Electronic Supplementary Material (ESI) for Chemical Science.

Supporting Information

Transition Metal Catalyzed Diastereoselective Synthesis of *syn*- and *anti*- δ-Vinyl-Lactams: Formal Total Synthesis of (−)-Cermizine C and (−)-Senepodine G

Johannes P. Schmidt and Bernhard Breit*

Institut für Organische Chemie, Albert-Ludwigs-Universität Freiburg, Albertstraße 21, 79104, Freiburg, Germany

Table of Contents

General and Materials

FCC (Flash Column Chromatography) was accomplished using MACHEREY-NAGEL silica gel 60 ® (230-400 mesh).

TLC (Thin Layer Chromatography) was performed on aluminum plates pre-coated with silica gel (MERCK, $60F_{254}$), which were visualized by UV fluorescence (λ_{max} = 254 nm) and/or by staining with 1% w/v $KMnO_4$ in 0.5 M aqueous K_2CO_3.

NMR (Nuclear Magnetic Resonance) spectra were acquired on a BRUKER Avance 400 spectrometer (400 MHz and 100.6 MHz for ^1H and ^{13}C respectively) and/or on a VARIAN Mercury (300 MHz and 75.5 MHz for ^1H and ^{13}C respectively). All ^1H NMR spectra are reported in parts per million (ppm) downfield of TMS and were measured relative to the signals at 7.26 ppm ($CHCl_3$). All ^{13}C-NMR spectra were reported in ppm relative to residual $CHCl_3$ (77.16 ppm) and were obtained with ^1H-decoupling. Data for ^1H-NMR are described as following: chemical shift (δ□in ppm), multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; quin, quintet; sx, sextet; m, multiplet; app, apparent; br, broad signal), coupling constant (Hz), integration. Data for ^{13}C-NMR spectra are described in terms of chemical shift (δ in ppm).

High resolution mass spectra (**HR-MS**) were obtained on a THERMO SCIENTIFIC Advantage and a THERMO SCIENTIFIC Exactive instrument (APCI/MeOH: spray voltage 4-5 kV, ion transfer tube: 250-300 °C, vaporizer: 300-400 °C).

Chiral HPLC was performed on a MERCK HITACHI HPLC apparatus (pump: L-7100, UV detector: D-7400, oven: L-7360; columns: Chiralpak AD-3, AD-H, Chiralcel OD-3, 25 cm, 4.6 mm, DAICEL; Lux A-2, C-1, C-2, C-4, 50 cm, 4.6 mm, PHENOMENEX; carrier gas: He).

GC

Chiral GC was performed on a Agilent Technologies 6890N network GC-System [Inlet: 200 °C, 1.13 bar; Column: Hydrodex-B-TBDAc 25m x 0.25mm , carrier gas He (constant flow 1 mL/min).

Optical Rotation

The optical rotation of chiral compounds was determined on an A. KRÜSS OPTRONIC P8000 T apparatus and transformed for a given temperature according to the following formula

$$[\alpha]_D^T = \frac{\alpha \cdot 100}{c \cdot d}$$

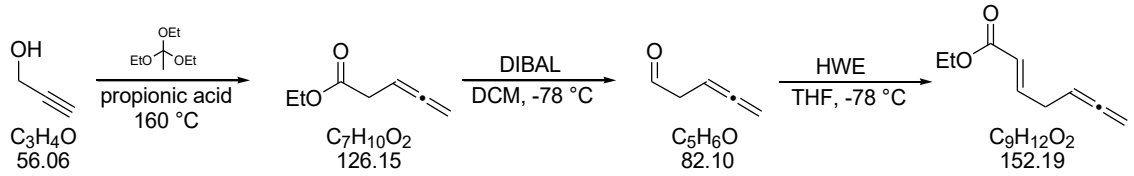
α: measured value for optical rotation; *c*: concentration in g/100 ml; *d*: length of the cuvette in dm; T: temperature in °C.

Solvents: 1,2-Dichloroethane (DCE) was freshly distilled over CaH_2 and degassed with argon prior to use. Toluene was freshly distilled over Sodium/Benzophenone and degassed with argon prior to use. Terahydrofuran (THF) was purchased in HPLC grade quality and was purified by continuous distillation over potassium under argon. Solvents employed for work-up and column chromatography were purchased in technical grade quality and distilled by rotary evaporator before use.

Ligand and Metal catalyst: The ligands were purchased from Sigma-Aldrich, ABCR, Alfa Aesar, TCI, ChemPur and used without further purification. Josiphos was either purchased from Sigma-Aldrich or received as a gift from Solvias. $[Rh(COD)Cl]_2$ and $Pd(dba)_2$ were purchased from Sigma-Aldrich

Preparation of starting materials

Synthesis of ethyl (E)-hepta-2,5,6-trienoate starting from propargyl alcohol



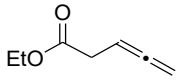
C_3H_4O
56.06

$C_7H_{10}O_2$
126.15

C_5H_6O
82.10

$C_9H_{12}O_2$
152.19

Synthesis of ethyl penta-3,4-dienoate 26



$C_7H_{10}O_2$
126.16

Prepared in analogy to a literature procedure.[1]

To a solution of propargyl alcohol (9.0 mL, 8.7 g, 0.16 mol, 0.5 equiv.) in triethyl orthoacetate (60 mL, 53 g, 0.32 mol, 1.0 equiv.) was added dropwise propionic acid (0.80 mL, 0.80 g, 11 mmol, 4.0 mol%) at 100 °C. The mixture was heated to 160 °C and resulting EtOH was continuously distilled off under atmospheric pressure for 1 h. Then another aliquot of propargyl alcohol (9.0 mL, 8.7 g, 0.16 mol, 0.5 equiv.) and propionic acid (0.80 mL, 0.80 g, 11 mmol, 4.0 mol%) were added dropwise and the mixture was stirred for another 1 h before a third portion of propionic acid (0.80 mL, 0.80 g, 11 mmol, 4.0 mol%) was added. The reaction was stirred for an additional hour and then cooled to room temperature and quenched by addition of aqueous HCl-solution (2 M, 100 mL). The organic layer was separated and the aqueous layer was extracted with Et_2O (3 × 100 mL). The combined organic layers were washed with brine (20 mL), dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue was purified by fractional distillation under reduced pressure ($bp_{46\ mbar}$: 75 °C). The title compound was obtained as colourless liquid (23 g, 0.24 mol, 76%).

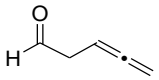
Analytical Data

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 1.27 (t, *J* = 7.1 Hz, 3H), 3.07 (dt, *J* = 7.4 Hz, *J* = 3.0 Hz, 2H), 4.16 (q, *J* = 7.1 Hz, 2H), 4.76 (dt, *J* = 2.9 Hz, *J* = 6.7 Hz, 2H), 5.27 (m_c, 1H) ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 14.3, 34.7, 60.9, 75.8, 83.6, 171.4, 209.5 ppm.

APCI-HRMS: *m/z* calcd for $C_7H_{10}O_2$ $[M+H]^+$ 127.0759, found 127.0759.

Synthesis of penta-3,4-dienal 27



C_5H_6O
82.10

Prepared in analogy to a literature procedure.[1]

At −80°C a solution of DIBAL-H (189 mL 189 mmol, 1.4 equiv., 1.0 M in CH_2Cl_2) was added dropwise over 90 min to a solution of ethylpenta-3,4-dienoate (17.1 g, 136 mmol, 1.0 equiv.) in CH_2Cl_2 (85 mL). The reaction mixture was stirred for 1 h and then transferred to an ice cold aqueous solution of HCl (2.0 M, 500 mL) at 0 °C. The layers were separated, the organic layer was washed with HCl (2.0 M, 2 × 500 mL) and the aqueous layer was extracted with CH_2Cl_2 (2 × 300 mL). The combined organic layers were washed with brine (50 mL), dried over Na_2SO_4, filtered over a silica pad and concentrated under reduced pressure. The crude product was purified by fractional distillation ($bp_{.250\ mbar}$: 65-78 °C). The title compound **123** was obtained as colourless liquid (5.47 g, 63.5 mmol, 47%).

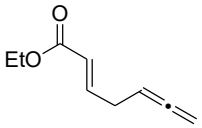
Analytical Data:

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 3.11 (dtd, *J* = 7.7, 3.0, 1.8 Hz, 2H), 4.79 (dt, *J* = 6.8, 3.0 Hz, 2H), 5.25 (m_c, 1H), 9.71 (t, *J* = 1.9 Hz, 1H) ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 42.8, 76.0, 81.1, 199.2, 210.1 ppm.

APCI-HRMS: *m/z* calcd for C_5H_6O $[M+NH_4]^+$ 100.0762, found 100.0757.

Synthesis of ethyl (*E*)-hepta-2,5,6-trienoate 28



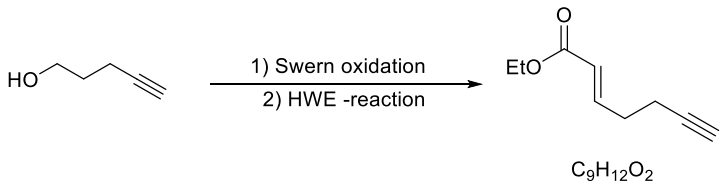
$C_9H_{12}O_2$
152.19

A suspension of NaH (60% in mineral oil, 1.1 g, 27 mmol, 1.1 equiv.) in dry THF (100 mL) was cooled to 0 °C and triethyl phosphonoacetate (6.9 g, 6.2 mL 31 mmol, 1.3 equiv.) was added dropwise to the reaction mixture. After complete addition, the suspension was stirred for 1 h at 0 °C and was then cooled to −78 °C. A solution of penta-4,5-dienal (2.0 g, 24 mmol, 1.0 equiv.) in dry THF (20 mL) was added dropwise to the reaction mixture at this temperature. The mixture was slowly warmed to −20 °C over 3 h and then quenched by the addition of aqueous saturated NH_4Cl-solution (50 mL). The layers were separated, the aqueous layer was extracted with Et_2O (3 × 100 mL) and the combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (60:1 Pentane:Et_2O). The title compound was obtained as colourless liquid (3.2 g, 21 mmol, 85%).

Analytical Data:

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 1.29 (t, *J* = 7.0 Hz, 3H), 2.87 – 2.93 (m, 2H), 4.19 (q, *J* = 7.0 Hz, 2H), 4.74 (dt, *J* = 6.8, 3.1 Hz, 2H), 5.12 (tt, *J* = 6.9 Hz, 1H), 5.89 (dt, *J* = 15.7, 1.7 Hz, 1H), 6.97 (dt, *J* = 15.6, 6.4 Hz, 1H) ppm.
^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 14.3, 31.2, 60.3, 75.8, 86.4, 122.2, 146.3, 166.5, 209.3 ppm.
APCI-HRMS: *m/z* calcd for $C_9H_{13}O_2$ $[M+H]^+$ 153.0910, found 153.0909.

Synthesis of ethyl (*E*)-hept-2-en-6-ynoate 29



$C_9H_{12}O_2$

Prepared in analogy to a literature procedure.[2]

To a solution of oxalyl chloride (2.5 mL, 28 mmol, 1.4 equiv.) in DCM (100 mL) was added DMSO (3.6 mL, 51 mmol, 2.6 equiv) dropwise at −78 °C. The mixture was stirred for 15 min at this temperature then 4-pentyn-1-ol (1.7 g, 20 mmol, 1.0 equiv.) in DCM (25 mL) was added dropwise. The mixture was stirred for further 15 min before NEt_3 (14 mL, 10 mmol, 5.1 equiv.) was added. After the addition, the mixture was stirred for 30 min at −78 °C and then allowed to warm to room temperature and stirred for further 3 h.

A solution of LiCl (1.6 g, 37 mmol, 1.9 equiv.), triethyl phosphonoacetate (7.2 mL, 37 mmol, 1.9 equiv.) and DBU (5.1 mL, 37 mmol, 1.9 equiv.) in acetonitrile (70 mL) was prepared and stirred for 1h. The SWERN solution was carefully concentrated in vacuo and the Horner Wadsworth Emmons solution was added. The reaction was stirred at room temperature overnight. The reaction was quenched with saturated NH_4Cl solution (40 mL) and concentrated. The residue was extracted with Et_2O (4 × 50 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed under vacuum and the crude product was purified by flash chromatography on silica gel (40:1 Pentane:Et_2O) to give the title compound as a colourless oil (2.7 g, 17 mmol, 85%).

Analytical Data

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 1.29 (t, *J* = 7.1 Hz, 3H), 2.00 (t, *J* = 2.6 Hz, 1H), 2.33-2.38 (m, 2H), 2.40-2.47 (m, 2H), 4.20 (q, *J* = 7.1 Hz), 5.89 (dt, *J* = 15.7, 1.6 Hz, 1H), 6.97 (dt, *J* = 15.7, 6.5 Hz, 1H) ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 14.3, 17.5, 60.4, 69.5, 82.8, 122.7, 146.3, 166.4 ppm.

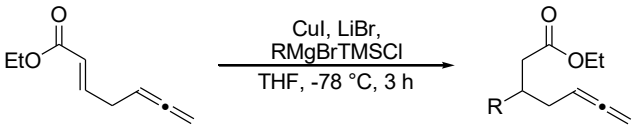
APCI-HRMS: *m/z* calcd for $C_9H_{16}O_2N$ $[M+NH_4]^+$ 170.1176, found 170.1177.

General Procedure substrate synthesis

General procedure GRIGNARD synthesis (GP1):

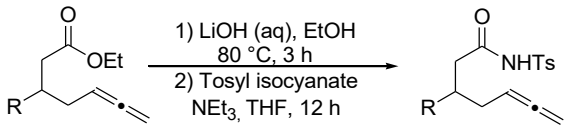
To a suspension of magnesium (1.2 equiv.) and iodide (catalytic amount) in THF (1.0 M) corresponding bromide (15 mmol) was added dropwise. After the reaction stopped refluxing, the mixture was heated to 80 °C for 1 h. Afterwards the solution was cooled to room temperature and directly used in the substrate synthesis or was stored in the freezer.

General procedure for the MICHAEL-Addition (GP 2):



A mixture of CuI (10 mol%) and LiBr (20 mol%) was carefully dried and cooled to room temperature under vacuum and backfilled with argon using a standard SCHLENK line apparatus, before extra dry or freshly distilled THF (1.0 M) was added. The mixture was stirred at room temperature for 15 min and then cooled to −78 °C. A solution of ethyl (*E*)-hepta-2,5,6-trienoate (1.0 equiv) in extra dry or freshly distilled THF (0.3 M) and TMSCl (1.1 equiv.) was added at this temperature. The mixture was stirred for 15 min before the GRIGNARD reagent in THF (1.5 equiv.) was added dropwise and stirred for 3 h at −78 °C. The reaction was quenched by the addition of aqueous saturated NH_4Cl-solution. The layers were separated, the aqueous layer was extracted with Et_2O (4 × 30 mL), the combined organic layer were washed with brine (40 mL) and dried over Na_2SO_4. The solvent was removed and the residue was purified by flash chromatography on silica gel using a mixture of pentane and ether.

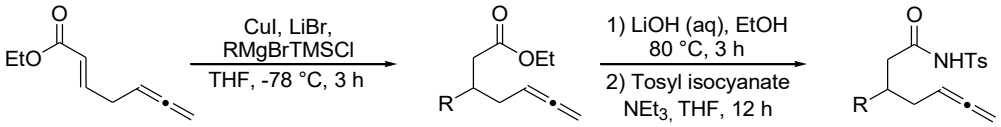
General procedure hydrolysis followed by amidation (GP 3):



To a solution of ethyl 3-ethylhepta-5,6-dienoate in EtOH (1.0 M) was added aqueous LiOH (3.0 M, 4.0 equiv.). The mixture was heated to 80 °C and stirred for 3 h. The reaction was concentrated under vacuum and the residue was diluted with H_2O (10 mL). The mixture was neutralized with aqueous HCl (2.0 M) and extracted with EtOAc (4 × 20 mL). The organic layer was separated, washed with brine (15 mL), H_2O (15 mL) and dried over Na_2SO_4.

The crude product was dissolved in THF (0.3 M) and tosyl isocyanate (1.0 equiv.) was added dropwise at room temperature. The solution was stirred for 10 min then NEt_3 (1.1 equiv.) was added. The mixture was stirred for another 14 h at room temperature then quenched by the addition of saturated NH_4Cl solution (30 mL). The layers were separated, the aqueous phase was extracted with EtOAc (2 × 50 ml), the combined organic layers were dried over Na_2SO_4. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography on silica gel (hexanes:EtOAc).

General procedure MICHAEL-Addition followed by hydrolysis and amidation (GP 4):

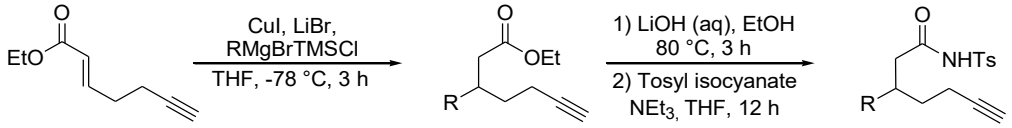


A mixture of CuI (10 mol%) and LiBr (20 mol%) was carefully dried and cooled to room temperature under vacuum and backfilled with argon using a standard SCHLENK line apparatus, before extra dry or freshly distilled THF (1.0 M) was added. The mixture was stirred at room temperature for 15 min and then cooled to −78 °C. A solution of ethyl (*E*)-hepta-2,5,6-trienoate (1.0 equiv) in extra dry or freshly distilled THF (2.0 M) and TMSCl (1.1 equiv.) was added at this temperature. The mixture was stirred for 15 min before the GRIGNARD reagent in THF(1.5 equiv.) was added dropwise and stirred for 3 h at −78 °C. The reaction was quenched by the addition of aqueous saturated NH_4Cl-solution. The layers were separated, the aqueous layer was extracted with Et_2O (4 × 30 mL), the combined organic layer were washed with brine (40 mL) and dried over Na_2SO_4.

The solvent was removed and the crude product was dissolved in EtOH (1.0 M). A solution of aqueous LiOH (3.0 M, 4.0 equiv.) was added and the mixture was heated to 80 °C and stirred for 3 h. The reaction was concentrated under vacuum and the residue was diluted with H_2O (10 mL). The mixture was neutralized with aqueous HCl (2.0 M) and extracted with EtOAc (4 × 20 mL). The organic layer was separated, washed with brine (15 mL), H_2O (15 mL) and dried over Na_2SO_4.

The solvent was removed under reduced pressure and the crude product was dissolved in THF (0.3 M) and tosyl isocyanate (1.0 equiv.) was added dropwise at room temperature. The solution was stirred for 10 min and then NEt_3 (1.1 equiv.) was added and stirred overnight at room temperature. The reaction was quenched by the addition of saturated NH_4Cl solution (30 mL). The layers were separated, the aqueous phase was extracted with EtOAc (2 × 50 ml), the combined organic layers were dried over Na_2SO_4. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography on silica gel (hexanes:EtOAc).

General procedure for MICHAEL-Addition followed by hydrolysis and amidation towards the alkyne substrates (GP 5):



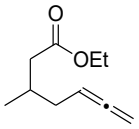
A mixture of CuI (10 mol%) and LiBr (20 mol%) was carefully dried and cooled to room temperature under vacuum and backfilled with argon using a standard SCHLENK line apparatus, before extra dry or freshly distilled THF (1.0 M) was added. The mixture was stirred at room temperature for 15 min and then cooled to −78 °C. A solution of ethyl (*E*)-hept-2-en-6-ynoate (1.0 equiv) in extra dry or freshly distilled THF (2.0 M) and TMSCl (1.1 equiv.) was added at this temperature. The mixture was stirred for 15 min before the GRIGNARD reagent in THF (1.5 equiv.) was added dropwise and stirred for 3 h at −78 °C. The reaction was quenched by the addition of aqueous saturated NH_4Cl-solution. The layers were separated, the aqueous layer was extracted with Et_2O (4 × 30 mL), the combined organic layer were washed with brine (40 mL) and dried over Na_2SO_4.

The solvent was removed and the crude product was dissolved in EtOH (1.0 M). A solution of aqueous LiOH (3.0 M, 4.0 equiv.) was added and the mixture was heated to 80 °C and stirred for 3 h. The reaction was concentrated under vacuum and the residue was diluted with H_2O (10 mL). The mixture was neutralized with aqueous HCl (2.0 M) and extracted with EtOAc (4 × 20 mL). The organic layer was separated, washed with brine (15 mL), H_2O (15 mL) and dried over Na_2SO_4.

The solvent was removed under reduced pressure and the crude product was dissolved in THF (0.3 M) and tosyl isocyanate (1.0 equiv.) was added dropwise at room temperature. The solution was stirred for 10 min and then NEt_3 (1.1 equiv.) was added and stirred overnight at room temperature. The reaction was quenched by the addition of saturated NH_4Cl solution (30 mL). The layers were separated, the aqueous phase was extracted with EtOAc (2 × 50 ml), the combined organic layers were dried over Na_2SO_4. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography on silica gel (hexanes:EtOAc).

Substrate synthesis allenes

Synthesis of ethyl 3-methylhepta-5,6-dienoate 30



$C_{10}H_{16}O_2$
168.24

The reaction was performed according to **general procedure 2** with (*E*)-hepta-2,5,6-trienoate (1.0 g, 6.6 mmol, 1.0 equiv.) and methylmagnesium bromide in THF (3.3 mL, 9.9 mmol, 3.0 M). The desired product was obtained a colourless liquid (0.98 g, 5.8 mmol, 88%).

Analytical Data

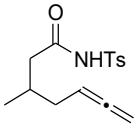
^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 0.98 (d, *J* = 6.4, 3H), 1.25 (t, *J* = 7.1, 3H), 1.95 – 2.16 (m, 4H), 2.30 – 2.41 (m, 1H), 4.09 – 4.17 (m, 2H), 4.65 (dt, *J* = 6.7, 2.7, 2.7, 2H), 5.00 – 5.11 (m, 1H) ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = δ = 14.4, 19.6, 30.7, 35.7, 41.2, 60.2, 74.4, 87.7, 173.1, 209.4 ppm.

APCI-HRMS: *m/z* calcd for $C_{10}H_{20}O_2N$ $[M+NH_4]^+$ 186.1489 found 186.1489

GC: Hydrodex-B-TBDAc 25m x 0.25mm, 80 °C, isothermal [50% ee. t_R = 29.0 min (minor), 30.0 min (major)]

Synthesis of 3-methyl-N-tosylhepta-5,6-dienamide 31



$C_{15}H_{19}NO_3S$
293.38

The reaction was performed according to **general procedure 3** with ethyl 3-methylhepta-5,6-dienoate (0.98 g, 5.8 mmol). The desired product was obtained as colourless oil (1.6 g, 5.3 mmol, 91%).

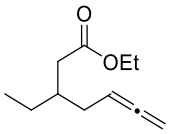
Analytical Data

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 0.90 (d, *J* = 6.4 Hz, 3H), 1.86 – 1.97 (m, 2H), 1.97 – 2.11 (m, 2H), 2.32 (m, 1H), 2.44 (s, 3H), 4.64 (dt, *J* = 6.6, 2.8 Hz, 2H), 4.86 – 5.04 (m, 1H), 7.30 – 7.39 (m, 2H), 7.94 (m, 2H), 8.35 (s, 1H) ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 19.5, 21.8, 30.5, 35.3, 42.9, 74.7, 87.3, 128.5, 129.7, 135.8, 145.2, 170.0, 209.3 ppm.

ESI-HRMS: *m/z* calcd for $C_{15}H_{19}O_3NNaS$ $[M+Na]^+$ 316.0978 found 316.0979.

Synthesis of ethyl 3-ethylhepta-5,6-dienoate 32



$C_{11}H_{18}O_2$
182.26

The reaction was performed according to **general procedure 2** with (*E*)-hepta-2,5,6-trienoate (1.0 g, 6.6 mmol, 1.0 equiv.) and ethylmagnesium bromide in THF (9.9 mL, 9.9 mmol, 1.5 equiv. 1.0 M). The desired product was obtained a colourless liquid (1.0 g, 5.7 mmol, 86%).

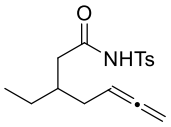
Analytical Data

^{1}H-NMR (400.1 MHz, $CDCl_3$): 0.90 (t, *J* = 7.4 Hz, 3H), 1.26 (t, *J* = 7.1Hz, 3H), 1.38 (m, 2H), 1.93 (dt, J = 13.0, 6.5 Hz, 1H), 1.97 – 2.15 (m, 2H), 2.21 – 2.36 (m, 2H), 4.13 (tt, *J* = 7.1, 7.1 Hz, 2H), 4.64 (dt, *J* = 6.6, 2.7 Hz, 2H), 5.03 (tt, *J* = 7.1, 1H) ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 11.0, 14.4, 26.3, 32.6, 36.8, 38.5, 60.2, 74.3, 87.5, 173.4, 209.4 ppm.

APCI-HRMS: *m/z* calcd for $C_{11}H_{22}O_2N$ $[M+NH_4]^+$ 200.1645, found 200.1645

Synthesis of 3-ethyl-N-tosylhepta-5,6-dienamide 33



$C_{16}H_{21}NO_3S$
307.41

The reaction was performed according to **general procedure 3** with ethyl 3-ethylhepta-5,6-dienoate (1.0 g, 5.7 mmol, 1.0 equiv.). The desired product was obtained as colourless oil (1.5 g, 4.9 mmol, 84%)

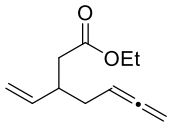
Analytical Data [4]

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 0.82 (t, *J* = 7.4 Hz, 3H), 1.13 – 1.37 (m, 2H), 1.81 – 1.96 (m, 2H), 1.96 – 2.04 (m, 1H), 2.20 (m, 2H), 2.44 (s, 3H), 4.65 (dt, *J* = 6.7, 2.7 Hz, 2H), 4.87 – 5.01 (m, 1H), 7.34 (d, *J* = 8.6 Hz, 2H), 7.94 (d , *J*=8.4 Hz, 2H), 8.25 (s, 1H) ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 11.0, 21.8, 26.2, 32.1, 36.6, 40.4, 74.8, 77.3, 87.1, 128.5, 129.7, 135.7, 145.2, 170.2, 209.3 ppm.

APCI-HRMS: *m/z* calcd for $C_{16}H_{22}O_3NS$ $[M+H]^+$ 308.1315 found 308.1315

Synthesis of ethyl 3-vinylhepta-5,6-dienoate 34



$C_{11}H_{16}O_2$
180.25

The reaction was performed according to **general procedure 2** with (E)-hepta-2,5,6-trienoate (1.0 g, 6.6 mmol, 1.0 equiv) and vinylmagnesium bromide (10 mL, 9.9 mmol, 1.0 M). The desired product was obtained a colourless liquid (0.88 g, 4.9 mmol, 75%).

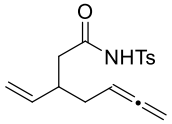
Analytical Data

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 1.25 (t, *J* = 7.1 Hz, 3H), 2.12 (ddt, *J* = 7.4, 6.8, 2.8 Hz, 2H), 2.31 (dd, *J* = 15.0, 8.3 Hz, 1H), 2.45 (dd, *J* = 15.0, 6.1 Hz, 1H), 2.62 – 2.74 (m, 1H), 4.12 (q, *J* = 7.2 , 2H), 4.66 (dt, *J* = 6.6, 2.8 Hz, 2H), 5.01 – 5.09 (m, 3H), 5.72 (m, 1H).ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 14.4, 33.7, 39.1, 40.1, 60.3, 74.7, 87.3, 115.3, 140.3, 172.4, 209.4 ppm.

APCI-HRMS: *m/z* calcd for $C_{11}H_{20}O_2N$ $[M+NH_4]^+$ 198.1489 found 198.1488

Synthesis of N-tosyl-3-vinylhepta-5,6-dienamide 35



$C_{16}H_{19}NO_3S$
305.39

The reaction was performed according to **general procedure 3** with ethyl 3-vinylhepta-5,6-dienoate (0.88 g, 4.9 mmol, 1.0 equiv.). The desired product was obtained as colourless wax (1.4 g, 4.5 mmol, 91%)

Analytical Data

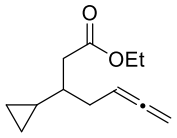
mp: 112 – 114 °C

^{1}H-NMR (500.1 MHz, $CDCl_3$): δ = 2.01 – 2.07 (m, 2H), 2.22 (dd, *J* = 15.1, 8.4 Hz, 1H), 2.40 (dd, *J* = 15.1, 5.6 Hz, 1H), 2.44 (s, 3H), 2.51 – 2.66 (m, 1H), 4.66 (ddd, *J* = 6.8, 3.2, 2.4 Hz, 2H), 4.86 – 5.08 (m, 3H), 5.61 (m, 1H), 7.30 – 7.41 (m, 2H), 7.88 – 7.99 (m, 2H), 8.12 (s, 1H). ppm.

^{13}C-NMR (126.6 MHz, $CDCl_3$): δ = 21.8, 33.3, 39.8, 40.9, 75.1, 86.8, 116.4, 128.5, 129.6, 135.6, 139.4, 145.2, 169.2, 209.3 ppm.

ESI-HRMS: *m/z* calcd for $C_{16}H_{19}O_3NNaS$ $[M+Na]^+$ 328.0978 found 328.0981.

Synthesis of ethyl 3-cyclopropylhepta-5,6-dienoate 36



$C_{12}H_{18}O_2$
194.27

The reaction was performed according to **general procedure 2** with ethyl 3-ethylhepta-5,6-dienoate (1.0 g, 5.7 mmol, 1.0 equiv.) cyclopropylmagnesium bromide (10 mL, 9.9 mmol, 1.0 M). The desired product was obtained as colourless liquid (0.92 g, 4.7 mmol, 83%).

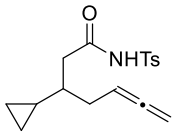
Analytical Data

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 0.12 – 0.20 (m, 2H), 0.38 – 0.53 (m, 2H), 0.59 – 0.72 (m, 1H), 1.26 (t, *J* = 7.1, 4H), 2.05 – 2.17 (m, 1H), 2.18 – 2.26 (m, 1H), 2.34 (dd, *J* = 14.6, 7.2 Hz, 1H), 2.44 (dd, *J* = 14.6, 6.8 Hz, 1H), 4.13 (m_c, 2H), 4.58 – 4.77 (m, 2H), 5.10 (dt, *J*=8.1, 6.7, 1H).ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 4.0, 4.3, 14.3, 15.9, 34.2, 39.6, 41.5, 60.2, 74.2, 87.5, 173.2, 209.4 ppm.

APCI-HRMS: *m/z* calcd for $C_{12}H_{22}O_2N$ $[M+NH_4]^+$ 212.1645 found 212.1644

Synthesis of 3-cyclopropyl-N-tosylhepta-5,6-dienamide 37



$C_{17}H_{21}NO_3S$
319.42

The reaction was performed according to **general procedure 3** with ethyl 3-cyclopropylhepta-5,6-dienoate (0.92 g, 4.7 mmol, 1.0 equiv). The desired product was obtained as colourless solid (1.3 g, 4.2 mmol, 89%)

mp Analytical Data

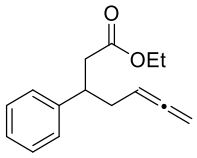
: 74 – 76 °C

^{1}H-NMR (500.1 MHz, $CDCl_3$): δ =-0.05 (ddt, *J* = 9.5, 5.5, 4.7 Hz, 1H), 0.03 – 0.12 (m, 1H), 0.29 (dddd, *J* = 9.3, 7.9, 5.6, 4.5 Hz, 1H), 0.43 (dddd, *J* = 9.2, 8.1, 5.6, 4.4 Hz, 1H), 0.54 (ddd, *J* = 9.9, 8.0, 4.9 Hz, 1H), 0.99 – 1.21 (m, 1H), 1.91 – 2.05 (m, 1H), 2.14 (dddd, *J* = 14.3, 7.3, 5.1, 3.0, 1H), 2.23 (dd, *J* = 14.4, 7.3 Hz, 1H), 2.39 (dd, *J* = 14.5, 6.2 Hz, 1H), 2.44 (s, 3H), 4.66 (dt, *J* = 6.7, 2.8 Hz, 2H), 5.01 (ddt, *J* = 7.9, 6.8, 6.5 Hz, 1H), 7.29 – 7.44 (m, 2H), 7.92 – 7.99 (m, 3H), 8.00 (s, 1H) ppm.

^{13}C-NMR (126.6 MHz, $CDCl_3$): δ = 4.2, 4.4, 15.8, 21.8, 33.7, 41.5, 41.7, 87.2, 129.6, 135.6, 145.2, 169.9, 209.3 ppm.

ESI-HRMS: *m/z* calcd for $C_{17}H_{21}O_3NNaS$ $[M+Na]^+$ 342.1134 found 342.1135.

Synthesis of ethyl 3-phenylhepta-5,6-dienoate 38



$C_{15}H_{18}O_2$
230.31

The reaction was performed according to **general procedure 2** with (E)-hepta-2,5,6-trienoate (1.0 g, 6.6 mmol, 1.0 equiv.) and phenylmagnesium bromide (10 mL, 9.9 mmol, 1.0 M). The desired product was obtained a colourless liquid (1.4 g, 6.2 mmol, 93%).

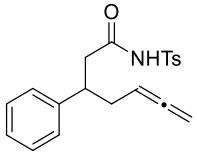
Analytical Data

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 1.14 (t, *J* = 7.1 Hz, 3H), 2.36 (ddt, *J* = 7.3, 7.1, 2.8 Hz, 2H), 2.58 (dd, *J* = 15.3, 8.4 Hz, 1H), 2.73 (dd, *J* = 15.3, 6.7 Hz, 1H), 3.19 – 3.31 (m, 1H), 4.03 (q, *J* = 7.2 Hz, 2H), 4.60 (dt, *J*=6.7, 4.0 Hz 2H), 4.95 (ddt, *J* = 7.1, 4.0, 2.8 Hz, 1H), 7.16 – 7.24 (m, 3H), 7.26 – 7.33 (m, 2H) ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 14.2, 35.5, 40.7, 42.2, 60.3, 74.7, 87.5, 126.7, 127.6, 128.5, 143.5 172.3, 209.4 ppm.

APCI-HRMS: *m/z* calcd for $C_{15}H_{22}O2N$ $[M+NH_4]^+$ 248.1645 found 248,1647

Synthesis of 3-phenyl-N-tosylhepta-5,6-dienamide 39



$C_{20}H_{21}NO_3S$
355.45

The reaction was performed according to **general procedure 3** with ethyl ethyl 3-phenylhepta-5,6-dienoate (1.4 g, 6.2 mmol, 1.0 equiv.). The desired product was obtained as yellow wax (1.9 g, 5.6 mmol, 90%)

Analytical Data

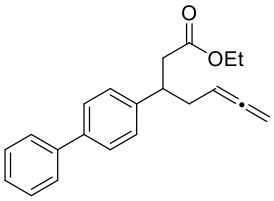
mp: 79 – 81 °C

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 2.20 – 2.31 (m, 2H), 2.44 (s, 3H), 2.48 (dd, *J* = 15.0, 8.7, 1H), 2.67 (dd, *J* = 15.0, 6.1, 1H), 3.13 (m_c, 1H), 4.49 – 4.65 (m, 2H), 4.85 (ddt, *J* = 7.7, 7.7, 6.8, 1H), 7.01 – 7.06 (m, 2H), 7.15 – 7.23 (m, 3H), 7.26 – 7.29 (m, 2H), 7.71 – 7.80 (m, 2H), 8.46 (s, 1H) ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 21.7, 35.1, 41.9, 42.7, 75.0, 87.1, 126.9, 127.4, 128.3, 128.7, 129.6, 135.5, 142.5, 145.0, 169.5, 209.3 ppm.

ESI-HRMS: *m/z* calcd for $C_{20}H_{21}O_3NNaS$ $[M+Na]^+$ 378.1134 found 378.1136.

Synthesis of ethyl 3-([1,1'-biphenyl]-4-yl)hepta-5,6-dienoate 40



$C_{21}H_{22}O_2$
306.41

The reaction was performed according to **general procedure 2** with (E)-hepta-2,5,6-trienoate (1.0 g, 6.6 mmol, 1.0 equiv.) and biphenylmagnesium bromide (10 mL, 9.9 mmol, 1.0 M). The desired product was obtained a colourless liquid (1.5 g, 4.8 mmol, 72%).

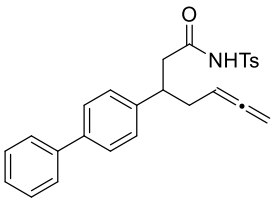
Analytical Data

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ =1.16 (t, *J* = 7.1 Hz, 3H), 2.39 (m, 2H), 2.62 (dd, *J* = 15.3, 8.5 Hz, 1H), 2.77 (dd, *J* = 15.3, 6.6 Hz, 1H), 3.30 (m_c, 1H), 4.06 (q, *J* = 7.1 Hz, 2H), 4.63 (dt, *J* = 6.3, 2.9 Hz, 2H), 4.99 (dd, *J* = 7.5, 7.0, 1H), 7.24 – 7.36 (m, 3H), 7.40 – 7.46 (m, 2H), 7.50 – 7.62 (m, 4H). ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 14.2, 35.5, 40.7, 41.8, 60.4, 74.8, 87.5, 127.1, 127.2, 127.2, 128.0, 128.8, 139.5, 141.0, 142.6, 172.3, 209.4 ppm.

ESI-HRMS: *m/z* calcd for $C_{21}H_{23}O_2$ $[M+H]^+$ 307.1693 found 307.1700

Synthesis of 3-([1,1'-biphenyl]-4-yl)-N-tosylhepta-5,6-dienamide 41



$C_{26}H_{25}NO_3S$
431.55

The reaction was performed according to **general procedure 3** with ethyl 3-([1,1'-biphenyl]-4-yl)hepta-5,6-dienoate (1.5 g, 4.8 mmol, 1.0 equiv.). The desired product was obtained as colourless wax (1.8 g, 4.1 mmol, 86%)

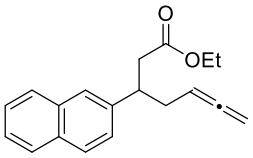
Analytical Data

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 2.25 – 2.37 (m, 5H), 2.42 – 2.58 (m, 1H), 2.72 (dd, *J* = 15.0, 5.8 Hz, 1H), 3.18 (m_c, 1H), 4.61 (ddd, *J* = 5.6, 2.8, 2.8 Hz, 2H), 4.91 (ddt, *J* = 6.9, 6.9, 6.9 Hz, 1H), 7.06 – 7.13 (m, 2H), 7.17 – 7.22 (m, 2H), 7.32 – 7.38 (m, 1H), 7.39 – 7.48 (m, 4H), 7.52 – 7.59 (m, 2H), 7.72 – 7.78 (m, 2H), 8.11 (s, 1H) ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 21.6, 35.1, 41.6, 42.8, 42.9, 75.1, 87.2, 127.0, 127.4, 127.4, 127.8, 127.8, 128.3, 128.3, 128.9, 129.6, 135.5, 140.7, 141.5, 145.0, 209.4 ppm.

ESI-HRMS: *m/z* calcd for $C_{26}H_{25}O_3NNaS$ $[M+Na]^+$ 454.1447 found 454.1443.

Synthesis of ethyl 3-(naphthalen-2-yl)hepta-5,6-dienoat 42



$C_{19}H_{20}O_2$
280.37

The reaction was performed according to **general procedure 2** with (E)-hepta-2,5,6-trienoate (1.0 g, 6.6 mmol, 1.0 equiv.) and naphthylmagnesium bromide (10 mL, 9.9 mmol, 1.0 M). The desired product was obtained a colourless liquid (1.4 g, 4.9 mmol, 75%).

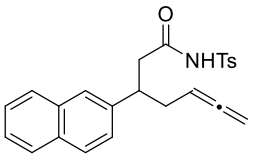
Analytical Data

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 1.12 (t, *J* = 7.1 Hz, 3H), 2.38 – 2.55 (m, 2H), 2.70 (dd, *J* = 15.3, 8.5 Hz, 1H), 2.82 (dd, *J* = 15.3, 6.6 Hz, 1H), 3.43 (dddd, *J* = 8.5, 7.1, 6.9, 6.1 Hz, 1H), 4.02 (m, 2H), 4.51 – 4.69 (m, 2H), 4.97 (dd, *J* = 6.8, 6.5 Hz, 1H), 7.32 – 7.39 (m, 1H), 7.39 – 7.51 (m, 2H), 7.60 – 7.67 (m, 1H), 7.73 – 7.85 (m, 3H) ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 14.2, 35.4, 40.7, 42.3, 60.4, 74.8, 87.5, 125.5, 125.9, 126.0, 126.2, 127.7, 127.8, 128.2, 132.5, 133.6, 141.0, 172.2, 209.4 ppm.

ESI-HRMS: *m/z* calcd for $C_{19}H_{20}O_2Na$ $[M+Na]^+$ 303.1356 found 303.1360

Synthesis of 3-(naphthalen-2-yl)-N-tosylhepta-5,6-dienamide 43



$C_{24}H_{23}NO_3S$
405.51

The reaction was performed according to **general procedure 3** with ethyl 3-(naphthalen-2-yl)hepta-5,6-dienoat (1.4 g, 4.9 mmol, 1.0 equiv.). The desired product was obtained as colourless oil (1.7 g, 4.3 mmol, 88%)

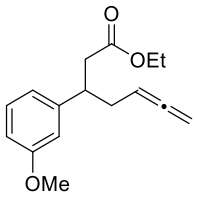
Analytical Data

^{1}H-NMR (500.1 MHz, $CDCl_3$): δ = 2.26 – 2.42 (m, 5H), 2.58 (dd, *J* = 15.0, 9.4 Hz, 1H), 2.76 (dd, *J* = 15.0, 5.7 Hz, 1H), 3.30 (m_c, 1H), 4.51 – 4.64 (m, 2H), 4.81 – 4.92 (m, 1H), 6.88 – 6.98 (m, 2H), 7.20 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.41 – 7.50 (m, 3H), 7.52 – 7.56 (m, 2H), 7.63 – 7.70 (m, 2H), 7.76 – 7.80 (m, 1H), 8.60 (s, 1H) ppm.

^{13}C-NMR (126.6 MHz, $CDCl_3$): δ = 21.7, 35.3, 42.2, 42.4, 75.1, 87.1, 125.3, 125.7, 126.1, 126.4, 127.6, 127.9, 127.9, 128.4, 129.4, 132.5, 133.5, 135.1, 139.7, 144.8, 169.5, 209.3 ppm.

ESI-HRMS: *m/z* calcd for $C_{24}H_{22}O_3NS$ $[M-H]^+$ 404.1326 found 404.1325.

Synthesis of ethyl 3-(3-methoxyphenyl)hepta-5,6-dienoate 44



$C_{16}H_{20}O_3$
260.33

The reaction was performed according to **general procedure 2** with (E)-hepta-2,5,6-trienoate (1.0 g, 6.6 mmol, 1.0 equiv.) and (3-methoxyphenyl)magnesium bromide (10 mL, 9.9 mmol, 1.0 M). The desired product was obtained a colourless liquid (1.0 g, 3.9 mmol, 60%).

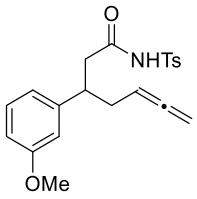
Analytical Data

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 1.16 (t, *J* = 7.1, 3H), 2.30 – 2.40 (m, 2H), 2.57 (dd, *J* = 15.3, 8.3 Hz, 1H), 2.71 (dd, *J* = 15.3, 6.8 Hz, 1H), 3.22 (dddd, *J* = 8.4, 7.1 Hz, 1H), 3.79 (s, 3H), 4.05 (q, *J* = 7.1 Hz, 2H), 4.55 – 4.70 (m, 2H), 4.89 – 5.01 (m, 1H), 6.68 – 6.77 (m, 2H), 6.76 – 6.84 (m, 1H), 7.15 – 7.24 (m, 1H) ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 14.2, 35.4, 40.6, 42.2, 55.2, 60.4, 74.7, 87.5, 111.9, 113.6, 120.0, 129.4, 145.2, 159.7, 172.3, 209.3 ppm.

APCI-HRMS: *m/z* calcd for $C_{16}H_{24}O_3N$ $[M+NH_4]^+$ 278.1751 found 278.1752.

Synthesis of ethyl 3-(3-methoxyphenyl)hepta-5,6-dienoate 45



$C_{21}H_{23}NO_4S$
385.48

The reaction was performed according to **general procedure 3** ethyl 3-(3-methoxyphenyl)hepta-5,6-dienoate (1.0 g, 3.9 mmol, 1.0 equiv.). The desired product was obtained as colourless wax (1.3 g, 3.5 mmol, 90%)

Analytical Data

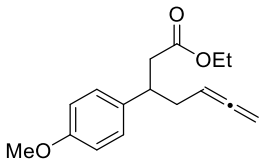
^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 2.04 – 2.27 (m, 2H), 2.36 (s, 3H), 2.40 (dd, *J* = 15.0, 8.8 Hz, 1H), 2.58 (dd, *J* = 15.0, 6.0 Hz, 1H), 3.02 (dddd, *J* = 8.9, 7.2, 7.2, 5.9 Hz, 1H), 3.65 (s, 3H), 4.45 – 4.56 (m,

2H), 4.78 (ddddd, *J* = 7.8, 6.8, 6.8, 6.8 Hr, 1H), 6.50 (dd, *J* = 2.5, 1.7 Hr, 1H), 6.55 – 6.60 (m, 1H), 6.65 (ddd, *J* = 8.2, 2.6, 0.9 Hz, 1H), 7.05 (dd, *J* = 8.3, 7.5 Hz, 1H), 7.15 – 7.22 (m, 2H), 7.63 – 7.70 (m, 2H), 8.43 (s, 1H).ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 21.7, 35.1, 42.0, 42.6, 55.2, 74.9, 87.2, 112.5, 113.2, 119.5, 128.3, 129.6, 129.7, 135.5, 144.2, 144.9, 159.8, 169. 5, 209.3 ppm.

APCI-HRMS: *m/z* calcd for $C_{21}H_{24}O_4NS$ $[M+H]^+$ 386.1421 found 386.1422.

Synthesis of ethyl 3-(4-methoxyphenyl)hepta-5,6-dienoate 46



$C_{16}H_{20}O_3$
260.33

The reaction was performed according to **general procedure 2** with (E)-hepta-2,5,6-trienoate (1.0 g, 6.6 mmol, 1.0 equiv.) and (4-methoxyphenyl)magnesium bromide (10 mL, 9.9 mmol, 1.0 M). The desired product was obtained a colourless liquid (1.2 g, 4.3 mmol, 65%).

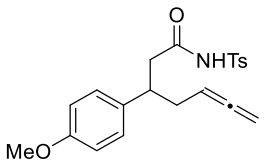
Analytical Data

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 1.16 (t, *J* = 7.1 Hz, 3H), 2.32 (m, 2H), 2.54 (dd, *J* = 15.2, 8.6 Hz, 1H), 2.70 (dd, *J* = 15.2, 6.6 Hz, 1H), 3.19 (tt, *J* = 8.5, 7.1 Hz, 1H), 3.78 (s, 3H), 4.03 (qd, *J* = 7.1, 1.3 Hz, 2H), 4.46 – 4.68 (m, 2H), 4.94 (tt, *J* = 7.3, 6.7 Hz, 1H), 6.83 (d, *J*=8.8, 2H), 7.11 (dd, *J* = 8.8, 0.5 Hz, 2H) ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 14.2, 35.6, 40.9, 41.4, 55.3, 60.3, 74.6, 87.6, 113.9, 128.5, 135.6, 158.3, 172.4, 209.3 ppm.

ESI-HRMS: *m/z* calcd for $C_{16}H_{20}O_3Na$ $[M+Na]^+$ 283.1305 found 283.1302.

Synthesis of 3-(4-methoxyphenyl)-N-tosylhepta-5,6-dienamide 47



$C_{21}H_{23}NO_4S$
385,48

The reaction was performed according to **general procedure 3** ethyl 3-(4-methoxyphenyl)hepta-5,6-dienoate (1.2 g, 4.3 mmol, 1.0 equiv.). The desired product was obtained as colourless wax (1.5 g, 3.9 mmol, 93%)

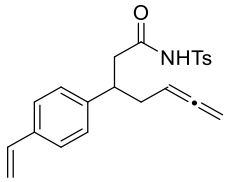
Analytical Data

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 2.11 – 2.19 (m, 2H), 2.33 – 2.39 (m, 4H), 2.57 (dd, *J* = 14.9, 5.9 Hz, 1H), 3.00 (dddd, *J* = 9.0, 7.2, 7.2, 5.8 Hz, 1H), 3.70 (s, 3H), 4.47 – 4.56 (m, 2H), 4.71 – 4.84 (m, 1H), 6.63 – 6.69 (m, 2H), 6.85 – 6.90 (m, 2H), 7.18 – 7.22 (m, 2H), 7.66 – 7.70 (m, 2H), 8.28 (s, 1H).ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 21.7, 35.3, 41.2, 42.9, 55.3, 74.9, 87.2, 114.2, 128.3, 128.3, 129.6, 134.4, 135.6, 144.9, 158.5, 169.5, 209.3 ppm

APCI-HRMS: *m/z* calcd for $C_{21}H_{24}O_4NS$ $[M+H]^+$ 386.1421 found 386.1422.

Synthesis of N-tosyl-3-(4-vinylphenyl)hepta-5,6-dienamide 48



$C_{22}H_{23}NO_3S$
381,49

The reaction was performed according to **general procedure 4** with (E)-hepta-2,5,6-trienoate (1.0 g, 6.6 mmol, 1.0 equiv.) and (4-vinylphenyl)magnesium bromide (10 mL, 9.9 mmol, 1.0 M). Ethyl 3-([1,1'-biphenyl]-4-yl)hepta-5,6-dienoate (1.2 g, 4.6 mmol). The desired product was obtained as yellow wax (1.1 g, 2.8 mmol, 60%)

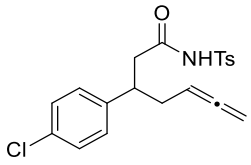
Analytical Data

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 2.22 – 2.27 (m, 2H), 2.41 – 2.52 (m, 4H), 2.68 (dd, *J* = 15.0, 5.9 Hz, 1H), 3.07 – 3.16 (m, 1H), 4.52 – 4.63 (m, 2H), 4.81 – 4.91 (m, 1H), 5.24 (dd, *J* = 10.9, 1.0 Hz, 1H), 5.70 (dd, *J* = 17.6, 1.0 Hz, 1H), 6.66 (dd, *J* = 17.6, 10.9 Hz, 1H), 6.95 – 7.01 (m, 2H), 7.18 – 7.27 (m, 4H), 7.69 – 7.76 (m, 2H), 8.48 (s, 1H) ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 21.7, 35.1, 41.7, 42.6, 75.1, 87.1, 113.6, 126.5, 127.6, 128.2, 129.6, 135.5, 136.3, 136.5, 142.1, 145.0, 169.4, 209.3 ppm.

ESI-HRMS: *m/z* calcd for $C_{22}H_{23}O_3NNaS$ $[M+Na]^+$ 404.1291 found 404.1289.

Synthesis of 3-(4-chlorophenyl)-N-tosylhepta-5,6-dienamide 49



$C_{20}H_{20}ClNO_3S$
389,89

The reaction was performed according to **general procedure 4** with (E)-hepta-2,5,6-trienoate (1.0 g, 6.6 mmol, 1.0 equiv.). The desired product was obtained as colourless wax (1.4 g, 3.5 mmol, 53%)

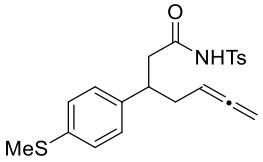
Analytical Data

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 2.19 – 2.29 (m, 2H), 2.41 (dd, *J* = 15.1, 9.3 Hz, 1H), 2.47 (s, 3H), 2.68 (dd, *J* = 15.1, 5.7 Hz, 1H), 3.12 (m, 1H), 4.54 – 4.63 (m, 2H), 4.85 (m, 1H), 6.92 – 6.96 (m, 2H), 7.10 (dd, *J* = 8.5, 1.3 Hz, 2H), 7.27 – 7.34 (m, 2H), 7.71 – 7.77 (m, 2H), 8.30 (s, 1H) ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 21.8, 34.9, 41.4, 42.6, 75.3, 86.9, 128.3, 128.8, 128.8, 129.6, 132.6, 132.6, 135.4, 140.9, 145.2, 168.9, 209.4 ppm.

ESI-HRMS: *m/z* calcd for $C_{20}H_{20}O_3NClNaS$ $[M+Na]^+$ 412.0745 found 412.0747.

Synthesis of 3-(4-(methylthio)phenyl)-N-tosylhepta-5,6-dienamide 50



$C_{21}H_{23}NO_3S_2$
401,54

The reaction was performed according to **general procedure 4** with (E)-hepta-2,5,6-trienoate (1.0 g, 6.6 mmol, 1.0 equiv.). The desired product was obtained as colourless solid (1.3 g, 3.2 mmol, 49%)

Analytical Data

mp: 102 – 104 °C

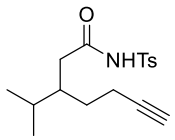
^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 2.20 – 2.27 (m, 2H), 2.39 – 2.44 (m, 1H), 2.45 (s, 3H), 2.46 (s, 3H), 2.66 (ddd, *J* = 15.0, 5.8, 0.8 Hz, 1H), 3.08 (ddd, *J* = 9.1, 7.4, 5.8 Hz, 1H), 4.59 (ddt, *J* = 6.7, 5.6, 1.7 Hz, 2H), 4.57 – 4.61 (m, 1H), 6.94 (m, 2H), 7.03 – 7.09 (m, 2H), 7.26 – 7.31 (m, 2H), 7.72 – 7.77 (m, 2H), 8.12 (s, 1H) ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 15.9, 21.8, 35.0, 41.4, 42.7, 75.1, 87.1, 126.9, 127.9, 128.3, 129.6, 135.4, 136.7, 139.2, 142.1, 145.1, 209.3 ppm.

ESI-HRMS: *m/z* calcd for $C_{21}H_{23}O_3NNaS_2$ $[M+Na]^+$ 424.1012 found 424.1017.

Substrate synthesis alkynes:

Synthesis of 3-isopropyl-N-tosylhept-6-ynamide 51



$C_{17}H_{23}NO_3S$
321.44

The reaction was performed according to **general procedure 5** with ethyl (E)-hept-2-en-6-ynoate (1.0 g, 6.6 mmol, 1.0 equiv.). The desired product was obtained as colourless wax (1.6 g, 4.9 mmol, 75%).

Analytical Data

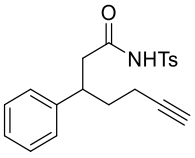
mp: 87 – 89 °C

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 0.74 – 0.82 (m, 6H), 1.29 – 1.38 (m, 1H), 1.53 (dtd, *J* = 13.4, 7.5, 5.8 Hz, 1H), 1.63 – 1.71(m, 1H), 1.80 – 1.91 (m, 1H), 1.95 – 1.97 (m, 1H), 2.05 – 2.14 (m, 3H), 2.24 (dd, *J* = 15.5, 6.2 Hz, 1H), 2.45 (s, 3H), 7.34 (dd, *J* = 8.6, 0.7 Hz, 2H), 7.94 (dd, *J* = 8.4, 0.6 Hz, 2H), 8.31 (s, 1H). ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 16.5, 18.5, 19.2, 21.8, 29.5, 29.6, 37.9, 39.9, 69.1, 84.1, 128.5, 129.7, 135.6, 145.2, 170.47 ppm.

ESI-HRMS: *m/z* calcd for $C_{17}H_{23}O_{3N}NaS$ $[M+Na]^+$ 344.1291 found 344.1282.

Synthesis of 3-phenyl-N-tosylhept-6-ynamide 52



$C_{20}H_{21}NO_3S$
355.45

The reaction was performed according to **general procedure 5** with ethyl (E)-hept-2-en-6-ynoate (1.0 g, 6.6 mmol, 1.0 equiv.). The desired product was obtained as colourless wax (1.6 g, 4.9 mmol, 55%).

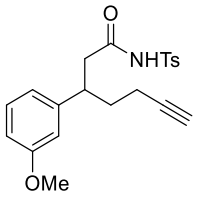
Analytical Dat^x

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 1.60 – 1.83 (m, 3H), 1.83 – 1.87 (m, 1H), 1.87 – 1.99 (m, 1H), 2.37 (s, 3H), 2.39 – 2.56 (m, 2H), 3.09 (dddd, *J* = 9.8, 8.4, 6.5, 4.9 Hz, 1H), 6.93 – 7.01 (m, 2H), 7.11 – 7.17 (m, 3H), 7.19 – 7.24 (m, 2H), 7.66 – 7.71 (m, 2H), 8.27 (s, 1H).ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 16.4, 21.8, 34.6, 41.0, 43.6, 69.1, 83.5, 127.2, 127.4, 128.3, 128.9, 129.6, 135.5, 141.7, 145.0, 169.1 ppm.

ESI-HRMS: *m/z* calcd for $C_{20}H_{22}O_3NS$ $[M+H]^+$ 356.1314 found 356.1315.

Synthesis of 3-(3-methoxyphenyl)-N-tosylhept-6-ynamide 53



$C_{21}H_{23}NO_4S$
385.48

The reaction was performed according to **general procedure 5** with ethyl (E)-hept-2-en-6-ynoate (1.0 g, 6.6 mmol, 1.0 equiv.). The desired product was obtained a colourless liquid (1.0 g, 2.6 mmol, 40%).

Analytical Data

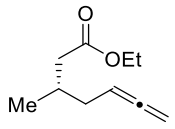
^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 1.58 – 1.95 (m, 5H), 2.44 (s, 3H), 2.46 – 2.64 (m, 2H), 3.13 (dddd, *J* = 9.8, 8.5, 6.5, 5.0 Hz, 1H), 3.73 (s, 3H), 6.59 (dd, *J* = 2.6, 1.7 Hz, 1H), 6.65 (ddd, *J* = 7.7, 1.7, 1.0 Hz, 1H), 6.73 (ddd, *J* =8.2, 2.6, 0.9 Hz, 1H), 7.14 (dd, *J* = 8.3, 7.6 Hz, 1H), 7.24 – 7.30 (m, 2H), 7.72 – 7.77 (m, 2H), 8.51 (s, 1H) ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 16.4, 21.7, 34.6, 41.1, 43.5, 55.2, 69.1, 83.5, 112.6, 113.4, 119.5, 128.3, 129.6, 129.4, 135.5, 143.4, 144.9, 159.9, 169.2 ppm.

ESI-HRMS: *m/z* calcd for $C_{21}H_{24}O_4Na$ $[M+Na]^+$ 283.1302 found 283.1305

Enantioselective preparation of starting material

Synthesis of ethyl (S)-3-methylhepta-5,6-dienoate 54



$C_{10}H_{16}O_2$
168,24

CuI (1.0 mol%) and S-Tol-Binap (20 mol%) were dissolved in *t*-BuOMe (40 mL) and stirred under argon at room Temperature for 1 h until a yellow suspension was observe. The mixture was cooled to −50 °C and ethyl (*E*)-hepta-2,5,6-trienoate (2.0 g, 13 mmol) was added and stirred for 15 min. Then MeMgBr in THF (6.5 mL, 20 mmol, 3.0 M, 1.5 equiv.) was added dropwise. The mixture was stirred at −50 °C for 2 h, then quenched by the addition of aqueous saturated NH_4Cl-solution. The layers were separated, the aqueous layer was extracted with Et_2O (4 × 30 mL), the combined organic layers were washed with brine (40 mL) and dried over Na_2SO_4. The solvent was removed and the residue was purified by flash chromatography on silica gel (Pentane:Et_2O = 60:1). The Product was obtained as colourless oil (1.0 g, 6.2 mmol, 48%).

Analytical Data

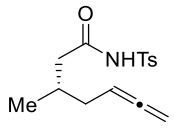
^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 0.98 (d, *J* = 6.4, 3H), 1.25 (t, *J* = 7.1, 3H), 1.95 – 2.16 (m, 4H), 2.30 – 2.41 (m, 1H), 4.09 – 4.17 (m, 2H), 4.65 (dt, *J* = 6.7, 2.7, 2.7, 2H), 5.00 – 5.11 (m, 1H) ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = δ = 14.4, 19.6, 30.7, 35.7, 41.2, 60.2, 74.4, 87.7, 173.1, 209.4 ppm.

APCI-HRMS: *m/z* calcd for $C_{10}H_{20}O_2N$ $[M+NH_4]^+$ 186.1489 found 186.1489

GC: Hydrodex-B-TBDAc 25m x 0.25mm, 80 °C, isothermal [95% ee. t_R = 28.9 min (minor), 29.7 min (major)], $[\alpha]_D^{25}$= −12 (c = 0.59 $CHCl_3$).

Synthesis of (S)-3-methyl-N-tosylhepta-5,6-dienamide 16



$C_{15}H_{19}NO_3S$
293,38

(S)-3-methylhepta-5,6-dienoate (0.6 g, 3.6 mmol, 1.0 equiv.) was dissolved in EtOH (4 mL) and a solution aqueous LiOH (15 mL, 3.0 M) was added. The mixture was heated to 80 °C and stirred for 3 h. The reaction was concentrated under vacuum and the residue was diluted with H_2O (10 mL), acidified with aqueous HCl (2.0 M) and execrated with EtOAc (4 × 20 mL). The organic layer was separated, washed with brine (15 mL), H_2O (15 mL) and dried over Na_2SO_4.

The crude product was dissolved in THF (12 mL), tosyl isocyanate (0.55 mL, 3.6 mmol, 1.0 equiv.) was added dropwise and the solution was stirred for 10 min at room temperature before NEt_3 (0.55 mL, 4.0 mmol, 1.1 equiv.) was added. The mixture was stirred for another 14 h at room temperature, quenched by the addition of saturated NH_4Cl solution (30 ml). The layers were separated, the aqueous phase was extracted with EtOAc (2 × 50 mL), the combined organic layers were dried over Na_2SO_4. The solvent was removed under vacuum and the crude product was purified by flash chromatography on silica gel (hexanes:EtOAc = 6:1). The Product was obtained as colourless oil (0.97 g, 3.3 mmol, 92%)

***Analytical Data*[1]**

H-NMR (400.1 MHz, $CDCl_3$): δ = 0.90 (d, *J* = 6.4 Hz, 3H), 1.86 – 1.97 (m, 2H), 1.97 – 2.11 (m, 2H), 2.32 (m, 1H), 2.44 (s, 3H), 4.64 (dt, *J* = 6.6, 2.8 Hz, 2H), 4.86 – 5.04 (m, 1H), 7.30 – 7.39 (m, 2H), 7.94 (m, 2H), 8.35 (s, 1H) ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 19.5, 21.8, 30.5, 35.3, 42.9, 74.7, 87.3, 128.5, 129.7, 135.8, 145.2, 170.0, 209.3 ppm.

ESI-HRMS: *m/z* calcd for $C_{15}H_{19}O_3NNaS$ $[M+Na]^+$ 316.0978 found 316.0979.

$[\alpha]_D^{25}$= − 10 (c = 0.97 $CHCl_3$)

General Procedure catalysis

General Procedure towards the *syn*-configurated Lactam (GP 6)

A 10 mL screw-cap flask was flame-dried, cooled to room temperature under vacuum and backfilled with argon (Argon 5.0 Sauerstoffwerk Friedrichshafen) using a standard SCHLENK line apparatus. The screw-cap flask was charged with amide (0.3 mmol, 1.0 equiv.) the flask was evacuated for 15 min and backfilled with argon three times. Then $[Rh(COD)Cl]_2$ (3.7 mg, 0.0075 mmol, 2.5 mol%), dppf (8.3 mg, 0.015 mmol, 5.0 mol%) and HOAcCl (5.7 mg, 0.06 mmol, 20 mol%) was added under a flow of argon followed by freshly distilled DCE (0.3 M). The flask was sealed and stirred at room temperature overnight. The solvent was removed and by ^{1}H-NMR spectroscopy and, if desired, purified by flash chromatography on silica gel using DCM.

General Procedure towards the *anti*-configurated Lactam (GP 7)

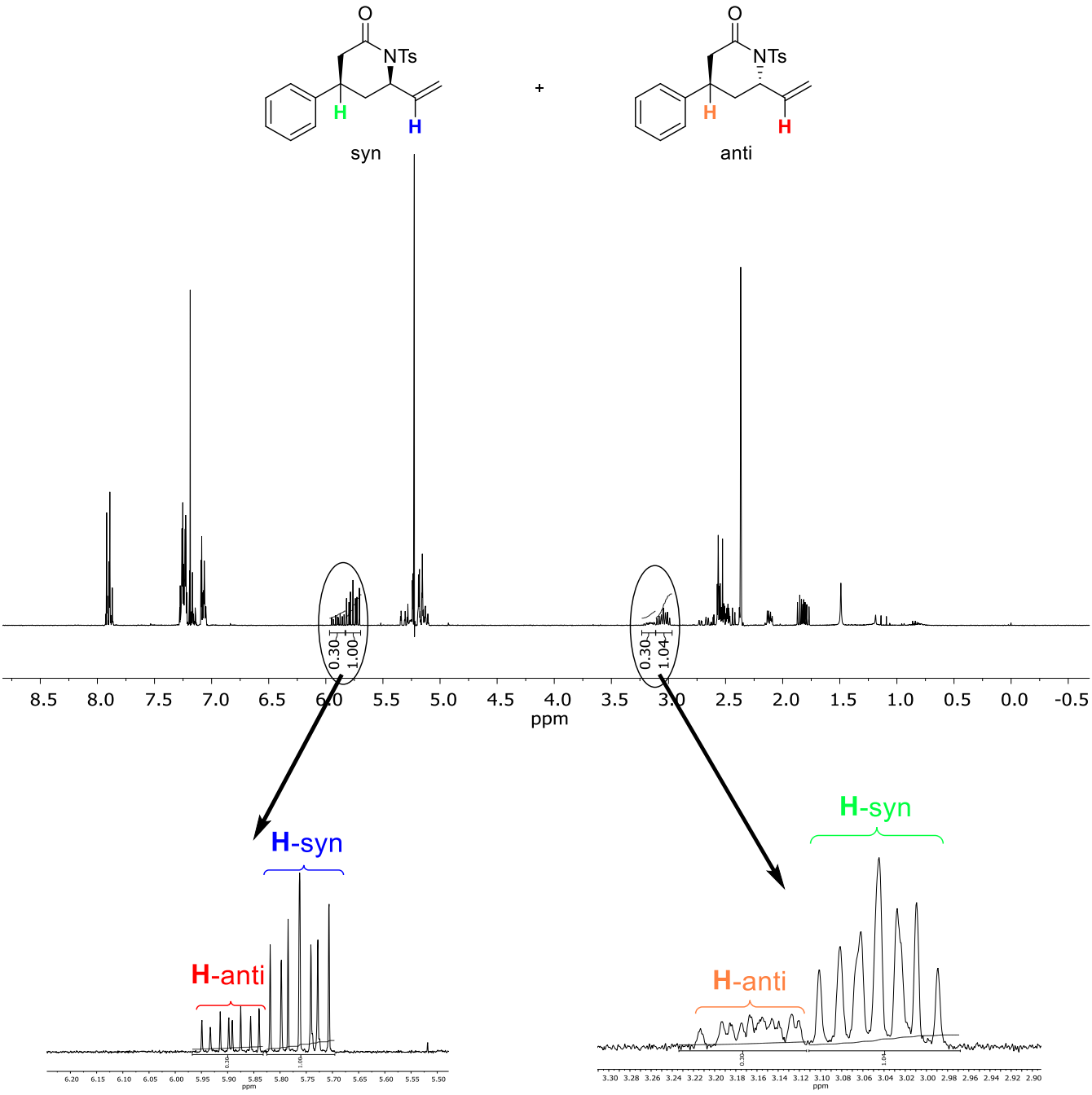
A 10 mL screw-cap flask was flame-dried, cooled to room temperature under vacuum and backfilled with argon (Argon 5.0 Sauerstoffwerk Friedrichshafen) using a standard SCHLENK line apparatus. The screw-cap flask was charged with the amide (0.3 mmol, 1.0 equiv.) the flask was evacuated for 15 min and backfilled with argon three times. Then $Pd(dba)_2$ (4.3 mg, 0.0075 mmol, 2.5 mol%), dppf (8.3 mg, 0.015 mmol, 5.0 mol%) and HOAcCl (5.7 mg, 0.06 mmol, 20 mol%) was added under a flow of argon followed by freshly distilled DCE (0.3 M). The flask was sealed and stirred at 80 °C overnight. The solvent was removed and by ^{1}H-NMR spectroscopy and, if desired, purified by flash chromatography on silica gel using DCM.

General Procedure towards the *syn*-configurated Lactam starting from the alkyne substrates (GP 8)

A 10 mL screw-cap flask was flame-dried, cooled to room temperature under vacuum and backfilled with argon (Argon 5.0 Sauerstoffwerk Friedrichshafen) using a standard SCHLENK line apparatus. The screw-cap flask was charged with amide (0.3 mmol, 1.0 equiv.) the flask was evacuated for 15 min and backfilled with argon three times. Then $[Rh(COD)Cl]_2$ (3.7 mg, 0.0075 mmol, 2.5 mol%), dppf (8.3 mg, 0.015 mmol, 5.0 mol%) and HOAcCl (5.7 mg, 0.06 mmol, 20 mol%) was added under a flow of argon followed by freshly distilled DCE (0.3 M). The flask was sealed and stirred at 80 °C overnight. The solvent was removed and by ^{1}H-NMR spectroscopy and, if desired, purified by flash chromatography on silica gel using DCM.

.

General Procedure for the determination of the d.r. - ratio



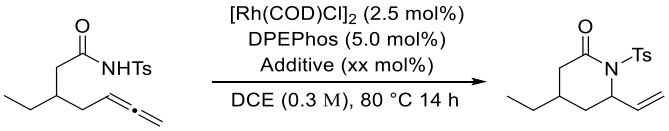
Calculation:

d.r = H-syn/(H-anti+H-syn) = 1.0/1.3 = 24/76 (syn/anti)

Condition screening

Condition screening Rh-catalysis

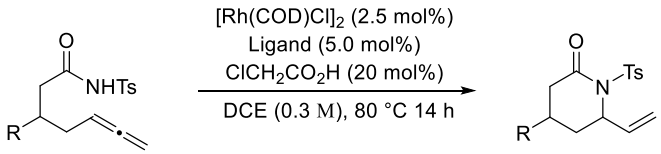
Additive-Screening:



#	Additive	mol%	Yield /%[(a)]	d.r. *(anti/syn)*[(b)]
1	-	-	19	-
2	**$PhCMe_2CO_2H$**	**40**	**96**	**34/66**
3	PPTS	20	65	28/72
4	PPTS/LiCl	40/30	90	35/65
5	Acetic acid	20	54	26/74
6	Glycolic acid	20	90	26/74
7	**Chloroacetic acid**	**20**	**96**	**20/80**
8	Chloroacetic acid /LiCl	20/30	93	20/80
9	Chloroacetic acid /LiBr	20/30	60	50/50
10	Bromoacetic acid	20	94	24/76
11	Dichloroacetic acid	20	79	23/77
12	Cyancoacetic acid	20	74	24/76
13	Phenylacetic acid	20	93	27/73
14	Salicylic acid	20	82	24/76
15	Succinic acid	20	77	24/76
16	Citric acid	20	69	25/75
17	2,6-Dichloronicotinic acid	20	48	25/75
18	4-Bromobenzoic acid	20	64	20/80
19	Malonic acid	40	70	24/76
20	BF_3*OEt	20	-	-
21	TFA	20	-	-

All reactions were performed on a 0.3 mmol scale. (a) NMR-Yield; (b) determined by ^{1}H-NMR analysis of the crude product

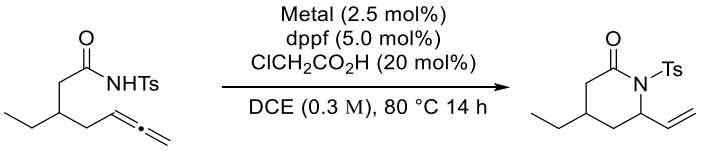
Ligand-Screening:



#	R	Ligand	Yield /%[a, b]	d.r. *(anti/syn)*[c]
1	Et	DPEPhos	96	20/80
2	Et	DPEPhos-Cy	33	37/62
3	Et	Xantphos	-	-
4	Et	Xphos	-	-
5	Et	BrettPhos	-	-
6	Et	dppp	24	38/62
7	Et	dppm	15	41/59
8	Et	*rac*-BINAP	72	25/75
9	Et	*rac*-DIOP	69	25/75
10	Et	DPEPhos	96	20/80
11	Et	DPPF	90	15/85
12	Ph	DPEPhos	96	27/73
13	Ph	DPPF	94	14/86
14	Ph	DPPF-Cy	29	22/78
15	Ph	DPPF-*t*Bu	-	-
16	Ph	DPPF-*i*Pr	40	24/76
17	Ph	SL-J003-rac	77	35/65

All reactions were performed on a 0.3 mmol scale. (a) NMR-Yield; (b) determined by ^{1}H-NMR analysis of the crude product

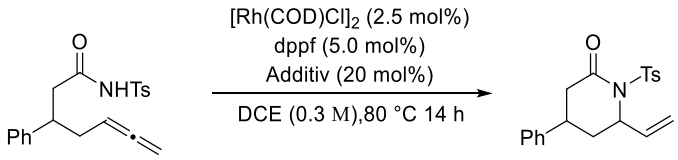
Metal-Screening:



#	Metal	Yield /%[(a)]	d.r. *(anti/syn)*[(b)]
1	$[Rh(COD)Cl]_2$	96	20/80
2	[Rh(COD)acac]	-	-
3	$[Rh(COD)OMe]_2$	-	-
4	$[Rh(COD)OH]_2$	86	76/24
5	$[Rh(COD)BF_4]$	20	81/19
6	[Rh(COD)Barf]	traces	-
7	[Rh(nbd)acac]	-	-
8	$[Ir(COD)Cl]_2$	-	-

All reactions were performed on a 0.3 mmol scale. (a) NMR-yield; (b) determined by ^{1}H-NMR analysis of the crude product

Enhanced additive-screening

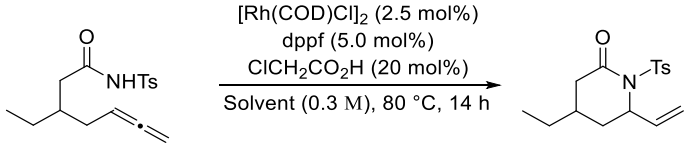


#	Additive	mol%	Yield /%[(a)]	d.r. *(anti/syn)*[(b)]
1	-	-	20	15/85
2	Chloroacetic acid	20	94	14/86
3	Chloroacetic acid	100	94	17/83
4	$PhCMe_2CO_2H$	20	98	35/65
5	Benzoic acid	20	79	23/76
6	Phenylacetic acid	20	93	27/73
7	4-Bromobenzoic acid	20	64	13/87
8	Diphenylacetic acid	20	95	30/70
9	Naphtoic acid	20	83	19/81
10	Lactic acid	20	81	15/85
11	(L)-phenylalanine	20	49	12/88
12	(L)-Leucin	20	68	13/87

13	(L)-N-benzoyl-Phenylalanine	20	95	29/71
14	Diphenylphosphate	20	80	12/88
15	(-)-Binolphosphate	20	81	13/87
16	(*R*)-Binolphosphate-trifluoromethylphenyl	20	70	16/84
17	Dichloroacetic acid	20	82	20/80
18	Acetic acid	20	55	75/25

All reactions were performed on a 0.3 mmol scale. (aNMR-Yield; (b) determined by ^{1}H-NMR analysis of the crude product

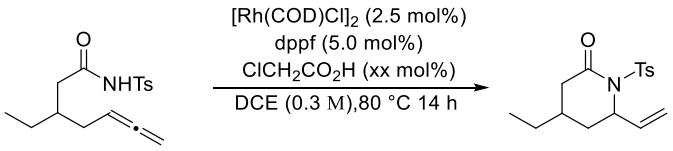
Solvent-Screening:



#	Solvent	Yield /%[(a)]	d.r. *(anti/syn)*[(b)]
1	**DCE**	**96**	**20/80**
2	DCM	82	19/81
3	Toluene	32	28/72
4	MeCN	81	22/78
5	EtOH	45	32/68
6	THF	47	25/75
7	Et_2O	50	21/79
8	DCE/EtOH (5:1)	89	23/77
9	DCE/EtOH (9:1)	93	19/81
10	PhF	82	20/80

All reactions were performed on a 0.3 mmol scale. (a) NMR-Yield; (b) determined by ^{1}H-NMR analysis of the crude product

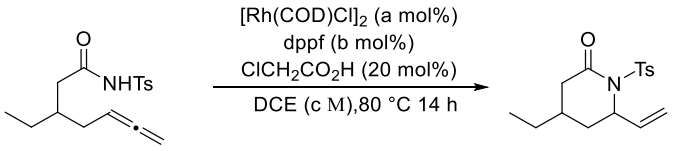
Additive concentration screening:



#	xx mol%	Yield /%[a]	d.r. *(anti/syn)*[b]
1	5.0	82	17/83
2	10	86	17/83
3	**20**	**96**	**20/80**
4	40	76	18/82
5	60	73	19/81

All reactions were performed on a 0.3 mmol scale. (a) NMR-Yield; (b) determined by ^{1}H-NMR analysis of the crude product

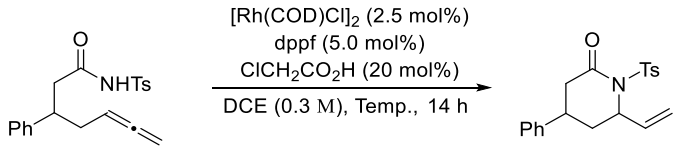
Metal, ligand and solvent concentration screening:



#	a mol%	b mol%	c M/L	Yield /%[a]	d.r. *(anti/syn)*[b]
1	2.5	5.0	0.20	89	18/82
2	2.5	5.0	0.24	93	19/81
3	2.5	5.0	**0.30**	**96**	**20/80**
4	2.5	5.0	0.45	82	20/80
5	2.5	5.0	0.65	74	21/79
6	2.0	5.0	0.24	89	20/80
7	1.25	2.5	0.30	81	18/82
8	2.5	10	0.3	94	26/74

All reactions were performed on a 0.3 mmol scale. (a) NMR-Yield; (b) determined by ^{1}H-NMR analysis of the crude product

Temperature screening:

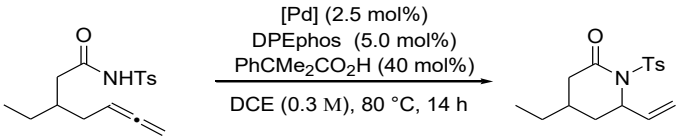


#	Temp. / C°	Yield /%[a]	d.r. *(anti/syn)*[b]
1	80	95	86/14
2	60	94	84/16
3	40	95	88/12
4	30	94	89/11
5	**Room Temperature**	**92**	**91/9**
6	20	82	92/8
7	10	0	0
8	0	0	0

All reactions were performed on a 0.3 mmol scale. (a) NMR-Yield; (b) determined by ^{1}H-NMR analysis of the crude product

Optimization Pd-catalysis

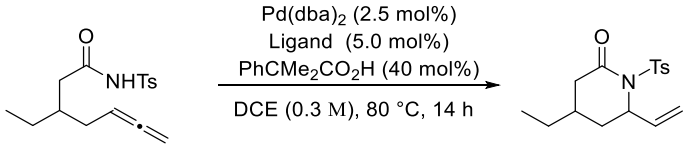
Metal-Screening:



#	Metal	Yield /%[a]	d.r. *(anti/syn)*[b]
1	$Pd_2(dba)_3$	58	87/13
2	$Pd(dba)_2$	45	90/10
3	$[Pd(\eta_3\text{-allyl})Cl]_2$	31	87/13
4	$Pd(PPh_3)_4$	48	88/12

All reactions were performed on a 0.3 mmol scale. (a) NMR-Yield; (b) determined by ^{1}H-NMR analysis of the crude product

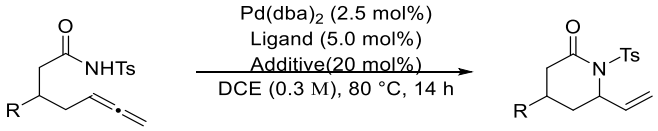
Ligand-Screening:



#	Ligand	Yield /%[(a)]	*d.r. (anti/syn)*[(b)]
1	DPEPhos	45	90/10
2	dppf	51	88/12
3	DPEPhos-Cy	11	n.d.
4	rac-Binap	59	60/40

All reactions were performed on a 0.3 mmol scale. (a) NMR-Yield; (b) determined by ^{1}H-NMR analysis of the crude product

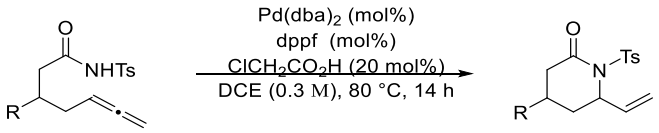
Additive-Screening:



#	R	Ligand	Additive	Yield /%[(a)]	d.r. *(anti/syn)*[(b)]
1	Et	DPEPhos	Benzoic acid / 20 mol%	47	86/14
2	Et	DPEPhos	$PhCMe_2CO_2H$ / 20 mol%	58	87/13
3	Et	DPEPhos	$ClCH_2CO_2H$ / 20 mol%	**87**	**87/13**
4	Et	DPEPhos	$ClCH_2CO_2H$ / LiCl 20/30 mol%	81	87/13
5	Et	DPEPhos	$ClCH_2CO_2H$ / LiBr 20/30 mol%	19	1/2
6	Et	DPEPhos	PPTS / LiCl 20/30 mol%	-	-
7	Et	dppf	$ClCH_2CO_2H$ / 20 mol%	90	90/10
8	Ph	dppf	-	15	82/18
9	Ph	dppf	$PhCMe_2CO_2H$ / 20 mol%	55	87/13
10	**Ph**	**dppf**	$ClCH_2CO_2H$ **/ 20 mol%**	**96**	**94/6**
11	Ph	dppf	Dichloroacetic acid/ 20 mol%	81	84/16
12	Ph	dppf	Acetic acid / 20 mol%	42	71/29

All reactions were performed on a 0.3 mmol scale. (a) NMR-Yield; (b) determined by ^{1}H-NMR analysis of the crude product

Metal / Ligand concentration screening:

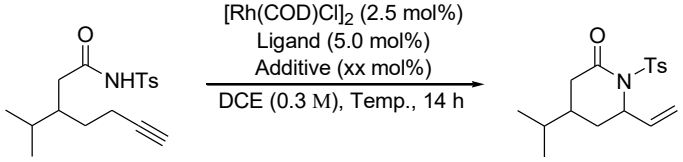


#	R	$Pd(dba)_2$	dppf	Yield	*d.r. (anti/syn)*
1	Et	2.5 mol%	5.0 mol%	90	90/10
2	Et	2.5 mol%	2.5 mol%	14	n.d.
3	Et	2.5 mol%	3.0 mol%	42	90/10

All reactions were performed on a 0.3 mmol scale. (a) NMR-Yield; (b) determined by ^{1}H-NMR analysis of the crude product

Condition screening alkine

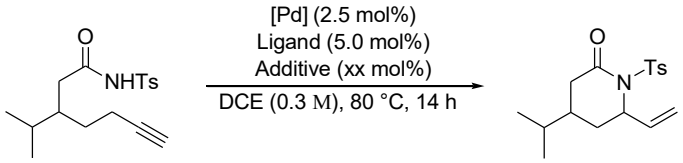
Rh-catalysis:



#	Ligand	Temp.	Additive / xx mol%	Yield /%[(a)]	d.r. *(anti/syn)*[(b)]
1	DPEPhos	80 °C	HOAcCl / 20	29	20/80
2	DPEphos	80 °C	$PhCMe_2CO_2H$ / 40	84	30/70
3	Xantphos	80 °C	$PhCMe_2CO_2H$ / 40	-	-
4	*rac*-BINAP	80 °C	$PhCMe_2CO_2H$ / 40	37	33/67
5	dppp	80 °C	$PhCMe_2CO_2H$ / 40	42	20/80
6	dppf	80 °C	$PhCMe_2CO_2H$ / 40	77	30/70
7	**dppf**	**80 °C**	$ClCH_2CO_2H$ / **20**	**86**	**16/84**
8	dppf	60 °C	$ClCH_2CO_2H$ / 20	53	11/89
9	dppf	Rt.	$ClCH_2CO_2H$ / 20	19	10/90

All reactions were performed on a 0.3 mmol scale. (a) NMR-Yield; (b) determined by ^{1}H-NMR analysis of the crude product

Pd-catalysis:



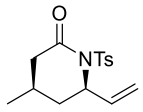
#	Metal	Ligand	Additive / xx mol%	Yield /%[(a)]	d.r. *(anti/syn)*[(b)]
1	$Pd(dba)_2$	DPEPhos	-	-	-
2	$Pd(dba)_2$	DPEPhos	$PhCMe_2CO_2H$ / 40	-	-
3	$Pd(dba)_2$	dppf	$ClCH_2CO_2H$ / 20	-	-
4	$Pd_2(dba)_3$	dppf	$ClCH_2CO_2H$ / 20	-	-
5	$[Pd(\eta_3\text{-allyl})Cl]_2$	DPEPhos	$PhCMe_2CO_2H$ / 40	-	-
6	$[Pd(\eta_3\text{-allyl})Cl]_2$	dppf	$ClCH_2CO_2H$ / 20	-	-
7	$PdPPh_3$	dppf	$ClCH_2CO_2H$ / 20	-	-

All reactions were performed on a 0.3 mmol scale. (a) NMR-Yield; (b) determined by ^{1}H-NMR analysis of the crude product

Synthesis and characterisation of lactams

Synthesis and characterisation of *syn*-lactams

Synthesis of 4-methyl-1-tosyl-6-vinylpiperidin-2-one 3a



$C_{15}H_{19}NO_3S$
293.38

The reaction was performed according to **general procedure 6** with 3-methyl-N-tosylhepta-5,6-dienamide (88 mg, 0.3 mmol, 1.0 equiv.). The reaction mixture was filtered, concentrated and the **d.r.** ratio (**d.r. = 78/22**) was determined by ^{1}H-NMR spectroscopy of the crude product. After purification by flash chromatography on silica gel (DCM) the product was obtained as colourless wax (82 mg, 0.28 mmol, 92%).

Analytical Data[3]

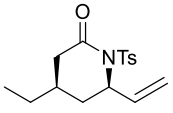
^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 0.95 (d, *J* = 6.5 Hz, 0.7H) [a], 1.02 (d, *J* = 6.5 Hz, 2.2H) [b], 1.44 (ddd, *J* = 14.0, 8.8, 5.8 Hz, 1H), 1.90 – 2.04 (m, 1H), 2.08 (dd, *J* = 16.1, 12.1 Hz, 1H), 2.24 – 2.36 (m, 1H), 2.36 – 2.47 (m, 4H), 5.06 – 5.16 (m, 1H), 5.16 – 5.33 (m, 2H), 5.72 – 5.94 (m, 1H), 7.24 – 7.33 (m, 2H), 7.91 (dd, *J* = 8.4, 4.7 Hz, 2H).ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 21.6, 21.7, 26.1, 37.2, 42.1, 58.3, 116.2, 129.07,129.16, 129.43, 136.70, 137.4, 139.2, 144.60, 171.3 ppm.

