Supporting Information

Ni-catalyzed reductive and merged photocatalytic cross-coupling reactions toward sp^3/sp^2 functionalized isoquinolones: Creating diversity at C-6 and C-7 to address bioactive analogs

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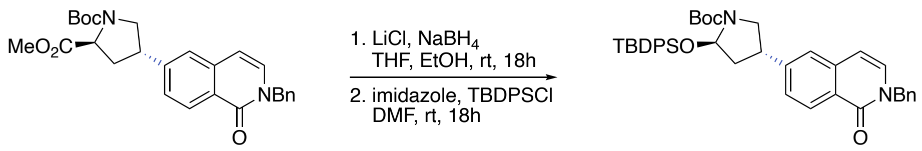
1. Supplementary reactions and control experiments.

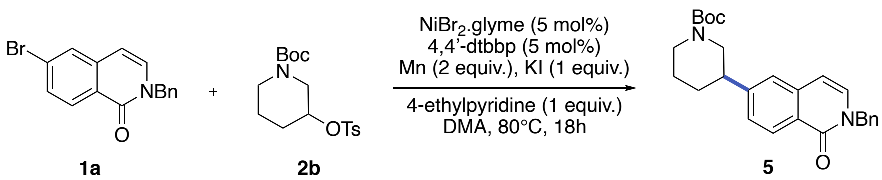
1.1. Transformation of compound 13 into 15



13 **15**

13 (190 mg, 0.41 mmol, 1 equiv.) in THF (1 mL) was successively treated by LiCl (52 mg, 1.23 mmol, 3 equiv.) and $NaBH_4$ (47 mg, 1.23 mmol, 3 equiv.). EtOH (2.1 mL) was then added and the mixture was allowed to stir at rt overnight. The conversion was checked by TLC. The reaction was quenched upon addition of water. The crude product was extracted with EtOAc, concentrated, dried over Na_2SO_4 and used in the next step without further purification.
The crude was taken up in DMF and treated by imidazole (42 mg, 0.62 mmol, 1.5 equiv.) and TBDPS-Cl (0.11 mL, 0.41 mmol, 1 equiv.) overnight at rt. The conversion was checked by TLC. The reaction was quenched upon addition of water. After extraction with EtOAc, the organic layer was dried over Na_2SO_4. The crude product was purified on SiO_2 using hexane/EtOAc: 9/1 to 7/3 to afford a white solid (132 mg, 49% yield) whose spectral data matched those of **15**.

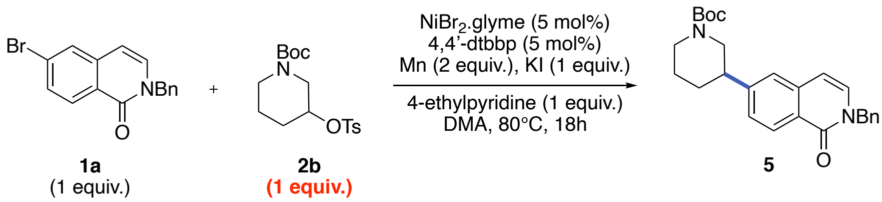
1.2. Reaction of 1a with 5 equiv. 2b



1a (1 equiv.) **2b** **(5 equiv.)** **5**

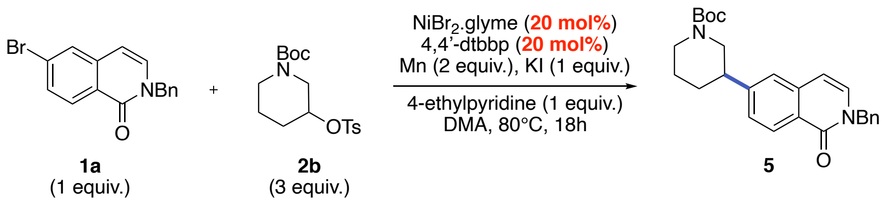
A sealed tube was charged with **1a** (50 mg, 0.159 mmol, 1 equiv.), $NiBr_2$.glyme (2.5 mg, 0.00795 mmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-dipyridyl (2.1 mg, 0.00795 mmol, 0.05 equiv.), potassium iodide (26 mg, 0.159 mmol, 1 equiv.) and manganese (17.5 mg, 0.318 mmol, 2 equiv.) and was purged with argon. A solution of **2b** (283 mg, 0.795 mmol, 5 equiv.) in DMA (0.8 mL) was then added followed by 4-ethylpyridine (18 μL, 0.159 mmol, 1 equiv.). The tube was sealed and the resulting mixture was stirred at 80°C for 18 hours. Completion of the reaction was checked by TLC (hexane/EtOAc = 6/4). After cooling down to room temperature, the mixture was filtered over a pad of celite and rinsed with acetonitrile. After evaporation, the crude was purified over SiO_2 using hexane/EtOAc = 8/2 to 6/4 as eluent affording **5** (27 mg, 41% yield) and biaryl **4** (7 mg, 19%).

1.3. Reaction of 1a with 1 equiv. 2b



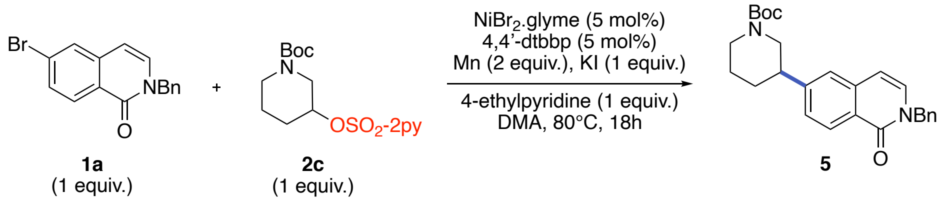
A sealed tube was charged with **1a** (108 mg, 0.344 mmol, 1 equiv.), $NiBr_2$.glyme (5.3 mg, 0.0172 mmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-dipyridyl (4.6 mg, 0.0172 mmol, 0.05 equiv.), potassium iodide (57 mg, 0.344 mmol, 1 equiv.) and manganese (38 mg, 0.688 mmol, 2 equiv.) and was purged with argon. A solution of **2b** (122 mg, 0.344 mmol, 1 equiv.) in DMA (1.7 mL) was then added followed by 4-ethylpyridine (39 µL, 0.344 mmol, 1 equiv.). The tube was sealed and the resulting mixture was stirred at 80°C for 18 hours. Completion of the reaction was checked by TLC (hexane/EtOAc = 6/4). After cooling down to room temperature, the mixture was filtered over a pad of celite and rinsed with acetonitrile. After evaporation, the crude was purified over SiO_2 using hexane/EtOAc = 8/2 to 6/4 as eluent affording **5** (30 mg, 21% yield) and biaryl **4** (30 mg, 37%).

1.4. Reaction of 1a with 3 equiv. 2b and 20 mol% NiBr2.glyme and 4,4'-dtbp



A sealed tube was charged with **1a** (50 mg, 0.159 mmol, 1 equiv.), $NiBr_2$.glyme (9.8 mg, 0.0318 mmol, 0.2 equiv.), 4,4'-di-*tert*-butyl-2,2'-dipyridyl (8.5 mg, 0.0318 mmol, 0.2 equiv.), potassium iodide (26 mg, 0.159 mmol, 1 equiv.) and manganese (17.5 mg, 0.318 mmol, 2 equiv.) and was purged with argon. A solution of **2b** (170 mg, 0.795 mmol, 3 equiv.) in DMA (0.8 mL) was then added followed by 4-ethylpyridine (18 µL, 0.159 mmol, 1 equiv.). The tube was sealed and the resulting mixture was stirred at 80°C for 18 hours. Completion of the reaction was checked by TLC (hexane/EtOAc = 6/4). After cooling down to room temperature, the mixture was filtered over a pad of celite and rinsed with acetonitrile. After evaporation, the crude was purified over SiO_2 using hexane/EtOAc = 8/2 to 6/4 as eluent affording **5** (28 mg, 42% yield) and biaryl **4** (13 mg, 35%).

1.5. Reaction of 1a with 1 equiv. 2c

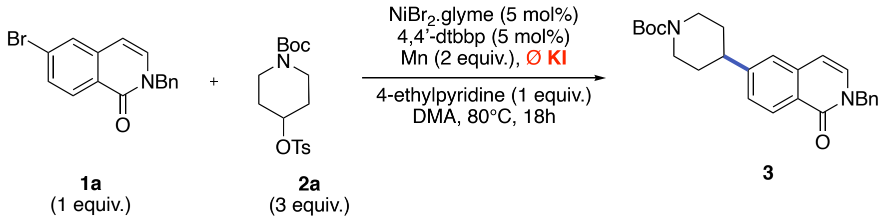


A sealed tube was charged with **1a** (108 mg, 0.344 mmol, 1 equiv.), $NiBr_2$.glyme (5.3 mg, 0.0172 mmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-dipyridyl (4.6 mg, 0.0172 mmol, 0.05 equiv.), potassium iodide (57 mg, 0.344 mmol, 1 equiv.) and manganese (38 mg, 0.688 mmol, 2 equiv.) and was purged with argon. A solution of **2c** (118 mg, 0.344 mmol, 1 equiv.) in DMA (1.7 mL) was then added followed by 4-ethylpyridine (39 μL, 0.344 mmol, 1 equiv.). The tube was sealed and the resulting mixture was stirred at 80°C for 18 hours. Completion of the reaction was checked by TLC (hexane/EtOAc = 6/4). After cooling down to room temperature, the mixture was filtered over a pad of celite and rinsed with acetonitrile. After evaporation, the crude was purified over SiO_2 using hexane/EtOAc = 8/2 to 6/4 as eluent affording **5** (28 mg, 19% yield) and biaryl **4** (24 mg, 30%).

1.6. Reaction of 1a with 1 equiv. 2d

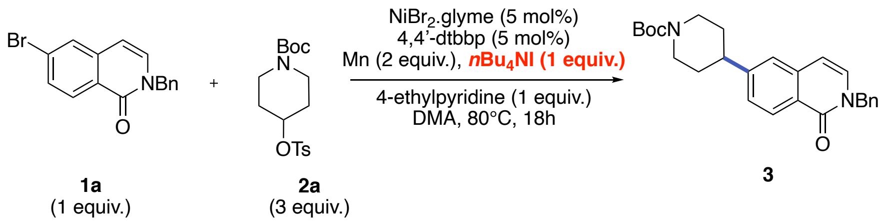
A sealed tube was charged with **1a** (50 mg, 0.159 mmol, 1 equiv.), $NiBr_2$.glyme (2.5 mg, 0.00795 mmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-dipyridyl (2.1 mg, 0.00795 mmol, 0.05 equiv.), potassium iodide (26 mg, 0.159 mmol, 1 equiv.) and manganese (17.5 mg, 0.318 mmol, 2 equiv.) and was purged with argon. A solution of **2d** (54 mg, 0.159 mmol, 1 equiv.) in DMA (0.8 mL) was then added followed by 4-ethylpyridine (18 μL, 0.159 mmol, 1 equiv.). The tube was sealed and the resulting mixture was stirred at 80°C for 18 hours. Completion of the reaction was checked by TLC (hexane/EtOAc = 6/4). After cooling down to room temperature, the mixture was filtered over a pad of celite and rinsed with acetonitrile. After evaporation, the crude was purified over SiO_2 using hexane/EtOAc = 8/2 to 6/4 as eluent affording **5** (8 mg, 12% yield) and biaryl **4** (23 mg, 31%).

1.7. Reaction of 1a with 3 equiv. 2a without KI



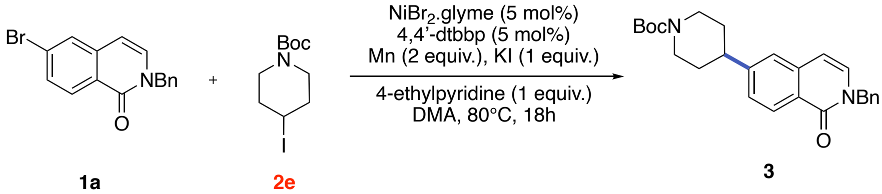
A sealed tube was charged with **1a** (50 mg, 0.159 mmol, 1 equiv.), $NiBr_2$.glyme (2.5 mg, 0.00795 mmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-dipyridyl (2.1 mg, 0.00795 mmol, 0.05 equiv.) and manganese (17.5 mg, 0.318 mmol, 2 equiv.) and was purged with argon. A solution of **2a** (170 mg, 0.477 mmol, 3 equiv.) in DMA (0.8 mL) was then added followed by 4-ethylpyridine (18 µL, 0.159 mmol, 1 equiv.). The tube was sealed and the resulting mixture was stirred at 80°C for 18 hours. TLC only showed traces of product. **1a** and **2a** were recovered.

1.8. Reaction of 1a with 3 equiv. 2a with *n*Bu_4NI



A sealed tube was charged with **1a** (50 mg, 0.159 mmol, 1 equiv.), $NiBr_2$.glyme (2.5 mg, 0.00795 mmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-dipyridyl (2.1 mg, 0.00795 mmol, 0.05 equiv.), *n*Bu_4NI (59 mg, 0.159 mmol, 1 equiv.) and manganese (17.5 mg, 0.318 mmol, 2 equiv.) and was purged with argon. A solution of **2a** (170 mg, 0.477 mmol, 3 equiv.) in DMA (0.8 mL) was then added followed by 4-ethylpyridine (18 µL, 0.159 mmol, 1 equiv.). The tube was sealed and the resulting mixture was stirred at 80°C for 18 hours. Completion of the reaction was checked by TLC (hexane/EtOAc = 6/4). After cooling down to room temperature, the mixture was filtered over a pad of celite and rinsed with acetonitrile. After evaporation, the crude was purified over SiO_2 using hexane/EtOAc = 8/2 to 6/4 as eluent affording **3** (35 mg, 53% yield) and and only traces amount of **4** on TLC.

1.9. Reaction of 1a with 3 equiv. 2e

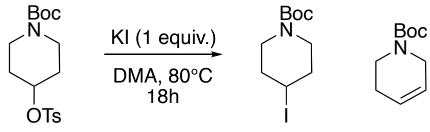


A sealed tube was charged with **1a** (40 mg, 0.127 mmol, 1 equiv.), $NiBr_2$.glyme (2.0 mg, 0.00635 mmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-dipyridyl (1.7 mg, 0.00635 mmol, 0.05 equiv.), potassium iodide (21 mg, 0.127 mmol, 1 equiv.) and manganese (14 mg, 0.254 mmol, 2 equiv.) and was purged with argon. A solution of **2e** (119 mg, 0.381 mmol, 3 equiv.) in DMA (0.64 mL) was then added followed by 4-ethylpyridine (14.4 µL, 0.127 mmol, 1 equiv.). The tube was sealed and the resulting mixture was stirred at 80°C for 18 hours. Completion of the reaction was checked by TLC (hexane/EtOAc = 6/4). After cooling down to room temperature, the mixture was filtered over a pad of celite and rinsed with acetonitrile. After evaporation, the crude was purified over SiO_2 using hexane/EtOAc = 8/2 to 6/4 as eluent affording **3** (38 mg, 71% yield) and no biaryl **4**.

1.10. Reaction with 1a and without the tosylate partner

A sealed tube was charged with **1a** (50 mg, 0.159 mmol, 1 equiv.), $NiBr_2$.glyme (2.5 mg, 0.00795 mmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-dipyridyl (2.1 mg, 0.00795 mmol, 0.05 equiv.), potassium iodide (26 mg, 0.159 mmol, 1 equiv.) and manganese (17.5 mg, 0.318 mmol, 2 equiv.) and was purged with argon. DMA (0.8 mL) was then added followed by 4-ethylpyridine (18 µL, 0.159 mmol, 1 equiv.). The tube was sealed and the resulting mixture was stirred at 80°C for 18 hours. The reaction was monitored by TLC (hexane/EtOAc = 6/4). After cooling down to room temperature, the mixture was filtered over a pad of celite and rinsed with acetonitrile. After evaporation, the crude was purified over SiO_2 using hexane/EtOAc = 8/2 to 6/4 as eluent affording biaryl **4** (3 mg, 8%) and a mixture of dehalogenated-**1a** : **1a** : 6-iodo-isoquinolone in a 4:62:34 NMR ratio.

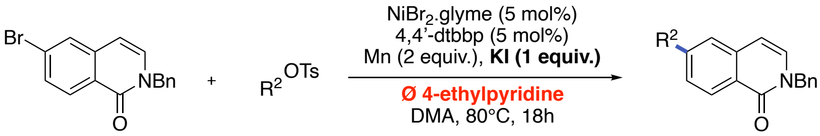
1.11. Control reaction of 2a with KI



2a **2e**

2a (50 mg, 0.141 mmol, 1 equiv.) and potassium iodide (23 mg, 0.141 mmol, 1 equiv) were stirred in DMA (0.7 mL) overnight at 80°C. After cooling down to rt, water was poured in the mixture followed by extraction with dichloromethane. The combined organic layers were washed with brine and dried over Na_2SO_4. After evaporation the crude was analyzed by ^1H NMR and showed the following product distribution: **2a**:**2e**:elimination = 0.07:1:0.17

1.12. Reactions without 4-ethylpyridine

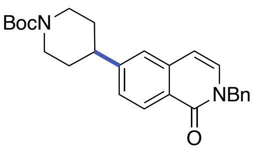


1a (1 equiv.) **2** (3 equiv.)

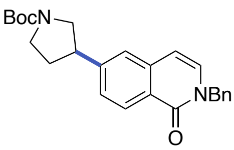
General procedure :

A sealed tube was charged with **1a** (1 equiv.), $NiBr_2$.glyme (0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-dipyridyl (0.05 equiv.), potassium iodide (1 equiv.) and manganese (2 equiv.) and was purged with argon. A solution of tosylate (3 equiv.) in DMA (0.2 M with respect to isoquinolone) was then added. The tube was sealed and the resulting mixture was stirred at 80°C for 18 hours. Completion of the reaction was checked by TLC (hexane/EtOAc = 6/4). After cooling down to room temperature, the mixture was filtered over a pad of celite and rinsed with acetonitrile. After evaporation, the crude was purified over SiO_2 using hexane/EtOAc = 8/2 to 6/4 as eluent.

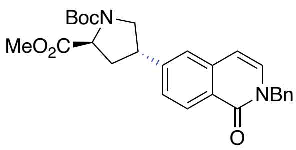
Following the above general procedure with **2a**, N-Boc-3-tosyloxypyrrolidine and N-Boc 4(*R)*-tosyloxy L-proline methyl ester respectively, the following products were obtained :



3: 87% (58 mg)

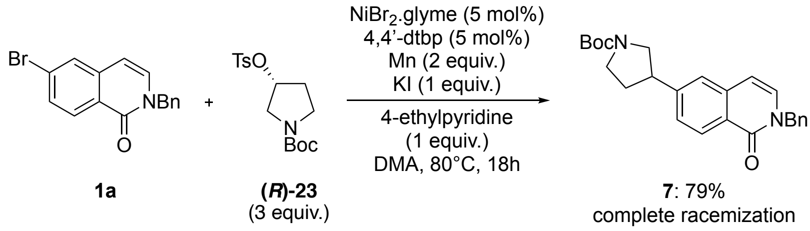


7: 70% (45 mg)

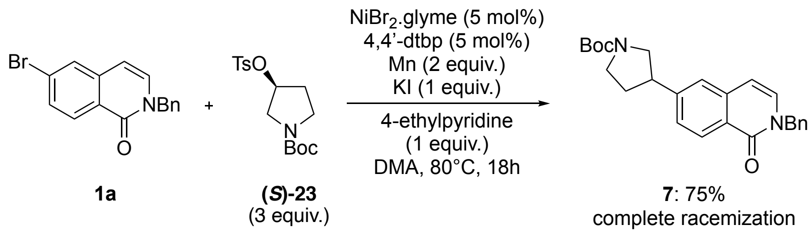


13: 81% (60 mg)

1.13. Reactions with (*R*)-23 and (*S*)-23

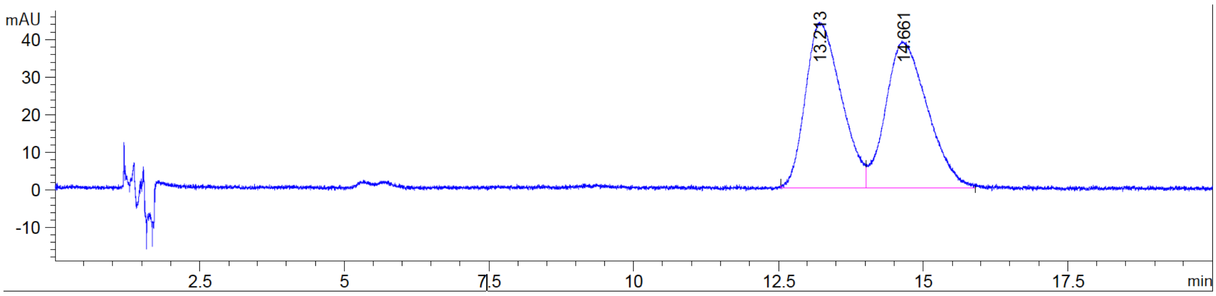


A sealed tube was charged with **1a** (50 mg, 0.159 mmol, 1 equiv.), $NiBr_2$.glyme (2.5 mg, 0.00795 mmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-dipyridyl (2.1 mg, 0.00795 mmol, 0.05 equiv.), potassium iodide (26 mg, 0.159 mmol, 1 equiv.) and manganese (17.5 mg, 0.318 mmol, 2 equiv.) and was purged with argon. A solution of **(*R*)-23** (163 mg, 0.477 mmol, 3 equiv.) in DMA (0.8 mL) was then added followed by 4-ethylpyridine (18 μL, 0.159 mmol, 1 equiv.). The tube was sealed and the resulting mixture was stirred at 80°C for 18 hours. Completion of the reaction was checked by TLC (hexane/EtOAc = 6/4). After cooling down to room temperature, the mixture was filtered over a pad of celite and rinsed with acetonitrile. After evaporation, the crude was purified over SiO_2 using hexane/EtOAc = 8/2 to 6/4 as eluent affording **7** (51 mg, 79% yield) with complete racemization as determined by chiral SFC analysis.

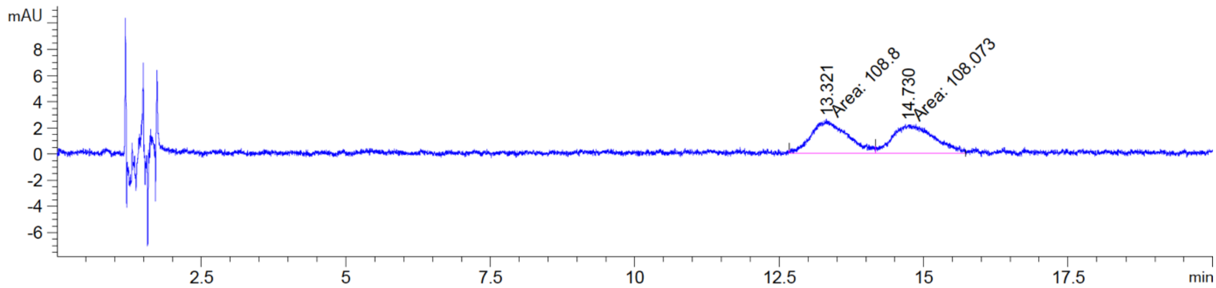


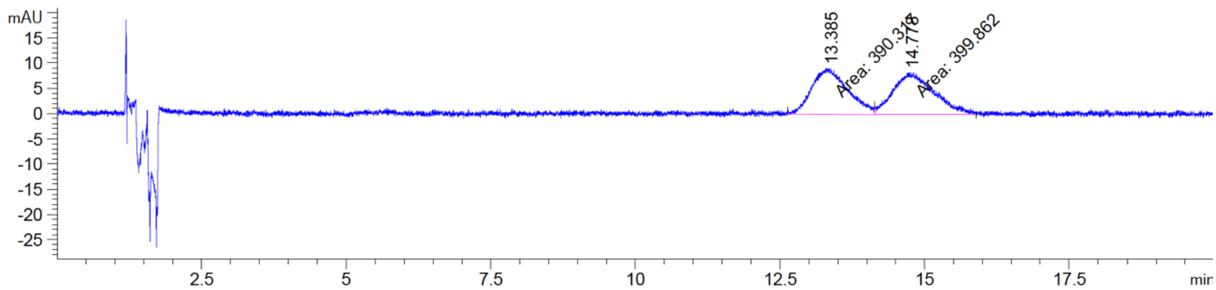
A sealed tube was charged with **1a** (50 mg, 0.159 mmol, 1 equiv.), $NiBr_2$.glyme (2.5 mg, 0.00795 mmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-dipyridyl (2.1 mg, 0.00795 mmol, 0.05 equiv.), potassium iodide (26 mg, 0.159 mmol, 1 equiv.) and manganese (17.5 mg, 0.318 mmol, 2 equiv.) and was purged with argon. A solution of **(*S*)-23** (163 mg, 0.477 mmol, 3 equiv.) in DMA (0.8 mL) was then added followed by 4-ethylpyridine (18 μL, 0.159 mmol, 1 equiv.). The tube was sealed and the resulting mixture was stirred at 80°C for 18 hours. Completion of the reaction was checked by TLC (hexane/EtOAc = 6/4). After cooling down to room temperature, the mixture was filtered over a pad of celite and rinsed with acetonitrile. After evaporation, the crude was purified over SiO_2 using hexane/EtOAc = 8/2 to 6/4 as eluent affording **7** (48 mg, 75% yield) with complete racemization as determined by chiral SFC analysis.

A vial containing a sample of both reaction mixtures was submitted to chiral SFC analysis to get retention times.

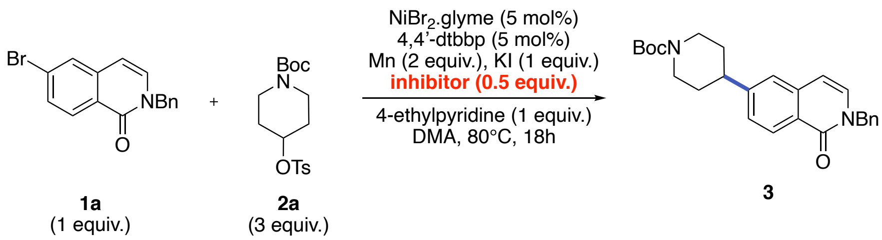


Each sample was then independently analyzed.





1.14. Reactions BHT, TEMPO and 1-chloro-2,4-dinitrobenzene



General procedure :

A sealed tube was charged with **1a** (50 mg, 0.159 mmol, 1 equiv.), $NiBr_2$.glyme (2.5 mg, 0.00795 mmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-dipyridyl (2.1 mg, 0.00795 mmol, 0.05

equiv.), potassium iodide (26 mg, 0.159 mmol, 1 equiv.), manganese (17.5 mg, 0.318 mmol, 2 equiv.) and inhibitor (0.5 equiv.) and was purged with argon. A solution of **2a** (170 mg, 0.477 mmol, 3 equiv.) in DMA (0.8 mL) was then added. The tube was sealed and the resulting mixture was stirred at 80°C for 18 hours. Completion of the reaction was checked by TLC (hexane/EtOAc = 6/4). After cooling down to room temperature, the mixture was filtered over a pad of celite and rinsed with acetonitrile. After evaporation, the crude was purified over SiO_2 using hexane/EtOAc = 8/2 to 6/4 as eluent.

Product **3** was isolated with 66% yield (44 mg) with BHT and 35% yield (23 mg) in the case of TEMPO.

There was no reaction with 1-choro-2,4-dinitrobenzene.

