Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

Synthesis and Hetero-Diels–Alder Reactions of Enantiomerically Pure Dihydro-1*H*-azepines

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Contents

General Experimental

Non-aqueous reactions were carried out in oven-dried glassware under an inert atmosphere of nitrogen unless otherwise stated.

Dichloromethane, diethyl ether, dimethylformamide, ethyl acetate, methanol, tetrahydrofuran and toluene were obtained by filtration through activated alumina columns. Bromoform and chloroform were washed with water, dried with calcium carbonate and distilled prior to use. *N*,*N*-diisopropylethylamine and triethylamine were distilled from calcium hydride and stored over potassium hydroxide. Acetone was used as supplied. Petroleum ether refers to the fraction of petroleum ether boiling between 40 °C and 60 °C.

Thin-layer chromatography was performed on Merck Kieselgel 60 F_{254} 0.25 mm precoated aluminium plates. Product spots were visualised under UV light (λ_{max} = 254 nm) and/or by staining with potassium permanganate or vanillin.

Column chromatography was performed using silica gel 60 (0.040 – 0.064 μm, Merck).

Infrared spectra were measured as neat samples on a Perkin-Elmer Spectrum RX FT-IR spectrometer. Absorption maxima (ν_{max}) are quoted in wavenumbers (cm^{-1}).

^{1}H NMR spectra were recorded on either a Bruker AV-400 (400 MHz) or Bruker AV-500 (500 MHz) spectrometer and reference relative to the residual non-deuterated solvent peak. Chemical shifts are reported in parts per million (ppm) with splittings reported as singlet (s), doublet (d), triplet (t), double of triplets (dt), double doublet of triplets (ddt), double doublet of quartets (ddq), heptet of doublets (heptd) or multiplet (m). Coupling constants (*J*) are measured in Hz and presented as observed. ^{13}C NMR spectra were recorded on either a Bruker AV-400 (101 MHz) or Bruker AV-500 (126 MHz) spectrometer and referenced relative to the residual non-deuterated solvent peak. Assignments of the ^{1}H and ^{13}C spectra were made by the analysis of δ/*J* values, COSY, DEPT-135, HSQC and HMBC as appropriate.

Mass spectra were recorded using Micromass AutoSpec Premier or Walters LCT Premier instruments under conditions of electrospray ionisation (ES), chemical ionisation (CI) or electron ionisation (EI).

Melting points were determined using a Stuart Scientific SMP1 melting point apparatus and are uncorrected.

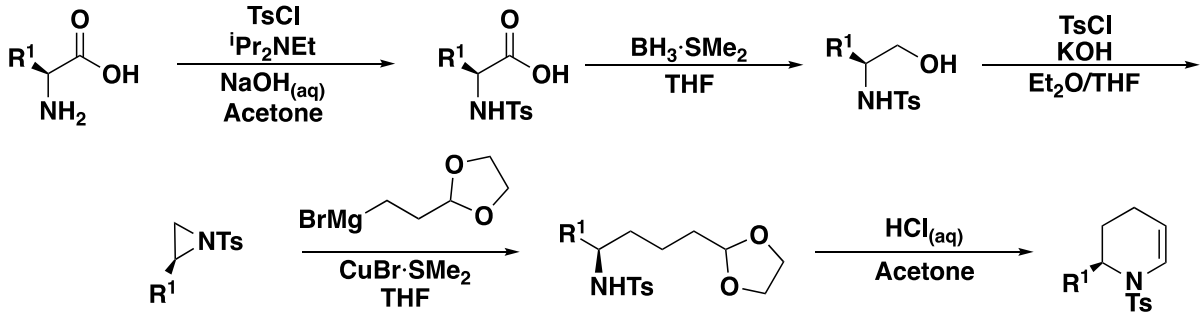
Optical rotatory powers were measured using a Bellingham+Stanley ADP410 Polarimeter.

Microwave reactions were performed using a Biotage Initiator EXP Microwave in sealed microwave vials purchased from Biotage.

Commercial reagents were used as supplied or purified by standard techniques where necessary.

Synthetic Procedures and Characterisation data

Tetrahydropyridines **1a-g** were synthesised following literature procedures reported by Craig *et al.*[1] and Harrity *et al.*[2] from naturally occurring L-amino acids. Exemplar procedures are herein reported:



Tosylation of amino acids

$NaOH_{(aq)}$ (2.00 M, 1.00 equiv.) and *N*,*N*-diisopropylethylamine (1.05 equiv.) was added to a stirring solution of amino acid (1.00 equiv.) and tosyl chloride (1.05 equiv.) in acetone (0.50 mL/mmol) at 0 °C. The reaction mixture was warmed to r.t and stirred for 16 h. The solution was extracted thrice with Et_2O and the collected organic layers were washed with an $NaOH_{(aq)}$ (2.00 M). The aqueous layers were acidified to pH 1 with concentrated hydrochloric acid (37%) and extracted thrice with EtOAc. The combined organic layers were washed with brine, dried (Na_2SO_4), filtered and concentrated under reduced pressure.

Reduction of tosyl-amino acids

Borane dimethylsulfide (3.0 equiv.) was added dropwise to a 0 °C solution of tosylated amino acid (1.0 equiv.) in THF (0.66 mL/mmol). Upon complete addition, the reaction mixture was stirred at 0 °C for 10 min before being warmed to r.t and stirred for 16 h. The reaction was quenched at 0 °C by the dropwise addition of $NaOH_{(aq)}$ (0.66 mL/mmol, 2.0 M) and upon complete addition, the mixture was warmed to r.t and

stirred for 3 h. The organic layer was separated and the aqueous layer was extracted four times with EtOAc. The combined organic layers were washed with brine, dried (Na_2SO_4), filtered and concentrated under reduced pressure. Purification by flash column chromatography was employed where appropriate.

Aziridine Formation

A solution of amino alcohol (1.0 equiv.), tosyl chloride (1.3 equiv.) and freshly ground KOH (4.0 equiv.) in 1:1 THF:Et_2O (5.0 mL/mmol) was heated to reflux for 3 h. The reaction mixture was then cooled to r.t and diluted with water. The organic layer was separated and the aqueous layer was extracted thrice with EtOAc. The combined organic layers were washed with brine, dried (Na_2SO_4), filtered and concentrated under reduced pressure. Purification by flash column chromatography was employed where appropriate.

Aziridine Ring Opening

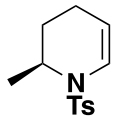
A solution of 2-(2-bromoethyl)-1,3-dioxolane (2.0 equiv.), magnesium turnings (4.0 equiv.) in THF (2.0 mL/mmol) was chilled to 0 °C and a single iodine crystal added to the mixture. The solution was stirred at this temperature for 30 min then warmed to r.t and stirred for 30 min. The solution was then cooled to –78 °C and copper bromide dimethyl-sulfide complex (0.20 equiv.) was added to the reaction mixture. After 1 h, a solution of aziridine (1.0 equiv.) in THF (1.0 mL/mmol) was added dropwise to the reaction mixture and stirred at –78 °C for 20 min before being warmed to r.t and stirred for 16 h. Water (1.0 mL) was added to the black solution, which was immediately filtered through celite®, washing with EtOAc. The filtrate was washed with water and this aqueous layer was extracted thrice with EtOAc. The combined organic layers were washed with brine, dried (Na_2SO_4), filtered and concentrated. Purification by flash column chromatography was employed where appropriate.

Deprotection/Cyclisation of sulfonamido-dioxolanes

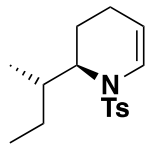
To 0 °C cooled solution of sulfonamide-dioxolane (1.0 equiv.) in acetone (20 mL/mmol) was added $HCl_{(aq)}$ (8.0 equiv., 1.00 M). The solution was stirred at this temperature for 10 min before being warmed to r.t and stirred for 16 h. The reaction mixture was neutralised by the addition of $K_2CO_{3(aq)}$ (8.0 equiv., 1.00 M), and the resultant solution was extracted thrice with EtOAc. The combined organic layers were washed with

brine, dried (Na_2SO_4), filtered and concentrated. Purification by flash column chromatography was employed where appropriate.

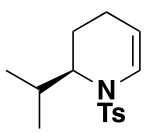
Characterisation data for Tetrahydropyridines **1a-g**:



(*S*)-2-Methyl-1-tosyl-1,2,3,4-tetrahydropyridine (1a): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO_2), 7.29 (d, *J* = 8.0 Hz, 2H, 2 × *meta*-SO_2), 6.62 (ddt, *J* = 8.3, 2.4, 1.5 Hz, 1H, NC*H*=), 4.99 (ddt, *J* = 8.5, 5.4, 1.7 Hz, 1H, NCHC*H*), 4.10 (dt, *J* = 6.7, 3.5 Hz, 1H, C*H*CH_3), 2.41 (s, 3H, Ar-CH_3), 2.10 – 1.91 (m, 1H, 1 × NCHCHC*H*$_2$), 1.90 – 1.74 (m, 1H, 1 × NCHCHC*H*2), 1.49 – 1.36 (m, 1H, 1 × NCHC*H*$_2$), 1.16 (d, *J* = 6.7 Hz, 3H, CHC*H*$_3$), 1.08 (tt, dt, *J* = 13.0, 5.1 Hz,1H, 1 × NCHC*H*$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.2 (*para*-SO_2), 136.4 (*ipso*-SO_2), 129.6 (2 × *meta*-SO_2), 126.8 (2 × *ortho*-SO_2), 123.2 (N*C*HCH), 107.6 (NCH*C*H), 48.5 (*C*HCH_3), 25.2 (NCH*C*H$_2$), 21.5 (Ar-CH_3), 18.2 (CH*C*H$_3$), 16.9 (NCHCH*C*H$_2$). ν_{max} 3065, 2973, 1645, 1597, 1338, 1163, 1099 cm^{-1}. m/z (ES+) (Found: $[M+H]^+$, 252.1053. $C_{13}H_{17}NO_2S$ requires $[M+H]^+$, 252.1058). $[\alpha]_D^{29}$ +270 (c 0.55 g/100 mL, $CHCl_3$). Data were in agreement with those previously reported.[2]

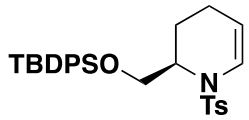


(*R*)-2-((*S*)-*sec*-Butyl)-1-tosyl-1,2,3,4-tetrahydropyridine (1b): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO_2), 7.28 (d, *J* = 7.9 Hz, 2H, 2 × *meta*-SO_2), 6.57 – 6.53 (m, 1H, NCH=), 5.09 (ddt, *J* = 8.3, 5.1, 1.8 Hz, 1H, NCH=C*H*), 3.57 (dt, *J* = 10.8, 3.3 Hz, 1H, NC*H*CH_2), 2.41 (s, 3H, Ar-CH_3), 1.86 (m, 2H, 1 × NCHCH$_2$C*H*$_2$ and 1 × C*H*$_2$CH$_3$), 1.75 – 1.60 (m, 2H, 1 × NCHCH$_2$C*H*$_2$ and 1 × NCHC*H*$_2$), 1.56 – 1.45 (m, 1H, C*H*CH_3), 1.26 – 1.12 (m, 1H, 1 × C*H*$_2$CH$_3$), 0.91 (t, *J* = 7.4 Hz, 3H, CH$_2$C*H*$_3$), 0.83 (d, *J* = 6.7 Hz, 3H, CHC*H*$_3$), 0.76 – 0.61 (m, 1H, 1 × NCHC*H*$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.2 (*para*-SO_2), 136.0 (*ipso*-SO_2), 129.6 (2 × *meta*-SO_2), 127.1 (2 × *ortho*-SO_2), 124.1 (NCH=), 111.7 (NCH=*C*H), 57.8 (N*C*HCH$_2$), 33.9 (*C*HCH$_3$), 26.0 (*C*H$_2$CH$_3$), 21.5 (Ar-CH_3), 20.8 (NCH*C*H$_2$), 17.6 (NCHCH$_2$*C*H$_2$), 15.0 (CH*C*H$_3$), 11.6 (CH$_2$*C*H$_3$). ν_{max} 2952, 1490, 1360, 1156, 1036 cm^{-1}. m/z (ES+) (Found: $[M+H]^+$, 294.1520. $C_{16}H_{23}NO_2S$ requires $[M+H]^+$, 294.1528). M.p. 75 – 76 °C. $[\alpha]_D^{24.9}$ +297 (c 2.55 g/100 mL, CH_2Cl_2).

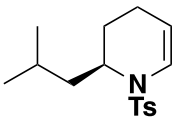


(*R*)-2-Isopropyl-1-tosyl-1,2,3,4-tetrahydropyridine (1c): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO_2), 7.28 (d, *J* = 8.0

Hz, 2H, 2 × *meta*-SO_2), 6.56 (dtd, *J* = 8.1, 2.0, 1.2 Hz, 1H, NC*H*=), 5.08 (ddt, *J* = 8.0, 5.0, 1.8 Hz, 1H, NCH=C*H*), 3.50 (dt, *J* = 10.8, 3.3 Hz, 1H, NC*H*CH_2), 2.41 (s, 3H, Ar-CH_3), 1.93 – 1.61 (m, 4H, C*H*(CH_3)$_2$, NCH=CHC*H*$_2$ and 1 × NCHC*H*$_2$), 1.09 (d, *J* = 6.6 Hz, 3H, 1 × CH(C*H*$_3$)$_2$), 0.88 (d, *J* = 6.7 Hz, 3H, 1 × CH(C*H*$_3$)$_2$), 0.76 – 0.64 (m, 1H, 1 × NCHC*H*$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.2 (*para*-SO_2), 136.2 (*ipso*-SO_2), 129.6 (2 × *meta*-SO_2), 127.1 (2 × *ortho*-SO_2), 124.0 (NCH=), 111.3 (NCH=*C*H), 59.1 (N*C*HCH_2), 27.6 (*C*H(CH_3)$_2$), 21.5 (Ar-CH_3), 20.8 (NCH*C*H_2), 20.5 (1 × CH(*C*H$_3$)$_2$), 19.0 (1 × CH(*C*H$_3$)$_2$), 17.6 (NCH=CH*C*H_2). ν_{max} 2968, 1642, 1595, 1397, 1336, 1249, 1166, 1090, 1007 cm^{-1}. m/z (EI+) (Found: [M]$^+$, 279.1306. $C_{15}H_{21}NO_2S$ requires [M]$^+$, 279.1293). M.p. 95 – 96 °C. $[\alpha]_D^{25.0}$ +403 (c 1.18 g/100 mL, CH_2Cl_2).

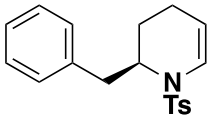


(*R*)-2-(((*tert*-Butyldiphenylsilyl)oxy)methyl)-1-tosyl-1,2,3,4-tetrahydropyridine (1d): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 – 7.59 (m, 6H, 2 × *ortho*-SO_2 and 4 × *ortho-meta*-SO_2), 6.55 (ddt, *J* = 8.4, 2.7, 1.3 Hz, 1H, NCH=), 4.94 – 4.87 (m, 1H, NCH=C*H*), 4.07 – 3.98 (m, 1H, NC*H*(CH_2)$_2$), 3.77 (dd, *J* = 10.1, 5.2 Hz, 1H, 1 × OCH_2), 3.56 (dd, *J* = 10.1, 9.9 Hz, 1H, 1 × OCH_2), 2.41 (s, 3H, Ar-CH_3), 2.04 – 1.96 (m, 1H, 1 × OCH_2CHC*H*$_2$), 1.81 – 1.67 (m, 2H, NCH=CHC*H*$_2$), 1.06 (s, 9H, C(CH_3)$_3$), 0.98 – 0.86 (dddd, *J* = 13.4, 11.4, 6.6, 4.3 Hz, 1H, 1 × OCH_2CHC*H*$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.3 (*para*-SO_2), 136.1 (*ipso*-SO_2), 135.6 (4 × *ortho*-Si), 133.4 (*ipso*-Si), 133.4 (*ipso*-Si), 129.7 (2 × *para*-Si), 129.6 (2 × *meta*-SO_2), 127.7 (2 × *meta*- Si), 127.7 (2 × *meta*-Si), 126.9 (2 × *ortho*-SO_2), 123.6 (NCH=), 108.4 (NCH=*C*H), 61.9 (OCH_2), 53.3 (N*C*H(CH_2)$_2$), 26.9 (C(*C*H$_3$)$_3$), 21.5 (Ar-CH_3), 19.4 (OCH_2CH*C*H_2), 19.2 (*C*(CH_3)$_3$), 16.8 (NCH=CH*C*H_2). ν_{max} 3070, 2930, 1648, 1597, 1472, 1428, 1360, 1347, 1265, 1167, 1103 cm^{-1}. m/z (ES+) (Found: [M+H]$^+$, 506.2174. $C_{29}H_{35}NO_3SSi$ requires [M+H]$^+$, 506.2185). $[\alpha]_D^{25.0}$ +53.7 (c 1.75 g/100 mL, CH_2Cl_2).

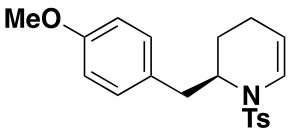


(*R*)-2-Isobutyl-1-tosyl-1,2,3,4-tetrahydropyridine (1e): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.2 Hz, 2H, 2 × *ortho*-SO_2), 7.27 (d, *J* = 7.7 Hz, 2H, 2 × *meta*-SO_2), 6.56 (dq, *J* = 8.2, 1.6 Hz, 1H, NCH=), 5.02 (ddt, *J* = 8.4, 5.3, 1.8 Hz, 1H, NCH=C*H*), 3.98 (dp, *J* = 9.6, 3.2 Hz, 1H, NC*H*(CH_2)), 2.40 (s, 3H, Ar-CH_3), 1.90 (dddt, *J* = 17.1, 12.7, 6.3, 2.3 Hz, 1H, 1 × NCH=CHC*H*$_2$), 1.81 – 1.65 (m, 2H, C*H*(CH_3)$_2$ and 1 × NCH=CHC*H*$_2$), 1.55 – 1.38 (m, 2H, 1 × C*H*$_2$(CH)$_2$ and

1 × NCH=CHCH$_2$C*H*$_2$), 1.15 (ddd, *J* = 13.8, 7.4, 6.4 Hz, 1H, 1 × C*H*$_2$(CH)$_2$), 0.95 (d, *J* = 6.5 Hz, 3H, 1 × CH(*C*H$_3$)$_2$), 0.90 (d, *J* = 6.6 Hz, 3H, 1 × CH(*C*H$_3$)$_2$), 0.89 – 0.81 (m, 1H, 1 × NCH=CHCH$_2$C*H*$_2$). ^{13}C NMR (101 MHz, CDCl$_3$) δ 143.2 (*para*-SO$_2$), 136.1 (*ipso*-SO$_2$), 129.5 (2 × *meta*-SO$_2$), 126.9 (2 × *ortho*-SO$_2$), 123.6 (NCH=), 109.5 (NCH=*C*H), 51.0 (N*C*H(CH$_2$)$_2$), 40.5 (*C*H$_2$(CH)$_2$), 24.0 (*C*H(CH$_3$)$_2$), 23.0 (NCH=CHCH$_2$*C*H$_2$), 22.6 (1 × CH(*C*H$_3$)$_2$), 22.5 (1 × CH(*C*H$_3$)$_2$), 21.5 (Ar-CH$_3$), 17.2 (NCH=CH*C*H$_2$). ν_{max} 2951, 1641, 1595, 1463, 1335, 1257, 1163, 1092, 1037 cm^{-1}. m/z (ES+) (Found: [M+H]$^+$, 294.1530. C$_{16}$H$_{23}$NO$_2$S requires [M+H]$^+$, 294.1528). M.p. 78 – 79 °C. $[\alpha]_D^{25.0}$ +299 (c 1.29 g/100 mL, CH$_2$Cl$_2$).



(*R*)-2-Benzyl-1-tosyl-1,2,3,4-tetrahydropyridine (1f): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.65 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO$_2$), 7.35 – 7.07 (m, 7H, 2 × *meta*-SO$_2$ and Ph), 6.72 – 6.63 (m, 1H, NC*H*CH), 5.05 (ddt, *J* = 8.4, 5.4, 1.7 Hz, 1H, NCHC*H*), 4.17 – 4.05 (m, 1H, NC*H*(CH$_2$)$_2$), 2.98 (dd, *J* = 13.3, 5.0 Hz, 1H, 1 × Ar-CH$_2$), 2.71 (dd, *J* = 13.4, 10.4 Hz, 1H, 1 × Ar-CH$_2$), 2.38 (s, 3H, Ar-CH$_3$), 2.07 (dddt, *J* = 18.7, 10.7, 3.6, 2.2 Hz, 1H, 1 × NCHCHC*H*$_2$), 1.80 (dtt, *J* = 18.2, 5.6, 1.6 Hz, 1H, 1 × NCHCHC*H*$_2$), 1.46 – 1.36 (m, 1H, 1 × NCHC*H*$_2$CH$_2$), 0.96 – 0.80 (m, 1H, 1 × NCHC*H*$_2$CH$_2$). ^{13}C NMR (101 MHz, CDCl$_3$) δ 143.3 (*para*-SO$_2$), 138.0 (*ipso*-CH$_2$), 136.3 (*ipso*-SO$_2$), 129.7 (2 × *meta*-SO$_2$), 129.4 (2 × *ortho*-CH$_2$), 128.5 (2 × *meta*-CH$_2$), 126.9 (2 × *ortho*-SO$_2$), 126.5 (*para*-CH$_2$), 123.5 (N*C*HCH), 108.2 (NCH*C*H), 54.3 (N*C*H(CH$_2$)$_2$), 38.1 (Ar-CH$_2$), 21.5 (Ar- CH$_3$), 21.0 (NCH*C*H$_2$CH$_2$), 17.0 (NCHCH*C*H$_2$). ν_{max} 3059, 3026, 2953, 1643, 1595, 1334, 1162 cm^{-1}. m/z (ES+) (Found: [M+H]$^+$, 328.1380. C$_{19}$H$_{21}$NO$_2$S requires [M+H]$^+$, 328.1371). M.p. 104 – 105 °C. $[\alpha]_D^{24.8}$ +279 (c 1.01 g/100 mL, CH$_2$Cl$_2$). Data were in agreement with those previously reported.[2]

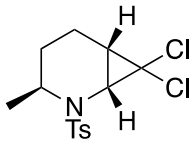


(*R*)-2-(4-Methoxybenzyl)-1-tosyl-1,2,3,4-tetrahydropyridine (1g): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.70 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO$_2$), 7.29 (d, *J* = 8.4 Hz, 2H, 2 × *meta*-SO$_2$), 7.15 (d, *J* = 8.6 Hz, 2H, 2 × *meta*-OCH$_3$), 6.86 (d, *J* = 8.6 Hz, 2H, 2 × *ortho*-OCH$_3$), 6.71 (ddt, *J* = 8.3, 2.2, 1.4 Hz, 1H, NC*H*CH), 5.09 (ddt, *J* = 8.5, 5.5, 1.7 Hz, 1H, NCHC*H*), 4.12 – 4.08 (m, 1H, NC*H*(CH$_2$)$_2$), 3.81 (s, 3H, OCH$_3$), 2.96 (dd, *J* = 13.6, 5.0 Hz, 1H, 1 × Ar-CH$_2$), 2.70 (dd, *J* = 13.6, 10.4 Hz, 1H, 1 × Ar-CH$_2$), 2.42 (s, 3H, Ar-CH$_3$), 2.18 – 2.02

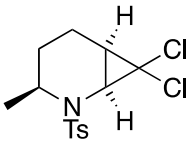
(m, 1H, 1 × NCHCHC*H*$_2$), 1.84 (dtt, *J* = 18.3, 5.7, 1.7 Hz, 1H, 1 × NCHCHC*H*$_2$), 1.53 – 1.41 (m, 1H, 1 × Ar-CH$_2$CHC*H*$_2$), 1.00 – 0.84 (m, 1H, 1 × Ar-CH$_2$CHC*H*$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.3 (*ipso*-OCH_3), 143.3 (*para*-SO_2), 136.3 (*ipso*-SO_2), 130.3 (2 × *meta*-OCH_3), 130.0 (*para*-OCH_3), 129.6 (2 × *meta*-SO_2), 126.8 (2 × *ortho*-SO_2), 123.5 (N*C*HCH), 113.9 (2 × *ortho*-OCH_3), 108.2 (NCH*C*H), 55.2 (OCH_3), 54.4 (N*C*H(CH$_2$)$_2$), 37.2 (Ar-CH$_2$), 21.5 (Ar-CH_3), 20.9 (Ar-CH$_2$CH*C*H$_2$), 17.0 (NCHCH*C*H$_2$). ν_{max} 3064, 2930, 1648, 1610, 1513, 1342, 1249, 1167 cm^{-1}. m/z (ES+) (Found: [M+H]$^+$, 328.1380. $C_{20}H_{23}NO_3S$ requires [M+H]$^+$, 328.1371). $[\alpha]_D^{25.3}$ +254 (c 1.87 g/100 mL, CH_2Cl_2).

General Procedure 1 – Dihalocyclopropanation

To a solution of tetrahydropyridine (1.0 equiv) and benzyltriethylammonium chloride (0.1 equiv.) in CHX_3 (4.5 mL/mmol) was added $NaOH_{(aq)}$ (50% w/v, 20 equiv.). The biphasic mixture was stirred vigorously at r.t for 16 h then water was added and the layers separated. The aqueous layer was extracted thrice with CH_2Cl_2 and the combined organic layers were washed with brine, dried (Na_2SO_4), filtered and concentrated under reduced pressure. Purification by flash column chromatography was employed where appropriate.



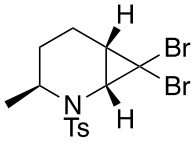
2a



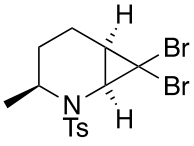
3a

(1*R*,3*S*,6*S*)-7,7-Dichloro-3-methyl-2-tosyl-2-azabicyclo[4.1.0]heptane (2a) and (1*S*,3*S*,6*R*)-7,7-dichloro-3-methyl-2-tosyl-2-azabicyclo[4.1.0]heptane (3a): Following **general procedure 1**, THP **1a** (126 mg, 0.50 mmol) was cyclopropanated in $CHCl_3$ and purification by flash column chromatography (9:1 pentane:Et$_2$O) afforded an inseparable 76:24 mixture of **2a** and **3a** as a colourless solid (149 mg, 0.45 mmol, 90%). R_f: 0.19 (9:1 pentane:Et$_2$O). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 – 7.79 (m, 4H, 2 × **2a**- and 2 × **3a**-*ortho*-SO_2), 7.36 – 7.28 (m, 4H, 2 × **2a**- and 2 × **3a**-*meta*-SO_2), 4.08 – 4.00 (m, 2H, **2a**/**3a**-NC*H*CH_3), 3.39 (d, *J* = 10.6 Hz, 1H, **3a**-NCHCCl_2), 3.33 (d, *J* = 10.1 Hz, 1H, **2a**-NCHCCl_2), 2.44 (s, 3H, **3a**-Ar-CH_3), 2.43 (s, 3H, **2a**-Ar-CH_3), 2.09 – 1.99 (m, 3H, (**2a**/**3a**-NCHC*H* and 1 × **3a**- NCHCHC*H*$_2$), 1.98 – 1.71 (m, 4H, 2 × **2a**-

NCHCHCH_2, 1 × **3a**-NCHCHCH_2 and 1 × **3a**-NCHCH_2), 1.53 – 1.38 (m, 3H, 2 × **2a**-NCHCH_2 and 1 × **3a**-NCHCH_2), 1.24 (d, J = 6.6 Hz, 3H, **3a**-NCHCH_3), 0.96 (d, J = 6.7 Hz, 3H, **2a**-NCHCH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.6 (**2a**/**3a**-*para*-SO_2), 137.7 (**2a**/**3a**-*ipso*-SO_2), 129.6 (2 × **2a**- and 2 × **3a**-*meta*-SO_2), 127.7 (2 × **3a**-*ortho*-SO_2), 127.5 (2 × **2a**-*ortho*-SO_2), 62.3 (**3a**-CCl_2), 62.0 (**2a**-CCl_2), 48.3 (**3a**-NCHCH$_3$), 46.5 (**2a**-NCHCH$_3$), 40.7 (**3a**-NCHCCl_2), 38.7 (**3a**-NCHCCl_2), 28.6 (**3a**-NCHCH$_2$), 28.4 (**3a**-NCHCH), 27.7 (**2a**-NCHCH$_2$), 27.3 (**2a**-NCHCH), 21.6 (*syn*/**2a**-Ar-CH$_3$), 20.2 (**3a**-NCHCH$_3$), 17.0 (**2a**-NCHCH$_3$), 12.6 (**3a**-NCHCHCH$_2$), 11.9 (**2a**-NCHCHCH$_2$). ν_{max} 2930, 1595, 1491, 1450, 1346, 1159, 1092, 1010 cm^{-1}. m/z (ES+) (Found: [M+H]$^+$, 334.0441. $C_{14}H_{18}NO_2SCl_2$ requires [M+H]$^+$, 334.0435). M.p. 89 – 91 °C.



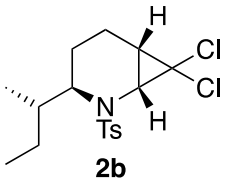
4a



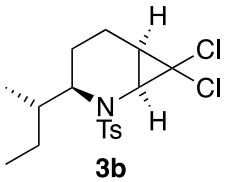
5a

(1*R*,3*S*,6*S*)-7,7-Dibromo-3-methyl-2-tosyl-2-azabicyclo[4.1.0]heptane (4a) and (1*S*,3*S*,6*R*)-7,7-dibromo-3-methyl-2-tosyl-2-azabicyclo[4.1.0]heptane (5a): Following **general procedure 1**, THP **1a** (126 mg, 0.50 mmol) was cyclopropanated in $CHBr_3$ and purification by flash column chromatography (8:2 pentane:Et_2O) afforded an inseparable 60:40 mixture of **4a** and **5a** as a colourless solid (167 mg, 0.39 mmol, 78%). R_f: 0.25 (8:2 pentane:Et_2O). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 8.3 Hz, 2H, 2 × **4a**-*ortho*-SO_2), 7.81 (d, J = 8.3 Hz, 2H, 2 × **5a**-*ortho*-SO_2), 7.35 – 7.29 (m, 4H, 2 × **5a** and 2 × **4a**-*meta*-SO_2), 4.08 – 3.94 (m, 2H, **5a**/**4a**-NCHCH$_3$), 3.39 (d, J = 10.1 Hz, 1H, **5a**-NCHCBr_2), 3.37 (d, J = 10.1 Hz, 1H, **4a**-NCHCBr_2), 2.44 (s, 3H, **5a**-Ar-CH$_3$), 2.43 (s, 3H, **4a**-Ar-CH$_3$), 2.16 – 2.06 (m, 3H, **5a**/**4a**-NCHCH and 1 × **5a**-NCHCHCH_2), 2.00 – 1.75 (m, 4H, 1 × **4a**-NCHCH_2, 1 × **5a**-NCHCHCH_2 and 2 × **4a**-NCHCHCH_2), 1.53 – 1.47 (m, 2H, 2 × **5a**-NCHCH_2), 1.44 – 1.36 (m, 1H, 1 × **4a**-NCHCH_2), 1.29 (d, J = 6.5 Hz, 3H, **5a**-NCHCH_3), 0.92 (d, J = 6.7 Hz, 3H, **4a**-NCHCH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.6 (**5a**/**4a**-*para*-SO_2), 137.5 (**4a**-*ipso*-SO_2), 136.7 (**5a**-*ipso*-SO_2), 129.7 (2 × **5a**-*meta*-SO_2), 129.6 (2 × **4a**-*meta*-SO_2), 127.8 (2 × **5a**-*ortho*-SO_2), 127.6 (2 × **4a**-*ortho*-SO_2), 48.5 (**5a**-NCHCH$_3$), 46.7 (**4a**-NCHCH$_3$), 41.6 (**5a**-NCHCBr_2), 39.5 (**4a**-NCHCBr_2), 36.6 (**5a**-CBr_2), 34.2 (**4a**-CBr_2), 29.8 (**5a**-NCHCH), 28.6 (**5a**-NCHCH$_2$), 28.4 (**4a**-NCHCH), 27.5 (**4a**-NCHCH$_2$), 21.6 (**5a**/**4a**-Ar-CH$_3$), 20.8 (**5a**-CHCH$_3$), 17.1 (**4a**-CHCH$_3$), 15.4 (**5a**-NCHCHCH$_2$), 13.5 (**4a**-NCHCHCH$_2$). ν_{max} 2960, 1595, 1446, 1383, 1327, 1159, 1126, 1092, 1006 cm^{-1}. m/z

(ES+) (Found: $[M+H]^+$, 421.9433. $C_{14}H_{18}NO_2SBr_2$ requires $[M+H]^+$, 421.9425). M.p. 79 – 81 °C.



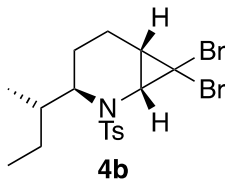
2b



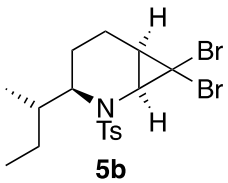
3b

(1*R*,3*R*,6*S*)-3-((*S*)-*sec*-Butyl)-7,7-dichloro-2-tosyl-2-azabicyclo[4.1.0]heptane (2b) and (1*S*,3*R*,6*R*)-3-((*S*)-*sec*-butyl)-7,7-dichloro-2-tosyl-2-azabicyclo[4.1.0]heptane (3b): Following **general procedure 1**, THP **1b** (733 mg, 2.50 mmol) was cyclopropanated in $CHCl_3$ and purification by flash column chromatography (9:1 pentane:Et_2O) afforded **2b** (568 mg, 1.51 mmol) and **3b** (142 mg, 0.38 mmol) as colourless solids (76% overall). R_f of **2b**: 0.33 (9:1 pentane:Et_2O). R_f of **3b**: 0.19 (9:1 pentane:Et_2O). **Characterisation of 2b:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO_2), 7.28 (d, *J* = 8.2 Hz, 2H, 2 × *meta*-SO_2), 3.64 (dt, *J* = 9.8, 3.2 Hz, 1H, NC*H*CH_2), 3.43 (d, *J* = 10.1 Hz, 1H, NCHCCl_2), 2.42 (s, 3H, Ar-CH_3), 1.99 (dd, *J* = 10.1, 8.0 Hz, 1H, NCHCCl_2C*H*), 1.87 (ddt, *J* = 14.9, 11.7, 8.0 Hz, 1H, 1 × NCHCH_2CH_2), 1.81 – 1.68 (m, 3H, 1 × NCHCH_2CH_2 and NCHCH_2CH_2), 1.68 – 1.51 (m, 1H, 1 × CH_2CH_3), 1.45 (dqt, *J* = 13.4, 6.6, 3.6 Hz, 1H, C*H*CH_3), 1.13 – 0.99 (m, 1H, 1 × CH_2CH_3), 0.87 (t, *J* = 7.4 Hz, 3H, CH_2CH_3), 0.84 (d, *J* = 6.7 Hz, 3H, CHCH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.4 (*para*-SO_2), 138.6 (*ipso*-SO_2), 129.4 (2 × *meta*-SO_2), 127.8 (2 × *ortho*-SO_2), 62.4 (CCl_2), 56.6 (N*C*HCH_2), 39.9 (N*C*HCC_2), 35.5 (*C*HCH_3), 27.9 (NCHCCl_2*C*H), 26.0 (*C*H_2CH_3), 23.6 (NCH*C*H_2CH_2), 21.6 (Ar-CH_2), 15.6 (CH*C*H_3), 13.0 (NCHCH_2*C*H_2), 11.8 (CH_2*C*H_3). ν_{max} 2967, 1599, 1454, 1342, 1163, 1096, 1018 cm^{-1}. m/z (CI+) (Found: $[M+H]^+$, 376.0897. $C_{17}H_{23}NO_2SCl_2$ requires $[M+H]^+$, 376.0905). M.p. 101 – 102 °C. $[\alpha]_D^{25.5}$ -110 (c 0.66 g/100 mL, CH_2Cl_2). **Characterisation of 3b:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO_2), 7.33 (d, *J* = 8.1 Hz, 2H, 2 × *meta*-SO_2), 3.34 (td, *J* = 6.0, 2.9 Hz, 1H, NC*H*CH_2), 3.30 (d, *J* = 10.2 Hz, 1H, NCHCCl_2), 2.44 (s, 3H, Ar-CH_3), 2.20 – 2.10 (m, 1H, NCHC*H*), 2.02 – 1.91 (m, 2H, NCHCCl_2C*H* and 1 × NCHCH_2CH_2), 1.79 – 1.71 (m, 1H, 1 × NCHCH_2), 1.53 – 1.42 (m, 2H, 1 × NCHCH_2CH_2 and 1 × CH_2CH_3), 1.29 – 1.10 (m, 2H, 1 × NCHCH_2 and 1 × CH_2CH_3), 0.85 (t, *J* = 7.4 Hz, 3H, CH_2CH_3), 0.80 (d, *J* = 6.7 Hz, 3H, CHCH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 143.8 (*para*-SO_2), 136.2 (*ipso*-SO_2), 129.7 (2 × *meta*-SO_2), 127.8 (2 × *ortho*-SO_2), 62.8 (CCl_2), 58.2 (N*C*HCH_2), 42.8 (N*C*HCCl_2), 36.9 (NCH*C*H), 28.9 (NCHCCl_2*C*H), 27.1 (*C*H_2CH_3), 22.5 (NCH*C*H_2), 21.6

(Ar-CH_3), 15.0 (NCHCH$_2$*C*H$_2$), 14.9 (CH*C*H$_3$), 12.2 (CH$_2$*C*H$_3$). ν_{max} 2967, 1598, 1342, 1161, 1096, 1018 cm^{-1}. m/z (ES+) (Found: [M+H]$^+$, 376.0915. $C_{14}H_{23}NO_2SCl_2$ requires [M+H]$^+$, 376.0905). M.p. 96 – 98 °C. $[\alpha]_D^{25.6}$ +75 (c 0.37 g/100 mL, CH_2Cl_2).



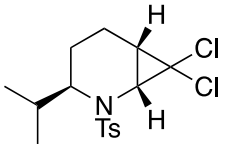
4b



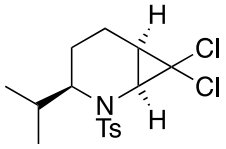
5b

(1*R*,3*R*,6*S*)-7,7-Dibromo-3-((*S*)-*sec*-butyl)-2-tosyl-2-azabicyclo[4.1.0]heptane (4b) and (1*S*,3*R*,6*R*)-7,7-dibromo-3-((*S*)-*sec*-butyl)-2-tosyl-2-azabicyclo[4.1.0]heptane (5b): Following **general procedure 1**, THP **1b** (293 mg, 1.00 mmol) was cyclopropanated in $CHBr_3$ and purification by flash column chromatography (9:1 pentane:Et_2O) afforded **4b** (184 mg, 0.40 mmol) and **5b** (101 mg, 0.22 mmol) as pale yellow solids (62% overall). R_f of **4b**: 0.46 (9:1 pentane:Et_2O). R_f of **5b**: 0.29 (95:5 pentane:Et_2O). **Characterisation of 4b:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO_2), 7.29 (d, *J* = 8.0 Hz, 2H, 2 × *meta*-SO_2), 3.67 (dt, *J* = 9.6, 3.5 Hz, 1H, NC*H*CH$_2$), 3.53 (d, *J* = 10.2 Hz, 1H, NCHCBr$_2$), 2.42 (s, 3H, Ar-CH_3), 2.08 (dd, *J* = 10.2, 8.3 Hz, 1H, NCHCBr$_2$C*H*), 1.90 (dddd, *J* = 16.6, 14.7, 6.4, 3.3 Hz, 1H, 1 × NCHCH$_2$C*H*$_2$), 1.78 – 1.55 (m, 4H, 1 × NCHCH$_2$C*H*$_2$, NCHC*H*$_2$CH$_2$ and 1 × C*H*$_2$CH$_3$), 1.45 (dtp, *J* = 13.3, 6.7, 3.3 Hz, 1H, C*H*CH$_3$), 1.11 – 1.00 (m, 1H, 1 × C*H*$_2$CH$_3$), 0.87 (t, *J* = 7.4 Hz, 3H, CH$_2$C*H*$_3$), 0.83 (d, *J* = 6.7 Hz, 3H, CHC*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.4 (*para*-SO_2), 138.7 (*ipso*-SO_2), 129.4 (2 × *meta*-SO_2), 127.9 (2 × *ortho*-SO_2), 56.8 (N*C*HCH$_2$), 41.0 (N*C*HCBr$_2$), 36.0 (*C*HCH$_3$), 34.2 (CBr$_2$), 28.6 (NCHCBr$_2$*C*H), 26.1 (*C*H$_2$CH$_3$), 23.9 (NCH*C*H$_2$CH$_2$), 21.6 (Ar-CH_3), 15.6 (CH*C*H$_3$), 14.9 (NCHCH$_2$*C*H$_2$), 11.8 (CH$_2$*C*H$_3$). ν_{max} 2963, 1595, 1327, 1159, 1092 cm^{-1}. m/z (ES+) (Found: [M+H]$^+$, 463.9911. $C_{17}H_{23}NO_2SBr_2$ requires [M+H]$^+$, 463.9894). M.p. 135 – 137 °C. $[\alpha]_D^{20.6}$ +19.6 (c 1.12 g/100 mL, CH_2Cl_2). **Characterisation of 5b:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.4 Hz, 2H, 2 × *ortho*-SO_2), 7.35 (d, *J* = 8.1 Hz, 1H, 2 × *meta*-SO_2), 3.29 (d, *J* = 10.2 Hz, 1H, NCHCBr$_2$), 3.25 (ddd, *J* = 6.2, 5.0, 3.2 Hz, 1H, NC*H*CH$_2$), 2.45 (s, 3H, Ar-CH_3), 2.27 (dddt, *J* = 11.1, 6.7, 4.4, 1.7 Hz, 1H, C*H*CH$_3$), 2.09 – 1.99 (m, 2H, NCHCBr$_2$C*H* and 1 × NCHCH$_2$C*H*$_2$), 1.81 – 1.72 (m, 1H, 1 × NCHC*H*$_2$CH$_2$), 1.48 – 1.34 (m, 2H, 1 × NCHCH$_2$C*H*$_2$ and 1 × C*H*$_2$CH$_3$), 1.34 – 1.23 (m, 1H, 1 × NCHC*H*$_2$CH$_2$), 1.21 – 1.11 (m, 1H, 1 × C*H*$_2$CH$_3$), 0.84 (d, *J* = 6.7 Hz, 3H, CHC*H*$_3$), 0.84 (t, *J* = 7.4 Hz, 3H, CH$_2$C*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.9 (*para*-SO_2), 135.8 (*ipso*-SO_2), 129.7 (2 × *meta*-SO_2), 128.0 (2 × *ortho*-SO_2), 58.4 (N*C*HCH$_2$),

43.7 (N*C*HCBr$_2$), 37.1 (*C*HCH$_3$), 36.1 (CBr$_2$), 30.5 (NCHCBr$_2$*C*H), 27.3 (*C*H$_2$CH$_3$), 22.4 (NCH*C*H$_2$CH$_2$), 21.6 (Ar-CH$_3$), 17.8 (NCHCH$_2$*C*H$_2$), 14.7 (CH*C*H$_3$), 12.2 (CH$_2$*C*H$_3$). ν_{max} 2922, 1595, 1326, 1159, 1092 cm^{-1}. m/z (ES+) (Found: [M+H]$^+$, 463.9912. $C_{17}H_{23}NO_2SBr_2$ requires [M+H]$^+$, 463.9894). M.p. 95 – 96 °C. $[\alpha]_D^{25.5}$ -110 (c 0.66 g/100 mL, CH_2Cl_2).



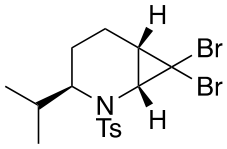
2c



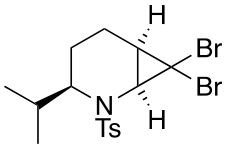
3c

(1*R*,3*S*,6*S*)-7,7-Dichloro-3-isopropyl-2-tosyl-2-azabicyclo[4.1.0]heptane (2c) and (1*S*,3*S*,6*R*)-7,7-dichloro-3-isopropyl-2-tosyl-2-azabicyclo[4.1.0]heptane (3c): Following **general procedure 1**, THP **1c** (140 mg, 0.50 mmol) was cyclopropanated in $CHCl_3$ and purification by flash column chromatography (85:15 pentane:Et_2O) afforded an inseparable 84:16 mixture of **2c** and **3c** as a colourless solid (127 mg, 0.35 mmol, 70%). R_f: 0.29 (85:15 pentane:Et_2O). **NMR assignment of 2c:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO_2), 7.28 (d, *J* = 8.0 Hz, 2H, 2 × *meta*-SO_2), 3.57 (ddd, *J* = 10.2, 4.0, 2.7 Hz, 1H, NC*H*CH$_2$), 3.44 (d, *J* = 10.1 Hz, 1H, NCHCCl$_2$), 2.41 (s, 3H, Ar-CH$_3$), 1.99 (dd, *J* = 10.1, 8.0 Hz, 1H, NCHCCl$_2$C*H*), 1.87 (ddt, *J* = 15.0, 12.2, 7.6 Hz, 1H, 1 × NCHCHCH$_2$), 1.80 – 1.69 (m, 3H, C*H*(CH$_3$)$_2$, 1 × NCHCHCH$_2$ and 1 × NCHCH$_2$), 1.62 – 1.49 (m, 1H, 1 × NCHC*H*$_2$), 0.96 (d, *J* = 6.8 Hz, 3H, 1 × CH(C*H*$_3$)$_2$), 0.89 (d, *J* = 6.7 Hz, 3H, 1 × CH(C*H*$_3$)$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.3 (*para*-SO_2), 138.6 (*ipso*-SO_2), 129.4 (2 × *meta*-SO_2), 127.7 (2 × *ortho*-SO_2), 62.3 (CCl$_2$), 57.8 (N*C*HCH$_2$), 39.7 (N*C*HCCl$_2$), 28.8 (NCH*C*H(CH$_3$)$_2$), 27.8 (NCHCCl$_2$*C*H), 23.8 (NCH*C*H$_2$), 21.6 (Ar-CH$_3$), 20.7 (1 × CH(*C*H$_3$)$_2$), 19.8 (1 × CH(*C*H$_3$)$_2$), 12.8 (NCHCH$_2$*C*H$_2$). **NMR assignment of 3c:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO_2), 7.33 (d, *J* = 8.3 Hz, 2H, 2 × *meta*-SO_2), 3.38 (td, *J* = 6.5, 2.5 Hz, 1H, NC*H*CH$_2$), 3.32 (d, *J* = 10.5 Hz, 1H, NCHCCl$_2$), 2.44 (s, 3H, Ar-CH$_3$), 2.34 (h, *J* = 6.8 Hz, 1H, C*H*(CH$_3$)$_2$), 2.05 – 1.91 (m, 2H, NCHCCl$_2$C*H* and 1 × NCHCHCH$_2$), 1.82 – 1.72 (m, 1H, 1 × NCHCHCH$_2$), 1.49 – 1.35 (m, 1H, 1 × NCHCH$_2$), 1.19 (dddd, *J* = 19.8, 10.0, 7.3, 5.6 Hz, 1H, 1 × NCHCH$_2$), 0.98 (d, *J* = 6.9 Hz, 3H, 1 × CH(C*H*$_3$)$_2$), 0.83 (d, *J* = 6.6 Hz, 3H, 1 × CH(C*H*$_3$)$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.7 (*para*-SO_2), 136.3 (*ipso*-SO_2), 129.7 (2 × *meta*-SO_2), 127.7 (2 × *ortho*-SO_2), 62.6 (CCl$_2$), 58.9 (N*C*HCH$_2$), 42.5 (N*C*HCCl$_2$), 29.9 (NCH*C*H(CH$_3$)$_2$), 28.4 (NCHCCl$_2$*C*H), 22.4 (NCH*C*H$_2$), 21.6 (Ar-CH$_3$), 20.6 (1 × CH(*C*H$_3$)$_2$), 18.5 (1 ×

$CH(CH_3)_2$), 14.3 ($NCHCH_2CH_2$). ν_{max} 2967, 1599, 1454, 1342, 1163, 1096, 1010 cm^{-1}. m/z (ES+) (Found: $[M+H]^+$, 362.0764. $C_{16}H_{21}NO_2SCl_2$ requires $[M+H]^+$, 362.0748). M.p. 154 – 156 °C.



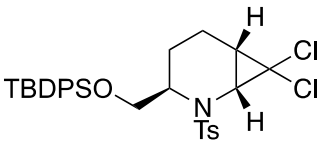
4c



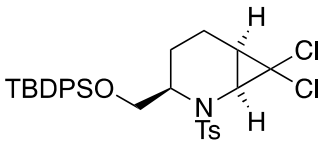
5c

(1*R*,3*S*,6*S*)-7,7-Dibromo-3-isopropyl-2-tosyl-2-azabicyclo[4.1.0]heptane (4c) and (1*S*,3*S*,6*R*)-7,7-dibromo-3-isopropyl-2-tosyl-2-azabicyclo[4.1.0]heptane (5c): Following **general procedure 1**, THP **1c** (279 mg, 1.00 mmol) was cyclopropanated in $CHBr_3$ and purification by flash column chromatography (9:1 pentane:Et_2O) afforded **4c** (173 mg, 0.38 mmol) and **5c** (116 mg, 0.26 mmol) as colourless solids (64% overall). R_f of **4c**: 0.44 (9:1 pentane:Et_2O). R_f of **5c**: 0.24 (9:1 pentane:Et_2O). **Characterisation of 4c:** ^1H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO_2), 7.29 (d, *J* = 7.7 Hz, 2H, 2 × *meta*-SO_2), 3.59 (dt, *J* = 10.0, 3.2 Hz, 1H, $NCHCH_2$), 3.54 (d, *J* = 10.2 Hz, 1H, $NCHCBr_2$), 2.42 (s, 3H, Ar-CH_3), 2.12 – 2.04 (m, 1H, $NCHCBr_2CH$), 1.96 – 1.83 (m, 1H, 1 × $NCHCH_2CH_2$), 1.79 – 1.60 (m, 4H, 1 × $NCHCH_2CH_2$, 2 × $NCHCH_2$ and $CH(CH_3)_2$), 0.96 (d, *J* = 6.8 Hz, 3H, 1 × $CH(CH_3)_2$), 0.88 (d, *J* = 6.7 Hz, 3H, 1 × $CH(CH_3)_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 143.4 (*para*-SO_2), 138.7 (*ipso*-SO_2), 129.5 (2 × *meta*-SO_2), 127.9 (2 × *ortho*-SO_2), 58.0 ($NCHCH_2$), 40.8 ($NCHCBr_2$), 34.1 (CBr_2), 29.2 ($CH(CH_3)_2$), 28.5 ($NCHCBr_2CH$), 24.1 ($NCHCH_2$), 21.6 (Ar-CH_3), 20.7 (1 × $CH(CH_3)_2$), 19.8 (1 × $CH(CH_3)_2$), 14.7 ($NCHCH_2CH_2$). ν_{max} 3030, 2960, 1599, 1464, 1327, 1252, 1156, 1092, 1047 cm^{-1}. m/z (ES+) (Found: $[M+H]^+$, 449.9742. $C_{16}H_{21}NO_2SBr_2$ requires $[M+H]^+$, 449.9738). M.p. 148 – 148 °C. $[\alpha]_D^{20.7}$ +23.7 (c 1.35 g/100 mL, CH_2Cl_2). **Characterisation of 5c:** ^1H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO_2), 7.34 (d, *J* = 7.8 Hz, 2H, 2 × *meta*-SO_2), 3.32 (d, *J* = 10.4 Hz, 1H, $NCHCBr_2$), 3.29 (td, *J* = 6.1, 2.6 Hz, 1H, $NCHCH_2$), 2.46 (s, *J* = 6.7 Hz, 1H, $CH(CH_3)_2$), 2.44 (s, 3H, Ar-CH_3), 2.13 – 1.99 (m, 2H, $NCHCBr_2CH$ and 1 × $NCHCH_2CH_2$), 1.81 – 1.71 (m, 1H, 1 × $NCHCH_2$), 1.41 – 1.30 (m, 1H, 1 × $NCHCH_2CH_2$), 1.29 – 1.18 (dddd, *J* = 12.8, 6.9, 4.2, 2.5 Hz, 1H, 1 × $NCHCH_2$), 0.96 (d, *J* = 6.9 Hz, 3H, 1 × $CH(CH_3)_2$), 0.86 (d, *J* = 6.7 Hz, 3H, 1 × $CH(CH_3)_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 143.8 (*para*-SO_2), 135.9 (*ipso*-SO_2), 129.7 (2 × *meta*-SO_2), 127.9 (2 × *ortho*-SO_2), 59.1 ($NCHCH_2$), 43.4 ($NCHCBr_2$), 36.1 (CBr_2), 30.3 ($CH(CH_3)_2$), 30.2 ($NCHCBr_2CH$), 22.4 ($NCHCH_2$), 21.6 (Ar-CH_3), 20.7 (1 × $CH(CH_3)_2$), 18.1 (1 ×

$CH(CH_3)_2$), 17.2 (NCHCH$_2$CH$_2$). ν_{max} 2967, 1595, 1450, 1349, 1163, 1092, 1006 cm^{-1}. m/z (ES+) (Found: $[M+H]^+$, 449.9742. $C_{16}H_{21}NO_2SBr_2$ requires $[M+H]^+$, 449.9738). M.p. 74 – 76 °C. $[\alpha]_D^{22.1}$ -37 (c 0.27 g/100 mL, CH_2Cl_2).



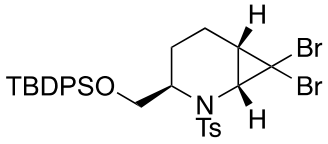
2d



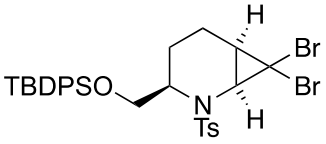
3d

(1*R*,3*R*,6*S*)-3-(((*tert*-Butyldiphenylsilyl)oxy)methyl)-7,7-dichloro-2-tosyl-2-azabicyclo[4.1.0]heptane (2d) and (1*S*,3*R*,6*R*)-3-(((*tert*-butyldiphenylsilyl)oxy)methyl)-7,7-dichloro-2-tosyl-2-azabicyclo[4.1.0]heptane (3d): Following **general procedure 1**, THP **1d** (108 mg, 0.21 mmol) was cyclopropanated in $CHCl_3$ and purification by flash column chromatography (95:5 pentane:EtOAc) afforded an inseparable 75:25 mixture of **2d** and **3d** as a colourless oil (68.4 mg, 0.12 mmol, 57%). R_f: 0.36 (95:5 pentane:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 – 7.65 (m, 4H, 2 × **2d**- and 2 × **3d**-*ortho*-SO_2), 7.64 – 7.52 (m, 8H, 4 × **2d**- and 4 × **3d**-*ortho*-Si), 7.50 – 7.36 (m, 12H, 4 × **2d**- and 4 × **3d**-*meta*- Si and 2 × **2d**- and 2 × **3d**-*para*-Si), 7.22 – 7.15 (m, 4H, 2 × **2d**- and 2 × **3d**-*meta*-SO_2), 4.03 – 3.97 (m, 1H, **2d**-NC*H*$(CH_2)_2$), 3.96 – 3.91 (m, 2H, **3d**-NC*H*$(CH_2)_2$ and 1 × **3d**-OCH_2), 3.48 (dd, *J* = 10.0, 5.1 Hz, 1H, 1 × **2d**-OCH_2), 3.41 – 3.32 (m, 2H, 1 × **2d**-OCH_2 and 1 × **3d**-OCH_2), 3.30 (d, *J* = 10.5 Hz, 1H, **3d**-NC*H*CH), 3.26 (d, *J* = 10.4 Hz, 1H, **2d**- NC*H*CH), 2.40 (s, 3H, **3d**-Ar-CH_3), 2.38 (s, 3H, **2d**-Ar-CH_3), 2.03 – 1.92 (m, 2H, 1 × **2d**- and 1 × **3d**-NCHC*H*$_2$CH$_2$), 1.89 – 1.81 (m, 2H, 1 × **2d**- and 1 × **3d**-NCHC*H*), 1.78 – 1.62 (m, 6H, 1 × **2d**- and 1 × **3d**-NCHC*H*$_2$CH$_2$, 2 × **2d**- and 2 × **3d**-NCHCH$_2$C*H*$_2$), 1.06 (s, 9H, **3d**-$C(CH_3)_3$), 1.04 (s, 9H, **2d**-$C(CH_3)_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.6 (**3d**-*para*-SO_2), 143.5 (**2d**-*para*-SO_2), 137.7 (**2d**-*ipso*- SO_2), 136.5 (**3d**-*ipso*-SO_2), 135.6 (2 × **3d**-*ortho*-Si), 135.5 (4 × **2d**-*ortho*-Si), 134.8 (2 × **3d**-*ortho*-Si), 133.4 (1 × **3d**-*ipso*-Si), 133.3 (1 × **3d**-*ipso*-Si), 133.1 (1 × **2d**-*ipso*-Si), 133.0 (1 × **2d**-*ipso*-Si), 129.9 (2 × **2d**-*para*-Si), 129.8 (1 × **3d**-*para*-Si), 129.7 (1 × **3d**-*para*-Si), 129.6 (2 × **3d**-*meta*-SO_2), 129.5 (2 × **2d**-*meta*-SO_2), 127.8 (4 × **2d**-*meta*-Si), 127.7 (4 × **3d**-*meta*-Si), 127.4 (2 × **3d**-*ortho*-SO_2), 127.3 (2 × **2d**-*ortho*-SO_2), 62.2 (**2d**-CCl_2), 61.8 (**2d**-OCH_2), 61.6 (**3d**-OCH_2), 60.4 (**3d**-CCl_2), 53.3 (**3d**-N*C*H$(CH_2)_2$), 51.1 (**2d**-N*C*H$(CH_2)_2$), 40.0 (**3d**-N*C*HCCl_2), 39.4 (**2d**-N*C*HCCl_2), 28.3 (**2d**-NCH*C*H), 28.1 (**3d**-NCH*C*H), 26.9 (**3d**-C(*C*$H_3)_3$), 26.8 (**2d**-C(*C*$H_3)_3$), 21.5 (**2d**/**3d**-Ar-CH_3 and **2d**/**3d**-NCH*C*H$_2$CH$_2$), 19.2 (**3d**-*C*$(CH_3)_3$), 19.1 (**2d**-*C*$(CH_3)_3$), 12.0 (**2d**-NCHCH$_2$*C*H$_2$), 11.9

(**2d**- NCHCH$_2$*C*H$_2$). ν_{max} 3071, 2956, 1595, 1428, 1349, 1163, 1111 cm^{-1}. m/z (ES+) (Found: [M+H]$^+$, 588.1575. $C_{30}H_{35}NO_3SiSCl_2$ requires [M+H]$^+$, 588.1562).

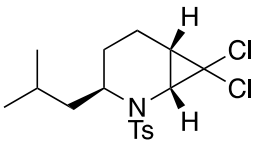


4d

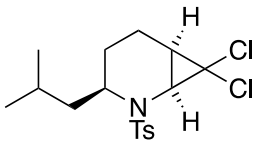


5d

(1*R*,3*R*,6*S*)-7,7-Dibromo-3-(((*tert*-butyldiphenylsilyl)oxy)methyl)-2-tosyl-2- azabicyclo[4.1.0]heptane (4d) and (1*S*,3*R*,6*R*)-7,7-dibromo-3-(((*tert*- butyldiphenylsilyl)oxy)methyl)-2-tosyl-2-azabicyclo[4.1.0]heptane (5d): Following **general procedure 1**, THP **1d** (108 mg, 0.21 mmol) was cyclopropanated in $CHBr_3$ and purification by flash column chromatography (9:1 pentane:Et_2O) afforded an inseparable 58:42 mixture of **4d** and **5d** as a yellow oil (75.5 mg, 0.11 mmol, 53%). R_f: 0.33 (9:1 pentane:Et_2O). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 – 7.67 (m, 4H, 2 × **4d**- and 2 × **5d**-*ortho*-SO_2), 7.64 – 7.56 (m, 8H, 4 × **4d**- and 4 × **5d**-*ortho*-Si), 7.50 – 7.36 (m, 12H, 4 × **4d**- and 4 × **5d**-*meta*-Si, 2 × **4d**- and 2 × **5d**-*para*-Si), 7.23 (d, *J* = 8.0 Hz, 2H, 2 × **5d**-*meta*-SO_2), 7.18 (d, *J* = 8.0 Hz, 2H, 2 × **4d**-*meta*-SO_2), 4.03 – 3.97 (m, 2H, **4d**-NC*H*$(CH_2)_2$ and 1 × **5d**-OCH_2), 3.94 – 3.89 (m, 1H, **5d**-NC*H*$(CH_2)_2$), 3.53 – 3.43 (m, 2H, 1 × **4d**-OCH_2 and 1 × **5d**-OCH_2), 3.35 – 3.28 (m, 3H, 1 × **4d**-OCH_2, **4d**-NC*H*CH and **5d**-NC*H*CH), 2.40 (s, 3H, **5d**-Ar-CH_3), 2.38 (s, 3H, **4d**-Ar-CH_3), 2.20 – 2.16 (m, 1H, 1 × **5d**-NCHC*H*$_2$CH$_2$), 2.04 – 1.92 (m, 4H, 1 × **4d**- and 1 × **5d**-NCHC*H*$_2$CH$_2$, 1 × **4d**- and 1 × **5d**-NCHC*H*), 1.81 – 1.60 (m, 5H, 1 × **4d**-NCHC*H*$_2$CH$_2$, 2 × **4d**- and 2 × **5d**-NCHCH$_2$C*H*$_2$), 1.06 (s, 9H, **4d**-C$(CH_3)_3$), 1.03 (s, 9H, **5d**-C$(CH_3)_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.7 (**5d**-*para*-SO_2), 143.5 (**4d**-*para*-SO_2), 137.7 (**4d**-*ipso*- SO_2), 136.3 (**5d**-*ipso*-SO_2), 135.6 (2 × **5d**-*ortho*-Si), 135.5 (2 × **5d**-*ortho*-Si), 135.5 (4 × **4d**-*ortho*-Si), 133.4 (1 × **5d**-*ipso*-Si), 133.3 (1 × **5d**-*ipso*-Si), 133.0 (1 × **4d**-*ipso*-Si), 133.0 (1 × **4d**-*ipso*-Si), 129.9 (2 × **4d**-*para*-Si), 129.7 (1 × **5d**-*para*-Si), 129.7 (1 × **5d**-*para*-Si), 129.6 (2 × **5d**-*meta*-SO_2), 129.6 (2 × **4d**-*meta*-SO_2), 127.7 (4 × **4d**- and 4 × **5d**-*meta*-Si), 127.6 (2 × **5d**-*ortho*-SO_2), 127.4 (2 × **4d**-*ortho*-SO_2), 62.2 (**5d**-OCH_2), 61.9 (**4d**-OCH_2), 53.4 (**5d**-N*C*H$(CH_2)_2$), 51.3 (**4d**-N*C*H$(CH_2)_2$), 40.8 (**5d**-N*C*HCH), 40.3 (**4d**-N*C*HCH), 36.4 (**5d**-CBr_2), 34.2 (**4d**-CBr_2), 29.5 (**5d**-NCH*C*H), 29.0 (**4d**-NCH*C*H), 26.9 (**5d**-C(*C*$H_3)_3$), 26.8 (**4d**-C(*C*$H_3)_3$), 21.7 (**4d**-NCH*C*H$_2$CH$_2$), 21.5 (**4d**/**5d**-Ar-CH_3), 21.5 (**5d**-NCH*C*H$_2$CH$_2$), 19.2 (**5d**-*C*$(CH_3)_3$), 19.1 (**4d**-*C*$(CH_3)_3$), 14.8 (**5d**-NCHCH$_2$*C*H$_2$), 13.6 (**4d**-NCHCH$_2$*C*H$_2$). ν_{max} 3071, 2956, 1595, 1428, 1349, 1163, 1096 cm^{-1}. m/z (ES+) (Found: [M+H]$^+$, 676.0559. $C_{30}H_{35}NO_3SiSBr_2$ requires [M+H]$^+$, 676.0552).



