Ketone-Derived 2,3-Dihydroquinazolinones in N-Heteroarene C-H Alkylation via C-C Bond Scission under Oxidative Metal Catalysis

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Table of contents

1 General Information

Analytic Methods:

All ^{1}H, ^{13}C and ^{19}F NMR spectra were recorded on a Bruker Advance III 500 MHz NMR spectrometer at room temperature unless otherwise noted. The chemicals shift (δ) values are quoted in ppm downfield of tetramethylsilane. The residual solvent signals were used as the references for ^{1}H and ^{13}C NMR spectra ($CDCl_3$: δ_H = 7.26 ppm, δ_C = 77.13 ppm; DMSO-d_6: δ_H = 2.50 ppm, δ_C = 39.52 ppm). ^{19}F NMR spectra are not calibrated by an internal reference. Coupling constants (J) are quoted in Hz. The following abbreviations are used for signal multiplicity: bs = broad signal, s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, dt = doublet of tripets, dq = doublet of quartets, tt = triplet of triplets, m = multiplet. High resolution mass spectra (HRMS) were recorded on Thermo Scientific™ Q Exactive™ Hybrid Quadrupole-Orbitrap Mass Spectrometer. Low resolution mass spectra (LRMS) were recorded using Thermo Scientific™ LCQ Fleet™ ion trap mass spectrometer. The ATR IR Spectra of solid and liquid compounds were recorded on a Shimadzu IRPrestige-21 FTIR spectrometer. The wave numbers are expressed in [cm^{-1}]. Melting points (uncorrected) of solid compounds were measured using one end closed glass capillaries in Stuart Melting Point SMP50 apparatus. On an electrochemical workstation from CH Instruments, Inc., cyclic voltammetry was carried out. Glassy carbon working electrode, graphite rod auxiliary electrode, and Ag wire pseudo-reference electrode were used to record CV. The ambient temperature is recorded as 27 ± 3 °C.

Reagents and Methods: All the chemicals were purchased from Sigma-Aldrich, TCI chemicals, Alfa Aesar, Acros Organics, Spectrochem, Avra, SRL, BLD Pharma and used without any further purification unless otherwise mentioned. Technical grade solvents: ethyl acetate, petroleum ether (40-60), hexane, acetone, dichloromethane were purchased from Merck and Avra and were used after distillation. purification as following: ethyl acetate, petroleum ether (40-60), dichloromethane, diethyl ether were purified by distillation. The following dry solvents were stored under molecular sieves with septa under nitrogen atmosphere and withdrawn using a syringe under positive nitrogen pressure: THF (from Spectrochem), Anhydrous *N,N*-Dimethylacetamide (DMA) and *N*-Methyl-2-pyrrolidone (NMP) were purchased from Sigma-Aldrich. Anhydrous *N,N*-Dimethylformamide (DMF), Dimethyl sulfoxide (DMSO) and Acetonitrile (MeCN) were purchased from Acros Organics. Dichloromethane (DCM) was purchased from Merck and was dried and distilled over CaH_2. Tetrahydrofuran (THF), Diethylether (Et_2O), and Toluene were purchased from Spectrochem and dried over KOH pallets or CaH_2 and distilled over Sodium wire/benzophenone. The following dry solvents: DCM, THF, Et_2O

and toluene were stored under molecular sieves with septa under nitrogen atmosphere and withdrawn using a syringe under positive nitrogen pressure The deuterated solvents, $CDCl_3$ (99.8%) and DMSO-d_6 (99.8%), were purchased from Sigma-Aldrich.

Silica Gel Aluminium TLC plates were purchased from Merck. TLC was visualized using shortwave UV-254 nm or the stain made out of phosphomolybdic acid or potassium permanganate then heating as the developer. Silica gel 230-400 mesh, purchased from Merck, was used for the column chromatography.

Note: No attempts were made to optimize the yields of the substrates.

2. Synthesis of Starting Materials

2.1 Synthesis of Ketone Derivatives

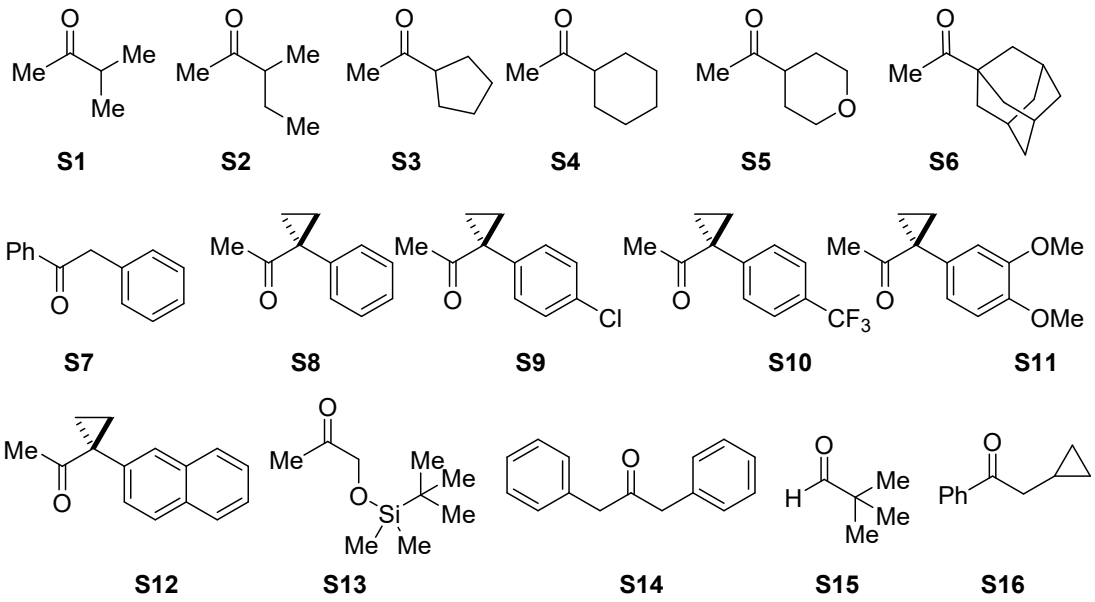
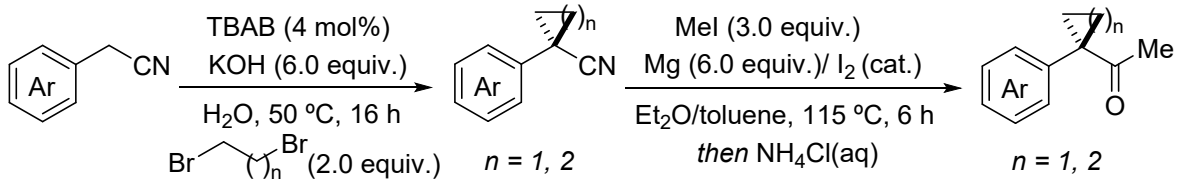


Figure S1: List of Ketones/Aldehydes

The ketones **S1**, **S2**, **S3**, **S4**, **S5**, **S6**, **S7** and **S14** were commercially procured. The aldehyde **S15** was also commercially procured. The ketones **S8**,[1] **S9**,[2] **S13**,[3] and **S16**[4] were prepared following the reported literatures.

