New Initiation Modes for Directed Carbonylative C-C Bond Activation: Rhodium-Catalyzed (3+1+2) Cycloadditions of Aminomethylcyclopropanes

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Supporting Information

Table of Contents

General Experimental Details. Starting materials sourced from commercial suppliers were used as received unless otherwise stated. Dry solvents, where necessary, were obtained by distillation using standard procedures or by passage through a column of anhydrous alumina using equipment from Anhydrous Engineering based on the Grubb's design.[1] Petrol refers to the fraction of petroleum ether boiling in the range of 40-60 °C. The removal of solvents *in vacuo* was achieved using both a Büchi rotary evaporator (bath temperatures up to 45 °C) at a pressure of either 15 mmHg (diaphragm pump) or 0.1 mmHg (oil pump), as appropriate, and a high vacuum line at r.t.. Reactions requiring anhydrous conditions were run under an atmosphere of dry nitrogen or argon; glassware, syringes and needles were either flame dried immediately prior to use or placed in an oven (200 °C) for at least 2 h and allowed to cool either in a desiccator or under an atmosphere of nitrogen or argon; liquid reagents, solutions or solvents were added *via* syringe through rubber septa; solid reagents were added *via* Schlenk type adapters. Commerically available Merck Kieselgel $60F_{254}$ aluminium backed plates were used for TLC analysis. Visualisation was achieved by either UV fluorescence, basic $KMnO_4$ solution and heat. Flash column chromatography (FCC) was performed using silica gel (Aldrich 40-63 μm, 230-400 mesh). The crude material was applied to the column as a solution in CH_2Cl_2 or by pre-adsorption onto silica, as appropriate. Melting points were determined using a Reichert melting point table and temperature controller and are uncorrected. Infra-red spectra were recorded in the range 4000-600 cm^{-1} on a Perkin Elmer Spectrum either as neat films or solids compressed onto a diamond window. Abbreviations used are: w (weak), m (medium) or s (strong). NMR spectra were recorded using either a Varian 400 MHz or Varian 500 MHz spectrometer. Chemical shifts (δ) are quoted in parts per million (ppm), coupling constants (*J*) are given in Hz to the nearest 0.5 Hz. Other abbreviations used are s (singlet), d (doublet), t (triplet), m (multiplet) and br. (broad). ^{1}H and ^{13}C NMR spectra were referenced to the appropriate residual solvent peak. ^{19}F spectra were referenced to CCl_3F as an external standard, ^{31}P spectra were referenced to H_3PO_4 as external standards. Assignments of ^{1}H NMR and ^{13}C NMR signals were made, where possible, using COSY, HMQC, HMBC, NOE and TOCSY experiments. Where mixtures of isomers (e.g. diastereomers and/or rotamers) have been characterized together, they are referred to as *A* and *B. Numbering systems for NMR signal assignments are specified on the structure and are not related to those used for the compound names*. Mass spectra were determined by the University of Bristol mass spectrometry service by either electron impact (ESI^+) or chemical ionization (CI^+) using a Fisons VG Analytical Autospec spectrometer.

Experimental Procedures and Data

General Procedure A for protection of cyclopropylmethanamines

To a stirred solution of cyclopropylamine (100 mol%) and triethylamine (120 mol%) in dichloromethane (0.2 M) was added the corresponding acid chloride/sulfonyl chloride (120 mol%) dropwise over 10 minutes at 0 °C under an atmosphere of nitrogen. The mixture was warmed to r.t. and stirred overnight. The mixture was diluted with water (10 mL/mmol) and extracted with dichloromethane (3 × 10 mL/mmol). Organic extracts were combined, washed with brine (10 mL/mmol), dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography under the conditions noted to yield the desired product.

General Procedure B for alkylation of protected cyclopropylmethanamines

To a solution of NaH (500 mol%, 60 % dispersion in mineral oil) in THF (0.3 M) was added a solution of protected aminocyclopropane (100 mol%) in THF (2.0 M) and the reaction was stirred at r.t. for 1 h. Allyl bromide (500 mol%) or (bromomethyl)cyclopropane (200 mol%) was added dropwise over 5 mintues at 0 °C and the reaction was stirred at r.t. for 18 h. Water (5 mL/mmol) was added and the mixture was extracted with Et_2O (3 × 2 mL/mmol). Then the organic extracts were combined, washed with brine (5 mL/mmol), dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography under the conditions noted to yield the desired product.

General Procedure C for preparation of substituted cyclopropylcarboxamides from substituted cyclopropanecarboxylic acid

To an ice-cold stirring solution of allylamine (100 mol%), EDCI (110 mol%) and DMAP (100 mol%) in anhydrous CH_2Cl_2 (0.5 M) under an atmosphere of nitrogen was added substituted cyclopropanecarboxylic acid (110 mol%) in CH_2Cl_2 (2.0 M) dropwise over 5 minutes. The mixture was warmed to r.t. and stirred overnight. Then the mixture was concentrated *in vacuo* and suspended in aq. 1M NaOH (5 mL/mmol) and extracted with EtOAc (3 × 5 mL/mmol). The organic extracts were combined and washed with 1M HCl (5 mL/mmol), brine (5 mL/mmol), dried over Na_2SO_4 and concentrated *in vacuo* to yield the desired product which was pure enough to be used without further purification.

General Procedure D for reduction of substituted cyclopropylcarboxamides

Substituted cyclopropylcarboxamides (100 mol%) in anhydrous THF (0.2 M) was added dropwise to an ice-cold suspension of $LiAlH_4$ (150 mol%) in THF (2.0 M) over 5 minutes. The solution was warmed to r.t. and then heated at reflux for 18 h. The reaction was cooled to r.t. and carefully added H_2O (0.5 mL/mmol), aq. 4M NaOH (0.5 mL/mmol), and H_2O (2 mL/mmol), and stirred for 0.5 h. Then the crude mixture was filtered through a pad of Celite®, the filtrate was extracted with Et_2O (3 × 5 mL/mmol) and the organic extracts combined and washed with brine (5 mL/mmol), dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography under the conditions noted to yield desired product.

General Procedure E for protection of substituted cyclopropylmethanamines

To a solution of cyclopropylmethanamine (100 mol%) in anhydrous toluene (0.2 M) was added potassium carbonate (200 mol%) and benzyl chloroformate/ sulfonyl chloride (200 mol%). The reaction mixture was heated to 50 °C and stirred overnight. The suspension was cooled to r.t. and water (10 mL/mmol) was added, the aqueous layer was extracted with EtOAc (3 × 10 mL/mmol) and the organic extracts combined, dried over Na_2SO_4 and concentrated *in vacuo.* The residue was purified by column chromatography under the conditions noted to yield the desired product.

General Procedure F for addition of Grignard reagent to imines

To a solution of imine (100 mol%) in THF (0.2 M) at -78 °C was added $BF_3.Et_2O$ (110 mol%) over 5 mintues, and the solution was stirred for 15 mins at -78 °C. Then the corresponding Grignard reagent (120 mol%) was added dropwise over 10 minutes. The solution was stirred at -78 °C for 6 h and then quenched with acetic acid (0.5 mL/mmol). The solution was warmed to r.t. and sat. aq. $NaHCO_3$ solution (15 mL/mmol) was added. The mixture was extracted with Et_2O (3 × 15 mL/mmol) and the organic extracts were combined, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography to yield the desired compound.

General Procedure G ('Conditions A'):

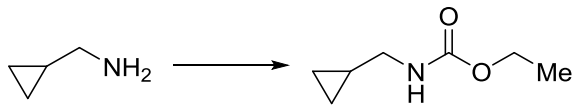
An oven dried reaction tube, fitted with a magnetic stirrer, was charged with $[Rh(cod)Cl]_2$ (3.75 mol%) and $AsPh_3$ (7.5 mol%), the tube was fitted with a rubber septum and purged with argon. Then cyclopropylmethanamine substrates (100 mol%) in anhydrous mesitylene (0.18

M) was added by syringe. The reaction mixture was purged with CO for 10 minutes and subsequently sparged with CO for ca. 10 seconds, then heated at 140 °C under a CO atmosphere (1 atm) for 72 h. The mixture was cooled to r.t., concentrated *in vacuo* and purified by flash column chromatography under the conditions noted to afford the desired product.

General Procedure H ('Conditions B'):

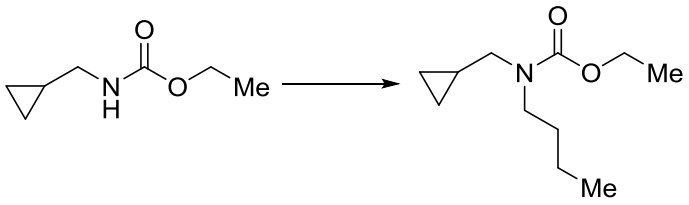
An oven dried reaction tube, fitted with a magnetic stirrer, was charged with $[Rh(CO)_2Cl]_2$ (5.0 mol%), Na_2SO_4 (20.0 mol%), the tube was fitted with a rubber septum and purged with argon. Cyclopropylmethanamine substrates (100 mol%) in anhydrous mesitylene (0.3 M) was added by syringe, then 1,4-oxathiane (30 mol%) was added by microlitre syringe. The reaction mixture was purged with CO for 10 minutes and subsequently sparged with CO for ca. 10 seconds, then heated at 140 °C under a CO atmosphere (1 atm) for 72 h. The mixture was cooled to r.t., concentrated *in vacuo* and purified by flash column chromatography under the conditions noted to afford the desired product.

Ethyl (cyclopropylmethyl)carbamate



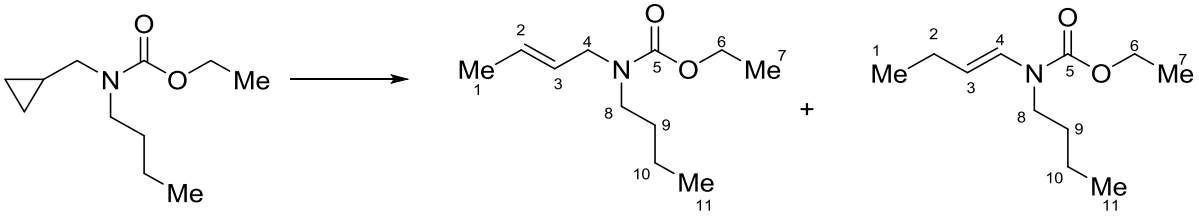
General procedure A: Cyclopropylmethylamine (0.82 g, 11.5 mmol) and ethyl carbonochloridate (1.21 mL, 12.7 mmol) were employed, the crude mixture was purified by flash column chromatography (0-30 % EtOAc/hexane) to afford the title compound (1.60 g, 97 %) as a colourless oil; ν_{max} / cm^{-1}: 3330 (m), 1691 (s), 1525 (s), 1242 (s), 1136 (m), 1030 (s); ^1H NMR ($CDCl_3$, 400 MHz): δ 4.85 (1H, br. m), 4.07 (2H, q, *J* = 7.0 Hz), 3.00 (2H, br. t, *J* = 6.5 Hz), 1.20 (3H, t, *J* = 7.0 Hz), 0.91 (1H, m), 0.47 – 0.43 (2H, m), 0.16 – 0.13 (2H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 156.7, 60.1, 45.9, 14.7, 11.1, 3.3; *m/z* (CI^+) HRMS: Calculated for $C_7H_{14}NO_2$: 144.1025. Found $[M+H]^+$: 144.1021.

Ethyl butyl(cyclopropylmethyl)carbamate (4a)



To a solution of ethyl (cyclopropylmethyl)carbamate (1.30 g, 9.1 mmol), NaOH (2.72 g, 68.2 mmol), K_2CO_3 (2.82 mg, 20.5 mmol) and NBu_4HSO_4 (308 mg, 0.9 mmol) in toluene (45 mL) was added 1-bromobutane (2.93 mL, 27.3 mmol). The reaction mixture was heated at reflux for 18 h and then cooled to r.t.. Water (100 mL) was added and the solution was extracted with Et_2O (3 × 30 mL). The organic extracts were combined, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography (5-10 % EtOAc/hexane) to afford the title compound **4a** (975 mg, 54 %) as a colourless oil; ν_{max} / cm^{-1}: 1693 (s), 1470 (m), 1421 (m), 1250 (m), 1169 (s), 1018 (m); ^1H NMR ($CDCl_3$, 400 MHz): δ 4.11 (2H, q, *J* = 7.0 Hz), 3.28 (2H, br. t, *J* = 7.5 Hz), 3.17 – 3.06 (2H, br. m), 1.56 – 1.48 (2H, m), 1.34 – 1.23 (5H, m), 1.00-0.89 (4H, m), 0.50 – 0.45 (2H, m), 0.23 – 0.16 (2H, br. m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 156.6, 61.0, 51.4, 47.2, 46.6*, 30.7, 30.4*, 20.2, 14.9, 14.0, 10.4, 3.6. **Doubling of some peaks due to two different conformers in solution. m/z* (CI^+) HRMS: Calculated for $C_{11}H_{22}NO_2$: 200.1651. Found $[M+H]^+$: 200.1648.

(*E*)-Ethyl but-2-en-1-yl(butyl)carbamate and (*E*)-ethyl but-1-en-1-yl(butyl)carbamate (10a)



4a **A** 3:1 mixture of stereoisomers **10a** **B**

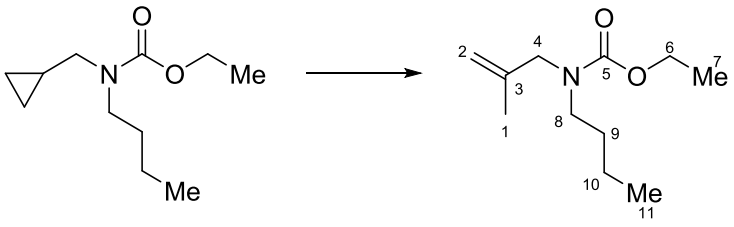
To a sealed tube containing $[Rh(cod)_2]BF_4$ (10.2 mg, 0.025 mmol) and triphenylphosphine (19.8 mg, 0.076 mmol) under an argon atmosphere was added carbamate **4a** (100 mg, 0.503 mmol) in anhydrous toluene (5.0 mL). The tube was sealed and heated to 140 °C for 4 h. The reaction was cooled to r.t. and concentrated *in vacuo. An in situ yield of alkene **10a**-A (11%) and vinyl carbamate **10a**-B (74%) was obtained by ^1H NMR against 1,4-dinitrobenzene as an*

internal standard. The residue was purified by flash column chromatography (0-3 % EtOAc/toluene) to afford vinyl carbamate **10a-**B (73 mg, 73 %) as a colourless oil and alkene **10a-**A (8 mg, 8 %, mixture of stereoisomers in a 3:1 (A:B) ratio) as colourless oils.

Data for alkene **10a-**A: ν_{max} / cm-1: 2959 (m), 1696 (s), 1467 (m), 1420 (m), 1380 (m), 1223 (s), 1149 (m), 1095 (m); ^{1}H NMR (CD_3CN, 400 MHz): δ 5.67-5.60 (2H, m, 1 × C**2**-H, A+B), 5.49 – 5.40 (2H, m, 1 × C**3**-H, A+B), 4.08 (4H, q, *J* = 7.0 Hz, 2 × C**6**-H_2, A+B), 3.91 (1H, br. d, *J* = 6.5 Hz, 1 × C**4**-H_2, B), 3.78 (2H, br. d, *J* = 6.0 Hz, 1 × C**4**-H_2, A), 3.20 (4H, t, *J* = 7.5 Hz, 2 × C**8**-H_2, A+B), 1.70 (6H, dd, *J* = 6.5, 1.5 Hz, 3 × C**1**-H_3, A+B), 1.54 – 1.48 (4H, m, 2 × C**9**-H_2, A+B), 1.34 – 1.27 (4H, m, 2 × C**10**-H_2, A+B), 1.23 (6H, t, *J* = 7.0 Hz, 3 × C**7**-H_3, A+B), 0.96 – 0.93 (6H, m, 3 × C**11**-H_3, A+B); ^{13}C NMR (CD_3CN, 100 MHz): δ 157.1 (C**5**, A+B), 128.8 (C**2**, A+B), 128.0 (C**3**, A), 127.8 (C**3**, B), 61.6 (C**6**, A+B), 49.3 (C**4**, A), 46.5 (C**8**, A+B), 44.0 (C**4**, B), 31.1 (C**9**, A+B), 20.7 (C**10**, A+B), 17.8 (C**1**, A), 15.1 (C**7**, A+B), 14.1 (C**11**, A+B), 13.0 (C**1**, B); *m/z* HRMS: (CI^+) Calculated for $C_{11}H_{22}NO_2$: 200.1651. Found $[M+H]^+$: 200.1656.

Data for vinyl carbamate **10a-**B: ν_{max} / cm^{-1}: 2960 (m), 1703 (s), 1661 (m), 1464 (m), 1411 (s), 1320 (m), 1245 (m), 1152 (s), 1030 (m); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.82 (1H, br. m, 1 × C**4**-H), 5.02 (1H, dt, *J* = 14.5, 6.5 Hz, 1 × C**3**-H), 4.17 (2H, q, *J* = 7.0 Hz, 2 × C**6**-H_2), 3.51 (2H, t, *J* = 7.5 Hz, 2 × C**8**-H_2), 2.11-2.06 (2H, m, 2 × C**2**-H_2), 1.54 (2H, tt, *J* = 7.5, 6.5 Hz, 2 × C**9**-H_2), 1.38-1.31 (2H, m, 2 × C**10**-H_2), 1.28 (3H, t, *J* = 7.0 Hz, 3 × C**7**-H_3), 1.02 (3H, t, *J* = 7.5 Hz, 3 × C**1/11**-H_3), 0.96 (3H, t, *J* = 7.5 Hz, 3 × C**1/11**-H_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 126.3 (C**4**), 111.2 (C**3**), 62.1 (C**6**), 43.9 (C**8**), 29.7 (C**9**), 23.9 (C**2**), 20.3 (C**10**), 14.9, 14.4, 13.7 (C**1**, C**7** and C**11**); *m/z* HRMS: (CI^+) Calculated for $C_{11}H_{22}NO_2$: 200.1651. Found $[M+H]^+$: 200.1645.

Ethyl butyl(2-methylallyl)carbamate (10a')

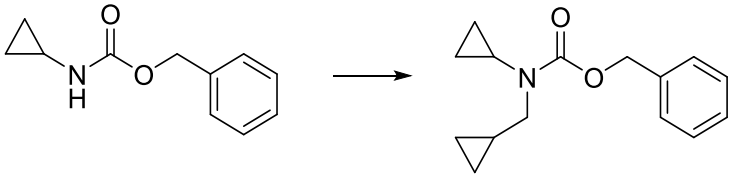


4a **10a'**

To a sealed tube containing $[Rh(cod)Cl]_2$ (6.2 mg, 0.012 mmol) and PPh_3 (19.8 mg, 0.076 mmol) under an argon atmosphere was added carbamate **4a** (100 mg, 0.503 mmol) in anhydrous toluene (5.0 mL). The tube was sealed and heated to 140 °C for 4 h. The reaction was cooled to r.t. and concentrated in *vacuo*. *An in situ yield was obtained by ^{1}H NMR against 1,4-dinitrobenzene as an internal standard; a 3% yield of alkene **10a'** and 93% of remaining starting material **4a** were observed. Extending the reaction time to 60 h resulted in a 26% in situ yield of alkene **10a'**, however, the product could not be readily separated from the starting material, the structure of alkene **10a'** was determined by analysis of the ^{1}H NMR of the reaction mixture.*

Data for alkene **10a'**: *Characteristic peaks only*: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.83-4.76 (2H, m, 2 × C**2**-$\underline{H}_2$), 3.80 (2H, br. m, 2 × C**4**-$\underline{H}_2$), 1.67 (3H, s, 3 × C**1**-$\underline{H}_3$).

Benzyl cyclopropyl(cyclopropylmethyl)carbamate (4b)

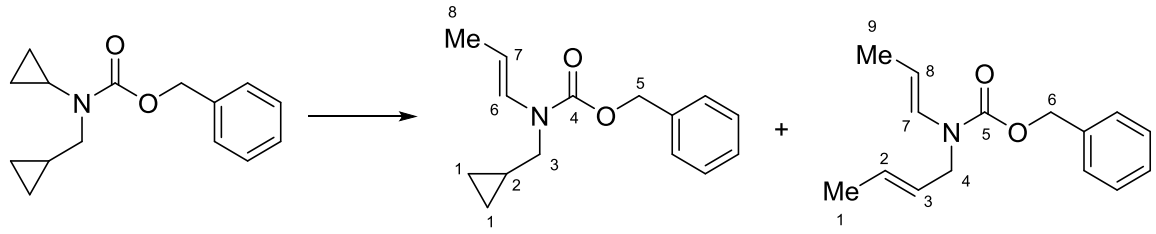


4b

To a solution of NaH (0.20 g, 5.0 mmol, 60% dispersion in mineral oil) in THF (5.0 mL) was added a solution of benzyl cyclopropylcarbamate (0.38 g, 2.5 mmol) (prepared according to literature procedure[2]) in THF (10 mL) and the reaction was stirred at r.t. for 1 h. (Bromomethyl)cyclopropane (0.65 g 5.0 mmol) was added dropwise over 5 mintues at r.t. and the reaction was heated to 50 °C and stirred for 12 h. Water (10 mL) was added and the mixture was extracted with Et_2O (3 × 5 mL), the organic extracts were combined, washed with brine (10 mL), dried over Na_2SO_4 and concentrated *in vacuo*. The crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound **4b** (0.44

g, 90 %) as a colorless oil; ν_{max} / cm^{-1}: 3081 (m), 1698 (s), 1453 (m), 1408 (s), 1277 (s), 1151 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 – 7.17 (5H, m), 5.15 (2H, s), 3.15 (2H, d, *J* = 6.9 Hz), 2.70 (1H, tt, *J* = 7.2, 3.9 Hz), 1.11 – 0.94 (1H, m), 0.82 – 0.73 (2H, m), 0.66 – 0.56 (2H, m), 0.50 – 0.42 (2H, m), 0.26 – 0.15 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.5, 137.0, 128.4, 127.8, 127.7, 66.9, 52.4, 29.1-28.8(m), 10.0, 8.3, 3.4; *m/z* (ESI^+) HRMS: Calculated for $C_{15}H_{19}NO_2Na$: 268.1308. Found $[M+Na]^+$: 268.1302.

Benzyl (*E*)-(cyclopropylmethyl) (prop-1-en-1-yl)carbamate and Benzyl ((*E*)-but-2-en-1-yl) ((*E*)-prop-1-en-1-yl)carbamate (11a and 11b)



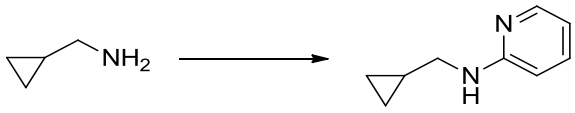
4b **11a** **11b**

Two oven dried reaction tubes (tube **I** and tube **II**), fitted with a magnetic stirrer, was charged with $[Rh(cod)_2]BF_4$ (4.10 mg, 0.01 mmol) and PPh_3 (7.86 mg, 0.03mmol). The tubes were fitted with a rubber septum and purged with argon. Benzyl cyclopropyl(cyclopropylmethyl)carbamate **4b** (49.20 mg, 0.20 mmol) in anhydrous toluene (2 mL) was added *via* syringe to each tube. The mixtures then were heated at 140 ^oC for 1h for tube **I**, and 3h for tube **II**. Then the reactions were cooled to r.t., concentrated *in vacuo* and purified by flash column chromatography (10 % EtOAc/Hex), respectively, the desired products were obtained as a mixture (for tube **I**, 92 %, **11a**/**11b**=13/1, for tube **II**, 90 %, **11a**/**11b** =7/3). *The products **11a** and **11b** could not be readily separated by column chromatography. The structure of the **11a** and **11b** were determined by analysis of the ^{1}H* NMR *of the mixture and corroborated by COSY data.*

Data for **11a**: *Characteristic peaks only*: ^{1}H NMR (400 MHz, CD_3CN, 65 ^oC): δ 5.21 (2H, s, 2 × C**5**-$\underline{H}_2$), 5.14 (1H, dq, *J* = 14.4, 6.6 Hz, 1 × C**7**-$\underline{H}$), 3.48 (2H, d, *J* = 6.7 Hz, 2 × C**3**-$\underline{H}_2$), 1.14 (1H, ttt, *J* = 8.1, 6.6, 5.0 Hz, 1 × C**2**-$\underline{H}$), 0.50 – 0.40 (2H, m, 2 × C**1**-$\underline{H}_2$), 0.34 – 0.18 (2H, m, 2 × C**1**-$\underline{H}_2$); *m/z* (ESI^+) HRMS: Calculated for $C_{15}H_{19}NO_2Na$: 268.1308. Found $[M+Na]^+$: 268.1295.

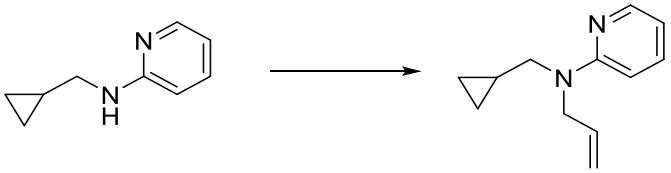
Data for **11b**: *Characteristic peaks only*: ^{1}H NMR (400 MHz, CD_3CN, 65 °C): δ 5.68 – 5.56 (1H, m, 1 × C**2**-H), 5.53 – 5.42 (1H, m, 1 × C**3**-H), 5.21 (2H, s, 1 × C**6**-H_2), 5.05 (2H, dq, *J* = 13.2, 6.5 Hz, 1 × C**8**-H), 4.15 – 4.06 (2H, m, 2 × C**4**-H_2). *m/z* (ESI^+) HRMS: Calculated for $C_{15}H_{19}NO_2Na$: 268.1308. Found $[M+Na]^+$: 268.1312.

_N_-(Cyclopropylmethyl)pyridin-2-amine



To a solution of cyclopropylmethanamine (1.42 g, 20 mmol) in DMSO (60 mL) at r.t. was added K_2CO_3 (5.52 g, 40 mmol) and 2-fluoropyridine (2.91 g, 30 mmol). The solution was stirred at 120 °C for 24 h and were cooled to r.t., then quenched with H_2O (60 mL) and extracted with EtOAc (2 × 60 mL), the organic extracts were combined, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography (10 % EtOAc/Hex) to yield the title compound (0.70 g, 24 %) as a colorless solid; m.p.: 43 – 45 °C (CH_2Cl_2/Hex); ν_{max} / cm^{-1}: 3270 (m), 3006 (m), 1600 (s), 1501 (m), 1444 (m), 1285 (m), 904 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.11 – 7.98 (1H, m), 7.45 – 7.34 (1H, m), 6.54 (1H, ddd, *J* = 7.2, 5.0, 1.1 Hz), 6.40 – 6.32 (1H, m), 4.64 (1H, br. s), 3.11 (2H, dd, *J* = 6.9, 5.7 Hz), 1.15 – 1.00 (1H, m), 0.56 – 0.50 (2H, m), 0.29 – 0.16 (2H, m); ^{13}C NMR: (100 MHz, $CDCl_3$): δ 158.8, 148.2, 137.3, 112.7, 106.6, 47.2, 10.8, 3.4; *m/z* (ESI^+) HRMS: Calculated for $C_9H_{13}N_2$: 149.1073. Found $[M+H]^+$: 149.1077.

_N_-Allyl-_N_-(cyclopropylmethyl)pyridin-2-amine (6a)

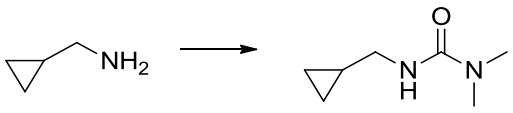


6a

General procedure B: *N*-(Cyclopropylmethyl)pyridin-2-amine (0.32 g, 2.1 mmol) and allyl bromide (1.26 g, 10.5 mmol) were employed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound **6a** (0.33 g, 85 %) as a colorless oil; ν_{max} / cm^{-1}: 3076 (m), 3004 (m), 1592 (s), 1485 (s), 1435 (m), 1244 (m), 977 (m); ^{1}H NMR (500 MHz, $CDCl_3$, 50 °C): δ 8.22 – 8.02 (1H, m), 7.46 – 7.31 (1H, m), 6.62 –

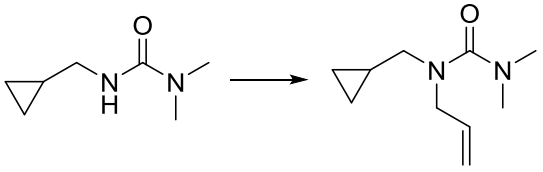
6.41 (2H, m), 5.86 (1H, ddt, *J* = 17.2, 10.2, 5.1 Hz), 5.21 – 5.04 (2H, m), 4.17 (2H, dd, *J* = 5.2, 1.8 Hz), 3.42 (2H, d, *J* = 6.5 Hz), 1.14 – 1.01 (1H, m), 0.58 – 0.39 (2H, m), 0.32 – 0.19 (2H, m); ^{13}C NMR: (127 MHz, $CDCl_3$, 50 °C): δ 158.3, 147.9, 136.9, 134.5, 115.7, 111.4, 106.0, 52.1, 50.7, 9.7, 3.6; *m/z* (ESI^+) HRMS: Calculated for $C_{12}H_{17}N_2$: 189.1386. Found $[M+H]^+$: 189.1393.

3-(Cyclopropylmethyl)-1,1-dimethylurea



General procedure A: Cyclopropylmethylamine (3.00 g, 42.0 mmol) and dimethylcarbamyl chloride (4.64 mL, 50.4 mmol) were employed, the crude mixture was recrystallized from Et_2O/Hex to yield the title compound (5.89 g, 80%) as a colorless solid; m.p.: 62 – 64 °C (EtOAc/Hex); ν_{max} / cm^{-1}: 3309 (s), 2919 (s), 1616 (s), 1532 (s), 1363 (s), 1223 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.53 (1H, br. s), 3.00 – 2.97 (2H, m), 2.83 (6H, s), 0.88 (1H, m), 0.41 – 0.37 (2H, m), 0.12 – 0.08 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.5, 45.8, 36.1, 11.3, 3.2; m/z (ESI^+) HRMS: Calculated for $C_7H_{14}N_2ONa$: 165.1001. Found $[M + Na]^+$: 165.0998.

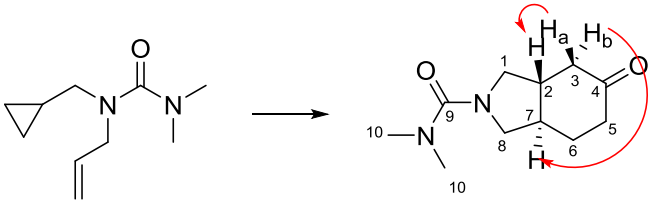
1-Allyl-1-(cyclopropylmethyl)-3,3-dimethylurea (6b)



6b

General procedure **B**: 3-(Cyclopropylmethyl)-1,1-dimethylurea (0.86 g, 6.0 mmol) allyl bromide (1.44 g, 12.0 mmol) were employed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound **6b** (0.95 g, 87 %) as a pale yellow oil; ν_{max} / cm^{-1}: 2920 (m), 1639 (s), 1488 (m), 1383 (m), 1198 (m), 1142 (m); ^{1}H NMR (400 MHz, $CDCl_3$, 50 °C): δ 5.87 – 5.68 (1H, m), 5.27 – 4.82 (2H, m), 3.95 – 3.79 (2H, m), 2.96 (2H, d, *J* = 6.7 Hz), 2.83 – 2.72 (6H, m), 1.01 – 0.88 (1H, m), 0.50 – 0.41 (2H, m), 0.16 – 0.05 (2H, m); ^{13}C NMR: (100 MHz, $CDCl_3$, 50 °C): δ 165.3, 134.9, 116.4, 52.2, 50.9, 38.6, 9.4, 3.5; *m/z* (ESI^+) HRMS: Calculated for $C_{10}H_{19}N_2O$: 183.1492. Found $[M+H]^+$: 183.1497.

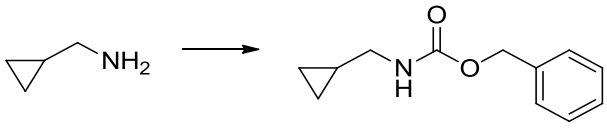
(3a*R, 7a*R**)-*N*,*N*-Dimethyl-5-oxooctahydro-2*H*-isoindole-2-carboxamide (8b)**



6b **8b**

General procedure G: Compound **3b** (27.3 mg, 0.15 mmol) was employed, the crude mixture was purified by column chromatography (80 % EtOAc/Hex) to yield the title compound **8b** (16.7 mg, 53 %, > 15:1 d.r.) as a colorless oil; ν_{max} / cm^{-1}: 2938 (m), 1711 (s), 1624 (s) 1500 (m), 1395 (s), 1369 (m); ^{1}H NMR (400 MHz, C_6D_6): δ 3.09 (1H, dd, *J* = 9.8, 6.6 Hz, 1 × C**8**-$\underline{H}_2$), 2.97 (1H, dd, *J* = 9.7, 6.6 Hz, 1 × C**1**-$\underline{H}_2$), 2.81 – 2.64 (2H, m, 1 × C**8**-$\underline{H}_2$, 1 × C**1**-$\underline{H}_2$), 2.49 (6H, s, 6 × C**10**-$\underline{H}_3$), 2.18 (1H, ddd, *J* = 14.0, 3.8, 1.9 Hz, 1 × C**5**-$\underline{H}_2$), 2.15 – 2.08 (1H, m, 1 × C**3**-$\underline{H}_2$), 1.68 – 1.59 (1H, m, 1 × C**3**-$\underline{H}_2$), 1.48 (1H, ddd, *J* = 13.9, 13.1, 0.9 Hz, 1 × C**5**-$\underline{H}_2$), 1.33 (1H, dddd, *J* = 12.4, 6.7, 3.4, 2.1 Hz, 1 × C**6**-$\underline{H}_2$), 1.15 – 1.04 (1H, m, 1 × C**2**-$\underline{H}$), 1.03 – 0.94 (1H, m, 1 × C**7**-$\underline{H}$), 0.86 – 0.70 (1H, m, 1 × C**6**-$\underline{H}_2$); ^{13}C NMR: (100 MHz, C_6D_6): δ 206.6 (C**4**), 162.6 (C**9**), 53.4 (C**1**), 52.5 (C**8**), 43.8 (C**5**), 43.4 (C**2**), 41.7 (C**7**), 39.7 (C**3**), 37.7 (C**10**), 26.4 (C**6**); *m/z* (ESI^+) HRMS: Calculated for $C_{11}H_{19}N_2O_2$: 211.1441. Found $[M+H]^+$: 211.1443. *The relative stereochemistry of this compound was corroborated by nOe experiments (as indicated on the compound structure). nOes were observed from C**3a**-H to C**2**-H, and from C**3b**-H to C**7**-H.*

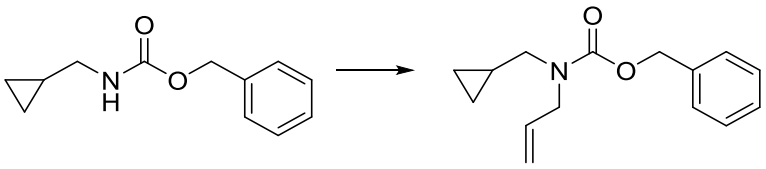
Benzyl (cyclopropylmethyl)carbamate



General procedure A: Cyclopropylmethylamine (3.00 g, 42.0 mmol) and benzyl chloroformate (8.57 g, 50.4 mmol) were employed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound (7.90 g, 92 %) as a colorless oil; ν_{max} / cm^{-1}: 3332 (s), 1694 (s), 1516 (s), 1456 (m), 1240 (s), 1131 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 – 7.26 (5H, m), 5.10 (2H, s), 4.88 (1H, br. s), 3.06 (2H, t, *J* = 6.5 Hz), 0.95 (1H, m), 0.51 – 0.47 (2H, m), 0.21 – 0.16 (2H, m); ^{13}C NMR: (100 MHz, $CDCl_3$) δ

156.3, 136.6, 128.5, 128.1, 128.0, 66.6, 46.0, 11.0, 3.2; *m/z* (ESI^+) HRMS: Calculated for $C_{12}H_{15}NO_2Na$: 228.0995. Found $[M+Na]^+$: 228.1004. *The spectroscopic properties of this compound consistent with the data available in the literature.*[3]

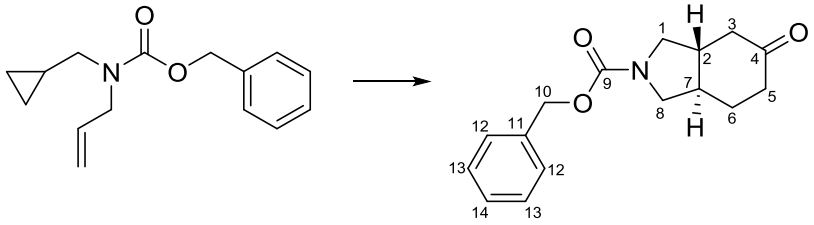
Benzylallyl(cyclopropylmethyl)carbamate (6c)



6c

General procedure B: Benzyl (cyclopropylmethyl)carbamate (4.49 g, 21.9 mmol) and allyl bromide (7.88 g, 65.7 mmol) were employed, the crude mixture which was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound **6c** (4.57 g, 85 %) as a colorless oil; ν_{max} / cm^{-1}: 1697 (s), 1514 (s), 1239 (s), 1132 (m), 1020 (m); ^1H NMR (500 MHz, CD_3CN, 65 °C): δ 7.7 – 7.0 (5H, m), 6.2 – 5.7 (1H, m), 5.4 – 4.9 (4H, m), 4.0 (2H, ddd, *J* = 5.7, 2.6, 1.5 Hz), 3.5 – 2.8 (2H, m), 1.2 – 0.9 (1H, m), 0.7 – 0.4 (2H, m), 0.2 (2H, m); ^{13}C NMR (126 MHz, CD_3CN, 65 °C) δ 155.9, 137.6, 134.5, 128.4, 127.8, 127.6, 116.9, 66.5, 51.1, 49.4, 9.9, 3.0, 2.8; HRMS: (CI^+) Calculated for $C_{15}H_{20}NO_2$: 246.1494. Found $[M + H]^+$: 246.1503.

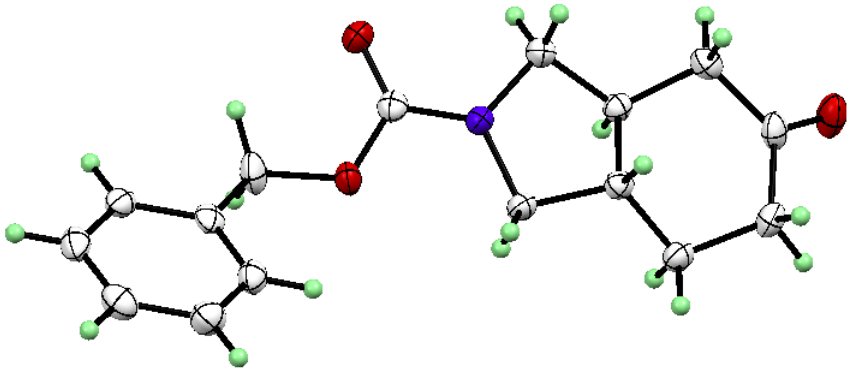
(3a*R, 7a*R**)-Benzyl 5-oxohexahydro-1*H*-isoindole-2(3*H*)-carboxylate (8c)**



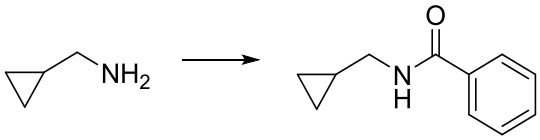
6c **8c**

General procedure G: Compound **6c** (36.8 mg, 0.15 mmol) was employed, the crude mixture was purified by column chromatography (33 % EtOAc/Hex) to yield the title compound **8c** (34.4 mg, 84 %, > 15:1 d.r. 1:1 mixture of rotamers *A:B*) as an off white solid; m.p.: 79 – 81 °C (EtOAc/Hex); ν_{max} / cm^{-1}: 1699 (s), 1419 (s) 1358 (s), 1170 (m), 1079 (m); ^1H NMR (400 MHz, $CDCl_3$): δ 7.36 – 7.28 (5H, m, 2 × C**12**-H, *A*+*B*, 2 × C**13**-H, *A*+*B*, 1 ×C**14**-H, *A*+*B*), 5.20 – 5.10 (2H, m, 2 ×C**10**-H_2, *A*+*B*), 3.81 – 3.67 (2H, m, 1 × C**8**-H, *A*+*B*, 1 × C**1**-H, *A*+*B*), 3.07 – 2.96 (2H, m, 1 × C**8**-H, *A*+*B*, 1 × C**1**-H, *A*+*B*), 2.66 – 2.56 (1H, m, 1

× C**3**-H$_2$, *A*+*B*), 2.53 – 2.47 (1H, m, 1 × C**5**-H$_2$, *A*+*B*), 2.40 – 2.30 (1H, m 1 × C**5**-H$_2$, *A*+*B*), 2.22 – 2.11 (2H, m, 1 × C**3**-H$_2$, *A*+*B*, 1 × C**6**-H$_2$, *A*+*B*), 2.10 – 1.91 (2H, m, 1 × C**2**-H, *A*+*B*, 1 × C**7**-H, *A*+*B*), 1.78 – 1.30 (1H, m, 1 × C**6**-H$_2$, *A*+*B*); ^{13}C NMR (100 MHz, $CDCl_3$): δ 209.0 (C**4**, *A*), 208.9 (C**4**, *B*), 154.8 (C**9**, *A*), 154.7 (C**9**, *B*), 136.8 (C**11**, *A*), 136.7 (C**11**, *B*), 128.5, 128.0, 127.9 (C**12**, *A*+*B*, C**13**, *A*+*B*, C**14**, *A*+*B*), 66.8 (C**10**, *A*+*B*), 51.2 (C**1**, *A*), 51.0 (C**1**, *B*), 50.4 (C**8**, *A*), 50.2 (C**8**, *B*), 44.4 (C**2**, *A*), 44.2 (C**3**, *A*), 44.2 (C**3**, *B*),43.7 (C**2**, *B*), 43.0 (C**7**, *A*), 42.3 (C**7**, *B*), 40.1 (C**5**, *A*), 40.0 (C**5**, *B*), 26.8 (C**6**, *A*+*B*); HRMS: (CI^+) Calculated for $C_{16}H_{19}NO_3$: 274.1443. Found $[M + H]^+$: 274.1445. *The structure and relative stereochemistry of this compound was determined unambiguously by X-ray crystallography.*

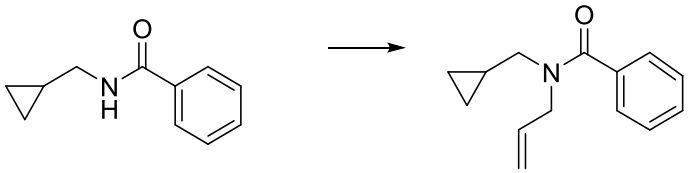


***N*-(Cyclopropylmethyl)benzamide**



General procedure A: Cyclopropylmethylamine (3.00 g, 42.0 mmol) and benzoyl chloride (7.06 g, 50.4 mmol) were employed, the crude mixture was recrystallized from Et_2O/Hex to yield the title compound (5.89 g, 80 %) as a colorless solid; m.p.: 78 – 80 °C (EtOAc/Hex); ν_{max} / cm^{-1}: 3306 (s), 2988 (s), 1631 (s), 1542 (s), 1492 (s), 1295 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 – 7.76 (2H, m), 7.47 (1H, m), 7.42 – 7.37 (2H, m), 6.40 (1H, br. s), 3.31 – 3.27 (2H, m), 1.04 (1H, m), 0.55 – 0.50 (2H, m), 0.27 – 0.23 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.4, 134.8, 131.3, 128.5, 126.9, 44.9, 10.7, 3.5; *m/z* (ESI^+) HRMS: Calculated for $C_{11}H_{13}NONa$: 198.0893. Found $[M + Na]^+$: 198.0889.

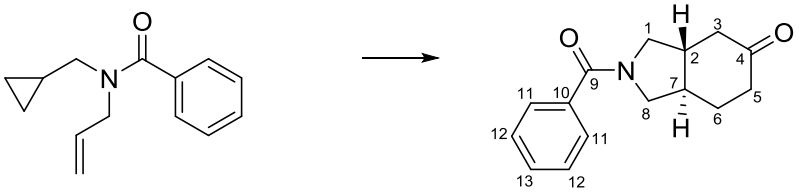
***N*-Allyl-*N*-(cyclopropylmethyl)benzamide (6d)**



6d

General procedure B: *N*-Allyl-*N*-(cyclopropylmethyl)benzamide (2.30 g, 13.1 mmol) was empolyed, the crude mixture was purified by column chromatography (66 % EtOAc/Hex) to yield the title compound **6d** (2.53 g, 90 %) as a yellow oil; ν_{max} / cm^{-1}: 2988 (m), 1629 (s), 1388 (m), 1414 (s), 1262 (s), 1075 (s); ^{1}H NMR (500 MHz, CD_3CN, 65 ^{o}C): δ 7.45 – 7.38 (5H, m), 5.87 (1H, br. s), 5.23 – 5.18 (2H, m), 4.10 (2H, br. s), 3.26 (2H, br. s), 1.03 (1H, br. s), 0.51 (2H, br. d, *J* = 7.8 Hz), 0.18 (2H, br. m); ^{13}C NMR (126 MHz, CD_3CN, 65 ^{o}C): δ 171.1, 137.6, 134.2, 129.0, 128.3, 126.4, 116.9, 51.6-48.8 (br), 9.6, 3.2, 3.1. *m/z* (ESI^+) HRMS: Calculated for $C_{14}H_{18}NO$: 216.1383. Found $[M + H]^+$: 216.1386.

(3a*R, 7a*R**)-2-Benzoyloctahydro-5*H*-isoindol-5-one (8d)**

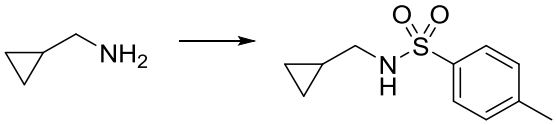


6d **8d**

General procedure G: Compound **6d** (32.3 mg, 0.15 mmol) was employed, the crude mixture was purified by column chromatography (80 % EtOAc/Hex) to yield the title compound **8d** (29.9 mg, 82 %, > 15:1 d.r., 1:1 mixture of rotamers *A:B*) as a colorless oil; ν_{max} / cm^{-1}: 2870 (m), 1710 (s), 1623 (s), 1575 (s), 1417 (s), 1028 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 – 7.48 (2H, m, 2 × C**12**-H, *A*+*B*), 7.43 – 7.36 (3H, m, 2 × C**11**-H, *A*+*B*, C**13**-H, *A*+*B*), 3.96 (0.5H, dd, *J* = 12.0, 7.5 Hz, 1 × C**1**-H_2, *A*), 3.90 (0.5H, dd, *J* = 12.0, 6.5 Hz, 1 ×C**8**-H_2, *A*), 3.63 (0.5H, dd, *J* = 10.0, 6.0 Hz, 1 ×C**1**-H_2, *B*), 3.57 (0.5H, dd, *J* = 10.1, 6.5 Hz, 1 ×C**8**-H_2, *B*), 3.32 – 3.15 (2H, m, 1 ×C**1**-H_2, *A*+*B*, 1 ×C**8**-H_2, *A*+*B*), 2.69 (0.50H, dt, *J* = 14.5, 3.0, 3.0 Hz, 1 ×C**3**-H_2, *A*), 2.55 – 2.45 (1.50H, m, 1 ×C**3**-H_2, *B*, 1 ×C**5**-H_2, *A*+*B*), 2.41 – 1.93 (5H, m, C**2**-H, *A*+*B*, 1 ×C**3**-H_2, *A*+*B*, 1 ×C**5**-H_2, *A*+*B*, 1 ×C**6**-H_2, *A*+*B*, C**7**-H, *A*+*B*),

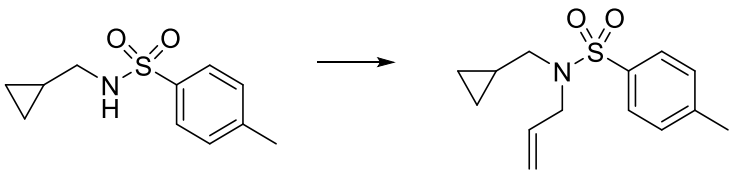
1.65 – 1.47 (1H, m, 1 ×C**6**-$\underline{H_2}$, *A*+*B*); ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.7 (C**4**, *A*), 208.6 (C**4**, *B*), 169.9 (C**9**, *A*+*B*), 136.5 (C**10**, *A*), 136.4 (C**10**, *B*), 130.1 (C**13**, *A*+*B*), 128.3 (C**11**, *A*), 128.3 (C**11**, *B*), 127.2 (C**12**, *A*), 127.1 (C**12**, *B*), 55.0 (C**8**, *A*), 53.9 (C**1**, *A*), 51.3 (C**8**, *B*), 50.5 (C**1**, *B*), 44.8 (C**2**, *A*), 44.3 (C**3**, *A*), 44.0 (C**3**, *B*), 43.3, 43.2 (C**2**, *B*, C**7**, *A*), 41.8 (C**7**, *B*), 40.2 (C**5**, *A*), 39.9 (C**5**, *B*), 26.9 (C**6**, *A*), 26.6 (C**6**, *B*); *m/z* (ESI$^+$) HRMS: Calculated for $C_{15}H_{17}NO_2Na$: 266.1151. Found, $[M + Na]^+$: 266.1143. *The relative stereochemistry of this compound was assigned by analogy to that of* ***8c****.*

***N*-(Cyclopropylmethyl)-4-methylbenzenesulfonamide**



General procedure A: Cyclopropylmethylamine (1.01 g, 14.1 mmol) and *p*-toluenesulfonyl chloride (3.22 g, 16.9 mmol) were employed, the crude mixture was purified by column chromatography (25 % EtOAc/Hex) to yield title sulfonamide (2.70 g, 85 %) as a colorless solid; m.p. 58 – 60 °C (CH_2Cl_2/Hex); ν_{max} / cm^{-1}: 3258 (m), 3004 (m), 2868 (m), 1595 (m), 1154 (s) 1091 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 – 7.66 (2H, m), 7.48 – 7.13 (2H, m), 4.71 (1H, br. s), 2.80 (2H, dd, *J* = 7.1, 5.9 Hz), 2.42 (3H, s), 0.86 (1H, dddd, *J* = 12.2, 8.1, 7.2, 2.8 Hz), 0.63 – 0.22 (2H, m), 0.13 – 0.02 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.3, 137.1, 129.6, 127.1, 48.3, 21.5, 10.7, 3.5; *m/z* (ESI$^+$) HRMS: Calculated for $C_{11}H_{15}NO_2SNa$: 248.0716. Found $[M+Na]^+$: 248.0714.

***N*-Allyl-*N*-(cyclopropylmethyl)-4-methylbenzenesulfonamide (6e)**

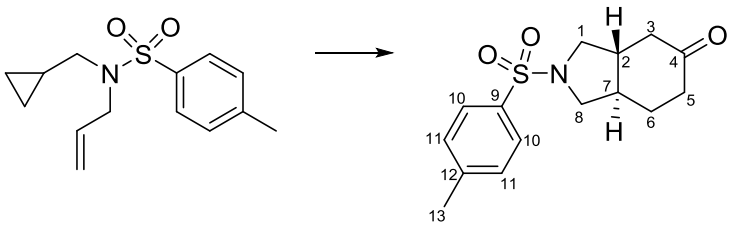


6e

General procedure B: *N*-(Cyclopropylmethyl)-4-methylbenzenesulfonamide (0.68 g, 3.0 mmol) and allyl bromide (1.80 g, 15.0 mmol) were empolyed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound **6e** (0.70 g, 88 %) as a colorless oil. ν_{max} / cm^{-1}: 1341 (s), 1305 (m), 1154 (s), 1091 (s), 1019 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (2H, d, *J* = 8.5 Hz), 7.26 (2H, d, *J* = 8.5 Hz), 5.64 (1H, ddt, *J* = 17.5,

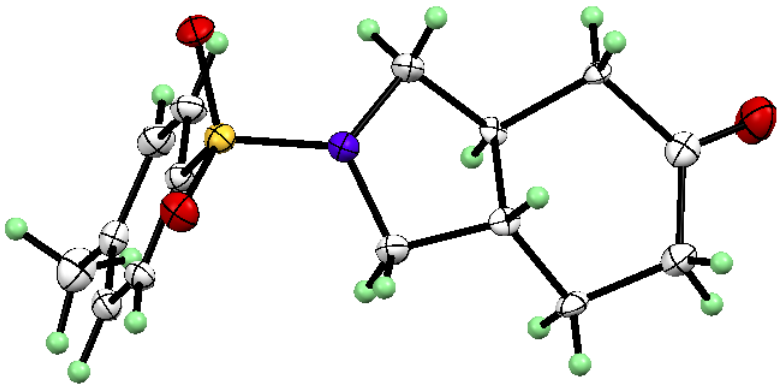
10.0, 6.0 Hz), 5.16 (1H, dd, *J* = 17.0, 1.5 Hz), 5.10 (1H, dd, *J* = 10.0, 1.5 Hz), 3.90 (2H, d, *J* = 6.0 Hz), 3.01 (2H, d, *J* = 7.0 Hz), 2.39 (3H, s), 0.85 (1H, m), 0.47 – 0.43 (2H, m), 0.13 (2H, dt, *J* = 6.0, 4.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.0, 137.6, 133.5, 129.6, 127.1, 188.3, 51.6, 50.0, 21.5, 9.6, 4.0; HRMS: (CI^+) Calculated for $C_{14}H_{20}NO_2S$: 266.1215. Found $[M + H]^+$: 266.1209.

(3a*R, 7a*R**)-2-Tosylhexahydro-1*H*-isoindol-5(6*H*)-one (8e)**

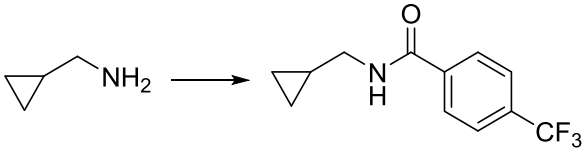


6e **8e**

General procedure G: Compound **6e** (39.8 mg, 0.15 mmol) was employed, the crude mixture was purified by column chromatography (33 % EtOAc/Hex) to yield the title compound **8e** (38.7 mg, 88 %, > 15:1 d.r.) as an off white solid; m.p.: 172 – 173 °C (CH_2Cl_2/Hex); ν_{max} / cm^{-1}: 1703 (m), 1338 (m), 1194 (m), 1156 (s), 1087 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (2H, d, *J* = 8.5 Hz, 2 × C**10**-H), 7.32 (2H, d, *J* = 8.5 Hz, 2 × C**11**-H), 3.66 (1H, dd, *J* = 9.5, 7.0 Hz, 1 × C**8**-H_2), 3.57 (1H. dd, *J* = 9.5, 7.0 Hz, 1 × C**1**-H_2), 2.94 (1H, dd, *J* = 10.5, 9.5 Hz, 1 × C**1**-H_2), 2.84 (1H. dd, *J* = 10.5, 9.5 Hz, 1 × C**8**-H_2), 2.51 (1H, ddd, *J* = 14.5, 4.0, 2.0 Hz, 1 × C**3**-H_2), 2.45 – 2.40 (4H, m, 1 × C**5**-H_2, 3 ×C**13**-H_3), 2.31 (1H, ddd, *J* = 15.5, 13.0, 6.5 Hz, 1 × C**5**-H_2), 2.15 – 2.07 (2H, m, 1 × C**3**-H_2, 1 × C**6**-H_2), 1.91 – 1.83 (1H, m, C**2**-H), 1.79 – 1.67 (1H, m, C**7**-H), 1.42 (1H, ddt, *J* = 13.0, 12.0, 5.0 Hz, 1 × C**6**-H_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.3 (C**4**), 143.6 (C**12**), 134.4 (C**9**), 129.8 (C**11**), 12.8 (C**10**), 52.6 (C**1**), 51.9 (C**8**), 44.2 (C**7**), 43.9 (C**3**), 42.7 (C**2**), 39.8 (C**5**), 26.5 (C**6**), 21.5 (C**13**); HRMS: (CI^+) Calculated for $C_{15}H_{20}NO_3S$: 294.1164. Found $[M + H]^+$: 294.1157. *The structure and relative stereochemistry of this compound was determined unambiguously by X-ray crystallography.*

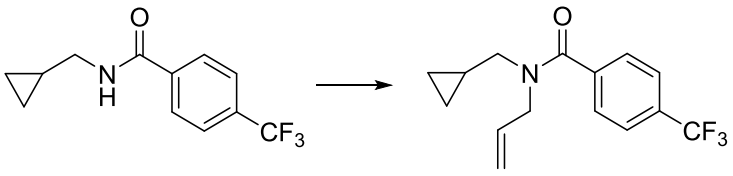


***N*-(Cyclopropylmethyl)-4-(trifluoromethyl)benzamide**



General procedure A: Cyclopropylmethylamine (1.42 g, 20.0 mmol) and 4-(trifluoromethyl)benzoyl chloride (3.56 mL, 24.0 mmol) were employed, the crude mixture was recrystallized from Et_2O/Hex to yield the title compound (4.10 g, 84 %) as a colourless solid; m.p.: 127 – 128 °C (EtOAc/Hex); ν_{max} / cm^{-1}: 3245 (s), 1642 (m), 1625 (s), 1557 (s), 1323 (s), 1154 (s), 1113 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (2H, d, *J* = 8.0 Hz), 7.67 (2H, d, *J* = 8.0 Hz), 6.42 (1H, br. s), 3.31 (2H, dd, *J* = 7.0, 5.5 Hz), 1.05 (1H, m, C**2**-H), 0.57 – 0.53 (2H, m), 0.29 – 0.25 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.2, 138.0, 133.0 (q, *J* = 32.5 Hz), 127.4, 125.5 (q, *J* = 4.0 Hz), 123.7 (q, *J* = 272.5 Hz), 45.1, 10.6, 3.5; *m/z* (ESI^+) HRMS: Calculated for $C_{12}H_{12}F_3NONa$: 266.0763. Found $[M + Na]^+$: 266.0764.

***N*-Allyl-N-(cyclopropylmethyl)-4-(trifluoromethyl)benzamide (6f)**

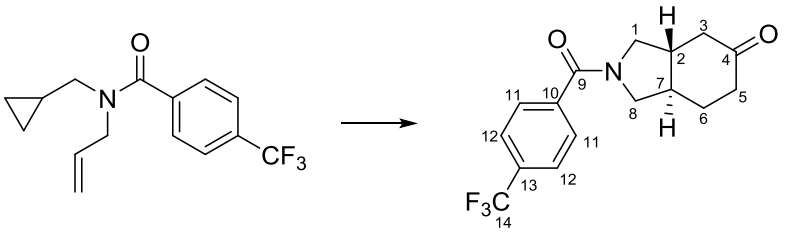


6f

General procedure B: *N*-(Cyclopropylmethyl)-4-(trifluoromethyl)benzamide (2.43 g, 10.0 mmol) and allyl bromide (4.33 mL, 50.0 mmol) were employed, the crude mixture was

purified by flash column chromatography (30 % EtOAc/Hex) to yield the compound **6f** (2.63 g, 93%) as a yellow oil; ν_{max} / cm^{-1}: 1686 (s), 1455 (m), 1169 (s), 1201 (s), 1137 (s); ^{1}H NMR (500 MHz, CD_3CN, 65 °C): 7.76 (2H, d, *J* = 8.0 Hz), 7.58 (2H, d, *J*=7.7 Hz), 5.87 (1H, br., s), 5.48 – 4.97 (2H, m), 4.10 (2H, br., s), 3.28 (2H, br., s), 1.05 (1H, br., s), 0.63 – 0.40 (2H, br., m), 0.20 (2H, br., s); ^{13}C NMR (126 MHz, CD_3CN, 65 °C): δ 169.8, 141.4, 133.8, 130.5 (q, *J* = 32.7, 32.0 Hz), 127.2, 125.3 (q, *J* = 3.9 Hz), 124.2 (q, *J* = 271.4 Hz), 116.4, 47.7-53.3 (br., m), 9.5, 3.2; ^{19}F NMR (377 MHz, $CDCl_3$): δ -62.8 (s, C<u>F</u>$_3$); *m/z* (ESI^+) HRMS: Calculated for $C_{15}H_{17}F_3NO$: 284.1257. Found $[M + H]^+$: 284.1252.

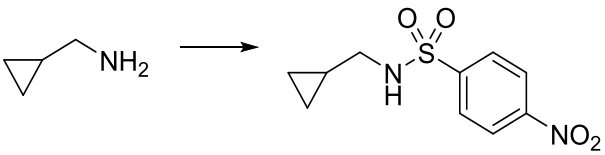
(3a*R, 7a*R**)-2-(4-(Trifluoromethyl)benzoyl)octahydro-5H-isoindol-5-one (8f)**



6f **8f**

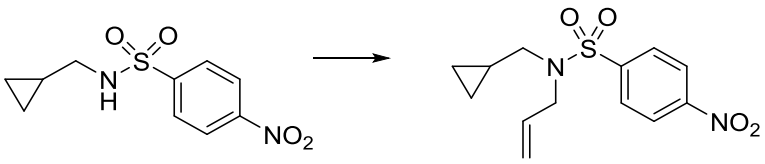
General procedure G: Compound **6f** (42.5 mg, 0.15 mmol) was employed, the crude mixture was purified by column chromatography (100 % EtOAc) to yield the title compound **8f** (33.7 mg, 72 %, > 15:1 d.r., 1:1 mixture of rotamers *A*:*B*) as a colorless oil; ν_{max} / cm^{-1}: 2967 (m), 1713 (s), 1627 (s), 1428 (s), 1322 (s), 1165 (s), 1123 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 – 7.60 (4H, m, 2 × C**11**-<u>H</u>, *A*+*B*, 2 × C**12**-<u>H</u>, *A*+*B*), 4.06 – 3.81 (1H, 1 × C**8**-<u>H</u>$_2$, *A*, 1 × C**1**-<u>H</u>$_2$, *A*), 3.68 – 3.40 (1H, m, 1 × C**8**-<u>H</u>$_2$, *B*, 1 × C**1**-<u>H</u>$_2$, *B*), 3.38 – 3.01 (2H, m, 1 × C**1**-<u>H</u>$_2$, *A*+*B*, 1 × C**8**-<u>H</u>$_2$, *A*+*B*), 2.69 (0.5H, dd, *J* = 14.5, 3.1 Hz, 0.50 × C**3**-<u>H</u>$_2$, *A*), 2.59 – 2.43 (1.50H, m, 0.50 × C**3**-<u>H</u>$_2$, *B*, 1 × C**5**-<u>H</u>$_2$, *A*+*B*), 2.42 – 1.95 (5H, m, 1 × C**3**-<u>H</u>$_2$, *A*+*B*, 1 × C**5**-<u>H</u>$_2$, *A*+*B*, 1 × C**6**-<u>H</u>$_2$, *A*+*B*, C**2**-<u>H</u>, *A*+*B*, C**7**-<u>H</u>, *A*+*B*), 1.60 (1H, m, 1 × C**6**-<u>H</u>$_2$, *A*+*B*); ^{13}C NMR (125 MHz, $CDCl_3$): δ 208.5 (C**4**, *B*), 208.4 (C**4**, *A*), 168.5 (C**9**, *A*+*B*), 139.9 (C**10**, *A*+*B*), 132.1 (q, *J* = 32.5.0 Hz, C**13**, *A*+*B*), 127.6 (C**11**, *B*), 127.6 (C**11**, *A*), 125.5 (q, *J* = 5.0 Hz, C**12**, *A*+*B*), 123.8 (q, *J* = 272.5 Hz, C**14**, *A*+*B*), 54.6 (C**1**, *A*), 53.9 (C**8**, *B*), 51.4 (C**1**, *B*), 50.6 (C**8**, *A*), 44.9 (C**2**, *A*), 44.4 (C**3**, *A*), 44.0 (C**3**, *B*), 43.5, 43.3 (C**2**, *B*, C**7**, *B*), 41.9 (C**7**, *A*), 40.2 (C**5**, *A*), 40.0 (C**5**, *B*), 26.9 (C**6**, *A*), 26.6 (C**6**, *B*); ^{19}F NMR (470 MHz, $CDCl_3$): δ -62.9 (s, C<u>F</u>$_3$, *A*), -63.0 (s, C<u>F</u>$_3$, *B*),; *m/z* (ESI^+) HRMS: Calculated for $C_{16}H_{17}F_3NO_2$: 312.1206. Found $[M + H]^+$: 312.1221. *The relative stereochemistry of this compound was assigned by analogy to that of* ***8c*** *and* ***8d****.*

***N*-(Cyclopropylmethyl)-4-nitrobenzenesulfonamide**



General procedure A: Cyclopropylmethylamine (1.07 g, 15.0 mmol) and *p*-toluenesulfonyl chloride (3.65 g, 16.5 mmol) were employed, the crude mixture was purified by column chromatography (25 % EtOAc/Hex) to yield title sulfonamide (3.34 g, 87 %) as an off-white solid; m.p. 114 – 116 °C (CH_2Cl_2/Hex); ν_{max} / cm^{-1}: 3285 (m), 1522 (s), 1431 (m), 1334 (s), 1157 (s) 1048 (s); ^{1}H NMR (400 MHz, $CDCl_3$): 8.47 – 8.21 (2H, m), 8.13 – 7.87 (2H, m), 5.23 (1H, t, *J* = 5.9 Hz), 2.88 (2H, dd, *J* = 7.2, 5.8 Hz), 0.97 – 0.76 (1H, m), 0.55 – 0.32 (2H, m), 0.11 (2H, t, *J* = 5.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.0, 146.2, 128.3, 124.4, 48.5, 10.8, 3.7; *m/z* (ESI^+) HRMS: Calculated for $C_{10}H_{12}N_2O_4SNa$: 279.0410. Found $[M+Na]^+$: 279.0397.

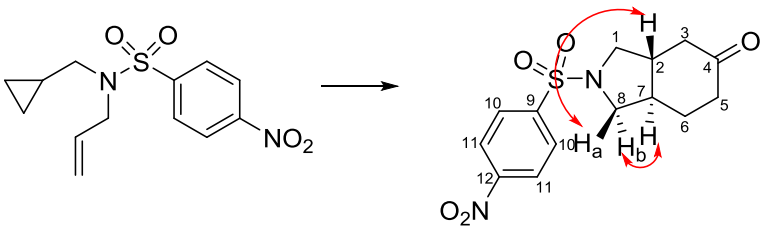
***N*-Allyl-*N*-(cyclopropylmethyl)-4-nitrobenzenesulfonamide (6g)**



6g

General procedure B: *N*-(Cyclopropylmethyl)-4-nitrobenzenesulfonamide (1.40 g, 5.5 mmol) and allyl bromide (3.30 g, 27.5 mmol) were employed, the crude mixture was purified by column chromatography (15 % EtOAc/Hex) to yield the title compound **6g** (1.48g, 91 %) as an off-white solid; m.p. 67 – 69 °C (CH_2Cl_2/Hex); ν_{max} / cm^{-1}: 1524 (s), 1346 (s), 1313 (m), 1150 (s), 1088 (m) 906 (m); ^{1}H NMR (400 MHz, $CDCl_3$): 8.45 – 8.19 (2H, m), 8.08 – 7.87 (2H, m), 5.62 (1H, ddt, *J* = 16.5, 10.2, 6.2 Hz), 5.30 – 4.96 (2H, m), 3.98 (2H, dd, *J*=6.3, 1.5 Hz), 3.10 (2H, d, *J* = 6.9 Hz), 0.95 – 0.72 (1H, m), 0.55 – 0.40 (2H, m), 0.17 (2H, dd, *J* = 4.9, 1.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.8, 146.6, 132.5, 128.2, 124.3, 119.1, 51.8, 50.0, 9.5, 4.1; *m/z* (ESI^+) HRMS: Calculated for $C_{13}H_{16}N_2O_4SNa$: 319.0723. Found $[M+Na]^+$: 319.0724.

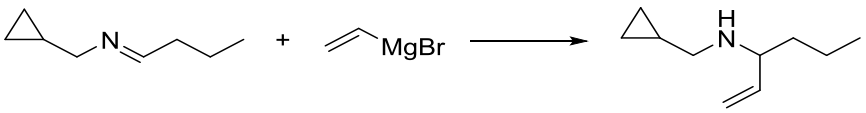
(3a*R, 7a*R**)-2-((4-Nitrophenyl)sulfonyl)octahydro-5*H*-isoindol-5-one (8g)**



6g **8g**

General procedure G: Compound **6g** (44.4 mg, 0.15 mmol) was employed, the crude mixture was purified by column chromatography (33 % EtOAc/Hex) to yield the title compound **8g** (18.1 mg, 37 %, > 15:1 d.r.) as an off white solid; m.p.: above 200 °C (CH_2Cl_2/Hex); ν_{max} / cm^{-1}: 2955 (m), 1706 (m), 1528 (m), 1348 (s), 1159 (s), 1033 (s); ^1H NMR (500 MHz, DMSO-d_6, 80 °C): δ 8.40 (1H, d, *J* = 8.9 Hz, 2 × C**11**-H), 8.07 (1H, d, *J* = 8.9 Hz, 2 × C**10**-H), 3.59 (1H, dd, *J* = 9.6, 7.1 Hz, 1 × C**1**-H_2), 3.52 (1H, dd, *J* = 9.5, 6.9 Hz, 1 × C**8**-H_2), 2.88 (1H, dd, *J* = 10.8, 9.4 Hz, 1 × C**8**-H_2), 2.81 (1H, dd, *J*=10.7, 9.6 Hz, 1 × C**1**-H_2), 2.34 – 2.21 (3H, m, 2 × C**3**-H_2, 1 × C**5**-H_2), 2.19 – 2.11 (1H, m, 1 × C**5**-H_2), 2.00 – 1.91 (1H, m, 1 × C**6**-H_2), 1.91 – 1.82 (1H, m, 1 × C**2**-H), 1.81 – 1.70 (1H, m, 1 × C**7**-H), 1.45 – 1.29 (1H, m, 1 × C**6**-H_2); ^{13}C NMR (126 MHz, DMSO-d_6, 80 °C): δ 209.0 (C**4**), 150.3 (C**12**), 142.8 (C**9**), 129.1 (C**10**), 125.2 (C**11**), 52.9 (C**8**), 52.2 (C**1**), 43.6 (C**7**), 43.4 (C**3**), 41.9 (C**2**), 39.7 (C**5**), 25.9 (C**6**); HRMS: (CI^+) Calculated for $C_{14}H_{16}N_2O_5SNa$: 347.0672. Found $[M + H]^+$: 347.0663. *The relative stereochemistry of this compound was corroborated by nOe experiments (as indicated on the compound structure). nOes were observed between C**8**$_a$-H and C**2**-H, C**8**$_b$-H and C**7**-H, no significant nOe was observed between C**2**-H and C**7**-H. The stereochemical assignment of this compound is consistent with that of **8e**.*

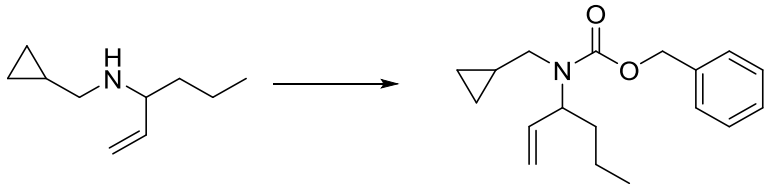
***N*-(Cyclopropylmethyl)hex-1-en-3-amine**



General procedure F: (*E*)-*N*-(cyclopropylmethyl)butan-1-imine (0.82 g, 6.6 mmol) (prepared according to literature procedure[4]) and vinylmagnesium bromide (6.6 mL, 13.2 mmol, 2.0 M in THF) were employed, the crude mixture was purified by column chromatography (66 % EtOAc/Hex) to yield the title compound (0.27 g, 27 %) as a red oil; ν_{max} / cm^{-1}: 3203 (m), 2958 (m), 1590 (m), 1428 (m), 1054 (s), 992 (s), 938 (s); ^1H NMR (400 MHz, $CDCl_3$): δ 6.51 (1H, br. s), 5.84 – 5.63 (1H, m), 5.51 (1H, dd, *J* = 10.2, 1.0 Hz), 5.42 (1H, dd, *J* = 16.9, 0.9 Hz), 3.63 (1H, td, *J* = 10.0, 4.1 Hz), 2.90 (2H, dd, *J* = 7.5, 1.8 Hz), 1.93

– 1.79 (1H, m), 1.79 – 1.62 (1H, m), 1.47 – 1.21 (2H, m), 1.19 – 1.11 (1H, m), 0.92 (3H, t, *J* = 7.3 Hz), 0.74 – 0.57 (2H, m), 0.44 – 0.24 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 131.5, 124.3, 62.4, 51.4, 33.4, 18.5, 13.3, 6.9, 4.5, 3.8; *m/z* (ESI$^+$) HRMS: Calculated for $C_{10}H_{20}N$: 154.1590. Found $[M+H]^+$: 154.1589.

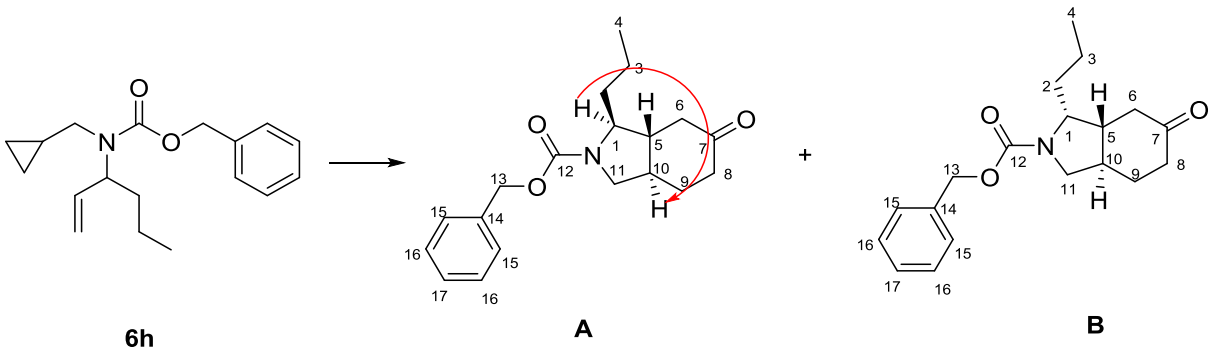
Benzyl (cyclopropylmethyl)(hex-1-en-3-yl)carbamate (6h)



6h

General Procedure E: *N*-(Cyclopropylmethyl)hex-1-en-3-amine (0.33 g, 2.2 mmol) and benzyl chloroformate (0.70 ml, 4.4 mmol) were employed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound **6h** (0.59 g, 92 %) as a colorless oil; ν_{max} / cm^{-1}: 2958 (m), 1692 (s), 1412 (m), 1255 (m), 1145 (m), 1087 (m), 696 (s); ^{1}H NMR (400 MHz, CD_3CN, 65 ^{o}C): δ 7.66 – 7.04 (5H, m), 5.97 (1H, ddd, *J* = 17.1, 10.5, 6.3 Hz), 5.36 – 4.90 (4H, m), 4.40 (1H, dtt, *J* = 8.1, 6.5, 1.5 Hz), 3.19 – 3.11 (1H, m), 3.10 – 3.03 (1H, m), 1.84 – 1.58 (2H, m), 1.52 – 1.24 (2H, m), 1.15 – 1.00 (1H, m), 0.94 (3H, t, *J* = 7.4 Hz), 0.59 – 0.35 (2H, m), 0.35 – 0.14 (2H, m); ^{13}C NMR (126 MHz, CD_3CN, 65 ^{o}C): δ 156.1, 138.5, 137.6, 128.3, 127.7, 127.6, 116.9, 66.4, 59.1, 49.3, 34.3, 19.3, 13.0, 11.0, 3.8, 3.6; *m/z* (ESI$^+$) HRMS: Calculated for $C_{18}H_{25}NO_2Na$: 310.1778. Found $[M+Na]^+$: 310.1763.

Benzyl-(1*S, 3a*R**, 7a*R**) and (1*R**, 3a*R**, 7a*R**)-6-oxo-1-propylhexahydro-1*H*-isoindole-2(3*H*)-carboxylate (8h)**



6h **A** **B**

8h

General procedure G: Compound **6h** (43.1 mg, 0.15 mmol) was employed, the crude mixture was purified by column chromatography (33 % EtOAc/Hex) to yield the title

compound **8h** (32.6 mg, 69 %, 1:1 mixture of rotamers *A:B*) as a colorless oil. A mixture of diastereomers A and B were obtained in a 3:1 (A:B) ratio. *Under general procedure **H**, title compound **8h** was obtained in 60 % yield (28.4 mg, 1:1 mixture of rotamers A:B) as a colorless oil. A mixture of diastereomers A and B were obtained in a 2:1 (A:B) ratio.*

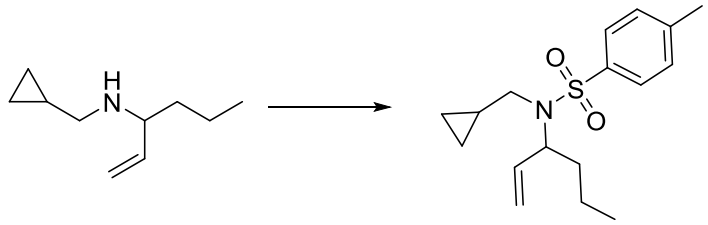
*The relative stereochemistry of major diastereomer A was corroborated by nOe experiments (as indicated on the compound structure). A nOes was observed from C**1**-H to C**9**-H, and no significant nOe was observed between C**5**-H and C**10**-H. The stereochemical assignment of major diastereomer A is consistent with that of major diastereomer A of **8l**. The relative stereochemistry of minor diastereomer B was tentatively assigned by analogy to that of minor diastereomer B of **8l**.*

ν_{max} / cm^{-1}: 2957 (m), 1698 (s), 1411 (m), 1356 (m), 1265 (m), 1075 (m); *m/z* (ESI^+) HRMS: Calculated for $C_{19}H_{25}NO_3Na$: 338.1727. Found $[M+Na]^+$: 338.1736

Data for mixture of diastereomers A and B: ^1H NMR (400 MHz, CD_3CN, 65 °C): δ 8.47 – 6.45 (10H, m, 2 × C**15**-H, A+B, 2 × C**16**-H, A+B, 1 × C**17**-H, A+B), 5.23 – 5.02 (4H, m, 2 × C**13**-H_2, A+B), 3.94 – 3.84 (2H, m, 1 × C**11**-H_2, A, 1 × C**1**-H, B), 3.70 – 3.57 (1H, br. m, 1 × C**11**-H_2, B), 3.51 (1H, dt, *J* = 9.6, 4.8 Hz, 1 × C**1**-H, A), 2.98 (1H, dd, *J* = 10.5, 10.5 Hz, 1 × C**11**-H_2, B) 2.94 – 2.79 (1H, m, 1 × C**11**-H_2, A), 2.53 (1H, dd, *J* = 14.5, 4.0 Hz, 1 × C**6**-H_2, A), 2.45 – 2.25 (8H, m, 1 × C**6**-H_2, A, 2 × C**8**-H_2, A, 2 × CH_2, B, 2 × CH_2, B, 1 × CH, B), 2.22 – 2.16 (1H, br. m, 1 × CH_2, B), 2.17 – 2.09 (1H, m, 1 × C**9**-H_2, , A), 2.04 – 2.03 (1H, m, 1 × CH, B), 2.02 – 1.98 (1H, m, 1 × C**10**-H, A), 1.89 – 1.72 (3H, m, 1 × C**5**-H, A, 2 × C**2**-H_2, A), 1.63 – 1.44 (4H, m, 1 × C**9**-H_2, A, 1 × CH_2, B, 1 × CH_2, B, 1 × CH_2, B), 1.33 – 1.28 (4H, m, 2 × C**3**-H_2, A, 1 × CH_2, B, 1 × CH_2, B), 0.98-0.84 (6H, m, 3 × C**4**-H_3, A, 3 × C**4**-H_3, B); ^{13}C NMR (126 MHz, CD_3CN): δ 209.2 (C**7**, B, *A*+*B*), 209.0 (C**7**, B, *A*+*B*), 155.1 (C**12**, A, *A*), 154.9 (C**12**, B, *A*), 154.8 (C**12**, B, *B*), 154.4 (C**12**, A, *B*), 137.7 (C**14**, A, *A*+*B*), 137.4 (C**14**, B, *A*+*B*), 128.4, 127.9, 127.8, 127.6, 127.5 (C**15**, A, *A*+*B*, C**16**, A, *A*+*B*, C**17**, A, *A*+*B*, C**15**, B, *A*+*B*, C**16**, B, *A*+*B*, C**17**, B, *A*+*B*), 66.3 (C**13**, A, *A*), 66.2 (C**13**, B, *A*), 66.0 (C**13**, B, *B*), 65.9 (C**13**, A, *B*), 62.5 (C**1**, A, *A*), 62.0 (C**1**, A, *B*), 59.5 (C**1**, B, *A*), 59.2 (C**1**, B, *B*), 51.2 (C**11**, A, *A*), 50.9 (C**11**, A, *B*), 50.5 (C**11**, B, *A*), 50.3 (C**11**, B, *B*), 49.5 (C**5**, A, *A*), 49.5 (C**5**, A, *B*), 47.5 (B, *A*), 46.8 (B, *B*), 44.5 (C**6**, A, *A*+*B*), 42.0 (B, *A*+*B*), 41.6 (C**10**, A, *A*), 41.6 (C**10**, A, *B*), 39.7 (B, *A*), 39.7 (B, *B*), 39.6 (C**8**, A, *A*+*B*), 39.0 (B, *A*), 38.1 (B, *B*), 34.4 (C**2**, A, *A*), 35.0 (C**2**, A, *B*), 33.1 (B, *A*), 32.9 (B, *B*), 27.4 (B, *A*), 27.3 (B, *B*), 25.8 (C**9**, A, *A*+*B*), 19.9 (B, *A*), 19.8 (B, *B*), 17.2 (C**3**, A, *A*), 17.0 (C**3**, A, *B*), 13.7 (C**4**, A, *A*), 13.6 (C**4**, A, *B*),

13.6 (C**4**, B, *A*), 13.5 (C**4**, B, *B*). *Minor diastereomer B could not be fully assigned based on the 1D and 2D NMR data.*

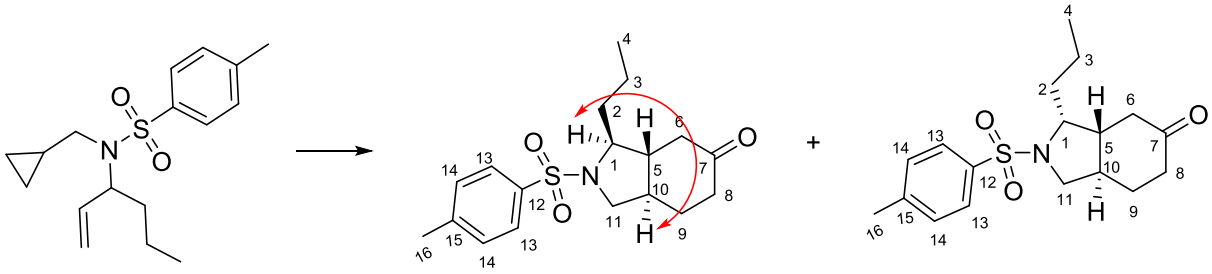
_N_-(Cyclopropylmethyl)-_N_-(hex-1-en-3-yl)-4-methylbenzenesulfonamide (6i)



6i

General Procedure E: *N*-(cyclopropylmethyl)hex-1-en-3-amine (0.15 g, 1.0 mmol) and *p*-toluenesulfonyl (0.39 g, 2.0 mmol) were employed, the crude mixture was purified by column chromatography (100 % Toluene) to yield the title compound **6i** (0.28 g, 90 %, > 15:1) as a yellow oil; ν_{max} / cm^{-1}: 2959 (m), 1458 (m), 1331 (s), 1154 (s), 1090 (s), 670 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (2H, d, *J* = 8.3 Hz), 7.25 (2H, d, *J* = 8.0 Hz), 5.57 (1H, ddd, *J* = 16.9, 10.6, 6.0 Hz), 5.40 – 4.76 (2H, m), 4.31 (1H, dt, *J* = 8.0, 6.5 Hz), 3.08 (1H, dd, *J* = 15.1, 6.4 Hz), 2.84 (1H, dd, *J* = 15.1, 7.1 Hz), 2.40 (3H, s), 1.89 – 1.48 (2H, m), 1.49 – 1.15 (2H, m), 1.07 – 0.97 (1H, m), 0.88 (3H, t, *J* = 7.3 Hz), 0.63 – 0.40 (2H, m), 0.41 – 0.11 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.7, 138.5, 136.8, 129.4, 127.2, 117.3, 59.2, 48.9, 34.5, 21.5, 19.5, 13.8, 12.0, 5.5, 4.8; *m/z* (ESI^+) HRMS: Calculated for $C_{17}H_{25}NO_2SNa$: 330.1498. Found $[M+Na]^+$: 330.1500.

(3*S, 3a*R**, 7a*R**) and (3*R**, 3a*R**, 7a*R**)-3-Propyl-2-tosylhexahydro-1*H*-isoindol-5(6*H*)-one (8i)**



6i **A** **B**

8i

General procedure G: Compound **6i** (46.1 mg, 0.15 mmol) was employed, the crude mixture was purified by column chromatography (33 % EtOAc/Hex) to yield the title

compound **8i** (32.2 mg, 64 %) as a colorless oil. A mixture of diastereomers A and B were obtained in a 8:1 (A:B) ratio. *Under general procedure **H**, title compound **8i** was obtained in 61 % yield (30.7 mg) as a colorless oil. A mixture of diastereomers A and B were obtained in a 3:1 (A:B) ratio.*

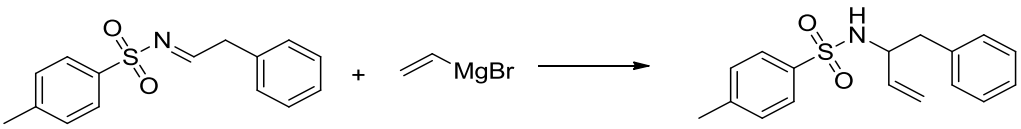
*The relative stereochemistry of major diastereomer A was corroborated by nOe experiments (as indicated on the compound structure). A nOe was observed between C**1**-H and C**10**-H, and no significant nOe was observed between C**5**-H and C**10**-H. The stereochemical assignment of major diastereomer A is consistent with that of major diastereomer A of **8l**. The relative stereochemistry of minor diastereomer B was tentatively assigned by analogy to that of minor diastereomer B of **8l**.*

ν_{max} / cm^{-1}: 2957 (m), 1712 (s), 1457 (m), 1341 (s), 1124 (s), 1089 (s); *m/z* (ESI^+) HRMS: Calculated for $C_{18}H_{25}NO_3SNa$: 358.1447. Found $[M+Na]^+$: 358.1455;

Data for major diastereomer A: ^1H NMR (500 MHz, $CDCl_3$): δ 7.72 (2H, d, *J* = 8.3 Hz, 2 × C**13**-H), 7.32 (2H, d, *J* = 8.1 Hz, 2 × C**14**-H), 3.71 (1H, dd, *J* = 11.4, 6.4 Hz, 1 × C**11**-H_2), 3.38 – 3.24 (1H, m, 1 × C**1**-H), 2.90 (1H, dd, *J* = 11.2 Hz, 11.2 Hz, 1 × C**11**-H_2), 2.53 (1H, ddd, *J* = 14.3, 3.9, 1.9 Hz, 1 × C**6**-H_2), 2.43 (3H, s, 3 × C**16**-H_3), 2.41 – 2.31 (1H, m, 1 × C**8**-H_2), 2.18 – 2.07 (1H, m, 1 × C**8**-H_2), 2.05 – 1.90 (2H, m, 1 × C**6**-H_2, 1 × C**9**-H_2), 1.85 – 1.62 (3H, m, 2 × C**2**-H_2, 1 × C**5**-H), 1.49 – 1.40 (1H, m, 1 × C**3**-H_2), 1.39 – 1.19 (3H, m, 1 × C**3**-H_2, 1 × C**9**-H_2, 1 × C**10**-H), 0.97 – 0.84 (3H, m, 1 × C**4**-H_3); ^{13}C NMR (126 MHz, $CDCl_3$): δ 208.6 (C**7**), 143.5 (C**15**), 135.5 (C**12**), 129.8 (C**14**), 127.3 (C**13**), 65.1 (C**1**), 53.0 (C**11**), 49.4 (C**5**), 45.0 (C**6**), 42.0 (C**10**), 39.5 (C**8**), 35.9 (C**2**), 25.9 (C**9**), 21.5 (C**16**), 17.6 (C**3**), 14.2 (C**4**).

Data for minor diastereomer B: *Characteristic peaks only*: ^1H NMR (500 MHz, $CDCl_3$): δ 3.68 – 3.58 (2H, m, 1 × C**11**-H_2, 1 × C**1**-H), 2.64 (1H, dd, *J* = 11.2 Hz, 11.2 Hz, 1 × C**11**-H_2).

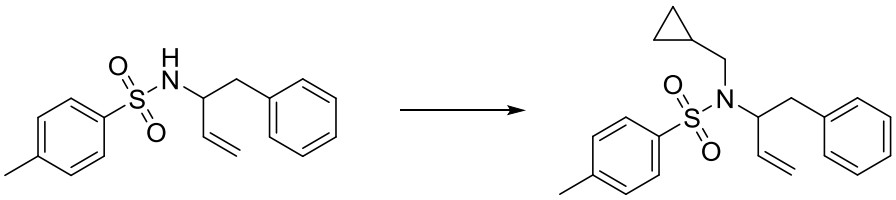
4-Methyl-*N*-(1-phenylbut-3-en-2-yl)benzenesulfonamide



General procedure F: (*E*)-4-Methyl-*N*-(2-phenylethylidene)benzenesulfonamide (2.44 g, 8.5 mmol) (prepared according to literature procedure[5]) and vinylmagnesium bromide (17.0

mL, 17.0 mmol, 1.0 M in THF) were employed, the crude mixture was purified by column chromatography (15 % EtOAc/Hex) to yield the title compound (2.14 g, 76 %) as a colorless oil; ν_{max} / cm^{-1}: 3274 (m), 2923 (m), 1413 (m), 1324 (s), 1153 (s), 1093 (s), 923 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (2H, d, *J* = 8.3 Hz), 7.33 – 6.98 (5H, m), 7.13 – 6.74 (2H, m), 5.85 – 5.42 (1H, m), 5.23 – 4.88 (2H, m), 4.68 (1H, d, *J* = 7.5 Hz), 4.31 – 3.79 (1H, m), 3.08 – 2.61 (2H, m), 2.40 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.1, 137.5, 137.2, 136.3, 129.5, 129.4, 128.5, 127.1, 126.8, 116.2, 56.9, 41.9, 21.5; *m/z* (ESI^+) HRMS: Calculated for $C_{17}H_{19}NO_2SNa$: 324.1029. Found $[M+Na]^+$: 324.1034;

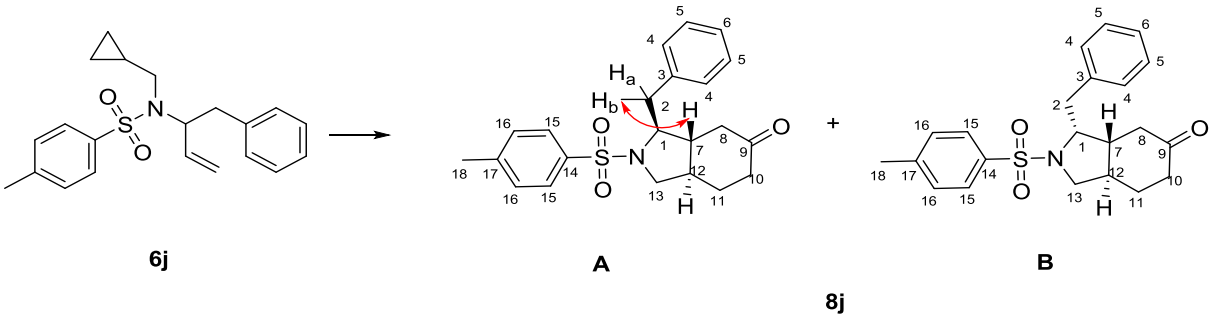
***N*-(Cyclopropylmethyl)-4-methyl-*N*-(1-phenylbut-3-en-2-yl)benzenesulfonamide (6j)**



6j

General procedure E: 4-Methyl-*N*-(1-phenylbut-3-en-2-yl)benzenesulfonamide (1.26 g, 4.0 mmol) and (bromomethyl)cyclopropane (1.08 g, 8.0 mmol) were employed, the crude mixture was purified by column chromatography (20 % EtOAc/Hex) to yield the title compound **6j** (0.79 g, 56 %) as a colorless oil; ν_{max} / cm^{-1}: 2924 (m), 1454 (m), 1330 (s), 1152 (s), 1090 (s), 1018 (m); ^{1}H NMR (400 MHz, , $CDCl_3$): δ 7.62 (2H, d, *J* = 8.0 Hz), 7.33 – 6.78 (7H, m), 5.77 (1H, ddd, *J* = 17.1, 10.5, 6.3 Hz), 5.08 (1H, d, *J* = 10.5 Hz), 4.99 (1H, d, *J* = 17.3 Hz), 4.70 – 4.54 (1H, m), 3.15 (1H, dd, *J* = 15.1, 6.6 Hz), 3.10 – 2.93 (3H, m), 2.39 (3H, s), 1.24 – 0.83 (1H, m), 0.67 – 0.42 (2H, m), 0.35 – 0.06 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.8, 138.4, 138.1, 135.7, 129.4, 129.3, 128.4, 127.2, 126.4, 118.4, 61.3 , 49.5 , 39.9 , 21.5 , 11.9 , 5.5 , 5.2; *m/z* (ESI^+) HRMS: Calculated for $C_{21}H_{25}NO_2SNa$: 378.1498. Found $[M+Na]^+$: 378.1507;

(3*S, 3a*R**, 7a*R**) and (3*R**, 3a*R**, 7a*R**)-3-benzyl-2-tosylhexahydro-1*H*-isoindol-5(6*H*)-one (8j)**



General procedure G: Compound **6j** (53.3 mg, 0.15 mmol) was employed, the crude mixture was purified by column chromatography (33 % EtOAc/Hex) to yield the title compound **8j** (37.4 mg, 65 %) as a colorless oil. A mixture of diastereomers A and B were obtained in a 5:1 (A:B) ratio. *Under general procedure **H**, title compound **8j** was obtained in 67 % yield (38.6 mg) as a colorless oil. A mixture of diastereomers A and B were obtained in a 3:1 (A:B) ratio.*

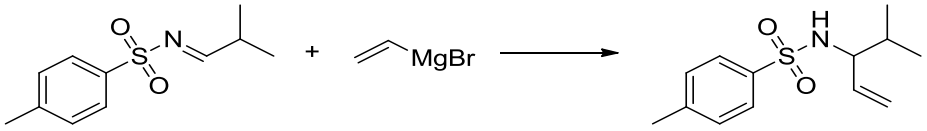
*The relative stereochemistry of major diastereomer A was corroborated by nOe experiments (as indicated on the compound structure). A nOe between C**2b**-H and C**7**-H was observed, and no significant nOe was observed between C**7**-H and C**12**-H. The stereochemical assignment of major diastereomer A is consistent with that of major diastereomer A of **8l**. The relative stereochemistry of minor diastereomer B was tentatively assigned by analogy to that of minor diastereomer B of **8l**.*

ν_{max} / cm^{-1}: 2925 (m), 1711 (s), 1339 (s), 1155 (s), 1089 (m), 1028 (m); *m/z* (ESI^+) HRMS: Calculated for $C_{22}H_{25}NO_3SNa$: 406.1447. Found $[M+Na]^+$: 406.1431;

Data for major diastereomer A: ^1H NMR (400 MHz, $CDCl_3$): δ 7.80 (2H, d, *J* = 8.2 Hz, 2 × C**15**-H), 7.45 – 7.05 (7H, m, 2 × C**16**-H, 2 × C**5**-H, 2 × C**4**-H, 1 × C**6**-H), 3.68 (1H, dd, *J* = 11.4, 6.1 Hz, 1 × C**13**-H_2), 3.50 (1H, ddd, *J* = 9.2, 7.7, 3.4 Hz, 1 × C**1**-H), 3.27 (1H, dd, *J* = 13.7, 3.4 Hz, 1 × C**2**-H_2), 3.07 (1H, dd, *J* = 13.7, 7.8 Hz, 1 × C**2**-H_2), 2.76 (1H, dd, *J* = 11.2, 11.2 Hz, 1 × C**13**-H_2), 2.45 (3H, s, 3× C**18**-H_3), 2.38 – 2.25 (1H, m, 1 × C**10**-H_2), 2.09 – 1.96 (1H, m, 1 × C**10**-H_2), 1.97 – 1.82 (2H, m, 1 × C**8**-H_2, 1 × C**11**-H_2), 1.73 (1H, dd, *J* = 13.8, 13.8 Hz, 1 × C**8**-H_2), 1.68 – 1.56 (1H, m, 1 × C**7**-H), 1.33 – 1.11 (2H, m, 1 × C**11**-H_2, 1 × C**12**-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.3 (C**9**), 143.7 (C**17**), 136.7 (C**3**), 135.1 (C**14**), 129.9, 129.8, 128.5, 127.4, 126.8 (C**15**, C**16**, C**4**, C**5**, C**6**), 66.0 (C**1**), 52.8 (C**13**), 49.2 (C**7**), 44.6 (C**8**), 41.7 (C**12**), 40.4 (C**2**), 39.3 (C**10**), 25.6 (C**11**), 21.6 (C**18**).

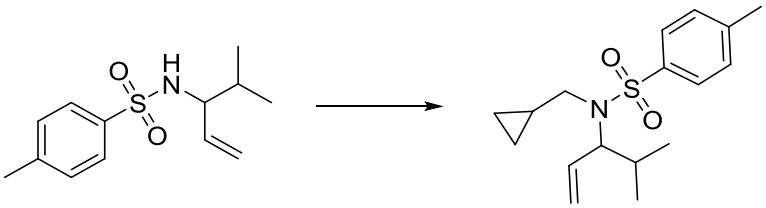
Data for minor diastereomer **B**: *Characteristic peaks only*: ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.06 (1H, ddd, *J* = 9.4, 7.7, 3.2 Hz, 1 × C**1**-H), 3.17 (1H, dd, *J* = 14.5, 3.3 Hz, 1 × C**2**-H_2), 2.96 (1H, dd, *J* = 14.6, 9.5 Hz, 1 × C**2**-H_2), 2.62 (1H, dd, *J* = 10.6, 9.1 Hz, 1 × C**13**-H_2), 2.25 – 2.16 (1H, m, 1 × C**7**-H), 1.50 – 1.42 (1H, m, 1 × C**12**-H);

4-Methyl-*N*-(4-methylpent-1-en-3-yl)benzenesulfonamide



General procedure F: (*E*)-4-Methyl-N-(2-methylpropylidene)benzenesulfonamide (1.40 g, 6.2 mmol) (prepared according to literature procedure[6]) and vinylmagnesium bromide (12.4 mL, 12.4 mmol, 1.0 M in THF) were employed, the crude mixture was purified by column chromatography (15 % EtOAc/Hex) to yield the title compound (1.44 g, 92 %) as a colorless solid; m.p.: 76 – 78 °C (CH_2Cl_2/Hex); ν_{max} / cm^{-1}: 3279 (m), 2962 (m), 1434 (m), 1323 (s), 1155 (s), 919 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 (2H, d, *J* = 8.3 Hz), 7.26 (2H, d, *J* = 8.5 Hz), 5.53 (1H, ddd, *J* = 17.1, 10.5, 6.7 Hz), 5.21 – 4.81 (2H, m), 4.59 – 4.56 (1H, br. m), 3.91 – 3.34 (1H, m), 2.41 (3H, s), 1.78 – 1.70 (1H, m), 0.83 (6H, dd, *J* = 6.8, 1.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.1, 138.1, 135.7, 129.4, 127.2, 116.6, 61.6, 32.7, 21.5, 18.2, 18.0; *m/z* (ESI^+) HRMS: Calculated for $C_{13}H_{19}NO_2SNa$: 276.1029. Found $[M+Na]^+$: 276.1039;

***N*-(Cyclopropylmethyl)-4-methyl-*N*-(4-methylpent-1-en-3-yl)benzenesulfonamide (6k)**

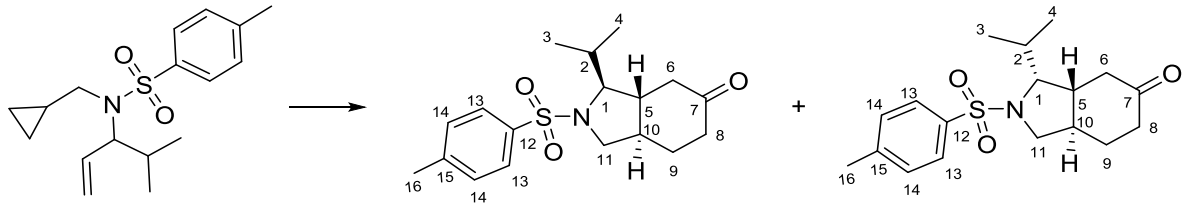


6k

General procedure E: 4-Methyl-*N*-(4-methylpent-1-en-3-yl)benzenesulfonamide (0.51 g, 2.0 mmol) and (bromomethyl)cyclopropane (0.54 g, 4.0 mmol) were employed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound **6k** (0.63 g, 92 %) as a colorless oil; ν_{max} / cm^{-1}: 2962 (m), 1333 (s), 1156 (s), 1090 (m), 1018 (m), 925 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (2H, d, *J* = 8.3 Hz), 7.23 (2H, d,

J = 8.0 Hz), 5.65 (1H, ddd, *J* = 17.1, 10.4, 8.7 Hz), 5.09 – 5.03 (1H, m), 4.95 (1H, ddd, *J* = 17.2, 1.7, 0.9 Hz), 3.86 (1H, dd, *J* = 10.6, 8.7 Hz), 3.07 (1H, dd, *J* = 15.1, 6.4 Hz), 2.91 (1H, dd, *J* = 15.1, 7.0 Hz), 2.39 (3H, s), 2.06 – 1.75 (1H, m), 1.14 – 0.93 (4H, m), 0.87 (3H, d, *J* = 6.5 Hz), 0.52 – 0.45 (2H, m), 0.35 – 0.07 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.6, 138.5, 135.1, 129.2, 127.4, 119.0, 67.5, 49.5, 30.4, 21.5 , 20.5, 20.3, 11.6, 5.8, 4.7; *m/z* (ESI^+) HRMS: Calculated for $C_{17}H_{25}NO_2SNa$: 330.1498. Found $[M+Na]^+$: 330.1501.