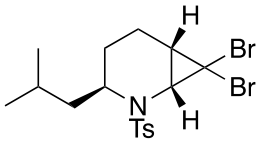
2e



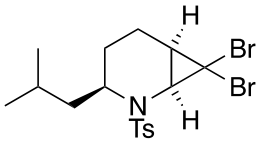
3e

(1*R*,3*S*,6*S*)-7,7-Dichloro-3-isobutyl-2-tosyl-2-azabicyclo[4.1.0]heptane (2e) and (1*S*,3*S*,6*R*)-7,7-dichloro-3-isobutyl-2-tosyl-2-azabicyclo[4.1.0]heptane (3e): Following **general procedure 1**, THP **1e** (1.17 g, 4.00 mmol) was cyclopropanated in $CHCl_3$ and purification by flash column chromatography (95:5 pentane:EtOAc) afforded **2e** (924 mg, 2.46 mmol) and **3e** (283 mg, 0.75 mmol) as colourless solids (81% overall). R_f of **2e**: 0.26 (95:5 pentane:EtOAc). R_f of **3e**: 0.19 (95:5 pentane:EtOAc). **Characterisation of 2e:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO_2), 7.30 (d, *J* = 8.1 Hz, 2H, 2 × *meta*-SO_2), 3.90 (dtd, *J* = 9.5, 4.5, 2.7 Hz, 1H, NC*H*$(CH_2)_2$), 3.35 (d, *J* = 10.2 Hz, 1H, NCHCCl_2), 2.43 (s, 3H, Ar-CH_3), 2.03 – 1.97 (m, 1H, NCHC*H*), 1.88 – 1.76 (m, 2H, NCHCH_2CH_2), 1.72 – 1.52 (m, 2H, NCHC*H*$_2$CH_2), 1.45 (dddd, *J* = 13.1, 11.5, 9.4, 6.6 Hz, 1H, C*H*$(CH_3)_2$), 1.30 (ddd, *J* = 13.6, 10.0, 5.0 Hz, 1H, 1 × C*H*$_2$CH$(CH_3)_2$), 1.13 – 1.01 (m, 1H, 1 × C*H*$_2$CH$(CH_3)_2$), 0.85 (d, *J* = 6.6 Hz, 3H, 1 × CH(C*H*$_3)_2$), 0.84 (d, *J* = 6.5 Hz, 3H, 1 × CH(C*H*$_3)_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.5 (*para*-SO_2), 137.8 (*ipso*-SO_2), 129.5 (2 × *meta*-SO_2), 127.6 (2 × *ortho*-SO_2), 62.3 (CCl_2), 49.2 (N*C*H$(CH_2)_2$), 39.6 (*C*H$_2$CH$(CH_3)_2$), 39.1 (N*C*HCCl_2), 27.8 (NCH*C*H), 24.9 (C*H*$(CH_3)_2$), 23.9 (NCH*C*H$_2$CH_2), 23.6 (1 × CH(*C*H$_3)_2$), 21.6 (1 × CH(*C*H$_3$) and Ar-CH_3), 12.1 (NCHCH$_2$*C*H$_2$). ν_{max} 2956, 1599, 1346, 1163, 1096, 1018 cm^{-1}. m/z (ES+) (Found: $[M+H]^+$, 376.0896. $C_{17}H_{23}NO_2SCl_2$ requires $[M+H]^+$, 376.0905). M.p. 116 – 117 °C. $[\alpha]_D^{20.5}$ +69 (c 0.84 g/100 mL, CH_2Cl_2). **Characterisation of 3e:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.2 Hz, 2H, 2 × *ortho*-SO_2), 7.33 (d, *J* = 8.2 Hz, 2H, 2 × *meta*-SO_2), 3.95 – 3.87 (m, 1H, NC*H*$(CH_2)_2$), 3.41 (d, *J* = 10.1 Hz, 1H, NCHCCl_2), 2.44 (s, 3H, Ar-CH_3), 2.09 – 1.97 (m, 2H, NCHC*H* and 1 × NCHCH$_2$C*H*$_2$), 1.71 – 1.63 (m, 1H, 1 × NCHC*H*$_2$CH_2), 1.56 – 1.41 (m, 2H, C*H*$_2$CH$(CH_3)_2$), 1.39 – 1.24 (m, 2H, 1 × NCHCH$_2$C*H*$_2$ and 1 × NCHC*H*$_2$CH_2), 0.97 (d, *J* = 6.1 Hz, 3H, 1 × CH(C*H*$_3)_2$), 0.87 (m, 4H, 1 × CH(C*H*$_3)_2$ and C*H*$(CH_3)_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.5 (*para*-SO_2), 137.0 (*ipso*-SO_2), 129.6 (2 × *meta*-SO_2), 127.6 (2 × *ortho*-SO_2), 62.3 (CCl_2), 51.3 (N*C*H$(CH_2)_2$), 41.0 (*C*H$_2$CH$(CH_3)_2$), 40.4 (N*C*HCCl_2), 28.2 (NCH*C*H), 25.9 (C*H*$(CH_3)_2$), 24.4 (NCH*C*H$_2$CH_2), 23.9 (1 × CH(*C*H$_3)_2$), 21.6 (Ar-CH_3), 21.2 (1 × CH(*C*H$_3)_2$), 12.3 (NCHCH$_2$*C*H$_2$). ν_{max} 2956, 1597, 1454, 1346, 1161,

1096, 1018 cm^{-1}. m/z (ES+) (Found: $[M+H]^+$, 376.0896. $C_{17}H_{23}NO_2SCl_2$ requires $[M+H]^+$, 376.0905). M.p. 51 – 52 °C. $[\alpha]_D^{24.7}$ -60 (c 0.07 g/100 mL, CH_2Cl_2).



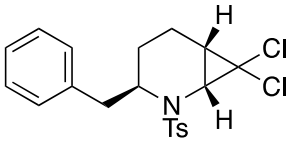
4e



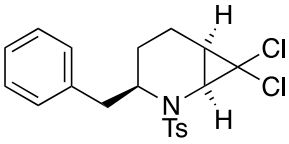
5e

(1*R*,3*S*,6*S*)-7,7-Dibromo-3-isobutyl-2-tosyl-2-azabicyclo[4.1.0]heptane (4e) and (1*S*,3*S*,6*R*)-7,7-dibromo-3-isobutyl-2-tosyl-2-azabicyclo[4.1.0]heptane (5e): Following **general procedure 1**, THP **1e** (440 mg, 1.50 mmol) was cyclopropanated in $CHBr_3$ and purification by flash column chromatography (95:5 pentane:EtOAc) afforded **4e** (246 mg, 0.53 mmol) and **5e** (198 mg, 0.43 mmol) as pale yellow solids (64% overall). R_f of **4e**: 0.52 (95:5 pentane:EtOAc). R_f of **5e**: 0.32 (95:5 pentane:EtOAc). **Characterisation of 4e:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO_2), 7.31 (d, *J* = 7.8 Hz, 2H, 2 × *meta*-SO_2), 3.90 (dq, *J* = 10.9, 3.7 Hz, 1H, NC*H*(CH_2)$_2$), 3.39 (d, *J* = 10.2 Hz, 1H, NCHCBr_2), 2.43 (s, 3H, Ar-CH_3), 2.13 – 2.03 (m, 1H, NCHC*H*), 1.91 – 1.67 (m, 3H, NCHCH_2C*H*$_2$ and 1 × NCHC*H*$_2$CH_2), 1.60 – 1.49 (ddd, *J* = 12.2, 7.3, 2.8 Hz, 1H, 1 × NCHC*H*$_2$CH_2), 1.48 – 1.36 (dqd, *J* = 9.6, 6.6, 4.8 Hz, 1H, C*H*(CH_3)$_2$), 1.33 – 1.22 (ddd, *J* = 13.6, 10.4, 4.7 Hz, 1H, 1 × C*H*$_2$CH(CH_3)$_2$), 1.05 – 0.95 (m, 1H, 1 × C*H*$_2$CH(CH_3)$_2$), 0.83 (d, *J* = 6.5 Hz, 6H, CH(C*H*$_3$)$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.6 (*para*-SO_2), 137.7 (*ipso*-SO_2), 129.5 (2 × *meta*-SO_2), 127.7 (2 × *ortho*-SO_2), 49.4 (N*C*H(CH_2)$_2$), 40.0 (N*C*HCBr_2), 39.6 (*C*H_2CH(CH_3)$_2$), 34.5 (CBr_2), 28.5 (NCH*C*H), 24.9 (*C*H(CH_3)$_3$), 24.0 (NCH*C*H_2CH_2), 23.6 (1 × CH(*C*H_3)$_2$), 21.6 (Ar- CH_3), 21.5 (1 × CH(*C*H_3)$_2$), 13.8 (NCHCH_2*C*H_2). ν_{max} 2956, 1595, 1454, 1341, 1159, 1092, 813 cm^{-1}. m/z (ES+) (Found: $[M+H]^+$, 463.9896. $C_{17}H_{23}NO_2SBr_2$ requires $[M+H]^+$, 463.9889). M.p. 107 – 109 °C. $[\alpha]_D^{21.6}$ +75 (c 0.61 g/100 mL, CH_2Cl_2). **Characterisation of 5e:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO_2), 7.33 (d, *J* = 8.0 Hz, 2H, 2 × *meta*-SO_2), 3.85 (ddd, *J* = 10.6, 5.4, 3.0 Hz, 1H, NC*H*(CH_2)$_2$), 3.40 (d, *J* = 10.2 Hz, 1H, NCHCBr_2), 2.44 (s, 3H, Ar-CH_3), 2.15 – 2.04 (m, 2H, NCHC*H* and 1 × NCHCH_2C*H*$_2$), 1.71 – 1.40 (m, 4H, C*H*$_2$CH(CH_3)$_2$, C*H*(CH_3)$_2$ and 1 × NCHC*H*$_2$CH_2), 1.38 – 1.16 (m, 2H, 1 × NCHCH_2C*H*$_2$ and 1 × NCHC*H*$_2$CH_2), 0.97 (d, *J* = 6.5 Hz, 3H, 1 × CH(C*H*$_3$)$_2$), 0.87 (d, *J* = 6.6 Hz, 1H, 1 × CH(C*H*$_3$)$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.6 (*para*-SO_2), 136.7 (*ipso*-SO_2), 129.6 (2 × *meta*-SO_2), 127.7 (2 × *ortho*-SO_2), 51.5 (N*C*H(CH_2)$_2$), 41.7 (*C*H_2CH(CH_3)$_3$), 41.3 (N*C*HCBr_2), 36.7 (CBr_2), 29.7 (NCH*C*H), 25.9 (*C*H(CH_3)$_2$), 24.4 (NCH*C*H_2CH_2),

23.9 (1 × CH(*C*H$_3$)$_2$), 21.6 (Ar- CH$_3$), 21.2 (1 × CH(*C*H$_3$)$_2$), 15.1 (NCHCH$_2$*C*H$_2$). ν_{max} 2956, 1595, 1454, 1342, 1159, 1092, 813 cm^{-1}. m/z (ES+) (Found: [M+H]$^+$, 463.9882. $C_{17}H_{23}NO_2SBr_2$ requires [M+H]$^+$, 463.9889). M.p. 83 – 85 °C. $[\alpha]_D^{23.9}$ -50 (c 0.12 g/100 mL, CH_2Cl_2).



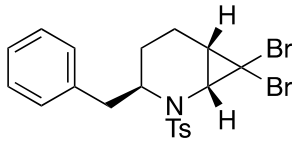
2f



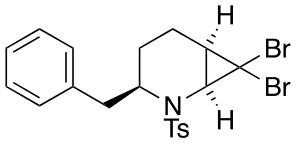
3f

(1*R*,3*R*,6*S*)-3-Benzyl-7,7-dichloro-2-tosyl-2-azabicyclo[4.1.0]heptane (2f) and (1*S*,3*R*,6*R*)-3-benzyl-7,7-dichloro-2-tosyl-2-azabicyclo[4.1.0]heptane (3f): Following **general procedure 1**, THP **1f** (164 mg, 0.50 mmol) was cyclopropanated in $CHCl_3$ and purification by flash column chromatography (9:1 pentane:Et_2O) afforded an inseparable 80:20 mixture of **2f** and **3f** as a colourless solid (173 mg, 0.42 mmol, 84%). R_f: 0.29 (9:1 pentane:Et_2O). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.4 Hz, 2H, 2 × **3f**-*ortho*-SO$_2$), 7.85 (d, *J* = 8.4 Hz, 2H, 2 × **2f**-*ortho*-SO$_2$), 7.38 – 7.18 (m, 10H, 2 × **2f**- and 2 × **3f**-*meta*-SO$_2$, 2 × **2f**- and 2 × **3f**-*meta*-CH$_2$, 1 × **2f**- and 1 × **3f**-*para*-CH$_2$), 7.15 – 7.08 (m, 4H, 2 × **2f**- and 2 × **3f**-*ortho*-CH$_2$), 4.07 (m, 2H, **2f**- and **3f**-NC*H*(CH$_2$)$_2$), 3.48 (d, *J* = 10.3 Hz, 1H, **2f**-NCHCCl$_2$), 3.42 (d, *J* = 10.3 Hz, 1H, **3f**-CHCCl$_2$), 3.29 – 3.22 (m, 1H, 1 × **3f**-ArCH$_2$), 2.72 (dd, *J* = 13.2, 4.2 Hz, 1H, 1 × **2f**-ArCH$_2$), 2.58 (m, 2H, 1 × **2f**- and 1 × **3f**-ArCH$_2$), 2.44 (s, 3H, **3f**-CH$_3$), 2.43 (s, 3H, **2f**-CH$_3$), 2.17 – 2.06 (m, 2H, **2f**- and **3f**-NCHC*H*)), 1.98 (ddd, *J* = 15.7, 12.4, 7.7 Hz, 2H, 1 × **2f**- and 1 × **3f**-NCHCHC*H*$_2$), 1.82 (dd, *J* = 15.3, 7.1 Hz, 2H, 1 × **2f**- and 1 × **3f**-NCHCHC*H*$_2$), 1.55 – 1.44 (m, 2H, 1 × **2f**- and 1 × **3f**-NCHC*H*$_2$CH$_2$), 1.38 (dddd, *J* = 14.2, 7.9, 2.6, 1.2 Hz, 2H, 1 × **2f**- and 1 × **3f**-NCHC*H*$_2$CH$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.7 (**2f**- and **3f**-*para*-SO$_2$), 137.7 (**2f**- and **3f**-*ipso*-SO$_2$), 137.6 (**2f**- and **3f**-*ipso*-CH$_2$), 129.7 (2 × **3f**-*meta*-SO$_2$), 129.7 (2 × **2f**-*meta*-SO$_2$), 129.4 (2 × **3f**-*meta*-CH$_2$), 128.9 (2 × **2f**-*ortho*-CH$_2$), 128.7 (2 × **2f**-*meta*-CH$_2$), 128.6 (2 × **3f**-*ortho*-CH$_2$), 127.6 (2 × **3f**-*ortho*-SO$_2$), 127.5 (2 × **2f**-*ortho*-SO$_2$), 126.7 (**2f**-*para*-CH$_2$), 126.5 (**3f**-*para*-CH$_2$), 62.3 (**3f**-CCl$_2$), 62.0 (**2f**-CCl$_2$), 54.6 (**3f**-N*C*H(CH$_2$)$_2$), 52.2 (**2f**-N*C*H(CH$_2$)$_2$), 40.4 (**3f**-N*C*HCCl$_2$), 39.0 (**2f**-N*C*HCCl$_2$), 38.7 (**3f**-CH$_2$Ph), 37.4 (**2f**-CH$_2$Ph), 28.1 (**3f**-NCH*C*H), 27.9 (**2f**-NCH*C*H), 23.0 (**3f**-NCH*C*H$_2$CH$_2$), 22.5 (**2f**-NCH*C*H$_2$CH$_2$), 21.6 (**2f**- and **3f**-CH$_3$), 12.2 (**3f**-NCHCH*C*H$_2$), 12.0 (**2f**-NCHCH*C*H$_2$). ν_{max} 3030, 2952, 1595, 1450, 1349, 1163, 1092 cm^{-1}. m/z (ES+)

(Found: $[M+H]^+$, 410.0754. $C_{20}H_{21}NO_2SCl_2$ requires $[M+H]^+$, 410.0748). M.p. 97 – 99 °C.

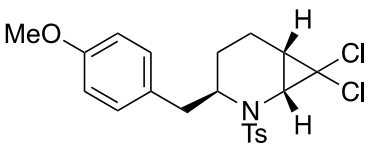


4f

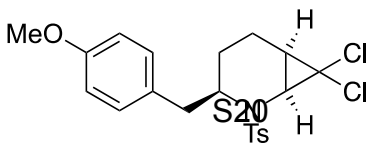


5f

(1*R*,3*R*,6*S*)-3-Benzyl-7,7-dibromo-2-tosyl-2-azabicyclo[4.1.0]heptane (4f) and (1*S*,3*R*,6*R*)-3-benzyl-7,7-dibromo-2-tosyl-2-azabicyclo[4.1.0]heptane (5f): Following **general procedure 1**, THP **1f** (652 mg, 2.00 mmol) was cyclopropanated in $CHBr_3$ and purification by flash column chromatography (8:2 hexane:Et_2O) afforded an inseparable 60:40 mixture of **4f** and **5f** as a pale yellow solid (888 mg, 1.78 mmol, 89%). R_f: 0.30 (8:2 hexane:Et_2O). ^1H NMR (400 MHz, $CDCl_3$) δ 7.91 – 7.85 (m, 4H, 2 × **4f**- and 2 × **5f**-*ortho*-SO_2), 7.39 – 7.19 (m, 12H, 2 × **4f**- and 2 × **5f**-*meta*-SO_2, 1 × **4f**- and 1 × **5f**-*para*-CH_2, 2 × **4f**- and 2 × **5f**-*meta*-CH_2 and 2 × **5f**-*ortho*-CH_2), 7.14 – 7.09 (m, 2H, 2 × **4f**-*ortho*-CH_2), 4.11 – 4.00 (m, 2H, **4f**- and **5f**-NC*H*$(CH_2)_2$), 3.54 (d, *J* = 10.2 Hz, 1H, **4f**-NCHCBr_2), 3.46 (d, *J* = 10.5 Hz, 1H, **5f**-NCHCBr_2), 3.35 – 3.27 (m, 1H, 1 × **5f**-Ar-CH_2), 2.76 – 2.65 (m, 2H, 1 × **5f**-Ar-CH_2 and 1 × **4f**-Ar-CH_2), 2.52 (dd, *J* = 13.3, 11.5 Hz, 1H, 1 × **4f**-Ar-CH_2), 2.45 (s, 3H, **5f**-Ar-CH_3), 2.43 (s, 3H, **4f**-Ar-CH_3), 2.25 – 2.12 (m, 3H, 1 × **4f**- and 1 × **5f**-NCHC*H* and 1 × **5f**-NCHCH_2C*H*$_2$), 2.07 – 1.93 (ddt, *J* = 16.0, 12.3, 8.1 Hz, 1H, 1 × **4f**-NCHCH_2C*H*$_2$), 1.82 – 1.73 (m, 1H, 1 × **4f**-NCHCH_2C*H*$_2$), 1.69 – 1.52 (m, 2H, 1 × **5f**-NCHC*H*$_2$CH_2 and 1 × **4f**-NCHC*H*$_2$CH_2), 1.41 – 1.31 (m, 2H, 1 × **5f**-NCHCH_2C*H*$_2$ and 1 × **4f**-NCHC*H*$_2$CH_2), 1.24 – 1.13 (m, 1H, 1 × **5f**-NCHC*H*$_2$CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.8 (**4f**-and **5f**-*para*-SO_2), 138.8 (**4f**-*ipso*-CH_2), 137.7 (**5f**-*ipso*-SO_2), 137.6 (**4f**-*ipso*-SO_2), 136.7 (**5f**-*ipso*-CH_2), 129.8 (2 × **5f**-*meta*-SO_2), 129.7 (2 × **4f**-*meta*-SO_2), 129.4 (2 × **5f**-*ortho*-CH_2), 128.8 (2 × **4f**-*ortho*-CH_2), 128.7 (2 × **4f**-*meta*-CH_2), 128.6 (2 × **5f**-*meta*-CH_2), 127.8 (2 × **4f**-*ortho*-SO_2), 127.6 (2 × **5f**-*ortho*-SO_2), 126.7 (**4f**-*para*-CH_2), 126.5 (**5f**-*para*-CH_2), 54.9 (**5f**-NC*H*$(CH_2)_2$), 52.5 (**4f**-NC*H*$(CH_2)_2$), 41.2 (**5f**-NCHCBr_2), 39.9 (**4f**-NCHCBr_2), 39.5 (**5f**-Ar-CH_2), 37.5 (**4f**-Ar-CH_2), 36.6 (**5f**-CBr_2), 34.0 (**4f**-CBr_2), 29.6 (**5f**-NCH*C*H), 28.6 (**4f**-NCH*C*H), 23.0 (**5f**-NCH*C*H_2CH_2), 22.7 (**4f**-NCH*C*H_2CH_2), 21.6 (**4f**- and **5f**-CH_3), 15.0 (**5f**-NCHCH_2*C*H_2), 13.7 (**4f**-NCHCH_2*C*H_2). ν_{max} 3027, 2941, 1599, 1495, 1454, 1346, 1159, 1092 cm^{-1}. m/z (ES+) (Found: $[M+H]^+$, 497.9732. $C_{20}H_{21}NO_2SBr_2$ requires $[M+H]^+$, 497.9738). M.p. 140 – 143 °C.

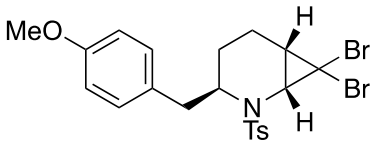


2g

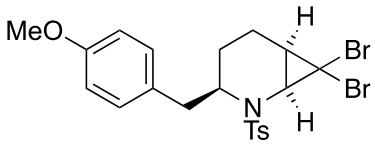


3g

(1*R*,3*R*,6*S*)-7,7-Dichloro-3-(4-methoxybenzyl)-2-tosyl-2-azabicyclo[4.1.0]heptane (2g) and (1*S*,3*R*,6*R*)-7,7-dichloro-3-(4-methoxybenzyl)-2-tosyl-2- azabicyclo[4.1.0]heptane (3g): Following **general procedure 1**, THP **1g** (194 mg, 0.50 mmol) was cyclopropanated in $CHCl_3$ and purification by flash column chromatography (85:15 pentane:Et_2O) afforded an inseparable 75:25 mixture of **2g** and **3g** as a colourless solid (170 mg, 0.39 mmol, 78%). R_f: 0.14 (85:15 pentane:Et_2O). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.3 Hz, 2H, 2 × **3g**-*ortho*-SO_2), 7.84 (d, *J* = 8.3 Hz, 2H, 2 × **2g**-*ortho*-SO_2), 7.33 (d, *J* = 7.9 Hz, 2H, 2 × **3g**-*meta*-SO_2), 7.31 (d, *J* = 7.9 Hz, 2H, 2 × **2g**-*meta*-SO_2), 7.14 (d, *J* = 8.5 Hz, 2H, 2 × **3g**-*meta*-OCH_3), 7.03 (d, *J* = 8.5 Hz, 2H, 2 × **2g**-*meta*-OCH_3), 6.84 (d, *J* = 8.7 Hz, 2H, 2 × **3g**-*ortho*-OCH_3), 6.81 (d, *J* = 8.7 Hz, 2H, 2 × **2g**-*ortho*-OCH_3), 4.05 – 3.96 (m, 2H, **2g**- and **3g**-NC*H*$(CH_2)_2$), 3.79 (s, 3H, **3g**-OCH_3), 3.78 (s, 3H, **2g**-OCH_3), 3.47 (d, *J* = 10.2 Hz, 1H, **2g**-NCHCCl_2), 3.4 (d, *J* = 10.2 Hz, 1H, **3g**-NCHCCl_2), 3.18 (dd, *J* = 14.6, 2.2 Hz, 1H, 1 × **3g**-Ar-CH_2), 2.65 (dd, *J* = 13.4, 4.2 Hz, 1H, 1 × **2g**-Ar-CH_2), 2.55 (dd, *J* = 13.4, 11.4 Hz, 1H, 1 × **3g**-Ar-CH_2), 2.50 (dd, *J* = 13.5, 11.3 Hz, 1H, 1 × **2g**-Ar-CH_2), 2.44 (s, 3H, **3g**-Ar-CH_3), 2.42 (s, 3H, **2g**-Ar-CH_3), 2.14 – 2.05 (m, 3H, **2g**- and **3g**-NCHC*H* and 1 × **3g**-NCHCH_2C*H*$_2$), 1.97 (ddt, *J* = 15.7, 12.3, 7.9 Hz, 2H, 1 × **2g**- and 1 × **3g**-NCHCH_2C*H*$_2$), 1.86 – 1.76 (m, 1H, 1 × **2g**-NCHCH_2C*H*$_2$), 1.60 – 1.46 (m, 2H, 1 × **2g**-and 1 × **3g**-NCHC*H*$_2$CH_2), 1.40 (dddd, *J* = 14.1, 7.8, 2.4, 1.1 Hz, 1H, 1 × **2g**-NCHC*H*$_2$CH_2), 1.22 – 1.10 (m, 1H, 1 × **3g**-NCHC*H*$_2$CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.4 (**2g**-*ipso*-OCH_3), 158.3 (**3g**-*ipso*-OCH_3), 143.7 (**3g**-*para*-SO_2), 143.7 (**2g**-*para*-SO_2), 137.8 (**2g**-*ipso*-SO_2), 136.9 (**3g**-*ipso*-SO_2), 130.7 (**3g**-*para*-OCH_3), 130.3 (**2g**-*para*-OCH_3 and 2 × **3g**-*meta*-OCH_3), 129.8 (2 × **2g**-*meta*-OCH_3), 129.7 (2 × **3g**-*meta*-SO_2), 129.6 (2 × **2g**-*meta*-SO_2), 127.6 (2 × **3g**-*ortho*-SO_2), 127.5 (2 × **2g**-*ortho*-SO_2), 114.1 (2 × **2g**-*ortho*-OCH_3), 114.0 (2 × **3g**-*ortho*-OCH_3), 62.3 (**3g**-CCl_2), 62.1 (**2g**-CCl_2), 55.2 (**2g**- and **3g**-OCH_3), 54.8 (**3g**-N*C*H$(CH_2)_2$), 52.4 (**2g**-N*C*H$(CH_2)_2$), 40.4 (**3g**-N*C*HCCl_2), 39.0 (**2g**-N*C*HCCl_2), 37.8 (**3g**-Ar-CH_2), 36.5 (**2g**-Ar-CH_2), 28.2 (**3g**-NCH*C*H), 27.9 (**2g**-NCH*C*H), 22.9 (**3g**-NCH*C*H_2CH_2), 22.5 (**2g**-NCH*C*H_2CH_2), 21.6 (**2g**- and **3g**-Ar-CH_3), 12.2 (**3g**-NCHCH_2*C*H_2), 12.0 (**2g**-NCHCH_2*C*H_2). ν_{max} 2997, 1610, 1513, 1450, 1346, 1249, 1163, 1096, 1033 cm^{-1}. m/z (ES+) (Found: $[M+H]^+$, 440.0860. $C_{21}H_{23}NO_3SCl_2$ requires $[M+H]^+$, 440.0854). M.p. 51 – 52 °C.



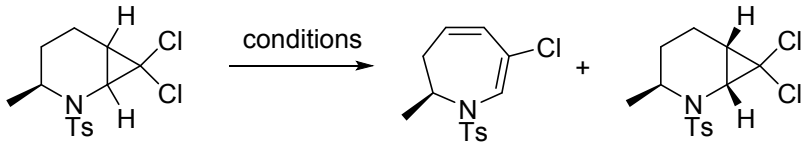
4g



5g

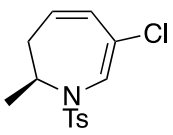
(1*R*,3*R*,6*S*)-7,7-Dibromo-3-(4-methoxybenzyl)-2-tosyl-2-azabicyclo[4.1.0]heptane (4g) and (1*S*,3*R*,6*R*)-7,7-dibromo-3-(4-methoxybenzyl)-2-tosyl-2- azabicyclo[4.1.0]heptane (5g): Following **general procedure 1**, THP **1g** (194 mg, 0.50 mmol) was cyclopropanated in $CHBr_3$ and purification by flash column chromatography (85:15 pentane:Et_2O) afforded an inseparable 62:38 mixture of **4g** and **5g** as a colourless solid (192 mg, 0.36 mmol, 73%). R_f: 0.13 (85:15 pentane:Et_2O). ^1H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.3 Hz, 4H, 2 × **4g**- and 2 × **5g**-*ortho*-SO_2), 7.38 – 7.31 (m, 4H, 2 × **4g**- and 2 × **5g**-*meta*-SO_2), 7.15 (d, *J* = 8.5 Hz, 2H, 2 × **5g**-*meta*-OCH_3), 7.02 (d, *J* = 8.6 Hz, 2H, 2 × **4g**-*meta*-OCH_3), 6.84 (d, *J* = 8.8 Hz, 2H, 2 × **5g**-*ortho*-OCH_3), 6.81 (d, *J* = 8.8 Hz, 2H, 2 × **4g**-*ortho*-OCH_3), 4.04 – 3.96 (m, 2H, **4g**-and **5g**-NC*H*$(CH_2)_2$), 3.79 (s, 3H, **5g**-OCH_3), 3.78 (s, 3H, **4g**-OCH_3), 3.52 (d, *J* = 10.2 Hz, 1H, **4g**-$NCHCBr_2$), 3.46 (d, *J* = 10.3 Hz, 1H, **5g**-$NCHCBr_2$), 3.23 (d, *J* = 13.3 Hz, 1H, 1 × **5g**-Ar-CH_2), 2.68 – 2.60 (m, 2H, 1 × **5g**-Ar-CH_2 and 1 × **4g**-Ar-CH_2), 2.46 (dd, *J* = 13.4, 11.5 Hz, 1H, 1 × **4g**-Ar-CH_2), 2.45 (s, 3H, **5g**-Ar-CH_3), 2.43 (s, 3H, **4g**-Ar-CH_3), 2.25 – 2.10 (m, 3H, 1 × **4g**- and 1 × **5g**-NCHC*H* and 1 × **5g**-$NCHCH_2CH_2$), 1.98 (ddt, *J* = 16.0, 12.4, 8.1 Hz, 1H, 1 × **4g**-$NCHCH_2CH_2$), 1.77 (dd, *J* = 15.3, 7.2 Hz, 1H, 1 × **4g**-$NCHCH_2CH_2$), 1.68 – 1.56 (m, 2H, 1 × **5g**-$NCHCH_2CH_2$ and 1 × **4g**-$NCHCH_2CH_2$), 1.41 – 1.32 (m, 2H, 1 × **4g**- and 1 × **5g**-$NCHCH_2CH_2$), 1.22 – 1.13 (m, 1H, 1 × **5g**-$NCHCH_2CH_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.4 (**4g**-*ipso*-OCH_3), 158.3 (**5g**-*ipso*-OCH_3), 143.8 (**4g**- and **5g**-*para*-SO_2), 137.7 (**4g**-*ipso*-SO_2), 136.7 (**5g**-*ipso*-SO_2), 130.8 (**5g**-*para*-OCH_3), 130.4 (2 × **5g**-*meta*-OCH_3), 129.8 (2 × **4g**-*meta*-OCH_3 and 2 × **5g**-*meta*-SO_2), 129.7 (2 × **4g**-*meta*-SO_2), 129.6 (2 × **4g**-*para*-OCH_3), 127.8 (2 × **5g**-*ortho*-SO_2), 127.6 (2 × **4g**-*ortho*-SO_2), 114.1 (2 × **4g**-*ortho*-OCH_3), 114.0 (2 × **5g**-*ortho*-OCH_3), 55.3 (**4g**- and **5g**- OCH_3), 55.0 (**5g**-N*C*H$(CH_2)_2$), 52.7 (**4g**-N*C*H$(CH_2)_2$), 41.3 (**5g**-N*C*HCBr_2), 40.0 (**4g**-N*C*HCBr_2), 38.6 (**5g**-Ar-CH_2), 36.6 (**4g**-Ar-CH_2), 36.6 (**5g**-CBr_2), 34.1 (**4g**-CBr_2), 29.6 (**5g**-NCH*C*H), 28.6 (**4g**-NCH*C*H), 22.9 (**5g**-NCH*C*H_2CH_2), 22.6 (**4g**-NCH*C*H_2CH_2), 21.6 (**4g**- and **5g**-Ar-CH_3), 15.0 (**5g**-$NCHCH_2CH_2$), 13.7 (**4g**-$NCHCH_2CH_2$). ν_{max} 3027, 2937, 1610, 1513, 1454, 1346, 1249, 1163, 1092, 1033 cm^{-1}. m/z (ES+) (Found: $[M+H]^+$, 527.9853. $C_{21}H_{23}NO_3SCl_2$ requires $[M+H]^+$, 527.9844). M.p. 71 – 74 °C.

Optimisation of the ring expansion reaction of 2a + 3a → 2a + 6

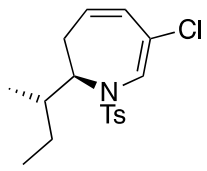


2a (major) + **3a** (minor) **6** **2a**

Entry	***Conditions***	***Result***
1	Ag_2CO_3 (1.5 equiv.), PhMe, 60 °C, 24 h	recovered SM
2	AgOTf (1.5 equiv.), PhMe, 60 °C, 24 h	recovered SM
3	$AgNO_3$ (1.5 equiv.), PhMe, 80 °C, 24 h	recovered SM
4	$AgBF_4$ (1.5 equiv.), PhMe, 80 °C, 24 h	recovered SM
5	$AgNO_3$ (1.5 equiv.), PhMe, 170 °C, µW, 5 h	minor converted
6	$AgPF_6$ (1.5 equiv.), PhMe, 150 °C, µW, 5 h	minor converted
7	$AgSbF_6$ (1.5 equiv.), PhMe, 150 °C, µW, 5 h	decomposition
8	PhMe, 150 °C, µW, 5 h	minor converted
9	K_2CO_3 (1.0 equiv.), PhMe, 150 °C, µW, 5 h	minor converted
10	PhMe, 130 °C, µW, 8 h	minor converted
11	K_2CO_3 (1.0 equiv.), PhMe, 130 °C, µW, 8 h	minor converted
12	HMPA, 80 °C, 24 h	recovered SM
13	NEt_3, 80 °C, 24 h	recovered SM
14	quinoline, 150 °C, 24 h	minor converted
15	*t*BuOH, 150 °C, µW, 5 h	minor converted
16	DMF, cat. HCl, 150 °C, µW, 5 h	minor converted
17	DMF, cat. HCl 200 °C	decomposition

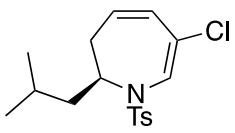


(*S*)-6-Chloro-2-methyl-1-tosyl-2,3-dihydro-1*H*-azepine (6): A solution of dichloride **2a/3a** (300 mg, 0.90 mmol) and potassium carbonate (124 mg, 0.90 mmol) in toluene (2.5 mL) was heated to 150 °C for 5 h under microwave irradiation. The brown solution was diluted with EtOAc (5.0 mL), filtered and concentrated under reduced pressure to afford a brown oil. Purification by flash column chromatography (95:5 pentane:Et_2O) afforded **6** as a colourless oil (58.5 mg, 0.196 mmol, 91% based on minor diastereoisomer conversion). R_f: 0.15 (95:5 pentane:Et_2O). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO_2), 7.32 (d, *J* = 8.6 Hz, 2H, 2 × *meta*-SO_2), 7.13 (s, 1H, NCH=), 6.03 (ddd, *J* = 11.6, 3.2, 1.7 Hz, 1H, NCHC$_q$C*H*), 5.67 – 5.60 (m, 1H, NCHCH_2C*H*), 4.53 – 4.45 (m, 1H, NC*H*CH_3), 2.43 (s, 3H, Ar-CH_3), 2.30 (ddd, *J* = 17.0, 8.4, 4.4 Hz, 1H, 1 × NCHC*H*$_2$), 1.83 – 1.76 (m, 1H, 1 × NCHC*H*$_2$), 0.90 (d, *J* = 6.9 Hz, 3H, NCHC*H*$_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.3 (*para*-SO_2), 135.2 (*ipso*-SO_2), 130.0 (2 × *meta*-SO_2), 129.2 (NCHC$_q$*C*H), 127.7 (NCHCH_2*C*H), 127.3 (2 × *ortho*-SO_2), 123.5 (NCH=), 114.0 (C$_q$Cl), 50.1 (N*C*HCH_3), 36.0 (CH_2), 21.6 (Ar-CH_3), 17.6 (CH*C*H$_3$). ν_{max} 3027, 2930, 1599, 1495, 1349, 1163, 1096 cm^{-1}. An accurate mass spectrum could not be generated for this compound by either ES or EI. $[\alpha]_D^{25.1}$ +29 (c 0.07 g/100 mL, CH_2Cl_2).

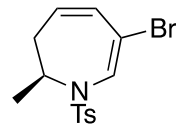


(*R*)-2-((*S*)-*sec*-Butyl)-6-chloro-1-tosyl-2,3-dihydro-1*H*-azepine (7): A solution of dichloride **3b** (100 mg, 0.27 mmol) and potassium carbonate (37.3 mg, 0.27 mmol) in toluene (2.5 mL) was heated to 150 °C for 5 h under microwave irradiation. The brown solution was diluted with EtOAc (5.0 mL), filtered and concentrated under reduced pressure to afford a brown oil. Purification by flash column chromatography (9:1 hexane:Et_2O) afforded **7** as a colourless oil (60.7 mg, 0.18 mmol, 67%). R_f: 0.31 (9:1 hexane:Et_2O). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO_2), 7.31 (d, *J* = 7.8 Hz, 2H, 2 × *meta*-SO_2), 7.15 (s, 1H, NCH=), 5.99 (ddd, *J* = 11.5, 3.0, 2.0 Hz, 1H, ClCC*H*CH), 5.66 (ddd, *J* = 12.2, 8.6, 3.6 Hz, 1H, ClCCHC*H*), 4.08 – 4.02 (m, 1H, NC*H*CH_2), 2.49 (ddd, *J* = 17.0, 8.2, 4.7 Hz, 1H, 1 × NCHC*H*$_2$), 2.42 (s, 3H, Ar-CH_3), 1.67 – 1.54 (m, 1H, 1 × C*H*$_2$$CH_3$), 1.34 – 1.17 (m, 2H, 1 × NCHC*H*$_2$ and C*H*CH_3), 1.08 (ddq, *J* = 14.0, 9.1, 7.1 Hz, 1H, 1 × C*H*$_2$$CH_3$), 0.85 (t, *J* = 7.4 Hz, 3H, CH_2C*H*$_3$), 0.73 (d, *J* = 6.6 Hz, 3H, CHC*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.2 (*para*-SO_2), 134.9

(*ipso*-SO_2), 130.0 (2 × *meta*-SO_2), 129.5 (ClC*C*HCH), 128.3 (ClCCH*C*H), 127.3 (2 × *ortho*-SO_2), 123.5 (NCH=), 115.5 (CCl), 59.3 (NC*H*CH_2), 33.7 (*C*HCH_3), 32.3 (NCH*C*H_2), 25.2 (*C*H_2CH_3), 21.6 (Ar-CH_3), 14.3 (CH*C*H_3), 11.1 (CH_2*C*H_3). ν_{max} 3042, 2963, 1595, 1461, 1353, 1245, 1167, 1088, 992 cm^{-1}. m/z (ES+) (Found: $[M+H]^+$, 340.1136. $C_{17}H_{22}NO_2SCl$ requires $[M+H]^+$, 340.1138). $[\alpha]_D^{25.7}$ +290 (c 0.74 g/100 mL, CH_2Cl_2).

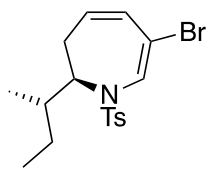


(*S*)-6-Chloro-2-isobutyl-1-tosyl-2,3-dihydro-1*H*-azepine (8): A solution of dichloride **3e** (140 mg, 0.37 mmol) and potassium carbonate (51.1 mg, 0.37 mmol) in toluene (2.5 mL) was heated to 150 °C for 5 h under microwave irradiation. The brown solution was diluted with EtOAc (5.0 mL), filtered and concentrated under reduced pressure to afford a brown oil. Purification by flash column chromatography (95:5 pentane:Et_2O) afforded **8** as a colourless oil (83.0 mg, 0.244 mmol, 66%). R_f: 0.22 (95:5 pentane:Et_2O). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.4 Hz, 2H, 2 × *ortho*-SO_2), 7.34 (d, *J* = 7.9 Hz, 2H, 2 × *meta*-SO_2), 7.14 (s, 1H, NCH=), 6.02 (ddd, *J* = 11.5, 3.2, 1.7 Hz, 1H, ClCC*H*CH), 5.64 (dddt, *J* = 11.6, 8.3, 3.3, 0.8 Hz, 1H, ClCCHC*H*), 4.43 (dq, *J* = 7.7, 4.1, 3.3 Hz, 1H, NC*H*$(CH_2)_2$), 2.45 (s, 3H, Ar-CH_3), 2.35 (ddd, *J* = 17.2, 8.4, 4.4 Hz, 1H, 1 × C*H*$_2$CH=), 1.64 (dqd, *J* = 17.3, 3.3, 0.8 Hz, 1H, 1 × C*H*$_2$CH=), 1.57 – 1.50 (m, 1H, C*H*$(CH_3)_2$), 1.17 (ddd, *J* = 13.9, 8.3, 6.5 Hz, 1H, 1 × C*H*$_2$CH$(CH_3)_2$), 1.01 – 0.95 (m, 1H, 1 × C*H*$_2$CH$(CH_3)_2$), 0.91 (d, *J* = 6.5 Hz, 3H, 1 × CH(C*H*$_3$)$_2$), 0.87 (d, *J* = 6.6 Hz, 3H, 1 × CH(C*H*$_3$)$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.2 (*para*-SO_2), 135.2 (*ipso*-SO_2), 130.0 (2 × *meta*-SO_2), 129.2 (ClC*C*HCH), 128.2 (ClCCH*C*H), 127.3 (2 × *ortho*-SO_2), 123.5 (NCH=), 115.1 (CCl), 52.5 (N*C*H$(CH_2)_2$), 40.1 (*C*H_2CH$(CH_3)_2$), 34.4 (*C*H_2CH=), 24.0 (*C*H$(CH_3)_2$), 22.5 (1 × CH(*C*H$_3$)$_2$), 22.5 (1 × CH(*C*H$_3$)$_2$), 21.6 (Ar-CH_3). ν_{max} 2960, 1595, 1342, 1167, 1096 cm^{-1}. m/z (ES+) (Found: $[M+H]^+$, 340.1145. $C_{17}H_{22}NO_2SCl$ requires $[M+H]^+$, 340.1138). $[\alpha]_D^{25.6}$ +260 (c 0.63 g/100 mL, CH_2Cl_2).

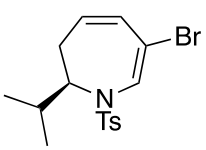


(*S*)-6-Bromo-2-methyl-1-tosyl-2,3-dihydro-1*H*-azepine (10): A solution of dibromide **4a/5a** (320 mg, 0.77 mmol) and potassium carbonate (106 mg, 0.77 mmol) in toluene (5.0 mL) was heated to 150 °C for 5 h under microwave irradiation. The brown solution was diluted with EtOAc (5.0 mL), filtered and concentrated under reduced pressure to afford a brown oil.

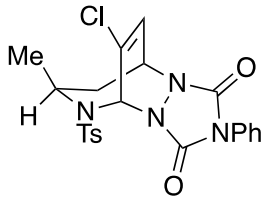
Purification by flash column chromatography (9:1 pentane:Et_2O) afforded **10** as a yellow oil (124 mg, 0.36 mmol, 86% based on minor diastereoisomer conversion). R_f: 0.24 (9:1 pentane:Et_2O). ^1H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO_2), 7.33 (d, *J* = 7.9 Hz, 2H, 2 × *meta*-SO_2), 7.28 (s, 1H, NCH=), 6.15 (ddd, *J* = 11.6, 3.2, 1.5 Hz, 1H, CBrC*H*CH), 5.55 (ddd, *J* = 11.2, 8.5, 3.6 Hz, 1H, CBrCHC*H*), 4.52 – 4.43 (m, 1H, NC*H*CH_3), 2.43 (s, 3H, Ar-CH_3), 2.30 (ddd, *J* = 17.1, 8.5, 4.6 Hz, 1H, 1 × CH_2), 1.85 – 1.73 (m, 1H, 1H, 1 × CH_2), 0.90 (dd, *J* = 6.8, 0.7 Hz, 3H, CHC*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.3 (*para*-SO_2), 135.1 (*ipso*-SO_2), 131.1 (CBr*C*HCH), 130.0 (2 × *meta*-SO_2), 127.8 (CBrCH*C*H), 127.3 (2 × *ortho*-SO_2), 125.8 (NCH=), 101.7 (CBr), 50.4 (N*C*HCH$_3$), 35.9 (CH_2), 21.6 (Ar-CH_3), 17.7 (CH*C*H$_3$). ν_{max} 3041, 2982, 1595, 1342, 1167, 1092, 984 cm^{-1}. m/z (ES-) (Found: $[M-H]^-$, 340.0011. $C_{14}H_{16}NO_2SBr$ requires $[M-H]^-$, 340.0007). $[\alpha]_D^{24.5}$ +100 (c 0.1 g/100 mL, CH_2Cl_2).



(*R*)-6-Bromo-2-((*S*)-*sec*-butyl)-1-tosyl-2,3-dihydro-1*H*-azepine (11): A solution of dibromide **5b** (100 mg, 0.21 mmol) and potassium carbonate (29.0 mg, 0.21 mmol) in toluene (2.5 mL) was heated to 150 °C for 5 h under microwave irradiation. The brown solution was diluted with EtOAc (5.0 mL), filtered and concentrated under reduced pressure to afford a brown oil. Purification by flash column chromatography (95:5 pentane:Et_2O) afforded **11** as a colourless solid (47.5 mg, 0.12 mmol, 59%). R_f: 0.29 (95:5 pentane:Et_2O). ^1H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO_2), 7.33 – 7.28 (m, 3H, 2 × *meta*-SO_2 and NCH=), 6.13 (ddd, *J* = 11.4, 3.7, 1.5 Hz, 1H, BrCC*H*CH), 5.62 – 5.52 (m, 1H, BrCCHC*H*), 4.08 – 4.00 (m, 1H, NC*H*CH_2), 2.53 – 2.44 (m, 1H, 1 × NCHC*H*$_2$), 2.42 (s, 3H, Ar-CH_3), 1.68 – 1.56 (dtt, *J* = 15.0, 7.5, 3.8 Hz, 1H, 1 × C*H*$_2$CH$_3$), 1.33 – 1.18 (m, 2H, 1 × NCHC*H*$_2$ and C*H*CH$_3$), 1.15 – 1.02 (m, 1H, 1 × C*H*$_2$CH$_3$), 0.86 (t, *J* = 7.4 Hz, 3H, CH$_2$C*H*$_3$), 0.73 (d, *J* = 6.7 Hz, 3H, CHC*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.2 (*para*-SO_2), 134.9 (*ipso*-SO_2), 131.4 (BrC*C*HCH), 130.0 (2 × *meta*-SO_2), 128.4 (BrCCH*C*H), 127.4 (2 × *ortho*-SO_2), 125.8 (NCH=), 103.5 (CBr), 59.6 (N*C*HCH$_2$), 33.8 (*C*HCH$_3$), 32.3 (NCH*C*H$_2$), 25.3 (*C*H$_2$CH$_3$), 21.6 (Ar-CH_3), 14.3 (CH*C*H$_3$), 11.2 (CH$_2$*C*H$_3$). ν_{max} 3083, 2967, 1592, 1353, 1170, 1092, 988 cm^{-1}. m/z (ES-) (Found: $[M-H]^-$, 382.0477. $C_{17}H_{22}NO_2SBr$ requires $[M-H]^-$, 382.0477). M.p. 95 – 96 °C. $[\alpha]_D^{23.2}$ +330 (c 0.03 g/100 mL, CH_2Cl_2).

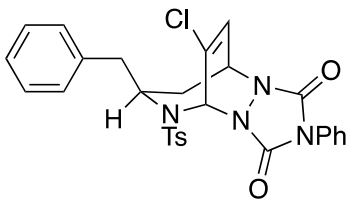


(*R*)-6-Bromo-2-isopropyl-1-tosyl-2,3-dihydro-1*H*-azepine (12): A solution of dibromide **5c** (100 mg, 0.22 mmol) and potassium carbonate (30.4 mg, 0.22 mmol) in toluene (2.0 mL) was heated to 150 °C for 5 h under microwave irradiation. The brown solution was diluted with EtOAc (5.0 mL), filtered and concentrated under reduced pressure to afford a brown oil. Purification by flash column chromatography (9:1 hexane:Et_2O) afforded **12** as a colourless oil (47.7 mg, 0.13 mmol, 59%). R_f: 0.31 (9:1 hexane:Et_2O). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO_2), 7.35 – 7.28 (m, 3H, 2 × *meta*-SO_2 and NCH=), 6.13 (dddd, *J* = 11.4, 3.3, 1.6, 0.6 Hz, 1H, CBrC*H*CH), 5.61 – 5.63 (m, 1H, CBrCHC*H*), 4.00 – 3.91 (m, 1H, NC*H*CH_2), 2.49 (dddd, *J* = 16.9, 8.6, 4.8, 0.7 Hz, 1H, 1 × CH_2), 2.42 (s, 3H, Ar-CH_3), 1.48 (dh, *J* = 10.7, 6.6 Hz, 1H, C*H*$(CH_3)_2$), 1.38 – 1.27 (m, 1H, 1 × CH_2), 0.92 (d, *J* = 6.6 Hz, 3H, 1 × CH(C*H*$_3)_2$), 0.78 (d, *J* = 6.6 Hz, 3H, 1 × CH(C*H*$_3)_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.2 (*para*-SO_2), 134.9 (*ipso*-SO_2), 131.4 (CBr*C*HCH), 130.0 (2 × *meta*-SO_2), 128.3 (CBrCH*C*H), 127.3 (2 × *ortho*-SO_2), 125.8 (NCH=), 103.1 (CBr), 61.0 (N*C*HCH_2), 32.4 (CH_2), 27.6 (*C*H$(CH_3)_2$) 21.6 (Ar-CH_3), 19.7 (1 × CH(*C*H$_3)_2$), 18.3 (1 × CH(*C*H$_3)_2$). m/z (ES+) (Found: $[M+H]^+$, 370.0463. $C_{16}H_{20}NO_2SBr$ requires $[M+H]^+$, 370.0471). m/z (ES+) (Found: $[M+H]^+$, 370.0463. $C_{16}H_{20}NO_2SBr$ requires $[M+H]^+$, 370.0471). $[\alpha]_D^{24.9}$ +212 (c 1.33 g/100 mL, CH_2Cl_2).



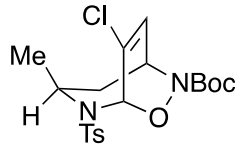
(5*R*,7*S*,9*S*)-12-Chloro-7-methyl-2-phenyl-6-tosyl-6,7,8,9-tetrahydro-1*H*,5*H*-5,9-etheno[1,2,4]triazolo[1,2-*a*][1,2,4]triazepine-1,3(2*H*)-dione (15): To a solution of chloride **6** (20.0 mg, 0.067 mmol) in CH_2Cl_2 (400 µL) was added 4-phenyl- 1,2,4-triazoline-3,5-dione (13.0 mg, 0.074 mmol). The reaction mixture turned bright red and the red colour faded as the reaction proceeded. After 5 minutes stirring at r.t, the reaction mixture was concentrated to afford **15** as a colourless solid (30.8 mg, 0.065 mmol, 97%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO_2), 7.51 – 7.35 (m, 5H, Ph), 7.29 (d, *J* = 8.0 Hz, 2H, 2 × *meta*-SO_2), 6.70 (t, *J* = 1.0 Hz, 1H, NCHN), 6.48 (dd, *J* = 7.0, 1.4 Hz, 1H, ClC=CH), 5.00 (td, *J* = 6.8, 1.4 Hz, 1H, =CHC*H*), 4.31 (p, *J* = 7.5 Hz, 1H, NC*H*CH_3), 2.42 (s, 3H, Ar-CH_3), 2.28 (ddd, *J* = 15.3, 7.8, 1.4 Hz, 1H, 1 × CH_2), 2.10 (ddd, *J* = 15.2, 6.7, 1.3 Hz, 1H, 1 × CH_2), 1.46 (d, *J* = 7.3 Hz, 3H, NCHC*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.6 (1 × CO), 150.6 (1 × CO), 144.3 (*para*-SO_2), 136.8 (*ipso*-SO_2), 131.1 (*ipso*-N),

130.2 (=CCl), 129.7 (2 × *meta*-SO_2), 129.2 (2 × *meta*-N), 128.4 (*para*-N), 127.4 (2 × *ortho*-SO_2), 127.1 (ClC=*C*H), 125.2 (2 × *ortho*-N), 68.3 (N_2CH), 49.5 (=CH*C*H), 48.7 (N*C*HCH$_3$), 39.4 (CH_2), 24.7 (NCH*C*H$_3$), 21.6 (Ar-CH_3). ν_{max} 3090, 2963, 1718, 1595, 1495, 1402, 1342, 1163, 1014 cm^{-1}. m/z (ES+) (Found: $[M+H]^+$ 473.1042. $C_{22}H_{21}N_4O_4SCl$ requires $[M+H]^+$, 473.1050). M.p. 194 – 195 °C. $[\alpha]_D^{24.8}$ -310 (c 0.09 g/100 mL, CH_2Cl_2).

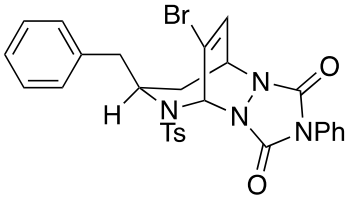


(5*R*,7*S*,9*S*)-7-Benzyl-12-chloro-2-phenyl-6-tosyl-6,7,8,9-tetrahydro-1*H*,5*H*-5,9- etheno[1,2,4]triazolo[1,2-*a*][1,2,4]triazepine-1,3(2*H*)-dione (16): A solution of dichloride **2f/3f** (82.1 mg, 0.20 mmol) and potassium carbonate (27.6 mg, 0.20 mmol) in toluene (2.0 mL) was heated to 150 °C for 5 h under microwave irradiation. The brown solution was diluted with EtOAc (5.0 mL), filtered and concentrated under reduced pressure to afford a brown oil. Purification by flash column chromatography (9:1 pentane: Et_2O) afforded a pale yellow oil, which was dissolved in CH_2Cl_2 (300 µL). 4-Phenyl-1,2,4- triazoline-3,5-dione (7.7 mg, 0.044 mmol) was added. The reaction mixture turned bright red and the red colour faded as the reaction proceeded. After 5 minutes stirring at r.t, the reaction mixture was concentrated and purification by flash column chromatography (6:4 Et_2O:pentane) afforded **16** as a colourless solid (18.3 mg, 0.033 mmol, 83% over 2 steps based on conversion of **3f**). R_f: 0.26 (6:4 Et_2O:pentane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.4 Hz, 2H, 2 × *ortho*-SO_2), 7.50 – 7.32 (m, 8H, 5 × N-Ph, 2 × *meta*-CH_2 and *para*-CH_2), 7.28 (d, *J* = 7.7 Hz, 2H, 2 × *meta*-SO_2), 7.22 – 7.17 (m, 2H, 2 × *ortho*-CH_2), 6.76 (s, 1H, N_2CH), 6.60 (dd, *J* = 7.0, 1.4 Hz, 1H, ClC=CH), 4.99 (td, *J* = 7.0, 1.2 Hz, 1H, =CHC*H*CH_2), 4.27 (ddd, *J* = 11.7, 7.8, 4.0 Hz, 1H, NC*H*$(CH_2)_2$), 3.26 (dd, *J* = 13.4, 3.9 Hz, 1H, 1 × Ar-CH_2), 3.03 (dd, *J* = 13.4, 11.5 Hz, 1H, 1 × Ar-CH_2), 2.41 (s, 3H, CH_3), 2.20 (dd, *J* = 15.6, 6.9 Hz, 1H, 1 × =CHCHC*H*$_2$), 1.92 (dd, *J* = 15.5, 7.9 Hz, 1H, 1 × =CHCHC*H*$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.5 (1 × CO), 150.6 (1 × CO), 144.4 (*para*-SO_2), 138.1 (*ipso*-CH_2), 136.7 (*ipso*-SO_2), 131.0 (*ipso*-N), 130.3 (CCl), 129.8 (2 × *meta*-SO_2), 129.3 (2 × *ortho*-CH_2), 129.2 (2 × *meta*-N), 128.9 (2 × *meta*-CH_2), 128.5 (*para*-N), 127.4 (2 × *ortho*-SO_2 and ClC=*C*H), 127.1 (*para*-CH_2), 125.2 (2 × *ortho*-N), 68.3 (N_2CH), 55.2 (N*C*H$(CH_2)_2$), 49.4 (=CH*C*HCH_2), 43.6 (Ar-CH_2), 34.2 (=CHCH*C*H_2), 21.6 (CH_3). ν_{max} 3030, 2960, 1718, 1595, 1454, 1349, 1163,

1096 cm^{-1}. An accurate mass spectrum could not be generated for this compound by either ES or EI. M.p. 101 – 102 °C. $[\alpha]_D^{24.3}$ +6.5 (c 0.31 g/100 mL, CH_2Cl_2).

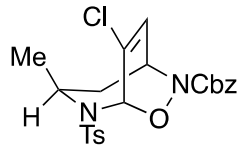


***tert*-Butyl (1*S*,3*S*,5*S*)-8-chloro-3-methyl-2-tosyl-7-oxa-2,6-diazabicyclo[3.2.2]non-8-ene-6-carboxylate (17)**: To a solution of chloride **6** (18.0 mg, 0.064 mmol) in CH_2Cl_2 (300 µL) was added *tert*-butyl hydroxycarbamate (18.8 mg, 0.141 mmol) and Bu_4NIO_4 (55.5 mg, 0.128 mmol). The reaction mixture was stirred at r.t for 18 h then concentrated under reduced pressure. Purification by flash column chromatography (6:4 pentane:Et_2O) afforded **17** as a colourless solid (20.1 mg, 0.047 mmol, 73%). R_f: 0.23 (6:4 Et_2O:pentane). ^1H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO_2), 7.29 (d, *J* = 7.7 Hz, 2H, 2 × *meta*-SO_2), 6.49 (dd, *J* = 7.5, 1.6 Hz, 1H, ClC=CH), 6.34 (s, 1H, OCH), 4.93 (t, *J* = 6.9 Hz, 1H, =CHC*H*CH_2), 3.94 – 3.86 (m, 1H, NC*H*CH_3), 2.41 (s, 3H, Ar-CH_3), 2.02 (ddd, *J* = 15.1, 7.9, 1.5 Hz, 1H, 1 × CH_2), 1.85 (ddd, *J* = 15.0, 6.5, 1.1 Hz, 1H, 1 × CH_2), 1.46 (s, 9H, $C(CH_3)_3$), 1.39 (d, *J* = 7.3 Hz, 3H, NCHC*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.4 (CO_2), 143.7 (*para*-SO_2), 136.3 (*ipso*-SO_2), 129.6 (2 × *meta*-SO_2), 129.4 (CCl), 128.1 (2 × *ortho*-SO_2), 127.6 (ClC=*C*H), 85.0 (OCH), 82.5 (*C*$(CH_3)_3$), 52.3 (=CH*C*HCH$_2$), 47.7 (N*C*HCH$_3$), 38.8 (CH_2), 28.2 (C(*C*H_3)$_3$), 23.7 (NCH*C*H$_3$), 21.6 (Ar-CH_3). ν_{max} 2978, 1722, 1648, 1599, 1353, 1163, 1111, 992 cm^{-1}. m/z (ES+) (Found: $[M+Na]^+$ 451.1082. $C_{22}H_{23}N_2O_5SCl$ requires $[M+Na]^+$, 451.1070). M.p. 70 – 71 °C. $[\alpha]_D^{23.8}$ +200 (c 0.01 g/100 mL, CH_2Cl_2).



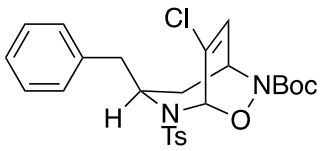
(5*R*,7*S*,9*S*)-7-Benzyl-12-bromo-2-phenyl-6-tosyl-6,7,8,9-tetrahydro-1*H*,5*H*-5,9-etheno[1,2,4]triazolo[1,2-*a*][1,2,4]triazepine-1,3(2*H*)-dione (18): A solution of dibromide **4f/5f** (120 mg, 0.24 mmol) and potassium carbonate (33.2 mg, 0.24 mmol) in toluene (2.0 mL) was heated to 150 °C for 5 h under microwave irradiation. The brown solution was diluted with EtOAc (5.0 mL), filtered and concentrated under reduced pressure to afford a brown oil. Purification by flash column chromatography (9:1 pentane: Et_2O) afforded a pale yellow oil, which was dissolved in CH_2Cl_2 (300 µL). 4-Phenyl-1,2,4- triazoline-3,5-dione was added until the red colour of the reaction mixture persisted. The reaction mixture was concentrated under reduced pressure and

purification by flash column chromatography (1:1 pentane:Et_2O) afforded **18** as a colourless solid (49.6 mg, 0.084 mmol, 88% over 2 steps based on conversion of **5f**). R_f: 0.22 (1:1pentane:Et_2O). ^1H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO_2), 7.51 – 7.31 (m, 8H, 2 × *meta*-CH_2, *para*-CH_2, 5 × N-Ph), 7.28 (d, *J* = 7.9 Hz, 2H, 2 × *meta*-SO_2), 7.22 – 7.17 (m, 2H, 2 × *ortho*-CH_2), 6.83 (dd, *J* = 7.0, 1.2 Hz, 1H, BrC=CH), 6.81 (s, 1H, CHN_2), 4.95 (t, *J* = 6.8 Hz, 1H, =CHC*H*CH_2), 4.27 (ddd, *J* = 11.6, 7.8, 3.9 Hz, 1H, NC*H*$(CH_2)_2$), 3.27 (dd, *J* = 13.5, 3.8 Hz, 1H, 1 × Ar-CH_2), 3.07 (dd, *J* = 13.4, 11.5 Hz, 1H, 1 × Ar-CH_2), 2.41 (s, 3H, CH_3), 2.20 (dd, *J* = 15.6, 6.9 Hz, 1H, 1 × =CHCHC*H*$_2$), 1.91 (dd, *J* = 15.6, 7.9 Hz, 1H, 1 × =CHCHC*H*$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.6 (1 × CO), 150.7 (1 × CO), 144.4 (*para*-SO_2), 138.2 (*ipso*-CH_2), 136.8 (*ipso*-SO_2), 131.9 (BrC=*C*H), 131.1 (*ipso*-N), 129.8 (2 × *meta*-SO_2), 129.4 (2 × *ortho*-CH_2), 129.2 (2 × *meta*-N), 129.0 (2 × *meta*-CH_2), 128.5 (*para*-N), 127.4 (2 × *ortho*- SO_2), 127.1 (*para*-CH_2), 125.2 (2 × *ortho*-N), 117.8 (CBr), 69.8 (CHN_2), 55.3 (N*C*H$(CH_2)_2$), 50.4 (=CH*C*HCH_2), 43.7 (Ar-CH_2), 34.1 (=CHCH*C*H_2), 21.6 (CH_3). ν_{max} 3063, 2926, 1774, 1710, 1621, 1498, 1402, 1349, 1163 cm^{-1}. m/z (ES+) (Found: $[M+H]^+$ 593.0866. $C_{28}H_{25}N_4O_4SBr$ requires $[M+H]^+$, 593.0858). M.p. 108 – 110 °C. $[\alpha]_D^{24.7}$ -310 (c 0.09 g/100 mL, CH_2Cl_2).

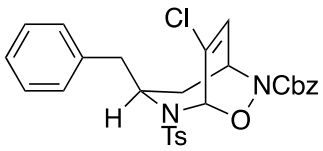


Benzyl (1*S*,3*S*,5*S*)-8-chloro-3-methyl-2-tosyl-7-oxa-2,6-diazabicyclo[3.2.2]non-8-ene-6-carboxylate (19): To a solution of chloride **6** (18.0 mg, 0.064 mmol) in CH_2Cl_2 (300 µL) was added benzyl hydroxycarbamate (23.6 mg, 0.141 mmol) and Bu_4NIO_4 (55.5mg, 0.128 mmol). The reaction mixture was stirred at r.t for 18 h then concentrated under reduced pressure. Purification by flash column chromatography (6:4 pentane:Et_2O) afforded **19** as a colourless solid (17.3 mg, 0.037 mmol, 58%). R_f: 0.16 (6:4 pentane:Et_2O). ^1H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.2 Hz, 2H, 2 × *ortho*-SO_2), 7.45 – 7.34 (m, 5H, 5 × Ph), 7.13 (d, *J* = 8.0 Hz, 2H, 2 × *meta*-SO_2), 6.47 (dd, *J* = 7.6, 1.6 Hz, 1H, ClC=CH), 6.37 (s, 1H, OCH), 5.20 (d, *J* = 12.3 Hz, 1H, 1 × OCH_2), 5.15 (d, *J* = 12.3 Hz, 1H, 1 × OCH_2), 5.02 (t, *J* = 6.7 Hz, 1H, =CHC*H*CH_2), 3.92 (p, *J* = 7.4 Hz, 1H, NC*H*CH_3), 2.36 (s, 3H, Ar-CH_3), 2.00 (dd, *J* = 15.1, 8.0 Hz, 1H, 1 × NCHC*H*$_2$), 1.84 (dd, *J* = 15.1, 6.1 Hz, 1H, 1 × NCHC*H*$_2$), 1.39 (d, *J* = 7.2 Hz, 3H, NCHC*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.9 (CO_2), 143.8 (*para*-SO_2), 136.0 (*ipso*-SO_2), 135.6 (*ipso*- CH_2), 129.8 (CCl), 129.5 (2 × *meta*-SO_2), 128.6 (2 × *meta*-CH_2), 128.5 (*para*-CH_2), 128.1 (2 × *ortho*-CH_2),

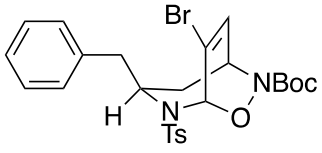
128.0 (2 × *ortho*-SO_2), 127.1 (ClC=*C*H), 85.3 (OCH), 68.1 (OCH_2), 52.3 (=CH*C*HCH_2), 47.7 (N*C*HCH$_3$), 39.2 (NCH*C*H$_2$), 23.7 (NCH*C*H$_3$), 21.6 (Ar-CH_3). ν_{max} 3068, 2930, 1703, 1648, 1595, 1349, 1290, 1163, 1103, 988 cm^{-1}. m/z (ES+) (Found: $[M+Na]^+$ 485.0915. $C_{22}H_{23}N_2O_5SCl$ requires $[M+Na]^+$, 485.0914). M.p. 50 – 54 °C. $[\alpha]_D^{21.1}$ -36.2 (c 1.27 g/100 mL, CH_2Cl_2).



