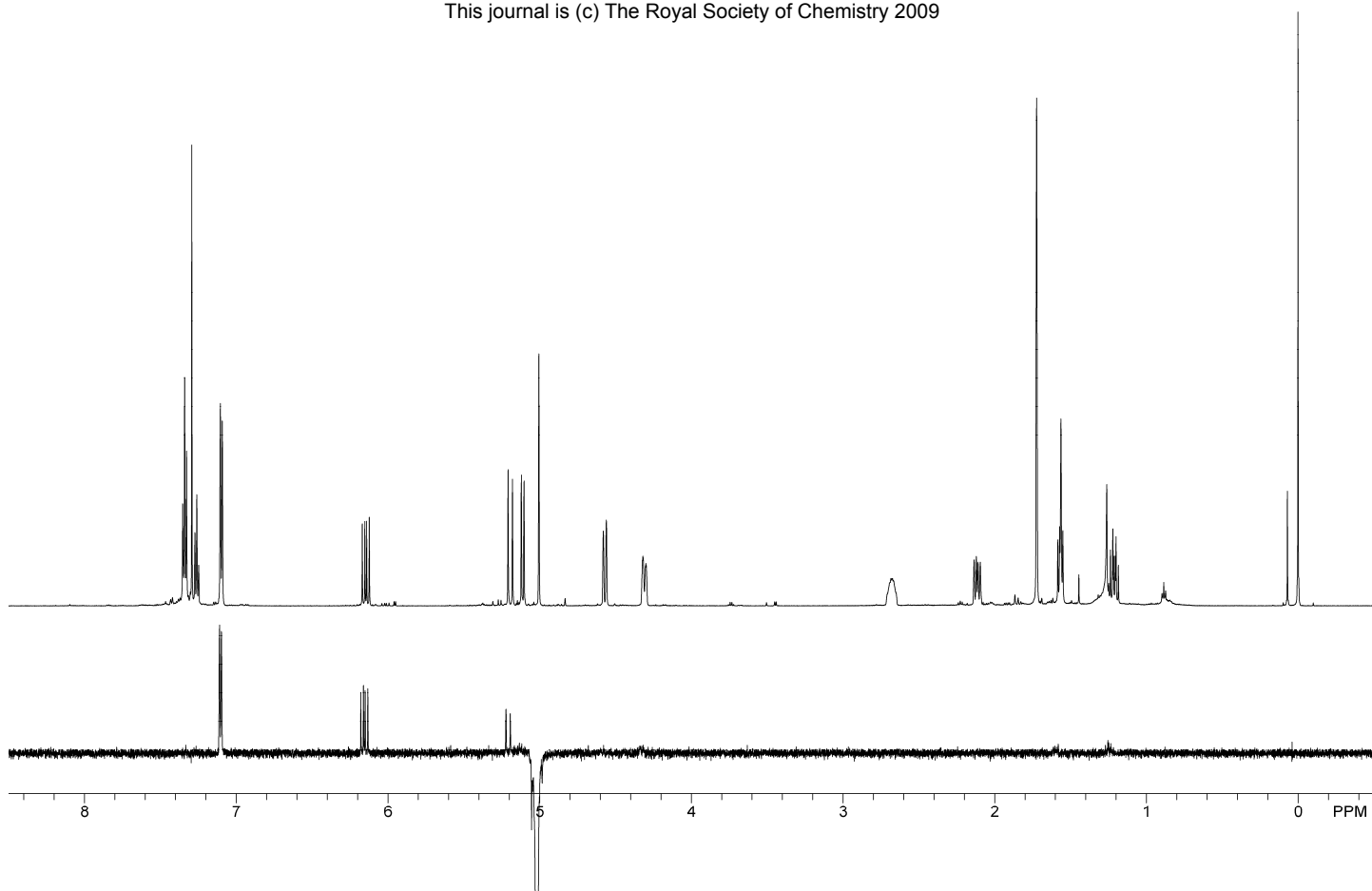


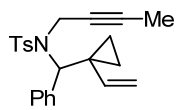


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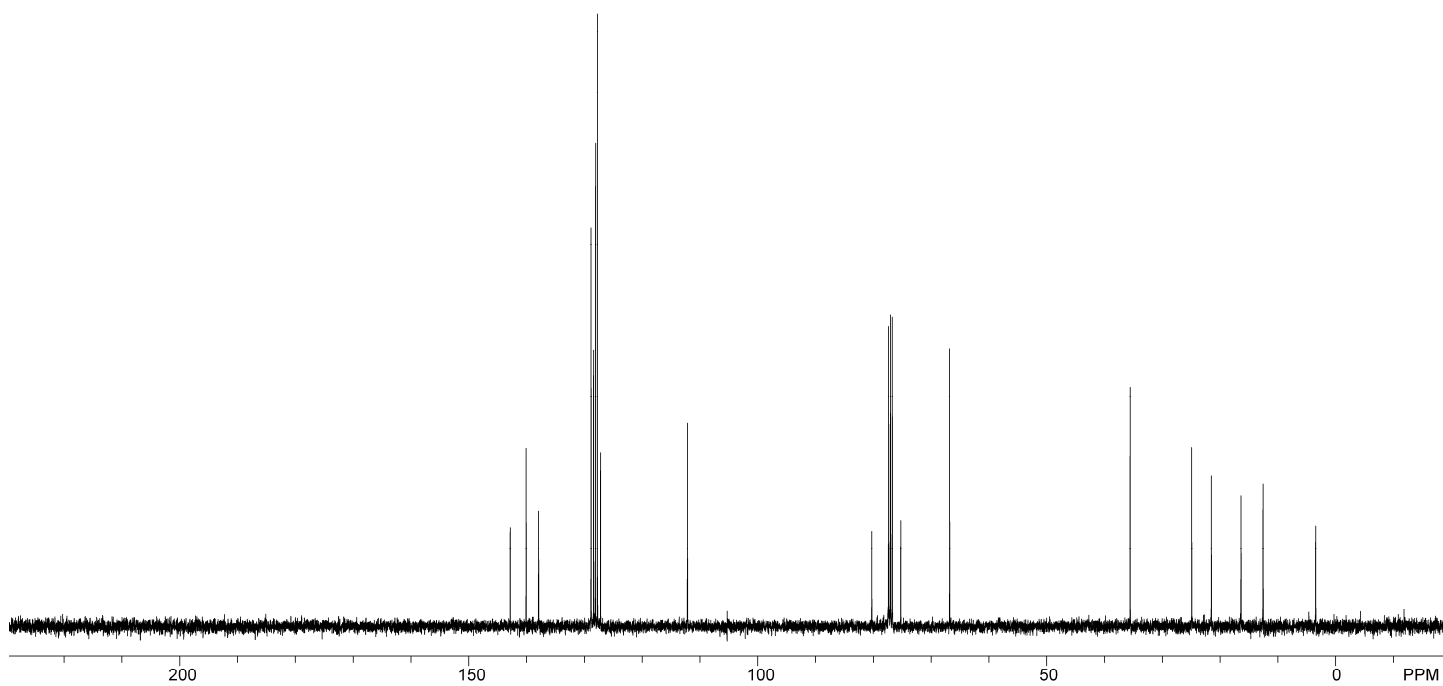
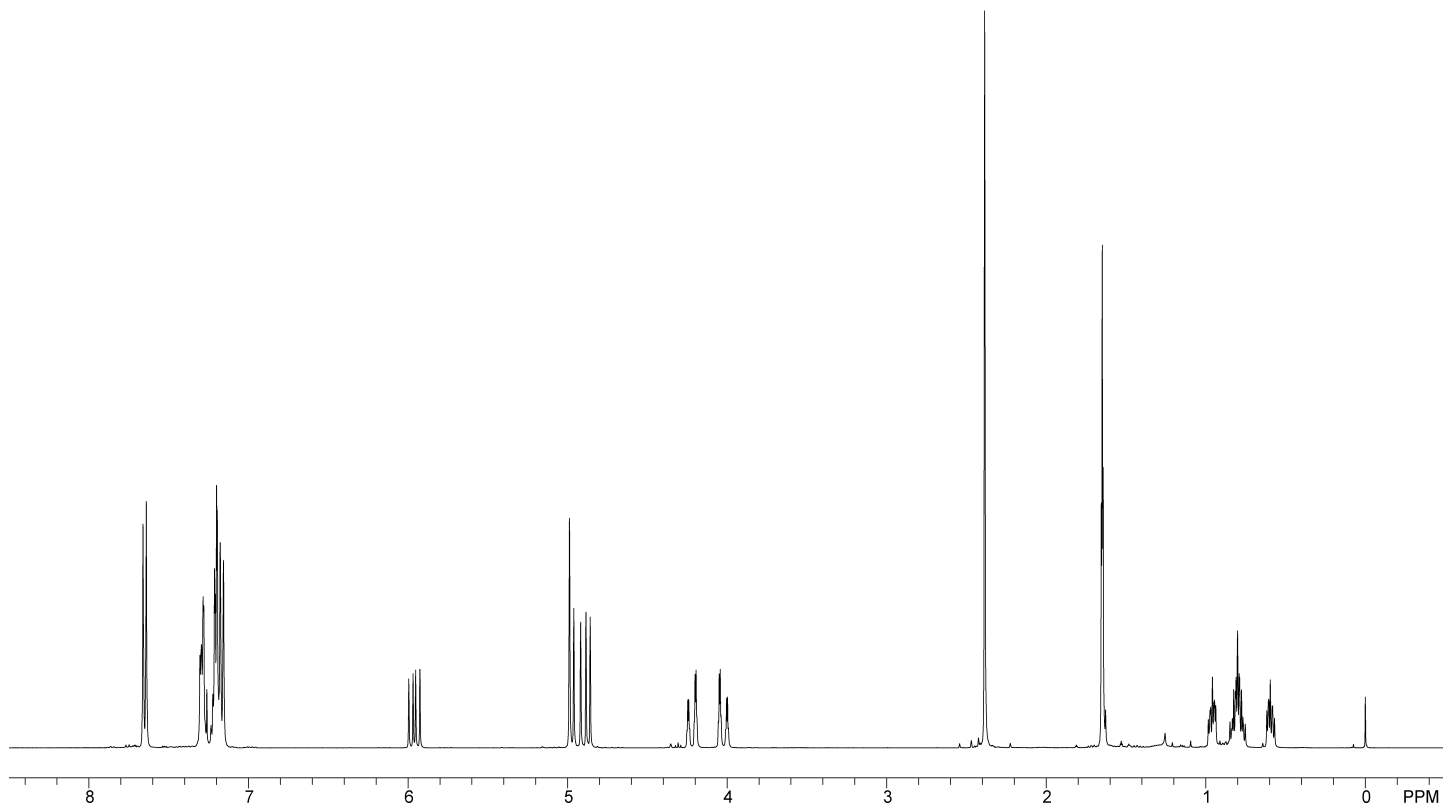


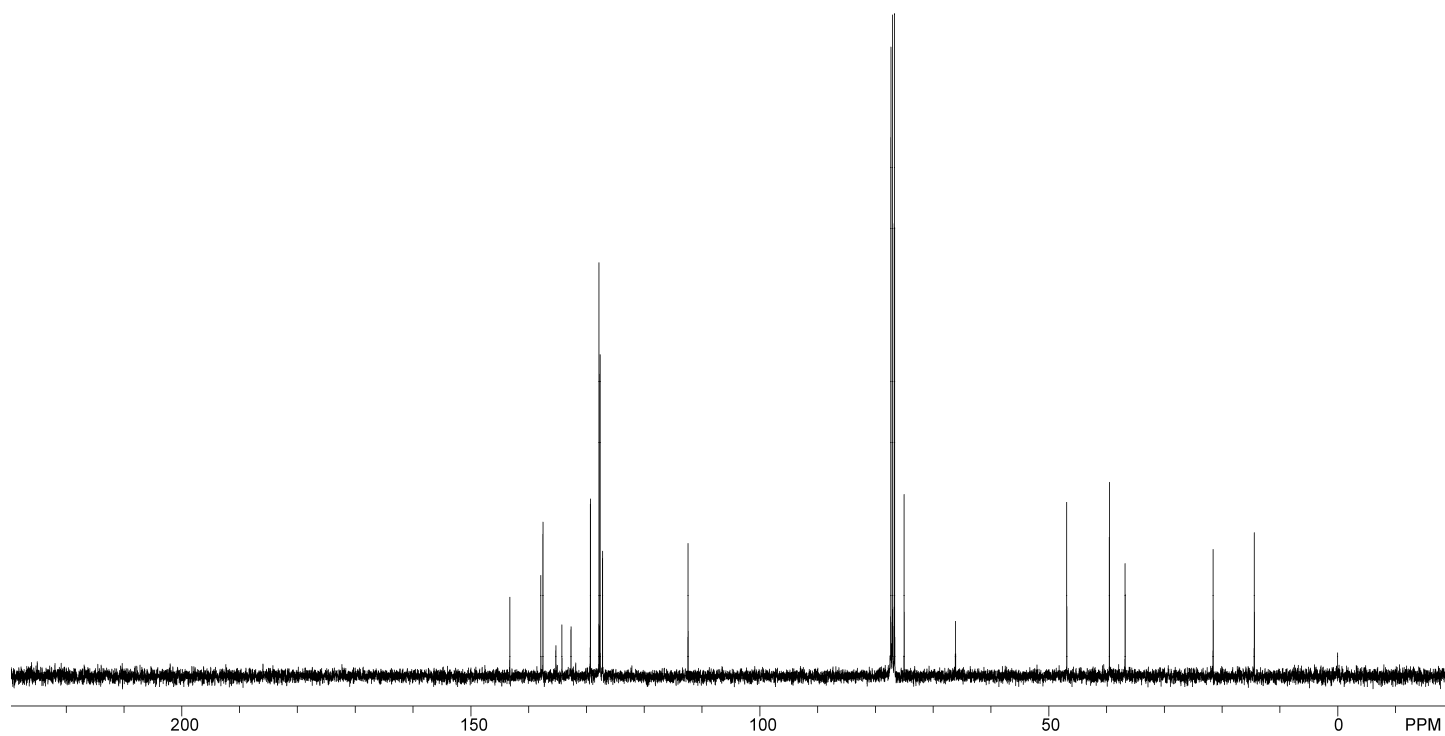
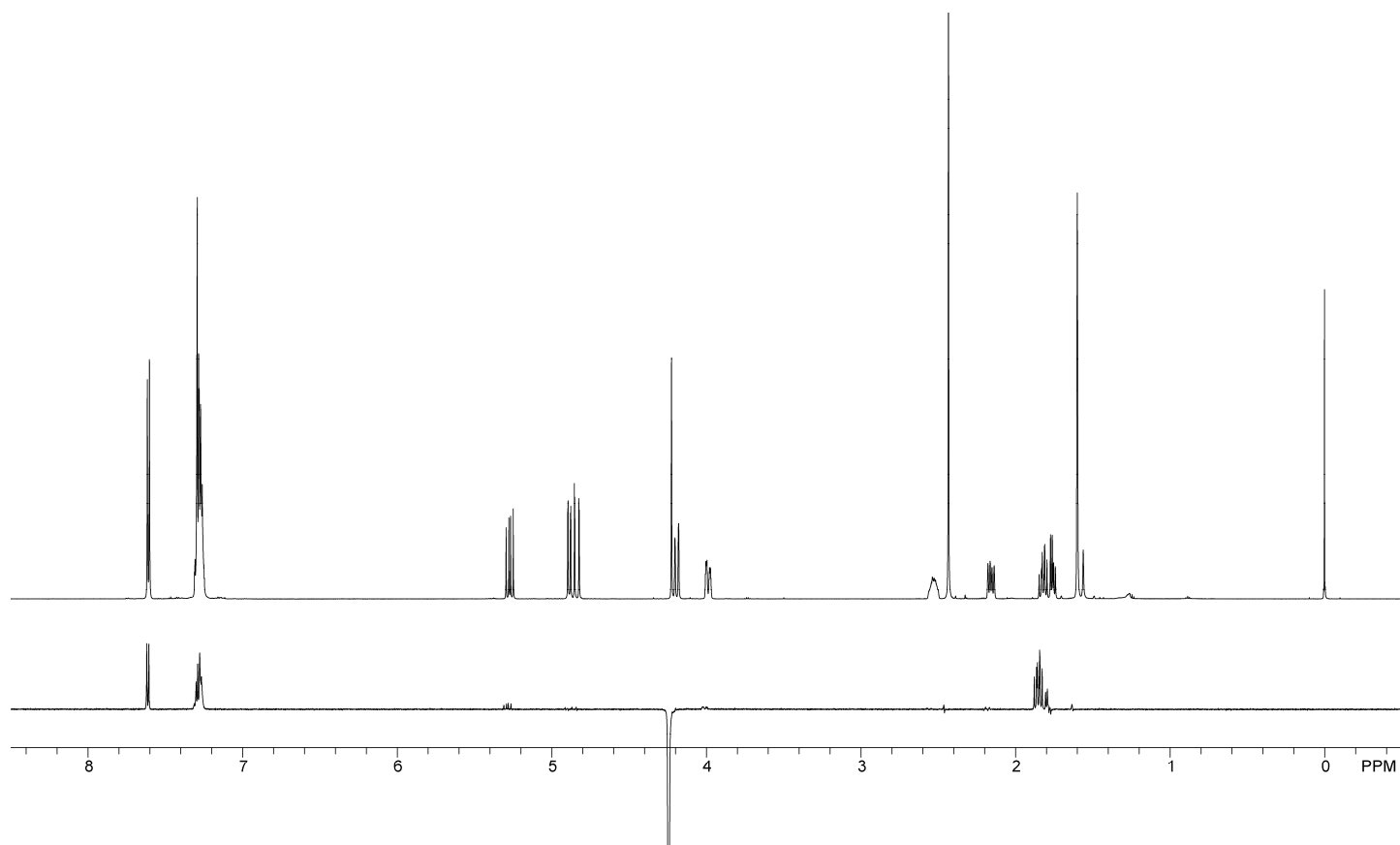
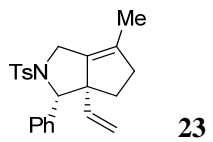


