Strain-enabled radical spirocyclization cascades: rapid access to spirocyclobutyl lactones and – lactams

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1. General methods

1.1 Solvents, Reagents, Glassware and Reaction Setup

Unless otherwise specified, all reactions were conducted under an inert atmosphere of nitrogen or argon using hot air oven dried (120 ºC) glassware utilizing standard Schlenk-line technique. Air and moisture-sensitive liquids and solutions were transferred via syringe into the reaction vessels through a rubber septum under inert atmosphere. Unless otherwise specified, all reagents were purchased of the highest commercial quality and used as received. Non-anhydrous solvents were purchased at the highest commercial quality and used as received. Organic solvents used for carrying out reactions were dried using standard methods. All work up and purification were carried out with reagent grade solvents in air. Temperature described below −5 °C was achieved using immersion cooler by Julabo.

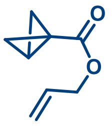
1.2 Analytical methods

Chromatography: Column chromatography was carried out using Sigma-Aldrich silica gel (60 Å, 230-400 mesh, 40-63 μm). Reactions were monitored by thin-layer chromatography (TLC), using aluminium-backed Merck Kieselgel 60 F254 fluorescent treated silica gel plates, which were visualized under UV light or by staining with aqueous basic $KMnO_4$, or phosphomolybdic acid solution in ethanol. **IR:** Infrared (FT-IR) spectra were recorded of neat sample on Bruker alfa FT-IR, νmax in cm–1 and the bands are characterized as strong (s), medium (m), and weak (w). **Melting Point:** Melting points were measured in open glass capillary on a Buchi M-560 melting point apparatus. **NMR:** NMR spectra were recorded on Bruker Ultrashield spectrometer at 400 MHz (for ^{1}H-NMR), 101 MHz (for ^{13}C-NMR), 376 MHz (for ^{19}F-NMR). Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as internal standard ($CDCl_3$: δ 7.26 ppm for 1H-NMR and δ 77.00 ppm for ^{13}C-NMR). For ^{1}H-NMR, data are reported as follows: chemical shift, multiplicity (s = singlet, brs = broad singlet, d = doublet, dd = doublet of doublets, ddd = doublet of doublet of doublets, t = triplet, q = quartet, dt = doublet of triplets, m = multiplet etc.), coupling constants (Hz) and integration. **NMR yields:** Following work up or/and solvent evaporator, dibromomethane (relative to limiting starting material) was added to the crude residue. The resultant mixture was dissolved in $CDCl_3$, and a 0.5 mL sample of the resultant solution taken for ^{1}H NMR analysis. Yields were calculated based on the integrals of known S3 product resonances relative to dibromomethane (2H, at 4.94 ppm in $CDCl_3$). MS: High Resolution Mass

Spectrometry (HRMS) was performed on Waters e2695 XEVO G2-XS Q-TOFinstrument. Photoreactions were conducted using Photocube with 457 nm using 100% intensity.

2. Preparation of Starting Materials:

2.1 Synthesis of bicyclo[1.1.0]butanes (BCBs):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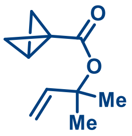
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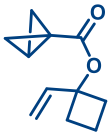
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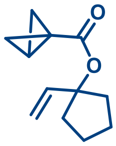
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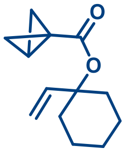
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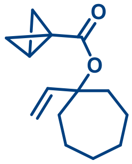
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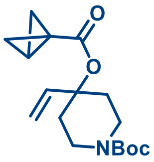
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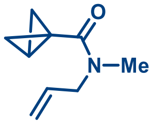
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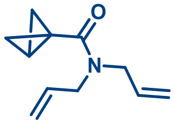
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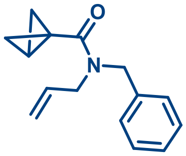
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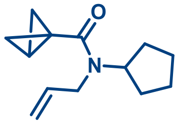
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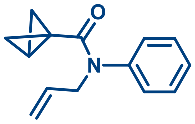
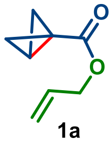
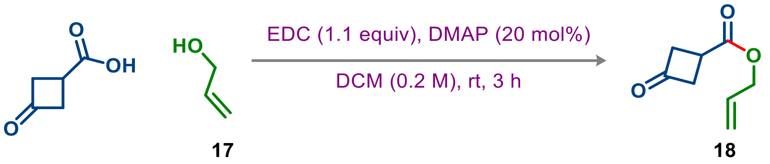

1l

BCB allyl esters and – amides (**1a-1l**) were synthesized using the following procedures.

Allyl-bicyclo[1.1.0]butane-1-carboxylate (1a)

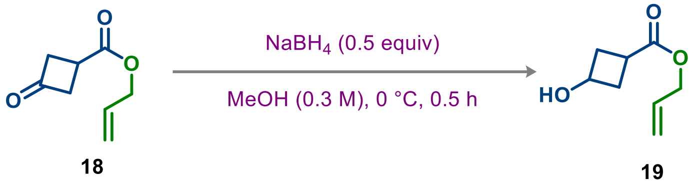

1a

Allyl 3-oxocyclobutane-1-carboxylate (18)



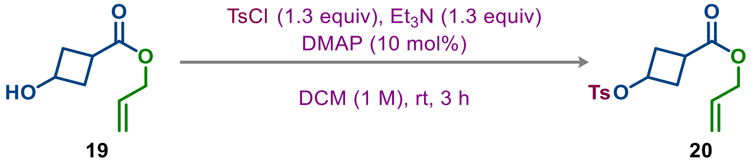
Following a slightly modified procedure,[1] to a stirred solution of 3-oxocyclobutane-1-carboxylic acid (1.00 g, 8.80 mmol, 1.00 equiv) in DCM (44 mL, 0.20 M) under nitrogen, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC) (1.85 g, 9.60 mmol, 1.10 equiv), allyl alcohol **17** (0.60 mL, 8.80 mmol, 1.00 equiv), and DMAP (0.21 g, 1.8 mmol, 0.20 equiv) were added and stirred. After 3 h, DCM (20 mL) was added to the reaction mixture and quenched with a saturated aqueous NH_4Cl solution (50 mL). The resulting reaction mixture was extracted with DCM (2 × 50 mL). The combined organic phases were dried over Na_2SO_4. The solvent was removed under vacuum to yield **18** as a light brown oil (1.08 g, 80%), which was used without further purification in the reduction reaction detailed below.

Allyl 3-hydroxycyclobutane-1-carboxylate (19)



Following a slightly modified procedure,[1] to a stirred solution of ketone **18** (1.08 g, 6.97 mmol, 1.00 equiv) in MeOH (23 mL, 0.30 M) at 0 °C (ice/water bath), $NaBH_4$ (132 mg, 3.49 mmol, 0.500 equiv) was added and stirred. After 30 minutes, the reaction mixture was quenched with a saturated aqueous NH_4Cl solution (25 mL). The reaction was extracted with DCM (3 × 25 mL) and the combined organic phases were washed with brine (25 mL) and dried over Na_2SO_4. The solvent was removed under vacuum to yield **19** as a light-yellow oil (800 mg, 73%), which was used without further purification in the tosylation reaction detailed below.

Allyl 3-(tosyloxy)cyclobutane-1-carboxylate (20)

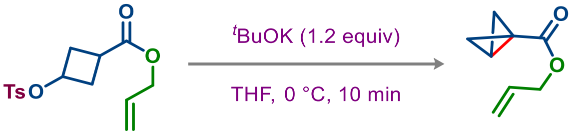


Following a slightly modified procedure,[1] to a stirred solution of alcohol **19** (800 mg, 5.12 mmol, 1.00 equiv) in DCM (6.0 mL, 1.0 M) under nitrogen at 0 °C (ice/water bath), 4-toluenesulfonyl chloride (1.30 g, 6.81 mmol, 1.30 equiv), Et_3N (0.95 mL, 6.8 mmol, 1.3 equiv), and DMAP (63 mg, 0.51 mmol, 0.10 equiv) were added and stirred at room temperature. After 3 h, DCM (40 mL) was added to the reaction mixture followed by water (40 mL). The organic phase was washed with brine (50 mL), dried over Na_2SO_4. The solvent was removed under vacuum. The crude product was purified by flash chromatography (silica, 1:19 v/v EtOAc:Hexane) to afford the desired product **20** as a brown oil (798 mg, 58%). **(See Spectra)**

- **TLC (EtOAc:Hexane, 1:19 v/v):** $R_f = 0.35$, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.77 (d, *J* = 8.0 Hz, 2H, Ar*H*), 7.33 (d, *J* = 8.0 Hz, 2H, Ar*H*), 5.87 (ddt, *J* = 16.5, 11.1, 5.8 Hz, 1H, alkene C*H*), 5.34 – 5.19 (m, 2H, alkene C*H*$_2$), 4.73 (p, *J* = 7.6 Hz, 1H, OC*H*), 4.54 (d, *J* = 5.8 Hz, 2H, OC*H*$_2$), 2.64 (p, *J* = 10.2, 7.7 Hz, 1H), 2.54 – 2.32 (m, 7H).
- **^{13}C NMR (101 MHz, $CDCl_3$):** δ 172.8, 144.9, 133.8, 131.8, 129.8, 127.8, 118.5, 69.5, 65.5, 34.1, 29.5, 21.6.

- **IR (Neat):** υ 2998 (w), 2952 (w), 1733 (s), 1363 (m), 1177 (s), 995 (w), 854 (w).
- **HRMS (ESI):** calcd. for $C_{15}H_{18}O_5SNa^+$ $[M+Na]^+$ 333.0773; found: 333.0774

Allyl-bicyclo[1.1.0]butane-1-carboxylate (1a)

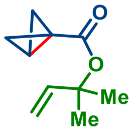


20 **1a**

Following a slightly modified procedure,[1] to a stirred solution of tosylate **20** (798 mg, 2.58 mmol, 1.00 equiv) in THF (13 mL, 0.20 M) under nitrogen at 0 °C (ice/water bath), ^{t}BuOK (347 mg, 3.09 mmol, 1.20 equiv, 0.73 M in THF) was added and stirred for 10 minutes. The resulting mixture was quenched with a saturated aqueous NH_4Cl solution (10 mL). The reaction mixture was extracted with DCM (3 × 30 mL) and the combined organic phases were dried over Na_2SO_4. The solvent was removed under vacuum. The crude product was purified by flash chromatography (silica, 1:49 v/v EtOAc:Hexane) to afford the desired product **1a** as a brown oil (180 mg, 50%). (See Spectra)

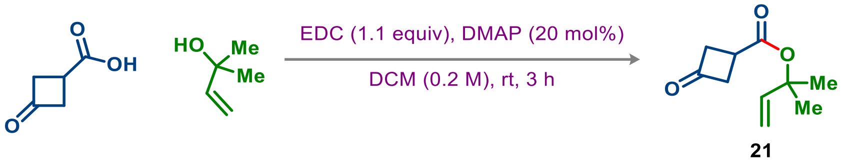
- **TLC (EtOAc:Hexane, 1:49 v/v):** $R_f = 0.71$, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 5.92 (ddt, *J* = 16.4, 10.8, 5.6 Hz, 1H, alkene C*H*), 5.33 – 5.17 (m, 2H, alkene C*H*$_2$), 4.60 (dt, *J* = 5.7, 1.5 Hz, 2H, OC*H*$_2$), 2.38 (d, *J* = 3.5 Hz, 2H, bicyclobutane C*H*$_2$), 2.10 (p, *J* = 3.2 Hz, 1H, bicyclobutane C*H*), 1.16 (d, *J* = 2.9 Hz, 2H, bicyclobutane C*H*$_2$).
- **^{13}C NMR (101 MHz, $CDCl_3$):** δ 172.8, 132.4, 117.9, 65.2, 35.6, 16.7, 9.0.
- **IR (Neat):** υ 2923 (s), 2854 (m), 1731 (w), 1457 (w), 1369 (w), 1180 (w), 818 (w).
- **Mass:** Not detected in HRMS (ESI, CI) and GCMS. However, the subsequent reaction product was fully characterized.

2-(λ^1-Oxidaneyl)but-3-en-2-yl-bicyclo[1.1.0]butane-1-carboxylate (1b)



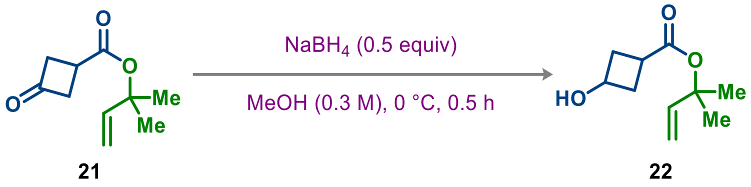
1b

2-Methylbut-3-en-2-yl 3-oxocyclobutane-1-carboxylate (21)



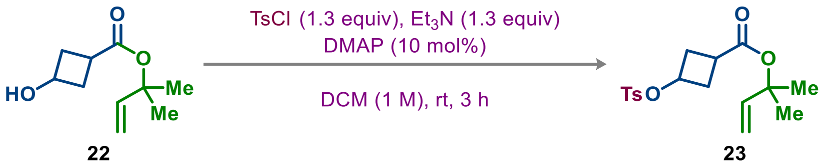
Following a slightly modified procedure,[1] to a stirred solution of 3-oxocyclobutane-1-carboxylic acid (1.00 g, 8.80 mmol, 1.00 equiv) in DCM (44 mL, 0.20 M) under nitrogen, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC)(1.85 g, 9.60 mmol, 1.10 equiv), 2-methylbut-3-en-2-ol (755 mg, 8.80 mmol, 1.00 equiv), and DMAP (210 mg, 1.80 mmol, 0.200 equiv) were added and stirred. After 3 h, DCM (20 mL) was added to the reaction mixture and quenched with a saturated aqueous NH_4Cl solution (50 mL). The resulting reaction mixture was extracted with DCM (2 × 50 mL). The combined organic phases were dried over Na_2SO_4. The solvent was removed under vacuum to yield **21** as a light brown oil (780 mg, 49%), which was used without further purification in the reduction reaction detailed below.

2-Methylbut-3-en-2-yl 3-hydroxycyclobutane-1-carboxylate (22)



Following a slightly modified procedure, [1] to a stirred solution of ketone **21** (456 mg, 2.50 mmol, 1.00 equiv) in MeOH (8 mL, 0.3 M) at 0 °C (ice/water bath), $NaBH_4$ (47.0 mg, 1.25 mmol, 0.500 equiv) was added and stirred at 0 °C. After 30 minutes, the reaction mixture was quenched with a saturated aqueous NH_4Cl solution (25 mL). The reaction was extracted with DCM (3 × 25 mL) and the combined organic phases were washed with brine (25 mL) and dried over Na_2SO_4. The solvent was removed under vacuum to yield **22** as a light-yellow oil (400 mg, 86%), which was used without further purification in the tosylation reaction detailed below.

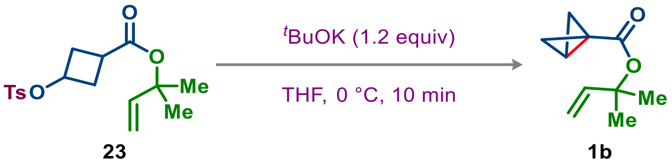
2-Methylbut-3-en-2-yl 3-(tosyloxy)cyclobutane-1-carboxylate(23)



Following a slightly modified procedure,[1] to a stirred solution of alcohol **22** (400 mg, 2.17 mmol, 1.00 equiv) in DCM (2.2 mL, 1.0 M) under nitrogen at 0 °C (ice/water bath), 4-toluenesulfonyl chloride (550 mg, 2.89 mmol, 1.30 equiv), Et_3N (0.403 mL, 2.89 mmol, 1.30 equiv), and DMAP (27 mg, 0.22 mmol, 0.10 equiv) were added and warm up to room temperature. After 3 h, DCM (40 mL) was added to the reaction mixture followed by water (40 mL). The organic phase was washed with brine (50 mL), dried over Na_2SO_4. The solvent was removed under vacuum. The crude product was purified by flash chromatography (silica, 1:19 v/v EtOAc:Hexane) to afford the desired product **23** as a brown oil (610 mg, 82%). **(See Spectra)**

- **TLC (EtOAc:Hexane, 1:19 v/v):** R_f = 0.32, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.77 (d, *J* = 8.0 Hz, 2H, Ar*H*), 7.33 (d, *J* = 8.0 Hz, 2H, Ar*H*), 6.12 – 5.94 (m, 1H, alkene C*H*), 5.19 – 5.03 (m, 2H, alkene *CH₂*), 4.71 (p, *J* = 7.5 Hz, 1H, OC*H*), 2.62 – 2.29 (m, 8H), 1.48 (d, *J* = 1.2 Hz, 6H, 2 x C*H₃*).
- **^{13}C NMR (101 MHz, $CDCl_3$):** δ 172.0, 144.9, 142.1, 133.8, 129.8, 127.8, 112.9, 81.2, 69.6, 34.0, 30.4, 26.3, 21.6.
- **IR (Neat):** υ 2923 (w), 2854 (w), 1728 (s), 1365 (s), 1179 (s), 1127 (m), 858 (m), 819 (m).
- **HRMS (ESI):** calcd. for $C_{17}H_{22}O_5SNa^+$ $[M+Na]^+$ 361.1086; found: 361.1083

2-(λ^1-Oxidaneyl)but-3-en-2-yl-bicyclo[1.1.0]butane-1-carboxylate (1b)



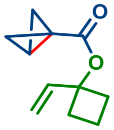
Following a slightly modified procedure,[1] to a stirred solution of tosylate **23** (600 mg, 1.77 mmol, 1.00 equiv) in THF (9 mL, 0.20 M) under nitrogen at 0 °C (ice/water bath), ^{t}BuOK (239 mg, 2.13 mmol, 1.20 equiv, 0.730 M in THF) was added and stirred for 10 minutes. The resulting mixture was quenched with a saturated aqueous NH_4Cl solution (10 mL) and extracted with DCM (3 × 30 mL) and the combined organic phases were dried over Na_2SO_4. The solvent was removed under vacuum. The crude product was purified by flash chromatography (silica, 1:49 v/v EtOAc:Hexane) to afford the desired product **1b** as a brown oil (230 mg, 78%). **(See Spectra)**

- **TLC (EtOAc:Hexane, 1:49 v/v): R_f = 0.75, $KMnO_4$**
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 6.06 (dd, *J* = 17.5, 10.9 Hz, 1H, alkene C*H*), 5.23 – 5.01 (m, 2H, alkene C*H₂*), 2.41 – 2.23 (m, 2H, bicyclobutane C*H₂*), 2.01 (p, *J* = 3.2 Hz, 1H,

bicyclobutane C*H*), 1.51 (s, 6H, 2 x C*H*$_3$), 1.09 (dd, *J* = 2.8, 1.2 Hz, 2H, bicyclobutane C*H*$_2$).

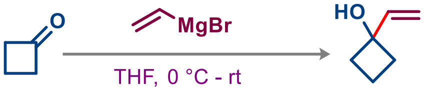
- **^{13}C NMR (101 MHz, CDCl$_3$):** δ 172.0, 142.7, 112.4, 80.6, 35.4, 26.5, 16.0, 9.9.
- **IR (Neat):** υ 2923 (s), 2854 (w), 1733 (s), 1460 (w), 1159 (m), 1119 (s), 1021 (w).
- **HRMS (ESI):** calcd. for $C_{10}H_{14}O_2H^+$ $[M+H]^+$ 167.1072; found: 167.1076

1-Vinylcyclobuty-bicyclo[1.1.0]butane-1-carboxylate (1c)



1c

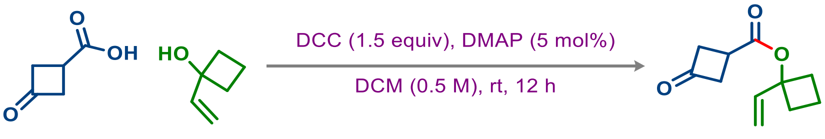
1-Vinylcyclobutan-1-ol (24)



24

Following a slightly modified procedure,[2] to a solution of vinylmagnesium bromide (20 mL, 1.0 M in THF, 2.0 equiv) in THF (20 mL), cyclobutanone (700 mg, 10.0 mmol,1.00 equiv) was added drop-wise at 0 °C under nitrogen. After 12 h stirring at room temperature, the reaction mixture was quenched with aqueous NH_4Cl (70 mL) at 0 °C and extracted with Et_2O (3 × 70 mL). The combined organic layers were washed with brine (100 mL) and dried over Na_2SO_4. The solvent was removed under vacuum to yield **24** as a light-yellow oil (800 mg, 82%), which was used in the next step without further purification.

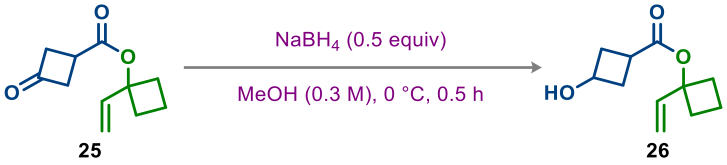
1-Vinylcyclobutyl 3-oxocyclobutane-1-carboxylate (25)



24 25

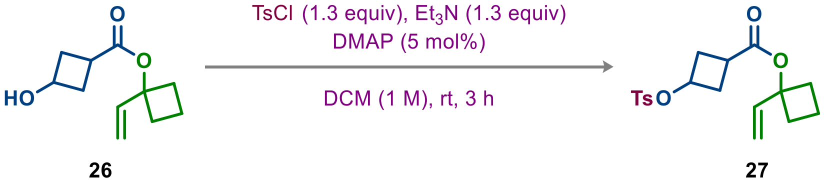
Following a slightly modified procedure,[3] to a solution of 3-oxocyclobutanecarboxylic acid (920 mg, 8.00 mmol, 1.00 equiv) in dry DCM (16 mL, 0.5 M,), alcohol **24** (0.79 g, 8.0 mmol, 1.0 equiv), DMAP (49 mg, 0.40 mmol, 0.05 equiv) and DCC (2.48 g, 12.0 mmol, 1.50 equiv) were added under nitrogen. After 12 h stirring at room temperature, the reaction mixture was filtrated, and the precipitate (dicyclohexylurea) was rinsed with DCM (10 mL). The filtrate was concentrated in vacuum to yield **25** as a light-yellow oil (995 mg, 63%), which was used in the next step without further purification.

1-Vinylcyclobutyl 3-hydroxycyclobutane-1-carboxylate (26)



Following a slightly modified procedure,[1] to a stirred solution of ketone **25** (971 mg, 5.00 mmol, 1.00 equiv) in MeOH (17 mL, 0.30 M) at 0 °C (ice/water bath), $NaBH_4$ (95.0 mg, 1.25 mmol, 0.500 equiv) was added. After stirring at 0 °C for 30 minutes, the reaction mixture was quenched with a saturated aqueous NH_4Cl solution (60 mL). The reaction was extracted with DCM (3 × 25 mL) and the combined organic phases were washed with brine (50 mL) and dried over Na_2SO_4. The solvent was removed under vacuum to yield **26** as a light-yellow oil (623 mg, 63%), which was used without further purification in the tosylation reaction detailed below.

1-Vinylcyclobutyl 3-(tosyloxy)cyclobutane-1-carboxylate (27)



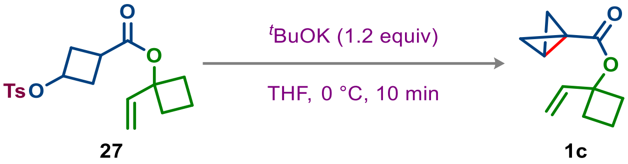
Following a slightly modified procedure,[1]to a stirred solution of alcohol **26** (450 mg, 2.29 mmol, 1.00 equiv) in DCM (2.3 mL, 1.0 M) under nitrogen at 0 °C (ice/water bath), 4-toluenesulfonyl chloride (568 mg, 2.98 mmol, 1.30 equiv), Et_3N (0.426 mL, 2.98 mmol, 1.30 equiv), and DMAP (15 mg, 0.12 mmol, 0.050 equiv) were added. After stirring 3 hat room temperature, DCM (40 mL) was added to the reaction mixture followed by water (40 mL). The organic phase was washed with brine (50 mL), dried over Na_2SO_4. The solvent was removed under vacuum. The crude product was purified by flash chromatography (silica, 1:19 v/v EtOAc:Hexane) to afford the desired product **27** as a brown oil (470 mg, 59%). **(See Spectra)**

- **TLC (EtOAc:Hexane, 1:9 v/v):** $R_f = 0.41$, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.75 (d, *J* = 7.9 Hz, 2H, Ar*H*), 7.32 (d, *J* = 8.0 Hz, 2H, Ar*H*), 6.06 (dd, *J* = 17.4, 10.7 Hz, 1H, alkene C*H*), 5.27 – 5.09 (m, 2H, alkene C*H*$_2$), 4.70

(p, J = 7.6 Hz, 1H, OCH), 2.63 – 2.51 (m, 1H), 2.47 – 2.23 (m, 11H), 1.86 – 1.73 (m, 1H), 1.63 (p, J = 9.3 Hz, 1H).

- **^{13}C NMR (101 MHz, CDCl$_3$):** δ 171.5, 144.8, 137.9, 133.7, 129.8, 127.7, 113.6, 81.1, 69.5, 33.8, 33.8, 29.8, 21.5, 13.7.
- **IR (Neat):** υ 2933 (w), 2950 (w), 1728 (s), 1360 (s), 1171 (s), 855 (s), 816 (s), 557 (m).
- **HRMS (ESI):** calcd. for $C_{18}H_{22}O_5SNa^+$ $[M+Na]^+$ 373.1086; found: 373.1084

1-Vinylcyclobutyl-bicyclo[1.1.0]butane-1-carboxylate (1c)

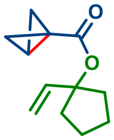


Following a slightly modified procedure,[1] to a stirred solution of tosylate **27** (470 mg, 1.34 mmol, 1.00 equiv) in THF (7 mL, 0.20 M) under nitrogen at 0 °C (ice/water bath), ^{t}BuOK (181 mg, 1.61 mmol, 1.20 equiv, 0.730 M in THF) was added and stirred for 10 minutes at 0 °C. The resulting mixture was quenched with a saturated aqueous NH_4Cl solution (10 mL). The reaction mixture was extracted with DCM (3 × 30 mL) and the combined organic phases were dried over Na_2SO_4. The solvent was removed under vacuum. The crude product was purified by flash chromatography (silica, 1:49 v/v EtOAc:Hexane) to afford the desired product **1c** as a brown oil (170 mg, 71%).

(See Spectra)

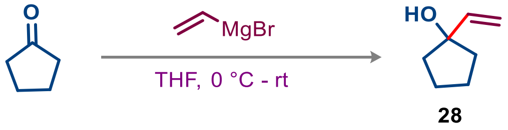
- **TLC (EtOAc:Hexane, 1:19 v/v):** R_f = 0.73, $KMnO_4$.
- **^{1}H NMR (400 MHz, CDCl$_3$):** δ 6.15 (dd, J = 17.3, 10.8 Hz, 1H, alkene CH), 5.35 – 5.11 (m, 2H, alkene CH_2), 2.39 – 2.28 (m, 6H), 2.04 (p, J = 3.3 Hz, 1H, bicyclobutane CH), 1.91 – 1.78 (m, 1H), 1.68 (p, J = 10.7, 9.9 Hz, 1H), 1.12 (d, J = 2.8 Hz, 2H, bicyclobutane CH_2).
- **^{13}C NMR (101 MHz, CDCl$_3$):** δ 171.6, 138.6, 113.2, 80.8, 35.5, 34.0, 16.2, 13.8, 9.4.
- **IR (Neat):** υ 2924 (m), 2854 (w), 1730 (s), 1366 (m), 1178 (s), 1098 (w), 820 (m).
- **HRMS (ESI):** calcd. for $C_{11}H_{14}O_2Na^+$ $[M+Na]^+$ 201.0891; found: 201.0896

1-Vinylcyclopentyl-bicyclo[1.1.0]butane-1-carboxylate (1d)



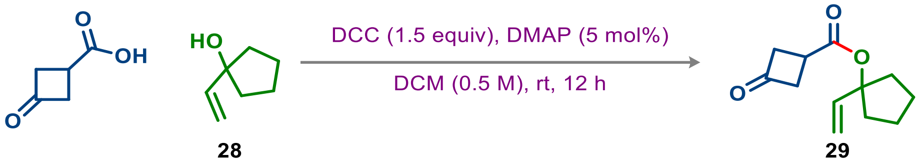
1d

1-Vinylcyclopentan-1-ol (28)



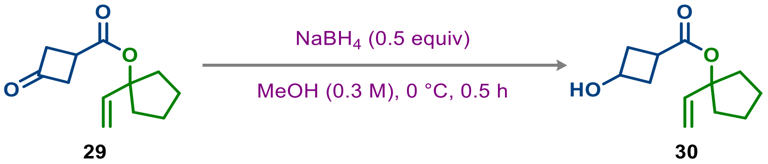
Following a slightly modified procedure,[2] to a solution of vinylmagnesium bromide (44 mL, 1.0 M in THF, 2.0 equiv) in THF (44 mL), cyclopetanone (1.8 g, 22 mmol, 1.0 equiv) was added drop-wise at 0 °C under nitrogen. After 12 h stirring at room temperature, the reaction mixture was quenched with aqueous NH_4Cl (250 mL) at 0 °C and extracted with Et_2O (3 × 170 mL). The combined organic layers were washed with brine (150 mL) and dried over Na_2SO_4. The solvent was removed under vacuum to yield **28** as a light-yellow oil (1.1 g, 44%), which was used in the next step without further purification.

1-Vinylcyclopentyl 3-oxocyclobutane-1-carboxylate (29)



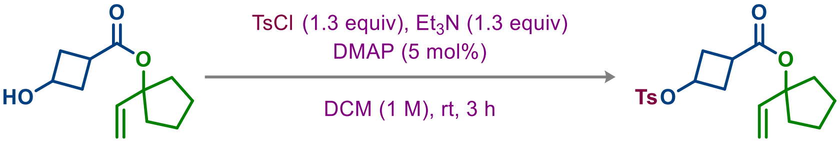
Following a slightly modified procedure,[3] to a solution of 3-oxocyclobutanecarboxylic acid (204 mg, 1.78 mmol, 1.00 equiv) in dry DCM (3.6 mL, 0.5 M,), alcohol **28** (200 mg, 1.78 mmol, 1.00 equiv), DMAP (11.0 mg, 0.089 mmol, 0.05 equiv) and DCC (551 mg, 2.67 mmol, 1.50 equiv) were added under nitrogen. After 12 h stirring at room temperature, the reaction mixture was filtrated, and the precipitate (dicyclohexylurea) was rinsed with DCM (5 mL). The filtrate was concentrated in vacuum to yield **29** as a light-yellow oil (190 mg, 51%), which was used in the next step without further purification.

1-Vinylcyclopentyl 3-hydroxycyclobutane-1-carboxylate (30)



Following a slightly modified procedure,[1] to a stirred solution of ketone **29** (190 mg, 0.912 mmol, 1.00 equiv) in MeOH (3 mL, 0.3 M) at 0 °C (ice/water bath), $NaBH_4$ (18 mg, 0.46 mmol, 0.50 equiv) was added. After stirring at 0 °C for 30 minutes, the reaction mixture was quenched with a saturated aqueous NH_4Cl solution (10 mL). The reaction was extracted with DCM (3 × 10 mL) and the combined organic phases were washed with brine (10 mL) and dried over Na_2SO_4. The solvent was removed under vacuum to yield **30** as a light-yellow oil (170 mg, 89%), which was used without further purification in the tosylation reaction detailed below.

1-Vinylcyclopentyl 3-(tosyloxy)cyclobutane-1-carboxylate (31)

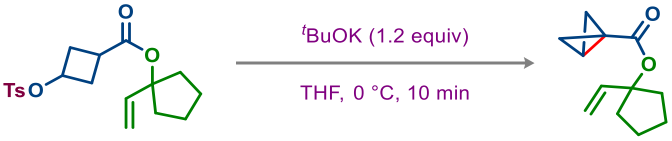


30 **31**

Following a slightly modified procedure,[1] to a stirred solution of alcohol **30** (170 mg, 0.808 mmol , 1.00 equiv) in DCM (0.8 mL, 1.0 M) under nitrogen at 0 °C (ice/water bath), 4-toluenesulfonyl chloride (201 mg, 1.05 mmol, 1.30 equiv), Et_3N (0.105 mL, 1.05 mmol, 1.30 equiv), and DMAP (5.0 mg, 0.04 mmol, 0.05 equiv) were added. After stirring for 3 h at room temperature, DCM (10 mL) was added to the reaction mixture followed by water (10 mL). The organic phase was washed with brine (10 mL), dried over Na_2SO_4. The solvent was removed under vacuum. The crude product was purified by flash chromatography (silica, 1:19 v/v EtOAc:Hexane) to afford the desired product **31** as a brown oil (160 mg, 55%). **(See Spectra)**

- **TLC (EtOAc:Hexane, 1:9 v/v):** $R_f = 0.42$, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.77 (d, *J* = 7.9 Hz, 2H. Ar*H*), 7.33 (d, *J* = 8.0 Hz, 2H, Ar*H*), 6.09 (dd, *J* = 17.5, 10.9 Hz, 1H, alkene C*H*), 5.15 – 5.01 (m, 2H, alkene CH_2), 4.71 (p, *J* = 7.5 Hz, 1H, OC*H*), 2.61 – 2.31 (m, 9H), 2.13 – 2.02 (m, 2H), 1.85 (dt, *J* = 13.3, 7.5 Hz, 2H), 1.68 – 1.62 (m, 3H).
- **^{13}C NMR (101 MHz, $CDCl_3$):** δ 172.0, 144.9, 139.9, 133.8, 129.8, 127.8, 113.3, 91.0, 69.6, 37.5, 33.9, 30.3, 23.1, 21.6.
- **IR (Neat):** υ 2955 (w), 2873 (w), 1729 (s), 1364 (s), 1176 (s), 858 (m), 818 (m).
- **HRMS (ESI):** calcd. for $C_{19}H_{24}O_5SNa^+$ $[M+Na]^+$ 387.1242; found: 387.1242

1-Vinylcyclopentyl-bicyclo[1.1.0]butane-1-carboxylate (1d)

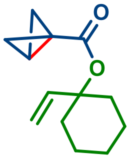


31 **1d**

Following a slightly modified procedure,[1] to a stirred solution of tosylate **31** (160 mg, 0.440 mmol, 1.00 equiv) in THF (2.3 mL, 0.2 M) under nitrogen at 0 °C (ice/water bath), ^{t}BuOK (60.0 mg, 0.527 mmol, 1.20 equiv, 0.73 M in THF) was added and stirred for 10 minutes. The resulting mixture was quenched with a saturated aqueous NH_4Cl solution (10 mL) andextracted with DCM (3 × 10 mL) and the combined organic phases were dried over Na_2SO_4. The solvent was removed under vacuum. The crude product was purified by flash chromatography (silica, 1:49 v/v EtOAc:Hexane) to afford the desired product **1d** as a brown oil (60 mg, 71%). **(See Spectra)**

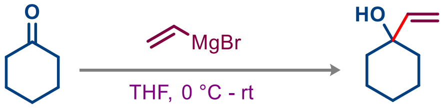
- **TLC (EtOAc:Hexane, 1:19 v/v):** R_f = 0.51, $KMnO_4$.
- **^{1}H NMR (400 MHz, CDCl$_3$):** δ 6.15 (dd, *J* = 17.5, 10.9 Hz, 1H, alkene C*H*), 5.20 – 5.05 (m, 2H, alkene C*H*$_2$), 2.32 (d, *J* = 3.4 Hz, 2H), 2.19 – 2.10 (m, 2H), 2.00 (p, *J* = 3.3 Hz, 1H, bicyclobutane C*H*), 1.92 – 1.83 (m, 2H, cyclopentyl C*H*$_2$), 1.74 – 1.59 (m, 4H, cyclopentyl C*H*$_2$), 1.11 (d, *J* = 2.7 Hz, 2H, bicyclobutane C*H*$_2$).
- **^{13}C NMR (101 MHz, CDCl$_3$):** δ 172.1, 140.5, 112.8, 90.5, 37.7, 35.5, 23.3, 16.0, 9.8.
- **IR (Neat):** υ 2923 (s), 2856 (m), 1725 (m), 1457 (w), 1179 (w), 755 (w), 570 (w).
- **HRMS (ESI):** calcd. for $C_{12}H_{16}O_2Na^+$ $[M+Na]^+$ 215.1048; found: 215.1256

1-Vinylcyclohexyl-bicyclo[1.1.0]butane-1-carboxylate (1e)



1e

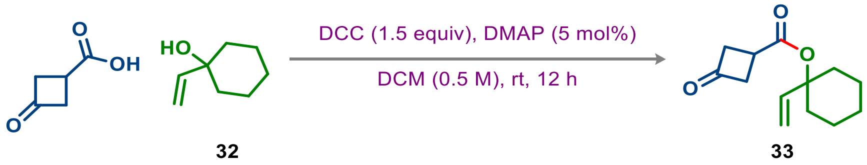
1-Vinylcyclohexan-1-ol (32)



32

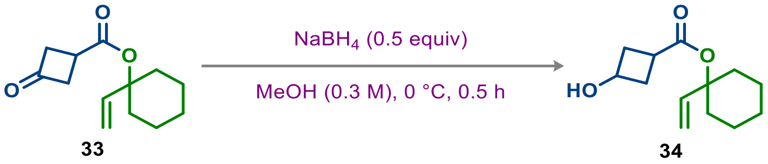
Following a slightly modified procedure,[2] to a solution of vinylmagnesium bromide (44 mL, 1.0 M in THF, 2.0 equiv) in THF (44 mL), cyclohexanone (2.16 g, 22.0 mmol, 1.00 equiv) was added drop-wise at 0 °C under nitrogen. After 12 h stirring at room temperature, the reaction mixture was quenched with aqueous NH_4Cl (250 mL) at 0 °C and extracted with Et_2O (3 × 170 mL). The combined organic layers were washed with brine (150 mL) and dried over Na_2SO_4. The solvent was removed under vacuum to yield **32** as a light-yellow oil (1.5 g, 54%), which was used in the next step without further purification.

1-Vinylcyclohexyl 3-oxocyclobutane-1-carboxylate (33)



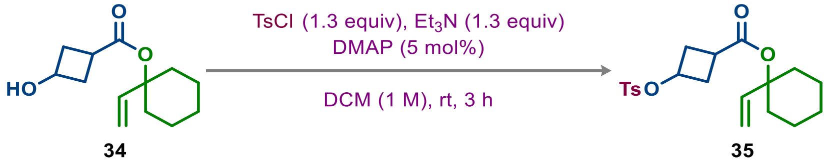
Following a slightly modified procedure,[3] to a solution of 3-oxocyclobutanecarboxylic acid (452 mg, 3.96 mmol, 1.00 equiv) in dry DCM (7.8 mL, 0.5 M,), alcohol **32** (500 mg, 3.96 mmol, 1.00 equiv), DMAP (26 mg, 0.20 mmol, 0.05 equiv) and DCC (1.23 g, 5.94 mmol, 1.50 equiv) were added under nitrogen. After 12 h stirring at room temperature, the reaction mixture was filtrated, and the precipitate (dicyclohexylurea) was rinsed with DCM (10 mL). The filtrate was concentrated in vacuum to yield **33** as a light-yellow oil (550 mg, 63%), which was used in the next step without further purification.

1-Vinylcyclohexyl 3-hydroxycyclobutane-1-carboxylate (34)



Following a slightly modified procedure,[1] to a stirred solution of ketone **33** (550 mg, 2.47 mmol, 1.00 equiv) in MeOH (8 mL, 0.3 M) at 0 °C (ice/water bath), NaBH$_4$ (47.0 mg, 1.24 mmol, 0.500 equiv) was added. After stirring for 30 minutes at 0 °C, the reaction mixture was quenched with a saturated aqueous NH$_4$Cl solution (25 mL). The reaction was extracted with DCM (3 × 20 mL) and the combined organic phases were washed with brine (25 mL) and dried over Na$_2$SO$_4$. The solvent was removed under vacuum to yield **34** as a light-yellow oil (540 mg, 97%), which was used without further purification in the tosylation reaction detailed below.

1-Vinylcyclohexyl 3-(tosyloxy)cyclobutane-1-carboxylate (35)

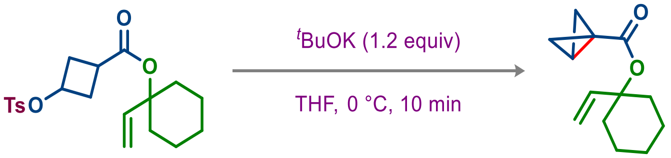


Following a slightly modified procedure,[1] to a stirred solution of alcohol **34** (539 mg, 2.40 mmol, 1.00 equiv) in DCM (2.4 mL, 1.0 M) under nitrogen at 0 °C (ice/water bath), 4-toluenesulfonyl chloride (594 mg, 3.12 mmol, 1.30 equiv), Et$_3$N (0.436 mL, 3.12 mmol, 1.30 equiv), and DMAP

(15 mg, 0.12 mmol, 0.05 equiv) were added. After stirring.at room temperature for 3 h, DCM (20 mL) was added to the reaction mixture followed by water (20 mL). The organic phase was washed with brine (20 mL), dried over Na_2SO_4. The solvent was removed under vacuum. The crude product was purified by flash chromatography (silica, 1:19 v/v EtOAc:Hexane) to afford the desired product **35** as a brown oil (300 mg, 34%). **(See Spectra)**

- **TLC (EtOAc:Hexane, 1:9 v/v):** $R_f = 0.4$, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.77 (d, *J* = 8.1 Hz, 2H, Ar*H*), 7.33 (d, *J* = 8.0 Hz, 2H, Ar*H*), 6.03 (dd, *J* = 17.6, 11.0 Hz, 1H, alkene C*H*), 5.30 – 4.96 (m, 2H, alkene C*H*$_2$), 4.71 (p, *J* = 7.6 Hz, 1H, OC*H*), 2.66 – 2.27 (m, 8H), 2.13 (dt, *J* = 14.5, 3.5 Hz, 2H, cyclohexyl C*H*$_2$), 1.57 – 1.39 (m, 7H), 1.28 – 1.13 (m, 1H).
- **^{13}C NMR (101 MHz, $CDCl_3$):** δ 171.7, 144.9, 141.5, 133.7, 129.8, 127.8, 113.9, 82.2, 69.6, 34.6, 34.0, 30.4, 25.2, 21.8, 21.6.
- **IR (Neat):** υ 2933 (m), 2859 (w), 1727 (s), 1364 (s), 1179 (s), 817 (m), 561 (m).
- **HRMS (ESI):** calcd. for $C_{20}H_{26}O_5SNa^+$ $[M+Na]^+$ 401.1399; found: 401.1395

1-Vinylcyclohexyl-bicyclo[1.1.0]butane-1-carboxylate (1e)



35 1e

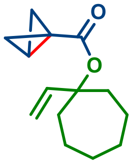
Following a slightly modified procedure,[1] to a stirred solution of tosylate **35** (210 mg, 0.555 mmol, 1.00 equiv) in THF (2.8 mL, 0.20 M) under nitrogen at 0 °C (ice/water bath), ^{t}BuOK (75.0 mg, 0.665 mmol, 1.20 equiv, 0.73 M in THF) was added and stirred for 10 minutes at 0 °C. The resulting mixture was quenched with a saturated aqueous NH_4Cl solution (25 mL). The reaction mixture was extracted with DCM (3 × 25 mL) and the combined organic phases were dried over Na_2SO_4. The solvent was removed under vacuum. The crude product was purified by flash chromatography (silica, 1:49 v/v EtOAc:Hexane) to afford the desired product **1d** as a brown oil (70 mg, 62%). **(See Spectra)**

- **TLC (EtOAc:Hexane, 1:19 v/v):** $R_f = 0.46$, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 6.11 (dd, *J* = 17.6, 11.0 Hz, 1H, alkene C*H*), 5.25 – 4.99 (m, 2H, alkene C*H*$_2$), 2.34 (d, *J* = 3.4 Hz, 2H, bicyclobutane C*H*$_2$), 2.23 – 2.14 (m, 2H,

cyclohexyl C*H*$_2$), 2.01 (d, *J* = 3.5 Hz, 1H, bicyclobutane C*H*), 1.64 – 1.44 (m, 7H), 1.31 – 1.23 (m, 1H), 1.12 (d, *J* = 2.8 Hz, 2H, bicyclobutane C*H*$_2$).

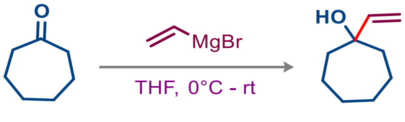
- **^{13}C NMR (101 MHz, CDCl$_3$):** δ 171.7, 142.2, 113.3, 81.6, 35.5, 34.9, 25.3, 21.9, 16.0, 9.9.
- **IR (Neat):** υ 2932 (m), 2859 (w), 1709 (s), 1392 (m), 1197 (s), 1132 (s), 884 (m), 757 (m).
- **HRMS (ESI):** calcd. for $C_{13}H_{18}O_2Na^+$ $[M+Na]^+$ 229.1204; found: 229.1210

1-Vinylcycloheptyl-bicyclo[1.1.0]butane-1-carboxylate (1f)



1f

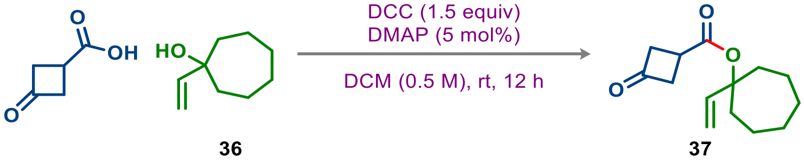
1-Vinylcycloheptan-1-ol (36)



36

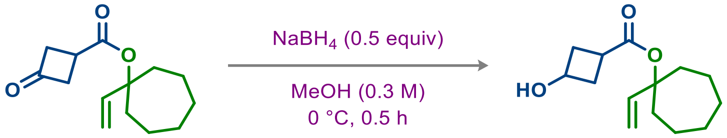
Following a slightly modified procedure,[2] to a solution of vinylmagnesium bromide (44 mL, 1.0 M in THF, 2.0 equiv) in THF (44 mL), cycloheptanone (2.47 g, 22.0 mmol, 1.00 equiv) was added drop-wise at 0 °C under nitrogen. After 12 h stirring at room temperature, the reaction mixture was quenched with aqueous NH_4Cl (250 mL) at 0 °C and extracted with Et_2O (3 × 170 mL). The combined organic layers were washed with brine (150 mL) and dried over Na_2SO_4. The solvent was removed under vacuum to yield **36** as a light-yellow oil (2.1 g, 68%), which was used in the next step without further purification.

1-Vinylcycloheptyl 3-oxocyclobutane-1-carboxylate (37)



Following a slightly modified procedure,[3] to a solution of 3-oxocyclobutanecarboxylic acid (1.71 g, 15.0 mmol, 1.00 equiv) in dry DCM (30 mL, 0.5 M,), alcohol **36** (2.1 g, 15 mmol, 1.0 equiv), DMAP (92 mg, 0.75 mmol, 0.05 equiv) and DCC (4.60 g, 22.5 mmol, 1.50 equiv) were added under nitrogen. After 12 h stirring at room temperature, the reaction mixture was filtrated, and the precipitate (dicyclohexylurea) was rinsed with DCM (30 mL). The filtrate was concentrated in vacuum to yield **37** as a light-yellow oil (2.2 g, 57%), which was used in the next step without further purification.

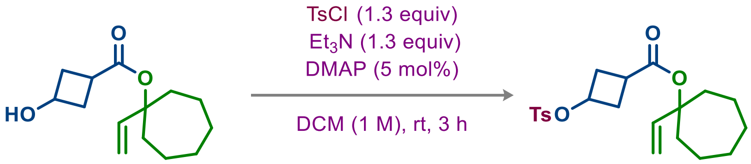
1-Vinylcycloheptyl 3-hydroxycyclobutane-1-carboxylate (38)



37 **38**

Following a slightly modified procedure,[1] to a stirred solution of ketone **37** (2.00 g, 8.46 mmol, 1.00 equiv) in MeOH (28 mL, 0.3 M) at 0 °C (ice/water bath), $NaBH_4$ (160 mg, 4.23 mmol, 0.500 equiv) was added. After 30 minutes stirring at room temperature, the reaction mixture was quenched with a saturated aqueous NH_4Cl solution (60 mL). The reaction was extracted using DCM (3 × 40 mL) and the combined organic phases were washed with brine (40 mL) and dried over Na_2SO_4. The solvent was removed under vacuum to yield **38** as a light-yellow oil (1.81 g, 90%), which was used without further purification in the tosylation reaction detailed below.

1-Vinylcycloheptyl 3-(tosyloxy)cyclobutane-1-carboxylate (39)



38 **39**

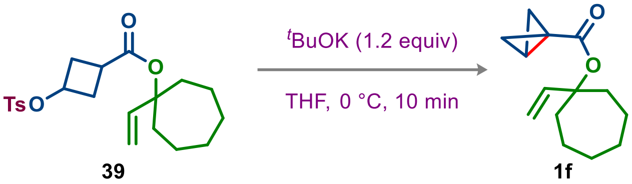
Following a slightly modified procedure,[1] to a stirred solution of alcohol **38** (1.40 g, 5.87 mmol, 1.00 equiv) in DCM (6.0 mL, 1.0 M) under nitrogen at 0 °C (ice/water bath), 4-toluenesulfonyl chloride (1.45 g, 7.63 mmol, 1.30 equiv), Et_3N (1.06 mL, 7.63 mmol, 1.30 equiv), and DMAP (36.0 mg, 0.293 mmol, 0.05 equiv) were added. After 3 h stirring.at room temperature, DCM (50 mL) was added to the reaction mixture followed by water (40 mL). The organic phase was washed with brine (40 mL), dried over Na_2SO_4. The solvent was removed under vacuum. The crude product was purified by flash chromatography (silica, 1:19 v/v EtOAc:Hexane) to afford the desired product **39** as a brown oil (680 mg, 30%). **(See Spectra)**

- **TLC (EtOAc:Hexane, 1:9 v/v):** R_f = 0.49, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.76 (d, *J* = 7.9 Hz, 2H, Ar*H*), 7.32 (d, *J* = 8.0 Hz, 2H, Ar*H*), 6.00 (dd, *J* = 17.6, 10.9 Hz, 1H, alkene C*H*), 5.10 – 5.00 (m, 2H, alkene CH_2), 4.70

(p, *J* = 7.4 Hz, 1H, OC*H*), 2.61 – 2.33 (m, 11H), 2.05 (dd, *J* = 14.9, 7.9 Hz, 2H, cycloheptyl C*H*$_2$), 1.88 (ddd, *J* = 14.6, 9.1, 2.6 Hz, 2H, cycloheptyl C*H*$_2$), 1.59 – 1.40 (m, 5H).

- **^{13}C NMR (101 MHz, CDCl$_3$):** δ 171.8, 144.8, 142.4, 133.7, 129.8, 127.7, 112.6, 86.4, 69.6, 38.1, 33.9, 30.3, 29.1, 22.2, 21.6.
- **IR (Neat):** υ 2930 (w), 2859 (w), 1729 (s), 1365 (s), 1177 (s), 812 (m), 754 (m).
- **HRMS (ESI):** calcd. for $C_{21}H_{28}O_5SNa^+$ [M+H]$^+$ 415.1555; found: 415.1557

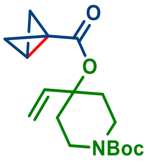
1-Vinylcycloheptyl-bicyclo[1.1.0]butane-1-carboxylate (1f)



Following a slightly modified procedure,[1] to a stirred solution of tosylate **39** (500 mg, 1.27 mmol, 1.00 equiv) in THF (7 mL, 0.2 M) under nitrogen at 0 °C (ice/water bath), ^{t}BuOK (171 mg, 1.53 mmol, 1.20 equiv, 0.73 M in THF) was added and stirred for 10 minutes 0 °C. The resulting mixture was quenched with a saturated aqueous NH_4Cl solution (25 mL) and extracted with DCM (3 × 25 mL) and the combined organic phases were dried over Na_2SO_4. The solvent was removed under vacuum. The crude product was purified by flash chromatography (silica, 1:49 v/v EtOAc:Hexane) to afford the desired product **1f** as a brown oil (150 mg, 54%). (See Spectra)

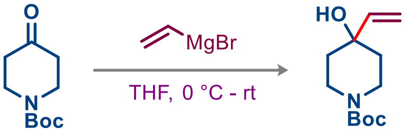
- **TLC (EtOAc:Hexane, 1:19 v/v):** R$_f$ = 0.53, KMnO$_4$.
- **^{1}H NMR (400 MHz, CDCl$_3$):** δ 6.09 (dd, *J* = 17.6, 11.0 Hz, 1H, alkene C*H*), 5.14 – 5.01 (m, 2H, alkene C*H*$_2$), 2.32 (d, *J* = 3.4 Hz, 2H, bicyclobutane C*H*$_2$), 2.13 (dd, *J* = 14.8, 7.7 Hz, 2H, cycloheptyl C*H*$_2$), 1.99 (p, *J* = 3.2 Hz, 1H, bicyclobutane C*H*), 1.87 (dd, *J* = 14.5, 9.0 Hz, 2H, cycloheptyl C*H*$_2$), 1.63 – 1.43 (m, 8H, cycloheptyl C*H*$_2$), 1.10 (d, *J* = 2.7 Hz, 2H, bicyclobutane C*H*$_2$).
- **^{13}C NMR (101 MHz, CDCl$_3$):** δ 171.8, 143.1, 112.1, 85.7, 38.3, 35.5, 29.0, 22.4, 15.9, 9.9.
- **IR (Neat):** υ 2927 (m), 2858 (w), 1709 (s), 1452 (w), 1395 (m), 1196 (s), 1143 (s), 756 (m).
- **HRMS (ESI):** calcd. for $C_{14}H_{20}O_2Na^+$ [M+Na]$^+$ 243.1361; found: 243.1363

Tert-butyl 4-((-bicyclo[1.1.0]butane-1-carbonyl)oxy)-4-vinylpiperidine-1-carboxylate (1g)



1g

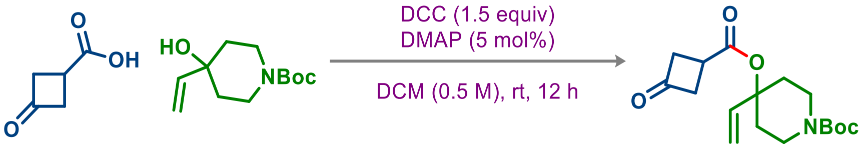
Tert-butyl 4-hydroxy-4-vinylpiperidine-1-carboxylate (40)



40

Following a slightly modified procedure,[2] to a solution of vinylmagnesium bromide (44 mL, 1.0 M in THF, 2.0 equiv) in THF (44 mL), *tert*-butyl 4-oxopiperidine-1-carboxylate (4.38 g, 22 mmol, 1.00 equiv) was added drop-wise at 0 °C under nitrogen. After 12 h stirring at room temperature, the reaction mixture was quenched with aqueous NH_4Cl (250 mL) at 0 °C and extracted with Et_2O (3 × 170 mL). The combined organic layers were washed with brine (150 mL) and dried over Na_2SO_4. The solvent was removed under vacuum to yield **40** as a light-yellow oil (3.5 g, 70%), which was used in the next step without further purification.

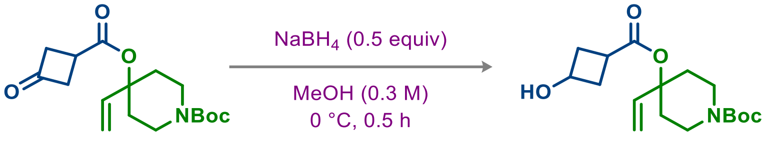
Tert-butyl 4-((3-oxocyclobutane-1-carbonyl)oxy)-4-vinylpiperidine-1-carboxylate (41)



40 **41**

Following a slightly modified procedure,[3] to a solution of 3-oxocyclobutanecarboxylic acid (418 mg, 3.67 mmol, 1.00 equiv) in dry DCM (7.4 mL, 0.5 M,), alcohol **40** (835 mg, 3.67 mmol, 1.00 equiv), DMAP (23 mg, 0.18 mmol, 0.05 equiv) and DCC (1.14 g, 5.50 mmol, 1.50 equiv) were added under nitrogen. After 12 h stirring at room temperature, the reaction mixture was filtrated, and the precipitate (dicyclohexylurea) was rinsed with DCM (10 mL). The filtrate was concentrated under vacuum to yield **41** as a light-yellow oil (798 mg, 67%), which was used in the next step without further purification.

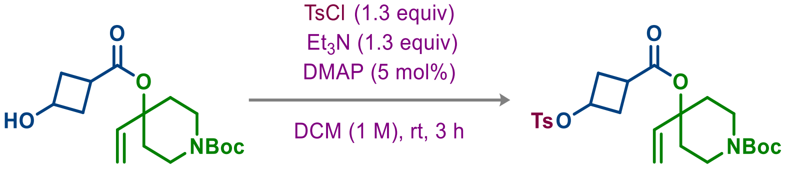
Tert-butyl 4-((3-hydroxycyclobutane-1-carbonyl)oxy)-4-vinylpiperidine-1-carboxylate (42)



41 **42**

Following a slightly modified procedure,[1] to a stirred solution of ketone **41** (798 mg, 2.47 mmol, 1.00 equiv) in MeOH (8 mL, 0.3 M) at 0 °C (ice/water bath), $NaBH_4$ (47.0 mg, 1.24 mmol, 0.500 equiv) was added. After 30 minutes stirring at 0 °C, the reaction mixture was quenched with a saturated aqueous NH_4Cl solution (25 mL) andextracted with DCM (3 × 25 mL) and the combined organic phases were washed with brine (25 mL) and dried over Na_2SO_4. The solvent was removed under vacuum to yield **38** as a light-yellow oil (775 mg, 96%), which was used without further purification in the tosylation reaction detailed below.

Tert-butyl 4-((3-(tosyloxy)cyclobutane-1-carbonyl)oxy)-4-vinylpiperidine-1-carboxylate (43)



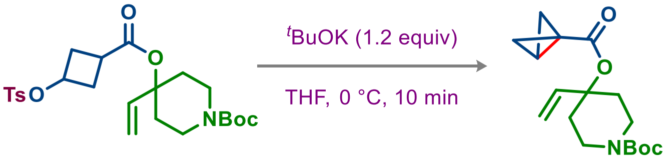
42 **43**

Following a slightly modified procedure,[1] to a stirred solution of alcohol **42** (755 mg, 2.32 mmol, 1.00 equiv) in DCM (2.3 mL, 1.0 M) under nitrogen at 0 °C (ice/water bath), 4-toluenesulfonyl chloride (575 mg, 3.02 mmol, 1.30 equiv), Et_3N (0.431 mL, 3.02 mmol, 1.30 equiv), and DMAP (15 mg, 0.12 mmol, 0.05 equiv) were added. After 3 h stirring.at room temperature, DCM (50 mL) was added to the reaction mixture followed by water (40 mL). The organic phases were washed with brine (40 mL), dried over Na_2SO_4. The solvent was removed under vacuum. The crude product was purified by flash chromatography (silica, 1:19 v/v EtOAc:Hexane) to afford the desired product **43** as a brown oil (1.02 g, 90%). **(See Spectra)**

- **TLC (EtOAc:Hexane, 2:8 v/v):** $R_f = 0.2$, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.76 (d, *J* = 8.0 Hz, 2H, Ar*H*), 7.33 (d, *J* = 8.0 Hz, 2H, Ar*H*), 6.03 (dd, *J* = 17.6, 11.0 Hz, 1H, alkene C*H*), 5.19 – 5.11 (m, 2H, alkene C*H*$_2$), 4.71 (p, *J* = 7.5 Hz, 1H, OC*H*), 3.79 (d, *J* = 13.4 Hz, 2H, piperidinyl C*H*$_2$), 3.08 – 2.90 (m, 2H, piperidinyl C*H*$_2$), 2.67 – 2.52 (m, 1H, C*H*COO), 2.52 – 2.27 (m, 7H), 2.20 – 2.10 (m, 2H, piperidinyl C*H*$_2$), 1.68 (ddd, *J* = 14.9, 11.4, 4.6 Hz, 2H, piperidinyl C*H*$_2$), 1.44 (s, 9H, ^{t}Bu*H*).

- **^{13}C NMR (101 MHz, CDCl$_3$):** δ 171.6, 154.5, 144.9, 139.8, 133.6, 129.8, 127.6, 115.0, 79.9, 79.6, 69.3, 39.4, 33.9, 33.8, 30.2, 28.3, 21.5.
- **IR (Neat):** υ 2926 (w), 2862 (w), 1731 (w), 1690 (s), 1365 (m), 1169 (s), 819 (m).
- **HRMS (ESI):** calcd. for $C_{24}H_{33}NO_7SNa^+$ $[M+Na]^+$ 502.1875; found: 502.1875

***Tert*-butyl 4-((-bicyclo[1.1.0]butane-1-carbonyl)oxy)-4-vinylpiperidine-1-carboxylate (1g)**

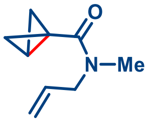


43 1g

Following a slightly modified procedure,[1] to a stirred solution of tosylate **43** (1.02 g, 2.09 mmol, 1.00 equiv) in THF (11 mL, 0.20 M) under nitrogen at 0 °C (ice/water bath), ^{t}BuOK (281 mg, 2.51 mmol, 0.73 M in THF) was added and stirred for 10 minutes at 0 °C. The resulting mixture was quenched with a saturated aqueous NH_4Cl solution (30 mL). The reaction mixture was extracted with DCM (3 × 30 mL) and the combined organic phases were dried over Na_2SO_4. The solvent was removed under vacuum. The crude product was purified by flash chromatography (silica, 1:49 v/v EtOAc:Hexane) to afford the desired product **1g** as a brown oil (500 mg, 78%). **(See Spectra)**

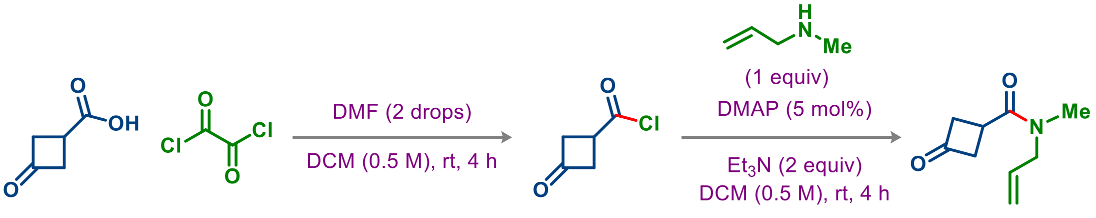
- **TLC (EtOAc:Hexane, 1:9 v/v):** R_f = 0.33, $KMnO_4$.
- **^{1}H NMR (400 MHz, CDCl$_3$):** δ 6.10 (dd, *J* = 17.6, 11.0 Hz, 1H, alkene C*H*), 5.31 – 5.06 (m, 2H, alkene C*H*$_2$), 3.97 – 3.76 (m, 2H, piperidinyl C*H*$_2$), 3.03 (t, *J* = 12.4 Hz, 2H, piperidinyl C*H*$_2$), 2.38 – 2.16 (m, 4H), 2.06 (p, *J* = 3.2 Hz, 1H, bicyclobutane C*H*), 1.72 – 1.64 (m, 2H, piperidinyl C*H*$_2$), 1.45 (s, 9H, ^{t}Bu*H*), 1.14 (d, *J* = 2.8 Hz, 2H, bicyclobutane C*H*$_2$).
- **^{13}C NMR (101 MHz, CDCl$_3$):** δ 171.6, 154.8, 140.6, 114.5, 79.6, 79.4, 35.6, 34.3, 28.4, 16.6, 9.8. One carbon was not resolved at 101 MHz.
- **IR (Neat):** υ 2927 (w), 2932 (w), 1697 (s), 1398 (m), 1191 (m), 1149 (s), 760 (w).
- **HRMS (ESI):** calcd. for $C_{17}H_{25}NO_4Na^+$ $[M+Na]^+$ 330.1681; found: 330.1681

***N*-Allyl-*N*-methylbicyclo[1.1.0]butane-1-carboxamide (1h)**



1h

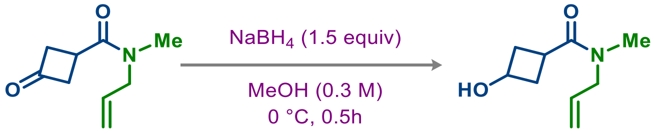
N-Allyl-*N*-methyl-3-oxocyclobutane-1-carboxamide (44)



44

Following a slightly modified procedure,[4] to a solution of 3-oxocyclobutanecarboxylic acid (1.00 g, 8.76 mmol, 1.00 equiv) in DCM (17.0 mL), oxalyl chloride (1.88 mL, 22.0 mmol, 2.50 equiv) and DMF (two drops) were added at 0 °C. After 4 h stirring at room temperature, the reaction mixture was concentrated under vacuum and used directly in the next step. To a mixture of the *N*-methy-allylamine (640 mg, 8.76 mmol, 1.00 equiv), DMAP (54.0 mg, 0.44 mmol, 0.05 equiv) and Et_3N (2.44 mL, 17.5 mmol, 2.00 equiv) in DCM (8 mL), acyl chloride in DCM (8 mL) was added at 0 °C. After 4 h stirring at room temperature, the reaction mixture was washed with 5% HCl (10 mL), brine (15 mL) and H_2O (15 mL). The organic layer was dried over Na_2SO_4, filtered. The solvent was removed under vacuum to yield **44** as a light-yellow oil (874 mg, 60%), which was used without further purification in the reaction detailed below.

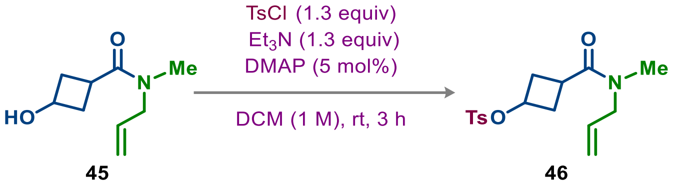
N-Allyl-3-hydroxy-*N*-methylcyclobutane-1-carboxamide (45)



44 **45**

Following a slightly modified procedure,[3] to a stirred solution of ketone **44** (874 mg, 5.23 mmol, 1.00 equiv) in MeOH (17.5 mL, 0.30 M) at 0 °C (ice/water bath), $NaBH_4$ (298 mg, 7.85 mmol, 1.50 equiv) was added and stirred at 0 °C. After 30 minutes, the reaction mixture was quenched with a saturated aqueous NH_4Cl solution (40 mL) and extracted with DCM (3 × 40 mL) and the combined organic phases were washed with brine (40 mL) and dried over Na_2SO_4. The solvent was removed under vacuum to yield **45** as a light-yellow oil (690 mg, 78%), which was used without further purification in the tosylation reaction detailed below.

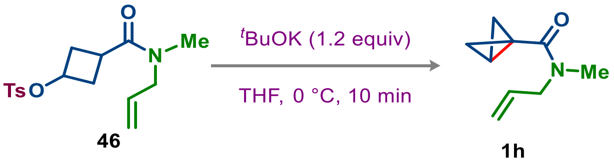
3-(Allyl(methyl)carbamoyl)cyclobutyl 4-methylbenzenesulfonate (46)



Following a slightly modified procedure,[3] to a stirred solution of alcohol **45** (690 mg, 4.08 mmol, 1.00 equiv) in DCM (4.1 mL, 1.0 M) under nitrogen at 0 °C (ice/water bath), 4-toluenesulfonyl chloride (1.01 g, 6.81 mmol, 1.30 equiv), Et_3N (0.74 mL, 5.3 mmol, 1.3 equiv), and DMAP (25 mg, 0.20 mmol, 0.05 equiv) were added. After 3 h stirring at room temperature, DCM (40 mL) was added to the reaction mixture followed by water (40 mL). The organic phase was washed with brine (50 mL), dried over Na_2SO_4. The solvent was removed under vaccum. The crude product was purified by flash chromatography (silica, 4:6 v/v EtOAc:Hexane) to afford the desired product **46** as a brown oil (963 mg, 73%). **(See Spectra)**

- **TLC (EtOAc:Hexane, 4:6 v/v):** R_f = 0.2, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** For both rotamers: δ 7.74 (d, *J* = 7.9 Hz, 2H), 7.31 (d, *J* = 7.9 Hz, 2H), 5.66 (ddt, *J* = 16.2, 10.3, 5.4 Hz, 1H), 5.18 – 4.98 (m, 2H), 4.75 (dp, *J* = 15.6, 7.7 Hz, 1H), 3.91 (d, *J* = 5.9 Hz, 1H), 3.75 (d, *J* = 4.8 Hz, 1H), 2.85 (s, 2H), 2.80 (s, 1H), 2.68 (dq, *J* = 17.4, 8.7 Hz, 1H), 2.42 (d, *J* = 8.6 Hz, 7H).
- **^{13}C NMR (101 MHz, $CDCl_3$):** For both rotamers: δ 172.1, 171.6, 144.8, 133.9, 132.6, 132.4, 129.7, 127.7, 117.3, 116.7, 69.8, 69.7, 51.5, 50.1, 34.0, 33.7, 28.7, 28.1, 21.5.even carbons were not resolved at 101 MHz.
- **IR (Neat):** υ 3464 (w), 2924 (w), 1638 (s), 1356 (s), 1174 (s), 915 (m), 844 (s), 561 (m).
- **HRMS (ESI):** calcd. for $C_{16}H_{21}NO_4SH^+$ $[M+H]^+$ 324.1270; found: 324.1273

N-Allyl-*N*-methylbicyclo[1.1.0]butane-1-carboxamide (1h)



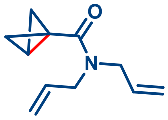
Following a slightly modified procedure,[3] to a stirred solution of tosylate **46** (940 mg, 2.91 mmol, 1.00 equiv) in THF (13 mL, 0.20 M) under nitrogen at 0 °C (ice/water bath), ^{t}BuOK (392 mg, 3.49 mmol, 1.20 equiv, 0.73 M in THF) was added and stirred for 10 minutes at 0 °C. The resulting mixture was quenched with a saturated aqueous NH_4Cl solution (20 mL) and extracted with DCM

(3 × 30 mL) and the combined organic phases were dried over Na_2SO_4. The solvent was removed under vacuum. The crude product was purified by flash chromatography (silica, 3:7 v/v EtOAc:Hexane) to afford the desired product **1h** as a brown oil (186 mg, 42%).

(See Spectra)

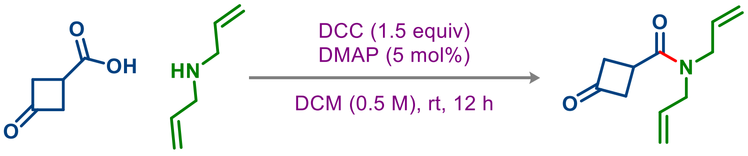
- **TLC (EtOAc:Hexane, 3:7 v/v):** $R_f = 0.12$, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** For both rotamers: δ 5.85 – 5.70 (m, 1H), 5.27 – 5.03 (m, 2H), 4.25 (d, *J* = 4.7 Hz, 1.1H), 3.99 (d, *J* = 5.9 Hz, 0.9H), 3.17 (s, 1.3H), 2.91 (s, 1.7H), 2.23 (d, *J* = 3.4 Hz, 2H), 1.91 (d, *J* = 7.4 Hz, 1H), 1.11 (d, *J* = 33.4 Hz, 2H).
- **^{13}C NMR (101 MHz, $CDCl_3$):** For both rotamers: δ 171.8, 133.7, 132.9, 117.4, 116.8, 53.0, 50.2, 37.1, 36.5, 35.9, 33.4, 13.8, 12.7, 8.0. wo carbons were not resolved at 101MHz.
- **IR (Neat):** υ 2955 (m), 2922 (s), 2856 (w), 1624 (w), 1460 (w), 1376 (w), 1268 (w), 755 (s).
- **HRMS (ESI):** calcd. for $C_9H_{13}NOH^+$ $[M+H]^+$ 152.1075; found: 152.1077

N,*N*-Diallylbicyclo[1.1.0]butane-1-carboxamide (1i)



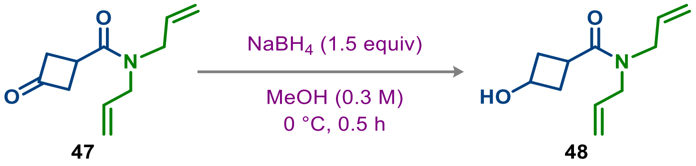
1i

N,*N*-Diallyl-3-oxocyclobutane-1-carboxamide (47)



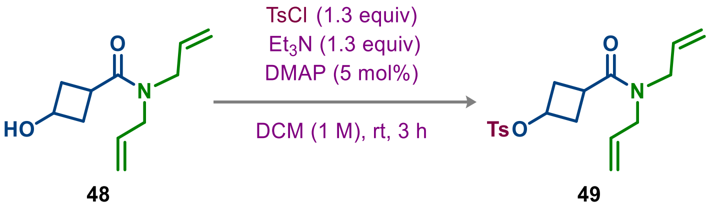
Following a slightly modified procedure,[3] to a solution of 3-oxocyclobutanecarboxylic acid (1.14 g, 10.0 mmol, 1.00 equiv) in dry DCM (20 mL, 0.50 M) under nitrogen, diallylamine (971 mg, 1.23 mL, 10.0 mmol, 1.00 equiv), DMAP (61 mg, 0.50 mmol, 0.05 equiv) and DCC (3.09 g, 15.0 mmol, 1.50 equiv) were added. After 12 h stirring at room temperature, the reaction mixture was filtrated, and the precipitate (dicyclohexylurea) was rinsed with DCM (10 mL). The filtrate was concentrated in vacuum to yield **47** as a light-yellow oil (1.21 g, 63%), which was used without further purification in the reduction reaction detailed below.

N,N-Diallyl-3-hydroxycyclobutane-1-carboxamide (48)



Following a slightly modified procedure,[3] to a stirred solution of ketone **47** (1.21 g, 6.26 mmol, 1.00 equiv) in MeOH (21 mL, 0.30 M) at 0 °C (ice/water bath), $NaBH_4$ (357 mg, 9.39 mmol, 1.50 equiv) was added and stirred. After 30 minutes, the reaction mixture was quenched with a saturated aqueous NH_4Cl solution (40 mL). The reaction was extracted with DCM (3 × 40 mL) and the combined organic phases were washed with brine (40 mL), dried over Na_2SO_4. The solvent was removed under vacuum to yield **48** as a light-yellow oil (1.12 g, 91%), which was used without further purification in the tosylation reaction detailed below.

3-(Diallylcarbamoyl)cyclobutyl 4-methylbenzenesulfonate (49)

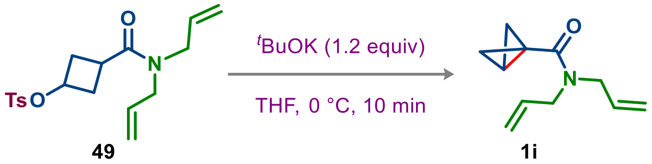


Following a slightly modified procedure,[3] to a stirred solution of alcohol **48** (1.12 g, 6.26 mmol, 1.00 equiv) in DCM (7.0 mL, 1.0 M) under nitrogen at 0 °C (ice/water bath), 4-toluenesulfonyl chloride (1.42 g, 7.46 mmol, 1.30 equiv), Et_3N (1.04 mL, 7.46 mmol, 1.30 equiv), and DMAP (35 mg, 0.29 mmol, 0.05 equiv) were added. After 3 h stirring at room temperature, DCM (35 mL) was added to the reaction mixture followed by water (50 mL). The organic phase was washed with brine (50 mL), dried over Na_2SO_4. The solvent was removed under vacuum. The crude product was purified by flash chromatography (silica, 1.5:8.5 v/v EtOAc:Hexane) to afford the desired product **49** as a brown oil (923 mg, 46%). **(See Spectra)**

- **TLC (EtOAc:Hexane, 2:8 v/v):** $R_f = 0.21$, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.75 (d, *J* = 8.0 Hz, 2H, Ar*H*), 7.31 (d, *J* = 8.0 Hz, 2H, Ar*H*), 5.74 – 5.58 (m, 2H, 2 x alkene C*H*), 5.09 (ddd, *J* = 29.5, 15.8, 6.8 Hz, 4H, 2 x alkene CH_2), 4.74 (p, *J* = 7.7 Hz, 1H, OC*H*), 3.91 (d, *J* = 5.9 Hz, 2H, NCH_2), 3.73 (d, *J* = 4.8 Hz, 2H, NCH_2), 2.78 – 2.61 (m, 1H), 2.48 – 2.31 (m, 7H).

- **^{13}C NMR (101 MHz, CDCl$_3$):** δ 171.9, 144.8, 133.9, 132.8, 132.7, 129.8, 127.7, 117.3, 116.7, 69.8, 48.6, 48.0, 34.0, 28.3, 21.6.
- **IR (Neat):** υ 3078 (w), 2927 (w), 2859 (w), 1638 (s), 1413 (m), 1356 (s), 1174 (s), 844 (m).
- **HRMS (ESI):** calcd. for $C_{18}H_{23}NO_4SNa^+$ $[M+Na]^+$ 372.1245; found: 372.1242

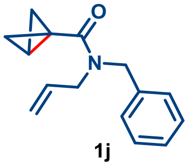
N,N-Diallylbicyclo[1.1.0]butane-1-carboxamide (1i)



Following a slightly modified procedure,[3] to a stirred solution of tosylate **49** (900 mg, 2.64 mmol, 1.00 equiv.) in THF (13.5 mL, 0.20 M) under nitrogen at 0 °C (ice/water bath), ^{t}BuOK (355 mg, 3.17 mmol, 1.20 equiv, 0.73 M in THF) was added and stirred for 10 minutes. The resulting mixture was quenched with a saturated aqueous NH_4Cl solution (50 mL) and extracted with DCM (3 × 50 mL) and the combined organic phases were dried over Na_2SO_4. The solvent was removed under vacuum. The crude product was purified by flash chromatography (silica, 1:19 v/v EtOAc:Hexane) to afford the desired product **1i** as a brown oil (324 mg, 69%). **(See Spectra)**

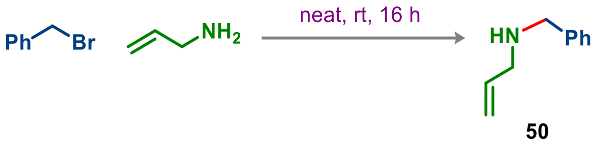
- **TLC (EtOAc:Hexane, 2:8 v/v):** R_f = 0.30, $KMnO_4$.
- **^{1}H NMR (400 MHz, CDCl$_3$): δ** 5.78 (ddt, *J* = 16.2, 10.5, 5.5 Hz, 2H, 2 x alkene C*H*), 5.26 – 5.06 (m, 4H, 2 x alkene C*H*$_2$), 4.23 (d, *J* = 5.0 Hz, 2H, NC*H*$_2$), 3.96 (d, *J* = 6.1 Hz, 2H, NC*H*$_2$), 2.26 (d, *J* = 3.4 Hz, 2H, bicyclobutane C*H*$_2$), 1.99 – 1.91 (m, 1H, bicyclobutane C*H*), 1.08 (d, *J* = 2.4 Hz, 2H, bicyclobutane C*H*$_2$).
- **^{13}C NMR (101 MHz CDCl$_3$):** δ 171.5, 133.9, 133.0, 117.4, 116.9, 49.7, 47.7, 36.6, 13.0, 8.1.
- **IR (Neat):** υ 3080 (w), 2927 (w), 1623 (s), 1460 (m), 1415 (m), 1218 (m), 753 (m).
- **HRMS (ESI):** calcd. for $C_{11}H_{15}NOH^+$ $[M+H]^+$ 178.1232; found: 178.1233

N,N-Diallylbicyclo[1.1.0]butane-1-carboxamide (1j)



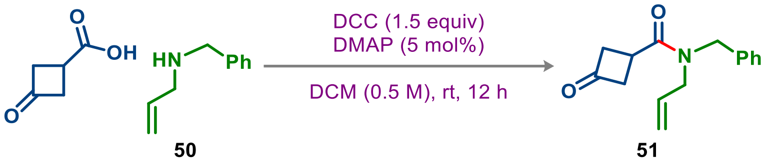
1j

N-Benzylprop-2-en-1-amine (50)



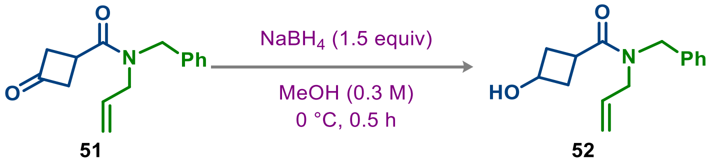
Following a slightly modified procedure,[5] benzyl bromide (1.19 mL, 10.0 mmol, 1.00 equiv) was added slowly to allylamine (4.49 mL, 60.0 mmol, 6.00 equiv) neat at room temperature and stirred for 16 h. The reaction was quenched with 1 M NaOH (20 mL) and extracted with Et_2O (3 x 30 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under vacuum. The crude product was passed through silica gel with EtOAc to afford **50** as a pale-yellow liquid (1.08 g, 70%), which was used in the next step without further purification.

N-Allyl-*N*-benzyl-3-oxocyclobutane-1-carboxamide (51)



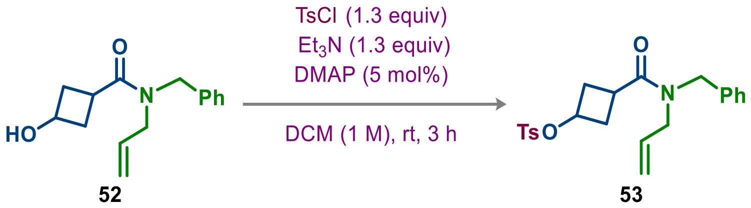
Following a slightly modified procedure,[3] to a stirred solution 3-oxocyclobutanecarboxylic acid (542 mg, 4.75 mmol, 1.00 equiv) in DCM (9 mL, 0.5 M) under nitrogen, amine **50** (700 mg, 4.75 mmol, 1.00 equiv), DMAP (30 mg, 0.24 mmol, 0.05 equiv) and DCC (1.47 g, 7.13 mmol, 1.50 equiv) were added. After 12 h stirring at room temperature, the reaction mixture was filtrated, and the precipitate (dicyclohexylurea) was rinsed with DCM (20 mL). The filtrate was concentrated in vacuum to yield **51** as a light-yellow oil (830 mg, 71%), which was used without further purification in the reduction reaction detailed below.

N-Allyl-*N*-benzyl-3-hydroxycyclobutane-1-carboxamide (52)



Following a slightly modified procedure,[3] to a stirred solution of ketone **51** (830 mg, 3.41 mmol, 1.00 equiv) in MeOH (11.5 mL, 0.300 M) at 0 °C (ice/water bath), $NaBH_4$ (194 mg, 5.12 mmol, 1.50 equiv) was added. After 30 minutes stirring at 0 °C, the reaction mixture was quenched with a saturated aqueous NH_4Cl solution (40 mL). The reaction was extracted with DCM (3 × 40 mL) and the combined organic phases were washed with brine (40 mL), dried over Na_2SO_4. The solvent was removed under vacuum to yield **52** as a light-yellow oil (790 mg, 94%), which was used without further purification in the tosylation reaction detailed below.

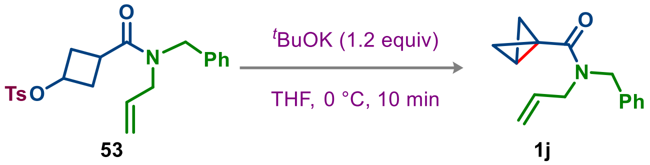
3-(Allyl(benzyl)carbamoyl)cyclobutyl 4-methylbenzenesulfonate (53)



Following a slightly modified procedure,[3] to a stirred solution of alcohol **52** (790 mg, 3.22 mmol, 1.00 equiv) in DCM (3.5 mL, 1.0 M) under nitrogen at 0 °C (ice/water bath), 4-toluenesulfonyl chloride (798 mg, 4.19 mmol, 1.30 equiv), Et_3N (0.59 mL, 4.2 mmol, 1.3 equiv), and DMAP (20 mg, 0.16 mmol, 0.10 equiv) were added. After 3 h stirring at room temperature, DCM (40 mL) was added to the reaction mixture followed by water (40 mL). The organic phase was washed with brine (50 mL), dried over Na_2SO_4. The solvent was removed under vacuum. The crude product was purified by flash chromatography silica, 2:8 v/v EtOAc:Hexane to afford the desired product **53** as a brown oil (796 mg, 67%). **(See Spectra)**

- **TLC (EtOAc:Hexane, 4:6 v/v):** R_f = 0.51, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** For both rotamers: δ 7.74 (dd, *J* = 14.6, 7.9 Hz, 2H), 7.34 – 7.21 (m, 5H), 7.19 – 7.15 (m, 1H), 7.06 (d, *J* = 7.4 Hz, 1H), 5.83 – 5.53 (m, 1H), 5.09 (ddd, *J* = 37.7, 17.2, 10.4 Hz, 2H), 4.75 (p, *J* = 7.6 Hz, 0.61H), 4.66 (q, *J* = 7.7 Hz, 0.4H), 4.52 (s, 1.14H), 4.38 (s, 0.8H), 3.94 (d, *J* = 6.0 Hz, 0.8H), 3.69 (d, *J* = 4.8 Hz, 1.04H), 2.83 – 2.66 (m, 1H), 2.58 – 2.34 (m, 6H), 2.33 – 2.21 (m, 1H).
- **^{13}C NMR (101 MHz, $CDCl_3$):** For both rotamers: δ 172.1, 144.7, 144.6, 137.0, 133.5, 133.5, 132.3, 129.6, 129.6, 128.6, 128.3, 127.8, 127.5, 127.5, 127.3, 127.1, 125.9, 117.4, 116.7, 69.7, 49.4, 48.3, 48.1, 48.0, 33.9, 28.1, 21.4. even carbons were not resolved at 101 MHz.
- **IR (Neat):** υ 2926 (w), 2857 (w), 1639 (s), 1356 (s), 1173 (s), 844 (s), 661 (s), 555 (s).
- **HRMS (ESI):** calcd. for $C_{22}H_{25}NO_4SH^+$ $[M+H]^+$ 400.1583; found: 400.1582

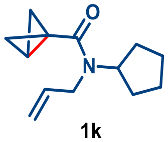
N-Allyl-*N*-benzylbicyclo[1.1.0]butane-1-carboxamide (1j)



Following a slightly modified procedure,[3] to a stirred solution of tosylate **53** (760 mg, 1.90 mmol, 1.00 equiv) in THF (9.5 mL, 0.20 M) under nitrogen at 0 °C (ice/water bath), ${}^tBuOK$ (256 mg, 2.28 mmol, 1.20 equiv, 0.73 M in THF) was added and stirred for 10 minutes. The resulting mixture was quenched with a saturated aqueous NH_4Cl solution (30 mL) and extracted with DCM (3 × 30 mL) and the combined organic phases were dried over Na_2SO_4. The solvent was removed under vacuum. The crude product was purified by flash chromatography (silica, 1.5:8.5 v/v EtOAc:Hexane) to afford the desired product **1j** as a brown oil (240 mg, 55%). **(See Spectra)**

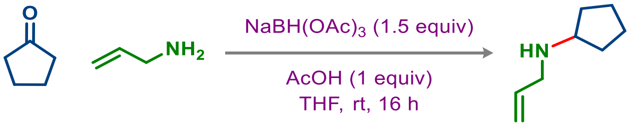
- **TLC (EtOAc:Hexane, 2:8 v/v):** R_f = 0.50, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** For both rotamers: δ 7.50 – 7.12 (m, 5H), 5.81 (ddt, *J* = 16.4, 10.4, 5.5 Hz, 1H), 5.18 (td, *J* = 28.8, 24.1, 13.6 Hz, 2H), 4.91 (s, 0.86H), 4.63 (s, 1.2H), 4.26 – 4.15 (m, 1.1H), 3.98 (d, *J* = 6.1 Hz, 0.84H), 2.29 (d, *J* = 38.3 Hz, 2H), 2.05 (s, 0.7H), 1.95 – 1.84 (m, 0.3H), 1.12 (d, *J* = 12.9 Hz, 2H).
- **^{13}C NMR (101 MHz, $CDCl_3$):** For both rotamers: δ 171.8, 137.3, 133.7, 132.7, 128.7, 128.5, 128.3, 127.3, 126.5, 117.7, 117.1, 50.7, 49.5, 47.7, 36.7, 33.4, 25.4, 24.8, 14.6, 13.2, 8.1.Three carbon were not resolved at 101 MHz.
- **IR (Neat):** υ 3030 (w), 2927 (m), 2860 (w), 1620 (s), 1456 (m), 1419 (s), 1211 (m), 701 (s).
- **HRMS (ESI):** calcd. for $C_{15}H_{17}NOH^+$ $[M+H]^+$ 228.1388; found: 228.1390

N-Allyl-*N*-cyclopentylbicyclo[1.1.0]butane-1-carboxamide (1k)



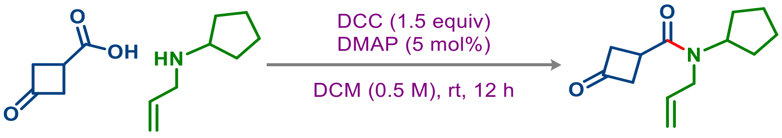
1k

N-Allylcyclopentanamine (54)



Following a slightly modified procedure,[6] to a solution of cyclopentanone (1.33 mL, 15.0 mmol, 1.00 equiv) in dry THF (37.5 mL), allyl amine (1.23 mL, 16.5 mmol, 1.10 equiv), sodium triacetoxyborohydride (4.8 g, 3.0 mmol, 1.5 equiv) and glacial acetic acid (0.855 mL, 15.0 mmol, 1.00 equiv) were added under nitrogen at room temperature. After stirring 16 h, the reaction mixture was quenched by 1 M aqueous HCl (80 mL) and extracted with EtOAc (2 x 80 mL). The aqueous phase was then basified to pH 12 by the addition of 5 M NaOH and extracted with EtOAc (2 x 50 mL). The combined organic phases were dried over anhydrous $MgSO_4$, and the solvent was removed under vacuum to afford the amine **54** as a light-yellow liquid (1.21 g, 64%), which was used in the next step without further purification.

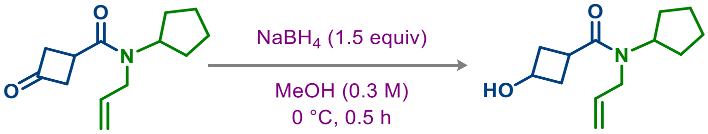
N-Allyl-*N*-cyclopentyl-3-oxocyclobutane-1-carboxamide (55)



54 **55**

Following a slightly modified procedure,[3] to a solution of 3-oxocyclobutanecarboxylic acid (1.0 g, 8.8 mmol, 1.0 equiv) in dry DCM (17 mL, 0.50 M), amine **54** (1.1 mL, 8.8 mmol, 1.0 equiv), DMAP (54 mg, 0.44 mmol, 0.05 equiv) and DCC (2.70 g, 13.2 mmol, 1.50 equiv) were added. After 12 h stirring at room temperature, the reaction mixture was filtrated, and the precipitate (dicyclohexylurea) was rinsed with DCM (20 mL). The filtrate was concentrated under vacuum to yield **55** as a light-yellow oil (905 mg, 46%), which was used without further purification in the reduction reaction detailed below.

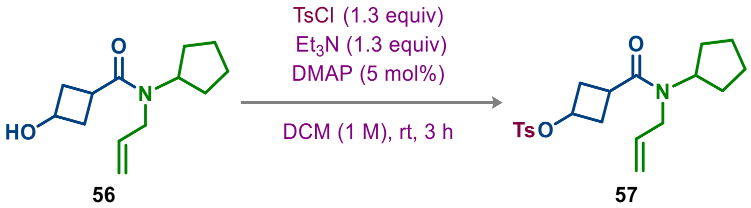
N-Allyl-*N*-cyclopentyl-3-hydroxycyclobutane-1-carboxamide (56)



55 **56**

Following a slightly modified procedure,[3] to a stirred solution of ketone **55** (600 mg, 2.71 mmol, 1.00 equiv) in MeOH (9 mL, 0.3 M) at 0 °C (ice/water bath), $NaBH_4$ (155 mg, 4.07 mmol, 1.50 equiv) was added. After 30 minutes stirring at 0 °C, the reaction mixture was quenched with a saturated aqueous NH_4Cl solution (25 mL) and extracted with DCM (3 × 25 mL) and the combined organic phases were washed with brine (25 mL) and dried over Na_2SO_4. The solvent was removed under vacuum to yield **56** as a light-yellow oil (535 mg, 88%), which was used without further purification in the tosylation reaction detailed below.

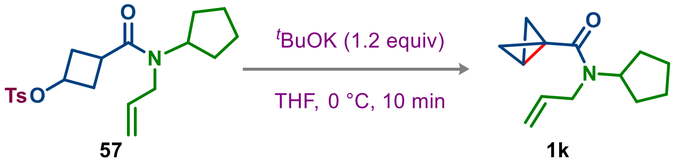
3-(Allyl(cyclopentyl)carbamoyl)cyclobutyl 4-methylbenzenesulfonate (57)



Following a slightly modified procedure,[3] to a stirred solution of alcohol **56** (548 mg, 2.71 mmol, 1.00 equiv) in DCM (3.0 mL, 1.0 M) under nitrogen at 0 °C (ice/water bath), 4-toluenesulfonyl chloride (672 mg, 3.52 mmol, 1.30 equiv), Et_3N (0.49 mL, 3.5 mmol, 1.3 equiv), and DMAP (17 mg, 0.14 mmol, 0.10 equiv) were added. After 3 h stirring at room temperature, DCM (25 mL) was added to the reaction mixture followed by water (25 mL). The organic phases were washed with brine (25 mL), dried over Na_2SO_4. The solvent was removed under vacuum. The crude product was purified by flash chromatography (silica, 1.5:8.5 v/v EtOAc:Hexane) to afford the desired product **57** as a brown oil (585 mg, 57%). **(See Spectra)**

- **TLC (EtOAc:Hexane, 2:8 v/v):** R_f = 0.23, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** For both rotamers: δ 7.77 (d, *J* = 7.9 Hz, 2H), 7.32 (dd, *J* = 8.4, 2.4 Hz, 2H), 5.86 – 5.70 (m, 1H), 5.18 – 5.01 (m, 2H), 4.83 – 4.59 (m, 1.5H), 3.95 (t, *J* = 8.4 Hz, 0.5H), 3.84 – 3.78 (m, 1H), 3.70 (dt, *J* = 4.2, 2.1 Hz, 1H), 2.79 (p, *J* = 8.7 Hz, 0.5H), 2.64 (p, *J* = 9.4, 7.5 Hz, 0.5H), 2.54 – 2.39 (m, 6H), 2.37 – 2.26 (m, 1H), 1.82 – 1.62 (m, 4H), 1.56 – 1.34 (m, 4H).
- **^{13}C NMR (101 MHz, $CDCl_3$):** For both rotamers: δ 172.7, 171.5, 144.8, 144.7, 135.0, 134.9, 134.0, 133.9, 129.8, 129.8, 127.7, 116.0, 115.4, 70.0, 69.9, 58.3, 56.2, 45.7, 44.3, 34.2, 34.1, 30.0, 29.1, 29.0, 28.8, 23.8, 21.6. Three carbon were not resolved at 101 MHz.
- **IR (Neat):** υ 2945 (m), 2865 (w), 1637 (s), 1446 (w), 1362 (m), 1178 (s), 852 (m).
- **HRMS (ESI):** calcd. for $C_{20}H_{27}NO_4SH^+$ $[M+H]^+$ 378.1739; found: 378.1742

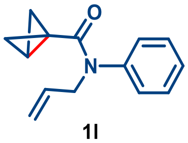
N-Allyl-*N*-cyclopentylbicyclo[1.1.0]butane-1-carboxamide (1k)



Following a slightly modified procedure,[3] to a stirred solution of tosylate **57** (550 mg, 1.46 mmol, 1.00 equiv) in THF (7.5 mL, 0.20 M) under nitrogen at 0 °C (ice/water bath), ^{t}BuOK (196 mg, 1.75 mmol, 1.20 equiv, 0.73 M in THF) was added and stirred for 10 minutes. The resulting mixture was quenched with a saturated aqueous NH_4Cl solution (25 mL) andextracted with DCM (3 × 25 mL) and the combined organic phases were dried over Na_2SO_4. The solvent was removed under vacuum. The crude product was purified by flash chromatography (silica, 1:9 v/v EtOAc:Hexane) to afford the desired product **1k** as a brown oil (165 mg, 55%). **(See Spectra)**

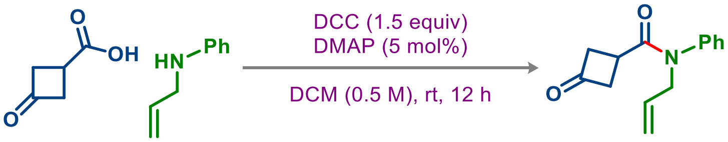
- **TLC (EtOAc:Hexane, 2:8 v/v):** $R_f = 0.37$, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 5.86 (ddt, *J* = 15.8, 10.2, 5.0 Hz, 1H), 5.26 – 5.01 (m, 2H), 4.76 (d, *J* = 21.3 Hz, 1H), 4.02 (s, 2H), 2.21 (d, *J* = 3.4 Hz, 2H), 1.92 – 1.52 (m, 9H), 1.05 (s, 2H).
- **^{13}C NMR (101 MHz, $CDCl_3$):** δ 171.2, 136.0, 115.5, 58.5, 36.5, 24.0, 12.1, 8.7. Two carbons were not resolved at 101 MHz.
- **IR (Neat):** υ 2949 (m), 2868 (w), 1678 (w), 1617 (s), 1417 (s), 1200 (m), 1160 (w), 746 (m).
- **HRMS (ESI):** calcd. for $C_{13}H_{19}NOH^+$ $[M+H]^+$ 206.1545; found: 206.1547

N-Allyl-*N*-phenylbicyclo[1.1.0]butane-1-carboxamide (1l)



1l

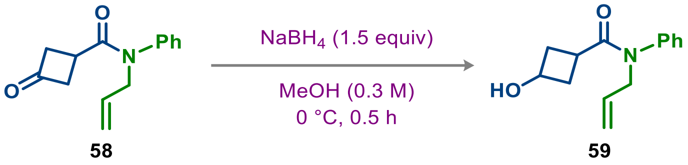
N-Allyl-3-oxo-*N*-phenylcyclobutane-1-carboxamide (58)



58

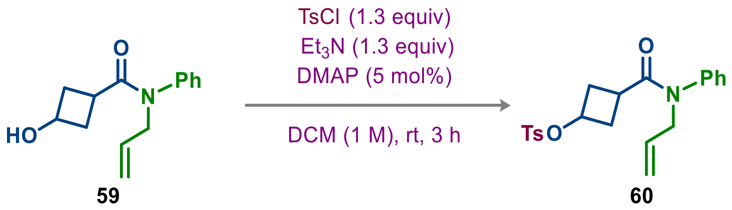
Following a slightly modified procedure,[3] to a stirred solution of 3-oxocyclobutane-1-carboxylic acid (2.00 g, 17.5 mmol, 1.00 equiv) in DCM (35 mL, 0.50 M) under nitrogen, *N*-phenyl-allylamine (2.38 mL, 17.5 mmol, 1.00 equiv), DCC (5.43 g, 26.3 mmol, 1.50 equiv), and DMAP (107 mg, 0.880 mmol, 0.05 equiv) were added. After 12 h stirring at room temperature, the reaction mixture was filtrated, and the precipitate (dicyclohexylurea) was rinsed with DCM (20 mL). The filtrate was concentrated in vacuum to yield **58** as a light-yellow oil (2.77 g, 69%), which was used without further purification in the reduction reaction detailed below.

N-Allyl-3-hydroxy-*N*-phenylcyclobutane-1-carboxamide (59)



Following a slightly modified procedure,[3] to a stirred solution of ketone **58** (2.77 g, 12.1 mmol, 1.00 equiv) in MeOH (42 mL, 0.30 M) at 0 °C (ice/water bath), $NaBH_4$ (687 mg, 18.1 mmol, 1.50 equiv) was added and stirred. After 30 minutes stirring at 0 °C, the reaction mixture was quenched with a saturated aqueous NH_4Cl solution (70 mL), and extracted with DCM (3 × 80 mL) and the combined organic phases were washed with brine (25 mL) and dried over Na_2SO_4. The solvent was removed under vacuum to yield **59** as a light-yellow oil (2.23 g, 80%), which was used without further purification in the tosylation reaction detailed below.

3-(Allyl(phenyl)carbamoyl)cyclobutyl 4-methylbenzenesulfonate (60)



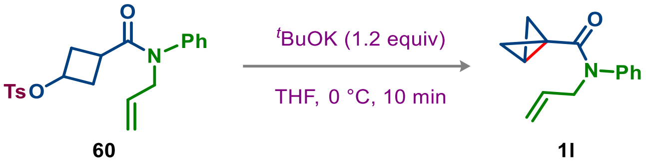
Following a slightly modified procedure,[3] to a stirred solution of alcohol **59** (1.41 g, 6.11 mmol, 1.00 equiv) in DCM (6.2 mL, 1.0 M) under nitrogen at 0 °C (ice/water bath), 4-toluenesulfonyl chloride (1.21 g, 7.94 mmol, 1.30 equiv), Et_3N (1.11 mL, 7.94 mmol, 1.30 equiv), and DMAP (37 mg, 0.31 mmol, 0.10 equiv) were added. After 3 h stirring at room temperature, DCM (60 mL) was added to the reaction mixture followed by water (60 mL). The organic phase was washed with brine (60 mL), dried over Na_2SO_4. The solvent was removed under vacuum. The crude product was purified by flash chromatography silica, 2:8 v/v EtOAc:Hexane to afford the desired product **60** as a brown oil (1.48 mg, 63%). **(See Spectra)**

- **TLC (EtOAc:Hexane, 4:6 v/v):** $R_f = 0.53$, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.72 (d, *J* = 7.9 Hz, 2H, Ar*H*), 7.41 – 7.26 (m, 5H, Ar*H*), 7.08 – 6.99 (m, 2H, Ar*H*), 5.80 (ddt, *J* = 16.7, 9.9, 6.3 Hz, 1H, alkene C*H*), 5.06 (dd, *J* =

23.8, 13.6 Hz, 2H, alkene C*H*$_2$), 4.50 (p, 1H, OC*H*), 4.23 (d, *J* = 6.4 Hz, 2H, NC*H*$_2$), 2.42 (d, *J* = 6.9 Hz, 6H), 2.04 (dp, *J* = 11.5, 3.9, 3.3 Hz, 2H).

- **^{13}C NMR (101 MHz, CDCl$_3$):** δ 171.7, 144.7, 141.6, 133.9, 132.7, 129.7, 129.6, 128.2, 127.7, 118.1, 69.8, 52.5, 34.4, 29.5, 21.6. One Carbon was not resolved at 101 MHz.
- **IR (Neat):** υ 3328 (w), 2923 (s), 2853 (m), 1627 (w), 1576 (w), 1458 (w), 1243 (w), 649 (w).
- **HRMS (ESI):** calcd. for $C_{21}H_{23}NO_4SH^+$ $[M+H]^+$ 386.1426; found: 386.1423

N-Allyl-*N*-phenylbicyclo[1.1.0]butane-1-carboxamide (1l)

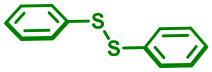


Following a slightly modified procedure,[3] to a stirred solution of tosylate **60** (1.3 g, 3.4 mmol, 1.0 equiv) in THF (17 mL, 0.20 M) under nitrogen at 0 °C (ice/water bath), ^{t}BuOK (454 mg, 4.05 mmol, 1.20 equiv, 0.73 M in THF) was added and stirred for 10 minutes. The resulting mixture was quenched with a saturated aqueous NH_4Cl solution (50 mL) and extracted with DCM (3 × 40 mL) and the combined organic phases were dried over Na_2SO_4. The solvent was removed under vacuum. The crude product was purified by flash chromatography (silica, 1.5:8.5 v/v EtOAc:Hexane) to afford the desired product **1l** as a brown oil (430 mg, 60%). **(See Spectra)**

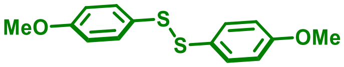
- **TLC (EtOAc:Hexane, 2:8 v/v):** R_f = 0.35, $KMnO_4$.
- **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.35 (t, *J* = 7.7 Hz, 2H, Ar*H*), 7.25 (q, *J* = 4.3, 3.9 Hz, 3H, Ar*H*), 5.88 (ddt, *J* = 16.6, 10.4, 6.0 Hz, 1H, alkene C*H*), 5.18 – 5.02 (m, 2H, alkene C*H*$_2$), 4.38 (d, *J* = 6.0 Hz, 2H, NC*H*$_2$), 2.05 (p, *J* = 2.8 Hz, 1H, bicyclobutane C*H*), 1.81 (d, *J* = 3.3 Hz, 2H, bicyclobutane C*H*$_2$), 0.77 (d, *J* = 2.4 Hz, 2H, bicyclobutane C*H*$_2$).
- **^{13}C NMR (101 MHz, CDCl$_3$** δ 171.4, 143.8, 133.3, 129.0, 127.6, 126.6, 117.3, 52.8, 37.1, 17.1, 10.1.
- **IR (Neat):** υ 3055 (w), 2930 (w), 2859 (w), 1629 (s), 1590 (m), 1398 (s), 1221 (s), 748 (s).
- **HRMS (ESI):** calcd. for $C_{14}H_{15}NONa^+$ $[M+Na]^+$ 236.1051; found: 236.1052

2.2 Synthesis of diradical Precursors:

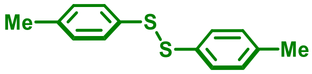
2.2.1 Synthesis of homodiradical precursors:



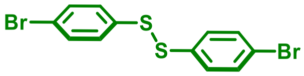
2a



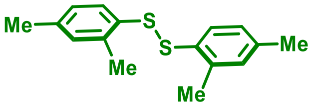
2b



2c

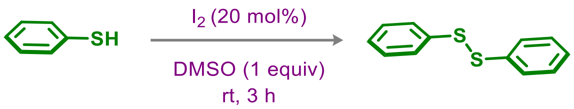


2d



2e

1,2-Diphenyldisulfane (2a)



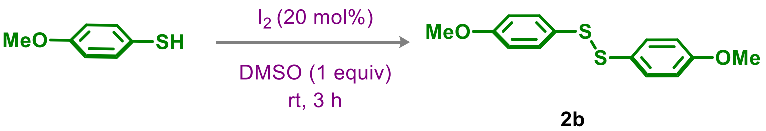
2a

Following a slightly modified procedure,[7] to a solution of iodine (510 mg, 2.00 mmol, 0.200 equiv) in DMSO (0.37 mL, 10 mmol, 1.0 equiv), thiophenol (1.02 mL, 1.10 g, 10.0 mmol, 1.00 equiv) was added. After stirring for 3 h at room temperature, the reaction mixture was quenched by $Na_2S_2O_3$ (50 mL) and extracted with EtOAc (3 x 60 mL) .The combined organic phases were dried over $MgSO_4$. The solvent was removed under vaccum. The crude product was purified by flash column chromatography using hexane as mobile phase to afford the pure product **2a** as a white solid (989 mg, 90%).

- **TLC (EtOAc:Hexane, 1:99 v/v):** $R_f = 0.7$, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.54 – 7.48 (m, 4H, Ar*H*), 7.35 – 7.28 (m, 4H, Ar*H*), 7.26 – 7.19 (m, 2H, Ar*H*).
- **^{13}C NMR (101 MHz, $CDCl_3$** δ 137.0, 129.1, 127.5, 127.1.

  The characterization data matched the reported values.[7]

1,2-Bis(4-methoxyphenyl)disulfane



2b

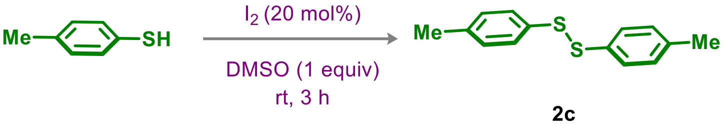
Following a slightly modified procedure,[7] to a solution of iodine (1.02 g, 4.00 mmol, 0.200 equiv) in DMSO (0.74 mL, 20 mmol, 1.0 equiv), 4-methoxybenzenethiol (2.8 g, 20 mmol, 1.0 equiv) was added. After stirring for 3 h at room temperature, the reaction mixture was quenched by $Na_2S_2O_3$

(100 mL) and extracted with EtOAc (3 x 70 mL) .The combined organic phases were dried over $MgSO_4$. The solvent was removed under vaccum. The crude product was purified by flash column chromatography using hexane as mobile phase to afford the pure product **2b** as a white solid (1.68 g, 61%).

- **TLC (EtOAc:Hexane, 1:19 v/v):** R_f = 0.65, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.40 (d, *J* = 8.4 Hz, 4H, Ar*H*), 6.84 (d, *J* = 8.6 Hz, 4H, Ar*H*), 3.80 (s, 6H, 2 x ArOCH_3).
- **^{13}C NMR (101 MHz, $CDCl_3$** δ 159.9, 132.6, 128.4, 114.6, 55.3.

  The characterization data matched the reported values.[7]

1,2-Di-*p*-tolyldisulfane (2c)



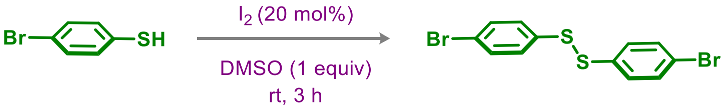
2c

Following a slightly modified procedure,[7] to a solution of iodine (510 mg, 2.00 mmol, 0.200 equiv) in DMSO (0.37 mL, 10 mmol, 1.0 equiv), 4-methylbenzenethiol (1.24 g, 10 mmol, 1.0 equiv) was added. After stirring for 3 h at room temperature, the reaction mixture was quenched by $Na_2S_2O_3$ (50 mL) and extracted with EtOAc (3 x 40 mL) .The combined organic phases were dried over $MgSO_4$. The solvent was removed under vaccum. The crude product was purified by flash column chromatography using hexane as mobile phase to afford the pure product **2c** as a white solid (915 mg, 74%).

- **TLC (EtOAc:Hexane, 1:99 v/v):** R_f = 0.71, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.40 (d, *J* = 7.9 Hz, 4H, Ar*H*), 7.11 (d, *J* = 7.9 Hz, 4H, Ar*H*), 2.33 (s, 6H, 2 x ArCH_3).
- **^{13}C NMR (101 MHz, $CDCl_3$:** δ 137.4, 133.9, 129.8, 128.5, 21.0.

  The characterization data matched the reported values.[7]

1,2-Bis(4-bromophenyl)disulfane (2d)



2d

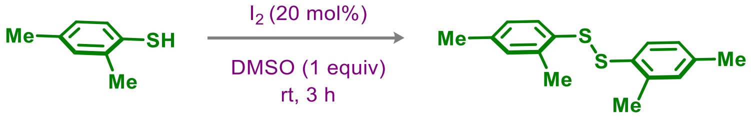
Following a slightly modified procedure,[7] to a solution of iodine (255 mg, 1.00 mmol, 0.200 equiv) in DMSO (0.185 mL, 5.00 mmol, 1.00 equiv), 4-bromobenzenethiol (945 mg, 5.00 mmol, 1.00

equiv) was added. After stirring for 3 h at room temperature, the reaction mixture was quenched by $Na_2S_2O_3$ (30 mL) and extracted with EtOAc (3 x 30 mL) .The combined organic phases were dried over $MgSO_4$. The solvent was removed under vaccum. The crude product was purified by flash column chromatography using hexane as mobile phase to afford the pure product **2d** as a white solid (770 mg, 81%).

- **TLC (EtOAc:Hexane, 1:99 v/v):** R_f = 0.79, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.43 (dd, *J* = 8.5, 1.4 Hz, 4H. Ar*H*), 7.34 (dd, *J* = 8.5, 1.4 Hz, 4H, Ar*H*).
- **^{13}C NMR (101 MHz, $CDCl_3$** δ 135.7, 132.2, 129.4, 121.5.

  The characterization data matched the reported values.[7]

1,2-Bis(2,4-dimethylphenyl)disulfane (2e)



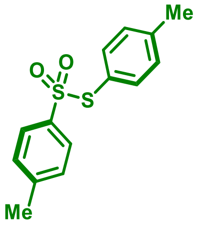
2e

Following a slightly modified procedure,[7] to a solution of iodine (255 mg, 1.00 mmol, 0.200 equiv) in DMSO (0.185 mL, 5.00 mmol, 1.00 equiv), 2,4-dimethylbenzenethiol (691 mg, 5.00 mmol, 1.00 equiv) was added. After stirring for 3 h at room temperature, the reaction mixture was quenched by $Na_2S_2O_3$ (30 mL) and extracted with EtOAc (3 x 30 mL) .The combined organic phases were dried over $MgSO_4$. The solvent was removed under vaccum. The crude product was purified by flash column chromatography using hexane as mobile phase to afford the pure product **2e** as a white solid (393 mg, 57%).

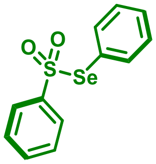
- **TLC (EtOAc:Hexane, 1:99 v/v):** R_f = 0.77, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.42 (dd, *J* = 8.0, 2.8 Hz, 2H, Ar*H*), 7.03 (s, 2H, Ar*H*), 6.96 (d, *J* = 8.0 Hz, 2H, Ar*H*), 2.41 (s, 6H, 2 x ArC*H*$_3$), 2.32 (s, 6H, 2 x ArC*H*$_3$).
- **^{13}C NMR (101 MHz, $CDCl_3$)** δ 138.3, 137.8, 132.3, 131.2, 130.5, 127.3, 21.0, 20.1.