***tert*-Butyl (1*S*,3*S*,5*S*)-3-benzyl-8-chloro-2-tosyl-7-oxa-2,6-diazabicyclo[3.2.2]non-8-ene-6-carboxylate (20)**: A solution of dichloride **2f/3f** (82.1 mg, 0.20 mmol) and potassium carbonate (27.6 mg, 0.20 mmol) in toluene (2.0 mL) was heated to 150 °C for 5 h under microwave irradiation. The brown solution was diluted with EtOAc (5.0 mL), filtered and concentrated under reduced pressure to afford a brown oil. Purification by flash column chromatography (9:1 pentane: Et_2O) afforded a pale yellow oil, which was dissolved in CH_2Cl_2 (300 µL). *tert*-Butyl hydroxycarbamate (11.7 mg, 0.088 mmol) and Bu_4NIO_4 (34.7 mg, 0.080 mmol) was added and the reaction mixture was stirred at r.t for 18 h then concentrated under reduced pressure. Purification by flash column chromatography (8:2 pentane:Et_2O) afforded **20** as a colourless solid (11.4 mg, 0.023 mmol, 58% over 2 steps based on conversion of **3f**). R_f: 0.22 (8:2 pentane:Et_2O). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.4 Hz, 2H, 2 × *ortho*-SO_2), 7.34 – 7.20 (m, 5H, 2 × *meta*-SO_2, 2 × *meta*-CH_2 and *para*-CH_2), 7.18 – 7.11 (m, 2H, 2 × *ortho*-CH_2), 6.61 (dd, *J* = 7.5, 1.6 Hz, 1H, ClC=CH), 6.43 (s, 1H, OCH), 4.89 (t, *J* = 7.0 Hz, 1H, =CHC*H*CH_2), 3.85 (ddd, *J* = 11.7, 7.9, 3.8 Hz, 1H, NC*H*$(CH_2)_2$), 3.19 (dd, *J* = 13.4, 3.7 Hz, 1H, 1 × Ar-CH_2), 3.00 (dd, *J* = 13.4, 11.6 Hz, 1H, 1 × Ar-CH_2), 2.39 (s, 3H, Ar-CH_3), 1.93 (dd, *J* = 15.3, 6.5 Hz, 1H, 1 × =CHCHC*H*$_2$), 1.65 (dd, *J* = 15.3, 7.9 Hz, 1H, 1 × =CHCHC*H*$_2$), 1.44 (s, 9H, C$(CH_3)_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.3 (CO_2), 143.8 (*para*-SO_2), 138.6 (*ipso*-CH_2), 136.2 (*ipso*- SO_2), 129.7 (2 × *meta*-SO_2 and CCl), 129.3 (2 × *ortho*-SO_2), 128.8 (2 × *meta*-SO_2), 128.2 (2 × *ortho*-SO_2), 127.8 (ClC=*C*H), 126.8 (*para*-CH_2), 85.0 (OCH), 82.5 (*C*$(CH_3)_3$), 54.4 (N*C*H$(CH_2)_2$), 52.3 (=CH*C*HCH$_2$), 42.6 (Ar-CH_2), 33.7 (=CHCH*C*H$_2$), 28.2 (C(*C*H$_3$)$_3$), 21.6 (Ar-CH_3). ν_{max} 2978, 1722, 1644, 1599, 1368, 1163, 1092, 1028 cm^{-1}. m/z (ES+) (Found: $[M+Na]^+$ 527.1390. $C_{25}H_{29}N_2O_5SCl$ requires $[M+Na]^+$, 527.1383). M.p. 68 – 69 °C. $[\alpha]_D^{25.2}$ -6.1 (c 0.33 g/100 mL, CH_2Cl_2).

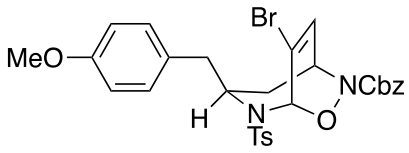


Benzyl (1*S*,3*S*,5*S*)-3-benzyl-8-chloro-2-tosyl-7-oxa-2,6-diazabicyclo[3.2.2]non-8-ene-6-carboxylate (21): A solution of dichloride **2f/3f** (82.1 mg, 0.20 mmol) and potassium carbonate (27.6 mg, 0.20 mmol) in toluene (2.0 mL) was heated to 150 °C for 5 h under microwave irradiation. The brown solution was diluted with EtOAc (5.0 mL), filtered and concentrated under reduced pressure to afford a brown oil. Purification by flash column chromatography (9:1 pentane:Et_2O) afforded a pale yellow oil, which was dissolved in CH_2Cl_2 (300 µL). Benzyl hydroxycarbamate (14.7 mg, 0.088 mmol) and Bu_4NIO_4 (34.7 mg, 0.080 mmol) was added and the reaction mixture was stirred at r.t for 18 h then concentrated under reduced pressure. Purification by flash column chromatography (8:2 pentane:Et_2O) afforded **21** as a colourless solid (11.4 mg, 0.021 mmol, 52% over 2 steps based on conversion of **3f**). R_f: 0.22 (8:2 pentane:Et_2O). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO_2), 7.42 – 7.34 (m, 5H, OCH_2*Ph*), 7.32 – 7.28 (m, 2H, 2 × *meta*-CH_2CH), 7.25 – 7.19 (m, 1H, *para*-CH_2CH), 7.17 – 7.11 (m, 4H, 2 × *meta*-SO_2 and 2 × *ortho*-CH_2CH), 6.59 (dd, *J* = 7.6, 1.6 Hz, 1H, ClC=CH), 6.45 (s, 1H, OCH), 5.18 (d, *J* = 12.3 Hz, 1H, 1 × OCH_2), 5.13 (d, *J* = 12.2 Hz, 1H, 1 × OCH_2), 5.00 (t, *J* = 6.3 Hz, 1H, =CHC*H*CH_2), 3.86 (ddd, *J* = 11.7, 8.0, 3.8 Hz, 1H, NC*H*$(CH_2)_2$), 3.18 (dd, *J* = 13.4, 3.7 Hz, 1H, 1 × Ar-C*H*$_2$CH), 3.00 (dd, *J* = 13.4, 11.5 Hz, 1H, 1 × Ar-C*H*$_2$CH), 2.35 (s, 3H, CH_3), 1.93 (dd, *J* = 15.4, 6.3 Hz, 1H, 1 × =CHCHC*H*$_2$), 1.64 (dd, *J* = 15.3, 8.2 Hz, 1H, 1 × =CHCHC*H*$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.9 (CO_2), 143.9 (*para*-SO_2), 138.5 (*ipso*-CH_2CH), 136.0 (*ipso*-SO_2), 135.6 (*ipso*-OCH_2), 130.0 (CCl), 129.6 (2 × *meta*-SO_2), 129.3 (2 × *ortho*-CH_2CH), 128.8 (2 × *meta*-CH_2CH), 128.6 (2 × *meta*-OCH_2), 128.5 (*para*-OCH_2), 128.1 (2 × *ortho*- SO_2), 128.1 (2 × *ortho*-OCH_2), 127.5 (=CH), 126.8 (*para*-CH_2CH), 85.3 (OCH), 68.2 (OCH_2), 54.3 (N*C*H$(CH_2)_2$), 52.3 (=CH*C*HCH_2), 42.6 (Ar-*C*H$_2$CH), 34.1 (=CHCH*C*H$_2$), 21.5 (CH_3). ν_{max} 3064, 2922, 1703, 1599, 1498, 1454, 1353, 1290, 1163, 1092, 1029 cm^{-1}. m/z (ES+) (Found: $[M+Na]^+$ 561.1230. $C_{28}H_{27}N_2O_5SCl$ requires $[M+Na]^+$, 561.1227). M.p. 72 – 74 °C. $[\alpha]_D^{23.8}$ -3.3 (c 0.60 g/100 mL, CH_2Cl_2).



***tert*-Butyl (1*S*,3*S*,5*S*)-3-benzyl-8-bromo-2-tosyl-7-oxa-2,6-diazabicyclo[3.2.2]non-8-ene-6-carboxylate (22)**: A

solution of dibromide **4f/5f** (375 mg, 0.77 mmol) and potassium carbonate (106 mg, 0.77 mmol) in toluene (5.0 mL) was heated to 150 °C for 5 h under microwave irradiation. The brown solution was diluted with EtOAc (5.0 mL), filtered and concentrated under reduced pressure to afford a brown oil. Purification by flash column chromatography (9:1 pentane:Et_2O) afforded a yellow oil that was dissolved in CH_2Cl_2 (700 µL). Benzyl hydroxycarbamate (225 mg, 1.69 mmol) and Bu_4NIO_4 (667 mg, 1.54 mmol) was added and the reaction mixture was stirred at r.t for 18 h, then concentrated under reduced pressure. Purification by flash column chromatography (9:1 pentane:EtOAc) afforded **22** as a colourless solid (114 mg, 0.21 mmol, 68% over 2 steps based on conversion of **5f**). R_f: 0.17 (9:1 pentane:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.4 Hz, 2H, 2 × *ortho*-SO_2), 7.34 – 7.21 (m, 5H, 2 × *meta*-SO_2, 2 × *meta*-CH_2 and *para*-CH_2), 7.18 – 7.11 (m, 2H, 2 × *ortho*-CH_2), 6.85 (dd, *J* = 7.5, 1.5 Hz, 1H, =C*H*CHCH$_2$), 6.48 (s, 1H, NCHO), 4.86 (t, *J* = 6.9 Hz, 1H, =CHC*H*CH$_2$), 3.85 (ddd, *J* = 11.6, 7.8, 3.8 Hz, 1H, NC*H*(CH_2)$_2$), 3.20 (dd, *J* = 13.4, 3.7 Hz, 1H, 1 × Ar-CH_2), 3.04 (dd, *J* = 13.4, 11.6 Hz, 1H, 1 × Ar-CH_2), 2.39 (s, 3H, Ar-CH_3), 1.93 (dd, *J* = 15.4, 6.6 Hz, 1H, 1 × =CHCHC*H*$_2$), 1.65 (dd, *J* = 15.4, 7.9 Hz, 1H, 1 × =CHCHC*H*$_2$), 1.45 (s, 9H, C(CH_3)$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.5 (CO_2), 143.8 (*para*-SO_2), 138.7 (*ipso*-CH_2), 136.2 (*ipso*- SO_2), 132.6 (=*C*HCHCH$_2$), 129.7 (2 × *meta*-SO_2), 129.3 (2 × *ortho*-CH_2), 128.8 (2 × *meta*- CH_2), 128.2 (2 × *ortho*-SO_2), 126.8 (*para*-CH_2), 117.6 (CBr), 86.4 (NCHO), 82.5 (*C*(CH_3)$_3$), 54.5 (N*C*H(CH_2)$_2$), 53.5 (=CH*C*HCH$_2$), 42.6 (Ar-CH_2), 33.6 (=CHCH*C*H$_2$), 28.2 (C(*C*H$_3$)$_3$), 21.6 (Ar-CH_3). ν_{max} 3064, 2978, 1718, 1599, 1349, 1245, 1159, 1088 cm^{-1}. m/z (ES+) (Found: [M+Na]$^+$, 571.0882. $C_{25}H_{29}N_2O_5SBr$ requires [M+Na]$^+$, 571.0878). M.p. 85 – 86 °C. $[\alpha]_D^{23.5}$ -44 (c 0.09 g/100 mL, CH_2Cl_2).

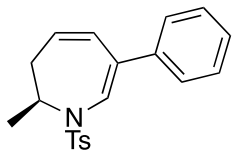


Benzyl (1*S*,3*S*,5*S*)-8-bromo-3-(4-methoxybenzyl)-2-tosyl-7-oxa-2,6-diazabicyclo[3.2.2]non-8-ene-6-carboxylate (23): A solution of dibromide **4g/5g** (93.0 mg, 0.185 mmol) and potassium carbonate (25.6 mg, 0.185 mmol) in toluene (3.0 mL) was heated to 150 °C for 5 h under microwave irradiation. The brown solution was diluted with EtOAc (5.0 mL), filtered and concentrated under reduced pressure to afford a brown oil. This was dissolved in CH_2Cl_2 (400 µL) and benzyl hydroxycarbamate (44.0 mg, 0.264 mmol) and Bu_4NIO_4 (104 mg, 0.240 mmol) were added. The reaction mixture was stirred at r.t for 20 min

then concentrated under reduced pressure. Purification by flash column chromatography (6:4 pentane:Et_2O) afforded **23** as a colourless solid (24.9 mg, 0.057 mmol, 77% over 2 steps based on conversion of **5g**). R_f: 0.15 (6:4 pentane:Et_2O). ^1H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO_2), 7.42 – 7.32 (m, 5H, 5 × Ph), 7.14 (d, *J* = 8.0 Hz, 2H, 2 × *meta*-SO_2), 7.06 (d, *J* = 8.5 Hz, 2H, 2 × *meta*-OCH_3), 6.87 – 6.78 (m, 3H, 2 × *ortho*-OCH_3 and BrC=CH), 6.50 (s, 1H, OCH), 5.18 (d, *J* = 12.3 Hz, 1H, 1 × OCH_2), 5.14 (d, *J* = 12.3 Hz, 1H, 1 × OCH_2), 4.97 (t, *J* = 7.2 Hz, 1H, =CHC*H*CH_2), 3.87 – 3.79 (m, 1H, NC*H*$(CH_2)_2$), 3.78 (s, 3H, OCH_3), 3.13 (dd, *J* = 13.6, 3.7 Hz, 1H, 1 × ArC*H*$_2$CH), 2.97 (dd, *J* = 13.6, 11.4 Hz, 1H, 1 × ArC*H*$_2$CH), 2.35 (s, 3H, Ar-CH_3), 1.95 (dd, *J* = 15.4, 6.4 Hz, 1H, 1 × =CHCHC*H*$_2$), 1.68 – 1.58 (m, 1H, 1 × =CHCHC*H*$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.4 (*ipso*-OCH_3), 155.0 (CO_2), 143.9 (*para*-SO_2), 136.0 (*ipso*-SO_2), 135.5 (*ipso*-Ph), 132.1 (BrC=*C*H), 130.5 (*para*-OCH_3), 130.2 (2 × *meta*-OCH_3), 129.6 (2 × *meta*-SO_2), 128.6 (2 × *meta*-Ph), 128.4 (*para*-Ph), 128.1 (2 × *ortho*-Ph), 128.0 (2 × *ortho*-SO_2), 117.8 (Br*C*=CH), 114.2 (2 × *ortho*-OCH_3), 86.7 (OCH), 68.1 (OCH_2), 55.2 (OCH_3), 54.6 (N*C*H$(CH_2)_2$), 53.4 (=CH*C*HCH_2), 41.8 (Ar*C*H$_2$CH), 33.9 (=CHCH*C*H$_2$), 21.5 (Ar-CH_3). ν_{max} 3090, 2945, 1715, 1610, 1513, 1443, 1286, 1249, 1156, 1088 cm^{-1}. m/z (ES+) (Found: $[M+Na]^+$, 635.0835. $C_{29}H_{29}N_2O_6SBr$ requires $[M+Na]^+$, 635.0827). M.p. 144 – 145 °C. $[\alpha]_D^{24.8}$ -17 (c 0.12 g/100 mL, CH_2Cl_2).

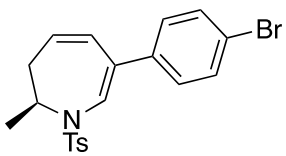
General Procedure 2 – Suzuki Coupling

To a solution of dihydroazepine (1.0 equiv), boronic acid (1.1 equiv.) and Cs_2CO_3 (2.0 equiv.) in 1,4-dioxane:water (5:1, 20 mL/mmol) was added $Pd(PPh_3)_4$ (0.05 equiv.) and the reaction mixture was heated to 85 °C for 1 h. Upon cooling to r.t, the reaction mixture was diluted with water (20 mL/mmol) and EtOAc (20 mL/mmol) and the layers separated. The aqueous layer was extracted thrice with EtOAc and the combined organic layers were washed with brine, dried (Na_2SO_4), filtered and concentrated under reduced pressure. Purification by flash column chromatography was employed where appropriate.

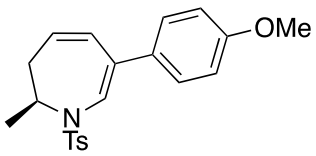


(*S*)-2-Methyl-6-phenyl-1-tosyl-2,3-dihydro-*1H*-azepine (24): Following **general procedure 2**, bromide **10** (39 mg, 0.11 mmol)

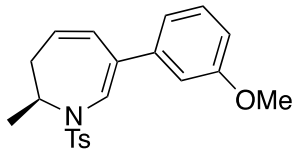
and phenylboronic acid (15 mg, 0.13 mmol) were subjected to Suzuki coupling conditions. Purification by flash column chromatography (9:1 pentane:Et_2O) afforded **24** as a colourless oil (30 mg, 0.09 mmol, 77%). R_f: 0.29 (9:1 pentane:Et_2O). ^1H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO_2), 7.38 – 7.22 (m, 7H, Ph and 2 × *meta*-SO_2), 7.08 (s, 1H, $NCHC_q$), 6.23 (ddd, *J* = 11.4, 3.1, 1.3 Hz, 1H, $NCHC_qCH$), 5.81 – 5.72 (m, 1H, $NCHCH_2CH$), 4.64 – 4.53 (m, 1H, $NCHCH_3$), 2.42 (s, 3H, Ar-CH_3), 2.34 (ddd, *J* = 17.0, 8.3, 4.4 Hz, 1H, 1 × CH_2), 1.96 (dq, *J* = 17.0, 3.2 Hz, 1H, 1 × CH_2), 0.98 (d, *J* = 6.8 Hz, 3H, $NCHCH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.9 (*para*-SO_2), 143.1 (*ipso*-Ph), 135.7 (*ipso*-SO_2), 129.9 (2 × *meta*-SO_2), 128.6 ($NCHC_qCH$), 128.3 (2 × *ortho*-Ph), 127.5 ($NCHCH_2CH$), 127.2 (2 × *ortho*-SO_2 and 2 × *meta*-Ph), 126.5 (*para*-Ph), 124.9 ($NCHC_q$), 121.2 ($NCHC_q$), 50.6 ($NCHCH_3$), 36.2 (CH_2), 21.6 (Ar-CH_3), 17.7 ($NCHCH_3$). ν_{max} 3030, 2930, 1592, 1346, 1163, 1092 cm^{-1}. m/z (CI+) (Found: $[M+H]^+$, 340.1360. $C_{20}H_{21}NO_2S$ requires $[M+H]^+$, 340.1366). $[\alpha]_D^{23.3}$ +160 (c 0.11 g/100 mL, CH_2Cl_2).



(*S*)-6-(4-Bromophenyl)-2-methyl-1-tosyl-2,3-dihydro-1*H*-azepine (25): Following **general procedure 2**, bromide **10** (50 mg, 0.15 mmol) and 4-bromophenylboronic acid (32 mg, 0.16 mmol) were subjected to Suzuki coupling conditions. Purification by flash column chromatography (9:1 hexane:EtOAc) afforded **25** as a pale yellow oil (33 mg, 0.08 mmol, 53%). R_f: 0.27 (9:1 hexane:EtOAc). ^1H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO_2), 7.45 (d, *J* = 8.5 Hz, 2H, 2 × *ortho*-Br), 7.31 (d, *J* = 8.2 Hz, 2H, 2 × *meta*-SO_2), 7.21 (d, *J* = 8.5 Hz, 2H, 2 × *meta*- Br), 7.07 (s, 1H, $NCHC_q$), 6.15 (ddd, *J* = 11.4, 3.1, 1.4 Hz, 1H, $CHCHCH_2$), 5.82 – 5.72 (m, 1H, $CHCHCH_2$), 4.63 – 4.52 (m, 1H, $NCHCH_3$), 2.42 (s, 3H, Ar-CH_3), 2.39 – 2.29 (m, 1H, 1 × CH_2), 2.02 – 1.83 (m, 1H, 1 × CH_2), 0.96 (d, *J* = 6.4 Hz, 3H, $CHCH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.0 (*para*-SO_2), 142.1 (*para*-Br), 135.5 (*ipso*-SO_2), 131.4 (2 × *ortho*-Br), 129.9 (2 × *meta*-SO_2), 128.8 (2 × *meta*-Br), 128.1 ($CHCHCH_2$), 127.8 ($CHCHCH_2$), 127.2 (2 × *ortho*-SO_2), 125.1 ($NCHC_q$), 120.4 (*ipso*-Br), 119.7 ($NCHC_q$), 50.7 ($NCHCH_3$), 36.1 (CH_2), 21.6 (Ar-CH_3), 17.8 ($NCHCH_3$). ν_{max} 3064, 2922, 1592, 1346, 1163, 1092 cm^{-1}. m/z (CI+) (Found: $[M+H]^+$, 418.0481. $C_{20}H_{20}NO_2SBr$ requires $[M+H]^+$, 418.0471). $[\alpha]_D^{24.2}$ +61 (c 0.33 g/100 mL, CH_2Cl_2).

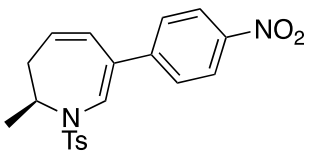


(*S*)-6-(4-Methoxyphenyl)-2-methyl-1-tosyl-2,3-dihydro-1*H*-azepine (26): Following **general procedure 2**, bromide **10** (40 mg, 0.12 mmol) and 4-methoxyphenylboronic acid (20 mg, 0.13 mmol) were subjected to Suzuki coupling conditions. Purification by flash column chromatography (9:1 pentane:Et_2O) afforded **26** as a colourless oil (34 mg, 0.09 mmol, 79%). R_f: 0.19 (9:1 pentane:Et_2O). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO_2), 7.30 (d, *J* = 8.4 Hz, 2H, 2 × *meta*-SO_2), 7.27 (d, *J* = 8.8 Hz, 2H, 2 × *meta*-OCH_3), 6.99 (s, 1H, $NCHC_q$), 6.88 (d, *J* = 8.7 Hz, 2H, 2 × *ortho*-OCH_3), 6.18 (ddd, *J* = 11.4, 3.0, 1.3 Hz, 1H, $NCHC_qCH$), 5.78 – 5.69 (m, 1H, $NCHCH_2CH$), 4.62 – 4.52 (m, 1H, $NCHCH_3$), 3.82 (s, 3H, OCH_3), 2.42 (s, 3H, Ar-CH_3), 2.32 (ddd, *J* = 17.0, 8.2, 4.4 Hz, 1H, 1 × CH_2), 1.95 (dq, *J* = 17.0, 3.4 Hz, 1H, 1 × CH_2), 0.97 (d, *J* = 6.8 Hz, 3H, $NCHCH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.5 (*ipso*-OCH_3), 143.8 (*para*-SO_2), 135.8 (*ipso*-SO_2), 135.6 (*para*-OCH_3), 129.8 (2 × *meta*-SO_2), 128.8 ($NCHC_qCH$), 128.3 (2 × *meta*-OCH_3), 127.4 ($NCHCH_2CH$), 127.2 (2 × *ortho*-SO_2), 123.9 ($NCHC_q$), 121.0 ($NCHC_q$), 113.7 (2 × *ortho*- OCH_3), 55.4 (OCH_3), 50.6 ($NCHCH_3$), 36.2 (CH_2), 21.6 (Ar-CH_3), 17.7 ($NCHCH_3$). ν_{max} 3030, 2930, 1592, 1510, 1342, 1245, 1163, 1092, 984 cm^{-1}. m/z (ES+) (Found: $[M+H]^+$ 370.1481. $C_{21}H_{23}NO_3S$ requires $[M+H]^+$, 370.1477). $[\alpha]_D^{24.6}$ +120 (c 0.05 g/100 mL, CH_2Cl_2).

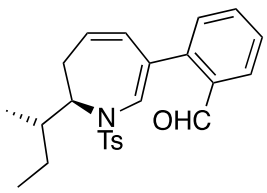


(*S*)-6-(3-Methoxyphenyl)-2-methyl-1-tosyl-2,3-dihydro-1*H*-azepine (27): Following **general procedure 2**, bromide **10** (34 mg, 0.10 mmol) and 3- methoxyphenylboronic acid (17 mg, 0.11 mmol) were subjected to Suzuki coupling conditions. Purification by flash column chromatography (9:1 pentane:Et_2O) afforded **27** as a colourless oil (27.7 mg, 0.075 mmol, 75%). R_f: 0.21 (9:1 pentane:Et_2O). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO_2), 7.30 (d, *J* = 8.4 Hz, 2H, 2 × *meta*-SO_2), 7.25 (t, *J* = 7.9 Hz, 1H, CH-*meta*-OCH_3), 7.09 (s, 1H, $NCHC_q$), 6.94 (ddd, *J* = 7.6, 1.8, 0.9 Hz, 1H, *para*-OCH_3), 6.87 (dd, *J* = 2.5, 1.7 Hz, 1H, OC_qCHC_q), 6.82 (ddd, *J* = 8.3, 2.6, 0.9 Hz, 1H, OC_qCHCH), 6.21 (ddd, *J* = 11.4, 3.1, 1.4 Hz, 1H, $NCHC_qCH$), 5.80 – 5.71 (m, 1H, $NCHCH_2CH$), 4.61 – 4.54 (m, 1H, $NCHCH_3$), 3.84 (s, 3H, OCH_3), 2.42 (s, 3H, Ar-CH_3), 2.33 (ddd, *J* = 16.9, 8.3, 4.4 Hz, 1H, 1 × CH_2), 1.95 (dq, *J* = 17.0, 3.3 Hz, 1H, 1 × CH_2), 0.97 (d, *J* = 6.8 Hz, 3H, $NCHCH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.6 (*ipso*-OCH_3), 144.6 (C_q-*meta*-OCH_3), 143.9 (*para*-SO_2), 135.7 (*ipso*-SO_2), 129.9 (2 × *meta*-SO_2),

129.3 (CH-*meta*-OCH_3), 128.6 ($NCHC_qCH$), 127.4 ($NCHCH_2CH$), 127.2 (2 × *ortho*-SO_2), 124.9 ($NCHC_q$), 121.0 ($NCHC_q$), 119.8 (*para*-OCH_3), 113.1 (OC_qCHC_q), 111.9 (OC_qCHCH), 55.3 (OCH_3), 50.6 ($NCHCH_3$), 36.2 (CH_2), 21.6 (Ar- CH_3), 17.7 ($NCHCH_3$). ν_{max} 3030, 2933, 1595, 1346, 1163, 1092, 1003 cm^{-1}. m/z (ES+) (Found: $[M+H]^+$ 370.1480. $C_{21}H_{23}NO_3S$ requires $[M+H]^+$, 370.1477). $[\alpha]_D^{24.6}$ +50 (c 0.04 g/100 mL, CH_2Cl_2).

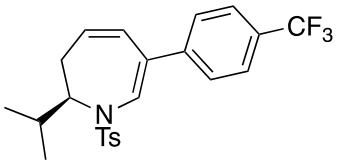


(*S*)-2-Methyl-6-(4-nitrophenyl)-1-tosyl-2,3-dihydro-1*H*-azepine (28): Following **general procedure 2**, bromide **10** (40.0 mg, 0.12 mmol) and 4-nitrophenylboronic acid (21.5 mg, 0.13 mmol) were subjected to Suzuki coupling conditions. Purification by flash column chromatography (9:1 hexane:EtOAc) afforded **28** as a yellow solid (33.6 mg, 0.087 mmol, 75%). R_f: 0.18 (9:1 hexane:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 8.8 Hz, 2H, 2 × *ortho*-NO_2), 7.69 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO_2), 7.48 (d, *J* = 8.8 Hz, 2H, 2 × *meta*-NO_2), 7.33 (d, *J* = 8.4 Hz, 2H, 2 × *meta*-SO_2), 7.26 (s, 1H, $NCHC_q$), 6.21 (ddd, *J* = 11.2, 3.2, 1.4 Hz, 1H, $CHCHCH_2$), 5.91 – 5.77 (m, 1H, $CHCHCH_2$), 4.62 – 4.52 (m, 1H, $NCHCH_3$), 2.44 (s, 3H, Ar-CH_3), 2.43 – 2.29 (m, 1H, 1 × CH_2), 1.92 (dq, *J* = 16.6, 3.0 Hz, 1H, 1 × CH_2), 0.98 (dd, *J* = 6.8, 0.8 Hz, 3H, $CHCH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.9 (*para*-NO_2), 146.3 (*ipso*-NO_2), 144.4 (*para*-SO_2), 135.1 (*ipso*-SO_2), 130.1 (2 × *meta*-SO_2), 128.4 ($CHCHCH_2$), 127.6 (2 × *meta*-NO_2), 127.3 ($CHCHCH_2$), 127.3 (2 × *ortho*-SO_2 and $NCHC_q$), 123.8 (2 × *ortho*-NO_2), 118.2 ($NCHC_q$), 51.0 ($NCHCH_3$), 36.0 (CH_2), 21.6 (Ar-CH_3), 18.0 ($CHCH_3$). ν_{max} 3075, 2922, 1580, 1513, 1338, 1167, 1092 cm^{-1}. m/z (CI+) (Found: $[M+H]^+$ 385.1204. $C_{20}H_{20}N_2O_4S$ requires $[M+H]^+$, 385.1217). M.p. 108 – 109 °C. $[\alpha]_D^{24.5}$ +80 (c 0.05 g/100 mL, CH_2Cl_2).



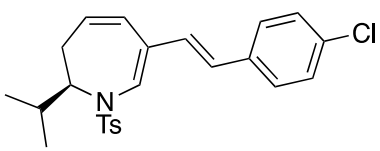
2-((*R*)-7-((*S*)-*sec*-Butyl)-1-tosyl-6,7-dihydro-1*H*-azepin-3-yl)benzaldehyde (29): Following **general procedure 2**, bromide **11** (25.0 mg, 0.065 mmol) and 2- formylphenylboronic acid (10.8 mg, 0.072 mmol) were subjected to Suzuki coupling conditions. Purification by flash column chromatography (8:2 hexane:Et_2O) afforded **29** as a pale yellow oil (23.2 mg, 0.057 mmol, 88%). R_f: 0.23 (8:2 hexane:Et_2O). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.01 (s, 1H, COH), 7.93 (dd, *J* = 7.8, 1.4 Hz, 1H, C*H*-*ortho*-

COH), 7.63 (d, *J* = 8.2 Hz, 2H, 2 × *ortho*-SO_2), 7.56 (td, *J* = 7.6, 1.6 Hz, 1H, C*H*-*para*-COH), 7.43 (t, *J* = 7.5 Hz, 1H, C*H*CHC_qCOH), 7.38 – 7.28 (m, 3H, 2 × *meta*-SO_2 and C*H*C_qC_qCOH), 6.89 (s, 1H, NCH=), 5.98 (ddd, *J* = 11.3, 3.2, 1.4 Hz, 1H, =C*H*$CHCH_2$), 5.73 (ddd, *J* = 11.4, 8.4, 3.4 Hz, 1H, =CHC*H*CH_2), 4.19 (dt, *J* = 10.8, 2.8 Hz, 1H, NC*H*CH_2), 2.61 (ddd, *J* = 16.9, 8.4, 4.6 Hz, 1H, 1 × NCHC*H*$_2$), 2.43 (s, 3H, Ar-CH_3), 1.68 (dtd, *J* = 15.1, 7.6, 3.1 Hz, 1H, 1 × C*H*$_2CH_3$), 1.56 – 1.37 (m, 2H, 1 × NCHC*H*$_2$ and C*H*CH_3), 1.13 (ddt, *J* = 14.0, 9.1, 7.1 Hz, 1H, 1 × C*H*$_2CH_3$), 0.90 (t, *J* = 7.4 Hz, 3H, CH_2C*H*$_3$), 0.81 (d, *J* = 6.7 Hz, 3H, CHC*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.8 (COH), 146.8 (*C*$_q$-*ortho*-COH), 144.2 (*para*-SO_2), 135.2 (*ipso*-SO_2), 134.2 (*C*$_q$-*ipso*-COH), 133.7 (*C*H-*para*-COH), 130.7 (*C*HC_qC_qCOH), 130.0 (2 × *meta*-SO_2), 129.8 (=*C*$HCHCH_2$), 127.9 (=CH*C*HCH_2), 127.8 (*C*H-*ortho*-COH), 127.5 (*C*$HCHC_qCOH$), 127.2 (2 × *ortho*-SO_2), 127.1 (NCH=), 119.0 (NCH*C*$_q$), 59.3 (N*C*HCH_2), 34.1 (*C*HCH_3), 32.7 (=CHCH*C*H_2), 25.3 (*C*H_2CH_3), 21.6 (Ar-CH_3), 14.5 (CH*C*H_3), 11.5 (CH_2*C*H_3). ν_{max} 3064, 2960, 1692, 1595, 1342, 1167, 1088, 988 cm^{-1}. m/z (ES+) (Found: [M+H]$^+$ 410.1791. $C_{24}H_{27}NO_3S$ requires [M+H]$^+$, 410.1790). $[\alpha]_D^{24.6}$ +123 (c 1.33 g/100 mL, CH_2Cl_2).

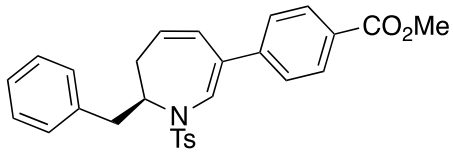


(*R*)-2-Isopropyl-1-tosyl-6-(4-(trifluoromethyl)phenyl)-2,3-dihydro-1*H*-azepine (30): Following **general procedure 2**, bromide **12** (45.0 mg, 0.12 mmol) and 4-(trifluoromethyl)phenylboronic acid (25.5 mg, 0.13 mmol) were subjected to Suzuki coupling conditions. Purification by flash column chromatography (95:5 hexane:Et_2O) afforded **30** as a yellow solid (47.1 mg, 0.108 mmol, 89%). R_f: 0.15 (95:5 hexane:Et_2O). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO_2), 7.61 (d, *J* = 8.2 Hz, 2H. 2 × *ortho*-CF_3), 7.45 (d, *J* = 8.3 Hz, 2H, 2 × *meta*-CF_3), 7.32 (d, *J* = 8.5 Hz, 2H, 2 × *meta*- SO_2), 7.18 (s, 1H, NCH=), 6.19 (ddd, *J* = 11.6, 3.1, 1.3 Hz, 1H, =C*H*$CHCH_2$), 5.89 – 5.77 (m, 1H, =CHC*H*CH_2), 4.09 (ddt, *J* = 10.8, 3.8, 1.4 Hz, 1H, NC*H*CH_2), 2.59 (ddd, *J* = 16.7, 8.5, 4.7 Hz, 1H, 1 × CH_2), 2.44 (s, 3H, Ar-CH_3), 1.65 (dp, *J* = 10.7, 6.9 Hz, 1H, C*H*$(CH_3)_2$), 1.51 (dq, *J* = 16.0, 2.7Hz, 1H, 1 × CH_2), 0.99 (d, *J* = 6.6Hz, 3H, 1 × CH(C*H*$_3)_2$), 0.86 (d, *J* = 6.6 Hz, 3H, 1 × CH(C*H*$_3)_2$). ^{19}F NMR (377 MHz, $CDCl_3$) δ -62.3. ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.7 (*para*-CF_3), 144.0 (*para*-SO_2), 135.3 (*ipso*-SO_2), 130.0 (2 × *meta*-SO_2), 128.5 (=CH*C*HCH_2), 128.3 (q, *J* = 91.5 Hz, *ipso*-CF_3), 128.1 (=*C*$HCHCH_2$), 127.4 (2 × *meta*-

CF_3), 127.3 (2 × *ortho*-SO_2), 126.1 (NCH=), 125.3 (q, *J* = 3.5 Hz, 2 × *ortho*- CF_3), 124.3 (q, *J* = 271.5 Hz, CF_3), 120.7 (NCH=C_q), 61.2 (N*C*HCH$_2$), 32.6 (CH_2), 27.8 (*C*H(CH_3)$_2$), 21.6 (Ar-CH_3), 19.8 (1 × CH(*C*H$_3$)$_2$), 18.4 (1 × CH(*C*H$_3$)$_2$). ν_{max} 2967, 1588, 1327, 1163, 1122, 1070, 988 cm^{-1}. m/z (ES+) (Found: $[M+H]^+$ 436.1564. $C_{23}H_{24}F_3NO_2S$ requires $[M+H]^+$, 436.1558). M.p. 104 – 106 °C. $[\alpha]_D^{22.4}$ +120 (c 0.15 g/100 mL, CH_2Cl_2).

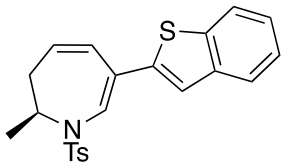


(*R*,*E*)-6-(4-Chlorostyryl)-2-isopropyl-1-tosyl-2,3-dihydro-1*H*-azepine (31): Following **general procedure 2**, bromide **12** (80.0 mg, 0.216 mmol) and (*E*)-4- chlorostyrylboronic acid (43.4 mg, 0.238 mmol) were subjected to Suzuki coupling conditions. Purification by flash column chromatography (9:1 pentane:Et_2O) afforded **31** as a colourless solid (75.5 mg, 0.176 mmol, 82%). R_f: 0.22 (9:1 pentane:Et_2O). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO_2), 7.37 – 7.22 (m, 6H, 2 × *meta*-SO_2, 2 × *ortho*-Cl and 2 × *meta*-Cl), 7.12 (s, 1H, NCHC_q), 6.74 (d, *J* = 16.0 Hz, 1H, Ar-CHC*H*), 6.51 (d, *J* = 16.0 Hz, 1H, Ar-C*H*CH), 6.36 (ddd, *J* = 11.3, 3.2, 1.3 Hz, 1H, NCHC_qC*H*), 5.82 (ddd, *J* = 11.6, 8.2, 3.4 Hz, 1H, NCHC_qCHC*H*), 4.04 – 3.97 (m, 1H, NC*H*CH_2), 2.51 (ddd, *J* = 16.9, 8.4, 4.7 Hz, 1H, 1 × CH_2), 2.41 (s, 3H, Ar-CH_3), 1.64 – 1.55 (m, 1H, C*H*(CH_3)$_2$), 1.53 – 1.43 (m, 1H, 1 × CH_2), 0.94 (d, *J* = 6.6 Hz, 3H, 1 × CH(C*H*$_3$)$_2$), 0.83 – 0.78 (d, *J* = 6.7 Hz, 3H, 1 × CH(C*H*$_3$)$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.0 (*para*-SO_2), 136.3 (*para*-Cl), 135.5 (*ipso*-SO_2), 132.3 (*ipso*-Cl), 131.9 (Ar-CH*C*H), 129.9 (2 × *meta*-SO_2), 128.8 (2 × *ortho*-Cl), 128.3 (NCHC_qCH*C*H), 127.9 (N*C*HC_q), 127.2 (2 × *ortho*-SO_2), 127.1 (2 × *meta*-Cl), 123.8 (NCHC_q*C*H), 123.2 (Ar-*C*HCH), 118.4 (NCH*C*$_q$), 61.3 (N*C*HCH_2), 32.3 (CH_2), 27.8 (*C*H(CH_3)$_2$), 21.6 (Ar-CH_3), 19.8 (1 × CH(*C*H$_3$)$_2$), 18.5 (1 × CH(*C*H$_3$)$_2$). ν_{max} 3034, 2963, 1625, 1580, 1491, 1341, 1267, 1163, 1088, 977 cm^{-1}. m/z (ES+) (Found: $[M+H]^+$ 428.1460. $C_{24}H_{26}NO_2SCl$ requires $[M+H]^+$, 428.1451). M.p. 60 – 61 °C. $[\alpha]_D^{24.9}$ -170 (c 0.06 g/100 mL, CH_2Cl_2).



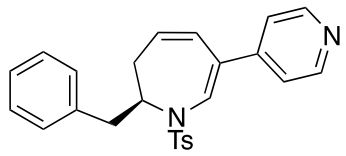
Methyl (*R*)-4-(7-benzyl-1-tosyl-6,7-dihydro-1*H*-azepin-3-yl)benzoate (32): A solution of dibromide **4f/5f** (150 mg, 0.30 mmol) and potassium carbonate (48 mg, 0.35 mmol) in toluene (5.0 mL) was heated to 150 °C for 5 h under microwave irradiation. The brown solution was diluted with EtOAc (5.0 mL), filtered

and concentrated under reduced pressure to afford a brown oil. Purification by flash column chromatography (9:1 pentane: Et_2O) afforded a pale yellow oil, which was subjected to **general procedure 2** with 4-methoxycarbonylphenylboronic acid (23.8 mg, 0.13 mmol). Purification by flash column chromatography (8:2 pentane:Et_2O) afforded **32** as a colourless solid (39.1 mg, 0.083 mmol, 69% over 2 steps based on conversion of **5f**). R_f: 0.19 (8:2 pentane:Et_2O). ^1H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.4 Hz, 2H, 2 × *ortho*-CO_2CH_3), 7.65 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO_2), 7.46 (d, *J* = 8.4 Hz, 2H, 2 × *meta*-CO_2CH_3), 7.32 – 7.18 (m, 6H, 2 × *meta*-SO_2, 2 × *meta*-CH_2, *para*-CH_2 and NCH=), 7.12 – 7.08 (m, 2H, 2 × *ortho*-CH_2), 6.33 (ddd, *J* = 11.4, 3.1, 1.4 Hz, 1H, C*H*CHCH$_2$), 5.81 (ddd, *J* = 11.5, 8.4, 3.3 Hz, 1H, CHC*H*CH$_2$), 4.65 (dddd, *J* = 10.1, 7.7, 5.0, 3.4 Hz, 1H, NC*H*$(CH_2)_2$), 3.94 (s, 3H, OCH_3), 2.69 – 2.56 (m, 2H, Ar-CH_2), 2.41 (s, 3H, Ar-CH_3), 2.28 (ddd, *J* = 17.0, 8.3, 4.3 Hz, 1H, 1 × CHCHC*H*$_2$), 1.85 (dq, *J* = 17.1, 3.2 Hz, 1H, 1 × CHCHC*H*$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.9 (CO_2), 147.6 (*para*-CO_2CH_3), 144.2 (*para*-SO_2), 137.7 (*ipso*-CH_2), 135.3 (*ipso*-SO_2), 130.0 (2 × *meta*-SO_2), 129.8 (2 × *ortho*-CO_2CH_3), 129.3 (2 × *ortho*-CH_2), 128.4 (2 × *meta*-CH_2), 128.3 (CH*C*HCH$_2$), 128.2 (*C*HCHCH$_2$ and NCH=*C*$_q$), 127.2 (2 × *ortho*-SO_2), 127.0 (2 × *meta*-CO_2CH_3), 126.6 (*para*-CH_2), 126.2 (NCH=), 120.3 (*ipso*-CO_2CH_3), 56.7 (N*C*H$(CH_2)_2$), 52.1 (OCH_3), 37.6 (Ar-CH_2), 33.1 (CHCH*C*H$_2$), 21.6 (Ar- CH_3). ν_{max} 3029, 2950, 1716, 1586, 1344, 1277, 1254, 1161, 1105, 1090, 1008 cm^{-1}. m/z (ES+) (Found: $[M+H]^+$ 474.1728. $C_{28}H_{27}NO_4S$ requires $[M+H]^+$, 474.1739). M.p. 65 – 66 °C. $[\alpha]_D^{23.8}$ +200 (c 0.03 g/100 mL, CH_2Cl_2).



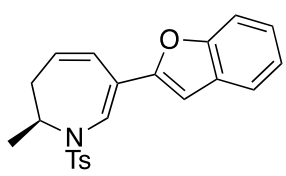
(*S*)-6-(Benzo[*b*]thiophen-2-yl)-2-methyl-1-tosyl-2,3-dihydro-1*H*-azepine (33): Following **general procedure 2**, bromide **10** (35.0 mg, 0.10 mmol) and benzo[*b*]thien-2-ylboronic acid (20.0 mg, 0.11 mmol) were subjected to Suzuki coupling conditions. Purification by flash column chromatography (9:1 pentane:Et_2O) afforded **33** as a pale yellow solid (34.4 mg, 0.087 mmol, 87%). R_f: 0.23 (9:1 pentane:Et_2O). ^1H NMR (400 MHz, $CDCl_3$) δ 7.76 (dd, *J* = 7.8, 1.2 Hz, 1H, SC_qC*H*CH), 7.72 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO_2), 7.69 (dd, *J* = 7.4, 1.2 Hz, 1H, $SC_qCHCHCHC$*H*), 7.51 (s, 1H, NCH=), 7.37 – 7.23 (m, 4H, 2 × *meta*-SO_2, SC_qCHC*H* and SC_qCHCHC*H*), 7.19 (s, 1H, $SC_qC_qCHC_q$), 6.42 (ddd, *J* = 11.4, 3.1, 1.4 Hz, 1H, $NCHC_qC$*H*), 5.86 – 5.78 (m, 1H, $NCHCH_2C$*H*), 4.66 – 4.55 (m, 1H, NC*H*CH_3), 2.43 (s,

3H, Ar-CH_3), 2.35 (ddd, *J* = 16.7, 8.3, 4.5 Hz, 1H, 1 × CH_2), 1.94 (dq, *J* = 16.9, 3.2 Hz, 1H, 1 × CH_2), 1.00 (d, *J* = 6.8 Hz, 3H, NCHC*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.4 ($SC_qC_qCHC_q$), 144.2 (*para*-SO_2), 140.5 ($SC_qC_qCHC_q$), 138.6 ($SC_qC_qCHC_q$), 135.3 (*ipso*-SO_2), 130.0 (2 × *meta*-SO_2), 127.8 ($NCHCH_2CH$), 127.3 (2 × *ortho*-SO_2), 127.2 ($NCHC_qCH$), 125.6 (NCH=), 124.4 ($SC_qCHCHCH$), 123.9 (SC_qCHCH), 123.0 ($SC_qCHCHCHCH$), 121.9 (SC_qCHCH), 118.9 ($SC_qC_qCHC_q$), 114.2 ($NCHC_q$), 51.1 ($NCHCH_3$), 35.9 (CH_2), 21.6 (Ar-CH_3), 18.0 ($NCHCH_3$). ν_{max} 3056, 2978, 1584, 1349, 1163, 1092 cm^{-1}. m/z (ES+) (Found: $[M+H]^+$ 396.1104. $C_{22}H_{21}NO_2S_2$ requires $[M+H]^+$, 396.1092). M.p. 59 – 61 °C. $[\alpha]_D^{24.2}$ -40 (c 0.15 g/100 mL, CH_2Cl_2).



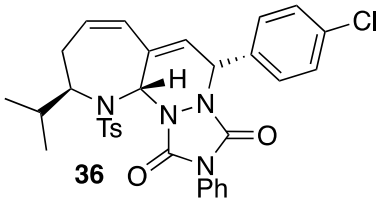
(*R*)-2-Benzyl-6-(pyridin-4-yl)-1-tosyl-2,3-dihydro-1*H*-azepine (34): A solution of dibromide **4f/5f** (150 mg, 0.30 mmol) and potassium carbonate (48 mg, 0.35 mmol) in toluene (5.0 mL) was heated to 150 °C for 5 h under microwave irradiation. The brown solution was diluted with EtOAc (5.0 mL), filtered and concentrated under reduced pressure to afford a brown oil. Purification by flash column chromatography (9:1 pentane: Et_2O) afforded a pale yellow oil, which was subjected to **general procedure 2** with 4-pyridinylboronic acid monohydrate (16.2 mg, 0.13 mmol). Purification by flash column chromatography (1:1 pentane:EtOAc) afforded **34** as a pale yellow solid (39.1 mg, 0.094 mmol, 78% over 2 steps based on conversion of **5f**). R_f: 0.17 (1:1 pentane:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, *J* = 6.3 Hz, 2H, 2 × *ortho*-N), 7.65 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO_2), 7.39 – 7.17 (m, 8H, 2 × *meta*-N, 2 × *meta*-SO_2, 2 × *meta*-CH_2, *para*-CH_2 and NCH=), 7.15 – 7.04 (m, 2H, 2 × *ortho*-CH_2), 6.31 (ddd, *J* = 11.3, 3.2, 1.4 Hz, 1H, C*H*$CHCH_2$), 5.84 (ddd, *J* = 11.5, 8.4, 3.4 Hz, 1H, =C*H*CH_2), 4.70 – 4.58 (m, 1H, NC*H*$(CH_2)_2$), 2.63 (d, *J* = 13.6 Hz, 1H, 1 × Ar-CH_2), 2.58 (d, *J* = 13.6 Hz, 1H, 1 × Ar-CH_2), 2.41 (s, 3H, CH_3), 2.28 (ddd, *J* = 17.0, 8.4, 4.4 Hz, 1H, 1 × =CHC*H*$_2$), 1.81 (dq, *J* = 17.0, 3.4 Hz, 1H, 1 × =CHC*H*$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.4 (*para*-N), 149.9 (2 × *ortho*-N), 144.4 (*para*-SO_2), 137.5 (*ipso*-CH_2), 135.1 (*ipso*-SO_2), 130.1 (2 × *meta*-SO_2), 129.3 (2 × *ortho*-CH_2), 128.8 (=*C*HCH_2), 128.5 (2 × *meta*-CH_2), 127.3 (2 × *ortho*-SO_2), 127.2 (*C*$HCHCH_2$), 127.0 (NCH=), 126.7 (*para*-CH_2), 121.6 (2 × *meta*-N), 118.1 (NCH=C_q), 56.8 (N*C*$H(CH_2)_2$, 37.7 (Ar-CH_2), 33.0 (=CH*C*H_2), 21.6 (CH_3). ν_{max} 3064, 3027, 2922, 1584, 1495, 1349, 1163, 1088,

1014 cm^{-1}. m/z (ES+) (Found: $[M+H]^+$ 417.1643. $C_{25}H_{24}N_2O_2S$ requires $[M+H]^+$, 417.1637). M.p. 58 – 59 °C. $[\alpha]_D^{24.4}$ +67 (c 0.15 g/100 mL, CH_2Cl_2).

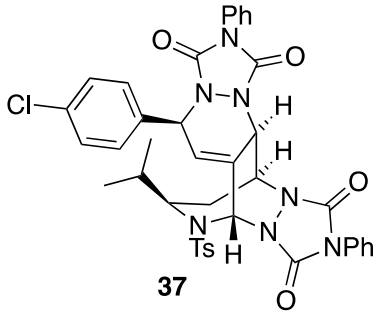


(*S*)-6-(Benzofuran-2-yl)-2-methyl-1-tosyl-2,3-dihydro-1*H*-azepine (35): Following **general procedure 2**, bromide **10** (35.0 mg, 0.10 mmol) and 2-benzofuranylboronic acid (18.2 mg, 0.11 mmol) were subjected to Suzuki coupling conditions. Purification by flash column chromatography (9:1 pentane:Et_2O) afforded **35** as a colourless solid (31.2 mg, 0.082 mmol, 82%). R_f: 0.19 (9:1 pentane:Et_2O). ^1H NMR (400 MHz, $CDCl_3$) δ 7.88 (s, 1H, NCH=), 7.75 (d, *J* = 8.4 Hz, 2H, 2 × *ortho*-SO_2), 7.51 – 7.41 (m, 2H, OC_qCHCH and $OC_qCHCHCHCH$), 7.32 (d, *J* = 8.1 Hz, 2H, 2 × *meta*-SO_2), 7.25 – 7.15 (m, 2H, OC_qCHCH and $OC_qCHCHCH$), 6.60 (s, 1H, OC_qCHC_q), 6.41 (ddd, *J* = 11.3, 3.1, 1.2 Hz, 1H, $NCHC_qCH$), 5.84 (ddd, *J* = 11.6, 8.4, 3.4 Hz, 1H, $NCHCH_2CH$), 4.64 – 4.57 (m, 1H, $NCHCH_3$), 2.43 (s, 3H, Ar-CH_3), 2.36 (ddd, *J* = 16.8, 8.4, 4.6 Hz, 1H, 1 × CH_2), 1.94 (dq, *J* = 16.9, 3.3 Hz, 1H, 1 × CH_2), 0.98 (d, *J* = 6.8 Hz, 3H, $NCHCH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.2 (OC_qCHC_q), 154.4 ($OC_qC_qCHC_q$), 144.2 (*para*-SO_2), 135.4 (*ipso*-SO_2), 130.0 (2 × *meta*-SO_2), 129.4 ($OC_qC_qCHC_q$), 127.7 ($NCHCH_2CH$), 127.3 (2 × *ortho*-SO_2), 125.2 (NCH=), 124.8 ($NCHC_qCH$), 123.7 (OC_qCHCH), 122.7 ($OC_qCHCHCH$), 120.2 ($OC_qCHCHCHCH$), 110.8 (OC_qCHCH), 109.6 ($NCHC_q$), 100.0 (OC_qCHC_q), 51.2 ($NCHCH_3$), 35.9 (CH_2), 21.6 (Ar-CH_3), 17.9 ($NCHCH_3$). ν_{max} 3038, 2933, 1599, 1349, 1256, 1167, 1092 cm^{-1}. m/z (ES+) (Found: $[M+H]^+$ 380.1307. $C_{22}H_{21}NO_3S$ requires $[M+H]^+$, 380.1320). M.p. 59 – 62 °C. $[\alpha]_D^{24.0}$ -200 (c 0.04 g/100 mL, CH_2Cl_2).

(2*R*,7*R*,12a*R*)-7-(4-Chlorophenyl)-2-isopropyl-10-phenyl-1-tosyl-2,3,7,12a-tetrahydro- 1*H*,9*H*-[1,2,4]triazolo[1',2':1,2]pyridazino[3,4-*b*]azepine-9,11(10*H*)-dione (36) and (5*R*,7*R*,13*S*,13a*R*,16*R*)-5-(4-chlorophenyl)-16-isopropyl-2,10-diphenyl-17-tosyl- 5,7,13,13a-tetrahydro-1*H*,9*H*-7,13-(epiminoethano)[1,2,4]triazolo[1',2':1,2]pyridazino[4,5-*c*][1,2,4]triazolo[1,2-*a*]pyridazine-1,3,9,11(2*H*,10*H*)-tetraone (37)



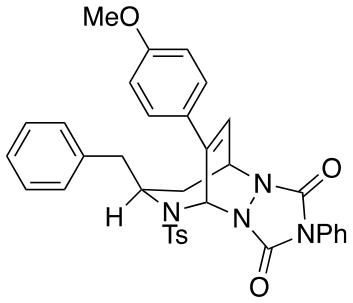
36



37

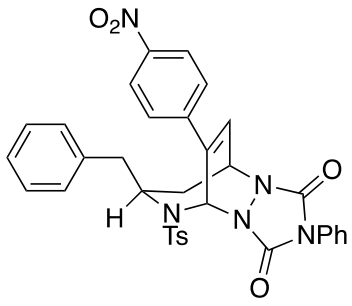
To a solution of chloride **31** (22.0 mg, 0.051 mmol) in CH_2Cl_2 (500 µL) was added 4-phenyl- 1,2,4-triazoline-3,5-dione (17.9 mg, 0.10 mmol). The reaction mixture stirred at r.t for 30 minutes and was then concentrated under reduced pressure. Purification by flash column chromatography (6:4 hexane:EtOAc) afforded **36** as a colourless solid (7.6 mg, 0.0126 mmol, 25%) and **37** as a colourless solid (24.5 mg, 0.0315 mmol, 62%). R_f of **36**: 0.36 (6:4 hexane:EtOAc) and R_f of **37**: 0.29 (6:4 hexane:EtOAc). **Characterisation of 36**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.5 Hz, 2H, 2 × *meta*-Cl), 7.63 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO_2), 7.44 – 7.28 (m, 7H, 2 × *ortho*-Cl and Ph), 7.12 (d, *J* = 8.0 Hz, 2H, 2 × *meta*- SO_2), 6.12 (s, 1H, TsNCHN), 5.85 (d, *J* = 11.5 Hz, 1H, *H*C=CHCH$_2$)), 5.70 – 5.61 (m, 1H, HC=C*H*CH$_2$ and Ar-CHC*H*), 5.25 (s, 1H, Ar-CHN), 4.05 (dt, *J* = 10.3, 7.6 Hz, 1H, NC*H*CH$_2$), 2.53 (t, *J* = 7.8 Hz, 2H, CH$_2$), 2.34 (dd, *J* = 7.5, 5.9 Hz, 1H, C*H*(CH$_3$)$_2$), 2.28 (s, 3H, Ar-CH$_3$), 1.07 (d, *J* = 6.7 Hz, 3H, 1 × CH(C*H*$_3$)$_2$), 1.02 (d, *J* = 6.6 Hz, 3H, 1 × CH(C*H*$_3$)$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.6 (1 × CO), 148.3 (1 × CO), 143.5 (*para*-SO_2), 138.1 (*ipso*-SO_2), 136.5 (*para*-Cl), 134.4 (*ipso*-Cl), 132.4 (TsNCH*C*$_q$), 130.8 (*ipso*-N), 129.7 (2 × *meta*-Cl), 129.7 (H*C*=CHCH$_2$), 129.1 (2 × *meta*-SO_2 and 2 × *ortho*-Cl), 128.9 (2 × *meta*-N), 128.2 (HC=*C*HCH$_2$), 127.9 (*para*-N), 127.9 (2 × *ortho*-SO_2), 126.1 (Ar-CH*C*H), 125.0 (2 × *ortho*-N), 66.1 (N*C*HCH$_2$), 62.3 (TsNCHN), 60.3 (Ar-CHN), 42.0 (*C*H(CH$_3$)$_2$), 29.0 (CH$_2$), 21.9 (1 × CH(*C*H$_3$)$_2$), 21.5 (Ar-CH$_3$), 18.3 (1 × CH(*C*H$_3$)$_2$). ν_{max} 2926, 1780, 1722, 1599, 1491, 1416, 1346, 1156, 1088 cm^{-1}. m/z (ES+) (Found: [M+H]$^+$, 603.1827. $C_{32}H_{31}N_4O_4SCl$ requires [M+H]$^+$, 603.1827). M.p. 189 – 191 °C. $[\alpha]_D^{22.6}$ -200 (c 0.04

g/100 mL, CH_2Cl_2). **Characterisation of 37**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.4 Hz, 2H, 2 × *ortho*-SO_2), 7.53 – 7.30 (m, 10H, 2 × Ph), 7.28 (d, *J* = 8.0 Hz, 2H, 2 × *meta*-SO_2), 7.07 (s, 4H, 2 × *ortho*-Cl and 2 × *meta*-Cl), 6.86 (s, 1H, TsNCHN), 6.36 – 6.29 (m, 2H, CH_2CHNCO and Ar-CHC*H*), 5.60 (t, *J* = 2.9 Hz, 1H, Ar-C*H*CH), 4.76 (t, *J* = 2.5 Hz, 1H, CH_2CHCHN), 3.85 (ddd, *J* = 9.6, 7.3, 2.8 Hz, 1H, TsNC*H*CH_2), 2.67 (ddd, *J* = 15.5, 6.9, 2.9 Hz, 1H, 1 × CH_2), 2.41 (s, 3H, Ar-CH_3), 2.23 – 2.12 (m, 1H, C*H*$(CH_3)_2$), 2.08 – 2.00 (m, 1H, 1 × CH_2), 1.16 (d, *J* = 6.6 Hz, 3H, 1 × CH(C*H*$_3)_2$), 1.11 (d, *J* = 6.6 Hz, 3H, 1 × CH(C*H*$_3)_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.7 (1 × CO), 151.4 (1 × CO), 149.5 (1 × CO), 149.2 (1 × CO), 144.5 (*para*-SO_2), 136.4 (*ipso*-SO_2), 135.1 (*ipso*-Cl), 134.3 (*para*-Cl), 131.0 (1 × *ipso*- N), 130.2 (1 × *ipso*-N), 129.7 (2 × *ortho*-Cl), 129.7 (2 × *meta*-SO_2), 129.1 (2 × *meta*-N), 129.0 (2 × *meta*-N), 128.7 (Ar-CH*C*H), 128.5 (1 × *para*-N), 128.4 (1 × *para*-N), 128.2 (2 × *meta*- Cl), 127.8 (2 × *ortho*-SO_2), 126.7 (TsNCH*C*$_q$), 125.2 (2 × *ortho*-N), 124.7 (2 × *ortho*-N), 70.5 (TsNCHN), 59.4 (N*C*HCH_2), 59.4 (CH_2CH*C*HN), 55.3 (Ar-*C*HCH), 49.1 (CH_2*C*HNCO), 33.1 (*C*H$(CH_3)_2$), 32.5 (CH_2), 21.6 (Ar-CH_3 and 1 × CH(*C*H$_3)_2$), 20.6 (1 × CH(*C*H$_3)_2$). ν_{max} 3068, 2967, 1774, 1715, 1595, 1502, 1413, 1163, 1088 cm^{-1}. m/z (ES+) (Found: $[M+H]^+$, 778.2200. $C_{40}H_{36}N_7O_6SCl$ requires $[M+H]^+$, 778.2215). M.p. 183 – 184 °C. $[\alpha]_D^{22.9}$ -200 (c 0.07 g/100 mL, CH_2Cl_2).



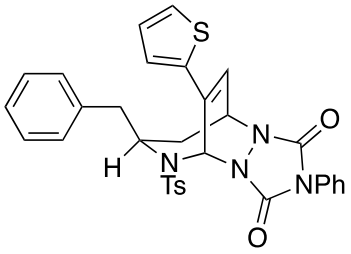
(5*R*,7*S*,9*S*)-7-Benzyl-12-(4-methoxyphenyl)-2-phenyl-6-tosyl-6,7,8,9-tetrahydro-1*H*,5*H*-5,9-etheno[1,2,4]triazolo[1,2-*a*][1,2,4]triazepine-1,3(2*H*)-dione (38): Following **general procedure 2**, bromide **18** (40.0 mg, 0.067 mmol) and 4- methoxyphenylboronic acid (15.8 mg, 0.074 mmol) were subjected to Suzuki coupling conditions. Purification by flash column chromatography (7:3 pentane:EtOAc) afforded **38** as a colourless solid (34.5 mg, 0.056 mmol, 84%). R_f: 0.28 (7:3 pentane:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.2 Hz, 2H, 2 × *ortho*-SO_2), 7.53 – 7.31 (m, 12H, 2 × Ph and 2 × *ortho*-OCH_3), 7.26 (s, 1H, =C*H*$CHCH_2$), 7.20 (d, *J* = 7.9 Hz, 2H, 2 × *meta*- SO_2), 6.96 (d, *J* = 8.8 Hz, 2H, 2 × *meta*-OCH_3), 4.76 (qd, *J* = 8.4, 2.7 Hz, 1H, NC*H*$(CH_2)_2$), 3.99 (d, *J* = 2.3 Hz, 1H, N_2CH), 3.89 (s, 3H, OCH_3), 3.83 (dd, *J* = 5.1, 2.3 Hz, 1H, =CHC*H*CH_2), 3.59 – 3.45 (m, 2H, 1 × Ar-CH_2 and 1 × =CHCHC*H*$_2$), 3.12 (dd, *J* = 13.4, 2.8 Hz, 1H, 1 × Ar-CH_2), 2.13 (s, 3H, Ar-CH_3), 2.11 – 2.04 (m, 1H, 1 ×

=CHCHC*H*$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.1 (*ipso*-OCH_3), 149.9 (1 × CO), 143.9 (1 × CO), 143.4 (*para*-SO_2), 137.4 (*ipso*-SO_2), 136.4 (*ipso*-CH_2), 130.7 (2 × *ortho*-CH_2), 130.5 (*ipso*-N), 129.0 (2 × *meta*-SO_2 and 2 × *meta*-N), 128.5 (2 × *meta*-CH_2), 128.2 (*para*-OCH_3), 128.1 (*para*-N), 127.3 (2 × *ortho*-SO_2), 126.9 (*para*-CH_2), 126.37, 124.7 (2 × *ortho*-N), 114.4 (=*C*HCHCH$_2$), 113.9 (2 × *meta*-OCH_3), 111.0 (N_2CHC_q), 60.6 (N*C*H(CH_2)$_2$), 60.5 (N_2CH), 58.0 (=CH*C*HCH$_2$), 55.3 (OCH_3), 41.6 (Ar-CH_2), 30.5 (=CHCH*C*H$_2$), 21.4 (Ar-CH_3). ν_{max} 3064, 2926, 1771, 1715, 1640, 1607, 1517, 1409, 1342, 1252, 1156, 1029 cm^{-1}. m/z (ES+) (Found: $[M+H]^+$ 621.2184. $C_{35}H_{32}N_4O_5S$ requires $[M+H]^+$, 621.2172).M.p. 127 – 128 °C. $[\alpha]_D^{24.1}$ +180 (c 0.29 g/100 mL, CH_2Cl_2).