2. NMR spectra

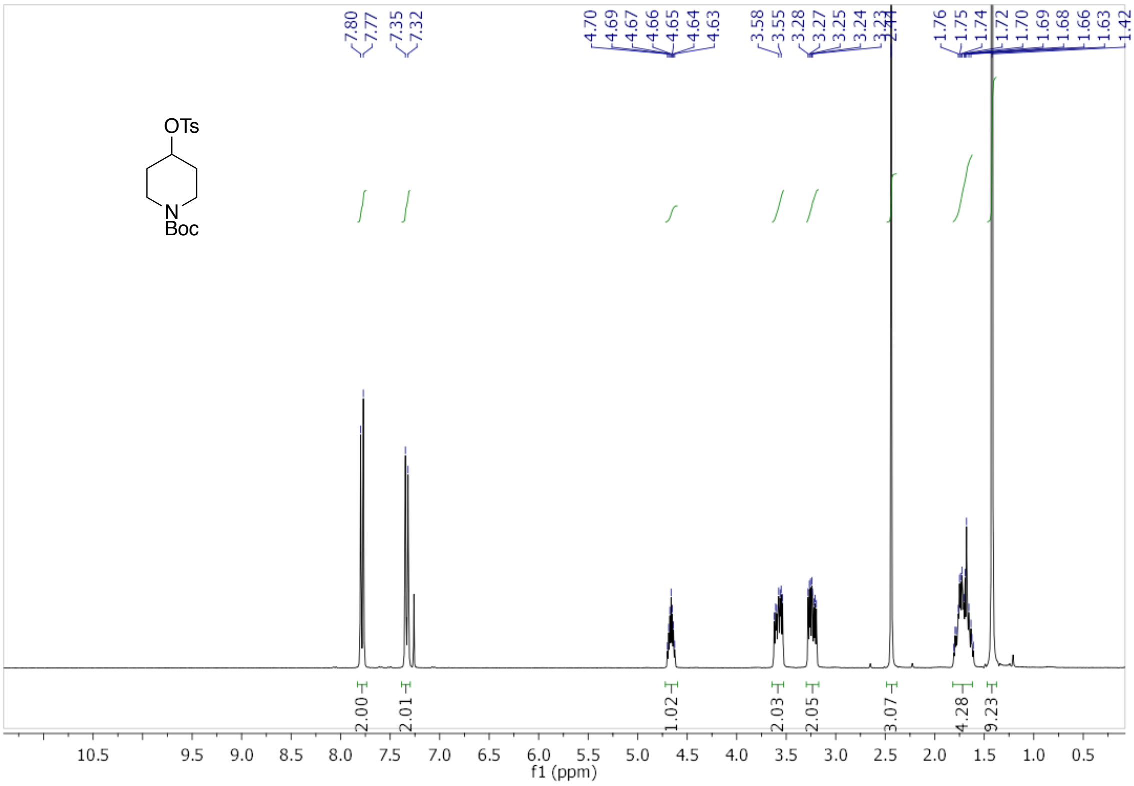


Figure S1: ^{1}H NMR (300 MHz, $CDCl_3$) of **2a**

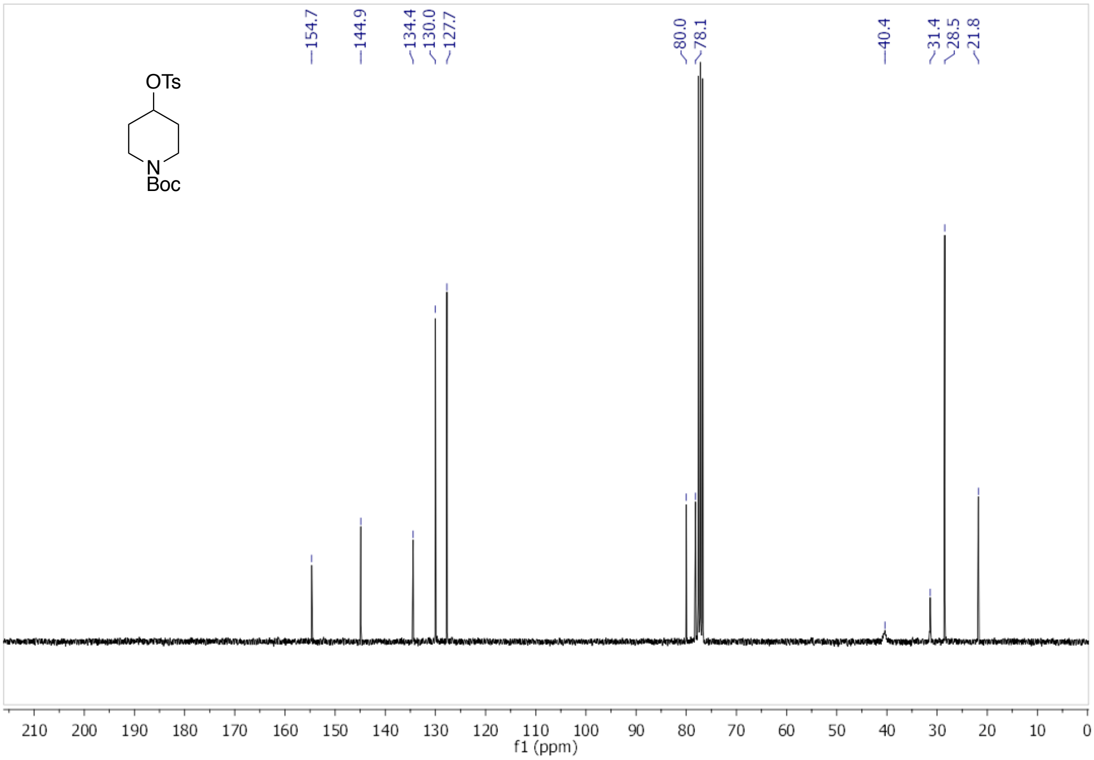


Figure S2 : ^{13}C NMR (75 MHz, $CDCl_3$) of **2a**

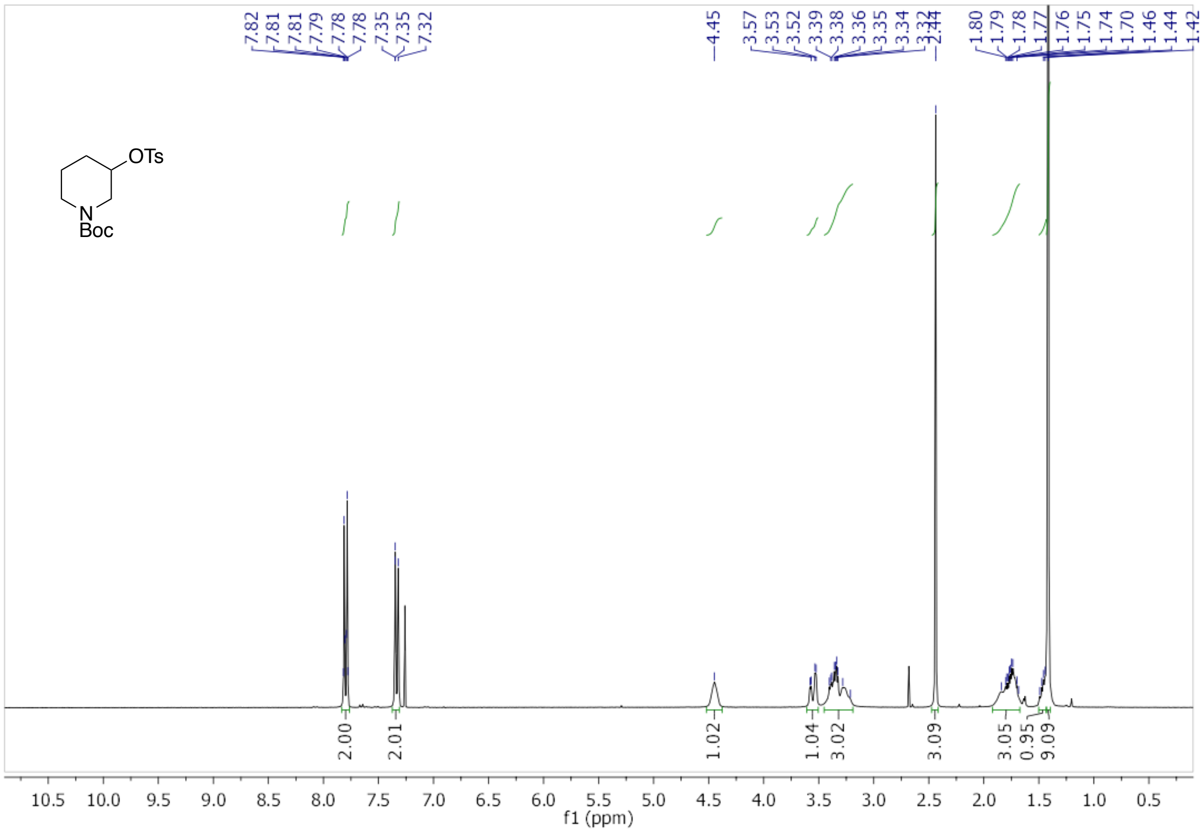


Figure S3: [1]H NMR (300 MHz, $CDCl_3$) of **2b**

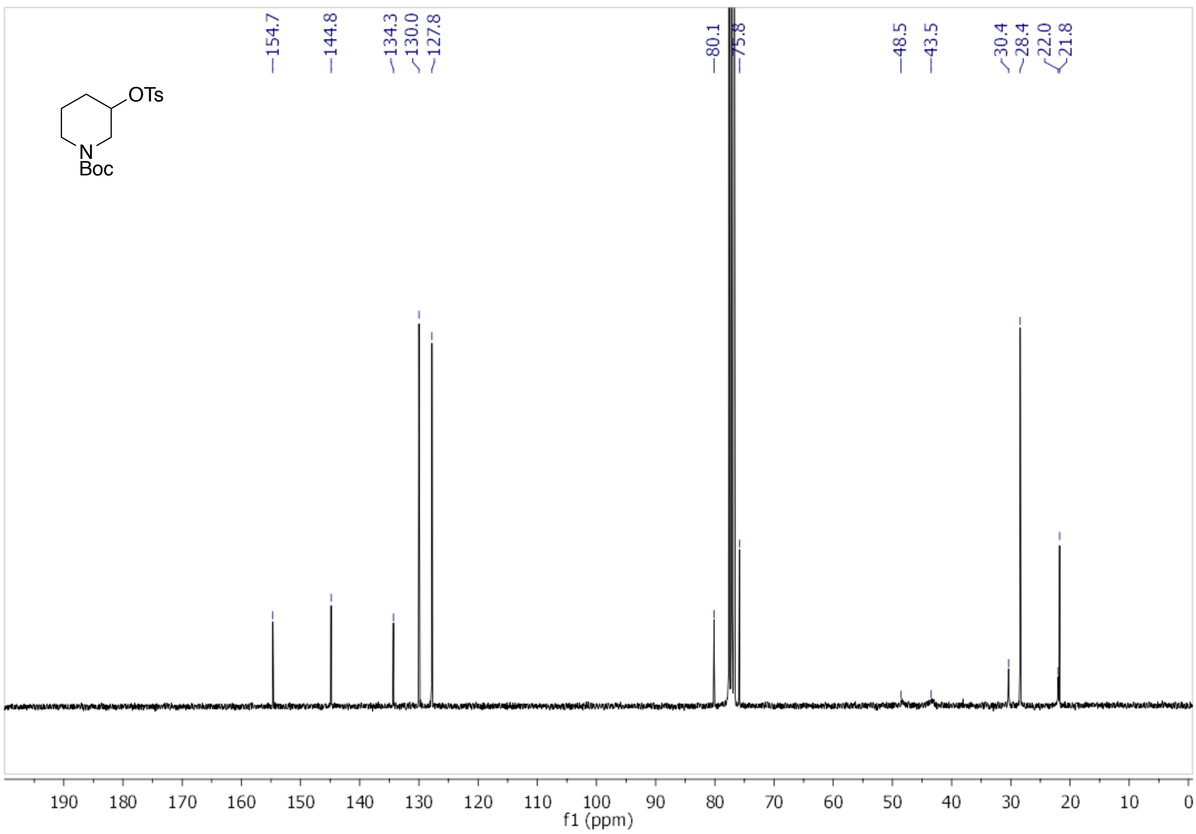


Figure S4: [13]C NMR (75 MHz, $CDCl_3$) of **2b**

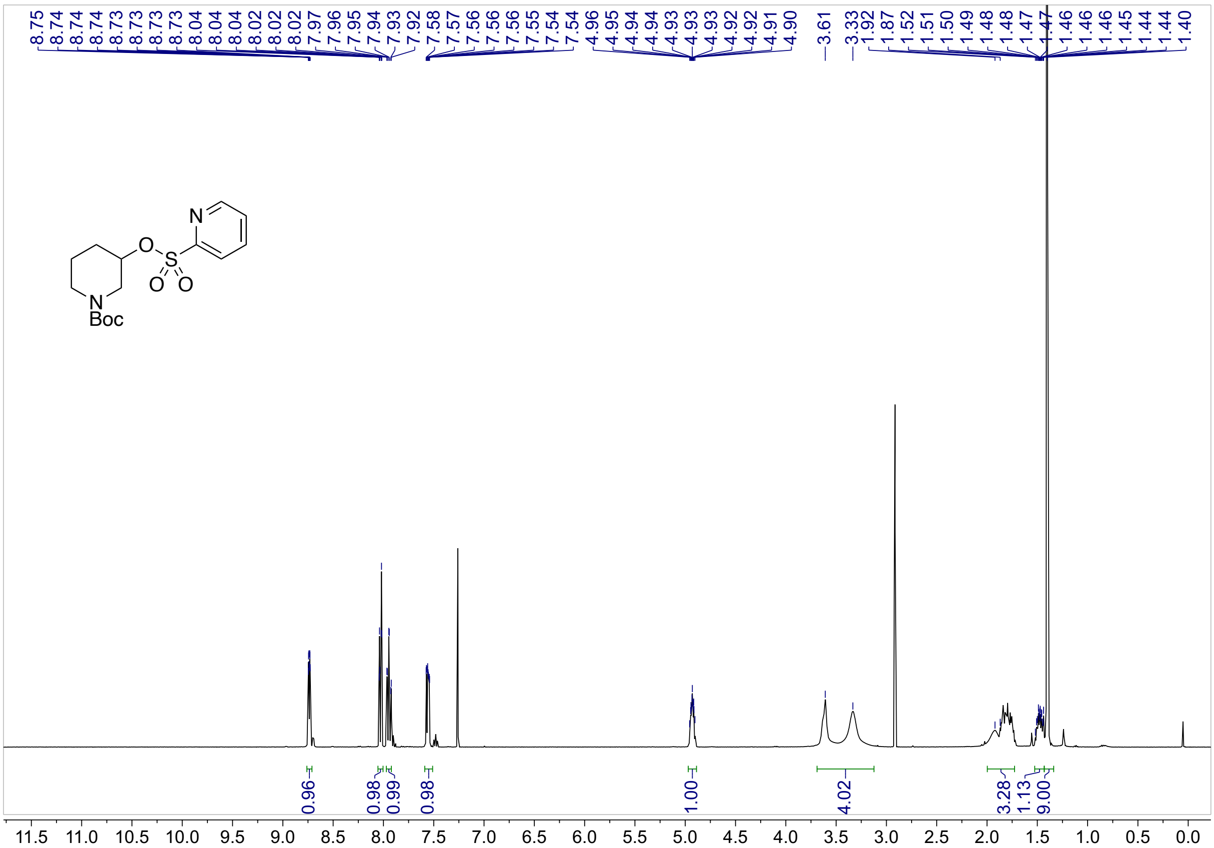


Figure S5 : ^{1}H NMR (400 MHz, $CDCl_3$) of **2c**

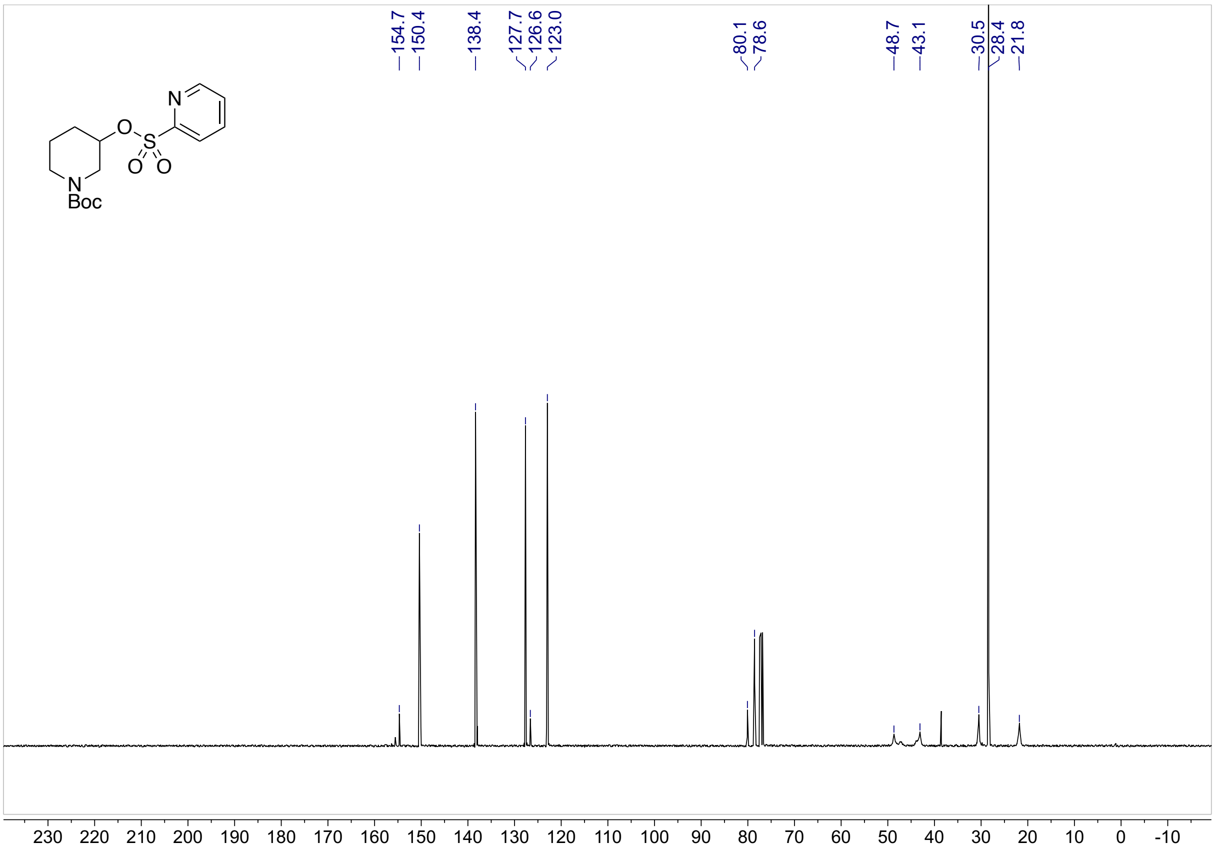


Figure S6 : ^{13}C NMR (101 MHz, $CDCl_3$) of **2c**

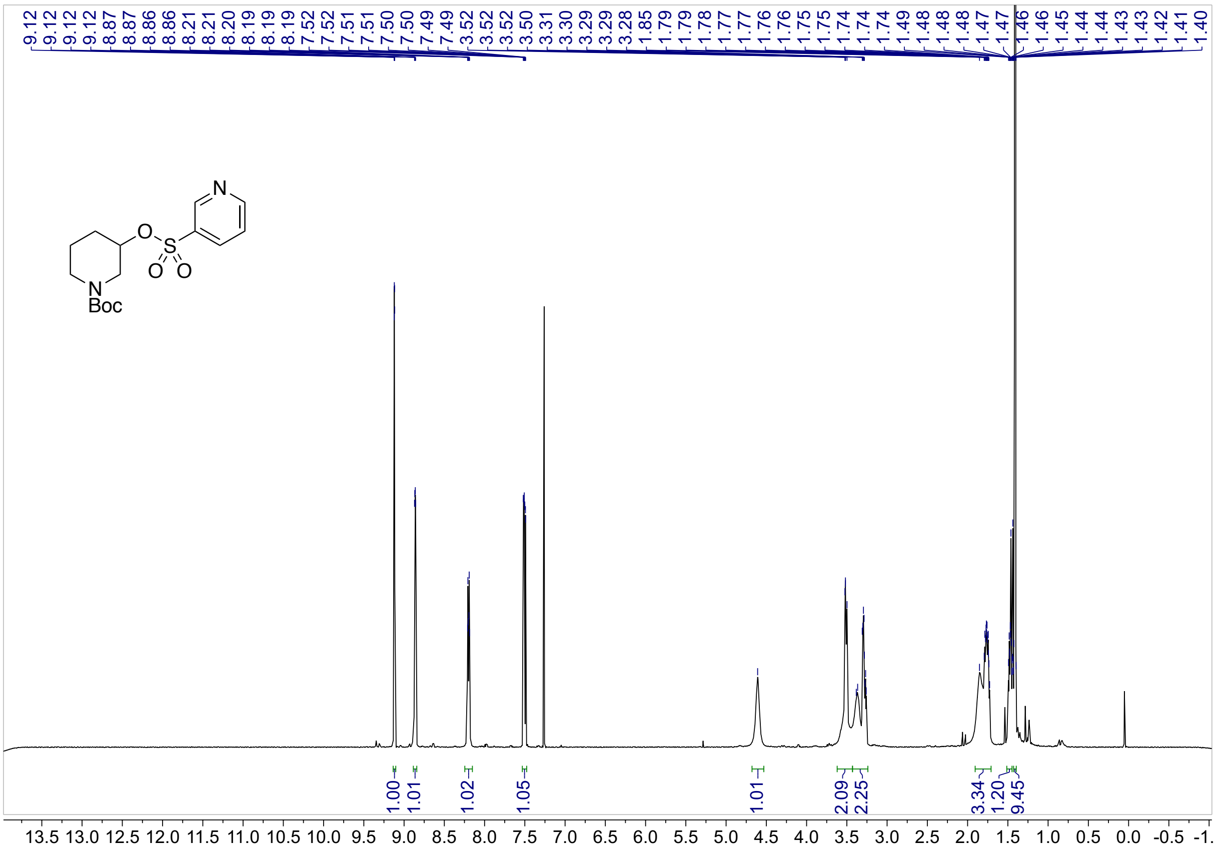


Figure S7: ^{1}H NMR (500 MHz, $CDCl_3$) of **2d**

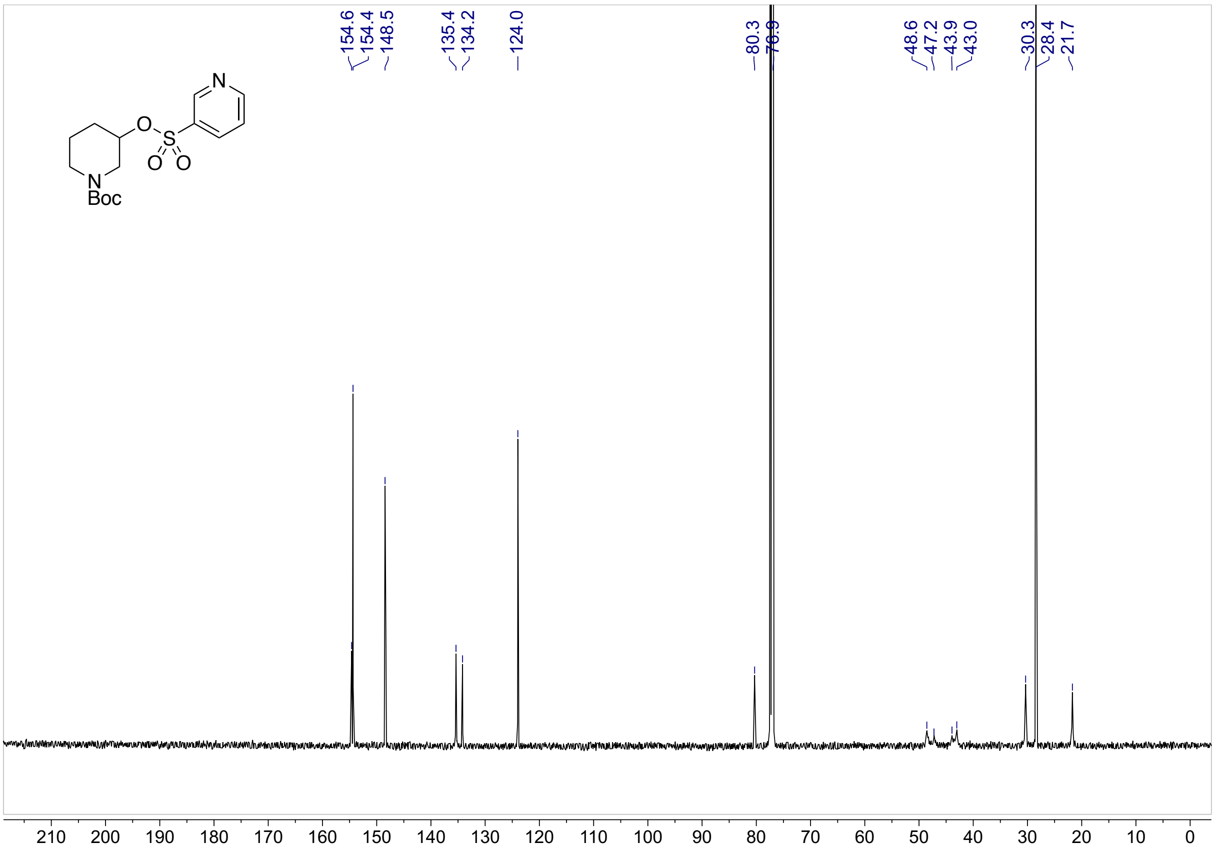


Figure S8: ^{13}C NMR (126 MHz, $CDCl_3$) of **2d**

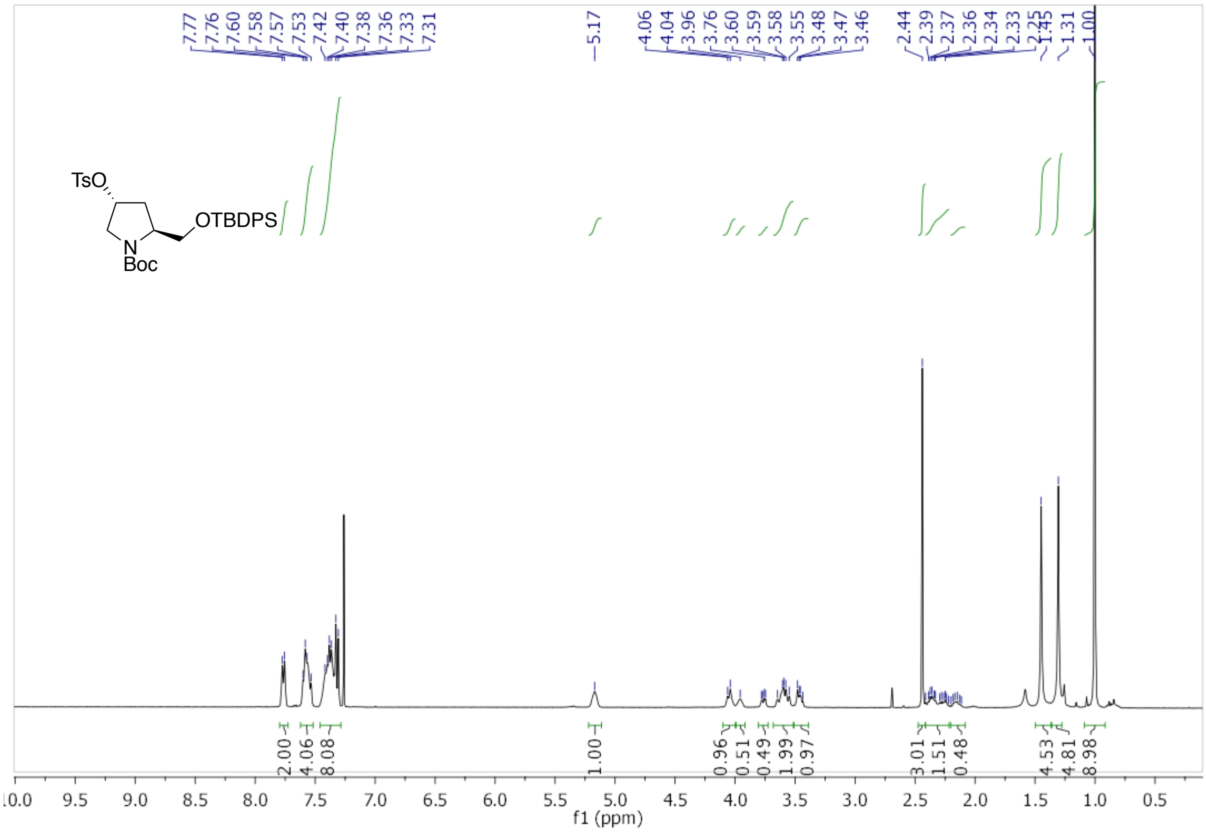


Figure S9: ^{1}H NMR (400 MHz, $CDCl_3$) of **S1**

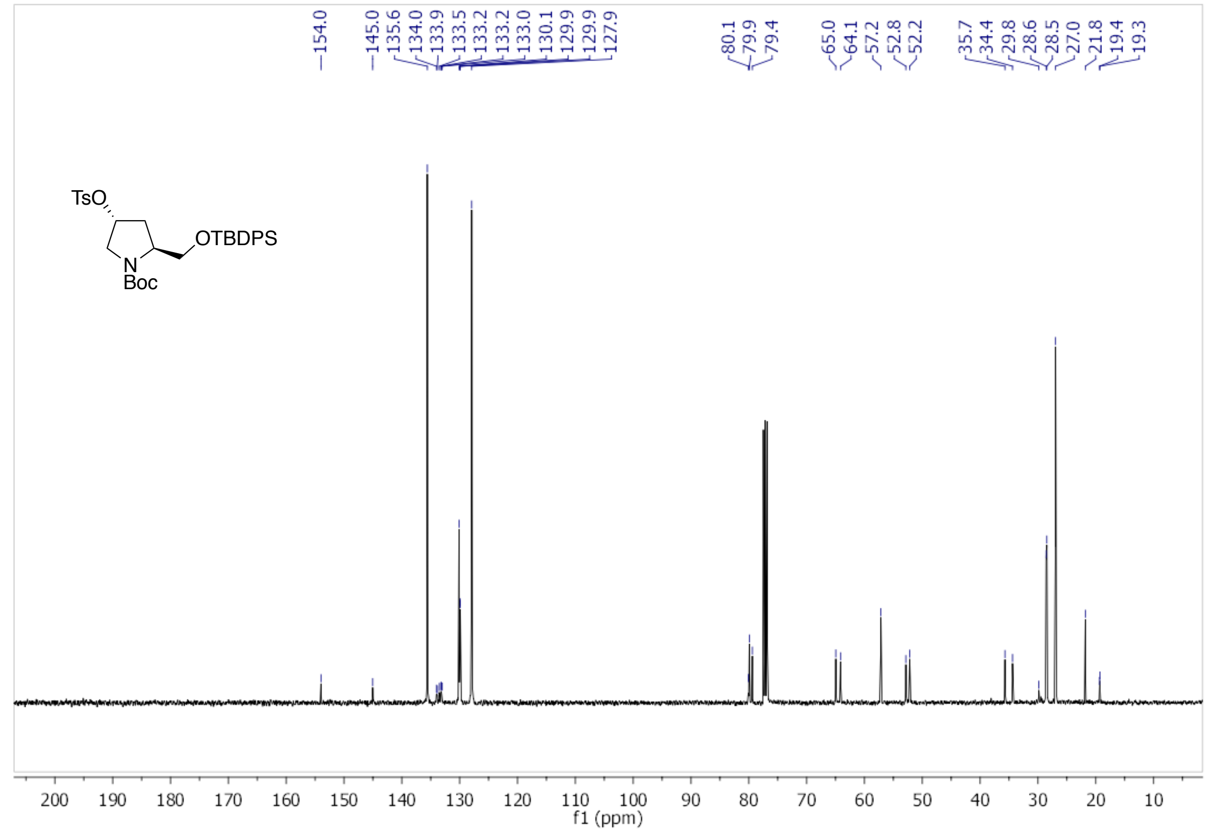


Figure S10: ^{13}C NMR (101 MHz, $CDCl_3$) of **S1**

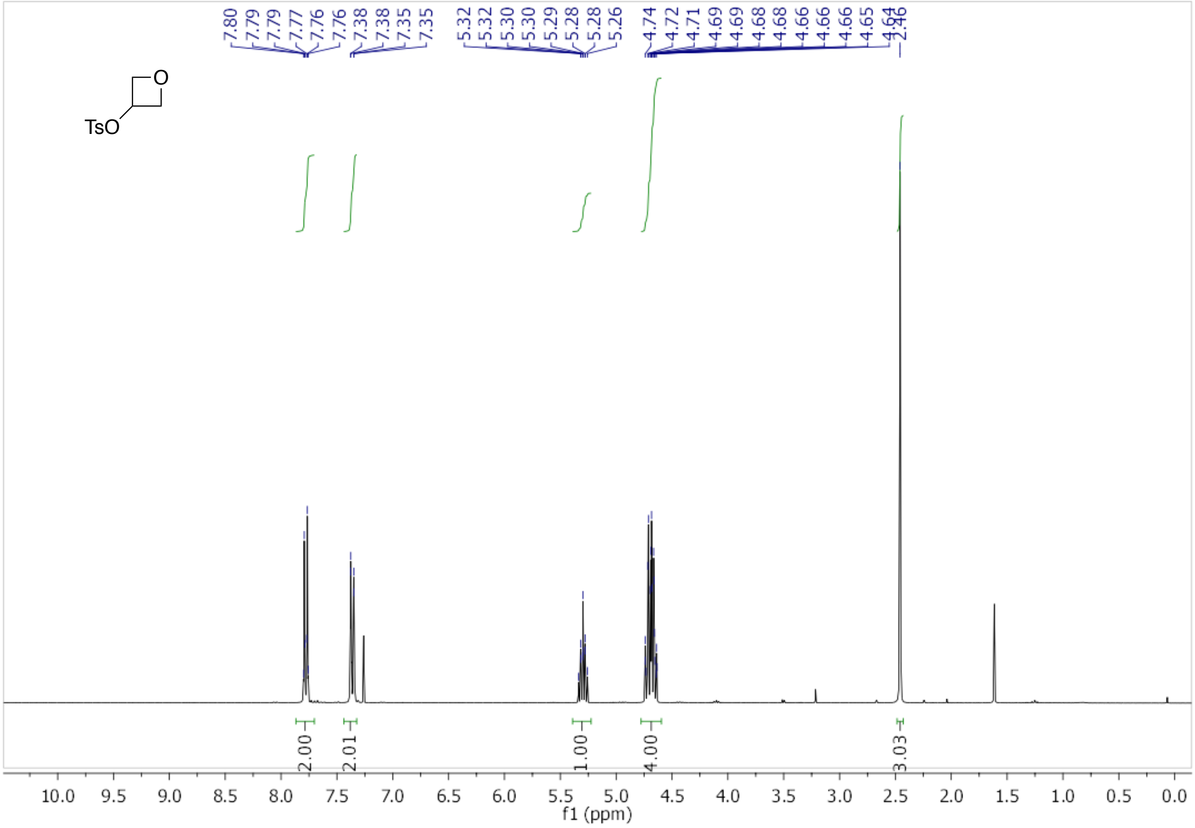


Figure S11 : ^{1}H NMR (300 MHz, $CDCl_3$) of **S2**

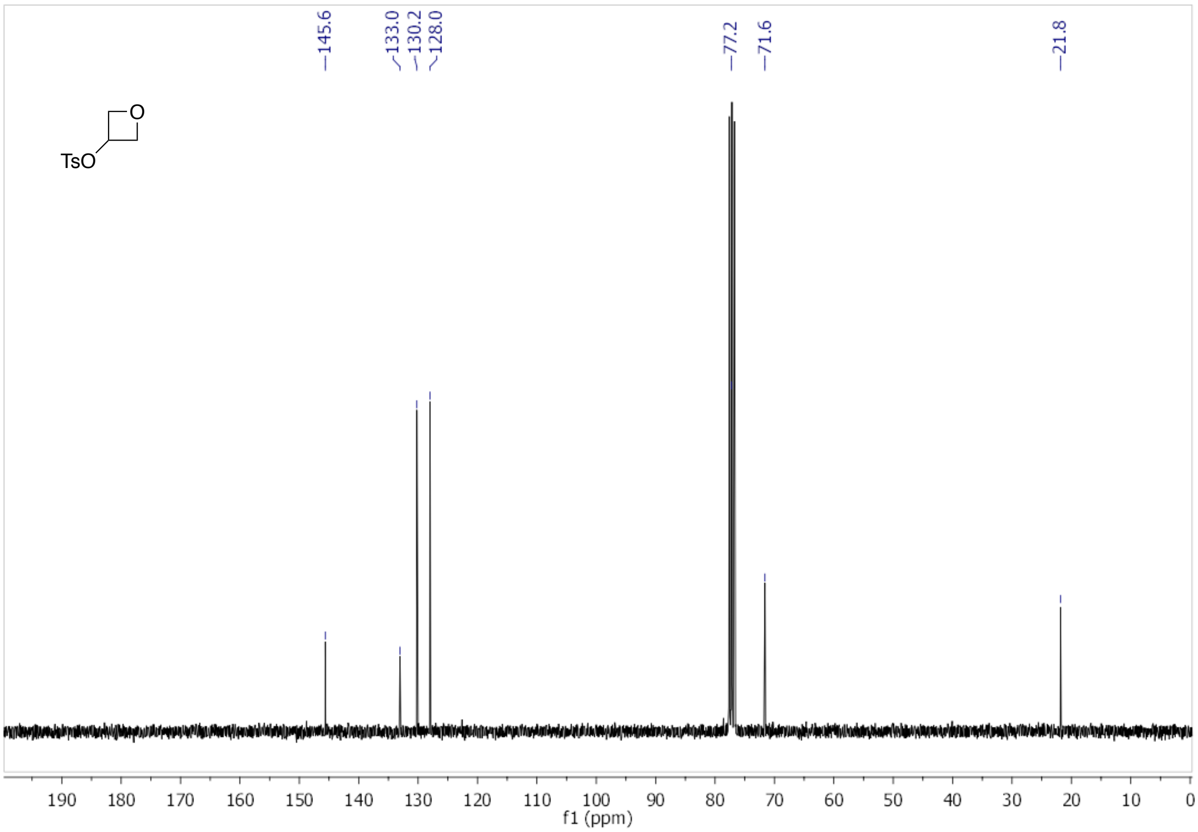


Figure S12 : ^{13}C NMR (75 MHz, $CDCl_3$) of **S2**

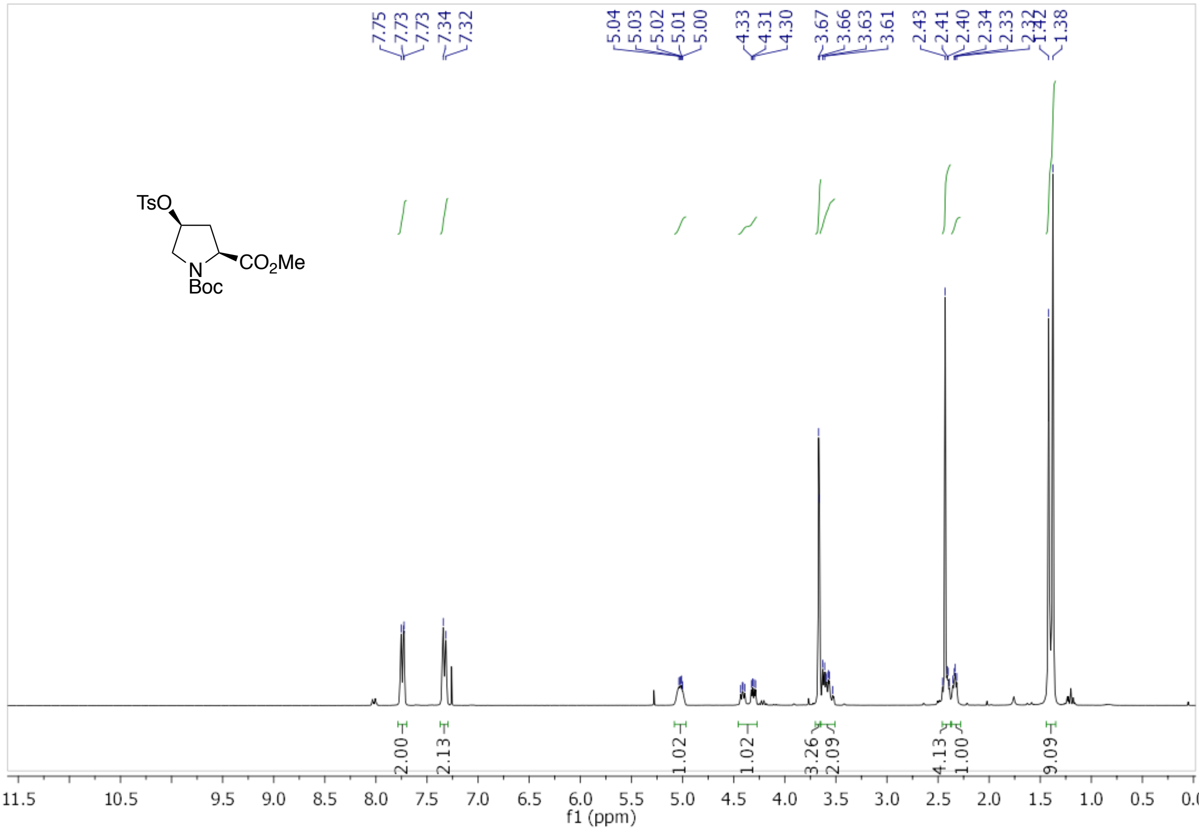