  The characterization data matched the reported values.[7]

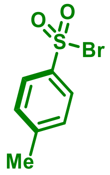
2.2.2 Synthesis of heterodiradical precursor:



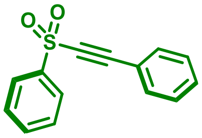
2f



2g

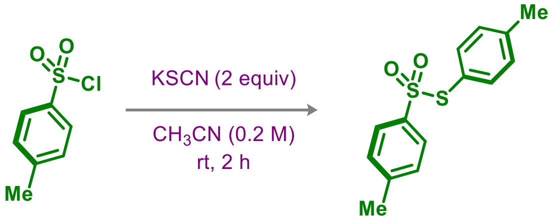


2h



2i

S-(*p*-Tolyl) 4-methylbenzenesulfonothioate (2f)



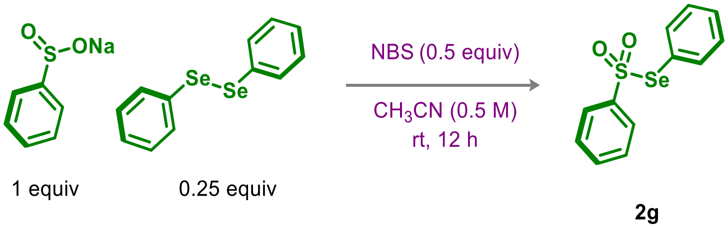
2f

Following a slightly modified procedure,[8] to a solution of 4-toluenesulfonyl chloride (953 mg, 5.00 mmol, 1.00 equiv) in CH_3CN (25 mL) under nitrogen, potassium thiocyante (971 mg, 10.0 mmol, 2.00 equiv) was added. Afer stirring for 2h at room temperature, the reaction mixture was filtrated. The precipitate was rinsed with DCM (20 mL). The filtrate was concentrated in vacuum. The crude product was purified by flash column chromatography using EtOAc:Hexane 1:19 mixture as mobile phase to afford the pure product **2f** as a brown liquid (423 mg, 31%).

- **TLC (EtOAc:Hexane, 1:19 v/v):** $R_f = 0.69$, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.44 (d, *J* = 8.0 Hz, 2H, Ar*H*), 7.21 (t, *J* = 7.6 Hz, 4H, Ar*H*), 7.13 (d, *J* = 7.9 Hz, 2H, Ar*H*), 2.41 (s, 3H, ArC*H*$_3$), 2.36 (s, 3H, ArC*H*$_3$).
- **^{13}C NMR (101 MHz, $CDCl_3$):** δ 144.6, 142.0, 140.3, 136.4, 130.1, 129.3, 127.5, 124.4, 21.8, 21.5

  The characterization data matched the reported values.[8]

Se-Phenyl benzenesulfonoselenoate (2g)



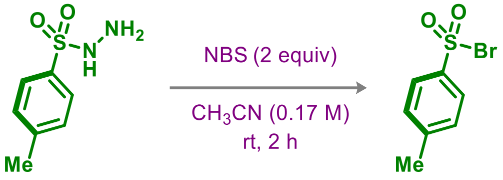
2g

Following a slightly modified procedure,[9] to a solution of $PhSO_2Na$ (1.64 g, 10.0 mmol, 1.00 equiv) in CH_3CN (20 mL), diselenide (785 mg, 2.50 mmol, 0.250 equiv) and NBS (890 mg, 5.00 mmol, 0.500 equiv) were added. After stirring for 12 h at room temperature, the reaction mixture was quenched with water (30 mL), and extracted with EtOAc (2 × 30 mL). The combined organic phases were dried over Na_2SO_4 and concentrated under vacuum. The crude product was purified by flash column chromatography using EtOAc:Hexane 1:19 mixture as an eluent to give **2g** as a yellow solid (995 mg, 67%).

- **TLC (EtOAc:Hexane, 1:19 v/v):** $R_f = 0.69$, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.58 – 7.46 (m, 6H, Ar*H*), 7.39 (t, *J* = 7.7 Hz, 2H, Ar*H*), 7.33 (t, *J* = 7.5 Hz, 2H, Ar*H*).
- **^{13}C NMR (101 MHz, $CDCl_3$** δ 145.1, 137.1, 133.5, 130.9, 129.5, 128.7, 127.8, 126.9.

  The characterization data matched the reported values.[9]

4-Methylbenzenesulfonyl bromide (2h)



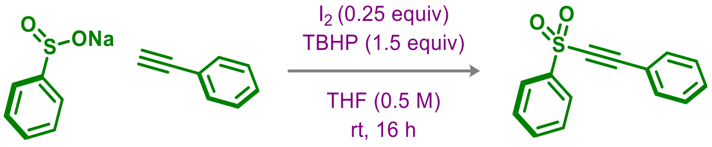
2h

Following a slightly modified procedure,[10] to a solution of 4-toluenesulfonyl hydrazide (931 mg, 5.00 mmol, 1.00 equiv) in MeCN (30 mL), *N*-bromosuccinimide (1.78 g, 10.0 mmol, 2.00 equiv) was added portion-wise. After stirring for 2 h at room temperature, the reaction mixture was diluted with saturated aqueous $NaHCO_3$ (30 mL) and extracted with DCM (2 x 30 mL). The combined organic phases were dried over Na_2SO_4 and concentrated under vacuum. The crude product was purified by flash column chromatography using EtOAc:Hexane 1:19 mixture to give **2h** as a white solid (636 mg, 54%).

- **TLC (EtOAc:Hexane, 1:19 v/v):** $R_f = 0.49$, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.89 (d, *J* = 8.0 Hz, 2H, Ar*H*), 7.40 (d, *J* = 8.0 Hz, 2H, Ar*H*), 2.49 (s, 3H, ArCH_3).
- **^{13}C NMR (101 MHz, $CDCl_3$)** δ 146.8, 144.7, 130.1, 126.6, 21.8

  The characterization data matched the reported values.[10]

((Phenylethynyl)sulfonyl)benzene (2i)



2i

Following a slightly modified procedure,[11] to a solution of ethynylbenzene (0.55 mL, 5.0 mmol, 1.0 equiv) in THF (20 mL), $PhSO_2Na$ (1.64 g, 10.0 mmol, 2.00 equiv), I_2 (634 mg, 2.50 mmol, 0.25 equiv), and TBHP (2.07 mL, 7.50 mmol, 1.50 equiv, 70 wt% in water) were added. After stirring for 16 h at room temperature, the reaction mixture was quenched by saturated $Na_2S_2O_3$ (20 mL) solution, diluted with H_2O (20 mL), and extracted with EtOAc (3×20 mL). The combined organic phases were washed with brine (30 mL), dried over anhydrous Na_2SO_4, and concentrated in vacuum. The crude product was purified by flash column chromatography using EtOAc:Hexane 1:19 mixture to give **2i** as a brown liquid (300 mg, 25%).

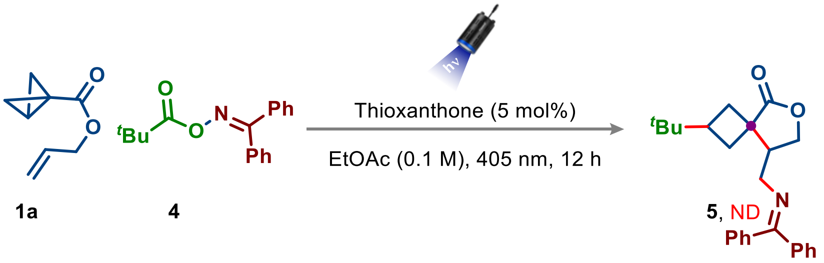
- **TLC (EtOAc:Hexane, 1:19 v/v):** R_f = 0.64, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.13 – 8.04 (m, 2H, Ar*H*), 7.72 – 7.65 (m, 1H, Ar*H*), 7.60 (t, *J* = 7.7 Hz, 2H, Ar*H*), 7.54 – 7.49 (m, 2H, Ar*H*), 7.48 – 7.44 (m, 1H, Ar*H*), 7.36 (t, *J* = 7.7 Hz, 2H, Ar*H*).
- **^{13}C NMR (101 MHz, $CDCl_3$)** δ 141.8, 134.3, 132.8, 131.7, 129.4, 128.7, 127.4, 117.8, 93.6, 85.3.

The characterization data matched the reported values.[11]

3. Procedure for the strain enabled radical cascade reactions:

3.1 PreliminaryExperiments:

2-(*Tert*-butyl)-8-(((diphenylmethylene)amino)methyl)-6-oxaspiro[3.4]octan-5-one (5)



An oven-dried 4 mL glass vial was charged with the BCB **1a** (21 mg, 0.15 mmol, 1.0 equiv),diphenylmethanone *O*-pivaloyl oxime **4** (43 mg, 0.15 mmol, 1.0 equiv) and thioxanthone (

1.6 mg, 5 mol%). Next, the vial was closed with a screw-cap septum. The vial was degassed and refilled with nitrogen using the Schlenk-line technique (three times). EtOAc(1.5 mL, 0.10 M) was added to the mixture and stirred for 12 h under the irradiation of a 457 nm Kessil lamp. The solvent was evaporated under vacuum. The crude reaction mixture was analyzed by ^{1}H NMR.

Allyl 1,3-diiodocyclobutane-1-carboxylate (6)

An oven-dried 4 mL glass vial was charged with the BCB **1a** (21 mg, 0.15 mmol, 1.0 equiv) and iodine (38 mg, 0.15 mmol, 1.0 equiv). Next, the vial was closed with a screw-cap septum. The vial was degassed and refilled with nitrogen using the Schlenk-line technique (three times). CH_3CN (1.5 mL, 0.10 M) was added to the mixture and stirred for 3 h under the irradiation of a 457 nm Kessil lamp. The solvent was evaporated under vacuum. The yield of the crude product was calculated by ^{1}H NMR using CH_2Br_2 as an internal standard. The crude product was purified using hexane as an eluent. **(See Spectra)**

- **TLC (EtOAc:Hexane, 1:19 v/v):** $R_f = 0.73$, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** For both diastereomers:δ 5.94 (ddq, *J* = 16.5, 11.0, 5.7 Hz, 1H, alkene C*H*), 5.45 – 5.26 (m, 2H, alkene C*H*$_2$), 4.75 (p, *J* = 8.1 Hz, 0.3H, C*H*I, for minor diastereomer), 4.68 (dt, *J* = 5.5, 1.3 Hz, 2H, allyl C*H*$_2$), 4.35 (p, 0.7H, C*H*I, for major diastereomer), 3.61 (ddd, *J* = 11.4, 7.8, 3.8 Hz, 1.5H, cyclobutane C*H*$_2$), 3.17 (td, *J* = 10.0, 3.6 Hz, 2.5H, cyclobutane C*H*$_2$).
- **^{13}C NMR (101 MHz, $CDCl_3$):** For both diastereomers: δ 172.2, 131.0, 119.2, 119.1, 66.9, 66.6, 52.2, 51.5, 29.7, 3.6. Four carbons were not resolved at 101 MHz.

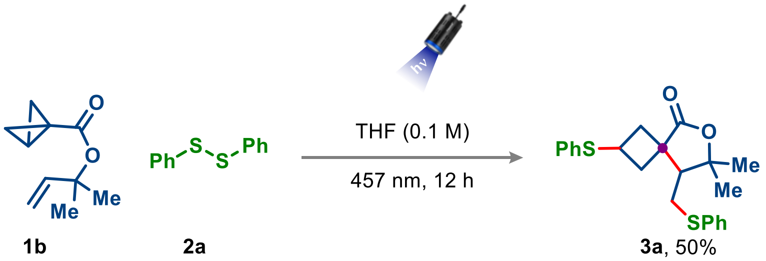
- **GCMS:** calcd. for $C_8H_{10}I_2O_2$ $^+$ $[M]^+$ 392; found 392.

2-Methylbut-3-en-2-yl 1,3-diiodocyclobutane-1-carboxylate (7)

An oven-dried 4 mL glass vial was charged with the BCB **1b** (25 mg, 0.15 mmol, 1.0 equiv) and iodine (38 mg, 0.15 mmol, 1.0 equiv). Next, the vial was closed with a screw-cap septum. The vial was degassed and refilled with nitrogen using the Schlenk-line technique (three times). CH_3CN (1.5 mL, 0.10 M) was added to the mixture and stirred for 3 h under the irradiation of a 457 nm Kessil lamp. The solvent was evaporated under vacuum. The yield of the crude product was calculated by ^{1}H NMR using CH_2Br_2 as an internal standard. The crude product was purified using hexane as an eluent. **(See Spectra)**

- **TLC (EtOAc:Hexane, 1:19 v/v):** $R_f = 0.75$, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** For both diastereomers: δ 6.17 – 6.00 (m, 1H, alkene C*H*), 5.28 – 5.08 (m, 2H, alkene C*H*$_2$), 4.73 (p, *J* = 8.0 Hz, 0.2H, for minor diastereomer), 4.31 (p, 0.8H, for major diastereomer), 3.59 – 3.49 (m, 1.5H, cyclobutane C*H*$_2$), 3.15 – 3.04 (m, 2.5H, cyclobutane C*H*$_2$), 1.56 (d, *J* = 5.2 Hz, 6H, C(C*H*$_3$)$_2$ for both diastereomers).
- **^{13}C NMR (101 MHz, $CDCl_3$):** For both diastereomers: δ 170.8, 141.4, 141.3, 113.7, 113.6, 82.8, 82.6, 52.1, 51.5, 25.9, 25.9, 21.3, 5.6, 3.8. Two carbons were not resolved at 101 MHz.
- **Mass:** Not detected in HRMS (ESI, CI).

7,7-Dimethyl-2-(phenylthio)-8-((phenylthio)methyl)-6-oxaspiro[3.4]octan-5-one (3a)



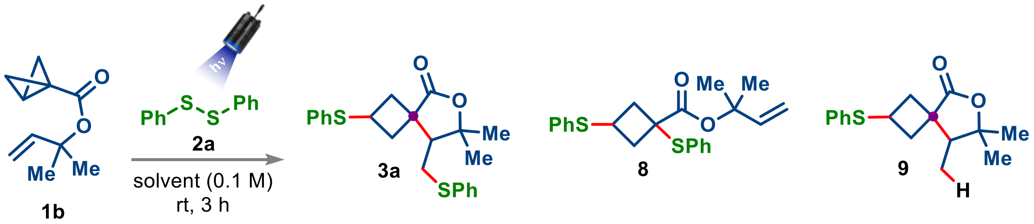
An oven-dried 4 mL glass vial was charged with the BCB **1b** (25 mg, 0.15 mmol, 1.0 equiv) and 1,2-diphenyldisulfane **2a** (33 mg, 0.15 mmol, 1.0 equiv). Next, the vial was closed with a screw-cap septum. The vial was degassed and refilled with nitrogen using the Schlenk-line technique (three times). THF (1.5 mL, 0.10 M) was added to the mixture and stirred for 3 h under the irradiation of a 457 nm Kessil lamp. The solvent was evaporated under vacuum. The yield of the crude product was calculated by ^{1}H NMR using CH_2Br_2 as an internal standard. The crude product was purified using EtOAc:hexane (1:19 v/v) as an eluent.(See Spectra)

- **TLC (EtOAc:Hexane, 1:9 v/v):** R_f = 0.32, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** For both diastereomers: δ 7.42 – 7.26 (m, 9H, Ar*H* for both diastereomers), 7.21 (qd, *J* = 5.8, 4.9, 2.3 Hz, 1H, Ar*H* for both diastereomers), 4.24 (p, *J* = 8.4 Hz, 0.2H, ArSC*H* for minor diastereomer), 4.09 (p, *J* = 8.7 Hz, 0.8H, ArSC*H* for major diastereomer), 3.20 (qd, *J* = 13.1, 7.2 Hz, 1H), 3.00 (dd, *J* = 13.0, 5.5 Hz, 0.3H), 2.90 – 2.75 (m, 2H), 2.58 (dtd, *J* = 12.6, 8.6, 8.1, 3.9 Hz, 1H), 2.50 – 2.30 (m, 1.7H), 2.28 – 2.10 (m, 1H), 1.50 (s, 1H), 1.46 (s, 2H), 1.22 (d, *J* = 3.5 Hz, 3H).
- **^{13}C NMR (101 MHz, $CDCl_3$):** For both diastereomers: δ 179.7, 178.5, 135.8, 134.8, 134.2, 131.1, 130.0, 129.9, 129.7, 129.4, 129.2, 129.0, 128.9, 127.2, 127.0, 126.9, 126.4, 85.1, 84.2, 51.3, 50.5, 45.4, 44.4, 37.5, 36.7, 35.6, 35.3, 35.2, 35.1, 31.1, 29.7, 28.6, 28.0, 23.2, 22.9. **One carbon was not resolved at 101 MHz.
- **HRMS (ESI):** calcd. for $C_{22}H_{25}O_2S_2^+$ $[M+H]^+$ 385.1296; found: 385.1295

3.2 Optimization of reaction conditions:

3.2.1 Optimization of reaction conditions using bifunctional reagent

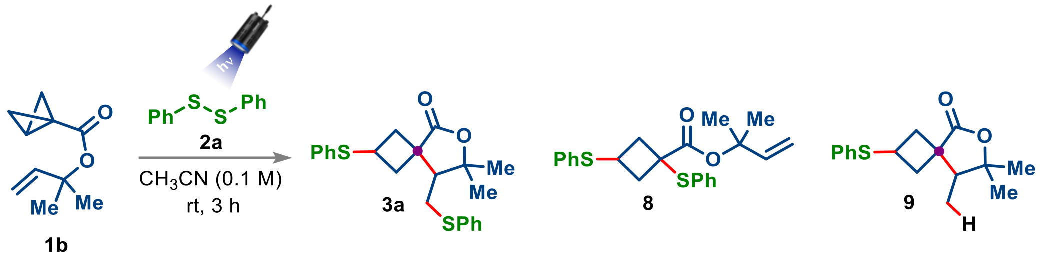
- **Screening of solvents:**



An oven-dried 4 mL glass vial was charged with the BCB **1b** (25 mg, 0.15 mmol, 1.0 equiv) and 1,2-diphenyldisulfane **2a** (33 mg, 0.15 mmol, 1.0 equiv). Next, the vial was closed with a screw-cap septum. The vial was degassed and refilled with nitrogen using the Schlenk-line technique (three times). Solvent (1.5 mL, 0.10 M) was added to the mixture and stirred for 3 h under the irradiation of a 457 nm Kessil lamp. The solvent was evaporated under vacuum. The yield of the crude product was calculated by ^{1}H NMR using CH_2Br_2 as an internal standard.

Entry	Solvent	3a	8	9
1	THF	50%	16%	26%
2	Et_2O	58%	18%	18%
3	DCM	55%	16%	8%
4	MeOH	67%	20%	7%
5	HFIP	69%	13%	3%
6	**CH_3CN**	**77%**	**9%**	**5%**

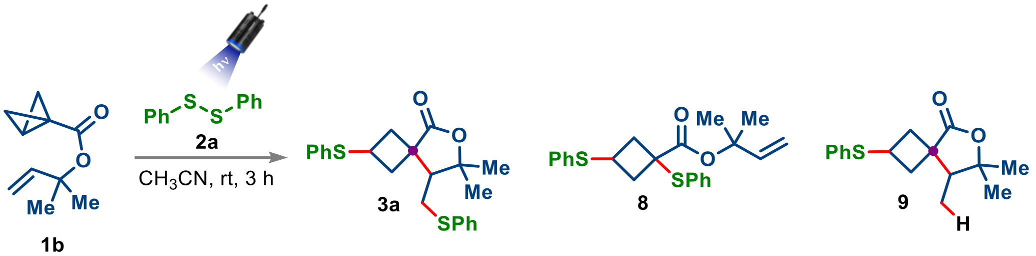
- **Screening of stoichiometry of the reagents:**



An oven-dried 4 mL glass vial was charged with the BCB **1b** (xx mmol) and 1,2-diphenyldisulfane **2a** (yy mmol). Next, the vial was closed with a screw-cap septum. The vial was degassed and refilled with nitrogen using the Schlenk-line technique (three times). CH_3CN (1.5 mL, 0.10 M) was added to the mixture and stirred for 3 h under the irradiation of a 457 nm Kessil lamp. The solvent was evaporated under vacuum. The yield of the crude product was calculated by ^1H NMR using CH_2Br_2 as an internal standard.

Entry	1b	2a	3a	8	9
1	**1**	**1**	**77%**	**9%**	**5%**
2	1	1.2	63%	13%	5%
3	1.2	1	70%	10%	5%

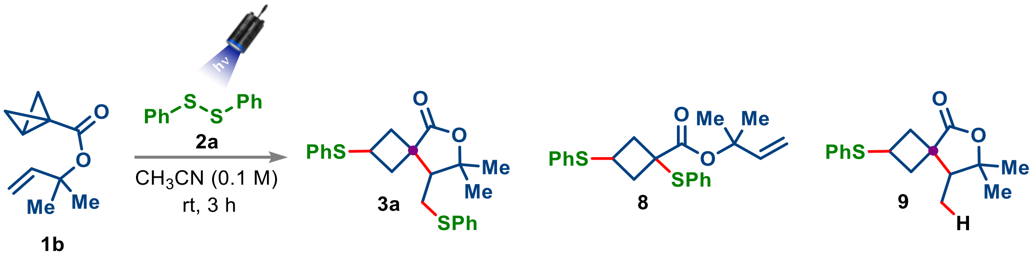
- **Effect of Concentration:**



An oven-dried 4 mL glass vial was charged with the BCB **1b** (25 mg, 0.15 mmol, 1.0 equiv) and 1,2-diphenyldisulfane **2a** (33 mg, 0.15 mmol, 1.0 equiv). Next, the vial was closed with a screw-cap septum. The vial was degassed and refilled with nitrogen using the Schlenk-line technique (three times). CH_3CN (x M) was added to the mixture and stirred for 3 h under the irradiation of a 457 nm Kessil lamp. The solvent was evaporated under vacuum. The yield of the crude product was calculated by ^1H NMR using CH_2Br_2 as an internal standard.

Entry	Solvent CH_3CN (x M)	3a	8	9
1	**0.1**	**77%**	**9%**	**5%**
2	0.05	50%	8%	7%
3	0.2	52%	13%	4%

- **Screening of light source:**

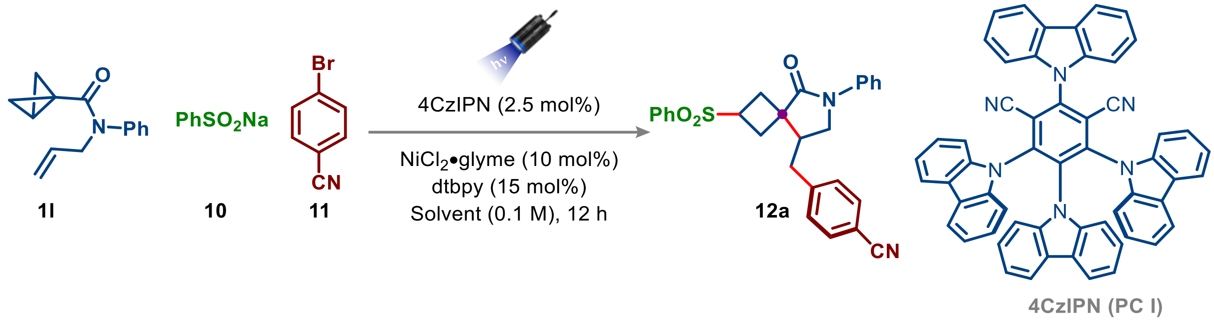


An oven-dried 4 mL glass vial was charged with the BCB **1b** (25 mg, 0.15 mmol, 1.0 equiv) and 1,2-diphenyldisulfane **2a** (33 mg, 0.15 mmol, 1.0 equiv). Next, the vial was closed with a screw-cap septum. The vial was degassed and refilled with nitrogen using the Schlenk-line technique (three times). CH_3CN (1.5 mL, 0.10 M) was added to the mixture and stirred for 3 h under the irradiation of a x nm Kessil lamp. The solvent was evaporated under vacuum. The yield of the crude product was calculated by ^1H NMR using CH_2Br_2 as an internal standard.

Entry	Light Source (x nm)	3a	8	9
1	**440**	**77%**	**9%**	**5%**
2	390	60%	21%	4%

3.2.2 Optimization of dual photoredox/nickel catalysis

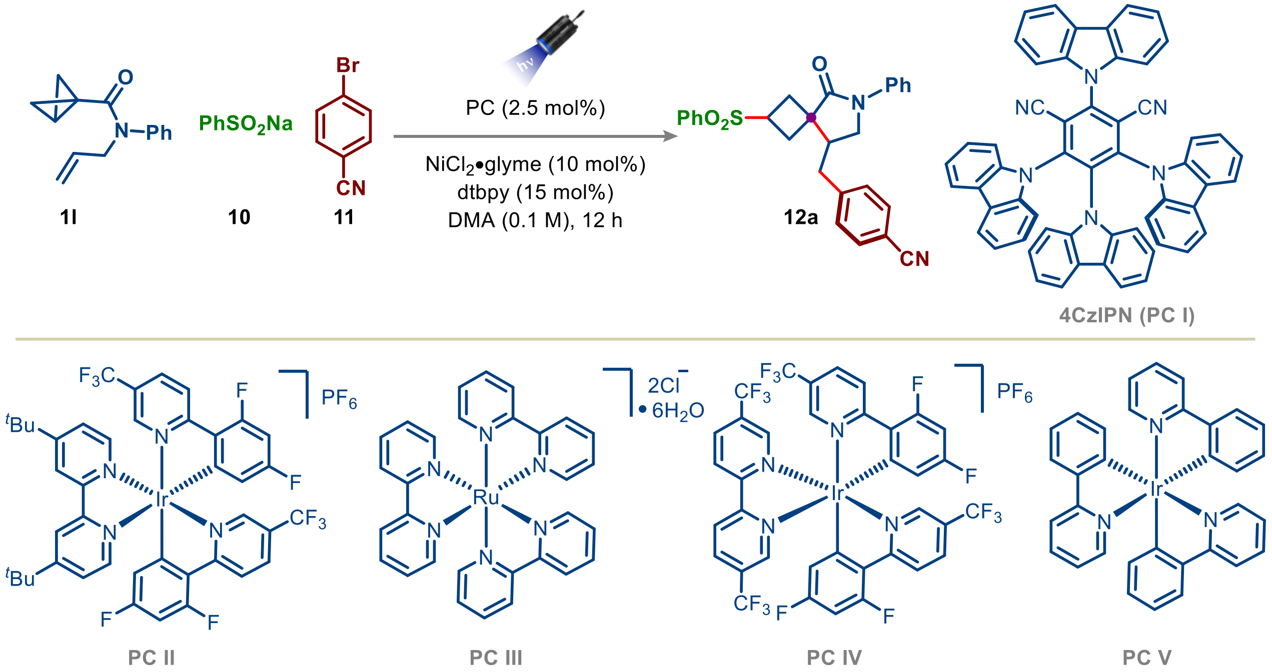
- **Solvent screening:**



An oven-dried 4 mL glass vial was charged with the BCB **1l** (32 mg, 0.15 mmol, 1.0 equiv), sodium benzenesulfinate **10** (37.0 mg, 0.225 mmol, 1.50 equiv), 4-bromobenzonitrile **11** (55 mg, 0.30 mmol, 2.0 equiv) and 4CzIPN (3.0 mg, 2.5 mol%), $NiCl_2$·glyme (3.3 mg, 10 mol%), dtbpy (6.0 mg, 15 mol%). Next, the vial was closed with a screw-cap septum. The vial was degassed and refilled with nitrogen using the Schlenk-line technique (three times). Solvent (1.5 mL, 0.10 M) was added to the mixture and stirred under the irradiation of a 457 nm Kessil lamp. After 12 h, the reaction mixture was quenched with H_2O (10.0 mL). The resulting reaction mixture was extracted with Et_2O (2 × 5.0 mL). The combined organic phases were dried over Na_2SO_4. The solvent was removed under vacuum. The yield of the crude product was calculated by ^1H NMR using CH_2Br_2 as an internal standard.

Entry	Solvent	12a
1	CH_3CN	10%
2	DCM	16%
3	DMSO	61%
4	DMF	60%
5	**DMA**	**64%**

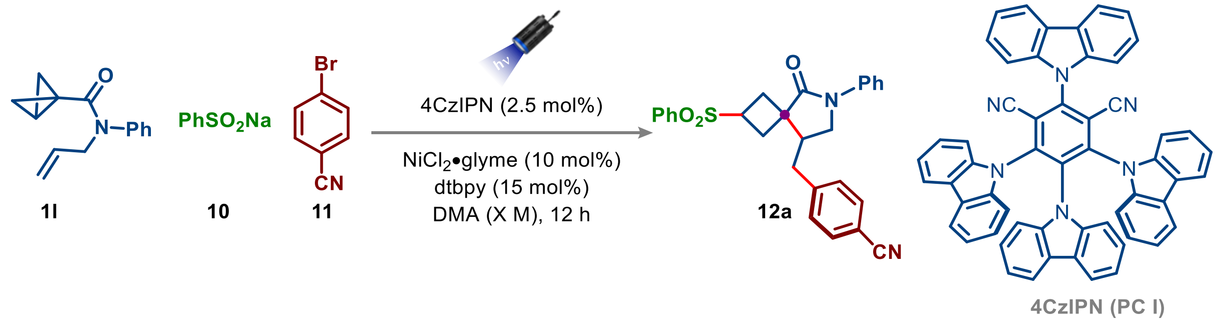
- **Photocatalyst screening:**



An oven-dried 4 mL glass vial was charged with the BCB **1l** (32 mg, 0.15 mmol, 1.0 equiv), sodium benzenesulfinate **10** (37.0 mg, 0.225 mmol, 1.50 equiv), 4-bromobenzonitrile **11** (55 mg, 0.30 mmol, 2.0 equiv) and PC (xx mg, 2.5 mol%), $NiCl_2$·glyme (3.3 mg, 10 mol%), dtbpy (6.0 mg, 15 mol%). Next, the vial was closed with a screw-cap septum. The vial was degassed and refilled with nitrogen using the Schlenk-line technique (three times). Solvent (1.5 mL, 0.10 M) was added to the mixture and stirred under the irradiation of a 457 nm Kessil lamp. After 12 h, the reaction mixture was quenched with H_2O (10.0 mL). The resulting reaction mixture was extracted with Et_2O (2 × 5.0 mL). The combined organic phases were dried over Na_2SO_4. The solvent was removed under vacuum. The yield of the crude product was calculated by ^{1}H NMR using CH_2Br_2 as an internal standard.

Entry	Photocatalyst	12a
1	PC I	64%
2	PC II	30%
3	PC III	60%
4	PC IV	46%
5	PC V	34%

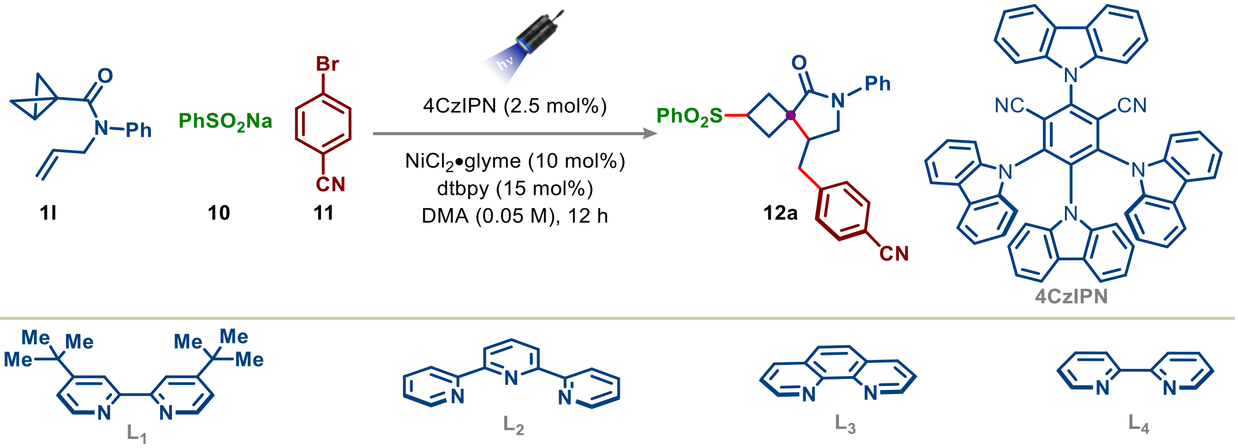
- **Effect of concentration:**



An oven-dried 4 mL glass vial was charged with the BCB **1l** (32 mg, 0.15 mmol, 1.0 equiv), sodium benzenesulfinate **10** (37.0 mg, 0.225 mmol, 1.50 equiv), 4-bromobenzonitrile **11** (55 mg, 0.30 mmol, 2.0 equiv) and 4CzIPN (3.0 mg, 2.5 mol%), $NiCl_2$·glyme (3.3 mg, 10 mol%), dtbpy (6.0 mg, 15 mol%). Next, the vial was closed with a screw-cap septum. The vial was degassed and refilled with nitrogen using the Schlenk-line technique (three times). DMA (x M) was added to the mixture and stirred under the irradiation of a 457 nm Kessil lamp. After 12 h, the reaction mixture was quenched with H_2O (10.0 mL). The resulting reaction mixture was extracted with Et_2O (2 × 5.0 mL). The combined organic phases were dried over Na_2SO_4. The solvent was removed under vacuum. The yield of the crude product was calculated by ^{1}H NMR using CH_2Br_2 as an internal standard.

Entry	DMA (x M)	12a
1	0.05	71%
2	0.1	64%
3	0.2	55%

- **Ligand screening:**

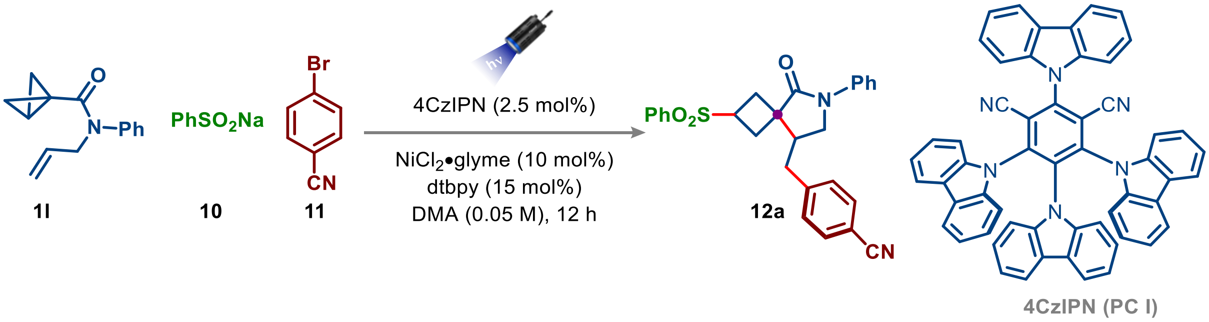


An oven-dried 4 mL glass vial was charged with the BCB **1l** (32 mg, 0.15 mmol, 1.0 equiv), sodium benzenesulfinate **10** (37.0 mg, 0.225 mmol, 1.50 equiv), 4-bromobenzonitrile **11** (55 mg, 0.30

mmol, 2.0 equiv) and 4CzIPN (3.0 mg, 2.5 mol%), $NiCl_2$·glyme (3.3 mg, 10 mol%), ligand (xx mg, 15 mol%). Next, the vial was closed with a screw-cap septum. The vial was degassed and refilled with nitrogen using the Schlenk-line technique (three times). DMA (3.0 mL, 0.05 M) was added to the mixture and stirred under the irradiation of a 457 nm Kessil lamp. After 12 h, the reaction mixture was quenched with H_2O (10.0 mL). The resulting reaction mixture was extracted with Et_2O (2 × 5.0 mL). The combined organic phases were dried over Na_2SO_4. The solvent was removed under vacuum. The yield of the crude product was calculated by ^1H NMR using CH_2Br_2 as an internal standard.

Entry	Ligand	12a
1	L_1	71%
2	L_2	26%
3	L_3	35%
4	L_4	63%

- **Control Experiments:**

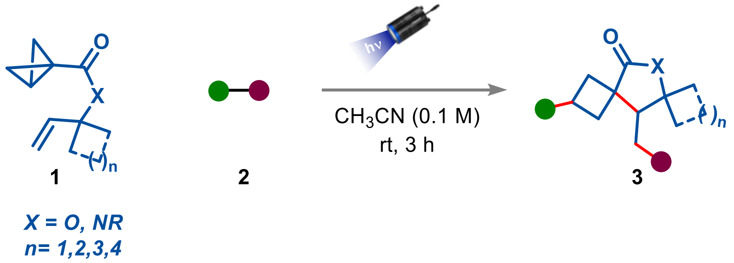


An oven-dried 4 mL glass vial was charged with the BCB **1l** (32 mg, 0.15 mmol, 1.0 equiv), sodium benzenesulfinate **10** (37.0 mg, 0.225 mmol, 1.50 equiv), 4-bromobenzonitrile **11**(55 mg, 0.30 mmol, 2.0 equiv) and 4CzIPN (3.0 mg, 2.5 mol%), $NiCl_2$·glyme (3.3 mg, 10 mol%), dtbpy (6.0 mg, 15 mol%). Next, the vial was closed with a screw-cap septum. The vial was degassed and refilled with nitrogen using the Schlenk-line technique (three times). DMA (3.0 mL, 0.05 M) was added to the mixture and stirred under the irradiation of a 457 nm Kessil lamp. After 12 h, the reaction mixture was quenched with H_2O (10.0 mL). The resulting reaction mixture was extracted with Et_2O (2 × 5.0 mL). The combined organic phases were dried over Na_2SO_4. The solvent was removed under vacuum. The yield of the crude product was calculated by ^1H NMR using CH_2Br_2 as an internal standard.

Entry	**Reaction component omitted**	**12a**
1	Photocatalyst	ND
2	Nickel catalyst	ND
3	Light	ND
4	Ligand	8%

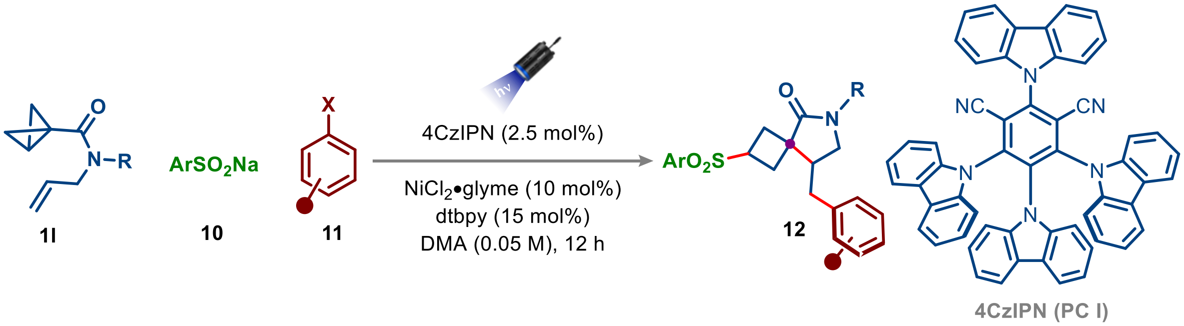
3.3 General Procedure

- **General Procedure A**



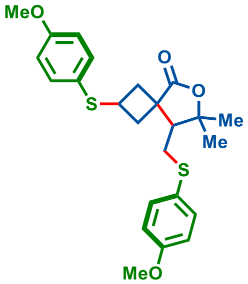
An oven-dried 10 mL glass vial was charged with the BCB **1** (0.3 mmol, 1 equiv) and the diradical precursor **2** (0.3 mmol, 1 equiv). Next, the vial was closed with a screw-cap septum. The vial was degassed and refilled with argon using the Schlenk-line technique (three times). CH_3CN (3.0 mL, 0.10 M) was added to the mixture and stirred for 3 h under the irradiation of a 457 nm Kessil lamp. The solvent was evaporated under reduced pressure. Finally, the crude product **3** was purified by flash column chromatography.

- **General Procedure B**



An oven-dried 25 mL glass vial was charged with the BCB **1** (0.30 mmol, 1.0 equiv), sodium arylsulfinate **10** (0.45 mmol, 1.5 equiv), aryl halide or alkenyl bromide **11** (0.60 mmol, 2.0 equiv) and 4CzIPN (6.0 mg, 2.5 mol%), $NiCl_2\cdot$glyme (6.6 mg, 10 mol%), dtbpy (12 mg, 15 mol%). Next, the vial was closed with a screw-cap septum. The vial was degassed and refilled with nitrogen using the Schlenk-line technique (three times). DMA (6.0 mL, 0.05 M) was added to the mixture and stirred under the irradiation of a 457 nm Kessil lamp. After 12 h, the reaction mixture was quenched with H_2O (20.0 mL). The resulting reaction mixture was extracted with Et_2O (2 × 10 mL). The combined organic phases were dried over Na_2SO_4. The solvent was removed under vacuum. Finally, the crude product **12** was purified by flash column chromatography.

2-((4-Methoxyphenyl)thio)-8-(((4-methoxyphenyl)thio)methyl)-7,7-dimethyl-6-oxaspiro[3.4]octan-5-one (3b)

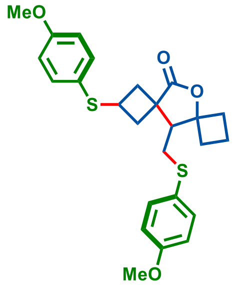


3b

Following the general procedure A, BCB **1b** (50 mg, 0.30 mmol, 1.0 equiv) and 1,2-bis(4-methoxyphenyl)disulfane **2b** (84 mg, 0.30 mmol, 1.0 equiv) were stirred for 3 h. Next, the reaction mixture was concentrated under vacuum. The crude product was purified by flash chromatography using (silica, 1:19 v/v EtOAc:Hexane) to afford the product **3b** as a brown sticky liquid (100 mg, 0.225 mmol, 75%, 1.1:1 *dr*, inseparable diastereomers). **(See Spectra)**

- **TLC (EtOAc:Hexane, 1:9 v/v):** R_f = 0.31, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.50 – 7.20 (m, 4H Ar*H* for both diastereomer), 6.87 (t, *J* = 9.2 Hz, 4H, Ar*H* for both diastereomer), 4.06 (p, *J* = 9.2, 8.7 Hz, 0.22H, ArSC*H* for minor diastereomer), 3.89 (p, *J* = 8.3, 7.8 Hz, 0.77H, ArSC*H* for major diastereomer), 3.84 – 3.76 (m, 6H, 2 x ArOCH_3 for both diastereomer), 3.11 (dd, *J* = 13.1, 7.6 Hz, 1H), 3.01 (dd, *J* = 13.2, 6.6 Hz, 1H), 2.80 (dd, *J* = 12.5, 8.9 Hz, 1H), 2.73 – 2.58 (m, 1H), 2.50 – 2.36 (m, 1.5H), 2.25 (q, *J* = 7.2, 6.2 Hz, 1H), 2.14 – 1.96 (m, 0.5H), 1.49 (s, 1H, OCCH_3 for both diastereomer), 1.42 (s, 2H, OCCH_3 for both diastereomer), 1.25 (s, 1H, OCCH_3 for both diastereomer), 1.18 (s, 2H, OCCH_3 for both diastereomer).
- **^{13}C NMR (101 MHz, $CDCl_3$): Major Diastereomer:** δ 178.5, 159.5, 159.4, 134.1, 133.6, 125.1, 125.0, 114.9, 114.6, 84.1, 55.4, 55.3, 51.4, 44.1, 37.3, 37.3, 35.1, 32.9, 28.1, 22.9. **Minor Diastereomer:** δ 179.8, 159.8, 159.5, 135.6, 133.8, 125.1, 123.4, 114.9, 114.6, 85.1, 55.4, 55.3, 50.5, 44.9, 36.7, 36.1, 34.9, 32.9, 28.7, 23.2.
- **IR (Neat):** υ 2926 (m), 2852 (w), 1762 (s), 1688 (w), 1590 (w), 1492 (s), 1283 (s), 1246 (s).
- **HRMS (ESI):** calcd. for $C_{24}H_{28}O_4S_2H^+$ $[M+H]^+$ 445.1507; found: 445.1508

2-((4-Methoxyphenyl)thio)-5-(((4-methoxyphenyl)thio)methyl)-10-oxadispiro[3.1.3^6.2^4]undecan-11-one (3c)



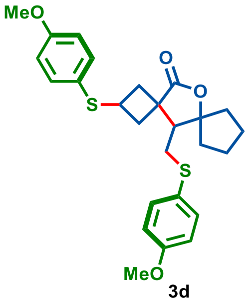
3c

Following the general procedure A, BCB **1c** (36 mg, 0.20 mmol, 1.0 equiv) and 1,2-bis(4-methoxyphenyl)disulfane **2b** (56 mg, 0.20 mmol, 1.0 equiv) were stirred for 3 h. Next, the reaction mixture was concentrated under vacuum. The crude product was purified by flash chromatography using (silica, 1:19 v/v EtOAc:Hexane) to afford the product **3c** as a brown liquid (60.0 mg, 0.131 mmol, 66%, 1.2:1 *dr*, inseparable diastereomers). **(See Spectra)**

- **TLC (EtOAc:Hexane, 1:9 v/v):** R_f = 0.21, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.34 (m, 4H, Ar*H* for both diastereomer), 7.00 – 6.71 (m, 4H, Ar*H* for both diastereomer), 3.98 (p, *J* = 8.5 Hz, 0.54H, ArSC*H* for major diastereomer), 3.85 – 3.78 (m, 6H, 2 x ArOCH_3 for both diastereomer), 3.74 (p, *J* = 8.9 Hz, 0.46H, ArSC*H* for minor diastereomer), 3.19 – 2.97 (m, 1H), 2.81 (d, *J* = 6.0 Hz, 1H), 2.65 – 2.10 (m, 9H), 1.97 (m, 1H), 1.75 – 1.66 (m, 1H).
- **^{13}C NMR (101 MHz, $CDCl_3$): Major Diastereomer:** δ 179.4, 159.6, 159.3, 134.3, 133.5, 125.5, 123.8, 114.8, 114.6, 87.2, 55.4, 55.3, 50.0, 45.3, 37.2, 36.5, 34.4, 33.7, 33.3, 29.8, 13.4.

  Minor Diastereomer: δ 177.9, 159.5, 159.4, 134.9, 133.7, 125.4, 124.7, 114.9, 114.6, 87.2, 55.4, 55.3, 49.4, 44.5, 38.3, 38.0, 34.3, 33.5, 33.4, 30.0, 13.9.
- **IR (Neat):** υ 2932 (m), 2843 (w), 1767 (m), 1493 (m), 1288 (m), 1245 (s), 827 (m).
- **HRMS (ESI):** calcd. for $C_{25}H_{28}O_4S_2Na^+$ $[M+Na]^+$ 479.1327; found: 479.1327

2-((4-Methoxyphenyl)thio)-5-(((4-methoxyphenyl)thio)methyl)-11-oxadispiro[3.1.4^6.2^4]dodecan-12-one (3d)



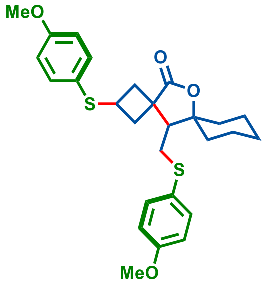
3d

Following the general procedure A, BCB **1d** (39 mg, 0.20 mmol, 1.0 equiv) and 1,2-bis(4-methoxyphenyl)disulfane **2b** (56 mg, 0.20 mmol, 1.0 equiv) were stirred for 3 h. Next, the reaction mixture was concentrated under vacuum. The crude product was purified by flash chromatography using (silica, 1:19 v/v EtOAc:Hexane) to afford the product **3d** as a brown sticky liquid (64 mg, 0.136 mmol, 68%, 1.2:1 *dr*, inseparable diastereomers)**.** **(See Spectra)**

- **TLC (EtOAc:Hexane, 1:9 v/v):** R_f = 0.23, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.40 – 7.25 (m, 4H, Ar*H* for both diastereomer), 6.91 – 6.80 (m, 4H, Ar*H* for both diastereomer), 4.03 (p, *J* = 8.6 Hz, 0.51H, ArSC*H* for major diastereomer), 3.87 (p, *J* = 9.0 Hz, 0.5H, ArSC*H* for minor diastereomer), 3.80 (dd, *J* = 8.5, 5.2 Hz, 6H, 2 x ArOCH_3 for both diastereomer), 3.07 (dd, *J* = 13.1, 7.9 Hz, 0.5H), 2.98 (dd, *J* = 13.1, 5.4 Hz, 0.5H), 2.82 – 2.56 (m, 2H), 2.54 – 2.13 (m, 3.5H), 2.03 – 1.90 (m, 0.5H), 1.88 – 1.50 (m, 8H).
- **^{13}C NMR (101 MHz, $CDCl_3$): Major Diastereomer:** δ 179.8, 159.6, 159.3, 135.3, 133.4, 125.3, 123.6, 114.8, 114.6, 95.7, 55.4, 55.3, 47.2, 45.3, 38.2, 37.0, 36.3, 34.3, 33.5, 33.4, 23.8, 22.8.

  Minor Diastereomer: δ 178.4, 159.5, 159.3, 134.1, 133.7, 125.2, 124.9, 114.9, 114.6, 94.8, 55.4, 55.3, 47.9, 44.5, 37.6, 37.0, 36.3, 34.5, 33.4, 33.3, 23.9, 22.8
- **IR (Neat):** υ 2930 (m), 2850 (w), 1760 (s), 1590 (w), 1492 (m), 1288 (m), 1244 (s), 827 (w).
- **HRMS (ESI):** calcd. for $C_{26}H_{30}O_4S_2Na^+$ $[M+Na]^+$ 493.1483; found: 493.1483

2-((4-Methoxyphenyl)thio)-5-(((4-methoxyphenyl)thio)methyl)-12-oxadispiro[3.1.5^6.2^4]tridecan-13-one (3e)



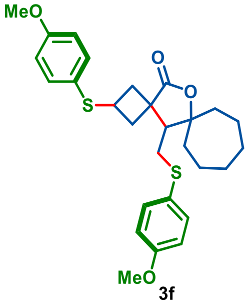
3e

Following the general procedure A, BCB **1e** (62 mg, 0.30 mmol, 1.0 equiv) and 1,2-bis(4-methoxyphenyl)disulfane **2b** (84 mg, 0.30 mmol, 1.0 equiv) were stirred for 3 h. Next, the reaction mixture was concentrated under vacuum. The crude product was purified by flash chromatography using (silica, 1:19 v/v EtOAc:Hexane) to afford the product **3e** as a brown sticky liquid (105 mg, 0.216 mmol, 72%, 1.1:1 *dr*, inseparable diastereomers). **(See Spectra)**

- **TLC (EtOAc:Hexane, 1:9 v/v):** R_f = 0.19, $KMnO_4$.
- **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.42 – 7.26 (m, 4H, Ar*H* for both diastereomer), 6.93 – 6.83 (m, 4H m, 4H, Ar*H* for both diastereomer), 4.10 (p, *J* = 8.6 Hz, 0.56H, ArSC*H* for major diastereomer), 3.94 (p, *J* = 8.9 Hz, 0.52H, ArSC*H* for minor diastereomer), 3.88 – 3.78 (m, 6H, 2 x ArOCH_3 for both diastereomer), 3.08 (d, *J* = 7.0 Hz, 1H), 2.83 (dd, *J* = 12.4, 8.9 Hz, 0.5H), 2.74 (d, *J* = 7.3 Hz, 1H), 2.70 – 2.60 (m, 1H), 2.52 – 2.38 (m, 1H), 2.29 (dd, *J* = 11.7, 9.1 Hz, 1.5H), 2.19 – 2.09 (m, 0.5H), 1.99 – 1.89 (m, 1H), 1.83 – 1.35 (m, 9.5H).
- **^{13}C NMR (101 MHz, CDCl$_3$): Major Diastereomer:** δ 180.0, 159.7, 159.3, 133.9, 133.4, 125.2, 125.2, 114.8, 114.6, 86.3, 55.4, 55.3, 50.8, 44.6, 37.2, 36.6, 36.4, 35.1, 32.7, 32.0, 25.0, 22.4, 21.3.

  Minor Diastereomer: δ 178.8, 159.5, 159.3, 135.4, 133.6, 125.2, 123.6, 114.9, 114.6, 85.5, 55.4, 55.3, 51.8, 43.7, 37.5, 37.2, 36.4, 35.3, 33.0, 31.7, 25.0, 22.3, 21.2.
- **IR (Neat):** υ 2928(m), 2854 (w), 1757 (s), 1492 (m), 1285 (m), 1243 (s), 1028 (m), 821 (m).
- **HRMS (ESI):** calcd. for $C_{27}H_{32}O_4S_2Na^+$ $[M+Na]^+$ 507.1640; found: 507.1642

2-((4-Methoxyphenyl)thio)-5-(((4-methoxyphenyl)thio)methyl)-13-oxadispiro[3.1.6^6.2^4]tetradecan-14-one (3f)



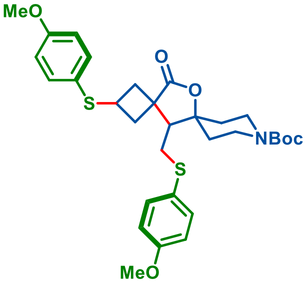
3f

Following the general procedure A, BCB **1f** (66 mg, 0.30 mmol, 1.0 equiv) and 1,2-bis(4-methoxyphenyl)disulfane **2b** (84 mg, 0.30 mmol, 1.0 equiv) were stirred for 3 h. Next, the reaction mixture was concentrated under vacuum. The crude product was purified by flash chromatography using (silica, 1:19 v/v EtOAc:Hexane) to afford the product **3f** as a brown sticky liquid (80 mg, 0.16 mmol, 54%, 1.5:1 *dr*, inseparable diastereomers). **(See Spectra)**

- **TLC (EtOAc:Hexane, 1:19 v/v):** R_f = 0.33, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.40 – 7.28 (m, 4H, Ar*H* for both diastereomer), 6.91 – 6.86 (m, 4H, Ar*H* for both diastereomer), 4.09 (p, *J* = 8.7 Hz, 0.6H, ArSC*H* for major diastereomer), 3.95 (p, *J* = 9.2 Hz, 0.4H, ArSC*H* for minor diastereomer), 3.84 – 3.80 (m, 6H, 2 x ArOCH_3 for both diastereomer), 3.12 (h, *J* = 5.7 Hz, 0.5H), 2.83 – 2.59 (m, 2.5H), 2.45 (ddt, *J* = 18.2, 13.2, 7.0 Hz, 1H), 2.31 – 2.20 (m, 1H), 2.11 (ddd, *J* = 18.1, 12.5, 6.1 Hz, 1H), 2.01 – 1.87 (m, 1H), 1.82 – 1.40 (m, 12H).
- **^{13}C NMR (101 MHz, $CDCl_3$): Major Diastereomer:** δ 180.1, 159.7, 159.3, 135.4, 133.4, 125.3, 123.6, 114.8, 114.6, 89.9, 55.36, 55.3, 51.9, 44.7, 41.8, 36.8, 36.3, 35.2, 34.7, 32.5, 29.3, 28.4, 23.0, 21.7

  Minor Diastereomer: δ 179.0, 159.5, 159.2, 133.9, 133.6, 125.3, 125.2, 115.0, 114.6, 88.9, 55.36, 55.3, 52.9, 43.8, 41.4, 37.6, 37.1, 35.3, 34.3, 32.8, 29.0, 28.2, 22.9, 21.6
- **IR (Neat):** υ 2929 (m), 2858 (w), 2361 (w), 1759 (s), 1492 (m), 1281 (s), 1247 (s), 753 (s).
- **HRMS (ESI):** calcd. for $C_{28}H_{34}O_4S_2H^+$ $[M+H]^+$ 499.1977; found: 499.1979

***Tert*-butyl 2-((4-methoxyphenyl)thio)-5-(((4-methoxyphenyl)thio)methyl)-13-oxo-12-oxa-9-azadispiro[3.1.56.24]tridecane-9-carboxylate (3g)**

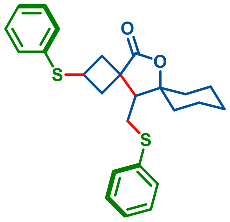


3g

Following the general procedure A, BCB **1g** (92 mg, 0.30 mmol, 1.0 equiv) and 1,2-bis(4-methoxyphenyl)disulfane **2b** (84 mg, 0.30 mmol, 1.0 equiv) were stirred for 3 h. Next, the reaction mixture was concentrated under vacuum. The crude product was purified by flash chromatography using (silica, 1:9 v/v EtOAc:Hexane) to afford the product **3g** as a brown sticky liquid (50.0 mg, 0.085 mmol, 28%, 1.5:1 *dr*, inseparable diastereomers). **(See Spectra)**

- **TLC (EtOAc:Hexane, 2:8 v/v):** R_f = 0.15, $KMnO_4$.
- **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.40 – 7.34 (m, 3H, Ar*H* for both diastereomer), 7.27 (d, *J* = 3.3 Hz, 1H, Ar*H* for both diastereomer), 6.92 – 6.87 (m, 4H, Ar*H* for both diastereomer), 4.15 – 3.94 (m, 3H), 3.89 (p, *J* = 8.7 Hz, 0.45H, ArSC*H* for minor diastereomer), 3.85 – 3.81 (m, 6H, 2 x ArOCH_3 for both diastereomer), 3.13 – 2.99 (m, 3H), 2.81 (dd, *J* = 12.5, 8.9 Hz, 0.5H), 2.76 – 2.63 (m, 2.5H), 2.51 – 2.40 (m, 1.5H), 2.27 (dd, *J* = 11.7, 9.0 Hz, 0.5H), 2.22 – 2.12 (m, 2H), 1.94 (dd, *J* = 9.2, 5.5 Hz, 1H), 1.67 (dd, *J* = 12.4, 4.7 Hz, 1.5H), 1.46 (d, *J* = 1.9 Hz, 9H).
- **^{13}C NMR (101 MHz, CDCl$_3$: Major Diastereomer:** δ 179.5, 159.8, 159.5, 154.6, 135.7, 133.5, 124.7, 123.2, 114.9, 114.6, 84.1, 79.8, 55.4, 50.1, 44.3, 37.2, 36.6, 36.2, 35.0, 32.5, 31.6, 29.7, 28.4.** Two carbons were not resolved at 101 MHz.
- **Minor Diastereomer:** δ 178.3, 159.6, 159.4, 154.6, 134.3, 133.8, 124.7, 115.0, 83.3, 79.9, 55.3, 51.1, 43.4, 37.2, 36.5, 35.2, 32.8, 31.9, 31.3. ** Six carbons were not resolved at 101 MHz.
- **IR (Neat):** υ 2955 (m), 2921 (s), 2854 (w), 1766 (m), 1690 (m), 1285 (w), 1245 (s), 1163 (w).
- **HRMS (ESI):** calcd. for $C_{31}H_{39}NO_6S_2Na^+$ $[M+Na]^+$ 608.2116; found: 608.2117

2-(Phenylthio)-5-((phenylthio)methyl)-12-oxadispiro[3.1.5^6.2^4]tridecan-13-one (3h)



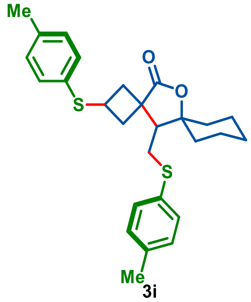
3h

Following the general procedure A, BCB **1e** (62 mg, 0.30 mmol, 1.0 equiv) and 1,2-diphenyldisulfane **2a** (66 mg, 0.30 mmol, 1.0 equiv) were stirred for 3 h. Next, the reaction mixture was concentrated under vacuum. The crude product was purified by flash chromatography using (silica, 1:49 v/v EtOAc:Hexane) to afford the product **3h** as a brown sticky liquid (60.0 mg, 0.141 mmol, 47%, 2:1 *dr*, inseparable diastereomers). **(See Spectra)**

- **TLC (EtOAc:Hexane, 1:19 v/v):** R_f = 0.41, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.43 – 7.15 (m, 10H, Ar*H* for both diastereomer), 4.27 (p, *J* = 8.6 Hz, 0.6H, ArSC*H* for major diastereomer), 4.14 (p, *J* = 8.7 Hz, 0.4H, ArSC*H* for minor diastereomer), 3.27 – 3.20 (m, 0.5H), 3.03 – 2.79 (m, 2H), 2.60 (ddt, *J* = 12.4, 8.1, 4.5 Hz, 1H), 2.49 (dd, *J* = 12.7, 8.7 Hz, 0.5H), 2.39 (dd, *J* = 11.8, 8.8 Hz, 0.5H), 2.31 – 2.22 (m, 1H), 2.10 – 2.03 (m, 0.5H), 1.92 (td, *J* = 13.3, 5.1 Hz, 0.5H), 1.85 – 1.45 (m, 9H), 1.27 – 1.18 (m, 1.5H).
- **^{13}C NMR (101 MHz, $CDCl_3$): Major Diastereomer:** δ 179.9, 135.1, 134.5, 130.9, 129.9, 129.2, 129.0, 126.9, 126.8, 86.3, 50.9, 45.1, 37.1, 35.5, 35.2, 32.1, 31.0, 29.7, 25.0, 22.4, 21.3

  Minor Diastereomer: δ 178.8, 135.9, 135.0, 130.0, 129.6, 129.3, 128.9, 127.1, 126.3, 85.5, 51.8, 44.0, 37.8, 36.3, 35.5, 35.3, 31.8, 25.0, 22.3, 21.2. One carbon was not resolved at 101 MHz.
- **IR (Neat):** υ 3059 (w), 2927 (s), 2856 (w), 1759 (s), 1442 (w), 1292 (w), 950 (w), 743 (w).
- **HRMS (ESI):** calcd. for $C_{25}H_{29}O_2S_2^+$ $[M+H]^+$ 425.1609; found: 425.1606

2-(*p*-Tolylthio)-5-((*p*-tolylthio)methyl)-12-oxadispiro[3.1.56.24]tridecan-13-one (3i)



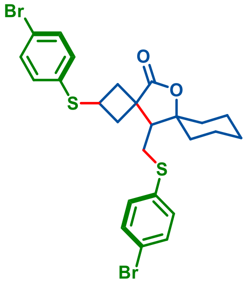
3i

Following the general procedure A, BCB **1e** (62 mg, 0.30 mmol, 1.0 equiv) and 1,2-di-*p*-tolyldisulfane **2c** (74 mg, 0.30 mmol, 1.0 equiv) were stirred for 3 h. Next, the reaction mixture was concentrated under vacuum. The crude product was purified by flash chromatography using (silica, 1:49 v/v EtOAc:Hexane) to afford the product **3i** as a brown sticky liquid (56.0 mg, 0.122 mmol, 42%, 1.3:1 *dr*, inseparable diastereomers). **(See Spectra)**

- **TLC (EtOAc:Hexane, 1:19 v/v):** R_f = 0.43, $KMnO_4$
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.34 – 7.10 (m, 8H, Ar*H* for both diastereomer), 4.20 (p, *J* = 8.6 Hz, 0.52H, ArSC*H* for major diastereomer), 4.05 (p, *J* = 8.7 Hz, 0.43H, ArSC*H* for minor diastereomer), 3.16 (d, *J* = 7.1 Hz, 0.5H), 2.93 – 2.81 (m, 1H), 2.77 – 2.71 (m, 1H), 2.57 – 2.50 (m, 1H), 2.45 (dd, *J* = 12.9, 8.8 Hz, 0.5H), 2.41 – 2.29 (m, 6H, 2 x ArCH_3 for both diastereomer), 2.24 – 2.16 (m, 1H), 2.03 – 1.88 (m, 1H), 1.84 – 1.48 (m, 9H), 1.19 (dq, *J* = 9.0, 5.9, 4.7 Hz, 1H), 0.94 – 0.82 (m, 1H).
- **^{13}C NMR (101 MHz, $CDCl_3$): Major Diastereomer:** δ 180.0, 137.2, 137.1, 132.0, 131.3, 130.5, 130.4, 129.7, 129.6, 86.3, 50.8, 44.9, 37.2, 36.1, 35.7, 35.4, 32.1, 31.8, 29.7, 25.0 , 22.5, 21.3, 21.1.

  Minor Diastereomer: δ 178.8, 137.4, 136.6, 131.8, 131.3, 130.7, 130.6, 130.1, 130.0, 85.5, 51.8, 43.9, 37.7, 36.8, 36.4, 35.4, 31.7, 31.5, 25.0, 22.4, 21.2, 21.1 One carbon was not resolved at 101 MHz.
- **IR (Neat):** υ 2927 (s), 2857 (w), 1761 (s), 1492 (w), 1450 (w), 951 (w), 804 (w).
- **HRMS (ESI):** calcd. for $C_{27}H_{33}O_2S_2^+$ $[M+H]^+$ 453.1922; found: 453.1925

2-((4-Bromophenyl)thio)-5-(((4-bromophenyl)thio)methyl)-12-oxadispiro[3.1.5^6.2^4]tridecan-13-one (3j)



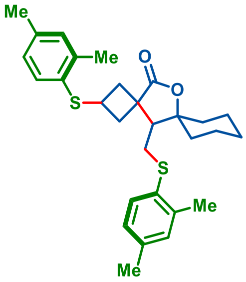
3j

Following the general procedure A, BCB **1e** (62 mg, 0.30 mmol, 1.0 equiv) and 1,2-bis(4-bromophenyl)disulfane **2d** (113 mg, 0.30 mmol, 1.00 equiv) were stirred for 3 h. Next, the reaction mixture was concentrated under vacuum. The crude product was purified by flash chromatography using (silica, 1:49 v/v EtOAc:Hexane) to afford the product **3j** as a brown sticky liquid (90.0 mg, 0.155 mmol, 52%, 1.5:1 *dr*, inseparable diastereomers). **(See Spectra)**

- **TLC (EtOAc:Hexane, 1:19 v/v):** R_f = 0.38, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.50 – 7.41 (m, 4H, Ar*H* for both diastereomer), 7.28 – 7.13 (m, 4H, Ar*H* for both diastereomer), 4.26 (p, *J* = 8.4 Hz, 0.6H, ArSC*H* for major diastereomer), 4.06 (p, *J* = 8.8 Hz, 0.4H, ArSC*H* for minor diastereomer), 3.22 – 3.16 (m, 0.5H), 3.07 – 2.94 (m, 1H), 2.89 – 2.75 (m, 1.5H), 2.64 – 2.55 (m, 1H), 2.49 – 2.19 (m, 2H), 2.12 – 2.05 (m, 0.5H), 1.90 – 1.64 (m, 6H), 1.59 – 1.45 (m, 2H), 1.25 – 1.13 (m, 1.5H), 0.92 – 0.85 (m, 1H).
- **^{13}C NMR (101 MHz, $CDCl_3$): Major Diastereomer:** δ 179.6, 134.3, 134.1, 132.0, 132.0, 131.4, 131.3, 120.9, 120.6, 86.2, 50.9, 45.2, 37.5, 37.0, 35.6, 35.2, 32.2, 31.3, 24.9, 22.4, 21.2.

  Minor Diastereomer: δ 178.5, 135.0, 134.2, 132.4, 132.3, 131.7, 131.2, 121.1, 120.3, 85.4, 51.8, 44.0, 37.7, 36.3, 35.6, 35.1, 31.8, 31.2, 22.3, 21.1. One carbon was not resolved at 101 MHz.
- **IR (Neat):** υ 2923 (s), 2853 (w), 1759 (m), 1687 (s), 1469 (m), 1247 (w), 741 (w).
- **HRMS (ESI):** calcd. for $C_{25}H_{27}Br_2O_2S_2^+$ $[M+H]^+$ 580.9819; found: 580.9817

2-((2,4-Dimethylphenyl)thio)-5-(((2,4-dimethylphenyl)thio)methyl)-12-oxadispiro[3.1.56.24]tridecan-13-one (3k)



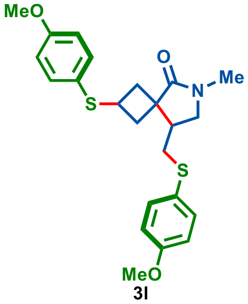
3k

Following the general procedure A, BCB **1e** (62 mg, 0.30 mmol, 1.0 equiv) and 1,2-bis(2,4-dimethylphenyl)disulfane **2e** (83 mg, 0.30 mmol, 1.0 equiv) were stirred for 3 h. Next, the reaction mixture was concentrated under vacuum. The crude product was purified by flash chromatography using (silica, 1:49 v/v EtOAc:Hexane) to afford the product **3k** as a brown sticky liquid (79.0 mg, 0.162 mmol, 55%, 1.2:1 *dr*, inseparable diastereomers). **(See Spectra)**

- **TLC (EtOAc:Hexane, 1:19 v/v):** R_f = 0.41, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.28 – 6.90 (m, 6H, Ar*H* for both diastereomer), 4.21 (p, *J* = 8.5 Hz, 0.5H, ArSC*H* for major diastereomer), 4.09 (p, *J* = 8.7 Hz, 0.5H, ArSC*H* for minor diastereomer), 3.14 (d, *J* = 7.0 Hz, 1H), 3.00 (dd, *J* = 12.6, 6.1 Hz, 0.5H), 2.92 – 2.76 (m, 2H), 2.64 – 2.57 (m, 1H), 2.48 (dd, *J* = 12.7, 8.8 Hz, 1H), 2.43 – 2.27 (m, 12H, 4 x ArCH_3 for both diastereomer), 2.11 (dd, *J* = 8.3, 6.1 Hz, 0.5H), 1.98 – 1.37 (m, 10H), 1.25 – 1.16 (m, 1H).
- **^{13}C NMR (101 MHz, $CDCl_3$): Major Diastereomer:** δ 180.0, 138.3, 137.8, 136.9, 136.0, 131.7, 131.5, 131.1, 130.6, 129.6, 129.3, 127.4, 127.1, 85.5, 52.1, 44.1, 38.0, 37.1, 36.4, 35.3, 35.2, 31.7, 30.6, 25.0, 22.3, 21.2, 20.9, 20.4, 20.4

  Major Diastereomer: δ 178.8, 138.4, 138.3, 136.7, 136.6, 131.4, 131.2, 130.9, 130.7, 130.4, 129.5, 127.3, 127.1, 86.3, 51.2, 45.3, 37.3, 35.5, 34.9, 32.0, 30.6, 22.4, 21.3, 20.8, 20.6, 20.4. Three carbons were not resolved at 101 MHz.
- **IR (Neat):** υ 2929 (m), 2857 (w), 1759 (s), 1444 (w), 1268 (m), 951 (w), 736 (s).
- **HRMS (ESI):** calcd. for $C_{29}H_{36}O_2S_2Na^+$ $[M+Na]^+$ 503.2054; found: 503.2057

2-((4-Methoxyphenyl)thio)-8-(((4-methoxyphenyl)thio)methyl)-6-methyl-6-azaspiro[3.4]octan-5-one (3l)

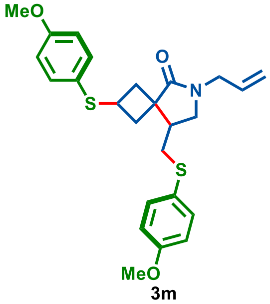


3l

Following the general procedure A, BCB **1h** (46 mg, 0.30 mmol, 1.0 equiv) and 1,2-bis(4-methoxyphenyl)disulfane **2b** (84 mg, 0.30 mmol, 1.0 equiv) were stirred for 3 h. Next, the reaction mixture was concentrated under vacuum. The crude product was purified by flash chromatography using (silica, 3:7 v/v EtOAc:Hexane) to afford the product **3l** as a brown sticky liquid (80.0 mg, 0.186 mmol, 62%, 1.5:1 *dr*, inseparable diastereomers). **(See Spectra)**

- **TLC (EtOAc:Hexane, 4:6 v/v):** R_f = 0.43, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.37 – 7.25 (m, 4H, Ar*H* for both diastereomer), 6.86 – 6.79 (m, 4H, Ar*H* for both diastereomer), 4.02 (p, *J* = 8.3 Hz, 0.40H, ArSC*H* for minor diastereomer), 3.85 – 3.74 (m, 6H, 2 x ArOCH_3 for both diastereomer), 3.57 (p, *J* = 8.7 Hz, 0.66H, ArSC*H* for major diastereomer), 3.40 – 3.33 (m, 1H), 3.16 (dd, *J* = 12.9, 4.2 Hz, 0.5H), 3.06 (ddd, *J* = 22.7, 10.0, 5.8 Hz, 1H), 2.89 (dd, *J* = 12.9, 3.8 Hz, 0.5H), 2.79 (d, *J* = 7.1 Hz, 3H, NCH_3 for both diastereomer), 2.69 (dd, *J* = 12.9, 10.6 Hz, 0.5H), 2.59 (ddd, *J* = 11.8, 8.0, 4.0 Hz, 3.5H), 2.12 (ddt, *J* = 28.9, 15.2, 5.7 Hz, 1.5H), 1.89 (dd, *J* = 11.7, 8.5 Hz, 0.5H).
- **^{13}C NMR (101 MHz, $CDCl_3$): Major Diastereomer:** δ 175.4, 159.3, 159.2, 134.1, 133.4, 125.2, 124.3, 114.8, 114.4, 55.3, 55.2, 51.2, 45.8, 40.6, 37.6, 36.7, 36.2, 32.3, 29.9.
  Minor Diastereomer: δ 177.3, 159.3, 159.1, 134.6, 134.0, 133.2, 125.2, 114.7, 114.4, 55.3, 55.2, 51.7, 45.7, 40.8, 38.4, 37.8, 36.1, 33.4, 29.8.
- **IR (Neat):** υ 2924 (m), 2841 (w), 1684 (s), 1590 (m), 1490 (s), 1281 (m), 1239 (s), 824 (m).
- **HRMS (ESI):** calcd. for $C_{23}H_{27}NO_3S_2Na^+$ $[M+Na]^+$ 452.1330; found: 452.1332

6-Allyl-2-((4-methoxyphenyl)thio)-8-(((4-methoxyphenyl)thio)methyl)-6-azaspiro[3.4]octan-5-one (3m)



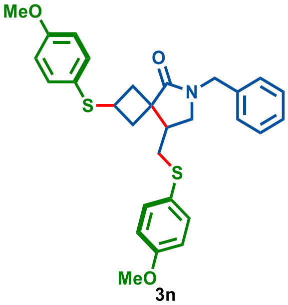
3m

Following the general procedure A, BCB **1i** (54 mg, 0.30 mmol, 1.0 equiv) and 1,2-bis(4-methoxyphenyl)disulfane **2b** (84 mg, 0.30 mmol, 1.0 equiv) were stirred for 3 h. Next, the reaction mixture was concentrated under vacuum. The crude product was purified by flash chromatography using (silica, 1:9 v/v EtOAc:Hexane) to afford the product **3m** as a brown sticky liquid (88.0 mg, 0.193 mmol, 64%, 1.5:1 *dr*, inseparable diastereomers). **(See Spectra)**

- **TLC (EtOAc:Hexane, 2:8 v/v):** R_f = 0.26, $KMnO_4$.
- **^{1}H NMR (400 MHz, CDCl3):** δ 7.34 – 7.25 (m, 4H, Ar*H* for both diastereomer), 6.86 – 6.82 (m, 4H, Ar*H* for both diastereomer), 5.63 (ddt, *J* = 16.6, 10.0, 6.3 Hz, 1H, alkene C*H* for both diastereomer), 5.18 – 5.09 (m, 2H, alkene C*H*$_2$ for both diastereomer), 4.02 (p, *J* = 8.3 Hz, 0.36H, ArSC*H* for minor diastereomer), 3.85 – 3.78 (m, 7H), 3.58 (p, *J* = 8.8 Hz, 0.64H, ArSC*H* for major diastereomer), 3.35 (ddd, *J* = 9.9, 7.1, 4.8 Hz, 1H), 3.16 (dd, *J* = 12.9, 4.3 Hz, 0.5H), 3.05 (ddd, *J* = 25.1, 10.1, 5.8 Hz, 1H), 2.89 (dd, *J* = 12.9, 3.7 Hz, 0.5H), 2.71 – 2.28 (m, 4.5H), 2.18 (ddd, *J* = 11.5, 8.1, 3.3 Hz, 1H), 2.12 – 2.02 (m, 1H), 1.92 (dd, *J* = 11.6, 8.6 Hz, 0.5H).
- **^{13}C NMR (101 MHz, CDCl$_3$): Major Diastereomer:** δ 175.2, 159.3, 159.3, 134.2, 133.6, 132.2, 125.3, 124.3, 118.1, 114.8, 114.5, 55.3, 55.3, 48.5, 46.2, 45.4, 40.7, 38.3, 37.6, 36.7, 32.2.

  Minor Diastereomer: δ 177.1, 159.3, 159.2, 134.6, 133.3, 132.1, 126.3, 125.2, 118.1, 114.8, 114.5, 55.2, 55.3, 49.0, 46.1, 45.3, 40.9, 37.7, 36.2, 36.1, 33.5
- **IR (Neat):** υ 2926 (w), 2841 (w), 1686 (s), 1591 (w), 1491 (m), 1282 (w), 1242 (s), 1029 (w).
- **HRMS (ESI):** calcd. for $C_{25}H_{30}NO_3S_2^+$ $[M+H]^+$ 456.1667; found: 456.1667

6-Benzyl-2-((4-methoxyphenyl)thio)-8-(((4-methoxyphenyl)thio)methyl)-6-azaspiro[3.4]octan-5-one (3n)



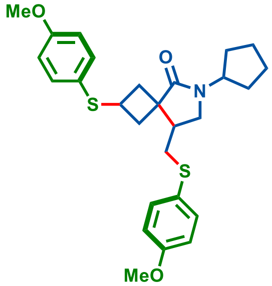
3n

Following the general procedure A, BCB **1j** (70 mg, 0.30 mmol, 1.0 equiv) and 1,2-bis(4-methoxyphenyl)disulfane **2b** (84 mg, 0.30 mmol, 1.0 equiv) were stirred for 3 h. Next, the reaction mixture was concentrated under vacuum. The crude product was purified by flash chromatography using (silica, 1:9 v/v EtOAc:Hexane) to afford the product **3n** as a brown sticky liquid (101 mg, 0.199 mmol, 67%, 1.7:1 *dr*, inseparable diastereomers). **(See Spectra)**

- **TLC (EtOAc:Hexane, 2:8 v/v):** R_f = 0.39, $KMnO_4$.
- **^{1}H NMR (400 MHz, CDCl3):** δ 7.34 – 7.14 (m, 9H, Ar*H* for both diastereomer), 6.86 – 6.79 (m, 4H, Ar*H* for both diastereomer), 4.45 – 4.35 (m, 2H, PhCH_2 for both diastereomer), 4.06 (p, *J* = 8.3 Hz, 0.4H, ArSC*H* for minor diastereomer), 3.79 (d, *J* = 4.5 Hz, 6H, 2 x ArOCH_3 for both diastereomer), 3.59 (p, *J* = 8.9 Hz, 0.6H, ArSC*H* for major diastereomer), 3.29 – 3.23 (m, 1H), 3.12 (dd, *J* = 12.8, 4.2 Hz, 0.5H), 2.99 (dd, *J* = 10.1, 5.4 Hz, 0.5H), 2.89 (ddd, *J* = 22.7, 11.5, 4.9 Hz, 0.5H), 2.60 (tdd, *J* = 20.9, 9.7, 6.6 Hz, 1.5H), 2.51 – 2.00 (m, 4H), 1.93 (dd, *J* = 11.6, 8.6 Hz, 0.5H), 1.78 – 1.71 (m, 0.5H).
- **^{13}C NMR (101 MHz, CDCl3): Major Diastereomer:** δ 175.4, 159.3, 159.3, 136.3, 134.1, 133.6, 133.3, 128.7, 128.1, 127.6, 125.2, 114.8, 114.5, 55.3, 55.2, 48.3, 46.8, 46.2, 40.6, 38.2, 37.6, 36.6, 32.2

  Minor Diastereomer: δ 177.3, 159.4, 159.2, 134.7, 128.7, 128.1, 127.5, 125.3, 124.4, 114.7, 114.5, 55.3, 55.2, 48.9, 46.7, 46.1, 40.9, 37.8, 36.2, 33.5. Three carbons were not resolved at 101 MHz.
- **IR (Neat):** υ 2923 (w), 2848 (w), 1685 (s), 1490 (s), 1281 (m), 1241 (s), 1028 (m), 824 (m).
- **HRMS (ESI):** calcd. for $C_{29}H_{32}NO_3S_2^+$ $[M+H]^+$ 506.1824; found: 506.1825

6-Cyclopentyl-2-((4-methoxyphenyl)thio)-8-(((4-methoxyphenyl)thio)methyl)-6-azaspiro[3.4]octan-5-one (3o)



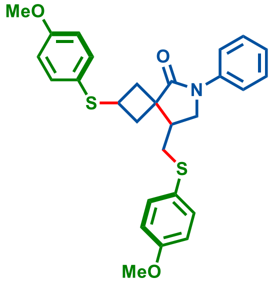
3o

Following the general procedure A, BCB **1k** (62 mg, 0.30 mmol, 1.0 equiv) and 1,2-bis(4-methoxyphenyl)disulfane **2b** (84 mg, 0.30 mmol, 1.0 equiv) were stirred for 3 h. Next, the reaction mixture was concentrated under vacuum. The crude product was purified by flash chromatography using (silica, 1:9 v/v EtOAc:Hexane) to afford the product **3o** as a brown sticky liquid (114 mg, 0.234 mmol, 78%, 1.3:1 *dr*, inseparable diastereomers). **(See Spectra)**

- **TLC (EtOAc:Hexane, 2:8 v/v):** R_f = 0.29, $KMnO_4$.
- **^{1}H NMR (400 MHz, CDCl3):** δ 7.35 – 7.25 (m, 4H, Ar*H* for both diastereomer), 6.87 – 6.81 (m, 4H, Ar*H* for both diastereomer), 4.47 – 4.36 (m, 1H, NC*H* for both diastereomer), 4.01 (p, *J* = 8.5 Hz, 0.4H, ArSC*H* for minor diastereomer), 3.84 – 3.77 (m, 6H, 2 x ArOCH_3 for both diastereomer), 3.56 (p, *J* = 9.1 Hz, 0.6H, ArSC*H* for major diastereomer), 3.36 – 3.30 (m, 1H), 3.16 – 3.07 (m, 1H), 3.01 (dd, *J* = 10.0, 5.7 Hz, 0.5H), 2.90 (dd, *J* = 12.9, 3.6 Hz, 0.5H), 2.66 – 2.56 (m, 1H), 2.51 – 2.26 (m, 3H), 2.17 (ddd, *J* = 11.7, 8.0, 3.4 Hz, 0.5H), 2.06 (dd, *J* = 12.0, 7.9 Hz, 0.5H), 1.93 – 1.53 (m, 7H), 1.40 (tt, *J* = 12.5, 7.3 Hz, 2H).
- **^{13}C NMR (101 MHz, CDCl3): Major Diastereomer:** δ 175.0, 159.3, 159.2, 134.2, 133.6, 125.3, 125.2, 114.8, 114.4, 55.3, 55.2, 52.4, 46.6, 44.5, 40.8, 38.1, 37.6, 36.5, 31.9, 28.8, 28.7, 24.3, 24.2.

  Minor Diastereomer: δ 177.0, 159.2, 159.1, 134.5, 133.3, 124.4, 114.7, 114.4, 55.3, 55.2, 52.3, 46.6, 45.0, 41.2, 37.7, 36.1, 36.0, 33.3, 28.8, 28.6, 24.3, 24.2. **One carbon was not resolved at 101 MHz.
- **IR (Neat):** υ 2929 (m), 2865 (w), 1680 (s), 1490 (m), 1282 (m), 1242 (s), 1176 (m), 1029 (m).
- **HRMS (ESI):** calcd. for $C_{27}H_{34}NO_3S_2^+$ $[M+H]^+$ 484.1980; found: 484.1978

2-((4-Methoxyphenyl)thio)-8-(((4-methoxyphenyl)thio)methyl)-6-phenyl-6-azaspiro[3.4]octan-5-one (3p)



3p

Following the general procedure A, BCB **1l** (64 mg, 0.30 mmol, 1.0 equiv) and 1,2-bis(4-methoxyphenyl)disulfane **2b** (84 mg, 0.30 mmol, 1.0 equiv) were stirred for 3 h. Next, the reaction mixture was concentrated under vacuum. The crude product was purified by flash chromatography using (silica, 1:9 v/v EtOAc:Hexane) to afford the product **3p** as a brown sticky liquid (121 mg, 0.246 mmol, 82%, 1.2:1 *dr*, separable diastereomers). **(See Spectra)**

Major Diastereomer:

- **TLC (EtOAc:Hexane, 2:8 v/v):** R_f = 0.26, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.59 (d, *J* = 8.1 Hz, 2H, Ar*H*), 7.35 (t, *J* = 9.0 Hz, 6H, Ar*H*), 7.13 (t, *J* = 7.4 Hz, 1H, Ar*H*), 6.88 – 6.81 (m, 4H, Ar*H*), 3.86 (p, *J* = 9.9, 6.7 Hz, 1H, ArSC*H*), 3.79 (s, 6H, 2 x ArOCH_3), 3.62 (dd, *J* = 9.8, 6.4 Hz, 2H), 3.23 (dd, *J* = 13.1, 4.1 Hz, 1H), 2.78 (dd, *J* = 13.1, 10.7 Hz, 1H), 2.57 (dd, *J* = 11.6, 9.4 Hz, 1H), 2.49 – 2.41 (m, 3H), 2.30 – 2.23 (m, 1H).
- **^{13}C NMR (101 MHz, $CDCl_3$):** δ 176.8, 159.5, 159.3, 139.3, 134.8, 133.5, 128.9, 125.0, 124.6, 124.2, 119.6, 114.9, 114.6, 55.4, 55.0, 50.4, 47.4, 40.5, 37.7, 36.1, 35.9, 33.4.
- **IR (Neat):** υ 2929 (w), 2838 (w), 1696 (s), 1593 (m), 1493 (s), 1392 (m), 1244 (s), 1030 (m).
- **HRMS (ESI):** calcd. for $C_{28}H_{30}NO_3S_2^+$ $[M+H]^+$ 492.1667; found: 492.1669

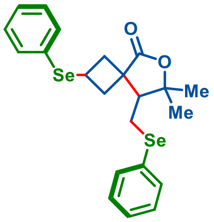
Minor Diastereomer:

- **TLC (EtOAc:Hexane, 2:8 v/v):** R_f = 0.27, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.60 (d, *J* = 8.1 Hz, 2H, Ar*H*), 7.39 – 7.28 (m, 6H, Ar*H*), 7.13 (t, *J* = 7.5 Hz, 1H, Ar*H*), 6.86 (dd, *J* = 8.4, 4.9 Hz, 4H, Ar*H*), 4.03 (p, *J* = 8.3 Hz, 1H, ArSC*H*), 3.85 – 3.76 (m, 7H), 3.55 (dd, *J* = 9.9, 6.1 Hz, 1H), 2.94 (dd, *J* = 13.1, 3.5 Hz,

1H), 2.78 – 2.63 (m, 1H), 2.61 – 2.46 (m, 2H), 2.24 – 2.11 (m, 2H), 2.00 (dd, *J* = 11.7, 8.4 Hz, 1H).

- **^{13}C NMR (101 MHz, CDCl$_3$):** δ 174.7, 159.4, 139.3, 134.5, 133.7, 128.8, 124.9, 124.8, 124.4, 119.4, 114.9, 114.5, 55.3, 55.3, 49.8, 47.4, 40.0, 38.1, 37.5, 36.3, 32.2. One carbon was not resolved at 101 MHz.
- **IR (Neat):** υ 2932 (w), 2838 (w), 1693 (s), 1593 (m), 1492 (s), 1392 (m), 1288 (m), 1243 (s), 827 (w).
- **HRMS (ESI):** calcd. for $C_{28}H_{29}NO_3S_2Na^+$ [M+Na]$^+$ 514.1487; found: 514.1484

7,7-Dimethyl-2-(phenylselanyl)-8-((phenylselanyl)methyl)-6-oxaspiro[3.4]octan-5-one (3q)



3q

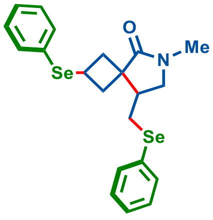
Following the general procedure A, BCB **1b** (50 mg, 0.30 mmol, 1.0 equiv) and 1,2-diphenyldiselane (94 mg, 0.30 mmol, 1.0 equiv) were stirred for 3 h. Next, the reaction mixture was concentrated under vacuum. The crude product was purified by flash chromatography using (silica, 1:19 v/v EtOAc:Hexane) to afford the product **3q** as a brown sticky liquid (45 mg, 0.094 mmol, 31%, 1.2:1 *dr*, inseparable diastereomers). **(See Spectra)**

- **TLC (EtOAc:Hexane, 1:9 v/v):** R$_f$ = 0.43, KMnO$_4$.
- **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.54 – 7.42 (m, 4H, Ar*H* for both diastereomer), 7.34 – 7.30 (m, 3H, Ar*H* for both diastereomer), 7.28 (t, *J* = 3.2 Hz, 3H, Ar*H* for both diastereomer), 4.29 (p, *J* = 8.9 Hz, 0.67H, ArSC*H* for major diastereomer), 4.10 (p, *J* = 9.0 Hz, 0.35H, ArSC*H* for minor diastereomer), 3.18 (dd, *J* = 12.4, 7.7 Hz, 0.5H), 3.06 (dd, *J* = 12.4, 6.6 Hz, 0.5H), 2.94 (dd, *J* = 12.7, 9.0 Hz, 0.5H), 2.87 – 2.80 (m, 0.5H), 2.72 (ddd, *J* = 15.7, 7.2, 3.8 Hz, 1H), 2.69 – 2.63 (m, 1H), 2.56 (ddd, *J* = 15.7, 11.7, 7.4 Hz, 1H), 2.43 (dd, *J* = 11.9, 9.3 Hz, 0.5H), 2.32 – 2.22 (m, 1H), 2.05 (dd, *J* = 8.9, 5.9 Hz, 0.5H), 1.46 (s, 2H), 1.41 (s, 1H), 1.18 (d, *J* = 2.9 Hz, 3H).
- **^{13}C NMR (101 MHz, CDCl$_3$): Major Diastereomer:** δ 179.6, 135.2, 133.2, 129.8, 129.4, 129.1, 129.1, 128.0, 127.7, 85.2, 51.3, 47.1, 36.8, 35.5, 29.6, 28.5, 23.2, 23.1.

Minor Diastereomer: δ 178.3, 133.4, 133.2, 129.5, 129.1, 127.9, 127.3, 84.5, 52.1, 46.0, 38.0, 35.8, 30.2, 27.9, 22.8. **Three carbon was not resolved at 101 MHz.

- **IR (Neat):** υ 2924 (m), 2853 (w), 1757 (s), 1435 (m), 1286 (s), 1066 (s), 933 (m), 736 (s).
- **HRMS (ESI):** calcd. for $C_{22}H_{24}O_2Se_2Na^+$ $[M+Na]^+$ 503.0005; found: 503.0002

6-Methyl-2-(phenylselanyl)-8-((phenylselanyl)methyl)-6-azaspiro[3.4]octan-5-one (3r)



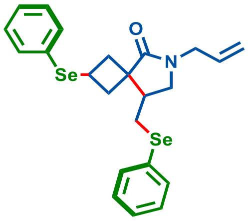
3r

Following the general procedure A, BCB **1h** (46 mg, 0.30 mmol, 1.0 equiv) and 1,2-diphenyldiselane (94 mg, 0.30 mmol, 1.0 equiv) were stirred for 3 h. Next, the reaction mixture was concentrated under vacuum. The crude product was purified by flash chromatography using (silica, 3:7 v/v EtOAc:Hexane) to afford the product **3r** as a brown sticky liquid (100 mg, 0.215 mmol, 72%, 1.2:1 *dr*, inseparable diastereomers). **(See Spectra)**

- **TLC (EtOAc:Hexane, 4:6 v/v):** $R_f = 0.49$, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.49 – 7.39 (m, 4H, Ar*H* for both diastereomer), 7.34 – 7.24 (m, 6H, Ar*H* for both diastereomer), 4.25 (p, *J* = 8.5 Hz, 0.45H, ArSC*H* for minor diastereomer), 3.83 (p, *J* = 9.0 Hz, 0.57H, ArSC*H* for major diastereomer), 3.36 (ddd, *J* = 13.8, 9.9, 7.1 Hz, 1H), 3.27 (dd, *J* = 12.1, 4.0 Hz, 0.5H), 3.02 (dd, *J* = 10.0, 5.5 Hz, 0.5H), 2.95 (dd, *J* = 10.1, 6.3 Hz, 0.5H), 2.87 (dd, *J* = 12.1, 3.6 Hz, 0.5H), 2.82 – 2.60 (m, 4.5H), 2.57 – 2.38 (m, 2.5H), 2.31 – 2.22 (m, 1H), 2.15 (dtd, *J* = 10.8, 6.8, 3.6 Hz, 0.5H), 2.04 (dd, *J* = 11.8, 8.7 Hz, 0.5H).
- **^{13}C NMR (101 MHz, $CDCl_3$): Major Diastereomer:** δ 175.2, 133.4, 132.7, 129.9, 129.2, 128.9, 128.6, 127.4, 127.1, 51.9, 48.2, 41.3, 39.0, 33.0, 30.7, 29.8, 28.0.

  Minor Diastereomer: δ 177.2, 134.4, 132.7, 129.5, 129.2, 128.9, 127.4, 127.2, 126.3, 52.4, 47.9, 41.6, 38.3, 34.1, 29.7, 29.4, 27.6.
- **IR (Neat):** υ 2925 (w), 2855 (w), 1685 (s), 1479 (w), 1434 (m), 1278 (w), 1023 (w), 736 (m).
- **HRMS (ESI):** calcd. for $C_{21}H_{23}NOSe_2H^+$ $[M+H]^+$ 466.0188; found: 466.0189

6-Allyl-2-(phenylselanyl)-8-((phenylselanyl)methyl)-6-azaspiro[3.4]octan-5-one (3s)

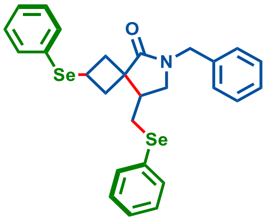


3s

Following the general procedure A, BCB **1i** (54 mg, 0.30 mmol, 1.0 equiv) and 1,2-diphenyldiselane (94 mg, 0.30 mmol, 1.0 equiv) were stirred for 3 h. Next, the reaction mixture was concentrated under vacuum. The crude product was purified by flash chromatography using (silica, 1:9 v/v EtOAc:Hexane) to afford the product **3s** as a brown sticky liquid (126 mg, 0.257 mmol, 88%, 1.2:1 *dr*, inseparable diastereomers). **(See Spectra)**

- **TLC (EtOAc:Hexane, 2:8 v/v):** R_f = 0.29, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.52 – 7.41 (m, 4H, Ar*H* for both diastereomer), 7.27 (dd, *J* = 7.2, 3.6 Hz, 6H, Ar*H* for both diastereomer), 5.69 – 5.57 (m, 1H, alkene C*H* for both diastereomer), 5.19 – 5.08 (m, 2H, alkene CH_2 for both diastereomer), 4.27 (p, *J* = 8.5 Hz, 0.47H, ArSC*H* for minor diastereomer), 3.90 – 3.76 (m, 2.53H), 3.42 – 3.26 (m, 1.5H), 3.02 (dd, *J* = 10.1, 5.6 Hz, 0.5H), 2.95 (dd, *J* = 10.1, 6.4 Hz, 0.5H), 2.88 (dd, *J* = 12.1, 3.7 Hz, 0.5H), 2.80 – 2.66 (m, 1.5H), 2.59 – 2.40 (m, 2.5H), 2.35 – 2.24 (m, 1H), 2.19 – 2.12 (m, 0.5H), 2.07 (dd, *J* = 11.8, 8.7 Hz, 0.5H).
- **^{13}C NMR (101 MHz, $CDCl_3$): Major Diastereomer:** δ 174.9, 134.5, 133.6, 132.9, 132.1, 129.3, 129.2, 129.0, 128.9, 127.5, 118.2, 49.3, 48.5, 45.4, 41.5, 38.9, 32.9, 30.7, 28.1.
  Minor Diastereomer: δ 177.0, 132.9, 132.1, 129.9, 129.3, 128.7, 127.4, 127.2, 49.8, 48.3, 45.3, 41.8, 38.3, 34.2, 29.5, 27.7. Three carbons were not resolved at 101 MHz.
- **IR (Neat):** υ 2924 (w), 2854 (w), 1687 (s), 1478 (w), 1435 (w), 1275 (w), 737 (m), 691 (w).
- **HRMS (ESI):** calcd. for $C_{23}H_{25}NOSe_2H^+$ $[M+H]^+$ 492.0345; found: 492.0346

6-Benzyl-2-(phenylselanyl)-8-((phenylselanyl)methyl)-6-azaspiro[3.4]octan-5-one (3t)



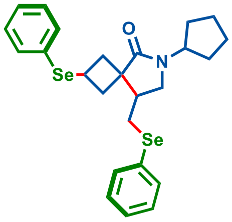
3t

Following the general procedure A, BCB **1j** (70 mg, 0.30 mmol, 1.0 equiv) and 1,2-diphenyldiselane (94 mg, 0.30 mmol, 1.0 equiv) were stirred for 3 h. Next, the reaction mixture was concentrated under vacuum. The crude product was purified by flash chromatography using (silica, 1:9 v/v EtOAc:Hexane) to afford the product **3t** as a brown sticky liquid (125 mg, 0.232 mmol, 77%, 1.2:1 *dr*, inseparable diastereomers). **(See Spectra)**

- **TLC (EtOAc:Hexane, 2:8 v/v):** R_f = 0.38, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.46 (ddt, *J* = 16.2, 8.3, 3.3 Hz, 3H, Ar*H* for both diastereomer), 7.39 – 7.35 (m, 1H, Ar*H* for both diastereomer), 7.32 – 7.22 (m, 9H, Ar*H* for both diastereomer), 7.15 (t, *J* = 7.4 Hz, 2H, Ar*H* for both diastereomer), 4.43 – 4.35 (m, 2H, PhC*H*$_2$ for both diastereomer), 4.29 (p, *J* = 8.7 Hz, 0.48H, ArSC*H* for minor diastereomer), 3.86 (p, *J* = 8.9 Hz, 0.52H, ArSC*H* for major diastereomer), 3.30 – 3.22 (m, 1.5H), 2.93 (dd, *J* = 10.1, 5.6 Hz, 0.5H), 2.87 – 2.83 (m, 1H), 2.78 – 2.67 (m, 1.5H), 2.57 (d, *J* = 9.4 Hz, 1.5H), 2.44 – 2.24 (m, 2H), 2.17 – 2.04 (m, 1H).
- **^{13}C NMR (101 MHz, $CDCl_3$): Major Diastereomer:** δ 175.2, 136.2, 133.5, 133.0, 132.9, 129.3, 129.0, 128.8, 128.7, 128.1, 127.6, 127.5, 127.2, 49.2, 48.5, 46.8, 41.4, 38.9, 33.0, 30.7, 28.0.

  Minor Diastereomer: δ 177.2, 136.2, 134.6, 130.1, 129.2, 129.2, 129.0, 128.7, 128.6, 127.6, 127.5, 127.4, 49.6, 48.3, 46.7, 41.7, 38.3, 34.2, 29.5, 27.6. One carbon was not resolved at 101 MHz.
- **IR (Neat):** υ 2923 (w), 2856 (w), 1687 (s), 1433 (m), 738 (m), 695 (w).
- **HRMS (ESI):** calcd. for $C_{27}H_{28}NOSe_2^+$ $[M+H]^+$ 542.0501; found: 542.0504

6-Cyclopentyl-2-(phenylselanyl)-8-((phenylselanyl)methyl)-6-azaspiro[3.4]octan-5-one (3u)



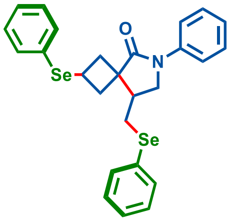
3u

Following the general procedure A, BCB **1k** (62 mg, 0.30 mmol, 1.0 equiv) and 1,2-diphenyldiselane (94 mg, 0.30 mmol, 1.0 equiv) were stirred for 3 h. Next, the reaction mixture was concentrated under vacuum. The crude product was purified by flash chromatography using (silica, 1:9 v/v EtOAc:Hexane) to afford the product **3u** as a brown sticky liquid (140 mg, 0.270 mmol, 90%, 1.3:1 *dr*, inseparable diastereomers). **(See Spectra)**

- **TLC (EtOAc:Hexane, 2:8 v/v):** $R_f = 0.33$, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.51 – 7.42 (m, 4H, Ar*H* for both diastereomer), 7.27 (dt, *J* = 10.3, 3.2 Hz, 6H, Ar*H* for both diastereomer), 4.41 (dt, *J* = 13.7, 8.0 Hz, 1H, NC*H* for both diastereomer), 4.25 (p, *J* = 8.5 Hz, 0.47H, ArSC*H* for minor diastereomer), 3.83 (p, *J* = 9.0 Hz, 0.53H, ArSC*H* for major diastereomer), 3.40 – 3.22 (m, 1.5H), 3.01 (dd, *J* = 10.0, 5.2 Hz, 0.5H), 2.91 (ddd, *J* = 15.3, 11.3, 4.8 Hz, 1H), 2.76 – 2.63 (m, 1.5H), 2.59 – 2.37 (m, 2.5H), 2.33 – 2.20 (m, 1H), 2.17 – 2.04 (m, 1H), 1.83 – 1.50 (m, 6H), 1.45 – 1.25 (m, 2H).
- **^{13}C NMR (101 MHz, $CDCl_3$): Major Diastereomer:** δ 174.8, 133.5, 133.0, 130.0, 129.4, 129.3, 129.0, 127.5, 127.1, 52.4, 49.0, 45.4, 41.6, 38.9, 32.7, 30.7, 28.8, 28.7, 28.1, 24.2, 24.2.

  Minor Diastereomer: δ 176.9, 134.3, 132.9, 129.2, 128.9, 128.8, 127.4, 127.3, 52.3, 48.8, 45.8, 42.1, 38.3, 34.0, 29.5, 28.8, 28.6, 27.7, 24.2, 24.1. One carbon was not resolved at 101 MHz.
- **IR (Neat):** υ 2928 (m), 2865 (w), 1678 (s), 1577 (w), 1477 (w), 1428 (m), 1277 (w), 737 (s).
- **HRMS (ESI):** calcd. for $C_{25}H_{30}NOSe_2^+$ $[M+H]^+$ 520.0658; found: 520.0660

6-Phenyl-2-(phenylselanyl)-8-((phenylselanyl)methyl)-6-azaspiro[3.4]octan-5-one (3v)



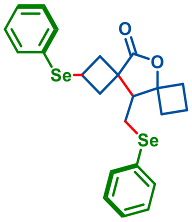
3v

Following the general procedure A, BCB **1l** (64 mg, 0.30 mmol, 1.0 equiv) and 1,2-diphenyldiselane (94 mg, 0.30 mmol, 1.0 equiv) were stirred for 3 h. Next, the reaction mixture was concentrated under vacuum. The crude product was purified by flash chromatography using (silica, 1:9 v/v EtOAc:Hexane) to afford the product **3v** as a brown sticky liquid (152 mg, 0.289 mmol, 96%, 1.1:1 *dr*, inseparable diastereomers). **(See Spectra)**

- **TLC (EtOAc:Hexane, 2:8 v/v):** R_f = 0.34, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.61 – 7.42 (m, 6H, Ar*H* for both diastereomer), 7.38 – 7.23 (m, 8H, Ar*H* for both diastereomer), 7.16 – 7.09 (m, 1H, Ar*H* for both diastereomer), 4.26 (p, *J* = 8.5 Hz, 0.5H, ArSC*H* for major diastereomer), 3.94 – 3.79 (m, 1.5H), 3.53 (dd, *J* = 9.9, 5.6 Hz, 0.5H), 3.45 (dd, *J* = 9.9, 6.3 Hz, 0.5H), 3.32 (dd, *J* = 12.3, 3.9 Hz, 0.5H), 2.93 – 2.51 (m, 4.5H), 2.44 – 2.23 (m, 1.5H), 2.14 (dd, *J* = 11.9, 8.6 Hz, 0.5H).
- **^{13}C NMR (101 MHz, $CDCl_3$): Major Diastereomer:** δ 174.4, 139.2, 133.7, 133.0, 129.4, 129.3, 129.1, 129.0, 128.8, 127.5, 127.3, 124.4, 119.4, 50.6, 49.7, 40.9, 38.9, 33.0, 30.4, 27.6

  Minor Diastereomer: δ 176.50, 132.9, 129.8, 129.2, 128.6, 128.7, 127.4, 124.5, 119.5, 51.0, 49.6, 41.4, 38.3, 34.0, 29.3, 27.3. Four carbons were not resolved at 101 MHz.
- **IR (Neat):** υ 2922 (m), 2854 (w), 1692 (s), 1590 (w), 1481 (m), 1389 (s), 1304 (m), 738 (s).
- **HRMS (ESI):** calcd. for $C_{26}H_{25}NOSe_2Na^+$ $[M+Na]^+$ 550.0165; found: 550.0167

2-(Phenylselanyl)-5-((phenylselanyl)methyl)-10-oxadispiro[3.1.3^6.2^4]undecan-11-one (3w)

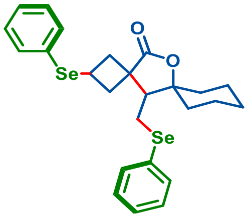


3w

Following the general procedure A, BCB **1c** (54 mg, 0.30 mmol, 1.0 equiv) and 1,2-diphenyldiselane (94 mg, 0.30 mmol, 1.0 equiv) were stirred for 3 h. Next, the reaction mixture was concentrated under vacuum. The crude product was purified by flash chromatography using (silica, 1:19 v/v EtOAc:Hexane) to afford the product **3w** as a brown sticky liquid (30 mg, 0.062 mmol, 21%, 1.3:1 *dr*, separable diastereomers).We could isolate only one diastereomer. **(See Spectra)**

- **TLC (EtOAc:Hexane, 1:9 v/v):** R_f = 0.29, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.53 – 7.46 (m, 4H, Ar*H*), 7.31 – 7.26 (m, 6H, Ar*H*), 4.22 (p, *J* = 8.6 Hz, 1H, ArSC*H*), 2.82 – 2.70 (m, 3H), 2.63 – 2.57 (m, 1H), 2.43 – 2.10 (m, 7H), 1.95 (ddq, *J* = 15.6, 10.4, 5.4 Hz, 1H), 1.68 (dq, *J* = 19.6, 8.4 Hz, 1H).
- **^{13}C NMR (101 MHz, $CDCl_3$):** δ 179.3, 134.5, 133.2, 129.3, 129.1, 127.7, 127.7, 87.4, 50.8, 47.5, 38.8, 34.4, 29.8, 29.4, 23.9, 13.4. Three carbons were not resolved at 101 MHz.
- **IR (Neat):** υ 2925 (m), 2855 (w), 1762 (s), 1436 (w), 1295 (m), 1068 (m), 947 (w), 739 (s).
- **HRMS (ESI):** calcd. for $C_{23}H_{24}O_2Se_2Na^+$ $[M+Na]^+$ 515.0005; found: 515.0008

2-(Phenylselanyl)-5-((phenylselanyl)methyl)-12-oxadispiro[3.1.5^6.2^4]tridecan-13-one (3x)



3x

Following the general procedure A, BCB **1e** (62 mg, 0.30 mmol, 1.0 equiv) and 1,2-diphenyldiselane (94 mg, 0.30 mmol, 1.0 equiv) were stirred for 3 h. Next, the reaction mixture was concentrated under vacuum. The crude product was purified by flash chromatography using (silica, 1:19 v/v EtOAc:Hexane) to afford the product **3x** as a brown sticky liquid (110 mg, 0.212 mmol, 70%, 1.6:1 *dr*, inseparable diastereomers). **(See Spectra)**

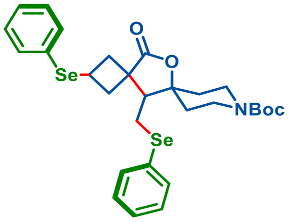
- **TLC (EtOAc:Hexane, 1:9 v/v):** R_f = 0.27, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.56 – 7.46 (m, 4H, Ar*H* for both diastereomer), 7.34 – 7.21 (m, 6H, Ar*H* for both diastereomer), 4.33 (p, *J* = 8.9 Hz, 0.6H, ArSC*H* for major diastereomer), 4.15 (p, *J* = 9.0 Hz, 0.4H, ArSC*H* for minor diastereomer), 3.16 – 3.10 (m, 0.5H), 2.97 (dd, *J* = 12.7, 8.9 Hz, 0.5H), 2.85 – 2.52 (m, 3.5H), 2.48 – 2.43 (m, 0.5H), 2.31

(dd, *J* = 11.9, 9.3 Hz, 0.5H), 2.22 (t, *J* = 7.1 Hz, 0.5H), 1.99 (dd, *J* = 8.7, 6.0 Hz, 0.5H), 1.88 (td, *J* = 13.1, 4.9 Hz, 0.5H), 1.80 – 1.36 (m, 9H), 1.23 – 1.06 (m, 1H).

- **^{13}C NMR (101 MHz, CDCl$_3$): Major Diastereomer:** δ 179.8, 135.0, 133.1, 129.3, 129.0, 127.8, 127.8, 127.6, 127.2, 86.4, 51.6, 46.8, 37.2, 37.0, 35.7, 31.9, 29.6, 24.9, 23.3, 22.4, 21.2.

  Minor Diastereomer: δ 178.5, 133.2, 133.2, 133.1, 129.4, 129.3, 129.0, 128.0, 85.8, 52.4, 45.7, 38.2, 36.2, 35.9, 31.6, 30.2, 23.4, 22.3, 21.1. Two carbons were not resolved at 101 MHz.
- **IR (Neat):** υ 2930 (m), 2858 (w), 1756 (s), 1437 (m), 1288 (m), 1204 (m), 948 (m), 737 (m).
- **HRMS (ESI):** calcd. for $C_{25}H_{28}O_2Se_2H^+$ [M+H]$^+$ 521.0498; found: 521.0500

***Tert*-butyl 13-oxo-2-(phenylselanyl)-5-((phenylselanyl)methyl)-12-oxa-9-azadispiro[3.1.5^6.2^4]tridecane-9-carboxylate (3y)**



3y

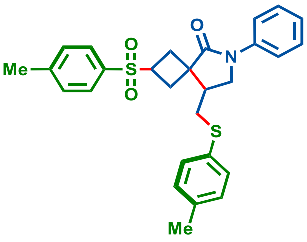
Following the general procedure A, BCB **1g** (92 mg, 0.30 mmol, 1.0 equiv) and 1,2-diphenyldiselane (94 mg, 0.30 mmol, 1.0 equiv) were stirred for 3 h. Next, the reaction mixture was concentrated under vacuum. The crude product was purified by flash chromatography using (silica, 1:9 v/v EtOAc:Hexane) to afford the product **3y** as a brown sticky liquid (55.0 mg, 0.089 mmol, 30%, 1.3:1 *dr*, inseparable diastereomers). **(See Spectra)**

- **TLC (EtOAc:Hexane, 2:8 v/v):** R$_f$ = 0.18, KMnO$_4$.
- **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.56 – 7.47 (m, 2.5H, Ar*H* for both diastereomer), 7.46 – 7.42 (m, 1H, Ar*H* for both diastereomer), 7.36 – 7.25 (m, 6.5H, Ar*H* for both diastereomer), 4.31 (p, *J* = 8.9 Hz, 0.67H, ArSC*H* for major diastereomer), 4.18 – 3.92 (m, 2.33H), 3.17 – 2.93 (m, 3H), 2.78 (dddd, *J* = 20.3, 12.3, 8.5, 3.7 Hz, 1H), 2.67 – 2.42 (m, 3H), 2.32 – 2.23 (m, 1H), 2.11 (td, *J* = 13.3, 5.3 Hz, 0.5H), 2.00 (dd, *J* = 9.8, 5.8 Hz, 1H), 1.75 – 1.63 (m, 2H), 1.48 (s, 9H, ^{t}Bu*H* for both diastereomer), 1.40 – 1.26 (m, 1.5H).

- **^{13}C NMR (101 MHz, CDCl$_3$): Major Diastereomer:** δ 179.2, 154.6, 135.2, 133.3, 129.5, 129.4, 129.1, 128.9, 128.0, 127.8, 84.2, 79.8, 50.9, 46.5, 39.1, 37.0, 35.6, 31.5, 30.0, 28.8, 26.9, 22.8. One carbon was not resolved at 101 MHz.