ESI-HRMS: *m/z* calcd for $C_{15}H_{22}O_3NNaS$ $[M+Na]^+$ 316.0978 found 316.0982.

HPLC: LC-4, λ = 236 nm, *n*-heptane:IPA = 85:15, 0.4 mL/min, 22 °C: t_r = 38.9 min (major) and t_r = 73.9 min (minor), 50% ee.

Synthesis of 4-ethyl-1-tosyl-6-vinylpiperidin-2-one 4a



$C_{16}H_{21}NO_3S$
307.41

The reaction was performed according to **general procedure 6** with 3-ethyl-N-tosylhepta-5,6-dienamide (93 mg, 0.3 mmol, 1.0 equiv.). The reaction mixture was filtered, concentrated and the **d.r.** ratio (**d.r. = 84/16**) was determined by ^{1}H-NMR spectroscopy of the crude product. After purification by flash chromatography on silica gel (DCM) the product was obtained as a colourless wax (90 mg, 0.29 mmol, 98%).

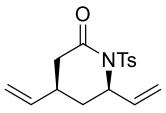
Analytical Data[3]

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 0.84-0.91 (m, 3H), 1.24-1.50 (m, 3H), 1.57-1.84 (m, 1H), 1.95-2.11 (m, 1H), 2.27-2.68 (m, 5H), 5.09-5.31 (m, 3H), 5.76-5.90 (m, 1H), 7.27-7.31 (m, 2H), 7.87-7.94 (m, 2H) ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 11.3, 21.7, 28.8, 29.1, 29.7, 32.7, 35.0, 39.8, 40.0, 58.2, 116.2, 117.6, 129.2, 129.4, 136.7, 137.4, 139.2, 144.6, 170.2, 171.5 ppm.

ESI-HRMS: *m/z* calcd for $C_{16}H_{22}O_3NS$ $[M+H]^+$ 308.1315, found 308.1317.

Synthesis of 1-tosyl-4,6-divinylpiperidin-2-one 5a



$C_{16}H_{19}NO_3S$
305.39

The reaction was performed according to **general procedure 6** with N-tosyl-3-vinylhepta-5,6-dienamide (92 mg, 0.3 mmol, 1.0 equiv.). The reaction mixture was filtered, concentrated and the **d.r.** ratio (**d.r. = 75/25**) was determined by ^{1}H-NMR spectroscopy of the crude product. After purification by flash chromatography on silica gel (DCM) the product was obtained as a colourless solid (88 mg, 0.29 mmol, 96%).

Analytical Data[3]

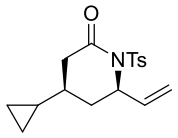
mp: 59 – 61 °C

^{1}H-NMR (500.1 MHz, $CDCl_3$): δ = 1.66 (ddd, *J* = 14.1, 8.5, 5.4 Hz, 1H), 2.25 – 2.40 (m, 2H), 2.42 (s, 3H), 2.50 (dd, *J* = 4.9, 1.9 Hz, 1H), 2.53 – 2.60 (m, 1H), 4.98 – 5.08 (m, 2H), 5.08 – 5.18 (m, 1H), 5.18 – 5.38 (m, 2H), 5.67 – 5.76 (m, 1H), 5.81 (ddd, *J* = 17.1, 10.4, 6.0 Hz, 1H), 7.27 – 7.31 (m, 2H), 7.91 – 7.93(m, 2H).ppm.

^{13}C-NMR (125.7 MHz, $CDCl_3$): δ = 21.7, 32.0, 34.7, 34.9, 39.4, 58.2, 114.9, 116.6, 129.2, 136.5, 137.1, 138.8, 139.8, 144.8, 170.7 ppm.

APCI-HRMS: *m/z* calcd for $C_{16}H_{20}O_3NS$ $[M+H]^+$ 306.1158 found 306.1157.

Synthesis of 4-cyclopropyl-1-tosyl-6-vinylpiperidin-2-one 6a



$C_{17}H_{21}NO_3S$
319.42

The reaction was performed according to **general procedure 6** with 3-cyclopropyl-N-tosylhepta-5,6-dienamide (96 mg, 0.3 mmol, 1.0 equiv.). The reaction mixture was filtered, concentrated and the **d.r.** ratio (**d.r. = 83/17**) was determined by ^{1}H-NMR spectroscopy of the crude product. After purification by flash chromatography on silica gel (DCM) the product was obtained as a colourless wax (89 mg, 0.28 mmol, 94%).

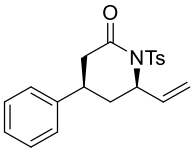
Analytical Data[3]

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = -0.01 – 0.18 (m, 2H), 0.35 – 0.51 (m, 2H), 0.56 – 0.61 (m, 1H), 1.06 – 1.17 (m, 1H), 1.71 (ddd, *J* = 14.1, 8.3, 5.2 Hz, 1H), 2.14 – 2.40 (m, 2H), 2.41 (s, 3H), 2.51 (ddd, *J* = 16.6, 5.0, 1.7 Hz, 1H), 5.13 (dddd, *J* = 9.4, 5.8, 3.4, 1.6 Hz, 1H), 5.18 – 5.29 (m, 2H), 5.85 (ddd, *J* = 17.1, 10.4, 5.8 Hz, 1H), 7.26 – 7.31 (m, 2H), 7.90 – 7.93 (m, 2H). ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 3.4, 3.7, 16.9, 21.7, 35.1, 36.6, 40.1, 58.1, 116.2, 129.1, 129.1, 129.2, 139.2, 144.6, 171.3 ppm.

ESI-HRMS: *m/z* calcd for $C_{17}H_{22}O_3NS$ $[M+H]^+$ 320.1315 found 320.1316.

Synthesis of 4-phenyl-1-tosyl-6-vinylpiperidin-2-one 2a



$C_{20}H_{21}NO_3S$
355.45

The reaction was performed according to **general procedure 6** with 3-phenyl-N-tosylhepta-5,6-dienamide (107 mg, 0.3 mmol, 1.0 equiv.). The reaction mixture was filtered, concentrated and the **d.r.** ratio (**d.r. = 91/9**) was determined by ^{1}H-NMR spectroscopy of the crude product. After purification by flash chromatography on silica gel (DCM) the product was obtained as a colourless solid (101 mg, 0.29 mmol, 92%).

Analytical Data[3]

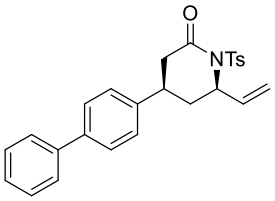
mp: 104 – 106 °C

^{1}H-NMR (500.1 MHz, $CDCl_3$): δ = 1.89 (ddd, *J* = 14.0, 10.3, 6.0 Hz, 1H), 2.44 (s, 3H), 2.54 – 2.67 (m, 3H), 3.00 – 3.17 (m, 1H), 5.13 – 5.35 (m, 3H), 5.83 (ddd, *J* = 16.8, 10.3, 6.3 Hz, 1H), 7.12 – 7.20 (m, 2H), 7.20 – 7.29 (m, 1H), 7.29 – 7.36 (m, 4H), 7.95 – 7.99 (m, 2H) ppm.

^{13}C-NMR (125.6 MHz, $CDCl_3$): δ = 21.8, 36.9, 37.1, 41.4, 58.3, 116.6, 126.7, 127.2, 129.0, 129.2, 129.3, 136.5, 139.2, 142.4, 144.8, 171.0 ppm.

APCI-HRMS: *m/z* calcd for $C_{16}H_{22}O_3NS$ $[M+H]^+$ 356.1242 found 356.1241.

Synthesis of 4-([1,1'-biphenyl]-4-yl)-1-tosyl-6-vinylpiperidin-2-one 7a



$C_{26}H_{25}NO_3S$
431.55

The reaction was performed according to **general procedure 6** with 3-([1,1'-biphenyl]-4-yl)-N-tosylhepta-5,6-dienamide (130 mg, 0.3 mmol, 1.0 equiv.). The reaction mixture was filtered, concentrated and the **d.r.** ratio (**d.r. = 91/9**) was determined by ^{1}H-NMR spectroscopy of the crude product. After purification by flash chromatography on silica gel (DCM) the product was obtained as a colourless wax (121 mg, 0.28 mmol, 93%).

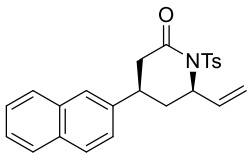
Analytical Data[3]

^{1}H-NMR (500.2 MHz, $CDCl_3$): δ =1.94 (ddd, *J* = 14.0, 10.3, 5.9 Hz, 1H), 2.45 (s, 3H), 2.57 – 2.72 (m, 3H), 3.17 (dd, *J* = 11.8, 10.7, 1H), 5.16 – 5.36 (m, 3H), 5.86 (ddd, *J* = 16.9, 10.3, 6.3 Hz, 1H), 7.20 – 7.25 (m, 2H), 7.31 – 7.37 (m, 3H), 7.42 – 7.46 (m, 2H), 7.54 – 7.58 (m, 4H), 7.98 – 8.02 (m, 2H) ppm.

^{13}C-NMR (125.7 MHz, $CDCl_3$): δ = 21.7, 36.6, 37.1, 41.4, 58.3, 116.6, 127.0, 127.1, 127.4, 127.7, 128.9, 129.2, 129.3, 136.5, 139.2, 140.2, 140.5, 141.3, 144.8, 170.9 ppm.

ESI-HRMS: *m/z* calcd for $C_{26}H_{25}O_3NNaS$ $[M+Na]^+$ 454.1447 found 454.1453.

Synthesis of (4-(naphthalen-2-yl)-1-tosyl-6-vinylpiperidin-2-one 8a



$C_{24}H_{23}NO_3S$
405.51

The reaction was performed according to **general procedure 6** with 3-(naphthalen-2-yl)-N-tosylhepta-5,6-dienamide (107 mg, 0.3 mmol, 1.0 equiv.). The reaction mixture was filtered, concentrated and the **d.r.** ratio (**d.r. = 91/9**) was determined by ^{1}H-NMR spectroscopy of the crude product. After purification by flash chromatography on silica gel (DCM) the product was obtained as a colourless wax (93 mg, 0.23 mmol, 78%).

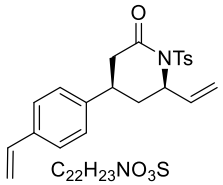
Analytical Data[3]

^{1}H-NMR (500.1 MHz, $CDCl_3$): δ = 2.00 (ddd, *J* = 14.1, 10.2, 5.9 Hz, 1H), 2.45 (s, 3H), 2.61 – 2.70 (m, 1H), 2.71 – 2.78 (m, 2H), 3.22 – 3.34 (m, 1H), 5.22 – 5.34 (m, 3H), 5.87 (ddd, *J* = 16.8, 10.3, 6.3 Hz, 1H), 7.28 (dd, *J* = 8.6, 1.9 Hz, 1H), 7.31 – 7.37 (m, 2H), 7.43 – 7.53 (m, 2H), 7.55 – 7.58 (m, 1H), 7.74 – 7.87 (m, 3H), 7.98 – 8.05 (m, 2H) ppm.

^{13}C-NMR (125.8 MHz, $CDCl_3$): δ = 21.8, 37.0, 37.0, 41.4, 58.4, 116.7, 125.0, 125.1, 126.0, 126.5, 127.7, 128.9, 129.3, 129.3, 129.6, 132.5, 133.5, 136.5, 139.2, 139.6, 144.8, 171.0 ppm.

APCI-HRMS: *m/z* calcd for $C_{24}H_{24}O_3NS$ $[M+H]^+$ 406.1471 found 406.14i69.

Synthesis of 1-tosyl-6-vinyl-4-(4-vinylphenyl)piperidin-2-one 9a



$C_{22}H_{23}NO_3S$
381.49

The reaction was performed according to **general procedure 6** with N-tosyl-3-(4-vinylphenyl)hepta-5,6-dienamide (114 mg, 0.3 mmol, 1.0 equiv.). The reaction mixture was filtered, concentrated and the **d.r.** ratio (**d.r. = 90/10**) was determined by ^{1}H-NMR spectroscopy of the crude product. After purification by flash chromatography on silica gel (DCM) the product was obtained as a colourless wax (96 mg, 0.25 mmol, 84%).

Analytical Data[3]

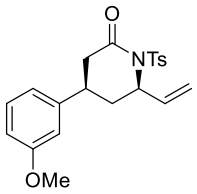
^{1}H-NMR (500.1 MHz, $CDCl_3$): δ = 1.88 (ddd, *J* = 14.0, 10.3, 6.0 Hz, 1H), 2.44 (s, 3H), 2.53 – 2.64 (m, 3H), 3.06 – 3.14 (m, 1H), 5.19 – 5.31 (m, 4H), 5.72 (dd, *J* = 17.6, 0.9 Hz, 1H), 5.83 (ddd, *J* = 16.8, 10.4,

6.3 Hz, 1H), 6.68 (dd, *J* = 17.6, 10.9 Hz, 1H), 7.10 – 7.12 (m, 2H), 7.29 – 7.33 (m, 2H), 7.34 – 7.39 (m, 2H), 7.93 – 8.00 (m, 2H) ppm.

^{13}C-NMR (125.8 MHz, $CDCl_3$): δ = 21.7, 36.6, 37.0, 41.3, 58.3, 114.1, 114.1, 116.6, 126.8, 126.9, 129.3, 129.3, 136.2, 136.6, 139.1, 141.9, 144.8, 170.1 ppm.

APCI-HRMS: *m/z* calcd for $C_{22}H_{23}O_3NNaS$ $[M+Na]^+$ 404.1291 found 404.1288.

Synthesis of 4-(3-methoxyphenyl)-1-tosyl-6-vinylpiperidin-2-one 10a



$C_{21}H_{23}NO_4S$
385.48

The reaction was performed according to **general procedure 6** with 3-(3-methoxyphenyl)-N-tosylhepta-5,6-dienamide (116 mg, 0.3 mmol, 1.0 equiv.). The reaction mixture was filtered, concentrated and the **d.r.** ratio (**d.r. = 90/10**) was determined by ^{1}H-NMR spectroscopy of the crude product. After purification by flash chromatography on silica gel (DCM) the product was obtained as a colourless wax (111 mg, 0.29 mmol, 96%).

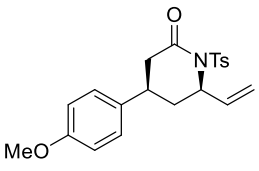
Analytical Data[3]

^{1}H-NMR (500.1 MHz, $CDCl_3$): δ = 1.88 (ddd, *J* = 14.1, 10.3, 6.0 Hz, 1H), 2.44 (s, 3H), 2.53 – 2.64 (m, 3H), 3.09 (dddd, *J* = 12.3, 10.7, 6.2, 4.8 Hz, 1H), 3.78 (s, 3H), 5.16 – 5.23 (m, 1H), 5.23 – 5.30 (m, 2H), 5.83 (ddd, *J* = 16.9, 10.3, 6.3 Hz, 1H), 6.68 (dd, *J* = 2.5, 1.8 Hz, 1H), 6.71 – 6.81 (m, 2H), 7.23 (m, 1H), 7.29 – 7.39 (m, 2H), 7.94 – 8.02 (m, 2H) ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 21.8, 37.0, 41.4, 55.3, 58.3, 112.1, 112.9, 116.7, 118.9, 129.2, 129.3, 130.0, 136.5, 139.2, 144.0, 144.8, 160.0, 170.9 ppm. ppm.

ESI-HRMS: *m/z* calcd for $C_{21}H_{23}O_4NNaS$ $[M+Na]^+$ 408.1240 found 405.1250

Synthesis of 4-(4-methoxyphenyl)-1-tosyl-6-vinylpiperidin-2-one 11a



$C_{21}H_{23}NO_4S$
385.48

The reaction was performed according to **general procedure 6** with 3-(4-methoxyphenyl)-N-tosylhepta-5,6-dienamide (116 mg, 0.3 mmol, 1.0 equiv.). The reaction mixture was filtered, concentrated and the **d.r.** ratio (**d.r. = 90/10**) was determined by ^{1}H-NMR spectroscopy of the crude

product. After purification by flash chromatography on silica gel (DCM) the product was obtained as a colourless wax (98 mg, 0.26 mmol, 85%).

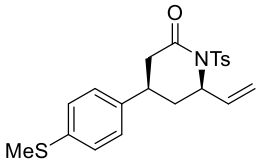
Analytical Data[3]

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 1.85 (ddd, *J* = 14.0, 10.4, 6.0 Hz, 1H), 2.44 (s, 4H), 2.52 – 2.60 (m, 2H), 2.60 (dd, *J* = 4.7, 2.2 Hz, 1H), 3.07 (dddd, *J* = 12.6, 10.5, 6.1, 4.6 Hz, 1H), 3.78 (s, 3H), 5.15 – 5.24 (m, 1H), 5.20 – 5.32 (m, 3H), 5.82 (ddd, *J* = 16.8, 10.3, 6.3 Hz, 1H), 6.77 – 6.90 (m, 2H), 7.01 – 7.09 (m, 2H), 7.29 – 7.42 (m, 2H), 7.89 – 8.04 (m, 2H) ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 21.8, 26.6, 33.2, 36.2, 37.4, 41.7, 55.4, 58.4, 114.4, 116.6, 127.7, 129.2, 129.3, 139.2, 144.8, 158.7, 171.1 ppm.

ESI-HRMS: *m/z* calcd for $C_{21}H_{24}O_4NS$ $[M+H]^+$ 386.1421 found 386.1424.

Synthesis of 4-(4-(methylthio)phenyl)-1-tosyl-6-vinylpiperidin-2-one 12a



$C_{21}H_{23}NO_3S_2$
401,54

The reaction was performed according to **general procedure 6** with 3-(4-(methylthio)phenyl)-N-tosylhepta-5,6-dienamide (120 mg, 0.3 mmol, 1.0 equiv.). The reaction mixture was concentrated and the **d.r.** ratio (**d.r. = 88/12**) was determined by ^{1}H-NMR spectroscopy of the crude product. After purification by flash chromatography on silica gel (DCM) the product was obtained as a colourless solid (112 mg, 0.28 mmol, 93%).

Analytical Data[3]

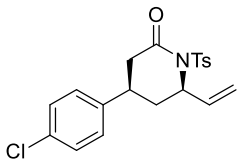
mp: 96 – 98 °C

^{1}H-NMR (500.1 MHz, $CDCl_3$): δ = 1.85 (ddd, *J* = 14.0, 10.3, 5.9 Hz, 1H), 2.43 (s, 3H), 2.46 (s, 3H), 2.52 – 2.63 (m, 3H), 3.08 (dddd, *J* = 12.3, 10.7, 6.2, 4.9 Hz, 1H), 5.17 – 5.22 (m, 1H), 5.22 – 5.30 (m, 2H), 5.82 (ddd, *J* = 16.8, 10.3, 6.3 Hz, 1H), 7.05 – 7.07 (m, 2H), 7.18 – 7.24 (m, 2H), 7.30 – 7.33 (m, 2H), 7.96 (dd, *J* = 8.5, 2.0 Hz, 2H) ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 16.0, 21.8, 36.5, 37.1, 41.4, 58.3, 116.7, 127.2, 127.3, 129.2, 129.3, 136.4, 137.4, 139.1, 144.8, 170.9 ppm.

ESI-HRMS: *m/z* calcd for $C_{21}H_{24}O_3NS_2$ $[M+Na]^+$ 402.1192 found 402.1199.

Synthesis of 4-(4-chlorophenyl)-1-tosyl-6-vinylidenepiperidin-2-one 13a



$C_{20}H_{20}ClNO_3S$
389.89

The reaction was performed according to **general procedure 6** with 3-(4-chlorophenyl)-N-tosylhepta-5,6-dienamide (117 mg, 0.3 mmol, 1.0 equiv.). The reaction mixture was filtered, concentrated and the **d.r.** ratio (**d.r. = 91/9**) was determined by ^{1}H-NMR spectroscopy of the crude product. After purification by flash chromatography on silica gel (DCM) the product was obtained as a colourless wax (100 mg, 0.26 mmol, 86%).

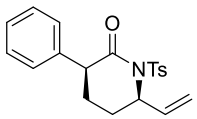
Analytical Data[3]

^{1}H-NMR (500.1 MHz, $CDCl_3$): δ = 1.84 (ddd, *J* = 14.0, 10.3, 5.9 Hz, 1H), 2.43 (s, 3H), 2.50 – 2.64 (m, 3H), 3.10 (dddd, *J* = 12.5, 10.6, 6.3, 4.6 Hz, 1H), 5.16 – 5.32 (m, 3H), 5.76 – 5.86 (m, 1H), 7.05 – 7.09 (m, 2H), 7.27 – 7.35 (m, 4H), 7.94 – 8.00 (m, 2H). ppm.

^{13}C-NMR (125.8 MHz, $CDCl_3$): δ = 21.8, 36.4, 37.0, 41.3, 58.2, 116.8, 128.1, 129.2, 129.3, 133.0, 136.4, 139.0,140.8, 144.9, 144.9, 170.6 ppm.

APCI-HRMS: *m/z* calcd for $C_{20}H_{20}O_3NClNaS$ $[M+Na]^+$ 412.0745 found 412.0750.

Synthesis of 3-phenyl-1-tosyl-6-vinylpiperidin-2-one 14a



$C_{20}H_{21}NO_3S$
355,45

The reaction was performed according to **general procedure 6** with 2-phenyl-N-tosylhepta-5,6-dienamide (107 mg, 0.3 mmol, 1.0 equiv.). The reaction mixture was filtered, concentrated and the **d.r.** ratio (**d.r. = 75/25**) was determined by ^{1}H-NMR spectroscopy of the crude product. After purification by flash chromatography on silica gel (DCM) the product was obtained as a colourless wax (82 mg, 0.23 mmol, 78%).

Analytical Data[3]

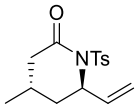
^{1}H-NMR (500.1 MHz, $CDCl_3$): δ = 1.74 – 1.92 (m, 1H), 2.05 – 2.22 (m, 2H), 2.22 – 2.38 (m, 1H), 2.41 – 2.43 (m, 3H), 3.66 – 3.84 (m, 1H), 5.24 – 5.47 (m, 3H), 5.85 – 6.12 (m, 1H), 6.93 – 7.14 (m, 2H), 7.17 – 7.26 (m, 3H), 7.26 – 7.32 (m, 2H), 7.87 – 8.03 (m, 2H) ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 21.7, 25.3, 25.6, 48.6, 58.7, 117.7, 127.0, 127.9, 128.5, 128.7, 129.1, 129.7, 137.4, 140.5, 144.8, 171.7 ppm.

ESI-HRMS: *m/z* calcd for $C_{20}H_{22}O_3NS$ $[M+Na]^+$ 356.1315 found 356.1315.

Synthesis and characterisation of *anti*-lactams

Synthesis of 4-methyl-1-tosyl-6-vinylpiperidin-2-one 3b



$C_{15}H_{19}NO_3S$
293.38

The reaction was performed according to **general procedure 7** with 3-methyl-N-tosylhepta-5,6-dienamide (88 mg, 0.3 mmol, 1.0 equiv.). The reaction mixture was filtered, concentrated and the **d.r.** ratio (**d.r. = 90/10**) was determined by ^{1}H-NMR spectroscopy of the crude product. After purification by flash chromatography on silica gel (DCM) the product was obtained as colourless wax (83 mg, 0.29 mmol, 98%).

Analytical Data[3]

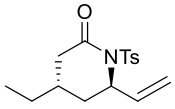
^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 0.95 (d, *J* = 6.5 Hz, 3H), 1.65 (ddd, *J* = 13.8, 12.4, 5.3 Hz, 1H), 1.88 – 2.03 (m, 2H), 2.05 – 2.12 (m, 1H), 2.41 (s, 3H), 2.52 (ddd, *J* = 17.7, 5.7, 2.0 Hz, 1H), 5.16 – 5.34 (m, 3H), 5.85 (ddd, *J* = 17.1, 10.5, 5.4 Hz, 1H), 7.23 – 7.34 (m, 2H), 7.85 – 8.00 (m, 2H) ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 21.3, 21.7, 23.2, 37.1, 41.8, 58.5, 117.6, 129.1, 129.4, 136.4, 137.4, 144.64, 170.1 ppm.

ESI-HRMS: *m/z* calcd for $C_{15}H_{20}O_3NS$ $[M+H]^+$ 294.1158 found 294.1158.

HPLC: LC-4, λ = 236 nm, *n*-heptane:IPA = 85:15, 0.4 mL/min, 22 °C: t_r = 45.2 min (major) and t_r = 77.5 min (minor), 50% ee.

Synthesis of 4-ethyl-1-tosyl-6-vinylpiperidin-2-one 4b



$C_{16}H_{21}NO_3S$
307.41

The reaction was performed according to **general procedure 7** with 3-ethyl-N-tosylhepta-5,6-dienamide (93 mg, 0.3 mmol, 1.0 equiv.). The reaction mixture was filtered, concentrated and the **d.r.** ratio (**d.r. = 90/10**) was determined by ^{1}H-NMR spectroscopy of the crude product. After purification by flash chromatography on silica gel (DCM) the product was obtained as a colourless wax (89 mg, 0.28 mmol, 96%).

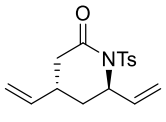
Analytical Data[3]

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 0.86 (t, *J* = 7.4 Hz, 3H), 1.20 – 1.34 (m, 2H), 1.61 (m, 1H), 1.77 – 1.93 (m, 1H), 1.98 (m, 2H), 2.41 (s, 3H), 2.55 (ddd, *J* = 17.6, 5.7, 2.0 Hz, 1H), 5.18 – 5.22 (m, 1H) 5.22 – 5.31 (m, 2H), 5.86 (ddd, *J* = 17.0, 10.5, 5.4 Hz, 1H), 7.26 – 7.35 (m, 2H), 7.84 – 7.96 (m, 2H).

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 10.9, 21.7, 28.8, 29.7, 35.0, 39.8, 58.4, 117.6, 129.1, 129.4, 136.5, 137.4, 144.6, 170.2 ppm.

ESI-HRMS: *m/z* calcd for $C_{16}H_{22}O_3NS$ $[M+H]^+$ 308.1315, found 308.1317.

Synthesis of 1-tosyl-4,6-divinylpiperidin-2-one 5b



$C_{16}H_{19}NO_3S$
305.39

The reaction was performed according to **general procedure 7** with N-tosyl-3-vinylhepta-5,6-dienamide (92 mg, 0.3 mmol, 1.0 equiv.). The reaction mixture was filtered, concentrated and the **d.r.** ratio (**d.r. = 92/8**) was determined by ^{1}H-NMR spectroscopy of the crude product. After purification by flash chromatography on silica gel (DCM) the product was obtained as a colourless wax (89 mg, 0.28 mmol, 93%).

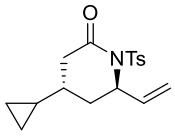
Analytical Data[3]

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 1.81 (m, 1H), 2.03 (ddt, *J* = 13.7, 3.5, 2.2 Hz, 1H), 2.19 (m, 1H), 2.42 (s, 3H), 2.57 (ddd, *J* = 17.8, 6.0, 2.0 Hz, 1H), 2.61 – 2.72 (m, 1H), 4.97 – 5.06 (m, 2H), 5.21 – 5.37 (m, 3H), 5.59 – 5.73 (m, 1H), 5.82 – 5.95 (m, 1H), 7.25 – 7.32 (m, 2H), 7.87 – 7.97 (m, 2H) ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 21.7, 32.0, 34.8, 39.0, 58.1, 114.9, 117.9, 129.1, 129.5, 136.4, 137.1, 139.7, 144.7, 169.5 ppm.

APCI-HRMS: *m/z* calcd for $C_{16}H_{20}O_3NS$ $[M+H]^+$ 306.1158 found 306.1157.

Synthesis of anti-4-cyclopropyl-1-tosyl-6-vinylpiperidin-2-one 6b



$C_{17}H_{21}NO_3S$
319.42

The reaction was performed according to **general procedure 7** with 3-cyclopropyl-N-tosylhepta-5,6-dienamide (96 mg, 0.3 mmol, 1.0 equiv.). The reaction mixture was filtered, concentrated and the **d.r.** ratio (**d.r. = 96/4**) was determined by ^{1}H-NMR spectroscopy of the crude product. After purification by flash chromatography on silica gel (DCM) the product was obtained as a colourless solid (89 mg, 0.29 mmol, 96%).

Analytical Data[3]

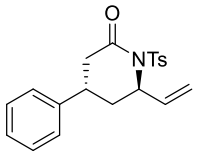
mp: 64 – 66 °C

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 0.04 – 0.16 (m, 2H), 0.42 – 0.47 (m, 2H), 0.45 – 0.57 (m, 1H), 1.05 – 1.44 (m, 1H), 1.80 (ddd, *J* = 13.7, 12.6, 5.3 Hz, 1H), 2.07 (ddt, *J* = 13.7, 3.6, 2.1, 2.1, 1H), 2.14 – 2.25 (m, 1H), 2.42 (s, 3H), 2.59 (ddd, *J* = 18.1, 6.1, 1.9 Hz, 1H), 5.05 – 5.36 (m, 3H), 5.63 – 5.91 (m, 1H), 7.26 – 7.30 (m, 2H), 7.71 – 8.12 (m, 2H) ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 3.1, 3.3, 16.4, 21.7, 33.7, 35.1, 39.9, 58.3, 117.6, 129.1, 129.4, 136.5, 137.3, 144.6, 170.2 ppm.

ESI-HRMS: *m/z* calcd for $C_{17}H_{22}O_3NS$ $[M+H]^+$ 320.1315 found 320.1315.

Synthesis of 4-phenyl-1-tosyl-6-vinylpiperidin-2-one 2b



$C_{20}H_{21}NO_3S$
355.45

The reaction was performed according to **general procedure 7** with 3-phenyl-N-tosylhepta-5,6-dienamide (107 mg, 0.3 mmol, 1.0 equiv.). The reaction mixture was filtered, concentrated and the **d.r.** ratio (**d.r. = 96/4**) was determined by ^{1}H-NMR spectroscopy of the crude product. After purification by flash chromatography on silica gel (DCM) the product was obtained as a colourless solid (101 mg, 0.29 mmol, 95%).

Analytical Data[3]

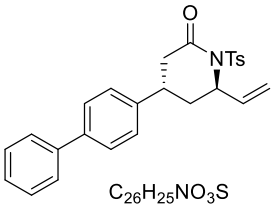
mp: 127 – 129 °C

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 2.16 – 2.24 (m, 2H), 2.44 (s, 3H), 2.50 (dd, *J* = 18.0, 11.7 Hz, 1H), 2.71 – 2.81 (m, 1H), 3.18 – 3.30 (m, 1H), 5.30 – 5.44 (m, 3H), 5.97 (ddd, *J* = 17.4, 10.6, 4.9 Hz, 1H), 7.11 – 7.15 (m, 2H), 7.21 – 7.26 (m, 1H), 7.29 – 7.34 (m, 4H), 7.94 – 7.98 (m, 2H) ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 21.7, 34.1, 36.2, 41.2, 58.3, 118.2, 126.6, 127.3, 129.0, 129.2, 129.6, 136.4, 137.1, 142.6, 144.8, 169.7 ppm.

APCI-HRMS: *m/z* calcd for $C_{16}H_{22}O_3NS$ $[M+H]^+$ 356.1242 found 356.1241.

Synthesis of 4-([1,1'-biphenyl]-4-yl)-1-tosyl-6-vinylpiperidin-2-one 7b



$C_{26}H_{25}NO_3S$
431.55

The reaction was performed according to **general procedure 7** with 3-([1,1'-biphenyl]-4-yl)-N-tosylhepta-5,6-dienamide (130 mg, 0.3 mmol, 1.0 equiv.). The reaction mixture was filtered, concentrated and the **d.r.** ratio (**d.r. = 86/14**) was determined by ^{1}H-NMR spectroscopy of the crude product. After purification by flash chromatography on silica gel (DCM) the product was obtained as a colourless solid (106 mg, 0.25 mmol, 82%).

Analytical Data[3]

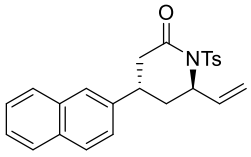
mp: 80 – 82 °C

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 2.18 – 2.26 (m, 2H), 2.44 (s, 3H), 2.54 (dd, *J* = 18.0, 11.6 Hz, 1H), 2.73 – 2.85 (m, 1H), 3.21 – 3.40 (m, 1H), 5.30 – 5.47 (m, 3H), 5.99 (ddd, *J* = 17.3, 10.6, 4.9 Hz, 1H), 7.20 – 7.22 (m, 2H), 7.31 – 7.34 (m, 3H), 7.41 – 7.45 (m, 2H), 7.53 – 7.57 (m, 4H), 7.96 – 7.98 (m, 2H). ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 21.8, 33.7, 36.2, 41.1, 58.3, 118.3, 127.0, 127.7, 128.9, 129.2, 129.6, 136.3, 137.1, 139.2, 140.3, 140.6, 141.6, 144.9, 169.6 ppm.

ESI-HRMS: *m/z* calcd for $C_{26}H_{25}O_3NNaS$ $[M+Na]^+$ 454.1447 found 454.1448.

Synthesis of 4-(naphthalen-2-yl)-1-tosyl-6-vinylpiperidin-2-one 8b



$C_{24}H_{23}NO_3S$
405.51

The reaction was performed according to **general procedure 7** with 3-(naphthalen-2-yl)-N-tosylhepta-5,6-dienamide (121 mg, 0.3 mmol, 1.0 equiv.). The reaction mixture was filtered, concentrated and the **d.r.** ratio (**d.r. = 82/18**) was determined by ^{1}H-NMR spectroscopy of the crude product. After purification by flash chromatography on silica gel (DCM) the product was obtained as a colourless solid (92 mg, 0.23 mmol, 75%).

Analytical Data[3]

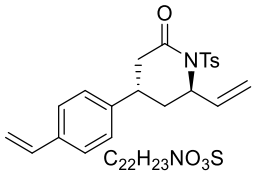
mp: 148 – 150 °C

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 2.23 – 2.32 (m, 2H), 2.44 (s, 3H), 2.62 (dd, *J* = 18.1, 11.5 Hz, 1H), 2.79 – 2.94 (m, 1H), 3.34 – 3.48 (m, 1H), 5.21 – 5.47 (m, 4H), 6.01 (ddd, *J* = 17.4, 10.5, 4.8 Hz, 1H), 7.24 – 7.28 (m, 1H), 7.30 – 7.34 (m, 2H), 7.45 – 7.48 (m, 2H), 7.55 – 7.61 (m, 1H), 7.79 – 7.82 (m, 2H), 7.96 – 7.99 (m, 2H) ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 21.8, 34.2, 36.2, 41.0, 58.3, 118.2, 124.9, 125.0, 126.0, 126.5, 127.7, 127.7, 128.8, 129.2, 129.6, 132.6, 133.6, 136.4, 137.2, 139.9, 144.9, 169.6 ppm.

APCI-HRMS: *m/z* calcd for $C_{24}H_{24}O_3NS$ $[M+H]^+$ 406.1471 found 406.1469

Synthesis of 1-tosyl-6-vinyl-4-(4-vinylphenyl)piperidin-2-one 9b



The reaction was performed according to **general procedure 7** with N-tosyl-3-(4-vinylphenyl)hepta-5,6-dienamide (114 mg, 0.3 mmol, 1.0 equiv.). The reaction mixture was filtered, concentrated and the **d.r.** ratio (**d.r. = 92/8**) was determined by ^{1}H-NMR spectroscopy of the crude product. After purification by flash chromatography on silica gel (DCM) the product was obtained as a colourless wax (107 mg, 0.28 mmol, 93%).

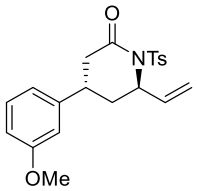
Analytical Data[3]

^{1}H-NMR (500.2 MHz, $CDCl_3$): δ = 2.15 – 2.19 (m, 2H), 2.43 (s, 3H), 2.48 (dd, *J* = 18.1, 11.7 Hz, 1H), 2.71 – 2.79 (m, 1H), 3.17 – 3.25 (m, 1H), 5.23 (dd, *J* = 10.9, 1.0 Hz, 1H), 5.30 – 5.42 (m, 3H), 5.71 (dd, *J* = 17.6, 0.9 Hz, 1H), 5.96 (ddd, *J* = 17.4, 10.5, 4.8 Hz, 1H), 6.67 (dd, *J* = 17.6, 10.9 Hz, 1H), 7.08 – 7.11 (m, 2H), 7.29 – 7.32 (m, 2H), 7.34 – 7.36 (m, 2H), 7.94 – 7.97 (m, 2H) ppm.

^{13}C-NMR (125.8 MHz, $CDCl_3$): δ = 21.7, 33.8, 36.0, 41.0, 58.2, 114.1, 118.2, 126.7, 129.1, 129.5, 136.2, 136.7, 137.0, 142.1, 144.8, 169.6 ppm.

ESI-HRMS: *m/z* calcd for $C_{22}H_{24}O_3NS$ $[M+H]^+$ 382.1471 found 382.1471.

Synthesis of 4-(3-methoxyphenyl)-1-tosyl-6-vinylpiperidin-2-one 10b



$C_{21}H_{23}NO_4S$
385.48

The reaction was performed according to **general procedure 7** with 3-(3-methoxyphenyl)-N-tosylhepta-5,6-dienamide (116 mg, 0.3 mmol, 1.0 equiv.). The reaction mixture was filtered, concentrated and the **d.r.** ratio (**d.r. = 91/9**) was determined by ^{1}H-NMR spectroscopy of the crude product. After purification by flash chromatography on silica gel (DCM) the product was obtained as a colourless solid (112 mg, 0.29 mmol, 97%).

Analytical Data[3]

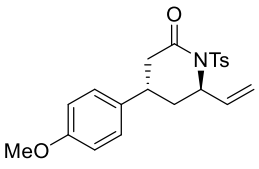
mp: 104 – 106 °C

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 2.15 – 2.20 (m, 2H), 2.43 (s, 3H), 2.49 (dd, *J* = 18.0, 11.6 Hz, 1H), 2.71 – 2.80 (m, 1H), 3.20 (ddt, *J*= 11.9, 9.5, 6.2, Hz 1H), 3.78 (s, 3H), 5.27 – 5.44 (m, 3H), 5.96 (ddd, *J* = 17.4, 10.5, 4.8 Hz, 1H), 6.67 (dd, *J* = 2.5, 1.8 Hz, 1H), 6.72 (ddt, *J* = 7.5, 1.4, 0.7, Hz, 1H), 6.77 (ddd, *J* = 8.3, 2.5, 1.0 Hz, 1H), 7.20 – 7.25 (m, 1H), 7.29 – 7.32 (m, 2H), 7.93 – 7.97 (m, 2H).

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 21.7, 34.1, 36.1, 41.1, 55.3, 58.2, 112.2, 112.7, 117.1, 118.8, 129.1, 129.5, 129.9, 136.3, 137.1, 144.3, 144.8, 160.1, 169.6 ppm.

ESI-HRMS: *m/z* calcd for $C_{21}H_{24}O_4NS$ $[M+H]^+$ 386.1421 found 386.1422.

Synthesis of 4-(4-methoxyphenyl)-1-tosyl-6-vinylpiperidin-2-one 11b



$C_{21}H_{23}NO_4S$
385.48

The reaction was performed according to **general procedure 7** with 3-(4-methoxyphenyl)-N-tosylhepta-5,6-dienamide (116 mg, 0.3 mmol, 1.0 equiv.). The reaction mixture was filtered, concentrated and the **d.r.** ratio (**d.r. = 88/12**) was determined by ^{1}H-NMR spectroscopy of the crude product. After purification by flash chromatography on silica gel (DCM) the product was obtained as a colourless solid (105 mg, 0.27 mmol, 91%).

Analytical Data[3]

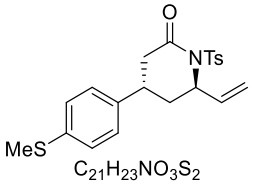
mp: 108 – 110 °C

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 2.11 – 2.21 (m, 2H), 2.43 (s, 3H), 2.44 – 2.51 (m, 1H), 2.69 – 2.79 (m, 1H), 3.18 (ddt, *J* = 11.9, 9.5, 6.2 Hz, 1H), 3.78 (s, 3H), 5.27 – 5.44 (m, 3H), 5.96 (ddd, *J* = 17.4, 10.5, 4.9 Hz, 1H), 6.80 – 6.89 (m, 2H), 7.03 – 7.14 (m, 2H), 7.27 – 7.38 (m, 2H), 7.92 – 7.98 (m, 2H) ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 21.7, 33.3, 36.4, 41.4, 55.4, 58.3, 114.4, 118.1, 127.5, 129.1 , 129.6, 134.7, 136.4, 137.2, 144.8, 158.8 , 169.8 ppm.

ESI-HRMS: *m/z* calcd for $C_{21}H_{24}O_4NS$ $[M+H]^+$ 386.1421 found 386.1422.

Synthesis of (4-(methylthio)phenyl)-1-tosyl-6-vinylpiperidin-2-one 12b



$C_{21}H_{23}NO_3S_2$
401.54

The reaction was performed according to **general procedure 7** with 3-(4-(methylthio)phenyl)-N-tosylhepta-5,6-dienamide (120 mg, 0.3 mmol, 1.0 equiv.). The reaction mixture was filtered, concentrated and the **d.r.** ratio (**d.r. = 92/8**) was determined by ^{1}H-NMR spectroscopy of the crude product. After purification by flash chromatography on silica gel (DCM) the product was obtained as a colourless solid (108 mg, 0.27 mmol, 90%).

Analytical Data[3]

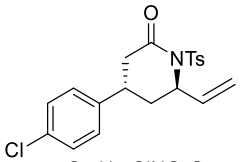
mp: 112 – 114 °C

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 2.12 – 2.19 (m, 2H), 2.44 – 2.46 (m, 7H), 2.68 – 2.78 (m, 1H), 3.19 (ddt, *J* = 12.1, 9.6, 6.3, 6.3 Hz, 1H), 5.27 – 5.46 (m, 3H), 5.95 (ddd, *J* = 17.4, 10.5, 4.8 Hz, 1H), 7.04 – 7.07 (m, 2H), 7.19 – 7.22 (m, 2H), 7.29 – 7.33 (m, 2H), 7.94 – 7.97 (m, 2H) ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 16.1, 21.7, 33.6, 36.2, 41.1, 58.2, 118.2, 127.1, 127.3, 129.2, 129.6, 136.3, 137.1, 137.4, 139.5, 144.9, 169.5 ppm.

ESI-HRMS: *m/z* calcd for $C_{21}H_{24}O_3NS_2$ $[M+H]^+$ 402.1192 found 402.1192.

Synthesis of 4-(4-chlorophenyl)-1-tosyl-6-vinylpiperidin-2-one 13b



$C_{20}H_{20}ClNO_3S$
389.89

The reaction was performed according to **general procedure 7** with 3-(4-chlorophenyl)-N-tosylhepta-5,6-dienamide (117 mg, 0.3 mmol, 1.0 equiv.). The reaction mixture was filtered, concentrated and the **d.r.** ratio (**d.r. = 91/9**) was determined by ^{1}H-NMR spectroscopy of the crude product. After purification by flash chromatography on silica gel (DCM) the product was obtained as a colourless wax (100 mg, 0.26 mmol, 86%).

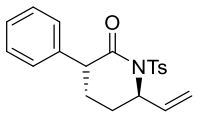
Analytical Data[3]

^{1}H-NMR (500.2 MHz, $CDCl_3$): δ = 2.10 – 2.19 (m, 1H), 2.44 (m, 4H), 2.52 – 2.61 (m, 1H), 2.70 – 2.78 (m, 1H), 3.16 – 3.25 (m, 1H), 5.28 – 5.44 (m, 3H), 5.95 (ddd, *J* = 17.4, 10.5, 4.8 Hz, 1H), 7.05 – 7.08 (m, 2H), 7.27 – 7.32 (m, 4H), 7.93 – 7.96 (m, 2H) ppm.

^{13}C-NMR (125.8 MHz, $CDCl_3$): δ = 21.7, 33.5, 36.0, 41.0, 58.1, 118.3, 127.9, 129.1, 129.2, 129.5, 133.0, 136.1, 136.9, 141.0, 144.9, 169.3 ppm.

ESI-HRMS: *m/z* calcd for $C_{20}H_{21}O_3NS$ $[M+H]^+$ 390.0927 found 390.0927.

Synthesis of 3-phenyl-1-tosyl-6-vinylpiperidin-2-one 14b



$C_{20}H_{21}NO_3S$
355.45

The reaction was performed according to **general procedure 7** with 2-phenyl-N-tosylhepta-5,6-dienamide (107 mg, 0.3 mmol, 1.0 equiv.). The reaction mixture was filtered, concentrated and the **d.r.** ratio (**d.r. = 1/1**) was determined by ^{1}H-NMR spectroscopy of the crude product. After purification by flash chromatography on silica gel (DCM) the product was obtained as a colourless solid (96 mg, 0.23 mmol, 90%).

Analytical Data[3]

mp: 114 – 116 °C

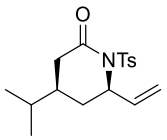
^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 1.93 – 2.18 (m, 4H), 2.41 (s, 3H), 3.48 – 3.57 (m, 1H), 5.32 – 5.53 (m, 3H), 5.98 (ddd, *J* = 17.0, 10.6, 4.6 Hz, 1H), 7.05 – 7.08 (m, 2H), 7.19 – 7.26 (m, 3H), 7.26 – 7.31 (m, 2H), 7.89 – 7.92 (m, 2H). ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 21.7, 26.7, 28.6, 51.6, 59.1, 118.2, 127.3, 128.5, 128.8, 129.2, 129.5, 136.4, 137.7, 139.6, 144.6, 171.6 ppm.

ESI-HRMS: *m/z* calcd for $C_{20}H_{22}O_3NS$ $[M+Na]^+$ 356.1315 found 356.1315.

Synthesis and characterisation of *syn*-lactams, starting from alkyne substrates.

Synthesis of 4-isopropyl-1-tosyl-6-vinylpiperidin-2-one 15a



$C_{17}H_{23}NO_3S$
321.44

The reaction was performed according to **general procedure 8** with 3-isopropyl-N-tosylhept-6-ynamide (97 mg, 0.3 mmol, 1.0 equiv.). The reaction mixture was filtered, concentrated and the **d.r.** ratio (**d.r. = 87/13**) was determined by ^{1}H-NMR spectroscopy of the crude product. After purification by flash chromatography on silica gel (DCM) the product was obtained as a colourless solid (71 mg, 0.22 mmol, 74%).

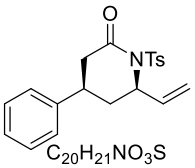
Analytical Data[3]

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 0.87 (dd, *J* = 11.2, 6.7 Hz, 6H), 1.44 – 1.56 (m, 2H), 1.58 – 1.74 (m, 2H), 2.12 (dd, *J* = 16.3, 12.9 Hz, 1H), 2.22 – 2.31 (m, 1H), 2.42 (s, 3H), 5.07 – 5.14 (m, 1H), 5.17 – 5.25 (m, 2H), 5.78 (ddd, *J* = 17.1, 10.4, 6.0 Hz, 1H), 7.27 – 7.30 (m, 2H), 7.90 – 7.94 (m, 2H).

^{13}C-NMR (100.6 MHz, $CDCl_3$): 19.4, 19.5, 21.7, 31.9, 32.6, 37.9, 57.9, 116.1, 129.1, 129.2, 136.6, 137.3, 139.4, 144.6, 171.9 ppm.

APCI-HRMS: *m/z* calcd for $C_{17}H_{24}O_3NS$ $[M+H]^+$ 322.1471 found 322.1471.

Synthesis of 4-phenyl-1-tosyl-6-vinylpiperidin-2-one 2a



$C_{20}H_{21}NO_3S$
355.45

The reaction was performed according to **general procedure 8** with 3-phenyl-N-tosylhept-6-ynamide (107 mg, 0.3 mmol, 1.0 equiv.). The reaction mixture was filtered, concentrated and the **d.r.** ratio (**d.r. = 82/18**) was determined by ^{1}H-NMR spectroscopy of the crude product. After purification by flash chromatography on silica gel (DCM) the product was obtained as a colourless solid (84 mg, 0.24 mmol, 79%).

Analytical Data[3]

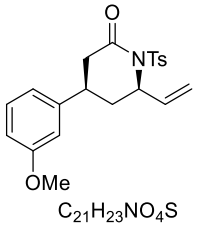
mp: 104 – 106 °C

^{1}H-NMR (500.1 MHz, $CDCl_3$): δ = 1.89 (ddd, *J* = 14.0, 10.3, 6.0 Hz, 1H), 2.44 (s, 3H), 2.54 – 2.67 (m, 3H), 3.00 – 3.17 (m, 1H), 5.13 – 5.35 (m, 3H), 5.83 (ddd, *J* = 16.8, 10.3, 6.3 Hz, 1H), 7.12 – 7.20 (m, 2H), 7.20 – 7.29 (m, 1H), 7.29 – 7.36 (m, 4H), 7.95 – 7.99 (m, 2H) ppm.

^{13}C-NMR (125.6 MHz, $CDCl_3$): δ = 21.8, 36.9, 37.1, 41.4, 58.3, 116.6, 126.7, 127.2, 129.0, 129.2, 129.3, 136.5, 139.2, 142.4, 144.8, 171.0 ppm.

APCI-HRMS: *m/z* calcd for $C_{16}H_{22}O_3NS$ $[M+H]^+$ 356.1242 found 356.1241.

Synthesis of 4-(3-methoxyphenyl)-1-tosyl-6-vinylpiperidin-2-one 10a



$C_{21}H_{23}NO_4S$
385.48

The reaction was performed according to **general procedure 8** with 3-(3-methoxyphenyl)-N-tosylhept-6-ynamide (116 mg, 0.3 mmol, 1.0 equiv.). The reaction mixture was filtered, concentrated and the **d.r.** ratio (**d.r. = 84/16**) was determined by ^{1}H-NMR spectroscopy of the crude product. After purification by flash chromatography on silica gel (DCM) the product was obtained as a colourless wax (101 mg, 0.26 mmol, 88%).

Analytical Data[3]

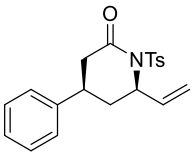
^{1}H-NMR (500.1 MHz, $CDCl_3$): δ = 1.88 (ddd, *J* = 14.1, 10.3, 6.0 Hz, 1H), 2.44 (s, 3H), 2.53 – 2.64 (m, 3H), 3.09 (dddd, *J* = 12.3, 10.7, 6.2, 4.8 Hz, 1H), 3.78 (s, 3H), 5.16 – 5.23 (m, 1H), 5.23 – 5.30 (m, 2H), 5.83 (ddd, *J* = 16.9, 10.3, 6.3 Hz, 1H), 6.68 (dd, *J* = 2.5, 1.8 Hz, 1H), 6.71 – 6.81 (m, 2H), 7.23 (m, 1H), 7.29 – 7.39 (m, 2H), 7.94 – 8.02 (m, 2H) ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 21.8, 37.0, 41.4, 55.3, 58.3, 112.1, 112.9, 116.7, 118.9, 129.2, 129.3, 130.0, 136.5, 139.2, 144.0, 144.8, 160.0, 170.9 ppm. ppm.

ESI-HRMS: *m/z* calcd for $C_{21}H_{23}O_4NNaS$ $[M+Na]^+$ 408.1240 found 405.1250.

Large scale catalysis

Synthesis of syn-4-phenyl-1-tosyl-6-vinylpiperidin-2-one 2a



$C_{20}H_{21}NO_3S$
355.45

A screw-cap flask was flame-dried, cooled to room temperature under vacuum and backfilled with argon using a standard SCHLENK line apparatus. The screw-cap flask was charged with 3-phenyl-N-tosylhepta-5,6-dienamide (500 mg, 1.40 mmol, 1.0 equiv.) the flask was evacuated for 15 min and backfilled with argon three times. Then $[Rh(COD)Cl]_2$ (17.3 mg, 0.035 mmol, 2.5 mol%), dppf (38.8 mg, 0.700 mmol, 5.0 mol%) and HOAcCl (26.5 mg, 0.28 mmol, 20 mol%) was added under a flow of argon followed by freshly distilled DCE (5 mL). The flask was sealed and stirred at room temperature overnight. The reaction mixture was filtered, concentrated and the **d.r.** ratio (**d.r. = 89/11**) was determined by ^{1}H-NMR spectroscopy of the crude product. After purification by flash chromatography on silica gel (DCM) the product was obtained as a colourless solid (472 mg, 1.33 mmol, 95%).

Analytical Data[3]

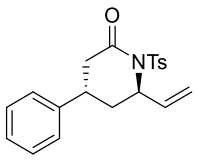
mp: 104 - 106 °C

^{1}H-NMR (500.1 MHz, $CDCl_3$): δ = 1.89 (ddd, *J* = 14.0, 10.3, 6.0 Hz, 1H), 2.44 (s, 3H), 2.54 – 2.67 (m, 3H), 3.00 – 3.17 (m, 1H), 5.13 – 5.35 (m, 3H), 5.83 (ddd, *J* = 16.8, 10.3, 6.3 Hz, 1H), 7.12 – 7.20 (m, 2H), 7.20 – 7.29 (m, 1H), 7.29 – 7.36 (m, 4H), 7.95 – 7.99 (m, 2H) ppm.

^{13}C-NMR (125.6 MHz, $CDCl_3$): δ = 21.8, 36.9, 37.1, 41.4, 58.3, 116.6, 126.7, 127.2, 129.0, 129.2, 129.3, 136.5, 139.2, 142.4, 144.8, 171.0 ppm.

APCI-HRMS: *m/z* calcd for $C_{16}H_{22}O_3NS$ $[M+H]^+$ 356.1242 found 356.1241.

Synthesis of anti-4-phenyl-1-tosyl-6-vinylpiperidin-2-one 2b



$C_{20}H_{21}NO_3S$
355.45

A screw-cap flask was flame-dried, cooled to room temperature under vacuum and backfilled with argon using a standard SCHLENK line apparatus. The screw-cap flask was charged with 3-phenyl-N-tosylhepta-5,6-dienamide (1.10g, 3.10 mmol, 1.0 equiv.) the flask was evacuated for 15 min and backfilled with argon three times. Then $Pd(dba)_2$ (44.5 mg, 0.078 mmol, 2.5 mol%), dppf (85.9 mg, 0.155 mmol, 5.0 mol%) and HOAcCl (59.0 mg, 0.62 mmol, 20 mol%) was added under a flow of argon followed by freshly distilled DCE (10 mL). The flask was sealed and stirred at 80 °C overnight. The flask was sealed and stirred at room temperature overnight. The reaction mixture was filtered, concentrated and the **d.r.** ratio (**d.r. = 92/8**) was determined by ^{1}H-NMR spectroscopy of the crude product. After purification by flash chromatography on silica gel (DCM) the product was obtained as a colourless solid (1.02 g, 2.88 mmol, 93%).

Analytical Data[3]

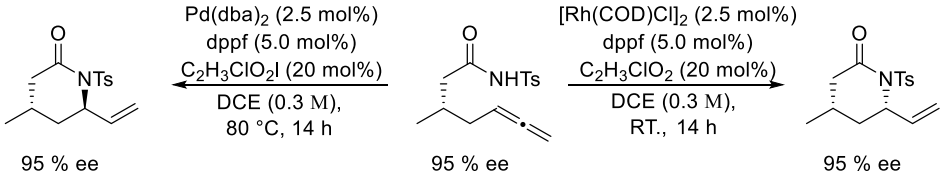
mp: 127 – 129 °C

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 2.16 – 2.24 (m, 2H), 2.44 (s, 3H), 2.50 (dd, *J* = 18.0, 11.7 Hz, 1H), 2.71 – 2.81 (m, 1H), 3.18 – 3.30 (m, 1H), 5.30 – 5.44 (m, 3H), 5.97 (ddd, *J* = 17.4, 10.6, 4.9 Hz, 1H), 7.11 – 7.15 (m, 2H), 7.21 – 7.26 (m, 1H), 7.29 – 7.34 (m, 4H), 7.94 – 7.98 (m, 2H) ppm.

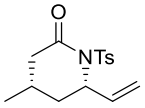
^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 21.7, 34.1, 36.2, 41.2, 58.3, 118.2, 126.6, 127.3, 129.0, 129.2, 129.6, 136.4, 137.1, 142.6, 144.8, 169.7 ppm.

APCI-HRMS: *m/z* calcd for $C_{16}H_{22}O_3NS$ $[M+H]^+$ 356.1242 found 356.1241.

Enantiomeric preparation of (4S,6S)-4-methyl-1-tosyl-6-vinylpiperidin-2-one and (4S,6R)-4-methyl-1-tosyl-6-vinylpiperidin-2-one



Synthesis of (4S,6S)-4-methyl-1-tosyl-6-vinylpiperidin-2-one 3a



$C_{15}H_{19}NO_3S$
293.38

A screw-cap flask was flame-dried, cooled to room temperature under vacuum and backfilled with argon using a standard SCHLENK line apparatus. The screw-cap flask was charged with (S)-3-methyl-N-tosylhepta-5,6-dienamide (88 mg, 0.30 mmol, 1.0 equiv.) the flask was evacuated for 15 min and backfilled with argon three times. Then $[Rh(COD)Cl]_2$ (3.7 mg, 0.0075 mmol, 2.5 mol%), dppf (8.3 mg, 0.015 mmol, 5.0 mol%) and HOAcCl (5.7 mg, 0.06 mmol, 20 mol%) was added under a flow of argon followed by freshly distilled DCE (1 mL). The flask was sealed and stirred at room temperature overnight. The reaction mixture was filtered, concentrated and the **d.r.** ratio (**d.r. = 78/22**) was determined by ^{1}H-NMR spectroscopy of the crude product. After purification by flash chromatography on silica gel (DCM) the product was obtained as a colourless solid (80 mg, 0.27 mmol, 91%).

Analytical Data[3]

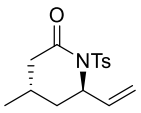
^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 0.95 (d, *J* = 6.5 Hz, 0.7H) [a], 1.02 (d, *J* = 6.5 Hz, 2.2H) [b], 1.44 (ddd, *J* = 14.0, 8.8, 5.8 Hz, 1H), 1.90 – 2.04 (m, 1H), 2.08 (dd, *J* = 16.1, 12.1 Hz, 1H), 2.24 – 2.36 (m, 1H), 2.36 – 2.47 (m, 4H), 5.06 – 5.16 (m, 1H), 5.16 – 5.33 (m, 2H), 5.72 – 5.94 (m, 1H), 7.24 – 7.33 (m, 2H), 7.91 (dd, *J* = 8.4, 4.7 Hz, 2H).ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 21.6, 21.7, 26.1, 37.2, 42.1, 58.3, 116.2, 129.07,129.16, 129.43, 136.70, 137.4, 139.2, 144.60, 171.3 ppm.

ESI-HRMS: *m/z* calcd for $C_{15}H_{22}O_3NNaS$ $[M+H]^+$ 316.0978 found 316.0982.

HPLC: LC-4, λ = 236 nm, *n*-heptane:IPA = 85:15, 0.4 mL/min, 22 °C: t_r = 38.8 min (minor) and t_r = 73.4 min (major), 95%ee; $[\alpha]_D^{25}$= − 67 (c = 1.0 $CHCl_3$)

Synthesis of (4S,6R)-4-methyl-1-tosyl-6-vinylpiperidin-2-one 3b



$C_{15}H_{19}NO_3S$
293,38

A screw-cap flask was flame-dried, cooled to room temperature under vacuum and backfilled with argon using a standard SCHLENK line apparatus. The screw-cap flask was charged with (S)-3-methyl-N-tosylhepta-5,6-dienamide (88 mg, 0.3 mmol, 1.0 equiv.) the flask was evacuated for 15 min and backfilled with argon three times. Then $Pd(dba)_2$ (4.3 mg, 0.0075 mmol, 2.5 mol%), dppf (8.3 mg, 0.015 mmol, 5.0 mol%) and HOAcCl (5.7 mg, 0.06 mmol, 20 mol%) was added under a flow of argon followed by freshly distilled DCE (10 mL). The flask was sealed and stirred at 80 °C overnight. The flask was sealed and stirred at room temperature overnight. The reaction mixture was filtered, concentrated and the **d.r.** ratio (**d.r. = 78/12**) was determined by ^{1}H-NMR spectroscopy of the crude product. After purification by flash chromatography on silica gel (DCM) the product was obtained as a colourless solid (84 mg, 0.29 mmol, 96%).

Analytical Data[3]

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 0.95 (d, *J* = 6.5 Hz, 3H), 1.65 (ddd, *J* = 13.8, 12.4, 5.3 Hz, 1H), 1.88 – 2.03 (m, 2H), 2.05 – 2.12 (m, 1H), 2.41 (s, 3H), 2.52 (ddd, *J* = 17.7, 5.7, 2.0 Hz, 1H), 5.16 – 5.34 (m, 3H), 5.85 (ddd, *J* = 17.1, 10.5, 5.4 Hz, 1H), 7.23 – 7.34 (m, 2H), 7.85 – 8.00 (m, 2H) ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 21.3, 21.7, 23.2, 37.1, 41.8, 58.5, 117.6, 129.1, 129.4, 136.4, 137.4, 144.64, 170.1 ppm.

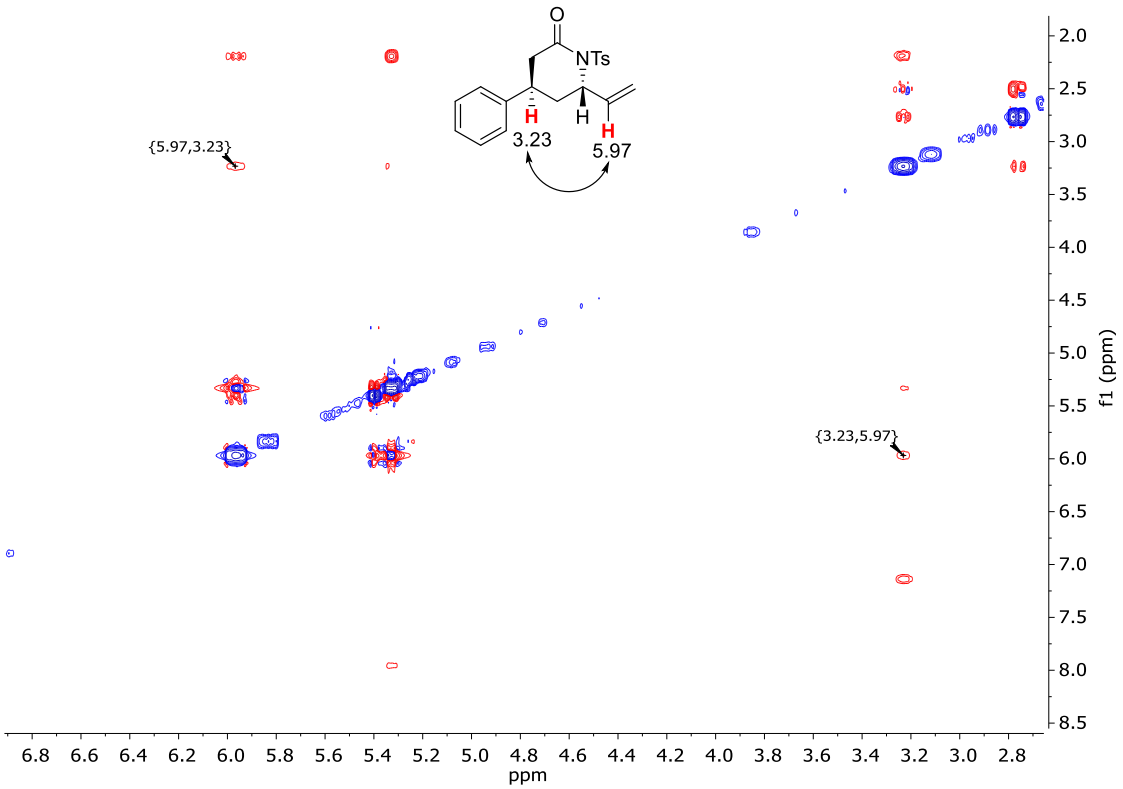
ESI-HRMS: *m/z* calcd for $C_{15}H_{20}O_3NS$ $[M+H]^+$ 294.1158 found 294.1158.

HPLC: LC-4, λ = 236 nm, *n*-heptane:IPA = 85:15, 0.4 mL/min, 22 °C: t_r = 44.6 min (major) and t_r = 77.6 min (minor), 95% ee. $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25}}$= − 19 (c = 0.61 $CHCl_3$)

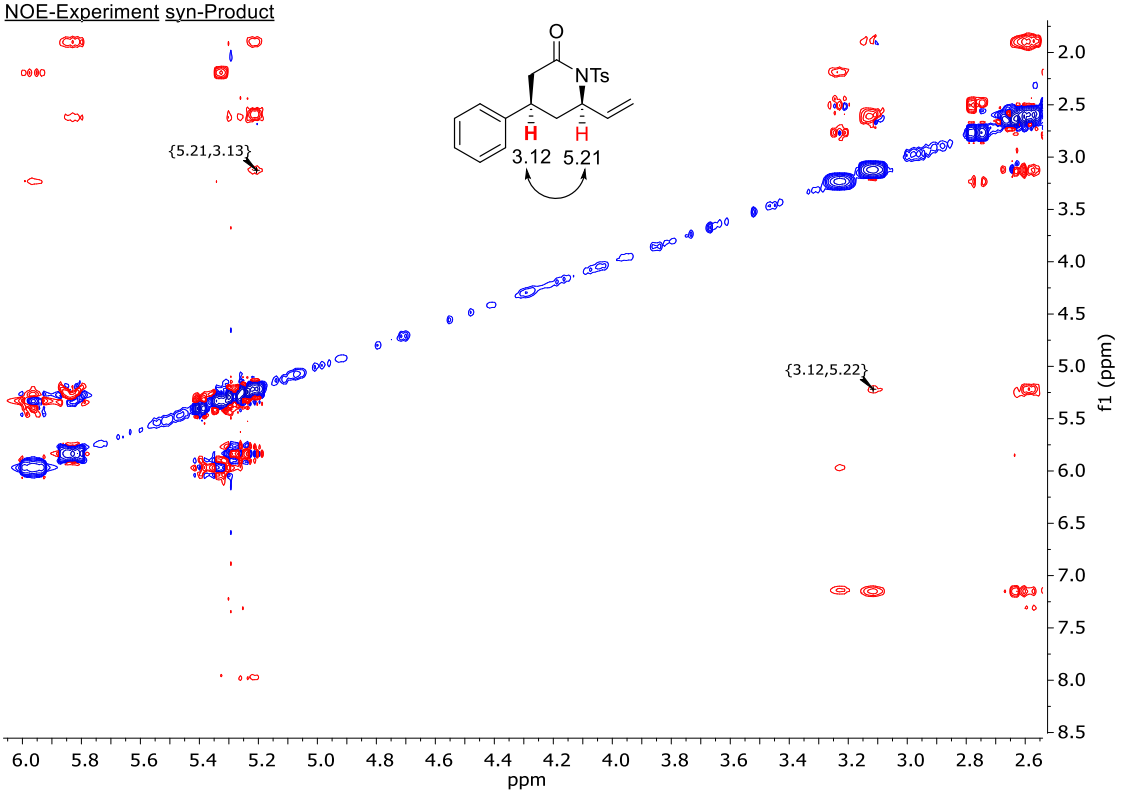
Relative configuration

NOE-Experiment

NOE-Experiment anti-Product

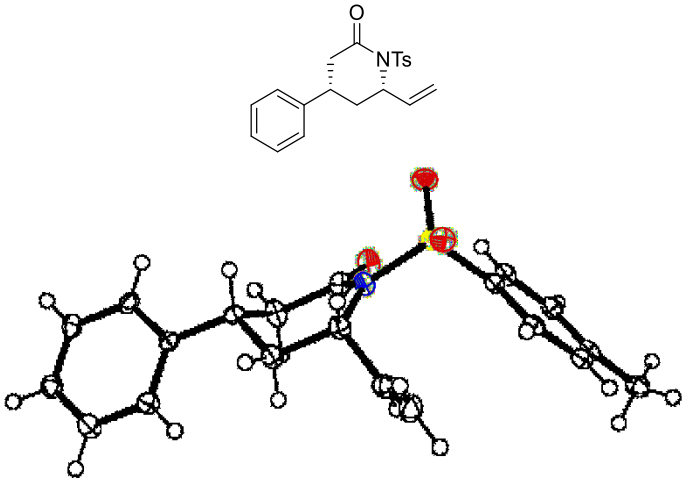


NOE-Experiment syn-Product



Crystal data

Crystal structure



Experimental. Single colourless block-shaped crystals of **2a** were obtained by recrystallisation from .... A suitable crystal (0.30×0.25×0.22) mm^3 was selected and mounted on a MITIGEN holder in perfluoroether oil on a Bruker SMART APEX2 area detector diffractometer. The crystal was kept at T = 100 K during data collection. Using **Olex2** (Dolomanov et al., 2009), the structure was solved with the **ShelXT** (Sheldrick, 2015) structure solution program, using the Intrinsic Phasing solution method. The model was refined with version 2018/3 of **ShelXL** (Sheldrick, 2015) using Least Squares minimisation.

Crystal Data. $C_{20}H_{21}NO_3S$, M_r = 355.44, monoclinic, $P2_1/n$ (No. 14), a = 8.136(8) Å, b = 17.429(15) Å, c = 13.045(14) Å, □ = 105.20(3)°, α = γ = 90°, V = 1785(3) $Å^3$, T = 100 K, Z = 4, Z' = 1, μ(MoK$_\alpha$) = 0.200, 20123 reflections measured, 4497 unique (R_{int} = 0.0302) which were used in all calculations. The final wR_2 was 0.0884 (all data) and R_1 was 0.0349 (I > 2(I)).

Compound	2a
CCDC	1845388
Formula	$C_{20}H_{21}NO_3S$
$D_{calc.}$/ g cm^{-3}	1.323
μ/mm^{-1}	0.200
Formula Weight	355.44
Colour	colourless
Shape	block
Size/mm^3	0.30×0.25×0.22
T/K	100
Crystal System	monoclinic
Space Group	$P2_1/n$
a/Å	8.136(8)
b/Å	17.429(15)
c/Å	13.045(14)
α/°	90
β/°	105.20(3)
γ/°	90
V/$Å^3$	1785(3)
Z	4
Z'	1
Wavelength/Å	0.710730
Radiation type	MoK□
Θ_{min}/°	1.996
Θ_{max}/°	28.643
Measured Refl.	20123
Independent Refl.	4497
Reflections Used	4117
R_{int}	0.0302
Parameters	311
Restraints	529
Largest Peak	0.376
Deepest Hole	-0.361
GooF	1.058
wR_2 (all data)	0.0884
wR_2	0.0863
R_1 (all data)	0.0383
R_1	0.0349

A colourless block-shaped crystal with dimensions 0.30×0.25×0.22 mm^3 was mounted on a MITIGEN holder in perfluoroether oil. X-ray diffraction data were collected using a Bruker SMART APEX2 area detector diffractometer equipped with a Oxford Cryosystems 800 low-temperature device, operating at T = 100 K.

Data were measured using ω and ϕ scans scans of 0.50 ° per frame for 40.00 s using MoK□ radiation (microfocus sealed X-ray tube, 50 kV, 1 mA). The total number of runs and images was based on the strategy calculation from the program **APEX2** (Bruker).The maximum resolution achieved was Θ = 28.643°.

Cell parameters were retrieved using the **SAINT** (Bruker, V8.38A, after 2013) software and refined using **SAINT** (Bruker, V8.38A, after 2013) on 9898 reflections, 49% of the observed reflections. Data reduction was performed using the **SAINT** (Bruker, V8.38A, after 2013) software which corrects for Lorentz polarisation. The final completeness is 99.90% out to 28.643° in Θ.

A multi-scan absorption correction was performed using SADABS-2016/2 (Bruker,2016/2) was used for absorption correction. wR_2(int) was 0.1108 before and 0.0416 after correction. The Ratio of minimum to maximum transmission is 0.9335. The λ/2 correction factor is Not present. The absorption coefficient μ of this material is 0.200 mm^{-1} at this wavelength (λ = 0.71073Å) and the minimum and maximum transmissions are 0.6962 and 0.7458..

The structure was solved in the space group $P2_1/n$ (# 14) by Intrinsic Phasing using the **ShelXT** (Sheldrick, 2015) structure solution program and refined by Least Squares using version 2018/3 of **ShelXL** (Sheldrick, 2015). All non-hydrogen atoms were refined anisotropically. Hydrogen atom positions were calculated geometrically and refined using the riding model.

_exptl_absorpt_process_details: SADABS-2016/2 (Bruker,2016/2) was used for absorption correction. wR_2(int) was 0.1108 before and 0.0416 after correction. The Ratio of minimum to maximum transmission is 0.9335. The λ/2 correction factor is Not present.

There is a single molecule in the asymmetric unit, which is represented by the reported sum formula. In other words: Z is 4 and Z' is 1.

Table 1: Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å²×10^3) for **10**. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{ij}.

Atom	x	y	z	U_{eq}
S1	3417.5(4)	5196.6(2)	8129.6(2)	17.73(8)
N1	5087.2(13)	5802.0(6)	8595.9(8)	18.6(2)
O1	6693.7(12)	5182.5(5)	7638.9(7)	25.2(2)
C1	4757.2(15)	6517.0(7)	9167.2(10)	19.4(2)
O2	4050.9(12)	4422.7(5)	8252.4(7)	24.7(2)
C2	3677.3(17)	7078.9(7)	8390.6(10)	23.7(3)
C3	2292.1(17)	7417.7(8)	8529.5(11)	28.6(3)
O3	2168.6(11)	5425.6(5)	8674.6(7)	21.61(19)
C4	6419(3)	6952.3(18)	9705(3)	24.1(6)
C5	8001.1(16)	6438.0(8)	9981.7(12)	15.5(3)
C6	8149(4)	6125(3)	8906(3)	23.5(6)
C7	6614.5(15)	5655.2(7)	8318.5(10)	20.7(2)
C8	9638(2)	6856.5(10)	10544.0(14)	15.6(3)
C9	9751(3)	7660.7(12)	10625.1(17)	19.8(4)
C10	11288(3)	8025.5(18)	11110(3)	24.1(5)
C11	12748(4)	7586.8(15)	11528(3)	22.4(5)

Atom	x	y	z	U_{eq}
C12	12662(3)	6784.8(16)	11462(2)	21.0(5)
C13	11119(3)	6422.9(13)	10973.2(16)	19.0(4)
C14	2618.8(15)	5403.8(7)	6759.0(9)	17.5(2)
C15	3317.2(15)	5046.0(7)	6004.2(10)	20.3(2)
C16	2657.3(16)	5227.6(7)	4929.8(10)	21.0(2)
C17	1306.8(15)	5747.4(7)	4594.2(10)	19.0(2)
C18	597.2(15)	6079.8(7)	5365.3(10)	18.8(2)
C19	1248.3(15)	5914.0(7)	6445.7(10)	18.2(2)
C20	646.0(18)	5950.7(8)	3428.0(10)	24.3(3)
C5A	8005(13)	6697(7)	9513(11)	22.2(18)
C8A	9629(17)	7032(8)	10272(12)	18(2)
C9A	9960(20)	7799(9)	10471(15)	20(2)
C10A	11550(30)	7988(15)	11150(30)	22(2)
C11A	12790(30)	7455(14)	11590(30)	22(2)
C12A	12400(30)	6684(14)	11420(20)	22(2)
C13A	10850(20)	6514(11)	10759(14)	23(2)
C4A	6487(13)	6753(10)	9996(10)	25.5(18)
C6A	8232(18)	5925(8)	9073(13)	18.9(19)

Table 2: Anisotropic Displacement Parameters ($\times 10^4$) **10**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2} \times U_{11} + ... + 2hka^* \times b^* \times U_{12}]$

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
S1	16.39(14)	16.01(15)	21.65(15)	-0.66(10)	6.49(11)	0.89(10)
N1	14.8(5)	19.2(5)	22.5(5)	-4.9(4)	6.0(4)	1.2(4)
O1	21.0(4)	29.5(5)	25.8(5)	-9.1(4)	7.7(4)	2.6(4)
C1	16.7(5)	19.1(6)	23.1(6)	-6.1(4)	6.5(4)	1.8(4)
O2	25.8(5)	17.2(4)	31.0(5)	1.1(4)	7.2(4)	3.4(4)
C2	29.7(7)	19.3(6)	23.0(6)	-2.5(5)	8.7(5)	0.2(5)
C3	24.9(6)	26.0(7)	30.7(7)	-5.1(5)	-0.3(5)	4.5(5)
O3	19.5(4)	23.2(4)	24.5(4)	0.4(3)	10.0(3)	0.2(3)
C4	15.9(8)	17.2(11)	35.1(14)	-5.0(9)	-0.7(8)	4.8(7)
C5	15.7(6)	15.4(6)	16.1(7)	1.4(5)	5.4(5)	1.9(5)
C6	19.4(9)	31.1(15)	22.2(11)	-7.3(9)	9.3(8)	-4.4(10)
C7	16.6(5)	25.4(6)	20.9(6)	-2.4(5)	6.5(4)	2.1(5)
C8	16.2(6)	16.9(8)	14.4(7)	1.1(5)	5.0(6)	1.8(6)
C9	16.4(8)	18.7(9)	24.9(9)	-0.5(6)	6.8(6)	1.6(6)
C10	19.8(11)	21.9(8)	30.8(9)	-4.2(7)	6.9(9)	0.1(8)
C11	18.1(8)	25.1(12)	23.8(10)	-0.3(9)	4.9(7)	-3.8(9)
C12	14.4(8)	27.3(11)	20.5(7)	0.2(7)	2.8(7)	0.0(7)
C13	17.1(9)	19.5(8)	18.9(9)	1.4(6)	1.8(7)	5.0(6)
C14	15.8(5)	15.8(5)	21.2(5)	-2.4(4)	5.6(4)	-2.1(4)
C15	16.1(5)	18.6(6)	26.9(6)	-5.2(5)	7.1(5)	-0.5(4)
C16	19.5(6)	21.2(6)	24.5(6)	-7.5(5)	9.9(5)	-4.4(5)
C17	19.4(6)	15.9(5)	22.5(6)	-3.3(4)	7.0(5)	-6.7(4)
C18	17.9(5)	15.0(5)	24.2(6)	-1.8(4)	7.0(5)	-1.9(4)
C19	17.6(5)	15.9(5)	22.8(6)	-3.2(4)	8.3(4)	-1.5(4)
C20	31.2(7)	21.1(6)	21.9(6)	-2.3(5)	9.3(5)	-3.7(5)
C5A	18(3)	26(3)	22(3)	1(3)	5(3)	0(3)
C8A	12(3)	21(4)	20(4)	4(3)	5(3)	2(3)
C9A	20(3)	18(3)	26(4)	2(3)	15(3)	3(3)
C10A	19(4)	21(3)	28(4)	2(3)	9(3)	-5(3)
C11A	16(3)	26(4)	24(4)	8(4)	7(3)	6(3)
C12A	23(4)	20(3)	23(4)	6(3)	6(3)	6(3)
C13A	21(4)	22(4)	21(4)	-3(3)	-1(3)	-1(3)
C4A	25(3)	26(4)	25(3)	-1(3)	5(3)	-4(3)
C6A	17(3)	18(4)	24(3)	0(3)	9(3)	7(3)

Table 3: Bond Lengths in Å for **10**.

Atom	Atom	Length/Å
S1	N1	1.7017(15)
S1	O2	1.4378(14)
S1	O3	1.4409(13)
S1	C14	1.772(2)
N1	C1	1.5117(17)
N1	C7	1.4058(19)
O1	C7	1.2243(17)
C1	C2	1.513(2)
C1	C4	1.549(3)
C1	C4A	1.588(10)
C2	C3	1.326(2)
C4	C5	1.532(3)
C5	C6	1.540(3)
C5	C8	1.527(2)
C6	C7	1.521(3)
C7	C6A	1.498(13)
C8	C9	1.407(3)
C8	C13	1.408(2)
C9	C10	1.398(3)
C10	C11	1.397(3)
C11	C12	1.401(3)
C12	C13	1.401(3)
C14	C15	1.4052(19)
C14	C19	1.4008(19)
C15	C16	1.399(2)
C16	C17	1.403(2)
C17	C18	1.4090(19)
C17	C20	1.517(2)
C18	C19	1.400(2)
C5A	C8A	1.543(13)
C5A	C4A	1.530(13)
C5A	C6A	1.493(14)
C8A	C9A	1.375(15)
C8A	C13A	1.368(15)
C9A	C10A	1.400(17)
C10A	C11A	1.381(17)
C11A	C12A	1.385(17)
C12A	C13A	1.364(16)

Table 4: Bond Angles in ° for **10**.

Atom	Atom	Atom	Angle/°
N1	S1	C14	106.35(6)
O2	S1	N1	108.22(8)
O2	S1	O3	118.91(6)
O2	S1	C14	109.24(6)
O3	S1	N1	104.60(8)
O3	S1	C14	108.77(8)
C1	N1	S1	117.32(9)
C7	N1	S1	118.16(10)
C7	N1	C1	124.06(10)
N1	C1	C2	110.52(12)
N1	C1	C4	112.35(12)
N1	C1	C4A	108.0(5)
C2	C1	C4	105.71(19)
C2	C1	C4A	122.9(7)
C3	C2	C1	124.17(13)
C5	C4	C1	113.58(19)
C4	C5	C6	104.7(3)
C8	C5	C4	114.01(15)
C8	C5	C6	109.90(15)
C7	C6	C5	113.6(2)
N1	C7	C6	115.90(17)
N1	C7	C6A	117.2(6)
O1	C7	N1	121.78(12)
O1	C7	C6	122.32(17)
O1	C7	C6A	118.9(6)
C9	C8	C5	122.94(16)
C9	C8	C13	118.20(17)
C13	C8	C5	118.83(17)
C10	C9	C8	121.4(2)
C11	C10	C9	119.7(3)
C10	C11	C12	119.9(2)
C13	C12	C11	120.1(2)
C12	C13	C8	120.7(2)
C15	C14	S1	120.52(11)
C19	C14	S1	118.49(9)
C19	C14	C15	120.96(12)
C16	C15	C14	118.82(13)
C15	C16	C17	121.47(11)
C16	C17	C18	118.49(12)
C16	C17	C20	120.44(11)
C18	C17	C20	121.07(13)
C19	C18	C17	121.08(13)
C18	C19	C14	119.14(11)
C4A	C5A	C8A	111.1(10)
C6A	C5A	C8A	114.6(10)
C6A	C5A	C4A	114.3(12)
C9A	C8A	C5A	125.7(13)
C13A	C8A	C5A	116.2(12)
C13A	C8A	C9A	118.1(14)
C8A	C9A	C10A	116.9(16)
C11A	C10A	C9A	124(2)
C10A	C11A	C12A	118(2)
C13A	C12A	C11A	116.7(18)
C12A	C13A	C8A	126.0(17)
C5A	C4A	C1	111.7(8)
C5A	C6A	C7	111.1(9)

Table 5: Hydrogen Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for **10**. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{ij}.

Atom	x	y	z	U_{eq}
H1A	4153.44	6374.33	9715.94	23
H1B	4002.87	6341.47	9615.23	23
H2	4013.05	7196.4	7763.69	28
H3A	1922.14	7312.54	9147.94	34
H3B	1669.87	7765.56	8010.46	34
H4A	6594.44	7365.45	9223.44	29
H4B	6286.61	7196.78	10363.51	29
H5	7808.05	6002.07	10434.81	19
H6A	8295.23	6561.13	8451.97	28
H6B	9181.55	5800.49	9026.87	28
H9	8762.32	7961.98	10344.73	24
H10	11340.8	8569.43	11154.66	29
H11	13796.46	7831.94	11856.42	27
H12	13652.59	6485.97	11748.69	25
H13	11070.03	5878.85	10931.02	23
H15	4221.22	4687.29	6219.52	24
H16	3134.65	4993.59	4416.17	25
H18	-338.52	6422.05	5148.23	23
H19	767.03	6144.56	6959.95	22
H20A	764.89	5506.21	2992.97	36
H20B	1303.52	6381.66	3259.5	36
H20C	-557.46	6095.63	3278.05	36
H5A	7727.6	7049.09	8886.73	27
H9A	9154.64	8182.67	10164.28	23
H10A	11793.99	8514.54	11310.26	27
H11A	13880.27	7613.01	12006.6	26
H12A	13172.93	6293.81	11751.63	26
H13A	10586.58	5985.89	10621.79	27
H4AA	6391.07	7286.34	10236.43	31
H4AB	6682.44	6413.44	10624.44	31
H6AA	8587.83	5552.4	9663.06	23
H6AB	9143.07	5951.06	8698.88	23

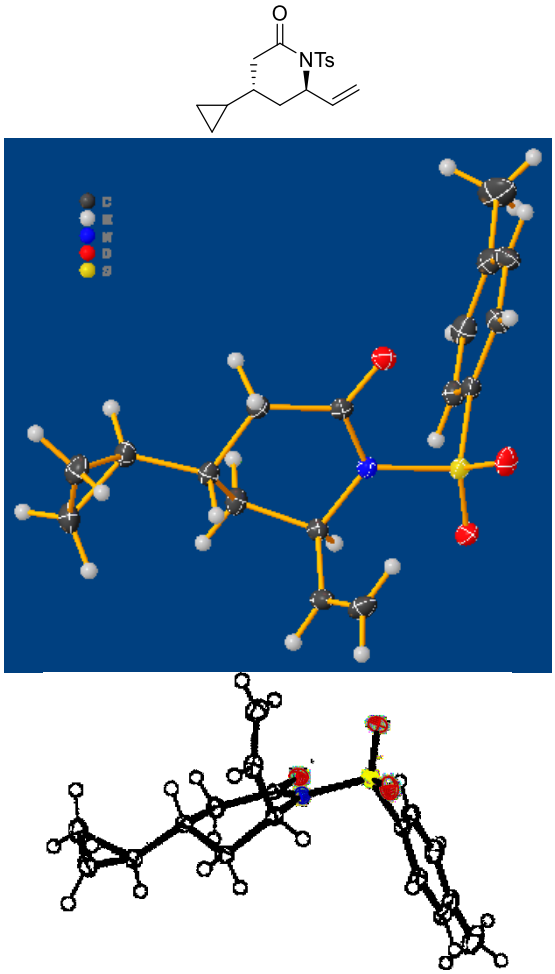
Table 6: Atomic Occupancies for all atoms that are not fully occupied in **10**.