Figure S13: ^1H NMR (300 MHz, $CDCl_3$) of **S3**

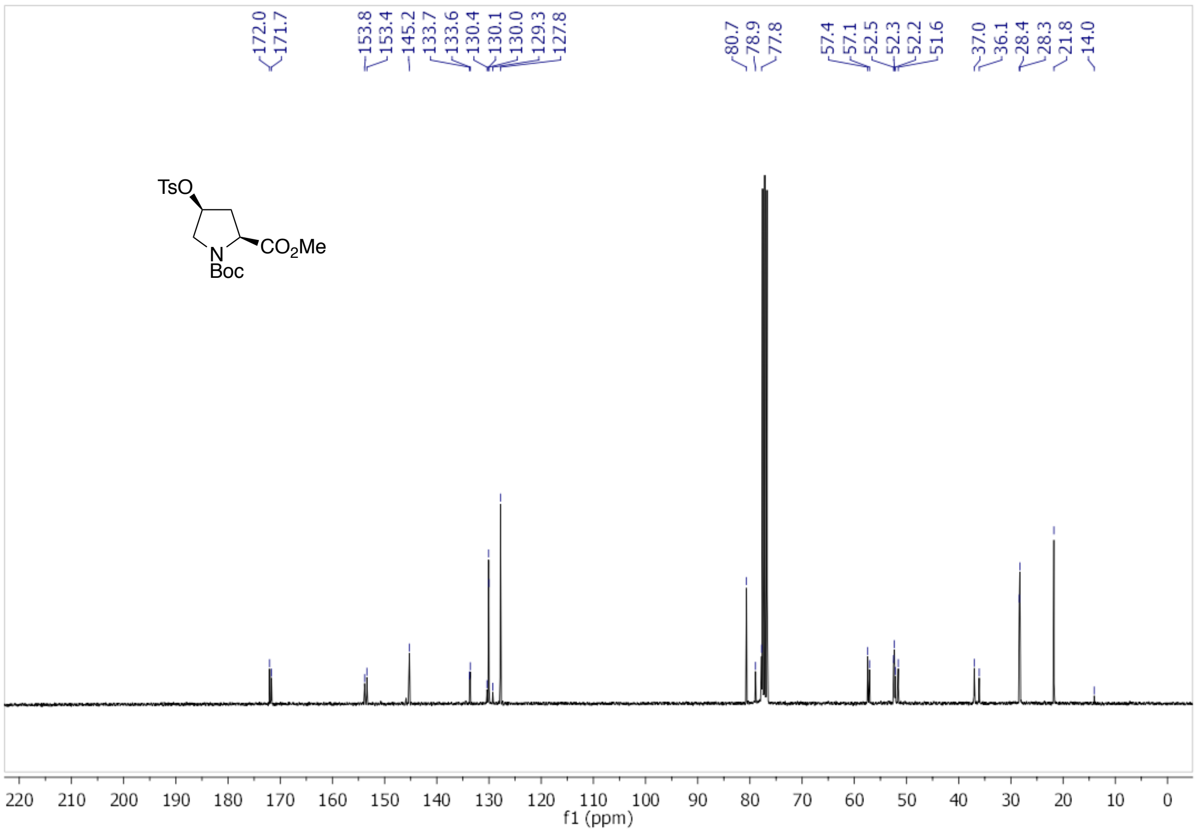


Figure S14: ^{13}C NMR (75 MHz, $CDCl_3$) of **S3**

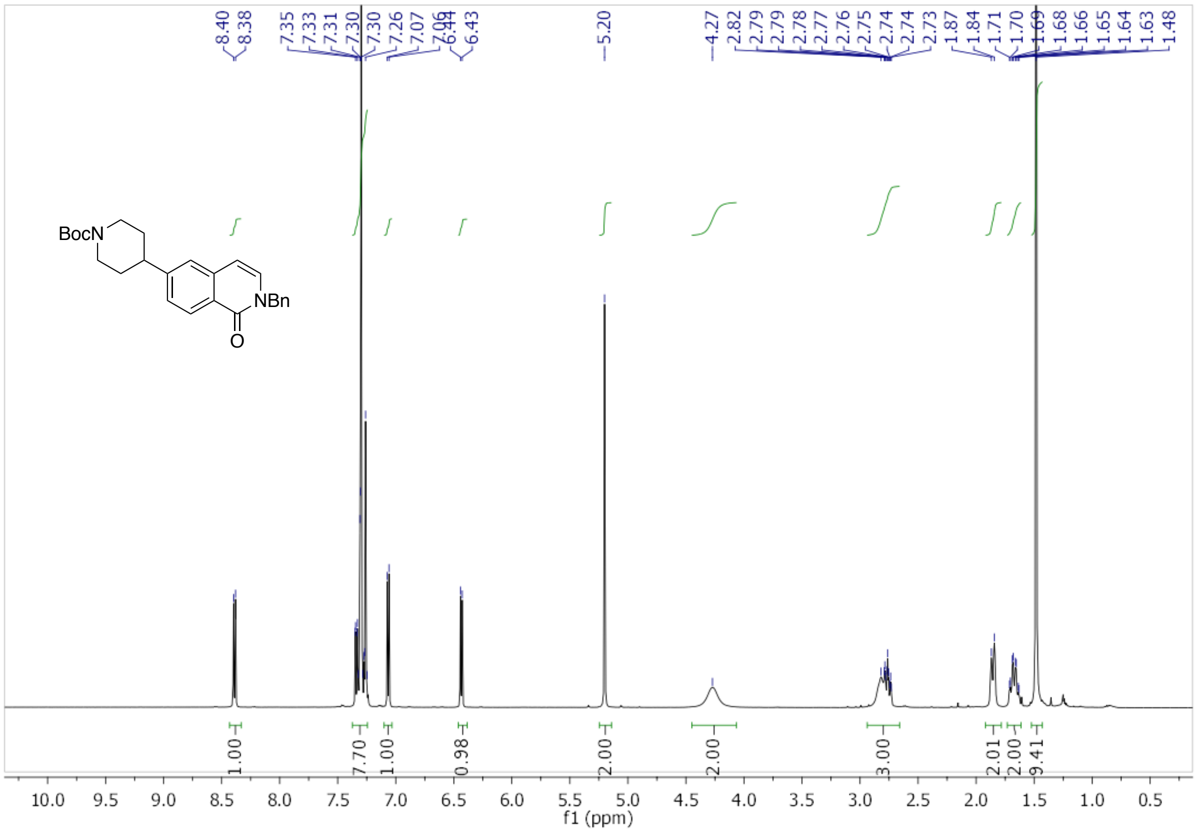


Figure S15: ^{1}H NMR (500 MHz, $CDCl_3$) of **3**

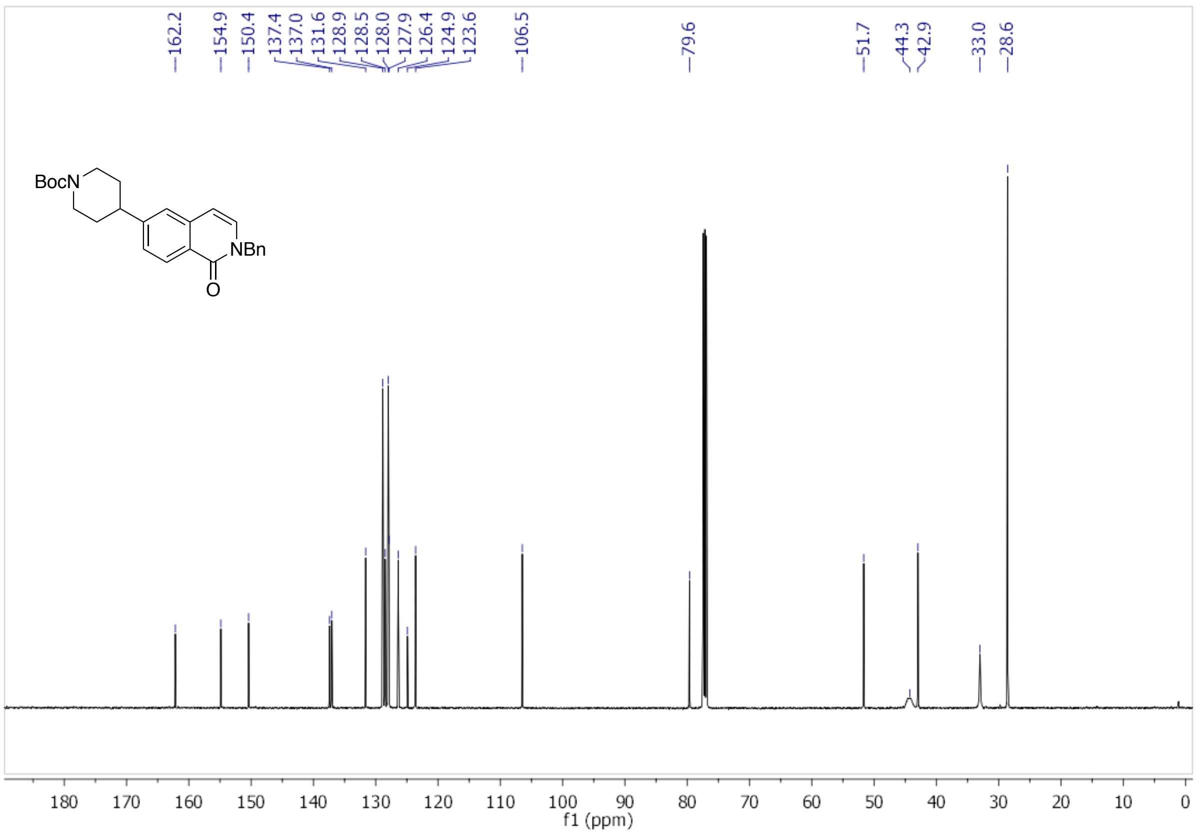


Figure S16: ^{13}C NMR (126 MHz, $CDCl_3$) of **3**

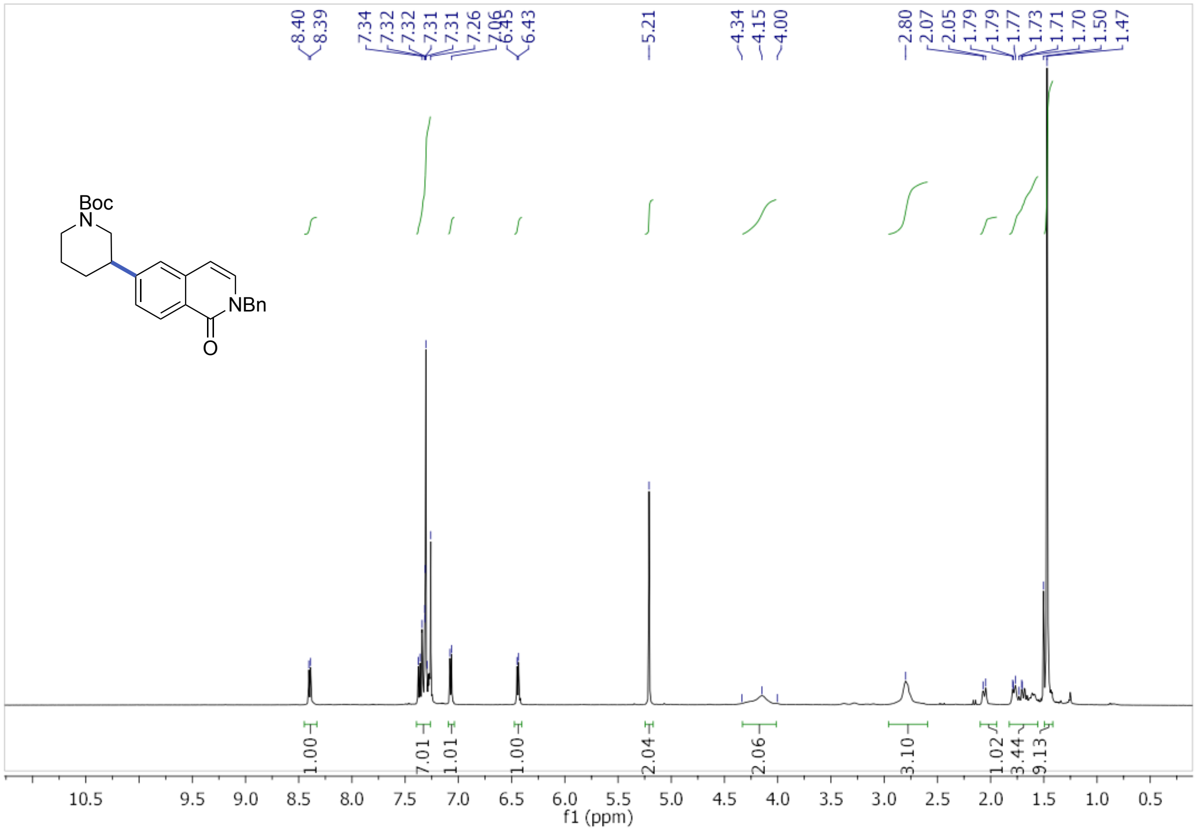


Figure S17: ^{1}H NMR (500 MHz, $CDCl_3$) of **5**

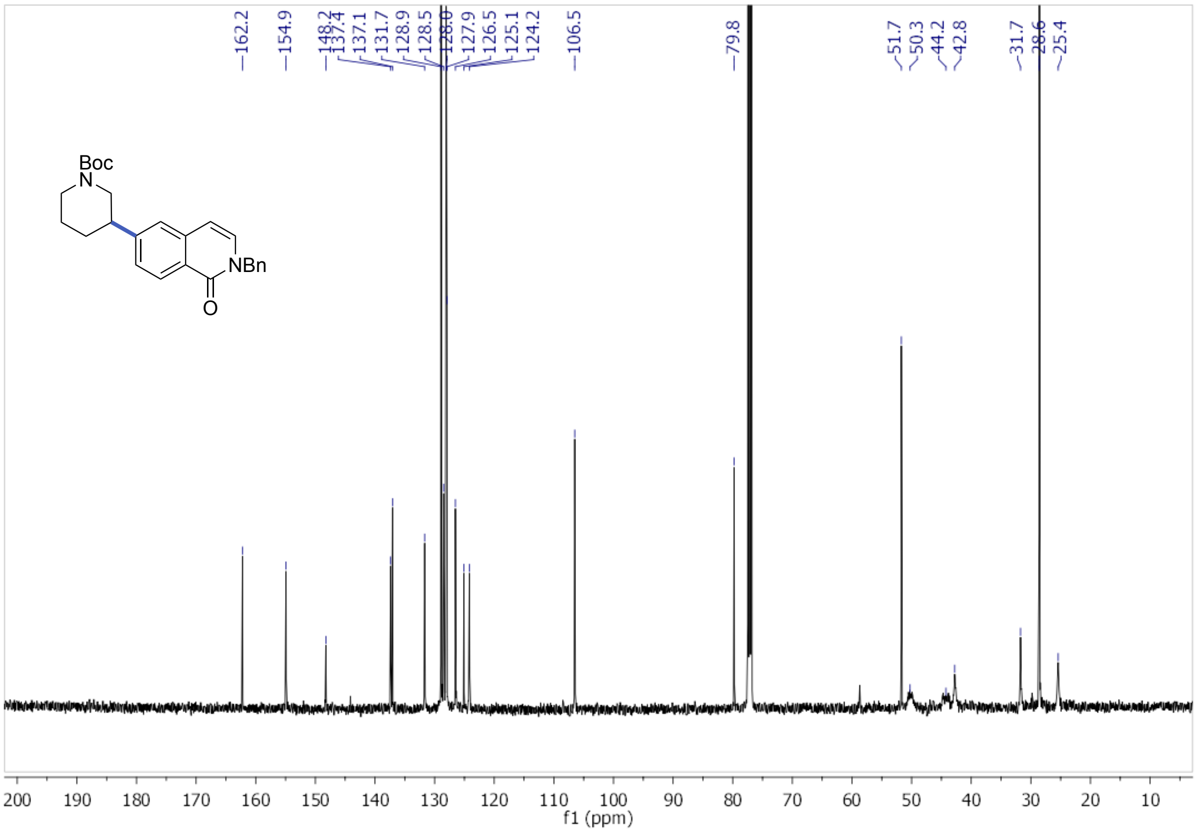


Figure S18: ^{13}C NMR (126 MHz, $CDCl_3$) of **5**

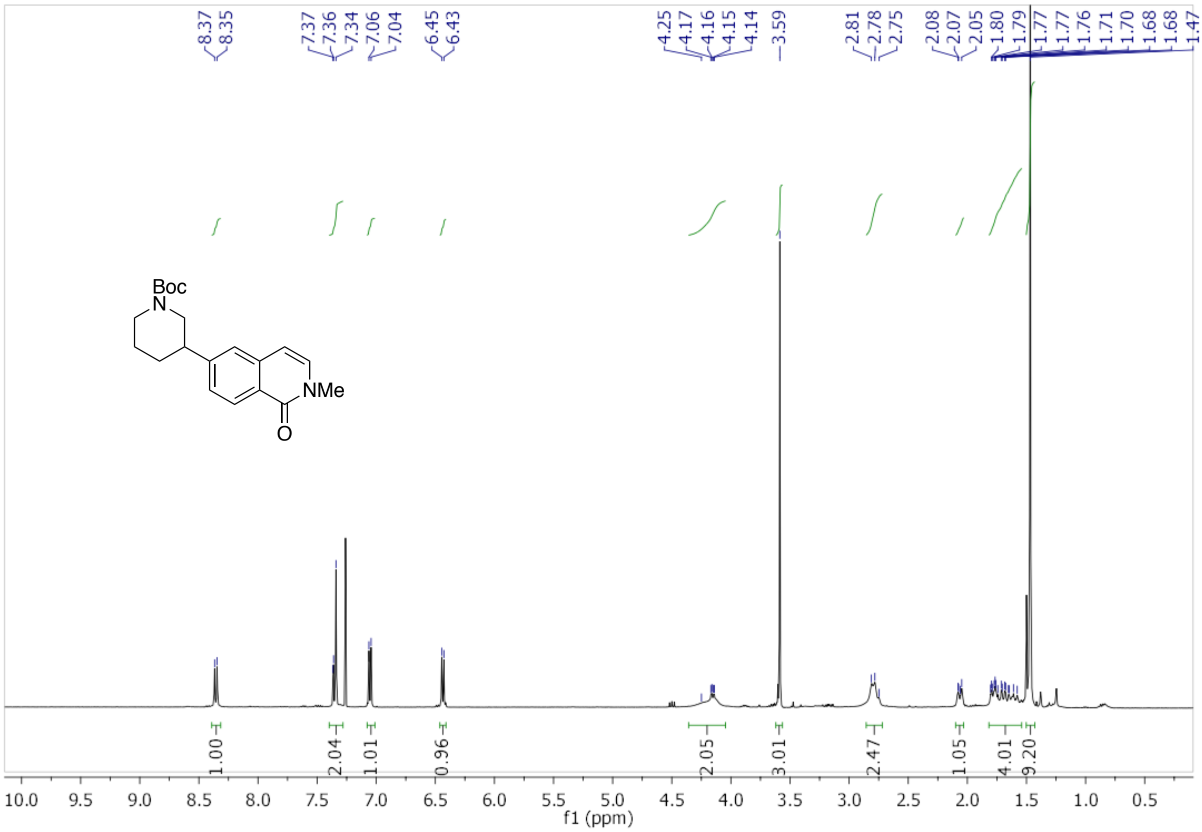


Figure S19: ^{1}H NMR (400 MHz, $CDCl_3$) of **6**

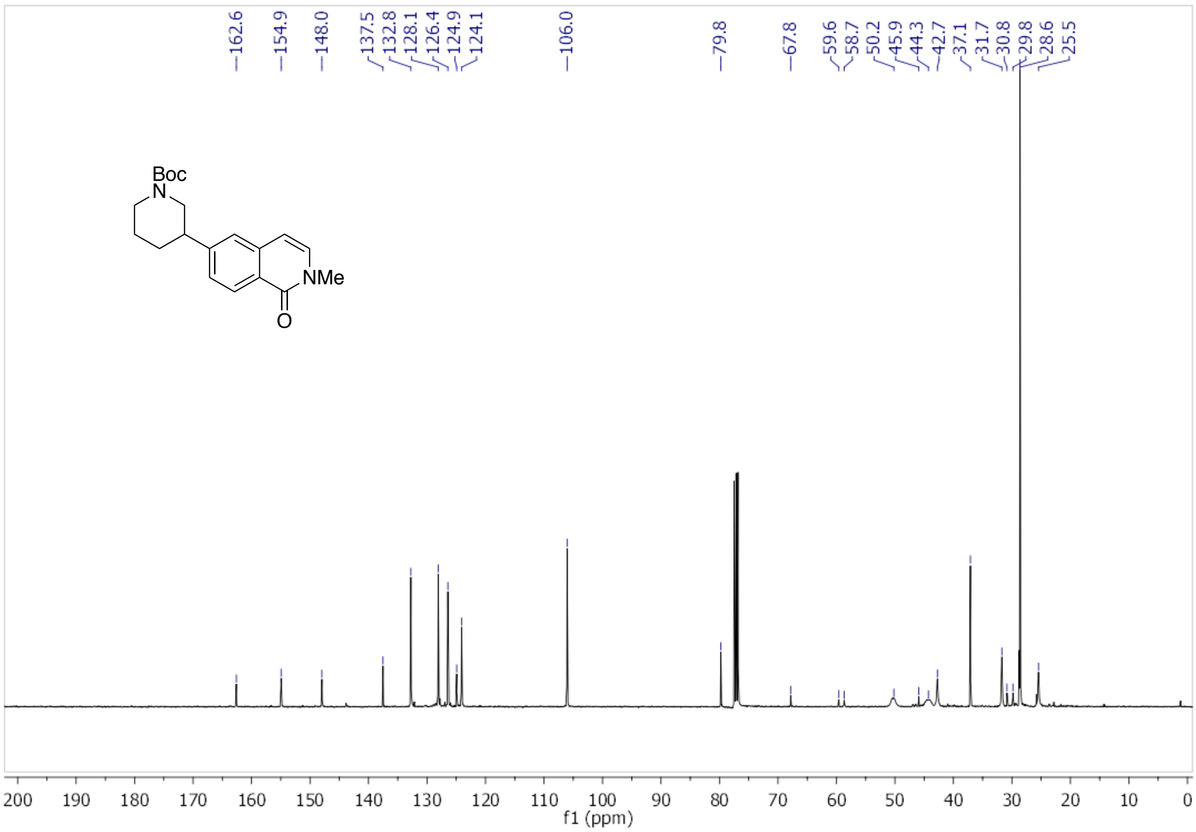


Figure S 20: ^{13}C NMR (75 MHz, $CDCl_3$) of **6**

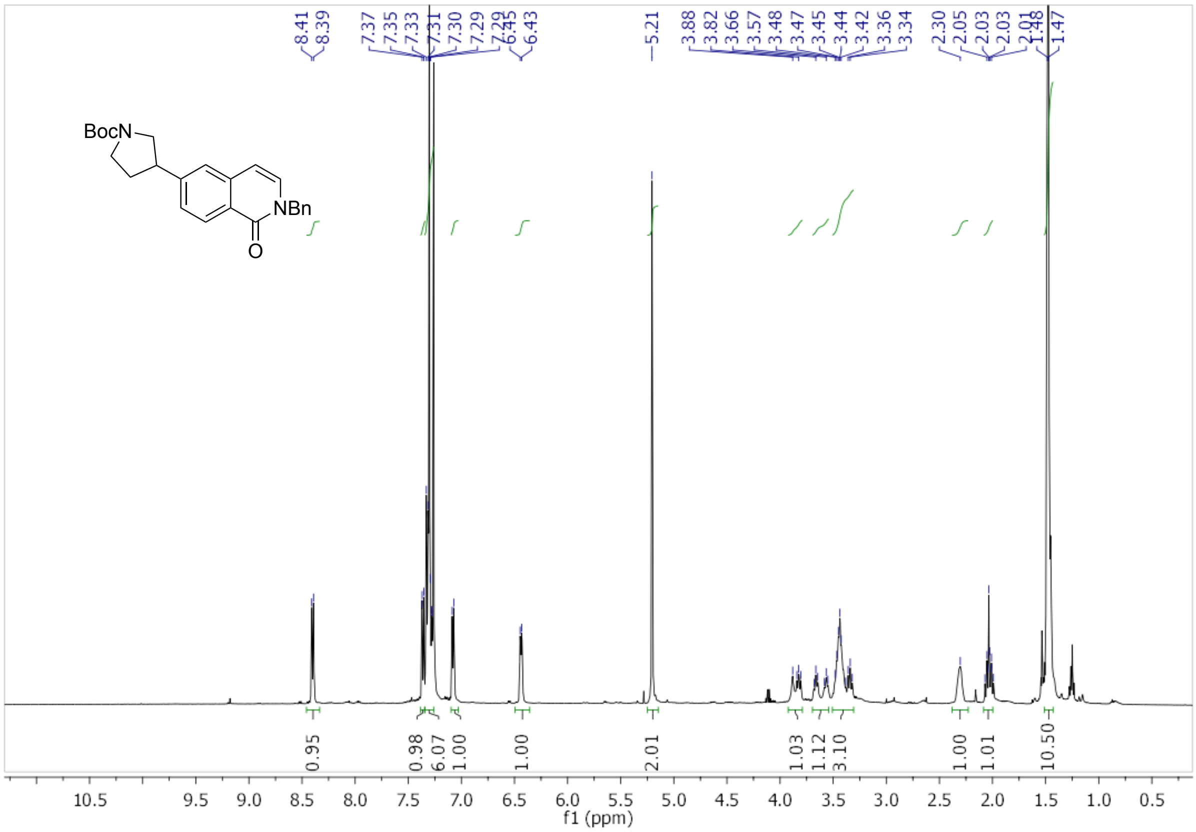


Figure S21: ^{1}H NMR (500 MHz, $CDCl_3$) of **7**

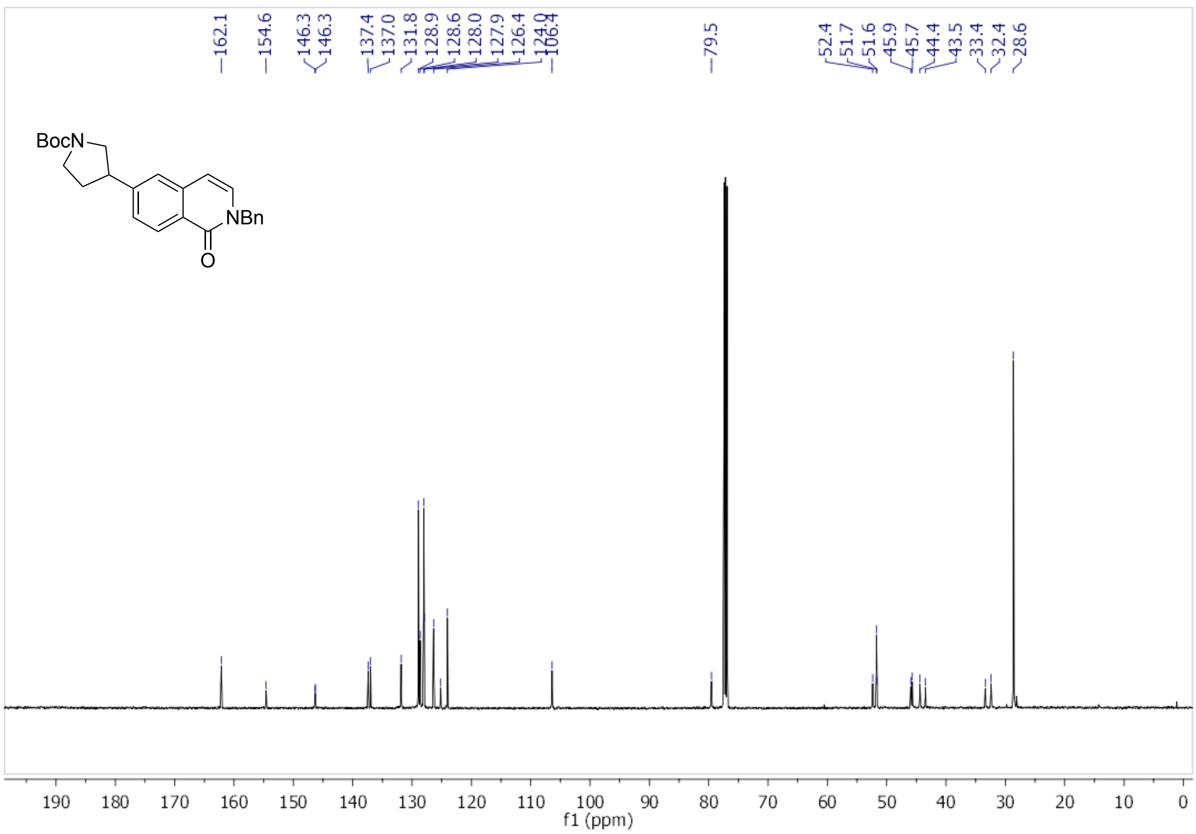


Figure S22: ^{13}C NMR (126 MHz, $CDCl_3$) of **7**

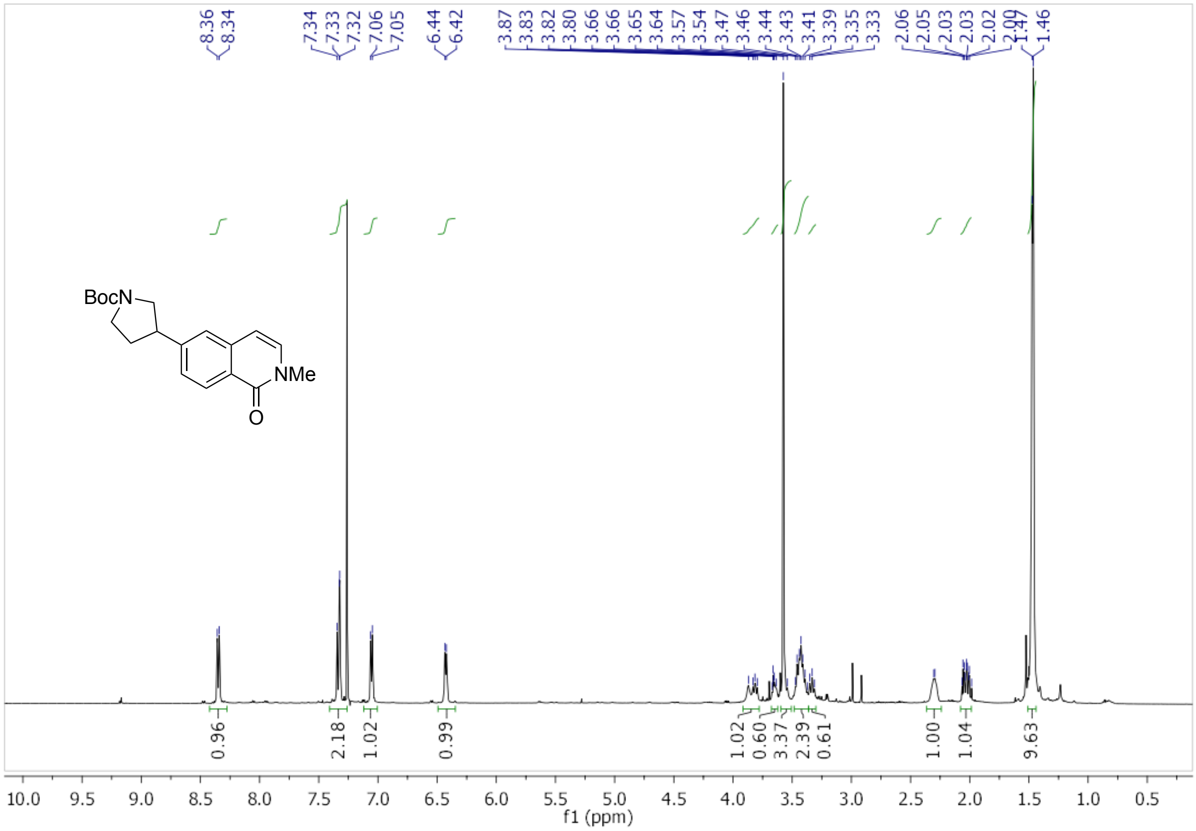


Figure S23: ^{1}H NMR (500 MHz, $CDCl_3$) of **8**

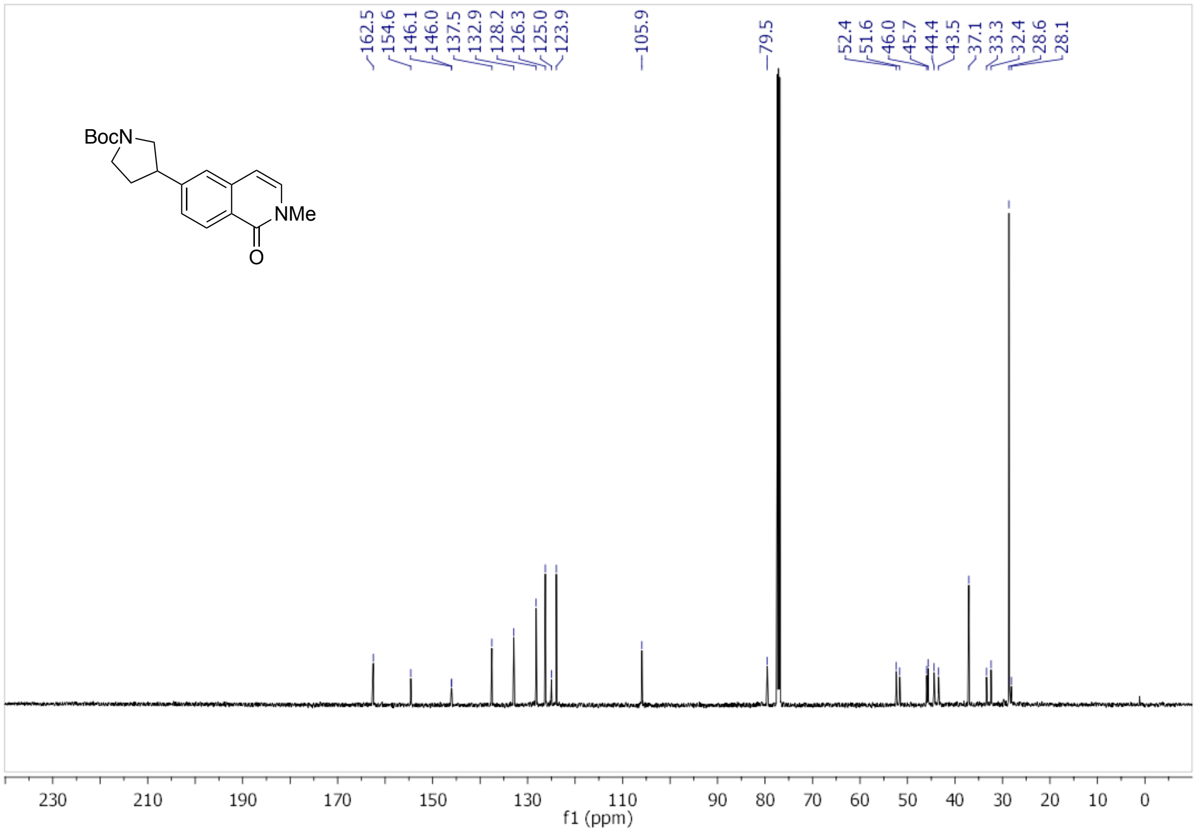


Figure S24: ^{13}C NMR (126 MHz, $CDCl_3$) of **8**

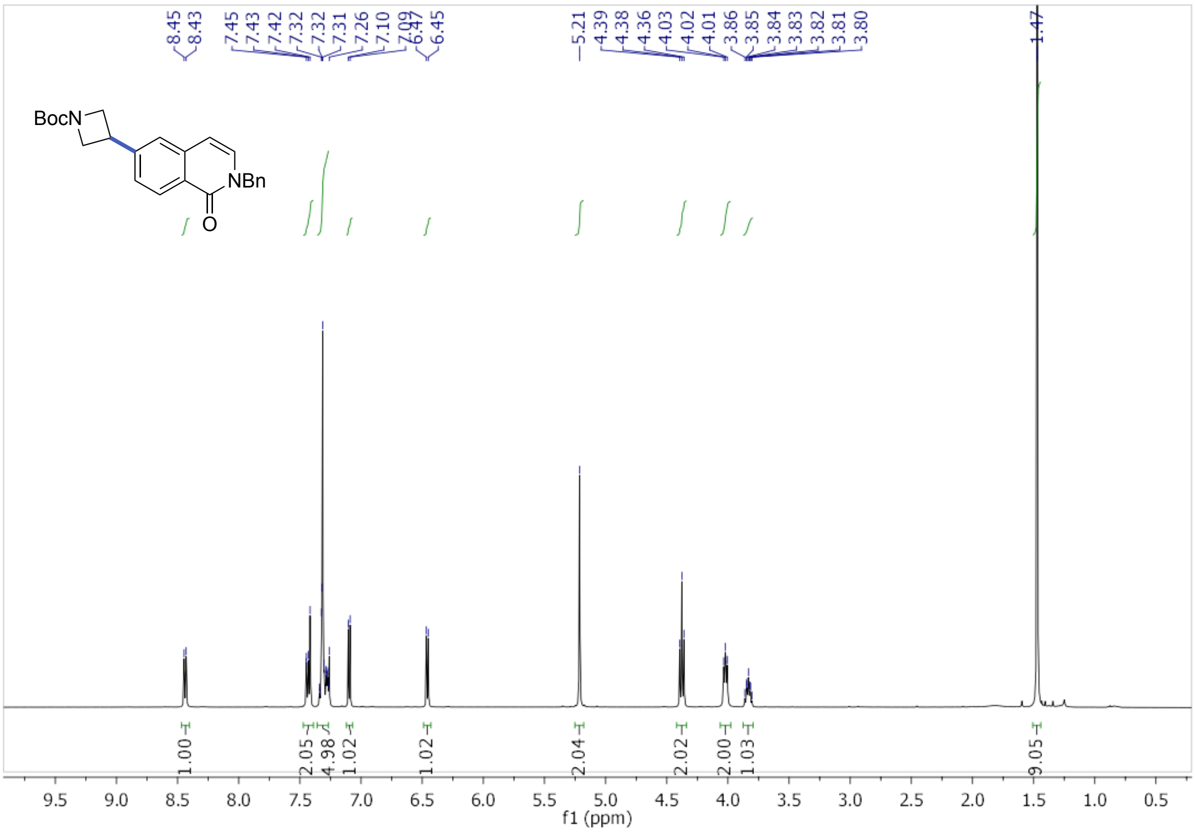


Figure S25: ^{1}H NMR (500 MHz, $CDCl_3$) of **9a**

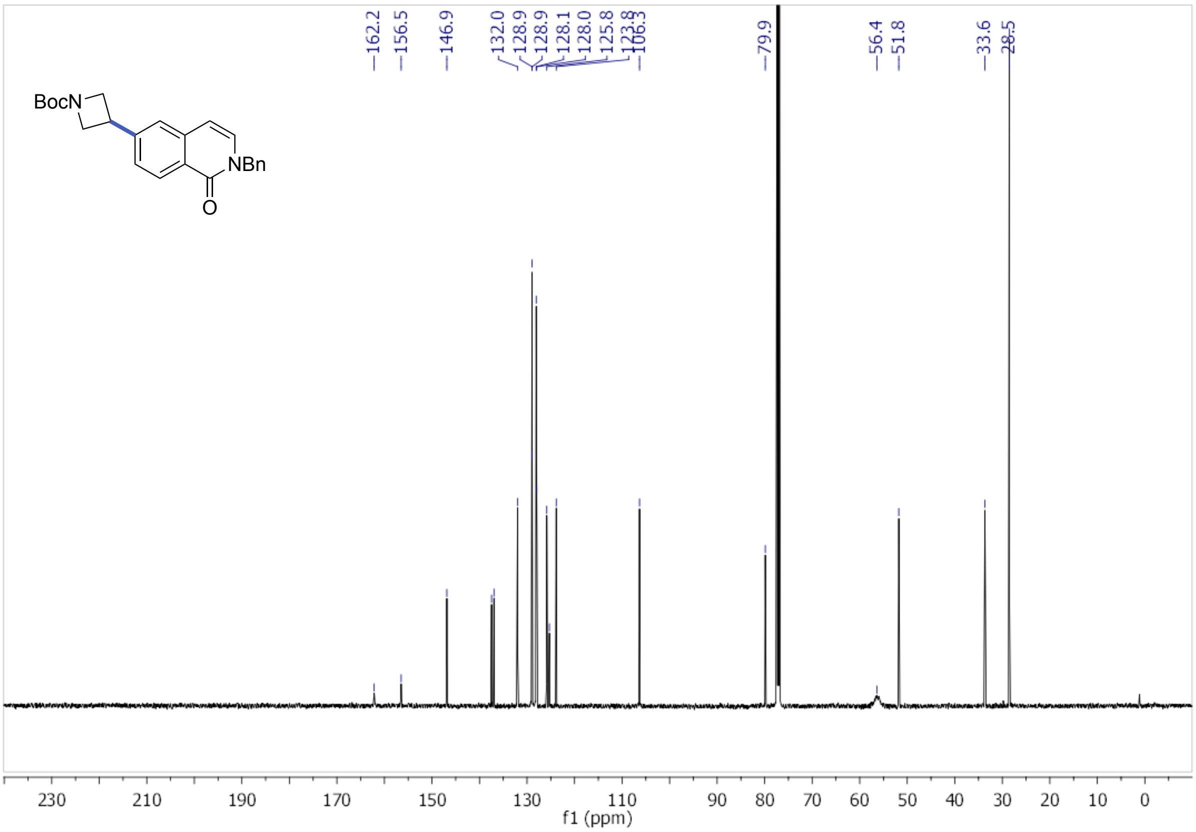