  Minor Diastereomer: δ 177.9, 154.5, 133.5, 133.3, 129.6, 128.9, 127.8, 127.4, 83.6, 79.8, 51.8, 45.4, 37.9, 36.2, 35.8, 31.3, 29.4, 23.0. Five carbons were not resolved at 101 MHz.
- **IR (Neat):** υ 2925 (m), 2856 (w), 1765 (m), 1733 (m), 1690 (s), 1366 (m), 1176 (s), 744 (w).
- **HRMS (ESI):** calcd. for $C_{29}H_{35}NO_4Se_2Na^+$ [M+Na]$^+$ 644.0795; found: 644.0794

6-Phenyl-8-((*p*-tolylthio)methyl)-2-tosyl-6-azaspiro[3.4]octan-5-one (3z)



3z

Following the general procedure A, BCB **1l** (64 mg, 0.30 mmol, 1.0 equiv) and *S*-(*p*-tolyl) 4-methylbenzenesulfonothioate **2f** (84 mg, 0.30 mmol, 1.0 equiv) were stirred for 3 h. Next, the reaction mixture was concentrated under vacuum. The crude product was purified by flash chromatography using silica, 2:8 v/v EtOAc:Hexane to afford the product **3z** as a brown sticky solid (120 mg, 0.224 mmol, 82%, 1.2:1 *dr*, separable diastereomers). **(See Spectra)**

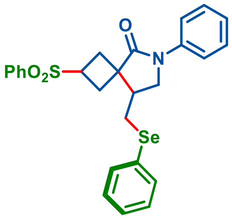
Major Diastereomer:

- **TLC (EtOAc:Hexane, 2:8 v/v):** $R_f = 0.13$, $KMnO_4$.
- **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.77 (d, *J* = 7.9 Hz, 2H, Ar*H*), 7.57 (d, *J* = 8.1 Hz, 2H, Ar*H*), 7.40 – 7.29 (m, 4H, Ar*H*), 7.28 – 7.21 (m, 2H, Ar*H*), 7.11 (t, *J* = 7.7 Hz, 3H, Ar*H*), 3.89 – 3.71 (m, 2H), 3.60 (dd, *J* = 10.0, 5.7 Hz, 1H), 3.19 (dd, *J* = 13.1, 4.6 Hz, 1H), 2.98 (dd, *J* = 11.9, 9.7 Hz, 1H), 2.90 – 2.77 (m, 2H), 2.52 – 2.41 (m, 4H), 2.37 – 2.27 (m, 4H), 2.15 – 2.04 (m, 1H).
- **^{13}C NMR (101 MHz, CDCl$_3$):** δ 173.3, 144.9, 139.0, 137.5, 134.2, 131.0, 130.8, 130.1, 130.0, 128.8, 128.7, 124.6, 119.4, 52.2, 49.7, 45.4, 39.9, 34.8, 31.2, 25.7, 21.6, 21.0.
- **IR (Neat):** υ 2923 (m), 2856 (w), 1693 (s), 1596 (w), 1494 (m), 1394 (m), 1305 (m), 1145 (s).
- **HRMS (ESI):** calcd. for $C_{28}H_{30}NO_3S_2^+$ [M+H]$^+$ 492.1667; found: 492.1668

Minor Diastereomer

- **TLC (EtOAc:Hexane, 2:8 v/v):** R_f = 0.12, $KMnO_4$.
- **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.74 (d, *J* = 7.9 Hz, 2H, Ar*H*), 7.56 (d, *J* = 8.2 Hz, 2H, Ar*H*), 7.38 – 7.29 (m, 6H, Ar*H*), 7.14 (d, *J* = 8.0 Hz, 3H, Ar*H*), 4.12 (p, *J* = 8.5 Hz, 1H, ArSC*H*), 3.91 (dd, *J* = 10.1, 7.3 Hz, 1H), 3.63 (dd, *J* = 10.1, 5.9 Hz, 1H), 3.42 (dd, *J* = 13.1, 3.4 Hz, 1H), 2.74 (ddd, *J* = 12.6, 9.6, 5.6 Hz, 2H), 2.62 – 2.30 (m, 10H).
- **^{13}C NMR (101 MHz, CDCl$_3$):** δ 175.8, 144.9, 138.9, 137.2, 134.8, 130.9, 130.8, 130.0, 129.9, 129.0, 128.2, 124.8, 119.7, 51.7, 50.4, 46.0, 40.1, 34.6, 30.9, 26.7, 21.6, 21.1.
- **IR (Neat):** υ 2922 (m), 2855 (w), 1697 (s), 1595 (w), 1493 (m), 1394 (m), 1279 (m), 1145 (s).
- **HRMS (ESI):** calcd. for $C_{28}H_{30}NO_3S_2^+$ $[M+H]^+$ 492.1667; found: 492.1666

6-Phenyl-8-((phenylselanyl)methyl)-2-(phenylsulfonyl)-6-azaspiro[3.4]octan-5- one (3aa)



3aa

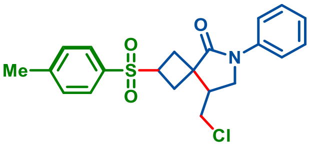
Following the general procedure A, BCB **1l** (64 mg, 0.30 mmol, 1.0 equiv) and *Se*-phenyl benzenesulfonoselenoate **2g** (90 mg, 0.30 mmol, 1.0 equiv) were stirred for 3 h. Next, the reaction mixture was concentrated under vacuum. The crude product was purified by flash chromatography using silica, 2:8 v/v EtOAc:Hexane to afford the product **3aa** as a brown solid (100 mg, 0.195 mmol, 65%, 1.3:1 *dr*, inseparable diastereomers). **(See Spectra)**

- **M.P.** 114 – 116 °C
- **TLC (EtOAc:Hexane, 2:8 v/v):** R_f = 0.15, $KMnO_4$.
- **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.96 – 7.84 (m, 2H, Ar*H* for both diastereomer), 7.72 – 7.48 (m, 7H, Ar*H* for both diastereomer), 7.40 – 7.25 (m, 5H, Ar*H* for both diastereomer), 7.19 – 7.11 (m, 1H, Ar*H* for both diastereomer), 4.16 (p, 0.47H, ArSC*H* for minor diastereomer), 4.00 – 3.72 (m, 1.6H), 3.57 (ddt, *J* = 9.5, 6.4, 3.6 Hz, 1H), 3.44 (dt, *J* = 12.2, 3.0 Hz, 0.5H), 3.23 (dd, *J* = 12.3, 4.2 Hz, 0.5H), 3.03 (dd, *J* = 12.0, 9.7 Hz, 0.5H), 2.92 – 2.73 (m, 2H), 2.63 – 2.47 (m, 2H), 2.45 – 2.28 (m, 1H), 2.19 – 2.08 (m, 0.5H).

- **^{13}C NMR (101 MHz, CDCl$_3$): Major Diastereomer:** δ 173.2, 138.9, 137.1, 133.8, 133.1, 129.3, 129.2, 128.7, 128.6, 128.5, 127.6, 124.5, 119.3, 51.9, 50.3, 45.8, 40.7, 30.7, 27.0, 25.4.

  Minor Diastereomer: δ 175.7, 138.8, 137.6, 133.8, 132.9, 129.3, 129.3, 128.8, 128.0, 127.5, 124.7, 119.5, 51.5, 51.1, 46.4, 40.9, 30.6, 27.1, 26.5. One carbon was not resolved at 101 MHz.
- **IR (Neat):** υ 3061 (w), 2932 (w), 1696 (s), 1492 (m), 1395 (m), 1308 (m), 1279 (m), 1147 (s).
- **HRMS (ESI):** calcd. for $C_{26}H_{26}NO_3SSe^+$ $[M+H]^+$ 512.0078; found: 512.0806

8-(Chloromethyl)-6-phenyl-2-tosyl-6-azaspiro[3.4]octan-5-one (3ab)



3ab

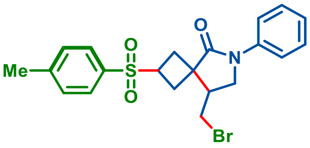
An oven-dried 10 mL glass vial was charged with the BCB **1l** (64 mg, 0.30 mmol, 1.0 equiv) and 4-methylbenzenesulfonyl chloride (58 mg, 0.30 mmol, 1.0 equiv). Next, the vial was closed with a screw-cap septum. The vial was degassed and refilled with argon using the Schlenk-line technique (three times). Solvent, CH_3CN (3.0 mL, 0.10 M) was added to the mixture and stirred for 3 h under the irradiation of a 390 nm Kessil lamp. The solvent was evaporated under reduced pressure. The crude reaction mixture was purified by flash column chromatography using EtOAc:Hexane 2:8 mixture as mobile phase to afford the pure product **3ab** as a brown sticky solid (75.0 mg, 0.186 mmol, 62%, 2:1 *dr*, inseparable diastereomers). **(See Spectra)**

- **TLC (EtOAc:Hexane, 2.5:7.5 v/v):** $R_f = 0.11$, $KMnO_4$.
- **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.76 (dd, *J* = 12.3, 7.9 Hz, 2H, Ar*H* for both diastereomer), 7.60 (d, *J* = 8.0 Hz, 2H, Ar*H* for both diastereomer), 7.43 – 7.32 (m, 4H, Ar*H* for both diastereomer), 7.15 (t, *J* = 7.2 Hz, 1H), 4.11 (p, 0.38H, ArSC*H* for minor diastereomer), 4.01 – 3.47 (m, 4.36H), 2.97 (q, *J* = 11.5, 11.1 Hz, 1.27H), 2.81 – 2.50 (m, 2H), 2.44 (s, 3H, ArCH_3 for both diastereomer), 2.31 – 2.16 (m, 2H).
- **^{13}C NMR (101 MHz, CDCl$_3$): Major Diastereomer:** δ 175.4, 145.0, 138.7, 134.7, 130.0, 129.0, 128.2, 125.1, 119.9, 51.8, 49.6, 45.2, 43.9, 42.5, 31.9, 26.5, 21.7.

Minor Diastereomer: δ 172.8, 138.8, 134.2, 129.0 , 128.7, 124.9, 119.5, 52.2, 48.9, 44.9, 43.6, 32.0, 25.5, 21.7. Three carbons were not resolved at 101MHz.

- **IR (Neat):** υ 2925 (w), 2856 (w), 1695 (s), 1596 (m), 1494 (m), 1399 (m), 1311 (m), 1144 (s).
- **HRMS (ESI):** calcd. for $C_{21}H_{23}ClNO_3S^+$ $[M+H]^+$ 404.1087; found: 404.1085

8-(Bromomethyl)-6-phenyl-2-tosyl-6-azaspiro[3.4]octan-5-one (3ac)



3ab

Following the general procedure A, BCB **1l** (64 mg, 0.30 mmol, 1.0 equiv) and 4-methylbenzenesulfonyl bromide **2h** (71 mg, 0.30 mmol, 1.0 equiv) were stirred for 3 h. Next, the reaction mixture was concentrated under vacuum. The crude product was purified by flash chromatography using silica, 2:8 v/v EtOAc:Hexane to afford the product **3ac** as a brown sticky solid (73 mg, 0.163 mmol, 54%, 2:1 *dr*, separable diastereomers). **(See Spectra)**

Major Diastereomer:

- **TLC (EtOAc:Hexane, 2.5:7.5 v/v):** $R_f = 0.15$, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.80 – 7.73 (m, 2H, Ar*H*), 7.62 – 7.57 (m, 2H, Ar*H*), 7.38 – 7.32 (m, 4H, Ar*H*), 7.18 – 7.11 (m, 1H, Ar*H*), 3.95 (dd, *J* = 10.1, 6.9 Hz, 1H), 3.83 (p, *J* = 9.9, 8.3 Hz, 1H. ArSC*H*), 3.62 (dt, *J* = 9.9, 4.7 Hz, 2H), 3.37 (dd, *J* = 10.4, 9.3 Hz, 1H), 3.03 – 2.90 (m, 2H), 2.84 – 2.75 (m, 1H), 2.44 (s, 3H, ArC*H*$_3$), 2.32 – 2.18 (m, 2H).
- **^{13}C NMR (101 MHz, $CDCl_3$):** δ 172.8, 145.0, 138.7, 134.2, 130.0, 128.9, 128.6, 124.9, 119.6, 52.1, 49.9, 45.5, 42.3, 31.8, 31.4, 25.3, 21.6.
- **IR (Neat):** υ 2923 (m), 2854 (w), 1697 (s), 1596 (w), 1494 (m), 1399 (m), 1279 (m), 1145 (s).
- **HRMS (ESI):** calcd. for $C_{21}H_{23}BrNO_3S^+$ $[M+H]^+$ 448.0582; found: 448.0585

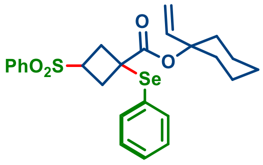
Minor Diastereomer:

- **TLC (EtOAc:Hexane, 2.5:7.5 v/v):** $R_f = 0.16$, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.77 – 7.73 (m, 2H, Ar*H*), 7.62 – 7.56 (m, 2H, Ar*H*), 7.40 – 7.33 (m, 4H, Ar*H*), 7.20 – 7.14 (m, 1H, Ar*H*), 4.12 (p, *J* = 8.4 Hz, 1H, ArSC*H*), 4.01 (dd,

J = 10.2, 7.3 Hz, 1H), 3.77 (dd, *J* = 10.4, 3.6 Hz, 1H), 3.65 (dd, *J* = 10.2, 5.1 Hz, 1H), 3.42 (t, *J* = 9.9 Hz, 1H), 2.82 – 2.64 (m, 3H), 2.61 – 2.46 (m, 2H), 2.45 (s, 3H, ArCH_3).

- **^{13}C NMR (101 MHz, $CDCl_3$):** δ 175.3, 145.0, 138.7, 134.6, 130.0, 129.0, 128.2, 125.1, 119.9, 51.7, 50.7, 45.9, 42.5, 32.0, 31.7, 26.3, 21.6.
- **IR (Neat):** υ 2923 (s), 2855 (w), 1694 (m), 1494 (m), 1398 (m), 1308 (m), 1146 (s), 1086 (w).
- **HRMS (ESI):** calcd. for $C_{21}H_{23}BrNO_3S^+$ $[M+H]^+$ 448.0582; found: 448.0583.

1-Vinylcyclohexyl (1s,3s)-1-(phenylselanyl)-3-(phenylsulfonyl)cyclobutane-1-carboxylate (3’)



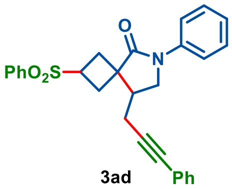
3'

Following general procedure A, BCB **1e** (31 mg, 0.15 mmol, 1.0 equiv) and *Se*-phenyl benzenesulfonoselenoate **2g** (45 mg, 0.15 mmol, 1.0 equiv) were stirred for 3 h. Next, the reaction mixture was concentrated under vacuum. The crude product was purified by flash chromatography using (silica, 2:8 v/v EtOAc:Hexane) to afford the product **3’** as a colourless liquid (68 mg, 0.135 mmol, 90%, 1.6:1 *dr*, inseparable diastereomers). **(See Spectra)**

- **TLC (EtOAc:Hexane, 2:8 v/v):** R_f = 0.15, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.84 – 7.76 (m, 2H, Ar*H* for both diastereomer), 7.67 – 7.52 (m, 5H, Ar*H* for both diastereomer), 7.42 – 7.27 (m, 3H, Ar*H* for both diastereomer), 6.13 – 5.95 (m, 1H, Alkene C*H* for both diastereomer), 5.31 – 5.07 (m, 2H, Alkene CH_2 for both diastereomer), 3.95 (p, *J* = 8.5 Hz, 0.66H, ArSC*H* for major diastereomer), 3.72 (p, *J* = 8.7 Hz, 0.40H, ArSC*H* for minor diastereomer), 3.17 – 3.05 (m, 1.2H), 2.90 – 2.74 (m, 1.6H), 2.40 – 2.29 (m, 1.2H), 2.16 (m, *J* = 14.2, 12.5, 7.0 Hz, 2H), 1.61 – 1.48 (m, 8H).
- **^{13}C NMR (101 MHz, $CDCl_3$):** δ 171.7, 171.5, 141.2, 141.0, 137.6, 137.5, 136.8, 136.8, 136.0, 134.0, 133.9, 129.4, 129.4, 129.2, 129.1, 128.4, 128.2, 127.7, 127.1, 114.5, 114.3, 83.6, 83.2, 53.5, 51.3, 41.9, 41.5, 34.8, 34.7, 34.7, 32.9, 26.9, 25.3, 25.2, 21.9, 21.9. **Two carbons were not resolved at 101 MHz.
- **IR (Neat):** υ 3063 (w), 2932 (s), 2857 (m), 1718 (s), 1442 (m), 1302 (s), 1241 (m), 1145 (s).

- **HRMS (ESI):** calcd. for $C_{25}H_{28}O_4SSeNa^+$ $[M+Na]^+$ 527.0771; found: 527.0772.

6-Phenyl-8-(3-phenylprop-2-yn-1-yl)-2-(phenylsulfonyl)-6-azaspiro[3.4]octan-5-one (3ad)



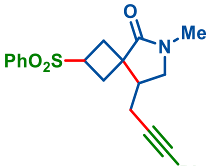
3ad

An oven-dried 10 mL glass vial was charged with the BCB **1l** (64 mg, 0.30 mmol, 1.0 equiv),((phenylethynyl)sulfonyl)benzene **2i** (146 mg, 0.600 mmol, 2.00 equiv), and AIBN (40 mg, 0.24 mmol, 0.80 equiv). Next, the vial was closed with a screw-cap septum. The vial was degassed and refilled with argon using the Schlenk-line technique (three times). Solvent, CH_3CN (3.0 mL, 0.10 M) was added to the mixture and stirred for 12 h at 80 °C. The solvent was evaporated under reduced pressure. The crude reaction mixture was purified by flash column chromatography using EtOAc:Hexane 3:7 mixture as mobile phase to afford the pure product **3ad** as a brown sticky solid (68 mg, 0.15 mmol, 50%, 1.6:1 *dr*, inseparable diastereomers).**(See Spectra)**

- **TLC (EtOAc:Hexane, 3:7 v/v):** $R_f = 0.10$, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.92 – 7.87 (m, 2.32H), 7.69 – 7.51 (m, 6H), 7.39 – 7.27 (m, 3.68H), 7.26 – 7.21 (m, 1.83H), 7.18 – 7.10 (m, 1.19H), 4.03 – 3.92 (m, 1.76H), 3.82 (p, *J* = 9.0 Hz, 0.30H), 3.61 (dd, *J* = 10.0, 4.1 Hz, 0.79H), 3.54 (dd, *J* = 10.1, 5.2 Hz, 0.23H), 3.42 (dd, *J* = 10.1, 3.9 Hz, 0.26H), 3.14 (t, *J* = 10.2 Hz, 0.30H), 3.06 – 2.89 (m, 2.20H), 2.73 – 2.58 (m, 2.62H), 2.47 – 2.41 (m, 0.80H), 2.34 – 2.18 (m, 1.1H).
- **^{13}C NMR (101 MHz, $CDCl_3$): Major Diastereomere:** δ 173.4, 139.0, 137.4, 133.8, 131.4, 129.3, 128.8, 128.5, 128.3, 128.2, 124.6, 122.7, 119.5, 85.7, 82.8, 52.2, 50.2, 45.3, 39.6, 31.6, 25.6, 20.5.

  Minor Diastereomer: δ 172.8, 138.7, 137.1, 133.9, 129.4, 128.9, 128.6, 124.9, 119.6, 52.1, 51.8, 46.3, 42.8, 31.3, 25.1. Seven carbons were not resolved at 101 MHz.
- **IR (Neat):** υ 2953 (w), 2919 (m), 2336 (w), 2249 (w), 1695 (s), 1492 (m), 1312 (m), 1146 (s).
- **HRMS (ESI):** calcd. for $C_{28}H_{25}NO_3SH^+$ $[M+H]^+$ 456.1633; found: 456.1637

6-Methyl-8-(3-phenylprop-2-yn-1-yl)-2-phenylsulfonyl-6-azaspiro[3.4]octan-5-one (3ae)

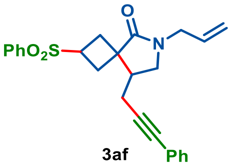


3ae

An oven-dried 10 mL glass vial was charged with the BCB **1h** (23 mg, 0.15 mmol, 1.0 equiv) and (phenylethynyl)sulfonyl)benzene **2i** (73 mg, 0.30 mmol, 2.0 equiv) and AIBN (20 mg, 0.12 mmol, 0.80 equiv). Next, the vial was closed with a screw-cap septum. The vial was degassed and refilled with argon using the Schlenk-line technique (three times). Solvent, dry CH_3CN (3.0 mL, 0.10 M) was added to the mixture and stirred for 12 h at 80 °C. The solvent was evaporated under reduced pressure. The crude product was purified by flash chromatography using (silica, 4:6 v/v EtOAc:Hexane) to afford the product **3ae** as a yellow sticky solid (41.0 mg, 0.103 mmol, 69%, 1.8:1 *dr*).**(See Spectra)**

- **TLC (EtOAc:Hexane, 5:5 v/v):** R_f = 0.1, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.92 – 7.83 (m, 2H), 7.71 – 7.63 (m, 1H), 7.55 (t, *J* = 7.7 Hz, 2H), 7.32 - 7.25 (m, 5H), 3.97 (p, *J* = 9.1 Hz, 1H), 3.50 (dd, *J* = 10.0, 6.4 Hz, 1H), 3.12 (dd, *J* = 10.1, 4.5 Hz, 1H), 3.02 – 2.88 (m, 2H), 2.86 (s, 3H), 2.64 (dd, *J* = 18.9, 9.4 Hz, 1H), 2.59 – 2.50 (m, 2H), 2.38 (ddd, *J* = 12.7, 8.2, 4.7 Hz, 1H), 2.16 (ddd, *J* = 12.4, 8.3, 4.7 Hz, 1H).
- **^{13}C NMR (101 MHz, $CDCl_3$):** δ 174.3, 137.4, 133.8, 131.5, 129.3, 128.6, 128.4, 128.2, 122.8, 86.0, 82.5, 52.5, 51.6, 43.7, 40.3, 31.8, 30.0, 25.7, 20.9.
- **IR (Neat):** υ 3010 (w), 2928 (m), 1686 (s), 1488 (m), 1439 (s), 1307 (m), 1144 (s), 1082 (m).
- **HRMS (ESI):** calcd. for $C_{23}H_{23}NO_3SNa^+$ $[M+Na]^+$ 416.1296; found: 416.1296.

6-Allyl-8-(3-phenylprop-2-yn-1-yl)-2-phenylsulfonyl-6-azaspiro[3.4]octan-5-one (3af)

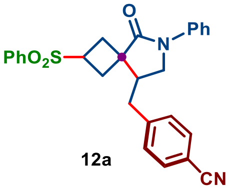


3af

An oven-dried 10 mL glass vial was charged with the BCB **1i** (27 mg, 0.15 mmol, 1.0 equiv) and (phenylethynyl)sulfonyl)benzene **2i** (73 mg, 0.30 mmol, 2.0 equiv) and AIBN (20 mg, 0.12 mmol, 0.80 equiv). Next, the vial was closed with a screw-cap septum. The vial was degassed and refilled with argon using the Schlenk-line technique (three times). Solvent, dry CH_3CN (3.0 mL, 0.10 M) was added to the mixture and stirred for 12 h at 80 °C. The solvent was evaporated under reduced pressure. The crude product was purified by flash chromatography using (silica, 3:7 v/v EtOAc:Hexane) to afford the product **3af** as a yellow sticky solid (41.0 mg, 0.098 mmol, 65%, 1.5:1 *dr*).**(See Spectra)**

- **TLC (EtOAc:Hexane, 3:7 v/v):** $R_f = 0.1$, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.88 – 7.84 (d, 2 H), 7.67 – 7.61 (t, 1H), 7.55 – 7.51 (m, 2H), 7.29 – 7.24 (m, 5H), 5.72 – 5.58 (m, alkene C*H*, 1H), 5.23 – 5.10 (m, alkene C*H*$_2$, 2H), 3.95 (p, 1H), 3.89 – 3.85 (d, 2H), 3.44 – 3.40 (dd, *J* = 10.2, 6.5 Hz, 1H), 3.10 – 3.06 (dd, *J* = 10.2, 6.5 Hz, 1H), 3.02 – 2.84 (m, 2H), 2.68 – 2.46 (m, 3H), 2.37 (ddd, *J* = 12.7, 8.2, 4.7 Hz, 1H), 2.15 (ddd, *J* = 12.4, 8.4, 4.7 Hz, 1H).
- **^{13}C NMR (101 MHz, $CDCl_3$):** δ 174.0, 137.4, 133.8, 132.1, 131.5, 129.4, 129.3, 128.6, 128.4, 128.3, 128.2, 122.8, 118.5, 86.0, 82.5, 52.4, 48.8, 45.5, 44.1, 40.3, 31.6.
- **IR (Neat):** υ 3060 (w), 2930 (m), 1685 (s), 1492 (m), 1440 (s), 1307 (m), 1276 (s), 1144 (s)
- **HRMS (ESI):** calcd. for $C_{25}H_{25}NO_3SNa^+$ $[M+Na]^+$ 442.1453; found: 442.1453.

4-((5-Oxo-6-phenyl-2-(phenylsulfonyl)-6-azaspiro[3.4]octan-8-yl)methyl)benzonitrile (12a)



12a

Following general procedure B, BCB **1l** (64 mg, 0.30 mmol, 1.0 equiv), sodium benzenesulfinate **10** (74 mg, 0.45 mmol, 1.5 equiv), 4-bromobenzonitrile **11**(110 mg, 0.600 mmol, 2.00 equiv) and 4CzIPN (6.0 mg, 2.5 mol%), $NiCl_2$·glyme (6.6 mg, 10 mol%), dtbpy (12 mg, 15 mol%) were added and stirred for 12 h. After the workup, the organic phases were concentrated under vacuum. The crude product was purified by flash chromatography using (silica, 4:6 v/v EtOAc:Hexane) to afford the product **12a** (93.0 mg, 0.204 mmol, 68%, 2:1 *dr*, separable diastereomers). **(See Spectra)**

Major Diastereomer:

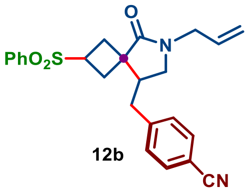
- **M.P.:** 75 - 80 °C
- **TLC (EtOAc:Hexane, 4:6 v/v):** $R_f = 0.11$, $KMnO_4$

- **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.90 (d, *J* = 7.7 Hz, 2H, Ar*H*), 7.68 (t, *J* = 7.3 Hz, 1H, Ar*H*), 7.60 (d, *J* = 7.9 Hz, 4H, Ar*H*), 7.53 – 7.48 (m, 2H, Ar*H*), 7.36 – 7.27 (m, 4H, Ar*H*), 7.12 (t, *J* = 7.4 Hz, 1H, Ar*H*), 3.79 (p, *J* = 9.1 Hz, 1H, PhSO$_2$C*H*), 3.55 (dd, *J* = 9.9, 5.5 Hz, 1H), 3.34 (dd, *J* = 10.0, 4.4 Hz, 1H), 3.08 (h, *J* = 9.9, 9.1 Hz, 2H), 2.94 (dd, *J* = 12.5, 10.0 Hz, 1H), 2.72 – 2.58 (m, 2H), 2.43 (ddd, *J* = 12.6, 8.2, 4.4 Hz, 1H), 2.20 (ddd, *J* = 12.6, 8.4, 4.4 Hz, 1H).
- **^{13}C NMR (101 MHz, CDCl$_3$):** δ 173.3, 143.7, 138.8, 137.1, 134.0, 132.7, 129.5, 129.4, 128.9, 128.6, 124.8, 119.3, 118.5, 111.0, 52.1, 49.1, 45.7, 41.6, 35.1, 31.0, 25.5.
- **IR (Neat):** υ 2929 (m), 2858 (w), 2227 (m), 1697 (s), 1599 (w), 1496 (m), 1281 (s), 1148 (s), 724 (m).
- **HRMS (ESI):** calcd. for $C_{27}H_{24}N_2O_3SNa^+$ $[M+Na]^+$ 479.1405; found: 479.1404

Minor Diastereomer:

- **TLC (EtOAc:Hexane, 4:6 v/v):** R_f = 0.19, $KMnO_4$
- **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.89 (d, *J* = 7.7 Hz, 2H, Ar*H*), 7.72 – 7.55 (m, 5H, Ar*H*), 7.50 (d, *J* = 8.2 Hz, 2H, Ar*H*), 7.33 (t, *J* = 7.8 Hz, 4H, Ar*H*), 7.14 (t, *J* = 7.3 Hz, 1H, Ar*H*), 4.16 (p, *J* = 8.4 Hz, 1H, PhSO$_2$C*H*), 3.63 (dd, *J* = 10.0, 6.5 Hz, 1H), 3.37 (dd, *J* = 10.0, 5.2 Hz, 1H), 3.27 (dd, *J* = 13.2, 3.2 Hz, 1H), 2.86 (dd, *J* = 12.2, 8.2 Hz, 1H), 2.77 – 2.44 (m, 5H).
- **^{13}C NMR (101 MHz, CDCl$_3$):** δ 175.7, 144.2, 138.8, 137.8, 133.9, 132.6, 129.6, 129.4, 129.0, 128.1, 125.0, 119.6, 118.6, 110.8, 51.6, 49.8, 46.4, 42.2, 35.3, 30.8, 26.5.
- **IR (Neat):** υ 2926 (m), 2856 (w), 2227 (w), 1686 (s), 1606 (w), 1492 (w), 1442 (m), 1281 (m), 1147 (s).
- **HRMS (ESI):** calcd. for $C_{27}H_{24}N_2O_3SNa^+$ $[M+Na]^+$ 479.1405; found: 479.1404

4-((6-Allyl-5-oxo-2-(phenylsulfonyl)-6-azaspiro[3.4]octan-8-yl)methyl)benzonitrile (12b)

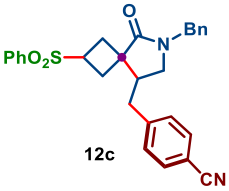


12b

Following general procedure B, BCB **1i** (53 mg, 0.30 mmol, 1.0 equiv), sodium benzenesulfinate **10** (74 mg, 0.45 mmol, 1.5 equiv), 4-bromobenzonitrile **11**(110 mg, 0.60 mmol, 2.0 equiv) and 4CzIPN (6.0 mg, 2.5 mol%), NiCl$_2$·glyme (6.6 mg, 10 mol%), dtbpy (12 mg, 15 mol%) were added and stirred for 12 h. After the workup, the organic phases were concentrated under vacuum. The crude product was purified by flash chromatography using (silica, 4:6 v/v EtOAc:Hexane) to afford the product **12b** (64.0 mg, 0.152 mmol, 51%, 2:1 *dr*, inseparable diastereomers). **(See Spectra)**

- **M.P.:** 125 - 130 °C
- **TLC (EtOAc:Hexane, 4:6 v/v):** $R_f = 0.06$, $KMnO_4$
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.85 (t, *J* = 8.7 Hz, 2H, Ar*H* for both diastereomers), 7.70 – 7.50 (m, 5H, Ar*H* for both diastereomers), 7.31 – 7.22 (m, 2H, Ar*H* for both diastereomers), 5.59 (ddt, *J* = 16.6, 10.4, 6.5 Hz, 1H, alkene C*H* for both diastereomers), 5.10 (td, *J* = 17.0, 8.4 Hz, 2H, alkene CH_2, for both diastereomers), 4.14 (p, *J* = 8.5 Hz, 0.25H, $PhSO_2CH$ for minor diastereomer), 3.92 – 3.65 (m, 2.75H), 3.01 (dtd, *J* = 20.7, 13.0, 12.0, 7.7 Hz, 2.5H), 2.82 (tq, *J* = 12.4, 7.6, 6.3 Hz, 1.5H), 2.66 – 2.28 (m, 4H), 2.08 (tt, *J* = 12.3, 6.2 Hz, 1H).
- **^{13}C NMR (101 MHz, $CDCl_3$):** δ 176.2, 173.9, 144.4, 144.0, 137.7, 137.1, 133.9, 133.8, 132.5, 131.8, 131.6, 129.5, 129.4, 129.3, 128.5, 128.0, 118.5, 118.5, 110.7, 110.5, 52.1, 51.6, 48.4, 47.6, 45.3, 45.2, 44.9, 44.4, 42.4, 42.1, 35.4, 35.2, 30.8, 30.5, 26.6, 25.3. Four peaks were not resolved at 101MHz.
- **IR (Neat):** υ 2928 (m), 2857 (w), 2226 (m), 1687 (s), 1607 (w), 1420 (m), 1278 (m), 1146 (m), 1085 (s).
- **HRMS (ESI):** calcd. for $C_{24}H_{24}N_2O_3SNa^+$ $[M+Na]^+$ 443.1405; found: 443.1402

4-((6-Benzyl-5-oxo-2-(phenylsulfonyl)-6-azaspiro[3.4]octan-8-yl)methyl)benzonitrile (12c)



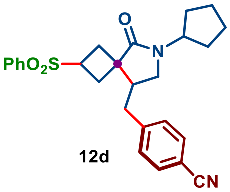
12c

Following general procedure B, BCB **1j** (69 mg, 0.30 mmol, 1.0 equiv), sodium benzenesulfinate **10** (74 mg, 0.45 mmol, 1.5 equiv), 4-bromobenzonitrile **11**(110 mg, 0.60 mmol, 2.0 equiv) and 4CzIPN (6.0 mg, 2.5 mol%), $NiCl_2$·glyme (6.6 mg, 10 mol%), dtbpy (12 mg, 15 mol%) were stirred for 12 h. After the workup, the organic phases were concentrated under vacuum. The crude product was purified by flash chromatography using (silica, 4:6 v/v EtOAc:Hexane) to afford the product **12c** (69 mg, 0.180 mmol, 60%, 2:1 *dr*, inseparable diastereomers). **(See Spectra)**

- **M.P.:** 178 - 184 °C

- **TLC (EtOAc:Hexane, 4:6 v/v):** R_f = 0.07, $KMnO_4$
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.89 (dd, *J* = 15.2, 7.4 Hz, 2H, Ar*H* for both diastereomers), 7.68 (q, *J* = 7.6 Hz, 1H, Ar*H* for both diastereomers), 7.58 (q, *J* = 7.9 Hz, 2H, Ar*H* for both diastereomers), 7.50 (d, *J* = 7.8 Hz, 1H, Ar*H* for both diastereomers), 7.45 (d, *J* = 6.9 Hz, 1H, Ar*H* for both diastereomers), 7.32 (d, *J* = 5.4 Hz, 3H, Ar*H* for both diastereomers), 7.22 – 7.13 (m, 2H, Ar*H* for both diastereomers), 7.01 (d, *J* = 7.8 Hz, 1H, Ar*H* for both diastereomers), 6.88 (d, *J* = 7.5 Hz, 1H, Ar*H* for both diastereomers), 4.63 (t, *J* = 13.8 Hz, 1H), 4.24 – 3.97 (m, 1.4H), 3.76 (p, 0.6H, $PhSO_2CH$ for major diastereomer), 3.24 – 2.82 (m, 3H), 2.80 – 2.51 (m, 2H), 2.51 – 2.04 (m, 4H).
- **^{13}C NMR (101 MHz, $CDCl_3$):** δ 176.2, 173.8, 144.3, 143.9, 137.8, 137.1, 136.1, 136.0, 134.0, 133.9, 132.4, 129.5, 129.5, 129.4, 128.8, 128.6, 128.5, 128.3, 128.1, 127.9, 127.9, 118.6, 118.5, 110.6, 110.5, 52.3, 51.7, 47.4, 46.7, 46.6, 46.6, 45.2, 44.7, 42.8, 42.2, 35.0, 35.0, 31.1, 30.9, 26.5, 25.2. Three carbons were not resolved at 101MHz.
- **IR (Neat):** υ 2926 (m), 2856 (w), 2227 (m), 1686 (s), 1492 (w), 1281 (m), 1147 (m), 696 (m).
- **HRMS (ESI):** calcd. for $C_{28}H_{27}N_2O_3S^+$ $[M+H]^+$ 471.1742; found: 471.1741

4-((6-Cyclopentyl-5-oxo-2-(phenylsulfonyl)-6-azaspiro[3.4]octan-8-yl)methyl)benzonitrile (12d)



12d

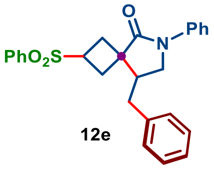
Following general procedure B, BCB **1k** (62 mg, 0.30 mmol, 1.0 equiv), sodium benzenesulfinate **10** (74 mg, 0.45 mmol, 1.5 equiv), 4-bromobenzonitrile **11**(110 mg, 0.60 mmol, 2.0 equiv) and 4CzIPN (6.0 mg, 2.5 mol%), $NiCl_2$·glyme (6.6 mg, 10 mol%), dtbpy (12 mg, 15 mol%) were stirred for 12 h. After the workup, the organic phases were concentrated under vacuum. The crude product was purified by flash chromatography using (silica, 4:6 v/v EtOAc:Hexane) to afford the product **12d** (81 mg, 0.18 mmol, 60%, 2:1 *dr*, inseparable diastereomers). **(See Spectra)**

- **M.P.:** 145 - 150 °C
- **TLC (EtOAc:Hexane, 4:6 v/v):** R_f = 0.05, $KMnO_4$
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.93 – 7.81 (m, 2H, Ar*H* for both diastereomers), 7.70 – 7.52 (m, 5H, Ar*H* for both diastereomers), 7.30 (d, *J* = 7.9 Hz, 1H, Ar*H* for both

diastereomers), 7.24 (s, 1H, Ar*H* for both diastereomers), 4.37 (h, *J* = 8.1 Hz, 1H), 4.13 (p, *J* = 8.5 Hz, 0.3H, $PhSO_2CH$ for minor diastereomer), 3.73 (p, *J* = 9.1 Hz, 0.7H, $PhSO_2CH$ for major diastereomer), 3.05 – 2.90 (m, 2H), 2.87 – 2.69 (m, 2H), 2.63 – 2.26 (m, 4H), 2.08 (ddd, *J* = 12.4, 8.3, 4.5 Hz, 1H), 1.81 – 1.67 (m, 2H), 1.53 (tt, *J* = 12.9, 7.1 Hz, 4H), 1.32 (tq, *J* = 15.8, 8.2 Hz, 2H).

- **^{13}C NMR (101 MHz, CDCl$_3$):** δ 176.1, 173.8, 144.6, 144.1, 137.8, 137.1, 133.9, 133.8, 132.5, 132.5, 129.5, 129.4, 129.3, 129.3, 128.5, 128.0, 118.6, 118.5, 110.7, 110.6, 52.5, 52.4, 52.2, 51.6, 45.4, 44.8, 44.4, 43.8, 42.6, 42.1, 35.2, 35.1, 30.8, 30.5, 28.7, 28.6, 26.4, 25.2, 23.9, 23.9, 23.9, 23.8. Two peaks were not resolved at 101 MHz.
- **IR (Neat):** υ 2949 (m), 2867 (w), 2226 (m), 1680 (s), 1607 (w), 1437 (m), 1280 (m), 1146 (m), 1085 (s).
- **HRMS (ESI):** calcd. for $C_{26}H_{28}N_2O_3SNa^+$ $[M+Na]^+$ 471.1718; found: 471.1715.

8-Benzyl-6-phenyl-2-(phenylsulfonyl)-6-azaspiro[3.4]octan-5-one (12e)



12e

Following general procedure B, BCB **1l** (64 mg, 0.30 mmol, 1.0 equiv), sodium benzenesulfinate **10** (74 mg, 0.45 mmol, 1.5 equiv), iodobenzene (122 mg, 0.600 mmol, 2.00 equiv) and 4CzIPN (6.0 mg, 2.5 mol%), $NiCl_2$·glyme (6.6 mg, 10 mol%), dtbpy (12 mg, 15 mol%) were stirred for 12 h. After the workup, the organic phases were concentrated under vacuum. The crude product was purified by flash chromatography using silica, 2:8 v/v EtOAc:Hexane to afford the product **12e** (107 mg, 0.247 mmol, 83%, 2:1 *dr*, separable diastereomers). (See Spectra)

Major Diastereomer:

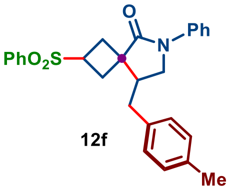
- **M.P.:** 140 – 150 °C
- **TLC (EtOAc:Hexane, 3:7 v/v):** R_f = 0.32, UV
- **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.91 (d, *J* = 8.3 Hz, 2H, Ar*H*), 7.68 (t, *J* = 7.4 Hz, 1H, Ar*H*), 7.57 (dd, *J* = 21.9, 7.9 Hz, 4H, Ar*H*), 7.31 (t, *J* = 7.6 Hz, 4H, Ar*H*), 7.24 – 7.20 (m, 1H, Ar*H*), 7.16 (d, *J* = 7.5 Hz, 2H, Ar*H*), 7.11 (t, *J* = 7.4 Hz, 1H, Ar*H*), 3.75 (p, *J* = 9.1 Hz, 1H, $PhSO_2CH$), 3.55 (dd, *J* = 10.0, 5.8 Hz, 1H), 3.39 (dd, *J* = 10.2, 4.9 Hz, 1H), 3.14 – 2.97 (m, 2H), 2.89 (dd, *J* = 12.4, 10.0 Hz, 1H), 2.69 – 2.56 (m, 2H), 2.46 (ddd, *J* = 12.6, 8.3, 4.4 Hz, 1H), 2.17 (ddd, *J* = 12.5, 8.4, 4.4 Hz, 1H).

- **^{13}C NMR (101 MHz, CDCl$_3$):** δ 173.8, 139.0, 138.0, 137.2, 133.9, 129.3, 128.9, 128.8, 128.6, 128.6, 126.9, 124.6, 119.4, 52.2, 49.5, 45.6, 42.0, 34.9, 30.8, 25.6.
- **IR (Neat):** υ 2928 (w), 2856 (w), 1696 (s), 1595 (w), 1493 (m), 1393 (m), 1312 (m), 1279 (m), 1214 (w), 1146 (s), 1085 (m), 757 (m), 725 (m), 693 (m).
- **HRMS (ESI):** calcd. for $C_{26}H_{26}NO_3S^+$ $[M+H]^+$ 432.1633; found: 432.1630.

Minor Diastereomer:

- **TLC (EtOAc:Hexane, 3:7 v/v):** $R_f = 0.5$, UV
- **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.90 (d, *J* = 7.7 Hz, 2H, Ar*H*), 7.66 (t, *J* = 7.4 Hz, 1H, Ar*H*), 7.61 – 7.49 (m, 4H, Ar*H*), 7.32 (td, *J* = 7.8, 7.2, 3.9 Hz, 4H, Ar*H*), 7.28 – 7.26 (m, 1H, Ar*H*), 7.20 (d, *J* = 7.5 Hz, 2H, Ar*H*), 7.13 (t, *J* = 7.4 Hz, 1H, Ar*H*), 4.19 (p, *J* = 8.6 Hz, 1H, PhSO$_2$C*H*), 3.61 (dd, *J* = 10.0, 6.8 Hz, 1H), 3.42 (dd, *J* = 10.0, 5.5 Hz, 1H), 3.19 (dd, *J* = 13.5, 3.5 Hz, 1H), 2.88 (dd, *J* = 12.0, 8.6 Hz, 1H), 2.73 (dd, *J* = 11.9, 8.6 Hz, 1H), 2.64 – 2.50 (m, 2H), 2.51 – 2.37 (m, 2H).
- **^{13}C NMR (101 MHz, CDCl$_3$):** δ 176.2, 139.0, 138.4, 137.9, 133.8, 129.3, 128.8, 128.8, 128.1, 126.7, 124.8, 119.6, 51.7, 50.1, 46.5, 42.4, 35.0, 30.8, 26.7. One carbon was not resolved at 101 MHz.
- **IR (Neat):** υ 2928 (w), 2859 (w), 1690 (s), 1596 (m), 1494 (m), 1394 (s), 1305 (s), 1146 (s), 1081 (s), 757 (s), 727 (s), 693 (s).
- **HRMS (ESI):** calcd. for $C_{26}H_{26}NO_3S^+$ $[M+H]^+$ 432.1633; found: 432.1631.

8-(4-Methylbenzyl)-6-phenyl-2-(phenylsulfonyl)-6-azaspiro[3.4]octan-5-one (12f)



12f

Following general procedure B, BCB **1l** (64 mg, 0.30 mmol, 1.0 equiv), sodium benzenesulfinate **10** (74 mg, 0.45 mmol, 1.5 equiv), 4-iodotoluene (130 mg, 0.60 mmol, 2.0 equiv) and 4CzIPN (6.0 mg, 2.5 mol%), NiCl$_2$·glyme (6.6 mg, 10 mol%), dtbpy (12 mg, 15 mol%) were stirred for 12 h. After workup, the organic phases were concentrated under vacuum. The crude product was purified by flash chromatography using silica, 2:8 v/v EtOAc:Hexane to afford the product **12f** (87.0 mg, 0.186 mmol, 62%, 2:1 *dr*, separable diastereomers). **(See Spectra)**

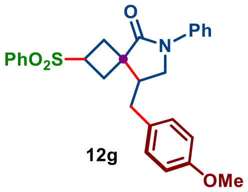
Major Diastereomer:

- **M.P.:** 192 – 196 °C
- **TLC (EtOAc:Hexane, 3:7 v/v):** R_f = 0.41, UV
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.91 (d, *J* = 8.0 Hz, 2H, Ar*H*), 7.68 (t, *J* = 7.4 Hz, 1H, Ar*H*), 7.57 (dd, *J* = 17.8, 7.7 Hz, 4H, Ar*H*), 7.35 – 7.26 (t, *J* = 8.0 Hz, 2H, Ar*H*), 7.14 – 7.07 (m, 3H, Ar*H*), 7.05 (d, *J* = 7.7 Hz, 2H, Ar*H*), 3.74 (p, *J* = 9.1 Hz, 1H, $PhSO_2CH$), 3.55 (dd, *J* = 10.0, 6.0 Hz, 1H), 3.38 (dd, *J* = 9.9, 5.7 Hz, 1H), 3.08 (t, *J* = 12.0 Hz, 1H), 2.99 (d, *J* = 9.7 Hz, 1H), 2.87 (t, *J* = 12.0 Hz, 1H), 2.66 – 2.53 (m, 2H), 2.46 (ddd, *J* = 12.6, 8.3, 4.3 Hz, 1H), 2.32 (s, 3H, $ArCH_3$), 2.15 (ddd, *J* = 12.4, 8.2, 4.3 Hz, 1H).
- **^{13}C NMR (101 MHz, $CDCl_3$):** δ 173.9, 139.1, 137.3, 136.4, 134.8, 133.8, 129.5, 129.3, 128.8, 128.6, 128.5, 124.5, 119.4, 52.1, 49.5, 45.6, 42.0, 34.4, 30.8, 25.6, 21.0.
- **IR (Neat):** υ 2924 (m), 2855 (w), 1695 (s), 1492 (m), 1391 (s), 1311 (s), 1277 (s), 1145 (s), 1084 (m), 757 (m), 725 (s), 625 (m).
- **HRMS (ESI):** calcd. for $C_{27}H_{28}NO_3S^+$ $[M+H]^+$ 446.1790; found: 446.1791.

Minor Diastereomer:

- **TLC (EtOAc:Hexane, 3:7 v/v):** R_f = 0.57, UV
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.90 (d, *J* = 7.6 Hz, 2H, Ar*H*), 7.66 (t, *J* = 7.5 Hz, 1H, Ar*H*), 7.61 – 7.49 (m, 4H, Ar*H*), 7.32 (t, *J* = 8.0 Hz, 2H, Ar*H*), 7.17 – 7.05 (m, 5H, Ar*H*), 4.19 (p, *J* = 8.5 Hz, 1H, $PhSO_2CH$), 3.60 (dd, *J* = 10.0, 6.8 Hz, 1H), 3.41 (dd, *J* = 10.0, 5.4 Hz, 1H), 3.18 – 3.10 (m, 1H), 2.88 (dd, *J* = 12.0, 8.7 Hz, 1H), 2.73 (dd, *J* = 11.8, 8.7 Hz, 1H), 2.60 – 2.50 (m, 2H), 2.49 – 2.38 (m, 2H), 2.34 (s, 3H, $ArCH_3$).
- **^{13}C NMR (101 MHz, $CDCl_3$):** δ 176.3, 139.0, 137.9, 136.2, 135.3, 133.8, 129.4, 129.3, 128.8, 128.6, 128.1, 124.7, 119.6, 51.7, 50.1, 46.5, 42.5, 34.6, 30.9, 26.7, 21.0.
- **IR (Neat):** υ 2924 (m), 2856 (w), 1691 (s), 1596 (w), 1495 (m), 1394 (s), 1305 (s), 1147 (s), 1084 (m), 759 (m), 726 (m), 691 (m).
- **HRMS (ESI):** calcd. for $C_{27}H_{28}NO_3S^+$ $[M+H]^+$ 446.1790; found: 446.1790.

8-(4-Methoxybenzyl)-6-phenyl-2-(phenylsulfonyl)-6-azaspiro[3.4]octan-5-one (12g)



12g

Following general procedure B, BCB **1l** (64 mg, 0.30 mmol, 1.0 equiv), sodium benzenesulfinate **10** (74 mg, 0.45 mmol, 1.5 equiv), 1-iodo-4-methoxybenzene **11**(140 mg, 0.600 mmol, 2.00 equiv) and 4CzIPN (6.0 mg, 2.5 mol%), $NiCl_2$·glyme (6.6 mg, 10 mol%), dtbpy (12 mg, 15 mol%) were stirred for 12 h. After the workup, the organic phases were concentrated under vacuum. The crude product was purified by flash chromatography using silica, 2:8 v/v EtOAc:Hexane to afford the product **12g** (103 mg, 0.223 mmol, 74%, 2:1 *dr*, separable diastereomers). **(See Spectra)**

Major Diastereomer:

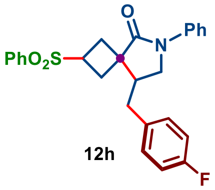
- **TLC (EtOAc:Hexane, 2:8 v/v):** R_f = 0.12, $KMnO_4$
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.91 (d, *J* = 7.7 Hz, 2H, Ar*H*), 7.68 (t, *J* = 7.4 Hz, 1H, , Ar*H*), 7.57 (dd, *J* = 20.1, 7.8 Hz, 4H, Ar*H*), 7.31 (t, *J* = 7.7 Hz, 2H, Ar*H*), 7.09 (dd, *J* = 18.8, 7.8 Hz, 3H, Ar*H*), 6.84 (d, *J* = 8.1 Hz, 2H, Ar*H*), 3.79 (s, 3H, $ArOCH_3$), 3.74 (p, *J* = 9.0 Hz, 1H, $PhSO_2CH$), 3.55 (dd, *J* = 9.9, 5.7 Hz, 1H), 3.37 (dd, *J* = 10.0, 5.1 Hz, 1H), 3.08 (dd, *J* = 11.8, 9.8 Hz, 1H), 2.98 (d, *J* = 9.5 Hz, 1H), 2.87 (dd, *J* = 12.2, 10.0 Hz, 1H), 2.63 – 2.52 (m, 2H), 2.45 (ddd, *J* = 12.4, 8.1, 4.2 Hz, 1H), 2.15 (ddd, *J* = 12.3, 8.3, 4.2 Hz, 1H).
- **^{13}C NMR (101 MHz, $CDCl_3$):** δ 173.9, 158.5, 139.1, 137.3, 133.9, 129.9, 129.6, 129.3, 128.8, 128.6, 124.6, 119.4, 114.3, 55.3, 52.2, 49.5, 45.6, 42.1, 34.1, 30.9, 25.6.
- **IR (Neat):** υ 2926 (m), 2855 (w), 2362 (m), 2334 (m), 1697 (s), 1601 (w), 1507 (m), 1279 (m), 1250 (m), 1147 (m).
- **HRMS (ESI):** calcd. for $C_{27}H_{27}NO_4SNa^+$ $[M+Na]^+$ 484.1558; found: 484.1558

Minor Diastereomer:

- **TLC (EtOAc:Hexane, 2:8 v/v):** R_f = 0.20, $KMnO_4$
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.90 (d, *J* = 7.7 Hz, 2H, Ar*H*), 7.70 – 7.51 (m, 5H, Ar*H*), 7.33 (t, *J* = 7.8 Hz, 2H, Ar*H*), 7.16 – 7.07 (m, 3H, Ar*H*), 6.91 – 6.81 (m, 2H, Ar*H*), 4.19 (p, *J* = 8.5 Hz, 1H, $PhSO_2CH$), 3.80 (d, *J* = 1.0 Hz, 3H, $ArOCH_3$), 3.61 (dd, *J* = 9.9, 6.8 Hz, 1H), 3.41 (dd, *J* = 10.0, 5.4 Hz, 1H), 3.12 (dd, *J* = 13.6, 3.6 Hz, 1H), 2.87 (dd, *J* = 12.0, 8.6 Hz, 1H), 2.72 (dd, *J* = 11.8, 8.7 Hz, 1H), 2.62 – 2.30 (m, 4H).
- **^{13}C NMR (101 MHz, $CDCl_3$):** δ 176.3, 158.4, 139.1, 137.9, 133.8, 130.4, 129.7, 129.3, 128.9, 128.2, 124.8, 119.7, 114.2, 55.3, 51.8, 50.1, 46.5, 42.6, 34.1, 31.0, 26.7.

- **IR (Neat):** υ 2928 (m), 2855 (w), 1691 (s), 1602 (w), 1506 (m), 1395 (m), 1306 (m), 1248 (s).
- **HRMS (ESI):** calcd. for $C_{27}H_{27}NO_4SNa^+$ $[M+Na]^+$ 484.1558; found: 484.1556.

8-(4-Fluorobenzyl)-6-phenyl-2-(phenylsulfonyl)-6-azaspiro[3.4]octan-5-one (12h)



12h

Following general procedure B, BCB **1l** (64 mg, 0.30 mmol, 1.0 equiv), sodium benzenesulfinate **10** (74 mg, 0.45 mmol, 1.5 equiv), 1-iodo-4-fluorobenzene (133 mg, 0.600 mmol, 2.00 equiv) and 4CzIPN (6.0 mg, 2.5 mol%), $NiCl_2$·glyme (6.6 mg, 10 mol%), dtbpy (12 mg, 15 mol%) were stirred for 12 h. After the workup, the organic phases were concentrated under vacuum. The crude product was purified by flash chromatography using silica, 2:8 v/v EtOAc:Hexane to afford the product **12h** (82.0 mg, 0.182 mmol, 61%, 2:1 *dr*, separable diastereomers). **(See Spectra)**

Major Diastereomer:

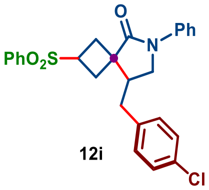
- **M.P.:** 175 – 185 °C
- **TLC (EtOAc:Hexane, 3:7 v/v):** $R_f = 0.54$, UV
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.91 (d, *J* = 7.9 Hz, 2H, Ar*H*), 7.72 – 7.64 (m, 1H, Ar*H*), 7.62 – 7.49 (m, 4H, Ar*H*), 7.31 (t, *J* = 7.2 Hz, 2H, Ar*H*), 7.16 – 7.06 (m, 3H, Ar*H*), 6.99 (t, *J* = 7.8 Hz, 2H, Ar*H*), 3.76 (p, *J* = 9.1 Hz, 1H, $PhSO_2CH$), 3.54 (dd, *J* = 10.2, 5.6 Hz, 1H), 3.36 (dd, *J* = 10.7, 5.0 Hz, 1H), 3.12 – 2.95 (m, 2H), 2.94 – 2.84 (m, 1H), 2.66 – 2.52 (m, 2H), 2.44 (ddd, *J* = 12.6, 8.2, 4.4 Hz, 1H), 2.17 (ddd, *J* = 12.5, 8.4, 4.4 Hz, 1H).
- **^{13}C NMR (101 MHz, $CDCl_3$):** δ 173.7, 161.7 (d, *J* = 245.5 Hz), 139.0, 137.2, 133.9, 133.6 (d, *J* = 3.3 Hz), 130.0 (d, *J* = 7.9 Hz), 129.3, 128.8, 128.6, 124.6, 119.3, 115.7 (d, *J* = 21.4 Hz), 52.1, 49.3, 45.6, 42.0, 34.1, 30.8, 25.5.
- **^{19}F NMR (377 MHz, $CDCl_3$):** δ -115.66
- **IR (Neat):** υ 2924 (m), 2855 (w), 1695 (s), 1597 (w), 1502 (s), 1447 (w), 1393 (s), 1311 (s), 1278 (s), 1218 (s), 1147 (s), 1086 (m), 821 (m), 759 (s), 726 (s), 691 (s).
- **HRMS (ESI):** calcd. for $C_{26}H_{24}FNO_3SNa^+$ $[M+Na]^+$ 472.1359; found: 472.1362.

Minor Diastereomer:

- **TLC (EtOAc:Hexane, 3:7 v/v):** $R_f = 0.66$, UV

- **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.89 (d, *J* = 8.2 Hz, 2H, Ar*H*), 7.66 (t, *J* = 7.5 Hz, 1H, Ar*H*), 7.61 – 7.49 (m, 4H, Ar*H*), 7.33 (t, *J* = 8.1 Hz, 2H, Ar*H*), 7.21 – 7.09 (m, 3H, Ar*H*), 7.01 (t, *J* = 8.7 Hz, 2H, Ar*H*), 4.18 (p, *J* = 8.5 Hz, 1H, PhSO$_2$C*H*), 3.61 (dd, *J* = 10.0, 6.8 Hz, 1H), 3.39 (dd, *J* = 10.0, 5.5 Hz, 1H), 3.16 (dd, *J* = 13.6, 3.5 Hz, 1H), 2.86 (dd, *J* = 12.1, 8.5 Hz, 1H), 2.71 (dd, *J* = 11.9, 8.6 Hz, 1H), 2.56 (m, 2H), 2.51 – 2.38 (m, 2H).
- **^{13}C NMR (101 MHz, CDCl$_3$):** δ 176.1, 161.6 (d, *J* = 245.0 Hz), 138.9, 137.8, 134.1 (d, *J* = 3.2 Hz), 133.8, 130.2 (d, *J* = 8.0 Hz), 129.3, 128.8, 128.1, 124.8, 119.6, 115.6 (d, *J* = 21.1 Hz), 51.7, 49.9, 46.4, 42.5, 34.2, 30.8, 26.6.
- **^{19}F NMR (377 MHz, CDCl$_3$):** δ -116.13
- **IR (Neat):** υ 2925 (w), 1689 (s), 1597 (m), 1502 (s), 1395 (s), 1306 (s), 1219 (s), 1145 (s), 1081 (s), 825 (w), 759 (s), 727 (s), 692 (s), 636 (s), 573 (s).
- **HRMS (ESI):** calcd. for $C_{26}H_{25}FNO_3S^+$ $[M+H]^+$ 450.1539; found: 450.1536.

8-(4-Chlorobenzyl)-6-phenyl-2-(phenylsulfonyl)-6-azaspiro[3.4]octan-5-one (12i)



12i

Following general procedure B, BCB **1l** (64 mg, 0.30 mmol, 1.0 equiv), sodium benzenesulfinate **10** (74 mg, 0.45 mmol, 1.5 equiv), 1-bromo-4-chlorobenzene (115 mg, 0.600 mmol, 2.00 equiv) and 4CzIPN (6.0 mg, 2.5 mol%), NiCl$_2$·glyme (6.6 mg, 10 mol%), dtbpy (12 mg, 15 mol%) were stirred for 12 h. After the workup, the organic phases were concentrated under vacuum. The crude product was purified by flash chromatography using silica, 2:8 v/v EtOAc:Hexane to afford the product **12i** (78.0 mg, 0.164 mmol, 56%, 2:1 *dr*, separable diastereomers). **(See Spectra)**

Major Diastereomer:

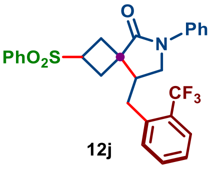
- **M.P.:** 195 – 206 °C
- **TLC (EtOAc:Hexane, 3:7 v/v):** R_f = 0.28, UV
- **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.92 (d, *J* = 8.0 Hz, 2H, Ar*H*), 7.70 (t, *J* = 7.2 Hz, 1H, Ar*H*), 7.64 – 7.52 (m, 4H, Ar*H*), 7.38 – 7.28 (m, 4H, Ar*H*), 7.18 – 7.09 (m, 3H, Ar*H*), 3.78 (p, *J* = 9.1 Hz, 1H, PhSO$_2$C*H*), 3.57 (dd, *J* = 10.0, 5.6 Hz, 1H), 3.38 (dd, *J* = 10.1, 4.9 Hz, 1H), 3.14 – 2.97 (m, 2H), 2.97 – 2.87 (m, 1H), 2.69 – 2.55 (m, 2H), 2.46 (ddd, *J* = 12.6, 8.2, 4.4 Hz, 1H), 2.19 (ddd, *J* = 13.1, 8.4, 4.3 Hz, 1H).

- **^{13}C NMR (101 MHz, CDCl$_3$):** δ 173.6, 138.9, 137.2, 136.5, 133.9, 132.7, 129.9, 129.3, 129.0, 128.8, 128.5, 124.6, 119.3, 52.1, 49.2, 45.6, 41.8, 34.3, 30.8, 25.5.
- **IR (Neat):** υ 2927 (w), 1642 (s), 1490 (m), 1401 (m), 1282 (w), 1147 (m), 1087 (m), 1013 (m), 802 (m), 760 (w), 724 (w), 690 (w).
- **HRMS (ESI):** calcd. for $C_{26}H_{25}ClNO_3S^+$ [M+H]$^+$ 466.1244; found: 466.1246.

Minor Diastereomer:

- **TLC (EtOAc:Hexane, 3:7 v/v):** R$_f$ = 0.42, UV
- **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.92 (d, *J* = 8.3 Hz, 2H, Ar*H*), 7.74 – 7.65 (m, 1H, Ar*H*), 7.63 – 7.57 (m, 2H, Ar*H*), 7.54 (d, *J* = 8.4 Hz, 2H, Ar*H*), 7.41 – 7.31 (m, 4H, Ar*H*), 7.17 (d, *J* = 7.9 Hz, 3H, Ar*H*), 4.20 (p, *J* = 8.7 Hz, 1H, PhSO$_2$C*H*), 3.63 (dd, *J* = 10.0, 6.8 Hz, 1H), 3.40 (dd, *J* = 10.2, 5.4 Hz, 1H), 3.19 (dd, *J* = 13.5, 3.6 Hz, 1H), 2.88 (dd, *J* = 12.1, 8.5 Hz, 1H), 2.74 (dd, *J* = 12.0, 8.5 Hz, 1H), 2.59 (ddd, *J* = 12.2, 9.0, 4.0 Hz, 2H), 2.54 – 2.40 (m, 2H).
- **^{13}C NMR (101 MHz, CDCl$_3$):** δ 176.0, 138.9, 137.8, 136.9, 133.9, 132.6, 130.1, 129.4, 128.9, 128.9, 128.1, 124.9, 119.6, 51.7, 49.9, 46.4, 42.4, 34.4, 30.8, 26.6.
- **IR (Neat):** υ 2934 (w), 1689 (s), 1595 (m), 1491 (s), 1395 (s), 1305 (s), 1144 (s), 1082 (s), 758 (s), 727 (s), 690 (s), 634 (s).
- **HRMS (ESI):** calcd. for $C_{26}H_{25}ClNO_3S^+$ [M+H]$^+$ 466.1244; found: 466.1241.

6-Phenyl-2-(phenylsulfonyl)-8-(2-(trifluoromethyl)benzyl)-6-azaspiro[3.4]octan-5-one (12j)



12j

Following general procedure B, BCB **1l** (64 mg, 0.30 mmol, 1.0 equiv), sodium benzenesulfinate **10** (74 mg, 0.45 mmol, 1.5 equiv), 1-iodo-2-(trifluoromethyl)benzene (163 mg, 0.600 mmol, 2.00 equiv) and 4CzIPN (6.0 mg, 2.5 mol%), NiCl$_2$·glyme (6.6 mg, 10 mol%), dtbpy (12 mg, 15 mol%) were stirred for 12 h. After the workup, the organic phases were concentrated under vacuum. The crude product was purified by flash chromatography using silica, 2:8 v/v EtOAc:Hexane to afford the product **12j** (39.0 mg, 0.078 mmol, 26%, 2:1 *dr*, separable diastereomers). **(See Spectra)**

Major Diastereomer:

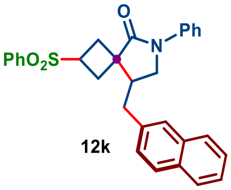
- **TLC (EtOAc:Hexane, 3:7 v/v):** R$_f$ = 0.32, UV

- **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.94 (d, *J* = 8.0 Hz, 2H, Ar*H*), 7.68 (d, *J* = 7.9 Hz, 2H, Ar*H*), 7.63 – 7.57 (m, 2H, Ar*H*), 7.54 (dd, *J* = 9.5, 2.6 Hz, 2H, Ar*H*), 7.49 (d, *J* = 7.6 Hz, 1H, Ar*H*), 7.37 (t, *J* = 7.7 Hz, 1H, Ar*H*), 7.35 – 7.29 (m, 2H, Ar*H*), 7.28 (s, 1H, Ar*H*), 7.12 (t, *J* = 7.4 Hz, 1H, Ar*H*), 3.83 (p, *J* = 9.1 Hz, 1H, PhSO$_2$C*H*), 3.53 (dd, *J* = 9.9, 6.2 Hz, 1H), 3.45 (dd, *J* = 10.0, 5.7 Hz, 1H), 3.25 (d, *J* = 12.1 Hz, 1H), 3.08 (dd, *J* = 12.0, 9.7 Hz, 1H), 2.97 – 2.88 (m, 1H), 2.74 (t, *J* = 12.6 Hz, 1H), 2.65 (d, *J* = 13.5 Hz, 1H), 2.46 (ddd, *J* = 12.7, 8.3, 4.3 Hz, 1H), 2.29 – 2.14 (m, 1H).
- **^{13}C NMR (101 MHz, CDCl$_3$):** δ 173.6, 139.0, 137.1, 136.7, 133.9, 132.1, 131.2, 129.3, 128.8, 128.6, 127.2, 126.8 (q, *J* = 11.2, Hz), 124.7, 124.6 (q, *J* = 290 Hz), 119.4, 52.1, 48.9, 45.9, 41.6, 31.4, 30.5, 25.4. ** One of the peaks was not resolved at 101 MHz.
- **^{19}F NMR (377 MHz, CDCl$_3$):** δ -58.67
- **IR (Neat):** υ 2922 (m), 2855 (w), 1697 (s), 1597 (w), 1493 (m), 1394 (m), 1310 (s), 1282 (s), 1149 (s), 1112 (s), 1034 (m), 762 (s), 726 (s), 690 (s).
- **HRMS (ESI):** calcd. for $C_{27}H_{24}F_3NO_3SNa^+$ $[M+Na]^+$ 522.1327; found: 522.1327.

Minor Diastereomer

- **TLC (EtOAc:Hexane, 3:7 v/v):** R_f = 0.45, UV.
- **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.94 – 7.87 (m, 2H, Ar*H*), 7.71 – 7.61 (m, 2H, Ar*H*), 7.58 (t, *J* = 7.9 Hz, 2H, Ar*H*), 7.52 (dd, *J* = 7.6, 5.0 Hz, 3H, Ar*H*), 7.35 (dt, *J* = 18.7, 7.5 Hz, 4H, Ar*H*), 7.17 – 7.09 (m, 1H, Ar*H*), 4.19 (p, *J* = 8.7 Hz, 1H, PhSO$_2$C*H*), 3.60 (dd, *J* = 9.9, 6.6 Hz, 1H), 3.45 (dd, *J* = 9.9, 5.9 Hz, 1H), 3.41 – 3.32 (m, 1H), 2.87 (dd, *J* = 12.1, 8.6 Hz, 1H), 2.79 – 2.68 (m, 2H), 2.60 (dddd, *J* = 20.6, 12.0, 8.0, 4.2 Hz, 2H), 2.46 (ddd, *J* = 12.2, 8.5, 3.7 Hz, 1H).
- **^{13}C NMR (101 MHz, CDCl$_3$):** δ 176.0, 138.9, 137.8, 137.3, 133.8, 132.1, 131.1, 129.4, 128.9, 128.2, 126.9, 126.6 (d, *J* = 5.8 Hz), 124.9, 119.7, 51.7, 49.9, 46.5, 42.1, 31.3, 30.3, 26.6. ** Two of the peaks were not resolved at 101 MHz.
- **^{19}F NMR (376 MHz, CDCl$_3$):** δ -58.62
- **IR (Neat):** υ 2924 (m), 2855 (w), 1691 (s), 1596 (w), 1494 (m), 1398 (m), 1308 (s), 1148 (s), 1116 (m), 1084 (m), 760 (m), 726 (m), 692 (m).
- **HRMS (ESI):** calcd. for $C_{27}H_{24}F_3NO_3SNa^+$ $[M+Na]^+$ 522.1327; found: 522.1325.

8-(Naphthalen-2-ylmethyl)-6-phenyl-2-(phenylsulfonyl)-6-azaspiro[3.4]octan-5-one (12k)



12k

Following general procedure B, BCB **1l** (64 mg, 0.30 mmol, 1.0 equiv), sodium benzenesulfinate **10** (74 mg, 0.45 mmol, 1.5 equiv), 2-bromonaphthalene (124 mg, 0.600 mmol, 2.00 equiv) and 4CzIPN (6.0 mg, 2.5 mol%), $NiCl_2$·glyme (6.6 mg, 10 mol%), dtbpy (12 mg, 15 mol%) were stirred for 12 h. After the workup, the organic phases were concentrated under vacuum. The crude product was purified by flash chromatography using silica, 2:8 v/v EtOAc:Hexane to afford the product **12k** (95.0 mg, 0.195 mmol, 65%, 2:1 *dr*, separable diastereomers). **(See Spectra)**

Major Diastereomer:

- **M.P.:** 188 – 195 °C
- **TLC (EtOAc:Hexane, 3:7 v/v):** R_f = 0.25, UV
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.88 (d, *J* = 7.7 Hz, 2H, Ar*H*), 7.85 – 7.72 (m, 3H, Ar*H*), 7.70 – 7.63 (m, 1H, Ar*H*), 7.63 – 7.45 (m, 7H, Ar*H*), 7.32 – 7.27 (m, 3H, Ar*H*), 7.10 (t, *J* = 7.4 Hz, 1H, Ar*H*), 3.79 (p, *J* = 9.1 Hz, 1H, $PhSO_2CH$), 3.55 (dd, *J* = 9.9, 5.9 Hz, 1H), 3.43 (dd, *J* = 9.9, 5.4 Hz, 1H), 3.19 (t, *J* = 10.0 Hz, 1H), 3.15 – 3.06 (m, 1H), 2.92 (dd, *J* = 12.4, 9.9 Hz, 1H), 2.83 – 2.69 (m, 2H), 2.51 (ddd, *J* = 12.6, 8.3, 4.4 Hz, 1H), 2.18 (ddd, *J* = 12.5, 8.4, 4.4 Hz, 1H).
- **^{13}C NMR (101 MHz, $CDCl_3$):** δ 173.8, 139.0, 137.2, 135.5, 133.8, 133.4, 132.3, 129.3, 128.8, 128.7, 128.5, 127.7, 127.4, 127.2, 126.6, 126.4, 125.8, 124.5, 119.3, 52.2, 49.5, 45.7, 41.8, 35.1, 30.9, 25.6.
- **IR (Neat):** υ 2923 (m), 2855(w), 1694 (s), 1493 (m), 1310 (s), 1275 (s), 1213 (w), 1144 (s), 1085 (m), 817 (w), 753 (m), 726 (s), 690 (m).
- **HRMS (ESI):** calcd. for $C_{30}H_{27}NO_3SNa^+$ $[M+Na]^+$ 504.1609; found: 504.1608.

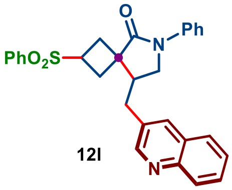
Minor Diastereomer:

- **TLC (EtOAc:Hexane, 3:7 v/v):** R_f = 0.41, UV
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.91 (d, *J* = 7.7 Hz, 2H, Ar*H*), 7.87 – 7.76 (m, 3H, Ar*H*), 7.66 (d, *J* = 6.3 Hz, 2H, Ar*H*), 7.62 – 7.54 (m, 2H, Ar*H*), 7.54 – 7.43 (m, 4H, Ar*H*), 7.39 – 7.28 (m, 3H, Ar*H*), 7.12 (t, *J* = 7.4 Hz, 1H, Ar*H*), 4.21 (p, *J* = 8.5 Hz, 1H, $PhSO_2CH$), 3.61

(dd, *J* = 10.0, 6.7 Hz, 1H), 3.47 (dd, *J* = 10.1, 5.4 Hz, 1H), 3.36 (dd, *J* = 13.2, 3.3 Hz, 1H), 2.94 (dd, *J* = 12.1, 8.6 Hz, 1H), 2.78 (dd, *J* = 11.9, 8.7 Hz, 1H), 2.74 – 2.66 (m, 1H), 2.65 – 2.54 (m, 2H), 2.50 (ddd, *J* = 12.2, 8.5, 3.7 Hz, 1H).

- **^{13}C NMR (101 MHz, CDCl$_3$):** δ 176.2, 139.0, 137.8, 135.9, 133.8, 133.5, 132.2, 129.4, 128.9, 128.6, 128.2, 127.7, 127.5, 127.3, 127.0, 126.3, 125.7, 124.8, 119.6, 51.7, 50.1, 46.5, 42.3, 35.2, 30.9, 26.7.
- **IR (Neat):** υ 2924 (m), 2856 (w), 1690 (s), 1596 (m), 1494 (m), 1394 (s), 1304 (s), 1145 (s), 1082 (s), 819 (m), 754 (s), 727 (s), 689 (s).
- **HRMS (ESI):** calcd. for $C_{30}H_{28}NO_3S^+$ [M+H]$^+$ 482.1790; found: 482.1794.

6-Phenyl-2-(phenylsulfonyl)-8-(quinolin-3-ylmethyl)-6-azaspiro[3.4]octan-5-one (12l)



12l

Following general procedure B, BCB **1l** (64 mg, 0.30 mmol, 1.0 equiv), sodium benzenesulfinate **10** (74 mg, 0.45 mmol, 1.5 equiv), 3-bromoquinoline **11**(125 mg, 0.600 mmol, 2.00 equiv) and 4CzIPN (6.0 mg, 2.5 mol%), NiCl$_2$·glyme (6.6 mg, 10 mol%), dtbpy (12 mg, 15 mol%) were stirred for 12 h. After the workup, the organic phases were concentrated under vacuum. The crude product was purified by flash chromatography using silica, 3:7 v/v EtOAc:Hexane to afford the product **12l** (92 mg, 0.185 mmol, 62%, 2:1 *dr*, separable diastereomers). **(See Spectra)**

Major Diastereomer:

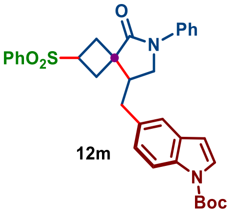
- **M.P.:** 155 - 160 °C
- **TLC (EtOAc:Hexane, 3:7 v/v):** R$_f$ = 0.08, KMnO$_4$
- **^{1}H NMR (400 MHz, CDCl$_3$):** δ 8.77 (d, *J* = 2.2 Hz, 1H, Ar*H*), 8.09 (d, *J* = 8.5 Hz, 1H, Ar*H*), 7.98 – 7.88 (m, 3H, Ar*H*), 7.80 – 7.65 (m, 3H, Ar*H*), 7.61 – 7.49 (m, 4H, Ar*H*), 7.29 (t, *J* = 8.1 Hz, 3H, Ar*H*), 7.10 (td, *J* = 8.6, 7.4, 1.2 Hz, 1H, Ar*H*), 3.86 (p, *J* = 9.1 Hz, 1H, PhSO$_2$C*H*), 3.63 – 3.53 (m, 1H), 3.42 (dd, *J* = 10.1, 5.2 Hz, 1H), 3.25 (d, *J* = 10.6 Hz, 1H), 3.12 (dd, *J* = 12.1, 9.7 Hz, 1H), 2.98 (dd, *J* = 12.5, 10.0 Hz, 1H), 2.83 – 2.72 (m, 2H), 2.52 (ddd, *J* = 12.7, 8.2, 4.4 Hz, 1H), 2.24 (ddd, *J* = 12.5, 8.3, 4.4 Hz, 1H).

- **^{13}C NMR (101 MHz, CDCl$_3$):** δ 173.5, 151.1, 147.2, 138.9, 137.2, 135.1, 134.0, 130.7, 129.5, 129.4, 129.2, 128.9, 128.6, 127.8, 127.3, 127.2, 124.7, 119.4, 52.2, 49.2, 45.8, 41.8, 32.3, 30.9, 25.6.
- **IR (Neat):** υ 2927 (w), 2856 (w), 2357 (w), 1696 (s), 1596 (m), 1494 (m), 1394 (m), 1312 (m), 1147 (m), 724 (m).
- **HRMS (ESI):** calcd. for $C_{29}H_{27}N_2O_3S^+$ $[M+H]^+$ 483.1742; found: 483.1742.

Minor Diastereomer:

- **TLC (EtOAc:Hexane, 3:7 v/v):** $R_f = 0.15$, $KMnO_4$
- **^{1}H NMR (400 MHz, CDCl$_3$):** δ 8.81 (d, *J* = 2.2 Hz, 1H, Ar*H*), 8.11 (d, *J* = 8.4 Hz, 1H, Ar*H*), 8.05 – 7.99 (m, 1H, Ar*H*), 7.90 (d, *J* = 7.7 Hz, 2H, Ar*H*), 7.81 (d, *J* = 8.2 Hz, 1H, Ar*H*), 7.69 (dt, *J* = 19.3, 7.4 Hz, 2H, Ar*H*), 7.57 (t, *J* = 7.6 Hz, 3H, Ar*H*), 7.50 (d, *J* = 8.2 Hz, 2H, Ar*H*), 7.31 (t, *J* = 7.8 Hz, 2H, Ar*H*), 7.12 (t, *J* = 7.4 Hz, 1H, Ar*H*), 4.20 (p, *J* = 8.4 Hz, 1H, PhSO$_2$C*H*), 3.64 (dd, *J* = 10.0, 6.1 Hz, 1H), 3.51 – 3.33 (m, 2H), 3.03 – 2.87 (m, 1H), 2.81 – 2.47 (m, 5H).
- **^{13}C NMR (101 MHz, CDCl$_3$):** δ 175.9, 151.4, 147.2, 138.8, 137.8, 135.2, 133.9, 131.2, 129.4, 129.3, 129.2, 128.9, 128.2, 127.9, 127.4, 127.1, 124.9, 119.6, 51.7, 50.0, 46.4, 42.2, 32.5, 30.8, 26.6.
- **IR (Neat):** υ 2938 (w), 2360 (m), 1692 (m), 1596 (m), 1495 (w), 1397 (m), 1306 (m), 1147 (m), 756 (s).
- **HRMS (ESI):** calcd. for $C_{29}H_{27}N_2O_3S^+$ $[M+H]^+$ 483.1742; found: 483.1740.

***tert*-Butyl 5-((5-oxo-6-phenyl-2-(phenylsulfonyl)-6-azaspiro[3.4]octan-8-yl)methyl)-1H-indole-1-carboxylate (12m)**



12m

Following general procedure B, BCB **1l** (64 mg, 0.30 mmol, 1.0 equiv), sodium benzenesulfinate **10** (74 mg, 0.45 mmol, 1.5 equiv), *tert*-butyl 5-bromo-1*H*-indole-1-carboxylate (124 mg, 0.600 mmol, 2.00 equiv) and 4CzIPN (6.0 mg, 2.5 mol%), NiCl$_2$·glyme (6.6 mg, 10 mol%), dtbpy (12 mg, 15 mol%) were stirred for 12 h. After the workup, the organic phases were concentrated under vacuum. The crude product was purified by flash chromatography using silica, 2:8 v/v EtOAc:Hexane to afford the product **12m** (105 mg, 0.184 mmol, 61%, 4:1 *dr*, separable diastereomers). **(See Spectra)**

Major Diastereomer:

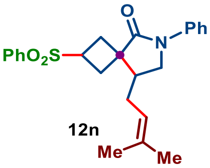
- **M.P.:** 198 – 210 °C
- **TLC (EtOAc:Hexane, 3:7 v/v):** R_f = 0.27, UV
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.90 (d, *J* = 8.1 Hz, 2H, Ar*H*), 7.71 – 7.63 (m, 1H, Ar*H*), 7.62 – 7.50 (m, 5H, Ar*H*), 7.42 – 7.27 (m, 4H, Ar*H*), 7.16 – 7.06 (m, 2H, Ar*H*), 6.50 (d, *J* = 3.7 Hz, 1H, Ar*H*), 3.76 (p, *J* = 9.1 Hz, 1H, $PhSO_2CH$), 3.52 (dd, *J* = 10.0, 5.6 Hz, 1H), 3.40 (dd, *J* = 10.1, 5.1 Hz, 1H), 3.20 – 3.05 (m, 2H), 2.88 (dd, *J* = 12.4, 9.9 Hz, 1H), 2.79 – 2.64 (m, 2H), 2.49 (ddd, *J* = 12.6, 8.2, 4.3 Hz, 1H), 2.16 (ddd, *J* = 12.5, 8.4, 4.4 Hz, 1H), 1.67 (s, 9H, $C(CH_3)_3$).
- **^{13}C NMR (101 MHz, $CDCl_3$):** δ 174.0, 149.6, 139.1, 137.3, 133.8, 132.2, 131.0, 129.3, 128.8, 128.6, 126.5, 124.7, 124.5, 120.7, 119.4, 115.4, 106.9, 83.8, 52.2, 49.5, 45.7, 42.4, 34.8, 30.9, 28.1, 25.7. ** One of the peaks was not resolved at 101 MHz.
- **IR (Neat):** υ 2975 (w), 2929 (w), 2857 (w), 1730 (s), 1698 (s), 1471 (m), 1376 (s), 1319 (s), 1217 (w), 1143 (s), 1085 (m), 762 (m), 728 (s).
- **HRMS (ESI):** calcd. for $C_{33}H_{35}N_2O_5S^+$ $[M+H]^+$ 571.2267; found: 571.2266.

Minor Diastereomer:

- **TLC (EtOAc:Hexane, 3:7 v/v):** R_f = 0.38, UV
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.09 (d, *J* = 8.5 Hz, 1H, Ar*H*), 7.94 – 7.87 (m, 2H, Ar*H*), 7.71 – 7.62 (m, 1H, Ar*H*), 7.63 – 7.49 (m, 5H, Ar*H*), 7.39 (d, *J* = 1.6 Hz, 1H, Ar*H*), 7.31 (t, *J* = 7.8 Hz, 2H, Ar*H*), 7.19 – 7.08 (m, 2H, Ar*H*), 6.53 (d, *J* = 3.7 Hz, 1H, Ar*H*), 4.20 (p, *J* = 8.5 Hz, 1H, $PhSO_2CH$), 3.57 (dd, *J* = 10.0, 6.8 Hz, 1H), 3.44 (dd, *J* = 10.0, 5.5 Hz, 1H), 3.29 (dd, *J* = 13.4, 3.4 Hz, 1H), 2.91 (dd, *J* = 12.0, 8.6 Hz, 1H), 2.75 (dd, *J* = 11.8, 8.7 Hz, 1H), 2.70 – 2.42 (m, 4H), 1.67 (s, 9H, $C(CH_3)_3$).
- **^{13}C NMR (101 MHz, $CDCl_3$):** δ 176.3, 149.6, 139.1, 137.9, 133.8, 132.7, 131.0, 129.3, 128.8, 128.2, 126.4, 125.0, 124.7, 120.8, 119.6, 115.3, 107.0, 83.7, 51.8, 50.1, 46.5, 42.8, 34.9, 30.9, 28.1, 26.7. ** One of the peaks was not resolved at 101 MHz.

- **IR (Neat):** υ 2933 (w), 1730 (s), 1692 (s), 1595 (w), 1472 (m), 1376 (s), 1345 (s), 1308 (s), 1258 (m), 1142 (s), 1083 (m), 761 (m), 728 (m), 690 (m).
- **HRMS (ESI):** calcd. for $C_{33}H_{35}N_2O_5S^+$ $[M+H]^+$ 571.2267; found: 571.2264.

8-(3-Methylbut-2-en-1-yl)-6-phenyl-2-(phenylsulfonyl)-6-azaspiro[3.4]octan-5-one (12n)



12n

Following general procedure B, BCB **1l** (64 mg, 0.30 mmol, 1.0 equiv), sodium benzenesulfinate **10** (74 mg, 0.45 mmol, 1.5 equiv), 1-bromo-2-methylprop-1-ene (81 mg, 0.60 mmol, 2.0 equiv) and 4CzIPN (6.0 mg, 2.5 mol%), $NiCl_2$·glyme (6.6 mg, 10 mol%), dtbpy (12 mg, 15 mol%) were stirred for 12 h. After the workup, the organic phases were concentrated under vacuum. The crude product was purified by flash chromatography using silica, 2:8 v/v EtOAc:Hexane to afford the product **12n** (45 mg, 0.110 mmol, 37%, 2:1 *dr*, separable diastereomers). **(See Spectra)**

Major Diastereomer:

- **TLC (EtOAc:Hexane, 2:8 v/v):** R_f = 0.19, $KMnO_4$
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.94 – 7.85 (m, 2H, Ar*H*), 7.67 (t, *J* = 7.2 Hz, 1H, Ar*H*), 7.61 – 7.54 (m, 4H, Ar*H*), 7.33 (t, *J* = 7.7 Hz, 2H, Ar*H*), 7.12 (t, *J* = 7.4 Hz, 1H, Ar*H*), 5.07 (t, *J* = 7.1 Hz, 1H, alkene C*H*), 3.84 – 3.65 (m, 2H), 3.36 (dd, *J* = 9.7, 5.5 Hz, 1H), 3.01 (dd, *J* = 11.8, 9.7 Hz, 1H), 2.83 (dd, *J* = 12.2, 10.1 Hz, 1H), 2.32 (tdd, *J* = 14.8, 9.9, 5.3 Hz, 3H), 2.12 (ddt, *J* = 15.1, 10.7, 5.8 Hz, 2H), 1.68 (s, 3H), 1.55 (s, 3H).
- **^{13}C NMR (101 MHz, $CDCl_3$):** δ 174.0, 139.2, 137.3, 135.0, 133.8, 129.3, 128.8, 128.6, 124.5, 120.2, 119.4, 52.2, 49.9, 45.4, 40.7, 31.1, 27.6, 25.8, 25.5, 17.9.
- **IR (Neat):** υ 2925 (m), 2857 (w), 1694 (s), 1595 (m), 1493 (m), 1392 (s), 1311 (s), 1280 (s), 1146 (s), 724 (s).
- **HRMS (ESI):** calcd. for $C_{24}H_{27}NO_3SNa^+$ $[M+Na]^+$ 432.1607; found: 432.1606.

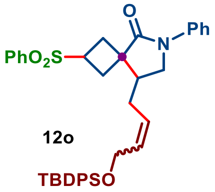
Minor Diastereomer:

- **TLC (EtOAc:Hexane, 2:8 v/v):** R_f = 0.28, $KMnO_4$
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.95 – 7.79 (m, 2H, Ar*H*), 7.68 – 7.61 (m, 1H, Ar*H*), 7.60 – 7.50 (m, 4H, Ar*H*), 7.35 (t, *J* = 7.8 Hz, 2H, Ar*H*), 7.18 – 7.08 (m, 1H, Ar*H*), 5.11 (t, *J* =

7.2 Hz, 1H, alkene C*H*), 4.16 (p, *J* = 8.6 Hz, 1H, $PhSO_2CH$), 3.81 (dd, *J* = 9.8, 7.0 Hz, 1H), 3.39 (dd, *J* = 9.8, 5.2 Hz, 1H), 2.79 (dd, *J* = 12.0, 8.8 Hz, 1H), 2.66 (dd, *J* = 11.7, 8.8 Hz, 1H), 2.49 (ddd, *J* = 12.0, 8.4, 3.9 Hz, 1H), 2.41 – 2.19 (m, 3H), 2.04 (dt, *J* = 14.5, 9.2 Hz, 1H), 1.61 (s, 3H), 1.59 (s, 3H).

- **^{13}C NMR (101 MHz, $CDCl_3$):** δ 176.5, 139.2, 138.0, 134.9, 133.8, 129.3, 128.9, 128.1, 124.7, 120.3, 119.7, 51.8, 50.6, 46.3, 41.1, 31.4, 27.7, 26.7, 25.9, 18.0.
- **IR (Neat):** υ 2928 (m), 1689 (s), 1596 (m), 1495 (m), 1398 (s), 1306 (s), 1147 (s), 727 (m).
- **HRMS (ESI):** calcd. for $C_{24}H_{27}NO_3SNa^+$ $[M+Na]^+$ 432.1607; found: 432.1610.

8-(4-((*tert*-Butyldiphenylsilyl)oxy)but-2-en-1-yl)-6-phenyl-2-(phenylsulfonyl)-6-azaspiro[3.4]octan-5-one (12o)



12o

Following general procedure B, BCB **1l** (64 mg, 0.30 mmol, 1.0 equiv), sodium benzenesulfinate **10** (74 mg, 0.45 mmol, 1.50 equiv), (*Z*)-((3-bromoallyl)oxy)(*tert*-butyl)diphenylsilane 225 mg, 0.600 mmol, 2.00 equiv) and 4CzIPN (6.0 mg, 2.5 mol%), $NiCl_2$·glyme (6.6 mg, 10 mol%), dtbpy (12 mg, 15 mol%) were stirred for 12 h. After the workup, the organic phases were concentrated under vacuum. The crude product was purified by flash chromatography using silica, 2:8 v/v EtOAc:Hexane to afford the product **12o** (130 mg, 0.200 mmol, 67%, 2:1 *dr*, separable diastereomers). **(See Spectra)**

Major Diastereomer with (1.5:1 *E/Z*):

- **TLC (EtOAc:Hexane, 2:8 v/v):** R_f = 0.08, $KMnO_4$
- **^1H NMR (400 MHz, $CDCl_3$):** δ 7.91 (dd, *J* = 7.5, 5.3 Hz, 2H, Ar*H* for both diastereomers), 7.70 – 7.53 (m, 9H, Ar*H* for both diastereomers), 7.46 – 7.30 (m, 8H, Ar*H* for both diastereomers), 7.12 (q, *J* = 7.5 Hz, 1H, Ar*H* for both diastereomers), 5.87 – 5.69 (m, 0.5H, alkene C*H* for both diastereomers), 5.63 (d, *J* = 3.7 Hz, 1H, alkene C*H* for both diastereomers), 5.44 – 5.29 (m, 0.5H, alkene C*H* for both diastereomers), 4.18 (d, *J* = 8.6 Hz, 2H), 3.79 (p, *J* = 9.1 Hz, 0.6H, $PhSO_2CH$ for major diastereomer), 3.71 – 3.60 (m, 1.4H), 3.37 (dd, *J* = 10.0, 5.8 Hz, 0.6H), 3.24 (dd, *J* = 9.9, 6.0 Hz, 0.4H), 3.03 (ddd, *J* =

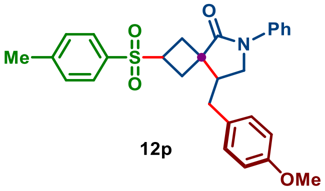
13.8, 11.9, 9.8 Hz, 1H), 2.81 (ddd, *J* = 34.7, 12.3, 10.1 Hz, 1H), 2.41 – 2.29 (m, 1.4H), 2.21 – 1.94 (m, 3.6H), 1.04 (dd, *J* = 15.4, 1.3 Hz, 9H, C(C*H*$_3$)$_3$ for both diastereomers).

- **^{13}C NMR (101 MHz, CDCl$_3$):** δ 173.8, 173.8, 139.1, 139.0, 137.3, 135.5, 135.4, 135.4, 133.8, 133.5, 133.5, 133.3, 133.31, 132.3, 132.2, 129.7, 129.6, 129.3, 128.8, 128.5, 127.7, 127.6, 127.6, 126.4, 126.0, 124.5, 119.4, 119.3, 63.8, 59.9, 52.1, 52.0, 49.6, 49.6, 45.3, 45.2, 40.2, 40.0, 31.7, 31.0, 30.7, 26.8, 26.7, 25.4, 19.2, 19.1. Eight peaks were not resolved at 101MHz.
- **IR (Neat):** υ 2935 (m), 2857 (w), 2360 (m), 1699 (s), 1596 (m), 1494 (m), 1393 (m), 1313 (m), 1279 (s), 1147 (s), 754 (s).
- **HRMS (ESI):** calcd. for $C_{39}H_{43}NO_4SSiNa^+$ [M+Na]$^+$ 672.2580; found: 672.2582.

Minor Diastereomer with (1.6:1 *E/Z*):

- **TLC (EtOAc:Hexane, 2:8 v/v):** R$_f$ = 0.11, KMnO$_4$
- **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.87 (dd, *J* = 12.9, 7.7 Hz, 2H, Ar*H* for both diastereomers), 7.72 – 7.61 (m, 5H, Ar*H* for both diastereomers), 7.59 – 7.49 (m, 4H, Ar*H* for both diastereomers), 7.45 – 7.28 (m, 8H, Ar*H* for both diastereomers), 7.14 (q, *J* = 7.5 Hz, 1H, Ar*H* for both diastereomers), 5.77 (dt, *J* = 12.2, 6.4 Hz, 0.5H, alkene C*H* for both diastereomers), 5.64 (d, *J* = 3.6 Hz, 1H, alkene C*H* for both diastereomers), 5.50 – 5.32 (m, 0.5H, alkene C*H* for both diastereomers), 4.29 – 4.05 (m, 3H), 3.73 (ddd, *J* = 12.3, 9.7, 7.0 Hz, 1H), 3.39 (dd, *J* = 10.0, 5.5 Hz, 0.7H), 3.27 (dd, *J* = 10.0, 5.5 Hz, 0.3H), 2.78 (dd, *J* = 12.0, 8.8 Hz, 0.6H), 2.71 – 2.13 (m, 5.4H), 1.99 (ddt, *J* = 23.8, 13.9, 7.1 Hz, 1H), 1.05 (d, *J* = 14.2 Hz, 9H, C(C*H*$_3$)$_3$ for both diastereomers).
- **^{13}C NMR (101 MHz, CDCl$_3$):** δ 176.3, 176.2, 139.1, 139.0, 137.9, 137.9, 135.5, 135.5, 135.5, 133.8, 133.7, 133.6, 133.5, 133.5, 132.2, 132.1, 129.7, 129.6, 129.3, 128.9, 128.1, 127.7, 127.6, 126.7, 126.3, 124.7, 119.7, 64.0, 60.0, 51.7, 51.6, 50.4, 50.3, 46.2, 46.0, 40.4, 40.2, 32.0, 31.1, 31.1, 26.8, 26.8, 26.7, 19.2, 19.1. Nine peaks were not resolved at 101MHz.
- **IR (Neat):** υ 2933 (m), 2856 (w), 1690 (s), 1595 (m), 1493 (m), 1394 (s), 1306 (s), 1145 (s), 693 (s).
- **HRMS (ESI):** calcd. for $C_{39}H_{43}NO_4SSiNa^+$ [M+Na]$^+$ 672.2580; found: 672.2579.

8-(4-Methoxybenzyl)-6-phenyl-2-tosyl-6-azaspiro[3.4]octan-5-one (12p)



12p

Following general procedure B, BCB **1l** (64 mg, 0.30 mmol, 1.0 equiv), sodium 4-methylbenzenesulfinate (80 mg, 0.45 mmol, 1.5 equiv), 4-bromobenzonitrile **11** (110 mg, 0.600 mmol, 2.00 equiv) and 4CzIPN (6.0 mg, 2.5 mol%), $NiCl_2$·glyme (6.6 mg, 10 mol%), dtbpy (12 mg, 15 mol%) were stirred for 12 h. After the workup, the organic phases were concentrated under vacuum. The crude product was purified by flash chromatography using silica, 2:8 v/v EtOAc:Hexane to afford the product **12p** (83 mg, 0.174 mmol, 58%, 1.2:1 *dr*, separable diastereomers). **(See Spectra)**

Major Diastereomer:

- **TLC (EtOAc:Hexane, 2:8 v/v):** R_f = 0.13, $KMnO_4$
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.78 (d, *J* = 7.9 Hz, 2H, Ar*H*), 7.54 (d, *J* = 8.1 Hz, 2H, Ar*H*), 7.36 (d, *J* = 8.0 Hz, 2H, Ar*H*), 7.30 (t, *J* = 7.8 Hz, 2H, Ar*H*), 7.09 (dd, *J* = 15.7, 7.9 Hz, 3H, Ar*H*), 6.83 (d, *J* = 8.2 Hz, 2H, Ar*H*), 3.78 (s, 3H, ArOCH_3), 3.72 (q, *J* = 9.1 Hz, 1H, ArSO$_2$C*H*), 3.54 (dd, *J* = 9.9, 6.1 Hz, 1H), 3.41 – 3.32 (m, 1H), 3.05 (dd, *J* = 12.0, 9.7 Hz, 1H), 3.00 – 2.92 (m, 1H), 2.85 (dd, *J* = 12.3, 10.0 Hz, 1H), 2.64 – 2.50 (m, 2H), 2.43-2.47 (m, 4H), 2.14 (ddd, *J* = 12.4, 8.4, 4.4 Hz, 1H).
- **^{13}C NMR (101 MHz, $CDCl_3$):** δ 173.9, 158.4, 144.8, 139.1, 134.3, 129.9, 129.8, 129.5, 128.7, 128.5, 124.5, 119.3, 114.2, 55.2, 52.2, 49.4, 45.5, 42.1, 33.9, 30.8, 25.5, 21.6.
- **IR (Neat):** υ 2930 (m), 2334 (w), 1695 (s), 1597 (w), 1504 (m), 1391 (m), 1311 (m), 1245 (s), 1143 (s).
- **HRMS (ESI):** calcd. for $C_{28}H_{29}NO_4SNa^+$ $[M+Na]^+$ 498.1715; found: 498.1714.

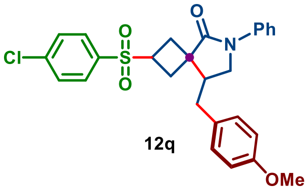
Minor Diastereomer:

- **TLC (EtOAc:Hexane, 2:8 v/v):** R_f = 0.21, $KMnO_4$
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.77 (d, *J* = 7.9 Hz, 2H, Ar*H*), 7.53 (d, *J* = 8.1 Hz, 2H, Ar*H*), 7.40 – 7.30 (m, 4H, Ar*H*), 7.12 (dd, *J* = 10.2, 7.8 Hz, 3H, Ar*H*), 6.86 (d, *J* = 8.2 Hz, 2H, Ar*H*), 4.15 (p, *J* = 8.5 Hz, 1H, ArSO$_2$C*H*), 3.80 (s, 3H, ArOCH_3), 3.60 (dd, *J* = 9.9, 6.8

Hz, 1H), 3.40 (dd, *J* = 10.0, 5.4 Hz, 1H), 3.12 (dd, *J* = 13.6, 3.6 Hz, 1H), 2.85 (dd, *J* = 12.1, 8.6 Hz, 1H), 2.70 (dd, *J* = 11.8, 8.6 Hz, 1H), 2.59 – 2.26 (m, 7H).

- **^{13}C NMR (101 MHz, CDCl$_3$):** δ 176.3, 158.3, 144.8, 139.1, 134.9, 130.4, 130.0, 129.7, 128.9, 128.2, 124.7, 119.6, 114.2, 55.3, 51.8, 50.0, 46.4, 42.6, 34.1, 31.0, 26.7, 21.6.
- **IR (Neat):** υ 2927 (m), 2856 (w), 2362 (m), 1691 (s), 1599 (m), 1506 (m), 1395 (m), 1307 (s), 1145 (s), 758 (m).
- **HRMS (ESI):** calcd. for $C_{28}H_{29}NO_4SNa^+$ $[M+Na]^+$ 498.1715; found: 498.1716.

2-((4-Chlorophenyl)sulfonyl)-8-(4-methoxybenzyl)-6-phenyl-6-azaspiro[3.4]octan-5-one (12q)



12q

Following general procedure B, BCB **1l** (64 mg, 0.30 mmol, 1.0 equiv), sodium 4-chlorobenzenesulfinate **10** (90 mg, 0.45 mmol, 1.5 equiv), 4-bromobenzonitrile **11**(110 mg, 0.600 mmol, 2.00 equiv) and 4CzIPN (6.0 mg, 2.5 mol%), NiCl$_2$·glyme (6.6 mg, 10 mol%), dtbpy (12 mg, 15 mol%) were added stirred for 12 h. After the workup, the organic phases were concentrated under vacuum. The crude product was purified by flash chromatography using silica, 2:8 v/v EtOAc:Hexane to afford the product **12q** (92.0 mg, 0.185 mmol, 62%, 2:1 *dr*, separable diastereomers). (See Spectra)

Major Diastereomer:

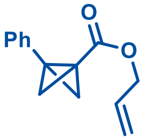
- **M.P.:** 95 - 100 °C
- **TLC (EtOAc:Hexane, 2:8 v/v):** R_f = 0.12, KMnO$_4$
- **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.82 (d, *J* = 8.3 Hz, 2H, Ar*H*), 7.58 – 7.49 (m, 4H, Ar*H*), 7.31 (t, *J* = 7.8 Hz, 2H, Ar*H*), 7.10 (dd, *J* = 15.9, 7.9 Hz, 3H, Ar*H*), 6.84 (d, *J* = 8.1 Hz, 2H, Ar*H*), 3.78 (s, 3H, ArOC*H*$_3$), 3.71 (p, *J* = 9.1 Hz, 1H, ArSO$_2$C*H*), 3.57 – 3.51 (m, 1H), 3.38 (dd, *J* = 10.0, 5.5 Hz, 1H), 3.06 (dd, *J* = 12.0, 9.7 Hz, 1H), 2.97 (d, *J* = 9.4 Hz, 1H), 2.84 (dd, *J* = 12.4, 9.9 Hz, 1H), 2.69 – 2.53 (m, 2H), 2.46 (ddd, *J* = 12.5, 8.3, 4.4 Hz, 1H), 2.14 (ddd, *J* = 12.5, 8.4, 4.3 Hz, 1H).
- **^{13}C NMR (101 MHz, CDCl$_3$):** δ 173.9, 158.4, 140.6, 139.0, 135.8, 130.0, 129.8, 129.6, 129.5, 128.8, 124.6, 119.3, 114.2, 55.2, 52.1, 49.5, 45.5, 42.0, 34.0, 30.8, 25.5.

- **IR (Neat):** υ 2933 (m), 2853 (w), 1696 (s), 1594 (m), 1507 (m), 1393 (m), 1316 (m), 1279 (s), 1148 (s), 757 (m).
- **HRMS (ESI):** calcd. for $C_{27}H_{26}ClNO_4SNa^+$ $[M+Na]^+$ 518.1169; found: 518.1167.

Minor Diastereomer:

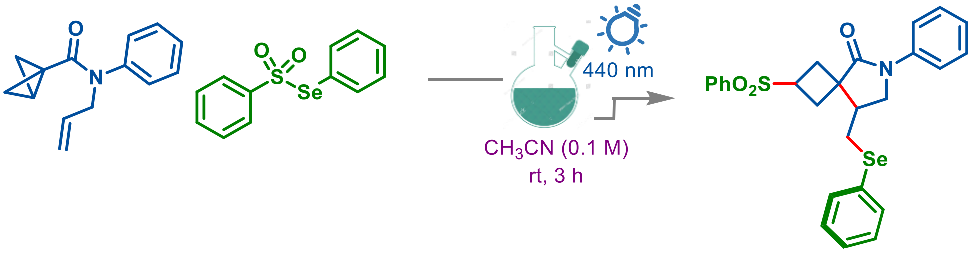
- **TLC (EtOAc:Hexane, 2:8 v/v):** $R_f = 0.19$, $KMnO_4$
- **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.83 (d, *J* = 8.3 Hz, 2H, Ar*H*), 7.59 – 7.49 (m, 4H, Ar*H*), 7.33 (t, *J* = 7.8 Hz, 2H, Ar*H*), 7.13 (dd, *J* = 11.6, 7.8 Hz, 3H, Ar*H*), 6.86 (d, *J* = 8.2 Hz, 2H, Ar*H*), 4.17 (p, *J* = 8.5 Hz, 1H, $ArSO_2CH$), 3.80 (s, 3H, $ArOCH_3$), 3.61 (dd, *J* = 10.0, 6.8 Hz, 1H), 3.41 (dd, *J* = 10.0, 5.4 Hz, 1H), 3.12 (dd, *J* = 13.8, 3.8 Hz, 1H), 2.85 (dd, *J* = 12.0, 8.6 Hz, 1H), 2.70 (dd, *J* = 11.8, 8.7 Hz, 1H), 2.63 – 2.20 (m, 4H).
- **^{13}C NMR (101 MHz, CDCl$_3$):** δ 176.1, 158.4, 140.7, 139.0, 136.4, 130.3, 129.7, 129.6, 128.9, 124.8, 119.7, 114.2, 55.3, 51.9, 50.1, 46.5, 42.6, 34.2, 30.9, 26.7. One carbon was not resolved at 101 MHz.
- **IR (Neat):** υ 2929 (m), 2855 (w), 1691 (s), 1590 (m), 1506 (m), 1395 (m), 1311 (m), 1248 (m), 1148 (s), 1086 (s), 757 (m).
- **HRMS (ESI):** calcd. for $C_{27}H_{26}ClNO_4SNa^+$ $[M+Na]^+$ 518.1169; found: 518.1168.

Unsuccessful substrate



4. Procedures for scale-up the reaction and product modifications

4.1 Reaction scale up

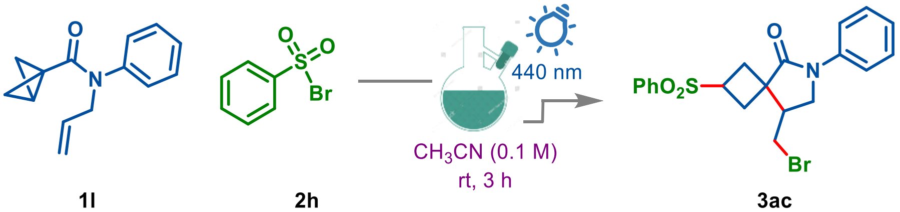


1l 2.0 mmol

2g 2.0 mmol

3aa Yield 70%

Following the general procedure A, an oven-dried 30 mL glass vial was charged with the BCB **1l** (427 mg, 2.00 mmol, 1.00 equiv) and interelement radical precursor **2g** (595 mg, 2.00 mmol, 1.00 equiv). Next, the vial was closed with a screw-cap septum. The vial was degassed and refilled with nitrogen using the Schlenk-line technique (three times). CH_3CN (20 mL, 0.10 M) was added to the mixture and stirred for 3 h under the irradiation of a 457 nm Kessil lamp. The solvent was evaporated under vacuum. The crude reaction mixture was purified by flash column chromatography using EtOAc:Hexane 1:9 mixture as mobile phase to afford the pure product **3aa** as a colorless sticky liquid (717 mg, 1.41 mmol, 70%).

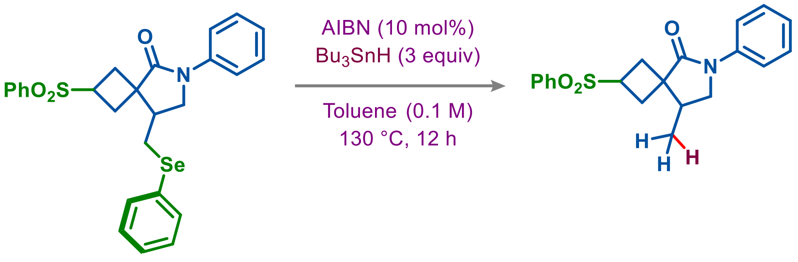


1l 2.0 mmol **2h** 2.0 mmol **3ac** Yield 50%

Following the general procedure A , an oven-dried 20 mL glass vial was charged with the BCB **1l** (427 mg, 2.00 mmol, 1.00 equiv) and the interelement radical precursor **2h** (471 mg, 2.00 mmol, 1.00 equiv). Next, the vial was closed with a screw-cap septum. The vial was degassed and refilled with nitrogen using the Schlenk-line technique (three times). CH_3CN (15 mL, 0.13 M) was added to the mixture and stirred for 3 h under the irradiation of a 457 nm Kessil lamp. The solvent was evaporated under vacuum. The crude reaction mixture was purified by flash column chromatography using EtOAc:Hexane 1:9 mixture as mobile phase to afford the pure product **3ac** as a colorless sticky liquid (450 mg, 1.00 mmol, 50%).

4.2 Product modifications

8-Methyl-6-phenyl-2-(phenylsulfonyl)-6-azaspiro[3.4]octan-5-one (13)



3aa **13**

To a solution of selenated compound **3aa** (52 mg, 0.10 mmol, 1.0 equiv) in toluene (1 mL) under nitrogen, AIBN (2.0 mg, 10 µmol, 1.0 mol%) and Bu_3SnH (54 mg, 0.30 mmol, 3.0 equiv) were added. After stirring at 130 °C for 12 h, the reaction mixture was cooled down to room temperature and the solvent was evaporated under vacuum. The crude reaction mixture was purified by flash column chromatography using EtOAc:Hexane 2:8 mixture as mobile phase to afford the pure product **13** as a brown sticky solid (28 mg, 79 µmol, 79%, 1.2:1 *dr*). **(See Spectra)**

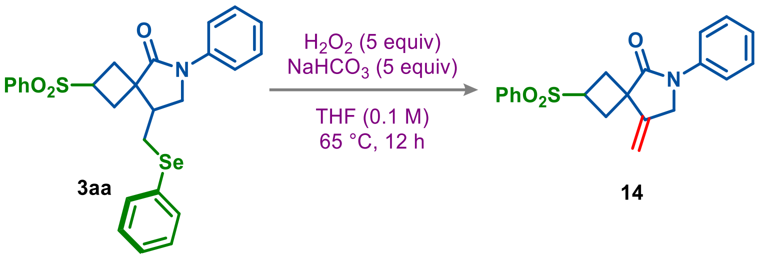
Major Diastereomer:

- **TLC (EtOAc:Hexane, 2:8 v/v):** R_f = 0.14, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.91 (d, *J* = 7.6 Hz, 2H, Ar*H*), 7.69 – 7.55 (m, 5H, Ar*H*), 7.34 (t, *J* = 7.8 Hz, 2H, Ar*H*), 7.12 (t, *J* = 7.4 Hz, 1H, Ar*H*), 3.83 – 3.70 (m, 2H), 3.32 (dd, *J* = 9.6, 6.2 Hz, 1H), 3.03 (dd, *J* = 11.9, 9.7 Hz, 1H), 2.78 (dd, *J* = 12.2, 10.0 Hz, 1H), 2.42 (h, *J* = 6.8 Hz, 1H), 2.30 (ddd, *J* = 12.5, 8.2, 4.5 Hz, 1H), 2.10 (ddd, *J* = 12.4, 8.3, 4.5 Hz, 1H), 1.19 (d, *J* = 6.9 Hz, 3H, CCH_3).
- **^{13}C NMR (101 MHz, $CDCl_3$):** δ 173.9, 139.2, 137.3, 133.8, 129.3, 128.8, 128.6, 124.5, 119.3, 52.2, 52.0, 45.8, 35.2, 30.7, 25.4, 14.1.
- **IR (Neat):** υ 2925 (w), 1696 (s), 1593 (w), 1494 (w), 1396 (s), 1311 (s), 1278 (s), 1147 (s).
- **HRMS (ESI):** calcd. for $C_{20}H_{21}NO_3SNa^+$ $[M+Na]^+$ 378.1140; found: 378.1141

Minor Diastereomer:

- **TLC (EtOAc:Hexane, 2:8 v/v):** R_f = 0.16, $KMnO_4$.
- **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.88 (dd, *J* = 7.2, 1.7 Hz, 2H, Ar*H*), 7.72 – 7.62 (m, 1H, Ar*H*), 7.57 (q, *J* = 7.6 Hz, 4H, Ar*H*), 7.42 – 7.29 (m, 2H, Ar*H*), 7.14 (t, *J* = 7.4 Hz, 1H, Ar*H*), 4.15 (p, *J* = 8.6 Hz, 1H, ArSC*H*), 3.87 (dd, *J* = 9.7, 7.1 Hz, 1H), 3.34 (dd, *J* = 9.7, 5.9 Hz, 1H), 2.75 (dd, *J* = 12.0, 8.7 Hz, 1H), 2.61 (dd, *J* = 11.8, 8.7 Hz, 1H), 2.50 (ddd, *J* = 12.0, 8.4, 3.8 Hz, 1H), 2.43 – 2.29 (m, 2H), 1.20 (d, *J* = 6.9 Hz, 3H, CCH_3).
- **^{13}C NMR (101 MHz, $CDCl_3$):** δ 176.5, 139.2, 138.0, 133.8, 129.3, 128.9, 128.1, 124.7, 119.6, 52.8, 51.6, 46.6, 35.4, 30.5, 26.3, 14.2.
- **IR (Neat):** υ 2929 (w), 1690 (s), 1596 (w), 1494 (m), 1399 (s), 1306 (s), 1147 (s), 726 (m).
- **HRMS (ESI):** calcd. for $C_{20}H_{22}NO_3S^+$ $[M+H]^+$ 356.1320; found: 356.1322

8-Methylene-6-phenyl-2-(phenylsulfonyl)-6-azaspiro[3.4]octan-5-one (14)



To a solution of selenated compound **3aa** (52 mg, 0.10 mmol, 1.0 equiv) in THF (1.0 mL) under nitrogen, $NaHCO_3$ (42 mg, 0.50 mmol, 5.0 equiv) and H_2O_2 (52 µL, 0.50 mmol, 5.0 equiv) were added. After stirring at 65 °C for 12 h, the reaction mixture was cooled down to room temperature and the solvent was evaporated under vacuum. The crude reaction mixture was purified by flash column chromatography using EtOAc:Hexane 2:8 mixture as mobile phase to afford the pure product **14** as a colorless solid (20 mg, 40 µmol, 41%, 1.2:1 *dr*). **(See Spectra)**

Major Diastereomer:

- **M.P.** 176 – 178 °C
- **TLC (EtOAc:Hexane, 2:8 v/v):** R_f = 0.14, $KMnO_4$.

  ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.95 – 7.90 (m, 2H, Ar*H*), 7.70 – 7.56 (m, 5H, Ar*H*), 7.40 – 7.34 (m, 2H, Ar*H*), 7.17 – 7.10 (m, 1H, Ar*H*), 5.35 (t, *J* = 2.3 Hz, 1H, alkene C*H*), 5.27 – 5.23 (m, 1H alkene C*H*), 4.37 (t, *J* = 2.1 Hz, 2H, NCH_2), 3.96 (p, *J* = 9.8, 8.3 Hz, 1H, ArSC*H*), 3.15 (td, *J* = 9.9, 2.7 Hz, 2H), 2.31 – 2.25 (m, 2H).

  ^{13}C NMR (101 MHz, CDCl$_3$): δ 172.9, 144.7, 138.6, 137.2, 133.9, 129.3, 128.9, 128.6, 124.8, 119.4, 107.7, 52.0, 51.3, 44.9, 32.6. One carbon was not resolved at 101 MHz.
- **IR (Neat):** υ 2924 (w), 2855 (w), 1700 (s), 1667 (w), 1496 (w), 1388 (m), 1302 (m), 1277 (m), 1146 (s).
- **HRMS (ESI):** calcd. for $C_{20}H_{19}NO_3SNa^+$ $[M+Na]^+$ 376.0983; found: 376.0983

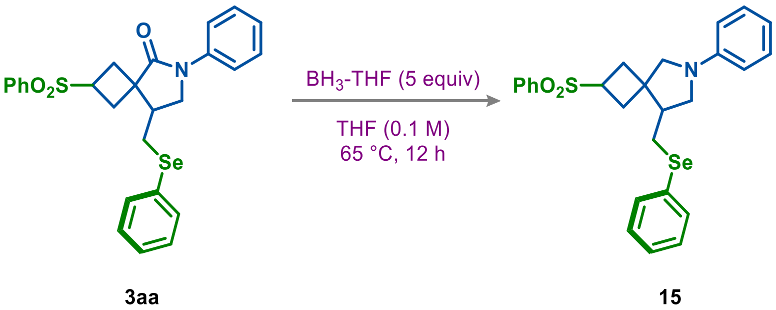
Minor Diastereomer:

- **M.P.** 162 – 164 °C
- **TLC (EtOAc:Hexane, 2:8 v/v):** R_f = 0.16, $KMnO_4$.
- **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.99 – 7.86 (m, 2H, Ar*H*), 7.72 – 7.53 (m, 5H, Ar*H*), 7.38 (t, *J* = 7.8 Hz, 2H, Ar*H*), 7.17 (t, *J* = 7.4 Hz, 1H, Ar*H*), 5.65 (d, *J* = 2.5 Hz, 1H, alkene C*H*),

5.39 (d, *J* = 2.5 Hz, 1H, alkene C*H*), 4.44 (d, *J* = 2.2 Hz, 2H, NC*H*$_2$), 4.21 (p, *J* = 8.7 Hz, 1H, ArSC*H*), 2.83 – 2.64 (m, 4H).