(3*S, 3a*R**, 7a*R**) and (3*R**, 3a*R**, 7a*R**)-3-Isopropyl-2-tosylhexahydro-1*H*-isoindol-5(6*H*)-one (8k)**



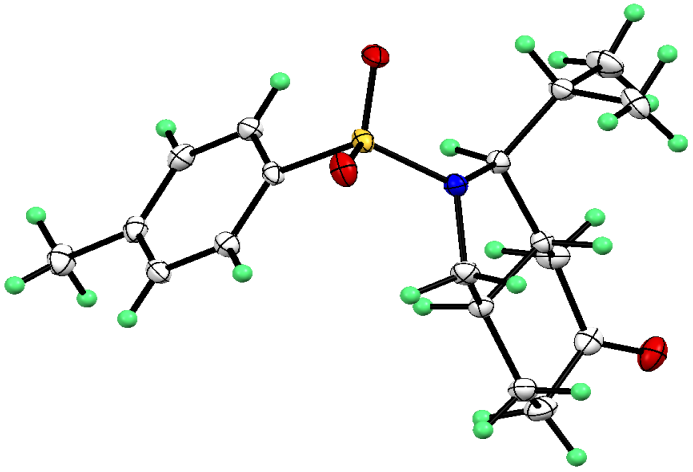
General procedure H: Compound **6k** (46.1 mg, 0.15 mmol) was employed, the crude mixture was purified by column chromatography (33 % EtOAc/Hex) to yield the title compound **8k** (33.8 mg, 67 %) as an off-white solid. A mixture of diastereomers A and B were obtained in a 10:1 (A:B) ratio. *Under general procedure **G**, title compound **8k** was obtained in 45 % yield (22.7 mg) as an off-white solid. A mixture of diastereomers A, B and C were obtained in a 14:2:1 (A:B:C) ratio.*

*Major diastereomer A could be recrystallized from the mixture (EtOAc/Hex), its structure and relative stereochemistry were determined unambiguously by X-ray crystallography. The relative stereochemistry of minor diastereomer B was tentatively assigned by analogy to that of minor diastereomer B of **8l**.*

ν_{max} / cm^{-1}: 2961 (m), 1709 (s), 1335 (s), 1156 (s), 1090 (m), 1002 (m); *m/z* (ESI^+) HRMS: Calculated for $C_{18}H_{25}NO_3SNa$: 358.1447. Found $[M+Na]^+$: 358.1452.

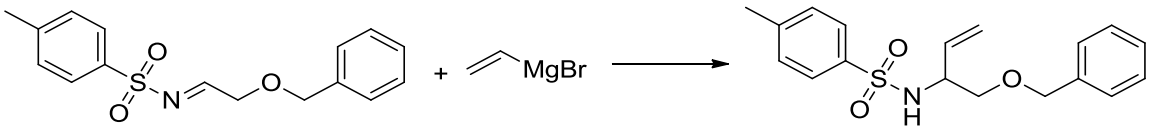
Data for major diastereomer A: m.p.: 100-102 °C (CH_2Cl_2/Hex); ^{1}H NMR (400 MHz, CD_3CN): δ 7.85 – 7.75 (2H, m, 2 × C**13**-H), 7.53 – 7.39 (2H, m, 2 × C**14**-H), 3.72 (1H, dd, *J* = 11.8, 6.5 Hz, 1 × C**11**-H_2), 3.34 (1H, dd, *J* = 9.1, 4.0 Hz, 1 × C**1**-H), 2.84 (1H, dd, *J* = 11.8 Hz, 11.8 Hz, 1 × C**11**-H_2), 2.50 – 2.42 (4H, m, 1 × C**6**-H_2, 3 × C**16**-H_3), 2.41 – 2.34 (1H, m, 1

× C**2**-H), 2.28 – 2.19 (1H, m, 1 × C**8**-H$_2$), 2.13 – 2.00 (2H, m, 1 × C**8**-H$_2$, 1 × C**6**-H$_2$), 1.94 – 1.81 (2H, m, 1 × C**5**-H, 1 × C**9**-H$_2$), 1.48 – 1.30 (1H, m, 1 × C**9**-H$_2$), 1.20 – 1.09 (1H, m, 1 × C**10**-H), 0.97 – 0.94 (6H, m, 3 × C**3**-H$_3$, , 3 × C**4**-H$_3$); ^{13}C NMR (100 MHz, CD_3CN): δ 207.1 (C**7**), 142.5 (C**15**), 134.2 (C**12**), 128.5 (C**14**), 126.1 (C**13**), 68.5 (C**1**), 51.9 (C**11**), 45.1 (C**6**), 43.2 (C**5**), 40.9 (C**10**), 37.6 (C**8**), 30.6 (C**2**), 23.5 (C**9**), 19.3 (C**16**), 17.4 (C**3**), 14.2 (C**4**);



Data for minor diastereomer B: *Characteristic peaks only*: ^{1}H NMR (400 MHz, CD_3CN): δ 7.73 – 7.70 (1H, m, 2 × C**13**-H), 3.60 – 3.51 (2H, m, 1 × C**11**-H$_2$, 1 × C**1**-H), 2.68 (1H, dd, *J* = 10.1 Hz, 10.1 Hz, 1 × C**11**-H$_2$).

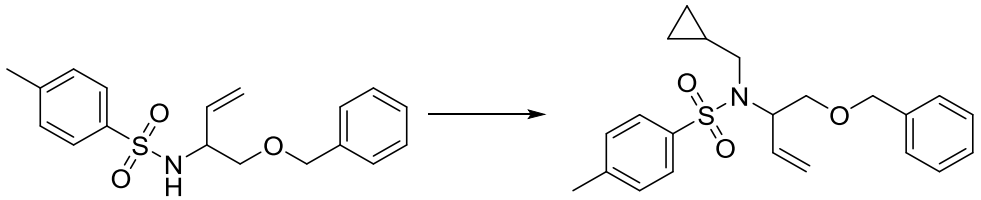
***N*-(1-(Benzyloxy)but-3-en-2-yl)-4-methylbenzenesulfonamide**



General procedure F: (*E*)-*N*-(2-(Benzyloxy)ethylidene)-4-methylbenzenesulfonamide (2.99 g, 9.5 mmol) (prepared according to literature procedure[7]) and vinylmagnesium bromide (19.0 mL, 19.0 mmol, 1.0 M in THF) were employed, the crude mixture was purified by column chromatography (15 % EtOAc/Hex) to yield the title compound (2.24 g, 73 %) as a colorless oil; ν_{max} / cm^{-1}: 3274 (m), 2901 (m), 1325 (m), 1160 (s), 1091 (s), 698 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (2H, d, *J* = 8.3 Hz), 7.45 – 7.26 (3H, m), 7.27 – 7.10 (4H, m), 5.69 (1H, ddd, *J* = 17.0, 10.4, 6.3 Hz), 5.16 (1H, dd, *J* = 17.2, 1.5 Hz), 5.09 (1H, dd, *J* = 10.5, 1.4 Hz), 4.98 (1H, br. s), 4.41 (2H, s), 3.96 – 3.88 (1H, m), 3.75 – 3.03 (2H, m), 2.41 (3H, s); ^{13}C

NMR (100 MHz, $CDCl_3$): δ 143.3, 137.6, 137.4, 135.1, 129.5, 128.4, 127.9, 127.7, 127.2, 117.5, 73.2, 71.8, 55.7, 21.5; *m/z* (ESI^+) HRMS: Calculated for $C_{18}H_{21}NO_3SNa$: 354.1134. Found $[M+Na]^+$: 354.1141.

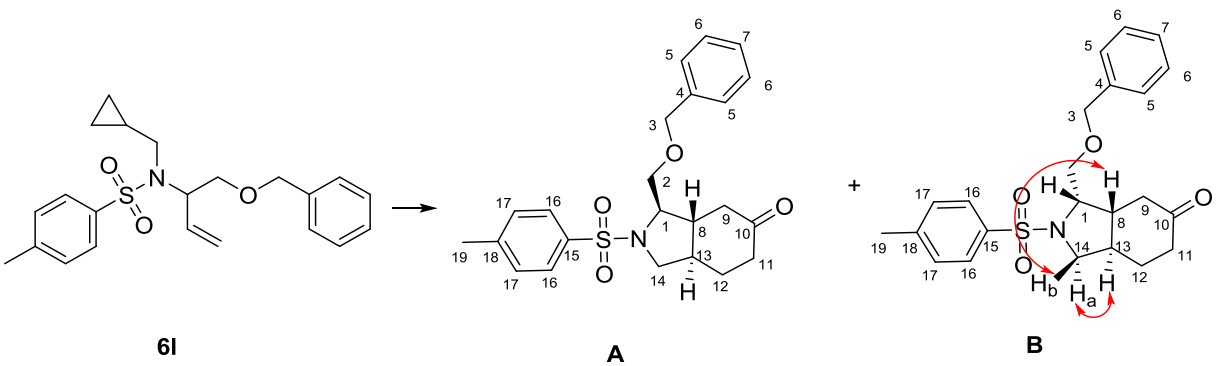
1-(Benzyloxy)-*N*-(cyclopropylmethyl)but-3-en-2-amine (6l)



6l

General procedure E: *N*-(1-(Benzyloxy)but-3-en-2-yl)-4-methylbenzenesulfonamide (0.46 g, 1.3 mmol) and (bromomethyl)cyclopropane (0.36 g, 2.6 mmol) were employed, the crude mixture was purified by column chromatography (20 % EtOAc/Hex) to yield the title compound **6l** (0.36 g, 71 %) as a colorless oil; ν_{max} / cm^{-1}: 3311 (w), 2858 (m), 1642 (m), 1240 (m), 1153 (m), 1090 (m); ^1H NMR (400 MHz, $CDCl_3$): δ 7.73 (2H, d, *J* = 8.3 Hz), 7.49 – 7.21 (5H, m), 7.18 (2H, d, *J* = 8.6 Hz), 6.12 – 5.54 (1H, m), 5.38 – 4.98 (2H, m), 4.75 – 4.57 (1H, m), 4.46 (2H, d, *J* = 3.0 Hz), 3.70 (2H, d, *J* = 6.9 Hz), 3.11 (1H, dd, *J* = 15.1, 6.8 Hz), 3.01 (1H, dd, *J* = 15.1, 6.7 Hz), 2.37 (3H, s), 1.04 – 0.85 (1H, m), 0.55 – 0.34 (2H, m), 0.30 – 0.06 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.7, 138.4, 137.8, 134.4, 129.3, 128.3, 127.7, 127.6, 127.3, 118.6, 73.0, 70.7, 58.7, 49.6, 21.5, 11.8, 5.1, 5.0; *m/z* (ESI^+) HRMS: Calculated for $C_{22}H_{27}NO_3SNa$: 408.1604. Found $[M+Na]^+$: 408.1617.

(3*R, 3a*R**, 7a*R**) and (3*S**, 3a*R**, 7a*R**)-3-((Benzyloxy)methyl)-2-tosylhexahydro-1*H*-isoindol-5(6*H*)-one (8l)**



6l **A** **B**

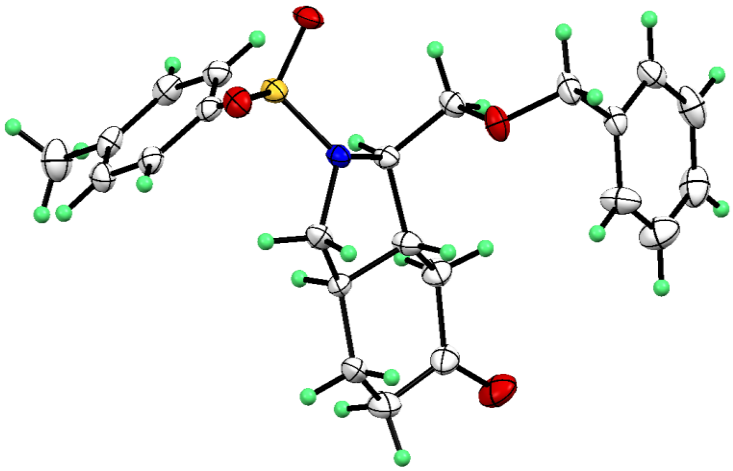
8l

General procedure H: Compound **6l** (57.8 mg, 0.15 mmol) was employed, the crude mixture was purified by column chromatography (33 % EtOAc/Hex) to yield the title compound **8l** (42.2 mg, 68 %) as an off-white soild. A mixture of diastereomers A and B were obtained in a 3:1 (A:B) ratio. *Under general procedure **G**, title compound **8l** was obtained in 61 % yield (37.9 mg) as an off-white solid. A mixture of diastereomers A and B were obtained in a 2:1 (A:B) ratio.*

*Diastereomer A and B could be separated by flash column chromatography (20 % EtOAc/hexane) using 60H silica. The structure and relative stereochemistry of major diastereomer A was determined unambiguously by X-ray crystallography. The relative stereochemistry of minor diastereomer B was corroborated by nOe experiments (as indicated on the compound structure). nOes were observed between C**14**$_a$-H and C**13**-H, C**14**$_b$ and C**8**, these results indicated a trans ring junction for diastereomer B (same as diastereomer A), which suggests that the stereochemistry at C**1** for diastereomer B is opposite to that of diastereomer A.*

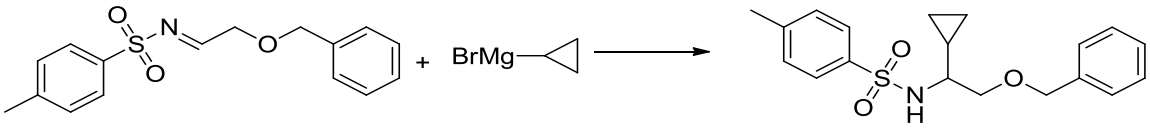
ν_{max} / cm^{-1}: 2885 (m), 1711 (s), 1343 (m), 1157 (s), 1088 (s), 662 (s); *m/z* (ESI^+) HRMS: Calculated for $C_{23}H_{27}NO_4SNa$: 436.1553. Found $[M+Na]^+$: 436.1544.

Data for major diastereomer A: m.p.: 132 – 135 °C (CH_2Cl_2/Hex); ^{1}H NMR (400 MHz, C_6D_6): δ 7.70 (2H, d, *J* = 8.1 Hz, 2 × C**16**-H), 7.36 – 7.08 (4H, m, 2 × C**6**-H, 2 × C**5**-H), 7.11 – 6.91 (1H, m, 1 × C**7**-H), 6.78 (2H, dd, *J* = 8.2, 2.0 Hz, 2 × C**17**-H), 4.27 (2H, s, 2 × C**3**-H_2), 3.89 (1H, dd, *J* = 9.6, 3.2 Hz, 1 × C**2**-H_2), 3.62 (1H, dd, *J* = 9.6, 6.7 Hz1 × C**2**-H_2), 3.49 (1H, dd, *J* = 11.0, 6.8 Hz, 1 × C**14**-H_2), 3.30 (1H, ddd, *J* = 9.6, 6.7, 3.2 Hz, 1 × C**1**-H), 2.63 (1H, ddd, *J* = 13.9, 3.7, 1.8 Hz, 1 × C**9**-H_2), 2.49 (1H, dd, *J* = 11.2, 1.4 Hz, 1 × C**14**-H_2), 2.01 – 1.88 (1H, m, 1 × C**11**-H_2), 1.86 (3H, s, 3 × C**19**-H_3), 1.68 – 1.53 (1H, m, 1 × C**8**-H), 1.52 – 1.39 (1H, m, 1 × C**9**-H_2), 1.27 (1H, td, *J* = 14.2, 6.8 Hz, 1 × C**11**-H_2), 1.13 – 0.94 (1H, m, 1 × C**12**-H_2), 0.94 – 0.72 (1H, m, 1 × C**13**-H), 0.62 – 0.40 (1H, m, 1 × C**12**-H_2); ^{13}C NMR (100 MHz, C_6D_6): δ 205.9 (C**10**), 142.7 (C**18**), 138.3 (C**4**), 136.5 (C**15**), 129.3 (C**16**), 128.3, 127.8, 127.5, 127.4 (C**5**, C**6**, C**7**, C**17**), 73.3 (C**3**), 72.0 (C**2**), 64.1 (C**1**), 52.9 (C**14**), 48.4 (C**8**), 44.5 (C**9**), 41.2 (C**13**), 38.8 (C**11**), 25.1 (C**12**), 20.7 (**C**19).



Data for minor diastereomer B: m.p.: 131 – 133 °C (CH_2Cl_2/Hex); ^{1}H NMR (400 MHz, C_6D_6): δ 7.68 (2H, d, *J* = 8.2 Hz, 2 × C**16**-H), 7.19 – 7.15 (4H, m, 2 × C**6**-H, 2 × C**5**-H), 7.08 – 6.99 (1H, m, 1 × C**7**-H), 6.78 (2H, d, *J* = 8.3 Hz, 2 × C**17**-H), 4.25 (2H, s, 2 × C**3**-H_2), 3.57 (3H, dt, *J* = 16.5, 6.7 Hz, 2 × C**2**-H_2, 1 × C**1**-H), 3.40 (1H, dd, *J* = 8.5, 6.6 Hz, 1 × C**14**-H_2), 2.38 – 2.17 (2H, m, 1 × C**14**-H_2, 1 × C**9**-H_2), 2.07 (1H, dd, *J* = 14.1, 14.1 Hz, 1 × C**9**-H_2), 1.99 – 1.88 (1H, m, 1 × C**11**-H_2), 1.87 (3H, s, 3 × C**19**-H_3), 1.82 – 1.70 (1H, m, 1 × C**13**-H), 1.52 (1H, td, *J* = 14.2, 6.3 Hz, 1 × C**11**-H_2), 1.19 – 1.09 (1H, m, 1 × C**12**-H_2), 1.04 – 0.89 (1H, m, 1 × C**8**-H), 0.37 – 0.25 (1H, m, 1 × C**12**-H_2). ^{13}C NMR (100 MHz, C_6D_6): δ 206.3 (C**10**), 142.8 (C**18**), 138.2 (C**4**), 134.9 (C**15**), 128.3 (C**16**), 127.6, 127.5, 127.5 (C**5**, C**6**, C**7**, C**17**), 73.4 (C**3**), 70.6 (C**2**), 60.5 (C**1**), 52.4 (C**14**), 46.3 (C**8**), 41.9 (C**9**), 39.3 (C**11**), 39.1 (C1**3**), 26.1 (C**12**), 20.7 (C**19**).

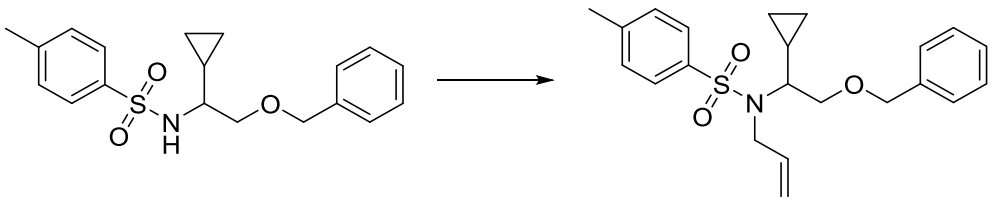
***N*-(2-(Benzyloxy)-1-cyclopropylethyl)-4-methylbenzenesulfonamide**



General procedure F: (*E*)-*N*-(2-(Benzyloxy)ethylidene)-4-methylbenzenesulfonamide (0.91 g, 3.0 mmol) and cyclopropylmagnesium bromide (0.86 g, 6.0 mmol) were employed, the crude mixture was purified by column chromatography (20 % EtOAc/Hex) to yield the title compound (0.68 g, 66 %) as a colorless oil; ν_{max} / cm^{-1}: 3276 (m), 2900 (m), 1321 (m), 1157 (m), 1084 (s), 1026 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (2H, d, *J* = 8.3 Hz), 7.40 – 7.04 (7H, m), 5.27 – 5.22 (1H, br. m), 4.40 (2H, s), 3.46 (1H, dd, *J* = 9.5, 4.4 Hz), 3.37 (1H, dd, *J* = 9.5, 4.2 Hz), 2.71 (1H, ddd, *J* = 8.6, 7.1, 4.3 Hz), 2.39 (3H, s), 0.96 (1H, ddt, *J* = 8.4, 4.9,

4.9 Hz), 0.52 – 0.40 (1H, m), 0.39 – 0.29 (1H, m), 0.24 – 0.14 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.0, 138.4, 137.9 129.4, 128.4, 127.7, 127.6, 127.1, 73.2, 72.0, 58.4, 21.5, 13.9, 3.9, 3.4; *m/z* (ESI^+) HRMS: Calculated for $C_{19}H_{23}NO_3SNa$: 368.1291. Found $[M+Na]^+$: 368.1289.

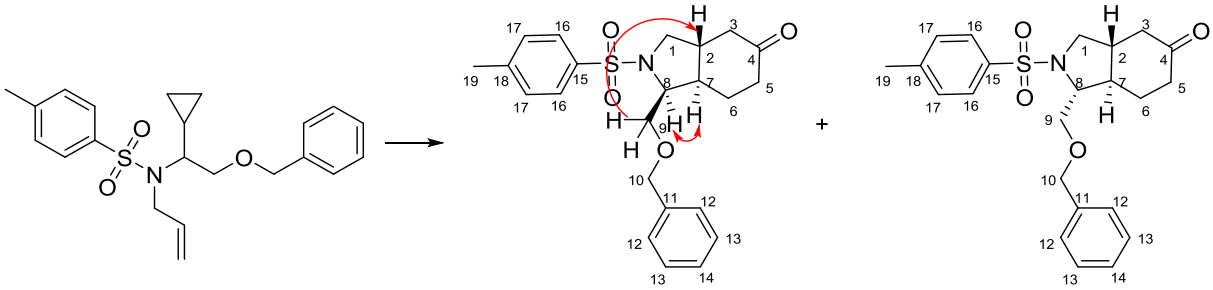
***N*-Allyl-*N*-(2-(benzyloxy)-1-cyclopropylethyl)-4-methylbenzenesulfonamide (6m)**



6m

General procedure B: *N*-(2-(benzyloxy)-1-cyclopropylethyl)-4-methylbenzenesulfonamide (0.65 g, 1.9 mmol) were employed, the mixture was purified by column chromatography (10 % EtOAc/Hex) to yield title amide **6m** (0.64 g, 88 %) as a colorless oil; ν_{max} / cm^{-1}: 2921 (m), 1698 (m), 1327 (m), 1154 (s), 1089 (m), 883 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (2H, d, *J* = 8.3 Hz), 7.38 – 7.27 (3H, m), 7.23 – 7.18 (2H, m), 7.15 (2H, d, *J* = 7.9 Hz), 5.83 (1H, ddt, *J* = 17.2, 10.1, 6.3 Hz), 5.11 (1H, dd, *J* = 17.2, 1.5 Hz), 5.02 (1H, dd, *J* = 10.2, 1.4 Hz), 4.43 (1H, d, *J* = 11.9 Hz), 4.36 (1H, d, *J* = 11.9 Hz), 3.94 (2H, ddt, *J* = 6.3, 3.1, 1.5 Hz), 3.66 – 3.56 (2H, m), 3.26 (1H, ddd, *J* = 9.9, 7.6, 4.9 Hz), 2.37 (3H, s), 0.99 (1H, ddt, *J* = 9.8, 8.0, 4.9 Hz), 0.68 – 0.52 (1H, m), 0.45 – 0.39 (1H, m), 0.36 – 0.23 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.6, 138.4, 138.0, 136.4, 129.1, 128.3, 127.6, 127.5, 127.5, 116.7, 72.9, 71.4, 63.3, 47.7, 21.5, 12.5, 6.2, 3.9; *m/z* (ESI^+) HRMS: Calculated for $C_{23}H_{27}NO_4SNa$: 408.1604. Found $[M+Na]^+$: 408.1596.

(1*S, 3a*R**, 7a*R**) and (1*R**, 3a*R**, 7a*R**)-1-((benzyloxy)methyl)-2-tosylhexahydro-1*H*-isoindol-5(6*H*)-one (8m)**



6m **A** **B**

8m

General procedure H: Compound **6m** was employed, the crude mixture was purified by column chromatography (33 % EtOAc/Hex) to yield the title compound **8m** (31.7 mg, 51 %) as a colorless oil. A mixture of diastereomers A and B were obtained in a 9:1 (A:B) ratio). *Under general procedure **G**, title compound **8m** was obtained in 26 % yield (16.2 mg) as a colorless oil. A mixture of diastereomers A and B were obtained in a 4:1 (A:B) ratio.*

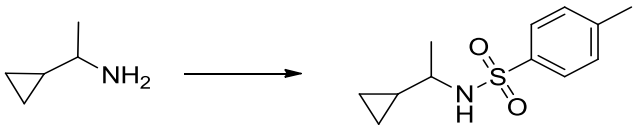
*The relative stereochemistry of major diastereomer A was corroborated by nOe experiments (as indicated on the compound structure). nOes were observed between C**7**-H and C**8**-H, from C**9**-H to C**2**-H, and no significant nOe was observed between C**7**-H and C**2**-H. The stereochemical assignment of major diastereomer A is consistent with that of major diastereomer A of **8n**. The relative stereochemistry of minor diastereomer B was tentatively assigned by analogy to that of minor diastereomer B of **8o**.*

ν_{max} / cm^{-1}: 2900 (m), 1712 (s), 1341 (m), 1161 (s), 1090 (s), 733 (s); *m/z* (ESI^+) HRMS: Calculated for $C_{23}H_{27}NO_4SNa$: 436.1553. Found $[M+Na]^+$: 436.1546.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 (2H, d, *J* = 8.2 Hz, 2 × C**16**-H), 7.55 – 6.98 (7H, m, 2 × C**17**-H, 2 × C**12**-H, 2 × C**13**-H, 1 × C**14**-H), 4.48 (2H, s, 2 × C**10**-H_2), 3.87 (1H, dt, *J* = 7.6, 4.5 Hz, 1 × C**8**-H), 3.65 (2H, d, *J* = 4.6 Hz, 2 × C**9**-H_2), 3.59 (1H, dd, *J* = 8.6, 6.6 Hz, 1 × C**1**-H_2), 2.68 (1H, dd, *J* = 10.6, 8.7 Hz, 1 × C**1**-H), 2.54 (1H, ddd, *J* = 14.1, 4.2, 1.9 Hz, 1 × C**3**-H_2), 2.48 – 2.31 (5H, m, 3 × C**19**-H_3, 1 × C**5**-H_2, 1 × C**2**), 2.19 – 2.02 (2H, m, 1 × C**5**-H_2, 1 × C**6**-H_2), 1.96 (1H, dd, *J* = 13.7, 13.7 Hz, 1 × C**3**-H_2), 1.80 – 1.65 (1H, m, 1 × C**6**-H_2), 1.64 – 1.57 (1H, m, 1 × C**7**-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.6 (C**4**), 143.6 (C**18**), 138.7 (C**11**), 134.1 (C**15**), 129.8 (C**17**), 128.4, 127.7, 127.7, 127.5 (C**16**, C**12**, C**13**, C1**4**), 73.6 (C**10**), 70.7 (C**9**), 60.4 (C**8**), 53.0 (C**1**), 45.5 (C**7**), 44.4 (C**3**), 40.9 (C**2**), 40.1 (C**5**), 24.2 (C**6**), 21.6 (C**19**).

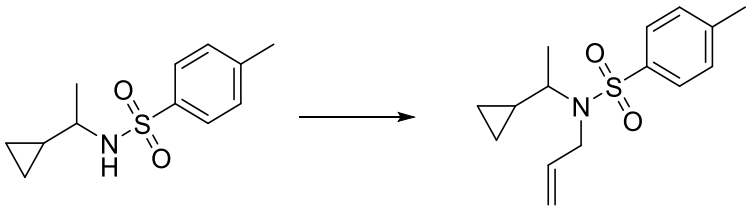
Data for minor diastereomer B: *Characteristic peaks only*: ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.30 (1H, ddd, *J* = 9.5, 6.4, 3.2 Hz, 1 × C**8**-H), 3.03 (1H, dd, *J* = 11.4 Hz, 1 × C**1**-H_2).

***N*-(1-Cyclopropylethyl)-4-methylbenzenesulfonamide**



General procedure A: 1-Cyclopropylethanamine (0.30 g, 3.5 mmol) and *p*-toluenesulfonyl chloride (0.83 g, 4.2 mmol) were employed, the crude mixture was purified by column chromatography (20 % EtOAc/Hex) to yield title sulfonamide (0.61 g, 71 %) as a colorless oil; ν_{max} / cm^{-1}: 3273 (m), 2972 (m), 1423 (m), 1320 (s), 1154 (s), 1089 (s), 970 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (2H, d, *J* = 8.3 Hz), 7.28 (2H, d, *J* = 8.0 Hz), 4.59 (1H, d, *J* = 6.4 Hz), 2.69 – 2.61 (1H, m), 2.42 (3H, s), 1.14 (3H, d, *J* = 6.6 Hz), 0.79 – 0.70 (1H, m), 0.44 (1H, dddd, *J* = 9.1, 8.3, 5.7, 4.5 Hz), 0.32 (1H, dddd, *J* = 9.1, 7.9, 5.6, 4.6 Hz), 0.12 (1H, dddd, *J* = 9.4, 5.6, 4.7, 4.7 Hz), 0.01 (1H, dddd, *J* = 9.6, 5.7, 4.8, 4.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.1, 138.1, 129.5, 127.1, 54.7, 21.5, 21.2, 17.9, 3.6, 3.3; *m/z* (ESI^+) HRMS: Calculated for $C_{12}H_{17}NO_2SNa$: 262.0872. Found $[M+Na]^+$: 262.0869.

***N*-Allyl-*N*-(1-cyclopropylethyl)-4-methylbenzenesulfonamide (6n)**

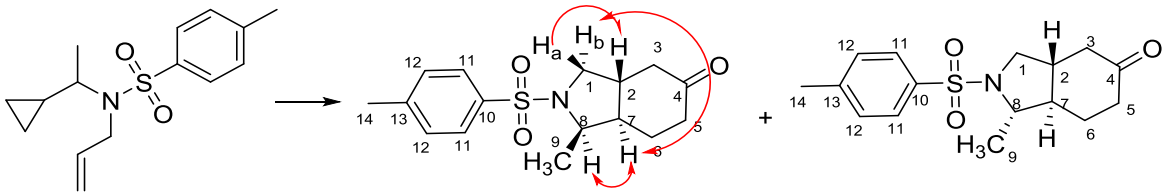


6n

General procedure B: *N*-(1-Cyclopropylethyl)-4-methylbenzenesulfonamide (0.52 g, 2.1 mmol) and allyl bromide (1.26 g, 10.5 mmol) were employed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound **6n** (0.53 g, 91 %) as a colorless oil; ν_{max} / cm^{-1}: 2974 (m), 1332 (s), 1151 (s), 1090 (s), 1038 (s), 879 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (2H, d, *J* = 8.1 Hz), 7.25 (2H, d, *J* = 8.0 Hz), 5.90 (1H, ddt, *J* = 16.9, 10.2, 6.2 Hz), 5.21 (1H, dd, *J* = 17.2, 1.7 Hz), 5.09 (1H, dd, *J* = 10.2, 1.3 Hz), 4.01 – 3.95 (1H, m), 3.90 – 3.84 (1H, m), 3.13 (1H, dq, *J* = 9.2, 6.8 Hz), 2.40 (3H, s), 1.13 (3H, dd, *J* = 6.8, 0.7 Hz), 0.86 (1H, qt, *J* = 8.5, 4.9 Hz), 0.53 (1H, tdd, *J* = 8.6, 7.0, 5.2

Hz), 0.34 (1H, ddt, *J* = 9.6, 8.4, 5.1 Hz), 0.17 (1H, ddd, *J* = 9.7, 4.9 Hz), 0.07 (1H, ddd, *J* = 9.9, 5.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.8, 138.6, 136.6, 129.4, 127.0, 116.6, 59.4, 46.5, 21.5, 18.9, 16.2, 5.5, 4.3; *m/z* (ESI^+) HRMS: Calculated for $C_{15}H_{21}NO_2SNa$: 302.1185. Found $[M+Na]^+$: 302.1178.

(1*R, 3a*R**, 7a*R**) and (1*S**, 3a*R**, 7a*R**)-1-Methyl-2-tosylhexahydro-1*H*-isoindol-5(6*H*)-one (8n)**



6n **A** **B**

8n

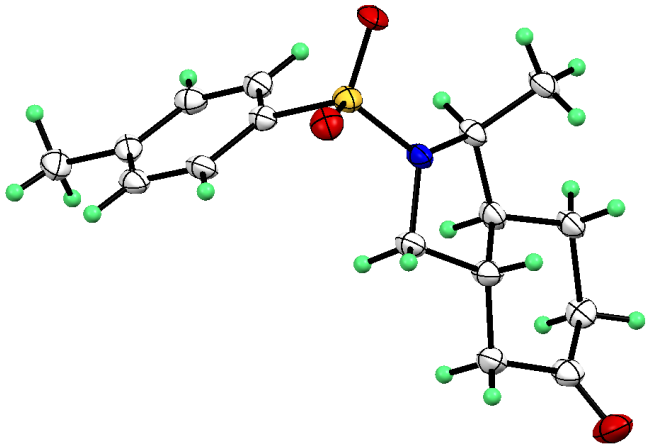
General procedure H: Compound **6n** (41.9 mg, 0.15 mmol) was employed, the crude mixture was purified by column chromatography (33 % EtOAc/Hex) to yield the title compound **8n** (27.6 mg, 60 %) as a colorless solid. A mixture of diastereomers A and B were obtained in a 6:1 (A:B) ratio. *Under general procedure **G**, title compound **8n** was obtained in 44 % yield (20.3 mg) as a colorless solid. A mixture of diastereomers A and B were obtained in a 3:1 (A:B) ratio.*

*Major diastereomers A was recrystallized from the mixture of A and B (EtOAc/Hex). The structure and relative stereochemistry of major diastereomers A was determined unambiguously by X-ray crystallography. At the same time, the relative stereochemistry of major diastereomers A was corroborated by nOe experiments (as indicated on the compound structure A). nOes between C**7**-H and C**8**-H, from C**1**$_a$-H to C**2**-H, between C**7**-H and C**1**$_b$-H were observed. The relative stereochemistry of minor diastereomer B was tentatively assigned by analogy to that of minor diastereomer B of **8o**.*

ν_{max} / cm^{-1}: 2971 (m), 1713 (s), 1338 (m), 1162 (m), 1043 (m), 816 (m); *m/z* (ESI^+) HRMS: Calculated for $C_{16}H_{21}NO_3SNa$: 330.1134. Found $[M+Na]^+$: 330.1147.

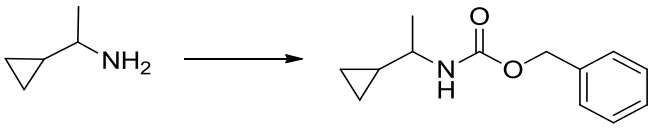
Data for major diastereomer A: m.p.: 159 – 160 °C (CH_2Cl_2/Hex);^{1}H NMR (400 MHz, C_6D_6): δ 7.74 (2H, d, *J* = 7.8 Hz, 2 × C**11**-H), 6.85 (2H, d, *J* = 8.1 Hz, 2 × C**12**-H), 3.91 (1H, td, *J* = 6.7, 6.7 Hz, 1 × C**8**-H), 3.22 (1H, dd, *J* = 8.7, 6.4 Hz, 1 × C**1**-H_2), 2.31 (1H, dd, *J* = 10.6, 8.7, Hz, 1 × C**1**-H_2), 2.06 (1H, ddd, *J* = 14.0, 4.1, 1.9 Hz, 1 × C**3**-H_2), 2.00 – 1.84 (4H,

m, 1 × C**5**-H$_2$, 3 × C**14**-H$_3$), 1.38 – 1.24 (2H, m, 1 × C**5**-H$_2$, 1 × C**2**-H), 1.13 (1H, dd, *J* =13.6, 13.6 Hz, 1 × C**3**-H$_2$), 0.97 – 0.88 (4H, m, 1 × C**6**-H$_2$, , 3 × C**9**-H$_3$), 0.86 – 0.76 (1H, m, 1 × C**7**-H), 0.76 – 0.62 (1H, m, 1 × C**6**-H$_2$); ^{13}C NMR (100 MHz, C_6D_6): δ 205.6 (C**4**), 142.6 (C**13**), 135.9 (C**10**), 129.3 (C**12**), 127.6 (C**11**), 56.9 (C**8**), 52.9 (C**1**), 45.0 (C**7**), 43.4 (C**3**), 39.5 (C**2**), 39.2 (C**5**), 23.5 (C**6**), 20.7 (C**14**), 17.7 (C**9**).



Data for minor diastereomer B: *Characteristic peaks only*: ^{1}H NMR (400 MHz, C_6D_6): δ 7.68 (2H, d, *J* = 8.2 Hz, 2 × C**11**-H$_2$), 6.80 (2H, d, *J* = 8.0 Hz, 2 × C**12**-H$_2$), 3.39 (1H, dd, *J* = 10.9, 6.5 Hz, × C**1**-H$_2$), 2.84 (1H, dt, *J* = 8.7, 6.1 Hz, 1 × C**8**-H), 2.58 (1H, dd, *J* = 10.7, 10.7 Hz, 1 × C**1**-H$_2$), 0.50 – 0.39 (1H, m, 1 × C**6**-H$_2$).

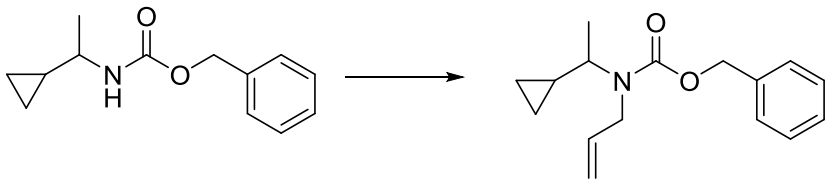
Benzyl (1-cyclopropylethyl)carbamate



General procedure A: 1-Cyclopropylethanamine (0.40 g, 4.7 mmol) and benzyl chloroformate (0.85 g, 5.6 mmol) were employed, the crude mixture was purified by column chromatography (20 % EtOAc/Hex) to yield title carbamate (0.42 g, 41 %) as a colorless oil; ν_{max} / cm^{-1}: 3329 (s), 2975 (m), 1679 (s), 1532 (s), 1362 (m), 1252 (s), 1058 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 – 7.26 (5H, m), 5.09 (2H, s), 4.76 (1H, s), 3.23 – 3.04 (1H, m), 1.21 (3H, d, *J* = 6.6 Hz), 0.81 – 0.78 (1H, m), 0.54 – 0.38 (2H, m), 0.38 – 0.30 (1H, m), 0.23 – 0.19 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.8, 136.7, 128.5, 128.1, 128.0, 66.5, 51.4,

20.6, 17.5, 3.1, 2.9; *m/z* (ESI$^+$) HRMS: Calculated for $C_{13}H_{17}NO_2SNa$: 242.1151. Found $[M+Na]^+$: 242.1157.

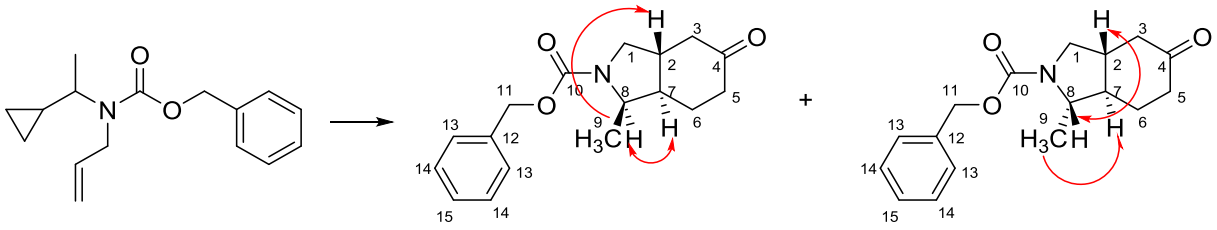
Benzyl allyl (1-cyclopropylethyl)carbamate (6o)



6o

General procedure B: Benzyl (1-cyclopropylethyl)carbamate (0.40 g, 1.8 mmol) and allyl bromide (1.11 g, 9.2 mmol) were employed was employed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound **6o** (0.40 g, 85 %) as a colorless oil; ; ν_{max} / cm^{-1}: 3079 (m), 1690 (s), 1408 (s), 1253 (s), 1136 (m), 1028 (m), 918 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 – 7.31 (5H, m), 5.91 (1H, ddt, *J* = 16.1, 10.4, 5.6 Hz), 5.24 – 5.02 (4H, m), 3.92 (2H, d, *J* = 5.8, Hz), 3.36 – 3.27 (1H, br. m), 1.23 (3H, dd, *J* = 6.8, 0.9 Hz), 1.10 – 0.90 (1H, m), 0.60 – 0.50 (1H, m), 0.40 (1H, tdd, *J* = 7.9, 2.5, 1.3 Hz), 0.25 (2H, br. s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.7, 137.6, 136.4, 128.3, 127.7, 127.6, 115.1, 66.3, 57.7, 46.0, 17.8, 15.4, 4.1, 3.3; *m/z* (ESI$^+$) HRMS: Calculated for $C_{16}H_{21}NO_2Na$: 282.1464. Found $[M+Na]^+$: 282.1470.

Benzyl (1*R, 3a*R**, 7a*R**) and (1*S**, 3a*R**, 7a*R**)-1-methyl-5-oxohexahydro-1*H*-isoindole-2(3*H*)-carboxylate (8o)**



6o **A** **B**

8o

General procedure H: Compound **6o** (38.9 mg, 0.15 mmol) was employed, the crude mixture was purified by column chromatography (33 % EtOAc/Hex) to yield the title compound **8o** (29.8 mg, 69 %) as a colorless oil. A mixture of diastereomers A and B were obtained in a 3:1 (A:B) ratio. *Under general procedure **G**, title compound **8o** was obtained in*

52 % yield (22.5 mg) as a colorless oil. A mixture of diastereomers A and B were obtained in a 1:1 (A:B) ratio.

*Diastereomer A and B could be separated by flash column chromatography (20 % EtOAc/hexane). The relative stereochemistry of major diastereomer A was corroborated by nOe experiments (as indicated on the compound structure A). nOes between C**7**-H and C**8**-H, and from C**9**-H to C**2**-H were observed. The stereochemical assignment of major diastereomer A is consistent with that of major diastereomer A of **8n**. The relative stereochemistry of minor diastereomer B was corroborated by nOe experiments (as indicated on the compound structure B). nOes between C**2**-H and C**8**-H, from C**9**-H to C**7**-H were observed.*

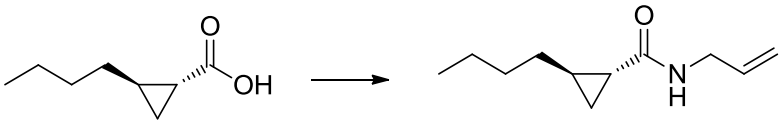
ν_{max} / cm^{-1}: 2935 (m), 1696 (s), 1410 (s), 1351 (m), 1090 (m), 770 (m); *m/z* (ESI^+) HRMS: Calculated for $C_{17}H_{21}NO_3Na$: 310.1414. Found $[M+Na]^+$: 310.1418.

Data for major diastereomer A: ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38 – 7.28 (5H, m, 2 × C**13**-H, *A*+*B*, 2 × C**14**-H, *A*+*B*, 1 × C**15**-H, *A*+*B*), 5.19 – 5.06 (2H, m, 2 × C**11**-H_2, *A*+*B*), 4.19 – 4.02 (1H, m, 1 × C**8**-H, *A*+*B*), 3.67 (1H, ddd, *J* = 10.3, 6.3, 6.3 Hz, 1 × C**1**-H_2, *A*+*B*), 3.03 (1H, ddd, *J* = 13.6, 10.1, 10.1 Hz, 1 × C**1**-H_2, *A*+*B*), 2.63 (1H, ddd, *J* = 26.6, 10.2, 2.0 Hz, 1 × C**3**-H_2, *A*+*B*), 2.54 – 2.47 (1H, m, 1 × C**5**-H_2, *A*+*B*), 2.36 – 2.27 (1H, m, 1 × C**5**-H_2, *A*+*B*), 2.24 – 2.14 (2H, m, 1 × C**3**-H_2, *A*+*B*, 1 × C**2**-H, *A*+*B*), 2.14 – 2.04 (1H, m, 1 × C**7**-H, *A*+*B*), 2.03 – 1.96 (1H, m, 1 × C**6**-H_2, *A*+*B*), 1.66 – 1.55 (1H, m, 1 × C**6**-H_2, *A*+*B*), 1.08 (3H, dd, *J* = 23.7, 6.6 Hz, 3 × C**9**-H_3, *A*+*B*); ^{13}C NMR (126 MHz, $CDCl_3$): δ 209.1 (C**4**, *A*), 209.0 (C**4**, *B*), 154.8 (C**10**, *A*), 154.5 (C**10**, *B*), 136.8 (C**12**, *A*), 136.8 (C**12**, *B*), 128.5, 128.5, 127.9, 127.9, 127.9 (C**13**, *A*+*B*, C**14**, *A*+*B*, C**15**, *A*+*B*), 66.8 (C**11**, *A*), 66.6 (C**11**, *B*), 55.2 (C**8**, *A*), 54.8 (C**8**, *B*), 51.3 (C**1**, *A*), 51.0 (C**1**, *B*), 46.0 (C**7**, *A*), 45.3 (C**7**, *B*), 44.8 (C**3**, *A*), 44.7 (C**3**, *B*), 40.4 (C**5**, *A*), 40.2 (C**5**, *B*), 40.2 (C**2**, *A*), 39.5 (C**2**, *B*), 24.5 (C**6**, *A*), 24.4 (C**6**, *B*), 15.8 (C**9**, *A*), 15.1 (C**9**, *B*).

Data for minor diastereomer B: ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41 – 7.27 (5H, m, 2 × C**13**-H, *A*+*B*, 2 × C**14**-H, *A*+*B*, 1 × C**15**-H, *A*+*B*), 5.21 – 5.04 (2H, m, 2 × C**11**-H_2, *A*+*B*), 3.96 – 3.76 (1H, m, 1 × C**1**-H_2, *A*+*B*), 3.49 – 3.33 (1H, m, 1 × C**8**-H, *A*+*B*), 3.03 (1H, dd, *J* = 10.7, 10.7 Hz, 1 × C**1**-H_2, *A*+*B*), 2.64 – 2.47 (2H, m, 1 × C**3**-H_2, *A*+*B*, 1 × C**5**-H_2, *A*+*B*), 2.33 (1H, ddd, J=15.2, 12.7, 6.6 Hz, 1 × C**5**-H_2, *A*+*B*), 2.22 – 2.05 (2H, m, 1 × C**3**-H_2, *A*+*B*, 1 × C**6**-H_2, *A*+*B*), 1.96 – 1.81 (1H, m, 1 × C**2**-H, *A*+*B*), 1.73 – 1.63 (1H, m, 1 × C**7**-H, *A*+*B*), 1.54 (1H,

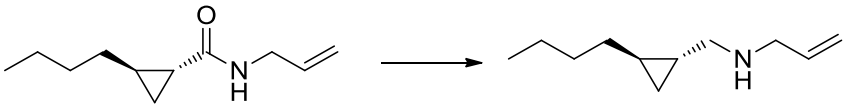
ddd, *J* = 12.6, 4.7, 4.7 Hz, 1 × C**6**-$\underline{H}_2$, *A*+*B*), 1.40 (3H, dd, *J* = 42.0, 6.0 Hz, 3 × C**9**-$\underline{H}_3$, *A*+*B*); ^{13}C NMR (126 MHz, $CDCl_3$): δ 209.1 (C**4**, *A*+*B*), 155.5 (C**10**, *A*), 154.9 (C**10**, *B*), 136.8 (C**12**, *A*), 136.7 (C**12**, *B*), 128.5 , 128.0 , 127.9 (C**13**, *A*+*B*, C**14**, *A*+*B*, C**15**, *A*+*B*), 67.1 (C**11**, *A*), 66.6 (C**11**, *B*), 58.2 (C**8**, *A*), 57.7 (C**8**, *B*), 51.8 (C**7**, *A*), 51.7 (C**1**, *A*), 51.5 (C**1**, *B*), 51.1 (C**7**, *B*), 44.1 (C**3**, *A*+*B*), 42.8 (C**2**, *A*), 42.7 (C**2**, *B*), 40.3 (C**5**, *A*+*B*), 26.6 (C**6**, *A*), 26.5 (C**6**, *B*), 19.8 (C**9**, *A*), 18.6 (C**9**, *B*).

(1*S, 2*S**)-*N*-Allyl-2-butylcyclopropane-1-carboxamide**



General procedure C: (1*S**, 2*S**)-2-Butylcyclopropanecarboxylic acid (1.50 g, 10.5 mmol, > 15:1 d.r.) (prepared according to literature procedure[2]) was employed and afforded the title compound (1.86 g, 98 %, > 15:1 d.r.) as an off-white solid which was pure enough to be used without further purification; m.p.: 48 – 50 °C (CH_2Cl_2/Hex); ν_{max} / cm^{-1}: 3283 (m), 2921 (m), 1638 (s), 1547 (s), 1235 (s), 916 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.85 (1H, dddd, *J* = 17.6, 7.4, 5.6, 1.8 Hz), 5.68 – 5.61 (1H, br. m), 5.22 – 5.10 (2H, m), 3.91 – 3.88 (2H, br. m), 1.38 – 1.24 (7H, m), 1.16 – 1.06 (2H, m), 0.90 – 0.86 (3H, m), 0.60 – 0.55 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.2, 134.5, 116.2, 42.1, 32.8, 31.4, 22.4, 22.3, 21.5, 14.4, 14.0; *m/z* (ESI^+) HRMS: Calculated for $C_{11}H_{19}NONa$: 204.1359. Found $[M+Na]^+$: 204.1363.

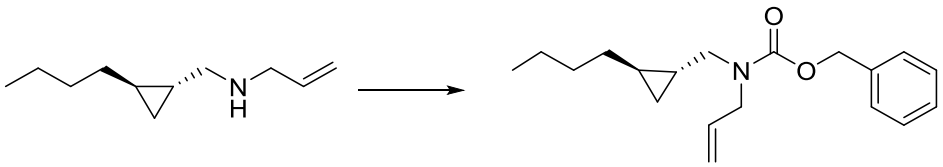
(1*S, 2*S**)-*N*-(2-Butylcyclopropyl)methyl)prop-2-en-1-amine**



General procedure D: (1*S**, 2*S**)-*N*-Allyl-2-butylcyclopropane-1-carboxamide (1.10 g, 6.1 mmol) was employed, the crude mixture was purified by column chromatography (100 % EtOAc) to yield the title compound (0.88 g, 87 %, > 15:1 d.r. 1:1 mixture of two rotamers) as a colorless oil; ν_{max} / cm^{-1}: 2919 (s), 2852 (m), 1455 (m), 992 (m), 915 (s), 727 (m); ^{1}H NMR (400 MHz CD_3CN) δ 5.88 (1H, ddt, *J* = 17.2, 10.2, 5.8 Hz), 5.19 – 5.17 (0.5H, m), 5.14 – 5.13 (0.5H, m), 5.06 – 5.05 (0.5H, m), 5.03 – 5.02 (0.5H, m), 3.21 (2H, dt, *J* = 5.8, 1.5 Hz), 2.47 (1H, dd, *J* = 12.0, 6.5 Hz), 2.36 (1H, dd, *J* = 12.1, 7.1 Hz), 1.43 – 1.15 (7H, m), 0.93 – 0.89 (3H, m), 0.68 – 0.61 (1H, m), 0.55 – 0.47 (1H, m), 0.28 – 0.19 (2H, m); ^{13}C NMR (100

MHz, CD_3CN): δ 138.0, 117.3, 53.5, 51.8, 33.3, 31.6, 22.2, 18.8, 17.4, 13.4, 9.9; *m/z* (ESI^+) HRMS: Calculated for $C_{11}H_{22}N$: 168.1747. Found $[M+H]^+$: 168.1749;

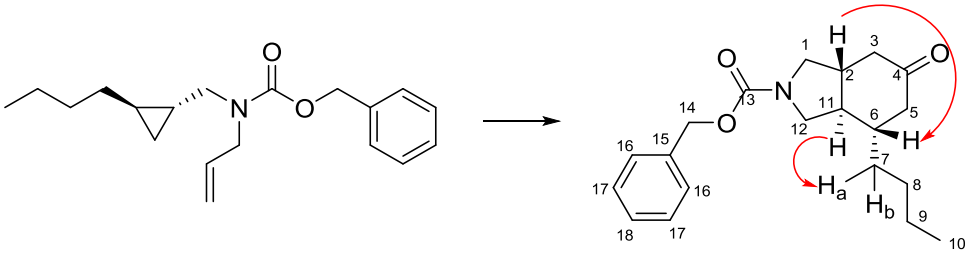
Benzyl (1*S, 2*S**)-allyl((-2-butylcyclopropyl)methyl)carbamate (6p)**



6p

General procedure E: (1*S**, 2*S**)-*N*-(2-Butylcyclopropyl)methyl)prop-2-en-1-amine (0.68 g, 5.3 mmol) and benzyl chloroformate (1.08 g, 6.4 mmol) were employed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound **6p** (1.24 g, 78 %, > 15:1 d.r.) as a colorless oil; ν_{max} / cm^{-1}: 2921 (m), 1694 (s), 1455 (s), 1404 (s), 1220 (s), 1158 (s); ^1H NMR (500 MHz, CD_3CN, 65 °C): δ 7.38 – 7.31 (5H, m), 5.88 – 5.80 (1H, m), 5.17 – 2.12 (4H, m), 4.01 – 3.93 (2H, m), 3.22 (1H, dd, *J* = 14.5, 6.4 Hz), 3.11 (1H, dd, *J* = 14.5, 7.3 Hz), 1.39 – 1.15 (6H, m), 0.91 – 0.89 (3H, m), 0.79 – 0.73 (1H, m), 0.67 – 0.61 (1H, m), 0.35 (1H, dt, *J* = 8.8, 4.7 Hz), 0.25 (1H, dt, *J* = 8.2, 4.8 Hz): ^{13}C NMR (126 MHz, CD_3CN, 65 °C): δ 155.8, 134.5, 128.3, 127.7, 127.6, 116.9, 115.6, 66.5, 50.6, 49.4, 33.0, 31.4, 22.1, 17.6, 17.5, 13.3, 10.1; *m/z* (ESI^+) HRMS: Calculated for $C_{19}H_{27}NO_2Na$: 324.1934. Found $[M+Na]^+$: 324.1943.

Benzyl (3a*R, 4*S**, 7a*R**)-4-butyl-6-oxooctahydro-2*H*-isoindole-2-carboxylate (8p)**

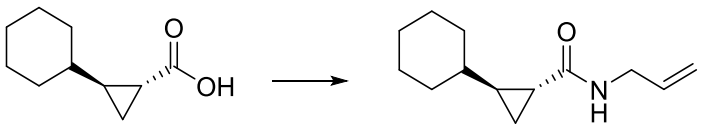


6p **8p**

General procedure H: Compound **6p** (45.2 mg, 0.15 mmol) was employed, the crude mixture was purified by column chromatography (33 % EtOAc/Hex) to yield the title compound **8p** (39.1 mg, 79 %, > 15:1 d.r. 1:1 mixture of rotamers *A:B*) as a colorless oil; *Under general procedure **G**, title compound **8p** was obtained in 54 % yield (26.8 mg, > 15:1 d.r. 1:1 mixture of rotamers A:B) as a colorless oil.*

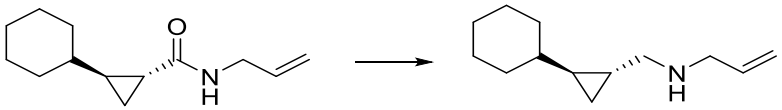
ν_{max} / cm^{-1}: 2925 (m), 1690 (s), 1402 (s), 1357 (s), 1112 (s), 697 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 – 7.30 (5H, m, 2 × C**16**-H, *A*+*B*, 2 × C**17**-H, *A*+*B*, 1 × C**18**-H, *A*+*B*), 5.18 – 5.11 (2H, m, 2 × C**14**-H, *A*+*B*), 3.86 (0.5H, dd, *J* = 10.4, 6.9 Hz, 0.5 × C**1**-H, *B*), 3.80 – 3.67 (1.5H, m, 1 × C**12**-H, *A*+*B*, 0.5 × C**1**-H, *A*), 3.06 – 2.97 (2H, m, 1 × C**12**-H, *A*+*B*, 1 × C**1**-H, *A*+*B*), 2.63 – 2.54 (2H, m, 1 × C**3**-H, *A*+*B*, 1 × C**5**-H, *A*+*B*), 2.24 – 2.15 (1H, m, 1 × C**3**-H, *A*+*B*), 2.05 – 1.92 (2H, m, 1 × C**5**-H, *A*+*B*, 1 × C**6**-H, *A*+*B*), 1.87 – 1.76 (1H, m, 1 × C**2**-H, *A*+*B*), 1.75 – 1.65 (1H, m, 1 × C**11**-H, *A*+*B*), 1.52 – 1.41 (1H, m, 1 × C**7**-H, *A*+*B*), 1.35 – 1.17 (5H, m, 1 × C**7**-H, *A*+*B*, 2 × C**8**-H, *A*+*B*, 2 × C**9**-H, *A*+*B*), 0.89 (3H, t, *J* = 6.9 Hz, 3 × C**10**-H, *A*+*B*). ^{13}C NMR (100 MHz, $CDCl_3$): 209.1 (C**4**, *A*), 209.1 (C**4**, *B*), 154.8 (C**13**, *A*+*B*), 136.8 (C**15**, *A*), 136.8 (C**15**, *B*), 128.5 (1 × C**Ar**, *A*+*B*), 128.1, 128.0, 128.0, 127.9 (2 ×C**Ar**, *A*+*B*), 66.9 (C**14**, *A*+*B*), 51.1 (C**12**, *A*), 50.8 (C**12**, *B*), 49.7 (C**1**, *A*), 49.4 (C**1**, *B*), 48.5 (C**2**, *A*), 47.8 (C**2**, *B*), 46.1(C**5**, *A*), 46.0(C**5**, *B*), 44.0(C**3**, *A*+*B*), 43.4 (C**6**, *A*), 42.7 (C**6**, *B*), 39.6 (C**11**, *A*), 39.5 (C**11**, *B*), 34.7 (C**7**, *A*) , 28.1 , 28.1, 22.7, (C**7**, *B*, C**8**, *A*+*B*, C**9**, *A*+*B*), 14.0(C**10**, *A*), 13.9 (C**10**, *B*); *m/z* (ESI^+) HRMS: Calculated for $C_{20}H_{27}NO_3Na$: 352.1883. Found $[M+Na]^+$: 352.1895; *The relative stereochemistry of this compound was corroborated by nOe experiments (as indicated on the compound structure). nOes from C**2**-H to C**6**-H, and from C**11**-H to C**7**$_a$-H were observed. The stereochemical assignment of this compound is consistent with that of **8q** and **8s**.*

(1*R, 2*S**)-*N*-Allyl-2-cyclohexylcyclopropanecarboxamide**



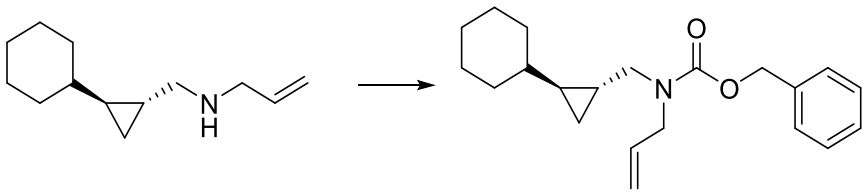
General procedure C: (1*R**, 2*S**)-2-Cyclohexylcyclopropanecarboxylic acid (0.98 g, 86 %, > 15:1 d.r.) (prepared according to literature procedure[2]) was employed and afforded the title compound (0.98 g, 86 %, > 15:1 d.r.) as a colorless solid which was pure enough to be used without further purification. m.p.: 93 – 95 °C (CH_2Cl_2/Hex); ν_{max} / cm^{-1}: 2920 (m), 2849 (m), 1697 (s), 1414 (m), 1228 (m), 1244 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.85 (1H, ddt, *J* = 17.1, 10.2, 5.7 Hz), 5.57 (1H, br. s), 5.30 – 4.87 (2H, m), 4.12 – 3.63 (2H, m), 1.80 – 1.66 (5H, m), 1.65 – 1.53 (3H, m), 1.29 – 1.01 (5H, m), 0.80 – 0.53 (2H, m); ^{13}C NMR (100 MHz, CD_3CN): δ 173.2, 134.5, 116.2, 42.1, 41.7, 32.7, 32.5, 28.0, 26.4 26.1, 21.1, 13.1; *m/z* (ESI^+) HRMS: Calculated for $C_{13}H_{21}NONa$: 230.1515. Found $[M+Na]^+$: 230.1519.

(1*R, 2*S**)-*N*-((-2-Cyclohexylcyclopropyl)methyl)prop-2-en-1-amine**



General procedure D: (1*R**, 2*S**)-*N*-Allyl-2-cyclohexylcyclopropanecarboxamide (0.57 g, 2.8 mmol) was employed, the crude mixture was purified by column chromatography (100 % EtOAc) to yield the title compound (0.49 g, 90 %, > 15:1 d.r.) as a colorless oil; ν_{max} / cm^{-1}: 2920 (m), 2849 (m), 1698 (m), 1414 (m), 1244 (m), 1228 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.96 (1H, ddt, *J* = 16.8, 10.2, 6.3 Hz), 5.53 – 4.91 (2H, m), 4.46 (1H, br. s), 3.39 (2H, d, *J* = 6.3 Hz), 2.99 – 2.22 (2H, m), 2.00 – 1.47 (5H, m), 1.18 – 0.92 (5H, m), 0.91 – 0.73 (1H, m), 0.67 – 0.51 (1H, m), 0.47 – 0.20 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 134.0, 118.4, 52.8, 51.0, 42.0, 33.1, 32.7, 26.5, 26.2, 24.8, 15.9, 9.7; *m/z* (ESI^+) HRMS: Calculated for $C_{13}H_{24}N$: 194.1903. Found $[M+H]^+$: 194.1908.

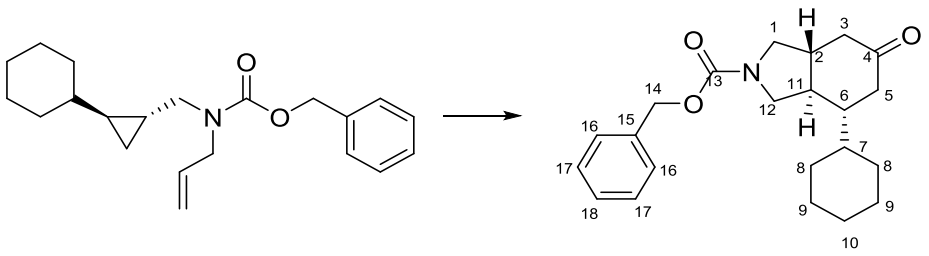
Benzyl (1*R, 2*S**)-allyl-((-2-cyclohexylcyclopropyl)methyl)carbamate (6q)**



6q

General procedure E: (1*R**, 2*S**)-*N*-((-2-Cyclohexylcyclopropyl)methyl)prop-2-en-1-amine (0.48 g, 2.5 mmol) and benzyl chloroformate (0.85 g, 5.0 mmol) were employed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound **6q** (0.54 g, 67 %, > 15:1 d.r.) as a colorless oil; ν_{max} / cm^{-1}: 2920 (m), 1697 (s), 1244 (m), 1229 (m), 1076 (s), 697 (s); ^{1}H NMR (500 MHz, CD_3CN, 65 ^{o}C): δ 7.80 – 6.97 (5H, m), 6.07 – 5.61 (1H, m), 5.51 – 4.65 (4H, m), 4.18 – 3.79 (2H, m), 3.24 (1H, dd, *J* = 14.5, 6.3 Hz), 3.09 (1H, dd, *J* = 14.6, 7.4 Hz), 1.80 – 1.47 (5H, br. m), 1.31 – 1.15 (3H, br. m), 1.13 – 0.94 (2H, br. m), 0.92 – 0.75 (1H, m), 0.71 – 0.57 (1H, m), 0.57 – 0.43 (1H, m), 0.46 – 0.11 (2H, m); ^{13}C NMR (126 MHz, CD_3CN, 65 ^{o}C): δ 155.8, 134.5, 128.3, 127.7, 127.7, 116.9, 66.5, 50.5, 49.4, 41.9, 32.7, 32.4, 26.3, 26.0, 24.2, 16.1, 8.7; *m/z* (ESI^+) HRMS: Calculated for $C_{21}H_{29}NO_2Na$: 350.2096. Found $[M+Na]^+$: 350.2091.

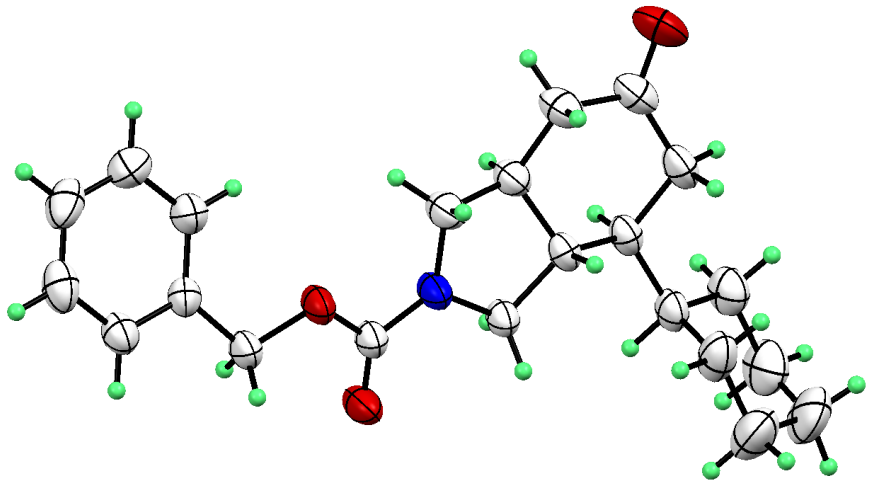
Benzyl (3a*R, 4*S**, 7a*R**)-4-cyclohexyl-6-oxohexahydro-1*H*-isoindole-2(3*H*)-carboxylate (8q)**



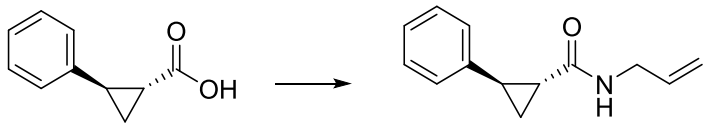
6q **8q**

General procedure H: Compound **6q** (49.1 mg, 0.15 mmol) was employed, the crude mixture was purified by column chromatography (30 % EtOAc/Hex) to yield the title compound **8q** (37.9 mg, 71 %, > 15:1 d.r. 1:1 mixture of rotamers *A:B*) as an off-white solid; *Under general procedure **G**, title compound **8q** was obtained in 38 % yield (20.3 mg, > 15:1 d.r. 1:1 mixture of rotamers A:B) as an off-white solid.*

m.p.: 112 – 114 °C (CH_2Cl_2/Hex); ν_{max} / cm^{-1}: 2922 (m), 2851 (m), 1693 (s), 1417 (s), 1357 (m), 1076 (m); ^1H NMR (400 MHz, $CDCl_3$): δ 7.68 – 7.26 (5H, m), 5.42 – 4.72 (2H, m), 3.85 (0.5H, dd, *J* = 10.4, 6.8 Hz), 3.82 – 3.56 (1.5H, m), 3.24 – 2.78 (2H, m), 2.70 – 2.48 (1H, m), 2.45 – 2.30 (1H, m), 2.25 – 2.09 (2H, m), 2.08 – 1.86 (2H, m), 1.84 – 1.57 (6H, m), 1.47 (1H, dd, *J* = 12.9, 12.9 Hz), 1.41 – 1.26 (1H, m), 1.27 – 0.89 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 209.9 (C**4**, *A*), 209.9 (C**4**, *B*), 154.8 (C**13**, *B*), 154.7(C**13**, *B*), 136.7, 128.5, 128.5, 128.1, 128.1, 128.0, 127.9 (C**Ar**, *A*+*B*), 66.9, 66.8*, 51.0, 50.7*, 49.6, 49.2*, 45.4, 44.9*, 44.8, 44.7*, 44.0, 44.0*, 43.6, 42.9*, 42.2, 41.9*, 40.8, 40.5*, 30.7, 30.5*, 27.5, 27.1*, 26.7, 26.7*, 26.5, 26.4*.**Doubling of some peaks due to two different conformers in solution. This compound could not be fully assigned based on the 1D and 2D NMR data, the structure and relative stereochemistry of this compound was determined unambiguously by X-ray crystallography.* *m/z* (ESI^+) HRMS: Calculated for $C_{22}H_{29}NO_3Na$: 378.2040. Found $[M+Na]^+$: 378.2053.

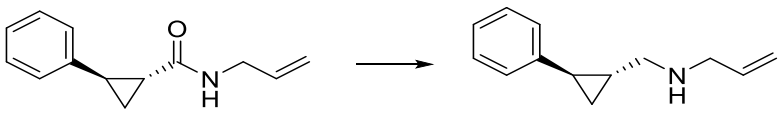


(1*S, 2*S**)-*N*-Allyl-2-phenylcyclopropanecarboxamide**



General procedure C: (1*S**, 2*S**)-2-Phenylcyclopropanecarboxylic acid (1.0 g, 6.2 mmol, > 15:1 d.r.) was employed and afforded the title compound (1.20 g, 92 %, > 15:1 d.r.) as a colorless solid which was pure enough to be used without further purification; m.p.: 91 – 93 °C (CH_2Cl_2/Hex); ν_{max} / cm^{-1}: 3250 (m), 1697 (s), 1632 (s), 1406 (s), 1239 (s), 696 (s); ^1H NMR (400 MHz, $CDCl_3$): δ 7.29 – 7.25 (2H, m), 7.22 – 7.14 (1H, m), 7.09 – 7.07 (2H, m), 6.02 – 5.67 (2H, m), 5.37 – 5.04 (2H, m), 3.93 – 3.90 (2H, m), 2.66 – 2.33 (1H, m), 1.70 – 1.50 (2H, m), 1.24 – 1.20 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) : δ 171.7, 140.8, 134.2, 128.4, 126.2, 126.0, 116.5, 42.3, 26.7, 25.1, 15.9; *m/z* (ESI^+) HRMS: Calculated for $C_{13}H_{15}NONa$: 224.1046. Found $[M+Na]^+$: 224.1049.

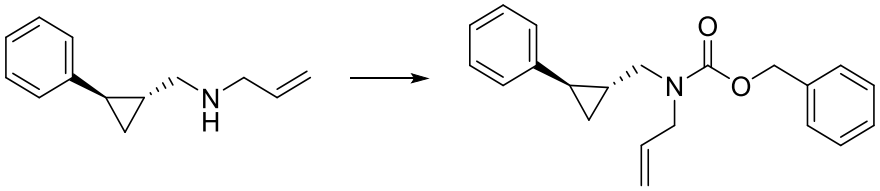
(1*S, 2*S**)-*N*-((-2-Phenylcyclopropyl)methyl)prop-2-en-1-amine**



General procedure D: (1*S**, 2*S**)-*N*-Allyl-2-phenylcyclopropanecarboxamide (1.13 g, 5.6 mmol) was employed, the crude mixture was purified by column chromatography (100 % EtOAc) to yield the title compound (0.90 g, 86 %, > 15:1 d.r. 1:1 mixture of two rotamers) as a colorless oil; ν_{max} / cm^{-1}: 2821 (m), 1702 (s), 1452 (m), 1417 (s), 697 (s); ^1H NMR (400

MHz, CD_3CN): δ 7.33 – 7.21 (2H, m), 7.19 – 7.12 (1H, m), 7.12 – 7.08 (2H, m), 5.91 (1H, ddt, *J* = 17.2, 10.3, 5.8 Hz), 5.20 – 5.19 (0.5H, m), 5.16 – 5.15 (0.5H, m), 5.05 (1H, ddt, *J* = 10.3, 2.1, 1.4 Hz) 3.25 – 3.23 (2H, m), 2.66 (1H, dd, *J* = 12.3, 6.2 Hz), 2.55 (2H, dd, *J* = 12.3, 7.0 Hz), 2.00 – 1.95 (1H, m), 1.75 (1H, dt, *J* = 8.6, 4.8 Hz), 1.56 (1H, br. d, *J* = 13.2 Hz), 1.29 – 1.21 (1H, m), 1.03 – 0.65 (2H, m); ^{13}C NMR (100 MHz, CD_3CN): δ 143.6, 137.8, 128.2, 125.5, 125.2, 117.3, 53.1, 51.7, 23.8, 21.7, 14.1; *m/z* (ESI^+) HRMS: Calculated for $C_{13}H_{18}N$: 188.1434. Found $[M+H]^+$: 188.1427.

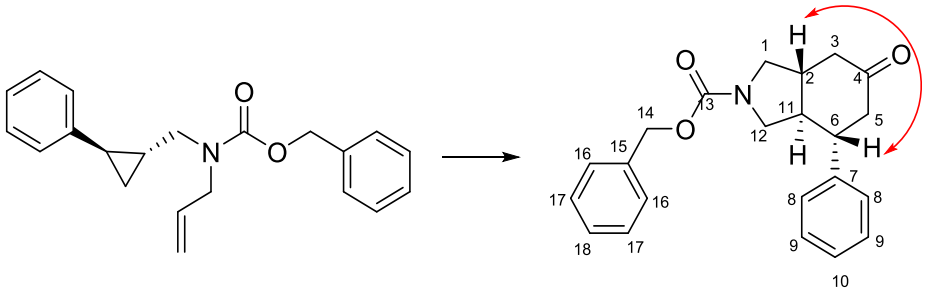
(1*S, 2*S**)-*N*-((-2-Phenylcyclopropyl)methyl)prop-2-en-1-amine (6r)**



6r

General procedure E: (1*S**, 2*S**)-*N*-((-2-Phenylcyclopropyl)methyl)prop-2-en-1-amine (0.73 g, 3.9 mmol) and benzyl chloroformate (1.33 g, 7.8 mmol) were employed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound **6r** (1.19 g, 95 %, > 15:1 d.r.) as a colorless oil; ν_{max} / cm^{-1}: 3028 (m), 1696 (s), 1455 (m), 1413 (s), 1240 (s), 697 (s); ^1H NMR (500 MHz, CD_3CN, 65 °C): δ 7.43 – 7.31 (5H, m), 7.30 – 7.23 (2H, m), 7.21 – 7.13 (1H, m), 7.11 – 7.02 (2H, m), 5.99 – 5.71 (1H, m), 5.36 – 4.89 (4H, m), 4.01 (2H, dt, *J* = 5.5, 1.6 Hz), 3.59 – 3.38 (1H, m), 3.34 – 3.27 (1H, m), 1.92 – 1.86 (1H, m), 1.43 – 1.29 (1H, m), 1.03 – 0.86 (2H, m); ^{13}C NMR (126 MHz, CD_3CN, 65 °C): δ 155.9, 142.8, 137.5, 134.4, 128.4, 128.2, 127.8, 127.7, 125.7, 125.4, 116.9, 66.6, 50.4, 49.6, 22.1, 21.9, 13.8; *m/z* (ESI^+) HRMS: Calculated for $C_{21}H_{23}NO_2Na$: 344.1621. Found $[M+Na]^+$: 344.1620.

Benzyl (3a*R, 4*S**, 7a*R**)-6-oxo-4-phenylhexahydro-1*H*-isoindole-2(3*H*)-carboxylate (8r)**

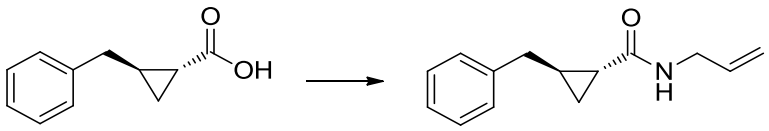


6r **8r**

General procedure H: Compound **6r** (48.2 mg, 0.15 mmol) was employed, the crude mixture was purified by column chromatography (33 % EtOAc/Hex) to yield the title compound **8r** (26.5 mg, 51 %, > 15:1 d.r. 1:1 mixture of rotamers *A:B*) as a colorless oil; *Under general procedure **G**, title compound **8r** was obtained in 27 % yield (14.1 mg, > 15:1 d.r. 1:1 mixture of rotamers A:B) as a colorless oil.*

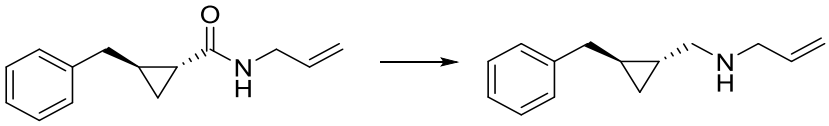
ν_{max} / cm^{-1}: 2884 (m), 1697 (s), 1417 (s), 1357 (s), 1135 (s), 699 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 – 6.69 (10H, m, 2 × C**8**-H, *A*+*B*, 2 × C**9**-H, *A*+*B*, C**10**-H, *A*+*B*, 2 × C**16**-H, *A*+*B*, 2 × C**17**-H, *A*+*B*, C**18**-H, *A*+*B*), 5.42 – 4.71 (2H, m, 2 × C**14**-H_2, *A*+*B*), 3.73 (1H, ddd, *J* = 21.3, 10.3, 7.0 Hz, 1 × C**1**-H_2, *A*+*B*), 3.41 (1H, ddd, *J* = 27.8, 10.6, 7.1 Hz, 1 × C**12**-H_2, *A*+*B*), 3.07 (1H, td, *J* = 10.5, 1.6 Hz, 1 × C**1**-H_2, *A*+*B*), 3.00 – 2.72 (2H, m, 1 × C**12**-H_2, *A*+*B*, 1 ×C**6**-H, *A*+*B*), 2.70 – 2.54 (2H, m, 1 × C**3**-H_2, *A*+*B*, 1 × C**5**-H_2, *A*+*B*), 2.55 – 2.43 (1H, m, 1 × C**5**-H_2, *A*+*B*), 2.36 – 2.19 (2H, m, 1 × C**11**-H, *A*+*B*, 1 × C**5**-H_2, *A*+*B*), 2.16 – 1.99 (1H, m, 1 × C**2**-H, *A*+*B*) ^{13}C NMR (100 MHz, $CDCl_3$): 208.0 (C**4**, *A*), 207.9 (C**4**, *B*), 154.7(C**13**, *A*+*B*), 141.6, 141.5, 136.7, 129.1, 129.0, 128.5, 128.4, 128.1, 128.0, 127.9, 127.4, 127.4, 126.6, 126.5 (C**7**, *A*+*B*, C**8**, *A*+*B*, C**9**, *A*+*B*, C**10**, *A*+*B*, C**15**, *A*+*B*, C**16**, *A*+*B*, C**17**, *A*+*B*, C**18**, *A*+*B*), 66.9 (C**14**, *A*+*B*), 51.3 (C**1**, *A*), 51.1 (C**1**, *B*), 49.7 (C**12**, *A*), 49.3 (C**12**, *B*), 48.8 (C**5**, *A*), 48.5 (C**5**, *B*), 48.4 (C**11**, *A*), 48.1 (C**11**, *B*), 45.9 (C**6**, *A*), 45.8 (C**6**, *B*), 44.0 (C**3**, *A*+*B*), 43.5 (C**2**, *A*), 42.8 (C**2**, *B*); *m/z* (ESI^+) HRMS: Calculated for $C_{22}H_{23}NO_3Na$: 372.1570. Found $[M+Na]^+$: 372.1574; *The relative stereochemistry of this compound was corroborated by nOe experiments (as indicated on the compound structure) A nOe was observed between C**2**-H and C**6**-H, and no significant nOe was observed between C**2**-H and C**11**-H. The stereochemical assignment of this compound is consistent with that of **8q** and **8s**.*

(1*R, 2*S**)-*N*-Allyl-2-benzylcyclopropanecarboxamide**



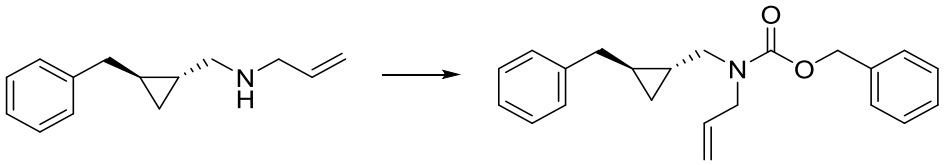
General procedure C: (1*R**, 2*S**)-2-Benzylcyclopropanecarboxylic acid (0.85 g, 4.8 mmol, > 15:1 d.r.) (prepared according to literature procedure[2]) was employed and afforded the title compound (0.92 g, 88 %, > 15:1 d.r.) as a colorless solid which was pure enough to be used without further purification. m.p.: 60 – 62 °C (CH_2Cl_2/Hex); ν_{max} / cm^{-1}: 3285 (m), 2912 (m), 1637 (m), 1546 (s), 1238 (s), 697 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.25 (2H, m), 7.25 – 7.16 (3H, m), 5.83 (1H, ddt, *J* = 17.2, 10.2, 5.6 Hz), 5.70 (1H, s), 5.32 – 4.88 (2H, m), 4.07 – 3.69 (2H, m), 2.67 (2H, d, *J* = 6.9 Hz), 1.85 – 1.59 (1H, m), 1.39 – 1.08 (2H, m), 0.86 – 0.59 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$): 172.7, 140.4, 134.4, 128.4, 128.3, 126.1, 116.2, 42.1, 38.4, 22.2, 21.5, 14.2; *m/z* (ESI^+) HRMS: Calculated for $C_{14}H_{17}NONa$: 238.1202. Found $[M+Na]^+$: 238.1207.

(1*R, 2*S**)-*N*-((2-Benzylcyclopropyl)methyl)prop-2-en-1-amine**



General procedure D: (1*R**, 2*S**)-*N*-Allyl-2-benzylcyclopropanecarboxamide (0.61 g, 2.8 mmol) was employed, the crude mixture was purified by column chromatography (100 % EtOAc) to yield the title compound (0.53 g, 92 %, > 15:1 d.r.) as a colorless oil; ν_{max} / cm^{-1}: 2915 (m), 1642 (m), 1452 (m), 1239 (m), 915 (s), 736 (s); ^{1}H NMR (400 MHz, CD_3CN): 7.37 – 7.25 (4H, m), 7.25 – 7.15 (1H, m), 5.87 (1H, ddt, *J* = 17.1, 10.2, 5.9 Hz), 5.24 – 5.07 (1H, m), 5.09 – 4.87 (1H, m), 3.16 (2H, dt, *J* = 5.8, 1.5 Hz), 2.58 (2H, d, *J* = 6.6 Hz), 2.51 (1H, dd, *J* = 12.1, 6.1 Hz), 2.38 (1H, dd, *J* = 12.2, 6.7 Hz), 1.65 (1H, br. s) 0.99 – 0.70 (2H, m), 0.56 – 0.25 (2H, m); ^{13}C NMR (100 MHz, CD_3CN): 142.3, 137.7, 128.3, 128.2, 125.8, 117.3, 53.1, 51.6, 39.1, 18.9, 18.7, 10.0; *m/z* (ESI^+) HRMS: Calculated for $C_{14}H_{20}N$: 202.1590. Found $[M+H]^+$: 202.1597.

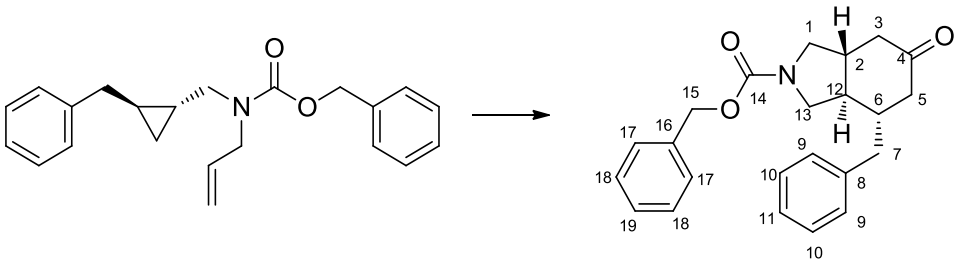
Benzyl (1*R, 2*S**)-allyl((2-benzylcyclopropyl)methyl)carbamate (6s)**



6s

General procedure E: (1*R**, 2*S**)-*N*-((2-Benzylcyclopropyl)methyl)prop-2-en-1-amine (0.50 g, 2.5 mmol) and benzyl chloroformate (0.84 g, 5.0 mmol) were employed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound **6s** (0.62 g, 75 %, > 15:1 d.r.) as a colorless oil; ν_{max} / cm^{-1}: 2917 (m), 1688 (s), 1455 (m), 1414 (s), 1226 (s), 737 (s); ^{1}H NMR (500 MHz, CD_3CN, 65 °C): δ 7.44 – 7.32 (5H, m), 7.32 – 7.27 (2H, m), 7.27 – 7.18 (3H, m), 5.89 – 5.70 (1H, m), 5.23 – 4.98 (4H, m), 4.11 – 3.72 (2H, m), 3.29 (1H, dd, *J* = 14.6, 5.5 Hz), 3.09 (1H, dd, *J* = 14.5, 7.1 Hz), 2.63 (1H, dd, *J* = 14.5, 5.8 Hz), 2.51 (1H, dd, *J* = 14.5, 6.6 Hz), 1.10 – 0.88 (2H, m), 0.63 – 0.30 (2H, m); ^{13}C NMR (126 MHz, CD_3CN, 65 °C): δ 155.8, 141.9, 137.5, 134.5, 128.4, 128.3, 128.2, 127.7, 127.6, 125.8, 116.9, 66.5, 50.3, 49.3, 39.0, 18.8, 17.6, 10.1; *m/z* (ESI^+) HRMS: Calculated for $C_{22}H_{25}NO_2Na$: 358.1778. Found $[M+Na]^+$: 358.1778.

Benzyl (3a*R, 4*S**, 7a*R**)-4-benzyl-6-oxohexahydro-1*H*-isoindole-2(3*H*)-carboxylate (8s)**

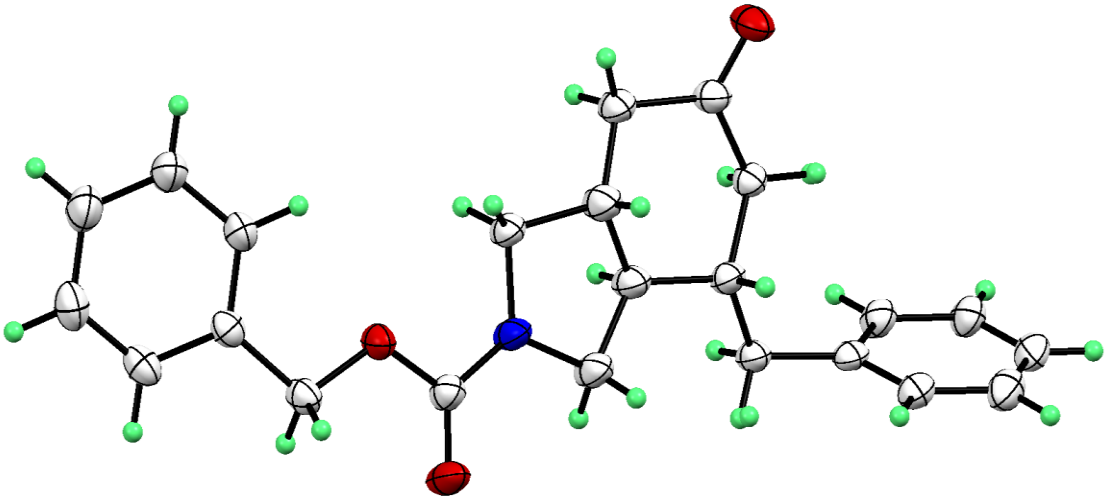


6s **8s**

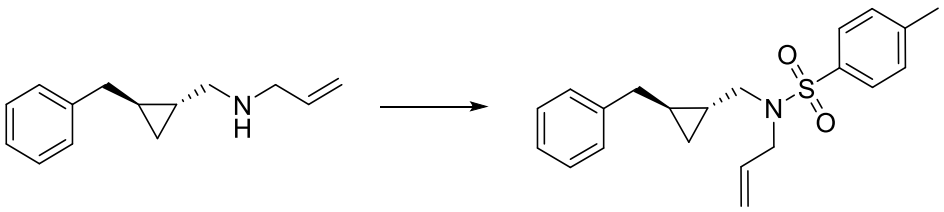
General procedure H: Compound **6s** (50.2 mg, 0.15 mmol) was employed, the crude mixture was purified by column chromatography (33 % EtOAc/Hex) to yield the title compound **8s** (46.8 mg, 86 %, > 15:1 d.r. 1:1 mixture of rotamers *A:B*) as an off-white solid; *Under general procedure **G**, title compound **8s** was obtained in 58 % yield (31.6 mg, > 15:1 d.r. 1:1 mixture of rotamers A:B) as an off-white solid.*

m.p.: 126 – 127 °C (CH_2Cl_2/Hex); ν_{max} / cm^{-1}: 2970 (m), 1696 (s), 1396 (s), 1357 (s), 1138 (m), 1059 (s); ^{1}H NMR (400 MHz, CD_3CN): δ 7.42 – 7.17 (8H, m, 8 × C**Ar**-H, *A*+*B*), 7.15 – 7.04 (2H, m, 2 × C**Ar**-H, *A*+*B*), 5.14 (2H, s, 2 × C**15**-$\underline{H}_2$, *A*+*B*), 3.92 (0.5H, dd, *J* = 10.5, 7.1

Hz, 1 × C**13**-H, *A*), 3.84 – 3.63 (1.5H, m, 1 × C**13**-H, *B*, 1 × C**1**-H, *A*+*B*), 3.14 – 2.91 (2H, m, 1 × C**1**-H, *A*+*B*, 1 × C**13**-H, *A*+*B*), 2.90 – 2.73 (1H, m, 1 × C**7**-H, *A*+*B*), 2.70 – 2.47 (2H, m, 1 × C**7**-H, *A*+*B*, 1 × C**3**-H, *A*+*B*), 2.45 – 2.31 (1H, m, 1 × C**5**-H, *A*+*B*), 2.28 – 2.11 (1H, m, 1 × C**3**-H, *A*+*B*), 2.10 – 1.94 (3H, m, 1 × C**5**-H, *A*+*B*, 1 × C**6**-H, *A*+*B*, 1 × C**2**-H, *A*+*B*), 1.95 – 1.77 (1H, m, 1 × C**12**-H, *A*+*B*); ^{13}C NMR (100 MHz, CD_3CN): δ 208.6 (C**4**, *A*), 208.5 (C**4**, *B*), 154.8 (C1**4**, *A*), 154.7 (C1**4**, *B*), 138.0, 137.8 (C1**5**, *B*), 136.7 , 129.1 , 129.1 , 128.5 , 128.5 , 128.0, 127.9 , 127.9 , 126.6 (C**Ar**, *A*+*B*), 66.9 (C1**5**, *A*+*B*), 50.9 (C**1**, *A*), 50.7 (C**1**, *B*), 49.7 (C**13**, *A*), 49.4 (C**13**, *B*), 48.2 (C**12**, *A*), 47.2 (C**12**, *B*), 45.9 (C**5**, *A*), 45.8 (C**5**, *B*), 43.8 (C**3**, *A*+*B*), 43.4 (C**2**, *A*) , 42.7 (C**2**, *B*), 41.5 (C**7**, *A*) , 41.3 (C**7**, *B*), 41.2 (C**6**, *A*+*B*); *m/z* (ESI^+) HRMS: Calculated for $C_{23}H_{25}NO_3Na$: 386.1727. Found $[M+Na]^+$: 386.1744; *The structure and relative stereochemistry of this compound was determined unambiguously by X-ray crystallography.*



(1*S, 2*S**)-*N*-Allyl-*N*-((-2-butylcyclopropyl)methyl)-4-methylbenzenesulfonamide (6t)**

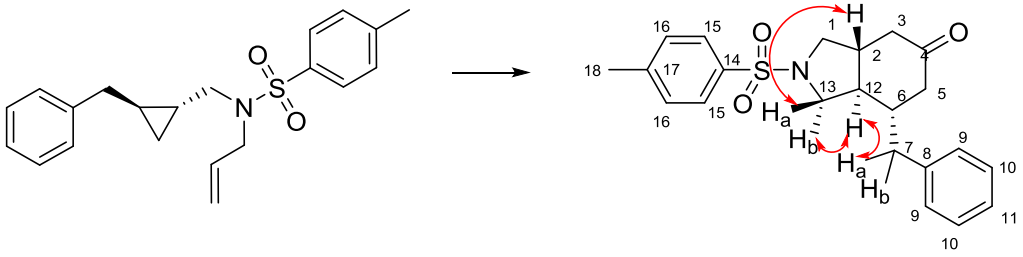


6t

General procedure E: (1*R**, 2*S**)-*N*-((2-Benzylcyclopropyl)methyl)prop-2-en-1-amine (0.50 g, 2.5 mmol) and *p*-toluenesulfonyl chloride (0.95 g, 5.0 mmol) were employed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title

compound **6t** (0.52 g, 61 %, > 15:1 d.r.) as a colorless oil; ν_{max} / cm^{-1}: 2918 (m), 1453 (m), 1340 (s), 1154 (s), 1090 (m), 911 (m), 754 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 – 7.57 (2H, m), 7.39 – 7.24 (4H, m), 7.23 – 7.17 (1H, m), 7.17 – 7.11 (2H, m), 5.56 (1H, ddt, *J* = 17.7, 9.5, 6.2 Hz), 5.24 – 4.79 (2H, m), 3.82 (1H, dd, *J* = 15.8, 6.0 Hz), 3.70 (1H, dd, *J* = 15.8, 6.3 Hz), 3.18 (1H, dd, *J* = 14.5, 6.2 Hz), 2.93 (1H, dd, *J* = 14.5, 7.2 Hz), 2.56 – 2.45 (2H, m), 2.42 (3H, s), 0.97 – 0.64 (2H, m), 0.58 – 0.22 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.0, 137.6, 133.4, 129.6, 128.3, 127.1, 126.0, 118.3, 50.6, 49.6, 39.2, 21.5, 19.4, 16.9, 11.0; *m/z* (ESI^+) HRMS: Calculated for $C_{21}H_{25}NO_2SNa$: 378.1498. Found $[M+Na]^+$: 378.1508.

(3a*R, 7*S**, 7a*R**) -7-Butyl-2-tosylhexahydro-1*H*-isoindol-5(6*H*)-one (8t)**



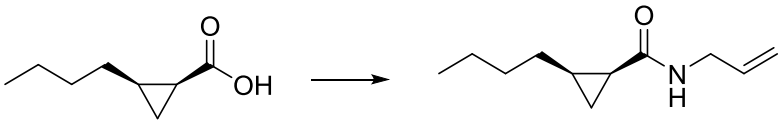
6t **8t**

General procedure H: Compound **6t** (53.3 mg, 0.15 mmol) was employed, the crude mixture was purified by column chromatography (30 % EtOAc/Hex) to yield the title compound **8t** (49.3 mg, 86 %, > 15:1 d.r.) as an off-white solid; *Under general procedure **G**, title compound **8t** was obtained in 66 % yield (37.8 mg, > 15:1 d.r.) as an off-white solid.*

m.p.: 160 – 162 °C (CH_2Cl_2/Hex); ν_{max} / cm^{-1}: 2940 (m), 1702 (m), 1337 (s), 1158 (s), 1087 (m), 1026 (m), 817 (m); ^{1}H NMR (400 MHz, C_6D_6): δ 7.84 (2H, d, *J* = 8.2 Hz, 2 × C**15**-H), 7.19 – 7.04 (3H, m, 2 × C**10**-H, 1 × C**11**-H), 6.96 (2H, d, *J* = 7.9 Hz, 2 × C**15**-H), 6.84 – 6.71 (2H, m, 2 × C**9**-H), 3.58 (1H, dd, *J* = 9.5, 7.0 Hz, 1 × C**13**-H), 3.31 (1H, dd, *J* =8.2, 7.1 Hz, 1 × C**1**-H), 2.74 – 2.44 (2H, m, 1 × C**1**-H, 1 × C**13**-H), 2.20 (1H, dd, *J* = 13.5, 4.8 Hz, 1 × C**7**-H), 2.13 – 1.96 (5H, m, 1 × C**3**-H, 1 × C**5**-H, 3 × C**18**-H), 1.91 (1H, dd, *J* = 13.5, 8.0 Hz, 1 × C**7**-H), 1.44 – 1.17 (3H, m, 1 × C**3**-H, 1 × C**5**-H, 1 × C**6**-H,), 1.16 – 0.98 (1H, m, 1 × C**2**-H), 1.00 – 0.79 (1H, m, 1 × C**12**-H); ^{13}C NMR (100 MHz, C_6D_6): δ 205.4 (C**4**), 142.8 (C**17**), 138.0 (C**8**), 135.9 (C**14**), 129.5 (C**16**), 129.1 (C**9**), 128.3 (C**10**), 127.6 (C**15**), 126.5 (C**11**), 52.1 (C**1**), 51.0 (C**13**), 46.7 (C**12**), 45.0 (C**5**), 42.7 (C**3**), 42.4 (C**2**), 40.8 (C**7**), 40.1 (C**6**), 20.8 (C**18**); *m/z* (ESI^+) HRMS: Calculated for $C_{22}H_{25}NO_3SNa$: 406.1447. Found $[M+Na]^+$:

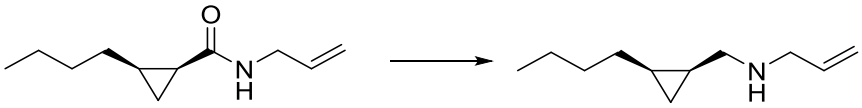
406.1440; *The relative stereochemistry of this compound was corroborated by nOe experiments (as indicated on the compound structure). nOes between C**12**-H and C**7$_a$**-H, C**12**-H and C**13$_b$**-H, C**2**-H and C**13$_a$**-H were observed. The stereochemical assignment of this compound is consistent with that of **8q** and **8s**.*

(1*S, 2*R**)-*N*-Allyl-2-butylcyclopropanecarboxamide**



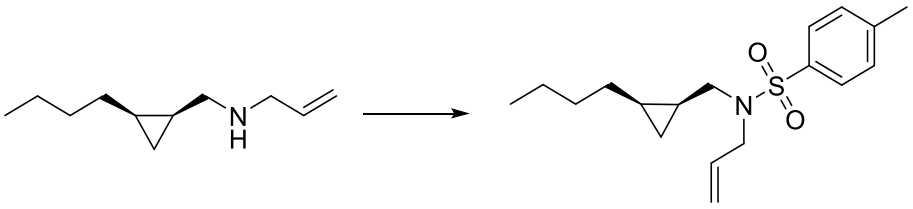
General procedure C: (1*S**, 2*R**)-2-Butylcyclopropanecarboxylic acid (1.00 g, 7.0 mmol, > 15:1 d.r.) (prepared according to literature procedure[2]) was employed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound (1.07 g, 84 %, > 15:1 d.r.) as an colorless oil. ν_{max} / cm^{-1}: 3300 (m), 2921 (m), 1641 (m), 1537 (m), 1240 (m), 1154 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.84 (1H, ddt, *J* = 17.2, 10.2, 5.7 Hz), 5.75 – 5.55 (1H, br. s), 5.31 – 4.85 (2H, m), 4.16 – 3.65 (2H, m), 1.53 – 1.40 (3H, m), 1.39 – 1.22 (4H, m), 1.16 – 1.04 (1H, m), 1.00 – 0.92 (1H, m), 0.91 – 0.82 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.4, 134.7, 116.1, 42.1, 32.0, 26.7, 22.4, 20.9 20.1, 14.1, 11.5; *m/z* (ESI$^+$) HRMS: Calculated for $C_{11}H_{19}NONa$: 204.1359. Found [M+Na]$^+$: 204.1357.

(1*S, 2*R**)-*N*-(2-Butylcyclopropyl)methyl)prop-2-en-1-amine**



General procedure D: (1*S**, 2*R**)-*N*-Allyl-2-butylcyclopropanecarboxamide (0.70 g, 3.9 mmol) was employed, the crude mixture was purified by column chromatography (100 % EtOAc) to yield the title compound (0.56 g, 86 %, > 15:1 d.r.) as a colorless oil; ν_{max} / cm^{-1}: 1696 (s), 1413 (m), 1240 (s), 1078 (m), 697 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.93 (1H, ddt, *J* = 16.9, 10.2, 6.0 Hz), 5.55 – 4.16 (2H, m), 3.64 – 2.98 (2H, m), 2.67 (1H, dd, *J* = 12.1, 6.9 Hz), 2.54 (1H, dd, *J* = 12.1, 7.4 Hz), 1.55 (1H, br. s), 1.47 – 1.26 (5H, m), 1.21 – 1.14 (1H, m), 1.03 – 0.93 (1H, m), 0.94 – 0.87 (3H, m), 0.85 – 0.72 (1H, m), 0.67 (1H, td, *J* = 8.3, 4.4 Hz), 0.01 (1H, q, *J* = 5.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.9, 115.8, 52.4, 49.1, 32.4, 28.3, 22.6, 15.8, 15.6, 14.1, 10.1; *m/z* (ESI$^+$) HRMS: Calculated for $C_{11}H_{22}N$: 168.1747. Found [M+H]$^+$: 168.1749.

