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ELECTRONIC SUPPLEMENTARY INFORMATION

Catalytic Asymmetric Synthesis of Chromenes and tetrahydroquinolines via Sequential Allylic Alkylation and Intramolecular Heck Coupling

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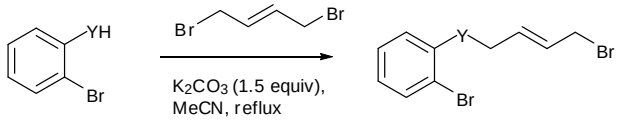
General procedures:

^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian AMX400 (400 and 100 MHz, respectively), a Varian VXR300 (300 and 75 MHz, respectively), or a Varian VXR200 NMR spectrometer (200 MHz and 75 MHz, respectively) with $CDCl_3$ as solvent. Chemical shifts were determined relative to the residual solvent peaks ($CHCl_3$, δ = 7.26 ppm for ^{1}H NMR, δ = 77.0 ppm for ^{13}C NMR). The following abbreviations are used to indicate signal multiplicity: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. Carbon assignments are based on APT ^{13}C-NMR experiments. Enantiomeric excesses were determined by chiral HPLC using a Shimadzu LC-10ADVP HPLC equipped with a Shimadzu SPD-M10AVP diode array detector or by capillary GC analysis (HP 6890, CP-Chiralsil-Dex-CB column (25 m x 0.25 mm) or Chiraldex B-PM (30 m x 0.25 mm x 0.25 μm)) using a flame ionization detector, in comparison with racemic products. Racemic products were obtained by the same procedure as the enantioselective allylic alkylation only using CuBr·SMe_2 (10 mol%), PPh_3 (20 mol%) and the corresponding Grignard reagent (1.70 eq.) at -80 °C in CH_2Cl_2. The ratio of regioisomers branch/linear (AAA) and exocyclic/endocyclic ratio (Heck coupling) were determined by ^{1}H NMR. Optical rotations were measured on a *Schmidt + Haensch* polarimeter (Polartronic MH8) with a 10 cm cell (*c* given in g/100 mL) at 20 °C. Thin-layer chromatography (TLC) was performed on Merck TLC Silica gel 60 Kieselguhr F_{254}. Flash chromatography was performed on silica gel Merck Type 9385 230-400 mesh. Mass spectra were recorded on a AEI-MS-902 mass spectrometer (EI+) or an LTQ Orbitrap XL (ESI+).

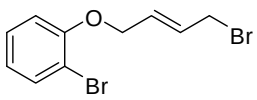
All reactions were carried out under a nitrogen atmosphere using oven dried glassware and using standard Schlenk techniques. CH_2Cl_2 was dried and distilled over calcium hydride. CuBr•SMe_2, Hoveyda-Grubbs 2nd generation catalysts, Wilkinson catalysts, (*R*,*R*)-Taniaphos and commercially available reagents were purchased from Aldrich, and used without further purification. Grignard reagents were purchased from Aldrich (MeMgBr, EtMgBr) or prepared from the corresponding alkyl bromides and magnesium turnings in Et_2O following standard procedures. Grignard reagents were titrated using *s*-BuOH and catalytic amounts of 1,10-phenanthroline.

Synthesis of Allylic bromides 1 and 2



1 Y = O
2 Y= NTs

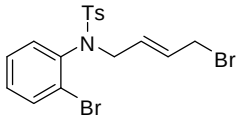
(*E*)-2-(4-Bromobut-2-enyloxy)-1-bromobenzene (1)



A suspension of *o*-bromophenol (10 mmol, 1.16 mL), 1,4-dibromobut-2-ene (40 mmol, 8.6 g) and K_2CO_3 (15 mmol, 2.05 g) in CH_3CN (100 mL) was heated at reflux temperature for 7 h. The reaction mixture was then concentrated and H_2O (100 mL) and Et_2O (100 mL) were added. The

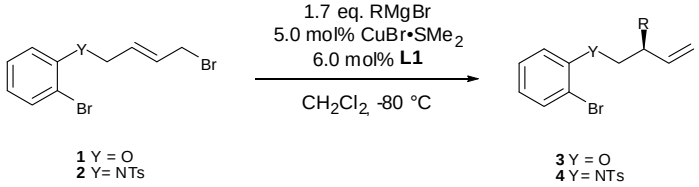
aqueous layer was separated and extracted with Et_2O (50 mL). The combined organic layer were dried ($MgSO_4$), filtered and concentrated in vacuo. Purification of the residue by flash chromatography (SiO_2, Et_2O/*n*-pentane gradient (1:99 to 5:95), R_f = 0.4) afforded **1** (2.9 g, 95% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (dd, *J* = 7.8 and 1.6 Hz, 1H), 7.27-7.23 (m, 1H), 6.88-6.83 (m, 2H), 6.15 (m, 1H), 6.01 (m, 1H), 4.58 (d, *J* = 4.9 Hz, 2H), 4.00 (d, *J* = 7.4 Hz, 2H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.7, 133.5, 129.4, 129.2, 128.4, 122.2, 113.6, 112.4. 68.2, 31.6. HRMS (EI, *m/z*): calcd for $C_{10}H_{10}Br_2O^+$: 307.9058; found: 307.9064.

(*E*)-*N*-(4-Bromobut-2-enyl)-*N*-(2-bromophenyl)-4-methylbenzenesulfonamide (2)



Prepared from *o*-bromophenyltosylamide (7.36 mmol, 2.4 g) following the procedure described for **1** (Reaction time = 16 h). Purification by column chromatography (SiO_2, Et_2O/*n*-pentane gradient (5:95 to 15:85), R_f = 0.4) afforded **2** (2.52 g, 75% yield) as a white solid, mp 90-91 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.2 Hz, 2H), 7.59 (d, *J* = 8.2 Hz, 1H), 7.30-7.24 (m, 3H), 7.21-7.16 (m, 1H), 7.11 (d, *J* = 7.9 Hz, 1H), 5.81-5.75 (m, 1H), 5.68-5.60 (m, 1H), 4.18 (m, 2H), 3.80 (d, *J* = 7.8 Hz, 2H), 2.44 (s, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.7, 137.5, 136.7, 133.9, 132.6, 131.0, 129.9, 129.5, 129.3, 127.9, 127.8, 125.6, 52.2, 31.2, 21.6. HRMS (EI, *m/z*): calcd for $C_{17}H_{17}Br_2NO_2S^+$: 458.9326; found: 458.9337.

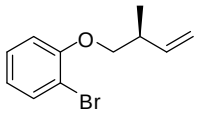
General procedure A: Enantioselective Cu-catalyzed synthesis of compounds 3 and 4



In a dry Schlenk tube equipped with septum and stirring bar, CuBr·SMe_2 (0.01 mmol, 2.05 mg, 5.0 mol%) and (*R*,*R*)-Taniaphos (**L1**) (0.012 mmol, 8.25 mg, 6 mol%) were dissolved in CH_2Cl_2 (2.0 mL) and stirred under nitrogen atmosphere at room temperature for 20 min. The mixture was cooled to -80 °C and a solution of Grignard reagent (solution in Et_2O, 1.7 eq.) in CH_2Cl_2 (1.0 mL) was added dropwise over 30 min via a syringe pump. Subsequently, a solution of allylic bromide **1** or **2** (0.2 mmol) in CH_2Cl_2 (1.0 mL) was added dropwise over 1 h via syringe pump. Once the addition was complete, the resulting mixture was stirred at -80 °C for 16h. The reaction was quenched by addition of MeOH (2.0 mL) and the mixture was allowed to warm up to rt. Saturated aqueous NH_4Cl solution (2 mL) was added and the organic phase separated. The aqueous phase was extracted with CH_2Cl_2 (2 x 10 mL). The combined organic phases were dried over $MgSO_4$ and concentrated under reduced pressure to yield the crude product which was purified by flash chromatography (SiO_2, EtOAc/Pentane). In accordance with the results

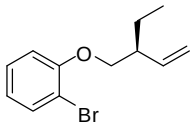
obtained in our previous work, the absolute configuration of these compounds is assumed to be (*S*).[1]

(+)-1-Bromo-2-(2methylbut-3-enyloxy)benzene (3a)



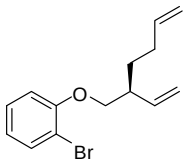
The title compound was prepared from **1** (3.0 mmol, 918 mg) following general procedure **A**. Purification by column chromatography (SiO_2, EtOAc/Pentane 1:99, R_f = 0.60) afforded **3a** (88% yield, 634 mg, 99% *ee*, $[\alpha]_D$ = +8.6 (*c* 1.0 in $CHCl_3$)) as a colorless oil. Enantiomeric excess determined for Heck product **5a**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (dd, *J* = 7.8 and 1.6 Hz, 1H), 7.24 (m, 1H), 6.84 (m, 2H), 5.92 (m, 1H), 5.13 (m, 2H), 3.95 (dd, *J* = 8.9 and 6.0 Hz, 1H), 3.83 (dd, *J* = 8.9 and 7.0 Hz, 1H), 2.75 (m, 1H), 1.20 (d, *J* = 6.8 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.3, 140.1, 133.3, 128.3, 121.7, 114.9, 113.2, 112.3, 73.4, 37.4, 16.5. HRMS (EI, *m/z*): calcd for $C_{11}H_{13}BrO^+$: 240.0150; found: 240.0136.

(+)-1-bromo-2-(2-ethylbut-3-enyloxy)benzene (3b)



The title compound was prepared from **1** (0.40 mmol, 120 mg) following general procedure **A**. Purification by column chromatography (SiO_2, EtOAc/Pentane 1:99, R_f = 0.7) afforded **3b** (97% yield, 97 mg, 99% *ee*, $[\alpha]_D^{20}$ = +28.0 (*c* 1.0 in $CHCl_3$)) as a colorless oil. Enantiomeric excess determined by chiral HPLC analysis, Chiralcel OD-H (99.75% *n*-heptane/0.25% *i*-PrOH), 40 °C, retention times (min) 13.2 (major) and 13.7 (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (dd, *J* = 7.9 and 1.6 Hz, 1H), 7.24 (m, 1H), 6.87 (dd, *J* = 8.2 and 1.3 Hz, 1H), 6.82 (m, 1H), 5.80 (m, 1H), 5.16 (m, 2H), 3.90-3.99 (m, 2H), 2.49 (m, 1H), 1.75 (m, 1H), 1.48 (m, 1H), 0.96 (t, *J* = 7.5 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.4, 138.9, 133.3, 128.3, 121.6, 116.4, 113.2, 112.4, 72.0, 45.2, 24.0, 11.4 ppm. HRMS (APCI+, *m/z*): calculated for $C_{12}H_{16}BrO$ [M+H$^+$]: 255.0385, found: 255.0381.

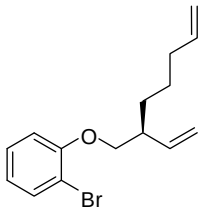
(+)-1-bromo-2-(2-vinylhex-5-enyloxy)benzene (3c)



[1] F. López, A. W. van Zijl, A. J. Minnaard and B. L. Feringa, *Chem. Commun.*, 2006, 409.

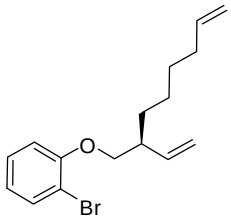
The title compound was prepared from **1** (0.65 mmol, 200 mg) following general procedure **A**. Purification by column chromatography (SiO_2, EtOAc/Pentane 1:99, R_f = 0.8) afforded **3c** (86% yield, 157 mg, 96% *ee*, $[\alpha]_D^{20}$ = +7.4 (*c* 1.0 in $CHCl_3$)) as a colorless oil. Enantiomeric excess determined by chiral HPLC analysis, Chiralcel OD-H (99.9 % *n*-heptane/0.1% *i*-PrOH, FL= 0.25 mL min^{-1}), 40 °C, retention times (min) 40.7 (major) and 43.1 (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (dd, *J* = 7.9 and 1.6 Hz, 1H), 7.24 (m, 1H), 6.87 (dd, *J* = 8.2 and 1.4 Hz, 1H), 6.82 (m, 1H), 5.81 (m, 2H), 5.17 (m, 2H), 5.00 (m, 2H), 4.00-3.90 (m, 2H), 2.60 (m, 1H), 2.18 (m, 1H), 2.10 (m, 1H), 1.81 (m, 1H), 1.57 (m, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.4, 138.8, 138.5, 133.3, 128.3, 121.7, 116.7, 114.7, 113.2, 112.4, 72.2, 43.0, 31.0, 30.2 ppm. HRMS (APCI+, *m/z*): calculated for $C_{14}H_{18}BrO$ [M+H$^+$]: 281.0541, found: 281.0536.

(+)-1-bromo-2-(2-vinylhept-6-enyloxy)benzene (3d)



The title compound was prepared from **1** (1.31 mmol, 400 mg) following general procedure **A**. Purification by column chromatography (SiO_2, EtOAc/Pentane 1:99, R_f = 0.8) afforded **3d** (90% yield, 348 mg, 95% *ee*, $[\alpha]_D^{20}$ = +28.0 (*c* 1.2 in $CHCl_3$)) as a colorless oil. Enantiomeric excess determined by chiral HPLC analysis, Chiralcel OD-H (99.9 % *n*-heptane/0.1% *i*-PrOH, FL= 0.25 mL min^{-1}), 40 °C, retention times (min) 40.0 (major) and 45.9 (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (dd, *J* = 7.9 and 1.6 Hz, 1H), 7.24 (m, 1H), 6.86 (dd, *J* = 8.3 and 1.3 Hz, 1H), 6.81 (m, 1H), 5.81 (m, 2H), 5.16 (m, 2H), 5.00 (m, 2H), 3.98-3.88 (m, 2H), 2.57 (m, 1H), 2.09 (m, 2H), 1.71 (m, 1H), 1.45 (m, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.4, 139.0, 138.7, 133.3, 128.3, 121.7, 116.4, 114.5, 113.2, 112.4, 72.3, 43.5, 33.8, 30.6, 26.2 ppm. HRMS (APCI+, *m/z*): calculated for $C_{15}H_{20}BrO$ [M+H$^+$]: 295.0698, found: 295.0692.

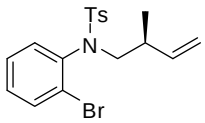
(+)-1-bromo-2-(2-vinyloct-7-enyloxy)benzene (3e)



The title compound was prepared from **1** (0.65 mmol, 200 mg) following general procedure **A**. Purification by column chromatography (SiO_2, EtOAc/Pentane 1:99, R_f = 0.8) afforded **3e** (94% yield, 190 mg, 97% *ee*, $[\alpha]_D^{20}$ = +24.0 (*c* 1.0 in $CHCl_3$)) as a colorless oil. Enantiomeric excess determined by chiral HPLC analysis, Chiralcel OD-H (99.9 % *n*-heptane/0.1% *i*-PrOH, FL= 0.25

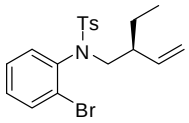
mL min^{-1}), 40 °C, retention times (min) 41.0 (major) and 44.0 (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (dd, *J* = 7.9 and 1.6 Hz, 1H), 7.24 (m, 1H), 6.87 (dd, *J* = 8.2 and 1.2 Hz, 1H), 6.82 (m, 1H), 5.81 (m, 2H), 5.15 (m, 2H), 4.95 (m, 2H), 3.98-3.88 (m, 2H), 2.56 (m, 1H), 2.07 (m, 2H), 1.71 (m, 1H), 1.45 (m, 5H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.4, 139.1, 139.0, 133.3, 128.3, 121.7, 116.4, 114.3, 113.1, 112.3, 72.3, 43.5, 33.7, 30.9, 28.9, 26.4 ppm. HRMS (APCI+, *m/z*): calculated for $C_{16}H_{22}BrO$ [M+H^+]: 309.0854, found: 309.0849.

(+)-*N*-(2-bromophenyl)-4-methyl-*N*-(2-methylbut-3-enyl)benzenesulfonamide (4a)



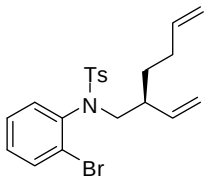
The title compound was prepared from **2** (1.0 mmol, 459 mg) following general procedure **A**. Purification by column chromatography (SiO_2, EtOAc/Pentane 10:90, R_f = 0.65) afforded **4a** (72% yield, 282 mg, 99% *ee*, $[\alpha]_D^{20}$ = +1.6 (*c* 14.9 in $CHCl_3$)) as a white solid, mp 78-79 °C. Enantiomeric excess determined by chiral HPLC analysis, Chiralpak AD (99% *n*-heptane/1% *i*-PrOH), 40 °C, retention times (min) 19.3 (major) and 20.9 (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (m, 3H), 7.25 (m, 4H), 7.16 (m, 1H), 5.67, (m, 1H), 4.97 (m, 2H), 3.53 (m, 2H), 2.43 (s major peak, 3H), 2.42 (s minor peak, 3H), 2.34 (m, minor peak, 1H), 2.21 (m, major peak, 1H), 1.07 (d, *J* = 6.7 Hz, major peak, 3H), 1.02 (d, *J* = 6.8 Hz, minor peak, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.5, 143.4, 141.1, 140.9, 138.2, 136.7, 136.4, 134.1, 133.4, 132.4, 129.6, 129.5, 129.4, 128.0, 127.9, 127.8, 127.7, 125.5, 124.8, 114.8, 114.7, 56.5, 37.0, 21.6, 18.0 ppm. HRMS (ESI+, *m/z*): calculated for $C_{18}H_{21}BrNO_2S$ [M+H^+]: 394.0476, found: 394.0471.

(+)-*N*-(2-bromophenyl)-*N*-(2-ethylbut-3-enyl)-4-methylbenzenesulfonamide (4b)



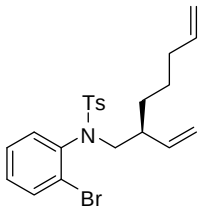
The title compound was prepared from **2** (0.30 mmol, 140 mg) following general procedure **A**. Purification by column chromatography (SiO_2, EtOAc/Pentane 10:90, R_f = 0.7) afforded **4b** (99% yield, 123 mg, 99% *ee*, $[\alpha]_D^{20}$ = +26.0 (*c* 1.0 in $CHCl_3$)) as a waxy solid. Enantiomeric excess determined for Heck product **6b**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (m, 3H), 7.28-7.11 (m, 5H), 5.55-5.39 (m, 1H), 5.01-4.86 (m, 2H), 3.65 (m, 1H), 3.48 (m, 1H), 2.41 (m, 3H), 2.13 (m, minor peak, 1H), 1.89 (m, major peak, 1H), 1.68 (m, major peak, 1H), 1.54 (m, minor peak, 1H), 1.20 (m, 1H), 0.82 (d, *J* = 7.3 Hz, minor peak, 3H), 0.78 (d, *J* = 7.4 Hz, major peak, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.4, 139.5, 139.4, 138.3, 138.0, 136.6, 136.5, 134.1, 134.0, 133.6, 132.5, 129.6, 129.5, 129.4, 127.9, 127.8, 127.7, 127.6, 125.5, 124.7, 116.8, 116.6, 55.4, 55.0, 45.3, 44.5, 25.0, 24.9, 21.6, 11.3, 11.2 ppm. HRMS (APCI+, *m/z*): calculated for $C_{19}H_{23}BrNO_2S$ [M+H^+]: 408.0633, found: 408.0638.

(+)-*N*-(2-bromophenyl)-4-methyl-*N*-(2-vinylhex-5-enyl)benzenesulfonamide (4c)



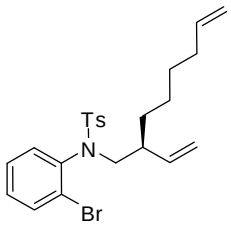
The title compound was prepared from **2** (0.50 mmol, 230 mg) following general procedure **A**. Purification by column chromatography (SiO_2, EtOAc/Pentane 10:90, R_f = 0.7) afforded **4c** (87% yield, 187 mg, 96% *ee*, $[\alpha]_D^{20}$ = +8.0 (*c* 1.0 in $CHCl_3$)) as a colorless oil. Enantiomeric excess determined by chiral HPLC analysis, Chiralpak AD (99.5 % *n*-heptane/0.5% *i*-PrOH), 40 °C, retention times (min) 27.9 (major) and 31.6 (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60-7.53 (m, 3H), 7.28-7.13 (m, 5H), 5.77-5.67 (m, 1H), 5.57-5.39 (m, 1H), 5.02 (m, 1H), 4.96-4.86 (m, 3H), 3.65 (m, 1H), 3.48 (m, 1H), 2.42 (m, 3H), 2.26 (m, minor peak, 1H), 2.00 (m, major peak, 1H), 1.89 (m, 1H), 1.71 (m, 1H), 1.60 (m, 1H), 1.26 (m, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.4, 139.5, 139.4, 138.3, 138.0, 136.6, 136.5, 134.1, 134.0, 133.7, 132.6, 129.6, 129.5, 129.4, 127.9, 127.8, 127.7, 127.6, 125.4, 124.6, 117.1, 116.8, 114.7, 114.5, 55.5, 55.1, 43.1, 42.5, 31.2, 31.1, 31.0, 30.9, 21.6 ppm. HRMS (APCI+, *m/z*): calculated for $C_{21}H_{25}BrNO_2S$ $[M+H^+]$: 434.0789, found: 434.0784.

(+)-*N*-(2-bromophenyl)-4-methyl-*N*-(2-vinylhept-6-enyl)benzenesulfonamide (4d)



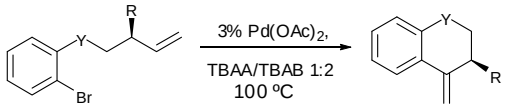
The title compound was prepared from **2** (0.87 mmol, 400 mg) following general procedure **A**. Purification by column chromatography (SiO_2, EtOAc/Pentane 10:90, R_f = 0.7) afforded **4d** (86% yield, 234 mg, 95% *ee*, $[\alpha]_D^{20}$ = +54.0 (*c* 1.9 in $CHCl_3$)) as a colorless oil. Enantiomeric excess determined for Heck product **6d**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59-7.53 (m, 3H), 7.29-7.13 (m, 5H), 5.80-5.68 (m, 1H), 5.57-5.39 (m, 1H), 5.01-4.87 (m, 4H), 3.65 (m, 1H), 3.48 (m, 1H), 2.42 (m, 3H), 2.25 (m, minor peak, 1H), 1.98 (m, major peak + CH_2, 3H), 1.63 (m, major peak, 1H), 1.50 (m, minor peak, 1H), 1.36 (m, 1H), 1.19 (m, 2H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.5, 139.6, 138.7, 138.0, 136.5, 132.5, 127.9, 127.6, 125.4, 124.7, 116.8, 116.5, 114.5, 114.4, 55.7, 55.1, 43.6, 42.9, 33.7, 31.5, 26.1, 21.6 ppm. HRMS (APCI+, *m/z*): calculated for $C_{22}H_{27}BrNO_2S$ $[M+H^+]$: 448.0946, found: 448.0941.

(+)-*N*-(2-bromophenyl)-4-methyl-*N*-(2-vinyloct-7-enyl)benzenesulfonamide (4e)



The title compound was prepared from **2** (0.50 mmol, 230 mg) following general procedure **A**. Purification by column chromatography (SiO_2, EtOAc/Pentane 10:90, R_f = 0.75) afforded **4e** (68% yield, 203 mg, 98% *ee*, $[\alpha]_D^{20}$ = +32.6 (*c* 1.2 in $CHCl_3$)) as a colorless oil. Enantiomeric excess determined for Heck product **6e**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60-7.53 (m, 3H), 7.28-7.11 (m, 5H), 5.82-5.71 (m, 1H), 5.56-5.39 (m, 1H), 5.00-4.86 (m, 4H), 3.65 (m, 1H), 3.48 (m, 1H), 2.42 (m, 3H), 2.21 (m, minor peak, 1H), 1.99 (m, major peak + CH_2, 3H), 1.63 (m, major peak, 1H), 1.47 (m, minor peak, 1H), 1.33-1.11 (m, 5H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.4, 139.8, 139.7, 139.0, 138.3, 138.0, 136.7, 136.5, 134.1, 134.0, 133.7, 132.5, 129.6, 129.5, 129.4, 127.9, 127.8, 127.7, 127.6, 125.5, 124.7, 116.7, 116.4, 114.2, 55.6, 55.2, 43.6, 42.9, 33.6, 31.9, 31.8, 28.9, 28.8, 26.3, 26.2, 21.6 ppm. HRMS (APCI+, *m/z*): calculated for $C_{23}H_{29}BrNO_2S$ [M+H$^+$]: 462.1102, found: 462.1097.

General procedure B: Synthesis of compounds 5 and 6 by intramolecular Heck reaction

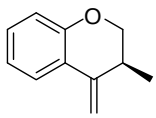


3 Y = O
4 Y= NTs

5 Y = O
6 Y= NTs

TBAB (1 g), TBAA (0.45 g, 1.5 mmol), $Pd(OAc)_2$ (3 mol%) and the corresponding AAA product (**3** or **4**) were stirred and heated at 100 °C for the indicated time (see Table 2). Water (3 mL) and EtOAc (3 mL) were added and, after cooling to r.t., the organic phase separated. The aqueous phase was extracted with EtOAc (2 x 5 mL). The combined organic phases were dried over $MgSO_4$ and concentrated under reduced pressure to yield the crude product which was purified by flash chromatography on silica gel, EtOAc/Pentane.

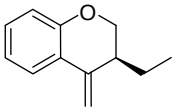
(+)-3-methyl-4-methylenechromene (5a)



The title compound was prepared from **3a** (0.29 mmol, 70 mg) following general procedure **B**. Reaction time: 15 min. Purification by column chromatography (SiO_2, EtOAc/Pentane 1:99, R_f = 0.4) afforded **5a** (93% yield, 43 mg, ratio exo:endo = 95:5, >99% *ee*, $[\alpha]_D^{20}$ = +18.3 (*c* 0.6 in

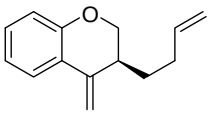
$CHCl_3$)) as a colorless oil. Enantiomeric excess determined by chiral GC analysis, Chiraldex B-PM column (30 m x 0.25 mm), 5 min isothermic 50 °C then 2 °C/min gradient to 175 °C, retention times (min) 44.5 (major) and 44.9 (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (dd, *J* = 7.9 and 1.6 Hz, 1H), 7.20-7.14 (m, 1H), 6.93-6.85 (m, 1H), 6.84 (dd, *J* = 8.2 and 1.0 Hz, 1H), 5.50 (d, *J* = 0.7 Hz, 1H), 4.94 (d, *J* = 1.4 Hz, 1H), 4.19 (dd, *J* = 10.5 and 3.5 Hz, 1H), 3.91 (dd, *J* = 10.5 and 7.3 Hz, 1H), 2.73 (m, 1H), 1.20 (d, *J* = 6.9 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.1, 142.6, 129.3, 124.9, 121.3, 120.7, 117.1, 105.2, 71.8, 34.0, 15.6 ppm. HRMS (EI, *m/z*) calculated for $C_{11}H_{12}O^+$: 160.0888, found: 160.0883.