- **^{13}C NMR (101 MHz, CDCl$_3$):** δ 175.9, 143.6, 138.5, 137.9, 133.8, 129.4, 129.0, 128.2, 125.0, 119.8, 110.9, 51.9, 50.5, 45.0, 34.2. One carbon was not resolved at 101 MHz.
- **IR (Neat):** υ 2925 (w), 1696 (s), 1593 (w), 1494 (w), 1396 (s), 1311 (s), 1278 (s), 1147 (s).
- **HRMS (ESI):** calcd. for $C_{20}H_{20}NO_3S^+$ $[M+H]^+$ 354.1164; found: 354.1163

6-Phenyl-8-((phenylselanyl)methyl)-2-(phenylsulfonyl)-6-azaspiro[3.4]octane (15)

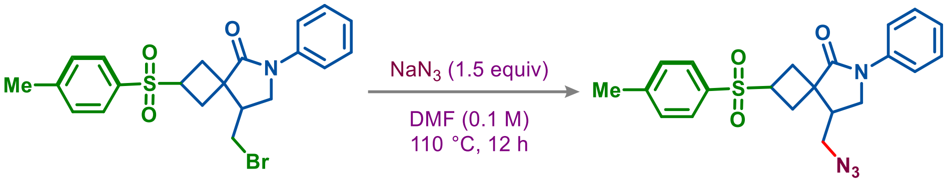


To a solution of **3aa** (52 mg, 0.10 mol, 1.0 equiv) in THF (1.0 mL), a solution of BH_3 •THF (0.5 mL, 1M, 0.5 mmol, 1 equiv) was added at room temperature. The resulting reaction mixture was heated to reflux for 12 h. After cooling down to room temperature, MeOH (2 mL) was added. After stirring for 30 minutes at room temperature, the solvent was evaporated under vacuum. The crude reaction mixture was purified by flash column chromatography using EtOAc:Hexane 2:8 mixture as mobile phase to afford the pure product **15** as a blue sticky solid (22 mg, 44 µmol, 44%, 1.1:1 *dr*, inseparable diastereomers). **(See Spectra)**

- **TLC (EtOAc:Hexane, 2:8 v/v):** R$_f$ = 0.18, KMnO$_4$.
- **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.87 (dd, *J* = 7.8, 2.8 Hz, 2H, Ar*H* for both diastereomer), 7.68 – 7.63 (m, 1H, Ar*H* for both diastereomer), 7.58 – 7.47 (m, 4H, Ar*H* for both diastereomer), 7.26 (s, 5H, Ar*H* for both diastereomer), 6.70 (q, *J* = 6.7 Hz, 1H, Ar*H* for both diastereomer), 6.50 (dd, *J* = 12.1, 8.1 Hz, 2H, Ar*H* for both diastereomer), 3.80 (p, *J* = 8.6 Hz, 0.48H, ArSC*H* for minor diastereomer), 3.67 (p, *J* = 8.5 Hz, 0.52H, ArSC*H* for major diastereomer), 3.51 – 3.44 (m, 2H), 3.37 – 3.22 (m, 2.5H), 3.09 (dd, *J* = 11.9, 3.7 Hz, 0.5H), 2.77 – 2.49 (m, 3H), 2.35 (dddd, *J* = 42.0, 21.7, 9.8, 3.9 Hz, 1.5H), 2.22 – 2.03 (m, 1.5H).

- **^{13}C NMR (101 MHz, CDCl$_3$): Major Diastereomer:** δ 147.1, 137.8, 133.1, 132.9, 129.3, 129.2, 128.3, 127.5, 116.2, 111.5, 59.1, 51.6, 46.3, 43.1, 32.5, 29.7, 27.4, 26.9. Two carbons were not resolved at 101 MHz.
- **Minor Diastereome**r: 147.2, 137.9, 133.8, 129.5, 129.3, 129.3, 128.2, 127.3, 116.3, 58.5, 52.0, 51.9, 46.6, 43.3, 32.2, 27.9, 26.9. Three carbons were not resolved at 101 MHz.
- **IR (Neat):** υ 2923 (m), 2852 (w), 1596 (m), 1476 (m), 1370 (m), 1306 (m), 1283 (m), 1145 (s).
- **HRMS (ESI):** calcd. for $C_{26}H_{28}NO_2SSe^+$ $[M+H]^+$ 498.1006; found: 498.1008

8-(Azidomethyl)-6-phenyl-2-tosyl-6-azaspiro[3.4]octan-5-one (16)



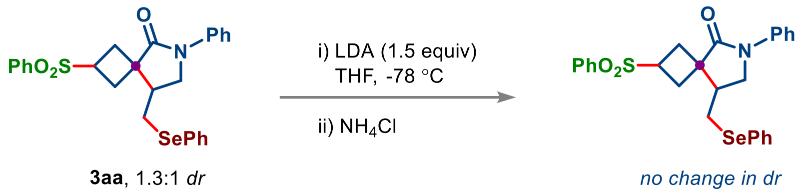
3ac **16**

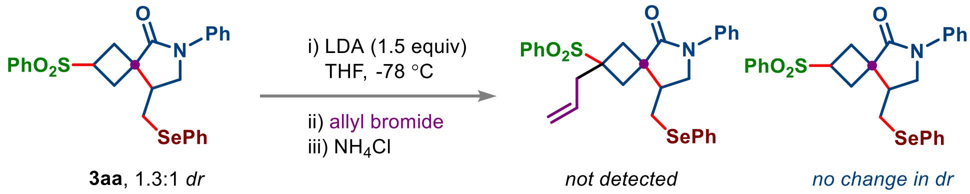
To a solution of **3ac** (44 mg, 0.10 mmol, 1.0 equiv) in DMF (1.0 mL), NaN$_3$ (10 mg, 0.15 mmol, 1.5 equiv) was added. After stirring at 110 °C for 12 h, the reaction mixture was extracted with EtOAc (2 x 5 mL). The organic phases were washed with brine (5 mL) and dried over MgSO$_4$. The solvent was evaporated under vacuum. The crude reaction mixture was purified by flash column chromatography using EtOAc:Hexane 1:9 mixture as mobile phase to afford the pure product **16** as a brown sticky solid (20 mg, 50 µmol, 50%, 2:1 *dr*, inseparable diastereomers). **(See Spectra)**

- **TLC (EtOAc:Hexane, 2.5:7.5 v/v):** $R_f = 0.15$, KMnO$_4$.
- **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.77 (dd, *J* = 14.8, 7.9 Hz, 2H, Ar*H* for both diastereomer), 7.60 (d, *J* = 8.0 Hz, 2H, Ar*H* for both diastereomer), 7.41 – 7.34 (m, 4H, Ar*H* for both diastereomer), 7.18 – 7.13 (m, 1H, Ar*H* for both diastereomer), 4.12 (p, *J* = 8.3 Hz, 0.3H, ArSC*H* for minor diastereomer), 3.94 – 3.76 (m, 1.7H), 3.65 – 3.44 (m, 3H), 3.02 – 2.90 (m, 1.5H), 2.73 – 2.64 (m, 0.5H), 2.58 – 2.52 (m, 1.5H), 2.45 (s, 3H, ArCH_3 for both diastereomer), 2.31 – 2.16 (m, 1.5H).
- **^{13}C NMR (101 MHz, CDCl$_3$): Major Diastereomer:** δ 173.0, 144.9, 138.8, 134.2, 130.0, 128.9, 128.6, 124.8, 119.4, 52.1, 51.2, 48.4, 44.4, 39.8, 31.9, 25.5, 21.7.
- **Minor Diastereomer:** δ 175.5, 145.0, 134.7, 129.0, 128.2, 125.0, 119.7, 51.8, 51.1, 49.3, 44.7, 40.0, 31.8, 21.6. Three carbons were not resolved at 101 MHz.

- **IR (Neat):** υ 2922 (s), 2855 (m), 2102 (s), 1696 (m), 1458 (m), 1281 (m), 1145 (m), 671 (w).
- **HRMS (ESI):** calcd. for $C_{21}H_{23}N_4O_3S^+$ $[M+H]^+$ 411.1491; found: 411.1495

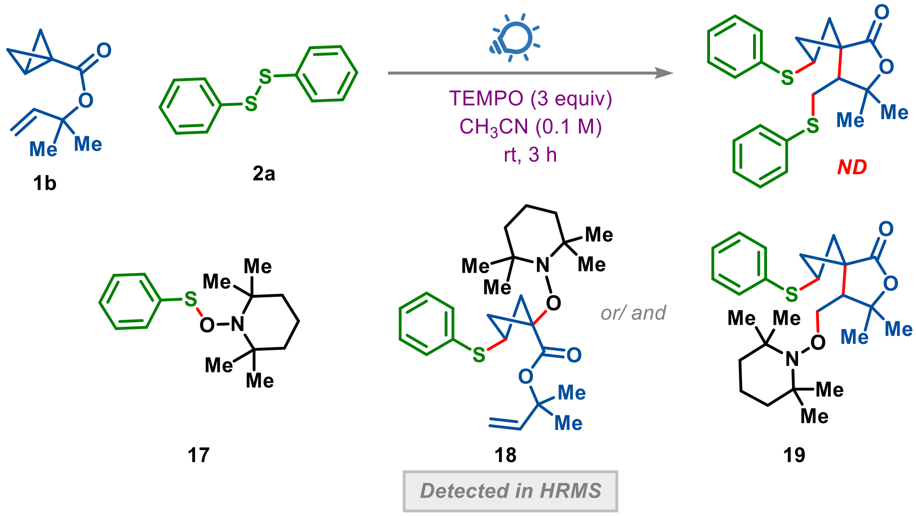
Experiments for epimerization (failed)





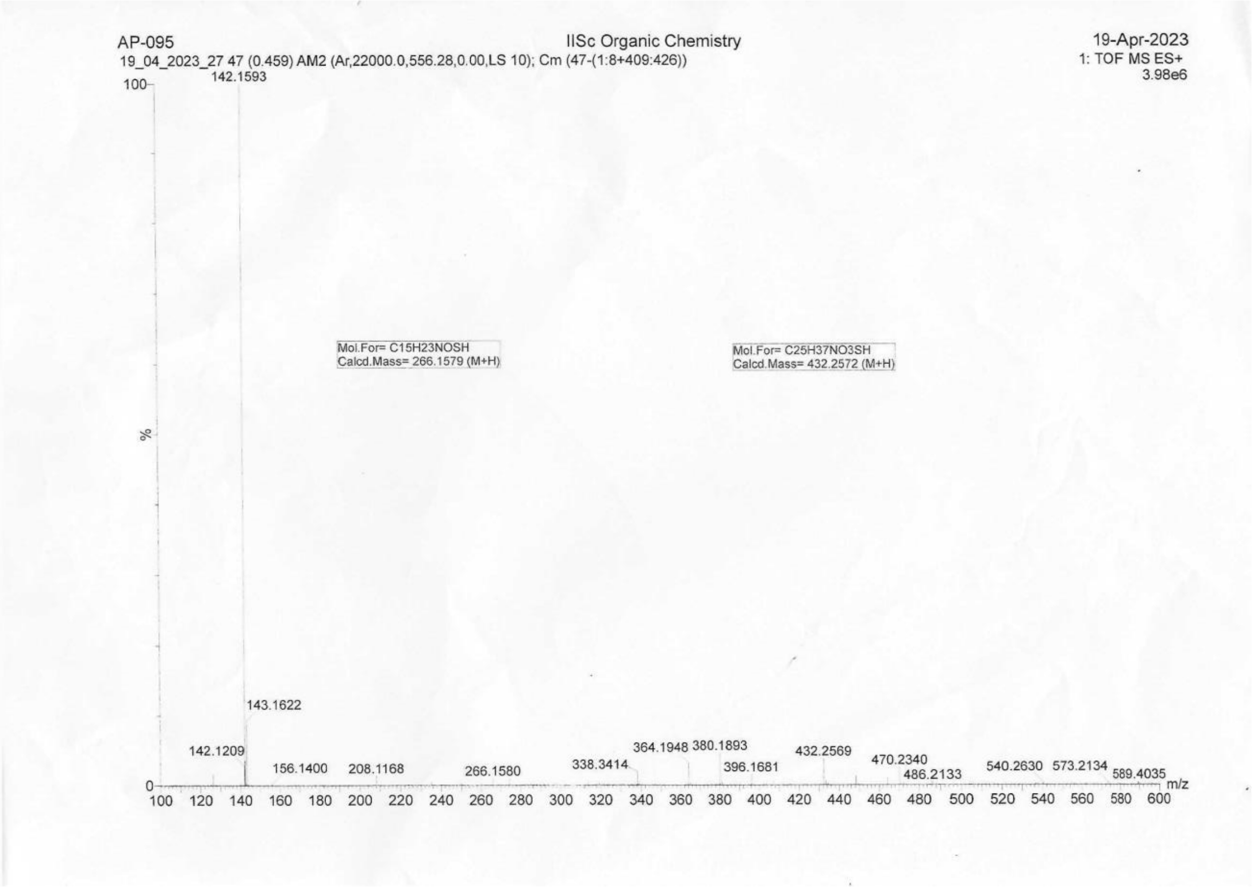
5. Mechanistic studies

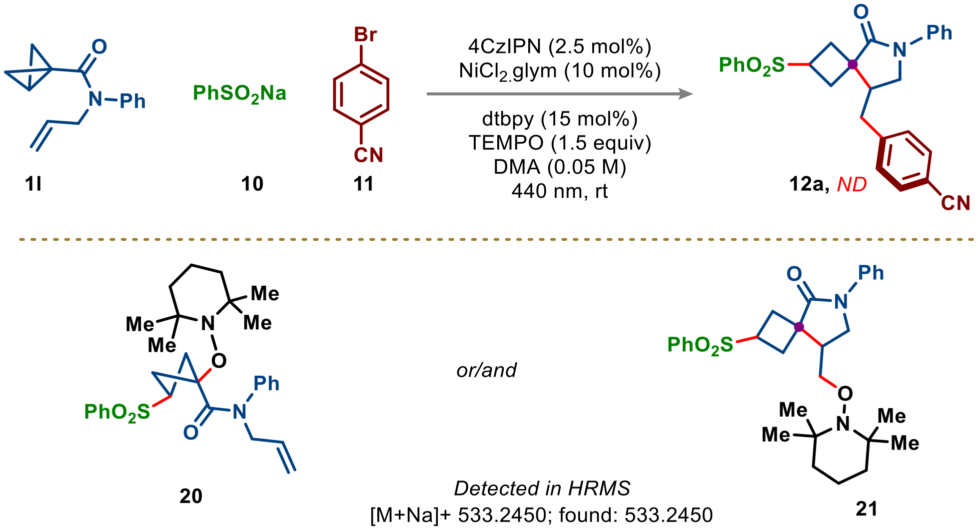
5.1 Radical trapping with TEMPO



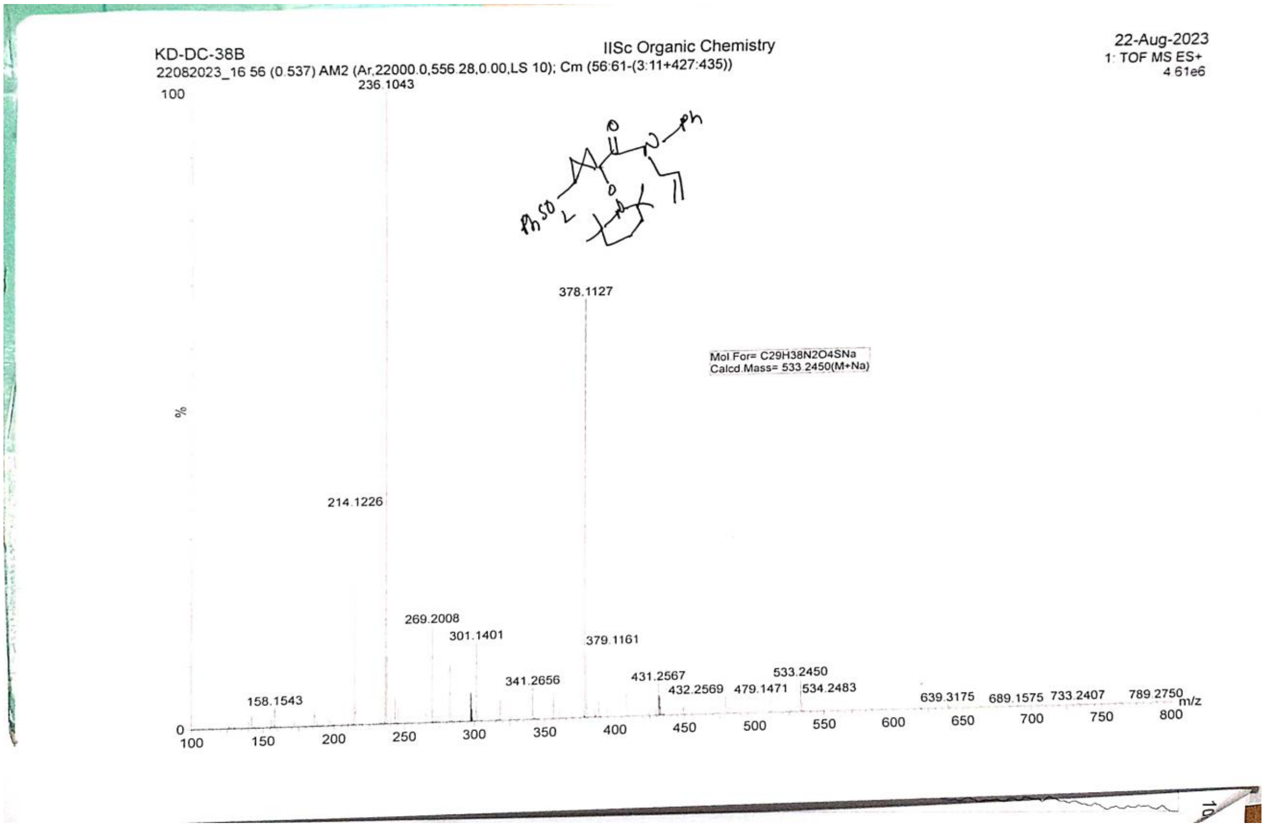
An oven-dried 4 mL glass vial was charged with the BCB **1b** (25 mg, 0.15 mmol, 1.0 equiv), 1,2-diphenyldisulfane **2a** (33 mg, 0.15 mmol, 1.0 equiv) and TEMPO (70.5 mg, 0.450 mmol, 3.00 equiv). Next, the vial was closed with a screw-cap septum. The vial was degassed and refilled with nitrogen using the Schlenk-line technique (three times). CH_3CN (1.5 mL, 0.10 M) was added to the mixture and stirred for 3 h under the irradiation of a 457 nm Kessil lamp. The solvent was evaporated under vacuum. ^{1}H NMR of the crude reaction mixture confirmed the absence of desired product formation andthe TEMPO adduct intermediates were detected in HRMS.

- **HRMS (ESI):** calcd. for $C_{15}H_{24}NOS^+$ $[M+H]^+$ 266.1579; found: 266.1580
  calcd. for $C_{25}H_{38}NO_3S^+$ $[M+H]^+$ 432.2572; found: 432.2569

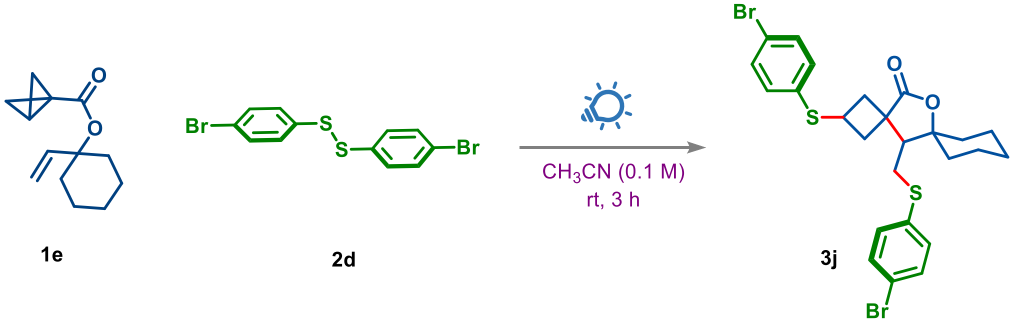


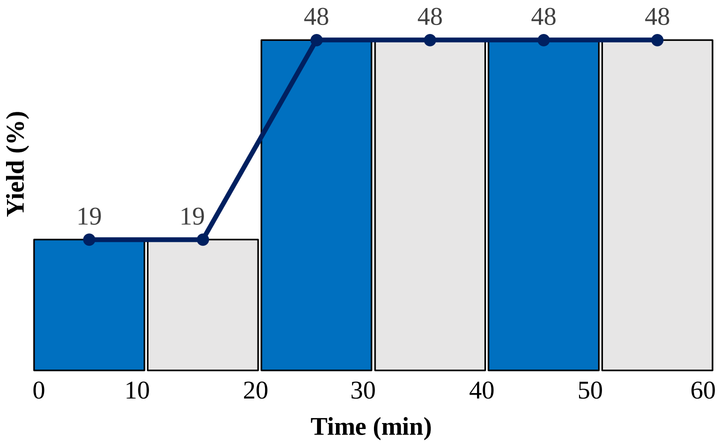


An oven-dried 4 mL glass vial was charged with the BCB **1l** (32 mg, 0.15 mmol, 1.0 equiv), sodium benzenesulfinate **10** (37.0 mg, 0.225 mmol, 1.50 equiv), 4-bromobenzonitrile **11** (55 mg, 0.30 mmol, 2.0 equiv) and 4CzIPN (3.0 mg, 2.5 mol%), $NiCl_2$·glyme (3.3 mg, 10 mol%), dtbpy (6.0 mg, 15 mol%), TEMPO (35 mg, 0.225 mmol, 1.50 equiv). Next, the vial was closed with a screw-cap septum. The vial was degassed and refilled with nitrogen using the Schlenk-line technique (three times). DMA (3.0 mL, 0.05 M) was added to the mixture and stirred under the irradiation of a 457 nm Kessil lamp. After 12 h, the reaction mixture was quenched with H_2O (10.0 mL). The resulting reaction mixture was extracted with Et_2O (2 × 5.0 mL). The combined organic phases were dried over Na_2SO_4. The solvent was removed under vacuum.



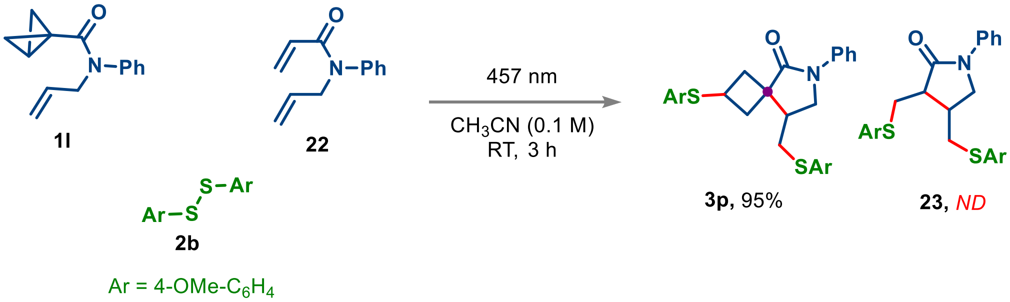
5.2 On-Off Experiment



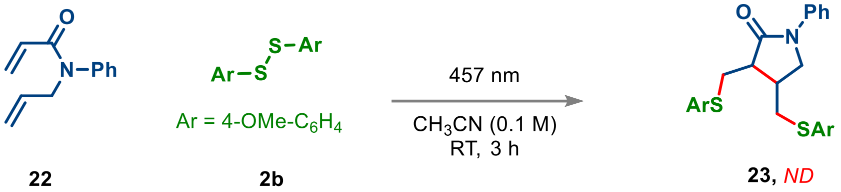


Reactions were carried out in 0.2 mmol scale. The isolated yield of the product **3j** in 0.3 mmol scale is 52%.

5.2 Control experiments

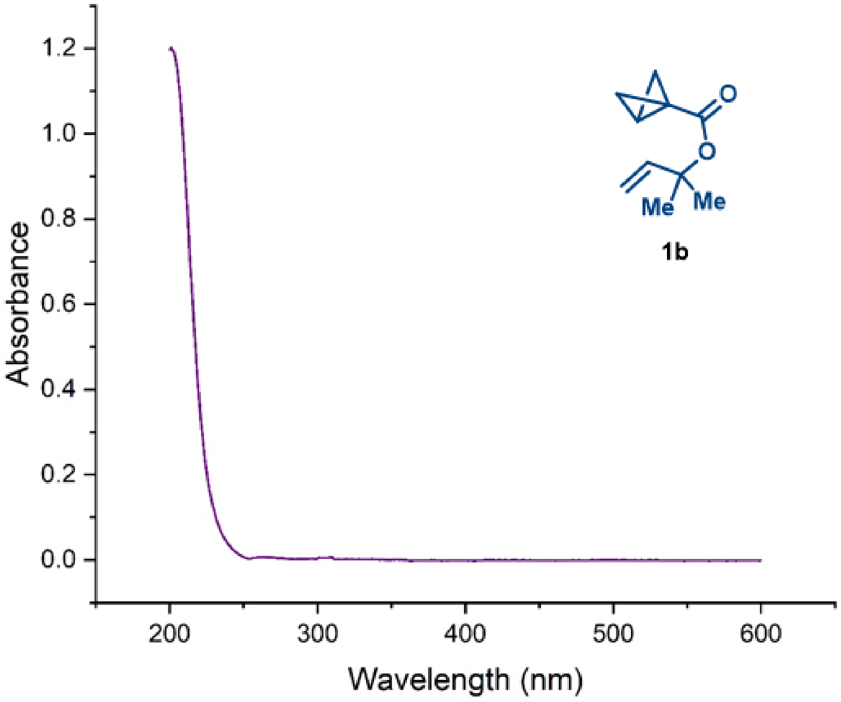


An oven-dried 4 mL glass vial was charged with the BCB **1b** (25 mg, 0.15 mmol, 1.0 equiv), 1,2-bis(4-methoxyphenyl)disulfane **2b** (42 mg, 0.15 mmol, 1.0 equiv) and *N*-allyl-*N*-phenylacrylamide (**22**) (30.5 mg, 0.150 mmol, 1.00 equiv). Next, the vial was closed with a screw-cap septum. The vial was degassed and refilled with nitrogen using the Schlenk-line technique (three times). CH$_3$CN (1.5 mL, 0.10 M) was added to the mixture and stirred for 3 h under the irradiation of a 457 nm Kessil lamp. The solvent was evaporated under vacuum. The yield of the crude product **3p** was calculated by ^{1}H NMR using CH_2Br_2 as an internal standard. Product **23** was not detected in either NMR or HRMS.



An oven-dried 4 mL glass vial was charged with *N*-allyl-*N*-phenylacrylamide (**22**) (30.5 mg, 0.150 mmol, 1.00 equiv) and 1,2-bis(4-methoxyphenyl)disulfane **2b** (42 mg, 0.15 mmol, 1.0 equiv). Next, the vial was closed with a screw-cap septum. The vial was degassed and refilled with nitrogen using the Schlenk-line technique (three times). CH_3CN (1.5 mL, 0.10 M) was added to the mixture and stirred for 3 h under the irradiation of a 457 nm Kessil lamp. The solvent was evaporated under vacuum. Product **23** was not detected in either NMR or HRMS.

5.2 UV-Vis spectra of BCB allyl ester 1b and diphenyl disulfide 2b



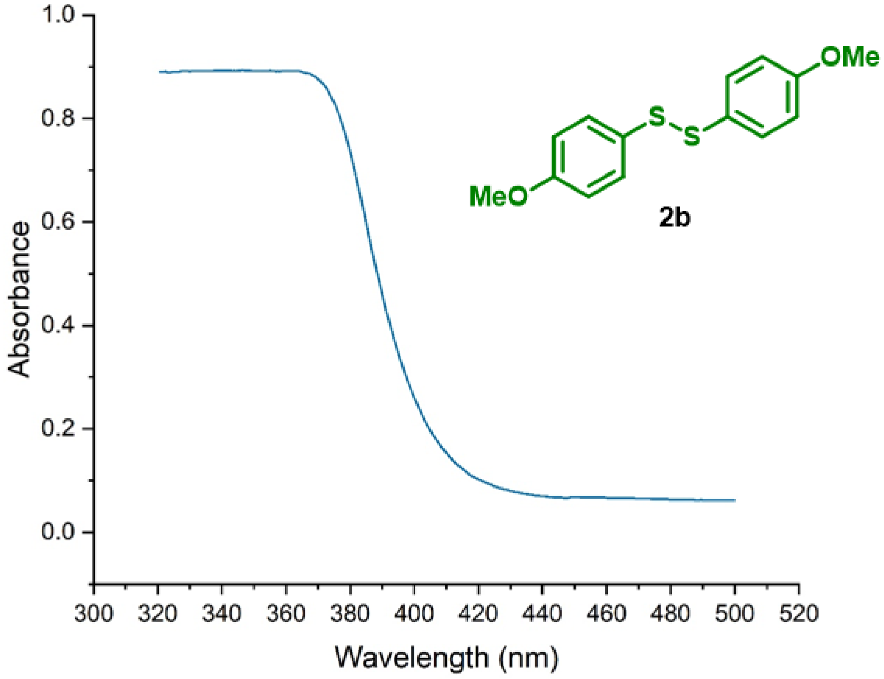
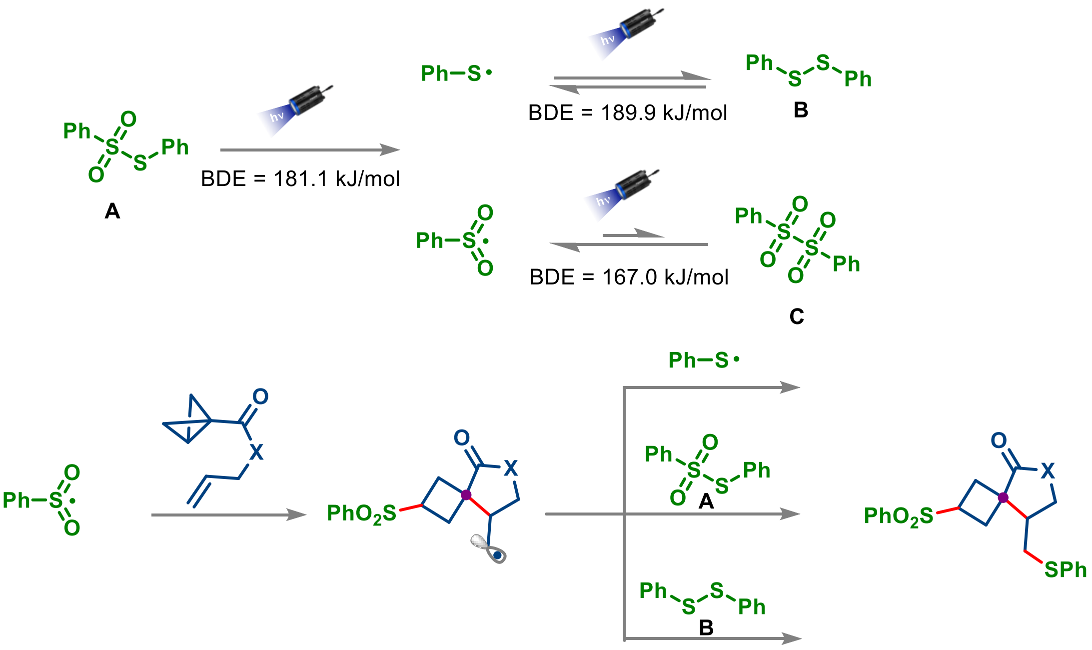


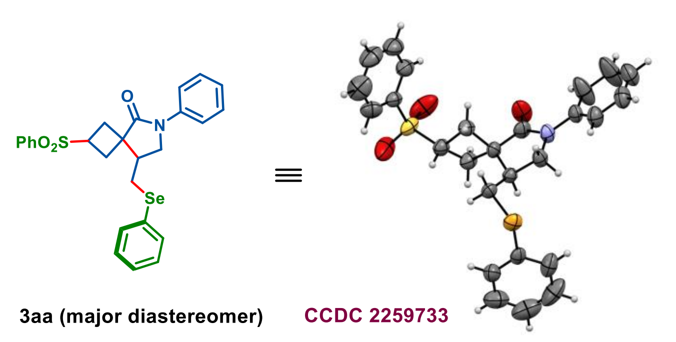
Figure 1: UV/Vis absorbance spectra of 1b and 2b in CH_3CN (0.001 M).

Mechanism for high chemoselectivity with interelement compounds



6. Crystallography Data

- Crystal structure and data of compound **3aa (major diastereomer)**



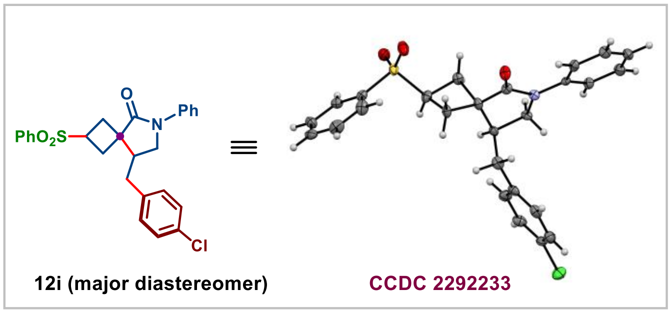
3aa (major diastereomer)

CCDC 2259733

Identification Code	SHELXL-2019/1
Empirical Formula	$C_{26}H_{25}NO_3SSe$
Molecular Weight	510.5210
Temperature	293K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	*P 21/n* (14)
Unit cell dimensions	a = 14.879(6); b = 8.126(3); c = 19.752(7)
Angles	α = 90; β = 99.543(12); γ = 90
Volume	2355.1 (15) Å^3
Z	4
Density (Calculated).	1.440 g/cm^3
Absorption coefficient	1.711 mm^{-1}
F (000)	1048.0
Theta range for data collection	2.716 to 27.160
Index ranges	-19<=h<=19, -10<=k<=10, -25<=l<=25
Reflections collected	57675
Independent reflections	5224 [R(int) = 0.0393]
Completeness	99.9 %
Structure Refinement	SHELXL-2019/1 (Sheldrick, 2019)'
Data/ restraints/ parameters	5224 / 0/ 292

Goodness of fit on F^2	1.122
Final R indices [1>2 sigma (1)]	$R_1 = 0.0759$; $wR_2 = 0.1560$
R indices (all data)	$R_1 = 0.1028$; $wR_2 = 0.1685$
Extinction coefficient	n/a
Largest diff. peak and hole	0.767 and -0.521 e. Å

- Crystal structure and data of compound **12i (major diastereomer)**



12i (major diastereomer)

CCDC 2292233

Identification Code	SHELXL-2019/1
Empirical Formula	$C_{26}H_{24}ClNO_3S$
Molecular Weight	465.97
Temperature	120K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	*P 21/n* (19)
Unit cell dimensions	a = 6.1782(2); b = 11.4363(4); c = 31.3637(9)
Angles	α = 90; β = 90; γ = 90
Volume	2216.03(12) $Å^3$
Z	4
Density (Calculated).	1.397 g/cm^3
Absorption coefficient	0.296 mm^{-1}
F (000)	976
Theta range for data collection	3.150 to 25.354

Index ranges	-7<=h<=7, -13<=k<=13, -37<=l<=37
Reflections collected	4064
Independent reflections	4064 [R(int) = 0.0550]
Completeness	99.9 %
Structure Refinement	SHELXL-2019/1 (Sheldrick, 2019)'
Data/restraints/parameters	4064/0/289
Goodness of fit on F^2	1.102
Final R indices [1>2 sigma (1)]	$R_1 = 0.0525$; $wR_2 = 0.1157$
R indices (all data)	$R_1 = 0.0550$; $wR_2 = 0.1143$
Extinction coefficient	n/a
Largest diff. peak and hole	0.311 and -0.259 e. Å

7. References

[1] B. D. Schwartz, A. P. Smyth, P. E. Nashar, M. G. Gardiner, L. R. Malins, *Org. Lett.* 2022, **24**, 1268-1273.

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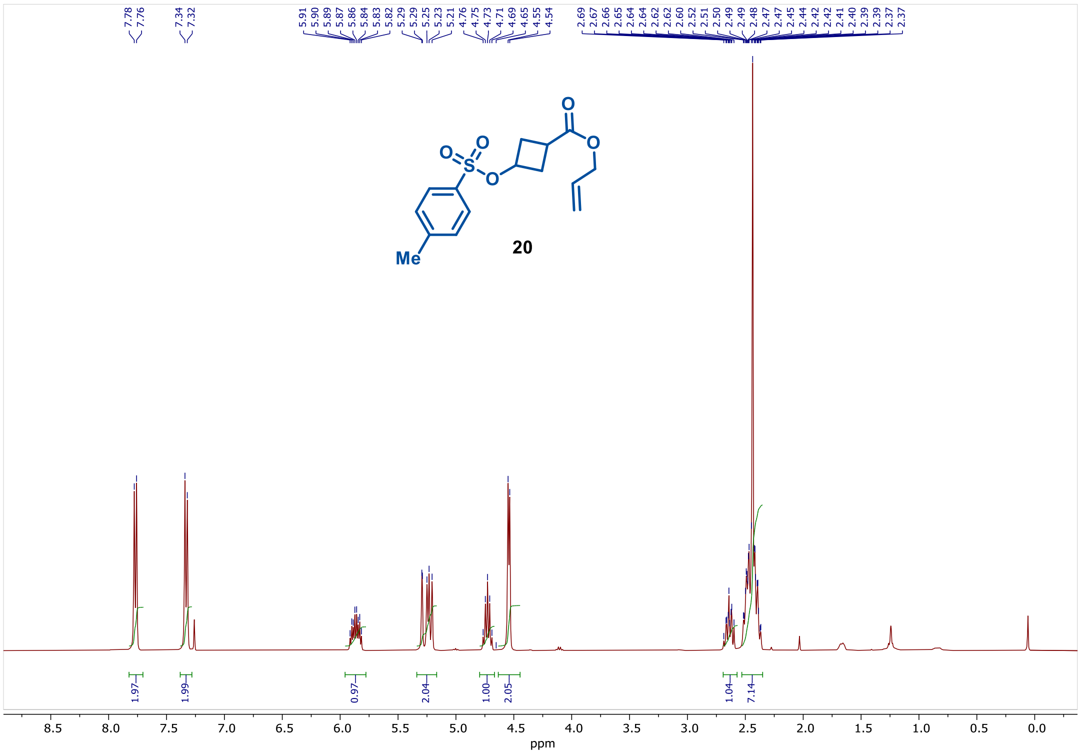
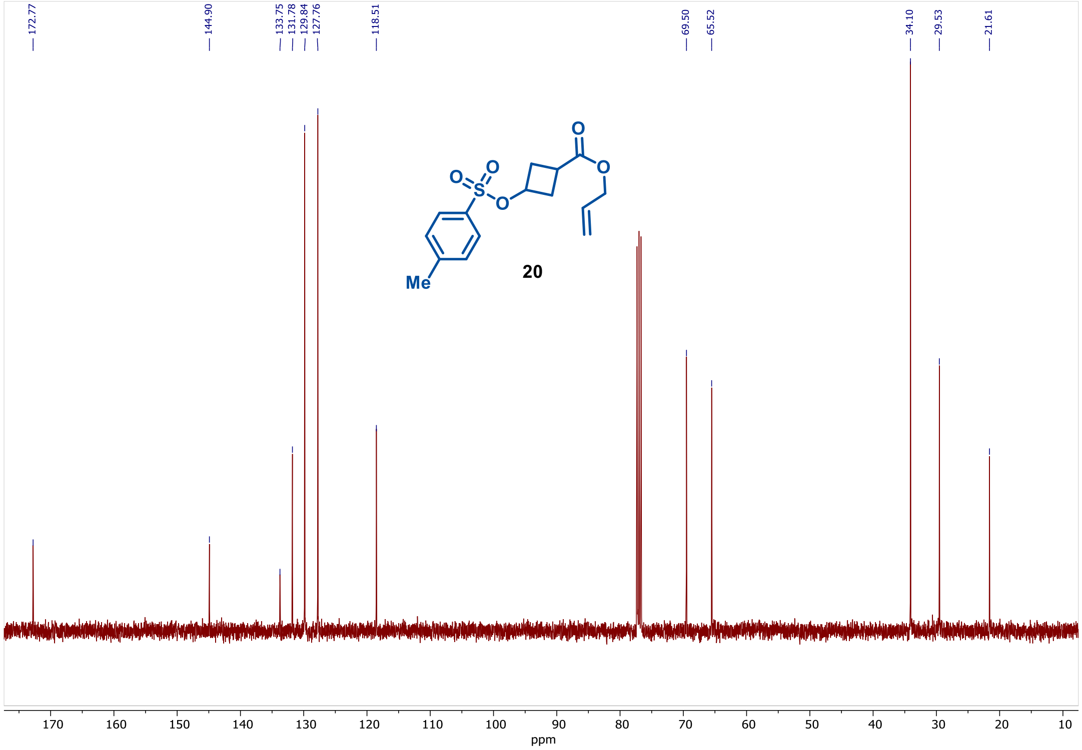
8. Spectra for new compounds

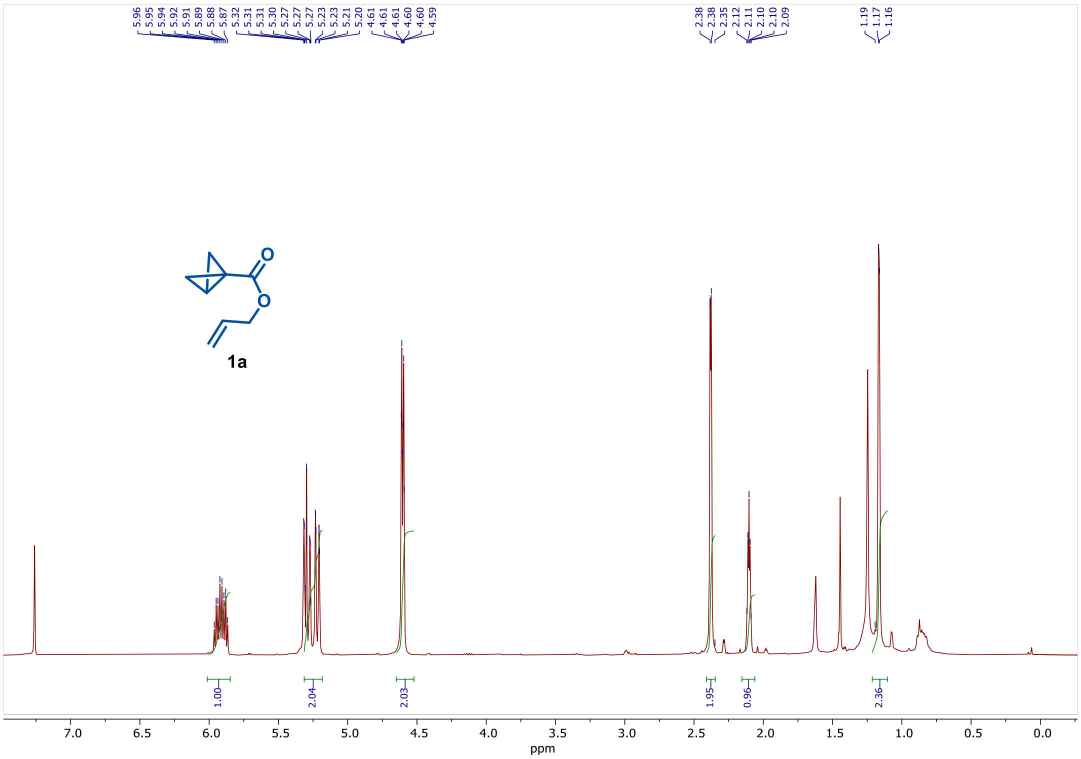
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **20** (**See Procedure**)



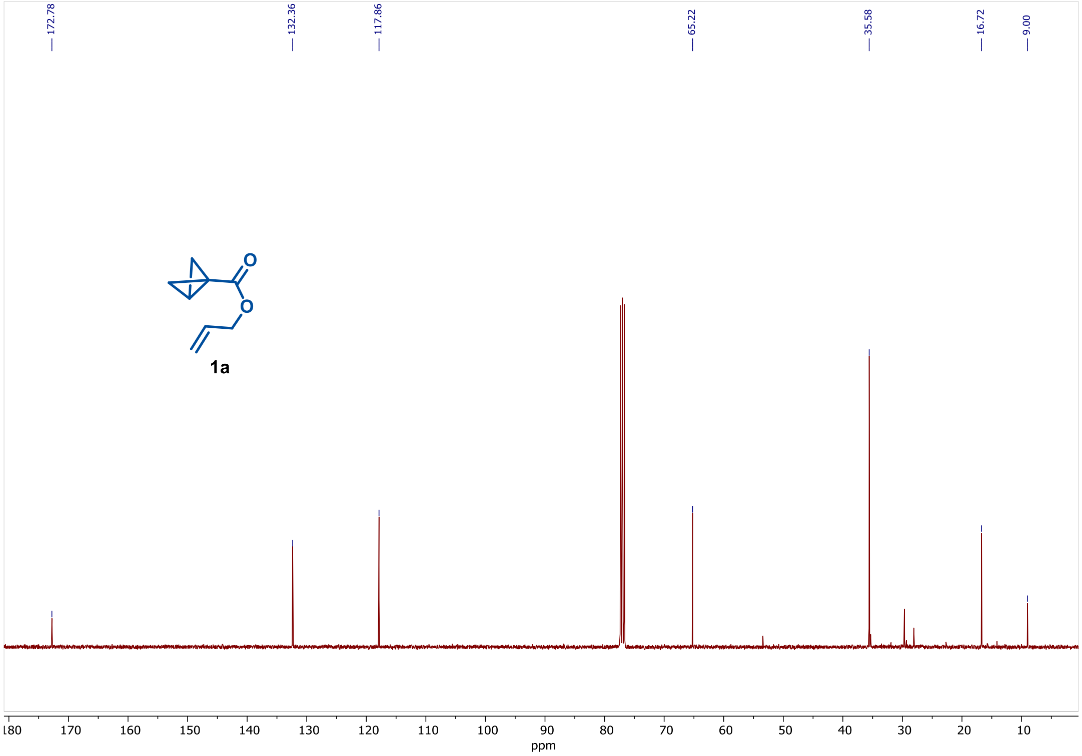
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **20**



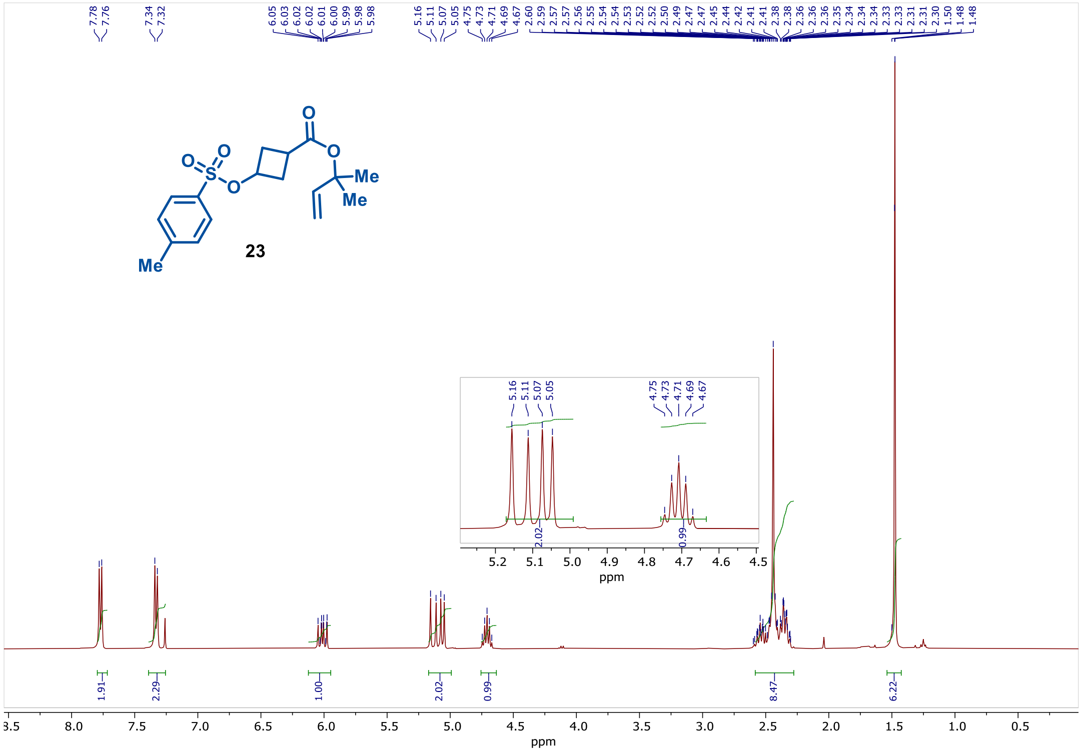
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **1a** (**See Procedure**)



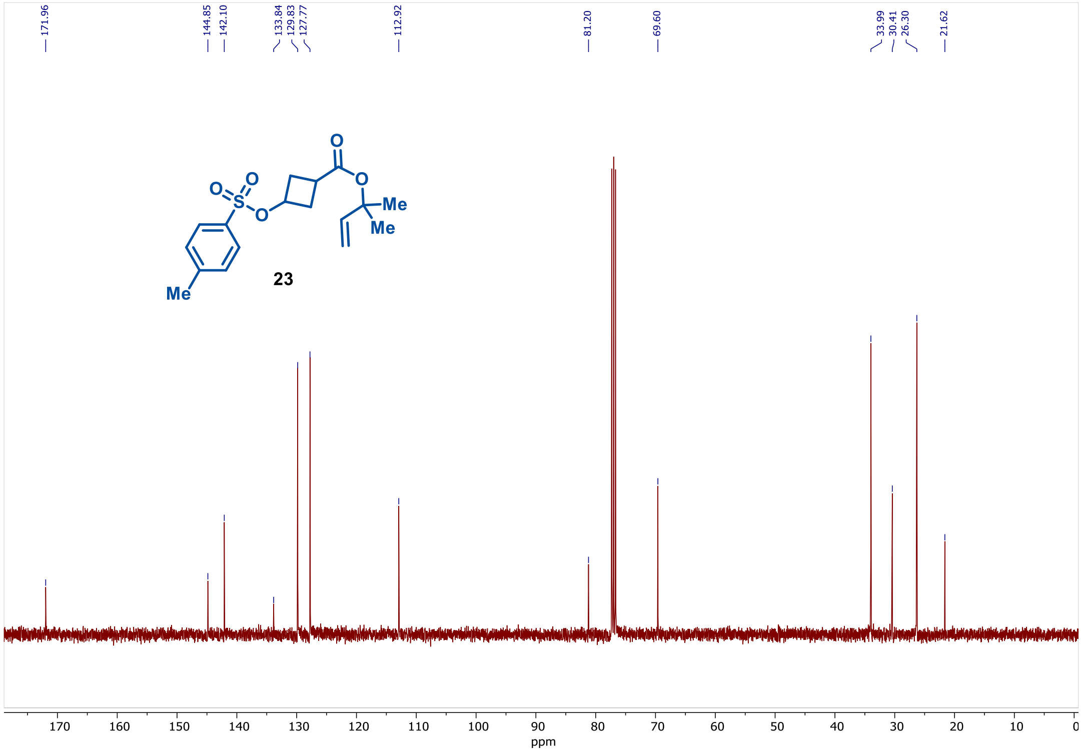
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **1a**



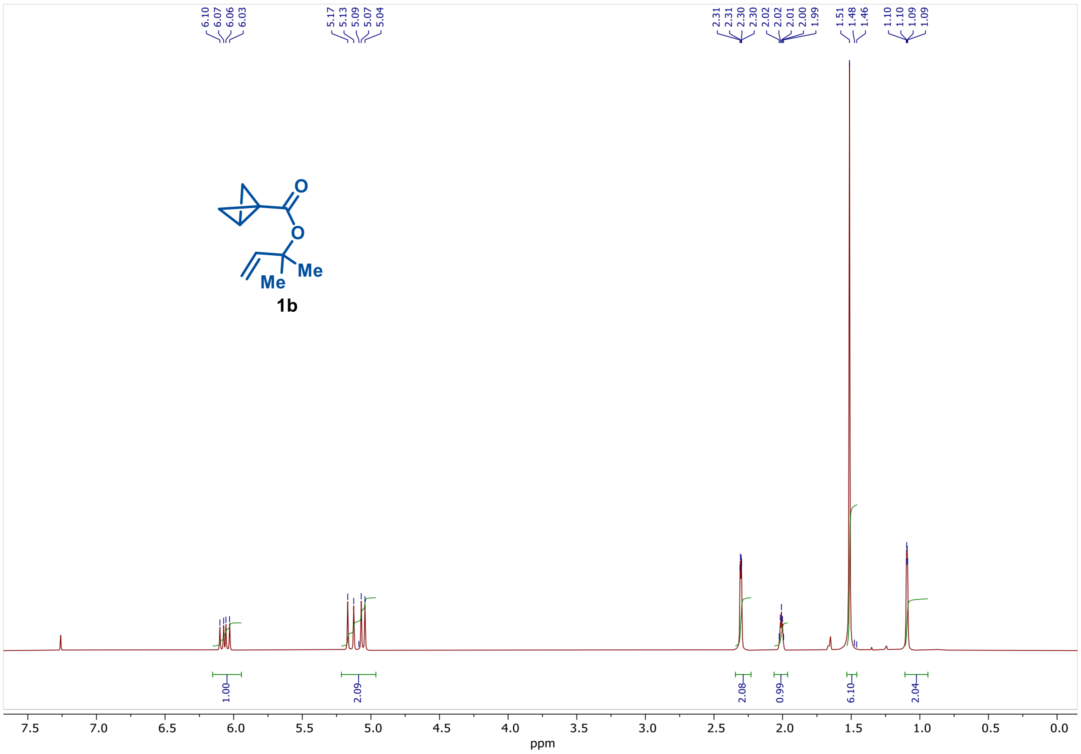
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **23** (**See Procedure**)



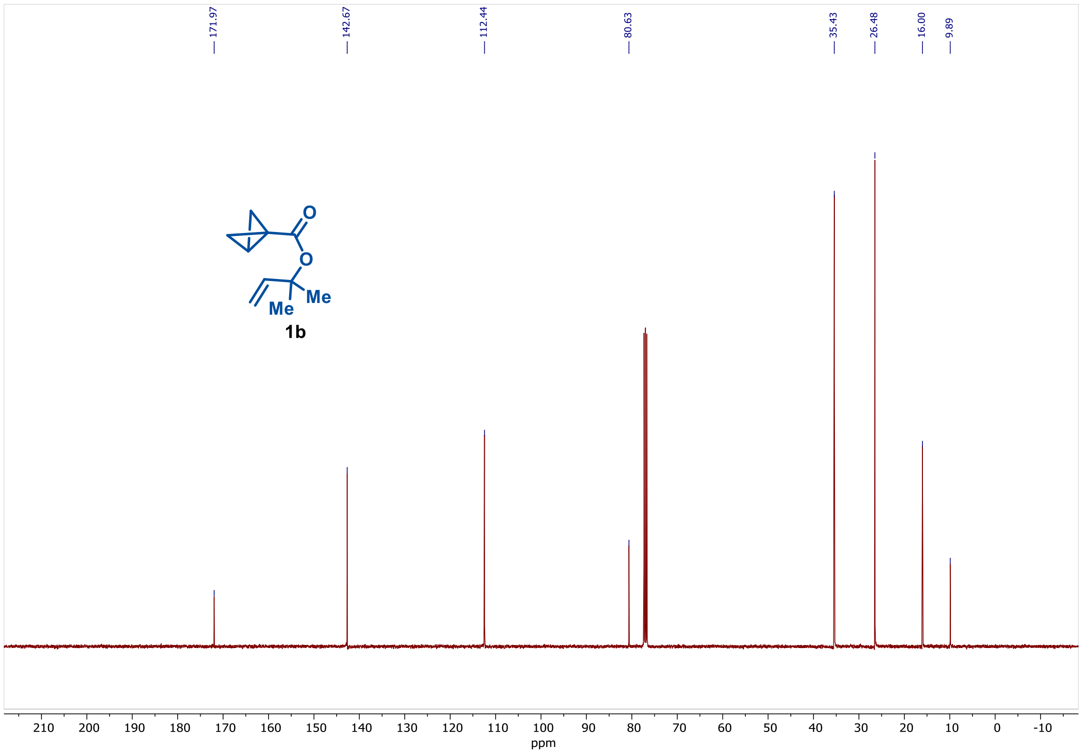
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **23**



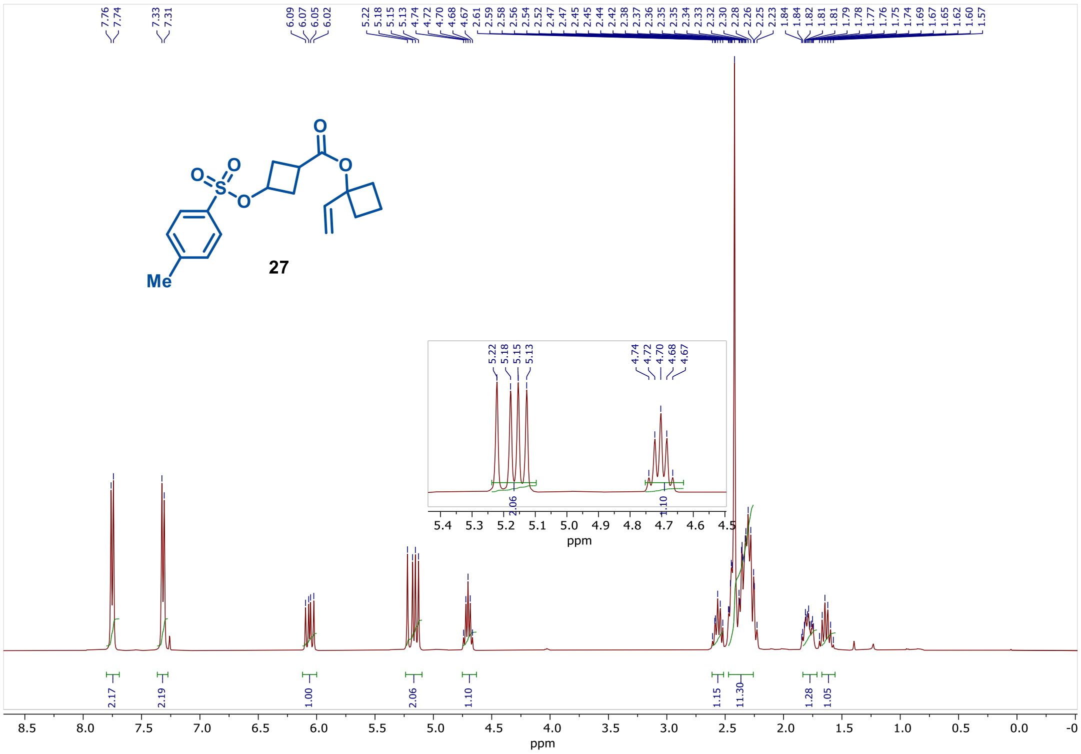
^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **1b** (**See Procedure**)



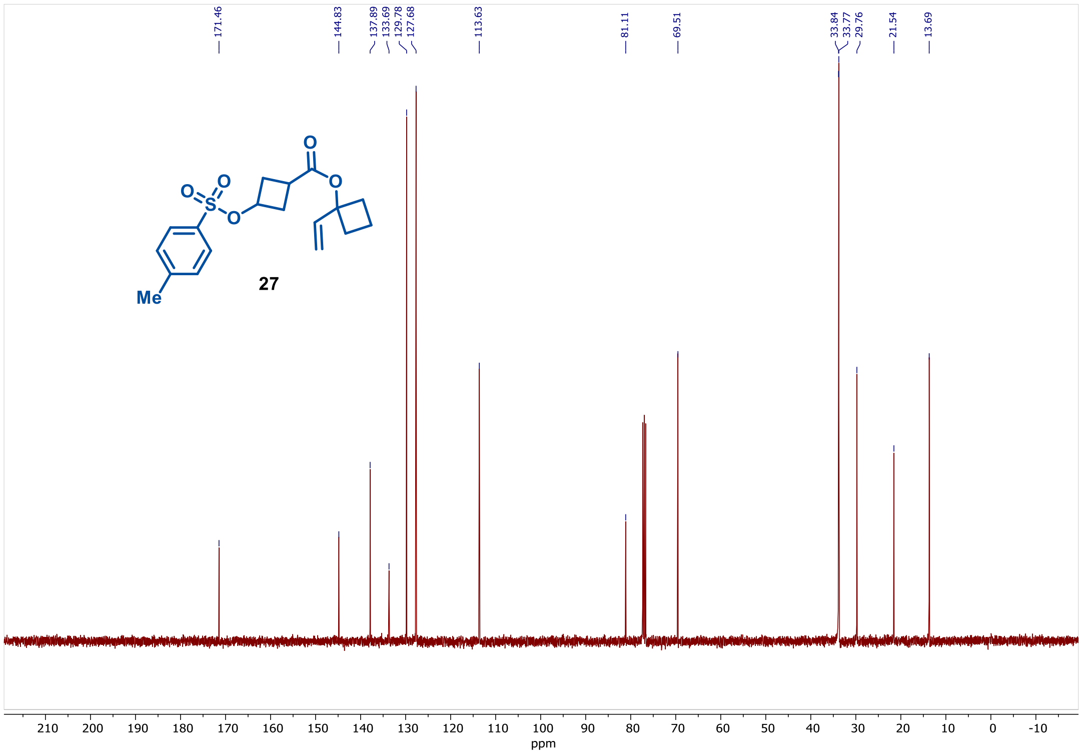
^{13}C NMR (101 MHz, $CDCl_3$) spectra of compound **1b**



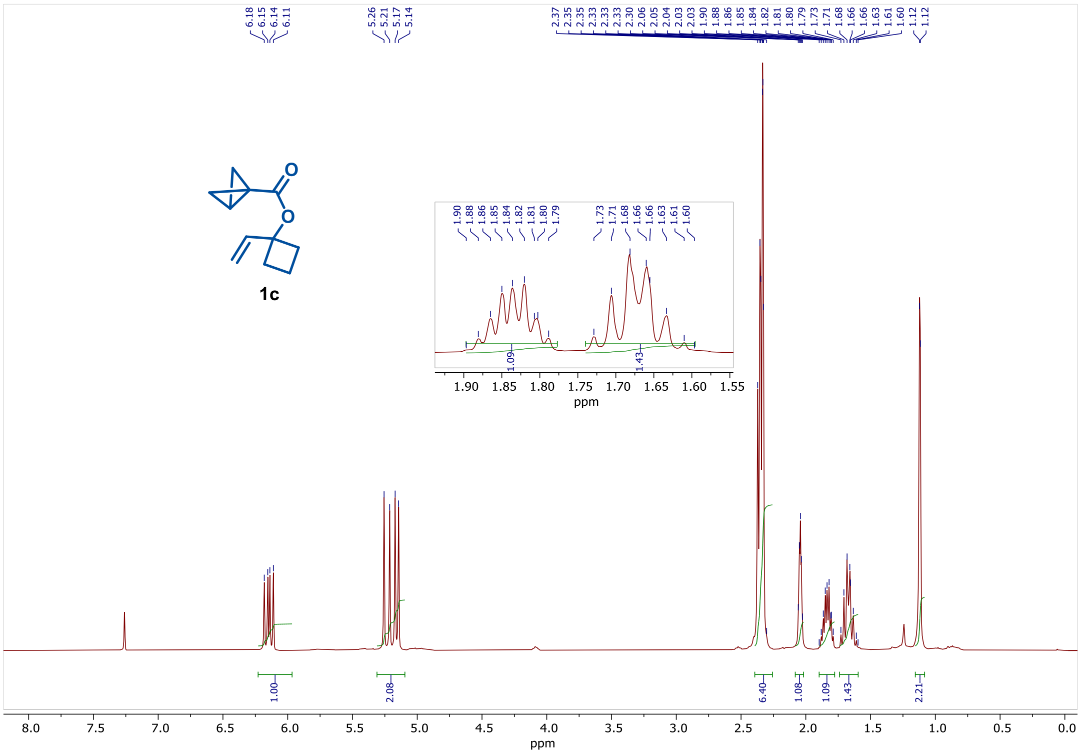
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **27** (**See Procedure**)



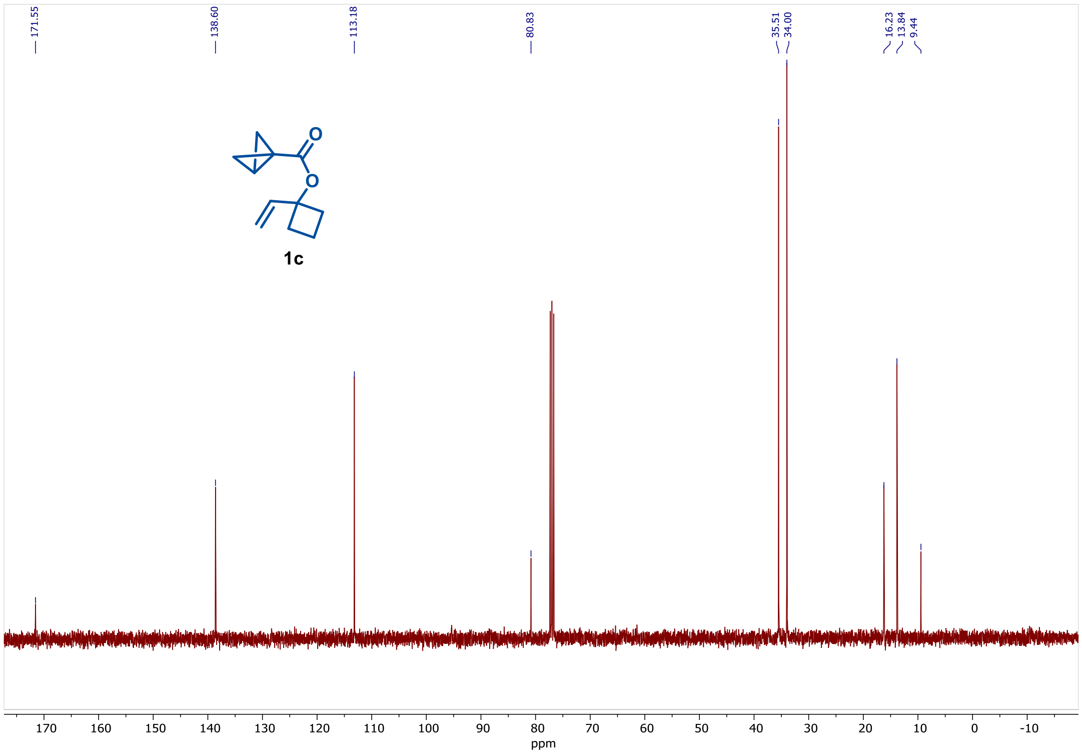
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **27**



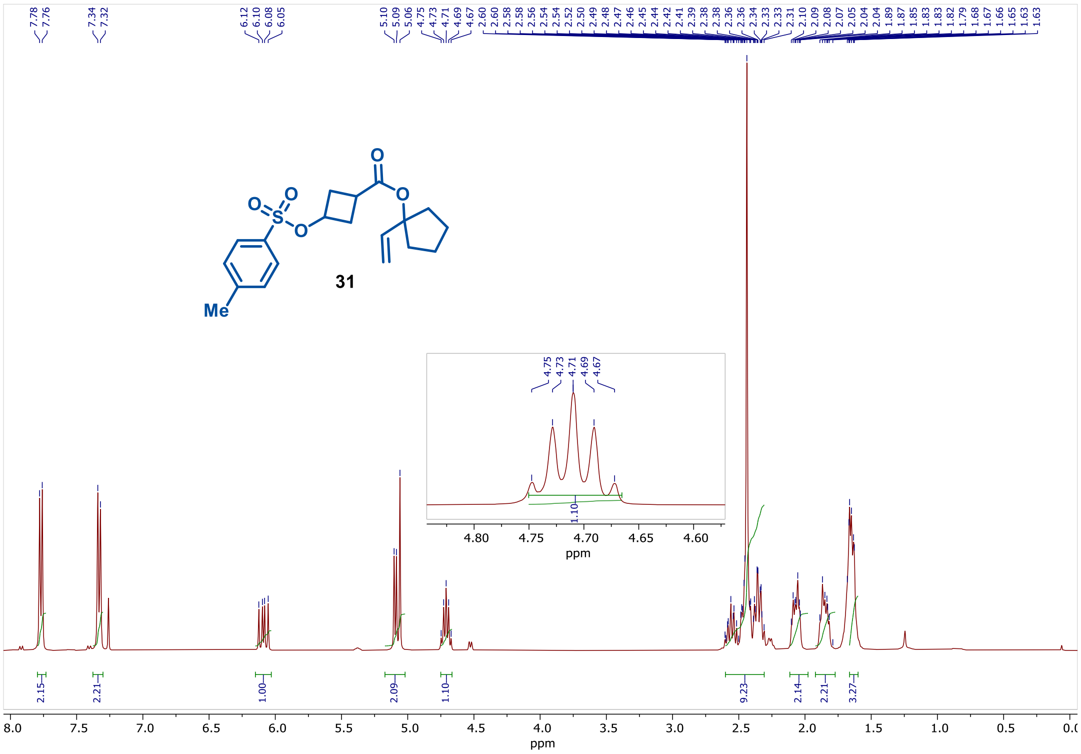
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **1c** (**See Procedure**)



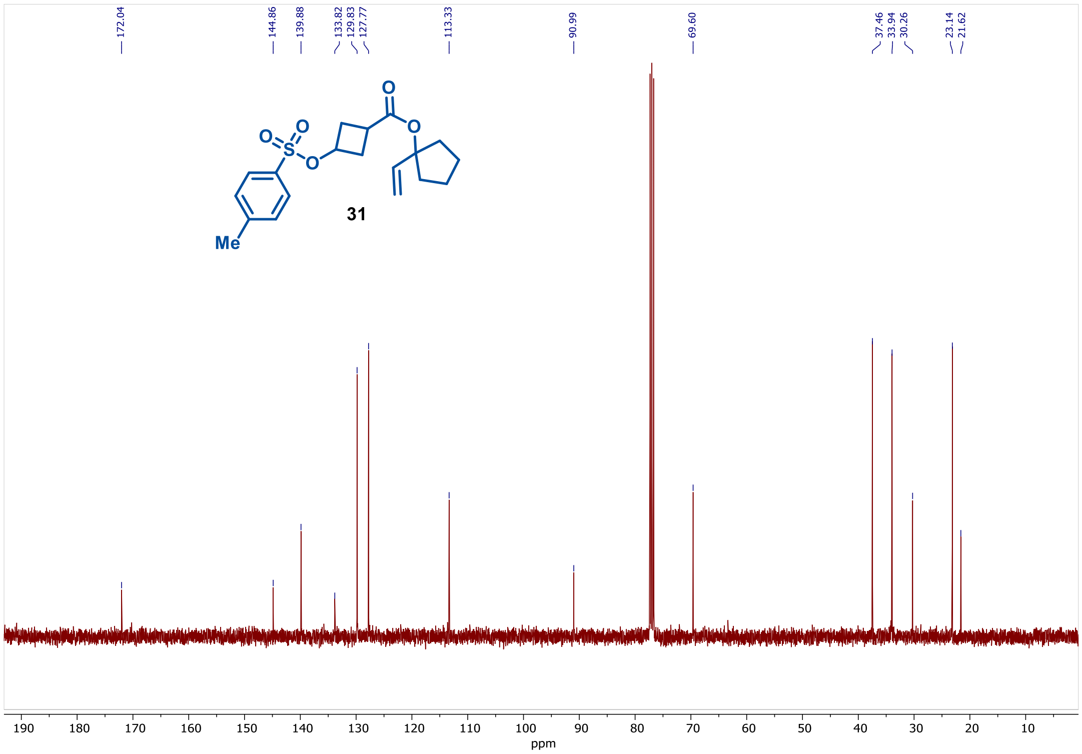
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **1c**



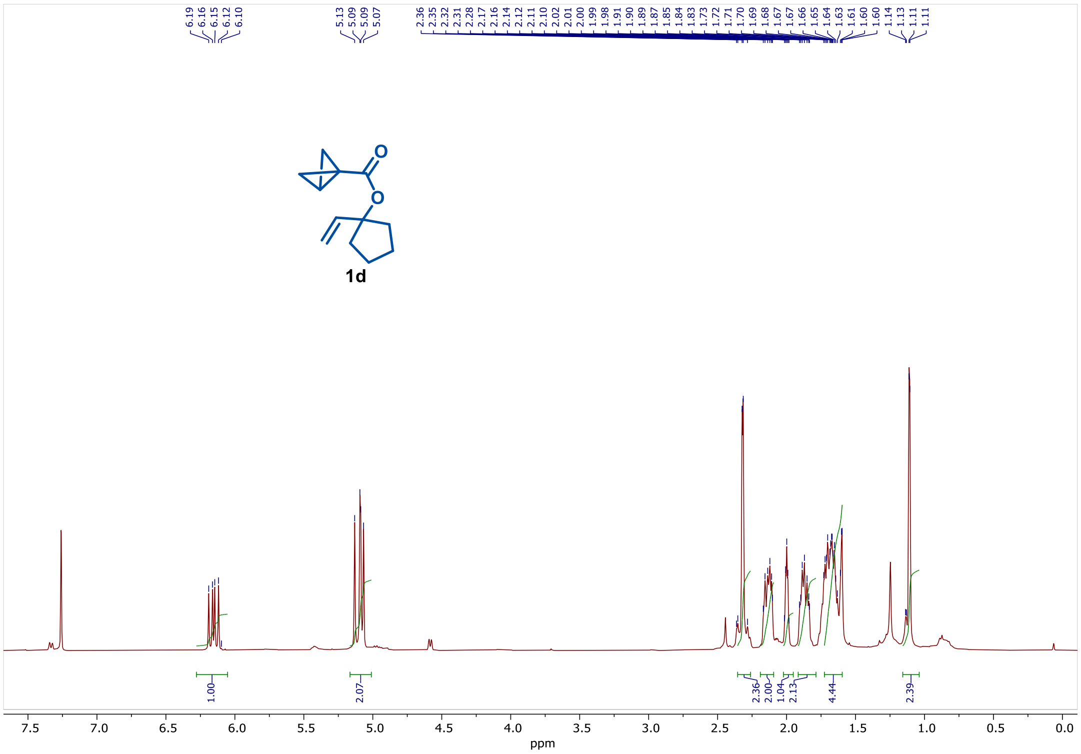
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **31** (**See Procedure**)



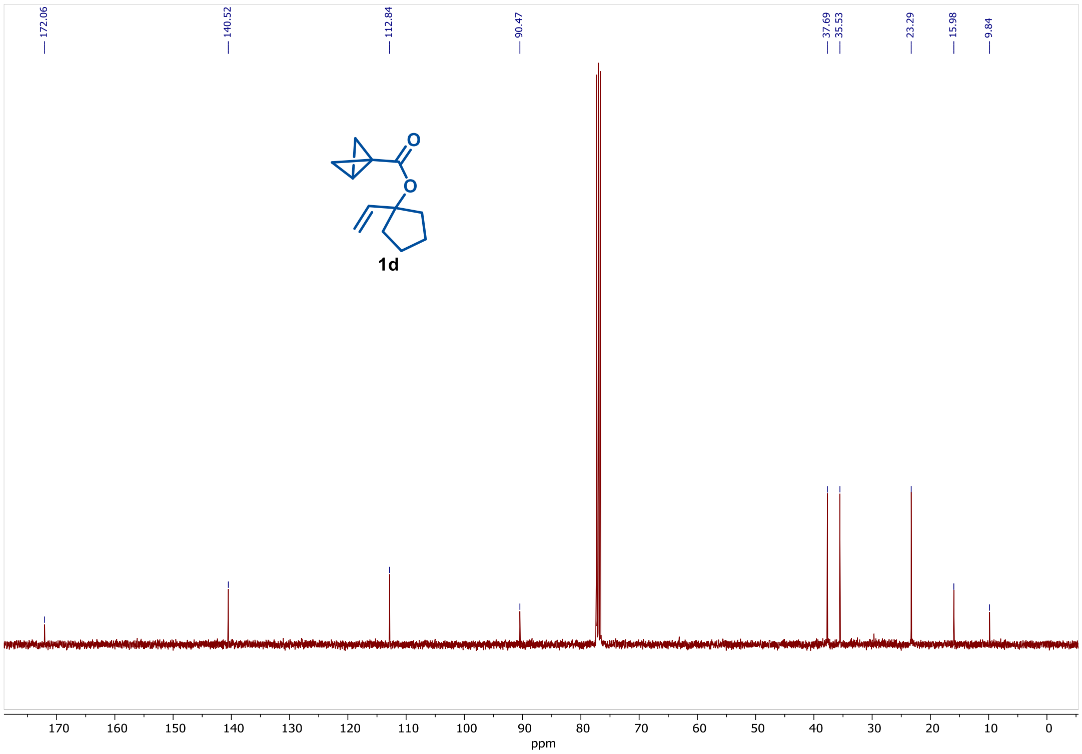
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **31**



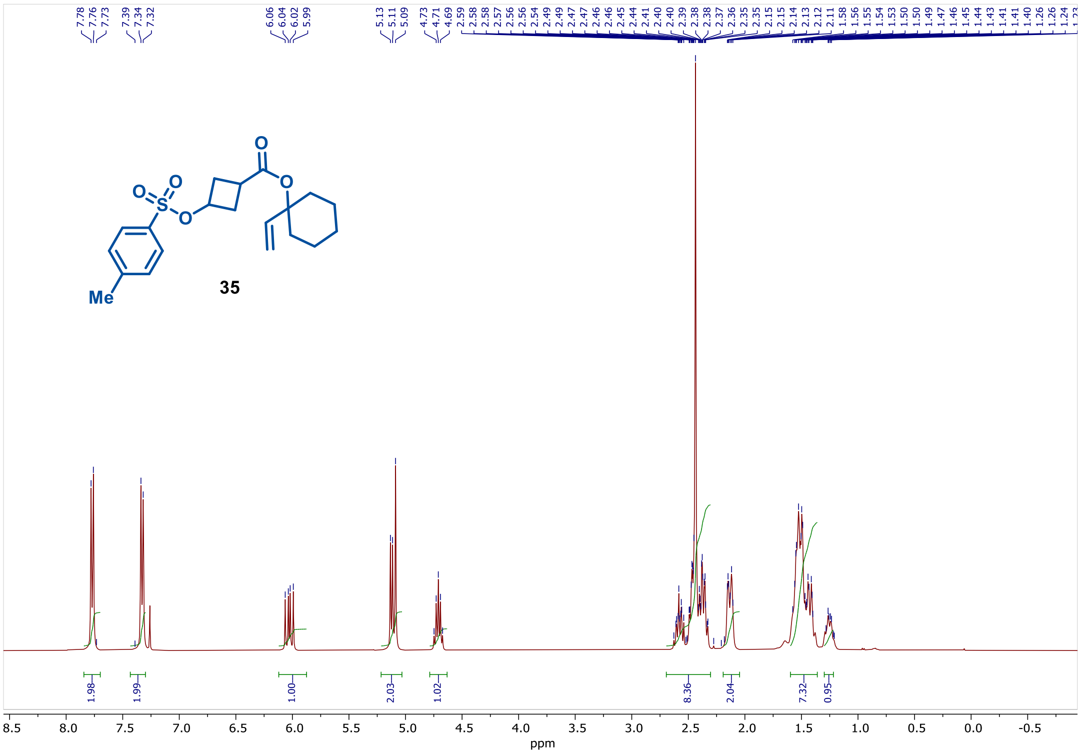
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **1d** (**See Procedure**)



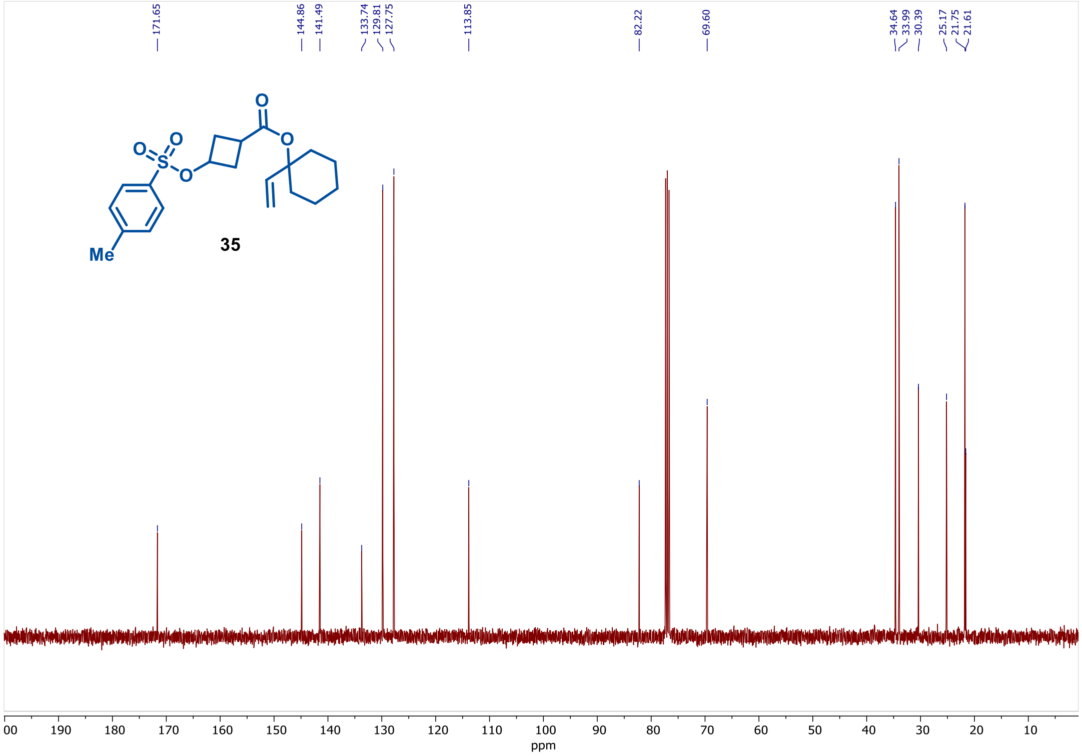
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **1d**



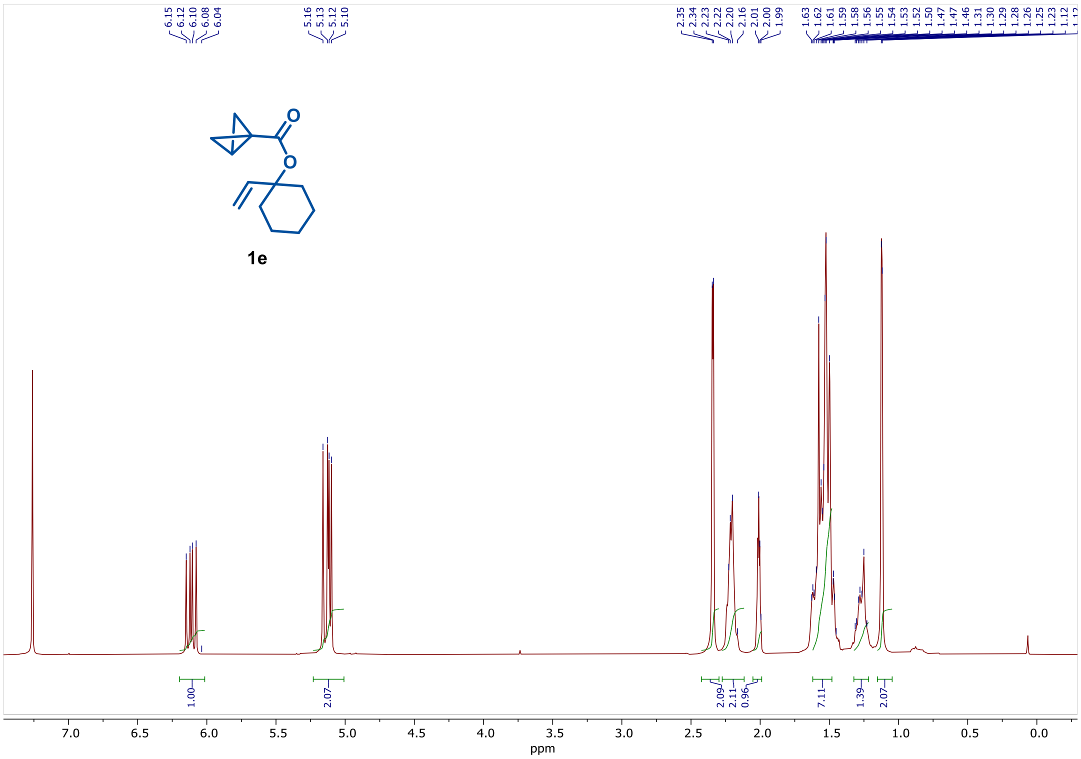
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **35** (**See Procedure**)



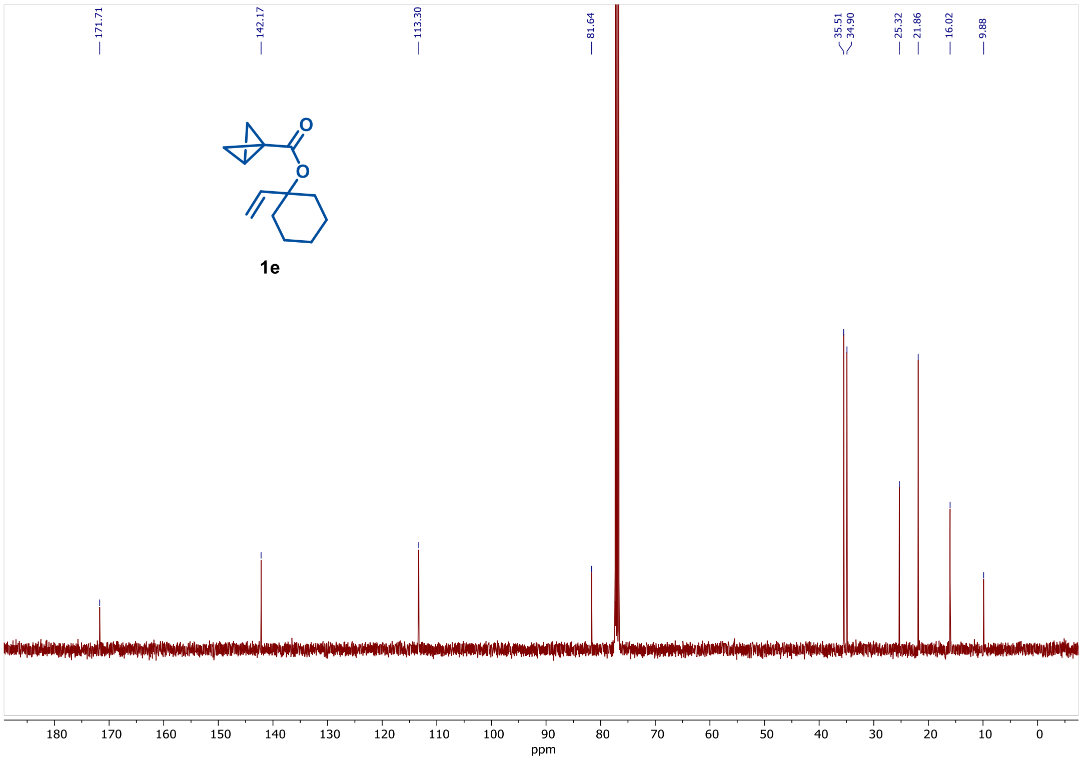
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **35**



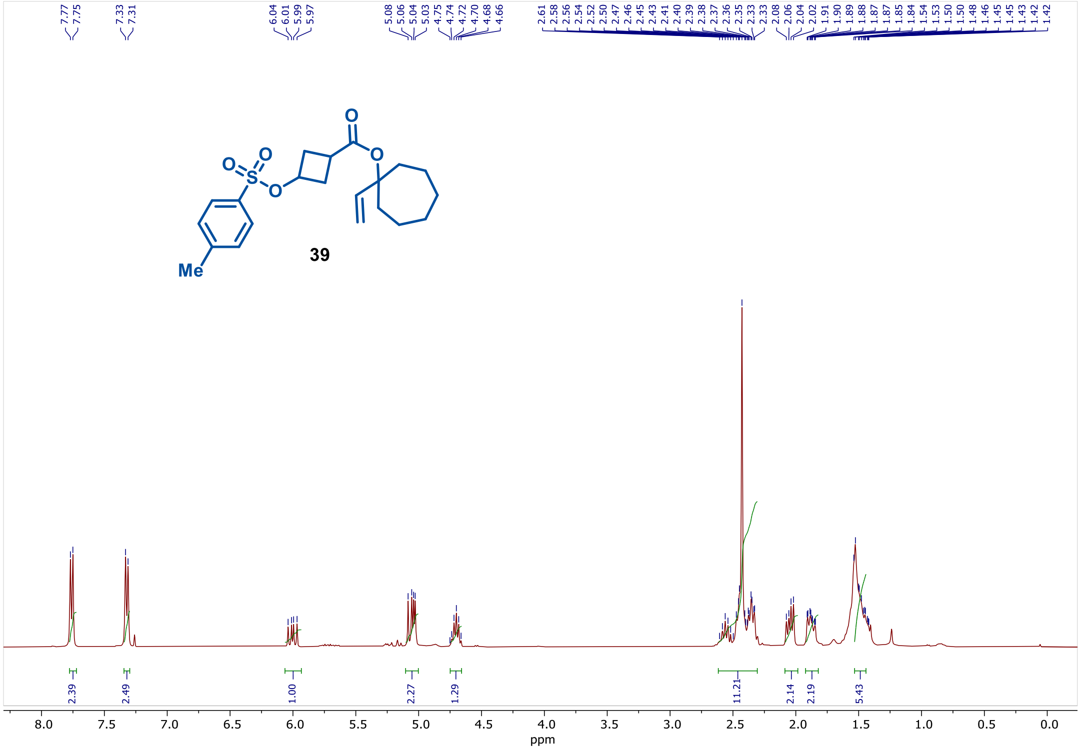
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **1e** ([See Procedure](#))



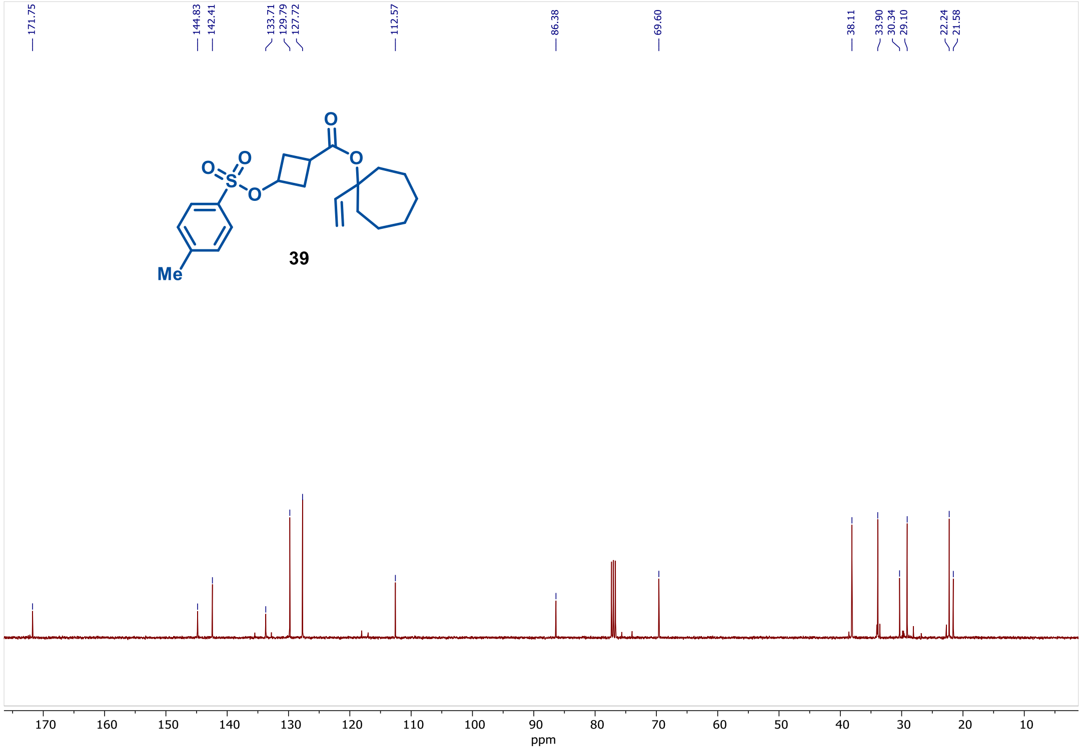
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **1e**



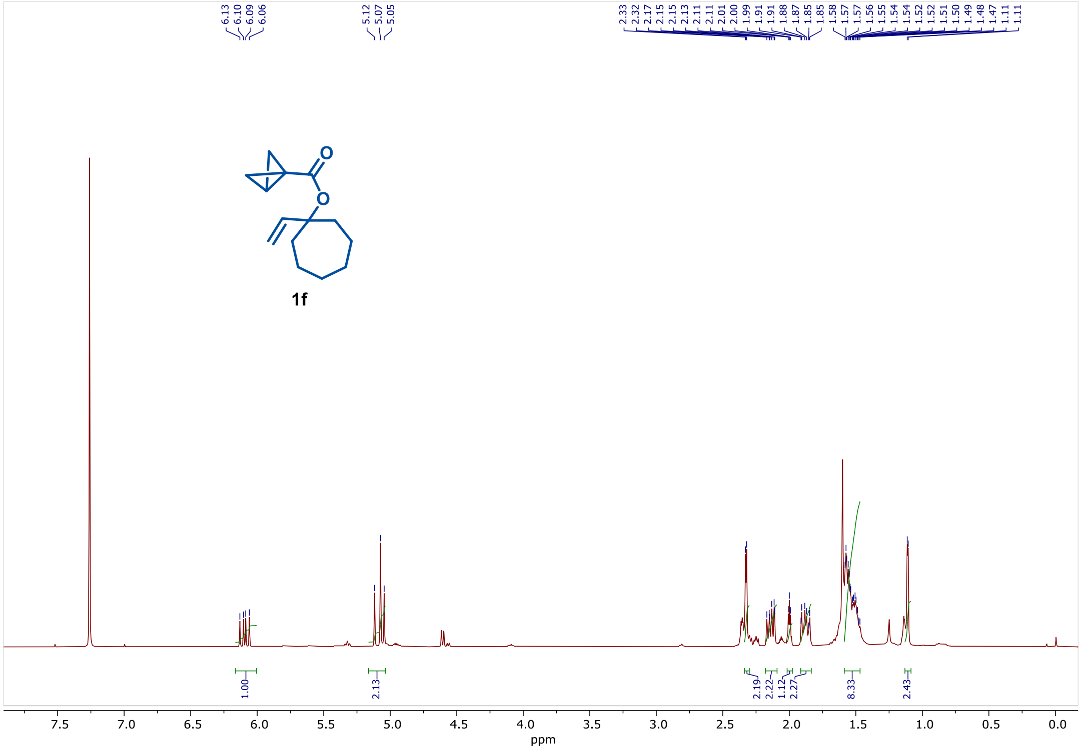
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **39** (**See Procedure**)



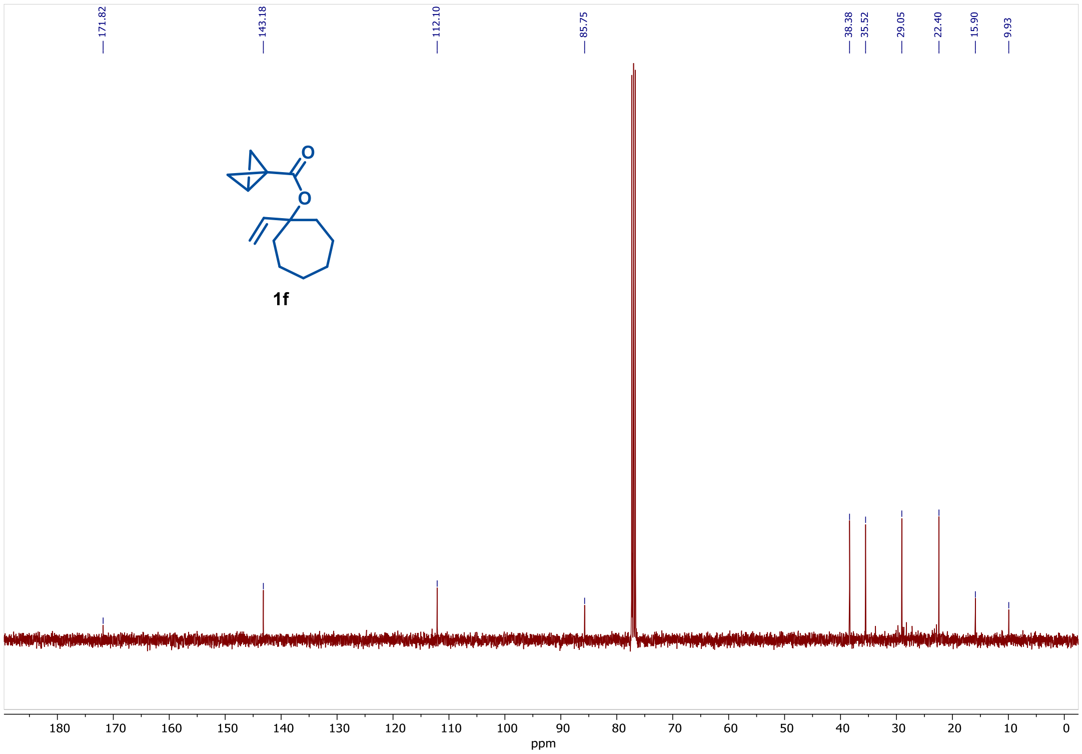
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **39**



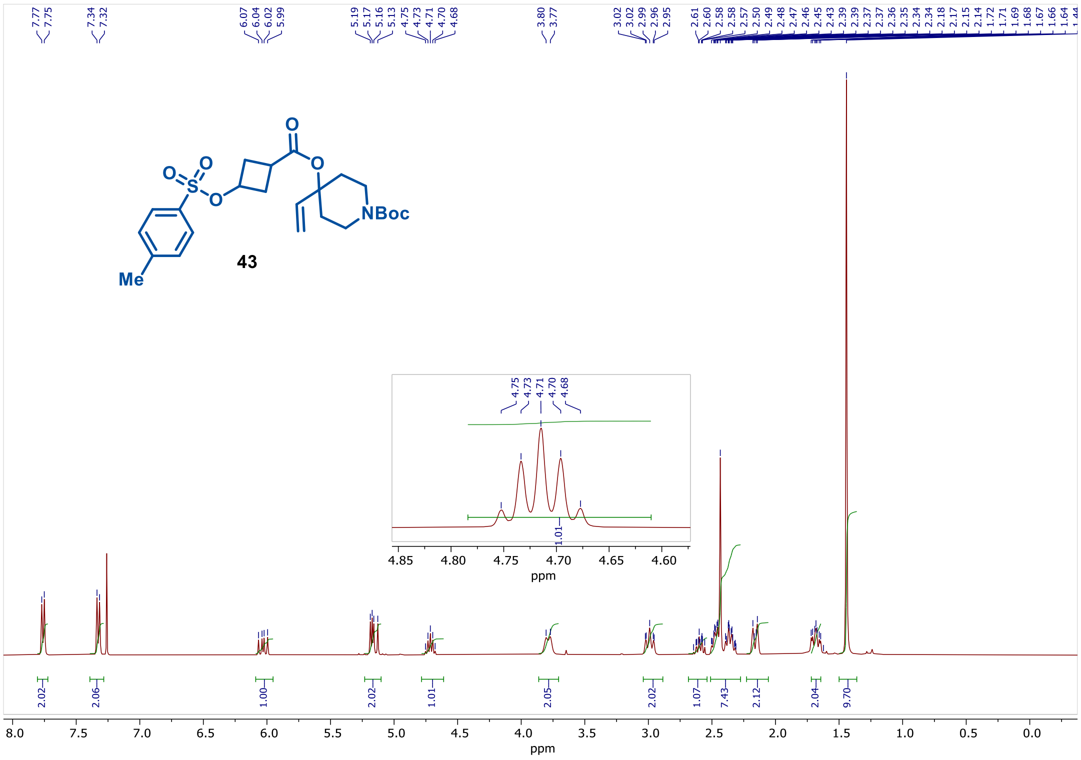
^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **1f** (See Procedure)



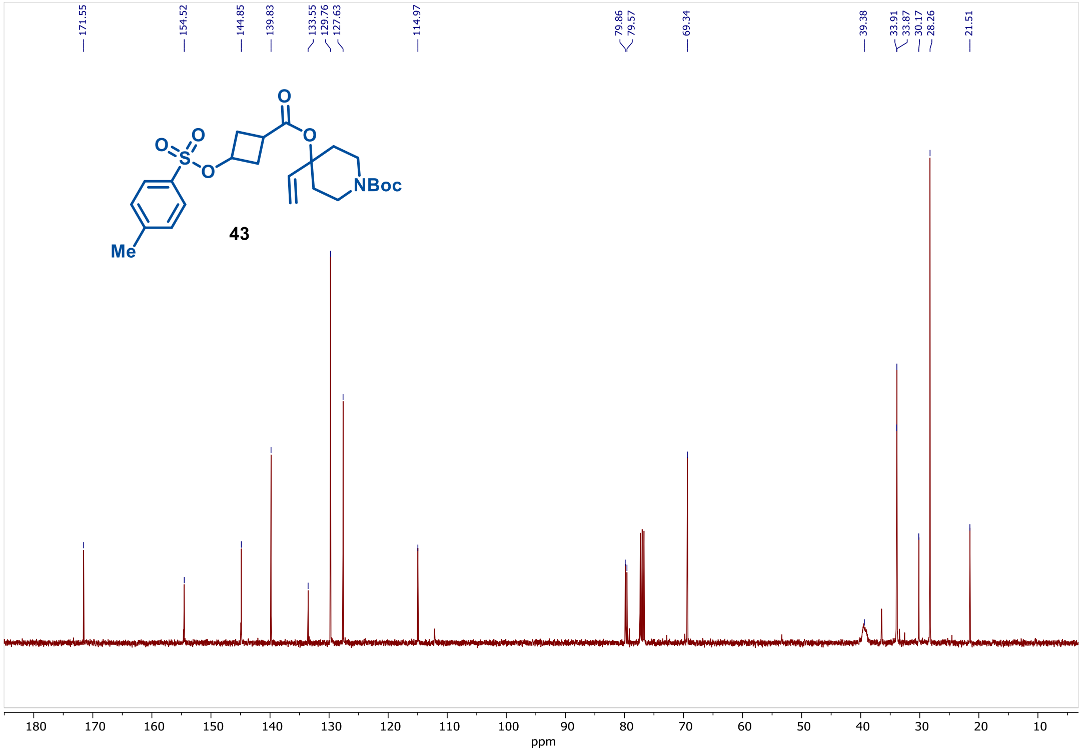
^{13}C NMR (101 MHz, $CDCl_3$) spectra of compound **1f**



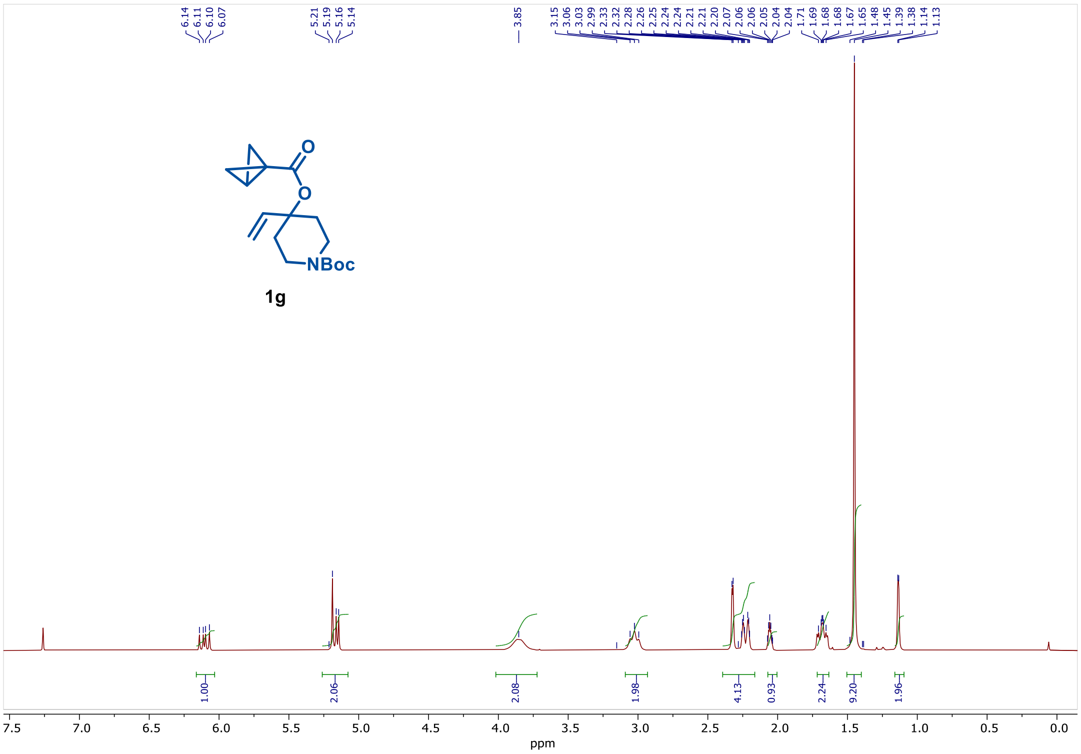
^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **43** (**See Procedure**)



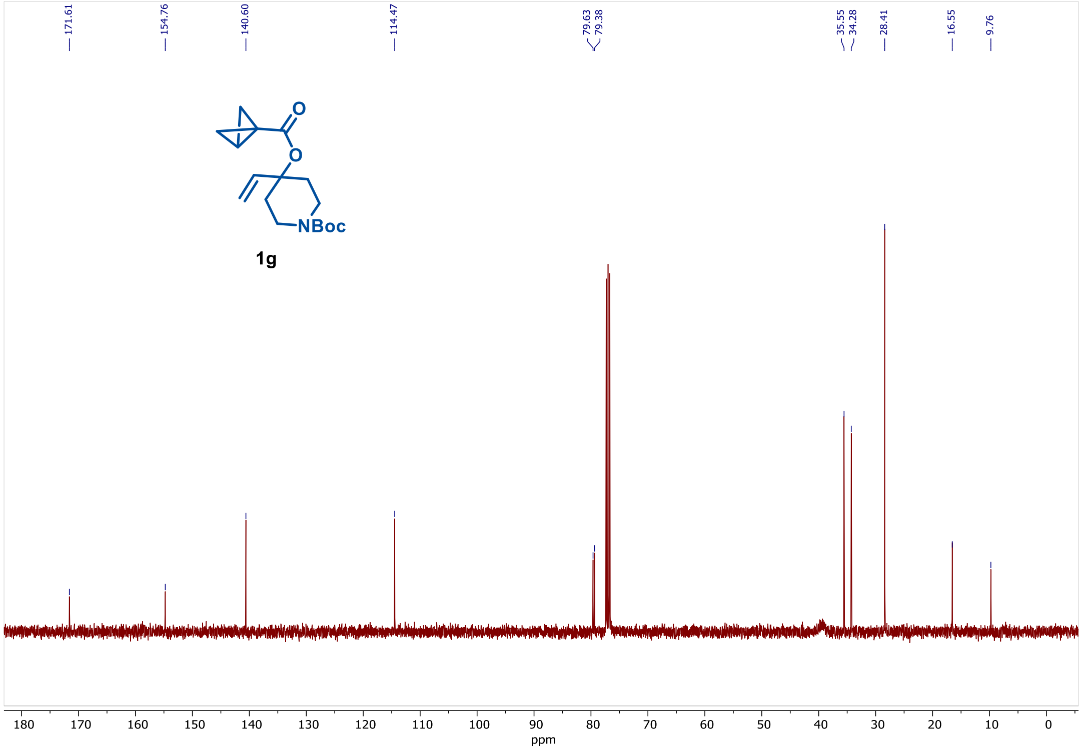
^{13}C NMR (101 MHz, $CDCl_3$) spectra of compound **43**



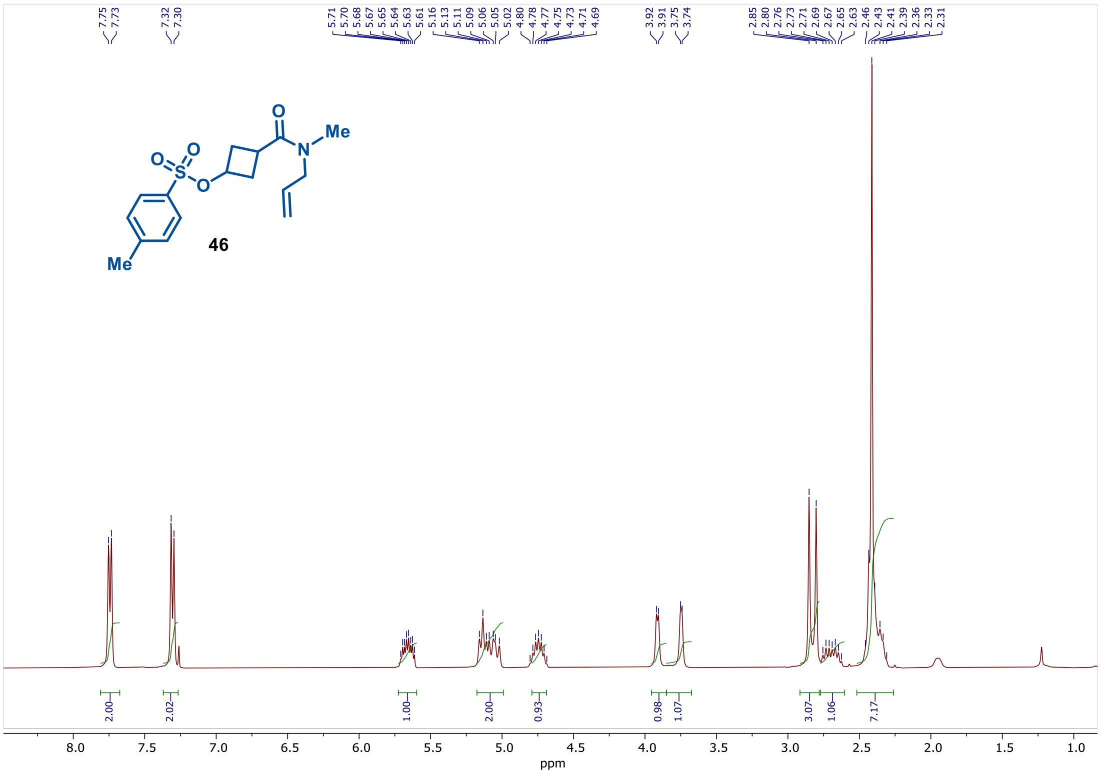
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **1g** (See Procedure)



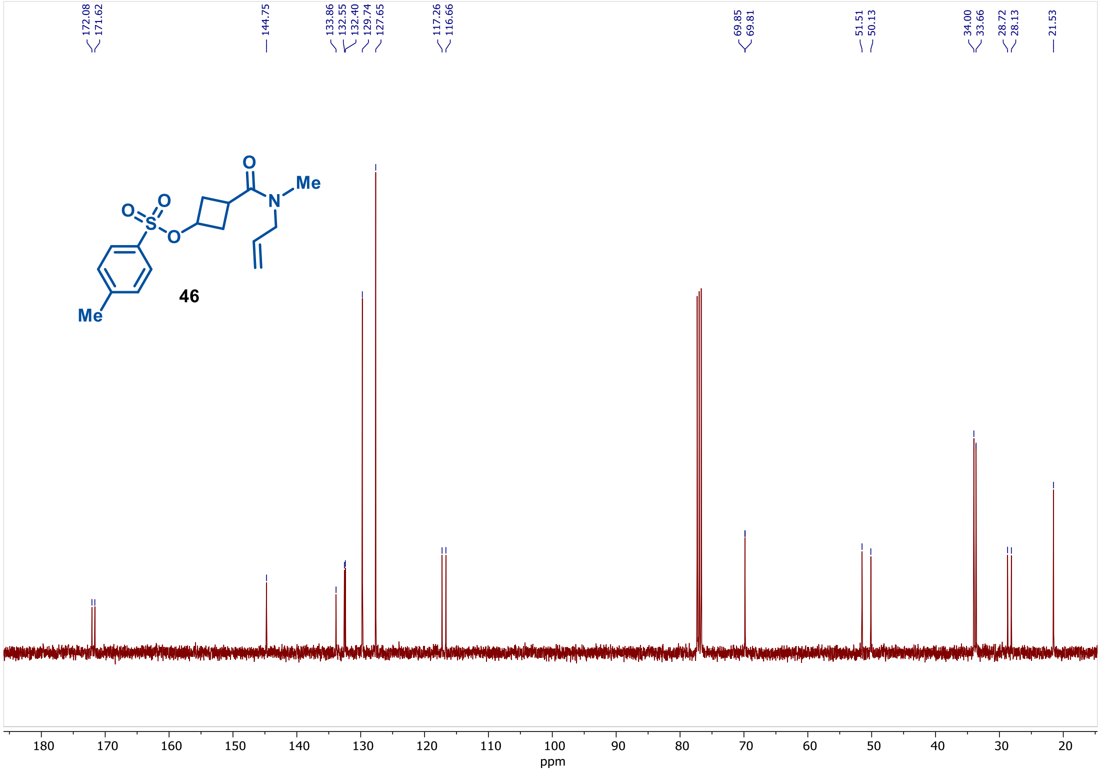
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **1g**