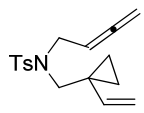


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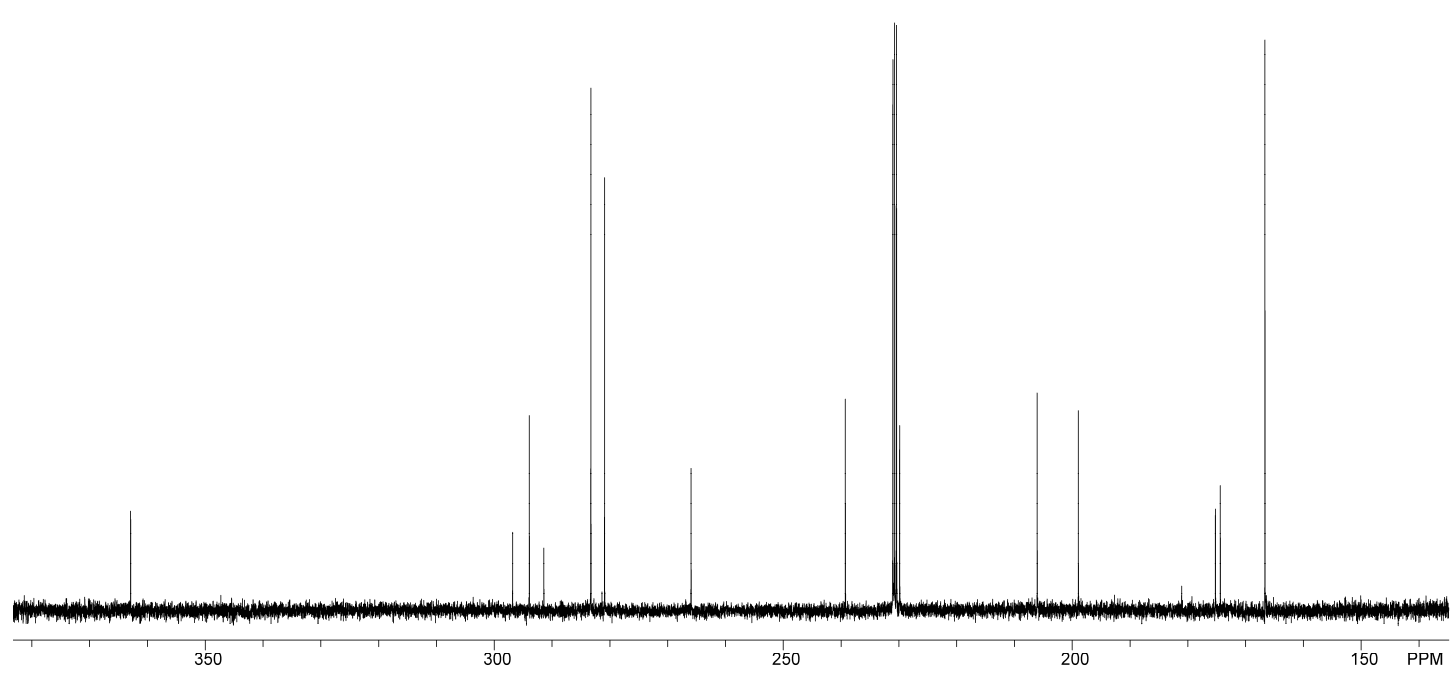
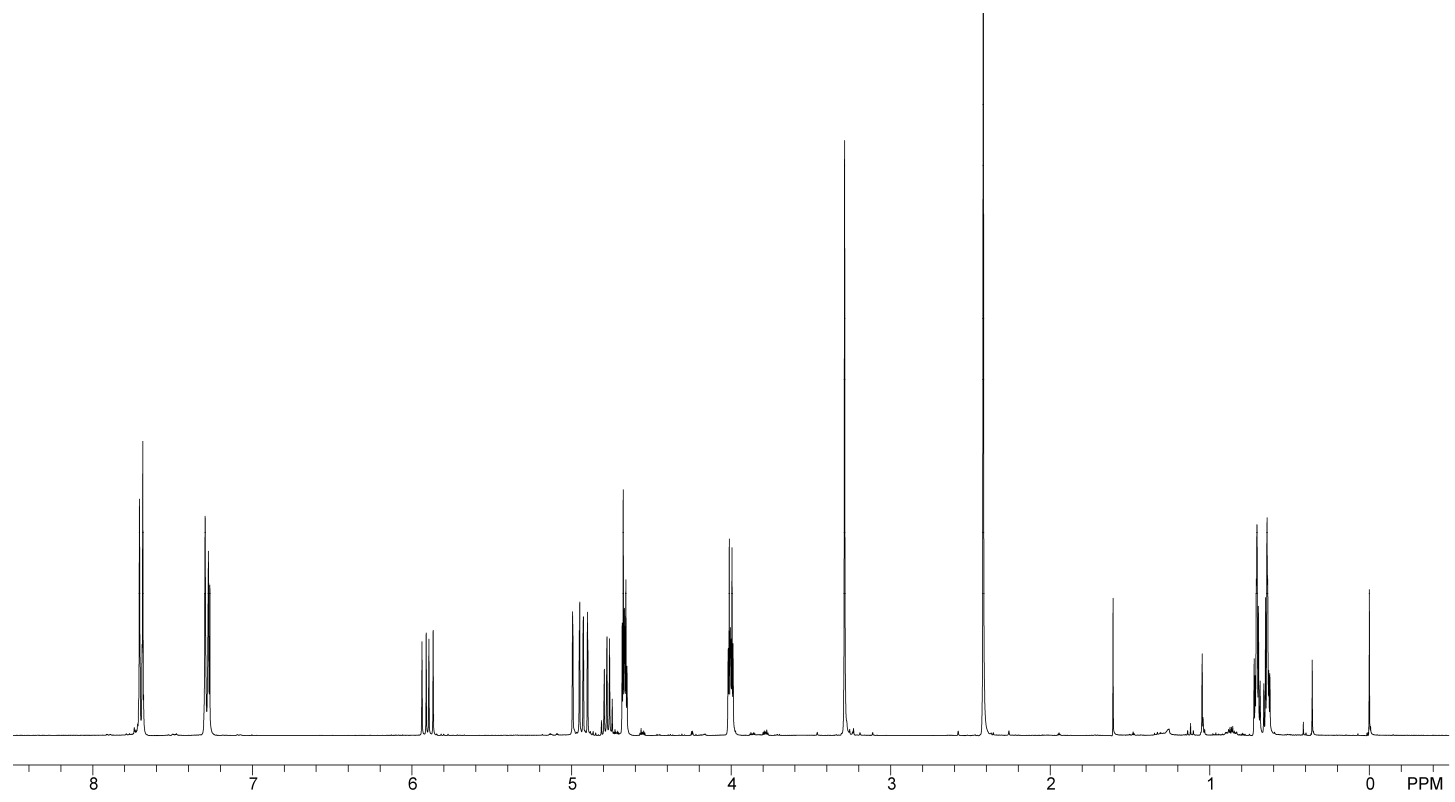
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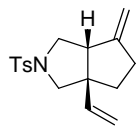






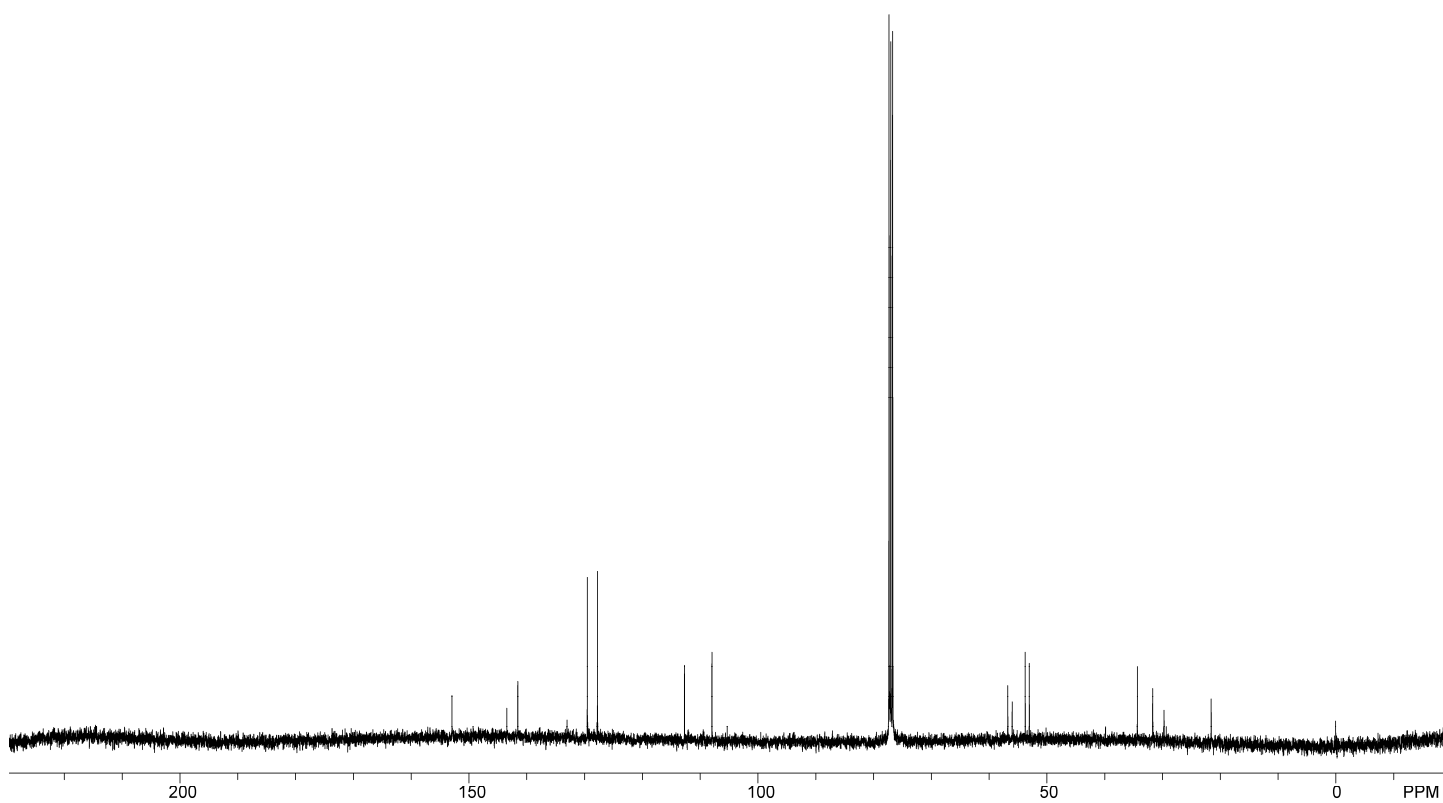
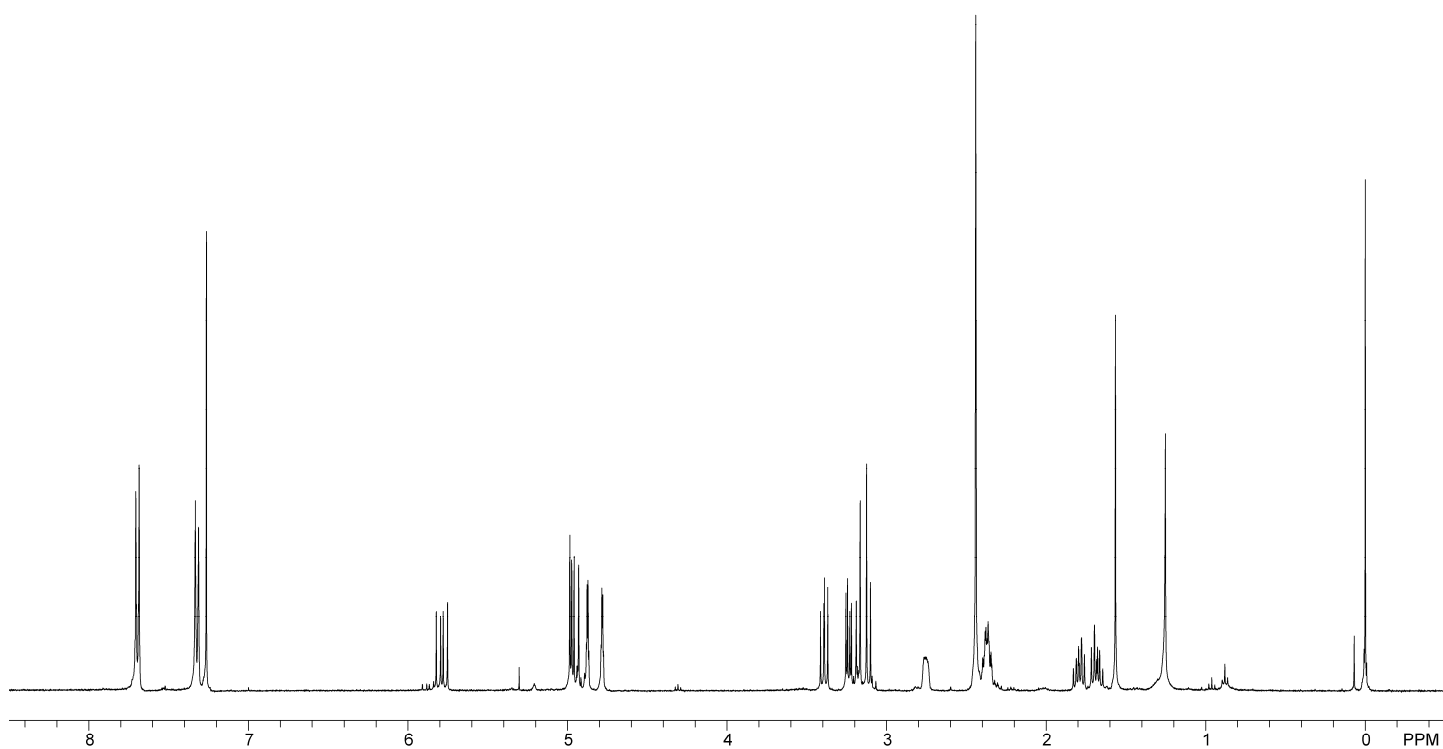
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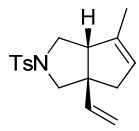