(-)-3-ethyl-4-methylenechromene (5b)



The title compound was prepared from **3b** (0.27 mmol, 70 mg) following general procedure **B**. Reaction time: 15 min. Purification by column chromatography (SiO_2, EtOAc/Pentane 1:99, R_f = 0.5) afforded **5b** (96% yield, 45 mg, ratio exo:endo = 98:2, 98% *ee*, $[\alpha]_D^{20}$ = -18.6 (*c* 1.0 in $CHCl_3$)) as a colorless oil. Enantiomeric excess determined by chiral GC analysis, Chiraldex B-PM column (30 m x 0.25 mm), 5 min isothermic 50 °C then 2 °C/min gradient to 175 °C, retention times (min) 47.2 (minor) and 47.7 (major). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (dd, *J* = 7.9 and 1.6 Hz, 1H), 7.19-7.15 (m, 1H), 6.92-6.88 (m, 1H), 6.83 (dd, *J* = 8.2 and 1.1 Hz, 1H), 5.52 (s, 1H), 4.89 (s, 1H), 4.20 (d, *J* = 3.1 Hz, 2H), 2.38 (m, 1H), 1.59 (m, 2H), 0.98 (t, *J* = 7.4 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.9, 140.8, 129.3, 125.0, 121.0, 120.6, 117.0, 107.0, 69.9, 42.2, 23.4, 11.8 ppm. HRMS (APCI+, *m/z*): calculated for $C_{12}H_{15}O$ [$M+H^+$]: 175.1123, found: 175.1118.

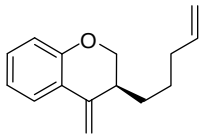
(+)-3-(but-3-enyl)-4-methylenechromene (5c)



The title compound was prepared from **3c** (0.25 mmol, 70 mg) following general procedure **B**. Reaction time: 1.5 h. Purification by column chromatography (SiO_2, EtOAc/Pentane 1:99, R_f = 0.7) afforded **5c** (84% yield, 42 mg, ratio exo:endo = >99:1, 96% *ee*, $[\alpha]_D^{20}$ = +42.6 (*c* 1.0 in $CHCl_3$)) as a colorless oil. Enantiomeric excess determined by chiral GC analysis, Chiraldex B-PM column (30 m x 0.25 mm), 5 min isothermic 50 °C then 2 °C/min gradient to 175 °C, retention times (min) 57.1 (minor) and 57.4 (major). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (dd, *J* = 7.9 and 1.6 Hz, 1H), 7.19-7.15 (m, 1H), 6.92-6.88 (m, 1H), 6.83 (dd, *J* = 8.2 and 1.1 Hz, 1H), 5.87-5.76 (m, 1H), 5.52 (s, 1H), 5.06-4.97 (m, 2H), 4.89 (s, 1H), 4.20 (d, *J* = 2.9 Hz, 2H), 2.52 (m, 1H), 2.15 (m, 2H), 1.65 (m, 2H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.8, 140.7, 138.3,

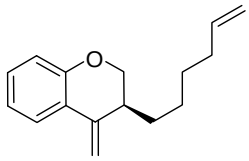
129.4, 125.1, 120.8, 120.7, 117.1, 115.0, 107.2, 70.1, 39.8, 31.2, 29.5 ppm. HRMS (APCI+, *m/z*): calculated for $C_{14}H_{17}O$ [M+H$^+$]: 201.1279, found: 201.1274.

(-)-4-methylene-3-(pent-4-enyl)chromene (5d)



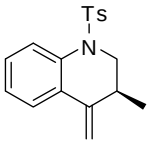
The title compound was prepared from **3d** (0.81 mmol, 240 mg) following general procedure **B**. Reaction time: 1.5 h. Purification by column chromatography (SiO_2, EtOAc/Pentane 1:99, R_f = 0.7) afforded **5d** (92% yield, 160 mg, ratio exo:endo = >99:1, 95% *ee*, $[\alpha]_D^{20}$ = -20.2 (*c* 0.4 in $CHCl_3$)) as a colorless oil. Enantiomeric excess determined for RCM product **9**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (dd, *J* = 7.9 and 1.6 Hz, 1H), 7.20-7.15 (m, 1H), 6.92-6.88 (m, 1H), 6.84 (dd, *J* = 8.2 and 1.1 Hz, 1H), 5.86-5.76 (m, 1H), 5.51 (s, 1H), 5.03-4.93 (m, 2H), 4.89 (s, 1H), 4.19 (d, *J* = 3.0 Hz, 2H), 2.49 (m, 1H), 2.07 (m, 2H), 1.60-1.45 (m, 4H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.9, 141.0, 138.6, 129.4, 125.1, 120.9, 120.7, 117.0, 114.6, 106.9, 70.1, 40.4, 33.7, 29.9, 26.6 ppm. HRMS (APCI+, *m/z*): calculated for $C_{15}H_{19}O$ [M+H$^+$]: 215.1436, found: 215.1430.

(-)-3-(hex-5-enyl)-4-methylenechromene (5e)



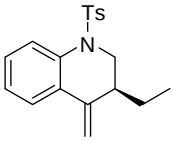
The title compound was prepared from **3e** (0.32 mmol, 100 mg) following general procedure **B**. Reaction time: 1.5 h. Purification by column chromatography (SiO_2, EtOAc/Pentane 1:99, R_f = 0.7) afforded **5e** (89% yield, 65 mg, ratio exo:endo = >99:1, 99% *ee*, $[\alpha]_D^{20}$ = -27.0 (*c* 1.0 in $CHCl_3$)) as a colorless oil. Enantiomeric excess determined by chiral HPLC analysis, Chiralcel OJ (99.8 % *n*-heptane/0.2% *i*-PrOH), 40 °C, retention times (min) 9.9 (minor) and 10.1 (major). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (dd, *J* = 7.9 and 1.6 Hz, 1H), 7.19-7.14 (m, 1H), 6.91-6.87 (m, 1H), 6.83 (dd, *J* = 8.2 and 1.1 Hz, 1H), 5.85-5.74 (m, 1H), 5.50 (s, 1H), 5.00-4.92 (m, 2H), 4.88 (s, 1H), 4.18 (d, *J* = 3.0 Hz, 2H), 2.47 (m, 1H), 2.05 (m, 2H), 1.54 (m, 2H), 1.40 (m, 4H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.9, 141.1, 138.9, 129.3, 125.1, 121.0, 120.7, 117.0, 114.3, 106.8, 70.1, 40.5, 33.7, 30.2, 28.8, 26.7 ppm. HRMS (APCI+, *m/z*): calculated for $C_{16}H_{21}O$ [M+H$^+$]: 229.1592, found: 229.1587.

(+)-3-methyl-4-methylene-1-tosyl-1,2,3,4-tetrahydroquinoline (6a)



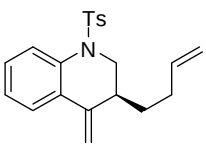
The title compound was prepared from **4a** (0.24 mmol, 95 mg) following general procedure **B**. Reaction time: 15 min. Purification by column chromatography (SiO_2, EtOAc/Pentane 10:90, R_f = 0.4) afforded **6a** (92% yield, 68 mg, ratio exo:endo = 95:5, 99% *ee*, $[\alpha]_D^{20}$ = 2.8 (*c* 1.0 in $CHCl_3$)) as a colorless oil. Enantiomeric excess determined by chiral HPLC analysis, Chiralpak AD (99.5 % *n*-heptane/0.5% *i*-PrOH), 40 °C, retention times (min) 23.3 (major) and 30.2 (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.4 Hz, 1H), 7.55-7.51 (m, 3H), 7.26-7.17 (m, 3H), 7.11-7.07 (m, 1H), 5.40 (d, *J* = 1.7 Hz, 1H), 4.86 (d, *J* = 1.8 Hz, 1H), 4.12 (dd, *J* = 13.3 and 4.9 Hz, 1H), 3.30 (dd, *J* = 13.3 and 10.4 Hz, 1H), 2.52 (m, 1H), 2.37 (s, 3H), 1.10 (d, *J* = 6.8 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.8, 143.6, 137.1, 136.2, 129.6, 128.4, 128.3, 127.0, 125.0, 124.9, 123.6, 108.6, 52.5, 33.3, 21.5, 17.6 ppm. HRMS (APCI+, *m/z*): calculated for $C_{18}H_{19}NNaO_2S$ $[M+H^+]$: 336.1034, found: 336.1029.

(-)-3-ethyl-4-methylene-1-tosyl-1,2,3,4-tetrahydroquinoline (6b)



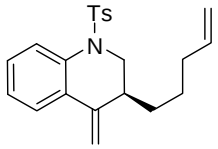
The title compound was prepared from **4b** (0.21 mmol, 86 mg) following general procedure **B**. Reaction time: 15 min. Purification by column chromatography (SiO_2, EtOAc/Pentane 10:90, R_f = 0.6) afforded **6b** (93% yield, 63 mg, ratio exo:endo = 98:2, 99% *ee*, $[\alpha]_D^{20}$ = -26.6 (*c* 1.0 in $CHCl_3$)) as a colorless oil. Enantiomeric excess determined by chiral HPLC analysis, Chiralcel OJ-H (99 % *n*-heptane/1% *i*-PrOH), 40 °C, retention times (min) 33.3 (major) and 41.4 (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (dd, *J* = 8.3 and 0.9 Hz, 1H), 7.57-7.55 (m, 2H), 7.49 (dd, *J* = 7.9 and 1.5 Hz, 1H), 7.20-7.18 (m, 3H), 7.07 (m, 1H), 5.33 (s, 1H), 4.79 (d, *J* = 1.1 Hz, 1H), 4.01 (dd, *J* = 13.1 and 4.7 Hz, 1H), 3.65 (dd, *J* = 13.1 and 8.0 Hz, 1H), 2.42-2.40 (m, 1H), 2.37 (s, 3H), 1.59-1.40 (m, 2H), 0.92 (t, *J* = 7.4 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.6, 142.5, 137.0, 136.2, 129.6, 128.4, 128.3, 127.1, 125.3, 124.7, 122.7, 109.6, 50.5, 41.1, 25.2, 21.5, 11.3 ppm. HRMS (APCI+, *m/z*): calculated for $C_{19}H_{22}NO_2S$ $[M+H^+]$: 328.1371, found: 328.1372.

(-)-3-(but-3-enyl)-4-methylene-1-tosyl-1,2,3,4-tetrahydroquinoline (6c)



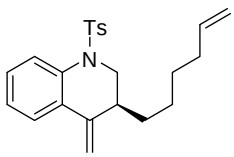
The title compound was prepared from **4c** (0.28 mmol, 120 mg) following general procedure **B**. Reaction time: 1 h. Purification by column chromatography (SiO_2, EtOAc/Pentane 10:90, R_f = 0.7) afforded **6c** (87% yield, 86 mg, ratio exo:endo = 98:2, 97% *ee*, $[\alpha]_D^{20}$ = -7.2 (*c* 0.7 in $CHCl_3$)) as a colorless oil. Enantiomeric excess determined by chiral HPLC analysis, Chiralcel OJ-H (99 % *n*-heptane/1% *i*-PrOH), 40 °C, retention times (min) 36.1 (major) and 41.0 (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (dd, *J* = 8.4 and 0.9 Hz, 1H), 7.59-7.56 (m, 2H), 7.49 (dd, *J* = 7.9 and 1.5 Hz, 1H), 7.21-7.19 (m, 3H), 7.07 (m, 1H), 5.82-5.72 (m, 1H), 5.34 (s, 1H), 5.06-4.98 (m, 2H), 4.81 (d, *J* = 1.0 Hz, 1H), 3.98 (dd, *J* = 13.1 and 4.6 Hz, 1H), 3.71 (dd, *J* = 13.1 and 7.5 Hz, 1H), 2.54 (m, 1H), 2.38 (s, 3H), 2.10 (m, 2H), 1.56 (m, 2H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.6, 142.6, 137.9, 137.0, 136.1, 129.6, 128.4, 127.9, 127.1, 125.4, 124.6, 122.5, 115.2, 109.8, 50.6, 38.9, 31.4, 30.8, 21.5 ppm. HRMS (APCI+, *m/z*): calculated for $C_{21}H_{24}NO_2S$ $[M+H^+]$: 354.1528, found: 354.1522.

(-)-4-methylene-3-(pent-4-enyl)-1-tosyl-1,2,3,4-tetrahydroquinoline (6d)



The title compound was prepared from **4d** (0.42 mmol, 190 mg) following general procedure **B**. Reaction time: 1 h. Purification by column chromatography (SiO_2, EtOAc/Pentane 10:90, R_f = 0.7) afforded **6d** (86% yield, 133 mg, ratio exo:endo = 98:2, 97% *ee*, $[\alpha]_D^{20}$ = -3.2 (*c* 1.0 in $CHCl_3$)) as a colorless oil. Enantiomeric excess determined by chiral HPLC analysis, Chiralcel OJ-H (99 % *n*-heptane/1% *i*-PrOH), 40 °C, retention times (min) 35.4 (major) and 40.6 (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (dd, *J* = 8.3 and 0.9 Hz, 1H), 7.57-7.55 (m, 2H), 7.48 (dd, *J* = 7.9 and 1.5 Hz, 1H), 7.23-7.18 (m, 3H), 7.09-7.05 (m, 1H), 5.83-5.72 (m, 1H), 5.32 (s, 1H), 5.01-4.93 (m, 2H), 4.79 (d, *J* = 1.1 Hz, 1H), 4.00 (dd, *J* = 13.1 and 4.7 Hz, 1H), 3.65 (dd, *J* = 13.1 and 7.9 Hz, 1H), 2.49 (m, 1H), 2.37 (s, 3H), 2.03 (m, 2H), 1.52-1.37 (m, 4H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.6, 142.7, 138.4, 137.0, 136.1, 129.6, 128.4, 128.2, 127.1, 125.4, 124.7, 122.6, 114.7, 109.6, 50.8, 39.4, 33.6, 31.8, 26.0, 21.5 ppm. HRMS (APCI+, *m/z*): calculated for $C_{22}H_{25}NNaO_2S$ $[M+Na^+]$: 390.1504, found: 390.1498.

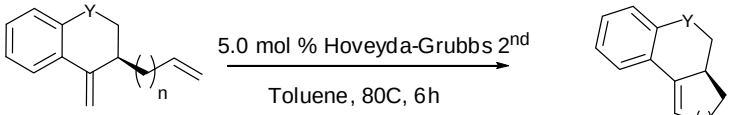
(+)-3-(hex-5-enyl)-4-methylene-1-tosyl-1,2,3,4-tetrahydroquinoline (6e)



The title compound was prepared from **4e** (0.29 mmol, 135 mg) following general procedure **B**. Reaction time: 1 h. Purification by column chromatography (SiO_2, EtOAc/Pentane 10:90, R_f = 0.8) afforded **6e** (77% yield, 85 mg, ratio exo:endo = 97:3, 98% *ee*, $[\alpha]_D^{20}$ = +7.6 (*c* 1.2 in

$CHCl_3$)) as a white waxy solid. Enantiomeric excess determined by chiral HPLC analysis, Chiralcel OJ-H (99 % *n*-heptane/1% *i*-PrOH), 40 °C, retention times (min) 29.5 (major) and 33.1 (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (dd, *J* = 8.3 and 0.9 Hz, 1H), 7.57-7.55 (m, 2H), 7.48 (dd, *J* = 7.9 and 1.5 Hz, 1H), 7.23-7.18 (m, 3H), 7.09-7.05 (m, 1H), 5.84-5.74 (m, 1H), 5.32 (s, 1H), 5.01-4.93 (m, 2H), 4.79 (d, *J* = 1.1 Hz, 1H), 3.99 (dd, *J* = 13.1 and 4.7 Hz, 1H), 3.64 (dd, *J* = 13.1 and 7.9 Hz, 1H), 2.47 (m, 1H), 2.37 (s, 3H), 2.03 (m, 2H), 1.56-1.26 (m, 6H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.6, 142.8, 138.7, 137.0, 136.1, 129.6, 128.4, 128.2, 127.1, 125.4, 124.7, 122.7, 114.4, 109.4, 50.8, 39.5, 33.6, 32.2, 28.8, 26.2, 21.5 ppm. HRMS (APCI+, *m/z*): calculated for $C_{23}H_{27}NNaO_2S$ [M+Na$^+$]: 404.1660, found: 404.1655.

General procedure C: RCM of compounds 5c, 6c and 5d

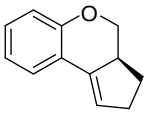


n= 2: **5c**, Y = O
n= 2: **6c**, Y= NTs
n= 3: **5d**, Y = O

n=1: **7**, Y = O
n=1: **8**, Y= NTs
n=2: **9**, Y = O

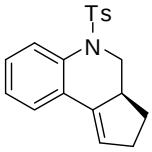
The corresponding diene was dissolved in degassed toluene (2-10 mM) under a N_2 atmosphere. Hoveyda-Grubbs 2nd generation catalyst (5 mol%) was tipped into the solution and then the stirred solution was heated for 6 h at 80 °C. The mixture was cooled down to room temperature and the solvent was removed under reduced pressure to yield the crude product which was purified by flash chromatography on silica gel, EtOAc/Pentane.

(+)-2,3,3a,4-tetrahydrocyclopenta[c]chromene (7)



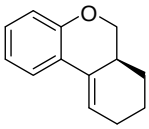
The title compound was prepared from **5c** (0.13 mmol, 25 mg) in toluene (15 mL) following general procedure **C**. Purification by column chromatography (SiO_2, EtOAc/Pentane 1:99, R_f = 0.7) afforded **7** (84% yield, 18 mg, 96% *ee*, $[\alpha]_D^{20}$ = +19.6 (*c* 1.1 in $CHCl_3$)) as a colorless oil. Volatile compound under vacuum pressure. Enantiomeric excess determined by chiral GC analysis, Chiraldex B-PM column (30 m x 0.25 mm), 5 min isothermic 50 °C then 2 °C/min gradient to 175 °C, retention times (min) 57.9 (major) and 58.4 (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (dd, *J* = 7.6 and 1.5 Hz, 1H), 7.19-7.11 (m, 1H), 6.90-6.86 (m, 2H), 6.06 (m, 1H), 4.52 (dd, *J* = 10.1 and 5.1 Hz, 1H), 3.67 (dd, *J* = 12.0 and 10.1 Hz, 1H), 3.10 (m, 1H), 2.54-2.49 (m, 2H), 2.24-2.17 (m, 1H), 1.49-1.39 (m, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.9, 136.9, 128.8, 125.1, 121.0, 120.7, 119.8, 117.1, 72.4, 41.9, 31.8, 27.5 ppm. HRMS (APCI+, *m/z*): calculated for $C_{12}H_{13}O$ [M+H$^+$]: 173.0966, found: 173.0961.

(+)-5-tosyl-3,3a,4,5-tetrahydro-2*H*-cyclopenta[c]quinoline (8)



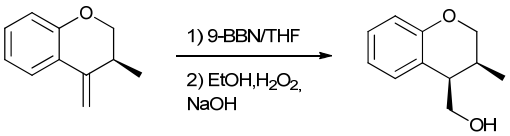
The title compound was prepared from **6c** (0.17 mmol, 60 mg) in toluene (15 mL) following general procedure **C**. Purification by column chromatography (SiO_2, EtOAc/Pentane 10:90, R_f = 0.7) afforded **8** (90% yield, 50 mg, 97% *ee*, $[\alpha]_D^{20}$ = +59.6 (*c* 1.4 in $CHCl_3$)) as a white waxy solid. Enantiomeric excess determined by chiral HPLC analysis, Chiralpak AD-H (99 % *n*-heptane/1% *i*-PrOH), 40 °C, retention times (min) 50.4 (major) and 52.8 (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.3 Hz, 1H), 7.54-7.52 (m, 3H), 7.22-7.18 (m, 3H), 7.12-7.08 (m, 1H), 6.10 (m, 1H), 4.58 (dd, *J* = 13.4 and 4.8 Hz, 1H), 2.99 (dd, *J* = 12.9 and 12.9 Hz, 1H), 2.51 (m, 1H), 2.37 (s, 3H), 2.36 (m, 1H), 2.09 (m, 1H), 1.38-1.26 (m, 2H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.5, 138.2, 137.3, 135.0, 129.6, 127.7, 127.0, 125.2, 125.0, 124.8, 124.7, 124.4, 52.0, 40.6, 31.5, 29.4, 21.5 ppm. HRMS (APCI+, *m/z*): calculated for $C_{19}H_{20}NO_2S$ [M+H$^+$]: 326.1215, found: 326.1210.

(+)-6a,7,8,9-tetrahydro-6*H*-benzo[c]chromene (9)



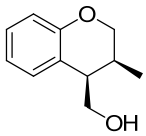
The title compound was prepared from **5d** (0.26 mmol, 55 mg) in toluene (26 mL) following general procedure **C**. Purification by column chromatography (SiO_2, EtOAc/Pentane 1:99, R_f = 0.7) afforded **9** (95% yield, 46 mg, 95% *ee*, $[\alpha]_D^{20}$ = +124.8 (*c* 1.0 in $CHCl_3$)) as a colorless oil. Enantiomeric excess determined by chiral GC analysis, Chiraldex B-PM column (30 m x 0.25 mm), 5 min isothermic 50 °C then 2 °C/min gradient to 175 °C, retention times (min) 66.2 (major) and 67.0 (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (dd, *J* = 7.9 and 1.6 Hz, 1H), 7.13-7.09 (m, 1H), 6.90-6.86 (m, 1H), 6.83 (dd, *J* = 8.2 and 1.1 Hz, 1H), 6.25 (m, 1H), 4.28 (dd, *J* = 10.4 and 4.6 Hz, 1H), 3.66 (dd, *J* = 12.0 and 10.4 Hz, 1H), 2.67 (m, 1H), 2.27 (m, 2H), 1.89 (m, 2H), 1.64 (m, 1H), 1.13 (m, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.1, 131.0, 128.2, 123.6, 121.7, 120.6, 118.6, 117.2, 71.3, 33.7, 25.9, 24.8, 21.4 ppm. HRMS (APCI+, *m/z*): calculated for $C_{13}H_{15}O$ [M+H$^+$]: 187.1123, found: 187.1121.

Stereoselective hydroboration-oxidation



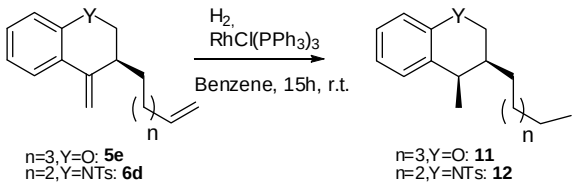
5a **10**

((+)-3-methylchroman-4-yl)methanol (10)

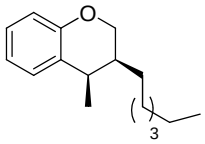


In an oven dried Schlenk tube equipped with septum and stirring bar under a N_2 atmosphere, chromene **5a** (0.28 mmol, 45 mg) was dissolved in anhydrous THF (0.5 mL), cooled to 0 °C and 9-BBN-THF (0.5M solution in THF, 0.42 mmol, 840 µL) was then added dropwise. The reaction mixture was stirred for 3 h, then it was allowed to reach rt, after which sequentially EtOH (2.5 mL), aq. NaOH (1M, 2.5 mL) and aq H_2O_2 (30%, 2.0 mL) were added. The resulting mixture was stirred overnight at rt and then quenched with aq $Na_2S_2O_3$ (10%, 10 mL). CH_2Cl_2 (20 mL) was added, the layers were separated and the aqueous layer was extracted with CH_2Cl_2 (20 mL). The combined organic layers were dried and concentrated *in vacuo*. Flash column chromatography (SiO_2, EtOAc/Pentane 3:7, R_f = 0.6) afforded **10** (81% yield, 40 mg, $[\alpha]_D^{20}$ = +79.0 (*c* 1.3 in $CHCl_3$)) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18-7.12 (m, 2H), 6.89-6.82 (m, 2H), 4.12-4.02 (m, 2H), 3.97-3.88 (m, 2H), 2.93 (m, 1H), 2.39-2.29 (m, 1H), 1.10 (d, *J* = 7.1 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.7, 129.3, 128.0, 122.4, 120.2, 116.8, 69.7, 63.7, 40.7, 29.2, 13.0 ppm. HRMS (APCI+, *m/z*): calculated for $C_{11}H_{15}O_2$ $[M+H^+]$: 179.1072, found: 179.1067.

Stereoselective hydrogenation



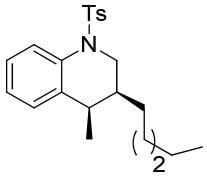
(+)-3-hexyl-4-methylchroman (11)



To an oven-dried flask was added $RhCl(PPh_3)_3$ (20 mg, 0.02 mmol) and a solution of **5e** (20 mg, 0.09 mmol) in benzene (2 mL). The flask was connected to a hydrogen balloon. After five vacuum/H_2-filling cycles, the reaction mixture was stirred at rt for 15 h. The resulting mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, EtOAc/Pentane 1:99, R_f = 0.7) afforded **11a** (96% yield, 20 mg, 9:1 d.r., $[\alpha]_D^{20}$ = +47.2 (*c* 1.0 in $CHCl_3$)) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14-7.07 (m, 2H), 6.89-6.77 (m, 2H), 4.17 (dd, *J* = 11.0 and 2.7 Hz, 1H, minor (*anti*)), 4.07 (ddd, *J* = 10.8, 3.6 and 1.2 Hz, 1H, major (*syn*)), 3.92 (dd, *J* = 10.6 and 10.6 Hz, 1H), 2.92 (m, 1H, major (*syn*)),

2.62 (m, 1H, minor (*anti*)), 2.07 (m, 1H), 1.43-1.24 (m, 10H), 1.17 (d, J = 7.2 Hz, 3H, major (*syn*)), 0.9 (d, 3H, minor (*anti*)), 0.9 (t, J = 6.6 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.9, 129.5, 128.2, 127.2, 120.0, 116.4, 66.2, 35.7, 32.3, 31.8, 29.5, 27.6, 26.9, 22.7, 17.4, 14.1 ppm. HRMS (APCI+, *m/z*): calculated for $C_{16}H_{25}O$ [M+H$^+$]: 233.1905, found: 233.1900.