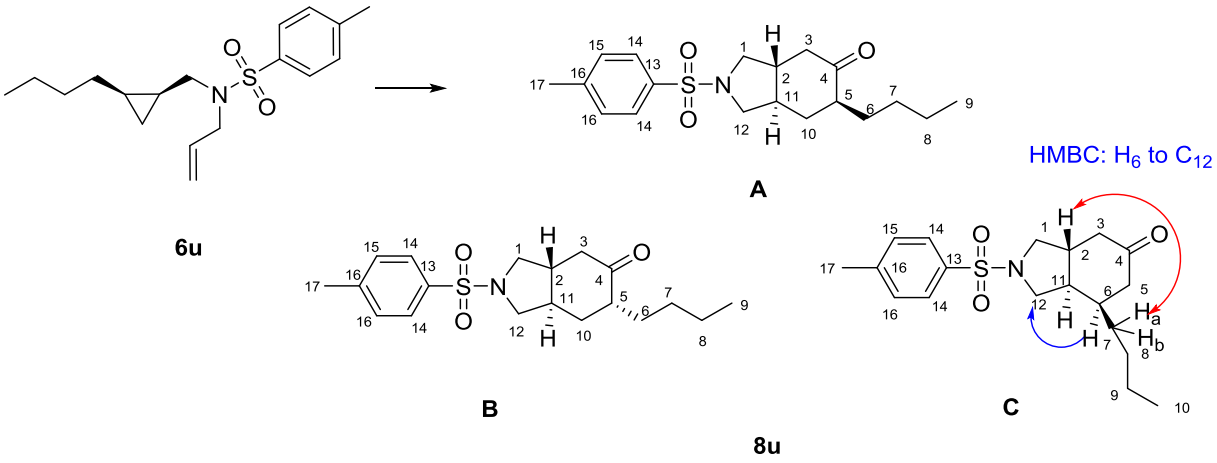
Benzyl (1*S, 2*R**)-allyl ((-2-butylcyclopropyl)methyl)carbamate (6u)**



6u

General procedure E: (1*S**, 2*R**)-*N*-(2-Butylcyclopropyl)methyl)prop-2-en-1-amine (0.27 g, 1.6 mmol) and *p*-toluenesulfonyl chloride (0.61 g, 3.2 mmol) were employed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound **6u** (0.33 g, 66 %, > 15:1 d.r.) as a colorless oil; ν_{max} / cm^{-1}: 2922 (m), 1697 (m), 1343 (m), 1154 (s), 1091 (s), 755 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (2H, d, *J* = 8.3 Hz), 7.44 – 6.93 (2H, m), 5.65 (1H, ddt, *J* = 17.2, 10.1, 6.2 Hz), 5.50 – 4.81 (2H, m), 4.21 – 3.71 (2H, m), 3.43 (1H, dd, *J* = 14.3, 5.5 Hz), 2.96 (1H, dd, *J* = 14.3, 8.5 Hz), 2.41 (3H, s), 1.47 – 1.24 (5H, m), 1.18 – 0.99 (1H, m), 0.93 – 0.82 (4H, m), 0.81 – 0.70 (1H, m), 0.66 (1H, td, *J* = 8.3, 4.5 Hz), 0.01 (1H, td, *J* = 5.4, 5.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.9, 137.6, 133.5, 129.6, 127.1, 118.2, 49.7, 47.0, 32.3, 28.3, 22.5, 21.5, 16.1, 14.1, 13.9, 11.2; *m/z* (ESI^+) HRMS: Calculated for $C_{18}H_{27}NO_2SNa$: 344.1655. Found $[M+Na]^+$: 344.1659;

(3a*R, 6*S**, 7a*R**) and (3a*R**, 6*R**, 7a*R**)-6-Butyl-2-tosylhexahydro-1*H*-isoindol-5(6*H*)-one and (3a*R**, 7*R**, 7a*R**)-7-butyl-2-tosylhexahydro-1*H*-isoindol-5(6*H*)-one (8u)**



6u **A** **B** **C** **8u**

General procedure G: Compound **6u** (48.2 mg, 0.15 mmol) was employed, the reaction was heated at 130 °C. The crude mixture was purified by column chromatography (33 %

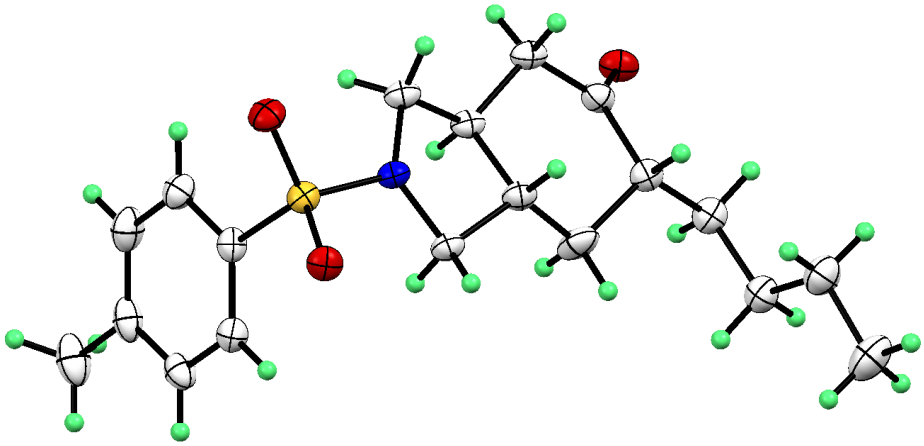
EtOAc/Hex) to yield the title compound **8u** (46.1 mg, 88 %) as a colorless oil. A mixture of diastereomers A and B and regioisomer C were obtained in a 5:1:1 (A:B:C) ratio; *Under general procedure **H**, title compound **8u** was obtained in 85 % yield (44.5 mg) as a colorless oil. A mixture of diastereomers A and B and regioisomer C were obtained in a 4:1:2 (A:B:C) ratio*

*Regioisomer C was separated from diastereomers A and B by flash column chromatography (20 % EtOAc/hexane). The regiochemistry of regioisomer C was confirmed by HMBC analysis (as indicated on the compound structure). The relative stereochemistry of regioisomer C was corroborated by nOe experiments (as indicated on the compound structure). A nOe between C**7**$_{\alpha}$-H and C**2**-H was observed, and no significant nOe was observed between C**2**-H and C**11**-H. Diastereomer A was recrystallized from the mixture of A and B (EtOAc/Hex), its structure and relative stereochemistry were determined unambiguously by X-ray crystallography. Diastereomer B could not be isolated in a pure form, and the proton signals for diastereomer B overlapped significantly with diastereomer A. Diastereomers A and B have the same chemical shift at C**12**-H$_2$ (for A: 3.64 ppm and 2.81 ppm; for B: 3.63 ppm and 2.80 ppm), which indicates that C**12** must be in a similar chemical environment, therefore ruling out the possibility of that B is a regioisomer of A. A TOCSY experiment irradiating C**2**-H of diastereomer B was utilized to enable coupling constant analysis of C**1**-H and C**1**2-H of diastereomer B : 3.63 (1H, dd, J = 9.8, 6.8 Hz, 1 × C**12**-H$_2$), 3.55 (1H, dd, J = 9.4, 7.5 Hz, 1 × C**1**-H$_2$), 2.94 (1H, dd, J = 10.2, 10.2 Hz, 1 × C**1**-H$_2$), 2.80 (1H, dd, J = 10.7, 9.2 Hz, 1 × C**12**-H$_2$); the coupling constant of **C1**-H and **C1**2-H observed for diastereomer A: 3.64 (1H, dd, J = 9.5, 7.0 Hz, 1 × C**12**-H$_2$), 3.54 (1H, dd, J = 9.7, 7.0 Hz, 1 × C**1**-H$_2$), 2.94 (1H, dd, J = 10.8, 9.7 Hz, 1 × C**1**-H$_2$), 2.81 (1H, dd, J = 10.9, 9.5 Hz, 1 × C**12**-H$_2$), these similar coupling constants indicated a trans ring junction for diastereomer B (same with diastereomer A) which suggesting that the stereochemistry at C5 was the opposite to that of diastereomer A.*

ν_{max} / cm^{-1}: 2927 (m), 1712 (s), 1340 (m), 1202 (m), 1157 (s), 1097 (m); *m/z* (ESI$^+$) HRMS: Calculated for $C_{19}H_{27}NO_3SNa$: 372.1604. Found $[M+Na]^+$: 372.1604.

Data for major diastereomer A: m.p.: 108 – 110 °C (CH_2Cl_2/Hex); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (2H, d, *J* = 8.2 Hz, 2 × C**14**-H), 7.31 (2H, d, *J* = 8.0 Hz, 2 × C**15**-H), 3.64 (1H, dd, *J* = 9.5, 7.0 Hz, 1 × C**12**-H$_2$), 3.54 (1H, dd, *J* = 9.7, 7.0 Hz, 1 × C**1**-H$_2$), 2.94 (1H,

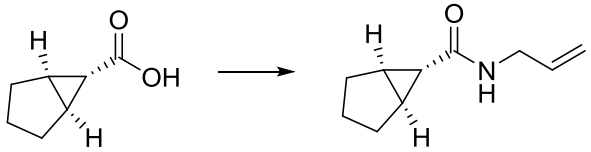
dd, *J* = 10.8, 9.7 Hz, 1 × C**1**-H$_2$), 2.81 (1H, dd, *J* = 10.9, 9.5 Hz, 1 × C**12**-H$_2$), 2.49 (1H, dd, *J* = 13.4, 3.9 Hz, 1 × C**3**-H$_2$), 2.43 (3H, s, 3 × C**17**-H$_3$), 2.27 – 2.08 (3H, m, 1 × C**10**-H$_2$, 1 × C**5**-H, 1 × C**3**-H$_2$), 2.04 – 1.86 (1H, m, 1 × C**11**-H), 1.83 – 1.72 (1H, m, 1 × C**6**-H$_2$), 1.72 – 1.51 (1H, m, 1 × C**2**-H), 1.41 – 0.95 (6H, m, 2 × C**8**-H$_2$, 2 × C**7**-H$_2$, 1 × C**10**-H$_2$, 1 × C**6**-H$_2$), 0.85 (3H, t, *J* = 7.0 Hz, 3 × C**9**-H$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 209.5 (C**4**), 143.5 (C**16**), 134.4 (C**13**), 129.8 (C**15**), 127.2 (C**14**), 52.6 (C**1**), 51.9 (C**12**), 48.7 (C**5**), 45.0 (C**2**), 44.1 (C**3**), 43.2 (C**11**), 33.1 (C**10**), 29.1 (C**7**), 28.5 (C**6**), 22.7 (C**8**), 21.5 (C**17**), 13.9 (C**9**). (*N.B. C7 and C**8** could not be assigned confidently*).



Data for minor diastereomer B **:** *Characteristic peaks only*: 7.71 (2H, d, *J* = 8.2 Hz, 2 × C**14**-H), 7.32 (2H, d, *J* = 8.0 Hz, 2 × C**13**-H) 3.63 (1H, dd, *J* = 9.8, 6.8 Hz, 1 × C**12**-H$_2$), 3.55 (1H, dd, *J* = 9.4, 7.5 Hz, 1 × C**1**-H$_2$), 2.94 (1H, dd, *J* = 10.2, 10.2 Hz, 1 × C**1**-H$_2$), 2.80 (1H, dd, *J* = 10.7, 9.2 Hz, 1 × C**12**-H$_2$). 2.42 – 2.34 (1H, m, 1 × C**2**-H).

Data for regioisomer C: m.p.: 129 – 132 °C (CH_2Cl_2/Hex); ^{1}H NMR (400 MHz, CD_3CN): δ 7.74 (2H, d, *J* = 8.3 Hz, 2 × C**14**-H), 7.43 (2H, d, *J* = 7.9 Hz, 2 × C**13**-H), 3.58 (1H, dd, *J* = 9.8, 6.9 Hz, , 1 × C**1**-H$_2$), 3.45 (1H, dd, *J* = 9.8, 7.6 Hz, 1 × C1**2**-H$_2$), 3.05 (1H, dd, *J* = 11.1, 9.8 Hz, 1 × C**12**-H$_2$), 2.88 (1H, dd, *J* = 10.5, 9.8 Hz, 1 × C**1**-H$_2$), 2.44 (3H, s, 3 × C**17**-H$_3$), 2.41 – 2.23 (3H, m, 1 × C**3**-H$_2$, 2 × C**5**-H$_2$), 2.17 (1H, m, 2 × C**11**-H), 2.17 – 2.06 (2H, m, 1 × C**3**-H$_2$, 1 × C**6**-H), 1.94 – 1.80 (1H, m, C**2**-H), 1.42 – 1.01 (5H, m, 2 × C**8**-H$_2$, 2 × C**9**-H$_2$, 1 × C**7**-H$_2$), 0.86 (3H, t, *J* = 7.1 Hz, 3 × C**10**-H$_3$), 0.84 – 0.73 (1H, m, 1 × C**7**-H$_2$); ^{13}C NMR (100 MHz, CD_3CN): δ 209.0 (C**4**), 143.8 (C**16**), 134.3 (C1**3**), 129.8 (C**15**), 127.3 (C**14**), 52.9 (C**1**), 48.6 (C**12**), 45.9 (C**11**), 44.6 (C**5**), 43.6 (C**3**), 37.9 (C**2**), 34.1 (C**6**), 29.6 (C**8**), 26.3 (C**9**), 22.4 (C**7**), 20.5 (C**17**), 13.2 (C**10**). (*N.B. C**8** and C**9** could not be assigned confidently*).

(1*R, 5*S**, 6*R**)-*N*-Allylbicyclo[3.1.0]hexane-6-carboxamide**



5:1 d.r. 10:1 d.r.

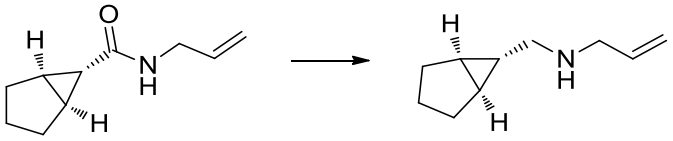
General procedure C: (1*R**, 5*S**, 6*R**)-Bicyclo[3.1.0]hexane-6-carboxylic acid (3.20 g, 25.4 mmol, 5:1 d.r.) (prepared according to literature procedure[2]) was employed and afforded the title compound (3.74 g, 88 %, 10:1 d.r.) as a off-white solid which can be recrystallized in Hex/EA to separate two diastereomers. Major diastereomer was obtained as a colorless soild and minor diastereomer was obtained as a colorless oil.

ν_{max} / cm^{-1}: 3287 (s), 2959 (m), 1632 (s), 1544 (s), 1410 (m), 1212 (m), 906 (s); *m/z* (ESI^+) HRMS: Calculated for $C_{10}H_{15}NONa$: 188.1046. Found $[M+Na]^+$: 188.1049.

Data for major diastereomer: m.p.: 118 – 120 °C (CH_2Cl_2/Hex); ^1H NMR (400 MHz, $CDCl_3$): δ 5.83 (1H, ddt, *J* = 17.2, 10.2, 5.7 Hz), 5.64 (1H, s), 5.32 – 4.84 (2H, m), 3.91 – 3.82 (2H, m), 1.88 – 1.65 (6H, m), 1.66 – 1.46 (1H, m), 1.14 (1H, t, *J* = 2.9 Hz), 1.12 – 0.93 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.9, 134.6, 116.2, 42.0, 27.4, 27.3, 23.4, 20.5.

Data for minor diastereomer: ^1H NMR (400 MHz, $CDCl_3$): δ 5.82 (1H, ddt, *J* = 17.3, 10.2, 5.8 Hz), 5.64 (1H, br. s), 5.26 – 4.96 (2H, m), 3.90 – 3.77 (2H, m), 2.01 – 1.90 (2H, m), 1.88 – 1.76 (2H, m), 1.69 – 1.39 (4H, m), 1.15 – 0.90 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.2, 134.3, 116.5, 41.9, 26.2, 24.2, 22.8, 22.3.

(1*R, 5*S**, 6*R**)-*N*-((Bicyclo[3.1.0]hexan-6-ylmethyl)prop-2-en-1-amine**

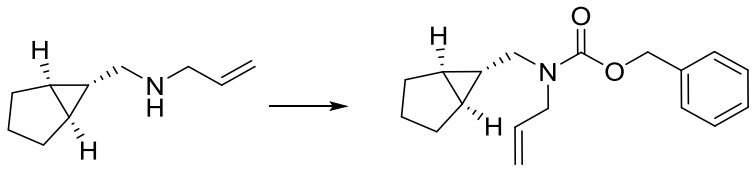


> 15:1 d.r. > 15:1 d.r.

General procedure D: (1*R**, 5*S**, 6*R**)-*N*-Allylbicyclo[3.1.0]hexane-6-carboxamide (2.60 g, 15.8 mmol) was employed, the crude mixture was purified by column chromatography (100 % EtOAc) to yield the title compound (2.29 g, 96 %, > 15:1 d.r.) as a colorless oil; ν_{max} / cm^{-1}: 3307 (m), 2859 (s), 1643 (m), 1449 (s), 1157 (m), 915 (s); ^1H NMR (400 MHz,

CD_3CN): δ 5.90 (1H, ddt, *J* = 17.2, 10.3, 5.9 Hz), 5.17 (1H, m), 5.05 (1H, m), 3.20 (2H, dt, *J* = 5.9, 1.5 Hz), 2.39 (2H, d, *J* = 6.9 Hz), 2.05 – 1.86 (1H, m), 1.82 – 1.60 (4H, m), 1.54 (1H, dt, *J* = 12.8, 8.0 Hz), 1.25 – 1.10 (1H, m), 1.10 – 1.05 (2H, m), 0.72 (1H, tt, *J* = 6.7, 3.1 Hz); ^{13}C NMR (100 MHz): δ 137.6, 117.3, 51.9, 51.6, 27.1, 23.0, 21.1, 19.0; *m/z* (ESI^+) HRMS: Calculated for $C_{10}H_{18}N$: 152.1434. Found $[M+H]^+$: 152.1434.

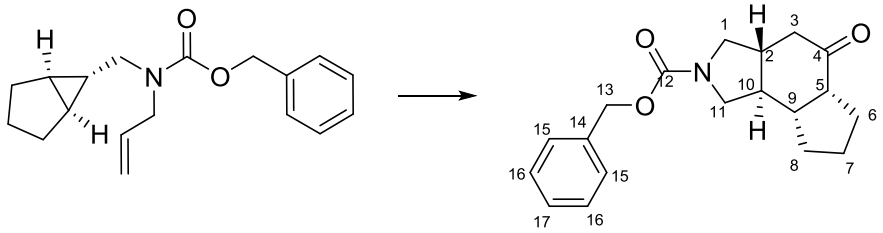
Benzyl (1*R, 5*S**, 6*R**)-allyl((-bicyclo[3.1.0]hexan-6-yl)methyl)carbamate (6v)**



6v

General procedure E: (1*R**, 5*S**, 6*R**)-*N*-((Bicyclo[3.1.0]hexan-6-ylmethyl)prop-2-en-1-amine (2.40 g, 15.6 mmol) and benzyl chloroformate (5.30 g, 31.2 mmol) were employed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound **6v** (4.12 g, 97 %, > 15:1 d.r.) as a colorless oil; ν_{max} / cm^{-1}: 2951 (m), 1696 (s), 1460 (m), 1412 (s), 1239 (s), 917 (m); ^{1}H NMR (400 MHz, CD_3CN, 65 ^{o}C): δ 7.69 – 7.07 (5H, m), 6.13 – 5.58 (1H, m), 5.36 – 4.72 (4H, m), 3.97 (2H, dt, *J* = 5.5, 1.5 Hz), 3.16 (2H, dd, *J* = 6.9, 1.1 Hz), 1.84 – 1.61 (4H, m), 1.63 – 1.37 (1H, m), 1.25 – 0.97 (3H, m), 0.81 (1H, tt, *J* = 6.7, 3.1 Hz); ^{13}C NMR (100 MHz, CD_3CN, 65 ^{o}C): 155.8, 134.6, 128.4, 128.3, 127.7, 127.6, 116.9, 66.5, 49.3, 49.2, 27.0, 23.2, 21.0, 18.2; *m/z* (ESI^+) HRMS: Calculated for $C_{18}H_{23}NO_2Na$: 308.1621. Found $[M+Na]^+$: 308.1624.

Benzyl (3a*R, 5a*R**, 8a*R**, 8b*R**)-5-oxodecahydrocyclopenta[e]isoindole-2(3*H*)-carboxylate (8v)**



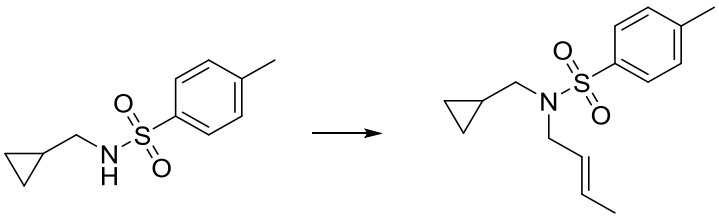
6v **8v**

In a glove box, an oven dried reaction tube, fitted with a magnetic stirrer, was charged with $[Rh(CH_2CH_2)_2Cl]_2$ (2.92 mg, 0.0075 mmol). Then took the reaction tube out of the glove box,

compound **6v** (42.80 mg, 0.15 mmol) in anhydrous 1, 2-dichlorobenzene (0.82 mL, 0.18 M) was added *via* syringe, then (7-*t*-BuO)-norbornadiene (2.6 uL, 0.015 mmol) was added by microlitre syringe. The reaction mixture was purged with CO for 10 minutes and subsequently sparged with CO for ca. 10 seconds, then heated at 140 °C under a CO atmosphere (1 atm) for 72 h. The mixture was cooled to r.t., concentrated *in vacuo.* The crude mixture was purified by column chromatography (30 % EtOAc/Hex) to yield the title compound **8v** (28.7 mg, 61 %, > 15:1 d.r. 1:1 mixture of rotamers *A:B*) as a colorless oil; *Under general procedure **G**, title compound **8v** was obtained in 20 % yield (9.4 mg, > 15:1 d.r. 1:1 mixture of rotamers A:B) as a colorless oil; Under general procedure **H**, title compound **8v** was obtained in 52 % yield (24.5 mg, > 15:1 d.r. 1:1 mixture of rotamers A:B) as a colorless oil;*

ν_{max} / cm^{-1}: 2945 (m), 1695 (s), 1416 (s), 1356 (s), 1122 (m), 1075 (s), 698 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 – 7.25 (5H, m, 2 × C**15**-H, *A*+*B*, 2 × C**16**-H, *A*+*B*, 1 × C**17**-H, *A*+*B*), 5.12 (2H, s, 2 × C**13**-H_2, *A*+*B*), 3.96 – 3.66 (2H, m, 1 × C**1**-H, *A*+*B*, 1 × C**11**-H, *A*+*B*), 3.13 – 2.87 (2H, m, 1 × C**1**-H, *A*+*B*, 1 × C**11**-H, *A*+*B*), 2.76 – 2.47 (2H, m, 1 × C**3**-H, *A*+*B*, 1 × C**5**-H, *A*+*B*), 2.34 – 2.08 (3H, m, 1 × C**2**-H, *A*+*B*, 1 × C**10**-H, *A*+*B*, 1 × C**3**-H, *A*+*B*,), 1.96 – 1.51 (6H, m, 2 × C**6**-H, *A*+*B*, 1 × C**8**-H, *A*+*B*, 2 × C**7**-H, *A*+*B*, 1 × C**9**-H, *A*+*B*), 1.50 – 1.29 (1H, m, 1 × C**8**-H, *A*+*B*); ^{13}C NMR (100 MHz, $CDCl_3$): δ 212.7 (C**4**, *A*), 212.6 (C**4**, *B*), 154.7 (C**12**, *A*), 154.6 (C**12**, *B*), 136.8 (C**14**, *A*), 136.8 (C**14**, *B*), 128.5, 128.0, 127.9 (C**15**, *A*+*B*, C**16**, *A*+*B*, C**17**, *A*+*B*,) 66.8 (C**13**, *A*), 66.8 (C**13**, *B*), 52.0 (C**5**, *A*), 52.0 (C**5**, *B*), 51.6 (C**1**, *A*), 51.3 (C**1**, *B*), 50.8 (C**11**, *A)*, 50.6 (C**11**, *B)*, 45.7 (C**9**, *A*) 44.9 (C**9**, *B*) 43.6 (C**10**, *A*), 43.5 (C**10**, *B*), 41.7 (C**3**, *A*), 41.6 (C**3**, *B*), 40.9 (C**2**, *A*+*B*), 31.9 (C**8**, *A*+*B*), 28.1, 28.0, 24.3, 24.2. (C**6**, *A*+*B*, C**7**, *A*+*B)* (*N.B. C**6** and C**7** could not be assigned confidently*). *m/z* (ESI^+) HRMS: Calculated for $C_{19}H_{23}NO_3Na$: 336.1570. Found $[M+Na]^+$: 336.1565; *The relative stereochemistry of this compound was assigned by analogy to that of **8q** and **8s**.*

(*E*)-*N*-(But-2-en-1-yl)-*N*-(cyclopropylmethyl)-4-methylbenzenesulfonamide (6w)



6w

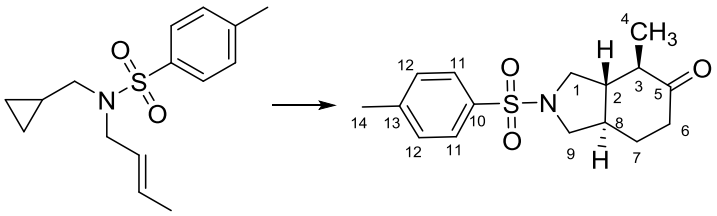
General procedure B: *N*-(Cyclopropylmethyl)-4-methylbenzenesulfonamide (1.72 g, 7.2 mmol) and (*E*)-1-bromobut-2-ene (1.92 g 14.4 mmol, *E*/*Z* = 17/1) were empolyed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound **6w** (1.89 g, 90 %, mixed with (*Z*)-isomer, *E*/*Z* = 14:1) as a colorless oil;

ν_{max} / cm^{-1}: 2918 (m), 1336 (s), 1154 (s), 1090 (m), 967 (m), 734 (s); *m/z* (ESI^+) HRMS: Calculated for $C_{15}H_{21}NO_2SNa$: 302.1185. Found $[M+Na]^+$: 302.1190.

Data for major *E*-isomer: ^1H NMR (400 MHz, $CDCl_3$): δ 7.68 (2H, d, *J* = 8.3 Hz), 7.29 – 7.24 (2H, m), 5.64 – 5.52 (1H, m), 5.32 – 5.22 (1H, m), 3.85 (2H, ddd, *J* = 6.6, 1.3, 1.3 Hz), 3.01 (2H, d, *J* = 6.8 Hz), 2.41 (3H, s), 1.70 – 1.56 (3H, m), 0.95 – 0.77 (1H, m), 0.52 – 0.38 (2H, m), 0.14 (2H, dt, *J* = 5.9, 4.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.8, 137.7, 129.8, 129.5, 127.1, 126.0, 51.3, 49.3, 21.5, 17.6, 9.7, 4.0.

Data for minor *Z*-isomer: *Characteristic peaks only*: ^1H NMR (400 MHz, $CDCl_3$): δ 3.98 (2H, d, *J* = 6.9 Hz)

(3a*S, 4*R**, 7a*R**)-4-Methyl-2-tosylhexahydro-1*H*-isoindol-5(6*H*)-one (8w)**

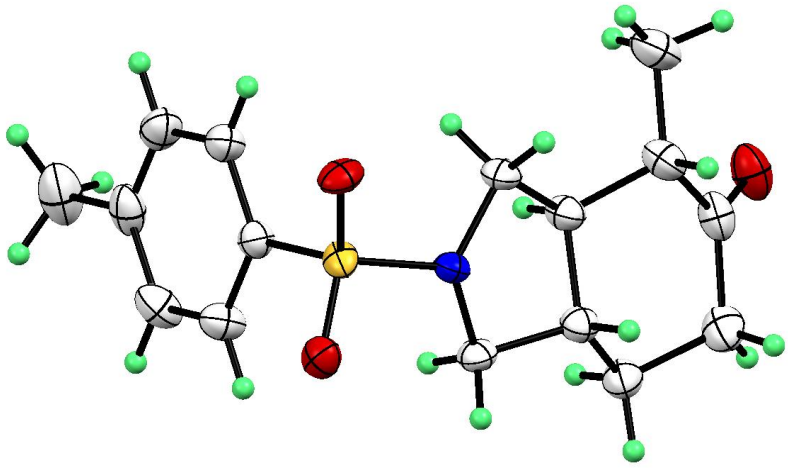


6w **8w**

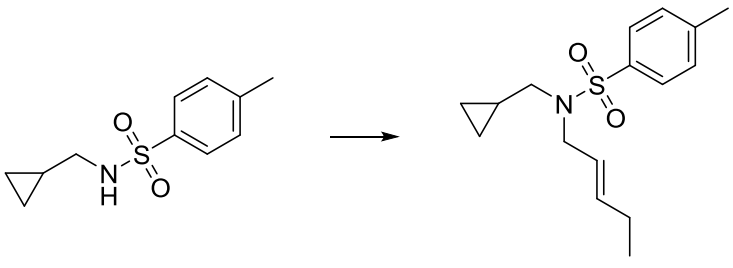
In a glove box, an oven dried reaction tube, fitted with a magnetic stirrer, was charged with $[Rh(CH_2CH_2)_2Cl]_2$ (2.92 mg, 0.0075 mmol). Then took the reaction tube out of the glove box, compound **6w** (41.90 mg, 0.15 mmol, mixed with (*Z*)-isomer, *E*/*Z* = 14:1) in anhydrous 1, 2-dichlorobenzene (0.82 mL, 0.18 M) was added *via* syringe, and 1,4-oxathiane (4.2 uL, 0.045 mmol) was added by microlitre syringe. The reaction mixture was purged with CO for 10 minutes and subsequently sparged with CO for ca. 10 seconds. Then the reaction heated at 140 °C under a CO atmosphere (1 atm) for 72 h. The mixture was cooled to r.t., concentrated *in vacuo.* The crude mixture was purified by column chromatography (33 % EtOAc/Hex) to yield the title compound **8w** (29.5 mg, 64 %, > 15:1 d.r.) as a colorless solid; *Under general procedure **G**, title compound **8w** was obtained in 56 % yield (25.8 mg,* > 15:1 d.r.*) as a*

*colorless solid; Under general procedure **H**, title compound **8w** was obtained in 59 % yield (27.2 mg, > 15:1 d.r.) as a colorless solid.*

m.p.: 102 – 104 °C (CH_2Cl_2/Hex); ν_{max} / cm^{-1}: 2954 (m), 1702 (s), 1393 (s), 1157 (s), 1110 (m), 1029 (m), 811 (m); ^1H NMR (400 MHz, $CDCl_3$): δ 7.71 (2H, d, *J* = 8.3 Hz, 2 × C**11**-H), 7.33 (2H, d, *J* = 8.5 Hz, 2 × C**12**-H), 3.65 (1H, dd, *J* = 9.5, 7.1 Hz, 1 × C**9**-H_2), 3.59 (1H, dd, *J* = 9.6, 7.1 Hz, 1 × C**1**-H_2), 3.00 (1H, dd, *J* = 10.8, 9.6 Hz, 1 × C**1**-H_2), 2.85 (1H, dd, *J* = 10.9, 9.5 Hz, 1 × C**9**-H_2), 2.47 – 2.39 (4H, m, 3 × C**14**-H_3, 1 × C**6**-H_2), 2.34 – 2.16 (2H, m, 1 × C**6**-H_2, 1 × C**3**-H), 2.09 (1H, dddd, *J* = 12.3, 6.4, 3.5, 2.0 Hz, 1 × C**7**-H_2), 2.04 – 1.95 (1H, m, 1 × C**8**-H), 1.54 – 1.35 (2H, m, 1 × C**7**-H_2, 1 × C**2**-H), 0.96 (3H, d, *J* = 6.5 Hz, 3 × C**4**-H_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 209.7 (C**5**), 143.5 (C**13**), 134.4 (C**10**), 129.8 (C**12**), 127.2 (C**11**), 52.3 (C**9**), 52.1 (C**1**), 51.0 (C**2**), 47.9 (C**3**), 42.9 (C**8**), 40.0 (C**6**), 27.1 (C**7**), 21.5 (C**14**), 12.4 (C**4**); *m/z* (ESI^+) HRMS: Calculated for $C_{16}H_{21}NO_3SNa$: 330.1134. Found $[M+Na]^+$: 330.1148. *The structure and relative stereochemistry of this compound was determined unambiguously by X-ray crystallography.*



(*E*) –*N*-(Cyclopropylmethyl)-4-methyl-*N*-(pent-2-en-1-yl)benzenesulfonamide (6x)



6x

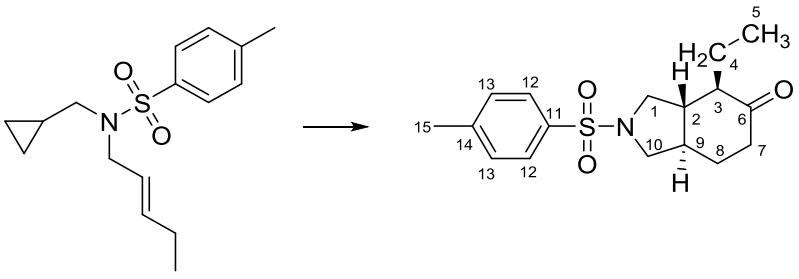
General procedure B: *N*-(Cyclopropylmethyl)-4-methylbenzenesulfonamide (0.27 g, 1.2 mmol) and (*E*)-1-bromopent-2-ene (0.21 g, 1.4 mmol, *E*/*Z* = 12:1) were empolyed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound **6x** (0.33 g, 79 %, mixed with (*Z*)-isomer, *E*/*Z* = 9:1) as a colorless oil.

ν_{max} / cm^{-1}: 2965 (m), 1598 (m), 1338 (m), 1154 (s), 905 (s), 727 (s); *m/z* (ESI^+) HRMS: Calculated for $C_{16}H_{23}NO_2SNa$: 316.1342. Found $[M+Na]^+$: 316.1345.

Data for major *E* isomer: ^1H NMR (400 MHz, $CDCl_3$): δ 7.68 (2H, d, *J* = 10.3 Hz), 7.27 (2H, d, *J* = 9.9 Hz), 5.68 – 5.52 (1H, m), 5.29 – 5.12 (1H, m), 3.85 (2H, d, *J* = 6.6 Hz), 3.01 (2H, dd, *J* = 6.9, 2.0 Hz), 2.40 (3H, s), 2.05 – 1.90 (2H, m), 0.98 – 0.82 (4H, m), 0.49 – 0.42 (2H, m), 0.19 – 0.08 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.8, 137.7, 136.7, 129.5, 127.1, 123.6, 51.3, 49.4, 25.1, 21.5, 13.2, 9.7, 4.0.

Data for minor isomer: *Characteristic peaks only*: 5.52 – 5.42 (1H, m), 3.96 (3H, d, *J* = 6.8 Hz).

(3a*S, 4*R**, 7a*R**)-4-Ethyl-2-tosylhexahydro-1*H*-isoindol-5(6*H*)-one (8x)**

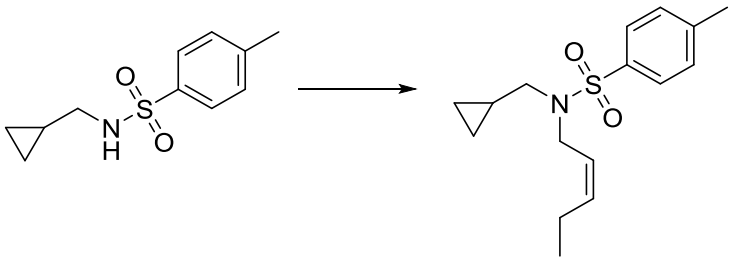


In a glove box, an oven dried reaction tube, fitted with a magnetic stirrer, was charged with $[Rh(CH_2CH_2)_2Cl]_2$ (2.92 mg, 0.0075 mmol) and Na_2SO_4 (4.26 mg, 0.03 mmol). Then took the reaction tube out of the glove box, compound **6x** (44.00 mg, 0.15 mmol, *E*/*Z* = 9:1) in anhydrous 1, 2-dichlorobenzene (0.82 mL, 0.18 M) was added *via* syringe, and 1,4-oxathiane (4.2 uL, 0.045 mmol) was added by microlitre syringe. The reaction mixture was purged with CO for 10 minutes and subsequently sparged with CO for ca. 10 seconds, then heated at 140 °C under a CO atmosphere (1 atm) for 72 h. The mixture was cooled to r.t., concentrated *in vacuo*. The crude mixture was purified by column chromatography (33 % EtOAc/Hex) to yield the title compound **8x** (25.2 mg, 52 %, > 15:1 d.r.) as a colorless solid;

*Under general procedure **G**, title compound **8x** was obtained in 49 % yield (23.8 mg, > 15:1 d.r.) as a colorless solid; Under general procedure **H**, title compound **8x** was obtained in 47 % yield (22.8 mg, > 15:1 d.r.) as a colorless solid.*

m.p.: 100 – 102 °C (CH_2Cl_2/Hex); ν_{max} / cm^{-1}: 1712 (m), 1343 (m), 1160 (m), 903 (s), 723 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (2H, d, *J* = 8.2 Hz, 2 × C**12**-H), 7.32 (2H, d, *J* = 7.8 Hz, 2 × C**13**-H), 3.67 – 3.55 (2H, m, 1 × C**10**-H_2, 1 × C**1**-H_2), 3.00 (1H, dd, *J* = 10.8, 9.6 Hz, 1 × C**1**-H_2), 2.84 (1H, dd, *J* = 10.9, 9.5 Hz, 1 × C**10**-H_2), 2.46 – 2.34 (4H, m, 1 × C**7**-H_2, 3 × C**15**-H_3), 2.34 – 2.18 (1H, m, 1 × C**7**-H_2), 2.15 – 1.91 (3H, m, 1 × C**8**-H_2, 1 × C**9**-H, 1 × C**3**-H), 1.63 – 1.47 (2H, m, 1 × C**4**-H_2, 1 × C**2**-H), 1.48 – 1.31 (2H, m, 1 × C**8**-H_2, 1 × C**4**-H_2), 0.83 (3H, t, *J* = 7.4 Hz, 3 × C**5**-H_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 209.4 (C**6**), 143.6 (C**14**), 134.4 (C**11**), 129.8 (C**13**), 127.2 (C**12**), 54.4 (C**3**), 52.1, 52.0 (C**1**, C**10**), 48.9 (C**2**), 43.2 (C**9**), 40.4 (C**7**), 27.2 (C**8**), 21.5 (C**15**), 20.2 (C**4**), 11.5 (C**5**). (*N.B. C**1** and C**10** could not be assigned confidently*). *m/z* (ESI^+) HRMS: Calculated for $C_{17}H_{23}NO_3Na$: 344.1291. Found $[M+Na]^+$: 344.1291; *The relative stereochemistry of this compound was assigned by analogy to that of **8w**.*

(*Z*)-*N*-(Cyclopropylmethyl)-4-methyl-*N*-(pent-2-en-1-yl)benzenesulfonamide (6x')

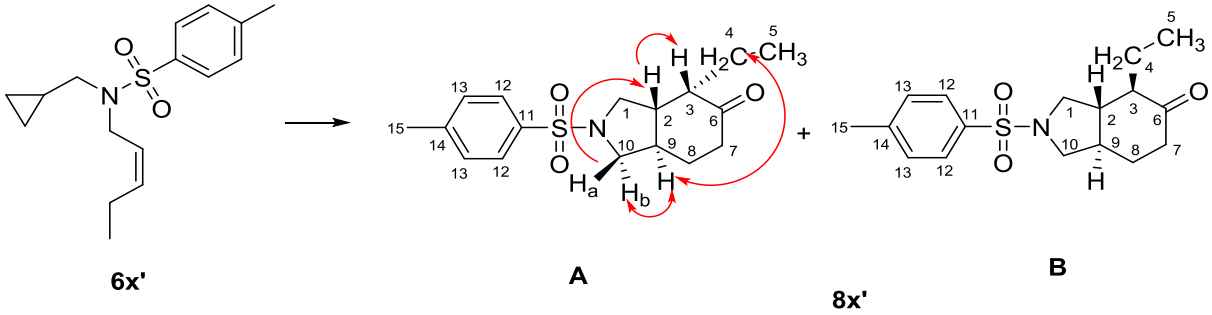


6x'

General procedure B: *N*-(Cyclopropylmethyl)-4-methylbenzenesulfonamide (0.64 g, 3 mmol) and (*Z*)-1-bromopent-2-ene (1.33 g, 9 mmol) (prepared according to literature procedure[8]) were empolyed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound **6x'** (0.66 g, 80 %) as a colorless oil; ν_{max} / cm^{-1}: 2965 (m), 1341 (m), 1153 (s), 1090 (m), 909 (m), 813 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (2H, d, *J* = 8.3 Hz), 7.26 (2H, d, *J* = 8.1 Hz), 5.54 – 5.36 (1H, m), 5.23 – 5.10 (1H, m), 3.96 (2H, dd, *J* = 6.7, 1.7 Hz), 3.01 (2H, dd, *J* = 6.9, 1.2 Hz), 2.40 (3H, s), 2.03 (2H, ddd, *J* = 7.5, 1.5, 1.5 Hz), 0.94 (3H, t, *J* = 7.5 Hz), 0.91 – 0.83 (1H, m), 0.49 – 0.44 (2H, m), 0.17 – 0.12 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.9, 137.6, 135.3, 129.5, 127.1, 123.9, 51.6,

44.1, 21.5, 20.6, 14.0, 9.7, 4.0; *m/z* (ESI$^+$) HRMS: Calculated for $C_{16}H_{23}NO_2SNa$: 316.1342. Found $[M+Na]^+$: 316.1360.

(3a*S*, 4*S***, 7a*R***) and (3a*S***, 4*R***, 7a*R***)-4-Ethyl-2-tosylhexahydro-1*H*-isoindol-5(6*H*)-one (8x')**



An oven dried reaction tube, fitted with a magnetic stirrer, was charged with $[Rh(cod)Cl]_2$ (2.77 mg, 0.0056 mmol) and $AsPh_3$ (3.45 mg, 0.011 mmol) and Na_2SO_4 (4.26 mg, 0.03 mmol). The tube was fitted with a rubber septum and purged with argon. Compound **6x'** (44.00 mg, 0.15 mmol) in anhydrous 1, 2-dichlorobenzene (0.82 mL, 0.18 M) was added *via* syringe. The reaction mixture was purged with CO for 10 minutes and subsequently sparged with CO for ca. 10 seconds, then heated at 140 °C under a CO atmosphere (1 atm) for 72 h. The mixture was cooled to r.t., concentrated *in vacuo*, the crude mixture was purified by column chromatography (33 % EtOAc/Hex) to yield the title compound **8x'** (24.3 mg, 50 %) as a colorless oil. A mixture of diastereomers A and B were obtained in a 7:1 (A:B) ratio. (There was a trace amount of unidentified impurity mixed in product). *Under general procedure **G**, title compound **8x'** was obtained in 46 % yield (22.4 mg) as a colorless oil, A mixture of diastereomers A and B were obtained in a 7:1 (A:B) ratio; Under general procedure **H**, title compound **8x'** was obtained in 57 % yield (27.7 mg) as a colorless oil, A mixture of diastereomers A and B were obtained in a 8:3 (A:B) ratio.*

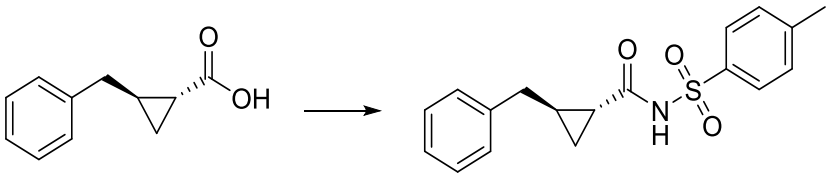
*The relative stereochemistry of major diastereomer A was corroborated by nOe experiments (as indicated on the compound structure A). nOes between C**9**-H and C**4**-H, C**10**$_b$-H and C**9**-H, from C**10**$_a$-H to C**2**-H, from C**2**-H to C**3**-H were observed. Analysis of relative stereochemistry of minor diastereomer B see **8x**.*

ν_{max} / cm^{-1}: 2963 (m), 1707 (s), 1339 (m), 1157 (s), 1092 (m), 815 (m); *m/z* (ESI$^+$) HRMS: Calculated for $C_{17}H_{23}NO_3SNa$: 344.1291. Found $[M+Na]^+$: 344.1307.

Data for major diastereomer A: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (2H, d, *J* = 8.3 Hz, 2 × C**12**-H), 7.32 (2H, d, *J* = 8.1 Hz, 2 × C**12**-H), 3.65 (1H, dd, *J* = 9.4, 7.0 Hz, 1 × C**10**-H_2), 3.36 (1H, dd, *J* = 9.7, 7.5 Hz, 1 × C**1**-H_2), 3.22 (1H, dd, *J* = 11.2, 9.8 Hz, 1 × C**1**-H_2), 2.73 (1H, dd, *J* = 10.6, 9.5 Hz, 1 × C**10**-H_2), 2.45 – 2.31 (5H, m, 1 × C**7**-H_2, 3 × C**15**-H_3, 1 × C**3**-H), 2.27 – 2.15 (1H, m, 1 × C**7**-H_2), 2.21 – 2.11 (1H, m, 1 × C**9**-H), 2.07 (1H, dddd, *J* = 12.6, 6.2, 3.9, 2.1 Hz, 1 × C**8**-H_2), 1.89 – 1.77 (1H, m, 1 × C**2**-H), 1.59 – 1.40 (2H, m, 2 × C**4**-H_2), 1.33 (1H, dddd, *J* = 13.3, 11.9, 4.7 4.7 Hz, 1 × C**8**-H_2), 0.81 (3H, t, *J* = 7.4 Hz, 3 × C**5**-H_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 211.9 (C**6**), 143.6 (C**14**), 134.3 (C**11**), 129.8 (C**13**), 127.3 (C**12**), 52.8 (C**3**), 52.2 (C**10**), 48.5 (C**1**), 47.6 (C**2**), 36.6 , 36.6 (C**7**, C**9**), 27.5 (**C8**), 21.5 (**C15**), 18.8 (**C4**), 11.8 (**C5**). (*N.B. C7 and C9 could not be assigned confidently*).

See compound **8x** for minor diastereomer

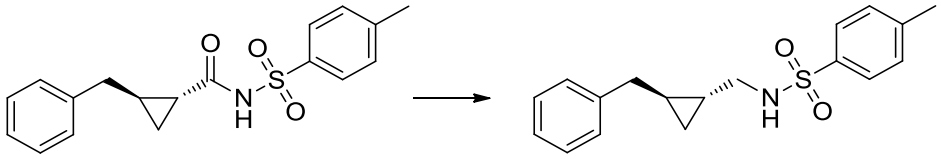
(1*R, 2*S**)-2-Benzyl-*N*-tosylcyclopropane-1-carboxamide**



To an ice-cold stirring solution of (1*R**, 2*S**)-2-Benzylcyclopropane-1-carboxylic acid (1.76 g, 10.0 mmol), EDCI (2.48 g, 13.0 mmol) and DMAP (1.71 g, 14.0 mmol) in anhydrous CH_2Cl_2 (25 mL) under an atmosphere of nitrogen was added *p*-methylbenzenesulfonamide (2.05 g, 12.0 mmol) in CH_2Cl_2 (2 mL). The mixture was heated to 50 °C and stirred for 24 h. Then the mixture was concentrated *in vacuo* and suspended in 1M NaOH (50 mL) and extracted with EtOAc (3 × 50 mL), the organic layers were combined and washed with 1M HCl (50 mL), brine (50 mL), dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography (20 % EtOAc/Hex) to yield the title compound (1.99 g, 61 %, > 15:1 d.r.) as a colorless solid; m.p.: 135 – 137 °C (CH_2Cl_2/Hex); ν_{max} / cm^{-1}: 3231 (m), 2921 (m), 1686 (m), 1453 (s), 1341 (m), 1175 (s), 1087 (s), 805 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.97 (1H, s), 7.91 (2H, d, *J* = 8.4 Hz), 7.36 – 7.29 (2H, m), 7.28 – 7.15 (3H, m), 7.14 – 7.04 (2H, m), 2.68 (1H, dd, *J* = 14.8, 6.4 Hz), 2.56 (1H, dd, *J* = 14.8, 7.0 Hz), 2.44 (3H, s), 1.77 – 1.61 (1H, m), 1.46 – 1.36 (1H, m), 1.26 (1H, ddd, *J* = 8.8, 4.4, 4.4 Hz), 0.84 (1H, ddd, *J* = 7.9, 6.6, 4.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.1, 145.0, 139.4, 135.6,

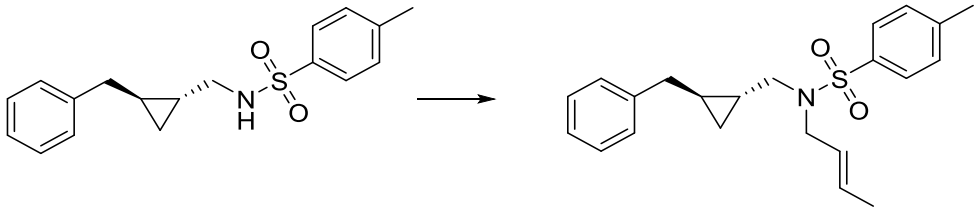
129.6, 128.4, 128.3, 128.2, 126.4, 37.9, 24.6, 21.7, 21.7, 16.3; *m/z* (ESI^+) HRMS: Calculated for $C_{18}H_{19}NO_3SNa$: 352.0978. Found $[M+Na]^+$: 352.0974.

(1*R, 2*S**)-*N*-((2-Benzylcyclopropyl)methyl)-4-methylbenzenesulfonamide**



General procedure D: (1*R**, 2*S**)-2-Benzyl-*N*-tosylcyclopropane-1-carboxamide (0.99 g, 3.0 mmol) was employed, the crude mixture was purified by column chromatography (15 % EtOAc/Hex) to yield the title compound (0.69 g, 74%, > 15:1 d.r.) as a colorless oil; ν_{max} / cm^{-1}: 3277 (m), 2921 (m), 1425 (m), 1321 (s), 1154 (s), 1054 (s), 813 (m); ^1H NMR (400 MHz, $CDCl_3$): δ 7.73 – 7.67 (2H, m), 7.31 – 7.26 (4H, m), 7.24 – 7.18 (1H, m), 7.17 – 7.11 (2H, m), 4.64 (1H, br. s), 2.96 – 2.71 (2H, m), 2.48 (2H, d, *J* = 6.4 Hz), 2.42 (3H, s), 0.83 – 0.72 (2H, m), 0.45 – 0.40 (1H, m), 0.39 – 0.33 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.3, 141.3, 137.0, 129.7, 128.4, 128.2, 127.1, 126.1, 47.6, 38.9, 21.5, 19.0, 18.0, 10.8; *m/z* (ESI^+) HRMS: Calculated for $C_{18}H_{21}NO_2SNa$: 338.1185. Found $[M+Na]^+$: 338.1194;

(1*R, 2*S**)-*N*-((-2-Benzylcyclopropyl)methyl)-*N*-(*E*-but-2-en-1-yl)-4methylbenzenevsulfonamide (6y)**



6y

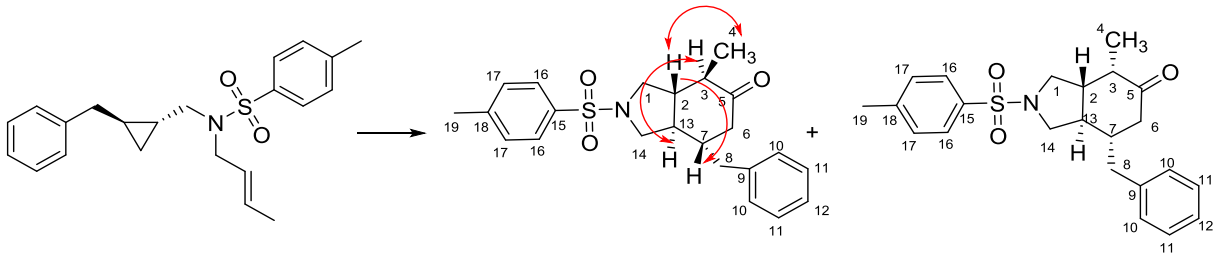
General procedure E: (1*R**, 2*S**)-*N*-((2-Benzylcyclopropyl)methyl)-4-methylbenzenesulfonamide (0.57 g, 1.8 mmol) and (*E*)-1-bromobut-2-ene (0.37 g, 2.7 mmol, *E*/*Z* = 17/1) were empolyed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound **6y** (0.59 g, 89 %, > 15:1 d.r. mixed with (*Z*)-isomer, *E*/*Z* = 10:1) as a colorless oil;

ν_{max} / cm^{-1}: 2916 (m), 1452 (m), 1335 (s), 1154 (s), 1090 (s), 932 (m); *m/z* (ESI^+) HRMS: Calculated for $C_{22}H_{27}NO_2SNa$: 392.1655. Found $[M+Na]^+$: 392.1649.

Data for major *E*-isomer A: ^{1}H NMR (400 MHz, $CDCl_3$): δ ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (2H, d, *J* = 8.3 Hz), 7.30 – 7.22 (4H, m), 7.23 – 7.09 (3H, m), 5.60 – 5.37 (1H, m), 5.20 (1H, dddd, *J* = 16.9, 8.3, 5.8, 1.7 Hz), 3.75 (1H, dd, *J* = 15.3, 6.5 Hz), 3.65 (1H, dd, *J* = 15.3, 6.8 Hz), 3.14 (1H, dd, *J* = 14.5, 6.1 Hz), 2.93 (1H, dd, *J* = 14.5, 7.0 Hz), 2.51 (2H, d, *J* = 6.5 Hz), 2.42 (3H, s), 1.61 (3H, dd, *J* = 6.5, 1.4 Hz), 0.91 – 0.72 (2H, m), 0.47 – 0.34 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.9, 141.3, 137.8, 129.8, 129.5, 128.3, 128.3, 127.1, 126.0, 125.9, 50.4, 49.0, 39.2, 21.5, 19.3, 17.6, 17.0, 11.1.

Data for minor *Z*-isomer B: *Characteristic peaks only*: ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.93 – 3.80 (2H, m).

(3a*S, 4*R**, 7*S**, 7a*R**) and (3a*S**, 4*S**, 7*S**, 7a*R**)-7-Benzyl-4-methyl-2-tosyloctahydro-5H-isoindol-5-one (8y)**



6y **A** **B**

8y

General procedure H: Compound **6y** (55.4 mg, 0.15 mmol, *E*/*Z* = 10:1) was employed, and the crude mixture was purified by column chromatography (33 % EtOAc/Hex) to yield the title compound **8y** (32.2 mg, 54 %) as an off-white solid. A mixture of diastereomers A and B were obtained in an 11:1 (A:B) ratio. *Under general procedure **G**, title compound **8y** was obtained in 19 % yield (11.3 mg) as an off-white solid, A mixture of diastereomers A and B were obtained in a 9:1 (A:B) ratio.*

*The relative stereochemistry of major diastereomer A was corroborated by nOe experiments (as indicated on the compound structure A). nOes between C**13**-H and C**3**-H, C**2**-H and C**4**-H, from C**2**-H to C**7**-H were observed. For minor diastereomer B, the coupling constants observed for C**1**-H and C**14**-H for diastereomer A and diastereomer B are similar with each other (for diastereomer A: (dd, J = 9.5, 7.1 Hz, 1 × C**1**-$\underline{H_2}$), (dd, J = 10.2, 10.2 Hz, 1 × C**14**-$\underline{H_2}$) for diastereomer B: characteristic peaks only: (dd, J = 9.8, 7.1 Hz, 1 × C**1**-$\underline{H_2}$), 3.14 (dd,*

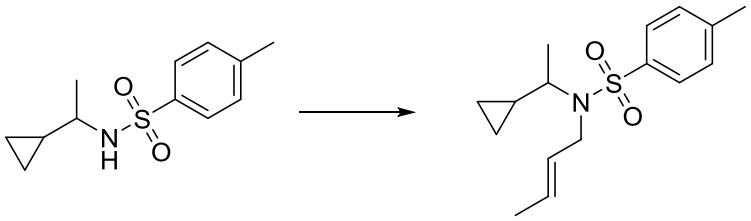
*J = 10.1, 10.1 Hz, 1 × C**14**-H$_2$)), these results indicated a trans ring junction for diastereomer B (same with diastereomer A). Combined with the stereochemical analysis results from **8t**, which was obtained as a single diasteromer, minor diastereomer B should have same stereochemistry with major diastereomer A at C**7**. The relative stereochemistry of C3 of diastereomer B was assigned by comparison to **8x'** and is believed to be formed from the 10 % Z-isomer of **6y**.*

ν_{max} / cm^{-1}: 2953 (m), 1695 (s), 1418 (s), 1357 (m), 1136 (m), 911 (m); *m/z* (ESI$^+$) HRMS: C alculated for $C_{23}H_{27}NO_3SNa$: 420.1604. Found $[M+Na]^+$: 420.1621.

Data for major diastereomer A: ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.75 – 7.61 (2H, m, 2 × C**16**-H), 7.35 (2H, d, *J* = 8.0 Hz, 2 × C**17**-H), 7.32 – 7.16 (3H, m, 2 × C**11**-H, 1 × C**12**-H), 7.03 (2H, dd, *J* = 6.9, 1.6 Hz, 2 × C**10**-H), 3.70 (1H, dd, *J* = 9.7, 7.0 Hz, 1 × C**14**-H$_2$), 3.58 (1H, dd, *J* = 9.5, 7.1 Hz, 1 × C**1**-H$_2$), 2.97 (1H, dd, *J* = 10.8, 9.6 Hz, 1 × C**1**-H$_2$), 2.86 (1H, dd, *J* = 10.2, 10.2 Hz, 1 × C**14**-H$_2$), 2.71 (1H, dd, *J* = 13.6, 4.6 Hz, 1 × C**8**-H$_2$), 2.49 – 2.39 (4H, m, 1 × C**8**-H$_2$, 3 × C**19**-H$_3$), 2.31 (1H, dd, *J* = 13.8, 3.4 Hz, 1 × C**6**-H$_2$), 2.15 (1H, dq, *J* = 13.0, 6.4 Hz, 1 × C**3**-H), 1.97 (1H, dd, *J* = 13.8, 12.7 Hz, 1 × C**6**-H$_2$), 1.93 – 1.85 (1H, m, 1 × C**7**-H), 1.84 – 1.74 (1H, m, 1 × C**13**-H), 1.56 – 1.45 (1H, m, 1 × C**2**-H), 0.94 (3H, d, *J* = 6.5 Hz, 3 × C**4**-H$_3$); ^{13}C NMR (126 MHz, $CDCl_3$): δ 209.3 (C**5**), 143.6 (C**18**), 137.7 (C**9**), 134.4 (C1**5**), 129.8 (C**17**), 129.0 (C**10**), 128.5 (C**12**), 127.3 (C**16**), 126.7 (C**11**), 51.8 (C**1**), 51.5 (C**14**), 49.9 (C**2**), 47.8 (C**13**), 47.4 (C**3**), 45.7 (C**6**), 41.5 (C**7**), 41.2 (C**8**), 21.6 (C**19**), 12.3 (C**4**).

Data for minor diastereomer B: *Characteristic peaks only*: ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.36 (1H, dd, *J* = 9.8, 7.1 Hz, 1 × C**1**-H$_2$), 3.14 (1H, dd, *J* = 10.1, 10.1 Hz, 1 × C**14**-H$_2$), 2.58 – 2.53 (1H, m, 1 × C**3**-H). 0.97 (1H, d, *J* = 7.4 Hz, 3 × C**4**-H$_3$).

(*E*)-*N*-(But-2-en-1-yl)-*N*-(1-cyclopropylethyl)-4-methylbenzenesulfonamide (6z)



6z

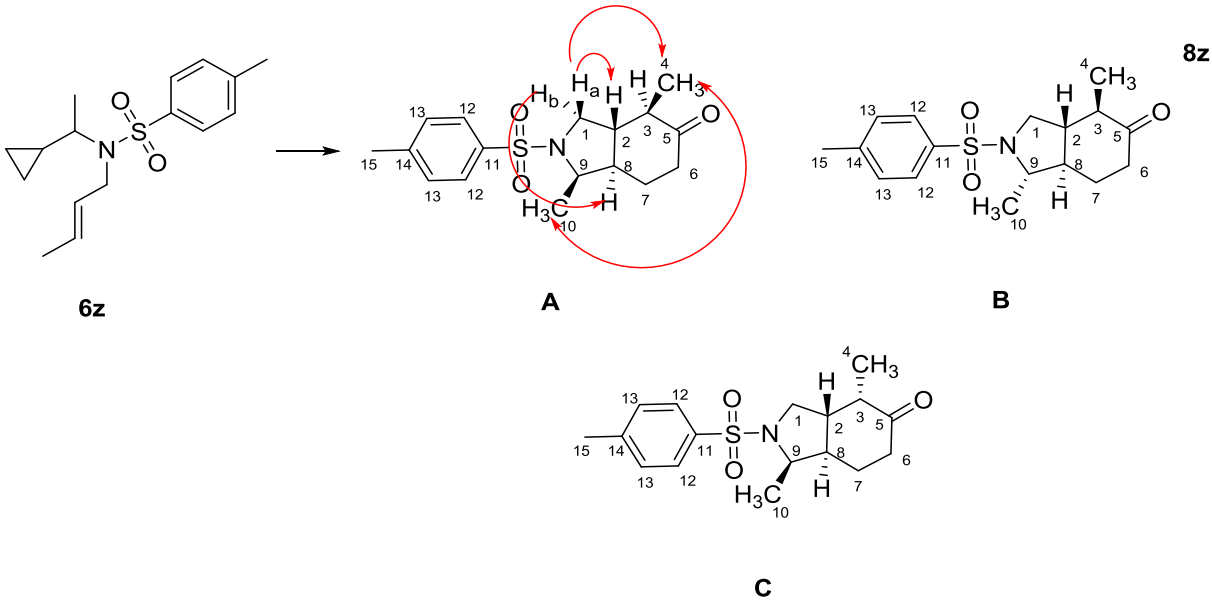
General procedure E: *N*-(1-Cyclopropylethyl)-4-methylbenzenesulfonamide (0.48 g, 2 mmol) and (*E*)-1-bromobut-2-ene (0.41g, 3.0 mmol, *E*/*Z* = 17:1) were empolyed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound **6z** (0.49 g, 85 %, mixed with (*Z*)-isomer, *E*/*Z* = 9:1) as a colorless oil.

ν_{max} / cm^{-1}: 2972 (s), 1450 (m), 1332 (s), 1150 (s), 1090 (s), 876 (m); *m/z* (ESI^+) HRMS: Calculated for $C_{16}H_{23}NO_2Na$: 316.1342. Found $[M+Na]^+$: 316.1346.

Data for major isomer: ^1H NMR (400 MHz, $CDCl_3$): δ 7.66 (2H, d, *J* = 8.2 Hz), 7.25 (2H, d, *J* = 8.7 Hz), 5.68 – 5.54 (1H, m), 5.54 – 5.40 (1H, m), 3.95 – 3.87 (1H, m), 3.86 – 3.78 (1H, m), 3.11 (1H, dq, *J* = 9.1, 6.8 Hz), 2.40 (3H, s), 1.65 (3H, dd, *J* = 6.3, 1.4 Hz), 1.13 (3H, d, *J* = 6.8 Hz), 0.88 (1H, dtt, *J* = 9.7, 8.1, 4.9 Hz), 0.53 (1H, dddd, *J* = 8.8, 8.0, 5.8, 4.3 Hz), 0.34 (1H, dddd, *J* = 8.9, 7.9, 5.5, 4.5 Hz), 0.17 (1H, dddd, *J* = 9.0, 5.4, 4.5, 4.5 Hz), 0.10 – 0.03 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.6, 138.8, 129.3, 129.0, 128.0, 127.0, 59.3, 45.9, 21.5, 19.1, 17.6, 16.2, 5.5, 4.2.

Data for minor isomer: *Characteristic peaks only*: ^1H NMR (400 MHz, $CDCl_3$): δ 4.04 (1H, dd, *J* = 16.9, 4.8 Hz).

(1*R, 3a*S**, 4*R**, 7a*R**) and (1*S**, 3a*S**, 4*R**, 7a*R**) and (1*R**, 3a*S**, 4*S**, 7a*R**)-1, 4-Dimethyl-2-tosyloctahydro-5*H*-isoindol-5-one (8z)**



General procedure H: Compound **6z** (44.0 mg, 0.15 mmol, mixed with (*Z*)-conformation isomer, *E*/*Z* = 9:1) was employed, the crude mixture was purified by column chromatography (33 % EtOAc/Hex) to yield the title compound **8z** (22.4 mg, 46 %) as a colorless oil. A mixture of diastereomers A, B and C were obtained in a 13:3:1 (A:B:C) ratio; *Under general procedure **G**, title compound **8z** was obtained in 21 % yield (10.3 mg) as a colorless oil, A mixture of diastereomers A, B and C were obtained in a 10:3:1 (A:B:C) ratio.*

*The relative stereochemistry of diastereomers A was corroborated by nOe experiments (as indicated on the compound structure A). nOes from C**1**$_a$-H to C**2**-H, from C**1**$_a$-H to C**4**-H, from C**1**$_b$-H to C**8**-H, and between C**4**-H to C**10**-H were observed. For minor diastereomer B, the coupling constants of C**9**-H (dt, J = 9.4, 6.0 Hz) are different from those of major diastereomer A (dt, J = 6.6, 6.6 Hz), and similar to coupling constants of C**8**-H for minor diastereomer B of product **8n** (dt, J = 8.7, 6.1 Hz). This indicates that diastereomer B and diastereomer B of **8n** have the same stereochemistry at ring junction and the **CH** position. At the same time, the coupling constants observed for C**4**-H of diastereomer A and diastereomer B are similar to each other (for diastereomer A: dd, J = 6.5, 0.8 Hz; for diastereomer B: dd, J = 6.6, 0.8 Hz), this indicates the same stereochemistry at C**3** for diastereomer A and diastereomer B. Based on these results, minor diastereomer B was assigned with the stereochemistry indicated on compound structure B. For minor diastereomer C: the coupling constants observed for C**9**-H of diastereomer A and diastereomer C are similar to each other (for diastereomer A: dt, J = 6.8, 6.8 Hz; for diastereomer B dt, J = 6.6, 6.6 Hz), indicating diastereomer C and diastereomer A have same stereochemistry at C**9** and the ring junction, which suggests that the stereochemistry at C3 for diastereomer C is opposite to that of diastereomer A.*

ν_{max} / cm^{-1}: 2970 (m), 1711 (s), 1339 (s), 1159 (m), 1037 (m), 816 (m); *m/z* (ESI^+) HRMS: Calculated for $C_{17}H_{23}NO_3Na$: 344.1291. Found $[M+Na]^+$: 344.1297.

Data for major diastereomer A**:** ^{1}H NMR (500 MHz, C_6D_6): δ 7.77 (2H, d, *J* = 8.0 Hz, 2 × C**12**-H), 6.92 – 6.81 (2H, m, 2 × C**13**-H), 3.69 (1H, dt, *J* = 6.8, 6.8 Hz, 1 × C**9**-H), 3.47 – 3.42 (1H, m, 1 × C**1**-H$_2$), 2.50 (1H, dd, *J* = 10.2, 8.6 Hz, 1 × C**1**-H$_2$), 2.06 – 1.96 (1H, m, 1 × C**6**-H$_2$), 1.90 (3H, s, 1 × C**15**-H$_2$), 1.44 – 1.36 (1H, m, 1 × C**6**-H$_2$), 1.33 – 1.24 (1H, m, 1 × C**2**-H), 1.23 – 1.15 (1H, m, 1 × C**3**-H), 1.06 – 0.98 (2H, m, 1 × C**7**-H$_2$, 1 × C**8**-H), 0.96 – 0.93 (3H, m), 1.02 – 0.96 (1H, m, 1 × C**7**-H$_2$); 0.76 (3H, dd, *J* = 6.5, 0.8 Hz, 3 × C**4**-H$_3$); ^{13}C NMR

(126 MHz, C_6D_6): δ 207.2 (C**5**), 142.6 (C**14**), 136.0 (C**11**), 129.3 (C**13**), 127.5 (C**12**), 57.4 (C**9**), 52.4 (C**1**), 47.5 (C**3**), 46.6 (C**2**), 45.4 (C**8**), 39.4 (C**6**), 24.2 (C**7**), 20.7 (C1**5**), 17.8 (C**10**), 12.2 (C**4**).

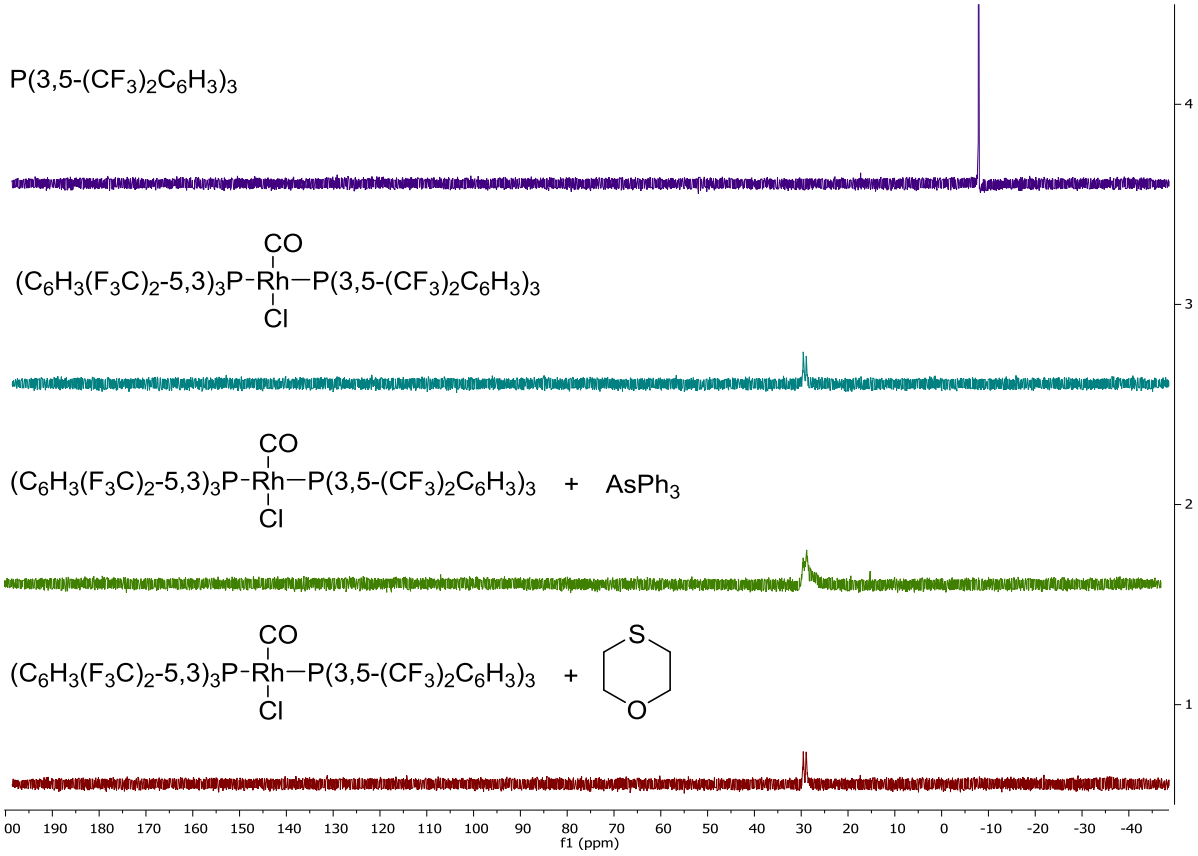
Data for minor diastereomer B: *Characteristic peaks only*: ^{1}H NMR (500 MHz, C_6D_6): δ 3.58 (1H, dd, *J* = 10.9, 7.0 Hz, 1 × C**1**-$\underline{H}_2$), 2.89 (1H, dt, *J* = 9.4, 6.0 Hz, 1 × C**9**-$\underline{H}$), 2.75 – 2.68 (1H, m, 1 × C**1**-$\underline{H}_2$), 0.72 (3H, dd, *J* = 6.6, 0.8 Hz, 3 × C**4**-$\underline{H}_3$).

Data for minor diastereomer C: *Characteristic peaks only*: ^{1}H NMR (500 MHz, C_6D_6): δ 3.30 (1H, dt, *J* = 6.6, 6.6 Hz, 1 × C**9**-$\underline{H}$), 3.25 – 3.18 (1H, m, 1 × C**1**-$\underline{H}_2$), 3.01 (1H, dd, *J* = 10.8, 4.6 Hz, 1 × C**1**-$\underline{H}_2$).

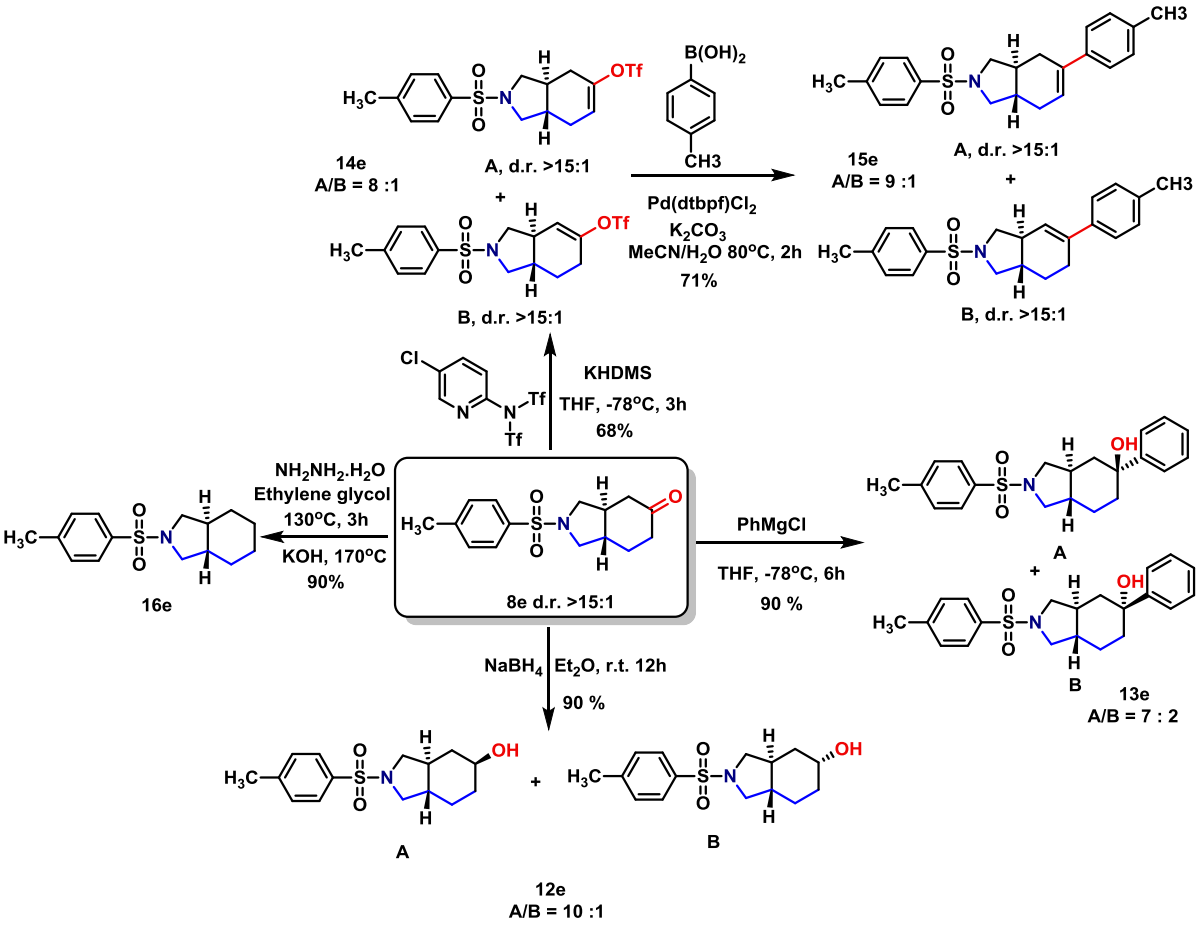
Binding Competition Studies.

$[Rh(CO)_2Cl]_2$ (1.94 mg, 0.005 mmol), and $P(3,5\text{-}(CF_3)_2C_6H_3)_3$ (13.4 mg, 0.020 mmol) and DCM (50 uL) were added to three NMR tubes (tube **I**, tube **II**, tube **III**), evolution of CO was noted on addition of CH_2Cl_2. After 10 minutes, $AsPh_3$ (6.12 mg, 0.020 mmol) was added to tube **II,** and 1,4-oxathiane (1.90 uL, 0.020 mmol) was added to tube **III.** These NMR tubes were left standing at r.t. for 15 minutes before the ^{31}P NMR analysis. ^{31}P NMR analysis of the three NMR tubes showed that trans-$Rh[P(3,5\text{-}(CF_3)_2C_6H_3)_3]_2(CO)Cl$ has formed in all three tubes ((^{31}P NMR (CH_2Cl_2, 162 MHz, 25 °C) tube **I**: δ 29.24 (d, *J* = 130.7 Hz), tube **II**: δ 29.18 (d, *J* = 130.0 Hz) and tube **III**: δ 29.23 (d, *J* = 128.9 Hz)), indicating that neither $AsPh_3$ nor 1,4-oxathiane undergo ligand exchange significantly with $Rh[P(3,5\text{-}(CF_3)_2C_6H_3)_3]_2(CO)Cl$.

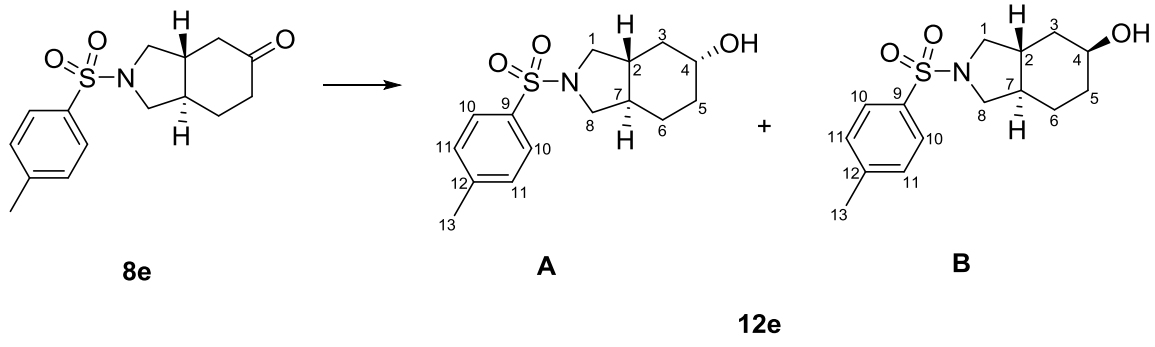
^{31}P spectra for binging competition studies:


P(3,5-(CF3)2C6H3)3
CO
(C6H3(F3C)2-5,3)3P-Rh-P(3,5-(CF3)2C6H3)3
Cl
CO
(C6H3(F3C)2-5,3)3P-Rh-P(3,5-(CF3)2C6H3)3 + AsPh3
Cl
CO
(C6H3(F3C)2-5,3)3P-Rh-P(3,5-(CF3)2C6H3)3 +
Cl
S
O
4
3
2
1
00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40
f1 (ppm)

Product Derivatization



(3a*R*, 5*R***, 7a*R***)-2-Tosyloctahydro-1*H*-isoindol-5-ol and (3a*R***, 5*S***, 7a*R***)-2-tosyloctahydro-1*H*-isoindol-5-ol (12e)**



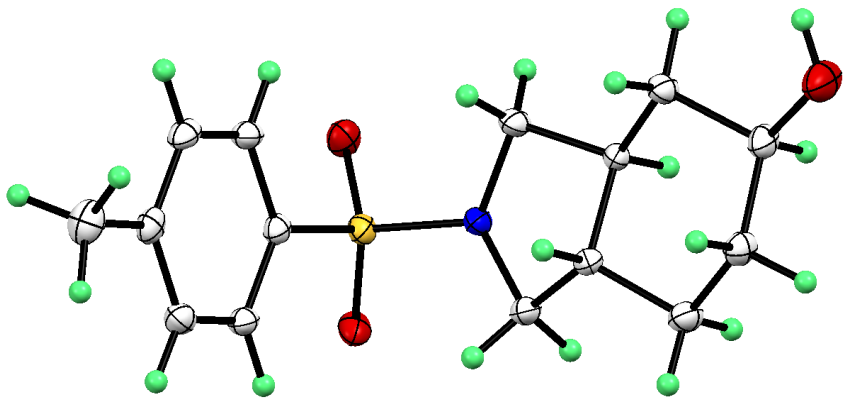
To a solution of cyclohexanone **8e** (73.3 mg, 0.25 mmol) in anhydrous Et_2O (1 mL) at 0 °C was added $NaBH_4$ (18.9 mg, 0.50 mmol) in two aliquots. Two drops of MeOH were added to facilitate the reaction, the mixture was warmed to r.t. and stirred overnight. Then the mixture was diluted with water (5 mL) and extracted with EtOAc (3 × 5 mL), the organic layers were

combined, washed with brine (5 mL), dried over Na_2SO_4 and concentrated *in vacuo*. The crude mixture was purified by column chromatography (50 % EtOAc/Hex) to yield the title compound **12e** (65.9 mg, 90 %) as an off-white solid. A mixture of diastereomers A and B were obtained in a 10:1 (A:B:C) ratio.

*Major diastereomer A was recrystallized from the mixture, and its structure and relative stereochemistry was determined unambiguously by X-ray crystallography. The relative stereochemistry of minor diastereomer B was assigned as the opposite diastereomer of major diastereomer A on position C**4**.*

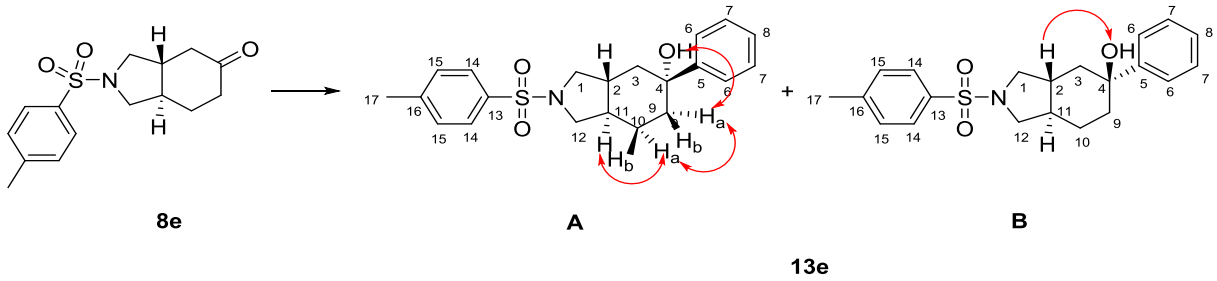
ν_{max} / cm^{-1}: 3408 (m), 2928 (m), 1335 (s), 1159 (s), 1092 (s), 1016 (s); *m/z* (ESI^+) HRMS: Calculated for $C_{15}H_{21}NO_3SNa$: 318.1134. Found $[M+Na]^+$: 318.1141.

Data for major diastereomer A: m.p.: 148 – 151 °C (CH_2Cl_2/Hex); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (2H, d, *J* = 7.9 Hz, 2 × C**10**-H), 7.30 (2H, d, *J* = 7.9 Hz, 2 × C**11**-H), 3.62 – 3.54 (1H, m, 1 × C**4**-H), 3.52 – 3.41 (2H, m, 1 × C**1**-H_2, 1 × C**8**-H_2), 2.83 – 2.69 (2H, m, 1 × C**1**-H_2, 1 × C**8**-H_2), 2.41 (3H, s, 3 × C**13**-H_3), 2.09 – 2.01 (1H, br. m, 1 × C**3**-H_2), 2.01 – 1.93 (1H, br. m, 1 × C**5**-H_2), 1.89 (1H, br. d, *J* = 12.6 Hz, (OH)), 1.83 – 1.77 (1H, br. m, 1 × C**6**-H_2), 1.43 – 1.14 (3H, m, 1 × C**5**-H_2, 1 × C**2**-H, 1 × C**7**-H), 1.09 – 0.95 (2H, m, 1 × C**3**-H_2, 1 × C**6**-H_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.3 (C1**2**), 134.6 (C**9**), 129.7 (C**11**), 127.2 (C1**0**), 70.0 (C**4**), 52.4, 52.3 (C**1**, C**8**), 43.8, 42.9 (C**2**, C**7**), 37.1 (C**3**), 34.6 (C**5**), 25.7 (C**6**), 21.5 (C**13**). (*N.B. C**1** and C**8**, C**2** and C**7** could not be assigned confidently*).



Data for minor diastereomer B: *Characteristic peaks only*: ^{1}H NMR (400 MHz, $CDCl_3$): 4.09 (1H, br. m, 1 × C**4**-H).

(3a*R*, 5*R***, 7a*R***) and (3a*R***, 5*S***, 7a*R***)-5-Phenyl-2-tosyloctahydro-1*H*-isoindol-5-ol (13e)**



To a stirring solution of **8e** (73.3 mg, 0.25 mmol) in anhydrous THF (1 mL) at -78 °C was added phenylmagnesium chloride (0.25 mL, 0.50 mmol, 2.0 M in THF) dropwise and the mixture was stirred at -78 °C for 6 h. Then the reaction mixture was quenched with sat. aq. NH_4Cl (1 mL), warmed to r.t., diluted with water (2 mL) and extracted with EtOAc (3 × 5 mL), the organic extracts were combined, washed with water (5 mL), brine (5 mL), dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography (33 % EtOAc/Hex) to yield the title compounds ***13e**-A* (64.8 mg, 69 %) as a colorless solid and the title compound ***13e**-B* (19.8 mg, 21%) as a colorless oil.

*The relative stereochemistry of major diastereomer A was corroborated by nOe experiments (as indicated on the compound structure A) nOes between OH and C**9**$_a$-H, C**9**$_a$-H and C**10**$_a$-H, C**10**$_a$-H and C**12**-H were observed. No significant nOe was observed between C**2**-H and C**11**-H. The relative stereochemistry of minor diastereomer B was corroborated by nOe experiments (as indicated on the compound structure B). A nOe from C**2**-H to OH was observed. No significant nOe was observed between C**2**-H and C**11**-H.*

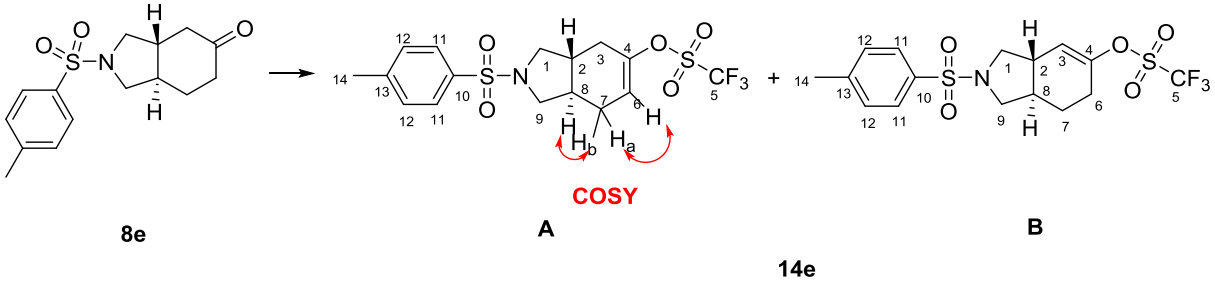
ν_{max} / cm^{-1}: 3236 (m), 2971 (m), 1340 (s), 1150 (s), 1042 (s), 1014 (m), 765 (s); *m/z* (ESI^+) HRMS: Calculated for $C_{21}H_{25}NO_3SNa$: 394.1447. Found $[M+Na]^+$: 394.1457.

Data for major diastereomer A: m.p.: 79 – 81 °C (CH_2Cl_2/Hex); ^1H NMR (400 MHz, $CDCl_3$): 7.65 (2H, d, *J* = 8.3 Hz, 2 × C**14**-H), 7.47 – 7.43 (2H, m, 2 × C**6**-H), 7.39 – 7.31 (2H, m, 2 × C**7**-H), 7.30 – 7.23 (3H, m, 2 × C**15**-H, 1 × C**8**-H), 3.50 – 3.40 (2H, m, 1 × C**1**-H_2, 1 × C**12**-H_2), 2.80 (1H, dd, *J* = 10.9, 9.2 Hz, 1 × C**1**-H_2), 2.68 (1H, dd, *J* = 11.0, 9.5 Hz, 1 × C**12**-H_2), 2.57 – 2.51 (2H, m, 1 × C**3**-H_2, 1 × C**9**-H_2), 2.40 (3H, s, 3 × C**17**-H_3), 2.01 (1H, br. s, OH), 1.86 – 1.82 (1H, m, 1 × C**10**-H_2), 1.71 (1H, td, *J* = 13.7, 4.1 Hz, 1 × C**9**-H_2), 1.56 – 1.37 (2H,

m, 1 × C**3**-H$_2$, 1 × C**2**-H), 1.37 – 1.22 (1H, m, 1 × C**11**-H), 1.19 – 1.08 (1H, m, 1 × C**10**-H$_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.0 (C**5**), 143.2 (C**16**), 134.8 (C**13**), 129.6 (C**15**), 128.7 (C**7**), 127.8 (C**8**), 127.2 (C**14**), 126.1 (C**6**), 73.7 (C**4**), 52.2, 52.1 (C**1**, C**12**), 44.5 (C**2**), 41.7 (C**11**), 40.7 (C**3**), 37.6 (C**9**), 25.7 (C**10**), 21.5 (C**17**).

Data for minor diastereomer B: ^{1}H NMR (400 MHz, $CDCl_3$): 7.72 (2H, d, *J* = 8.2 Hz, 2 × C**14**-H), 7.45 – 7.40 (2H, m, 2 × C**6**-H), 7.36 – 7.29 (4H, m, 2 × C**15**-H, 2 × C**7**-H), 7.28 – 7.22 (1H, m, 1× C**8**-H), 3.60 (1H, dd, *J* = 9.2, 6.7 Hz, 1 × C**12**-H$_2$), 3.52 (1H, dd, *J* = 9.2, 7.2 Hz, 1 × C**1**-H$_2$), 2.87 (2H, dd, *J* = 10.9, 9.3 Hz, 1 × C**1**-H$_2$, 1 × C**12**-H$_2$), 2.44 (3H, s, 3 × C**17**-H$_3$), 2.07 – 1.95 (1H, m, 1 × C**2**-H), 1.95 – 1.90 (1H, m, 1 × C**3**-H$_2$), 1.88 – 1.72 (3H, m, 2 × C**9**-H$_2$, 1 × C**10**-H$_2$), 1.63 (1H, br. s, OH), 1.60 – 1.49 (2H, m, 1 × C**10**-H$_2$, 1 × C**3**-H$_2$), 1.49 – 1.38 (1H, m, 1 × C**11**-H$_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.4 (C**5**), 143.2 (C**16**), 134.7 (C**13**), 129.7 (C**15**), 128.4 (C**7**), 127.3 (C**14**), 127.1 (C**8**), 124.2 (C**6**), 73.5 (C**4**), 52.6 (C**12**), 52.5 (C**1**), 43.9 (C**11**), 40.9 (C**3**), 39.9 (C**2**), 38.5 (C**9**), 24.0 (C**10**), 21.5 (C**17**).

(3a*R*, 7a*R***)-2-Tosyl-2,3,3a,4,7,7a-hexahydro-1*H*-isoindol-5-yl trifluoromethanesulfonate and (3a*S***, 7a*R***)-2-tosyl-2,3,3a,6,7,7a-hexahydro-1*H*-isoindol-5-yl trifluoromethanesulfonate (14e)**



To a solution of **8e** (105.0 mg, 0.36 mmol) in anhydrous THF (1.8 mL) at -78 °C was added potassium hexamethyldisilazide (KHMDS) (1 M in THF, 0.43 ml, 0.43 mmol) dropwise. Then the reaction was stirred at -78 °C for 10 minutes, and *N*-(5-chloro-2-pyridyl)bis(trifluoromethanesulfonimide) (Comin's reagent) (169.0 mg, 0.43 mmol) was added and the reaction was warmed slowly to r.t. over 3 h. The reaction was diluted with EtOAc (10 mL), washed with citric acid (10% w/v, 2 x 4 mL), H_2O (4 mL), and brine (4 mL), then dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound **14e** (82.3 mg, 68

%) as an off-white solid. A mixture of *regioisomers* A and B were obtained in a 8:1 (A:B) ratio.

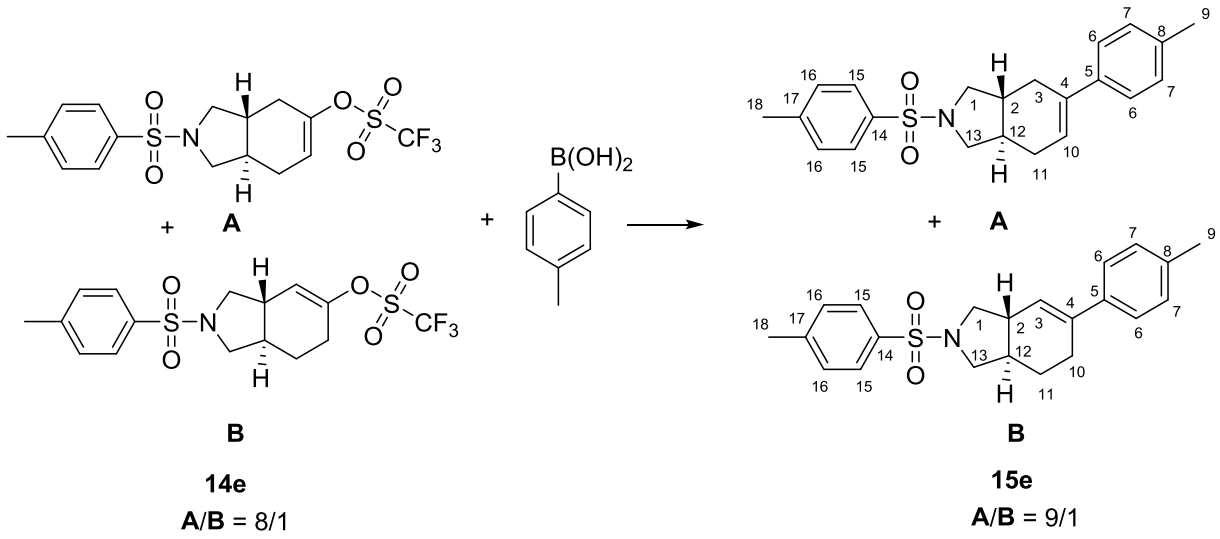
*The configuration of the enol triflate for major regioisomer A was determined by COSY data. Correlation between C**6**-H and C**7**-H$_a$, C**8**-H and C**7**-H$_b$ were observed.*

ν_{max} / cm^{-1}: 2935 (m), 1420 (s), 1342 (s), 1210 (s), 1009 (m), 859 (s); *m/z* (ESI$^+$) HRMS: Calculated for $C_{16}H_{18}NO_5S_2F_3Na$: 448.0471. Found $[M+Na]^+$: 448.0453

Data for major regioisomer A: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (2H, d, *J* = 8.3 Hz, 2 × C**11**-H), 7.32 (2H, d, *J* = 8.2 Hz, 2 × C**12**-H), 5.77 – 5.73 (1H, m, 1 × C**6**-H), 3.73 – 3.59 (2H, m, 1 × C**1**-H$_2$, 1 × C**9**-H$_2$), 2.96 – 2.79 (2H, m, 1 × C**1**-H$_2$, 1 × C**9**-H$_2$), 2.47 – 2.40 (4H, m, 3 × C**14**-H$_3$, 1 × C**8**-H$_2$, 1 × C**3**-H$_2$), 2.39 – 2.31 (1H, m, 1 × C**7**-H$_2$), 2.25 – 2.16 (1H, m, 1 × C**3**-H$_2$), 1.99 – 1.84 (2H, m, 1 × C**7**-H$_2$, 1 × C**2**-H), 1.80 – 1.70 (1H, m, 1 × C**8**-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.1 (C**4**), 143.6 (C**13**), 134.2 (C**10**), 129.8 (C**12**), 127.3 (C**11**), 118.4 (q, *J* = 320.2 Hz) (C**5**), 118.2 (C**6**), 52.2, 52.0 (C**1**, C**9**), 40.5 (C**8**), 39.1 (C**2**), 31.1 (C**3**), 26.1 (C**7**), 21.5 (C**14**). (*N.B. C**1** and C**9** could not be assigned confidently*)

Data for minor regioisomer B: *Characteristic peaks only*: ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.58 – 3.55 (2H, m, 1 × C**1**-H$_2$, 1 × C**9**-H$_2$).

(3a*R*, 7a*R***)-5-(*p*-Tolyl)-2-tosyl-2,3,3a,4,7,7a-hexahydro-1*H*-isoindole and (3a*R***, 7a*R***)-6-(*p*-tolyl)-2-tosyl-2,3,3a,4,5,7a-hexahydro-1*H*-isoindole (15e)**



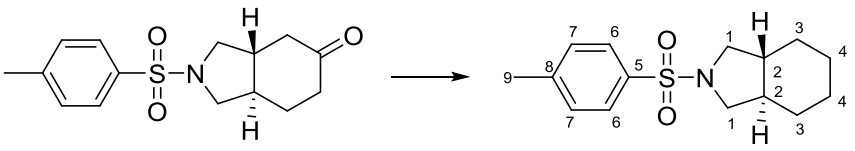
An oven dried reaction tube, fitted with a magnetic stirrer, was charged compound **14e** (33.6 mg, 0.1 mmol), *p*-tolylboronic acid (16.2 mg, 0.12 mmol), [Pd(dtbpf)Cl_2] (dtbpf = 1,1′ -Bis(di-tertbutylphosphino)ferrocene) (6.6 mg, 0.01 mmol), and K_2CO_3 (20.7 mg, 0.15 mmol). Then MeCN/H_2O(1:1, 1 mL) was added and the reaction tube was sealed under an argon atmosphere and heated to 80 °C for 2 h. The reaction mixture was cooled to r.t. and diluted with H_2O (5 mL). The aqueous phase was extracted with EtOAc (3 x 5 mL), the combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. The crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound **15e** (25.8 mg, 71 %) as an off-white solid. A mixture of *regioisomer* A and B were obtained in a 9:1 (A:B) ratio.

ν_{max} / cm^{-1}: 2921 (m), 1340 (s), 1158 (s), 1093 (m), 1040 (m), 917 (m); *m/z* (ESI^+) HRMS: Calculated for $C_{22}H_{25}NO_2SNa$: 390.1498. Found $[M+Na]^+$: 390.1508.

Data for major regioisomer A: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (2H, d, *J* = 8.3 Hz, 2 × C**15**-H), 7.32 (2H, d, *J* = 8.1 Hz, 2 × C**16**-H), 7.20 (2H, d, *J* = 8.3 Hz, 2 × C**6**-H), 7.10 (2H, d, *J* = 7.9 Hz, 2 × C**7**-H), 6.01 – 5.98 (1H, m, 1 × C**10**-H), 3.79 – 3.63 (2H, m, 1 × C**1**-H_2, 1 × C**13**-H_2), 3.01 – 2.81 (2H, m, 1 × C**1**-H_2, 1 × C**13**-H_2), 2.61 – 2.55 (1H, m, 1 × C**3**-H_2), 2.43 (3H, s, 3 × C**18**-H_3), 2.41 – 2.33 (1H, m, 1 × C**11**-H_2), 2.32 (3H, s, 3 × C**9**-H_3), 2.22 – 2.11 (1H, m, 1 × C**3**-H_2), 2.00 – 1.90 (1H, m, 1 × C**11**-H_2), 1.85 – 1.69 (2H, m, 1 × C**2**-H, 1 × C**12**-H_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.3 (C**17**), 138.7 (C**5**), 136.8 (C**8**), 136.1 (C**4**), 134.6 (C**14**), 129.7 (C**16**), 129.0 (C**7**), 127.3 (C**15**), 125.0 (C**6**), 122.6 (C**10**), 53.3, 53.2 (C**1**, C**13**), 40.9 (C**2**), 40.0 (C**12**), 31.0 (C**3**), 29.0 (C**11**), 21.5 (C**18**), 21.0 (C**9**). (*N.B. C**1** and C**13** could not be assigned confidently*).

Data for minor regioisomer B: *Characteristic peaks only*: ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.62 – 3.58 (2H, dd, *J* = 9.5, 6.9 Hz, 1 × C**1**-H_2, 1 × C**13**-H_2).

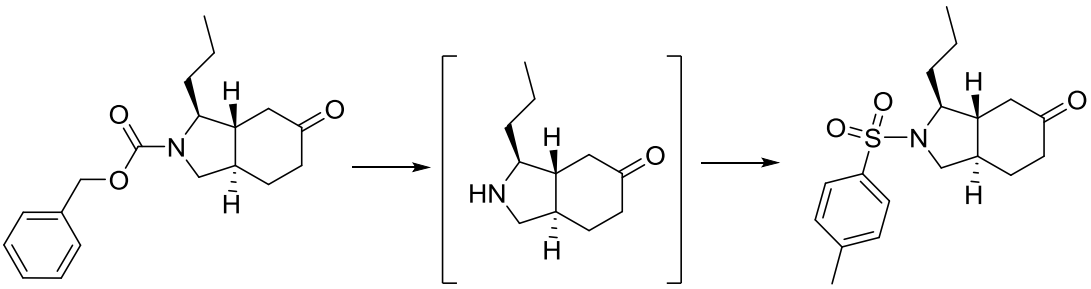
(3a*R, 7a*R**)-2-Tosyloctahydro-1*H*-isoindole (16e)**



8e **16e**

A stirred solution of **8e** (146.0 mg, 0.5 mmol) and hydrazinemonohydrate (0.25 ml, 5.0 mmol) in ethylene glycol (6 mL) was heated at 130 ^{o}C for 3 h. After removal of excess hydrazine hydrate under reduced pressure, KOH (330.0 mg, 5.0 mmol) was added to the mixture, and the reaction was heated at 170 ^{o}C for 16 h. The resulting solution was cooled to r.t., treated with saturated aq. NH_4Cl and extracted with diethyl ether (3 × 10 mL). The organic extracts were combined, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography (10 % EtOAc/hexane) to afford the title compound **16e** (124.6 mg, 90 %) as an off-white solid; m.p.: 105 - 107 °C ($CHCl_3$/Hex); ν_{max} / cm^{-1}: 2932 (m), 1341 (s), 1159 (s), 1092 (s), 1028 (s), 816 (m); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.71 (2H, d, *J* = 8.3 Hz, 2 × C**6**-H), 7.31 (2H, d, *J* = 7.9 Hz, 2 × C**7**-H), 3.50 (2H, dd, *J* = 9.4, 6.5 Hz, 2 × C**1**-H_2), 2.77 (2H, dd, *J* = 10.8, 9.3 Hz, 2 × C**1**-H_2), 1.85 – 1.76 (2H, m, 2 × C**4**-H_2), 1.76 – 1.66 (2H, m, 2 × C**3**-H_2), 1.37 – 1.20 (2H, m, 2 × C**2**-H), 1.21 – 1.07 (2H, m, 2 × C**3**-H_2), 1.04 – 0.84 (2H, m, 2 × C**4**-H_2); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 143.0 (C**8**), 134.9 (C**5**), 129.6 (C**7**), 127.3 (C**6**), 53.0 (C**1**), 44.4 (C**2**), 28.3 (C**4**), 25.3, 21.5 (C**3**); *m/z* (ESI$^+$) HRMS: Calculated for $C_{15}H_{22}NO_2S$: 280.1366. Found $[M+H]^+$: 280.1365.

Deprotection of Catalytic Products

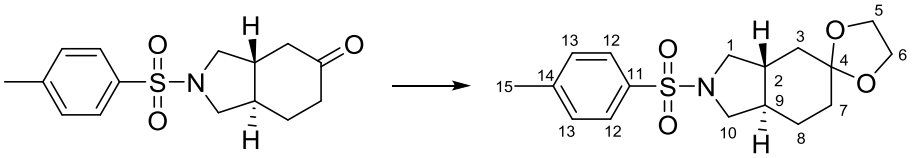


8h **8h'** **8i**

To a solution of **8h** (48.0 mg, 0.15 mmol, d.r.=3:1) in MeOH (5.0 mL) was added 10 wt. % palladium hydroxide on carbon (2.1 mg, 0.015 mmol) under the H_2 atmosphere (1 atm). Then evacuated and back-fill the flask with hydrogen three times. The reaction was stirred at 40 ^{o}C for 18 hours. The reaction mixture was then filtered through a short plug of silica, washed with MeOH, and concentrated *in vacuo* to afford **8h'** as a colorless oil which was directly dissolved in anhydrous toluene (2.0 ml), and then potassium carbonate (41.4 mg, 0.3 mmol) and sulfonyl chloride (57.0 mg, 0.3 mmol) were added to the solution. The reaction mixture was heated to 50 °C and stirred overnight. The suspension was cooled to r.t. and water (5 mL) was added, the aqueous layer was extracted with EtOAc (3 × 5 mL) and the

organic extracts combined, dried over Na_2SO_4 and concentrated *in vacuo.* The crude mixture was purified by column chromatography (33 % EtOAc/Hex) to yield the title compound **8i** (24.7 mg, 51 %) as a colorless oil. A mixture of diastereomers A and B were obtained in a 9:1 ratio.