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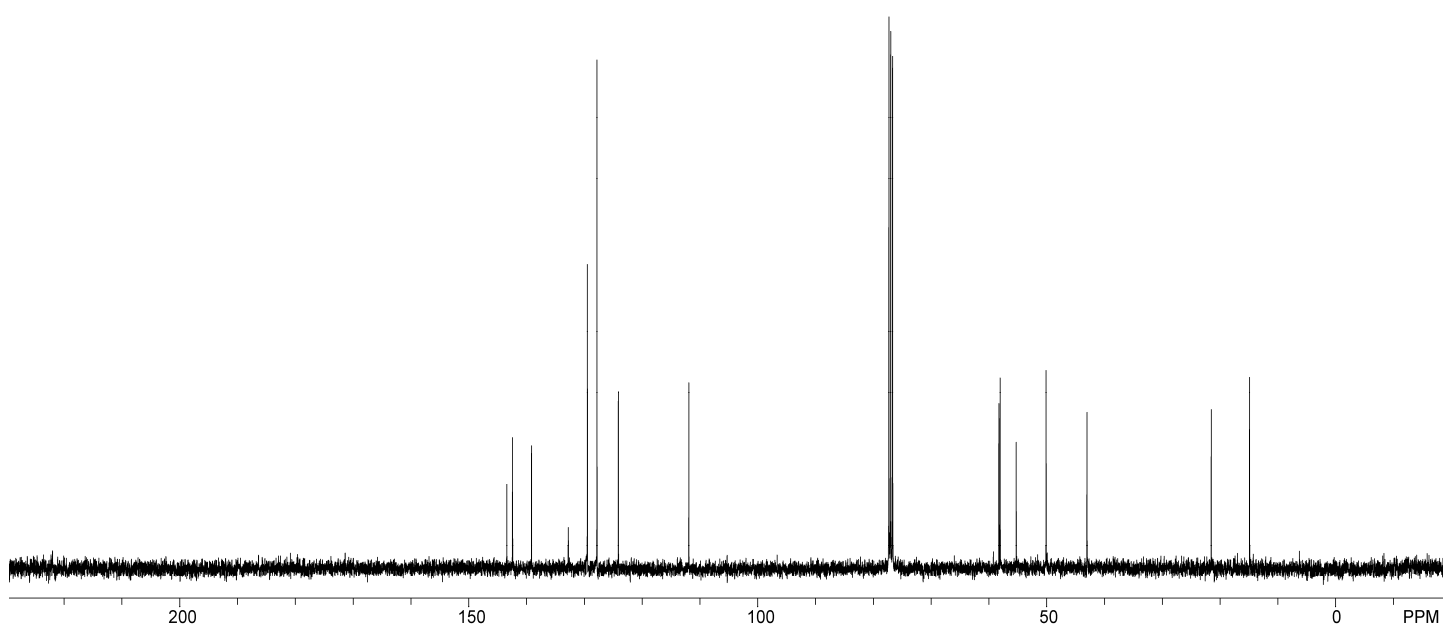
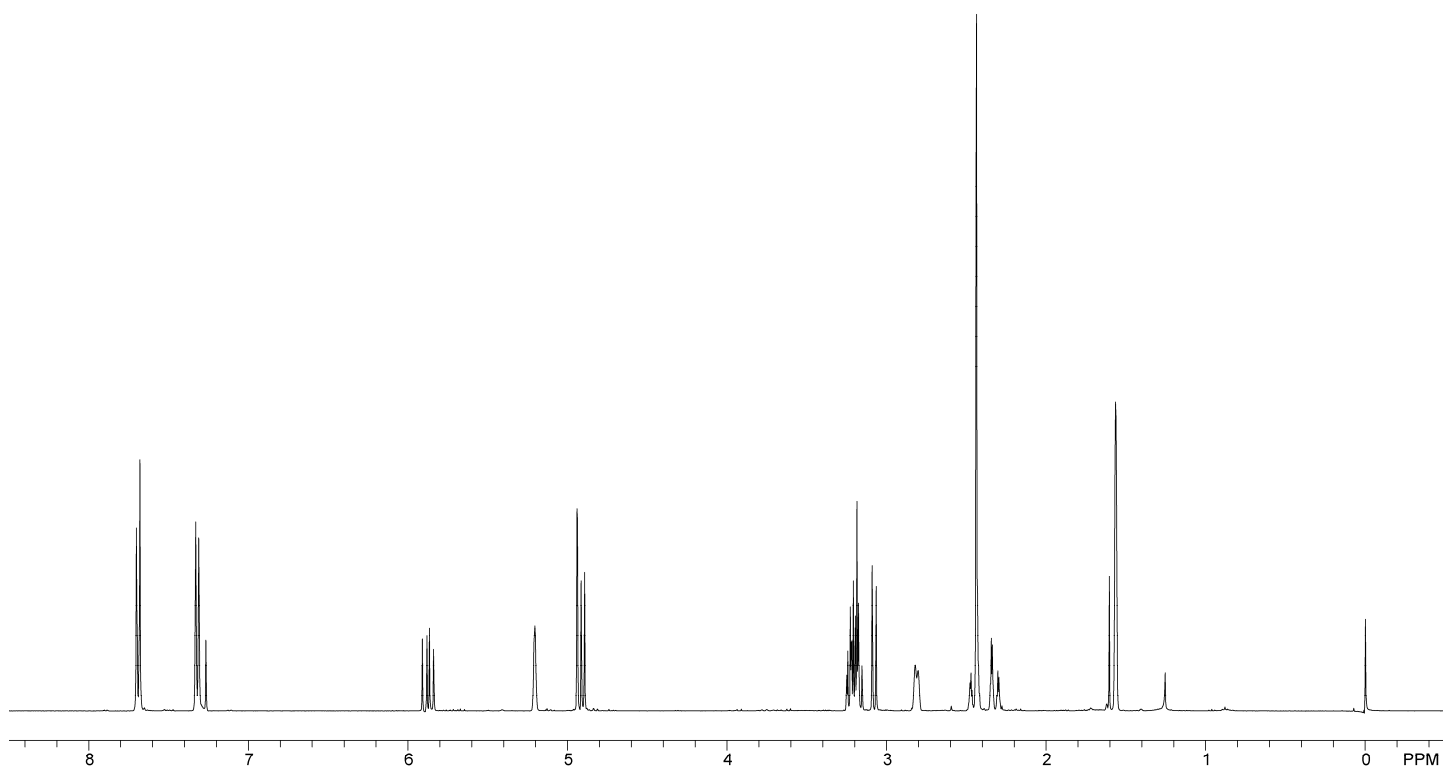
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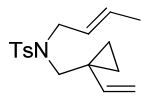




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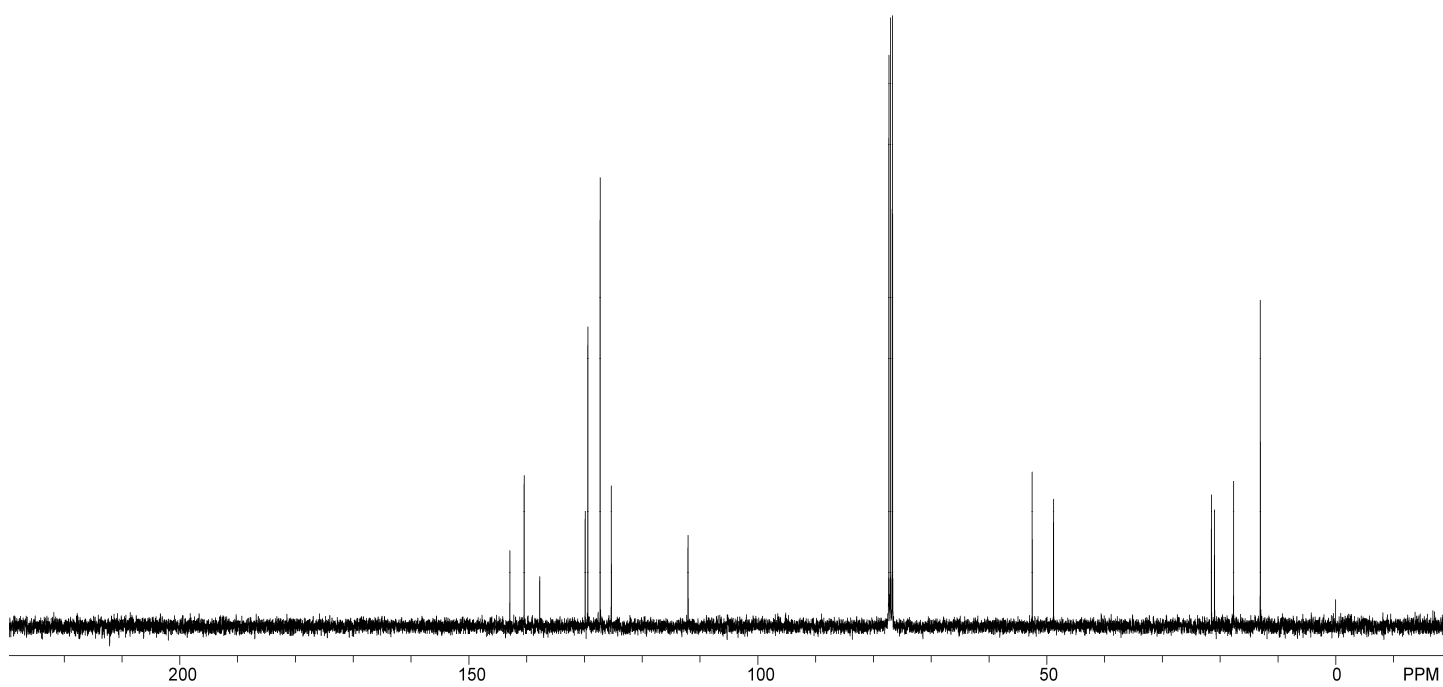
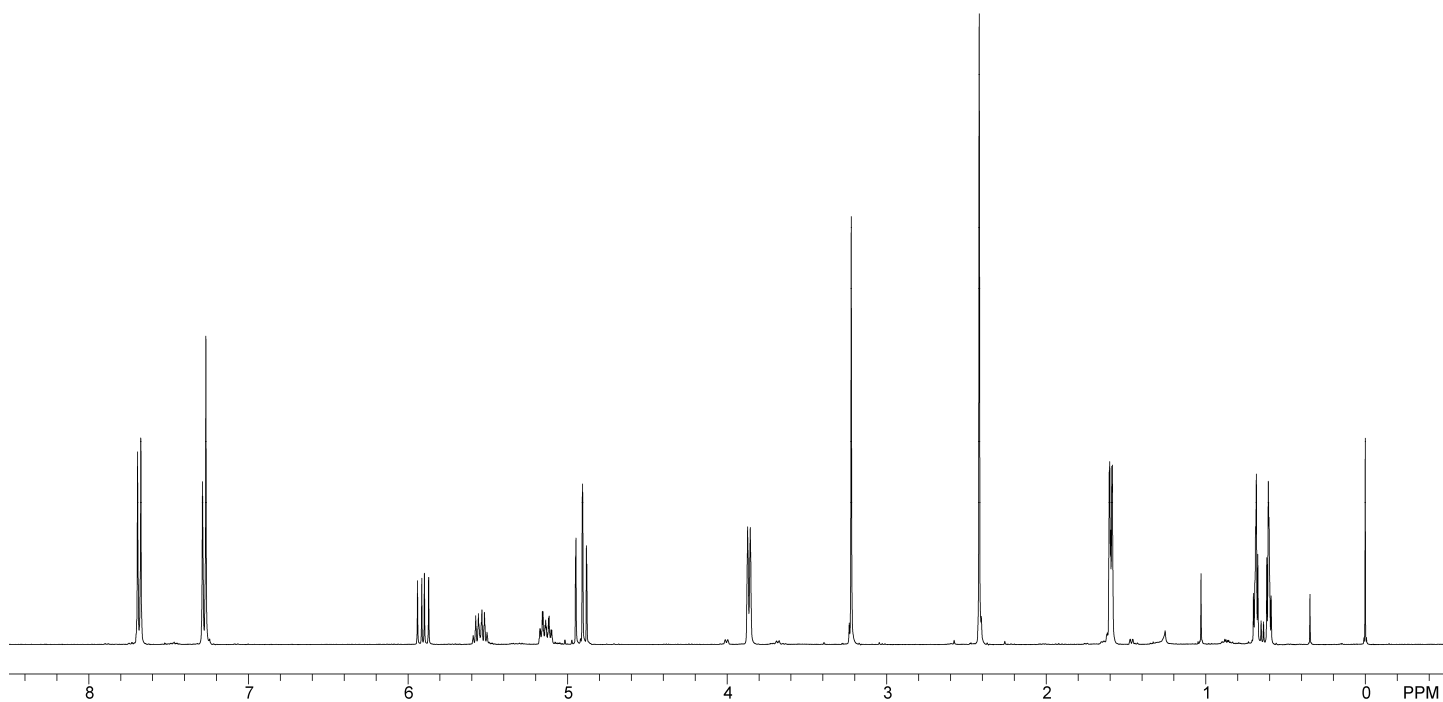
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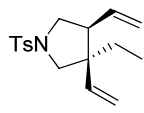