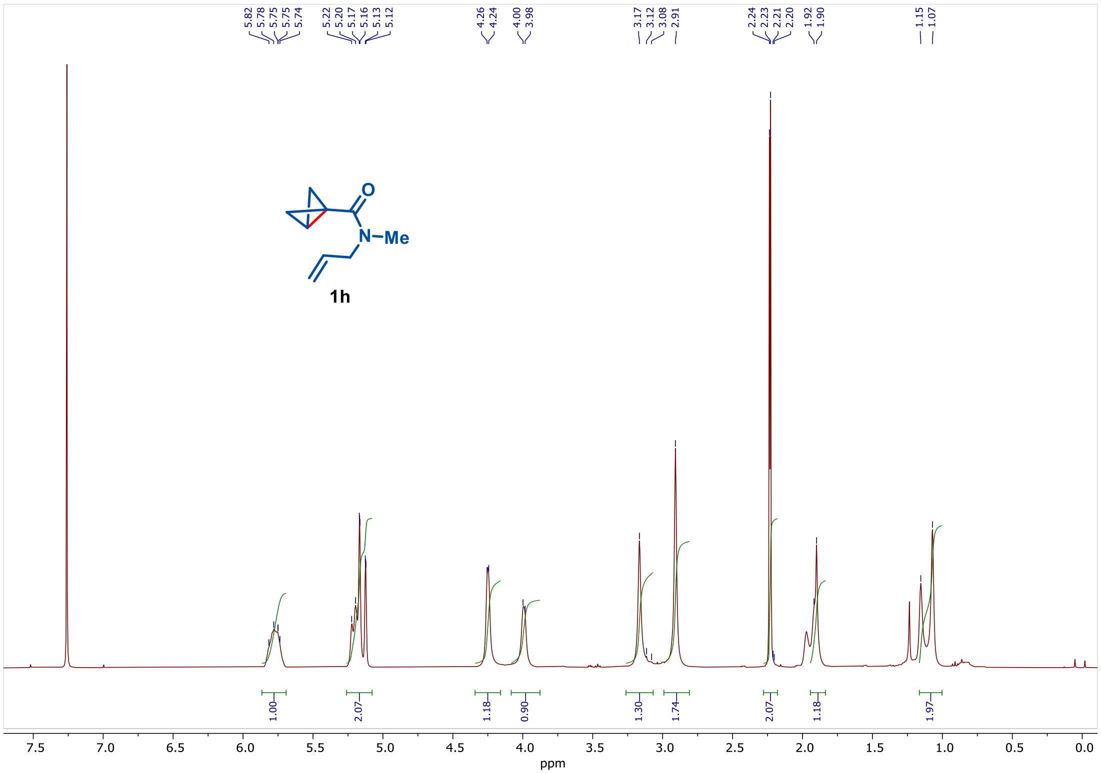
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **46** (**See Procedure**)



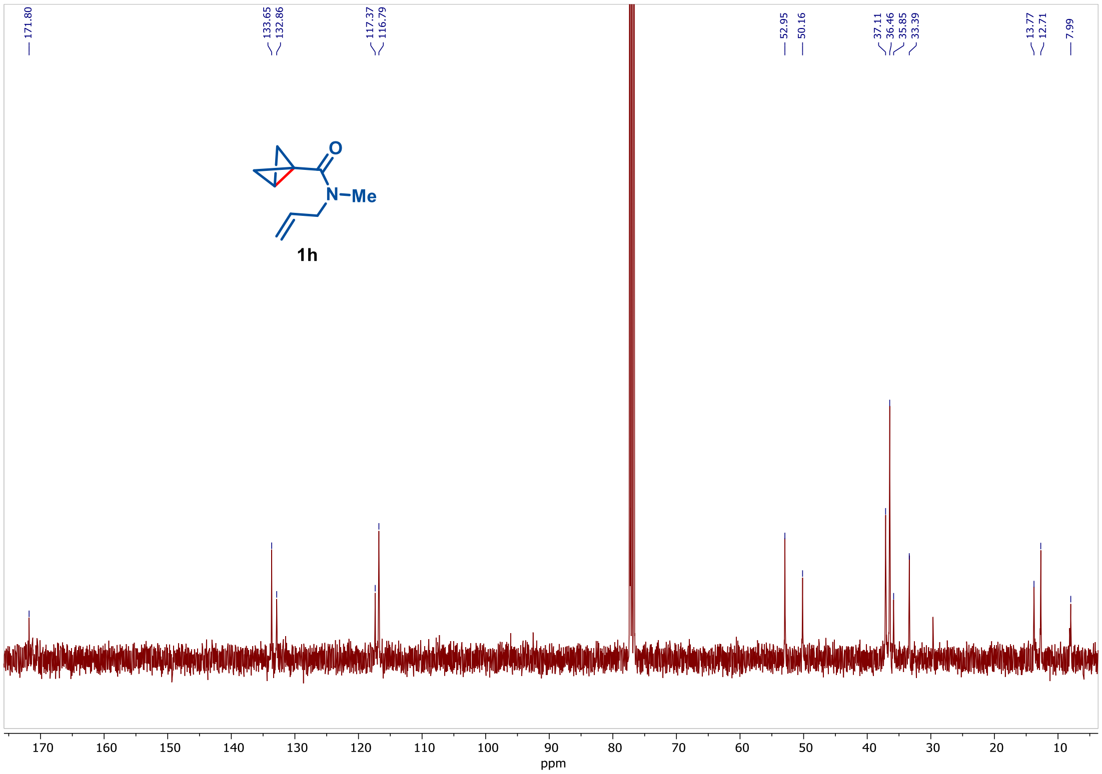
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **46**



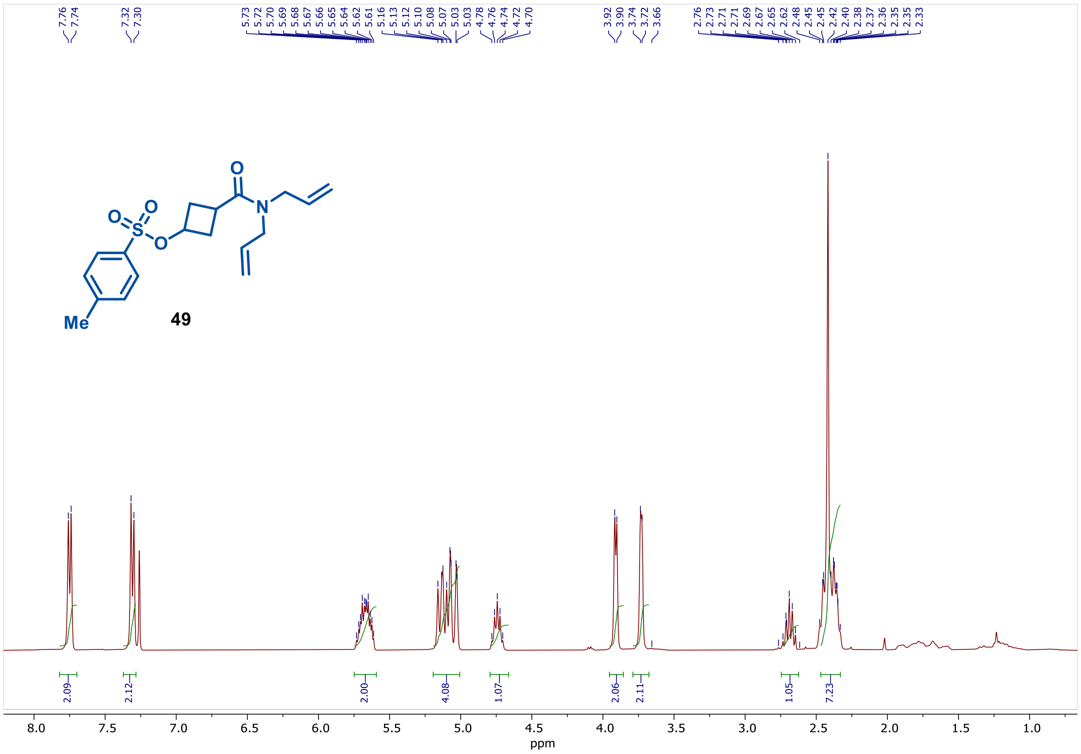
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **1h** (**See Procedure**)



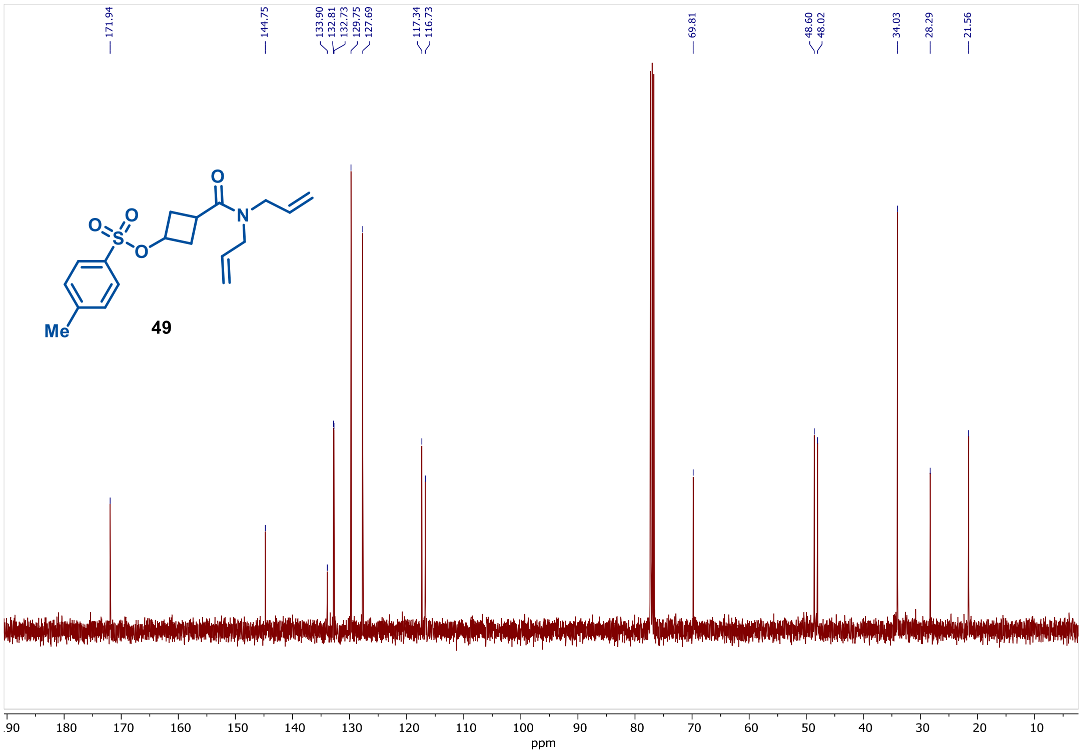
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **1h**



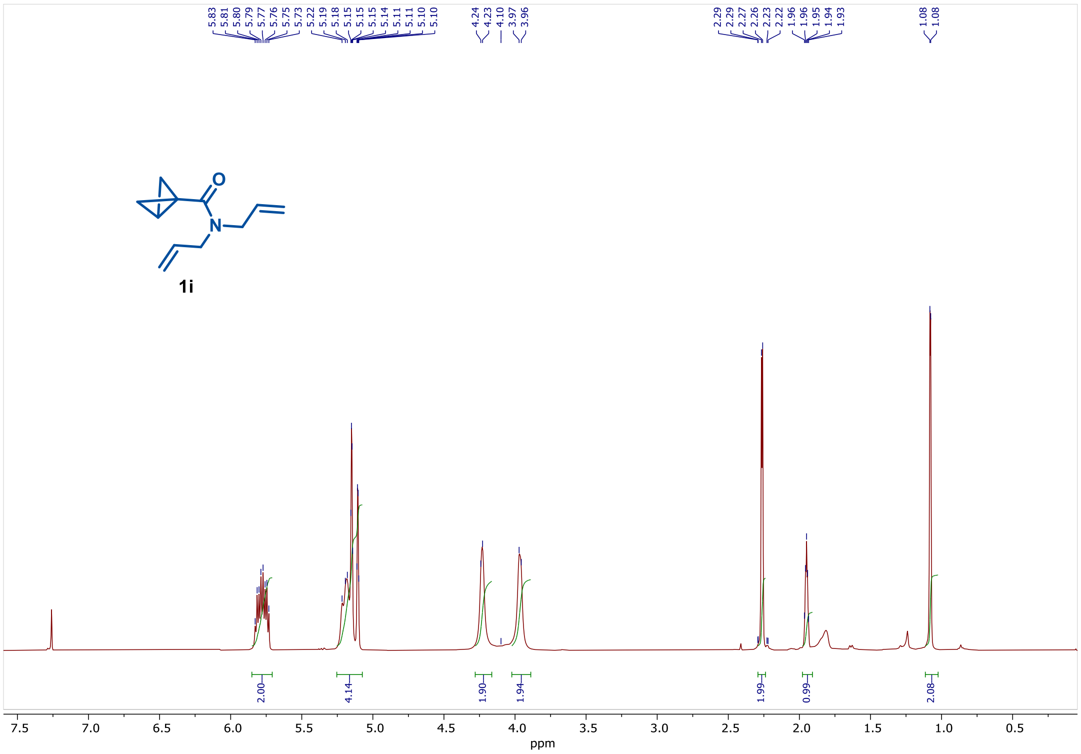
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **49** (**See Procedure**)



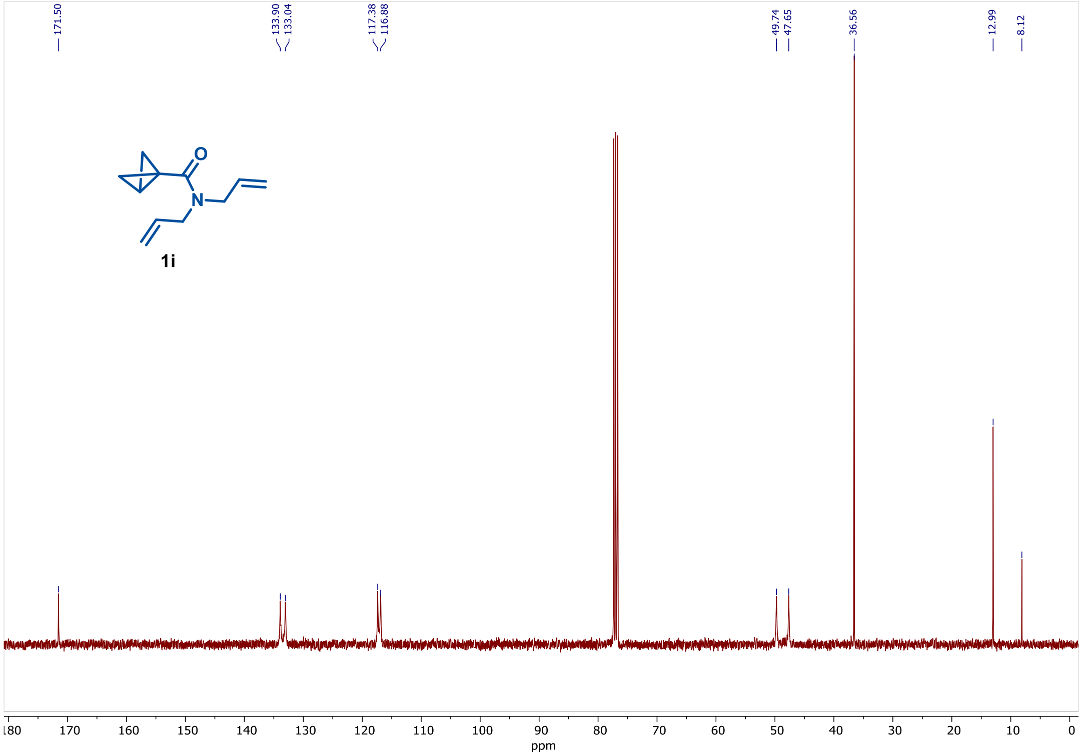
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **49**



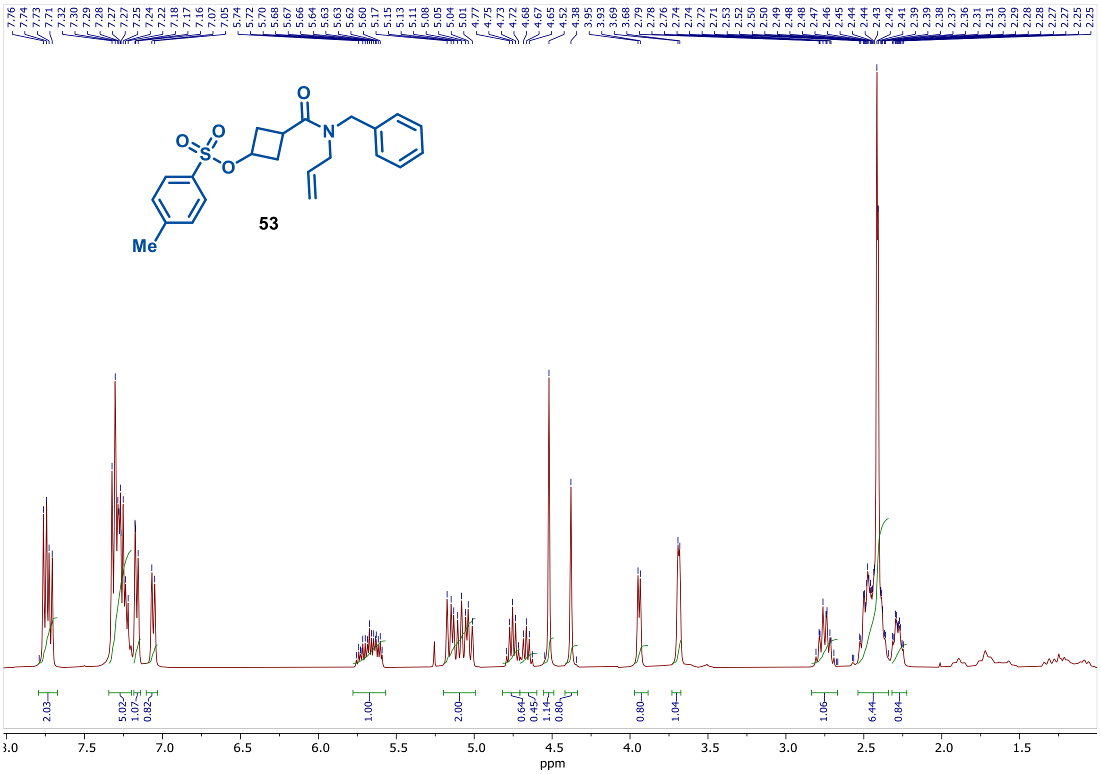
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **1i** (**See Procedure**)



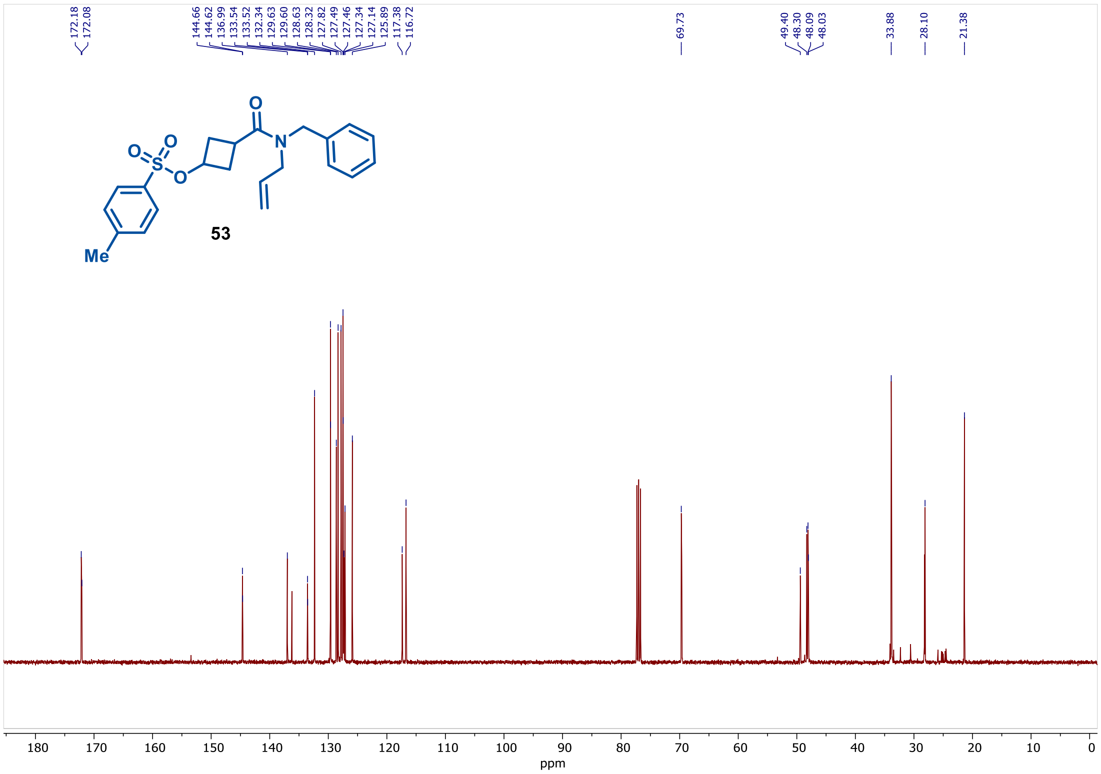
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **1i**



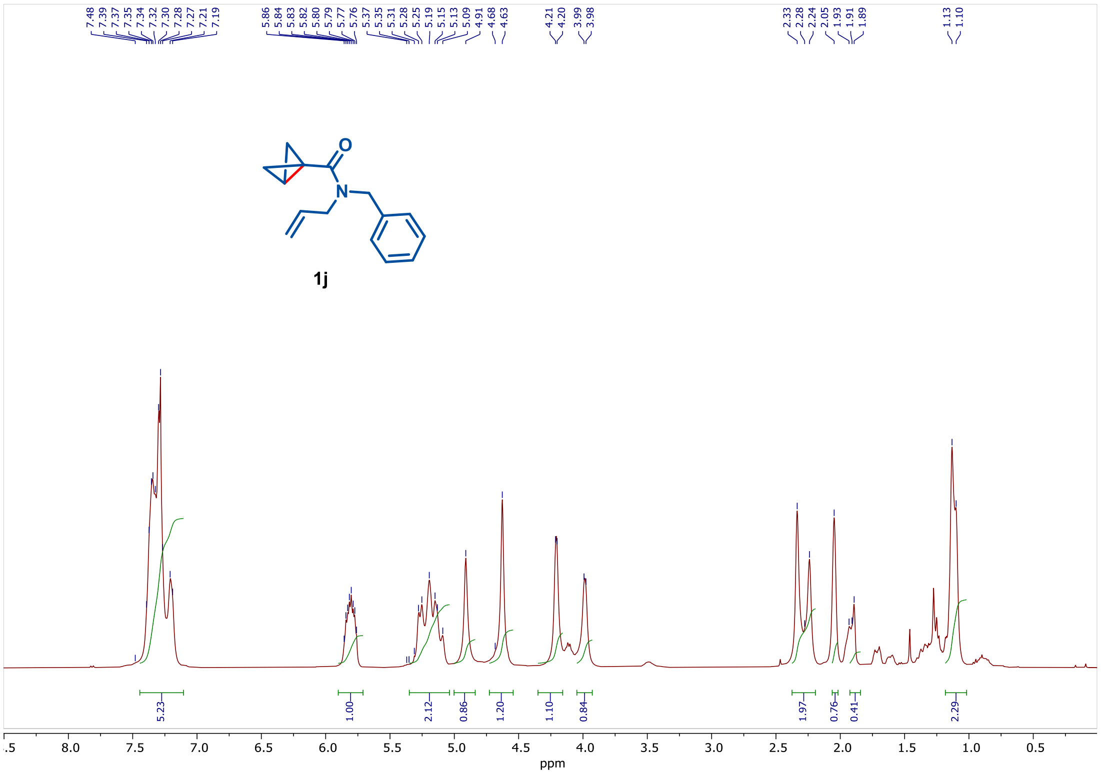
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **53** (**See Procedure**)



^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **53**



^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **1j** (**See Procedure**)



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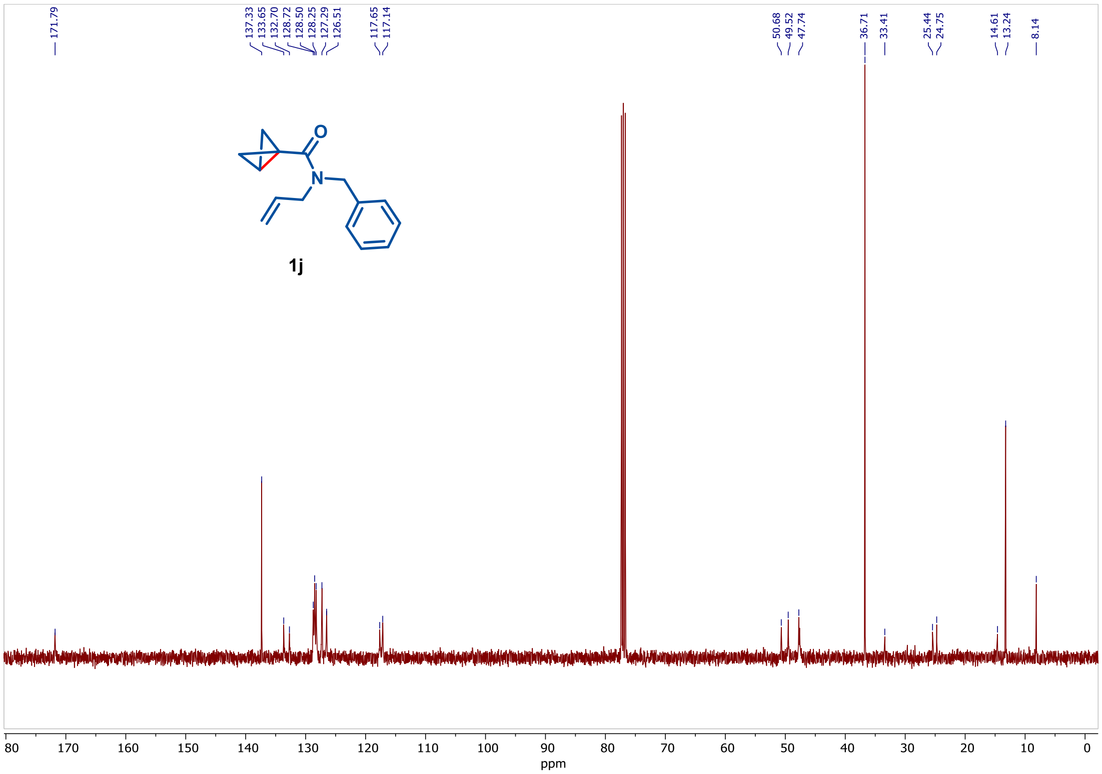
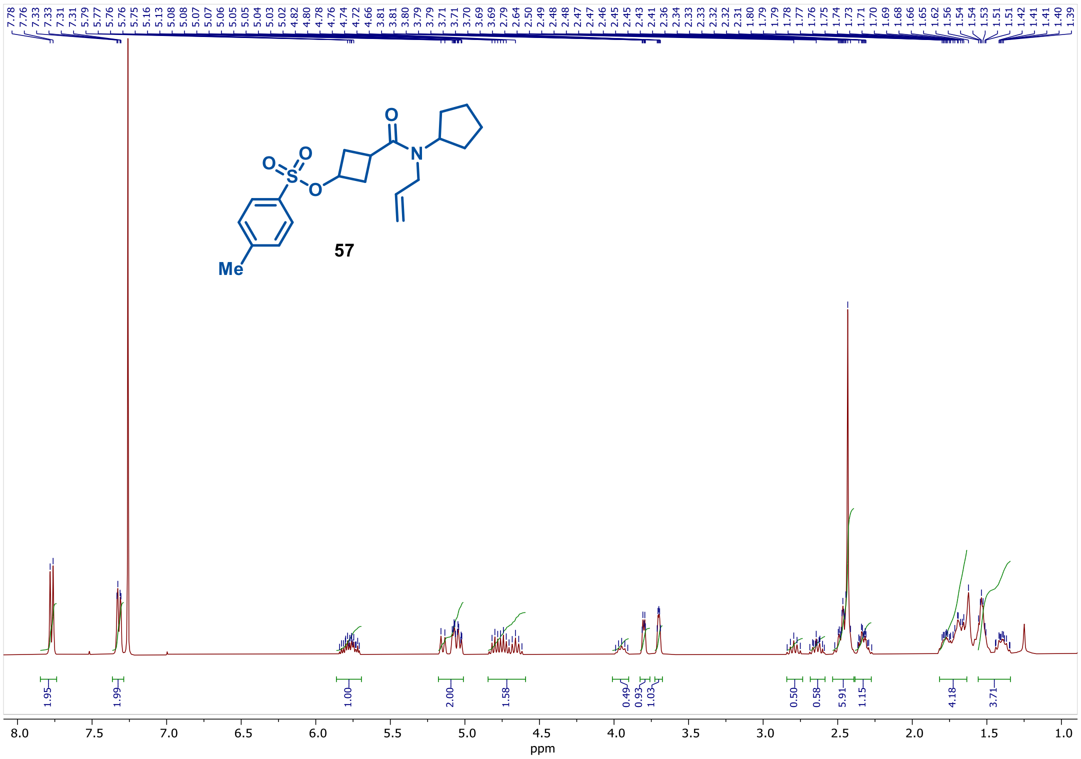
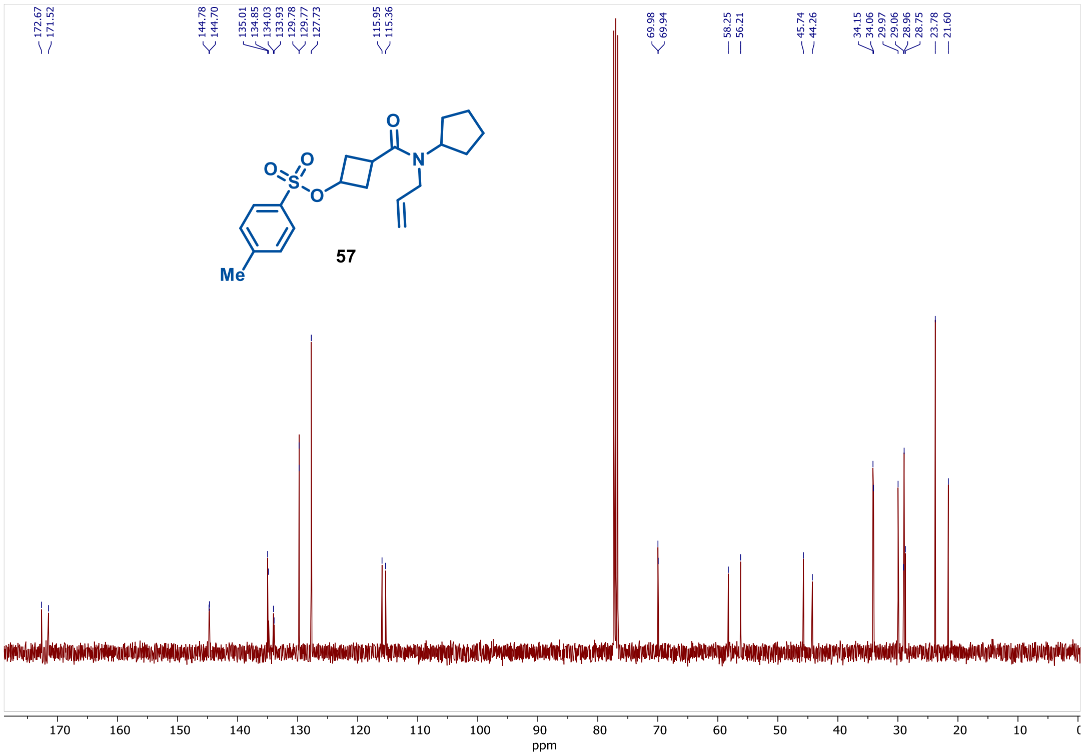


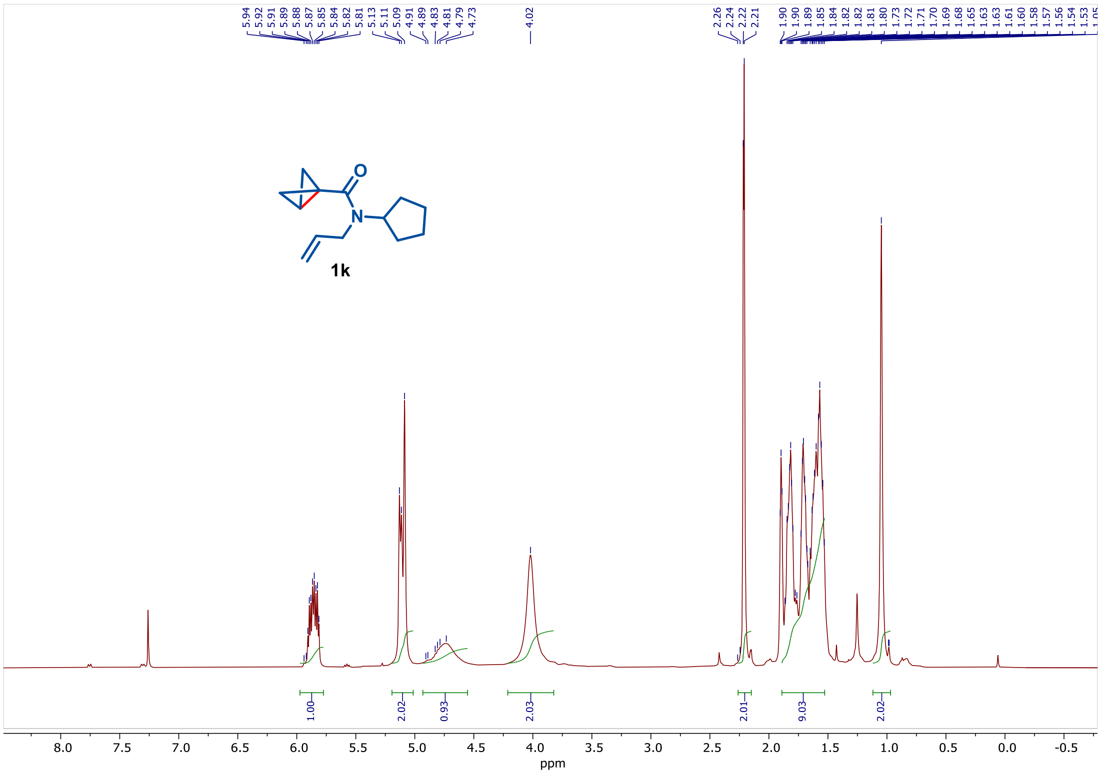
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **57** (**See Procedure**)



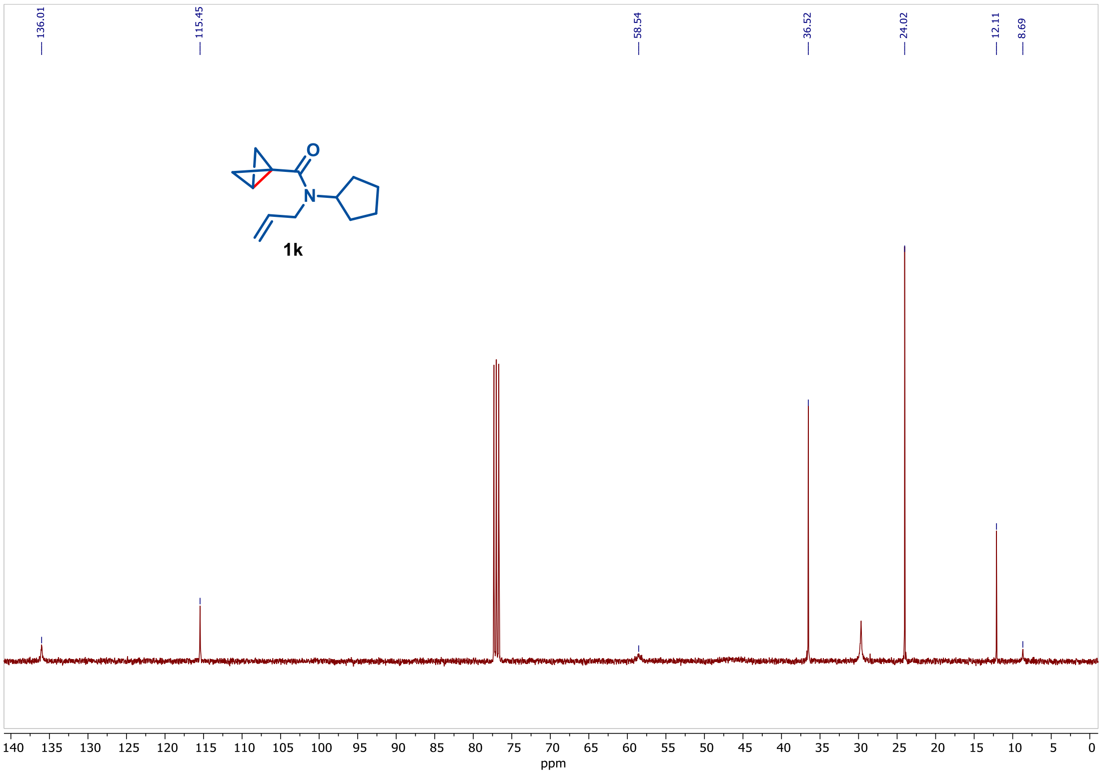
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **57**



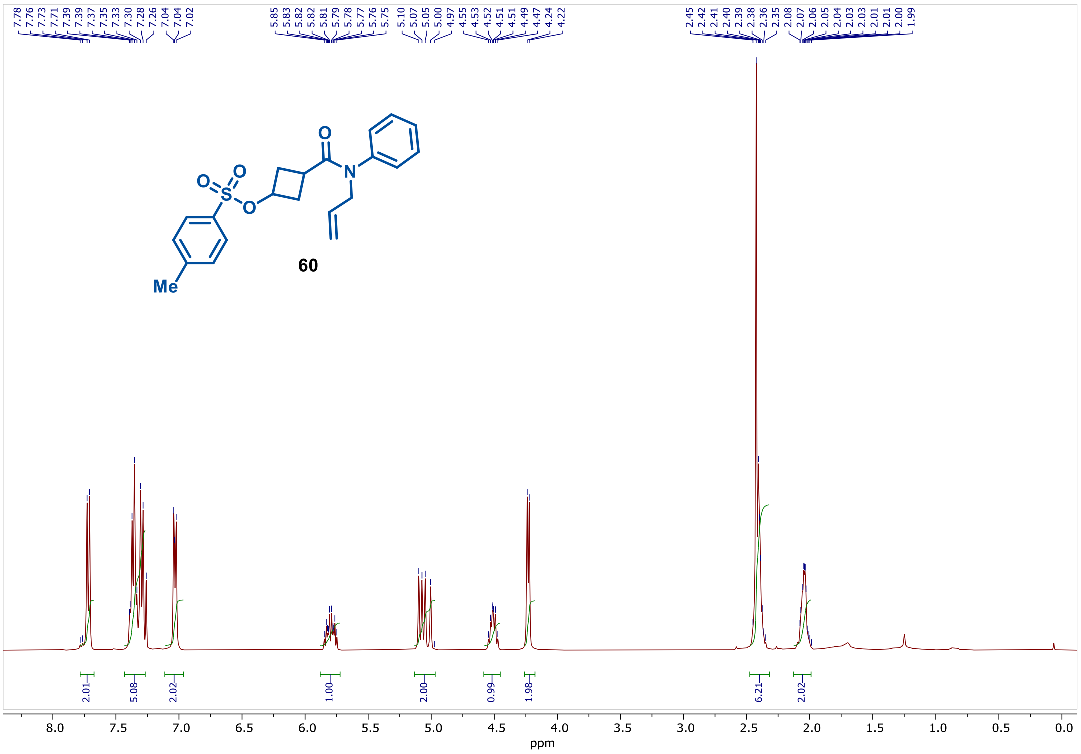
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **1k** (**See Procedure**)



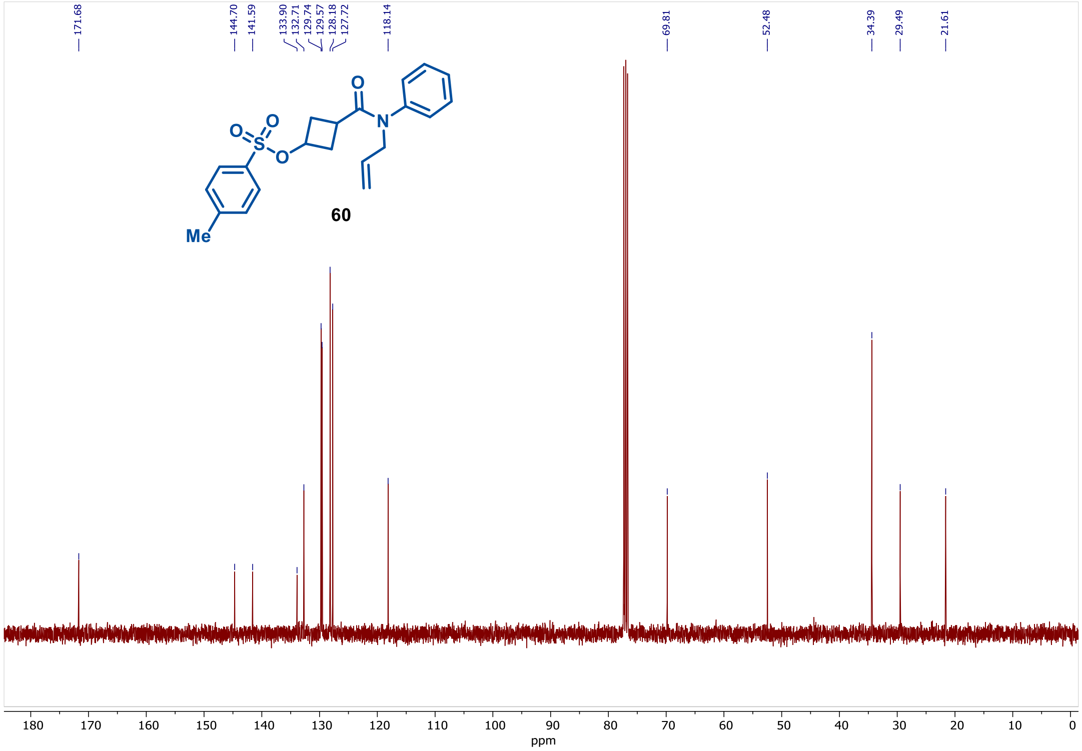
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **1k**



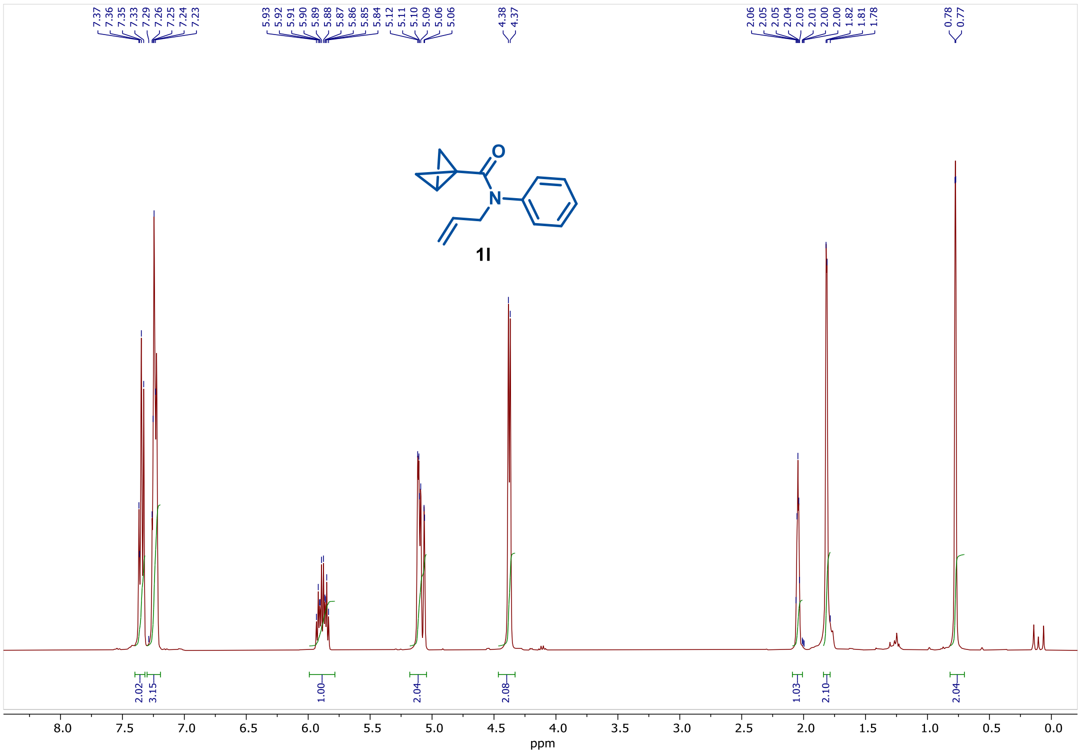
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **60** (**See Procedure**)



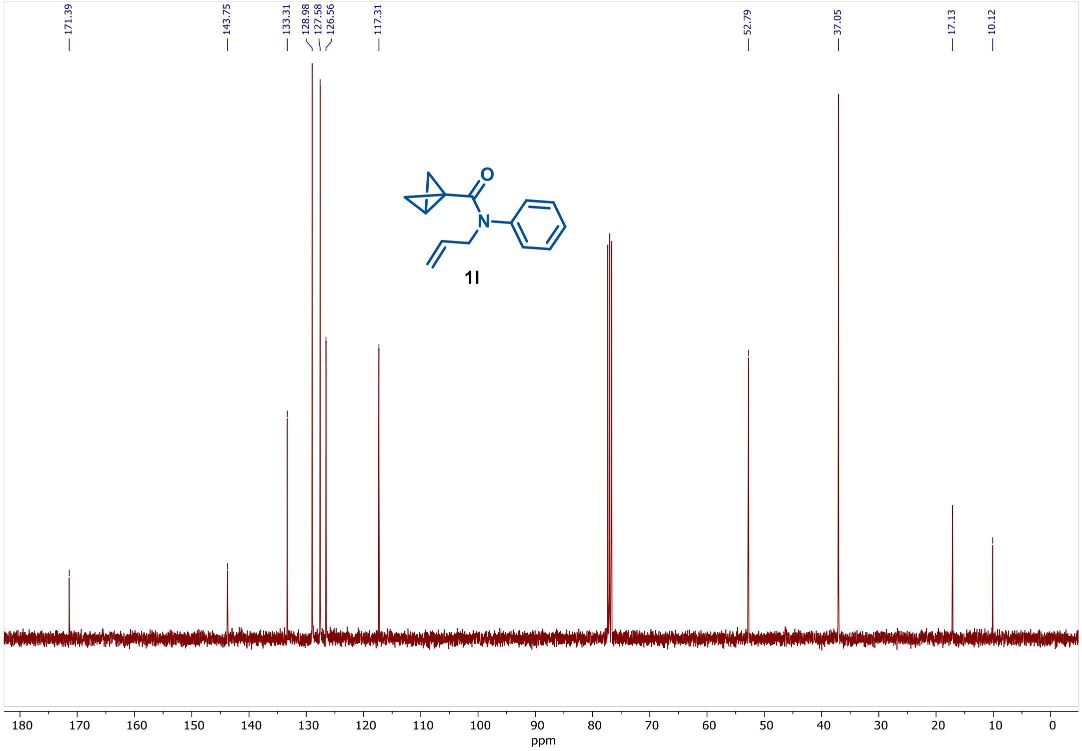
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **60**



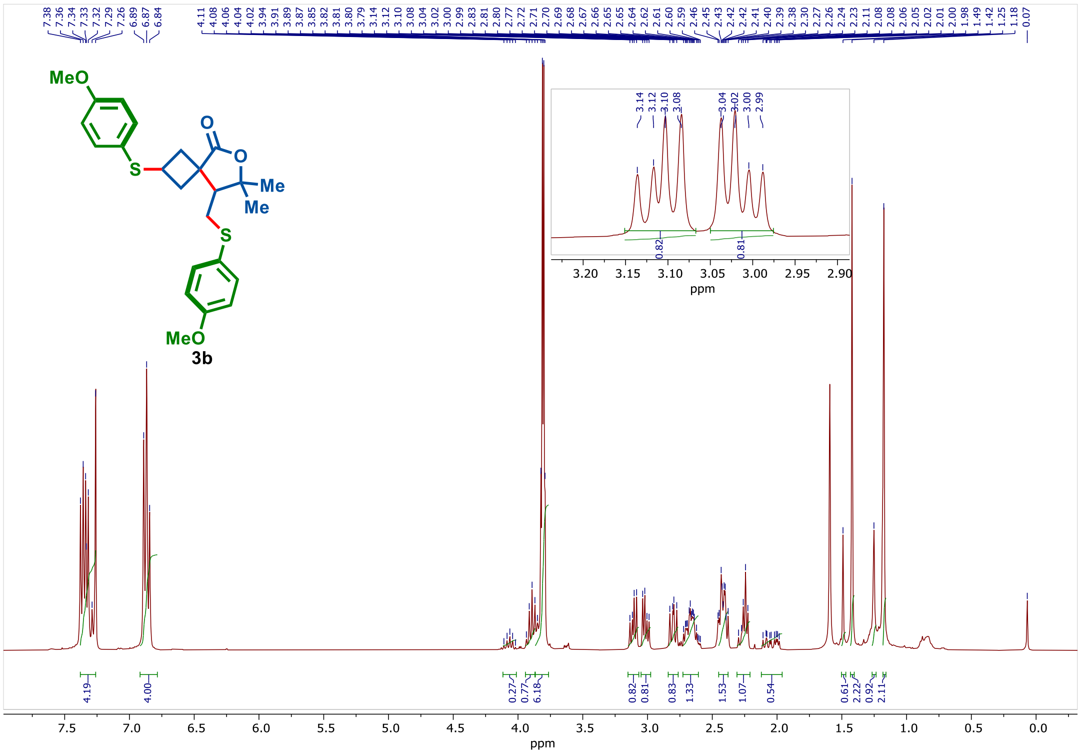
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **1l** (**See Procedure**)



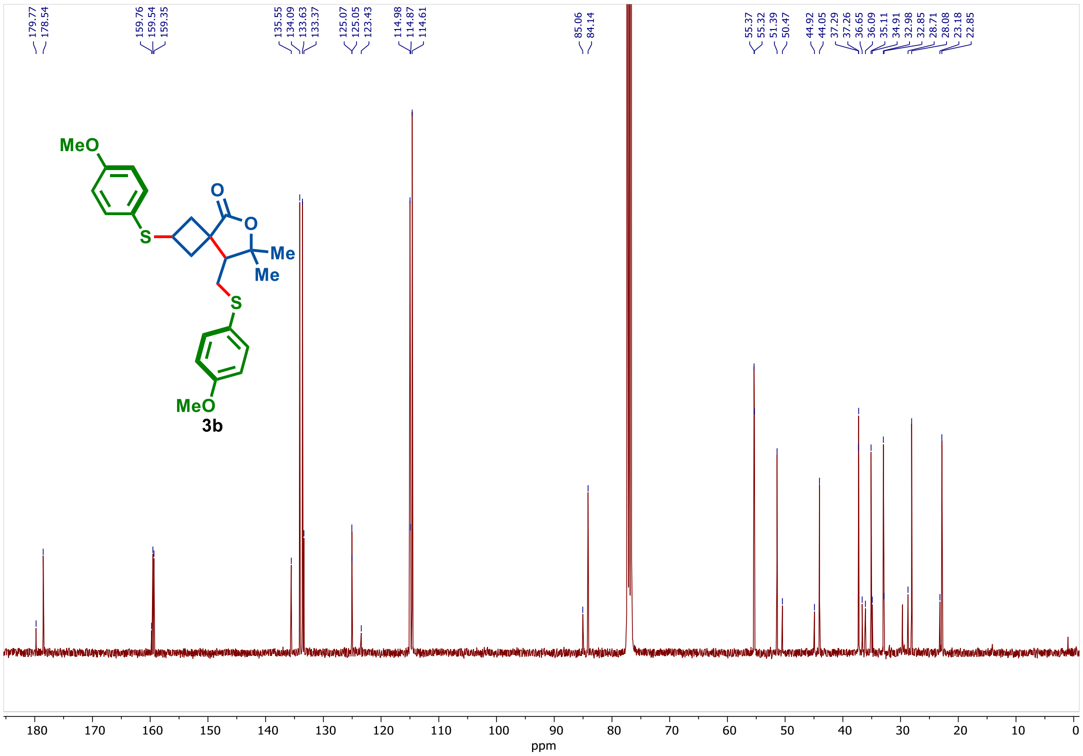
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **1l**



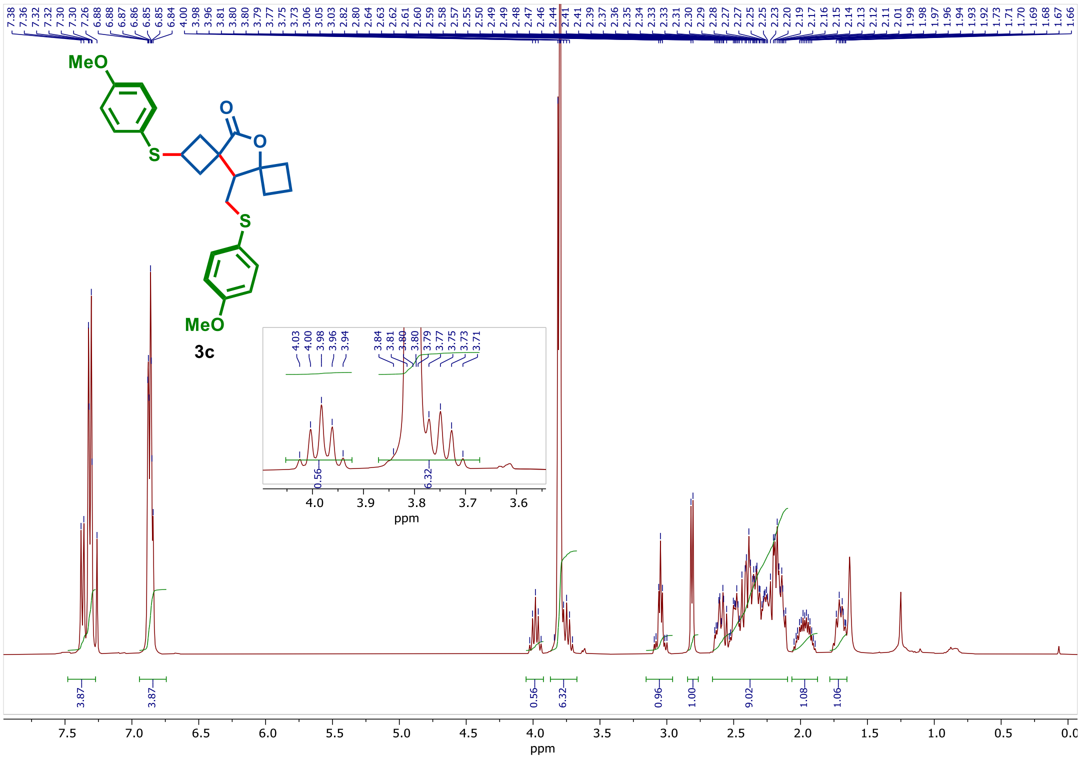
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **3b** (See Procedure)



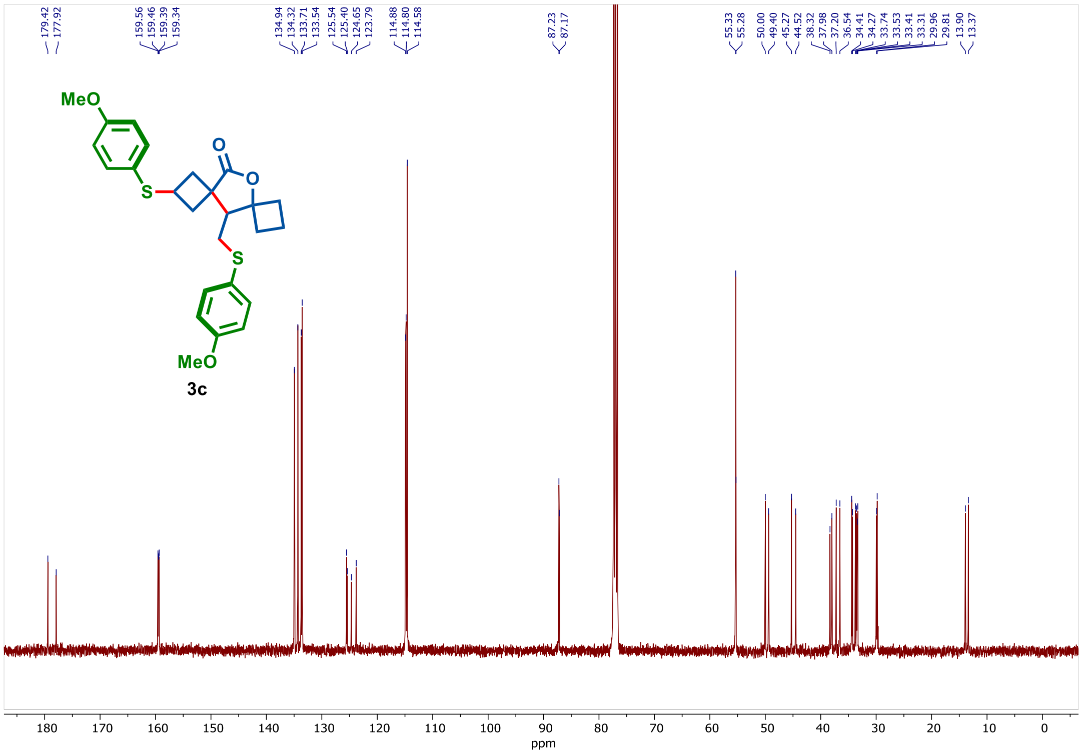
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **3b**



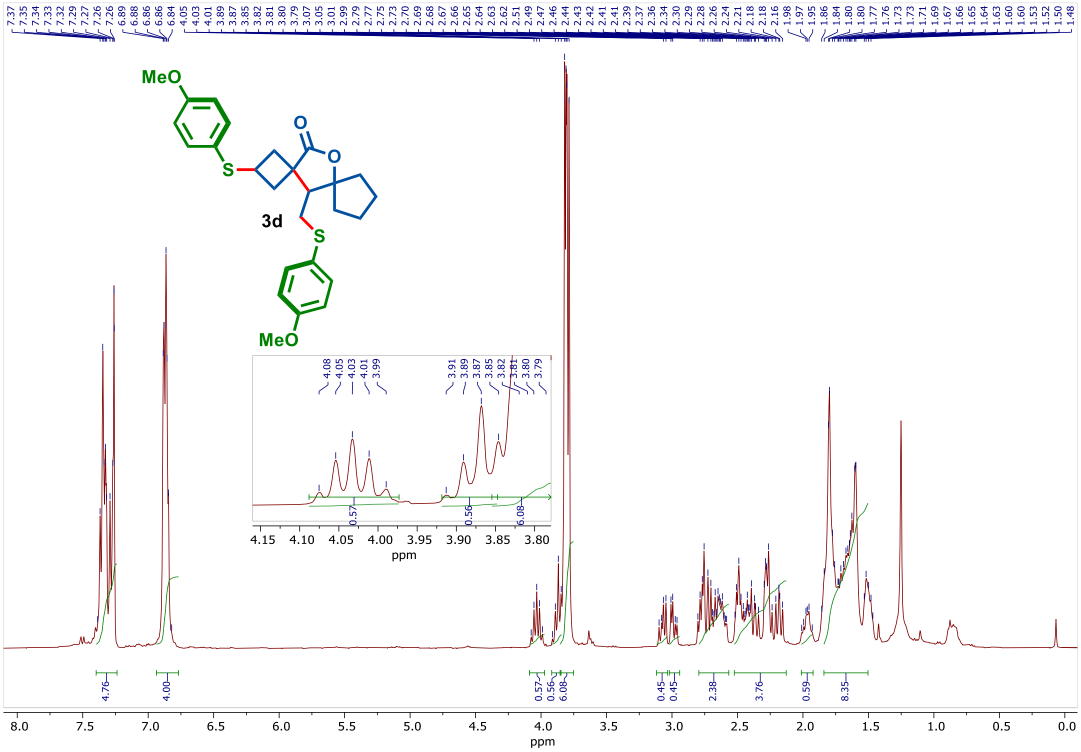
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **3c** (**See Procedure**)



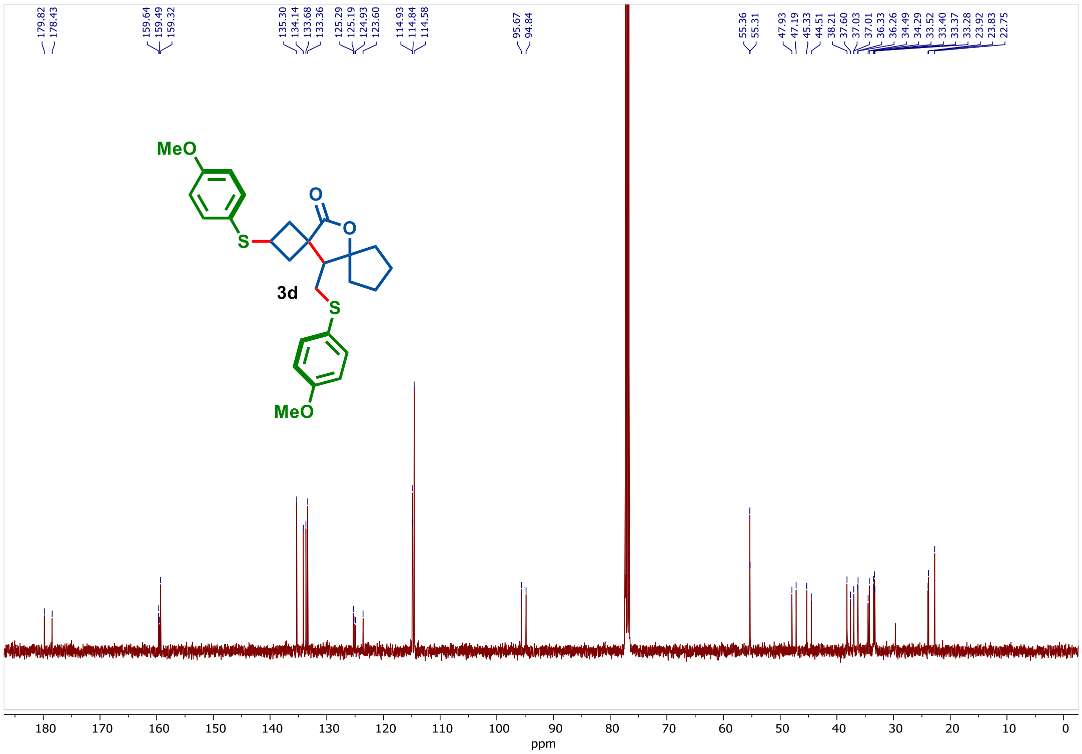
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **3c**



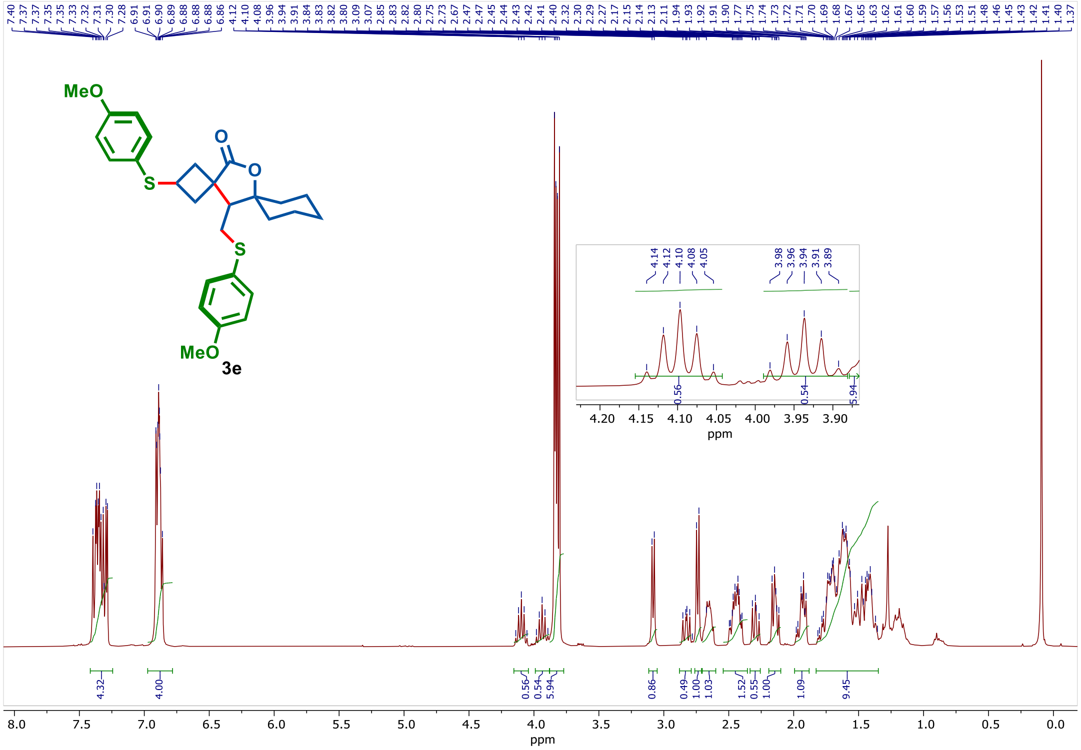
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **3d** (See Procedure)



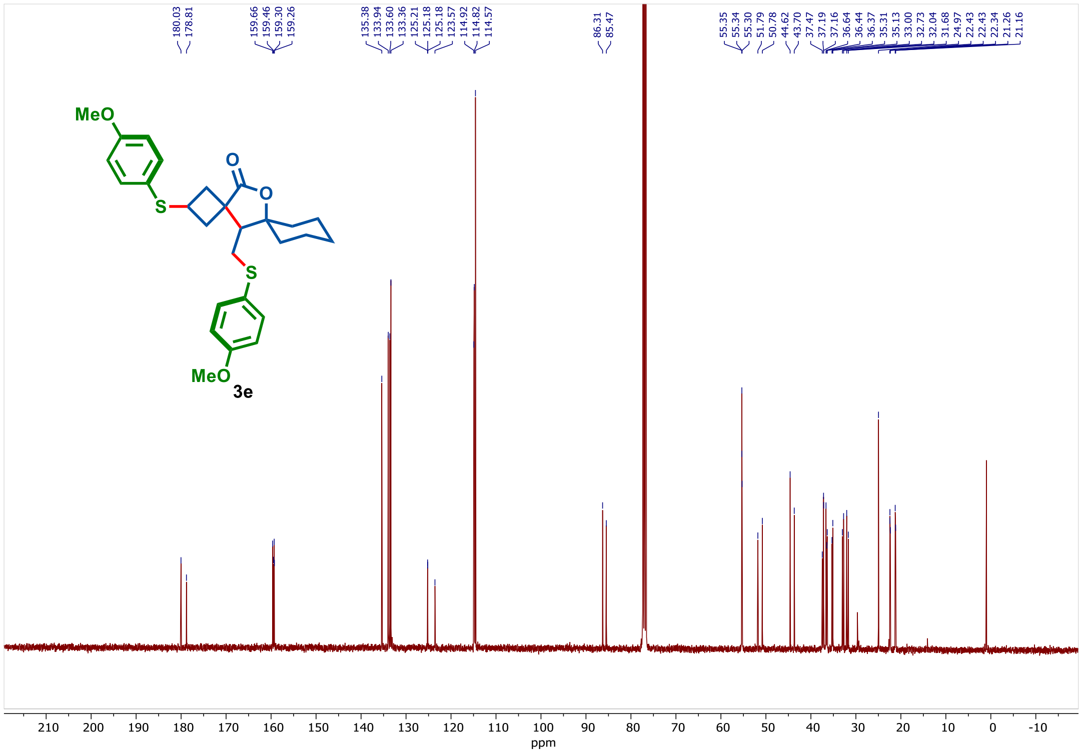
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **3d**



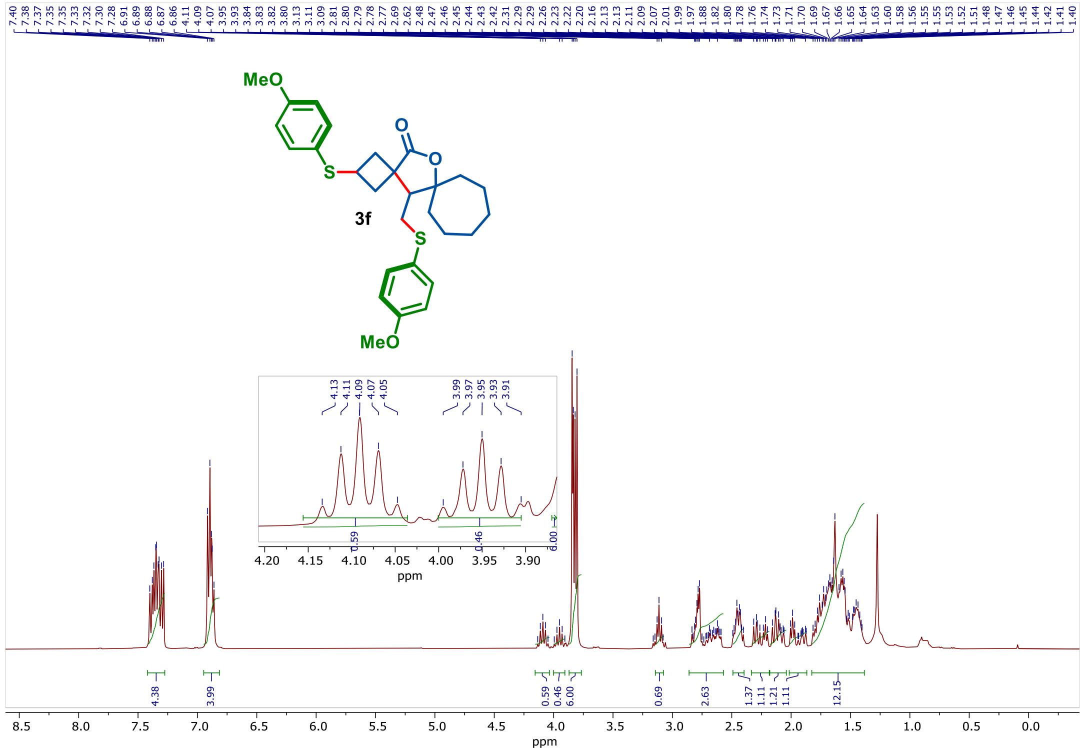
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **3e** (**See Procedure**)



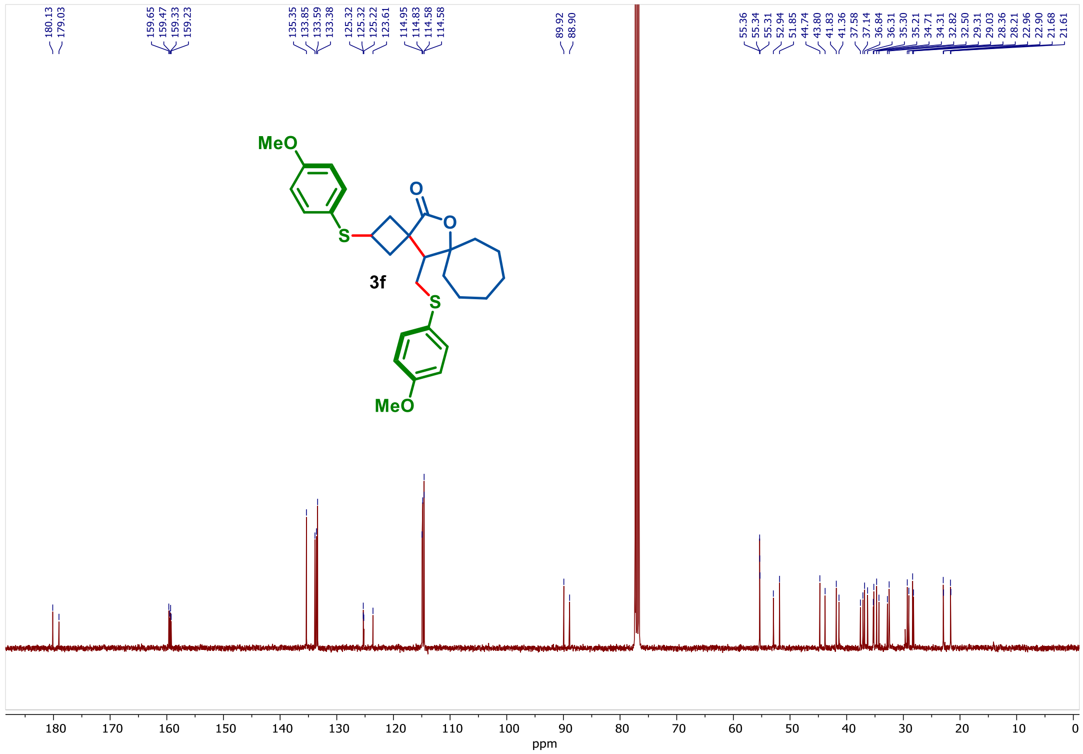
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **3e**



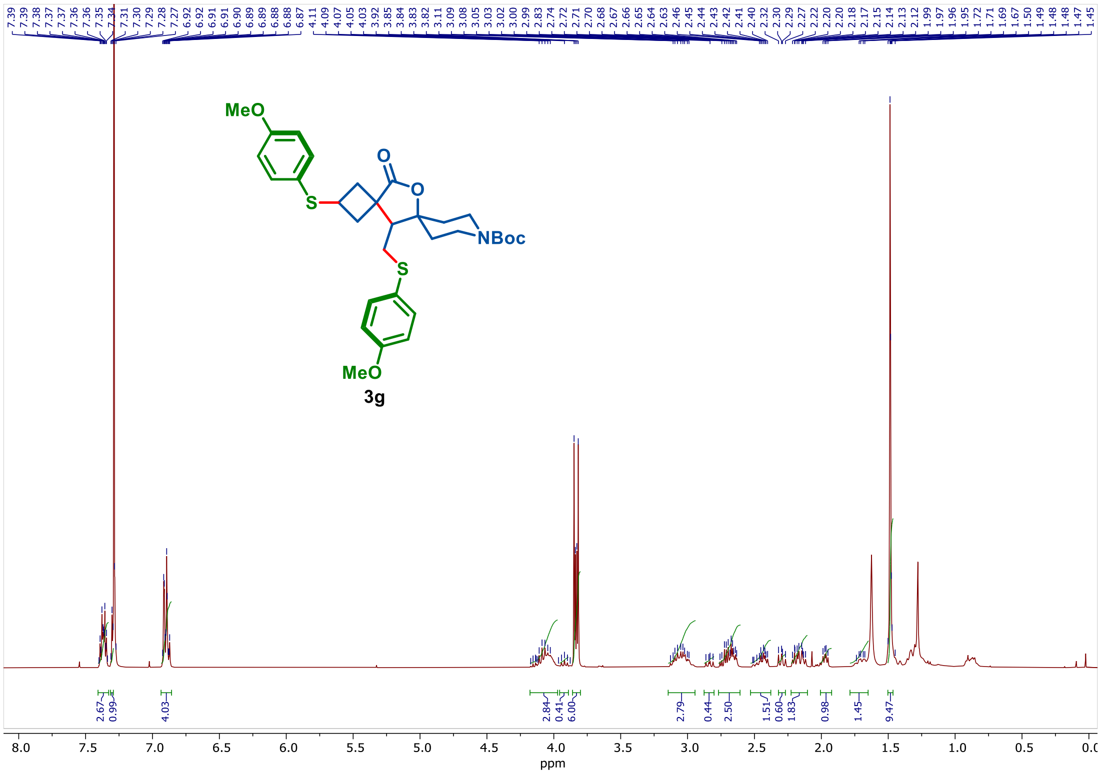
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **3f** (See Procedure)



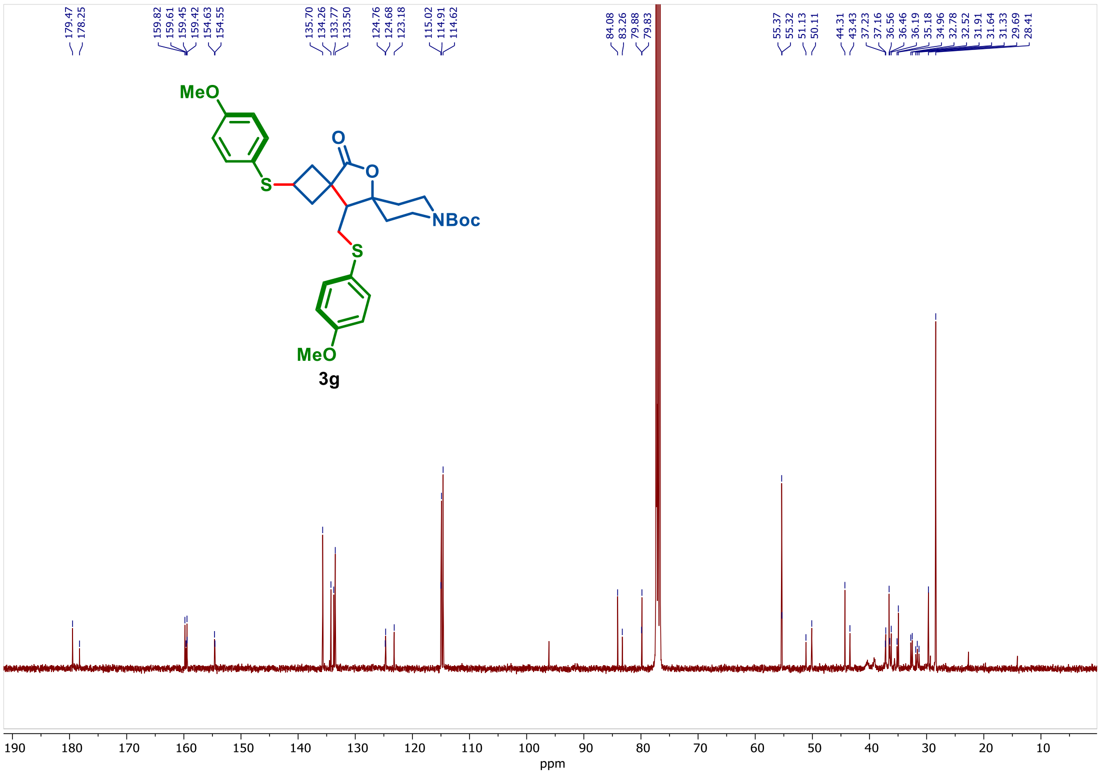
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **3f**



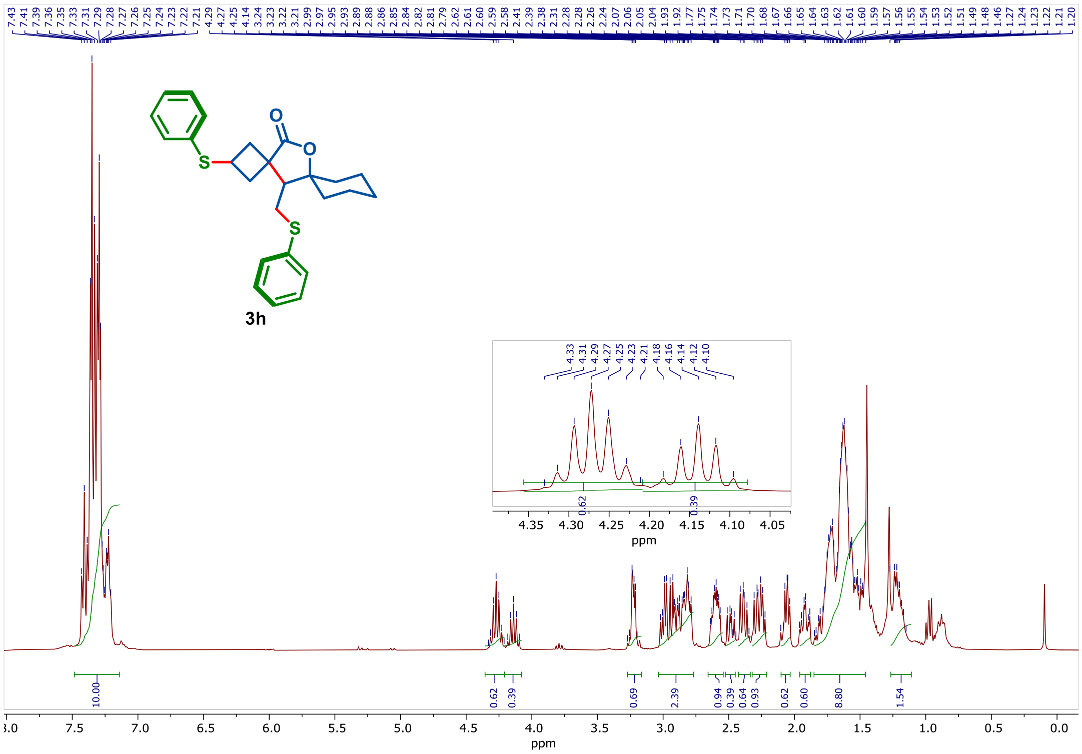
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **3g** (**See Procedure**)



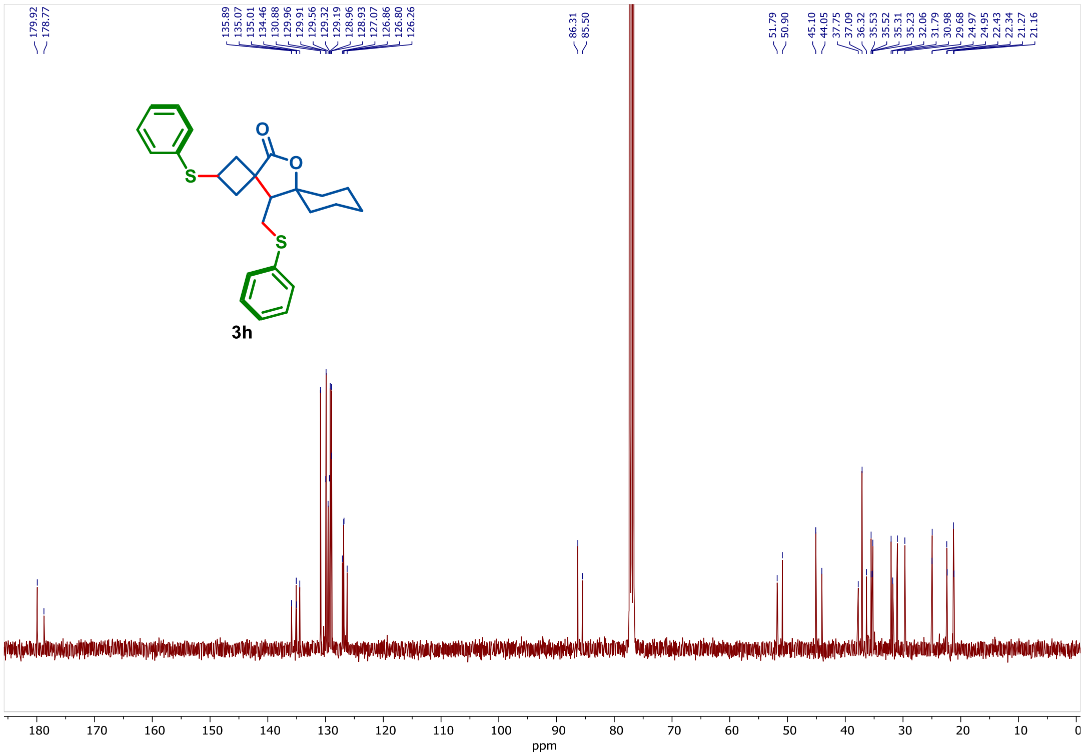
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **3g**



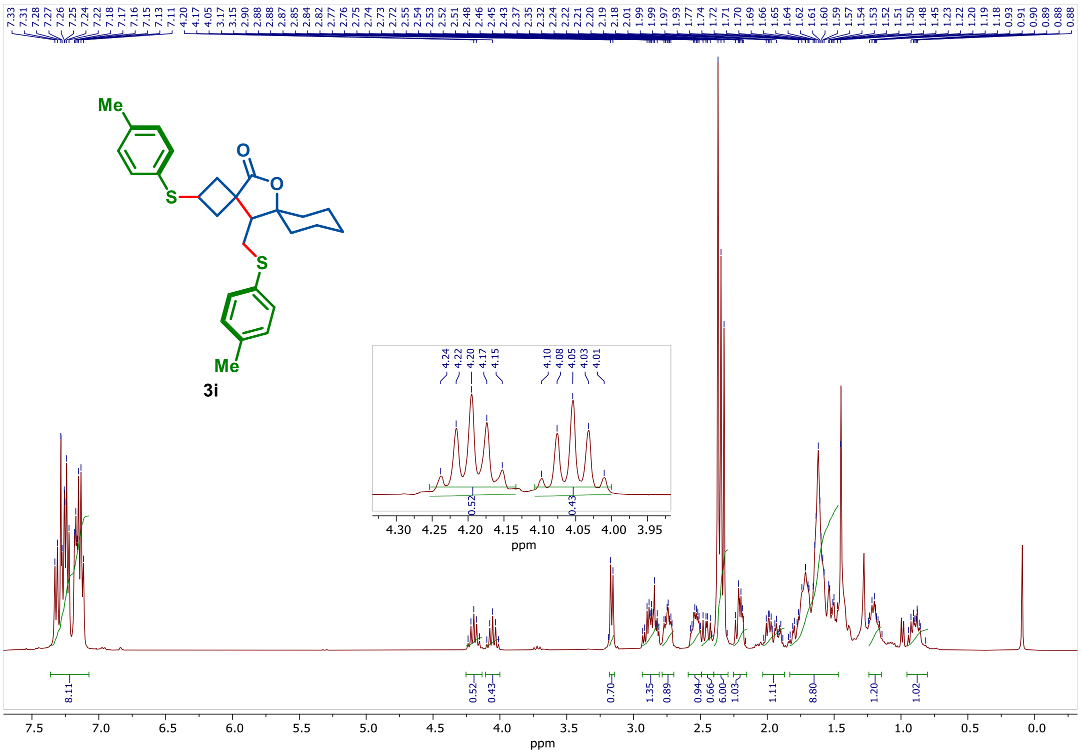
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **3h** (See Procedure)



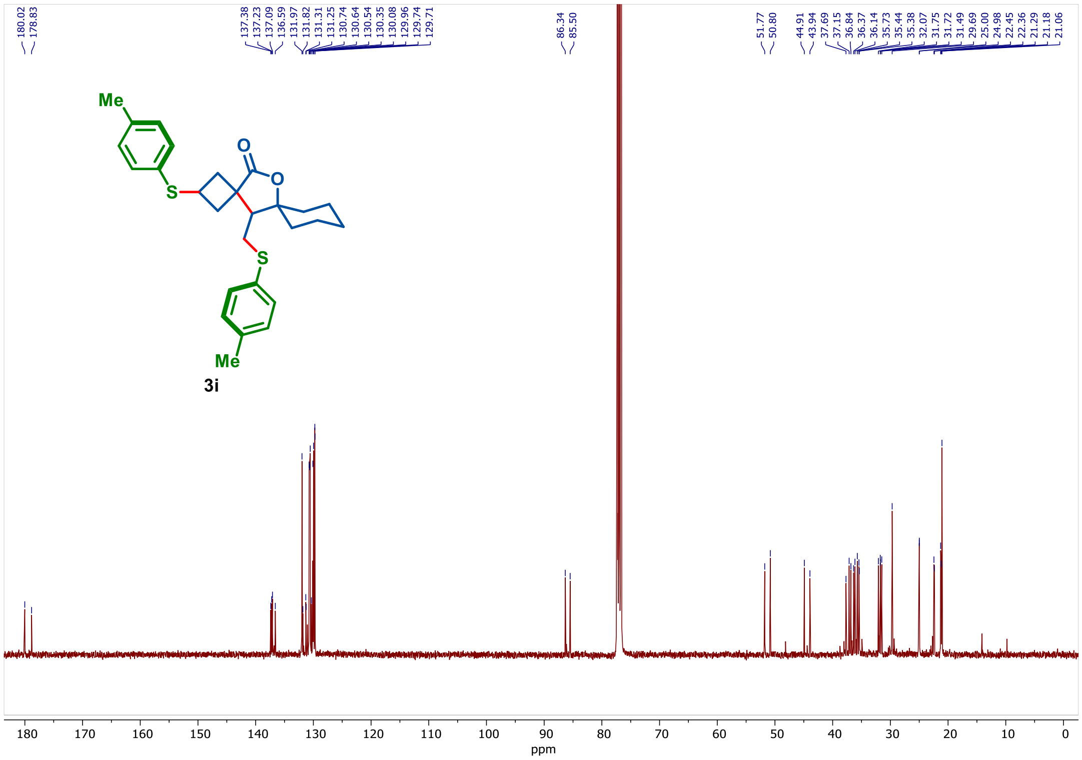
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **3h**



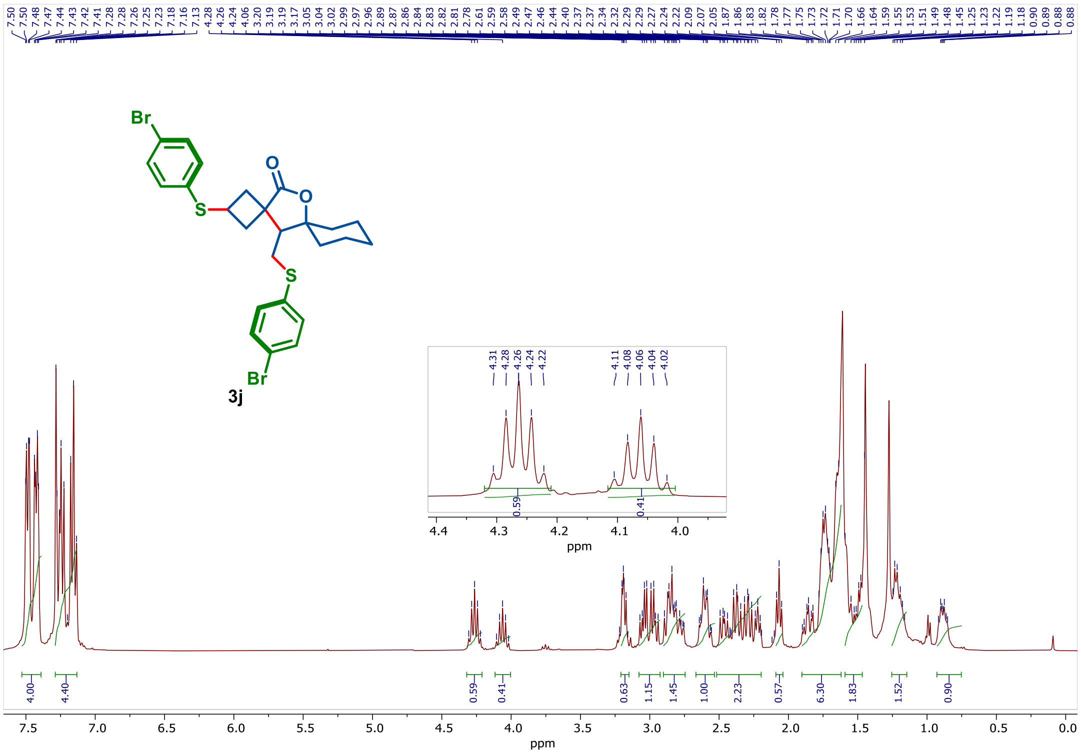
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **3i** (**See Procedure**)



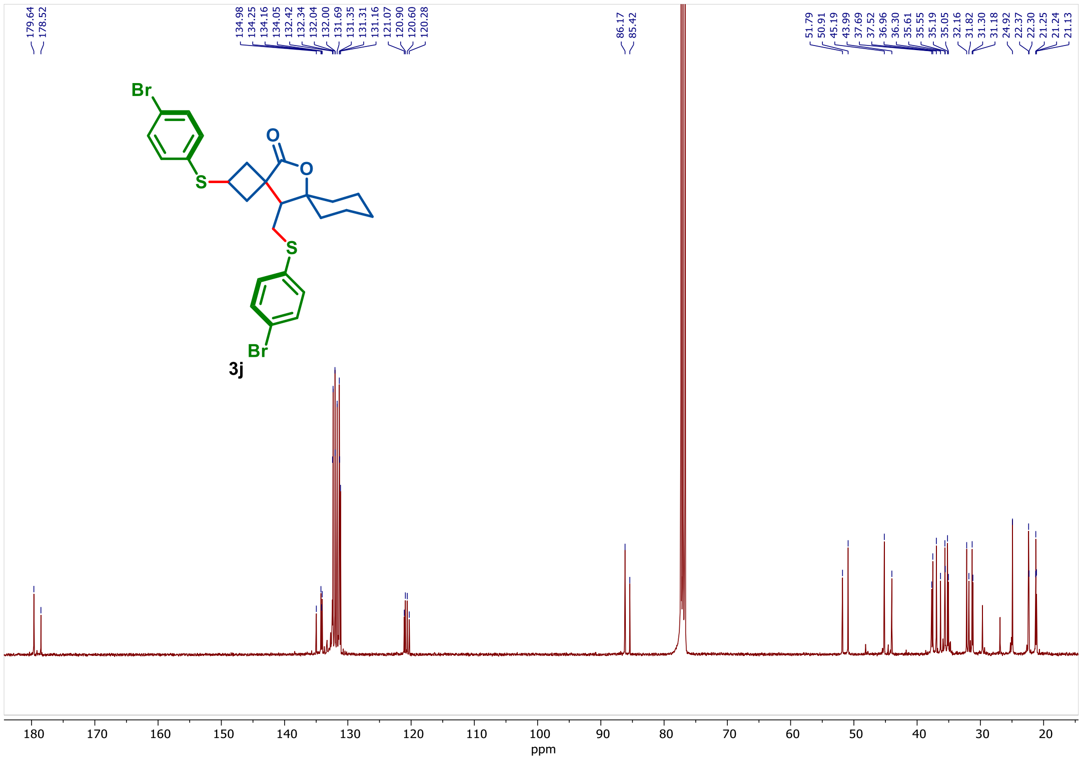
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **3i**



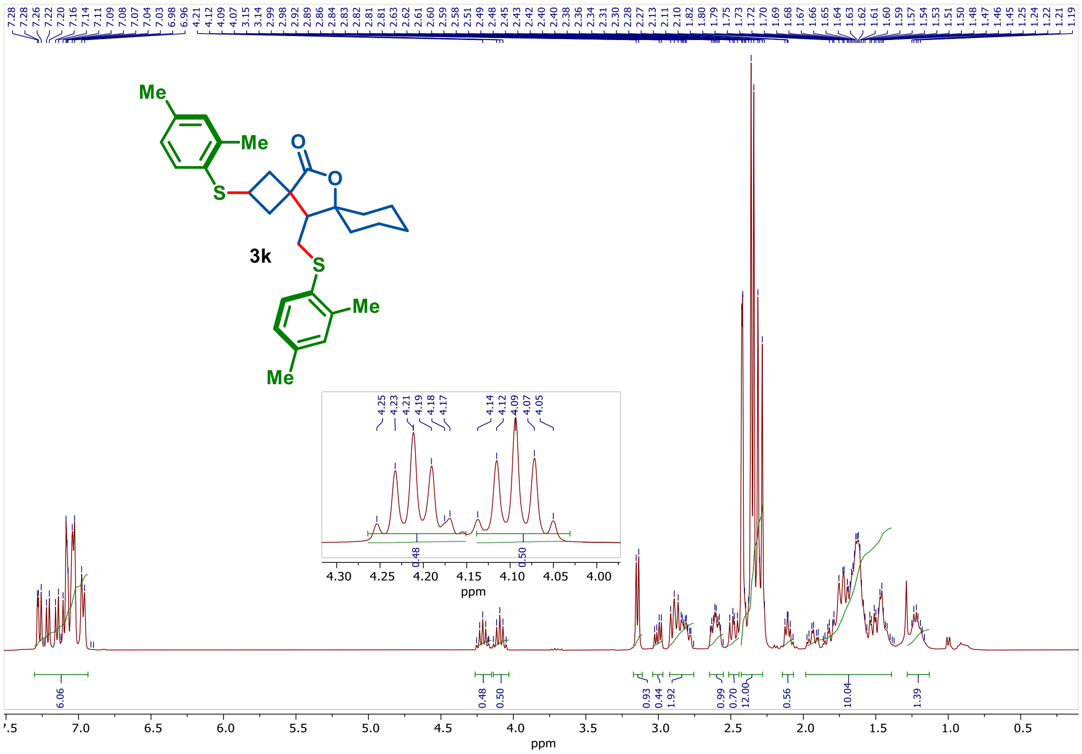
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **3j** (**See Procedure**)



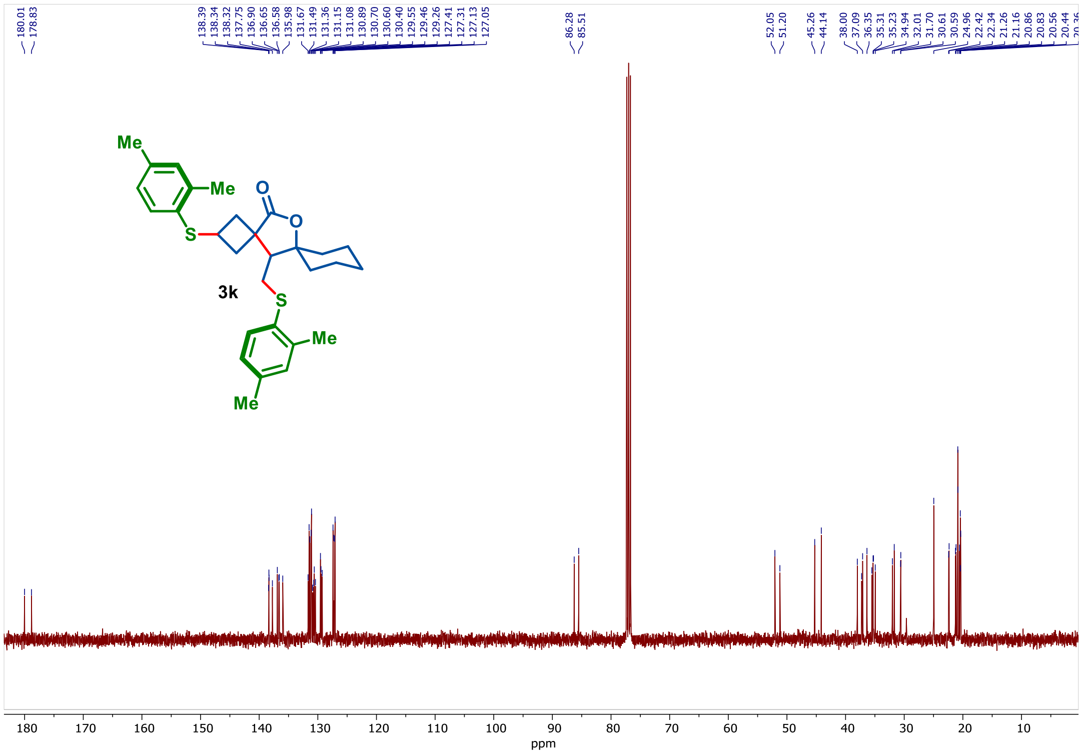
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **3j**



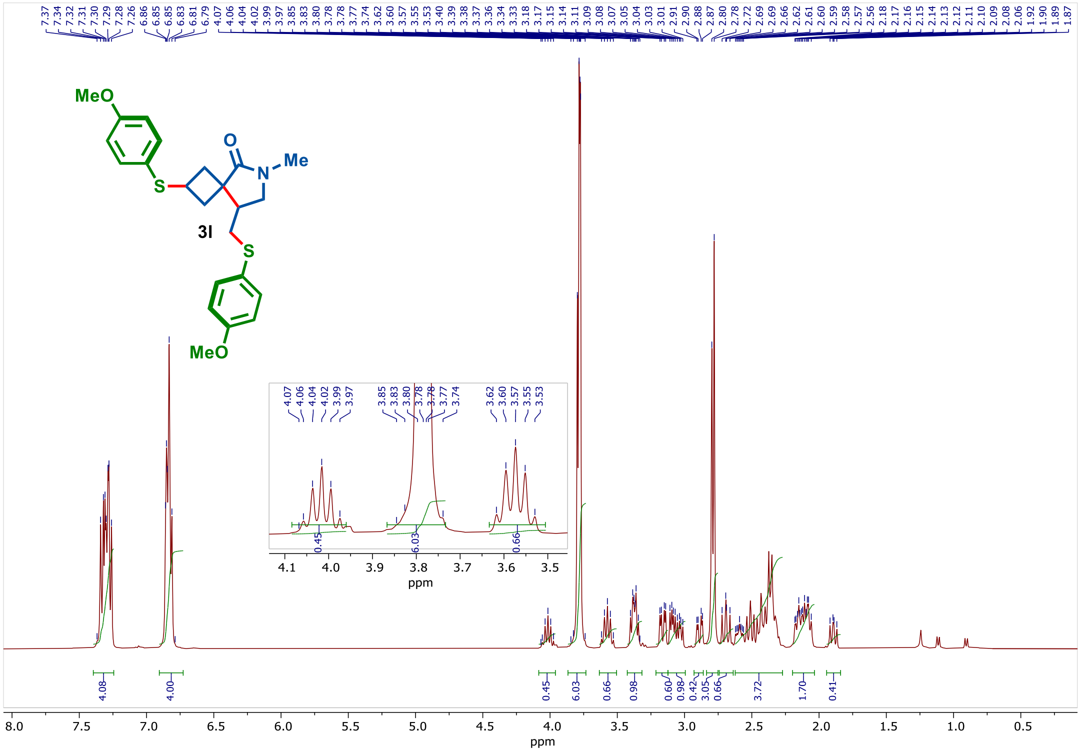
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **3k** (**See Procedure**)



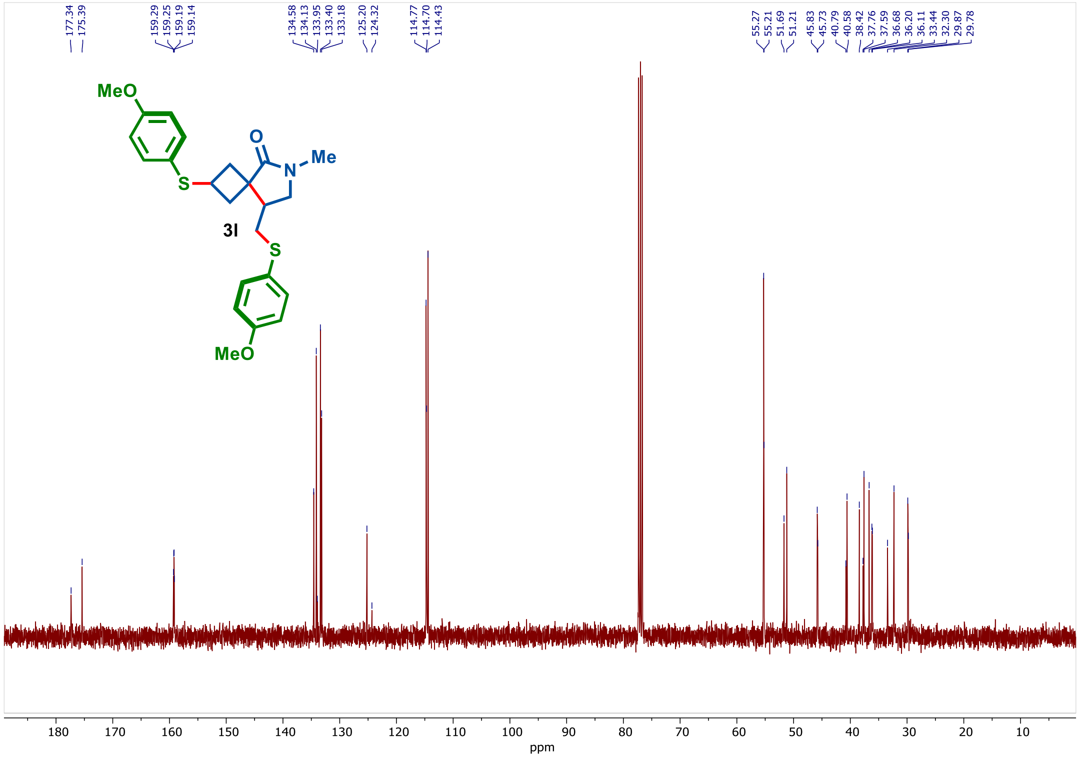
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **3k**



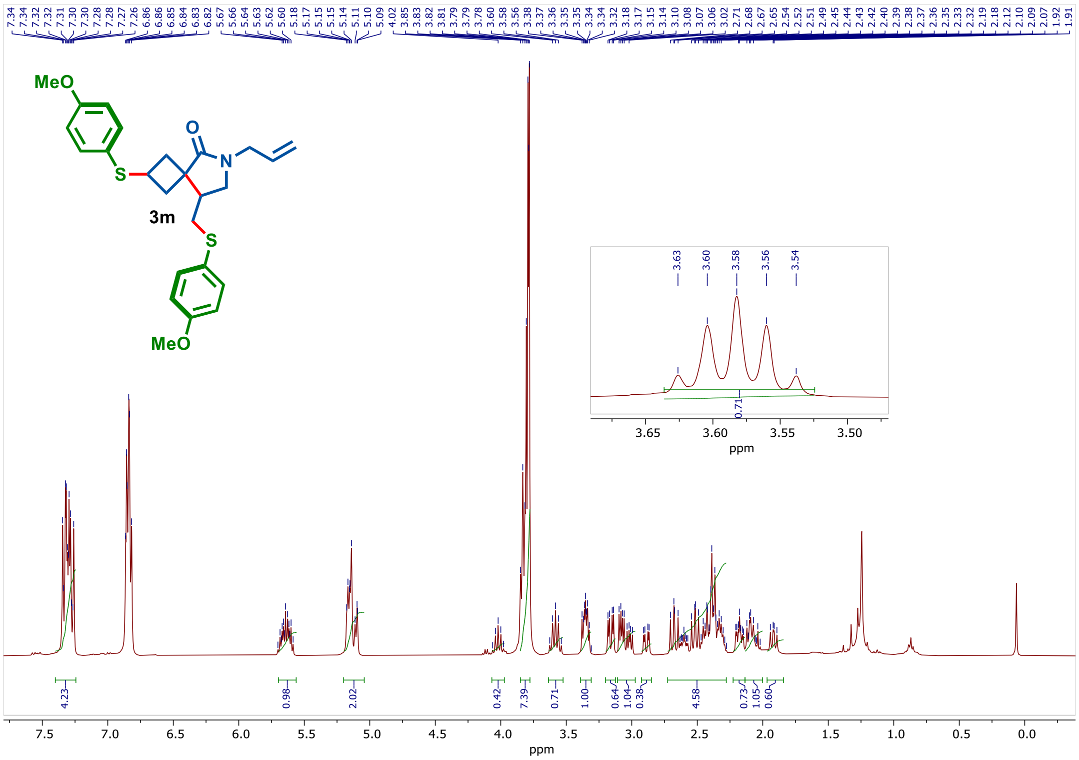
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **3l** (**See Procedure**)



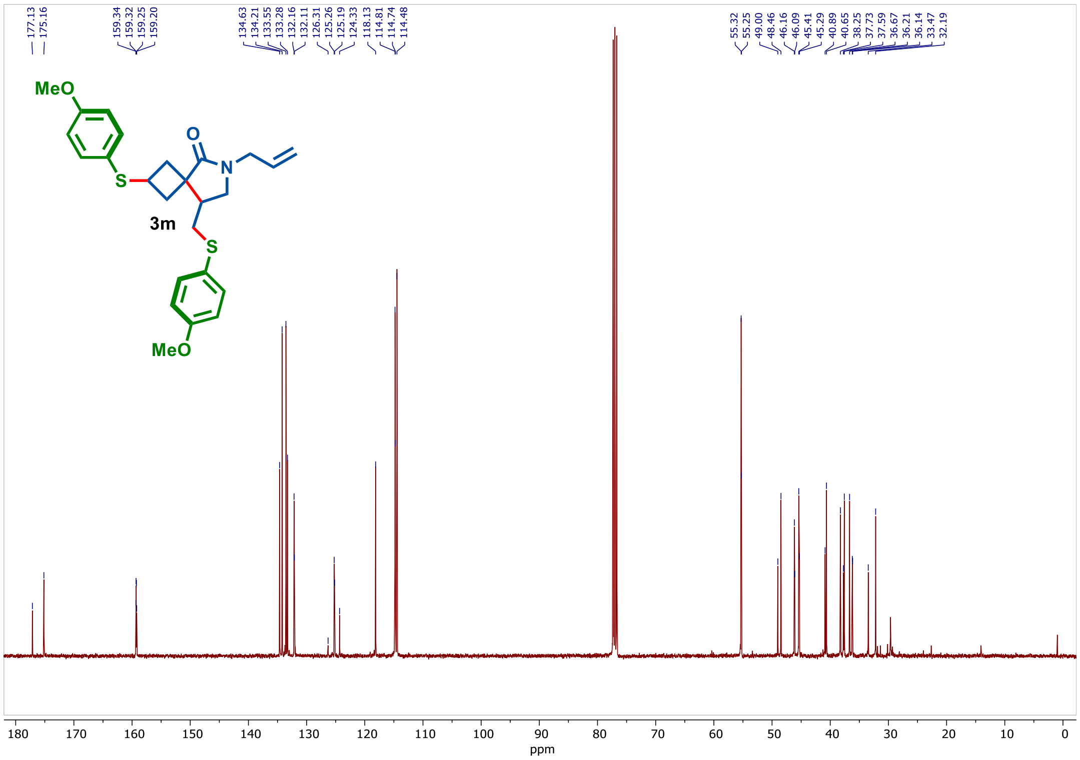
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **3l**



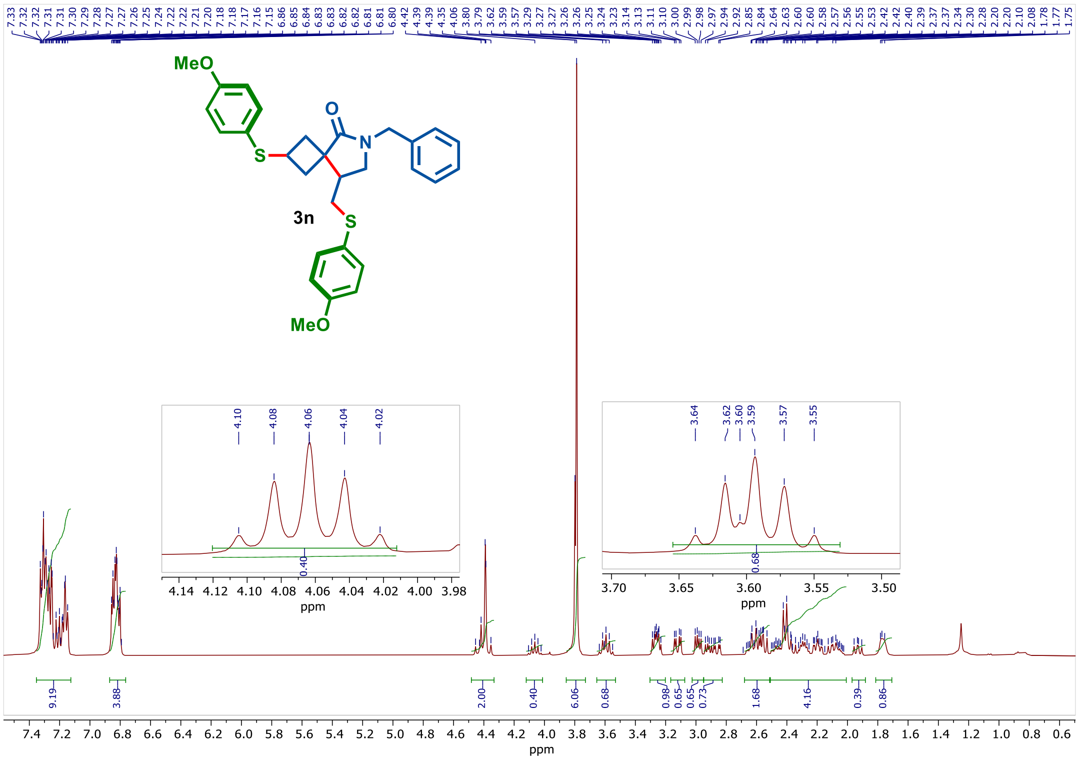
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **3m** (See Procedure)



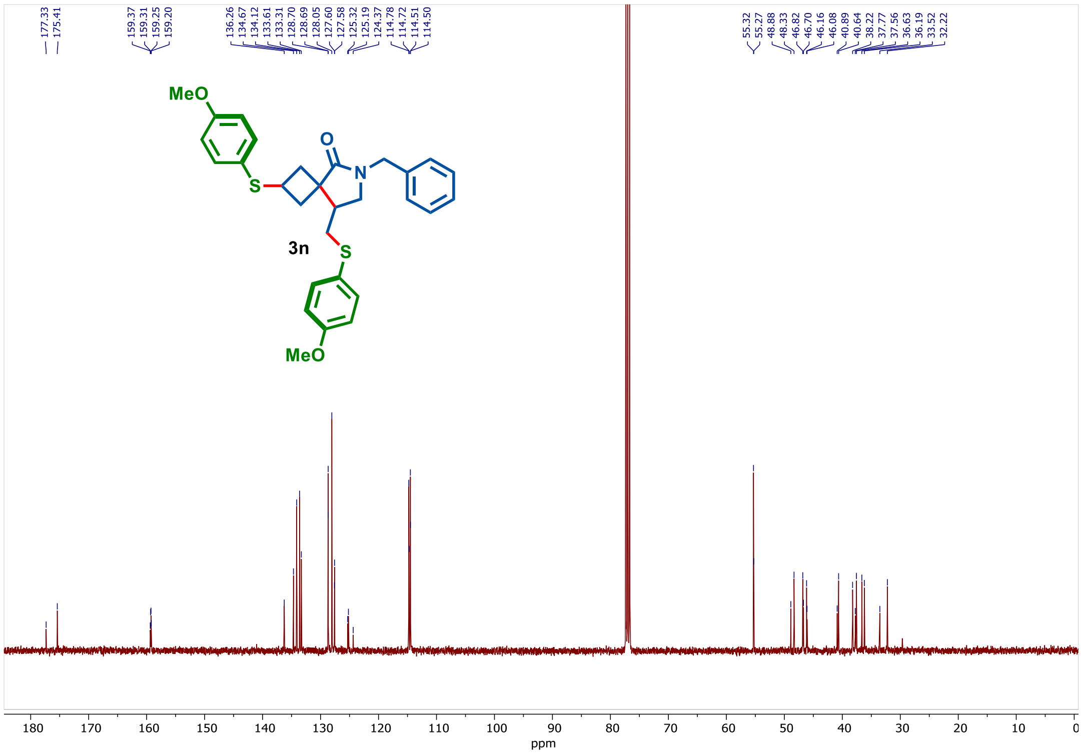
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **3m**