Figure S26: ^{13}C NMR (126 MHz, $CDCl_3$) of **9a**

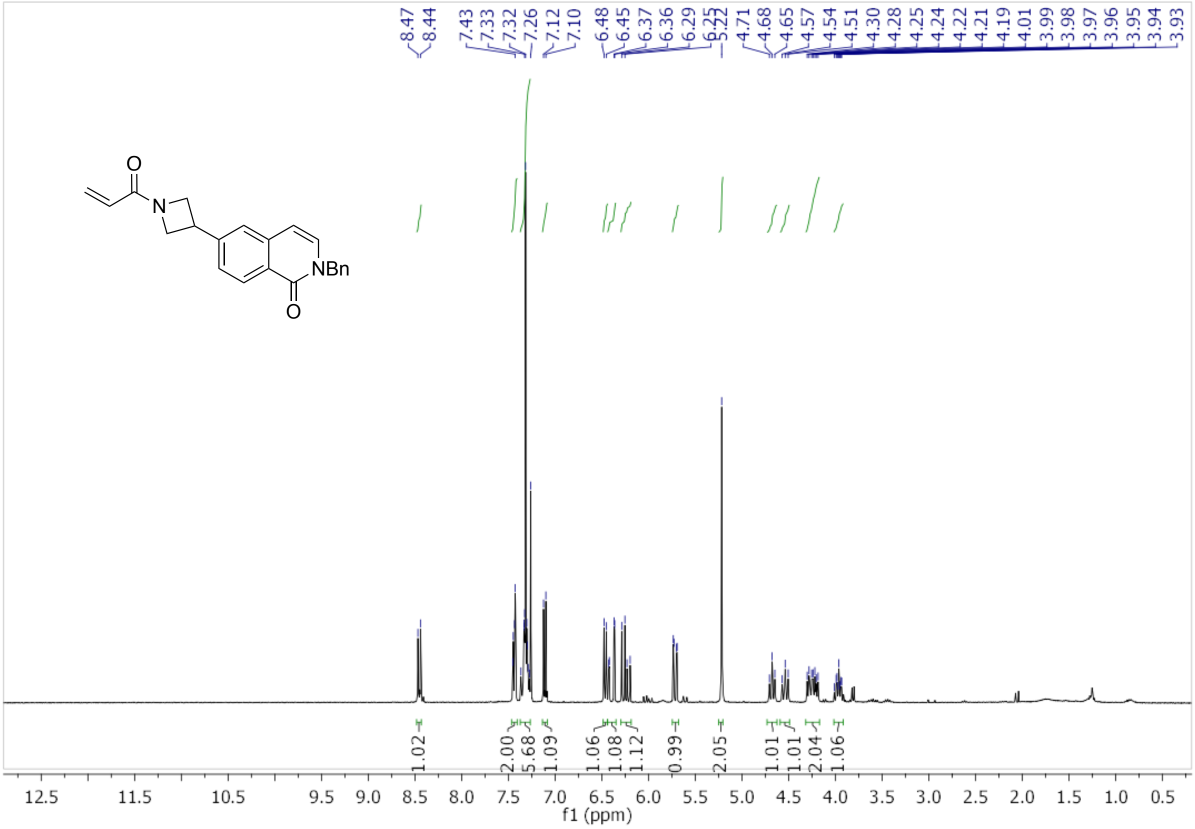


Figure S27: ^{1}H NMR (300 MHz, $CDCl_3$) of **9b**

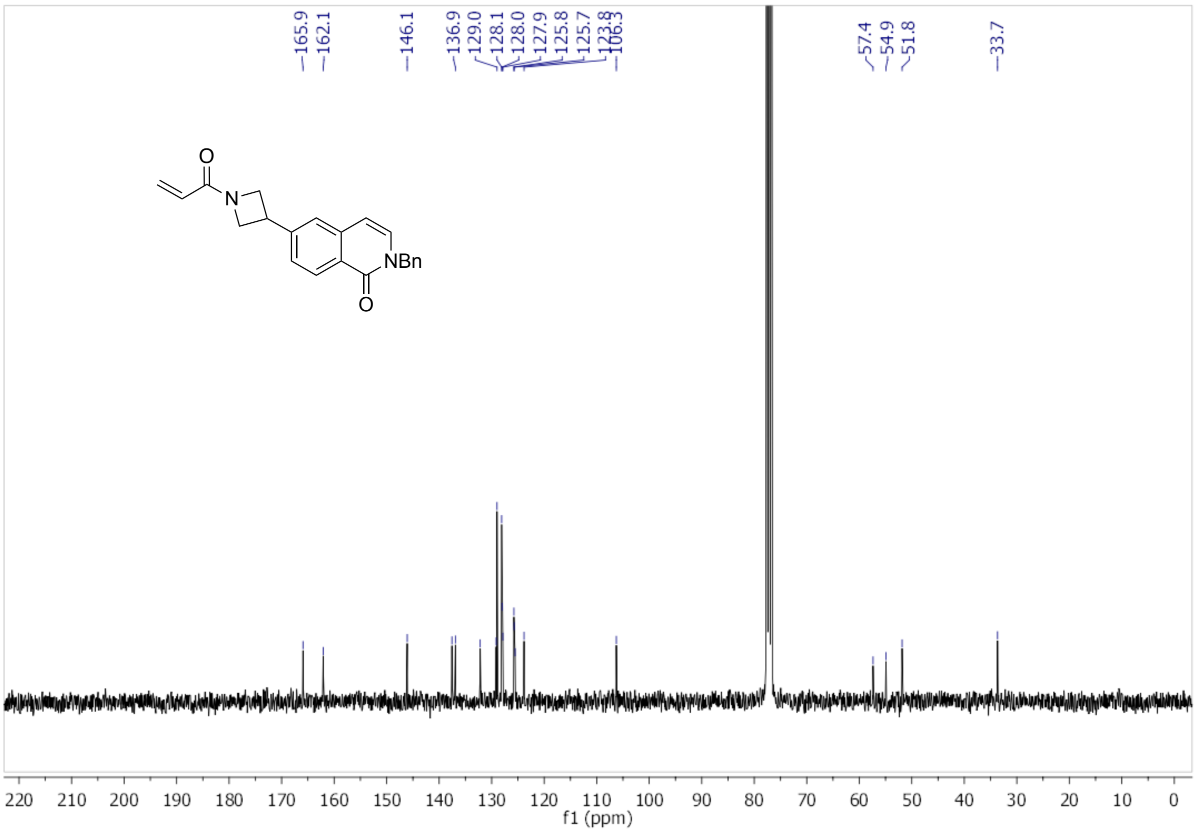


Figure S28: ^{13}C NMR (75 MHz, $CDCl_3$) of **9b**

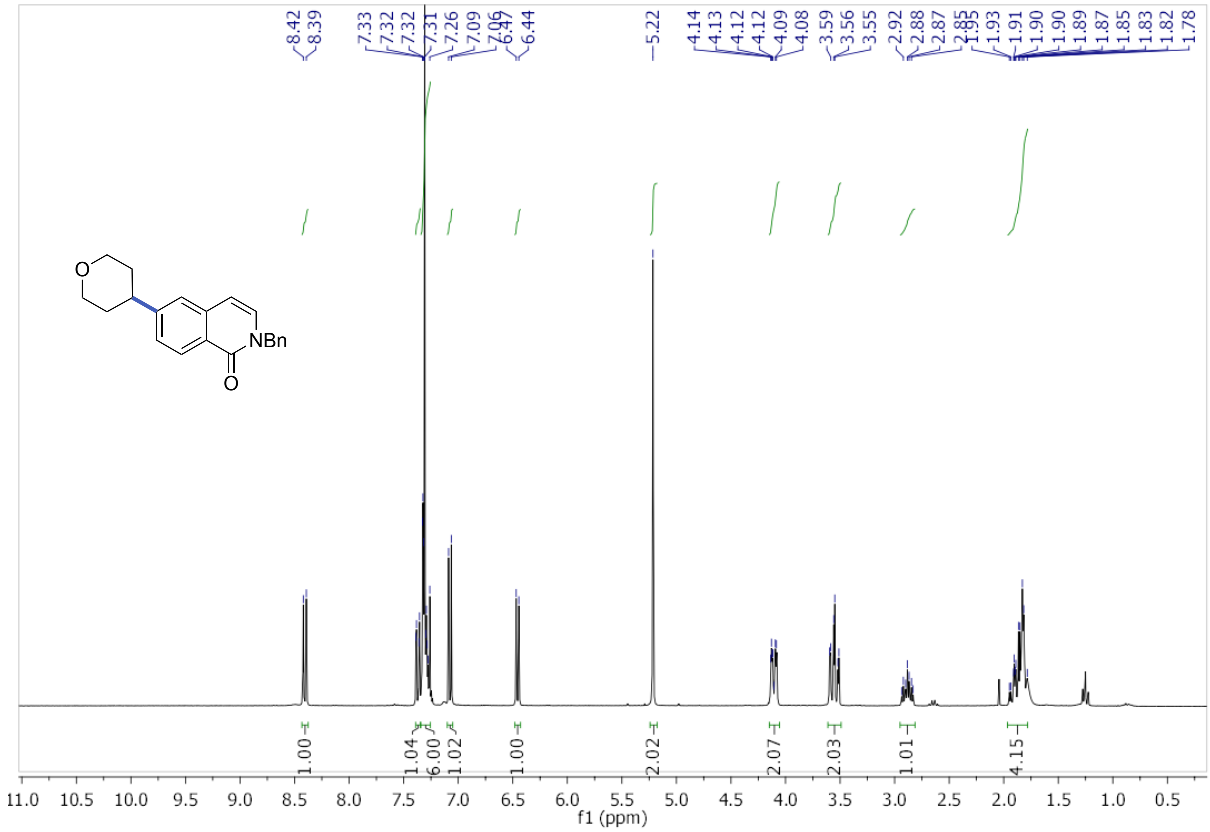


Figure S29: ^{1}H NMR (300 MHz, $CDCl_3$) of **11**

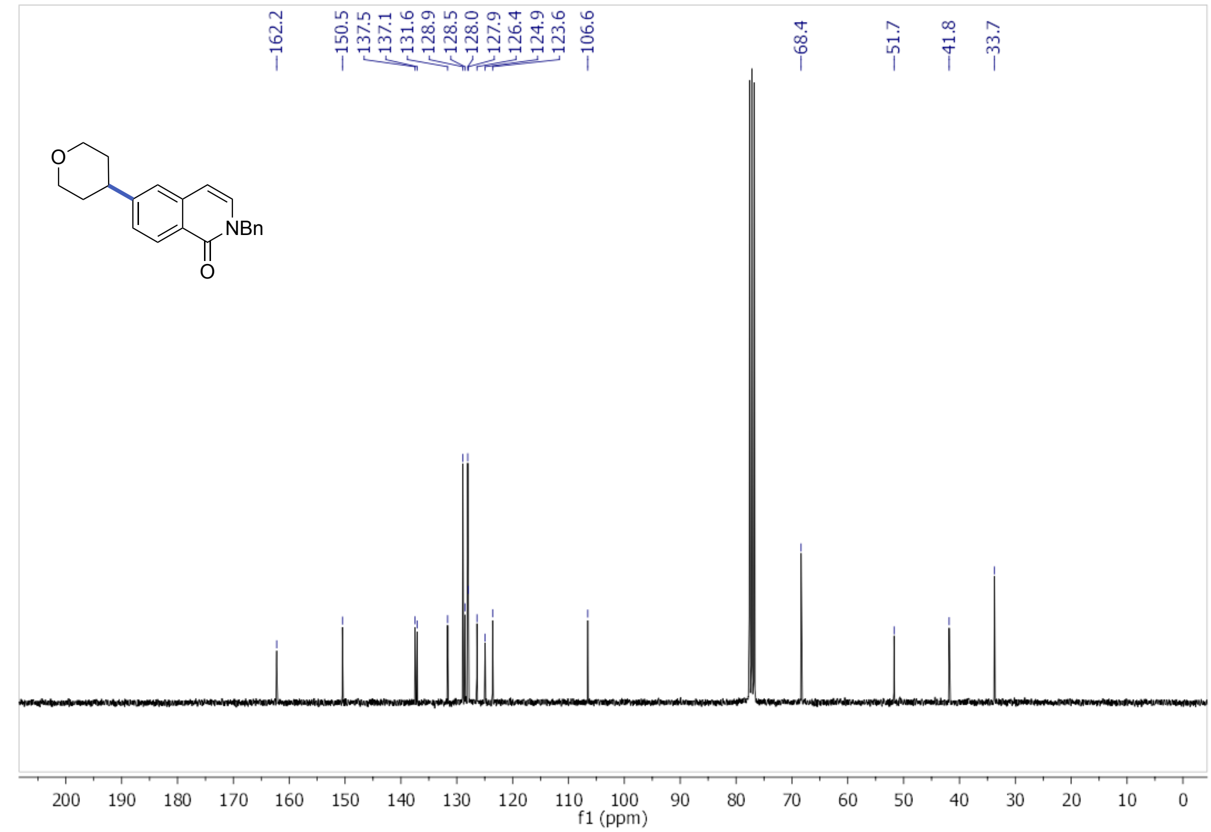


Figure S30: ^{13}C NMR (75 MHz, $CDCl_3$) of **11**

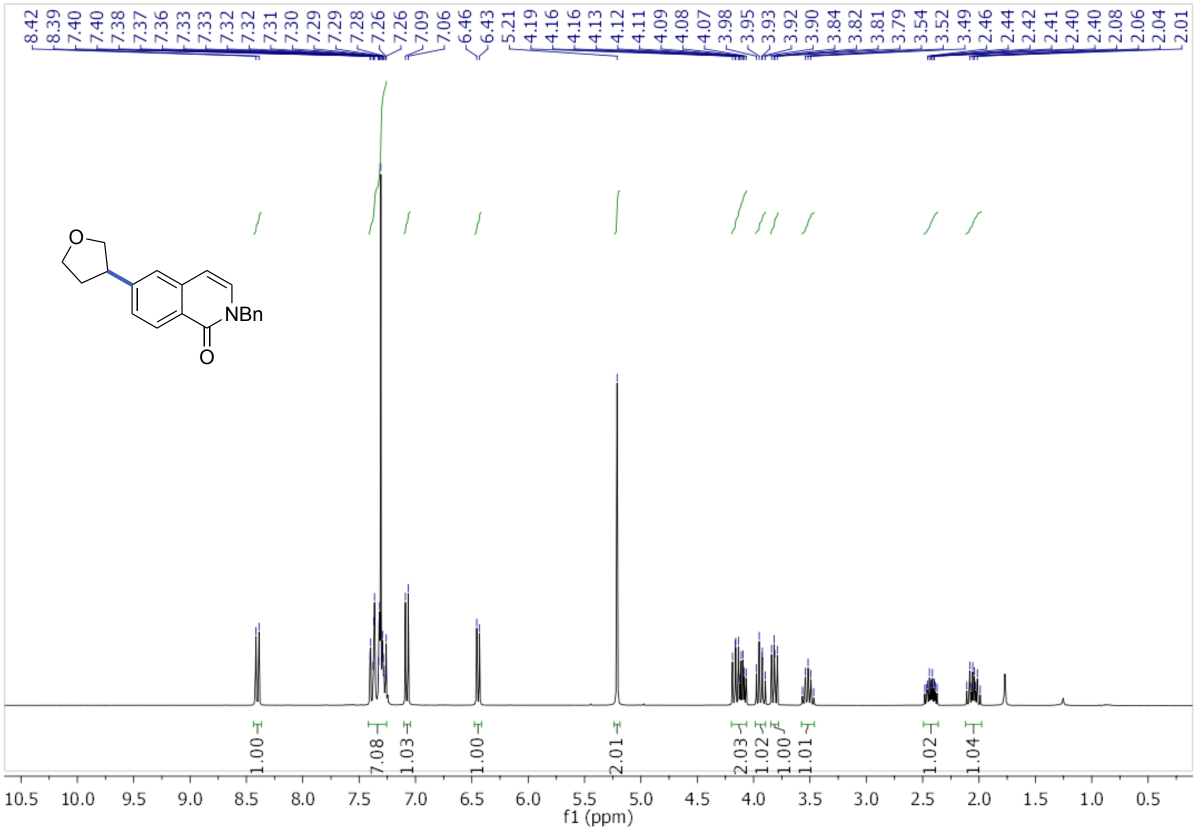


Figure S31: ^{1}H NMR (300 MHz, $CDCl_3$) of **12**

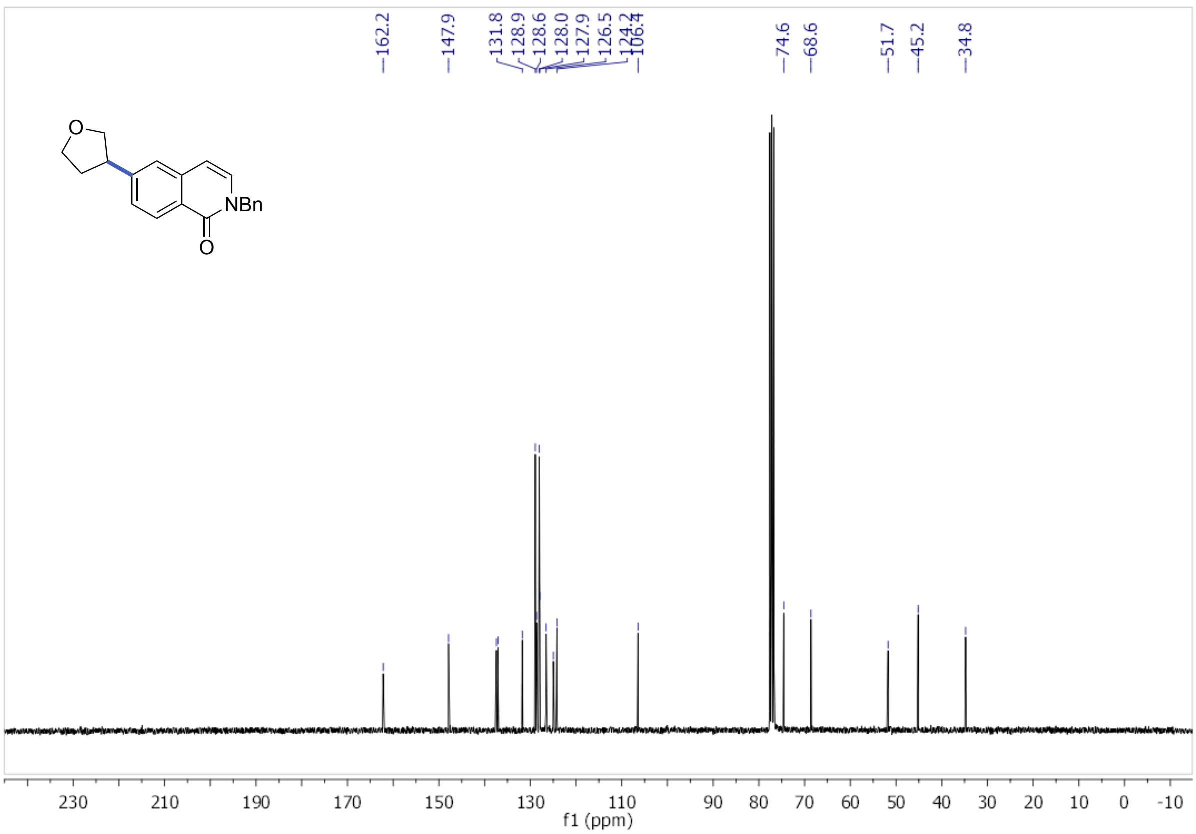


Figure S32 : ^{13}C NMR (75 MHz, $CDCl_3$) of **12**

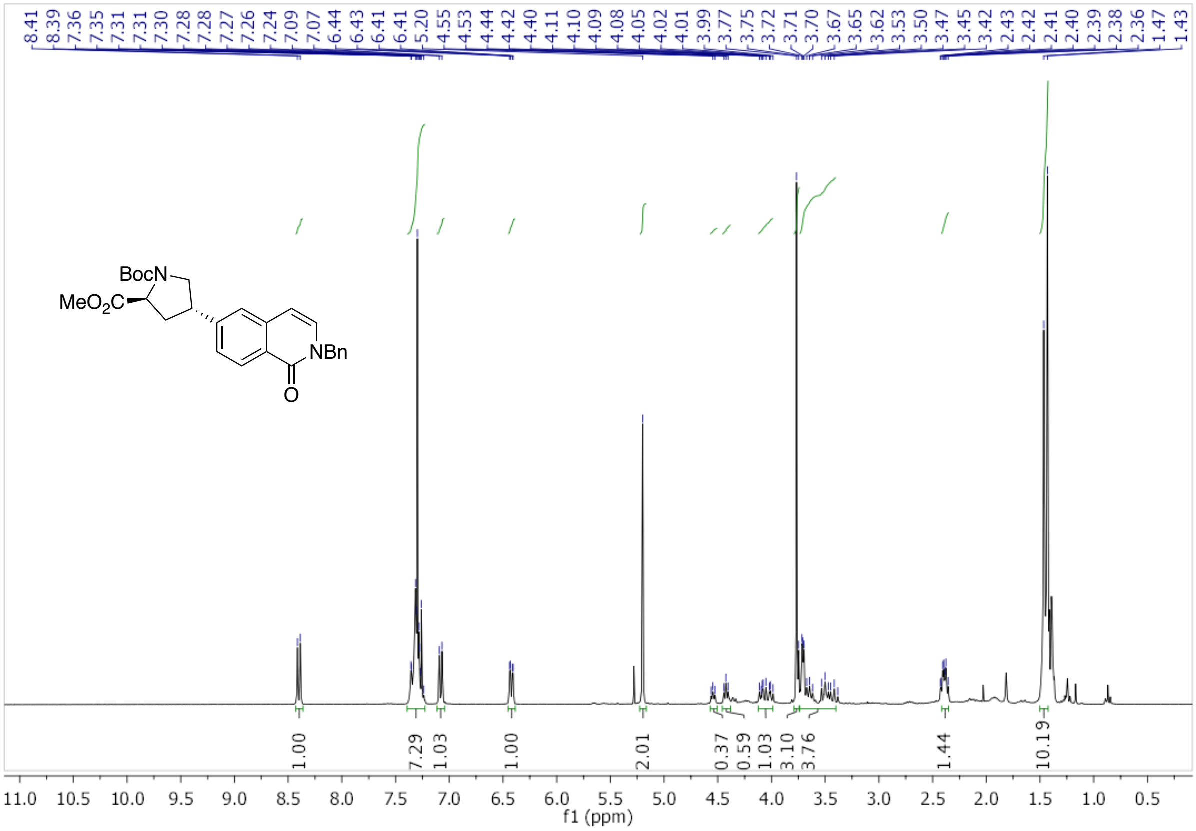


Figure S33: ^{1}H NMR (300 MHz, $CDCl_3$) of **13**

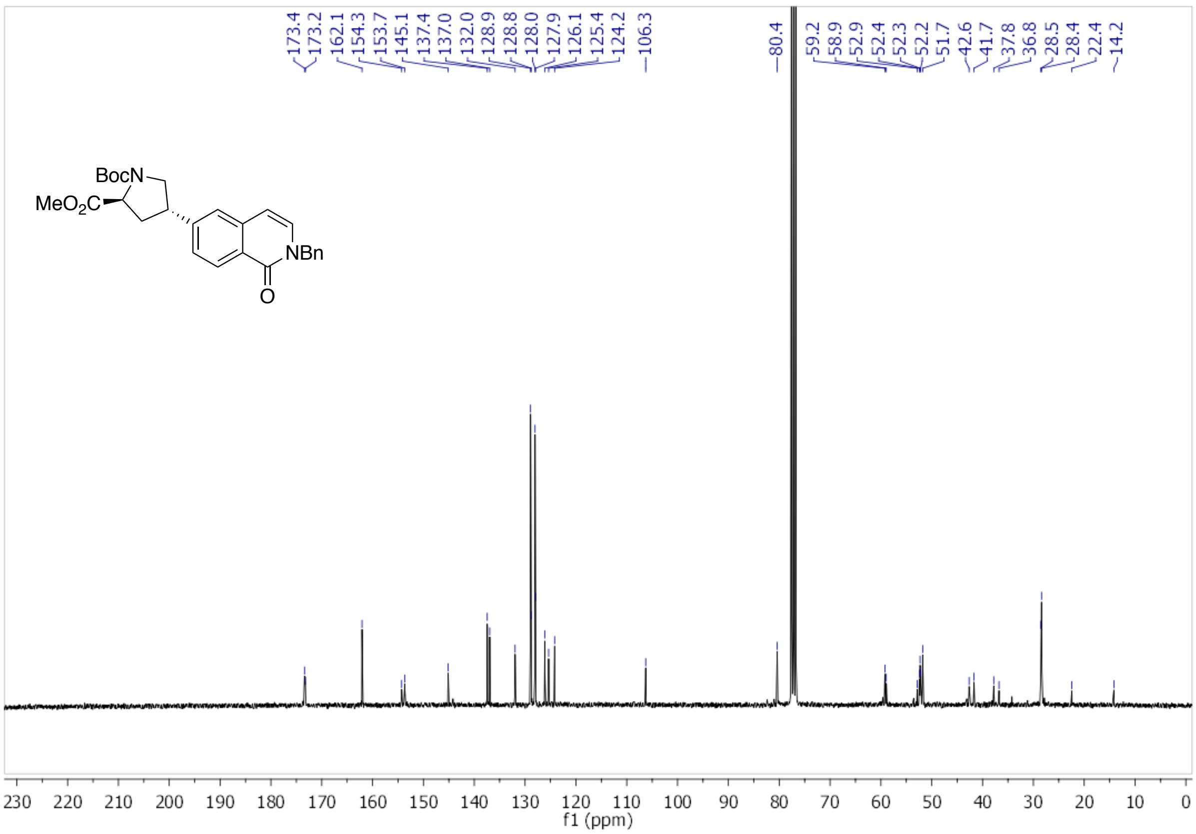


Figure S34: ^{13}C NMR (75 MHz, $CDCl_3$) of **13**

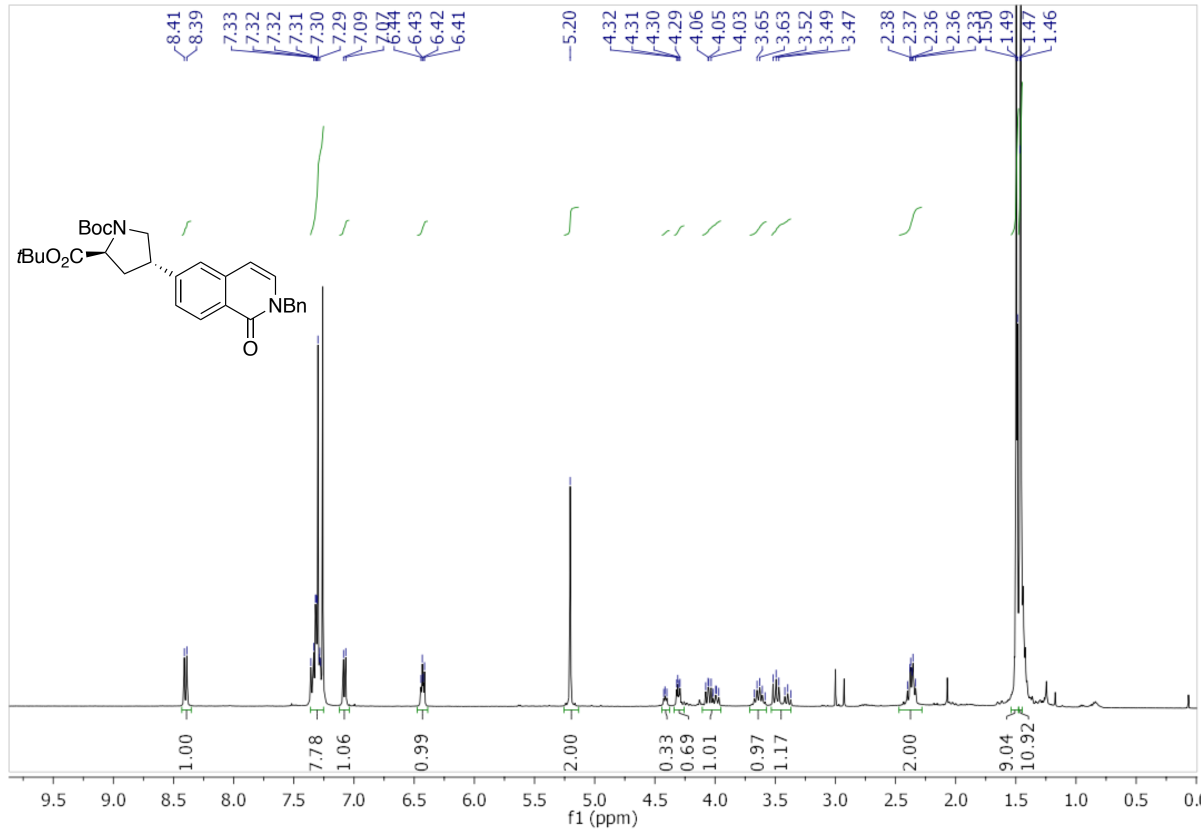


Figure S35: ^{1}H NMR (400 MHz, $CDCl_3$) of **14**

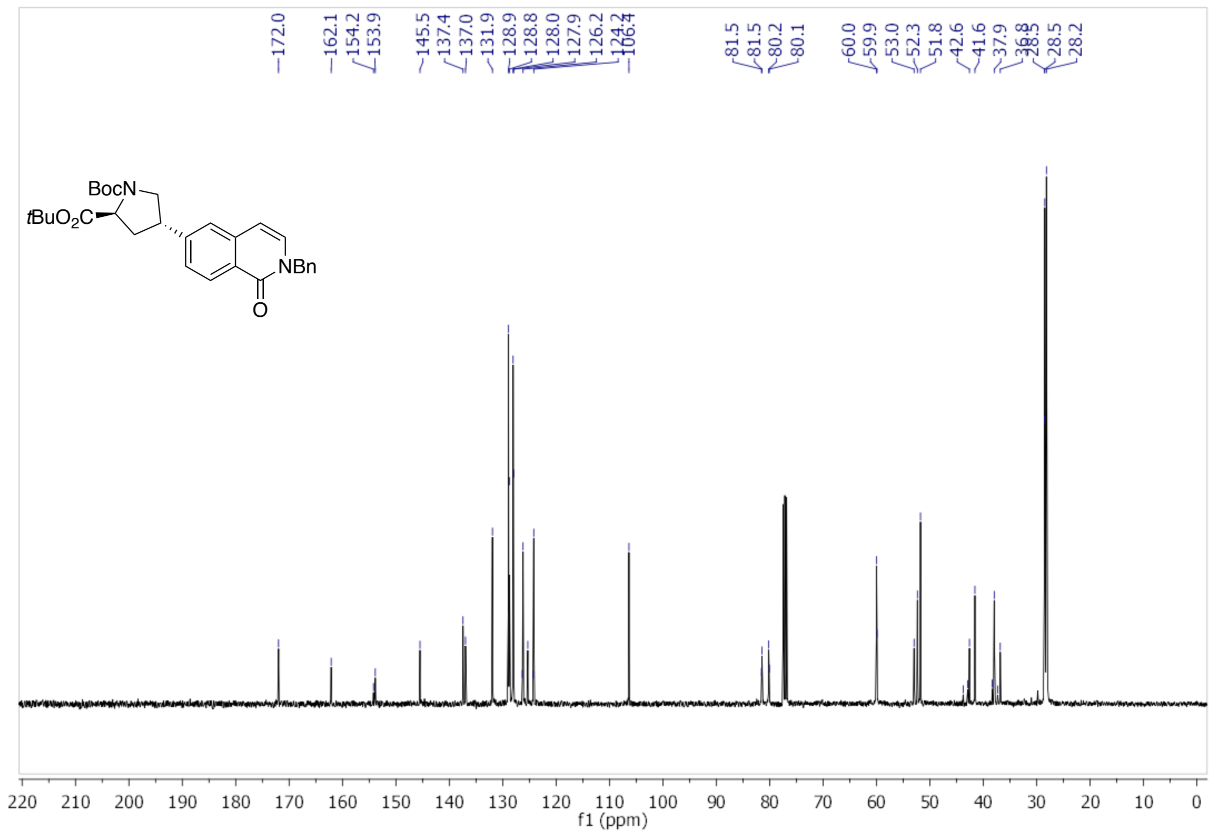


Figure S36: ^{13}C NMR (101 MHz, $CDCl_3$) of **14**

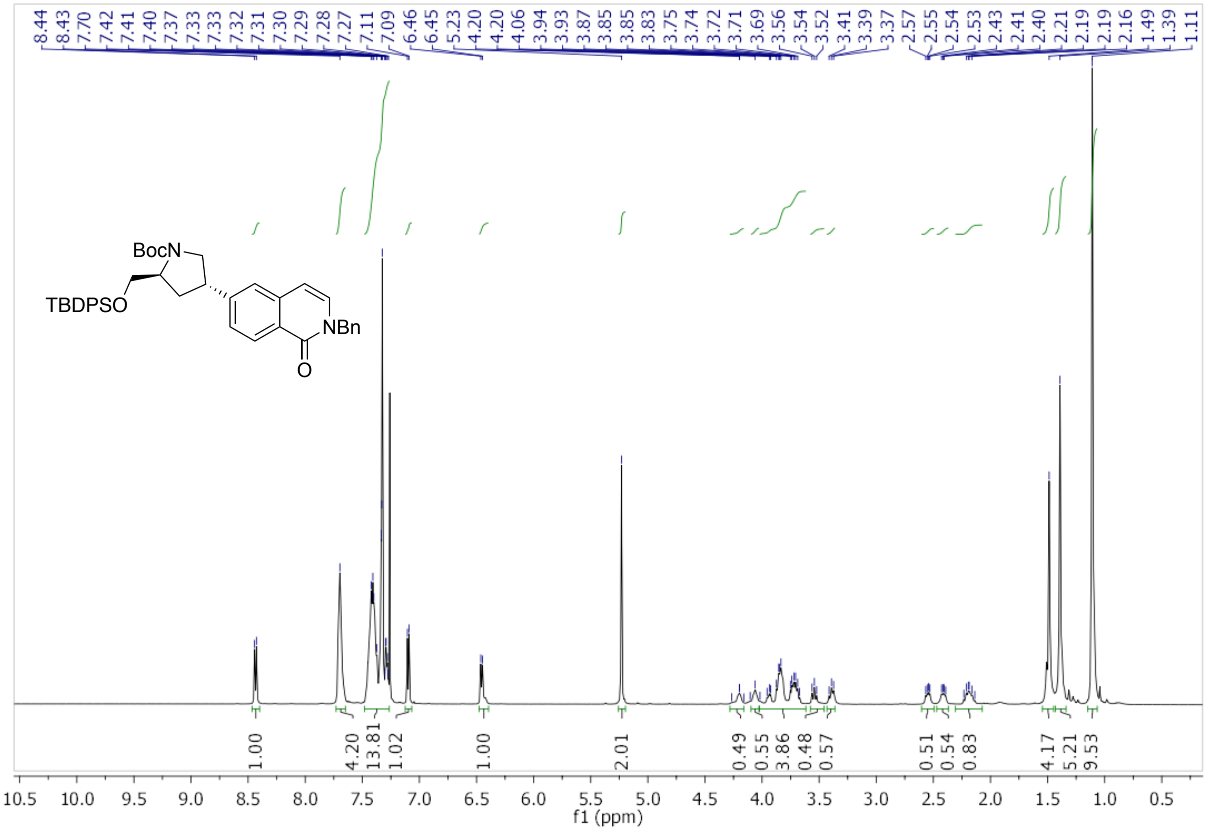


Figure S37: ^{1}H NMR (500 MHz, $CDCl_3$) of **15**

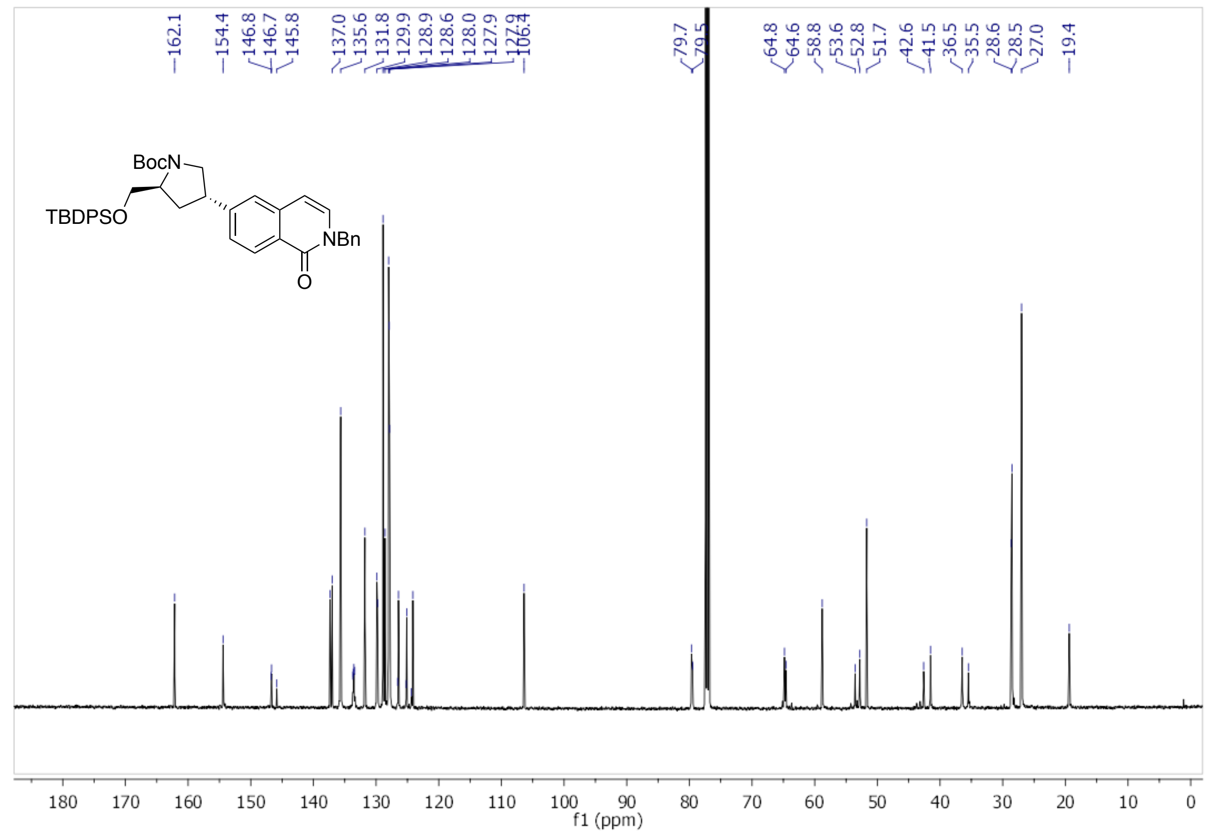


Figure S38: ^{13}C NMR (126 MHz, $CDCl_3$) of **15**