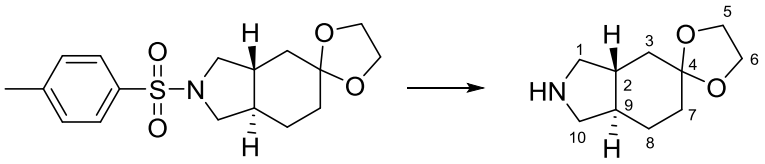
(3a*R, 7a*R**)-2-Tosyloctahydrospiro[isoindole-5,2'-[1,3]dioxolane] (17e)**



8e **17e**

To a flask equipped with a Dean–Stark apparatus under argon, was added **8e** (0.44g, 1.5 mmol), *p*-toluenesulfonic acid (15.0 mg, 0.09 mmol), ethylene glycol (0.9 mL, 15.0 mmol), and toluene (10 mL). The reaction solution was stirred under reflux for 5 h and water was removed through the Dean-Stark apparatus. The solution was cooled to 25 ^oC, diluted with aq. $NaHCO_3$, and extracted with diethyl ether (3 × 10 mL). The organic extracts were combined, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography (50 % EtOAc/hexane) to afford the title compound **17e** (0.50 g, 99 %) as a colorless solid; m.p.: 102 - 104 °C (CH_2Cl_2/Hex); ν_{max} / cm^{-1}: 2944 (m), 2880 (m), 1338 (s), 1157 (s), 1085 (s), 1035 (m); ^1H NMR ($CDCl_3$, 400 MHz): δ 7.69 (2H, d, *J* = 8.2 Hz, 2 × C**12**-H), 7.30 (2H, d, *J* = 7.8 Hz, 2 × C**13**-H), 3.94 – 3.84 (4H, m, 2 × C**5**-H_2, 2 × C**6**-H_2), 3.54 (1H, dd, *J* = 9.3, 6.8 Hz, 1 × C**1**-H_2), 3.48 (1H, dd, *J* = 9.3, 7.2 Hz, 1 × C**9**-H_2), 2.84 (1H, dd, *J* = 11.1, 9.3 Hz, 1 × C**9**-H_2), 2.77 (1H, dd, *J* = 10.9, 9.3 Hz, 1 × C**1**-H_2), 2.43 (3H, s, 3 × C**15**-H_3), 1.86 – 1.72 (3H, m, 1 × C**3**-H_2, 1 × C**7**-H_2, 1 × C**8**-H_2), 1.71 – 1.65 (1H, m, 1 × C**9**-H), 1.47 (1H, td, *J* = 13.6, 4.7 Hz, 1 × C**7**-H_2), 1.43 – 1.33 (1H, m, 1 × C**2**-H), 1.33 – 1.18 (2H, m, 1 × C**3**-H_2, 1 × C**8**-H_2); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 143.2 (C**14**), 134.7 (C**11**), 129.7 (C**13**), 127.2 (C**12**), 108.8 (C**4**), 64.4, 66.3(C**5**, C**6**), 52.3, 52.2 (C**1**, C**10**), 43.5 (C**2**), 42.2 (C**9**), 37.4 (C**8**), 34.3 (C**7**), 24.8 (C**3**), 21.5 (C**15**); *m/z* (ESI^+) HRMS: Calculated for $C_{17}H_{24}NO_4S$: 338.1421. Found $[M+H]^+$: 338.1425.

(3a*R, 7a*R**)-Octahydrospiro[isoindole-5,2'-[1,3]dioxolane] (18e)**

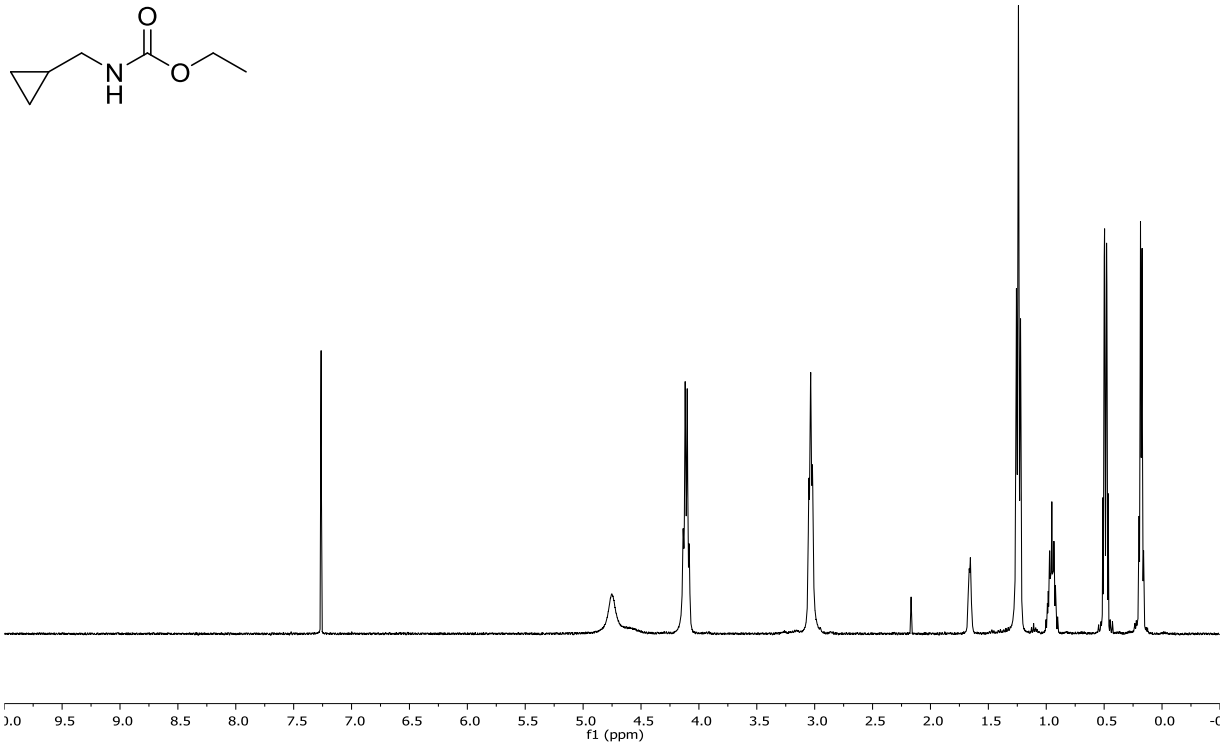


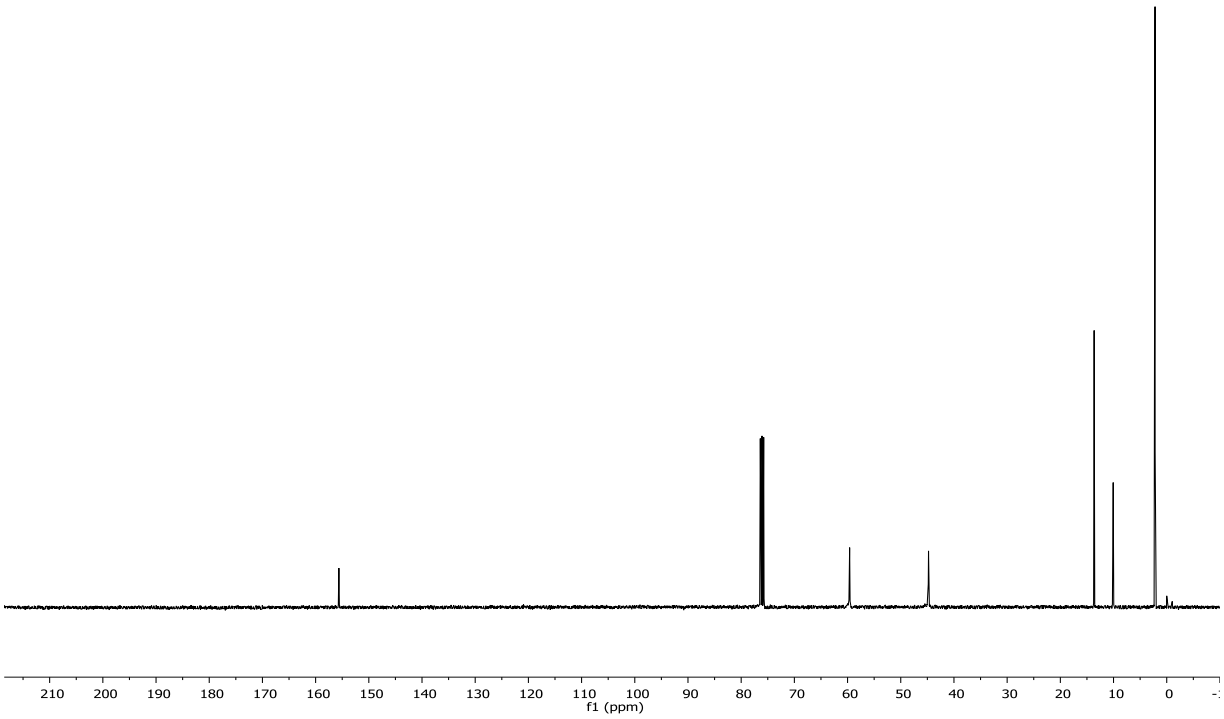
17e **18e**

Mg turnings (96.0 mg, 4.0 mmol) was added to a solution of **17e** (134.8 mg, 0.40 mmol) in dry MeOH (4 mL), and the mixture was refluxed for 24 hours. The suspension was cooled to r.t. and then was filtered through a short plug of silica, washed with MeOH, and concentrated *in vacuo*, The residue was purified by flash column chromatography (from 10 % MeOH/DCM to MeOH/DCM/NH_4OH = 8:1:0.1) to afford the title compound **18e** (67.9 mg, 93 %) as a red oil; ν_{max} / cm^{-1}: 3411 (s), 2928 (s), 2717 (m), 1361 (m), 1144 (s), 1069 (s), 948 (m); ^1H NMR ($CDCl_3$, 500 MHz): δ 4.05 – 3.75 (4H, m, 2 × C**5**-$\underline{H}_2$, 2 × C**6**-$\underline{H}_2$), 3.36 (1H, s, *br*. NH), 3.03 (2H, dd, *J* = 9.8, 7.0 Hz, 1 × C**1**-$\underline{H}_2$, 1 × C**10**-$\underline{H}_2$), 2.46 (2H, dd, *J* = 10.4, 10.4 Hz, 1 × C**1**-$\underline{H}_2$, 1 × C**10**-$\underline{H}_2$), 1.92 – 1.85 (1H, m, 1 × C**8**-$\underline{H}_2$), 1.84 – 1.73 (2H, m, 1 × C**3**-$\underline{H}_2$, 1 × C**7**-$\underline{H}_2$), 1.73 – 1.66 (1H, m, 1 × C**9**-$\underline{H}$), 1.52 (1H, td, *J* = 13.2, 4.4 Hz, 1 × C**7**-$\underline{H}_2$), 1.44 – 1.36 (1H, m, 1 × C**2**-$\underline{H}$), 1.35 – 1.23 (2H, m, 1 × C**3**-$\underline{H}_2$, 1 × C**8**-$\underline{H}_2$); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 109.6 (C**4**), 64.4, 64.3 (C**5**, C**6**), 50.5, 50.3 (C**1**, C**10**), 45.0 (C**2**), 43.7 (C**9**), 38.0 (C**8**), 34.9 (C**7**), 25.4 (C**3**); *m/z* (ESI^+) HRMS: Calculated for $C_{10}H_{17}NO_2$: 184.1332. Found $[M+H]^+$: 184.1333.

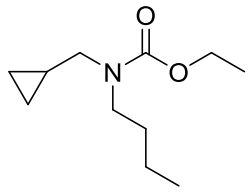
Copies of ^{1}H and ^{13}C NMR for Novel Compounds

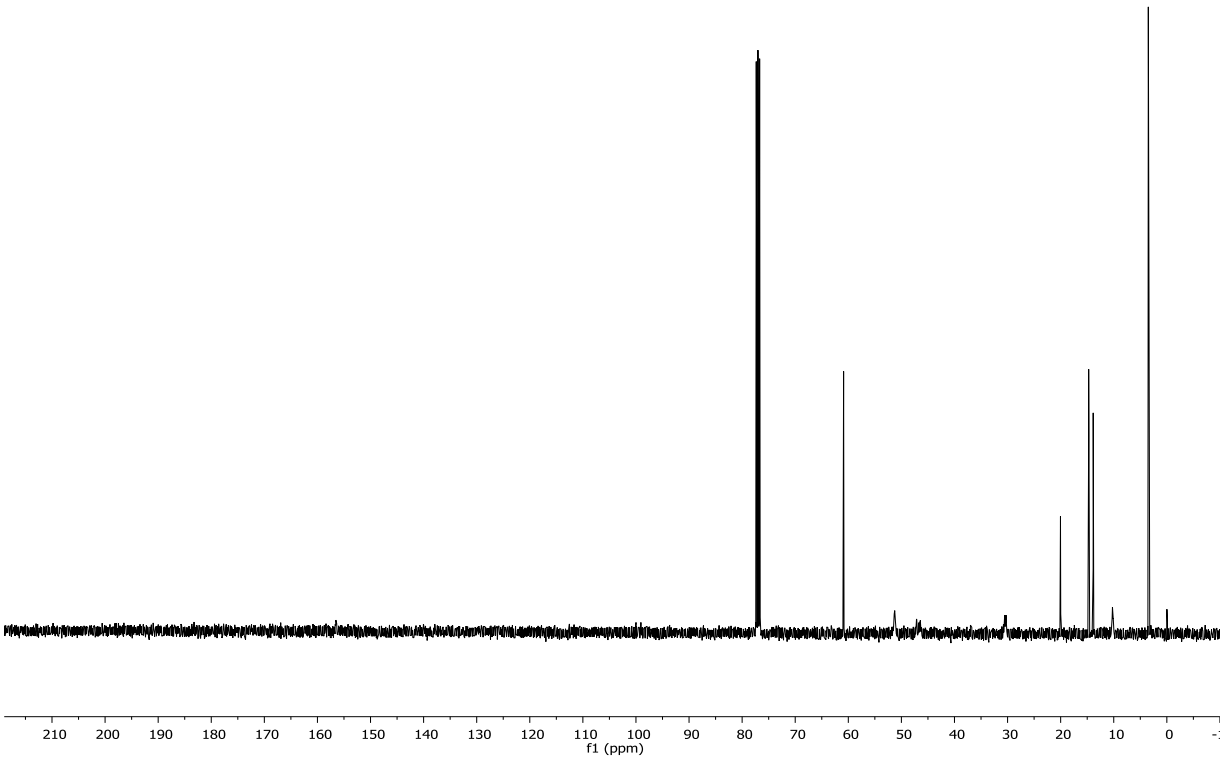
Ethyl (cyclopropylmethyl)carbamate



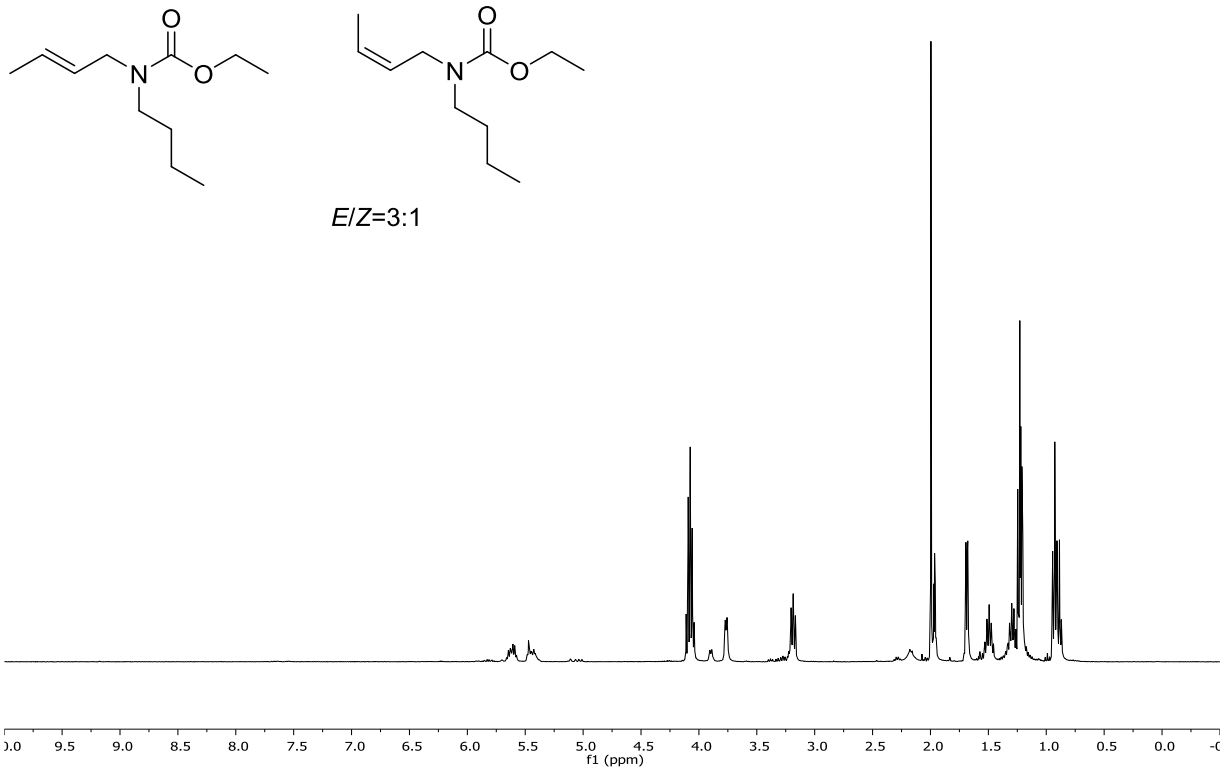


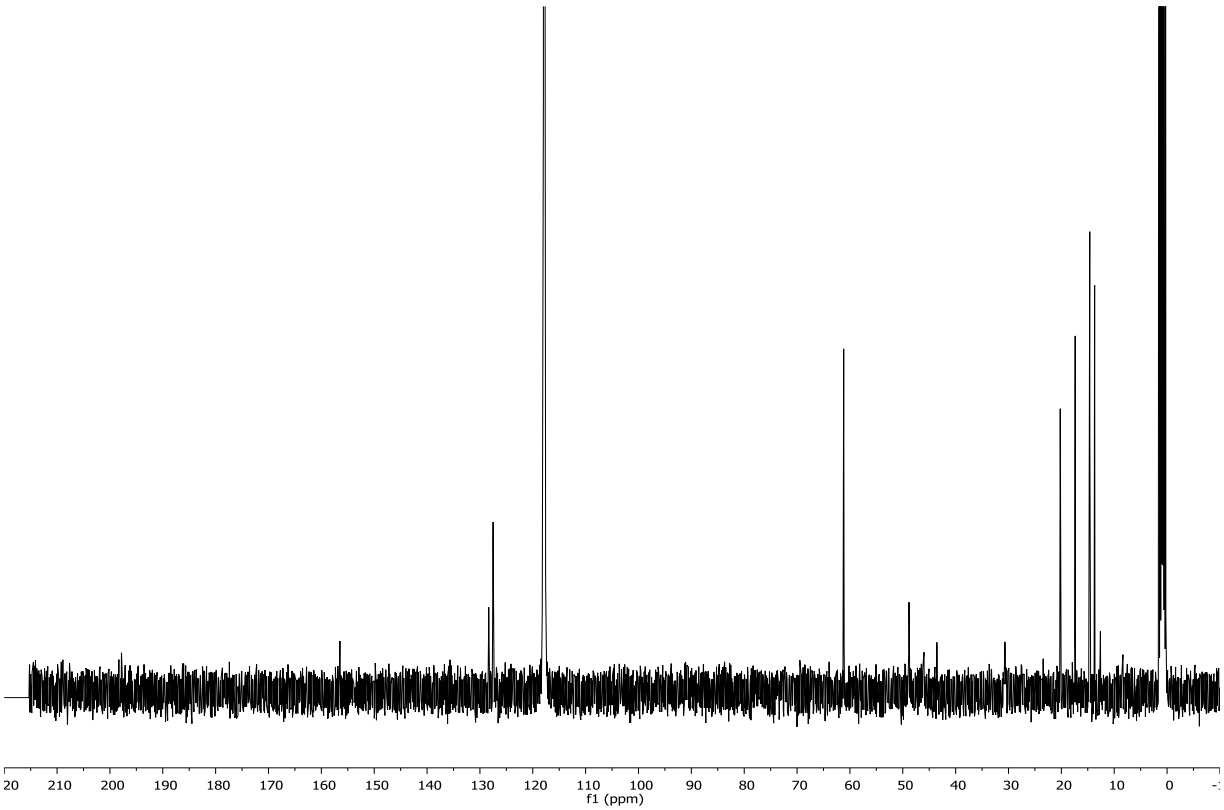
Ethyl butyl(cyclopropylmethyl)carbamate (4a)



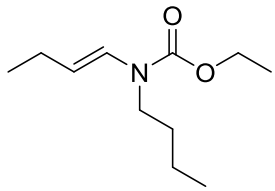


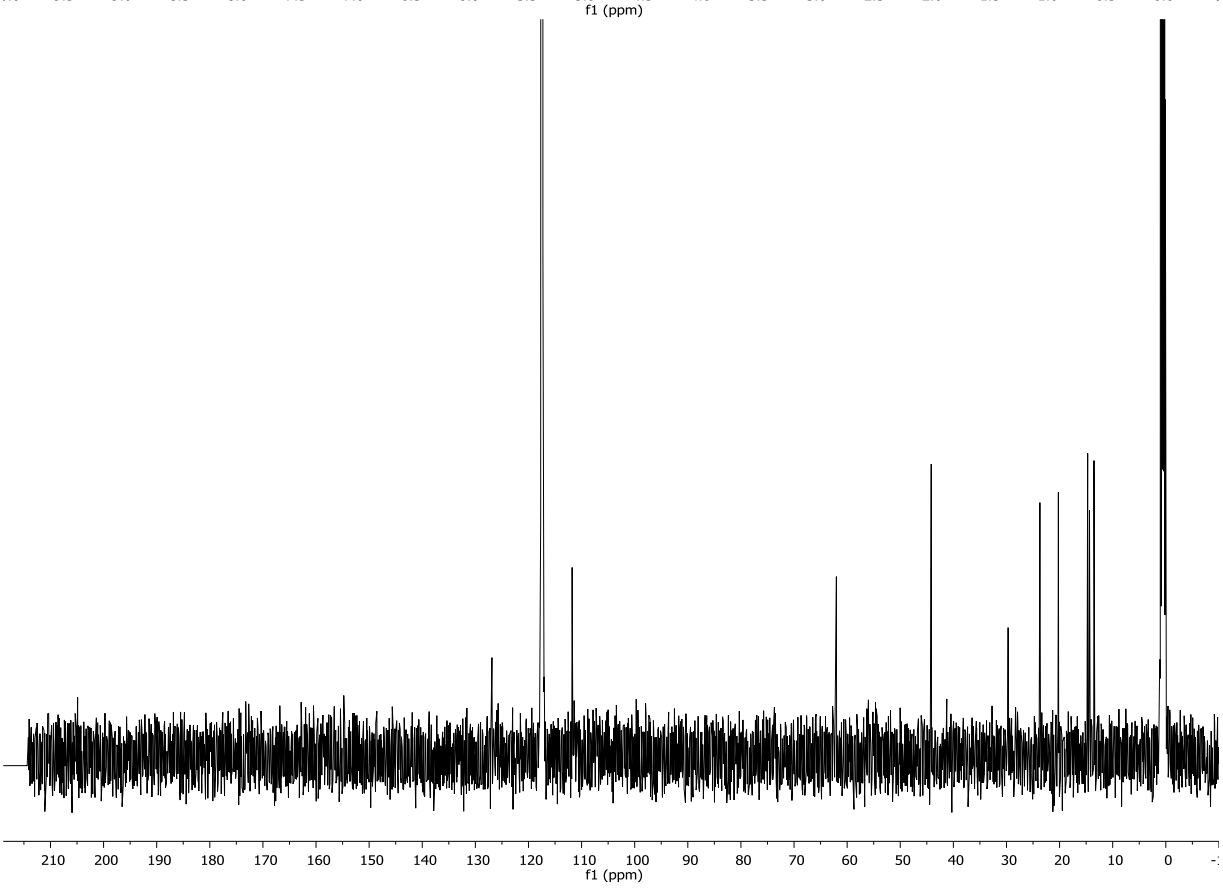
(*E*)-Ethyl but-2-en-1-yl(butyl)carbamate and (*Z*)-Ethyl but-2-en-1-yl(butyl)carbamate (10a-A)



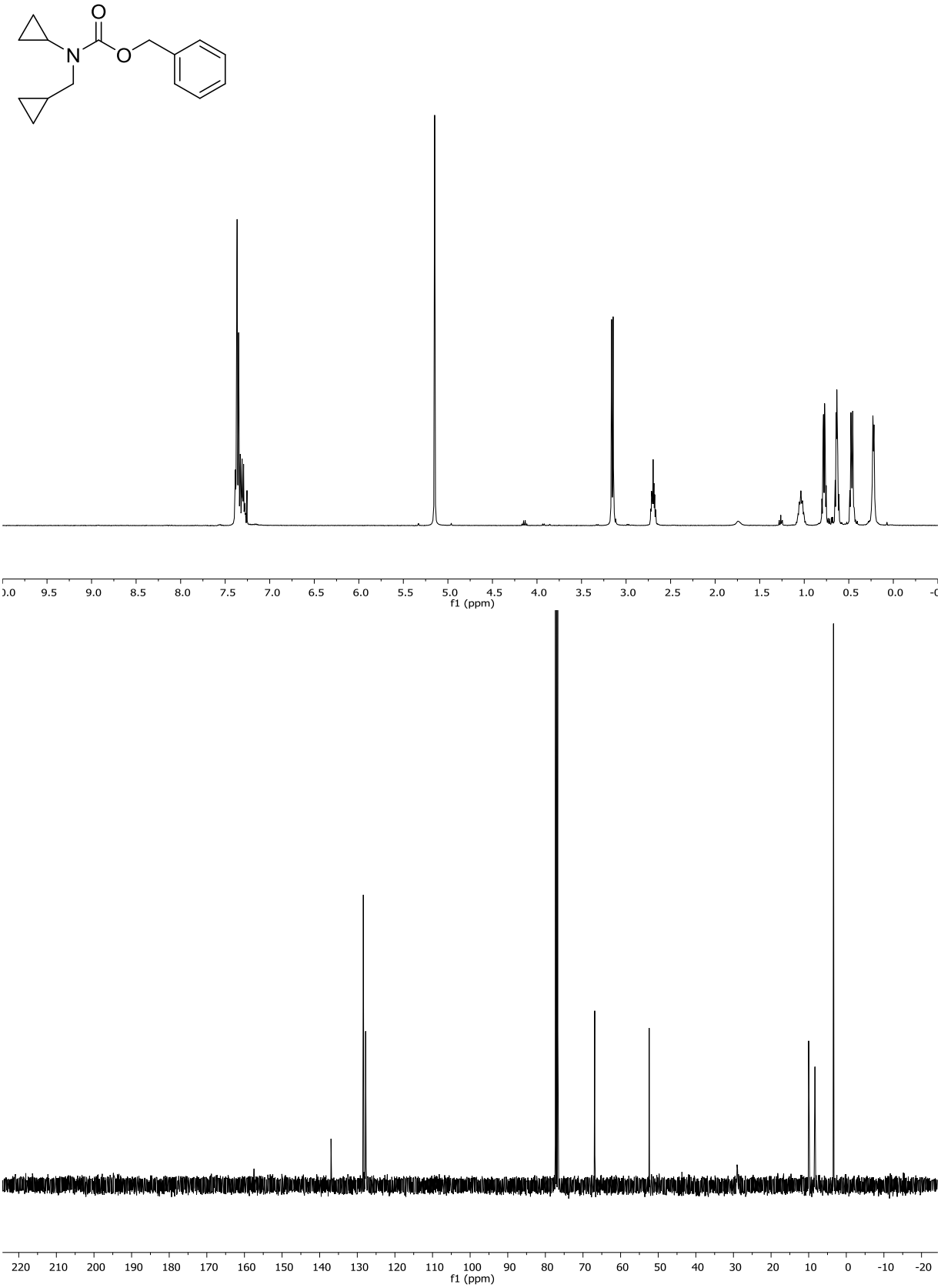


Ethyl (*E*)-but-1-en-1-yl(butyl)carbamate (10a-B)

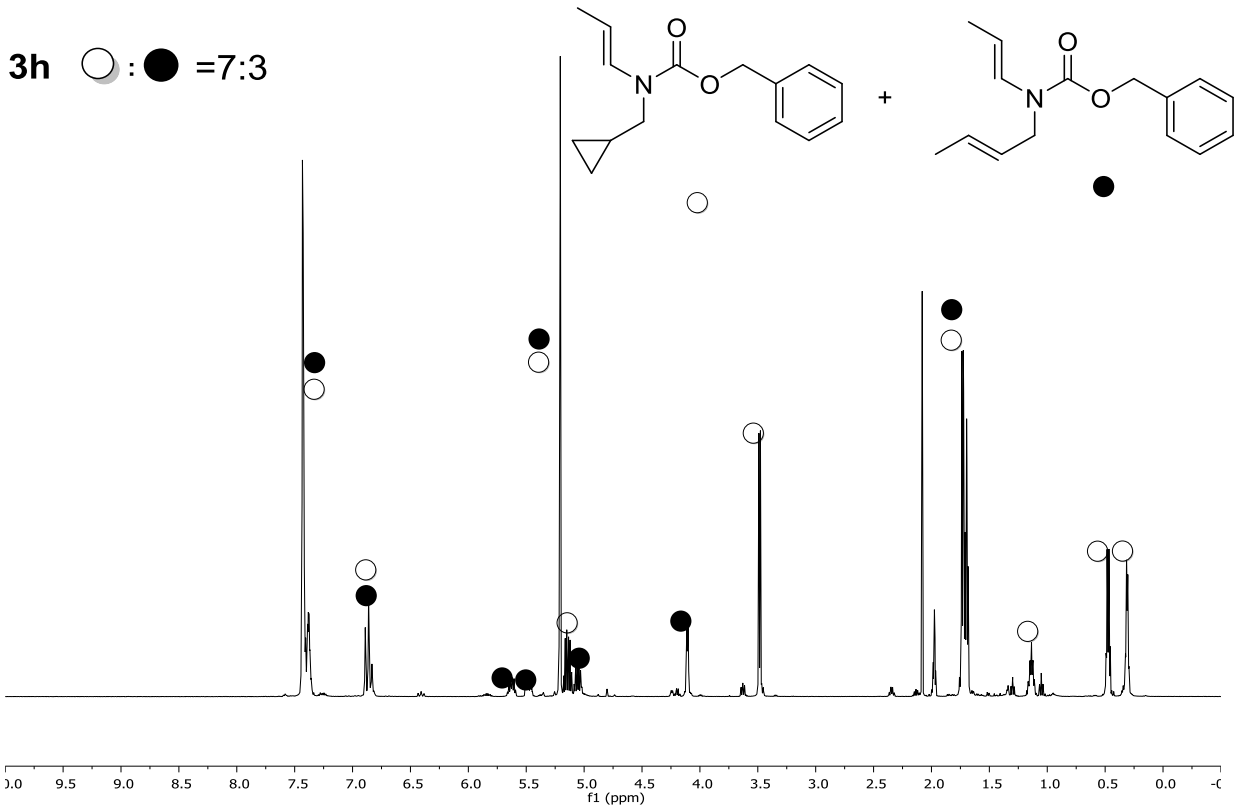




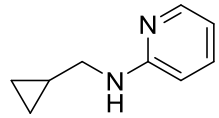
Benzyl cyclopropyl(cyclopropylmethyl)carbamate (4b)

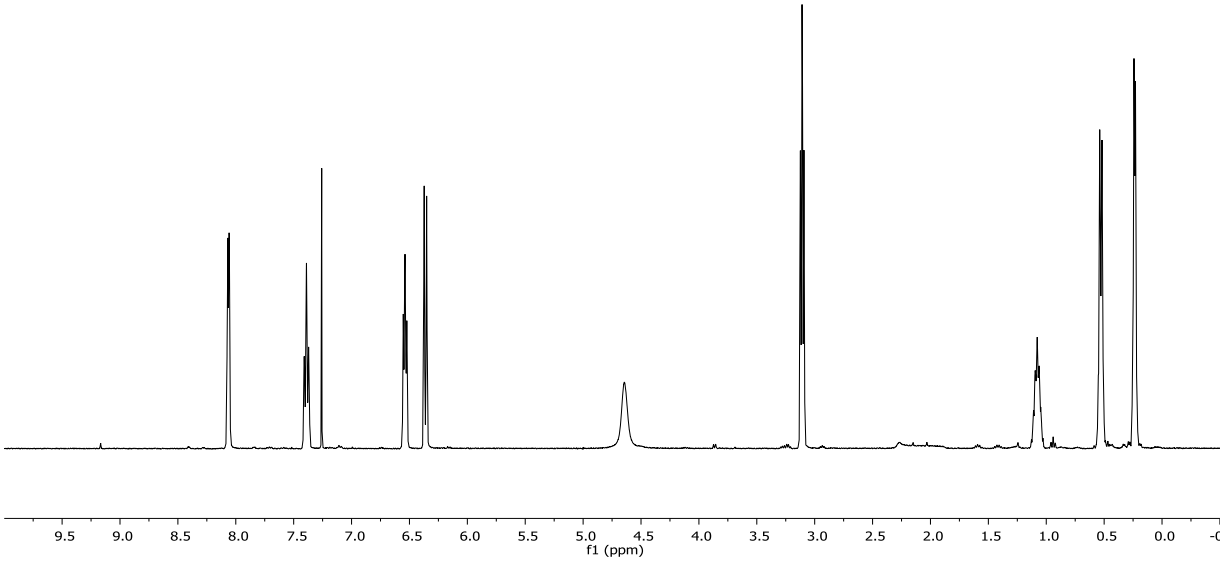


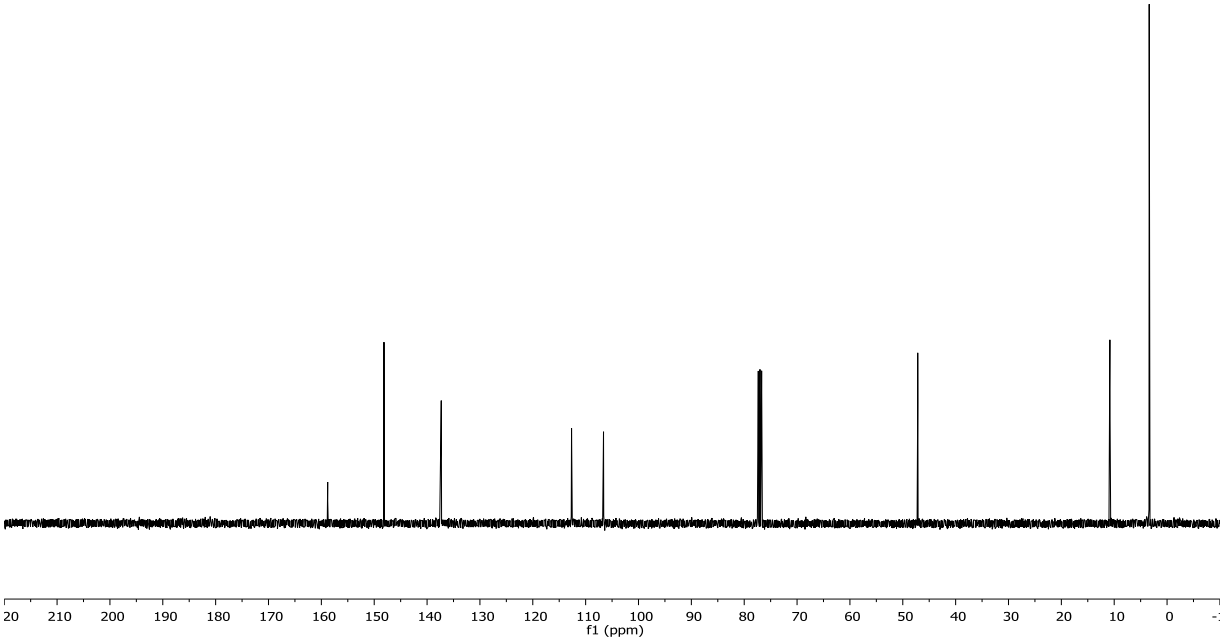
Benzyl (*E*)-(cyclopropylmethyl) (prop-1-en-1-yl)carbamate (11a) and Benzyl ((*E*)-but-2-en-1-yl)((*E*)-prop-1-en-1-yl)carbamate (11b)



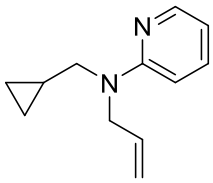
N-(Cyclopropylmethyl)pyridin-2-amine

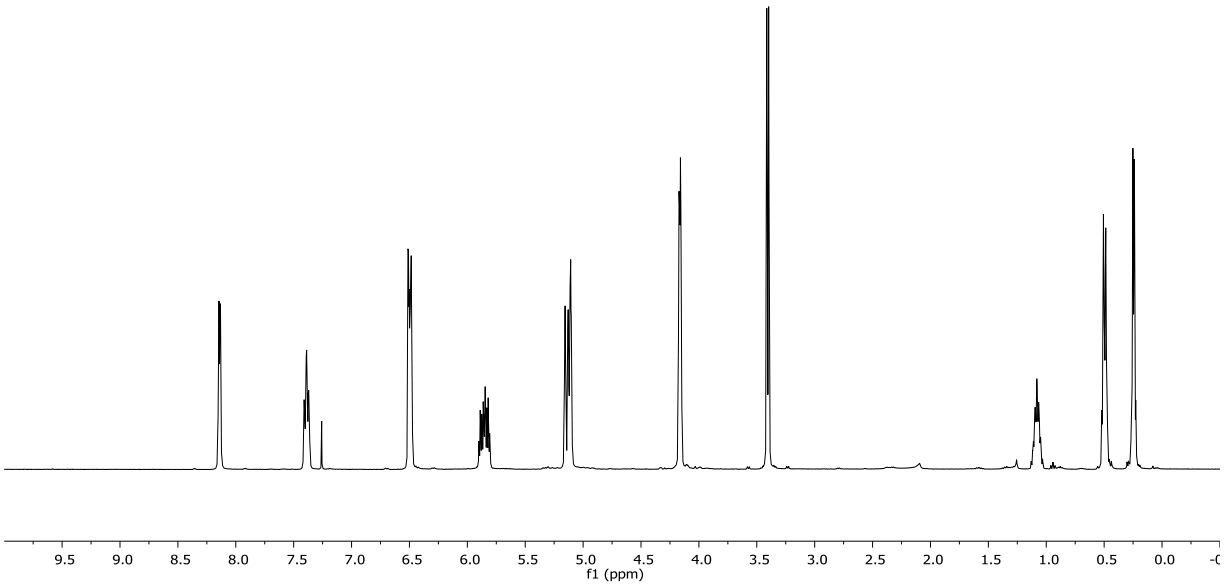


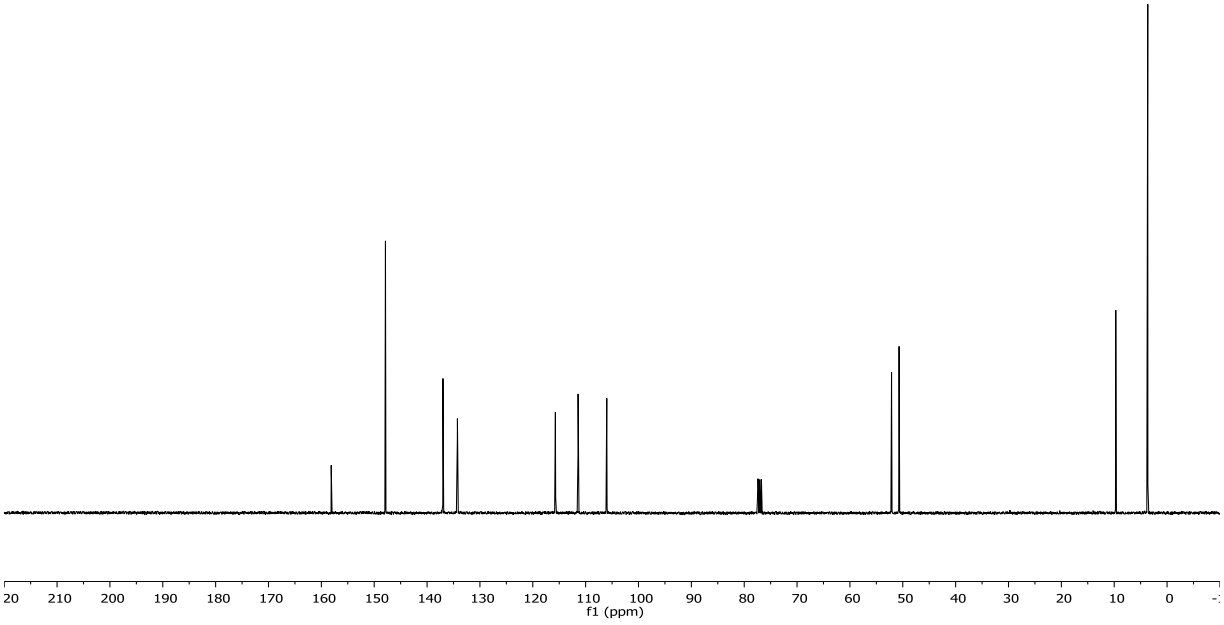




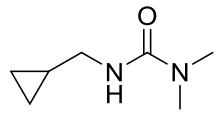
N-Allyl-*N*-(cyclopropylmethyl)pyridin-2-amine (6a)

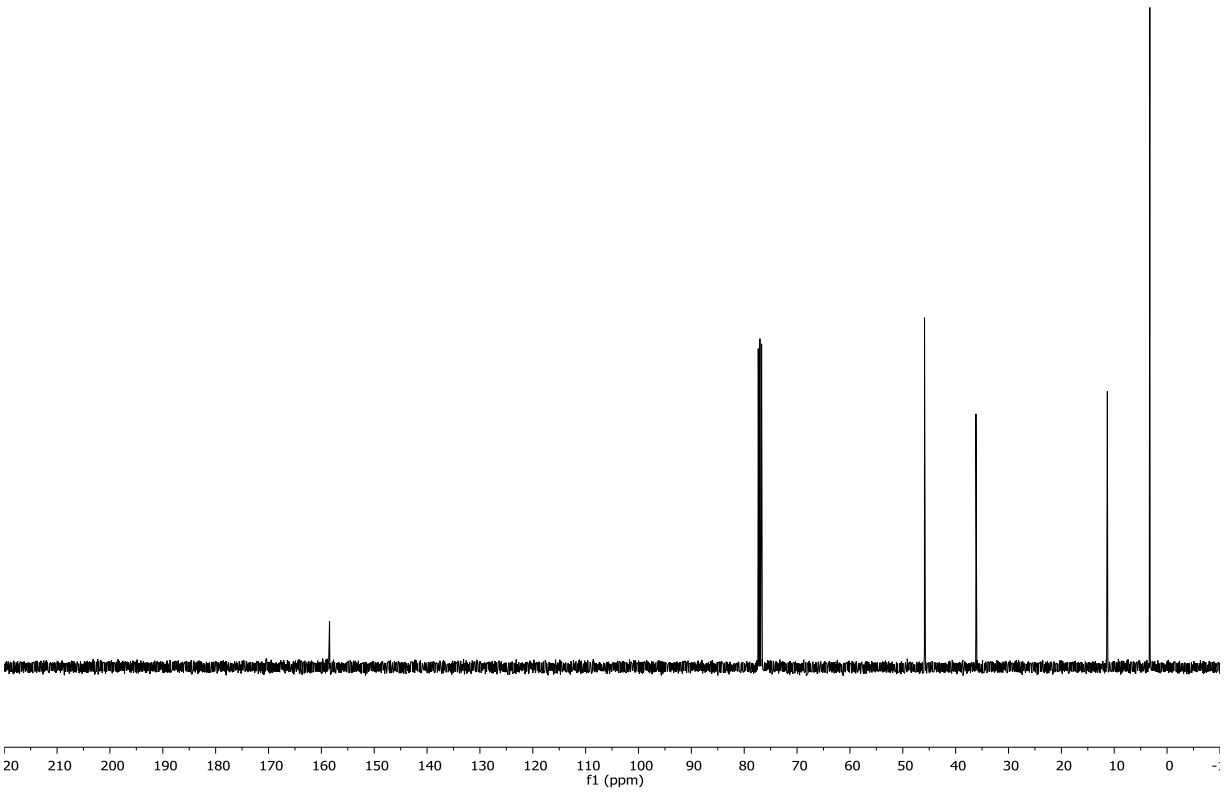




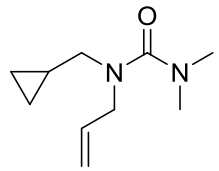


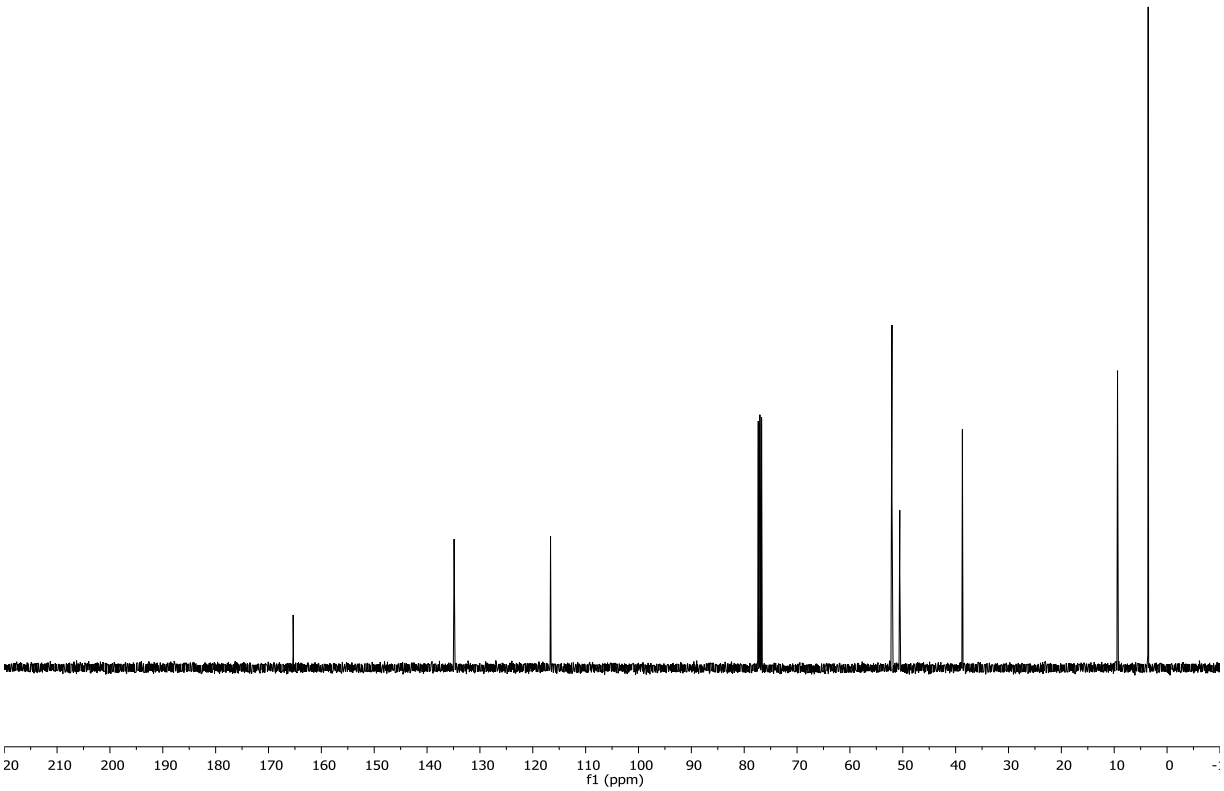
3-(Cyclopropylmethyl)-1,1-dimethylurea



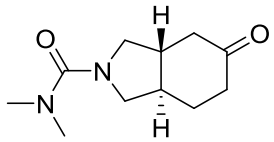


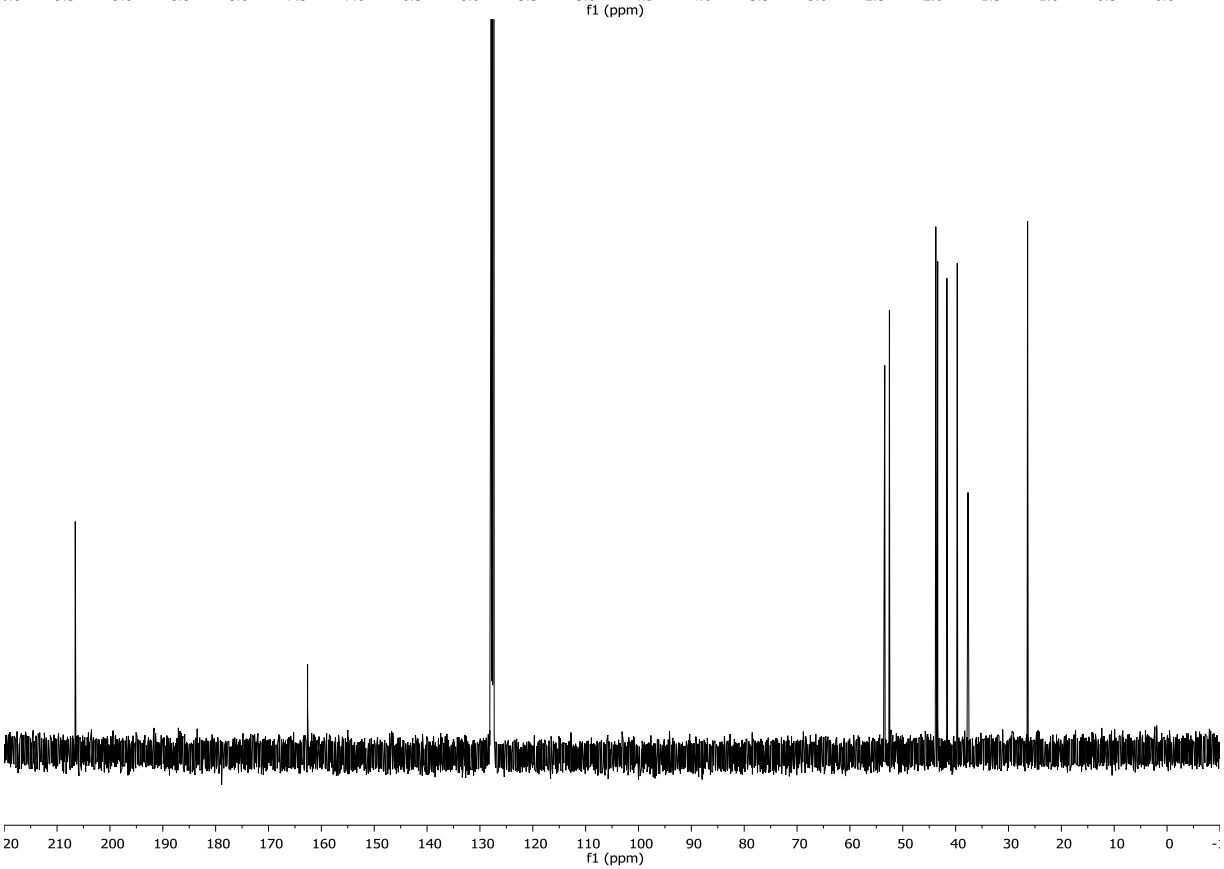
1-Allyl-1-(cyclopropylmethyl)-3,3-dimethylurea (6b)



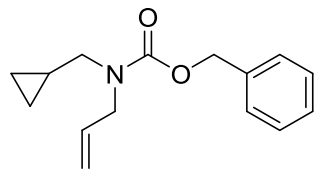


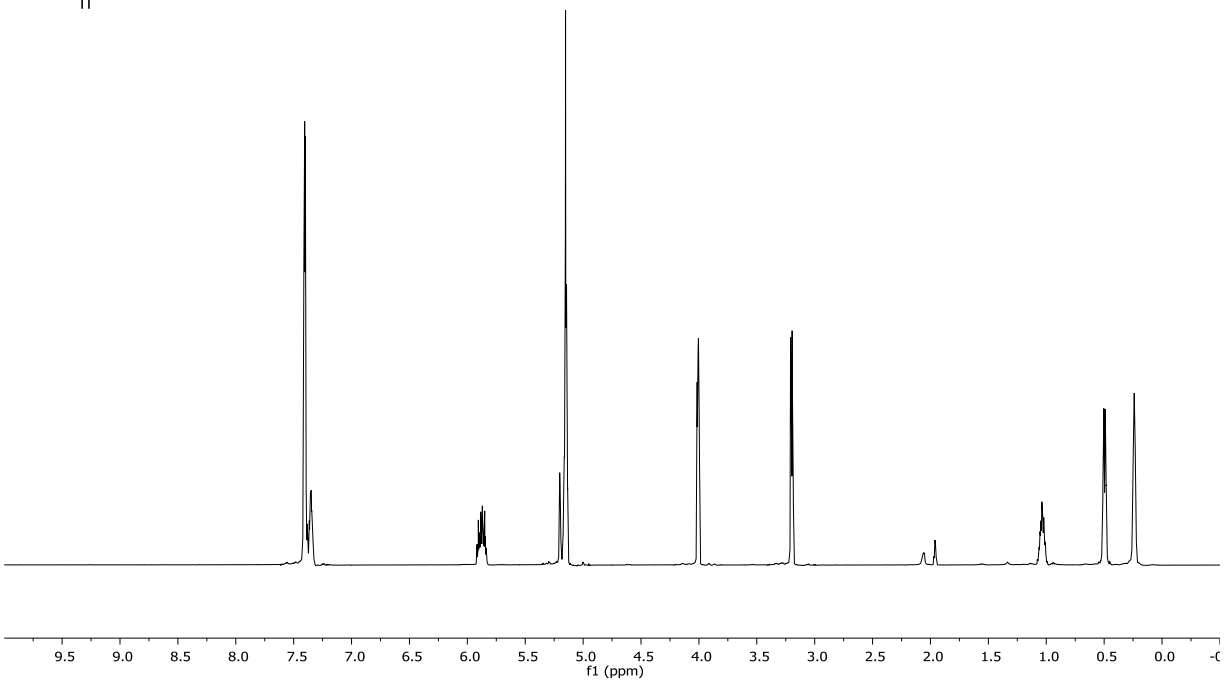
(3a*R, 7a*R**)-*N*,*N*-Dimethyl-5-oxooctahydro-2*H*-isoindole-2-carboxamide (8b)**

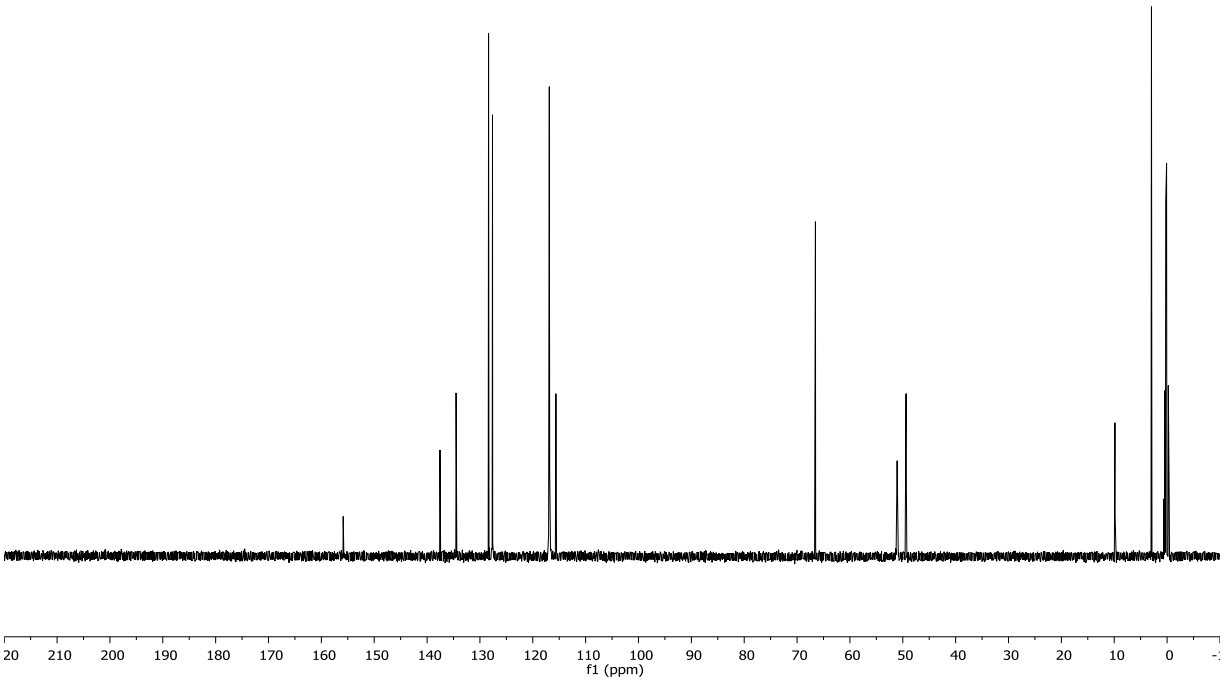




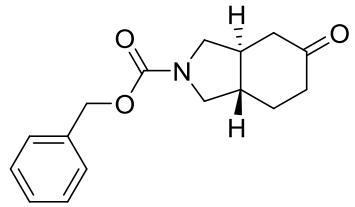
Benzylallyl(cyclopropylmethyl)carbamate (6c)

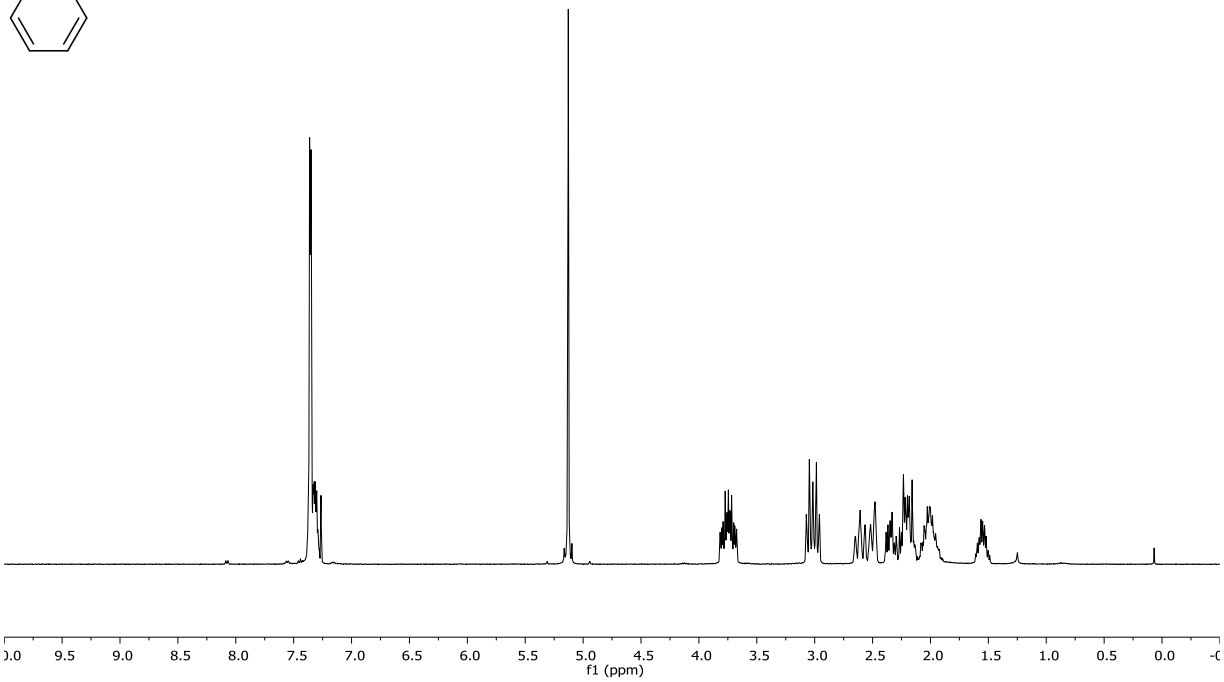


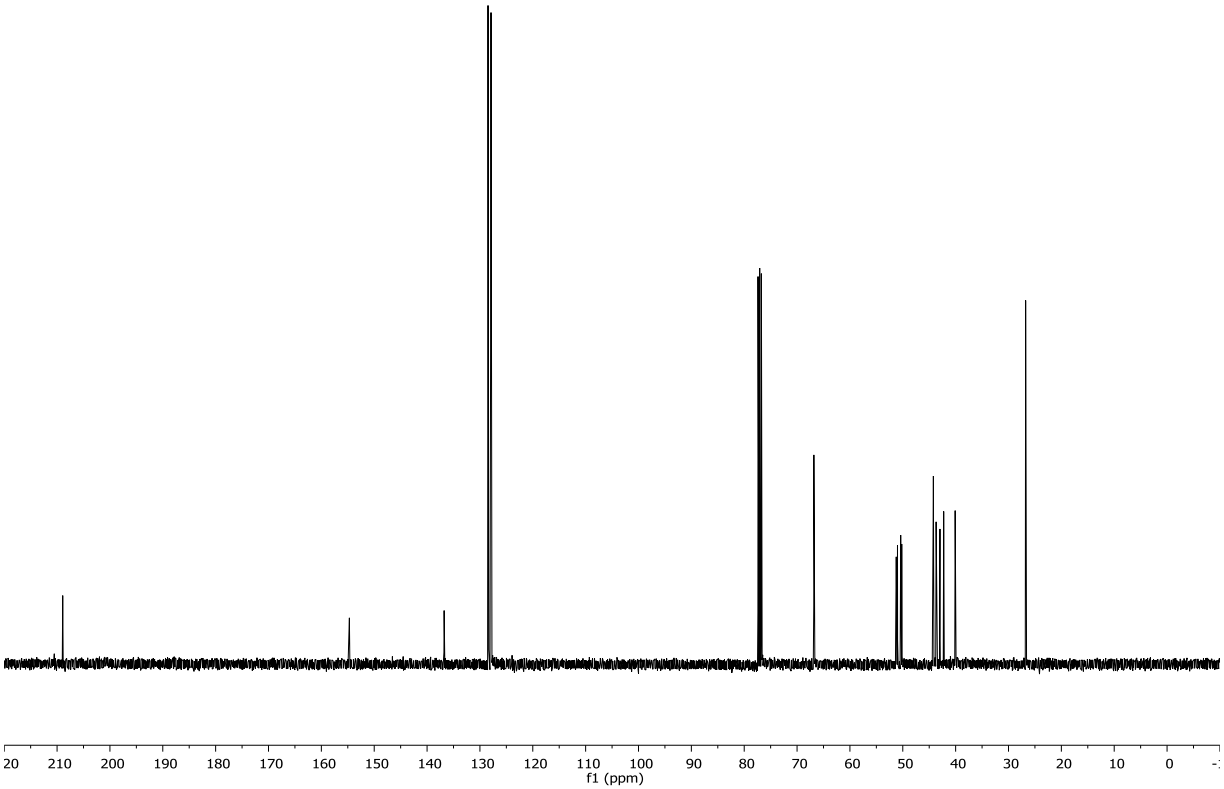




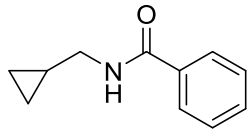
(3*aR, 7*aR**)-Benzyl 5-oxohexahydro-1*H*-isoindole-2(3*H*)-carboxylate (8c)**

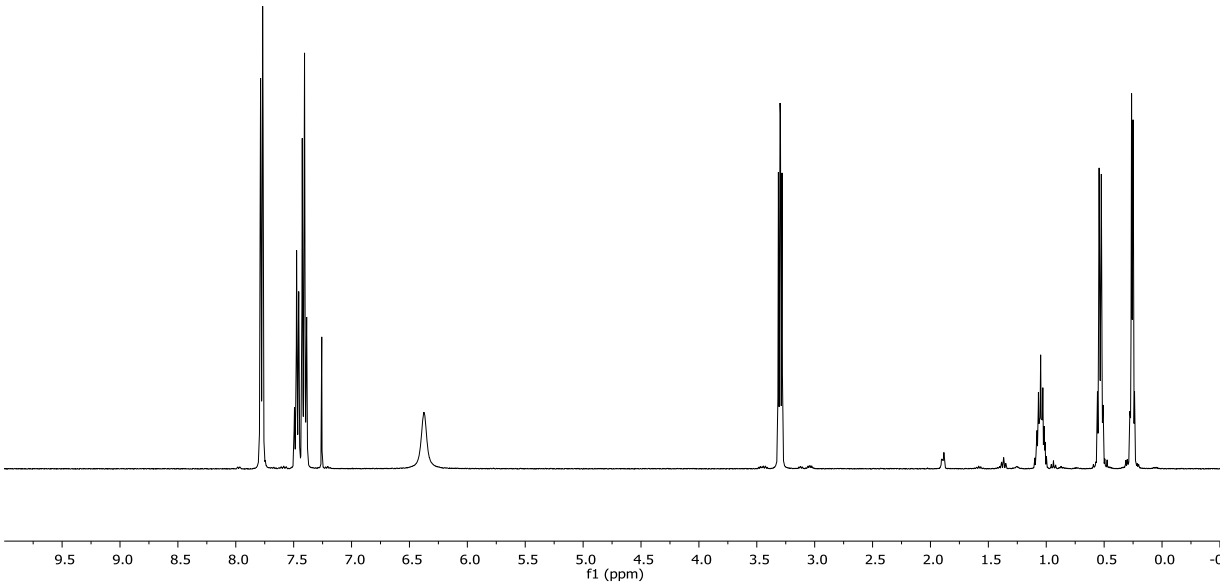


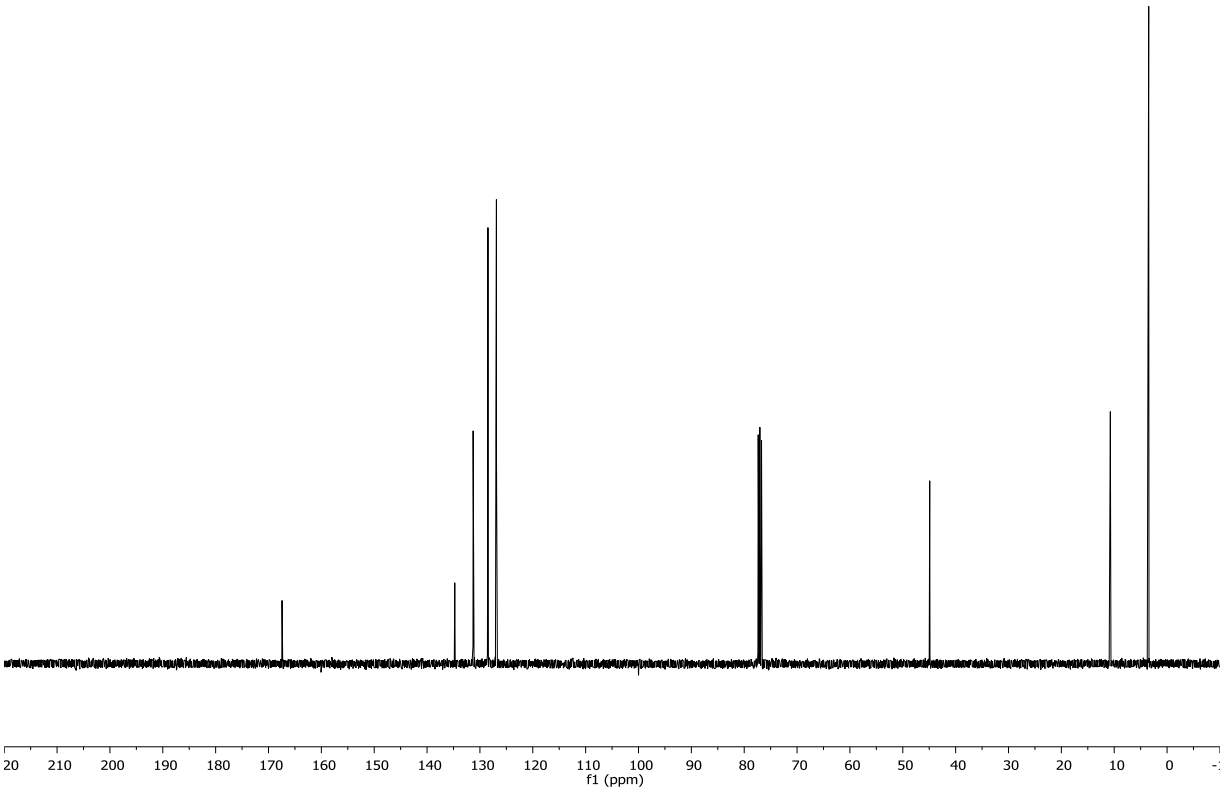




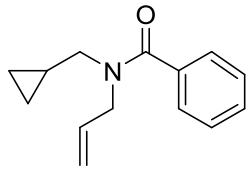
N-(Cyclopropylmethyl)benzamide

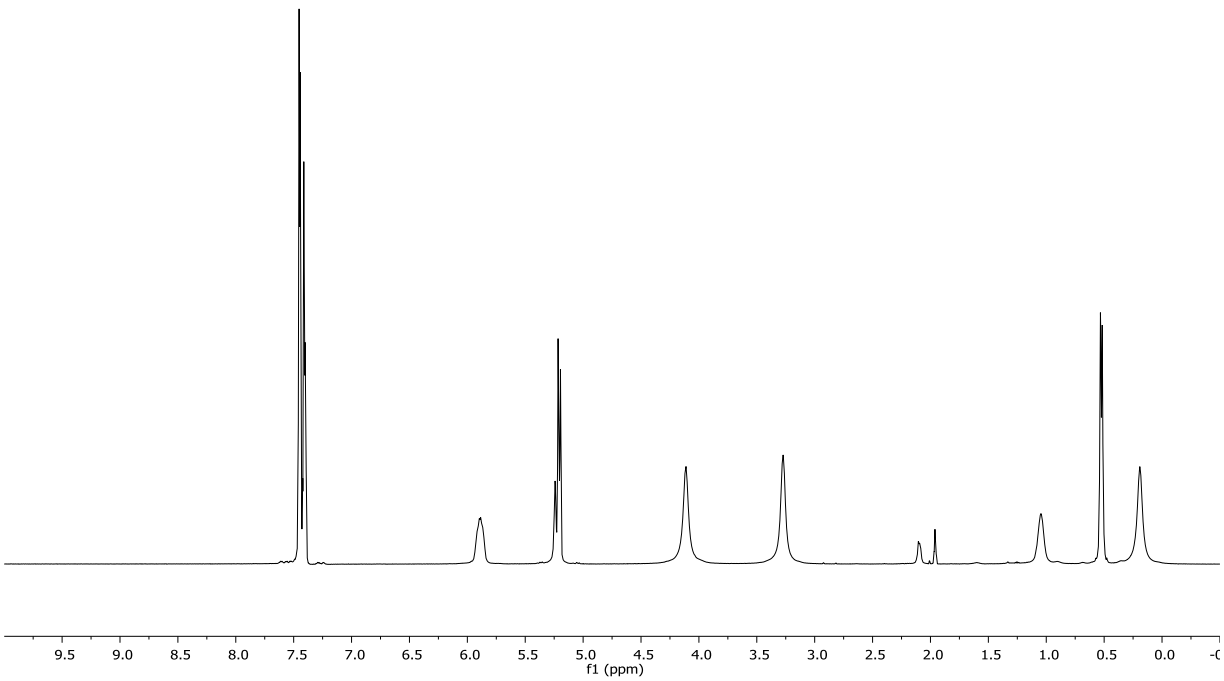


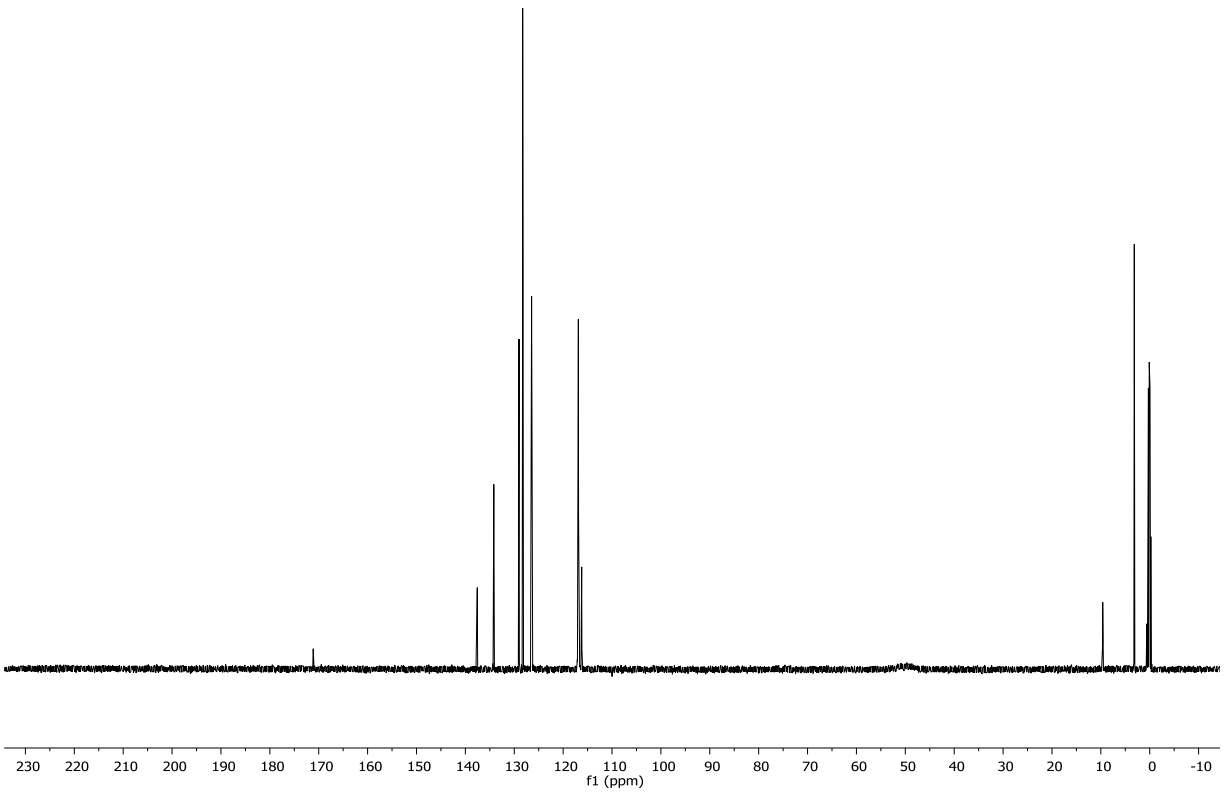




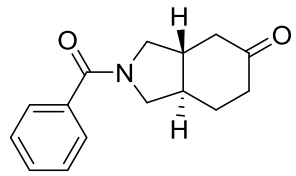
N-Allyl-*N*-(cyclopropylmethyl)benzamide (6d)

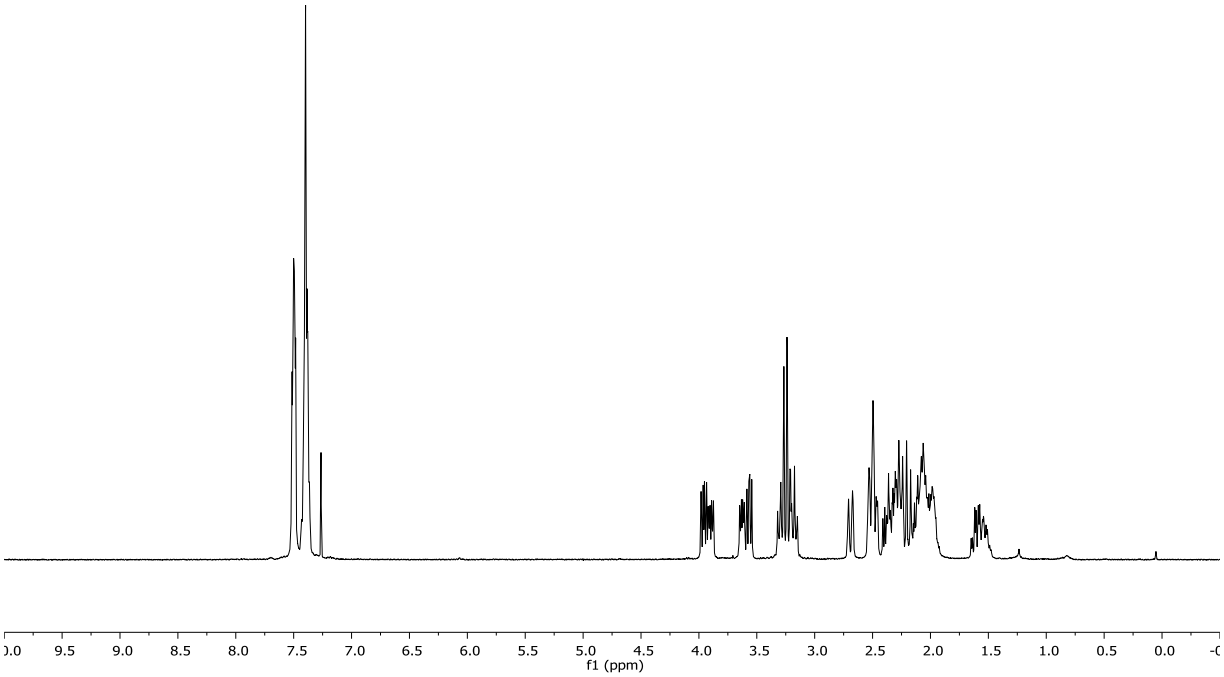


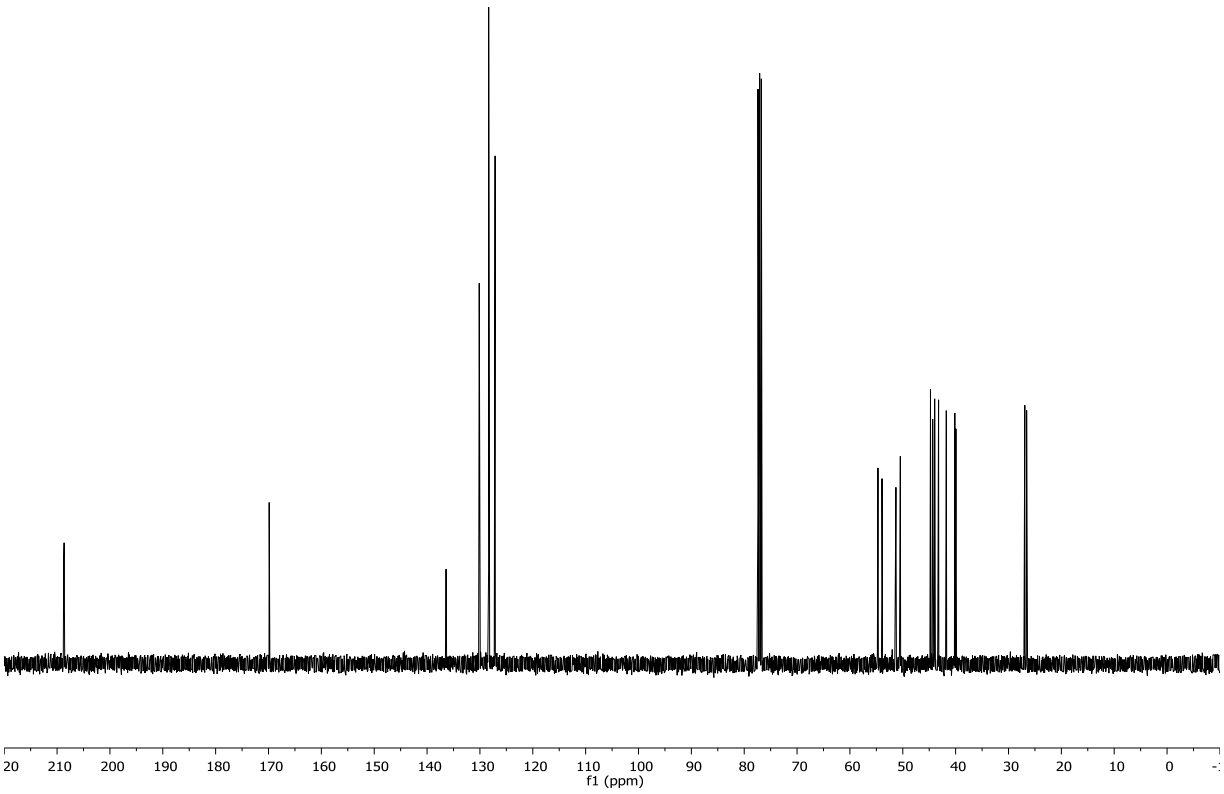




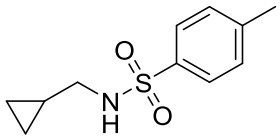
(3a*R, 7a*R**)-2-Benzoyloctahydro-5*H*-isoindol-5-one (8d)**

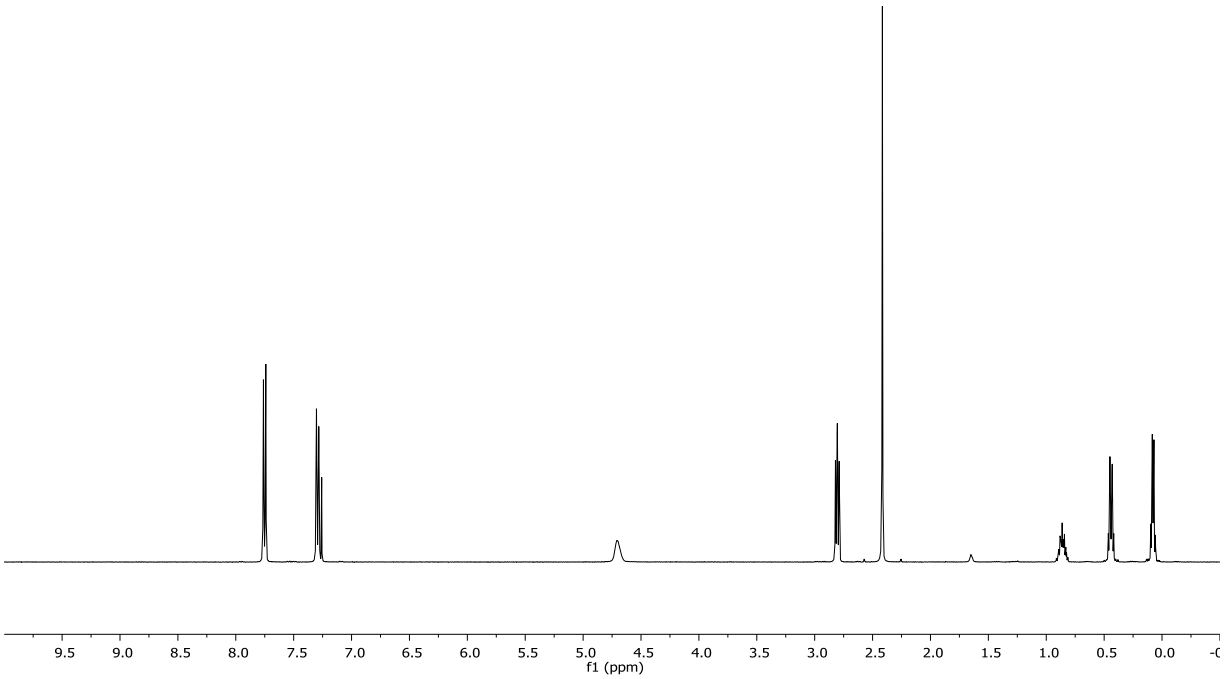


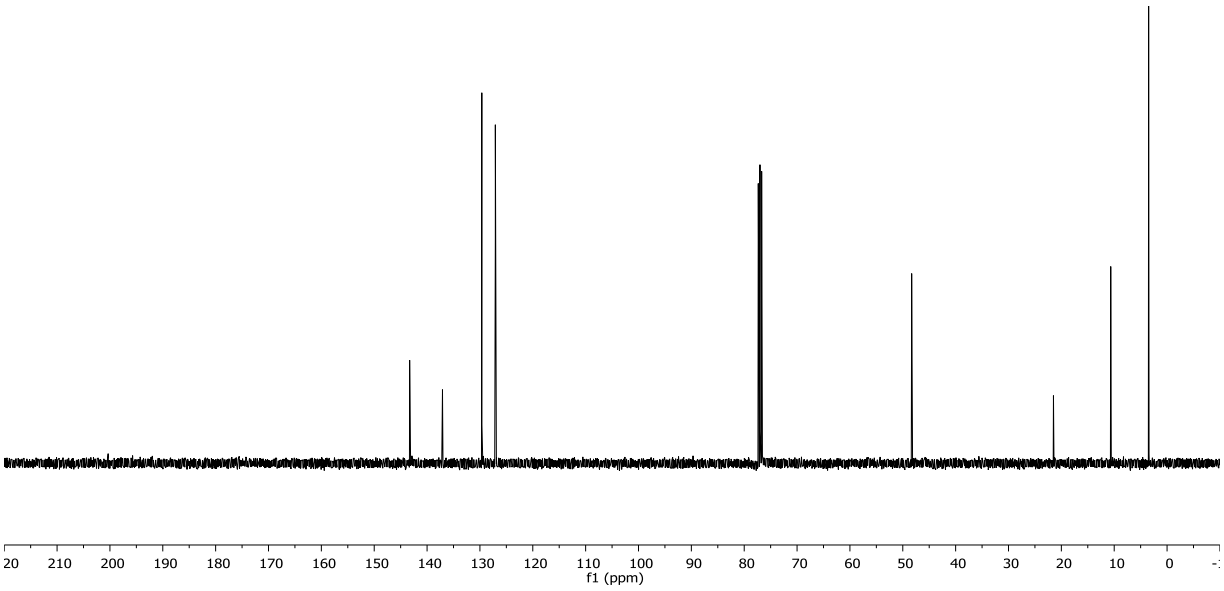




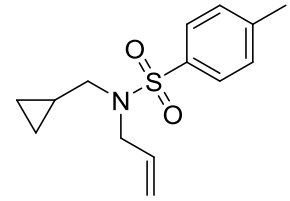
N-(Cyclopropylmethyl)-4-methylbenzenesulfonamide

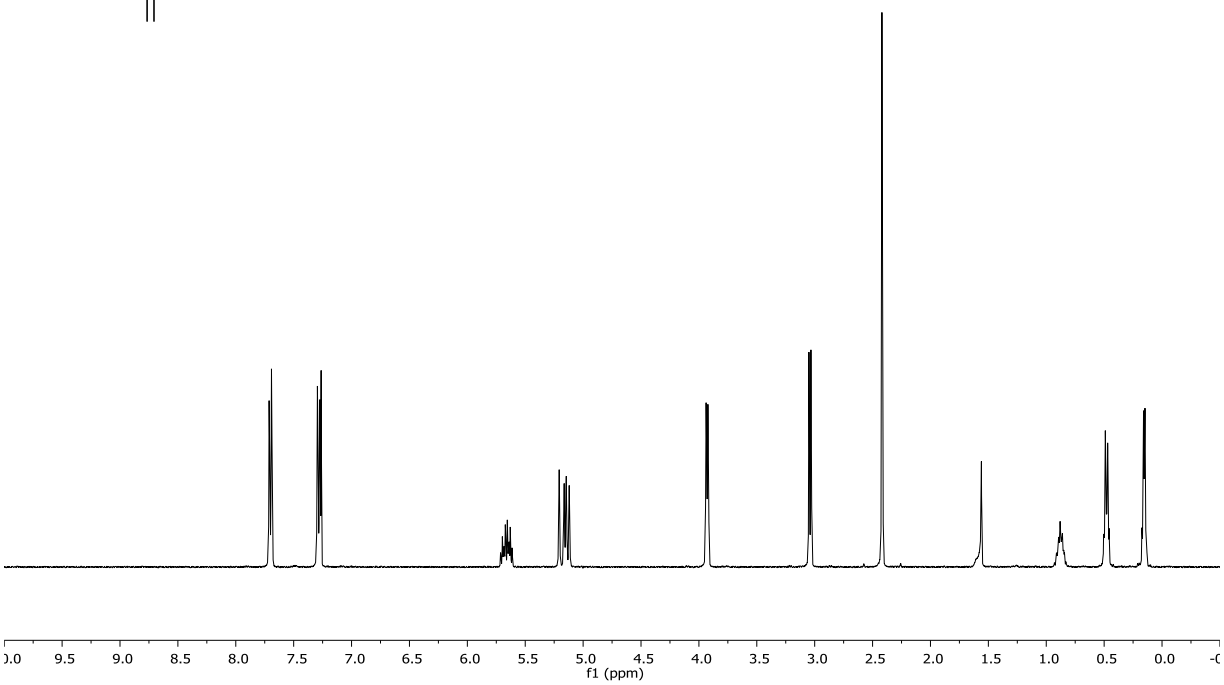


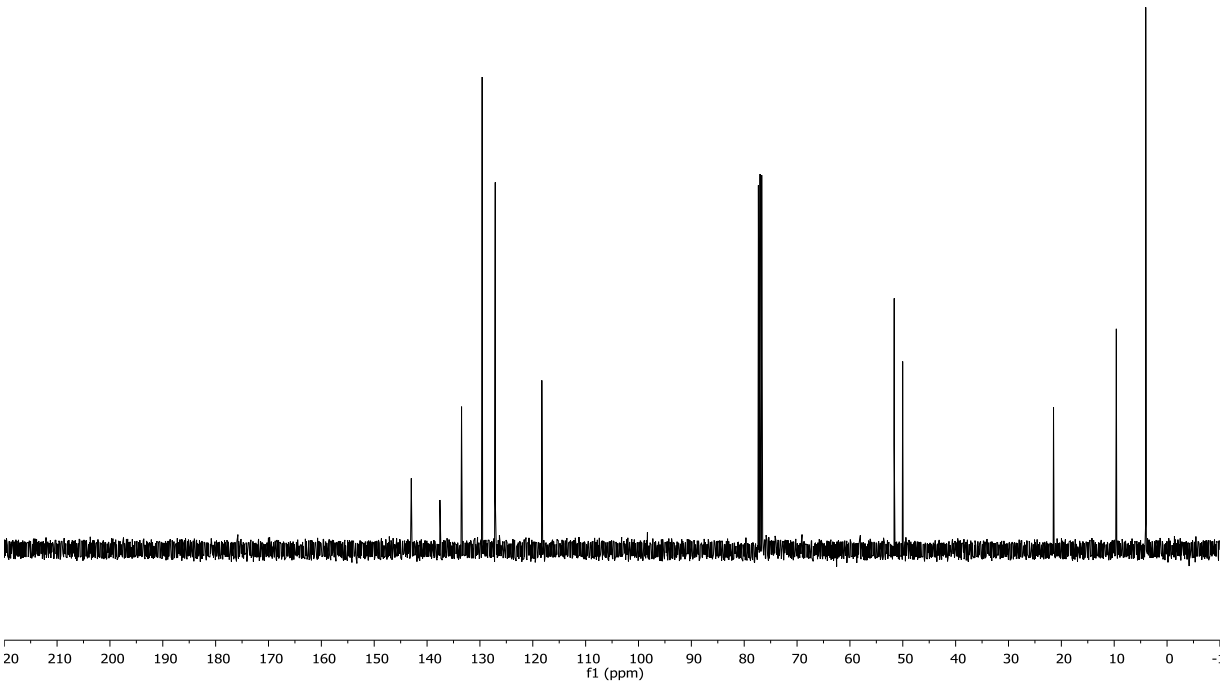




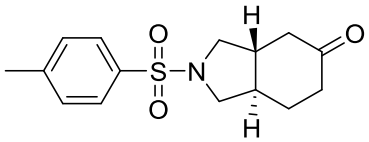
N-Allyl-*N*-(cyclopropylmethyl)-4-methylbenzenesulfonamide (6e)

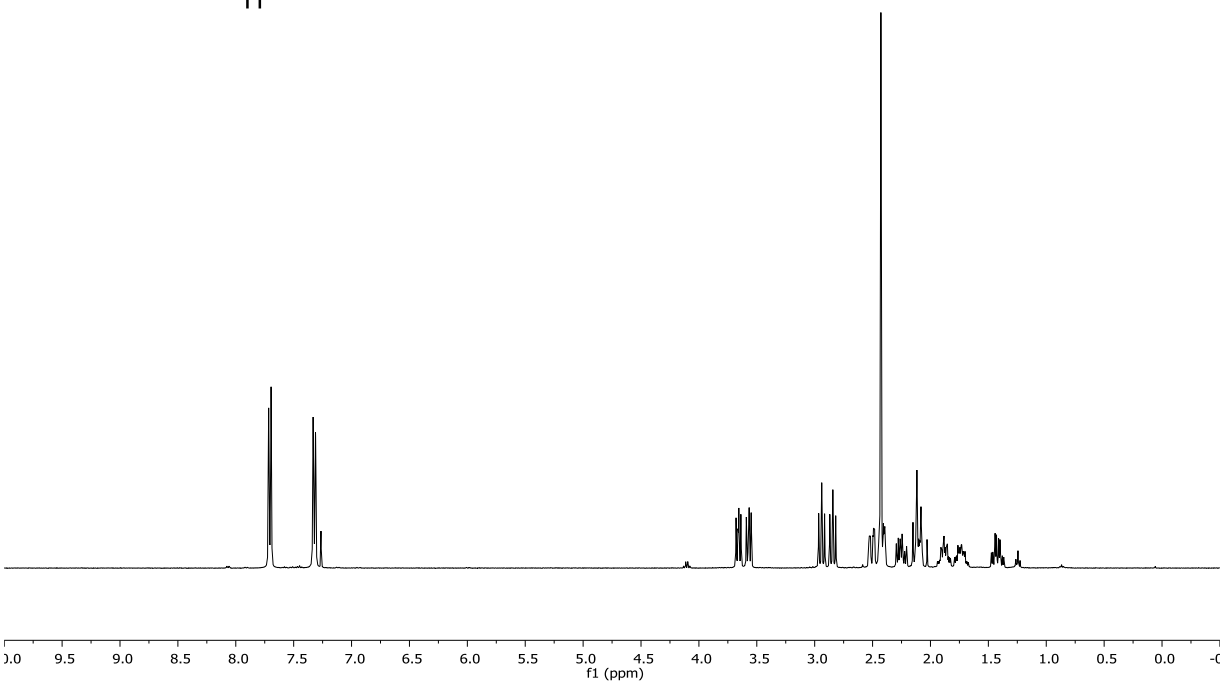


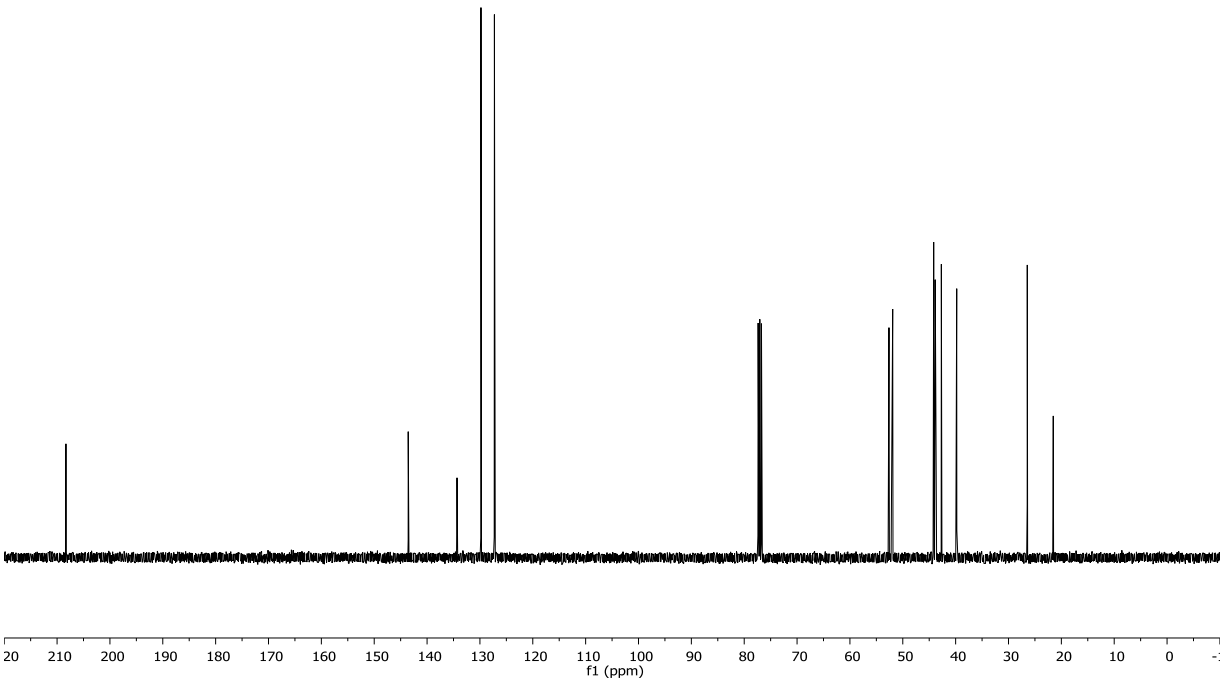




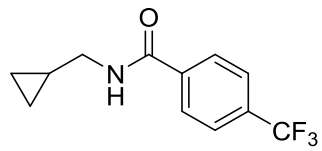
(3a*R, 7a*R**)-2-Tosylhexahydro-1*H*-isoindol-5(6*H*)-one (8e)**