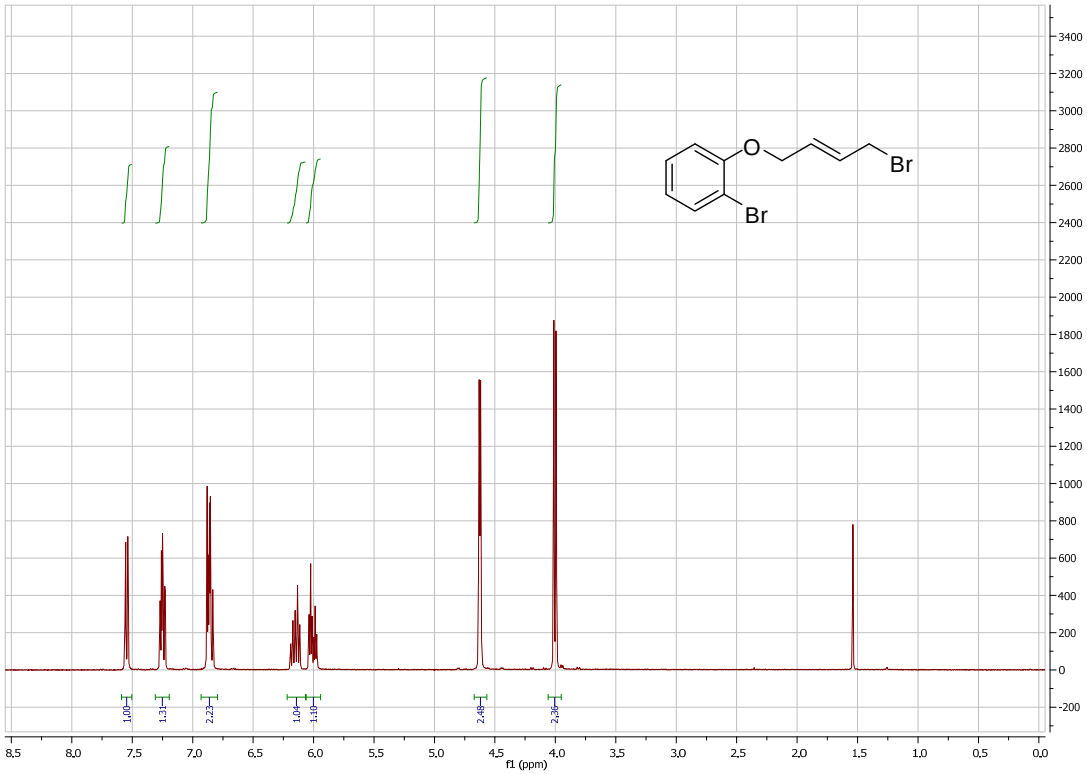
(+)-4-methyl-3-pentyl-1-tosyl-1,2,3,4-tetrahydroquinoline (12)

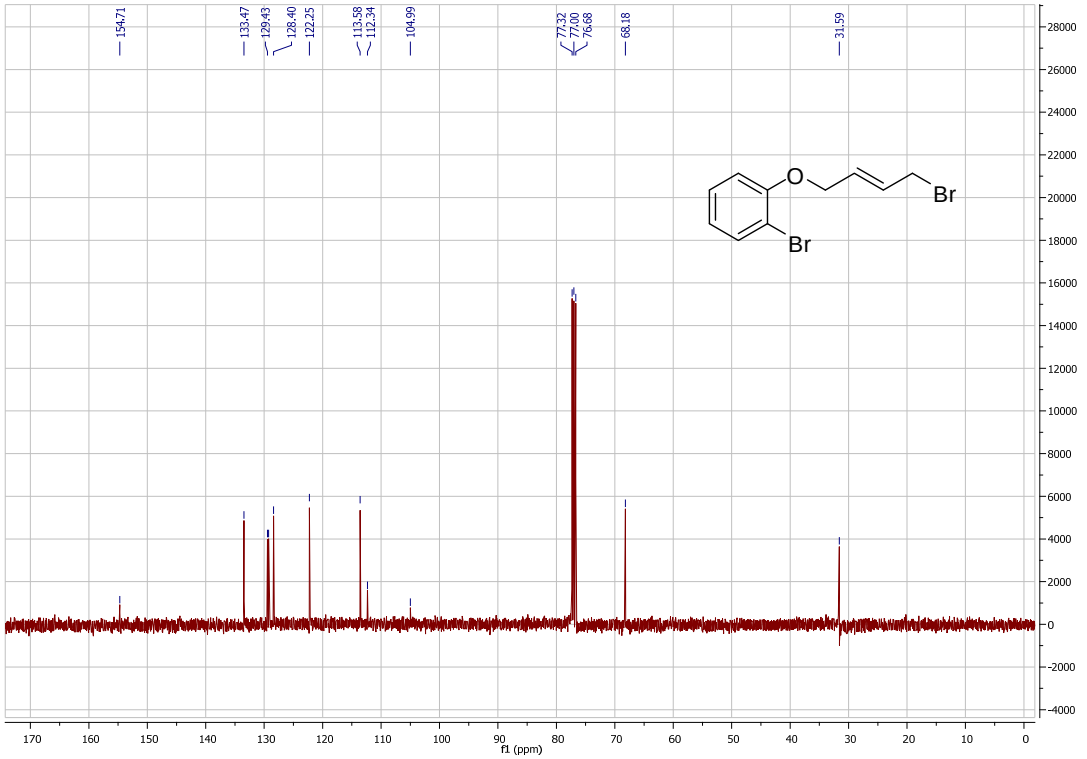


Compound prepared from **6d** (60 mg, 0.16 mmol) in benzene (2 mL) and $RhCl(PPh_3)_3$ (38 mg, 0.040 mmol) following the procedure described for **11a**. Purification by flash column chromatography (SiO_2, EtOAc/Pentane 10:90, R_f = 0.7) afforded **12** (98% yield, 58 mg, 10:1 d.r., $[\alpha]_D^{20}$ = +62.0 (*c* 1.1 in $CHCl_3$)) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 8.3 Hz, 1H), 7.50 (m, 2H), 7.20-7.14 (m, 3H), 7.03-7.01 (m, 2H), 4.13 (dd, J = 13.6 and 4.1 Hz, 1H, minor (*anti*)), 3.97 (ddd, J = 12.7, 4.2 and 0.9 Hz, 1H, major (*syn*)), 3.24 (dd, J = 12.1, 12.1 Hz, 1H, major (*syn*)), 3.15 (dd, J = 13.6, 10.2 Hz, 1H, minor (*anti*)), 2.64 (m, 1H), 2.35 (s, 3H), 1.65 (m, 1H), 1.32-1.19 (m, 8H), 0.88 (t, J = 7.1 Hz, 3H), 0.87 (d, 3H, J = 6.9 Hz, minor (*anti*)), 0.72 (d, J = 7.2 Hz, 3H, major (*syn*)) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.5, 135.9, 135.7, 135.5, 129.5, 128.9, 127.1, 126.6, 124.1, 122.9, 47.3, 35.5, 35.0, 31.8, 29.9, 26.6, 22.5, 21.5, 15.8, 14.0 ppm. HRMS (APCI+, *m/z*): calculated for $C_{22}H_{30}NO_2S$ [M+H$^+$]: 372.1997, found: 372.1992.

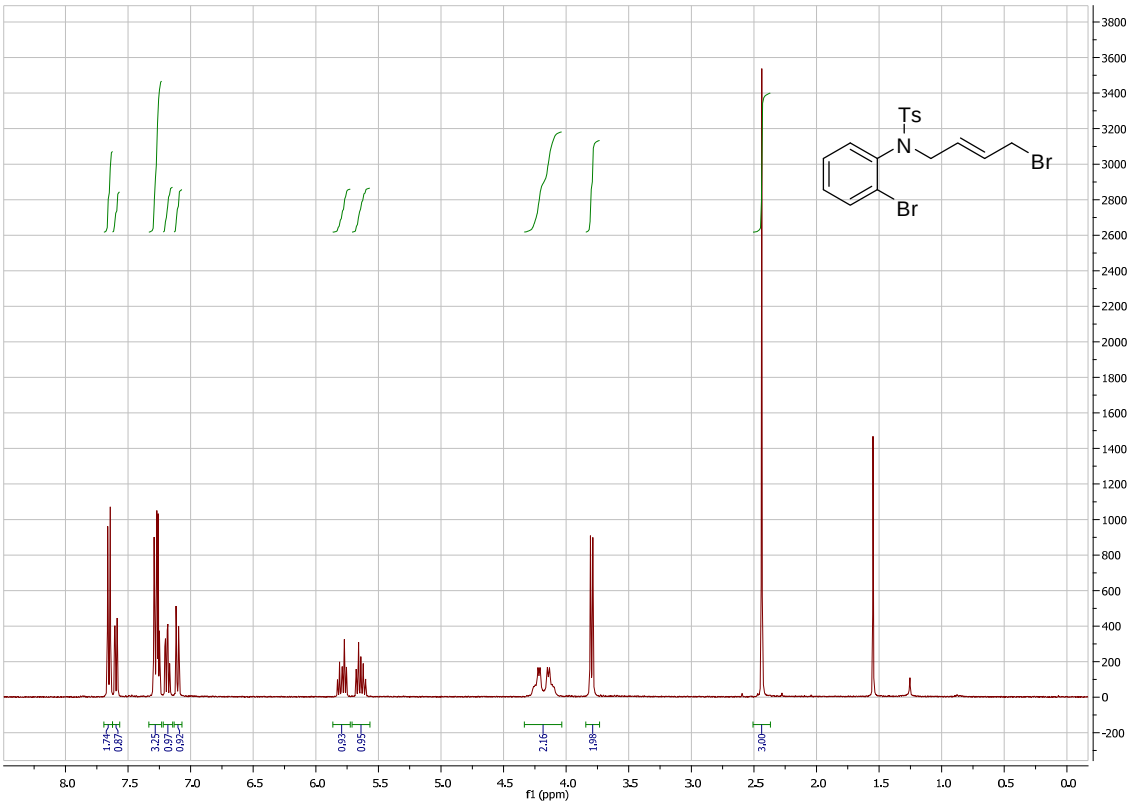
NMR spectra

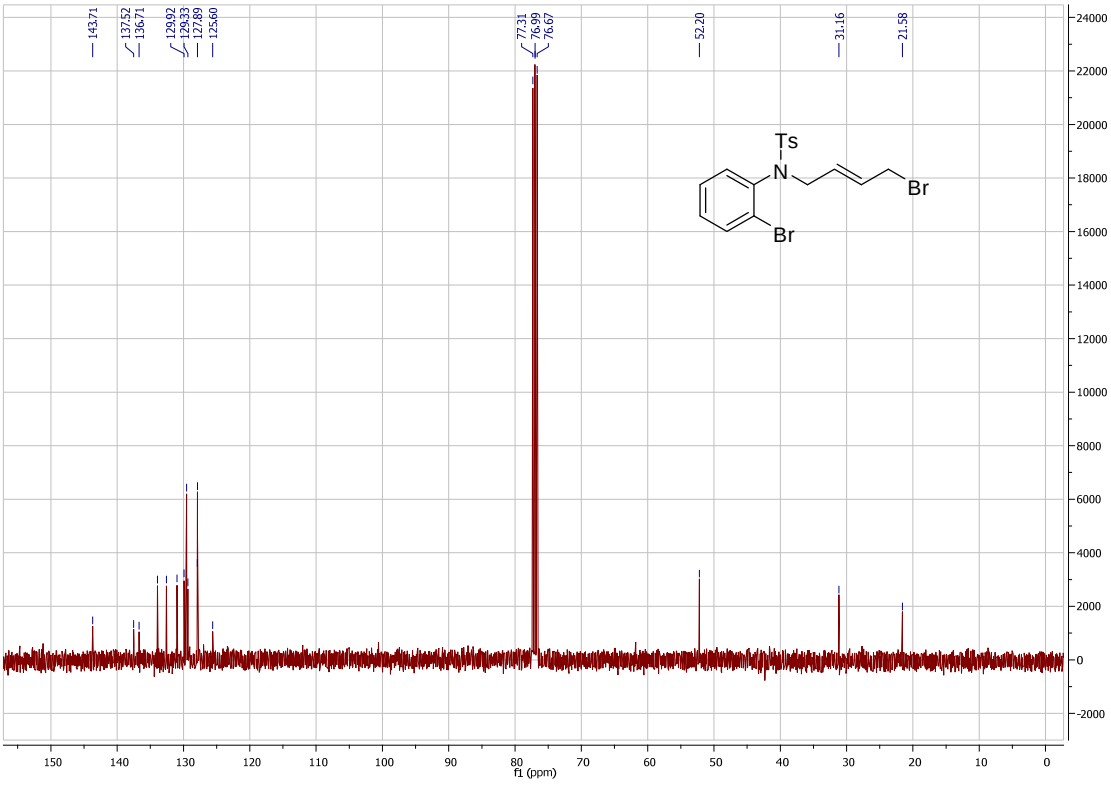
(*E*)-2-(4-Bromobut-2-enyloxy)-1-bromobenzene (1)



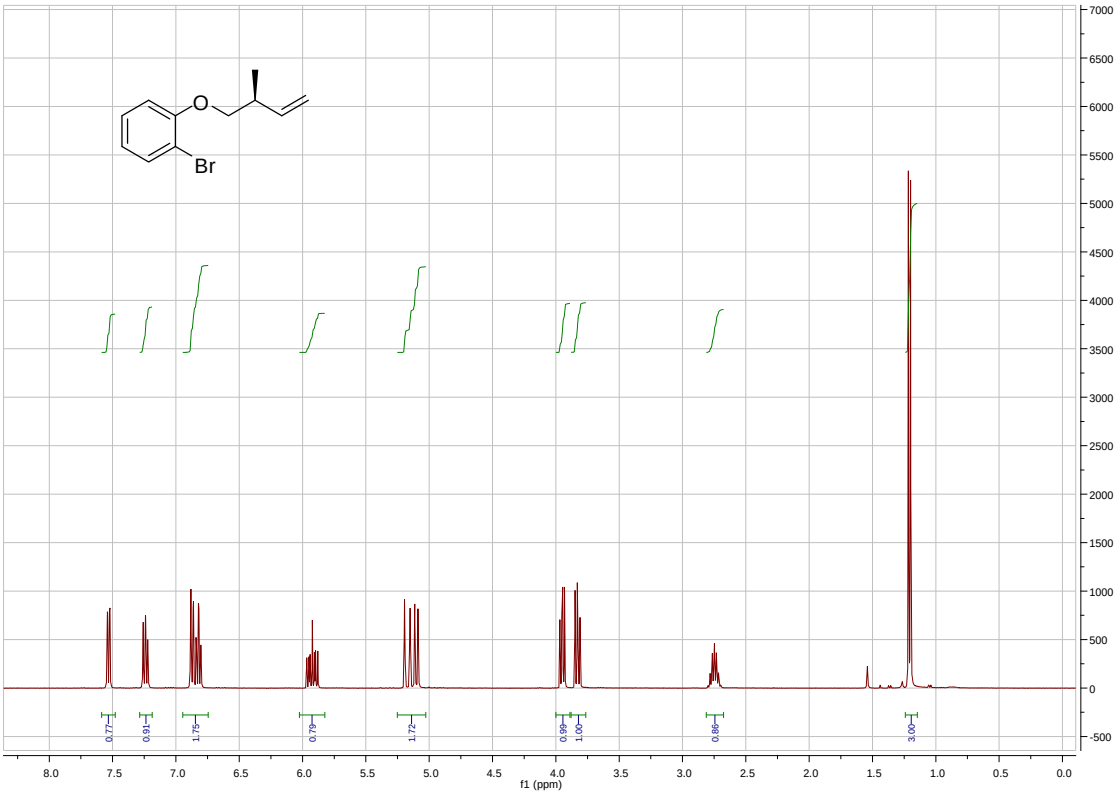


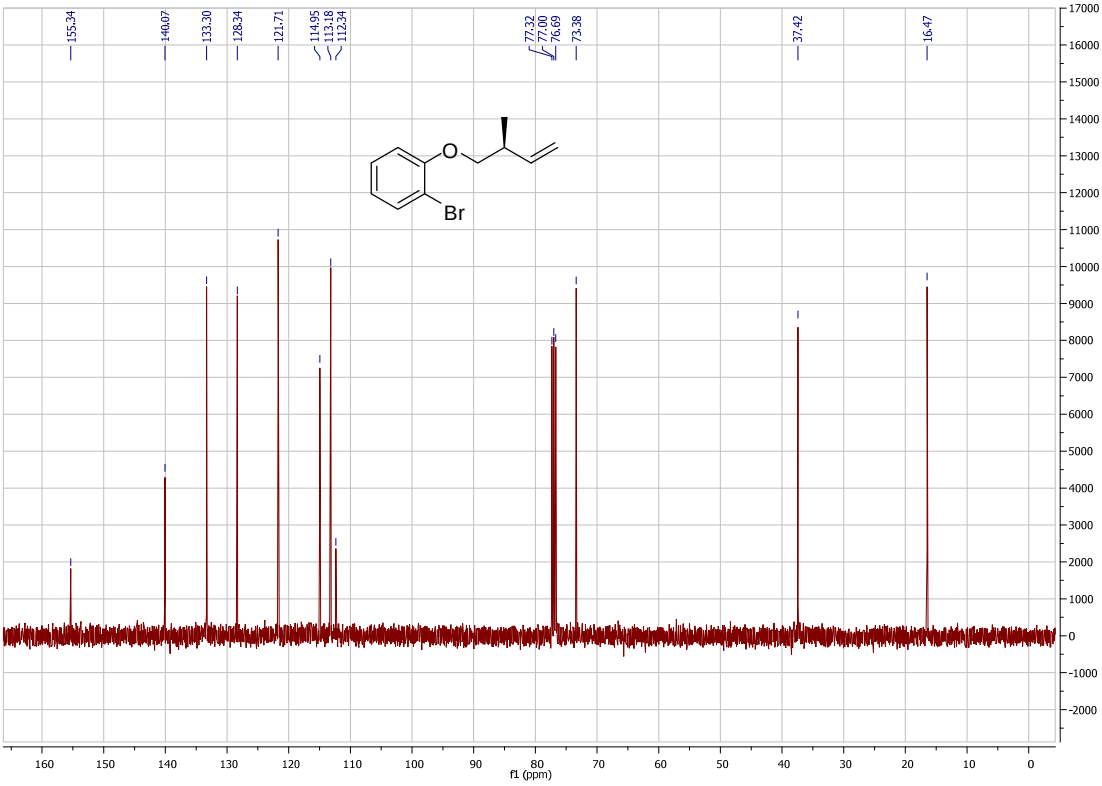
(*E*)-*N*-(4-Bromobut-2-enyl)-*N*-(2-bromophenyl)-4-methylbenzenesulfonamide (2)



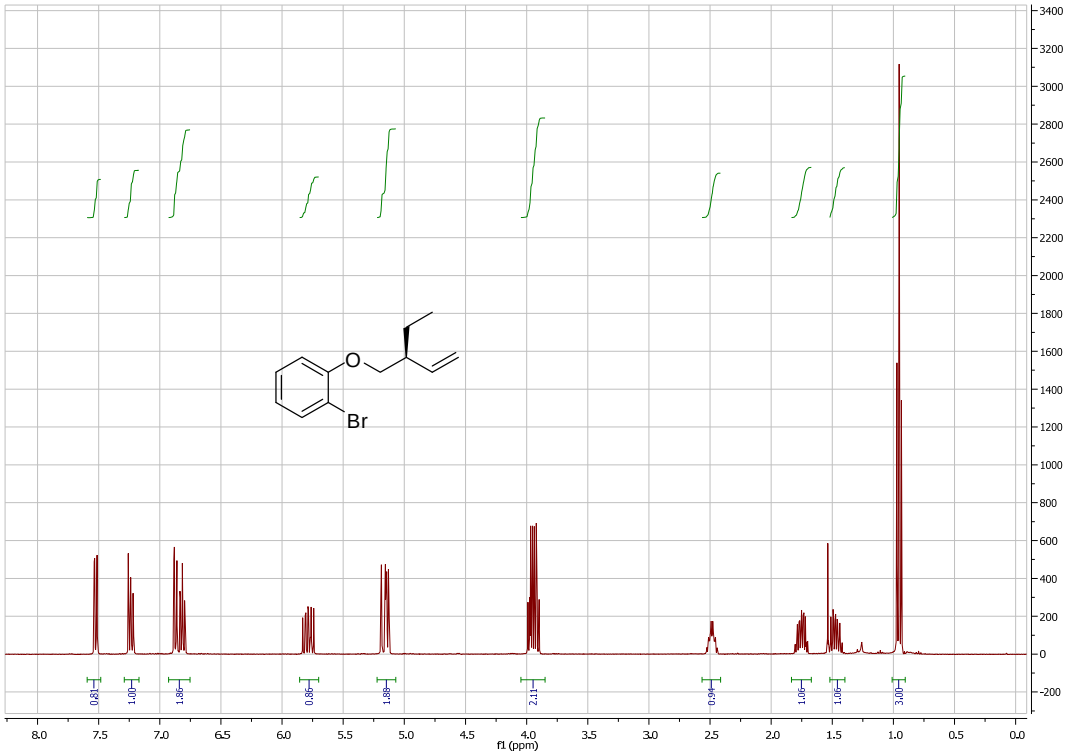


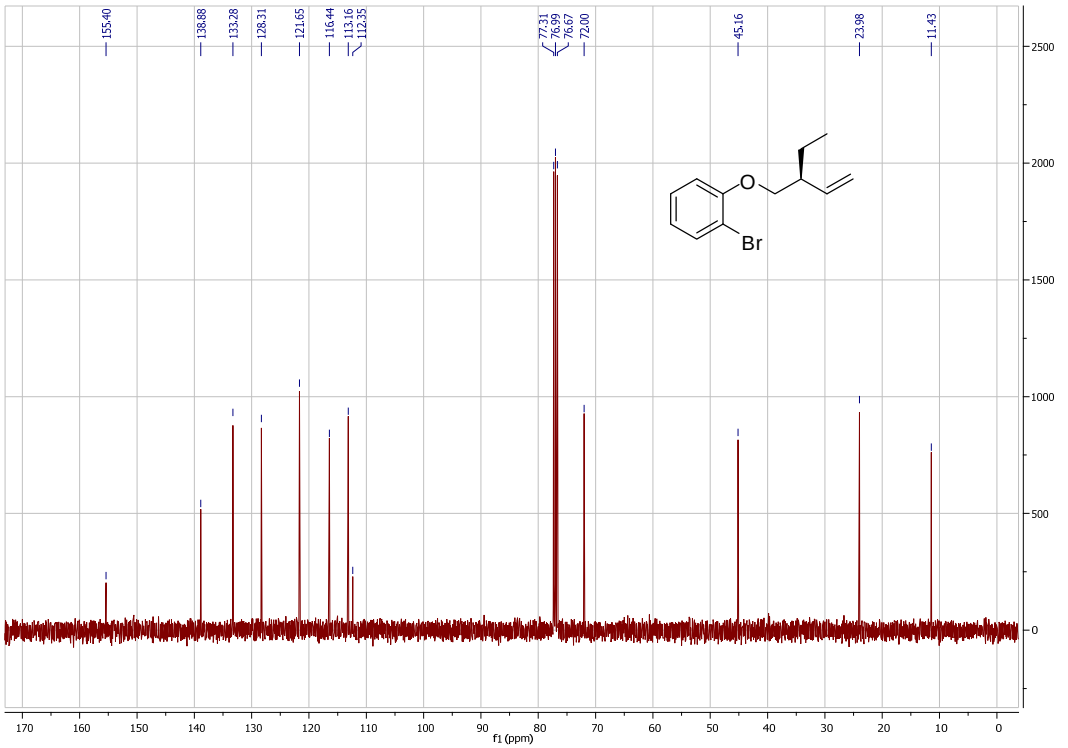
(+)-1-Bromo-2-(2methylbut-3-enyloxy)benzene (3a)