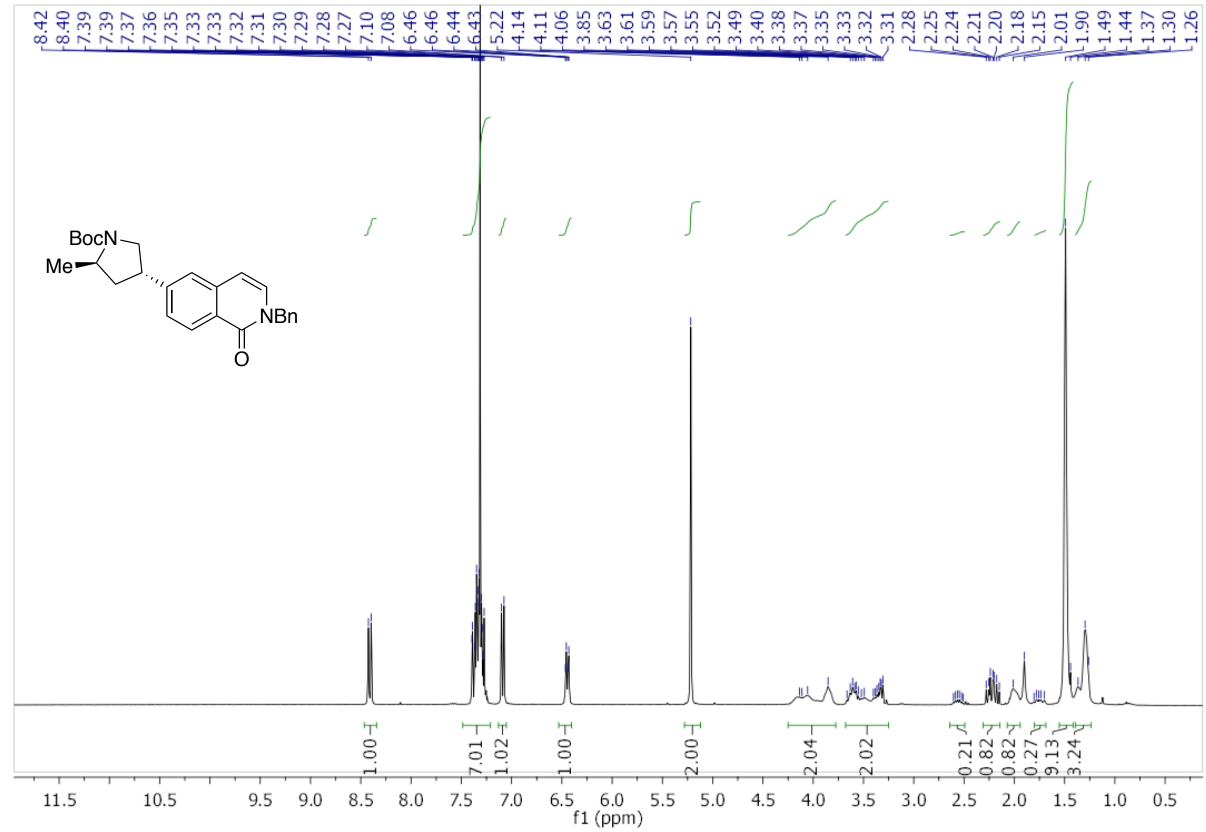


Figure S39: ^{1}H NMR (300 MHz, $CDCl_3$) of **16**

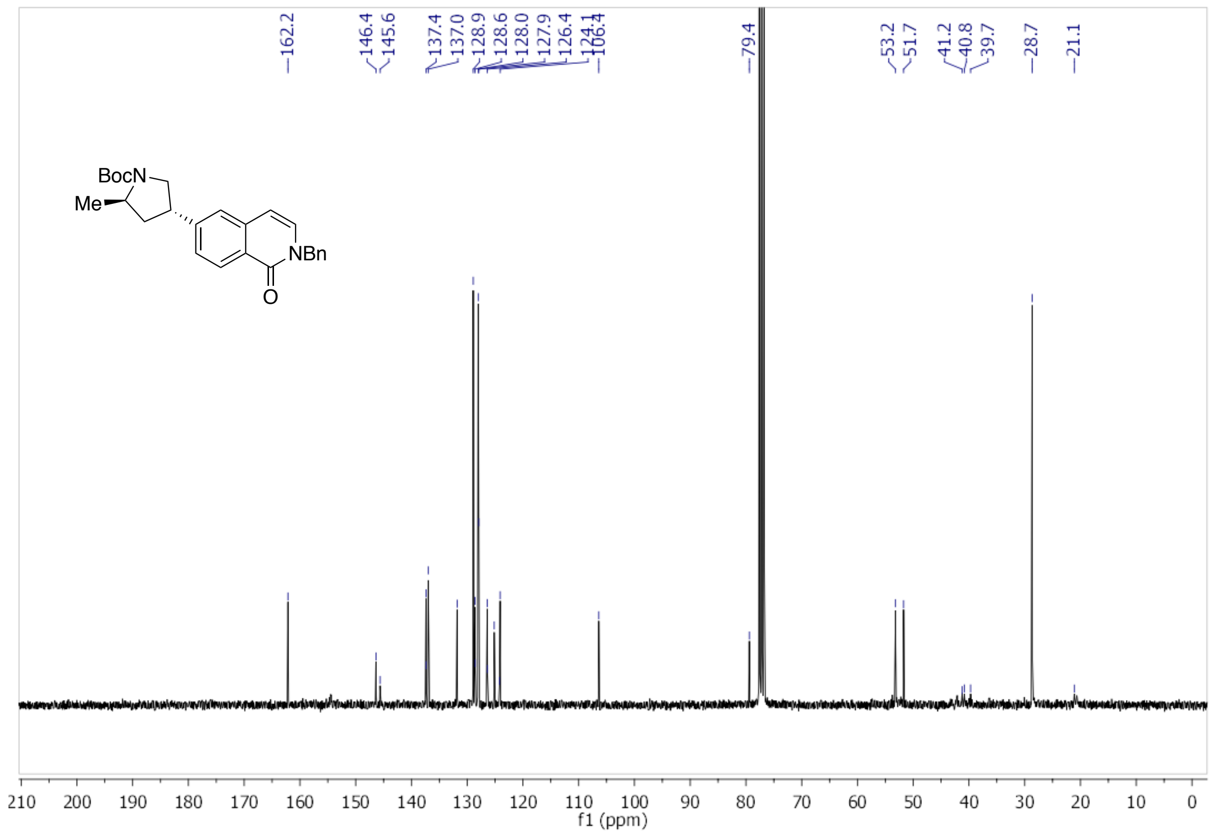


Figure S40: ^{13}C NMR (75 MHz, $CDCl_3$) of **16**

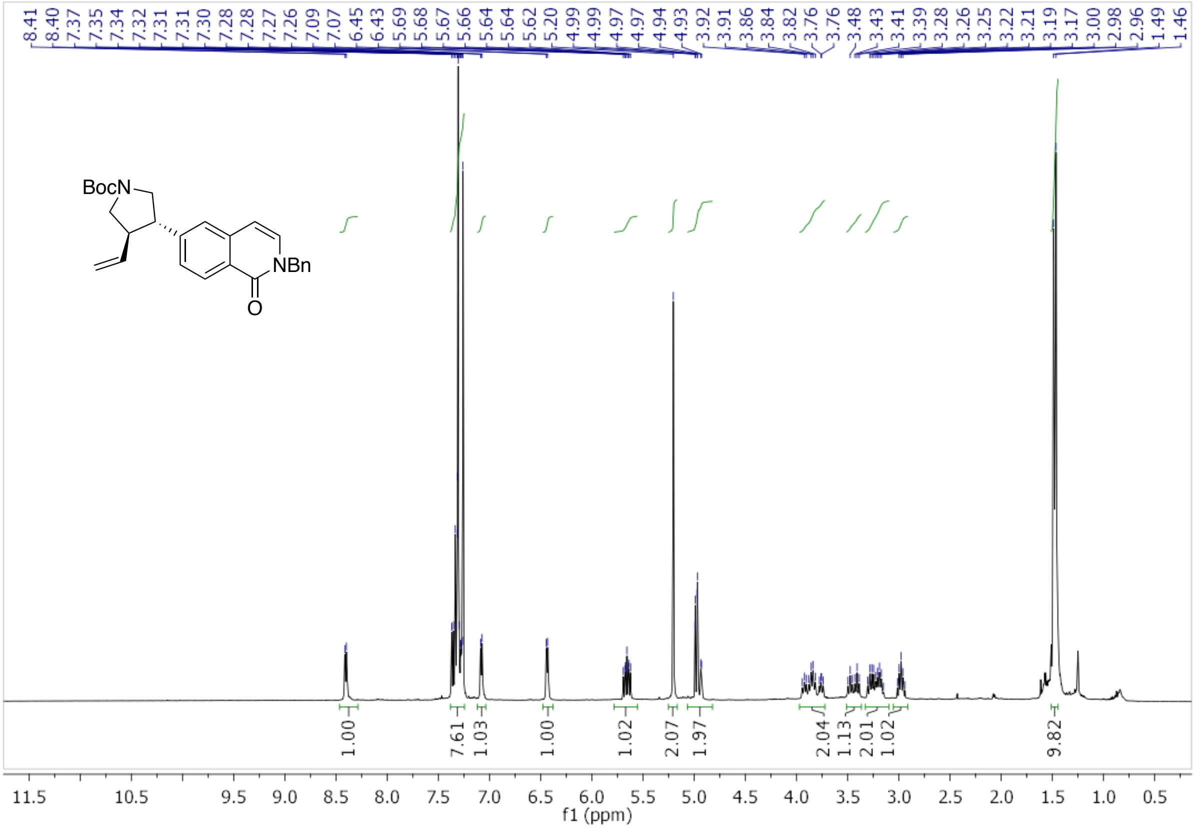


Figure S41: ^{1}H NMR (500 MHz, $CDCl_3$) of **17**

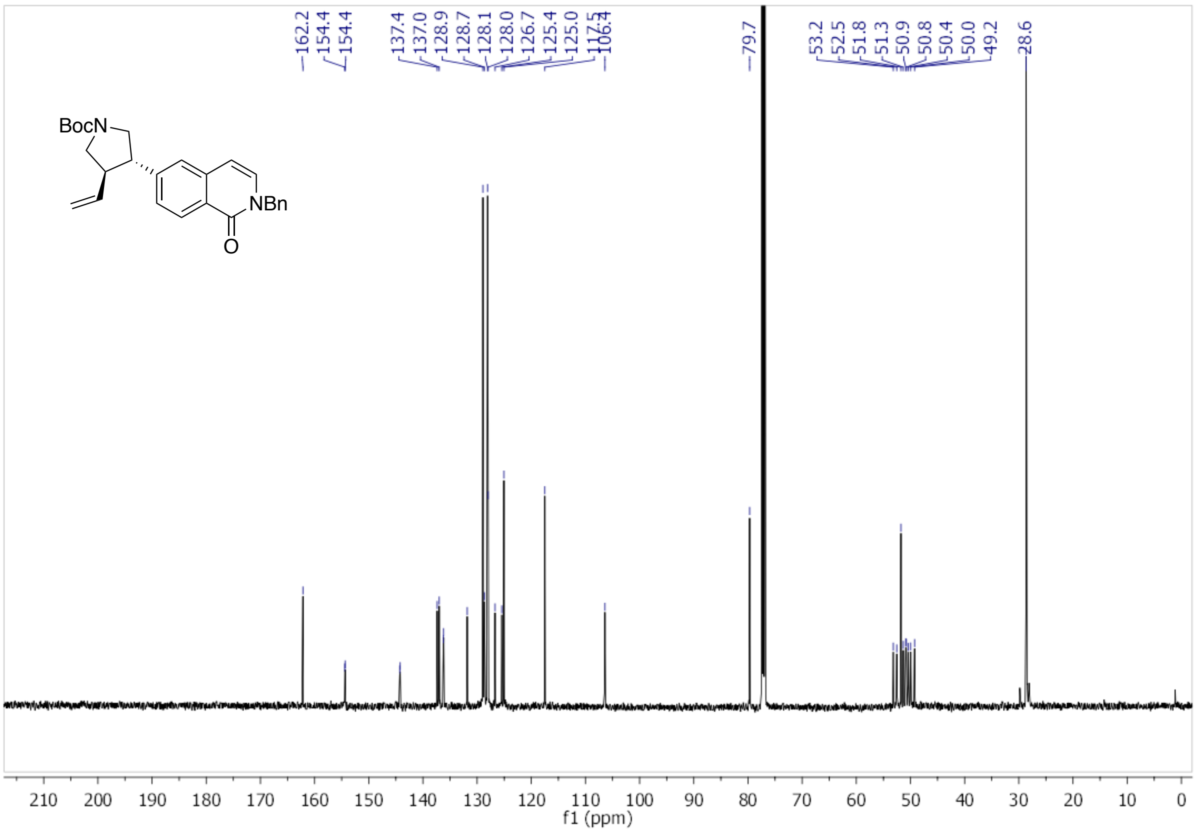


Figure S42: ^{13}C NMR (126 MHz, $CDCl_3$) of **17**

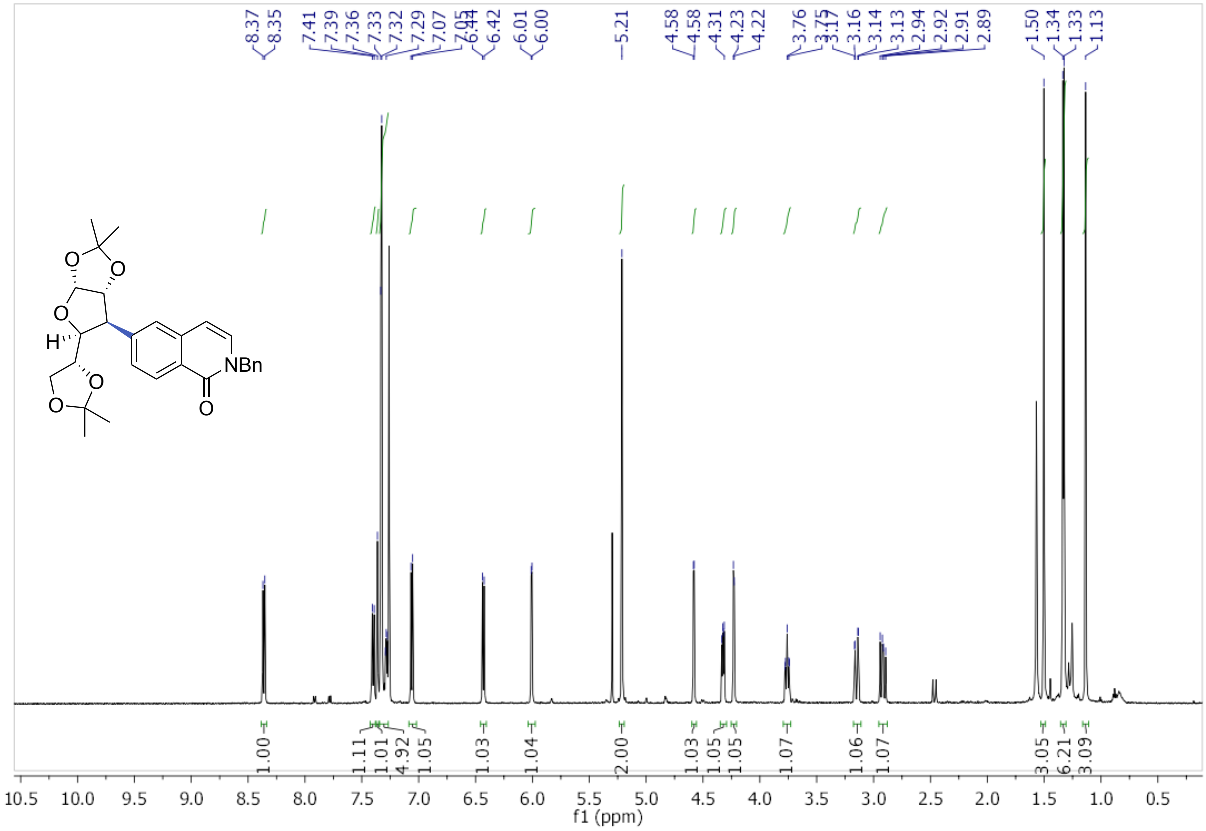


Figure S43: ^{1}H NMR (500 MHz, $CDCl_3$) of **18**

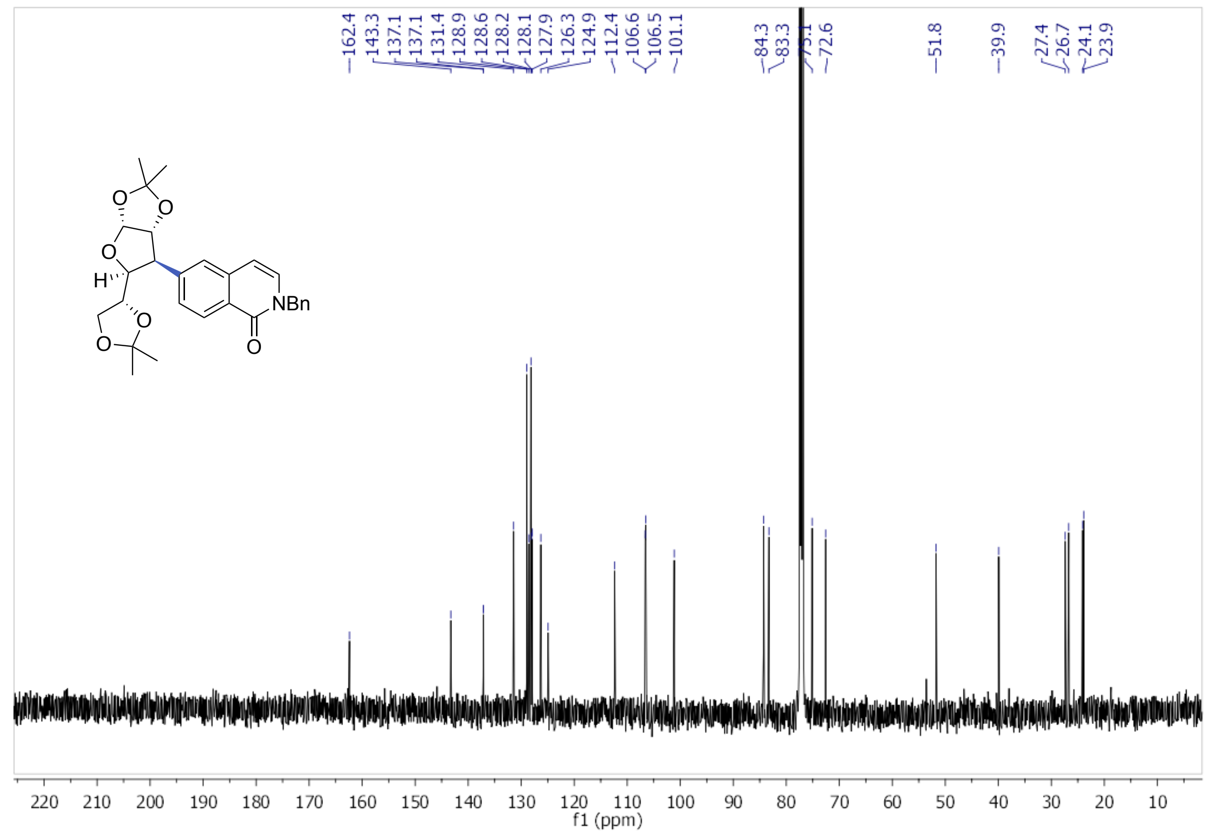


Figure S44: ^{13}C NMR (126 MHz, $CDCl_3$) of **18**

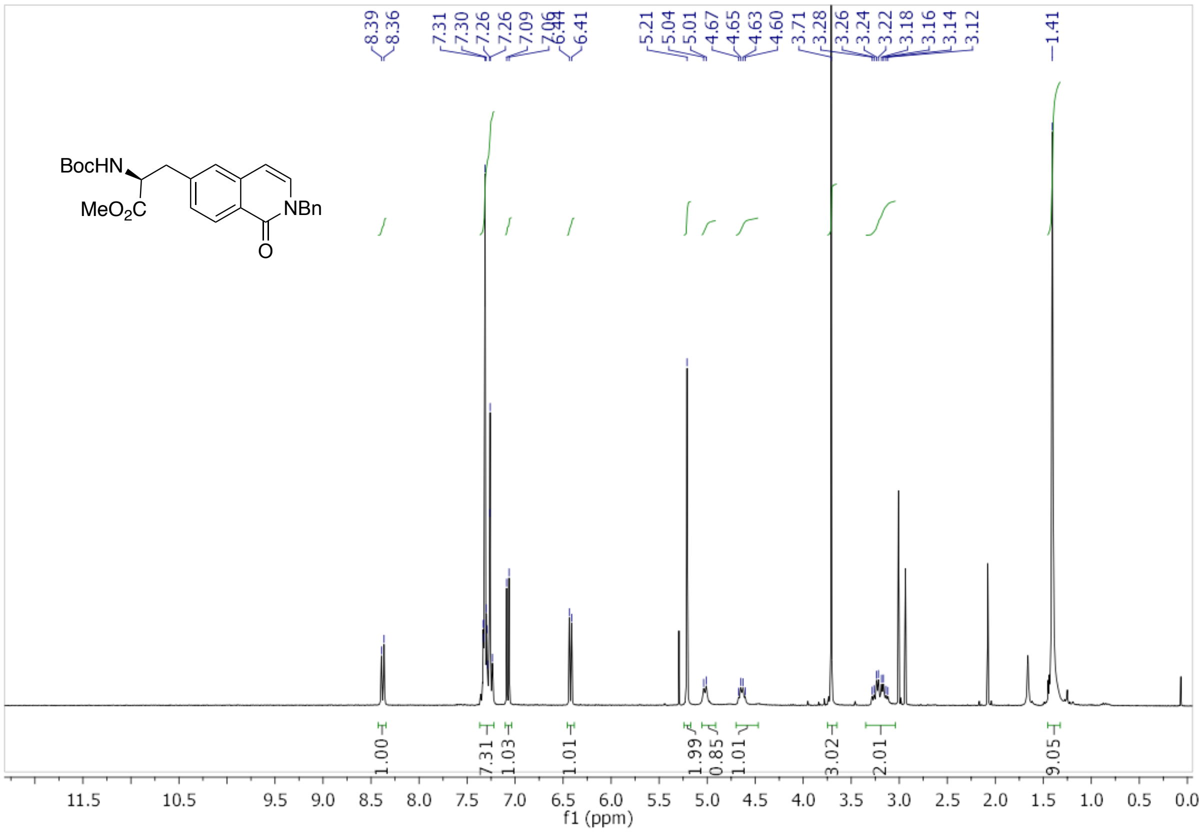


Figure S45: ^{1}H NMR (300 MHz, $CDCl_3$) of **19**

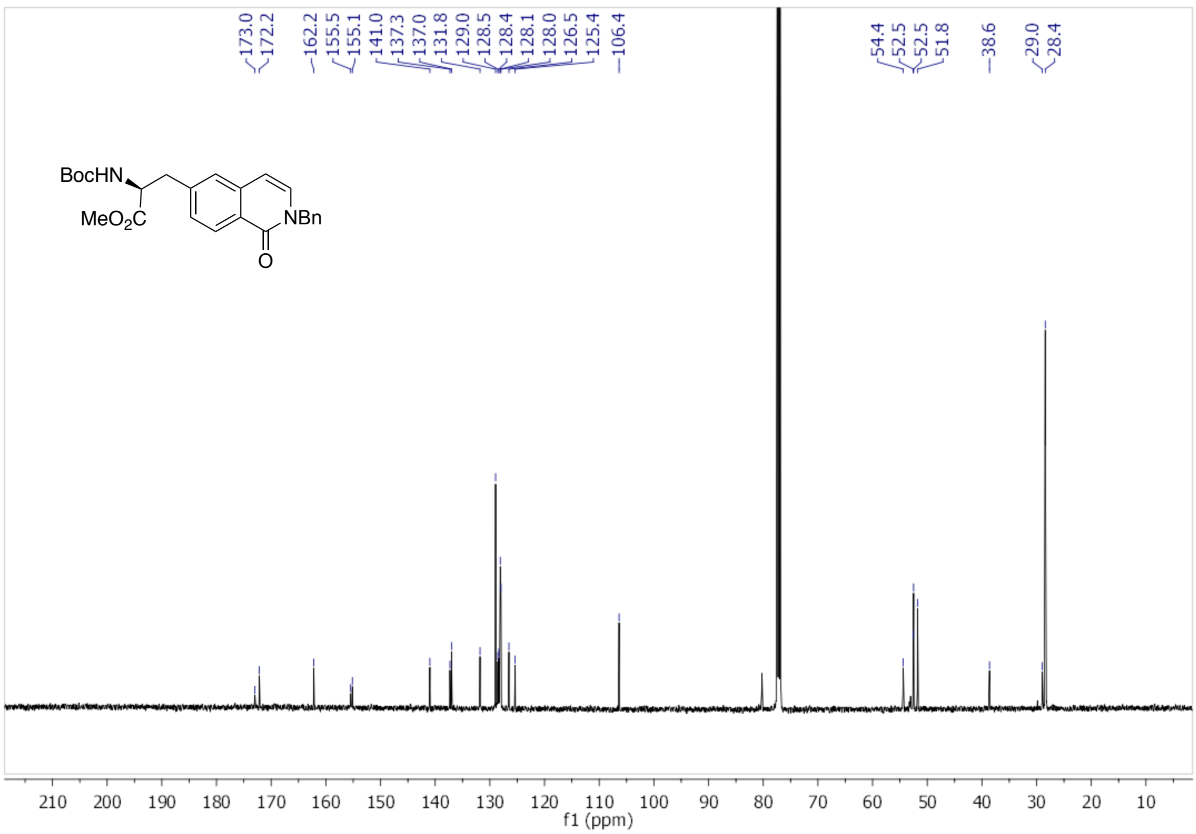


Figure S46: ^{13}C NMR (126 MHz, $CDCl_3$) of **19**

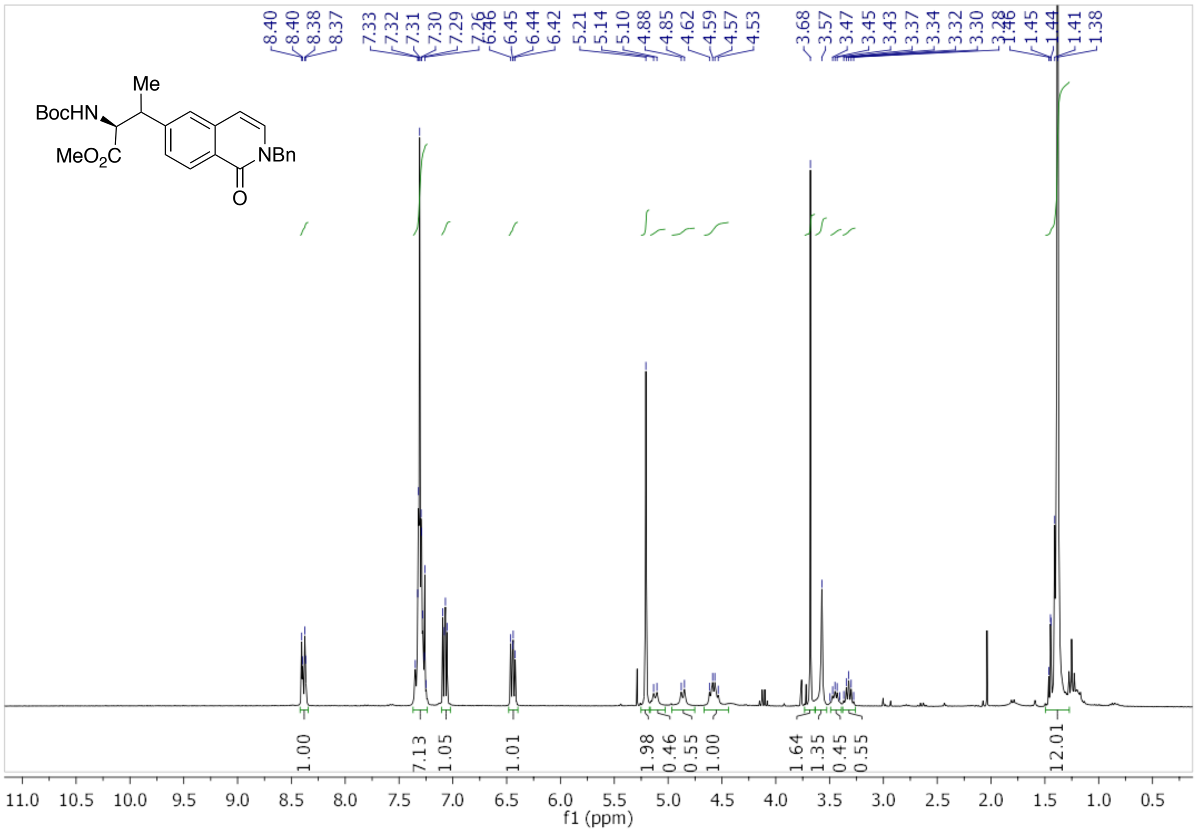


Figure S47: ^{1}H NMR (300 MHz, $CDCl_3$) of **20**

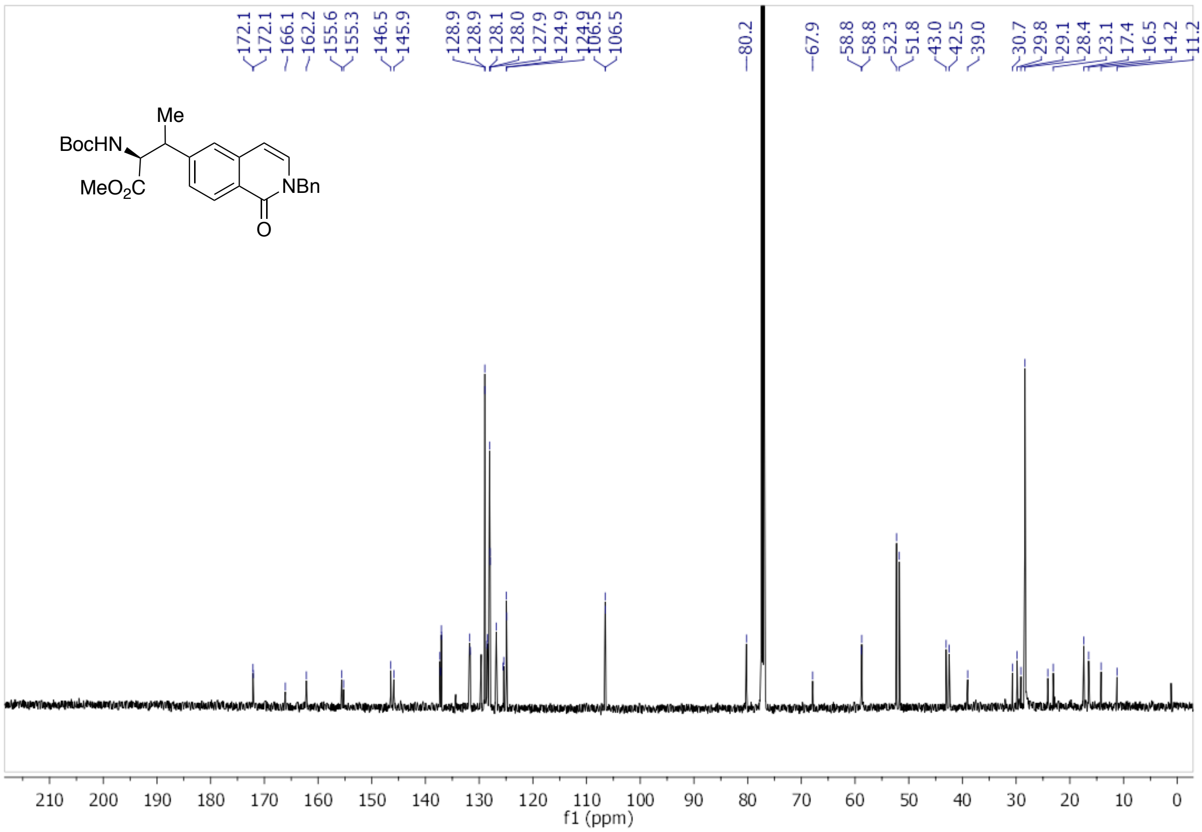


Figure S48: ^{13}C NMR (126 MHz, $CDCl_3$) of **20**

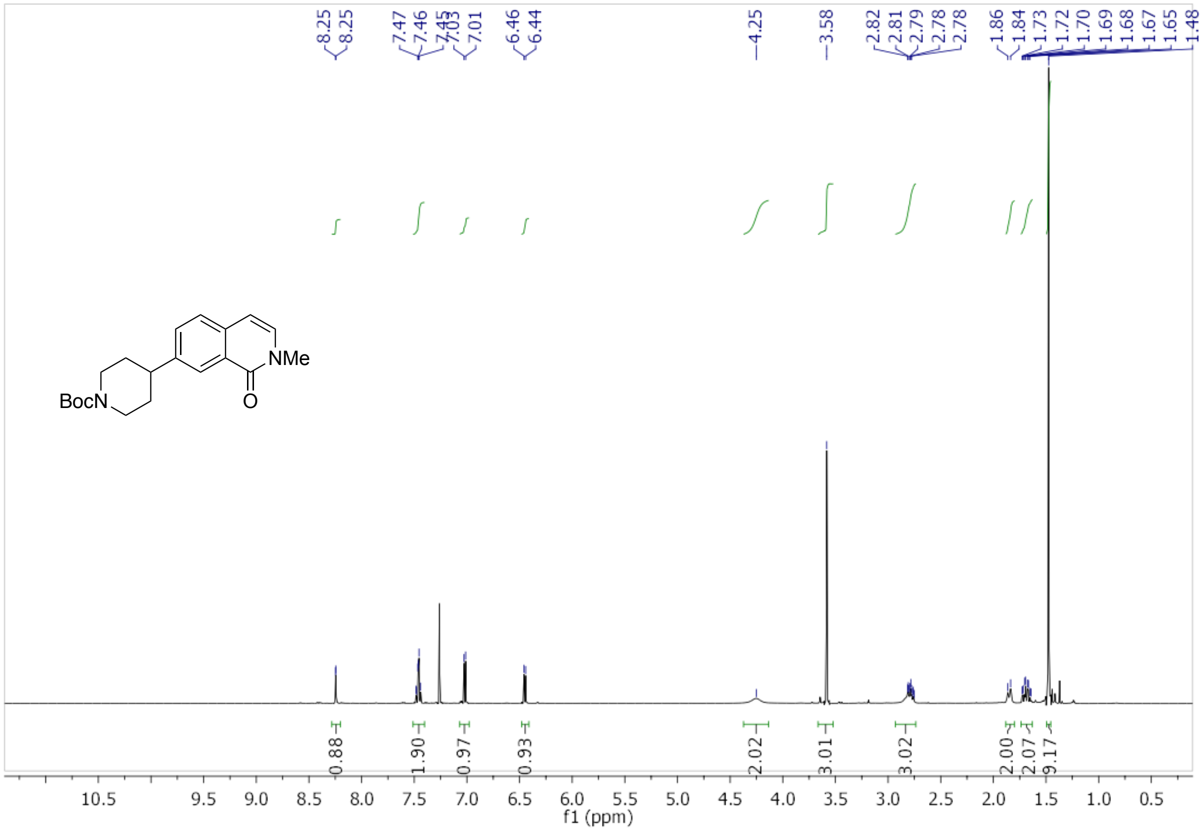


Figure S49: ^{1}H NMR (500 MHz, CDCl$_3$) of **21**

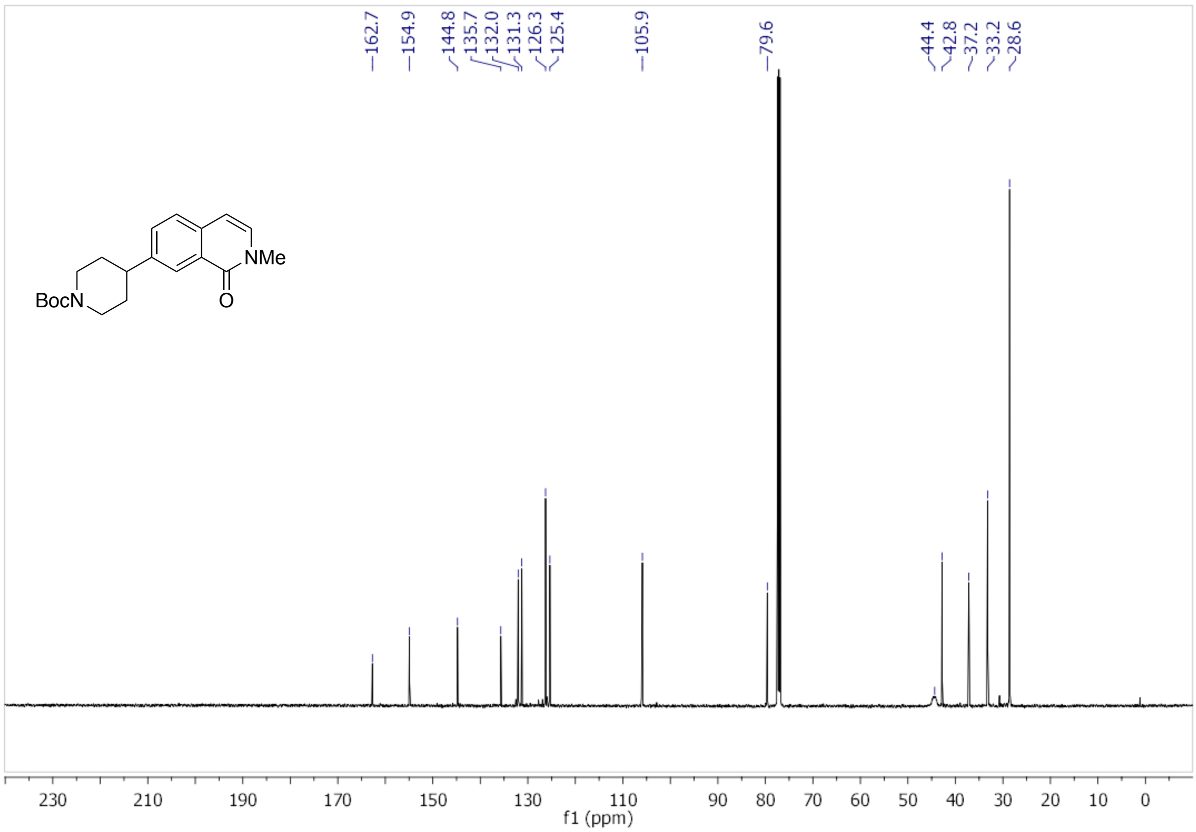


Figure S50: ^{13}C NMR (126 MHz, CDCl$_3$) of **21**

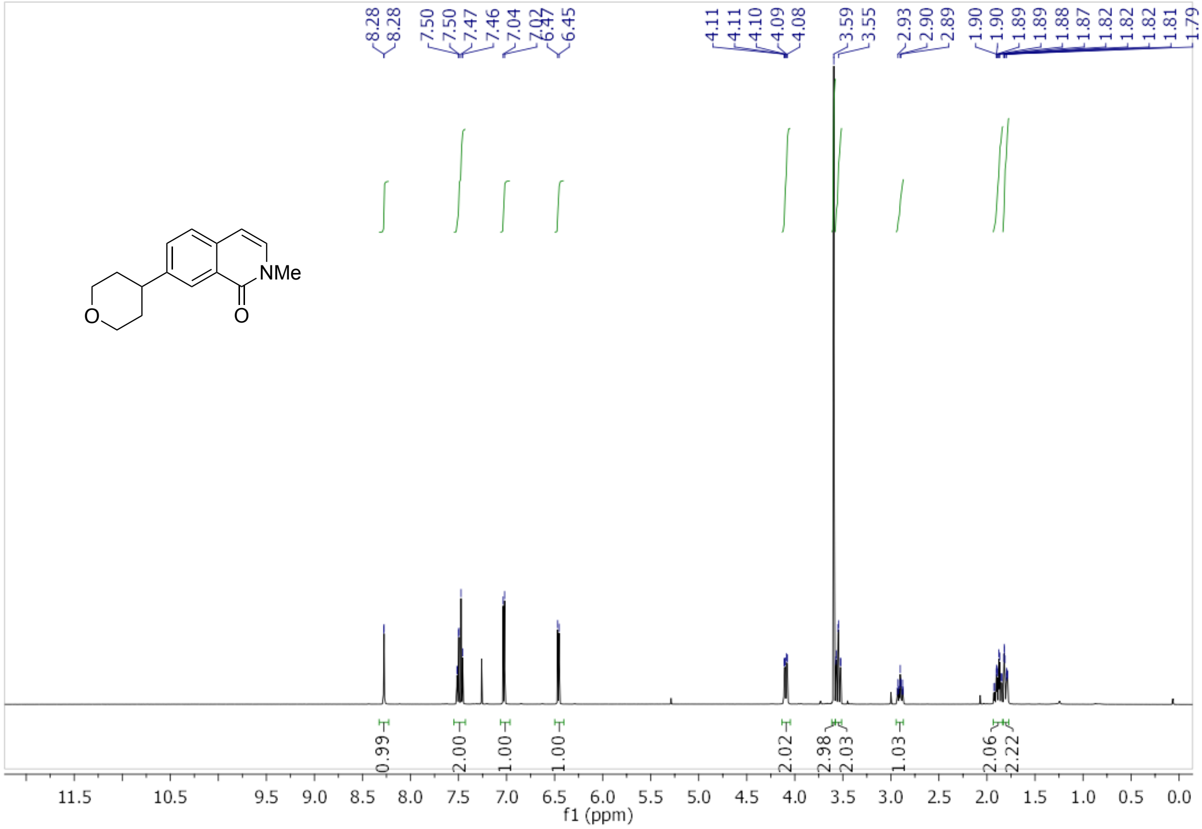