General procedure for the synthesis of 1-(1-Arylcycloalkyl)ethan-1-one derivatives (GP1)

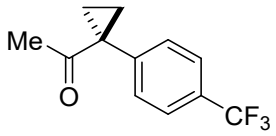


In a round bottom flask equipped with a Teflon-coated stirring bar, 2-arylacetonitrile (1.00 equiv.), KOH (6.00 equiv.) and tetrabutylammonium bromide (TBAB, 0.04 equiv.) were dissolved in water (5.0 M). The dibromoalkane (2.00 equiv.) was added dropwise to the reaction mixture. The resulting solution was heated at 50 ºC for 16 h. After cooling down to room temperature, the reaction mixture was diluted with water and extracted with dichloromethane. The organic phase was washed with 1N HCl solution and subsequently water followed by brine solution. The solvent was dried over anhydrous sodium sulfate and removed under reduced pressure. The crude mixture was purified by flash column chromatography through silica (eluent = petroleum ether/ethyl acetate) to afford 1-arylcycloalkane-1-carbonitrile, which was directly used in next step.

In a two neck round bottom flask with a Teflon-coated stirring bar under inert atmosphere, the Grignard reagent was prepared by the addition of methyl iodide (3.00 equiv.) into the mixture of magnesium (6.00 equiv.) and Iodine (catalytic amount) in dry diethyl ether (0.25 M) followed by stirring at room temperature for 2 h. Under inert atmosphere, in a separate two neck round bottom

flask equipped with a condenser and Teflon-coated stirring bar, the prepared Grignard reagent was dropwise added to the solution of 1-arylcycloalkane-1-carbonitrile (1.00 equiv.) in dry toluene (0.1 M) and the resulting mixture was refluxed at 115 ºC for 4 h. After cooling down to room temperature, the reaction mixture was quenched with aqueous ammonium chloride solution followed by extraction with diethyl ether. The resulting organic layers were dried over anhydrous sodium sulfate and concentrated under reduced pressure. The crude mixture was purified by flash column chromatography through silica (eluent = petroleum ether/ethyl acetate) to afford pure 1-(1-arylcycloalkyl)ethan-1-one (**S10-12**).

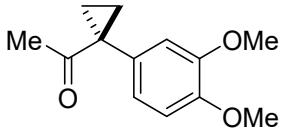
1-(1-(4-(Trifluoromethyl)phenyl)cyclopropyl)ethan-1-one (S10)



Following **GP-1**, the starting material 2-(4-(trifluoromethyl)phenyl)acetonitrile (1.85 g, 10.0 mmol) afforded 1-(1-(4-(trifluoromethyl)phenyl)cyclopropyl)ethan-1-one (**S10**) as white semi-solid (484 mg, 2.12 mmol, 21% overall yield after two steps).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 7.62 (d, *J* = 8.1 Hz, 2H), 7.49 (d, *J* = 8.0 Hz, 2H), 2.00 (s, 3H), 1.65 (q, *J* = 3.8 Hz, 2H), 1.19 (q, *J* = 3.8 Hz, 3H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 207.5, 145.2 (q, *J* = 1.2 Hz), 131.3, 129.9 (q, *J* = 32.6 Hz), 125.8 (q, *J* = 3.7 Hz), 123.1, 37.6, 29.3, 18.7; **^{19}F NMR (471 MHz, $CDCl_3$)** δ (ppm) = – 62.56; **HRMS (ESI):** m/z calc. for ($C_{12}H_{12}F_3O^+$) $[M+H]^+$: 229.0835; found: 229.0835; **IR (ATR) (ν cm^{-1}):** 2976, 2937, 2870, 1471, 1268, 1103, 1027, 808.

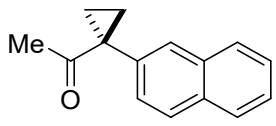
1-(1-(3,4-Dimethoxyphenyl)cyclopropyl)ethan-1-one (S11)



Following **GP-1**, the starting material 2-(3,4-dimethoxyphenyl)acetonitrile (2.66 g, 15.63 mmol) afforded the compound **S11** as pale yellow liquid (549 mg, 2.49 mmol, 16% overall yield after two steps).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 6.92 – 6.91 (m, 1H), 6.83 – 6.86 (m, 2H), 3.89 (s, 6H), 2.02 (s, 3H), 1.57 (dd, *J* = 6.5, 3.4 Hz, 2H), 1.16 (dd, *J* = 6.5, 3.4 Hz, 1H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 209.6, 149.0, 148.5, 133.8, 123.0, 113.9, 111.3, 56.1, 56.1, 37.4, 29.4, 19.1; **HRMS (ESI):** m/z calc. for ($C_{13}H_{17}O_3^+$) $[M+H]^+$: 221.1172; found: 221.1175; **IR (ATR) (ν cm^{-1}):** 3021, 1696, 1521, 1427, 1264, 1150, 1035, 986, 896.

1-(1-(Naphthalen-2-yl)cyclopropyl)ethan-1-one (S12)



Following **GP-1**, the starting material 2-(naphthalen-2-yl)acetonitrile (836 mg, 5.0 mmol) afforded the compound **S12** as pale yellow solid (595 mg, 2.83 mmol, 57% overall yield after two steps).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 7.82 – 7.86 (m, 4H), 7.48 – 7.53 (m, 3H), 2.04 (s, 3H), 1.68 (q, *J* = 3.6 Hz, 2H), 1.28 (q, *J* = 3.6 Hz, 2H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 209.1, 138.7, 133.5, 132.8, 129.5, 129.0, 128.5, 127.9, 127.8, 126.5, 126.3, 37.9, 29.8, 19.1. The spectroscopic data obtained were in agreement with the reported data for the compound **S14**.[5]