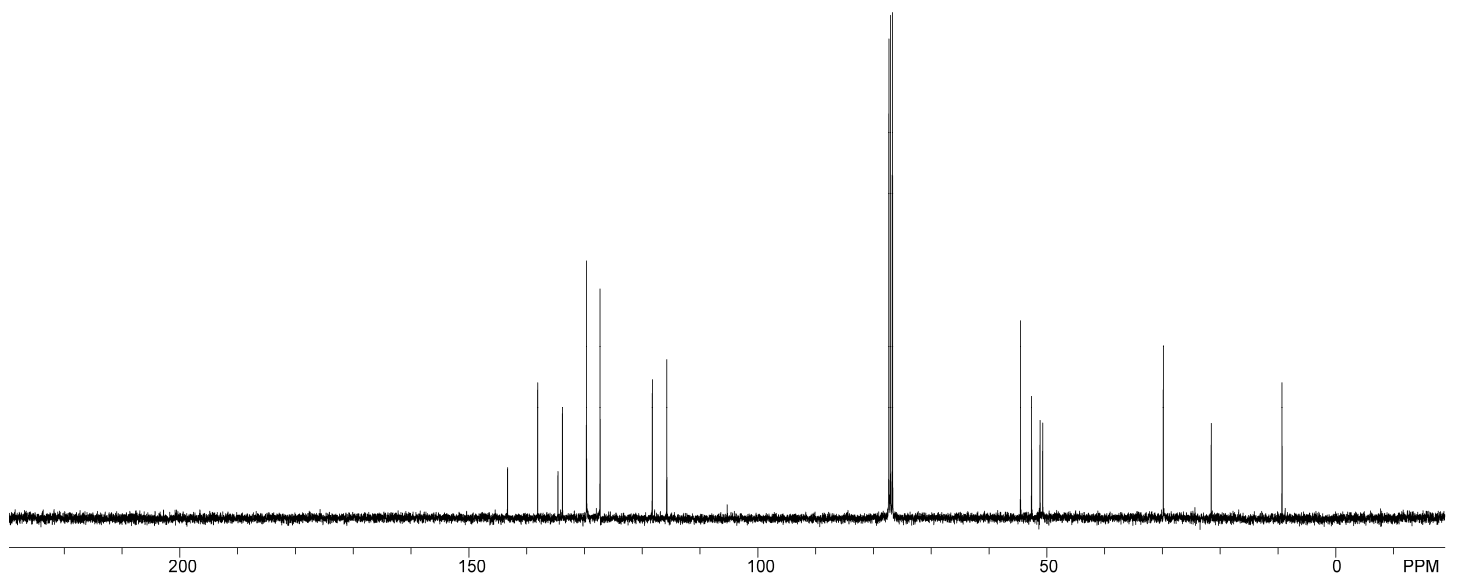
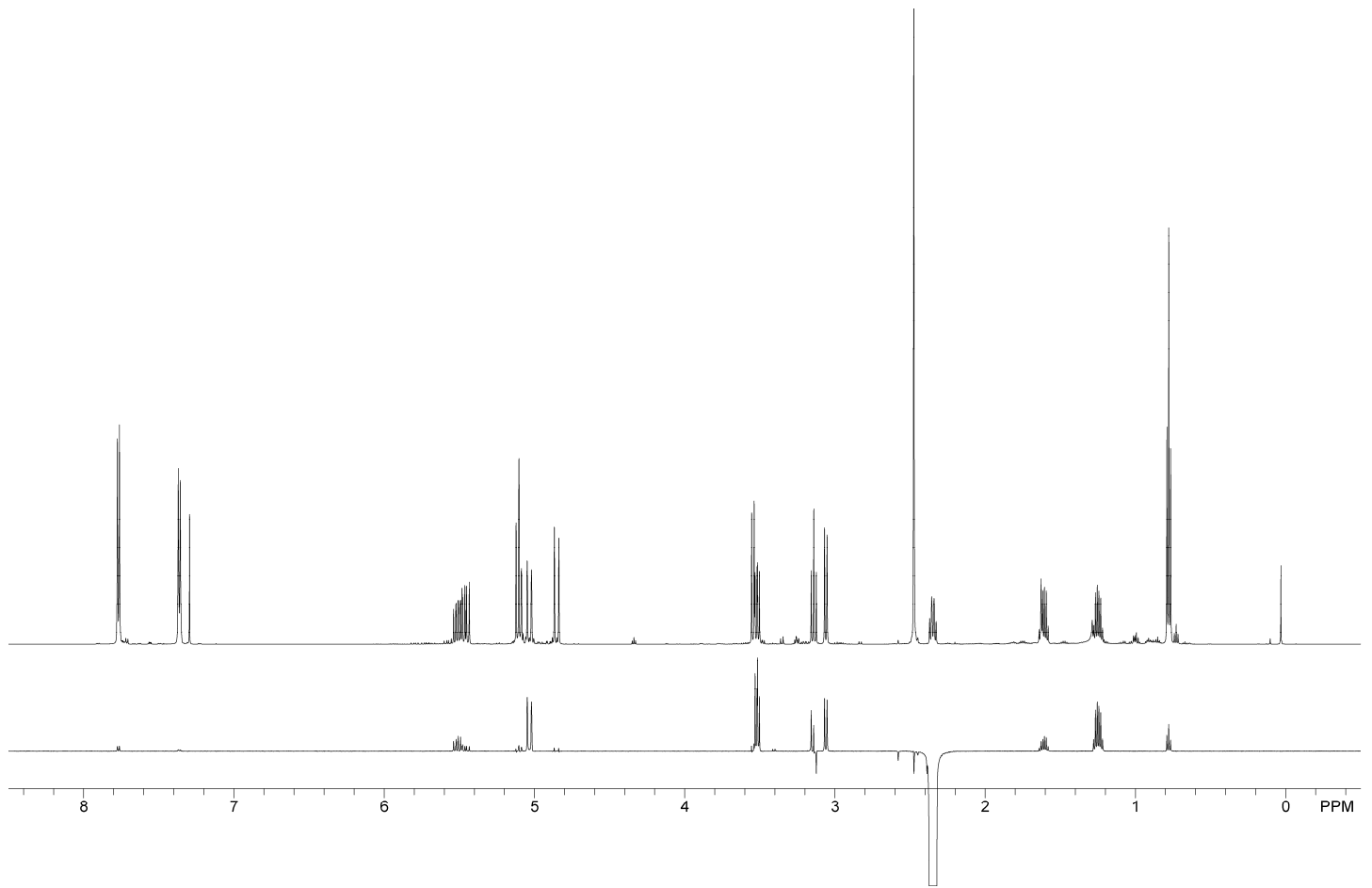
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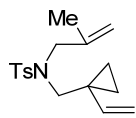
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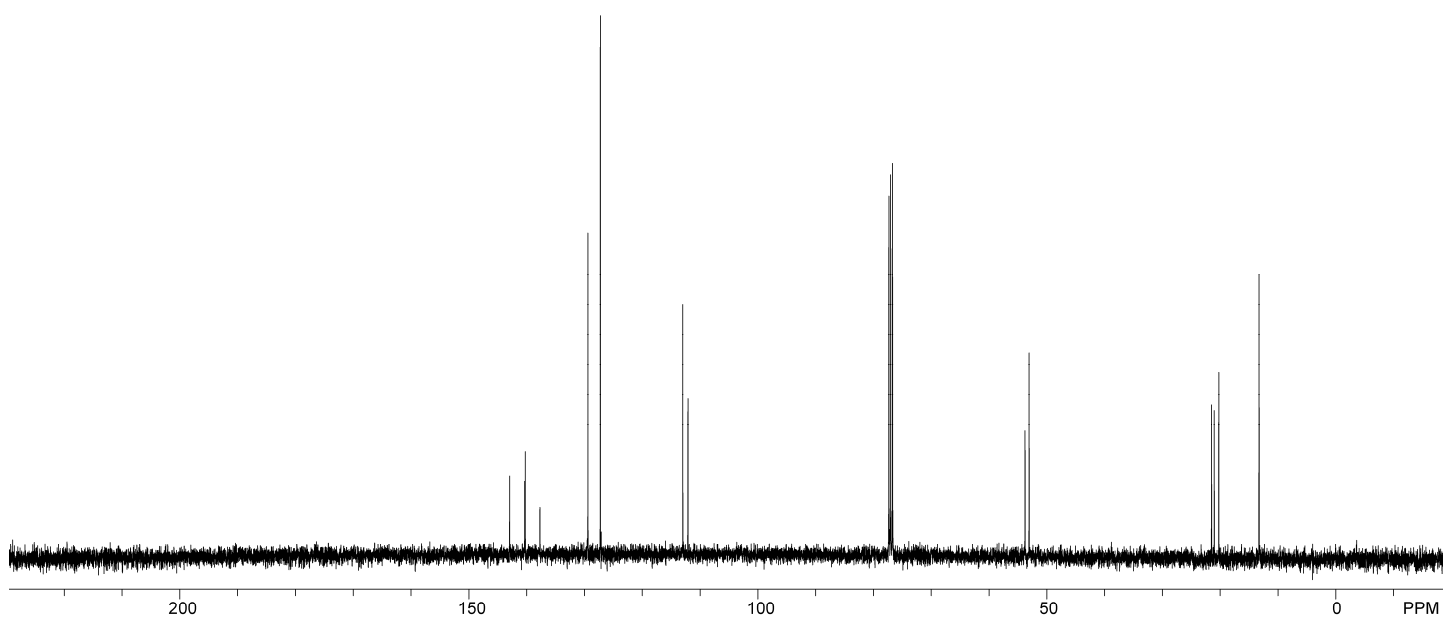
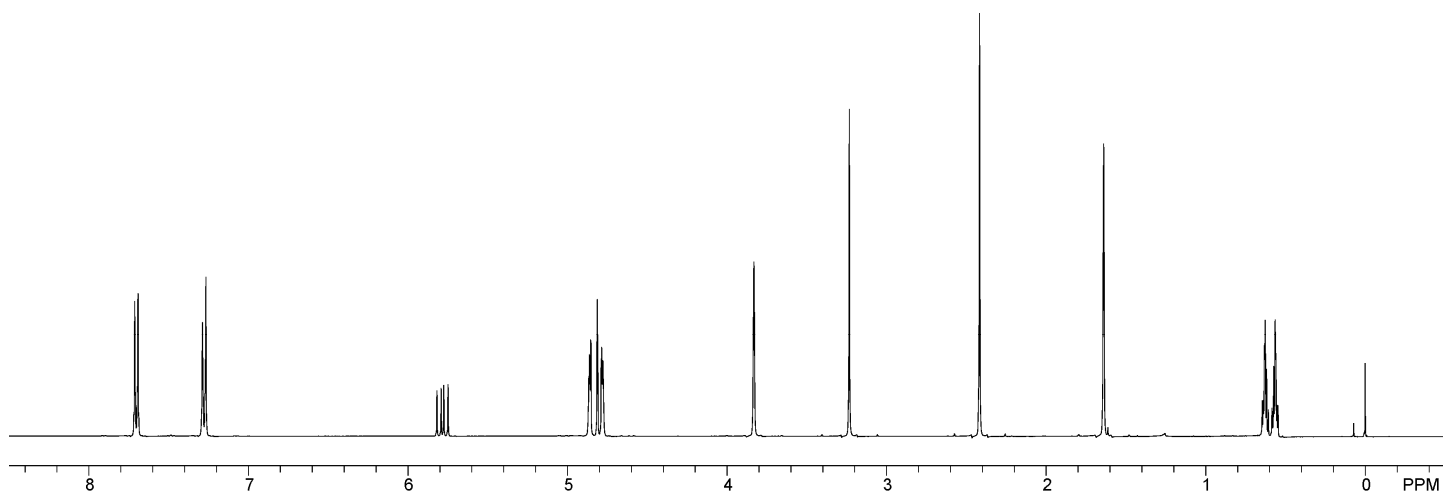
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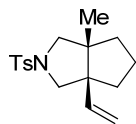




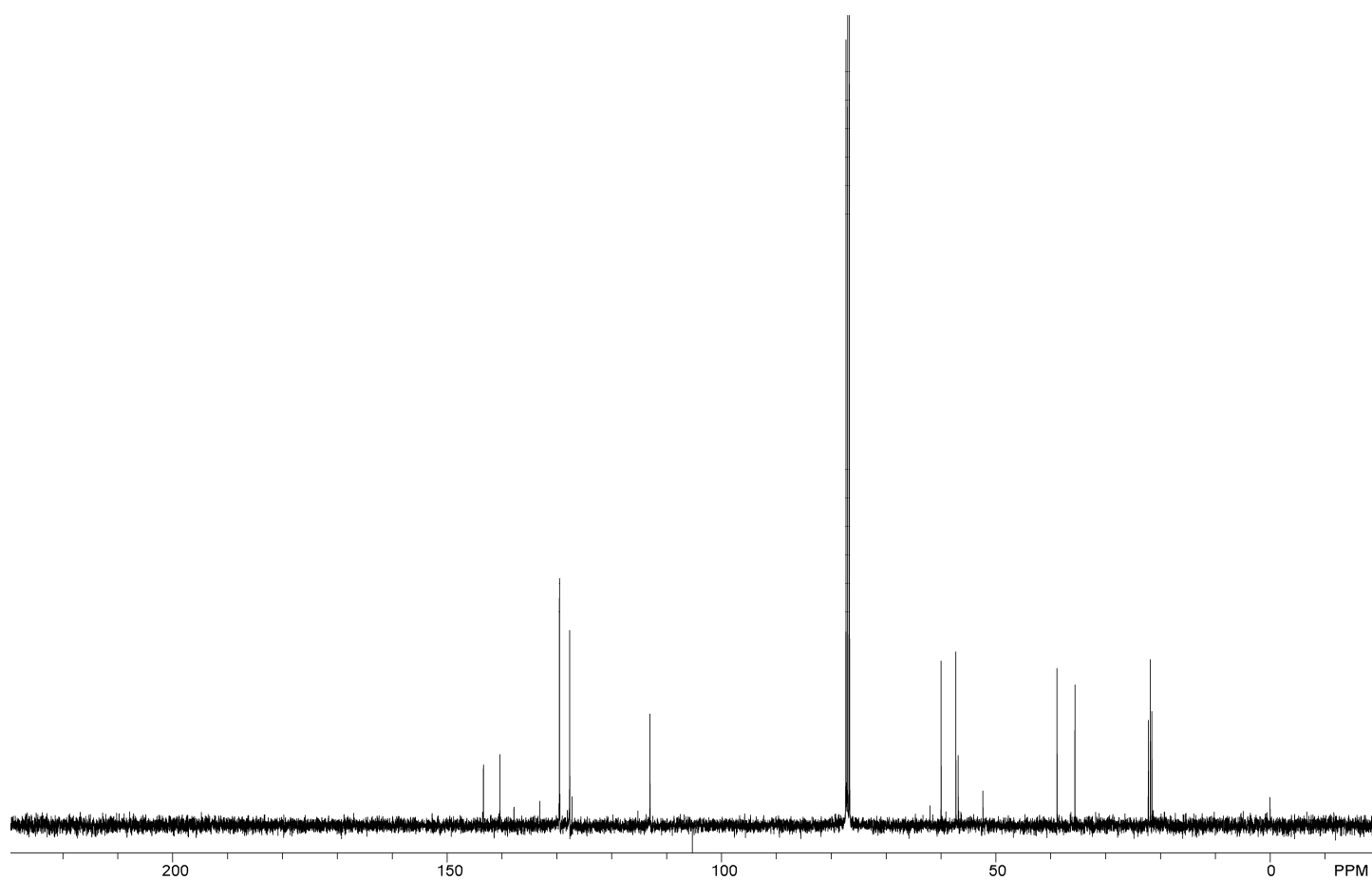
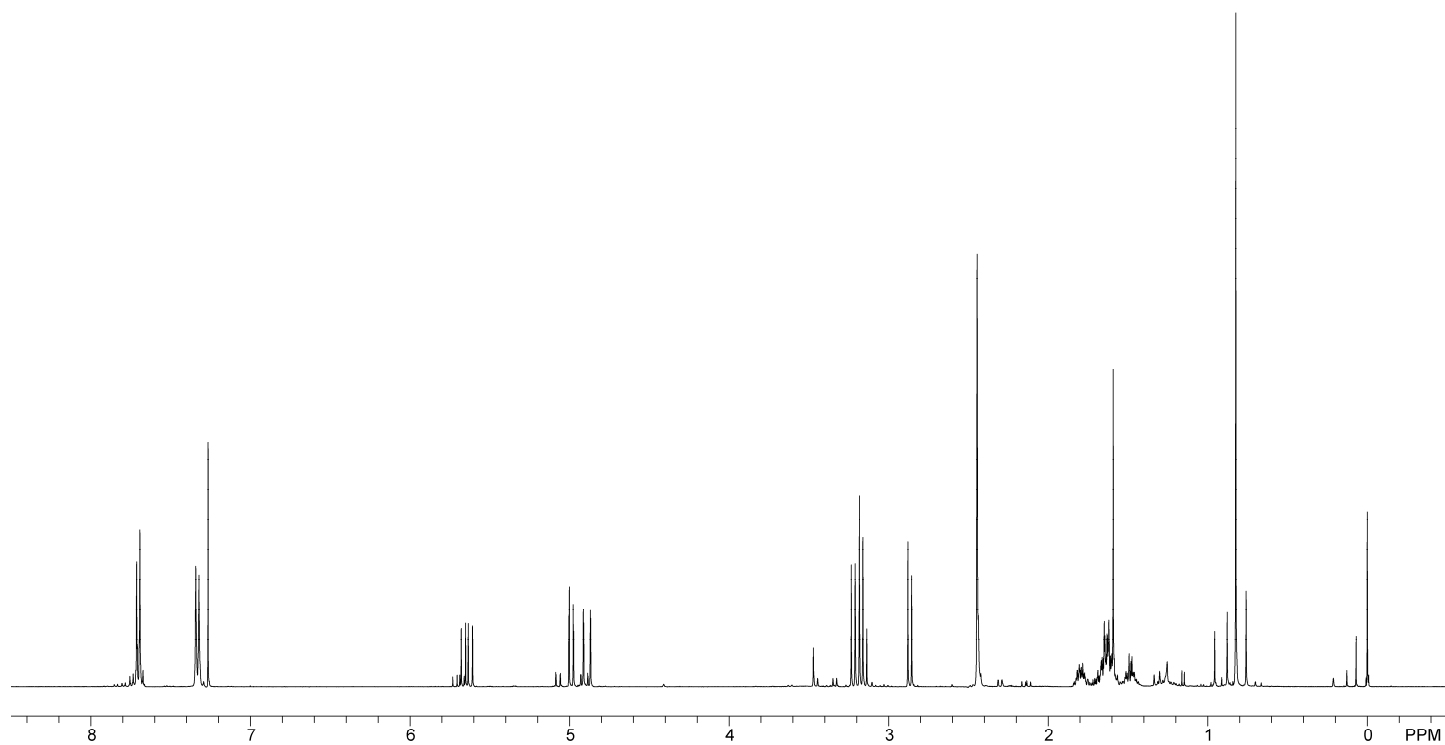
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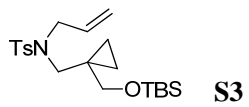
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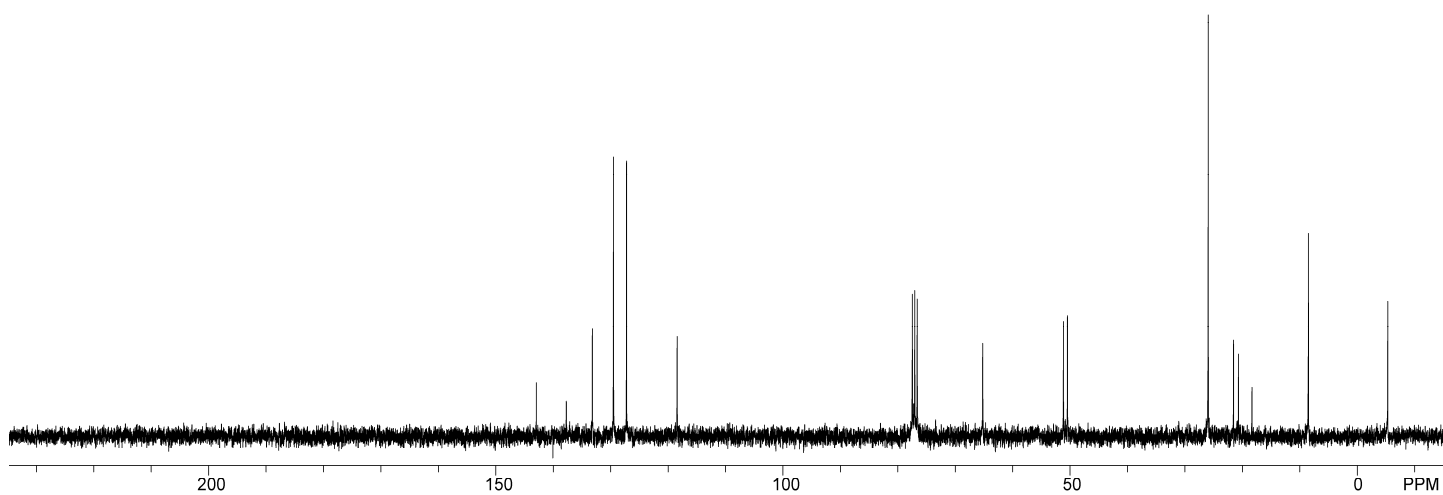
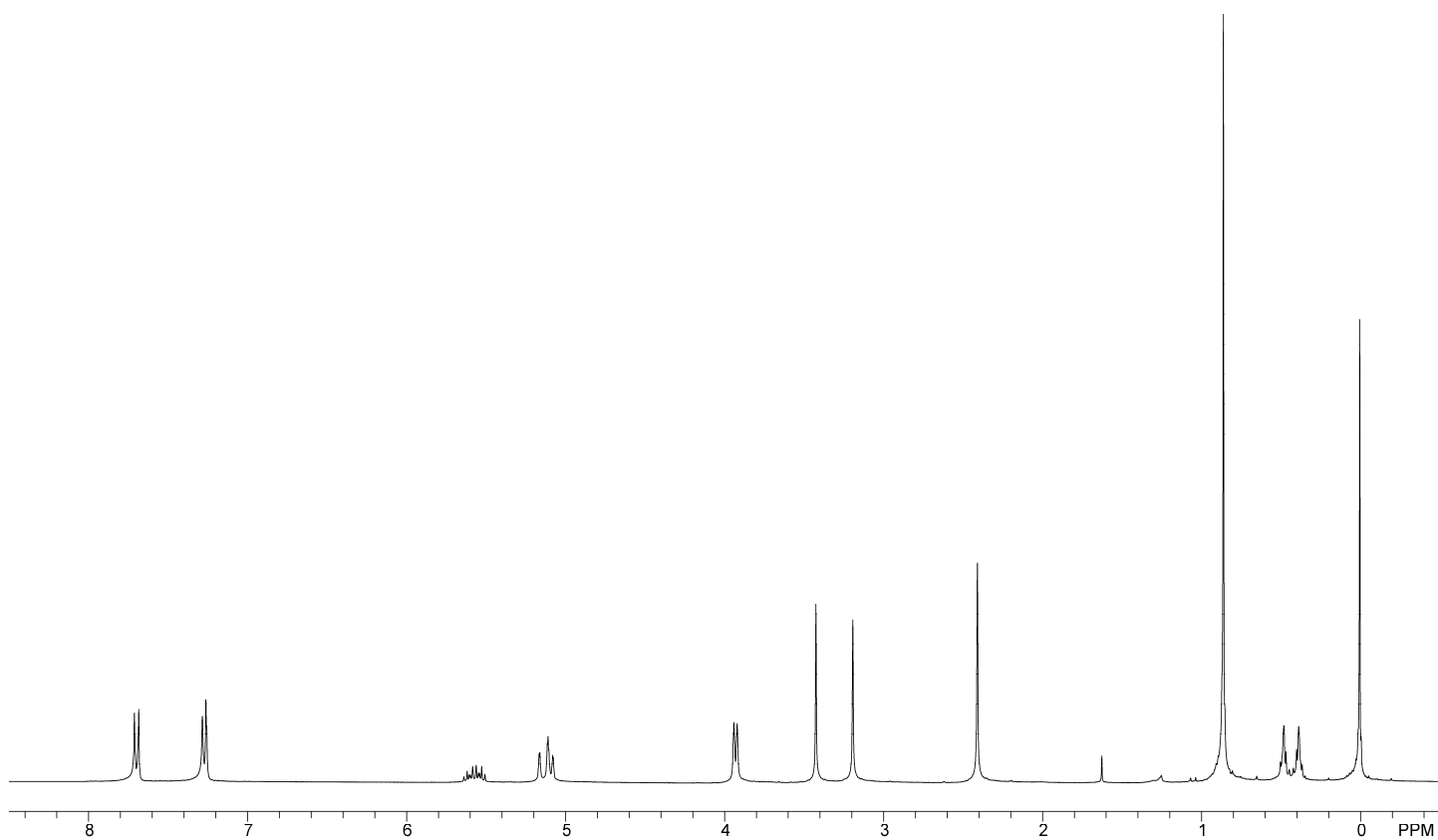