Figure S51: ^{1}H NMR (500 MHz, $CDCl_3$) of **22**

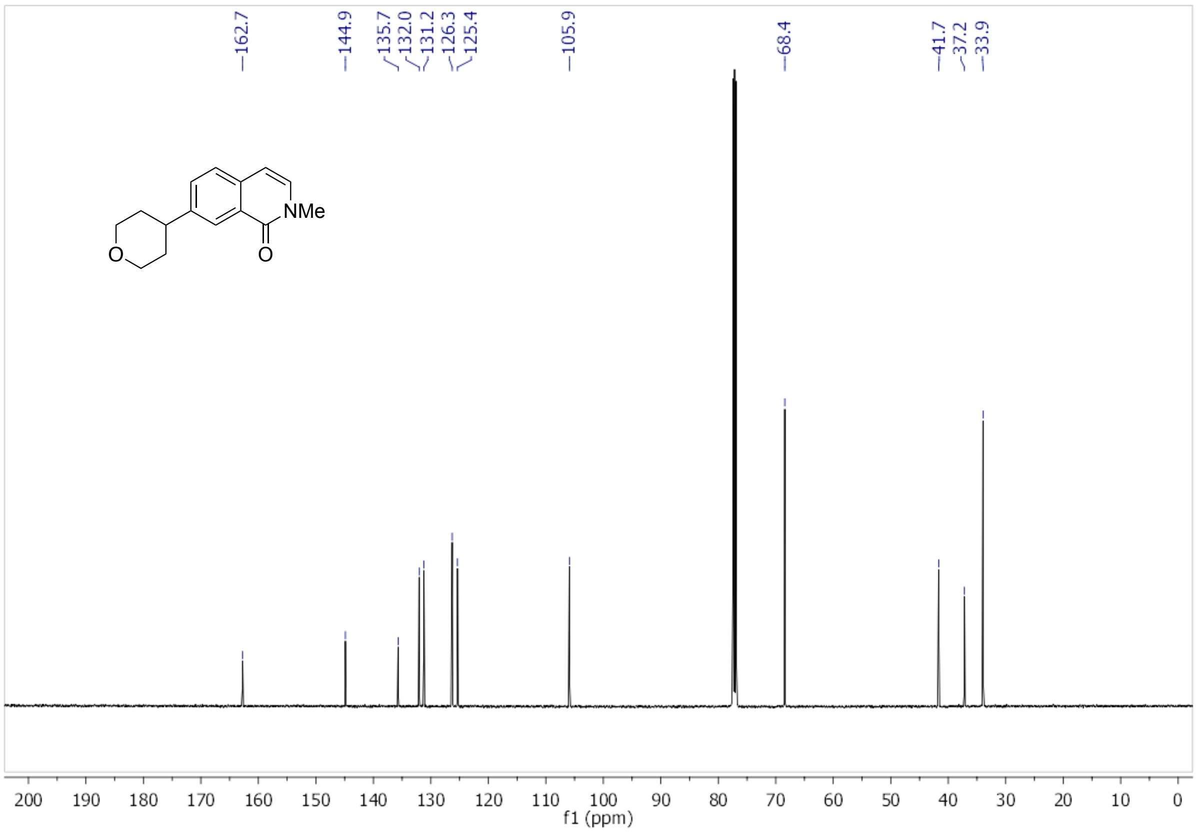


Figure S52: ^{13}C NMR (126 MHz, $CDCl_3$) of **22**

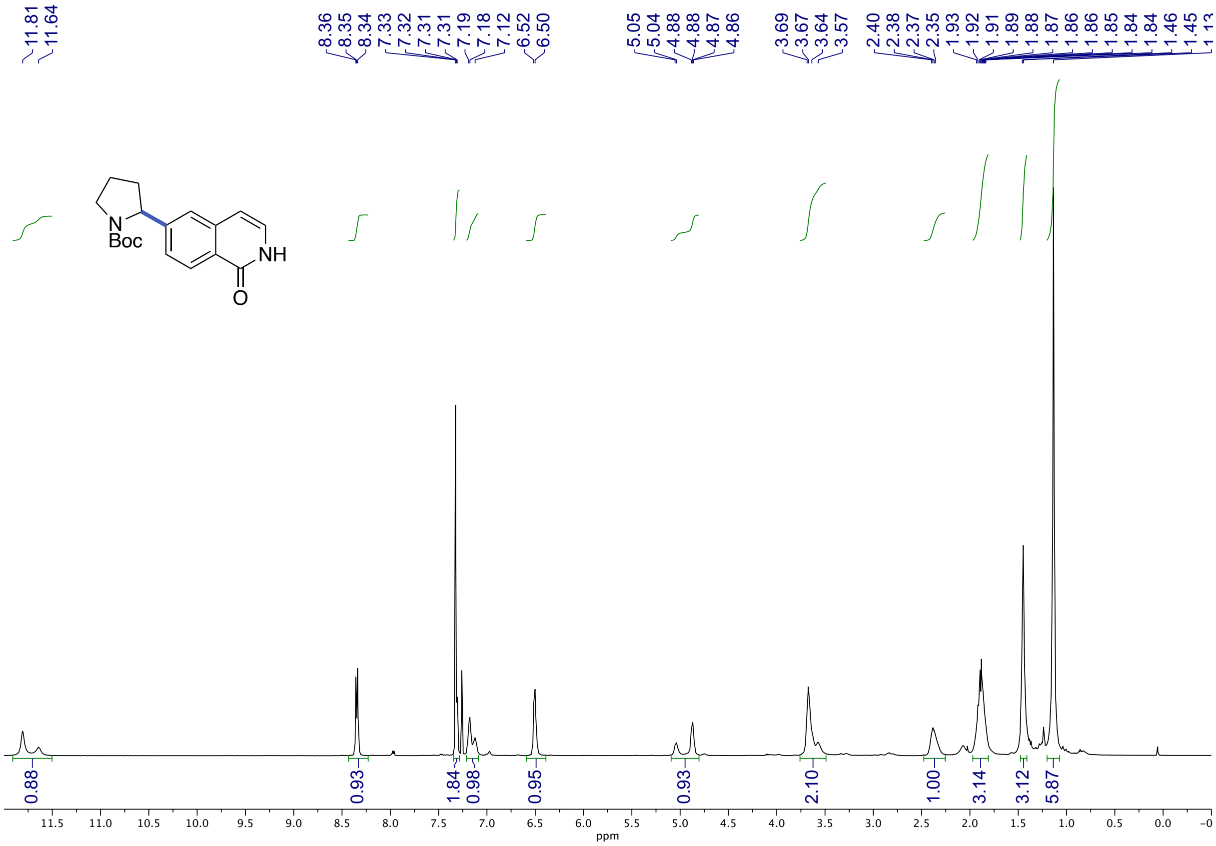


Figure S53: ^{1}H NMR (500 MHz, $CDCl_3$) of **27**

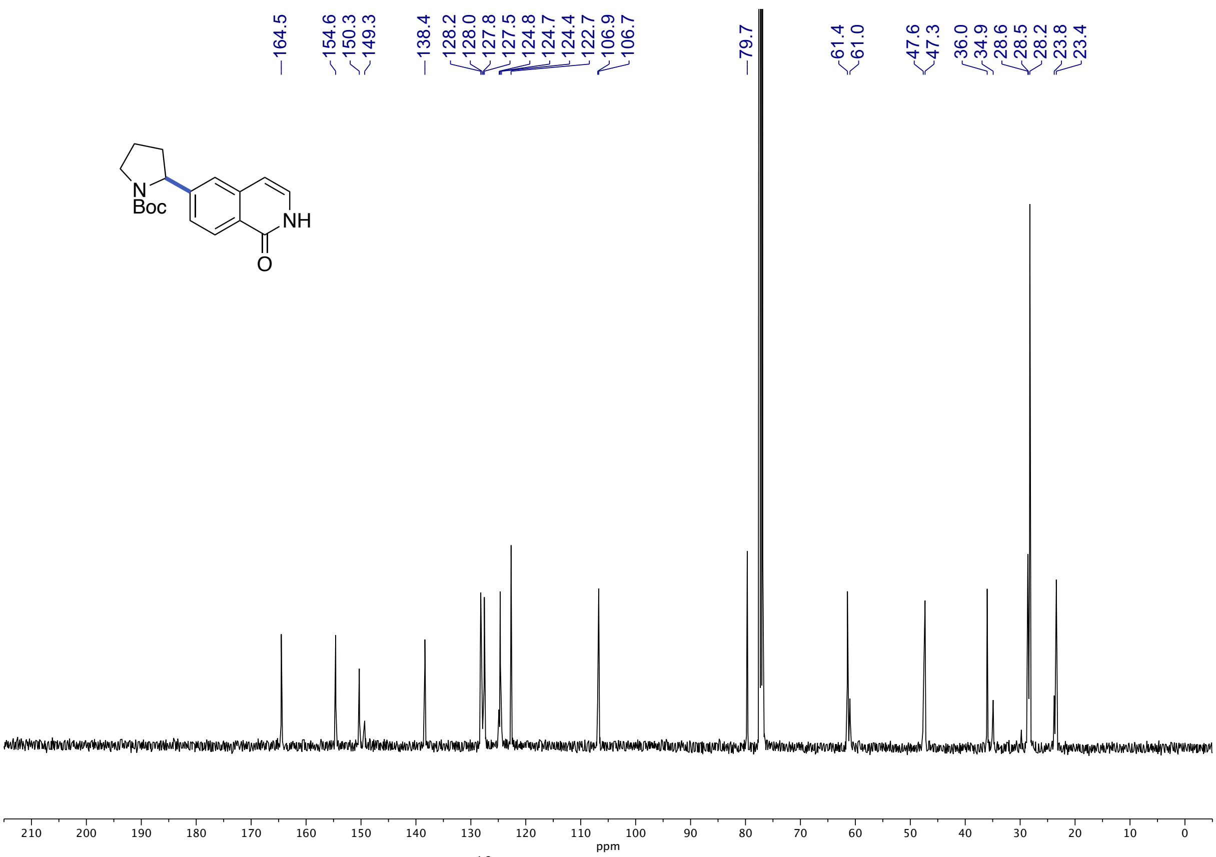


Figure S54: ^{13}C NMR (126 MHz, $CDCl_3$) of **27**

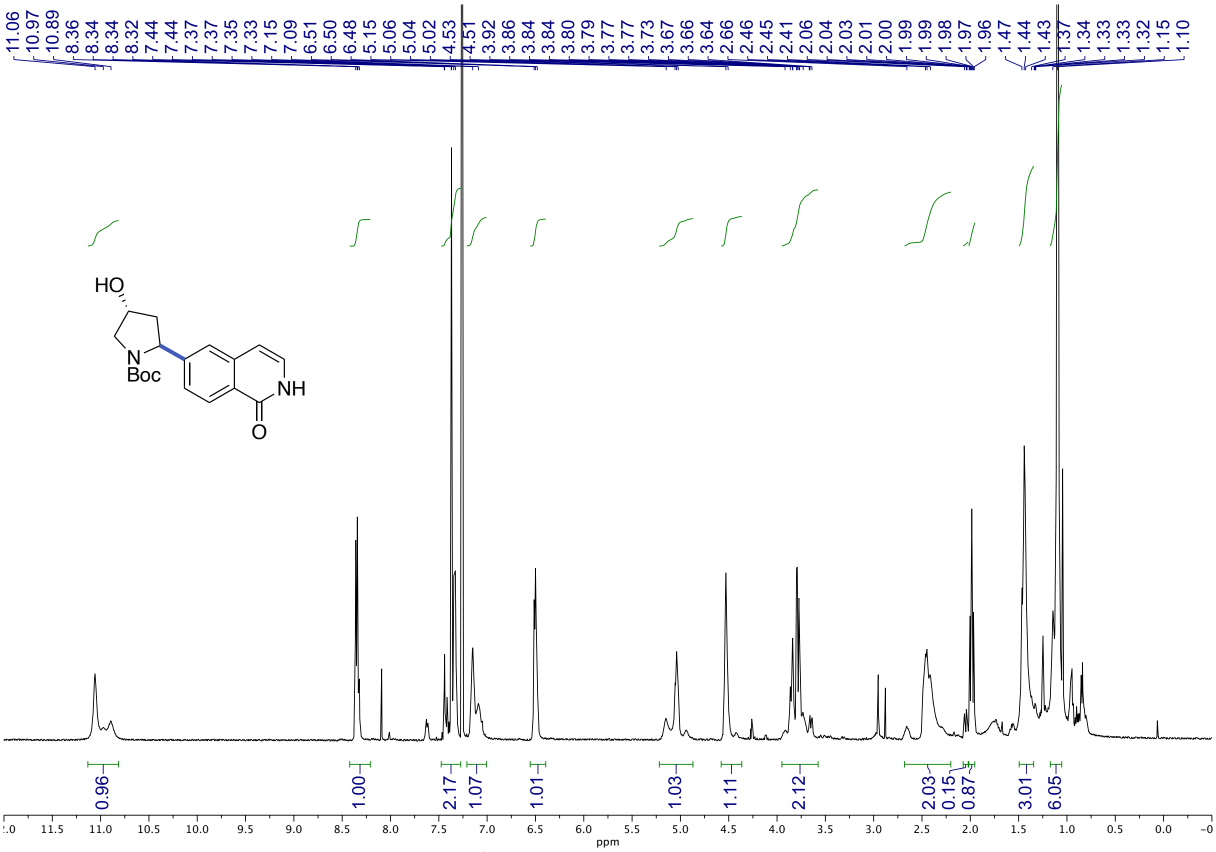


Figure S55: ^{1}H NMR (500 MHz, $CDCl_3$) of **28**

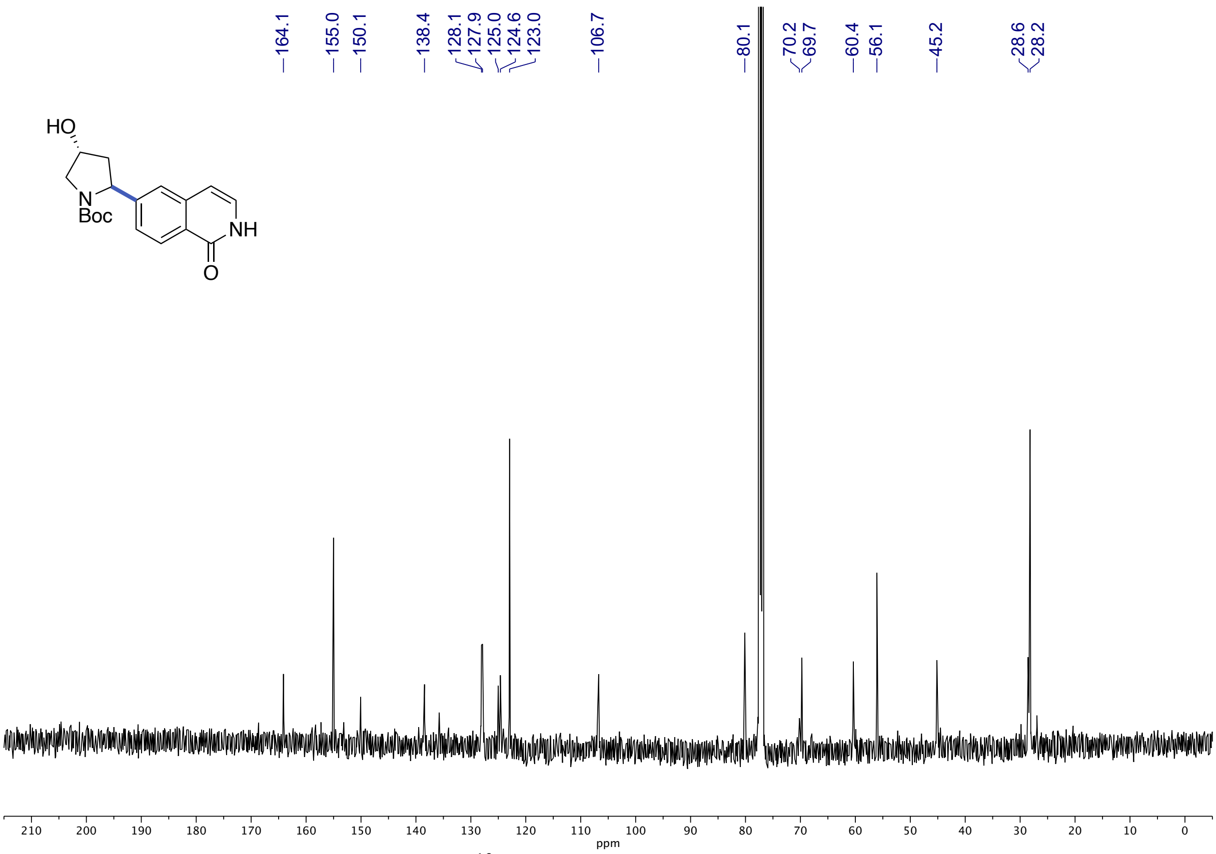


Figure S56: ^{13}C NMR (126 MHz, $CDCl_3$) of **28**

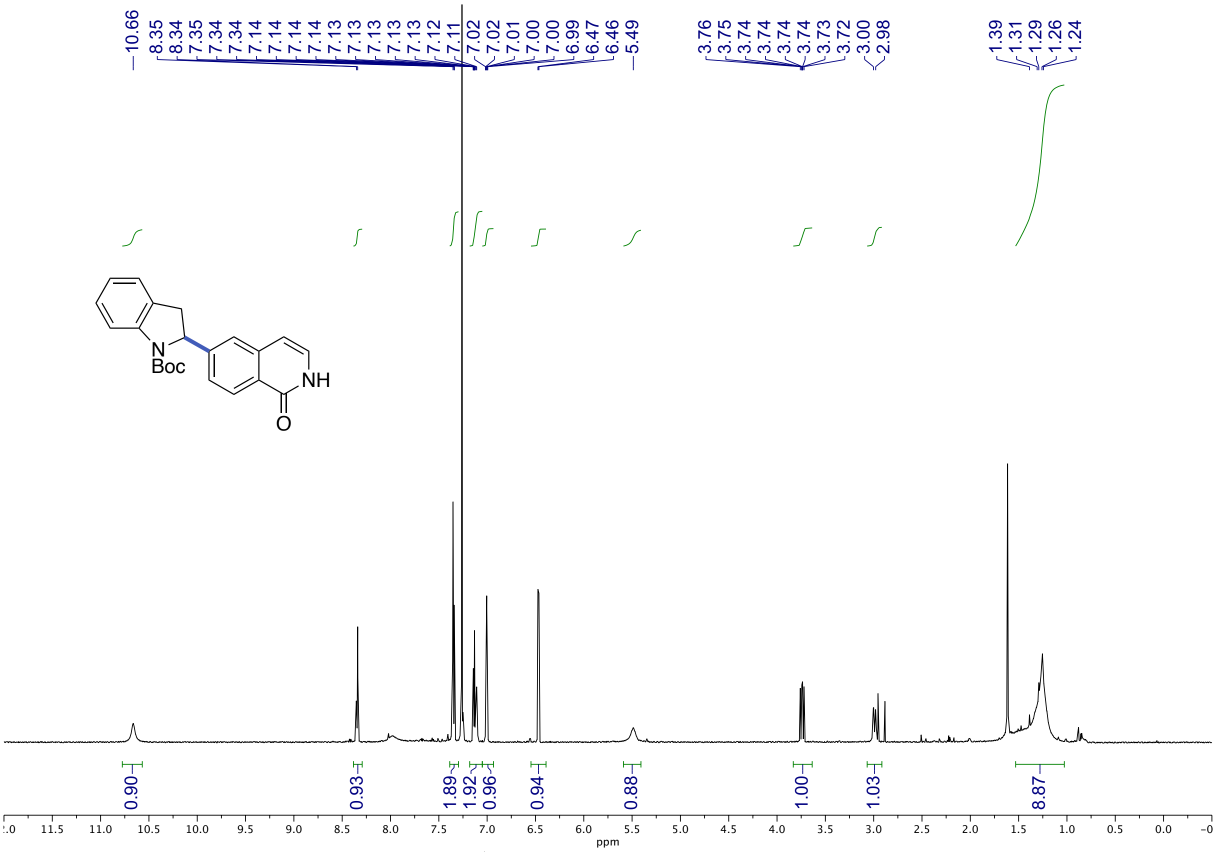


Figure S57: ^{1}H NMR (700 MHz, $CDCl_3$) of **29**

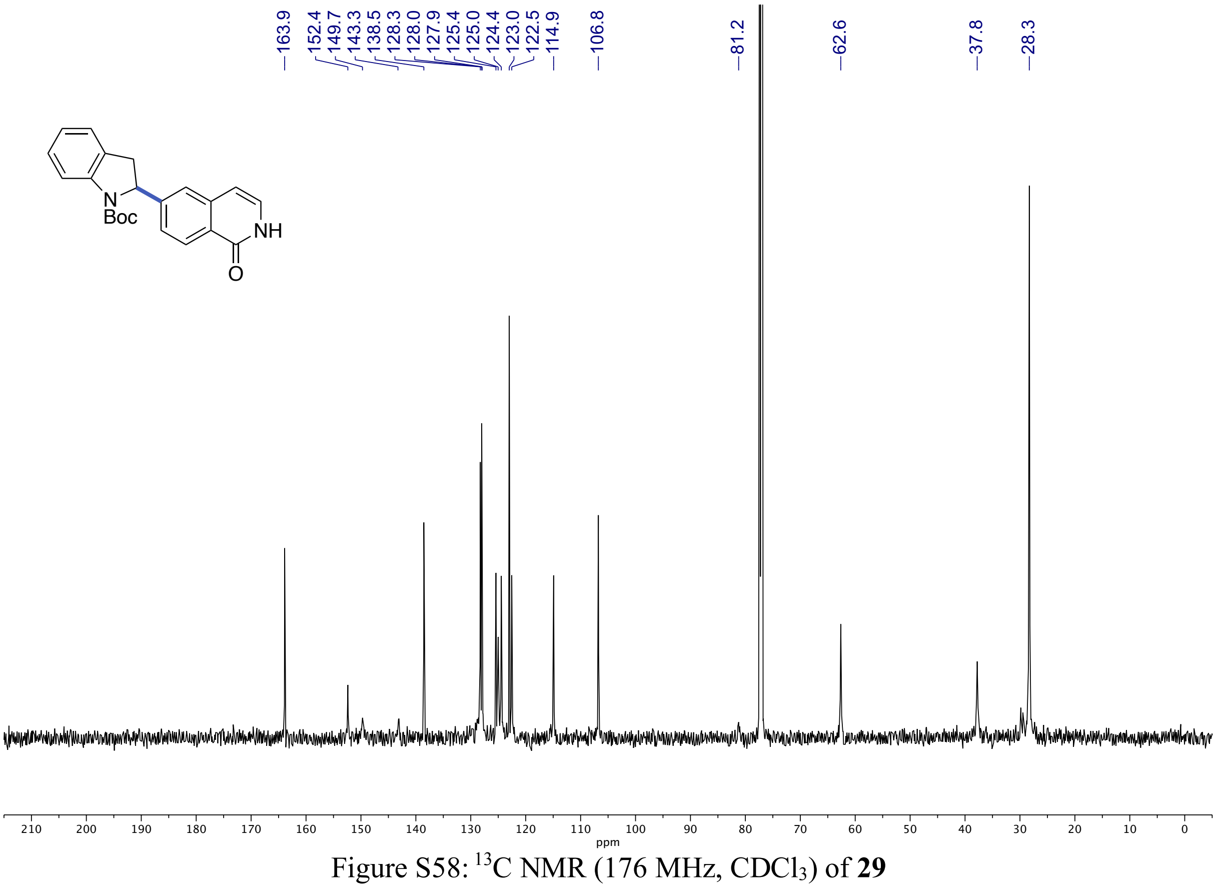


Figure S58: ^{13}C NMR (176 MHz, $CDCl_3$) of **29**

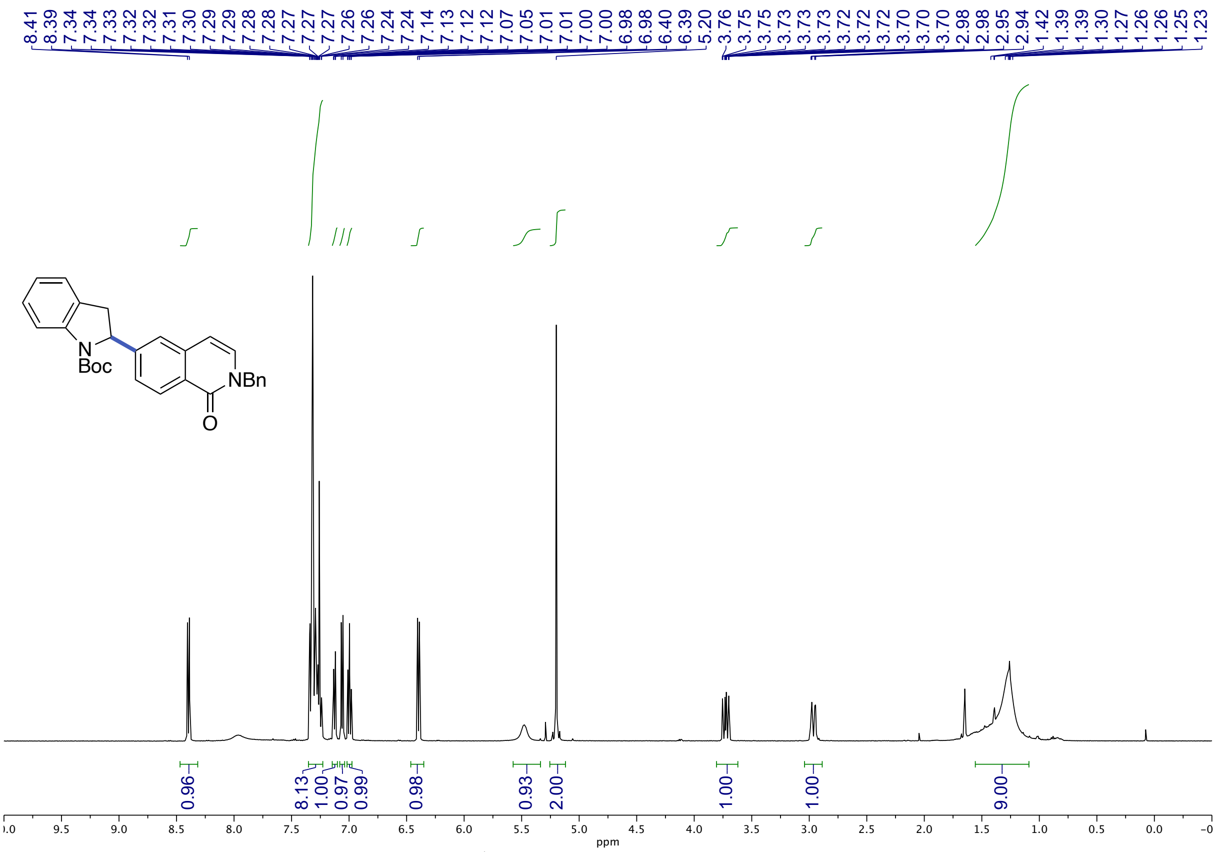


Figure S59: ^{1}H NMR (500 MHz, $CDCl_3$) of **30**

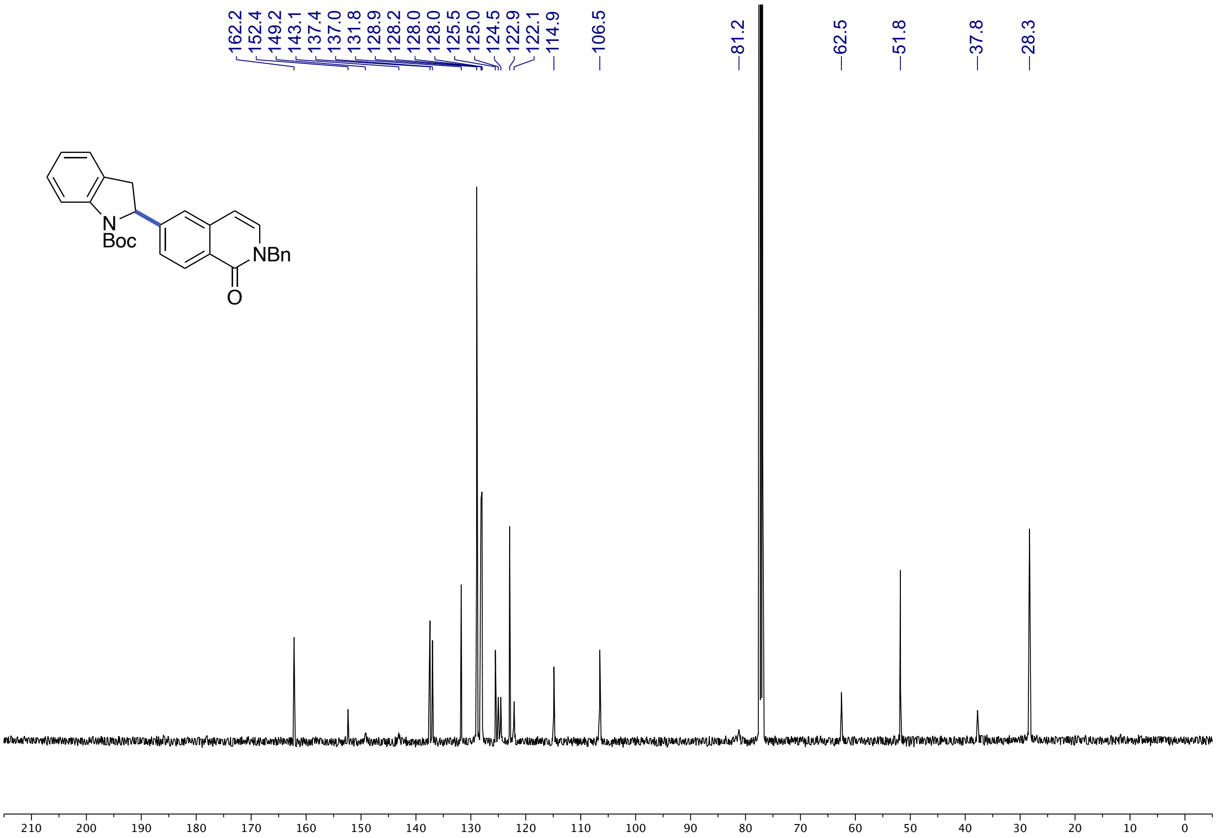


Figure S60: ^{13}C NMR (126 MHz, $CDCl_3$) of **30**

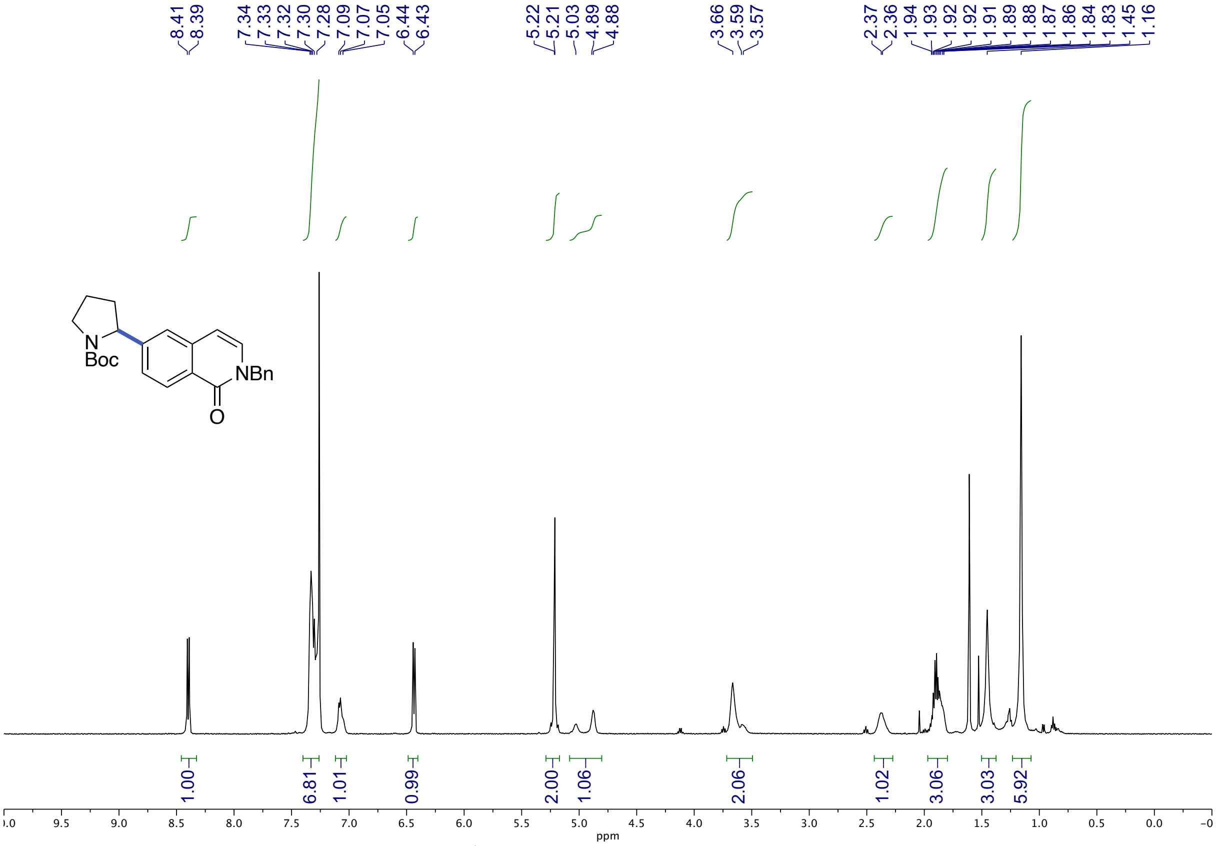


Figure S61: ^{1}H NMR (500 MHz, $CDCl_3$) of **31a**

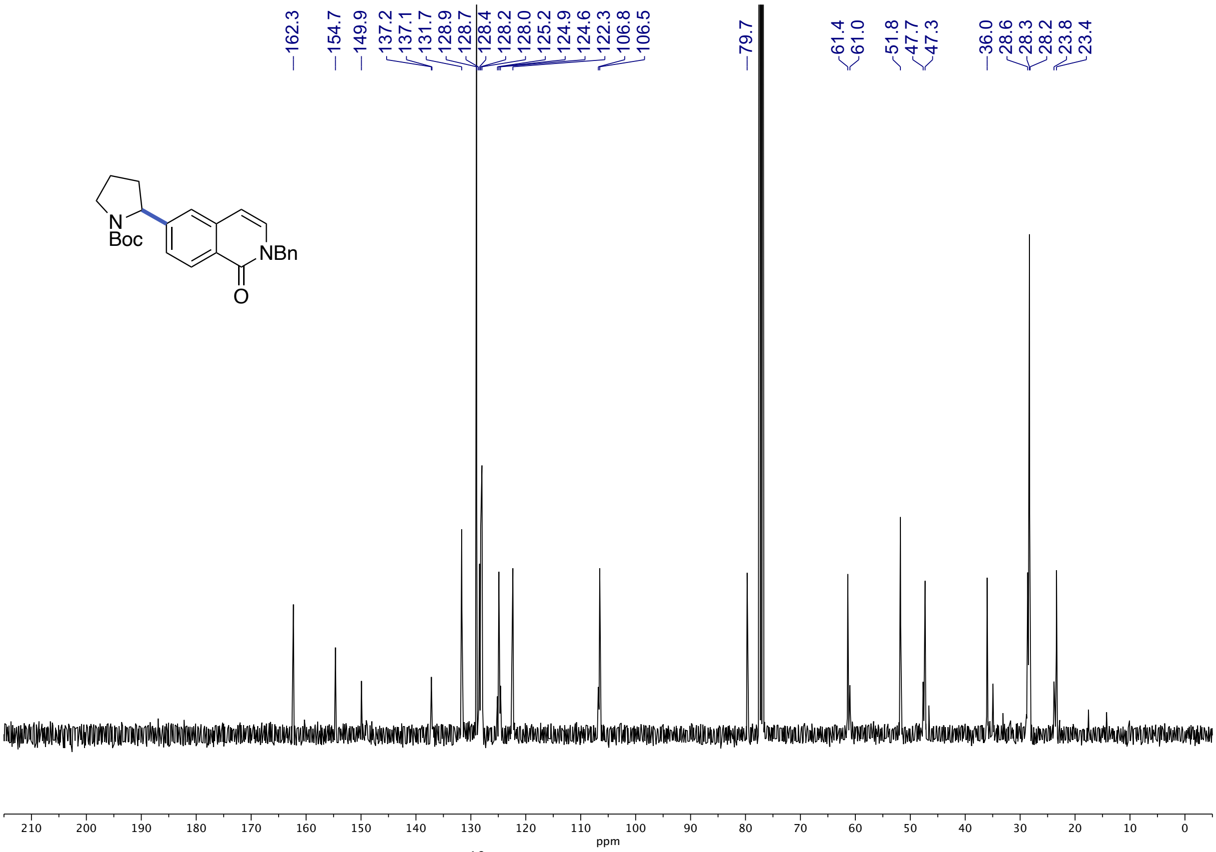


Figure S62: ^{13}C NMR (101 MHz, $CDCl_3$) of **31a**

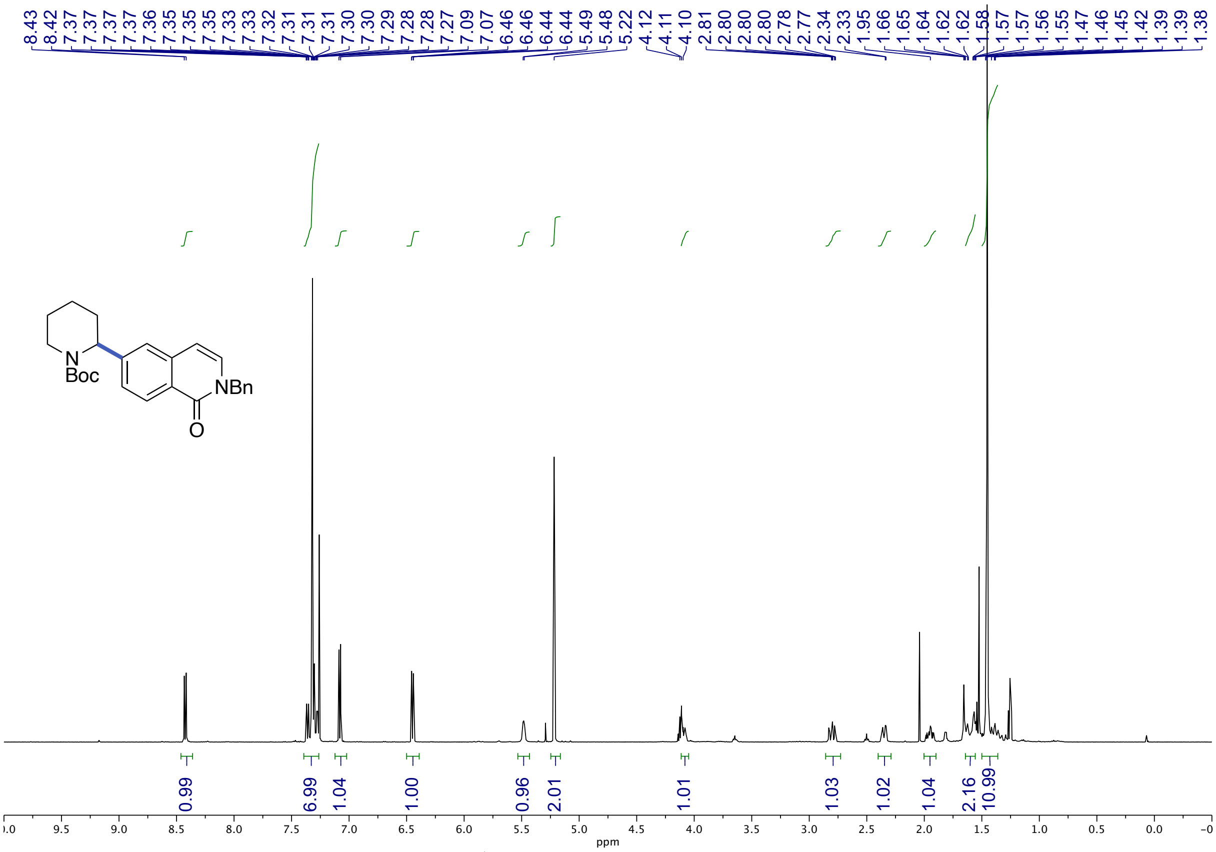


Figure S63: ^{1}H NMR (500 MHz, $CDCl_3$) of **32**