2.2 Synthesis of 2,3-Dihydroquinazolinone Derivatives

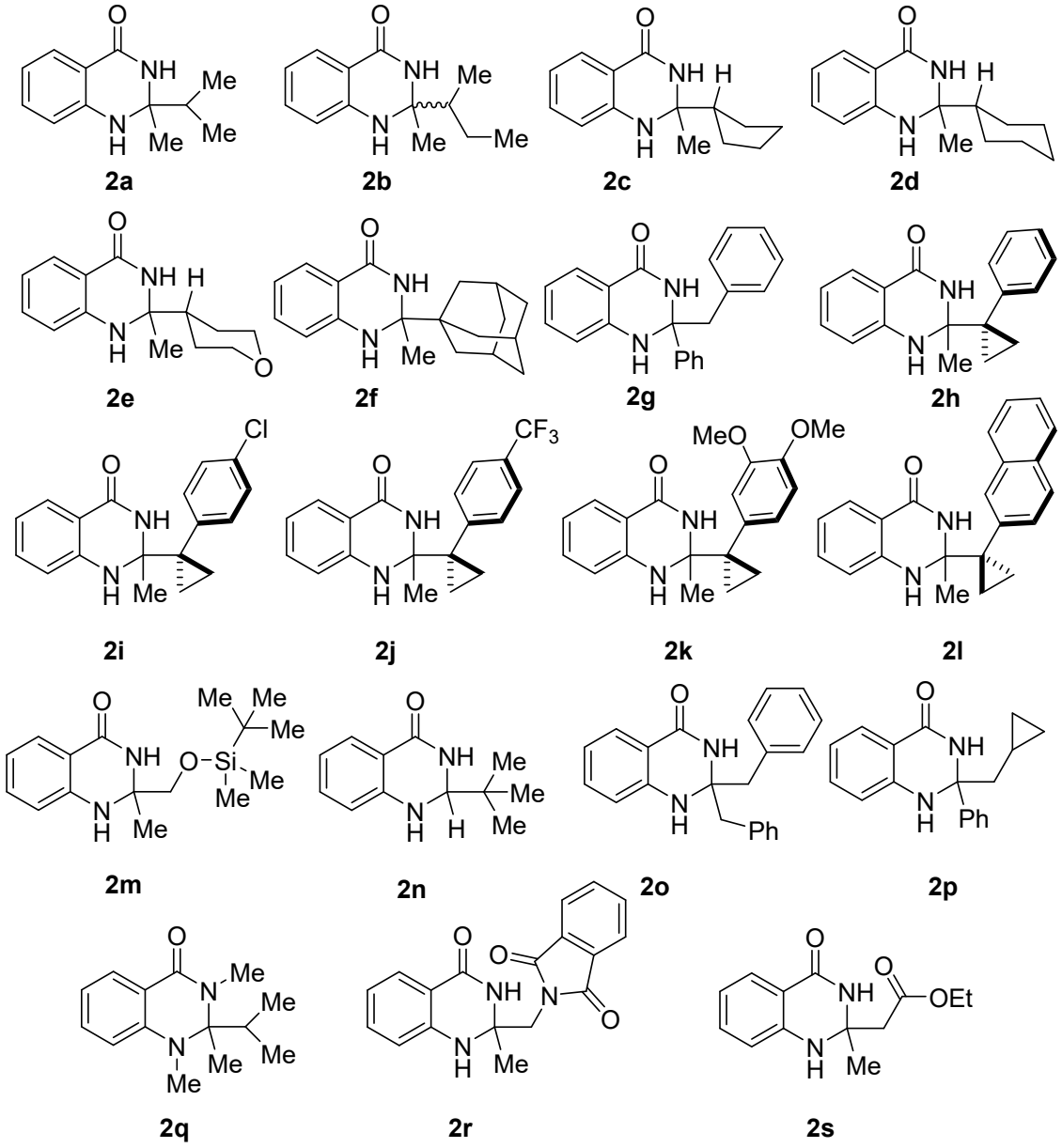
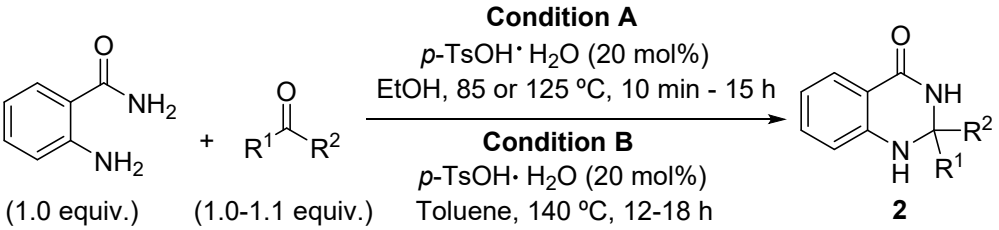


Figure S2: List of 2,3-Dihydroquinazolinone derivatives

Quinazolidinones **2g**,[6] **2m**,[4] **2n,**[7] **2p**[4], **2r**[4] and **2s**[8] were prepared following the reported literatures.

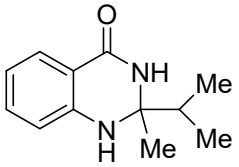
General procedure for the synthesis of Quinazolidinones (GP2)



Protocol A1: Following a modified procedure reported by Revathy et al.[9] in an oven-dried sealed tube equipped with a Teflon-coated stirring bar, anthranilamide (1.00 equiv.), ketone (1.00-1.10 equiv.) and *p*-toluenesulfonic acid (0.2 equiv.) were dissolved in absolute ethanol (2M). The resulting solution was heated at 85-125 ºC for 10 min - 15 h. After cooling down to room temperature, crushed ice was added to the reaction mixture and the solid was gradually precipitated out. The solid was filtered, washed with water and dried to deliver the product (**2**), which was further purified by recrystallization from ethanol (if required).

Protocol A2: Following a modified procedure reported by Revathy et al.[9] in an oven-dried sealed tube equipped with a Teflon-coated stirring bar, anthranilamide (1.00 equiv.), ketone (1.00-1.10 equiv.) and *p*-toluenesulfonic acid (0.2 equiv.) were dissolved in absolute ethanol (2M). The resulting solution was heated at 85-125 ºC for 10 min - 15 h. After cooling down to room temperature, the reaction mixture was concentrated under reduced pressure and the crude reaction mixture was purified by flash column chromatography through Silica gel (eluent: petroleum ether/ethyl acetate) to afford pure product **2**.

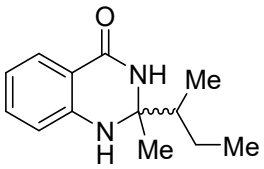
2-Isopropyl-2-methyl-2,3-dihydroquinazolin-4(1H)-one (2a)



Following **GP-2 (Protocol A1)**, Anthranilamide (2.72 g, 20 mmol) and 3-Methylbutan-2-one (**S1**, 1.72 g, 20 mmol) afforded the compound **2a** as white solid (3.57 g, 17.5 mmol, 87%). Reaction Temperature: 85 ºC.

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 7.86 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.28 (ddd, *J* = 8.2, 7.4, 1.6 Hz, 1H), 6.77 – 6.80 (m, 1H), 6.59 (dd, *J* = 8.1, 0.4 Hz, 1H), 5.84 (s, 1H), 4.13 (s, 1H), 2.01 – 2.09 (m, 1H), 1.44 (s, 3H), 1.02 (d, *J* = 6.9 Hz, 3H), 0.99 (d, *J* = 6.9 Hz, 3H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 164.1, 146.0, 134.2, 128.5, 118.6, 114.6, 114.4, 72.5, 37.8, 24.7, 17.2, 17.0. The spectroscopic data obtained were in agreement with the reported data for the compound **2a**.[10]

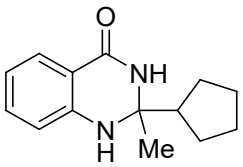
2-(*sec*-Butyl)-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (2b)



Following **GP-2 (Protocol A1)**, Anthranilamide (681 mg, 5.0 mmol) and 3-Methylpentan-2-one (**S2**, 501 mg, 5.0 mmol) afforded the compound **2b** as a white solid (570 mg, 2.61 mmol, 52%, as inseparable diastereomers, d.r. = 1:1). Reaction Temperature: 85 ºC.

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) (*mixture of diastereomers*) = 7.84 (d, *J* = 7.7 Hz, 1H), 7.24 – 7.28 (m, 1H), 6.75 – 6.78 (m, 1H), 6.59 (dd, *J* = 7.9, 3.0 Hz, 1H), 6.52 (bs, 1H), 4.29 (s, 1H) (*for one diastereomer*), 4.27 (s, 1H) (*for another diastereomer*),1.63 – 1.79 (m, 2H), 1.44 (s, 3H), 1.01 – 1.12 (m, 1H), 0.99 (d, *J* = 6.8 Hz, 3H) (*for one diastereomer*), 0.95 (d, *J* = 6.9 Hz, 3H) (*for another diastereomer*), 0.91 (q, *J* = 7.0 Hz, 3H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) (*mixture of diastereomers*) = 164.4, 164.3, 146.0, 146.0, 134.0, 134.0, 128.4, 128.4, 118.4, 118.3, 114.7, 114.6, 114.4, 72.7, 72.6, 44.7, 44.6, 24.9, 24.6, 24.0, 23.6, 13.5, 13.3, 12.7, 12.6; **HRMS (ESI):** m/z calc. for ($C_{13}H_{19}N_2O^+$) $[M+H]^+$: 219.1492; found: 219.1489; **IR (ATR) (ν cm^{-1}):** 3214, 2985, 1662, 1624, 1522, 1495, 1401, 823, 761, 657, 613; **Melting Point:** 206 °C.