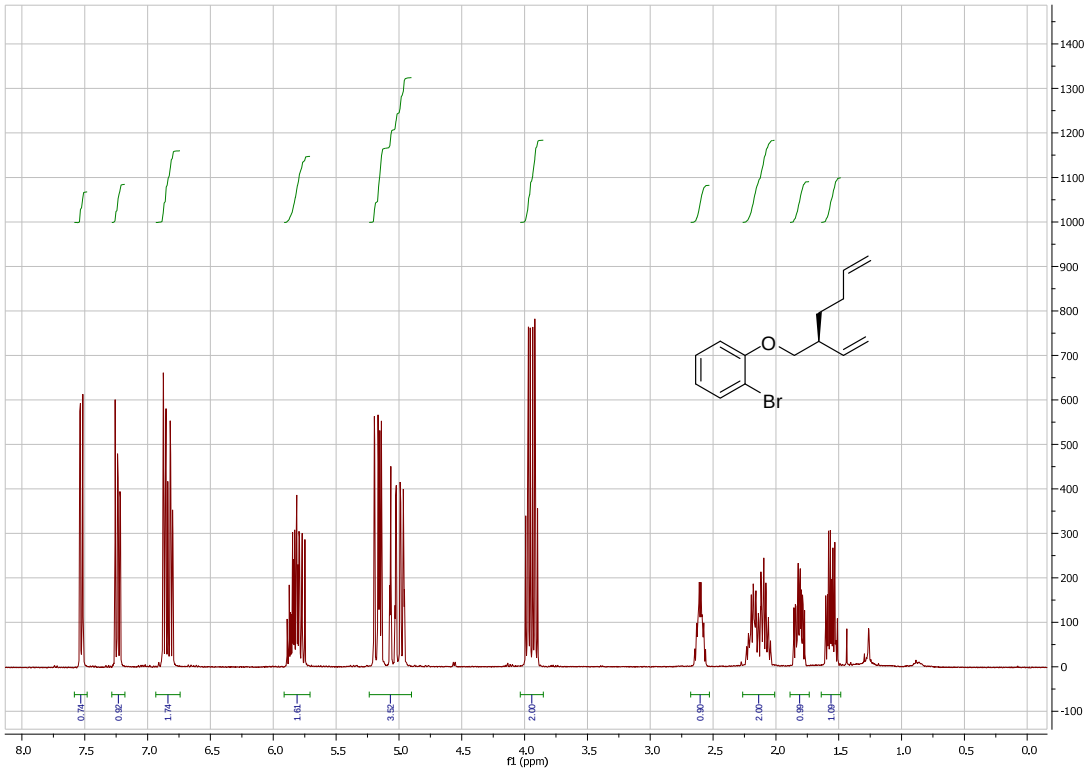


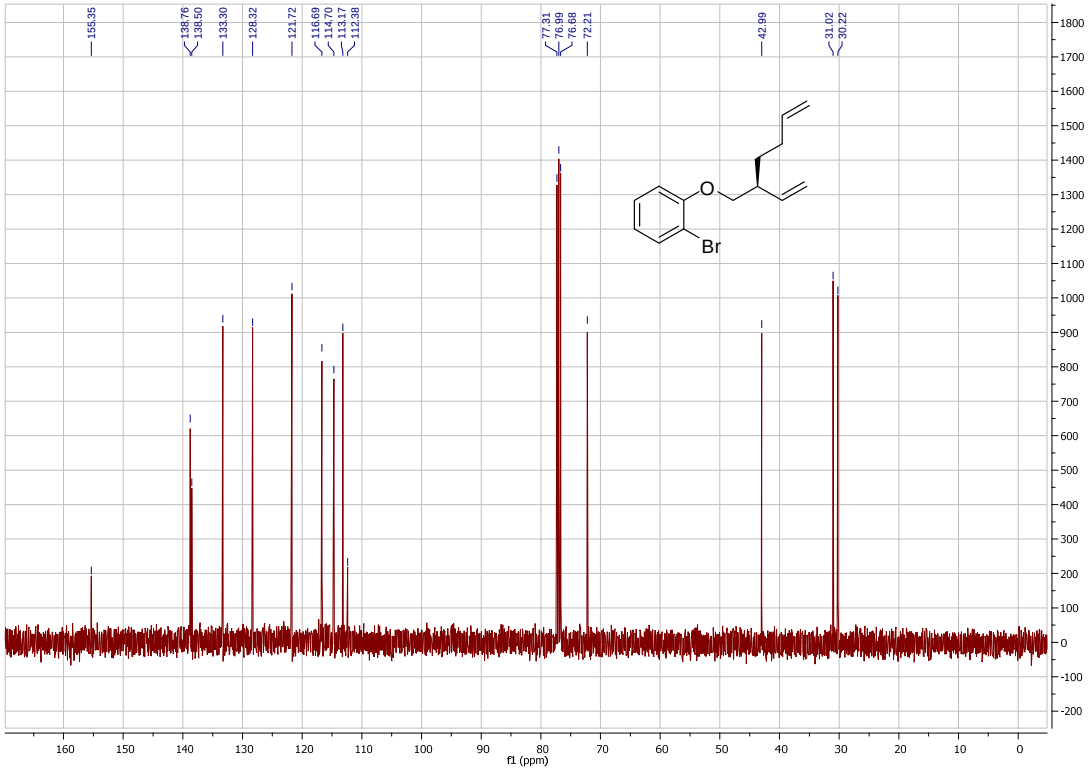
(+)-1-bromo-2-(2-ethylbut-3-enyloxy)benzene (3b)



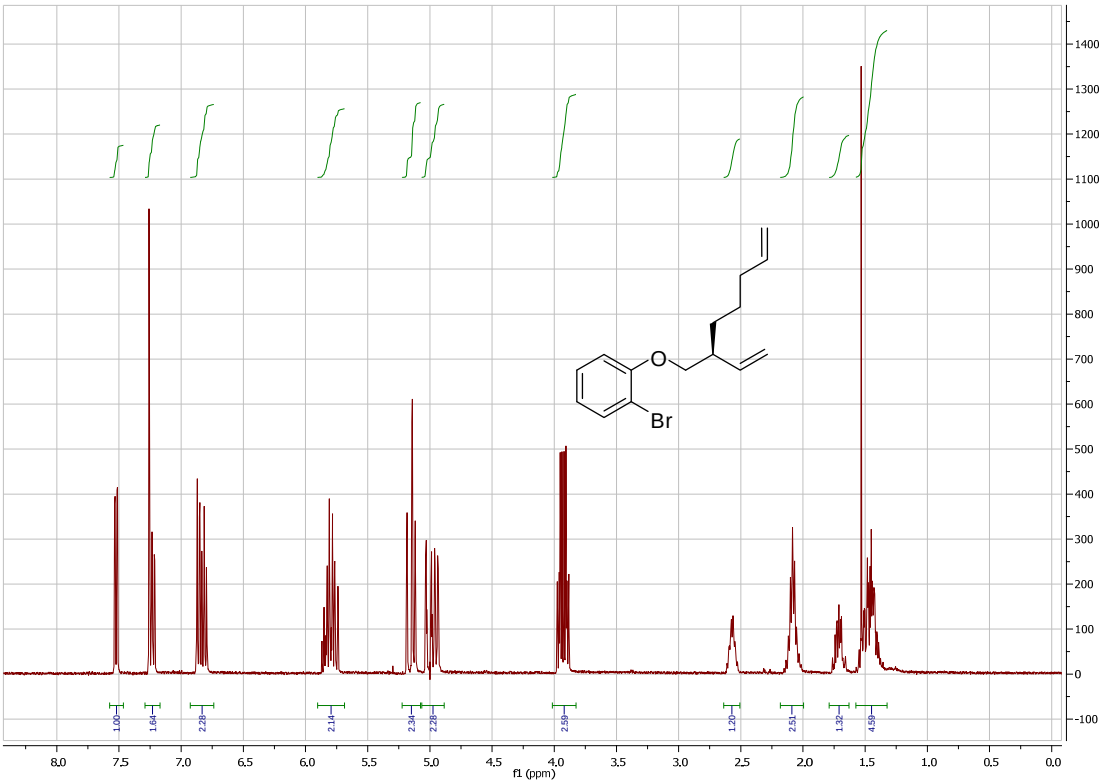


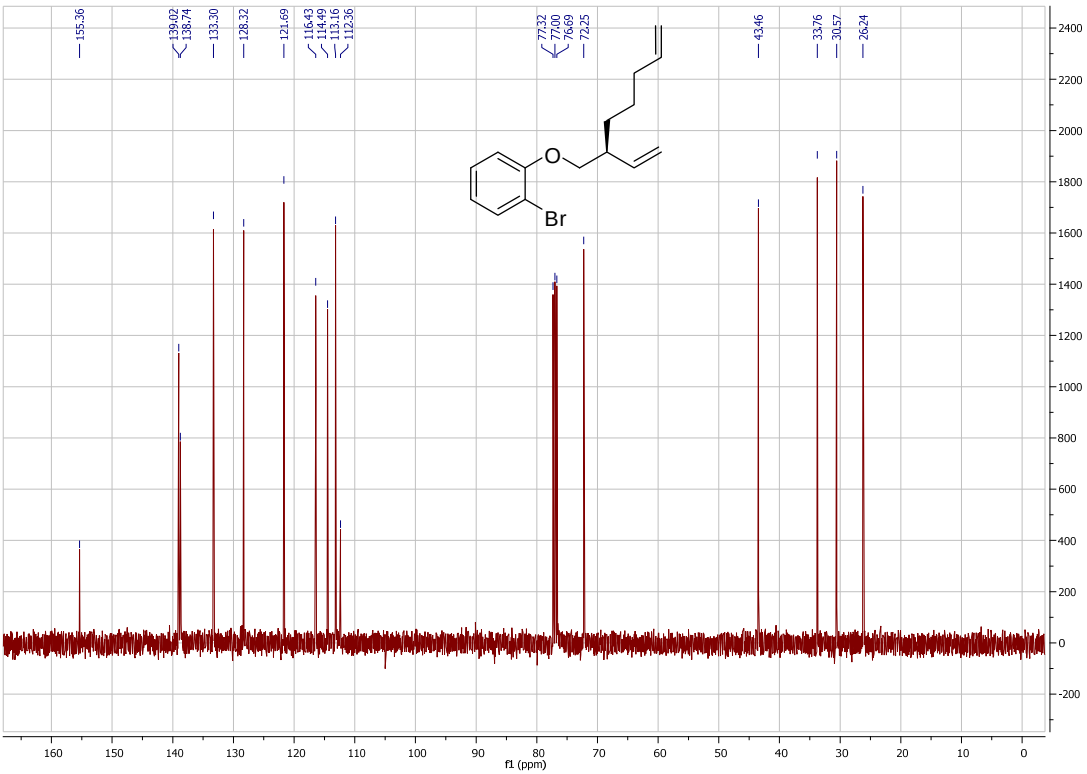
(+)-1-bromo-2-(2-vinylhex-5-enyloxy)benzene (3c)



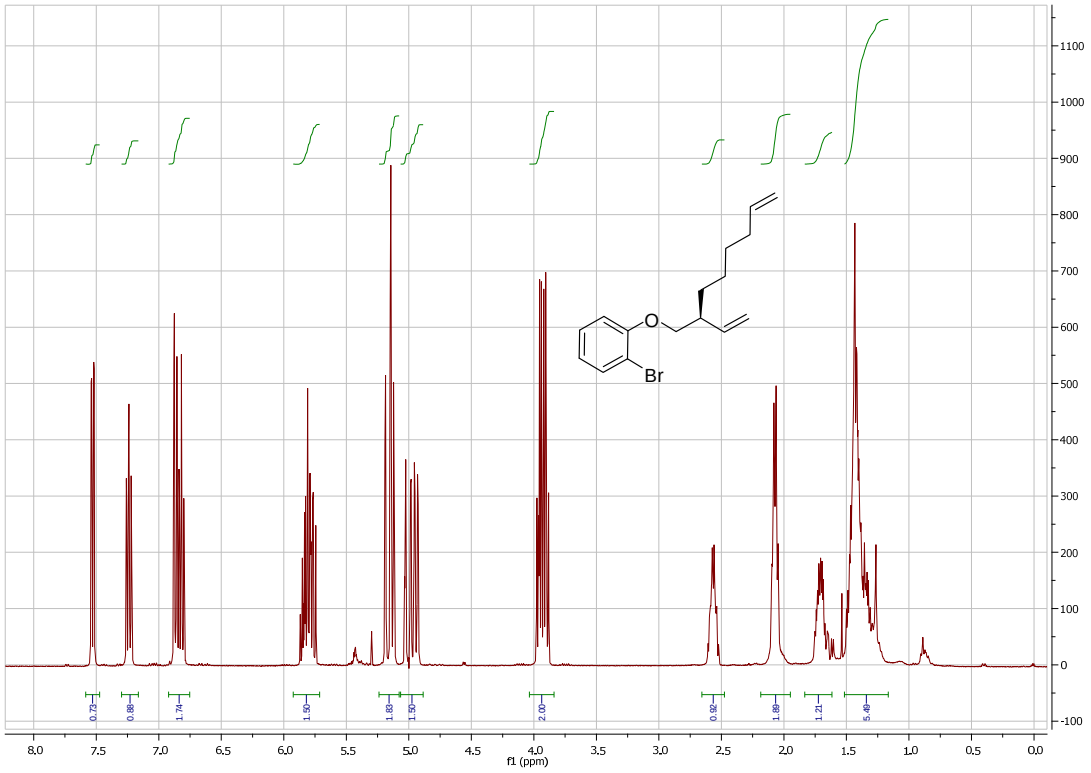


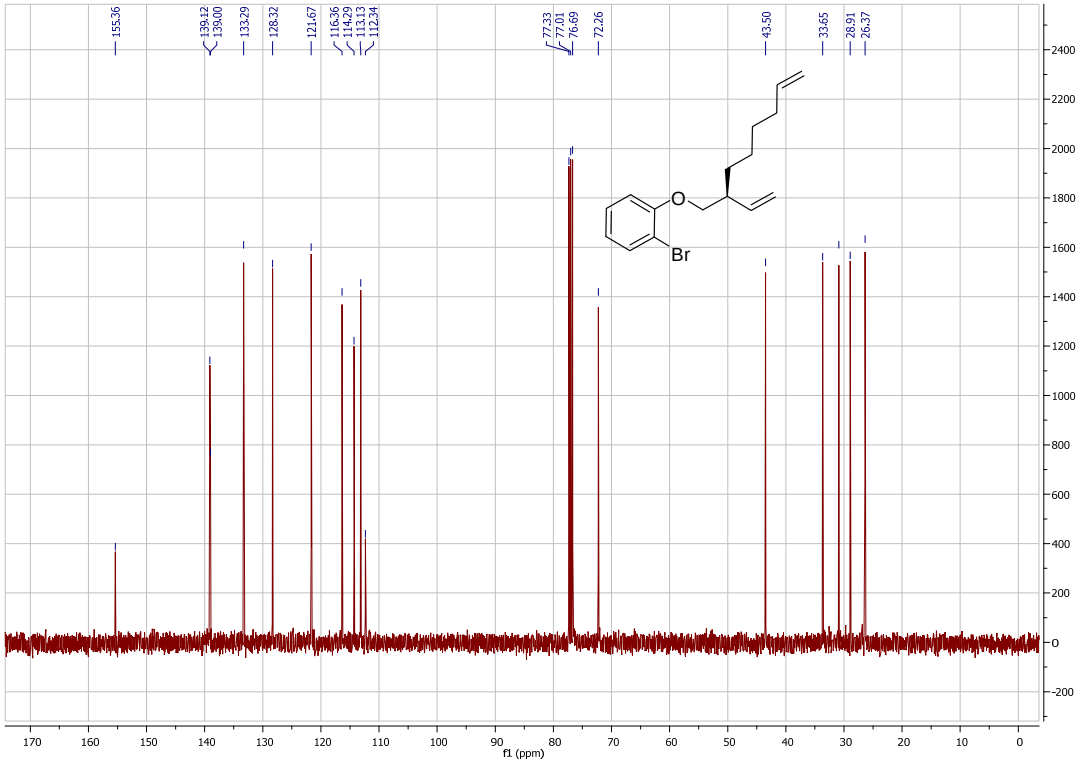
(+)-1-bromo-2-(2-vinylhept-6-enyloxy)benzene (3d)



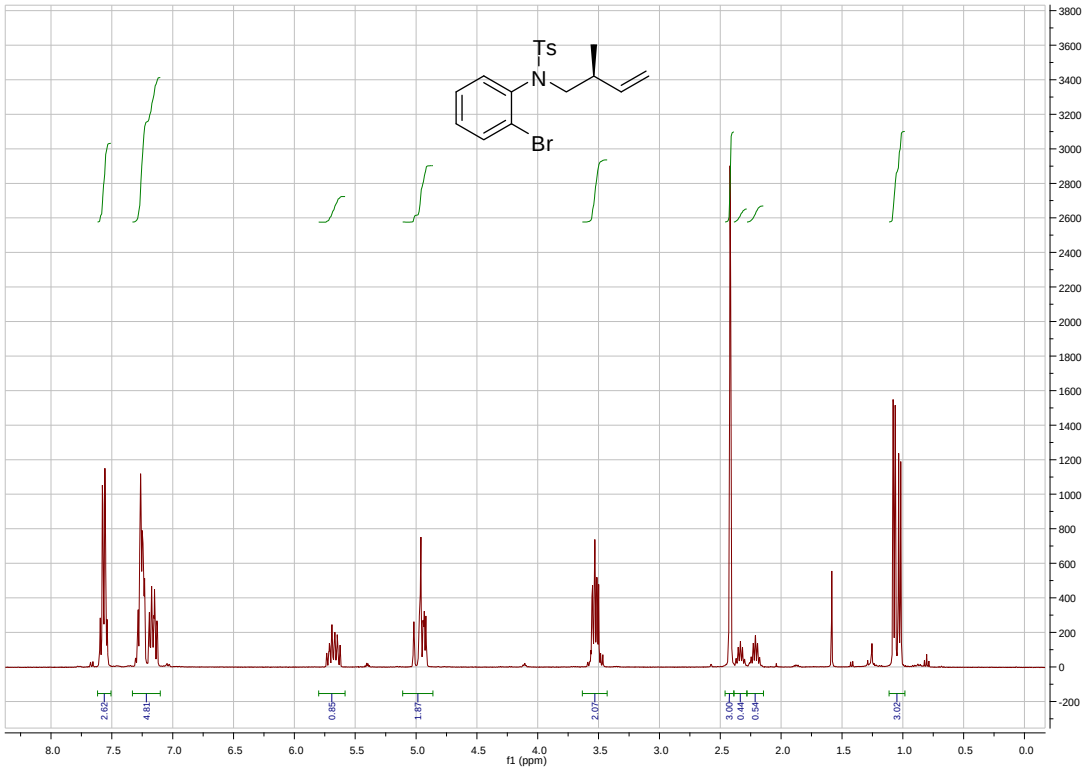


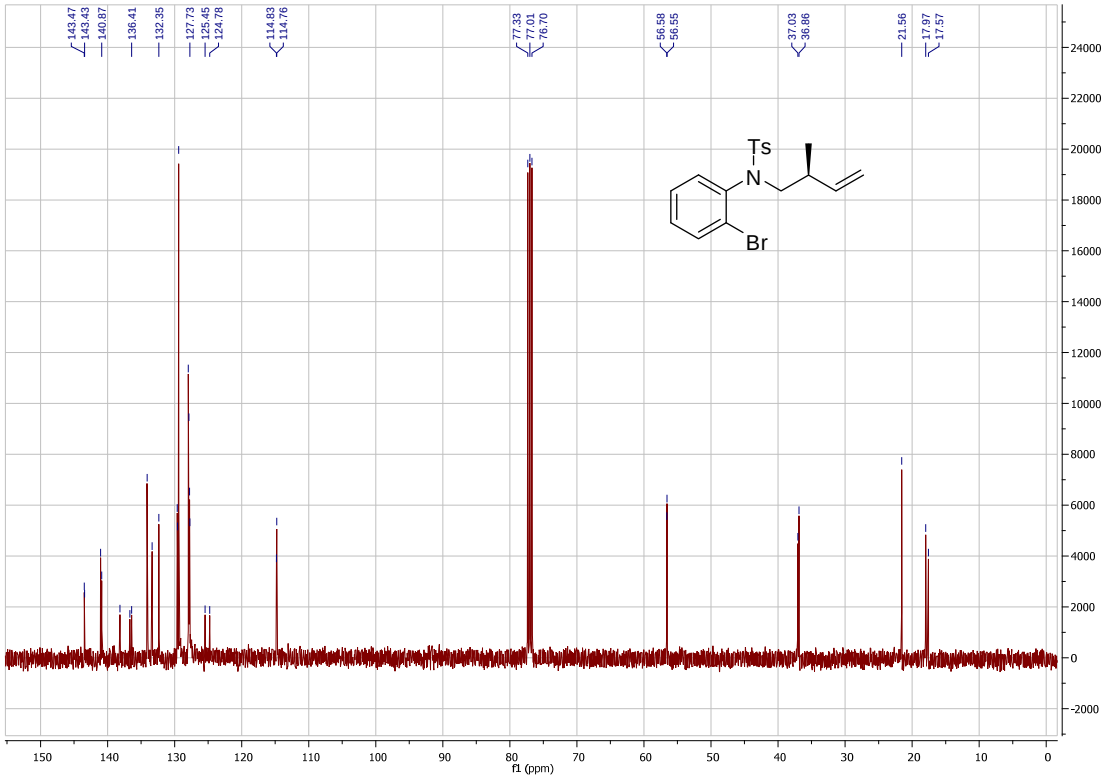
(+)-1-bromo-2-(2-vinyloct-7-enyloxy)benzene (3e)



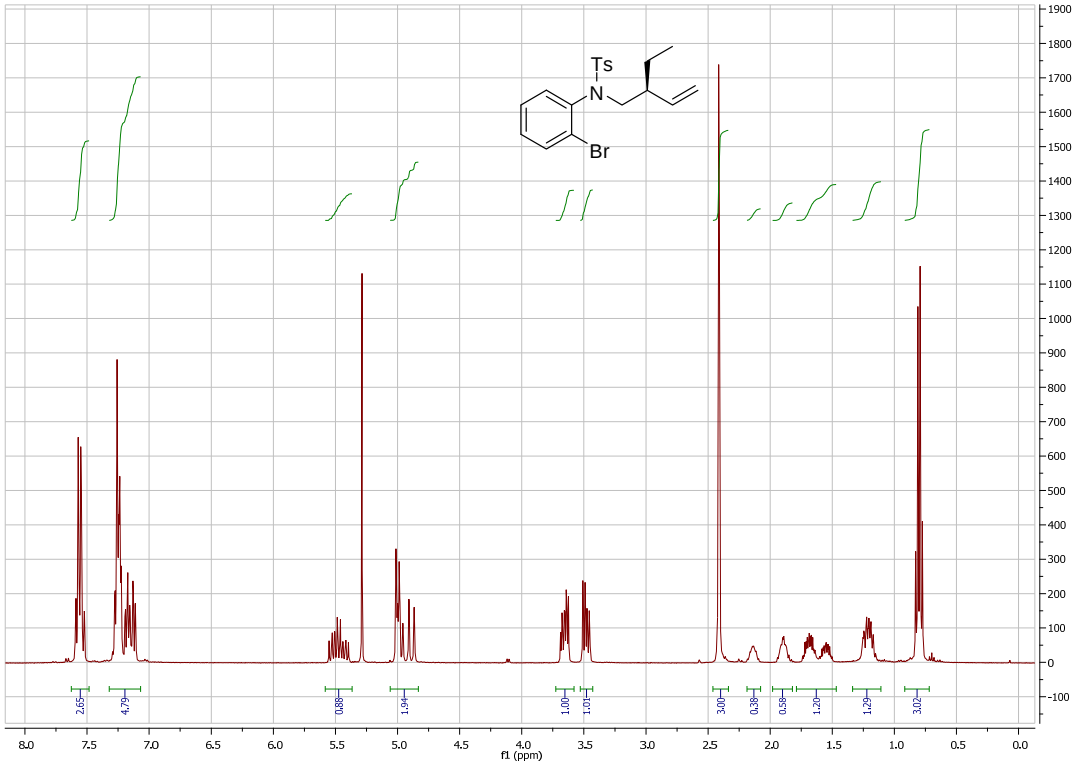


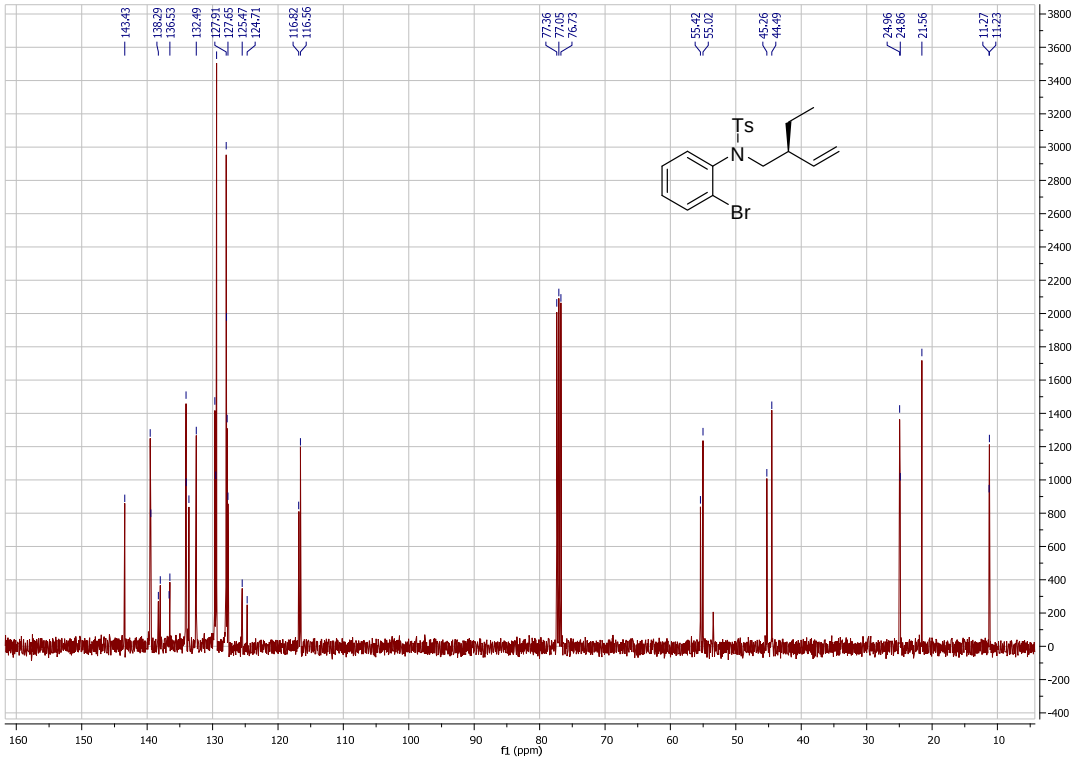
(+)-*N*-(2-bromophenyl)-4-methyl-*N*-(2-methylbut-3-enyl)benzenesulfonamide (4a)