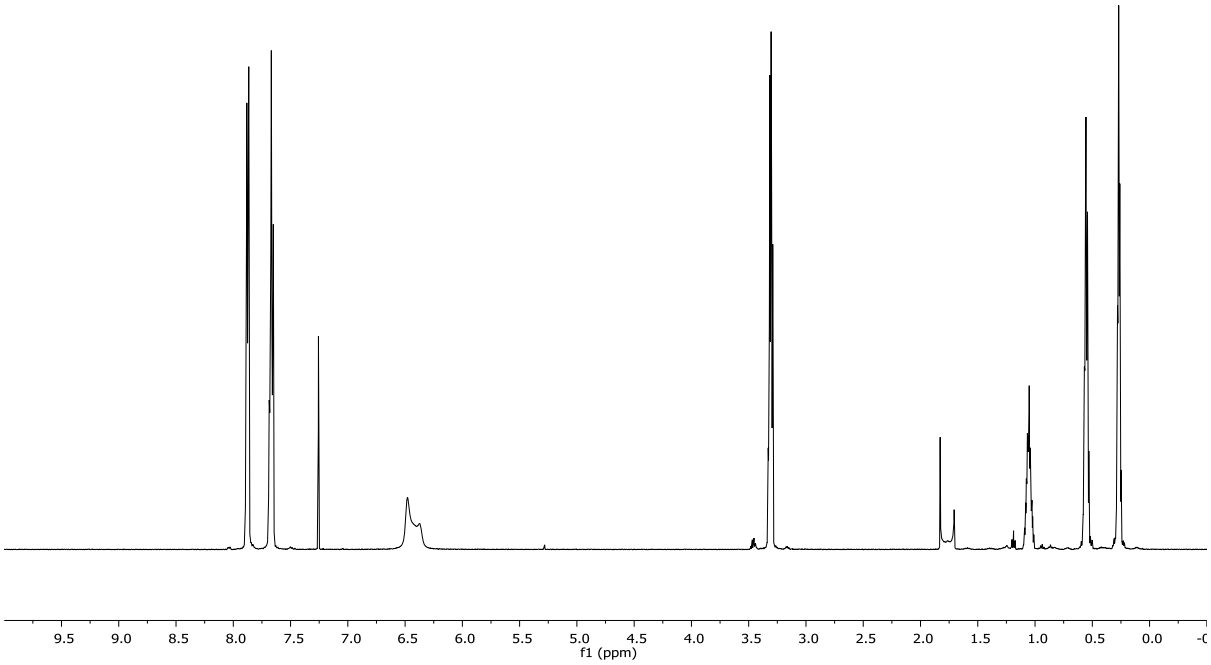


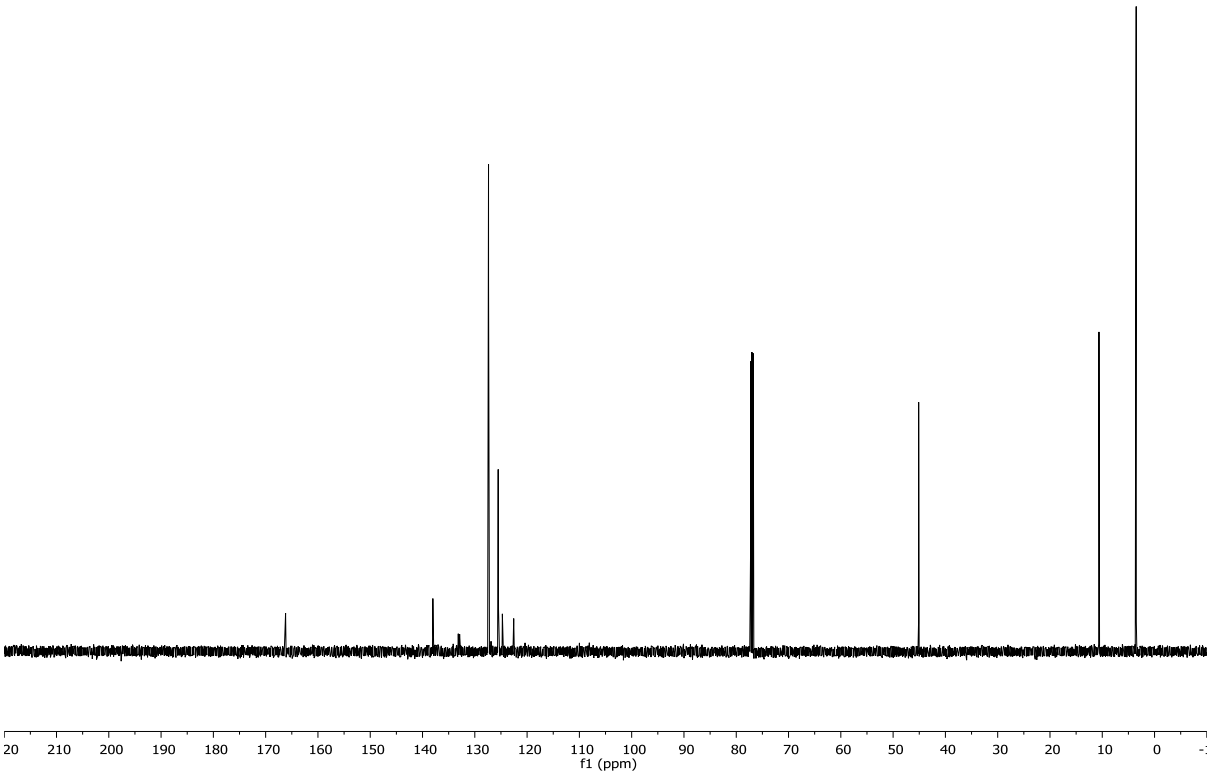


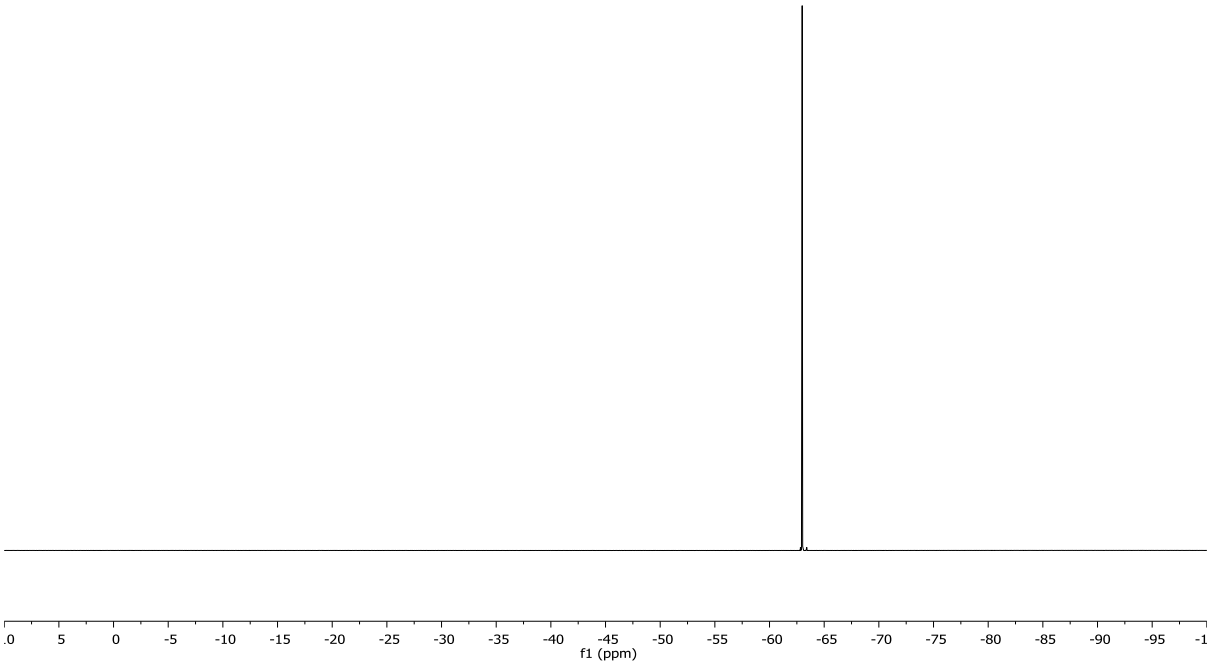


N-(Cyclopropylmethyl)-4-(trifluoromethyl)benzamide

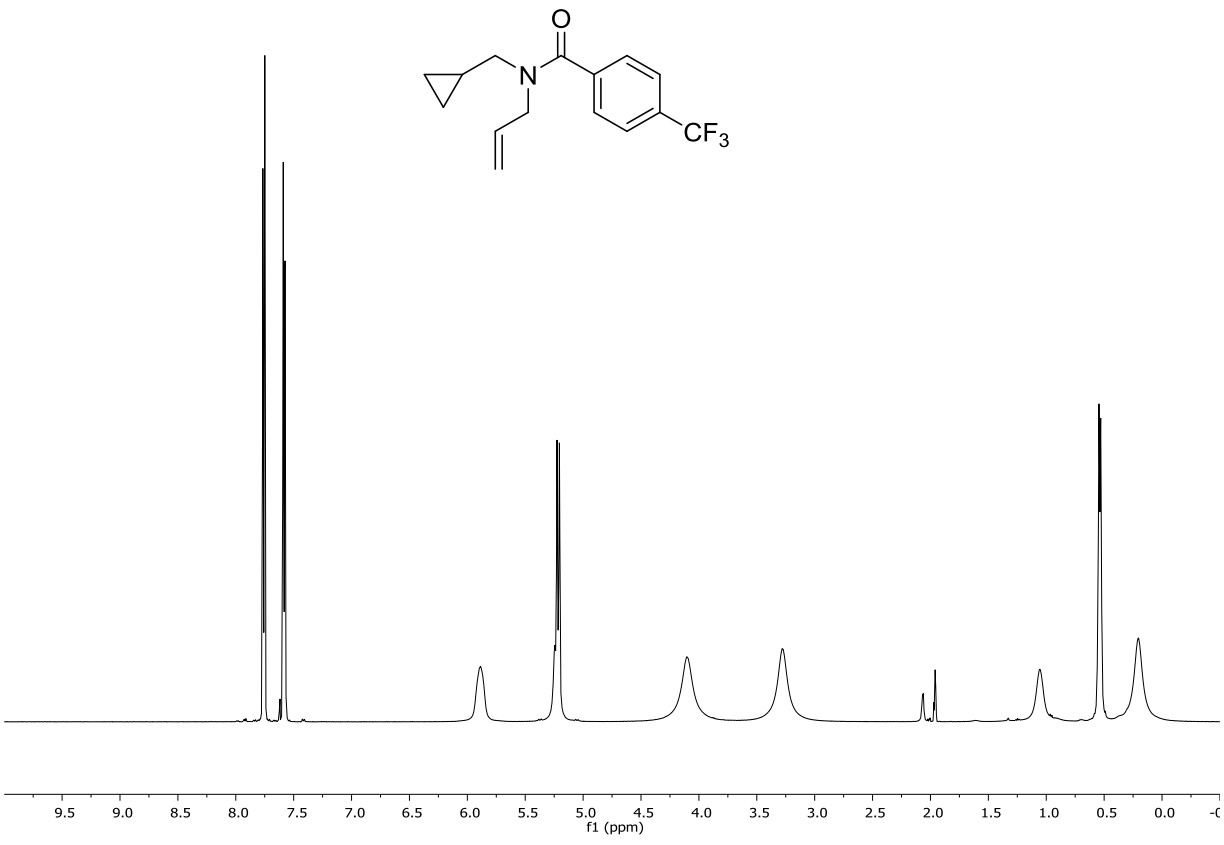


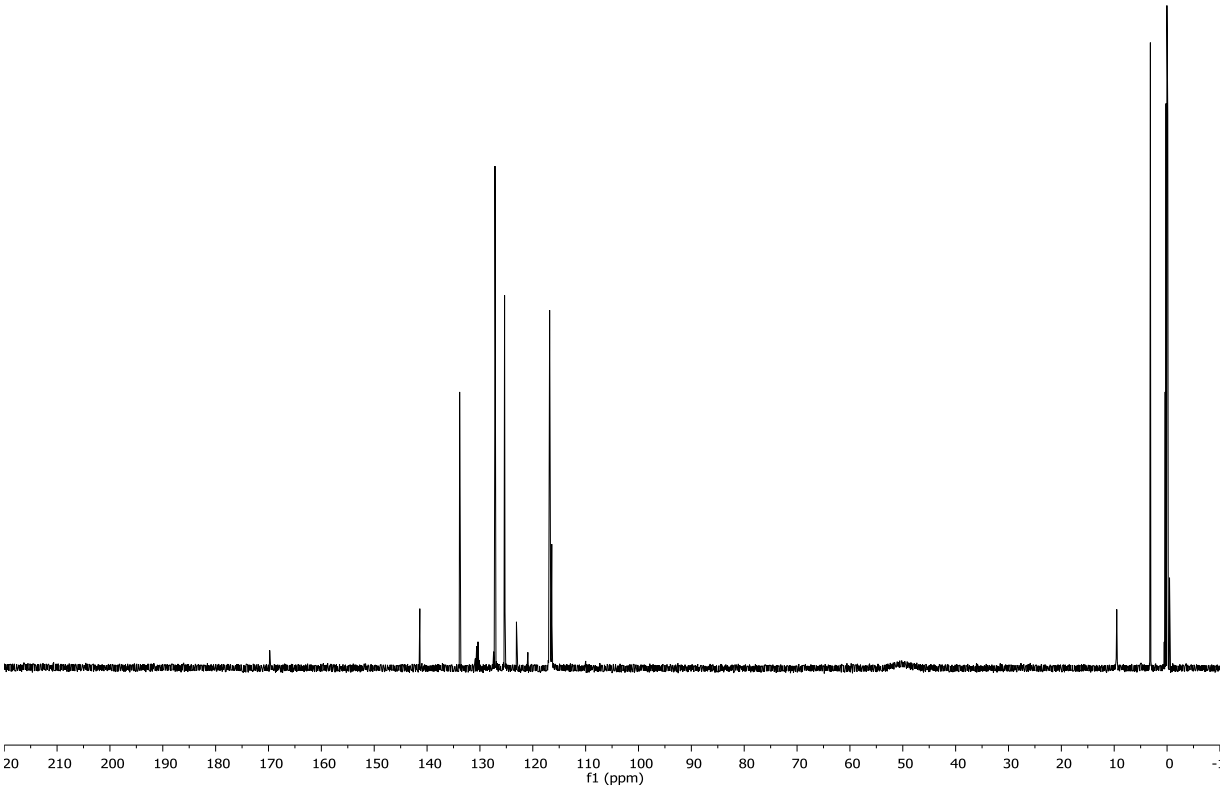






N-Allyl-N-(cyclopropylmethyl)-4-(trifluoromethyl)benzamide (6f)

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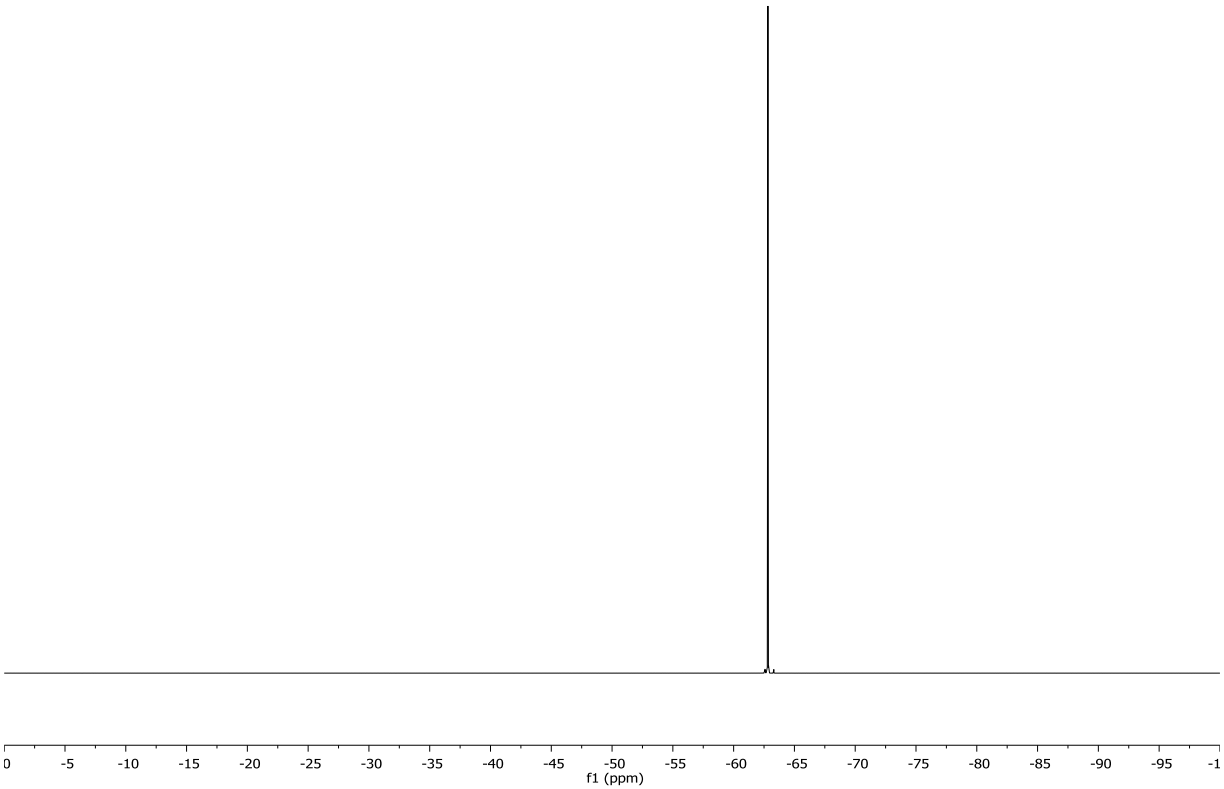
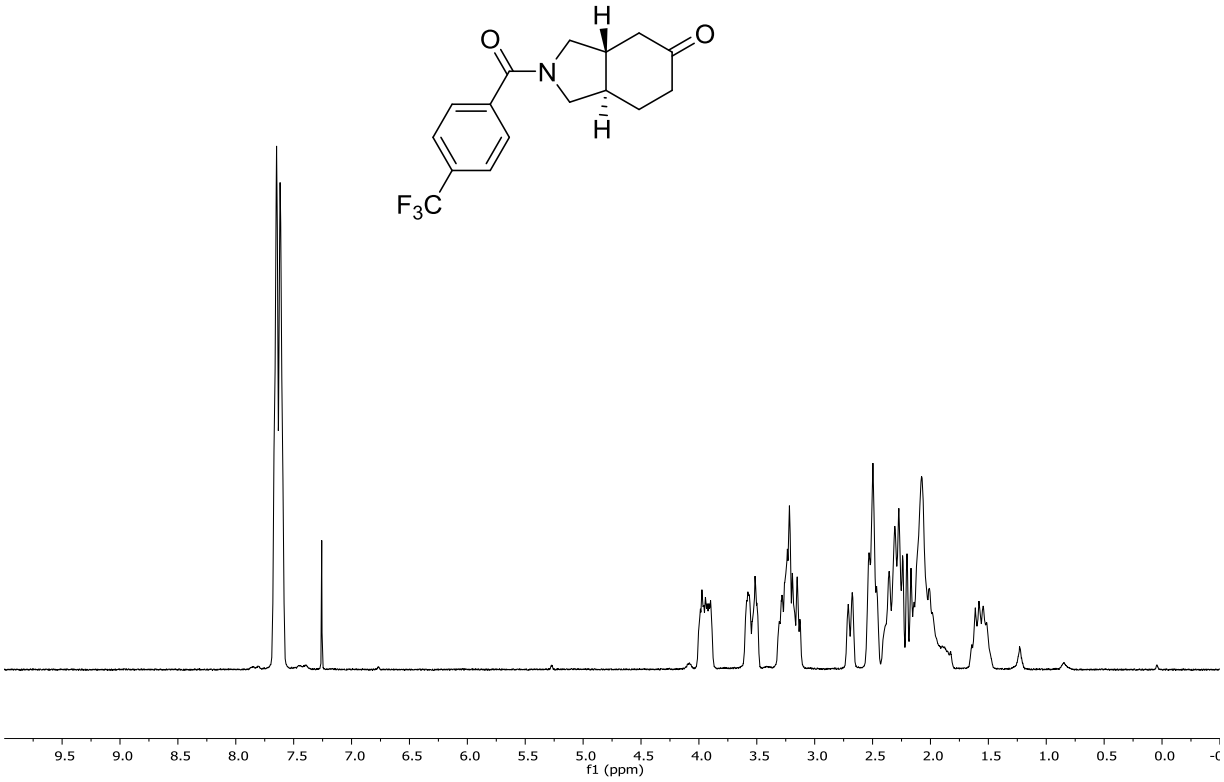
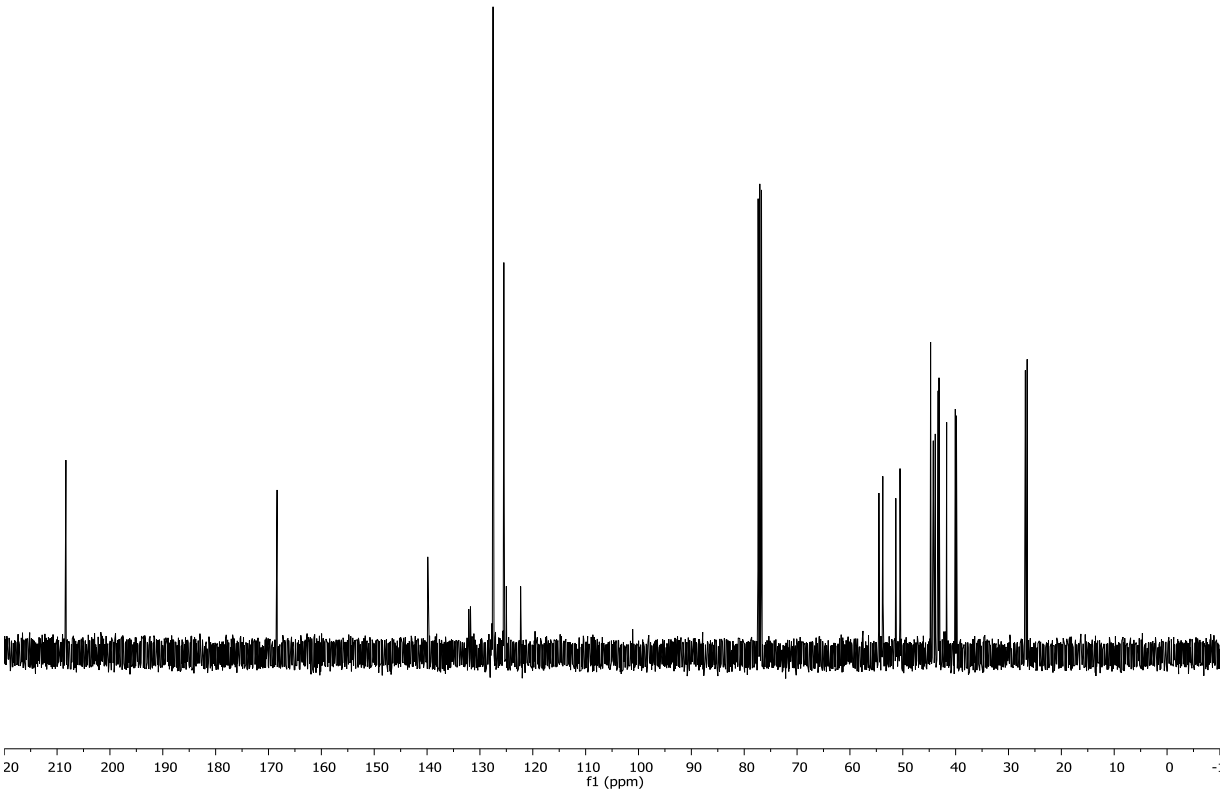
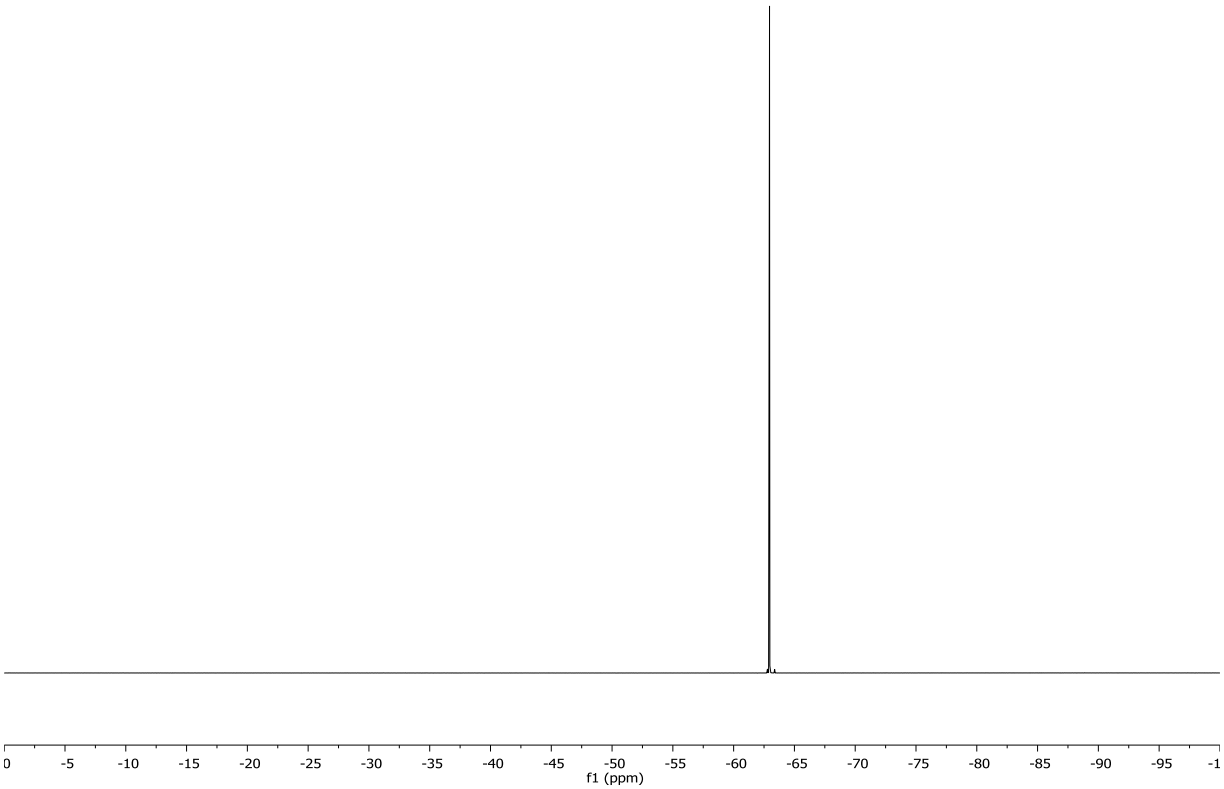
f1 (ppm)


0 -5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95
f1 (ppm)

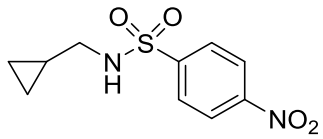
(3a*R, 7a*R**)-2-(4-(Trifluoromethyl)benzoyl)octahydro-5H-isoindol-5-one (8f)**

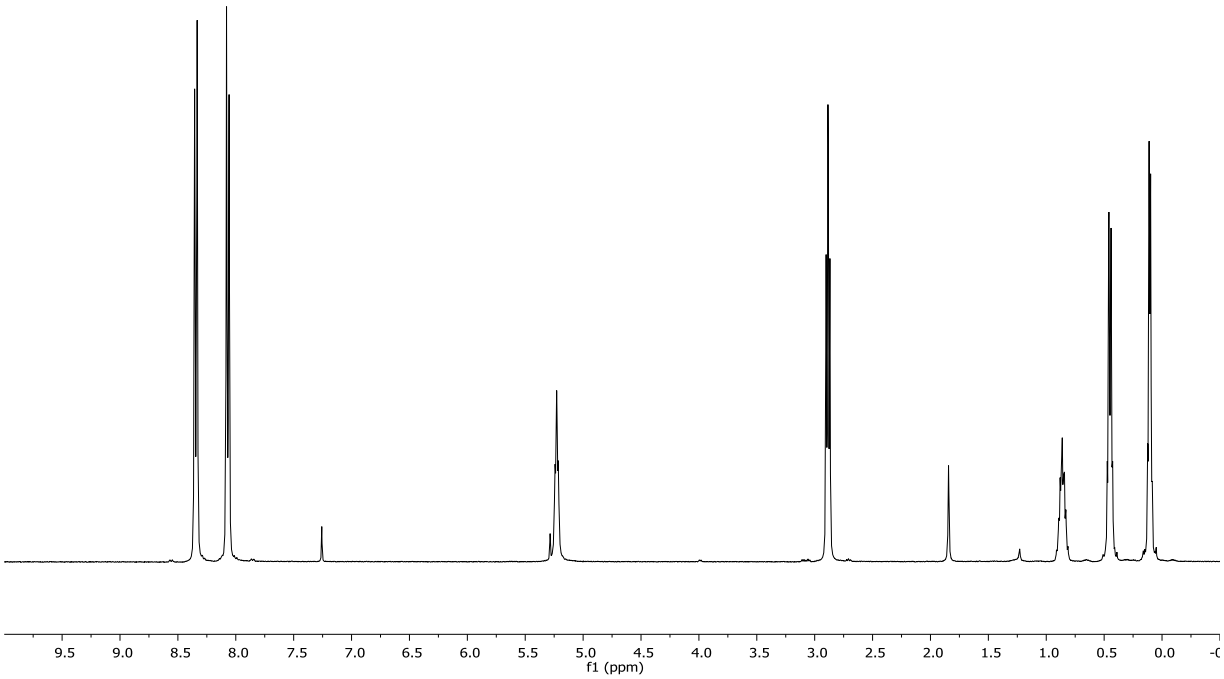


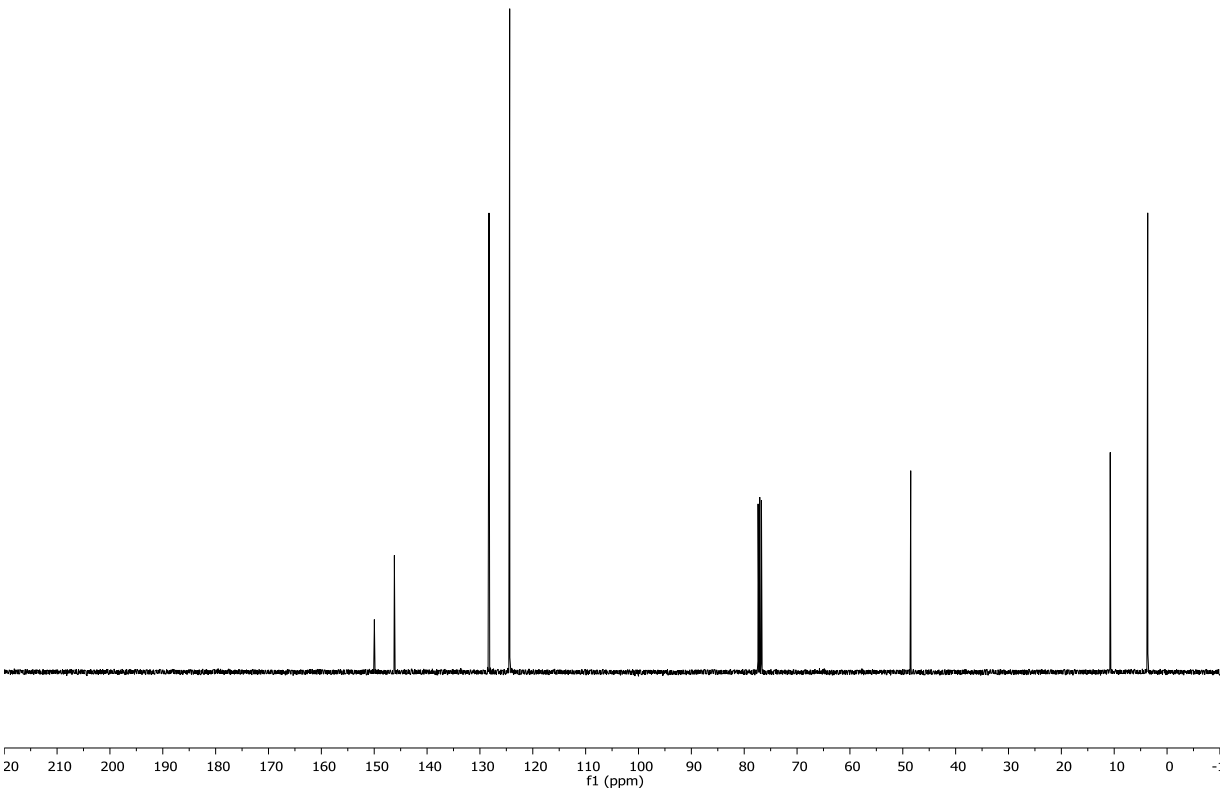



0
-5
-10
-15
-20
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-1
f1 (ppm)

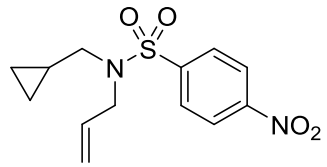
N-(Cyclopropylmethyl)-4-nitrobenzenesulfonamide

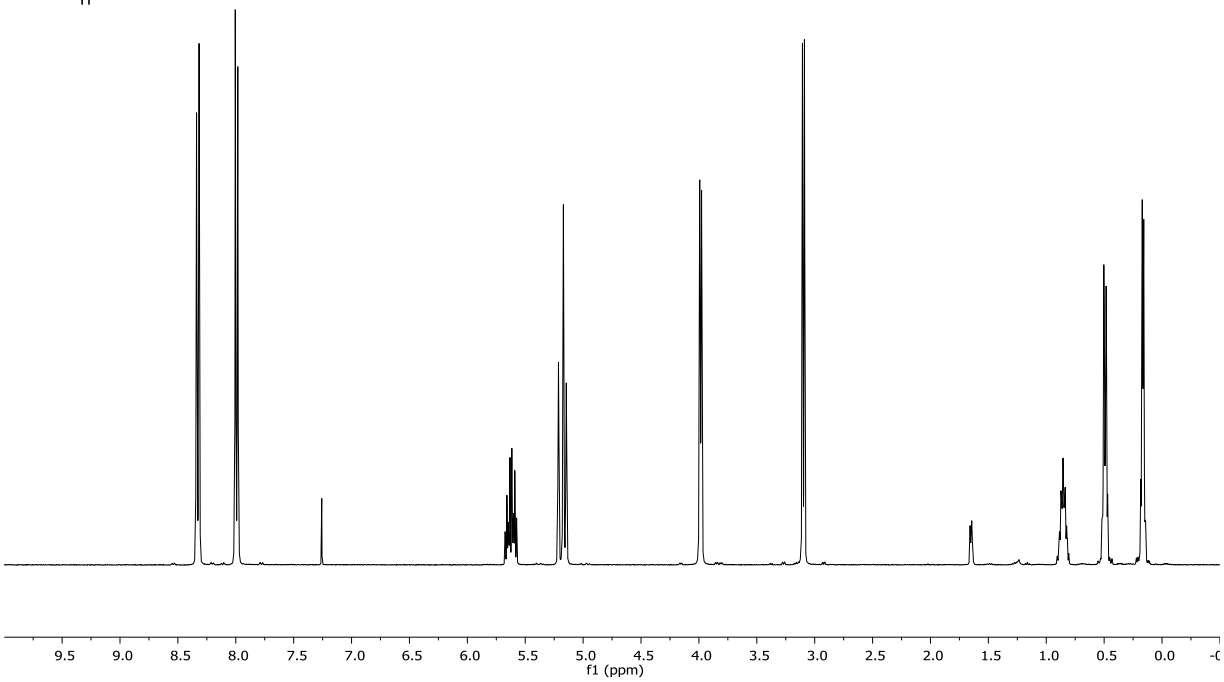


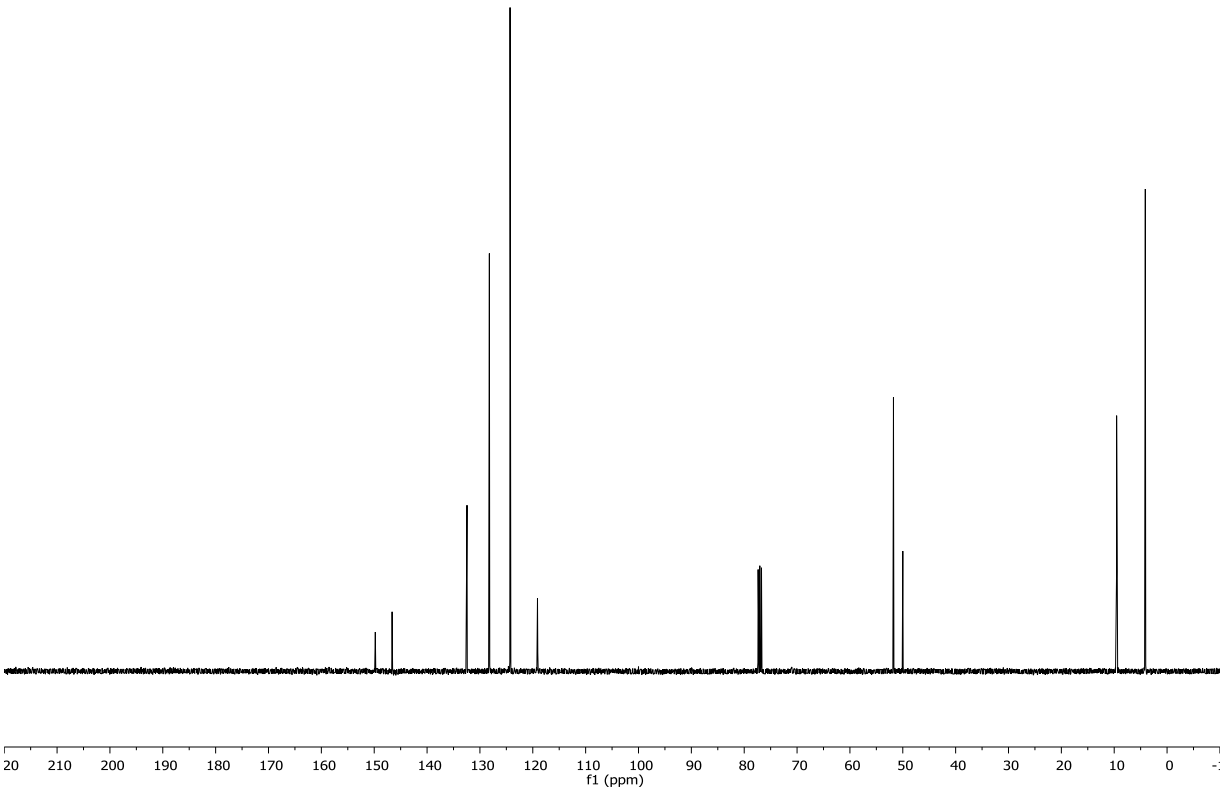




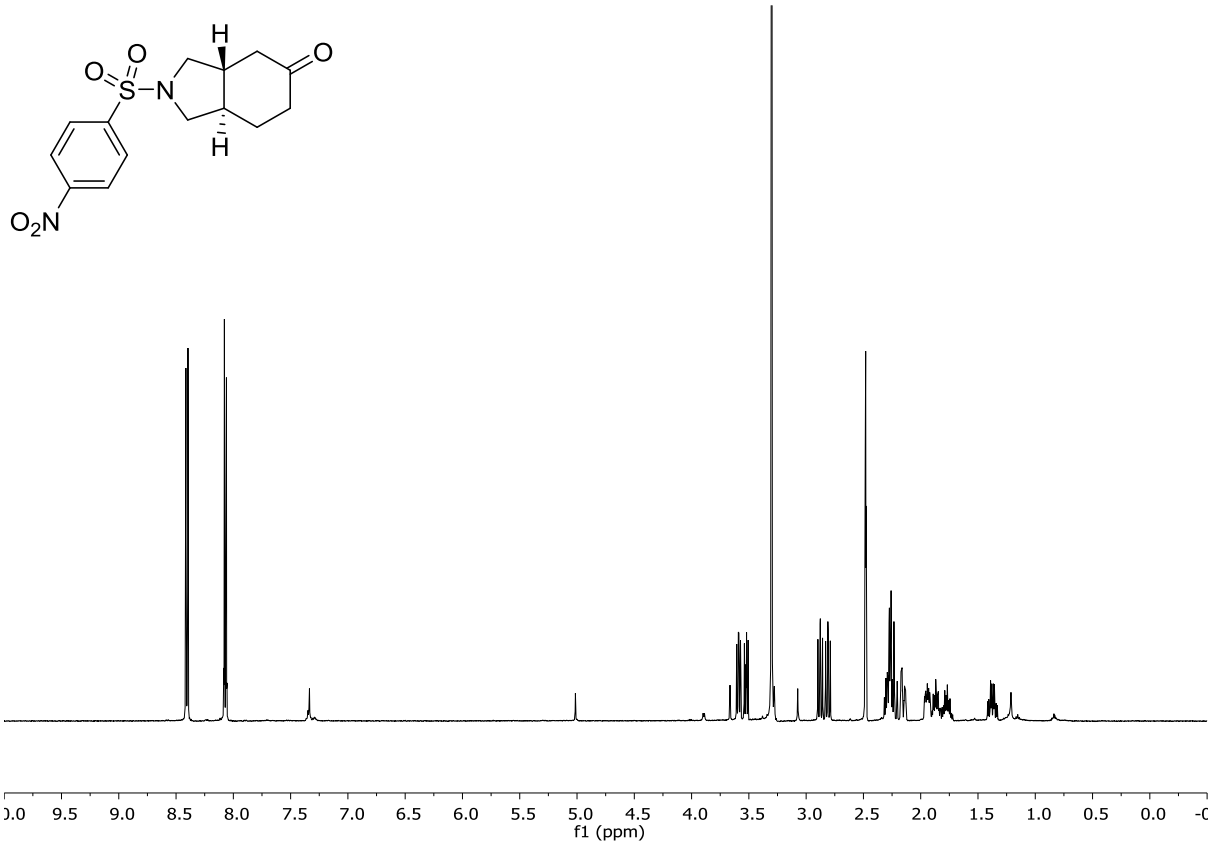
N-Allyl-*N*-(cyclopropylmethyl)-4-nitrobenzenesulfonamide (6g)

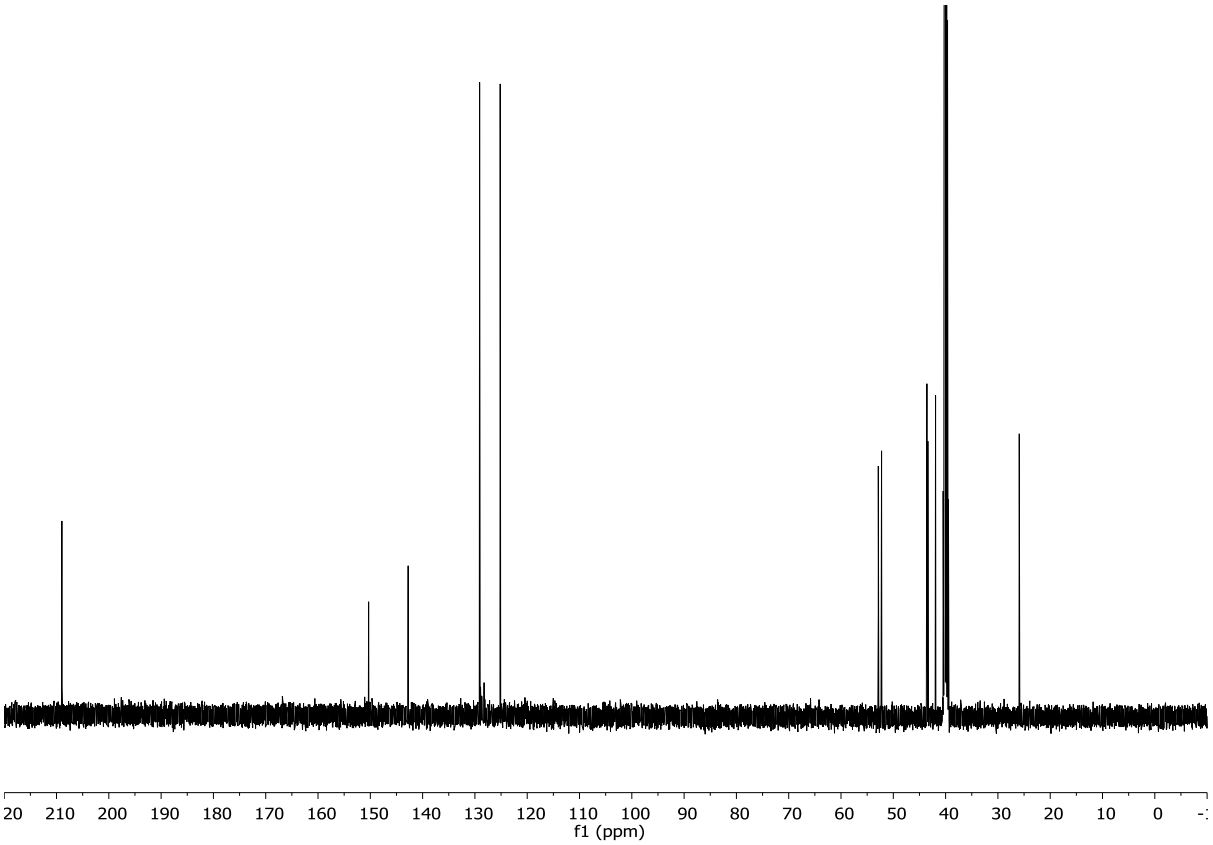




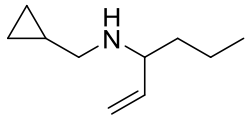


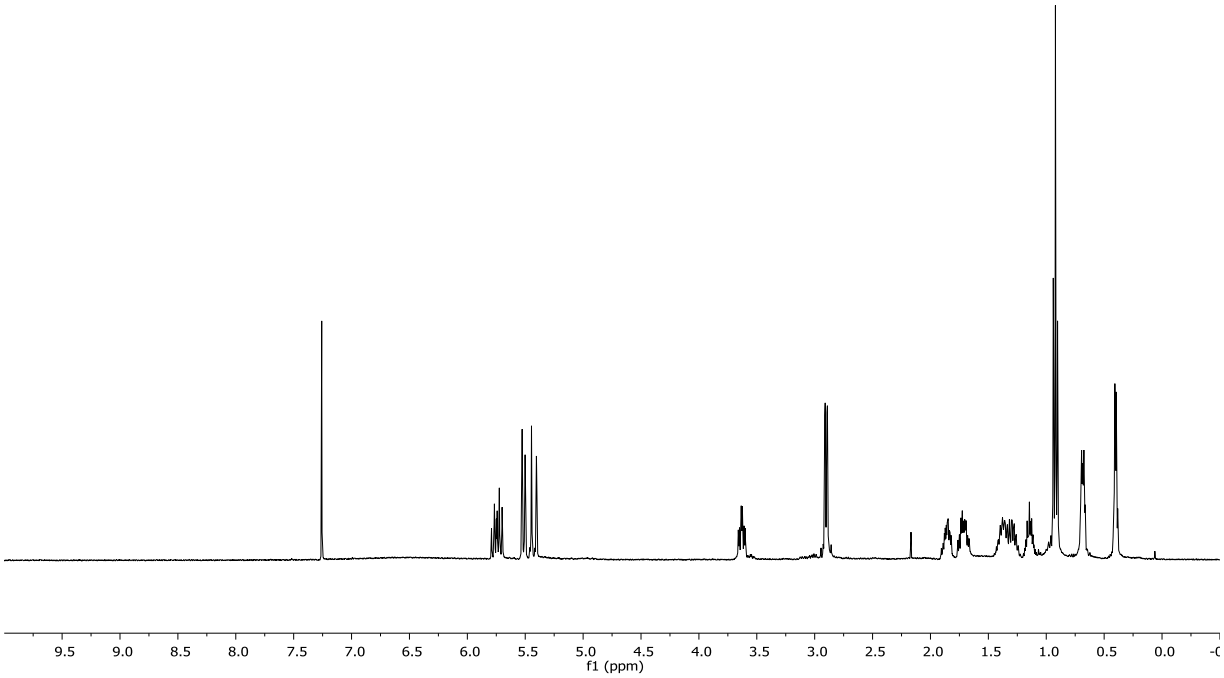
(3a*R, 7a*R**)-2-((4-Nitrophenyl)sulfonyl)octahydro-5*H*-isoindol-5-one (8g)

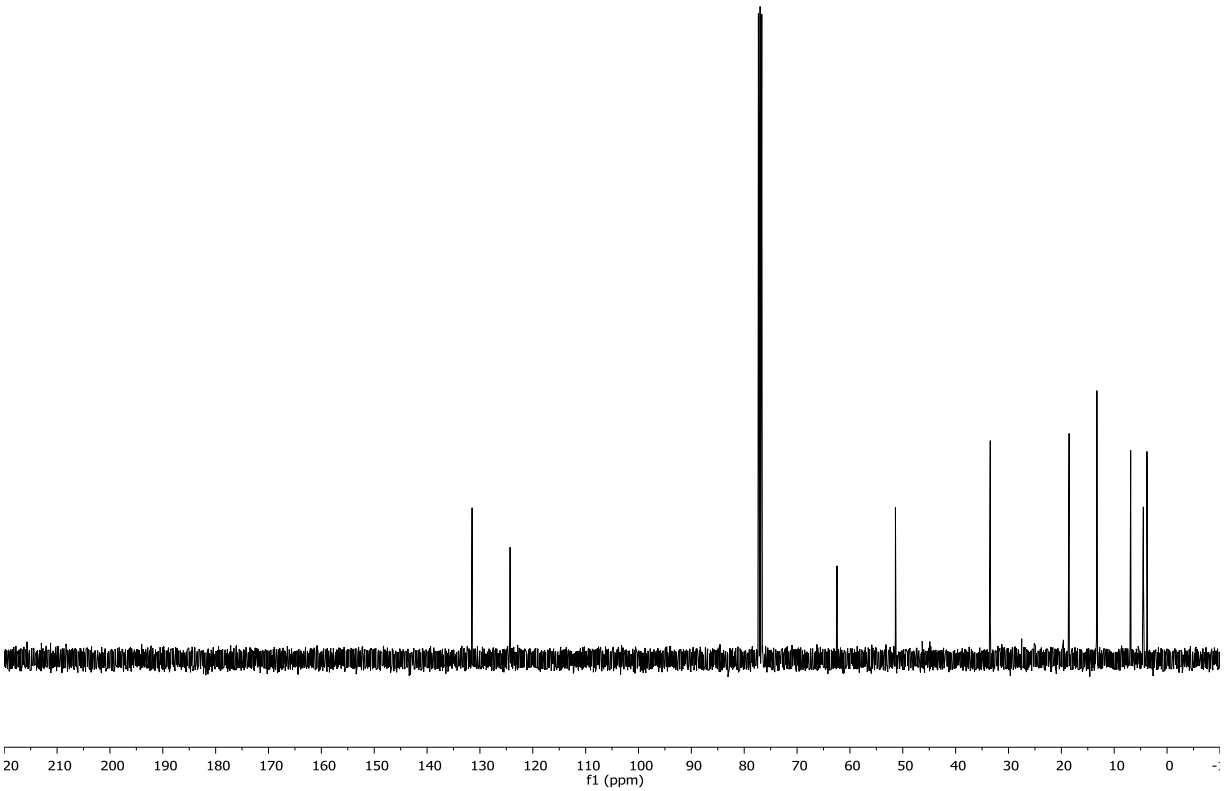




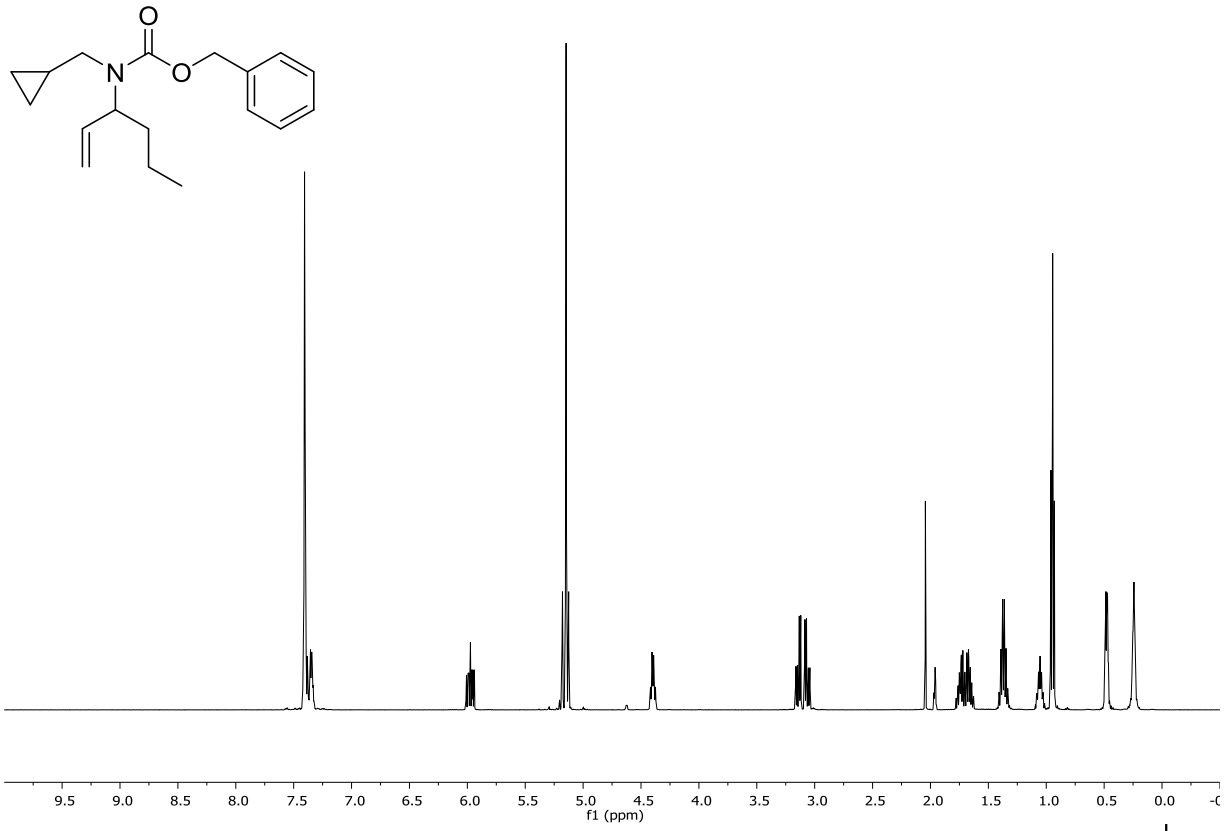
N-(Cyclopropylmethyl)hex-1-en-3-amine

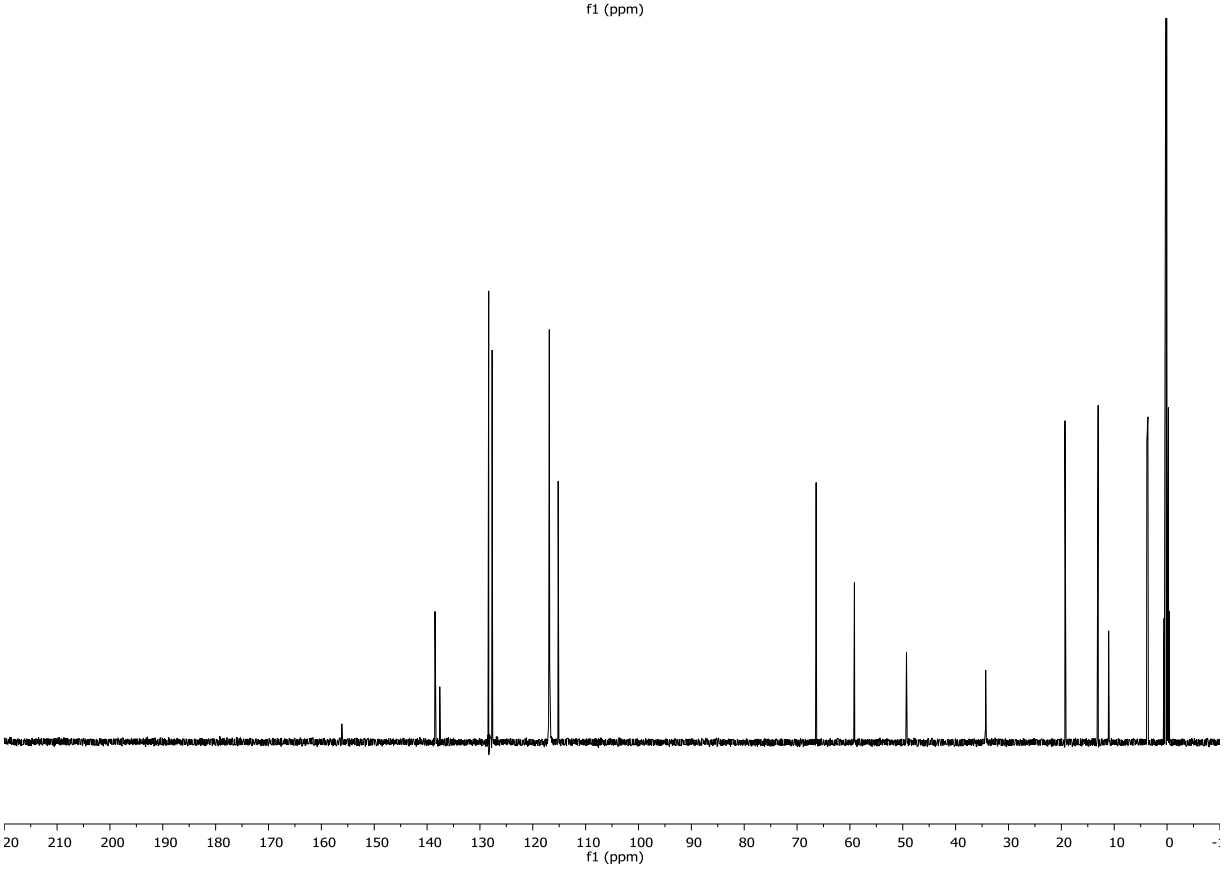




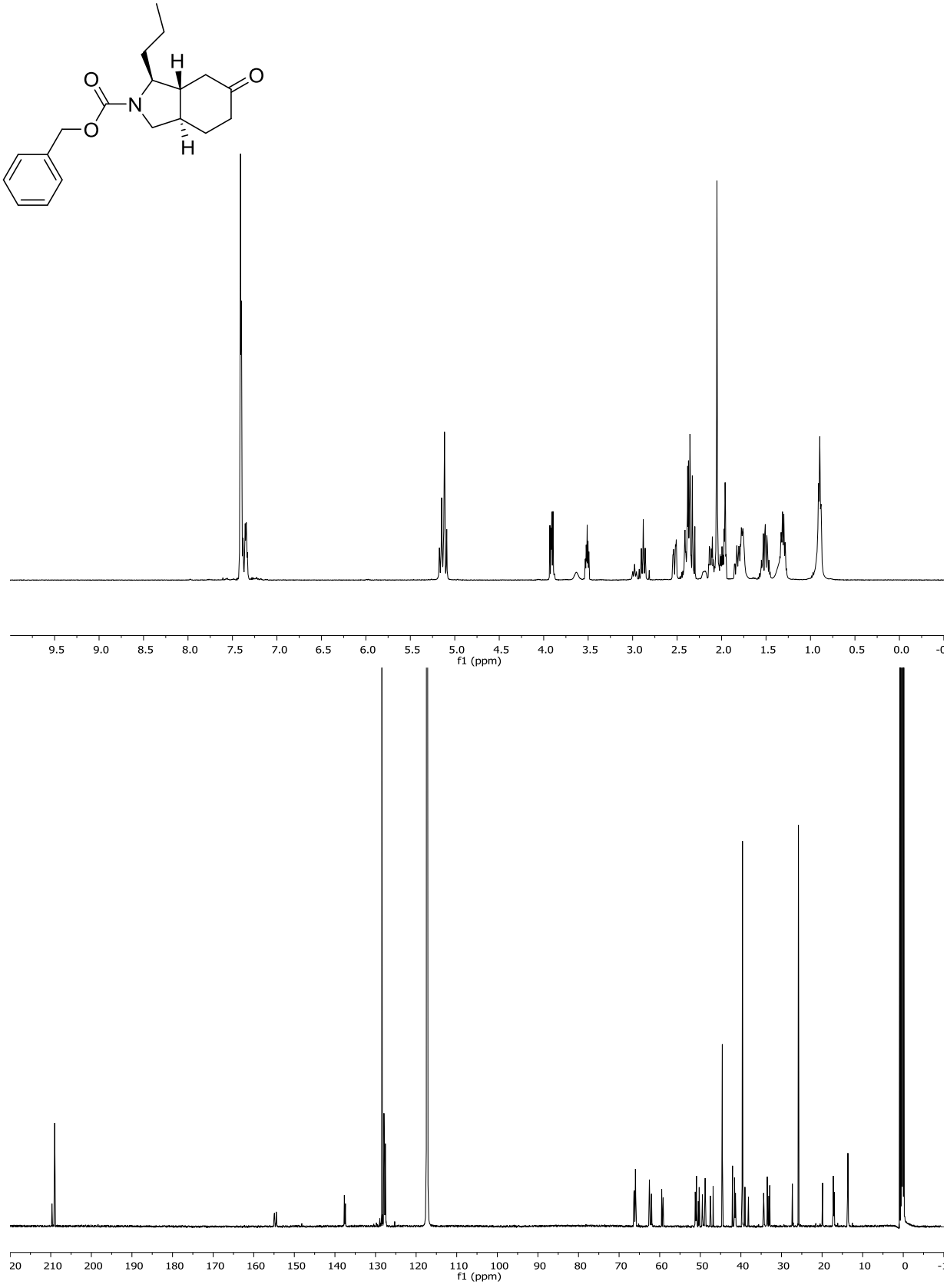


Benzyl (cyclopropylmethyl)(hex-1-en-3-yl)carbamate (6h)

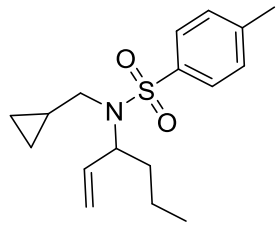


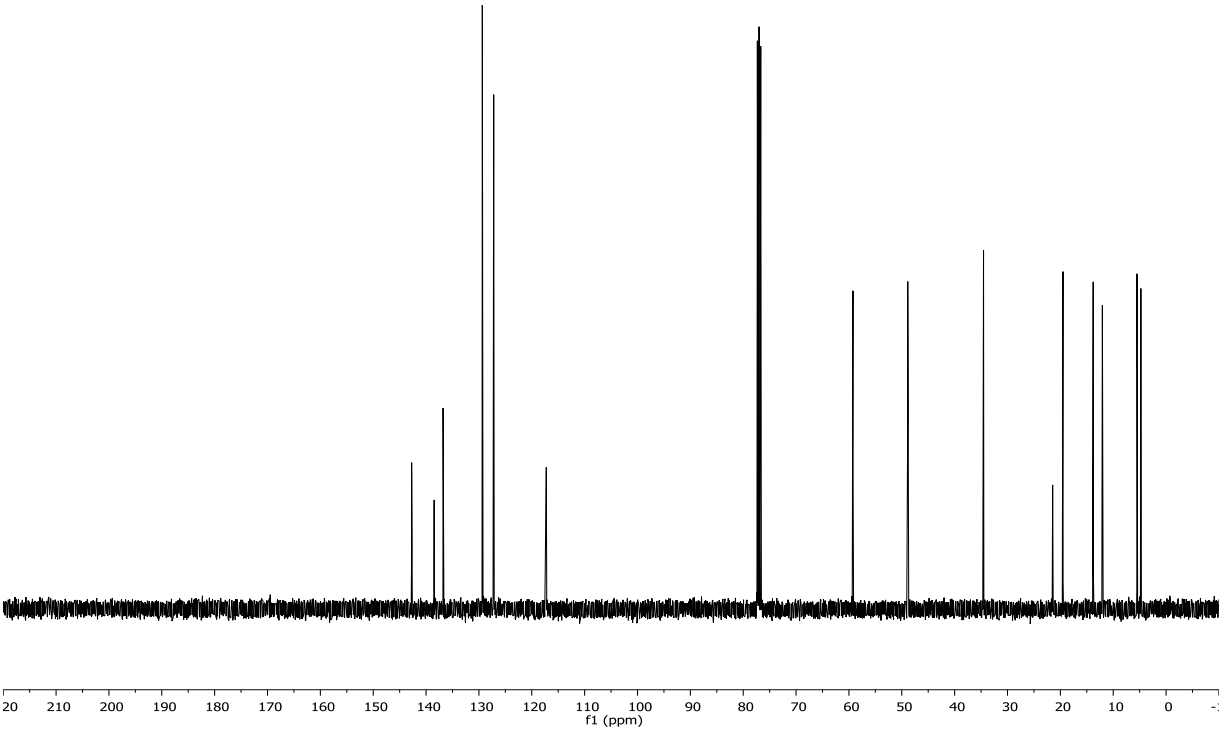


(1*S, 3a*R**, 7a*R**) and (1*R**, 3a*R**,7a*R**)-Benzyl 6-oxo-1-propylhexahydro-1*H*-isoindole-2(3*H*)-carboxylate (8h)**

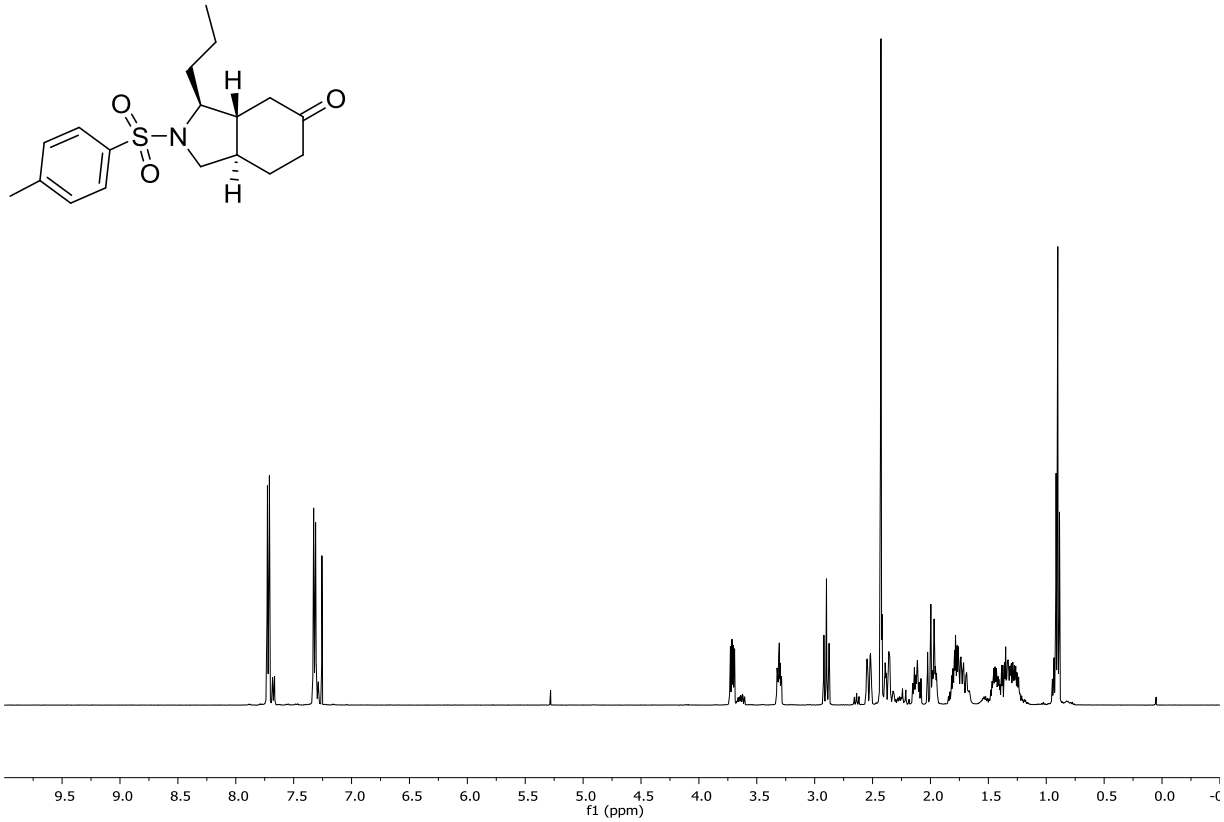


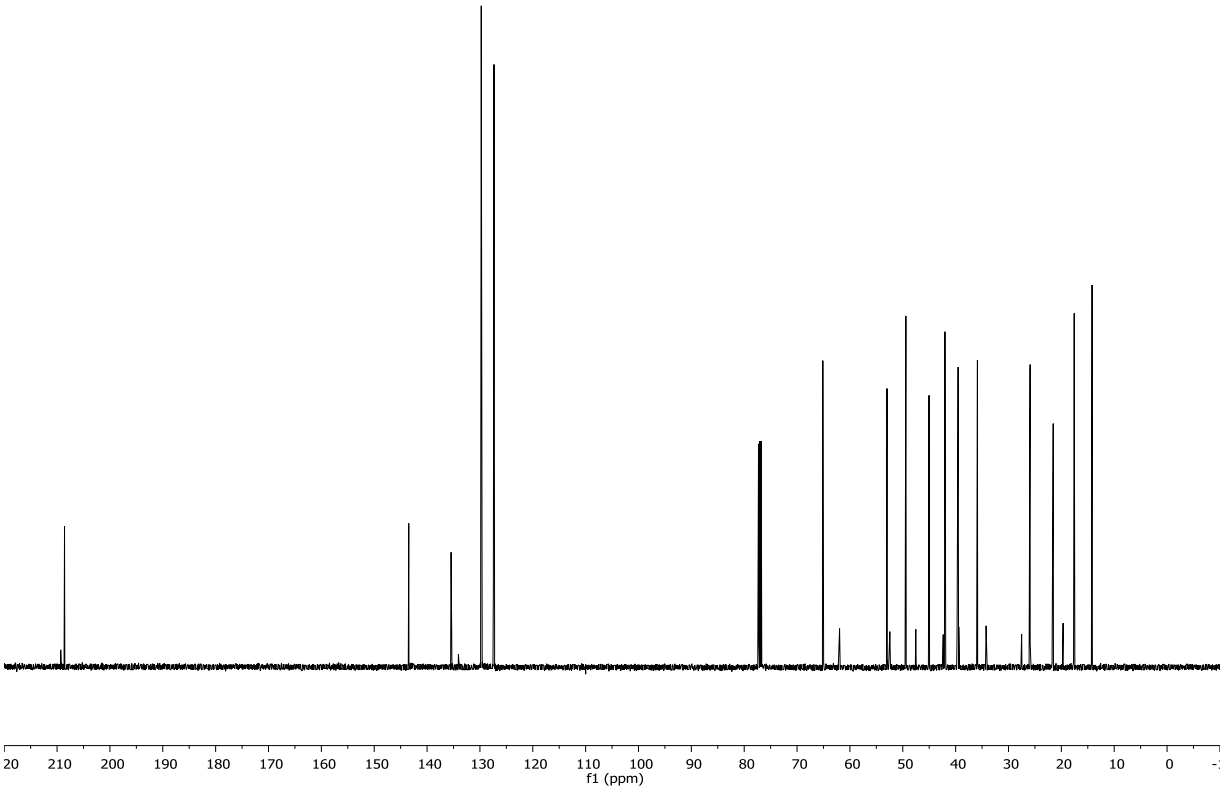
N-(Cyclopropylmethyl)-*N*-(hex-1-en-3-yl)-4-methylbenzenesulfonamide (6i)



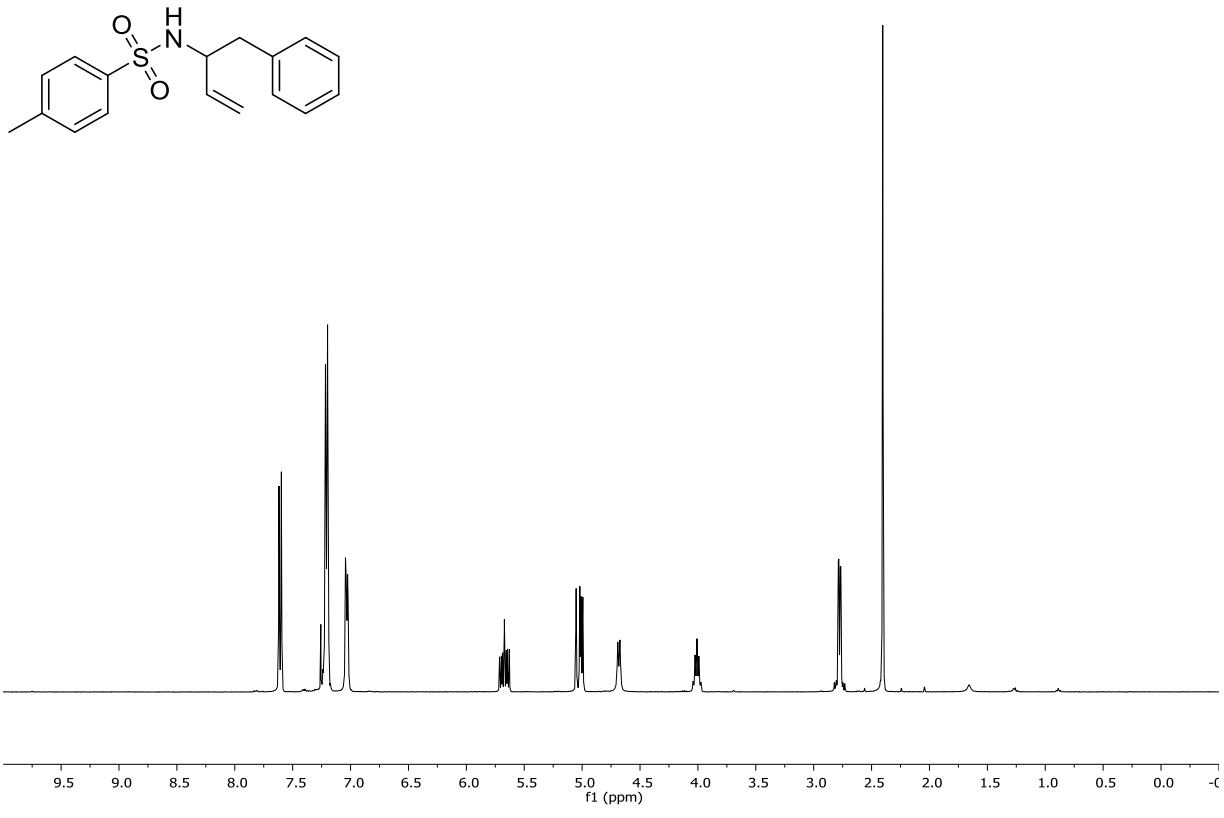


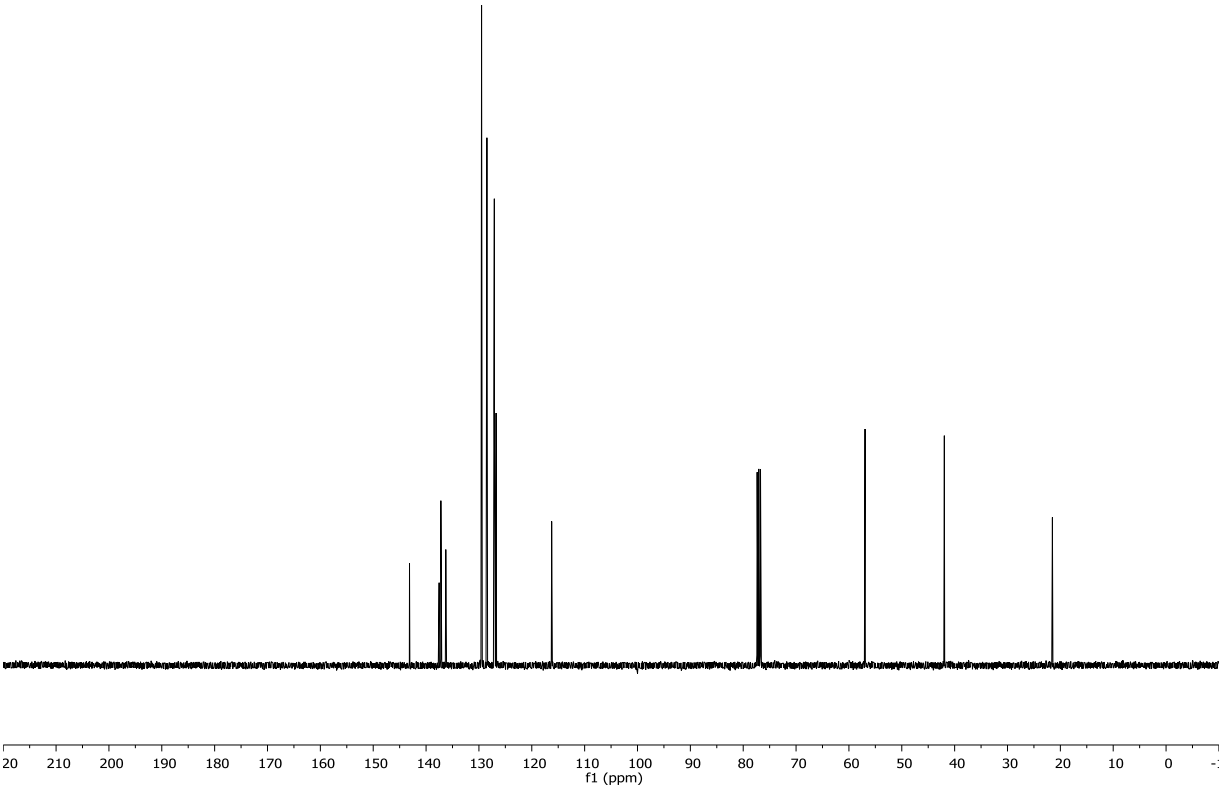
(3*S,3a*R**,7a*R**) and (3*R**,3a*R**,7a*R**)-3-Propyl-2-tosylhexahydro-1*H*-isoindol-5(6*H*)-one (8i)**



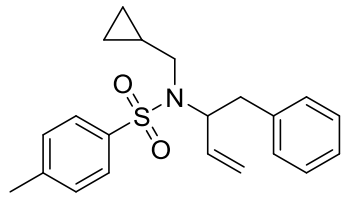


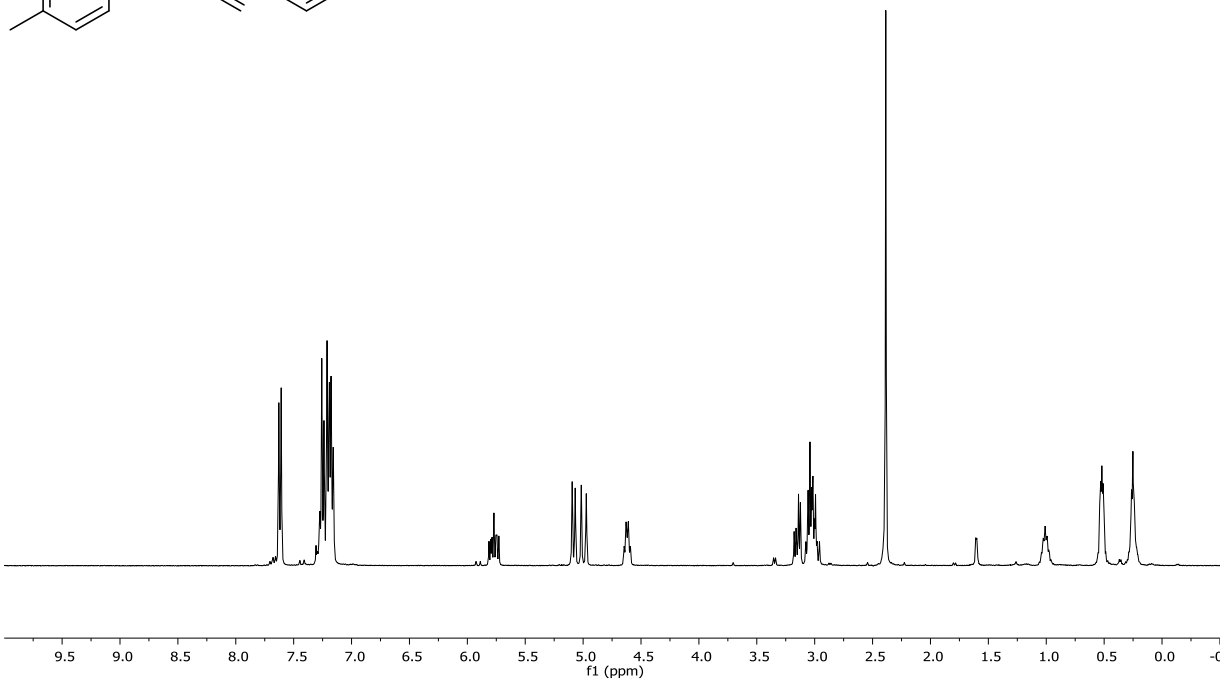
4-Methyl-*N*-(1-phenylbut-3-en-2-yl)benzenesulfonamide

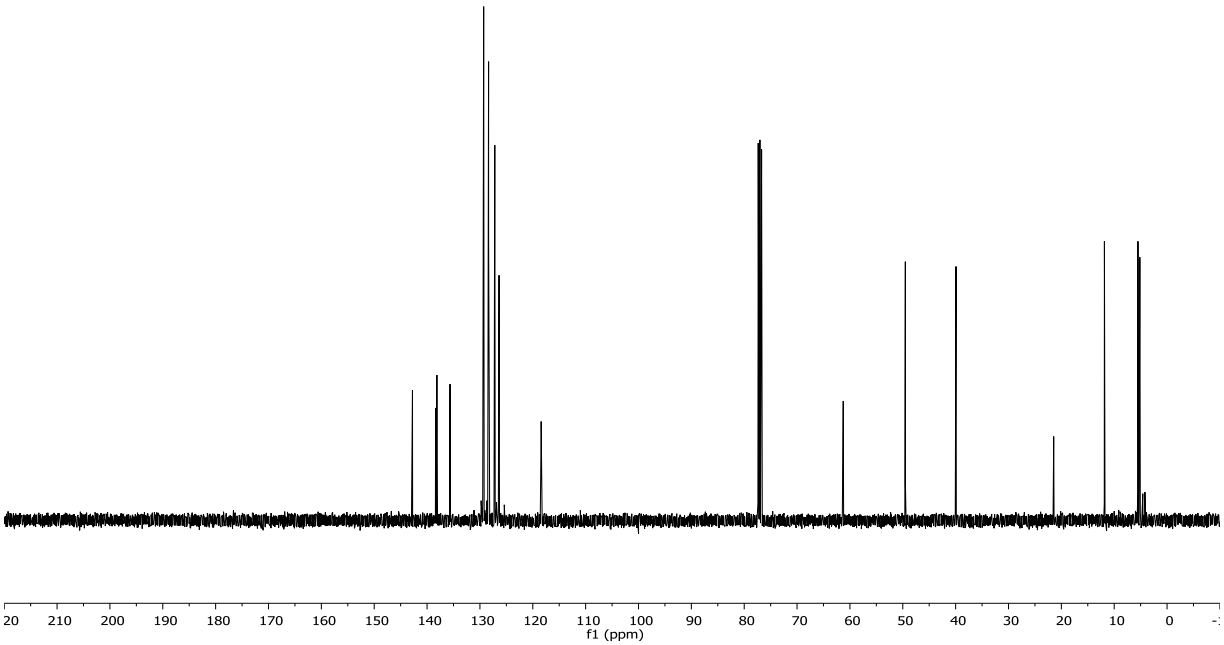




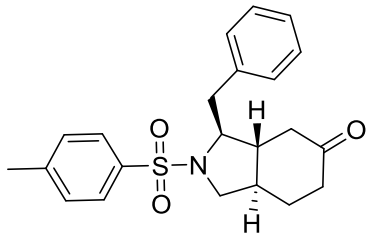
N-(Cyclopropylmethyl)-4-methyl-*N*-(1-phenylbut-3-en-2-yl)benzenesulfonamide (6j)

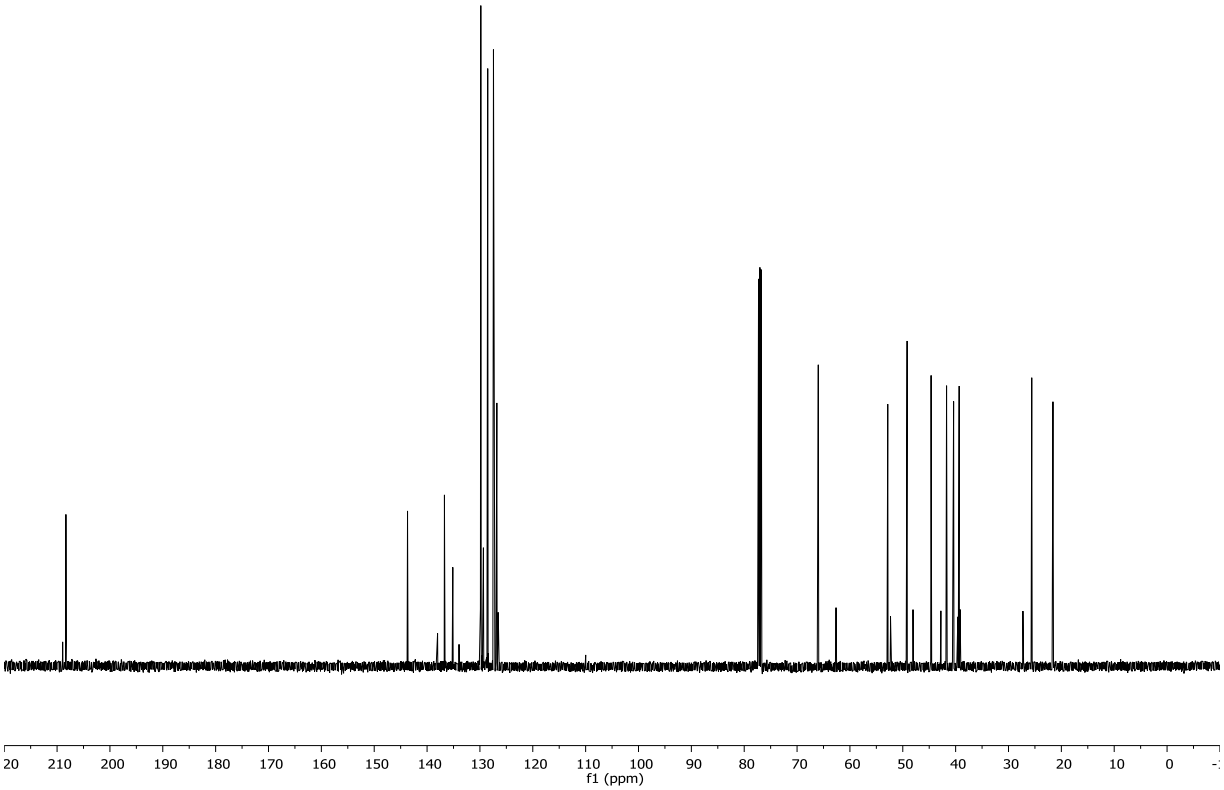




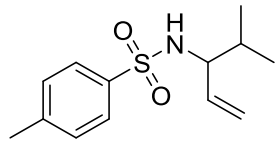


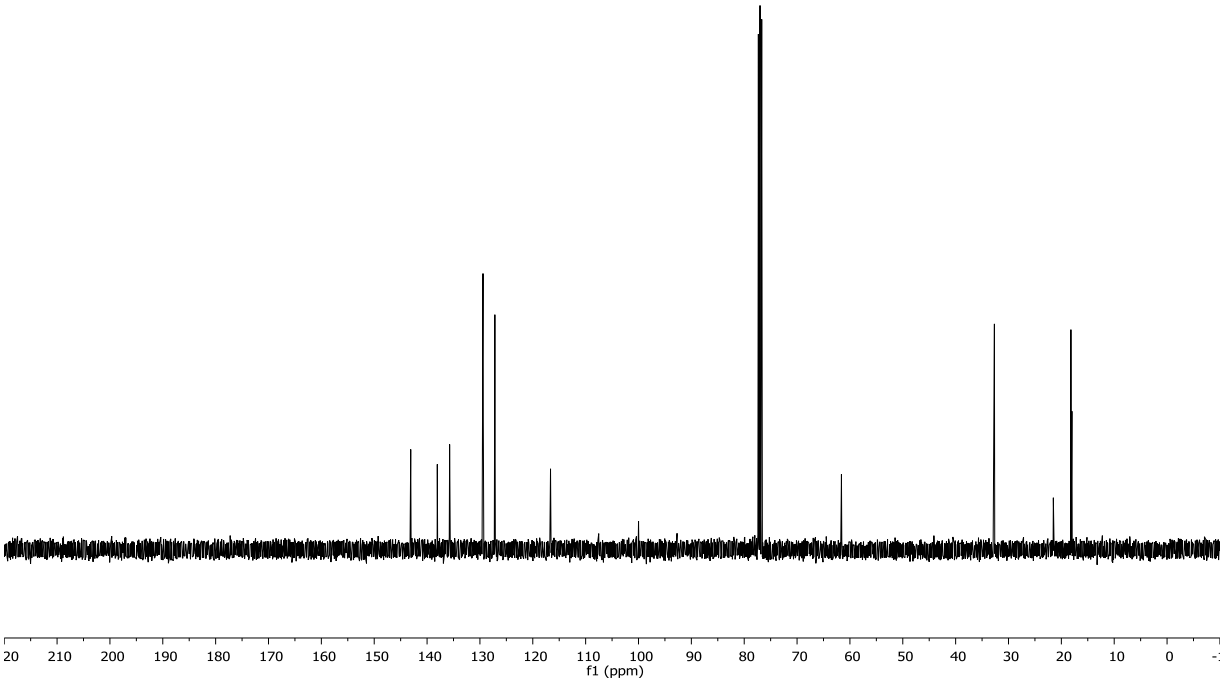
(3*S, 3a*R**, 7a*R**) and (3*R**, 3a*R**, 7a*R**)-3-Benzyl-2-tosylhexahydro-1*H*-isoindol-5(6*H*)-one (8j)**



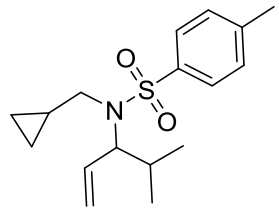


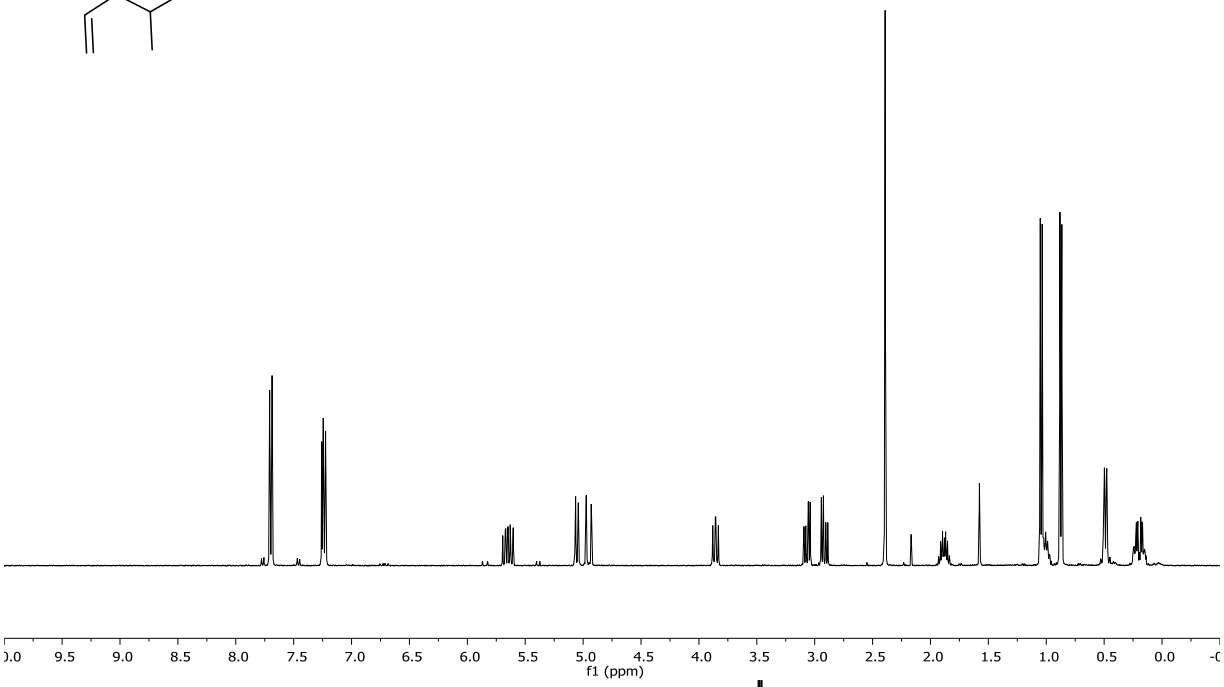
4-Methyl-*N*-(4-methylpent-1-en-3-yl)benzenesulfonamide

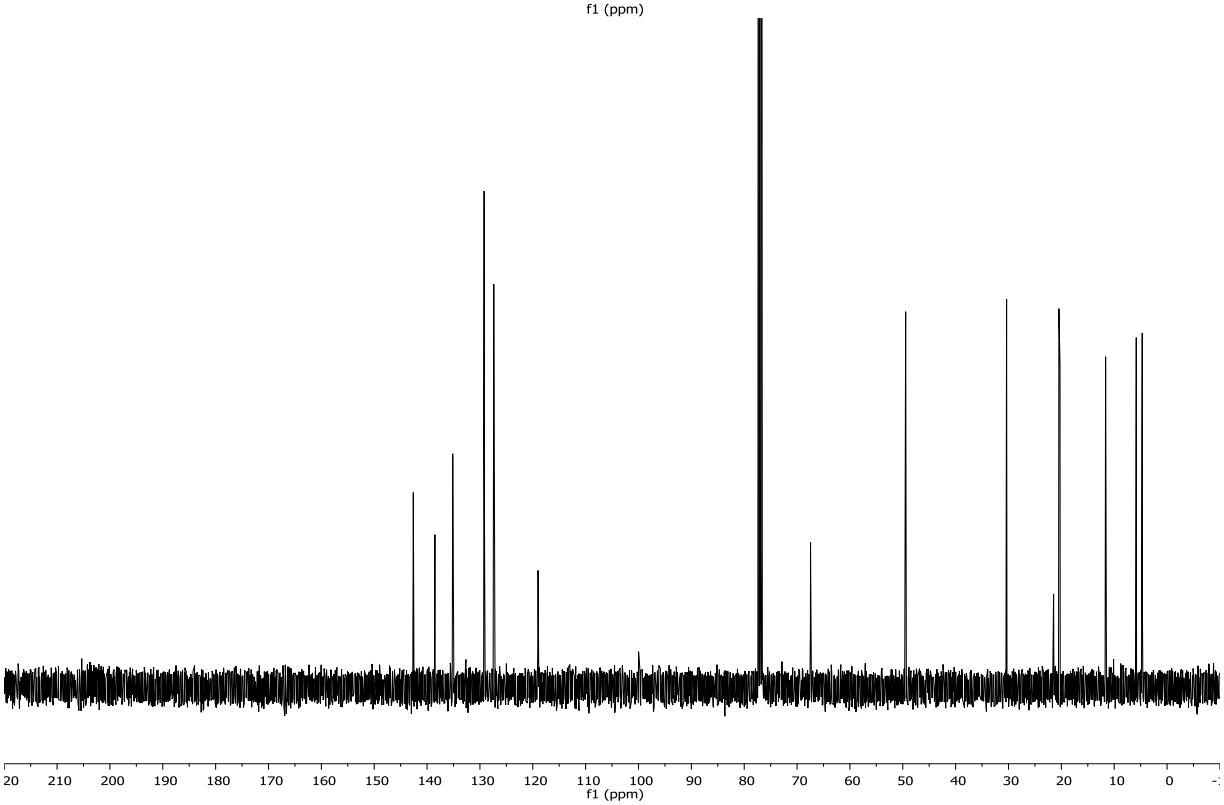




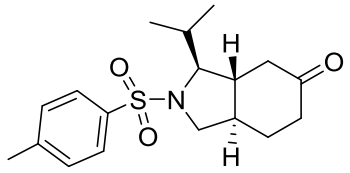
_N_-(Cyclopropylmethyl)-4-methyl-_N_-(4-methylpent-1-en-3-yl)benzenesulfonamide (6k)

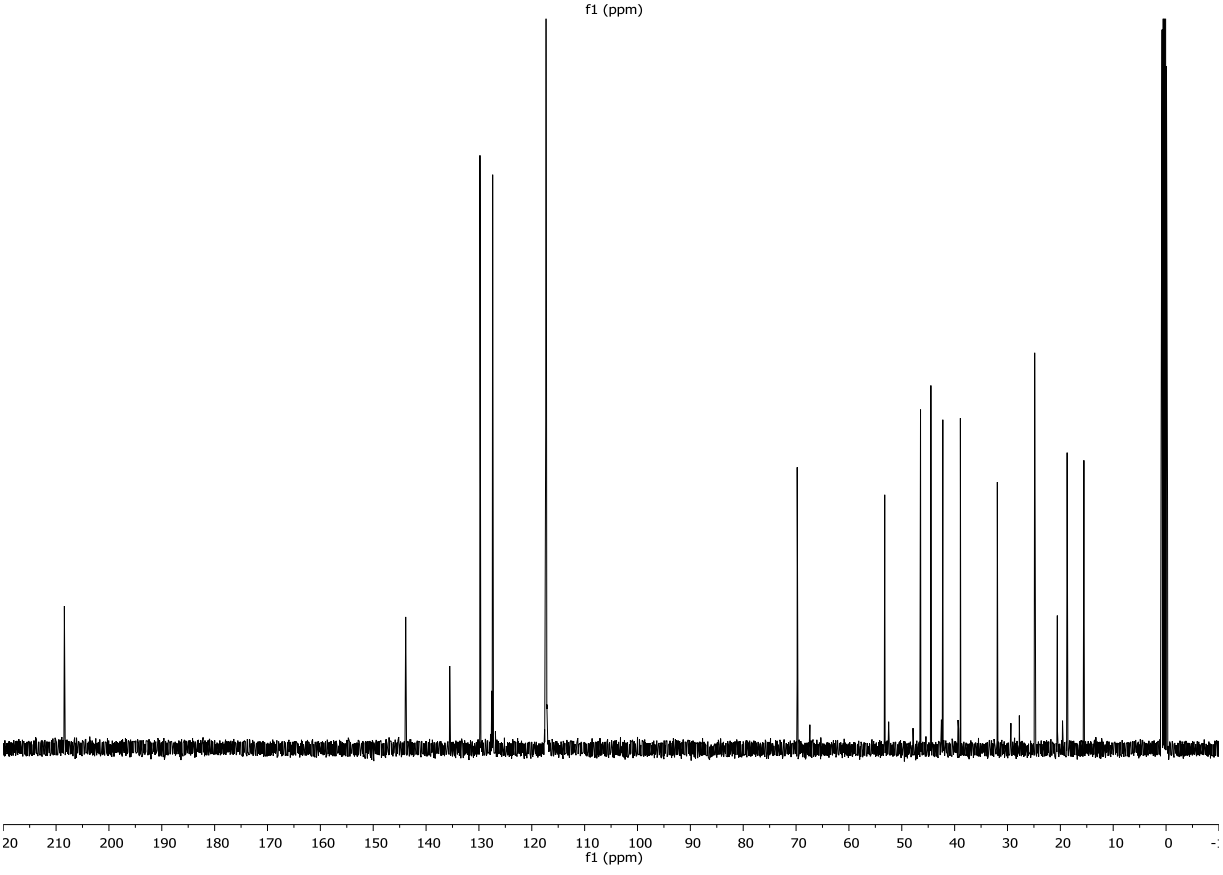




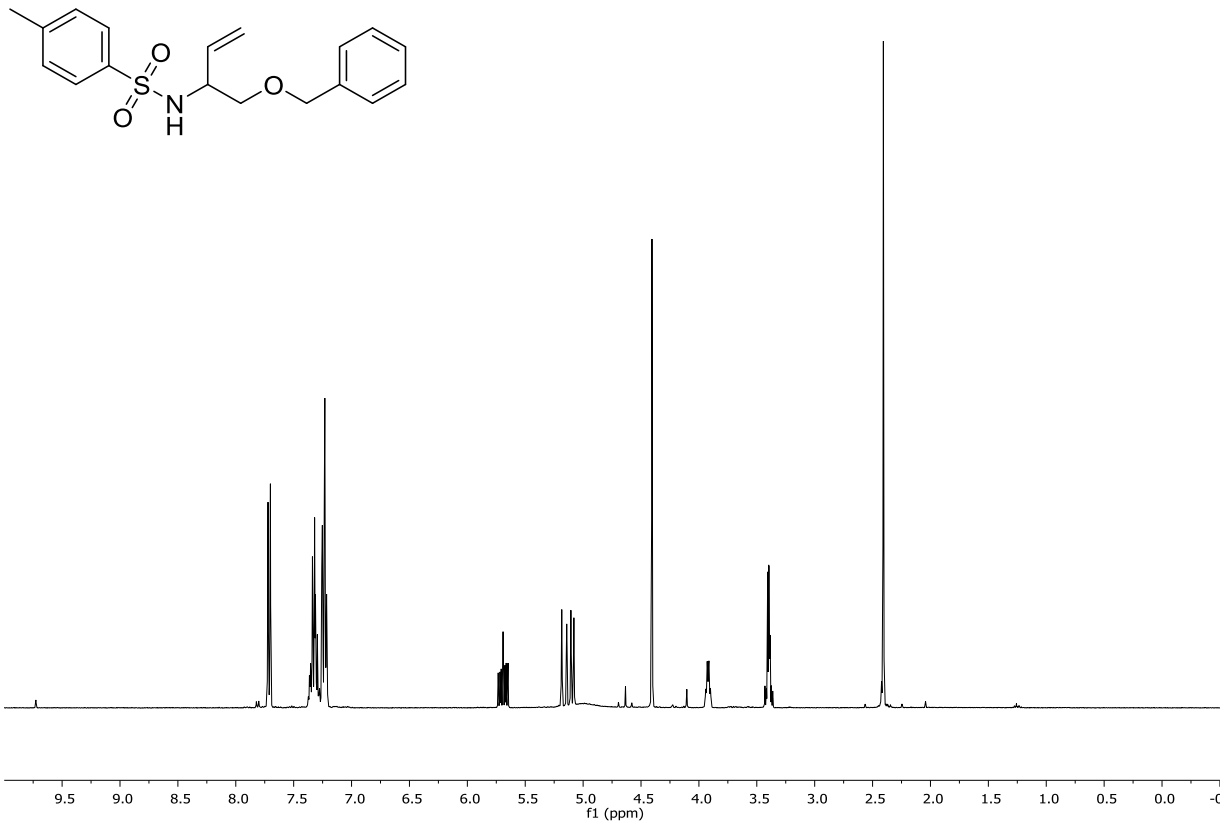


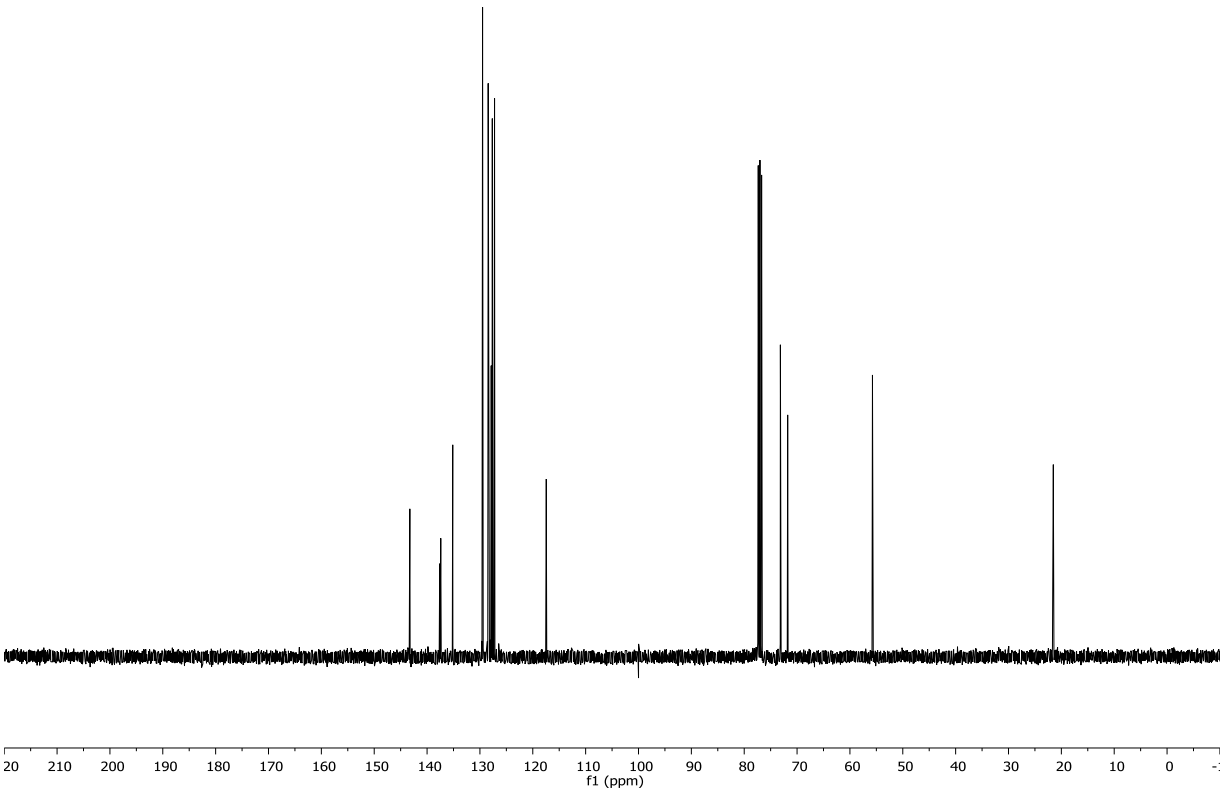
(3*S, 3a*R**, 7a*R**) and (3*R**, 3a*R**, 7a*R**) -3-Isopropyl-2-tosylhexahydro-1H-isoindol-5(6*H*)-one (8k)**