Atom	Occupancy
H1A	0.810(13)
H1B	0.190(13)
C4	0.810(13)
H4A	0.810(13)
H4B	0.810(13)
C5	0.889(4)
H5	0.889(4)
C6	0.827(15)
H6A	0.827(15)
H6B	0.827(15)
C8	0.889(4)
C9	0.889(4)
H9	0.889(4)
C10	0.889(4)
H10	0.889(4)
C11	0.889(4)
H11	0.889(4)
C12	0.889(4)
H12	0.889(4)

Atom	Occupancy
C13	0.889(4)
H13	0.889(4)
C5A	0.111(4)
H5A	0.111(4)
C8A	0.111(4)
C9A	0.111(4)
H9A	0.111(4)
C10A	0.111(4)
H10A	0.111(4)
C11A	0.111(4)
H11A	0.111(4)
C12A	0.111(4)
H12A	0.111(4)
C13A	0.111(4)
H13A	0.111(4)
C4A	0.190(13)
H4AA	0.190(13)
H4AB	0.190(13)
C6A	0.173(15)

Atom	Occupancy
H6AA	0.173(15)
H6AB	0.173(15)

Crystal Structure



Experimental. Single colourless needle-shaped crystals of **6b** were recrystallised from ethyl acetate by slow evaporation. A suitable crystal (0.15×0.09×0.05) mm^3 was selected and mounted on a MITIGEN holder in perfluoroether oil on a Bruker SMART APEX2 area detector diffractometer. The crystal was kept at T = 100(2) K during data collection. Using **Olex2** (Dolomanov et al., 2009), the structure was solved with the **ShelXT** (Sheldrick, 2015) structure solution program, using the Intrinsic Phasing solution method. The model was refined with version 2018/3 of **ShelXL** (Sheldrick, 2015) using Least Squares minimisation.

Crystal Data. $C_{17}H_{21}NO_3S$, M_r = 319.41, orthorhombic, $P2_12_12_1$ (No. 19), a = 5.89110(10) Å, b = 12.2990(3) Å, c = 22.4992(5) Å, $\alpha = \beta = \gamma = 90^\circ$, V = 1630.17(6) Å^3, T = 100(2) K, Z = 4, Z' = 1, μ(MoKα) = 0.210, 22098 reflections measured, 4988 unique (R_{int} = 0.0347) which were used in all calculations. The final wR_2 was 0.0890 (all data) and R_1 was 0.0359 (I > 2(I)).

Compound	6b
CCDC	1840179
Formula	$C_{17}H_{21}NO_3S$
$D_{calc.}$/ g cm^{-3}	1.301
μ/mm^{-1}	0.210
Formula Weight	319.41
Colour	colourless
Shape	needle
Size/mm^3	0.15×0.09×0.05
T/K	100(2)
Crystal System	orthorhombic
Flack Parameter	0.01(3)
Hooft Parameter	0.01(3)
Space Group	$P2_12_12_1$
a/Å	5.89110(10)
b/Å	12.2990(3)
c/Å	22.4992(5)
α/°	90
β/°	90
γ/°	90
V/Å^3	1630.17(6)
Z	4
Z'	1
Wavelength/Å	0.710730
Radiation type	MoKα
θ_{min}/°	1.810
θ_{max}/°	30.503
Measured Refl.	22098
Independent Refl.	4988
Reflections Used	4485
R_{int}	0.0347
Parameters	200
Restraints	0
Largest Peak	0.264
Deepest Hole	-0.327
GooF	1.030
wR_2 (all data)	0.0890
wR_2	0.0856
R_1 (all data)	0.0420
R_1	0.0359

A colourless needle-shaped crystal with dimensions 0.15×0.09×0.05 mm^3 was mounted on a MITIGEN holder in perfluoroether oil. X-ray diffraction data were collected using a Bruker SMART APEX2 area detector diffractometer equipped with a Oxford Cryosystems 800 low-temperature device, operating at T = 100(2) K.

Data were measured using ω and ϕ scans scans of 0.50 ° per frame for 60.00 s using MoK□ radiation (microfocus sealed X-ray tube, 50 kV, 1 mA). The total number of runs and images was based on the strategy calculation from the program **APEX2** (Bruker).The maximum resolution achieved was Θ = 30.503°.

Cell parameters were retrieved using the **SAINT** (Bruker, V8.38A, after 2013) software and refined using **SAINT** (Bruker, V8.38A, after 2013) on 6938 reflections, 31% of the observed reflections. Data reduction was performed using the **SAINT** (Bruker, V8.38A, after 2013) software which corrects for Lorentz polarisation. The final completeness is 100.00% out to 30.503° in Θ.

A multi-scan absorption correction was performed using SADABS-2016/2 (Bruker,2016/2) was used for absorption correction. wR_2(int) was 0.0887 before and 0.0413 after correction. The Ratio of minimum to maximum transmission is 0.9556. The λ/2 correction factor is Not present. The absorption coefficient μ of this material is 0.210 mm^{-1} at this wavelength (λ = 0.71073Å) and the minimum and maximum transmissions are 0.7132 and 0.7463.

The structure was solved in the space group $P2_12_12_1$ (# 19) by Intrinsic Phasing using the **ShelXT** (Sheldrick, 2015) structure solution program and refined by Least Squares using version 2018/3 of **ShelXL** (Sheldrick, 2015). All non-hydrogen atoms were refined anisotropically. Hydrogen atom positions were calculated geometrically and refined using the riding model.

_exptl_absorpt_process_details: SADABS-2016/2 (Bruker,2016/2) was used for absorption correction. wR_2(int) was 0.0887 before and 0.0413 after correction. The Ratio of minimum to maximum transmission is 0.9556. The λ/2 correction factor is Not present.

There is a single molecule in the asymmetric unit, which is represented by the reported sum formula. In other words: Z is 4 and Z' is 1.

The Flack parameter was refined to 0.01(3). Determination of absolute structure using Bayesian statistics on Bijvoet differences using the Olex2 results in 0.01(3). Note: The Flack parameter is used to determine chirality of the crystal studied, the value should be near 0, a value of 1 means that the stereochemistry is wrong and the model should be inverted. A value of 0.5 means that the crystal consists of a racemic mixture of the two enantiomers.

Table 7: Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for **22**. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{ij}.

Atom	x	y	z	U_{eq}
S1	9324.8(7)	4998.9(4)	5539.2(2)	16.18(10)
N1	8139(3)	4206.3(12)	6069.0(7)	15.4(3)
O1	11734(2)	4873.0(11)	5551.3(6)	22.3(3)
C1	8932(3)	4290.1(15)	6651.3(8)	15.8(4)
O2	8117(2)	4737.7(11)	5006.5(6)	21.9(3)
C2	7822(3)	3598.9(16)	7127.1(8)	19.0(4)
C3	6046(3)	2769.2(16)	6936.1(8)	17.4(4)
O3	10434(2)	4926.9(11)	6778.1(6)	19.1(3)

Atom	x	y	z	U_{eq}
C4	4726(3)	3255.1(16)	6418.6(8)	19.3(4)
C5	6272(3)	3462.2(15)	5888.8(8)	15.6(4)
C6	7145(4)	2402.7(15)	5640.5(8)	19.6(4)
C8	4493(3)	2434.7(15)	7436.7(9)	20.7(4)
C7	9289(4)	2109.7(17)	5595.8(9)	24.1(4)
C9	5038(4)	1436.5(18)	7798.2(9)	25.9(5)
C10	3092(3)	1423.8(17)	7360.9(9)	23.7(4)
C11	8617(3)	6335.9(15)	5742.0(8)	17.2(4)
C12	10131(3)	6957.2(16)	6066.3(9)	21.9(4)
C13	9537(4)	8013.8(16)	6215.8(9)	25.3(4)
C14	7459(4)	8455.3(16)	6044.3(9)	25.6(4)
C15	5979(4)	7819.2(16)	5710.2(9)	24.2(4)
C16	6535(3)	6755.5(16)	5556.9(9)	19.7(4)
C17	6805(6)	9588.7(19)	6228.6(12)	42.1(7)

Table 8: Anisotropic Displacement Parameters (×10^4) **22**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2} \times U_{11} + ... + 2hka^* \times b^* \times U_{12}]$

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
S1	16.54(19)	16.3(2)	15.7(2)	-0.10(18)	2.81(17)	0.01(18)
N1	16.9(7)	14.8(7)	14.3(7)	0.6(6)	1.4(6)	-0.4(6)
O1	17.7(6)	24.0(7)	25.3(7)	1.8(6)	7.2(6)	3.5(6)
C1	14.7(8)	15.3(8)	17.3(9)	-1.1(7)	-0.5(7)	4.1(6)
O2	28.7(8)	21.9(7)	15.2(6)	-0.3(5)	1.6(6)	-3.3(5)
C2	22.3(9)	20.3(9)	14.3(8)	0.4(7)	0.3(7)	-2.1(8)
C3	16.6(9)	18.6(9)	17.0(9)	0.9(7)	2.2(7)	1.6(7)
O3	16.3(6)	19.8(6)	21.3(6)	-2.6(5)	-0.1(5)	-0.2(6)
C4	14.5(8)	24.0(10)	19.5(9)	3.1(7)	0.8(7)	1.1(7)
C5	14.0(8)	16.9(9)	15.9(8)	1.6(7)	-1.7(7)	0.2(7)
C6	27.1(10)	16.1(9)	15.6(9)	-0.8(7)	-1.4(8)	-1.9(7)
C8	21.5(9)	18.4(9)	22.1(9)	1.6(7)	4.8(9)	1.4(8)
C7	31.8(10)	21.2(9)	19.2(9)	-3.7(7)	1.6(9)	6.3(8)
C9	30.7(11)	27.8(11)	19.2(9)	6.2(8)	2.4(8)	0.9(9)
C10	20.8(9)	25.8(10)	24.6(10)	6.3(8)	2.7(8)	-3.5(8)
C11	17.7(8)	16.7(9)	17.2(8)	1.1(7)	3.4(7)	0.1(7)
C12	22.3(9)	19.8(9)	23.6(9)	1.7(8)	-1.2(8)	-3.2(7)
C13	35.6(11)	17.6(9)	22.8(10)	-0.2(7)	-1.6(9)	-6.0(9)
C14	39.1(12)	16.7(9)	20.9(9)	3.9(8)	4.5(9)	2.9(9)
C15	26.2(10)	21.8(10)	24.6(10)	6.6(8)	3.1(8)	6.9(8)
C16	19.9(9)	19.8(9)	19.4(9)	2.8(7)	0.0(8)	0.2(7)
C17	71(2)	17.9(11)	37.4(14)	0.6(10)	2.7(14)	9.9(12)

Table 9: Bond Lengths in Å for **22**.

Atom	Atom	Length/Å
S1	N1	1.6910(16)
S1	O1	1.4277(14)
S1	O2	1.4302(14)
S1	C11	1.757(2)
N1	C1	1.395(2)
N1	C5	1.487(2)
C1	C2	1.515(3)
C1	O3	1.216(2)
C2	C3	1.523(3)
C3	C4	1.522(3)
C3	C8	1.508(3)
C4	C5	1.522(3)

Atom	Atom	Length/Å
C5	C6	1.508(3)
C6	C7	1.318(3)
C8	C9	1.507(3)
C8	C10	1.502(3)
C9	C10	1.511(3)
C11	C12	1.382(3)
C11	C16	1.395(3)
C12	C13	1.387(3)
C13	C14	1.394(3)
C14	C15	1.391(3)
C14	C17	1.504(3)
C15	C16	1.392(3)

Table 10: Bond Angles in ° for **22**.

Atom	Atom	Atom	Angle/°
N1	S1	C11	104.98(8)
O1	S1	N1	109.55(8)
O1	S1	O2	119.08(9)
O1	S1	C11	109.41(9)
O2	S1	N1	104.82(8)
O2	S1	C11	108.05(9)
C1	N1	S1	118.76(13)
C1	N1	C5	123.32(15)
C5	N1	S1	117.92(12)
N1	C1	C2	118.54(16)
O3	C1	N1	120.80(17)
O3	C1	C2	120.63(17)
C1	C2	C3	118.21(16)
C4	C3	C2	107.68(16)
C8	C3	C2	112.87(16)
C8	C3	C4	111.61(15)
C5	C4	C3	111.03(15)
N1	C5	C4	109.40(15)
N1	C5	C6	112.39(15)
C6	C5	C4	110.47(16)
C7	C6	C5	126.24(19)
C9	C8	C3	119.73(17)
C10	C8	C3	118.31(17)
C10	C8	C9	60.26(14)
C8	C9	C10	59.70(13)
C8	C10	C9	60.04(13)
C12	C11	S1	120.11(15)
C12	C11	C16	121.35(18)
C16	C11	S1	118.52(15)
C11	C12	C13	118.9(2)
C12	C13	C14	121.3(2)
C13	C14	C17	120.6(2)
C15	C14	C13	118.72(19)
C15	C14	C17	120.6(2)
C14	C15	C16	121.0(2)
C15	C16	C11	118.72(19)

Table 11: Torsion Angles in ° for **22**.

Atom	Atom	Atom	Atom	Angle/°
S1	N1	C1	C2	178.47(13)
S1	N1	C1	O3	0.6(2)
S1	N1	C5	C4	-152.69(13)
S1	N1	C5	C6	84.22(17)
S1	C11	C12	C13	179.41(16)
S1	C11	C16	C15	-179.20(15)
N1	S1	C11	C12	95.73(17)
N1	S1	C11	C16	-85.74(16)
N1	C1	C2	C3	5.6(3)
N1	C5	C6	C7	2.2(3)
O1	S1	N1	C1	52.40(16)
O1	S1	N1	C5	-128.36(14)
O1	S1	C11	C12	-21.76(18)
O1	S1	C11	C16	156.77(15)
C1	N1	C5	C4	26.5(2)
C1	N1	C5	C6	-96.6(2)
C1	C2	C3	C4	-35.5(2)
C1	C2	C3	C8	-159.11(16)
O2	S1	N1	C1	-178.73(13)
O2	S1	N1	C5	0.51(15)
O2	S1	C11	C12	-152.82(15)
O2	S1	C11	C16	25.71(18)
C2	C3	C4	C5	62.5(2)
C2	C3	C8	C9	-93.9(2)
C2	C3	C8	C10	-163.95(17)

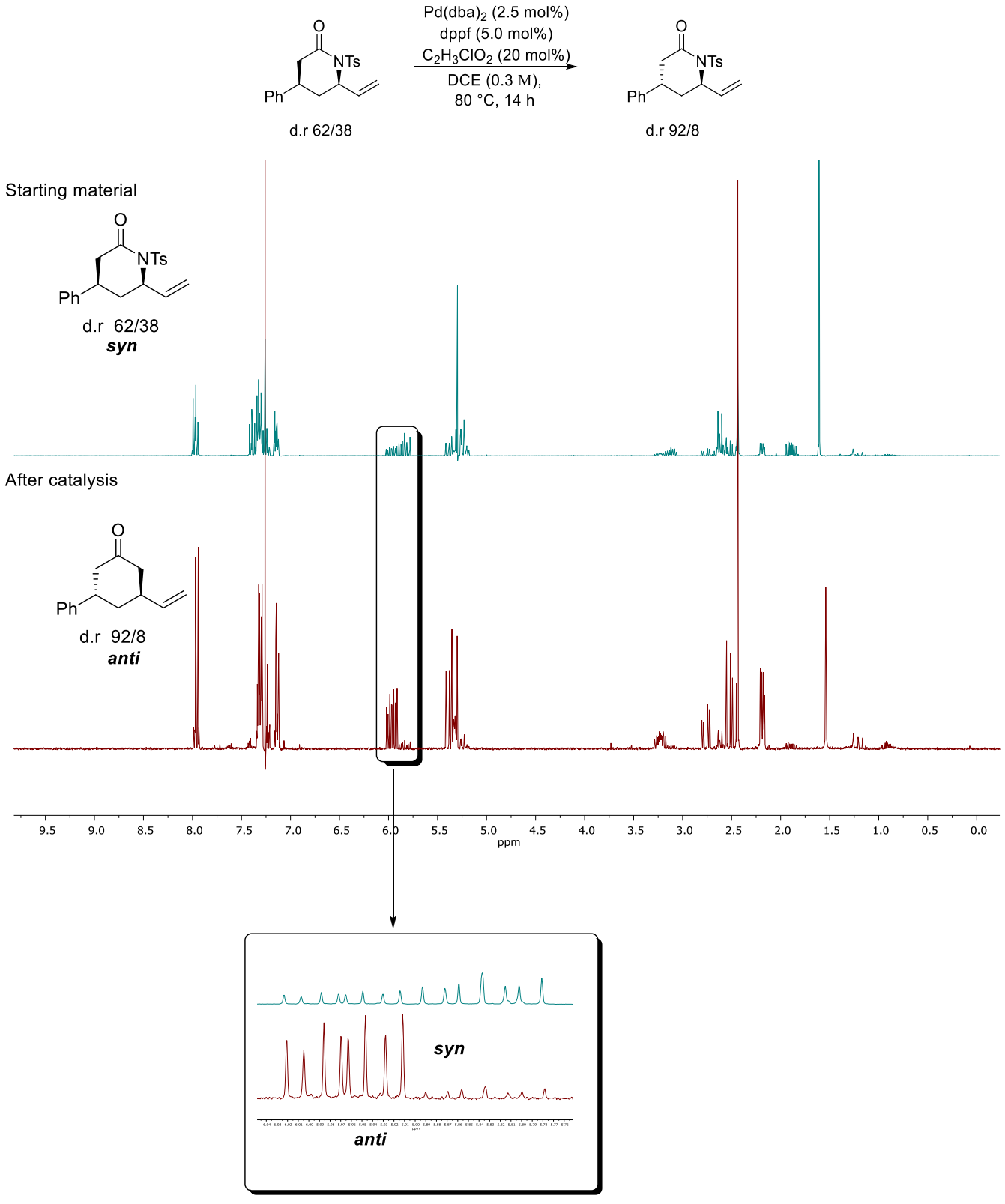
Atom	Atom	Atom	Atom	Angle/°
C3	C4	C5	N1	-58.2(2)
C3	C4	C5	C6	66.0(2)
C3	C8	C9	C10	-107.6(2)
C3	C8	C10	C9	109.94(19)
O3	C1	C2	C3	-176.51(17)
C4	C3	C8	C9	144.66(18)
C4	C3	C8	C10	74.6(2)
C4	C5	C6	C7	-120.3(2)
C5	N1	C1	C2	-0.7(3)
C5	N1	C1	O3	-178.57(16)
C8	C3	C4	C5	-173.15(16)
C11	S1	N1	C1	-64.99(15)
C11	S1	N1	C5	114.25(14)
C11	C12	C13	C14	-0.1(3)
C12	C11	C16	C15	-0.7(3)
C12	C13	C14	C15	-0.8(3)
C12	C13	C14	C17	177.8(2)
C13	C14	C15	C16	1.1(3)
C14	C15	C16	C11	-0.3(3)
C16	C11	C12	C13	0.9(3)
C17	C14	C15	C16	-177.6(2)

Table 12: Hydrogen Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for **22**. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{ij}.

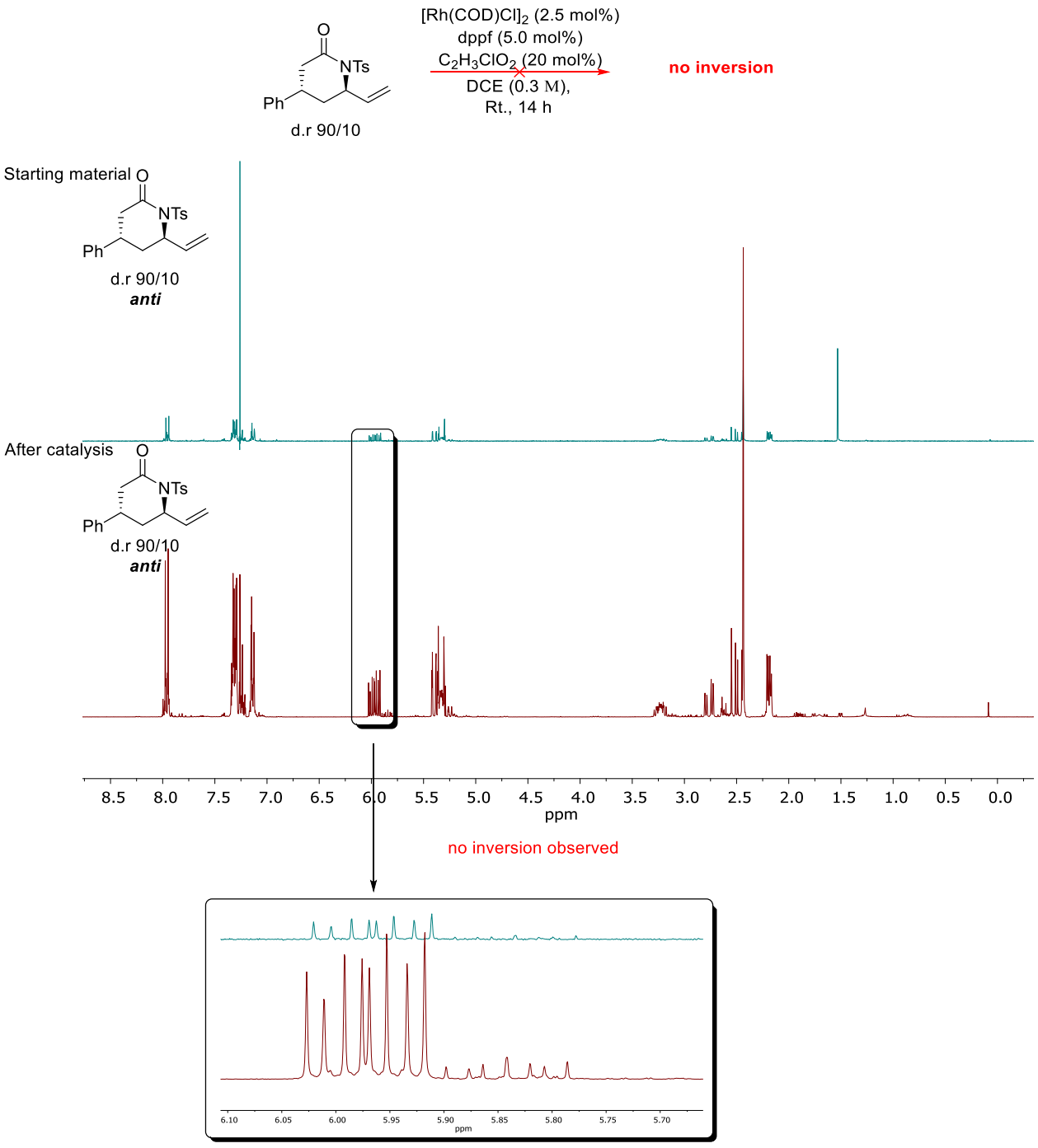
Atom	x	y	z	U_{eq}
H2A	7101.85	4095.58	7417.43	23
H2B	9039.58	3203.51	7339.95	23
H3	6854.36	2106.09	6789.92	21
H4A	3496.74	2750.48	6300.61	23
H4B	4019.98	3948	6545.15	23
H5	5360.89	3831.17	5572.77	19
H6	6042.1	1898.12	5503	24
H8	3747.24	3042.8	7657.9	25
H7A	10454.14	2586.64	5727.3	29
H7B	9670.82	1421.5	5432.14	29
H9A	4664.19	1448.65	8227.13	31
H9B	6423.73	1023.03	7694.11	31
H10A	3288.74	1001.39	6989.89	28
H10B	1529.6	1426.91	7522.79	28
H12	11553.23	6665.32	6184.92	26
H13	10567.4	8444.9	6439.3	30
H15	4569.08	8115.4	5584.93	29
H16	5515.09	6323.69	5330.5	24
H17A	8178.23	10012.41	6310.74	63
H17B	5864.52	9555.6	6587.44	63
H17C	5945.79	9936.3	5907.61	63

Thermodynamic and kinetic investigation

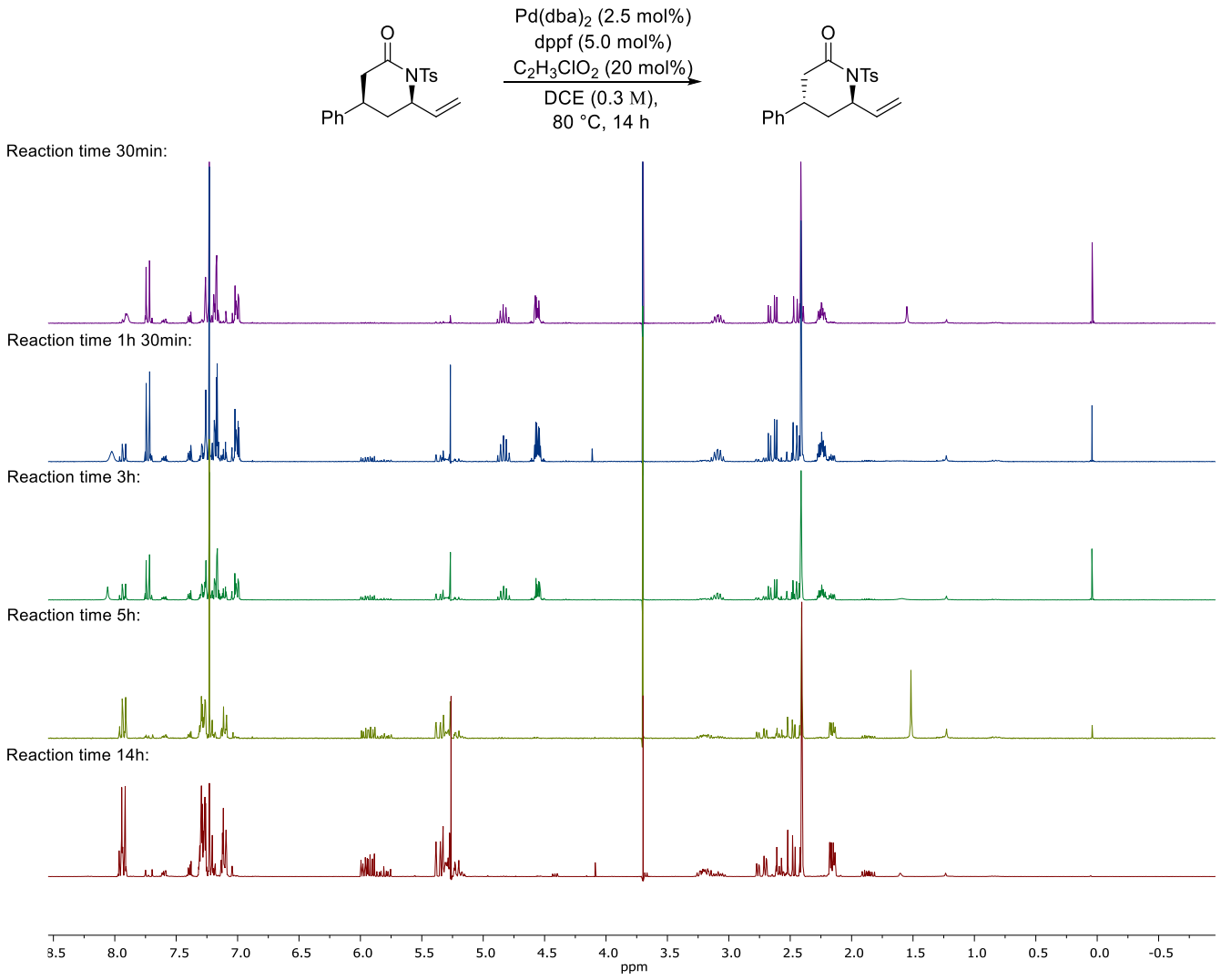
Inversion *syn* to *anti*



Inversion *anti* to *syn*



D.r. monitoring over 14 hours



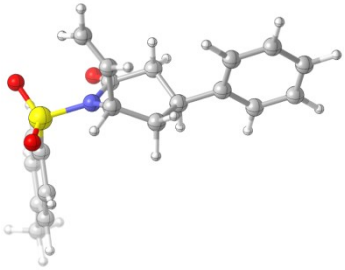
The experiment showed that the d.r., does not change during the reaction merely the yield increases over time.

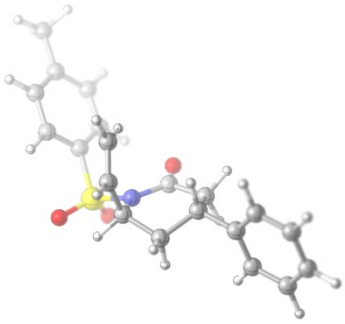
DFT calculations

Additional Information for DFT calculations

A conformer analysis was performed employing Spartan 10V1.10 with MMFF (Merck molecular force field). For the *anti*-diastereomer 13 conformers and for the *syn* diastereomer 9 conformers were found. For all conformers structure optimizations, using the BP86 functional in combination with the def2SVP2 basis set were carried out using Gaussian 09.[7] The most stable compounds were compared in energy and revealed that the *anti*-diastereomer is the more stable one.

	Syn	Anti
ΔE (kcal/mol)	-911211,96	-911213,32
ΔG (kcal/mol)	-911247,48	-911248,59





Cartesian coordinates for the optimized structures:

Syn:

C	1.68568	-0.26243	-1.33627
C	1.60709	0.01207	1.21385
N	-0.25205	-1.01686	0.01502
C	0.12705	-0.35402	1.18805
C	0.75434	-1.45008	-0.97197
C	2.07362	0.64411	-0.12358
S	-1.91706	-1.60329	-0.15876
O	-1.94929	-2.14324	-1.53871
O	-2.24496	-2.44826	1.00492
C	-2.92812	-0.11631	-0.12056
C	-4.59897	2.14463	-0.11328
C	-3.45862	0.33747	1.09949
C	-3.22226	0.52260	-1.33628
C	-4.05329	1.65383	-1.32027
C	-4.28983	1.46538	1.08910
C	-5.49854	3.35874	-0.09669
H	-5.08981	4.15195	0.56494
H	-6.50688	3.10446	0.29460
H	-5.62625	3.79070	-1.10870
H	-4.29145	2.16132	-2.26926
H	-2.81848	0.12314	-2.27833

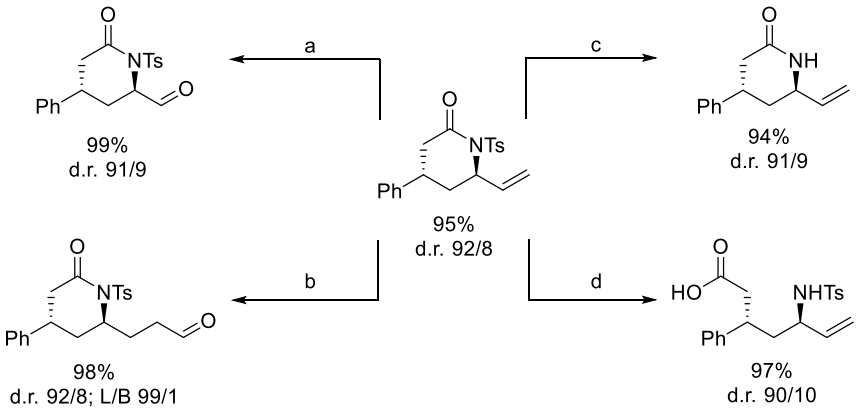
H	-4.70993	1.82956	2.04103
H	-3.20389	-0.18548	2.03107
H	2.18947	-0.91061	1.42493
H	1.75504	0.70659	2.06278
H	0.17832	-1.72286	-1.88408
H	1.18348	0.35940	-2.10476
H	2.59415	-0.67585	-1.82027
C	1.49814	-2.70918	-0.54769
C	1.13950	-3.54666	0.44118
O	-0.66369	-0.06871	2.08002
H	2.37396	-2.95163	-1.17827
H	1.71531	-4.46374	0.64304
H	0.24956	-3.35912	1.06593
H	1.51095	1.59619	-0.22687
C	3.55359	1.00974	-0.08738
C	6.30488	1.70525	0.00459
C	3.96340	2.35815	-0.15157
C	4.55057	0.01373	0.02578
C	5.91172	0.35605	0.07162
C	5.32543	2.70592	-0.10730
H	4.25946	-1.04899	0.08064
H	6.67192	-0.43650	0.16138
H	7.37251	1.97422	0.03984
H	5.62120	3.76595	-0.16095
H	3.20003	3.14956	-0.23841

Anti:

C	-2.13200	0.63346	1.16810
C	-1.76433	-0.12405	-1.18964
N	0.14425	0.69788	0.19704
C	-0.28293	0.24121	-1.05405
C	-0.61611	0.53799	1.45367
C	-2.55138	-0.40210	0.10737
S	1.66958	1.62580	0.27154
O	1.62919	2.62694	-0.80677
O	1.75161	2.03107	1.69450
C	3.00258	0.45785	-0.04600
C	5.18333	-1.25826	-0.49878
C	3.66710	-0.11061	1.05309
C	3.40778	0.20167	-1.36787
C	4.49407	-0.65769	-1.57937
C	4.75240	-0.96897	0.81475
C	6.35573	-2.17679	-0.75471
H	6.76340	-2.59615	0.18606
H	7.17922	-1.63938	-1.27223
H	6.06608	-3.02504	-1.41079
H	4.81794	-0.86672	-2.61225
H	2.86026	0.66026	-2.20237
H	5.28144	-1.41864	1.67080
H	3.33974	0.13067	2.07482
H	-1.82375	-0.97028	-1.90330
H	-2.20900	0.74773	-1.72208
H	-2.24045	-1.40025	0.48657
H	-0.33190	1.39497	2.10055

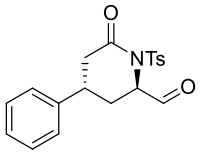
H	-2.37049	1.66364	0.82512
H	-2.68807	0.46939	2.11490
C	-0.26592	-0.73342	2.20666
C	0.50798	-1.74229	1.76979
C	-4.05706	-0.45494	-0.12261
C	-6.86493	-0.57701	-0.53248
C	-4.77571	-1.64525	0.12011
C	-4.77463	0.67556	-0.57585
C	-6.16345	0.61705	-0.77812
C	-6.16554	-1.70944	-0.08248
O	0.46447	0.21042	-2.02606
H	-0.72150	-0.79541	3.21280
H	0.69563	-2.62767	2.39786
H	0.99167	-1.71654	0.77951
H	-4.24398	1.62151	-0.77584
H	-6.70215	1.51111	-1.13097
H	-7.95384	-0.62360	-0.69241
H	-6.70397	-2.65078	0.11256
H	-4.23337	-2.53809	0.47412

Follow up Chemistry



Scheme: Follow-up chemistry. a) i) O_3, MeOH, −78 °C, ii) SMe_2, MeOH, −78 °C to rt, 99%; b) [{$Rh(CO)_2acac$}] (0.5 mol%), 6-DPPon (10 mol%), CO/H_2 (1:1, 10 bar), toluene, 80°C, 21 h, 98% (L/B 99/1); c) Li, naphthalene, THF, −78 °C to rt.; d) H_2O/IPA, LiOH, reflux, 17 h.

Synthesis of 6-oxo-4-phenyl-1-tosylpiperidine-2-carbaldehyde 18



$C_{19}H_{19}NO_4S$
357.42

A solution of 4-phenyl-1-tosyl-6-vinylpiperidin-2-one (82 mg, 0.23 mmol, 1.0 equiv.) in MeOH (3 mL) was cooled to −78 °C. Ozone was bubbled through the solution until the solution showed a blue colour (approx. 30 min) then, the reaction vessel was degassed with nitrogen until disappearance of the blue colour occurred. Me_2S (26 μL) was added and the reaction mixture was allowed to warm to room temperature. The solution was concentrated under recued pressure and the **d.r. (d.r. = 91/9)** was determined by 1H-NMR spectroscopy of the crude product. The residue was washed with pentane (5 mL) to obtain the desired product as white solid (81 mg, 0.22 mmol, 99%).

Analytical Data[3]

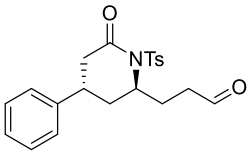
mp: decomposed at 213 °C

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 2.25 (ddd, *J* = 14.3, 12.6, 6.7 Hz, 1H), 2.46 (d, *J* = 0.7, 3H), 2.51 – 2.63 (m, 2H), 2.76 (ddd, *J* = 18.1, 5.6, 2.1 Hz, 1H), 2.84 – 2.93 (m, 1H), 5.21 (dd, *J* = 6.7, 2.6 Hz, 1H), 7.06 – 7.11 (m, 2H), 7.27 – 7.39 (m, 5H), 7.94 – 8.01 (m, 2H), 9.77 (s, 1H) Hz.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 21.8, 30.0, 34.7, 40.9, 63.6, 126.4, 127.7, 129.2, 129.3, 130.0, 135.5, 141.3, 145.4, 168.7, 197.1 ppm.

ESI-HRMS: *m/z* calcd for $C_{19}H_{20}O_4NS$ $[M+H]^+$ 358.1108 found 358.1107.

Synthesis of 3-6-oxo-4-phenyl-1-tosylpiperidin-2-yl)propanal 19



$C_{21}H_{23}NO_4S$
385.48

A solution of [$Rh(CO)_2$acac] (1.00 mg, 3.80 µmol, 1.2 mol%) and 6-DPPon (16.7 mg, 0.060 mmol, 20 mol%) in toluene (2.0 mL) was preformatted for 1 h at 80 °C (CO/H_2, 1:1, 10 bar). After this time the pressure was released and 4-phenyl-1-tosyl-6-vinylpiperidin-2-one (107 mg, 0.300 mmol, 1.0 equiv.) in toluene (1 mL) was added into the high-pressure autoclave and the mixture was flushed 3 times with CO/H_2. Afterwards CO/H_2 (1:1) was pressed on with 10 bar and the reaction-vessel was heated up to 80 °C and stirred for 21 h. The reaction mixture was filtrated, concentrated under reduced pressure and the L:B ratio (**L:B = 99:1**) and the d.r. (**d.r. = 92/8**) was determined by 1H-NMR spectroscopy of the crude product. After purification by flash column chromatography on silica (DCM:MeOH = 15:1) the product was obtained as colourless oil (113 mg, 0.29 mmol, 98%).

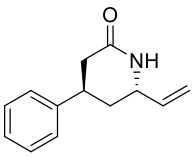
Analytical Data[3]

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 1.98 – 2.06 (m, 1H), 2.13 – 2.20 (m, 2H), 2.32 – 2.38 (m, 1H), 2.40 – 2.50 (m, 4H), 2.72 (ddt, *J* = 7.6, 6.9, 1.2, Hz, 2H), 2.82 (ddd, *J* = 18.2, 6.5, Hz, 1H), 3.33 (dddd, *J* = 12.8, 10.5, 6.5, 3.7 Hz, 1H), 4.67 (dtd, *J* = 8.4, 5.4, 5.4, 2.5 Hz, 1H), 7.12 – 7.15 (m, 2H), 7.29 – 7.34 (m, 5H), 7.90 – 7.93 (m, 2H), 9.85 (t, *J* = 1.0, Hz, 1H).

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 21.7, 27.4, 33.8, 34.5, 40.9, 56.0, 126.5, 127.3, 129.0, 129.0, 129.4, 136.4, 142.6, 144.9, 169.3, 200.5 ppm.

ESI-HRMS: *m/z* calcd for $C_{21}H_{23}O_4NNaS$ $[M+Na]^+$ 408.1240 found 408.1236.

Synthesis of 4-phenyl-6-vinylpiperidin-2-one 20



$C_{13}H_{15}NO$
201.26

Naphthalene (0.21 g 1.6 mmol, 6.8 equiv.) was dissolved in dry THF (3 mL). Lithium (12 mg, 1.6 mmol, 6.8 equiv.) was added, the mixture was sonicated for 30 min and then stirred at room temperature for 2 h in order to obtain a dark green Li-naphthalenide solution. 4-phenyl-1-tosyl-6-vinylpiperidin-2-one (82 mg, 0.23 mmol, 1.o equiv.) was dissolved in THF (1 mL), cooled to −78°C and the Li-naphthalenide solution (3 mL) was added dropwise at this temperature. The reaction was stirred for 30 min at −78 °C then allowed to warm to room temperature and stirred for further 2 h. The reaction was quenched through the addition of NH_4Cl (10 mL). The layers were separated, the aqueous layer was extracted with EE (2 × 15 mL), the combined organic layers were washed with brine (40 mL) and dried over Na_2SO_4. The reaction was, concentrated under reduced pressure and the **d.r.** (**d.r. = 91/9**) was determined by 1H-NMR spectroscopy of the crude product. The Residue was purified by flash chromatography on silica gel (DCM:MeOH = 40:1). The Product was obtained as brown oil (44 mg, 0.22 mmol, 94%).

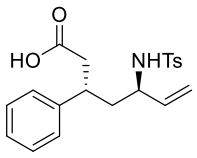
Analytical Data[3]

^{1}H-NMR (500.1 MHz, $CDCl_3$): δ = 1.91 – 2.03 (m, 1H), 2.10 – 2.22 (m, 1H), 2.54 (dd, *J* = 17.7, 9.5 Hz, 1H), 2.70 (ddd, *J* = 17.7, 5.5 Hz, 1.5, 1H), 3.21 (tdd, *J* = 9.4, 5.5, 3.2 Hz, 1H), 4.05 (ddtt, *J* = 5.6, 4.2, 2.7, 1.3 Hz, 1H), 5.21 – 5.31 (m, 2H), 5.88 (ddd, *J* = 17.1, 10.3, 5.3 Hz, 1H), 6.10 (s, 1H), 7.16 – 7.24 (m, 2H), 7.24 – 7.28 (m, 1H), 7.32 – 7.37 (m, 2H).

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 34.2, 34.8, 38.0, 52.9, 116.4, 126.8, 126.9, 128.9, 138.9, 143.1, 172.1 ppm.

ESI-HRMS: *m/z* calcd for $C_{20}H_{23}O_4NNaS$ $[M+Na]^+$ 224.1051 found 224.1050.

Synthesis of 5-((4-methylphenyl)sulfonamido)-3-phenylhept-6-enoic acid 21



$C_{20}H_{23}NO_4S$
373.47

To a solution of 4-phenyl-1-tosyl-6-vinylpiperidin-2-one (82 mg, 0.23 mmol, 1.o equiv.) in IPA (4 mL) was added LiOH (6.0 mg, 0.50 mmol, 2.1 equiv.) and H_2O (0.4 mL). The solution was refluxed overnight, cooled to room temperature and acidified with aqueous HCl (2 M). The layers were separated, the aqueous layer was execrated with EtOAc (3 × 10 mL). The combined organic layers were washed with brine (15 mL), H_2O (15 mL) and dried over Na_2SO_4.

The reaction mixture was concentrated under reduced pressure and the **d.r**. (**d.r. = 90/10**) was determined by 1H-NMR spectroscopy of the crude product. The product was obtained as a colourless wax (113 mg, 0.29 mmol, 97%), after purification by flash column chromatography on silica (DCM:MeOH = 15:1).

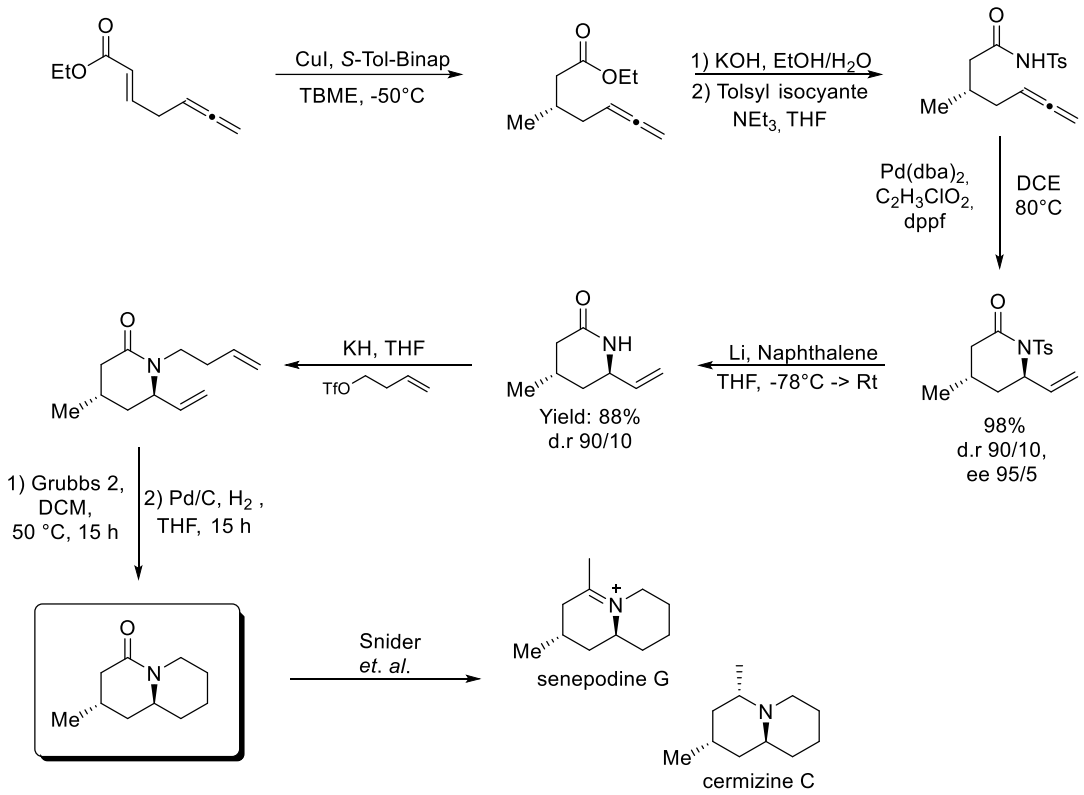
Analytical Data[3]

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 1.83 (ddd, *J* = 13.5, 9.8, 4.8 Hz, 1H), 1.97 (ddd, *J* = 13.5, 10.6, 5.0 Hz, 1H), 2.40 (s, 3H), 2.52 – 2.58 (m, 2H), 3.06 (dtd, *J* = 10.4, 7.4, 4.7 Hz, 1H), 3.39 (s, 1H), 4.84 – 5.07 (m, 3H), 5.51 (ddd, *J* = 17.4, 10.3, 7.4, 1H), 7.04 – 7.11 (m, 2H), 7.17 – 7.26 (m, 4H), 7.26 – 7.30 (m, 1H), 7.50 – 7.56 (m, 2H) ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 21.3, 38.3, 41.1, 41.4, 54.4, 117.7, 127.6, 127.3, 127.6, 128.8, 129.6, 136.5,137.5, 142.1, 143.3, 176.9 ppm.

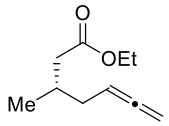
ESI-HRMS: *m/z* calcd for $C_{20}H_{23}O_4NNaS$ $[M+Na]^+$ 396.1240 found 396.1240

Formal total synthesis of Cermizine C and Senepodine G



Scheme: Enantioselective formal total synthesis of Cerminzine C and Senepodine G

Synthesis of ethyl (S)-3-methylhepta-5,6-dienoate 54



$C_{10}H_{16}O_2$
168.24

CuI (1.0 mol%) and S-Tol-Binap (20 mol%) was dissolved in *t*-BuOMe (40 mL) and stirred under argon at room Temperature for 1 h until a yellow suspension was observe. The mixture was cooled to −50 °C and ethyl (*E*)-hepta-2,5,6-trienoate (2.0 g, 13 mmol) was added and stirred for 15 min. Then MeMgBr in THF (6.5 mL, 20 mmol, 3.0 M, 1.5 equiv.) was added dropwise. The mixture was stirred at −50 °C for 2 h, then quenched by the addition of aqueous saturated NH_4Cl-solution. The layers were separated, the aqueous layer was extracted with Et_2O (4 × 30 mL), the combined organic layers were washed with brine (40 mL) and dried over Na_2SO_4. The solvent was removed and the residue was purified by flash chromatography on silica gel (Pentane:Et_2O = 60:1). The Product was obtained as colourless oil (1.0 g, 6.2 mmol, 48%).

Analytical Data

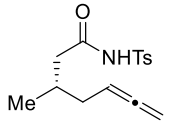
^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 0.98 (d, *J* = 6.4, 3H), 1.25 (t, *J* = 7.1, 3H), 1.95 – 2.16 (m, 4H), 2.30 – 2.41 (m, 1H), 4.09 – 4.17 (m, 2H), 4.65 (dt, *J* = 6.7, 2.7, 2.7, 2H), 5.00 – 5.11 (m, 1H) ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = δ = 14.4, 19.6, 30.7, 35.7, 41.2, 60.2, 74.4, 87.7, 173.1, 209.4 ppm.

APCI-HRMS: *m/z* calcd for $C_{10}H_{20}O_2N$ $[M+NH_4]^+$ 186.1489 found 186.1489

GC: Hydrodex-B-TBDAc 25m x 0.25mm, 80 °C, isothermal [94% ee. t_R = 28.9 min (minor), 29.7 min (major)], $[\alpha]_D^{25}$= −12 (c = 0.59 $CHCl_3$).

Synthesis of (S)-3-methyl-N-tosylhepta-5,6-dienamide 16



$C_{15}H_{19}NO_3S$
293.38

To (S)-3-methylhepta-5,6-dienoate (1.0 g, 5.9 mmol, 1.0 equiv.) was dissolved in EtOH (1 M) and a solution aqueous LiOH (3.0 M, 4.0 equiv.) was added. The mixture was heated to 80 °C and stirred for 3h. The reaction was concentrated under vacuum and the residue was diluted with H_2O (10 mL), acidified with aqueous HCl (2.0 M) and execrated with EtOAc (4 × 20 ml). The organic layer was separated, washed with brine (15 mL), H_2O (15 mL) and dried over Na_2SO_4.

The crude product was dissolved in THF (0.3 M), tosyl isocyanate (1.0 equiv.) was added dropwise and the solution was stirred for 10 min at room temperature and then NEt_3 (1.1 equiv.) was added. The mixture was stirred for another 14 h at room temperature, quenched by the addition of saturated NH_4Cl

solution (30 ml). The layers were separated, the aqueous phase was extracted with EtOAc (2 × 50 ml), the combined organic layers were dried over Na_2SO_4. The solvent was removed under vacuum and the crude product was purified by flash chromatography on silica gel (hexanes:EtOAc). The Product was obtained as yellow oil (1.6 mg, 5.5 mmol, 93%).

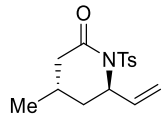
Analytical Data[4]

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 0.90 (d, *J* = 6.4 Hz, 3H), 1.86 – 1.97 (m, 2H), 1.97 – 2.11 (m, 2H), 2.32 (m, 1H), 2.44 (s, 3H), 4.64 (dt, *J* = 6.6, 2.8 Hz, 2H), 4.86 – 5.04 (m, 1H), 7.30 – 7.39 (m, 2H), 7.94 (m, 2H), 8.35 (s, 1H) ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 19.5, 21.8, 30.5, 35.3, 42.9, 74.7, 87.3, 128.5, 129.7, 135.8, 145.2, 170.0, 209.3 ppm.

ESI-HRMS: *m/z* calcd for $C_{15}H_{19}O_3NNaS$ $[M+Na]^+$ 316.0978 found 316.0979.

Synthesis of (S,R)-4-methyl-1-tosyl-6-vinylpiperidin-2-one 3b



$C_{15}H_{19}NO_3S$
293.38

A screw-cap flask was flame-dried, cooled to room temperature under vacuum and backfilled with argon using a standard SCHLENK line apparatus. The screw-cap flask was charged with (S)-3-methyl-N-tosylhepta-5,6-dienamide (900 mg, 3.1 mmol, 1.0 equiv.) the flask was evacuated for 15 min and backfilled with argon three times. Then $Pd(dba)_2$ (44.5 mg, 0.078 mmol, 2.5 mol%), dppf (85.9 mg, 0.155 mmol, 5.0 mol%) and HOAcCl (59.0 mg, 0.62 mmol, 20 mol%) was added under a flow of argon followed by freshly distilled DCE. The flask was sealed and stirred at 80 °C overnight. The reaction mixture concentrated and the **d.r.** ratio (**d.r. = 90/10**) was determined by ^{1}H-NMR spectroscopy of the crude product. The residue was purified by chromatography on silica gel (DCM). The Product was obtained as yellow oil (845 mg, 2.9 mmol, 93%).

Analytical Data[3,]

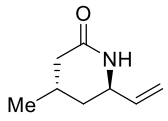
^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 0.95 (d, *J* = 6.5 Hz, 3H), 1.65 (ddd, *J* = 13.8, 12.4, 5.3 Hz, 1H), 1.88 – 2.03 (m, 2H), 2.05 – 2.12 (m, 1H), 2.41 (s, 3H), 2.52 (ddd, *J* = 17.7, 5.7, 2.0 Hz, 1H), 5.16 – 5.34 (m, 3H), 5.85 (ddd, *J* = 17.1, 10.5, 5.4 Hz, 1H), 7.23 – 7.34 (m, 2H), 7.85 – 8.00 (m, 2H) ppm.

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 21.3, 21.7, 23.2, 37.1, 41.8, 58.5, 117.6, 129.1, 129.4, 136.4, 137.4, 144.64, 170.1 ppm.

ESI-HRMS: *m/z* calcd for $C_{15}H_{20}O_3NS$ $[M+H]^+$ 294.1158 found 294.1158.

HPLC: LC-4, λ = 236 nm, *n*-heptane:IPA = 85:15, 0.4 mL/min, 22 °C: t_r = 44.6 min (major) and t_r = 77.6 min (minor), 95% ee. $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25}}$= − 19 (c = 0.61 $CHCl_3$)

Synthesis of (S,R)-4-methyl-6-vinylpiperidin-2-one 23



$C_8H_{13}NO$
139.20

Naphthalene (1.4 g, 11 mmol, 6.8 equiv.) was dissolved in dry THF (20 mL). Lithium (76 mg, 11 mmol, 6.8 equiv.) was added and the mixture was sonicated for 30 min and then stirred at room temperature for 2 h in order to obtain a dark green Li-naphthalenide solution. (S,R)-4-methyl-1-tosyl-6-vinylpiperidin-2-one (0.47 g, 1.6 mmol, 1.0 equiv.) was dissolved in dry THF (5 mL) and the Li-naphthalenide solution was added dropwise. The reaction was stirred at −78 °C for 30 min and then 1 h at room temperature, then quenched by the addition of saturated NH_4Cl solution (30 ml). The layers were separated, the aqueous phase was extracted with EtOAc (2 × 50 ml), the combined organic layers were dried over Na_2SO_4. The reaction mixture concentrated and the **d.r.** ratio (**d.r. = 90/10**) was determined by ^{1}H-NMR

spectroscopy of the crude product. The residue was purified by flash chromatography on silica gel (DCM:MeOH = 60:1). The Product was obtained as brown oil (196 mg, 1.41 mmol, 88%).

Analytical Data[3]

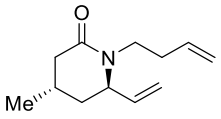
^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 0.99 – 1.03 (m, 3H), 1.59 – 1.76 (m, 2H), 1.92 – 2.03 (m, 1H), 2.00 – 2.10 (m, 1H), 2.45 (ddd, *J* = 17.1, 4.8, 1.5 Hz, 1H), 4.07 (ddt, *J* = 5.6, 2.9, 1.5, 1.5 Hz, 1H), 5.14 – 5.26 (m, 2H), 5.82 (ddd, *J* = 17.1, 10.3, 5.6 Hz, 1H), 6.04 (s, 1H) ppm

^{13}C-NMR (100.6 MHz, $CDCl_3$): 20.6, 23.5, 35.1, 39.3, 53.1, 115.8, 139.3, 172.5 ppm.

ESI-HRMS: *m/z* calcd for $C_8H_{14}ON$ $[M+H]^+$ 140.1069 found 140.1070.

$[\boldsymbol{\alpha}]_D^{25}$= –122 (c = 0.81 $CHCl_3$)

Synthesis of (S,R)-1-(but-3-en-1-yl)-4-methyl-6-vinylpiperidin-2-one 24



$C_{12}H_{19}NO$
193.29

(S,R)-4-methyl-6-vinylpiperidin-2-one (0.20 g, 1.4 mmol, 1.0 equiv) was dissolved in dry THF (12 mL) and cooled to −78 °C. KH (70 mg, 1.7 mmol, 1.2 equiv.) was added in small portions and the reaction was stirred at −78 °C for 1 h. Then freshly prepared[5] but-3-en-1-yl trifluoromethanesulfonate (0.39 g, 1.9 mmol, 1.3 equiv.) was added at this temperature and the reaction was stirred for further 30 min at this temperature. The reaction was warmed to room temperature and stirred for 2 h then quenched by the addition of saturated NH_4Cl solution (30 ml). The layers were separated, the aqueous phase was extracted with EtOAc (2 × 50 ml), the combined organic layers were dried over Na_2SO_4. The reaction mixture was concentrated and the **d.r.** ratio (**d.r. = 90/10**) was determined by ^{1}H-NMR spectroscopy of the crude product. The residue was purified by flash chromatography on silica gel (DCM:MeOH = 60:1). The Product was obtained as yellow oil (0.23 g, 1.2 mmol, 81%).

Analytical Data[3]

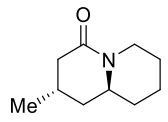
^{1}H-NMR (500.2 MHz, $CDCl_3$): δ = 0.94 (d, *J* = 6.4 Hz, 3H), 1.57 (ddd, *J* = 13.3, 11.7, 5.8 Hz, 1H), 1.70 – 1.73 (m, 1H), 1.93 (dd, *J* = 17.1, 11.1 Hz, 1H), 2.01 (ddddd, *J* = 11.3, 7.8, 6.1, 3.2, 1.7 Hz, 1H), 2.28 (dddd, *J* = 8.1, 6.8, 6.8, 1.2 Hz, 2H), 2.47 (ddd, *J* = 17.1, 5.1, 2.0 Hz, 1H), 2.70 (ddd, *J* = 13.4, 7.3, 7.3 Hz, 1H), 3.91 – 4.05 (m, 2H), 4.97 – 5.09 (m, 3H), 5.19 (ddd, *J*=10.3, 1.2, 1.2, 1H), 5.68 – 5.82 (m, 2H) ppm.

^{13}C-NMR (125.8 MHz, $CDCl_3$): 21.3, 23.3, 32.1, 36.4, 40.4, 45.1, 59.2, 116.5, 116.6, 135.7, 138.1, 170.0 ppm.

ESI-HRMS: *m/z* calcd for $C_{12}H_{20}ON$ $[M+H]^+$ 194.1539 found 194.1540.

$[\boldsymbol{\alpha}]_D^{25}$= –157 (c = 0.79 $CHCl_3$)

Synthesis of (S,S)-2-methyloctahydro-4H-quinolizin-4-one 25



$C_{10}H_{17}NO$
167.25

To a solution of (S,R)-1-(but-3-en-1-yl)-4-methyl-6-vinylpiperidin-2-one (80 mg, 0.41 mmol, 1.0 equiv.) in DCM (16 mL) was added GRUBBS II (12 mg, 0.014 mmol, 3.0 mol%). The reaction was heated to 50 °C and stirred overnight. The solution was cooled to room temperature and the solvent was removed under reduced pressure. The residue was dissolved in MeOH and palladium on charcoal (12 mg, 10% Pd) was added. The solution was hydrogenated at room temperature overnight. The reaction mixture was concentrated and the **d.r.** ratio (**d.r. = 90/10**) was determined by ^{1}H-NMR spectroscopy of the crude product. The residue was purified by flash chromatography on silica gel (DCM:MeOH = 60:1). The Product was obtained as colourless oil (68 mg, 0.40 mmol, 98%).

Analytic data[3, 6]

^{1}H-NMR (500.2 MHz, $CDCl_3$): δ = 0.96 (d, *J* = 6.4 Hz, 3H), 1.31 – 1.55 (m, 3H), 1.56 – 1.70 (m, 4H), 1.82 – 1.91 (m, 1H), 1.94 – 2.09 (m, 2H), 2.35 – 2.50 (m, 2H), 3.32 (ddd, *J* = 8.5, 6.3, 3.2 Hz, 1H), 4.74 (ddd, *J* = 13.0, 2.1, 2.1 Hz, 1H) ppm.

^{13}C-NMR (125.8 MHz, $CDCl_3$): 20.5, 24.5, 25.1, 25.5, 33.7, 36.9, 40.6, 43.2, 55.7, 168.6 ppm.

APCI-HRMS: *m/z* calcd for $C_{10}H_{18}ON$ $[M+H]^+$ 168.1383 found 168.1382.

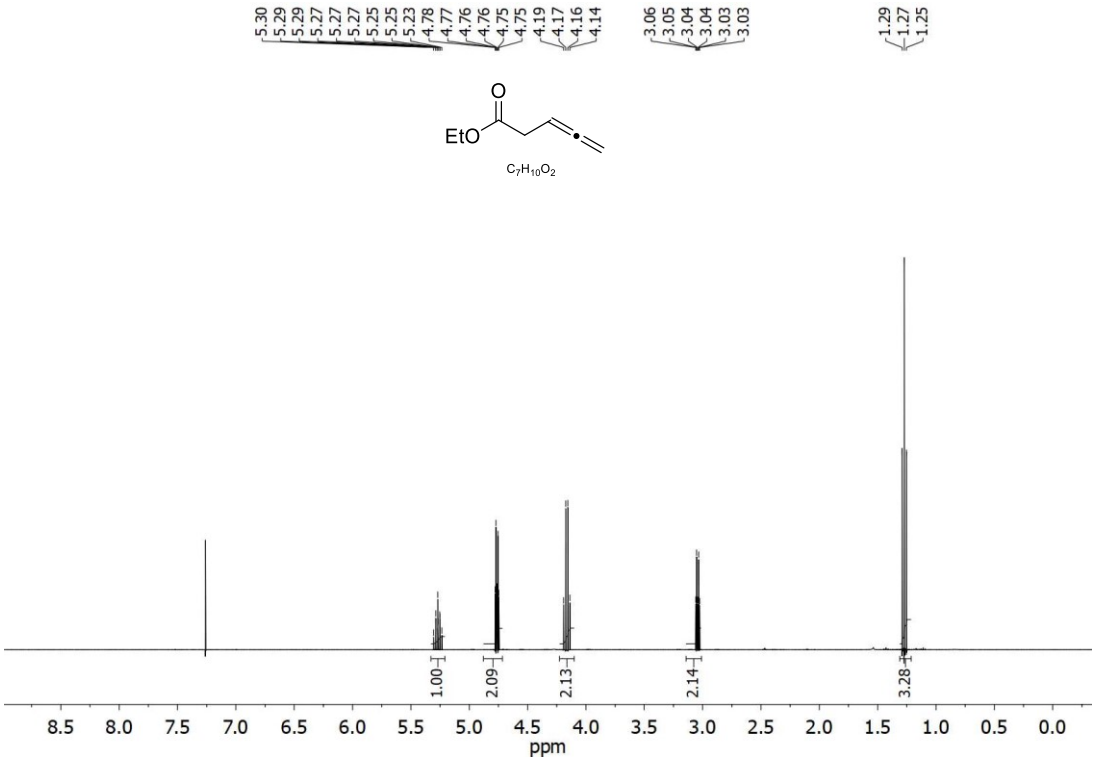
$[\alpha]_D^{25}$ = –24 (c = 0.81 $CHCl_3$)[5]