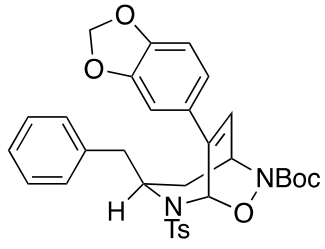


(5*R*,7*S*,9*S*)-7-Benzyl-12-(4-nitrophenyl)-2-phenyl-6-tosyl-6,7,8,9-tetrahydro-1*H*,5*H*-5,9-etheno[1,2,4]triazolo[1,2-*a*][1,2,4]triazepine-1,3(2*H*)-dione (39): Following **general procedure 2**, bromide **18** (30.0 mg, 0.051 mmol) and 4-nitrophenylboronic acid (9.3 mg, 0.056 mmol) were subjected to Suzuki coupling conditions. Purification by flash column chromatography (7:3 pentane:EtOAc) afforded **39** as a yellow solid (31.7 mg, 0.050 mmol, 98%). R_f: 0.15 (7:3 pentane:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 9.0 Hz, 2H, 2 × *ortho*-NO_2), 7.64 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO_2), 7.54 (d, *J* = 9.0 Hz, 2H, 2 × *meta*-NO_2), 7.52 – 7.34 (m, 11H, 2 × Ph and =C*H*CHCH$_2$), 7.20 (d, *J* = 8.3 Hz, 2H, 2 × *meta*-SO_2), 4.81 (dt, *J* = 8.5, 6.1 Hz, 1H, NC*H*(CH_2)$_2$), 3.85 (d, *J* = 2.2 Hz, 1H, NCHN), 3.81 (dd, *J* = 5.0, 2.2 Hz, 1H, =CHC*H*CH$_2$), 3.66 – 3.51 (m, 2H, 1 × Ar-CH_2 and 1 × =CHCHC*H*$_2$), 3.06 (dd, *J* = 13.4, 2.5Hz, 1H, 1 × Ar-CH_2), 2.19 – 2.13 (m, 1H, 1 × =CHCHC*H*$_2$), 2.12 (s, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.8 (2 × CO), 146.5 (*ipso*-NO_2), 143.8 (*para*-SO_2), 142.2 (*para*-NO_2), 137.3 (*ipso*-SO_2), 136.1 (*ipso*-CH_2), 131.0 (2 × *ortho*-CH_2), 130.2 (*ipso*-N), 129.2 (2 × *meta*-SO_2 and *para*-CH_2), 129.2 (2 × *meta*-N), 128.6 (2 × *meta*-CH_2), 128.5 (*para*-N), 127.3 (2 × *ortho*-SO_2), 125.2 (2 × *meta*-NO_2), 124.7 (2 × *ortho*-N), 123.9 (2 × *ortho*-NO_2), 118.3 (=*C*HCHCH$_2$), 108.7 (N_2CHC_q), 60.4 (N*C*H(CH_2)$_2$), 60.0 (NCHN), 58.3 (=CH*C*HCH$_2$), 41.5 (Ar-CH_2), 30.3 (=CHCH*C*H$_2$), 21.4 (CH_3). ν_{max} 3083, 2926, 1780, 1722, 1636, 1595, 1510, 1409, 1338, 1159 cm^{-1}. m/z (CI+) (Found: $[M+H]^+$,

636.1909. $C_{34}H_{29}N_5O_6S$ requires $[M+H]^+$, 636.1911). M.p. 148 – 149 °C. $[\alpha]_D^{23.7}$ +240 (c 0.09 g/100 mL, CH_2Cl_2).



(5*R*,7*S*,9*S*)-7-Benzyl-2-phenyl-12-(thiophen-2-yl)-6-tosyl-6,7,8,9-tetrahydro-1*H*,5*H*-5,9-etheno[1,2,4]triazolo[1,2-*a*][1,2,4]triazepine-1,3(2*H*)-dione (40): Following **general procedure 2**, bromide **18** (30.0 mg, 0.051 mmol) and thiophene-2- boronic acid pinacol ester (15.8 mg, 0.074 mmol) were subjected to Suzuki coupling conditions. Purification by flash column chromatography (7:3 pentane:EtOAc) afforded **40** as a yellow solid (30.0 mg, 0.050 mmol, 75%). R_f: 0.28 (7:3 pentane:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.3 Hz, 2H, 2 × *ortho*-SO_2), 7.51 – 7.29 (m, 10H, 2 × Ph), 7.21 – 7.16 (m, 3H, 2 × *meta*-SO_2 and SCH), 7.14 (s, 1H, =C*H*CHCH$_2$), 7.07 – 7.03 (m, 2H, SCHC*H* and SCHCHC*H*), 4.75 (tdd, *J* = 8.6, 6.7, 2.8 Hz, 1H, NC*H*(CH$_2$)$_2$), 4.00 (d, *J* = 2.3 Hz, 1H, NCHN), 3.80 (dd, *J* = 5.1, 2.3 Hz, 1H, =CHC*H*CH$_2$), 3.59 – 3.45 (m, 2H, 1 × Ar-CH$_2$ and 1 × =CHCHC*H*$_2$), 3.08 (dd, *J* = 13.5, 2.8 Hz, 1H, 1 × Ar-CH$_2$), 2.12 (s, 3H, CH_3), 2.10 – 2.00 (m, 1H, 1 × =CHCHC*H*$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.9 (1 × CO), 143.7 (1 × CO), 143.5 (*para*-SO_2), 140.5 (SC_q), 137.5 (*ipso*-SO_2), 136.4 (*ipso*-CH_2), 130.7 (2 × *ortho*-CH_2), 130.4 (*ipso*-N), 129.1 (2 × *meta*-N), 129.0 (2 × *meta*-SO_2), 128.6 (2 × *meta*-CH_2), 128.3 (*para*-N), 127.7 (SCH*C*H), 127.3 (2 × *ortho*-SO_2), 127.0 (*para*-CH_2), 124.7 (2 × *ortho*-N), 124.5 (SCHCH*C*H), 123.4 (SCH), 115.2 (=*C*HCHCH$_2$), 106.7 (N_2CHC_q), 60.9 (N_2CH), 60.6 (N*C*H(CH$_2$)$_2$), 58.1 (=CH*C*HCH$_2$), 41.6 (Ar-CH_2), 30.2 (=CHCH*C*H$_2$), 21.4 (CH_3). ν_{max} 3083, 2926, 1778, 1722, 1636, 1595, 1510, 1409, 1338, 1159 cm^{-1}. m/z (ES+) (Found: $[M+H]^+$ 597.1633. $C_{32}H_{29}N_4O_4S_2$ requires $[M+H]^+$, 597.1630). M.p. 227 – 228 °C. $[\alpha]_D^{24.2}$ +300 (c 0.06 g/100 mL, CH_2Cl_2).



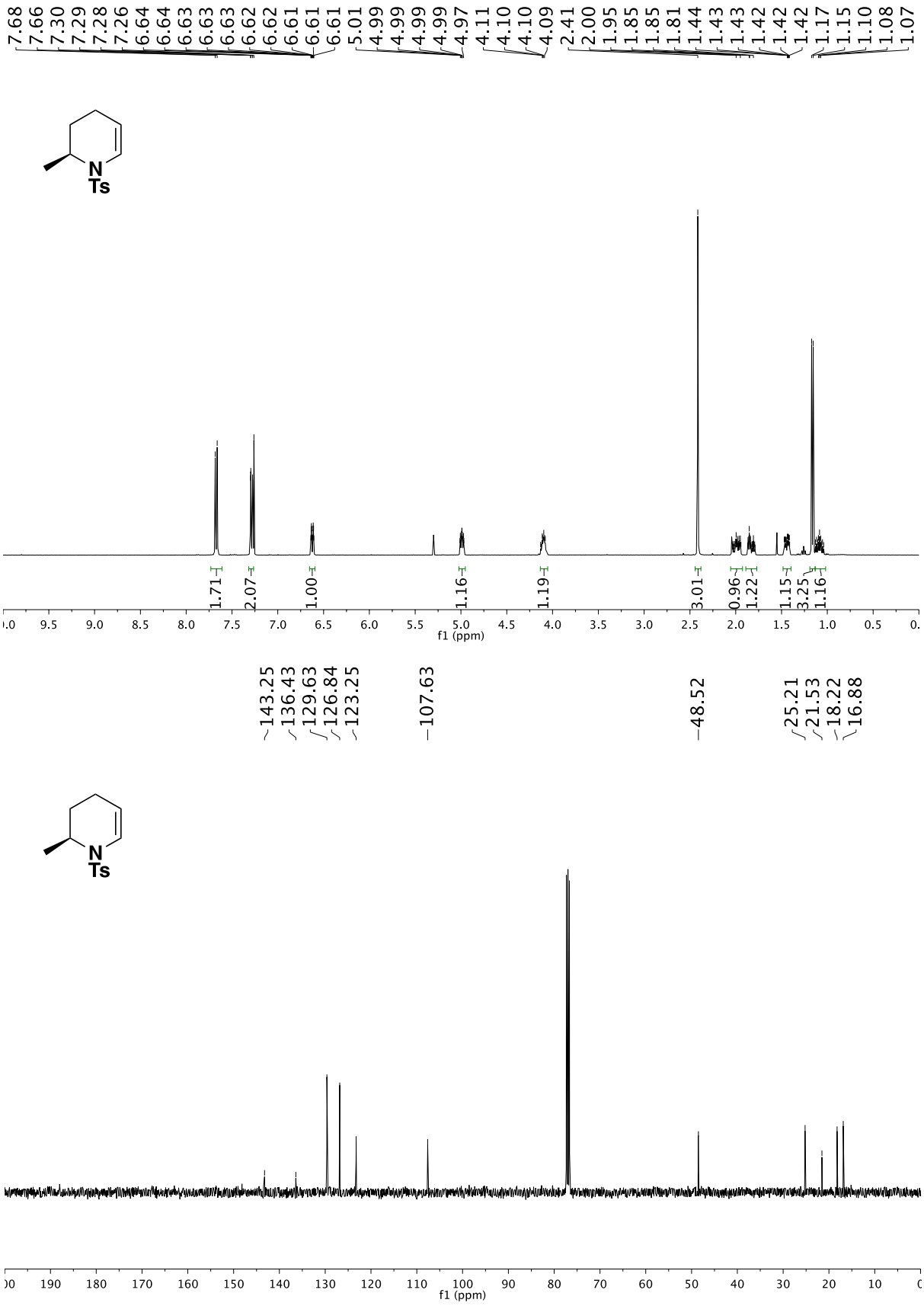
***tert*-Butyl (1*S*,3*S*,5*S*)-8-(benzo[*d*][1,3]dioxol-5-yl)-3-benzyl-2-tosyl-7-oxa-2,6- diazabicyclo[3.2.2]non-8-ene-6-carboxylate (41)**: Following **general procedure 2**, bromide **22** (20.0 mg, 0.0364 mmol) and 1,3-benzodioxole-5-boronic acid (6.6 mg, 0.040 mmol) were subjected to Suzuki coupling conditions. Purification by flash column chromatography (85:15

pentane:EtOAc) afforded **41** as a colourless solid (15.9 mg, 0.027 mmol, 75%). R_f: 0.17 (85:15 pentane:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.4 Hz, 2H, 2 × *ortho*-SO_2), 7.30 (d, *J* = 8.0 Hz, 2H, 2 × *meta*-SO_2), 7.28 – 7.25 (m, 2H, 2 × *meta*-CH_2), 7.22 – 7.17 (m, 1H, *para*-CH_2), 7.14 – 7.10 (m, 2H, 2 × *ortho*-CH_2), 7.06 (dd, *J* = 8.1, 1.8 Hz, 1H, CH-*para*-OCH_2), 7.02 (d, *J* = 1.8 Hz, 1H, CH-*ortho*-OCH_2/*ortho*-C_q), 6.91 (s, 1H, NCHO), 6.88 (d, *J* = 8.1 Hz, 1H, CH- *ortho*-OCH_2/*meta*-C_q), 6.68 (dd, *J* = 7.3, 1.4 Hz, 1H, =C*H*CHCH$_2$), 6.02 (d, *J* = 1.4 Hz, 1H, 1 × O_2CH_2), 6.01 (d, *J* = 1.4 Hz, 1H, 1 × O_2CH_2), 4.90 (t, *J* = 6.8 Hz, 1H, =CHC*H*CH$_2$), 3.89 (ddd, *J* = 11.5, 7.8, 3.6 Hz, 1H, NC*H*(CH_2)$_2$), 3.08 (dd, *J* = 13.3, 3.6 Hz, 1H, 1 × Ar-CH_2), 2.96 (dd, *J* = 13.3, 11.5 Hz, 1H, 1 × Ar-CH_2), 2.40 (s, 3H, Ar-CH_3), 1.96 (dd, *J* = 15.3, 6.6 Hz, 1H, 1 × =CHCHC*H*$_2$), 1.69 (dd, *J* = 15.2, 8.0 Hz, 1H, 1 × =CHCHC*H*$_2$), 1.43 (s, 9H, C(CH_3)$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.5 (CO_2), 148.4 (2 × *ipso*-OCH_2), 143.6 (*para*-SO_2), 138.9 (*ipso*-CH_2), 137.7 (C_q-*para*-OCH_2), 136.5 (*ipso*-SO_2), 129.6 (2 × *meta*-SO_2), 129.3 (2 × *ortho*-CH_2 and NCH*C*$_q$)), 128.7 (2 × *meta*-CH_2), 128.1 (2 × *ortho*-SO_2), 126.6 (*para*-CH_2), 123.6 (=*C*HCHCH$_2$), 119.2 (CH-*para*-OCH_2), 108.8 (CH-*ortho*-OCH_2/*meta*-C_q), 105.3 (CH- *ortho*-OCH_2/*ortho*-C_q), 101.4 (O_2CH_2), 82.5 (NCHO), 81.9 (*C*(CH_3)$_3$), 54.6 (N*C*H(CH_2)$_2$), 51.8 (=CH*C*HCH$_2$), 42.8 (Ar-CH_2), 33.7 (=CHCH*C*H$_2$), 28.2 (C(*C*H_3)$_3$), 21.5 (Ar-CH_3). ν_{max} 3064, 2978, 1718, 1599, 1491, 1327, 1245, 1163, 1096, 1040 cm^{-1}. m/z (ES+) (Found: [M+H]$^+$, 591.2154. $C_{32}H_{34}N_2O_7S$ requires [M+H]$^+$, 591.2165). M.p. 195 °C decomposed. $[\alpha]_D^{24.3}$ +270 (c 0.03 g/100 mL, CH_2Cl_2).

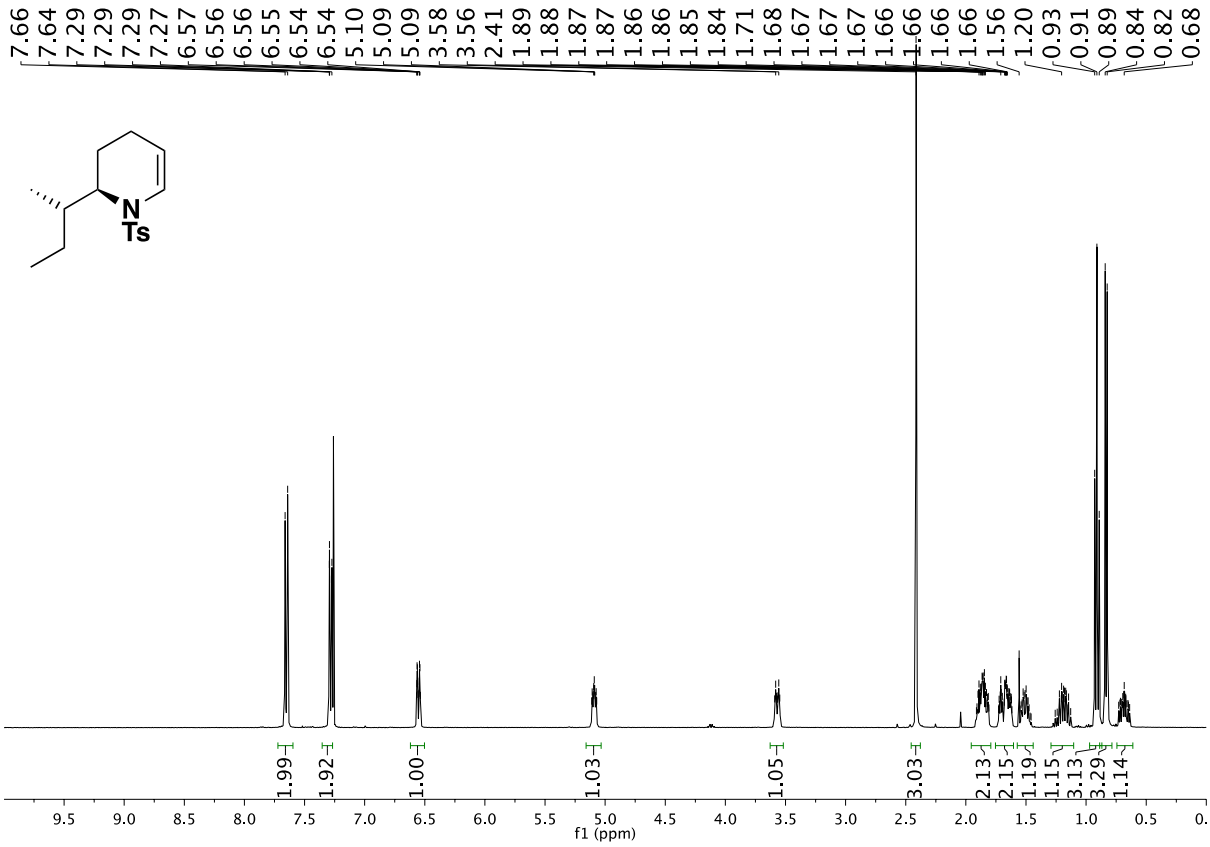
References

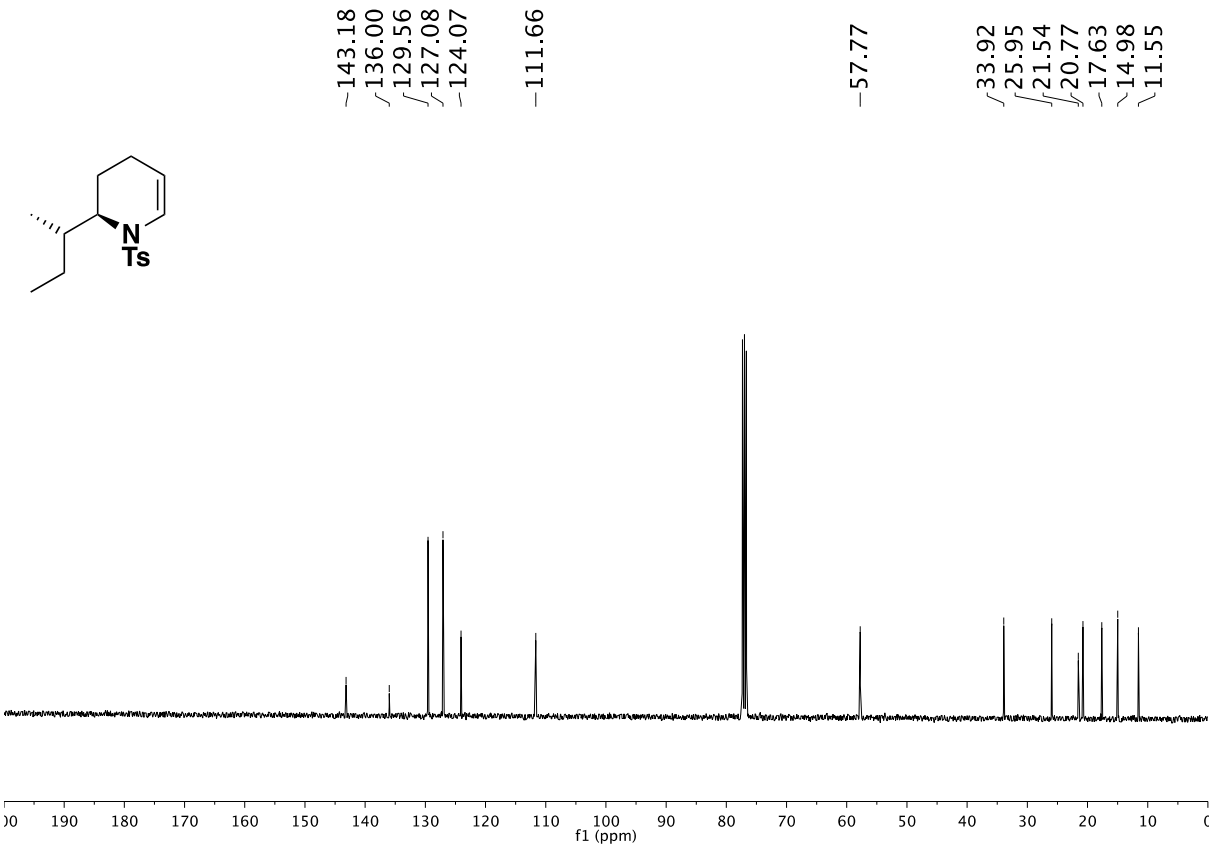
1) M. B. Berry and D. Craig, *Synlett*, **1992**, 41.
2) L. C. Pattenden, R. A. J. Wybrow, S. A. Smith and J. P. A. Harrity, *Org. Lett.*, 2006, **8**, 3090.

^{1}H and ^{13}C NMR Spectra of tetrahydropyridine 1a



^{1}H and ^{13}C NMR Spectra of tetrahydropyridine 1b

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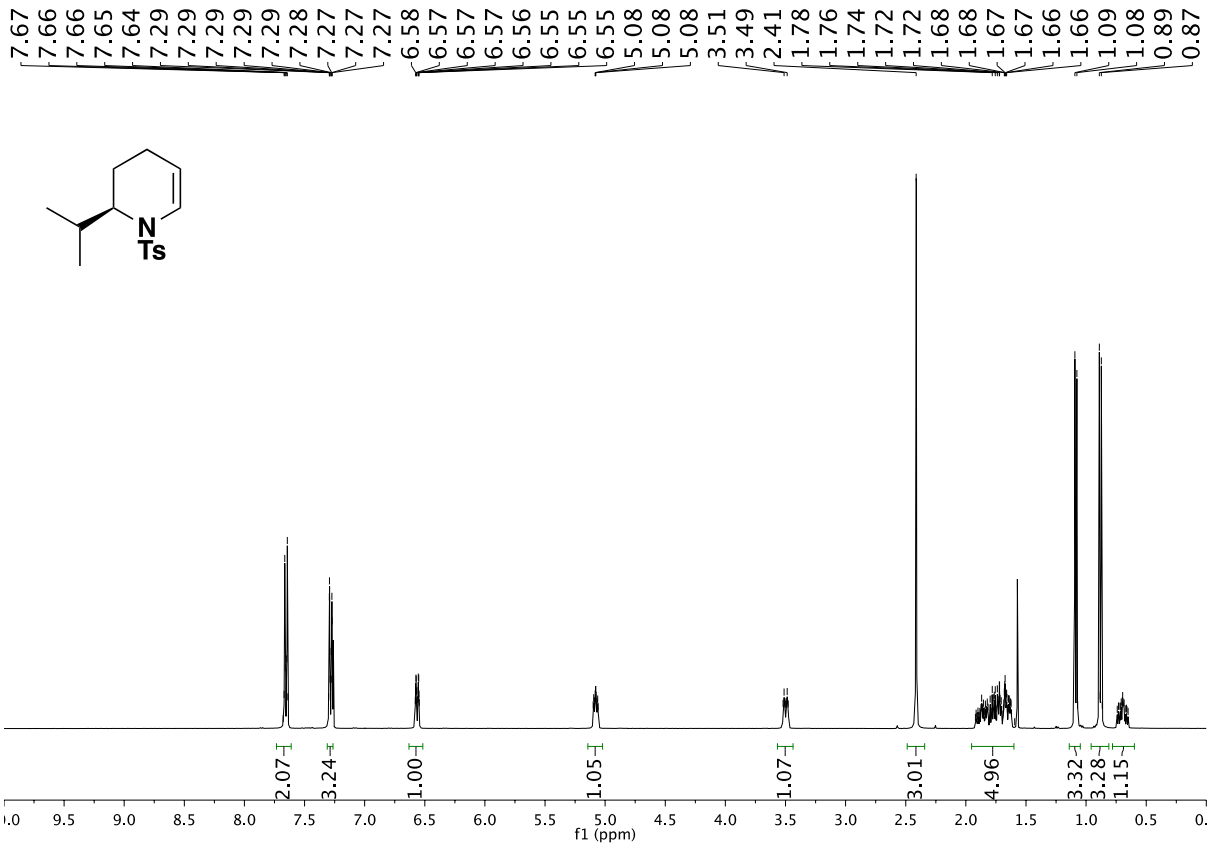
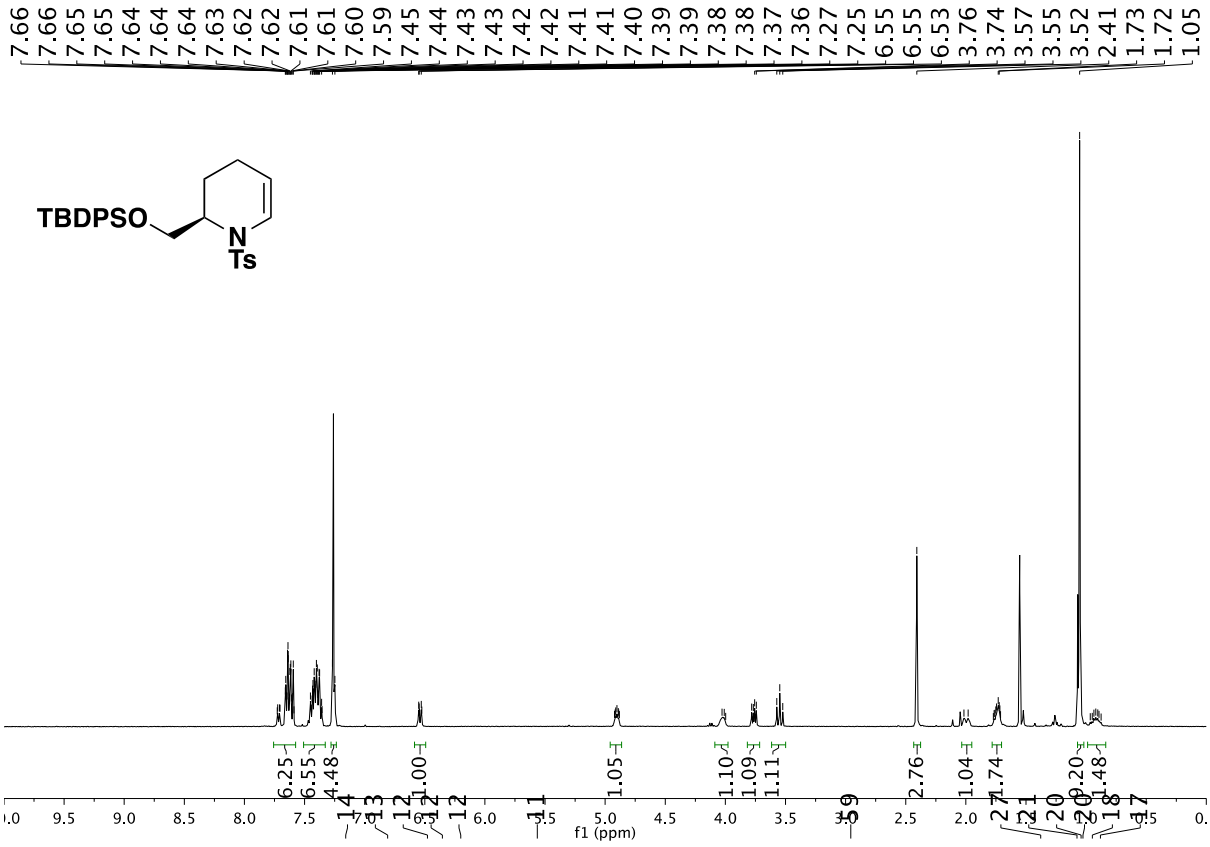
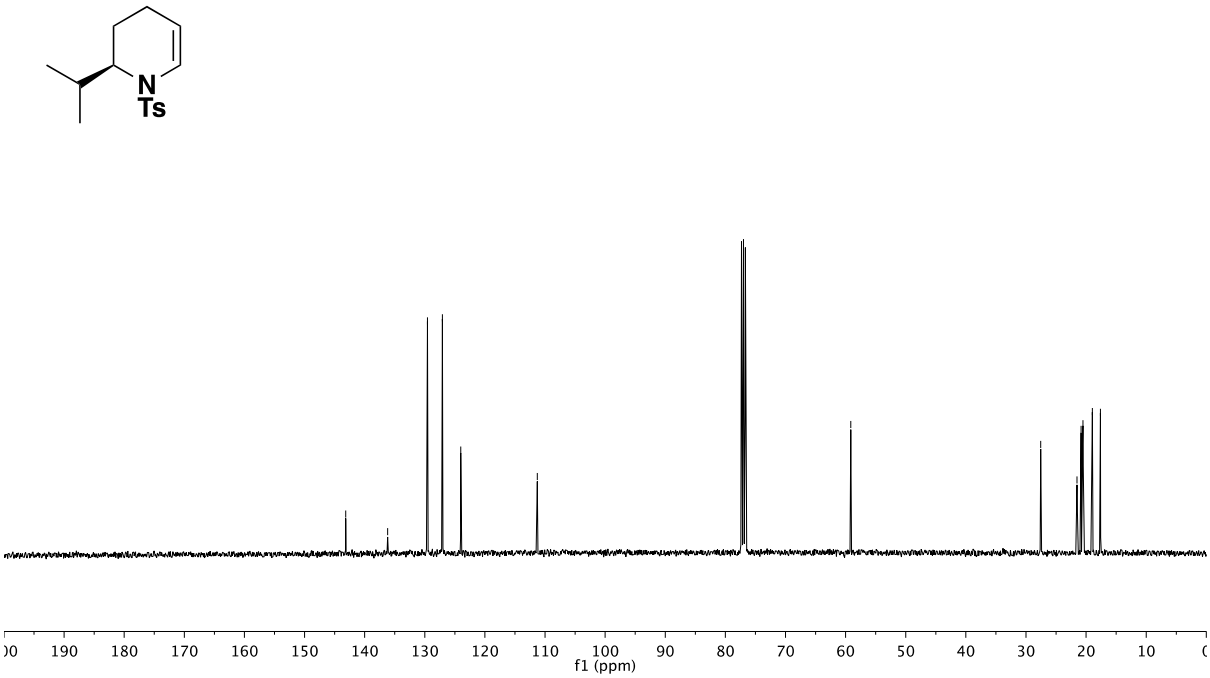
136.00
129.56
127.08
124.07
111.66
57.77
33.92
25.95
21.54
20.77
17.63
14.98
11.55
N
Ts
f1 (ppm)

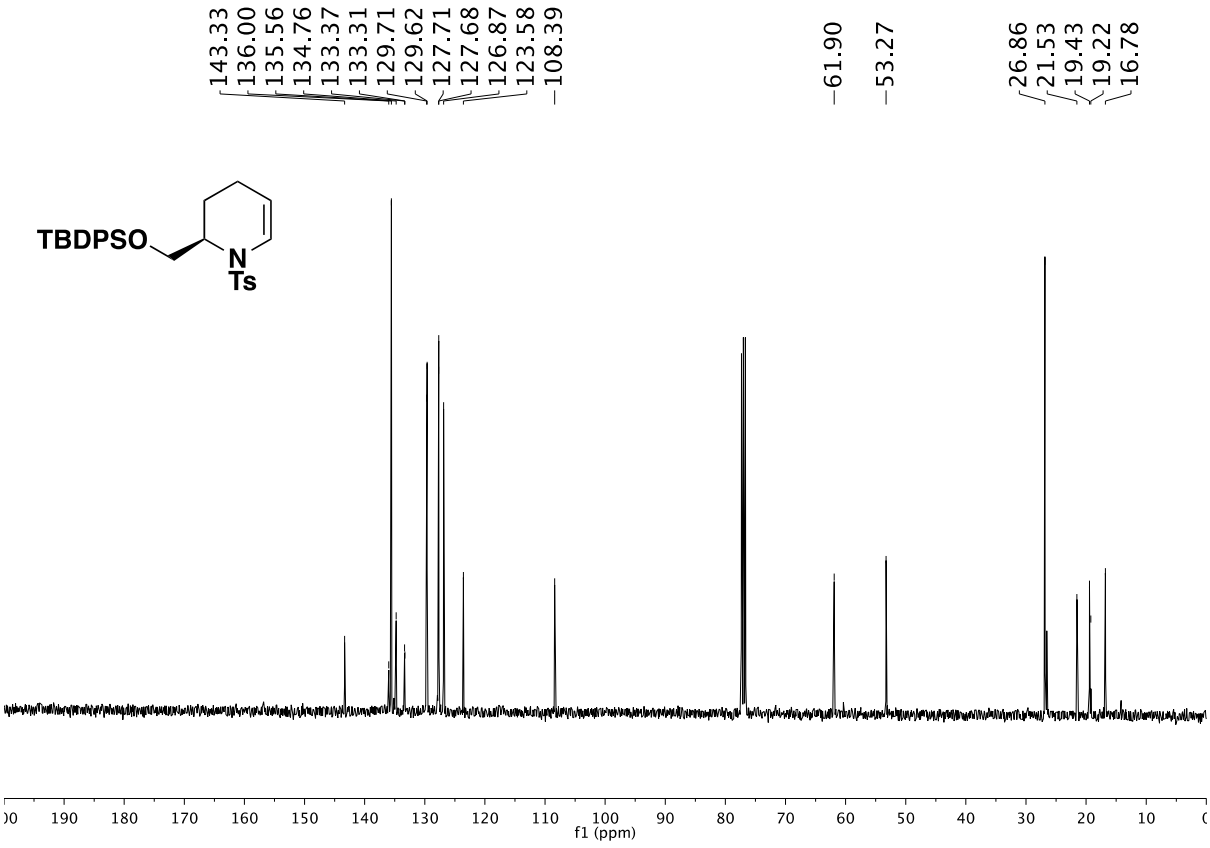
^{1}H and ^{13}C NMR Spectra of tetrahydropyridine 1c



^{1}H and ^{13}C NMR Spectra of tetrahydropyridine 1d



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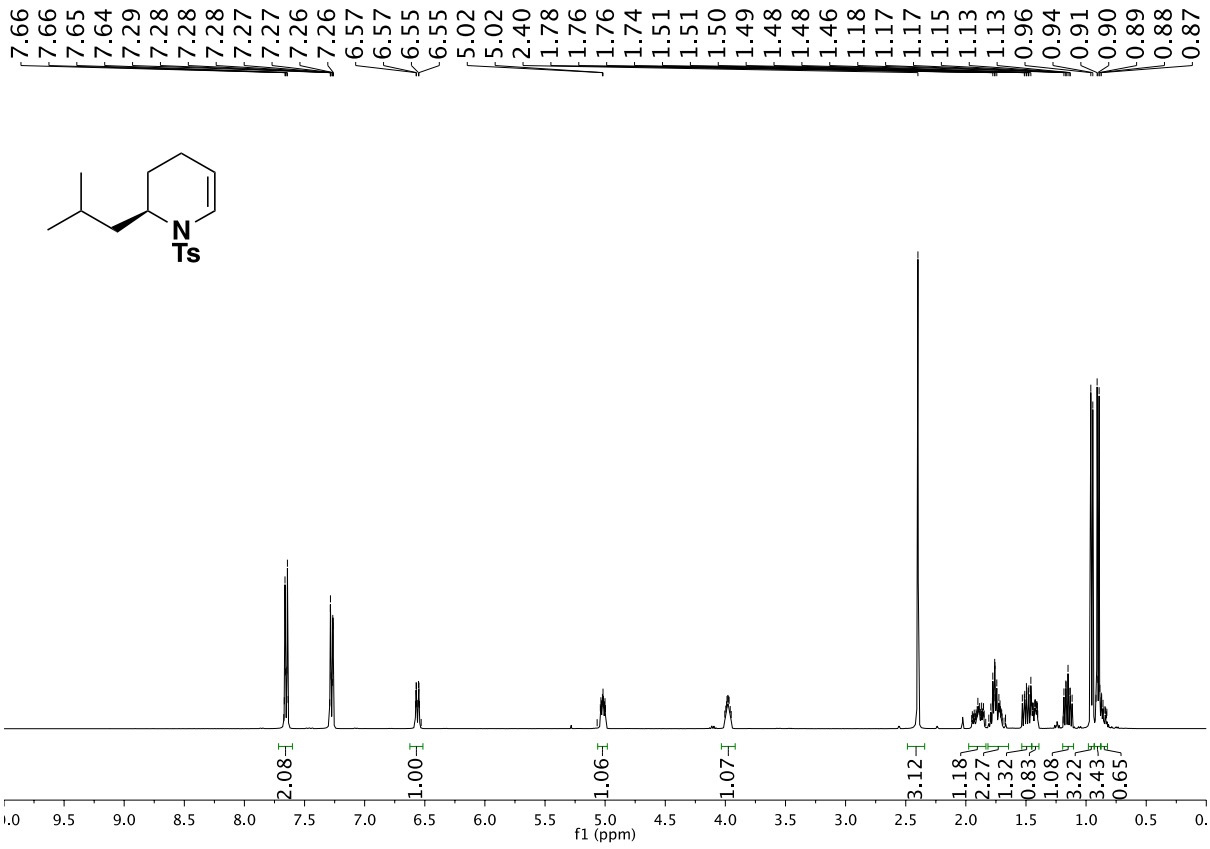
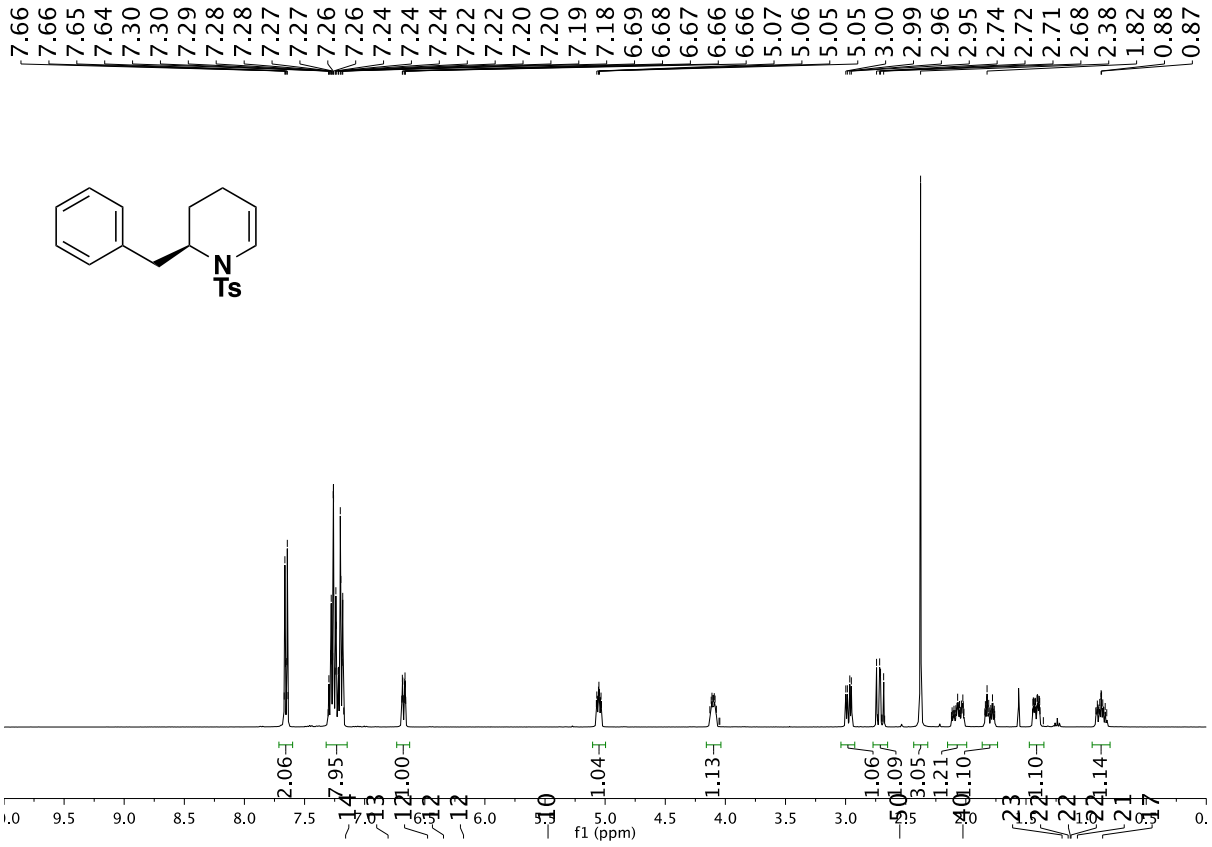
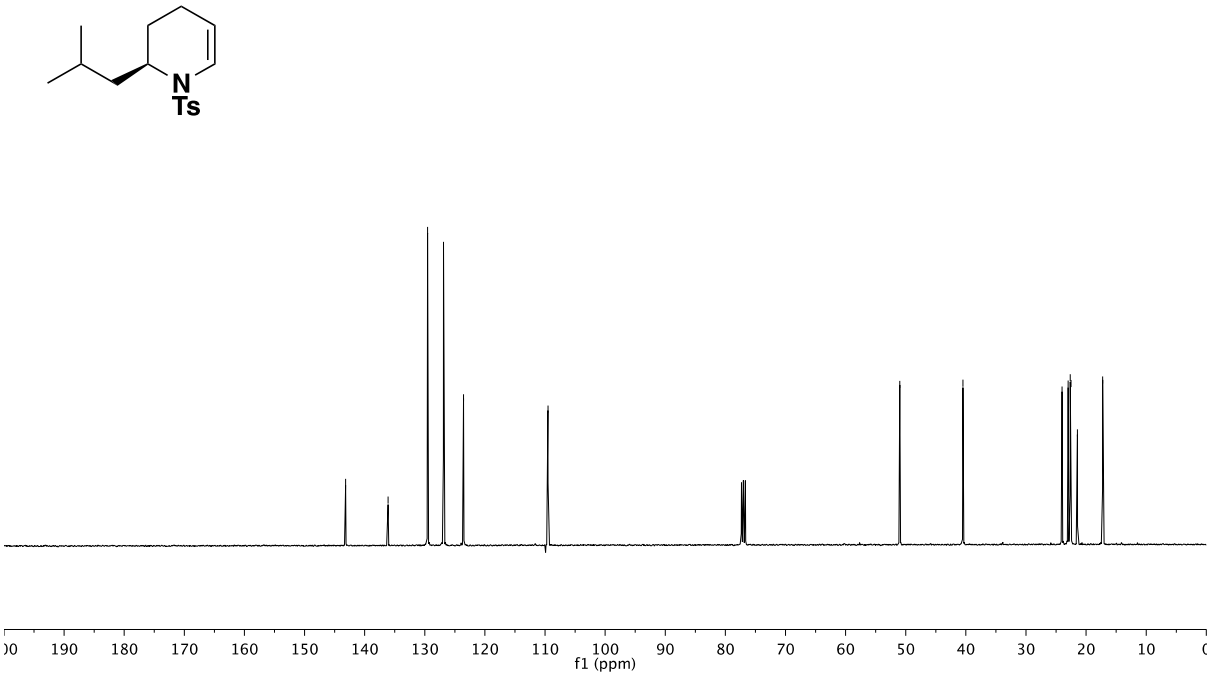
136.00
135.56
134.76
133.37
133.31
129.71
129.62
127.71
127.68
126.87
123.58
108.39
61.90
53.27
26.86
21.53
19.43
19.22
16.78
TBDPSO
N
Ts
f1 (ppm)

^{1}H and ^{13}C NMR Spectra of tetrahydropyridine 1e

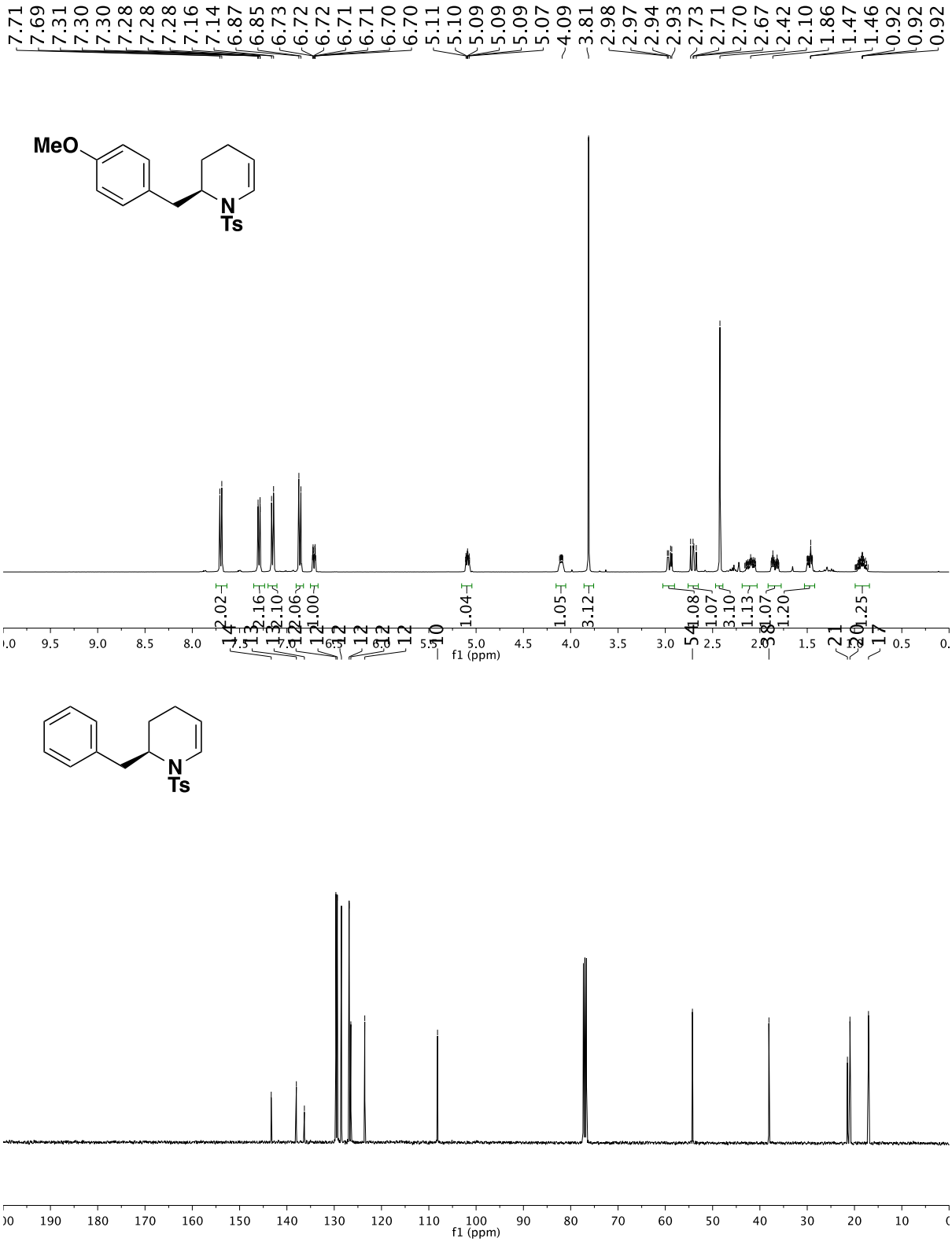


^{1}H and ^{13}C NMR Spectra of tetrahydropyridine 1f

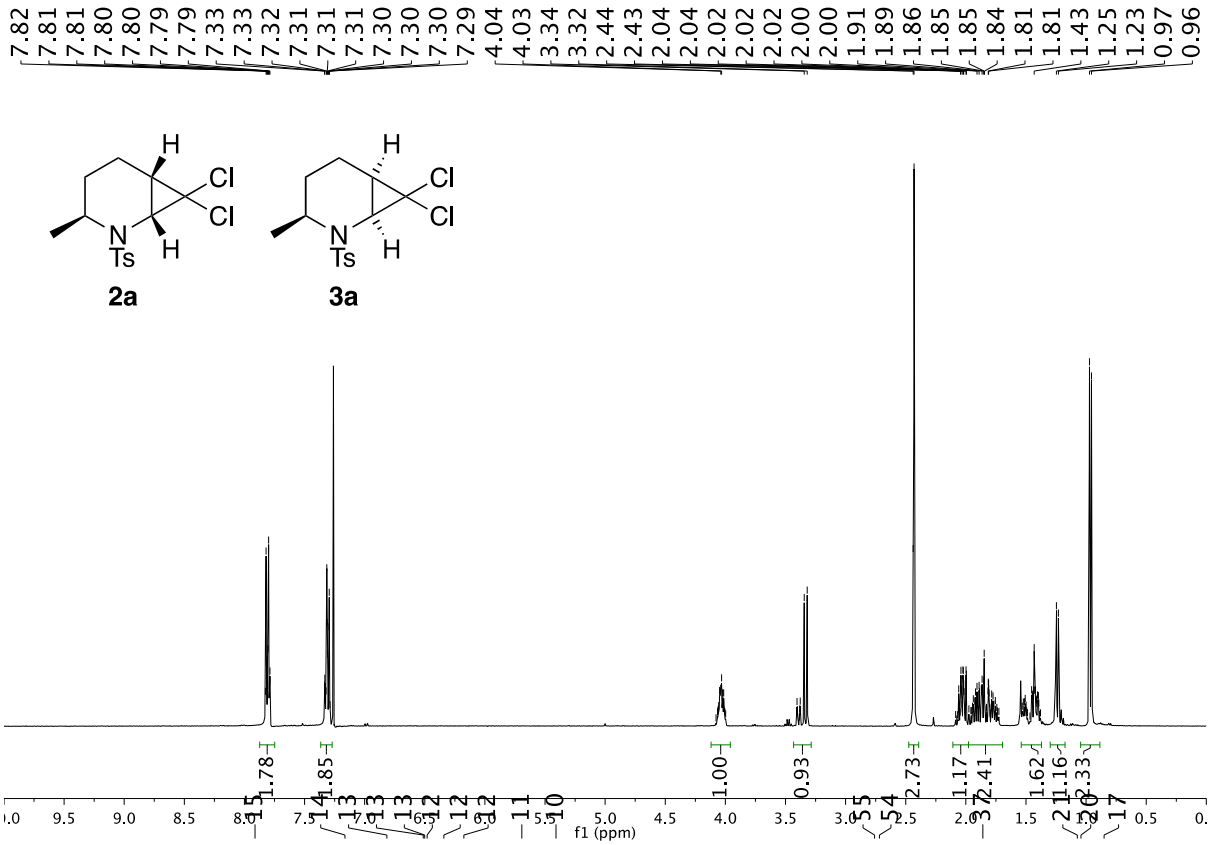


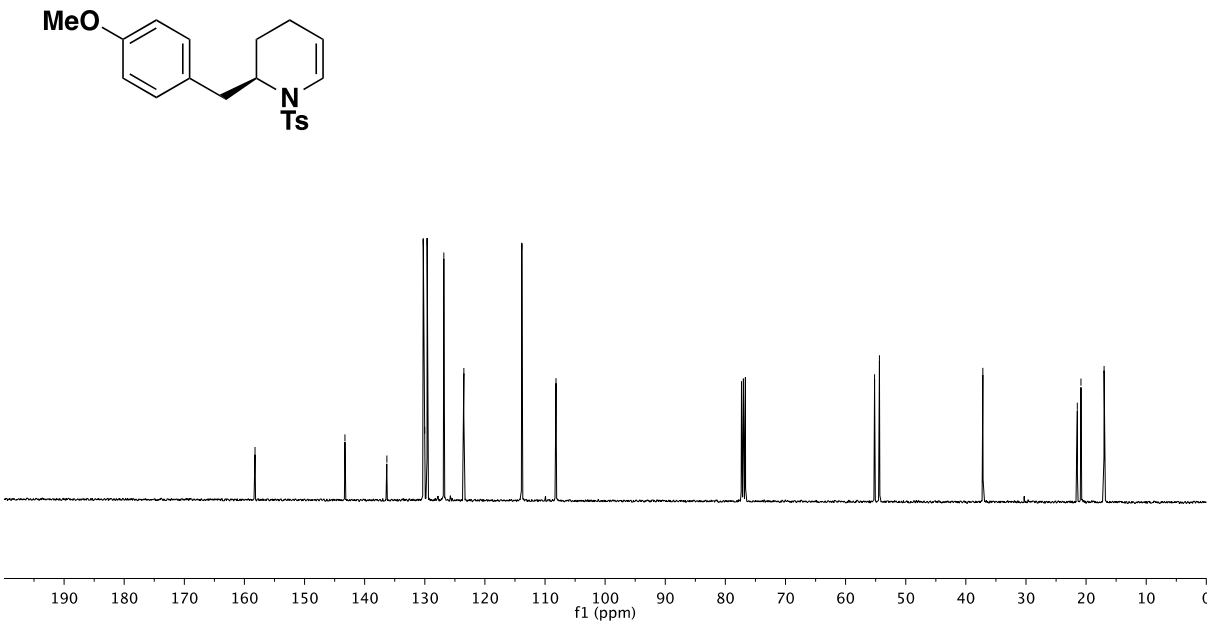


^{1}H and ^{13}C NMR Spectra of tetrahydropyridine 1g

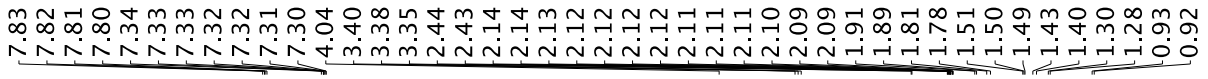


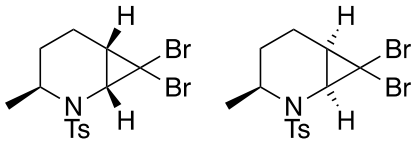
^{1}H and ^{13}C NMR Spectra of 2a/3a





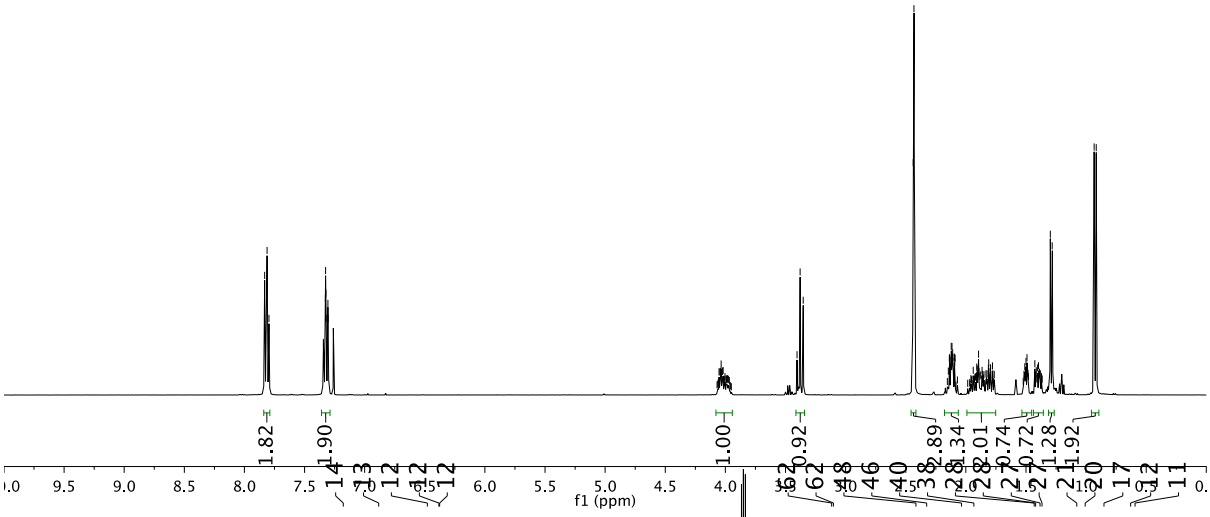
^{1}H and ^{13}C NMR Spectra of 4a/5a

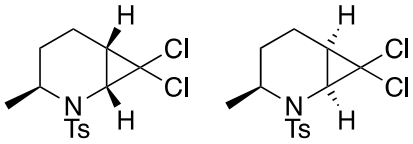




4a

5a

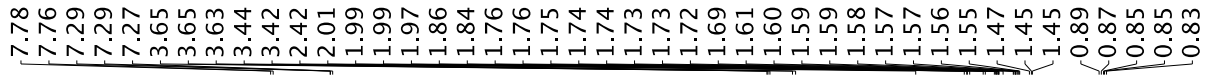


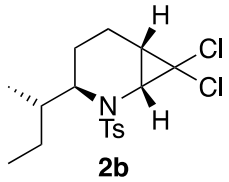


2a

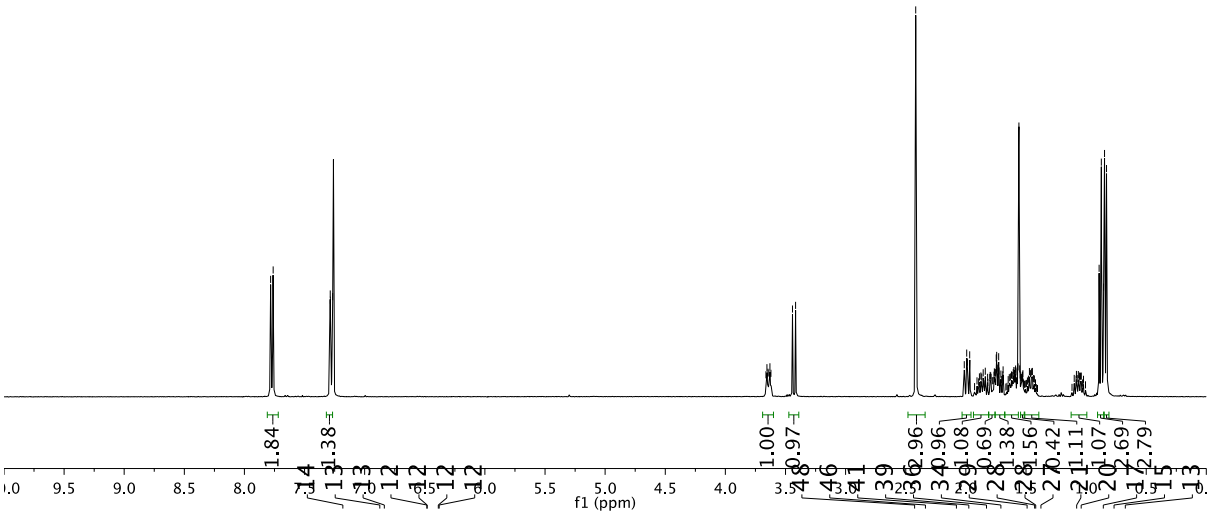
3a

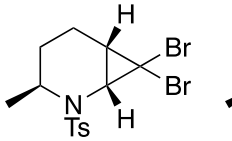
^{1}H and ^{13}C NMR Spectra of 2b



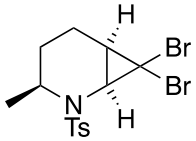


2b

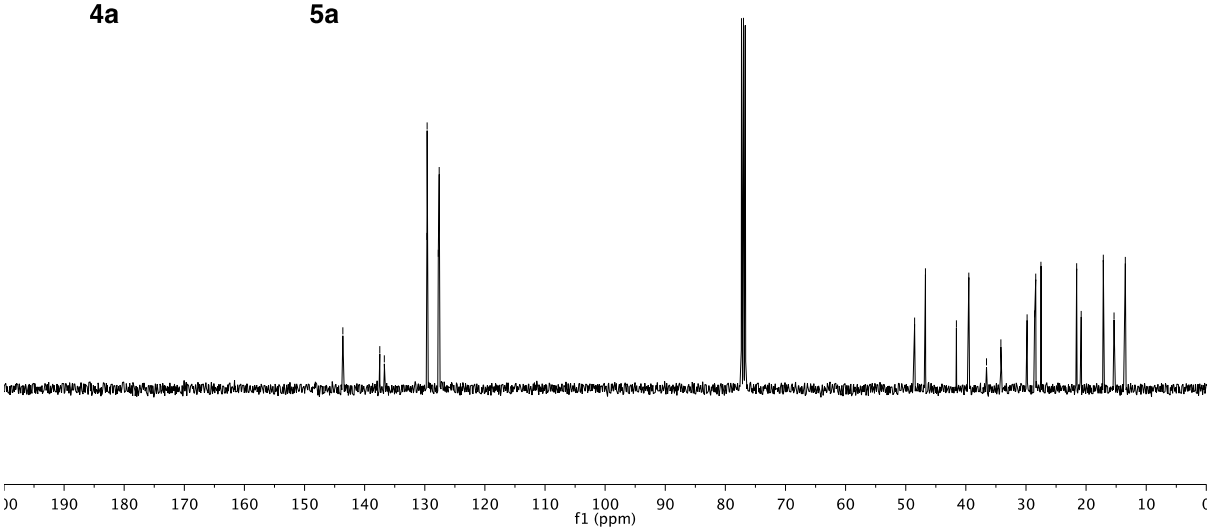




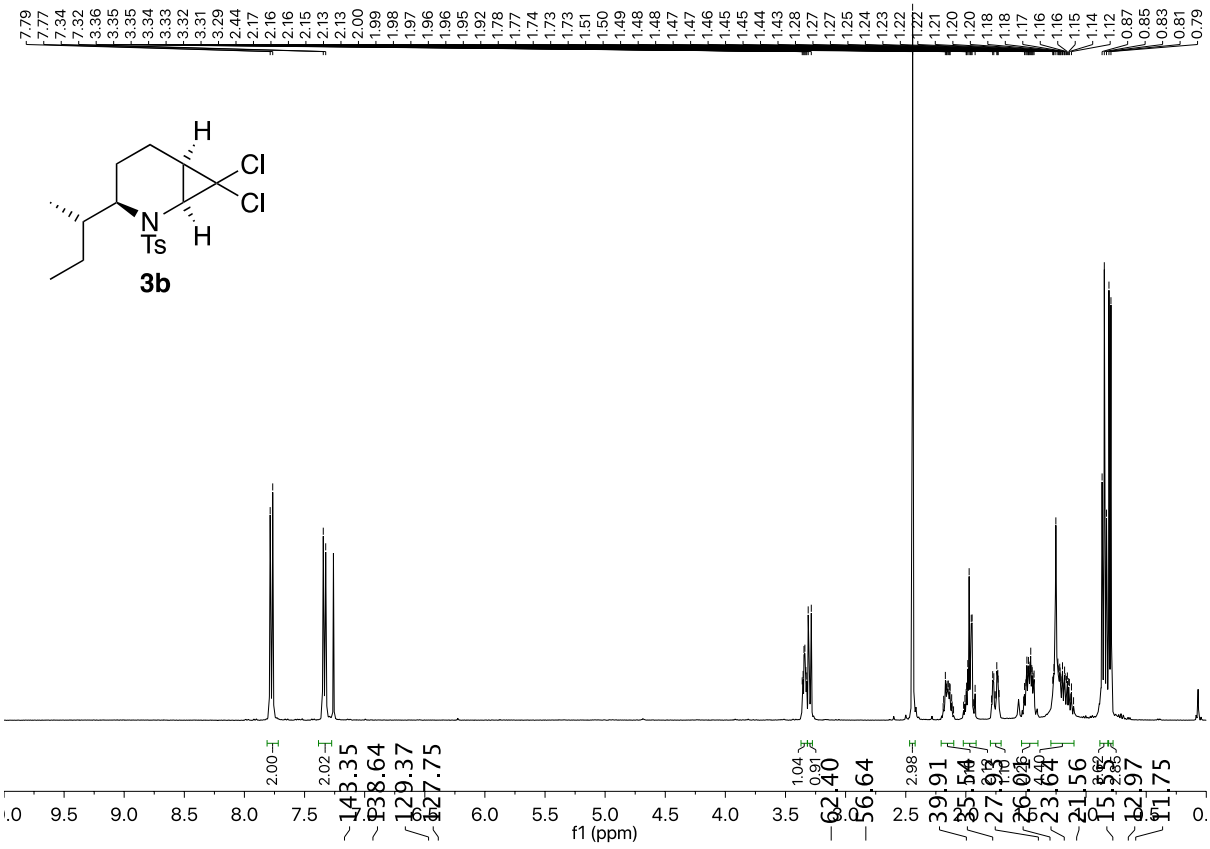
4a

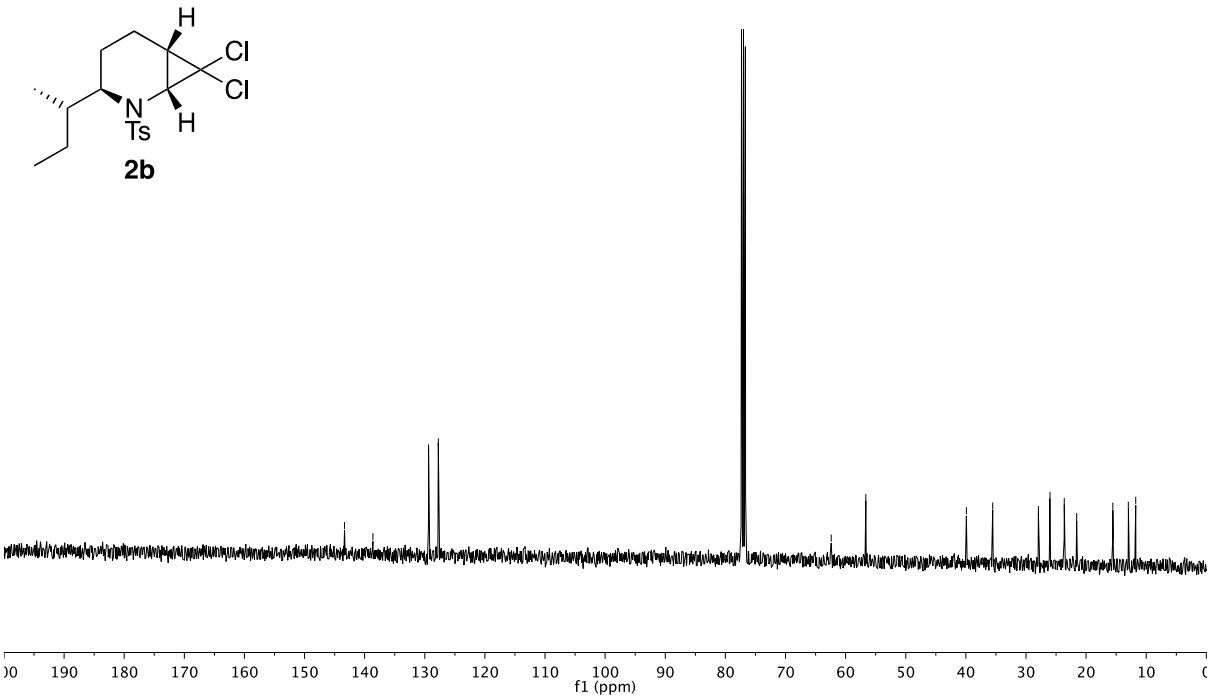


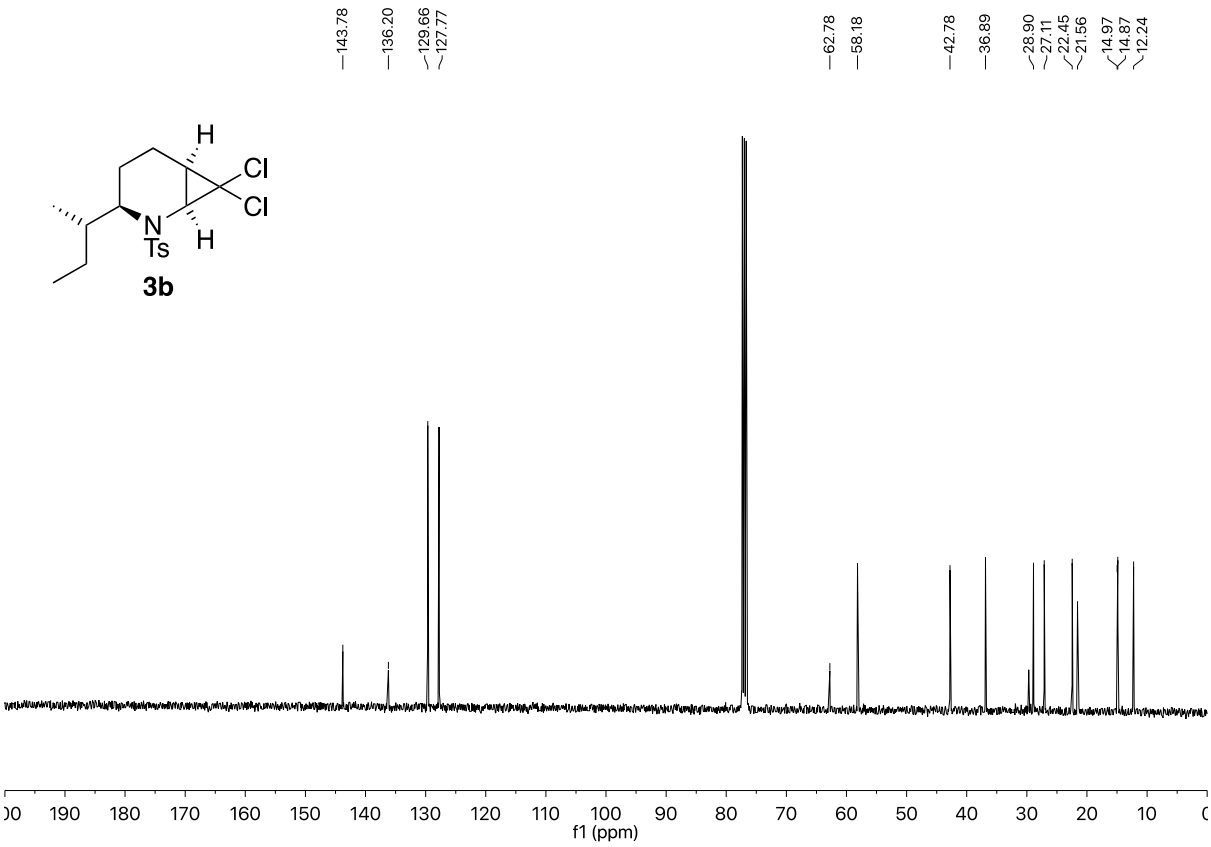
5a



^{1}H and ^{13}C NMR Spectra of 3b



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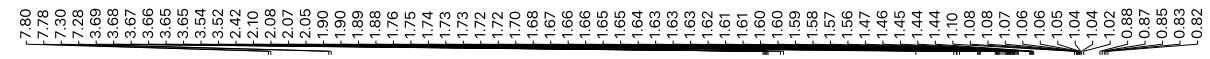
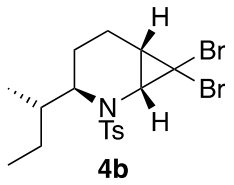
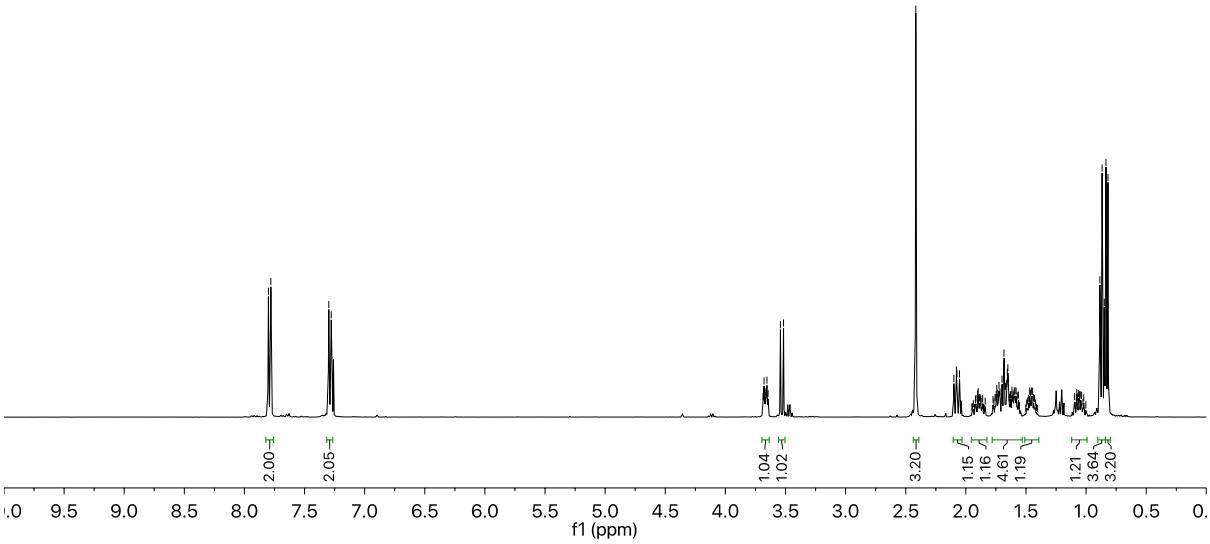
136.20
129.66
127.77
62.78
58.18
42.78
36.89
28.90
27.11
22.45
21.56
14.97
14.87
12.24
H
Cl
Cl
N
Ts
H
3b
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