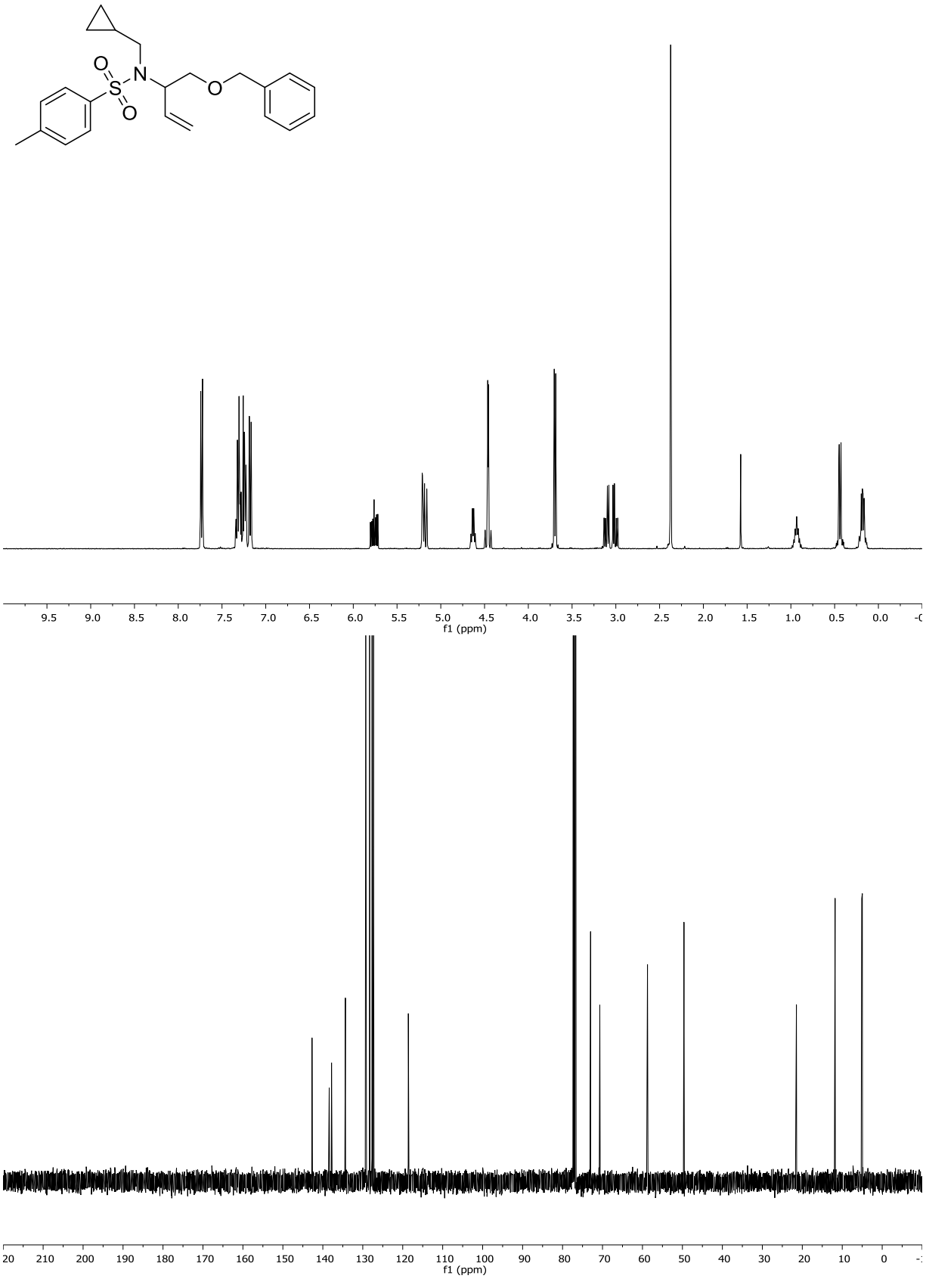


N-(1-(Benzyloxy)but-3-en-2-yl)-4-methylbenzenesulfonamide

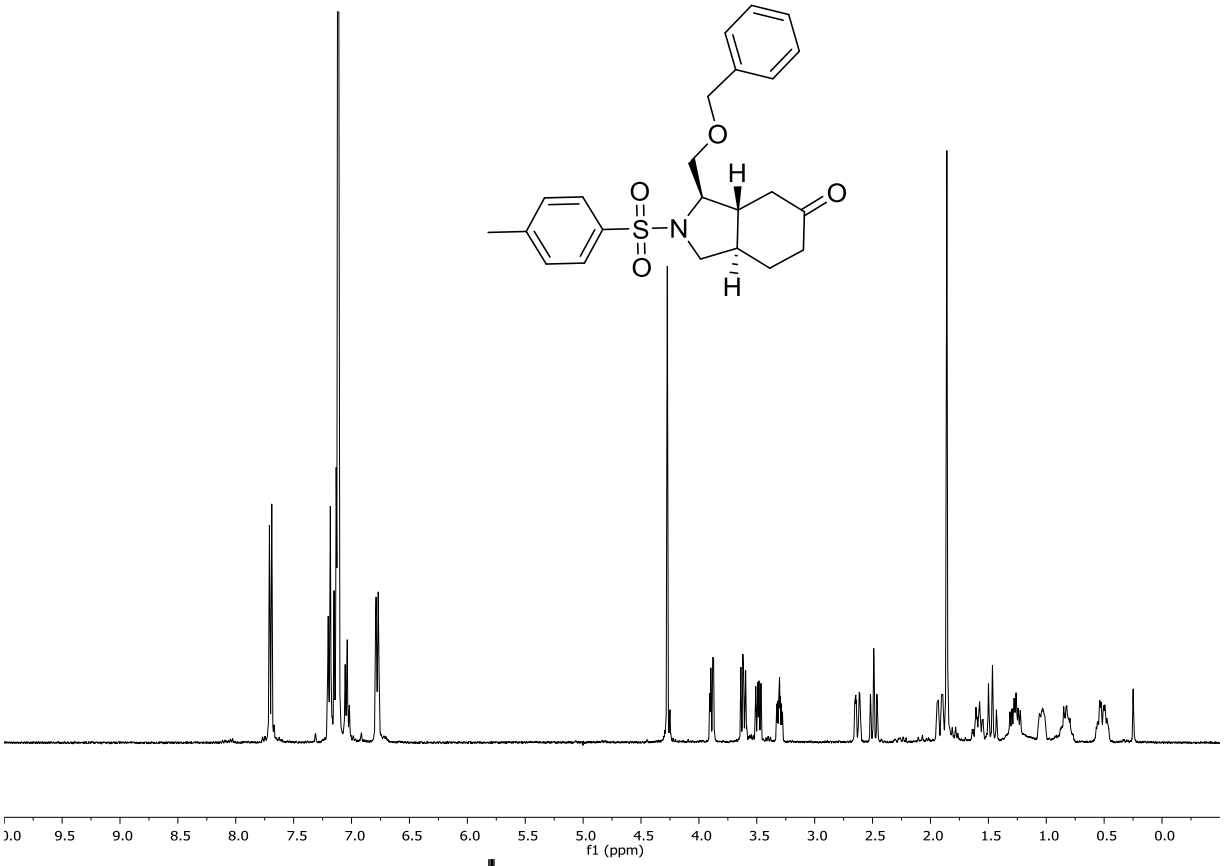


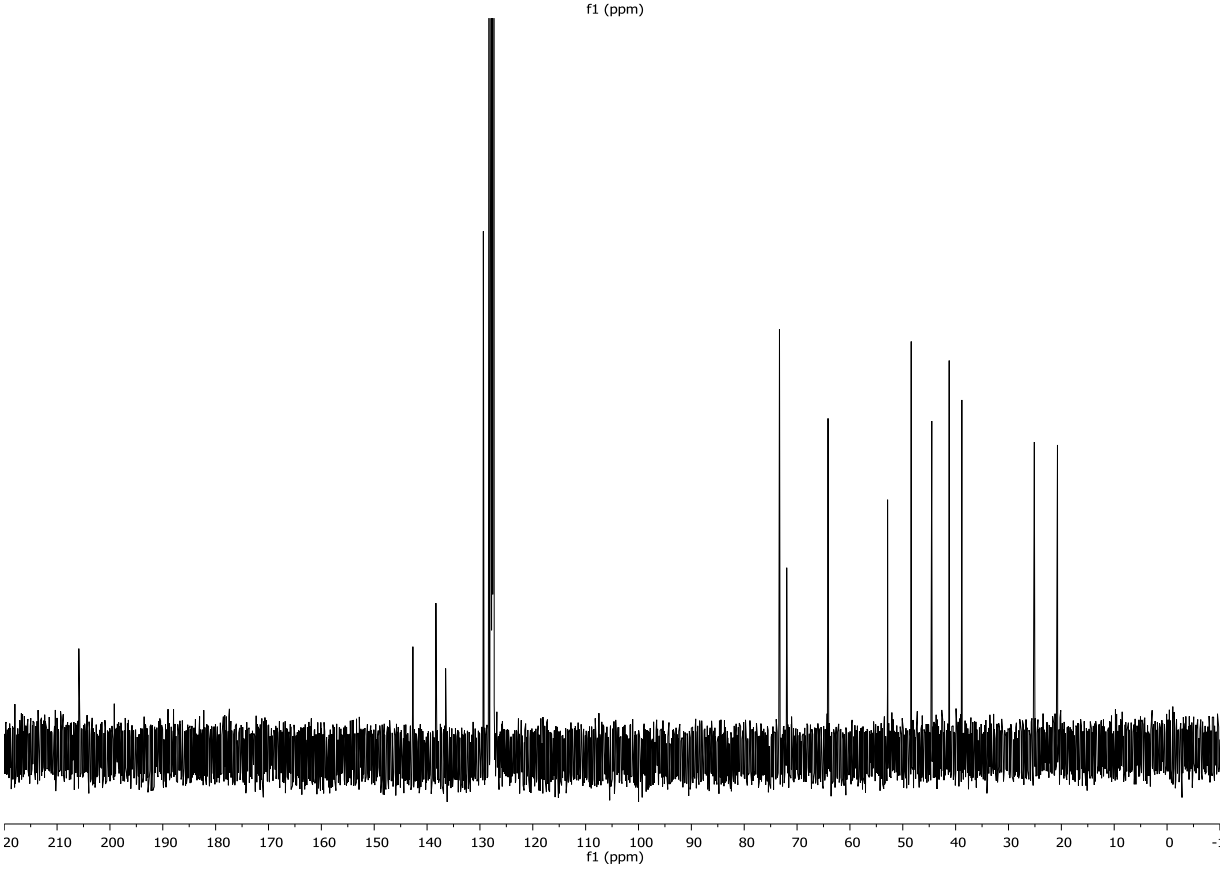


1-(Benzyloxy)-*N*-(cyclopropylmethyl)but-3-en-2-amine (6l)

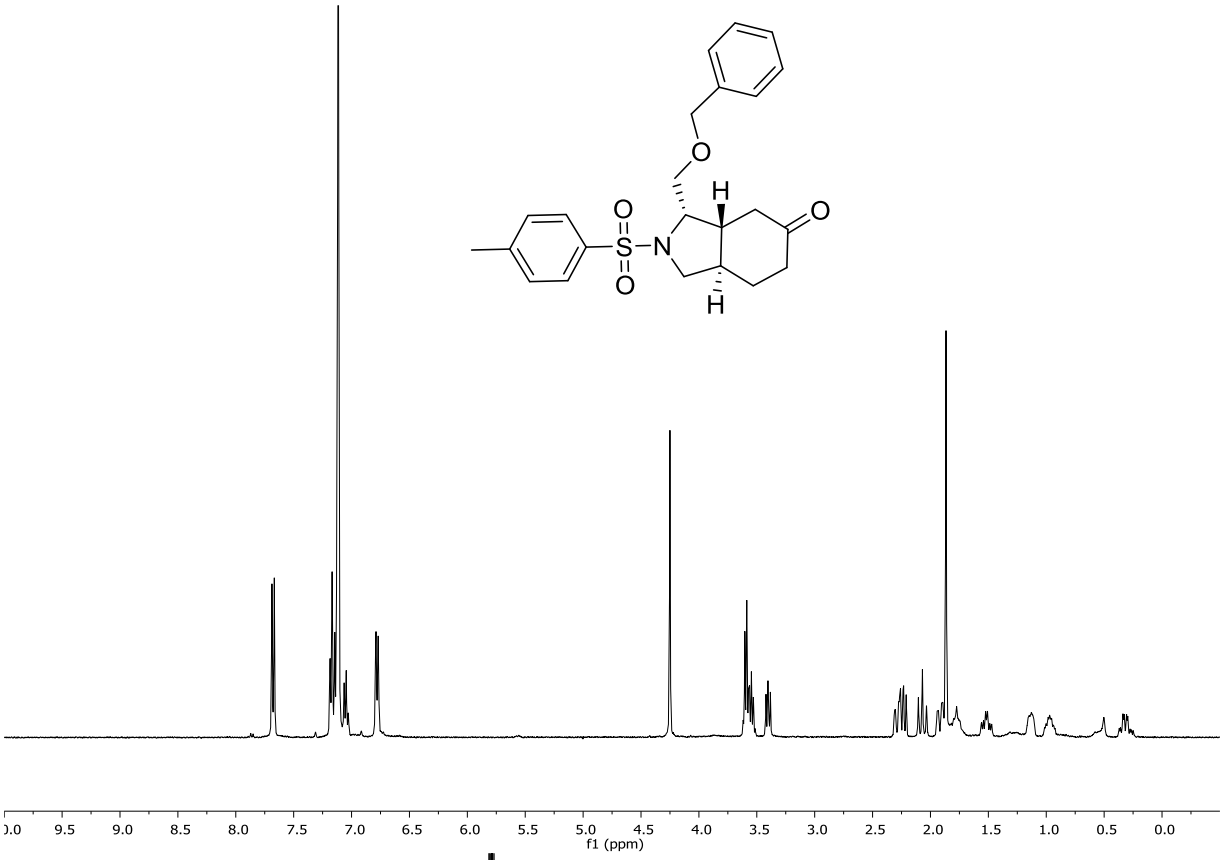


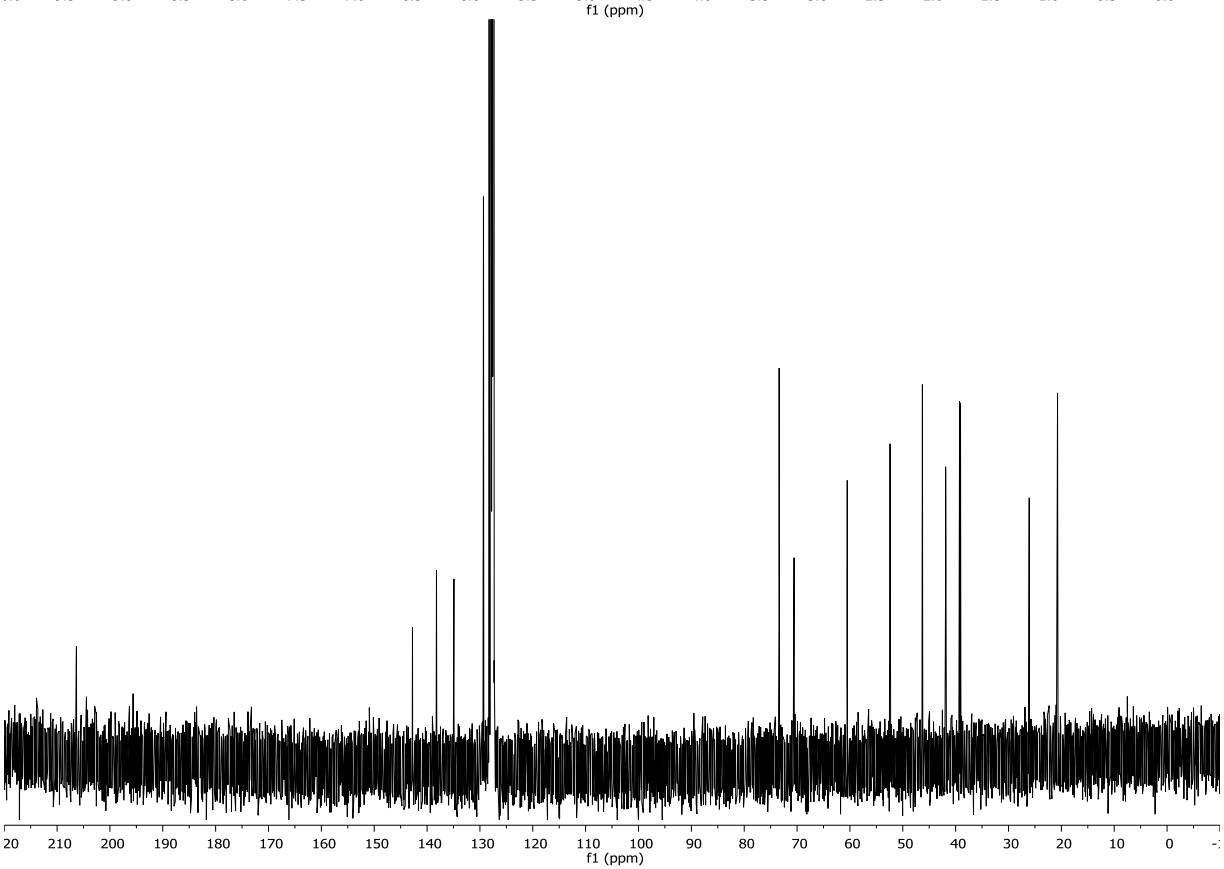
(3*R,3a*R**,7a*R**) -3-((Benzyloxy)methyl)-2-tosylhexahydro-1*H*-isoindol-5(6*H*)-one (8l-A)**



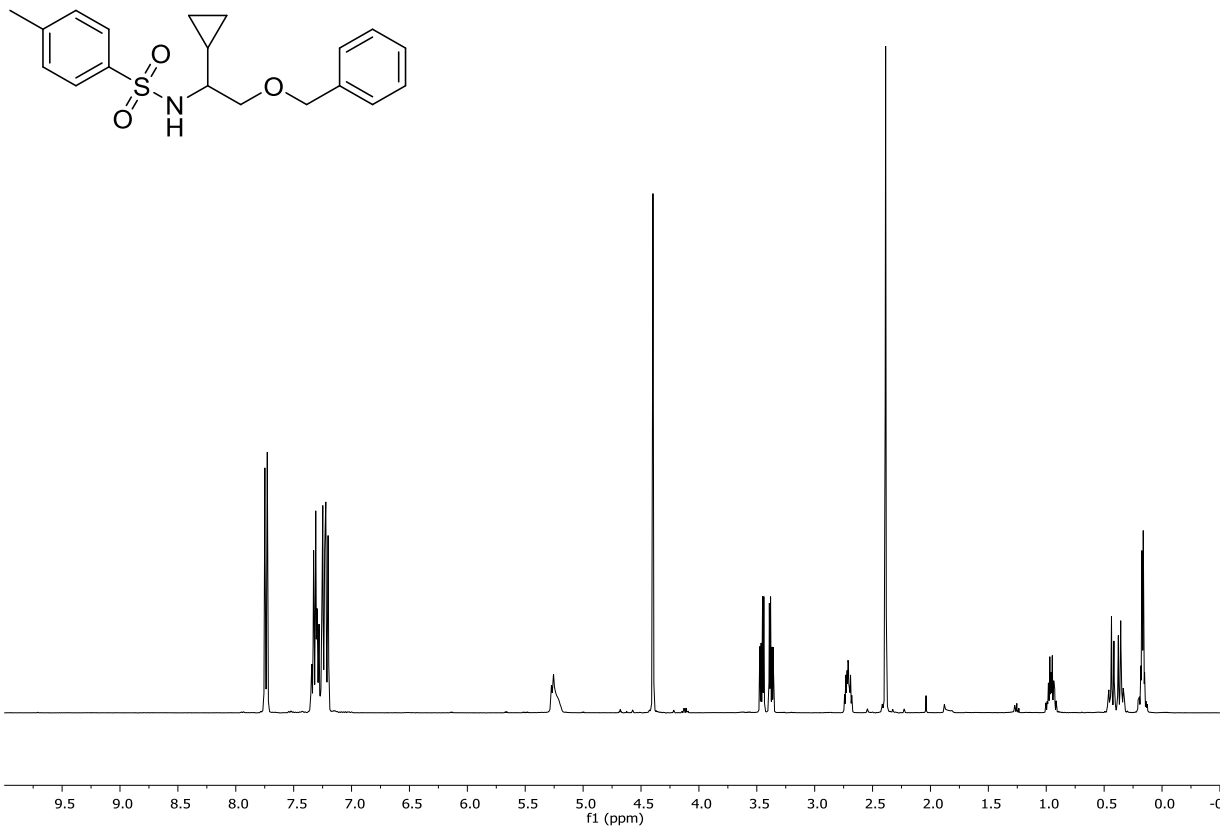


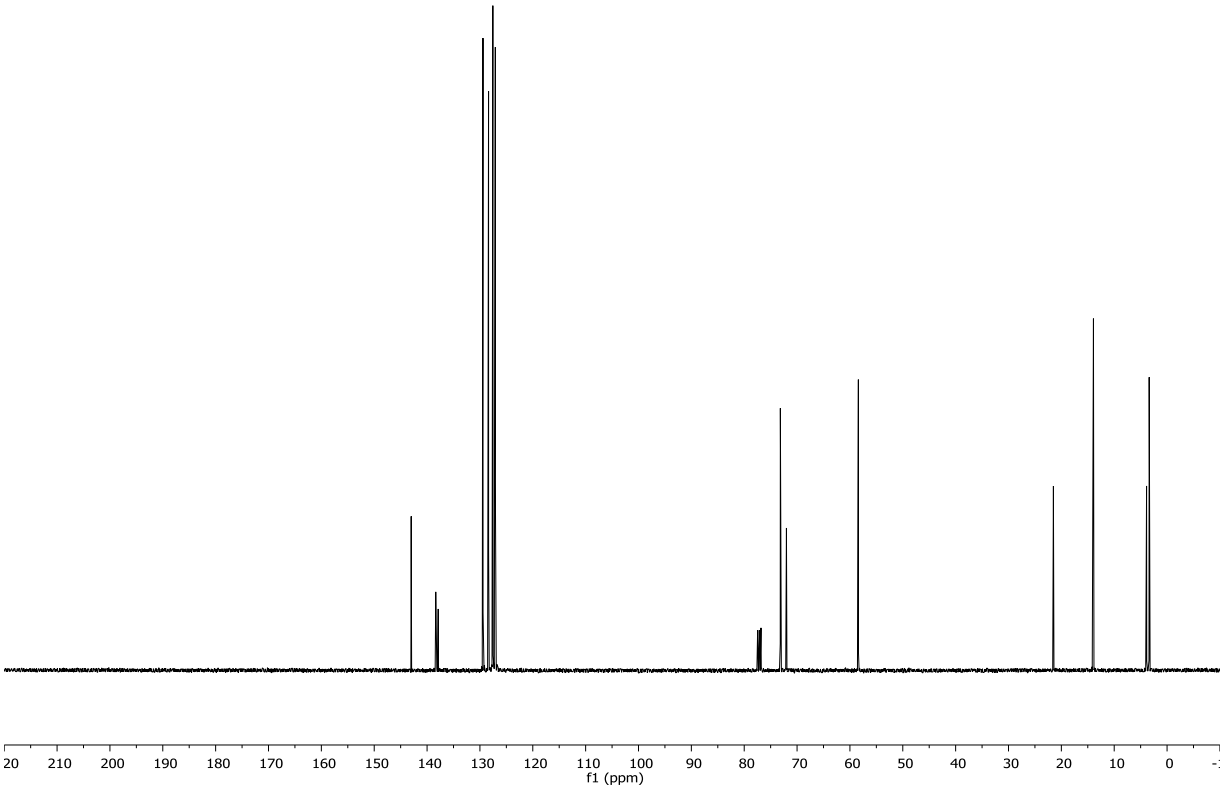
(3*S,3a*R**,7a*R**) -3-((Benzyloxy)methyl)-2-tosylhexahydro-1*H*-isoindol-5(6*H*)-one (8l-B)**



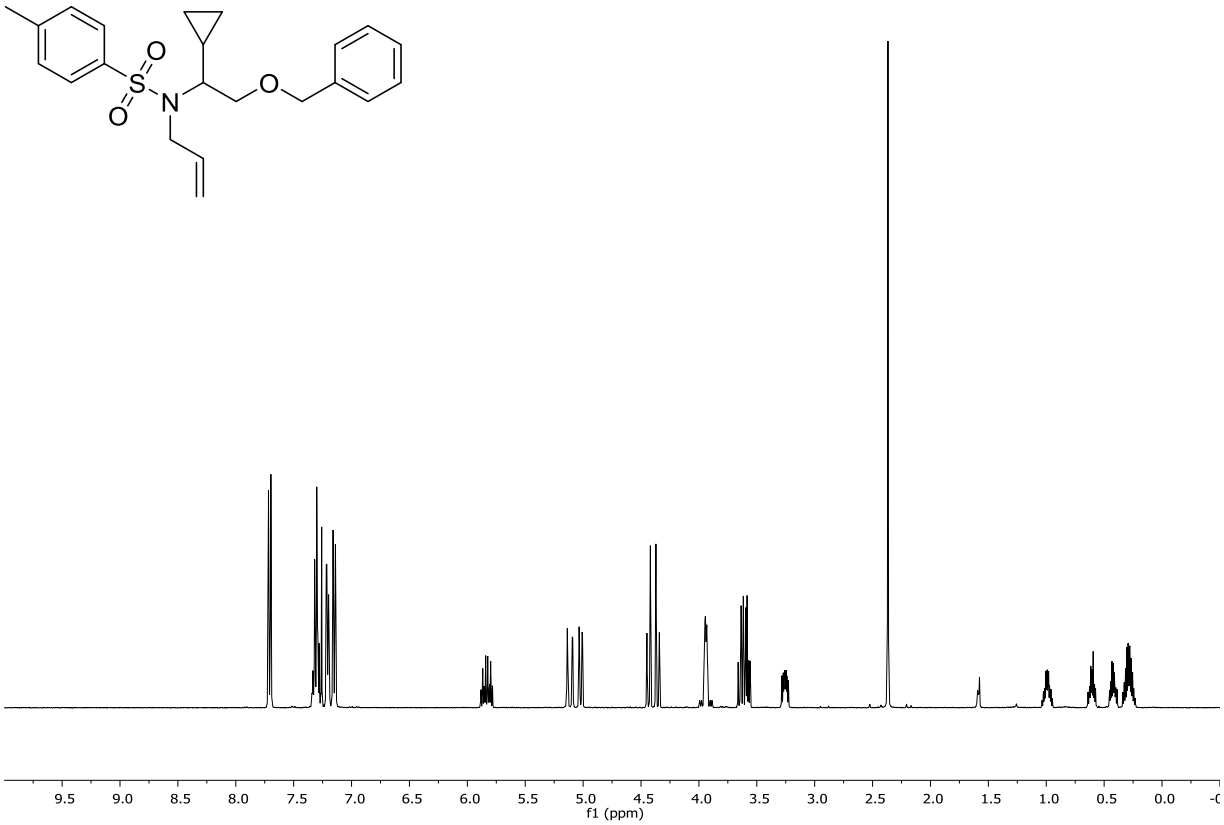


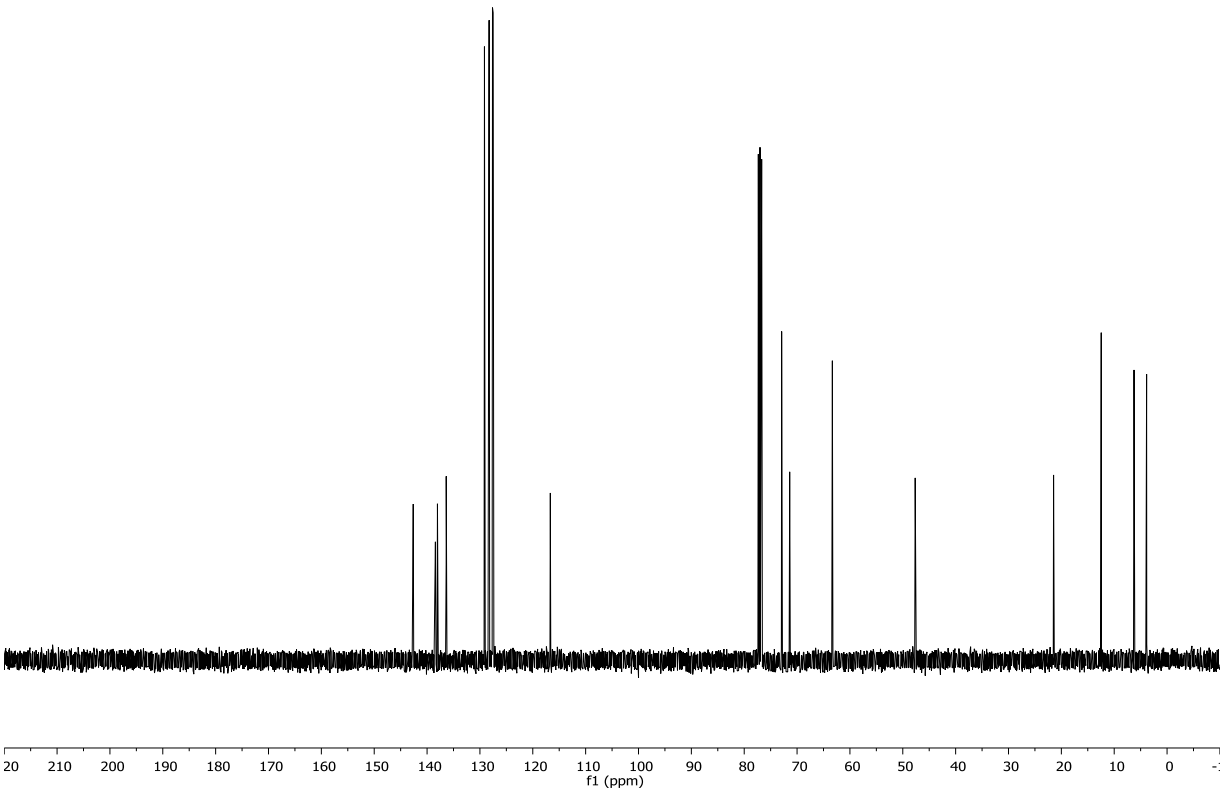
N-(2-(Benzyloxy)-1-cyclopropylethyl)-4-methylbenzenesulfonamide



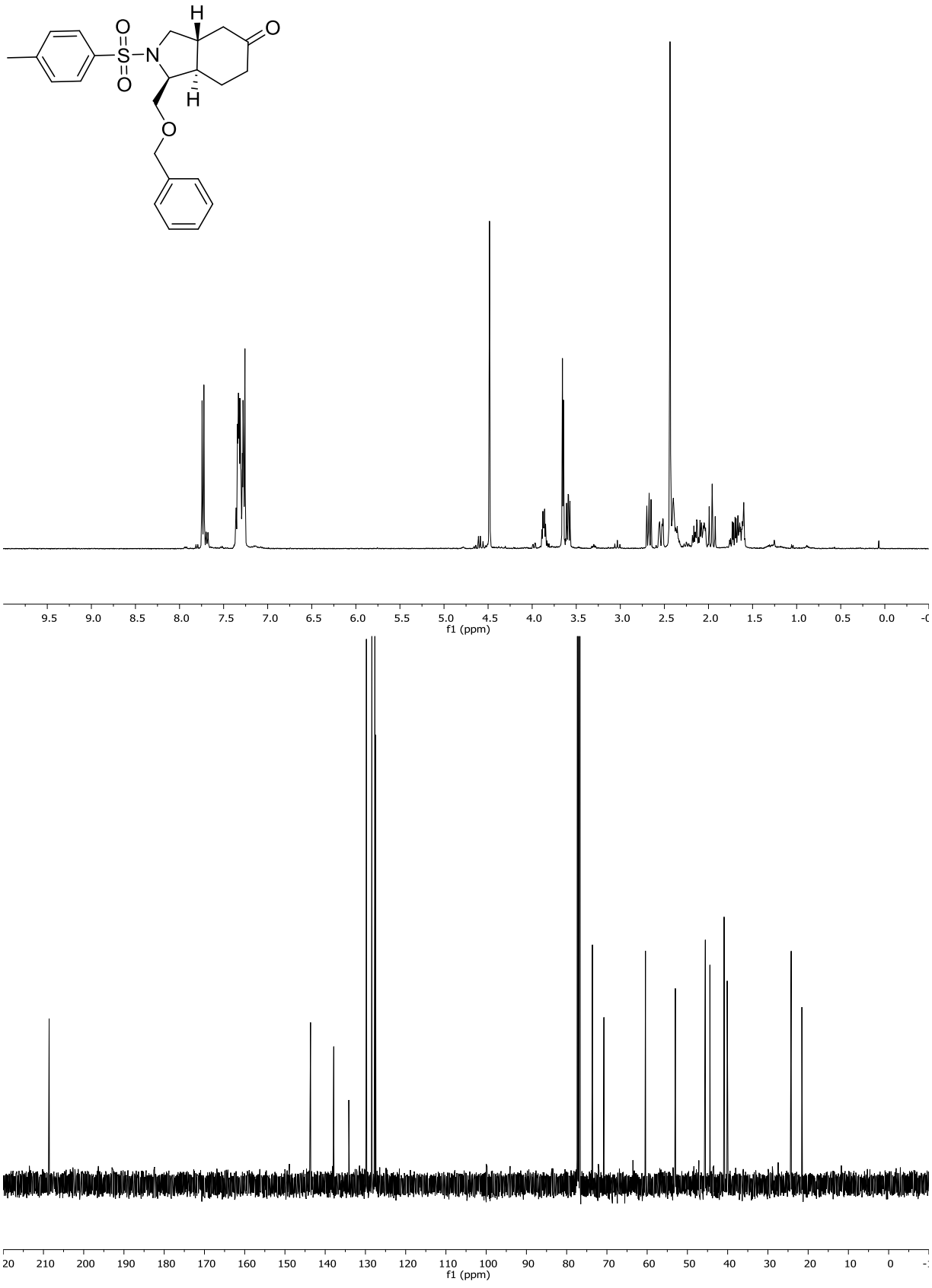


N-Allyl-*N*-(2-(benzyloxy)-1-cyclopropylethyl)-4-methylbenzenesulfonamide (6m)

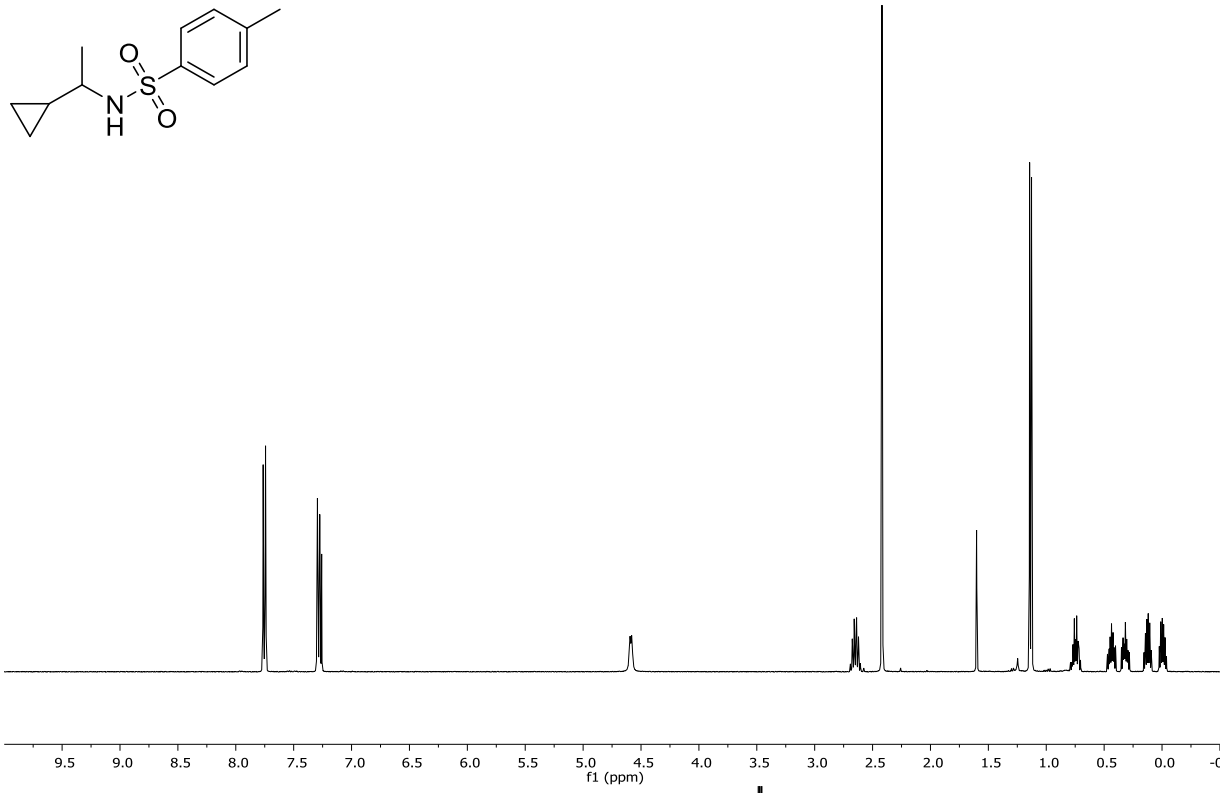


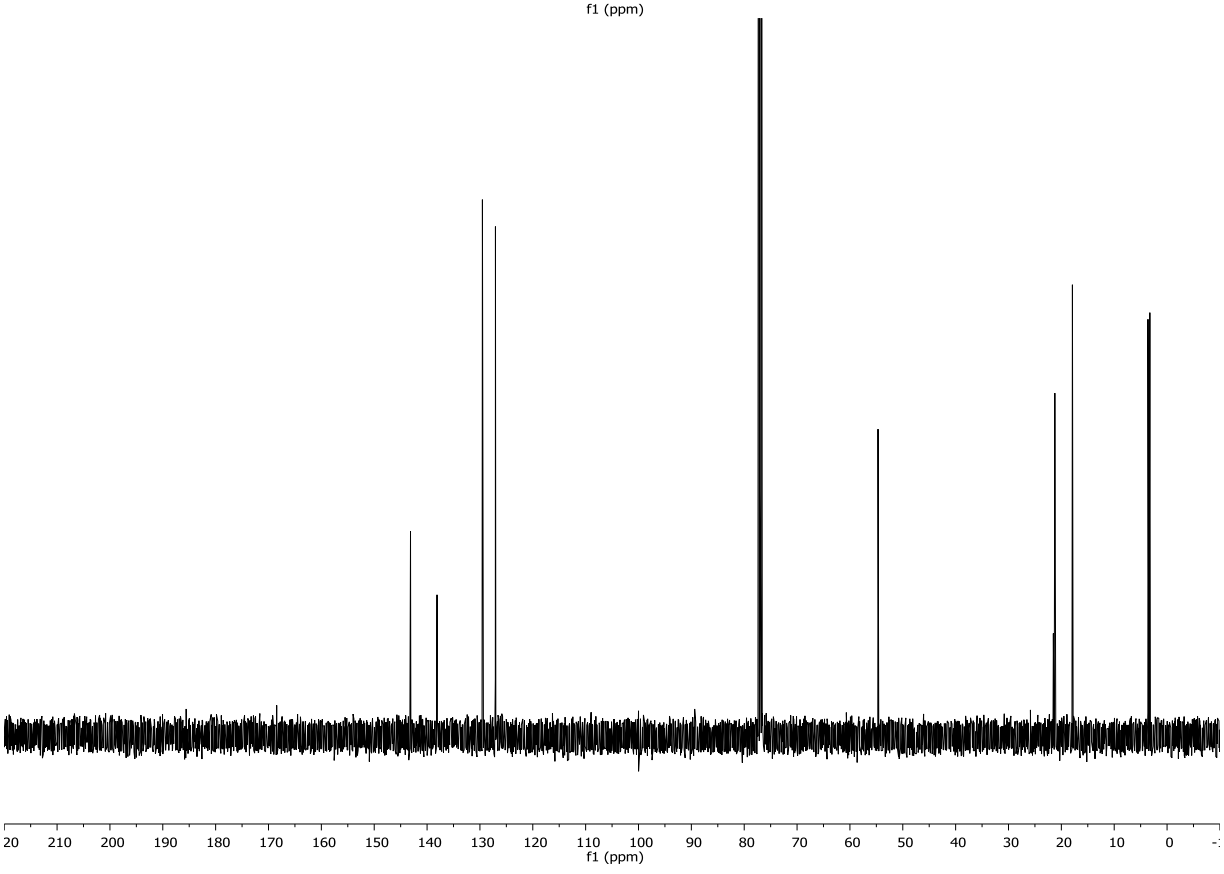


(1*S, 3a*R**, 7a*R**) and (1*R**,3a*R**,7a*R**)-1-((Benzyloxy)methyl)-2-tosylhexahydro-1*H*-isoindol-5(6*H*)-one (8m)**

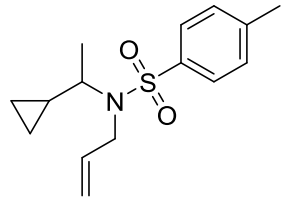


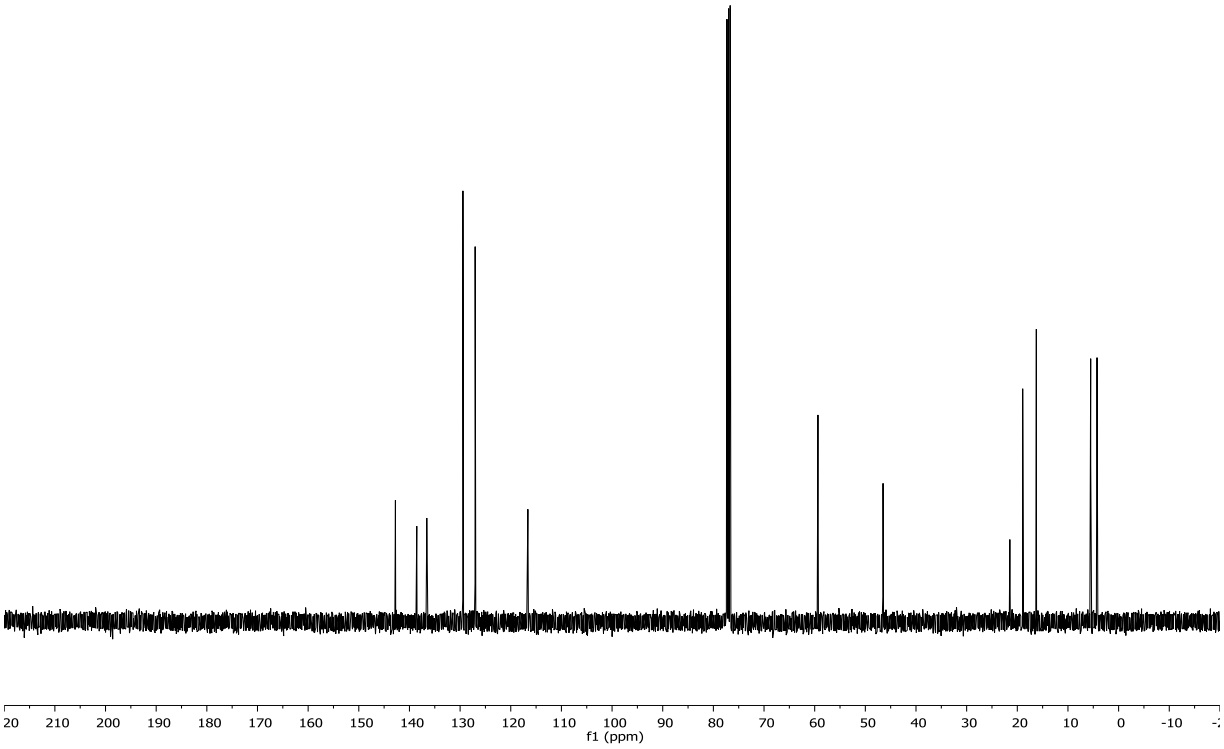
N-(1-Cyclopropylethyl)-4-methylbenzenesulfonamide



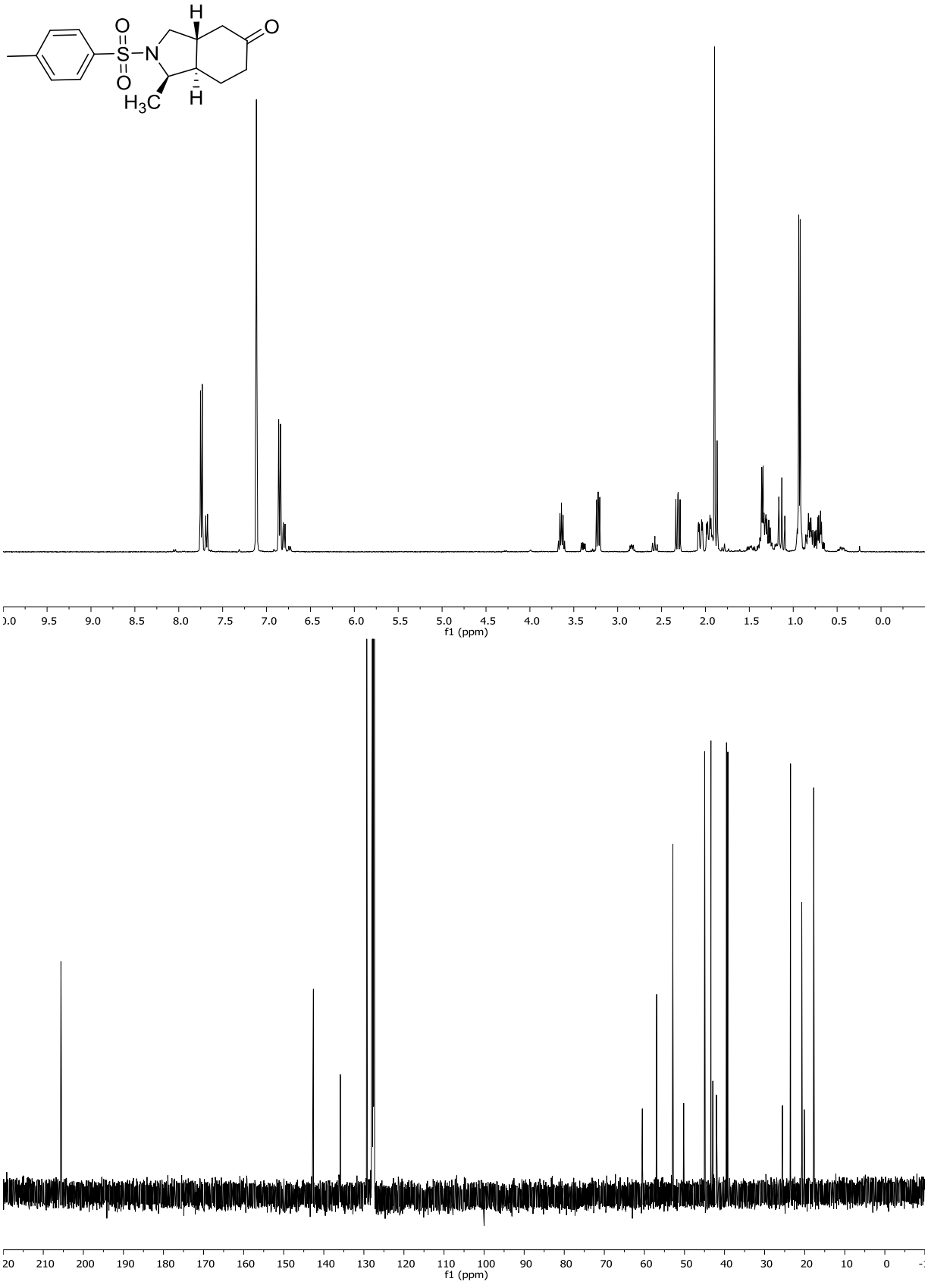


N-Allyl-*N*-(1-cyclopropylethyl)-4-methylbenzenesulfonamide (6n)

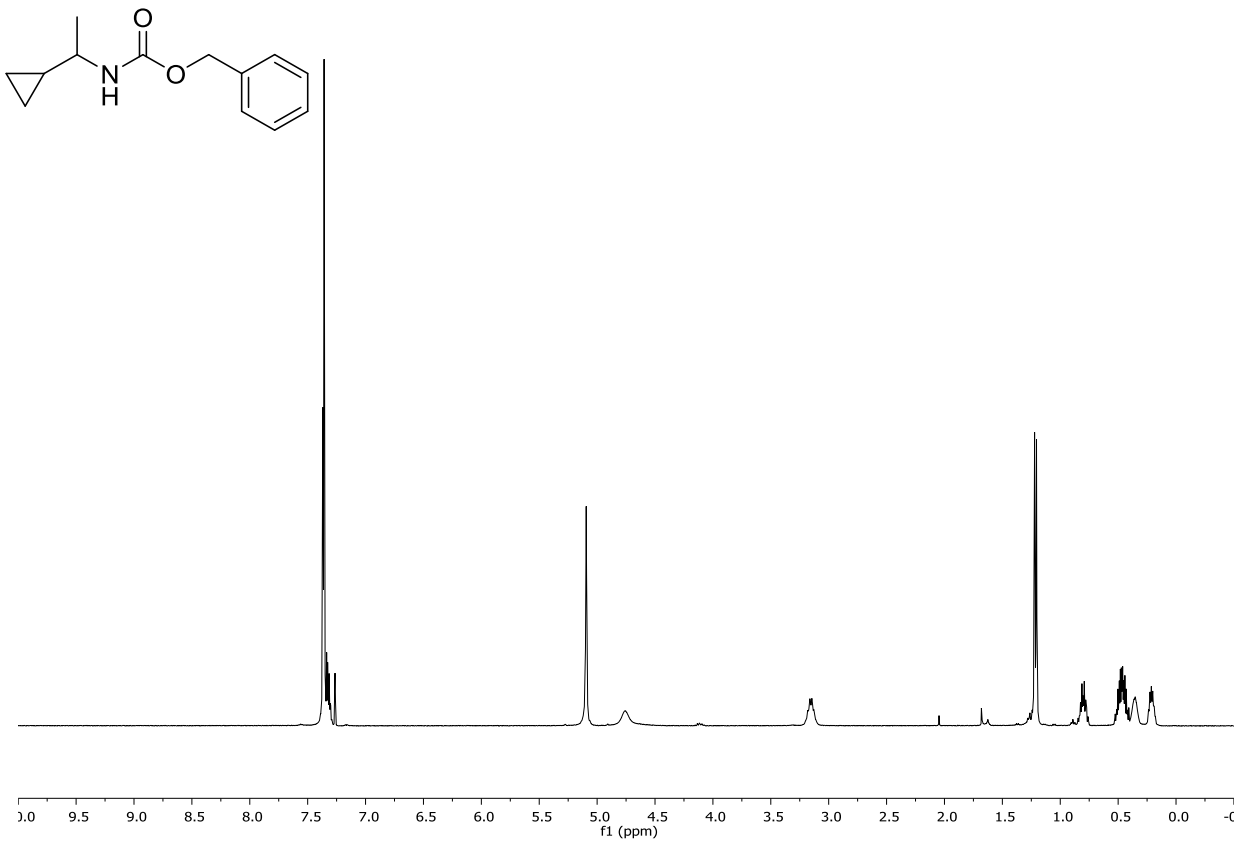


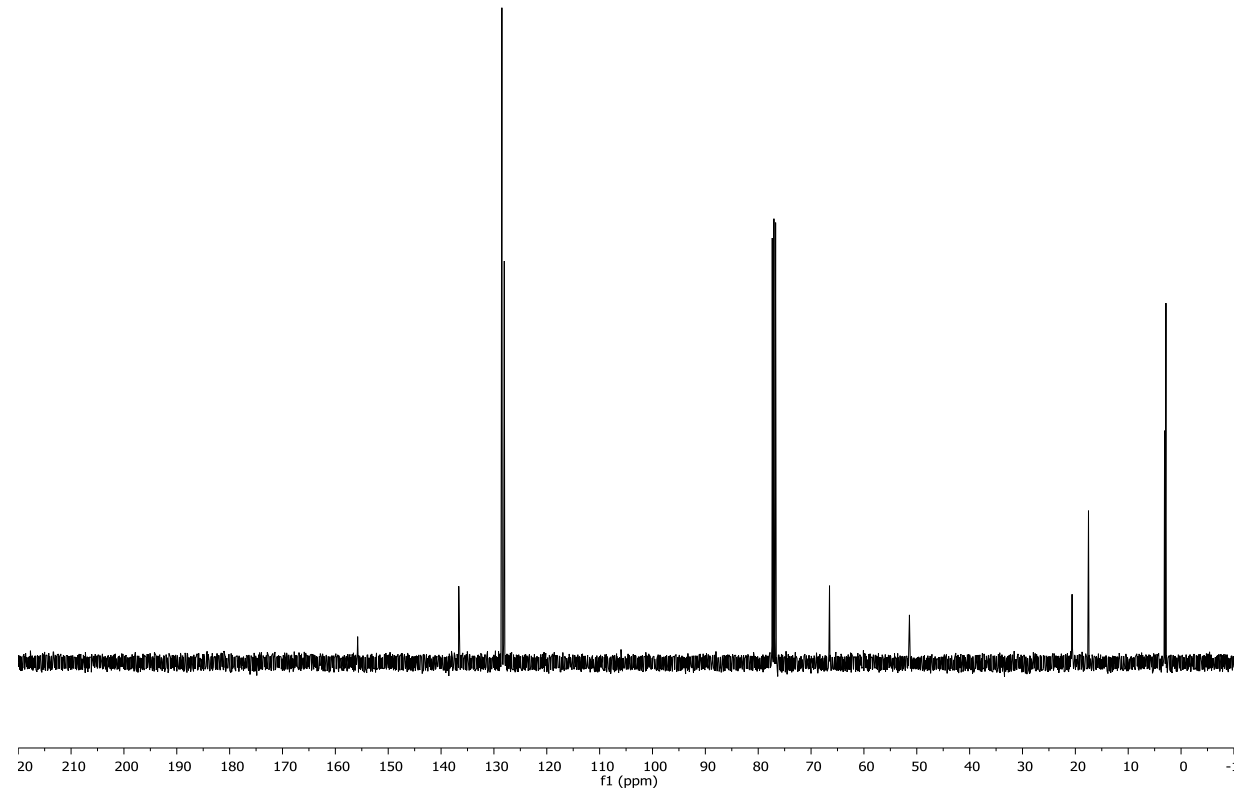


(1*R, 3a*R**, 7a*R**) and (1*S**, 3a*R**, 7a*R**)-1-Methyl-2-tosylhexahydro-1*H*-isoindol-5(6*H*)-one (8n)**

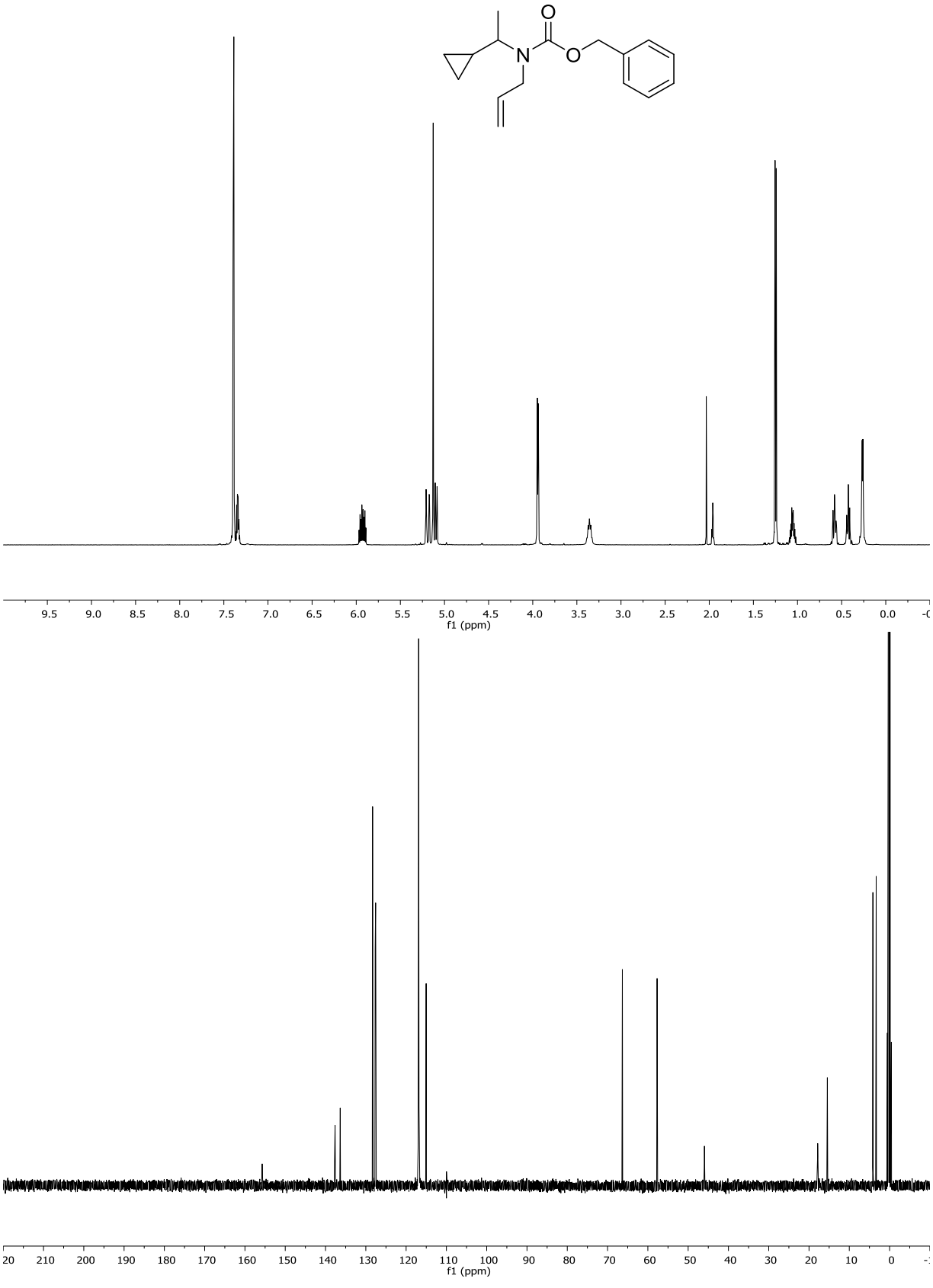


Benzyl (1-cyclopropylethyl)carbamate

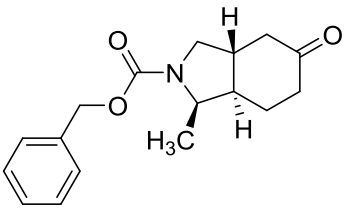


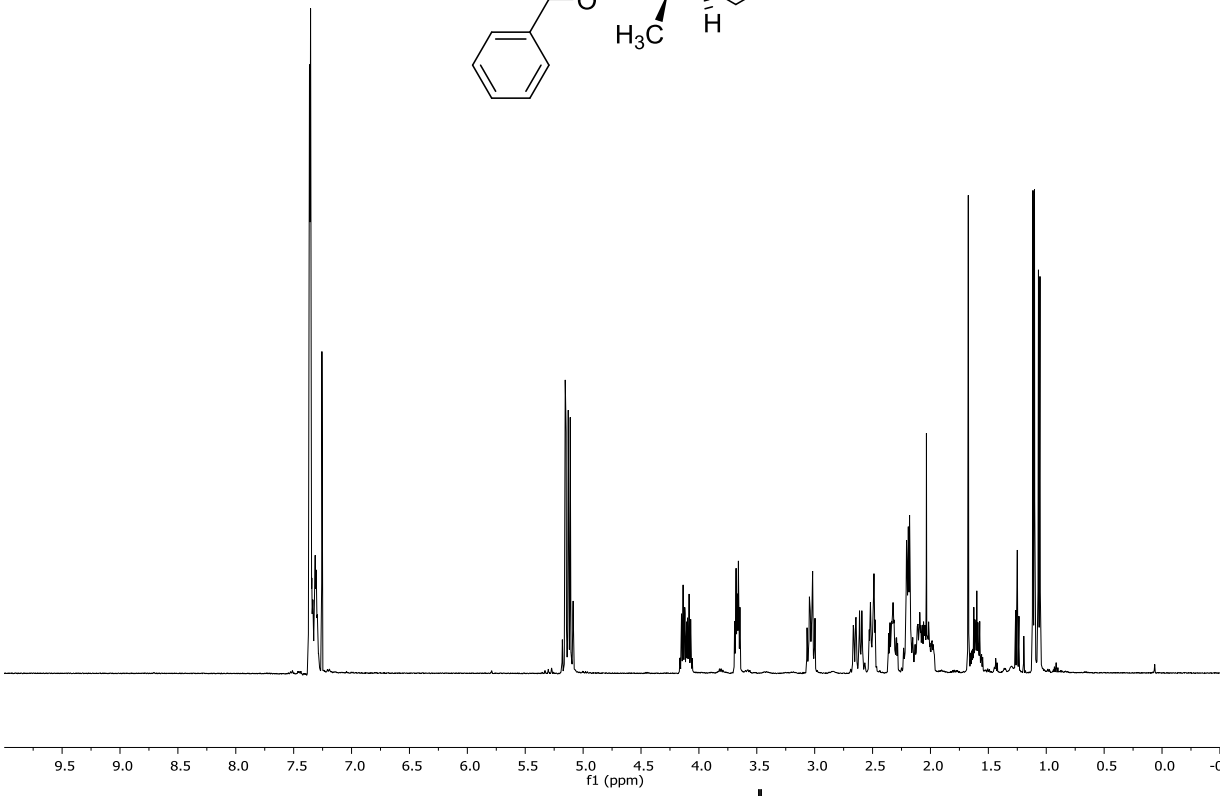


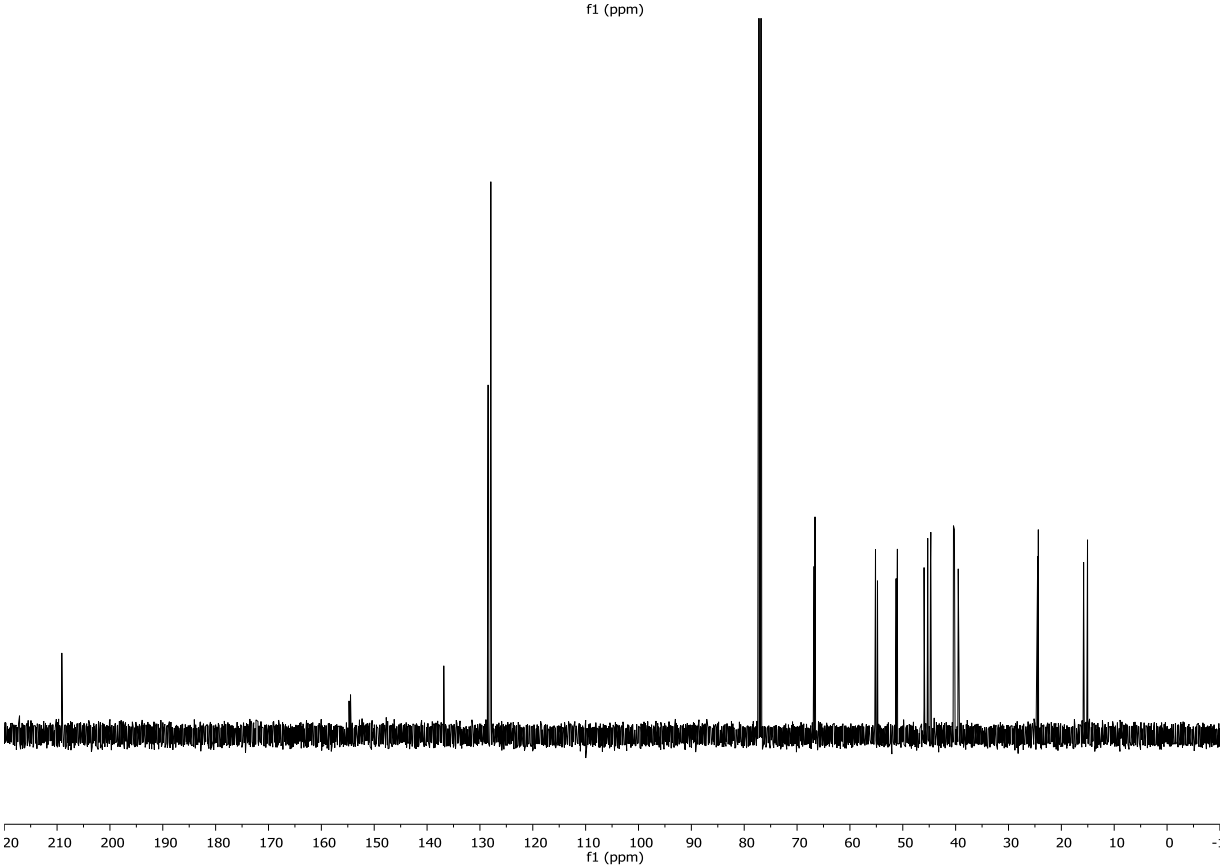
Benzyl allyl(1-cyclopropylethyl)carbamate (6o)



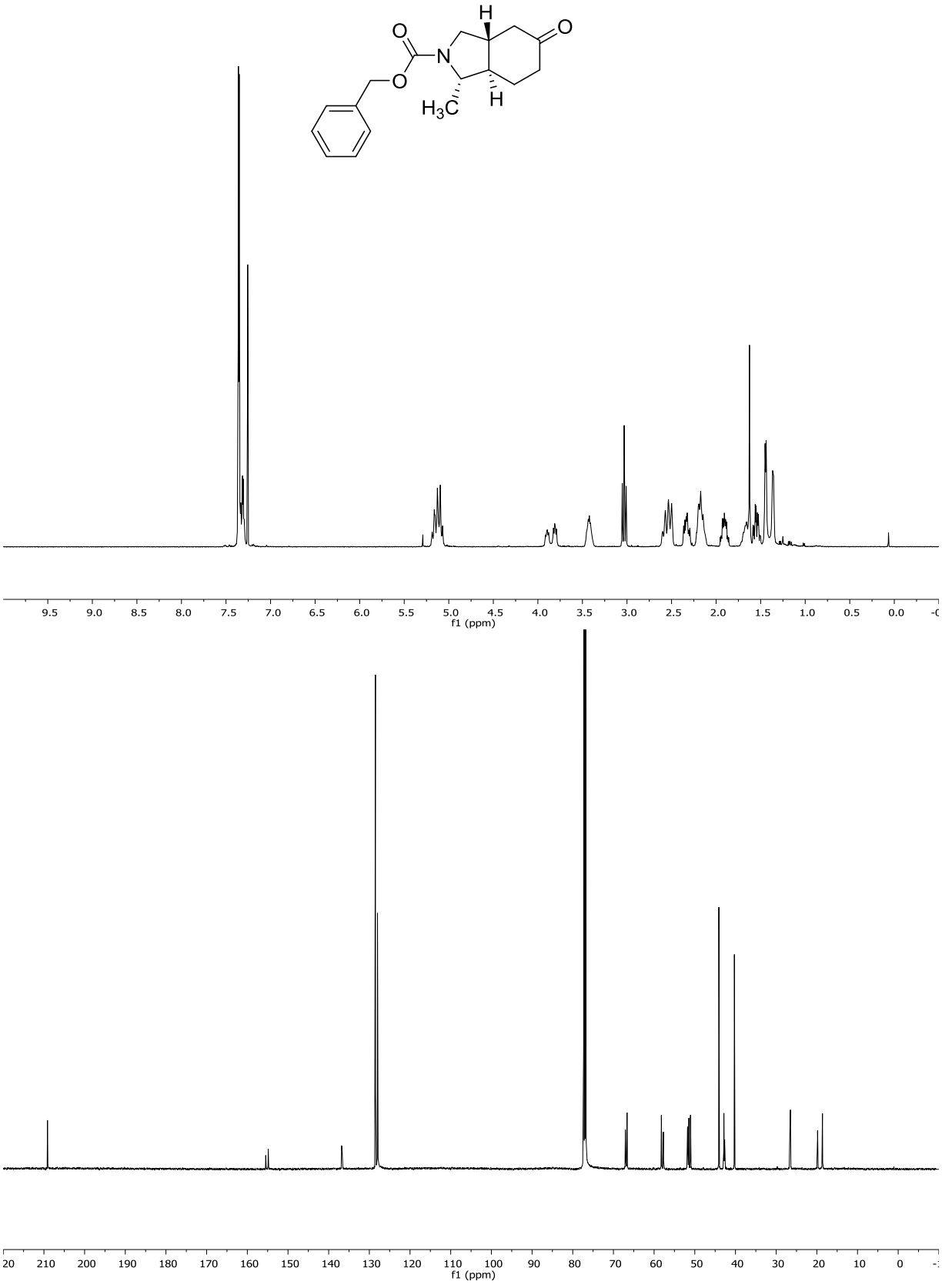
(1*R, 3a*R**, 7a*R**)-Benzyl 1-methyl-5-oxohexahydro-1*H*-isoindole-2(3*H*)-carboxylate (8o-A)**



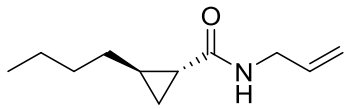


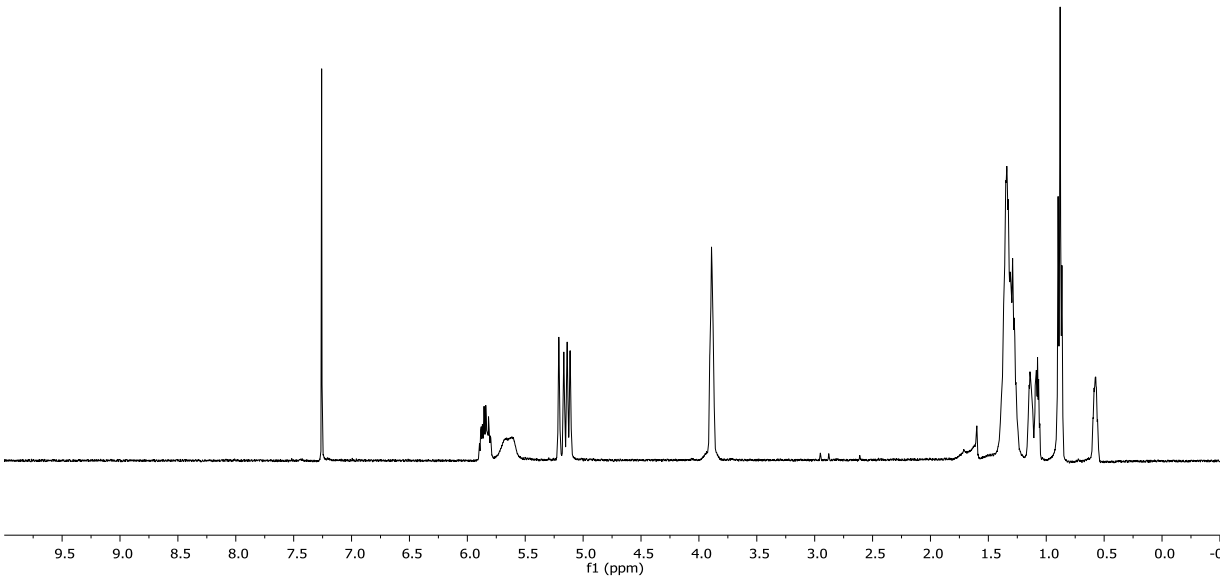


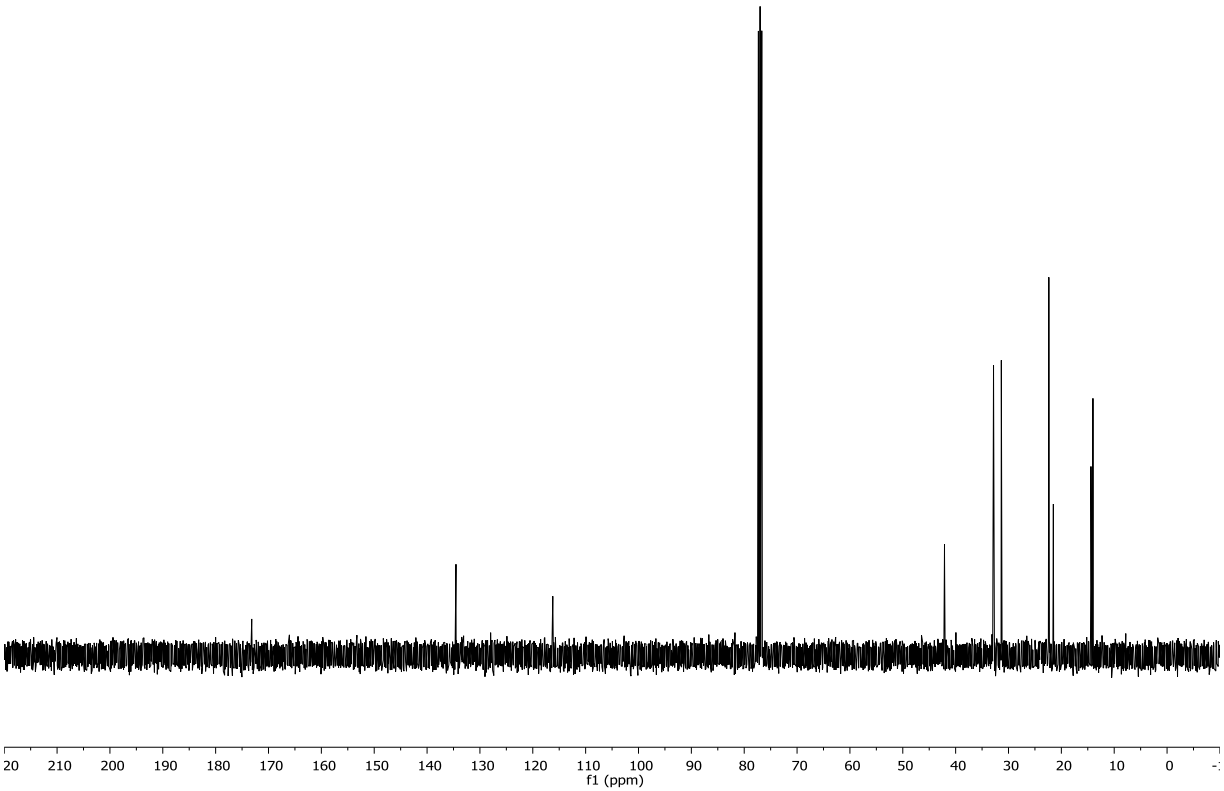
(1*S, 3a*R**, 7a*R**)-Benzyl 1-methyl-5-oxohexahydro-1*H*-isoindole-2(3*H*)-carboxylate (8o-B)**



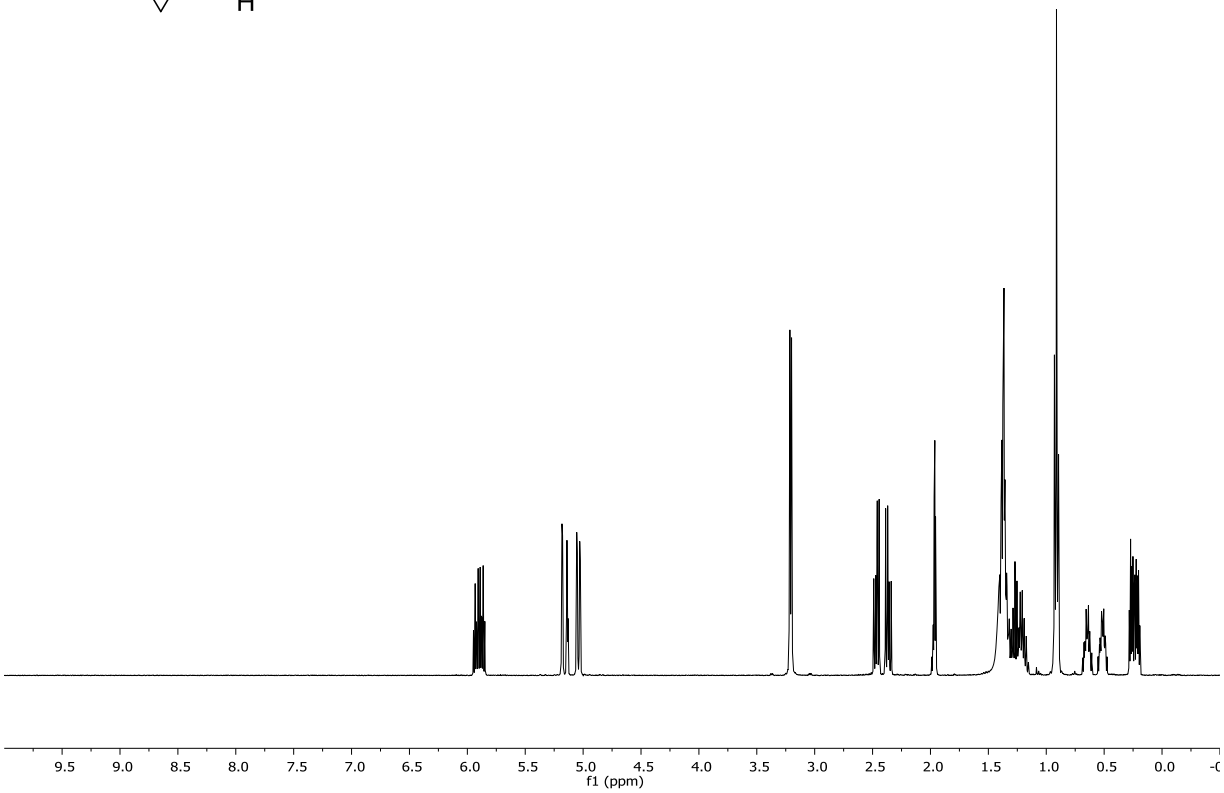
(1*S, 2*S**)-*N*-Allyl-2-butylcyclopropane-1-carboxamide**

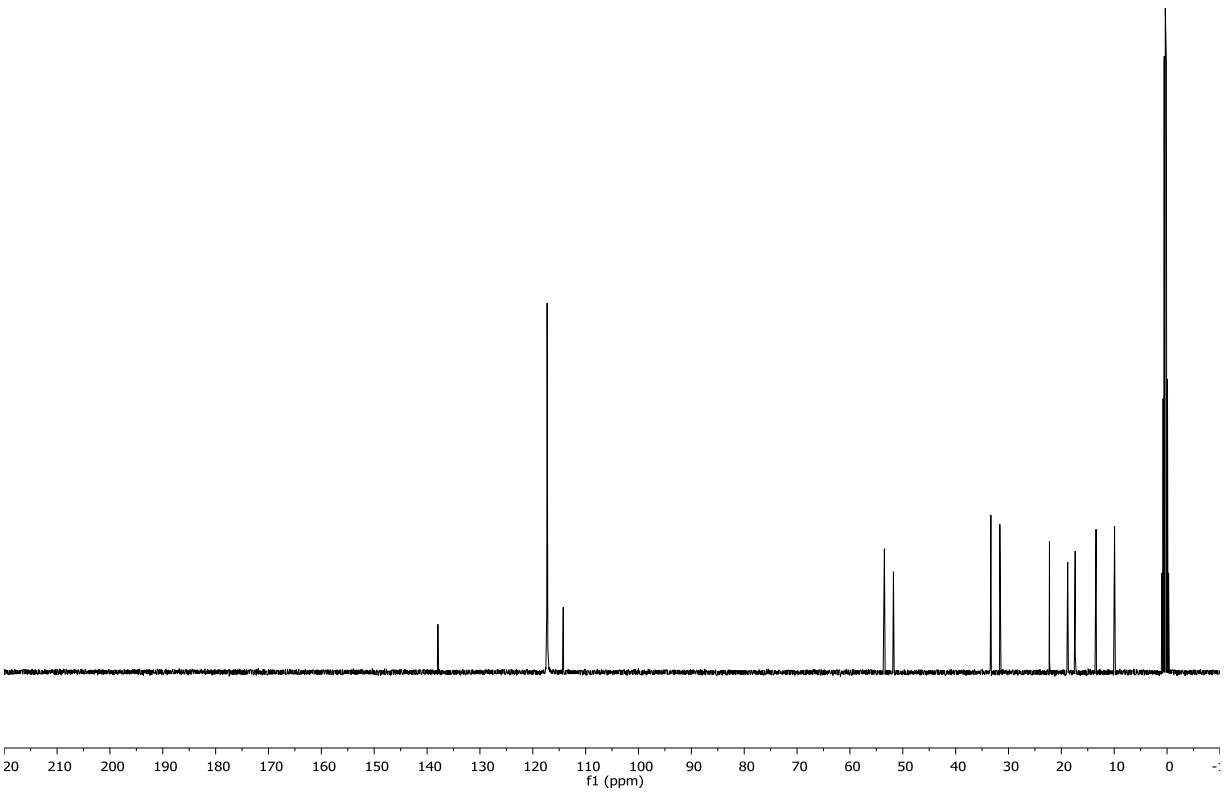




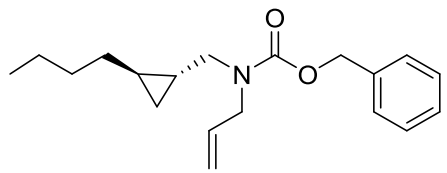


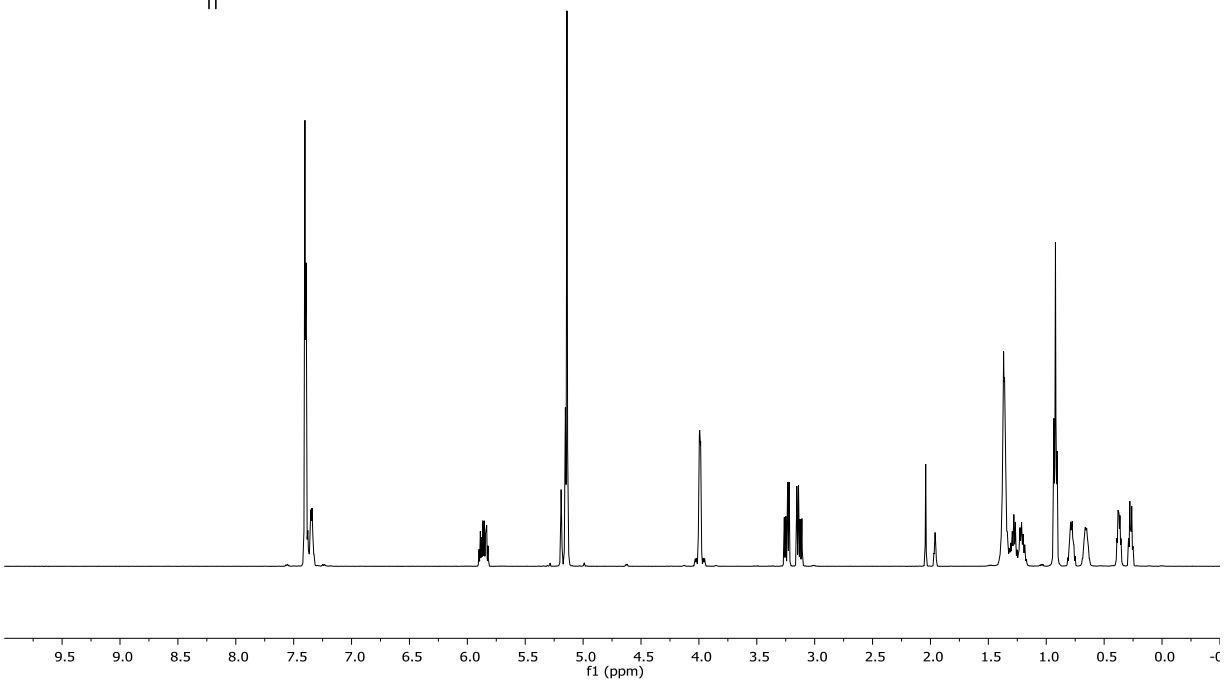
(1*S, 2*S**)-*N*-(2-Butylcyclopropyl)methyl)prop-2-en-1-amine**

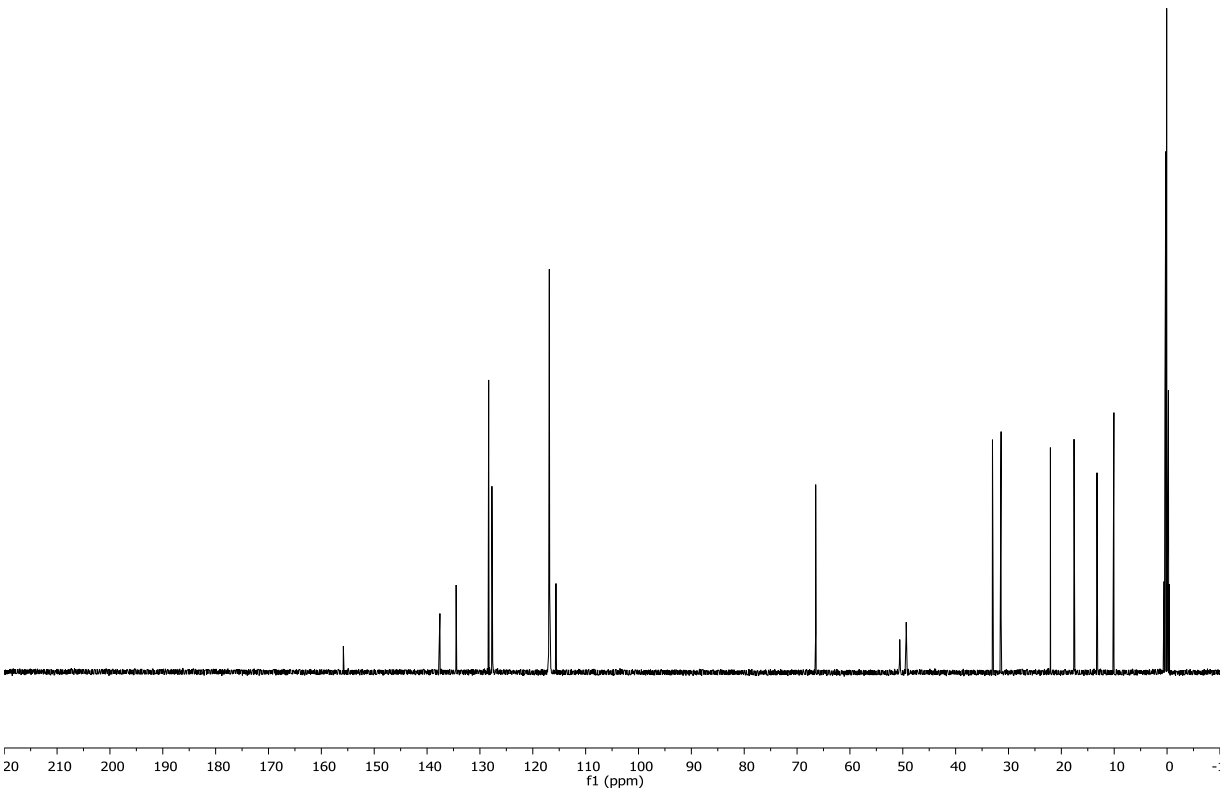




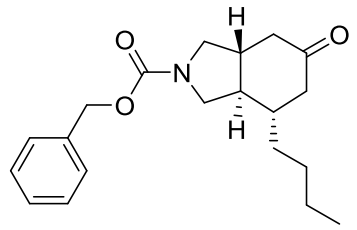
(1*S, 2*S**)-Benzyl allyl((-2-butylcyclopropyl)methyl)carbamate (6p)**

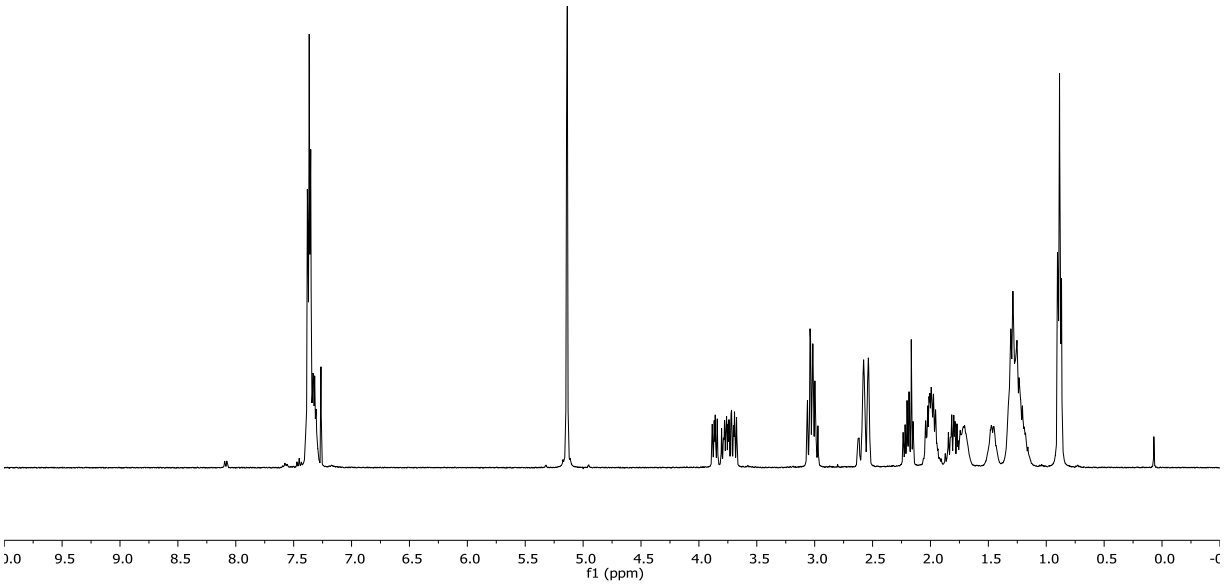


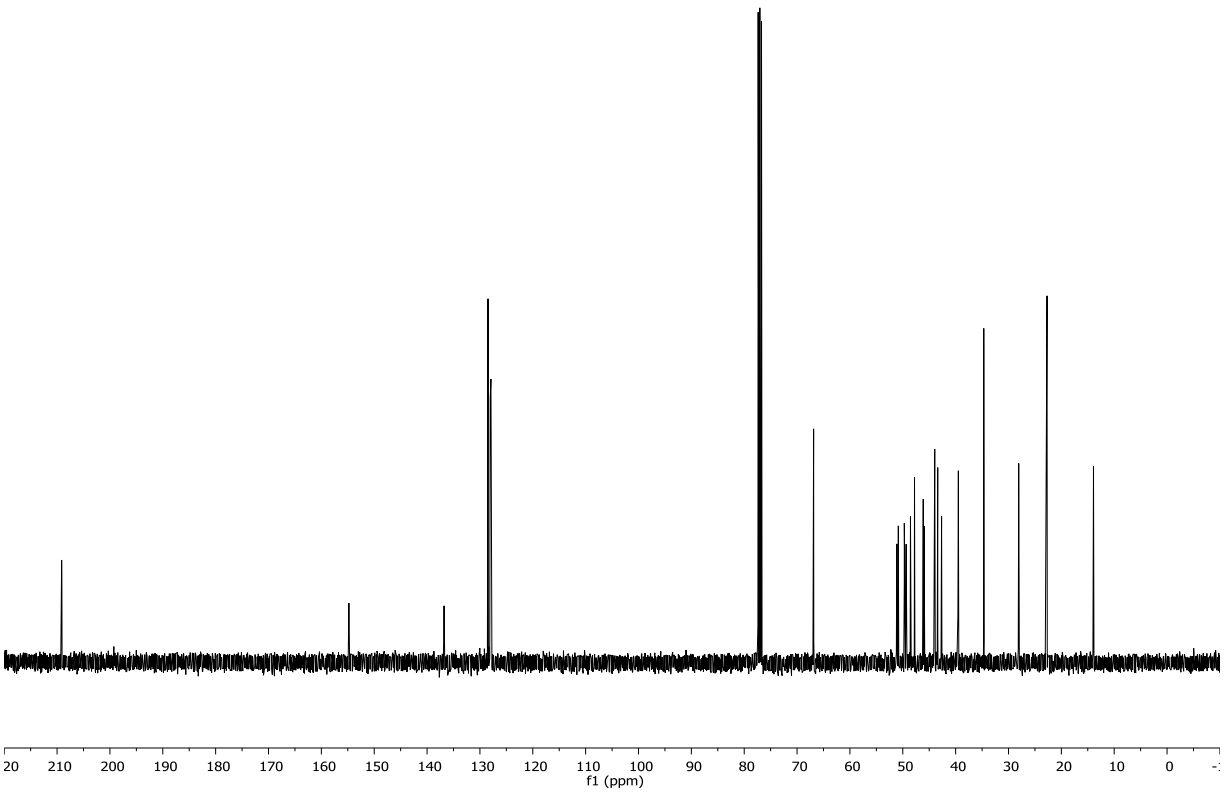




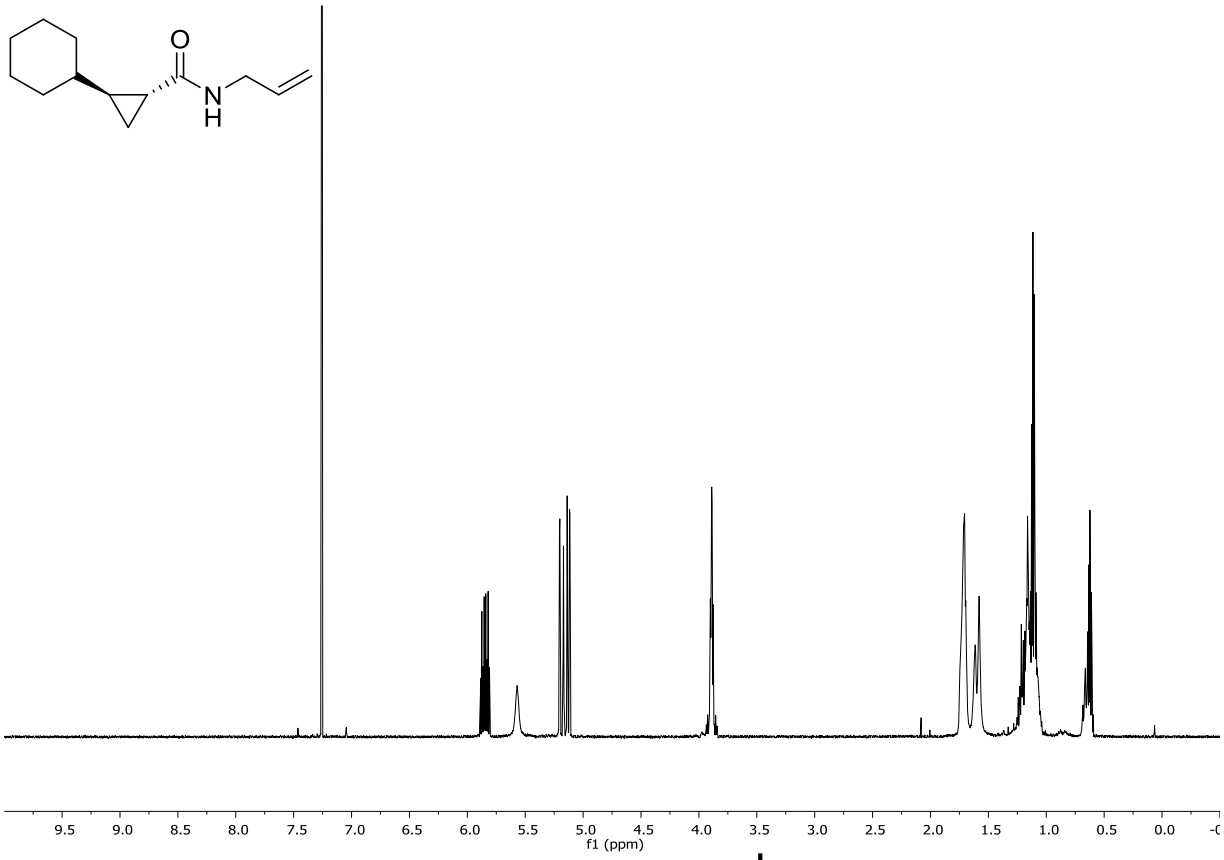
(3a*R, 4*S**, 7a*R**)-Benzyl-4-butyl-6-oxooctahydro-2*H*-isoindole-2-carboxylate (8p)**

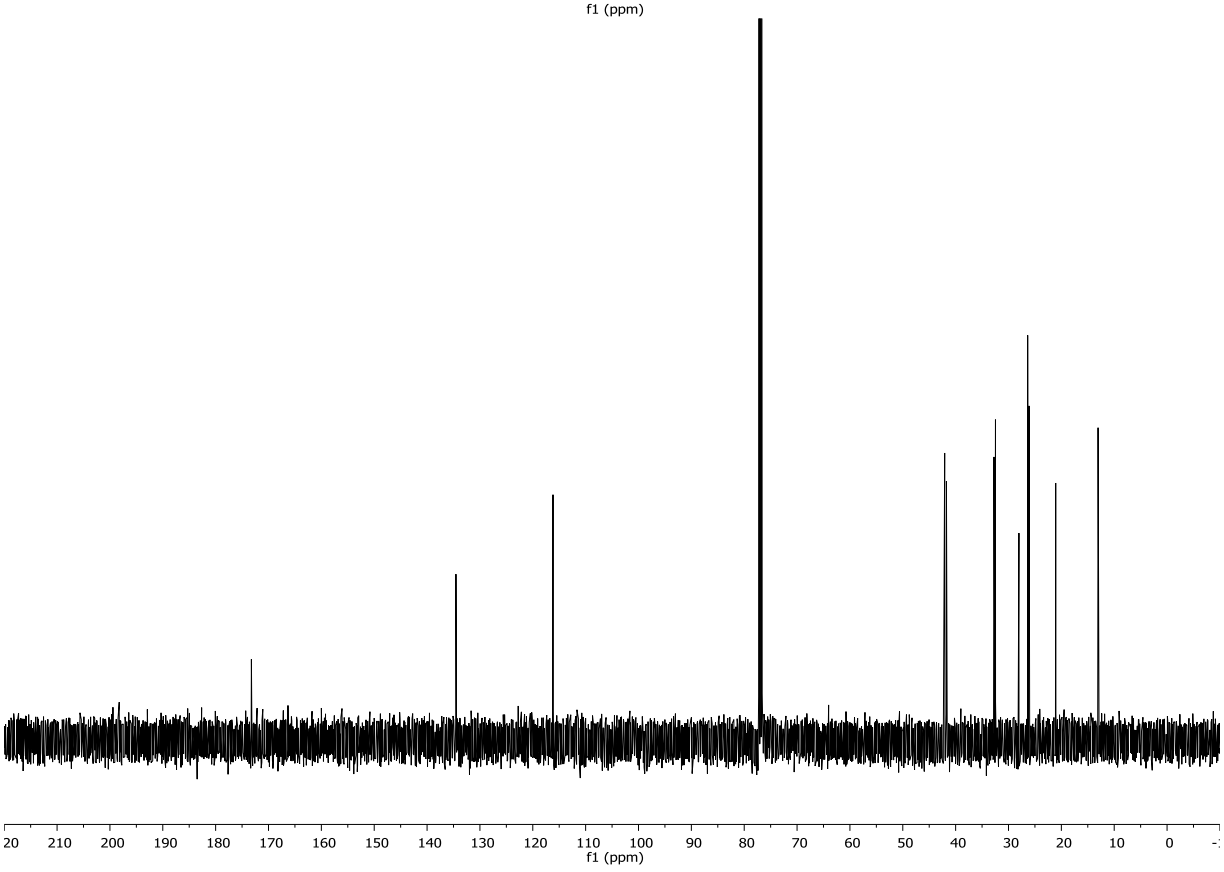




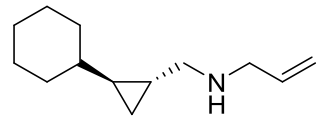


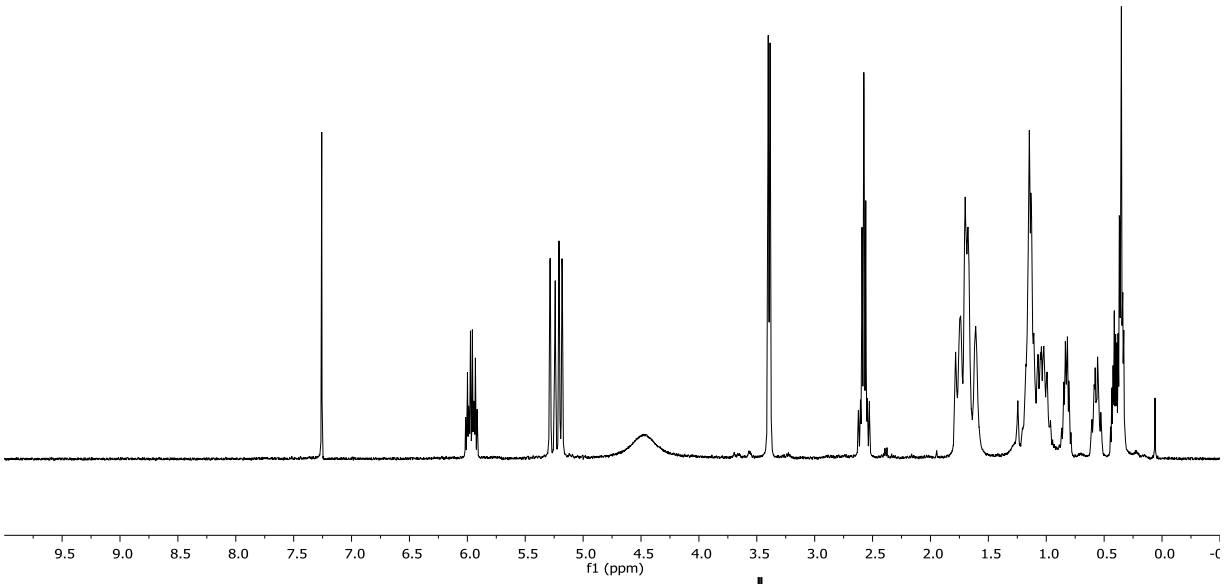
(1*R, 2*S**)-*N*-Allyl-2-cyclohexylcyclopropanecarboxamide**

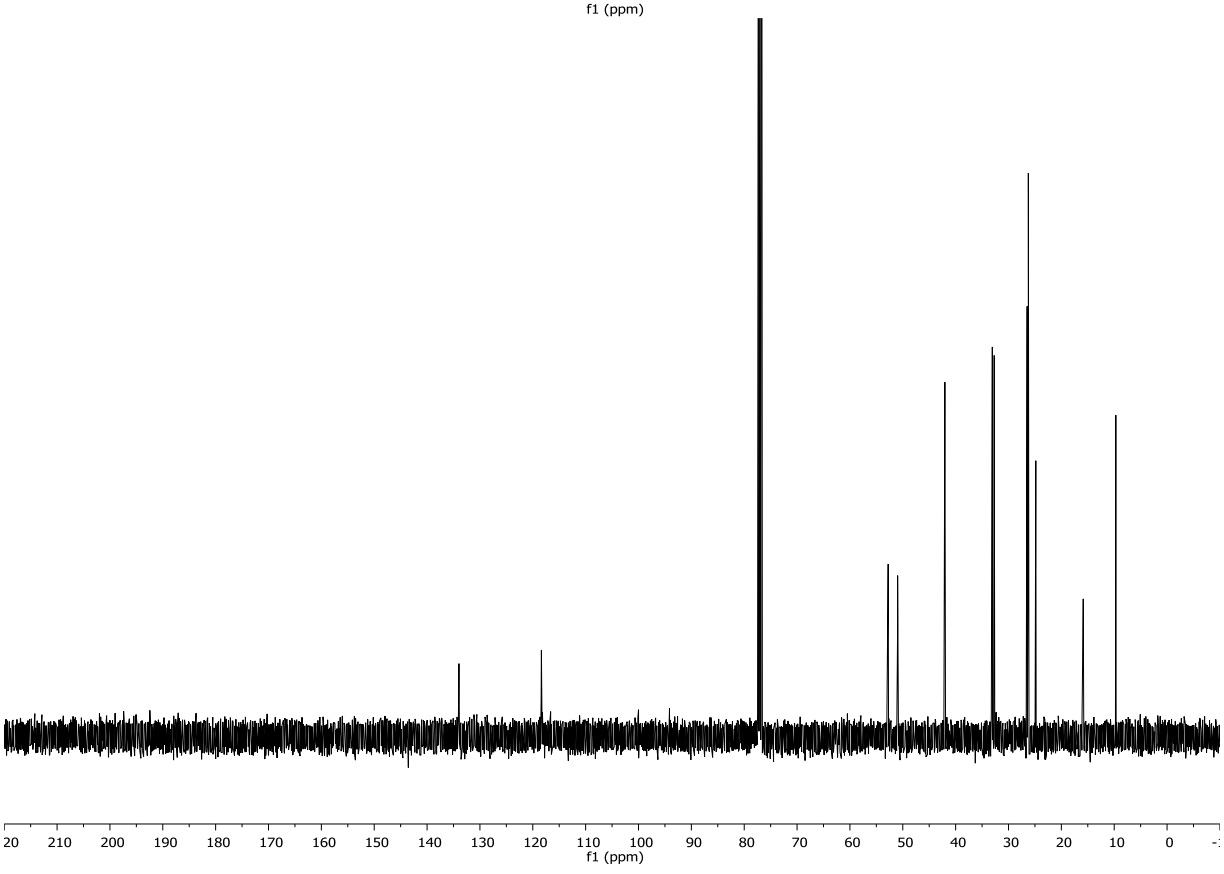




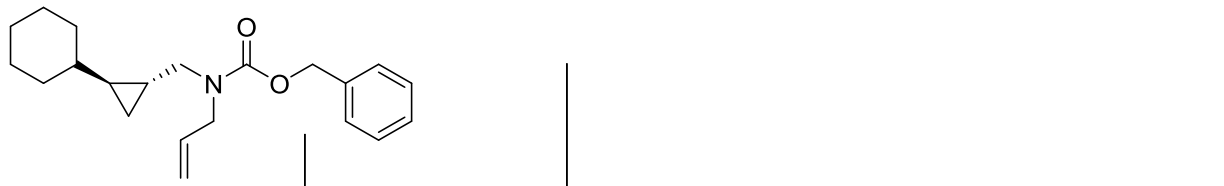
(1*R, 2*S**)-*N*-((-2-Cyclohexylcyclopropyl)methyl)prop-2-en-1-amine**