Analytic

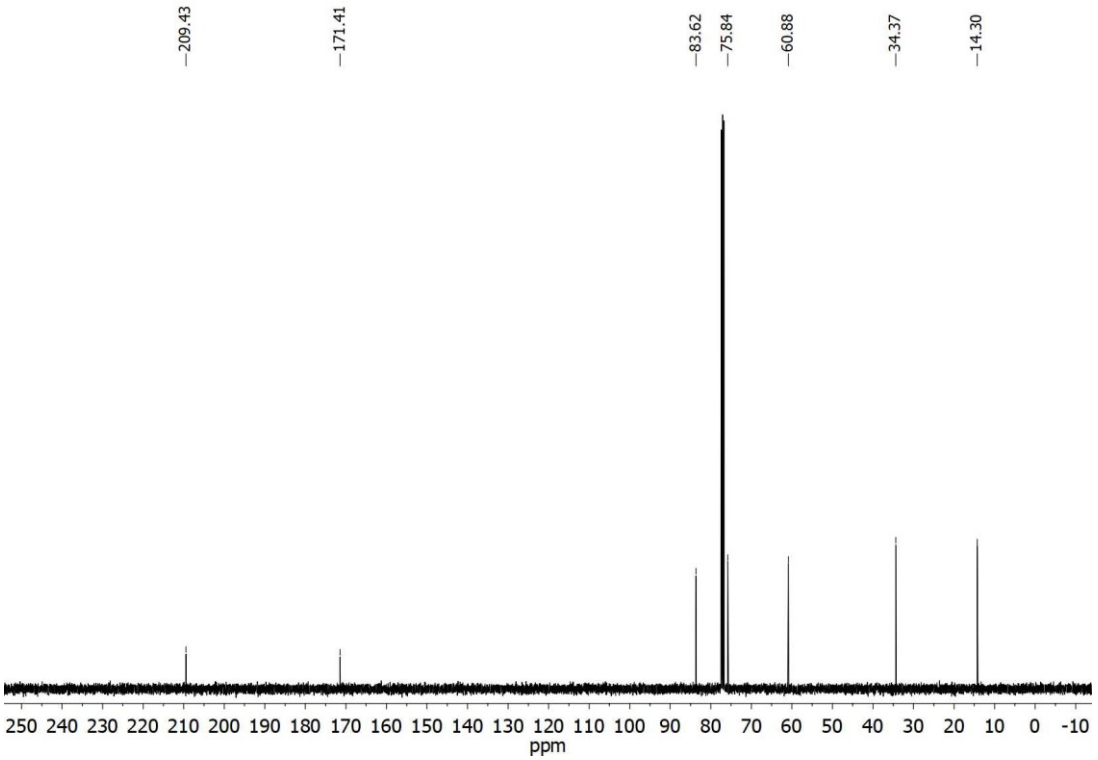
NMR

Ethyl penta-3,4-dienoate 26

^{1}H-NMR

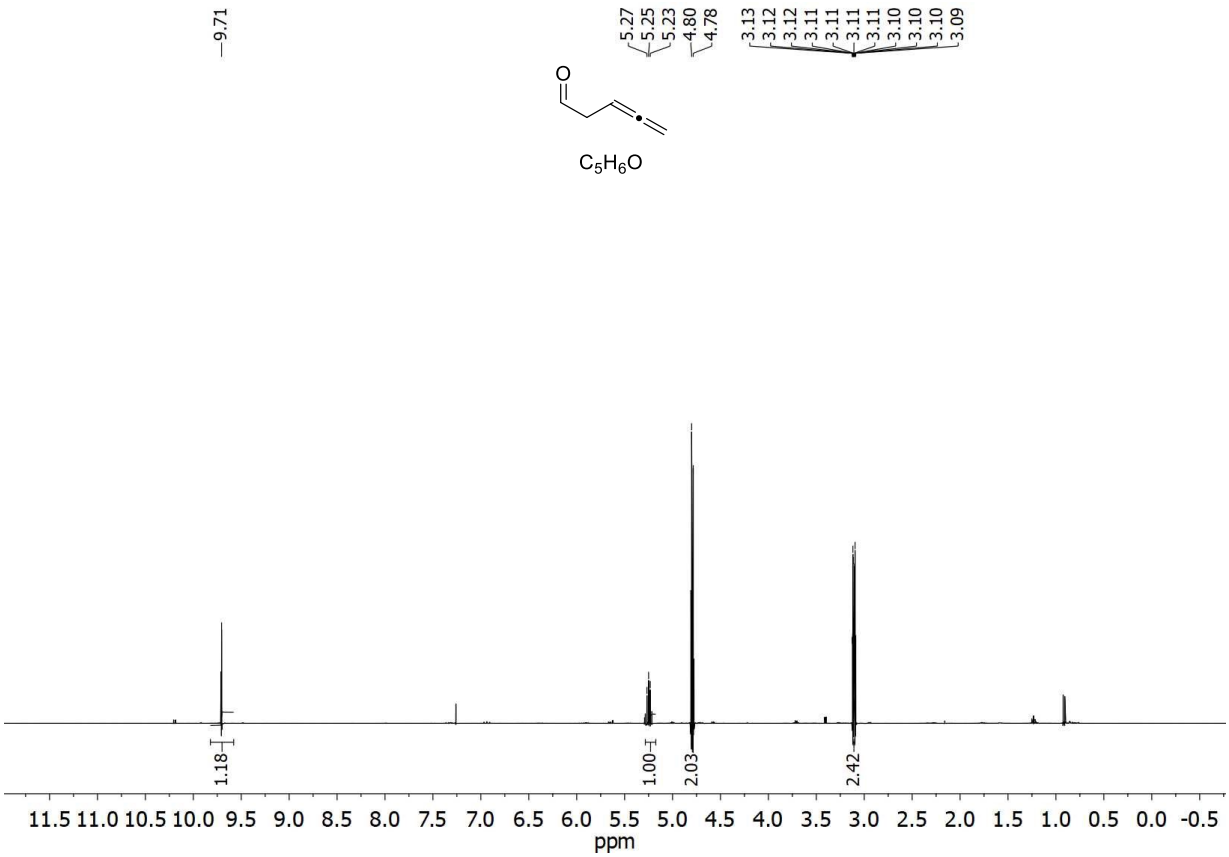


^{13}C-NMR

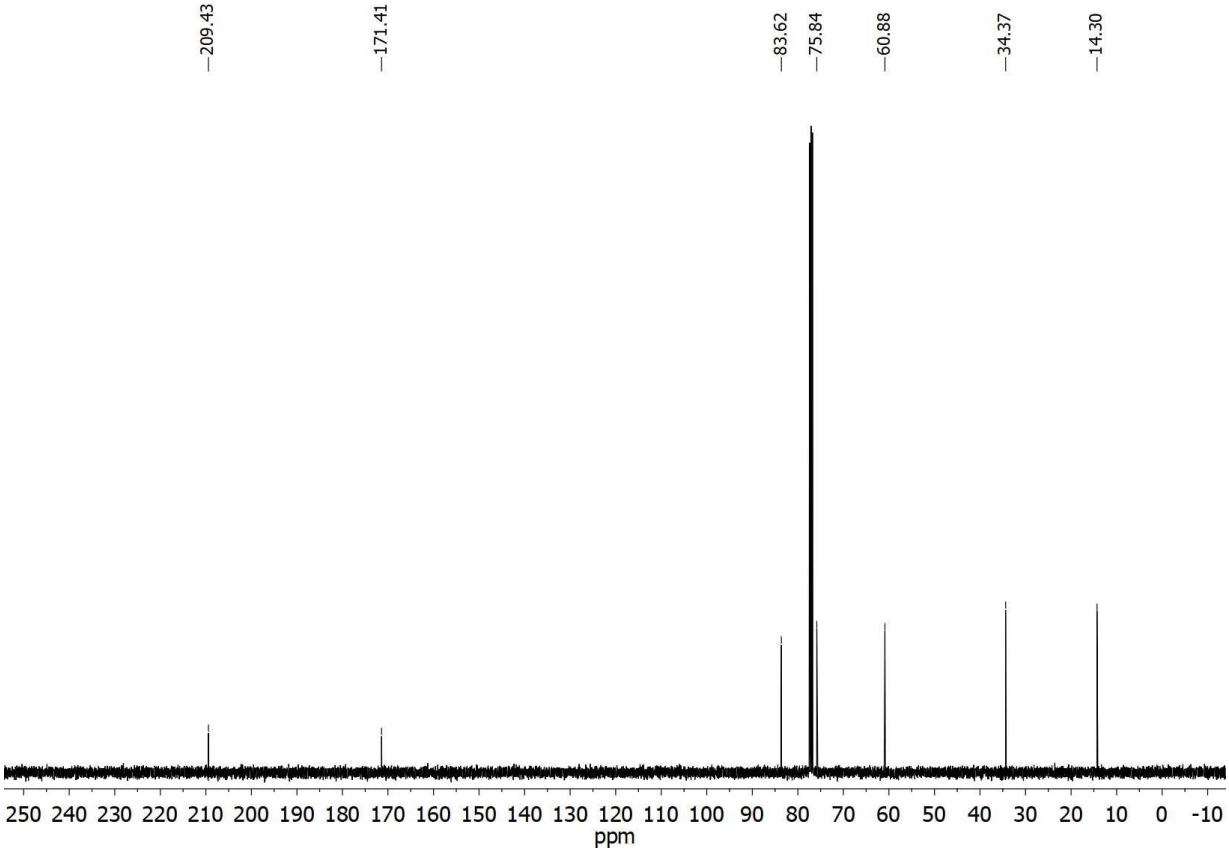


penta-3,4-dienal 27

^{1}H-NMR

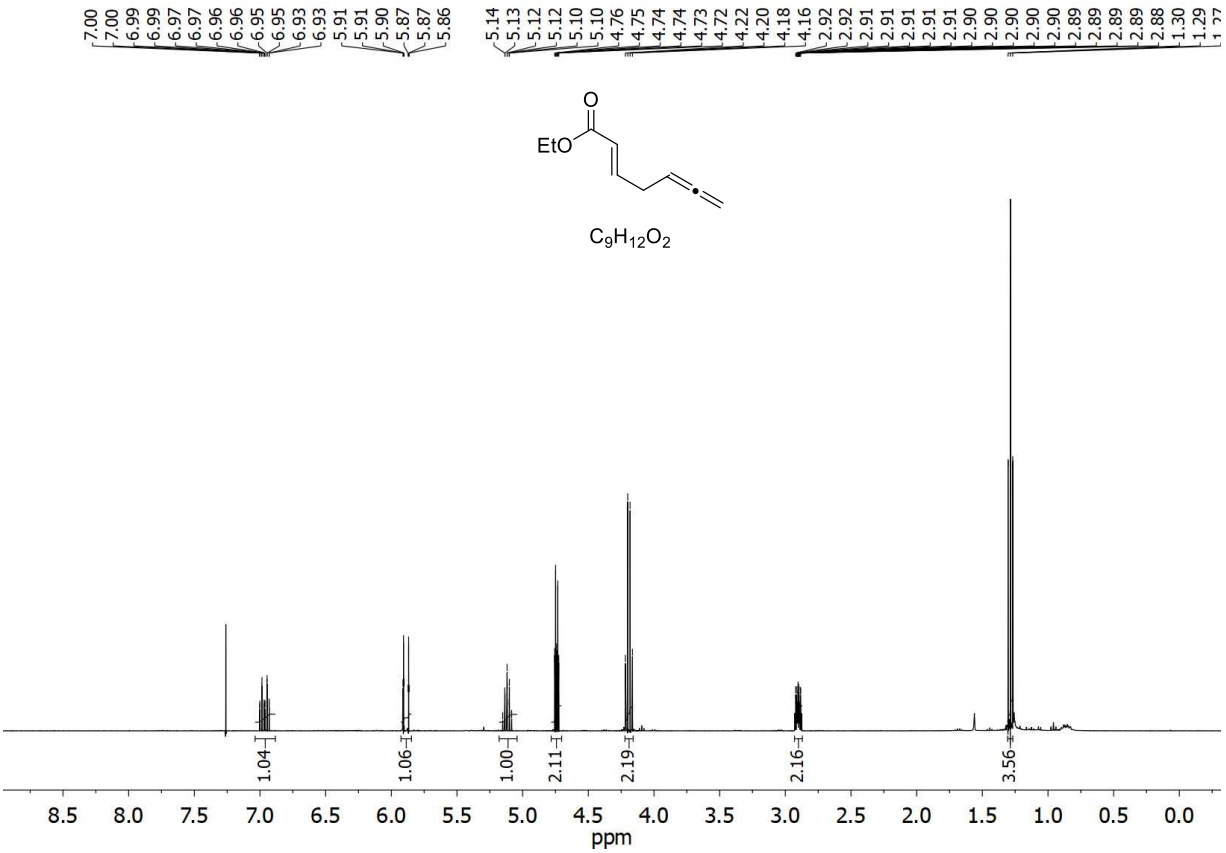


^{13}C-NMR

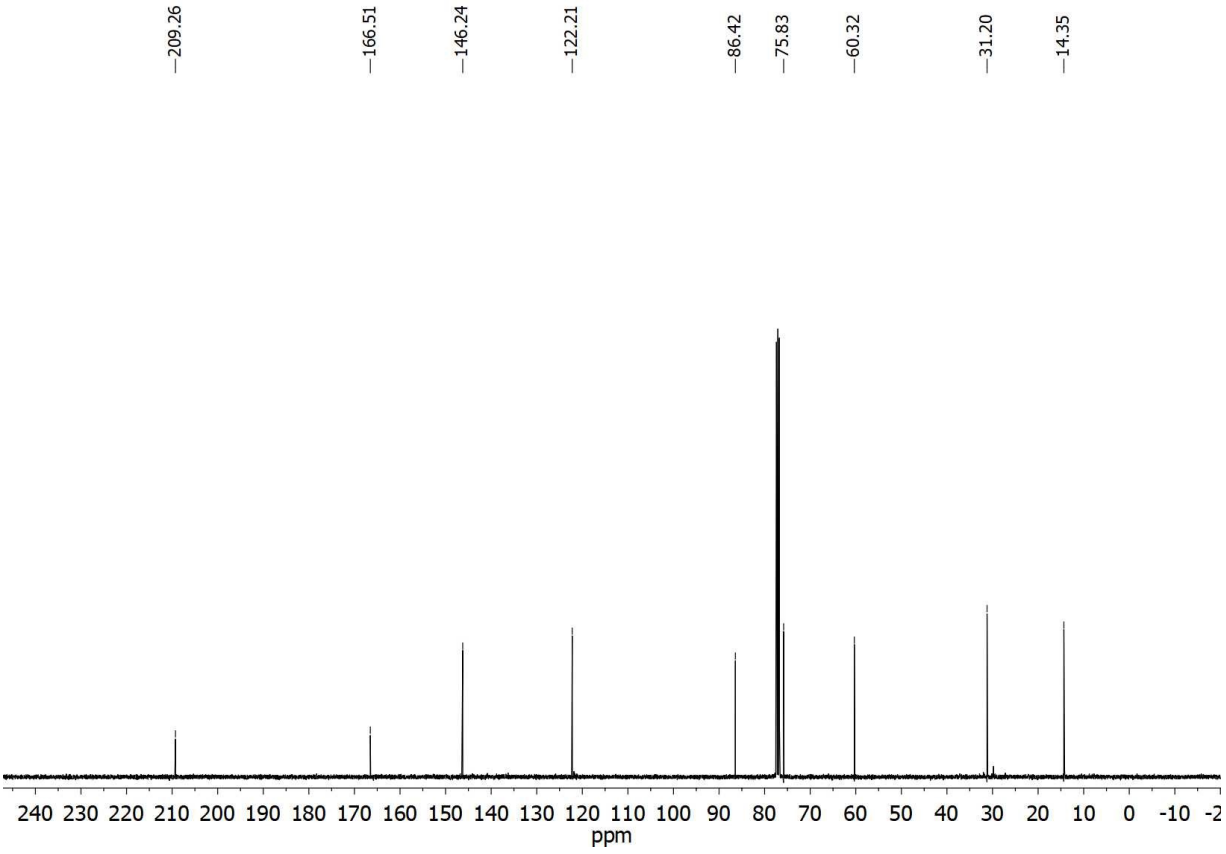


(*E*)-hepta-2,5,6-trienoate 28

^{1}H-NMR

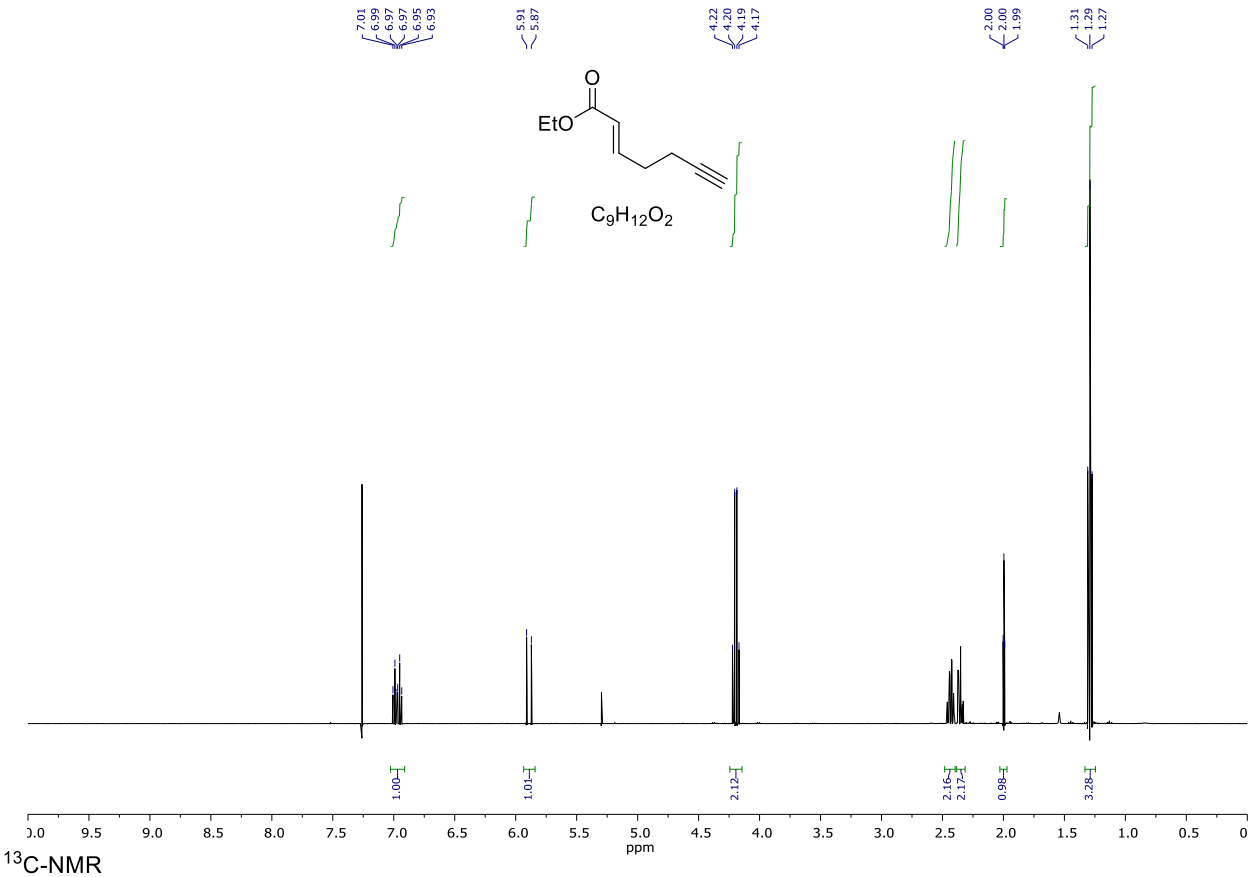


^{13}C-NMR

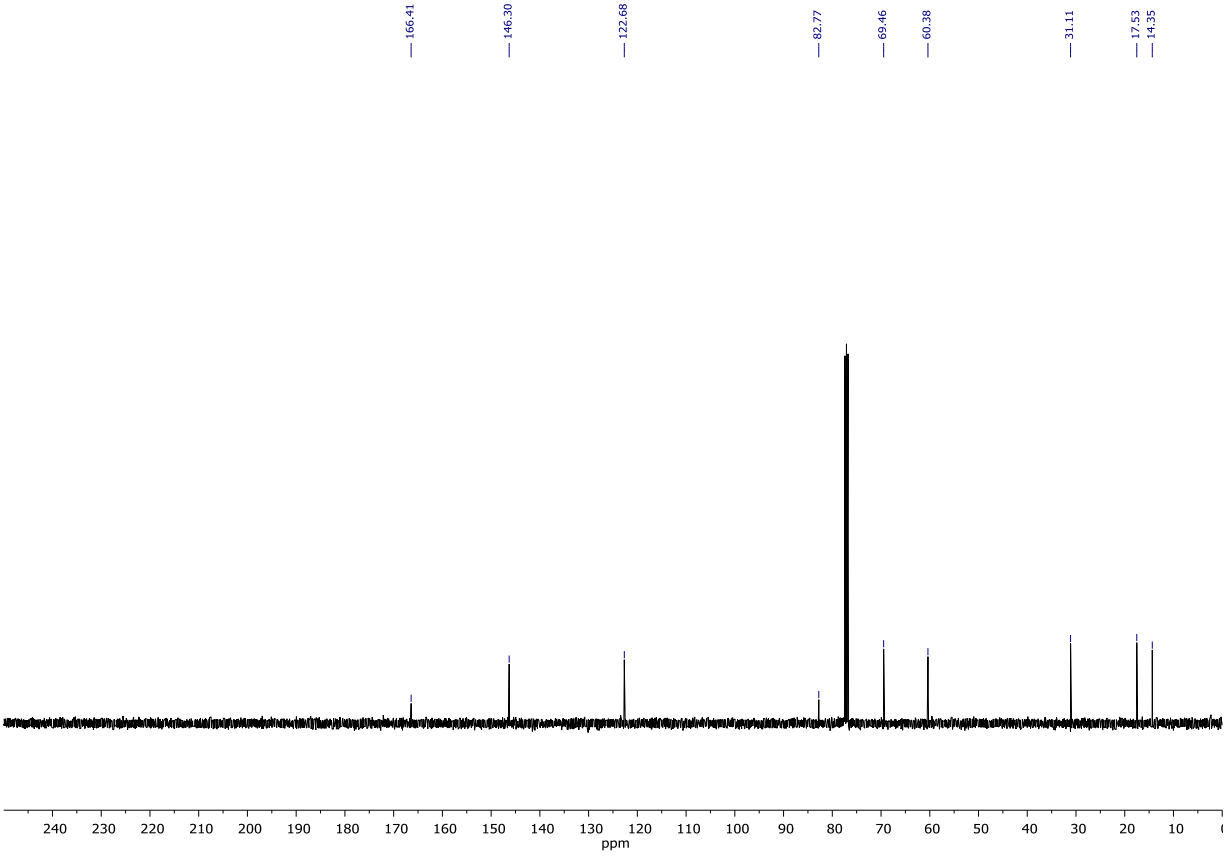


Ethyl (E)-hept-2-en-6-ynoate 29

^{1}H-NMR

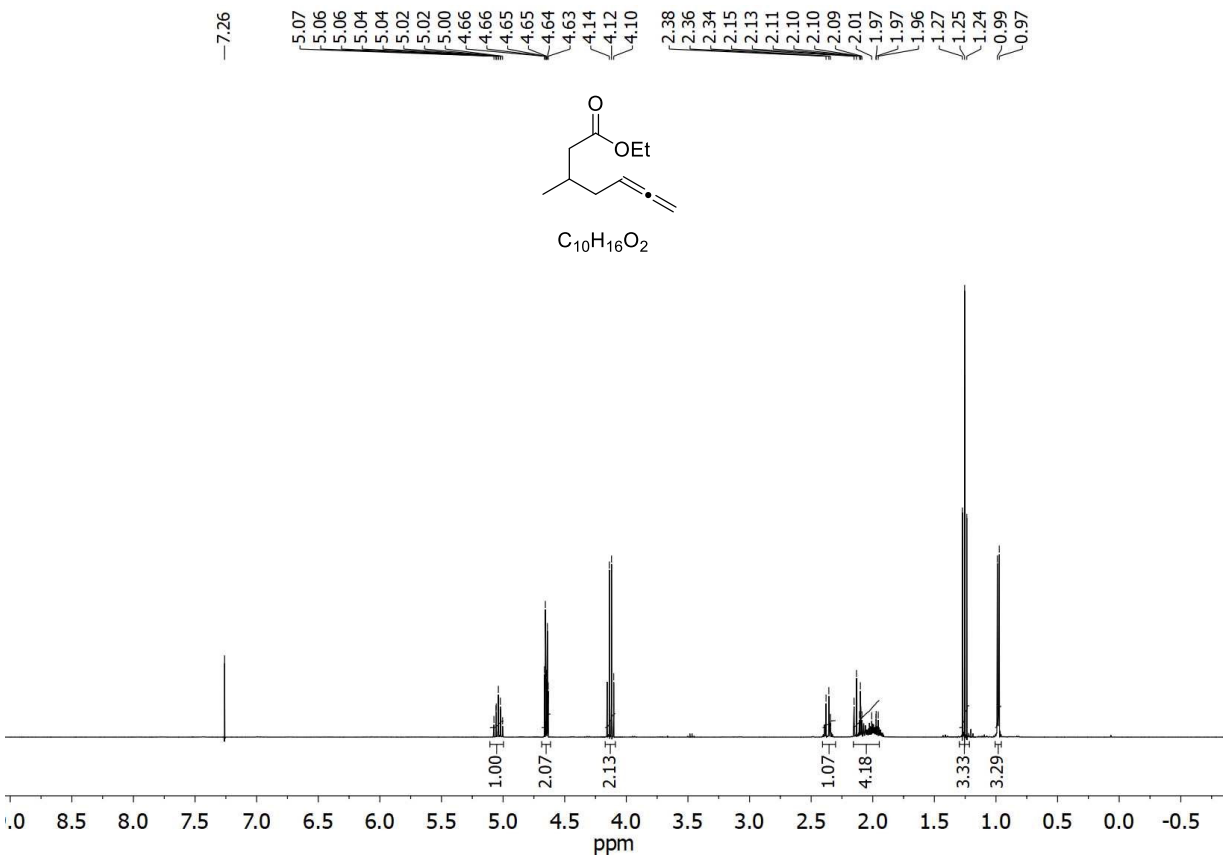


^{13}C-NMR



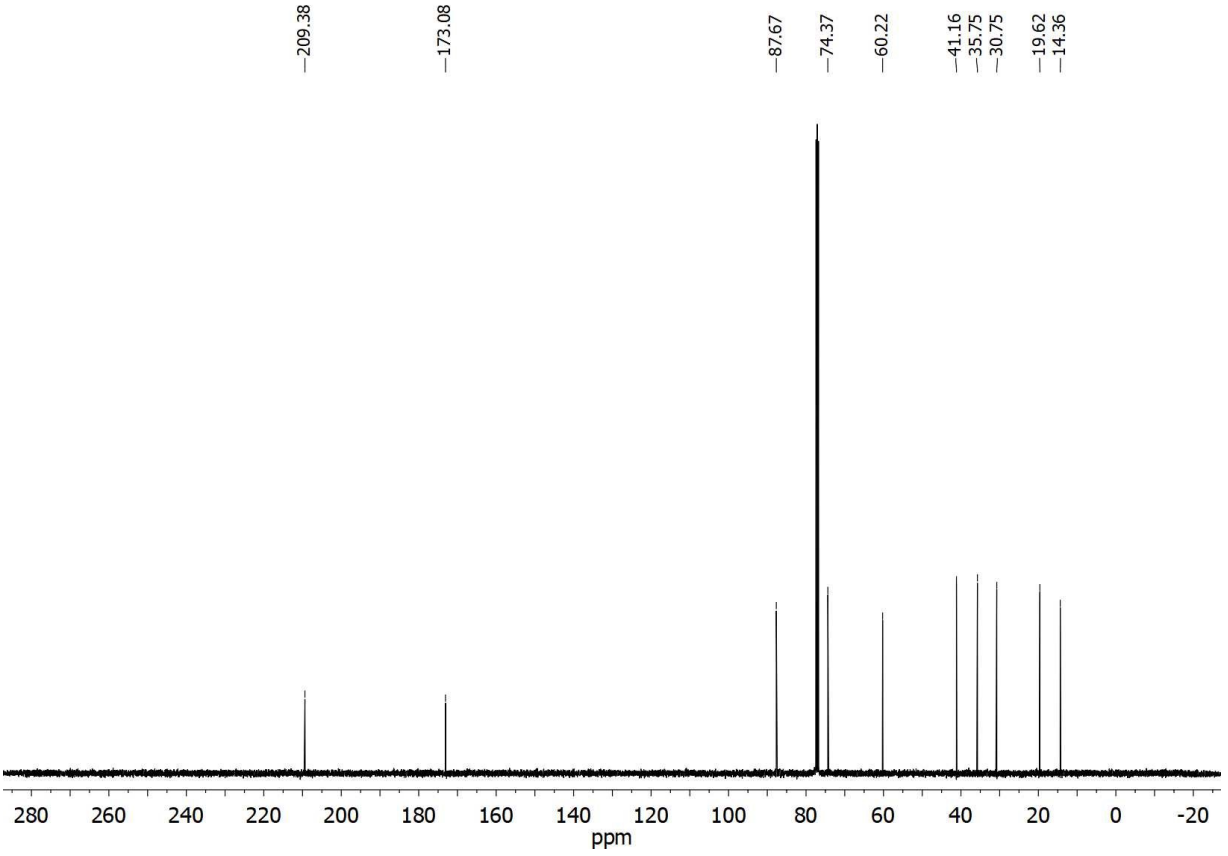
Ethyl 3-methylhepta-5,6-dienoate 30

^{1}H-NMR



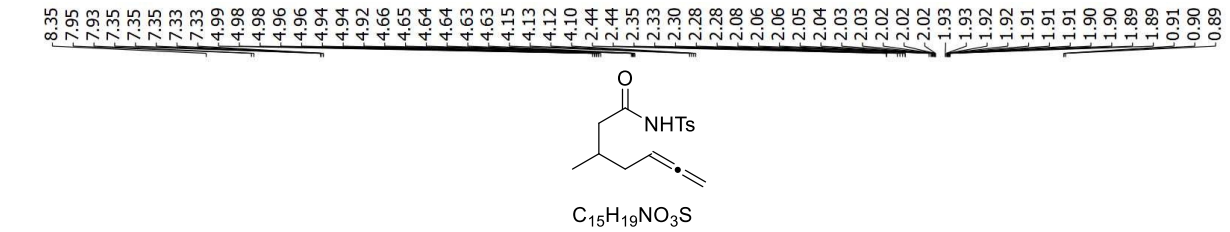
$C_{10}H_{16}O_2$

^{13}C-NMR

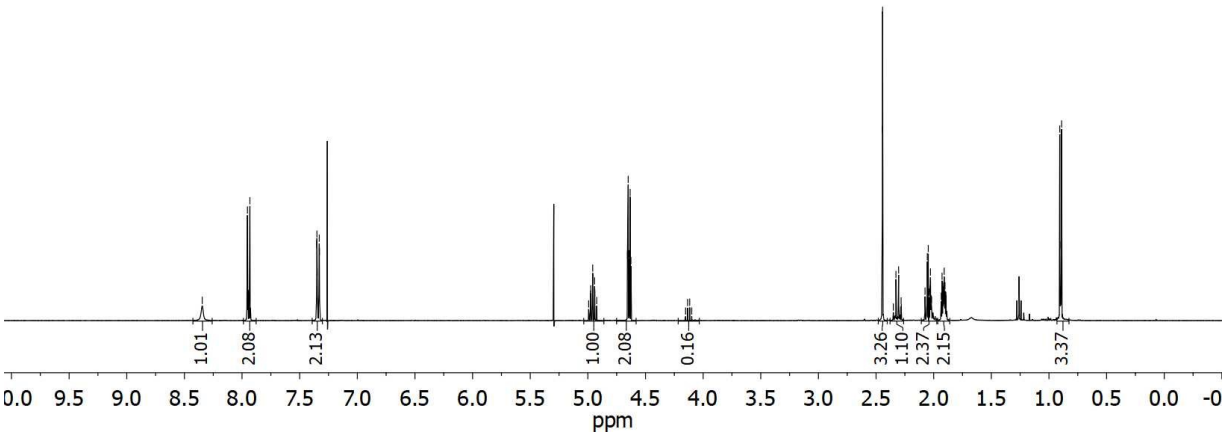


3-methyl-N-tosylhepta-5,6-dienamide 31

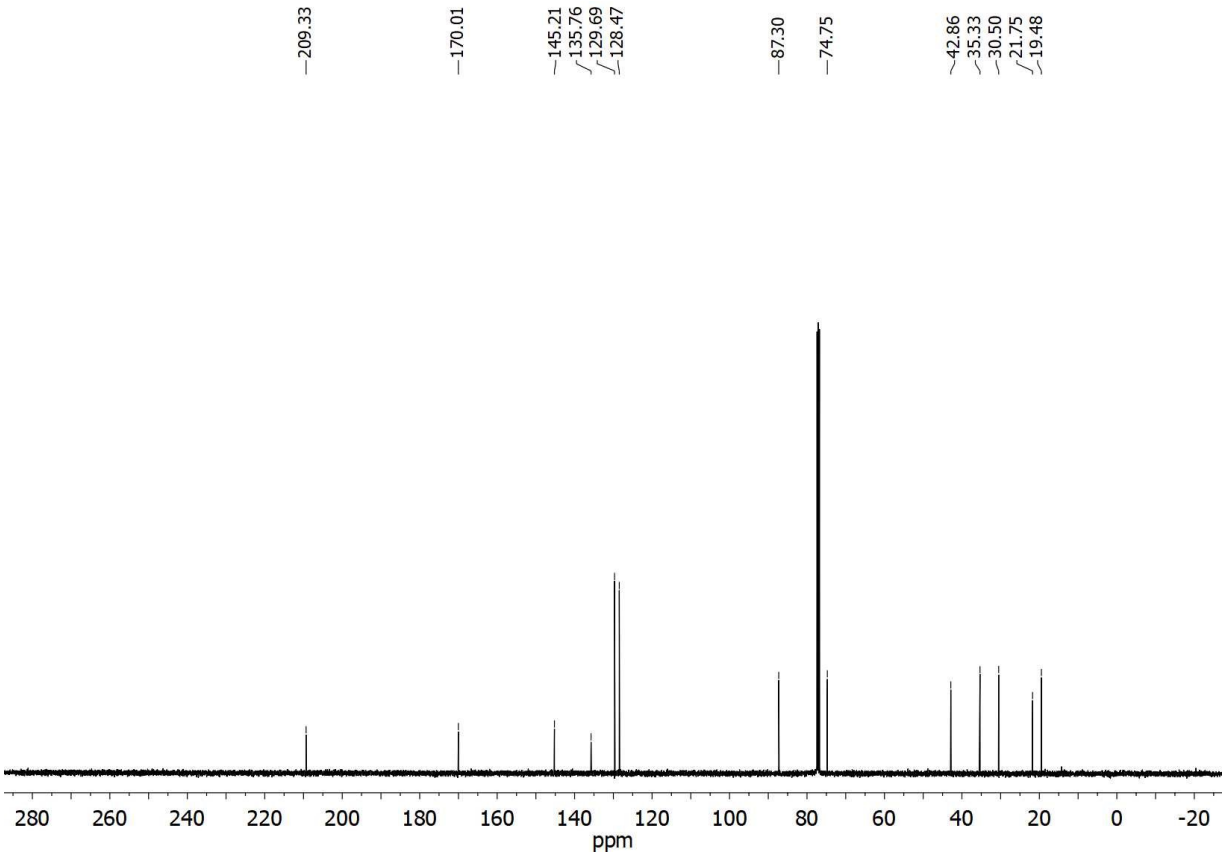
^{1}H-NMR



$C_{15}H_{19}NO_3S$

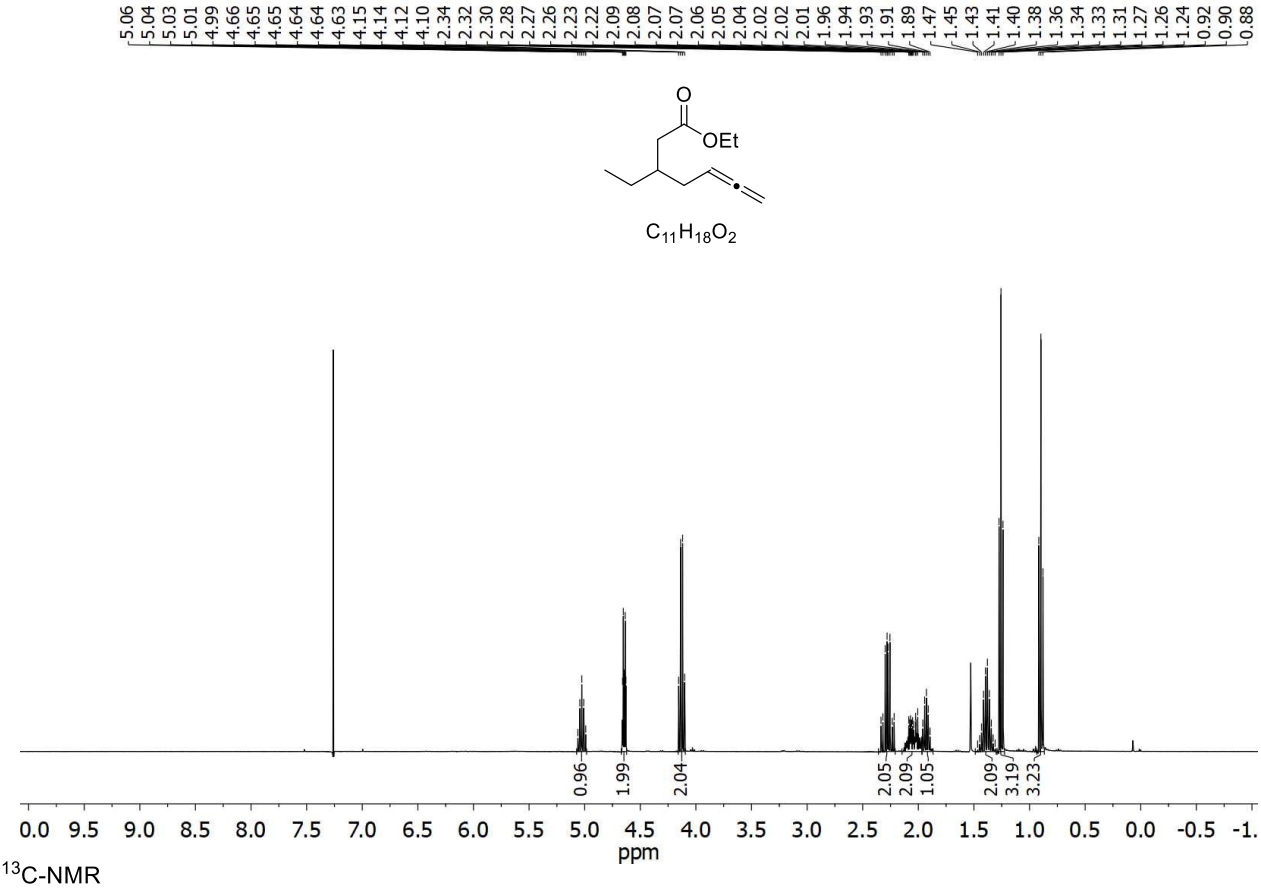


^{13}C-NMR

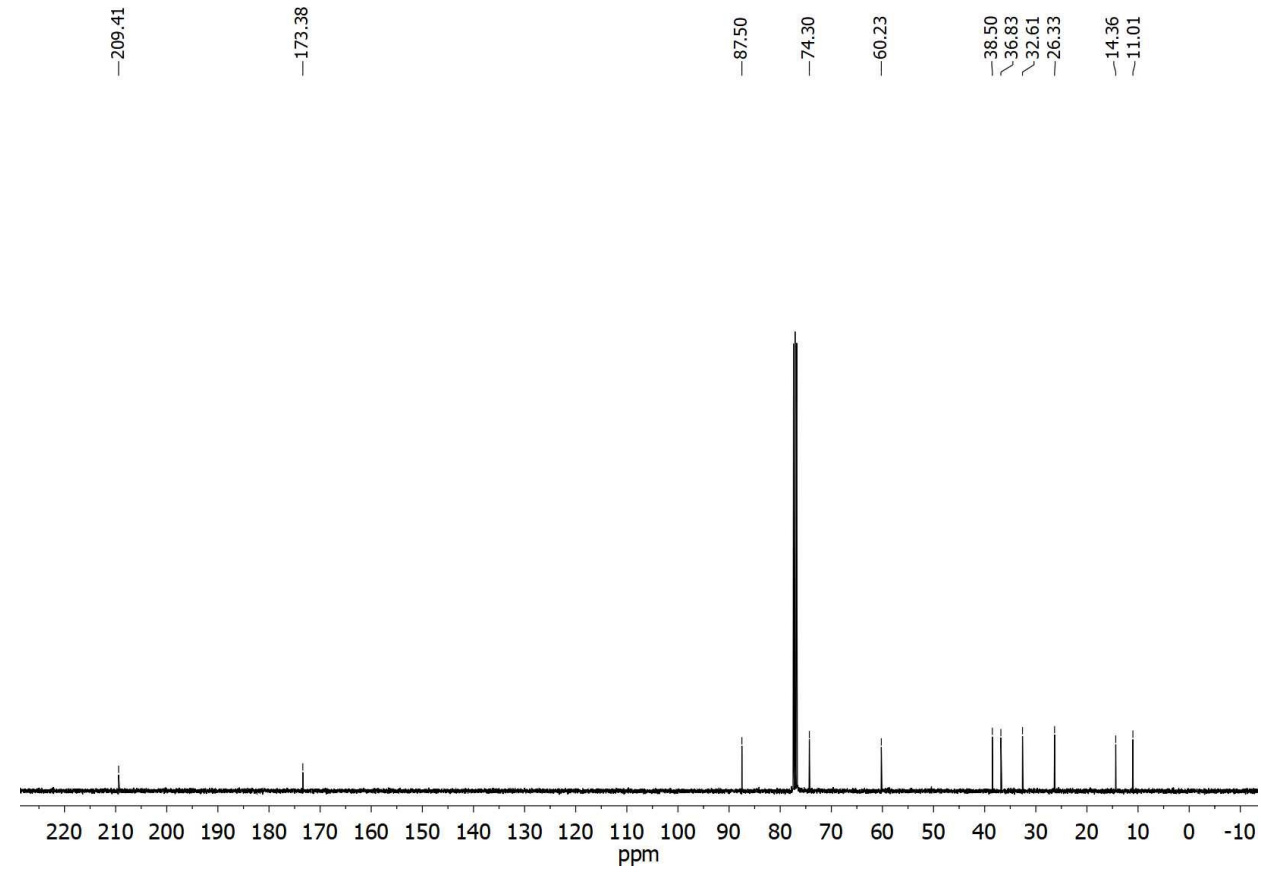


Ethyl 3-ethylhepta-5,6-dienoate 32

^{1}H-NMR

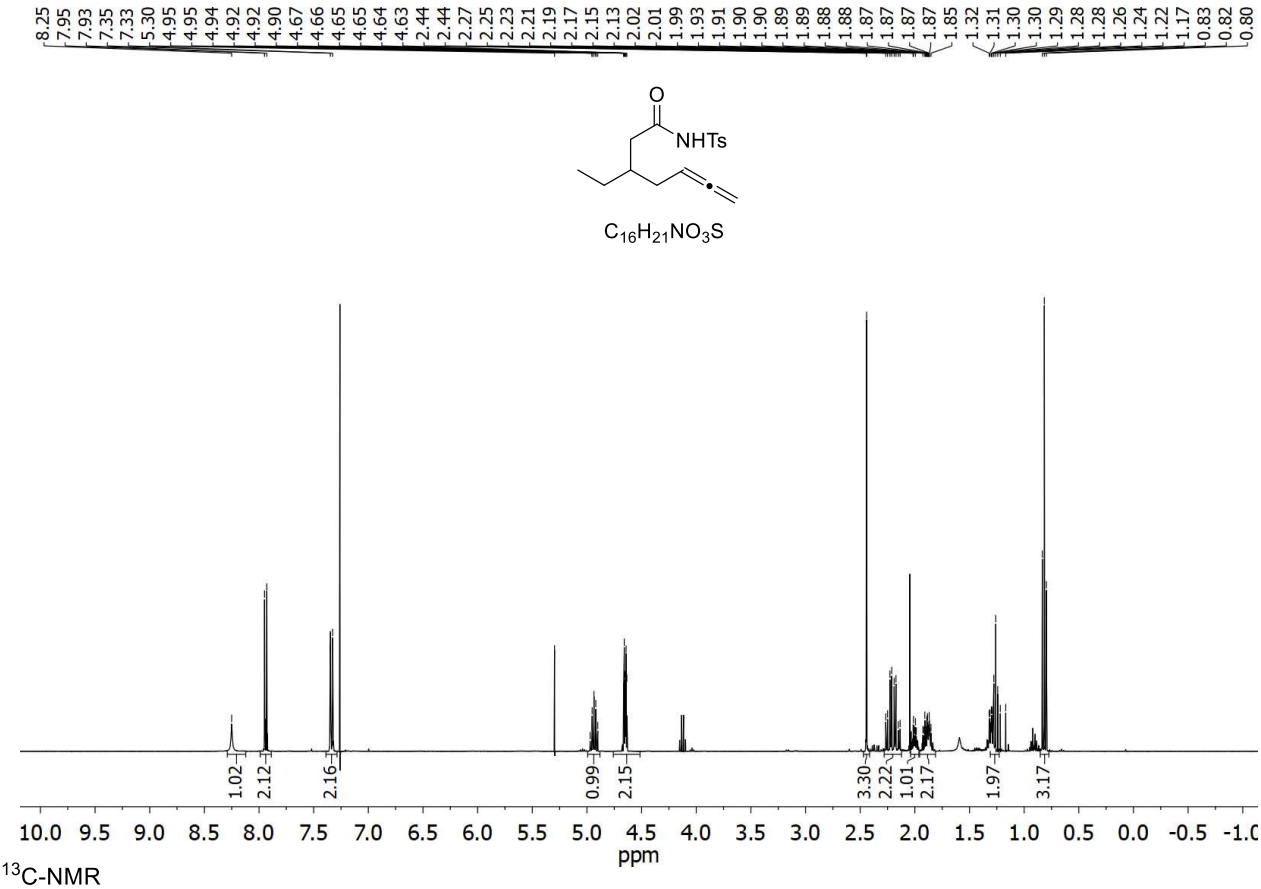


^{13}C-NMR

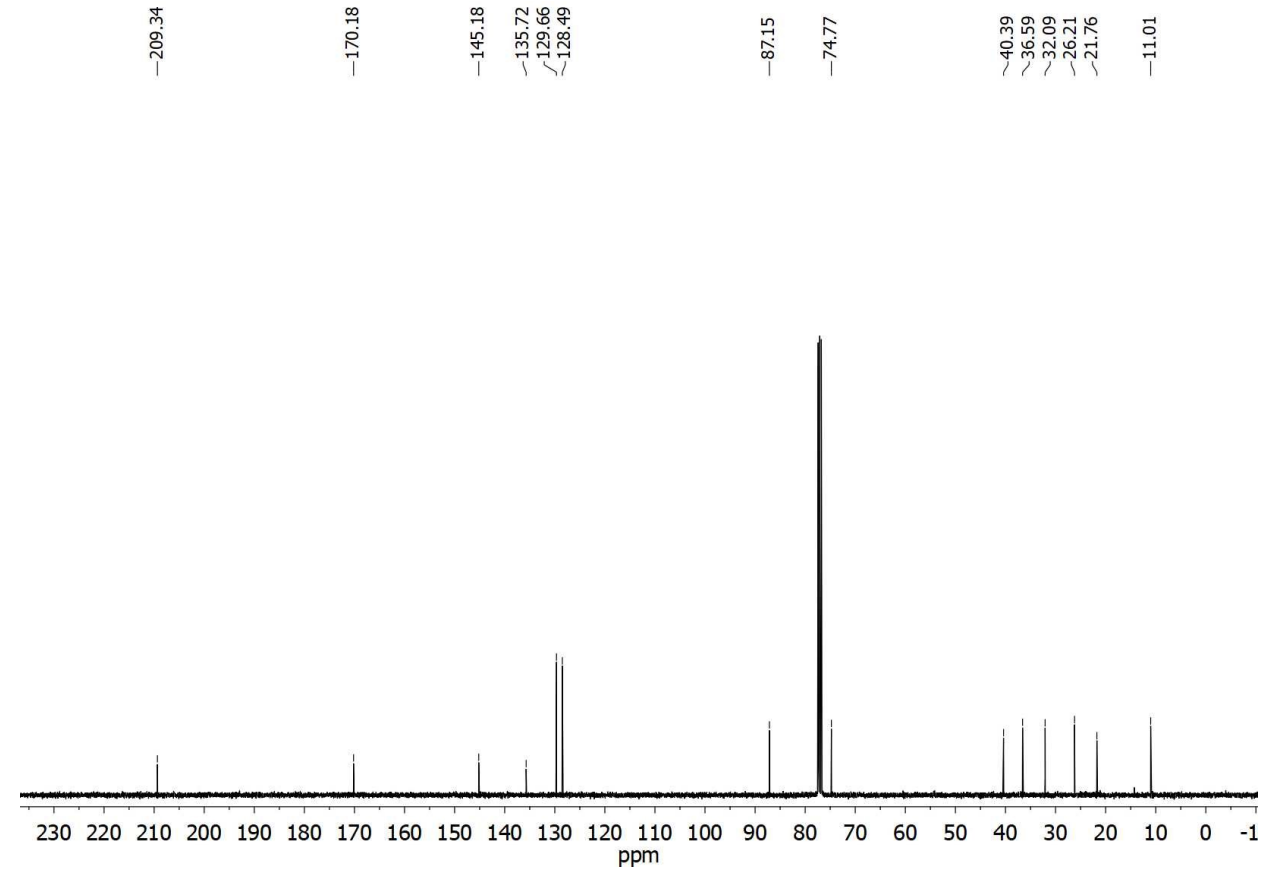


3-ethyl-N-tosylhepta-5,6-dienamide 33

^{1}H-NMR

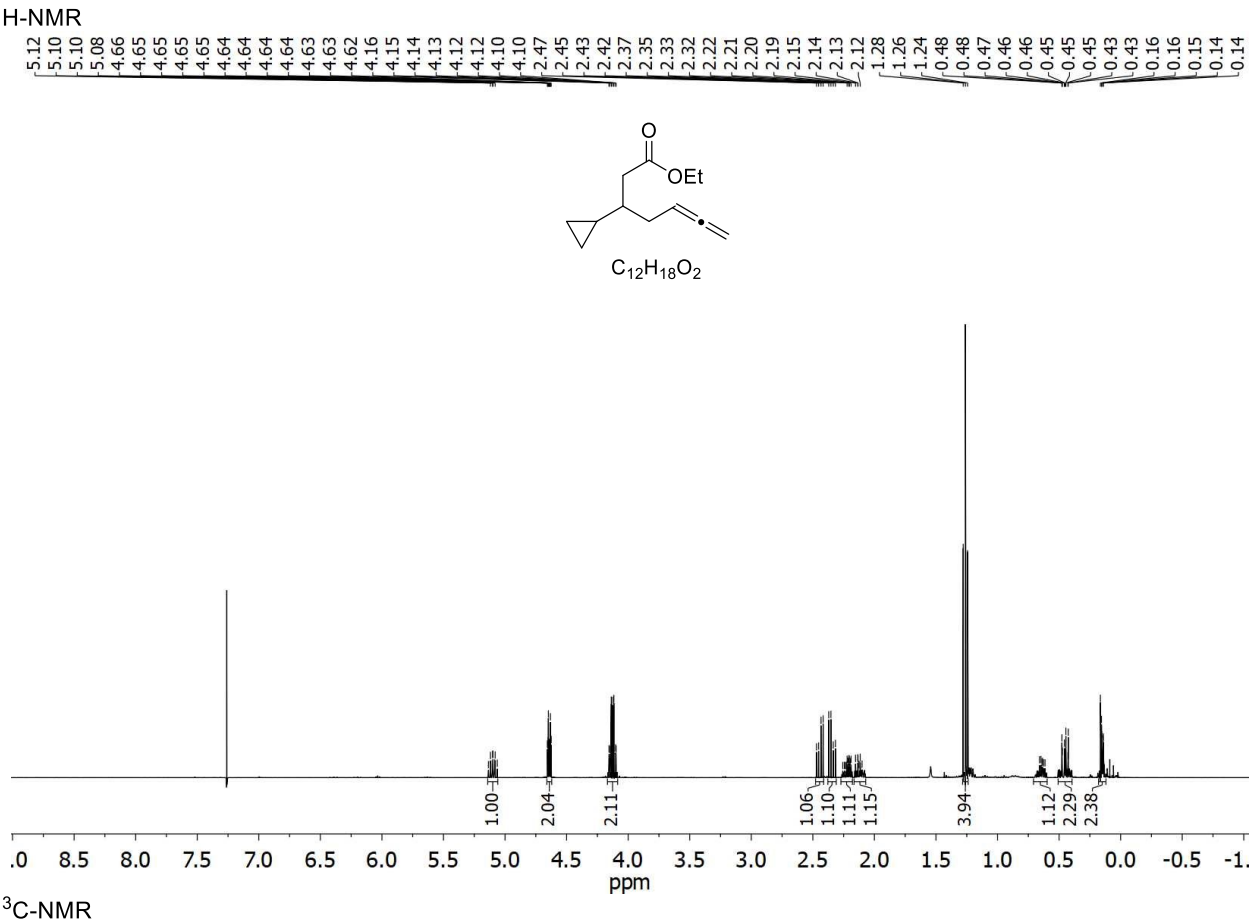


^{13}C-NMR

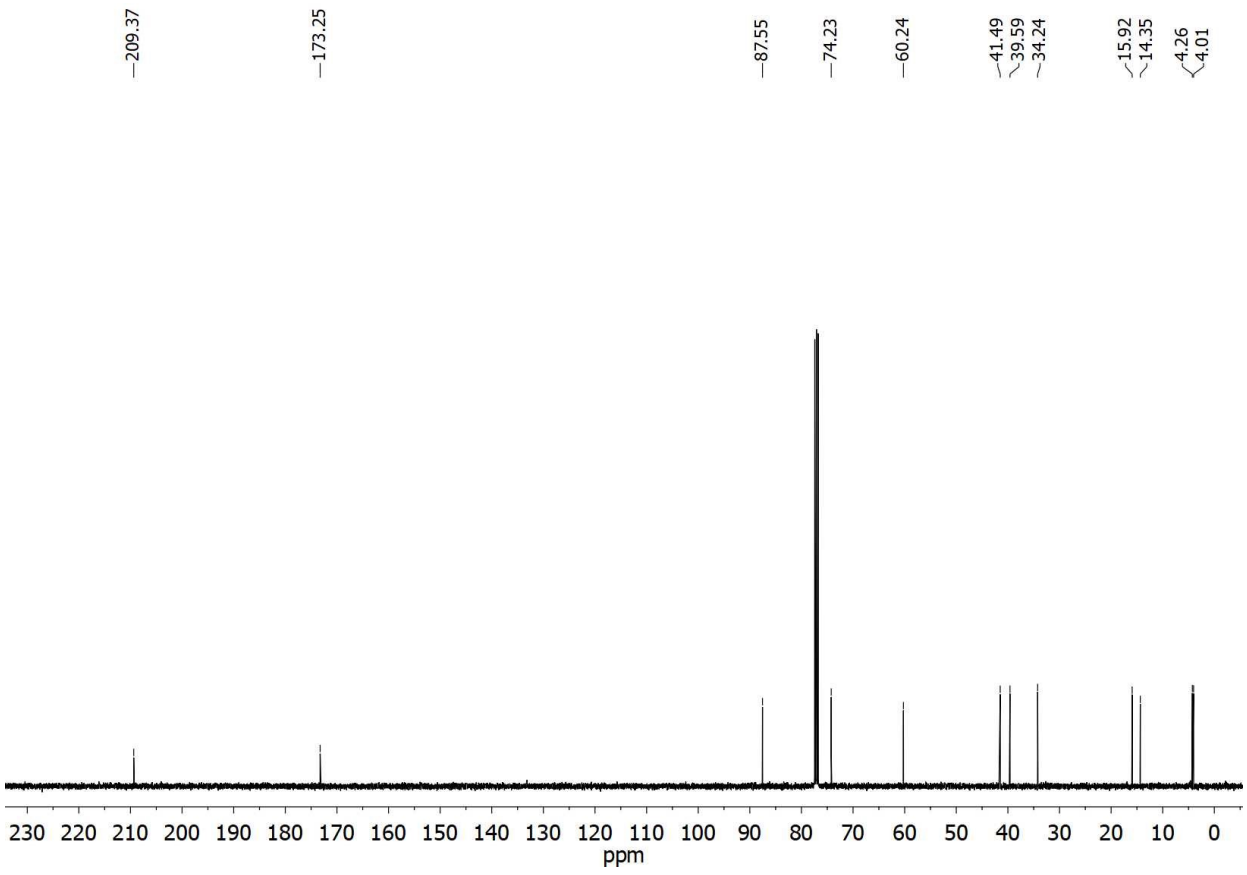


Ethyl 3-cyclopropylhepta-5,6-dienoate 34

^{1}H-NMR

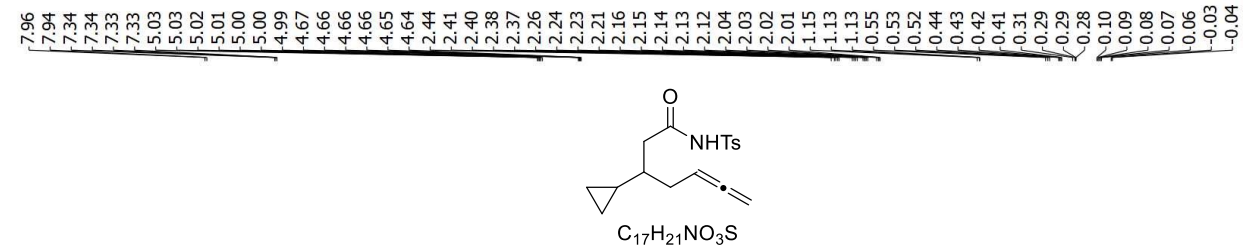


^{13}C-NMR

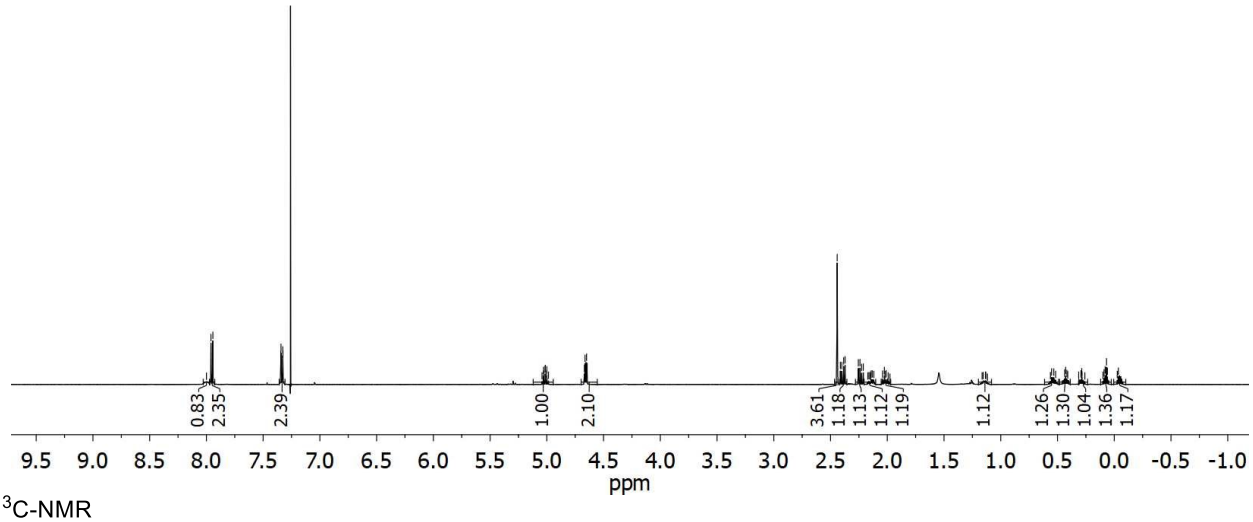


3-cyclopropyl-N-tosylhepta-5,6-dienamide 35

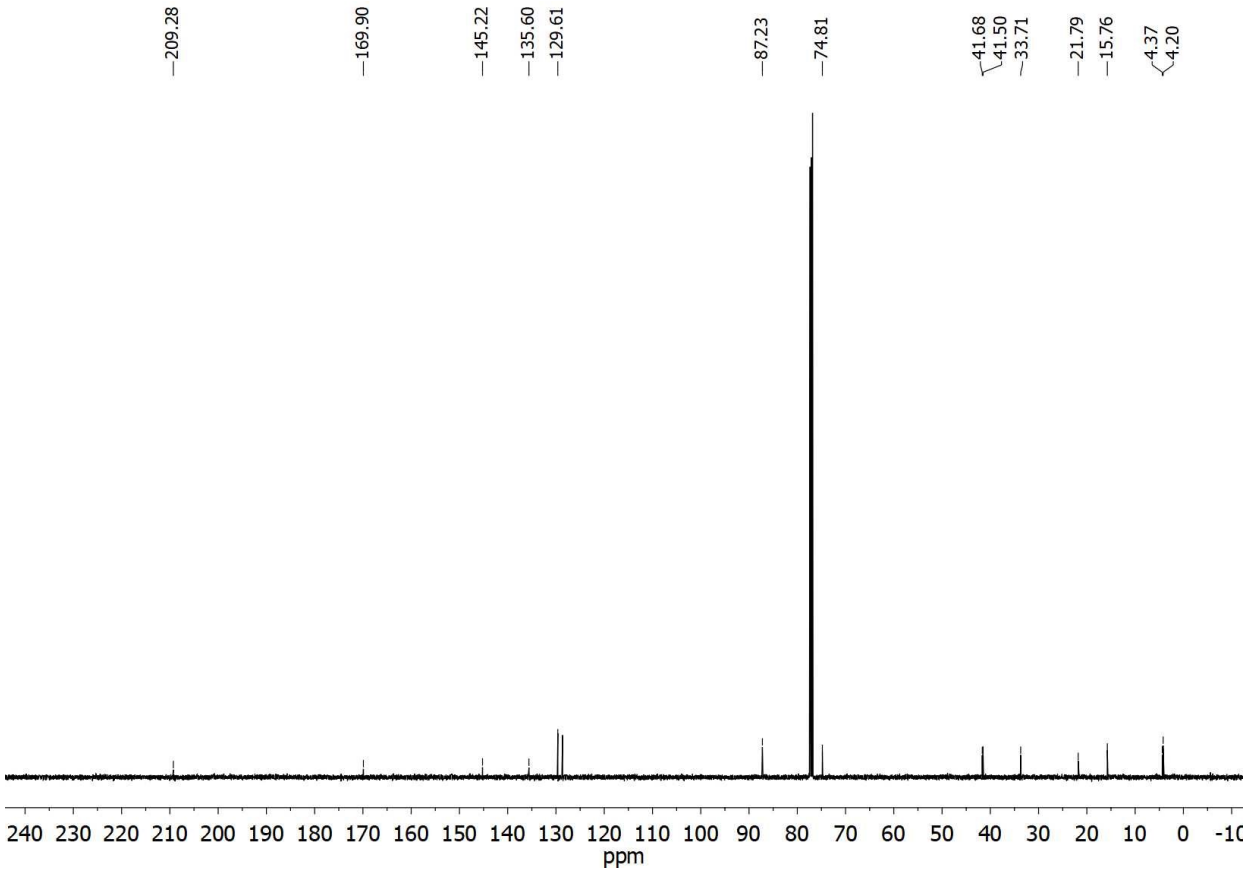
^{1}H-NMR



$C_{17}H_{21}NO_3S$

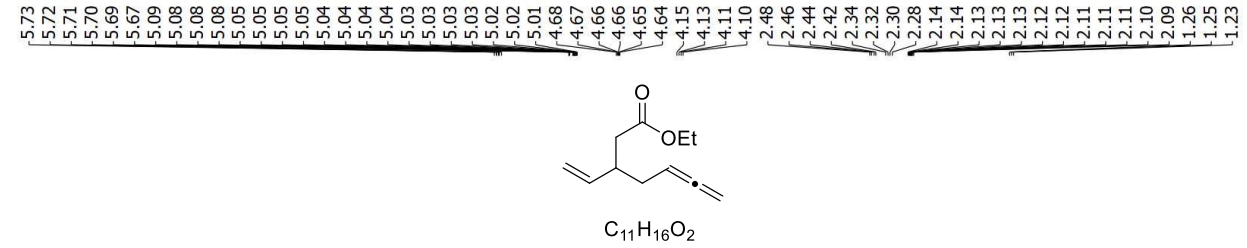


^{13}C-NMR

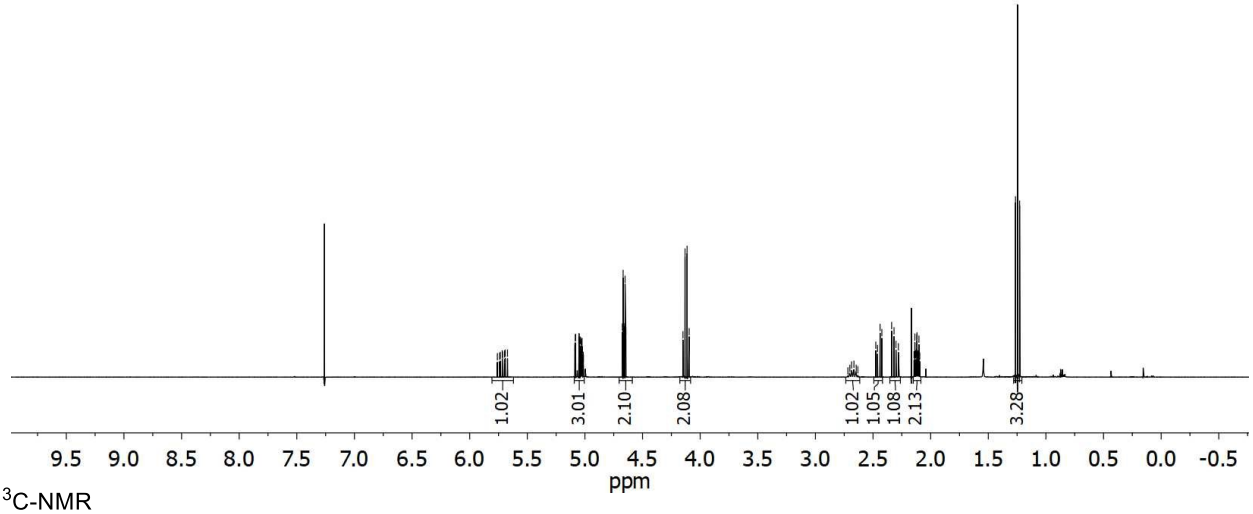


Ethyl 3-vinylhepta-5,6-dienoate 36

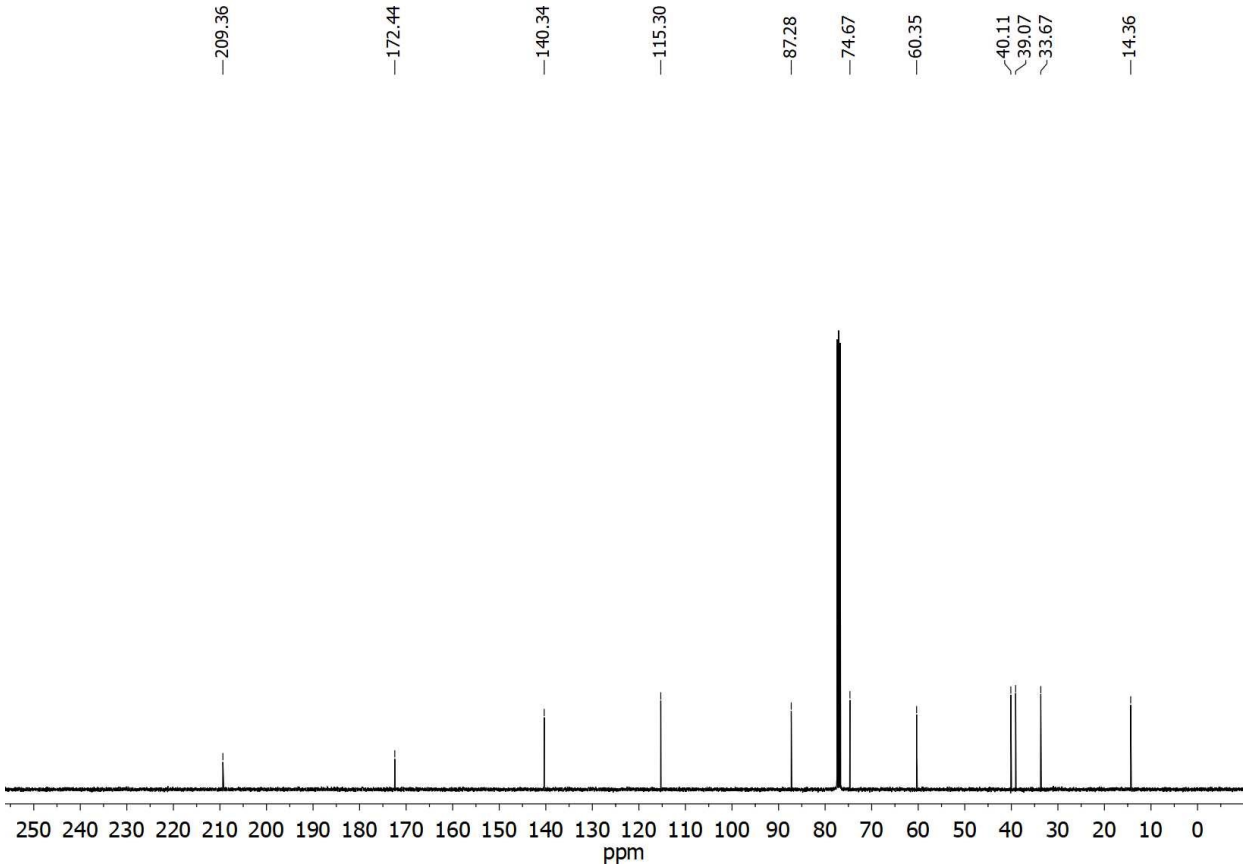
^{1}H-NMR



$C_{11}H_{16}O_2$

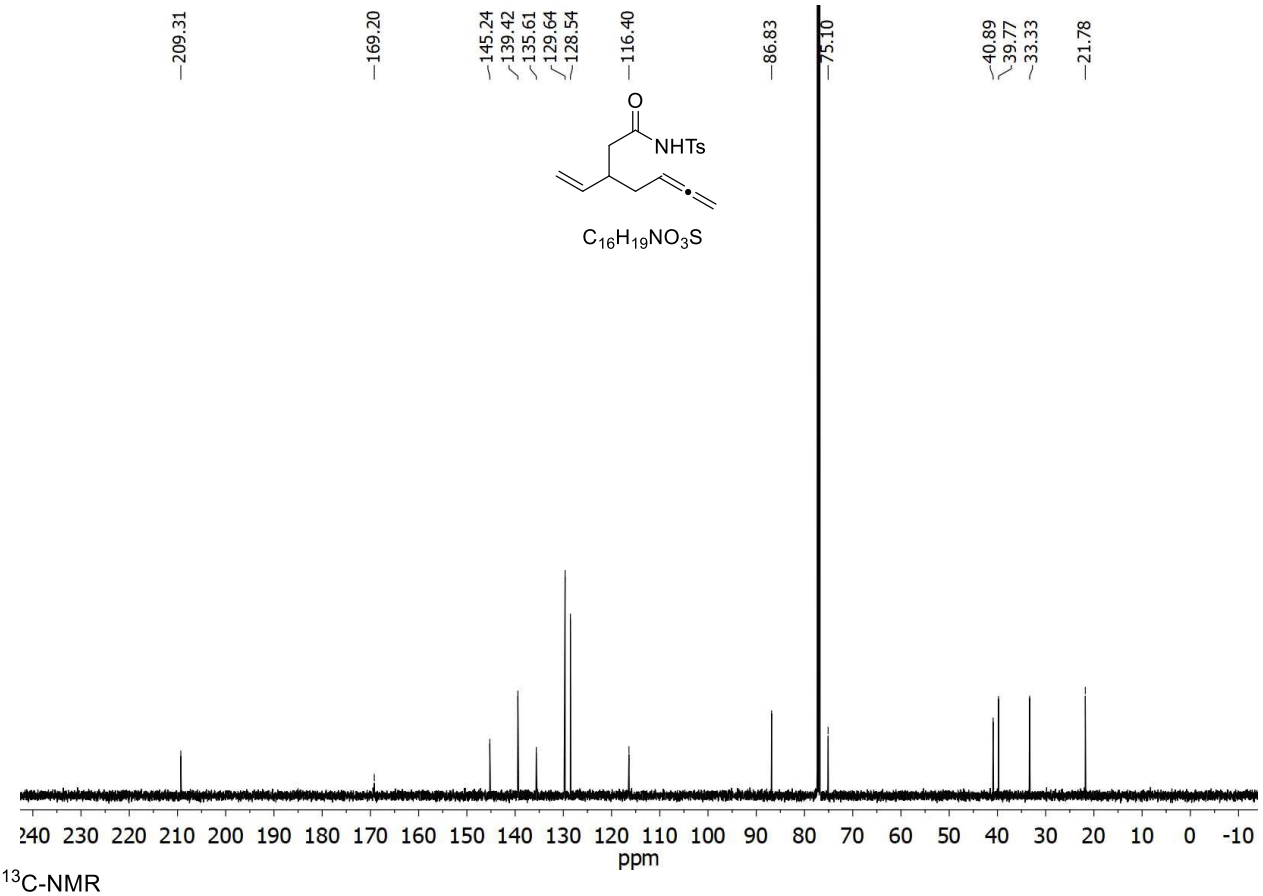


^{13}C-NMR

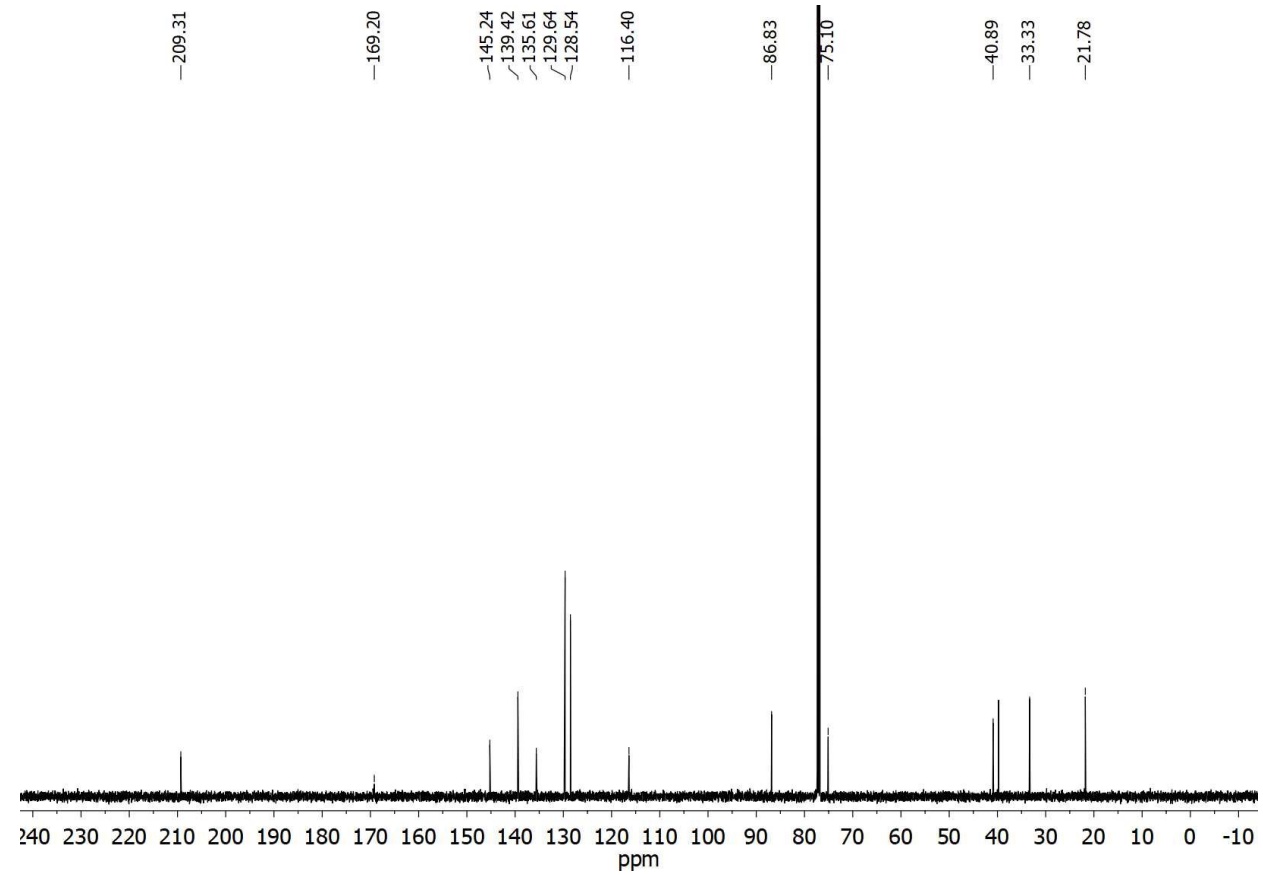


N-tosyl-3-vinylhepta-5,6-dienamide 37

^{1}H-NMR

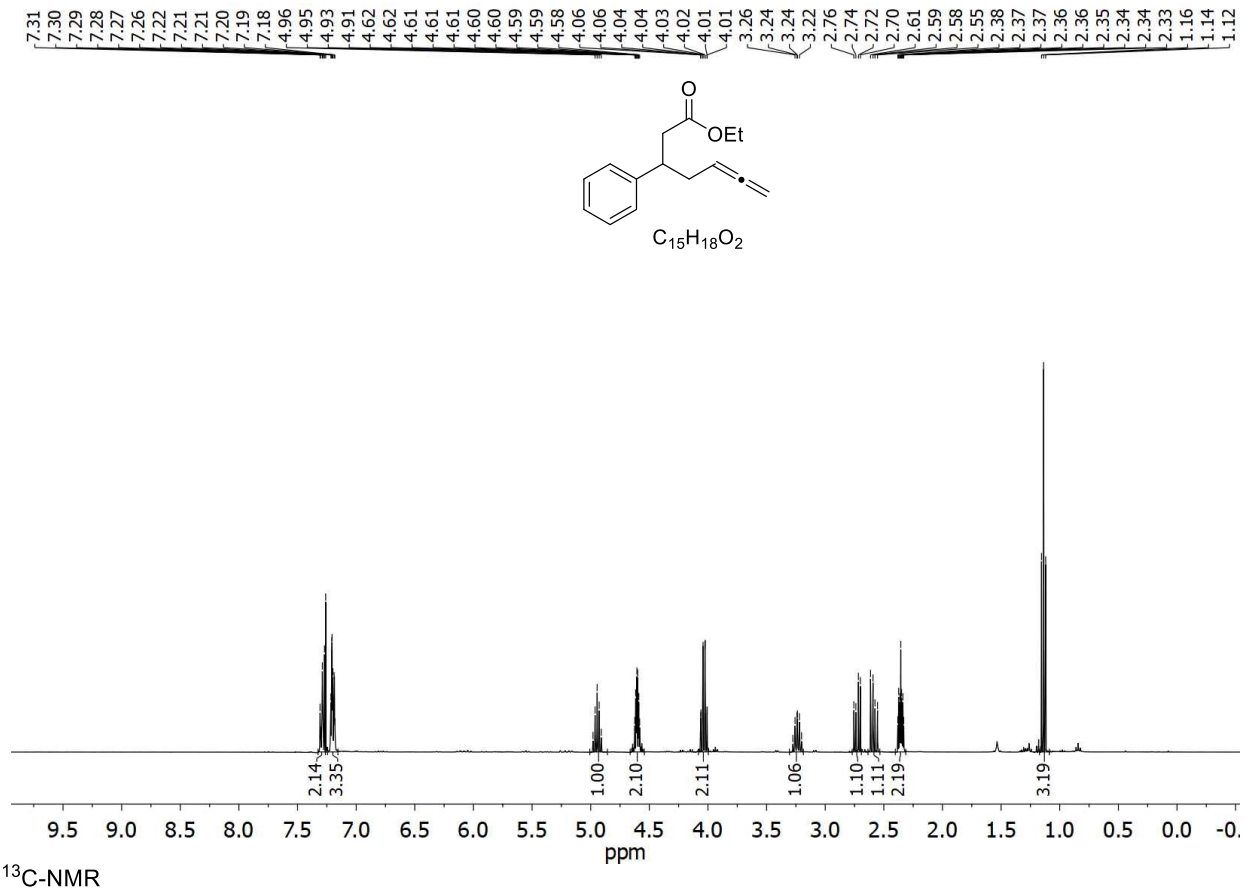


^{13}C-NMR

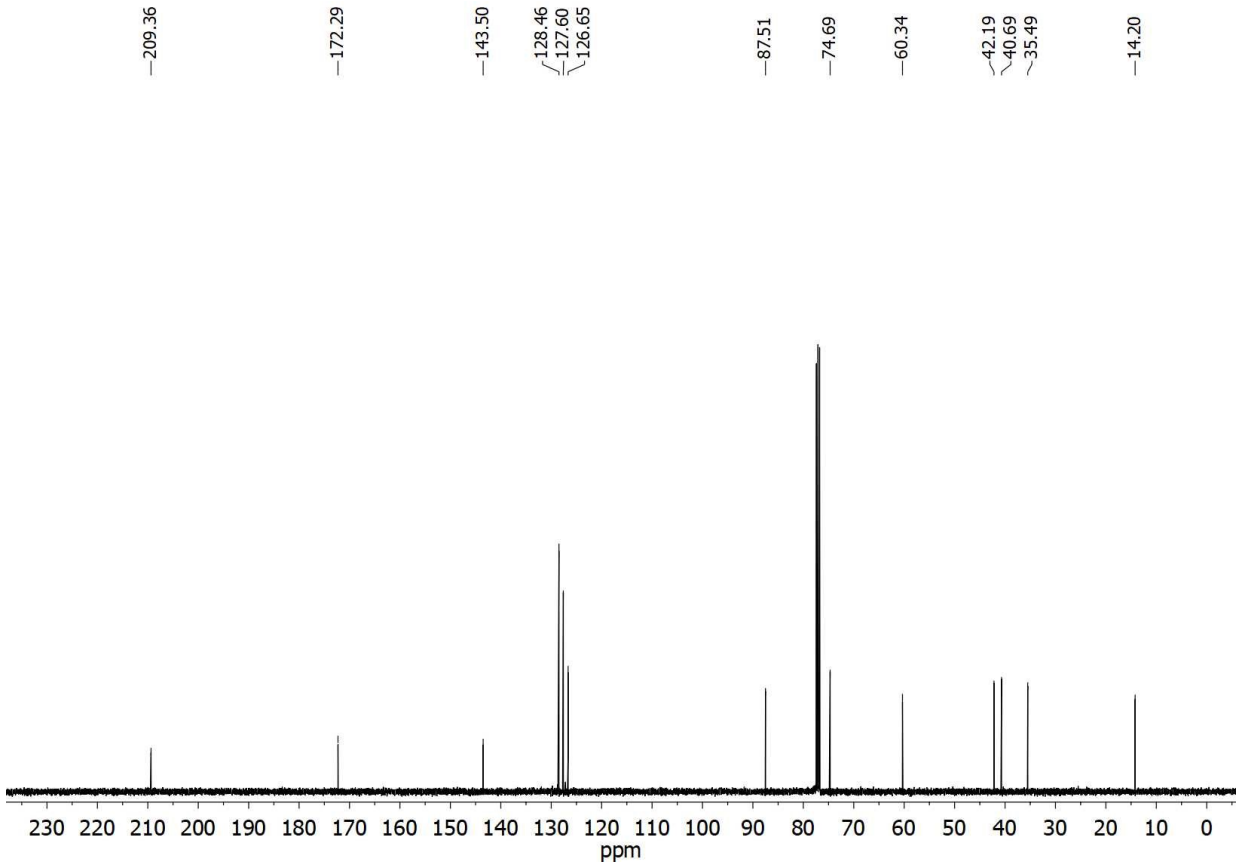


Ethyl 3-phenylhepta-5,6-dienoate 38

^{1}H-NMR

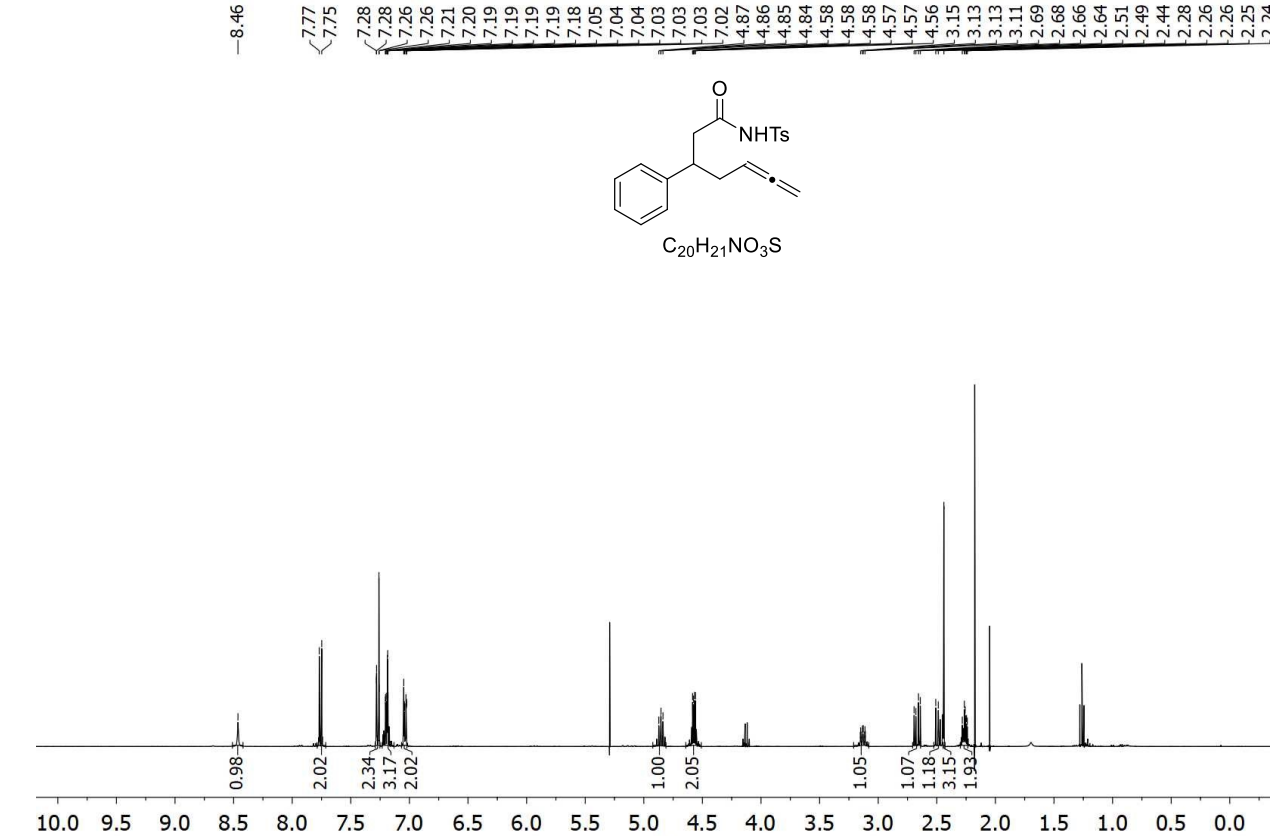


^{13}C-NMR

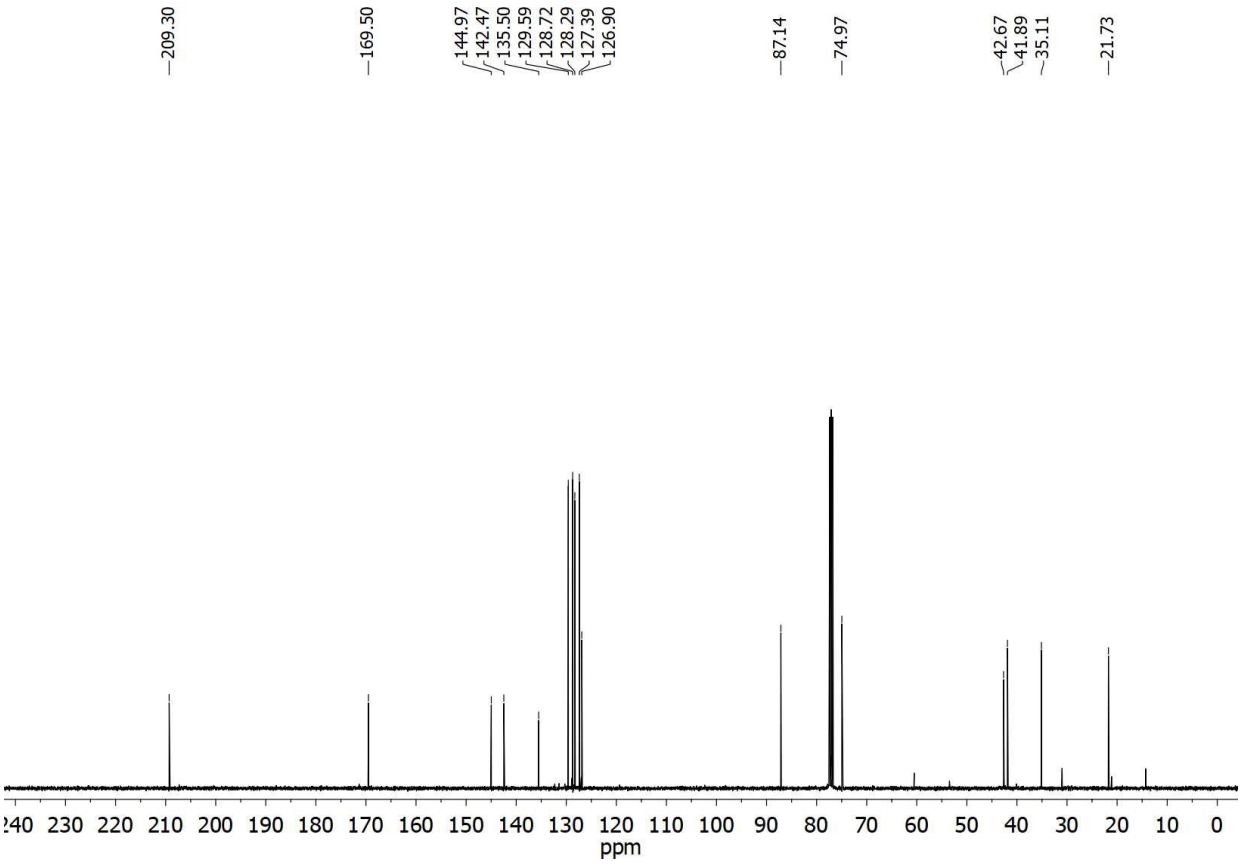


3-phenyl-N-tosylhepta-5,6-dienamide 39

^{1}H-NMR

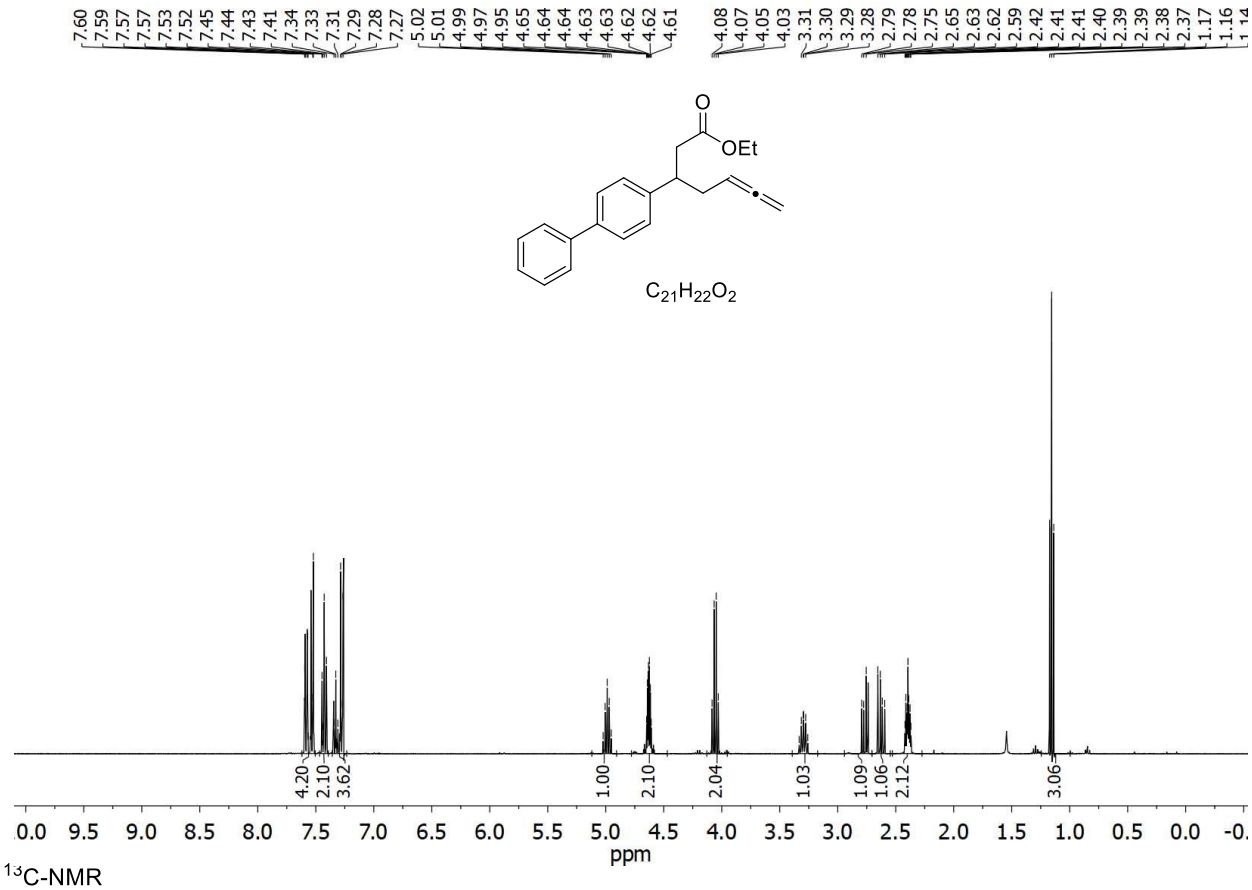


^{13}C-NMR

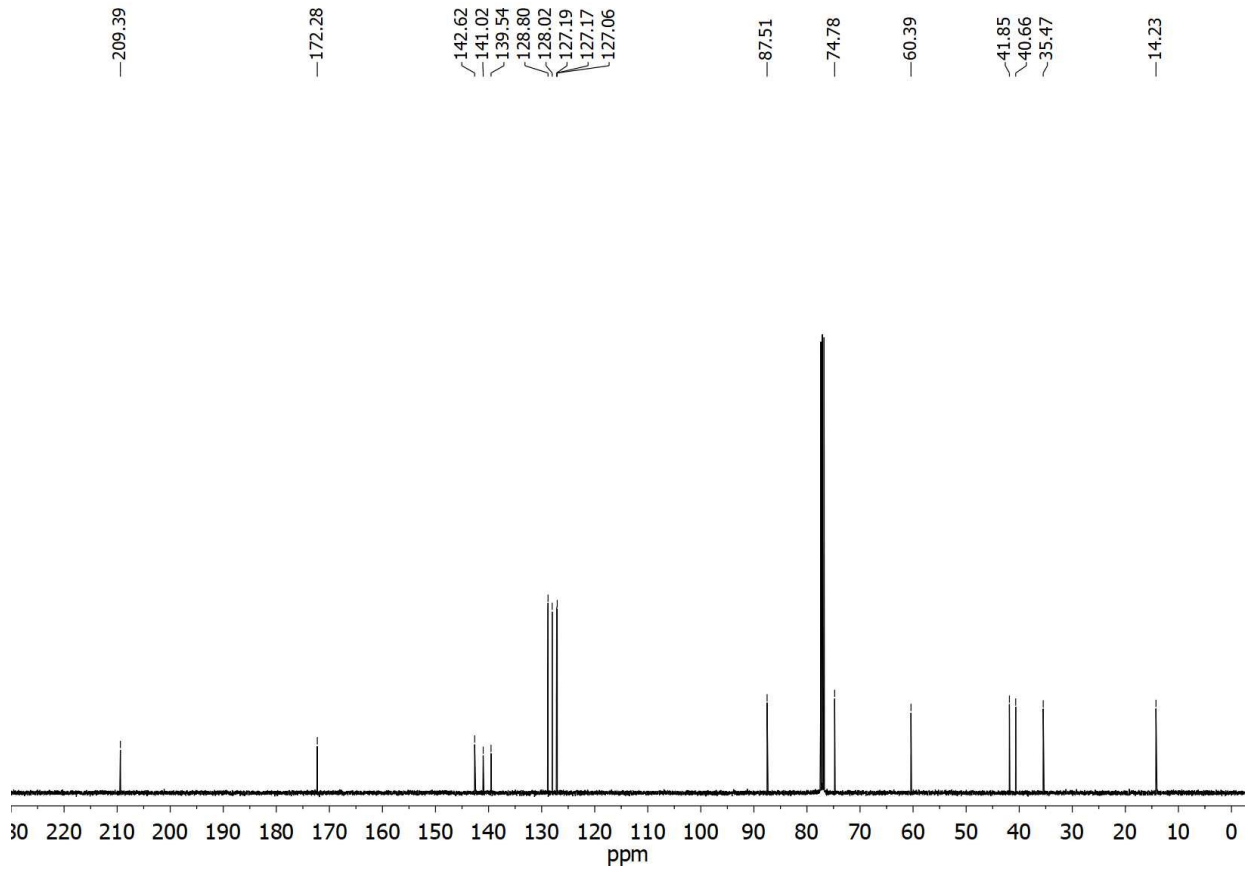


Ethyl 3-([1,1'-biphenyl]-4-yl)hepta-5,6-dienoate 40

^{1}H-NMR

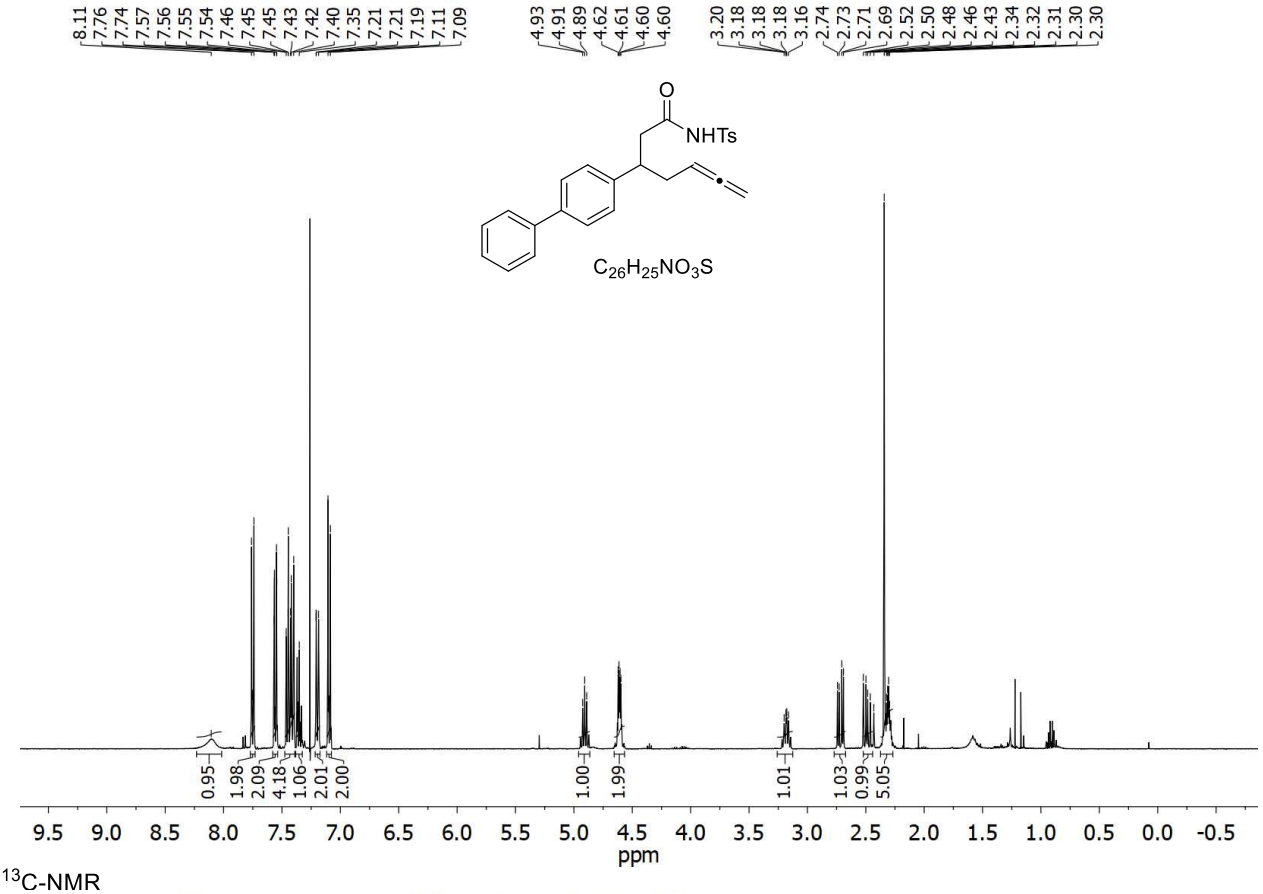


^{13}C-NMR

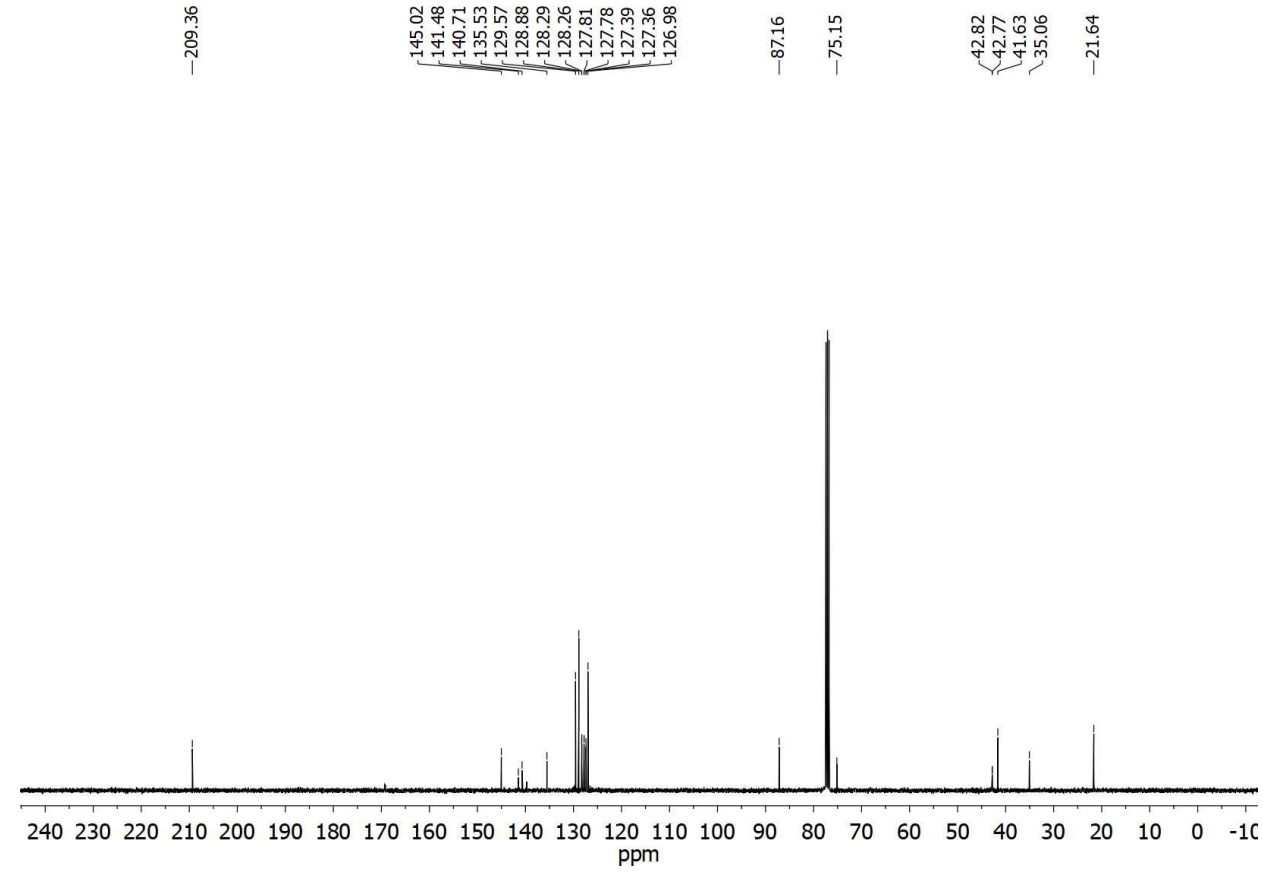


3-([1,1'-biphenyl]-4-yl)-N-tosylhepta-5,6-dienamide 41

^{1}H-NMR

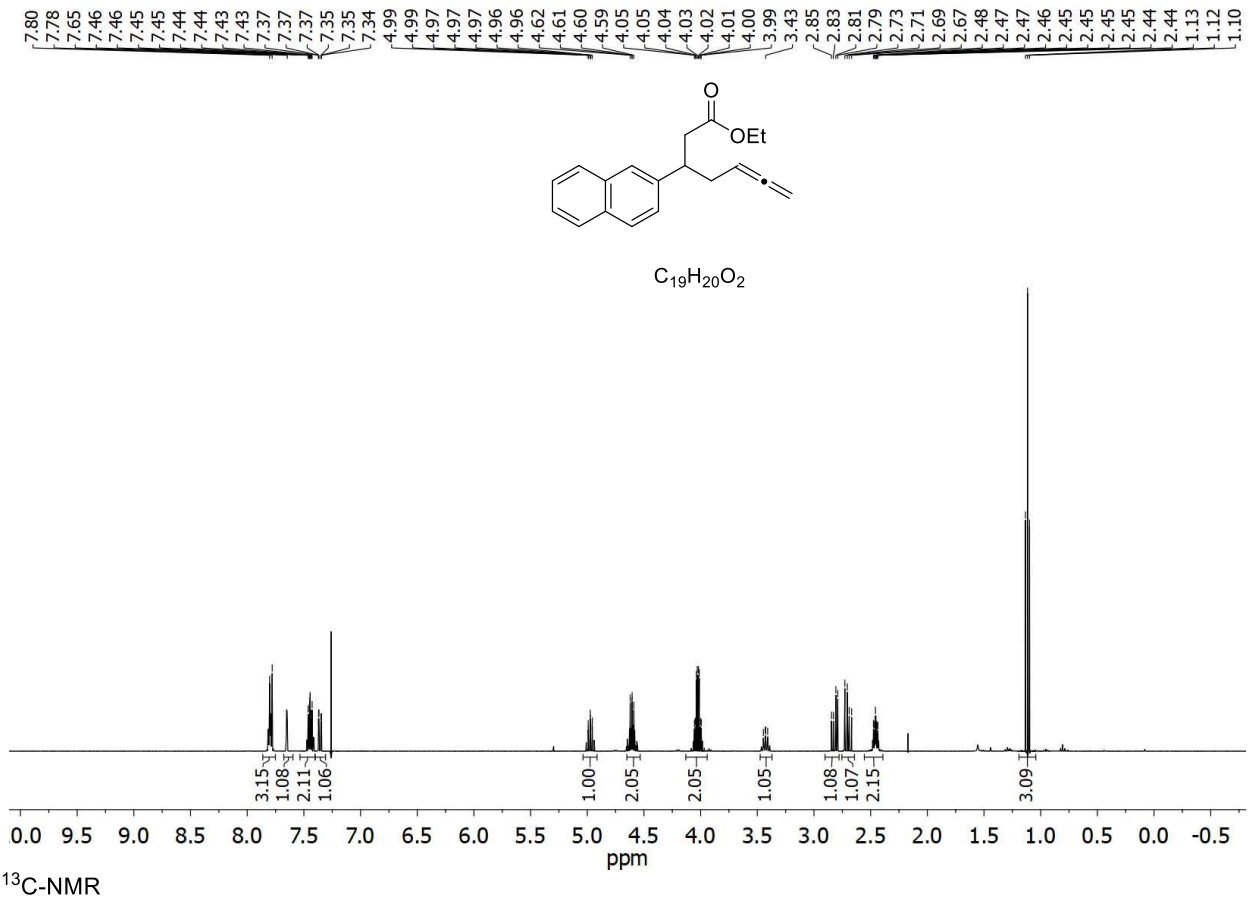


^{13}C-NMR



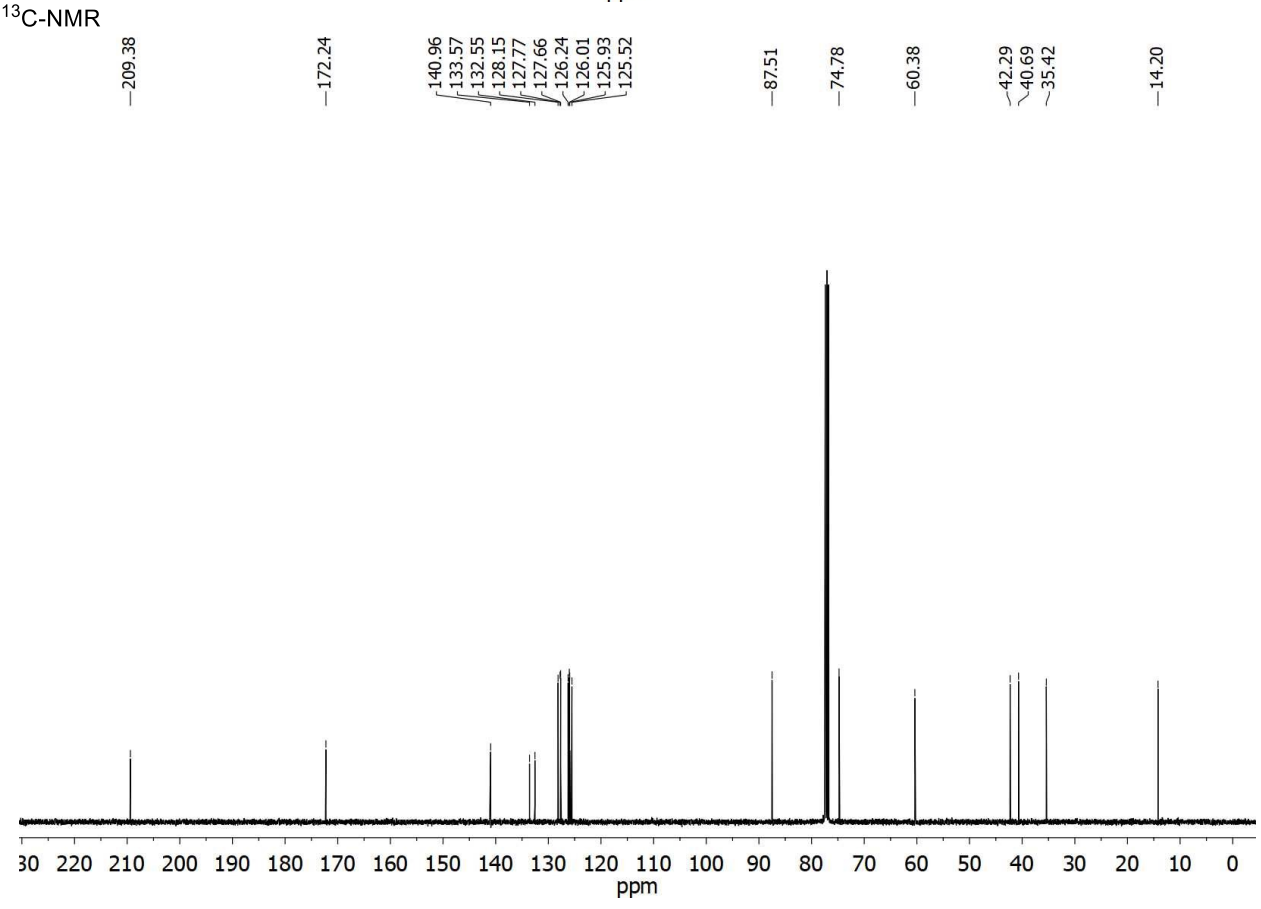
Ethyl 3-(naphthalen-2-yl)hepta-5,6-dienoat 42