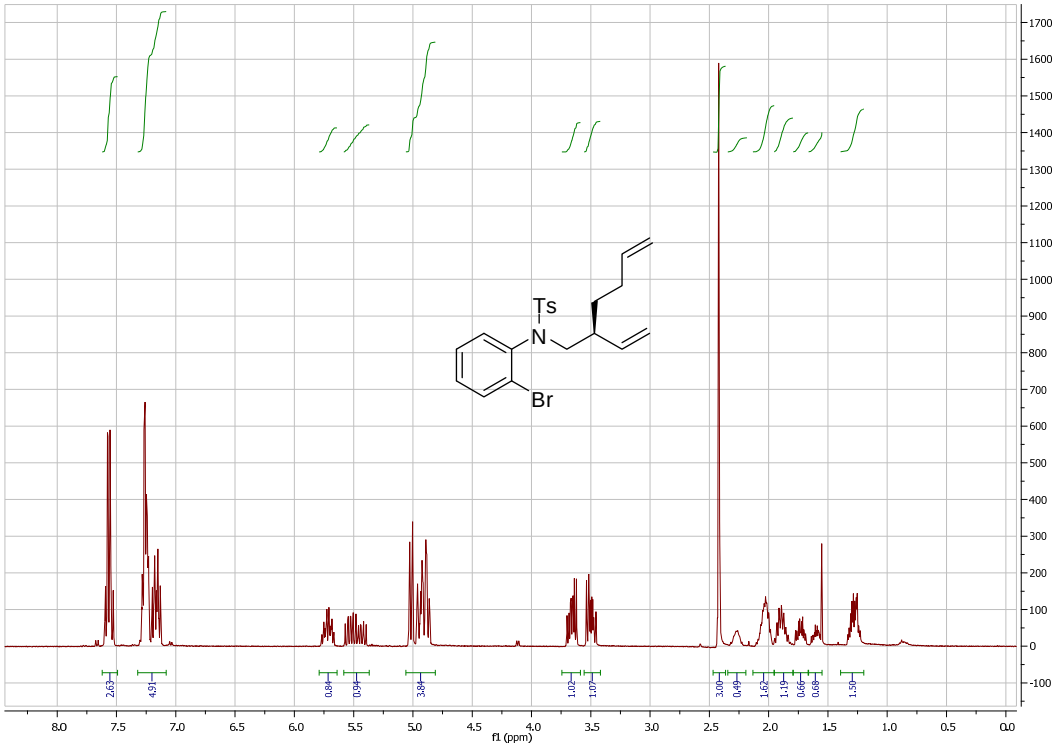


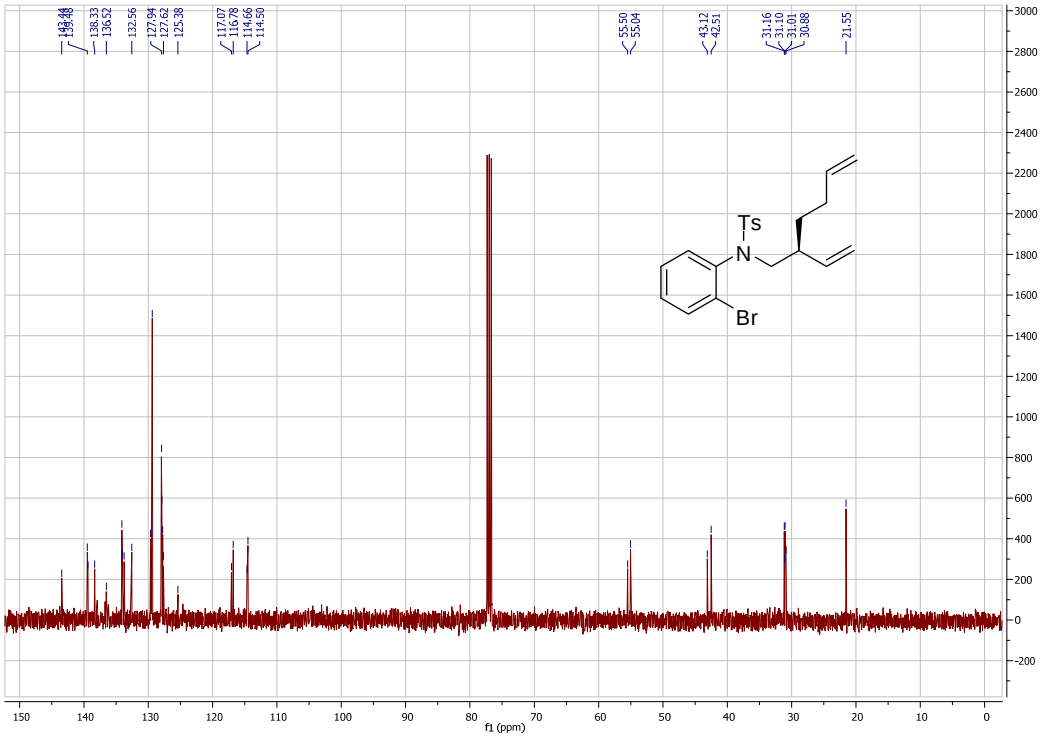
(+)-*N*-(2-bromophenyl)-*N*-(2-ethylbut-3-enyl)-4-methylbenzenesulfonamide (4b)



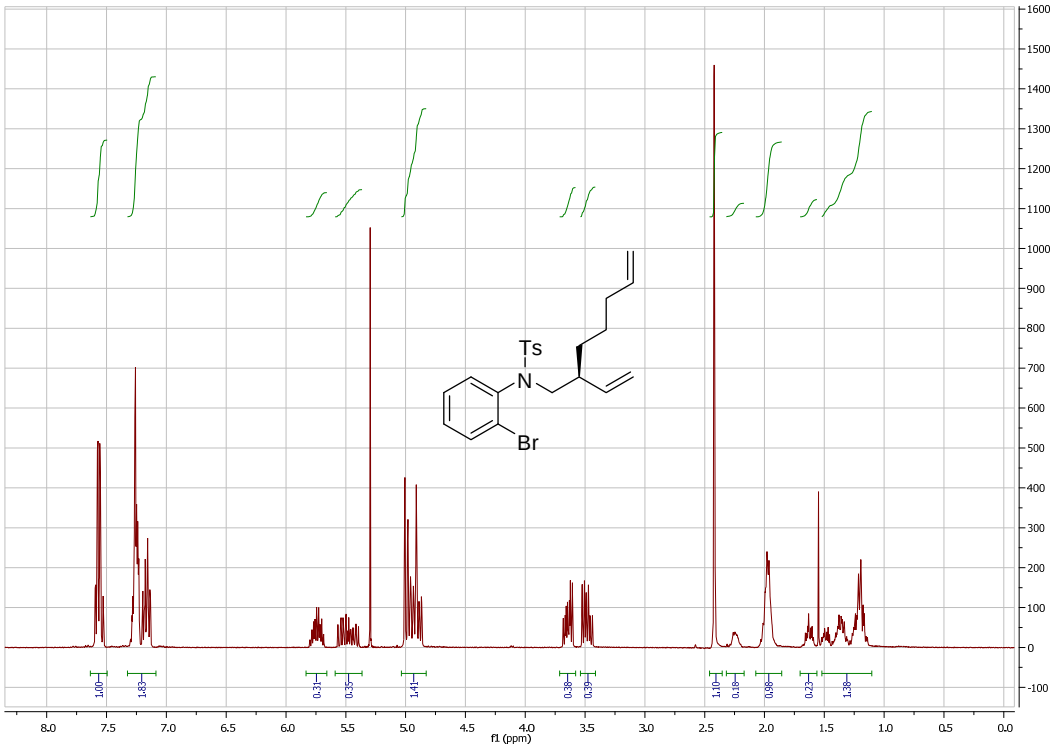


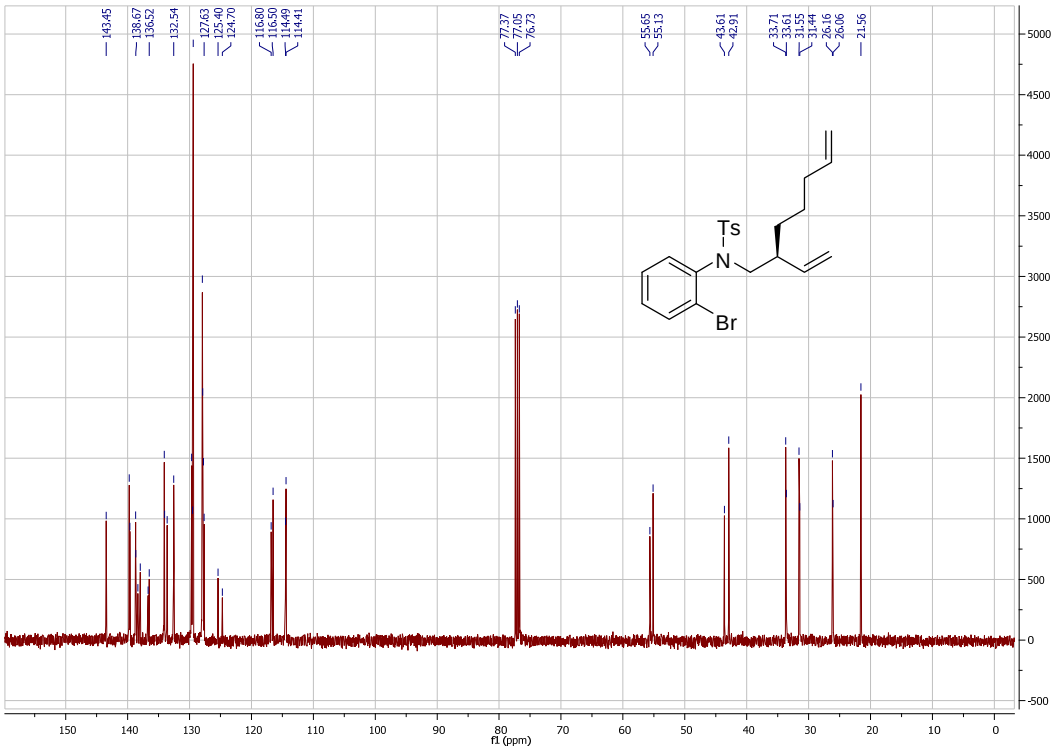
(+)-*N*-(2-bromophenyl)-4-methyl-*N*-(2-vinylhex-5-enyl)benzenesulfonamide (4c)



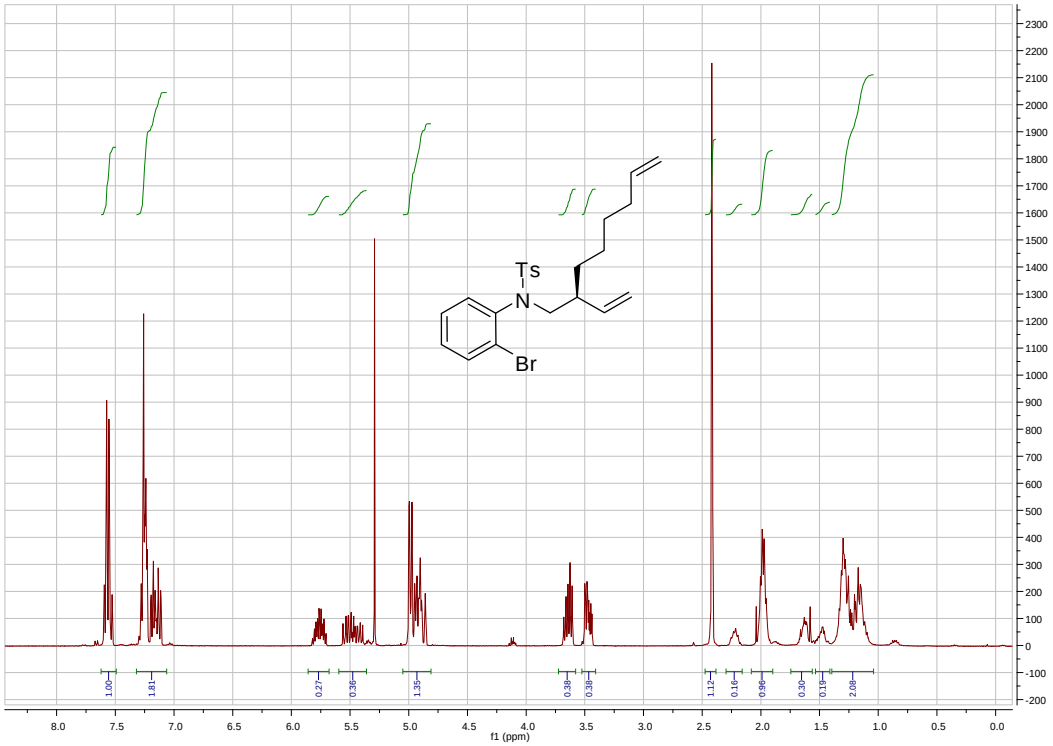


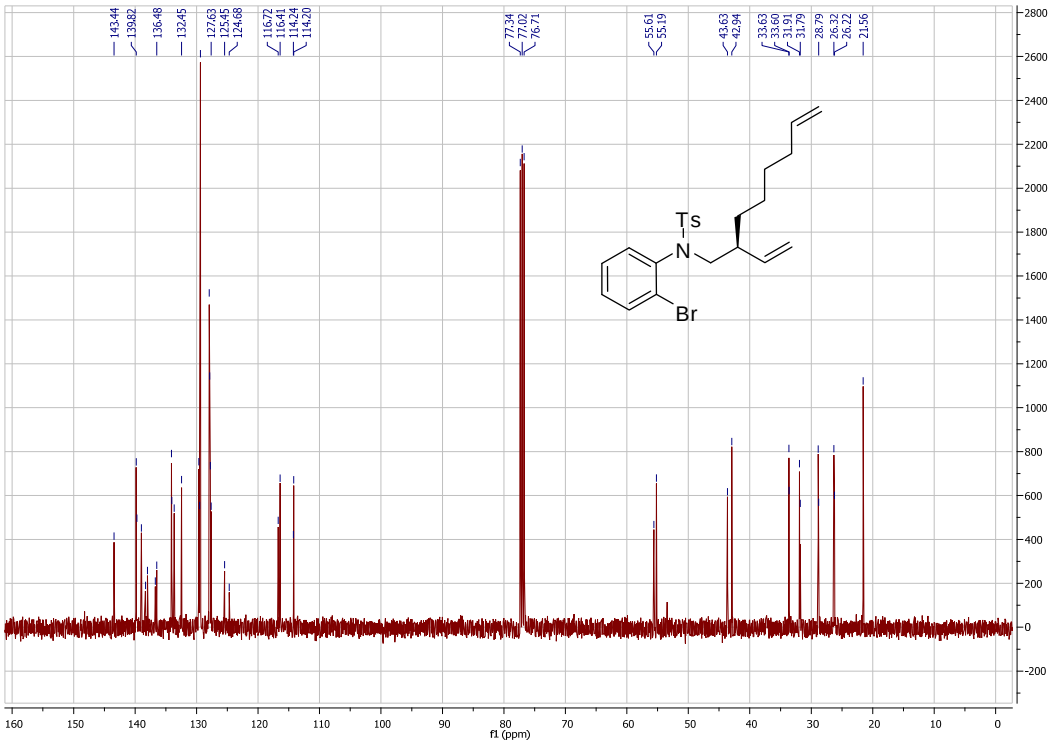
(+)-*N*-(2-bromophenyl)-4-methyl-*N*-(2-vinylhept-6-enyl)benzenesulfonamide (4d)



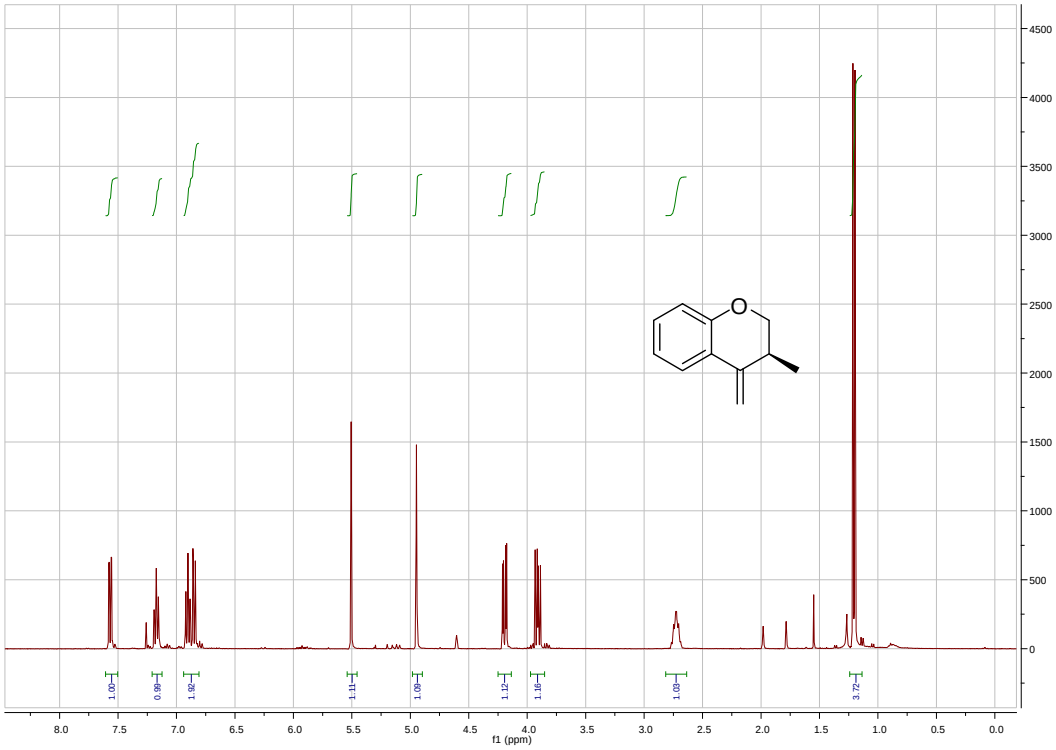


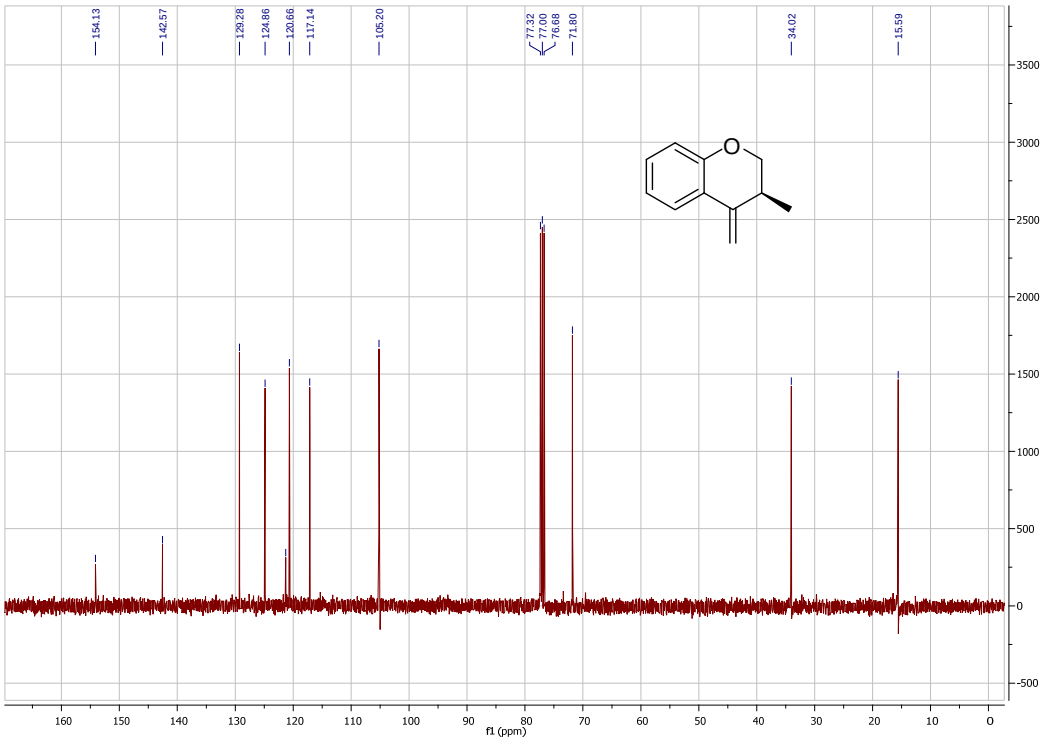
(+)-*N*-(2-bromophenyl)-4-methyl-*N*-(2-vinyloct-7-enyl)benzenesulfonamide (4e)



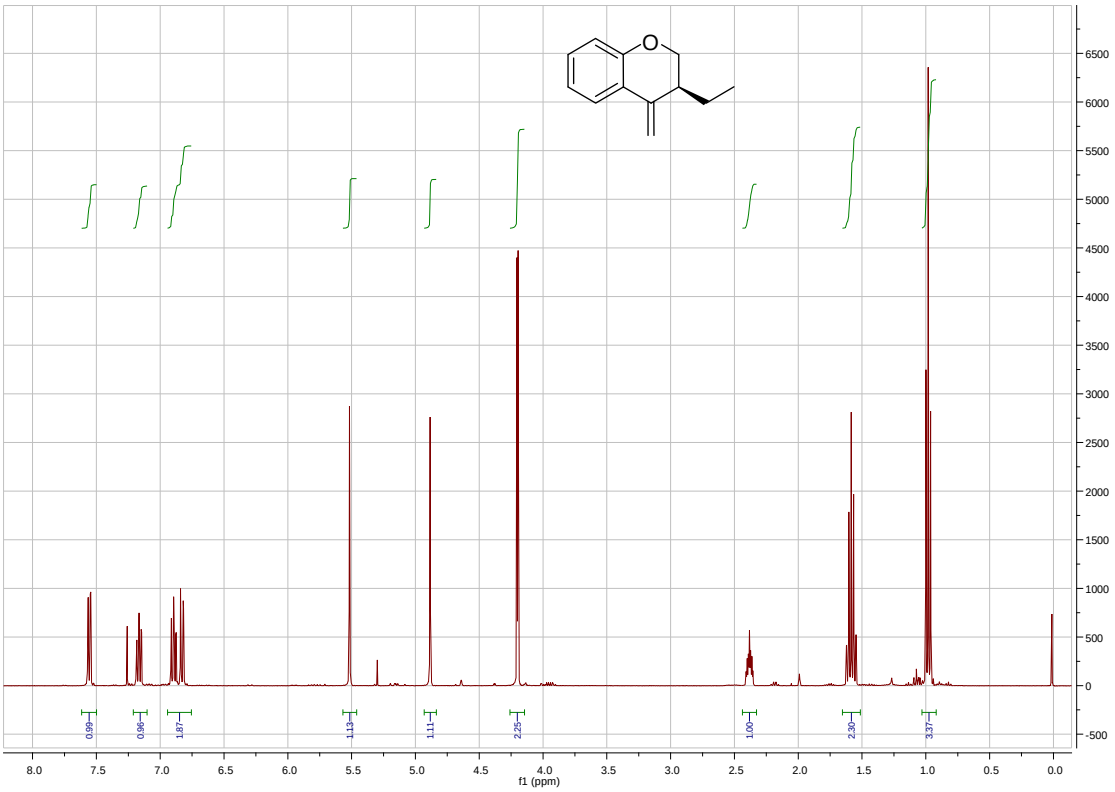


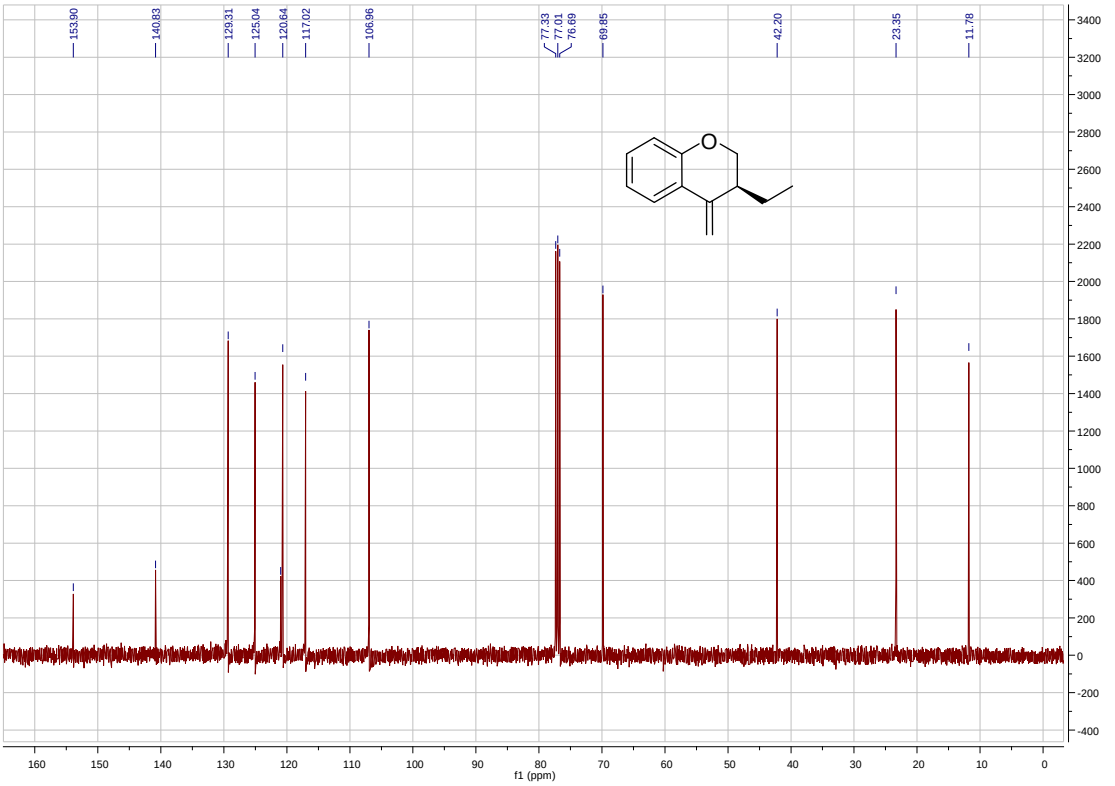
(+)-3-methyl-4-methylenechromene (5a)