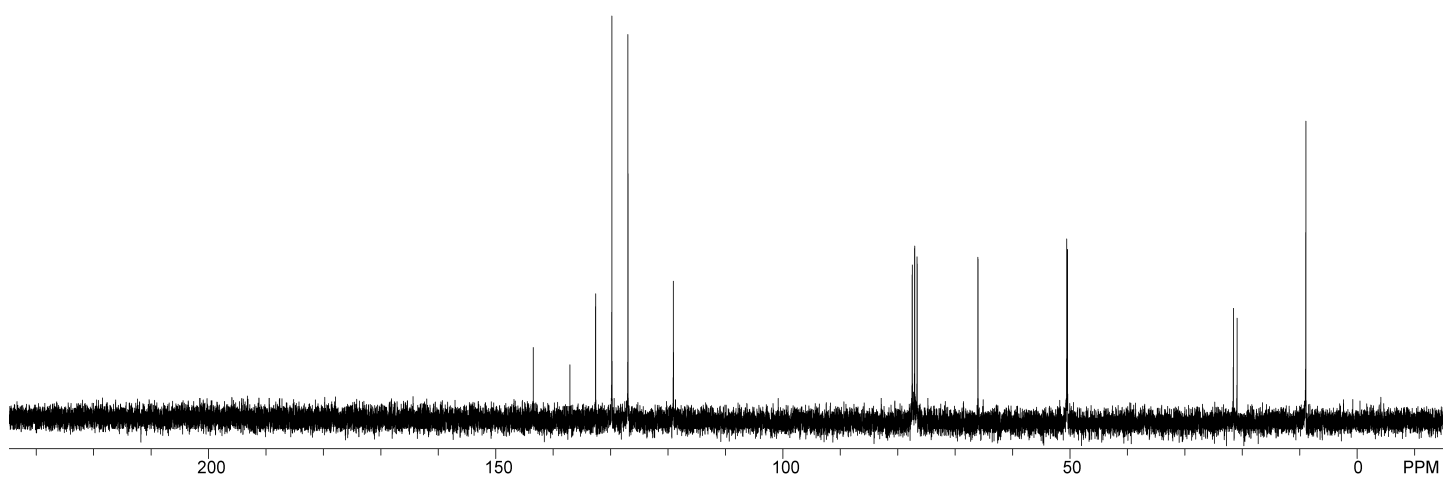
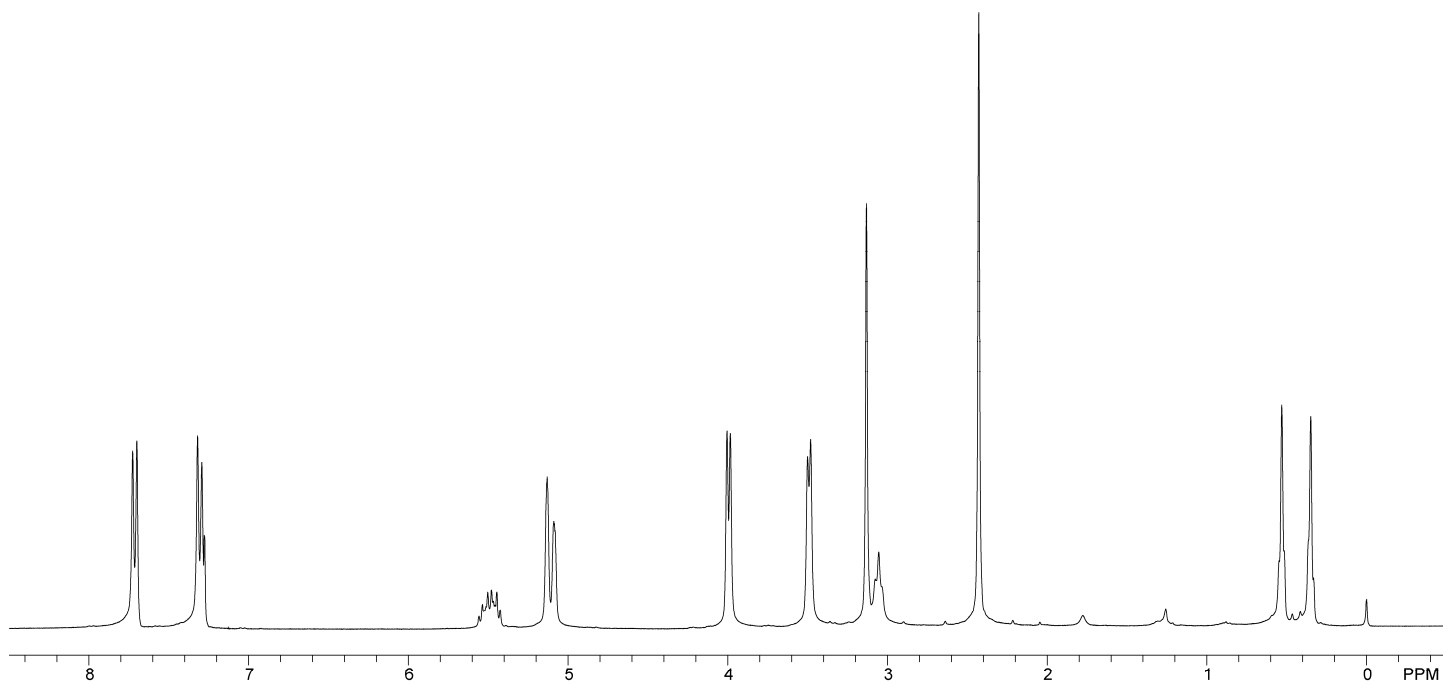
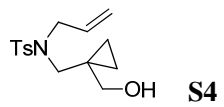
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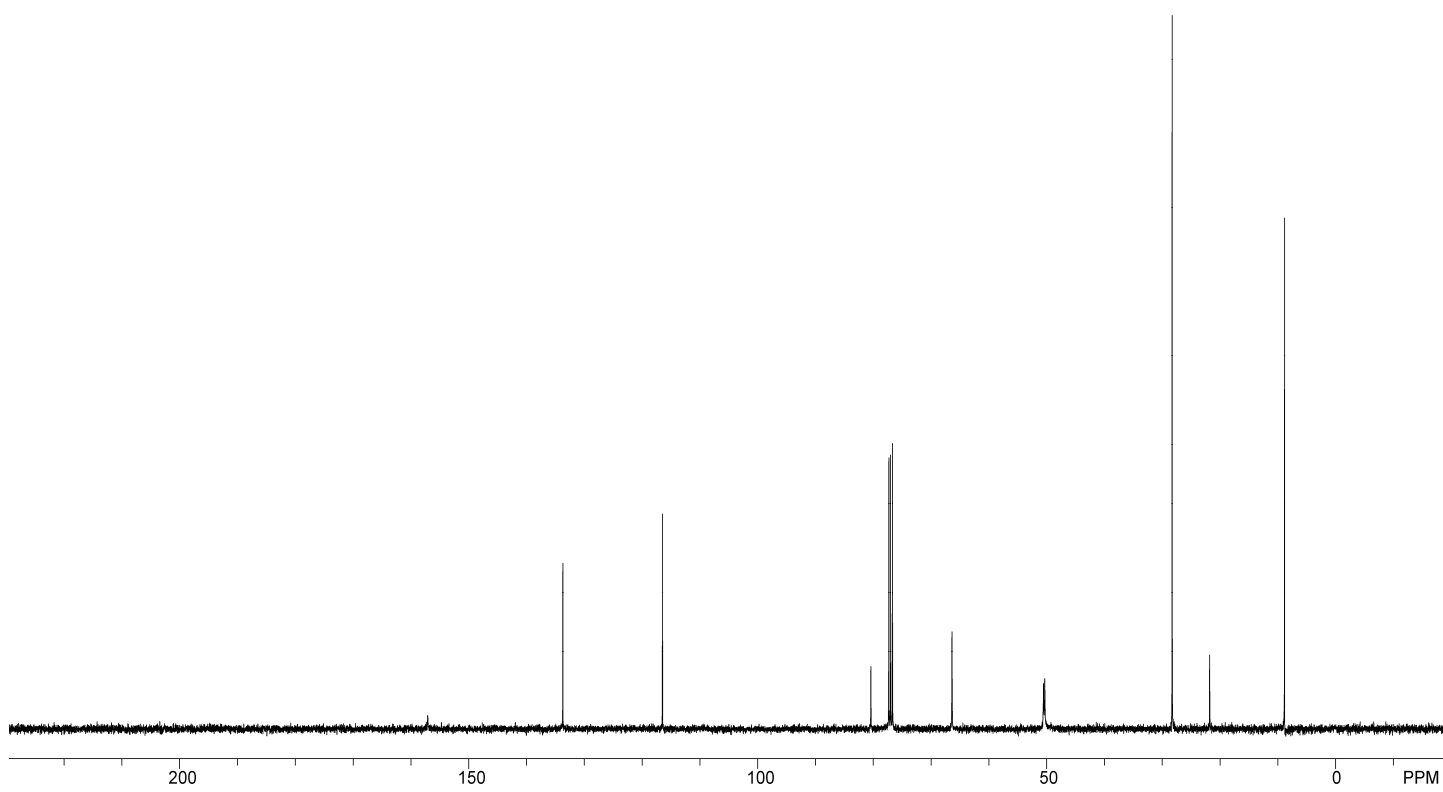
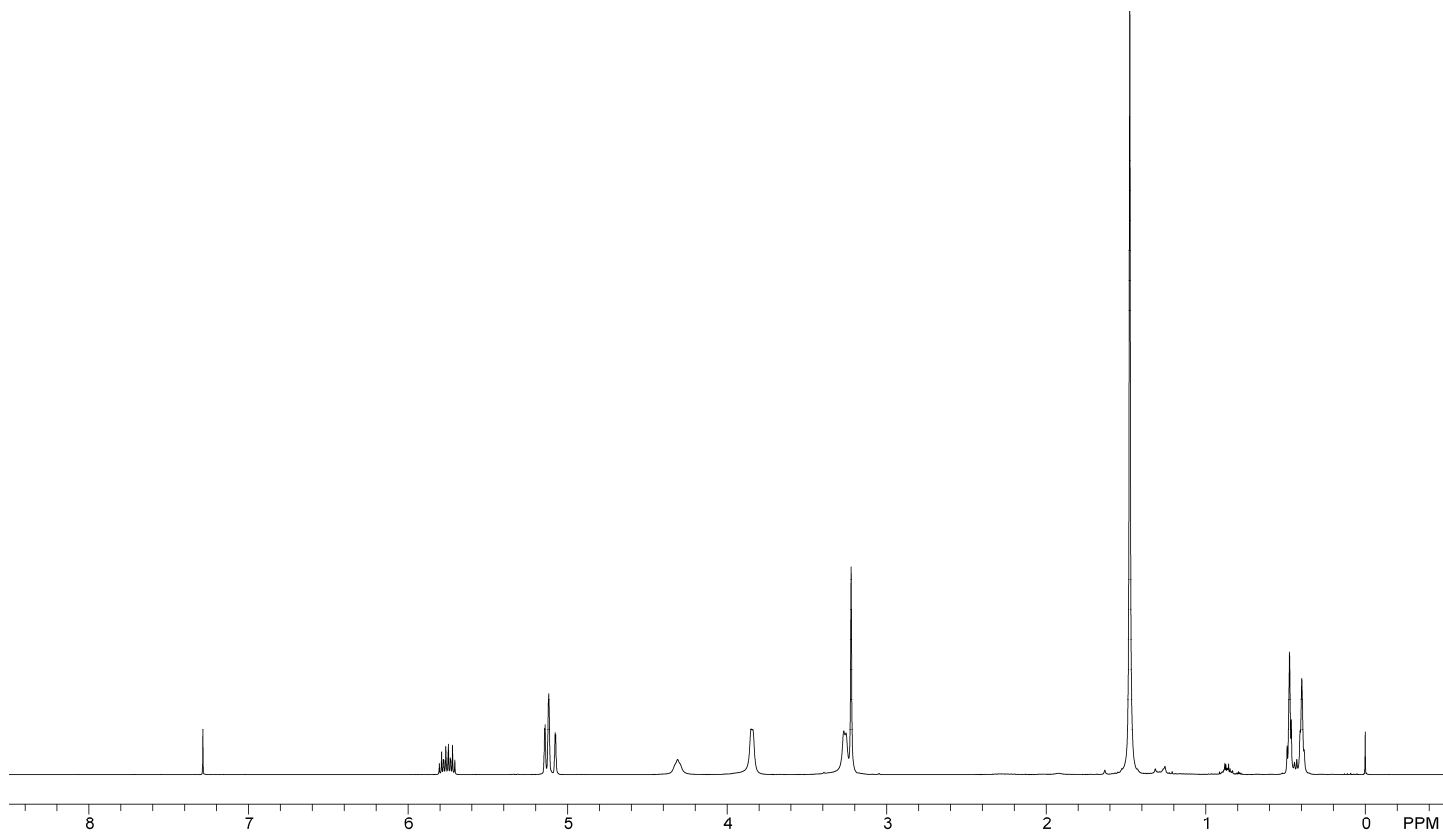
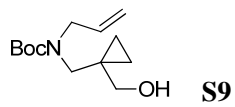