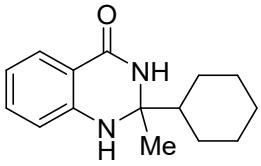
2-Cyclopentyl-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (2c)



Following **GP-2 (Protocol A1)**, Anthranilamide (681 mg, 5.0 mmol) and 1-Cyclopentylethan-1-one (**S3**, 561 mg, 5.0 mmol) afforded the compound **2c** as a white solid (900 mg, 3.91 mmol, 78%). Reaction Temperature: 85 ºC; Time: 15 min.

^{1}H NMR (500 MHz, DMSO-d_6) δ (ppm) = 7.87 (s, 1H), 7.52 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.15 – 7.18 (m, 1H), 6.65 (d, *J* = 7.8 Hz, 1H), 6.53 – 6.56 (m, 1H), 6.52 (bs, 1H), 2.15 – 2.22 (m, 1H), 1.43 – 1.56 (m, 8H), 1.32 (s, 3H); **^{13}C NMR (126 MHz, DMSO-d_6)** δ (ppm) = 163.0, 147.4, 133.3, 127.0, 115.8, 113.7, 113.4, 70.9, 50.8, 40.0, 39.9, 39.7, 39.5, 39.34, 39.2, 39.0, 26.84, 26.7, 26.5, 25.5, 25.3. The spectroscopic data obtained were in agreement with the reported data for the compound **2c**.[4]

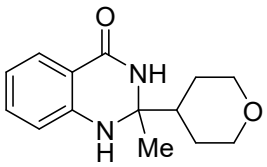
2-Cyclohexyl-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (2d)



Following **GP-2 (Protocol A1)**, Anthranilamide (2.72 g, 20.0 mmol) and 1-Cyclohexylethan-1-one (**S4**, 2.52 g, 20.0 mmol) afforded the compound **2d** as a white solid (3.95 g, 16.2 mmol, 81%) after recrystallization from ethanol. Reaction Temperature: 85 ºC.

^{1}H NMR (500 MHz, DMSO-d_6) δ (ppm) = 7.88 (s, 1H), 7.52 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.15 – 7.18 (m, 1H), 6.65 (d, *J* = 8.0 Hz, 1H), 6.60 (s, 1H), 6.53 – 6.56 (m, 1H), 1.68 – 1.79 (m, 4H), 1.52 – 1.58 (m, 2H), 1.29 (s, 3H), 0.98 – 1.10 (m, 5H); **^{13}C NMR (126 MHz, DMSO-d_6)** δ (ppm) = 162.9, 147.1, 133.2, 127.0, 115.8, 113.6, 113.5, 71.2, 47.9, 26.7, 26.4, 26.0, 26.0, 26.0, 24.9. The spectroscopic data obtained were in agreement with the reported data for the compound **2d**.[7]

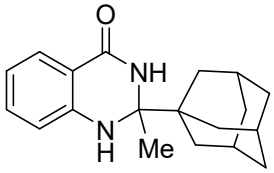
2-Methyl-2-(tetrahydro-2H-pyran-4-yl)-2,3-dihydroquinazolin-4(1*H*)-one (2e)



Following **GP-2 (Protocol A1)**, Anthranilamide (681 mg, 5.0 mmol) and 1-(Tetrahydro-2*H*-pyran-4-yl)ethan-1-one (**S5**, 641 mg, 5.0 mmol) afforded the compound **2e** as a white solid (560 mg, 2.27 mmol, 45%). Reaction Temperature: 85 ºC.

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 7.85 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.26 – 7.30 (m, 1H), 6.77 – 6.81 (m, 1H), 6.63 (s, 1H), 6.58 (d, *J* = 7.9 Hz, 1H), 4.21 (s, 1H), 4.02 (td, *J* = 11.2, 3.9 Hz, 2H), 3.30 (qd, *J* = 12.0, 2.1 Hz, 2H), 1.92 (tt, *J* = 12.2, 3.5 Hz, 1H), 1.72 – 1.73 (m, 1H), 1.61 – 1.64 (m, 1H), 1.44 – 1.55 (m, 2H), 1.48 (s, 3H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 164.3, 145.8, 134.2, 128.4, 118.6, 114.5, 114.4, 71.6, 67.9, 67.9, 45.6, 27.2, 27.0, 25.3; **HRMS (ESI):** m/z calc. for ($C_{14}H_{19}N_2O_2^+$) $[M+H]^+$: 247.1441; found: 247.1438; **IR (ATR) (ν cm^{-1}):** 3326, 3296, 2939, 1660, 1624, 1526, 1495, 1397, 1282, 1158, 1096, 860, 818, 760, 635; **Melting Point:** 195 °C.

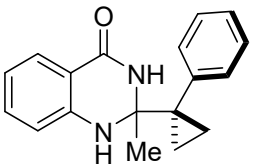
2-(Adamantan-1-yl)-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (2f)



Following **GP-2 (Protocol A1)**, the starting materials 2-Aminoanthranilamide (5.0 mmol) and 1-(Adamantan-1-yl)ethan-1-one (**S6**, 892 mg, 5.0 mmol) afforded the compound **2f** as a white solid (560 mg, 2.27 mmol, 45%). Reaction Temperature: 85 ºC.

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 7.82 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.25 (ddd, *J* = 8.2, 7.3, 1.6 Hz, 1H), 6.71 – 6.74 (m, 1H), 6.56 (d, *J* = 7.7 Hz, 1H), 5.91 (s, 1H), 4.17 (s, 1H), 2.04 – 2.06 (m, 3H), 1.60 – 1.72 (m, 12H), 1.44 (s, 3H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 164.2, 146.6, 134.2, 128.3, 117.9, 113.8, 113.3, 74.7, 41.7, 36.8, 35.8, 28.3, 23.5. The spectroscopic data obtained were in agreement with the reported data for the compound **2f**.[7]

2-Methyl-2-(1-phenylcyclopropyl)-2,3-dihydroquinazolin-4(1*H*)-one (2h)

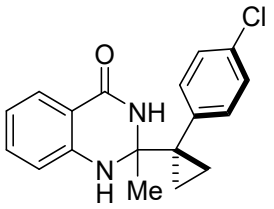


Following **GP-2 (Protocol A2)**, Anthranilamide (109 mg, 0.80 mmol) and 1-(1-phenylcyclopropyl)ethan-1-one (**S8**, 141 mg, 0.88 mmol) afforded the compound **2h** as light brown color solid (65 mg, 0.234 mmol, 29%). Reaction Temperature: 85 ºC.

^{1}H NMR (500 MHz, DMSO-d_6) δ (ppm) = 7.87 (s, 1H), 7.51 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.24 – 7.29 (m, 4H), 7.18 – 7.22 (m, 2H), 6.62 (d, *J* = 7.9 Hz, 1H), 6.56 (t, *J* = 7.8 Hz, 1H), 6.54 (s, 1H), 1.36 (s, 3H), 0.95 – 0.99 (m, 1H), 0.89 – 0.92 (m, 1H), 0.49 – 0.55 (m, 2H); **^{13}C NMR (126 MHz, DMSO-d_6)** δ (ppm) = 163.3, 146.9, 142.3, 133.3, 132.1, 127.6, 126.9, 126.5, 115.8, 113.9, 113.4, 69.9, 35.8, 26.6, 10.0, 7.4; **HRMS (ESI):** m/z calc. for ($C_{18}H_{19}N_2O^+$) $[M+H]^+$: 279.1492; found: 279.1491; **IR**

(ATR) (ν cm^{-1}): 3039, 3015, 2941, 2871, 2587, 1672, 1622, 1504, 1391, 761; **Melting Point:** 153-155 °C.