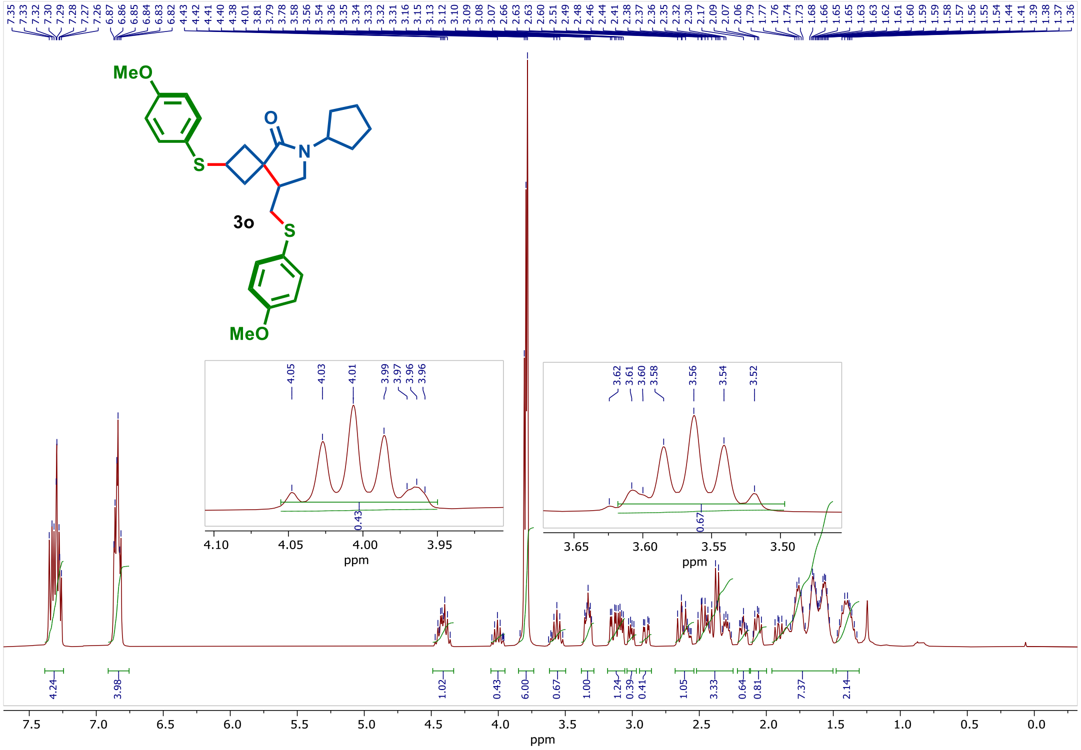
^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **3n** (See Procedure)



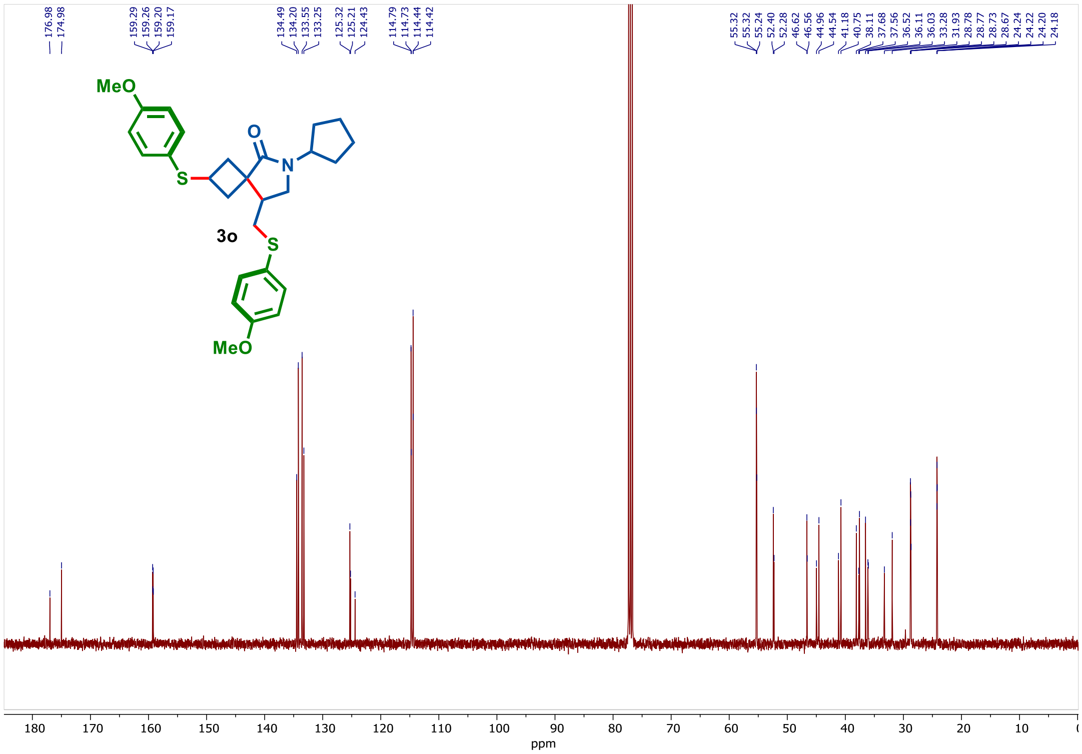
^{13}C NMR (101 MHz, $CDCl_3$) spectra of compound **3n**



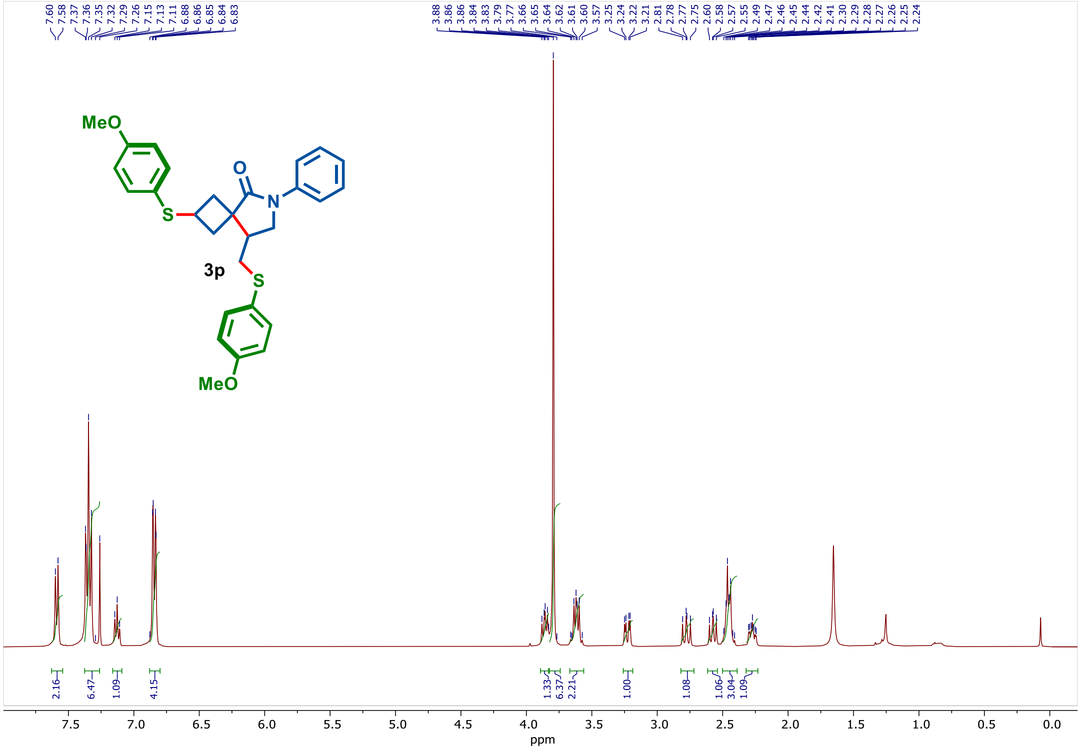
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **3o** (**See Procedure**)



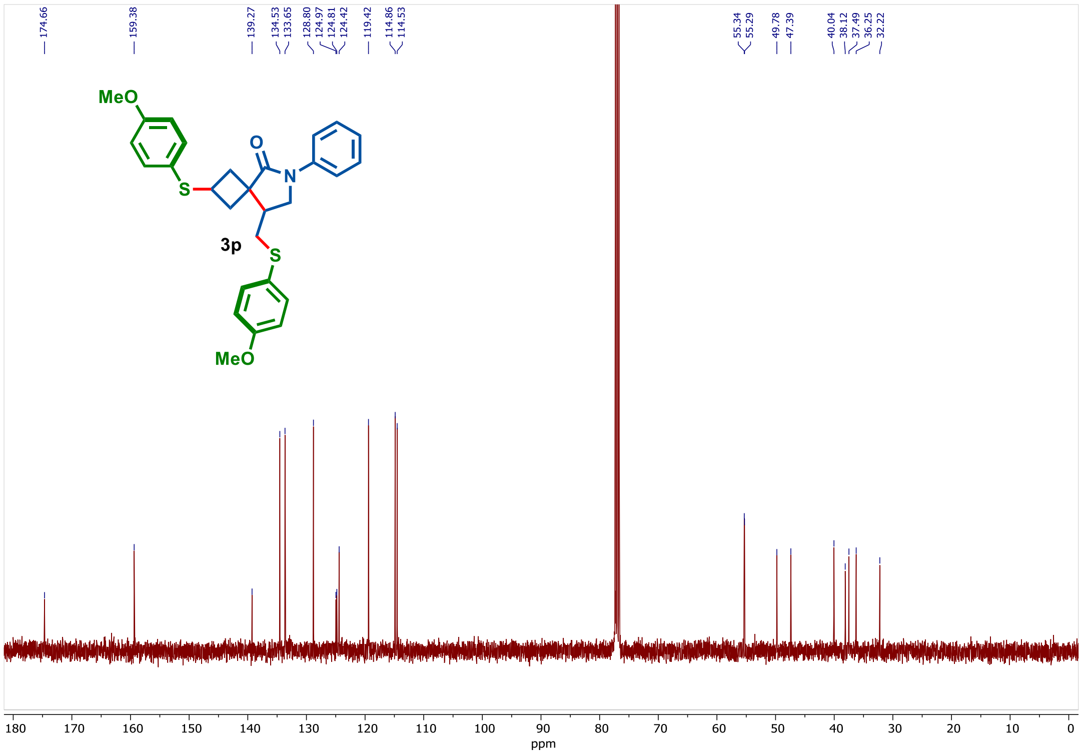
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **3o**



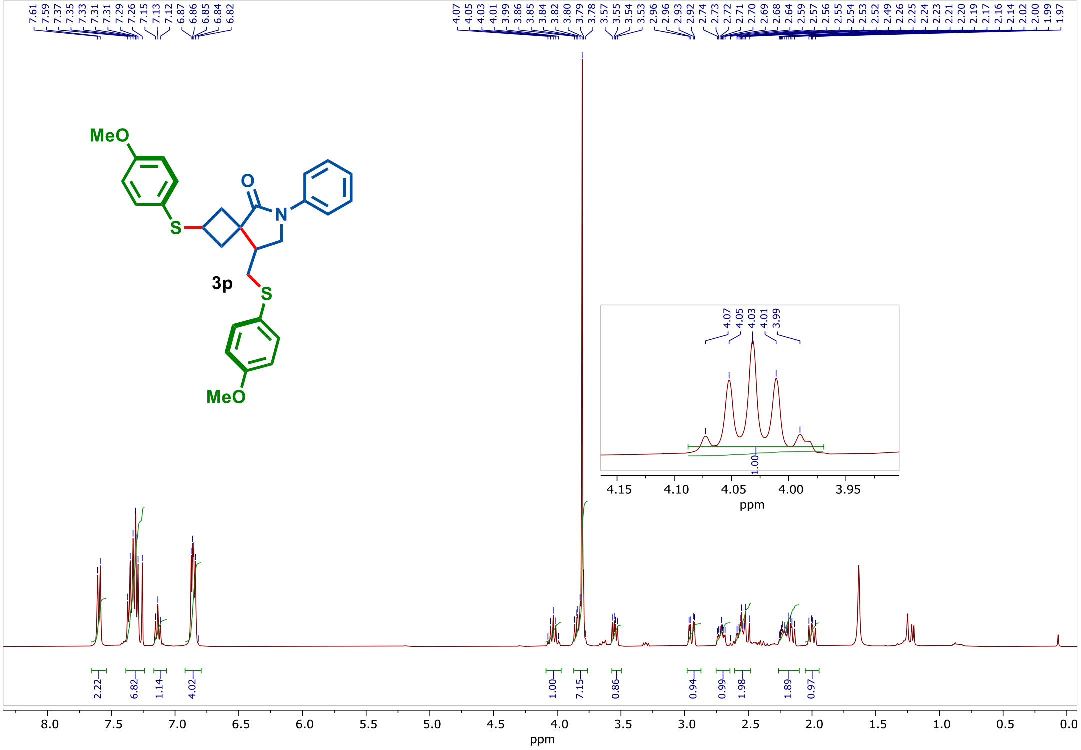
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **3p** (**See Procedure**)



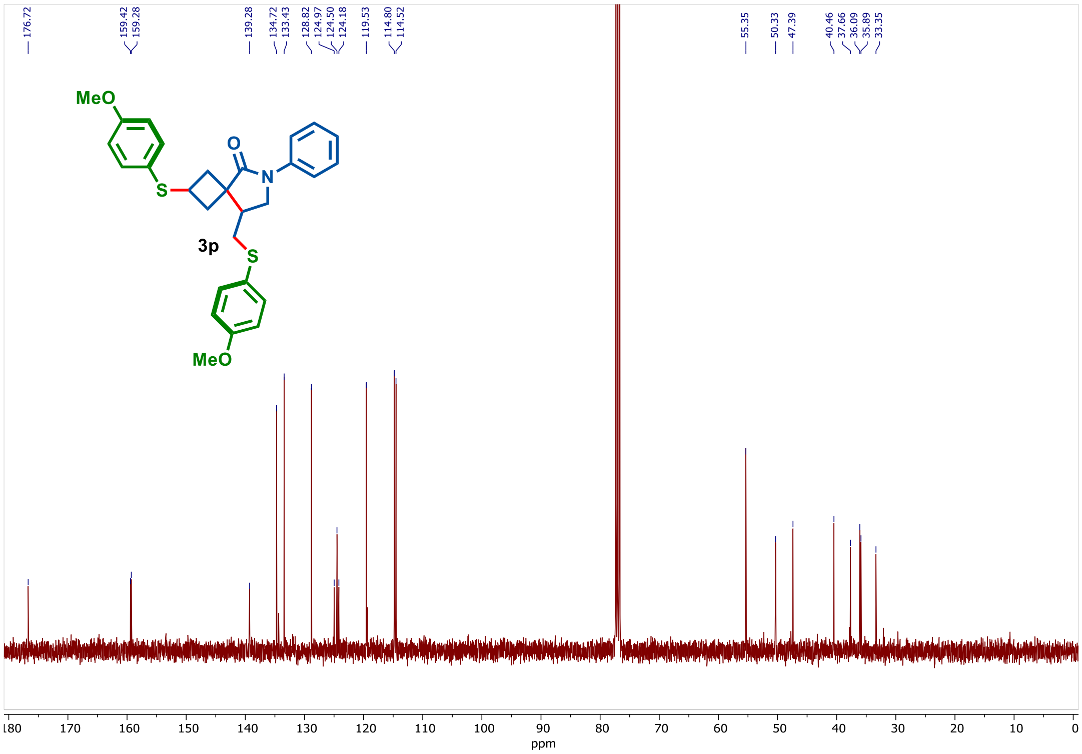
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **3p**



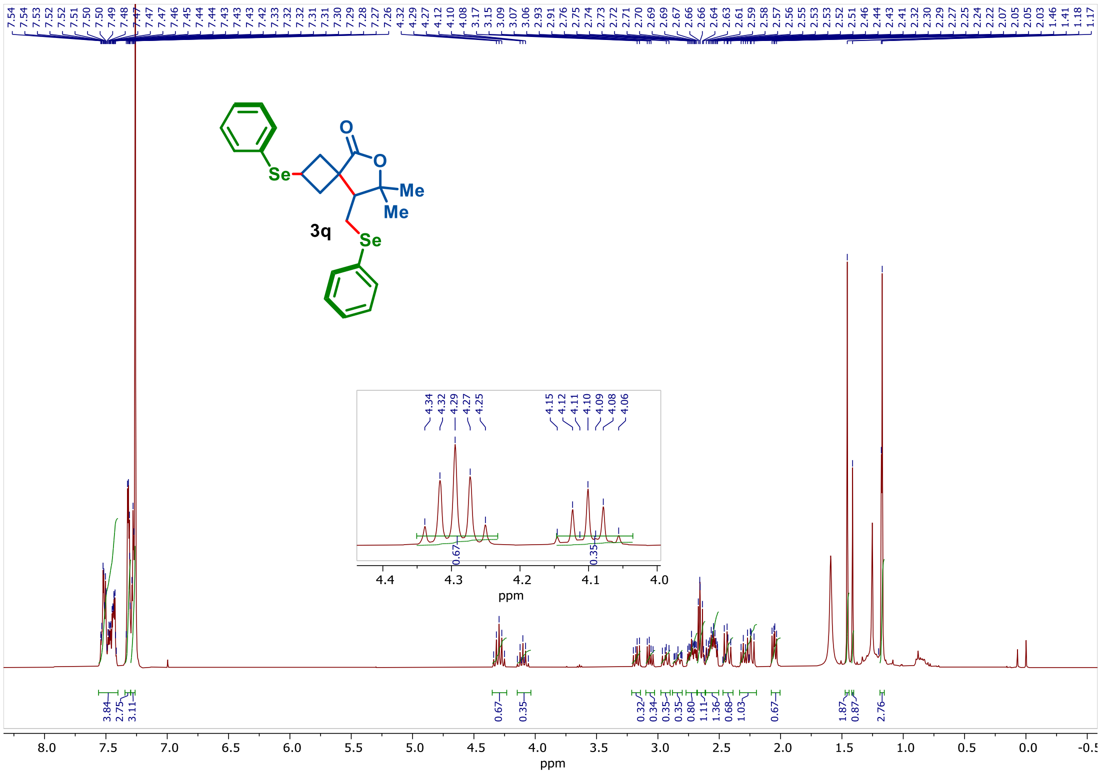
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **3p** (See Procedure)



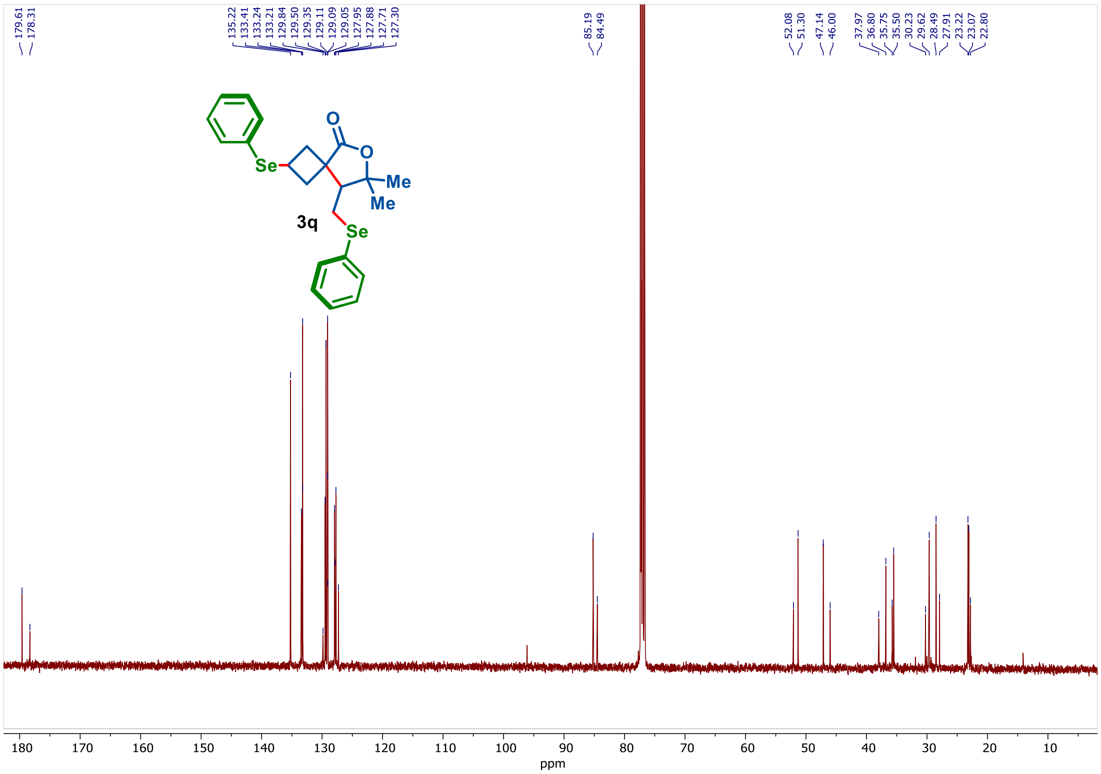
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **3p**



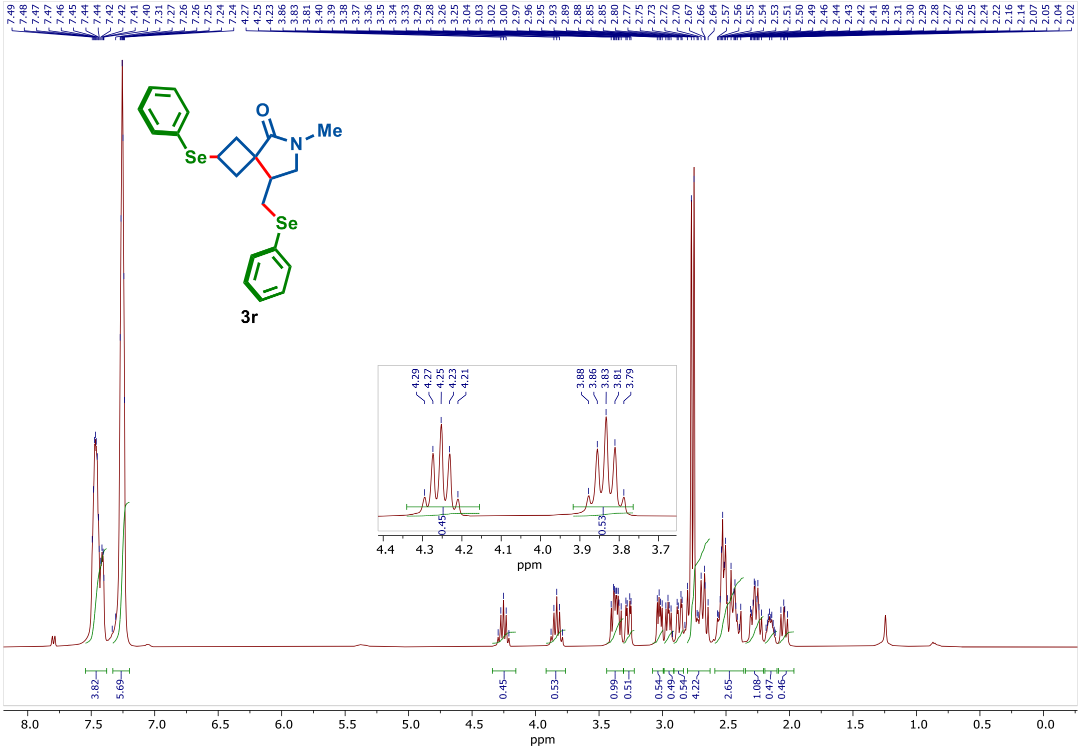
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **3q** (**See Procedure**)



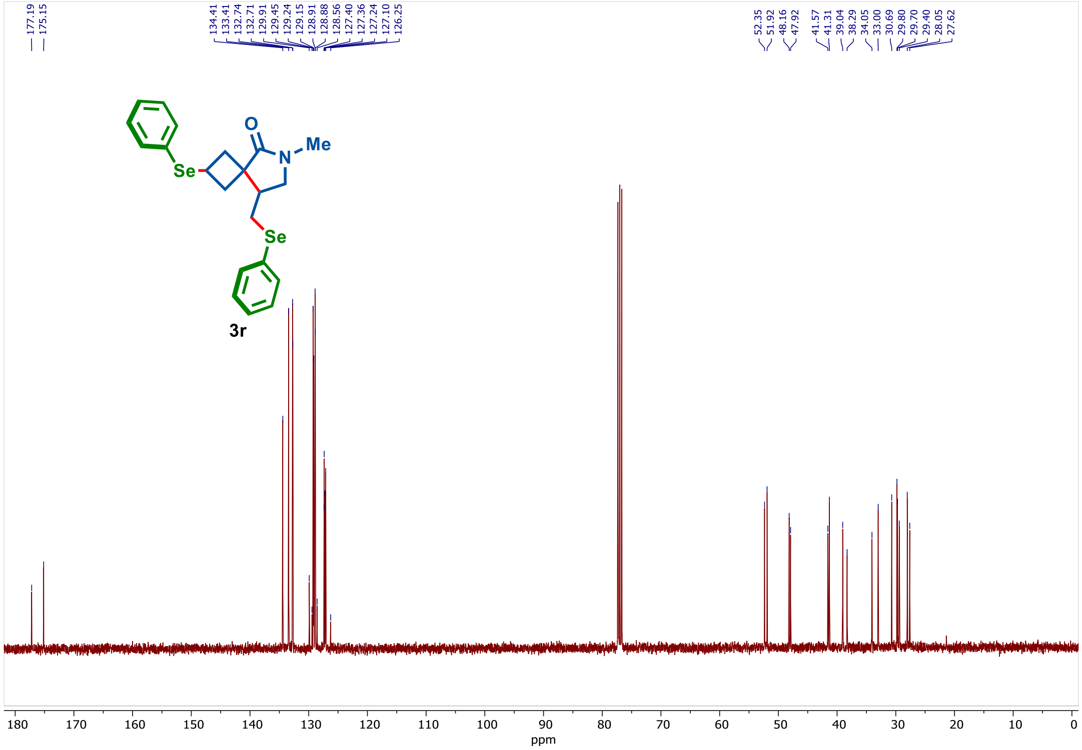
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **3q**



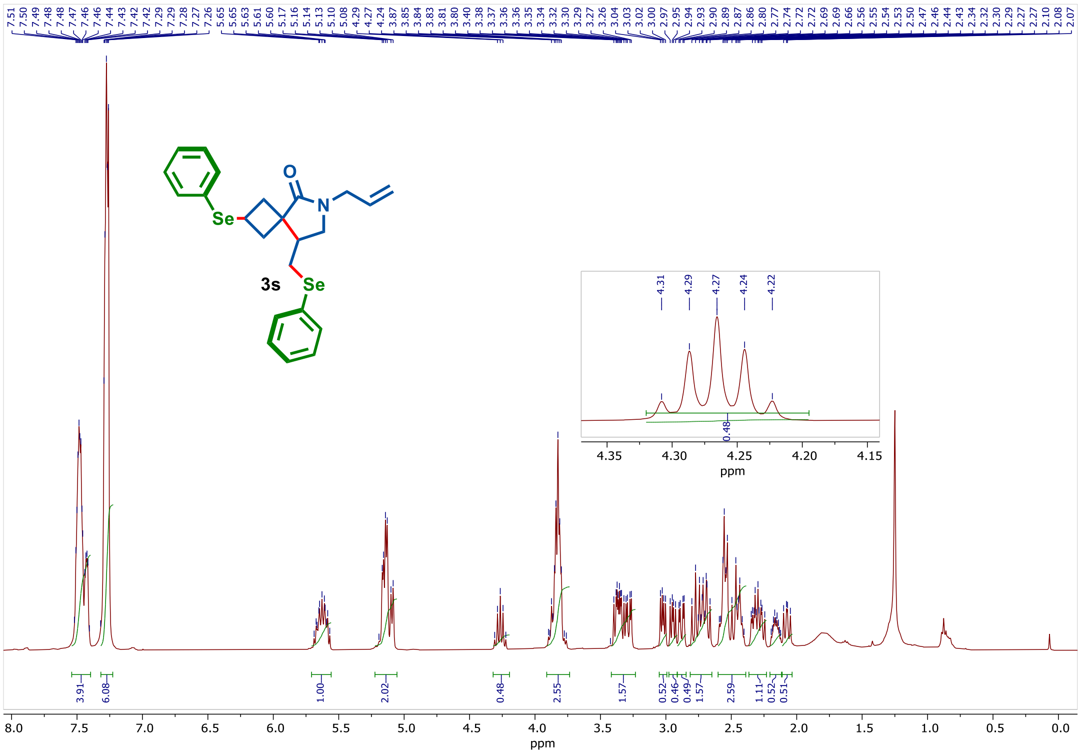
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **3r** (**See Procedure**)



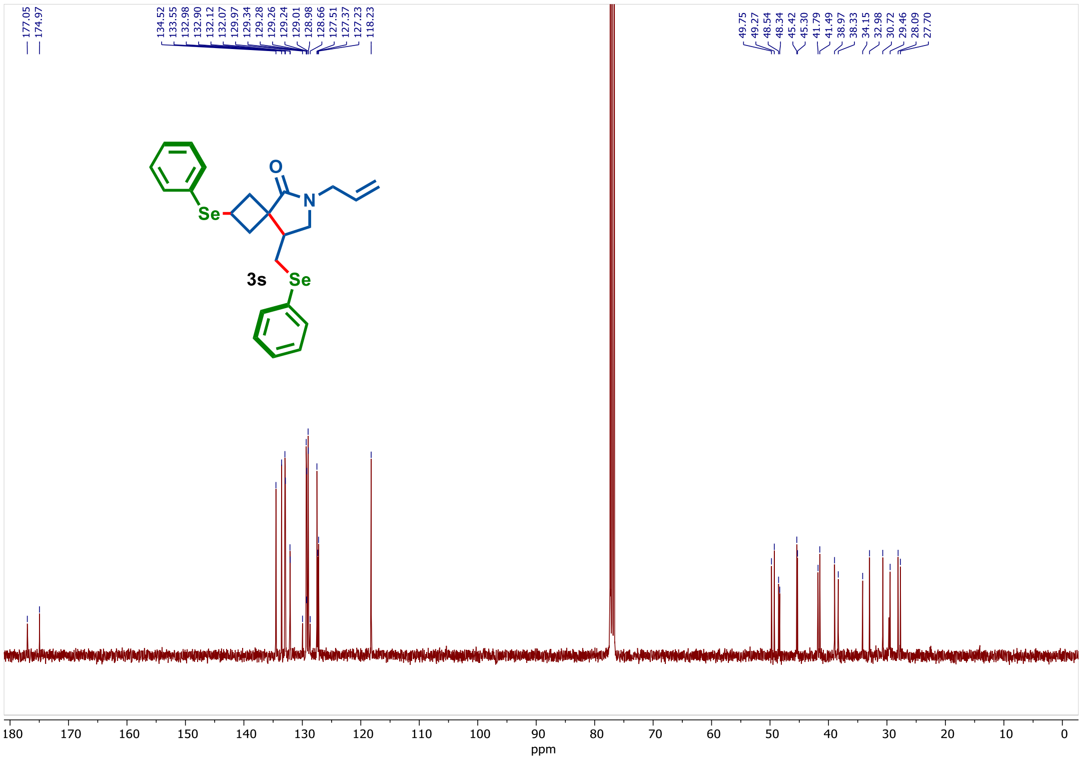
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **3r**



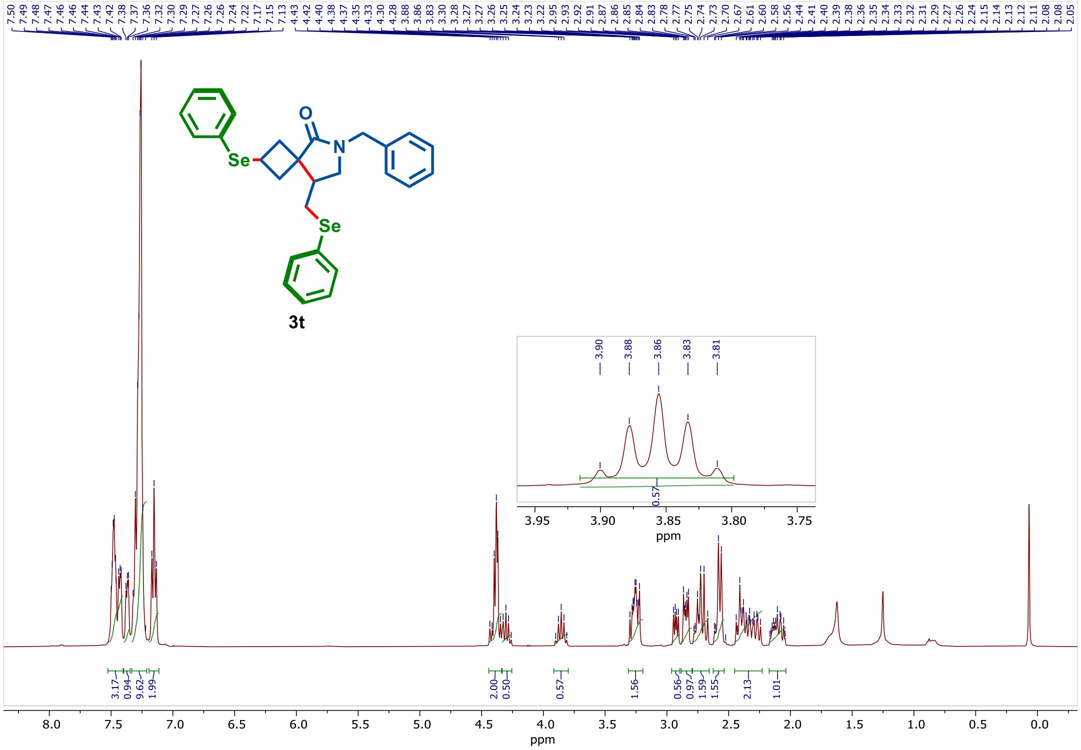
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **3s** (**See Procedure**)



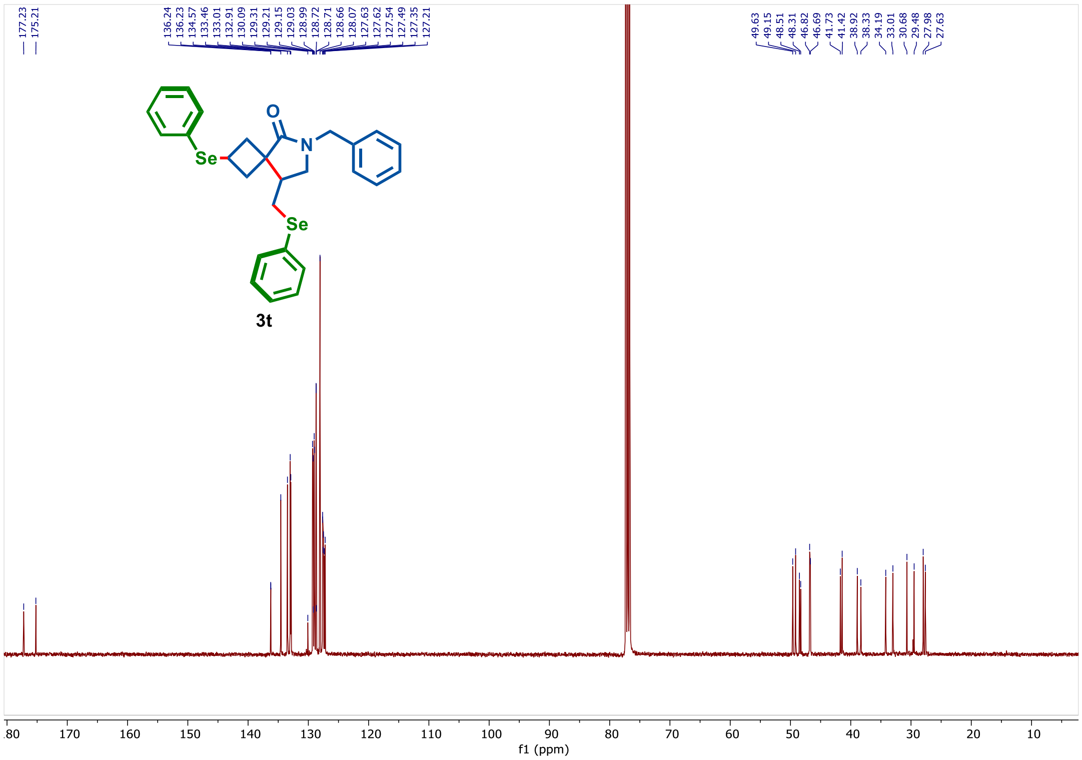
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **3s**



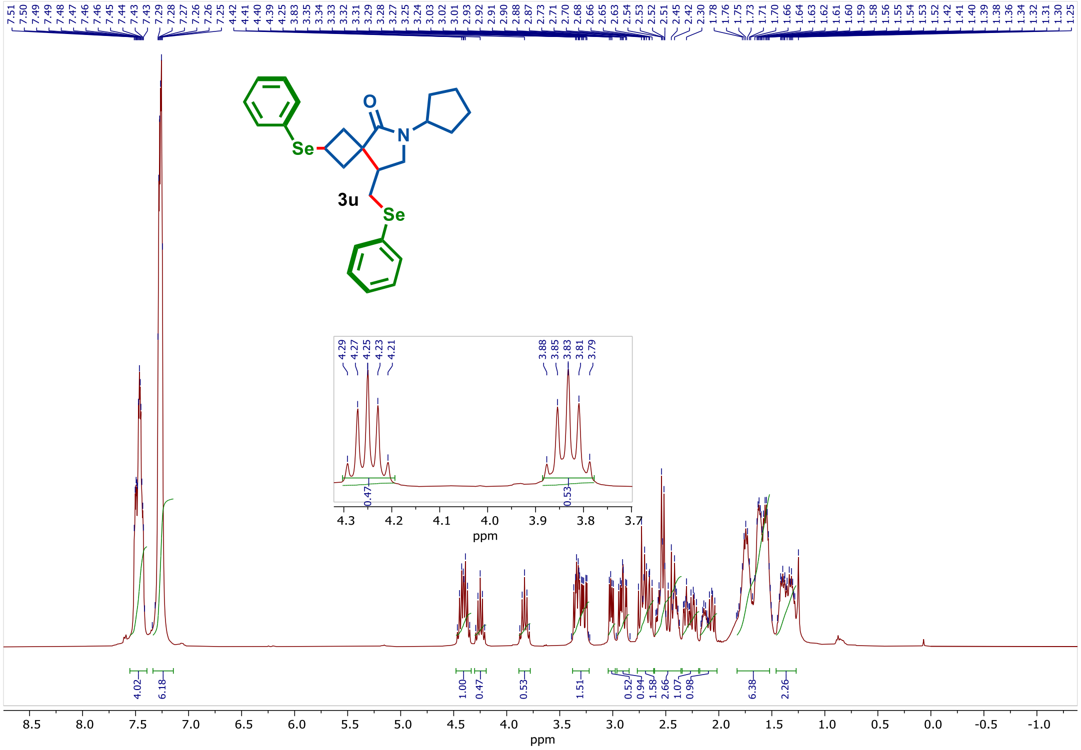
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **3t** (See Procedure)



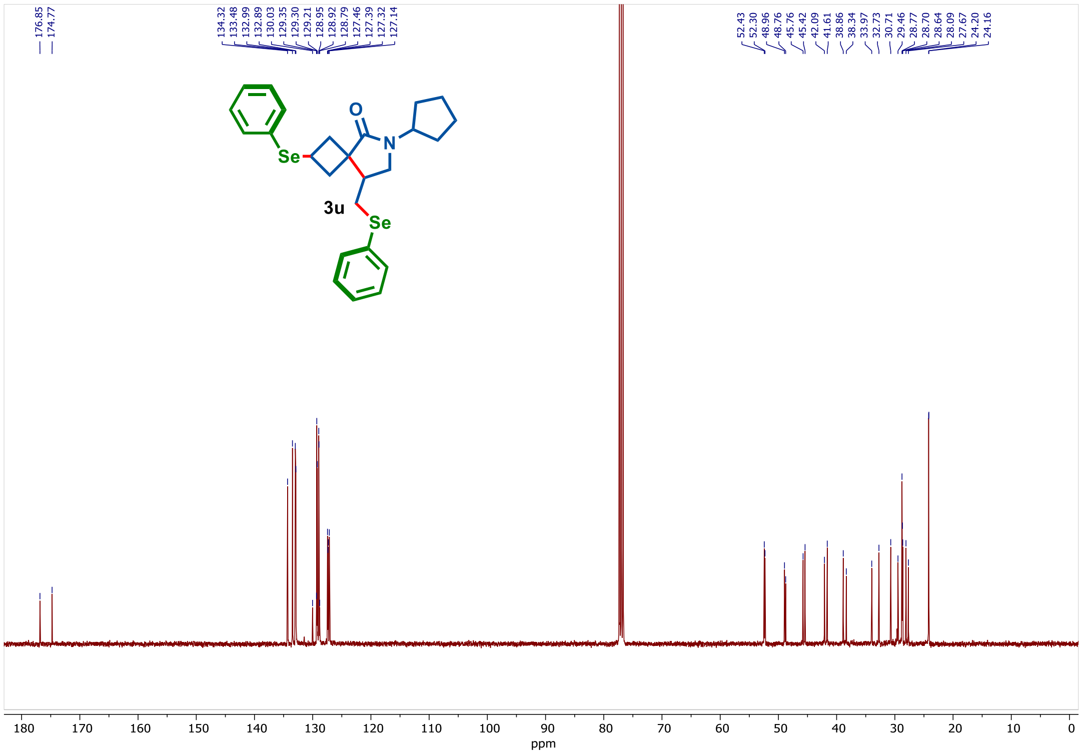
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **3t**



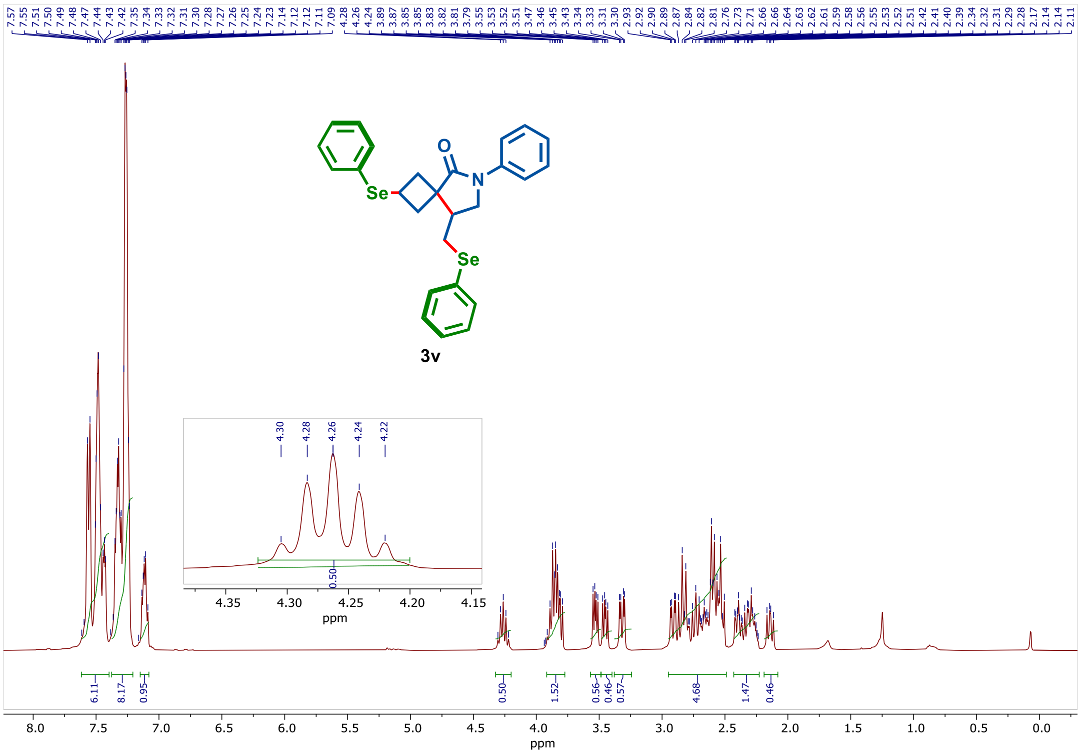
^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **3u** (See Procedure)



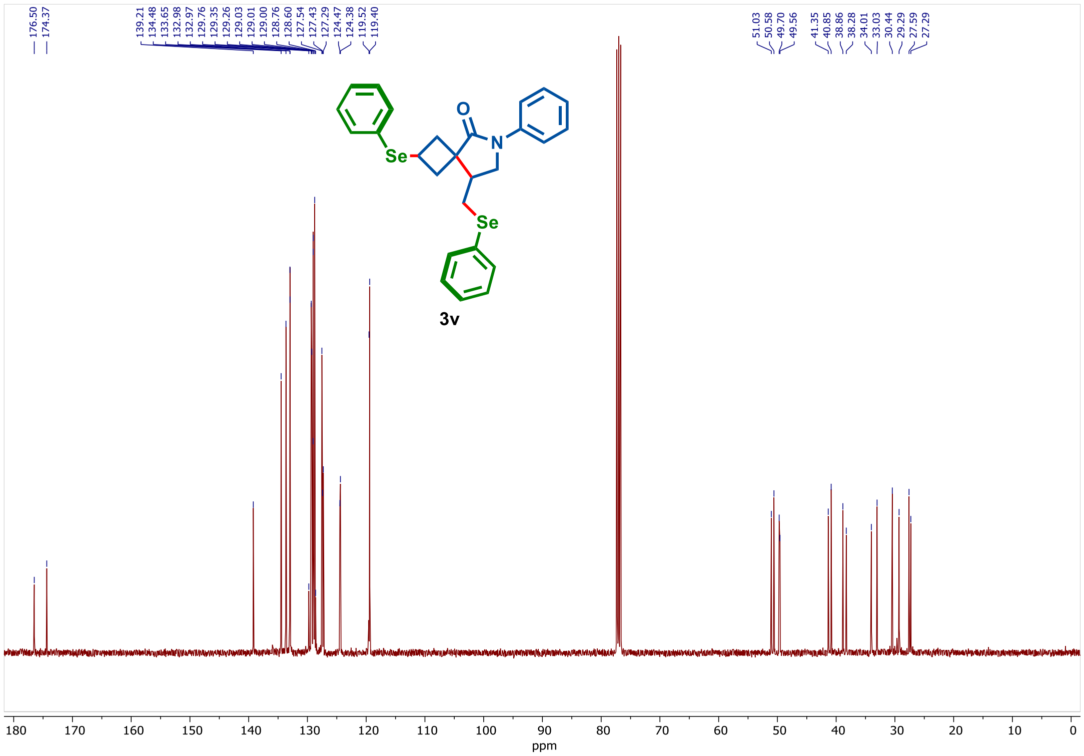
^{13}C NMR (101 MHz, $CDCl_3$) spectra of compound **3u**



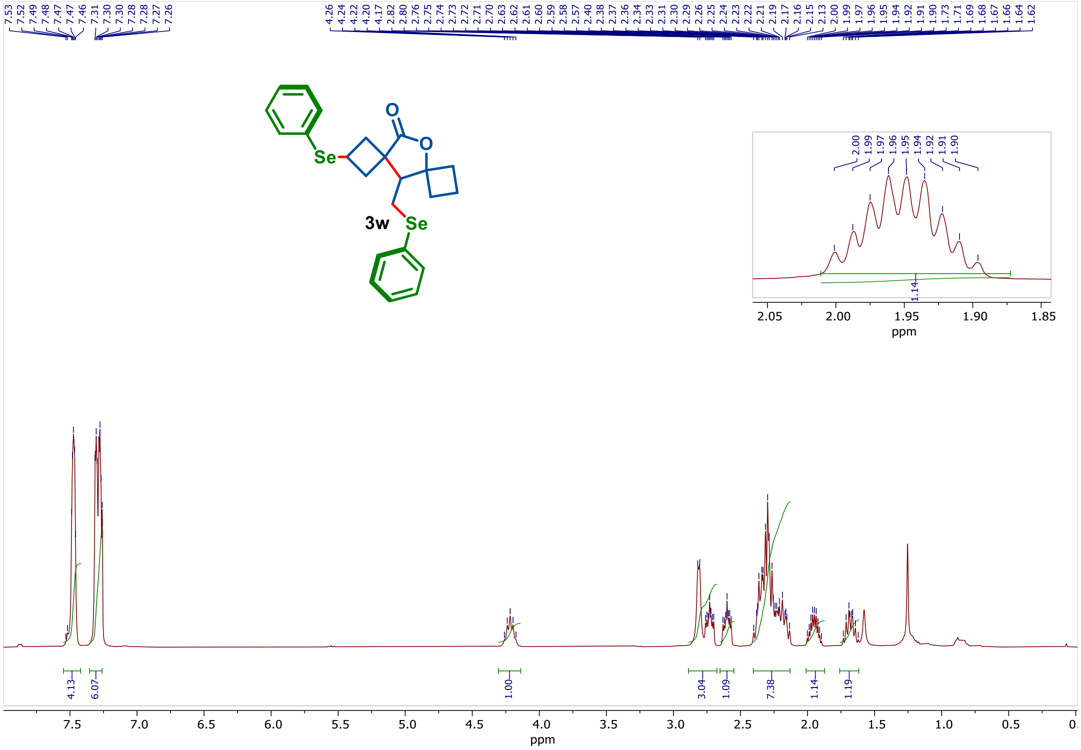
^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **3v** (**See Procedure**)



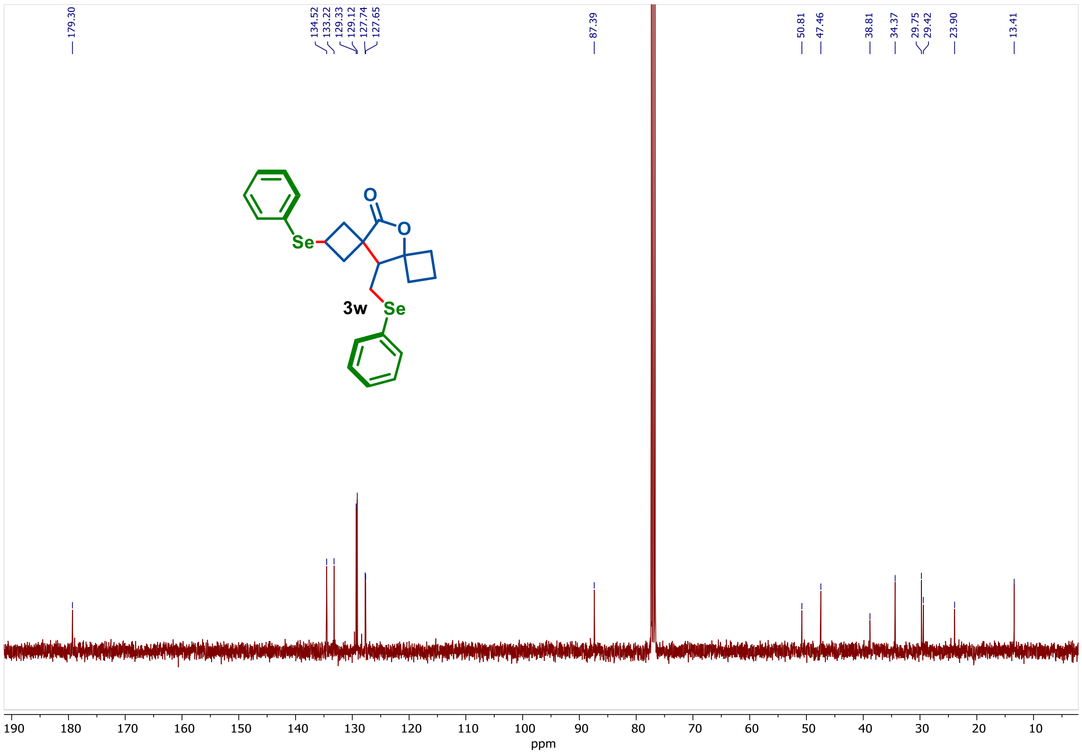
^{13}C NMR (101 MHz, $CDCl_3$) spectra of compound **3v**



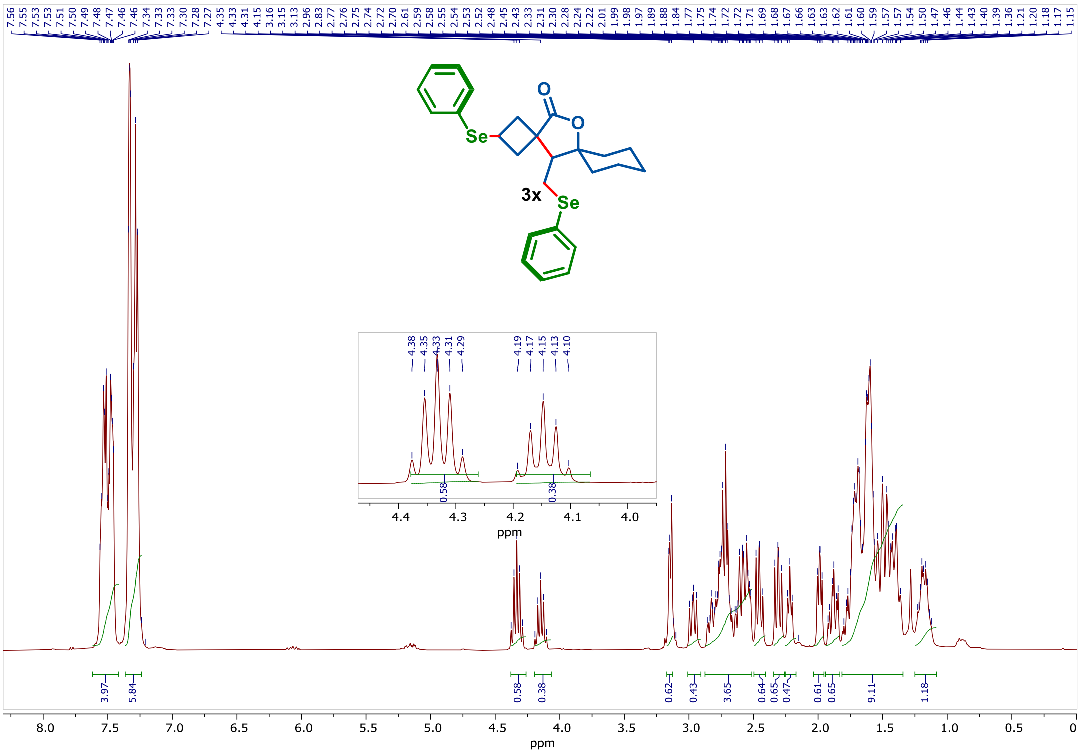
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **3w** (See Procedure)



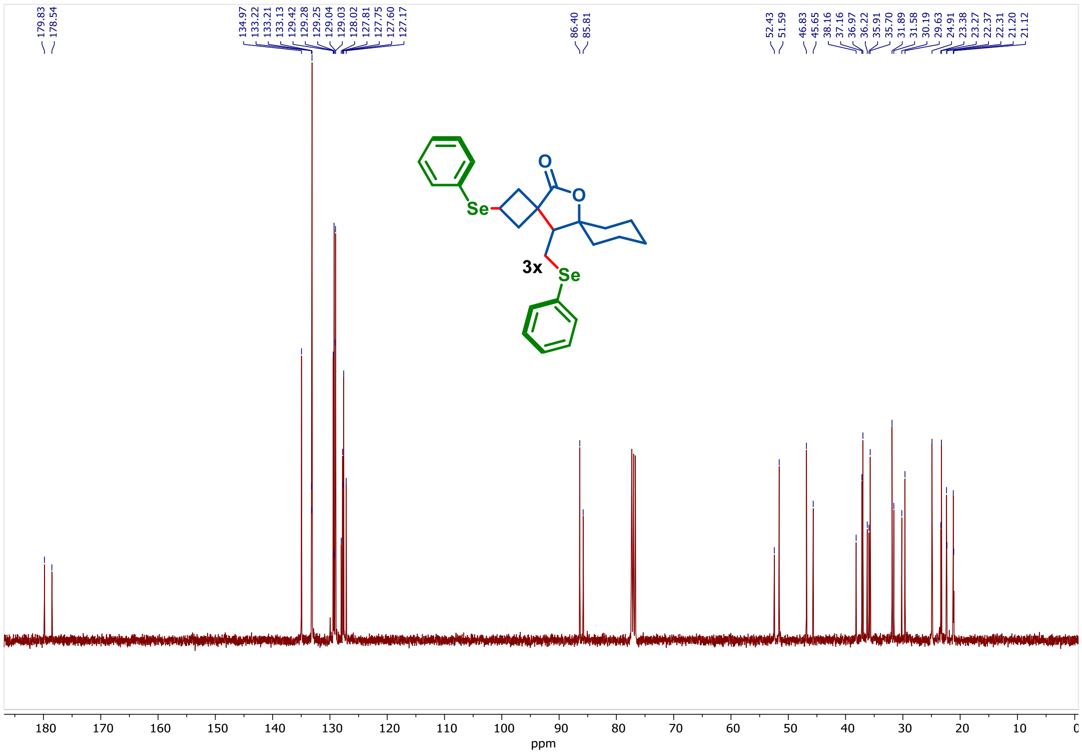
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **3w**



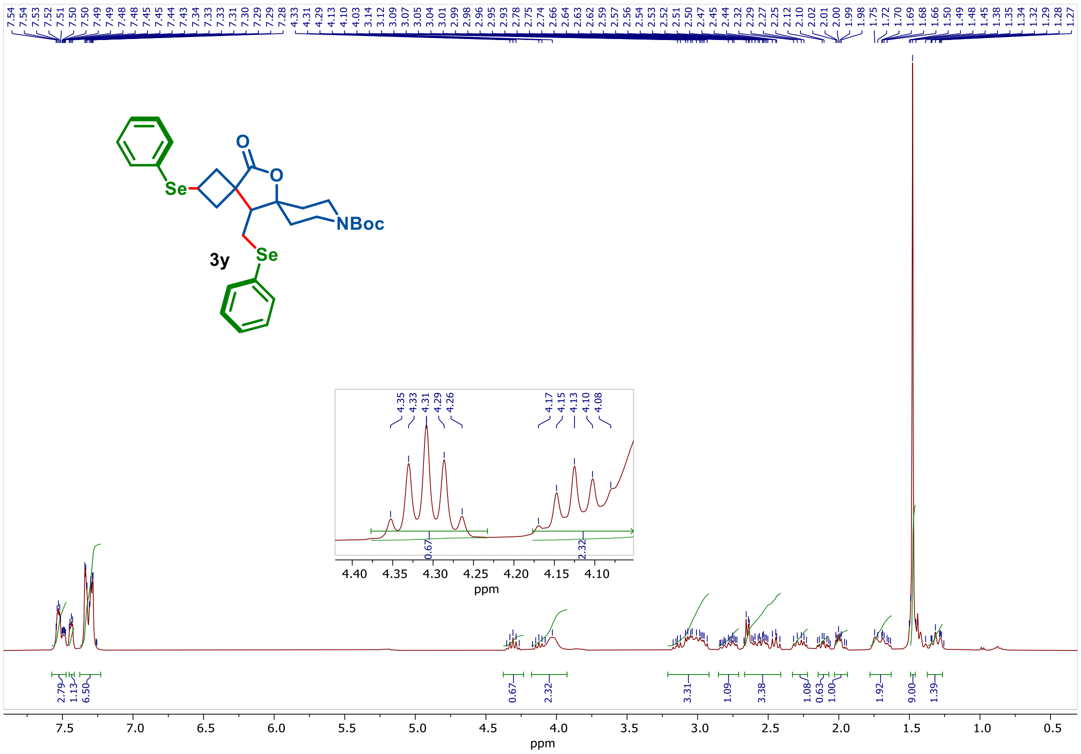
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **3x** (**See Procedure**)



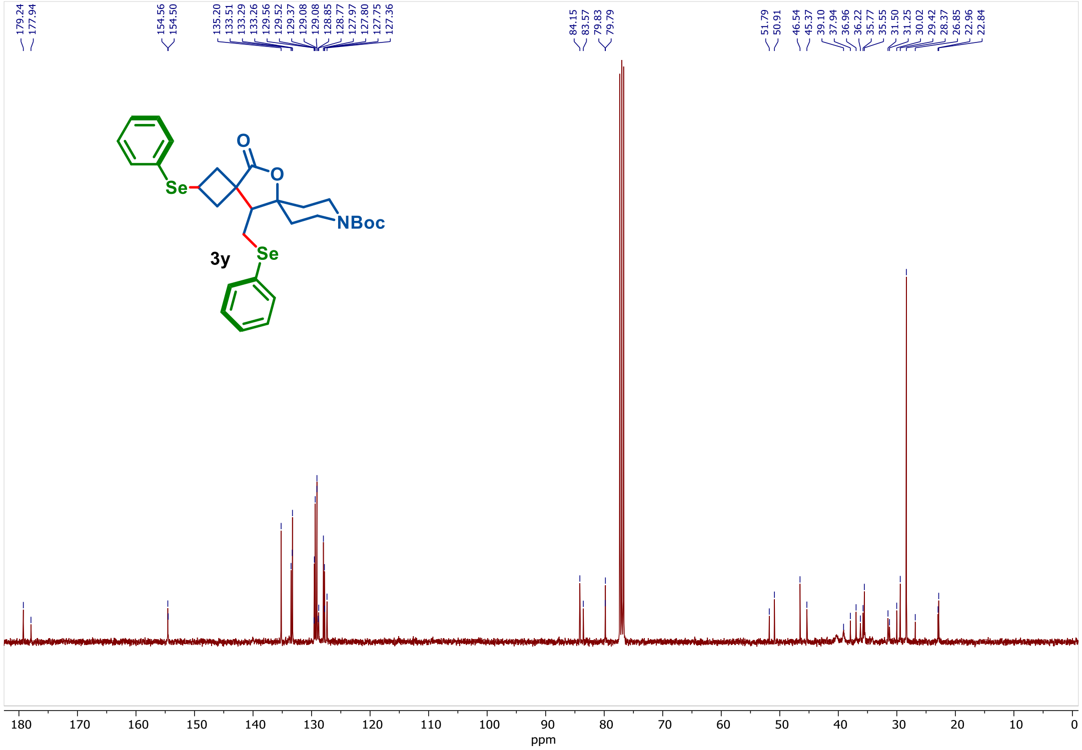
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **3x**



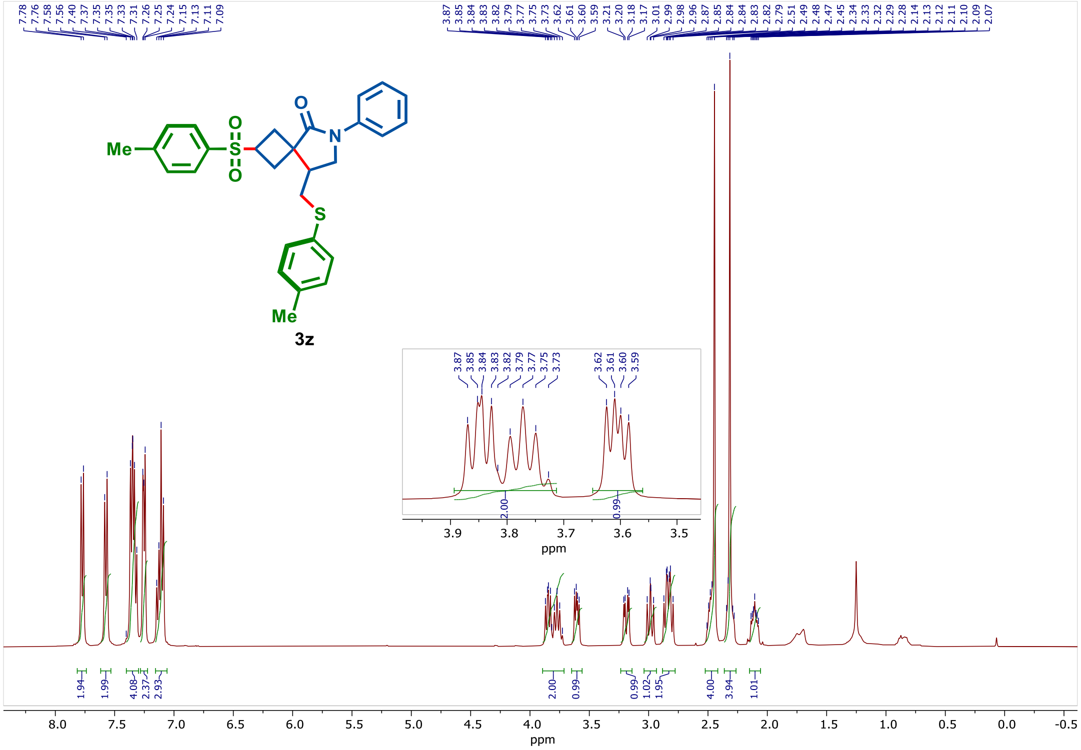
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **3y** (**See Procedure**)



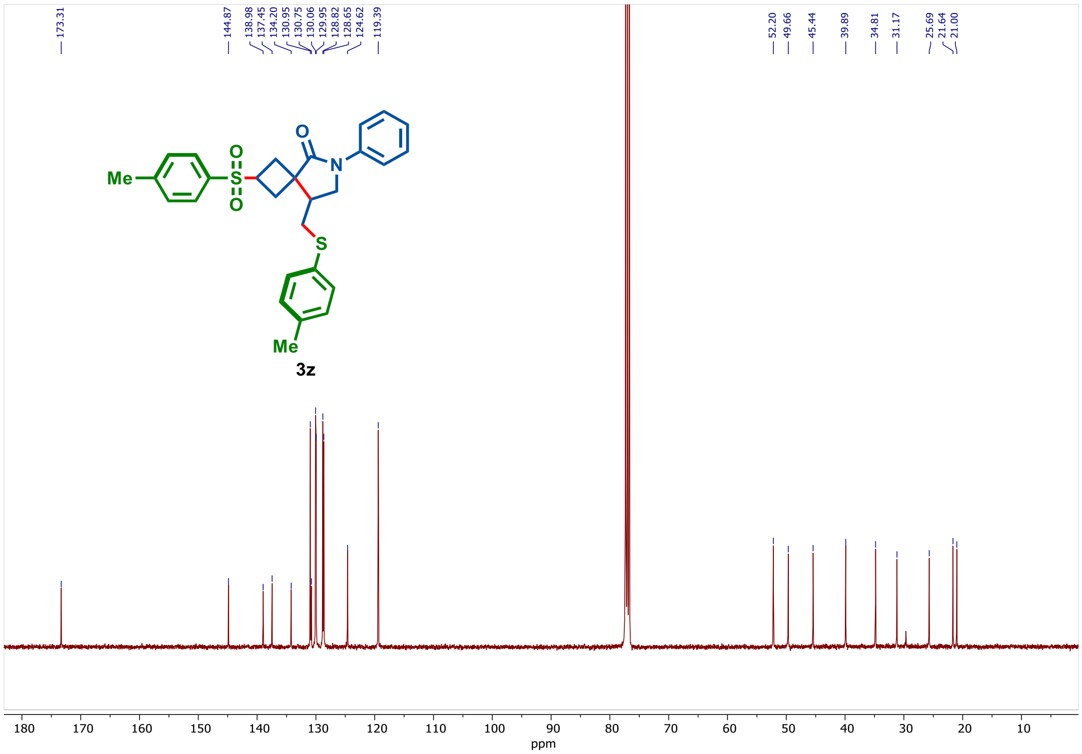
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **3y**



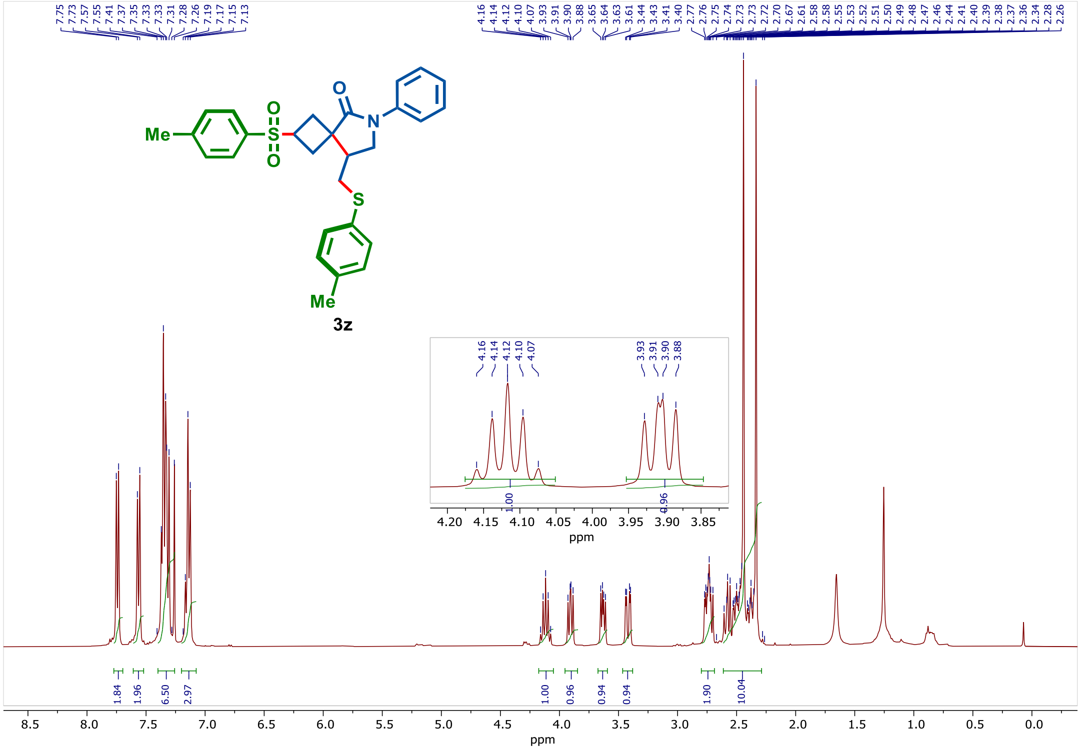
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **3z** (**See Procedure**)



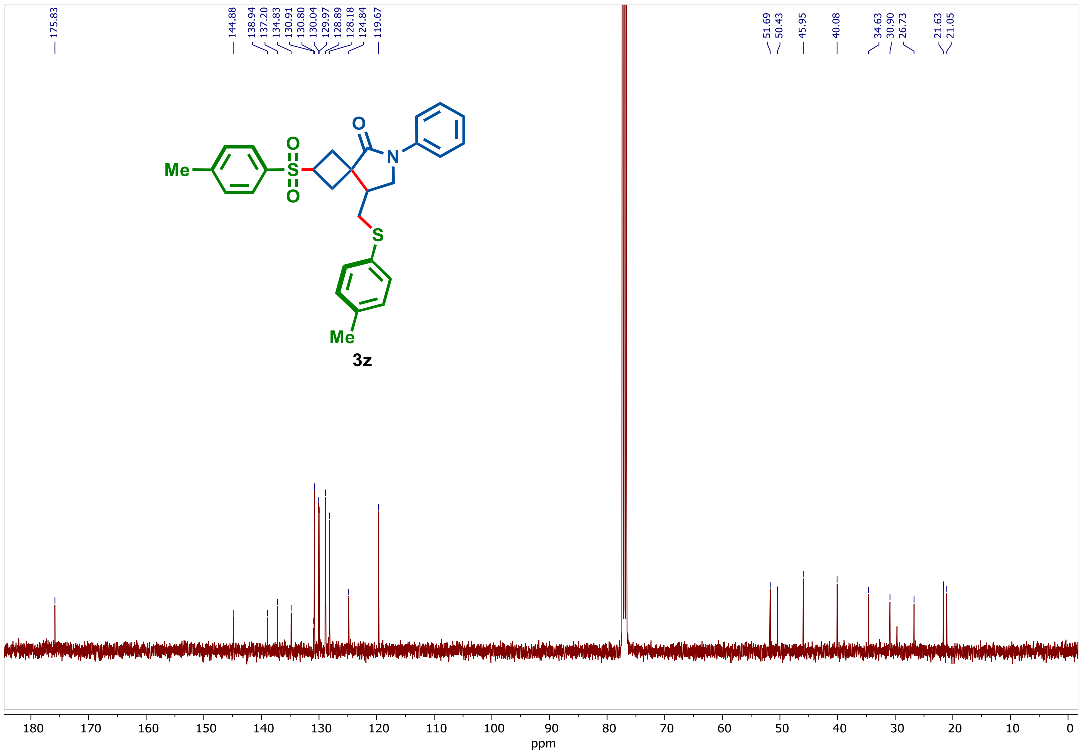
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **3z**



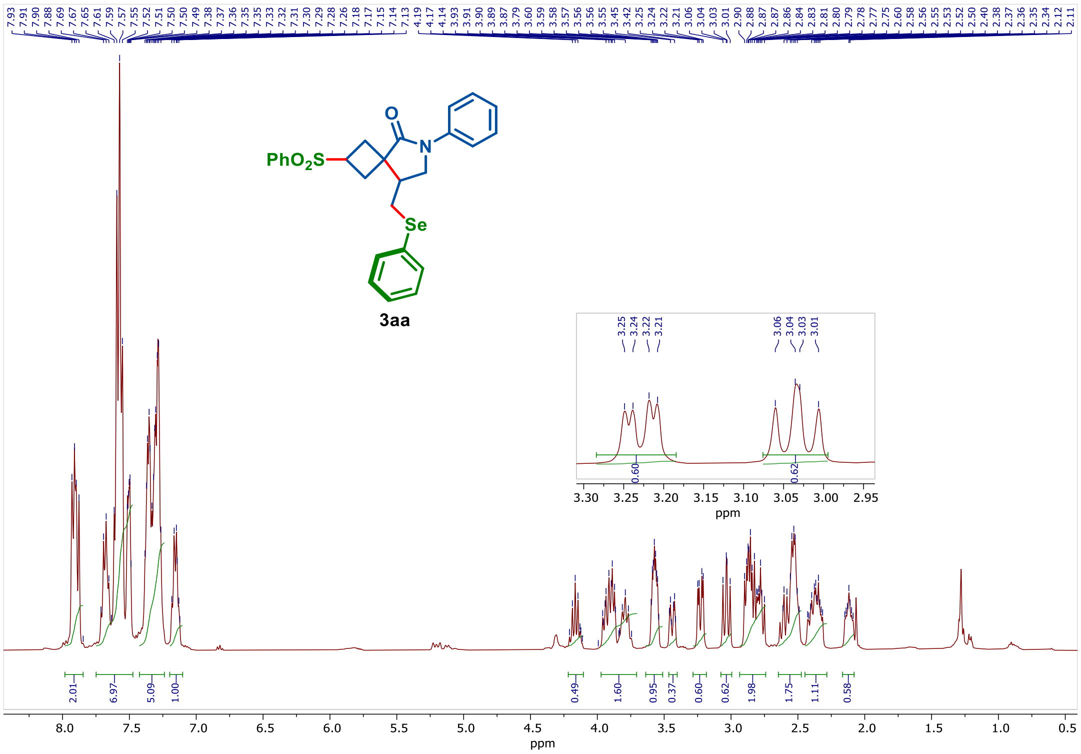
^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **3z** **(See Procedure)**



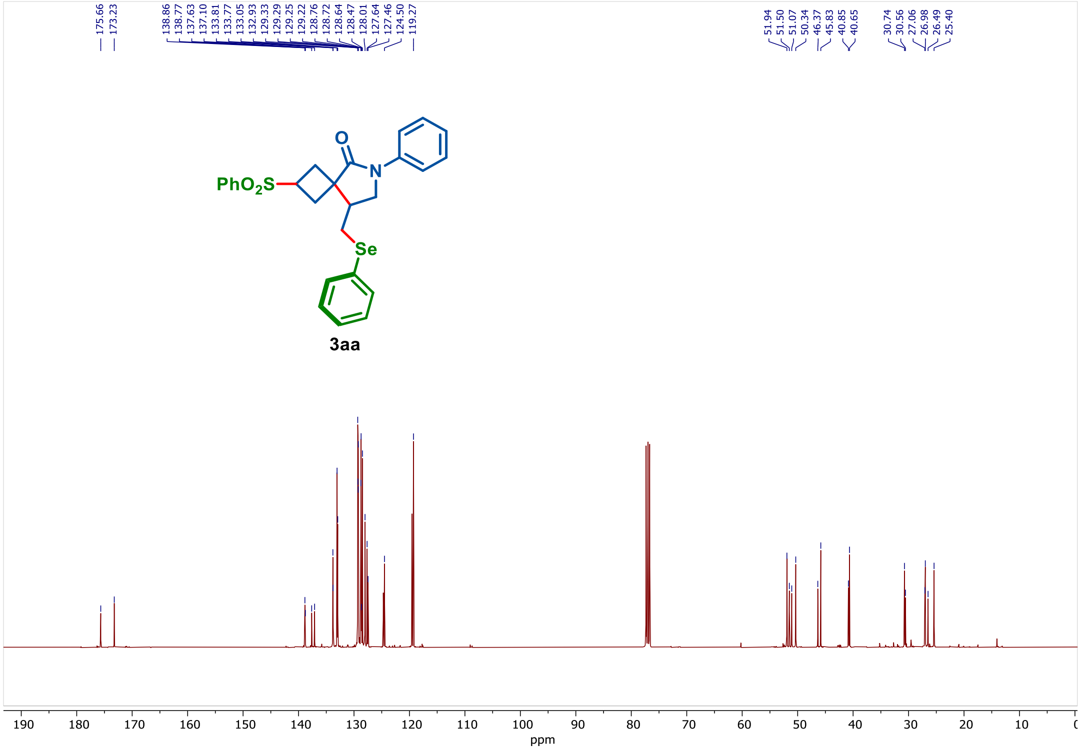
^{13}C NMR (101 MHz, $CDCl_3$) spectra of compound **3z**



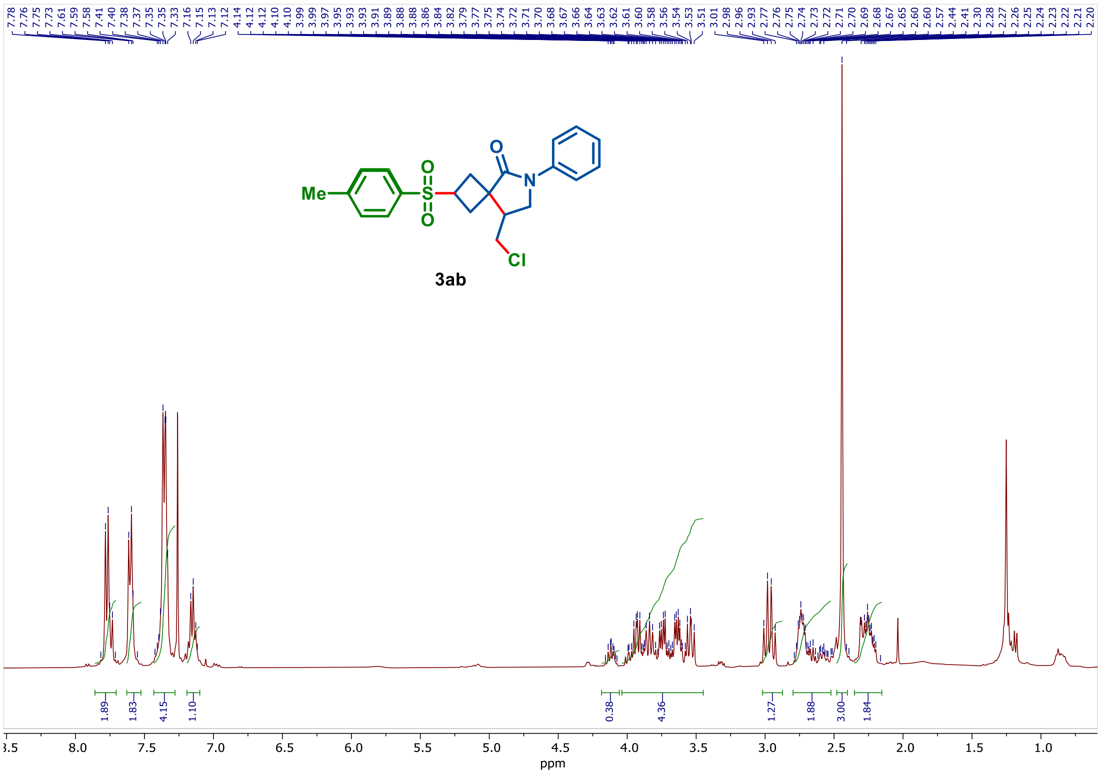
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **3aa** (**See Procedure**)



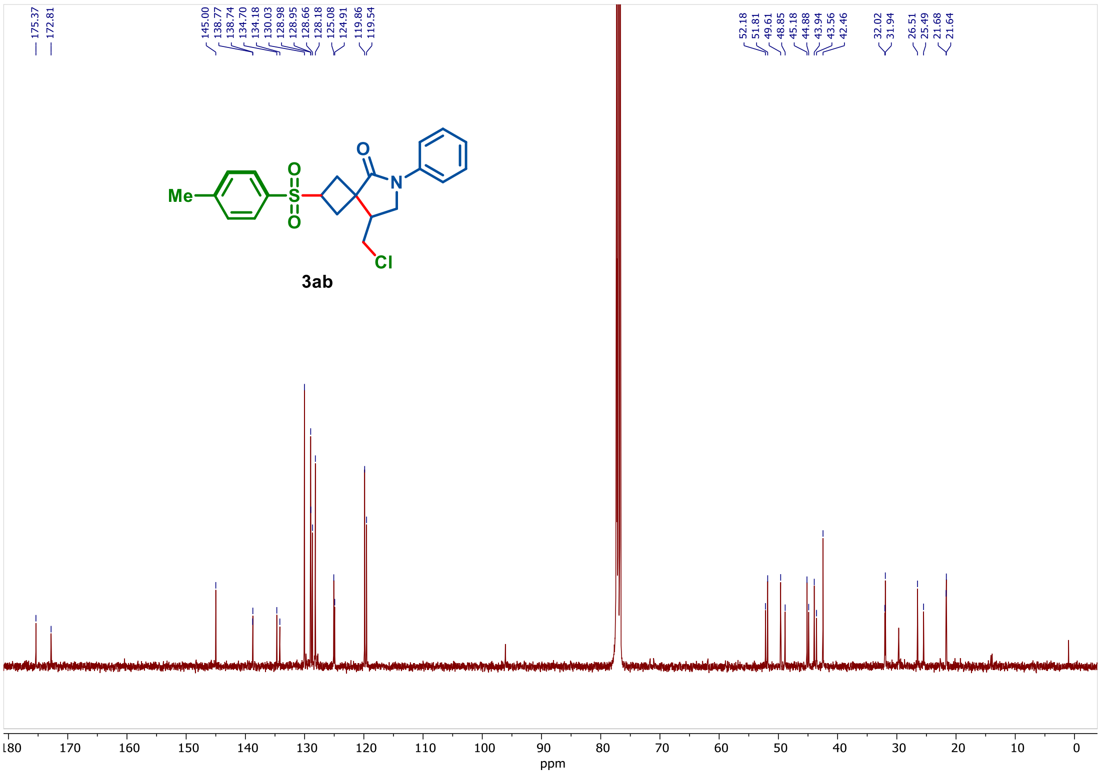
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **3aa**



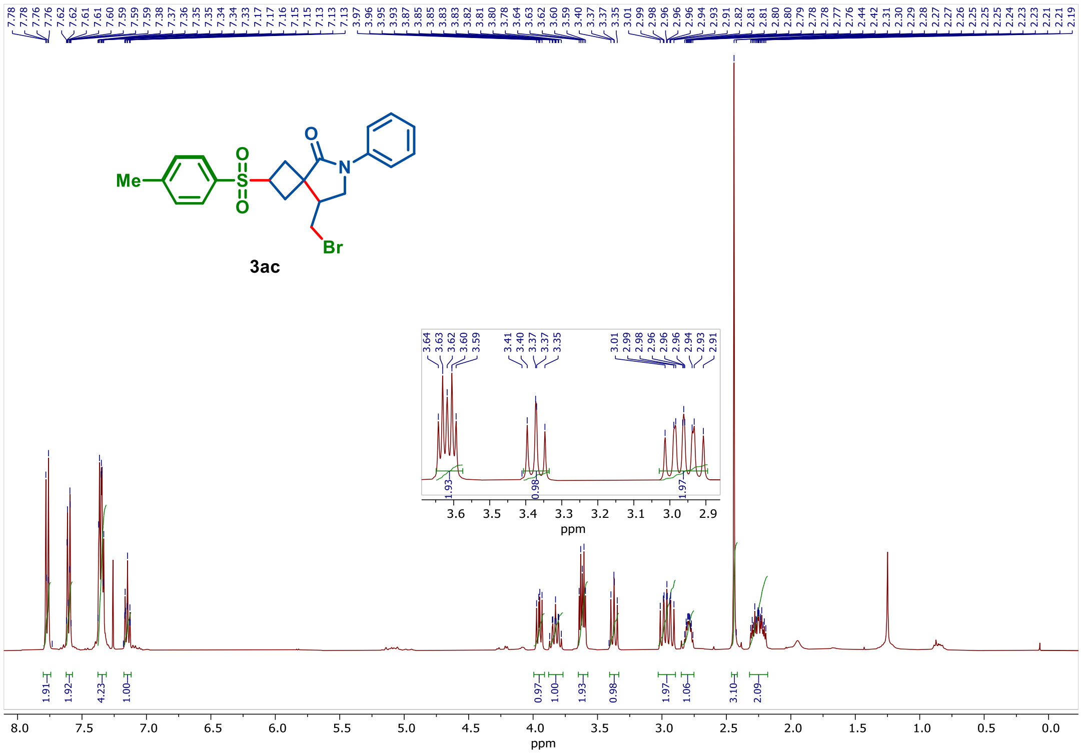
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **3ab** (**See Procedure**)



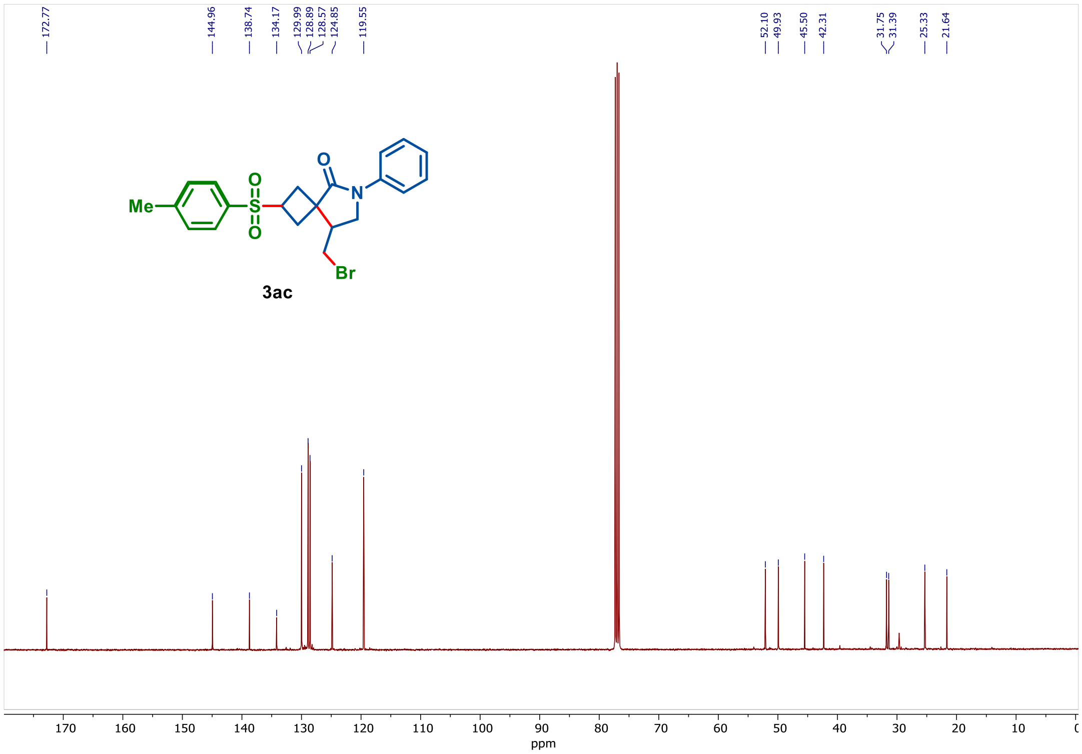
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **3ab**



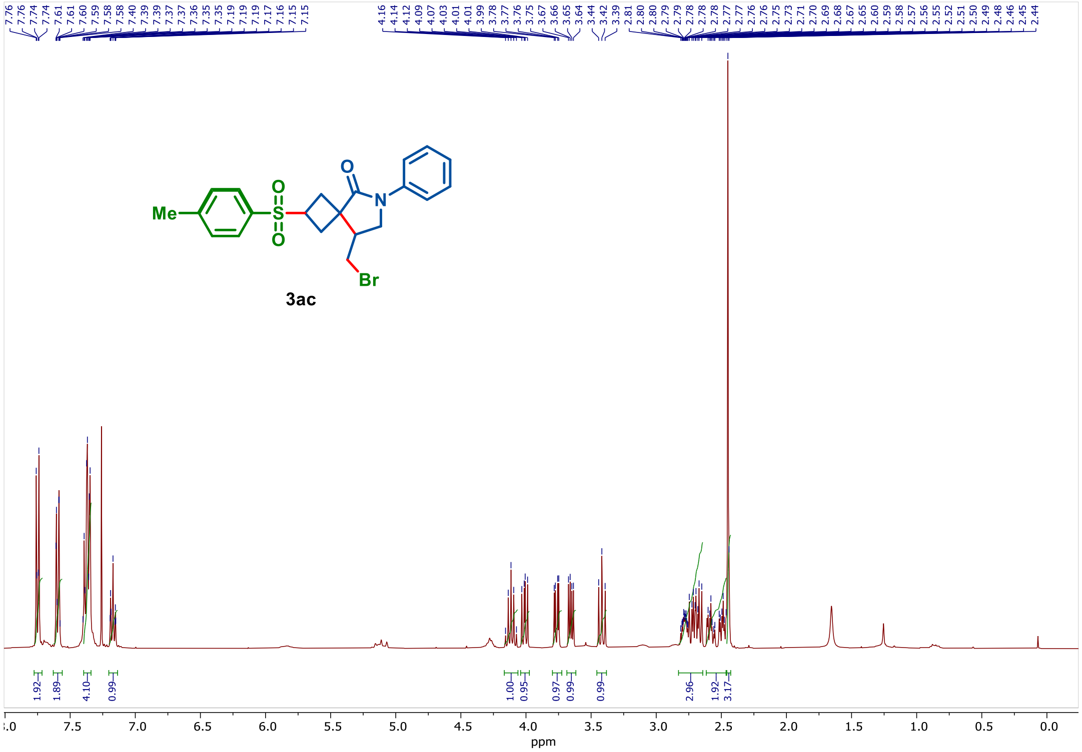
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **3ac** (**See Procedure**)



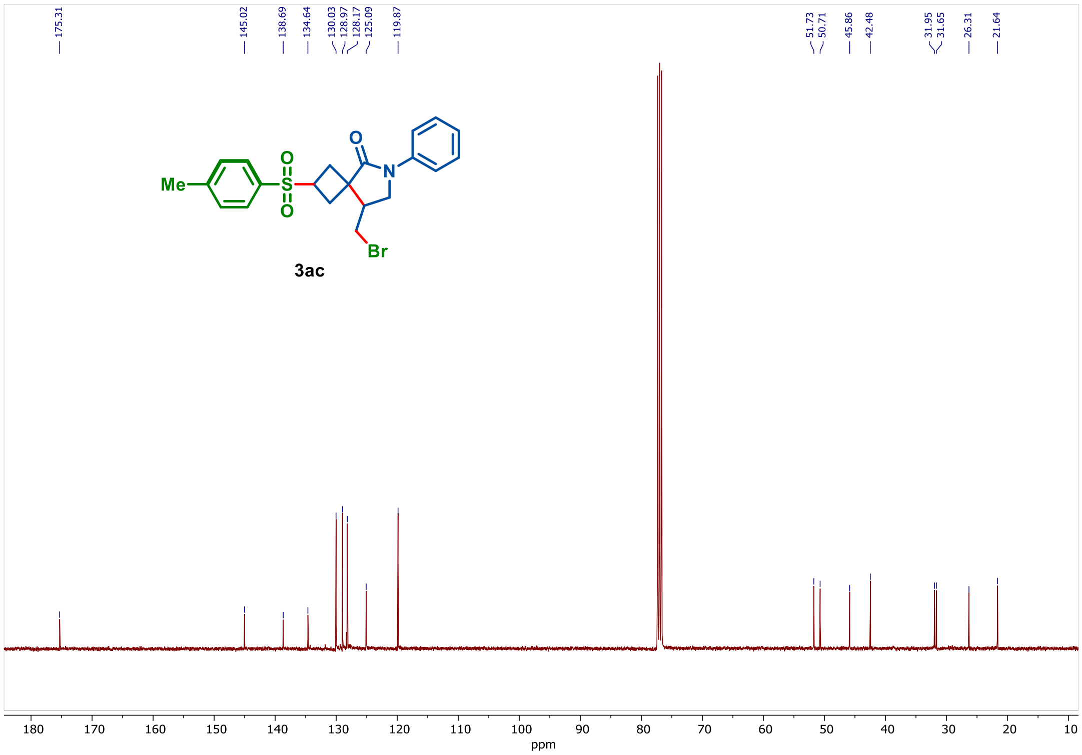
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **3ac**



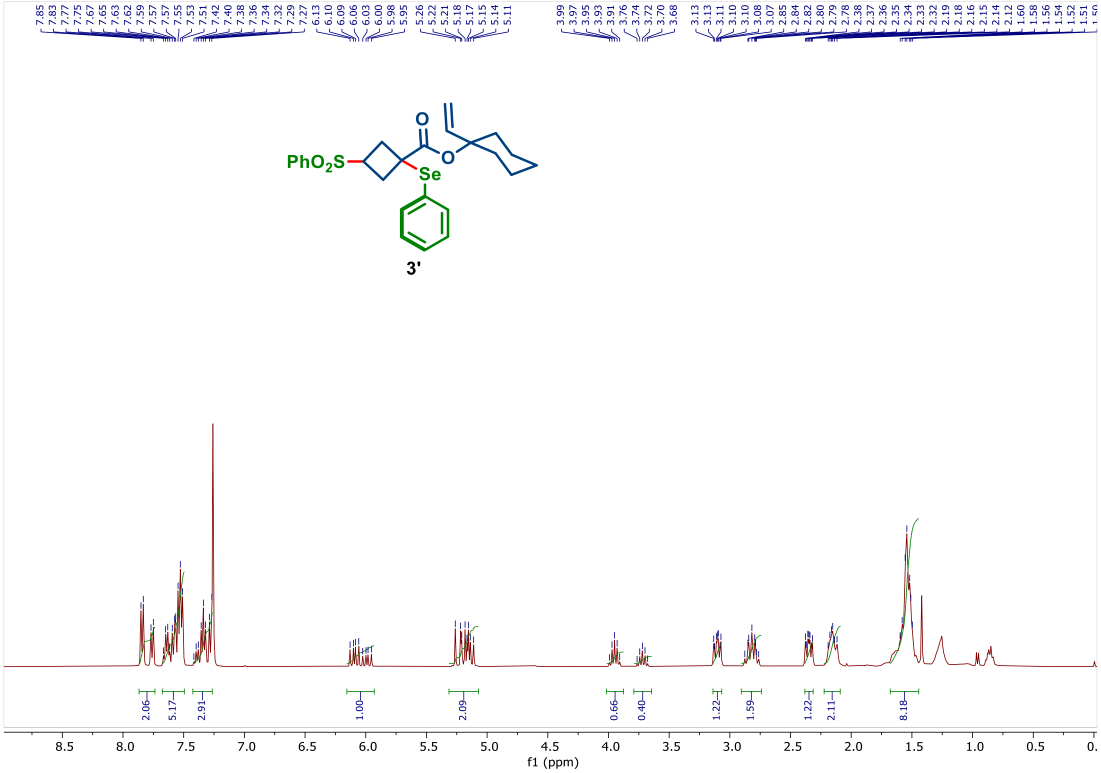
^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **3ac´**



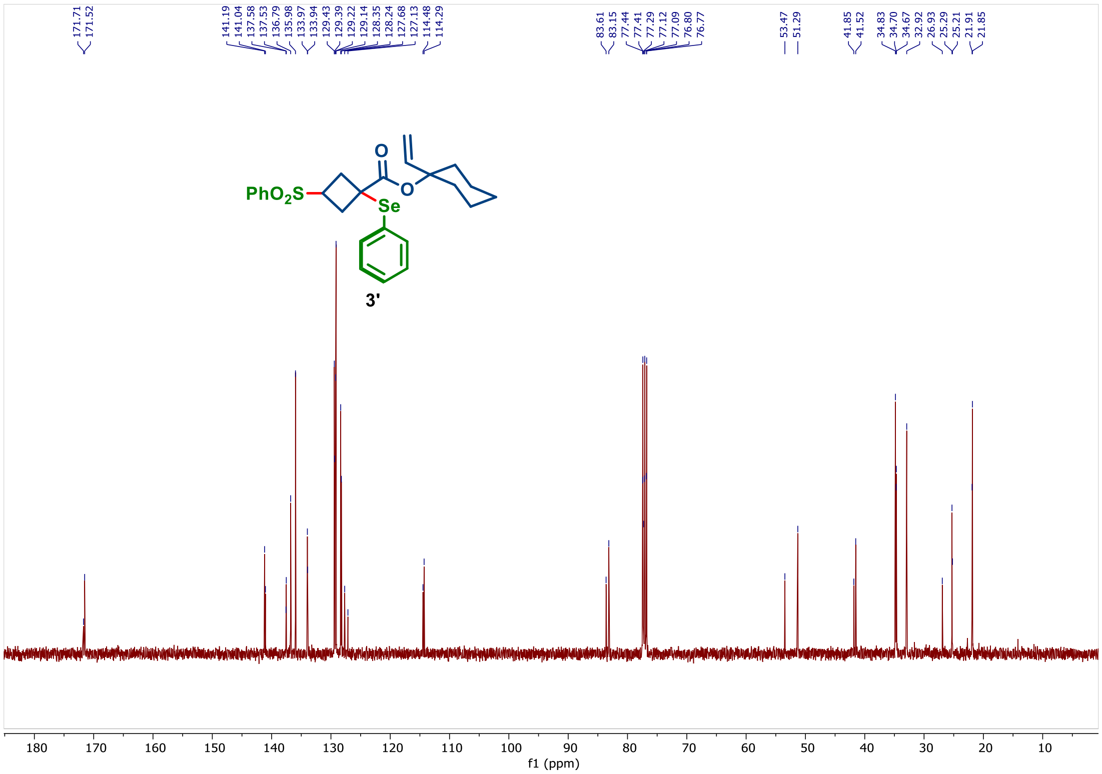
^{13}C NMR (101 MHz, $CDCl_3$) spectra of compound **3ac´**



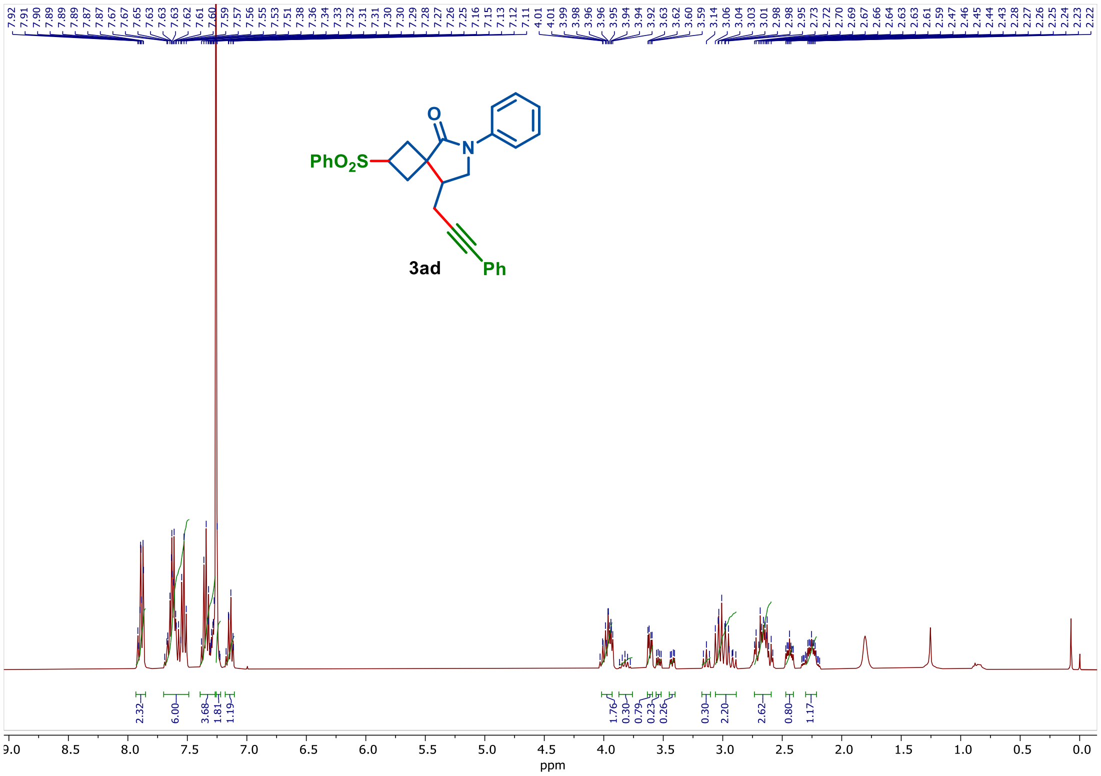
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **3’** **(See Procedure)**



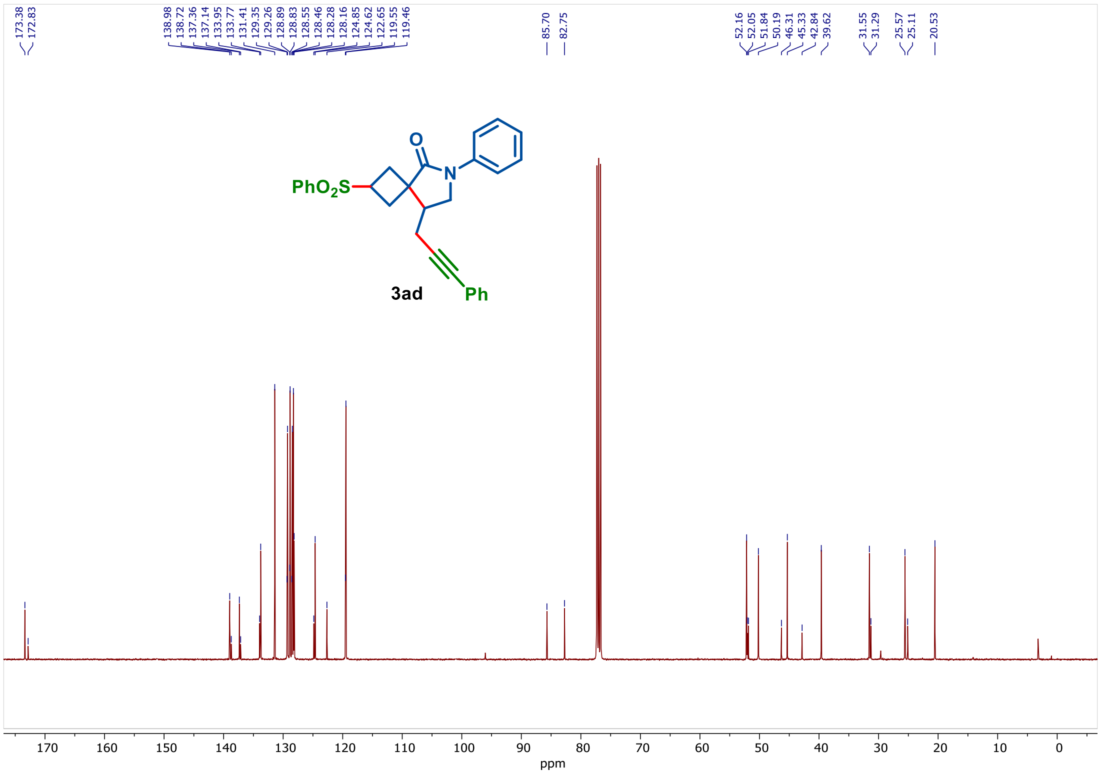
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **3’**



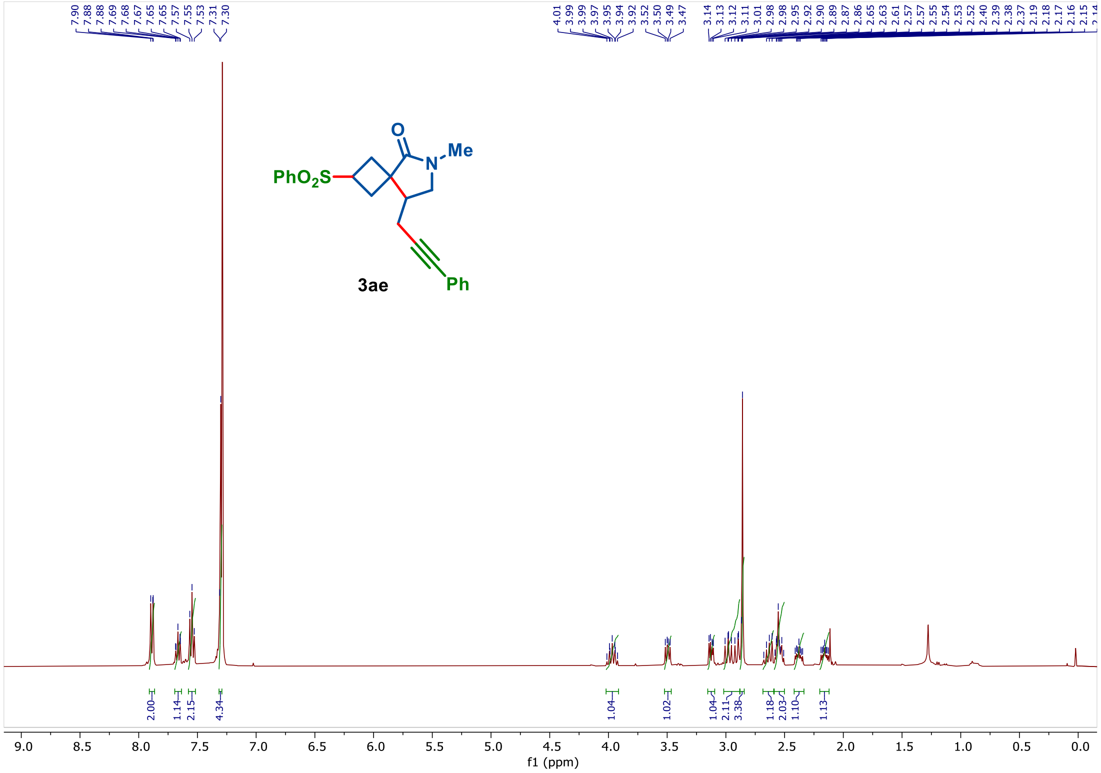
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **3ad** (See Procedure)



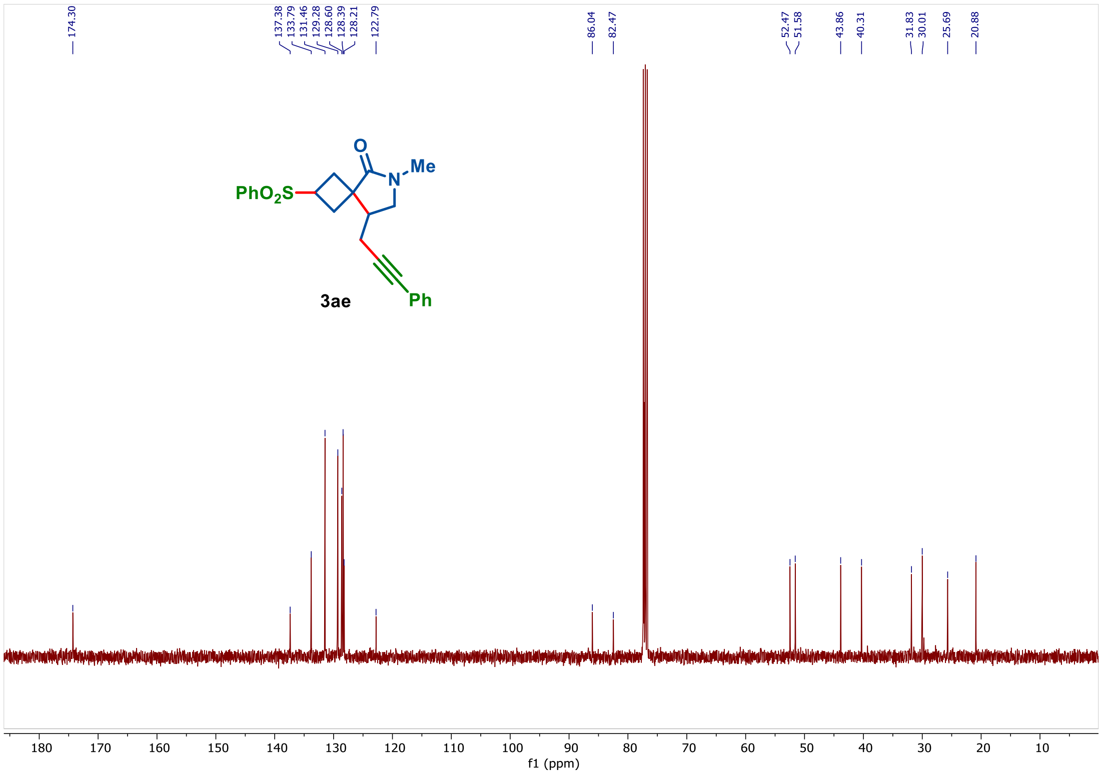
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **3ad**



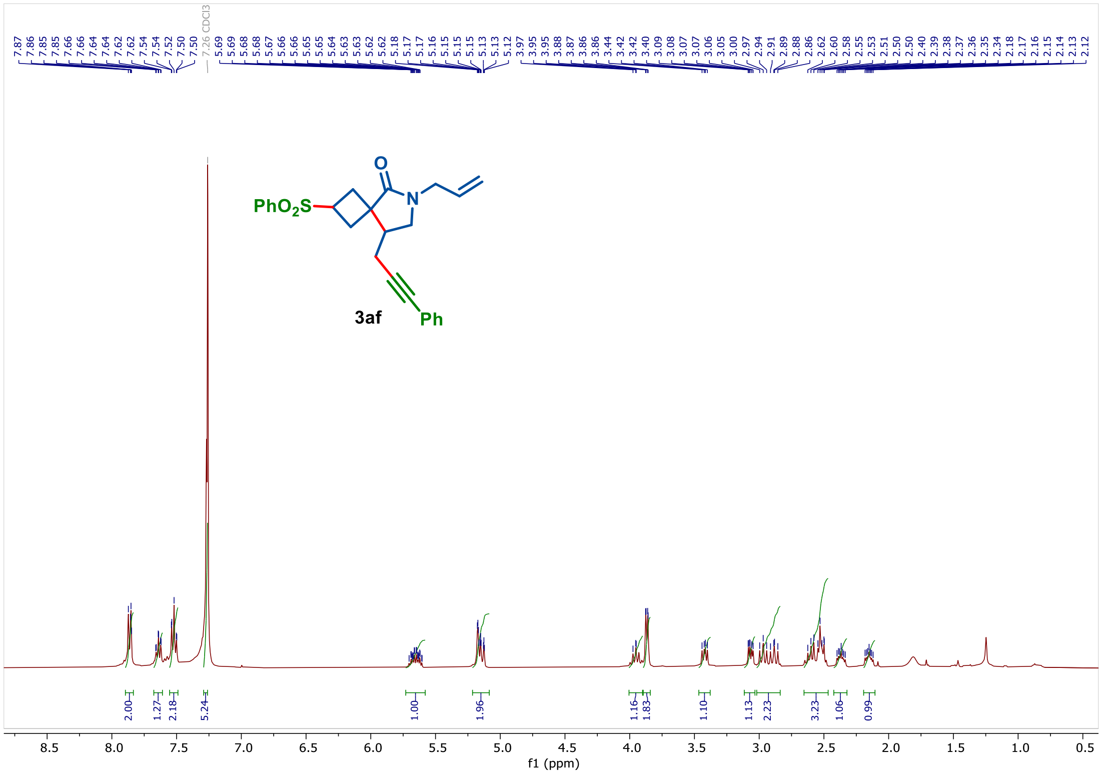
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **3ae** (See Procedure)



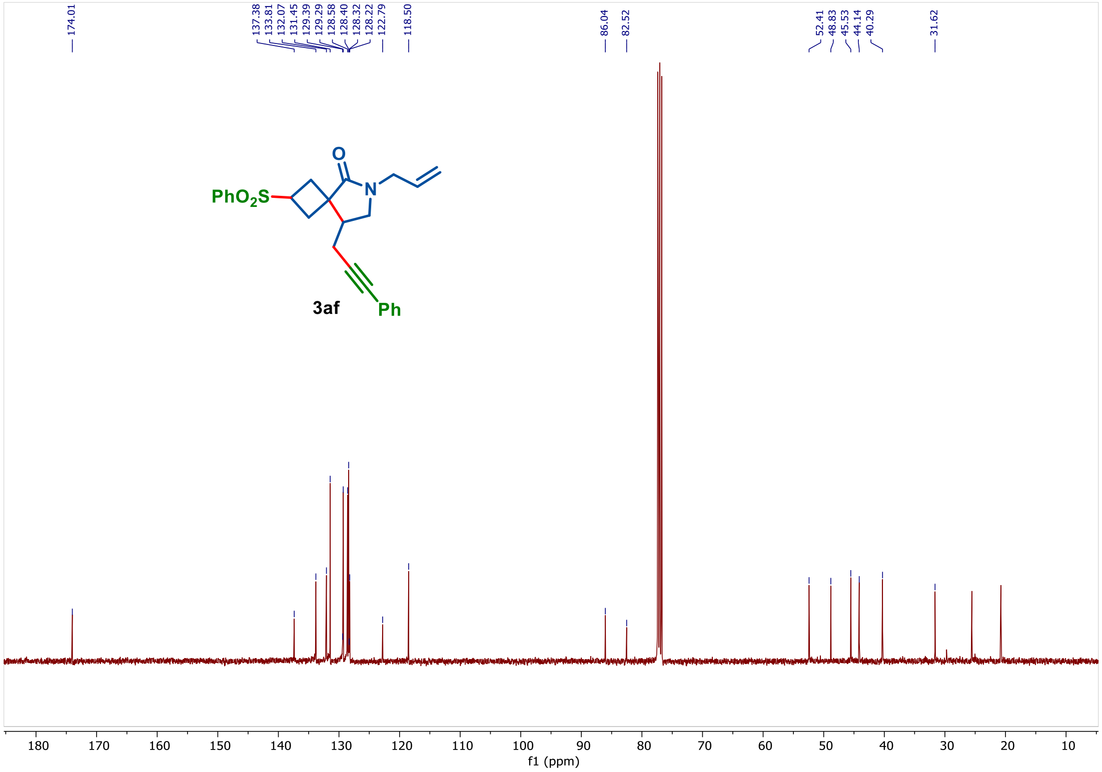
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **3ae**