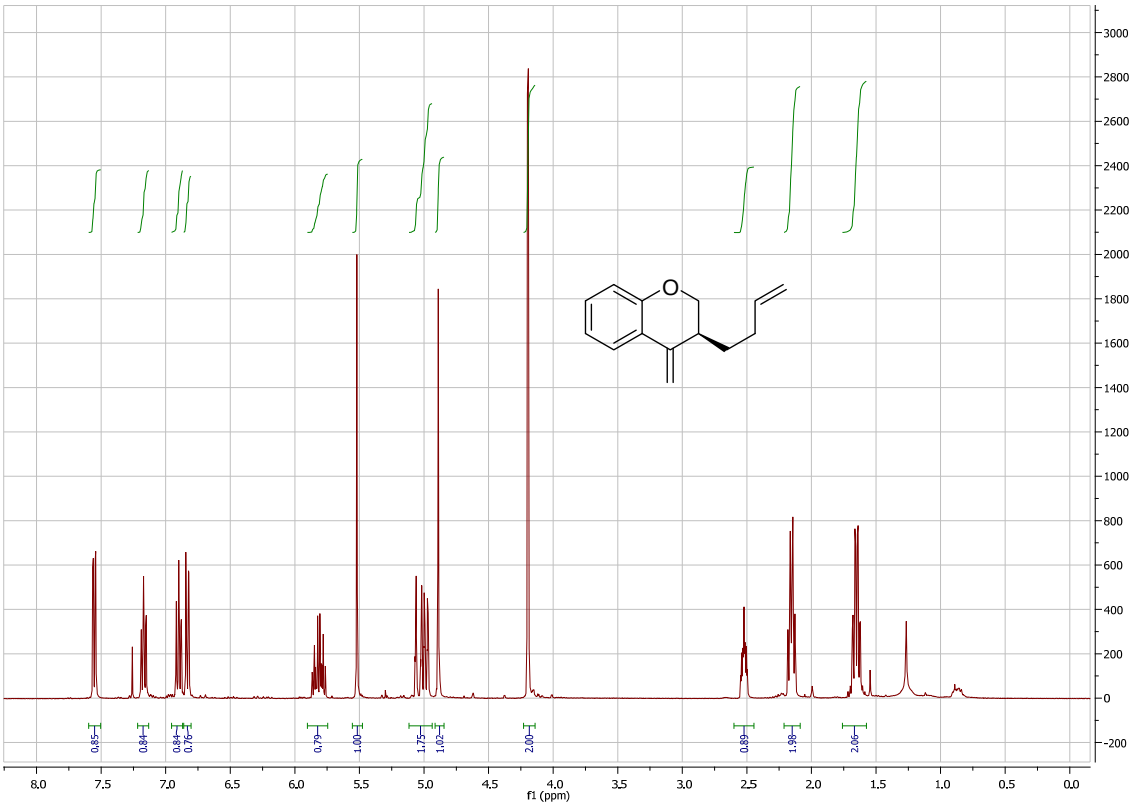


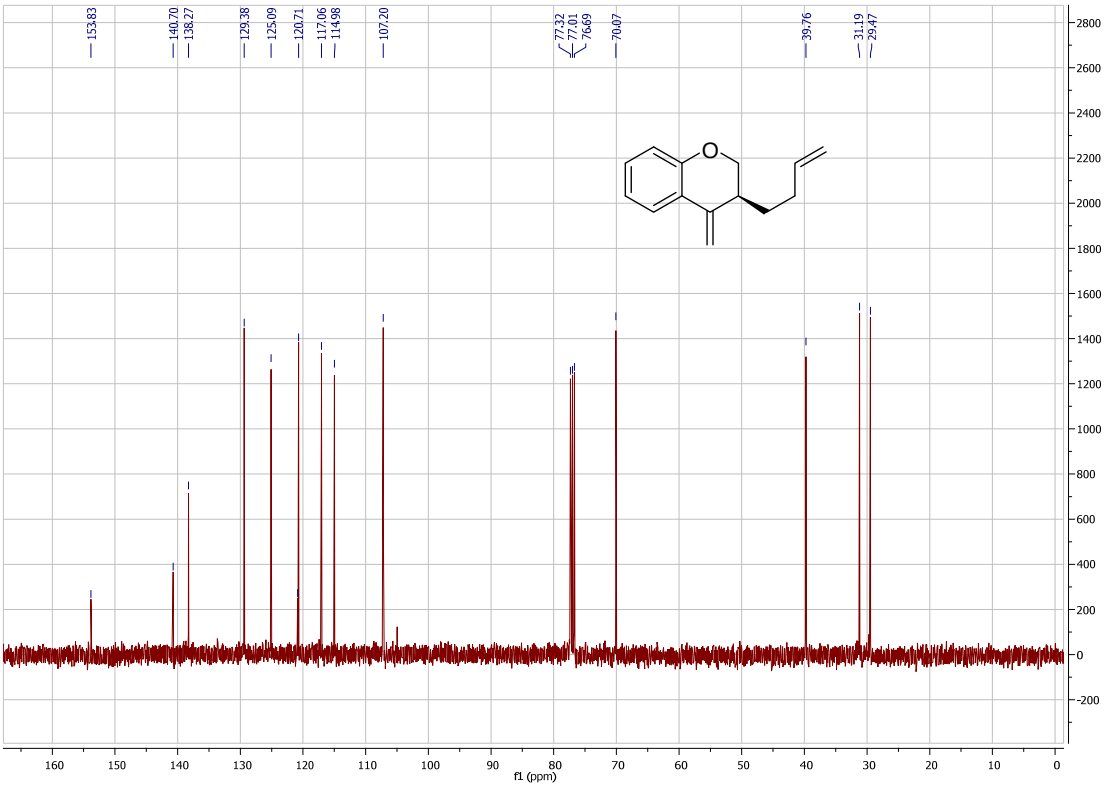
(-)-3-ethyl-4-methylenechromene (5b)



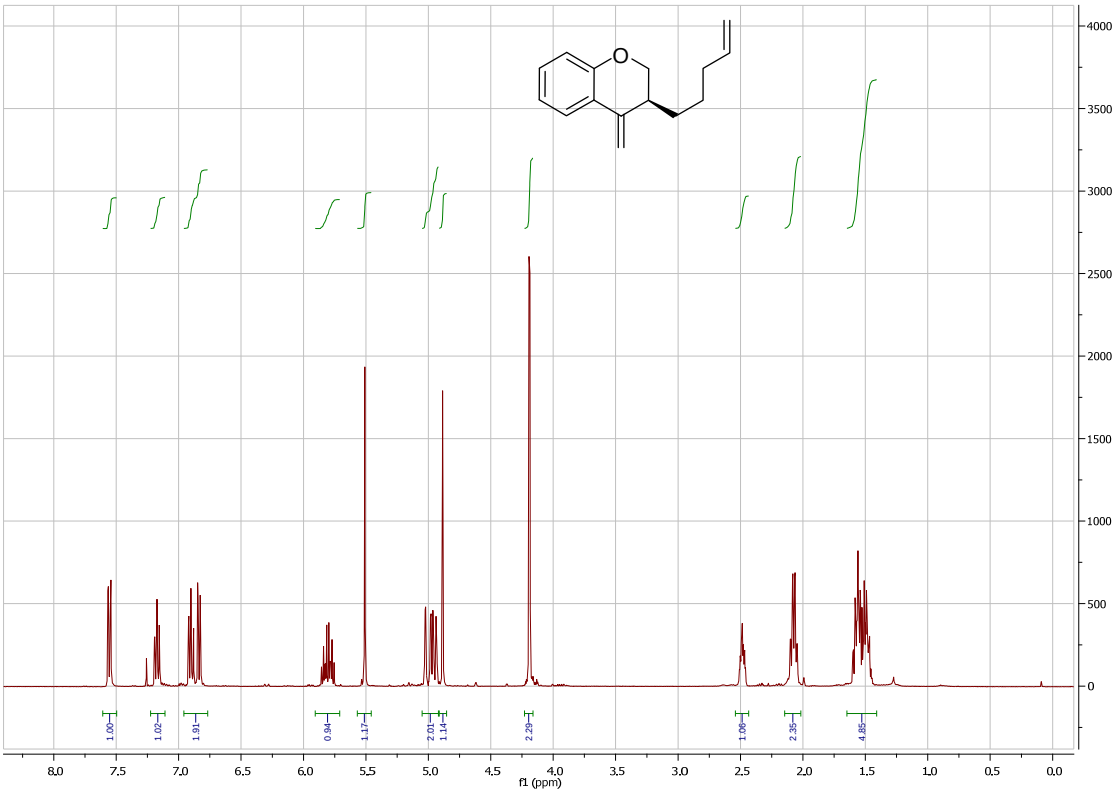


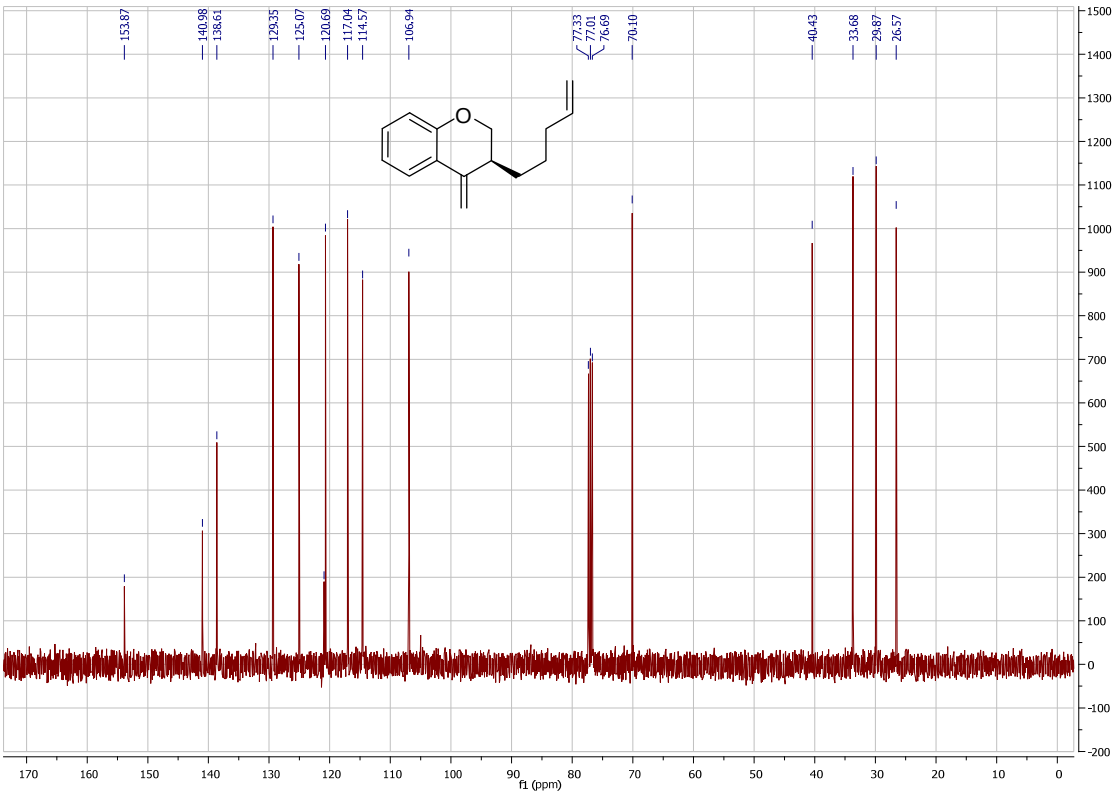
(+)-3-(but-3-enyl)-4-methylenechromene (5c)



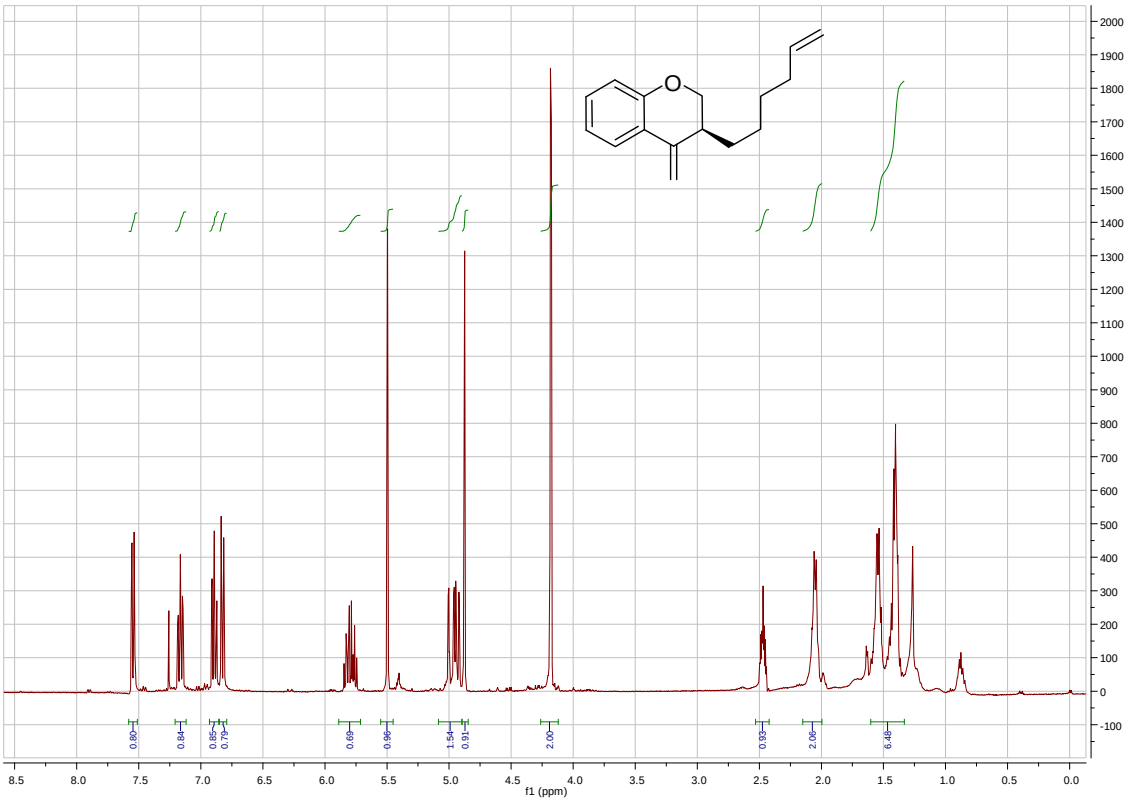


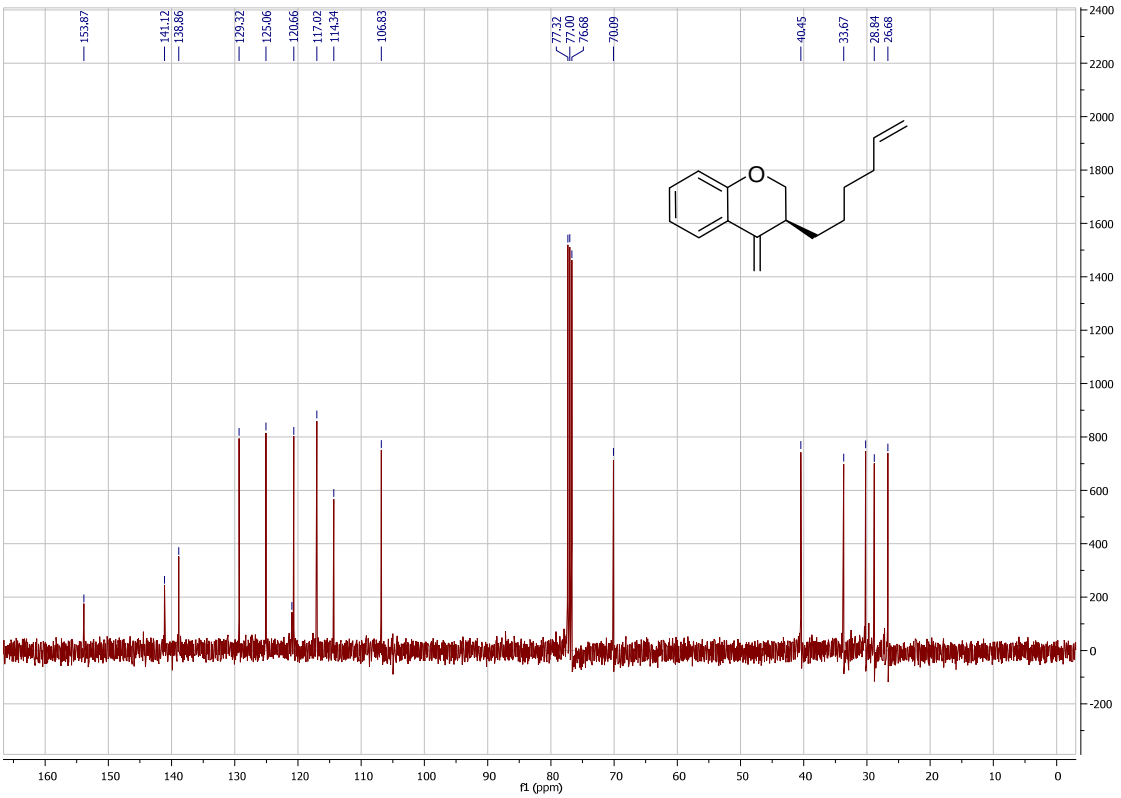
(-)-4-methylene-3-(pent-4-enyl)chromene (5d)



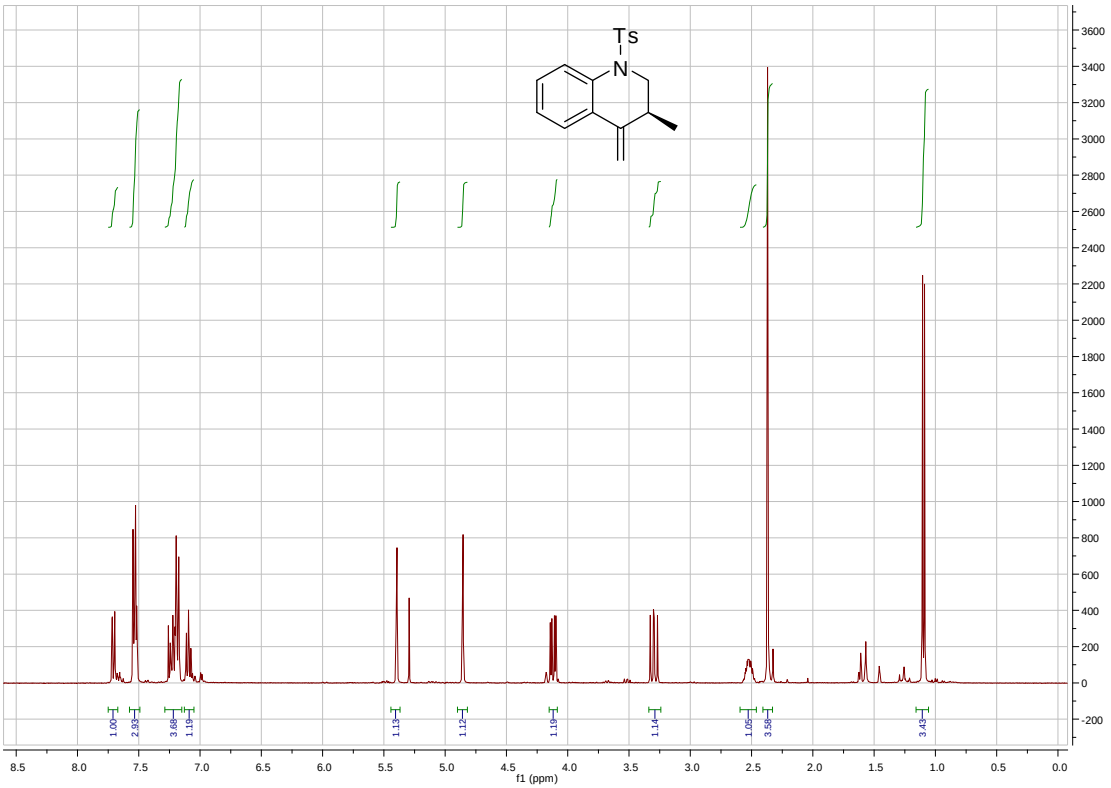


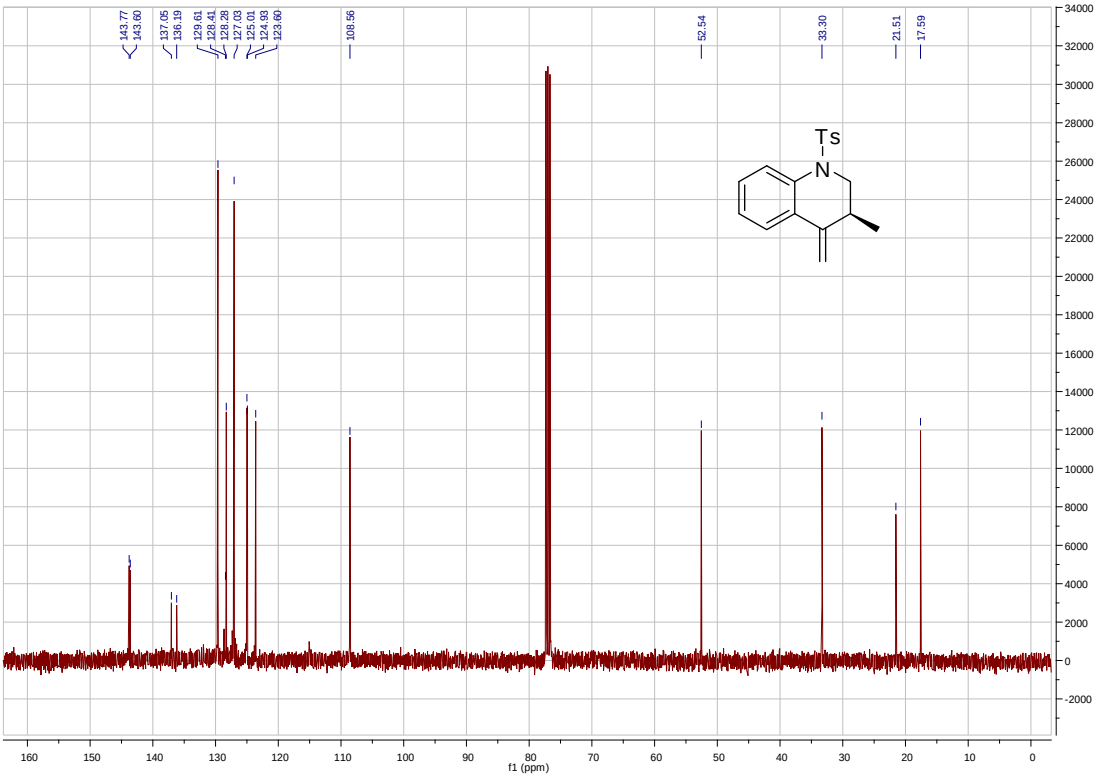
(-)-3-(hex-5-enyl)-4-methylenechromene (5e)



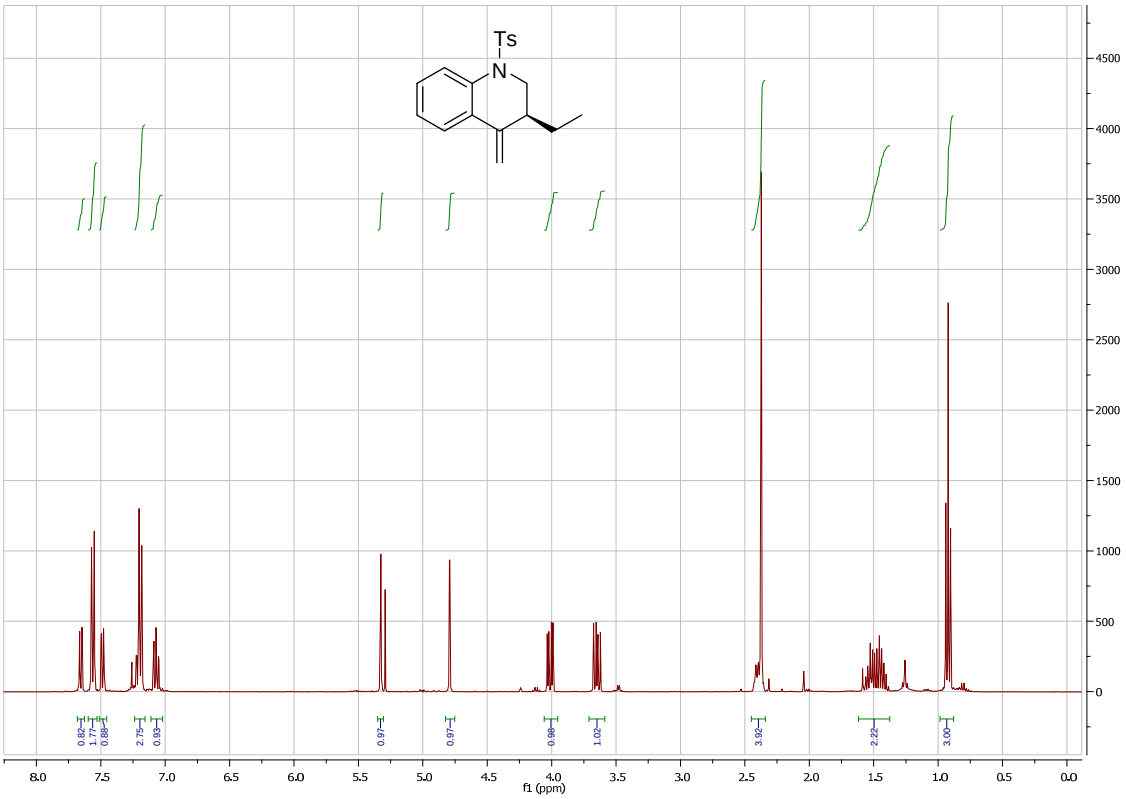


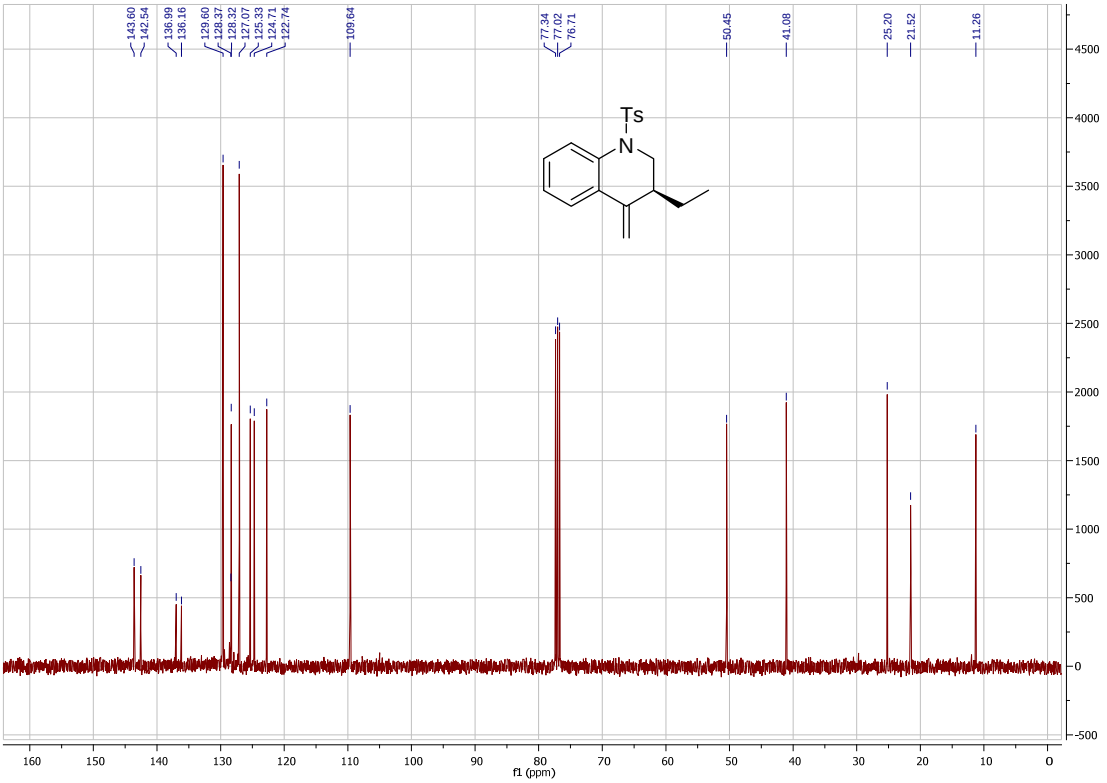
(+)-3-methyl-4-methylene-1-tosyl-1,2,3,4-tetrahydroquinoline (6a)