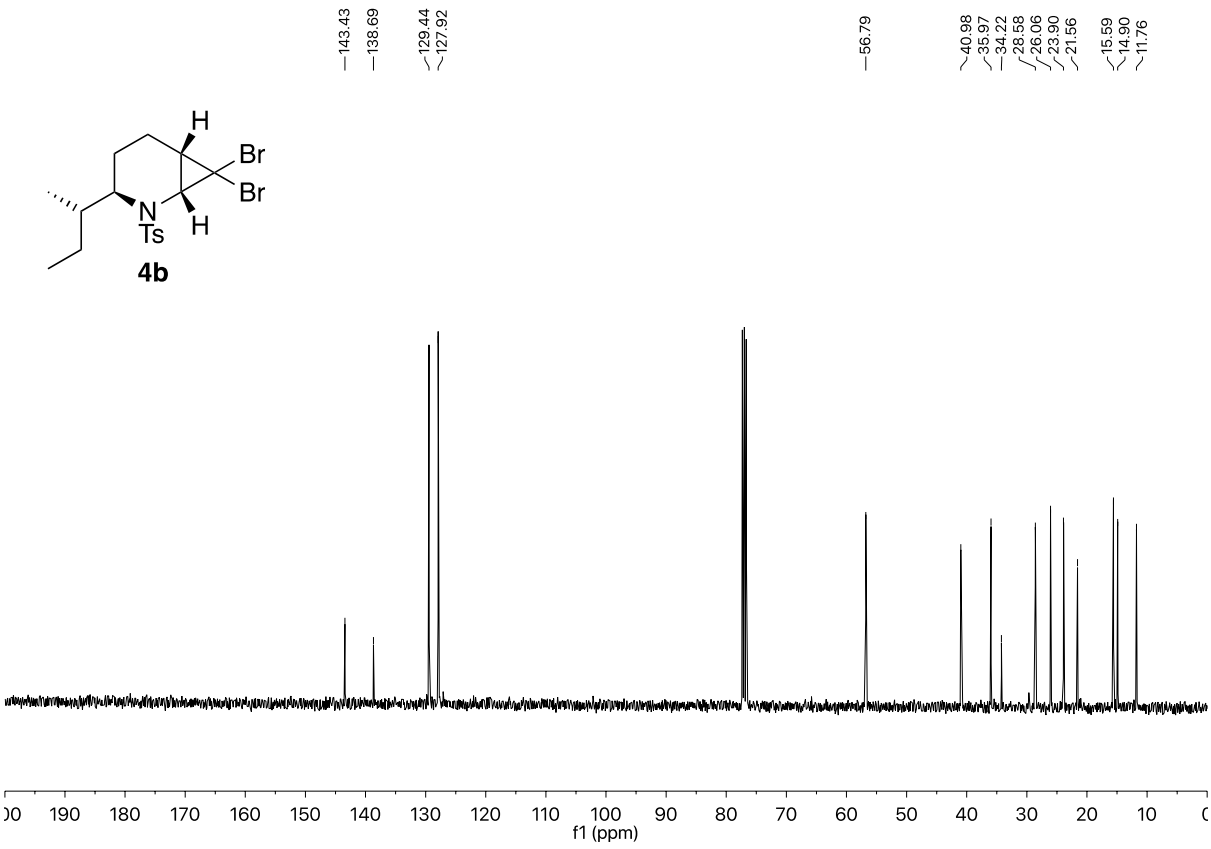
^{1}H and ^{13}C NMR Spectra of 4b





4b

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138.69
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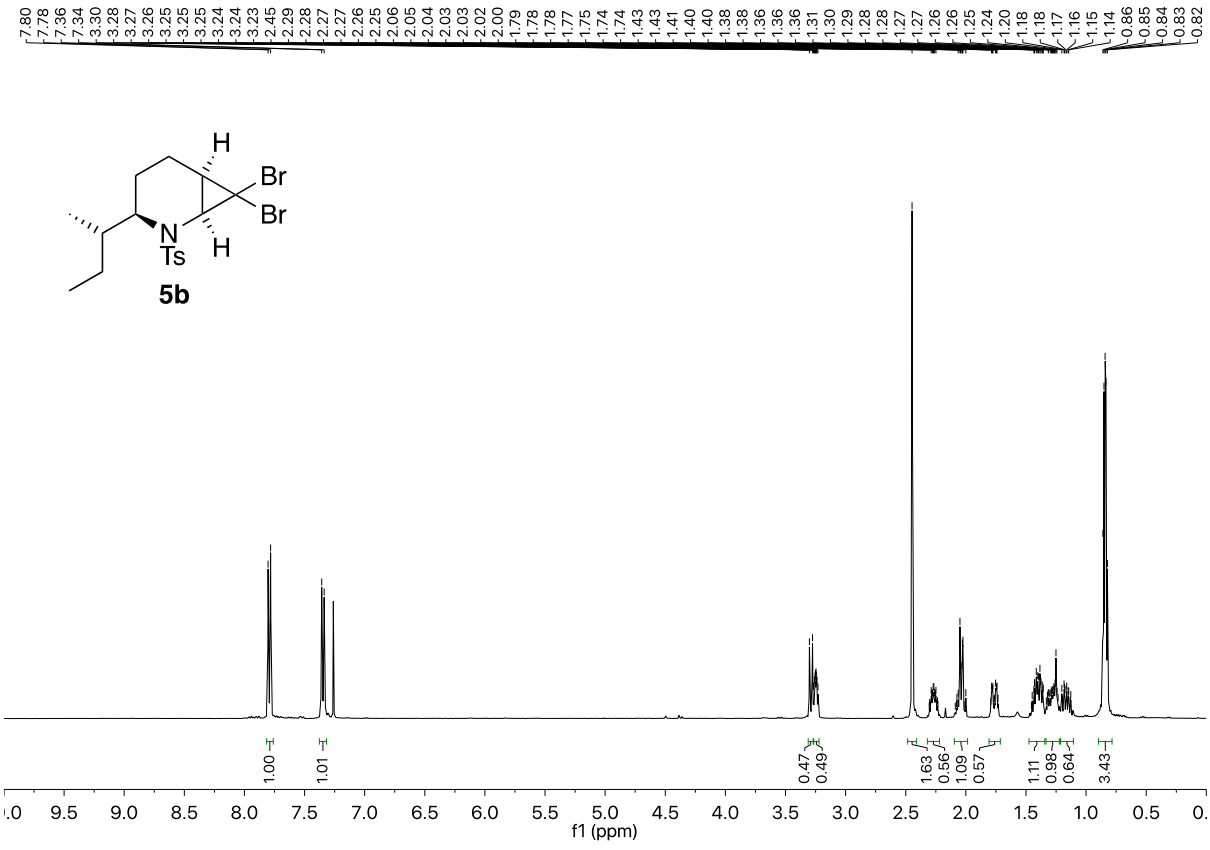
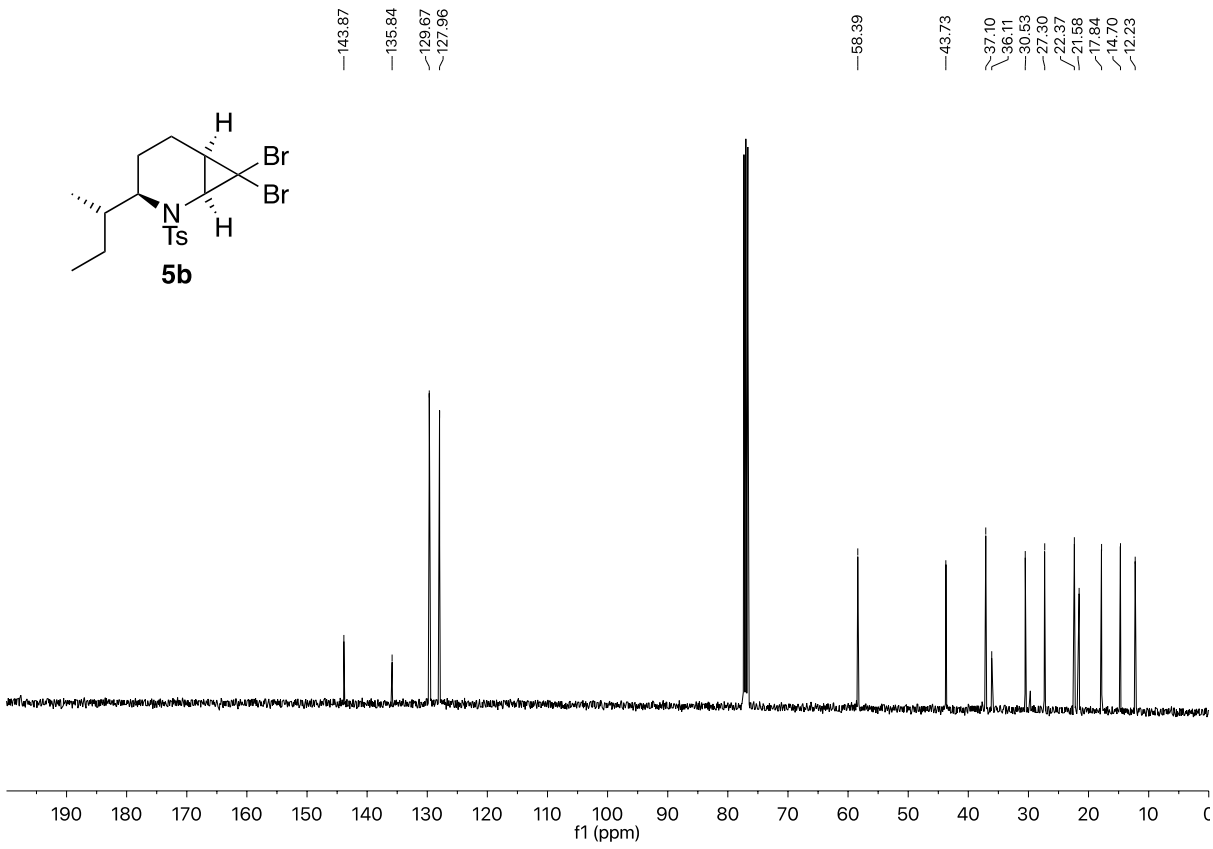
35.97
34.22
28.58
26.06
23.90
21.56
15.59
14.90
11.76
H
Br
Br
N
Ts
H
4b
f1 (ppm)

^{1}H and ^{13}C NMR Spectra of 5b

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58.39
43.73
37.10
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27.30
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21.58
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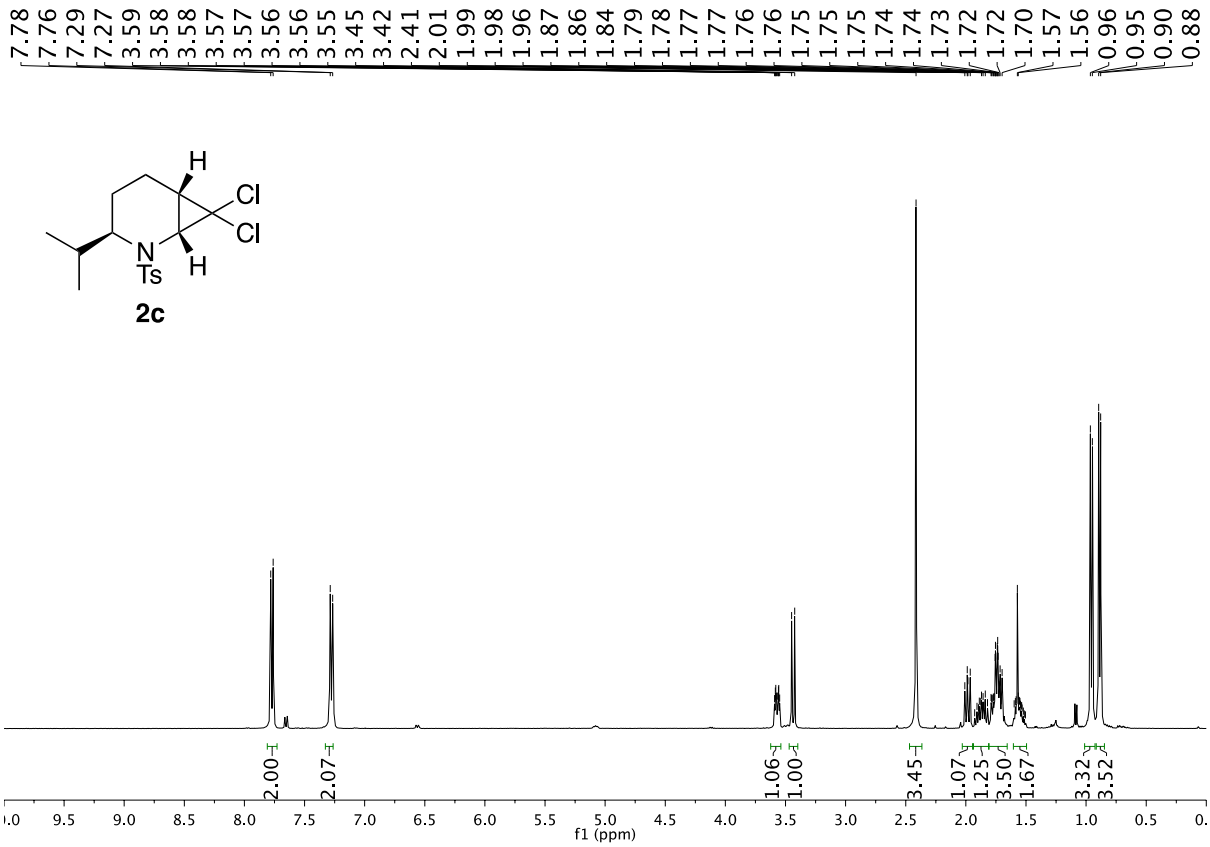
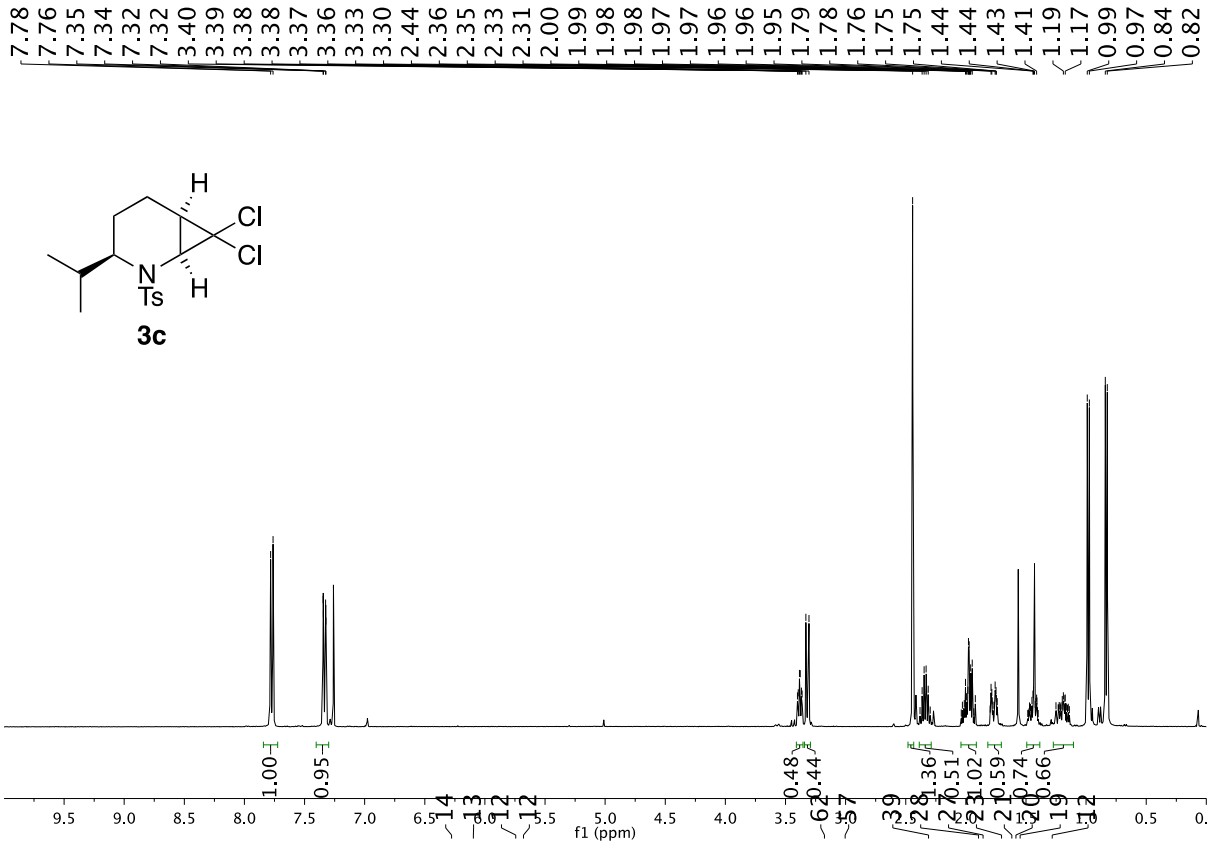
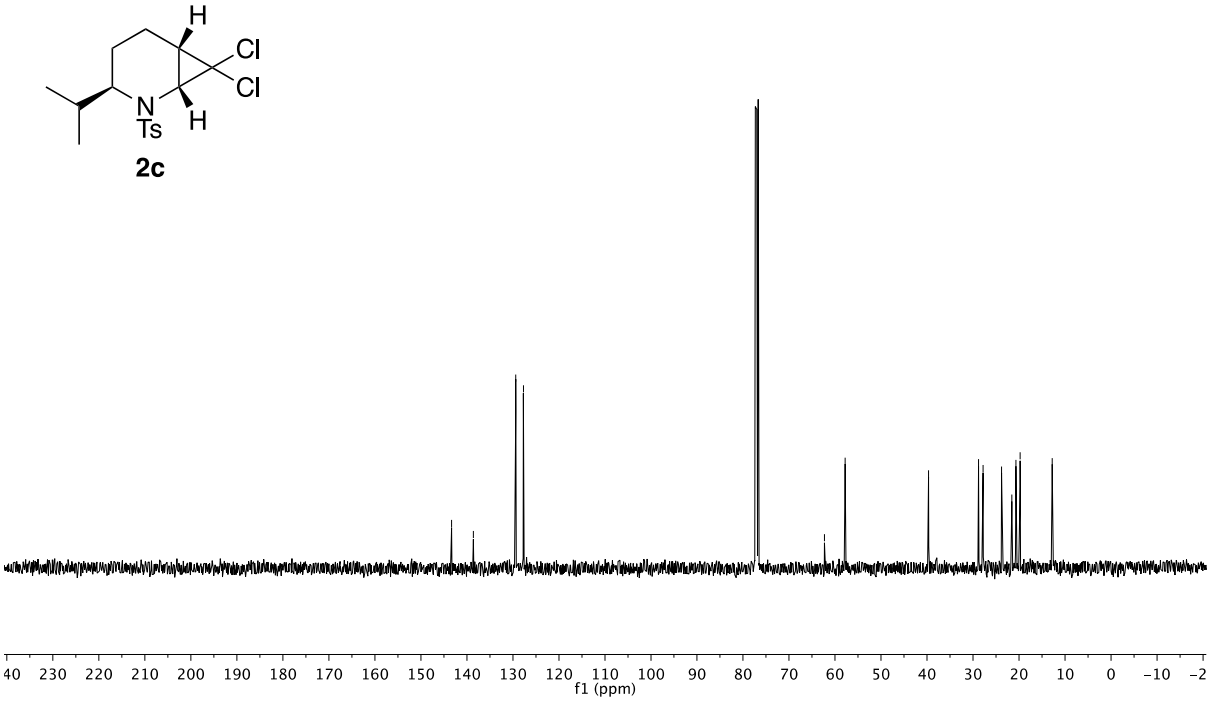
14.70
12.23
H
Br
Br
N
Ts
H
5b
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

^{1}H and ^{13}C NMR Spectra of 2c

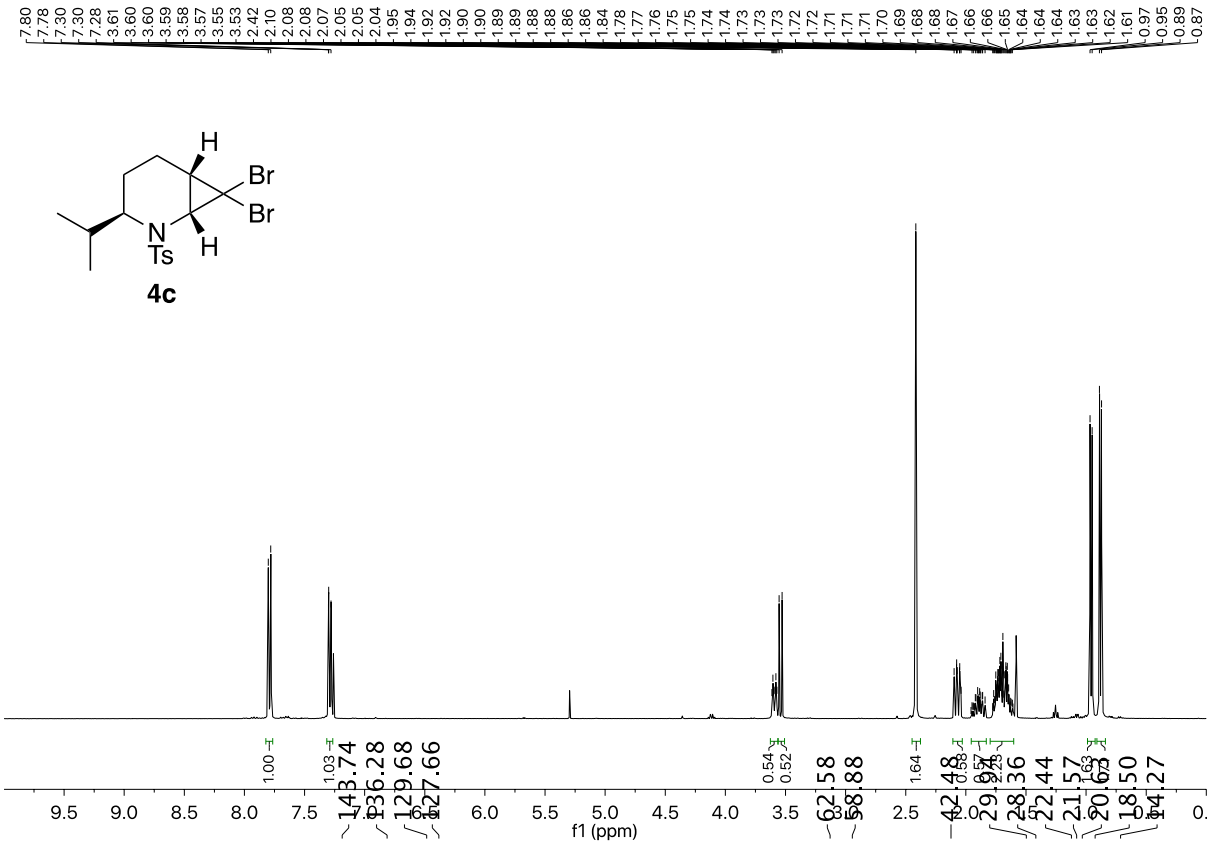


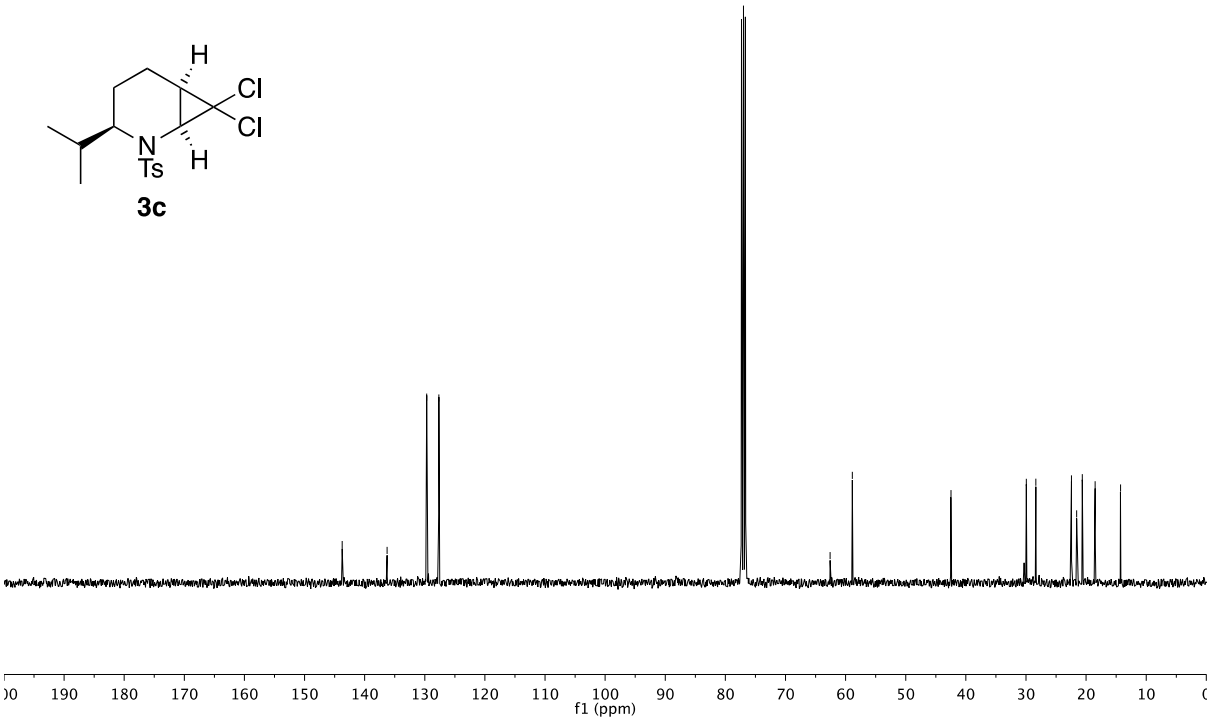
^{1}H and ^{13}C NMR Spectra of 3c

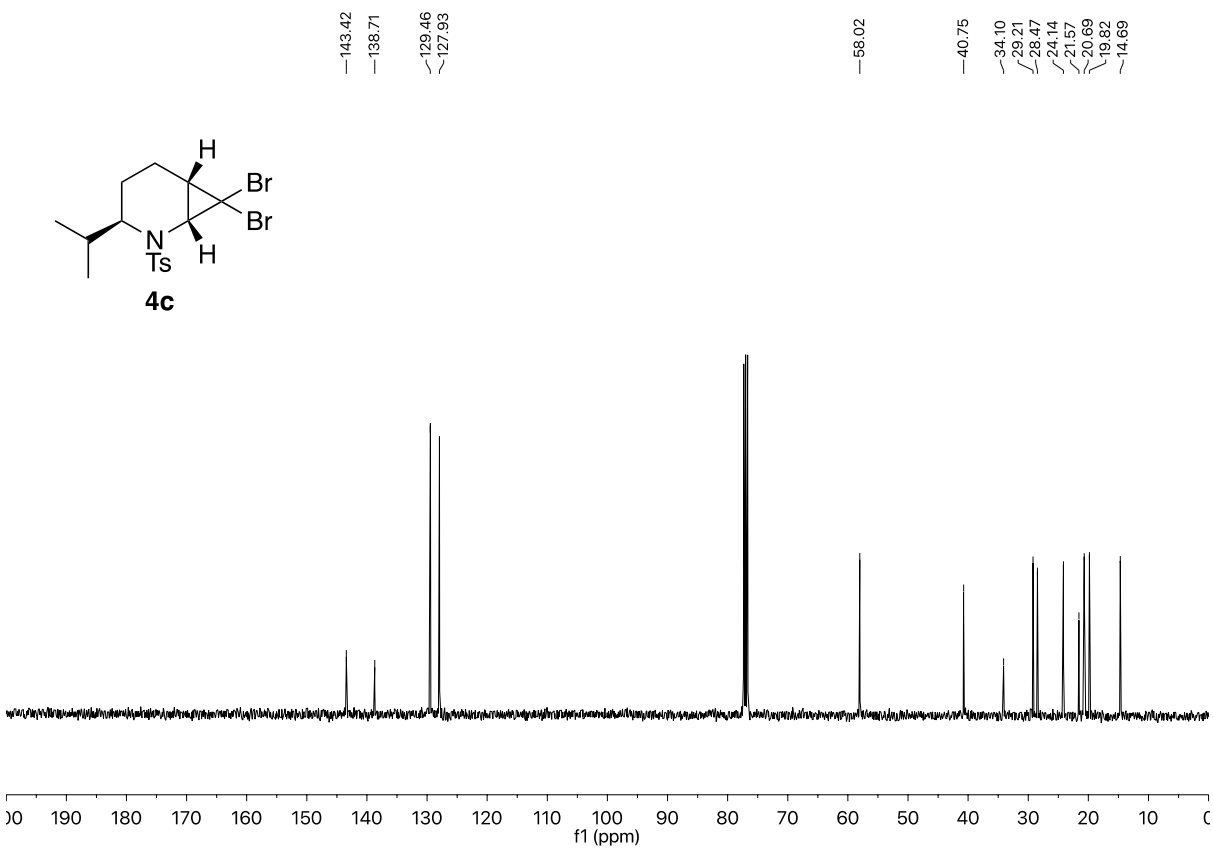




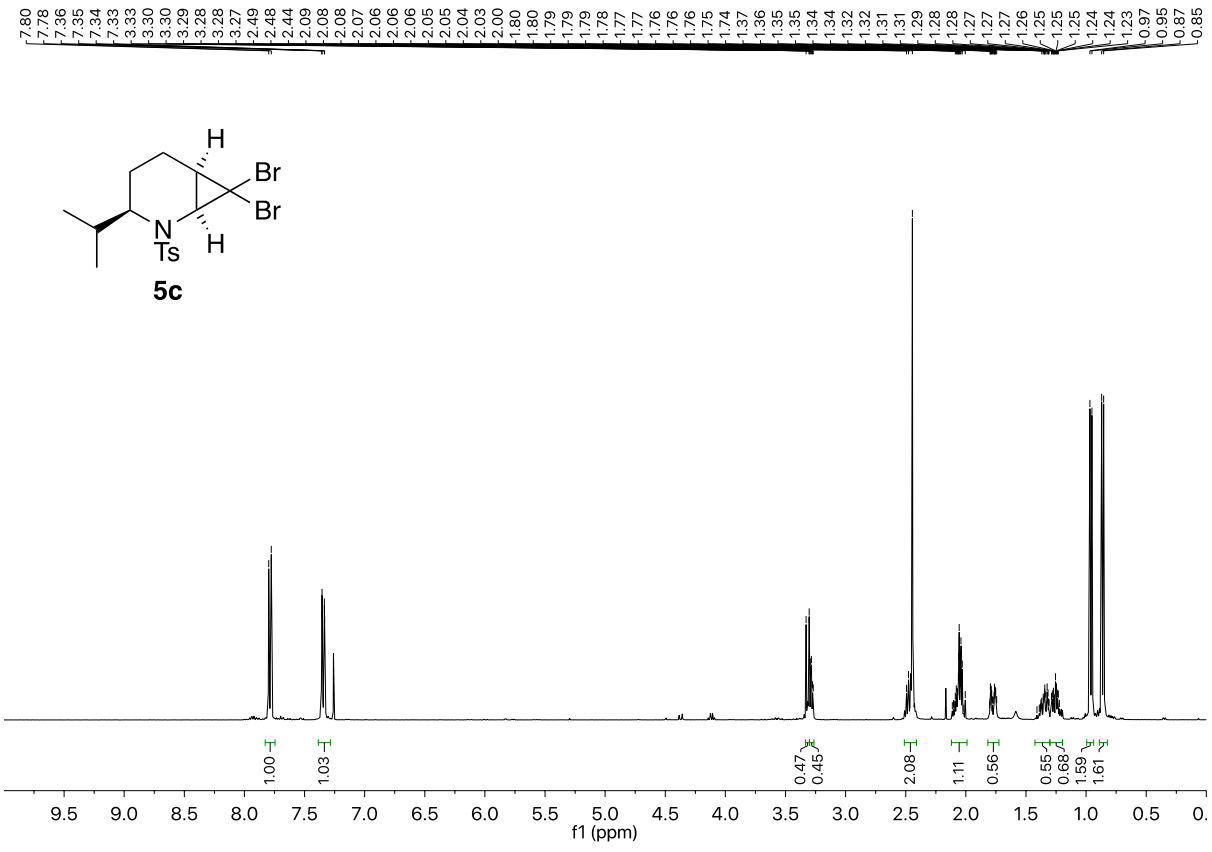
^{1}H and ^{13}C NMR Spectra of 4c



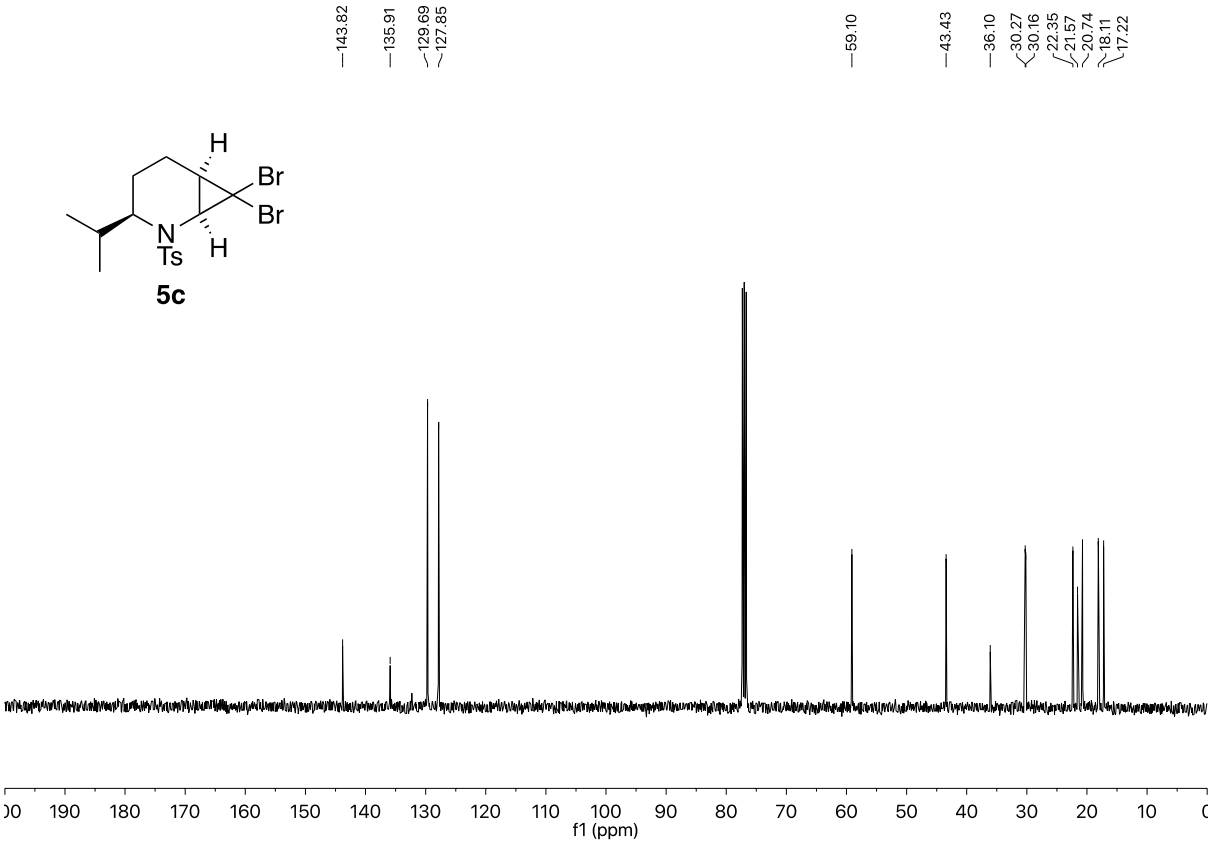



143.42
138.71
129.46
127.93
58.02
40.75
34.10
29.21
28.47
24.14
21.57
20.69
19.82
14.69
H
Br
Br
N
Ts
H
4c
f1 (ppm)

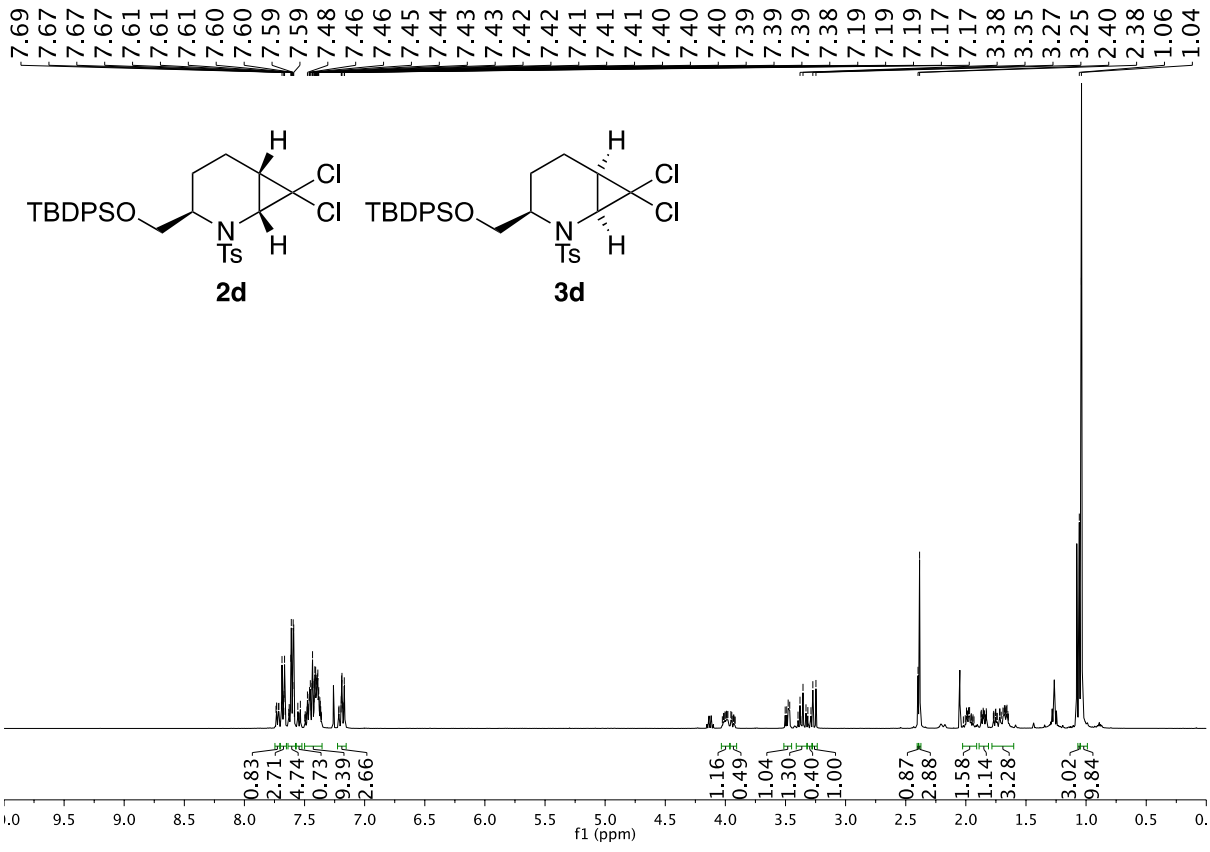
^{1}H and ^{13}C NMR Spectra of 5c



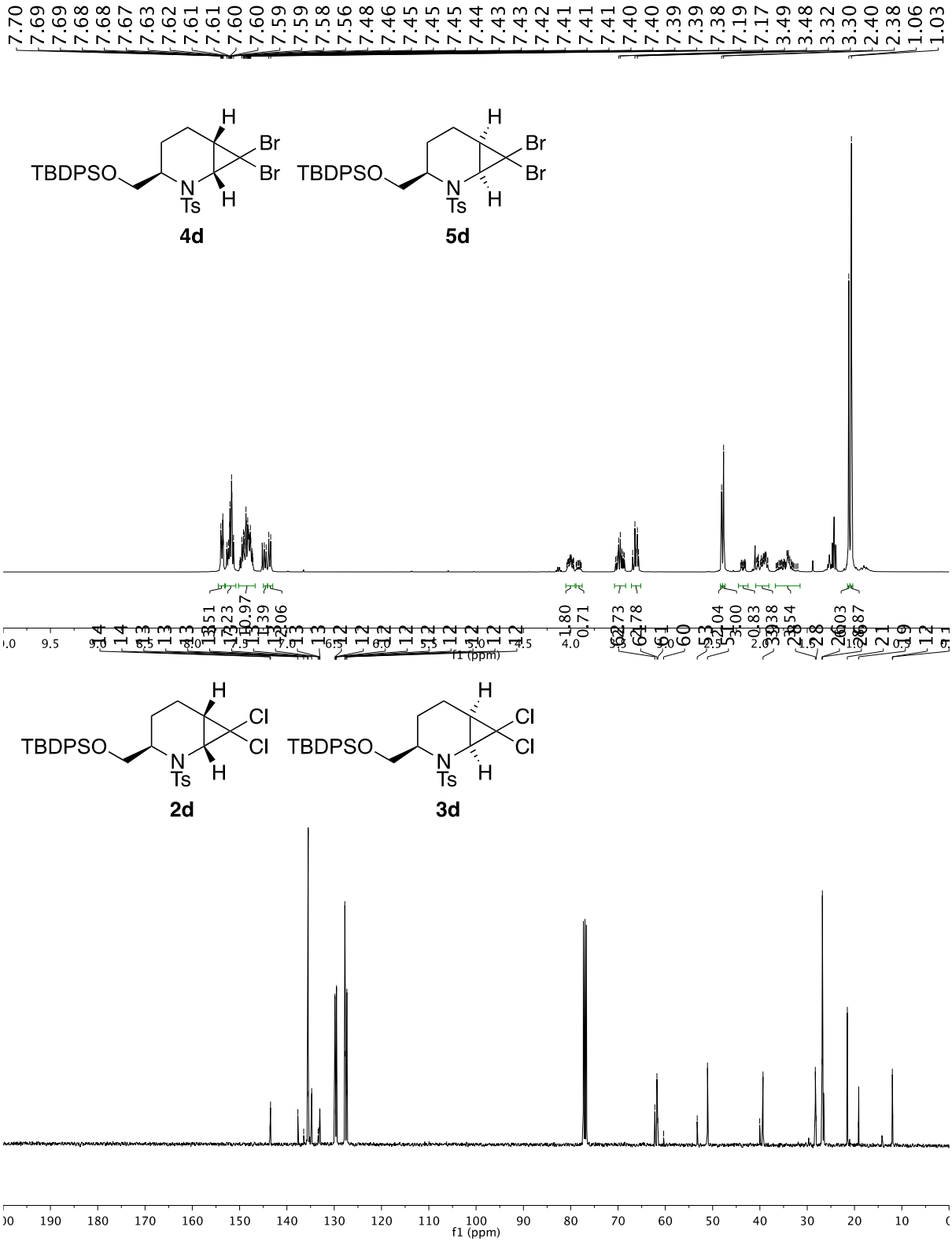
5c

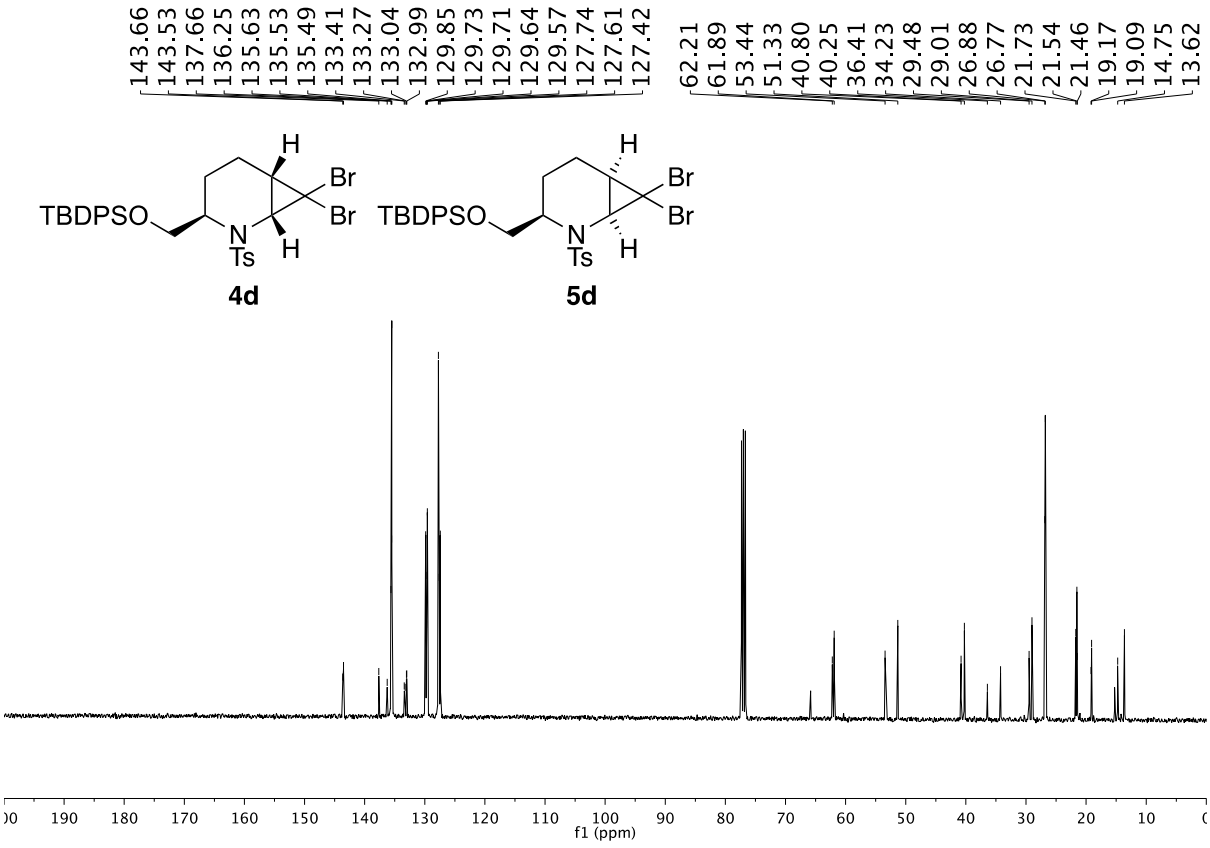

143.82
135.91
129.69
127.85
59.10
43.43
36.10
30.27
30.16
22.35
21.57
20.74
18.11
17.22
H
Br
Br
N
Ts
H
5c
f1 (ppm)

^{1}H and ^{13}C NMR Spectra of 2d/3d

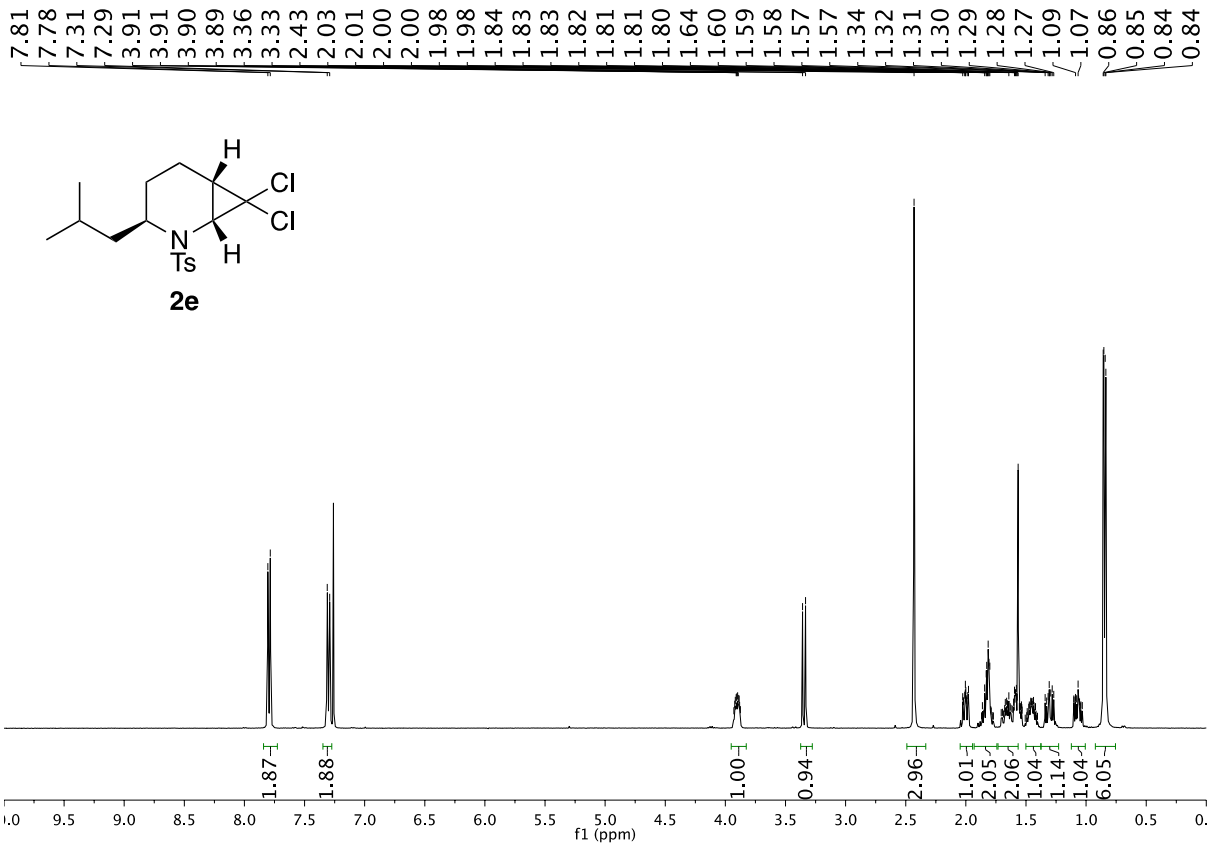


^{1}H and ^{13}C NMR Spectra of 4d/5d

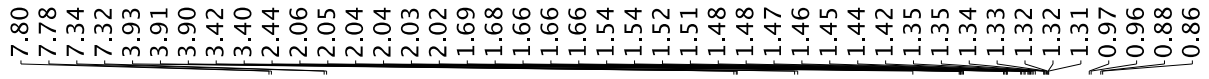


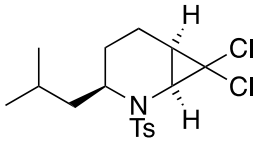

143.66
143.53
137.66
136.25
135.63
135.53
135.49
133.41
133.27
133.04
132.99
129.85
129.73
129.71
129.64
129.57
127.74
127.61
127.42
62.21
61.89
53.44
51.33
40.80
40.25
36.41
34.23
29.48
29.01
26.88
26.77
21.73
21.54
21.46
19.17
19.09
14.75
13.62
TBDPSO
Br
Br
H
N
Ts
H
4d
TBDPSO
Br
Br
H
N
Ts
H
5d
f1 (ppm)