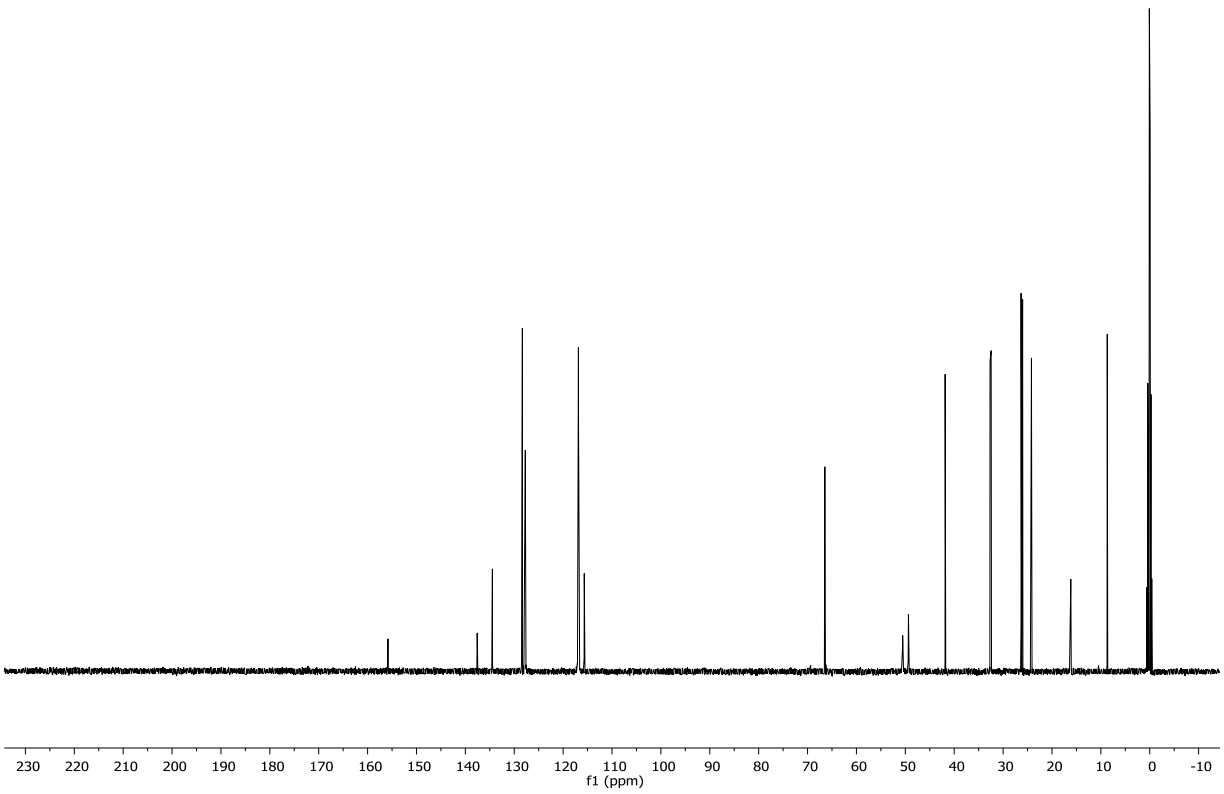




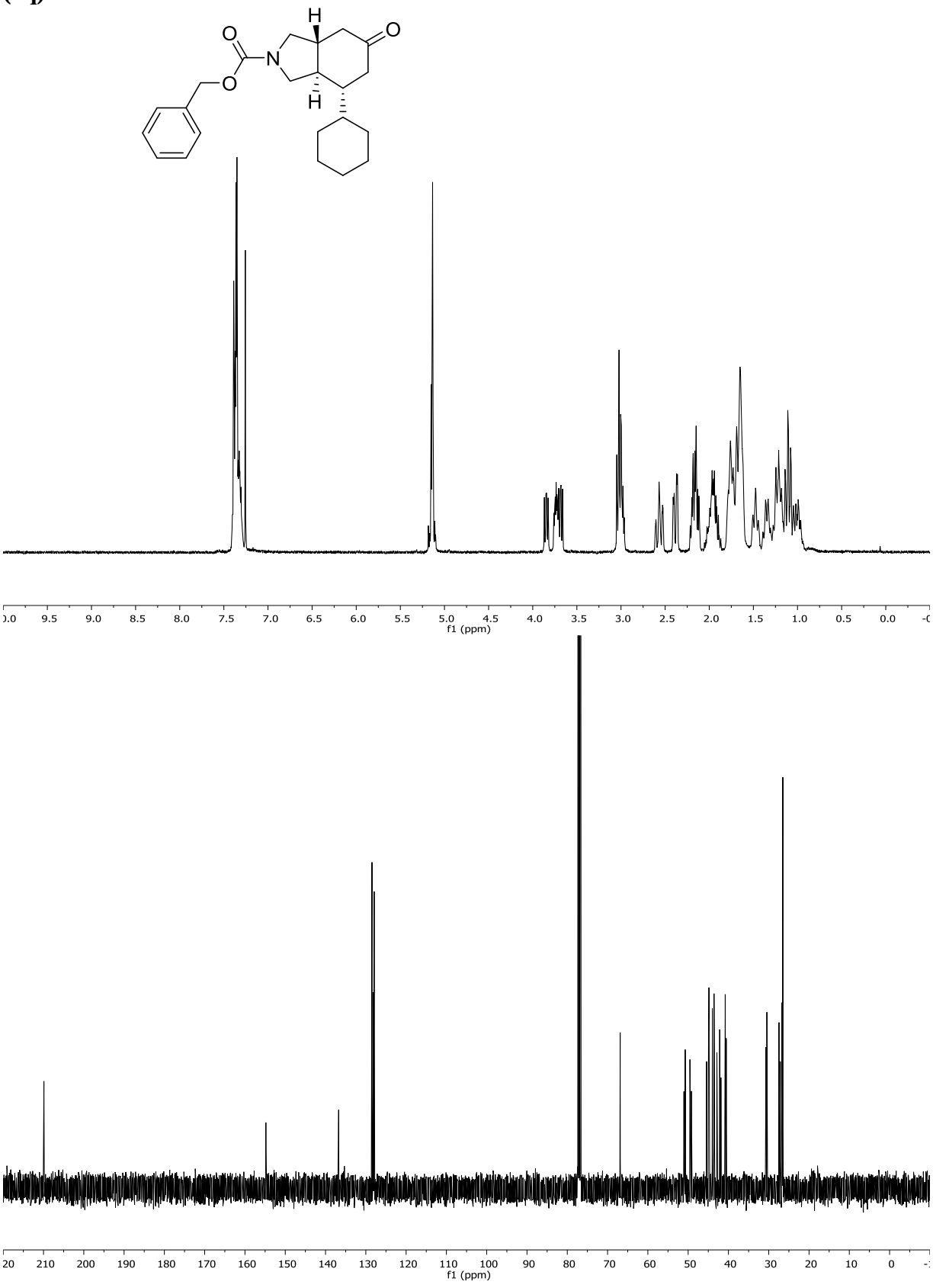


(1*R, 2*S**)-Benzyl allyl((-2-cyclohexylcyclopropyl)methyl)carbamate (6q)**

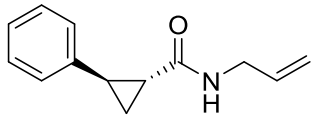


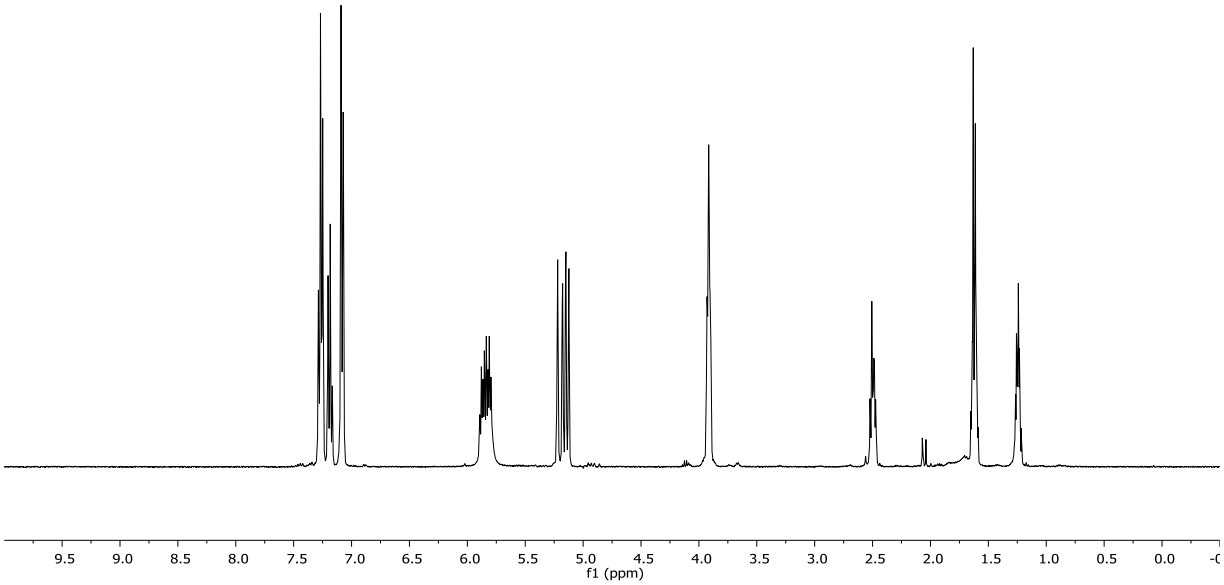


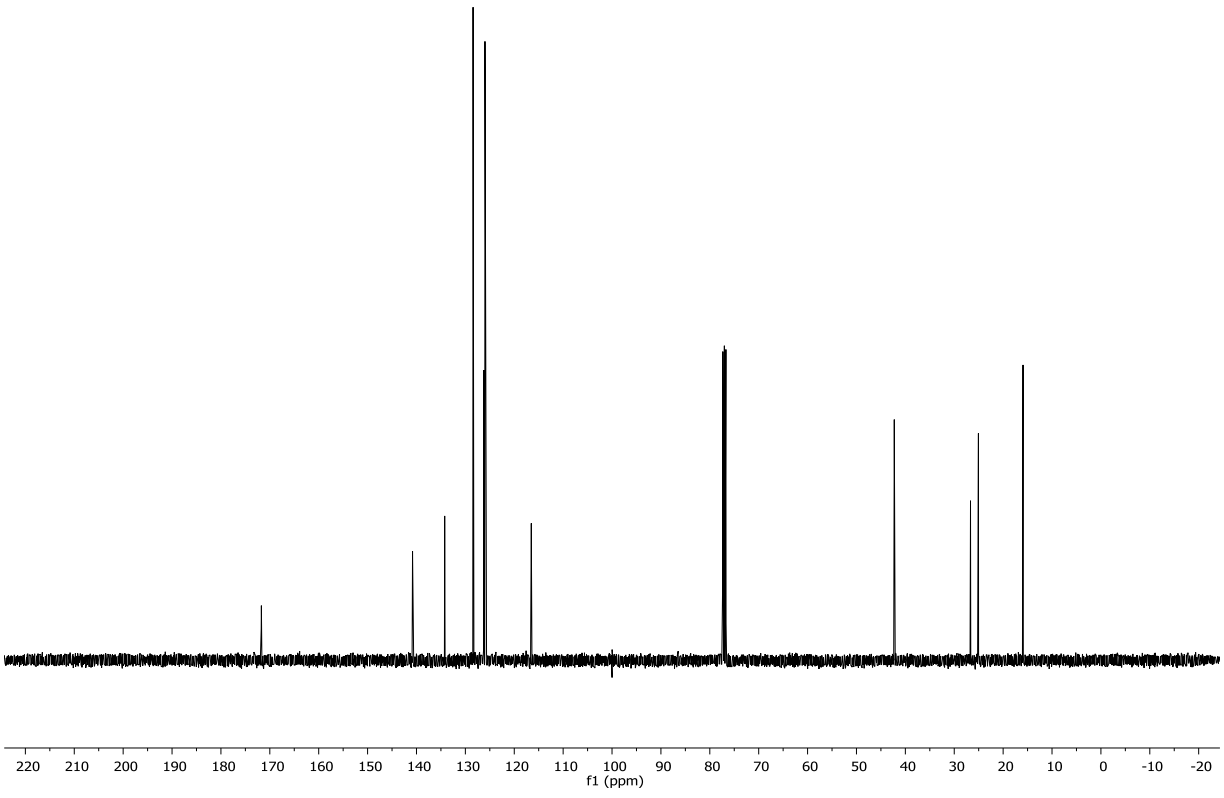
(3a*R, 4*S**, 7a*R**)-Benzyl 4-cyclohexyl-6-oxohexahydro-1*H*-isoindole-2(3*H*)-carboxylate (8q)**



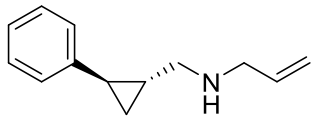
(1*S, 2*S**)-*N*-Allyl-2-phenylcyclopropanecarboxamide**

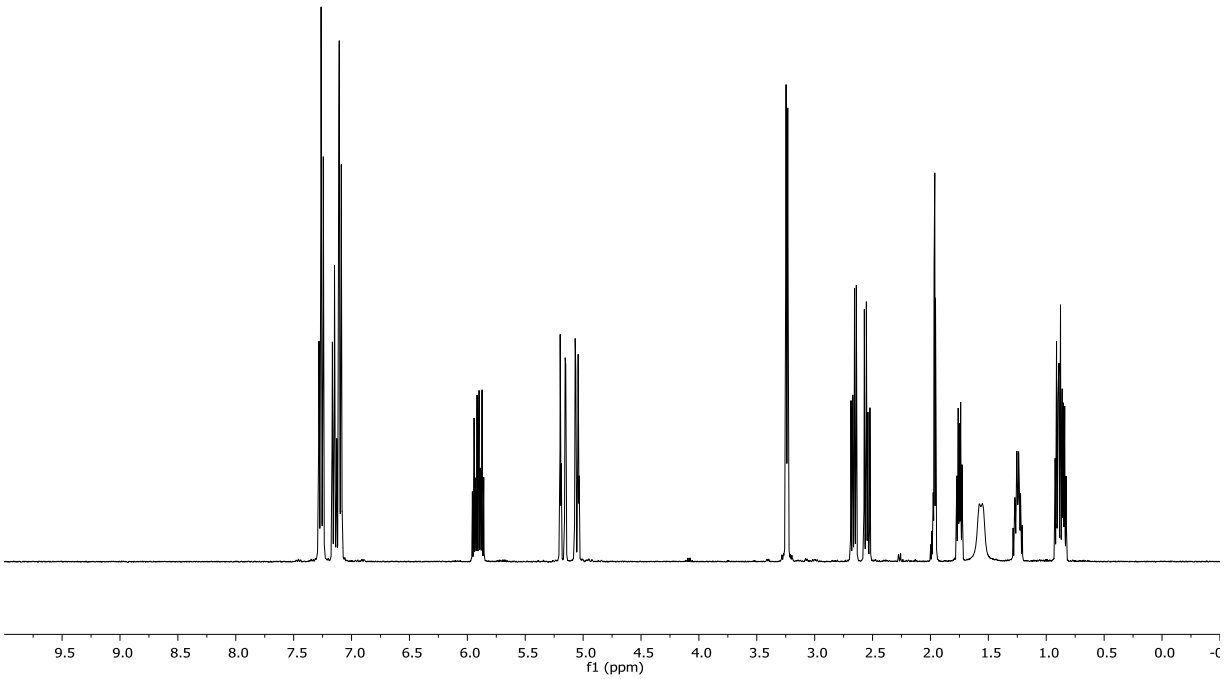


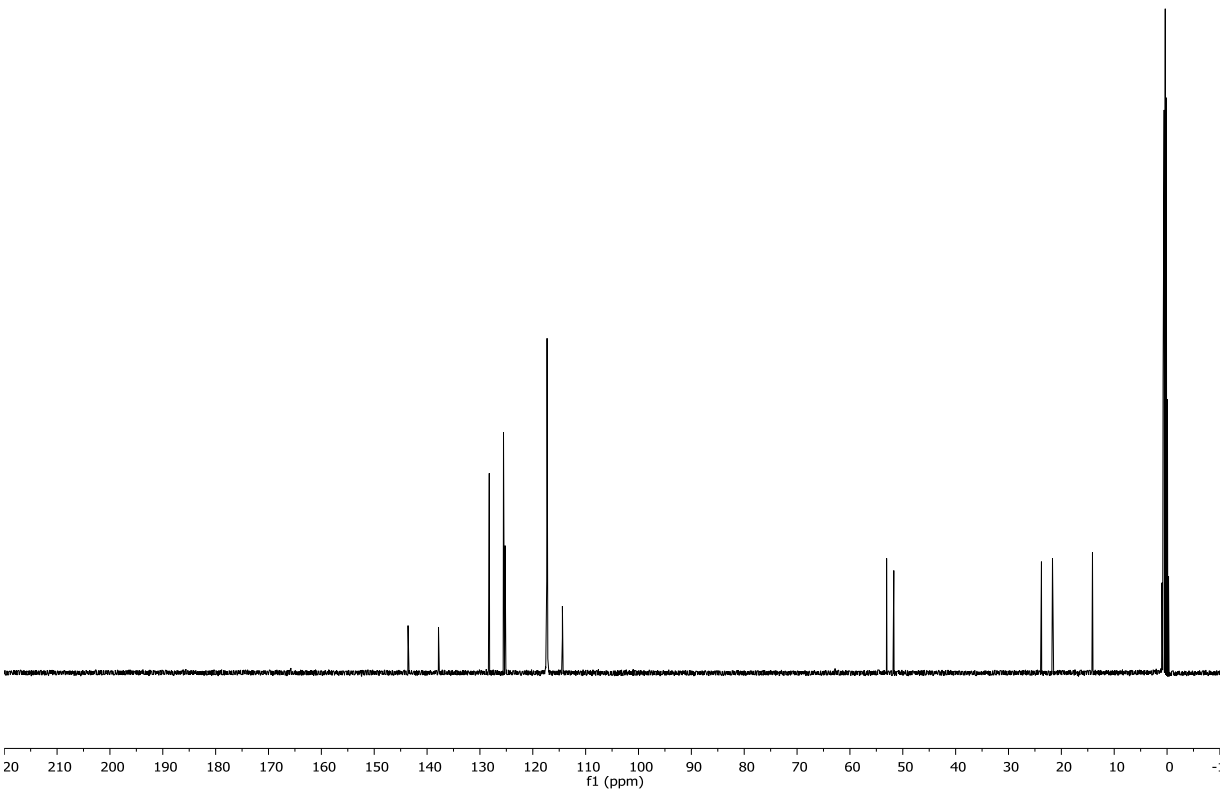




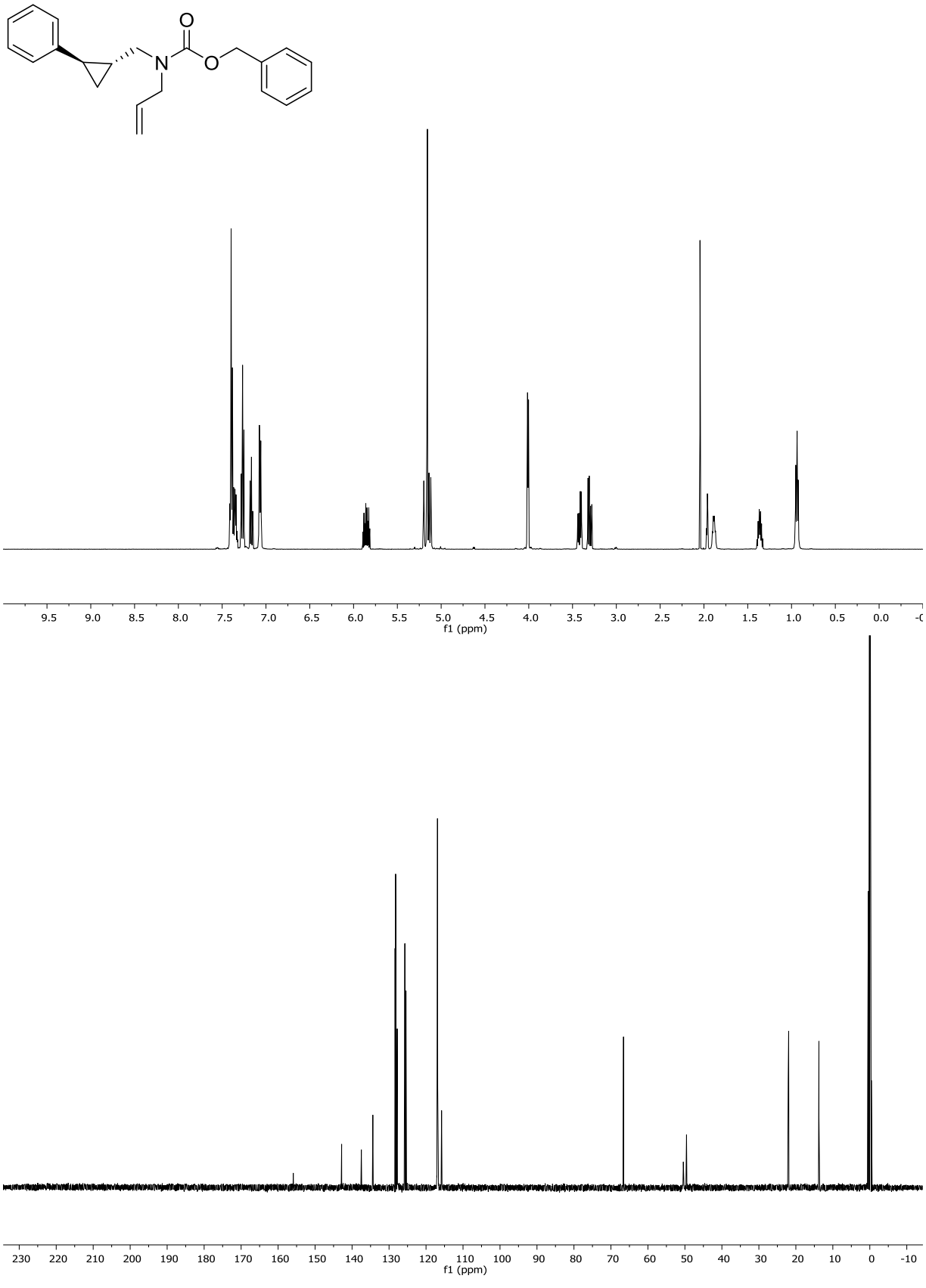
(1*S, 2*S**)-*N*-((-2-Phenylcyclopropyl)methyl)prop-2-en-1-amine**



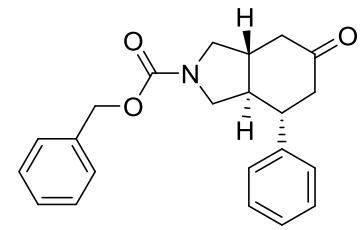


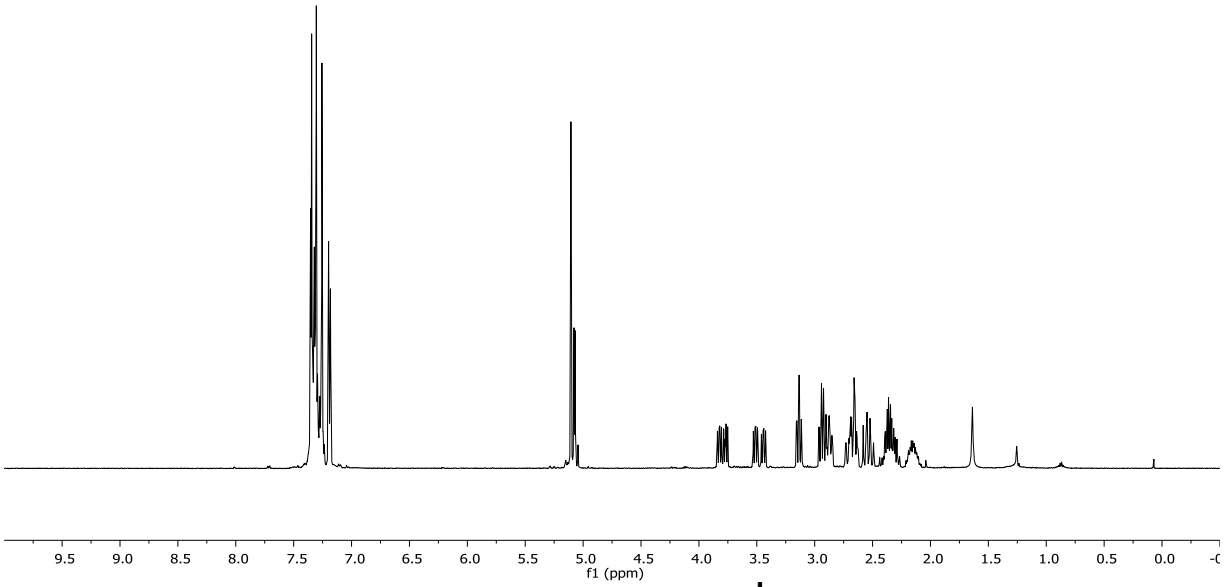


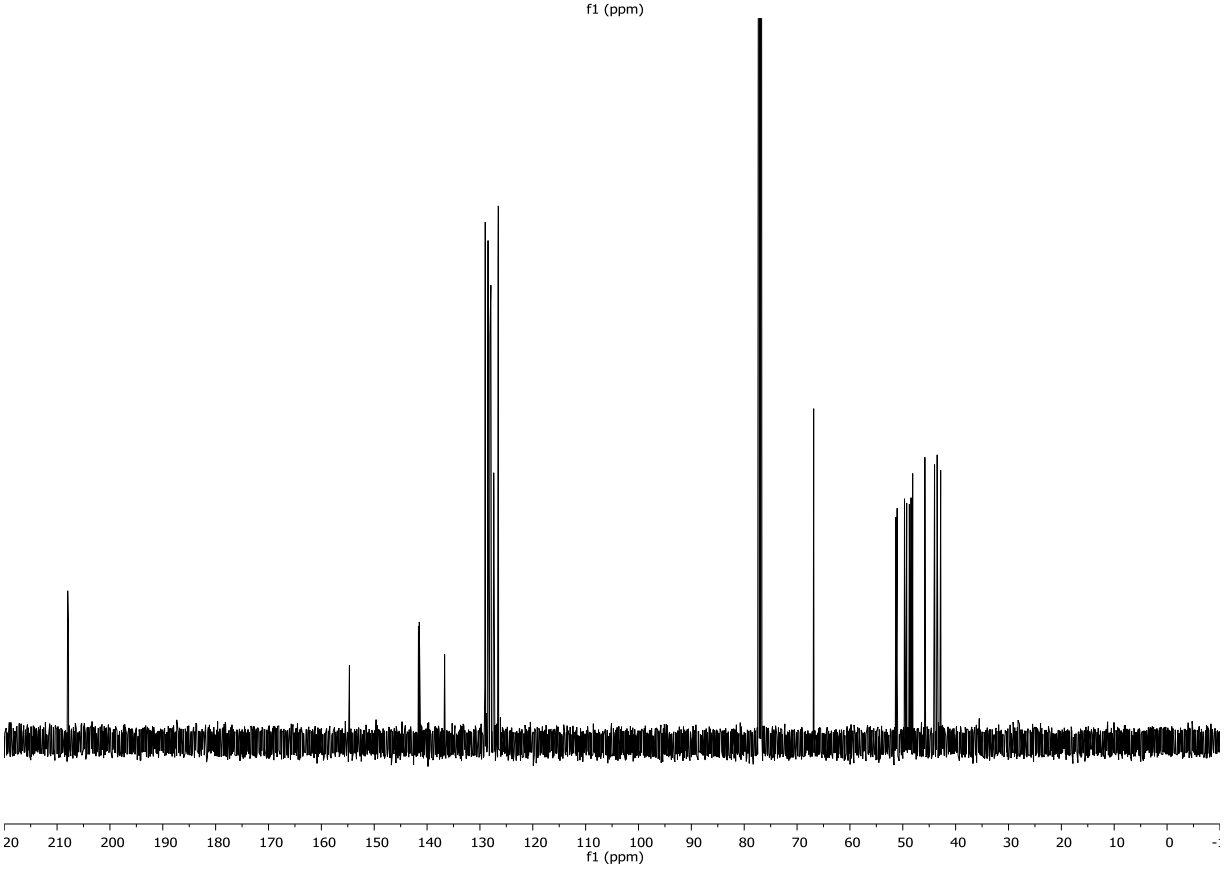
(1*S, 2*S**)-*N*-((-2-Phenylcyclopropyl)methyl)prop-2-en-1-amine (6r)**



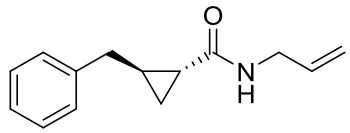
(3a*R,4*S**,7a*R**)-Benzyl 6-oxo-4-phenylhexahydro-1*H*-isoindole-2(3*H*)-carboxylate (8r)**

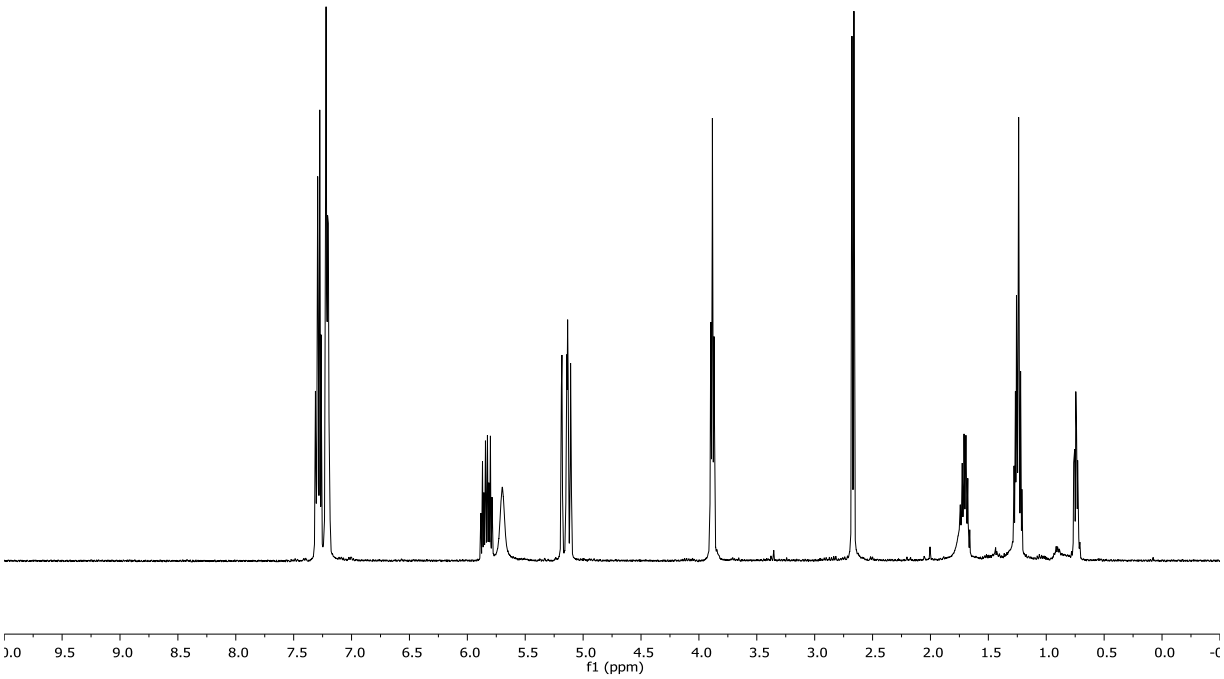


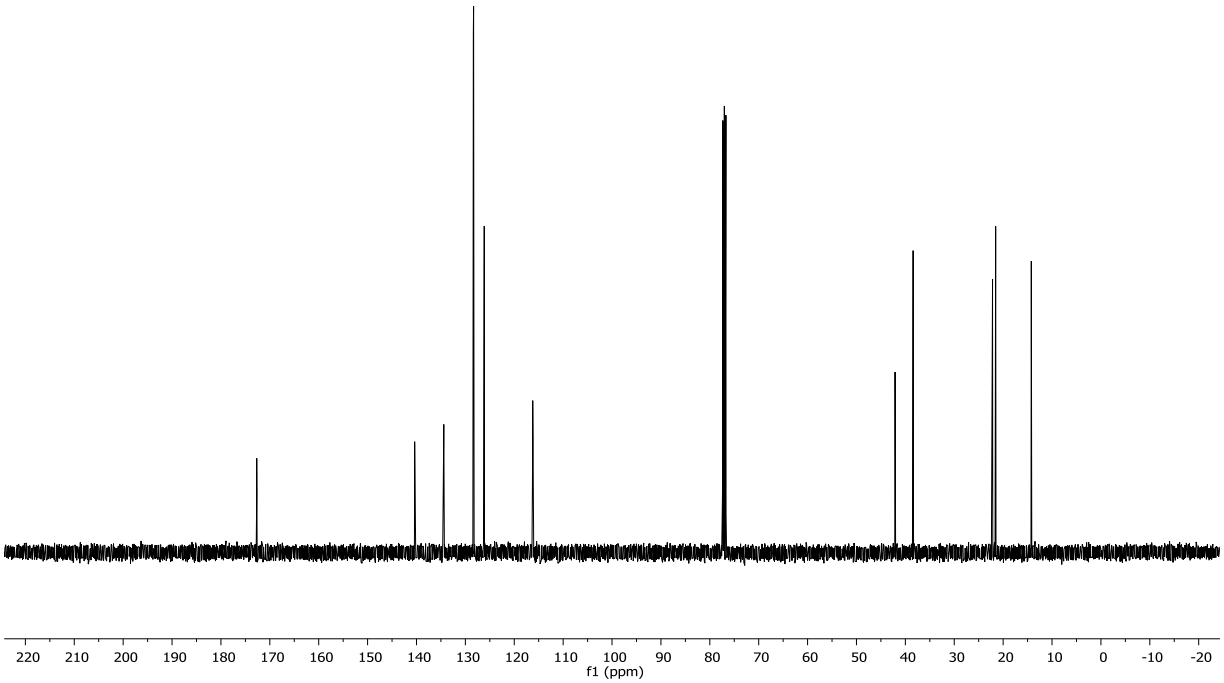




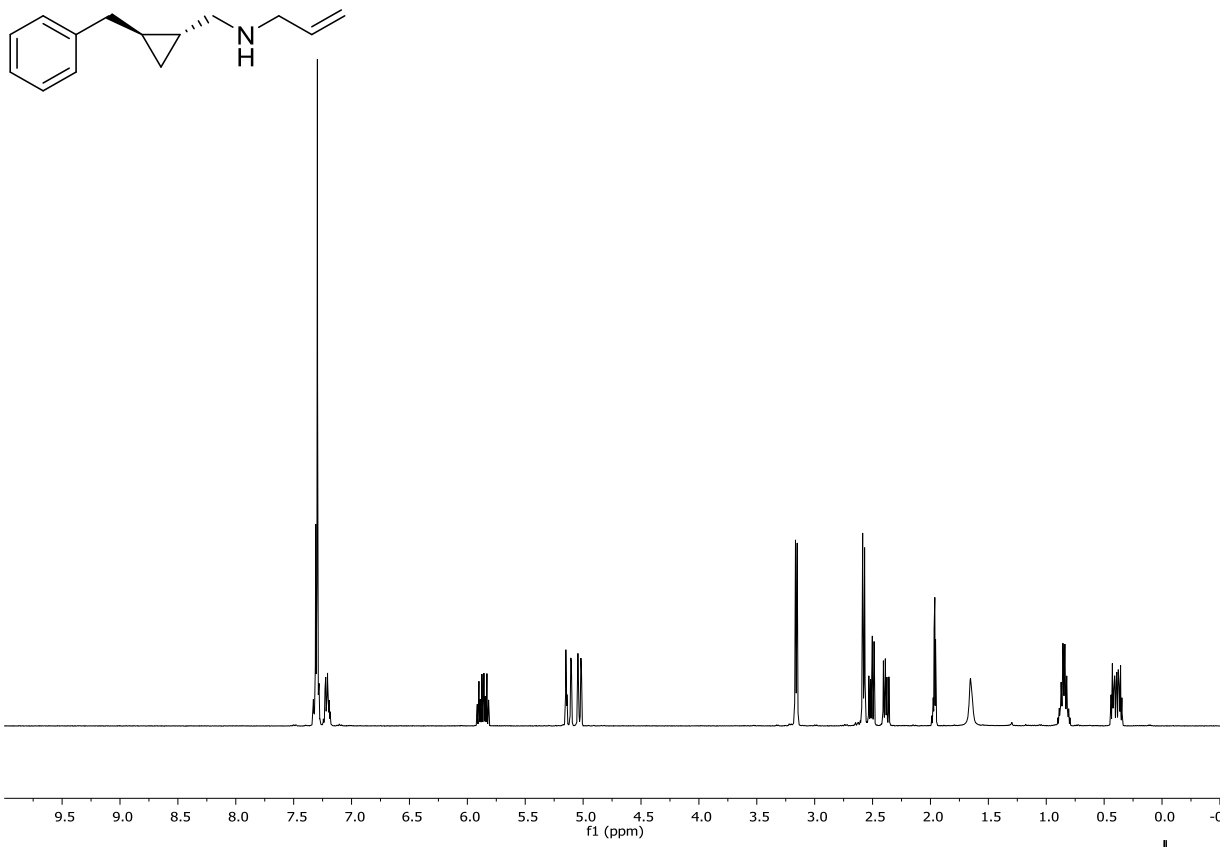
(1*R, 2*S**)-*N*-Allyl-2-benzylcyclopropanecarboxamide**

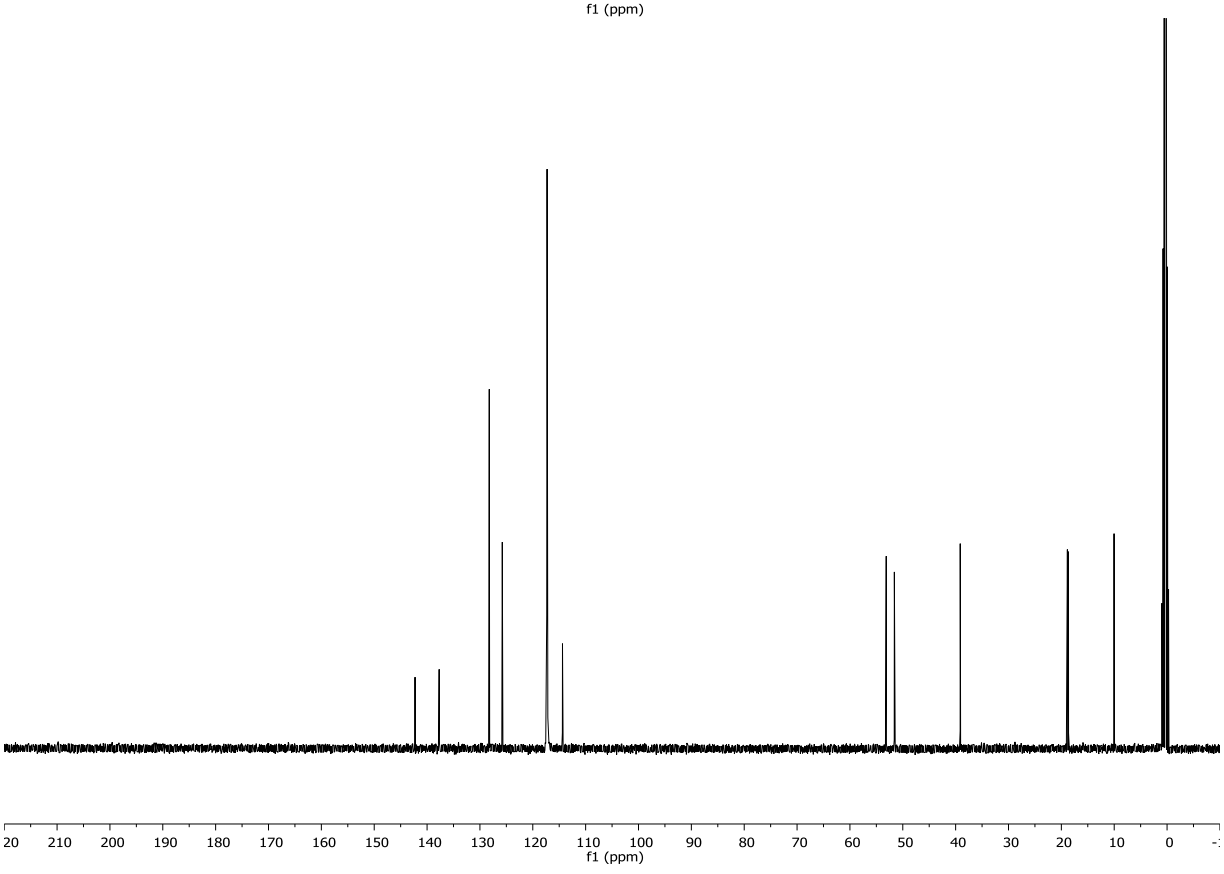




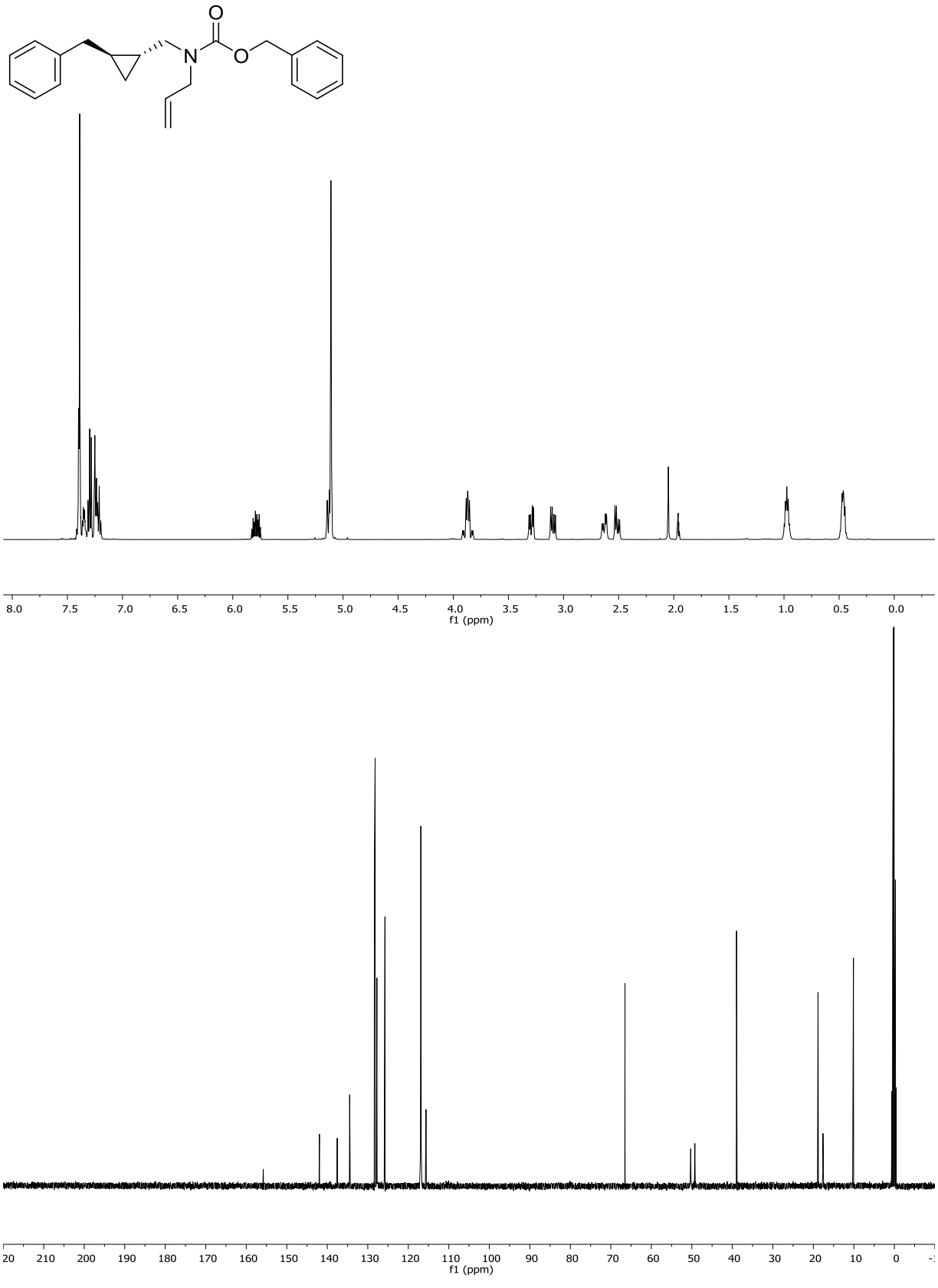


(1*R, 2*S**)-*N*-((2-Benzylcyclopropyl)methyl)prop-2-en-1-amine**

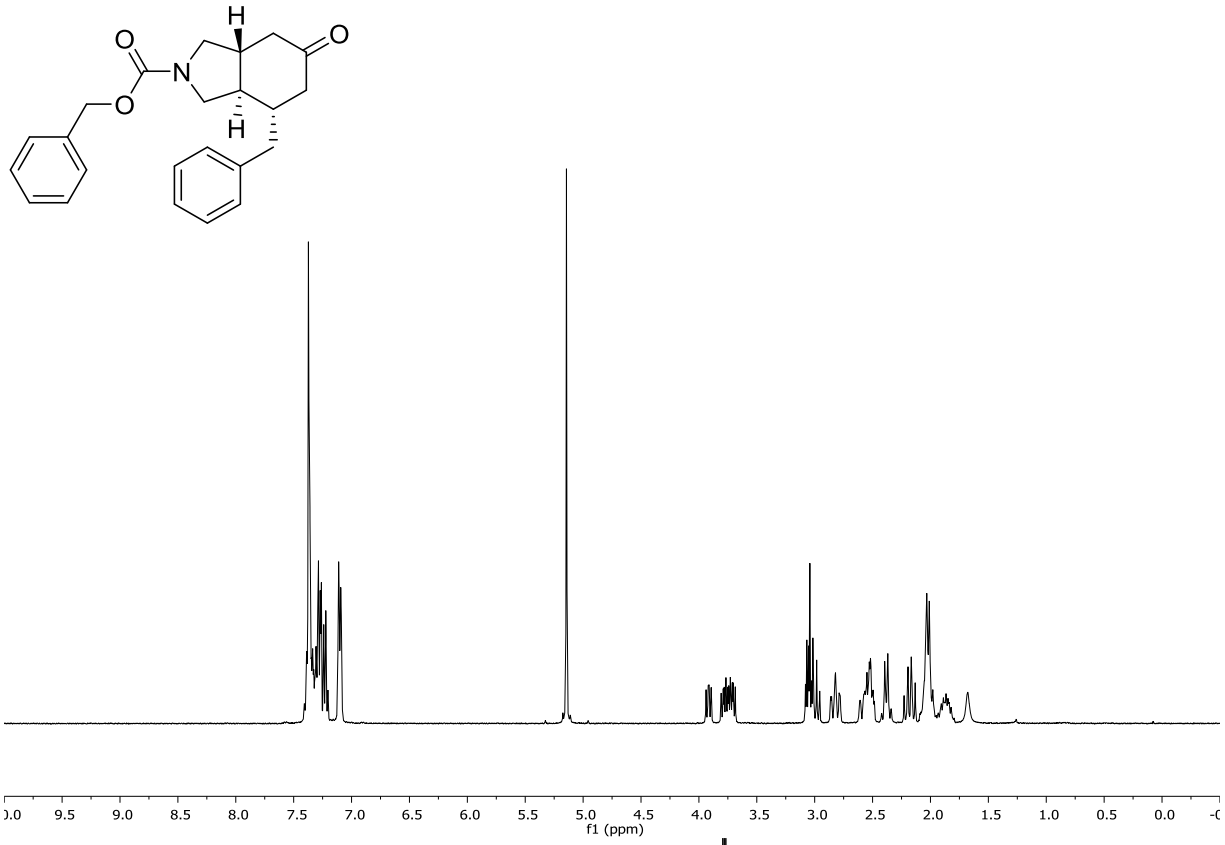


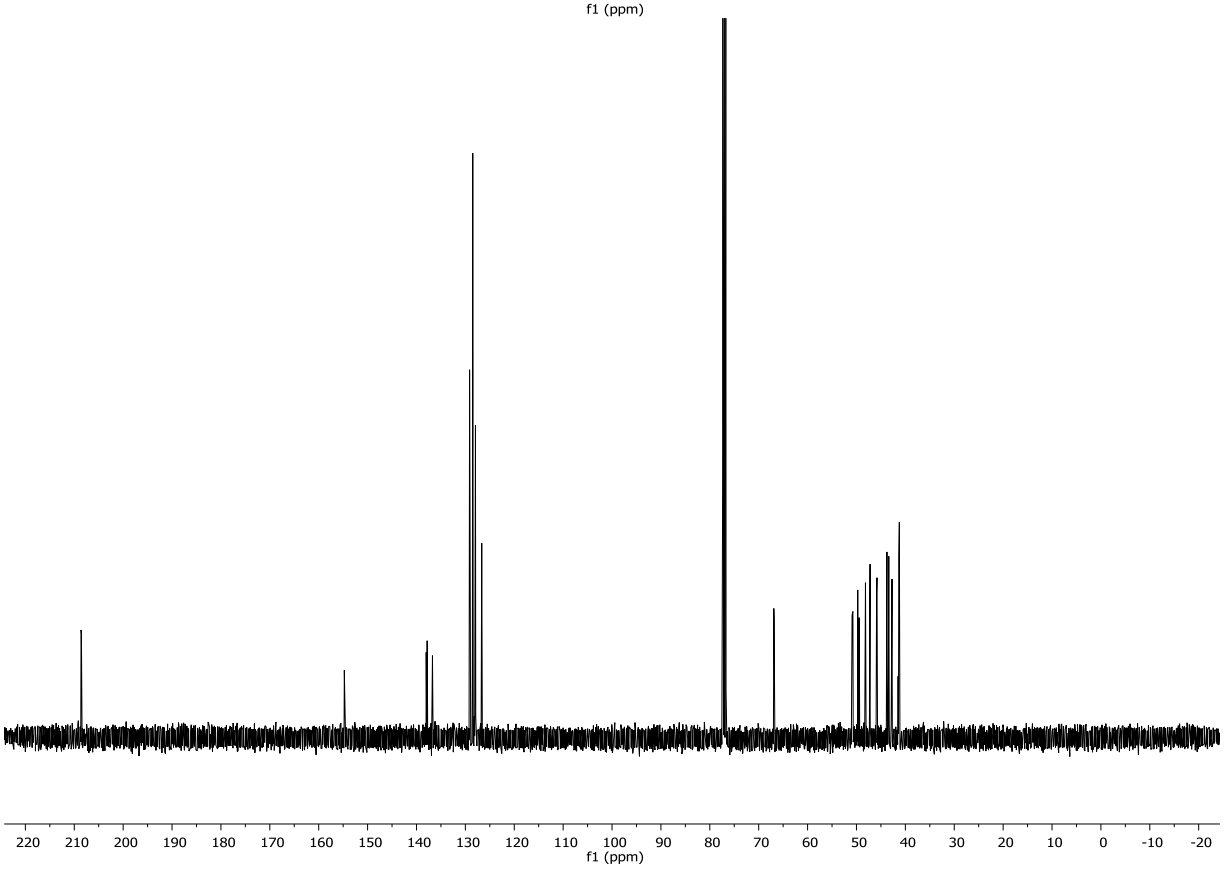


(1*R, 2*S**)-Benzyl allyl((2-benzylcyclopropyl)methyl)carbamate (6s)**

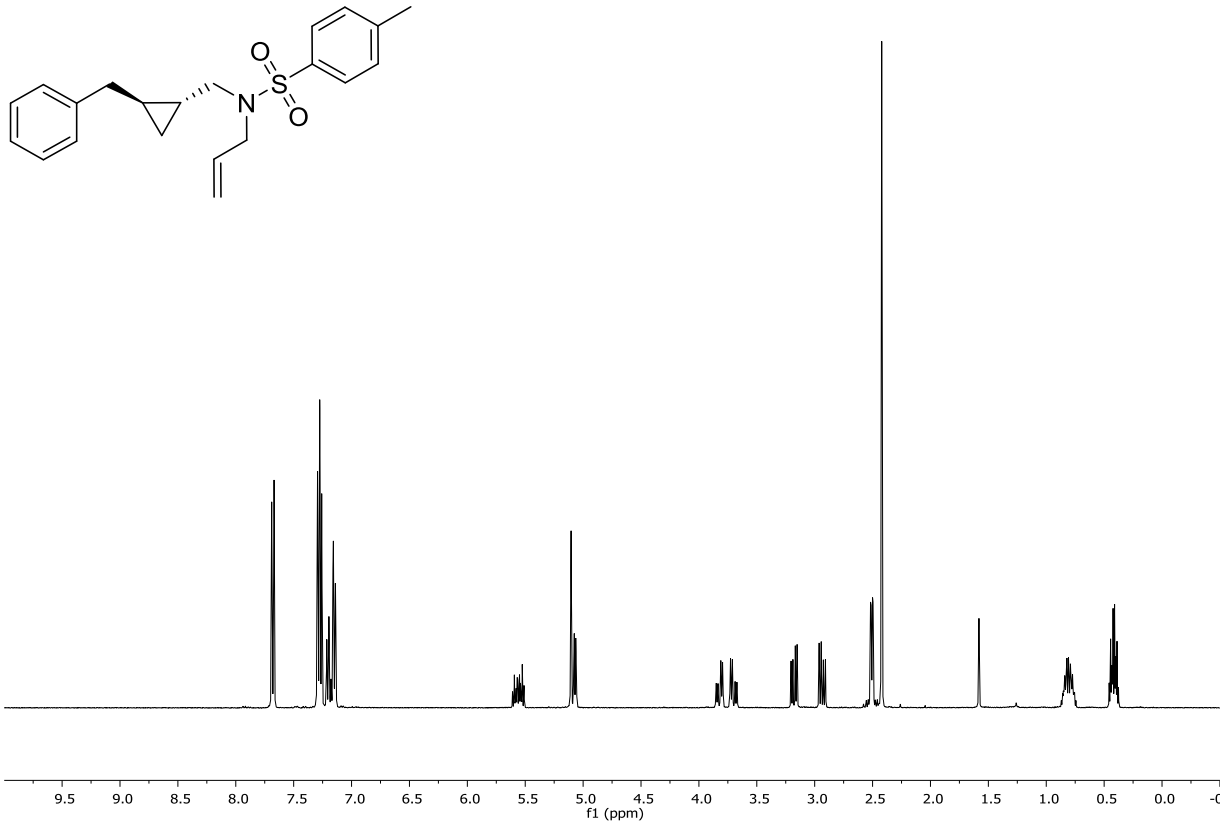


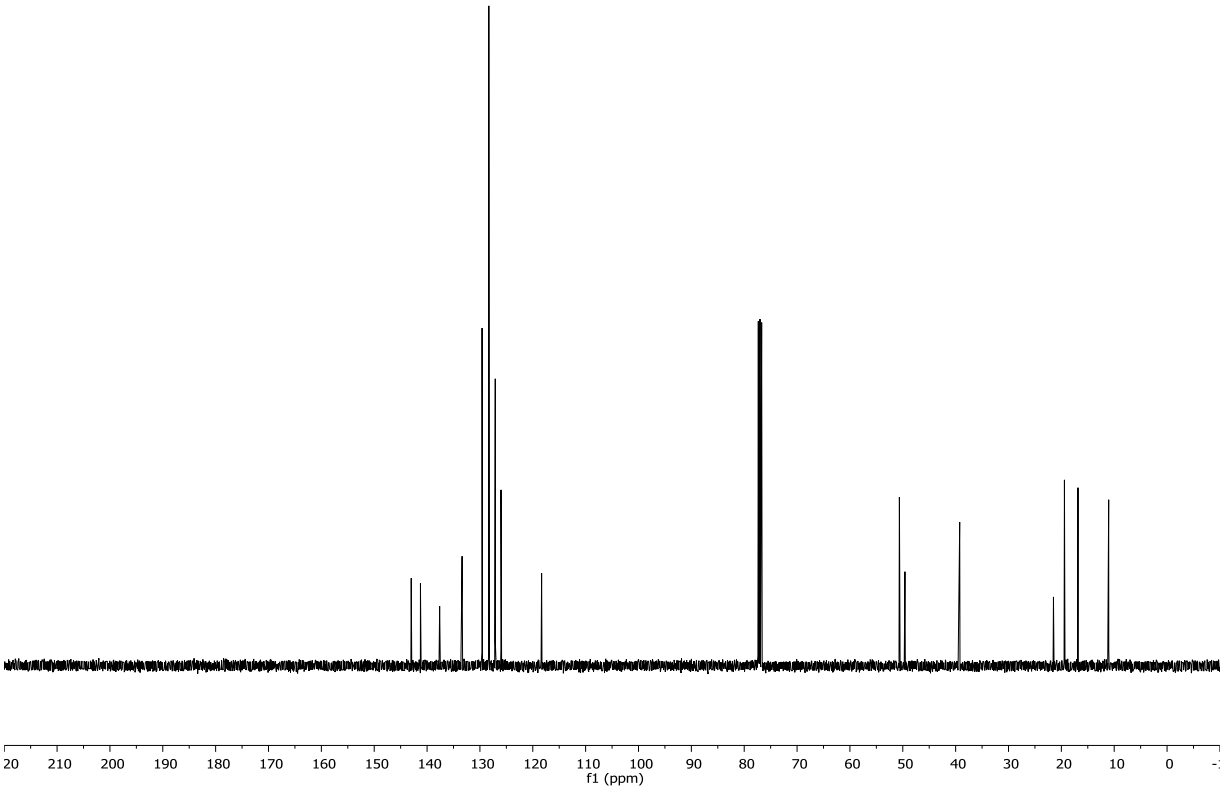
(3a*R, 4*S**, 7a*R**)-Benzyl 4-benzyl-6-oxohexahydro-1*H*-isoindole-2(3*H*)-carboxylate (8s)**



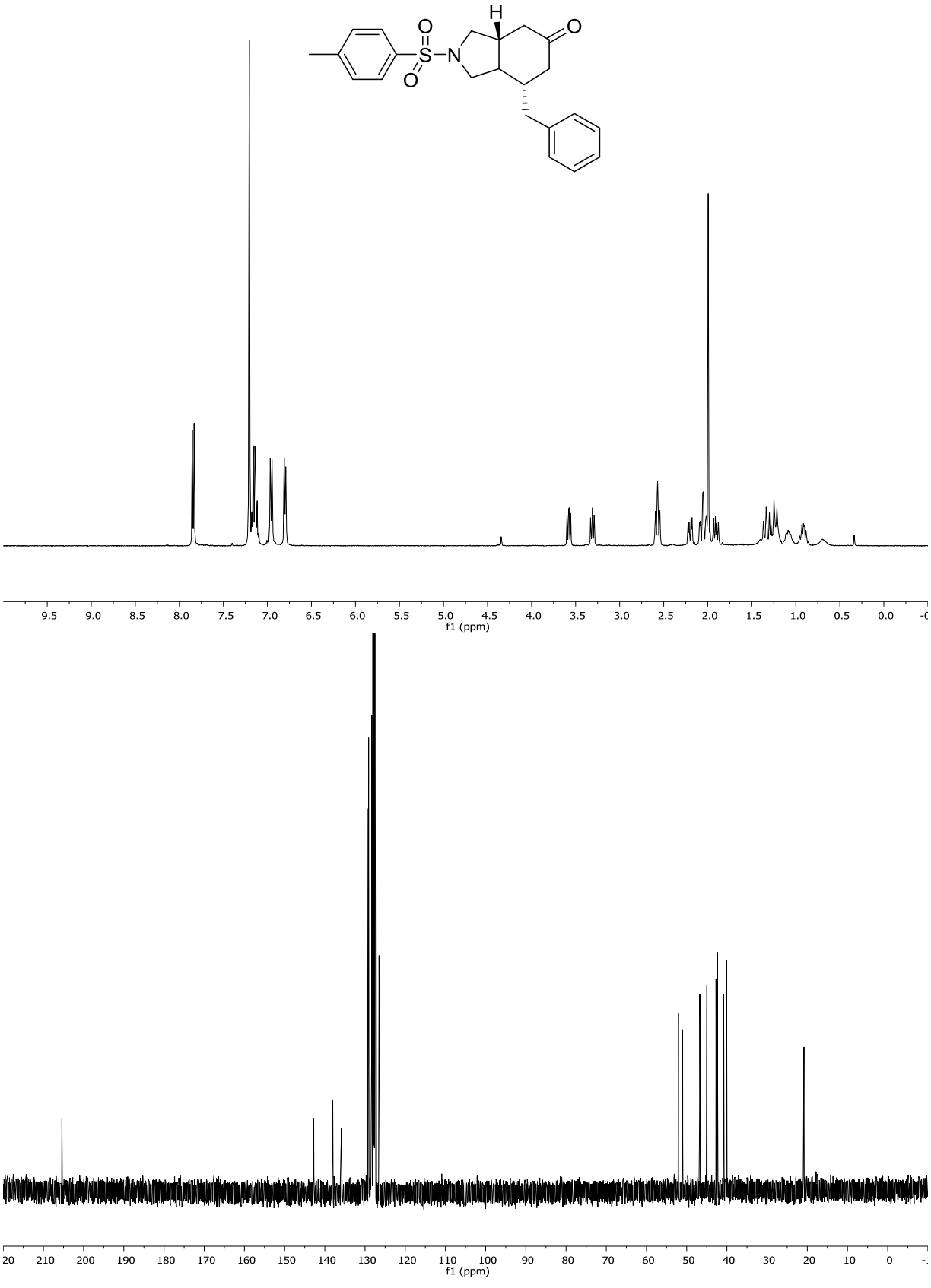


(1*S, 2*S**)-*N*-Allyl-*N*-((-2-butylcyclopropyl)methyl)-4-methylbenzenesulfonamide (6t)**

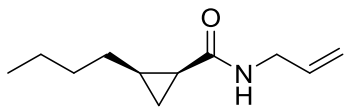


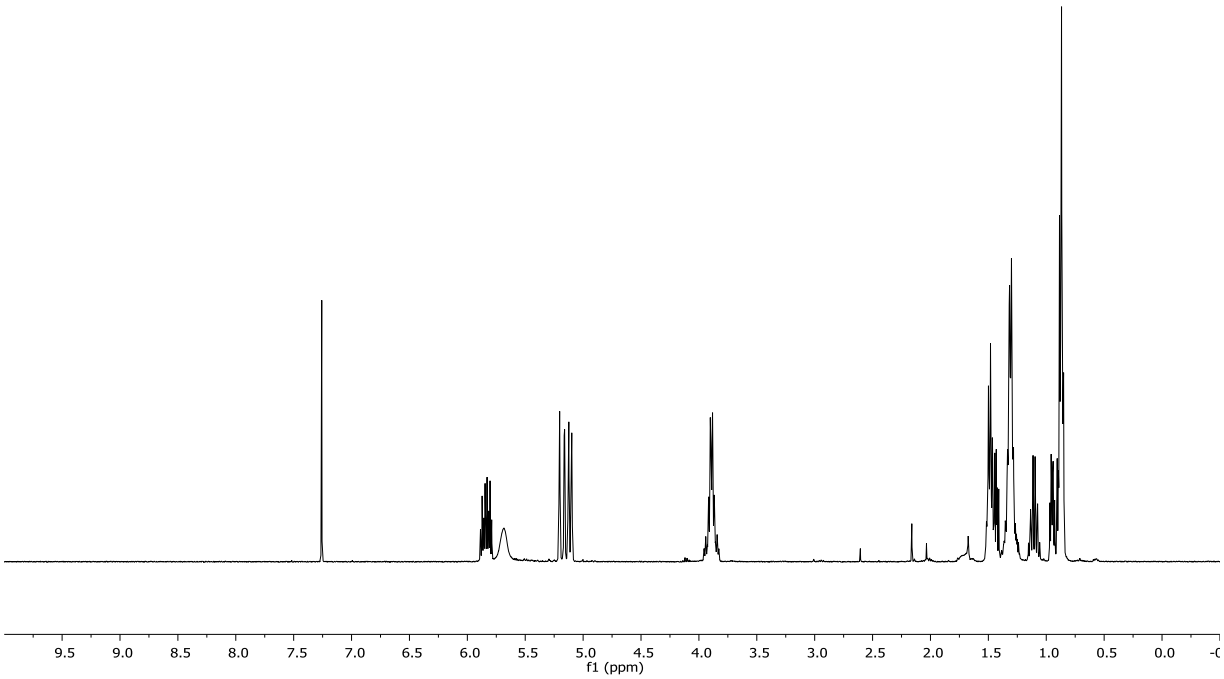


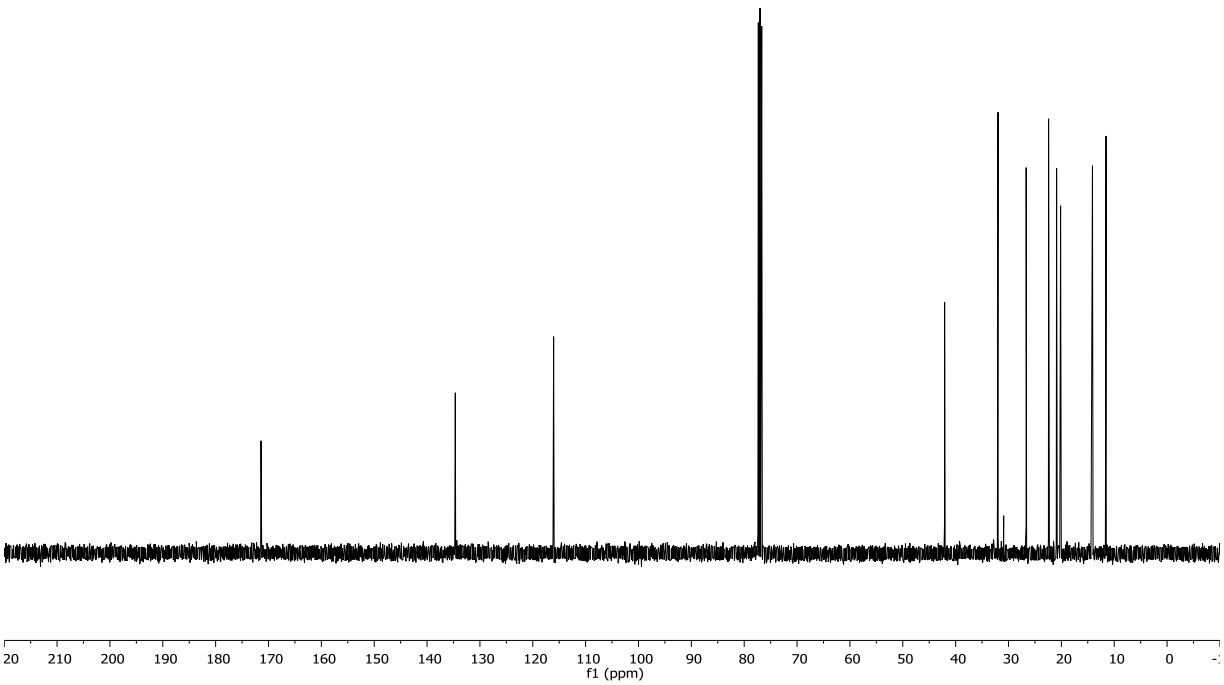
(3a*R, 7*S**, 7a*R**) -7-Butyl-2-tosylhexahydro-1*H*-isoindol-5(6*H*)-one (8t)**



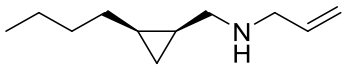
(1*S, 2*R**)-*N*-Allyl-2-butylcyclopropanecarboxamide**

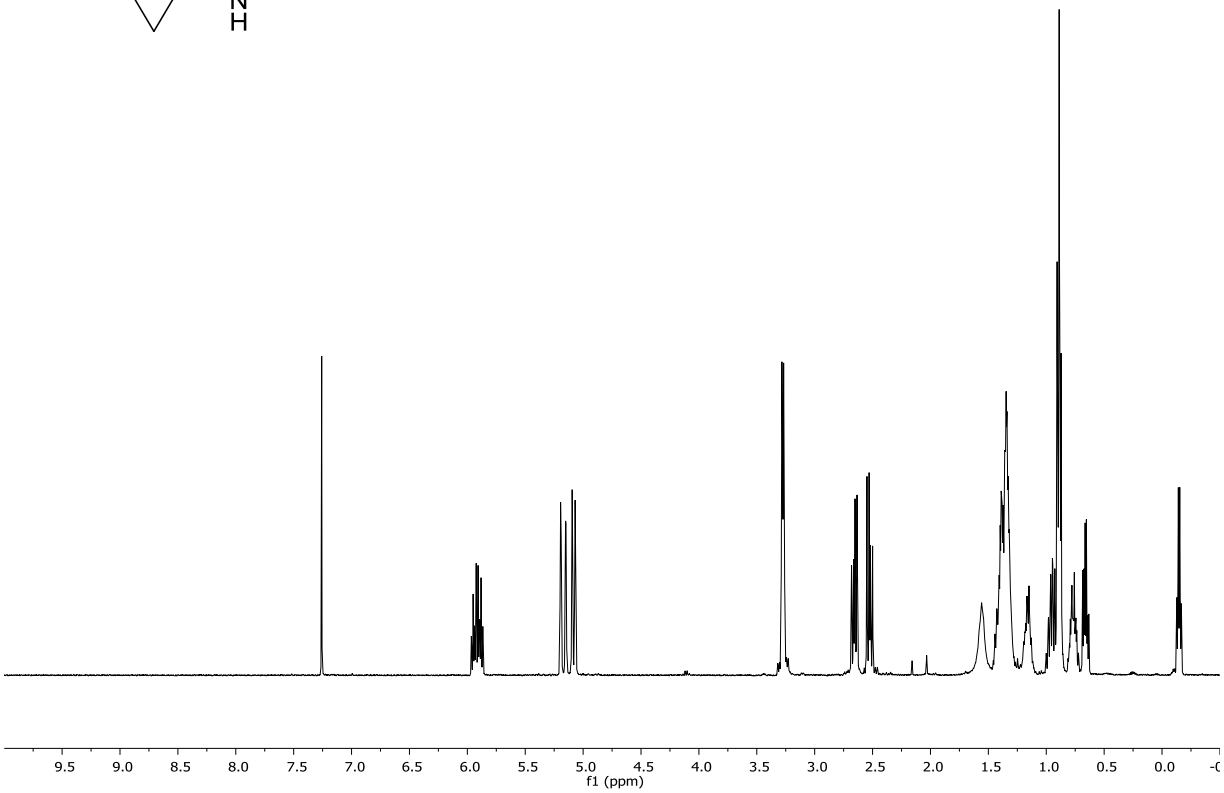


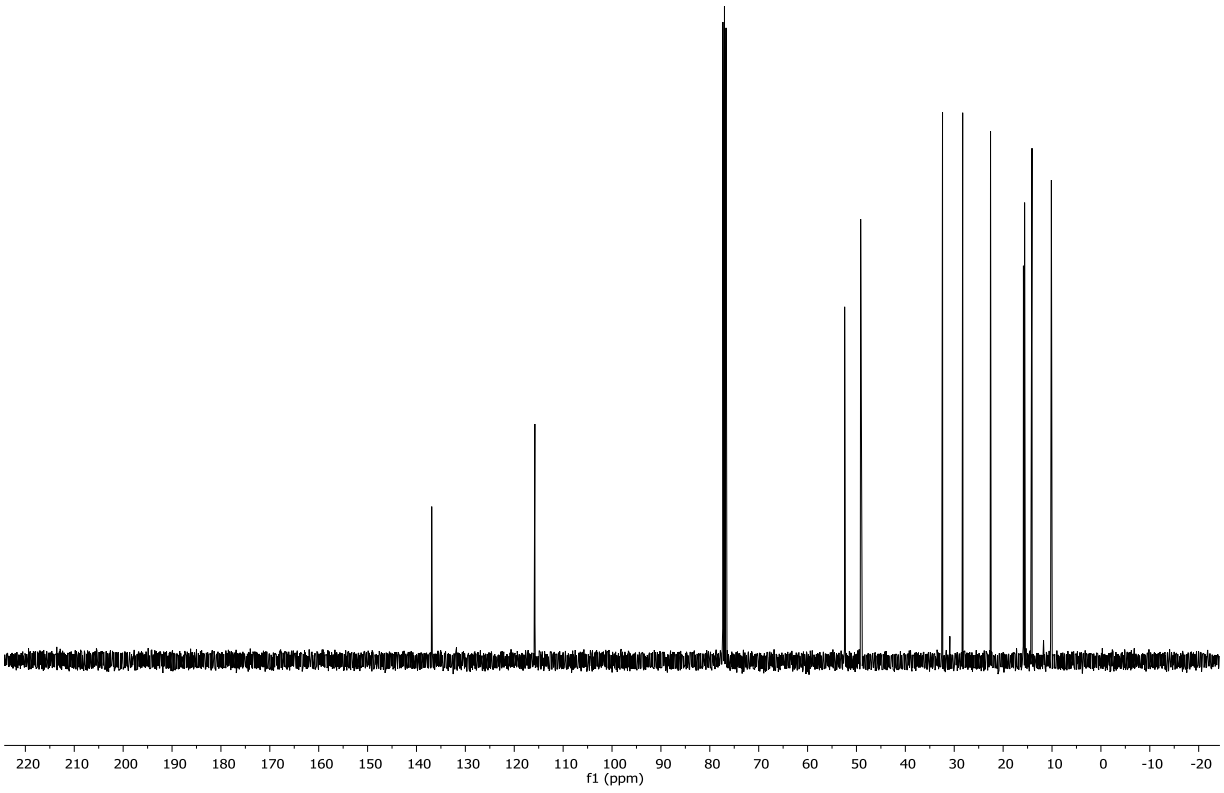




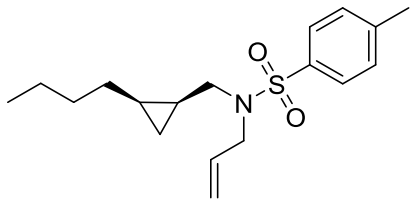
(1*S, 2*R**)-*N*-(2-Butylcyclopropyl)methyl)prop-2-en-1-amine**

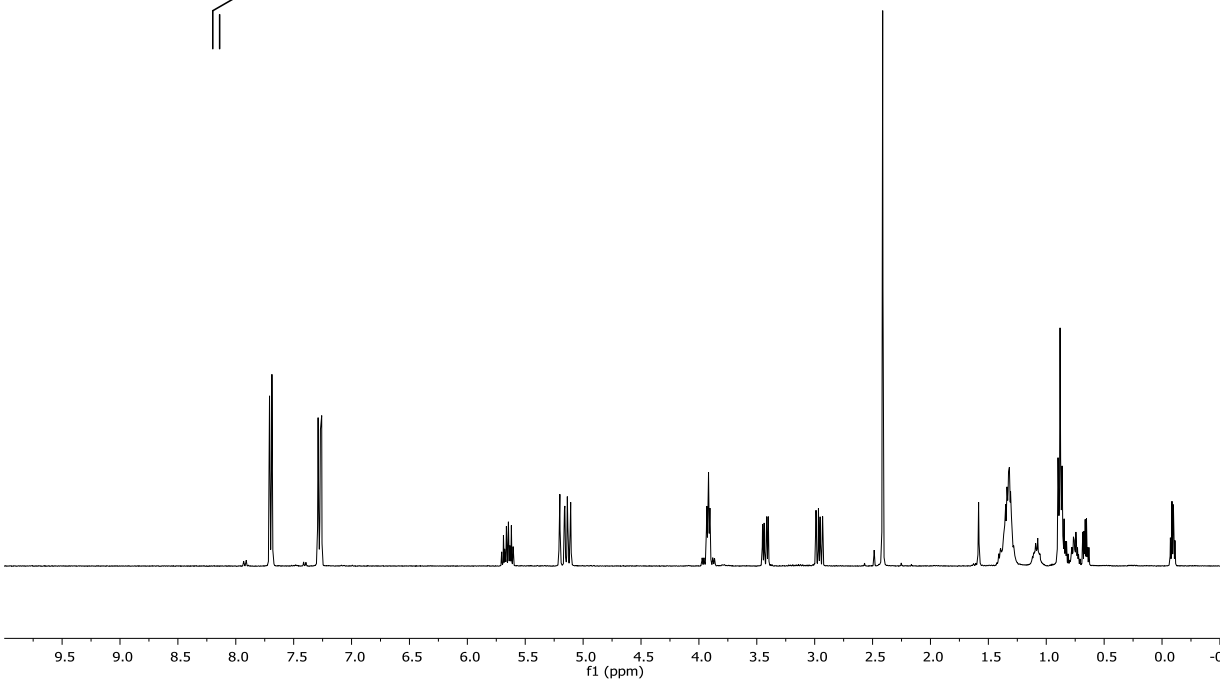


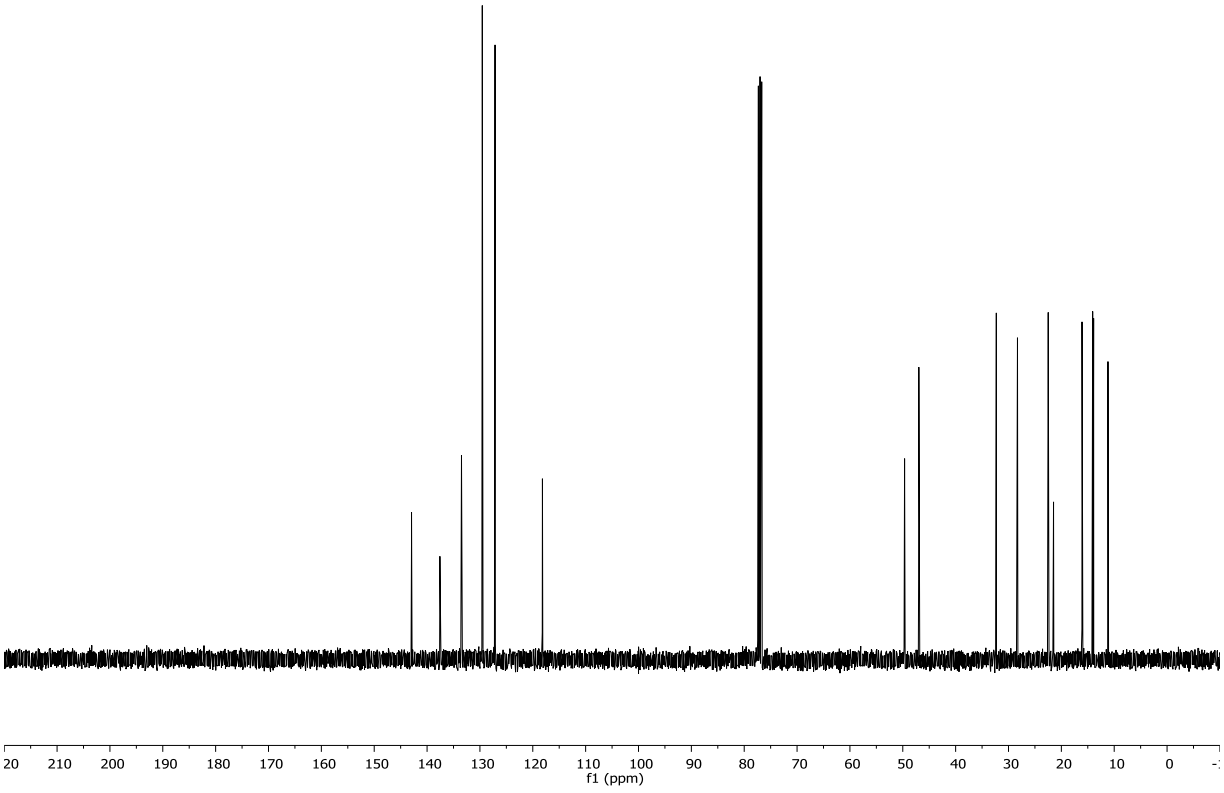




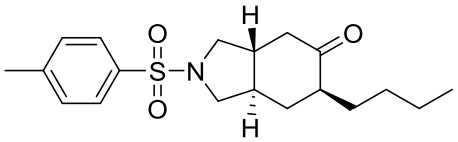
(1*S, 2*R**)-Benzyl allyl((-2-butylcyclopropyl)methyl)carbamate (6u)**

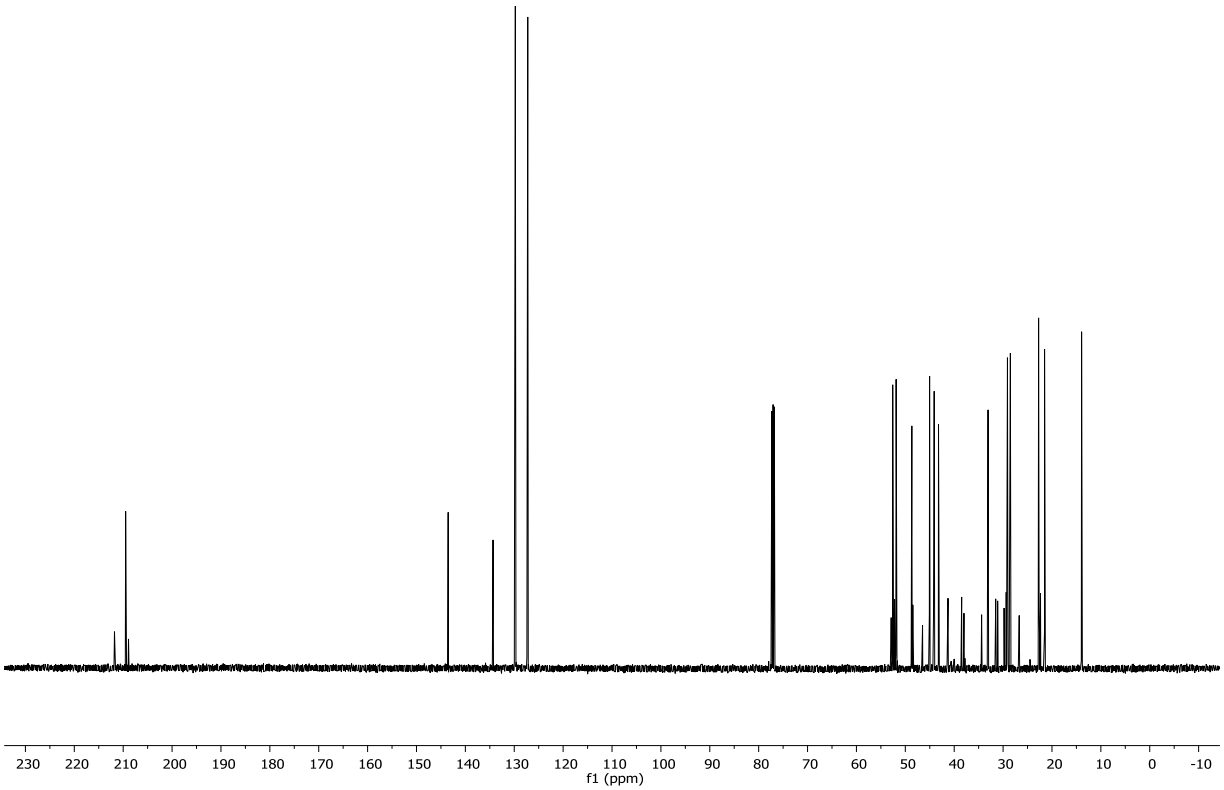




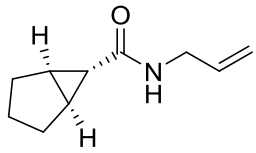


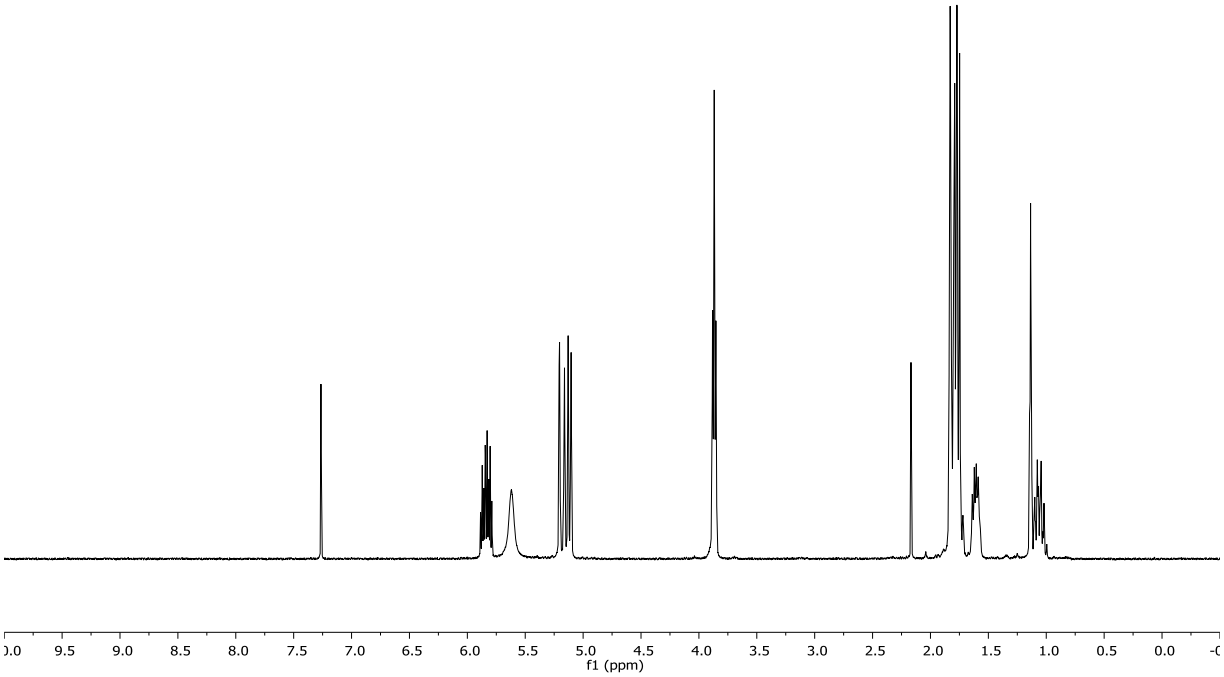
(3a*R, 6*S**, 7a*R**) and (3a*R**, 6*R**, 7a*R**) -6-Butyl-2-tosylhexahydro-1*H*-isoindol-5(6*H*)-one and (3a*R**, 7*R**, 7a*R**)-7-butyl-2-tosylhexahydro-1*H*-isoindol-5(6*H*)-one (8u)

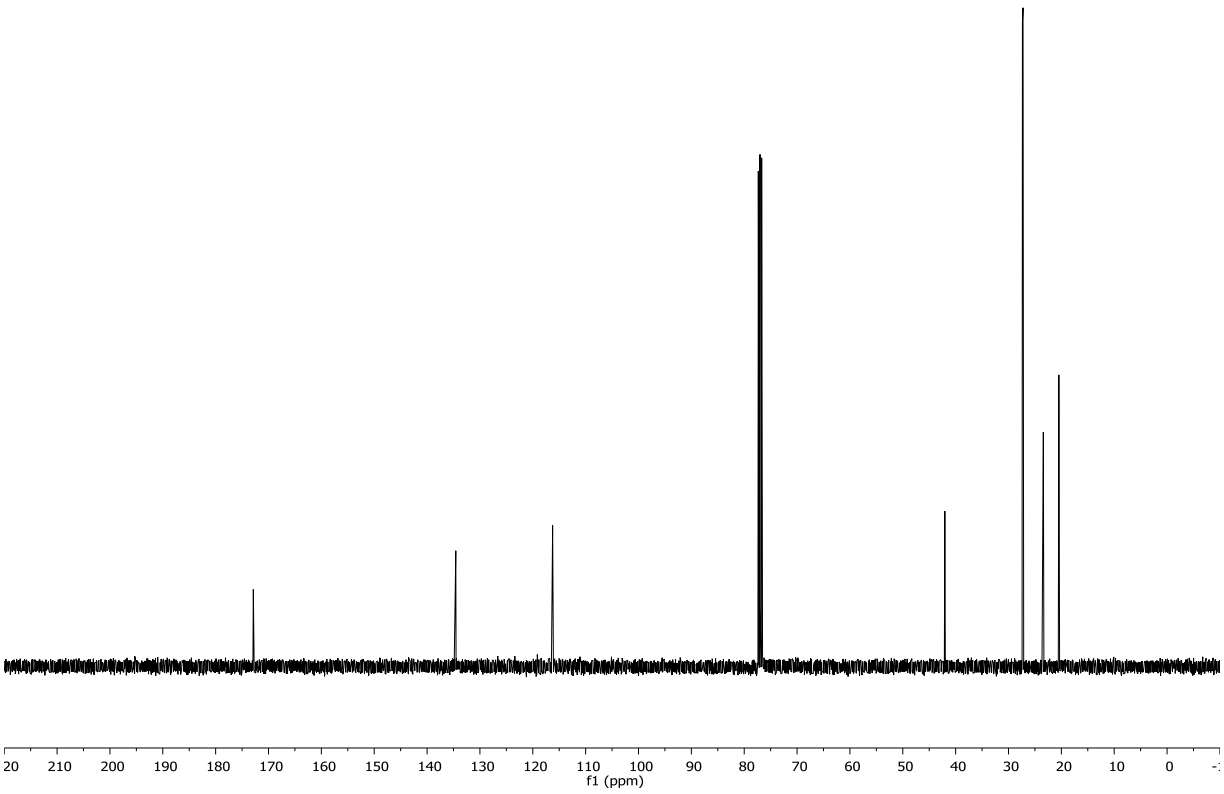




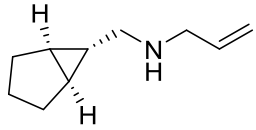
(1*R, 5*S**, 6*R**)-*N*-Allylbicyclo[3.1.0]hexane-6-carboxamide**

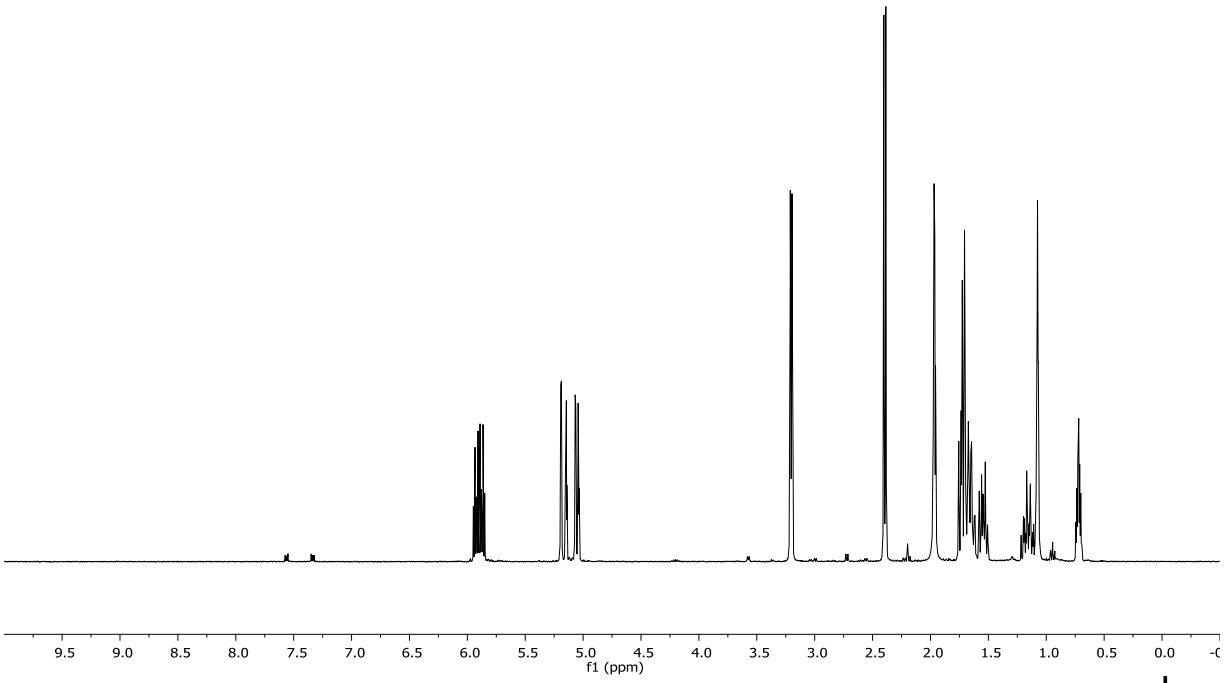


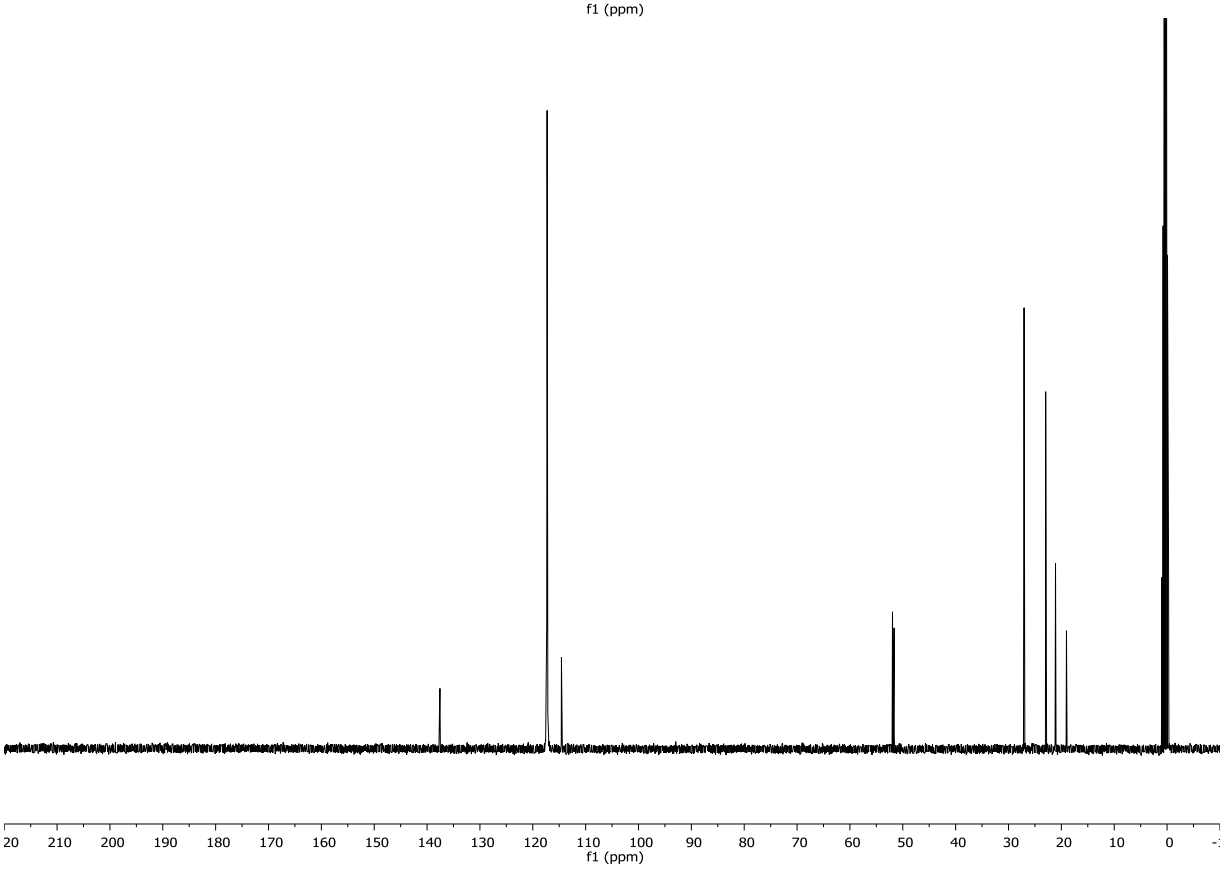




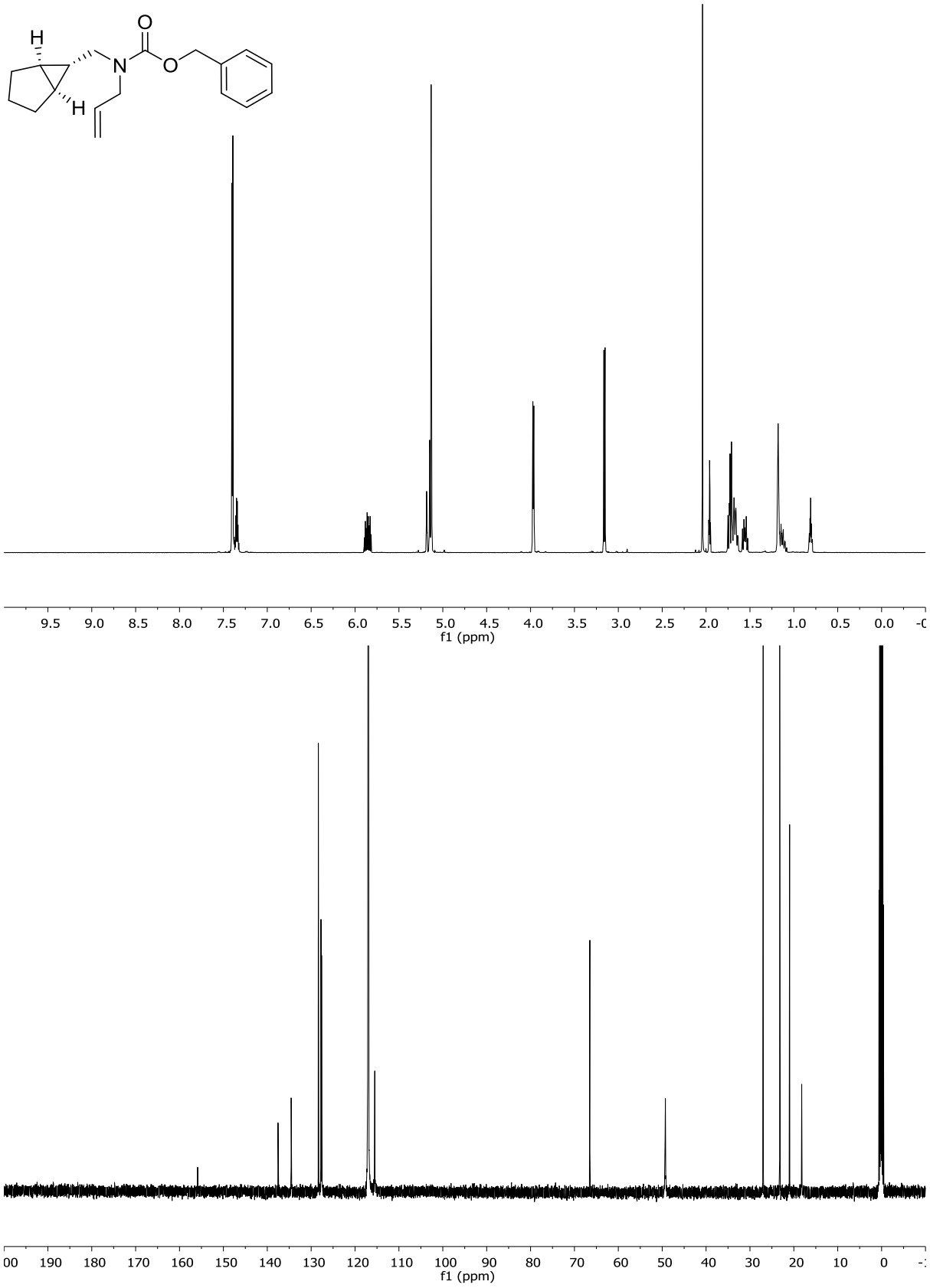
(1*R, 5*S**, 6*R**)-*N*-((Bicyclo[3.1.0]hexan-6-ylmethyl)prop-2-en-1-amine**