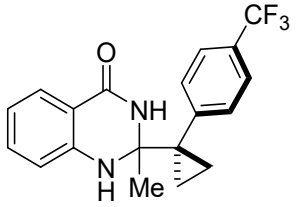
2-(1-(4-Chlorophenyl)cyclopropyl)-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (2i)



Following **GP-2 (Protocol A2)**, Anthranilamide (136 mg, 1.0 mmol) and 1-(1-(4-chlorophenyl)cyclopropyl)ethan-1-one (**S9**, 215 mg, 1.1 mmol) afforded the compound **2i** as white solid (200 mg, 0.639 mmol, 64%). Reaction Temperature: 125 ºC.

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 7.85 (d, *J* = 7.6 Hz, 1H), 7.30 – 7.34 (m, 1H), 7.29 (m, 4H),), 6.80 – 6.83 (m, 1H), 6.53 (d, *J* = 8.0 Hz, 1H), 6.37 (bs, 1H), 4.12 (s, 1H), 1.53 (s, 3H), 1.06 – 1.13 (m, 1H), 0.85 – 0.89 (m, 1H), 0.69 – 0.74 (m, 2H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 164.4, 145.9, 140.2, 134.4, 133.5, 133.5, 128.6, 128.4, 118.7, 114.9, 114.1, 70.5, 35.4, 28.1, 10.9, 7.8; **HRMS (ESI):** m/z calc. for ($C_{18}H_{18}ClN_2O^+$) $[M+H]^+$: 313.1102; found: 313.1099; **IR (ATR) (ν cm^{-1}):** 2941, 2868, 1690, 1622, 1496, 1478, 1406, 1298, 1263, 1098, 1020, 777; **Melting Point:** 154 °C.

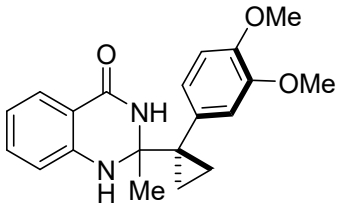
2-Methyl-2-(1-(4-(trifluoromethyl)phenyl)cyclopropyl)-2,3-dihydroquinazolin-4(1*H*)-one (2j)



Following **GP-2 (Protocol A2)**, Anthranilamide (109 mg, 0.80 mmol) and 1-(1-(4-(Trifluoromethyl)-phenyl)cyclopropyl)ethan-1-one (**S10**, 201 mg, 0.88 mmol) afforded the compound **2j** as white solid (182 mg, 0.525 mmol, 66%). Reaction Temperature: 125 ºC.

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 7.85 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.57 (d, *J* = 8.1 Hz, 2H), 7.49 (d, *J* = 8.0 Hz, 2H), 7.33 (td, *J* = 8.1, 1.5 Hz, 1H), 7.07 (s, 1H), 6.79 – 6.84 (m, 1H), 6.55 (d, *J* = 7.8 Hz, 1H), 4.15 (s, 1H), 1.56 (s, 3H), 1.13 – 1.16 (m, 1H), 0.96 – 0.99 (m, 1H), 0.71 – 0.77 (m, 2H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 164.8, 145.9, 145.8, 134.5, 132.6, 129.8 (q, *J* = 32.5 Hz), 128.4, 125.3 (q, *J* = 3.5 Hz), 123.1, 118.7, 114.9, 114.1, 70.4, 36.00, 27.9, 10.9, 7.6; **^{19}F NMR (471 MHz, $CDCl_3$)** δ (ppm) = – 62.53; **HRMS (ESI):** m/z calc. for ($C_{19}H_{18}F_3N_2O^+$) $[M+H]^+$: 347.1366; found: 347.1369; **IR (ATR) (ν cm^{-1}):** 3344, 3287, 3227, 3183, 3158, 3069, 3026, 1672, 1624, 1516, 1495, 1391, 1334, 1172, 1135, 1093, 1072, 1028, 913, 853, 737; **Melting Point:** 151-155 °C.

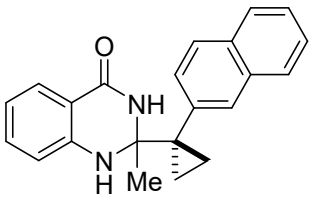
2-(1-(3,4-Dimethoxyphenyl)cyclopropyl)-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (2k)



Following **GP-2 (Protocol A2)**, Anthranilamide (136 mg, 1.0 mmol) and 1-(1-(3,4-dimethoxyphenyl)cyclopropyl)ethan-1-one (**S11**, 242 mg, 1.1 mmol) afforded the compound **2k** as white solid (225 mg, 0.665 mmol, 67%). Reaction Temperature: 100 ºC.

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 7.85 (d, *J* = 7.7 Hz, 1H), 7.31 (t, *J* = 7.6 Hz, 1H), 6.91 (d, *J* = 8.2 Hz, 1H), 6.79 – 6.85 (m, 2H), 6.53 (d, *J* = 8.0 Hz, 1H), 6.30 (s, 1H), 4.20 (s, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 1.55 (s, 3H), 1.03 – 1.07 (m, 1H), 0.80 – 0.88 (m, 1H), 0.72 – 0.76 (m, 2H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 164.3, 148.6, 148.5, 146.1, 134.3, 133.9, 128.4, 124.2, 118.6, 115.1, 114.9, 114.0, 111.0, 70.8, 56.1, 56.1, 35.6, 28.3, 11.1, 8.1; **HRMS (ESI):** m/z calc. for ($C_{20}H_{23}N_2O_3^+$) $[M+H]^+$: 339.1703; found: 339.1689; **IR (ATR) (ν cm^{-1}):**3336, 3014, 2948, 1668, 1622, 1523, 1469, 1415, 1390, 1340, 1259, 1140, 1035, 906, 863, 818, 762, 705, 651, 625; **Melting Point:** 175 °C.

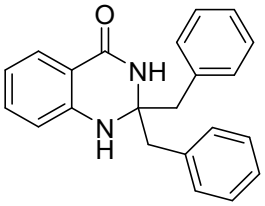
2-Methyl-2-(1-(naphthalen-2-yl)cyclopropyl)-2,3-dihydroquinazolin-4(1*H*)-one (2l)



Following **GP-2 (Protocol A2)**, Anthranilamide (136 mg, 1.0 mmol) and 1-(1-(4-chlorophenyl)cyclopropyl)ethan-1-one (**S12**, 231 mg, 1.1 mmol) afforded the compound **2l** as white solid (195 mg, 0.594 mmol, 59%). Reaction Temperature: 85 ºC.