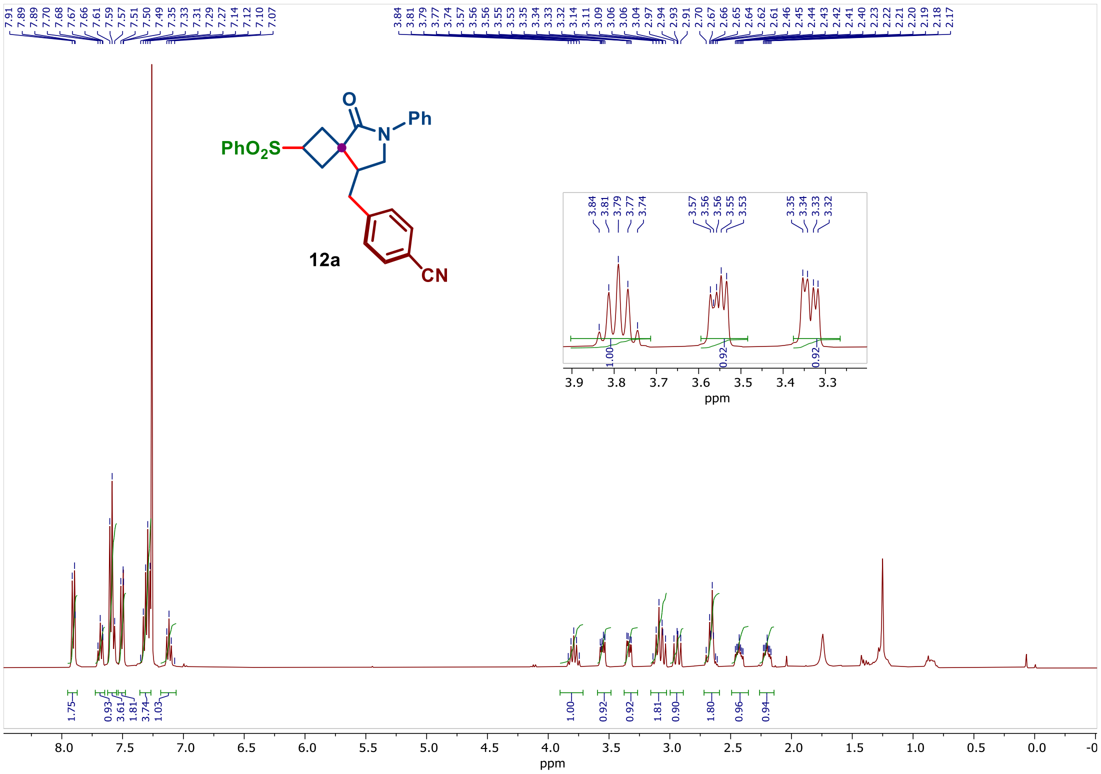
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **3af** (See Procedure)



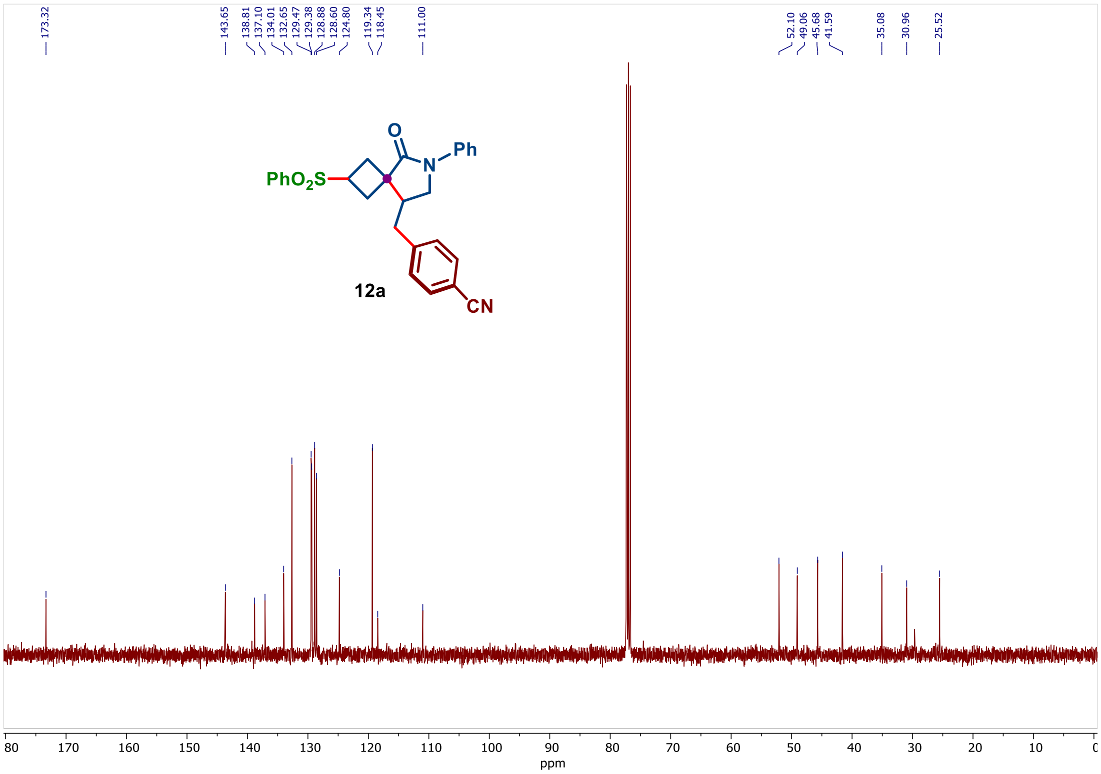
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **3af**



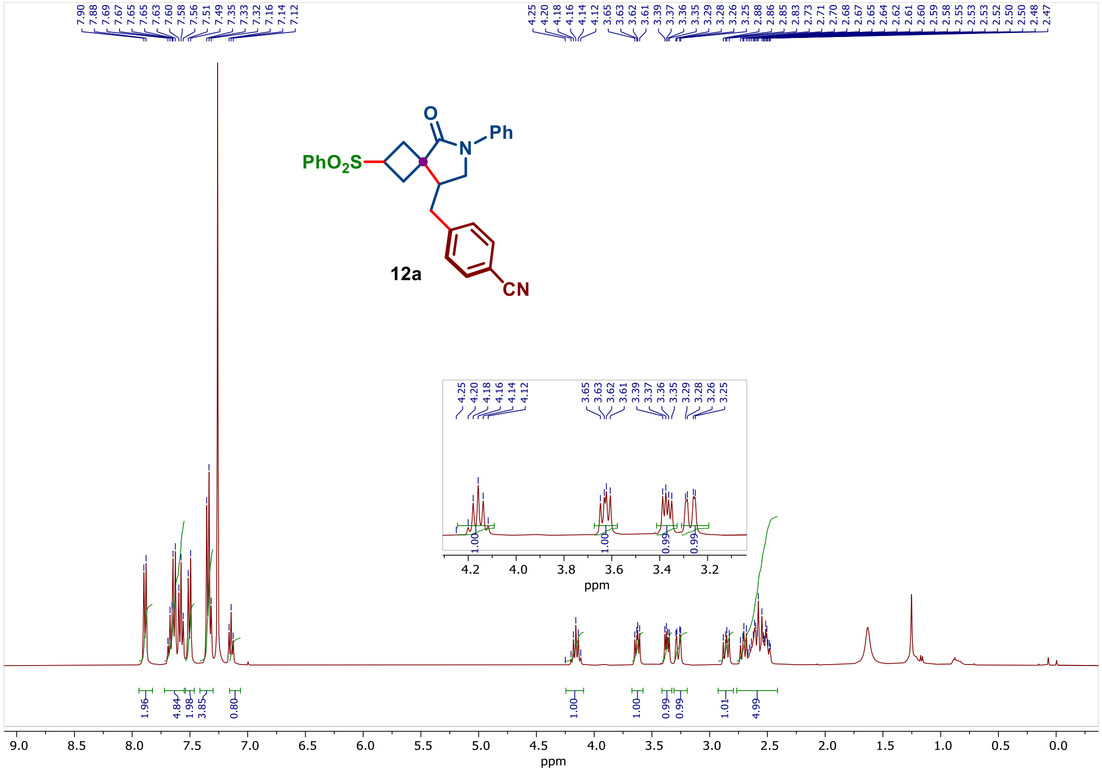
^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **12a (major)** (See Procedure)



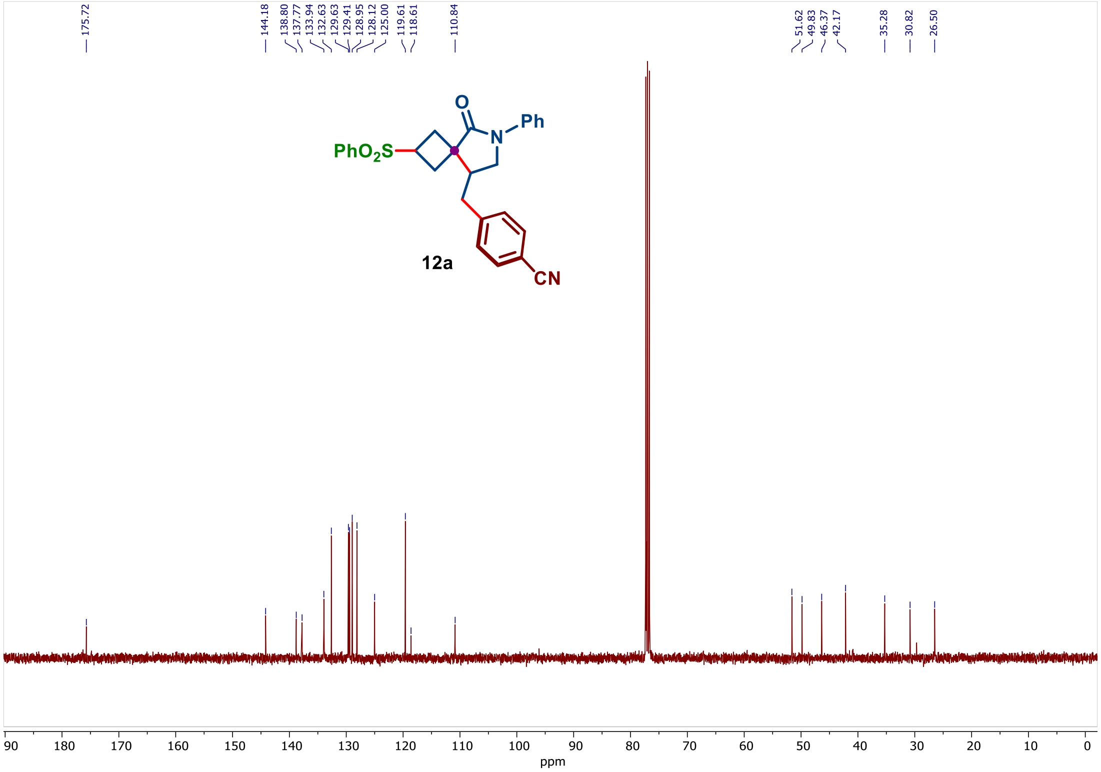
^{13}C NMR (101 MHz, $CDCl_3$) spectra of compound **12a (major)**



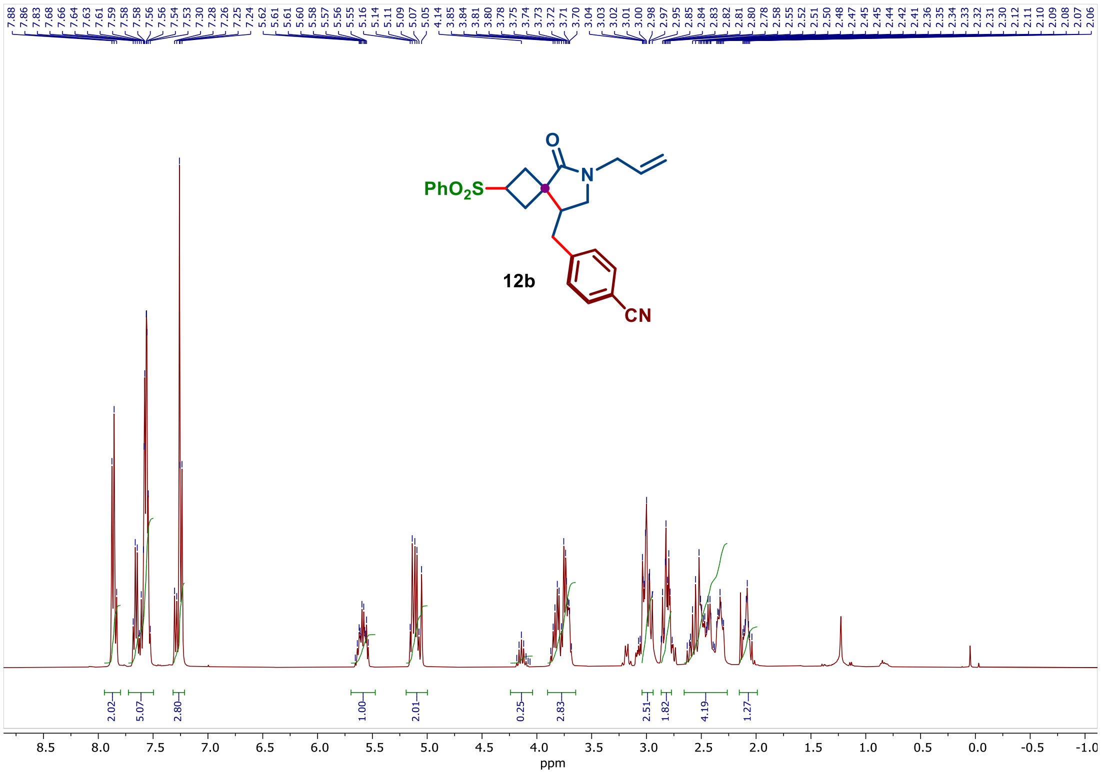
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **12a (minor)**



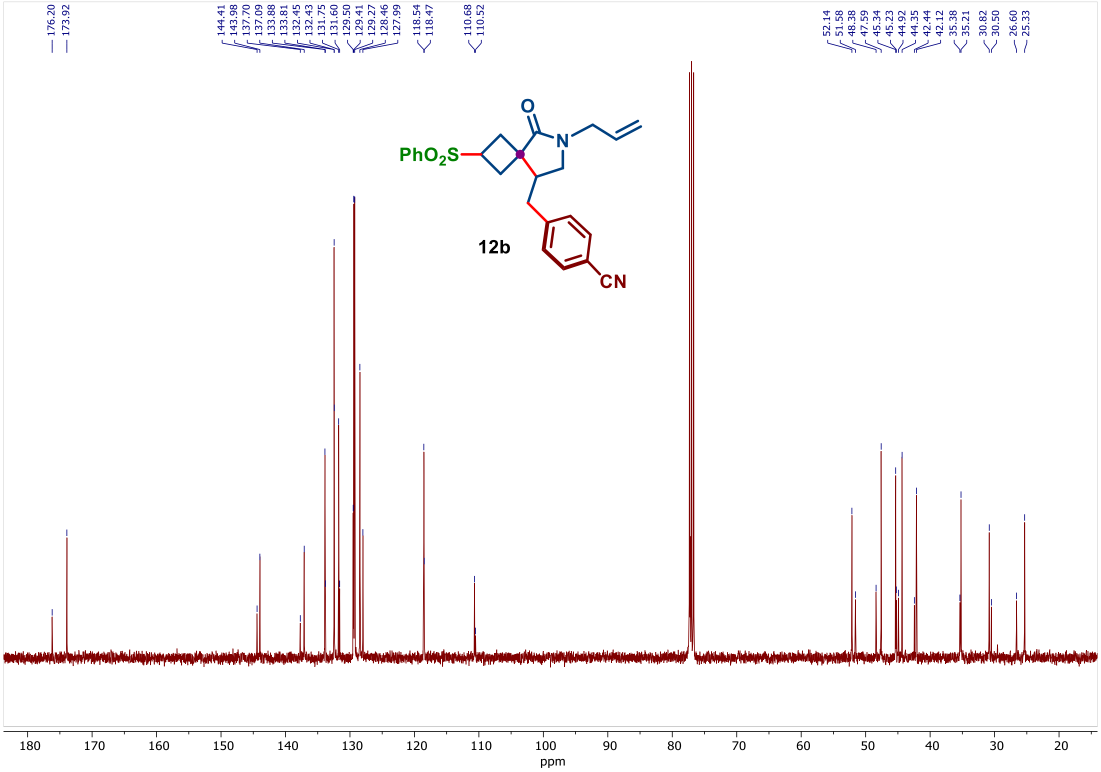
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **12a (minor)**



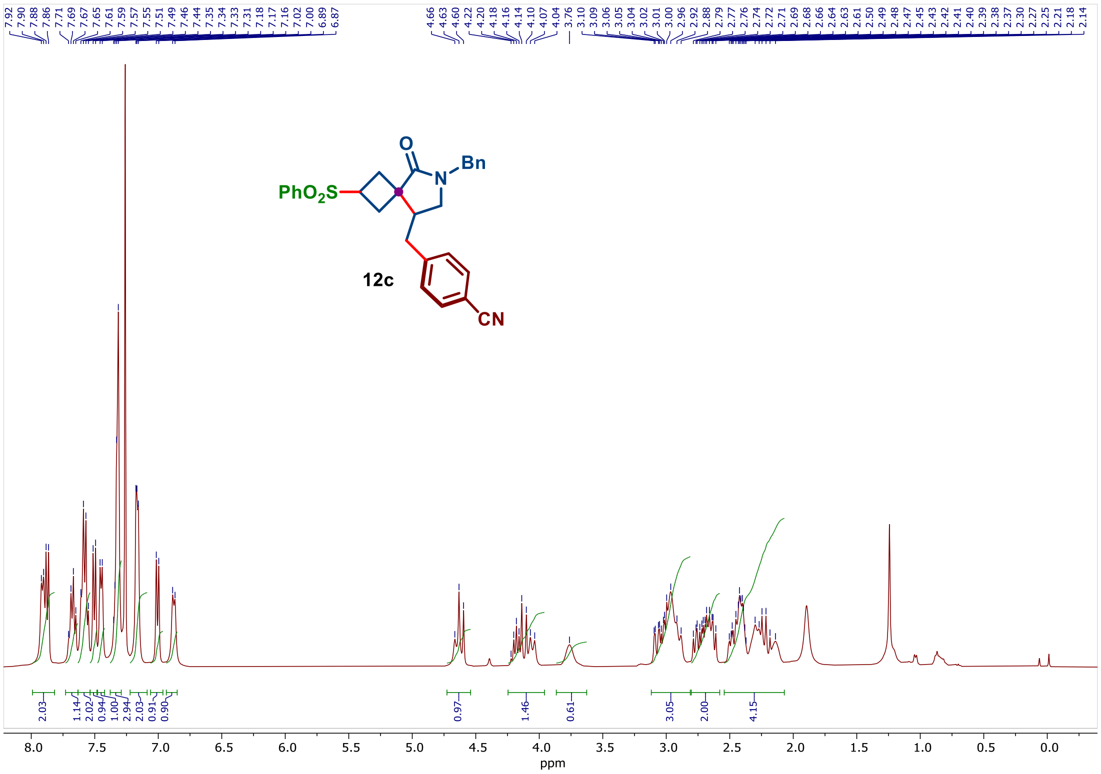
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **12b** (See Procedure)



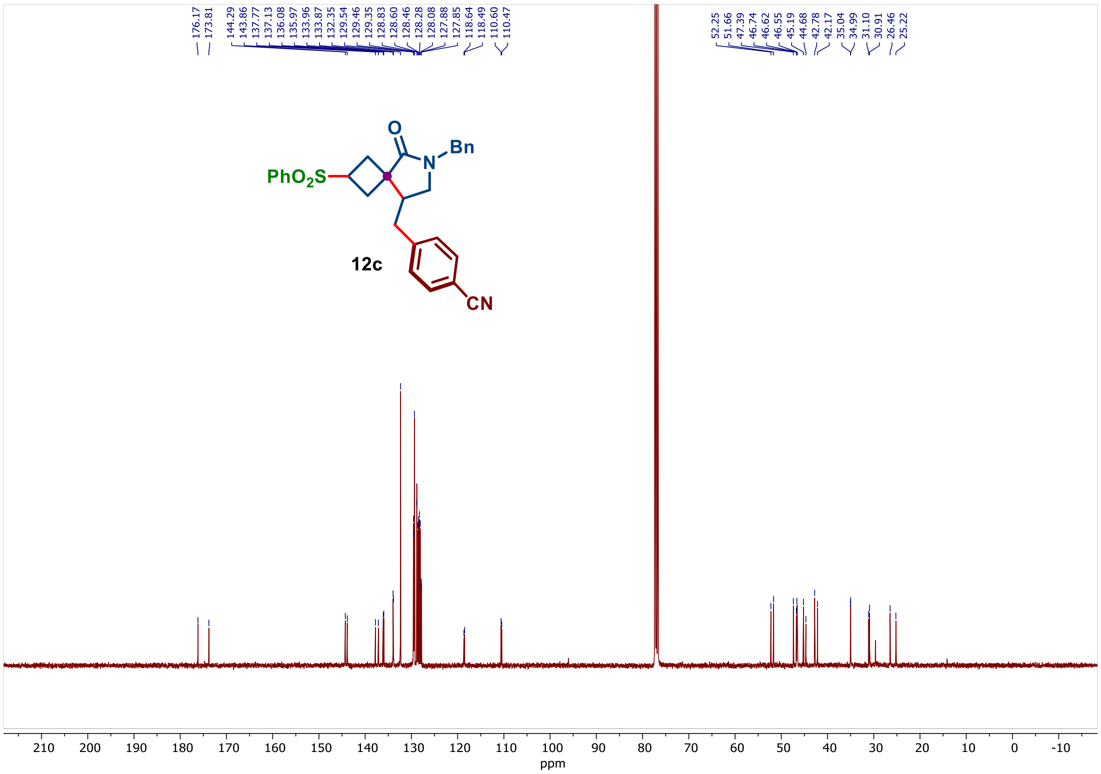
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **12b**



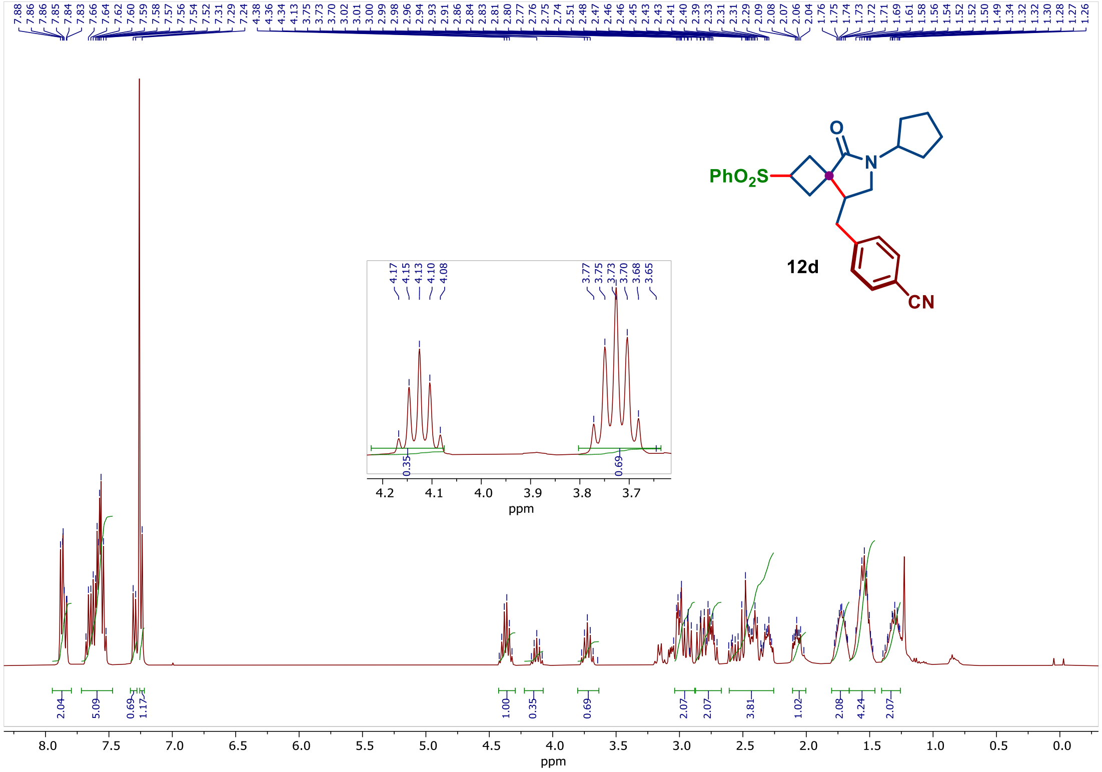
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **12c** (See Procedure)



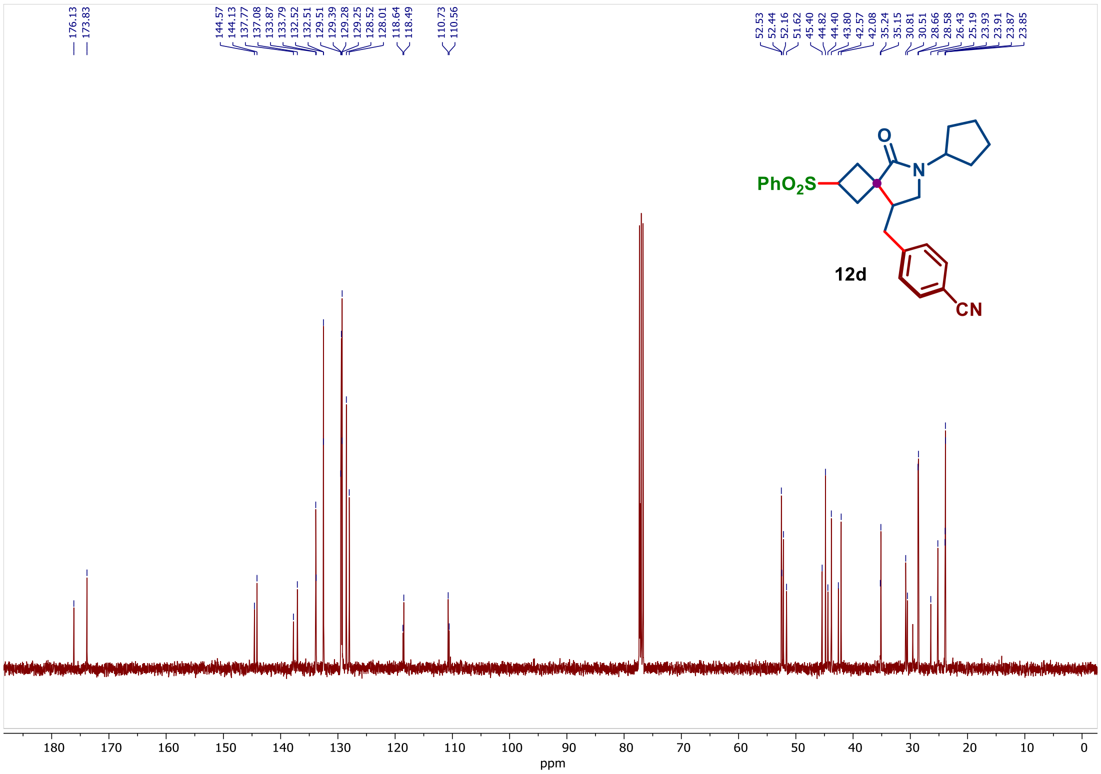
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **12c**



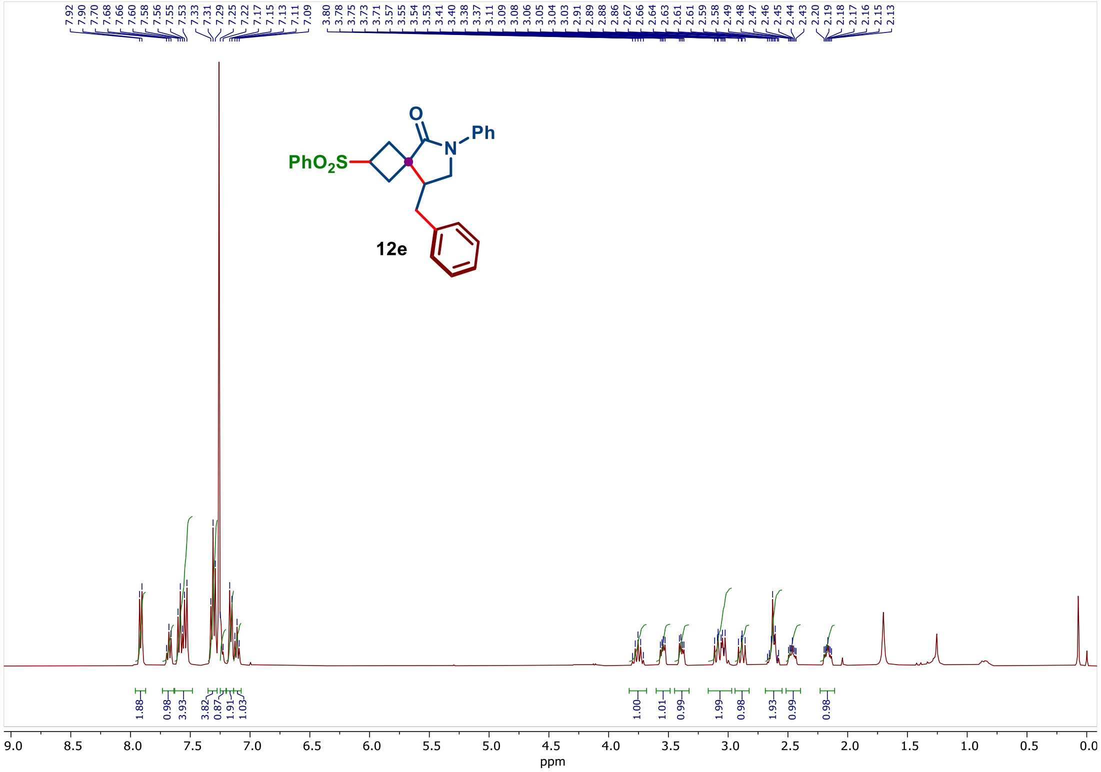
^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **12d** (See Procedure)



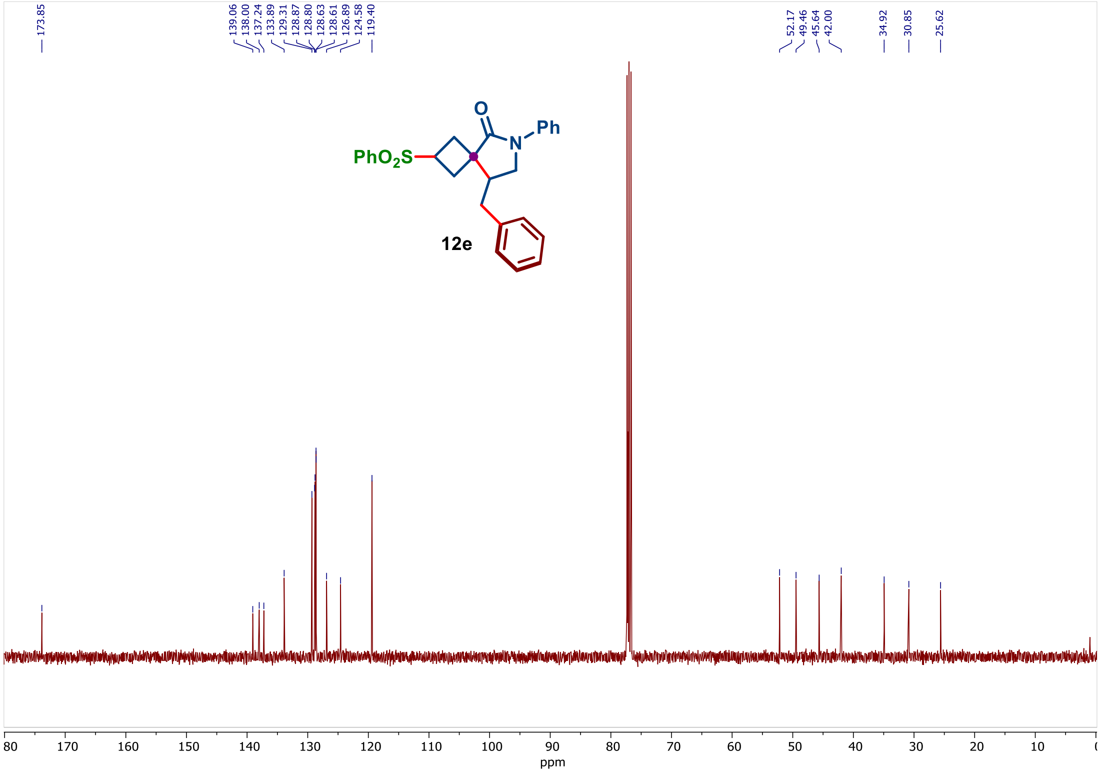
^{13}C NMR (101 MHz, $CDCl_3$) spectra of compound **12d**



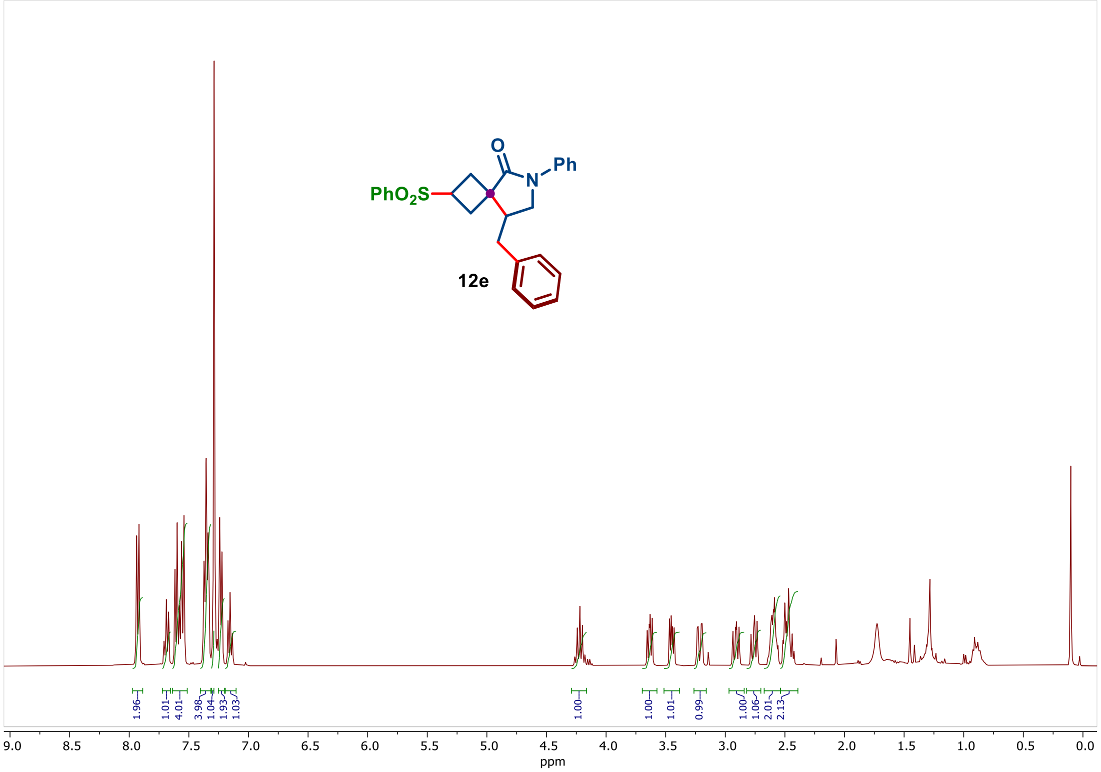
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **12e (major)** (See Procedure)



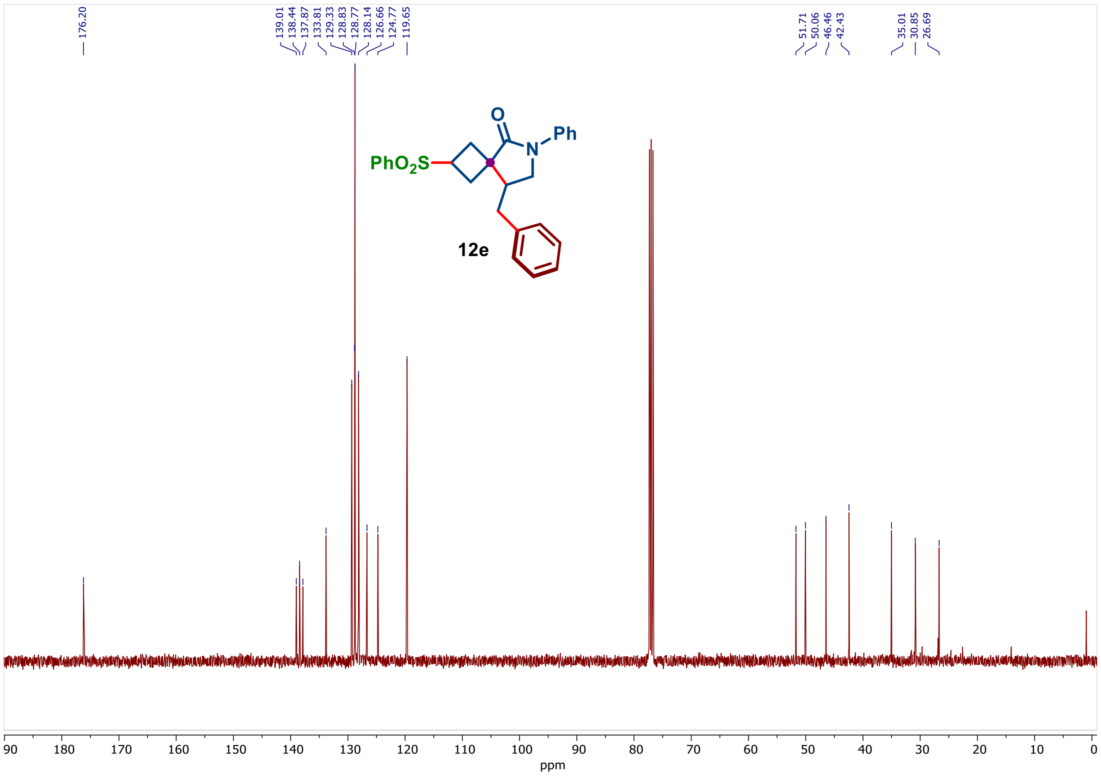
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **12e (major)**



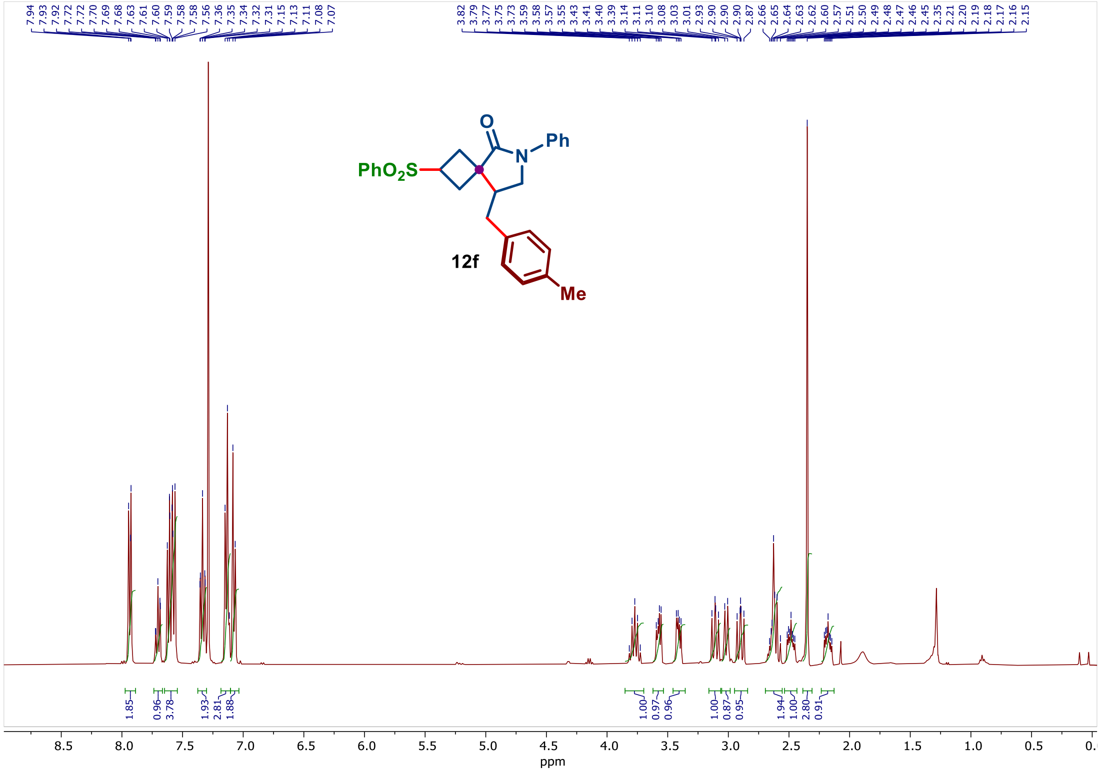
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **12e (minor)**



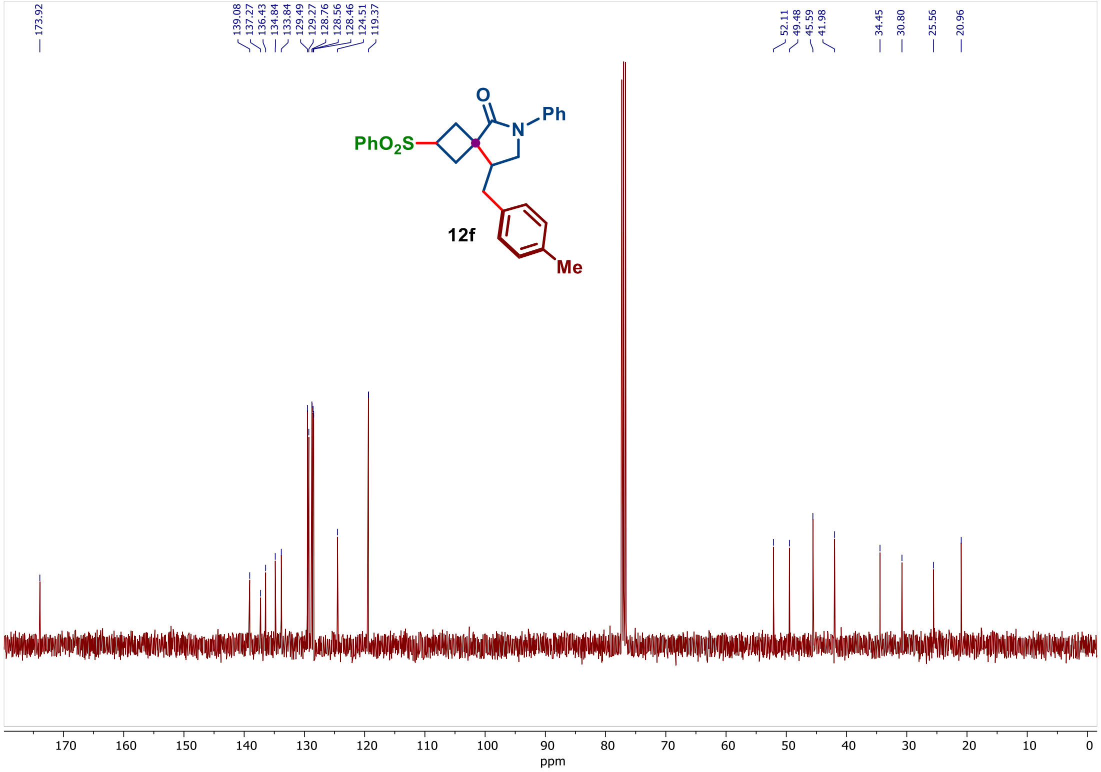
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **12e (minor)**



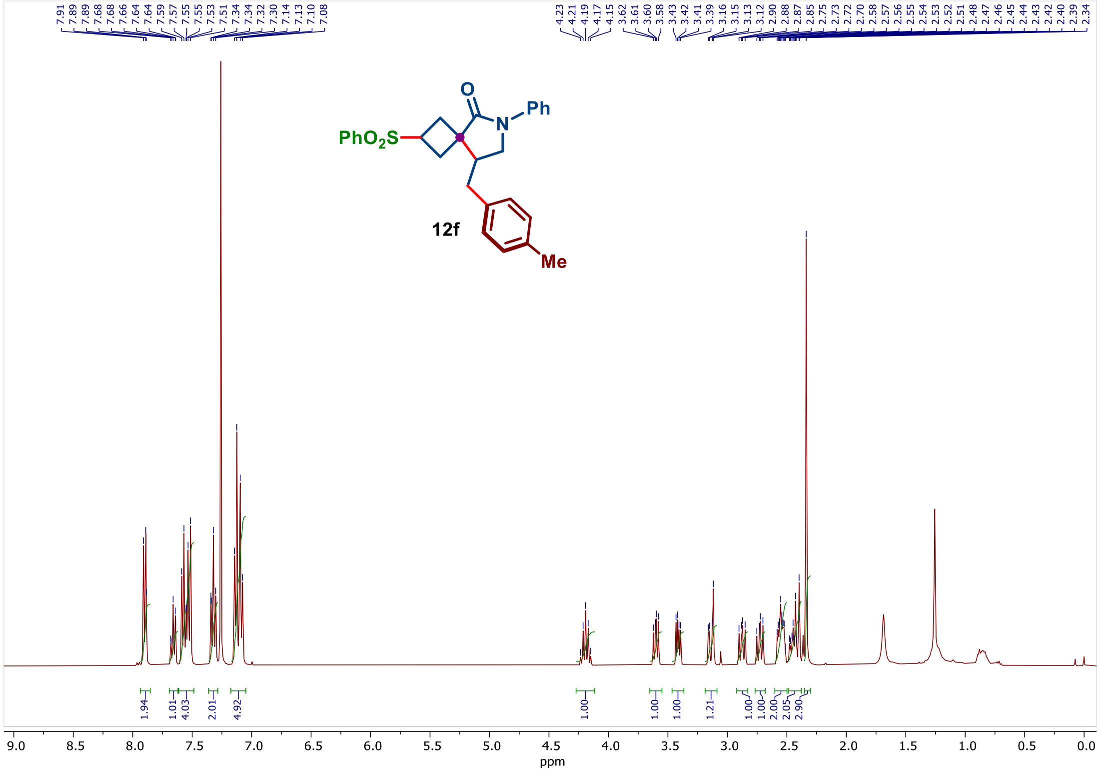
^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **12f (major)** (See Procedure)



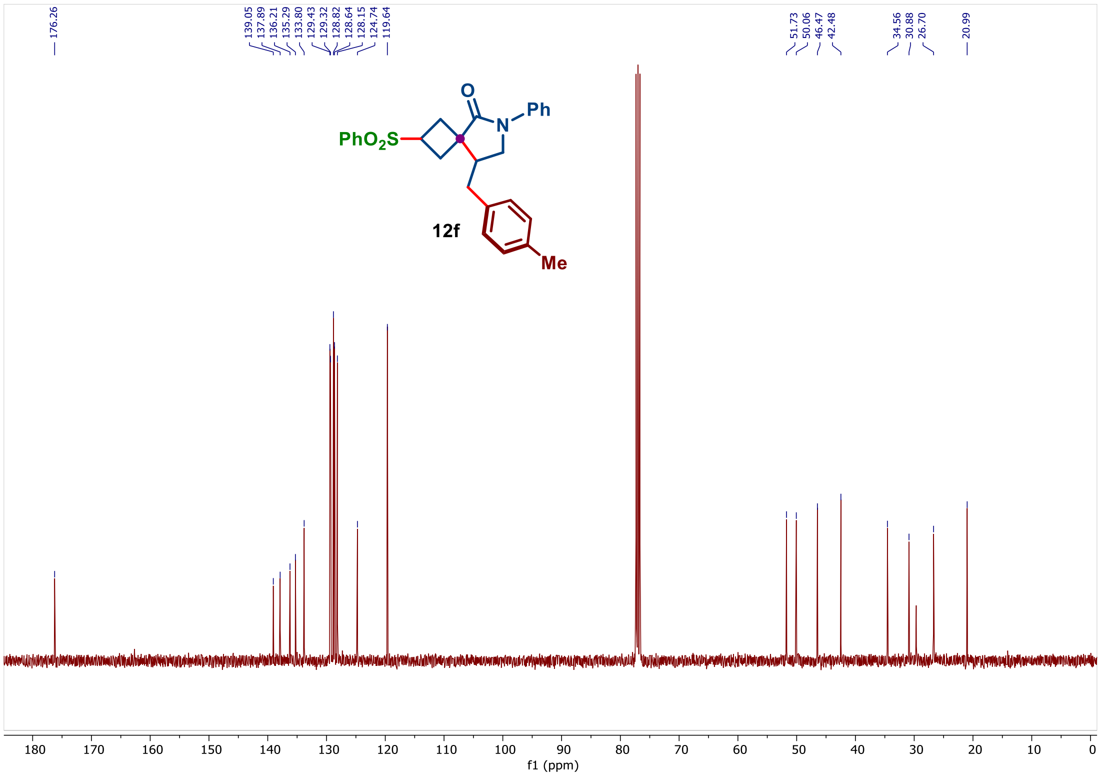
^{13}C NMR (101 MHz, $CDCl_3$) spectra of compound **12f (major)**



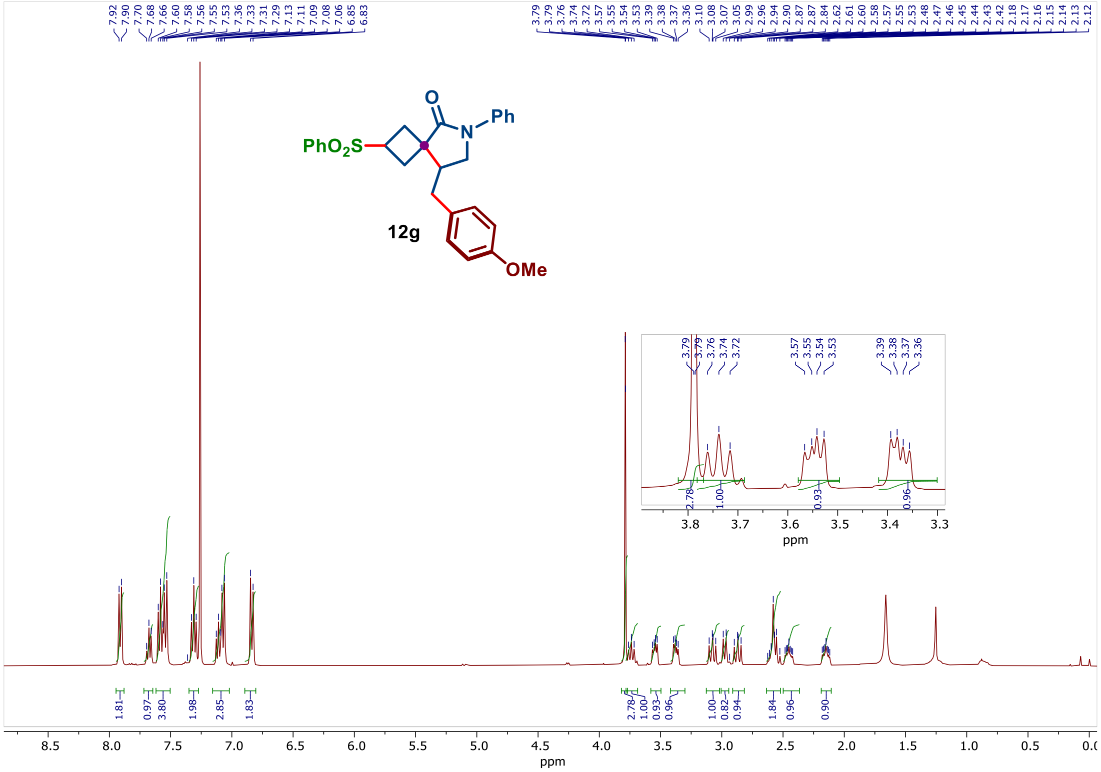
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **12f (minor)**



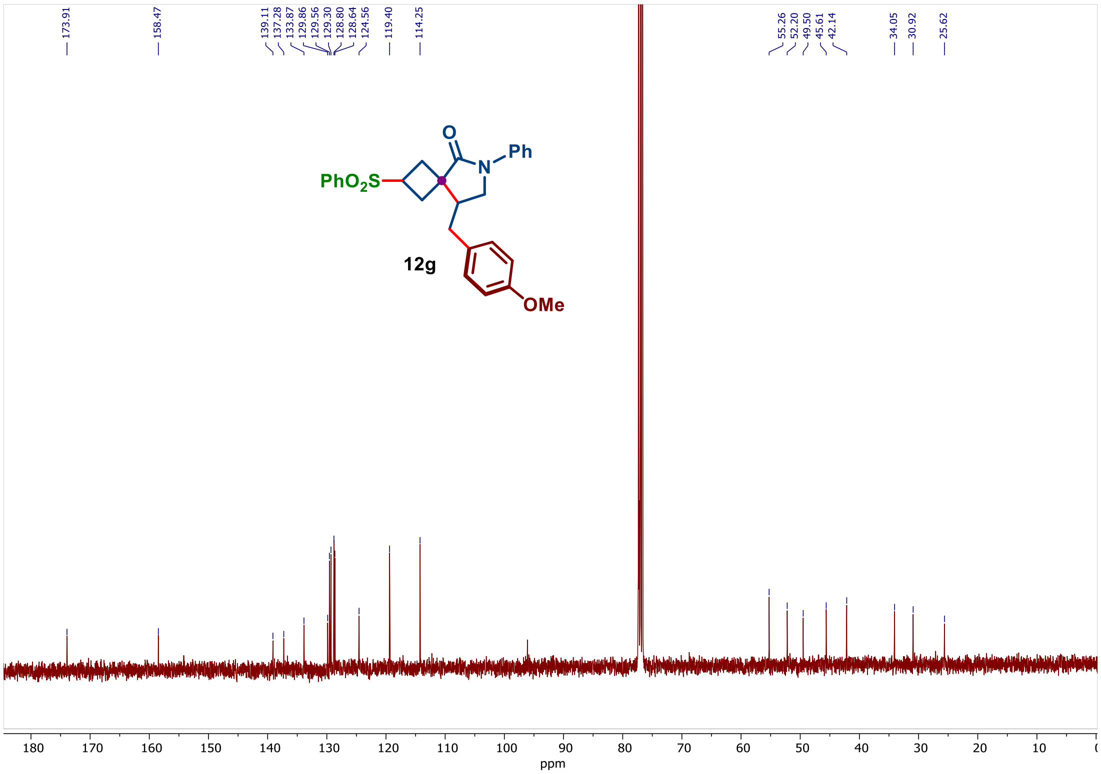
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **12f (minor)**



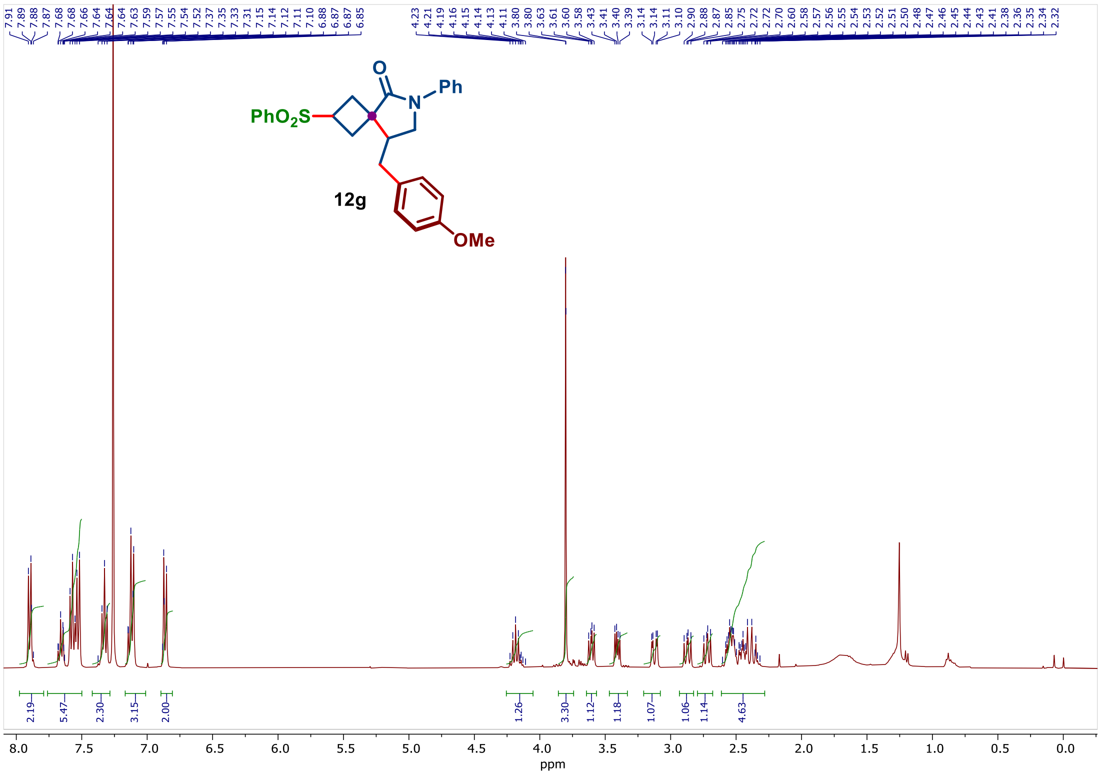
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **12g (major)**(See Procedure)



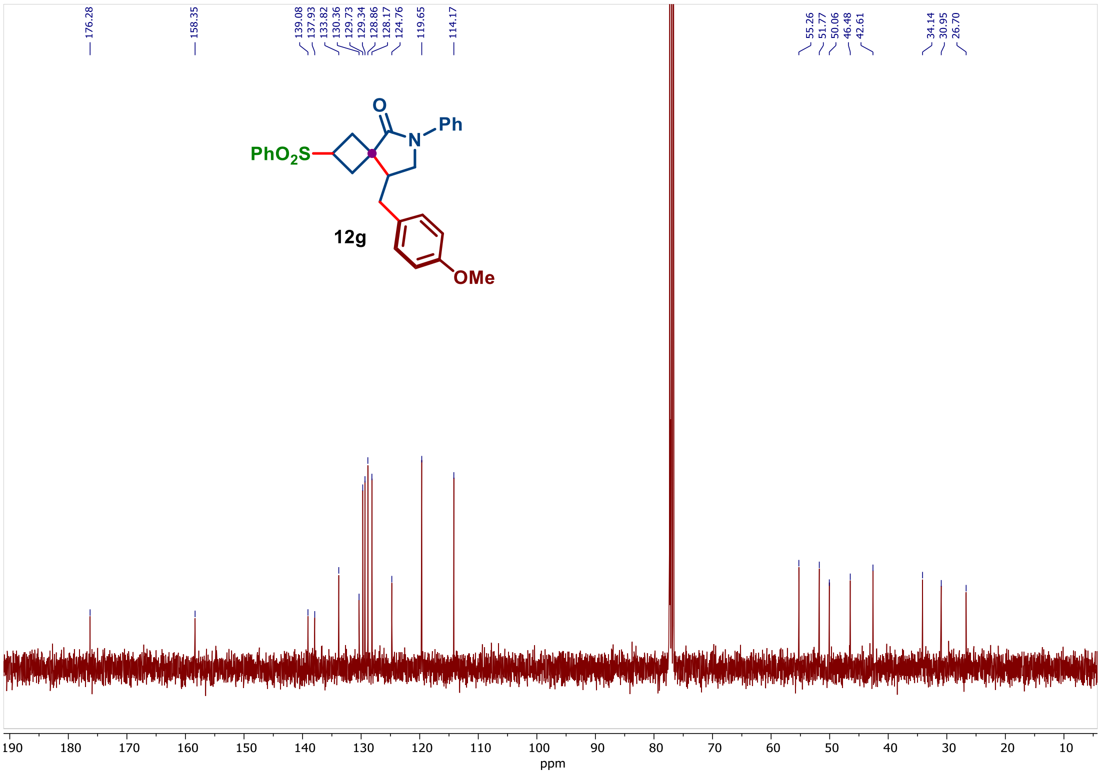
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **12g (major)**



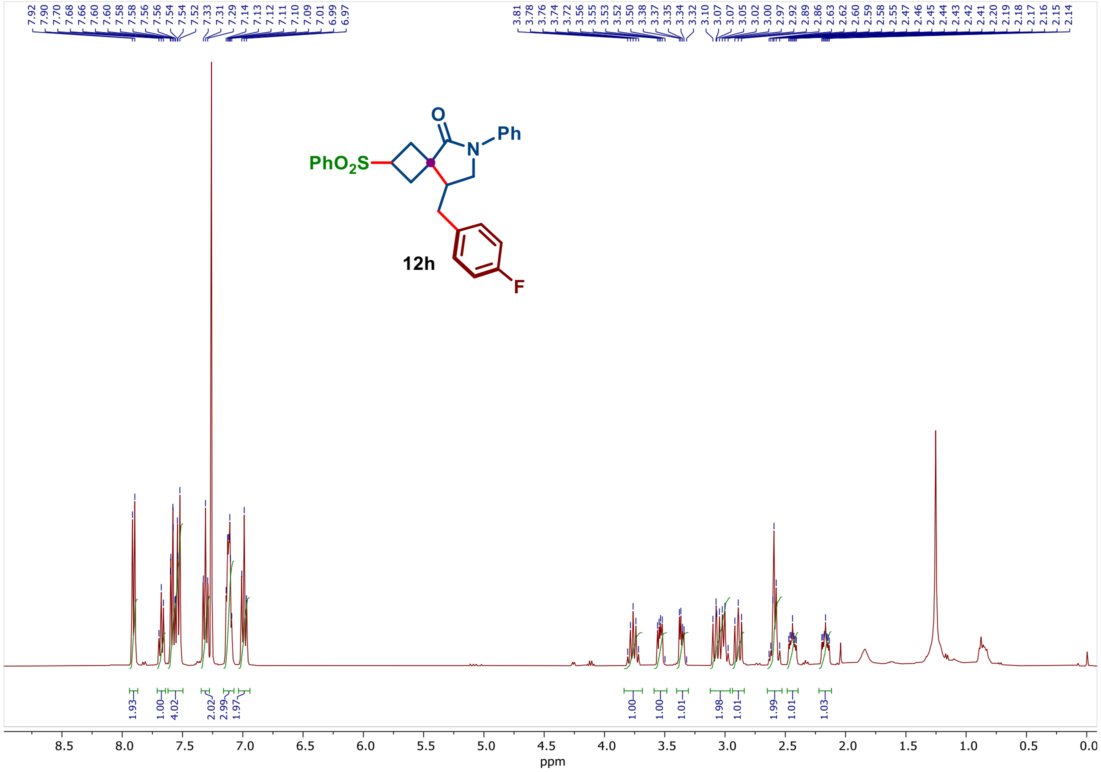
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **12g (minor)**



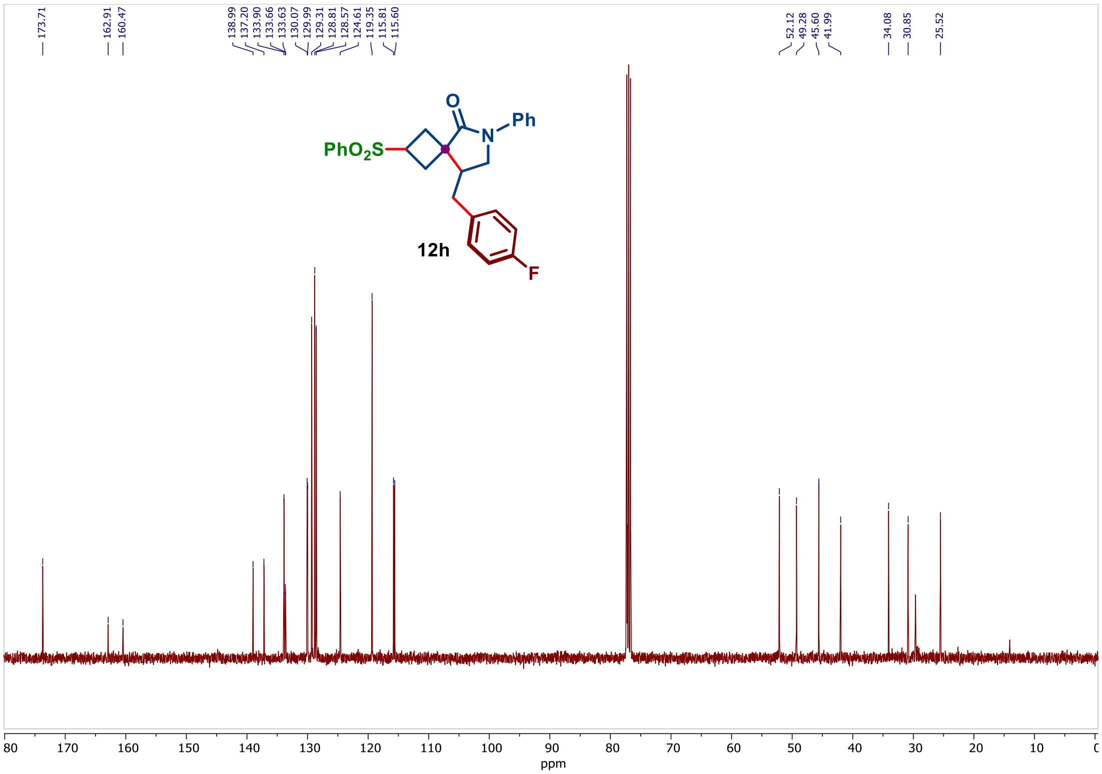
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **12g (minor)**



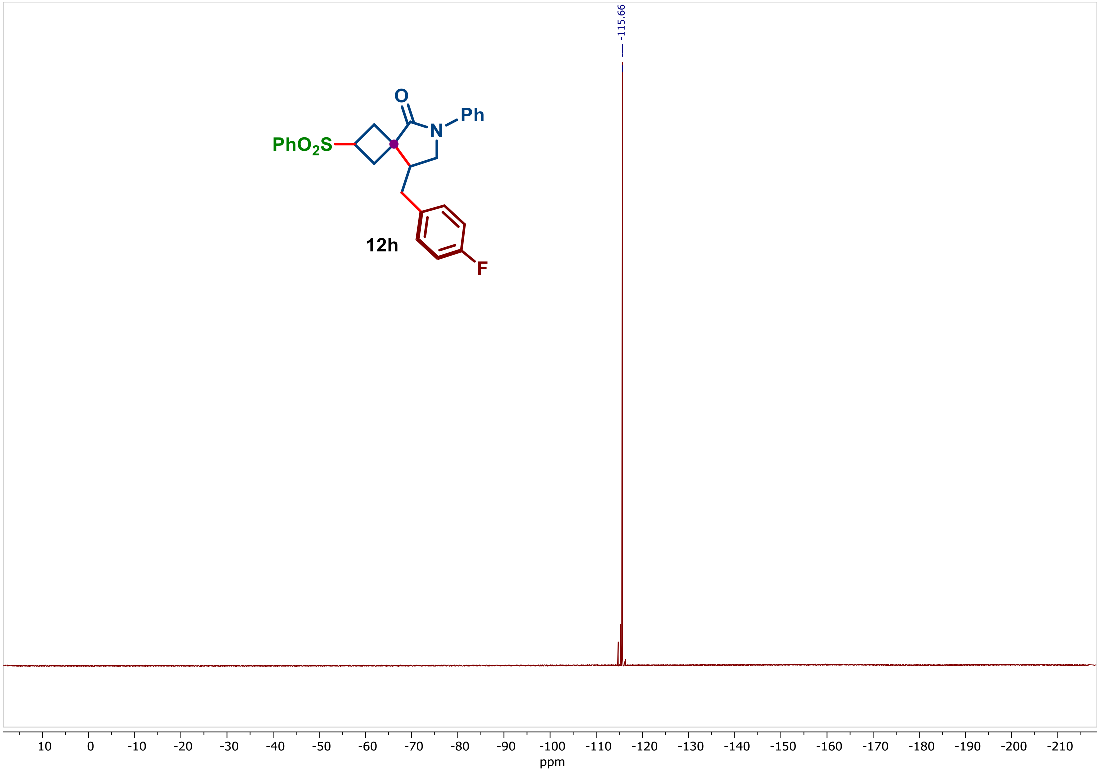
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **12h (major)** (See Procedure)



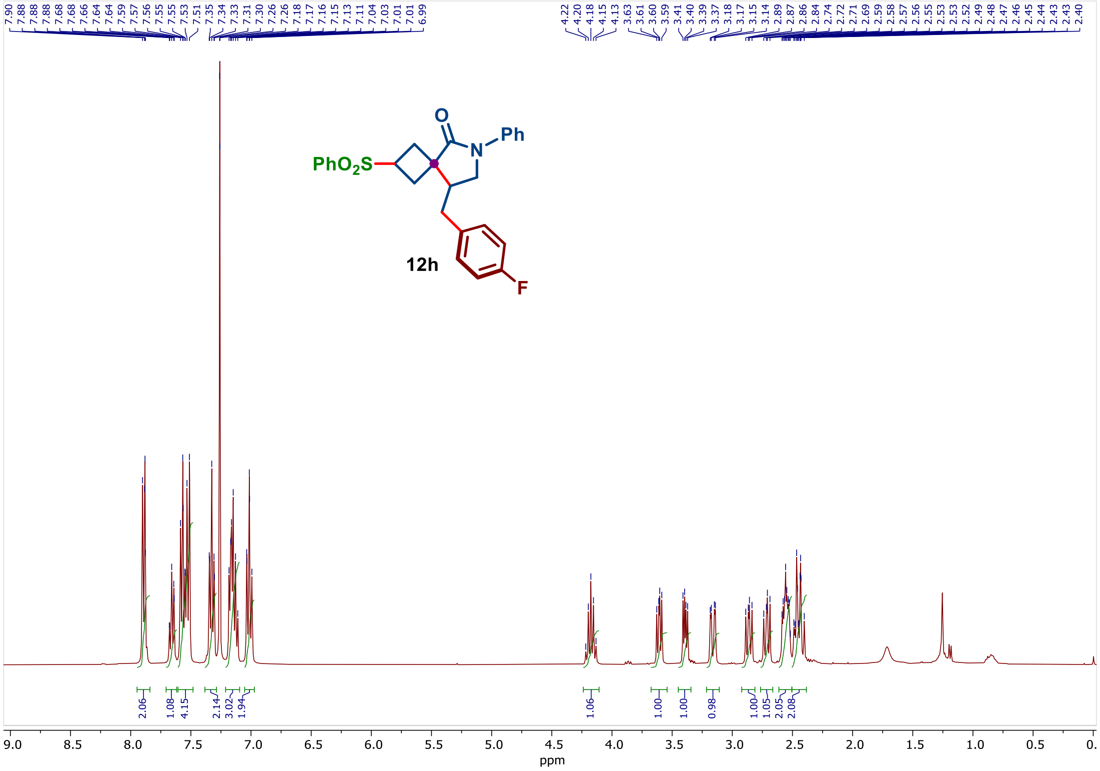
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **12h (major)**



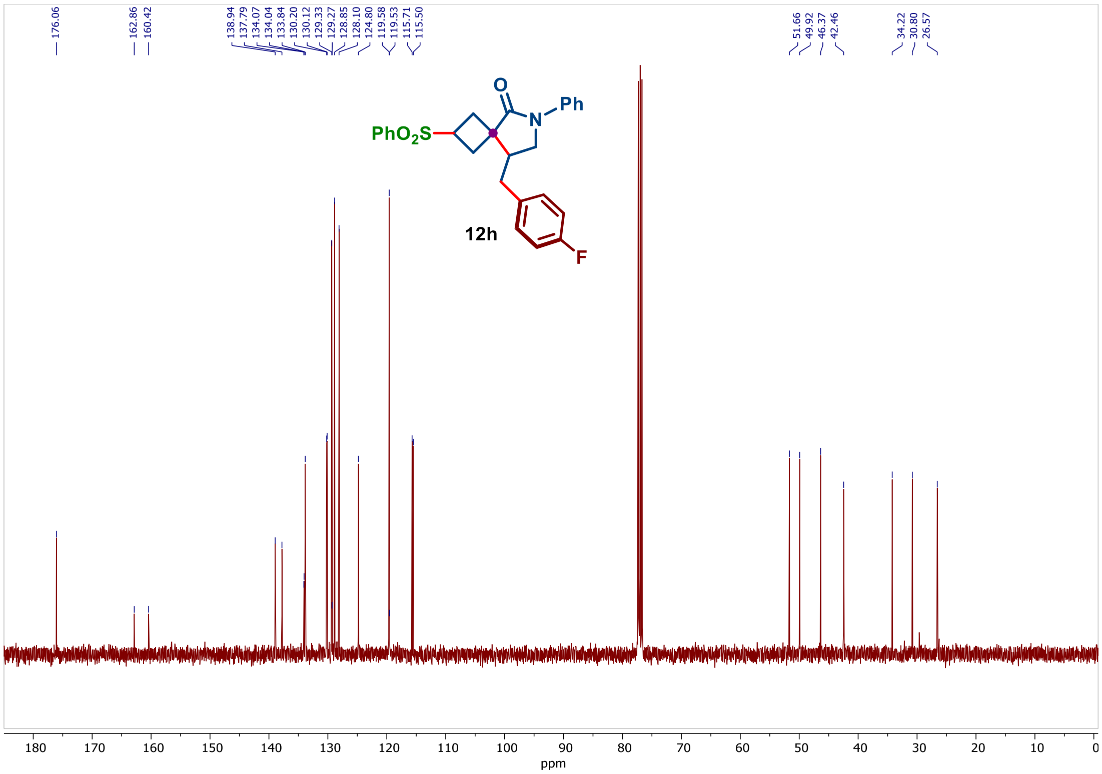
^{19}F NMR (377 MHz, CDCl$_3$) spectra of compound **12h (major)**



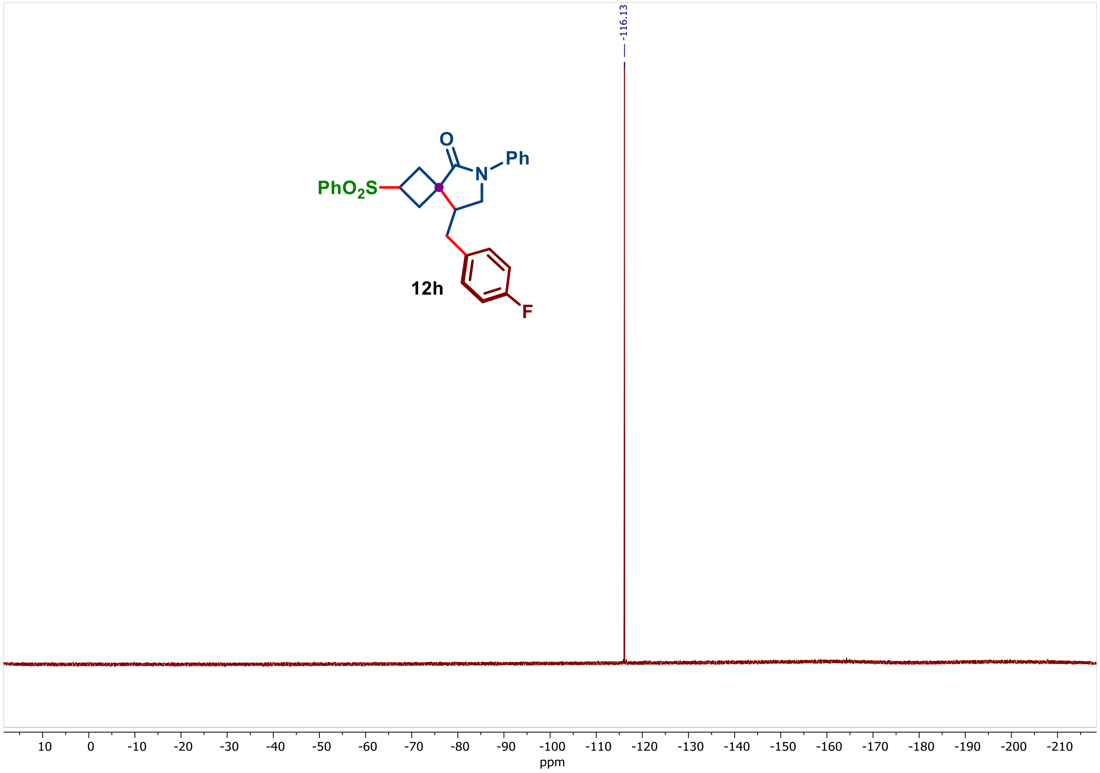
^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **12h (minor)**



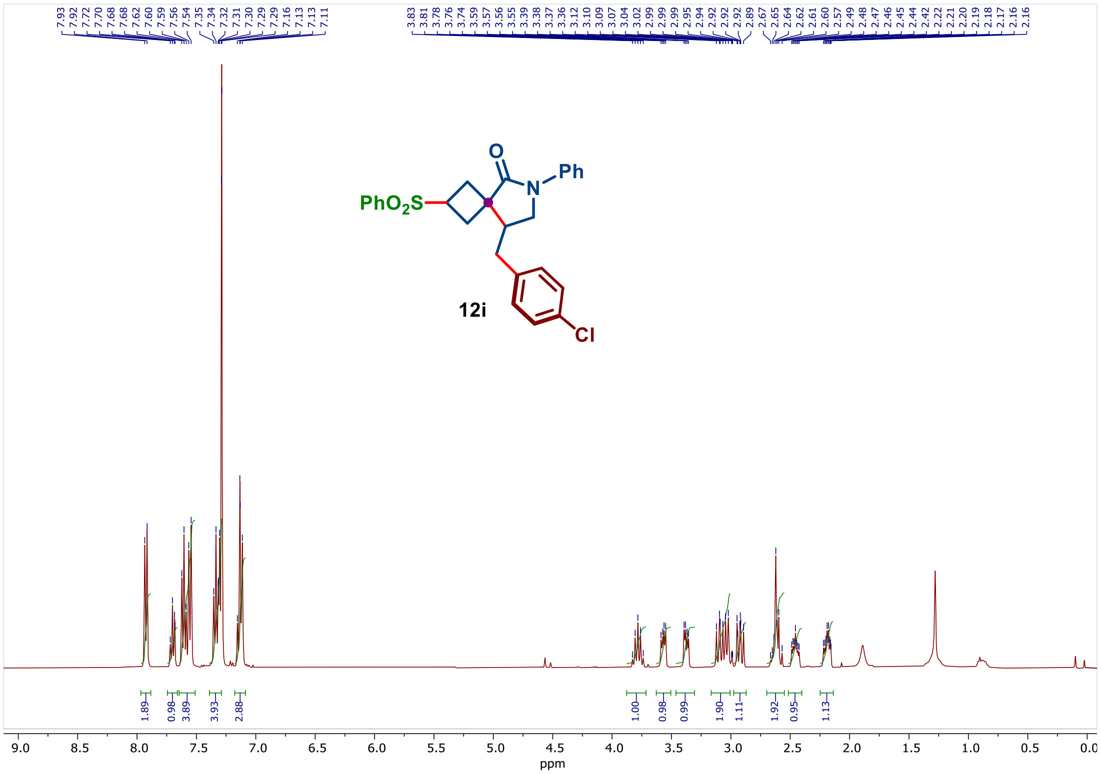
^{13}C NMR (101 MHz, $CDCl_3$) spectra of compound **12h (minor)**



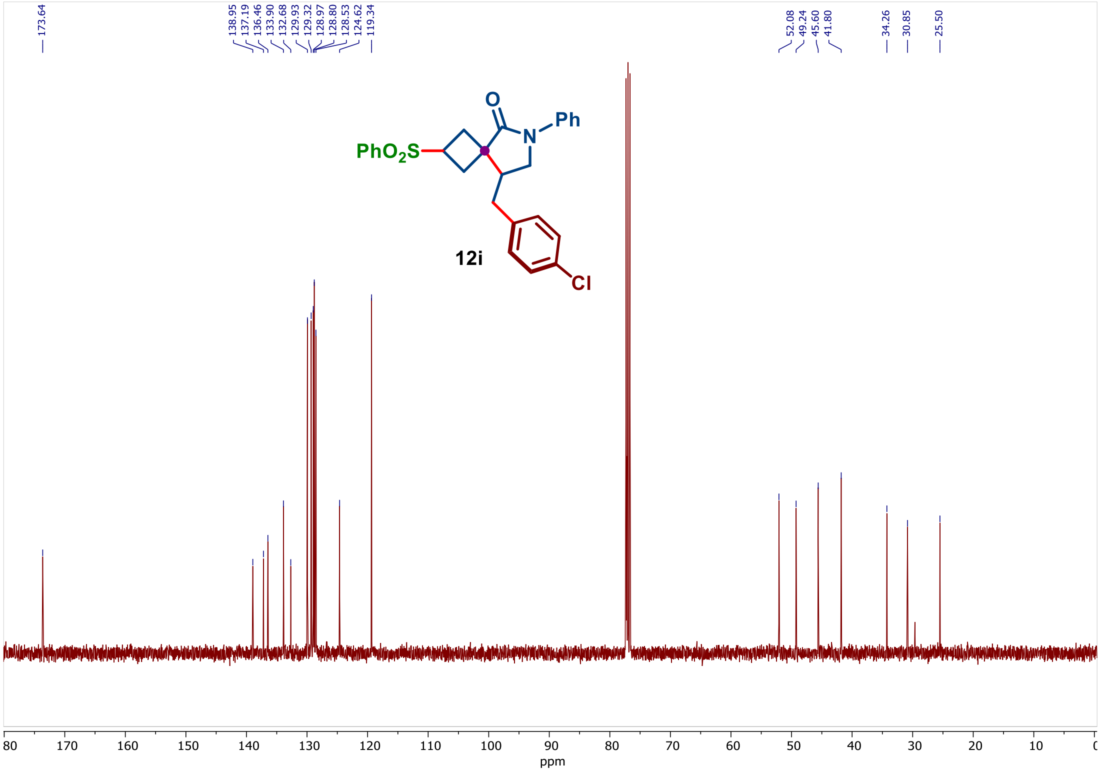
^{19}F NMR (377 MHz, $CDCl_3$) spectra of compound **12h (minor)**



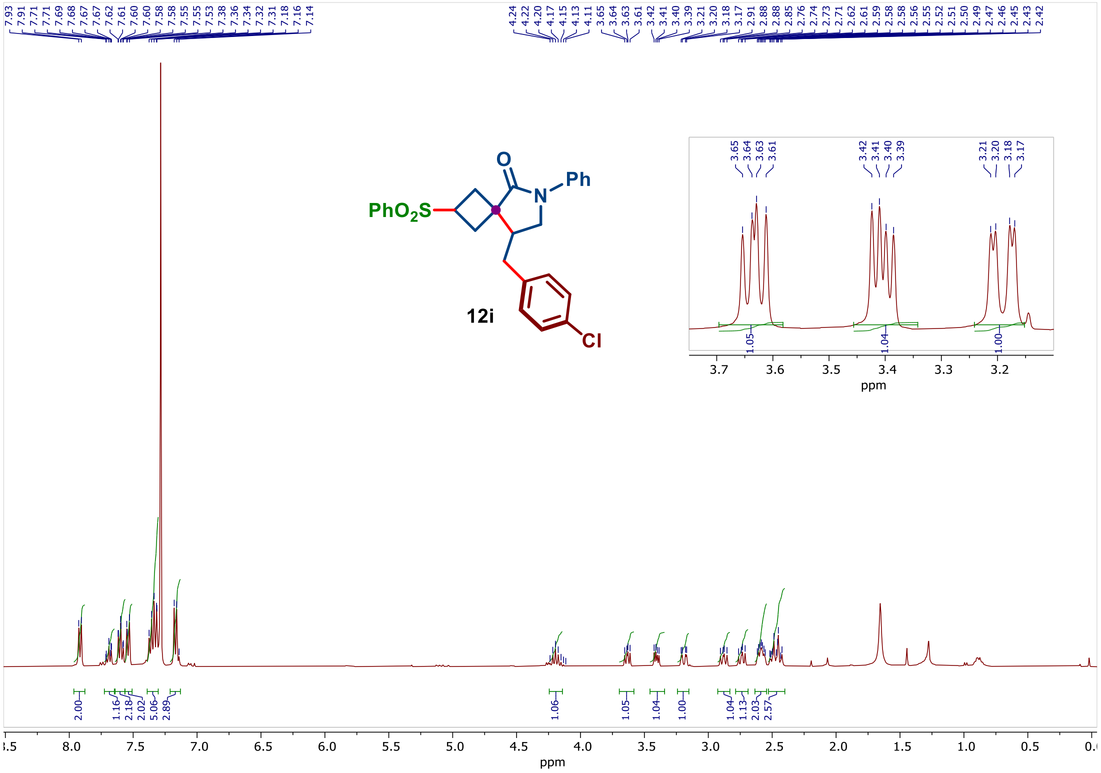
^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **12i (major)** (See Procedure)



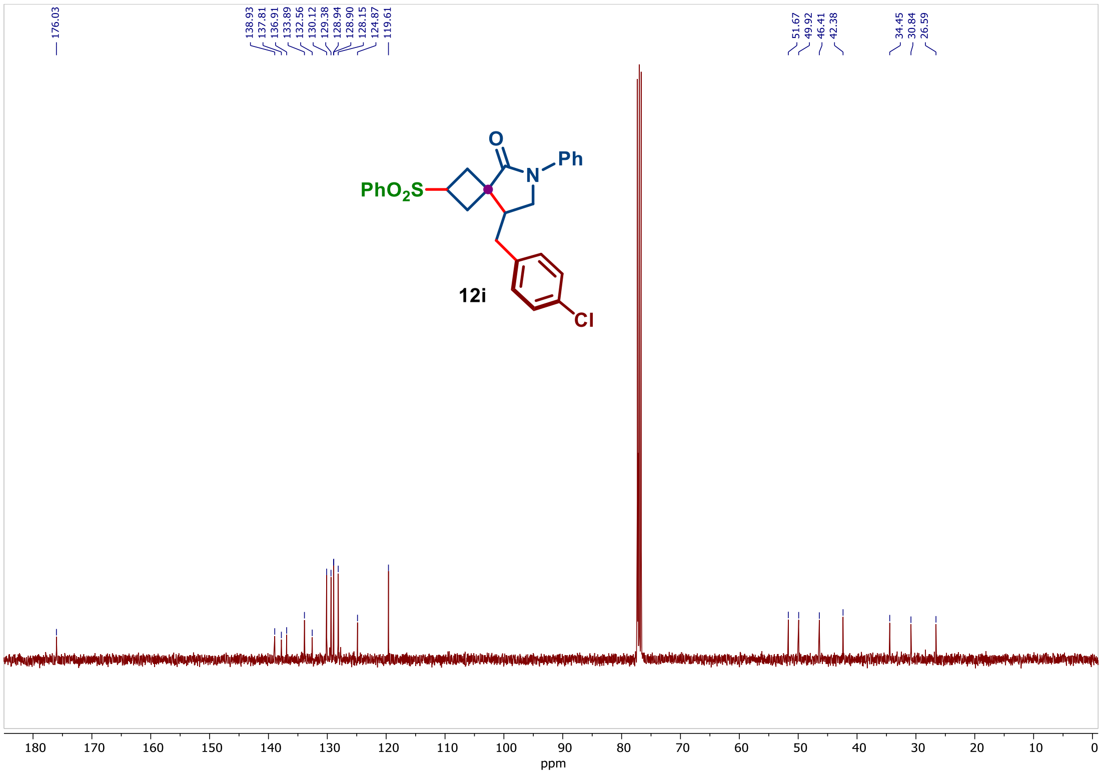
^{13}C NMR (101 MHz, $CDCl_3$) spectra of compound **12i (major)**



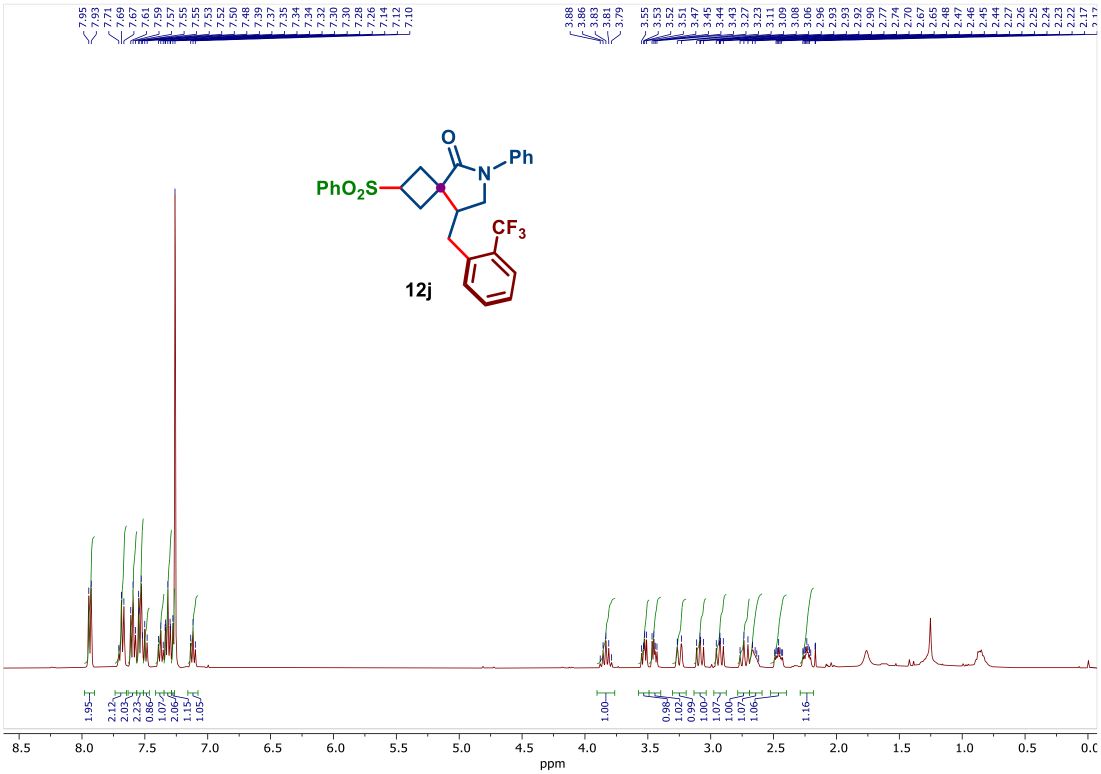
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **12i (minor)**



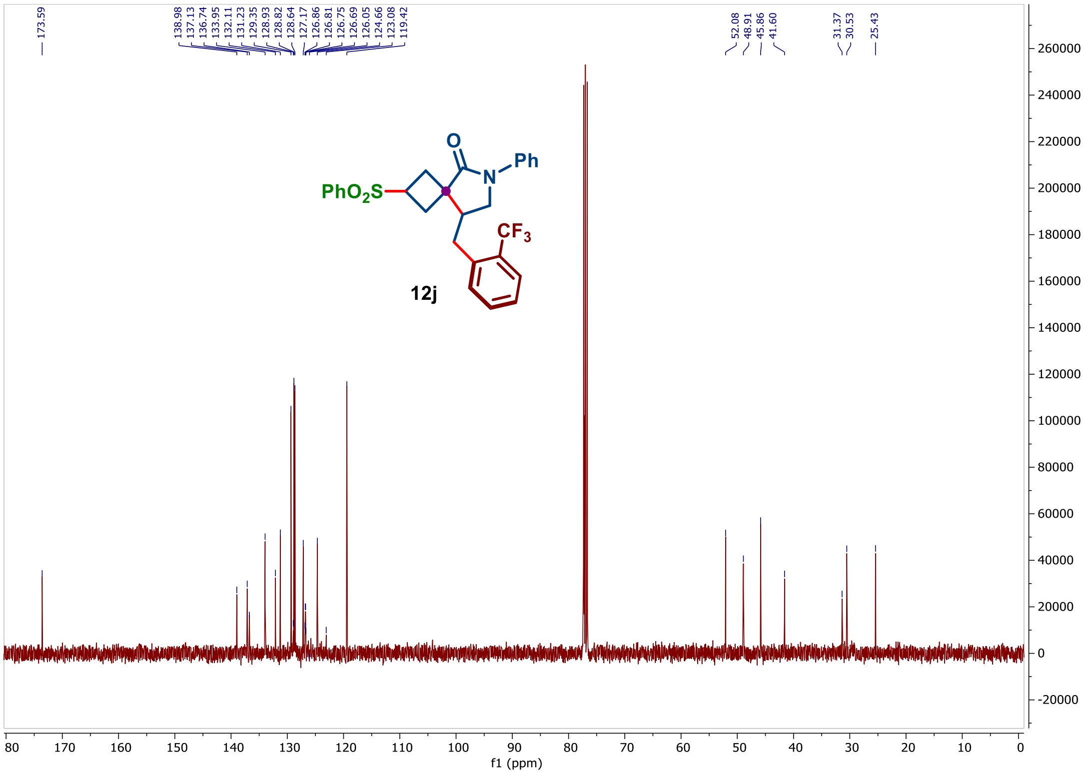
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **12i (minor)**



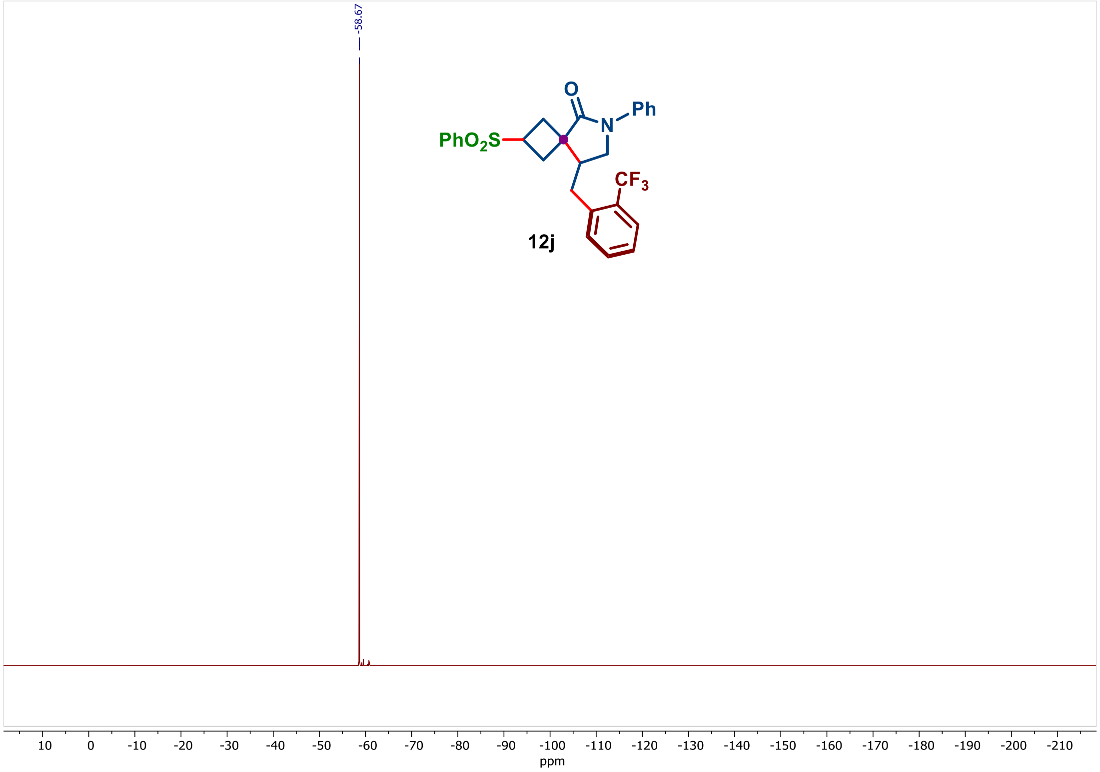
^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **12j (major)** (See Procedure)



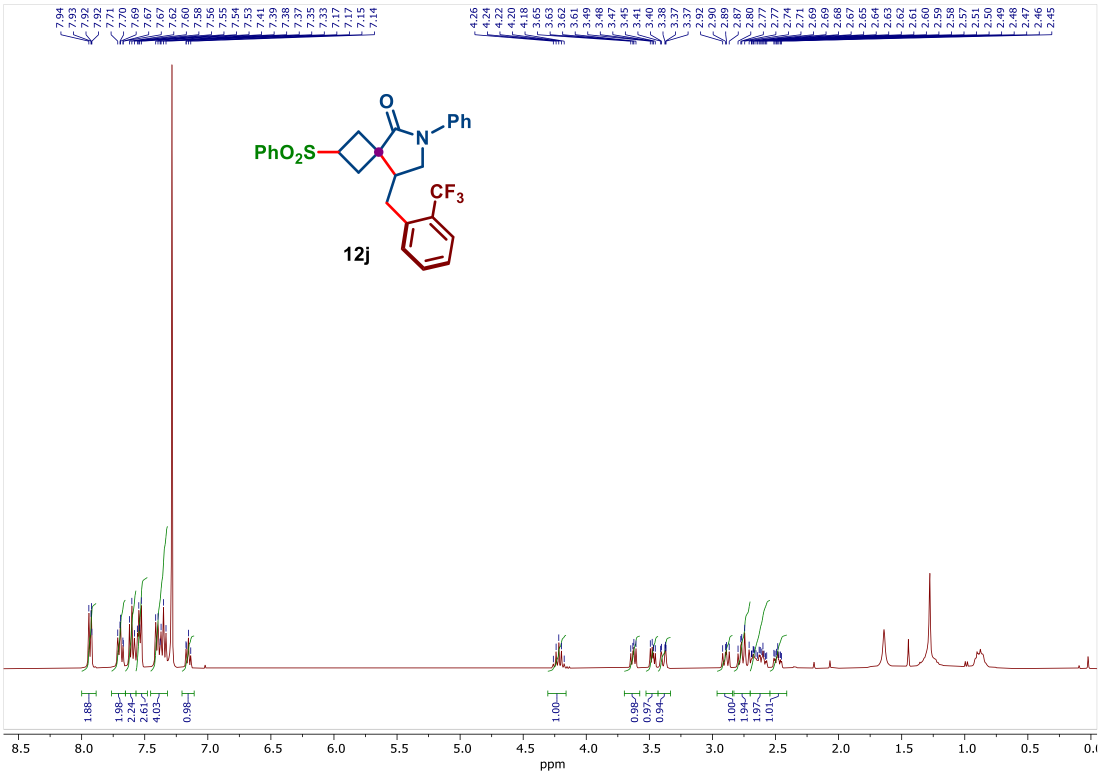
^{13}C NMR (101 MHz, $CDCl_3$) spectra of compound **12j (major)**



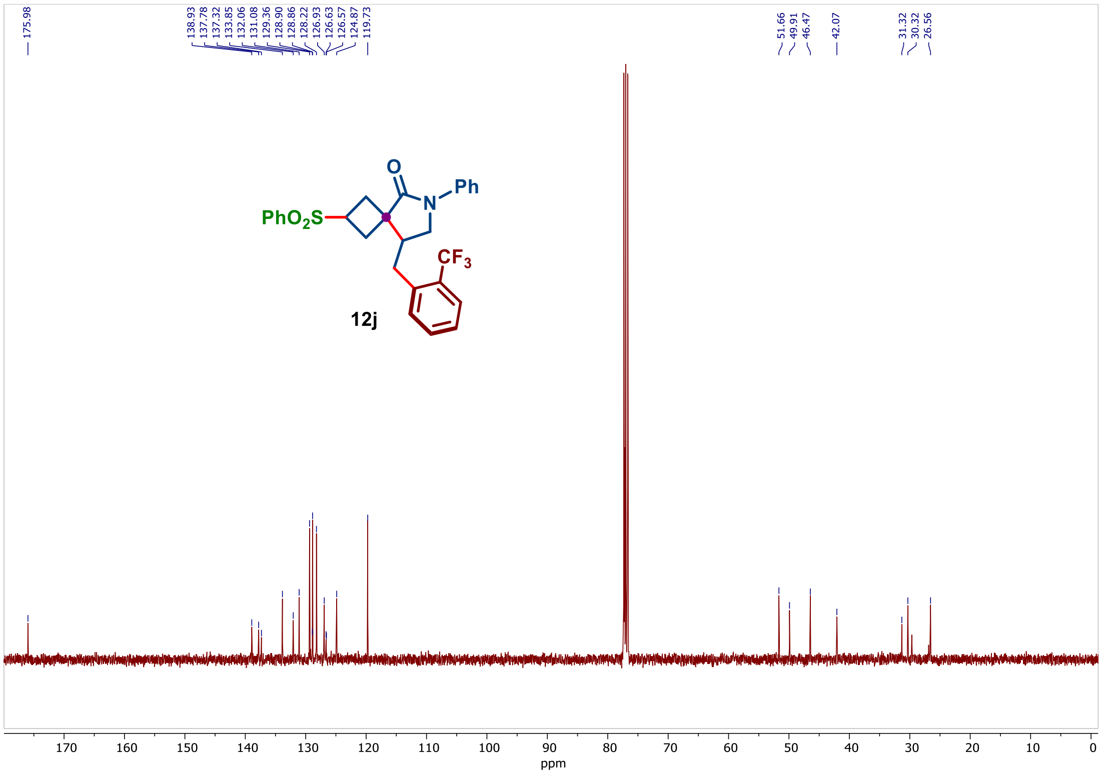
^{19}F NMR (377 MHz, $CDCl_3$) spectra of compound **12j (major)**



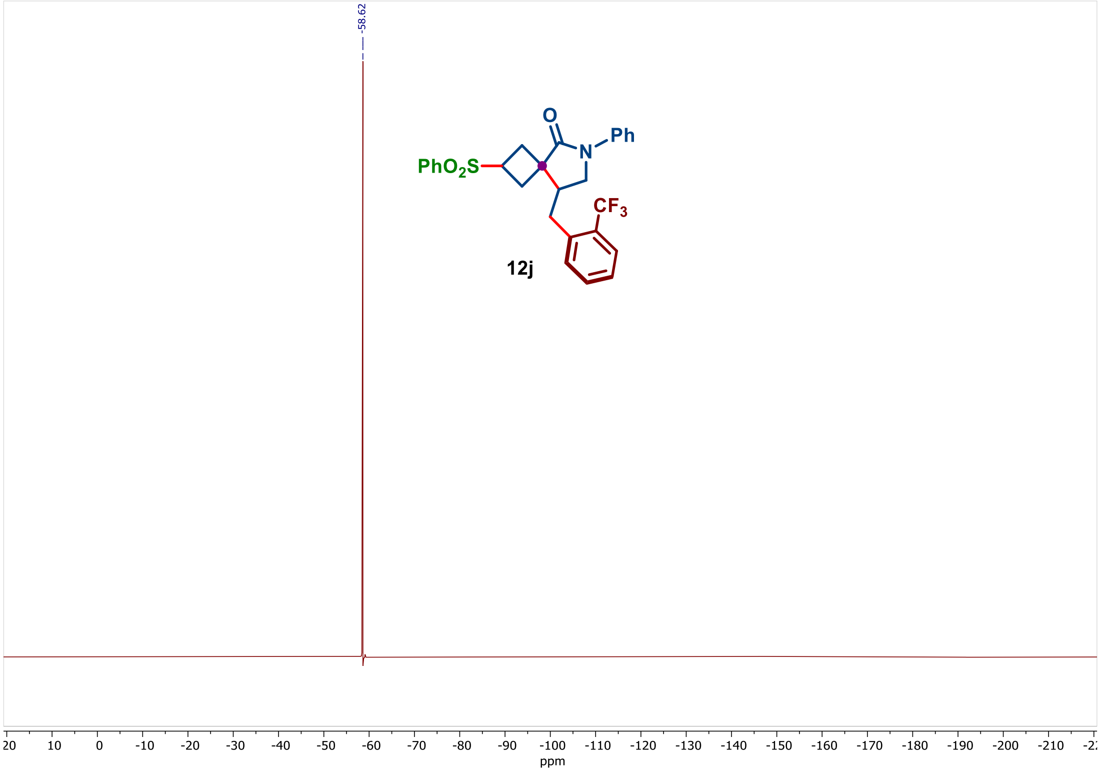
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **12j (minor)**



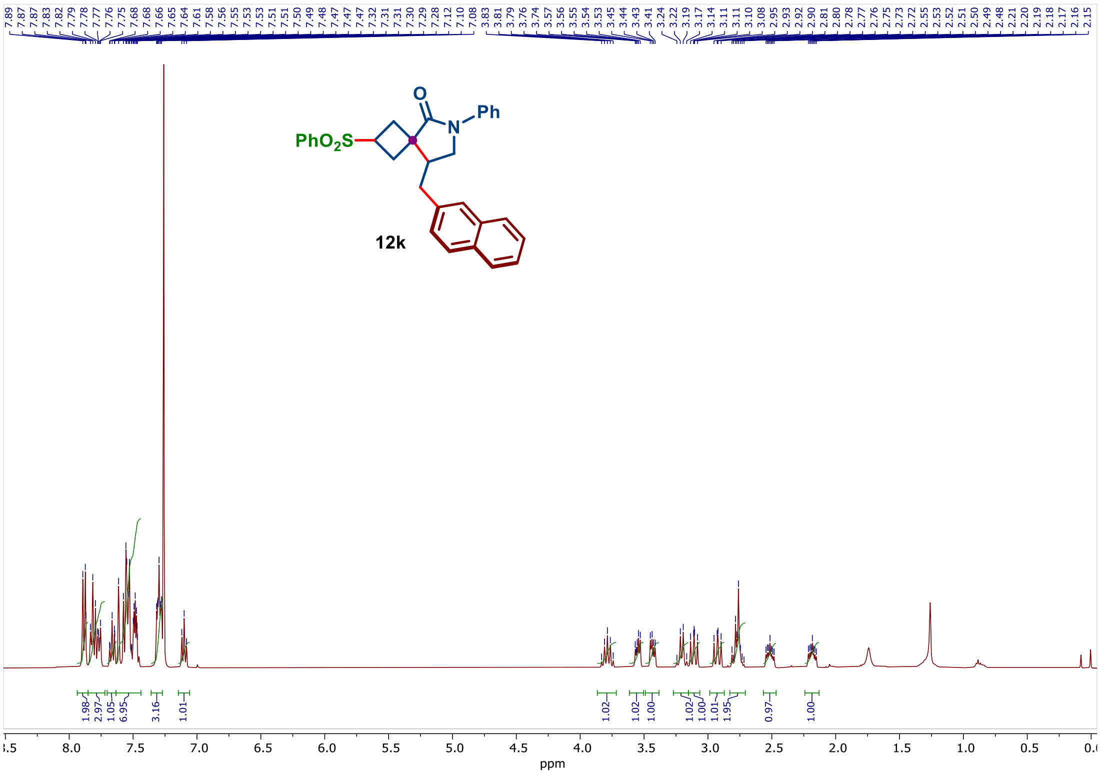
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **12j (minor)**



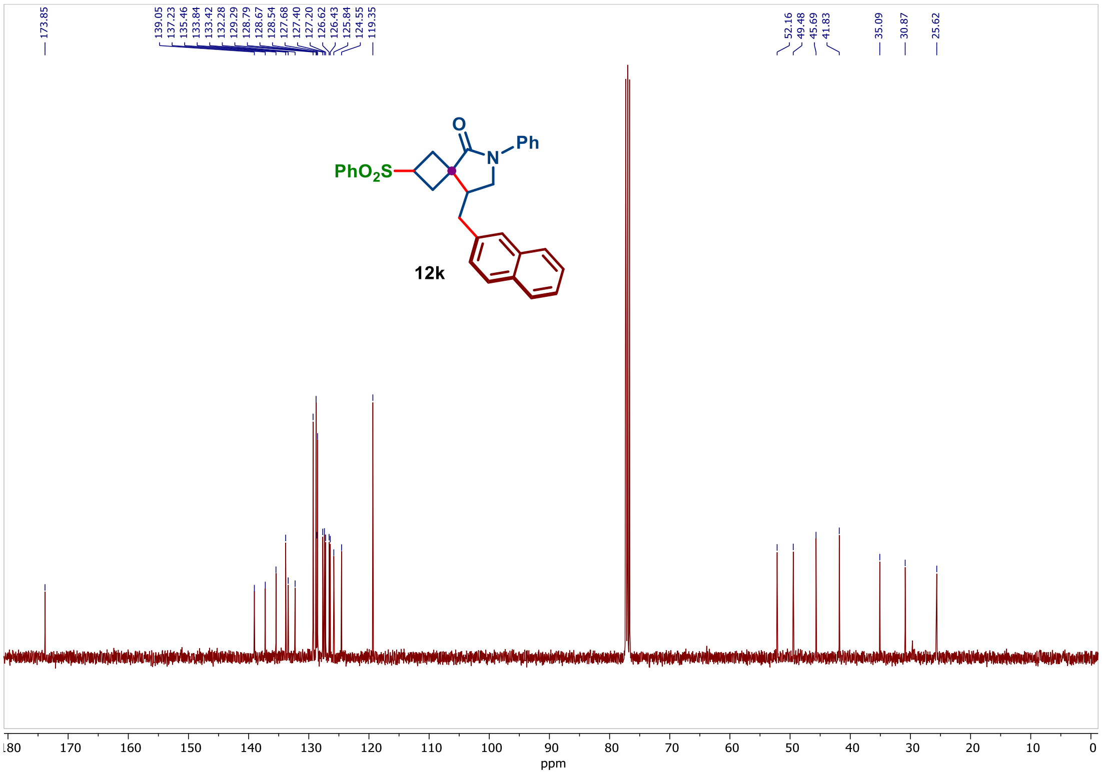
^{19}F NMR (377 MHz, CDCl$_3$) spectra of compound **12j (minor)**



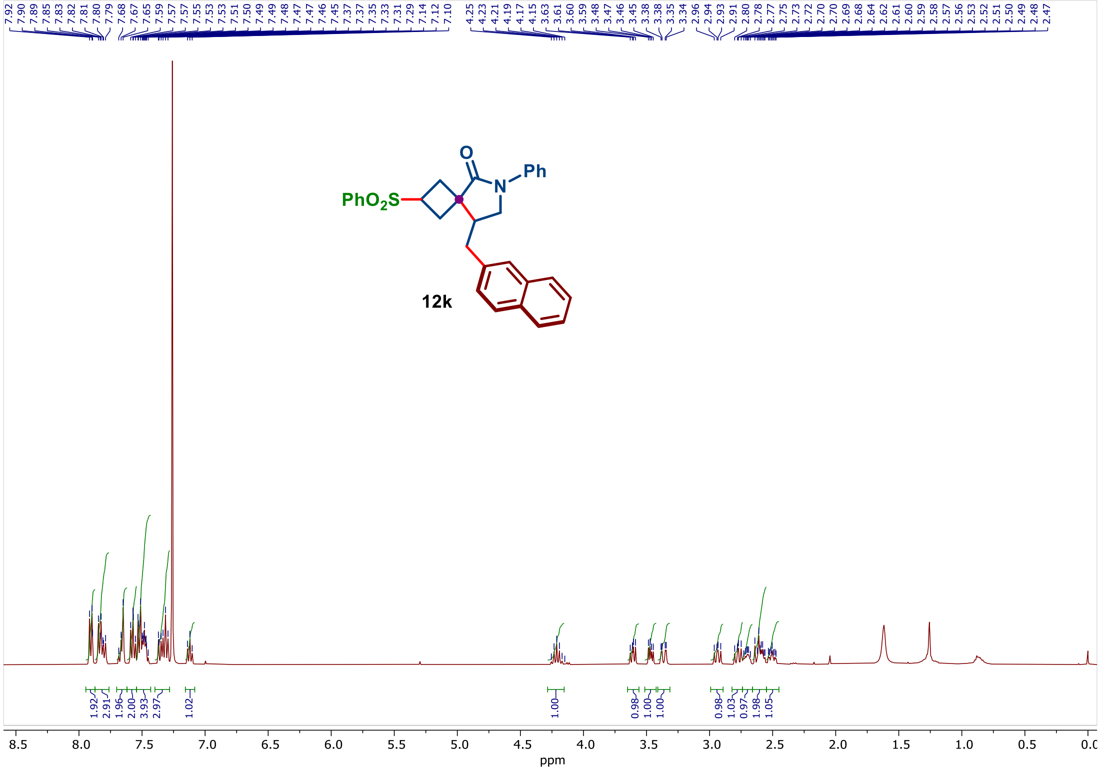
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **12k (major)** (See Procedure)