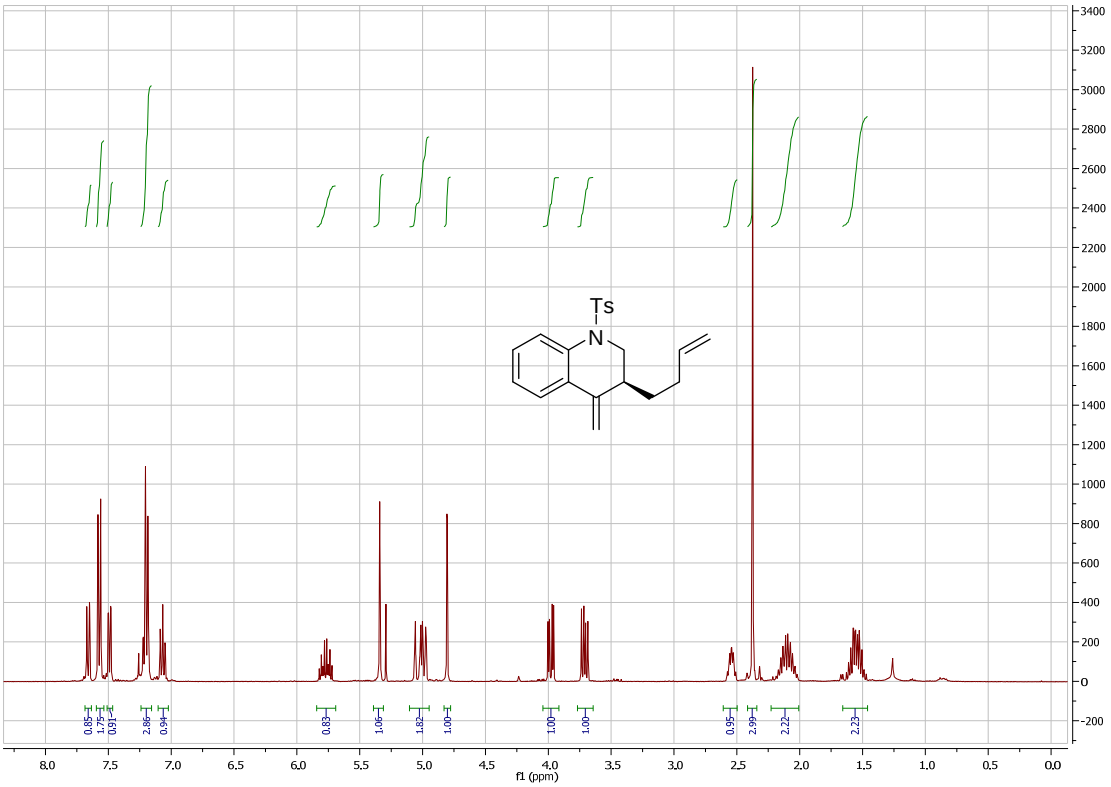


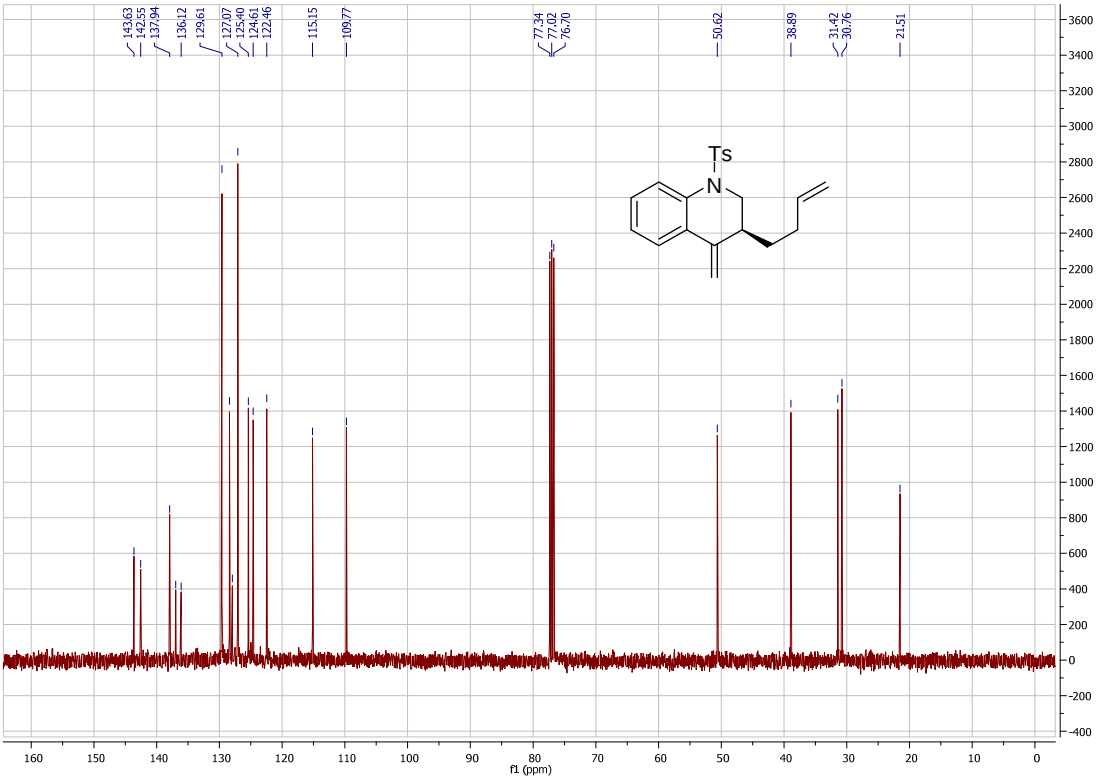
(-)-3-ethyl-4-methylene-1-tosyl-1,2,3,4-tetrahydroquinoline (6b)



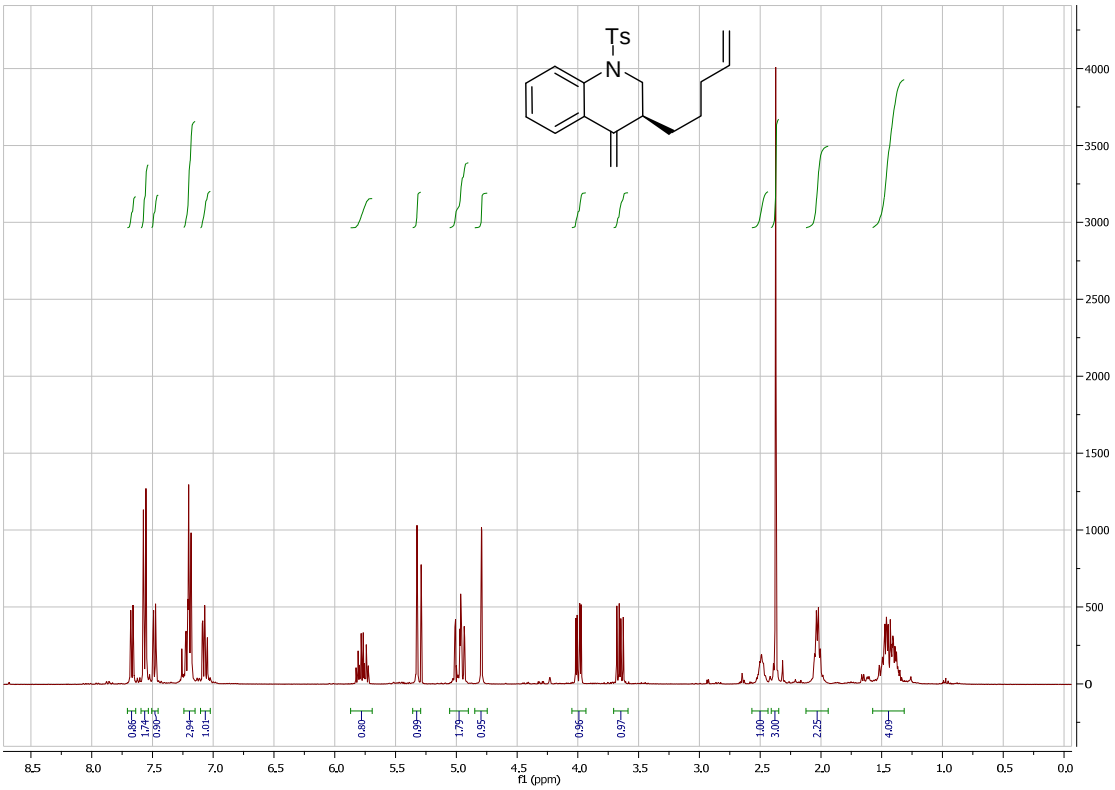


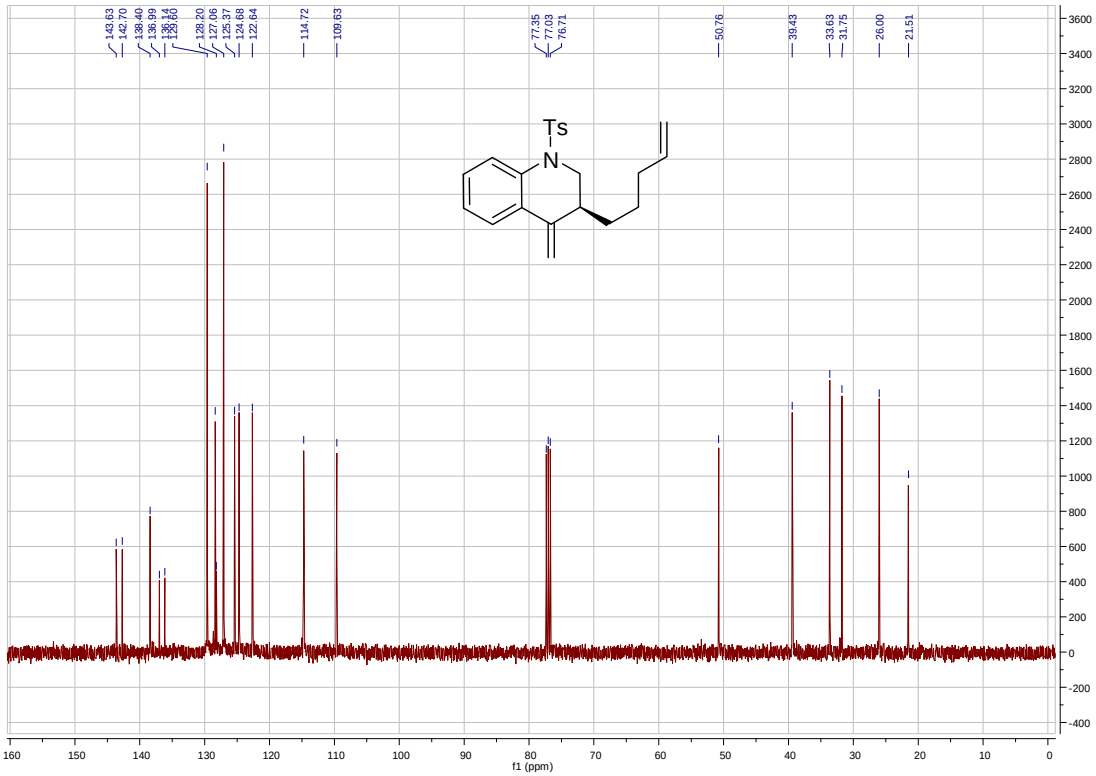
(-)-3-(but-3-enyl)-4-methylene-1-tosyl-1,2,3,4-tetrahydroquinoline (6c)



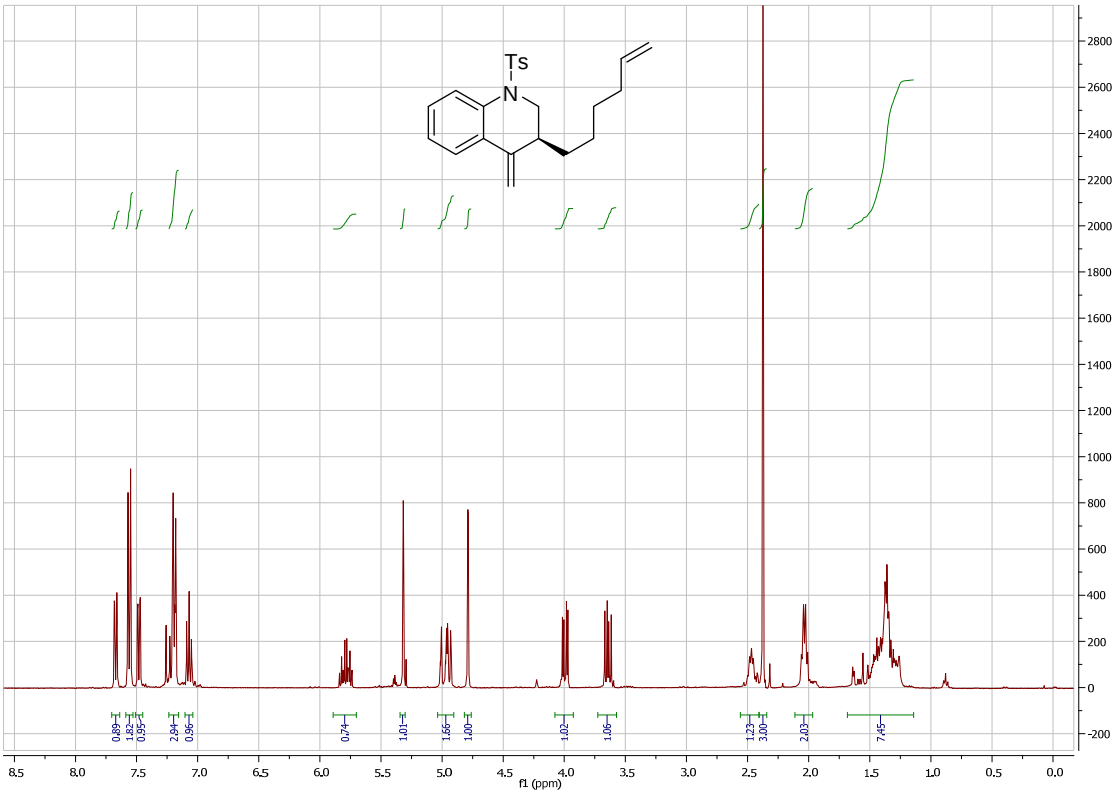


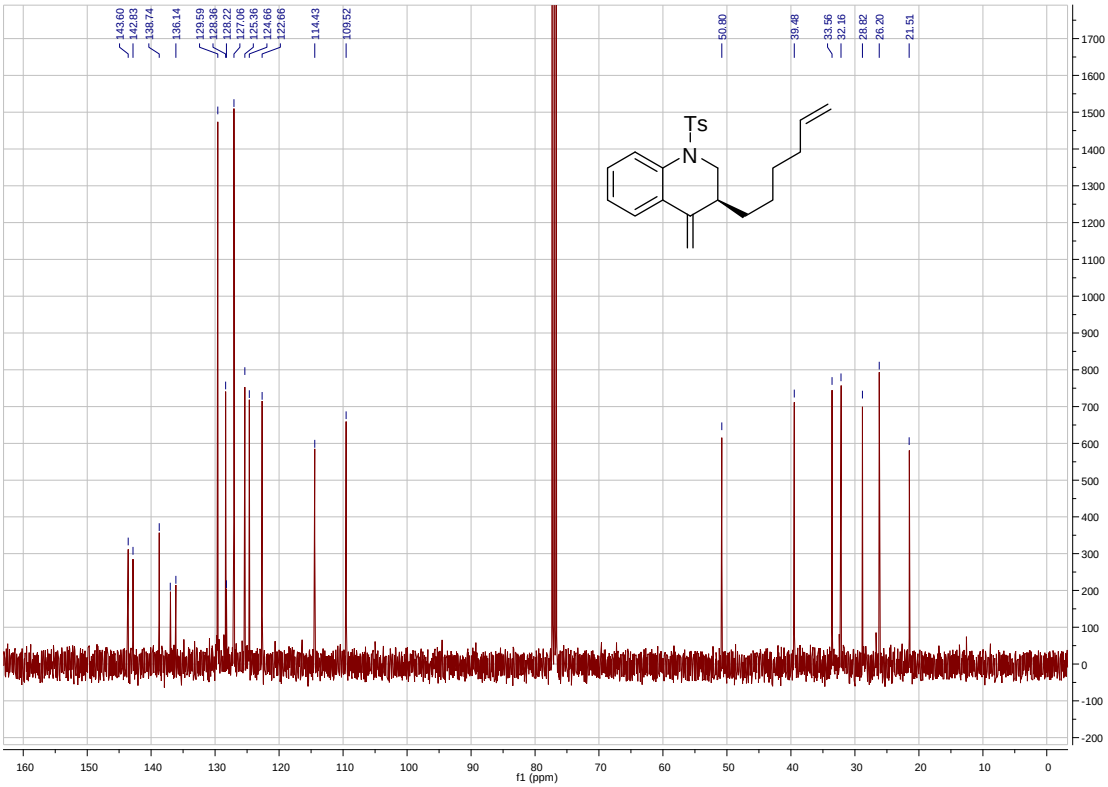
(-)-4-methylene-3-(pent-4-enyl)-1-tosyl-1,2,3,4-tetrahydroquinoline (6d)



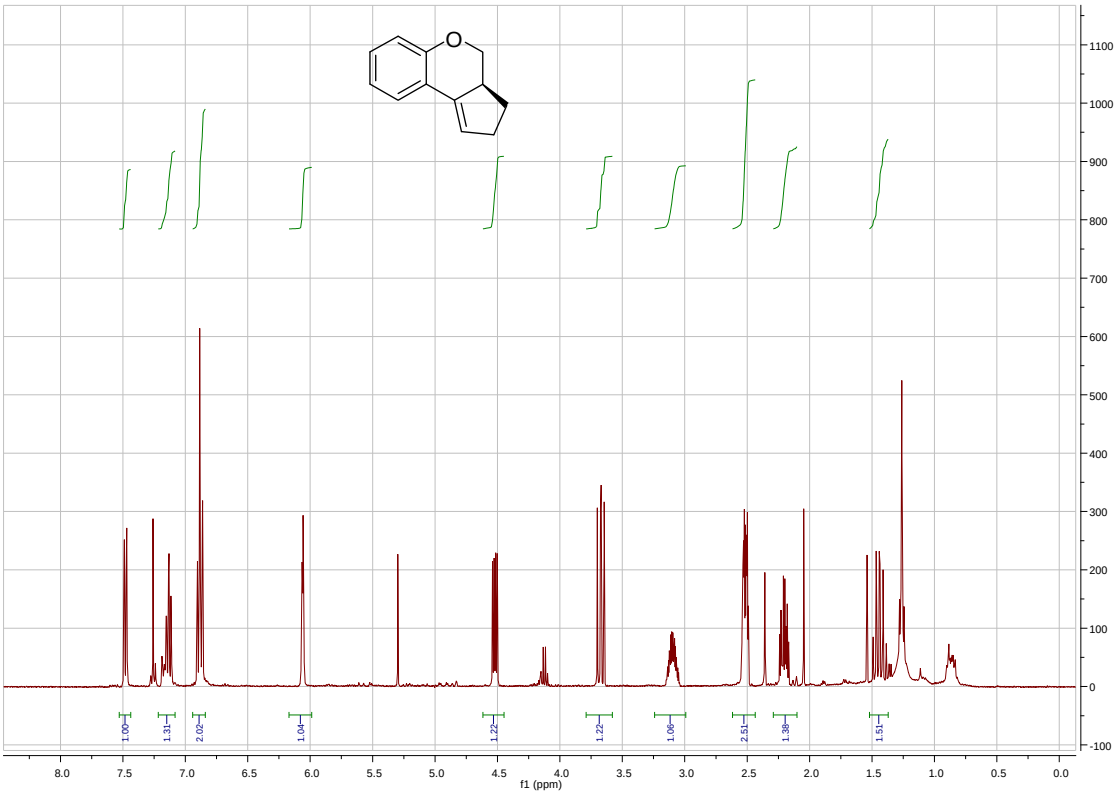


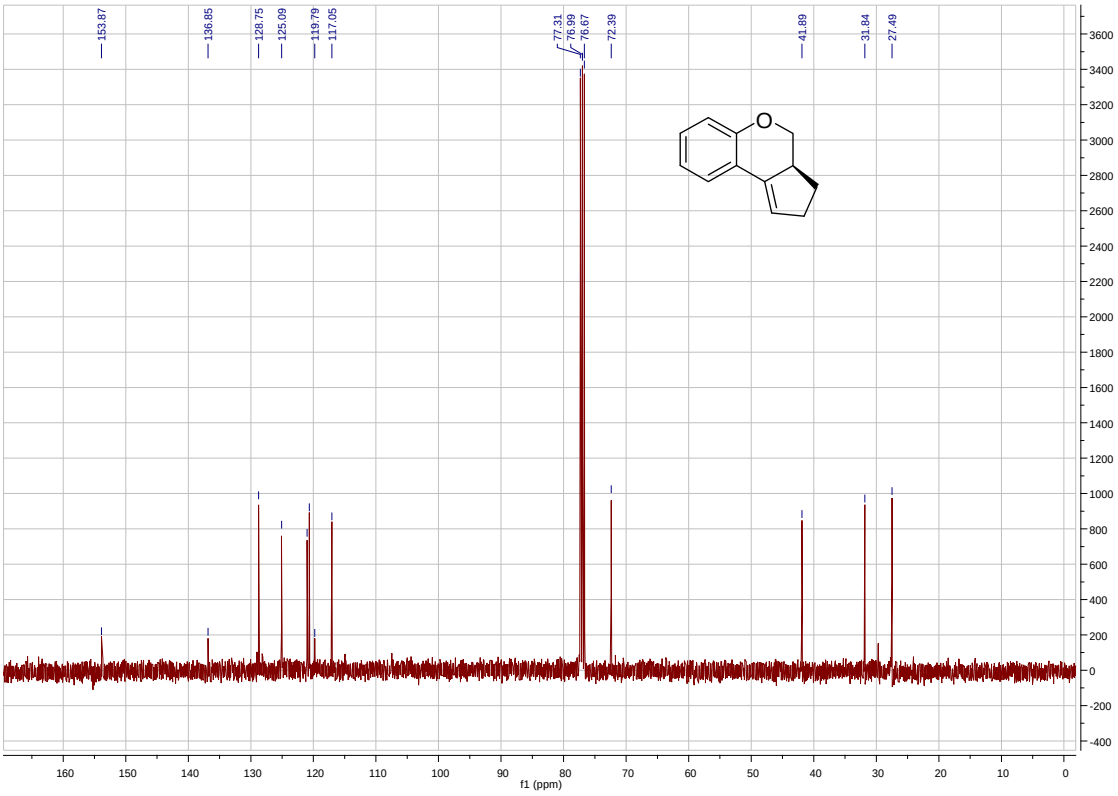
(+)-3-(hex-5-enyl)-4-methylene-1-tosyl-1,2,3,4-tetrahydroquinoline (6e)



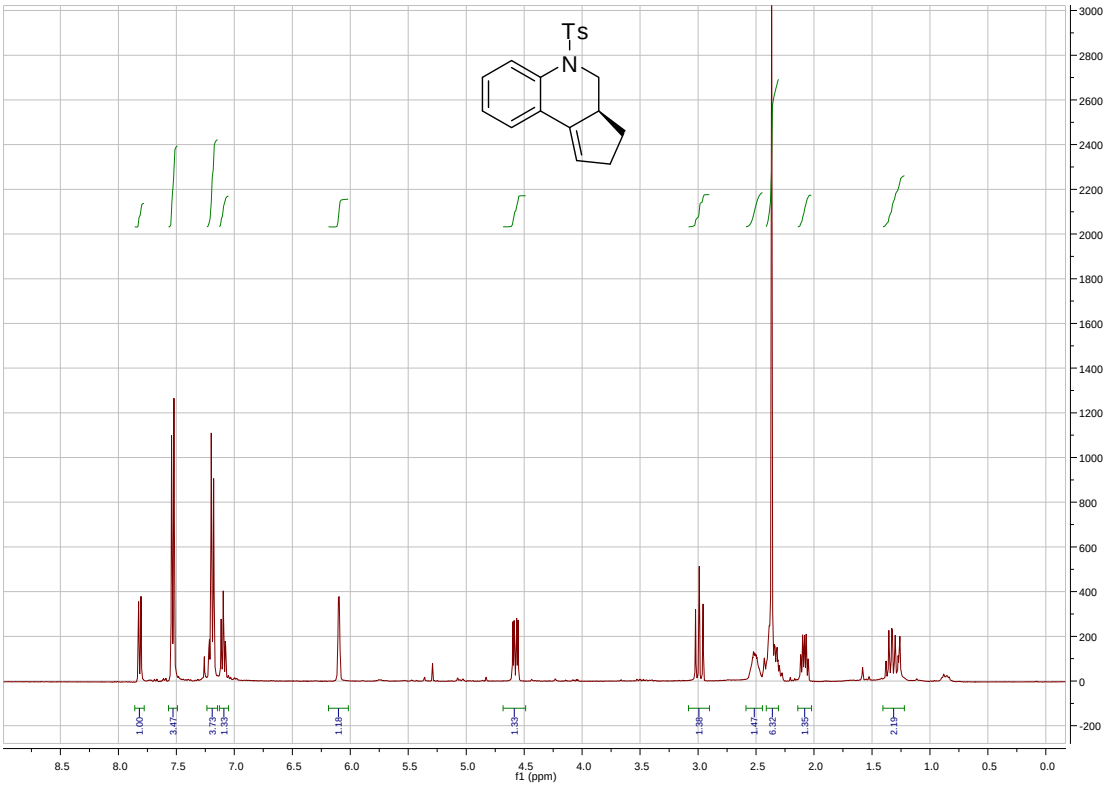


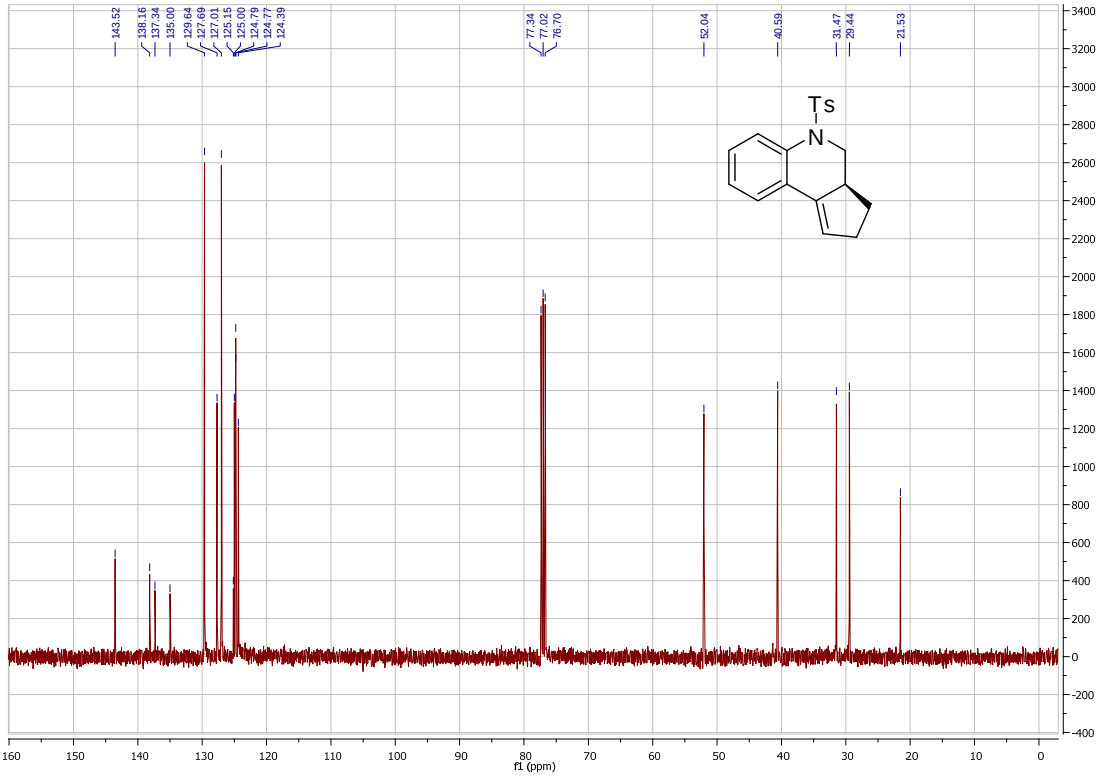
(+)-2,3,3a,4-tetrahydrocyclopenta[c]chromene (7)