^{1}H-NMR



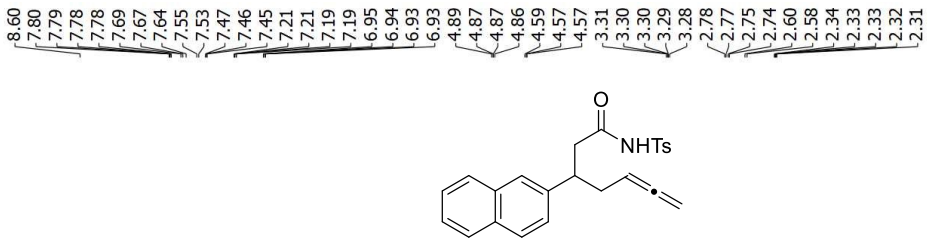
$C_{19}H_{20}O_2$

^{13}C-NMR

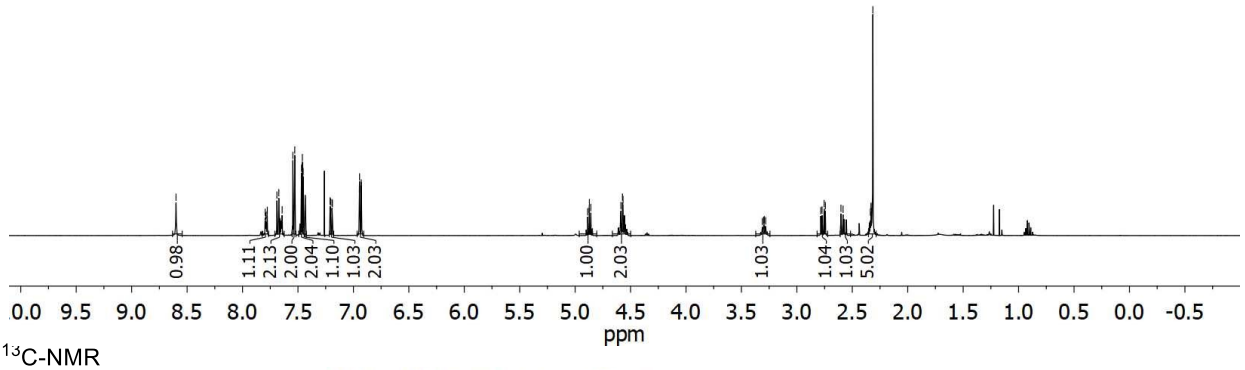


3-(naphthalen-2-yl)-N-tosylhepta-5,6-dienamide 43

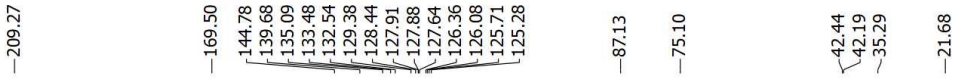
^{1}H-NMR

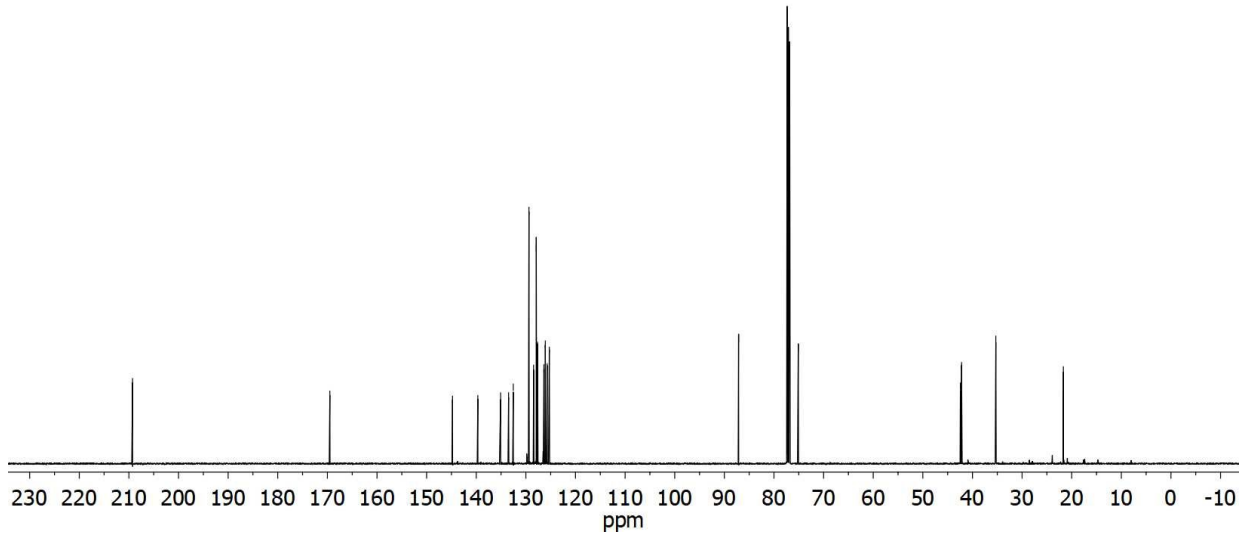


$C_{24}H_{23}NO_3S$



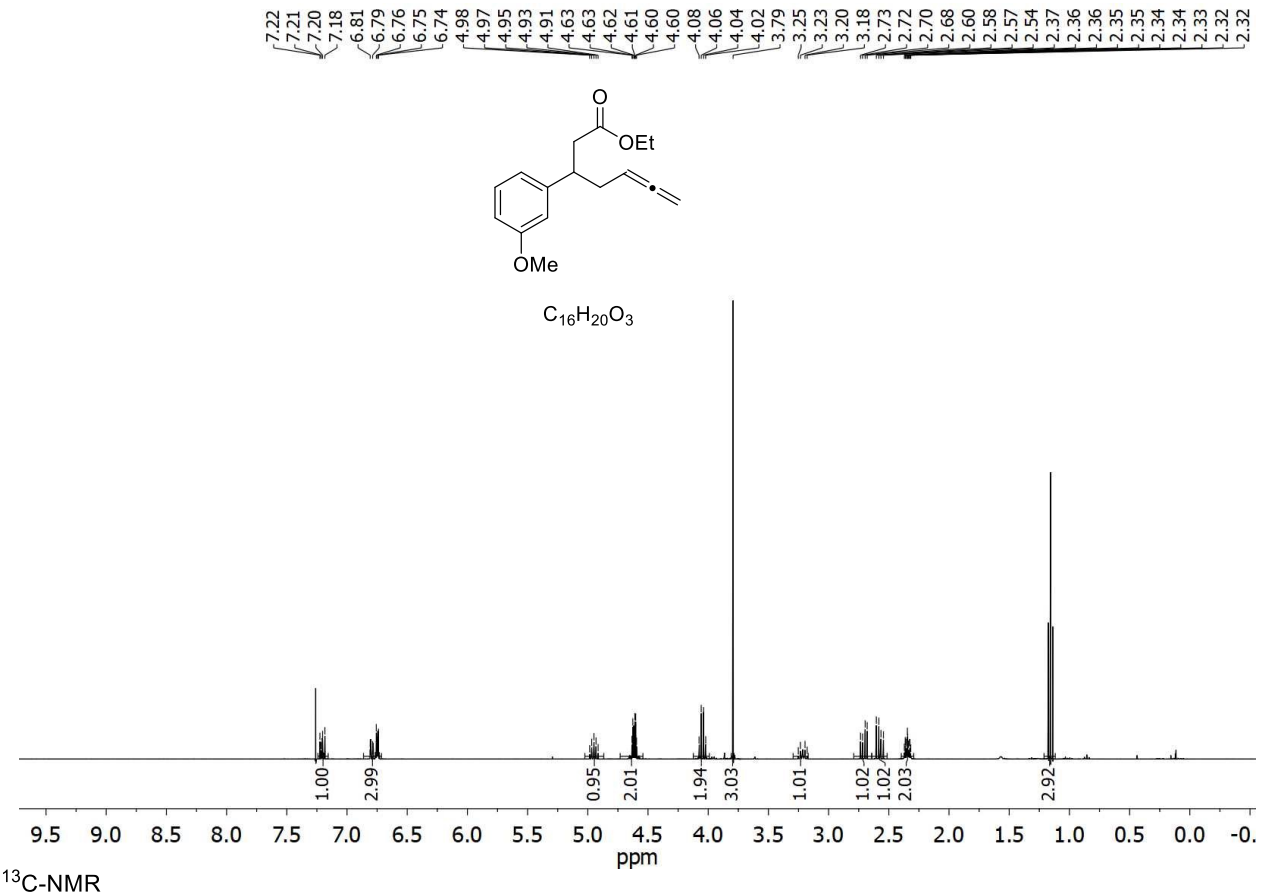
^{13}C-NMR



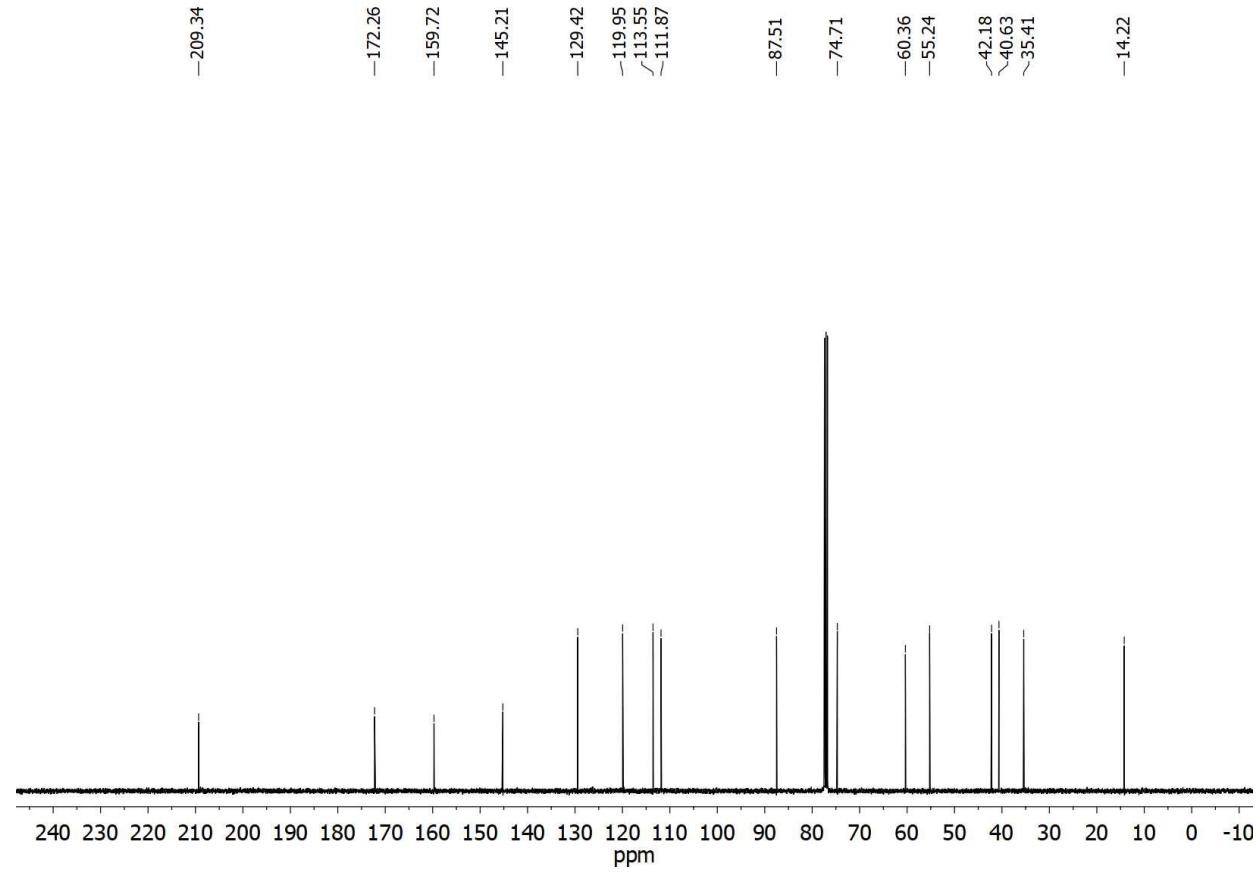


Ethyl 3-(3-methoxyphenyl)hepta-5,6-dienoate 44

^{1}H-NMR

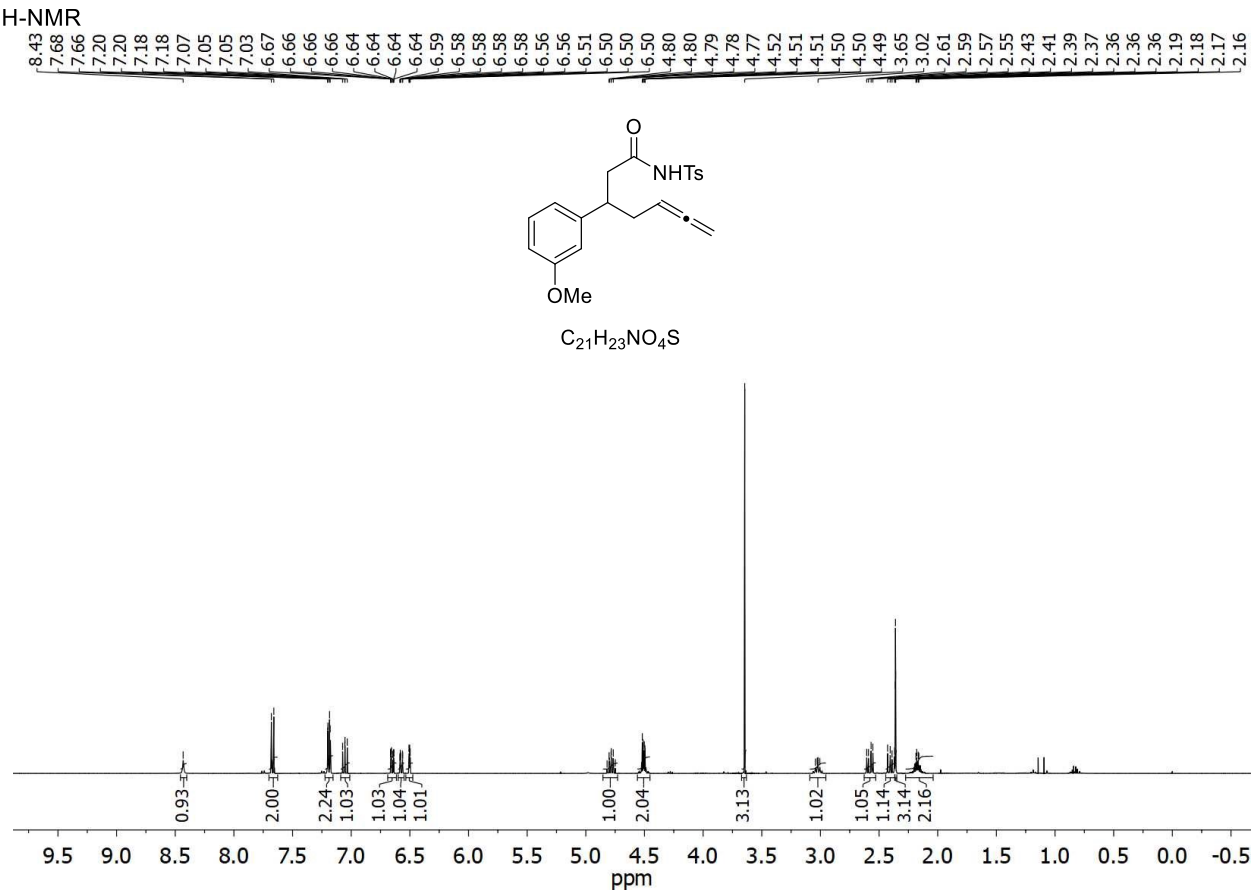


^{13}C-NMR



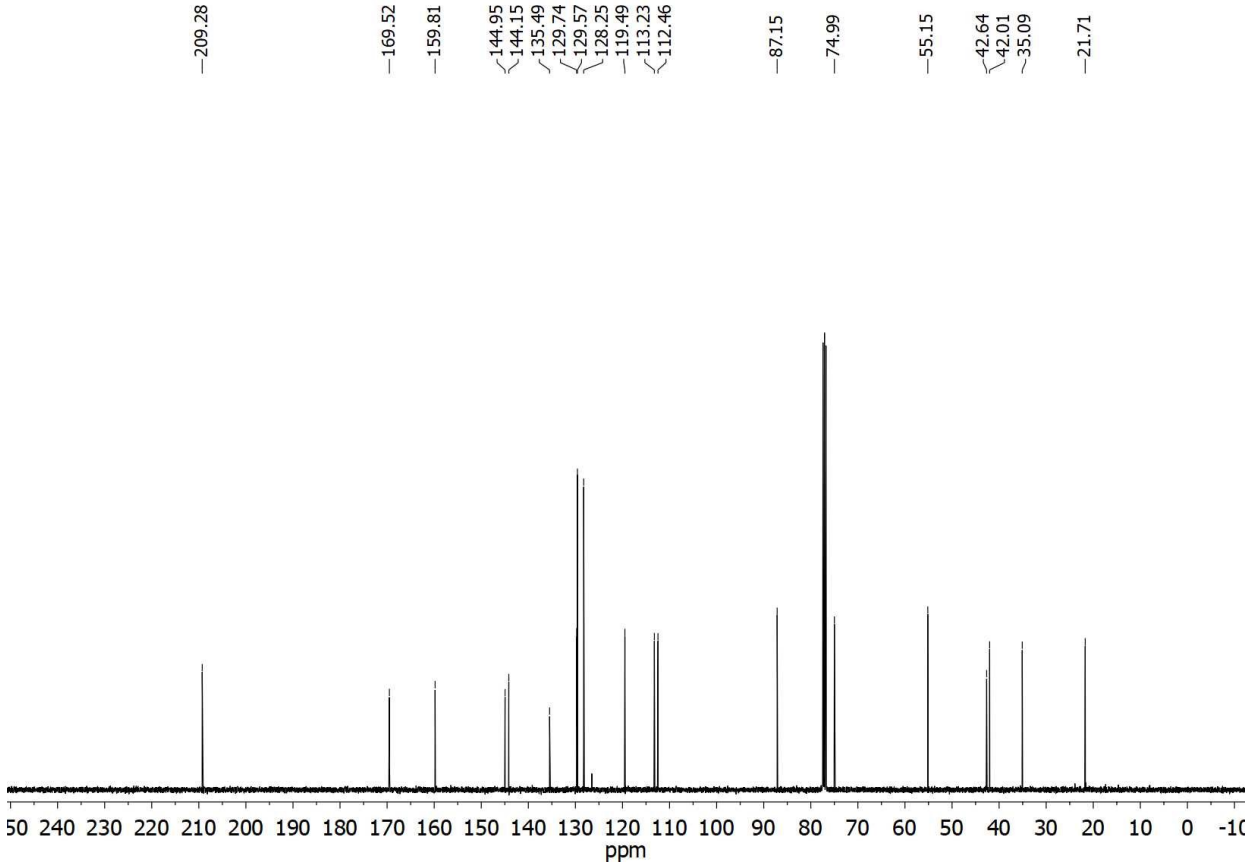
Ethyl 3-(3-methoxyphenyl)hepta-5,6-dienoate 45

^{1}H-NMR



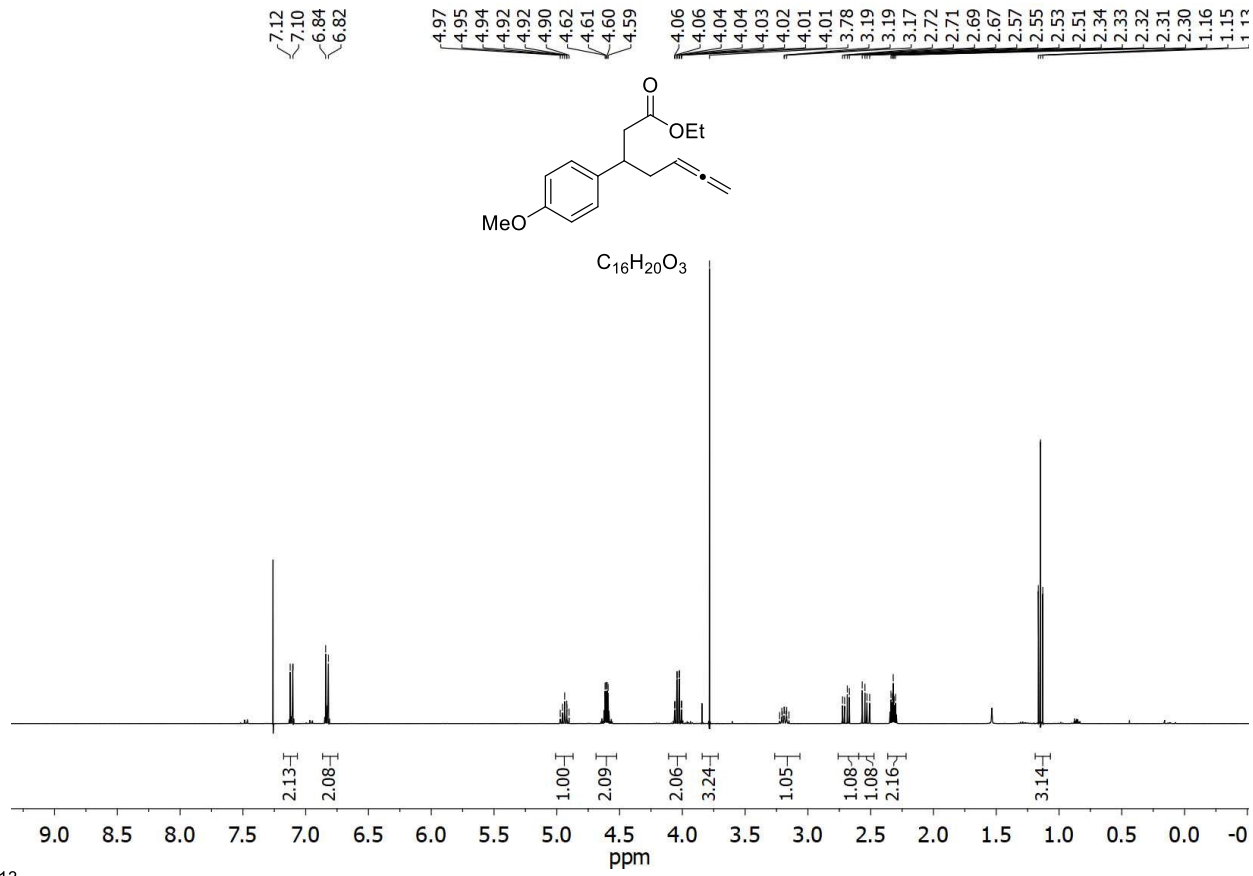
$C_{21}H_{23}NO_4S$

^{13}C-NMR

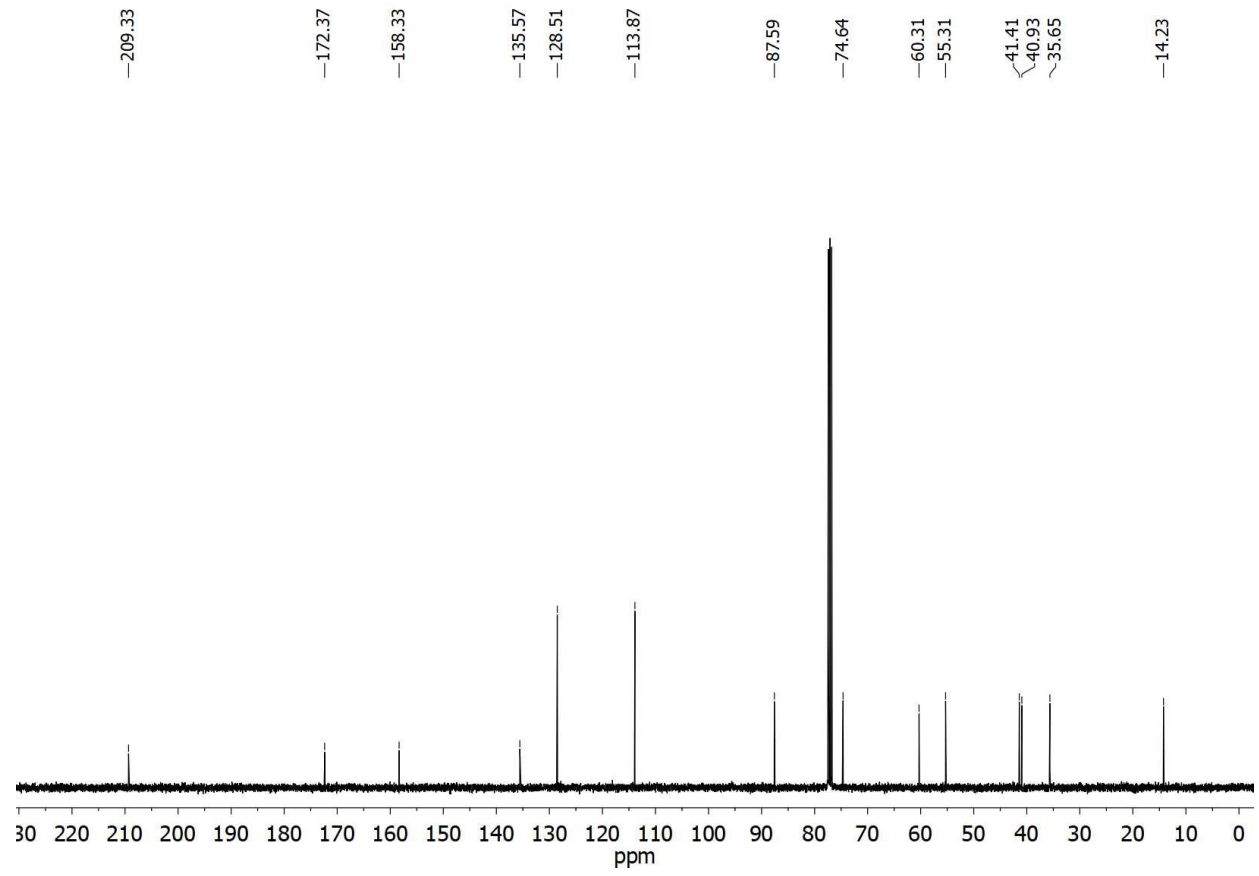


Ethyl 3-(4-methoxyphenyl)hepta-5,6-dienoate 46

^{1}H-NMR

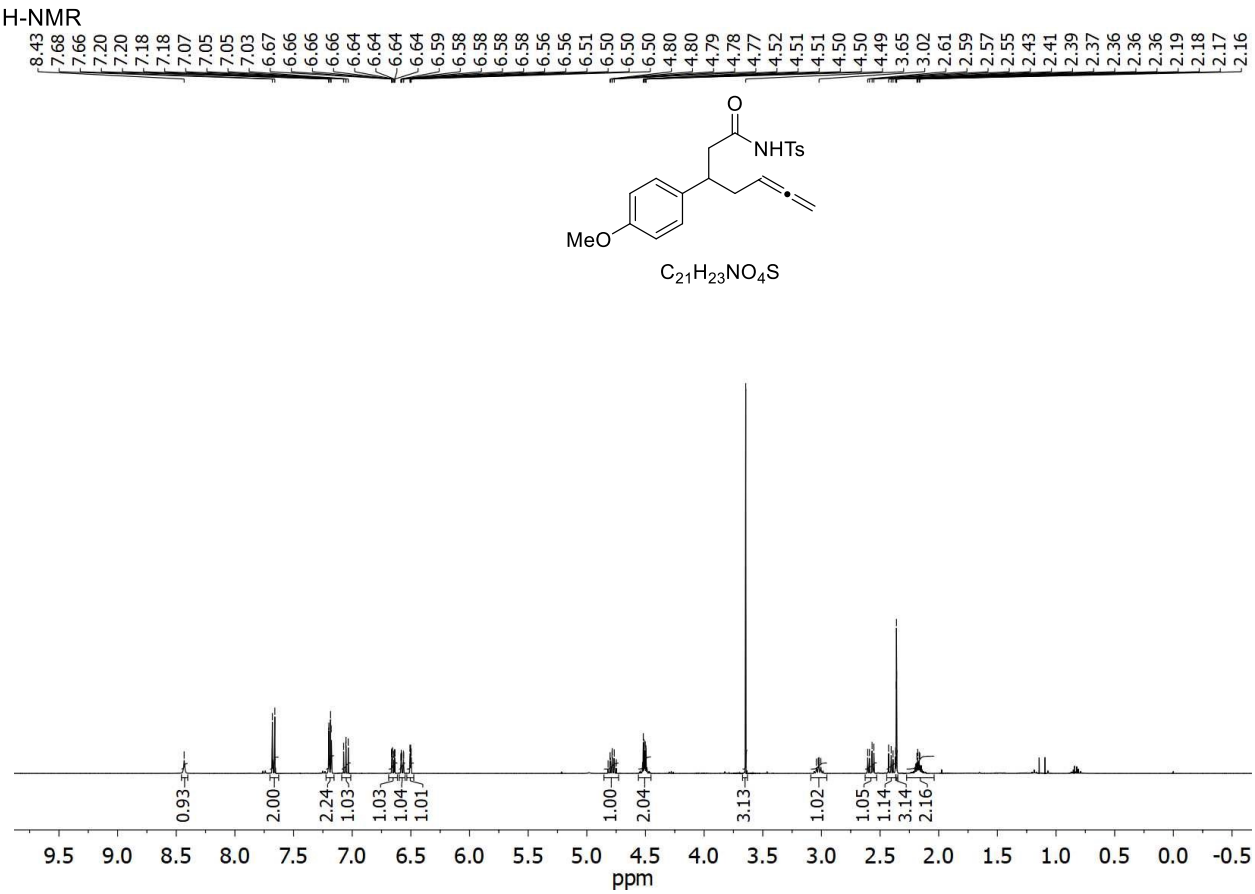


^{13}C-NMR

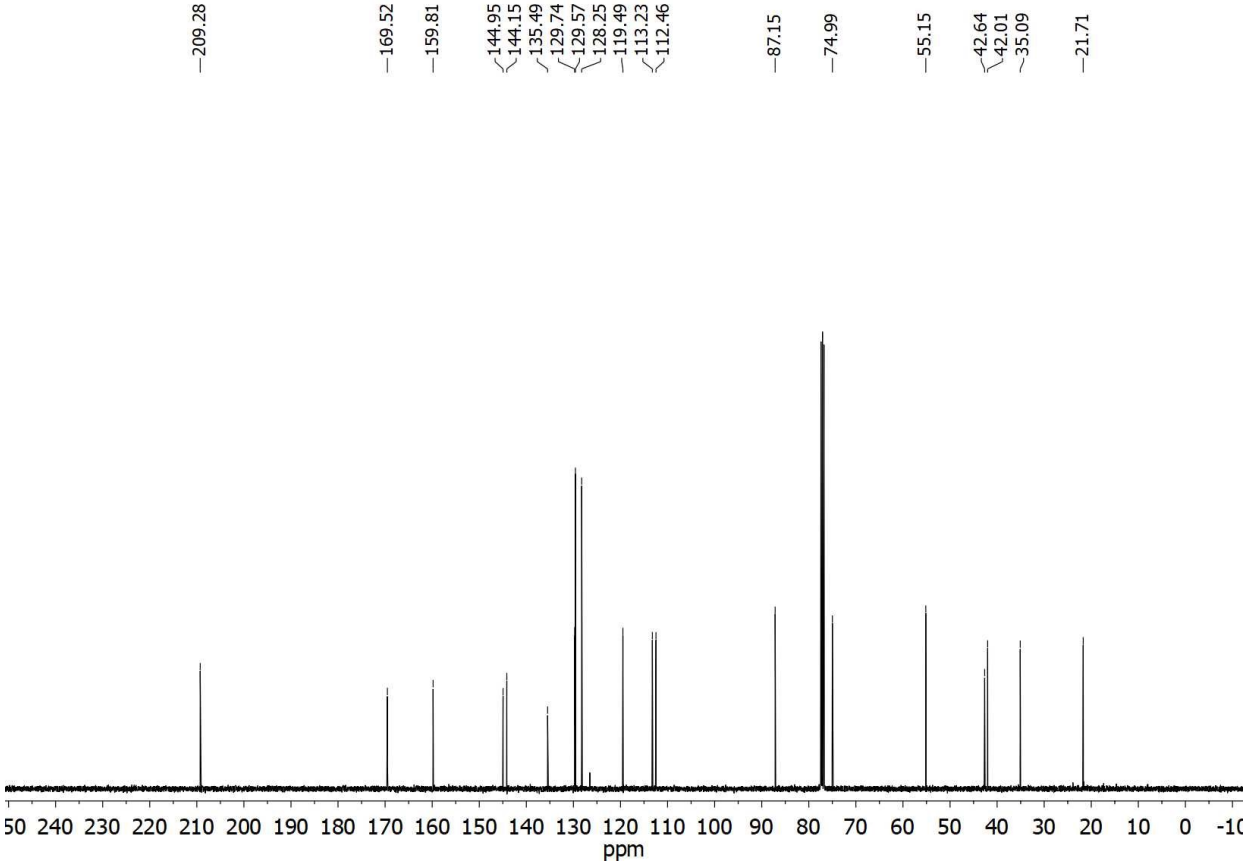


3-(4-methoxyphenyl)-N-tosylhepta-5,6-dienamide 47

^{1}H-NMR

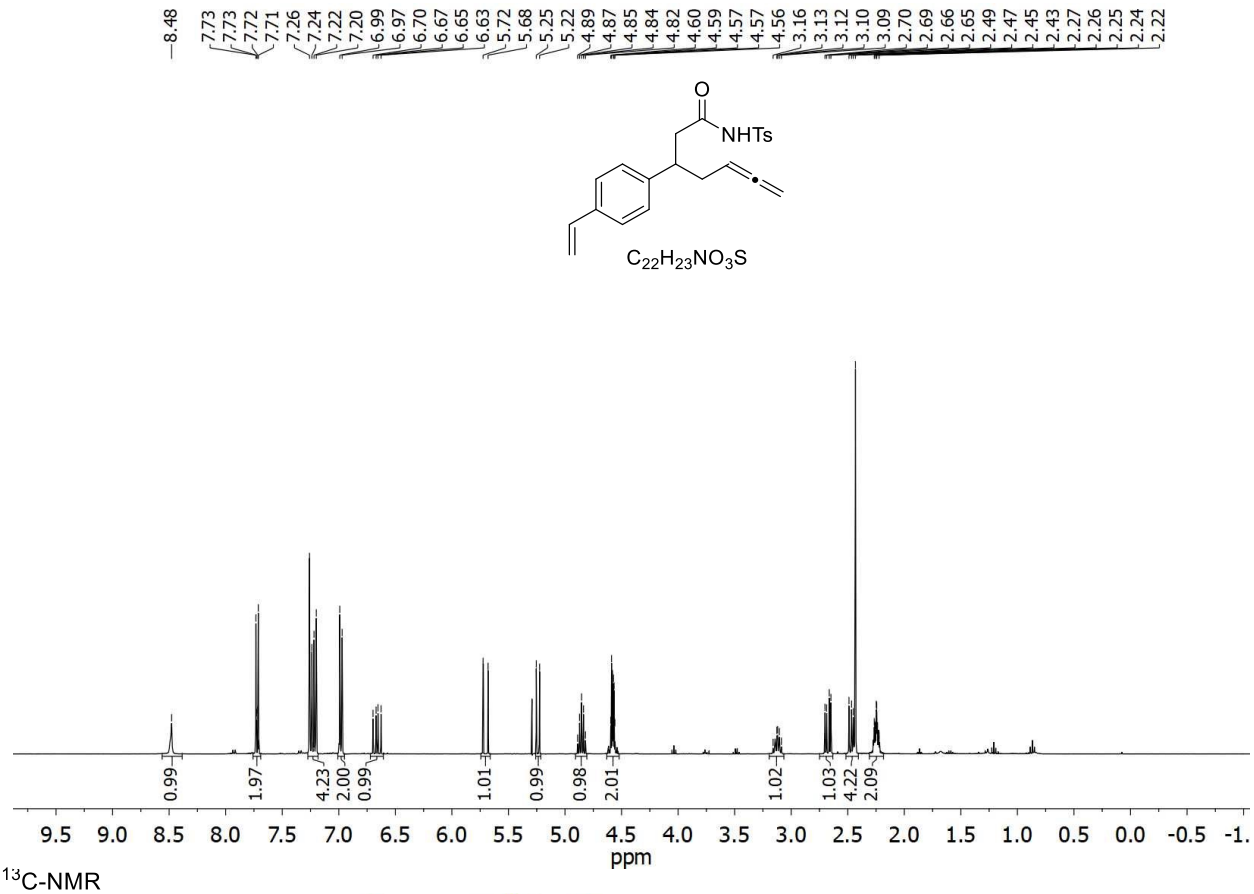


^{13}C-NMR

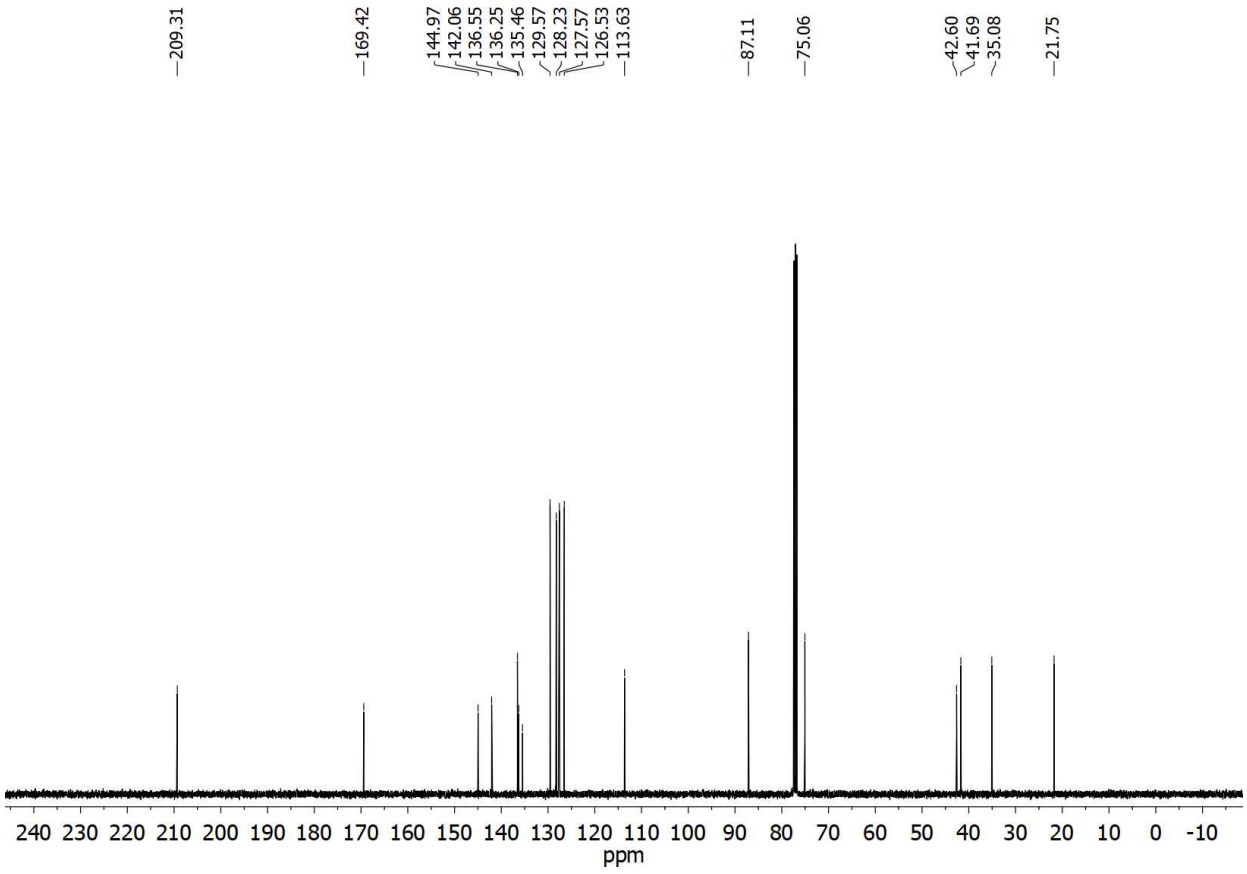


N-tosyl-3-(4-vinylphenyl)hepta-5,6-dienamide 48

^{1}H-NMR

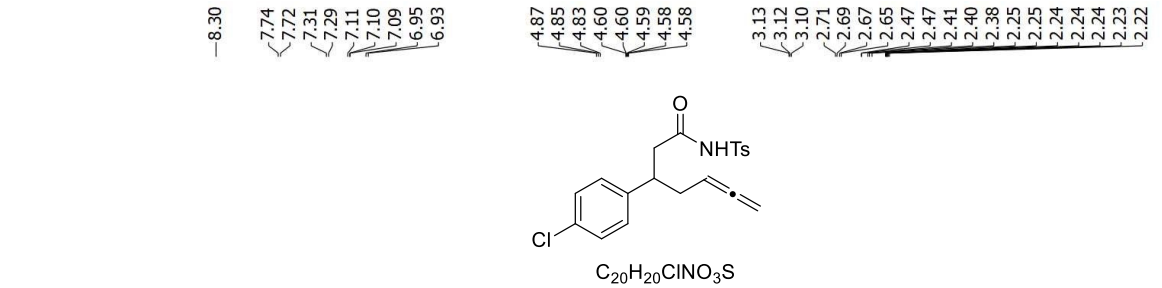


^{13}C-NMR

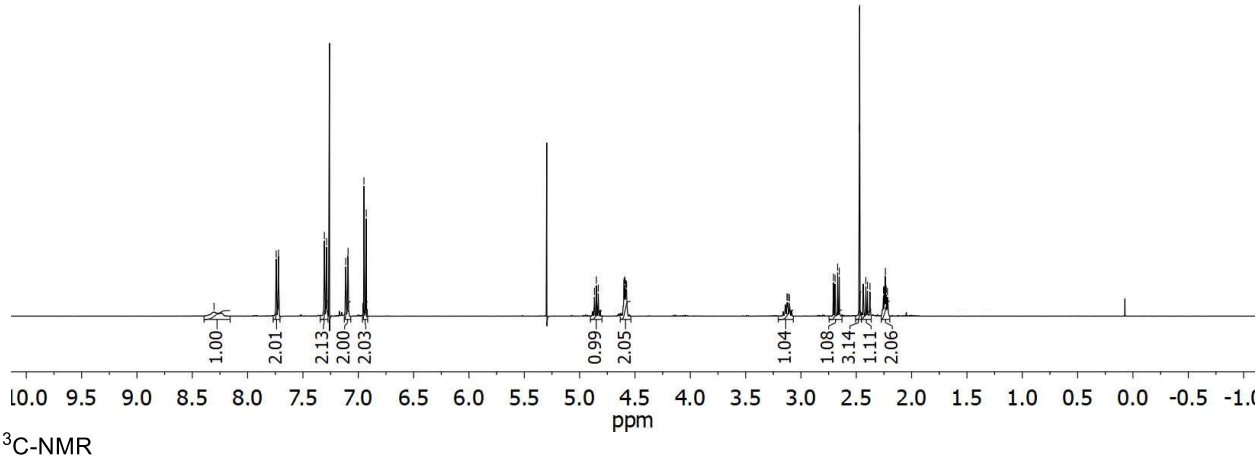


3-(4-chlorophenyl)-N-tosylhepta-5,6-dienamide 49

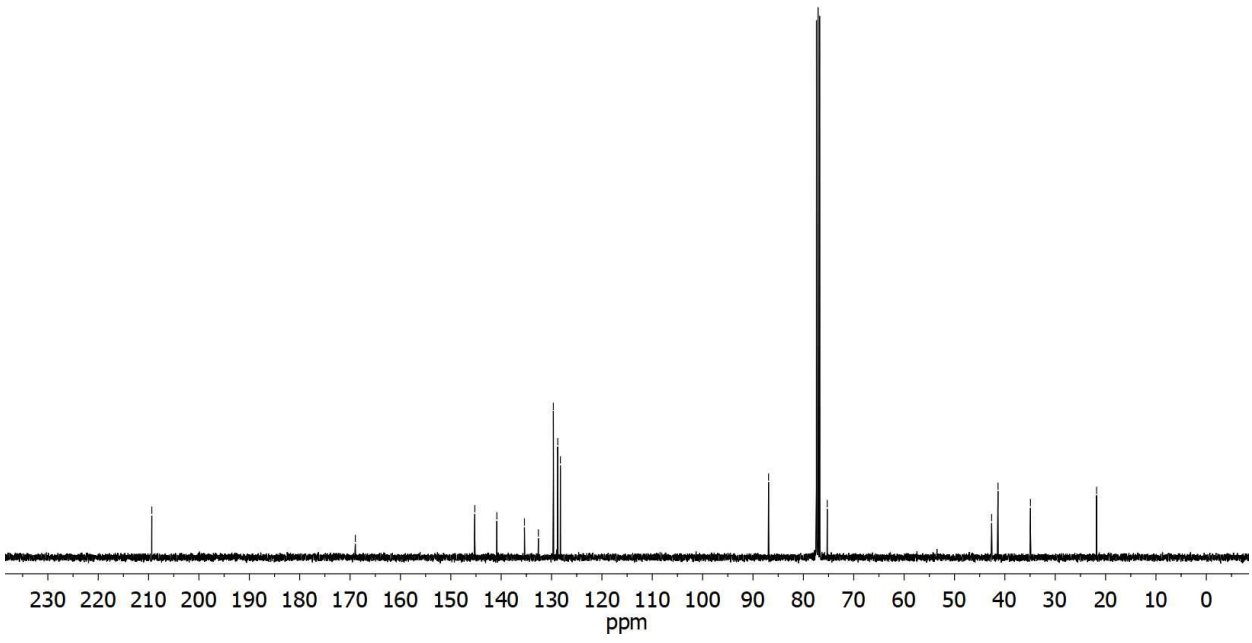
^{1}H-NMR



$C_{20}H_{20}ClNO_3S$

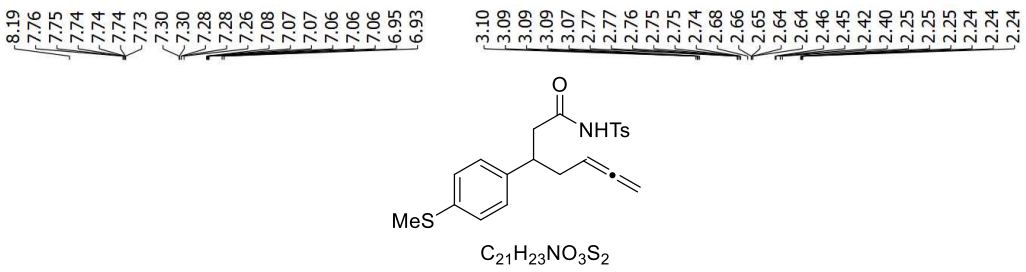


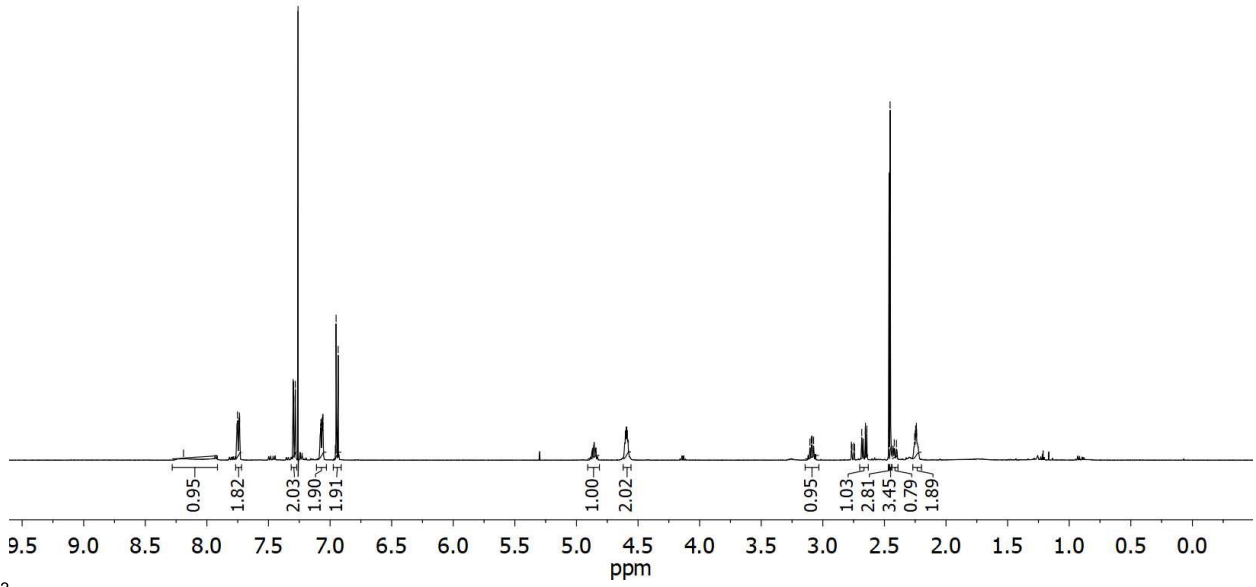
^{13}C-NMR



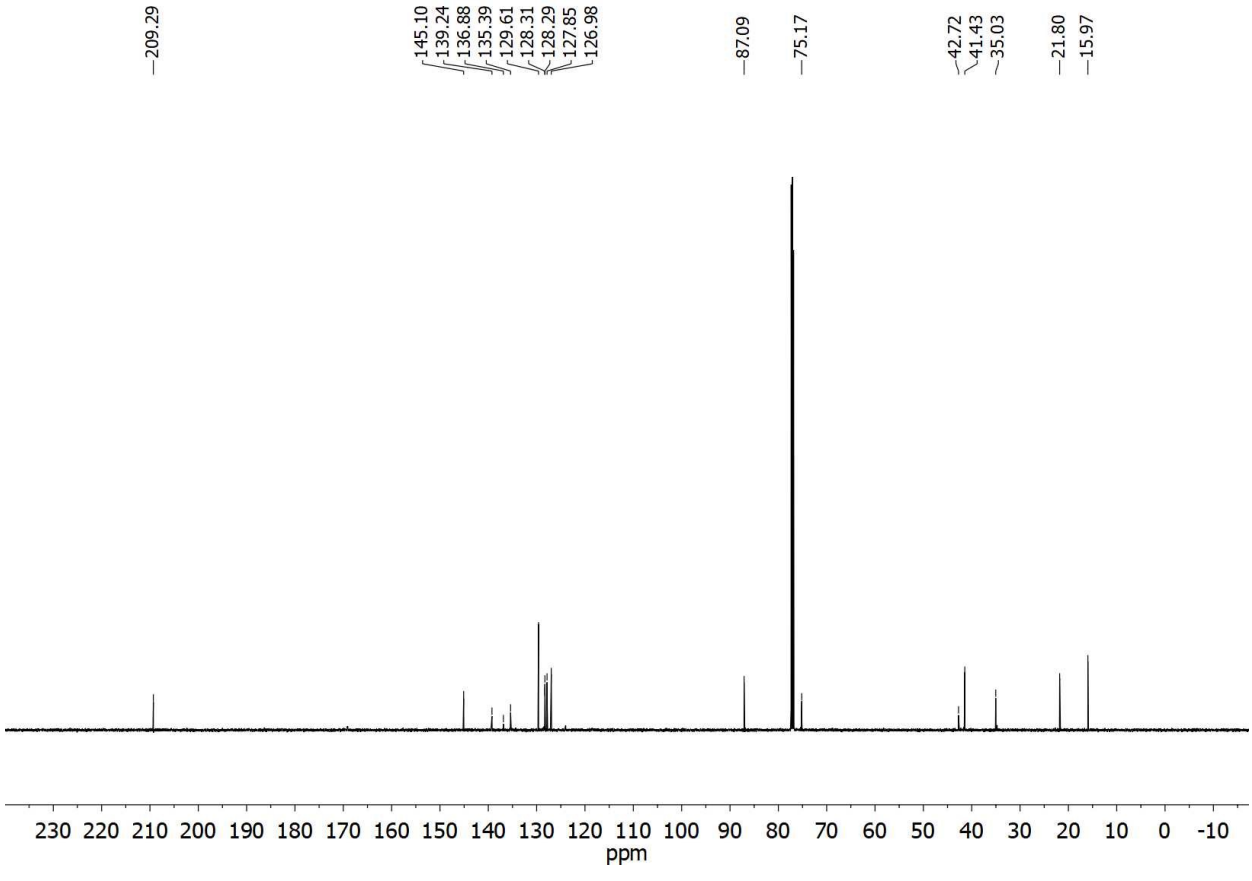
3-(4-(methylthio)phenyl)-N-tosylhepta-5,6-dienamide 50