^{1}H and ^{13}C NMR Spectra of 2e

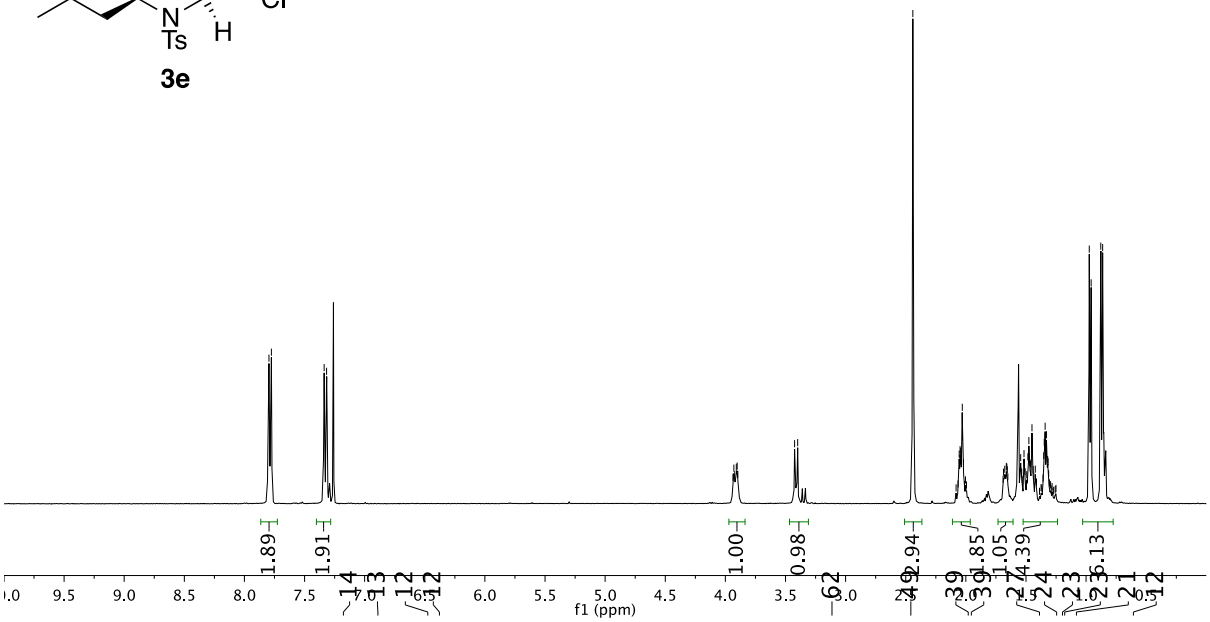


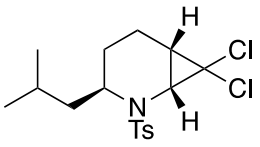
^{1}H and ^{13}C NMR Spectra of 3e





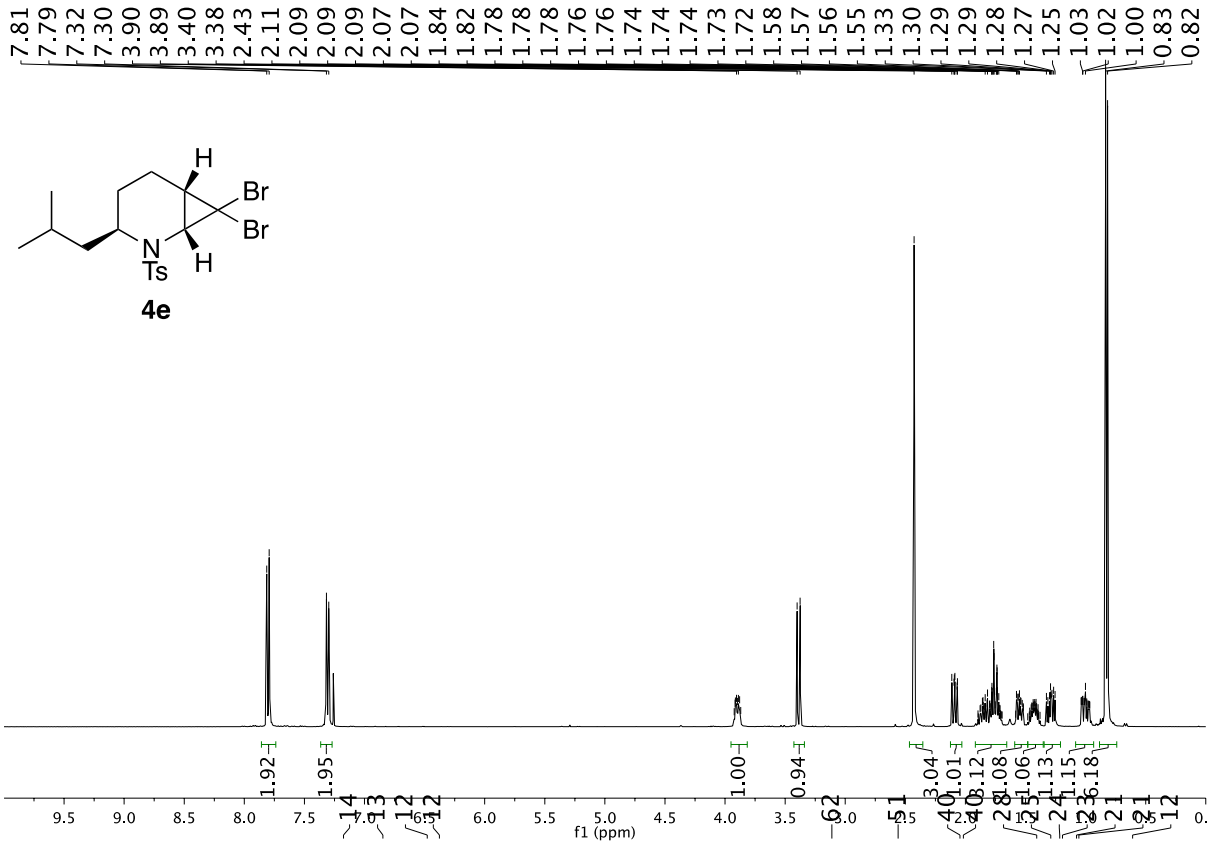
3e

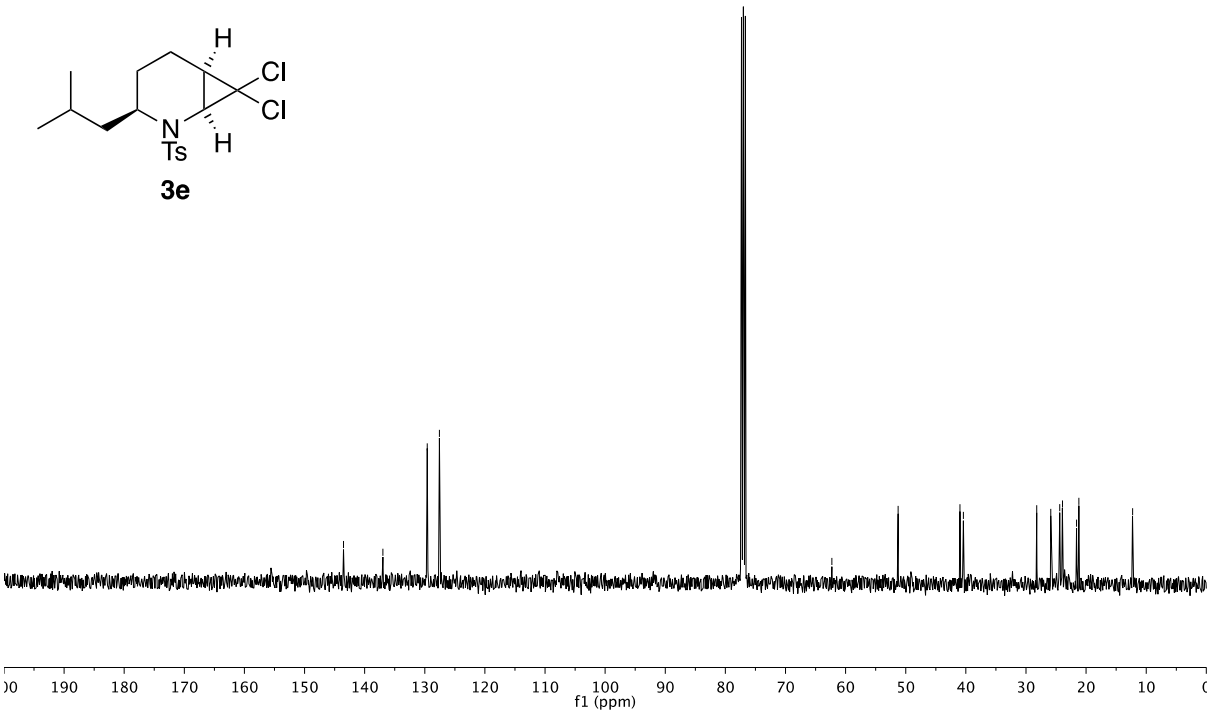




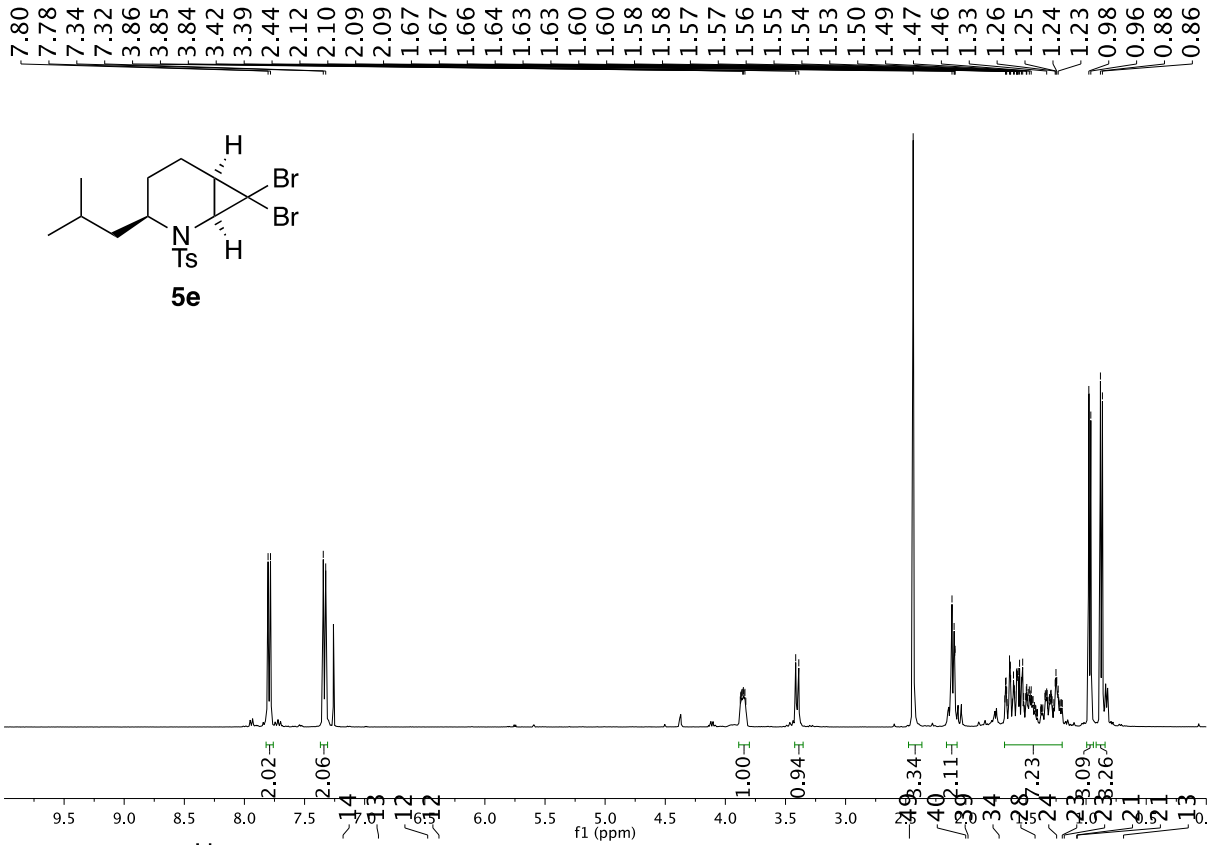
2e

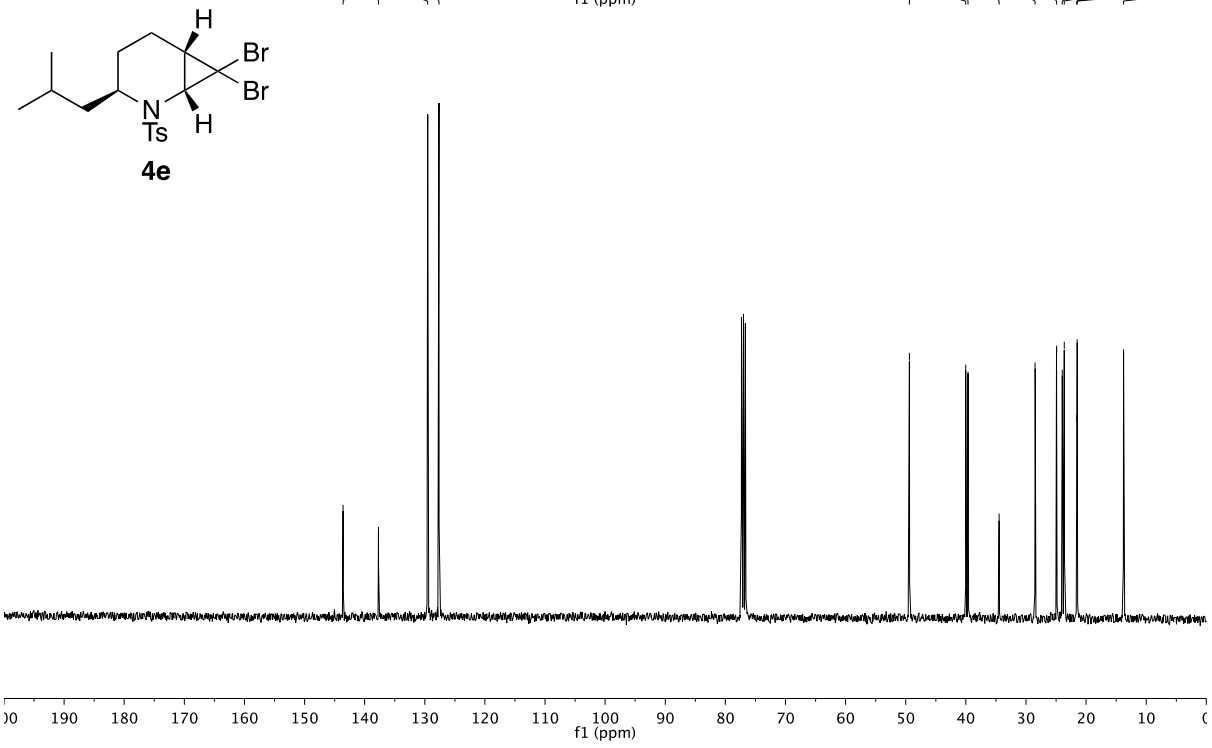
^{1}H and ^{13}C NMR Spectra of 4e



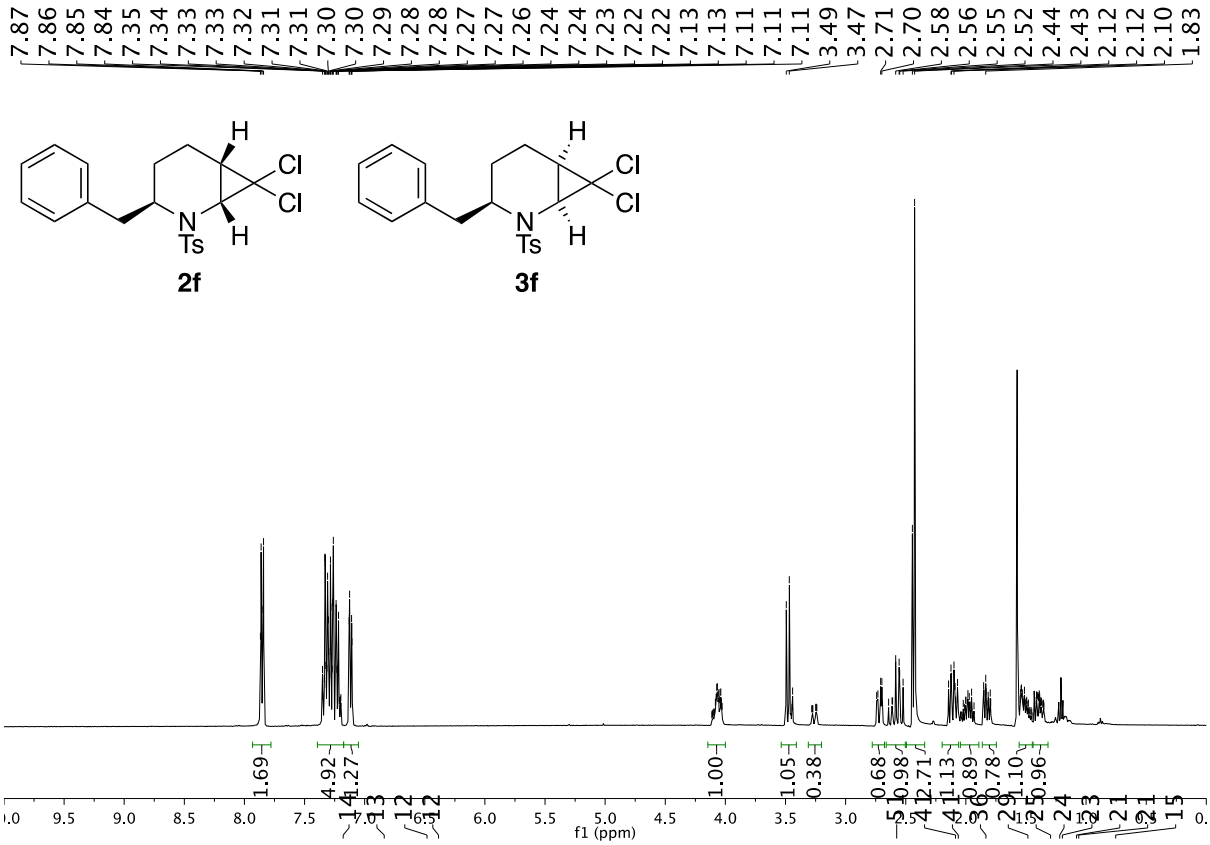


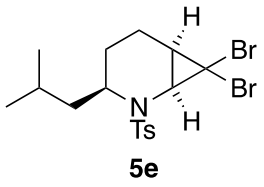
^{1}H and ^{13}C NMR Spectra of 5e



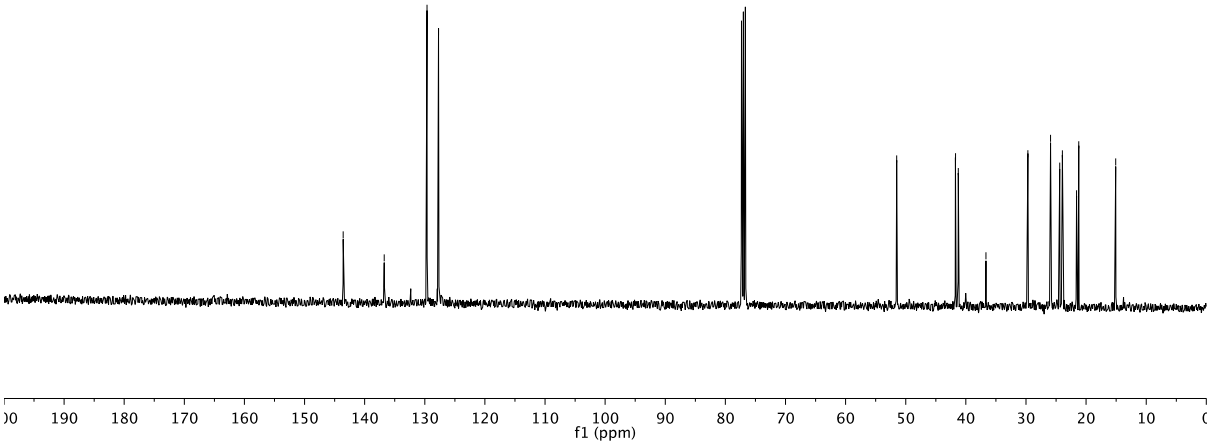


^{1}H and ^{13}C NMR Spectra of 2f/3f

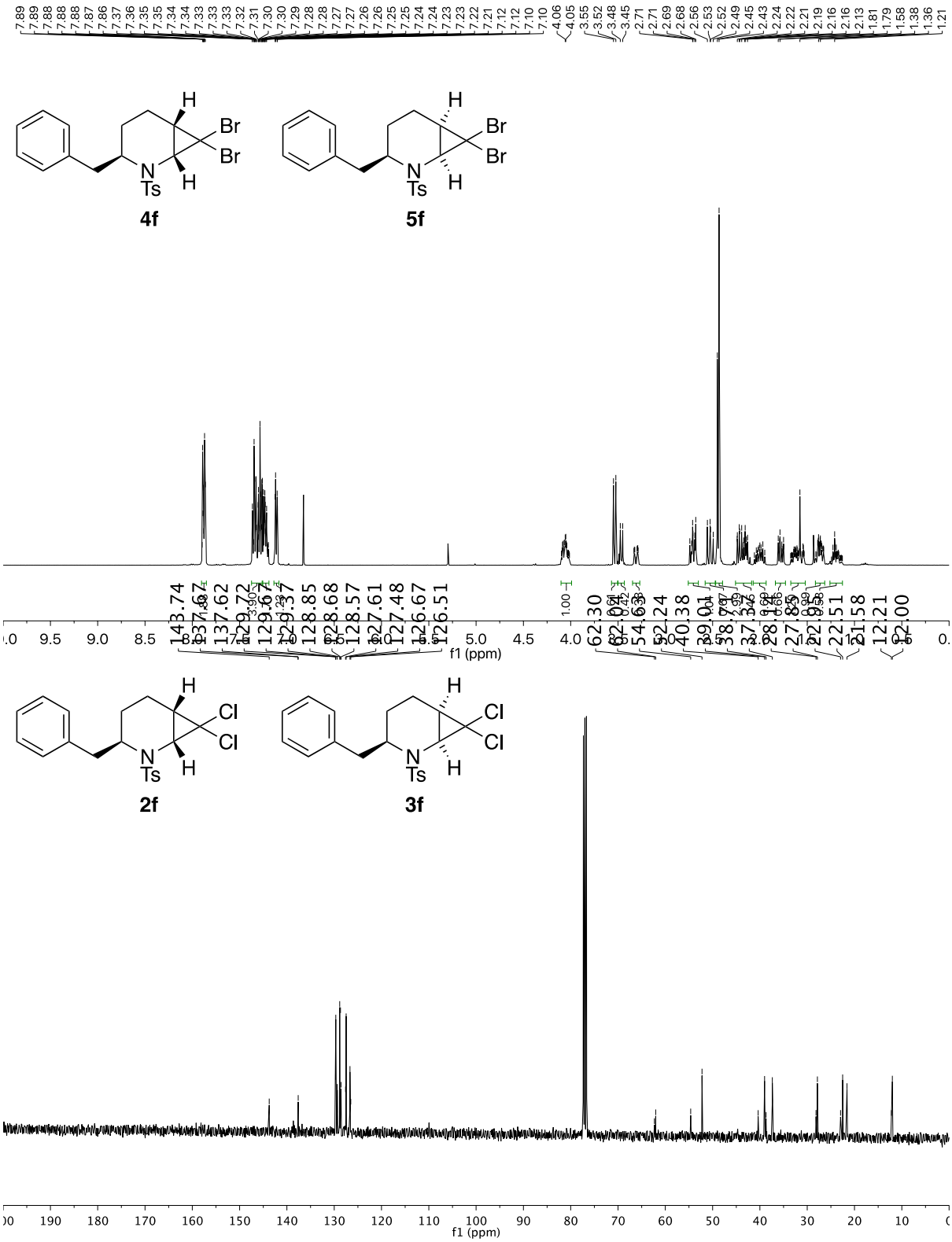


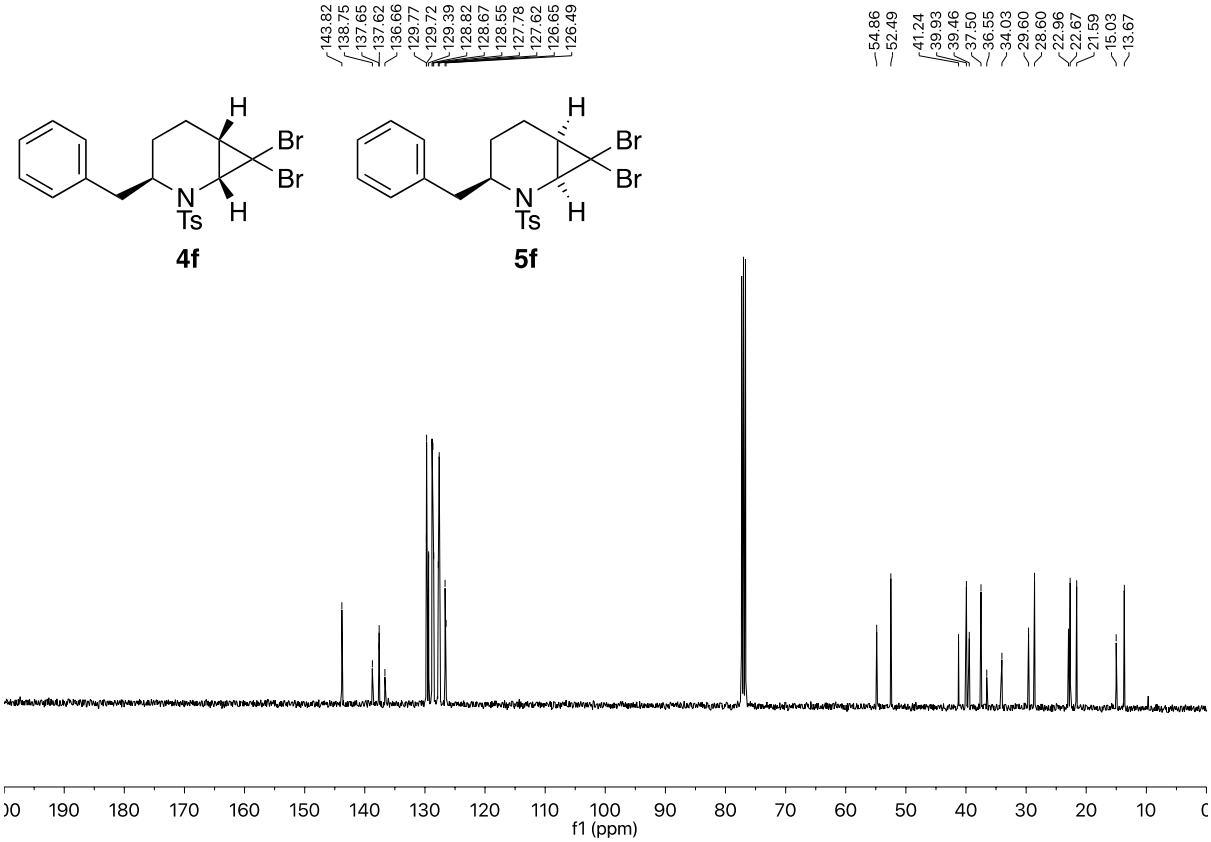


5e

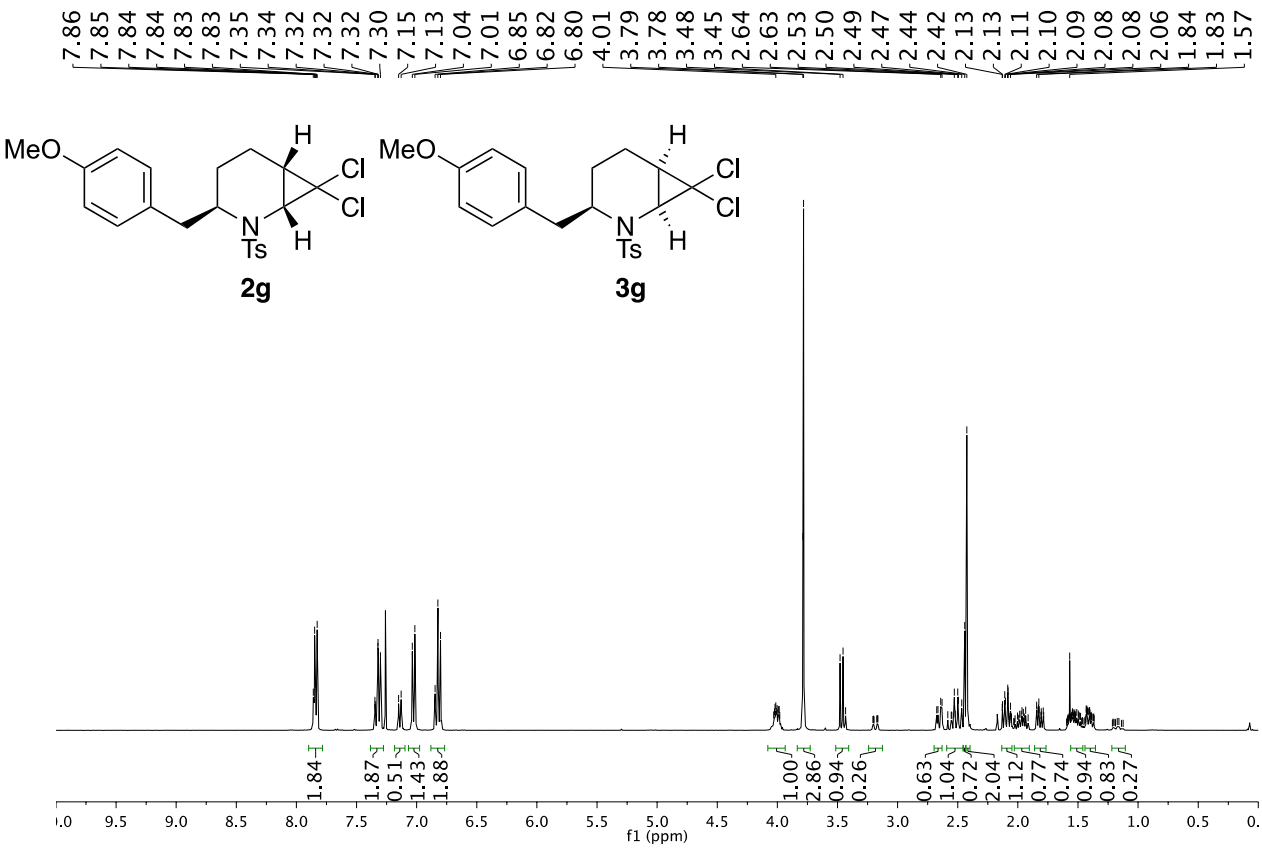


^{1}H and ^{13}C NMR Spectra of 4f/5f

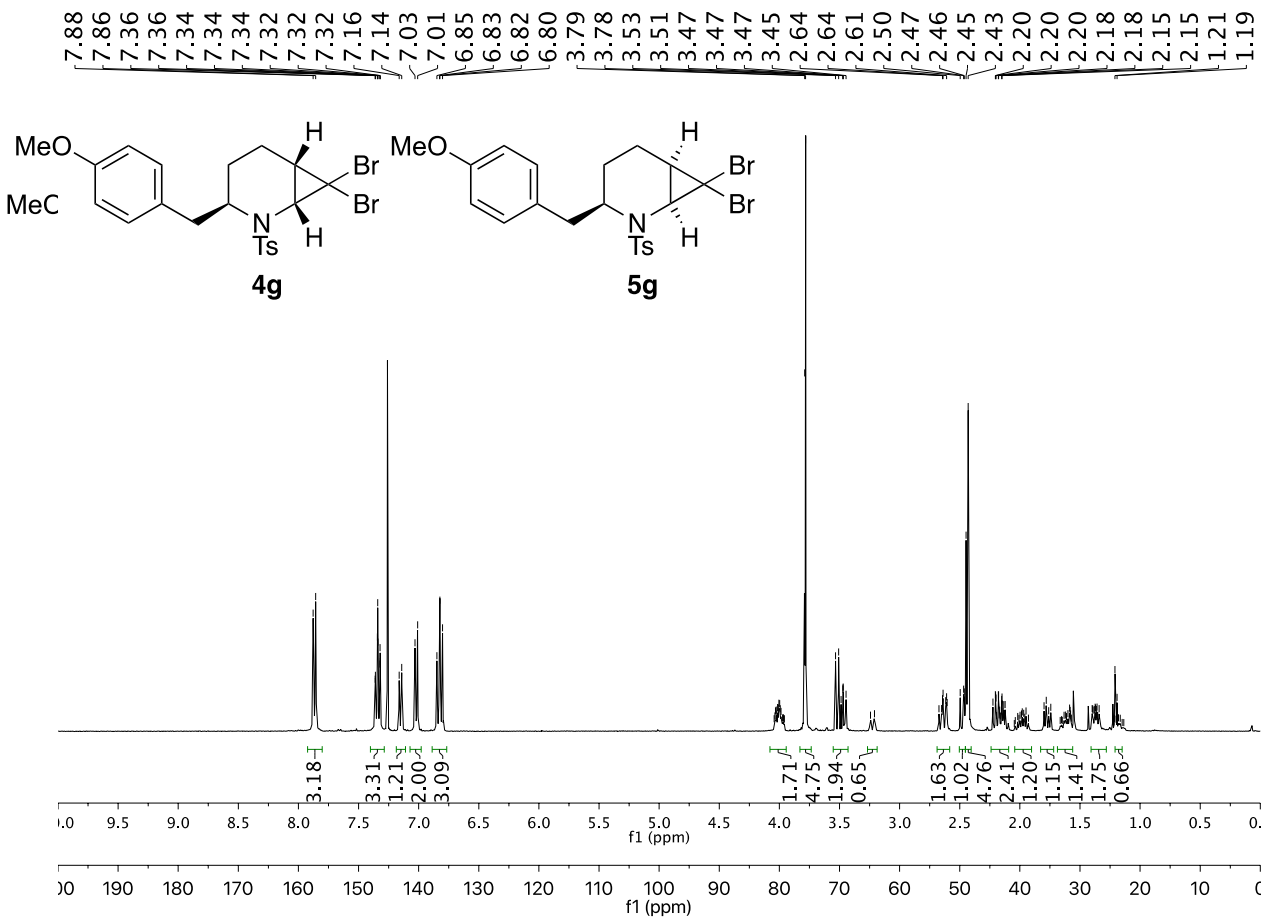



143.82
138.75
137.65
137.62
136.66
129.77
129.72
129.39
128.82
128.67
128.55
127.78
127.62
126.65
126.49
54.86
52.49
41.24
39.93
39.46
37.50
36.55
34.03
29.60
28.60
22.96
22.67
21.59
15.03
13.67
H
Br
Br
N
Ts
H
4f
H
Br
Br
N
Ts
H
5f
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

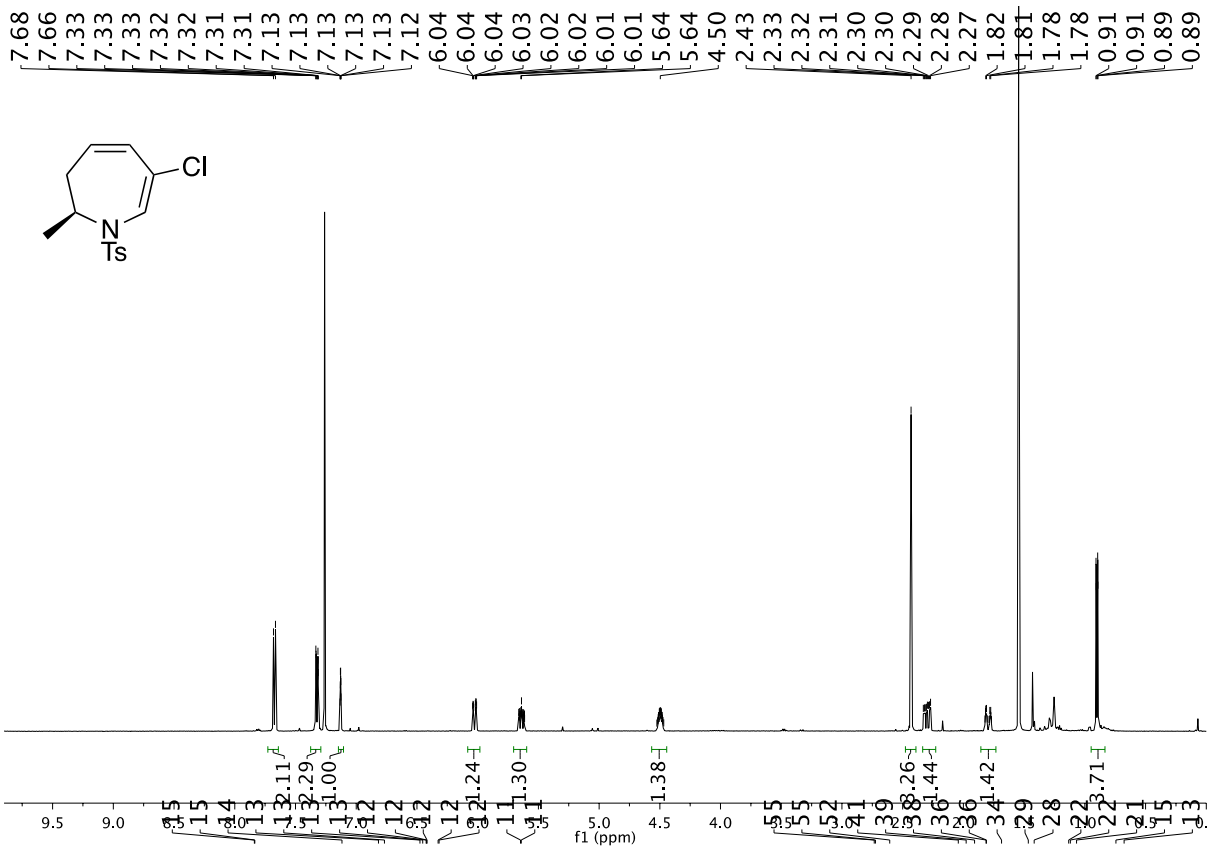
^{1}H and ^{13}C NMR Spectra of 2g/3g

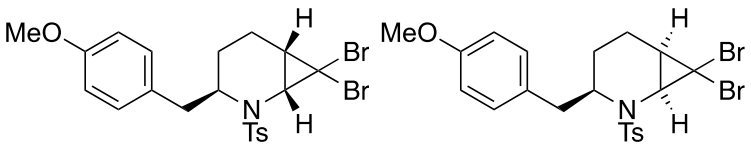


^{1}H and ^{13}C NMR Spectra of 4g/5g



^{1}H and ^{13}C NMR Spectra of 6

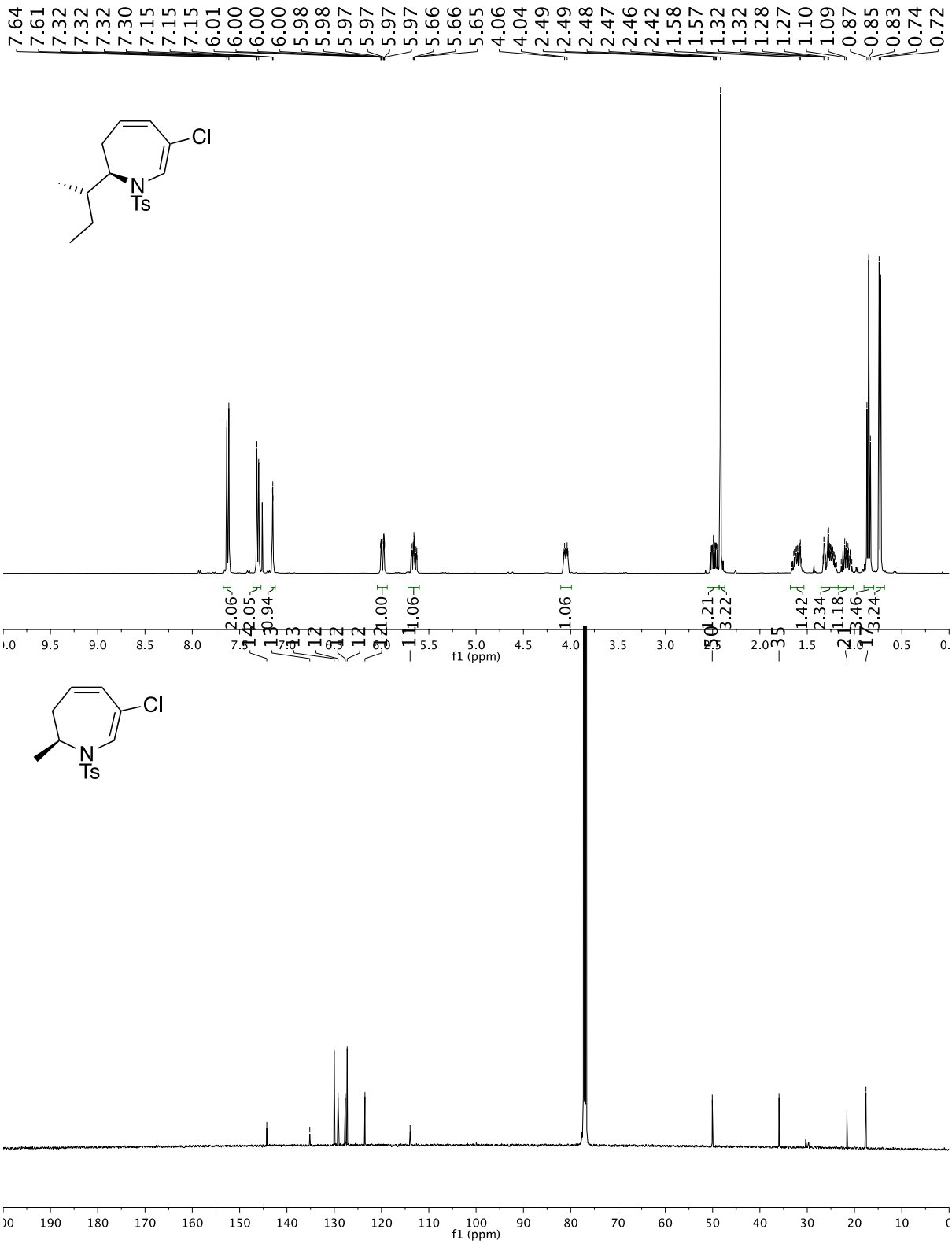




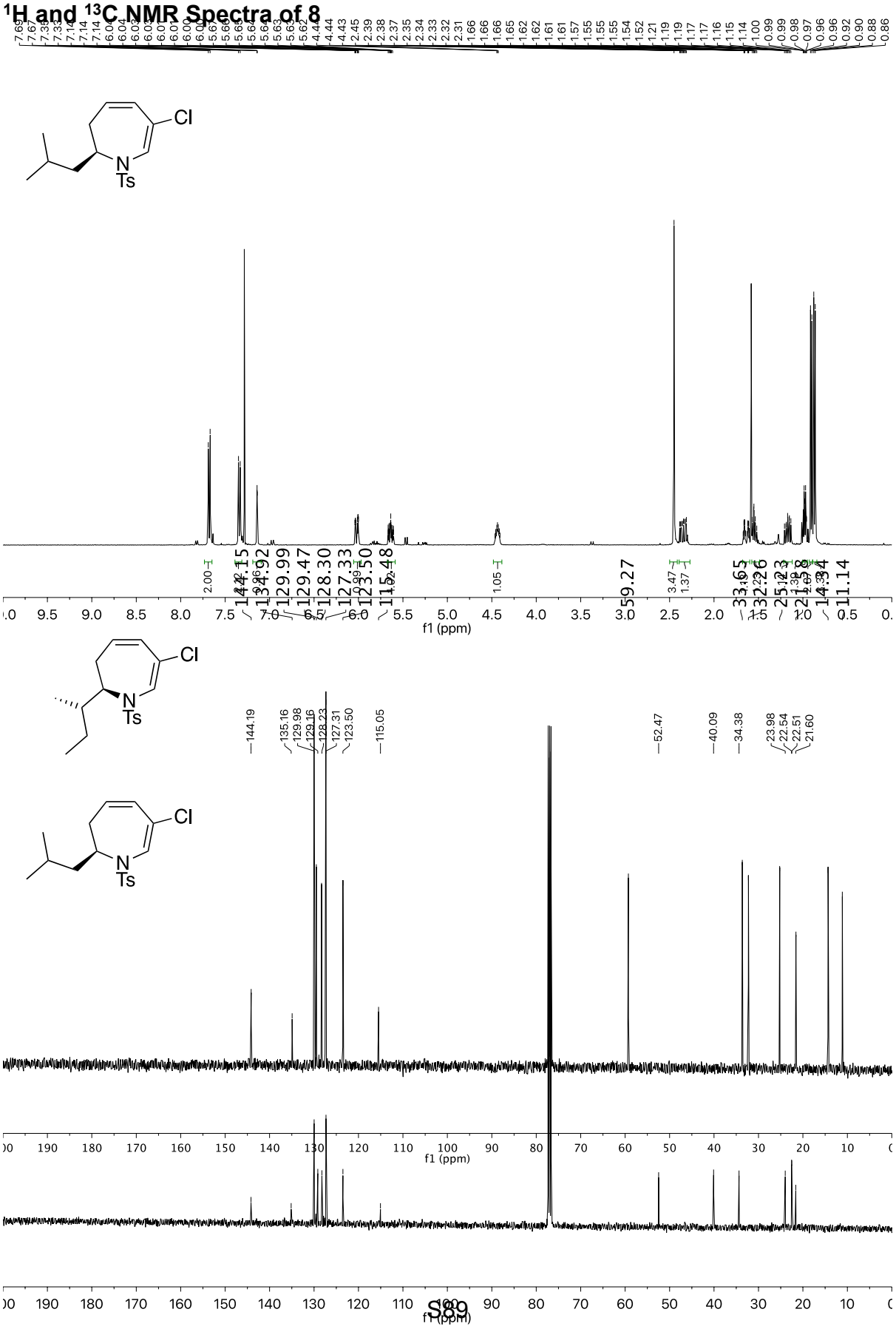
4g

5g

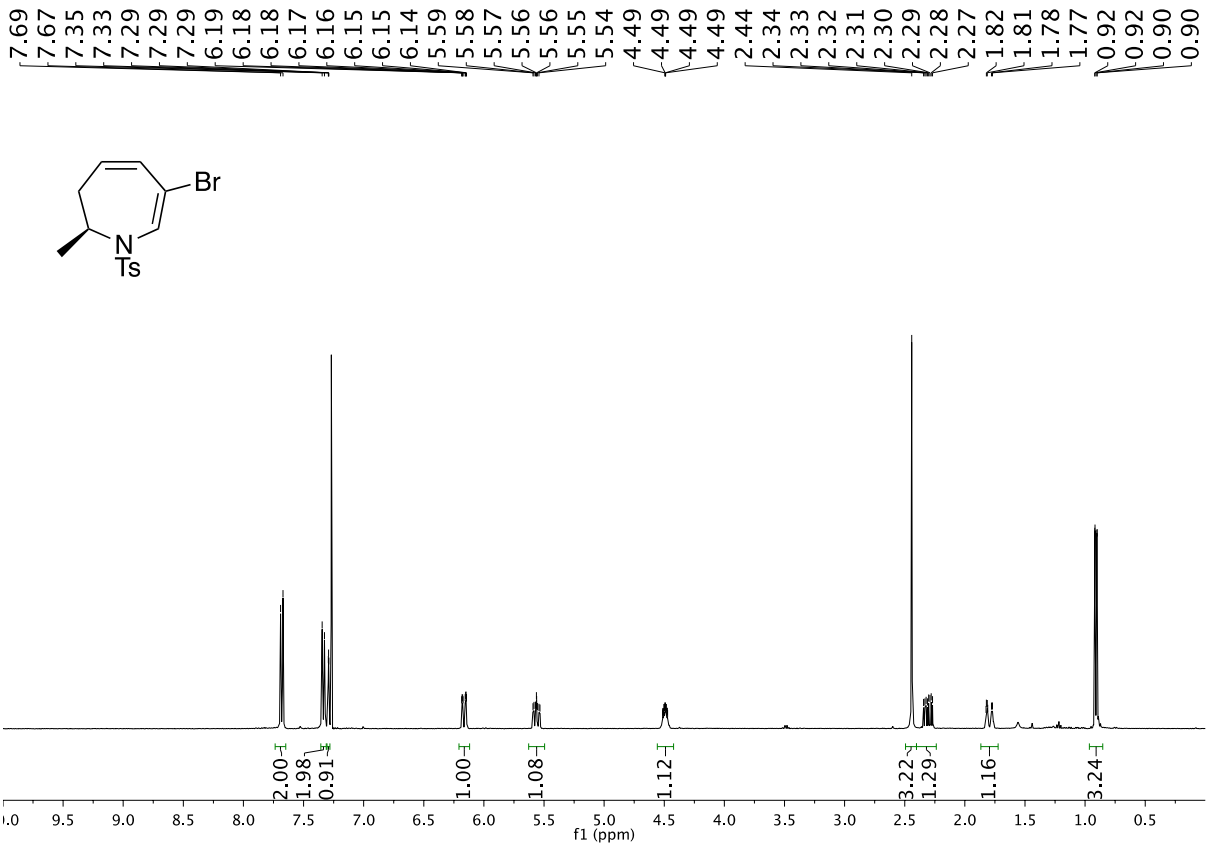
^{1}H and ^{13}C NMR Spectra of 7



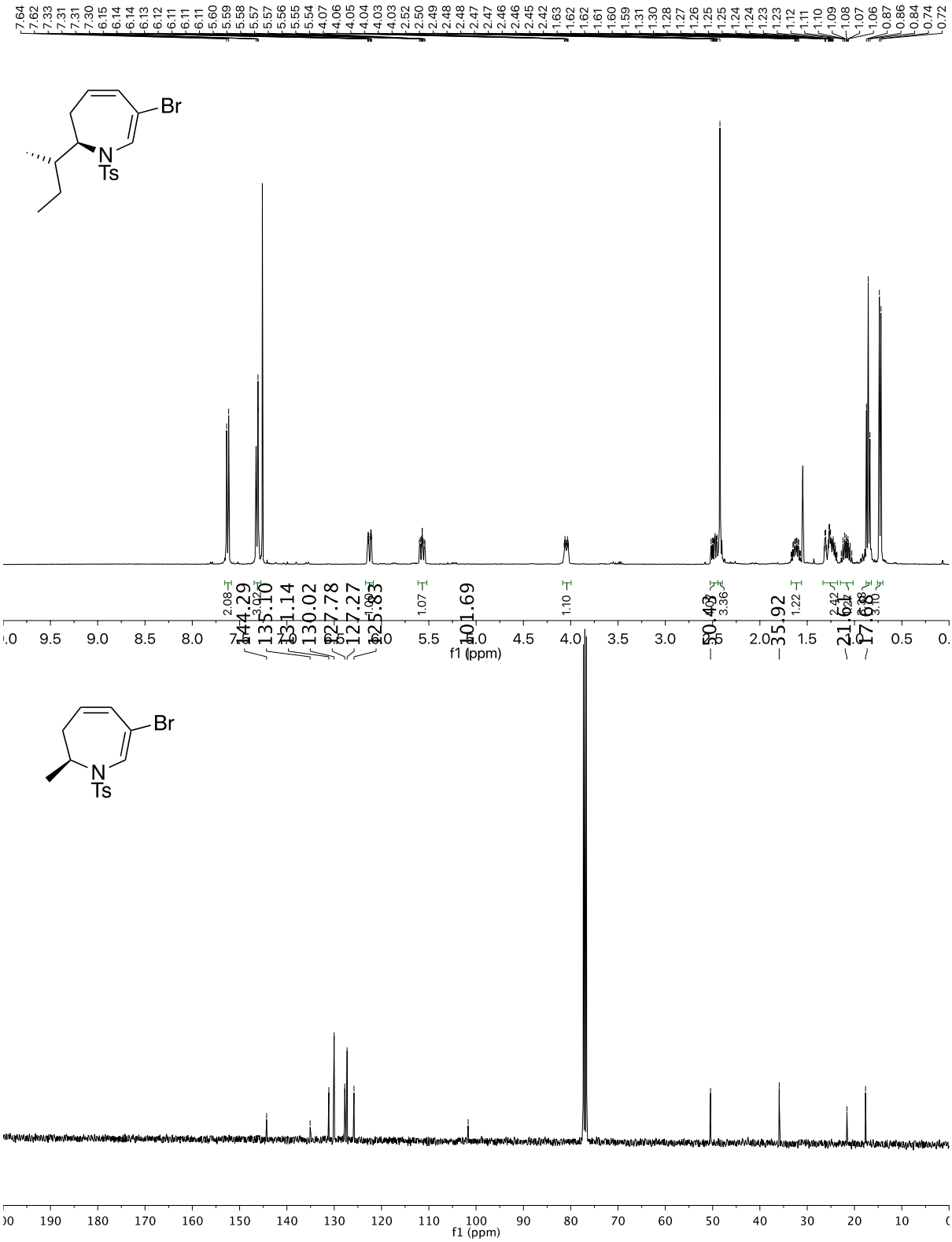
^{1}H and ^{13}C NMR Spectra of 8

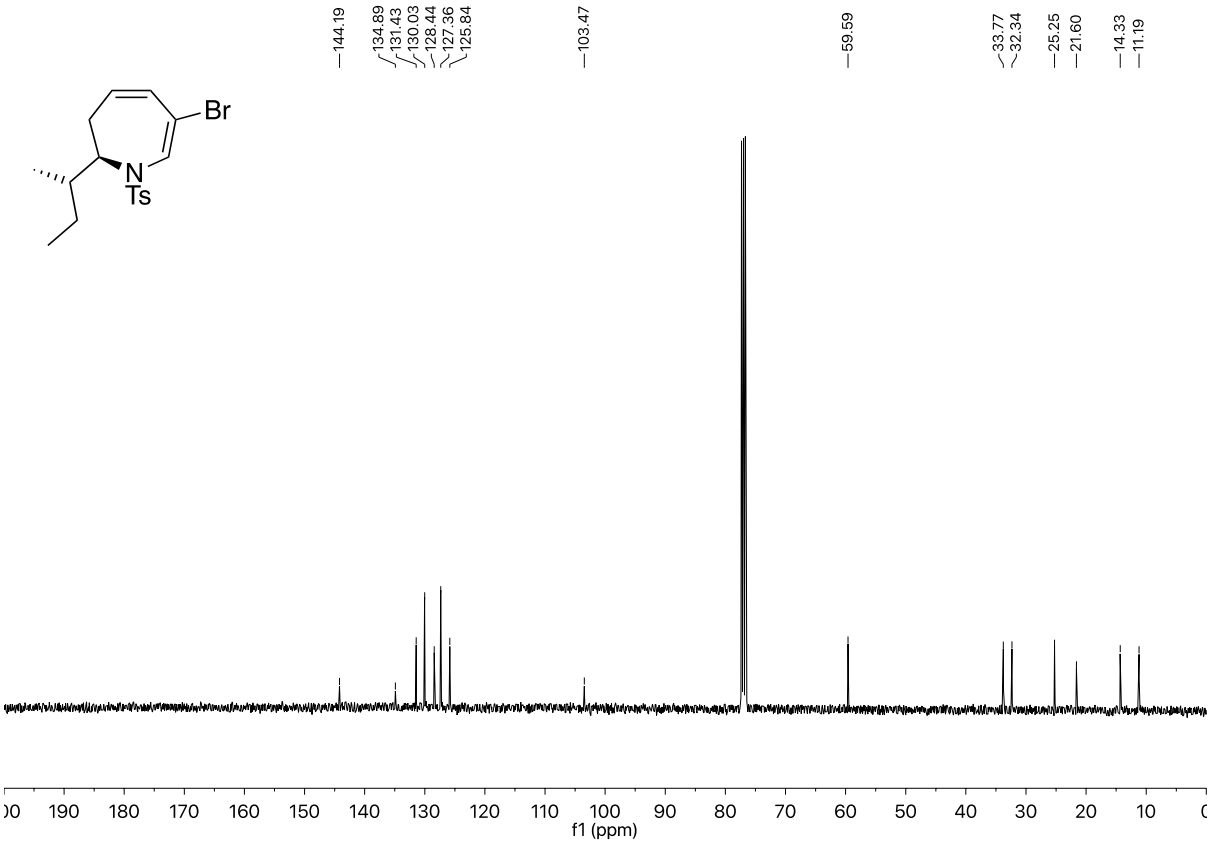


^{1}H and ^{13}C NMR Spectra of 10

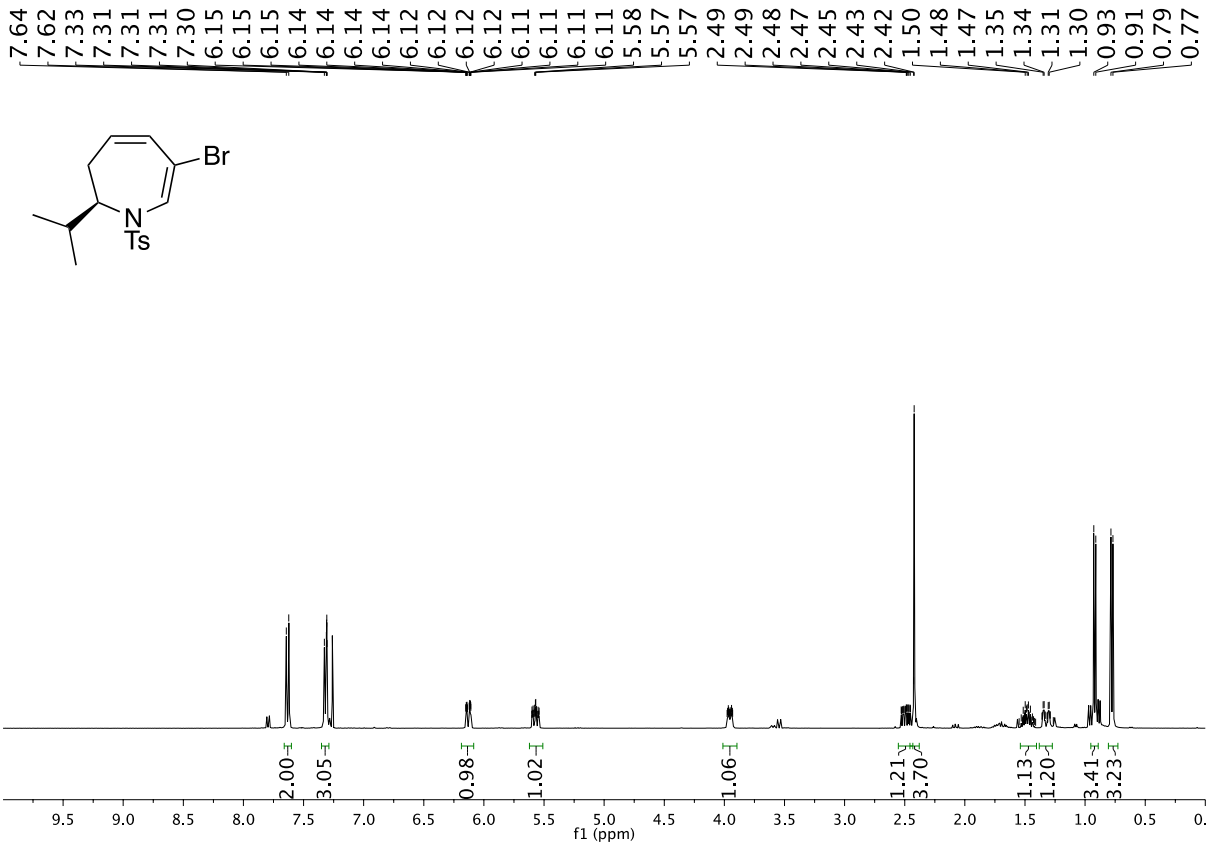


^{1}H and ^{13}C NMR Spectra of 11

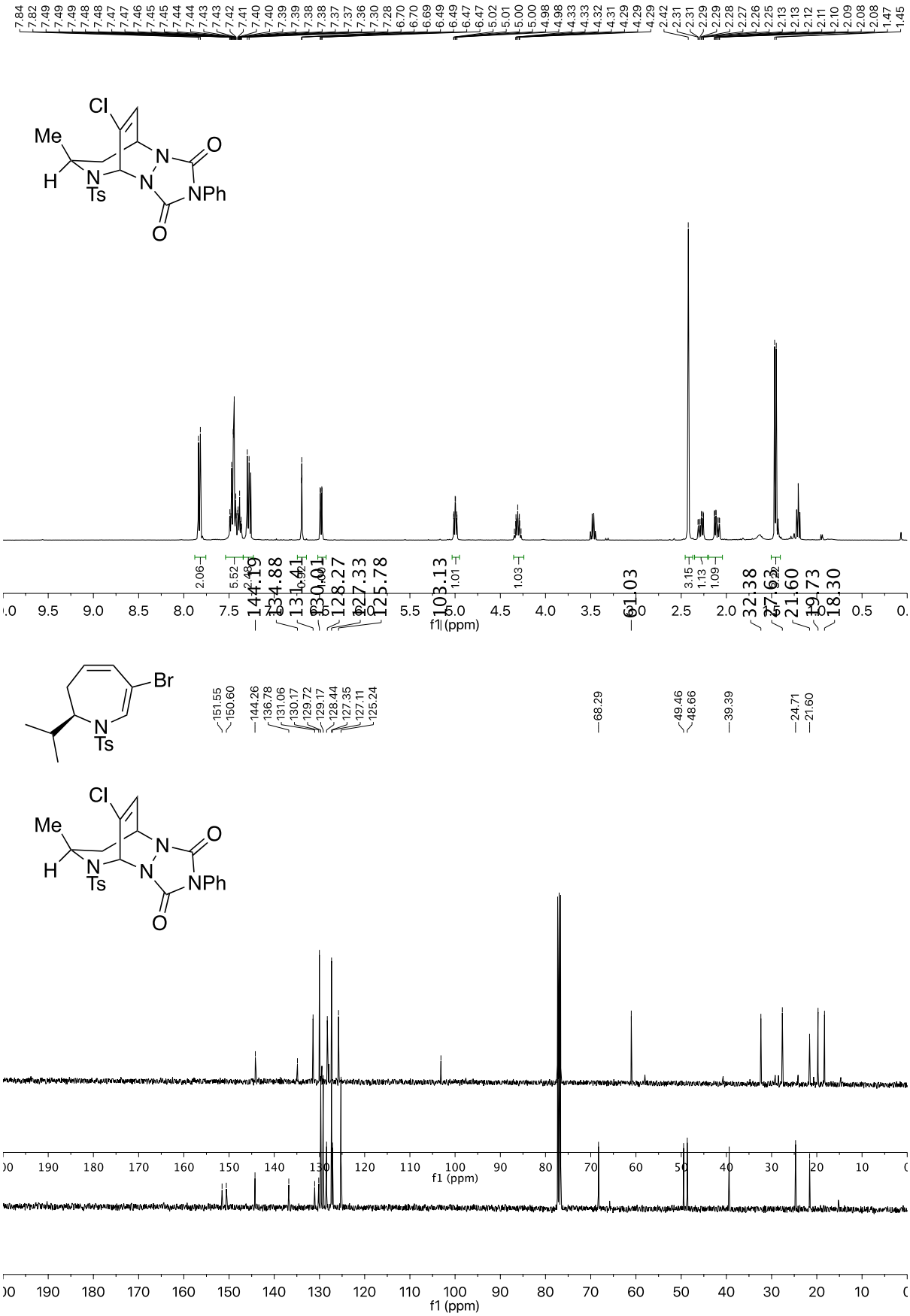



144.19
134.89
131.43
130.03
128.44
127.36
125.84
103.47
59.59
33.77
32.34
25.25
21.60
14.33
11.19
Br
N
Ts
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