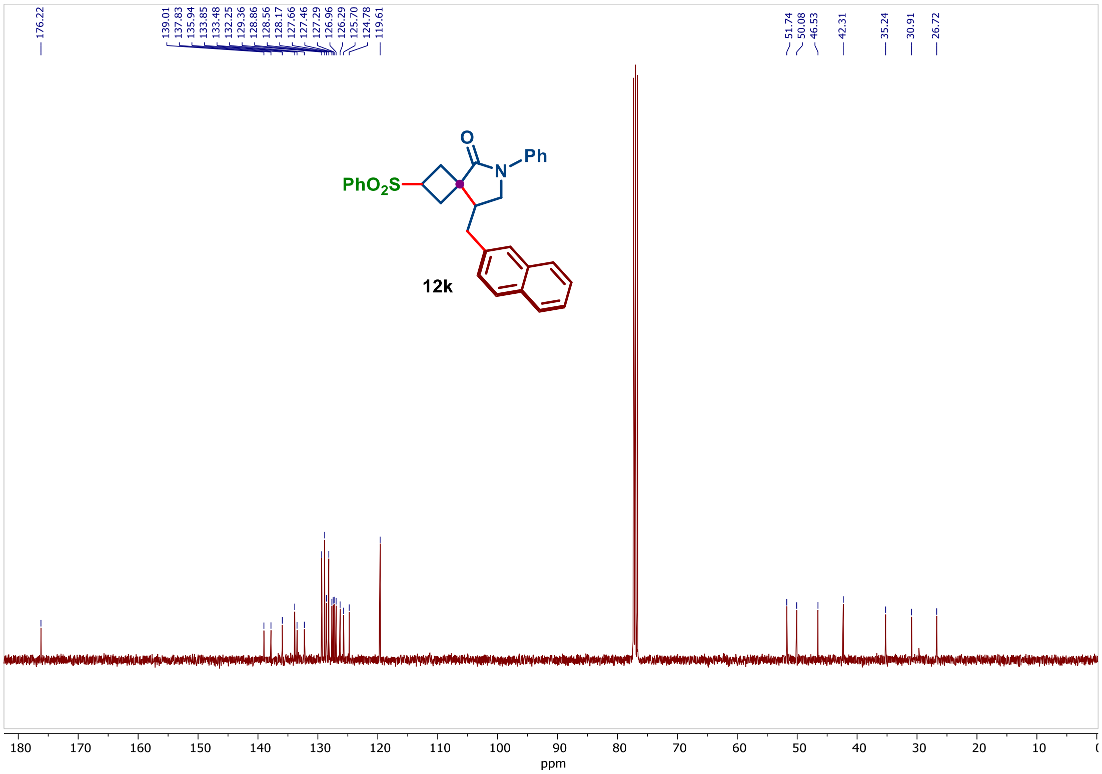
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **12k (major)**



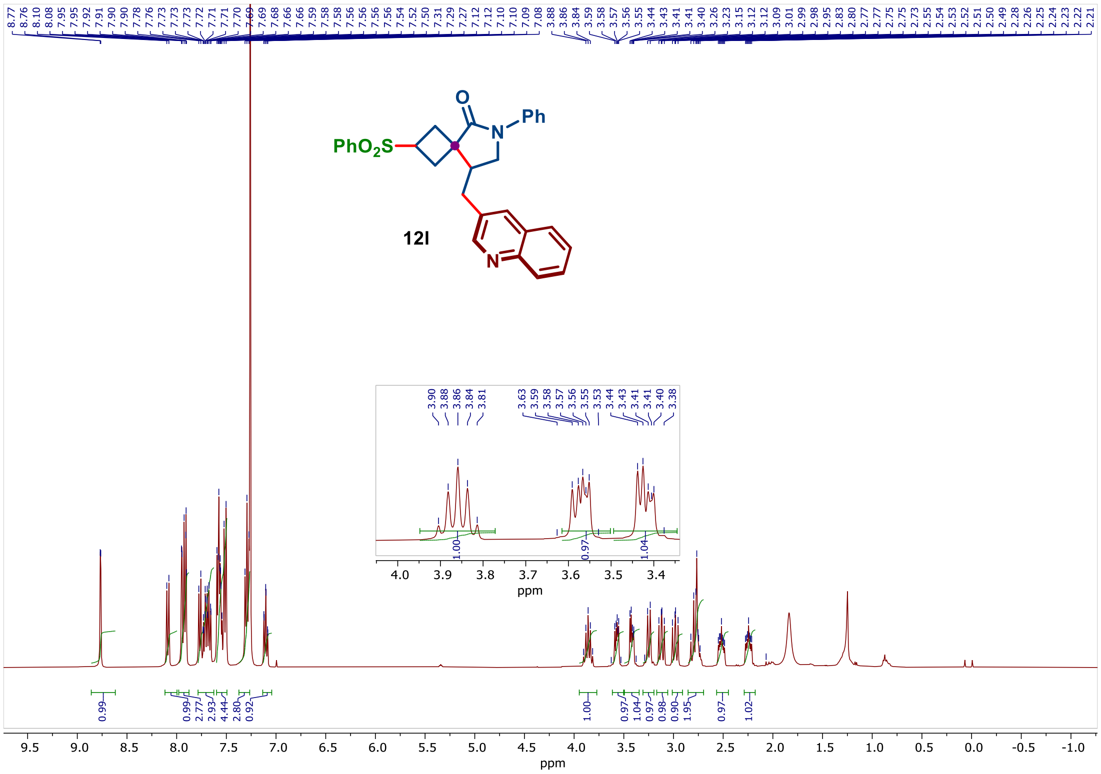
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **12k (minor)**



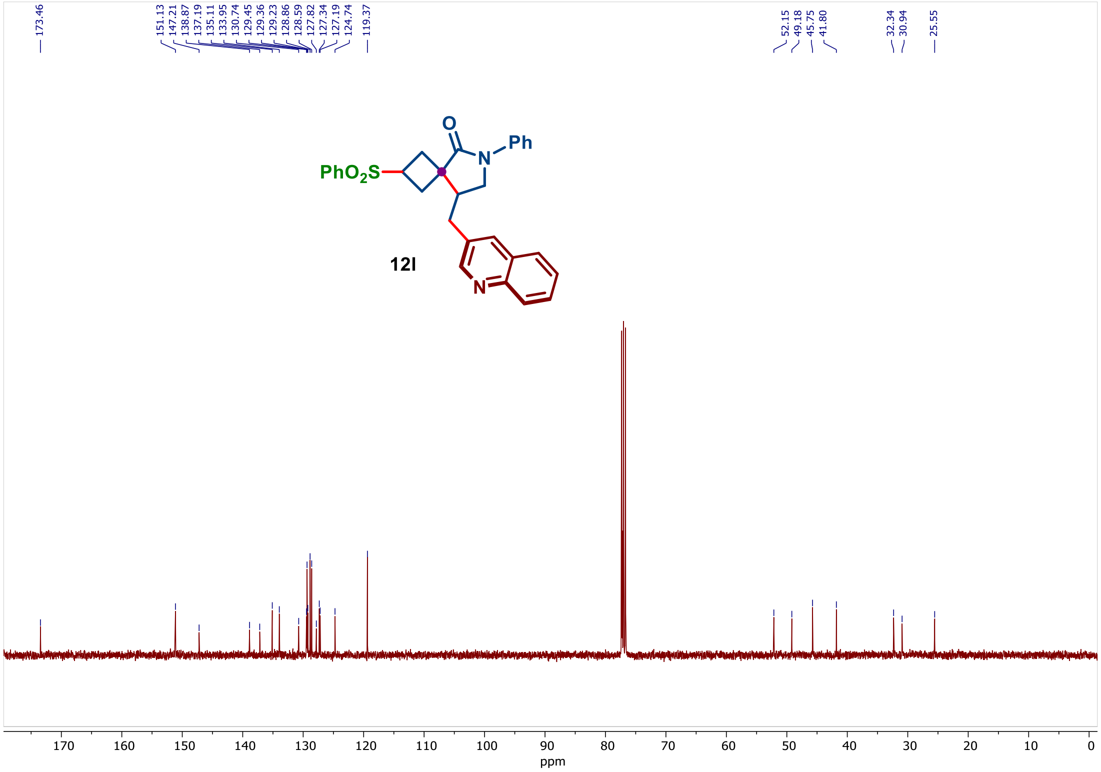
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **12k (minor)**



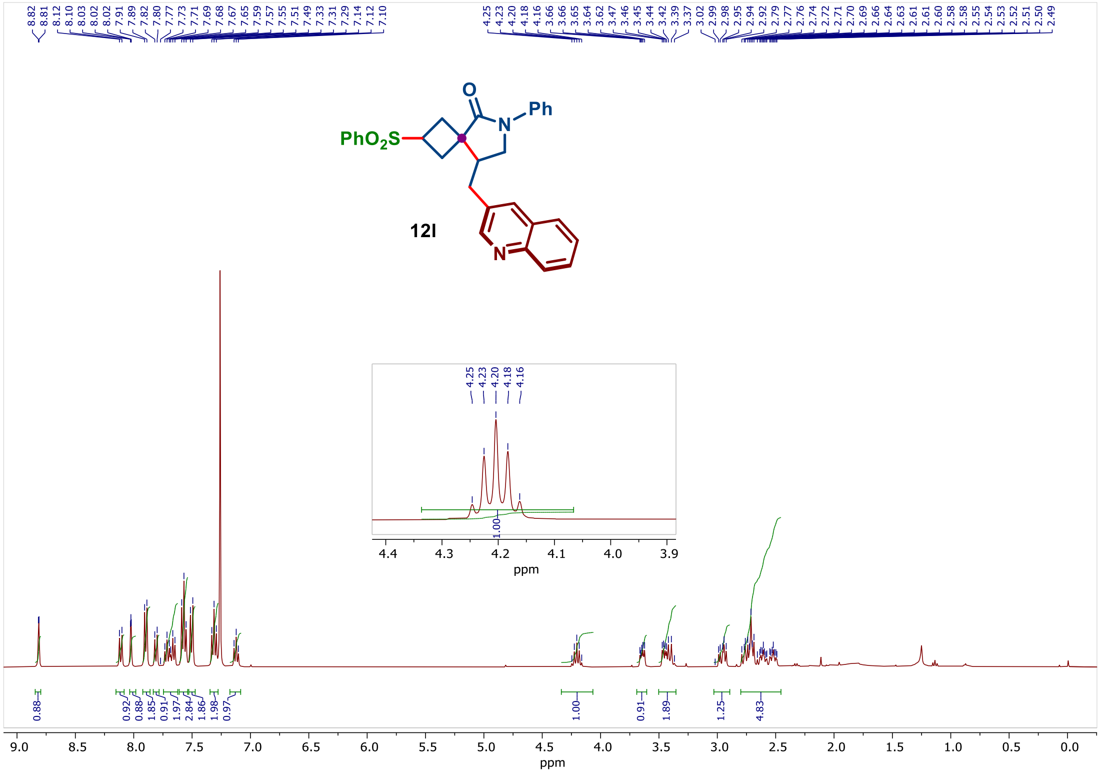
^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **12l (major)** (See Procedure)



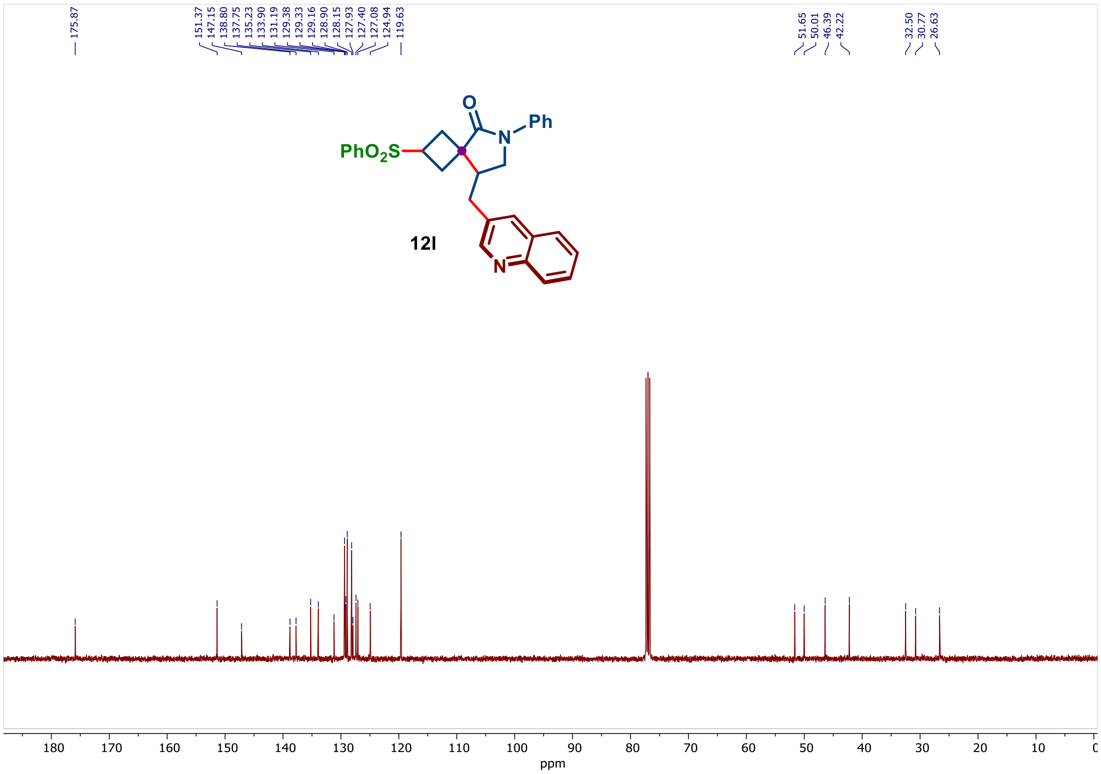
^{13}C NMR (101 MHz, $CDCl_3$) spectra of compound **12l (major)**



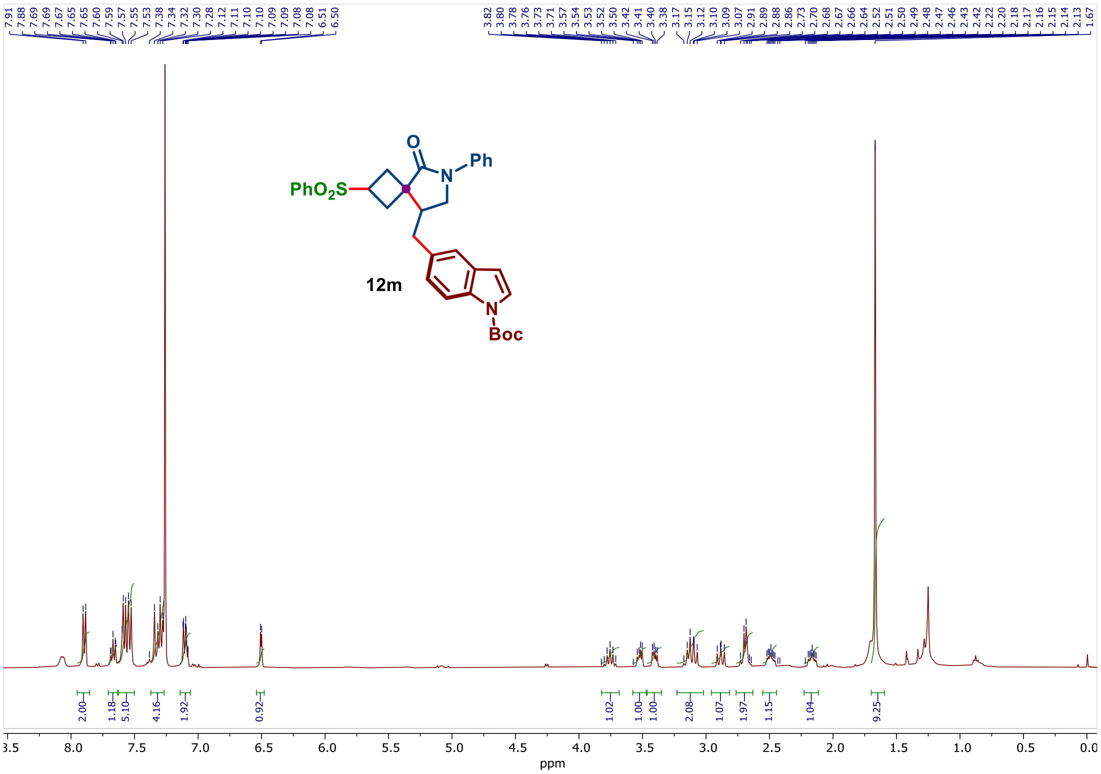
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **12l (minor)**



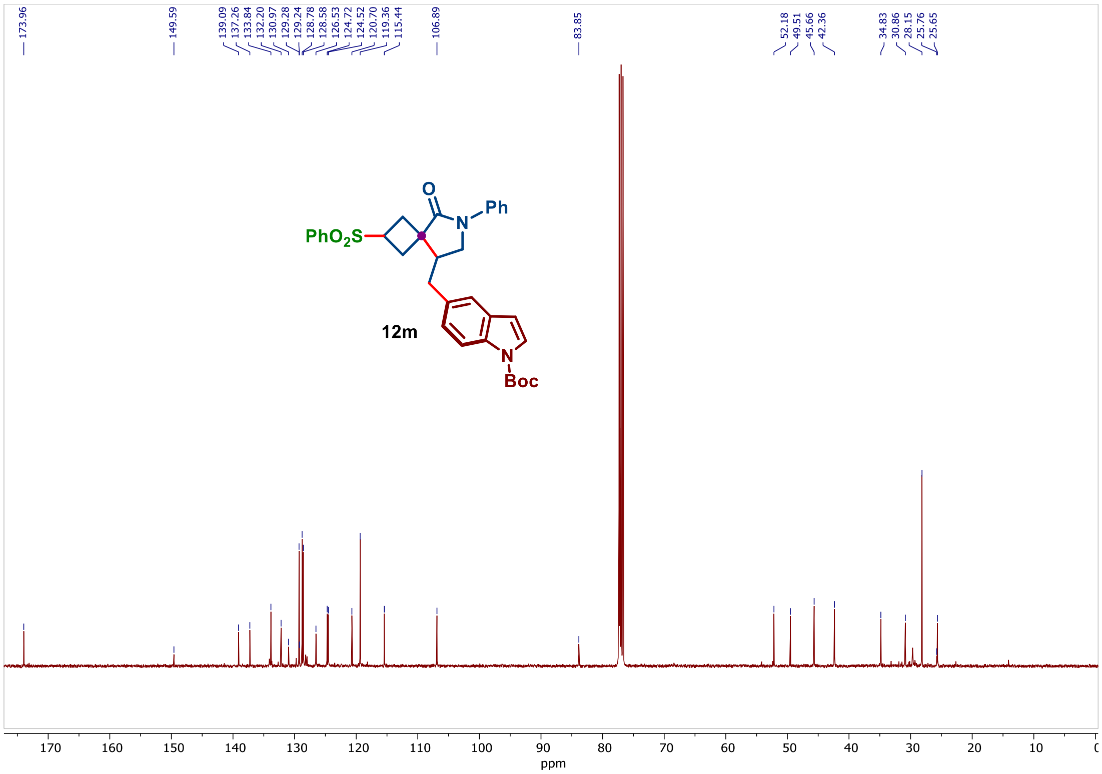
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **12l (minor)**



^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **12m (major)** (See Procedure)



^{13}C NMR (101 MHz, $CDCl_3$) spectra of compound **12m (major)**



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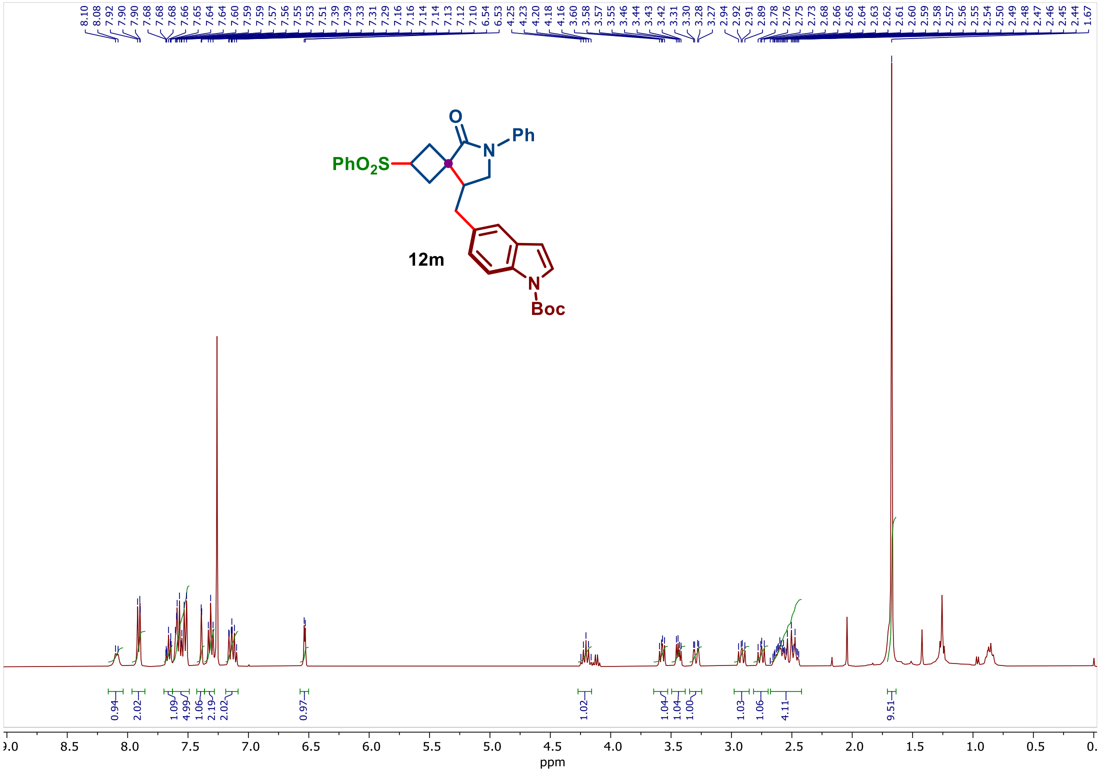
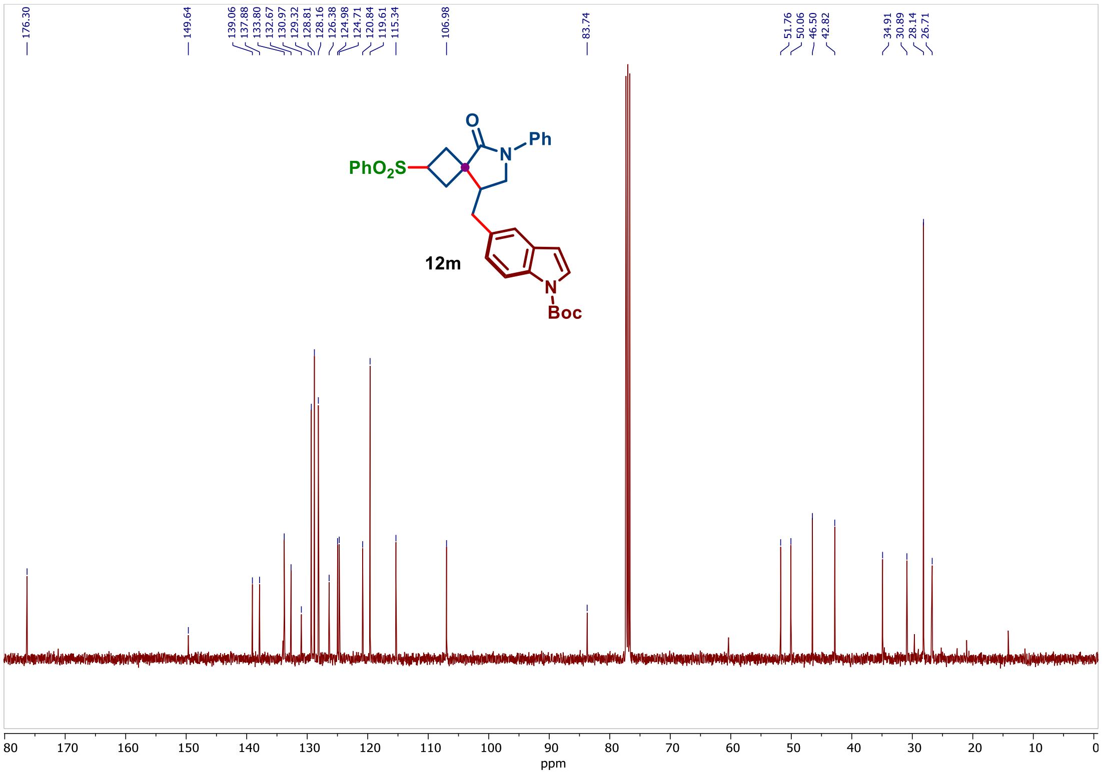
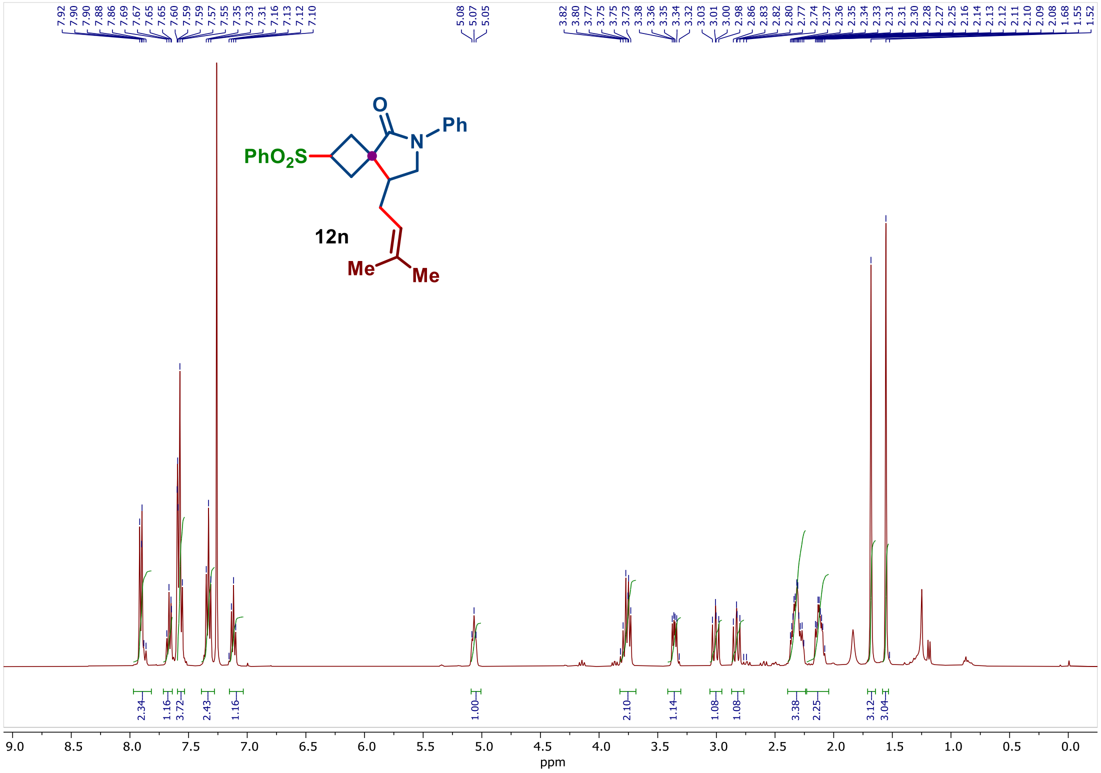


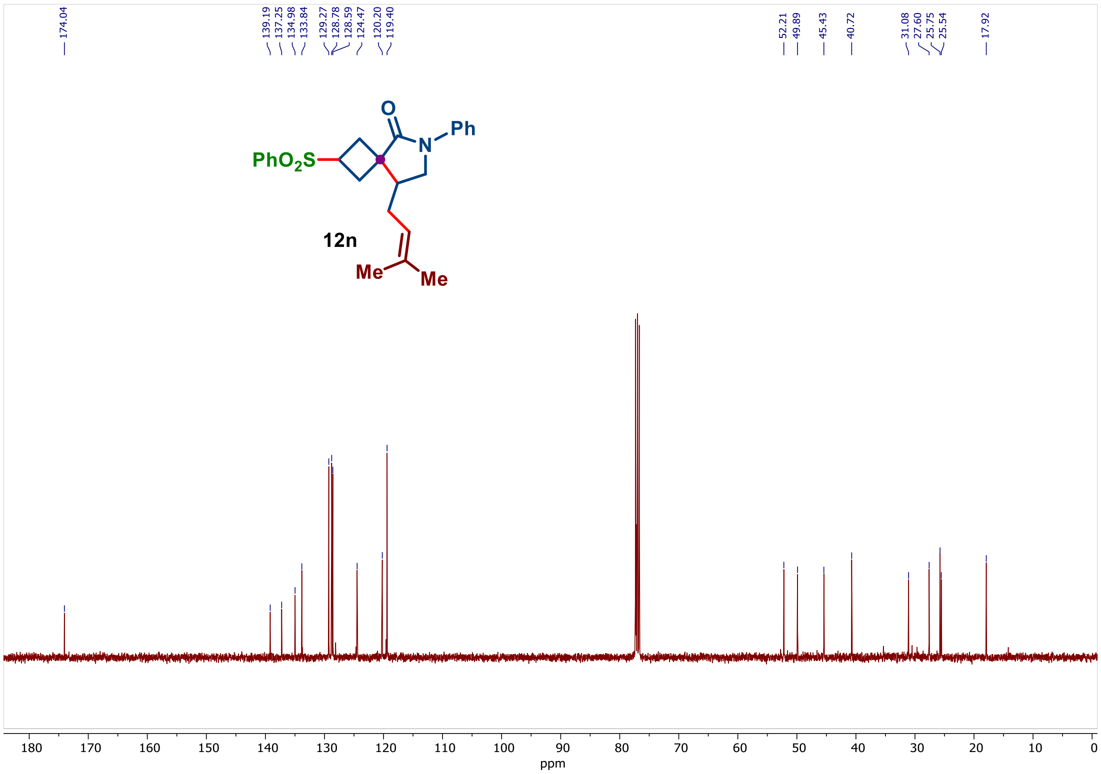
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **12m (minor)**



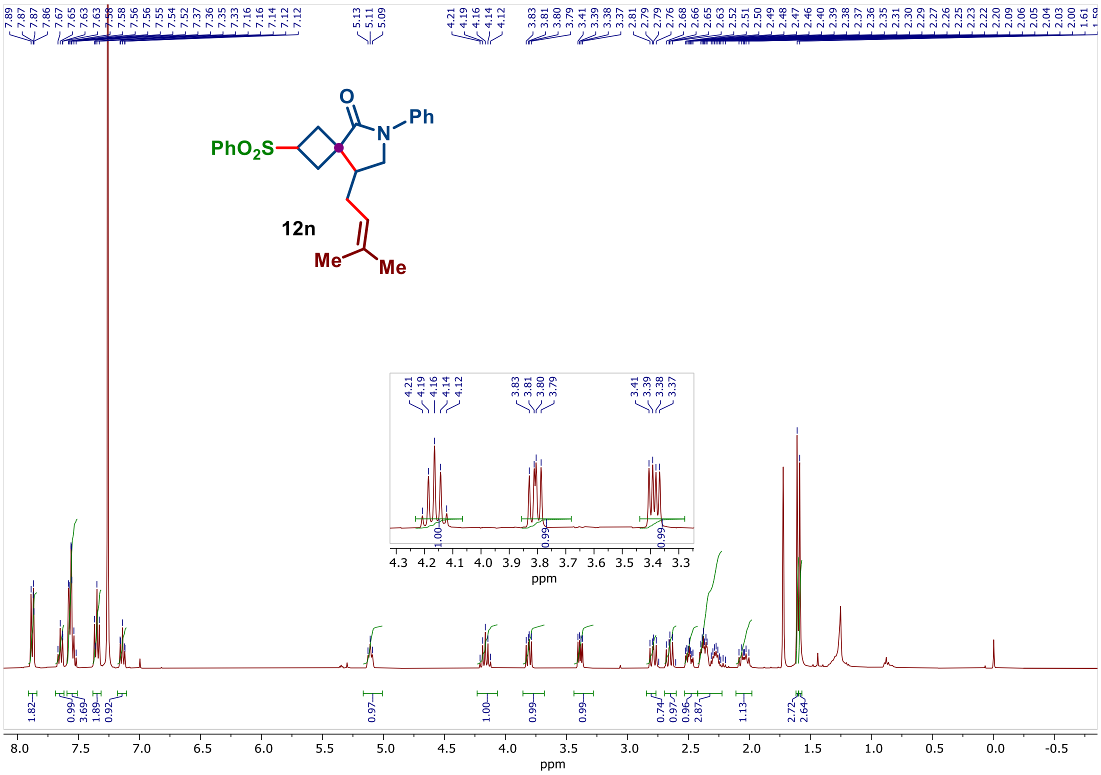
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **12n (major)** **(See Procedure)**



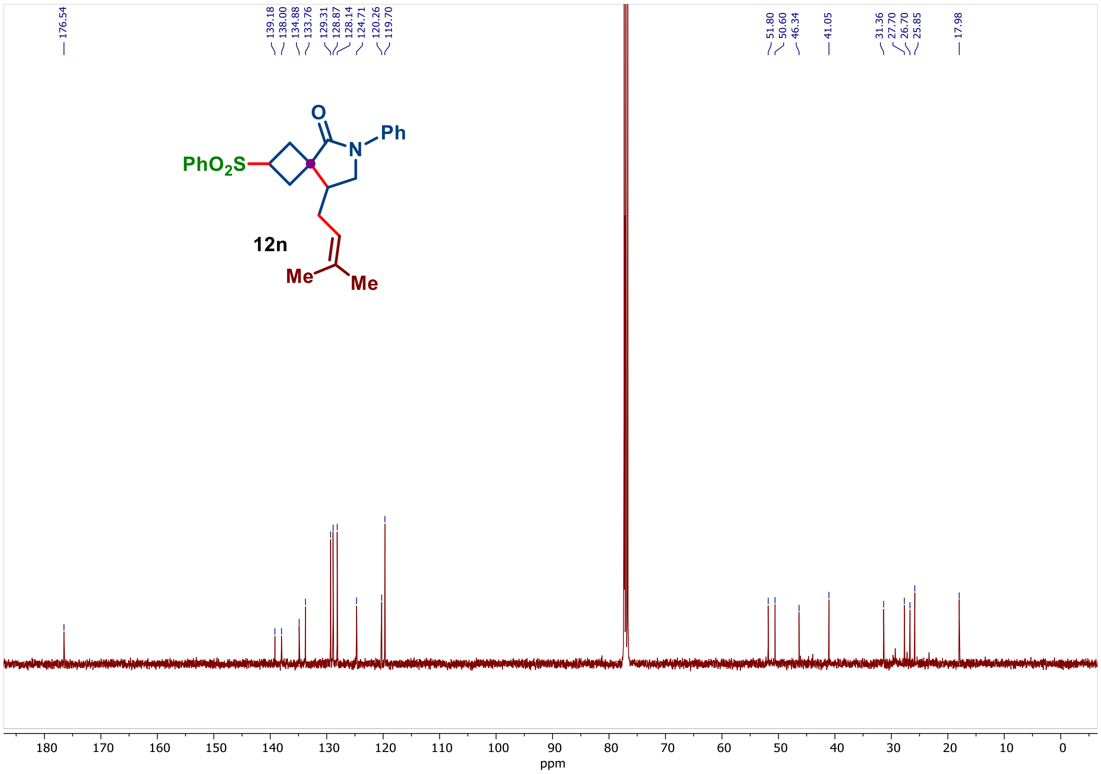
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **12n (major)**



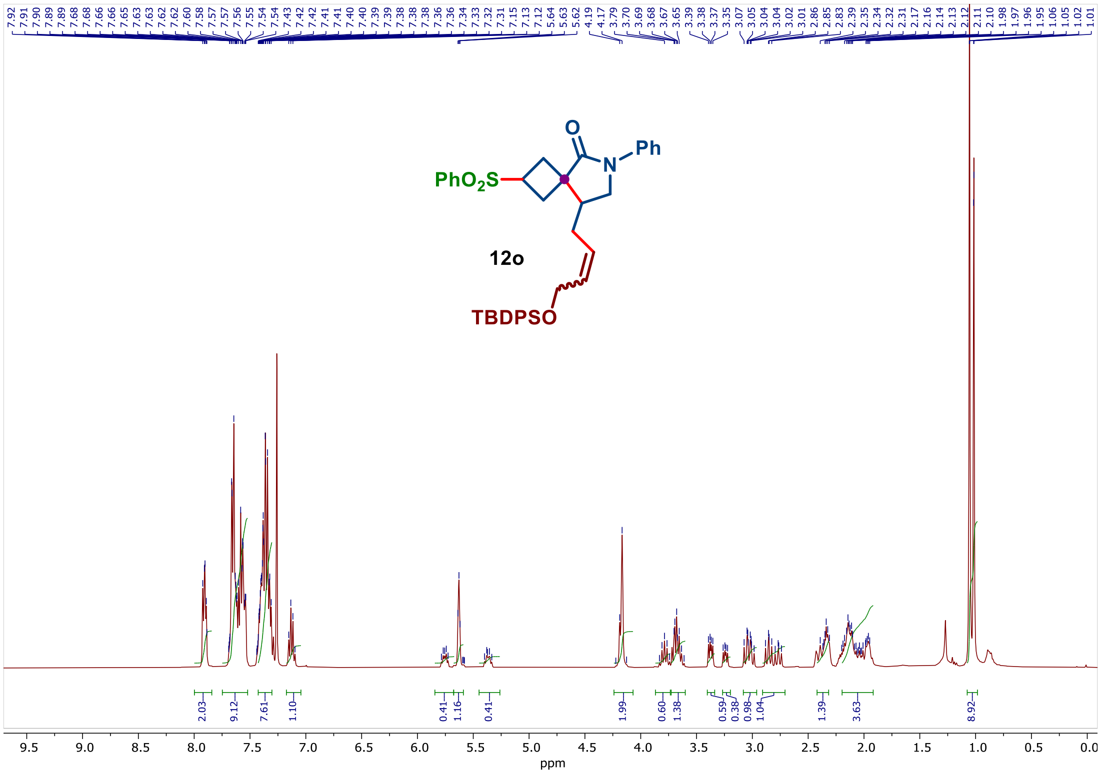
^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **12n (minor)**



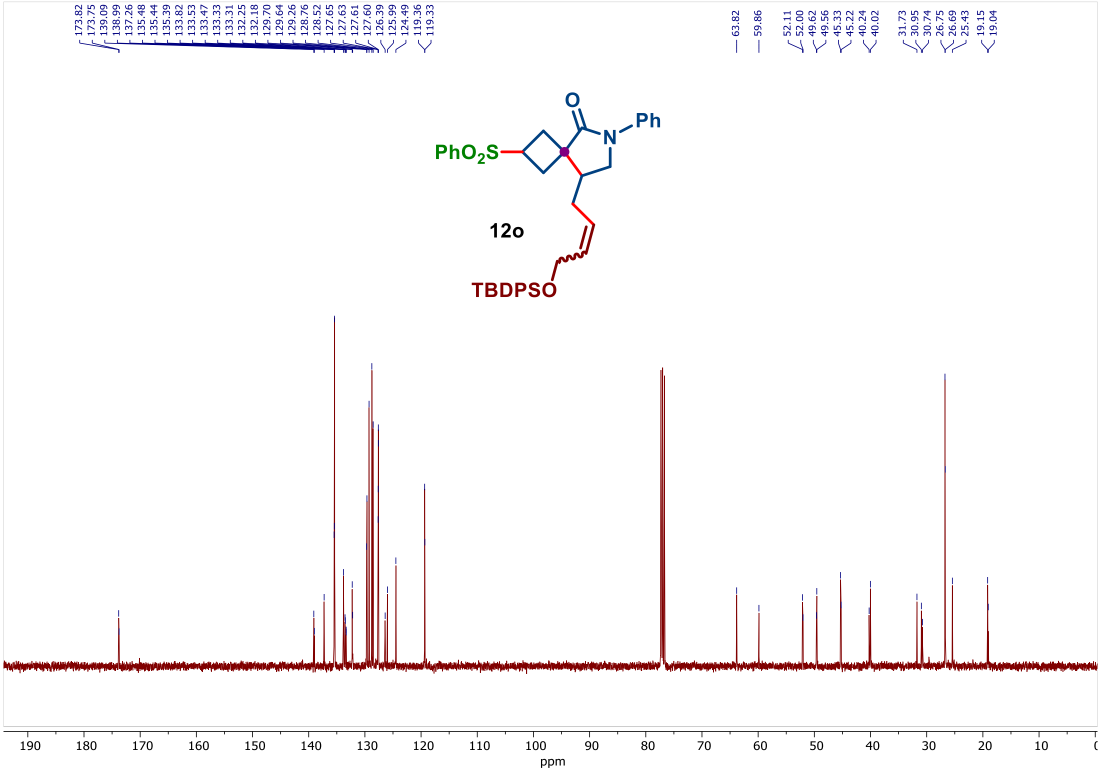
^{13}C NMR (101 MHz, $CDCl_3$) spectra of compound **12n (minor)**



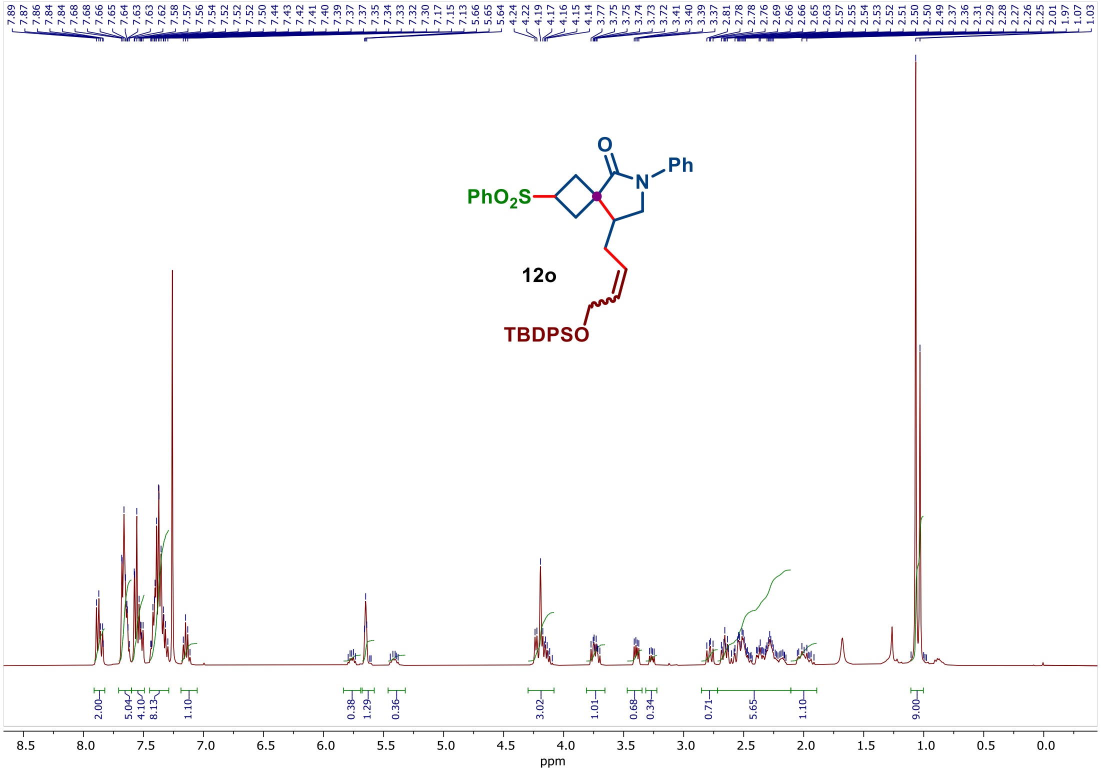
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **12o (major)** (See Procedure)



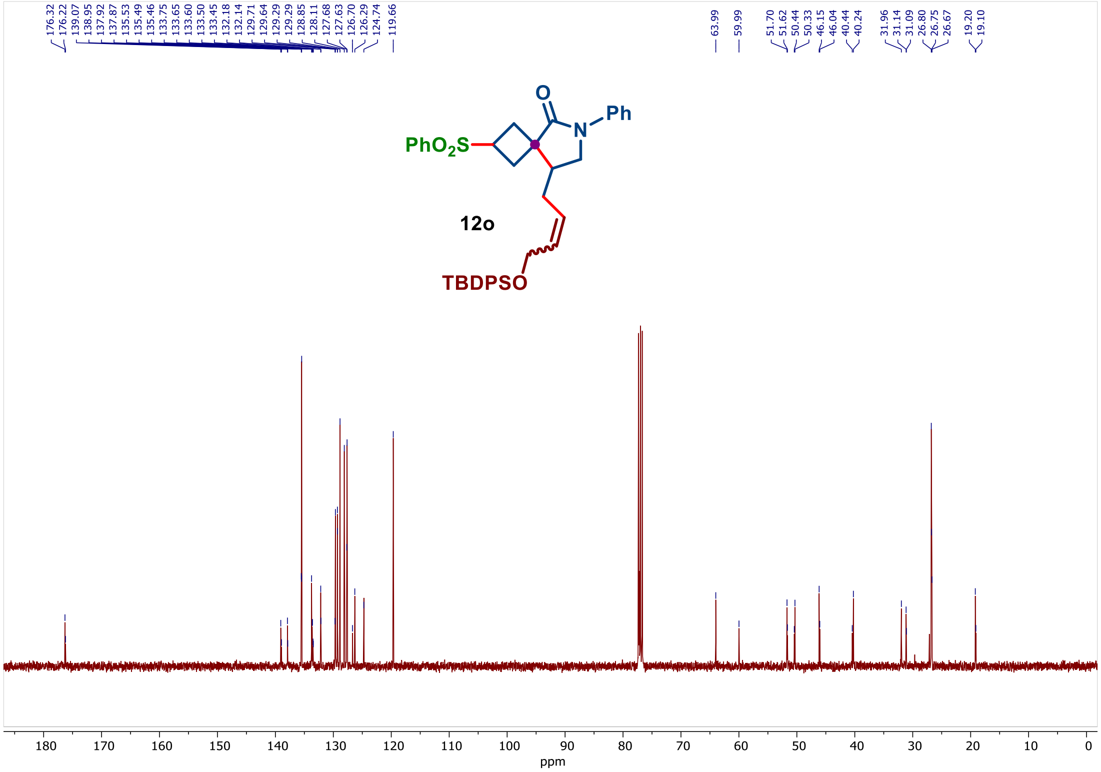
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **12o (major)**



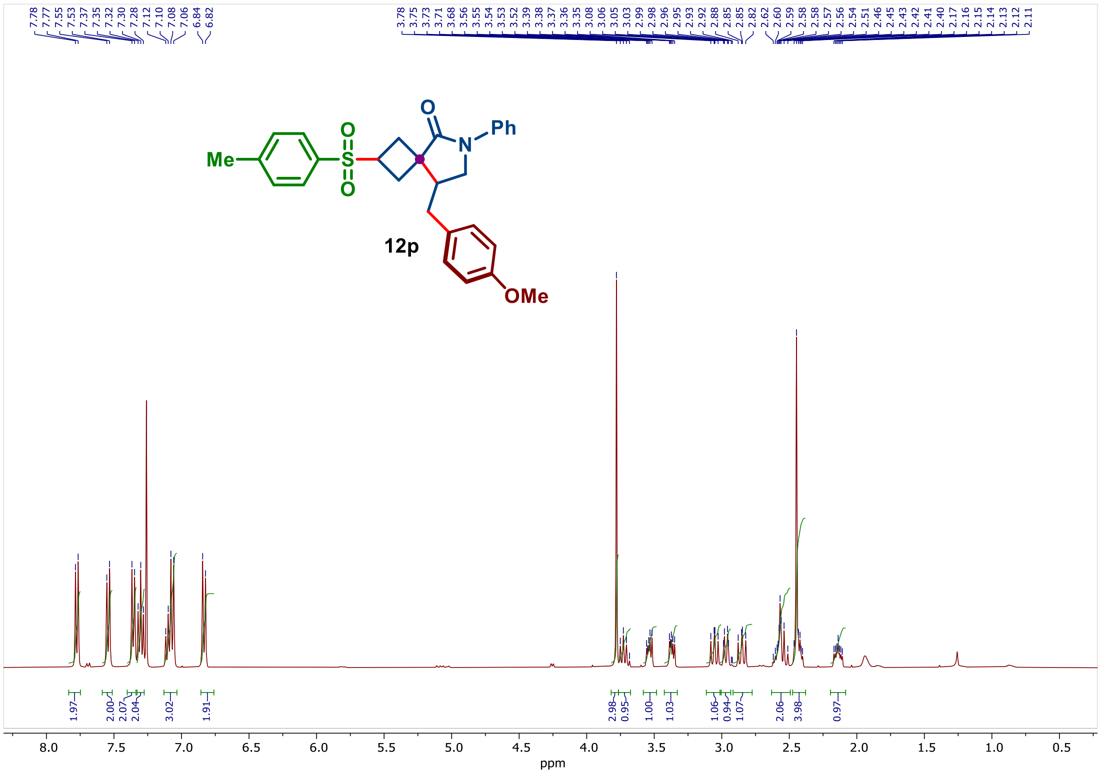
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **12o (minor)**



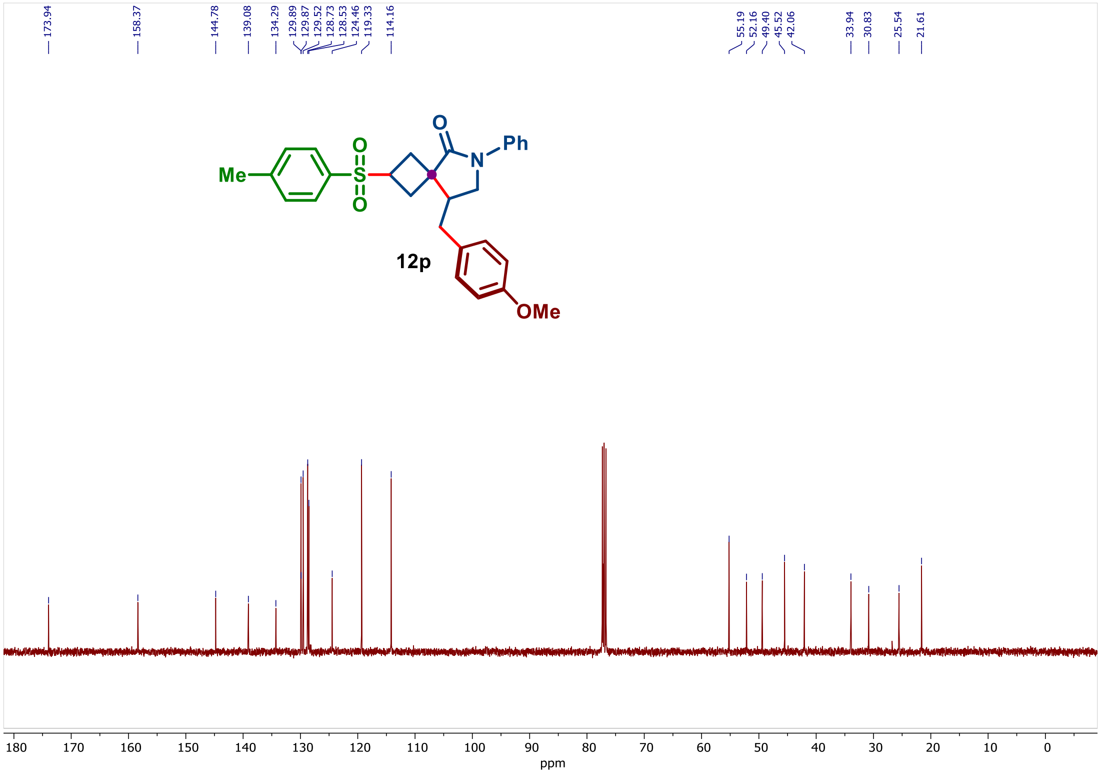
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **12o (minor)**



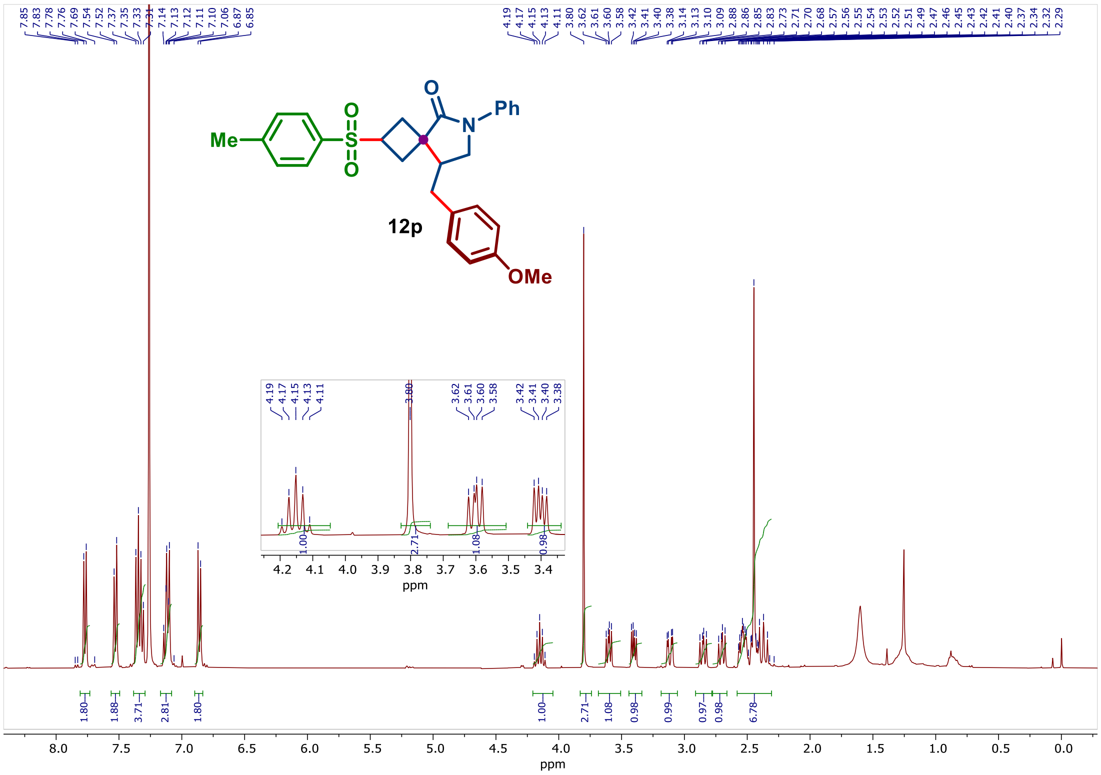
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **12p (major)** (See Procedure)



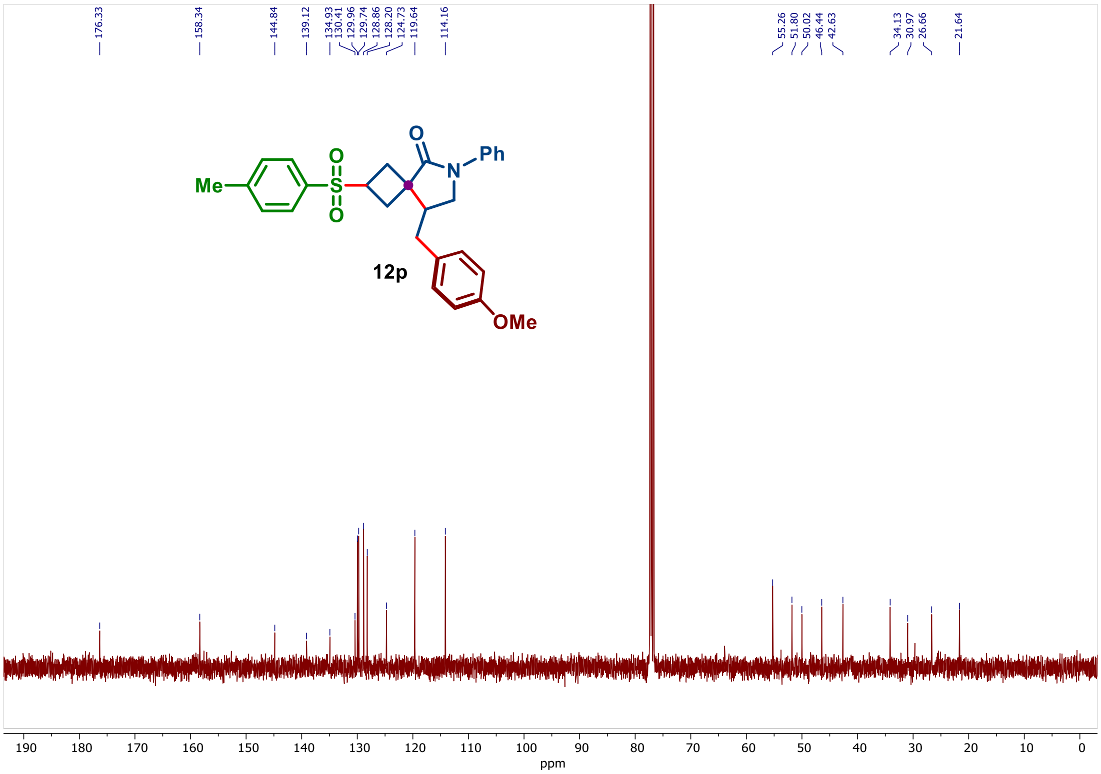
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **12p (major)**



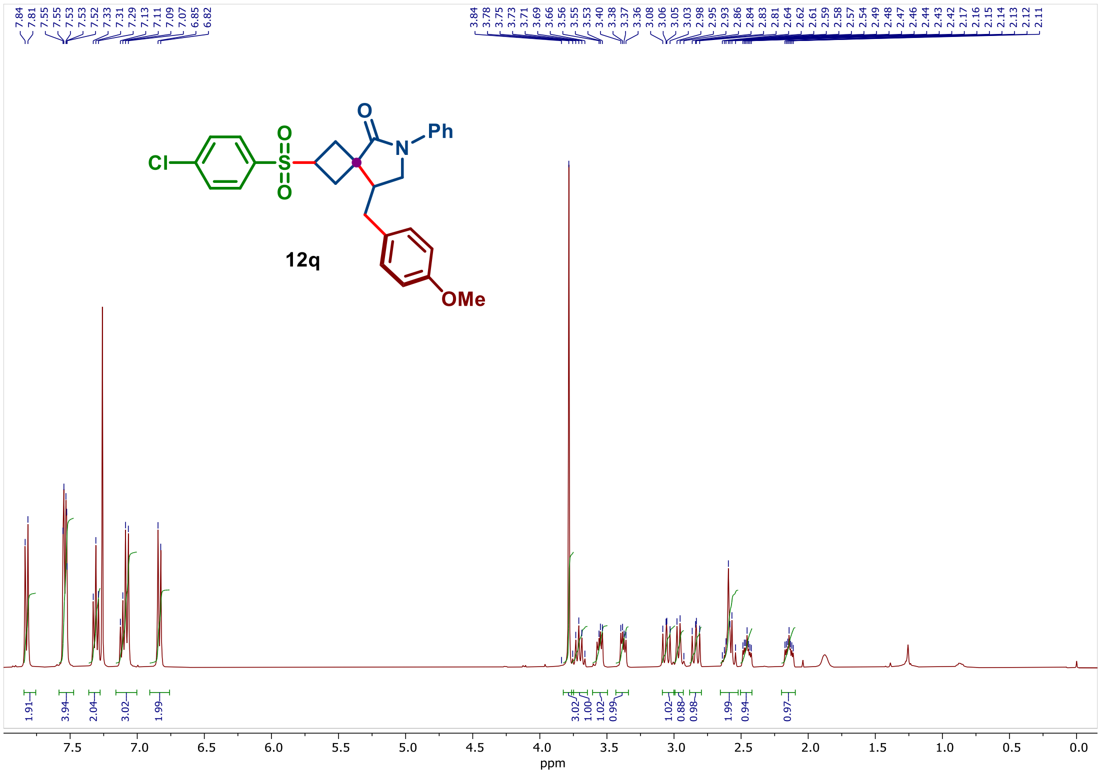
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **12p (minor)**



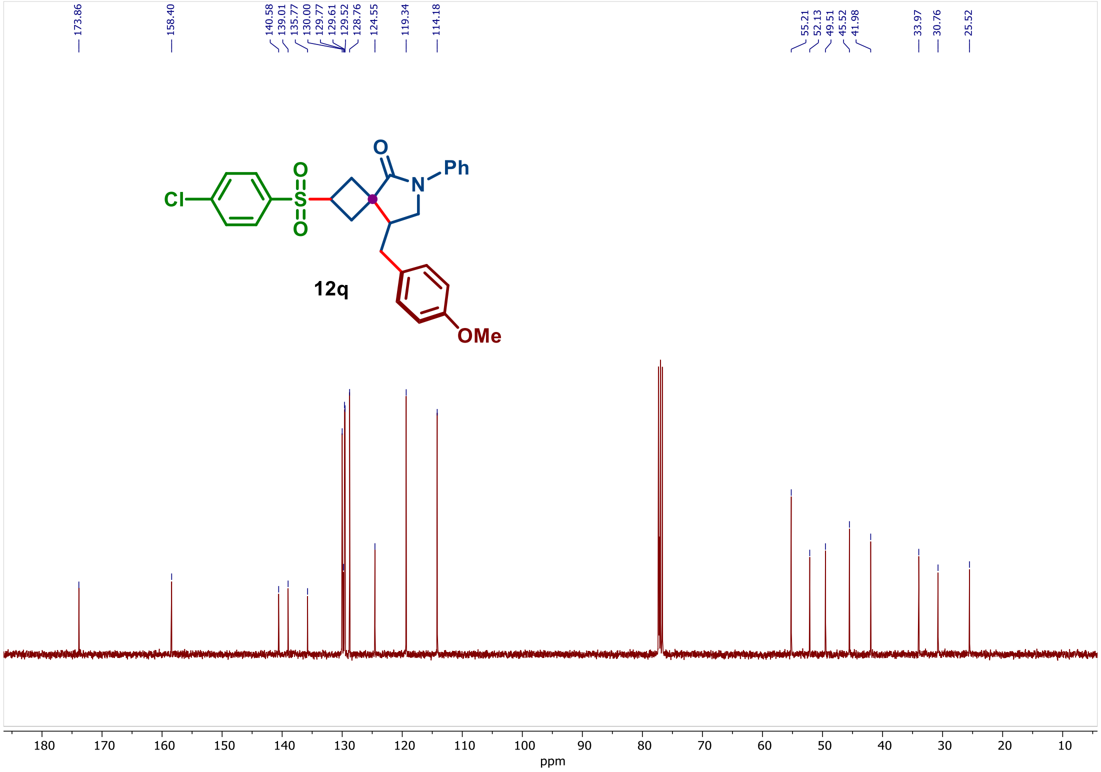
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **12p (minor)**



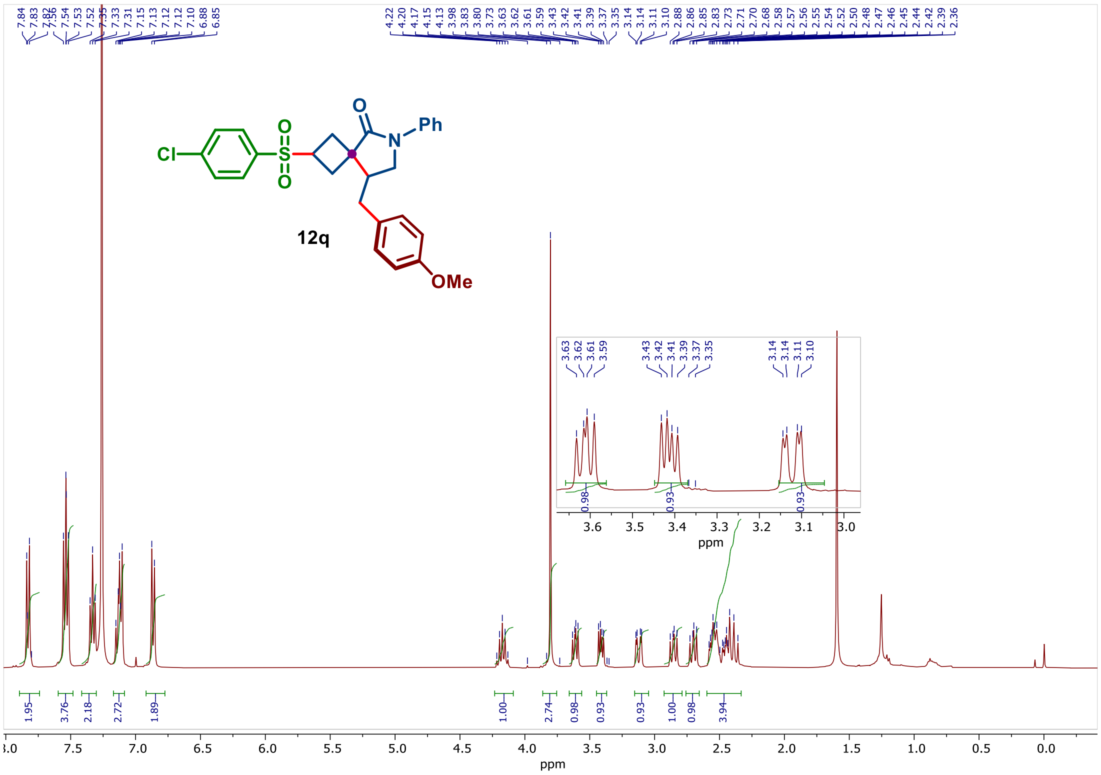
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **12q (major)** (See Procedure)



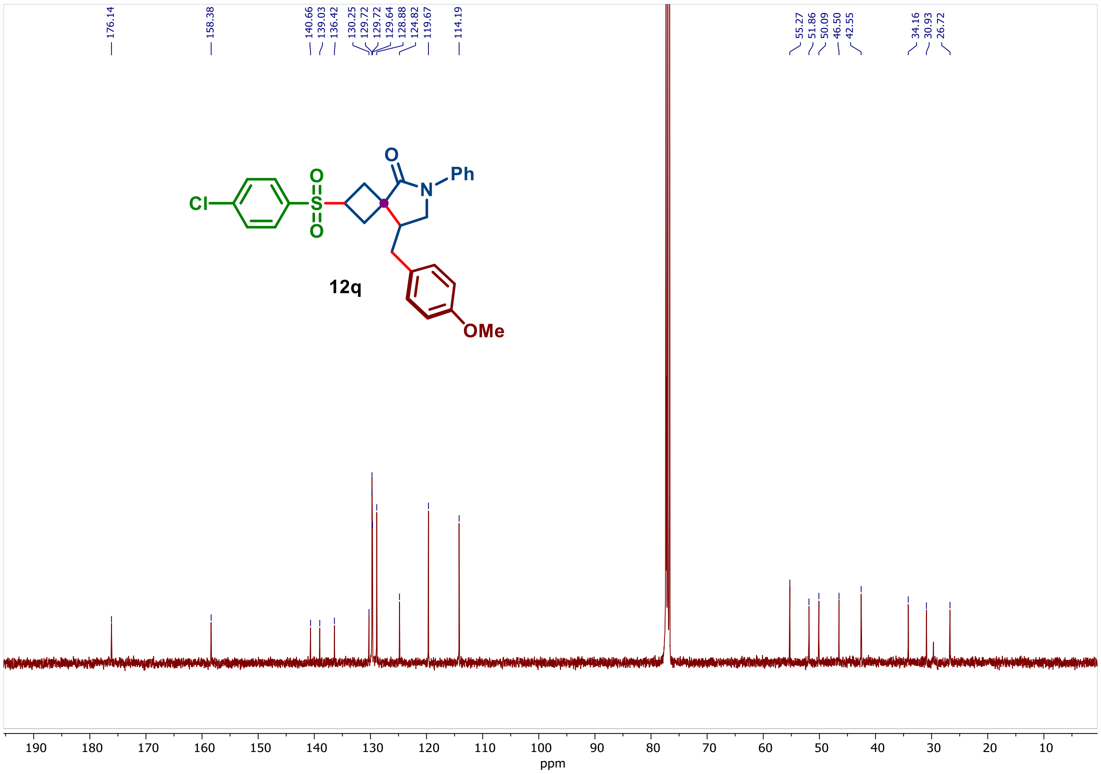
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **12q (major)**



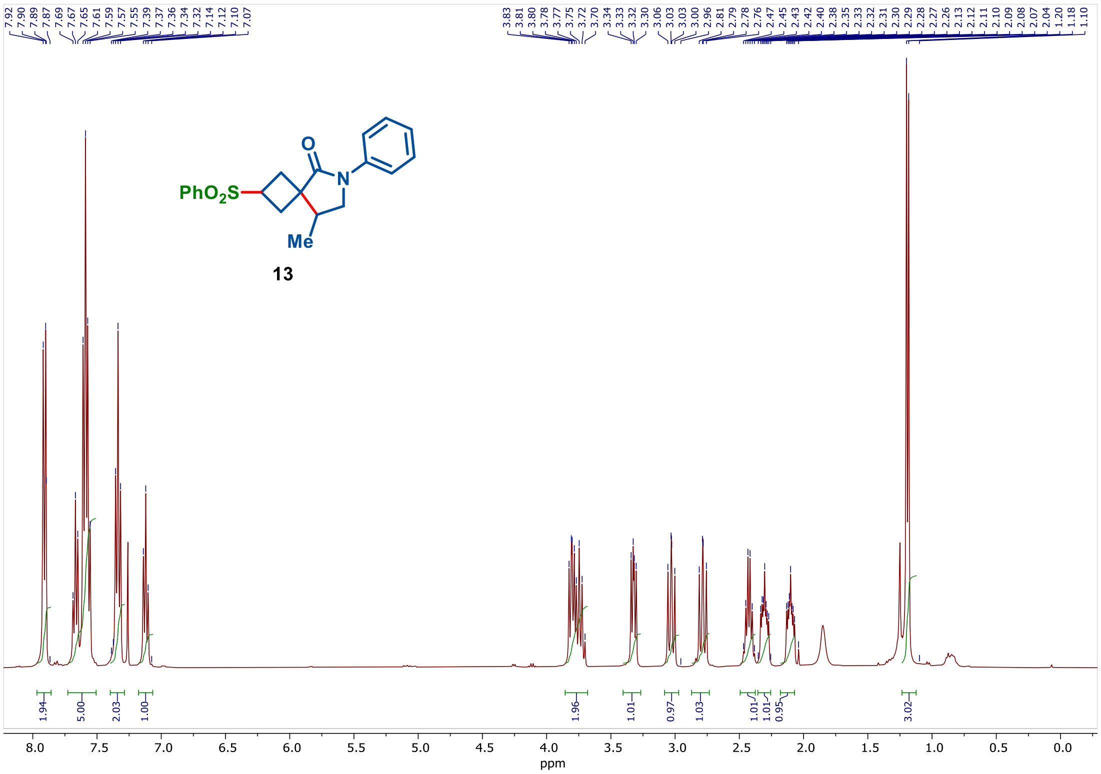
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **12q (minor) (See Procedure)**



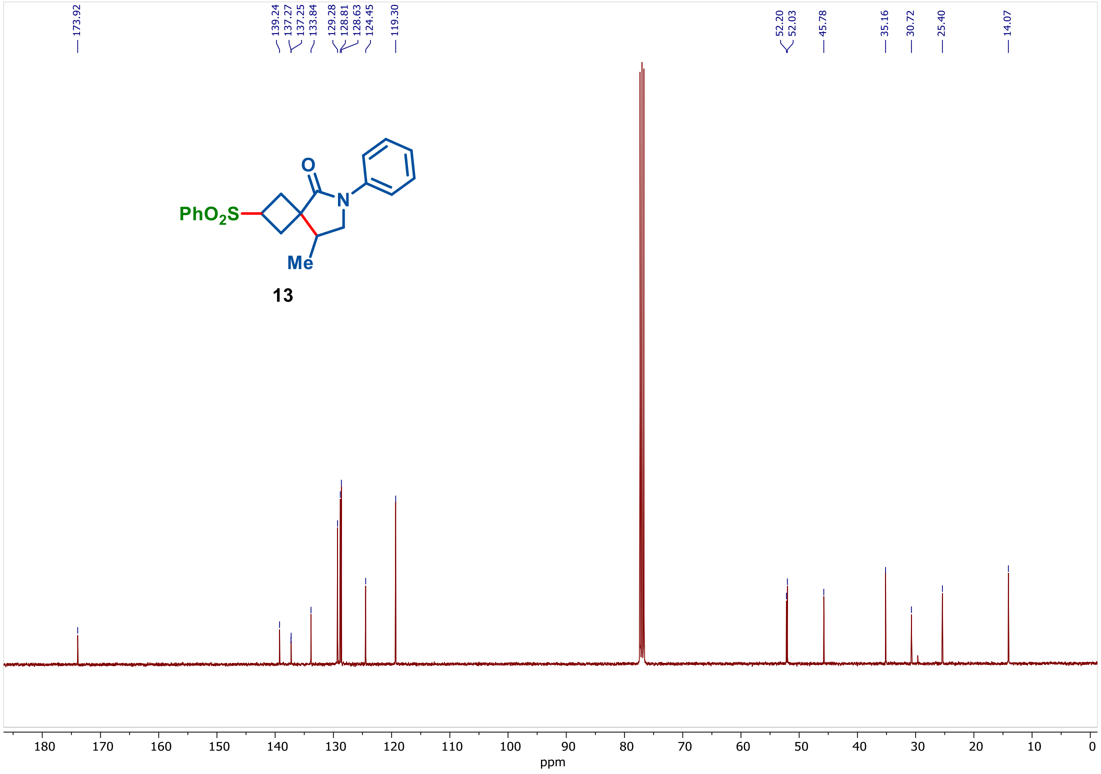
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **12q (minor)**



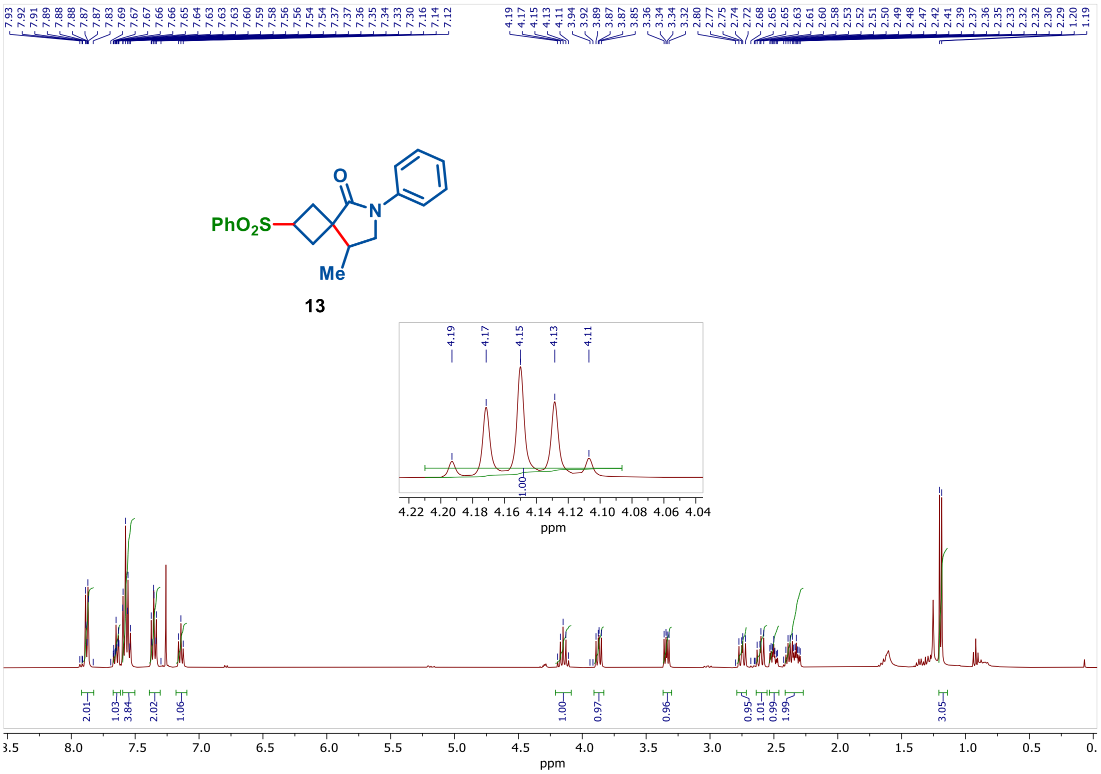
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **13 (major)** (**See Procedure**)



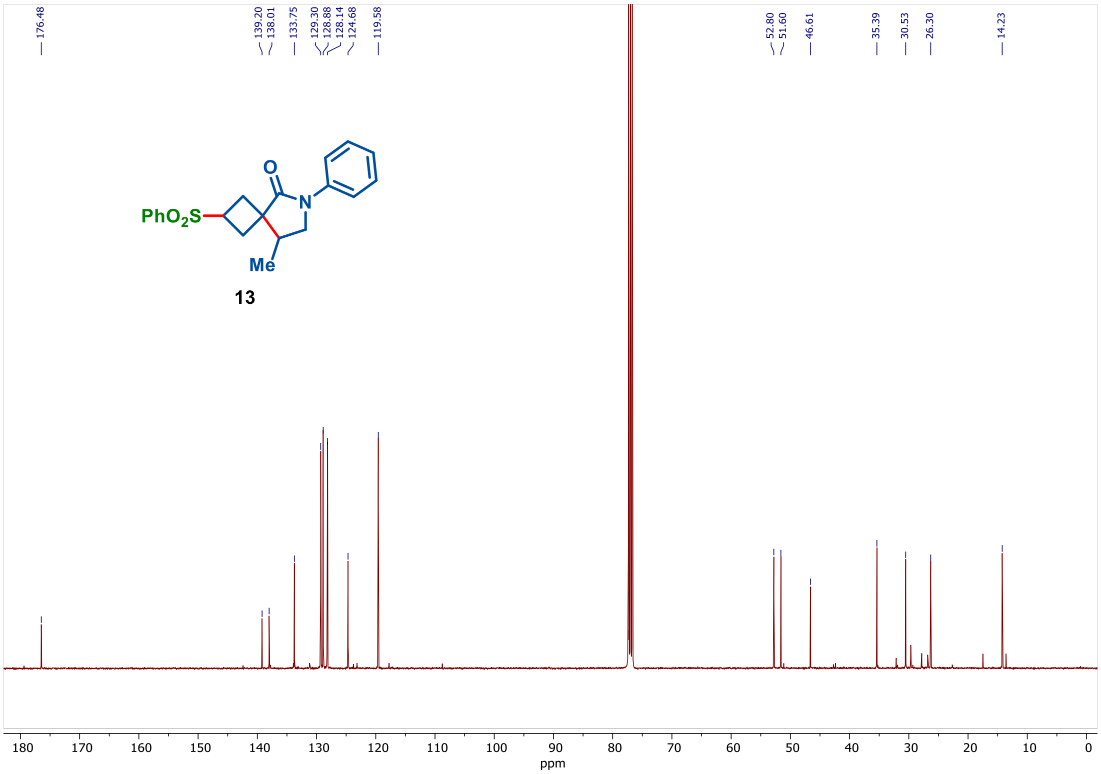
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **13 (major)**



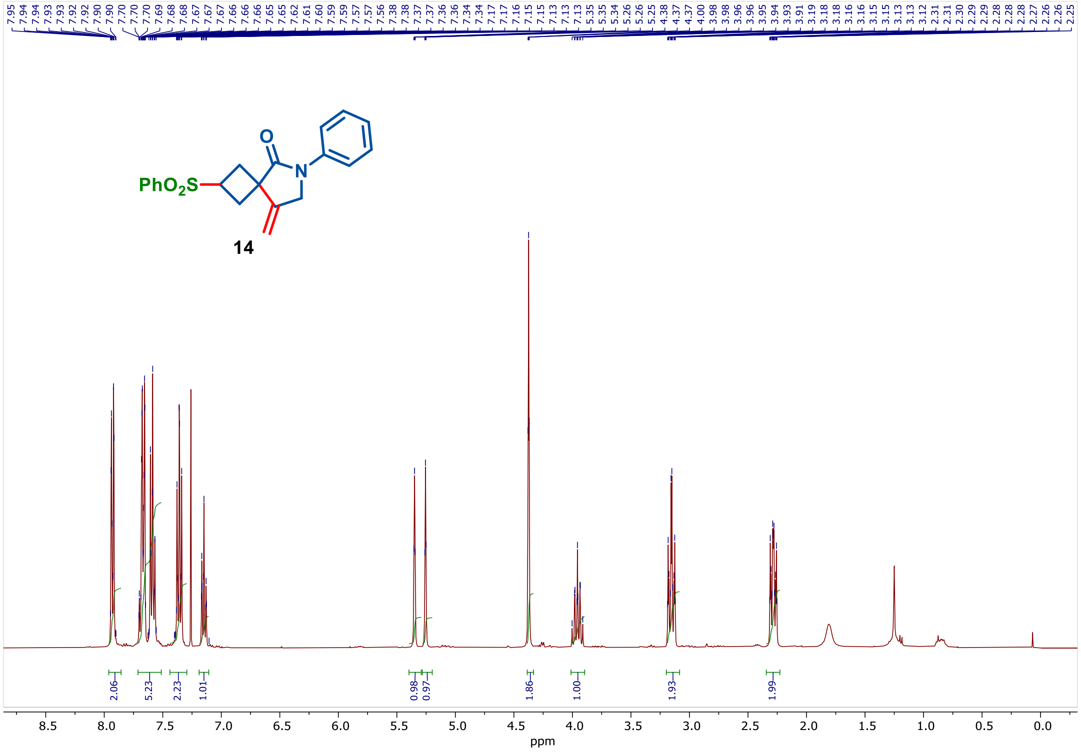
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **13 (minor)**



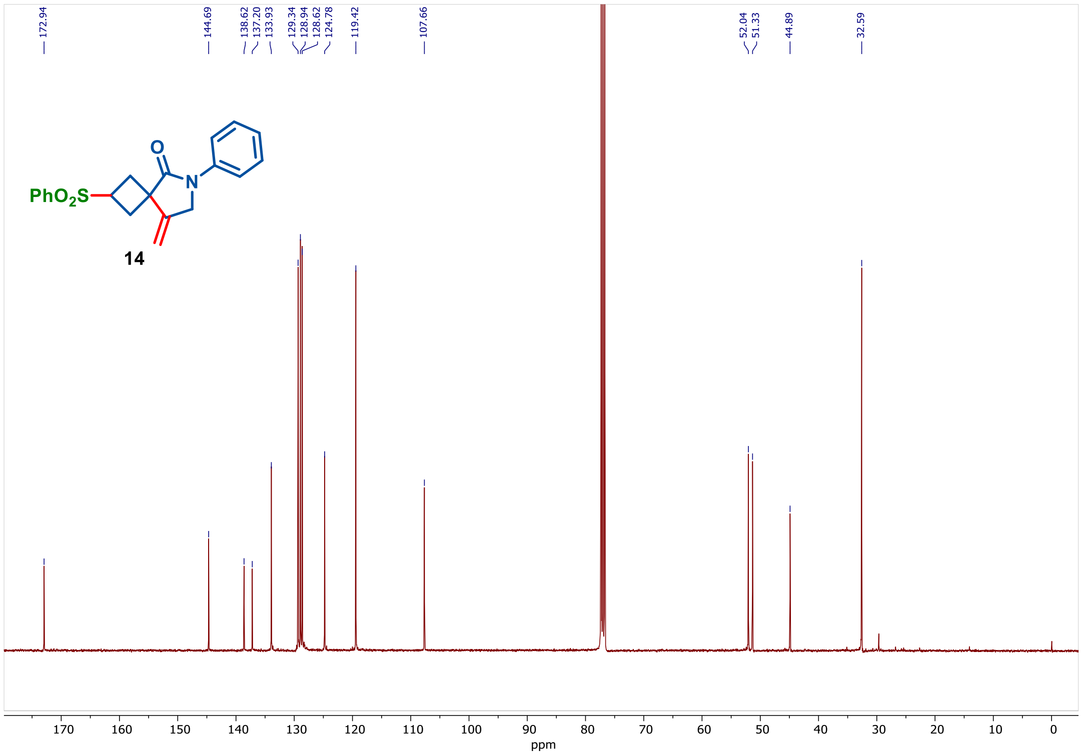
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **13 (minor)**



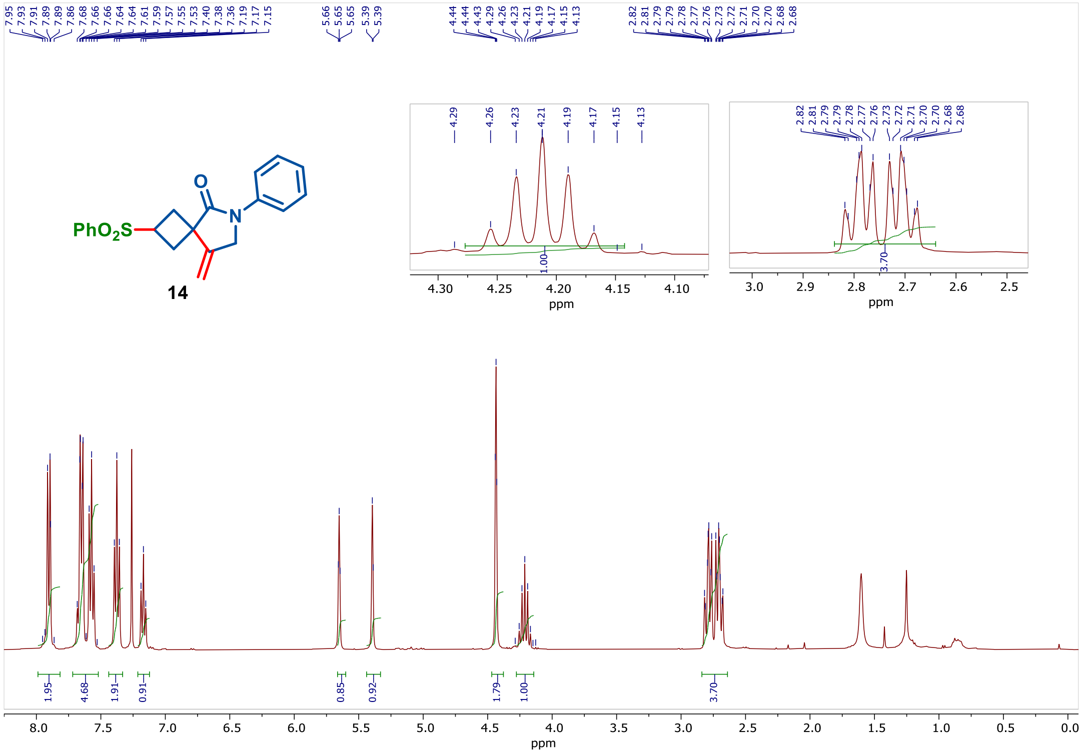
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **14 (major)** (**[See Procedure]**)



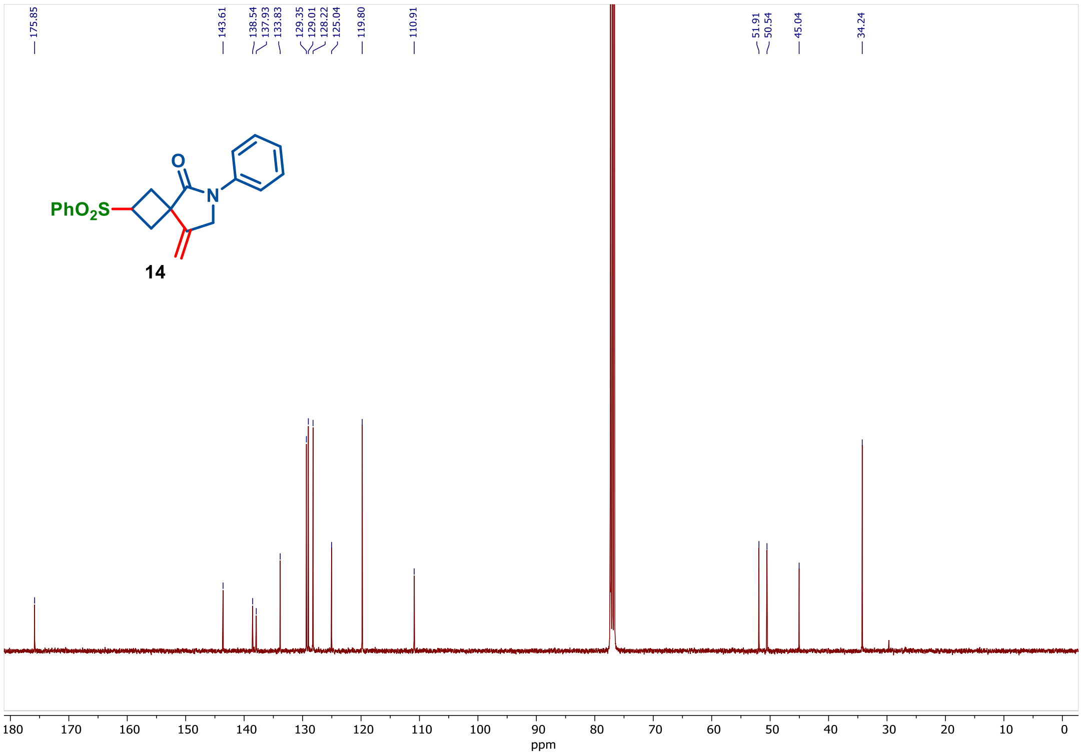
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **14 (major)**



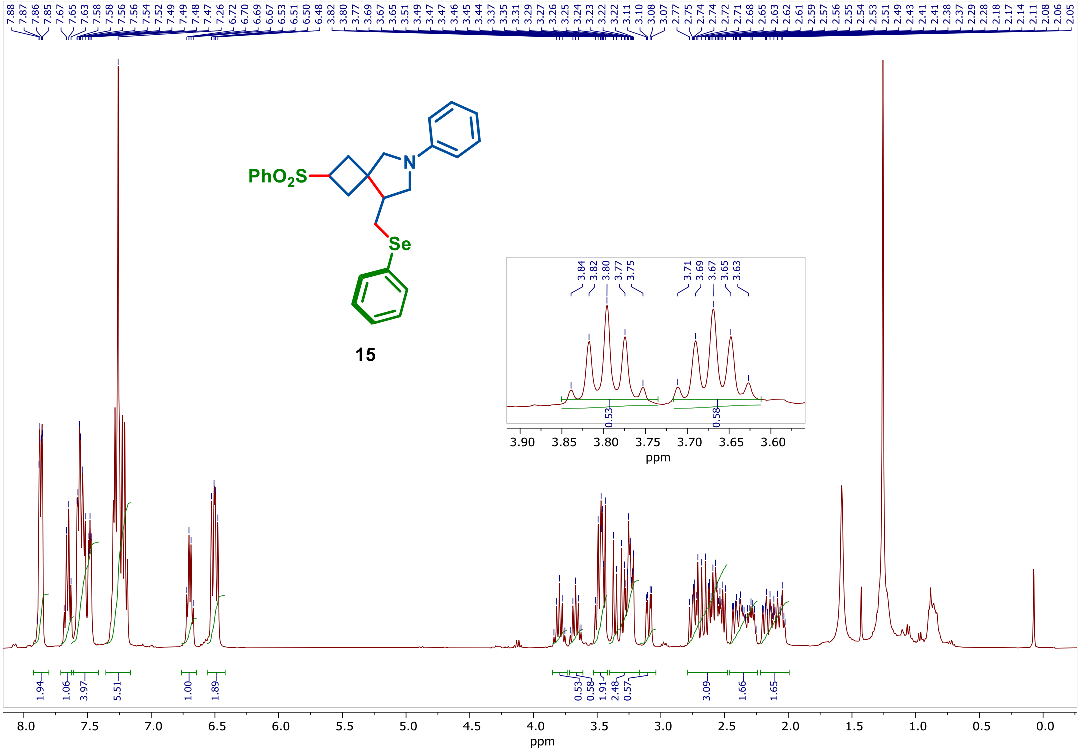
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **14 (minor)**



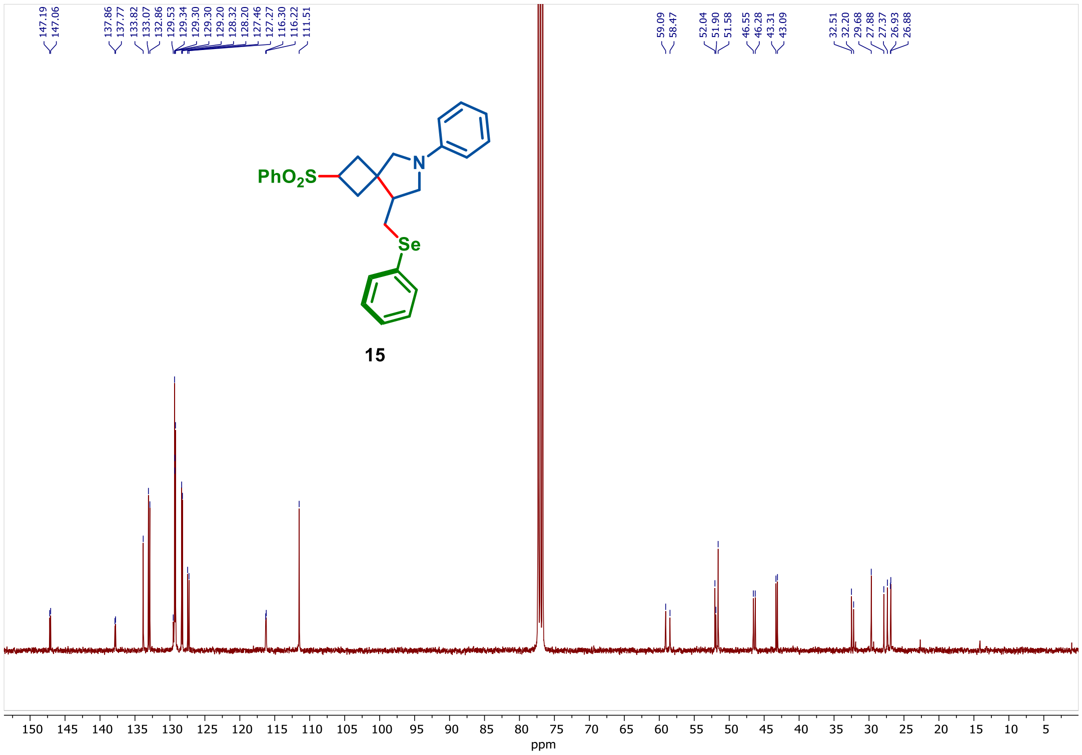
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **14 (minor)**



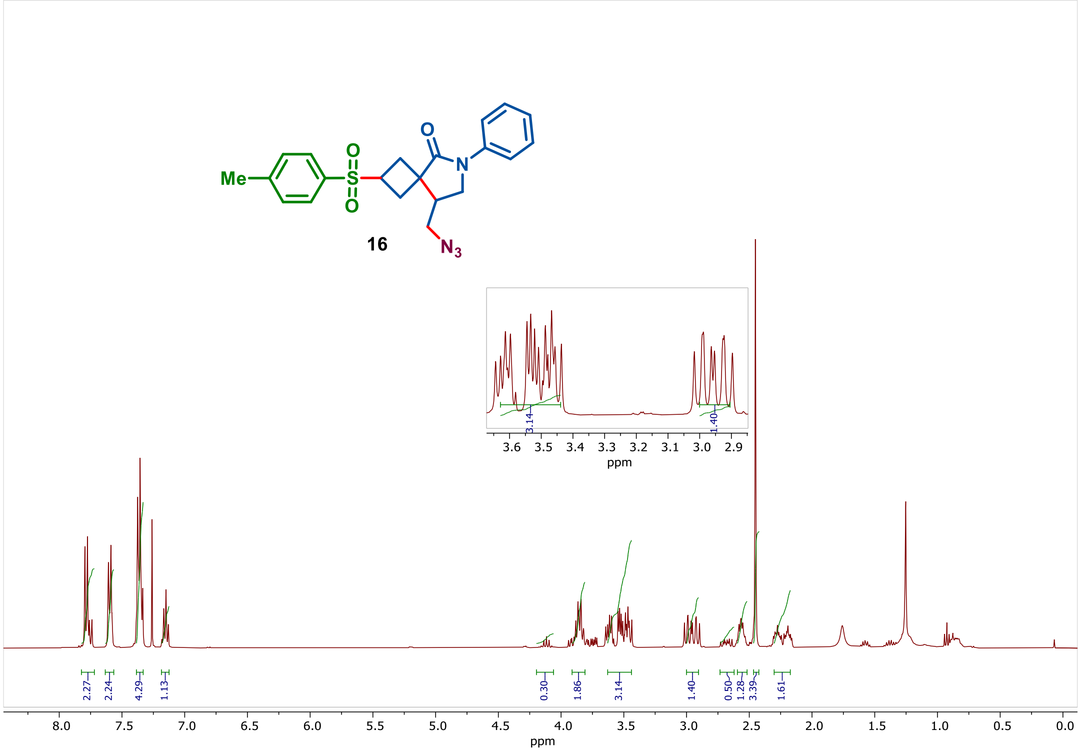
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **15** **(See Procedure)**



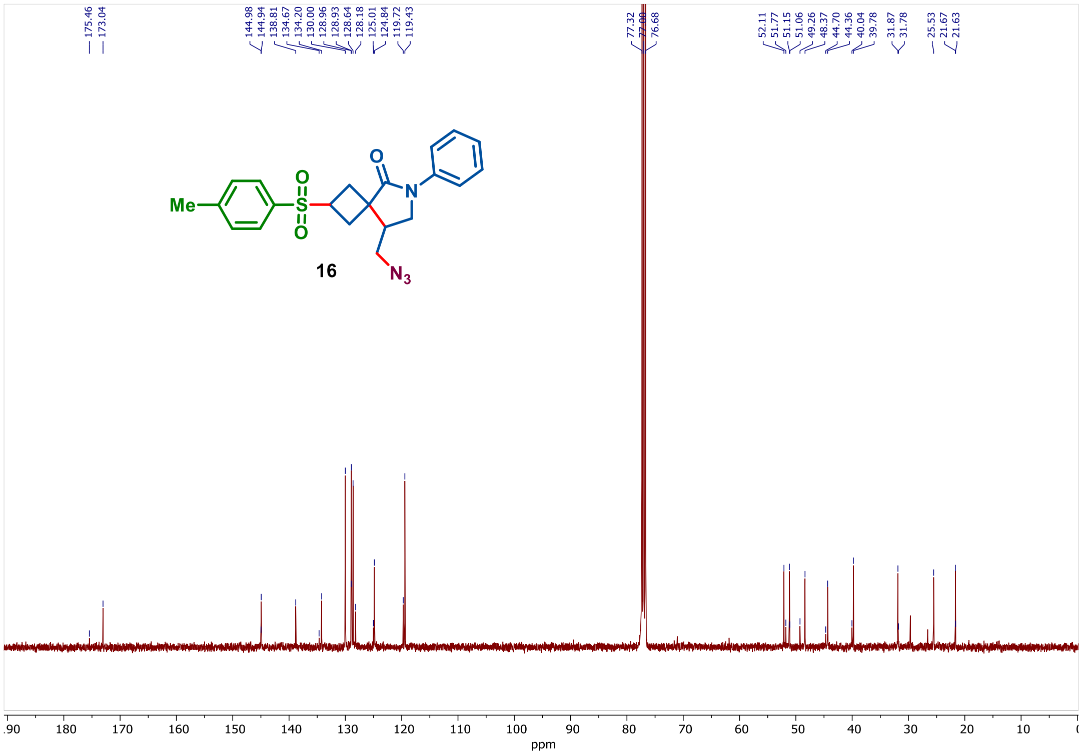
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **15**



^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **16** **(See Procedure)**

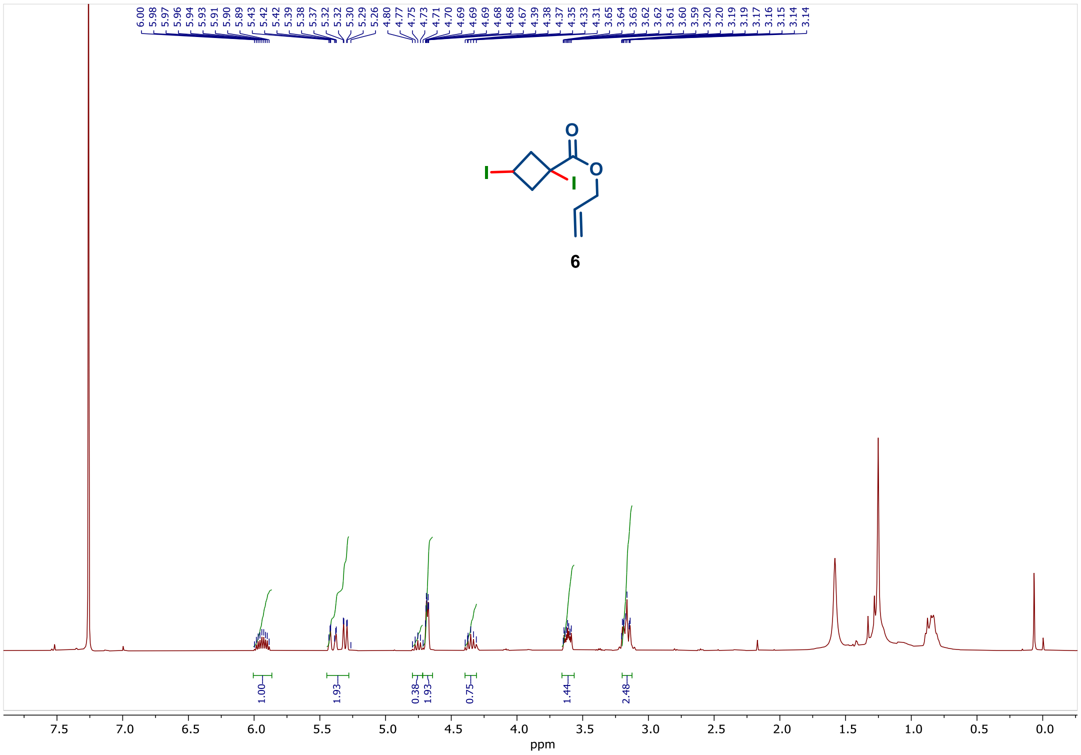


^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **16**

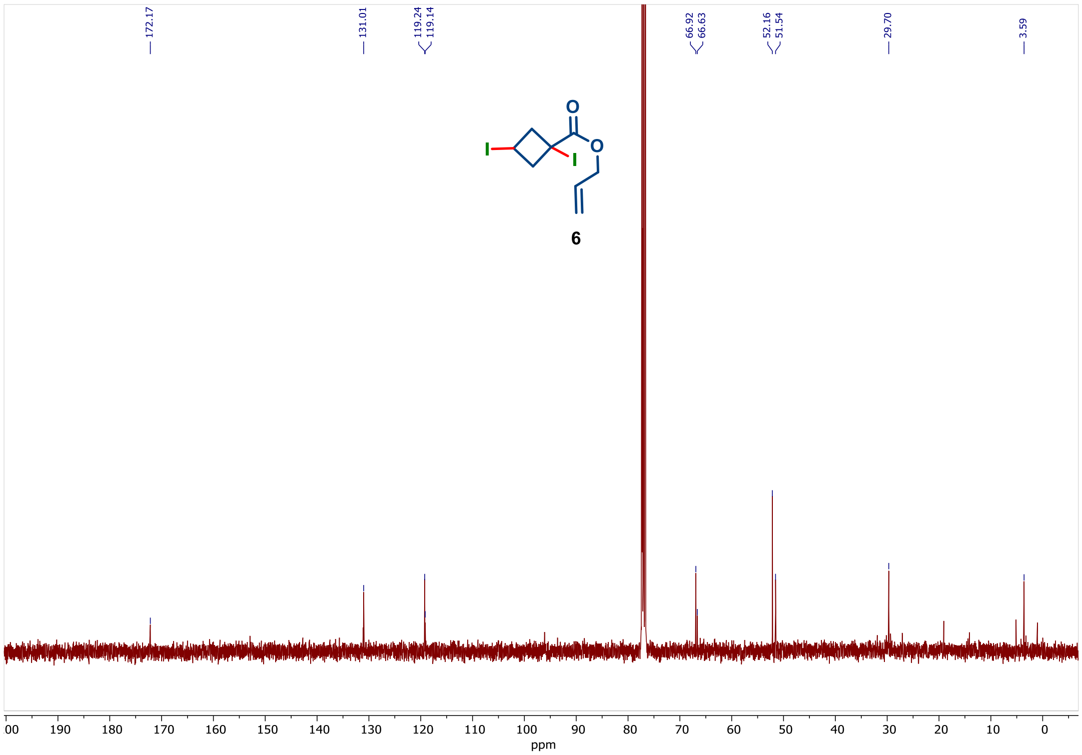


NMR spectra of preliminary experiments

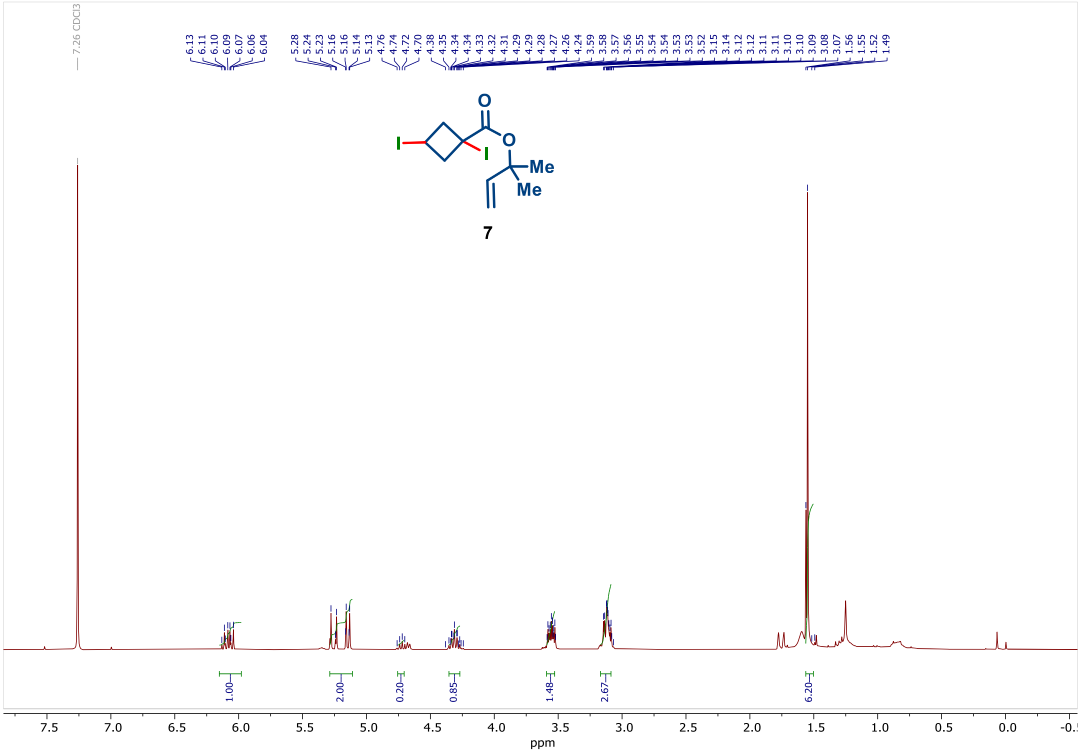
^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **6** (See Procedure)



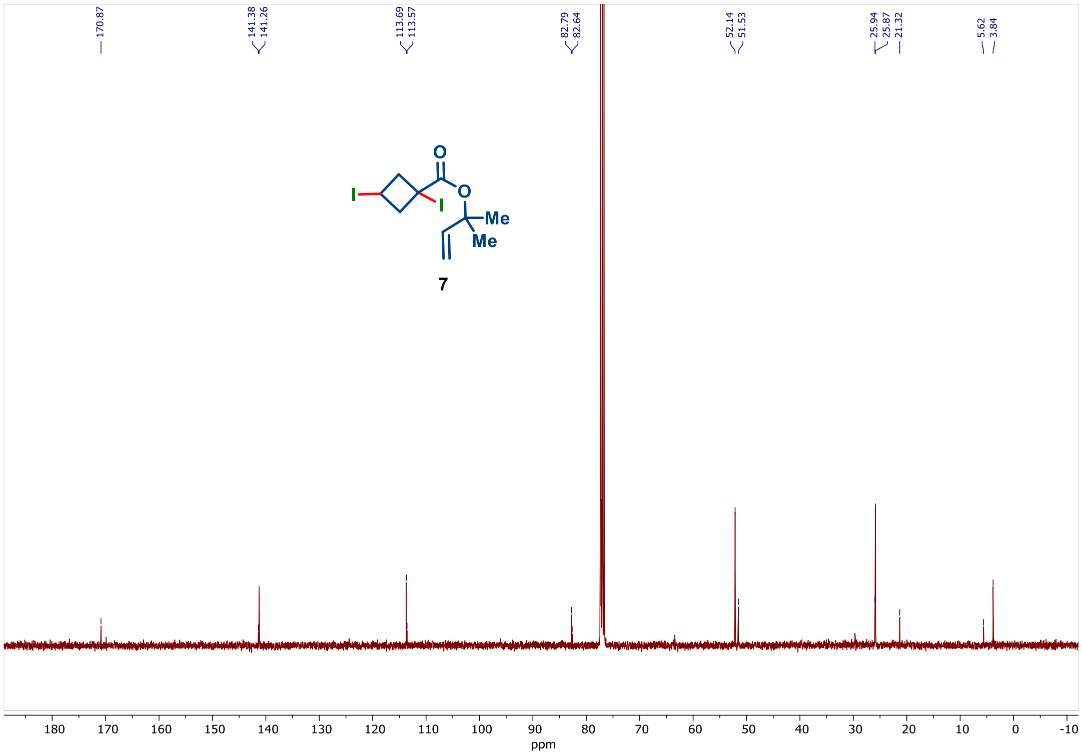
^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **6**



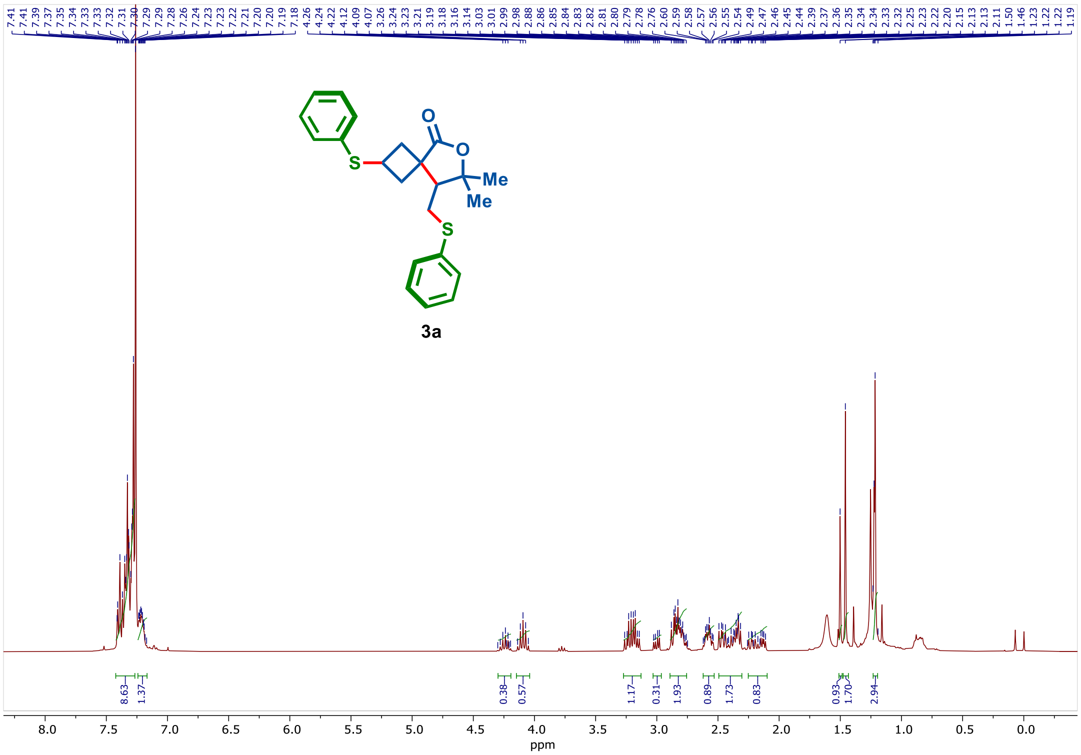
^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **7** **(See Procedure)**



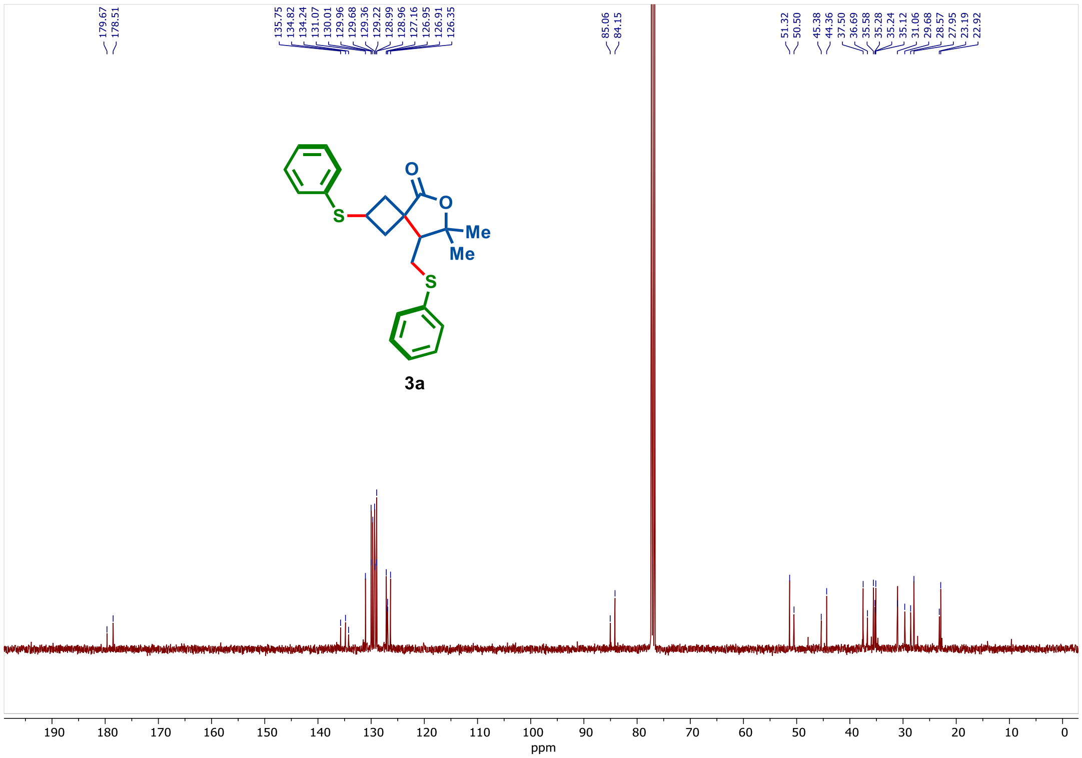
^{13}C NMR (101 MHz, $CDCl_3$) spectra of compound **7**



^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **3a** **(See Procedure)**



^{13}C NMR (101 MHz, CDCl$_3$) spectra of compound **3a**



^{1}H NMR (400 MHz, CDCl$_3$) spectra of compound **13** (HAT product)