^{1}H NMR (500 MHz, DMSO-d_6) δ (ppm) = 7.94 (s, 1H), 7.79 – 7.88 (m, 4H), 7.54 (d, *J* = 7.6 Hz, 1H), 7.45 – 7.50 (m, 2H), 7.42 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.23 – 7.26 (m, 1H), 6.64 (d, *J* = 8.0 Hz, 1H), 6.60 (s, 1H), 6.58 (t, *J* = 7.3 Hz, 1H), 1.43 (s, 3H); **^{13}C NMR (126 MHz, DMSO-d_6)** δ (ppm) = 163.3, 146.9, 139.8, 133.4, 132.6, 132.0, 130.8, 130.3, 127.7, 127.3, 126.9, 126.7, 125.8, 125.7, 115.9, 114.0, 113.4, 70.0, 36.0, 26.8, 10.2, 7.4; **HRMS (ESI):** m/z calc. for ($C_{22}H_{21}N_2O^+$) $[M+H]^+$: 329.1649; found: 329.1646; **IR (ATR) (ν cm^{-1}):**2936, 2867, 1685, 1623, 1475, 1390, 1284, 1235, 1195, 757; **Melting Point:** 141 °C.

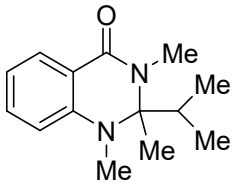
2,2-Dibenzyl-2,3-dihydroquinazolin-4(1*H*)-one (2o)



Following **GP-2 (Protocol A2)**, Anthranilamide (681 mg, 5.0 mmol) and 1,3-diphenylpropan-2-one (**S14**, 1.05 g, 5.0 mmol) afforded the compound **2o** as a white solid (780 mg, 2.38 mmol, 48%). Reaction Temperature: 85 ºC.

^{1}H NMR (500 MHz, DMSO-d_6) δ (ppm) = 7.96 (s, 1H), 7.24 – 7.28 (m, 5H), 7.19 – 7.22 (m, 4H), 7.12 – 7.15 (m, 2H), 7.07 – 7.09 (m, 1H), 6.77 (s, 1H), 6.55 – 6.58 (m, 1H), 6.35 – 6.39 (m, 1H), 3.01 (d, *J* = 13.4 Hz, 2H), 2.91 (d, *J* = 13.5 Hz, 2H); **^{13}C NMR (126 MHz, DMSO-d_6)** δ (ppm) = 163.0, 147.1, 136.3, 133.0, 131.0, 127.6, 126.6, 126.1, 115.4, 113.2, 112.3, 72.8, 46.7; **HRMS (ESI):** m/z calc. for ($C_{22}H_{21}N_2O^+$) $[M+H]^+$: 329.1649; found: 329.1644; **IR (ATR) (ν cm^{-1}):** 3394, 3321, 2972, 2937, 1663, 1496, 1465, 1389, 1275, 1163, 1038, 860, 758, 706; **Melting Point:** 174 °C.

2-Isopropyl-1,2,3-trimethyl-2,3-dihydroquinazolin-4(1*H*)-one (2q)



In a two neck round bottom flask with a Teflon-coated stirring bar under inert atmosphere, sodium hydride (0.4 mg, 10.0 mmol, 2.0 equiv., 60% in mineral oil) was added to the solution of 2-isopropyl-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (**2a**, 1.02 g, 5.00 mmol, 1.00 equiv.) in DMF (20 mL) at 0 ºC and stirred at room temperature for 30 min. Methyl iodide (622 µL, 10.0 mmol, 2.0 equiv.) was then added dropwise to the reaction mixture and allowed to stir at room temperature for another 12 h. The reaction mixture was quenched with aqueous ammonium chloride solution followed by extraction with ethyl acetate. The resulting organic layers were washed with water followed by brine solution, dried over anhydrous sodium sulfate and concentrated under reduced pressure. The crude mixture was purified by flash column chromatography through silica (eluent = petroleum ether/ethyl acetate) to afford pure 2-Isopropyl-1,2,3-trimethyl-2,3-dihydroquinazolin-4(1*H*)-one (**2q**, 705 mg, 3.03 mmol, 61%) as a colorless liquid.

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 7.94 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.35 – 7.39 (m, 1H), 6.89 – 6.92 (m, 1H), 6.81 (d, *J* = 8.1 Hz, 1H), 3.17 (s, 3H), 2.98 (s, 3H), 2.43 (sept, *J* = 6.9 Hz, 1H), 1.61 (s, 3H), 0.86 (d, *J* = 6.9 Hz, 3H), 0.75 (d, *J* = 6.9 Hz, 3H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 163.7, 147.5, 133.2, 128.1, 120.8, 119.6, 116.5, 79.2, 36.6, 36.1, 30.8, 18.1, 17.7, 16.8; **HRMS (ESI):** m/z calc. for ($C_{14}H_{20}N_2O^+$) $[M+H]^+$: 233.1449; found: 233.1445; **IR (ATR) (ν cm^{-1}):** 2939, 2869, 1648, 1612, 1498, 1399, 1342, 1315, 1222, 1116, 1046, 923, 760, 708.

2.3 Synthesis of *N*-Heteroarenes

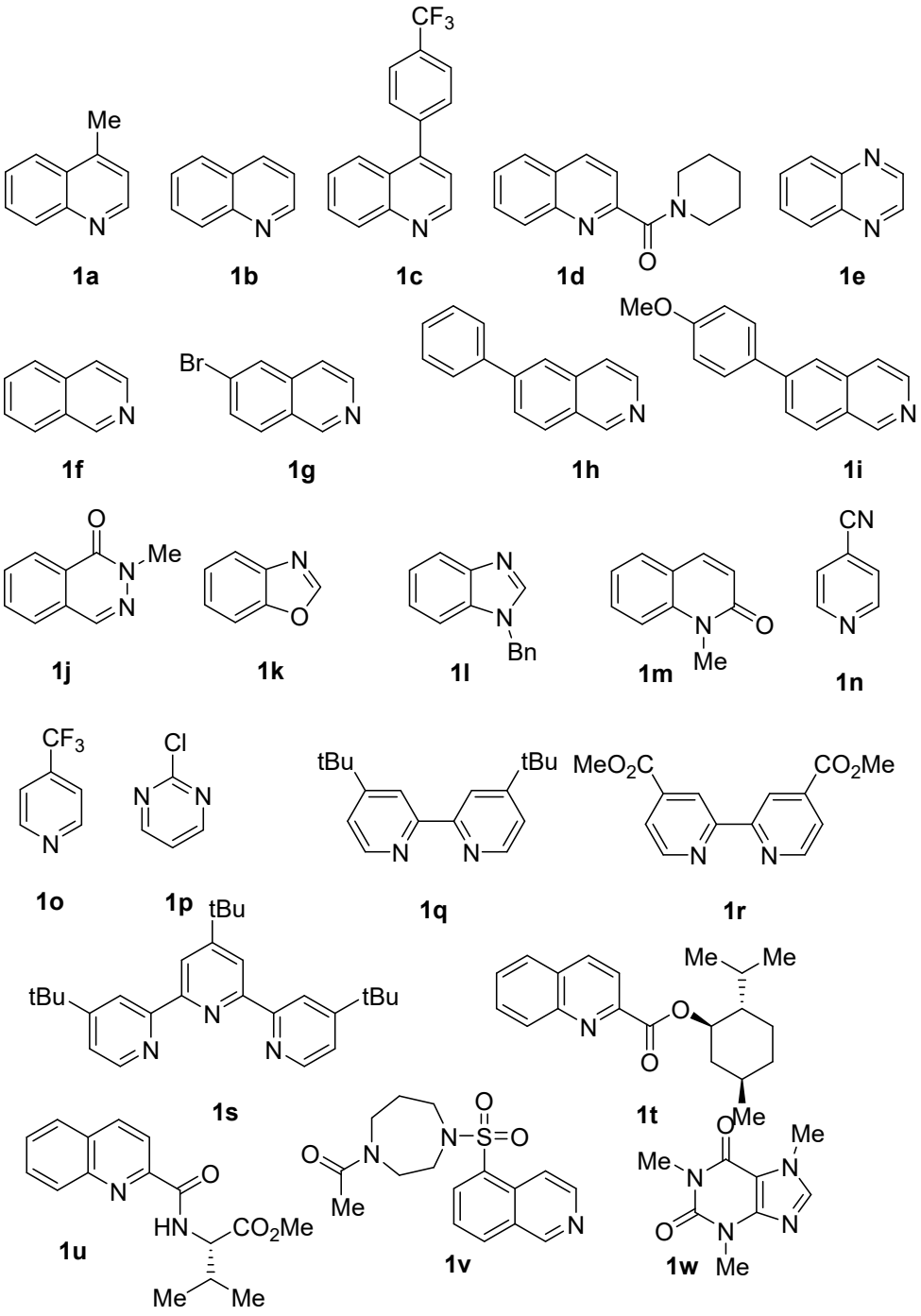
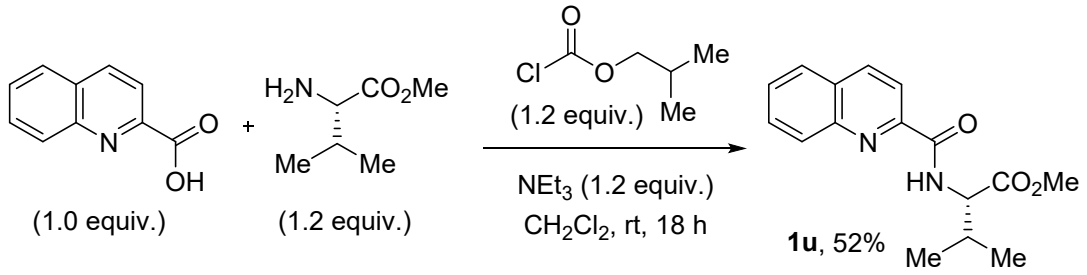