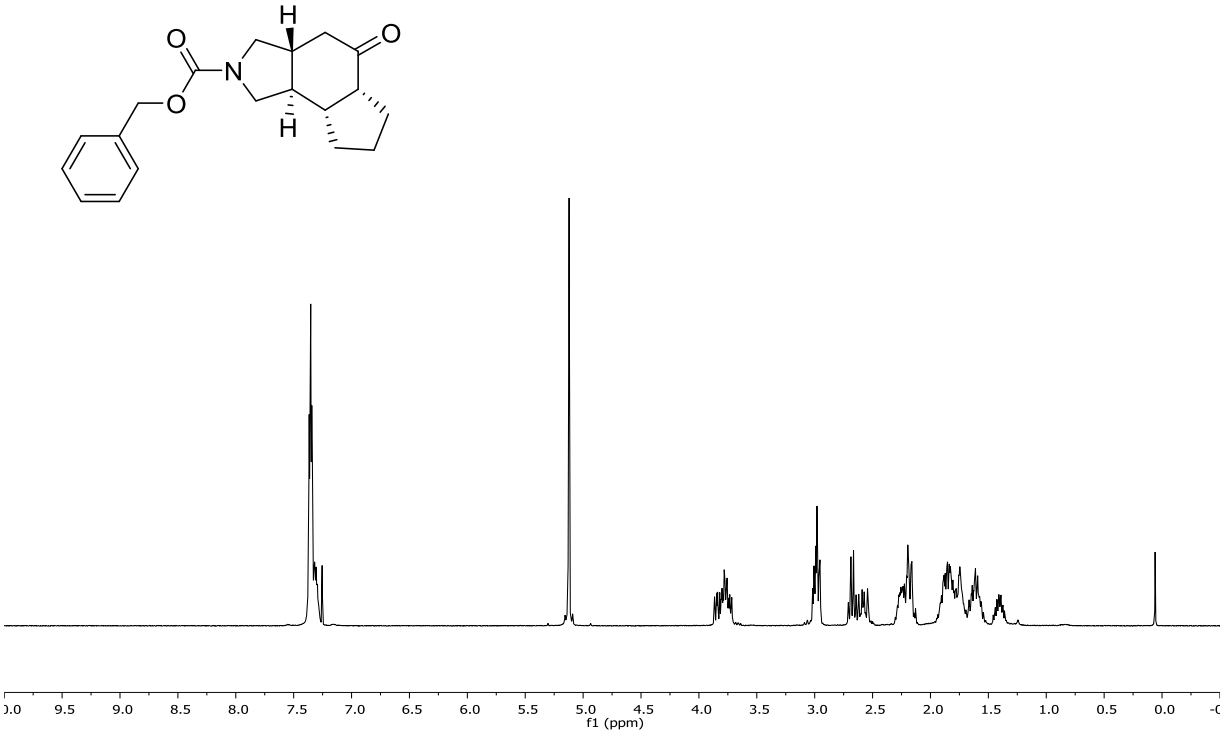


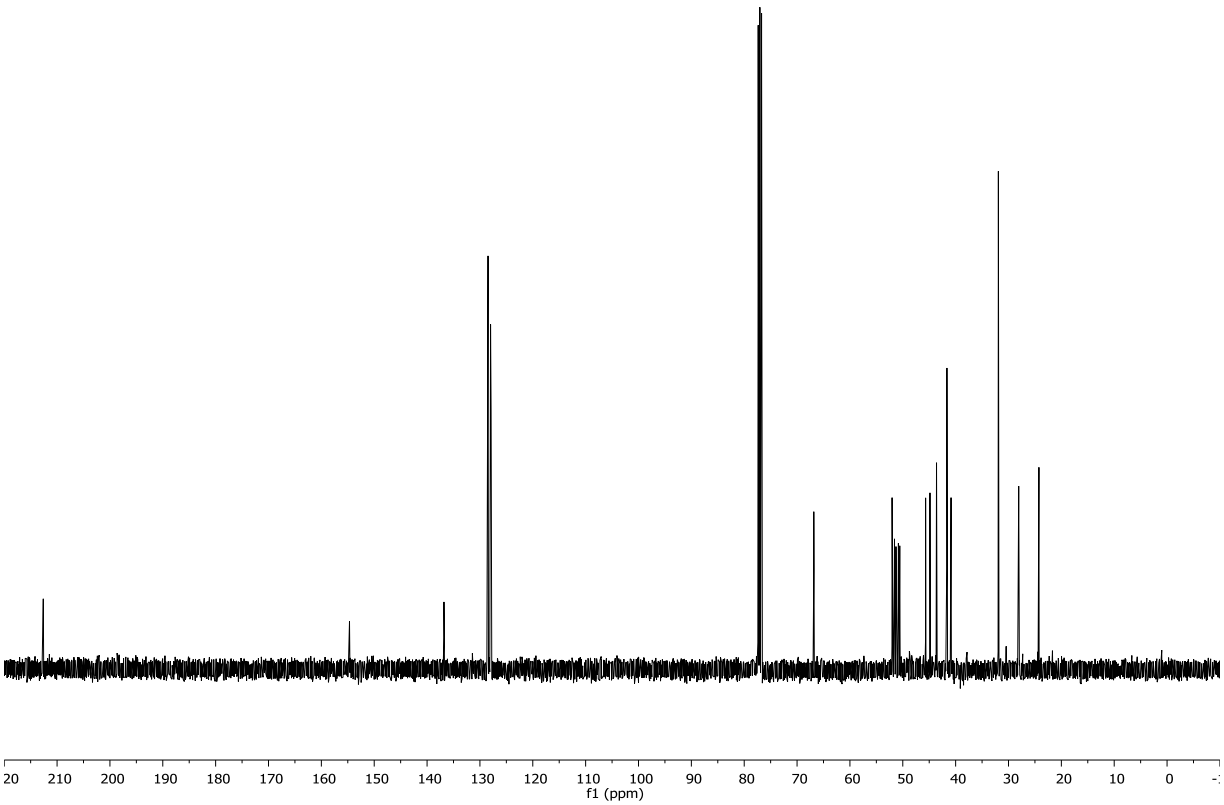


(1*R, 5*S**, 6*R**)-Benzyl allyl((-bicyclo[3.1.0]hexan-6-yl)methyl)carbamate (6v)**

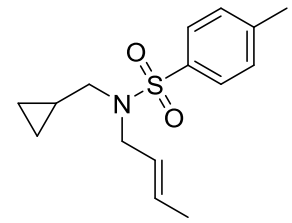


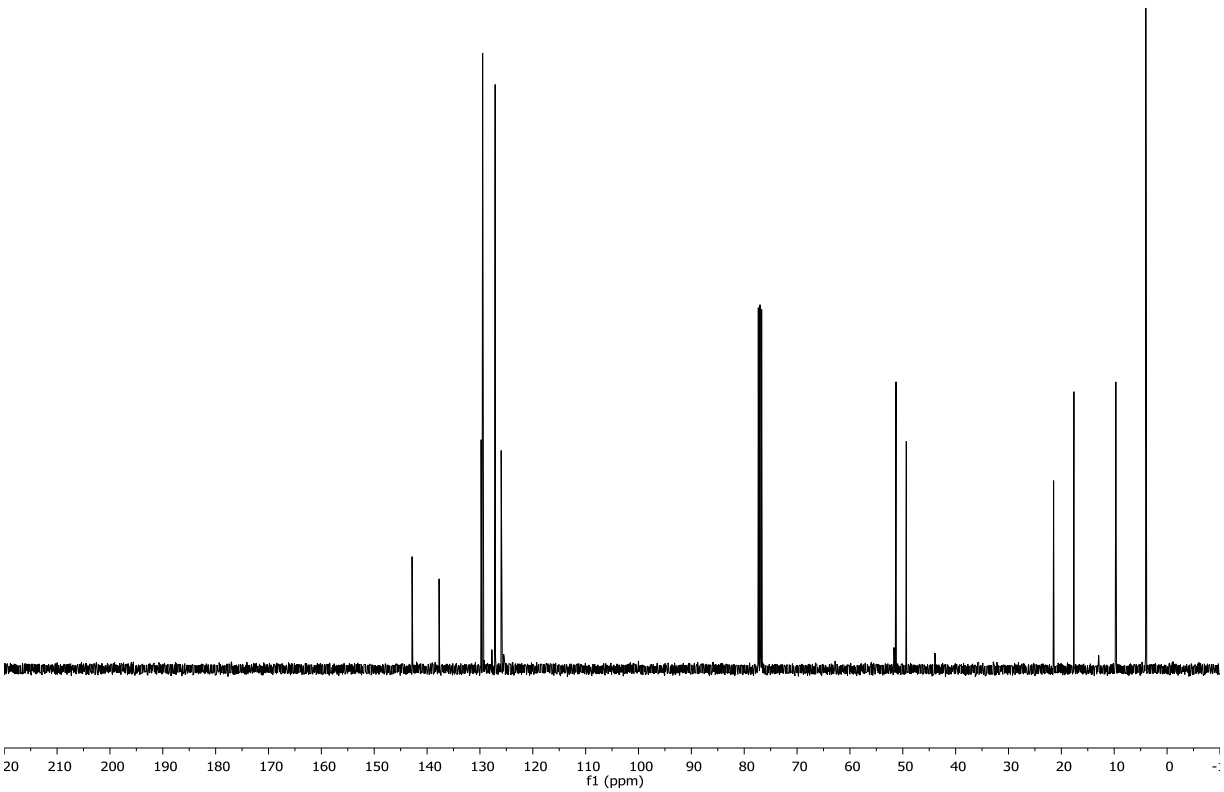
(3a*R, 5a*R**, 8a*R**, 8b*R**)-Benzyl 5-oxodecahydrocyclopenta[e]isoindole-2(3*H*)-carboxylate (8v)**



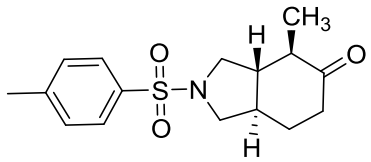


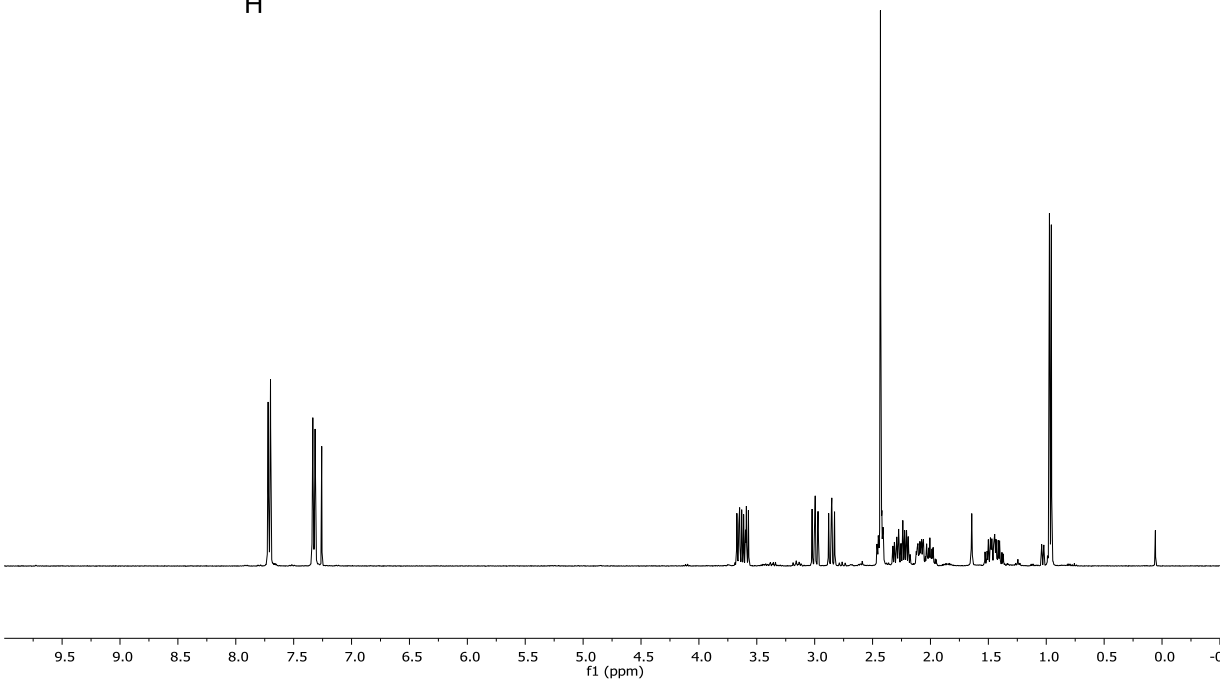
(*E*)-*N*-(But-2-en-1-yl)-*N*-(cyclopropylmethyl)-4-methylbenzenesulfonamide (6w)

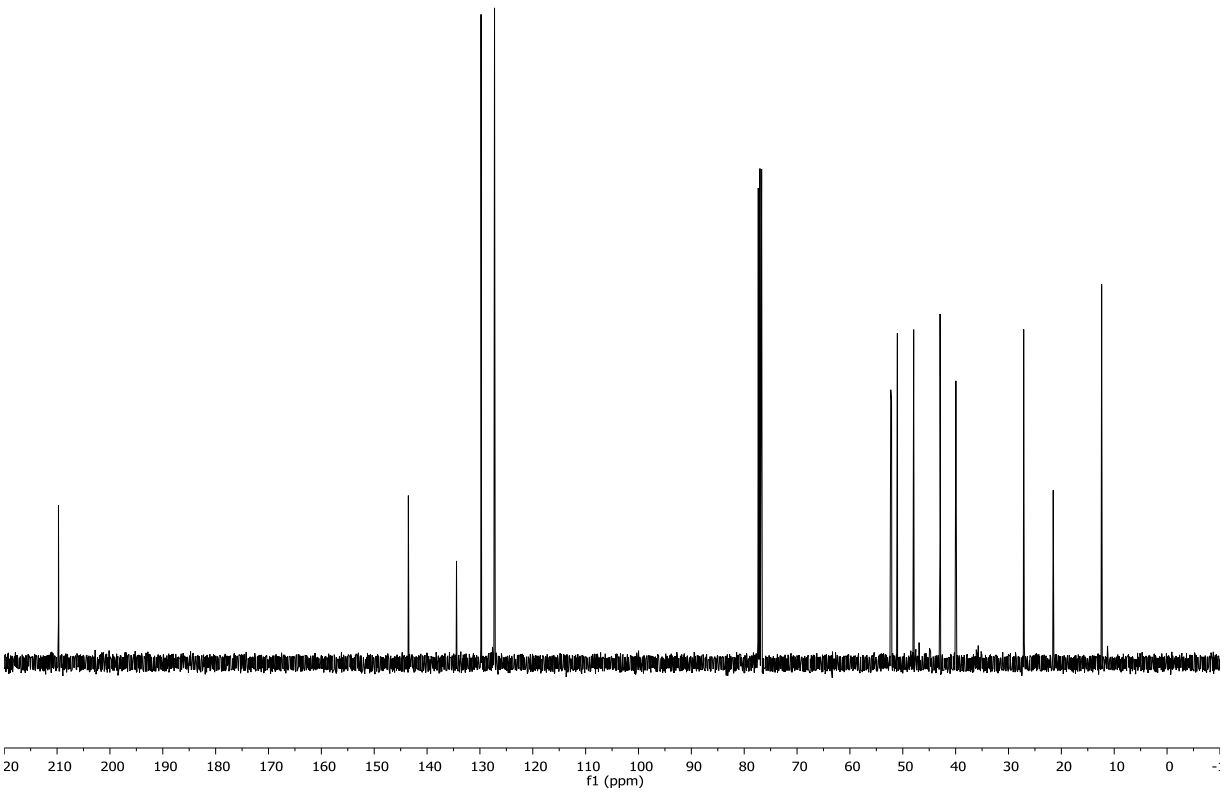




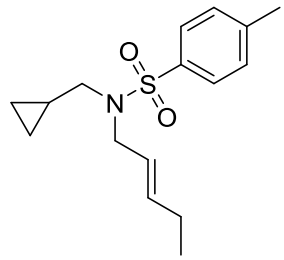
(3a*S, 4*R**, 7a*R**)-4-Methyl-2-tosylhexahydro-1*H*-isoindol-5(6*H*)-one (8w)**

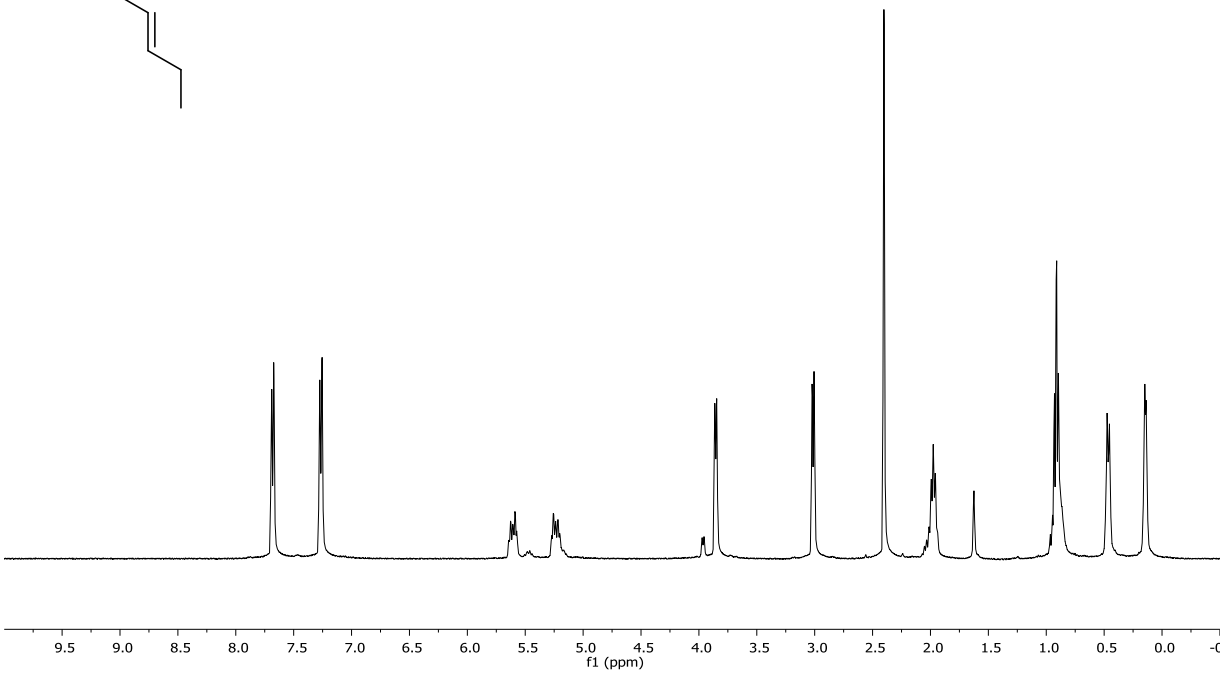


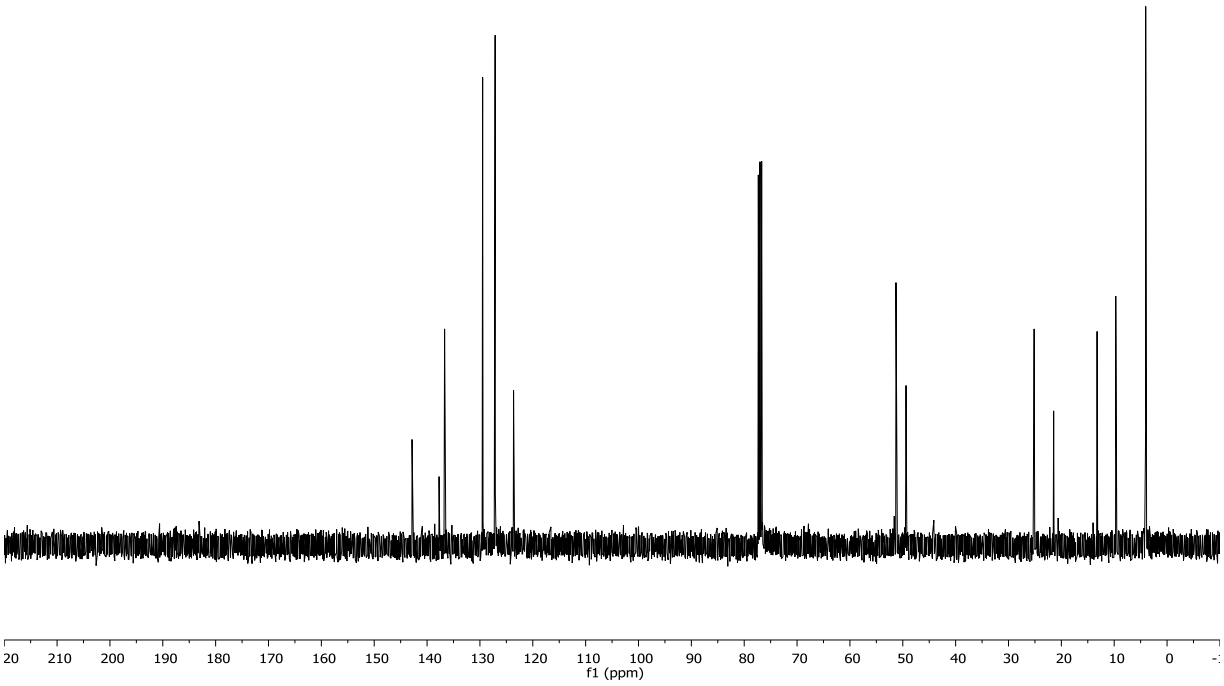




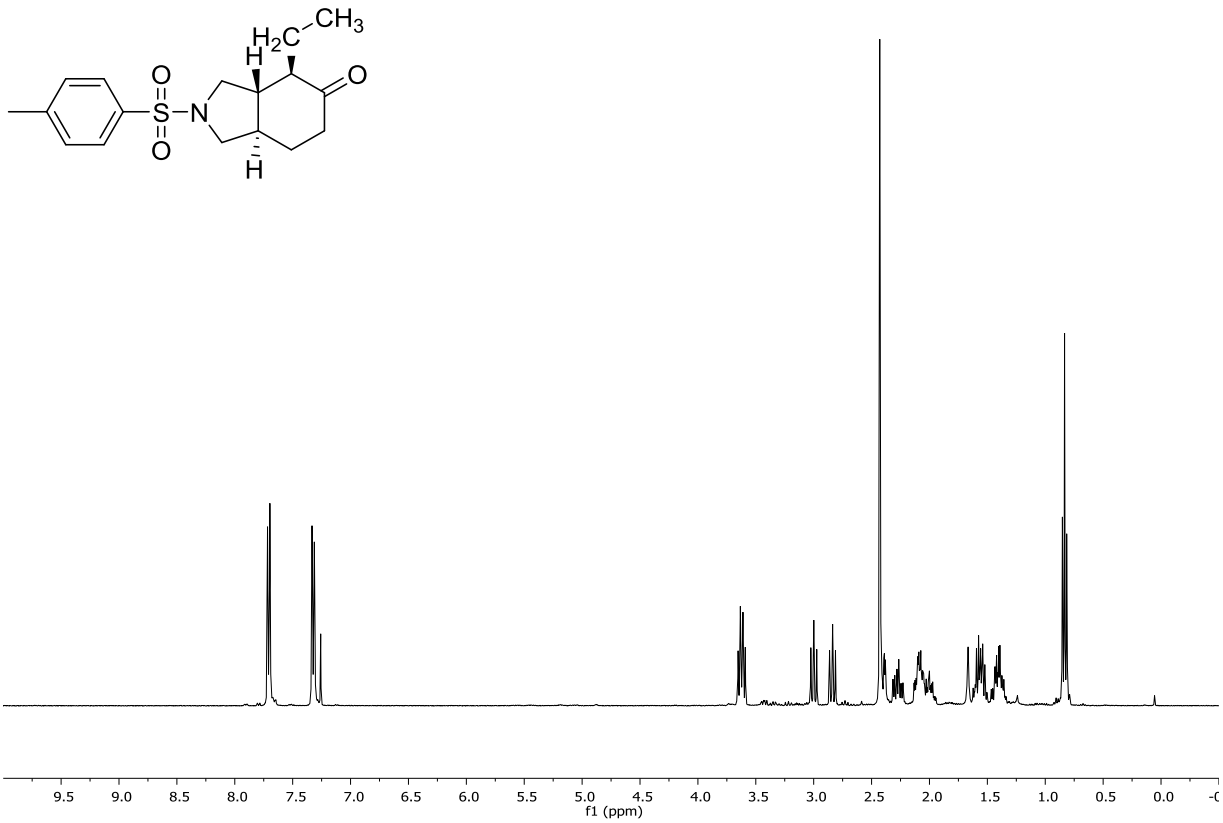
(*E*) –*N*-(Cyclopropylmethyl)-4-methyl-*N*-(pent-2-en-1-yl)benzenesulfonamide (6x)

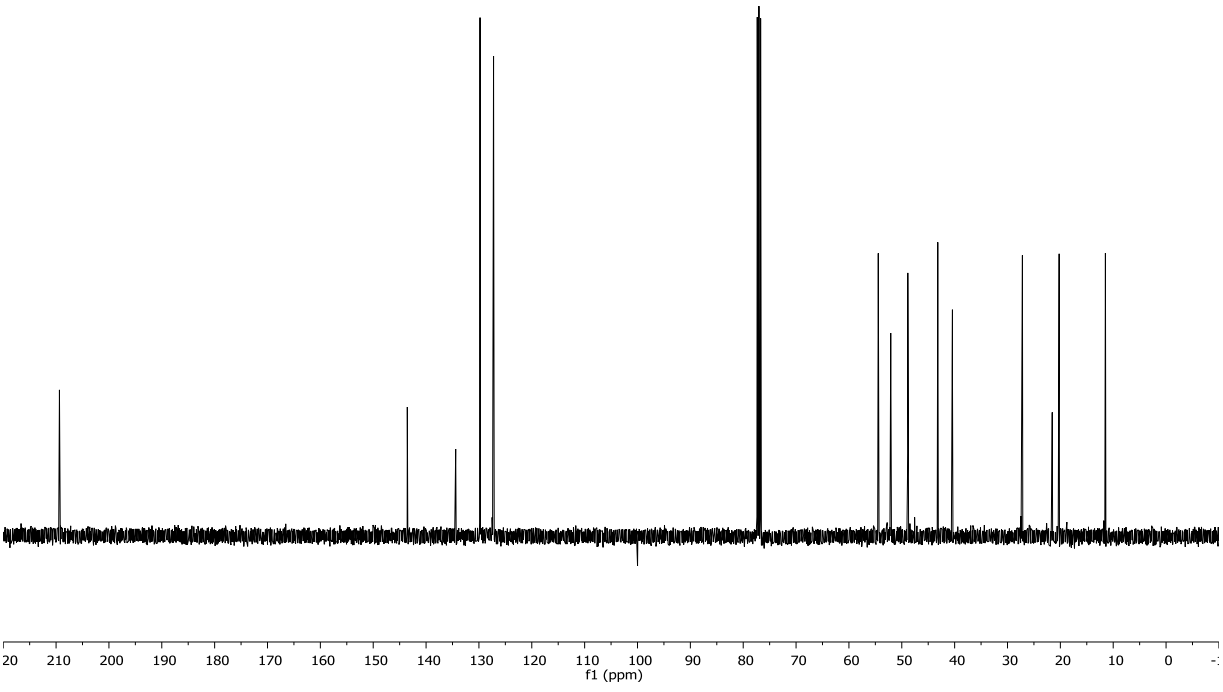




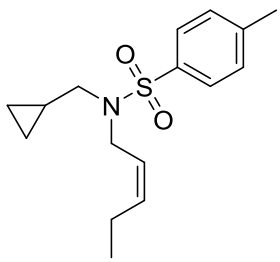


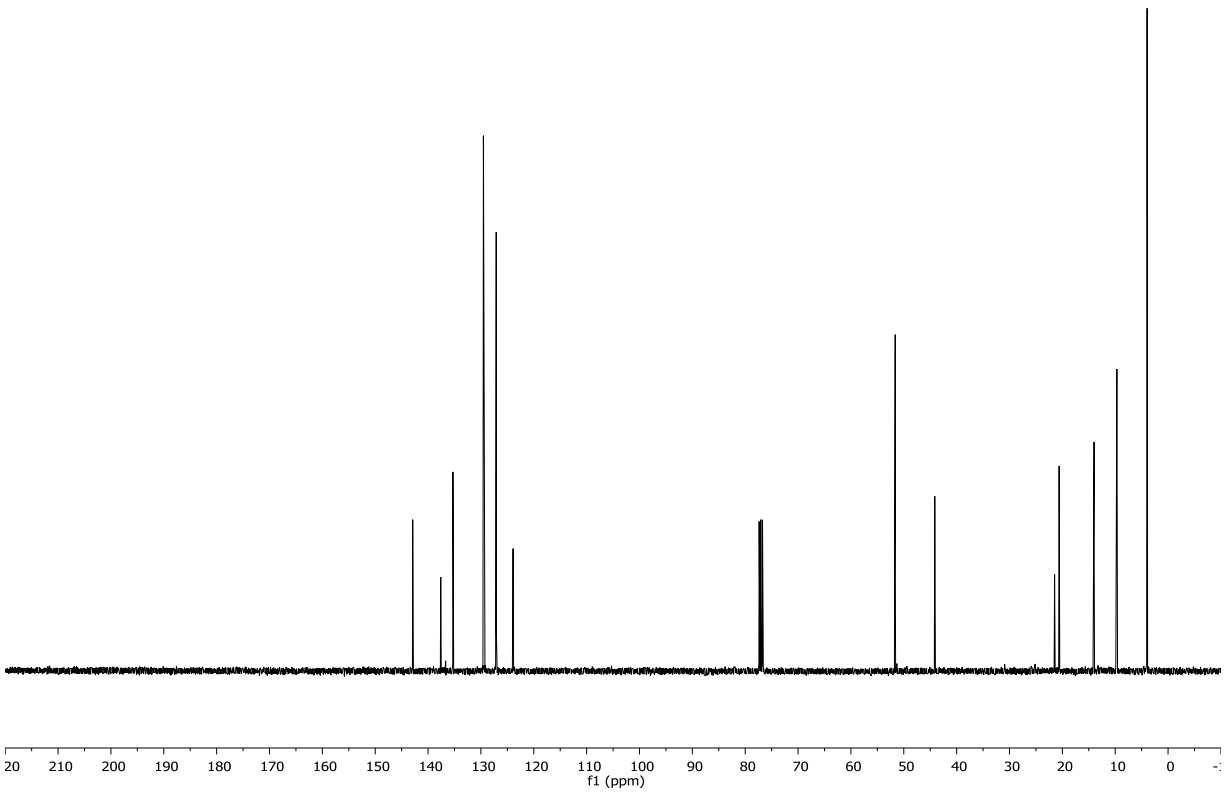
(3a*S, 4*R**, 7a*R**)-4-Ethyl-2-tosylhexahydro-1*H*-isoindol-5(6*H*)-one (8x)**



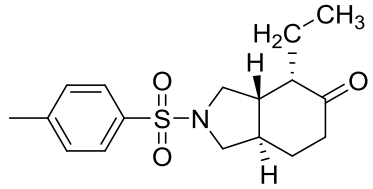


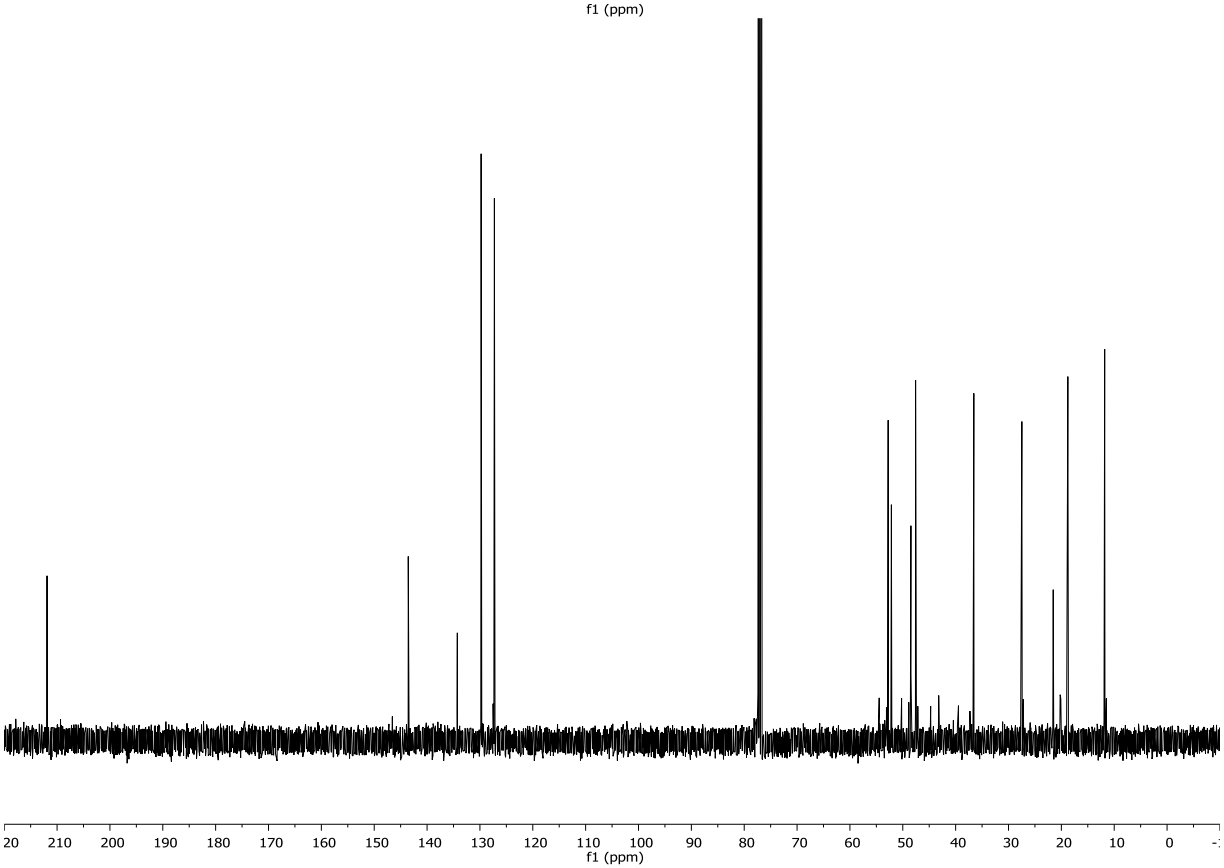
(*Z*)-*N*-(Cyclopropylmethyl)-4-methyl-*N*-(pent-2-en-1-yl)benzenesulfonamide (6x')



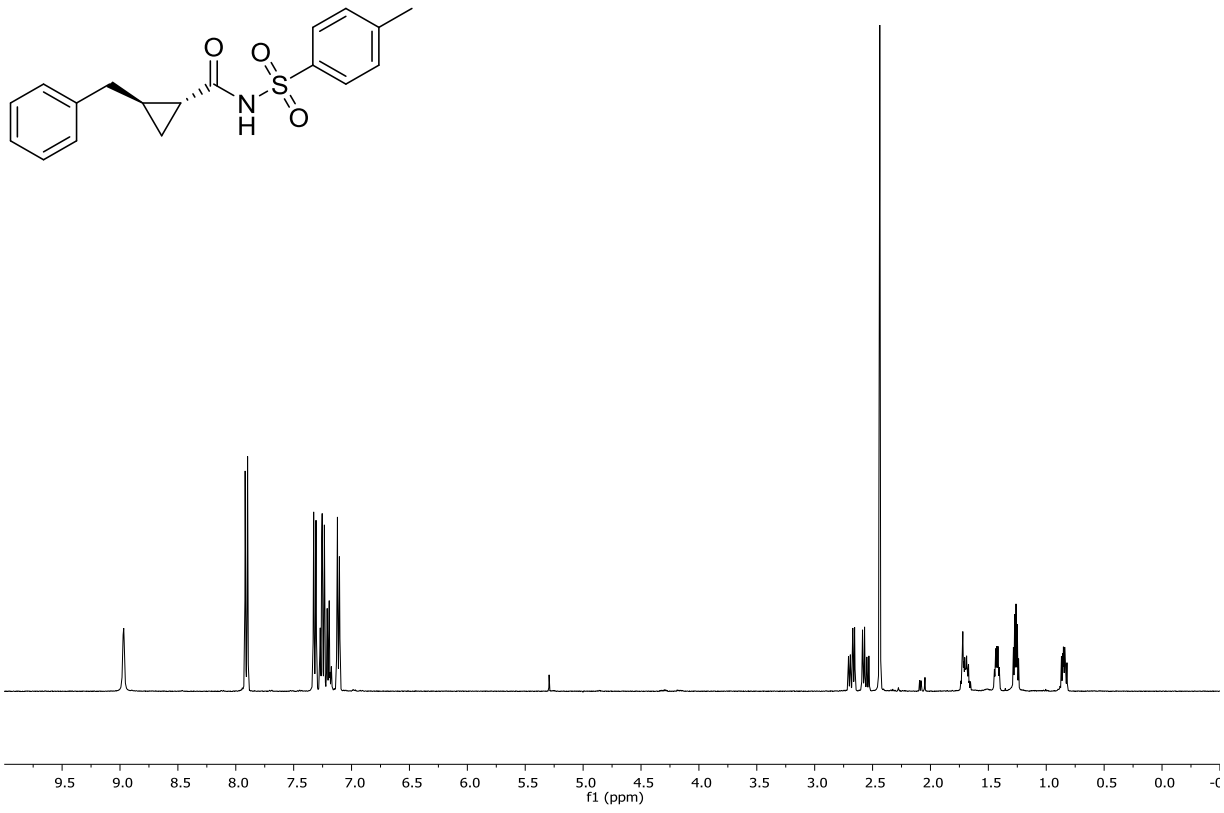


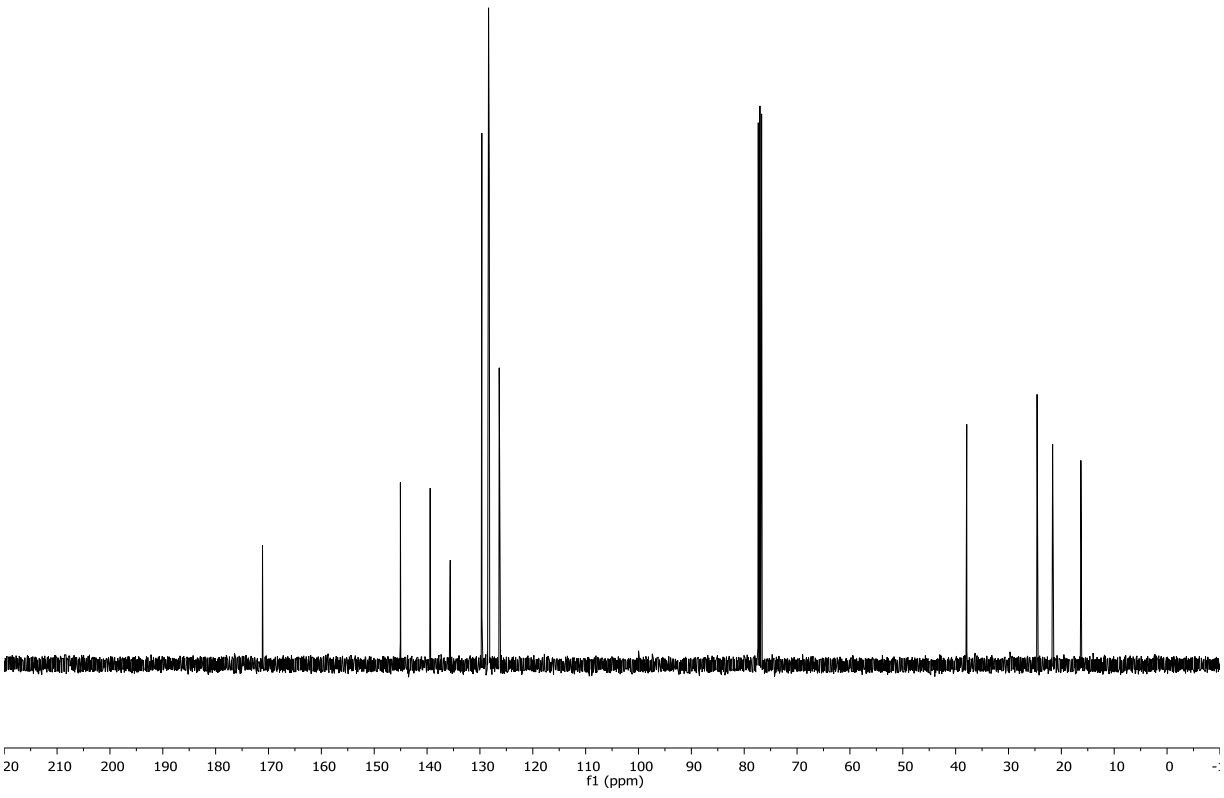
(3a*S, 4*S**, 7a*R**) and (3a*S**, 4*R**, 7a*R**)-4-Ethyl-2-tosylhexahydro-1*H*-isoindol-5(6*H*)-one (8x')**



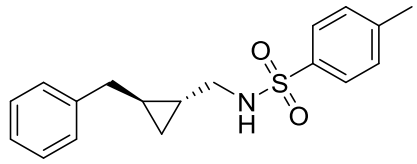


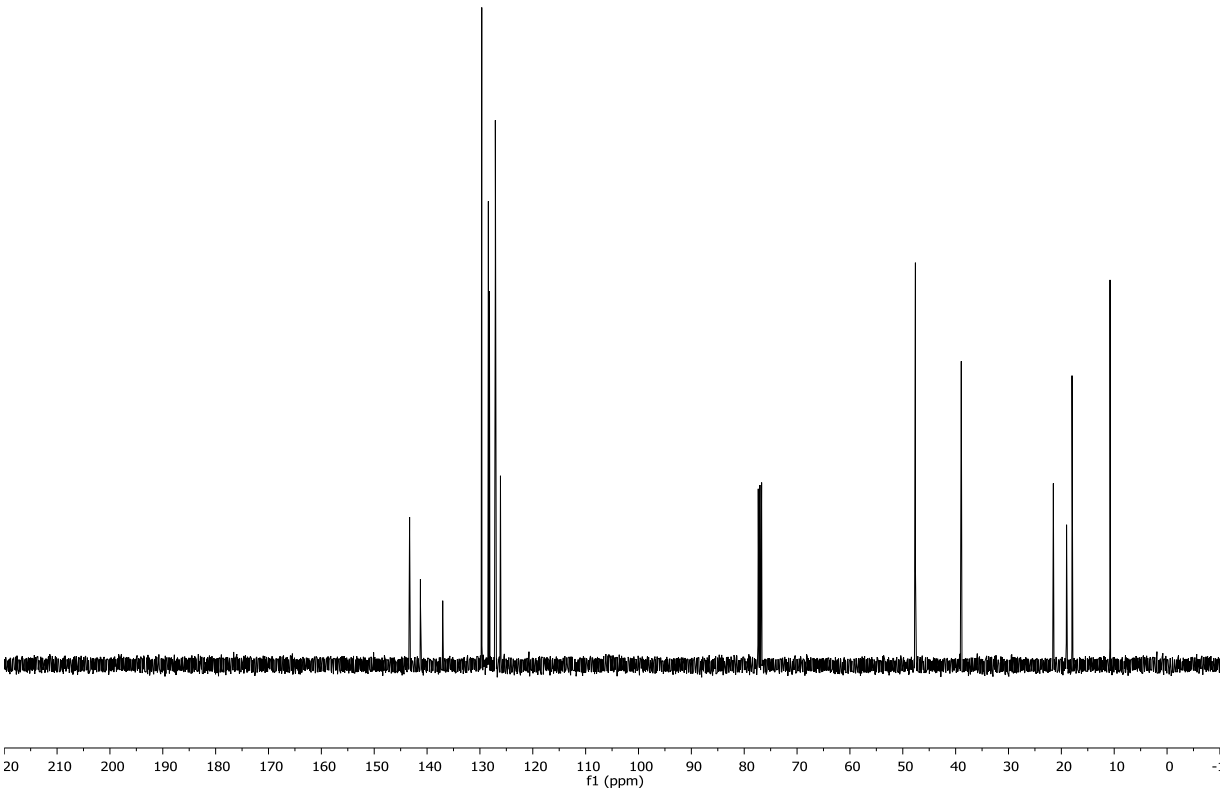
(1*R, 2*S**)-2-Benzyl-*N*-tosylcyclopropane-1-carboxamide**



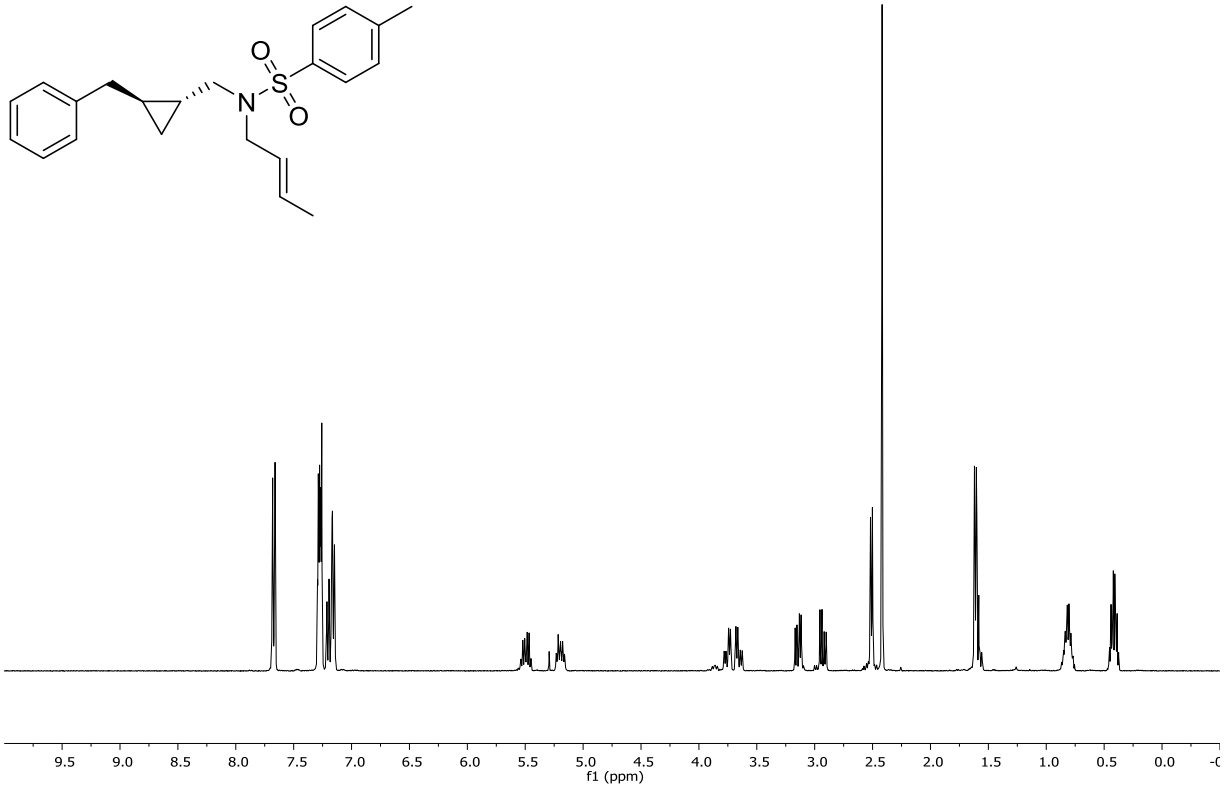


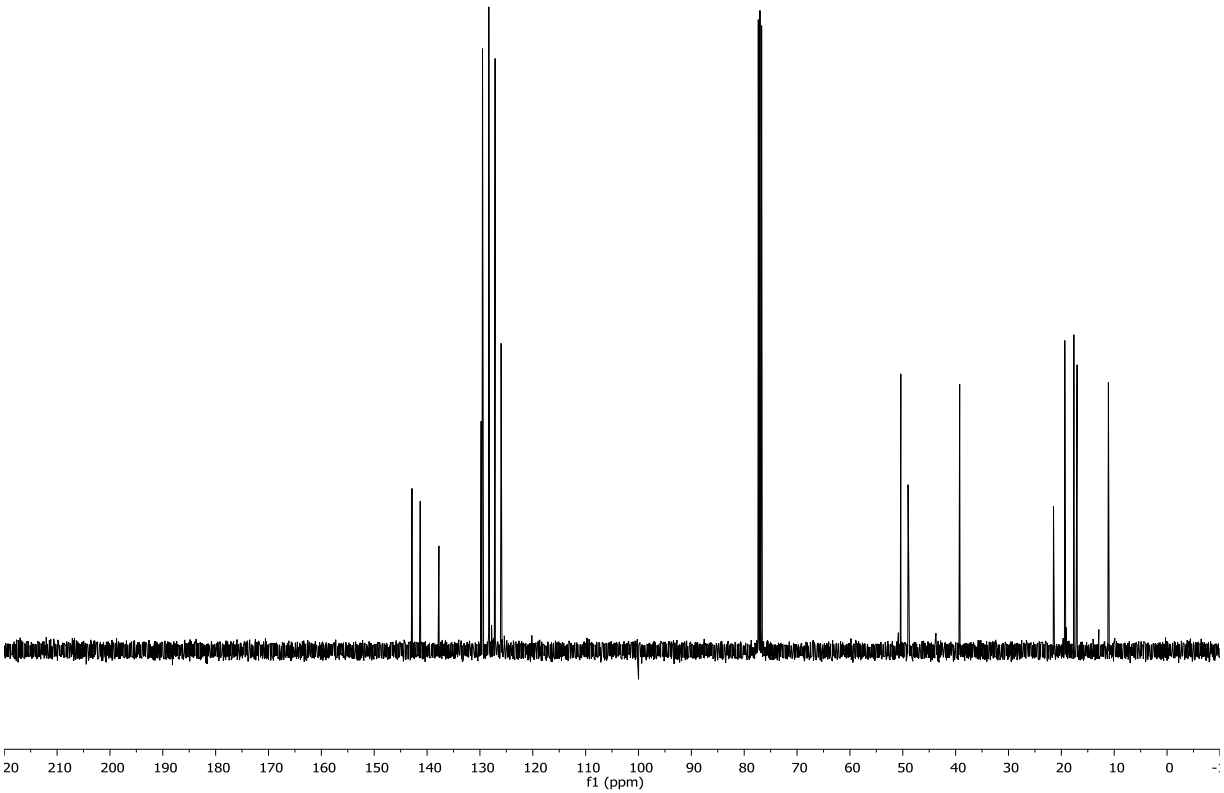
(1*R, 2*S**)-*N*-((2-Benzylcyclopropyl)methyl)-4-methylbenzenesulfonamide**



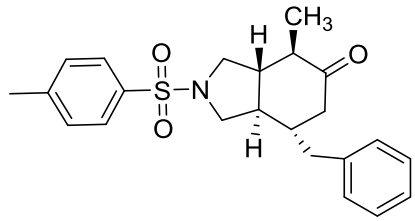


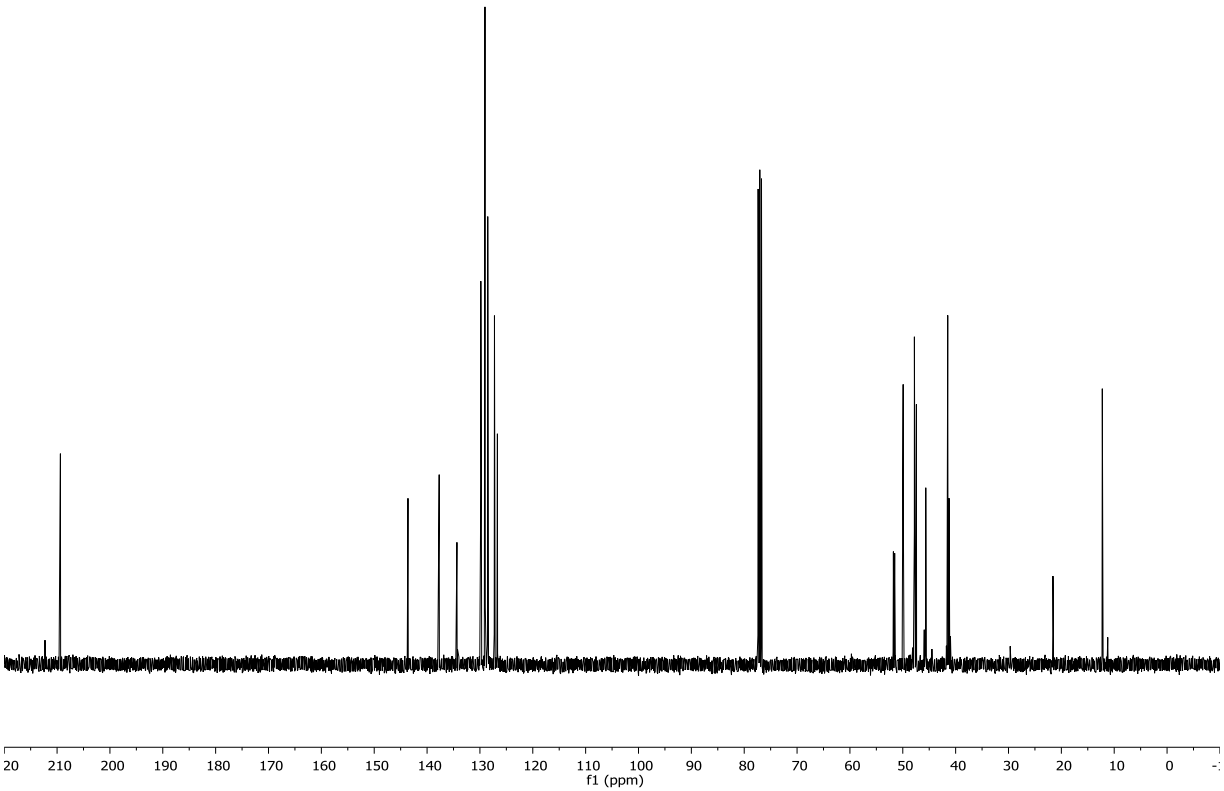
(1*R, 2*S**)-*N*-((-2-Benzylcyclopropyl)methyl)-*N*-(*E*-but-2-en-1-yl)-4-methylbenzenesulfon amide (6y)**



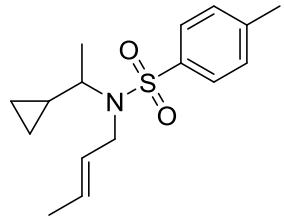


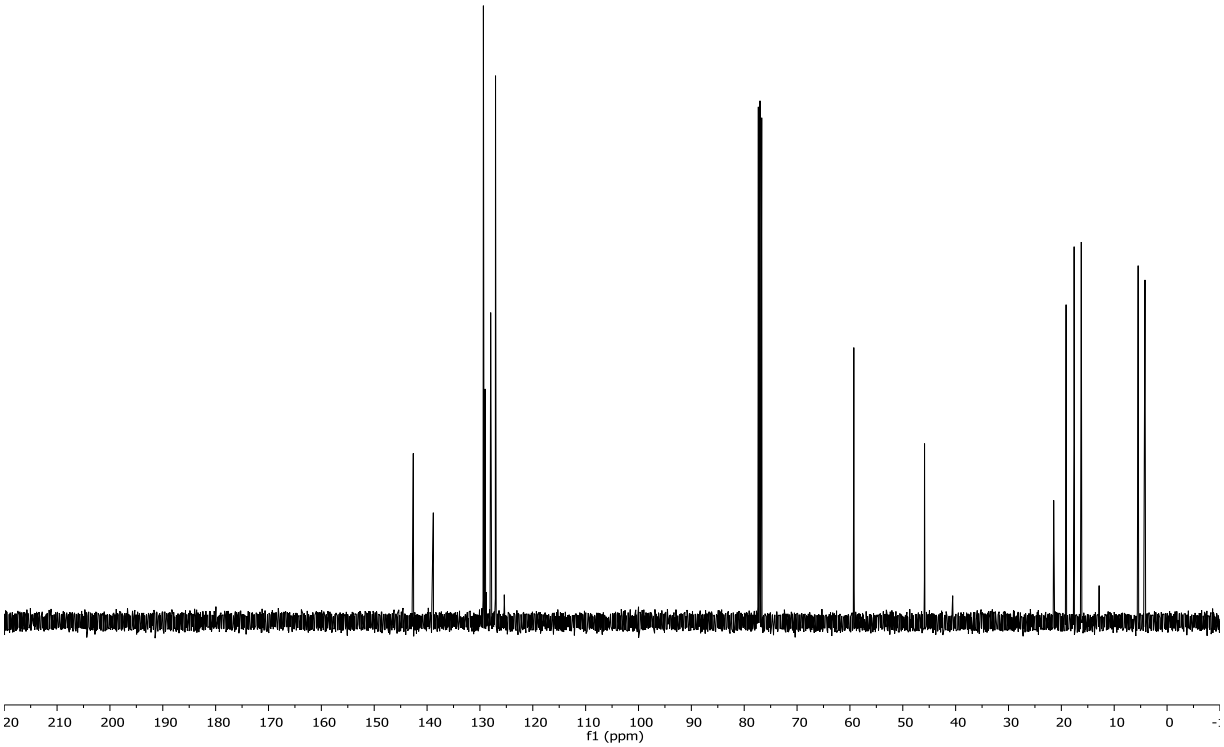
(3a*S, 4*R**, 7*S**, 7a*R**) and (3a*S**, 4*S**, 7*S**, 7a*R**)-7-Benzyl-4-methyl-2-tosyloctahydro-5*H*-isoindol-5-one (8y)**



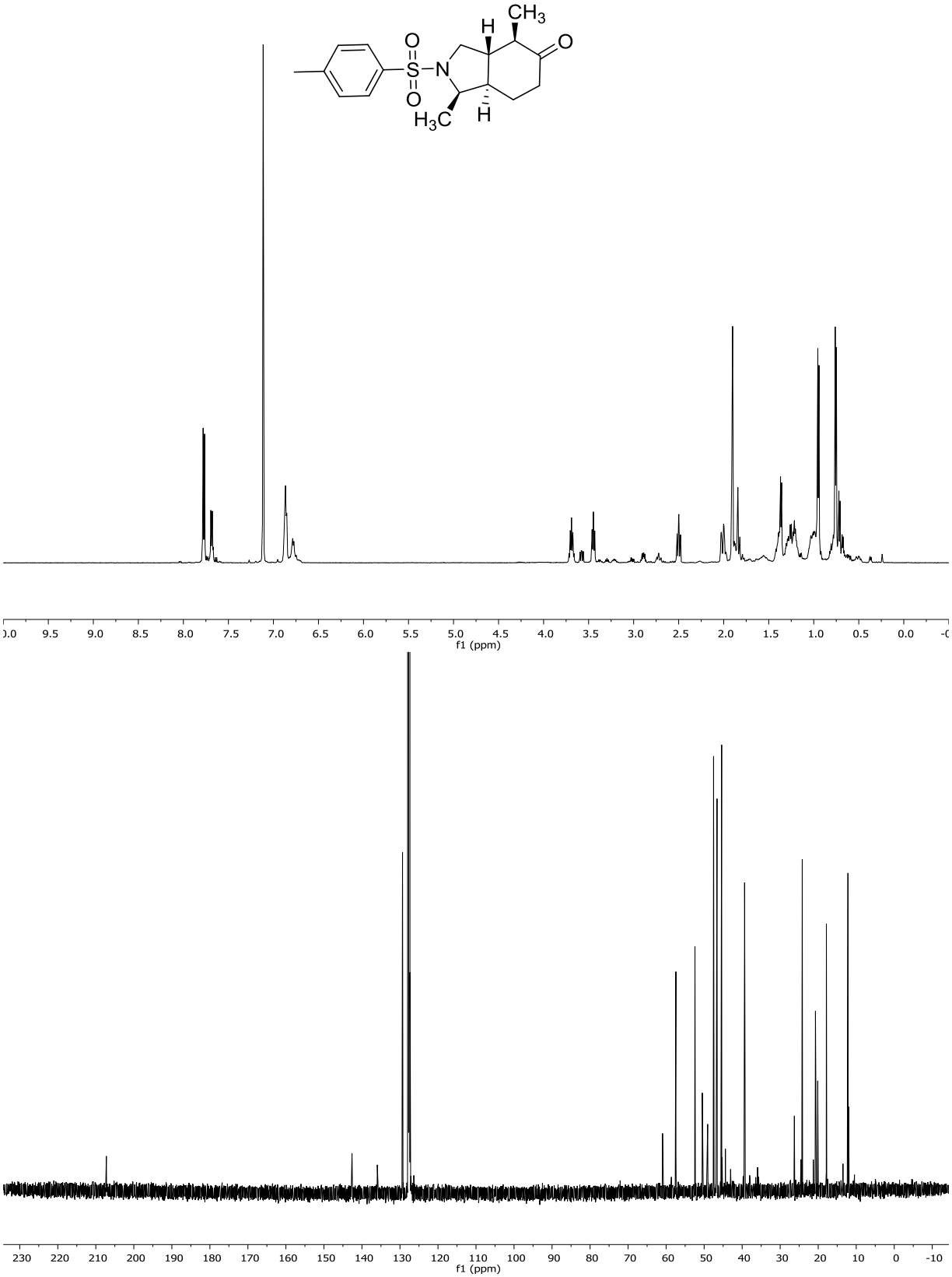


(*E*)-*N*-(But-2-en-1-yl)-*N*-(1-cyclopropylethyl)-4-methylbenzenesulfonamide (6z)

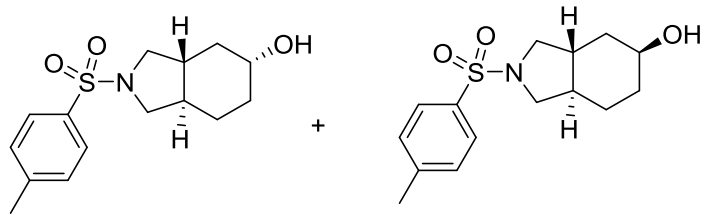


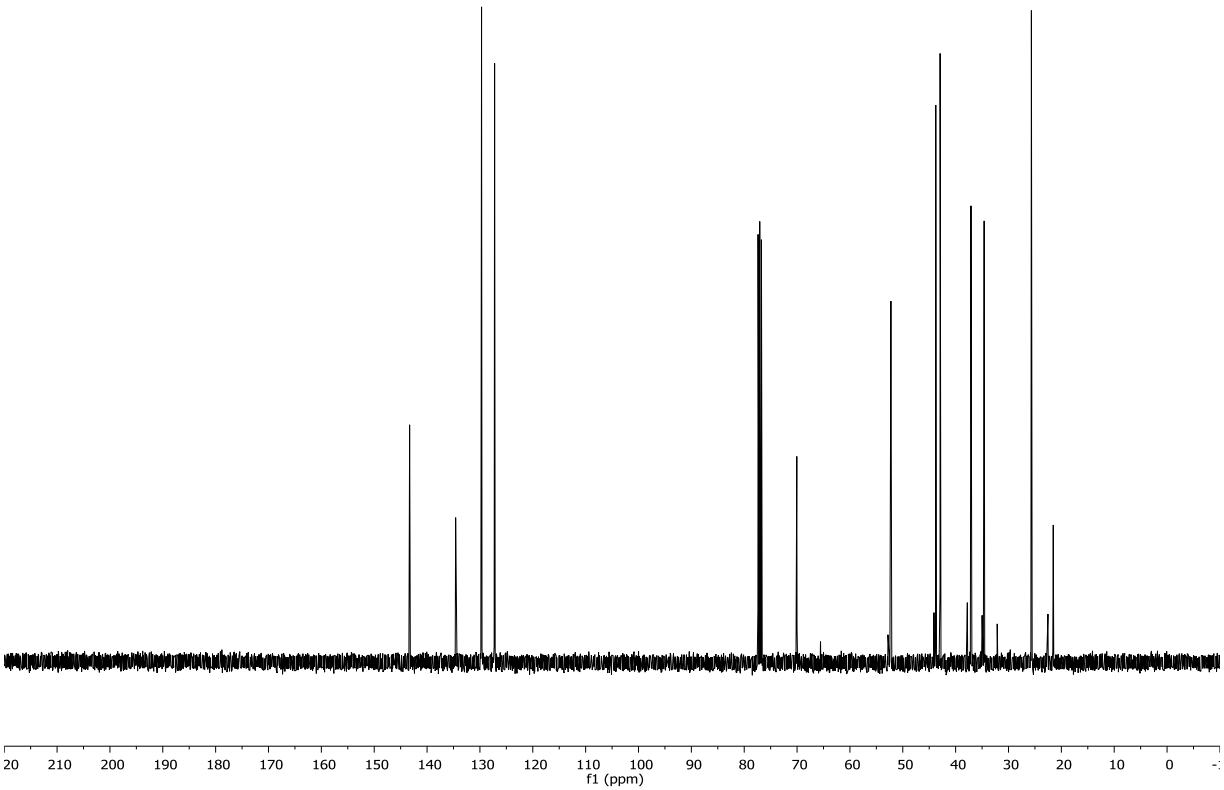


(1*R*, 3a*S***, 4*R***, 7a*R***) and (1*S***, 3a*S***, 4*R***, 7a*R***) and (1*R***, 3a*S***, 4*S***, 7a*R***)-1,4-Dimethyl-2-tosyloctahydro-5*H*-isoindol-5-one (8z)**

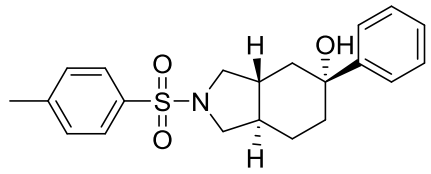


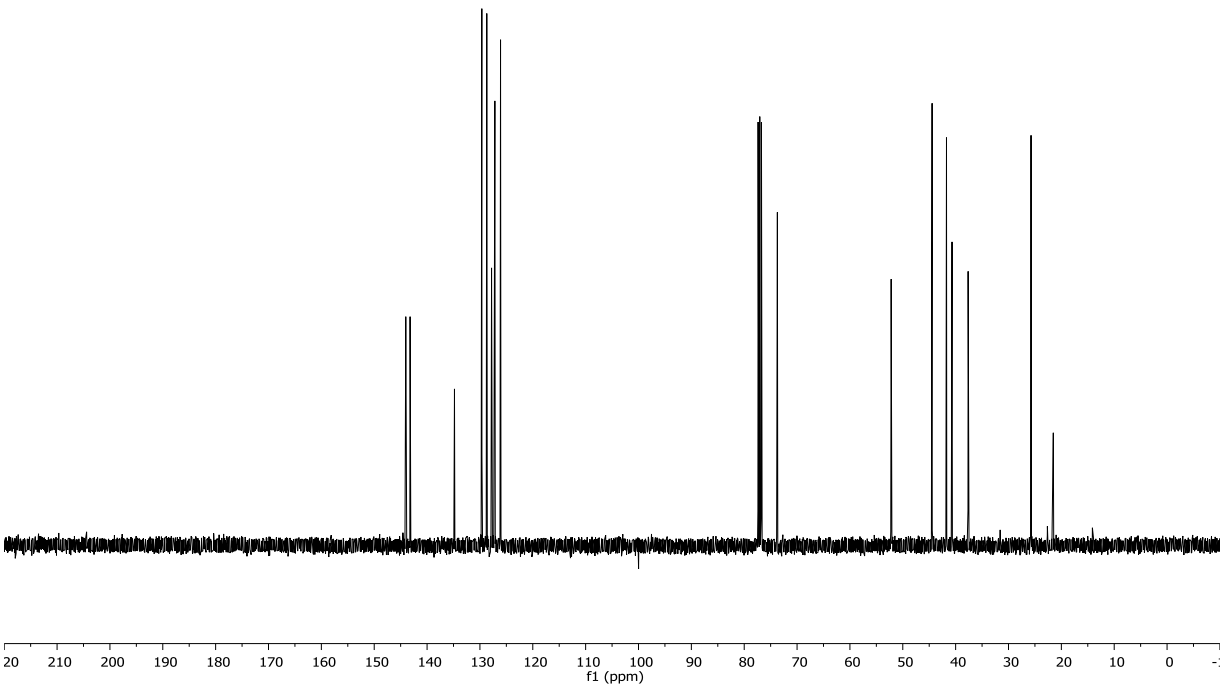
(3a*R, 5*R**, 7a*R**)-2-Tosyloctahydro-1*H*-isoindol-5-ol and (3a*R**, 5*S**, 7a*R**)-2-tosyloct-ahydro-1*H*-isoindol-5-ol (12e)



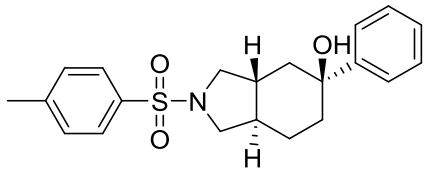


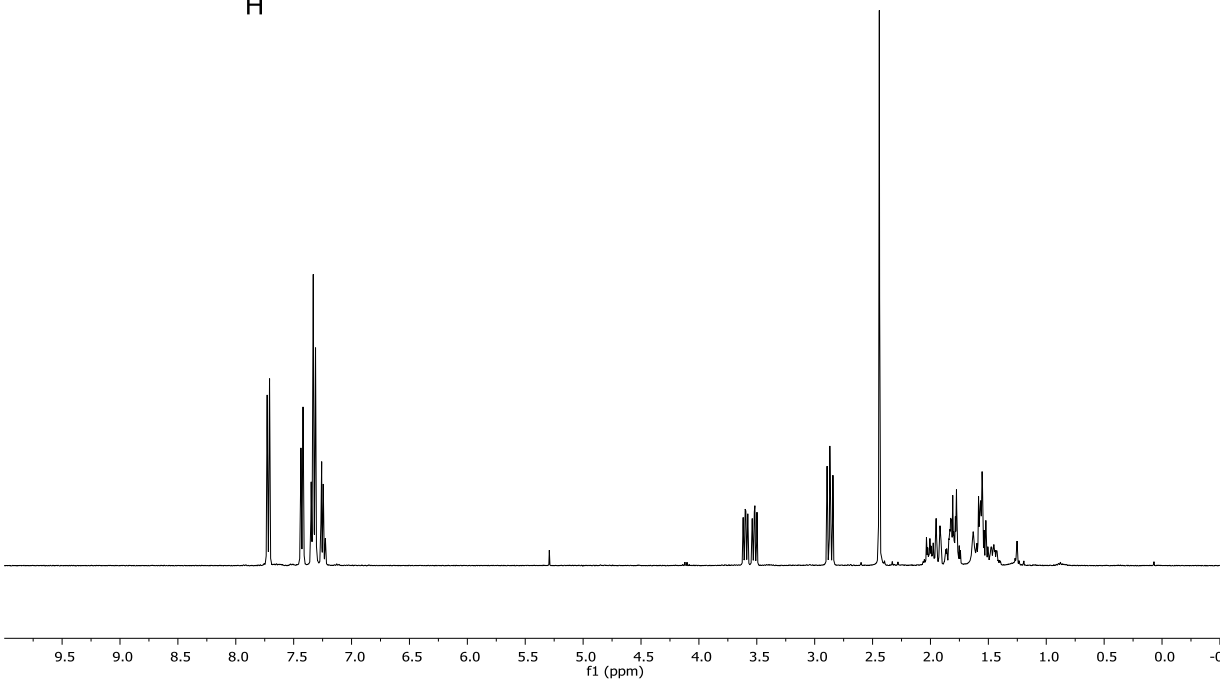
(3a*R, 5*R**, 7a*R**) -5-Phenyl-2-tosyloctahydro-1*H*-isoindol-5-ol (13e-A)**

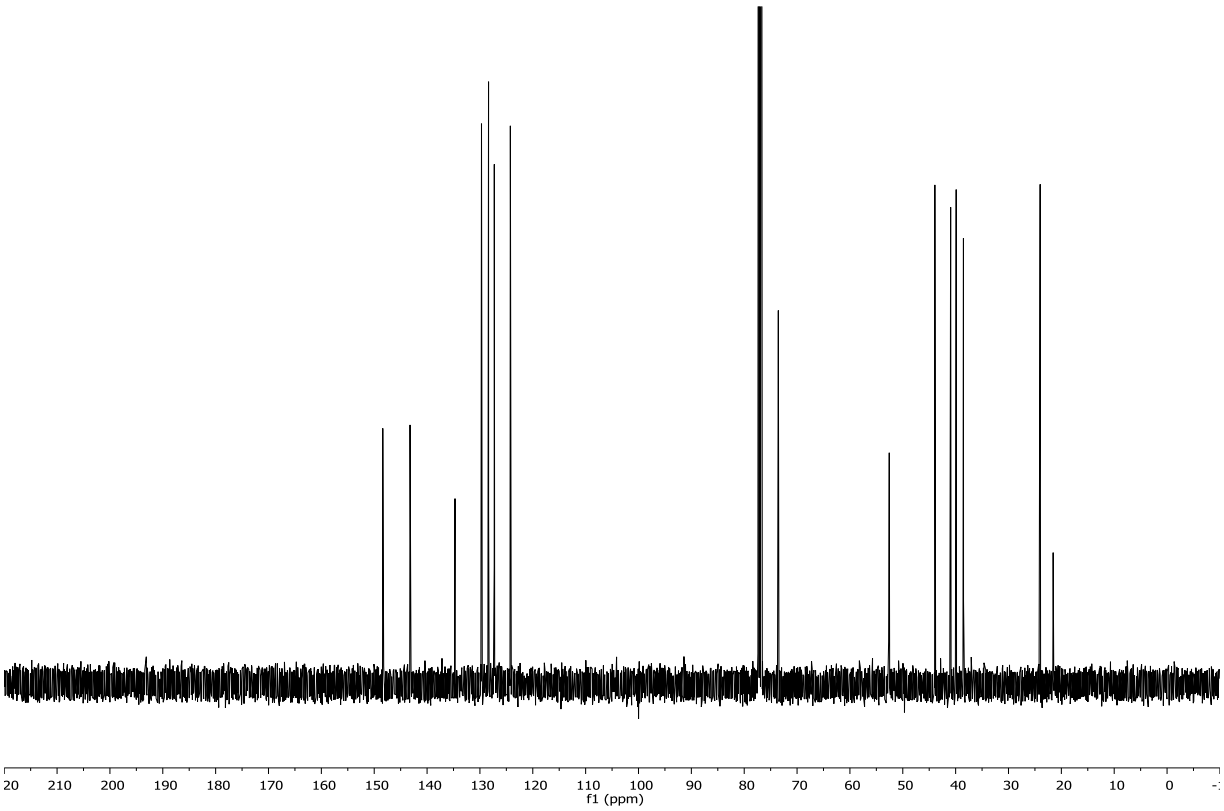




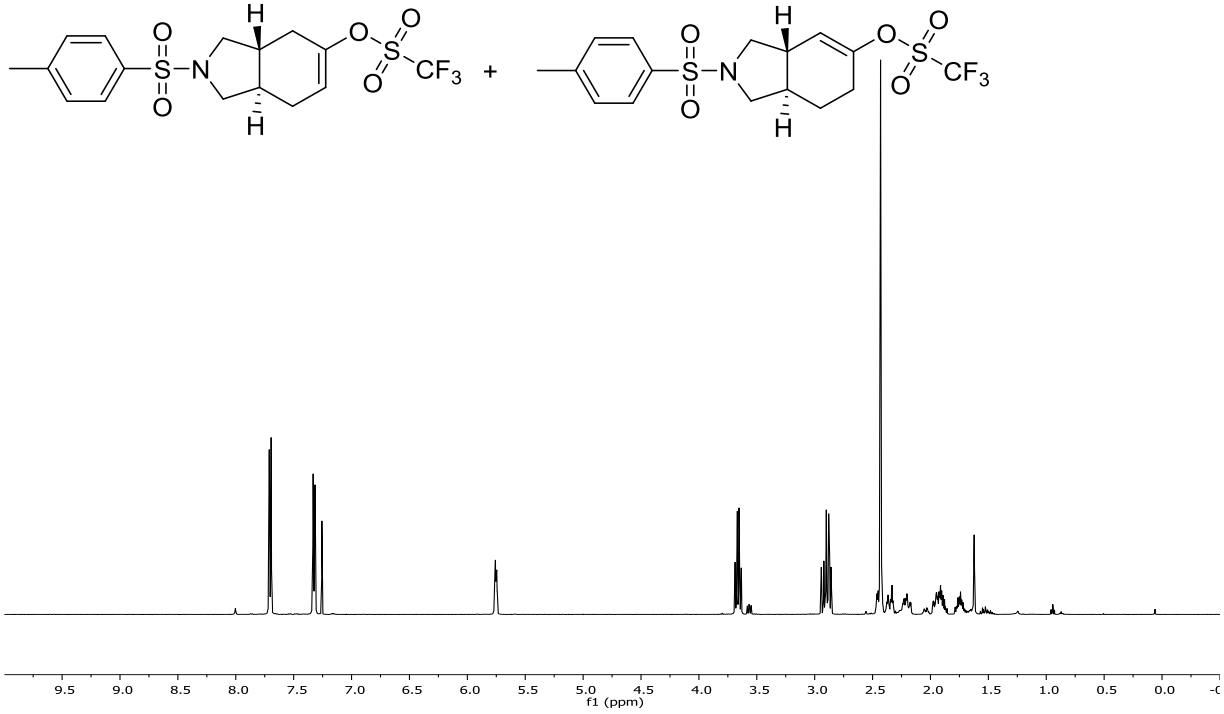
(3a*R, 5*S**, 7a*R**) -5-Phenyl-2-tosyloctahydro-1*H*-isoindol-5-ol (13e-B)**

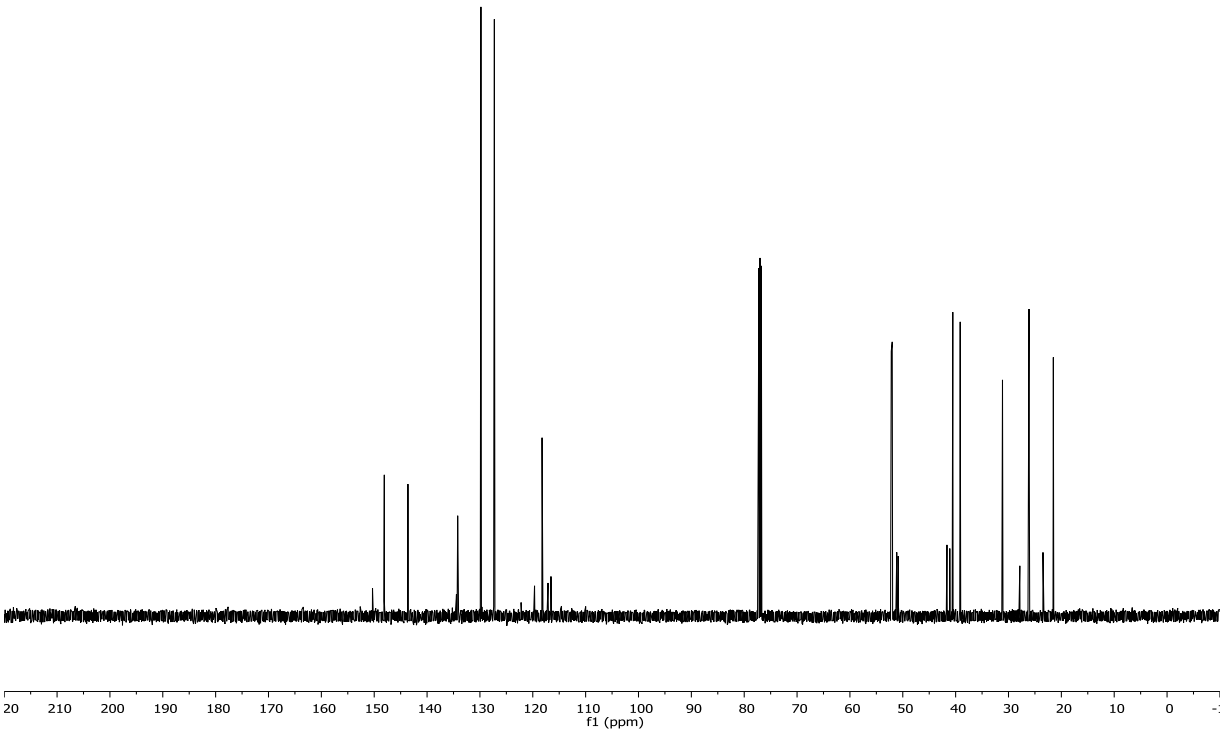


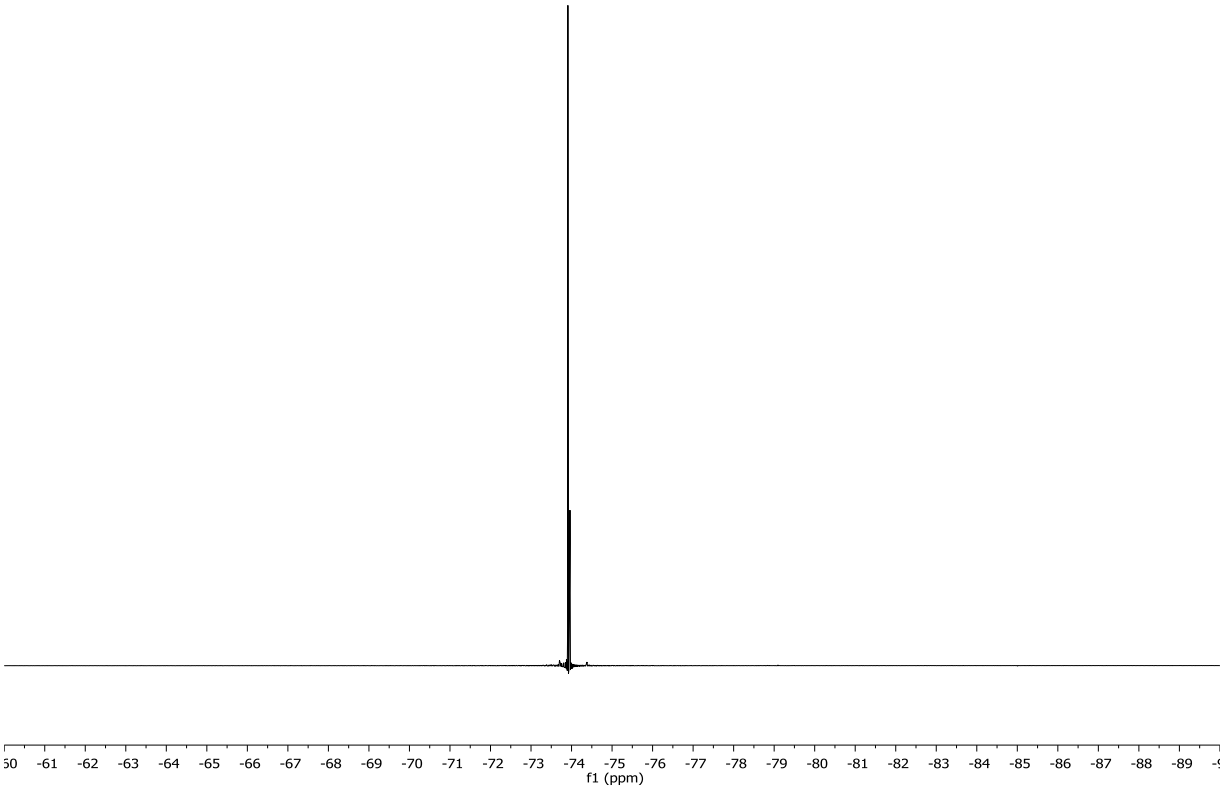




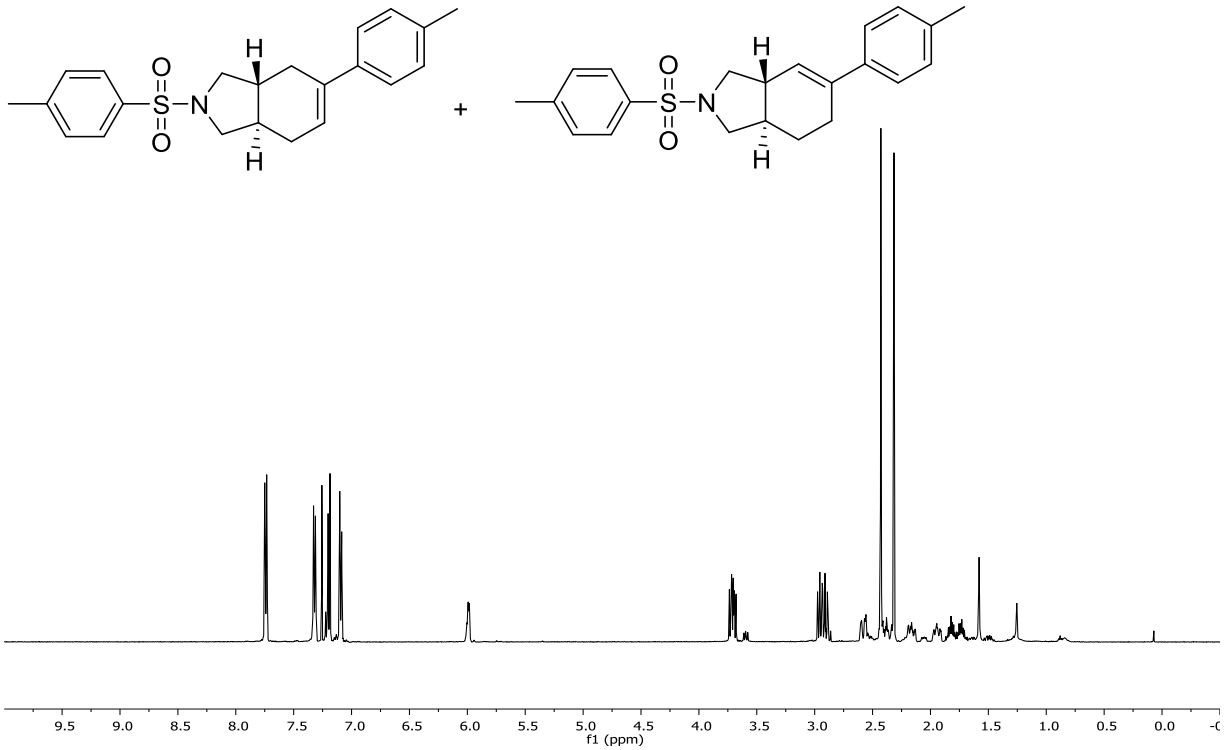
(3a*R*, 7a*R***)-2-Tosyl-2,3,3a,4,7,7a-hexahydro-1*H*-isoindol-5-yl trifluoromethanesulfonate and (3a*S***, 7a*R***)-2-tosyl-2,3,3a,6,7,7a-hexahydro-1*H*-isoindol-5-yl trifluoromethanesulfonate (14e)**

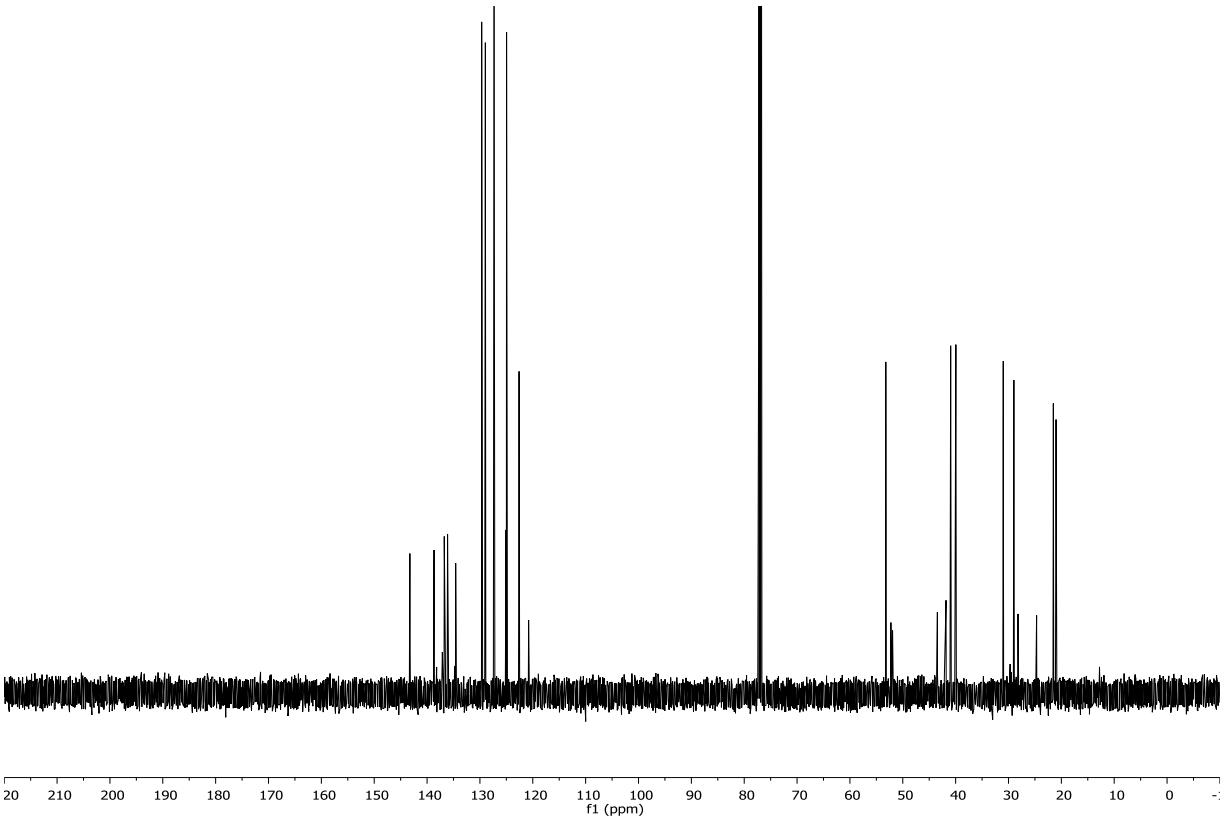




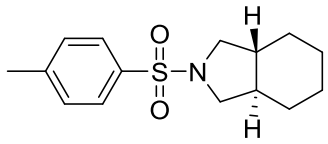

-60 -61 -62 -63 -64 -65 -66 -67 -68 -69 -70 -71 -72 -73 -74 -75 -76 -77 -78 -79 -80 -81 -82 -83 -84 -85 -86 -87 -88 -89
f1 (ppm)

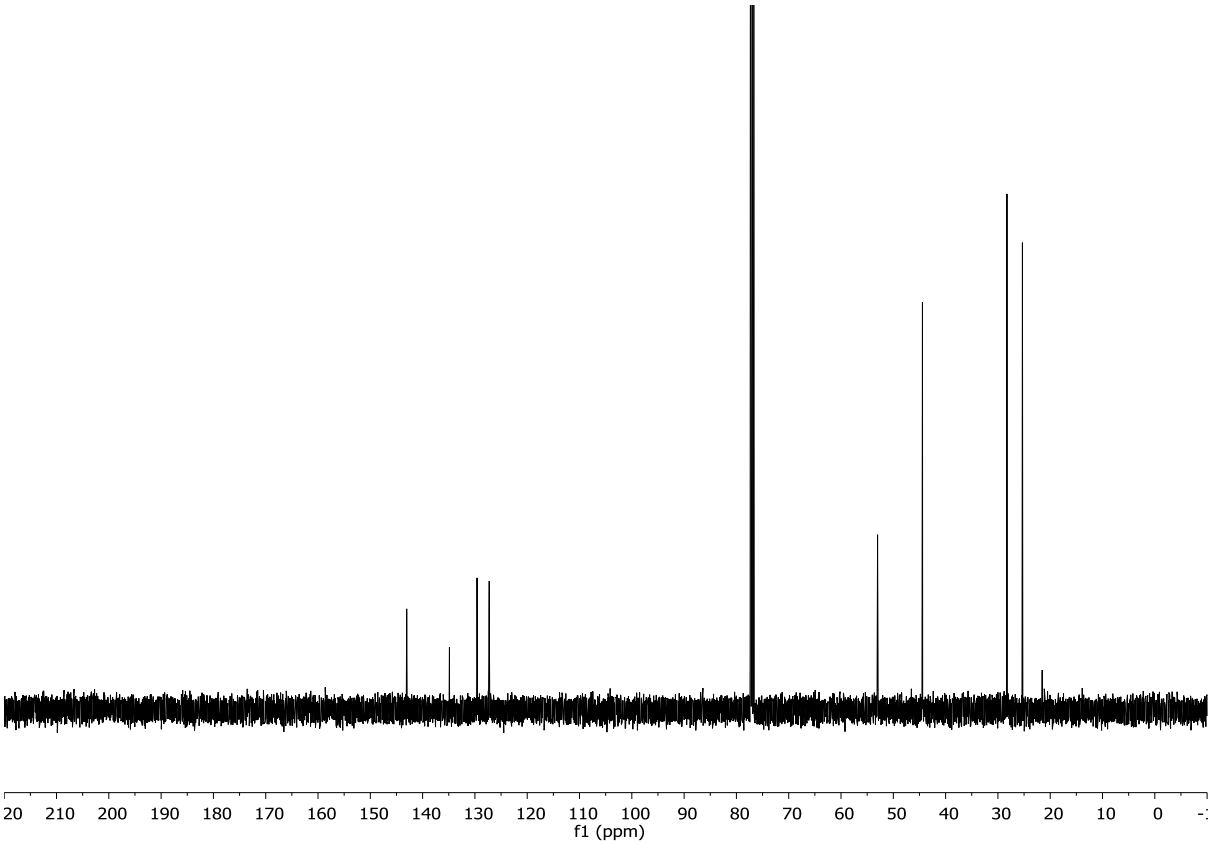
(3a*R, 7a*R**)-5-(*p*-Tolyl)-2-tosyl-2,3,3a,4,7,7a-hexahydro-1*H*-isoindole** and **(3a*R**, 7a*R**)-6-(p-tolyl)-2-tosyl-2,3,3a,4,5,7a-hexahydro-1*H*-isoindole (15e)**



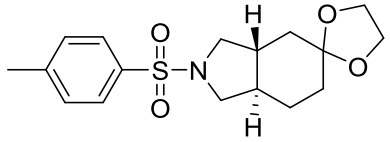


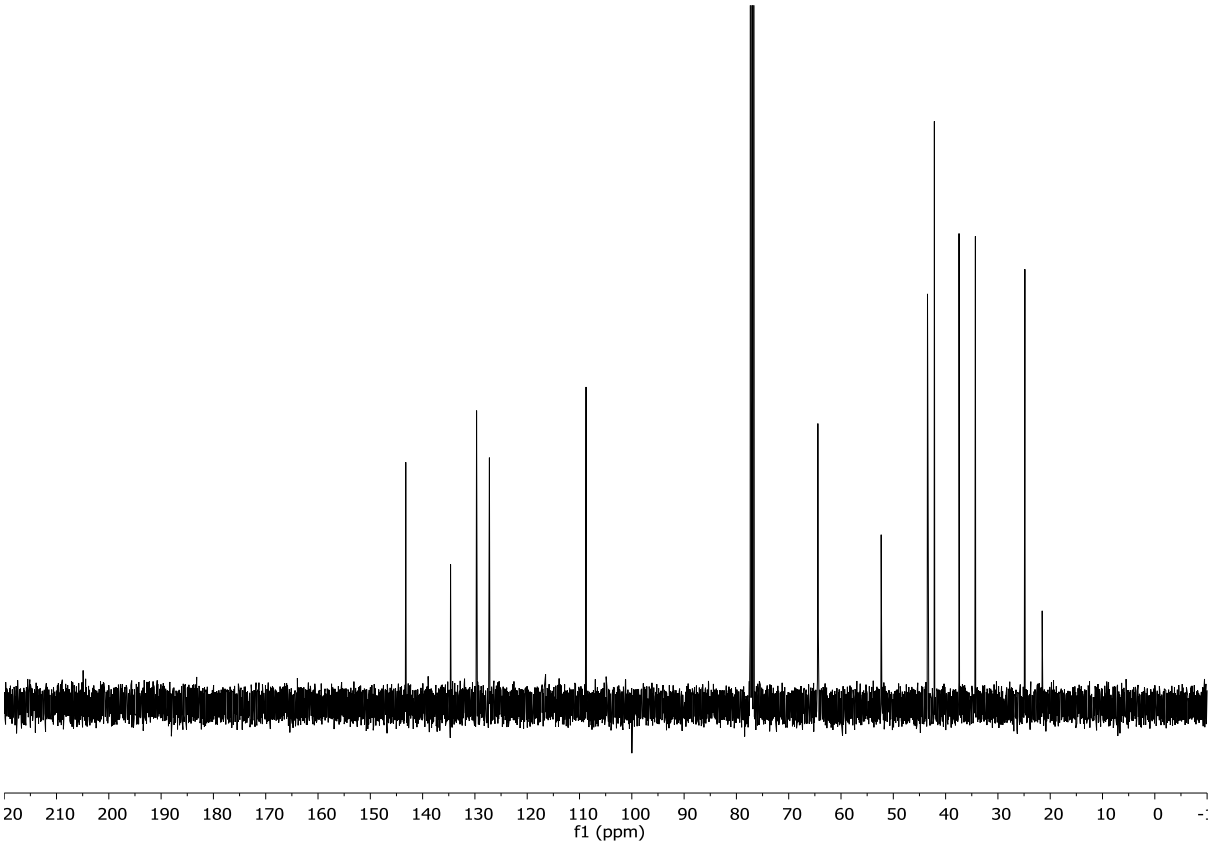
(3a*R, 7a*R**)-2-Tosyloctahydro-1H-isoindole (16e)**



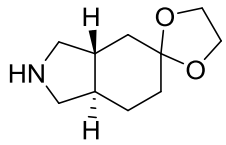


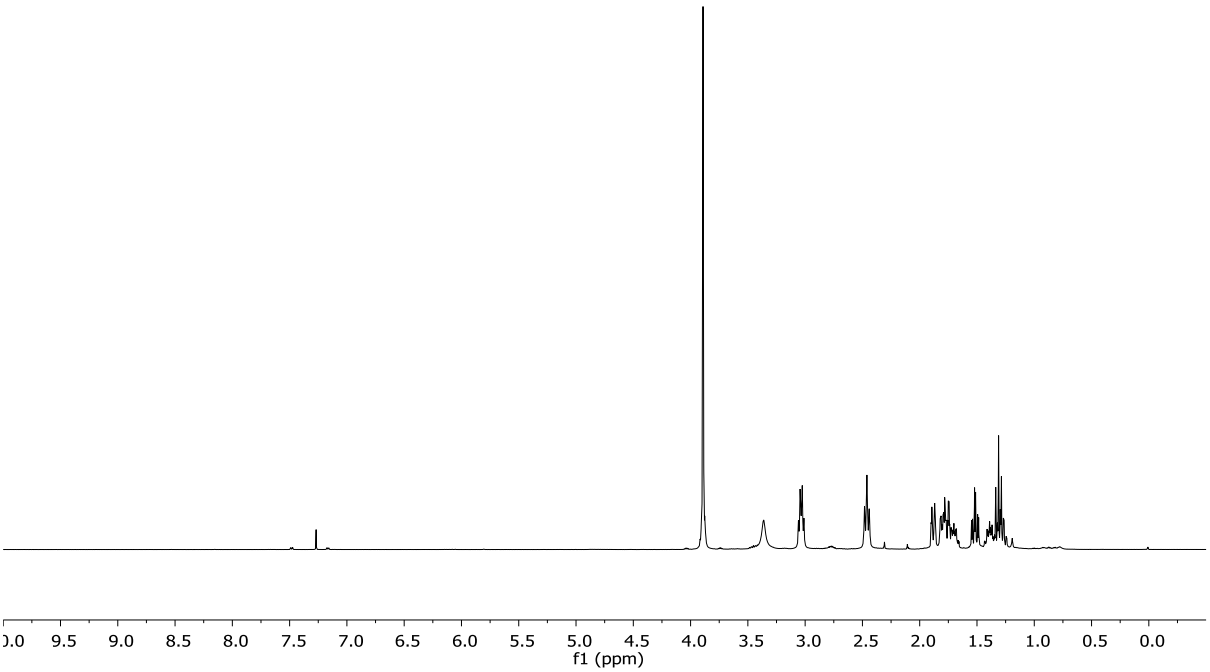
(3a*R, 7a*R**)-2-Tosyloctahydrospiro[isoindole-5,2'-[1,3]dioxolane] (17e)**

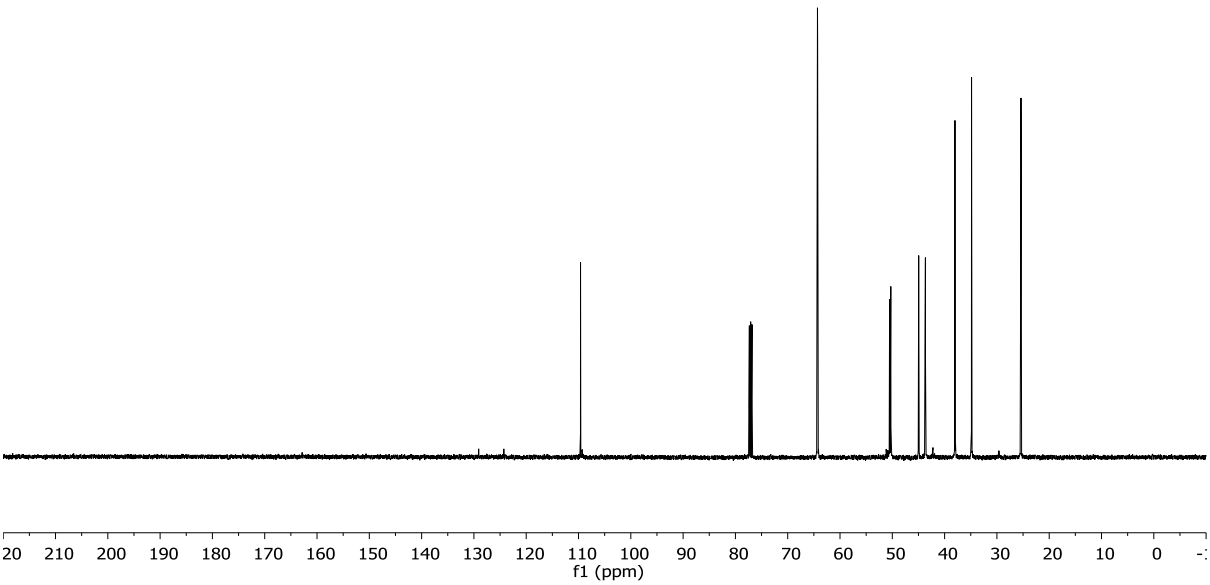




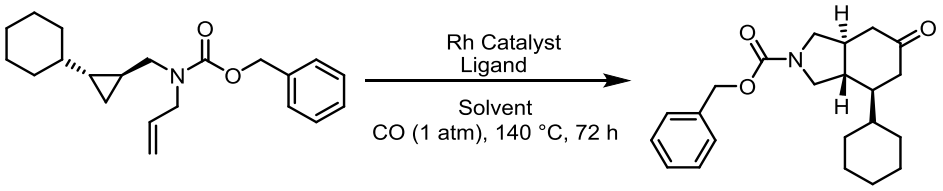
(3a*R, 7a*R**)-Octahydrospiro[isoindole-5,2'-[1,3]dioxolane] (18e)**





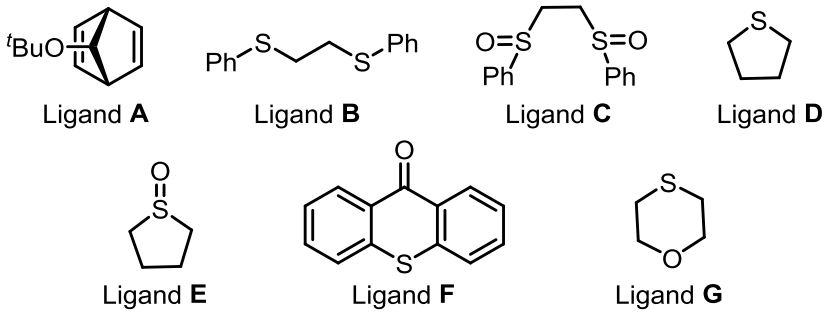


Selected Reaction Optimization Results



Rh catalyst (5 mol%)	Ligand (mol%)	Solvent (M)	Yield [a]
$[Rh(cod)Cl]_2$	$AsPh_3$ (10)	1,2-DCB (0.18)	39 %
$[Rh(CH_2CH_2)_2Cl]_2$	None	1,2-DCB (0.18)	44 %
$[Rh(CH_2CH_2)_2Cl]_2$	DMSO (30)	1,2-DCB (0.18)	52 %
$[Rh(CH_2CH_2)_2Cl]_2$	Ligand A (15)	1,2-DCB (0.18)	31 %
$[Rh(CH_2CH_2)_2Cl]_2$	Ligand B (15)	1,2-DCB (0.18)	(9 %)
$[Rh(CH_2CH_2)_2Cl]_2$	Ligand C (15)	1,2-DCB (0.18)	(36 %)
$[Rh(CH_2CH_2)_2Cl]_2$	Ligand D (30)	1,2-DCB (0.18)	54 %
$[Rh(CH_2CH_2)_2Cl]_2$	Ligand E (30)	1,2-DCB (0.18)	45 %
$[Rh(CH_2CH_2)_2Cl]_2$	Ligand F (30)	1,2-DCB (0.18)	49 %
$[Rh(CH_2CH_2)_2Cl]_2$	Ligand G (30)	1,2-DCB (0.18)	63 %
$[Rh(CO)_2Cl]_2$	Ligand G (30)	Mesitylene (0.3)	71 % [b]

[a] In situ yields are given in parentheses, in all case d.r >15:1; [b] Na_2SO_4 (20 mol%) was used as additive.



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