^{1}H-NMR



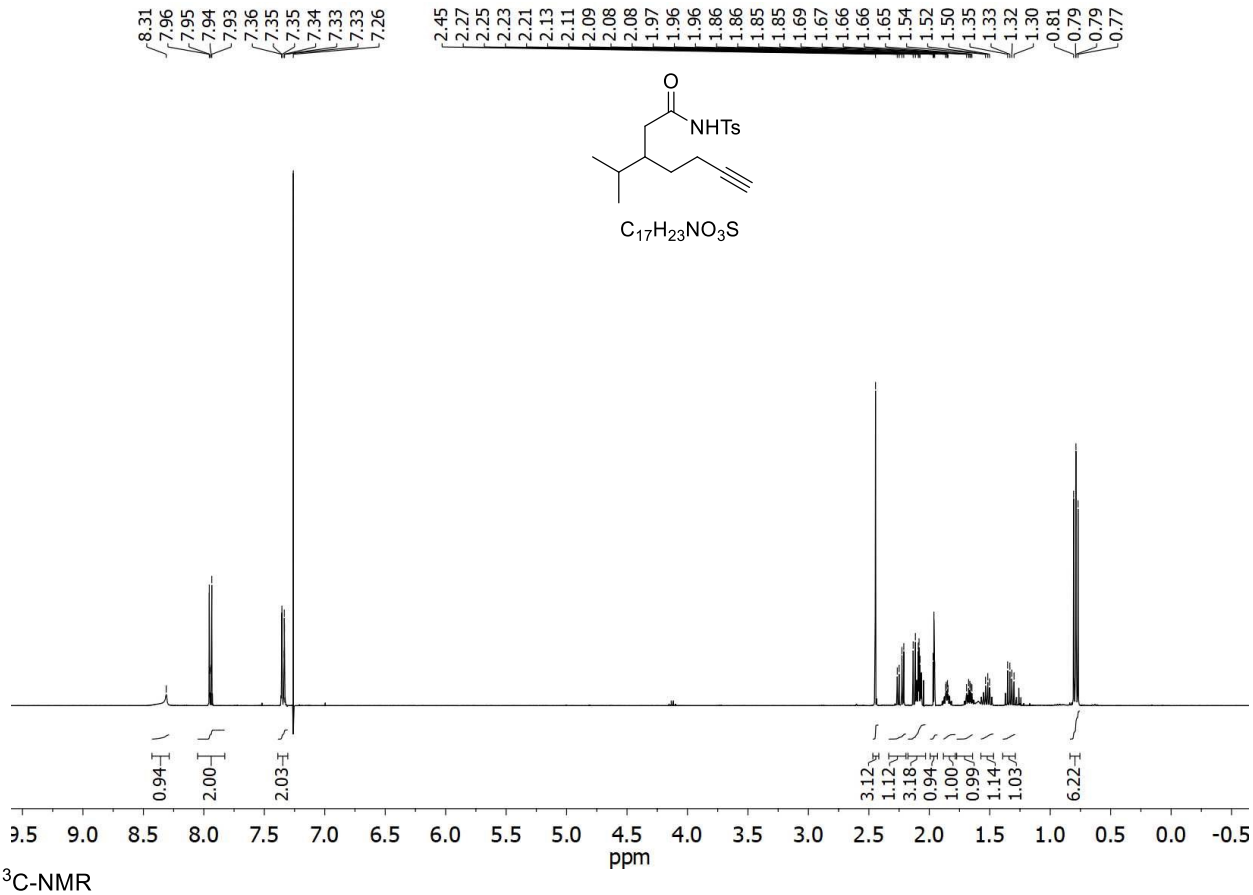


^{13}C-NMR

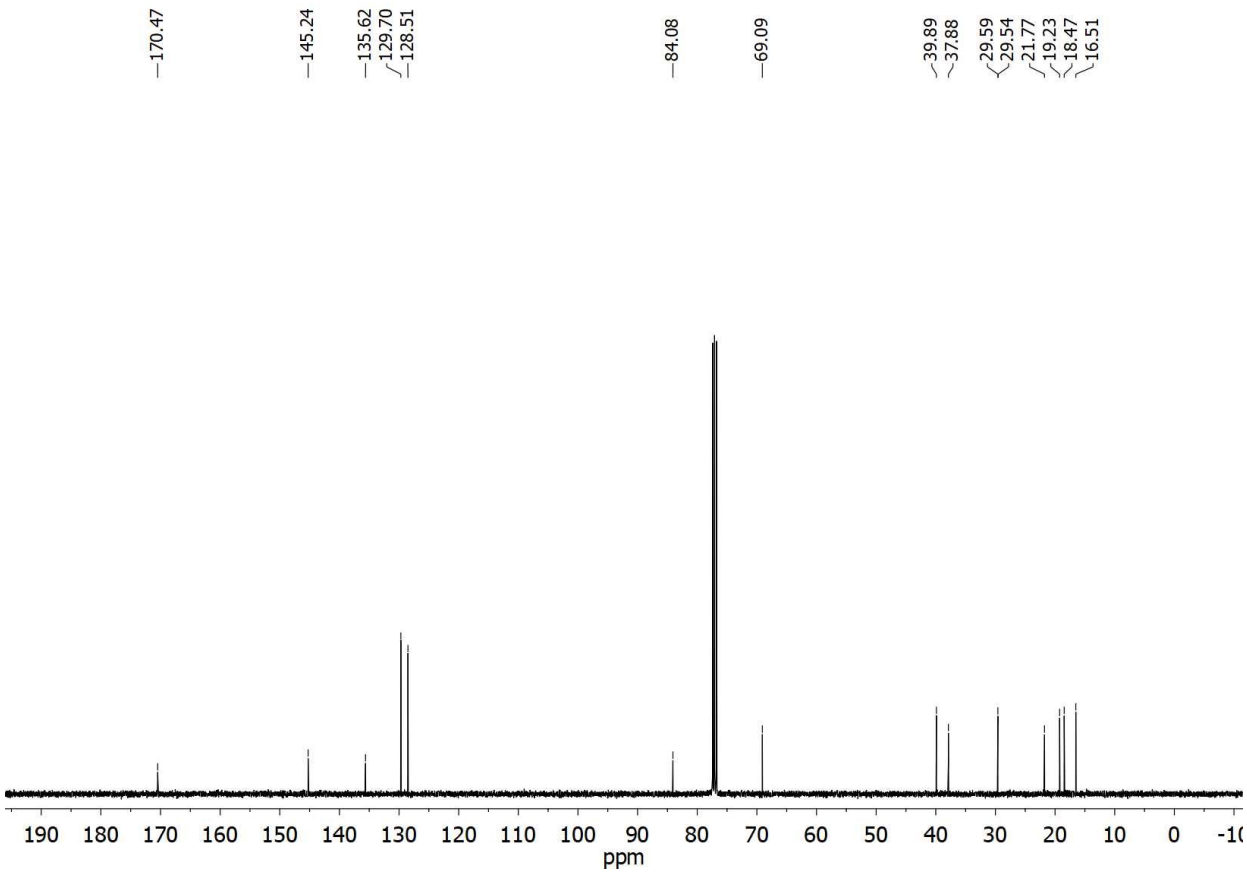


3-isopropyl-N-tosylhept-6-ynamide 51

^{1}H-NMR

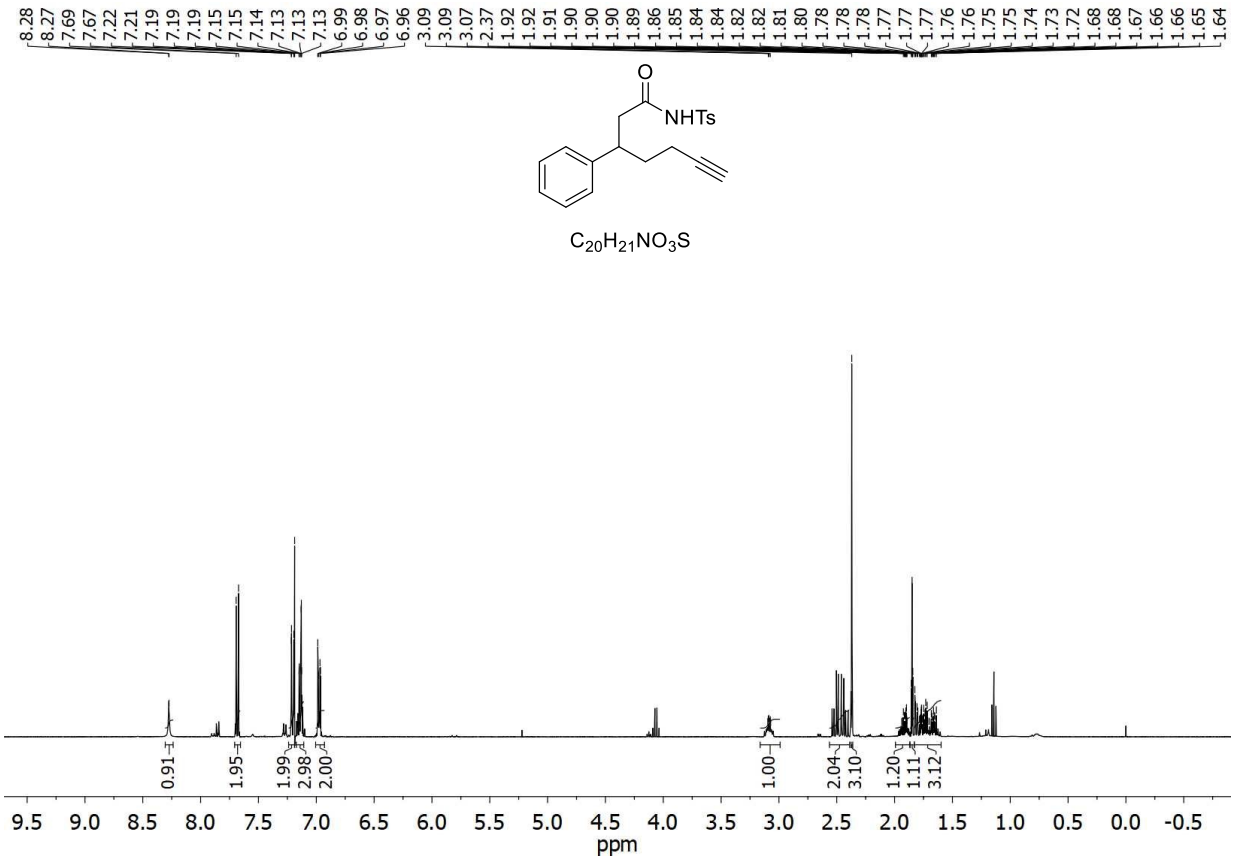


^{13}C-NMR



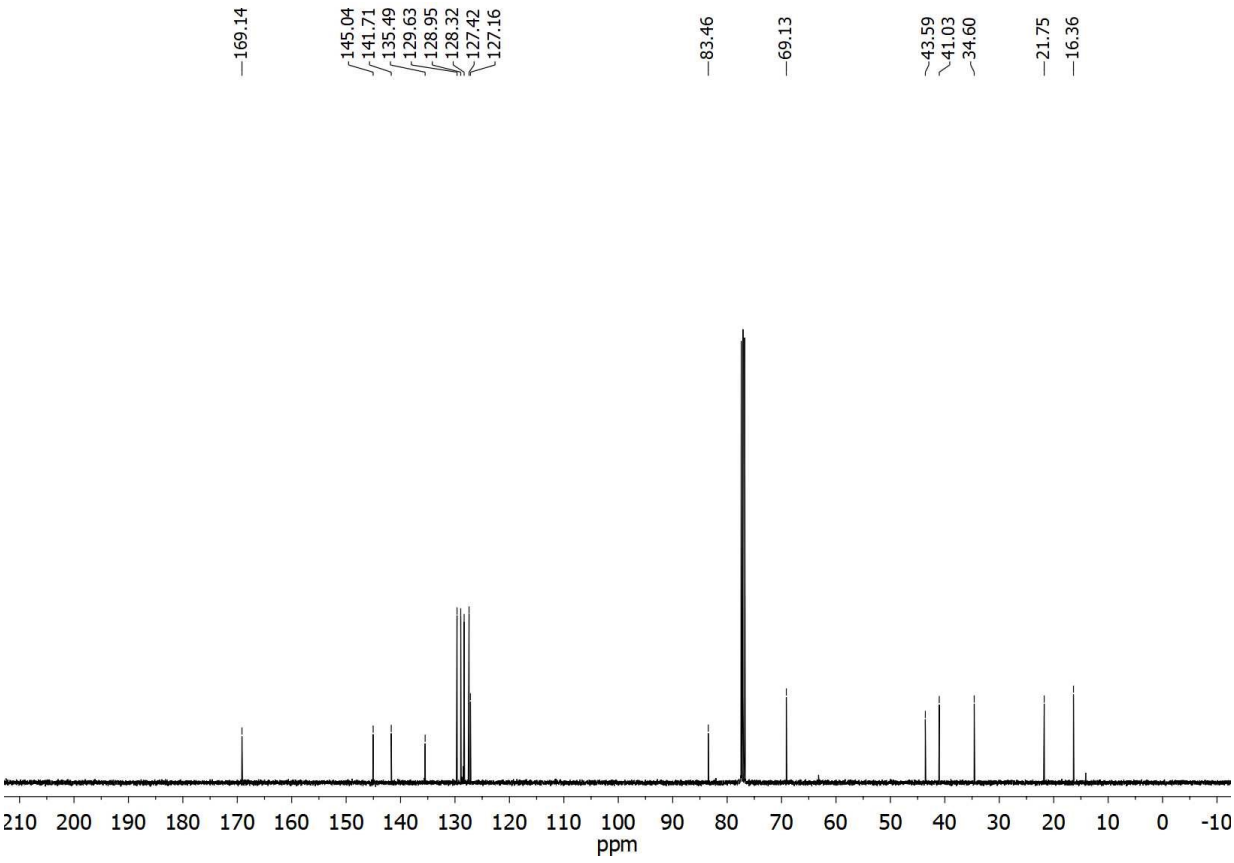
3-phenyl-N-tosylhept-6-ynamide 52

^{1}H-NMR



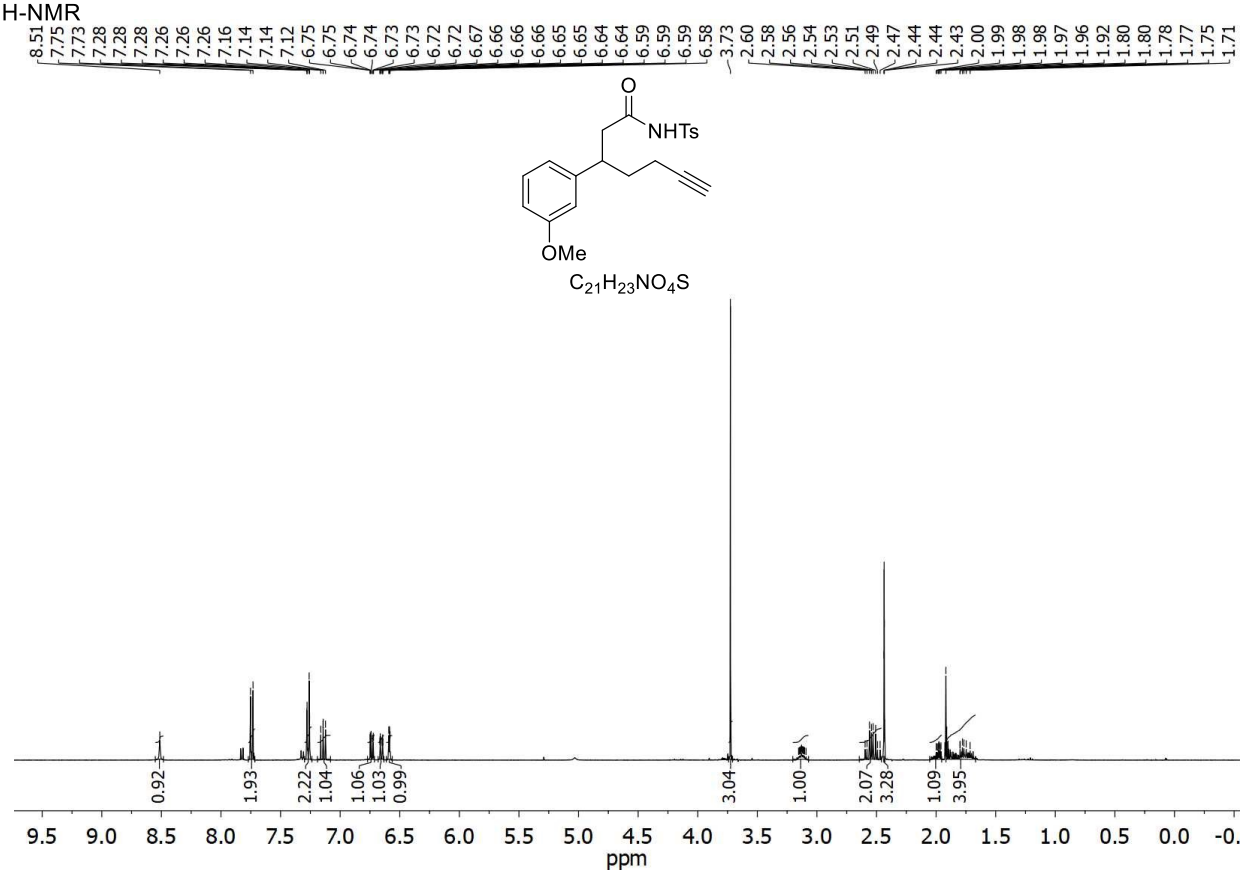
$C_{20}H_{21}NO_3S$

^{13}C-NMR

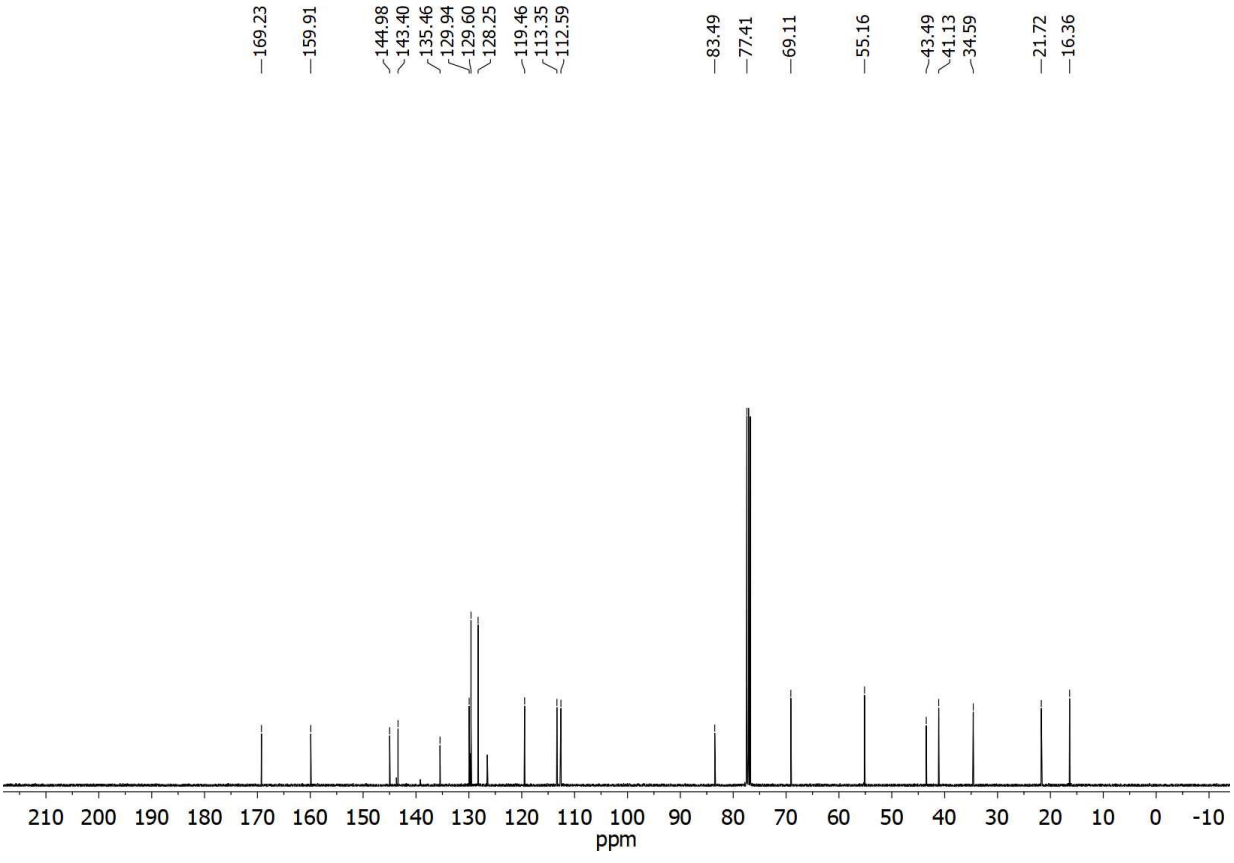


3-(3-methoxyphenyl)-N-tosylhept-6-ynamide 53

^{1}H-NMR



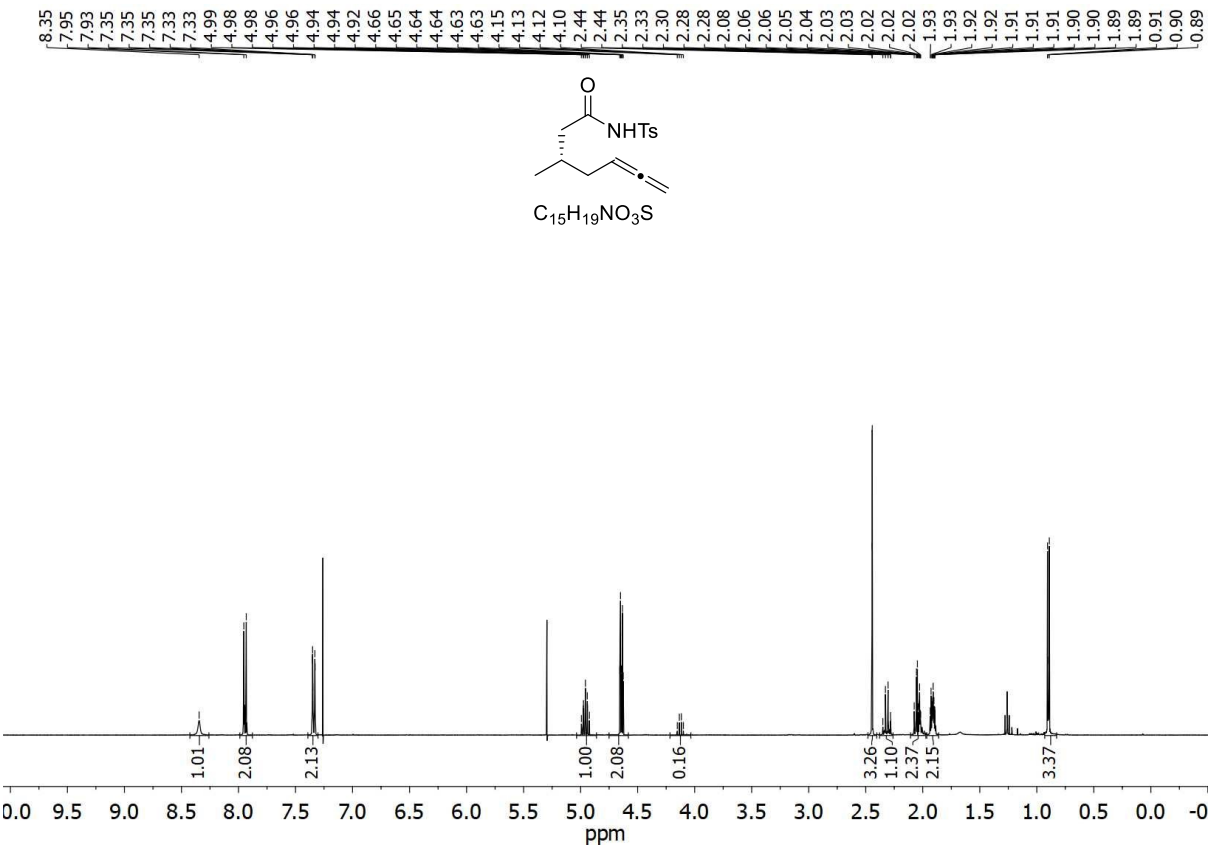
^{13}C-NMR



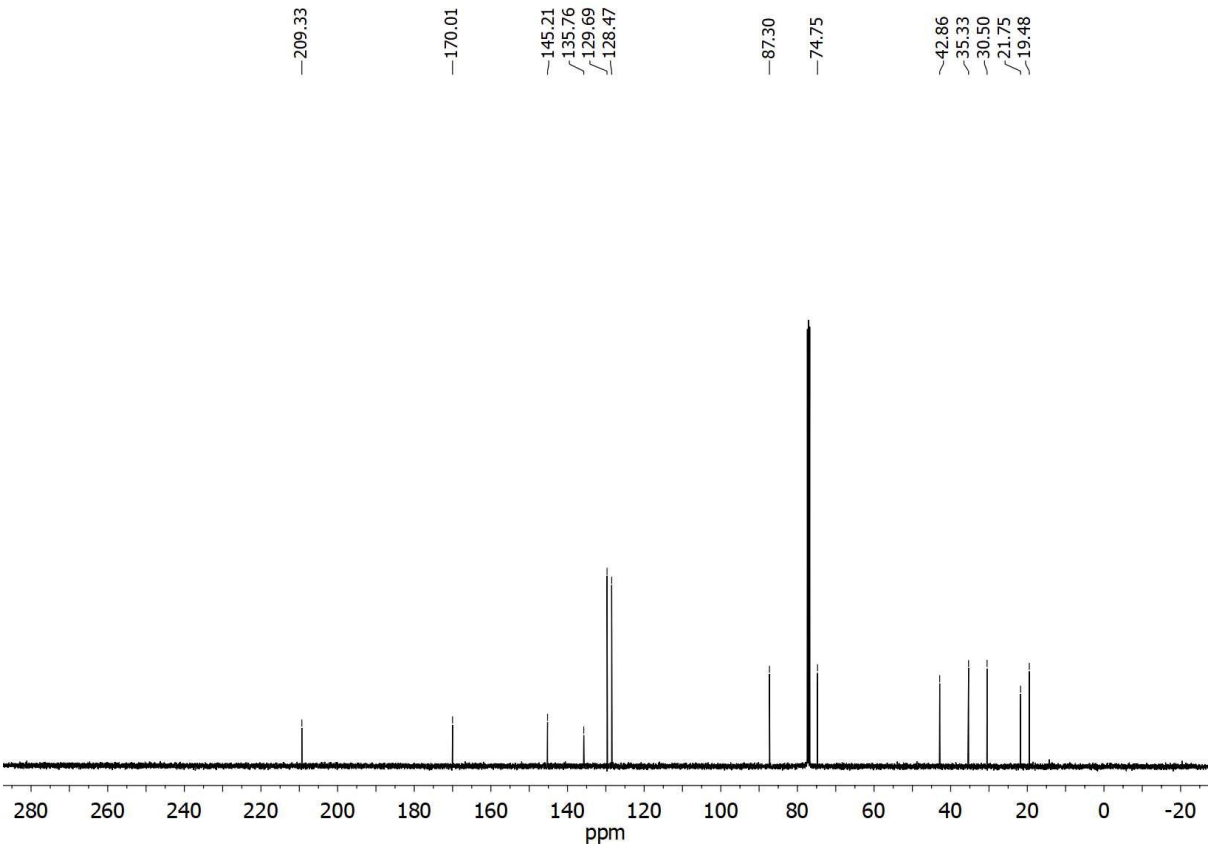
(S)-

3-methyl-N-tosylhepta-5,6-dienamide 16

^{1}H-NMR

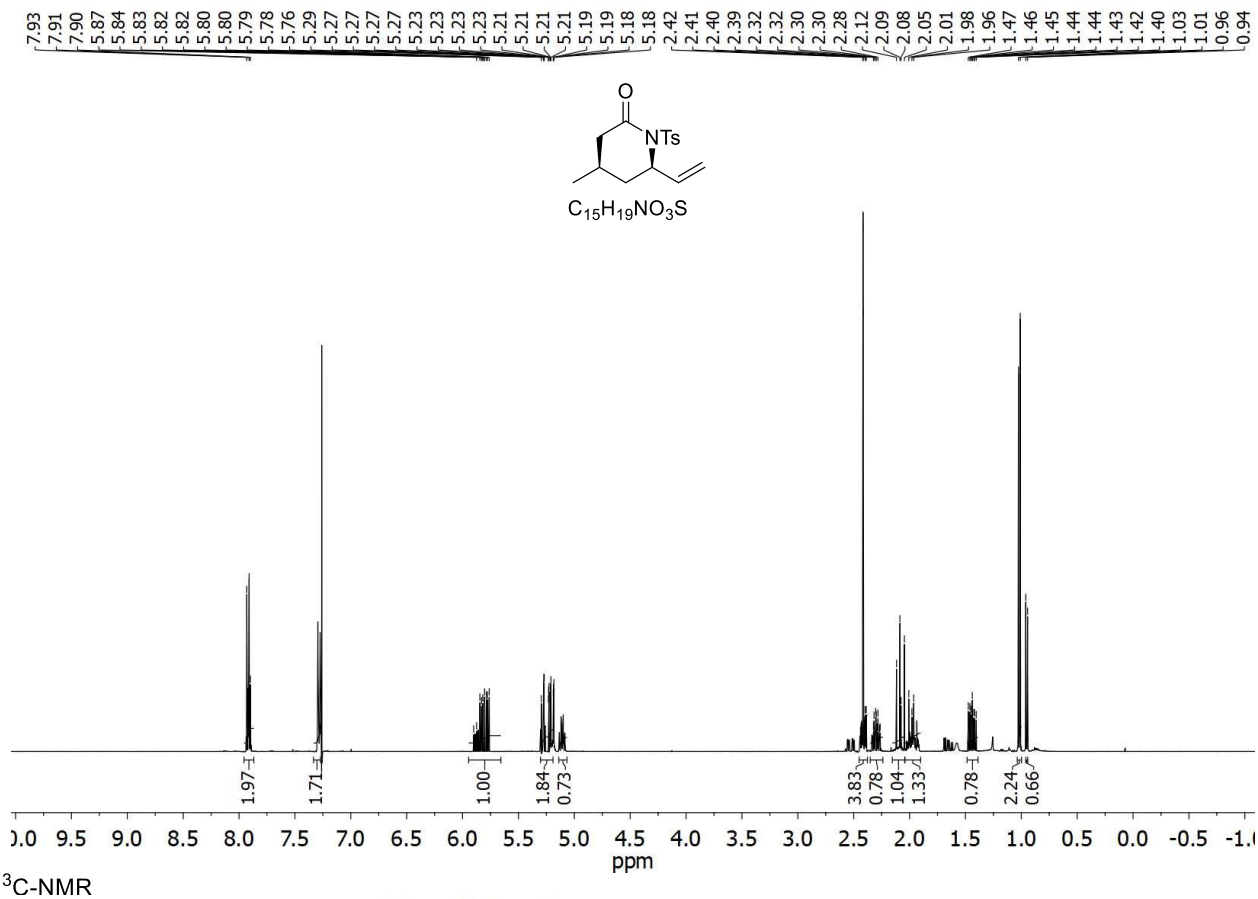


^{13}C-NMR

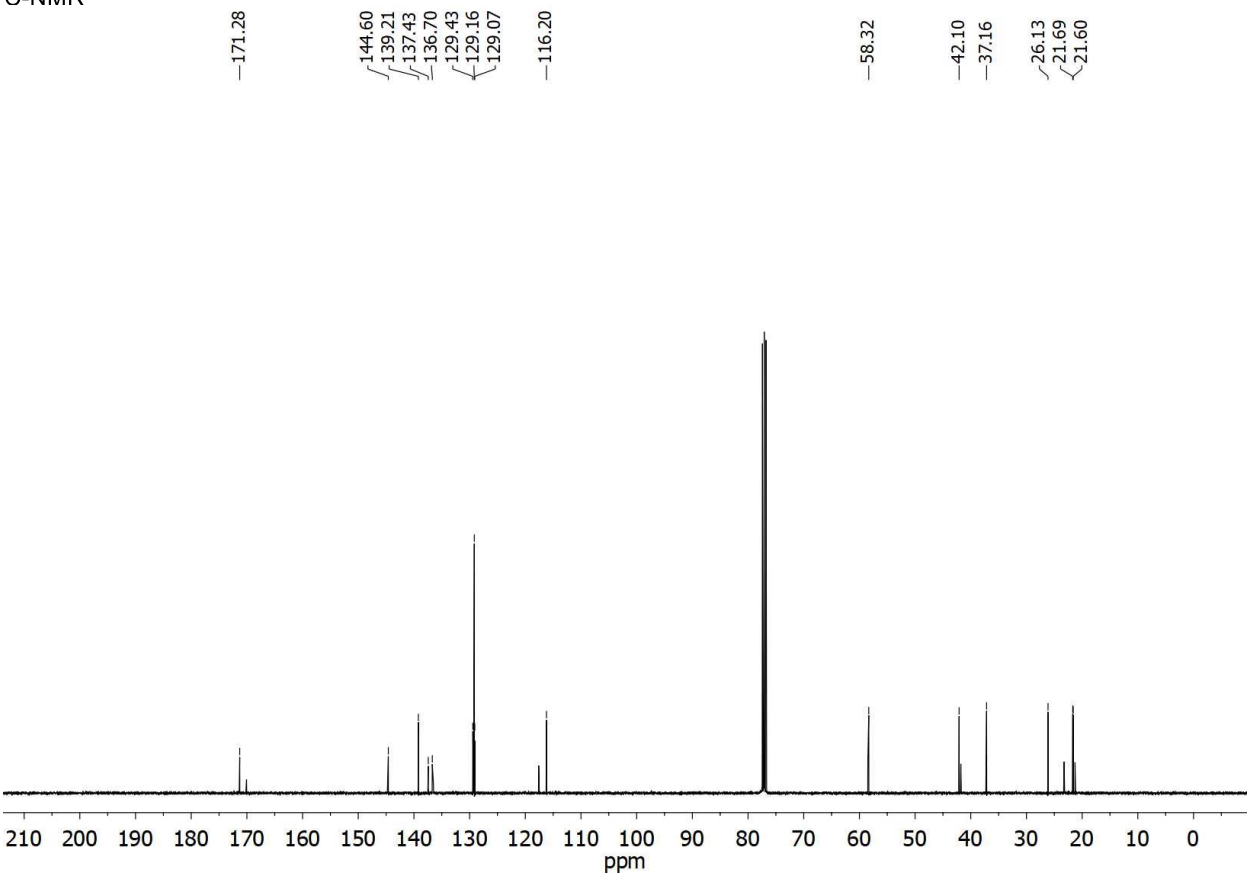


***syn*-4-methyl-1-tosyl-6-vinylpiperidin-2-one 3a**

^{1}H-NMR

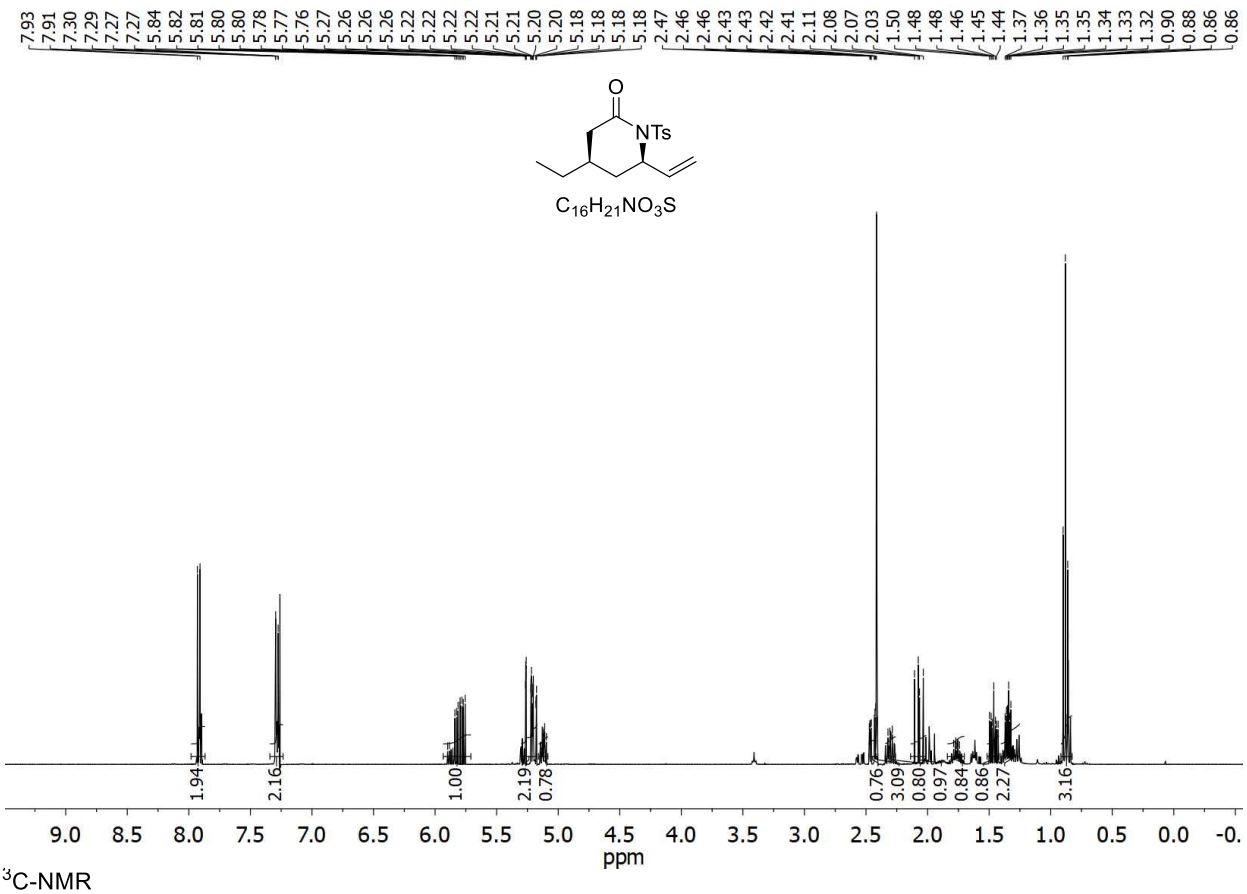


^{13}C-NMR

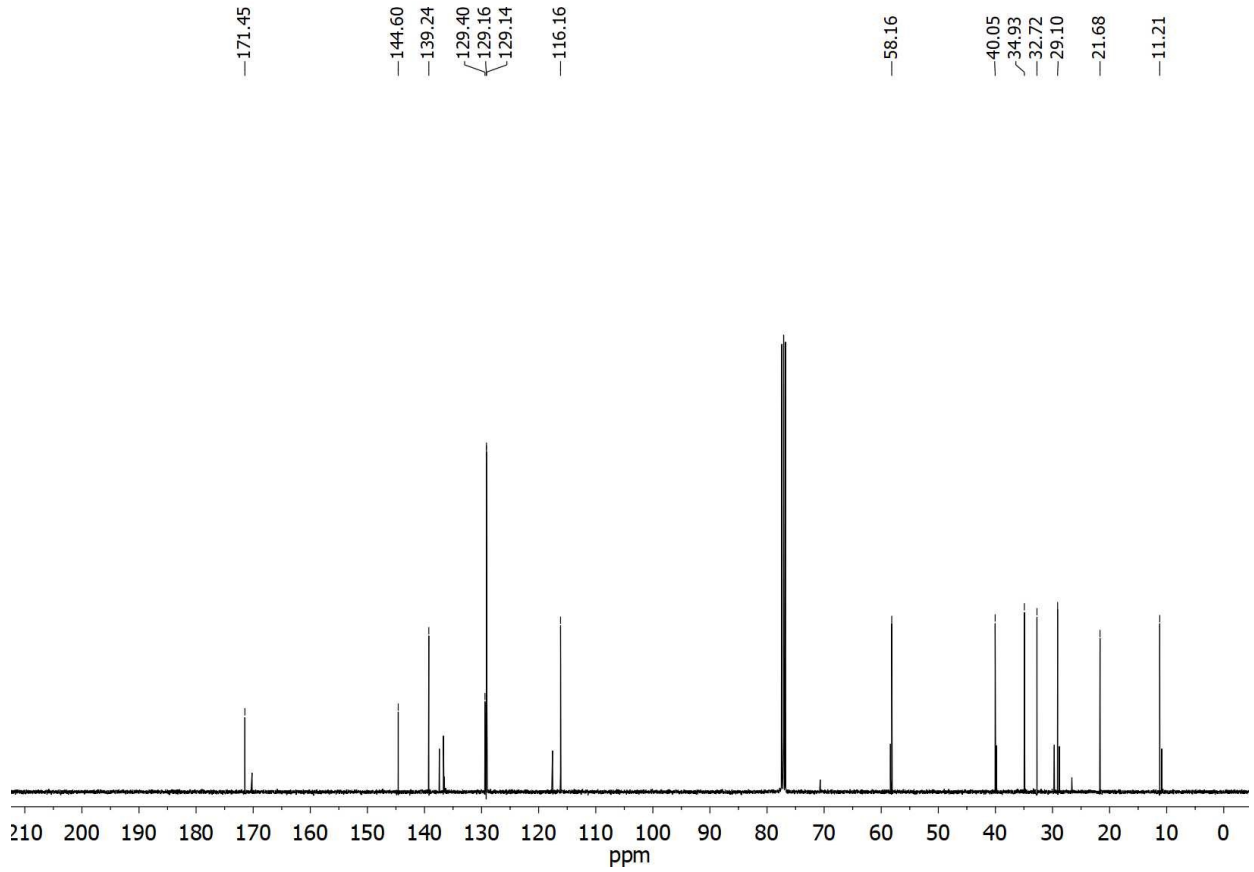


***syn*-4-ethyl-1-tosyl-6-vinylpiperidin-2-one 4a**

^{1}H-NMR

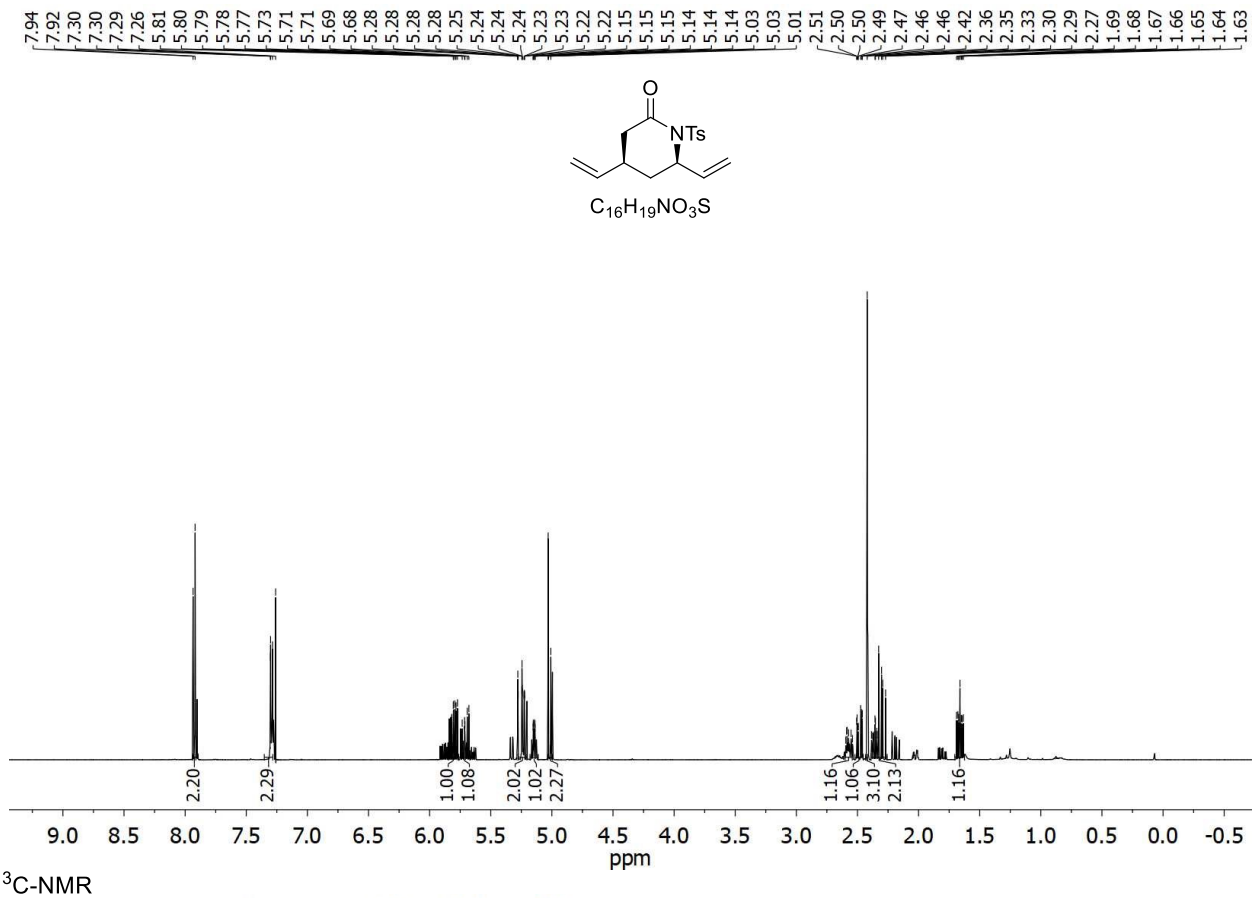


^{13}C-NMR

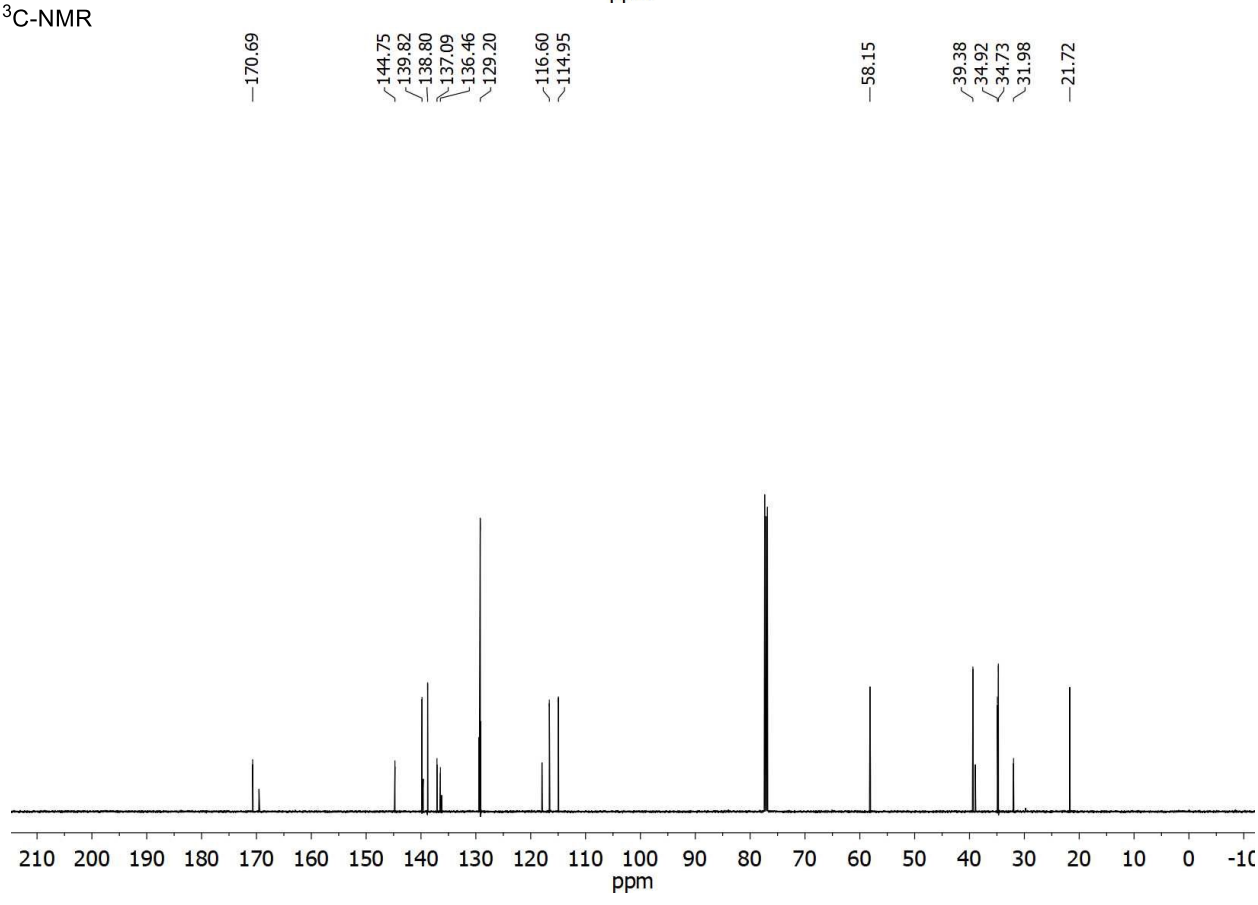


***syn*-1-tosyl-4,6-divinylpiperidin-2-one 5a**

^{1}H-NMR

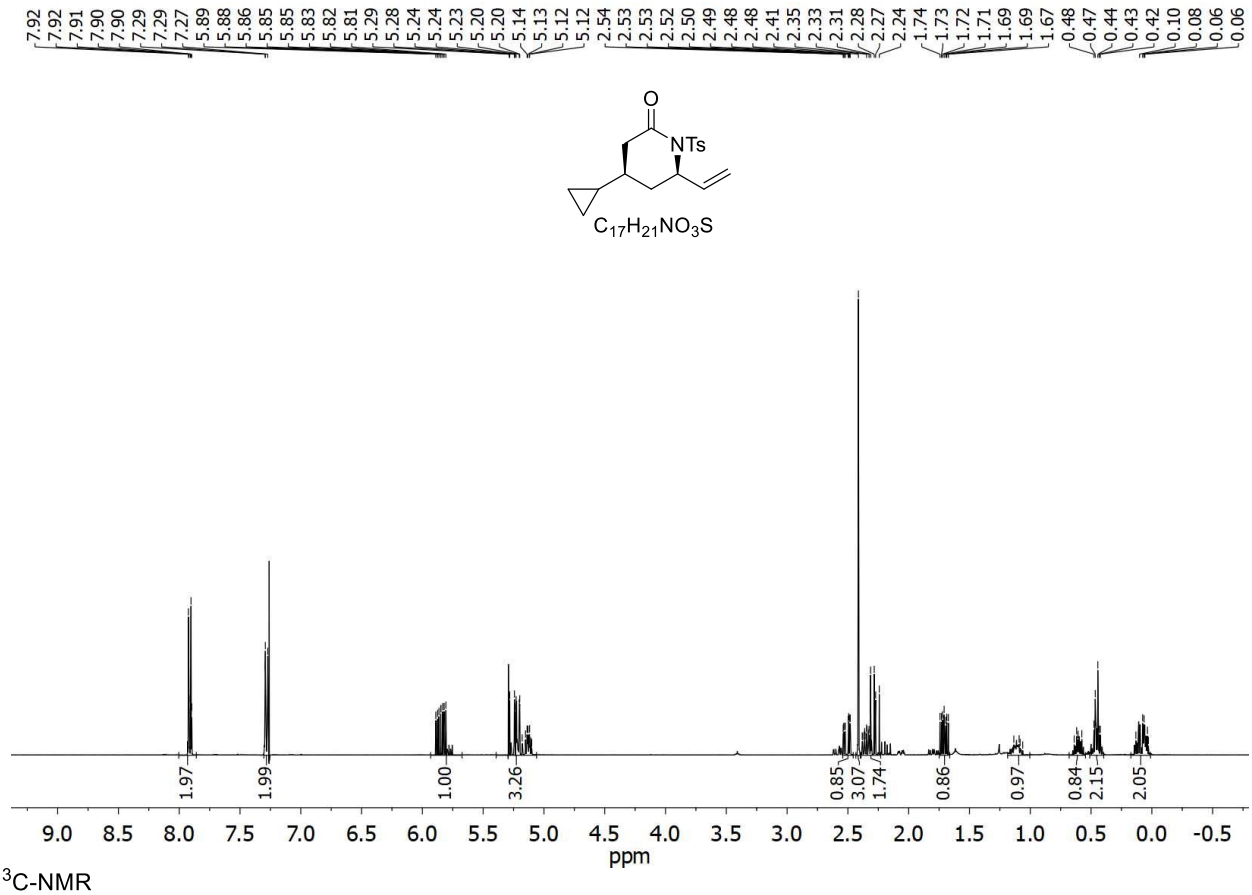


^{13}C-NMR

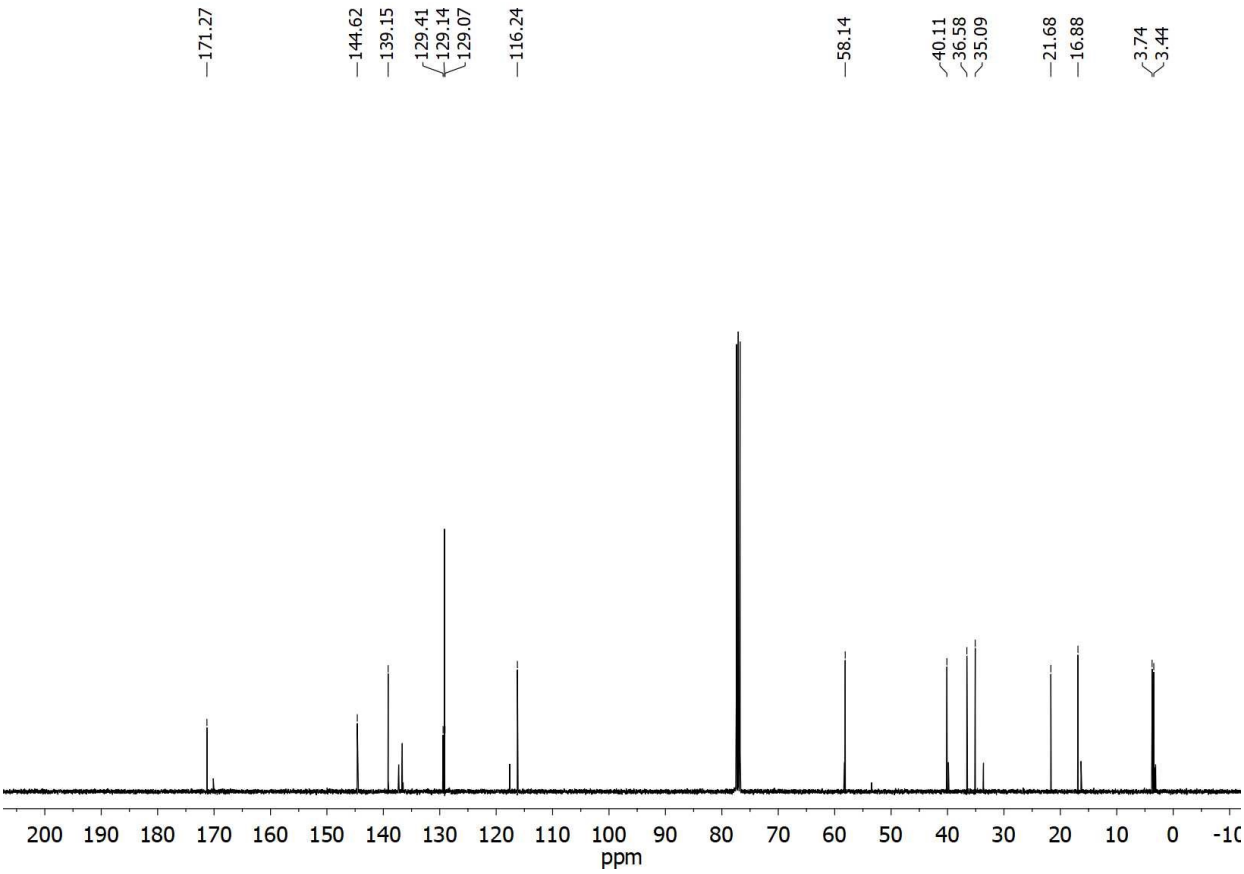


***syn*-4-cyclopropyl-1-tosyl-6-vinylpiperidin-2-one 6a**

^{1}H-NMR

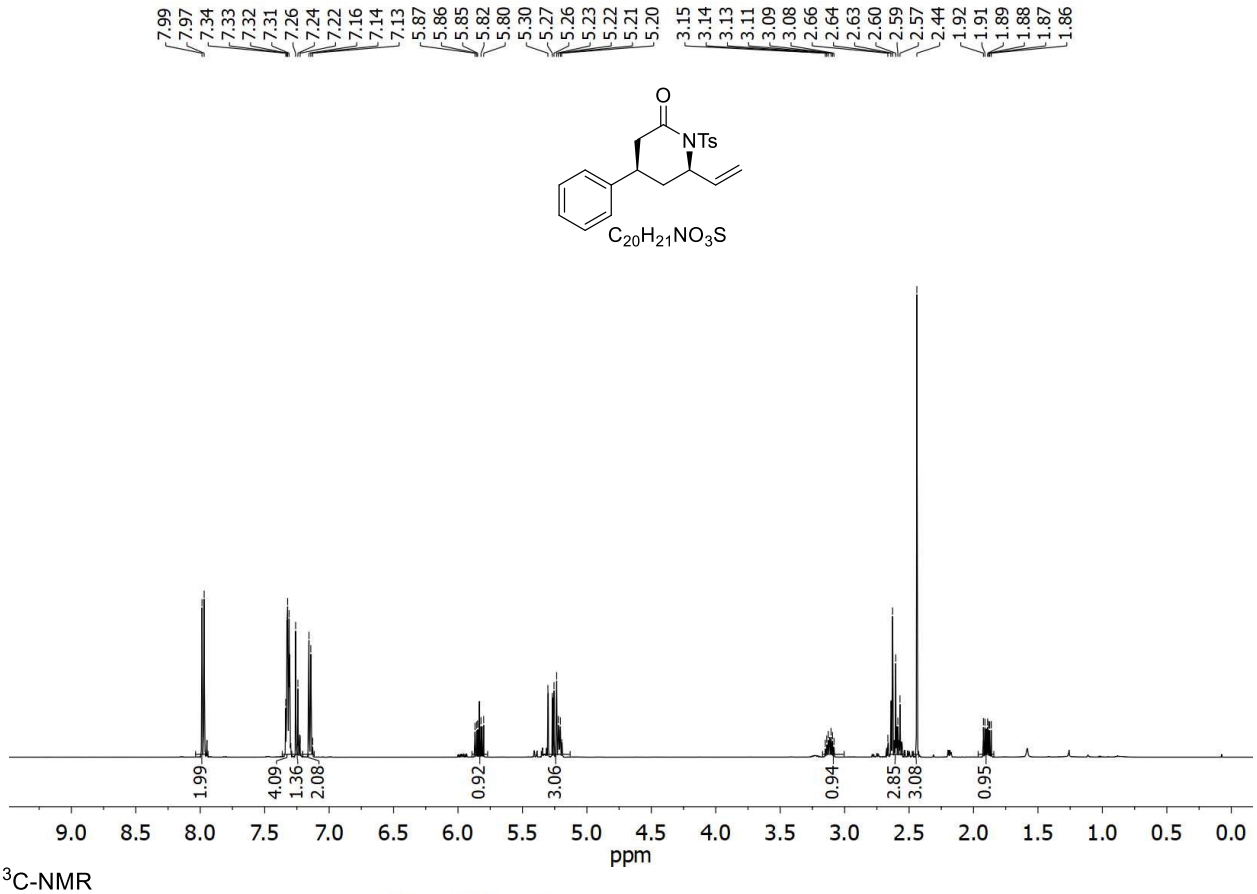


^{13}C-NMR

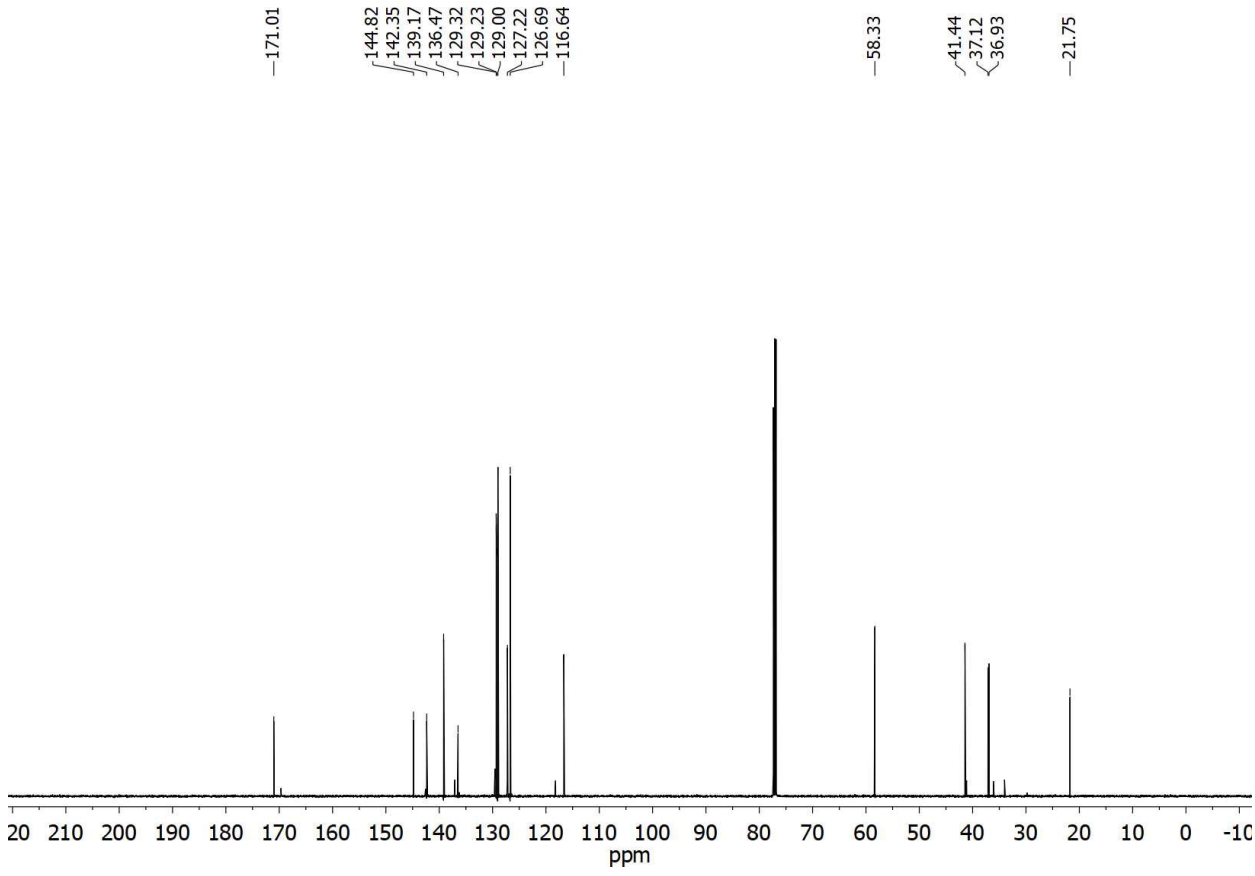


***syn*-4-phenyl-1-tosyl-6-vinylpiperidin-2-one 2a**

^{1}H-NMR

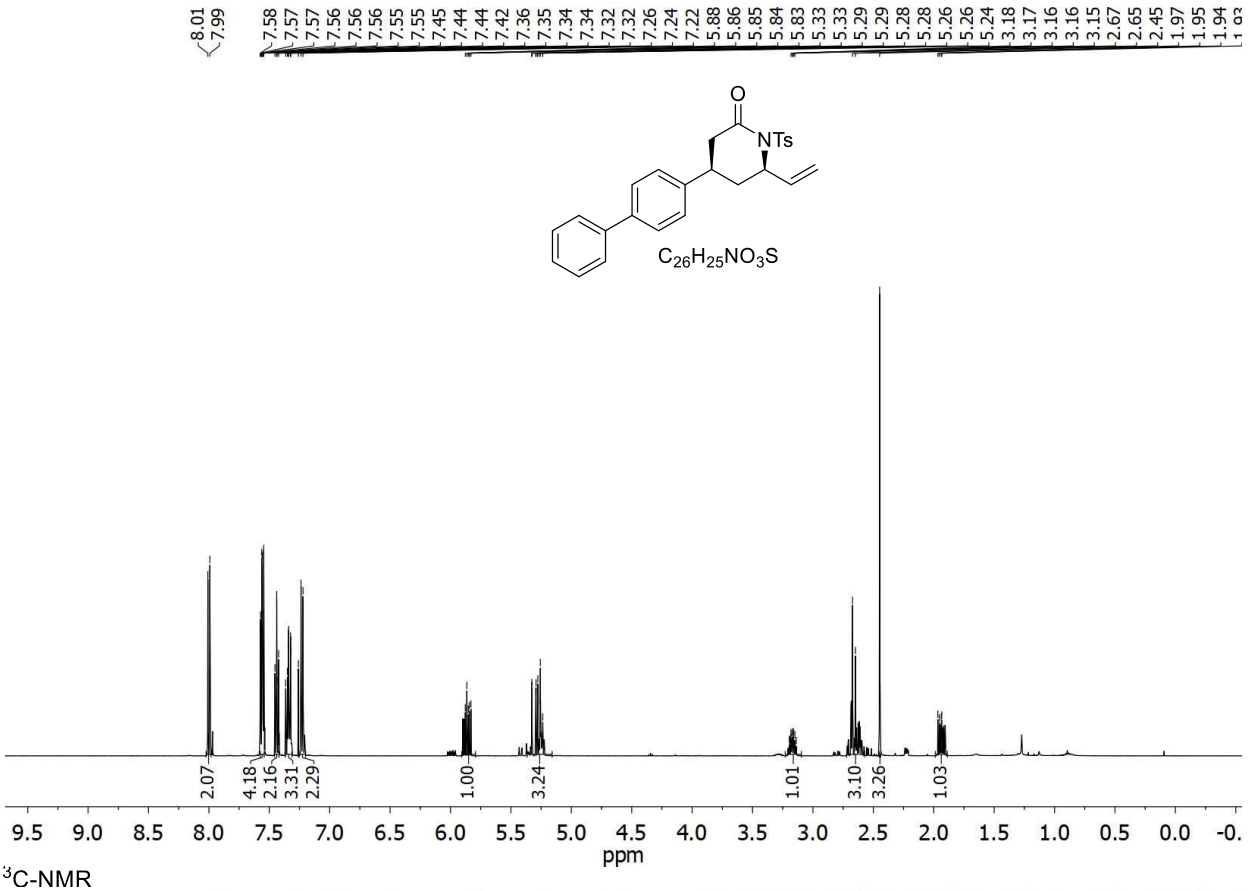


^{13}C-NMR

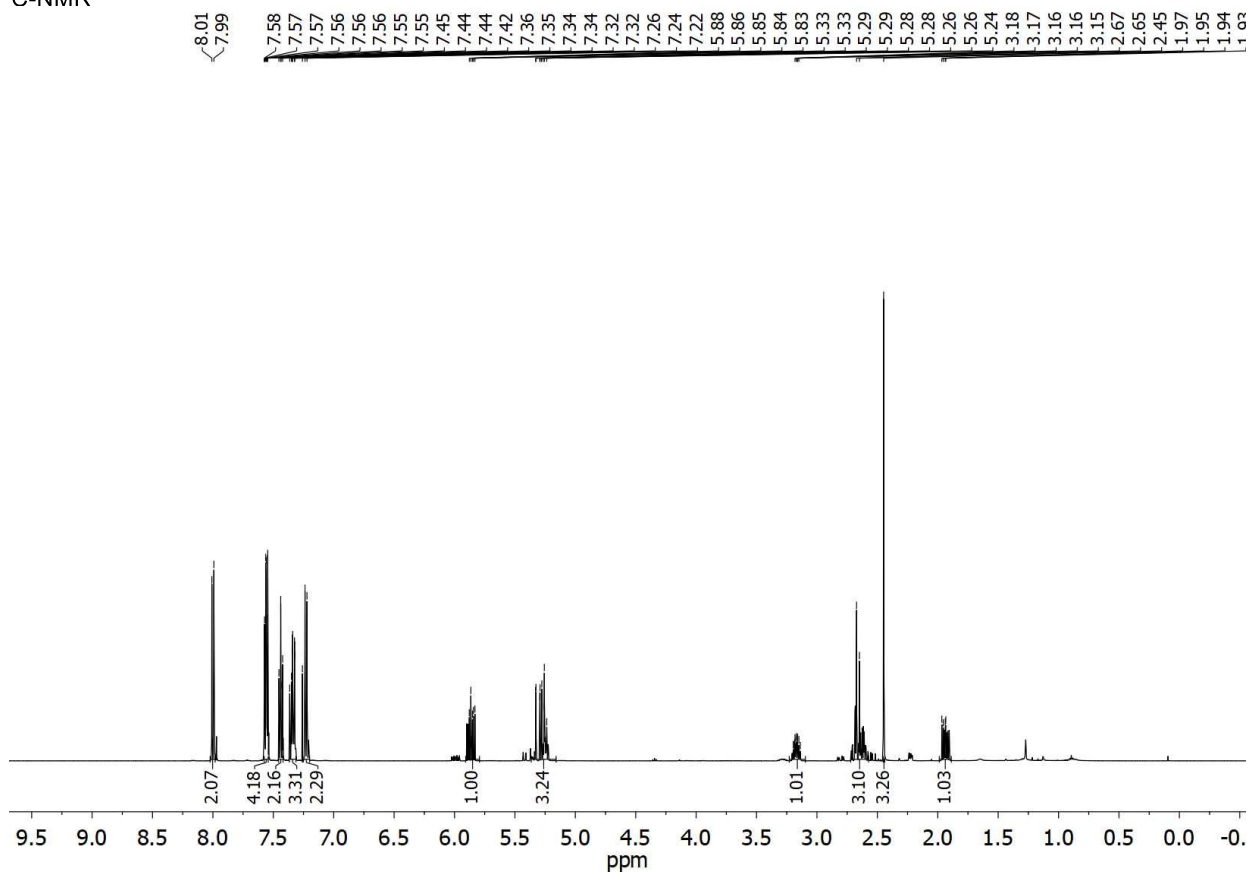


syn-4-([1,1'-biphenyl]-4-yl)-1-tosyl-6-vinylpiperidin-2-one 7a

^{1}H-NMR

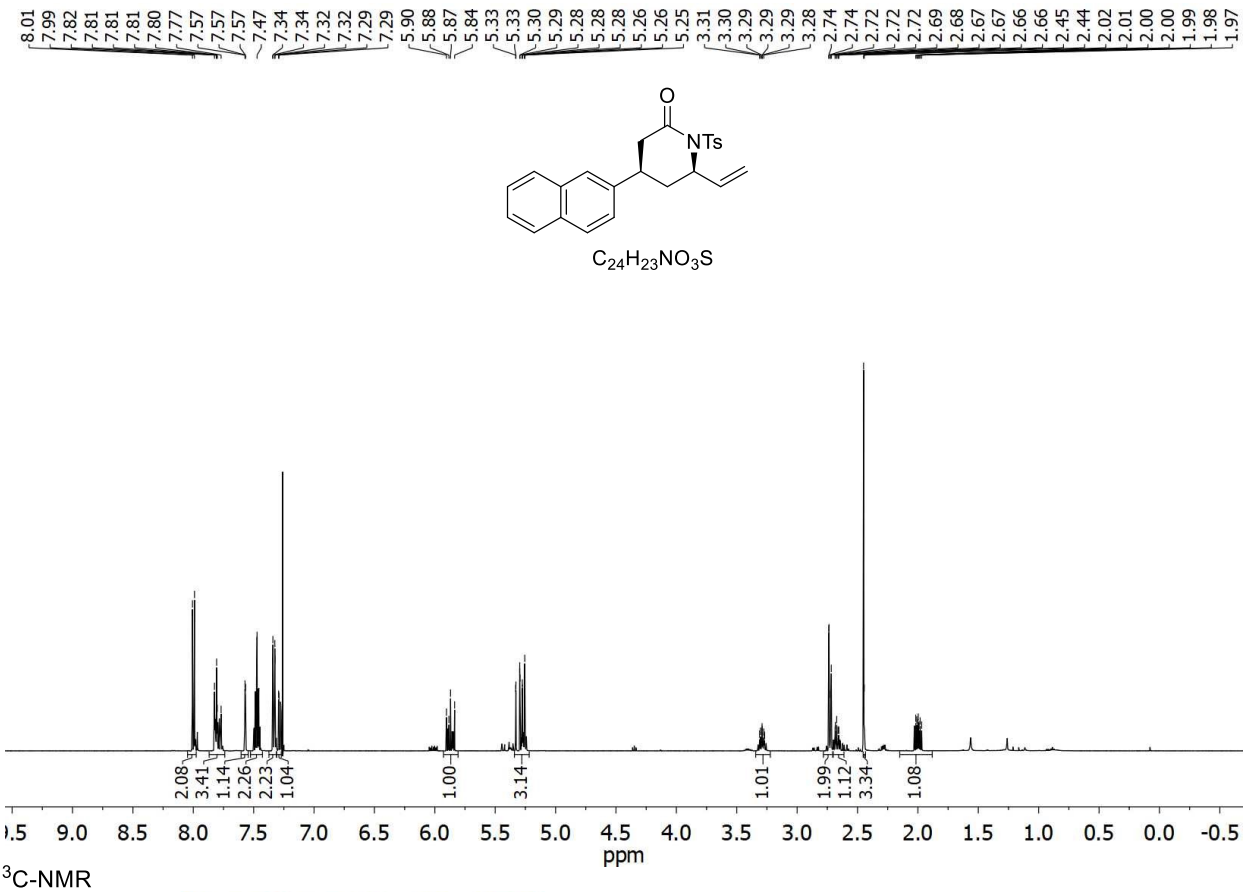


^{13}C-NMR

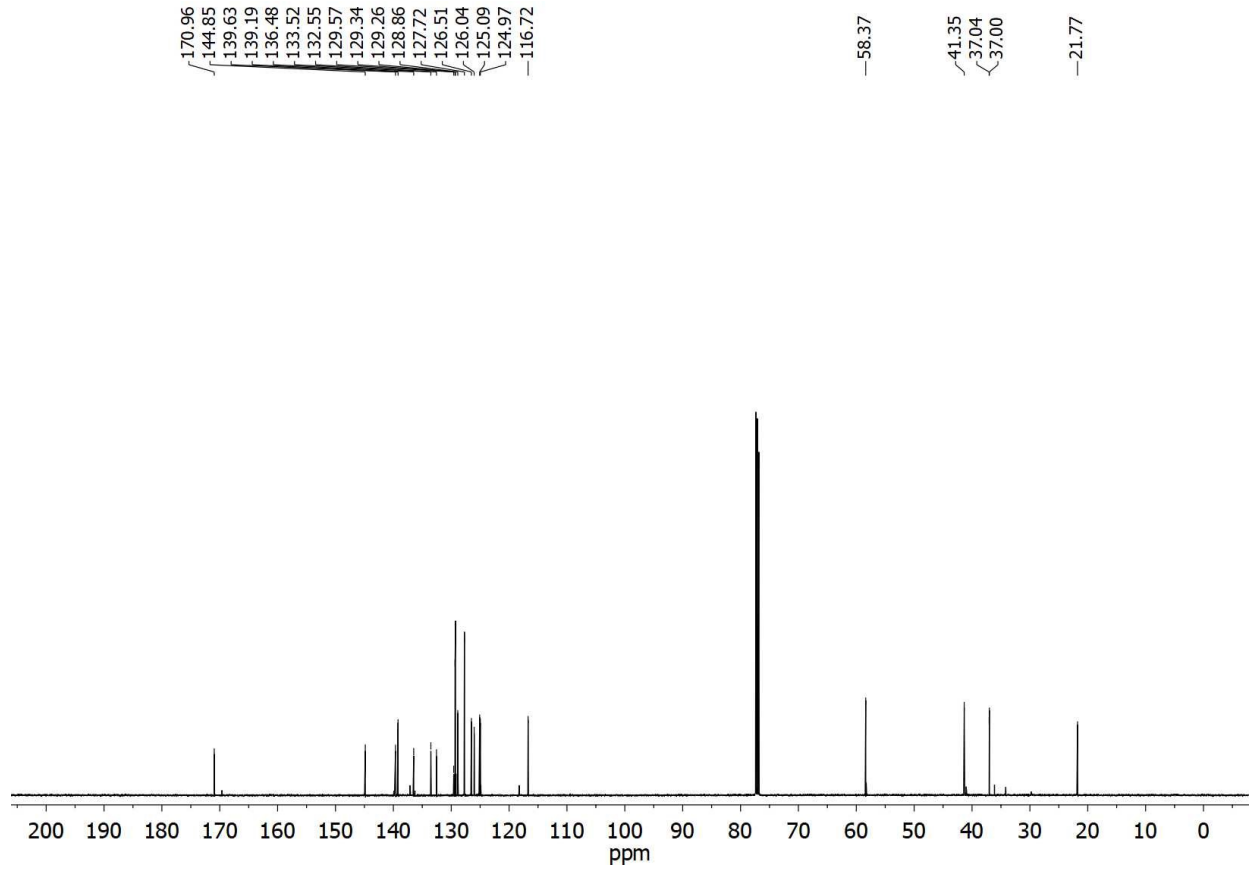


***syn*-(4-(naphthalen-2-yl)-1-tosyl-6-vinylpiperidin-2-one 8a**

^{1}H-NMR

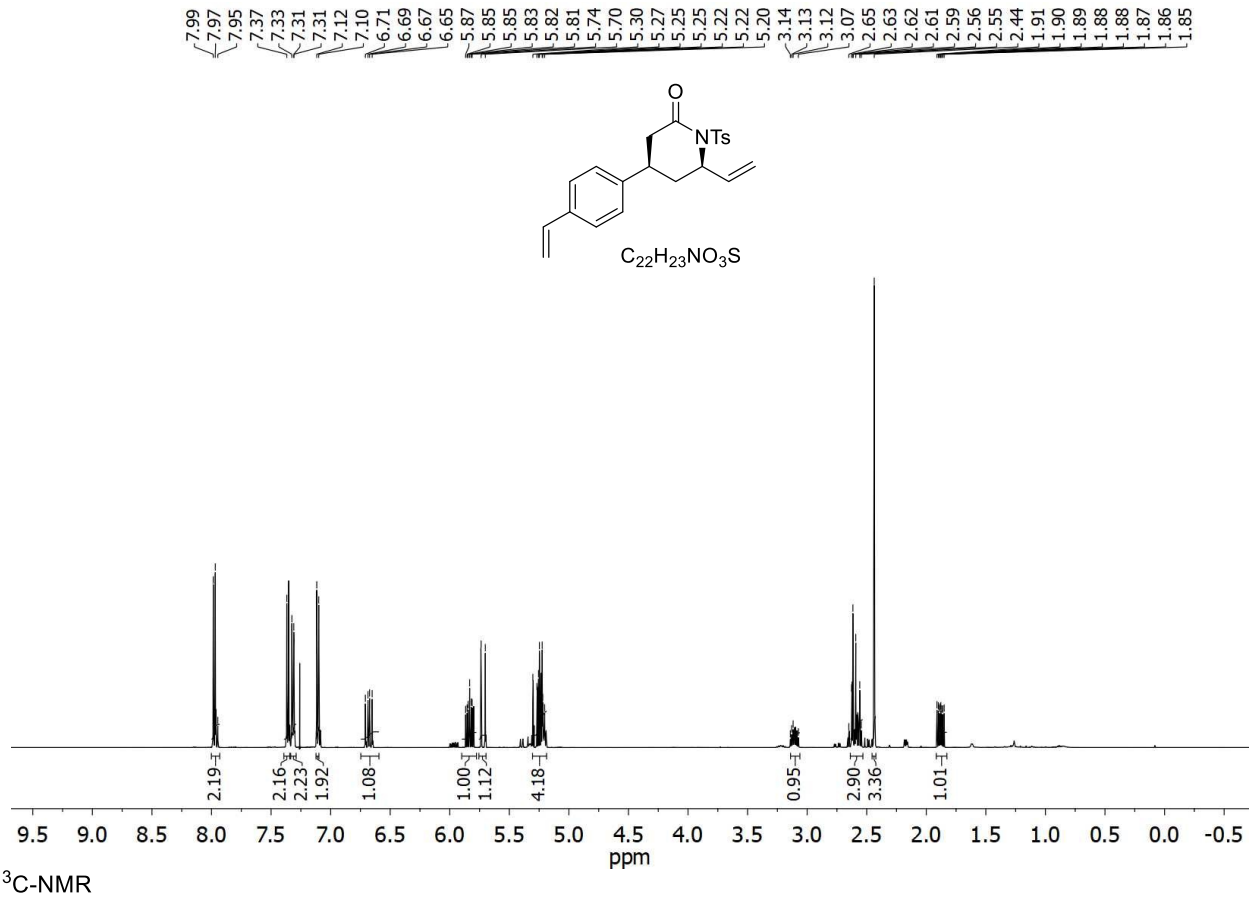


^{13}C-NMR

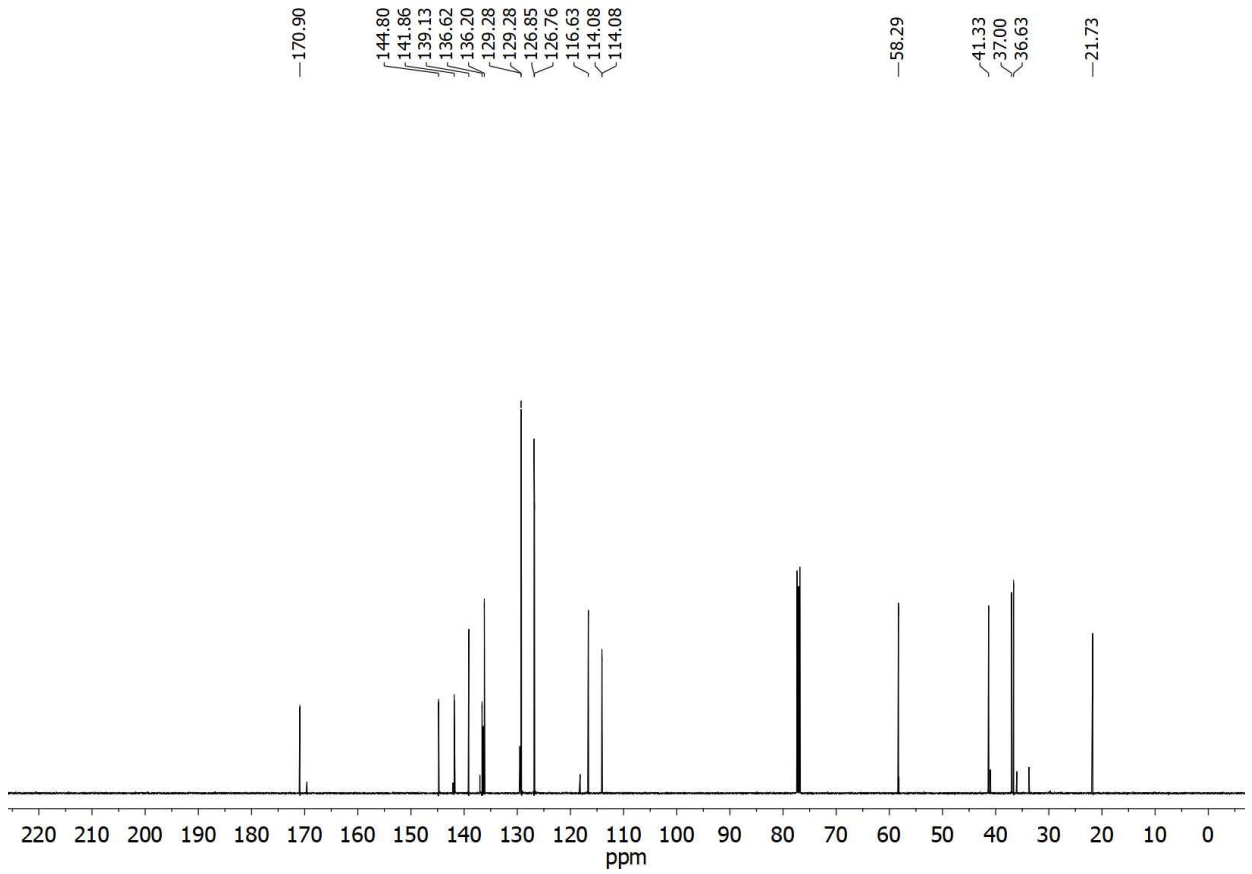


***syn*-1-tosyl-6-vinyl-4-(4-vinylphenyl)piperidin-2-one 9a**

^{1}H-NMR

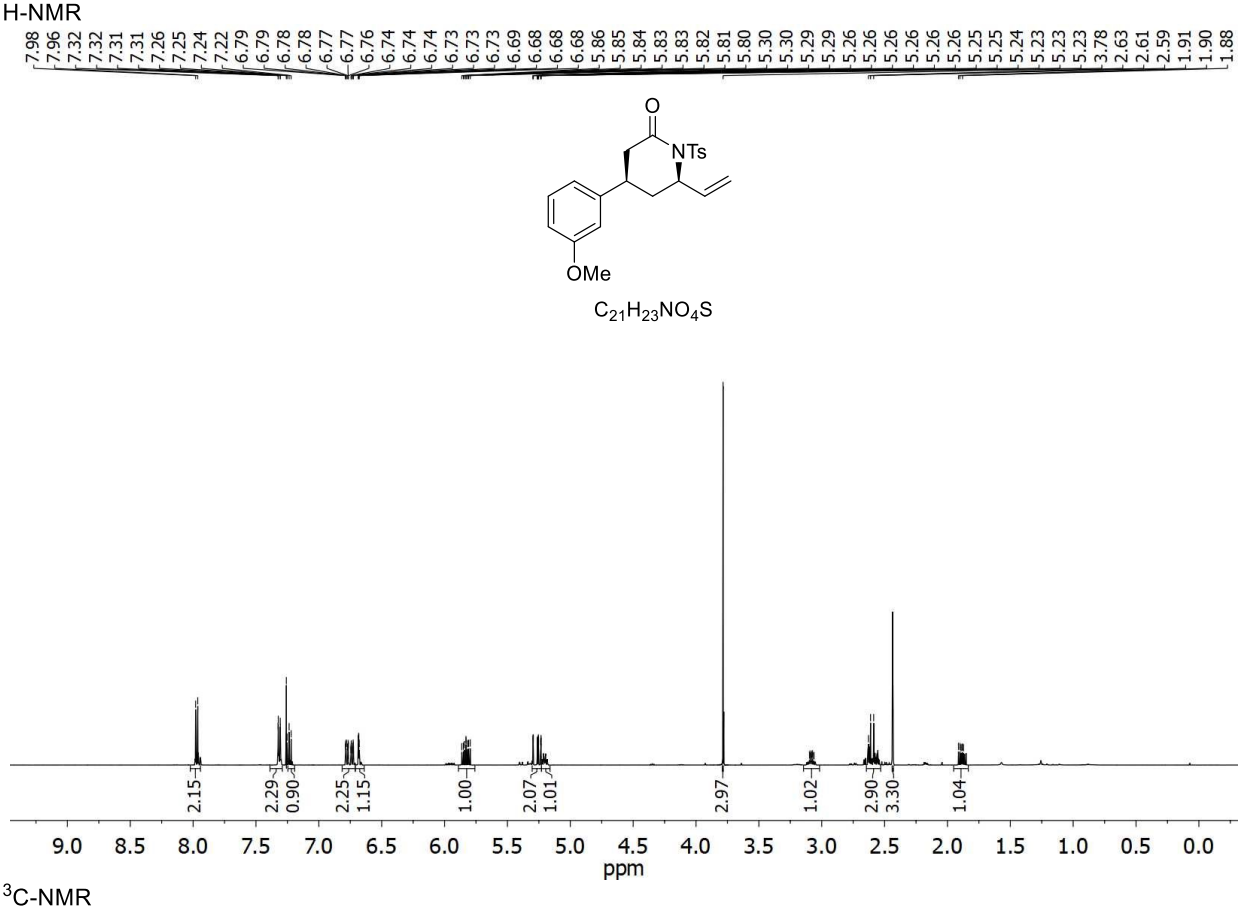


^{13}C-NMR

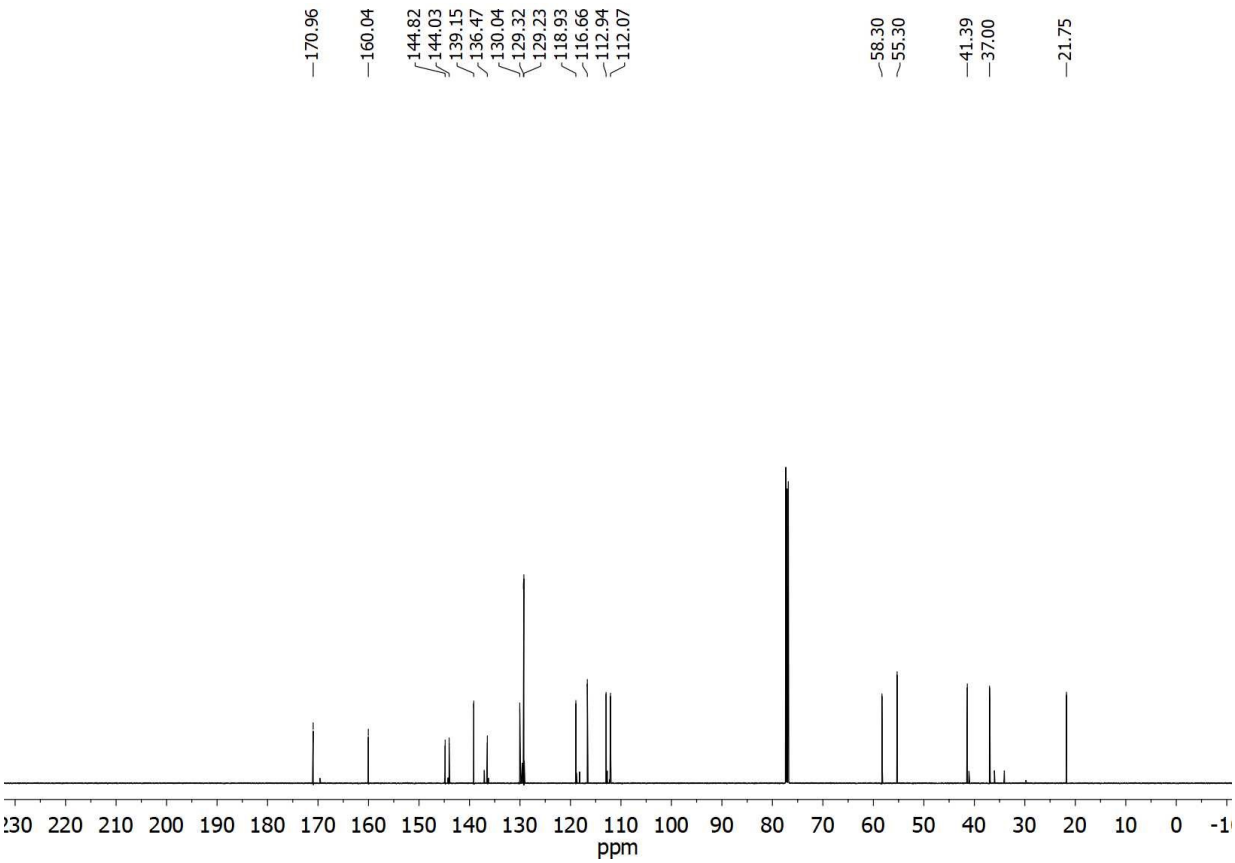


***syn*-4-(3-methoxyphenyl)-1-tosyl-6-vinylpiperidin-2-one 10a**

^{1}H-NMR

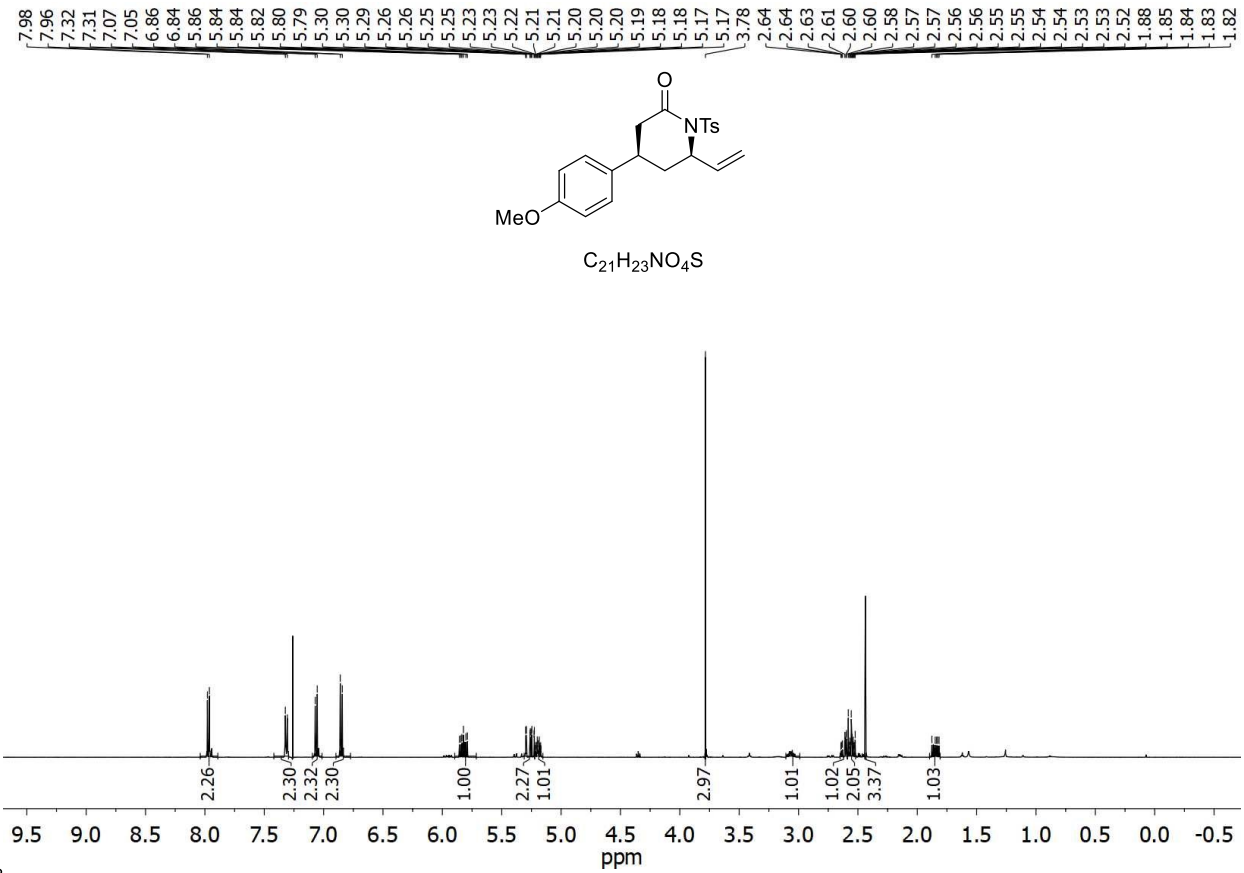


^{13}C-NMR



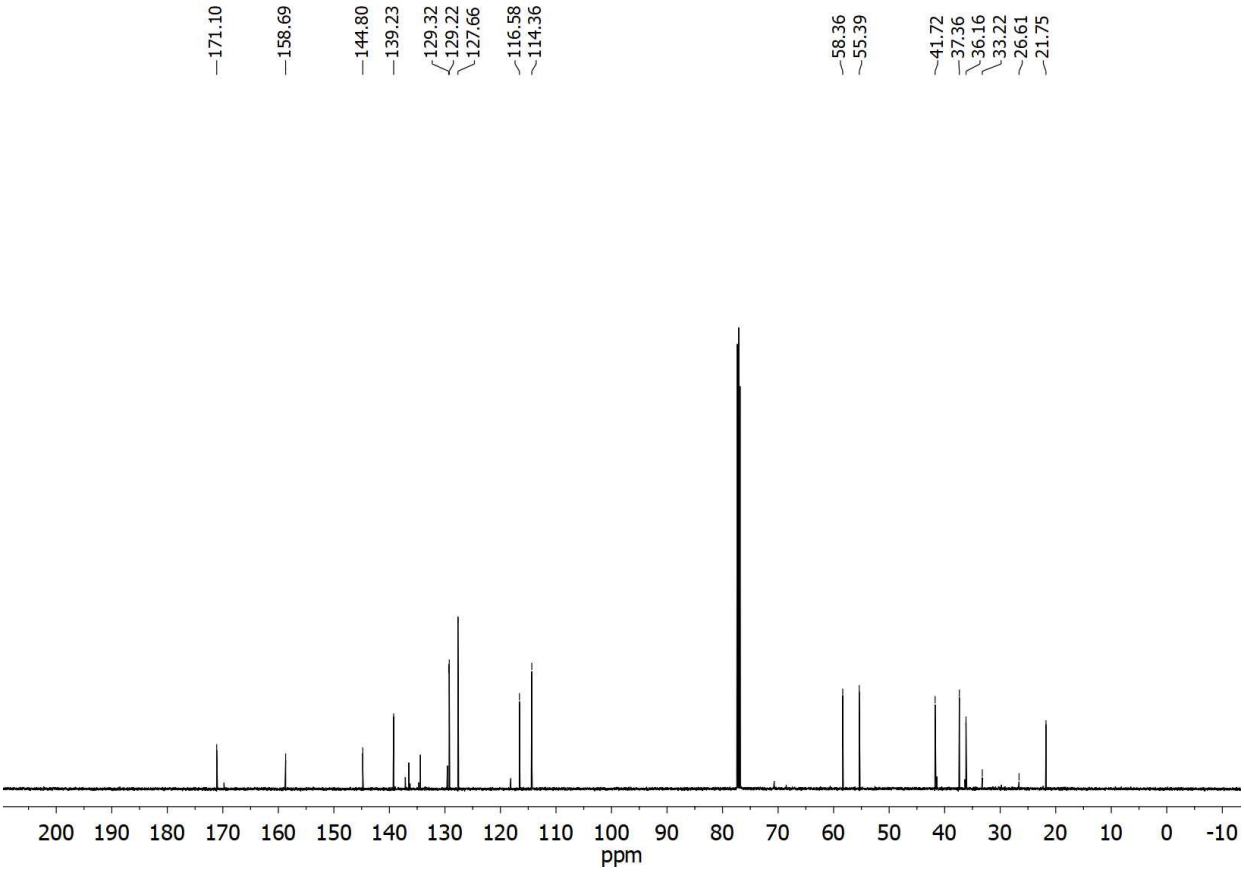
***syn*-4-(4-methoxyphenyl)-1-tosyl-6-vinylpiperidin-2-one 11a**

^{1}H-NMR



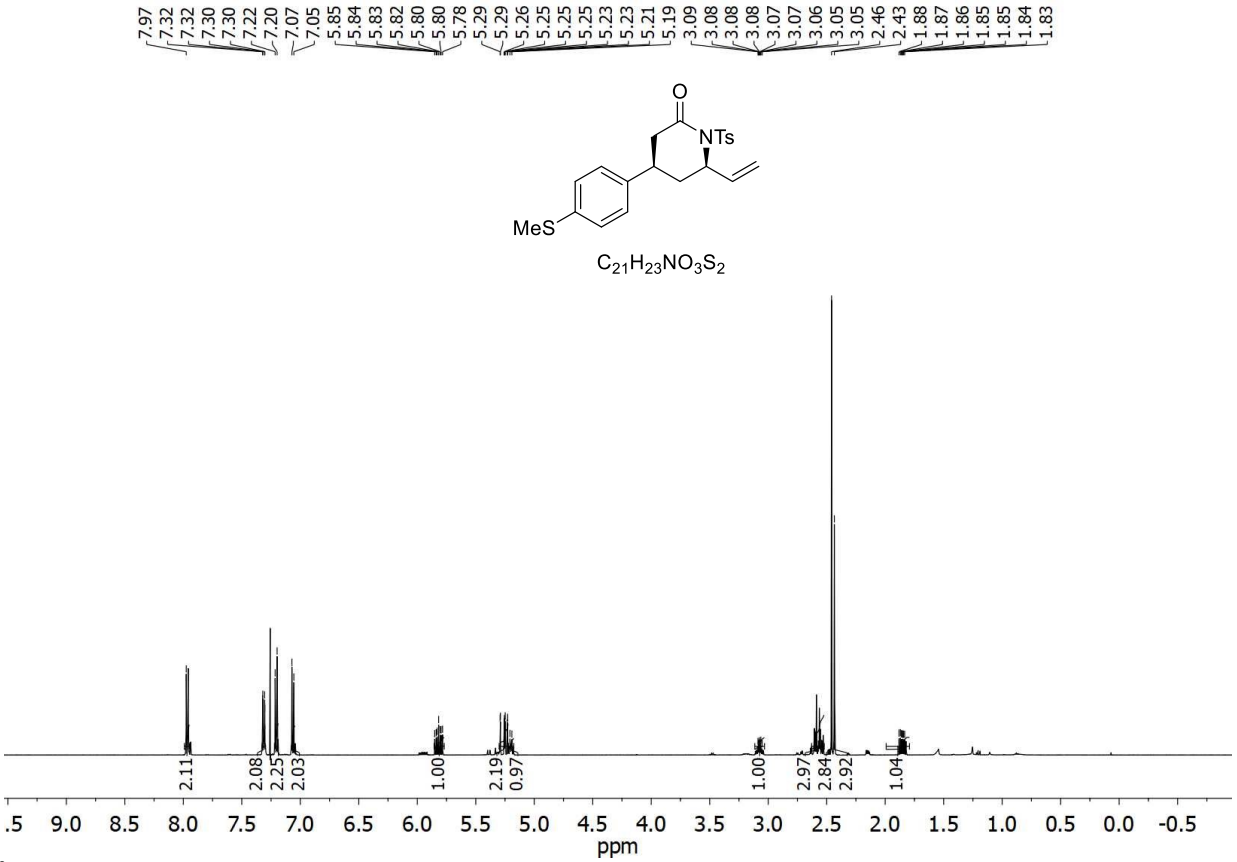
$C_{21}H_{23}NO_4S$

^{13}C-NMR

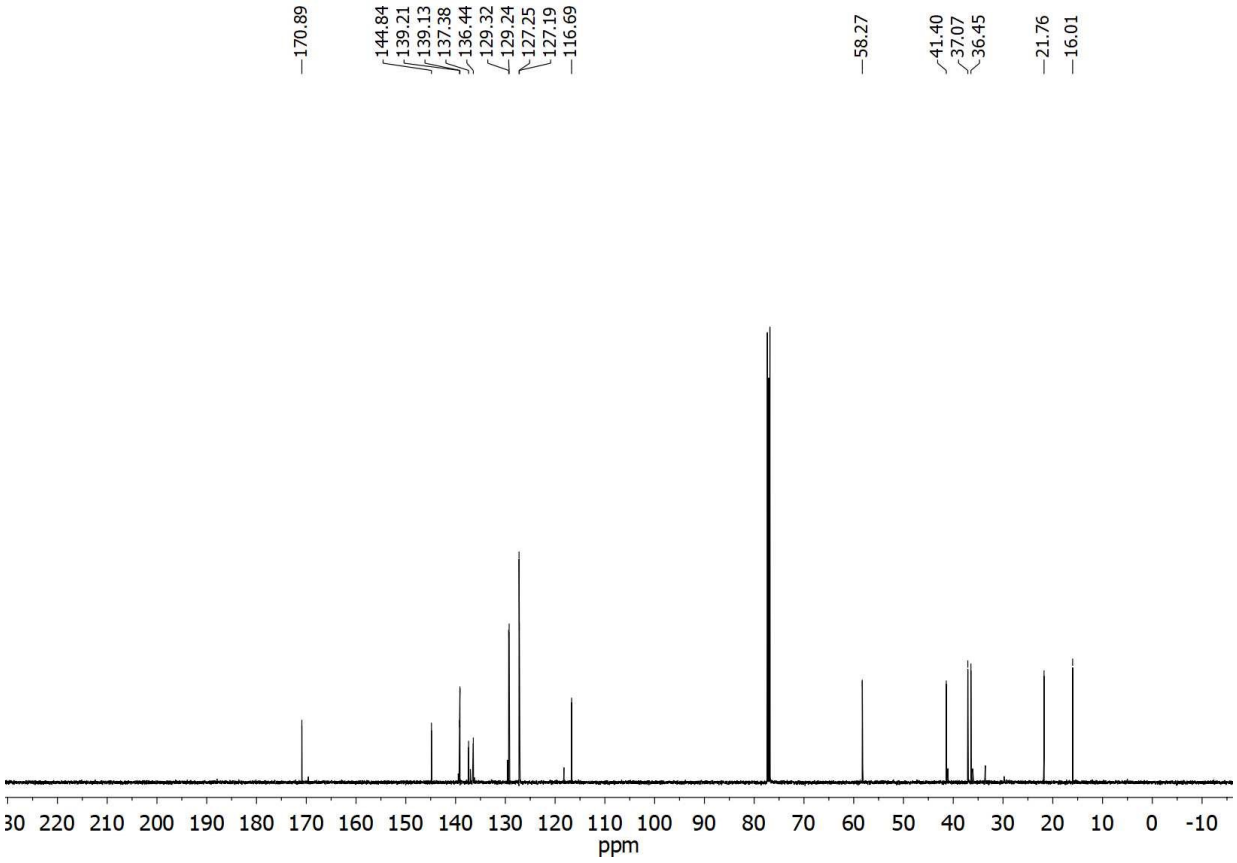


***syn*-4-(4-(methylthio)phenyl)-1-tosyl-6-vinylpiperidin-2-one 12a**

^{1}H-NMR

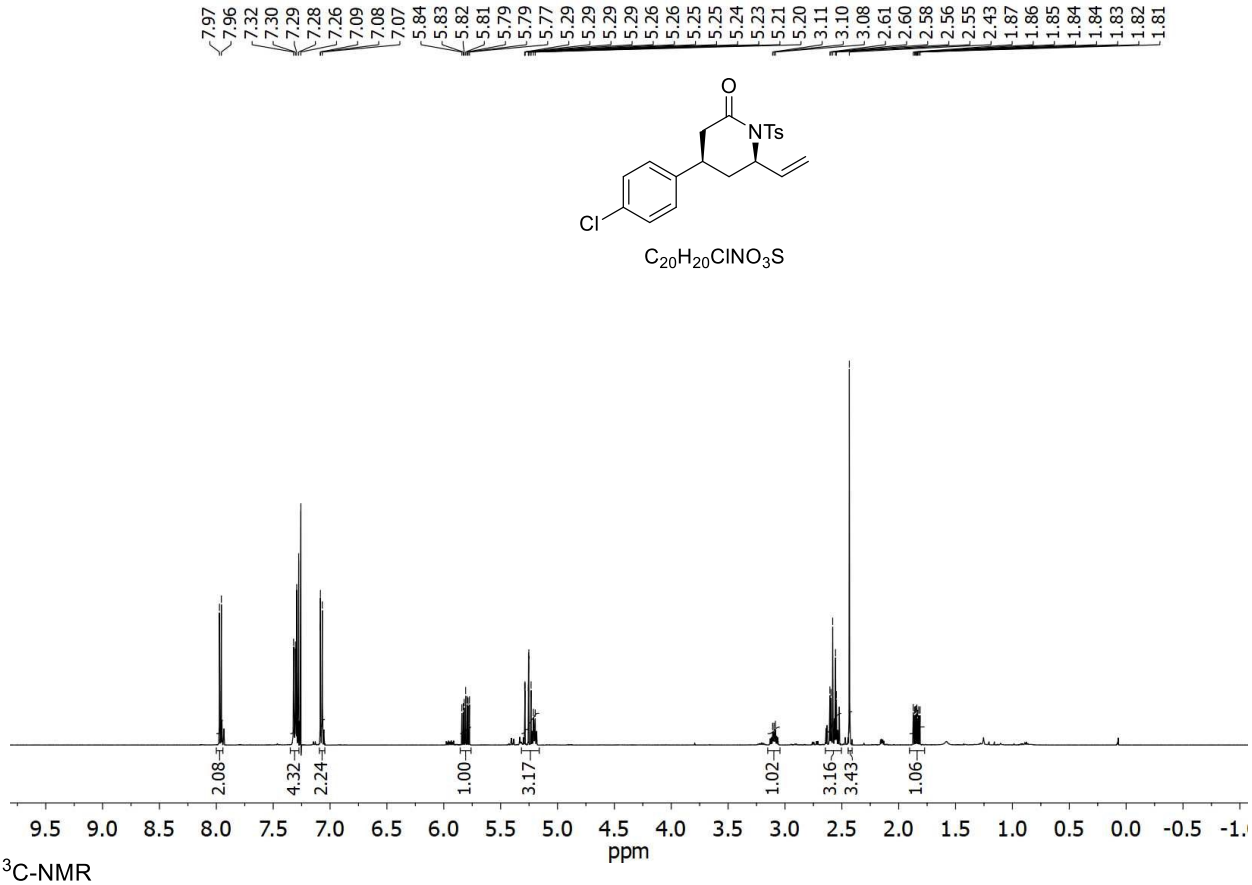


^{13}C-NMR

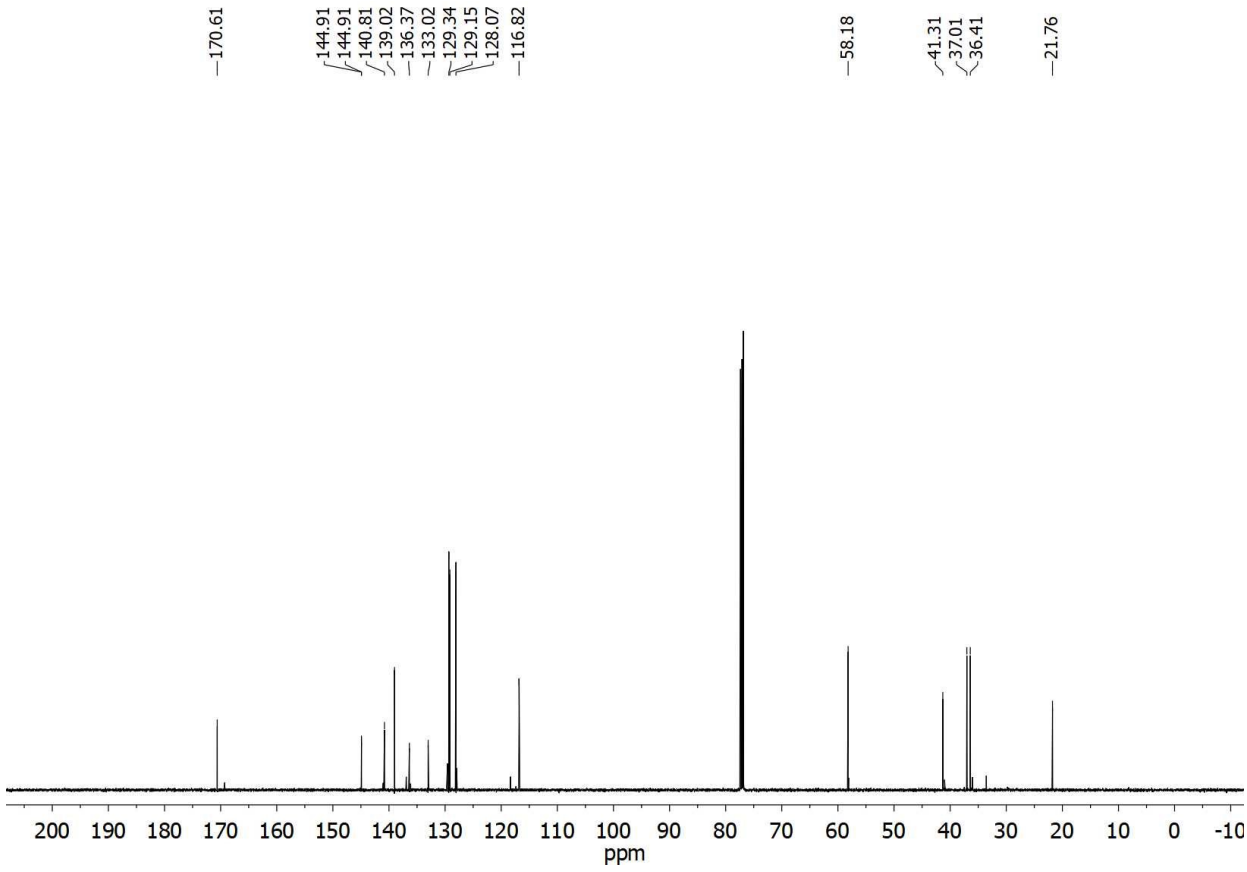


***syn*-4-(4-chlorophenyl)-1-tosyl-6-vinylidenepiperidin-2-one 13a**

^{1}H-NMR

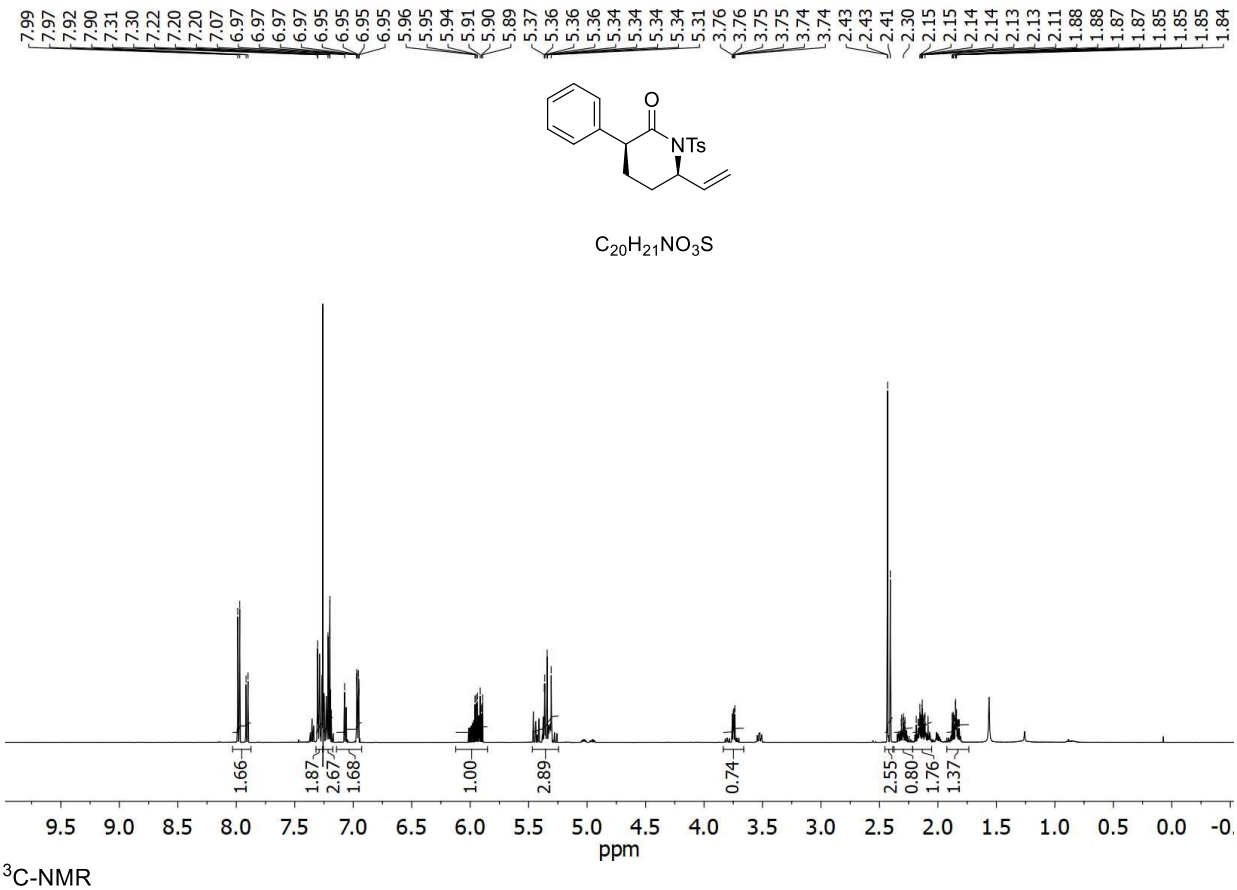


^{13}C-NMR



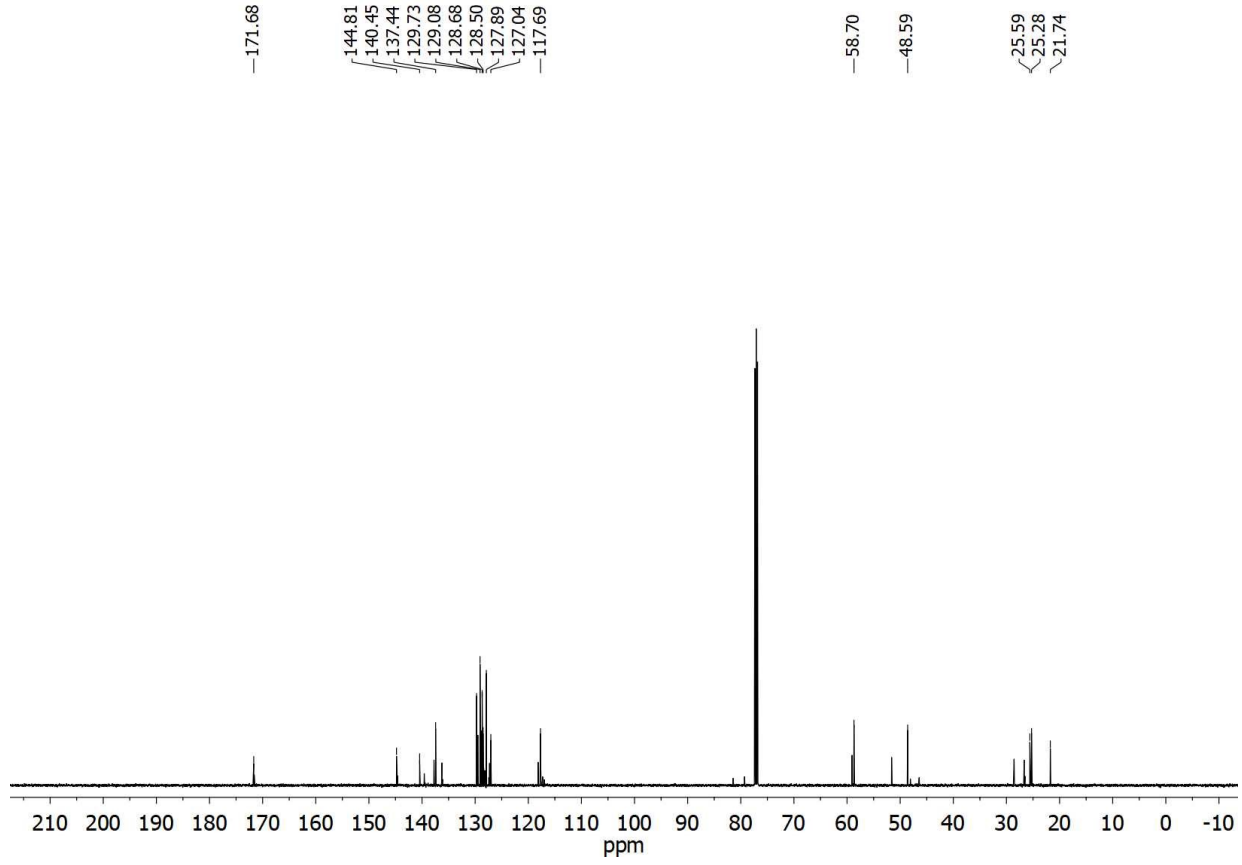
3-phenyl-1-tosyl-6-vinylpiperidin-2-one 14a