Figure S3: List of *N*-heteroarene compounds

N-Heteroarene **1a**, **1b**, **1e**, **1f**, **1g**, **1k**, **1n**, **1o**, **1p**, **1q**, **1r**, **1s** and **1w** were commercially procured. The *N*-heteroarene **1c**[11], **1d**[12], **1h**[13], **1i**[13], **1j**[14], **1l**[15], **1m**[16], **1t**[17] and **1v**,[18] were prepared following the reported literatures.

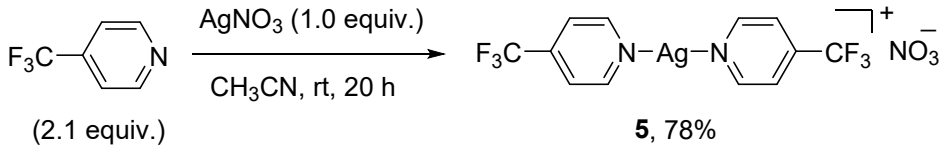
Synthesis of Methyl (quinoline-2-carbonyl)-*L*-valinate (1u)



In a round bottom flask with a Teflon-coated stirring bar, triethylamine (420 µL, 3.0 mmol, 1.2 equiv.) was added to the solution of quinoline-2-carboxylic acid (0.43 g, 2.5 mmol, 1.0 equiv.) in dichloromethane (15 mL). Then isobutylchloroformate (390 µL, 3.0 mmol, 1.2 equiv.) was added dropwise to the solution, cooled at 0 °C. After 10 min., the reaction mixture was warmed up to room temperature and allowed to stir for 20 min. Then, methyl L-valinate (0.40 g, 3.0 mmol, 1.2 equiv.) was added to the solution and stirred at room temperature for 18 h. The reaction mixture was quenched with aq. $NaHCO_3$ solution and extracted with dichloromethane. The organic layer was washed with water followed by brine solution, dried over anhydrous sodium sulfate and concentrated under reduced pressure. The crude mixture was purified by flash column chromatography through silica (eluent = petroleum ether/ethyl acetate) to afford pure methyl (quinoline-2-carbonyl)-*L*-valinate (**1u**, 373 mg, 1.3 mmol, 52%) as a pale yellow liquid.

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 8.73 (d, *J* = 9.0 Hz, 1H), 8.26 – 8.30 (m, 2H), 8.16 (d, *J* = 8.5 Hz, 1H), 7.86 (d, *J* = 8.1 Hz, 1H), 7.74 – 7.77 (m, 1H), 7.69 – 7.62 (m, 1H), 4.78 (dd, *J* = 9.2, 5.3 Hz, 1H), 3.78 (s, 3H), 2.31 – 2.40 (m, 1H), 1.06 (d, *J* = 2.2 Hz, 3H), 1.05 (d, *J* = 2.2 Hz, 3H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 172.5, 164.6, 149.4, 146.7, 137.6, 130.2, 130.1, 129.5, 128.1, 127.8, 119.0, 57.6, 52.3, 31.7, 19.3, 18.2; **HRMS (ESI):** m/z calc. for ($C_{16}H_{19}N_2O_3^+$) $[M+H]^+$: 287.1390; found: 287.1390; **IR (ATR) (ν cm^{-1}):** 1753, 1693, 1531, 1473, 1445, 1322, 1271, 1216, 1170, 854, 809, 781, 712, 660, 612.

2.4 Synthesis of well-defined Silver-pyridyl complex



Following a procedure reported by Baxter and Co-workers[19] in an oven-dried round bottom flask equipped with a Teflon-coated stirring bar, $AgNO_3$ (170 mg, 1.0 mmol, 1.0 equiv.) and 4-(trifluoromethyl)pyridine (116 µL, 2.1 mmol, 2.1 equiv.) were dissolved in acetonitrile (6.5 mL). The resulting solution was allowed to stir at rt for 20 h under dark. The solvent was removed under reduced pressure and the resulting solid was washed with diethyl ether. The obtained solid was dissolved in dichloromethane and passed through a celite pad. The removal of solvent afforded desired bis(4-(trifluoromethyl)pyridine)silver(I) nitrate (**5**, 360 mg, 0.78 mmol, 78%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 8.87 (bs, 4H), 7.59 (d, *J* = 5.5 Hz, 4H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 152.1, 139.6 (q, *J* = 34.6 Hz), 122.4 (q, *J* = 273.4 Hz), 120.5, 145.8, 134.5, 132.6, 129.8 (q, *J* = 32.5 Hz), 128.4, 125.3 (q, *J* = 3.5 Hz), 123.1, 118.7, 114.9, 114.1, 70.4, 36.00, 27.9, 10.9, 7.6; **^{19}F NMR (471 MHz, $CDCl_3$)** δ (ppm) = – 65.13; **LRMS (ESI):** m/z calc. for

($C_{12}H_8AgF_6N_2^+$) $[M\text{-}NO_3]^+$: 400.96; found: 401.56; **IR (ATR) (ν cm^{-1}):** 3368, 3306, 3025, 2859, 2362, 2335, 1658, 1562, 1431, 1363, 1345, 848, 818, 753, 701, 637, 617; **Melting Point:** 172 °C.