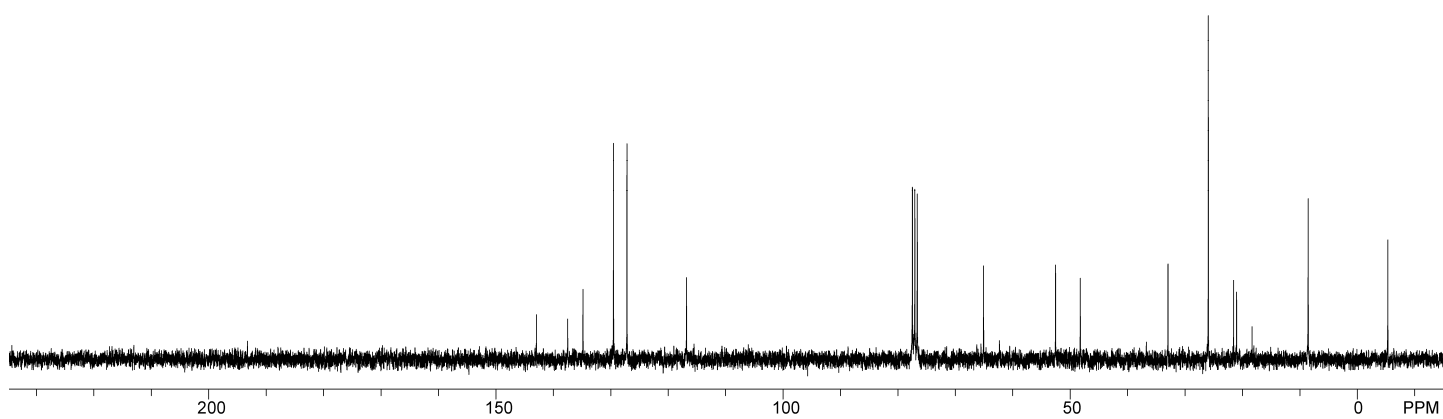
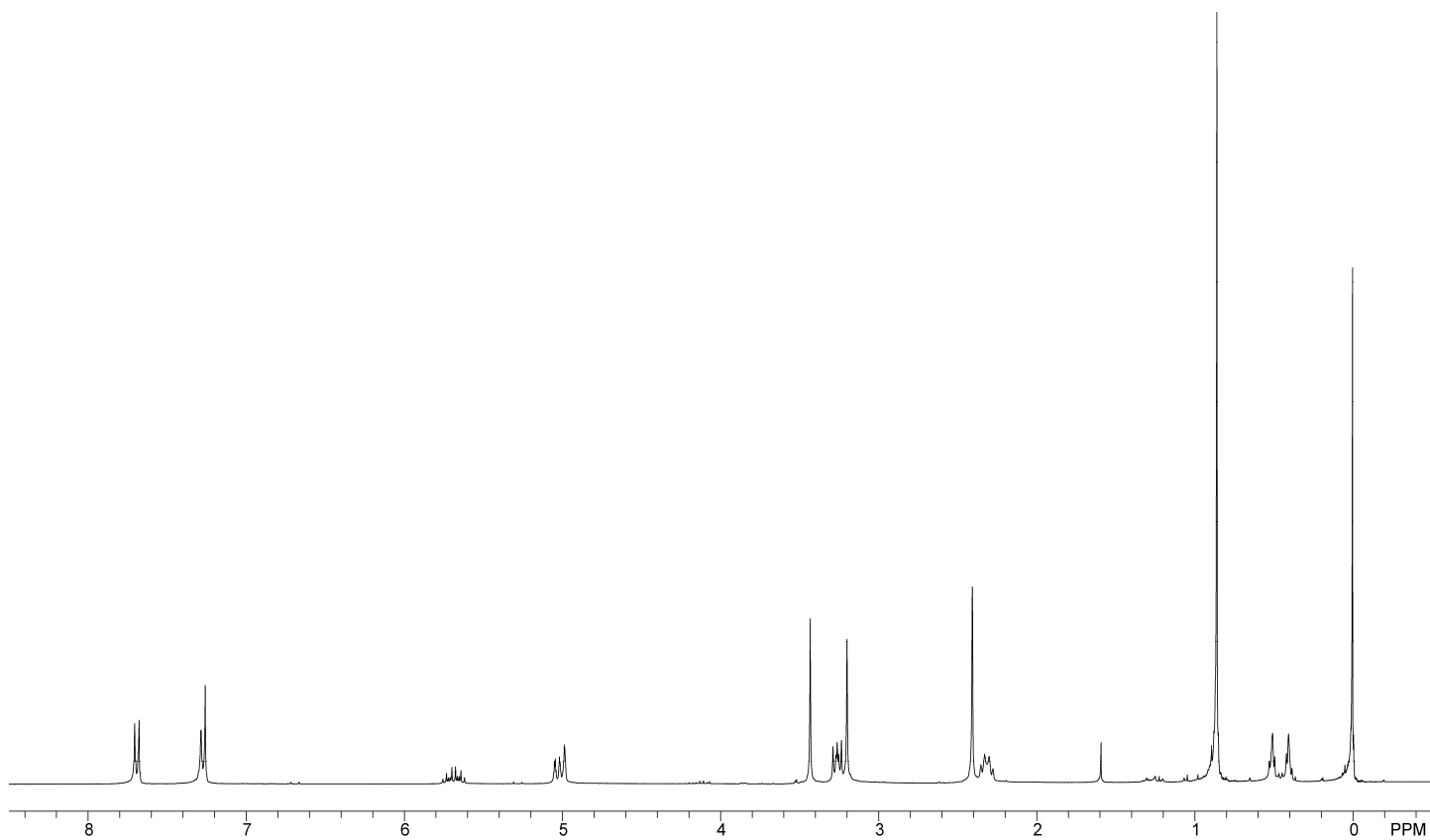
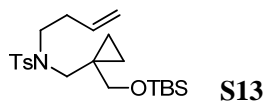


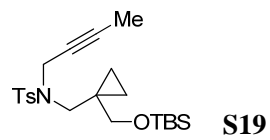
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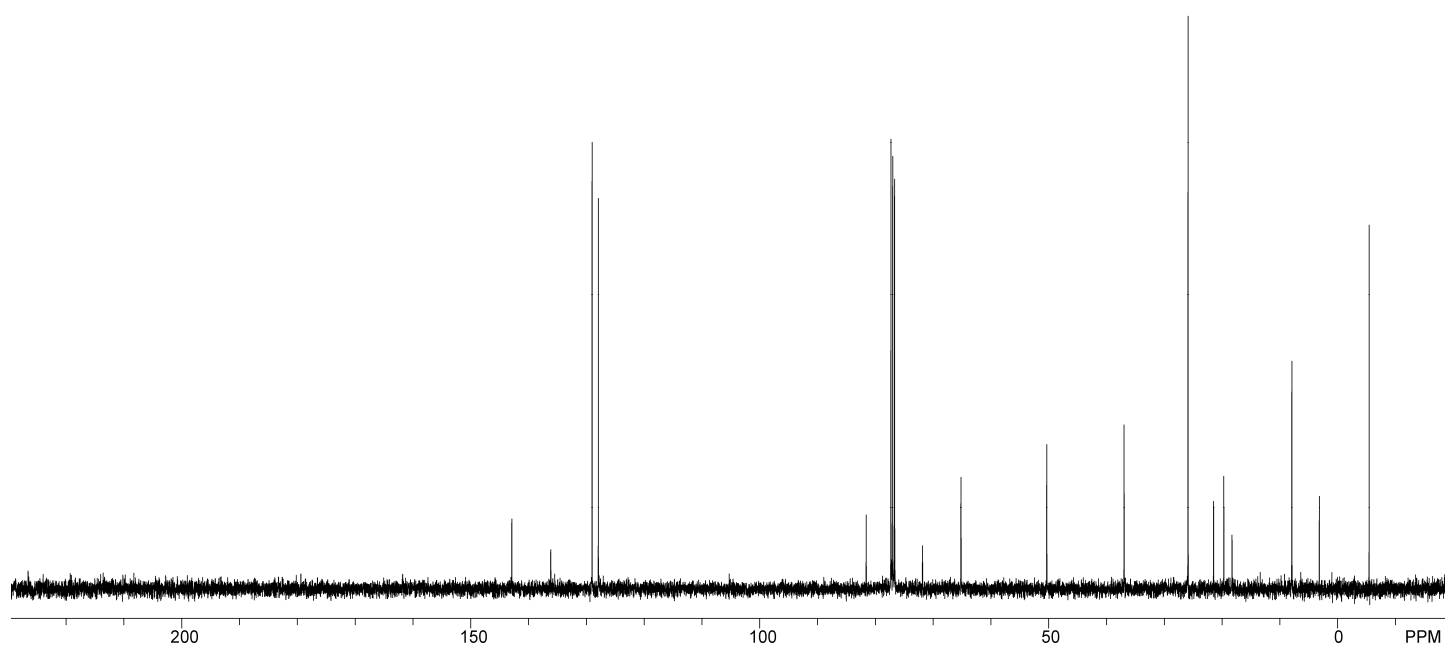
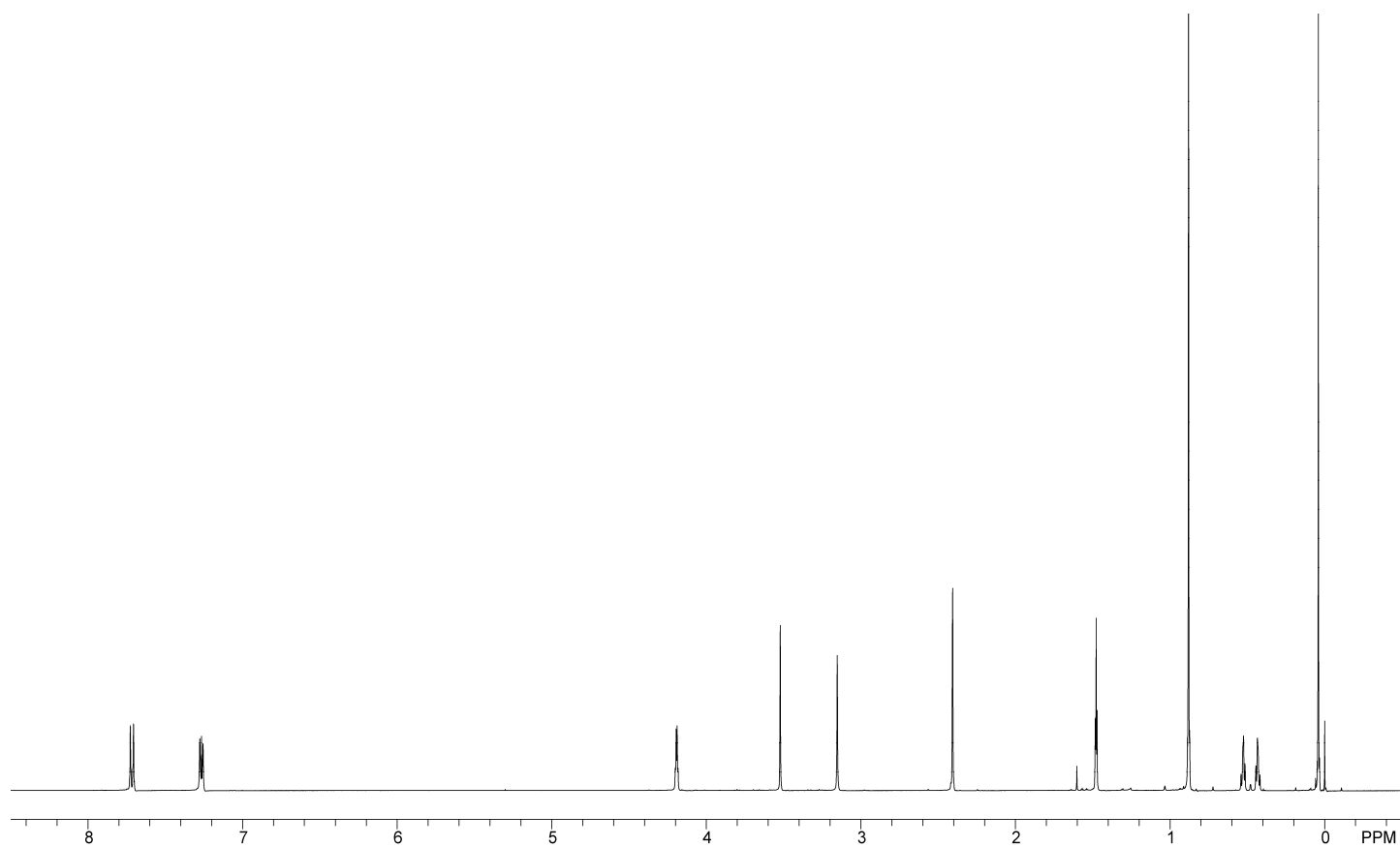


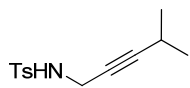






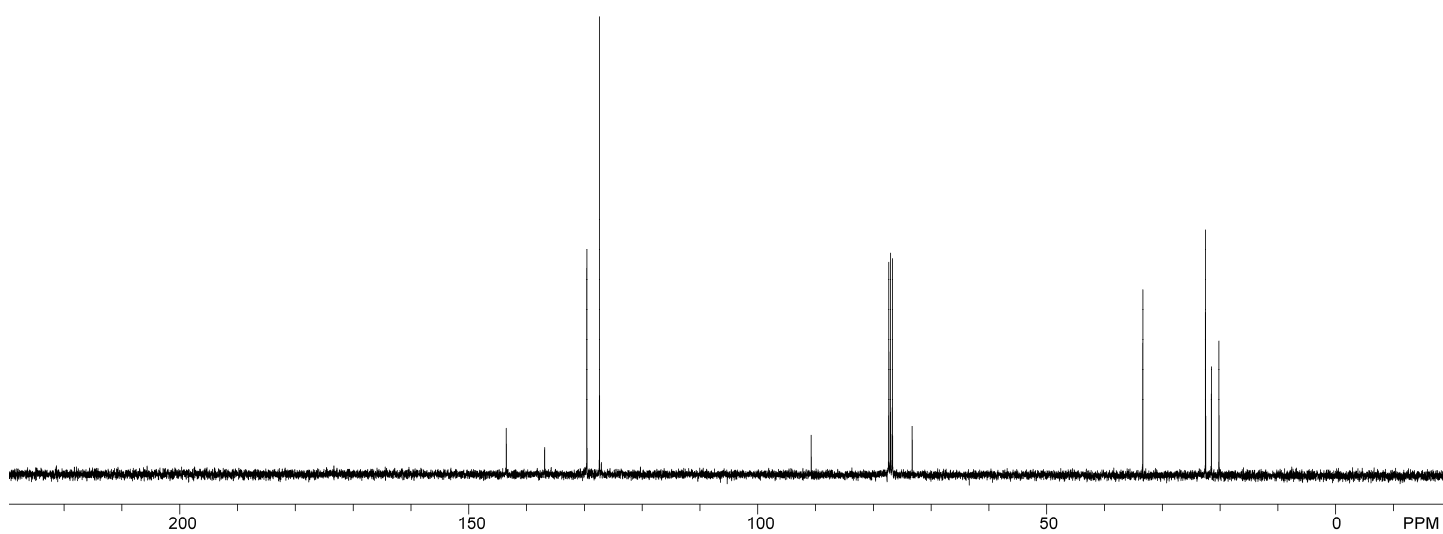
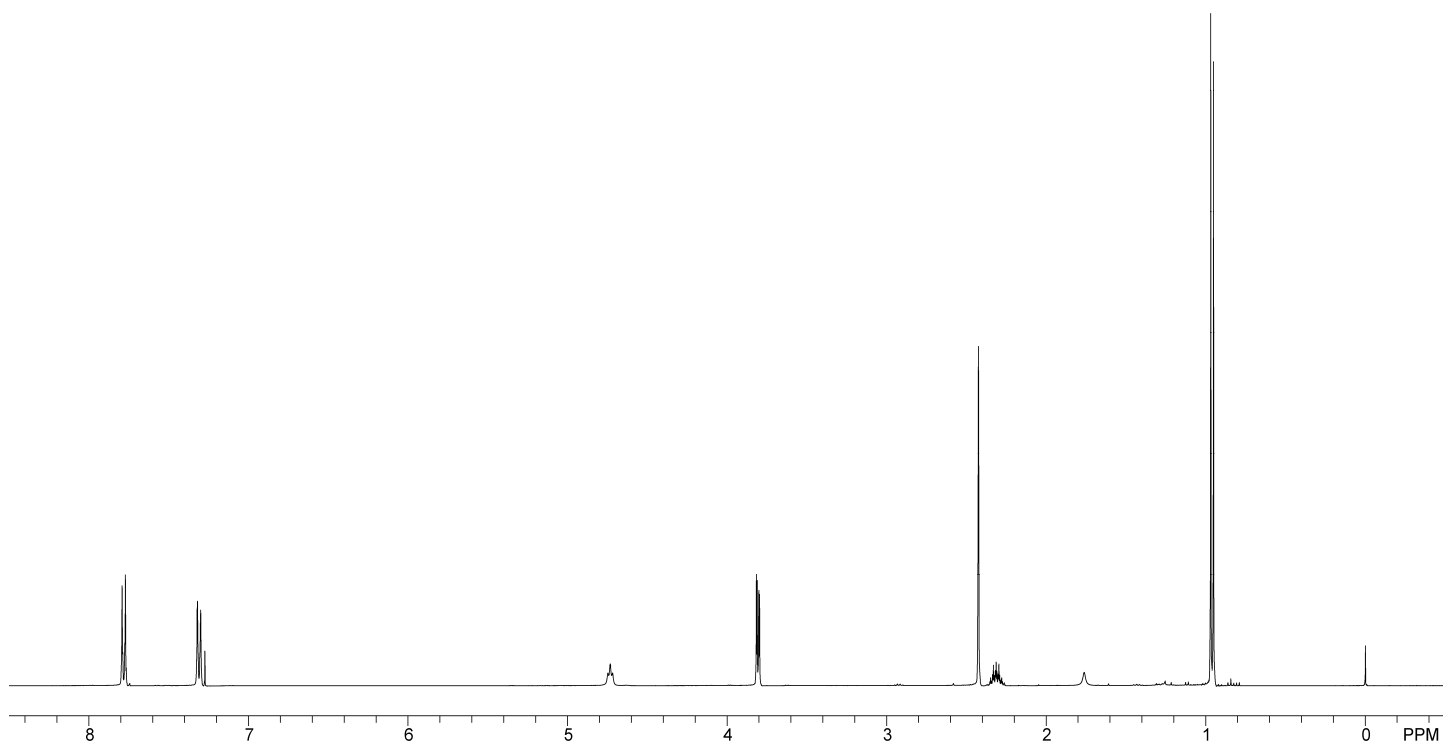
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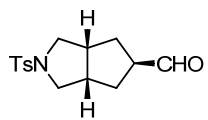