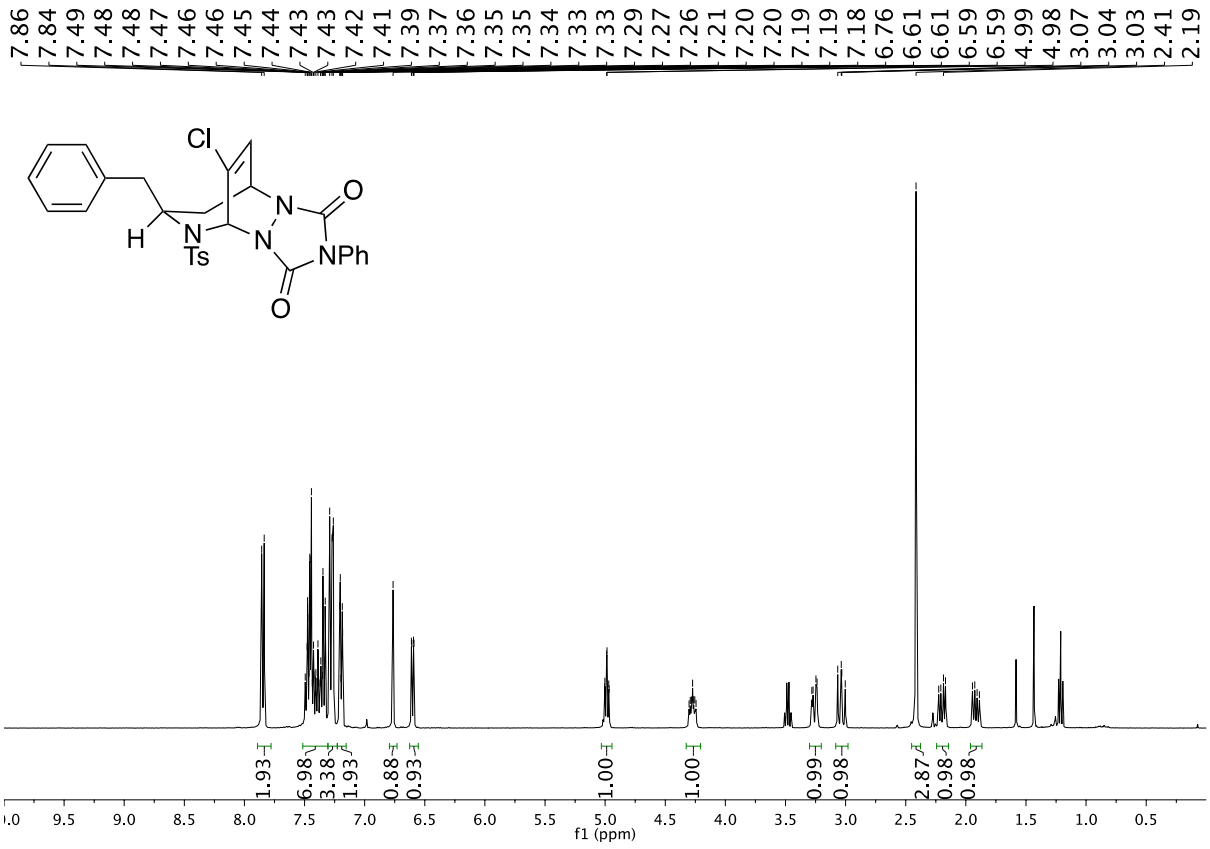
^{1}H and ^{13}C NMR Spectra of 12

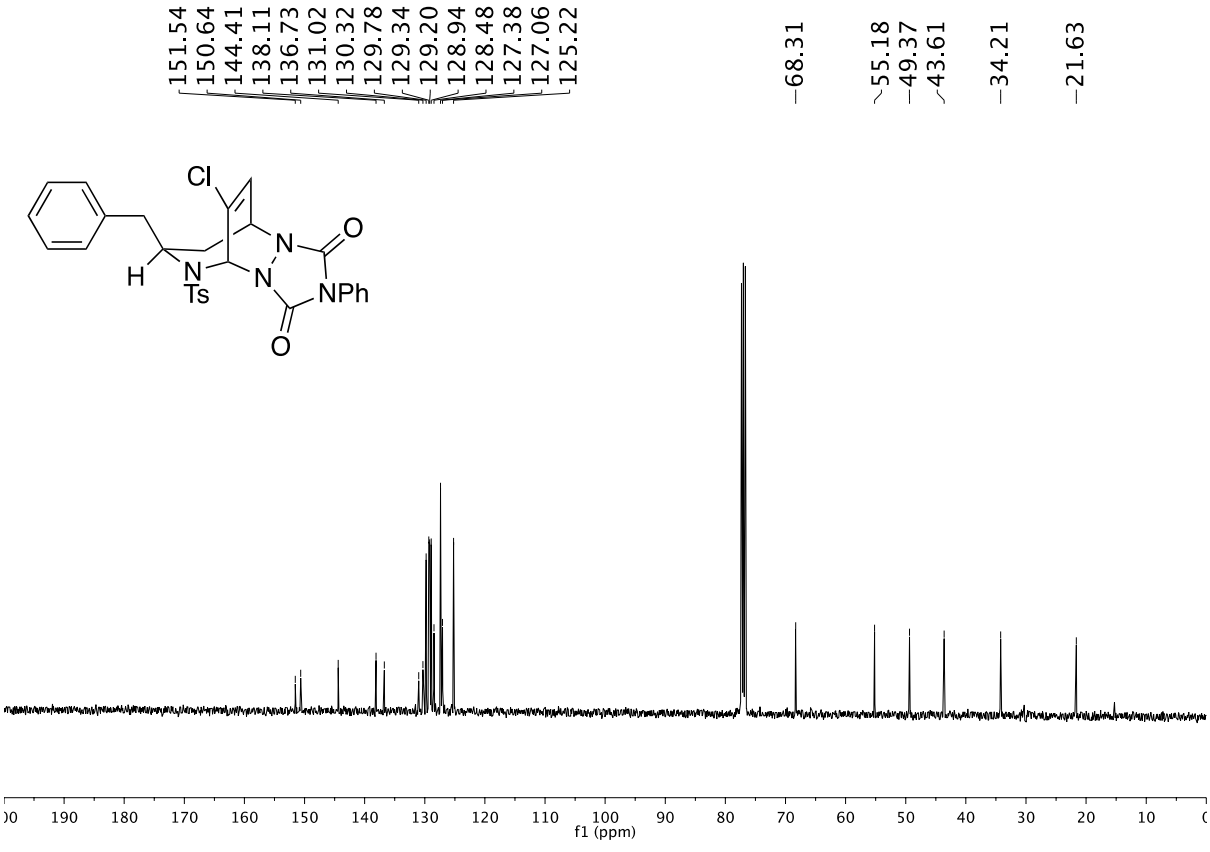


^{1}H and ^{13}C NMR Spectra of 15

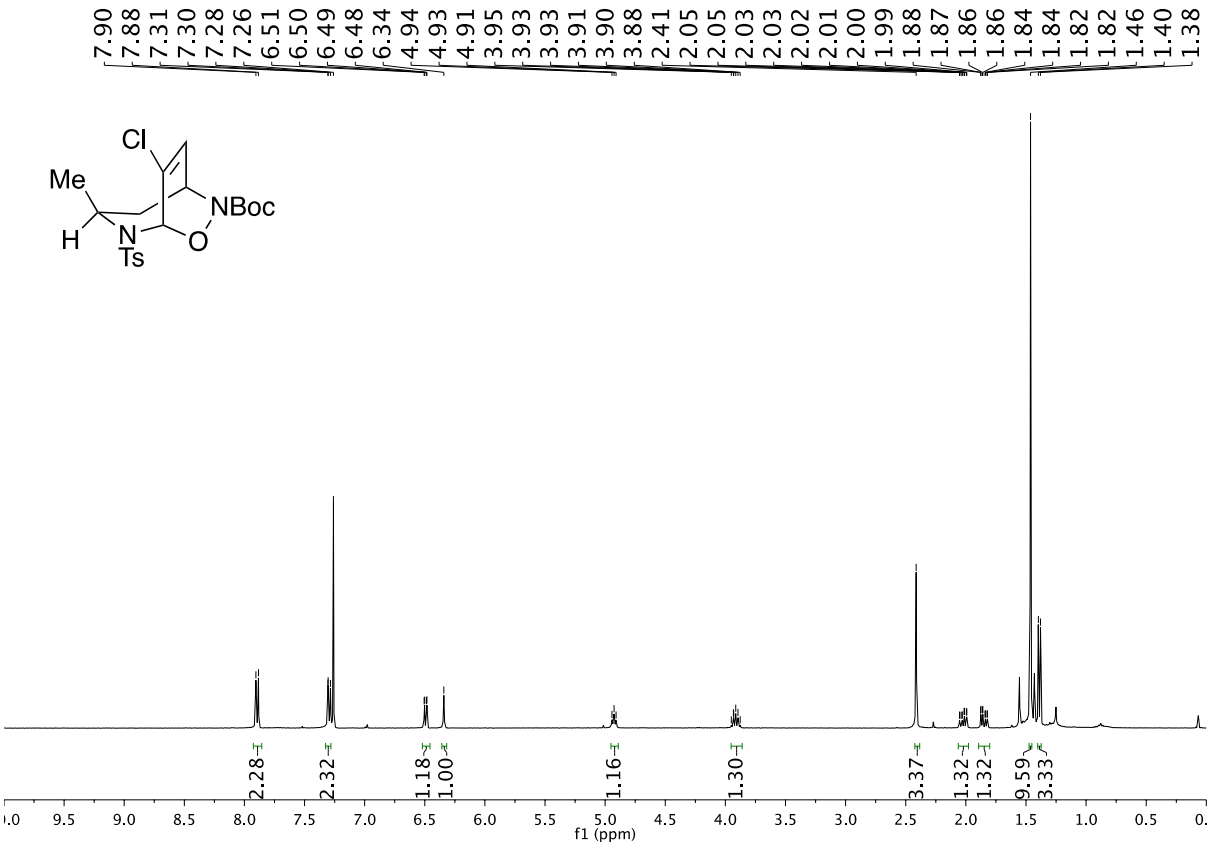


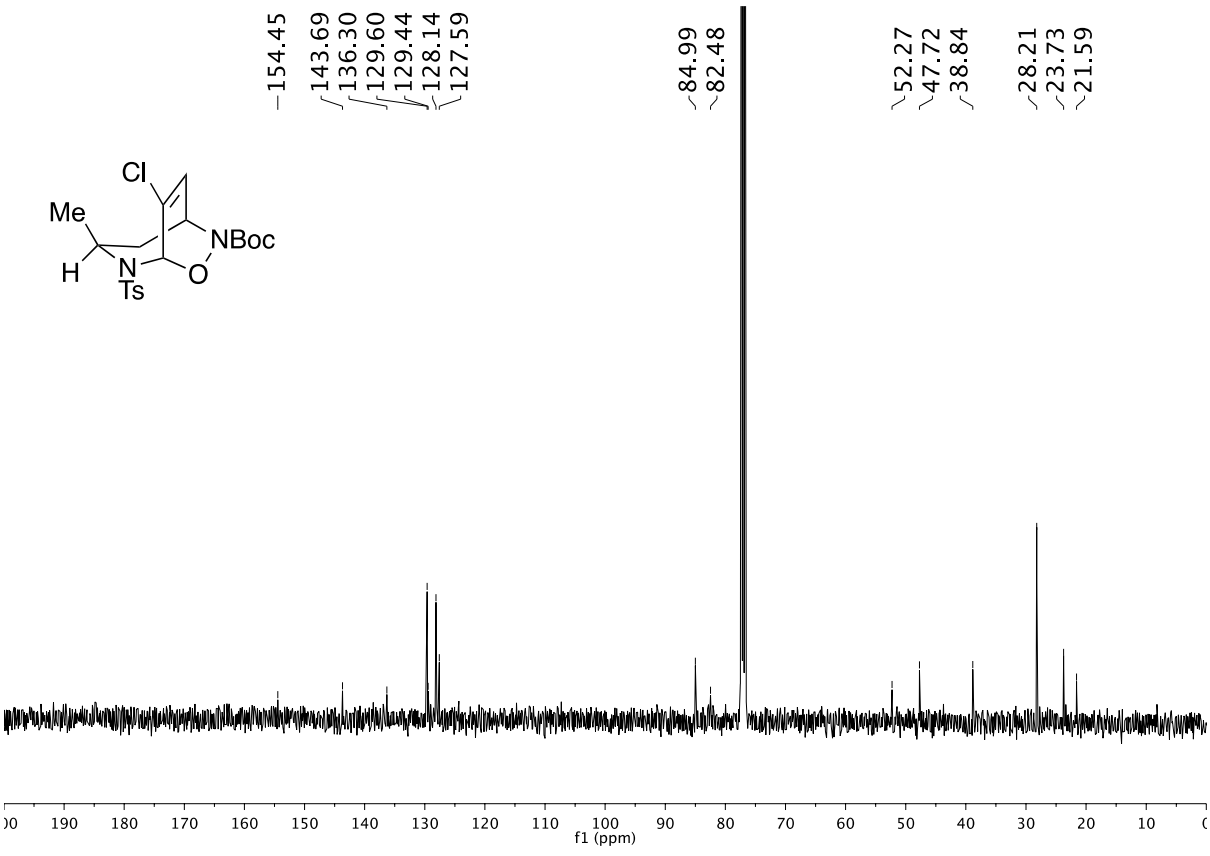
^{1}H and ^{13}C NMR Spectra of 16



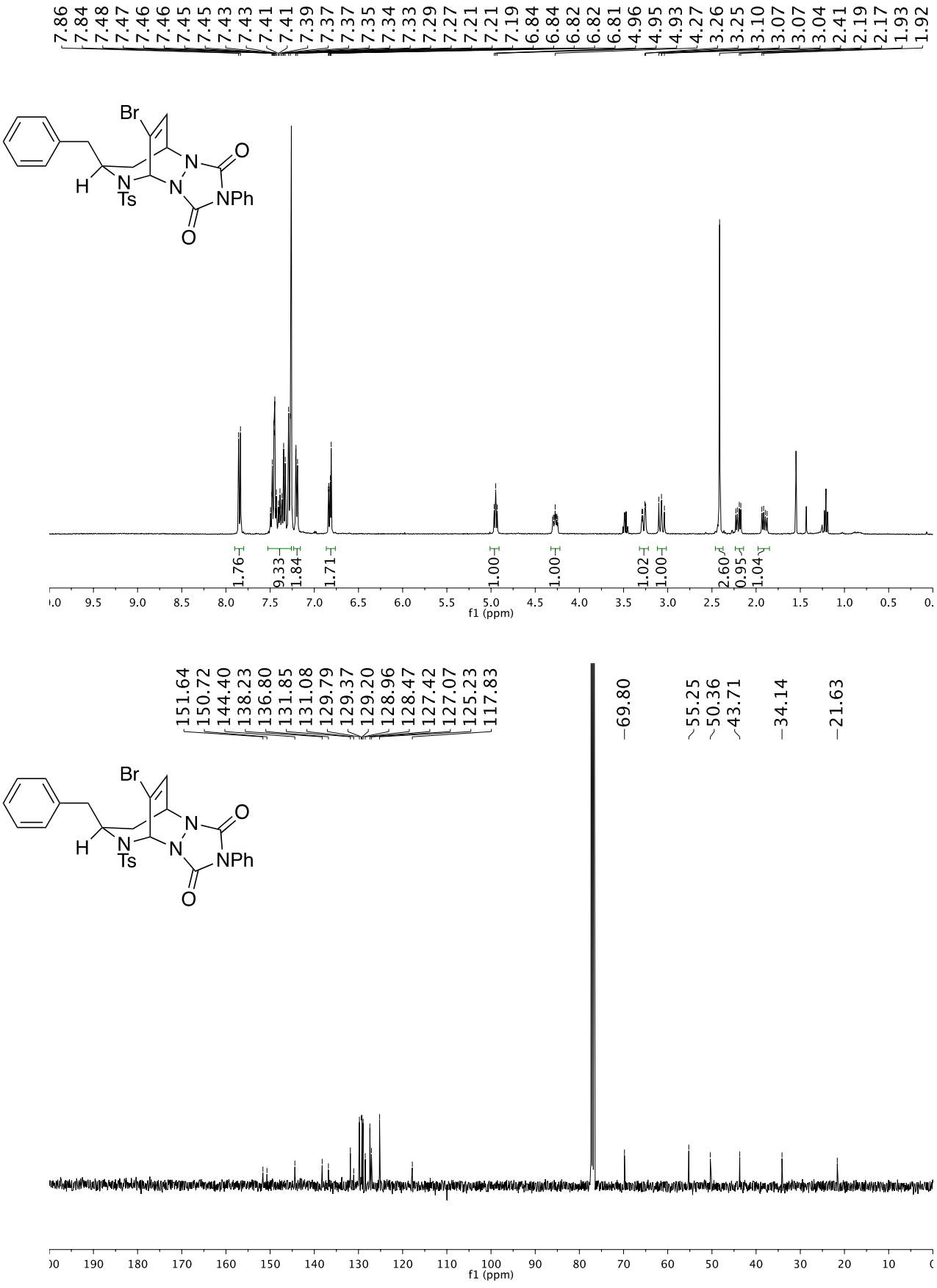


^{1}H and ^{13}C NMR Spectra of 17

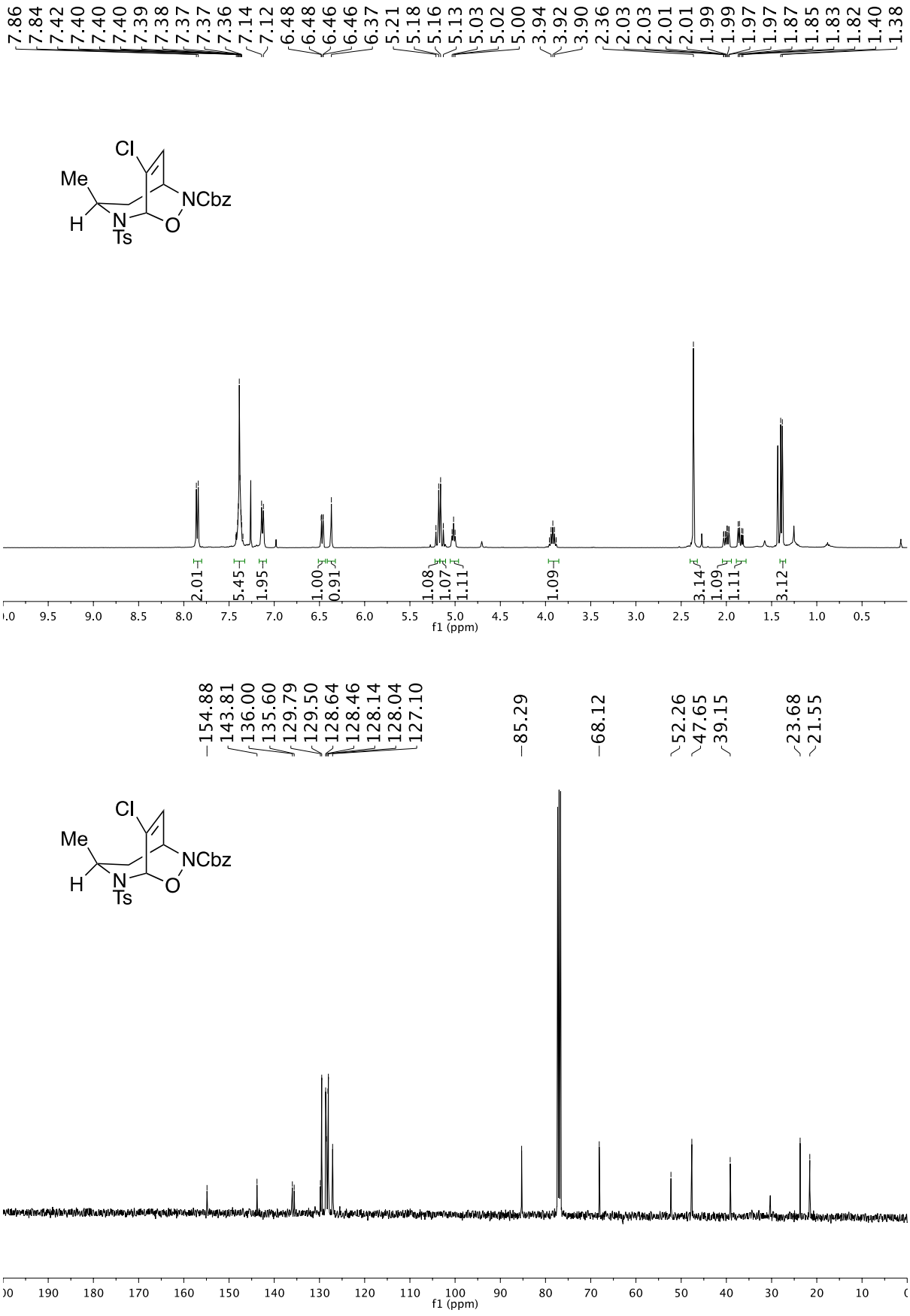




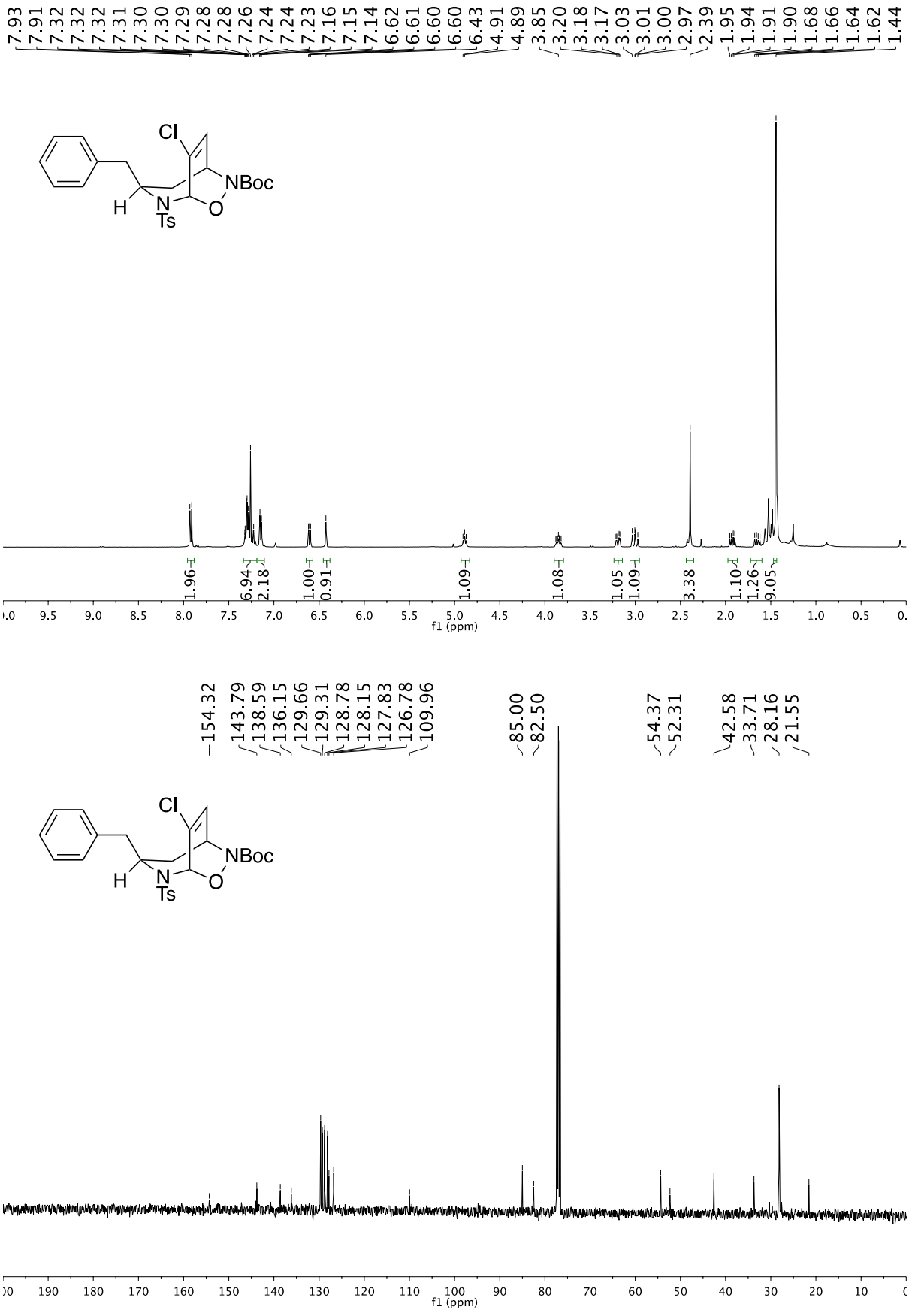
^{1}H and ^{13}C NMR Spectra of 18



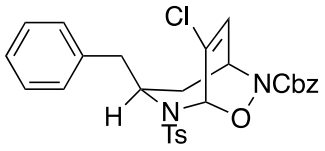
^{1}H and ^{13}C NMR Spectra of 19

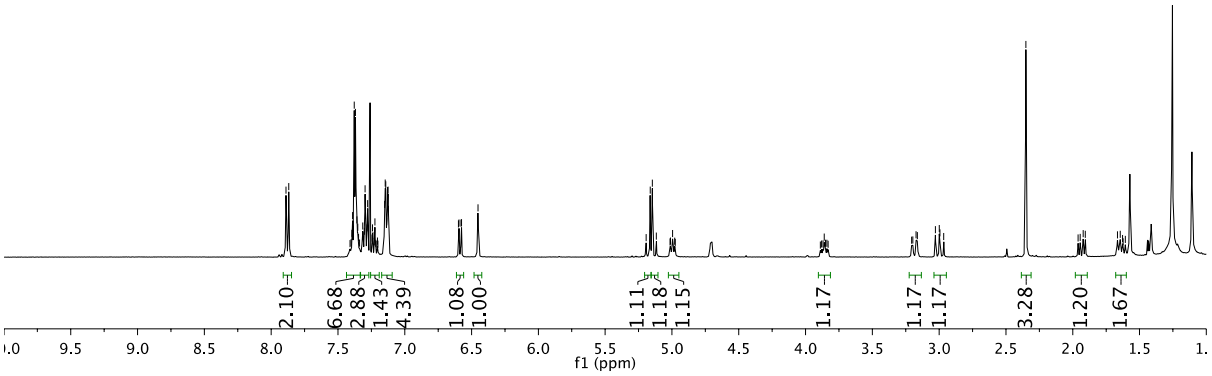


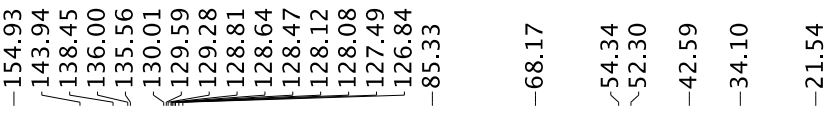
^{1}H and ^{13}C NMR Spectra of 20

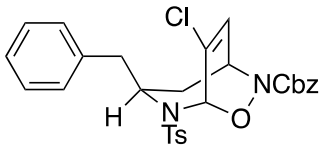


^{1}H and ^{13}C NMR Spectra of 21

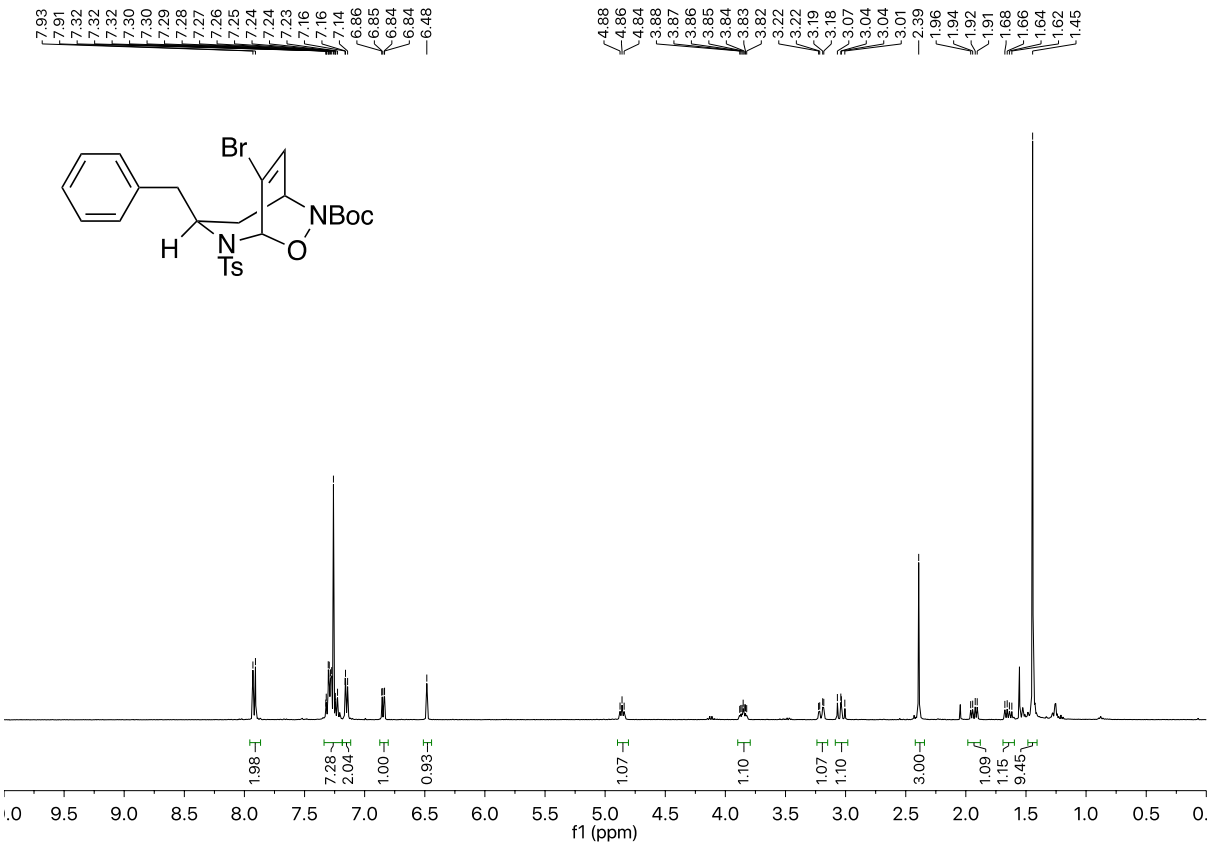


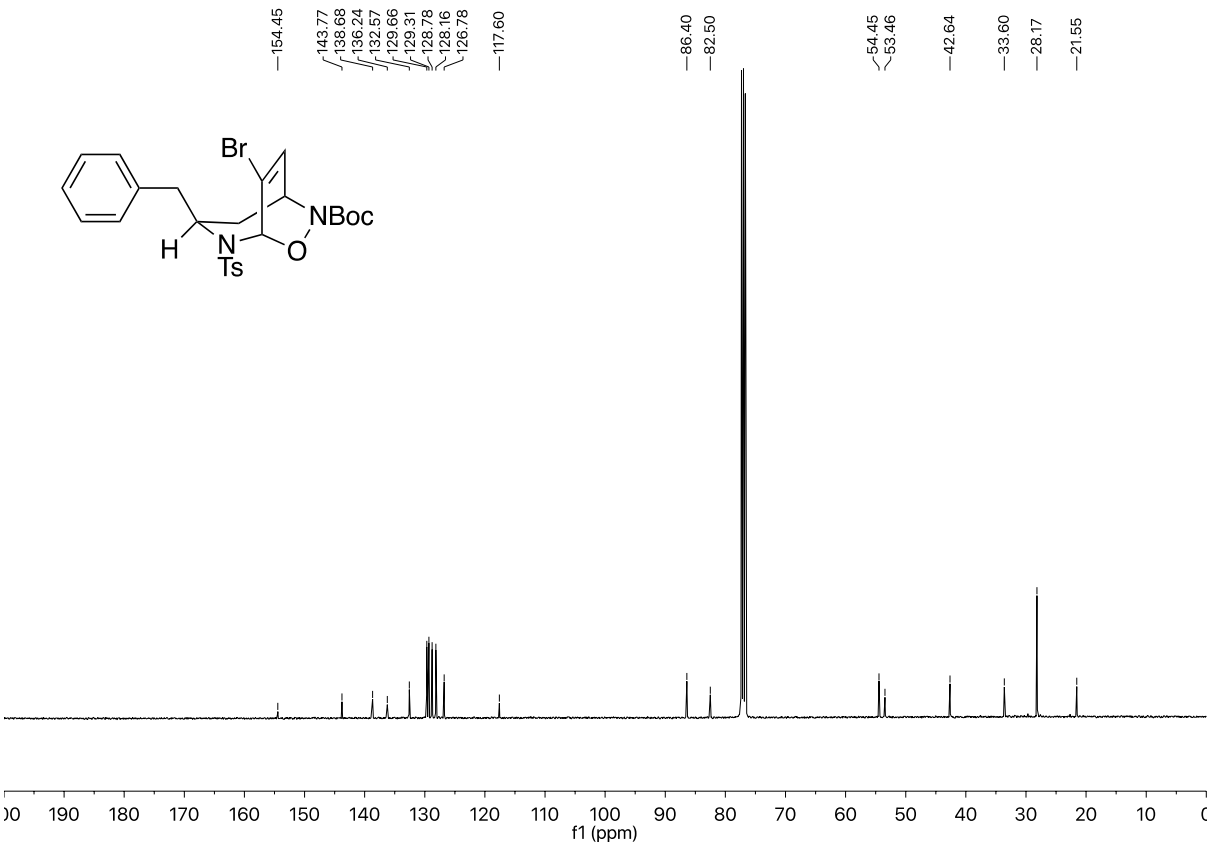




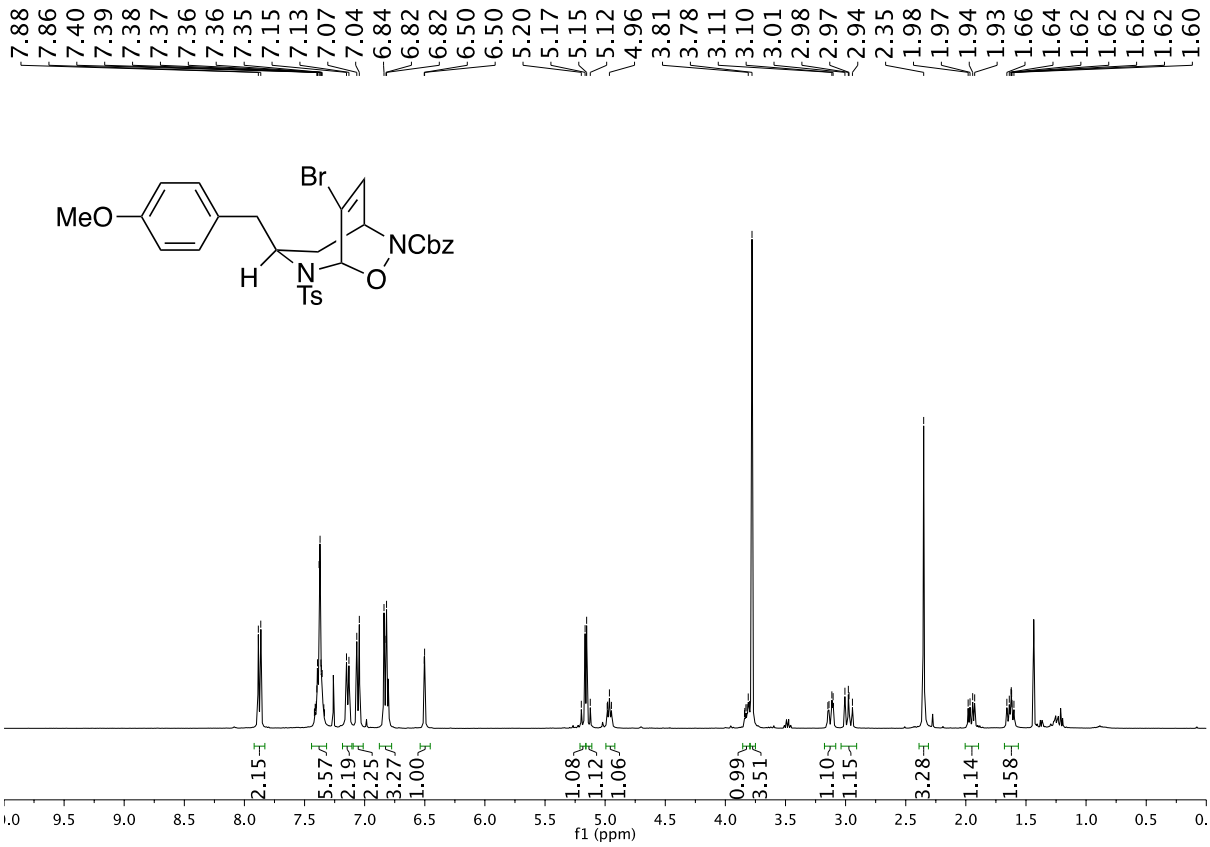


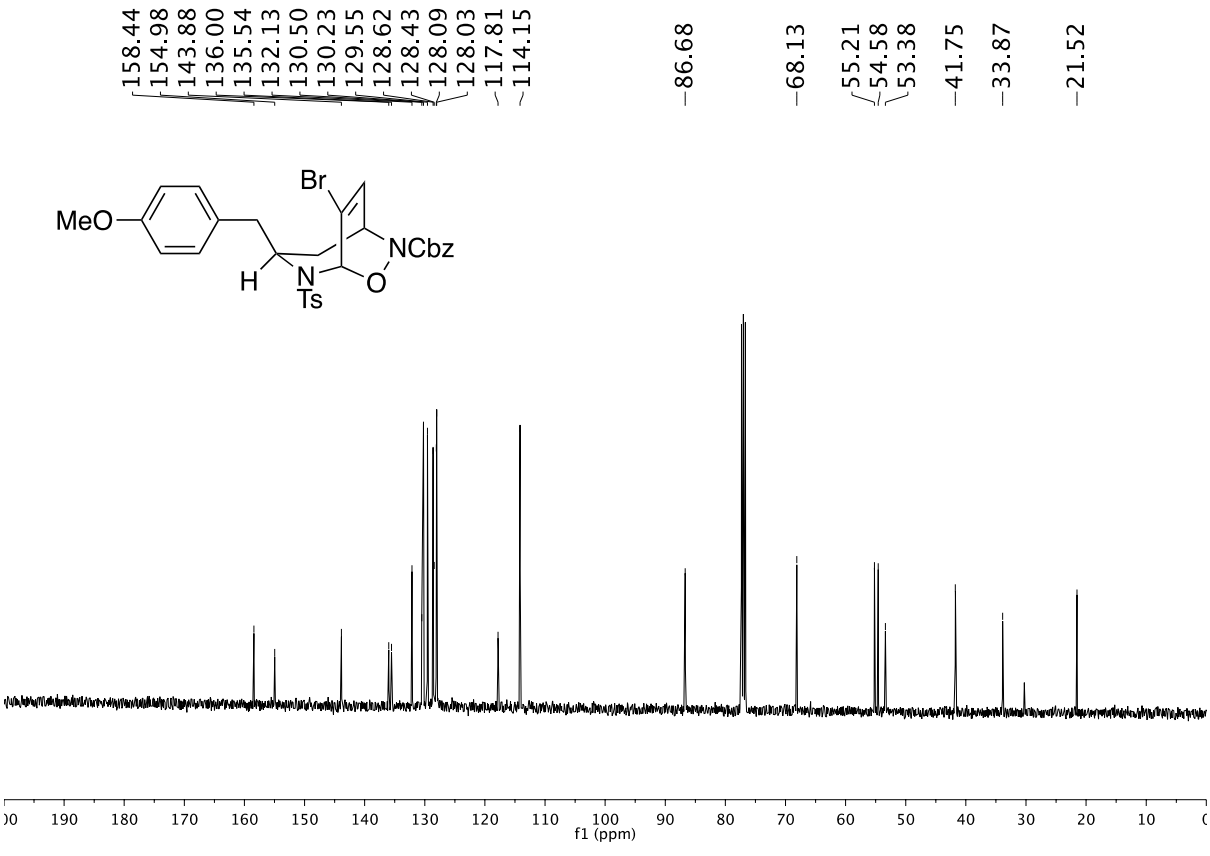
^{1}H and ^{13}C NMR Spectra of 22



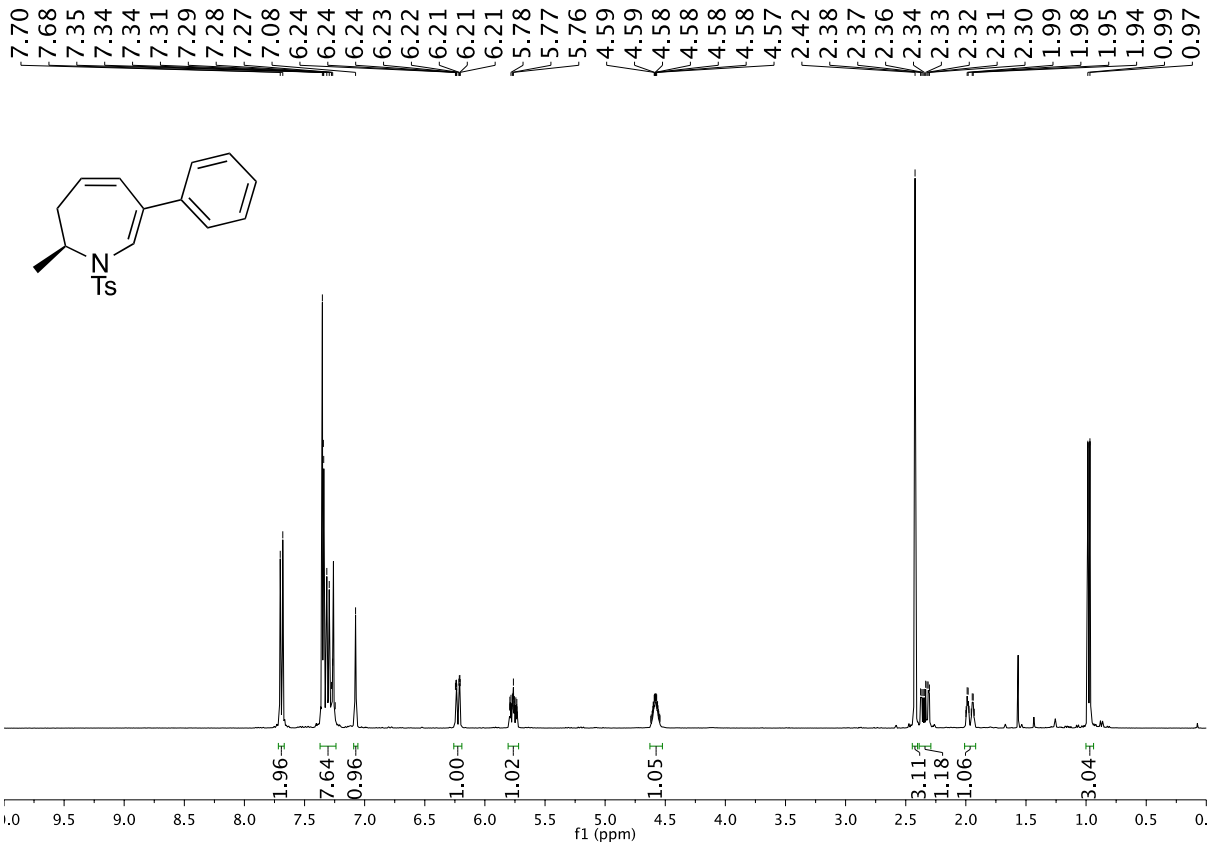


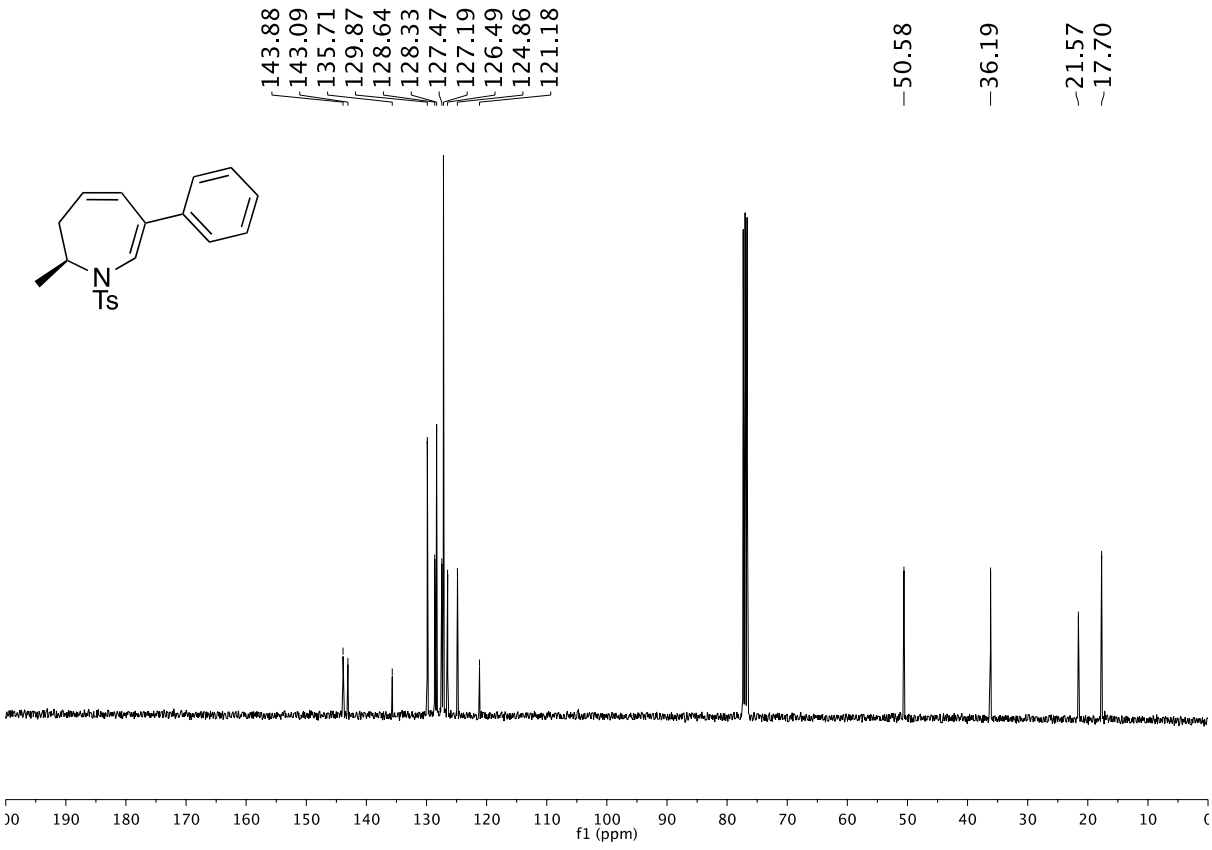
^{1}H and ^{13}C NMR Spectra of 23



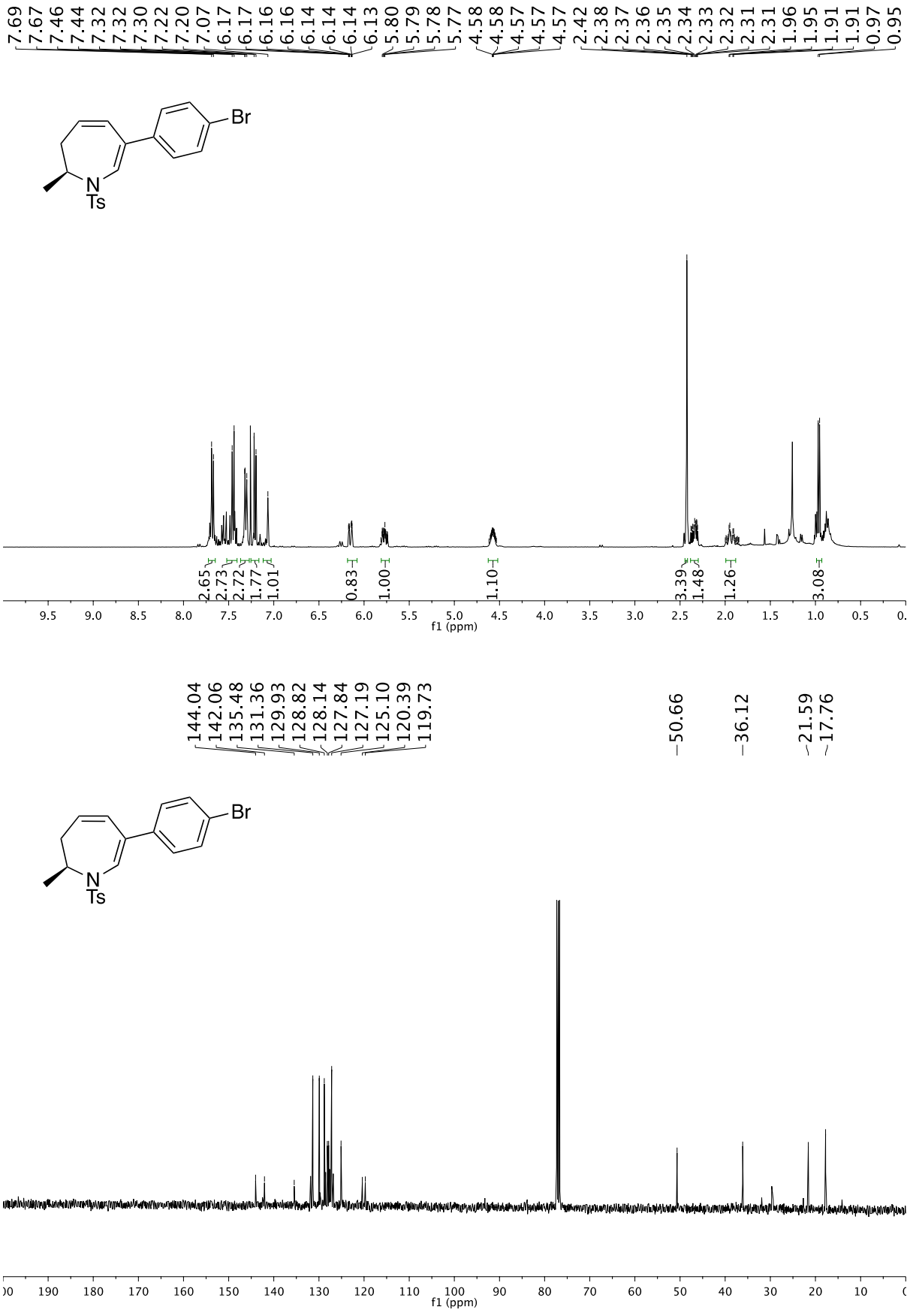


^{1}H and ^{13}C NMR Spectra of 24

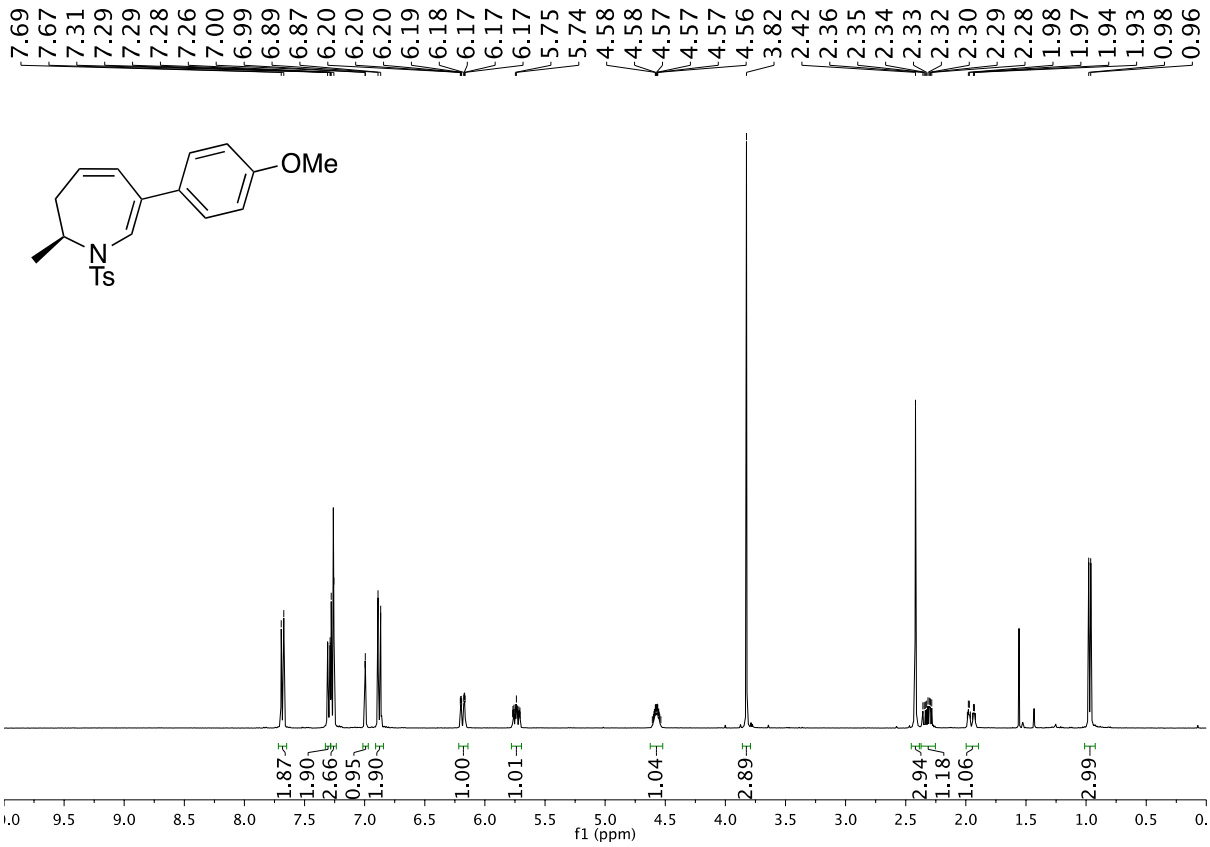


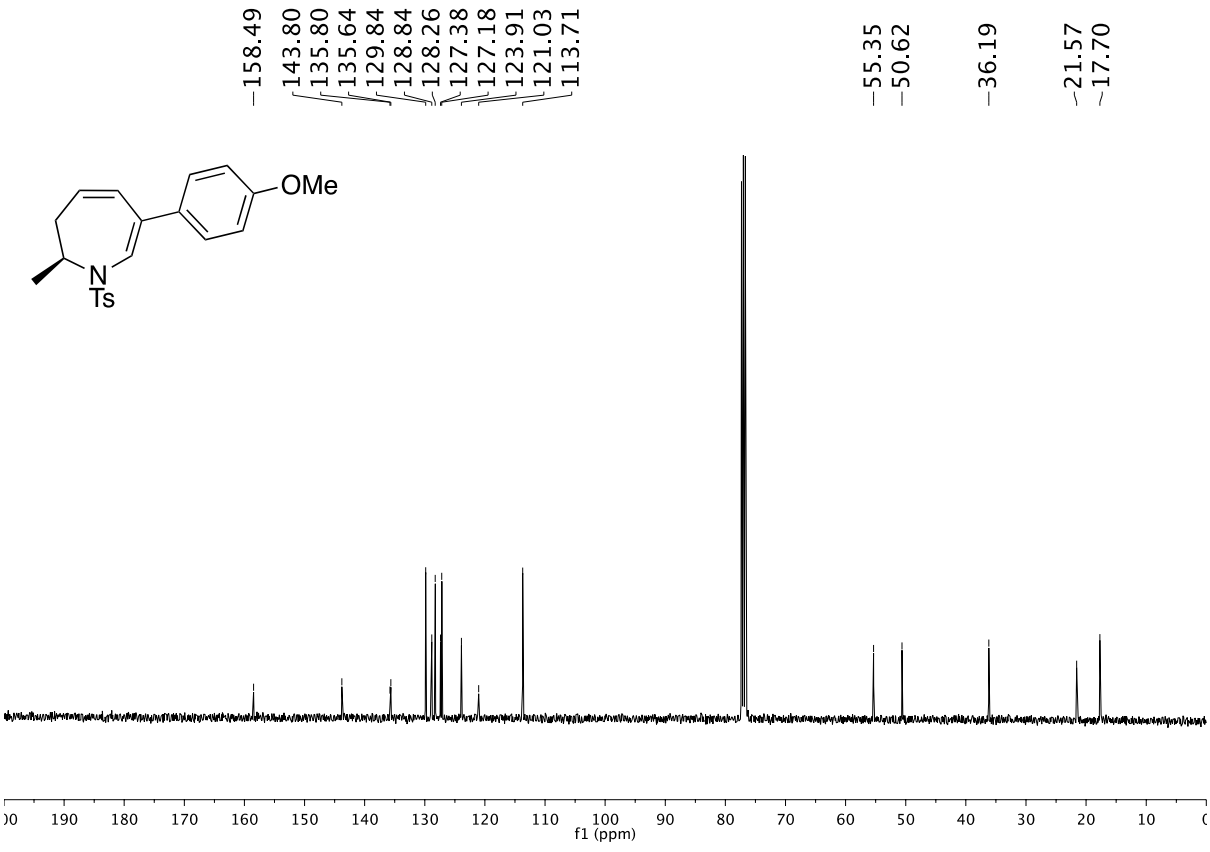


^{1}H and ^{13}C NMR Spectra of 25

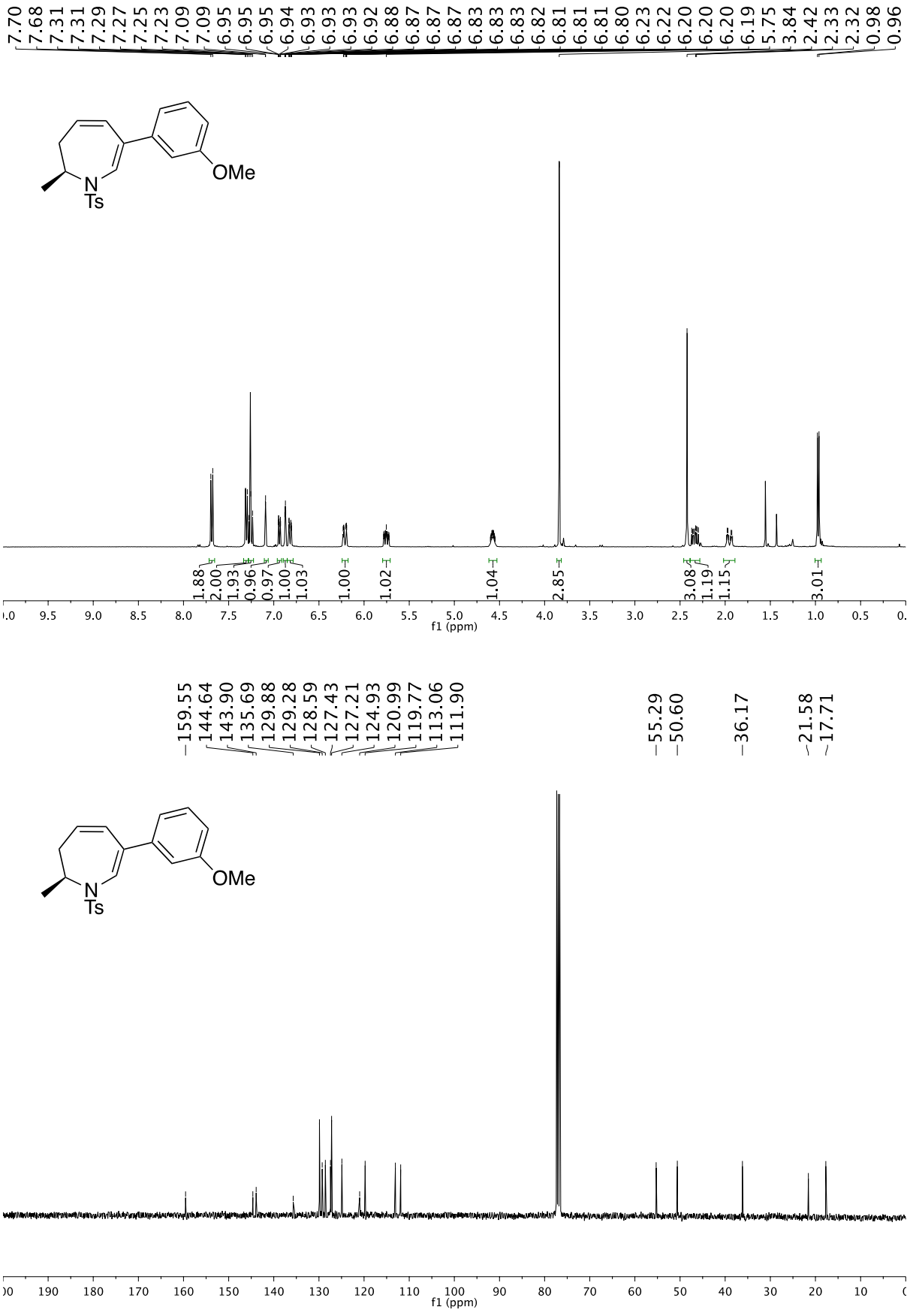


^{1}H and ^{13}C NMR Spectra of 26

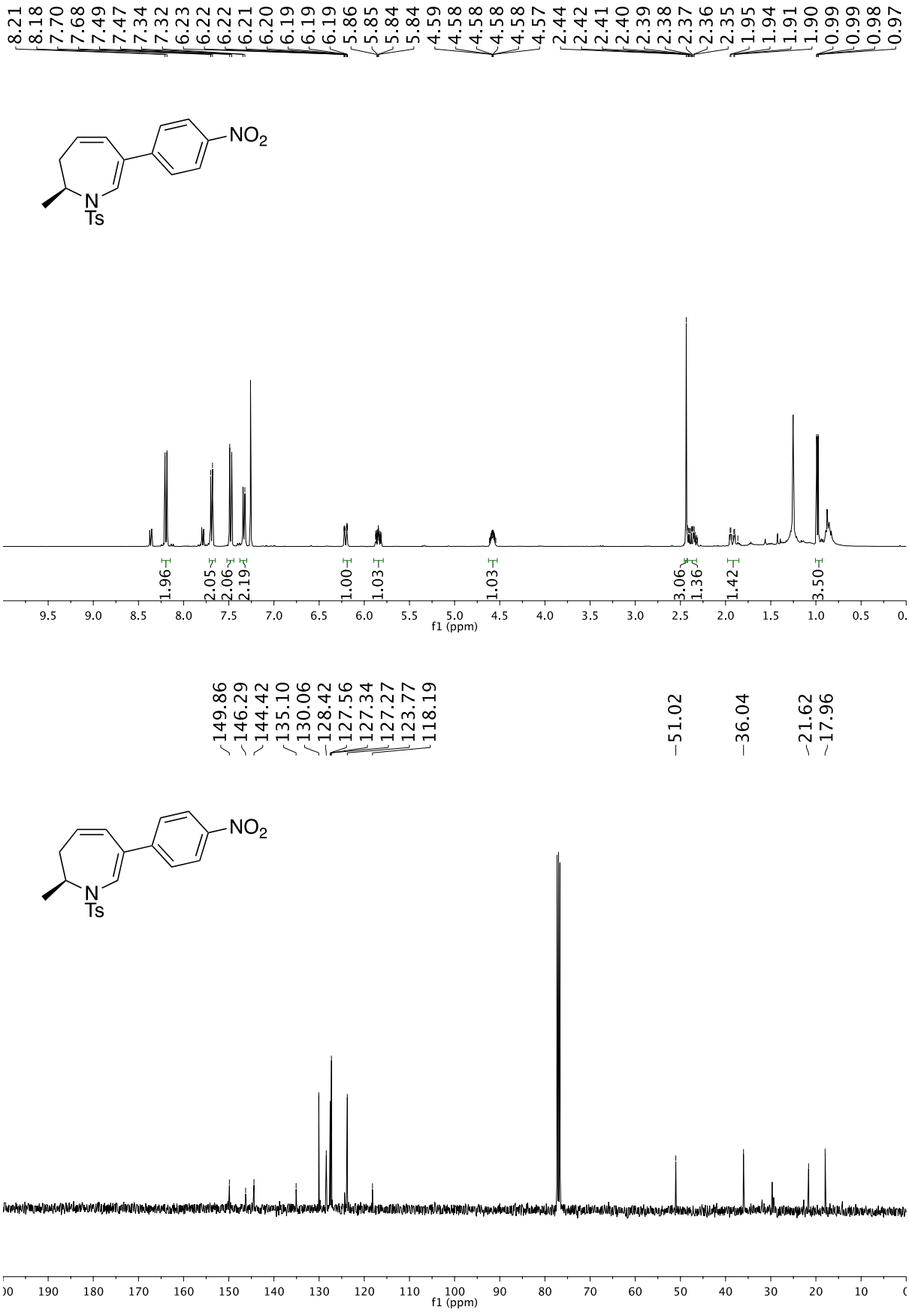




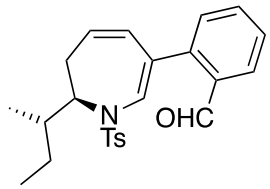
^{1}H and ^{13}C NMR Spectra of 27

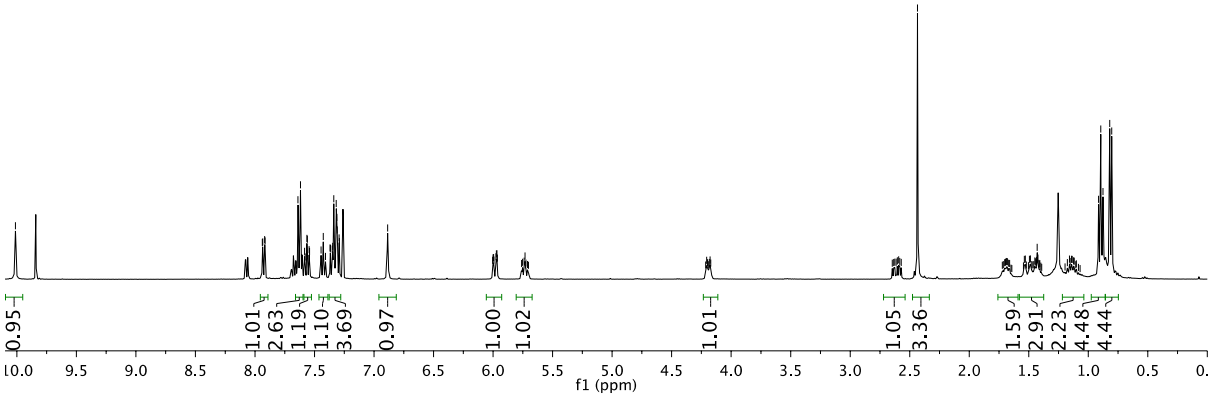


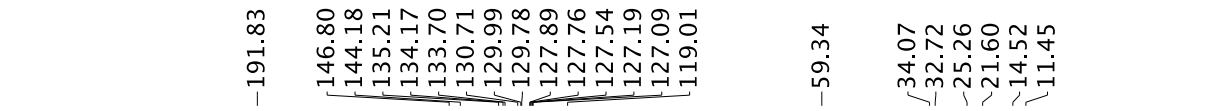
^{1}H and ^{13}C NMR Spectra of 28