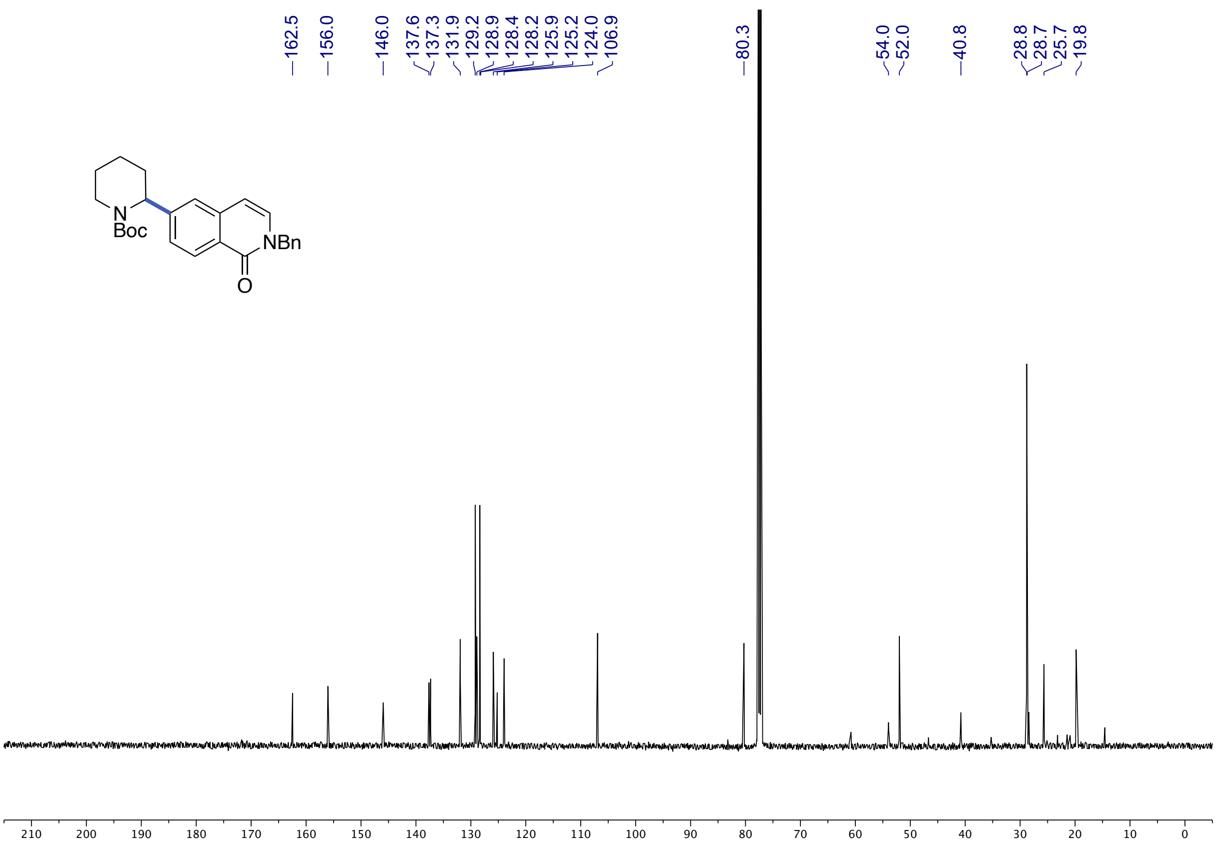


Figure S64: ^{13}C NMR (126 MHz, $CDCl_3$) of **32**

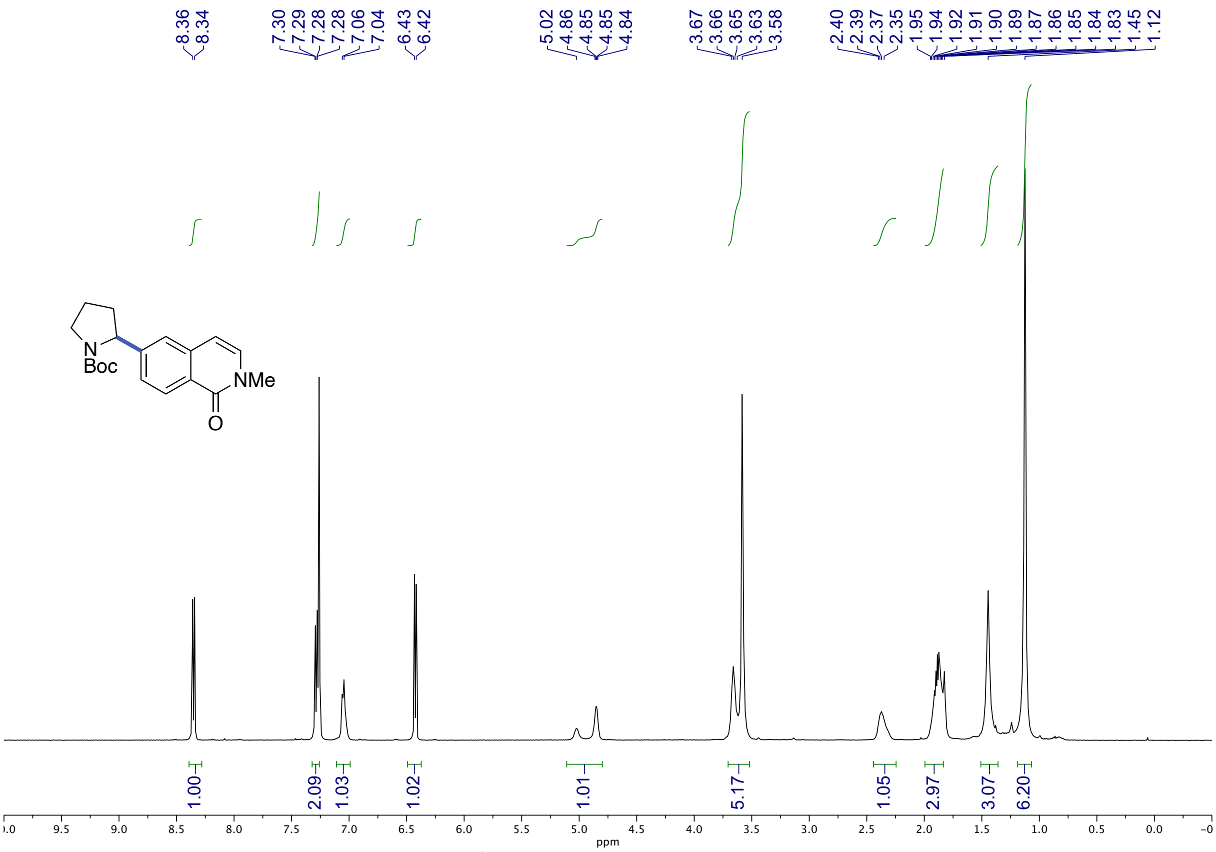


Figure S65: ^{1}H NMR (500 MHz, $CDCl_3$) of **33**

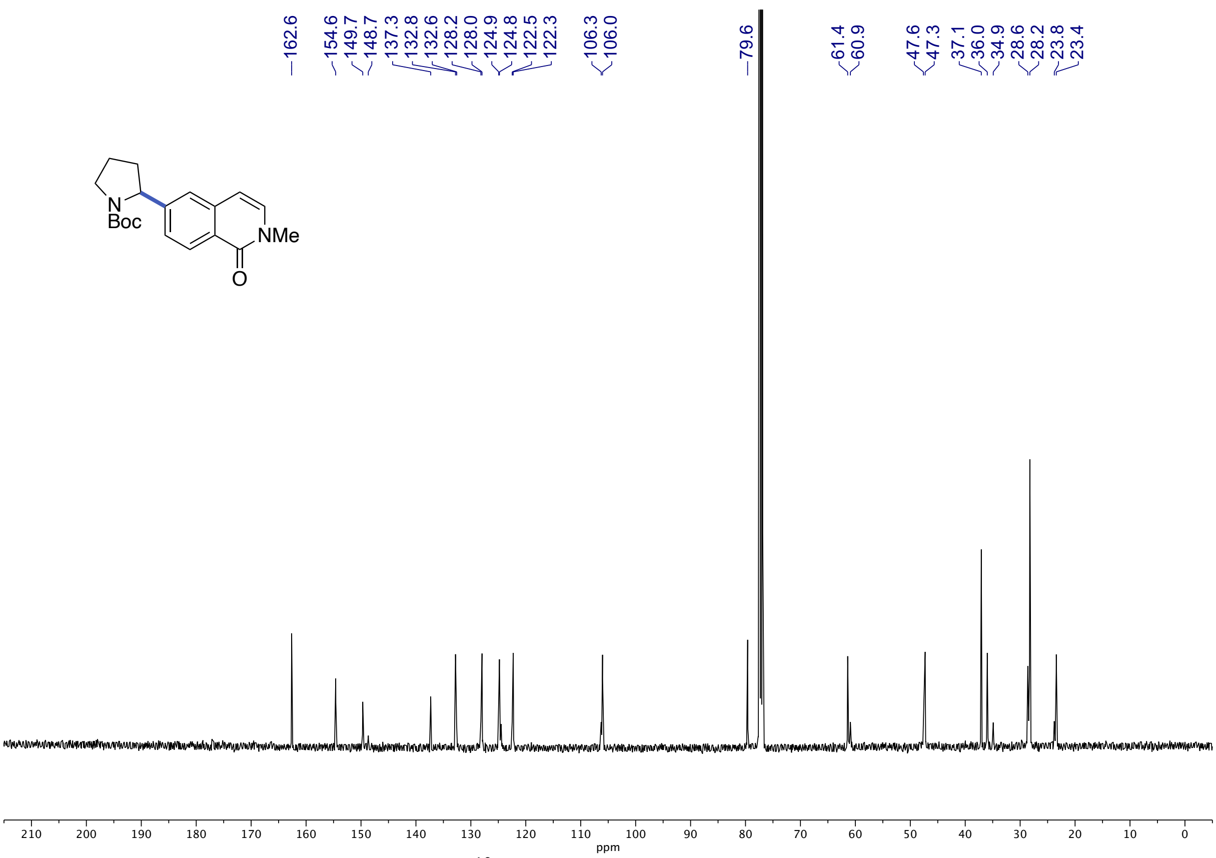


Figure S66: ^{13}C NMR (126 MHz, $CDCl_3$) of **33**

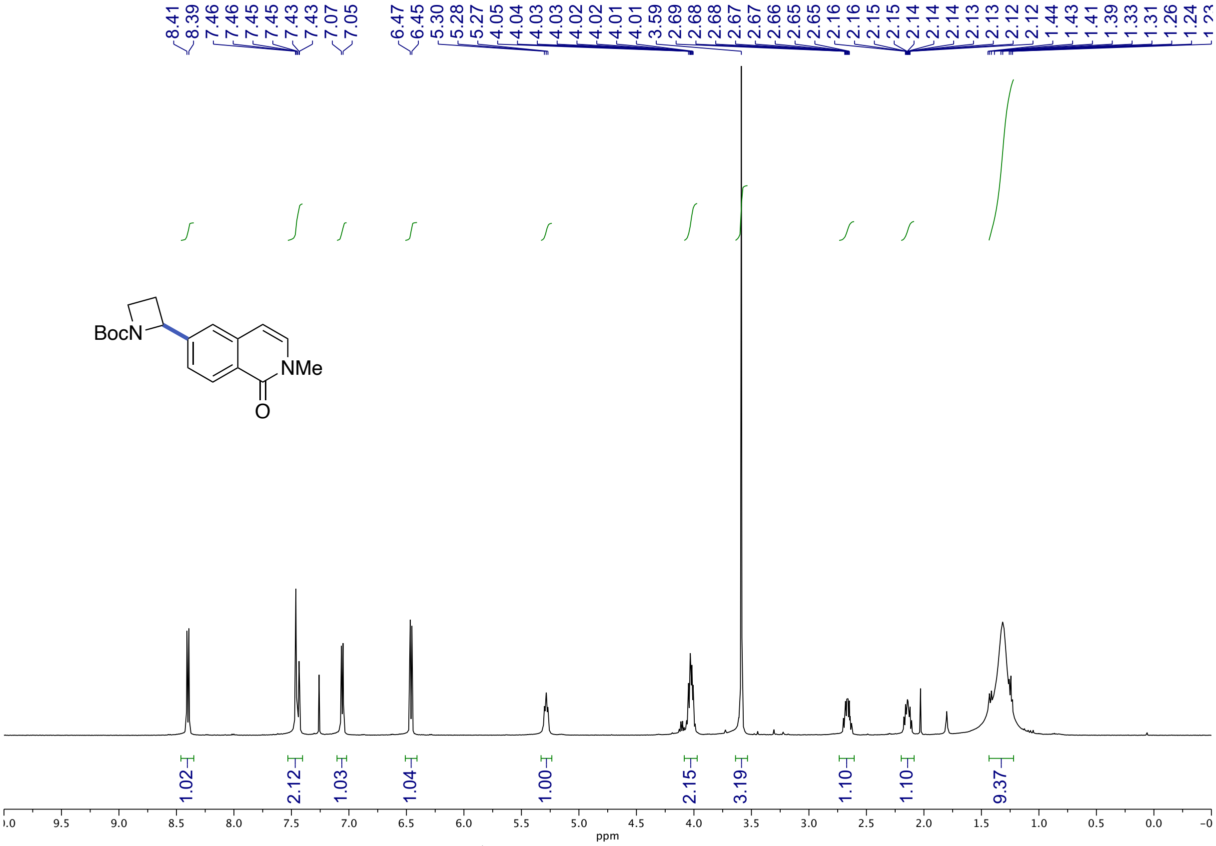


Figure S67: ^{1}H NMR (500 MHz, $CDCl_3$) of **34**

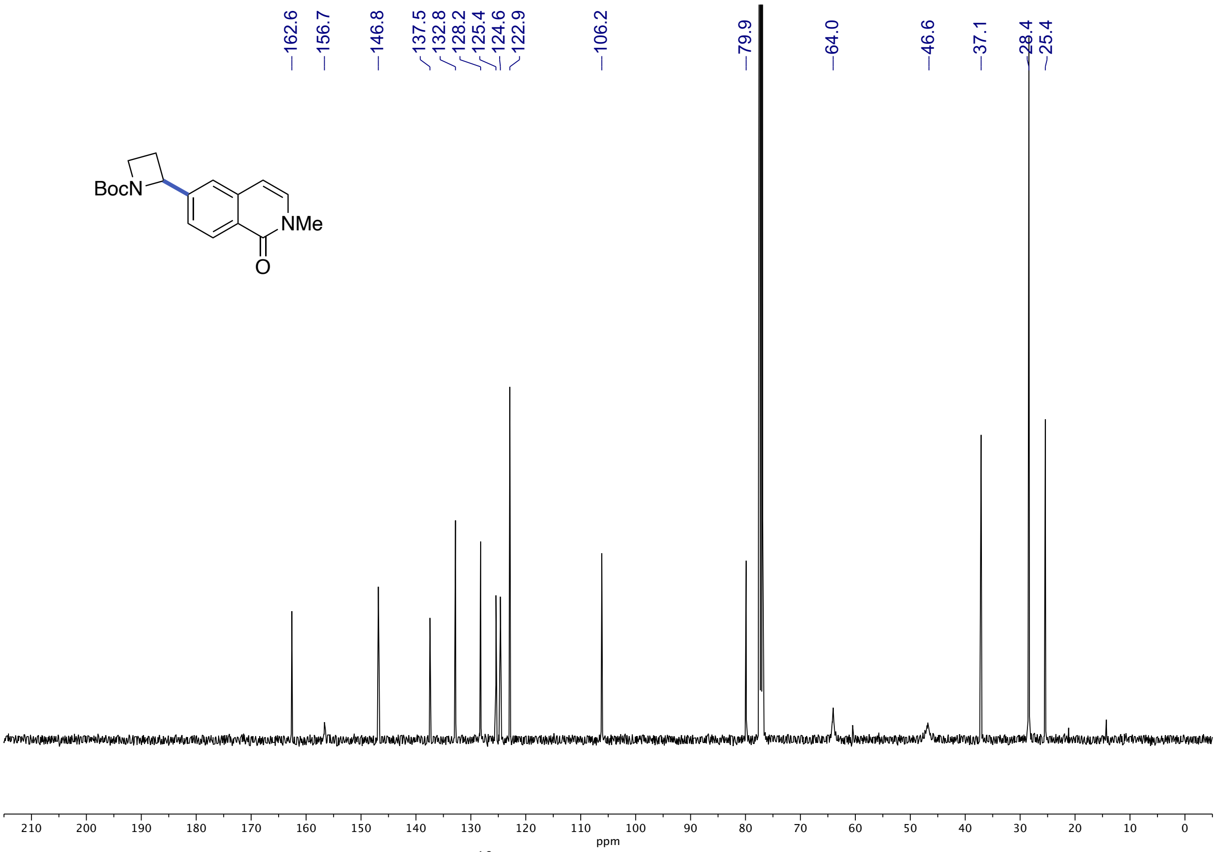


Figure S68: ^{13}C NMR (126 MHz, $CDCl_3$) of **34**

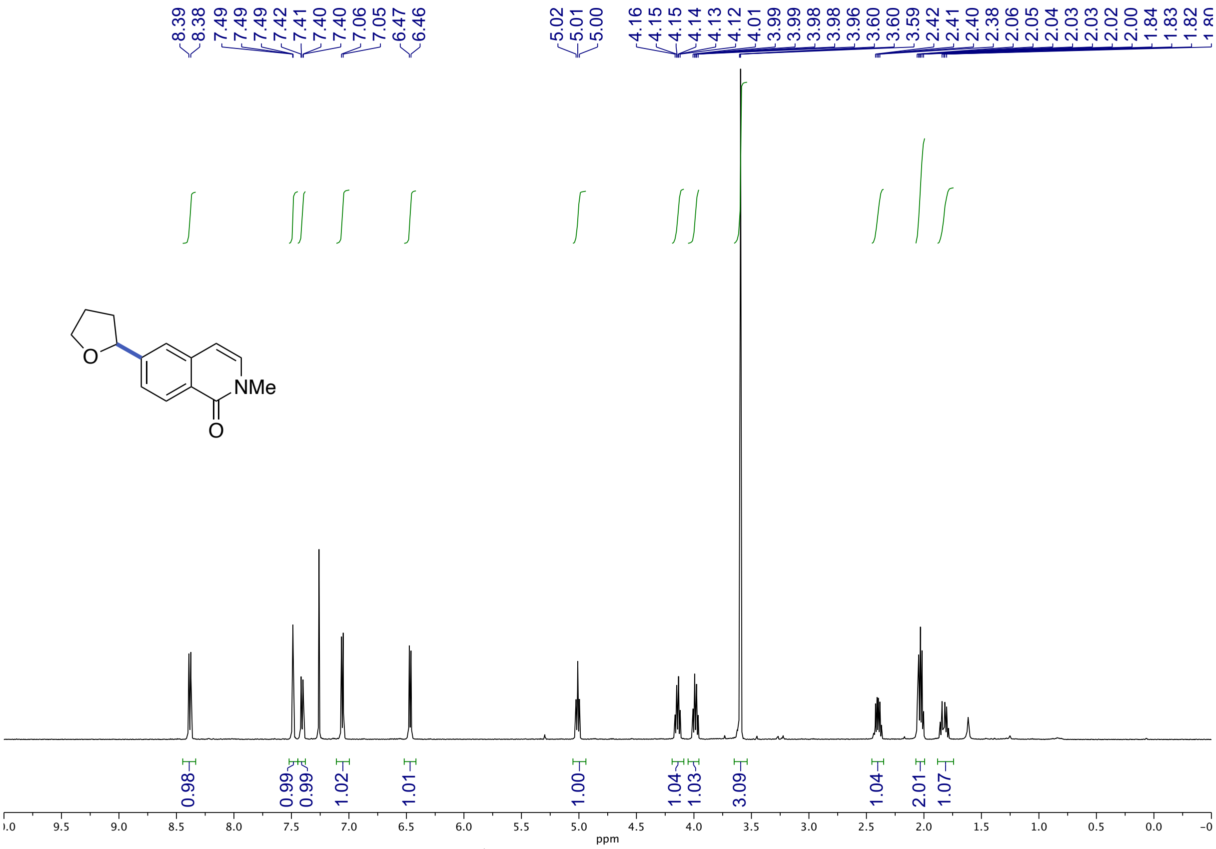


Figure S69: ^{1}H NMR (500 MHz, $CDCl_3$) of **35**

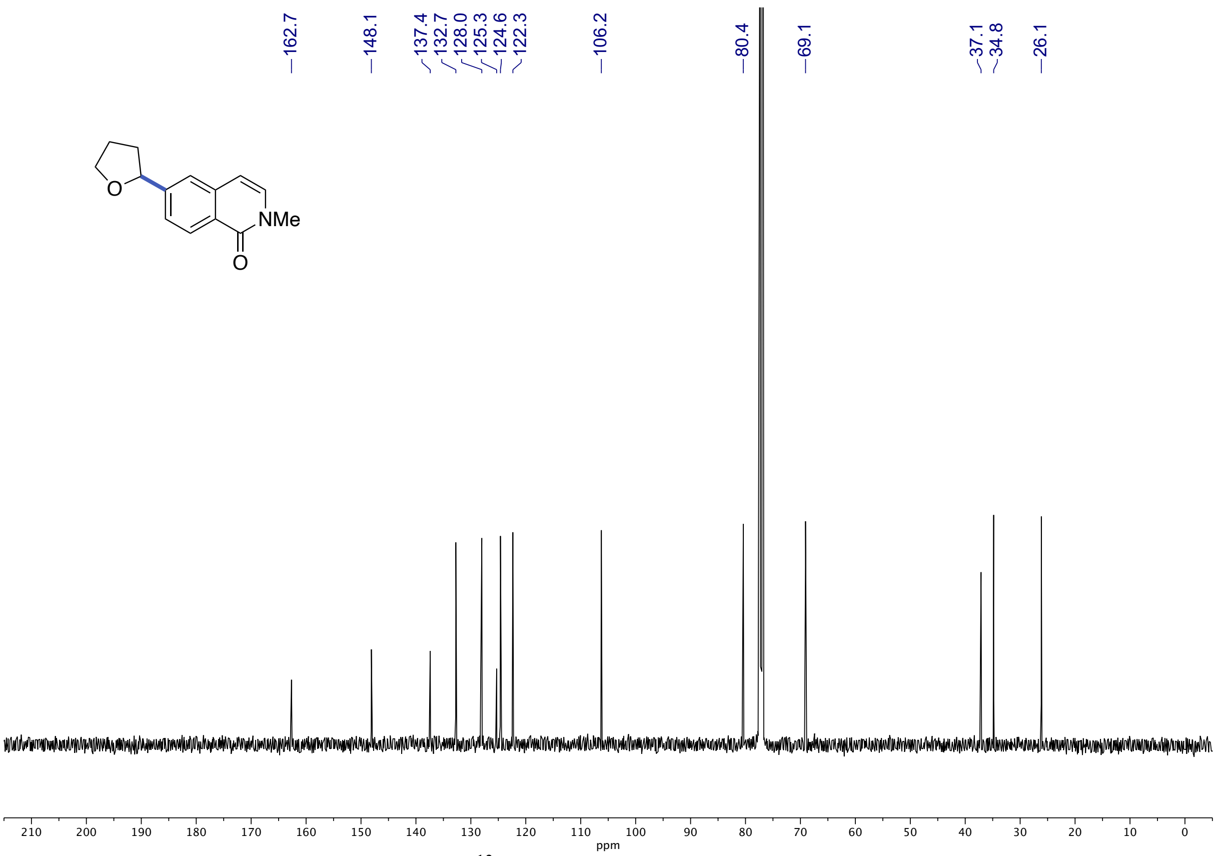


Figure S70: ^{13}C NMR (126 MHz, $CDCl_3$) of **35**

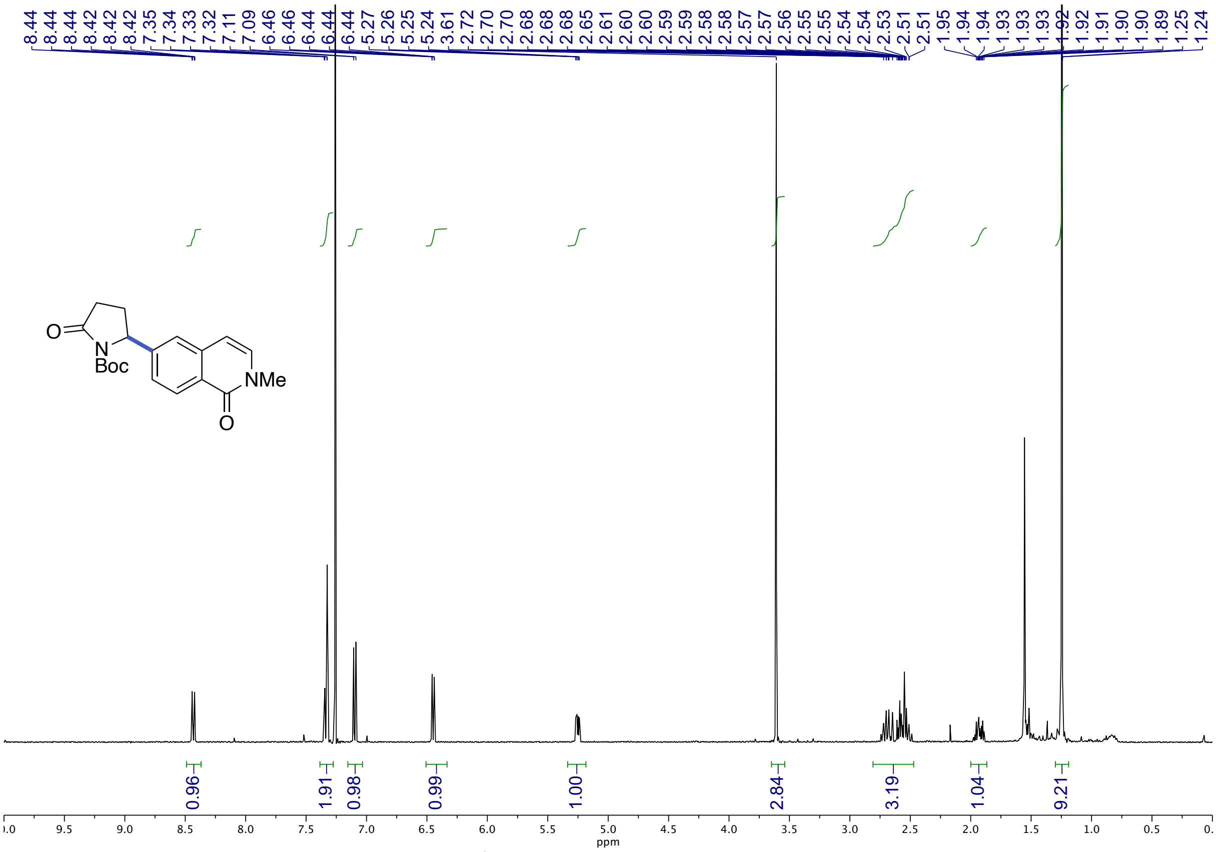


Figure S71: ^{1}H NMR (400 MHz, $CDCl_3$) of **36**

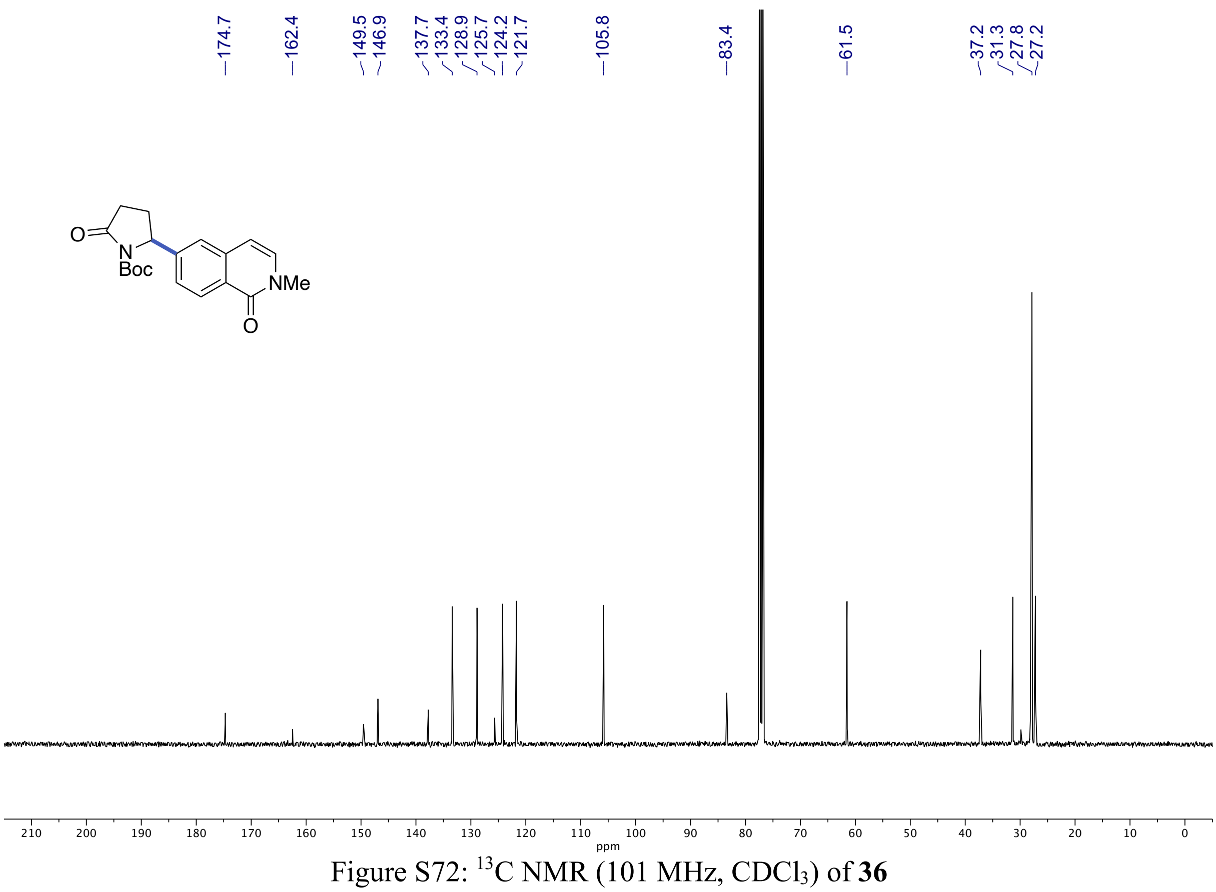


Figure S72: ^{13}C NMR (101 MHz, $CDCl_3$) of **36**

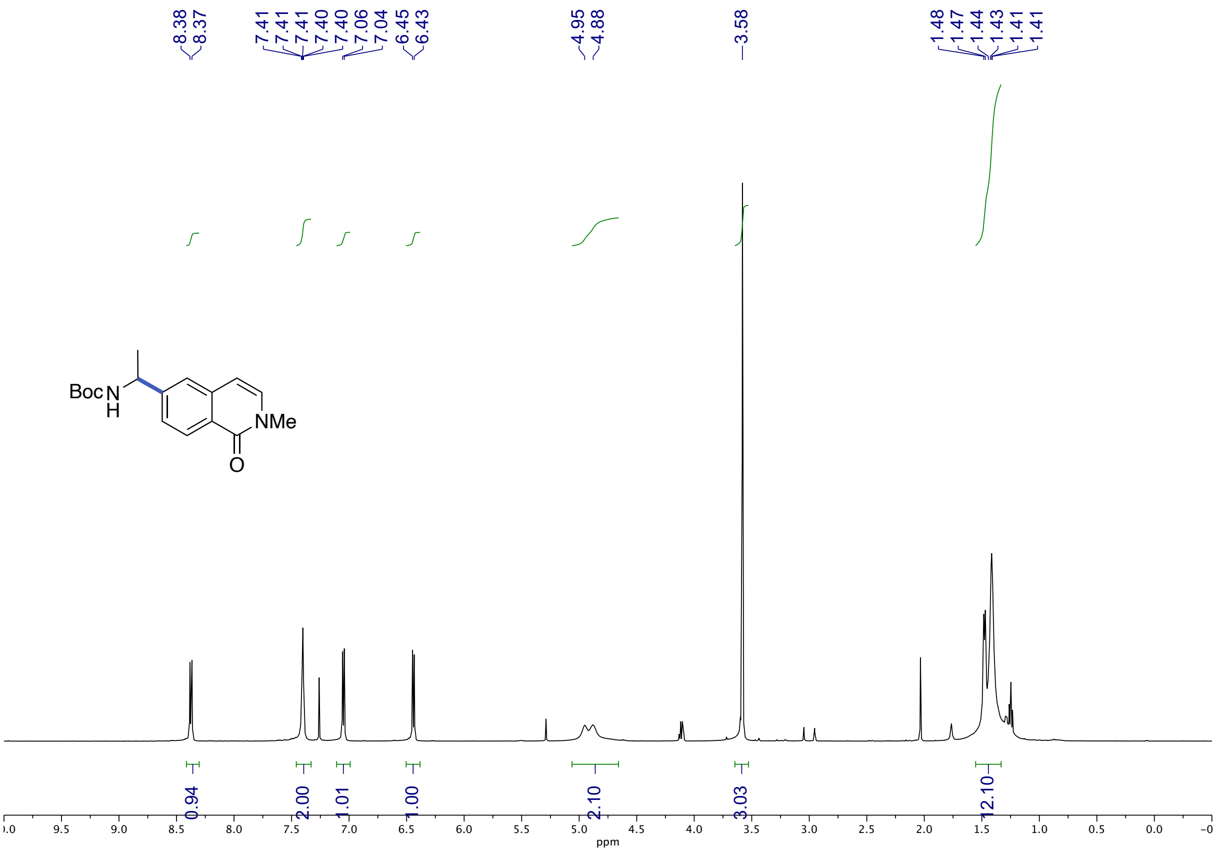


Figure S73: ^{1}H NMR (500 MHz, CDCl$_3$) of **38**

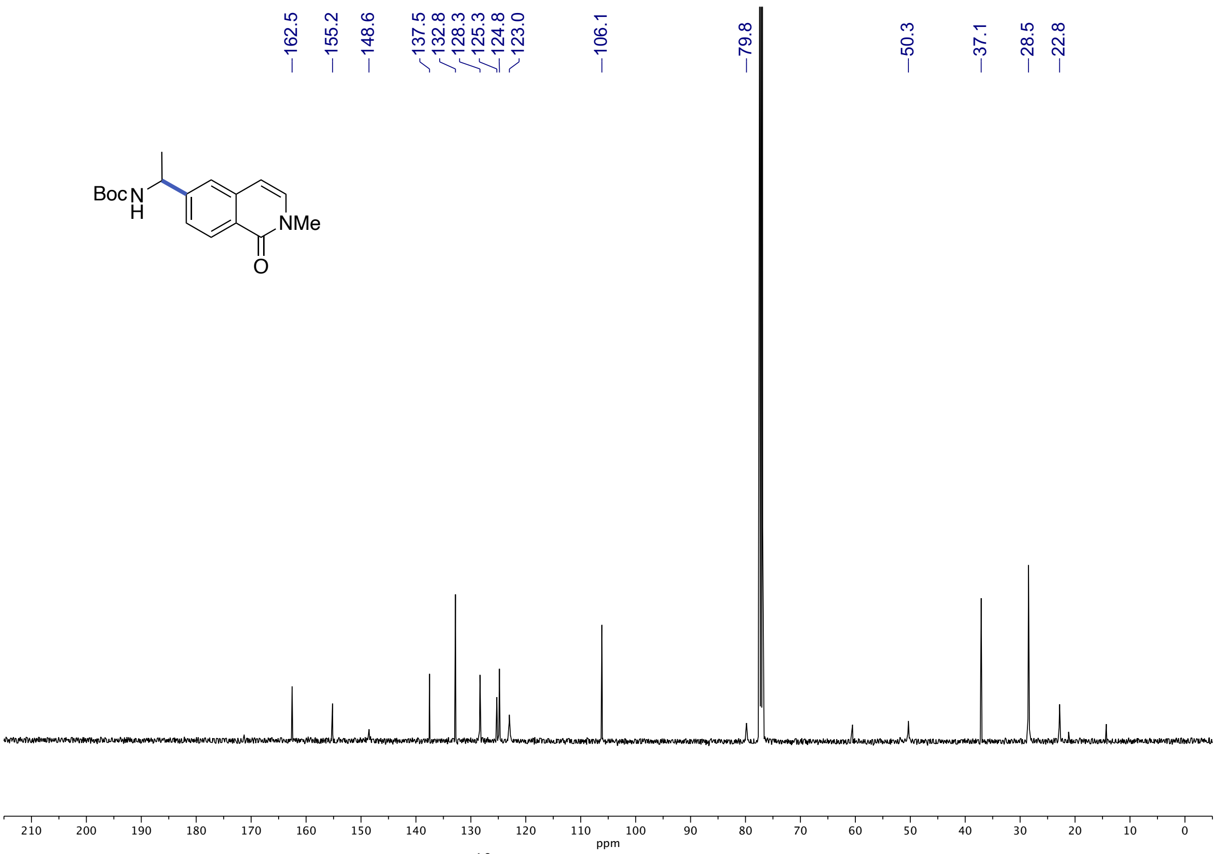


Figure S74: ^{13}C NMR (126 MHz, CDCl$_3$) of **38**

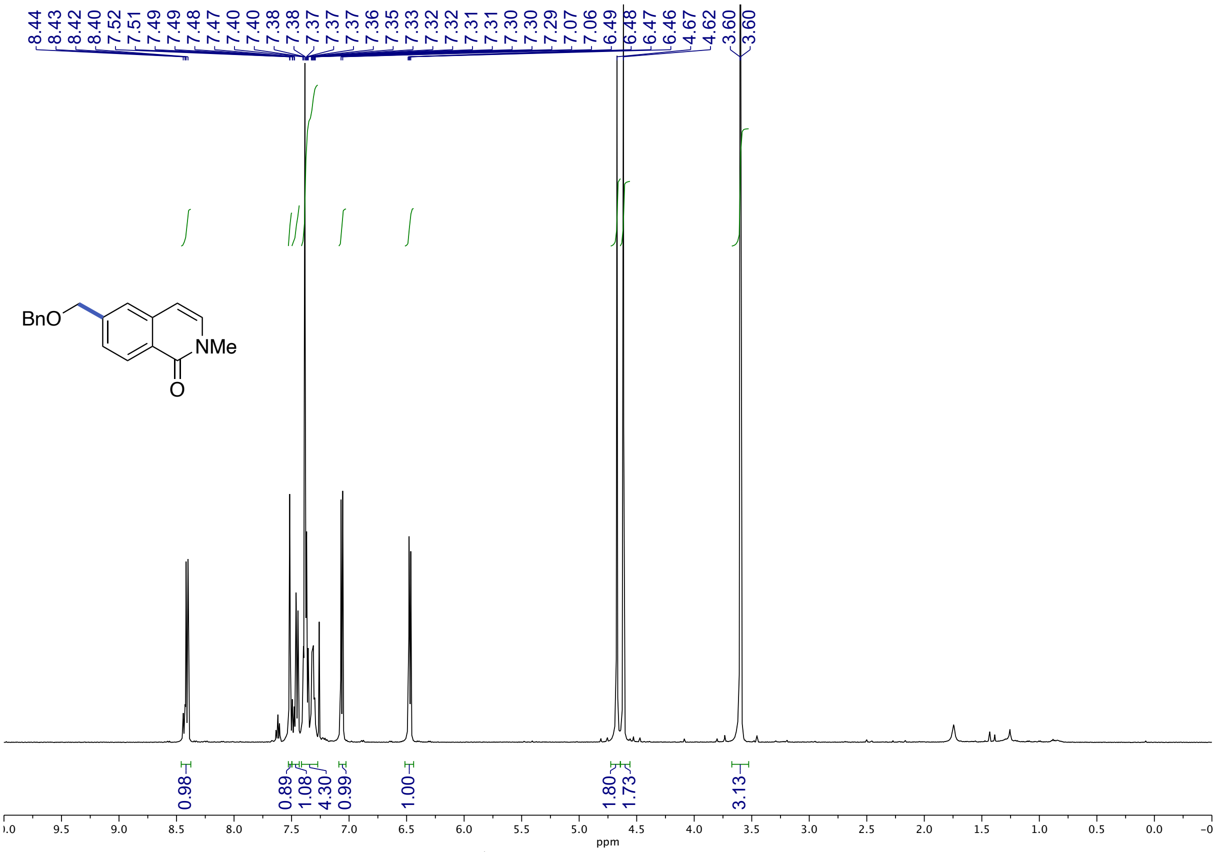


Figure S75: ^{1}H NMR (500 MHz, $CDCl_3$) of **39**

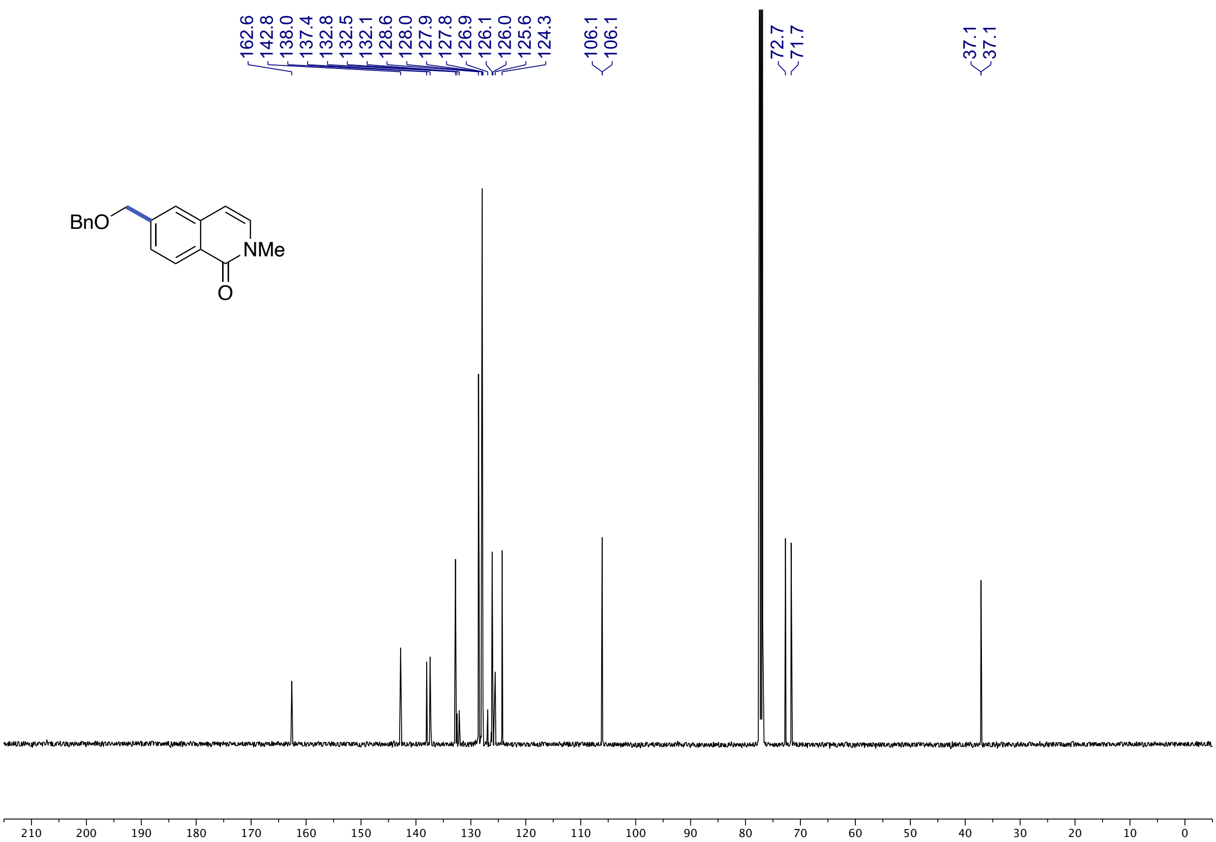