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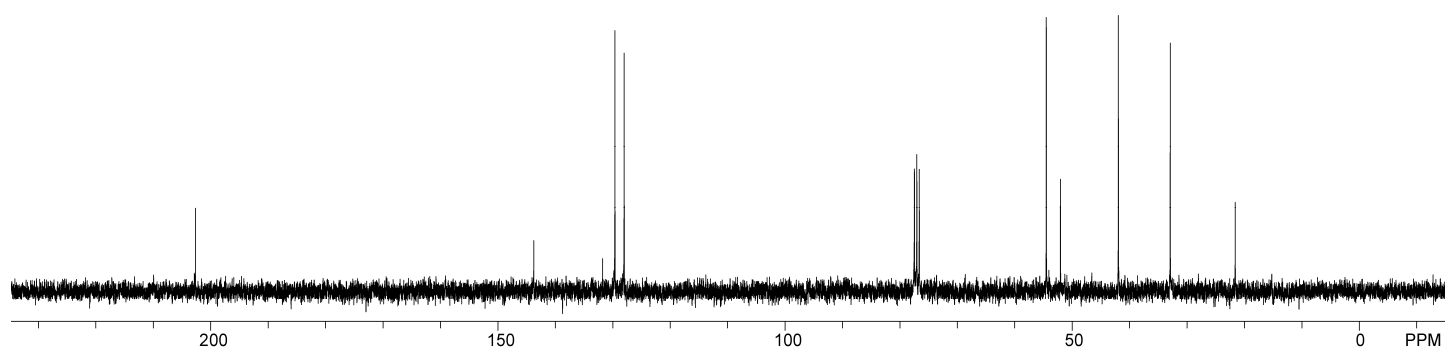
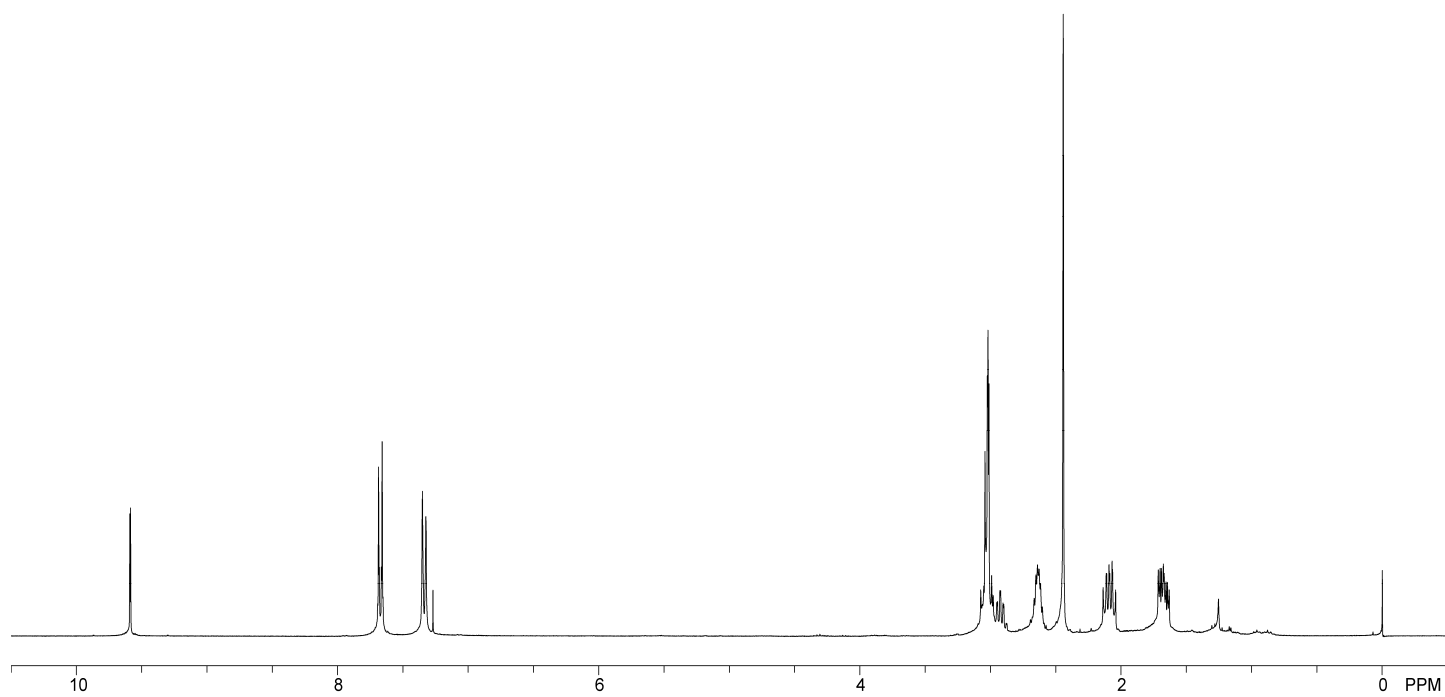
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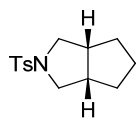




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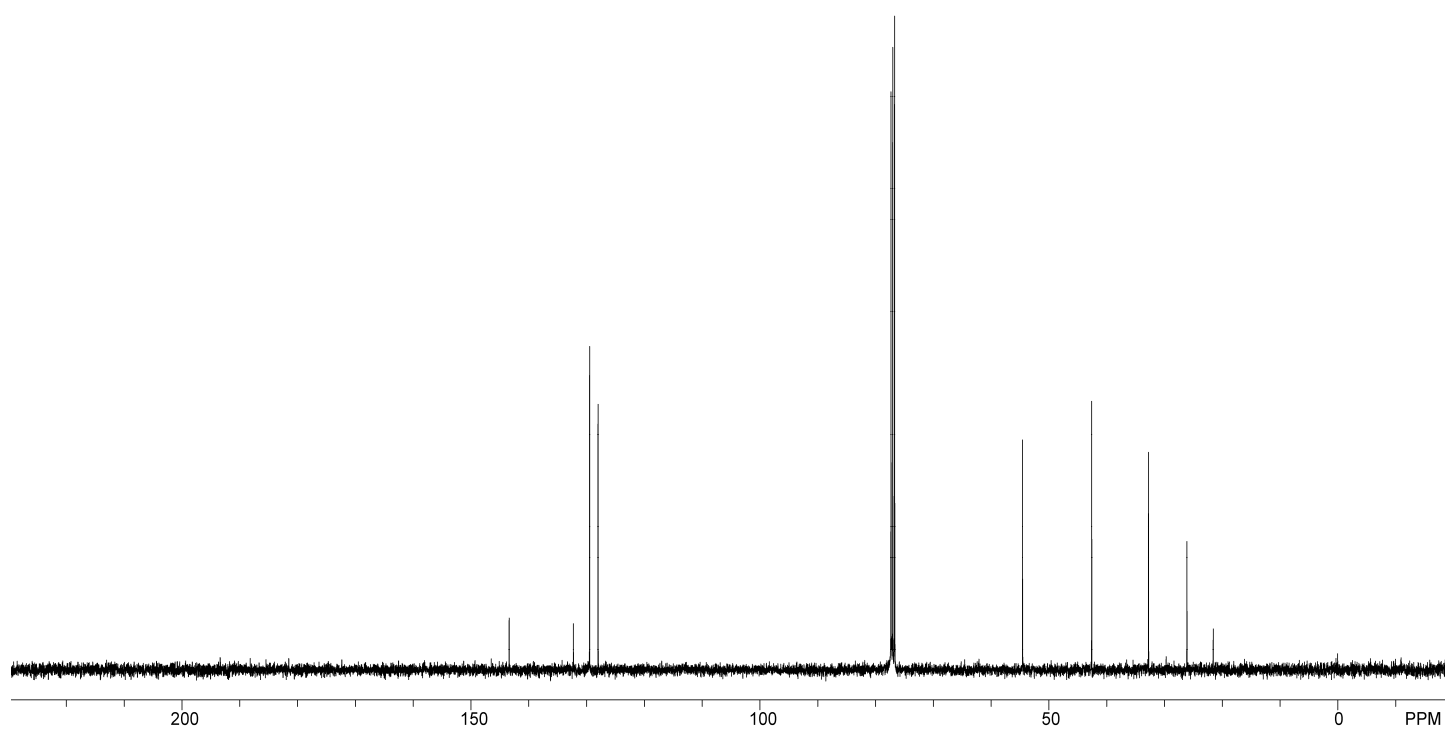
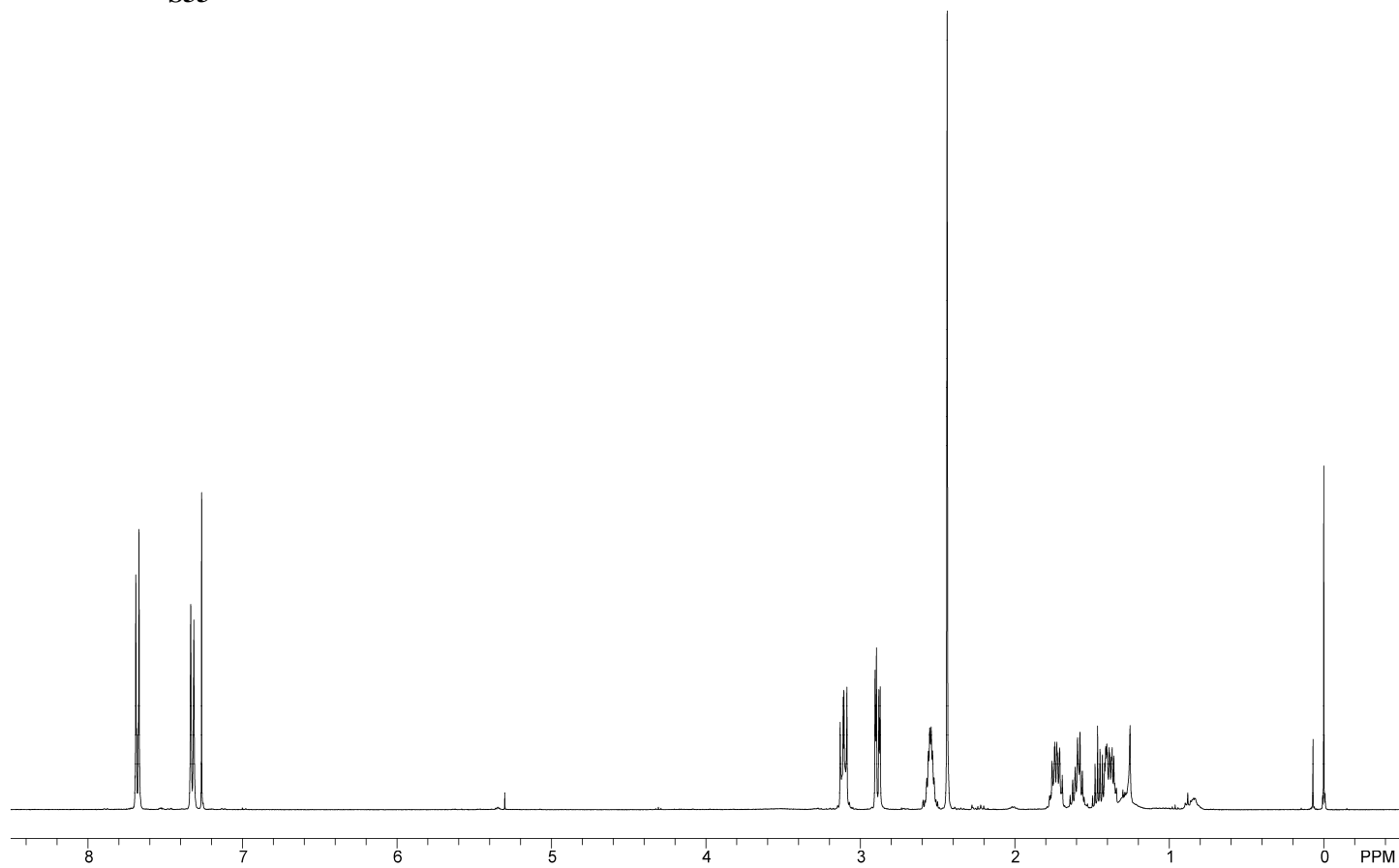
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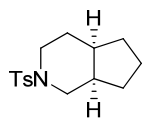