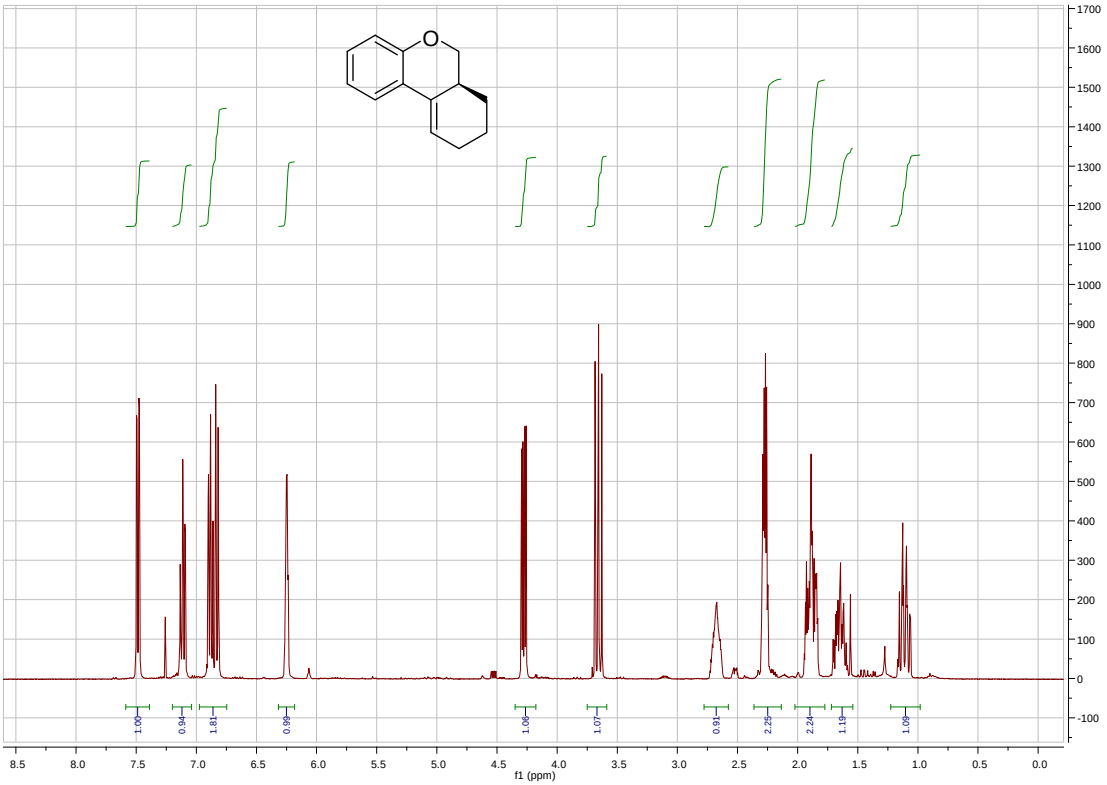


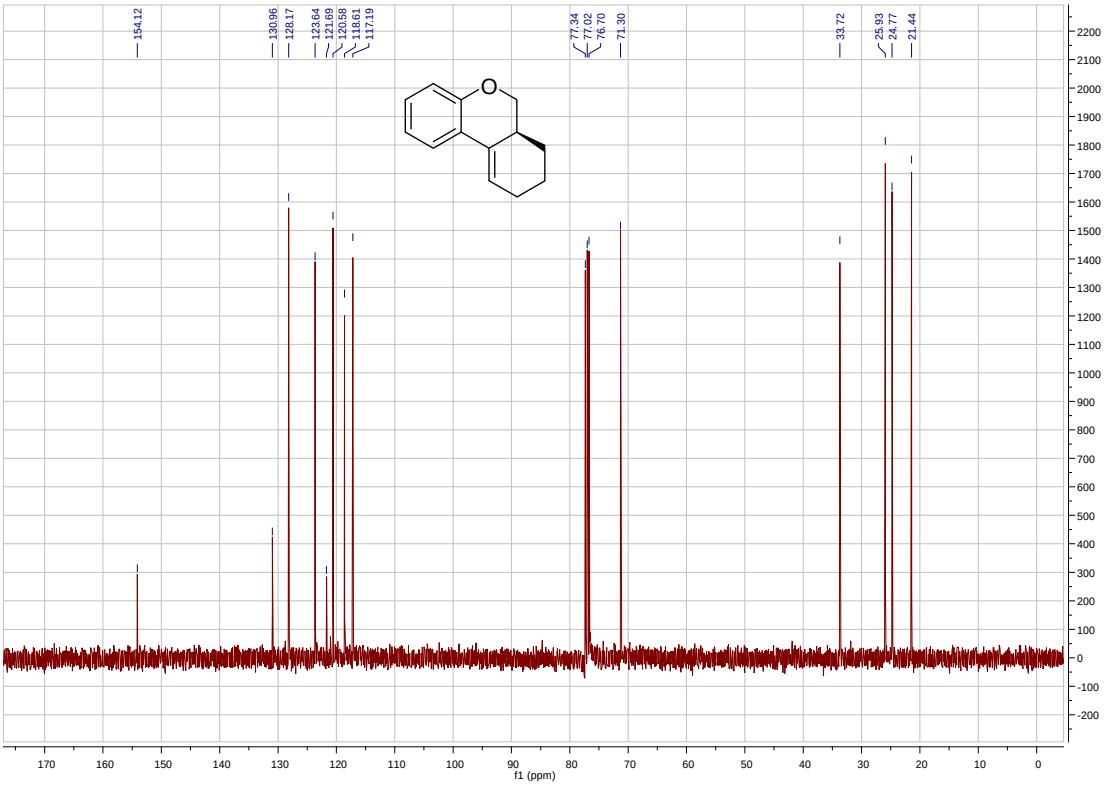
(+)-5-tosyl-3,3a,4,5-tetrahydro-2*H*-cyclopenta[c]quinoline (8)



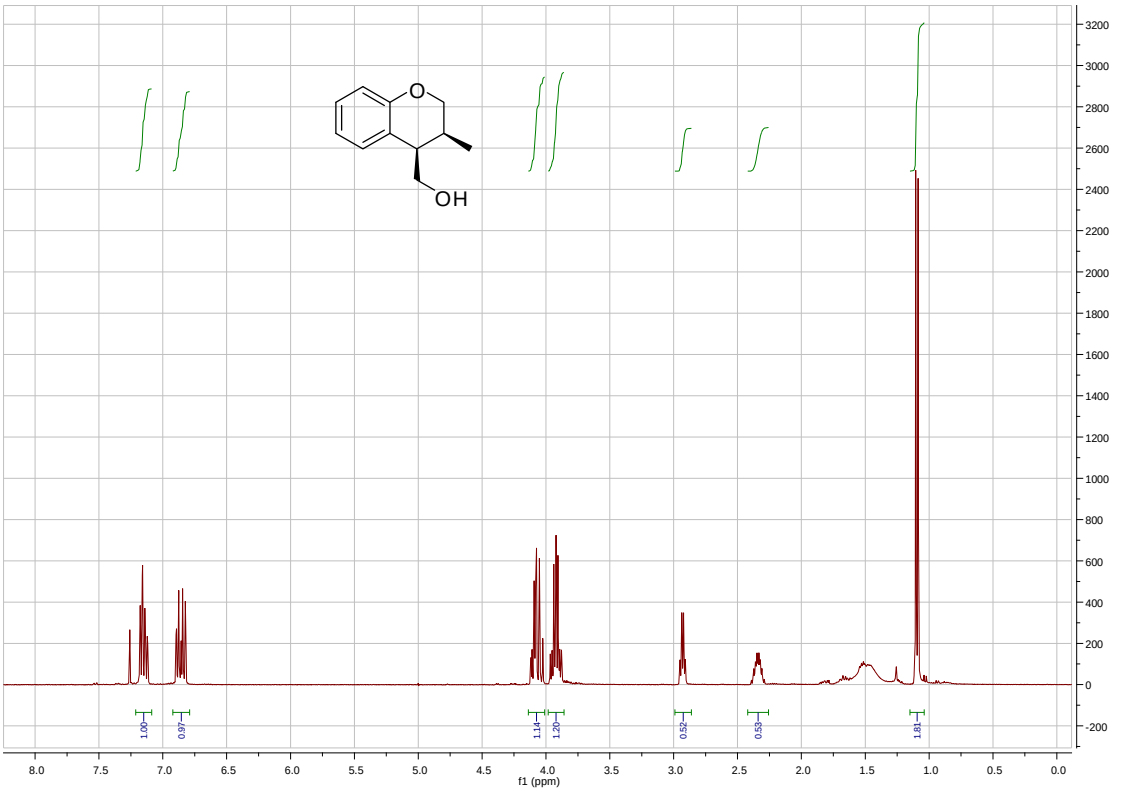


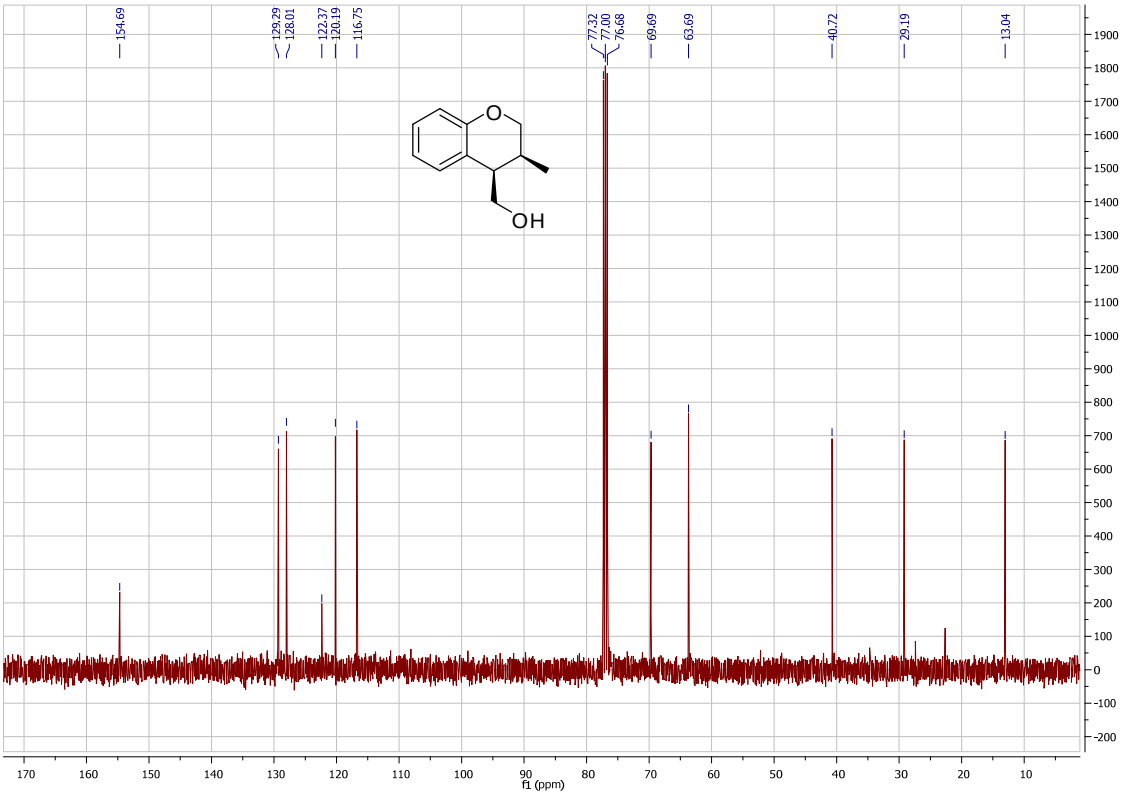
(+)-6a,7,8,9-tetrahydro-6*H*-benzo[c]chromene (9)



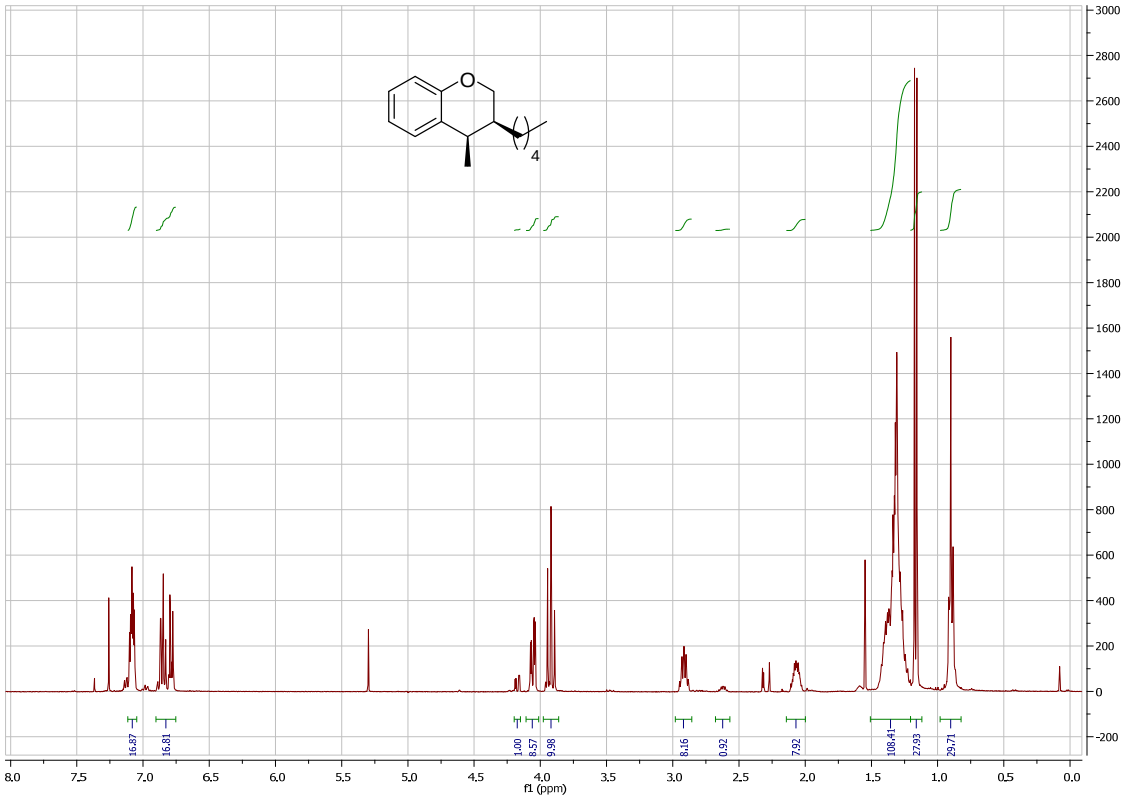


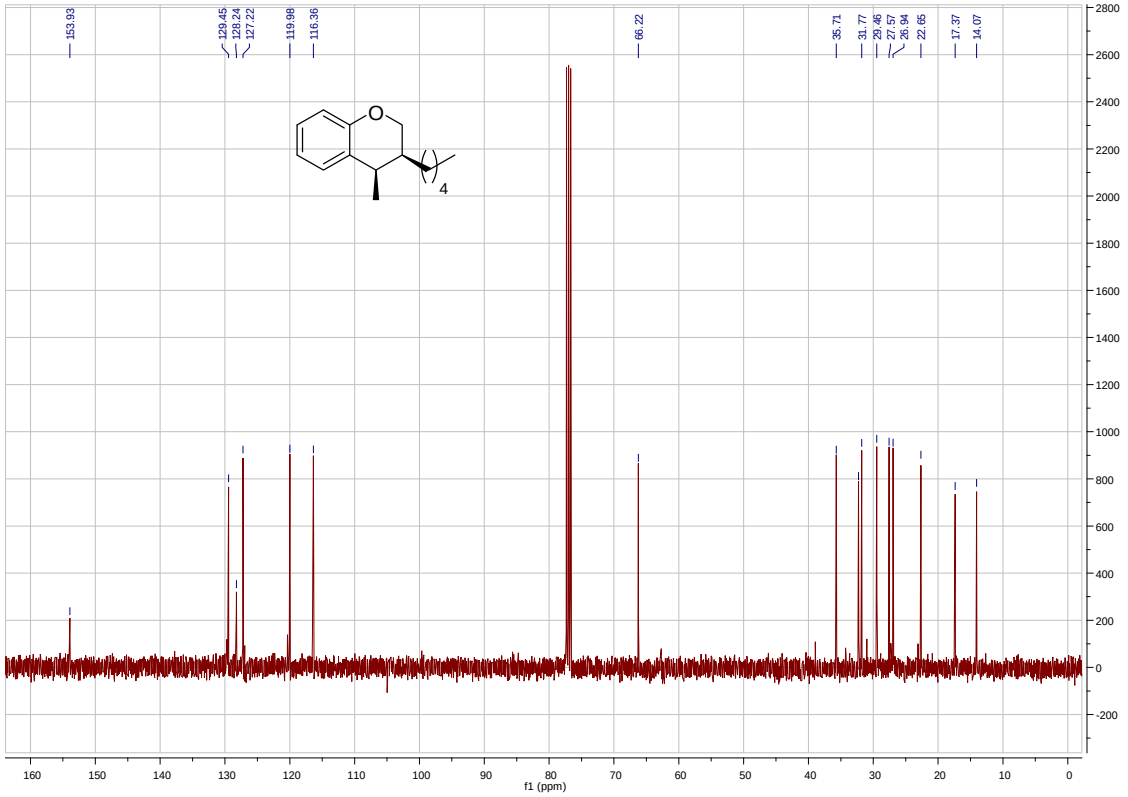
((+)-3-methylchroman-4-yl)methanol (10)



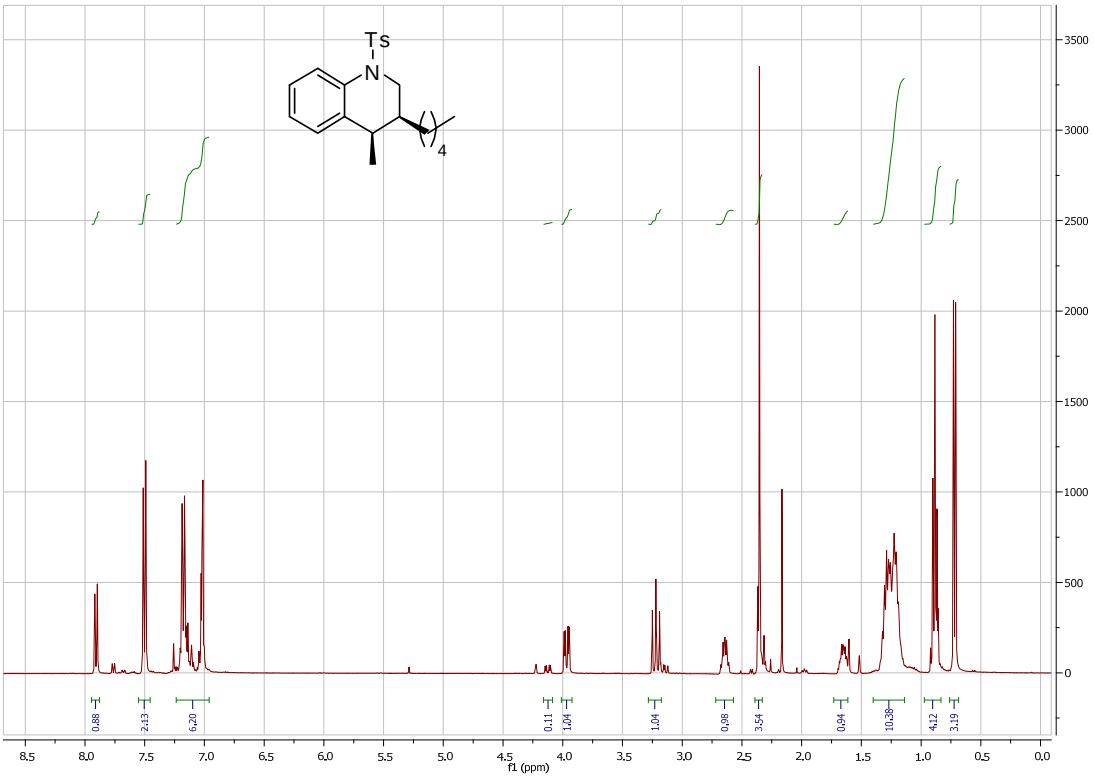


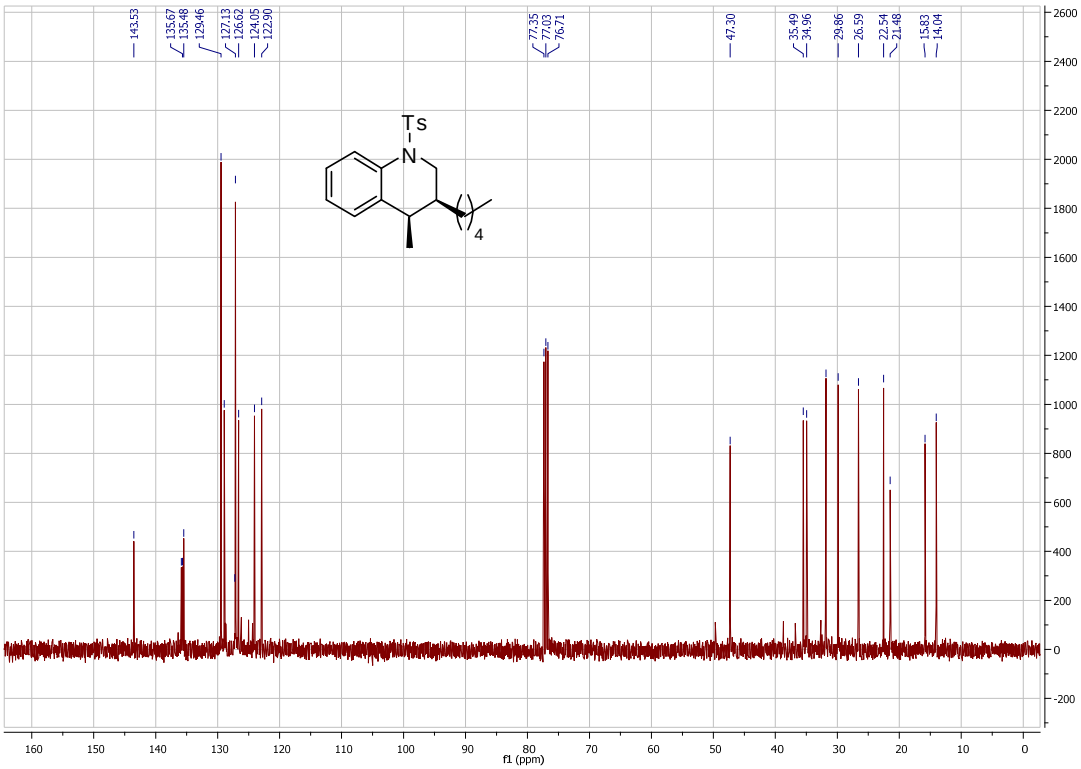
(+)-3-hexyl-4-methylchromane (11)





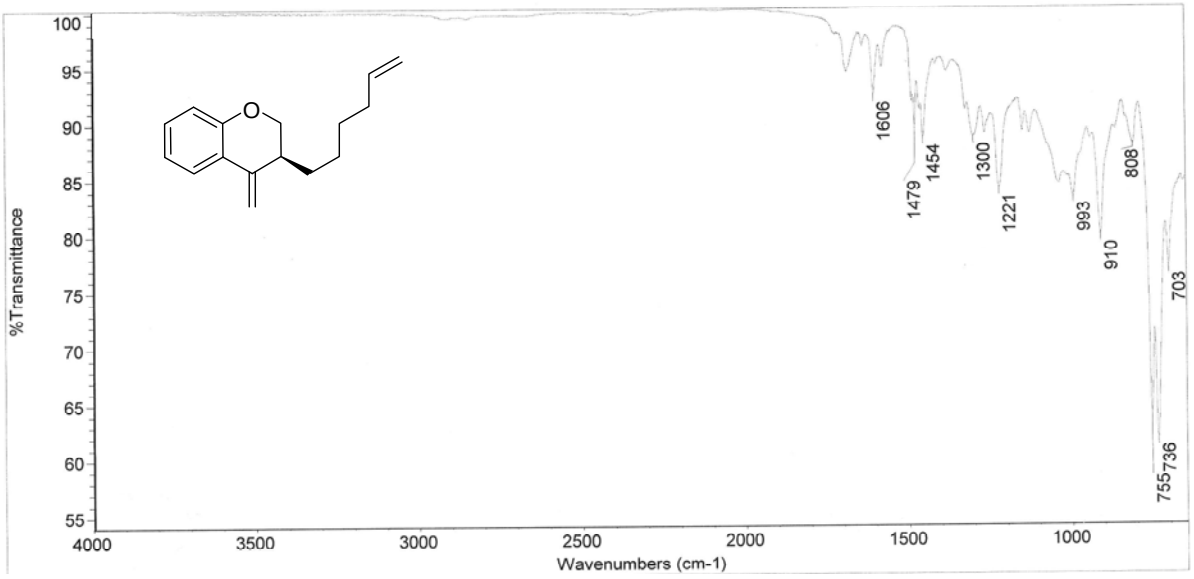
(+)-4-methyl-3-pentyl-1-tosyl-1,2,3,4-tetrahydroquinoline (12)





Selected IR spectra

Chromene **5e**



Tetrahydroquinoline **6c**