^{1}H-NMR



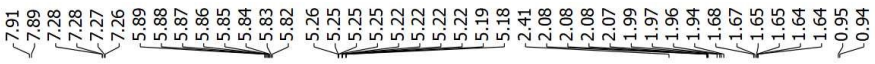
$C_{20}H_{21}NO_3S$

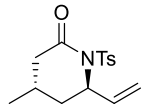
^{13}C-NMR



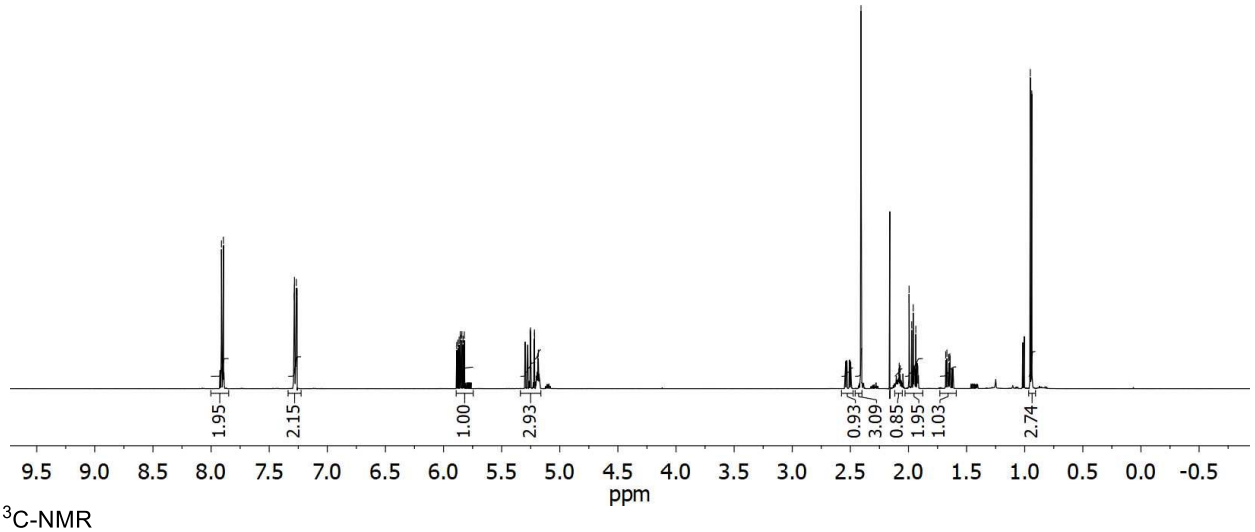
***anti*-4-methyll-1-tosyl-6-vinylpiperidin-2-one 3b**

^{1}H-NMR

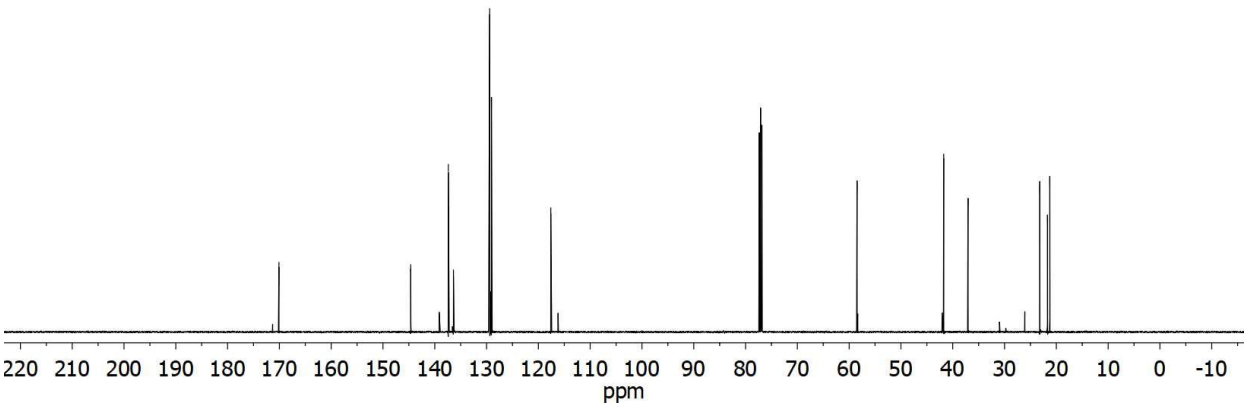




$C_{15}H_{19}NO_3S$

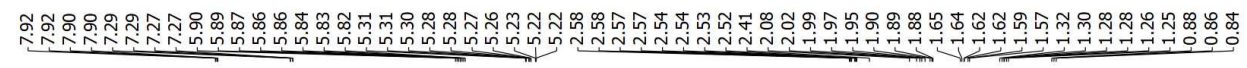


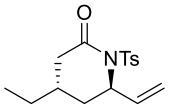
^{13}C-NMR



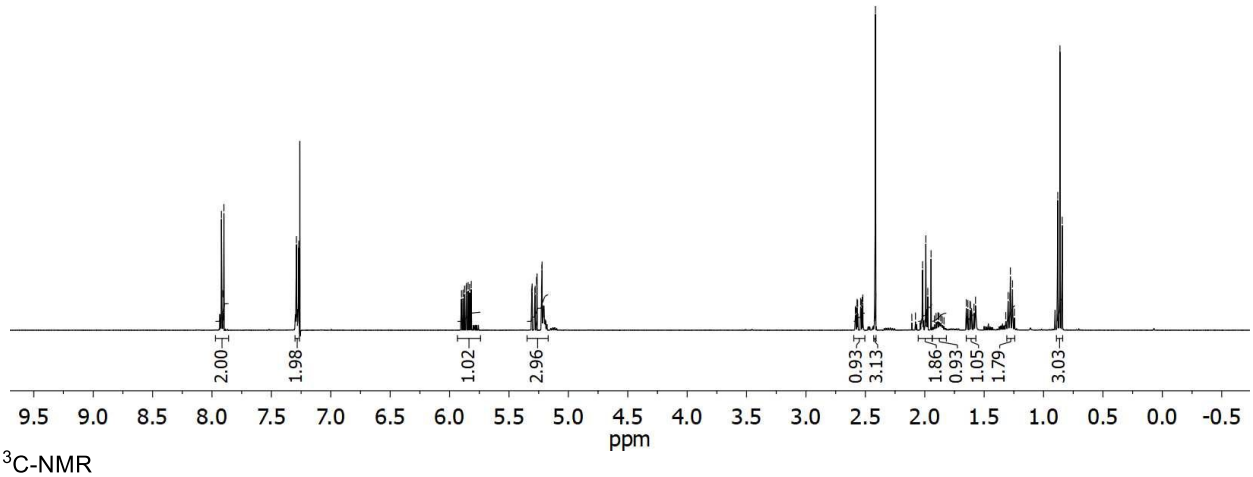
***anti*-4-ethyl-1-tosyl-6-vinylpiperidin-2-one 4b**

^{1}H-NMR

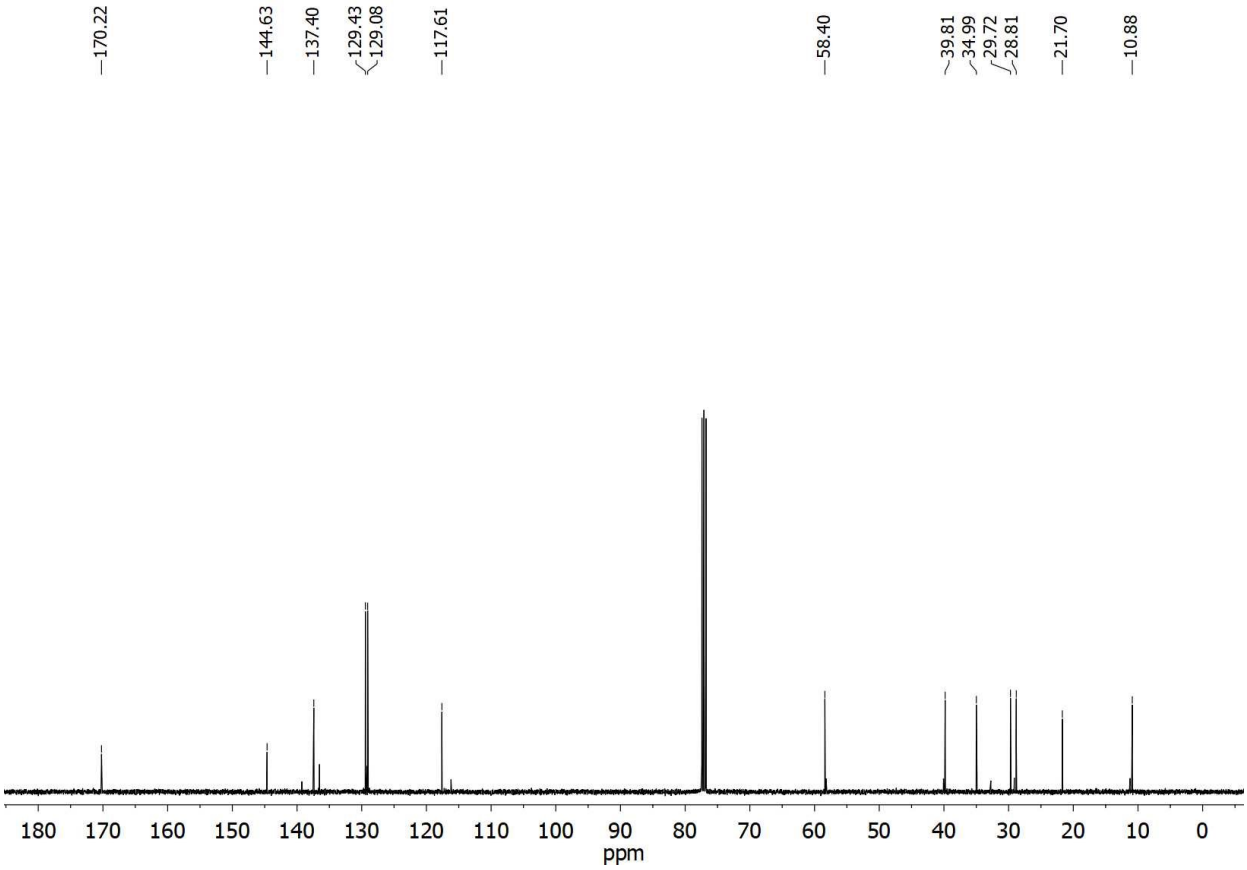




$C_{16}H_{21}NO_3S$

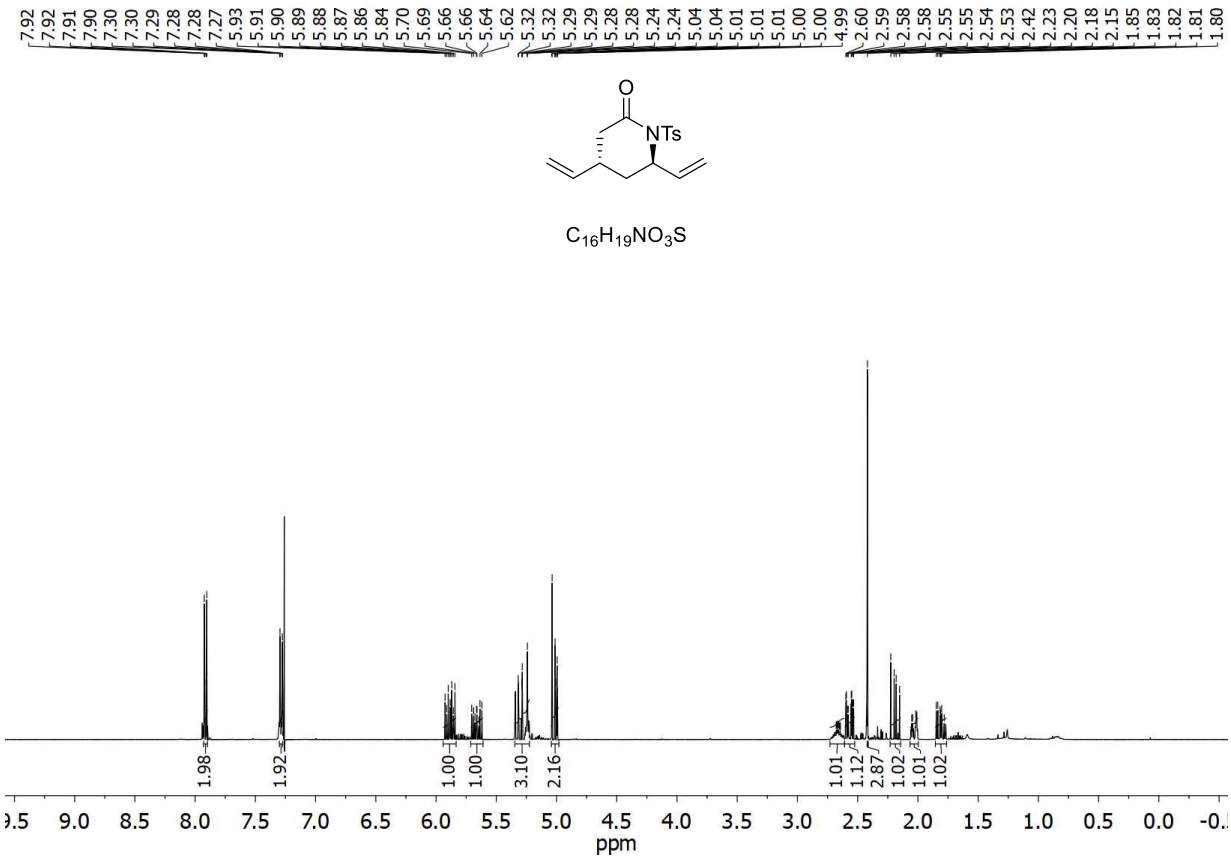


^{13}C-NMR



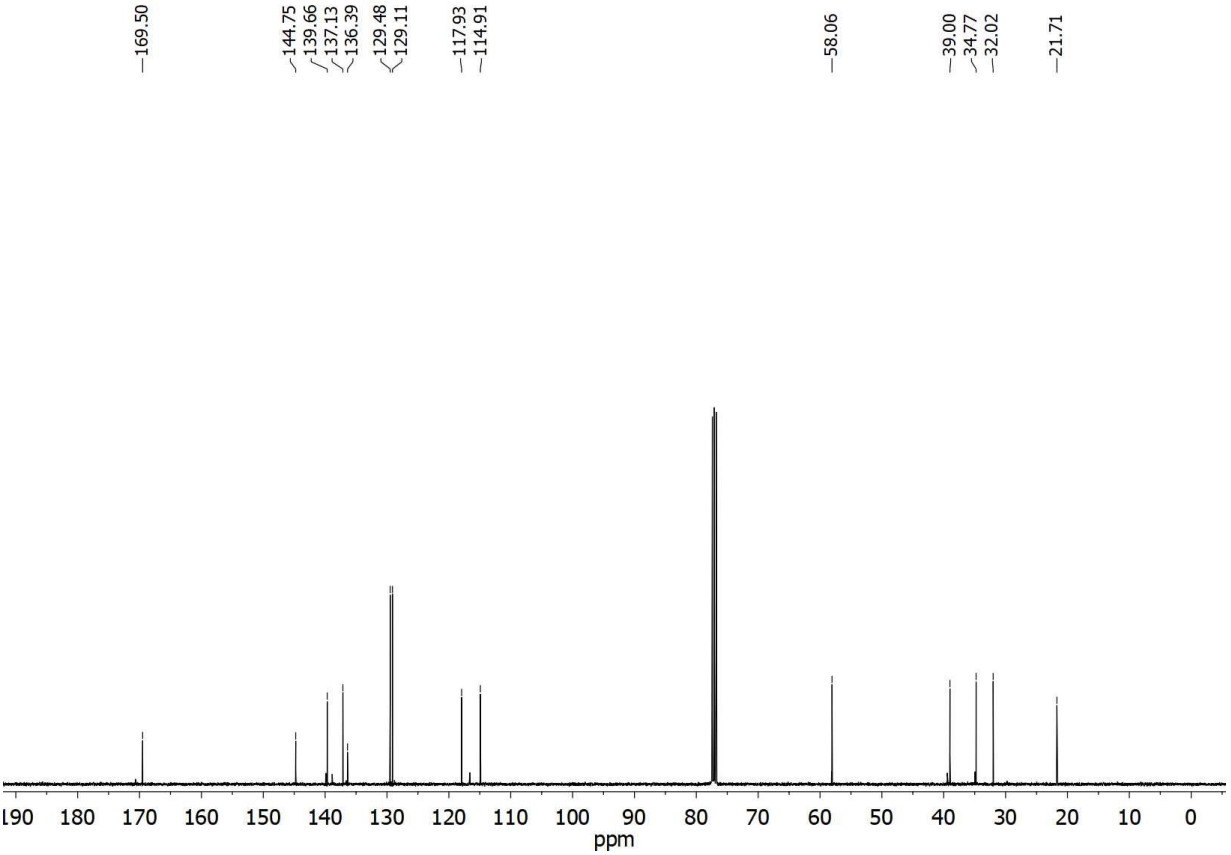
***anti*-1-tosyl-4,6-divinylpiperidin-2-one 5b**

^{1}H-NMR



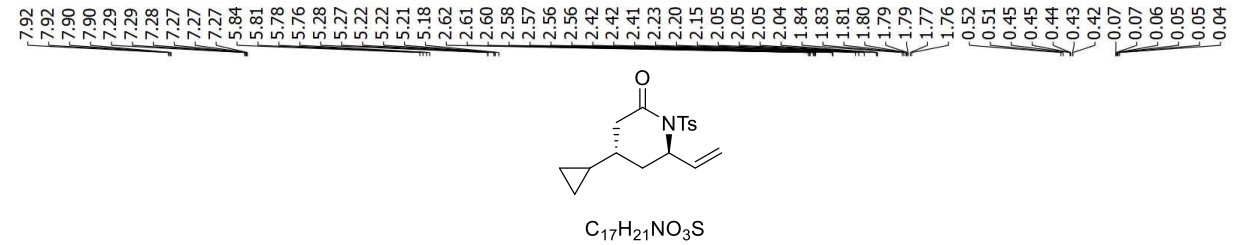
$C_{16}H_{19}NO_3S$

^{13}C-NMR

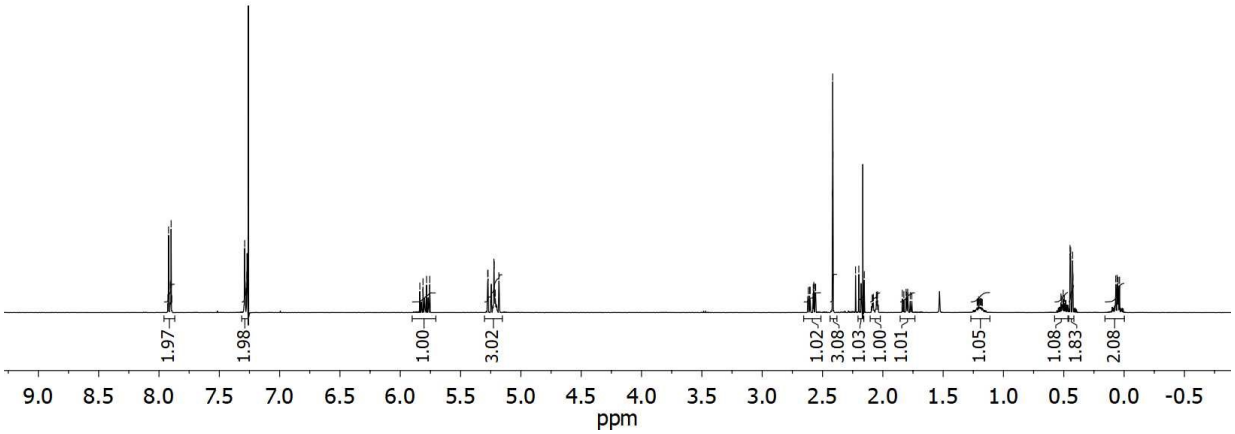


***anti*-4-cyclopropyl-1-tosyl-6-vinylpiperidin-2-one 6b**

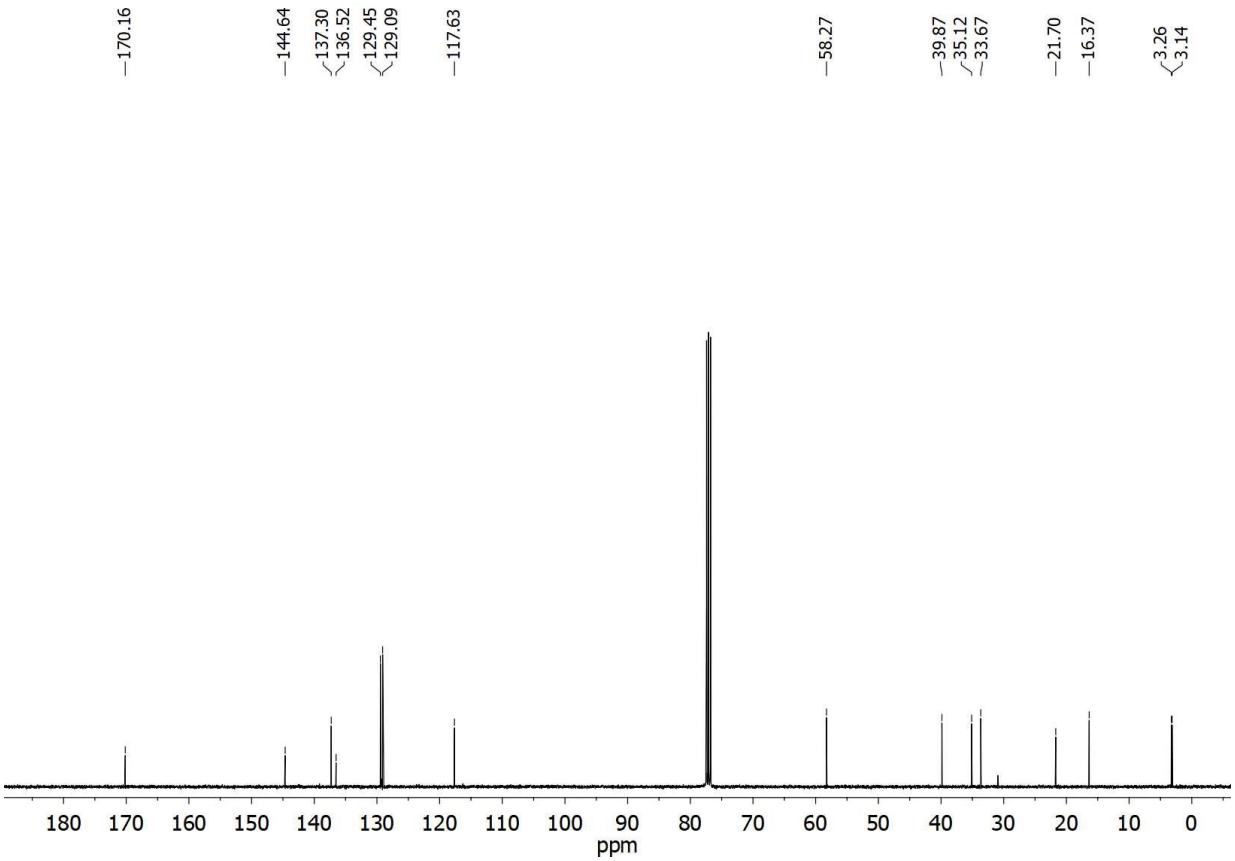
^{1}H-NMR



$C_{17}H_{21}NO_3S$

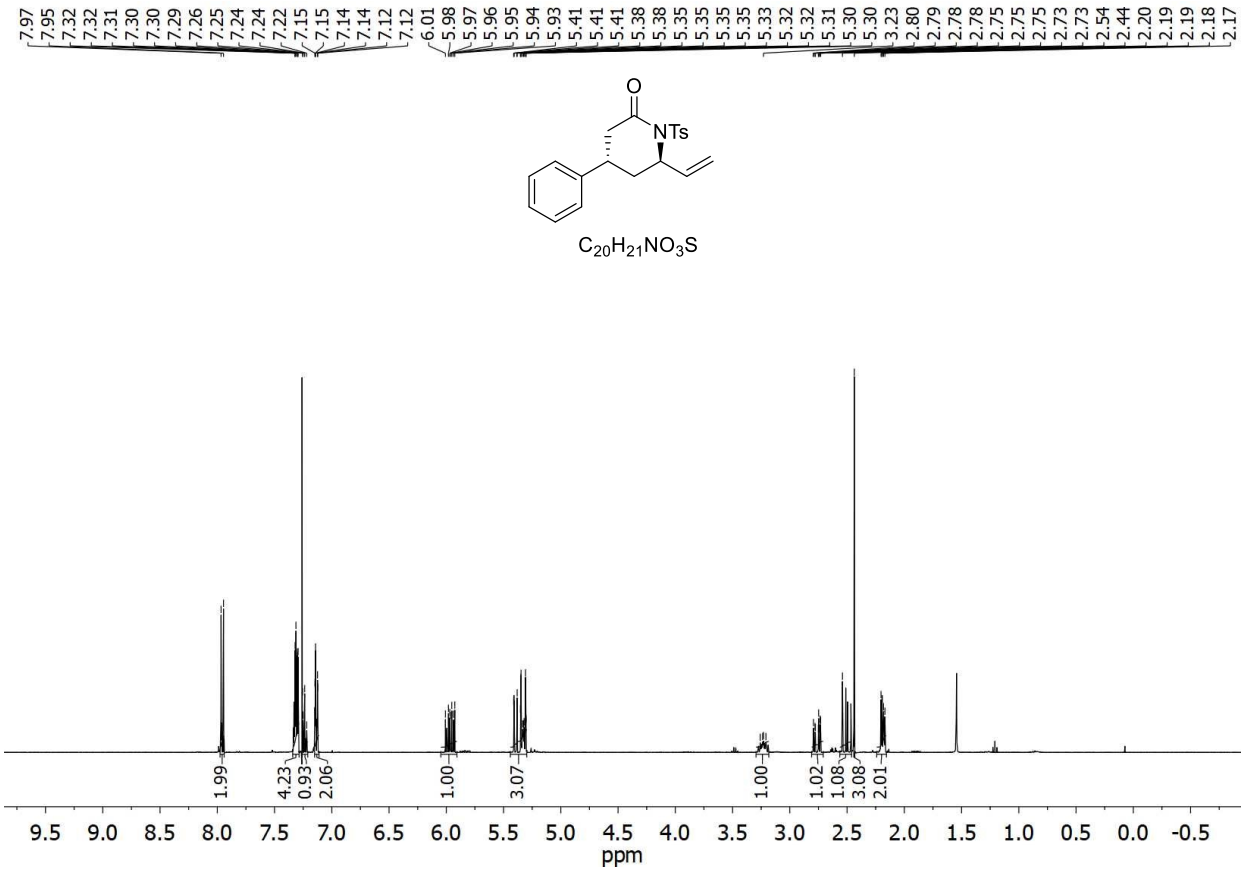


^{13}C-NMR

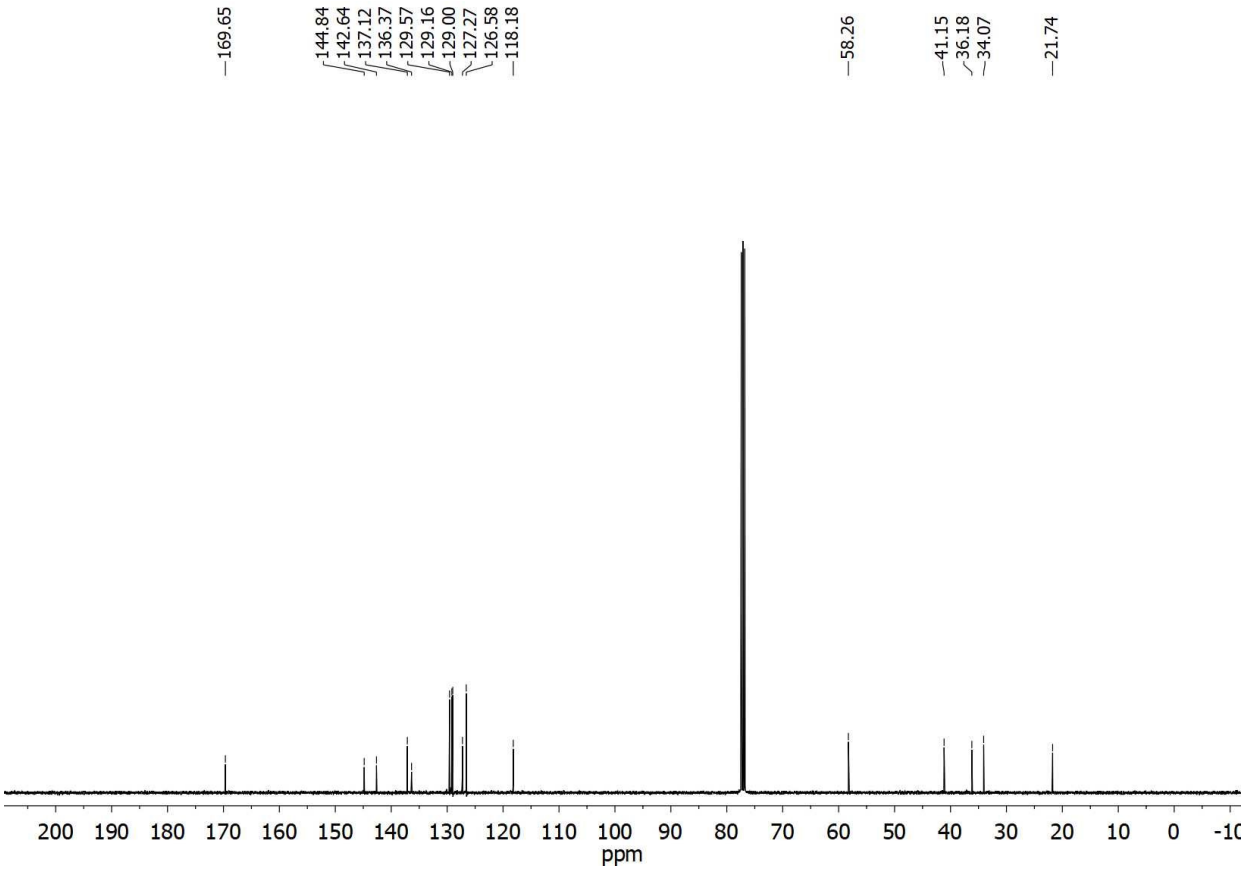


***anti*-4-phenyl-1-tosyl-6-vinylpiperidin-2-one 2b**

^{1}H-NMR



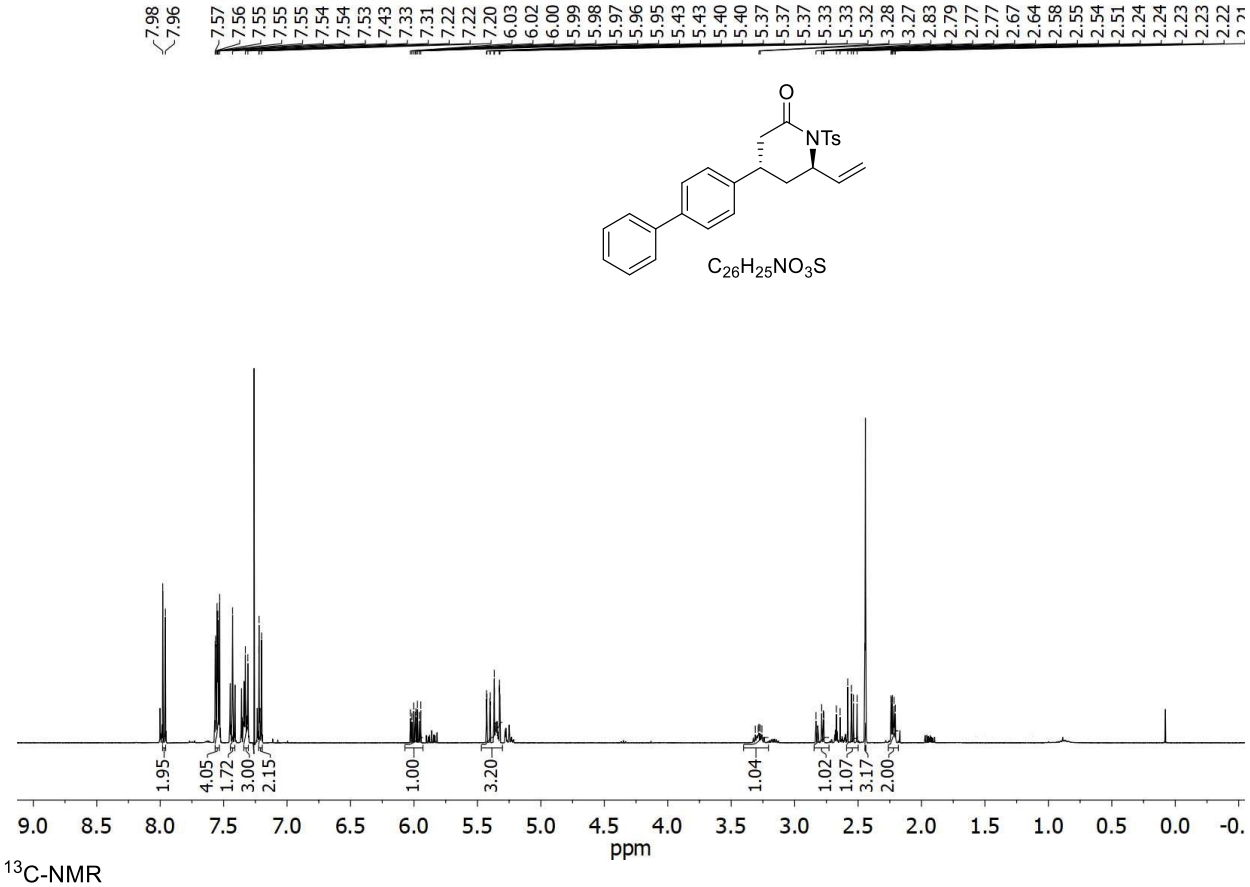
^{13}C-NMR



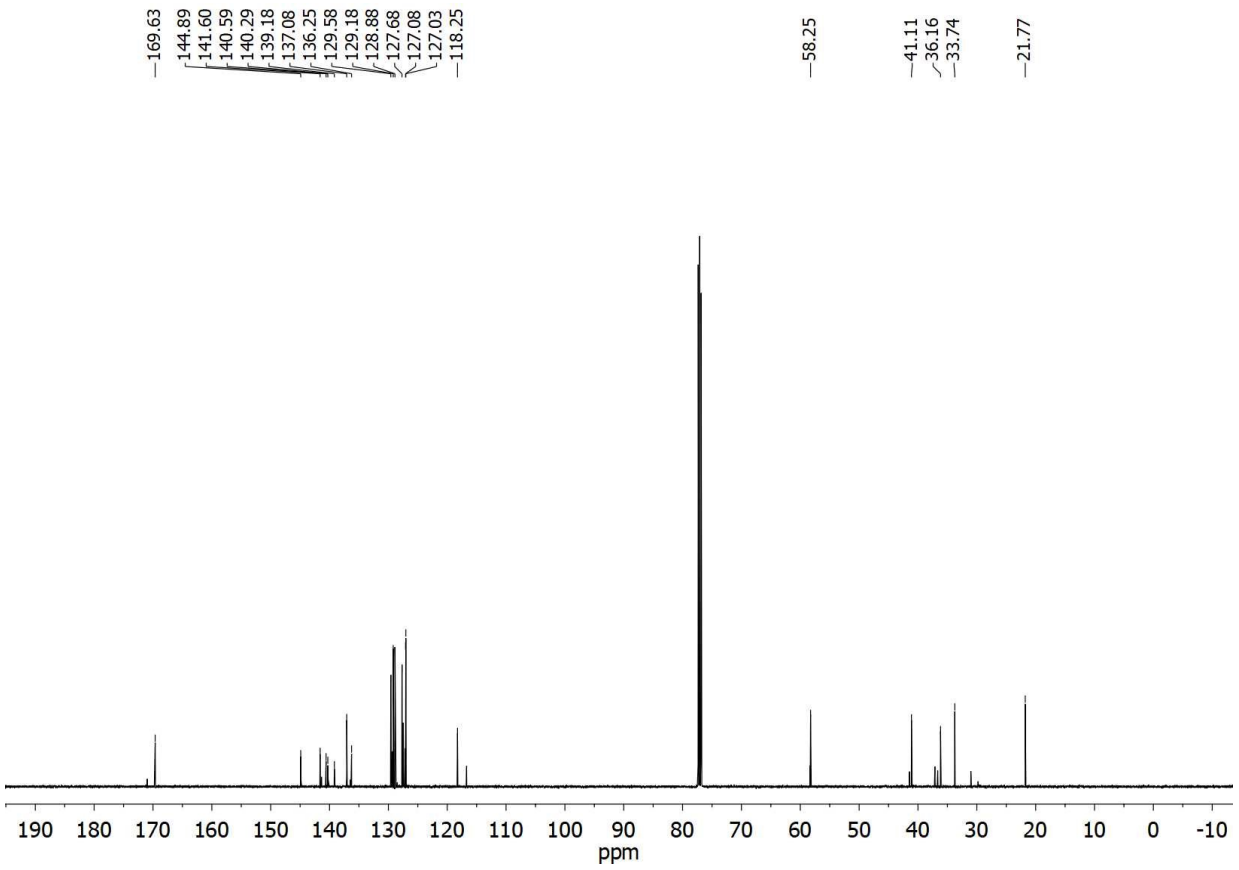
(

***anti*-4-([1,1'-biphenyl]-4-yl)-1-tosyl-6-vinylpiperidin-2-one 7b**

^{1}H-NMR

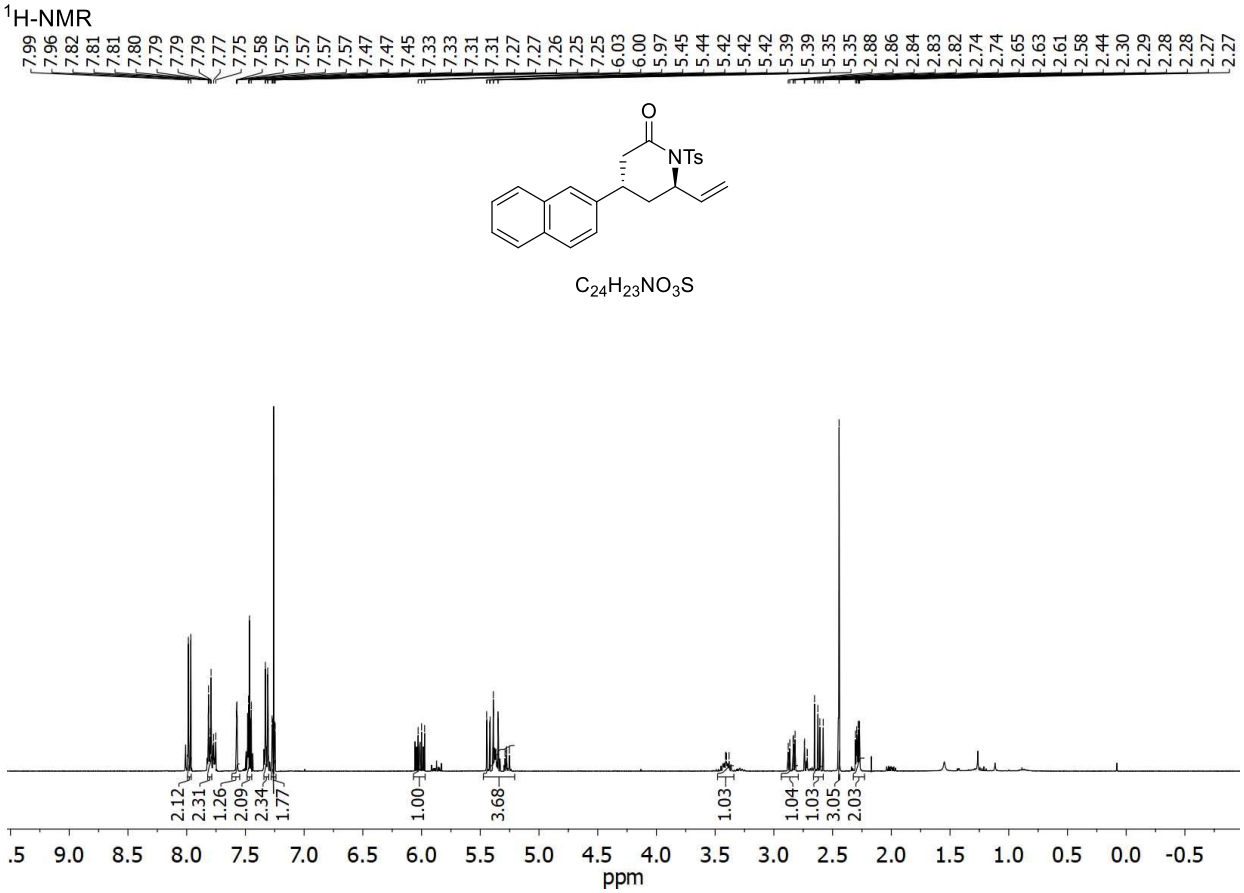


^{13}C-NMR



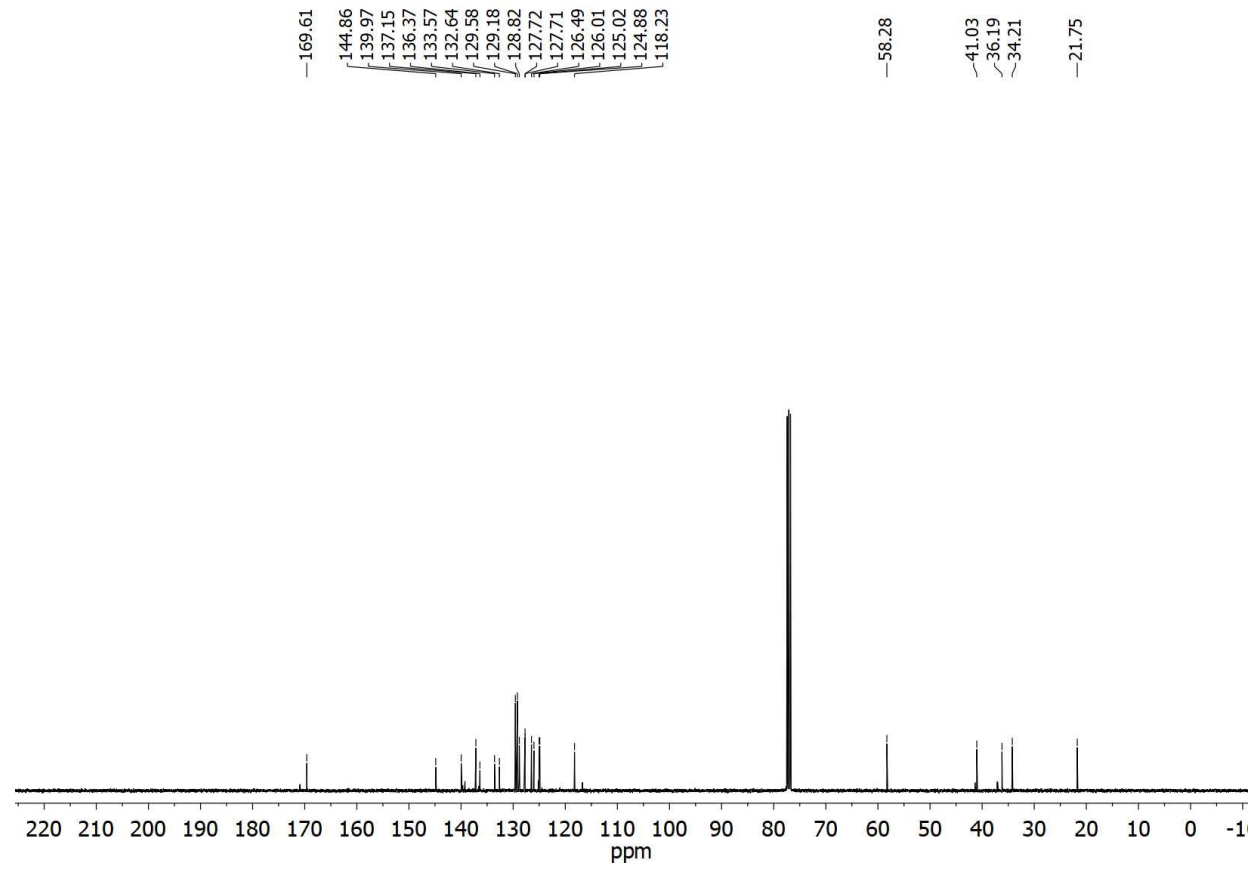
***anti*-4-(naphthalen-2-yl)-1-tosyl-6-vinylpiperidin-2-one 8b**

^{1}H-NMR



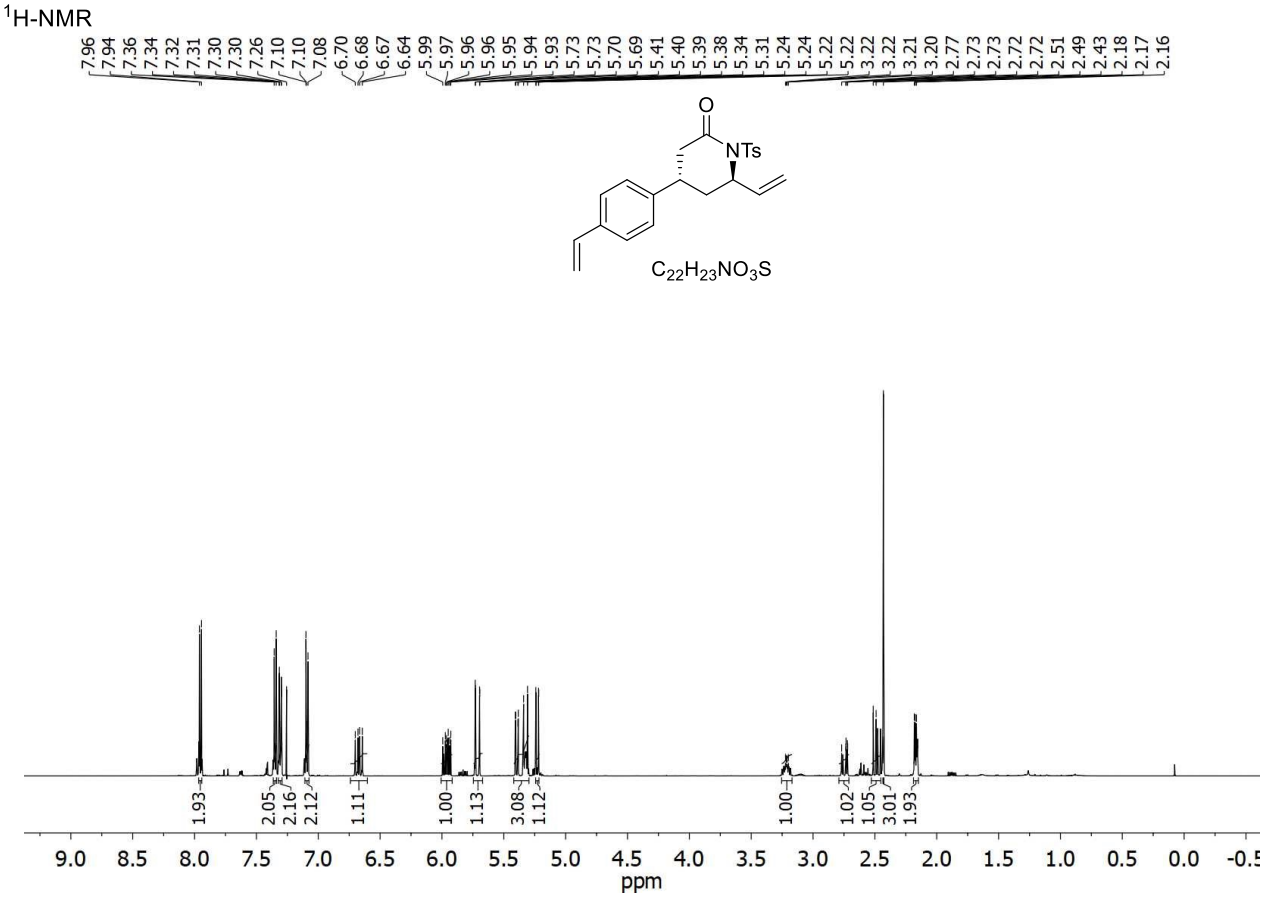
$C_{24}H_{23}NO_3S$

^{13}C-NMR

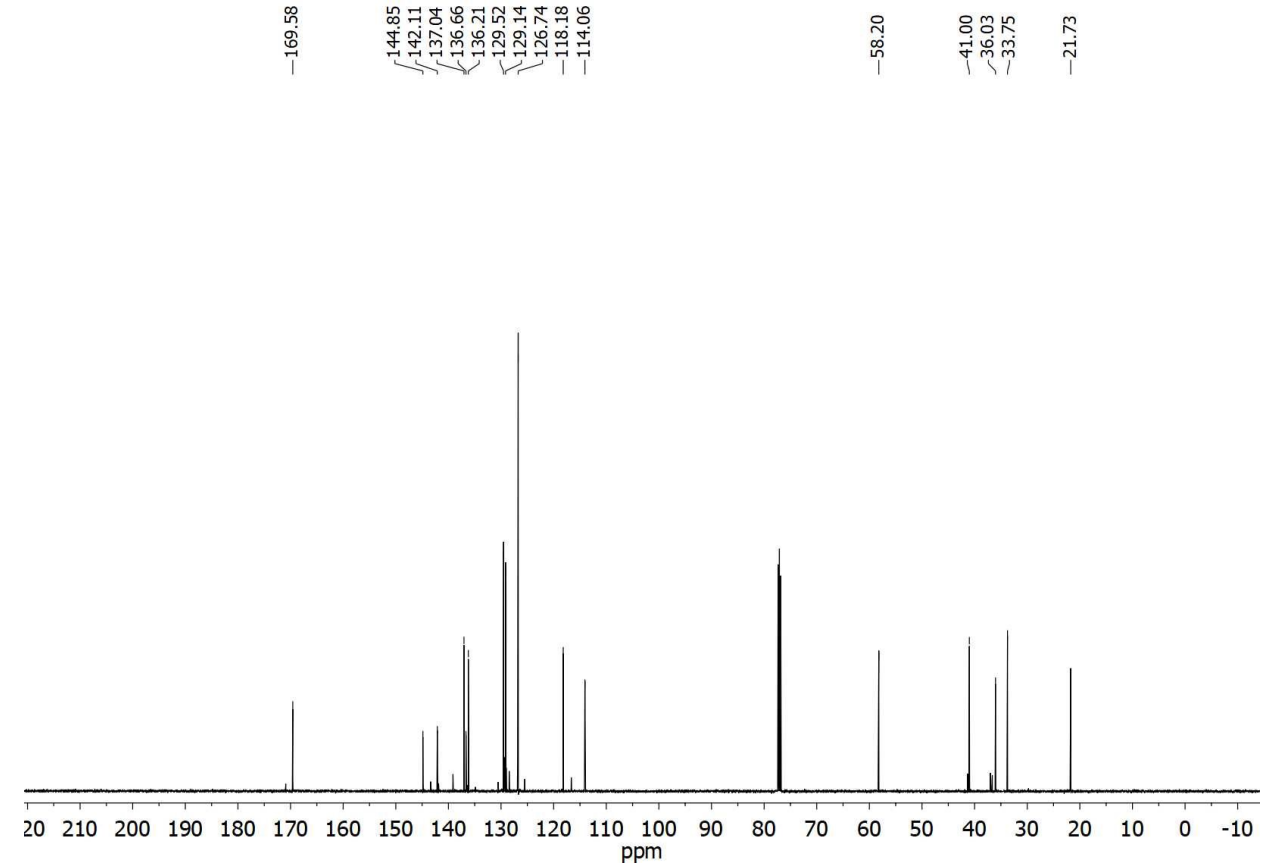


anti-1-tosyl-6-vinyl-4-(4-vinylphenyl)piperidin-2-one 9b

^{1}H-NMR

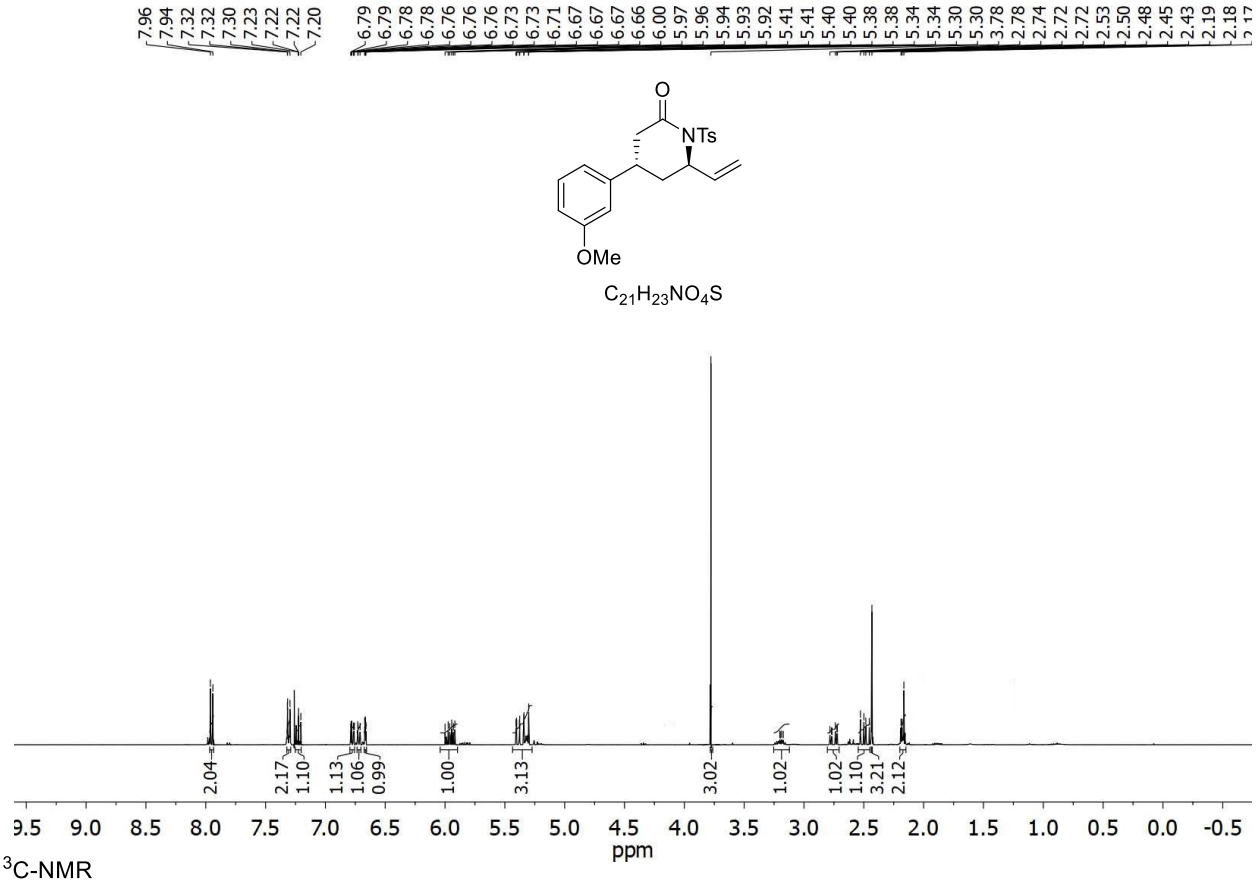


^{13}C-NMR

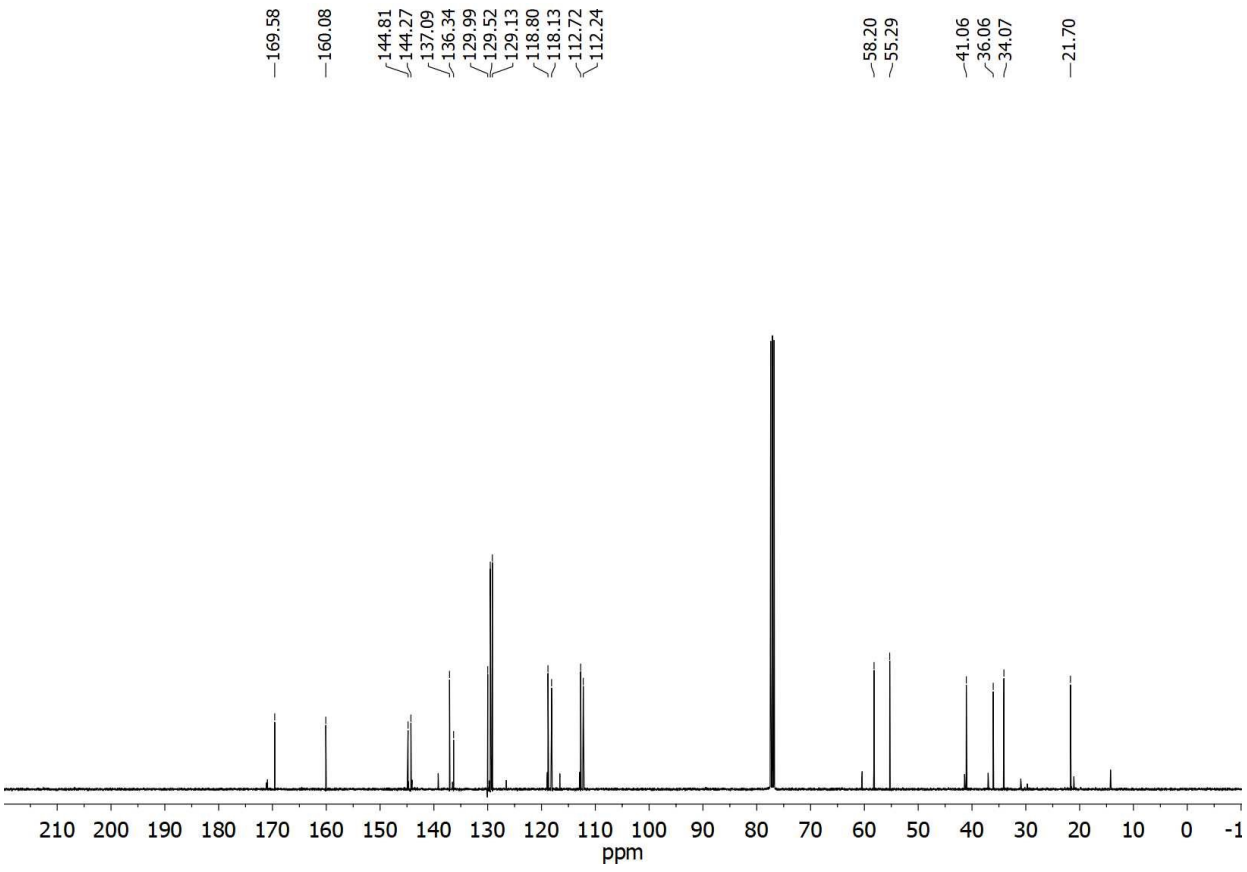


***anti*-4-(3-methoxyphenyl)-1-tosyl-6-vinylpiperidin-2-one 10b**

^{1}H-NMR

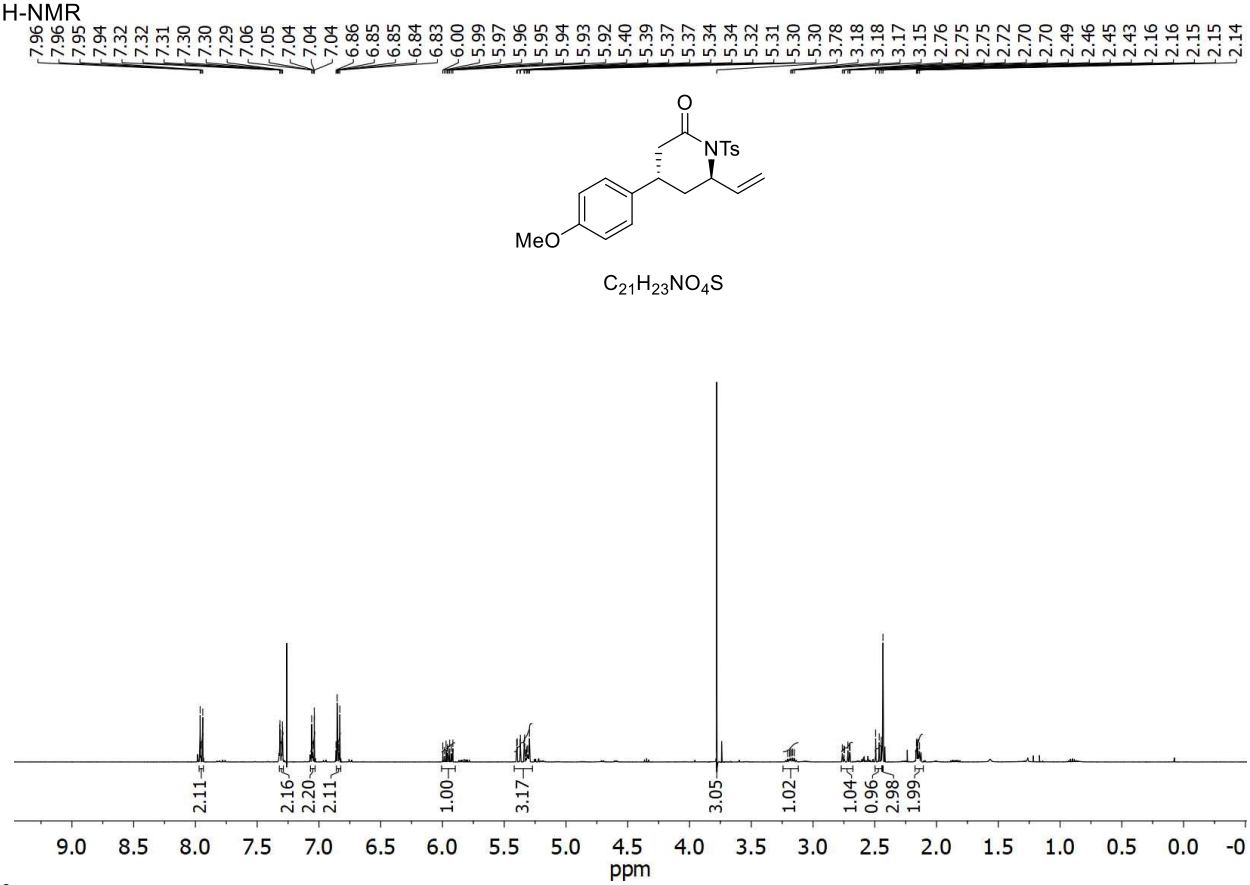


^{13}C-NMR



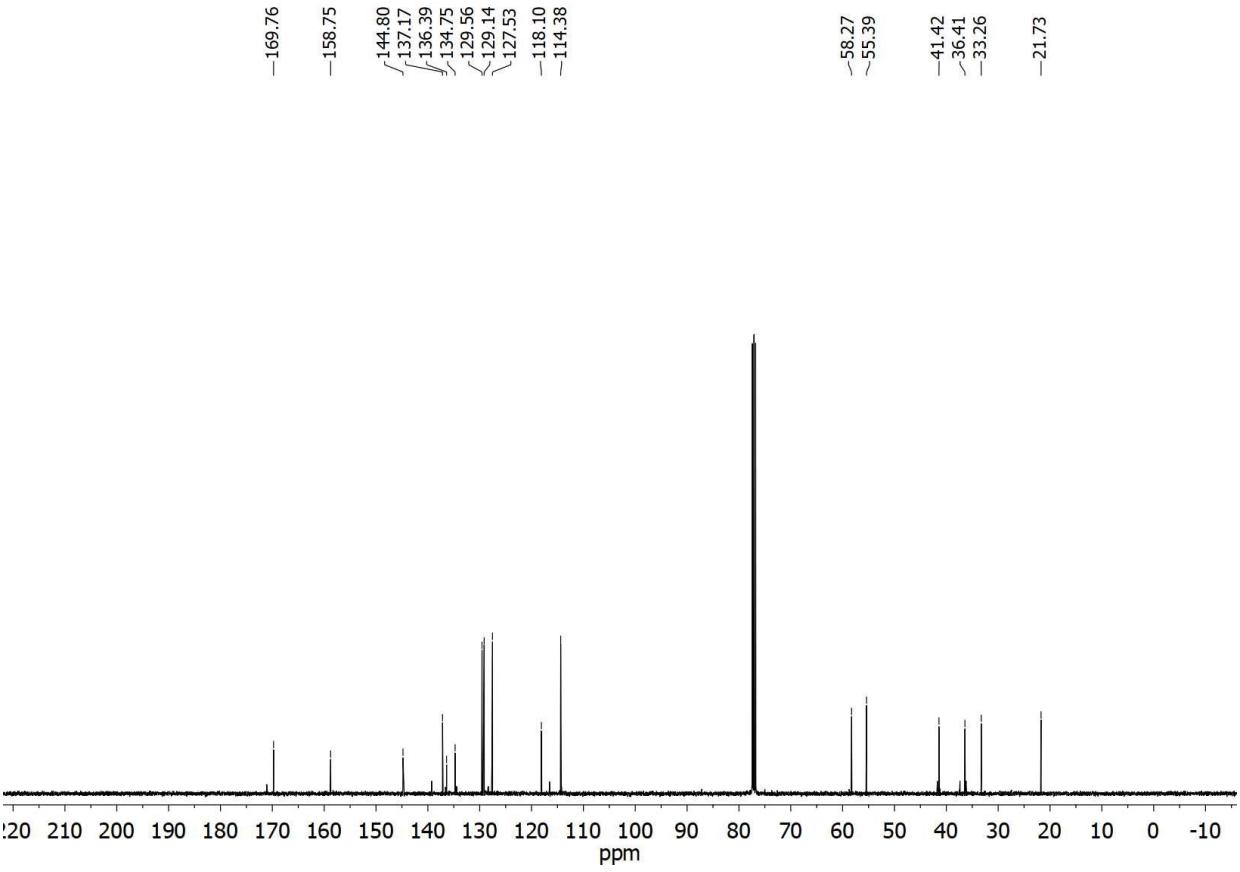
***anti*-4-(4-methoxyphenyl)-1-tosyl-6-vinylpiperidin-2-one 11b**

^{1}H-NMR



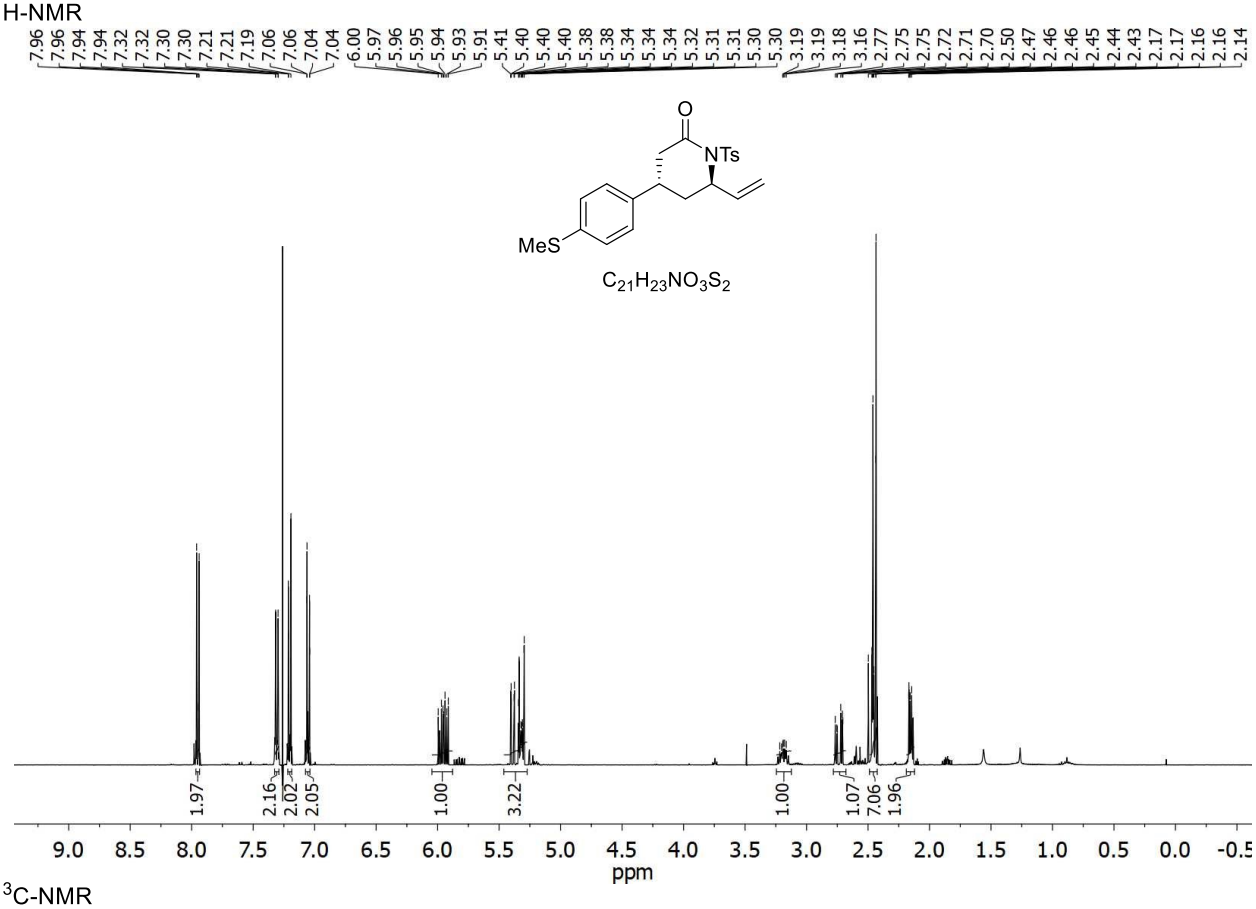
$C_{21}H_{23}NO_4S$

^{13}C-NMR

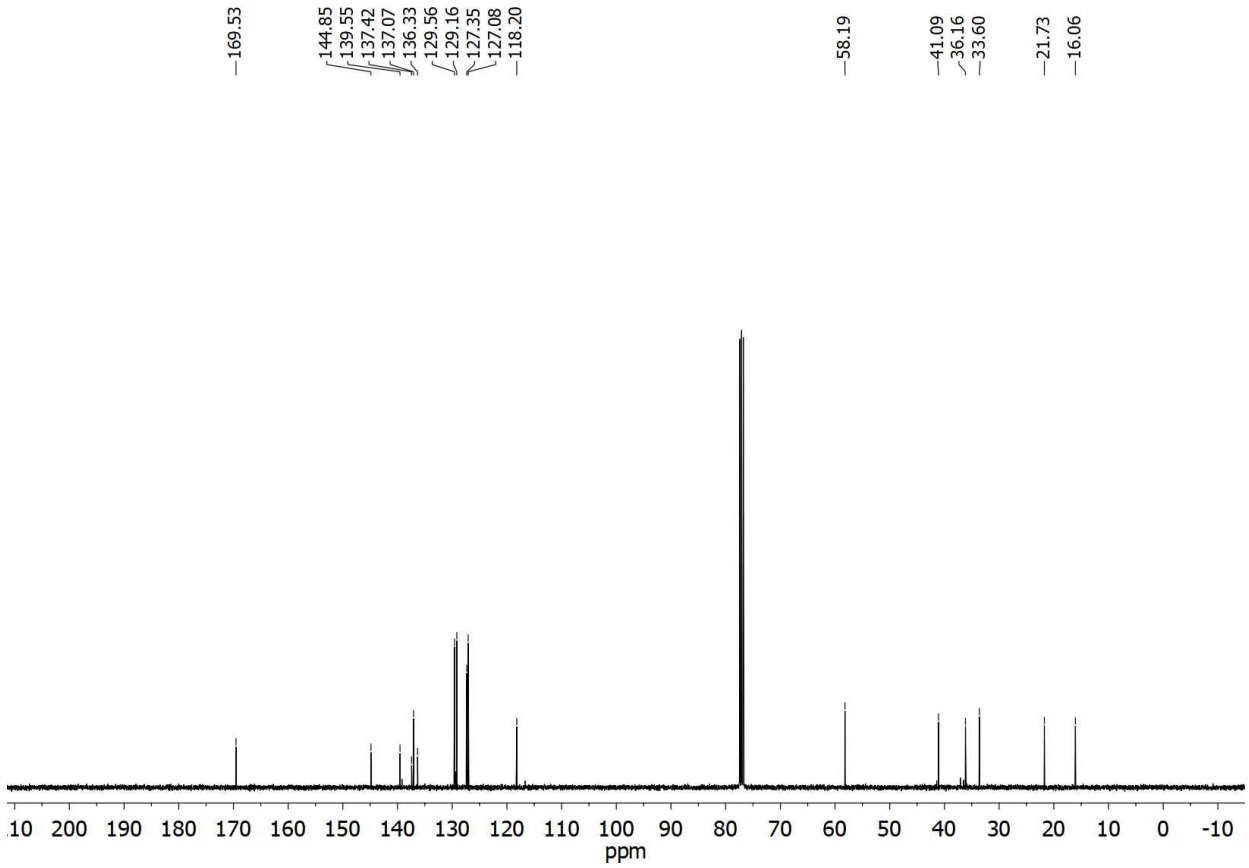


***anti*-(4-(methylthio)phenyl)-1-tosyl-6-vinylpiperidin-2-one 12b**

^{1}H-NMR

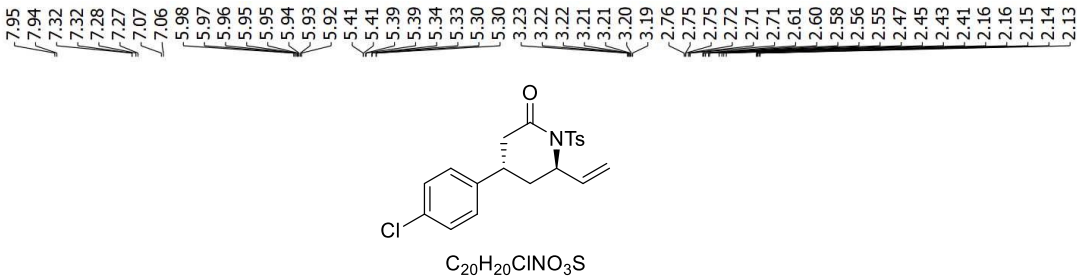


^{13}C-NMR

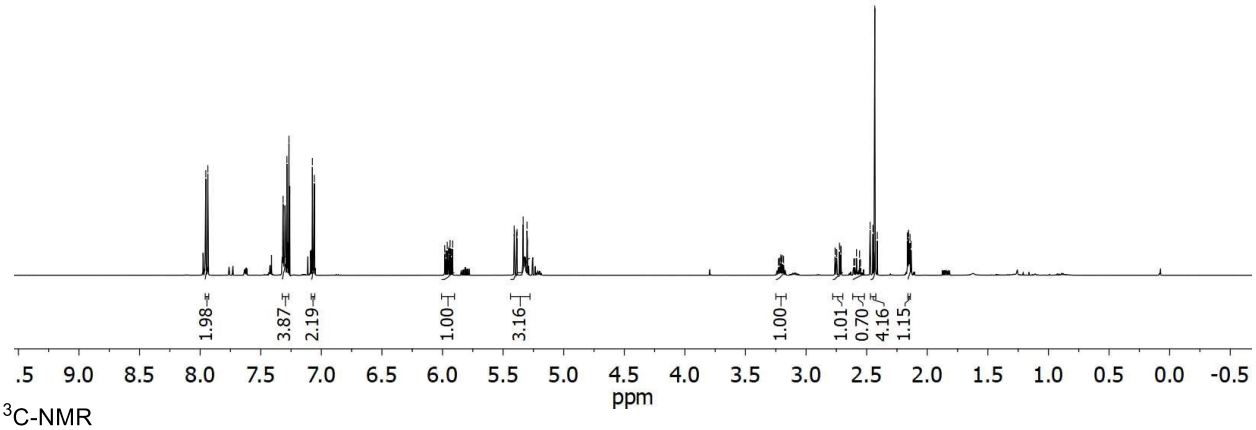


***anti*-4-(4-chlorophenyl)-1-tosyl-6-vinylpiperidin-2-one 13b**

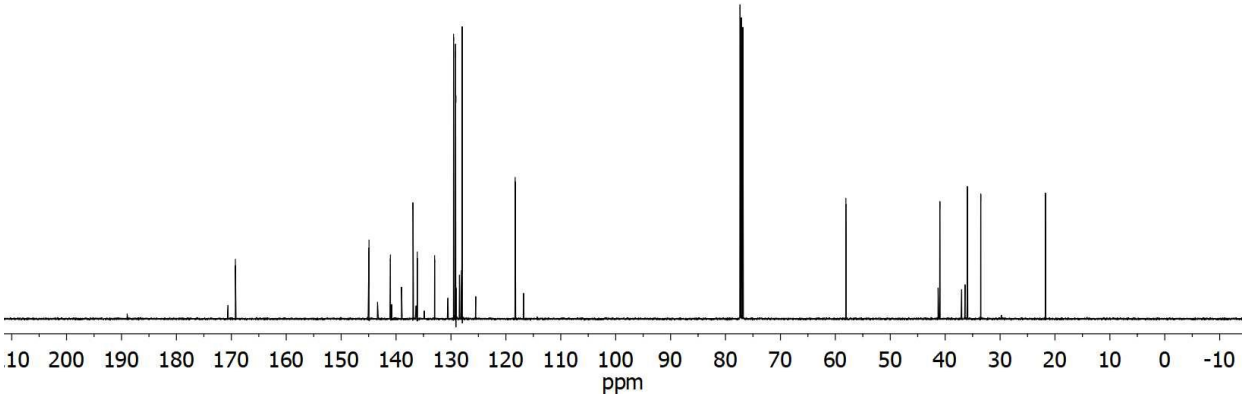
^{1}H-NMR



$C_{20}H_{20}ClNO_3S$

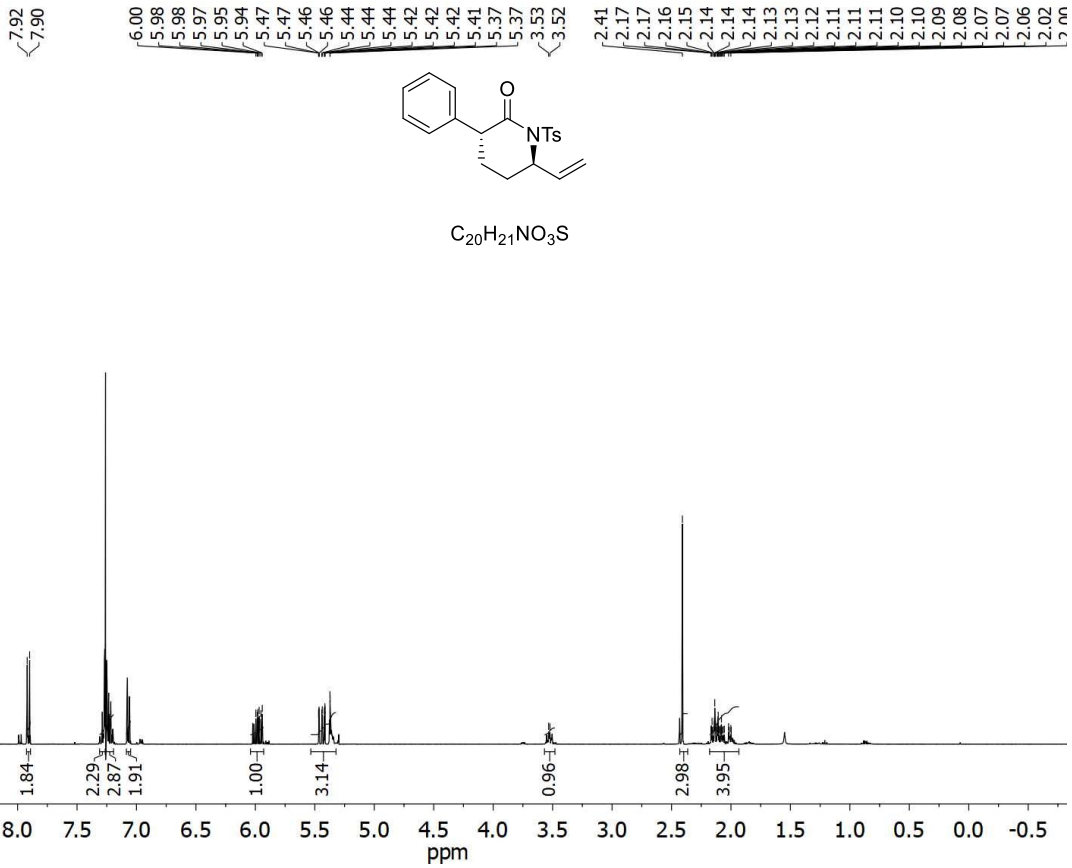


^{13}C-NMR



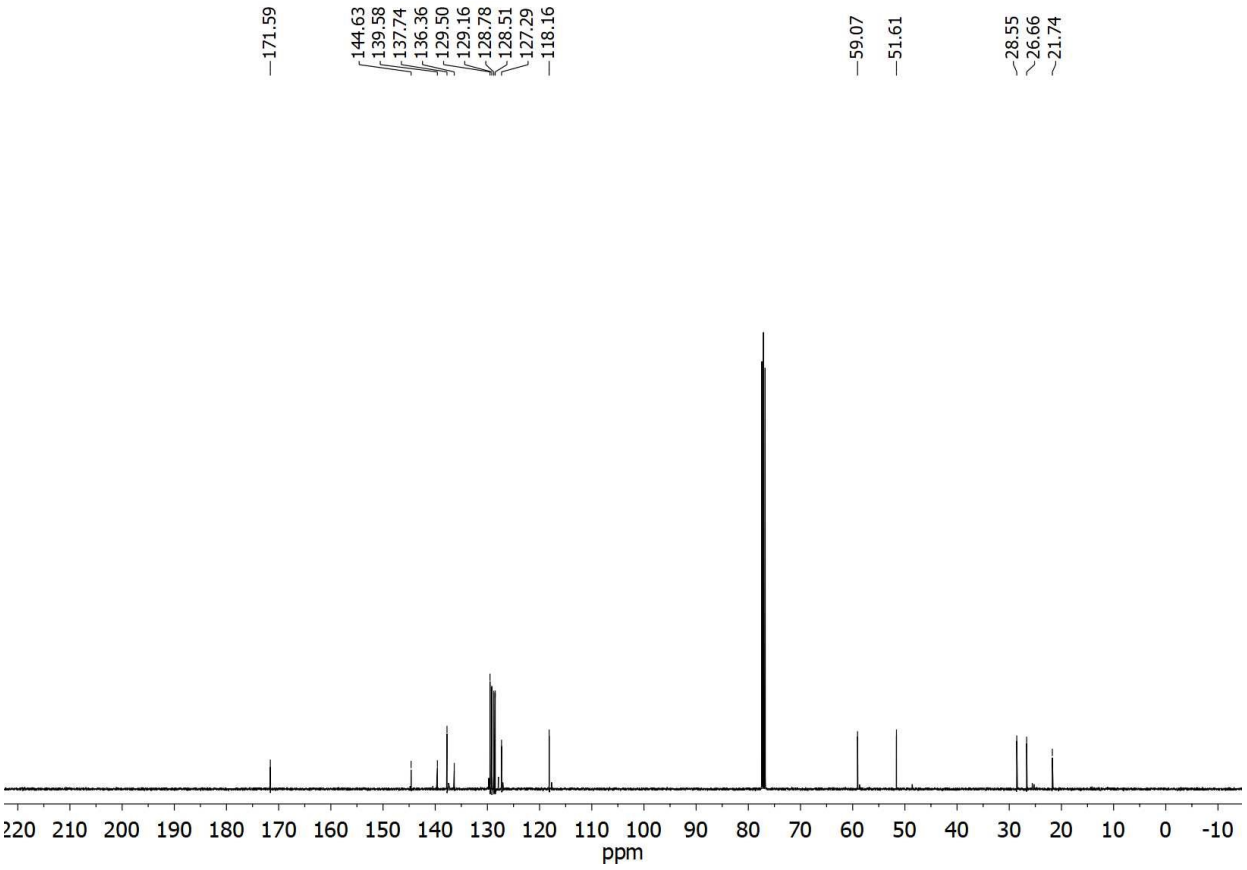
***anti*-3-phenyl-1-tosyl-6-vinylpiperidin-2-one 14b**