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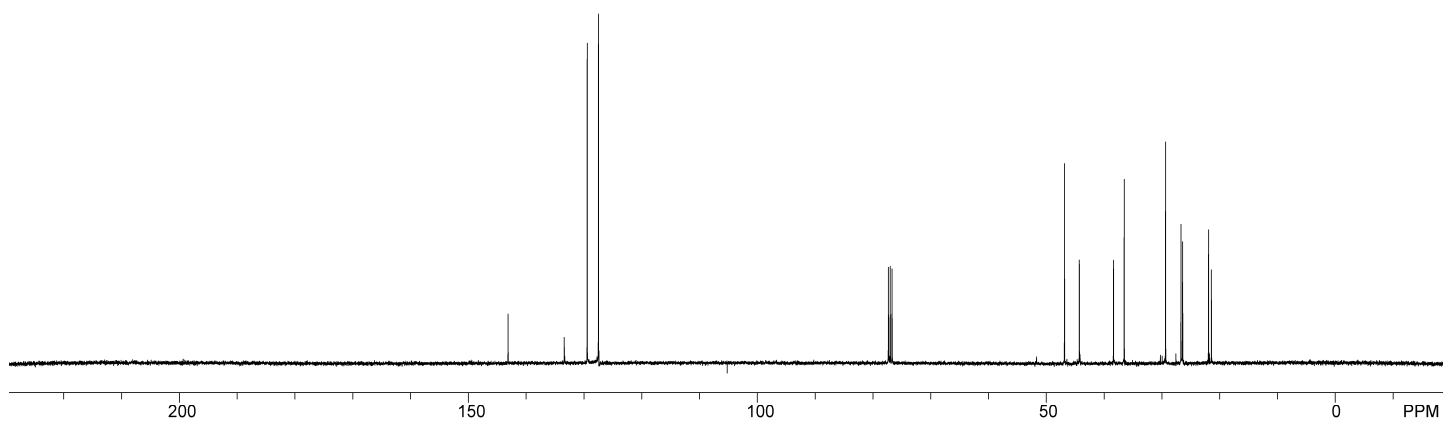
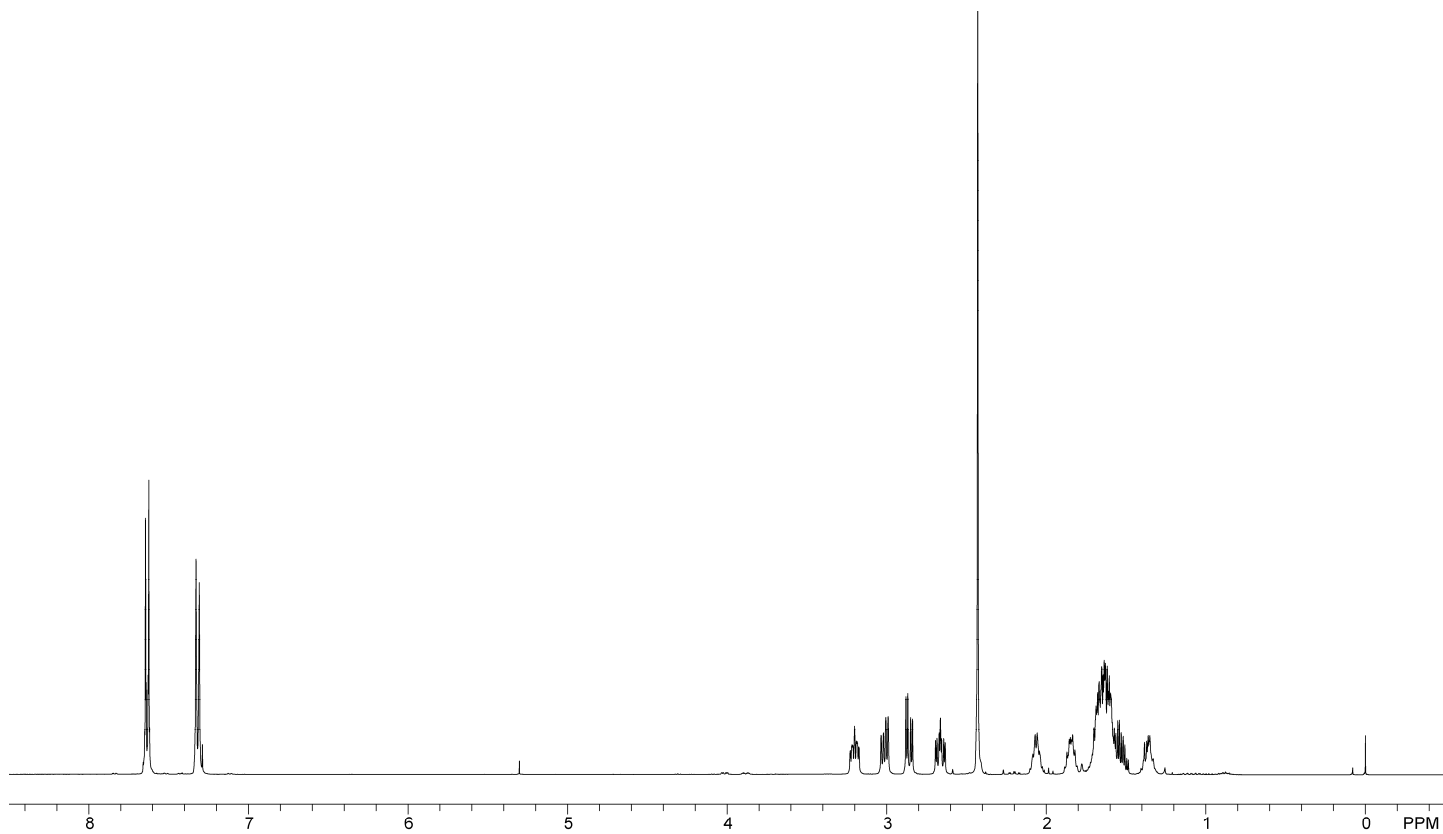


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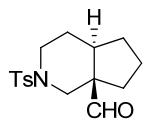


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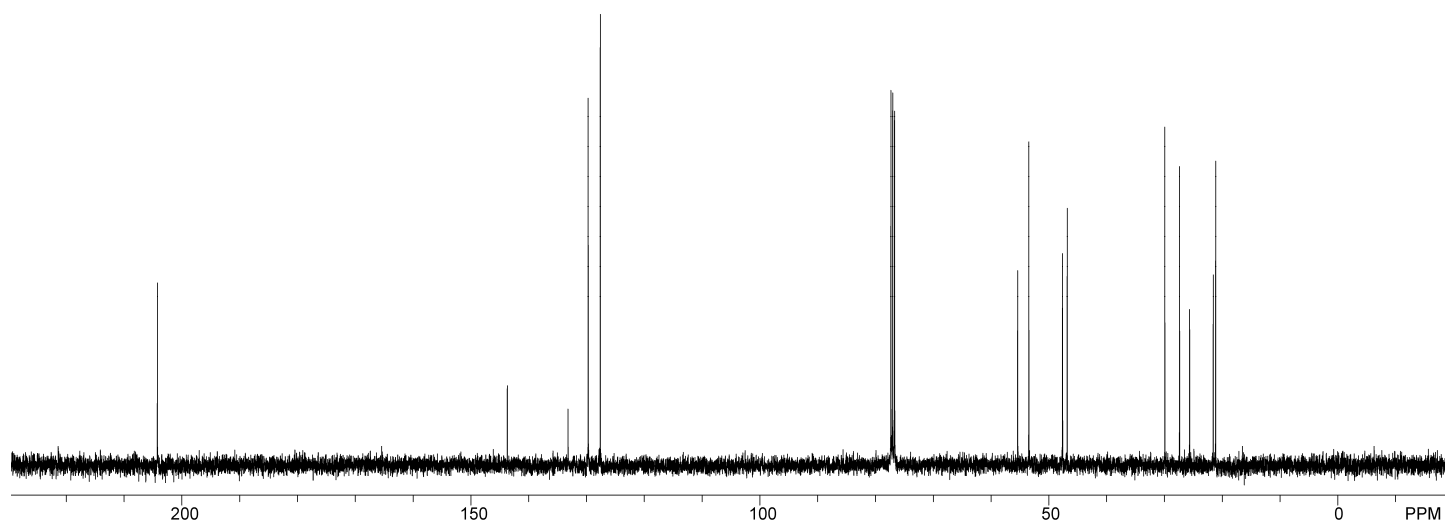
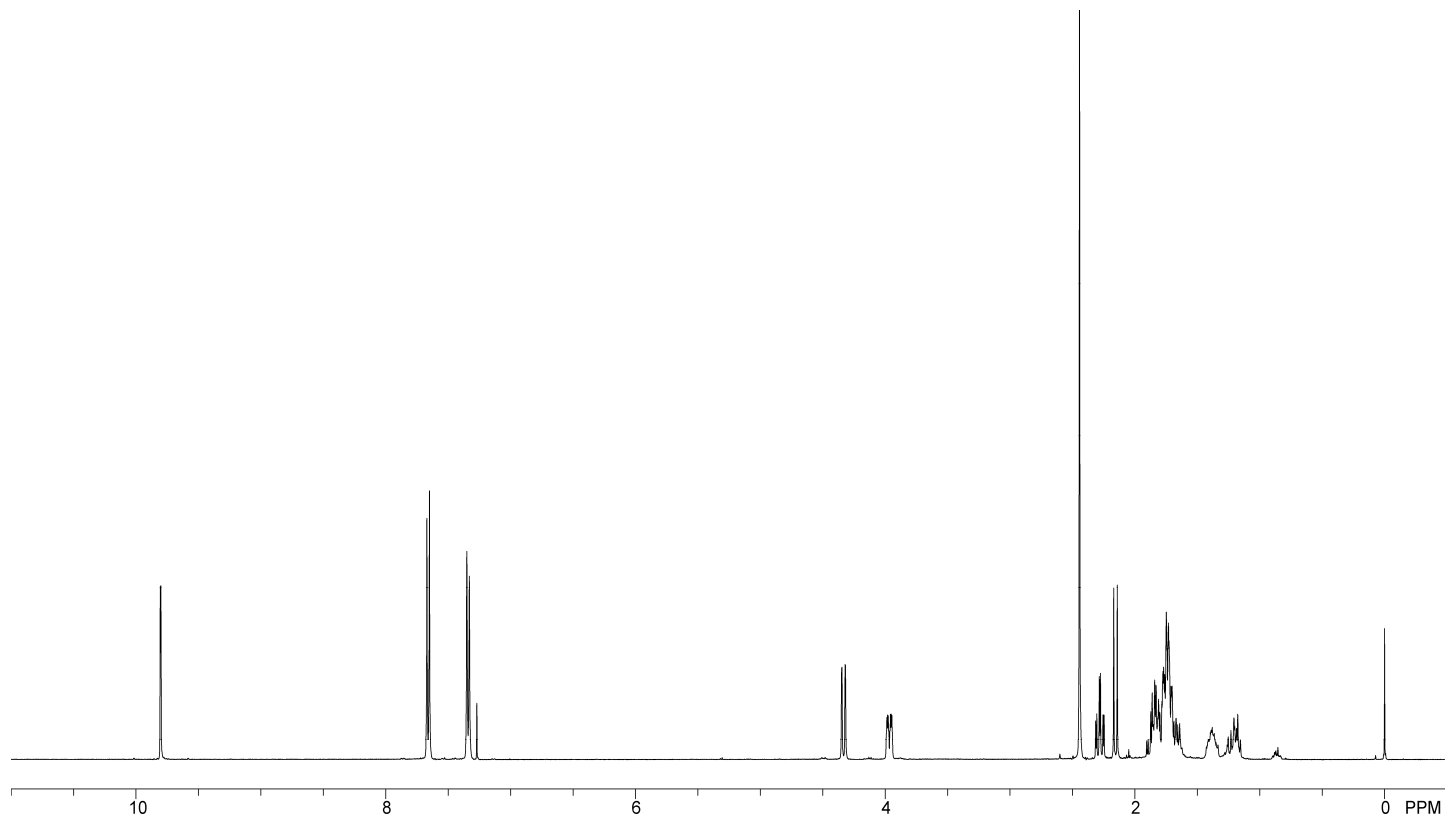


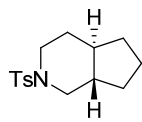
S61



S41

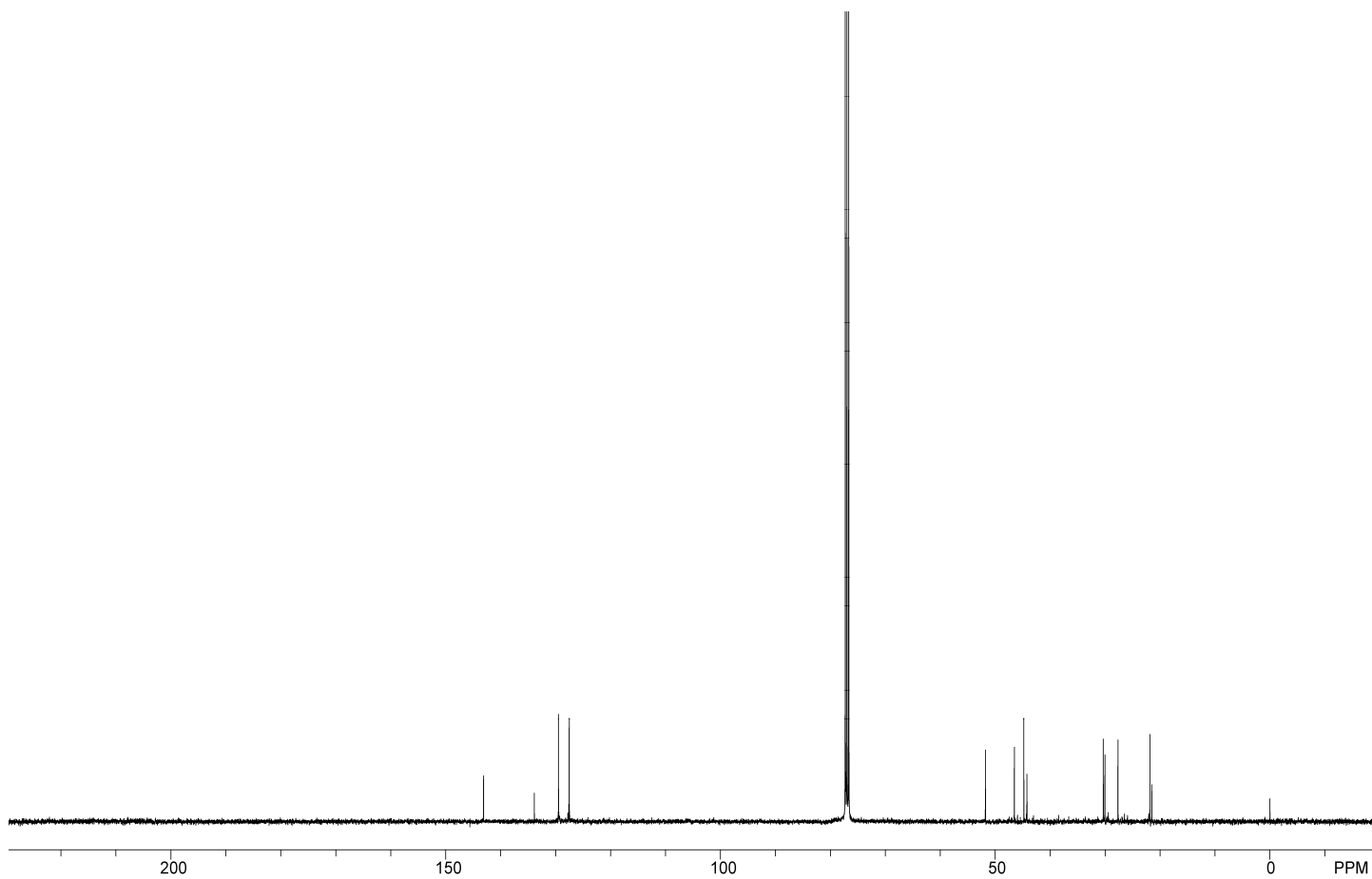
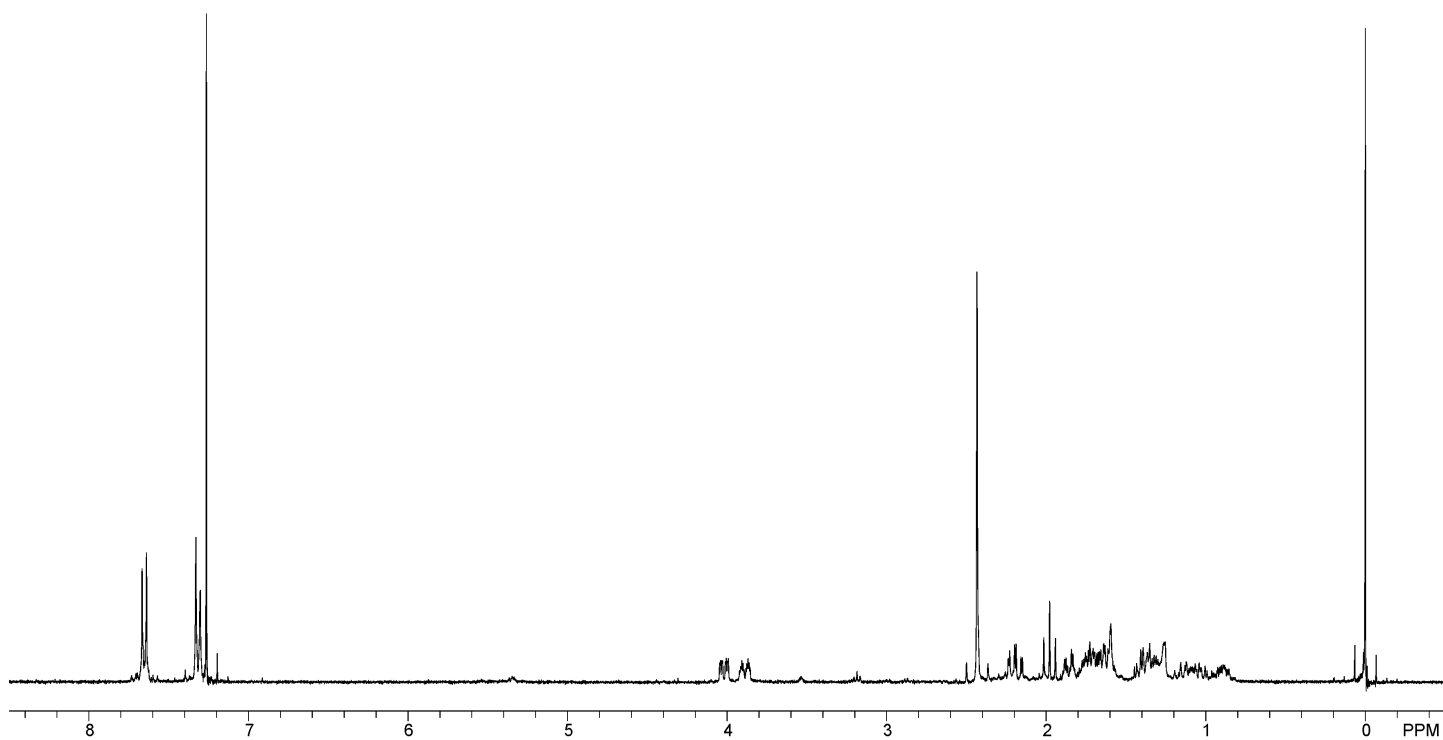
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