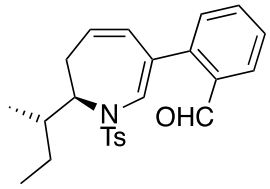


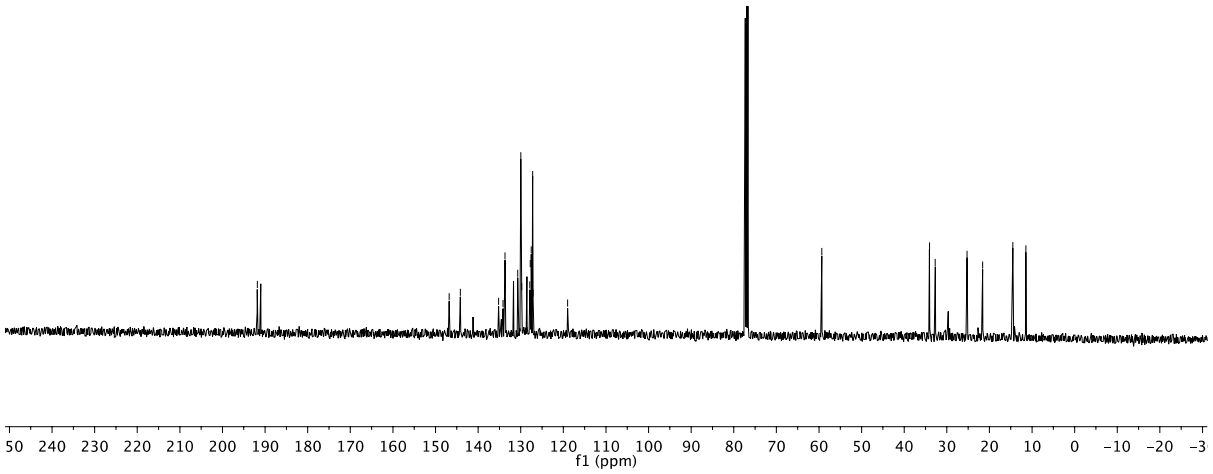
^{1}H and ^{13}C NMR Spectra of 29



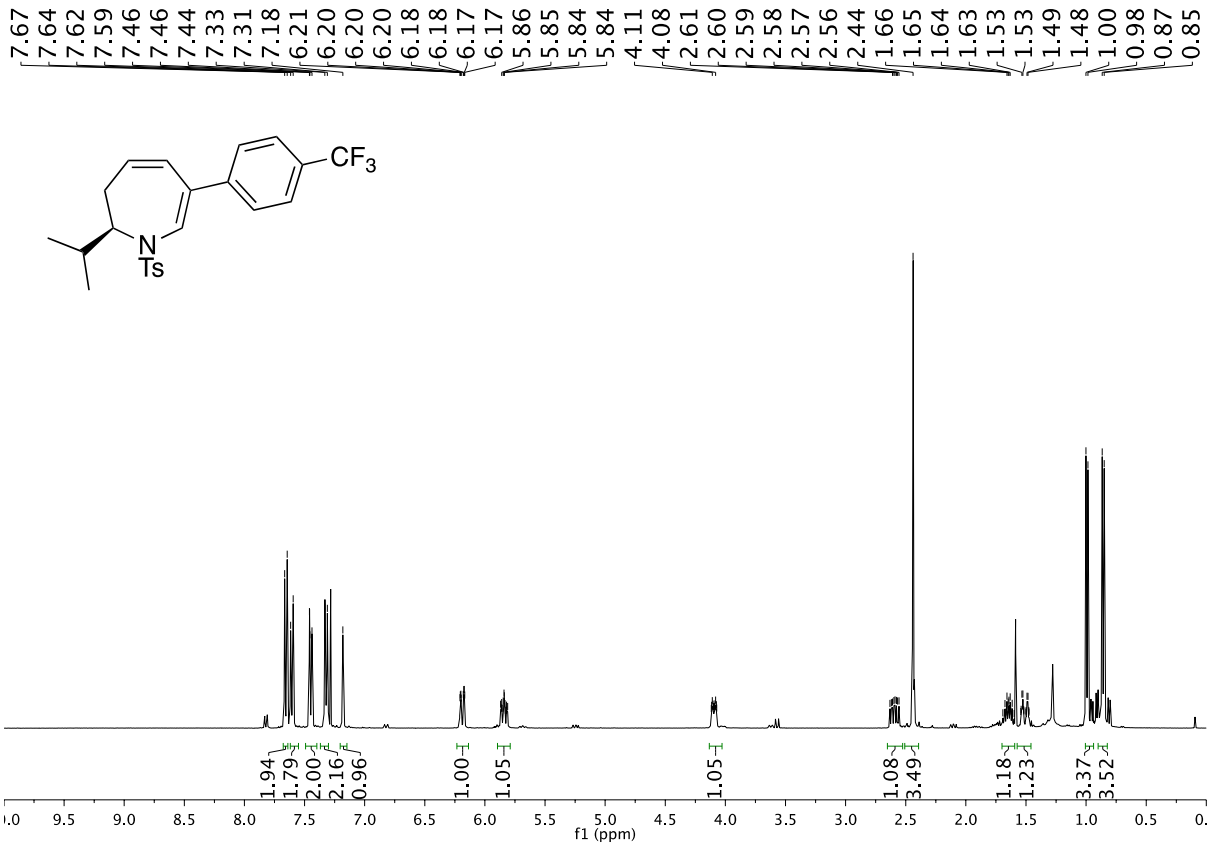


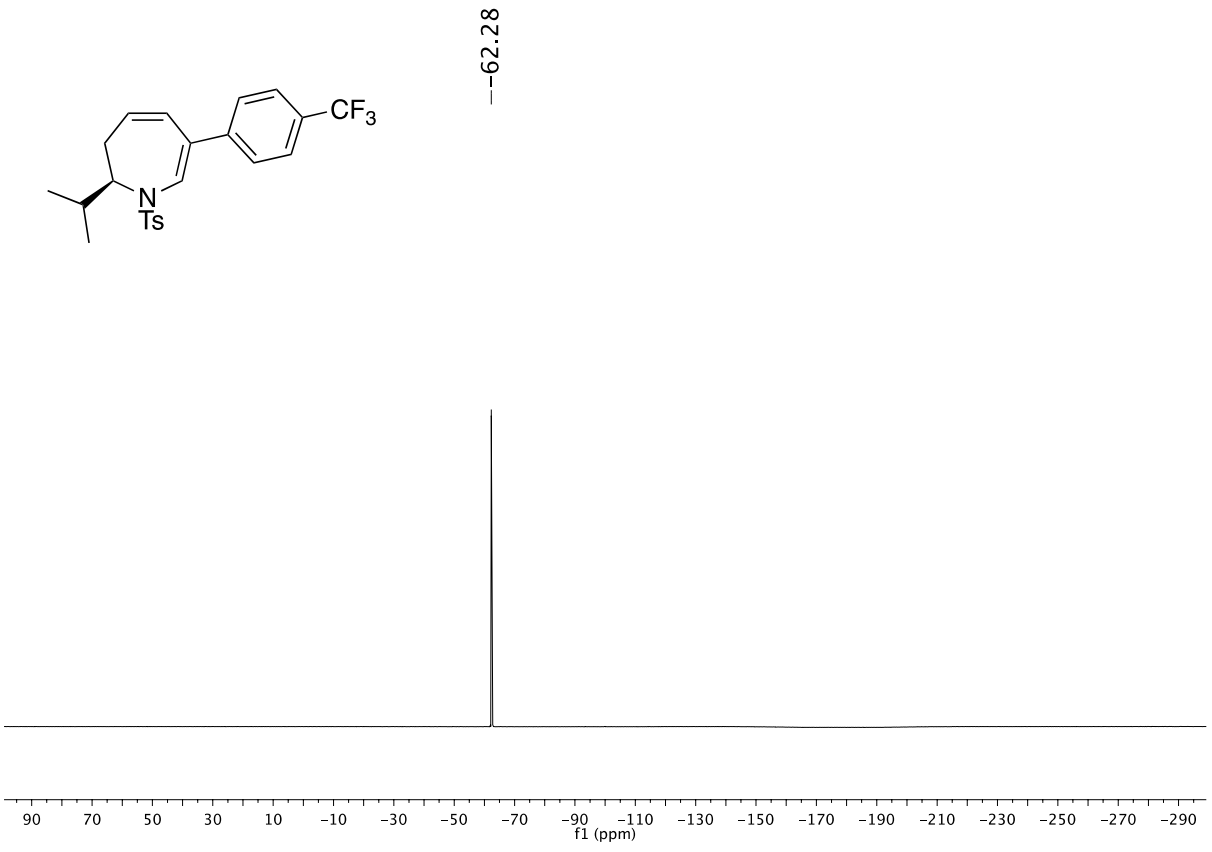


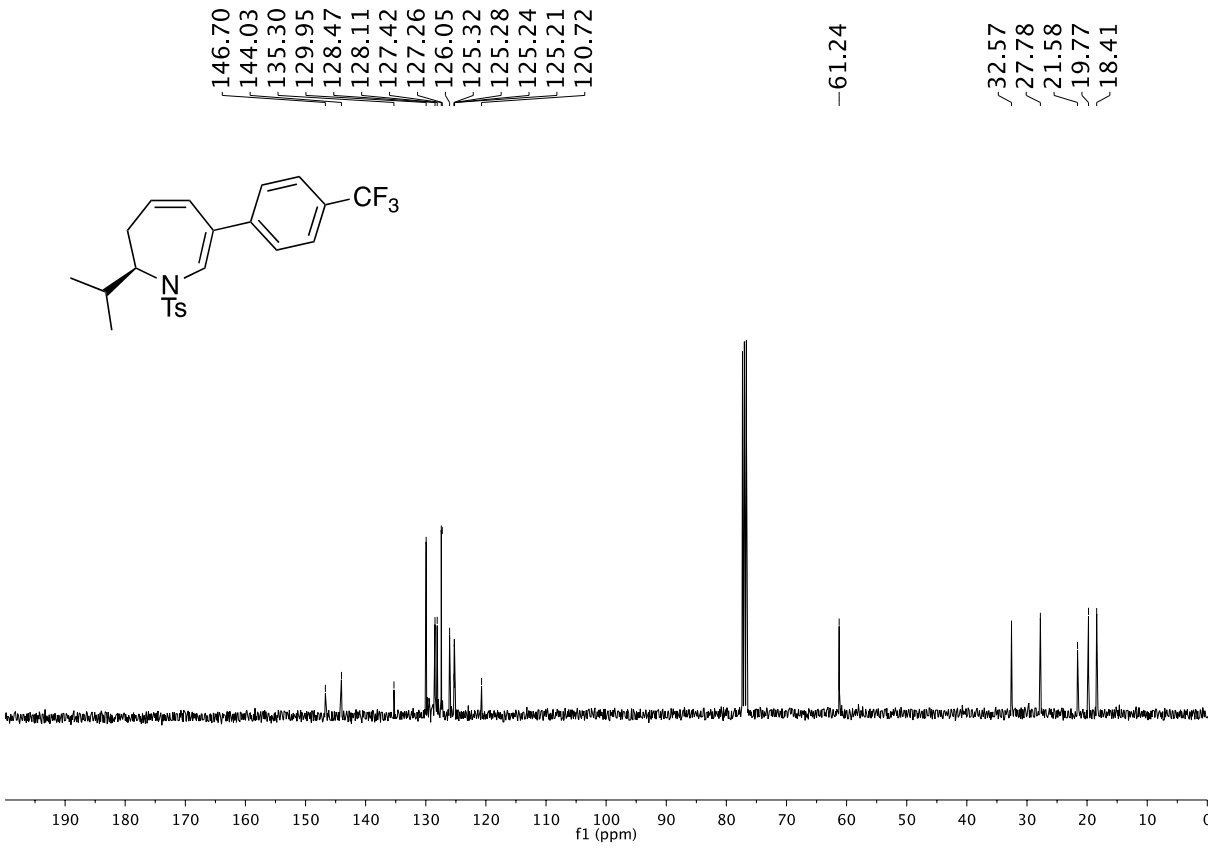




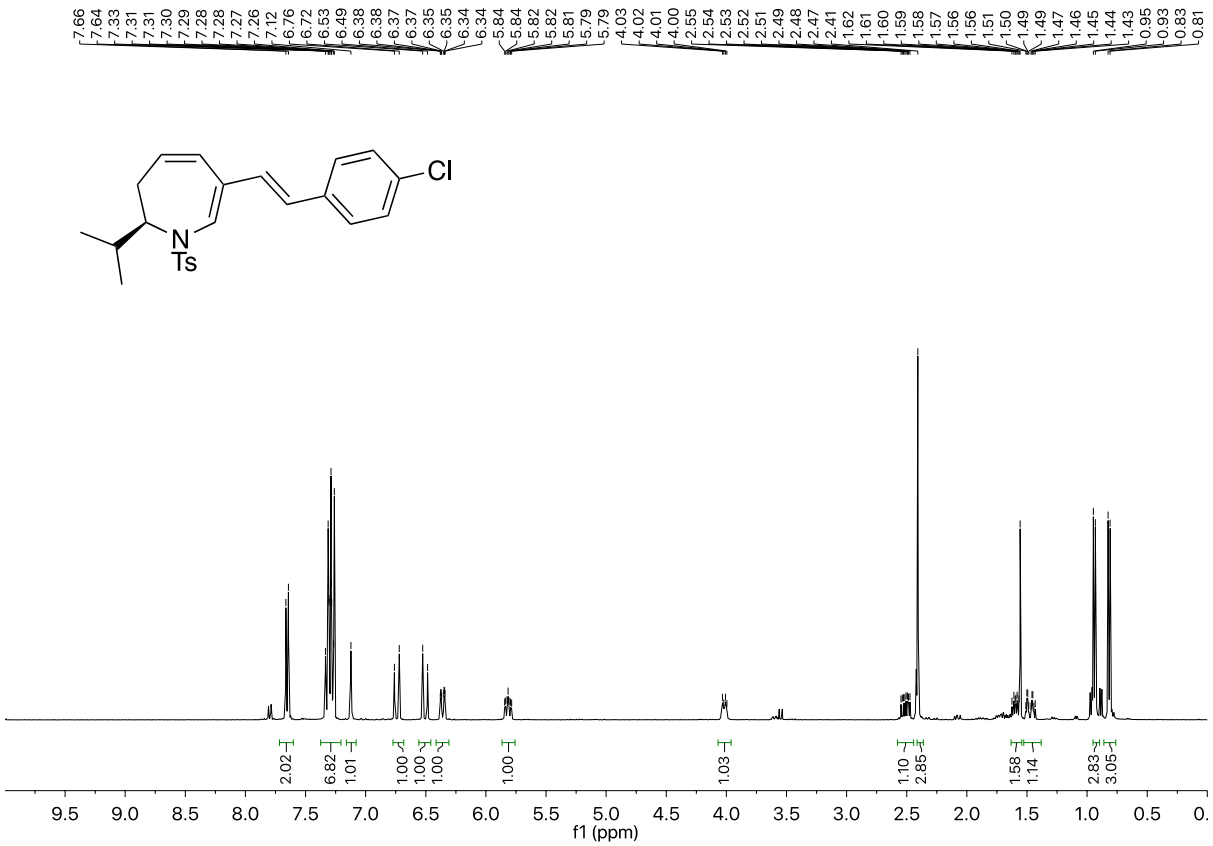
^{1}H, ^{19}F and ^{13}C NMR Spectra of 30

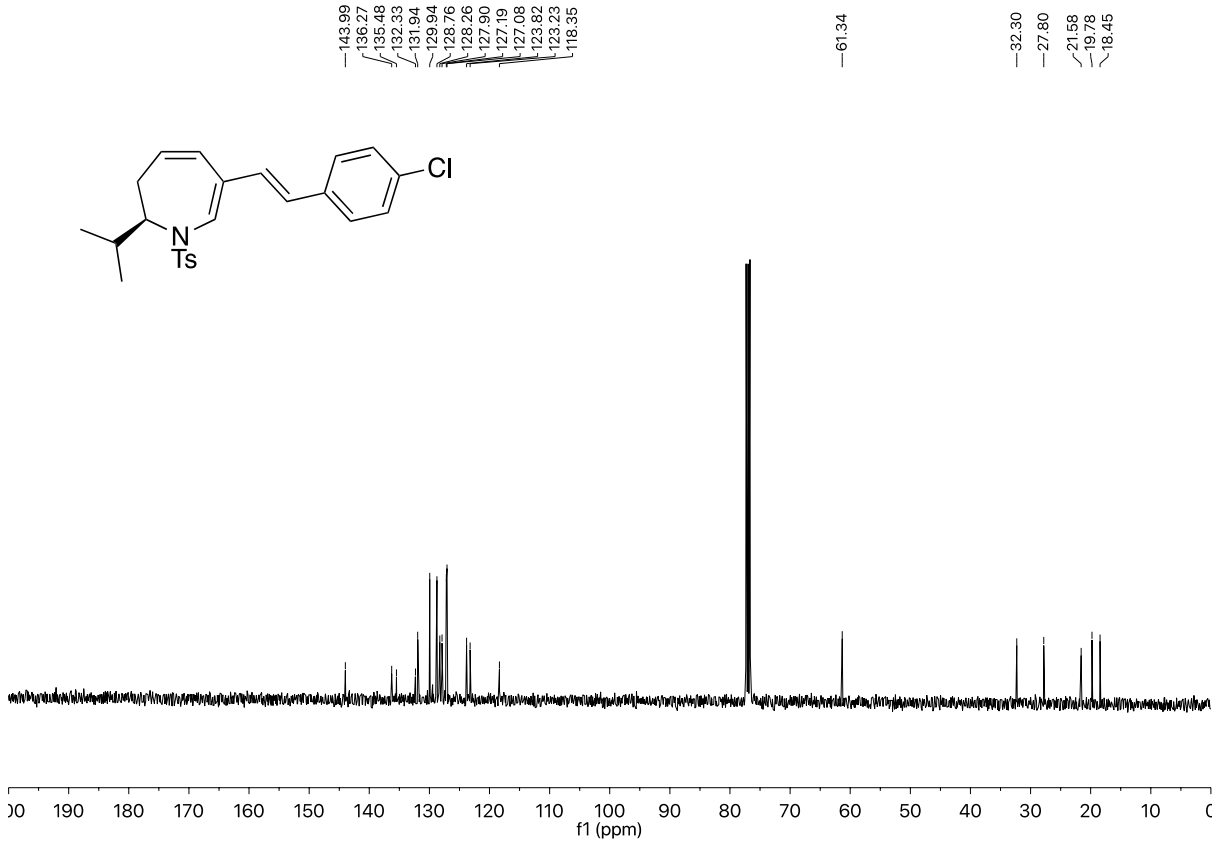




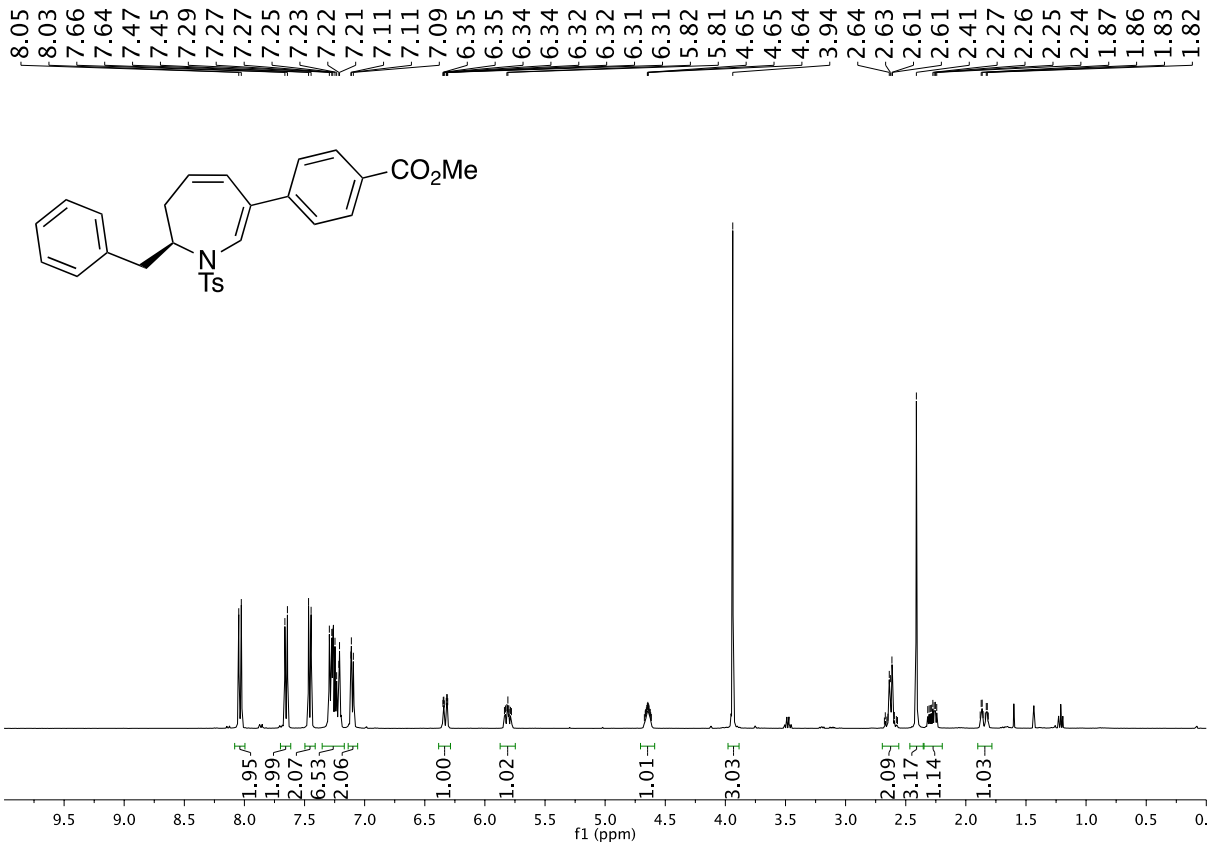

146.70
144.03
135.30
129.95
128.47
128.11
127.42
127.26
126.05
125.32
125.28
125.24
125.21
120.72
61.24
32.57
27.78
21.58
19.77
18.41
CF3
N
Ts
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

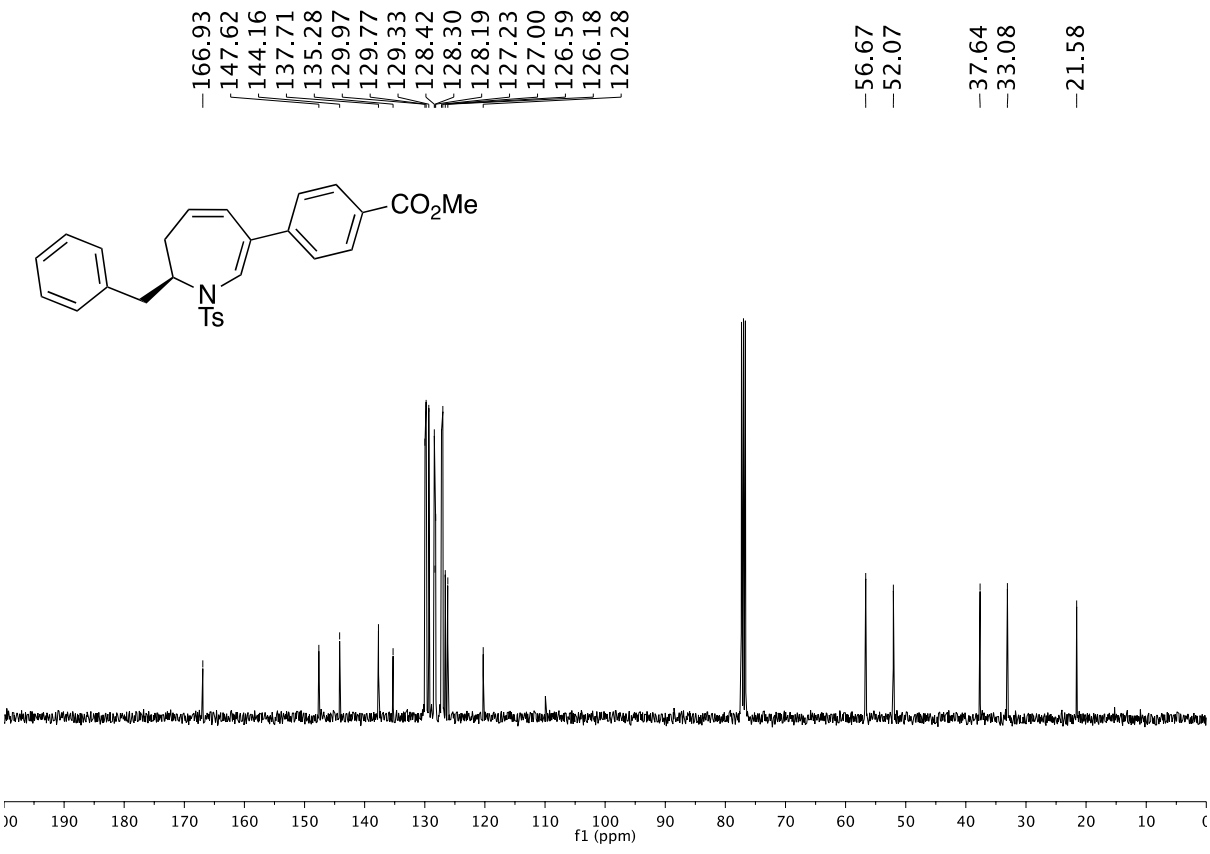
^{1}H and ^{13}C NMR Spectra of 31



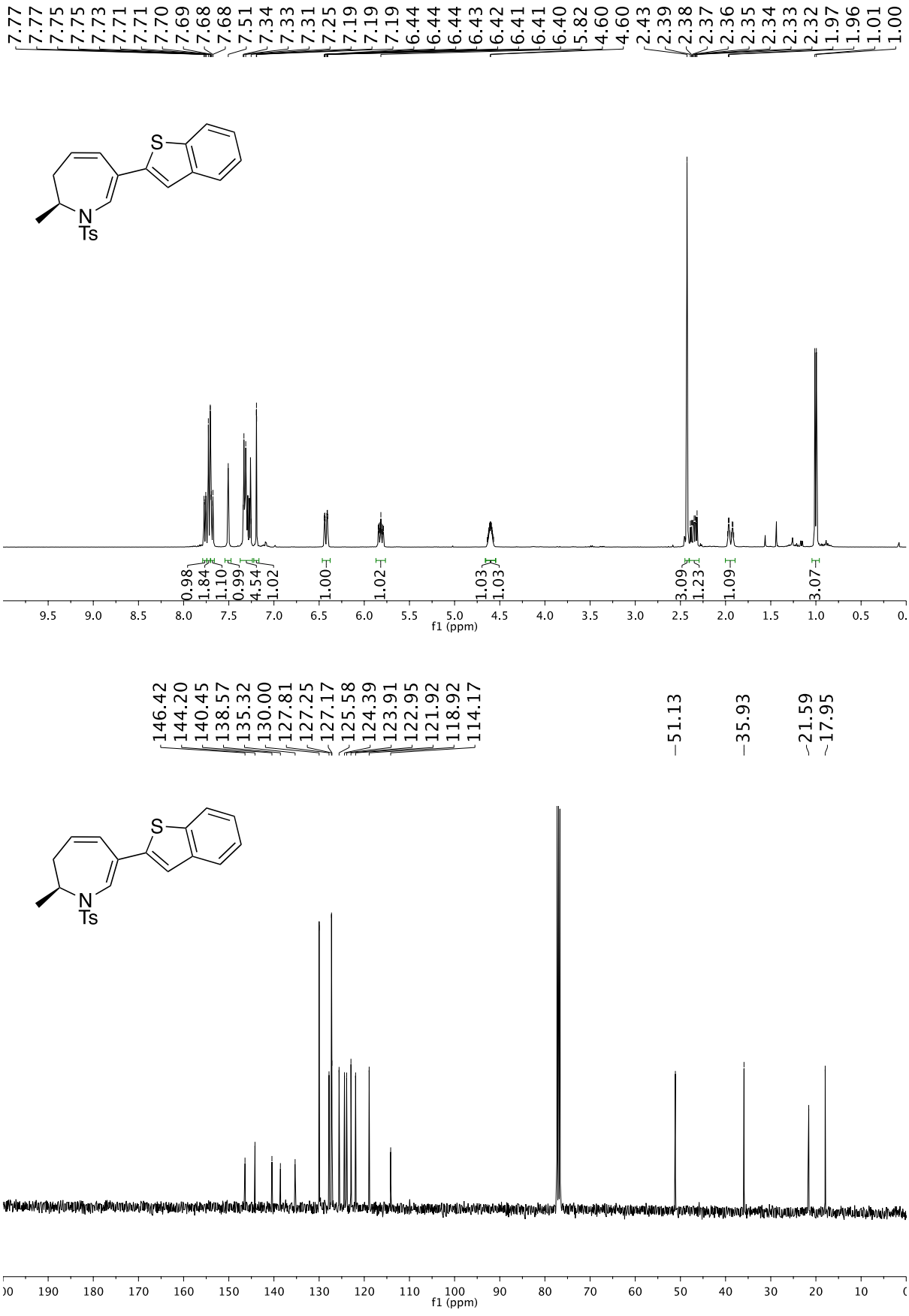


^{1}H and ^{13}C NMR Spectra of 32

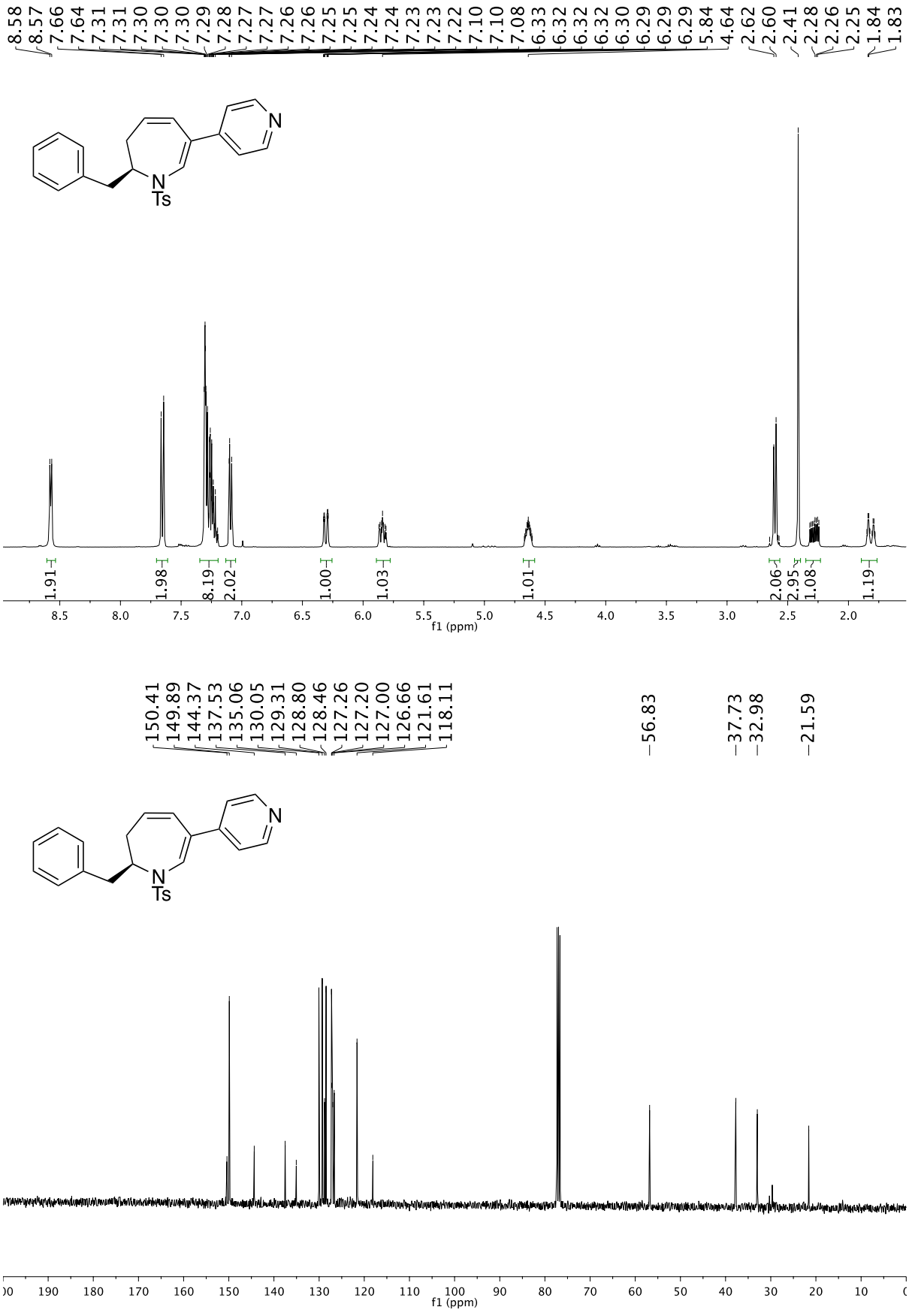




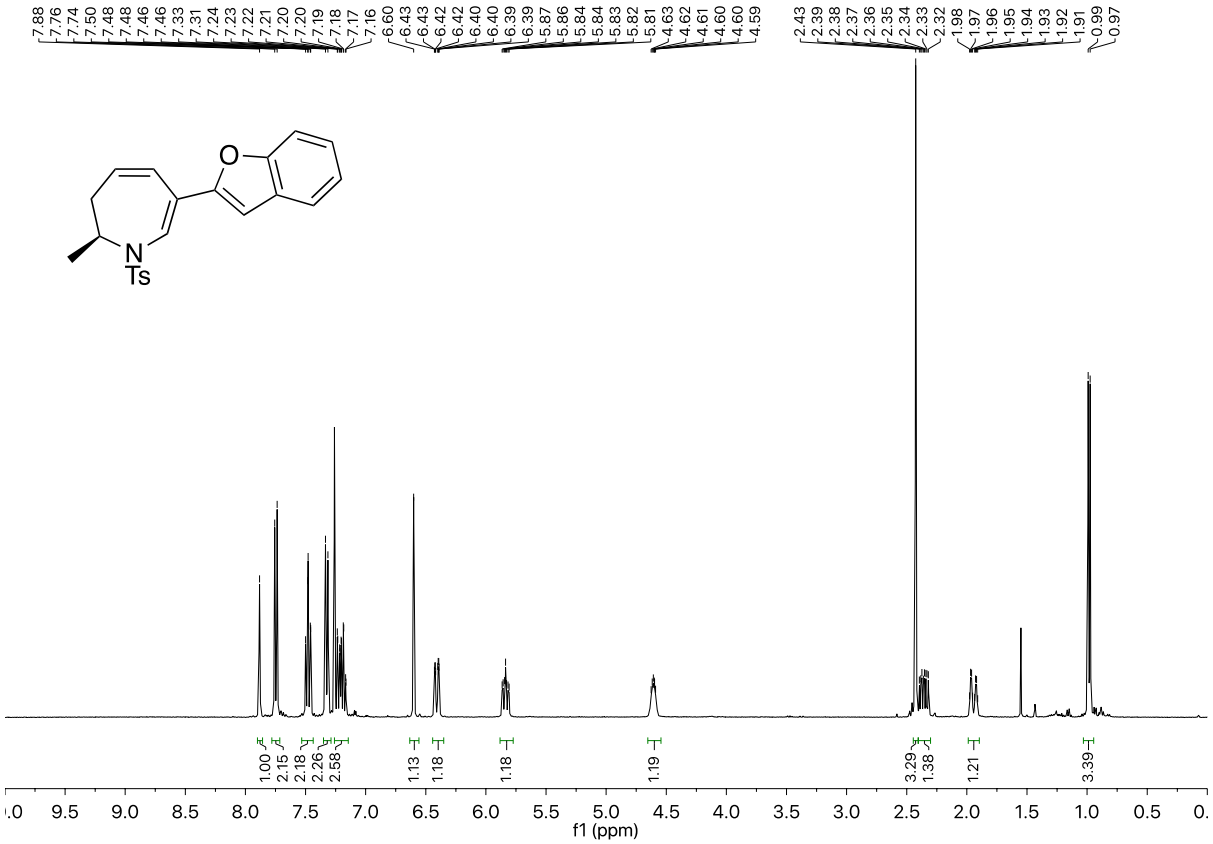
^{1}H and ^{13}C NMR Spectra of 33

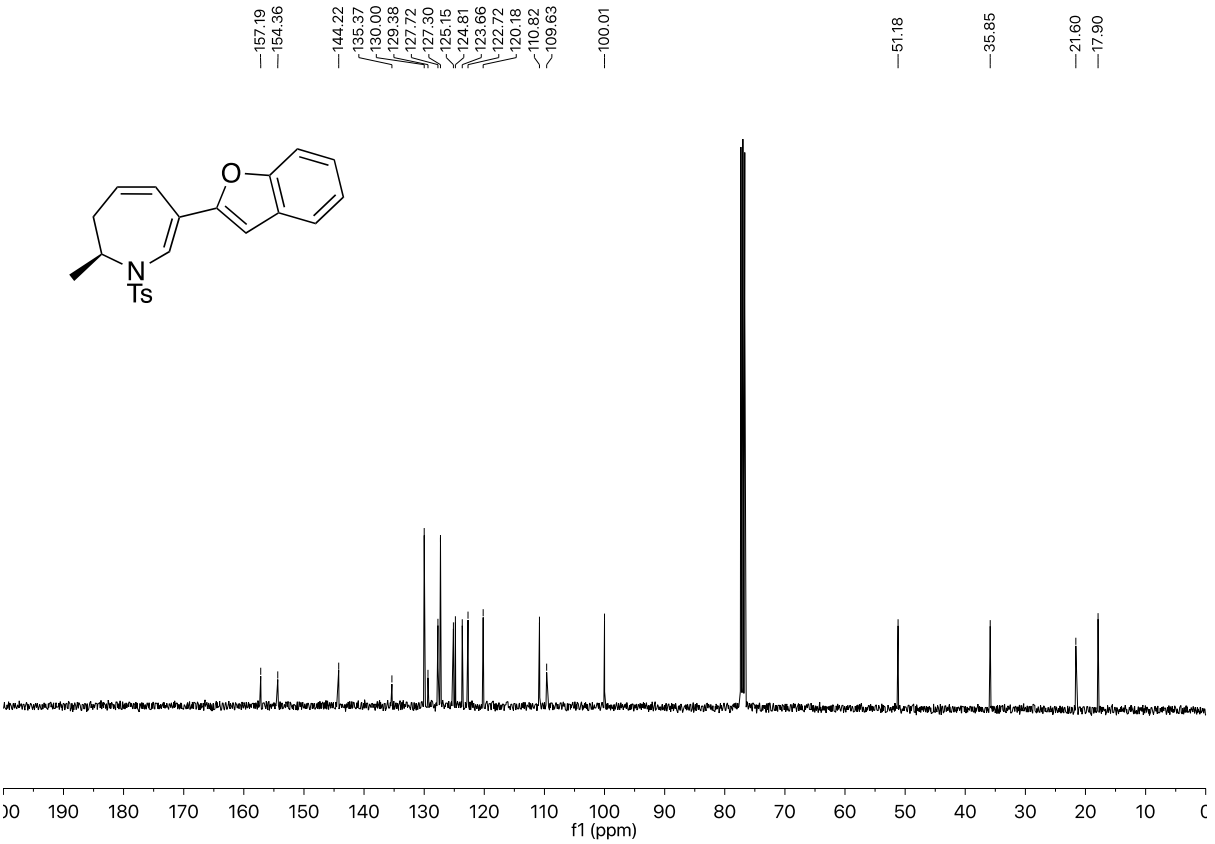


^{1}H and ^{13}C NMR Spectra of 34

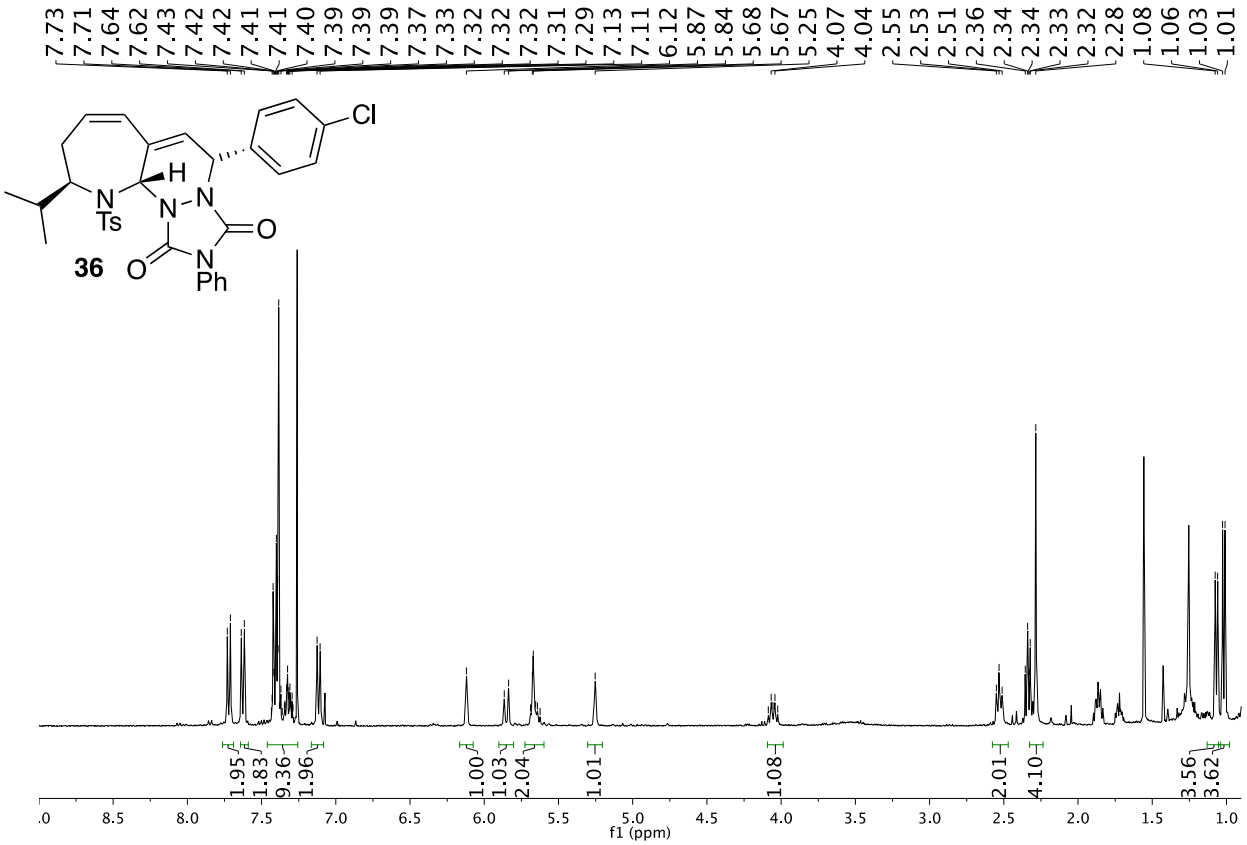


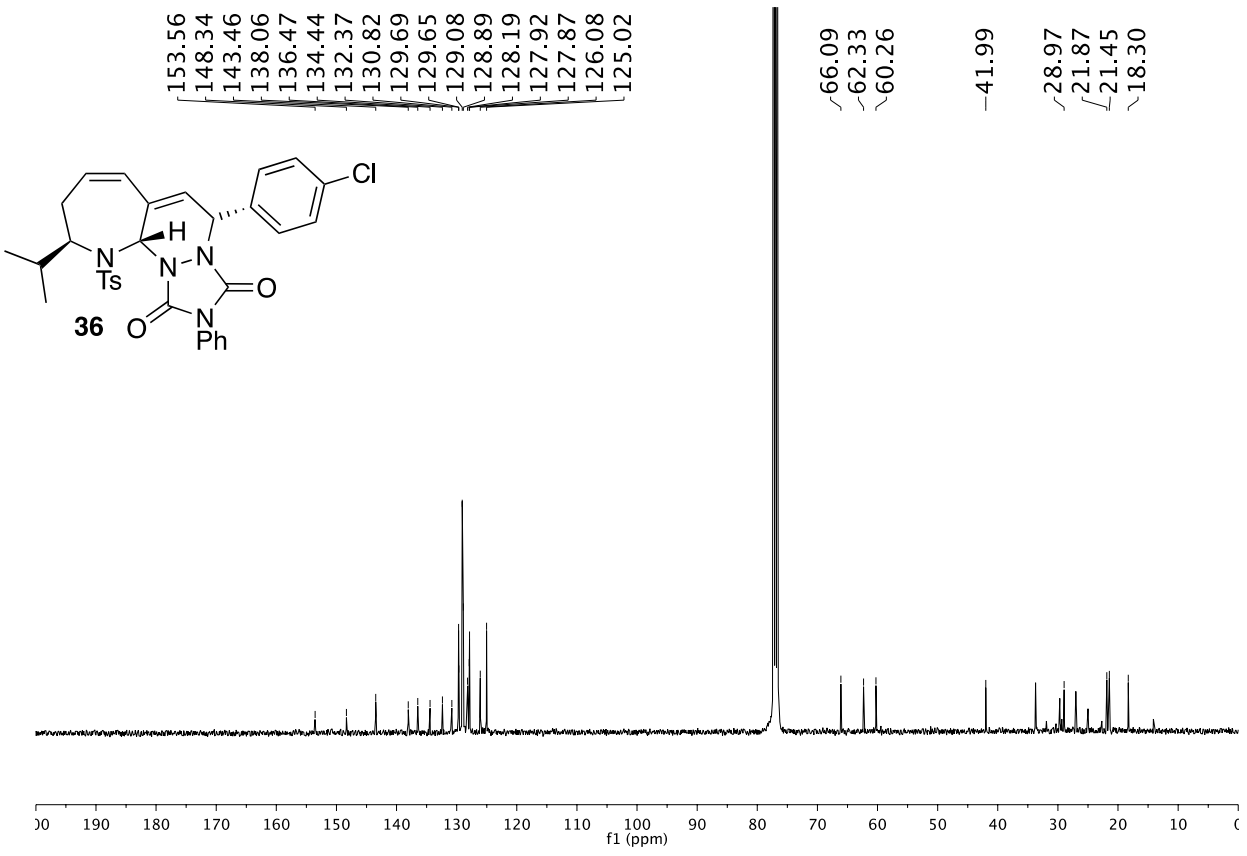
^{1}H and ^{13}C NMR Spectra of 35



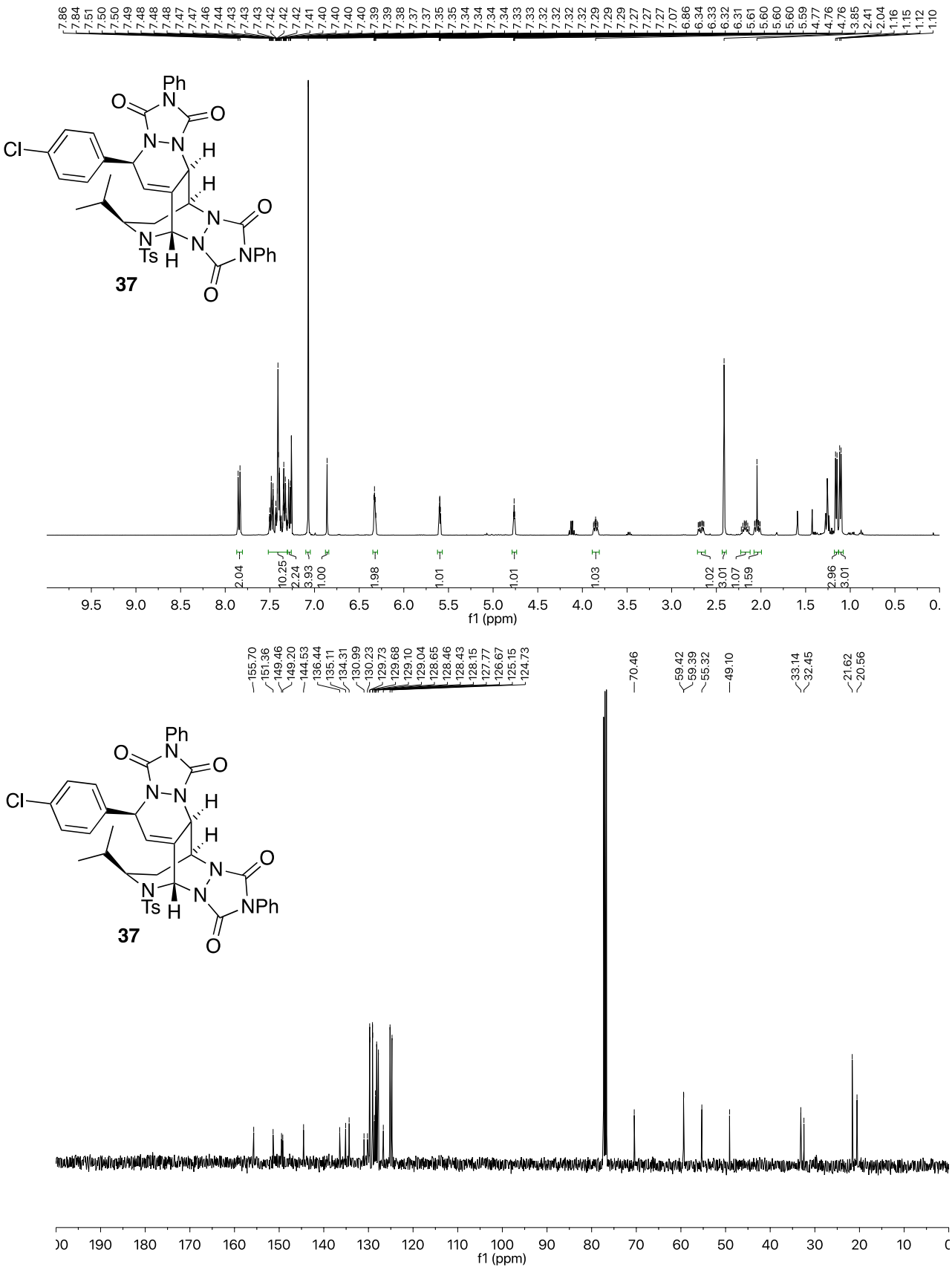


^{1}H and ^{13}C NMR Spectra of 36

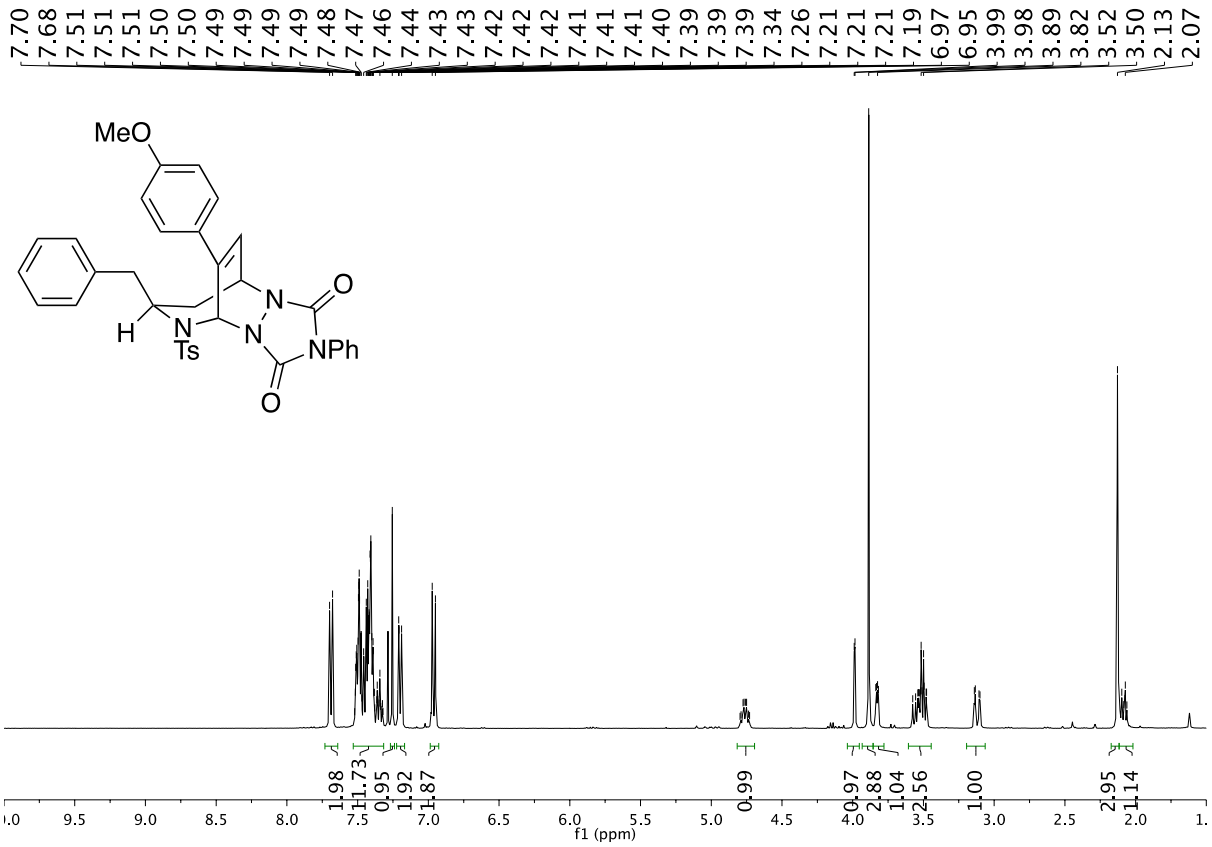


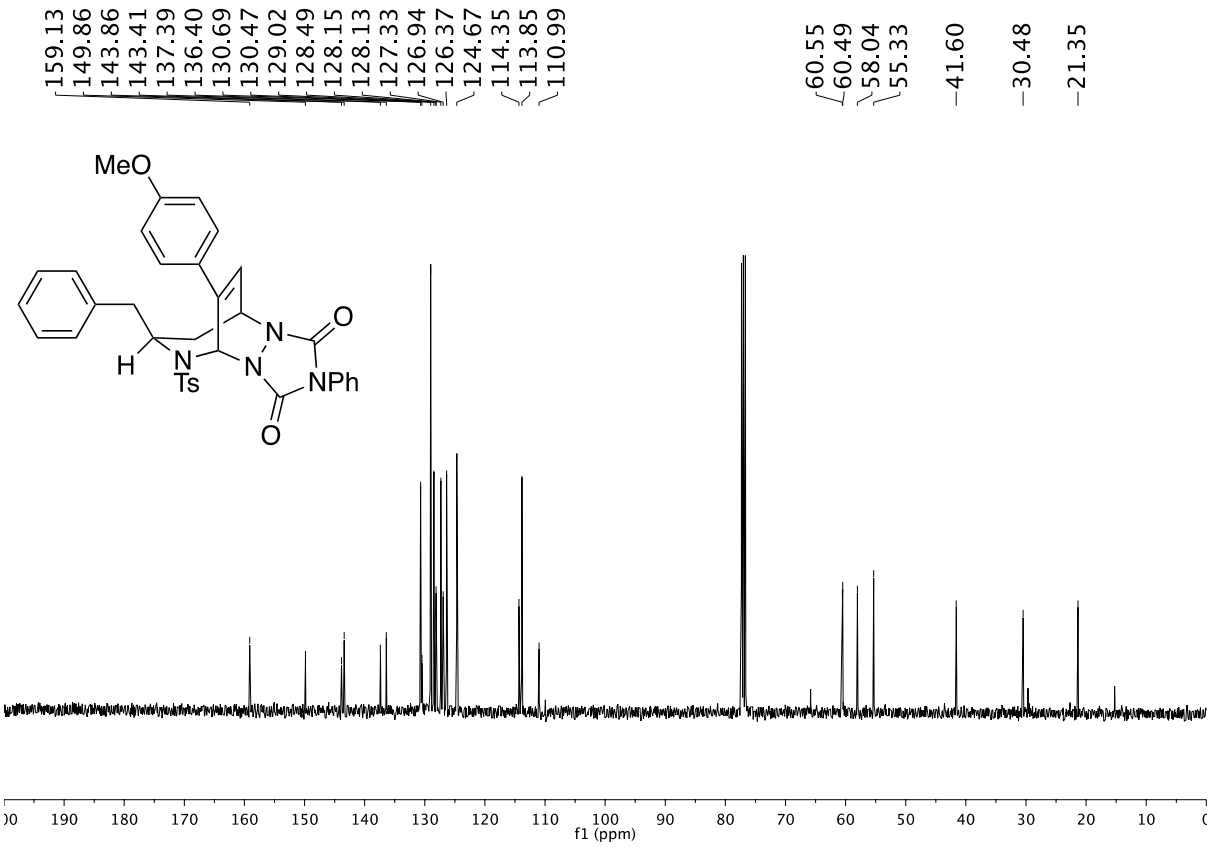


^{1}H and ^{13}C NMR Spectra of 37

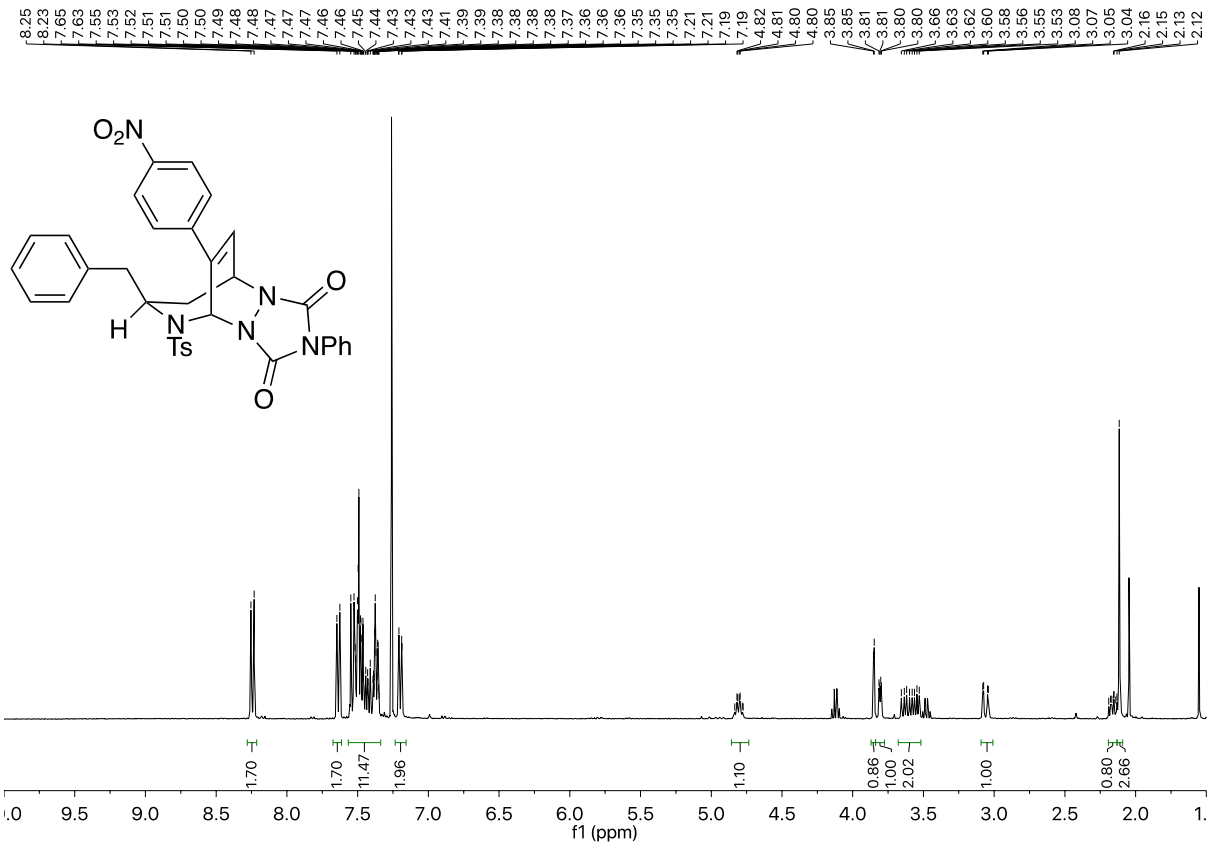


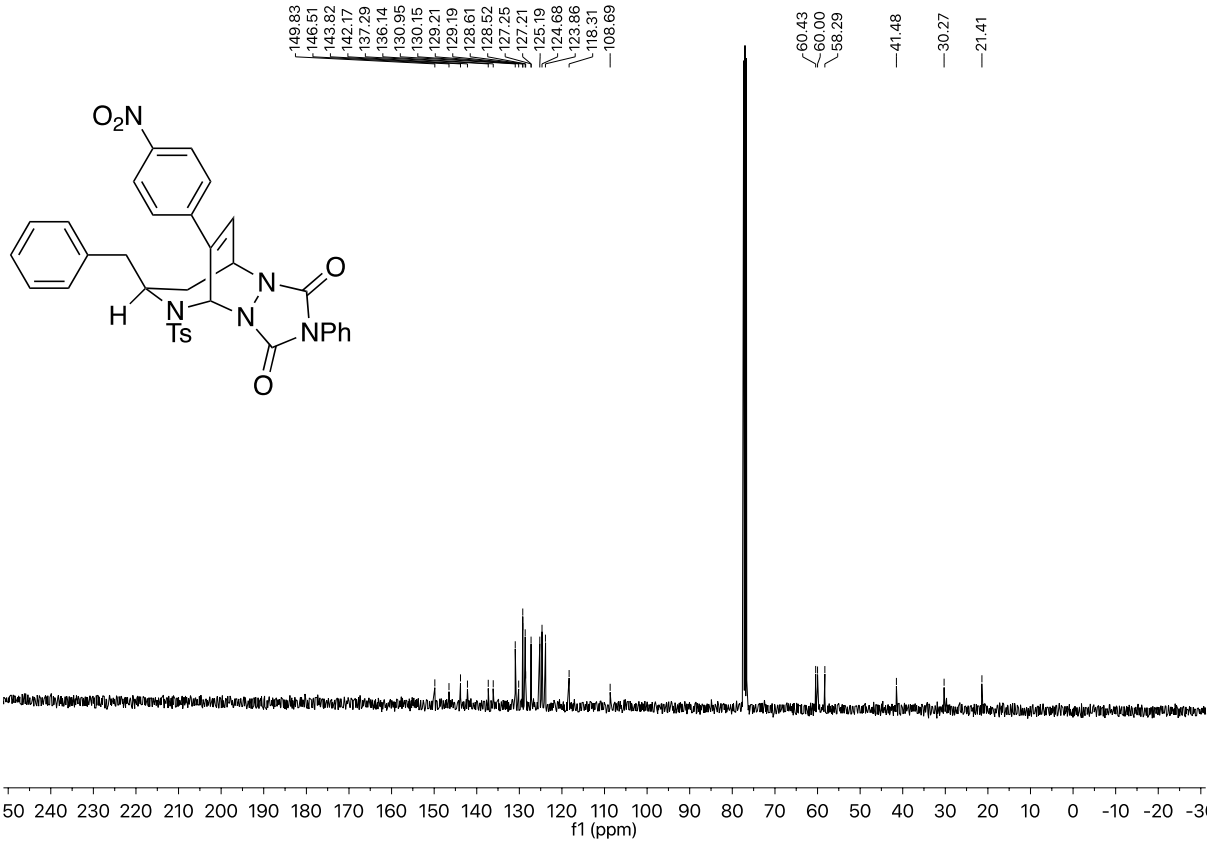
^{1}H and ^{13}C NMR Spectra of 38



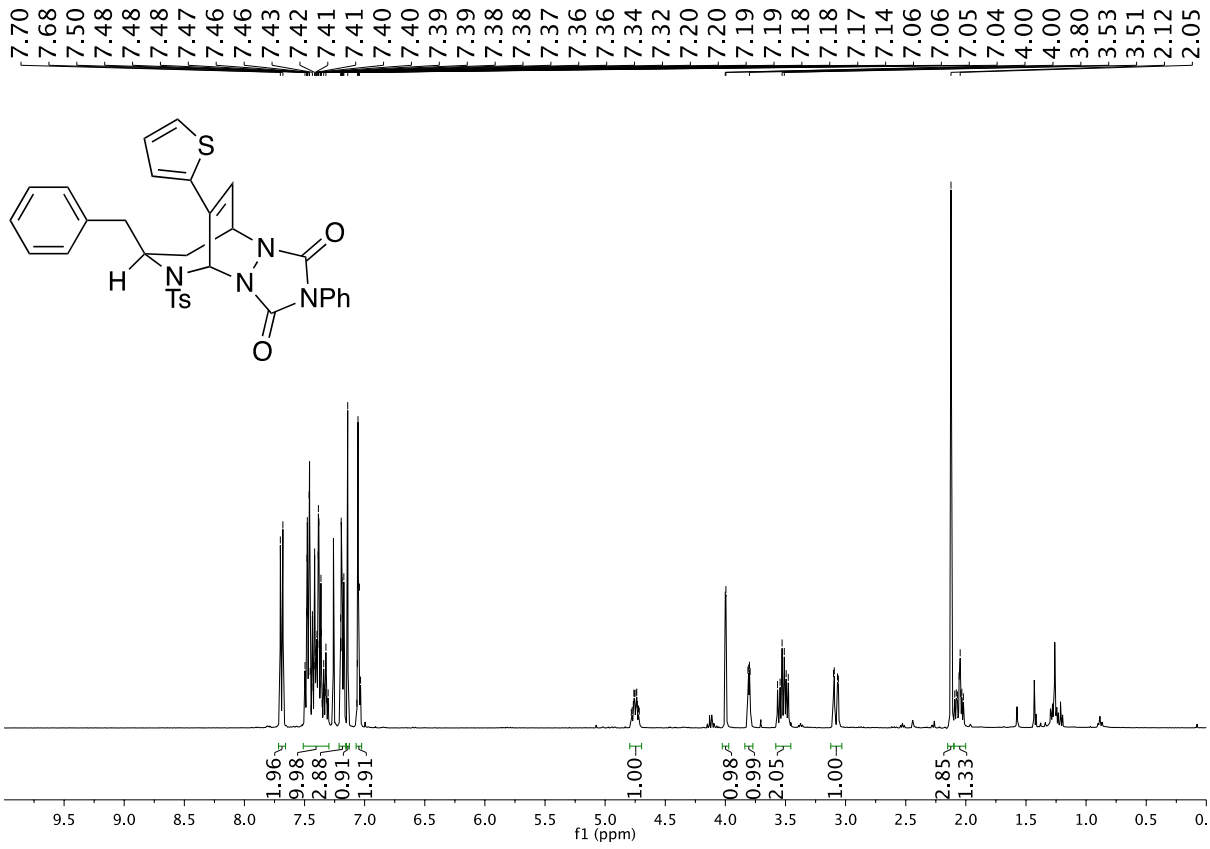


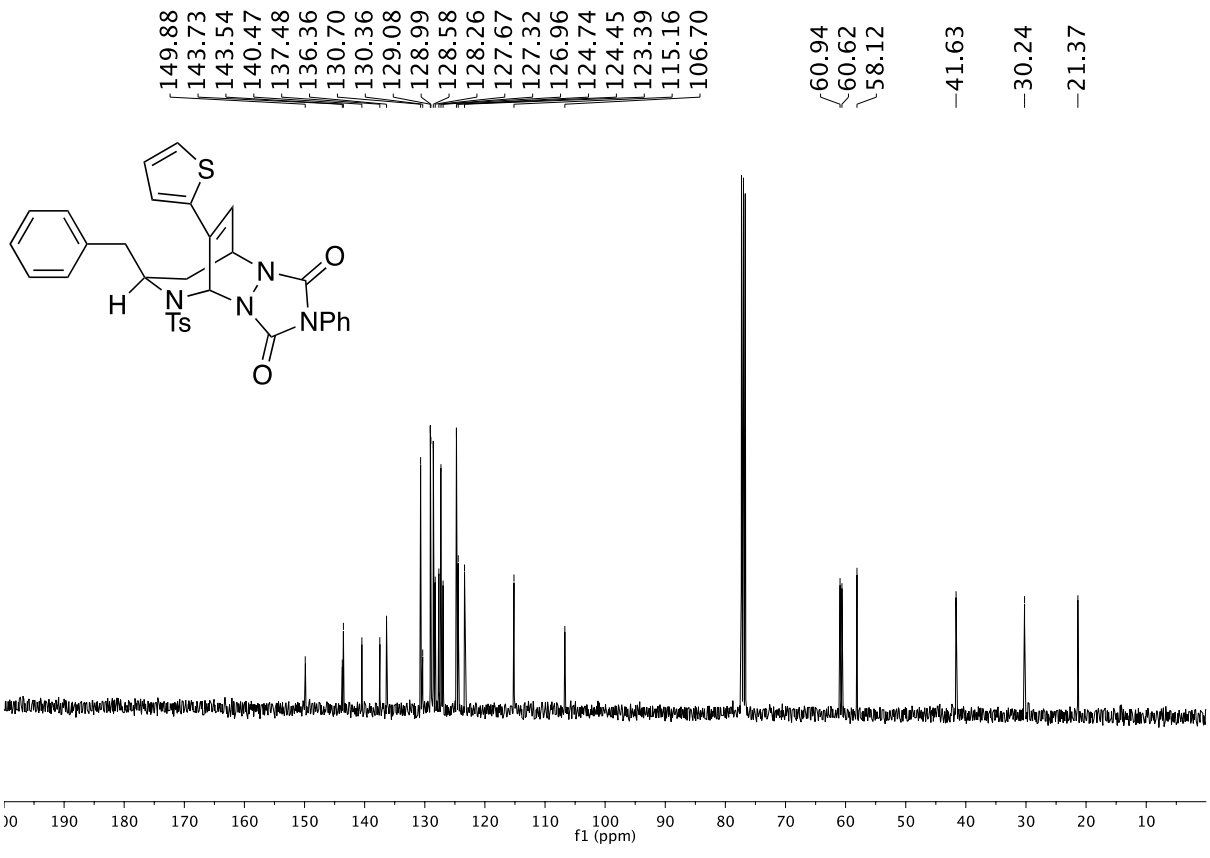
^{1}H and ^{13}C NMR Spectra of 39





^{1}H and ^{13}C NMR Spectra of 40





^{1}H and ^{13}C NMR Spectra of 41