Figure S76: ^{13}C NMR (126 MHz, $CDCl_3$) of **39**

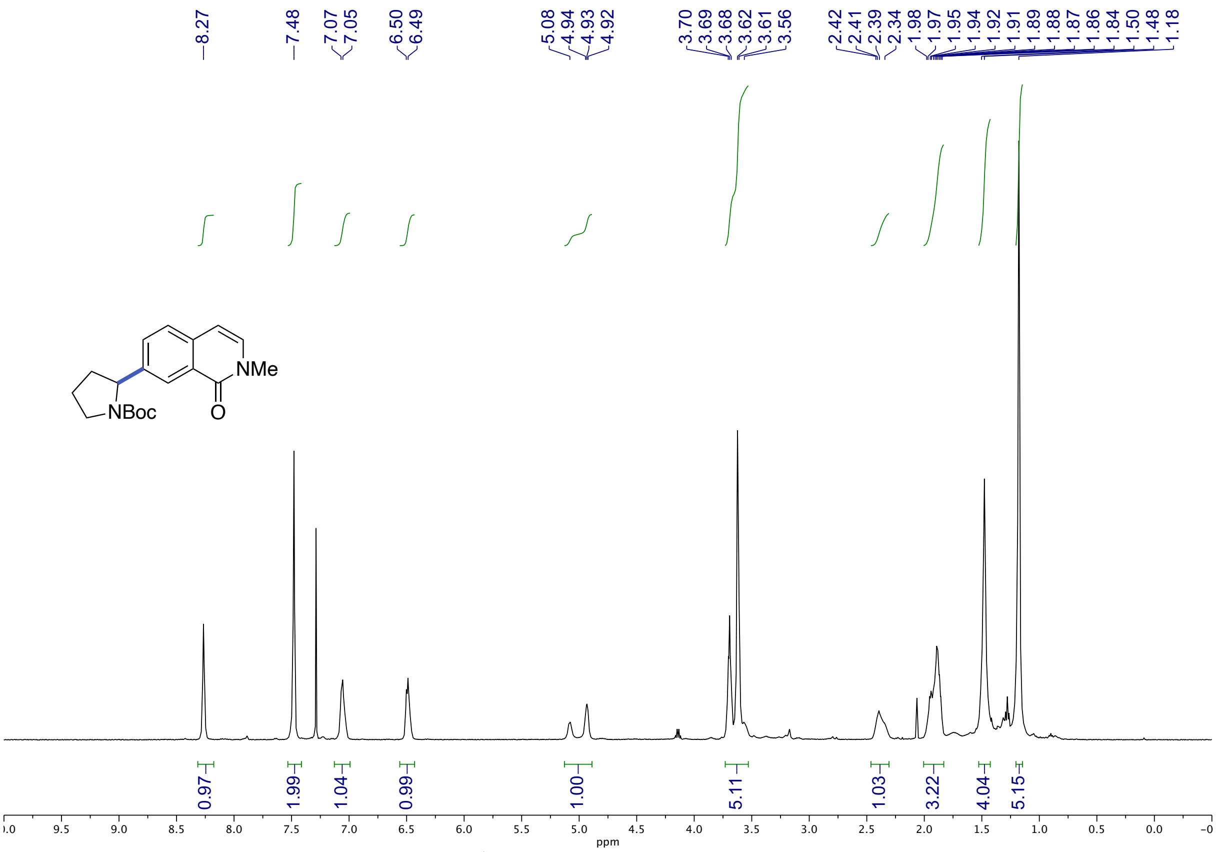


Figure S77: ^{1}H NMR (500 MHz, $CDCl_3$) of **40**

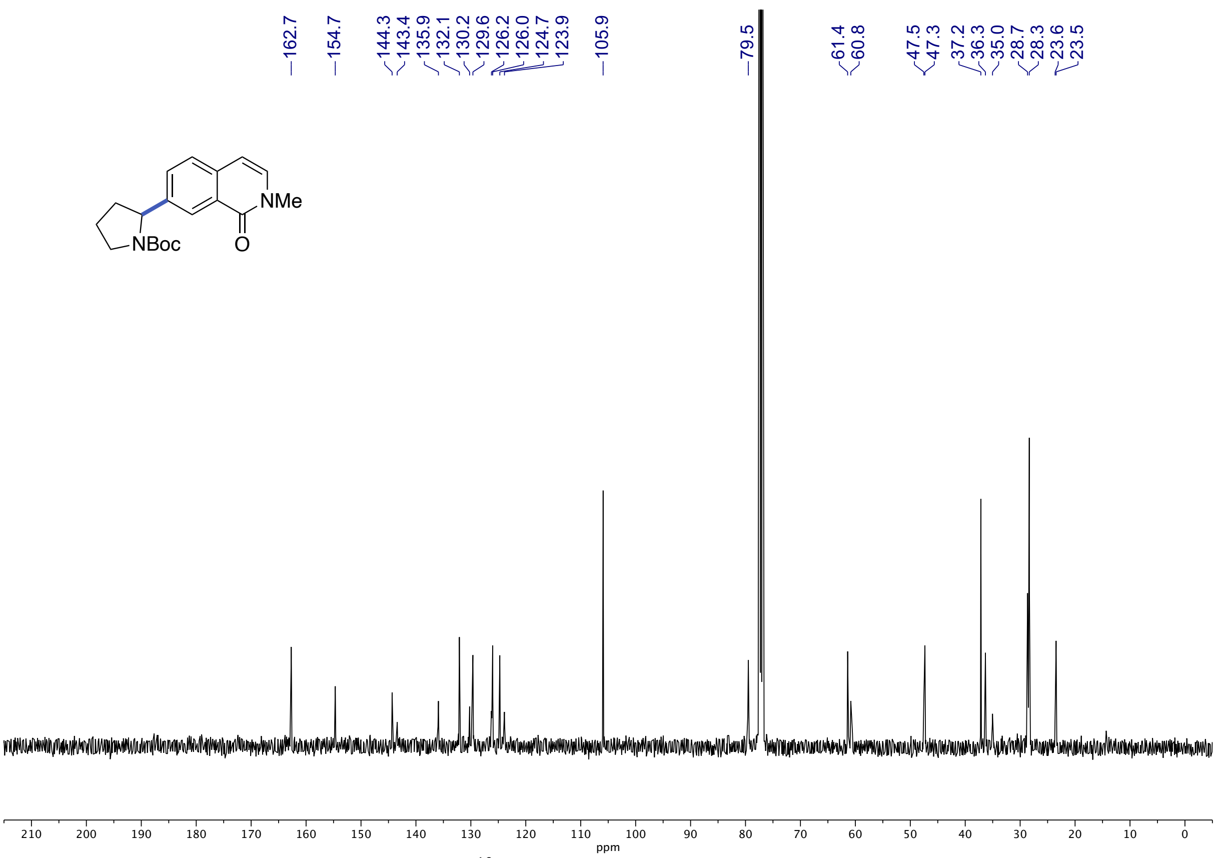


Figure S78: ^{13}C NMR (126 MHz, $CDCl_3$) of **40**

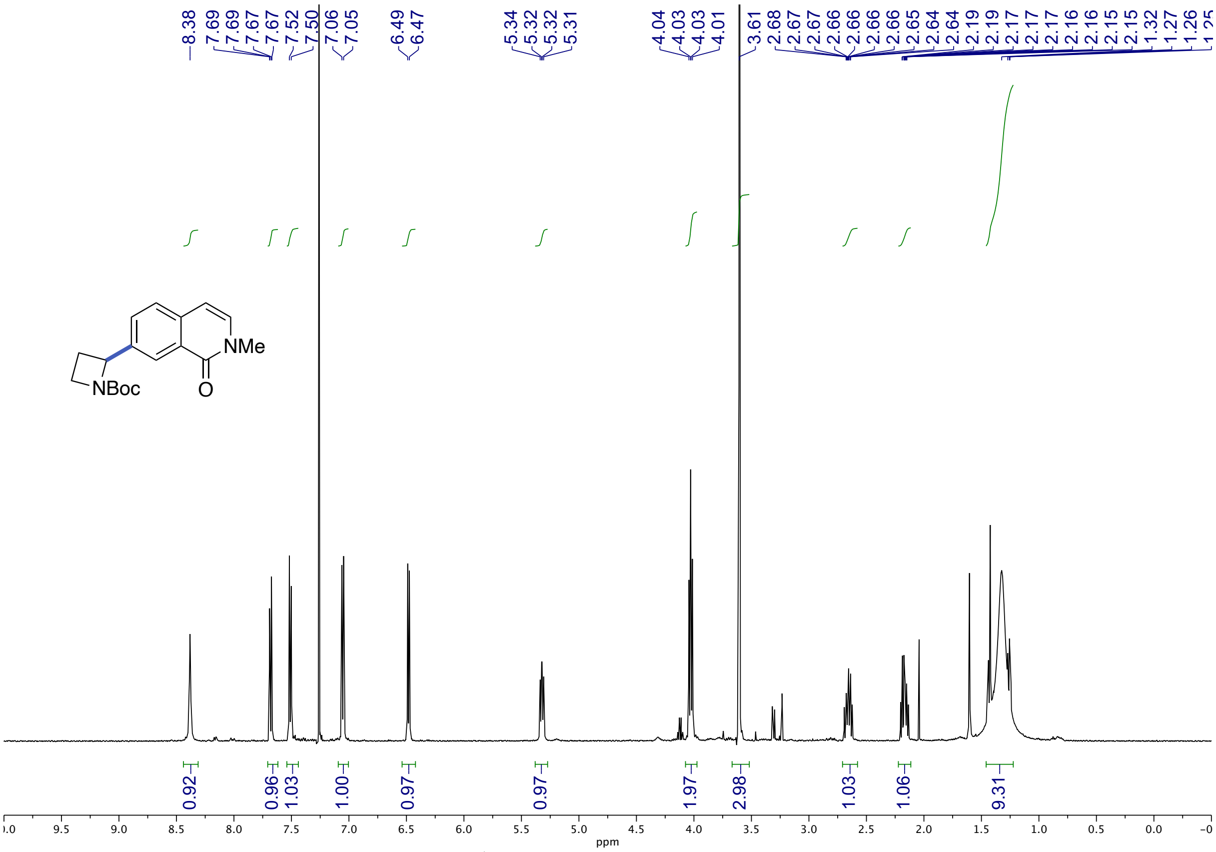


Figure S79: ^{1}H NMR (500 MHz, $CDCl_3$) of **41**

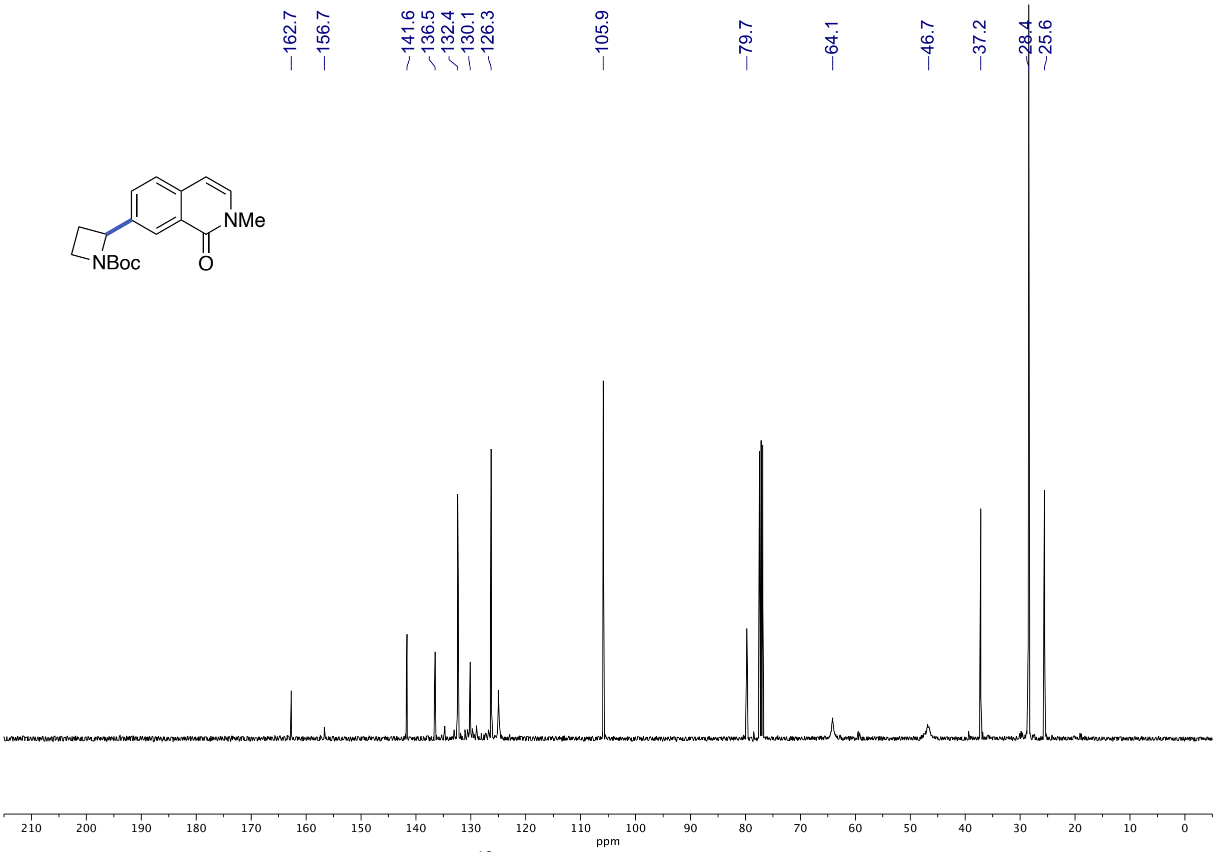


Figure S80: ^{13}C NMR (101 MHz, $CDCl_3$) of **41**

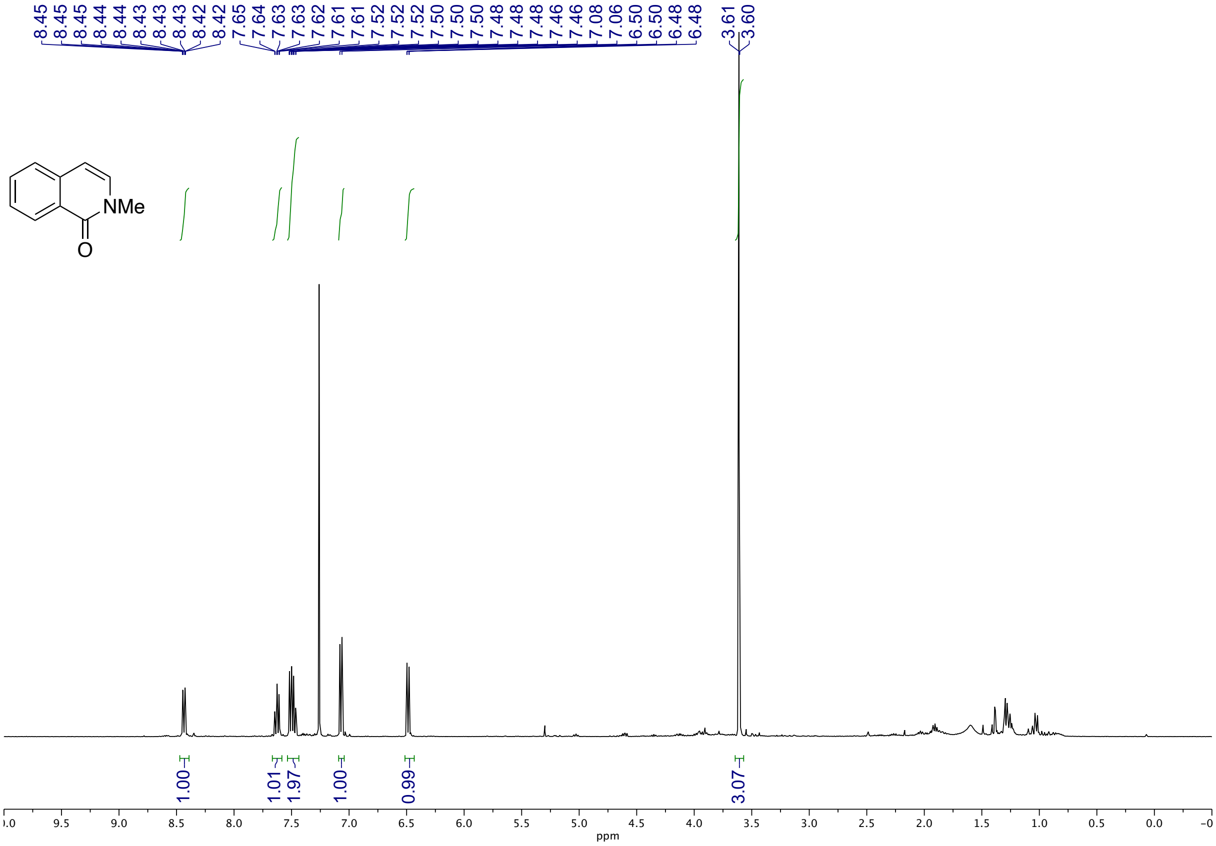


Figure S81: ^{1}H NMR (400 MHz, $CDCl_3$) of **S4**

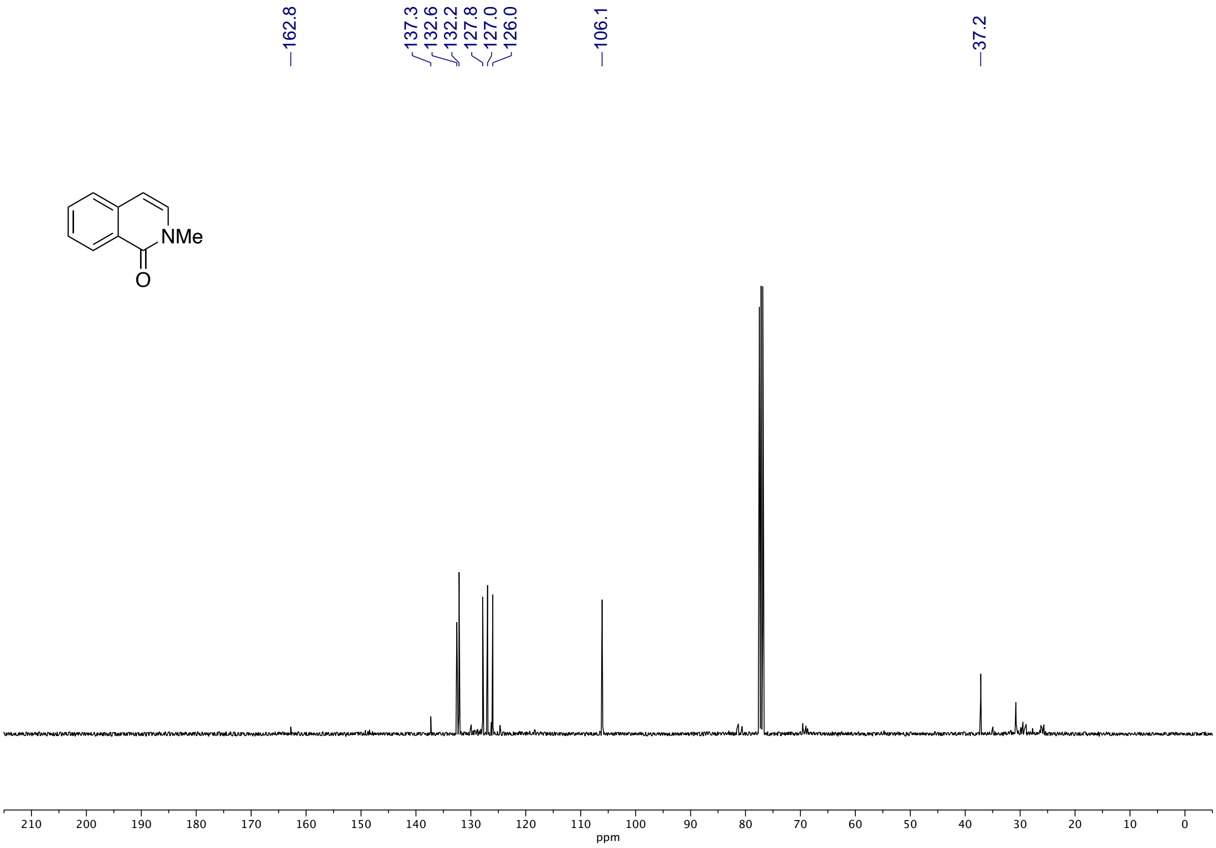


Figure S82: ^{13}C NMR (101 MHz, $CDCl_3$) of **S4**

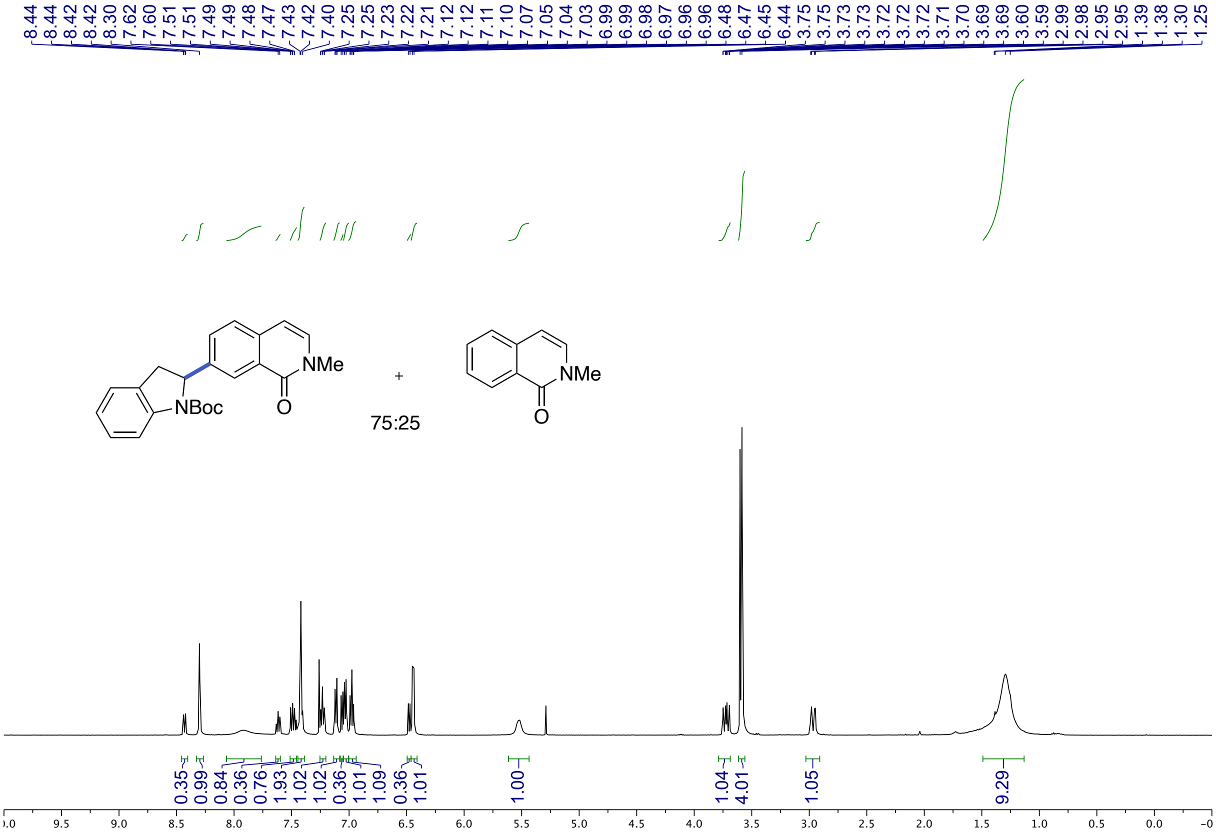


Figure S83: ^{1}H NMR (500 MHz, $CDCl_3$) of **42**+**S4**

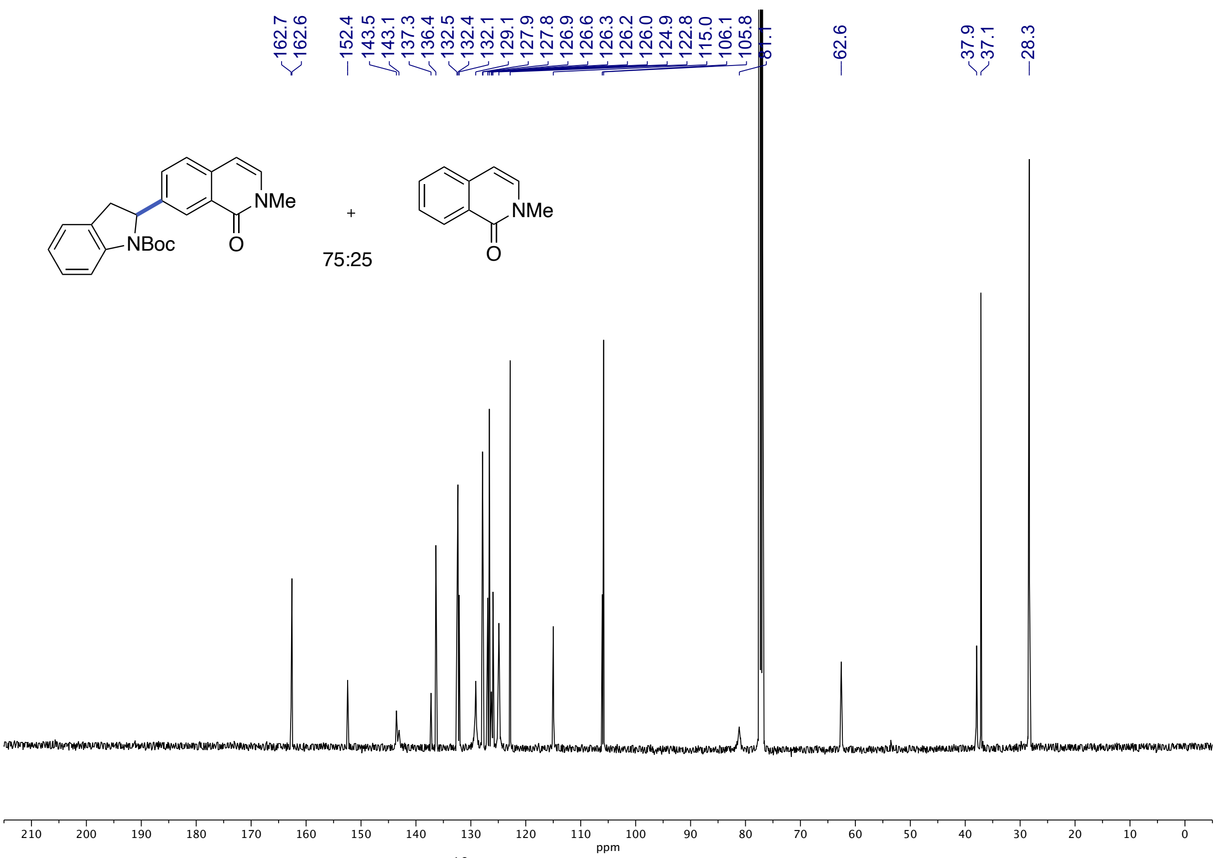


Figure S84: ^{13}C NMR (126 MHz, $CDCl_3$) of **42**+**S4**

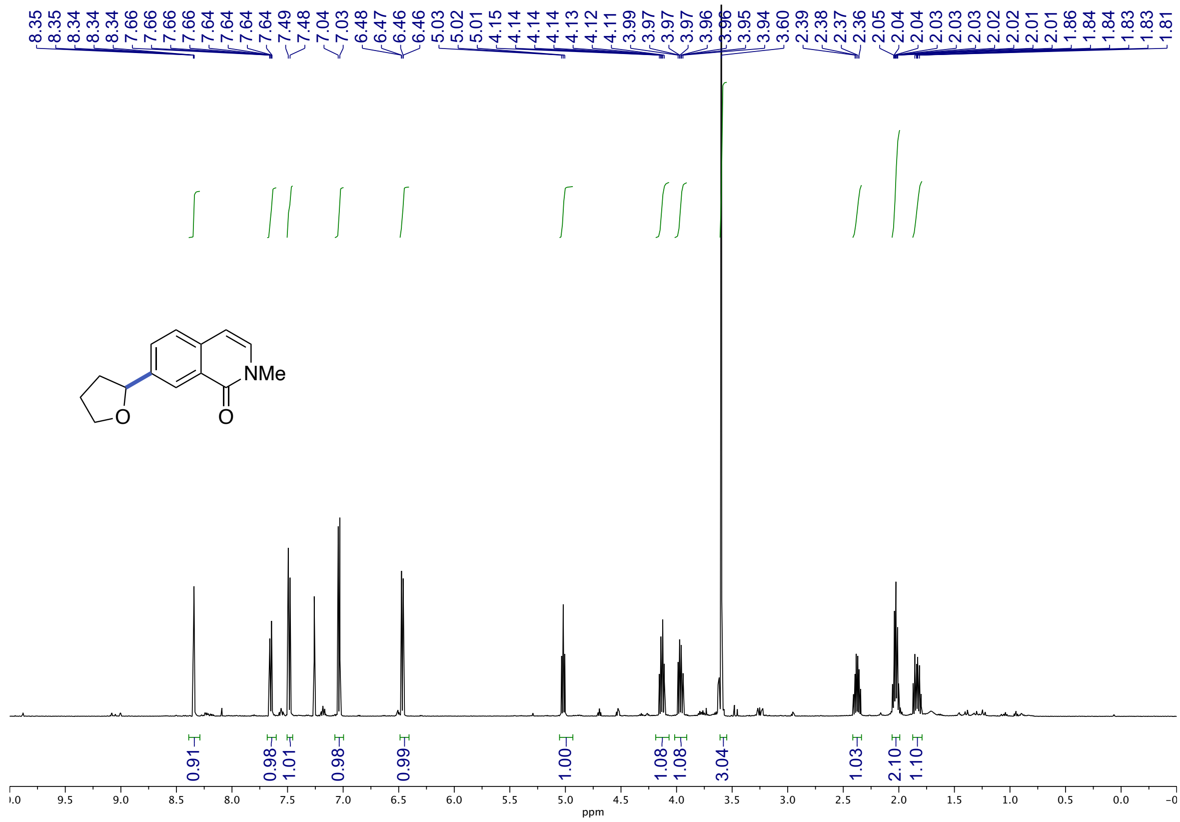


Figure S85: ^{1}H NMR (500 MHz, $CDCl_3$) of **43**

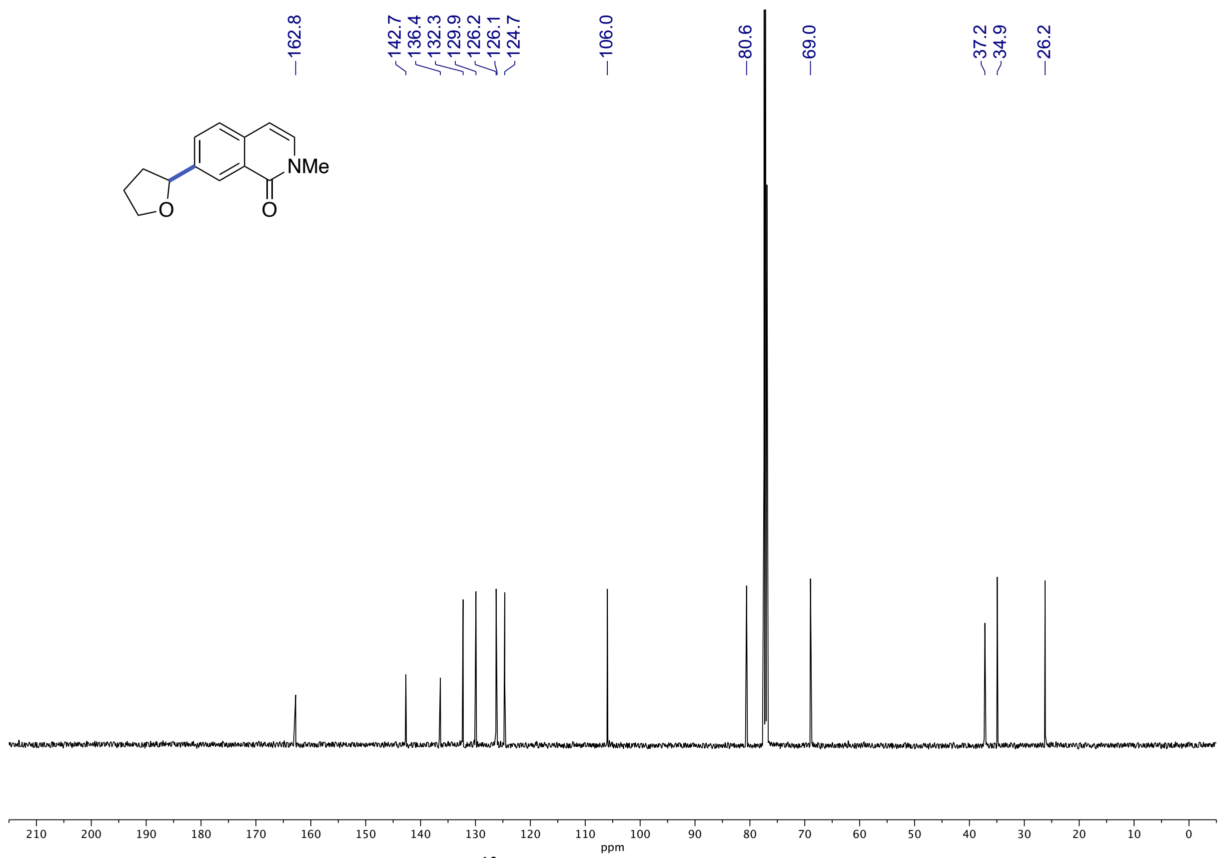


Figure S86: ^{13}C NMR (126 MHz, $CDCl_3$) of **43**

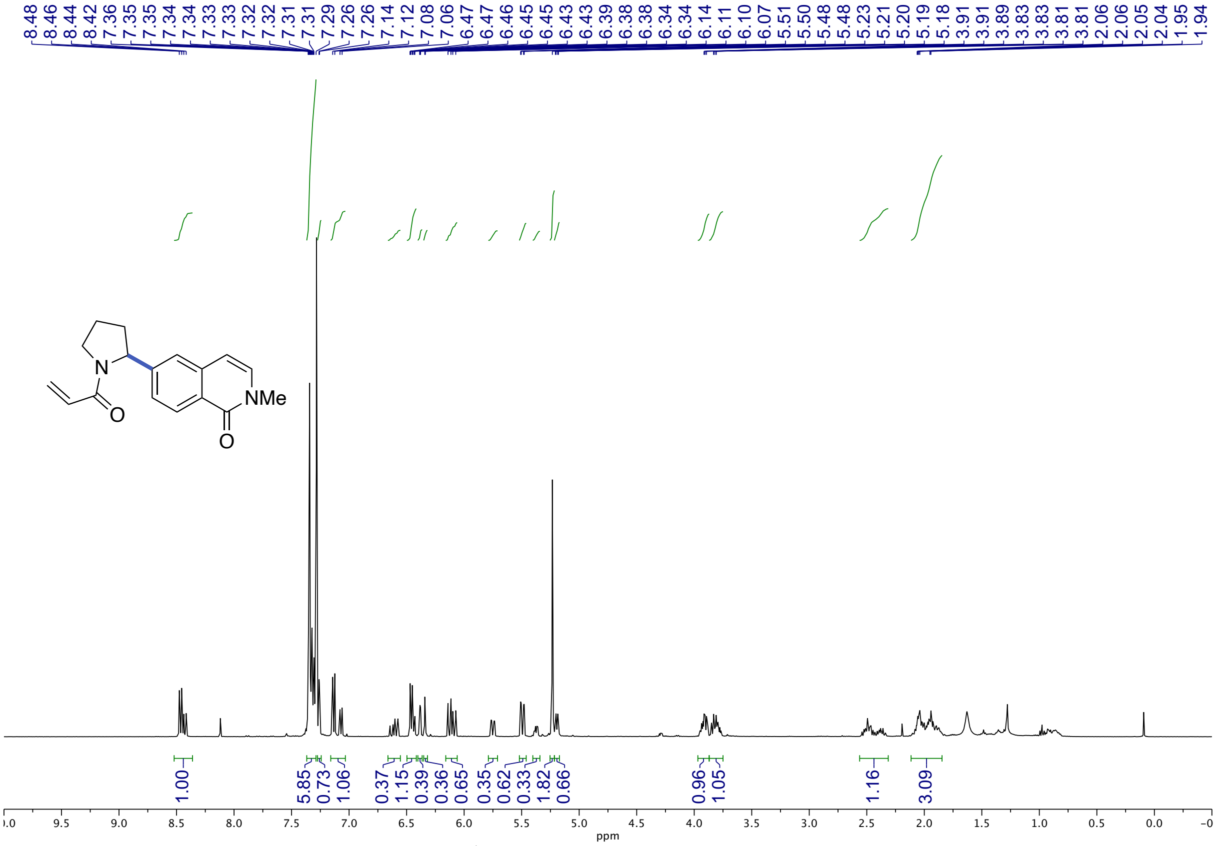


Figure S87: ^{1}H NMR (400 MHz, $CDCl_3$) of **31b**

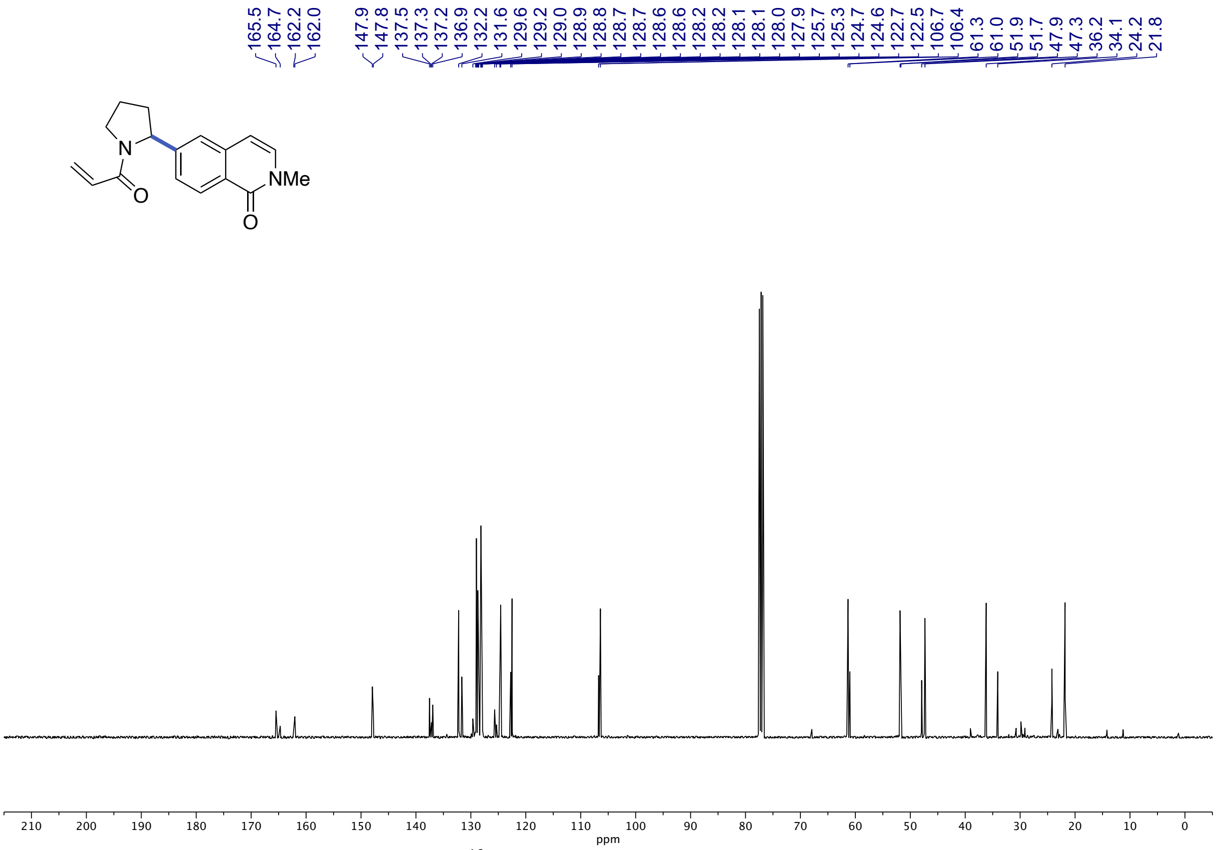


Figure S88: ^{13}C NMR (101 MHz, $CDCl_3$) of **31b**