^{1}H-NMR



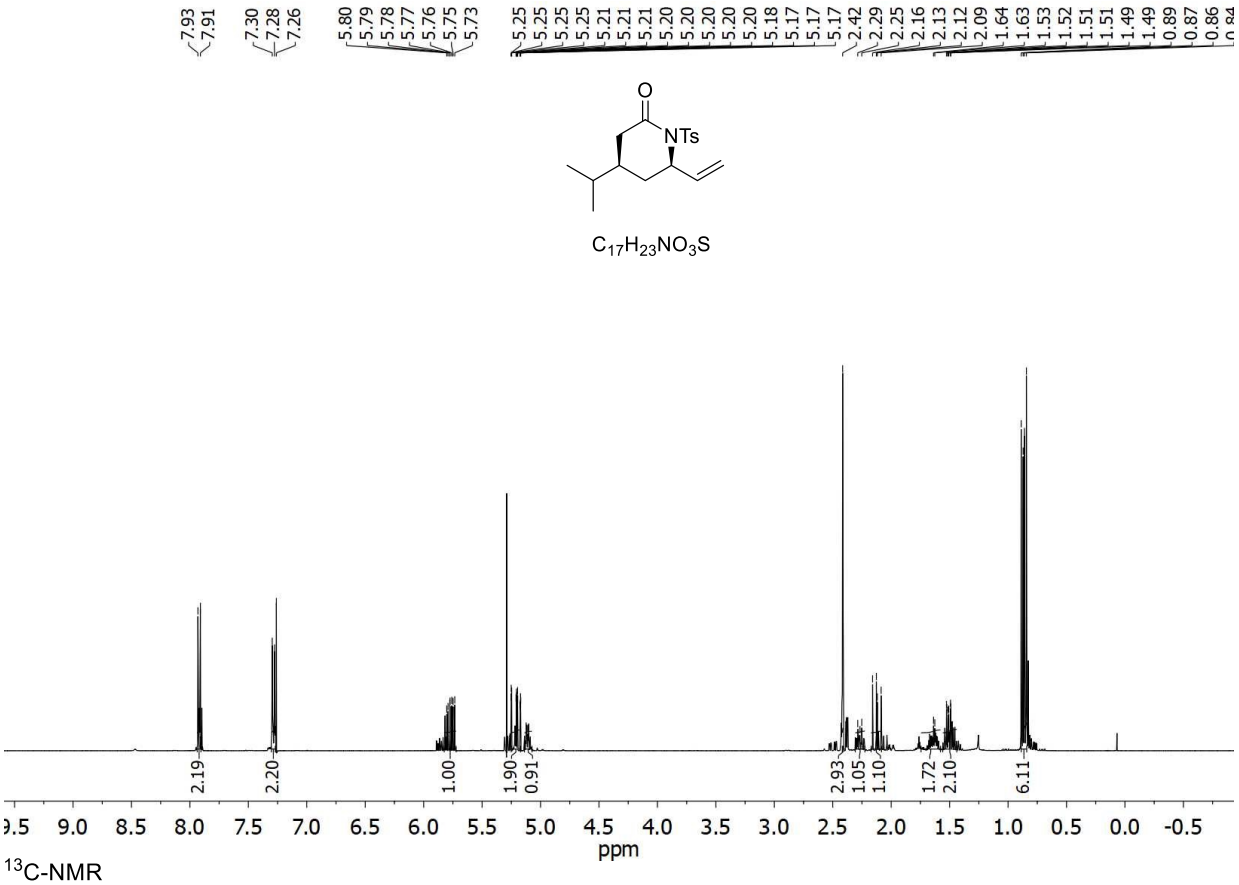
$C_{20}H_{21}NO_3S$

^{13}C-NMR

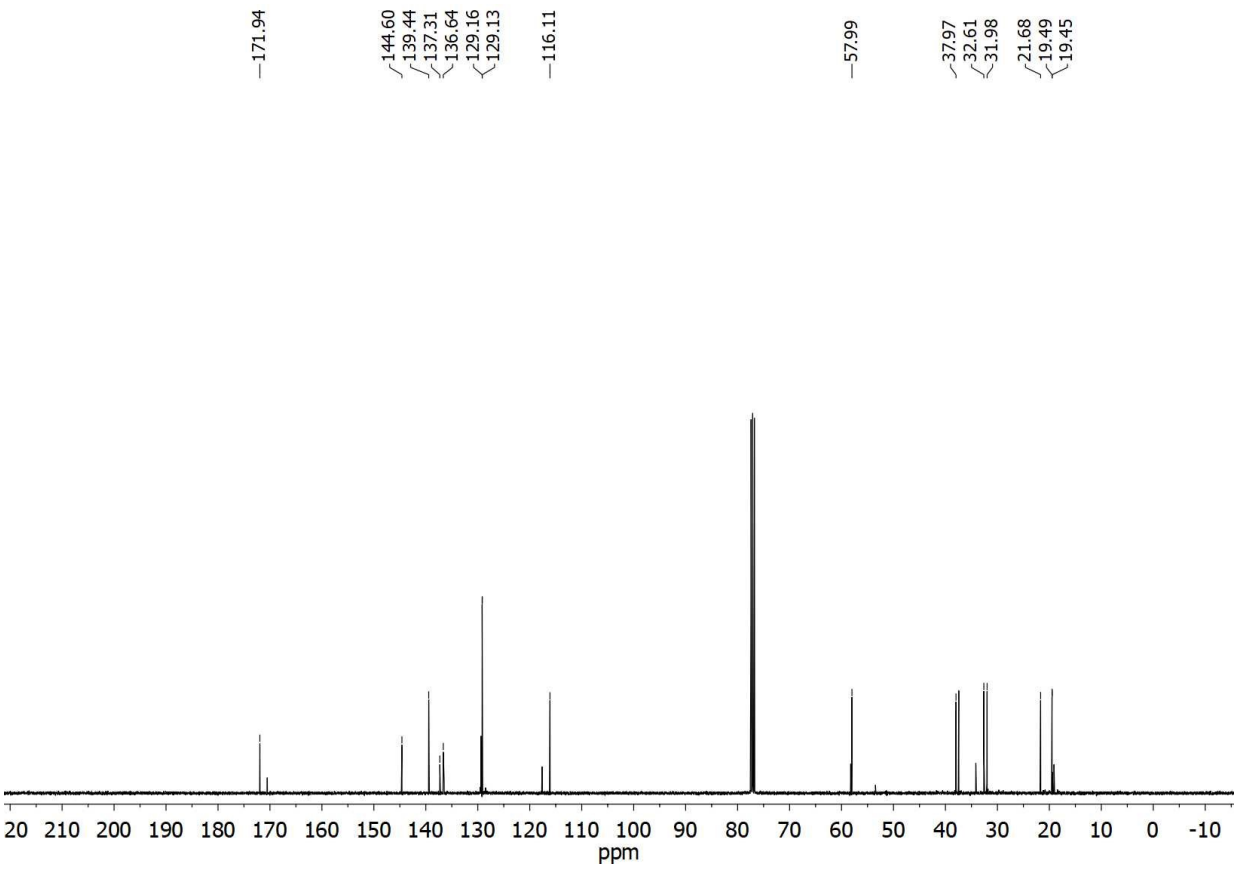


***syn*-4-isopropyl-1-tosyl-6-vinylpiperidin-2-one 15b**

^{1}H-NMR

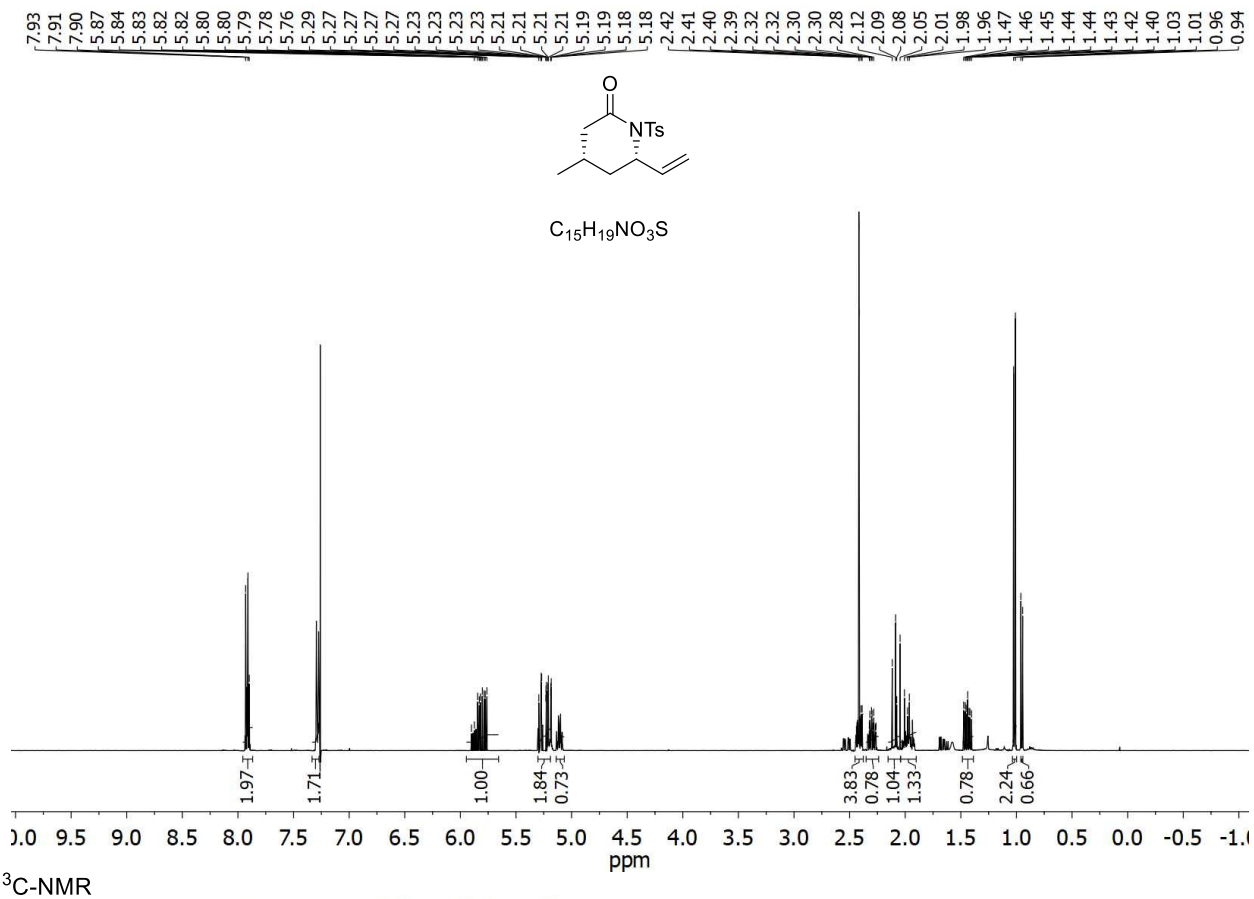


^{13}C-NMR

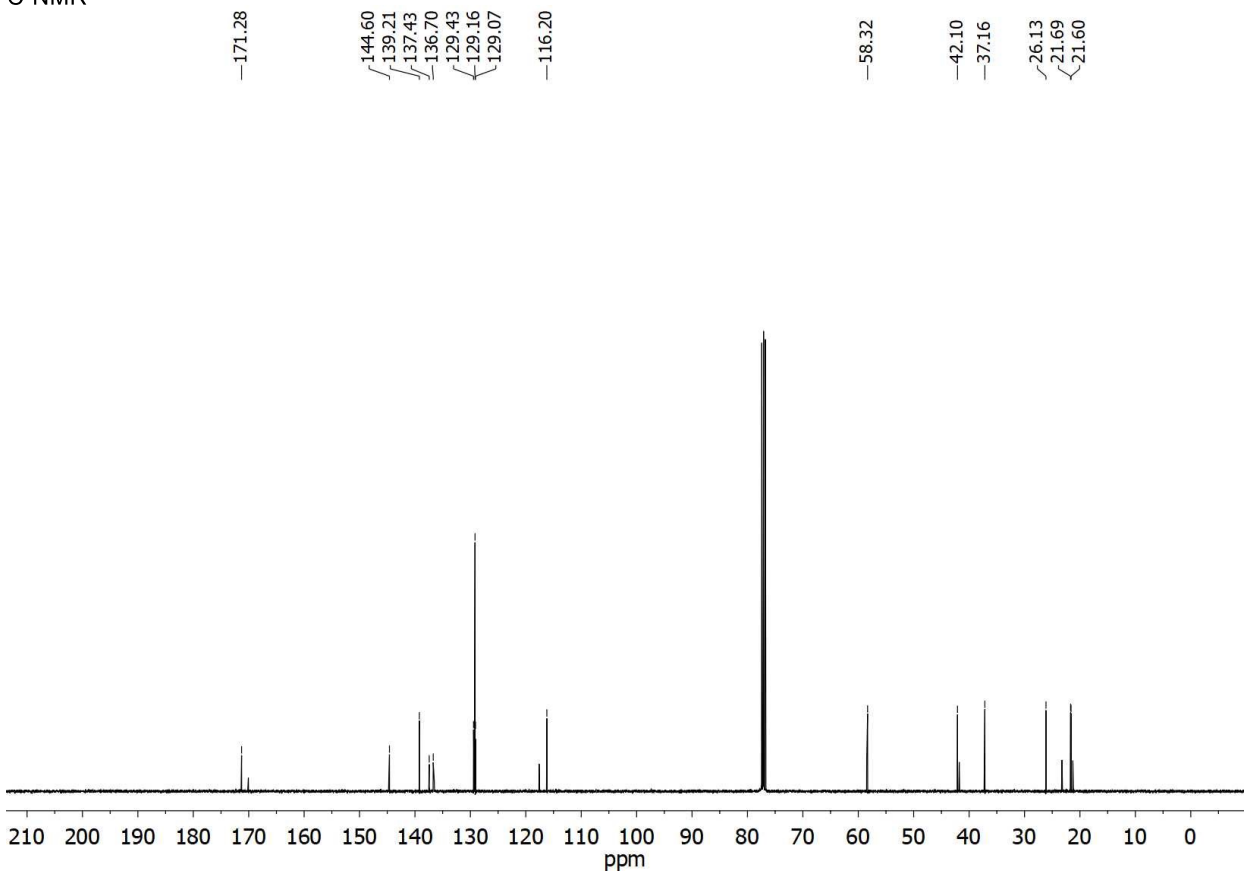


(4S,6S)-4-methyl-1-tosyl-6-vinylpiperidin-2-one 3a

^{1}H-NMR

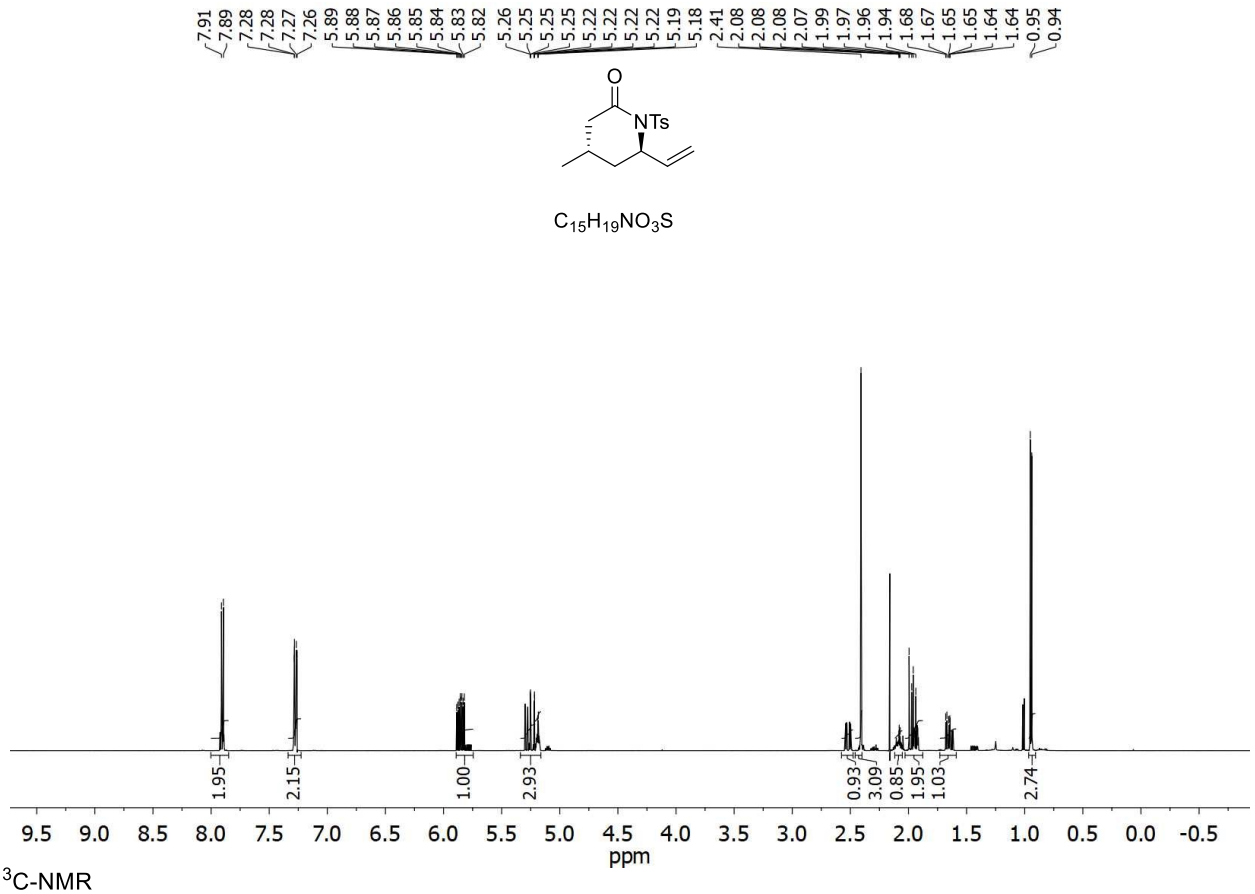


^{13}C-NMR



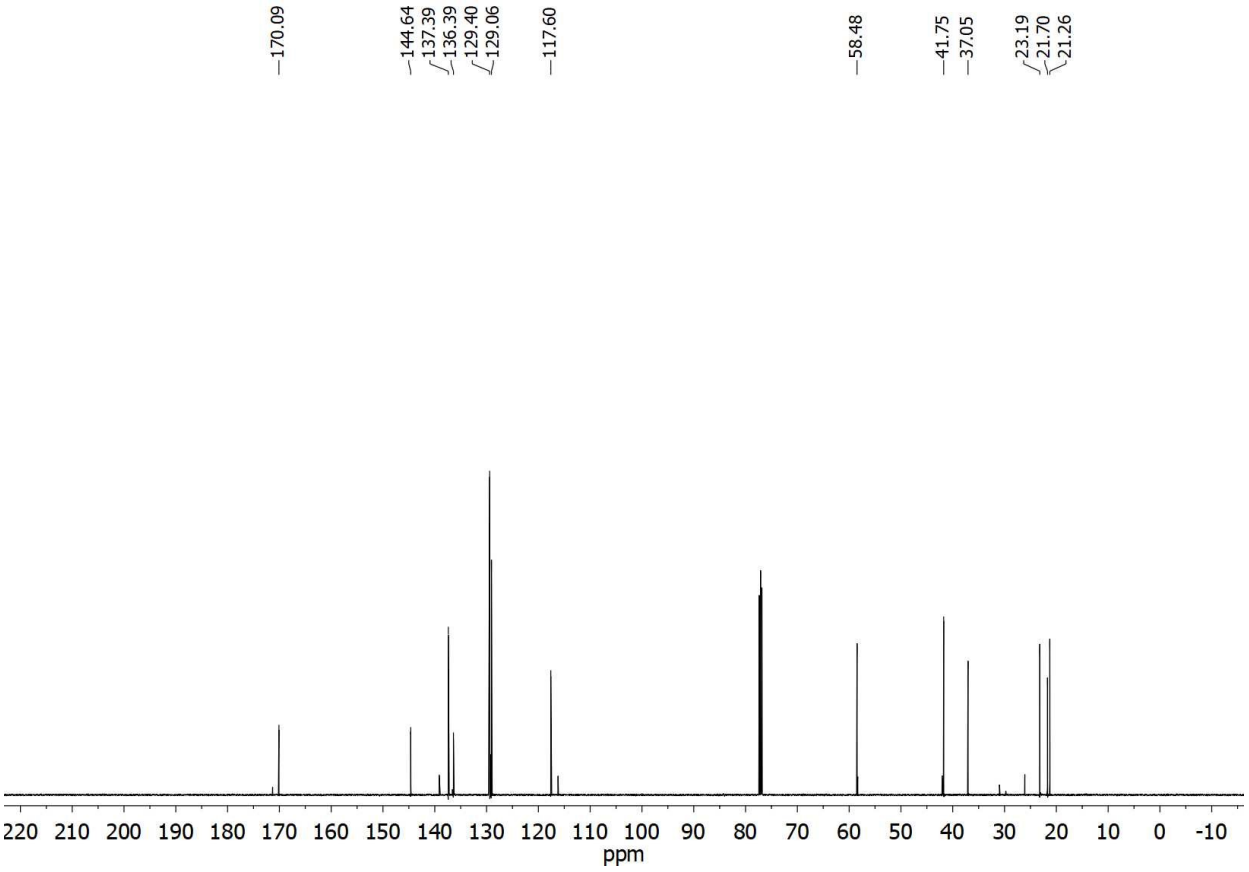
(4S,6R)-4-methyl-1-tosyl-6-vinylpiperidin-2-one 3b

^{1}H-NMR



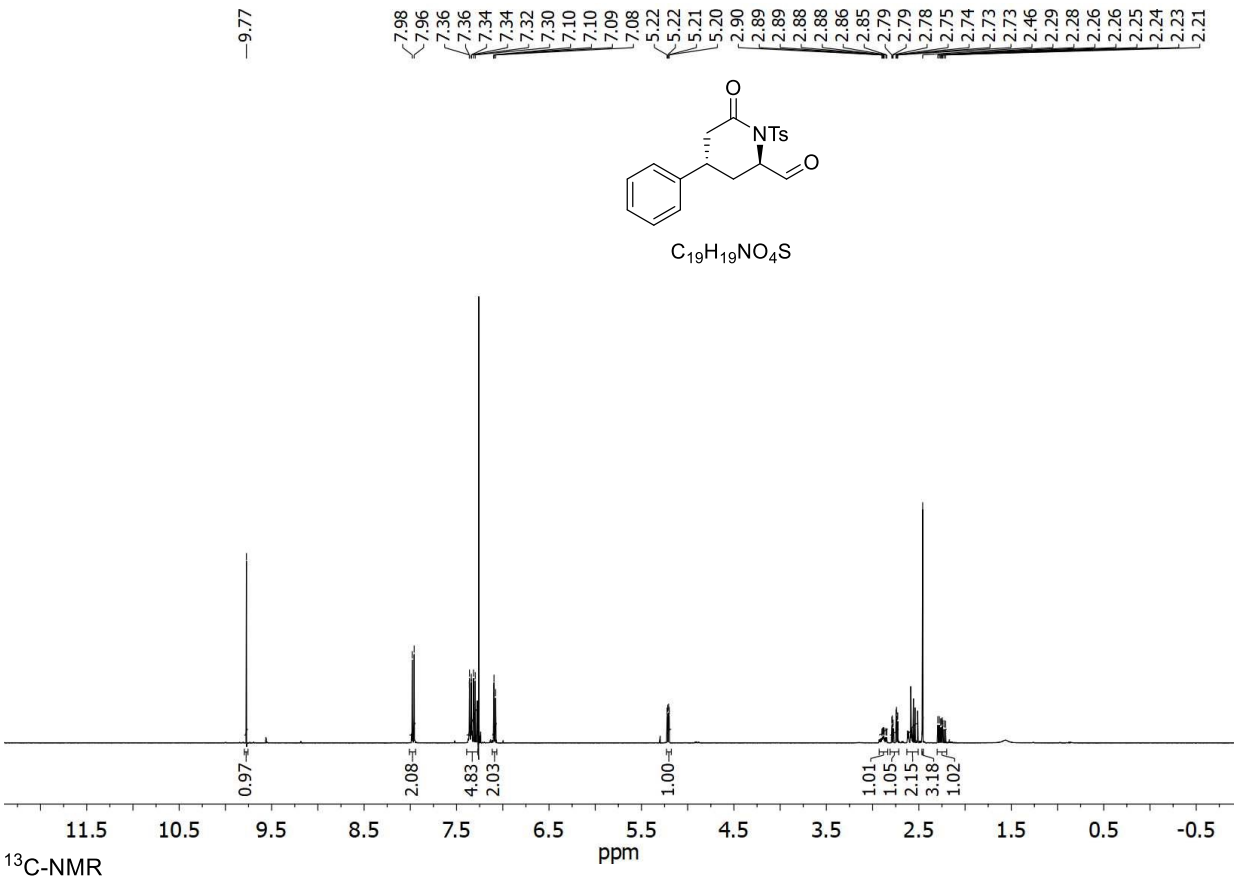
$C_{15}H_{19}NO_3S$

^{13}C-NMR

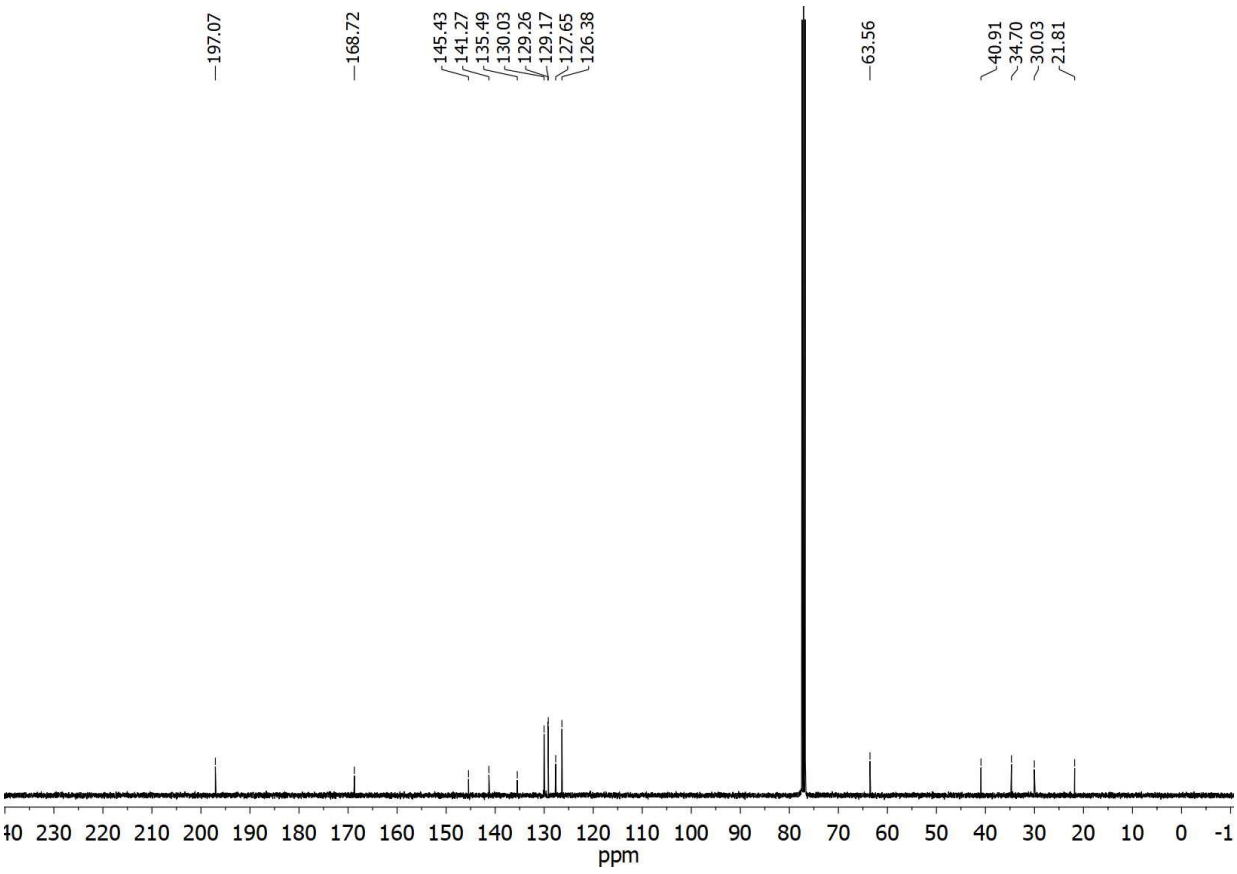


6-oxo-4-phenyl-1-tosylpiperidine-2-carbaldehyde 18

^{1}H-NMR

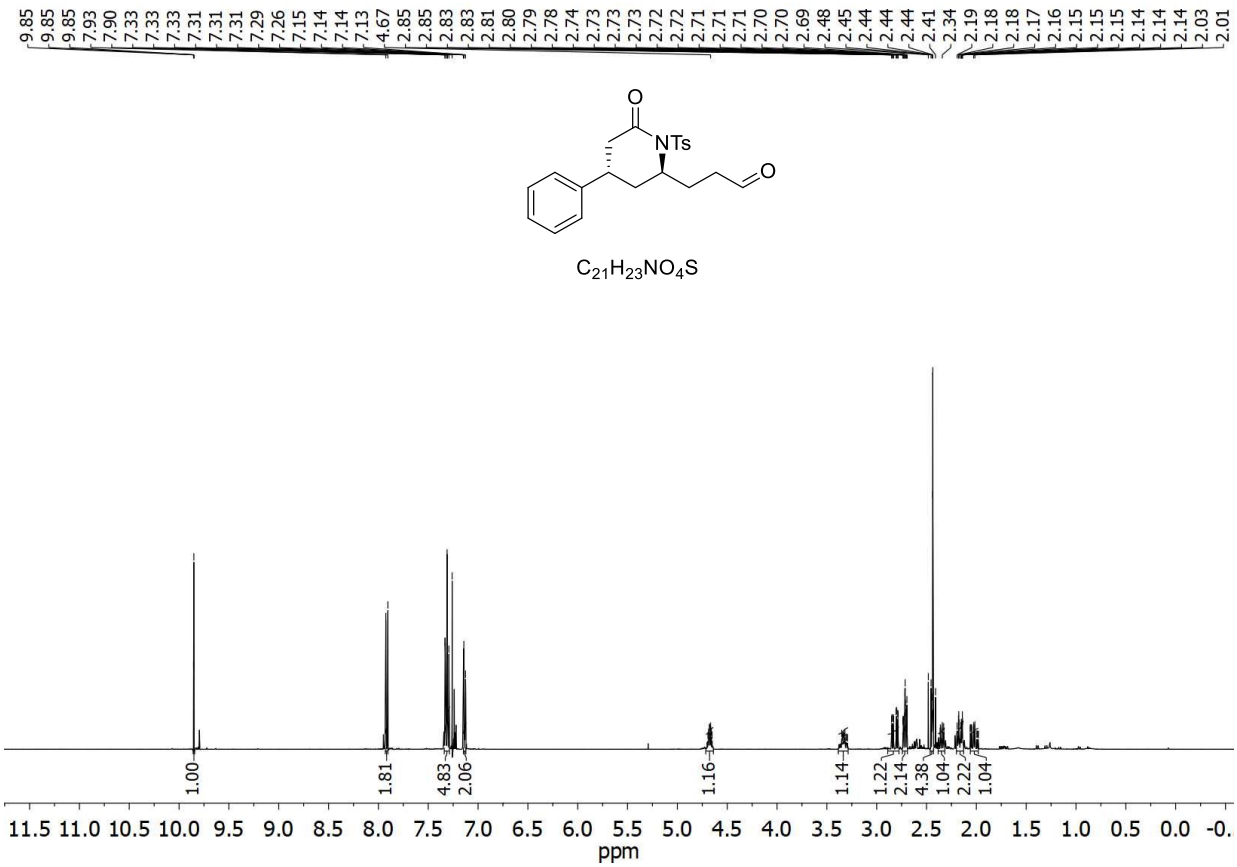


^{13}C-NMR



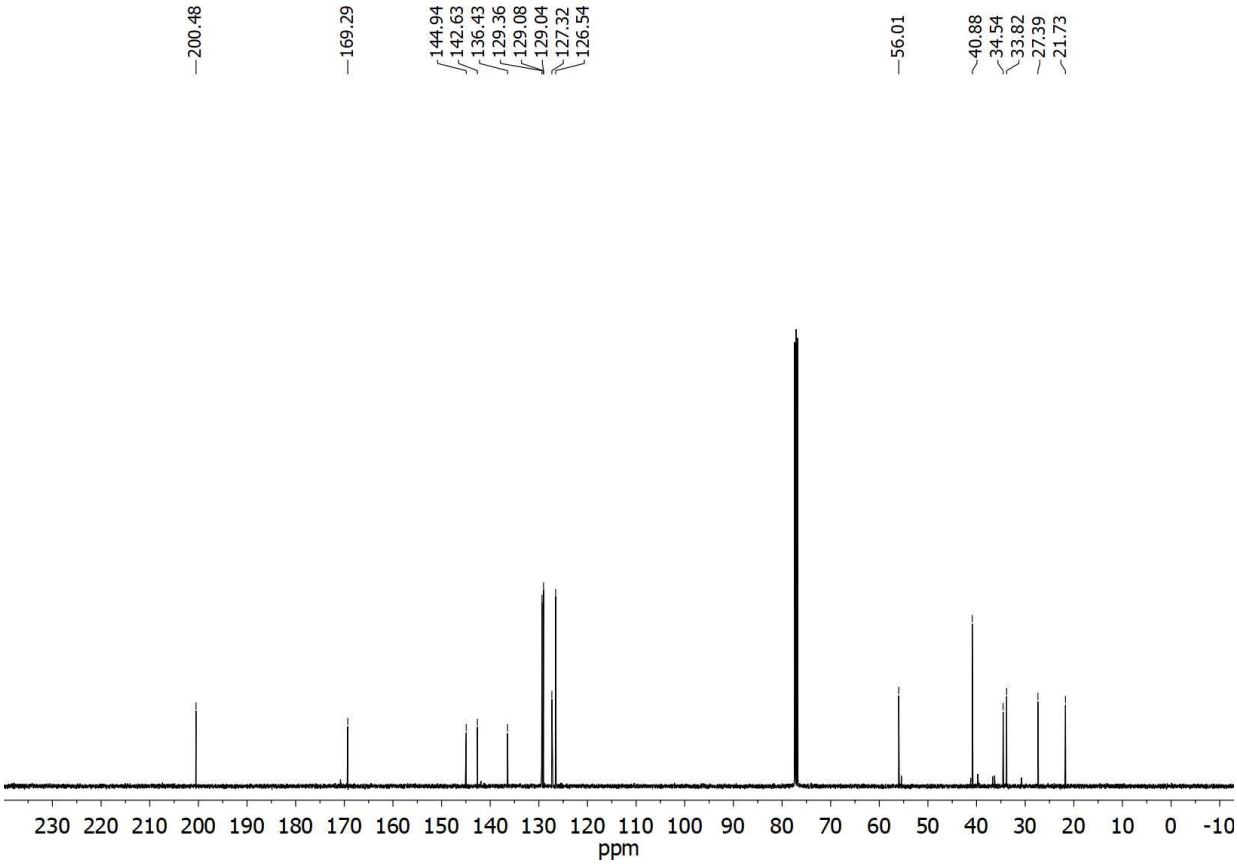
3-6-oxo-4-phenyl-1-tosylpiperidin-2-yl)propanal 19

^{1}H-NMR



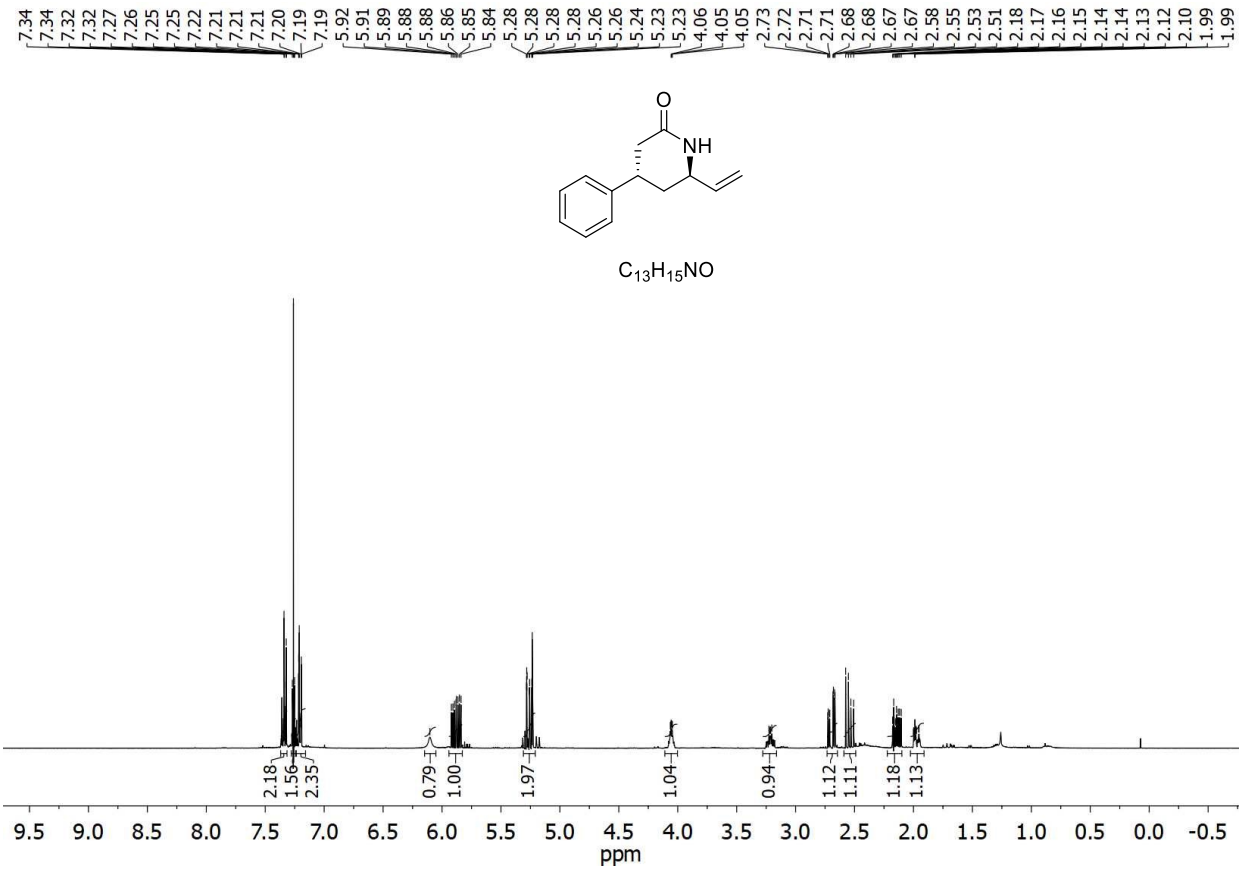
$C_{21}H_{23}NO_4S$

^{13}C-NMR



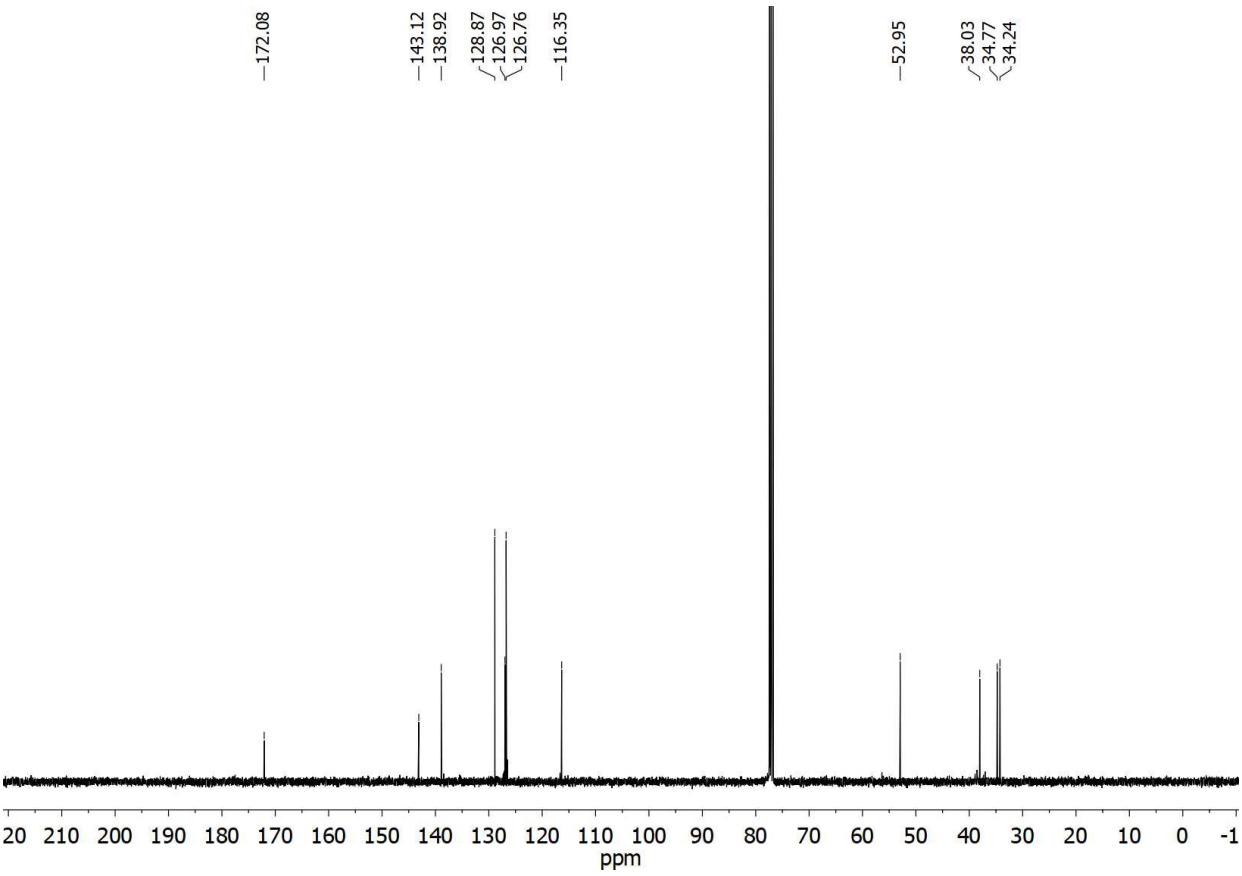
4-phenyl-6-vinylpiperidin-2-one 20

^{1}H-NMR



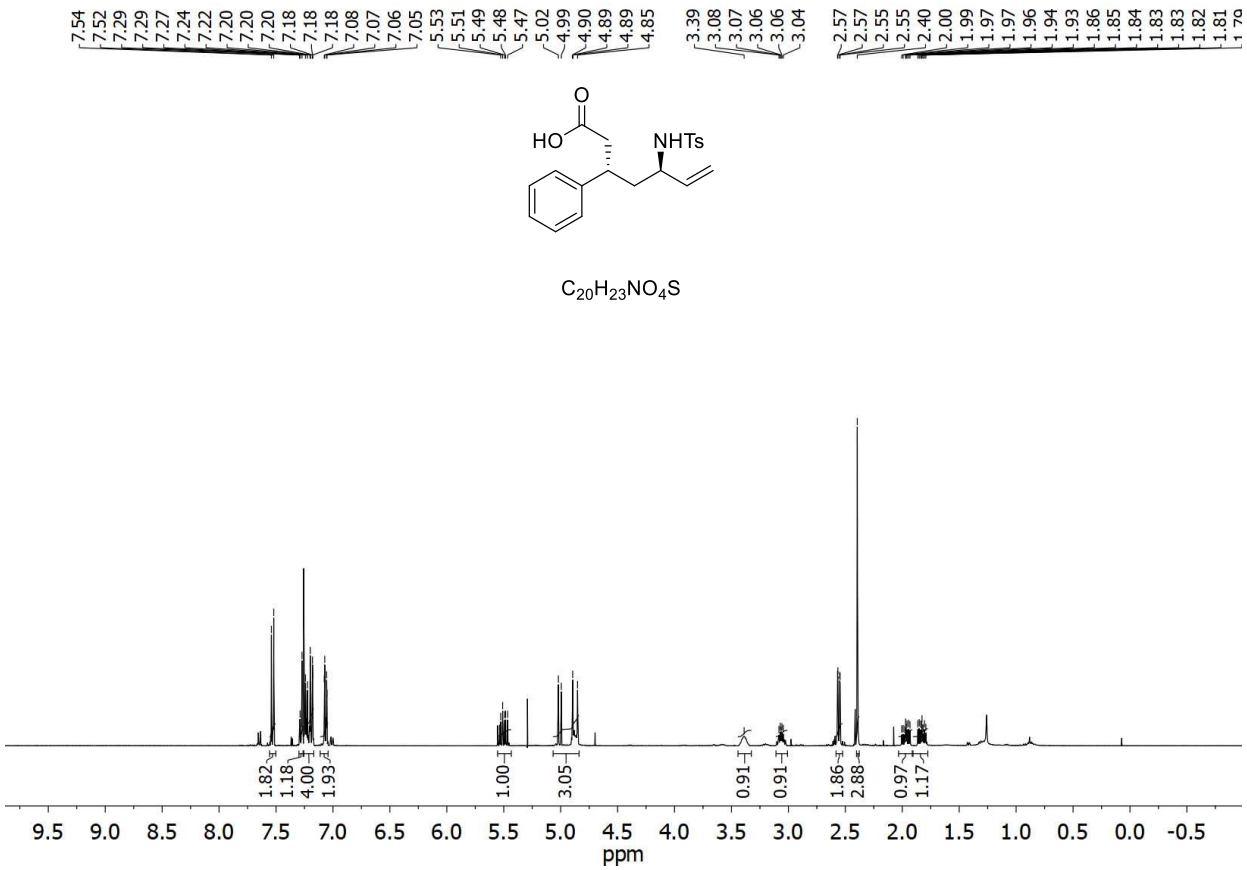
$C_{13}H_{15}NO$

^{13}C-NMR



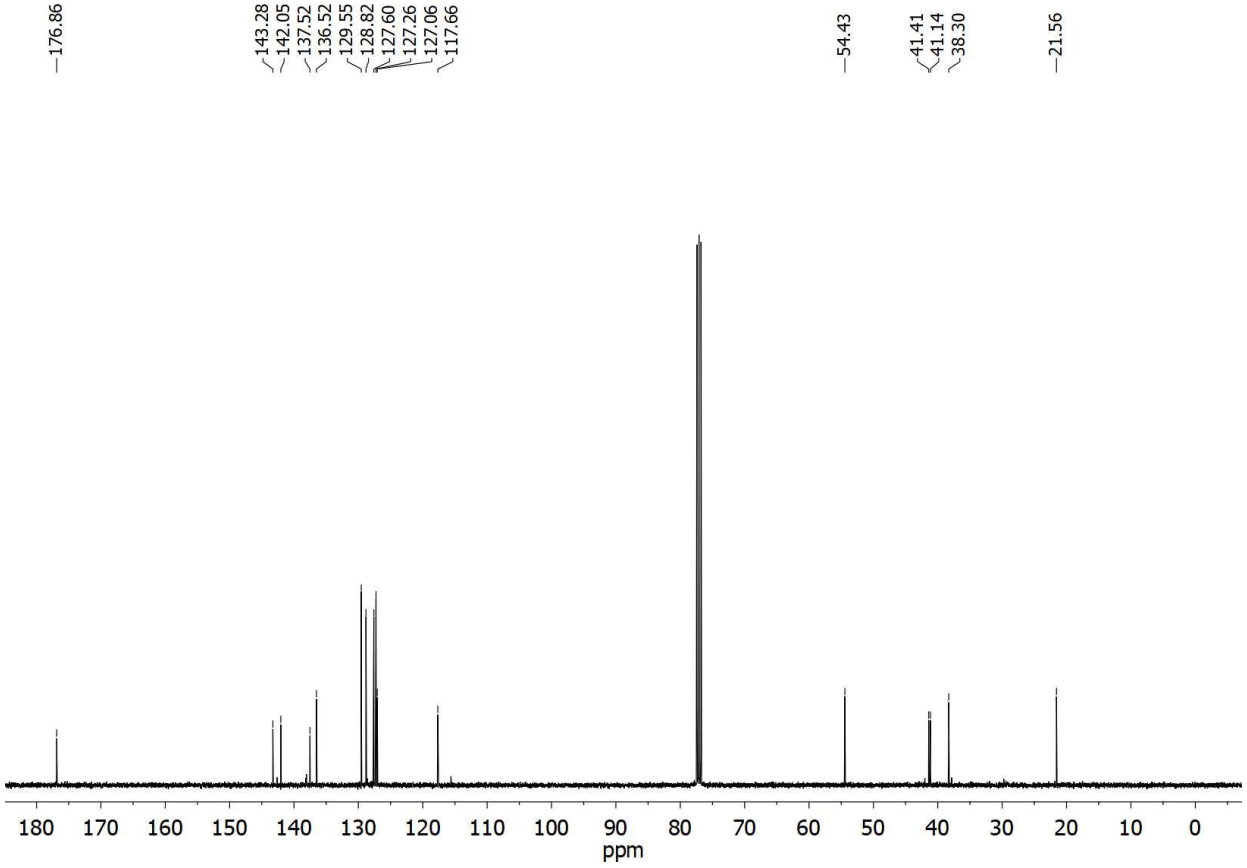
5-((4-methylphenyl)sulfonamido)-3-phenylhept-6-enoic acid 21

^{1}H-NMR



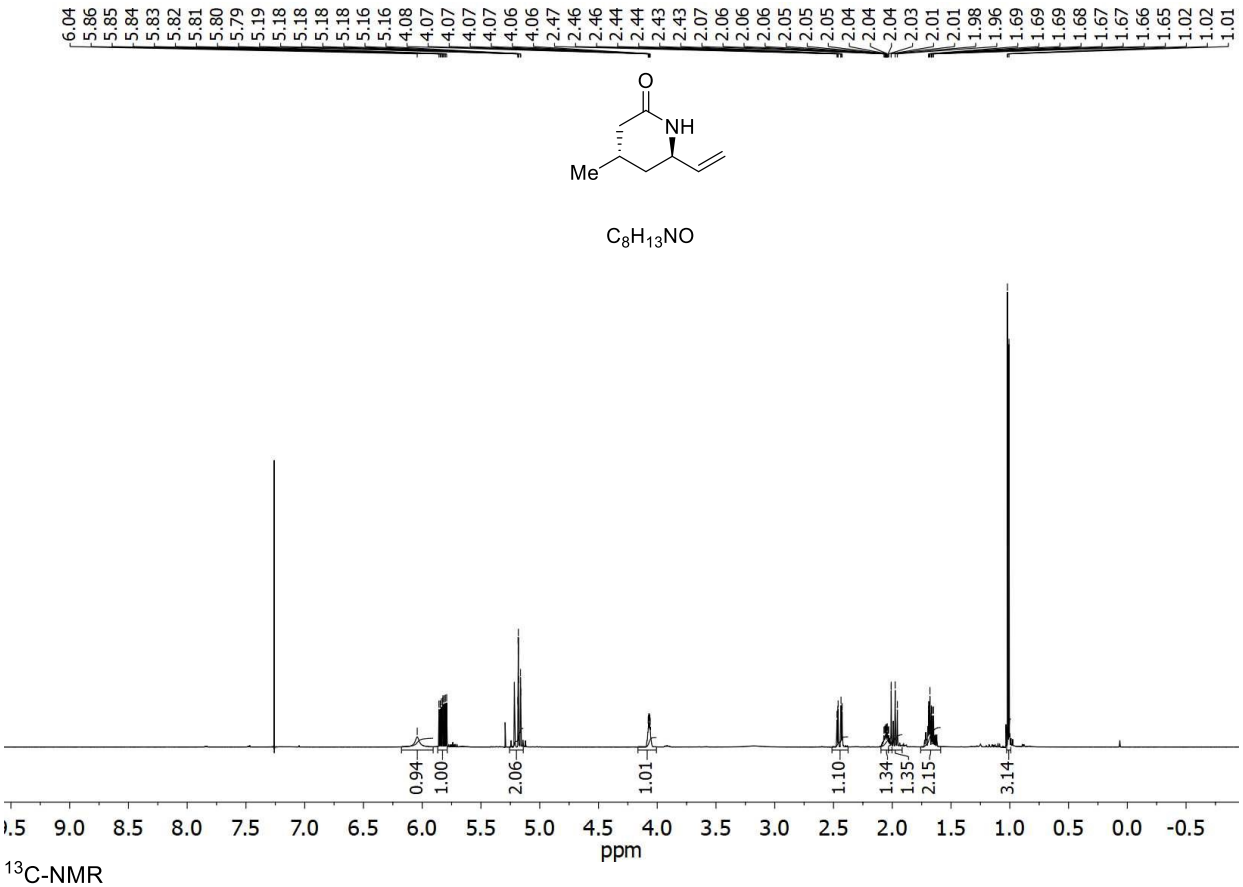
$C_{20}H_{23}NO_4S$

^{13}C-NMR



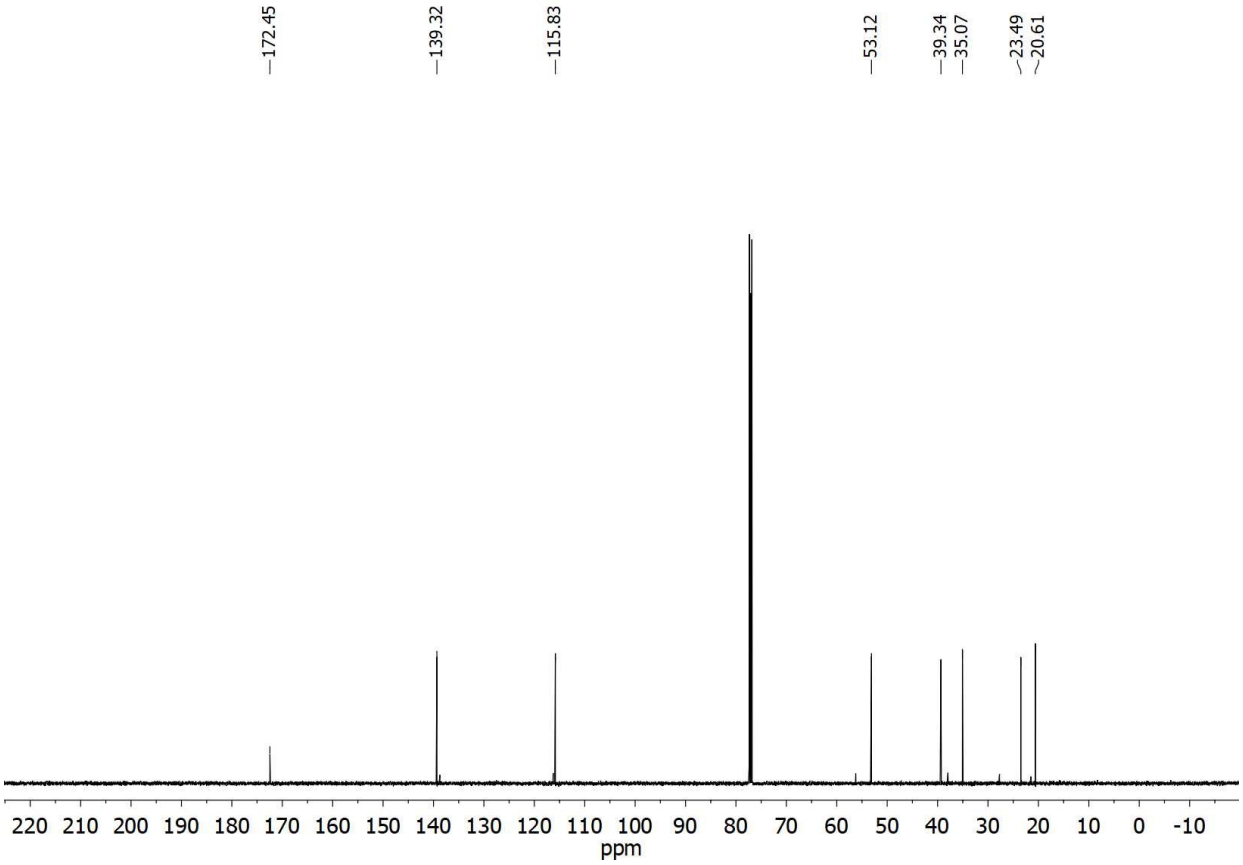
(S,R)-4-methyl-6-vinylpiperidin-2-one 23

^{1}H-NMR



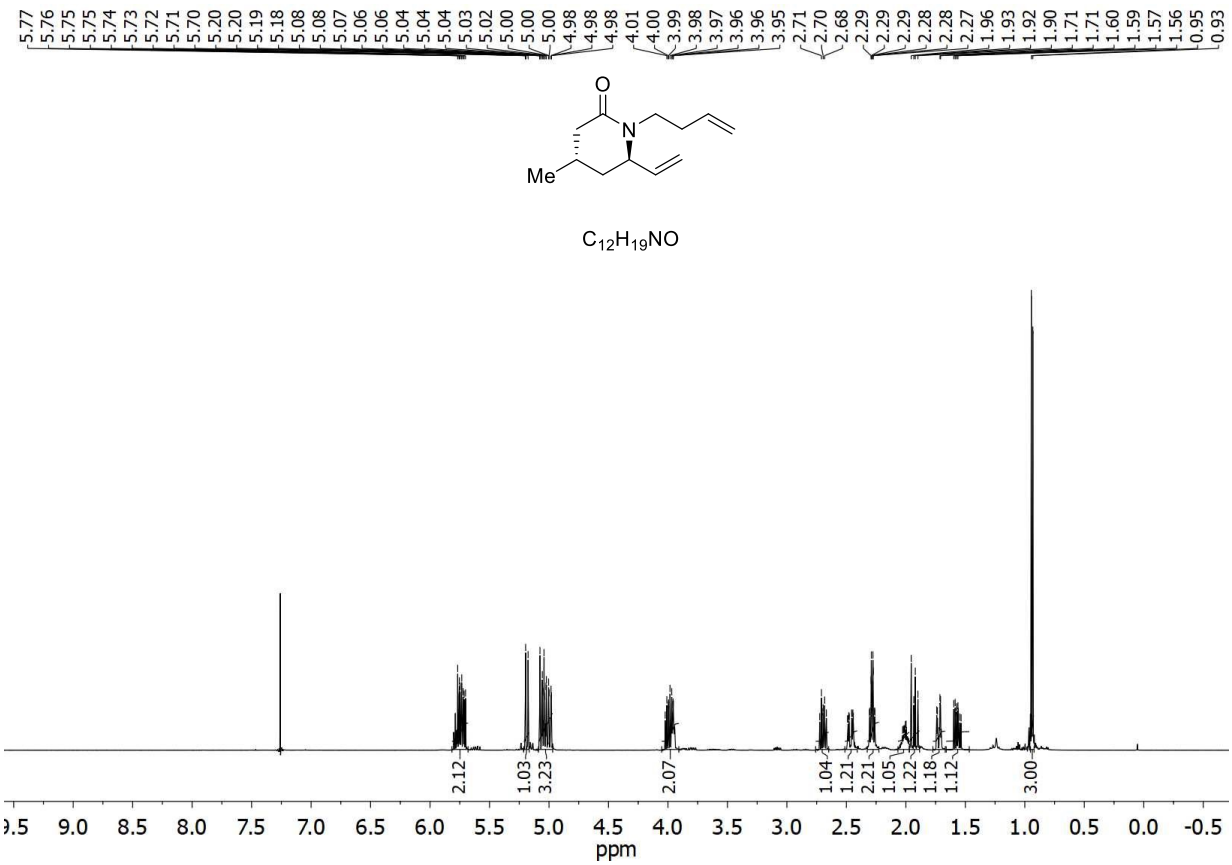
$C_8H_{13}NO$

^{13}C-NMR



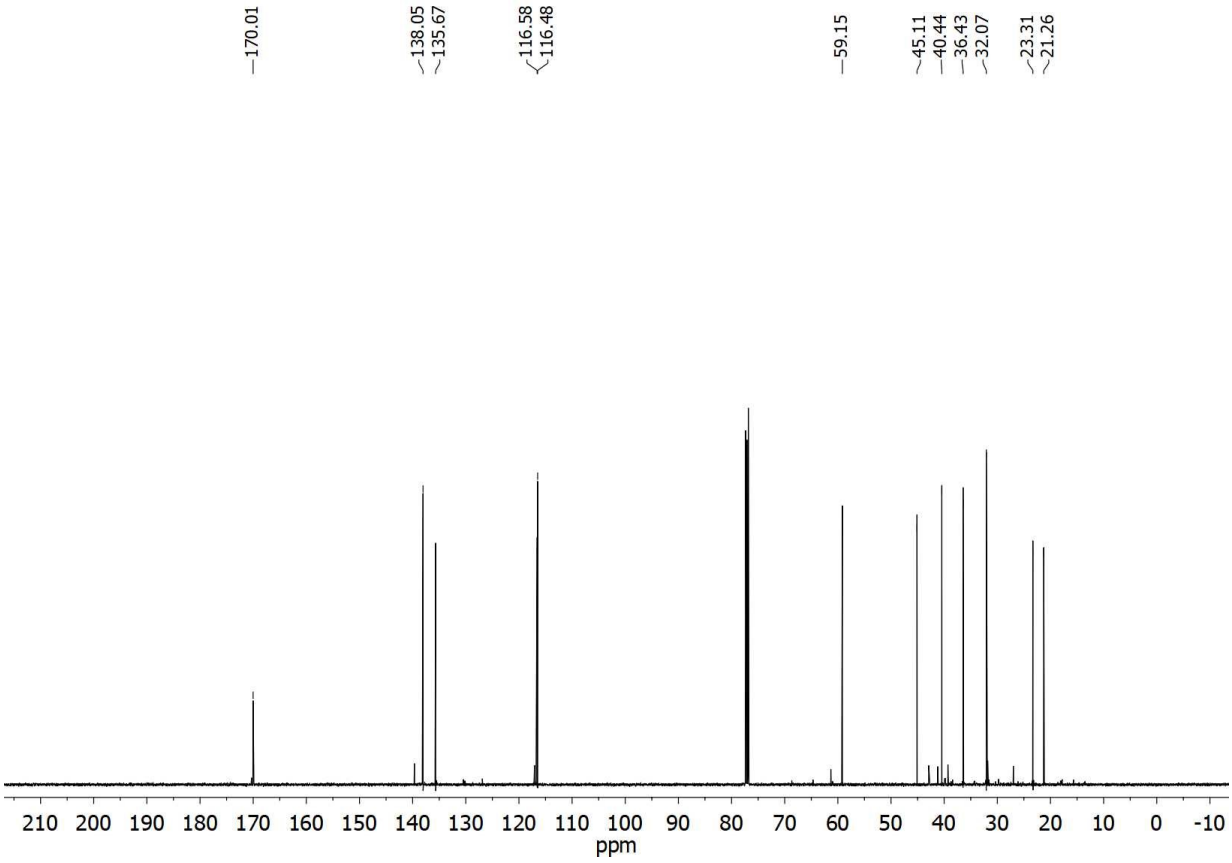
(*S*,*R*)-1-(but-3-en-1-yl)-4-methyl-6-vinylpiperidin-2-one 24

^{1}H-NMR



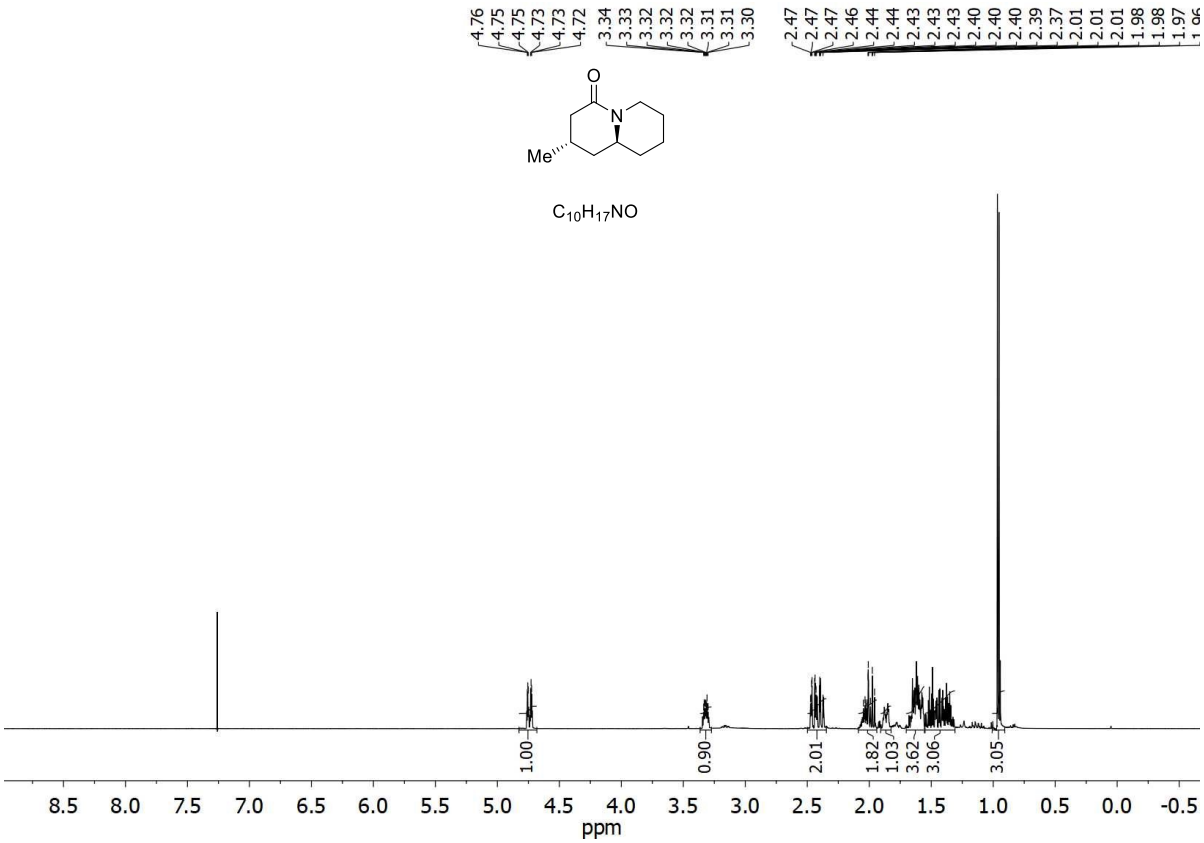
$C_{12}H_{19}NO$

^{13}C-NMR

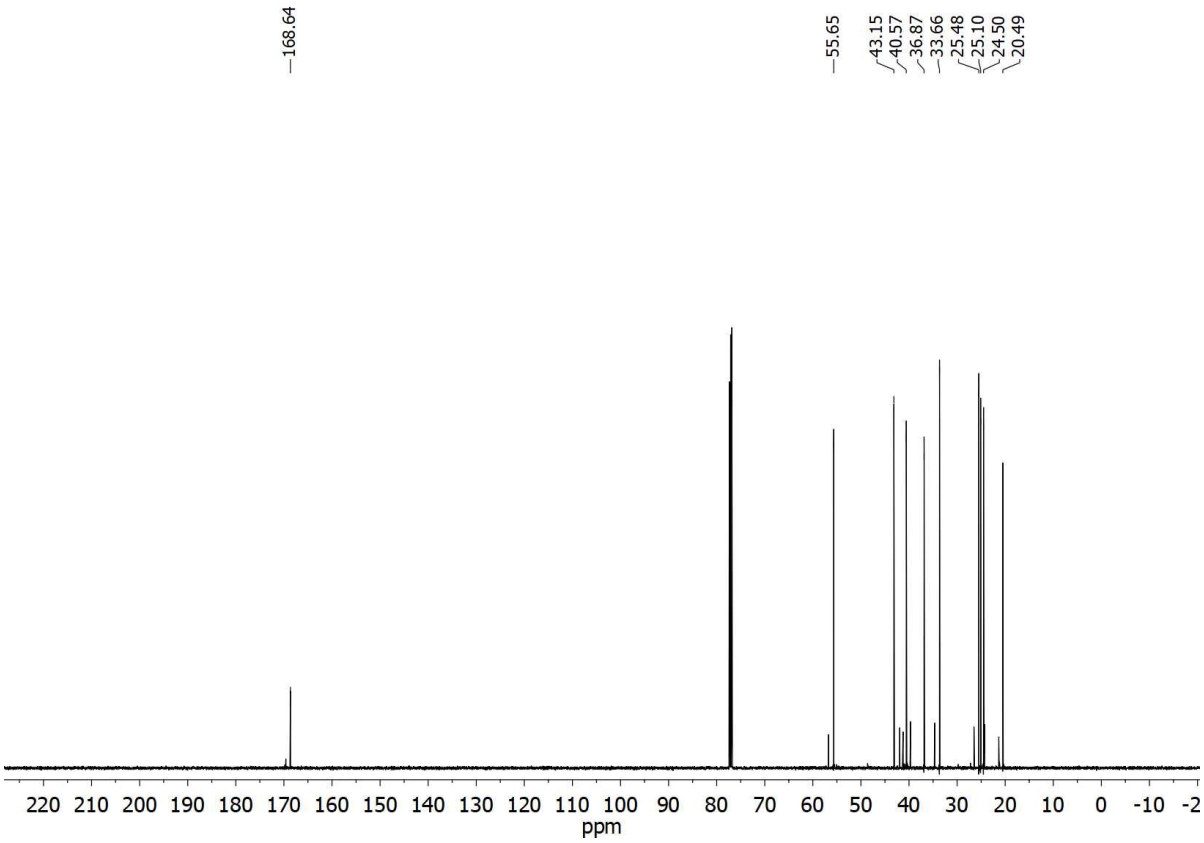


(*S*,*S*)-2-methyloctahydro-4H-quinolizin-4-one 25

^{1}H-NMR

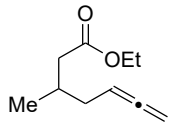


^{13}C-NMR

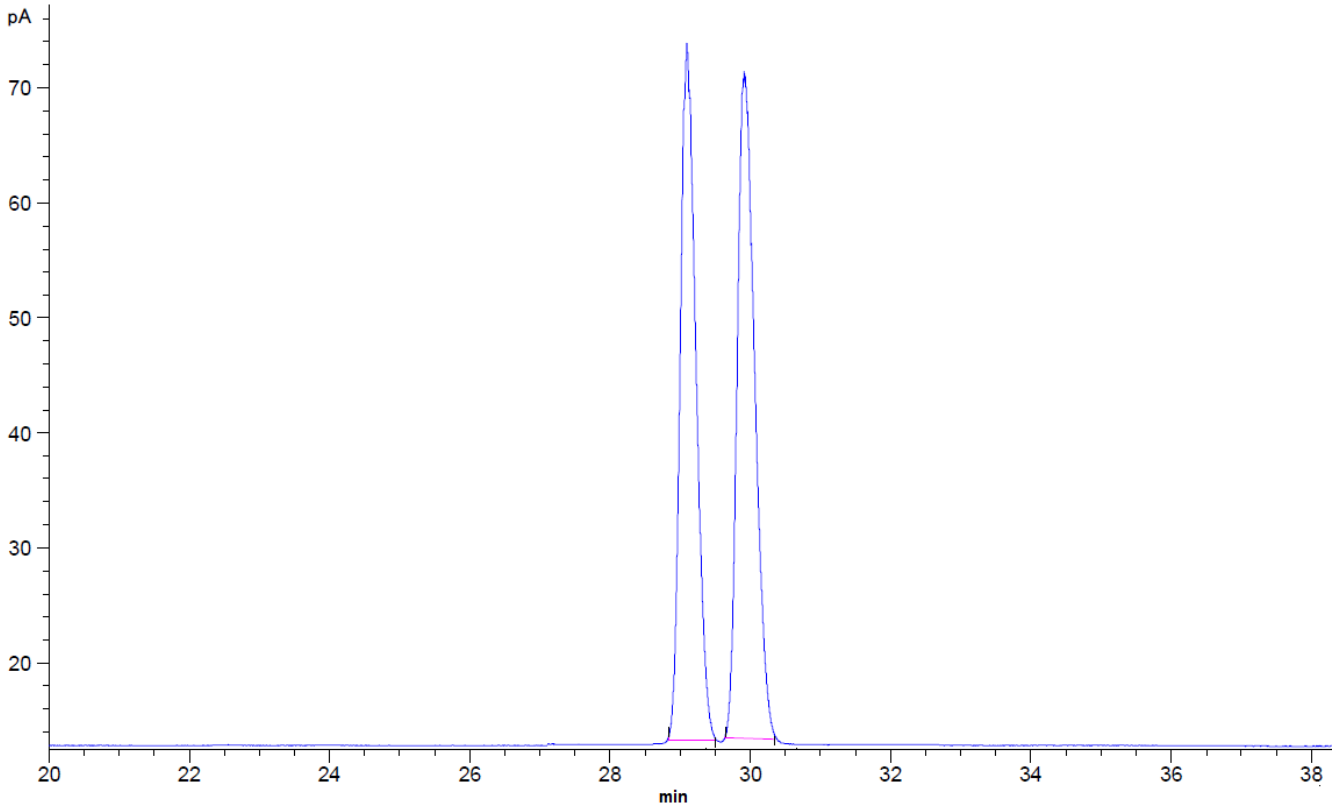


HPLC and GC-Results

GC – analysis of 3-methylhepta-5,6-dienoate

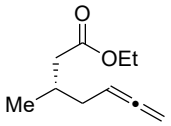


$C_{10}H_{16}O_2$
168.24

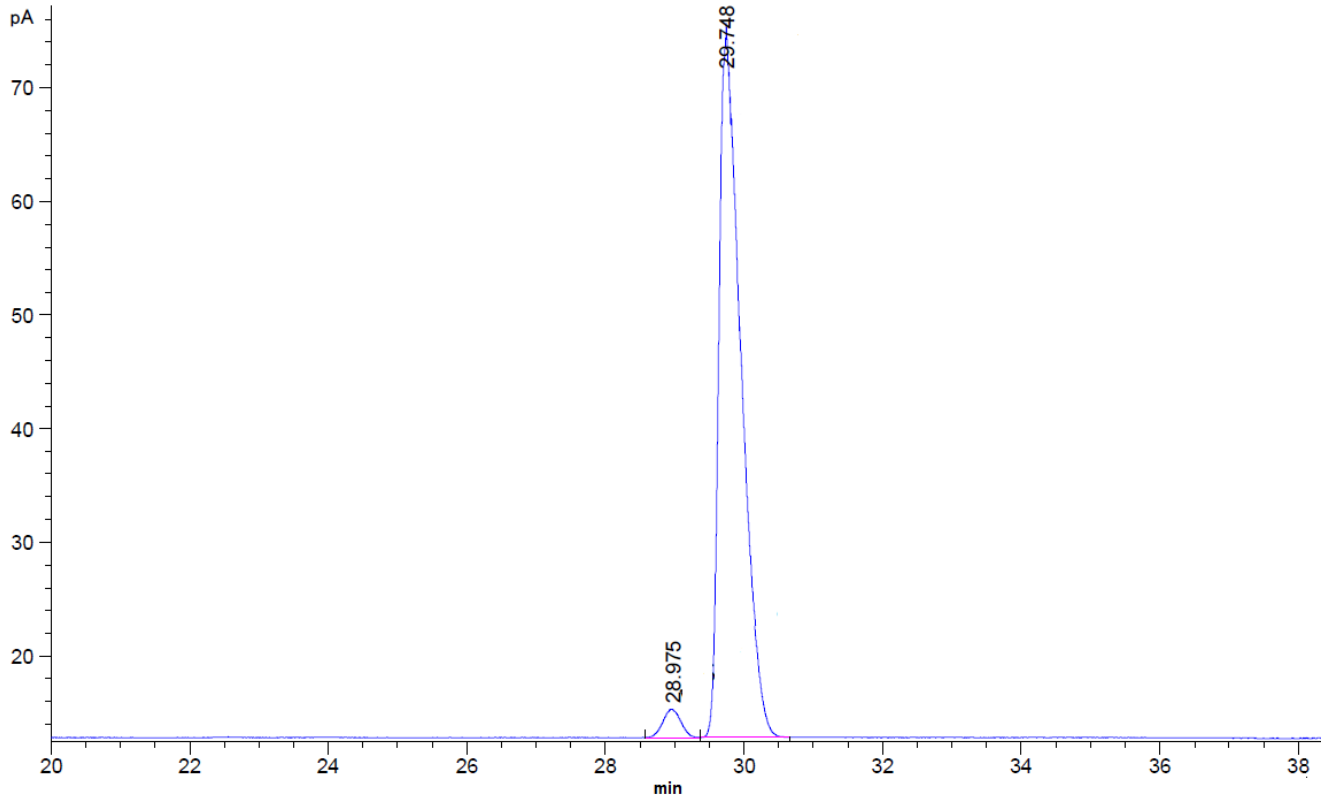


Peak Index	t [min]	Area [%]
1	29.005	49.17
2	30.048	50.83

GC – analysis of (S)-3-methylhepta-5,6-dienoate



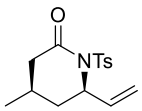
$C_{10}H_{16}O_2$
168.24



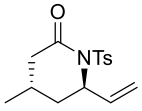
Peak Index	t [min]	Area [%]
1	28.975	3.17
2	29.748	96.83

HPLC- analysis of rac-4-methyl-1-tosyl-6-vinylpiperidin-2-one

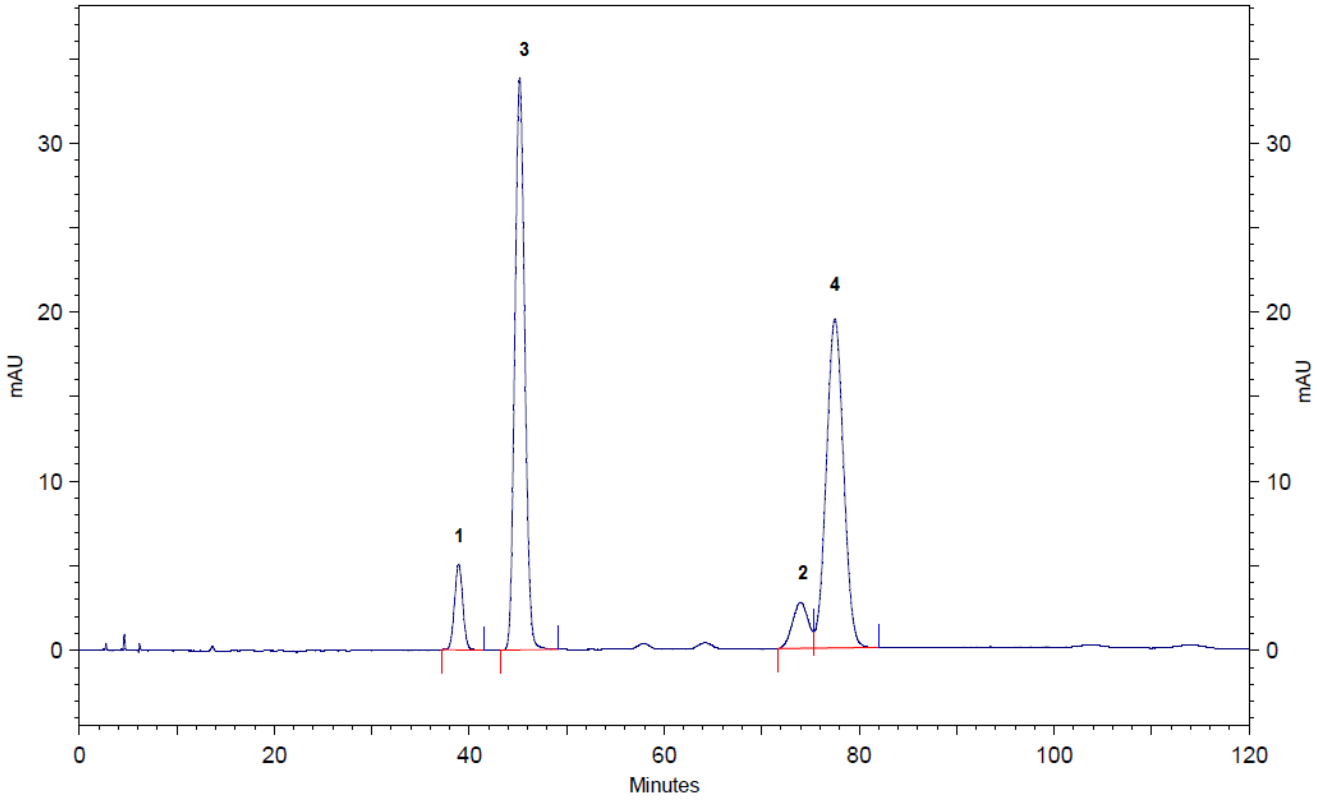
HPLC – Result of racemic mixture of *syn* and *anti* 4-methyl-1-tosyl-6-vinylpiperidin-2-one 3a/3b



$C_{15}H_{19}NO_3S$
(Peak Index 1 and 2)

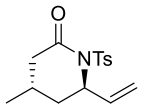


$C_{15}H_{19}NO_3S$
(Peak Index 3 and 4)

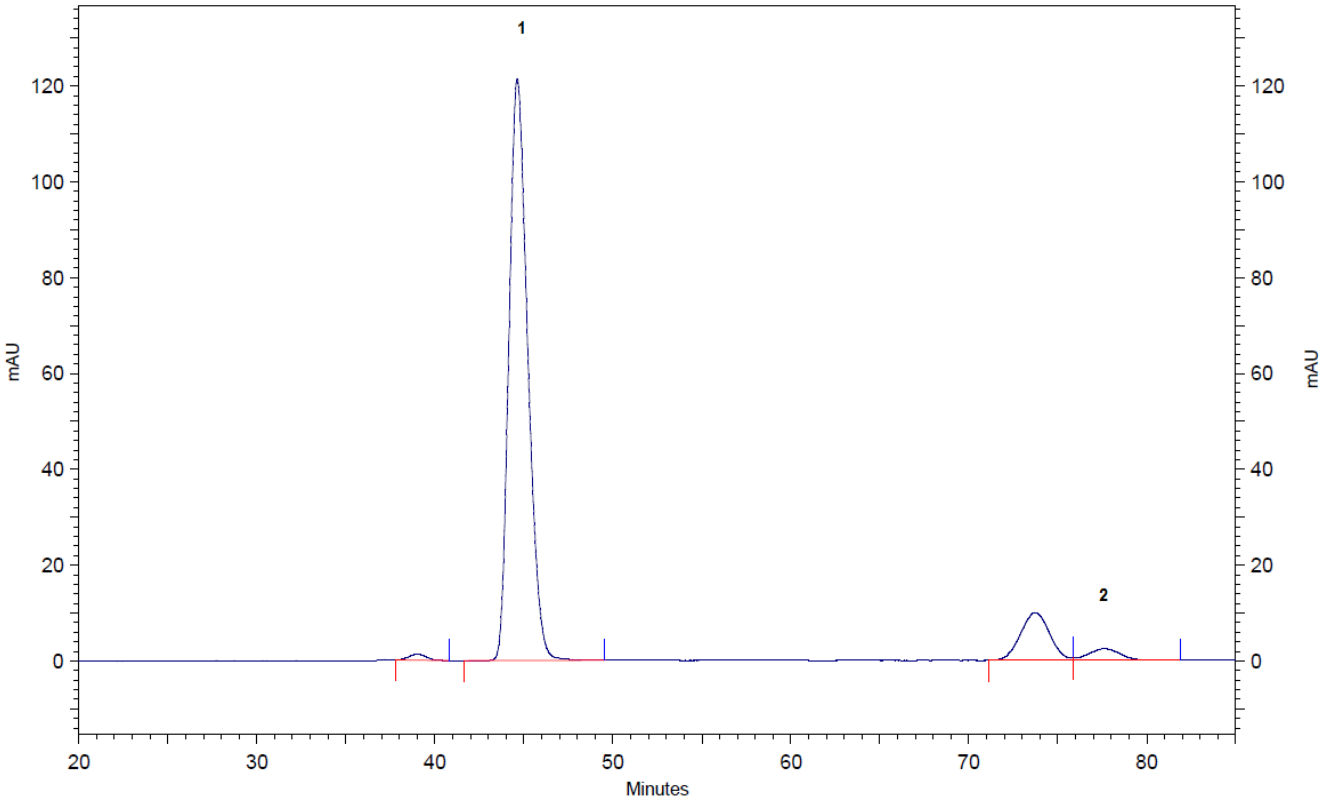


Peak Index	t [min]	Area [%]
1	38.91	5.62
2	73.98	5.60
3	45.17	44.33
4	77.51	44.45

HPLC – result of (4S,6R)-4-methyl-1-tosyl-6-vinylpiperidin-2-one 3b

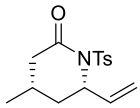


$C_{15}H_{19}NO_3S$

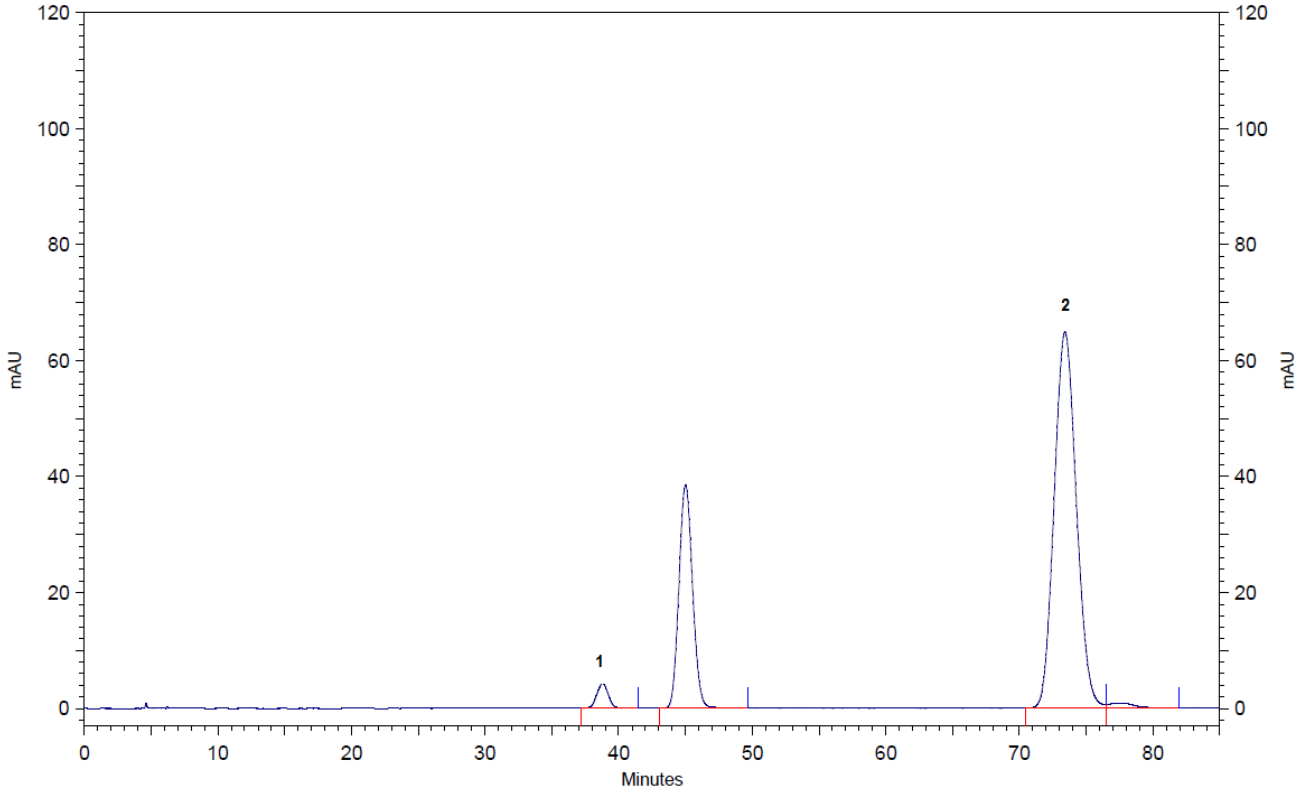


Peak Index	t [min]	Area [%]
1	44.63	96,92
2	77.62	3.08

HPLC – result of (4S,6R)-4-methyl-1-tosyl-6-vinylpiperidin-2-one 3b



$C_{15}H_{19}NO_3S$



Peak Index	t [min]	Area [%]
1	44.63	96,82
2	77.62	3.18

References

[1] P. Spreider, A. Haydl, M. Heinrich, B. Breit *Angew. Chem.* **2016**, *128,* 15798-15802; *Angew. Chem. Int. Ed.* **2015**, *55*, 15569-15573.

[2] M. W. Grafton, L. J. Farrugia, A. Sutherland, *J. Org. Chem.* **2013**, *78*, 7199 - 7207

[3] Separation of both diastereomers by column chromatography was not possible; Overlapping signals were discussed as multiplet.

[4] Separation by HPLC was not possible

[5] J. Scharfbier, M. Oestreich, *Synlett* **2016**, *27*, 1274-1276]

[6] B. B. Snider, J. F. Grabowski**,** *J. Org. Chem*. **2007**, *72*, 1039 – 1042.

[7] Gaussian 09, Revision B.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, T. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski; D. J. Fox, *Gaussian, Inc., Wallingford CT*, **2010**.