3. Optimization of reaction conditions

Optimized protocol for Silver-catalyzed alkylation of *N*-heteroarene with 2,3-Dihydro-quinazolidinone

In a heat gun-dried Schlenk tube equipped with a Teflon-coated stirring bar, Lepidine (**1a**, 0.1 mmol, 1.0 equiv.), 2-Isopropyl-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (**2a**) (0.25 mmol, 2.5 equiv.), $AgNO_3$ (0.02 mmol, 0.2 equiv.) and $K_2S_2O_8$ (0.2 mmol, 2.0 equiv.) were dissolved in dry DMF (1 mL) under inert atmosphere. The reaction mixture was stirred at room temperature for 24 h under dark condition. The reaction was quenched by the addition of brine solution (2 mL) and then extracted with ethyl acetate (3×5 mL). The combined organic layers were washed once again with water (5 mL), followed by brine (5 ml) and the solvents were removed under reduced pressure. The crude reaction mixture was purified by flash column chromatography through Silica gel (eluent: petroleum ether/ethyl acetate) to afford pure product **3aa** and the compound **4a** as side product.

Table S1: Optimization of Silver-catalyzed *sp2* C-H alkylation of *N*-Heteroarene.[a]

1a (1.0 equiv.) **2a** (2.5 equiv.) **3aa**

Entry	Deviation from standard condition	Yield (%)[b]
1	**none**	**92**
2	$AgBF_4$, instead of $AgNO_3$	54
3	CuBr, instead of $AgNO_3$	27
4	$FeCl_3$, instead of $AgNO_3$	38
5	$(NH_4)_2S_2O_8$, instead of $K_2S_2O_8$	81
6	$(BzO)_2$, instead of $K_2S_2O_8$	22
7	DTBP, instead of $K_2S_2O_8$	—
8	O_2 (1 bar), instead of $K_2S_2O_8$	—
9	NMP, instead of DMF	22
10	**2a** (2.0 equiv.) & $K_2S_2O_8$ (2.0 equiv.)	70
11	**2a** (1.5 equiv.) & $K_2S_2O_8$ (1.5 equiv.)	57
12	$AgNO_3$ (15 mol%)	72
13	w/o $K_2S_2O_8$	—
14	w/o $AgNO_3$	—

[a]Optimized reaction conditions: **1a** (0.10 mmol), **2a** (0.25 mmol), $AgNO_3$ (20 mol%), $K_2S_2O_8$ (0.2 mmol), DMF (1 mL) at rt for 24 h. [b]Isolated yield of **3aa**. DMF = *N,N*-dimethylformamide; NMP = *N*-Methyl-2-pyrrolidone; Bz = Benzoyl; DTBP = Di-*tert*-butylperoxide.

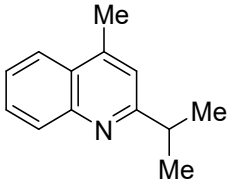
4 Synthesis and Characterization of Products

4.1 Synthesis and characterization of alkylated *N*-heteroarene products

General procedure: Silver-catalyzed alkylation of *N*-heteroarenes with 2,3-Dihydroquinazolidinones (GP3)

In a heat gun-dried Schlenk tube equipped with a Teflon-coated stirring bar, *N*-Heteroarene **1** (0.2 mmol, 1.0 equiv.), 2,3-Dihydroquinazolinone substrate (**2**) (0.5 mmol, 2.5 equiv.), $AgNO_3$ (0.04 mmol, 0.2 equiv.) and $K_2S_2O_8$ (0.4 mmol, 2.0 equiv.) were dissolved in dry DMF (2 mL) under inert atmosphere. The reaction mixture was stirred at room temperature for 24 h under dark condition. The reaction was quenched by the addition of brine solution (2 mL) and then extracted with ethyl acetate (3×5 mL). The combined organic layers were washed once again with water (5 ml), followed by brine (5 ml) and the solvents were removed under reduced pressure. The crude reaction mixture was purified by flash column chromatography through Silica gel (eluent: petroleum ether/ethyl acetate) to afford pure product **3**.

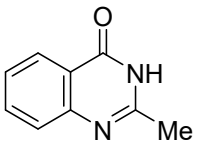
2-Isopropyl-4-methylquinoline (3aa)



Following **GP3**, the starting materials Lepidine (**1a**, 27 µL, 0.2 mmol, 1.0 equiv.) and 2-isopropyl-2-methyl-2,3-dihydroquinazolin-4(1H)-one (**2a,** 102 mg, 0.5 mmol) afforded the compound **3aa**, as a colorless liquid (34 mg, 0.184 mmol, 92%).

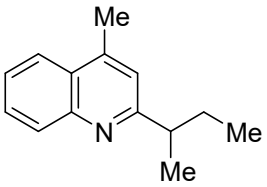
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 8.05 (d, *J* = 8.4 Hz, 1H), 7.94 (d, *J* = 8.3 Hz, 1H), 7.67 (ddd, *J* = 8.3, 6.9, 1.3 Hz, 1H), 7.50 (ddd, *J* = 8.1, 6.9, 1.1 Hz, 1H), 7.18 (s, 1H), 3.21 (sept, *J* = 7.0 Hz, 1H), 2.69 (s, 3H), 1.38 (d, *J* = 7.0 Hz, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 167.5, 147.7, 144.5, 129.6, 129.1, 127.2, 125.6, 123.7, 119.9, 37.4, 22.7, 19.0. The spectroscopic data obtained were in agreement with the reported data for the compound **3aa**.[20]

2-Methylquinazolin-4(3H)-one (4a)



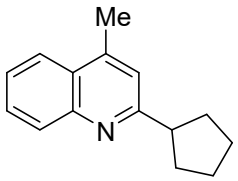
^{1}H NMR (500 MHz, DMSO-d6) δ (ppm) = 12.21 (s, 1H), 8.08 (d, *J* = 7.9 Hz, 1H), 7.78 (t, *J* = 7.6 Hz, 1H), 7.58 (d, *J* = 8.1 Hz, 1H), 7.46 (t, *J* = 7.5 Hz, 1H), 2.36 (s, 3H); **^{13}C NMR (126 MHz, DMSO-d6)** δ (ppm) = 162.2, 154.7, 149.5, 134.8, 127.1, 126.3, 126.1, 121.1, 21.9. The spectroscopic data obtained were in agreement with the reported data for the compound **4a**.[21]

2-(*sec*-Butyl)-4-methylquinoline (3ab)



Following **GP3**, the starting materials Lepidine (**1a**, 27 µL, 0.2 mmol, 1.0 equiv.) and 2-(*sec*-butyl)-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (**2b,** 109 mg, 0.5 mmol) afforded the compound **3ab**, as a colorless liquid (26 mg, 0.130 mmol, 65%).

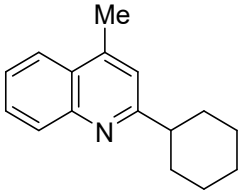
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 8.05 (dd, *J* = 8.4, 0.4 Hz, 1H), 7.95 (dd, *J* = 8.3, 0.9 Hz, 1H), 7.66 (ddd, *J* = 8.3, 6.9, 1.4 Hz, 1H), 7.50 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 7.13 (s, 1H), 2.92 – 2.99 (m, 1H), 2.69 (d, *J* = 0.7 Hz, 3H), 1.80 – 1.89 (m, 1H), 1.66 – 1.75 (m, 1H), 1.35 (d, *J* = 7.0 Hz, 3H), 0.89 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 166.9, 147.8, 144.3, 129.7, 129.0, 127.2, 125.5, 123.7, 120.3, 44.7, 30.1, 20.6, 19.0, 12.4. The spectroscopic data obtained were in agreement with the reported data for the compound **3ab**.[22]



Following **GP3**, the starting materials Lepidine (**1a**, 27 µL, 0.2 mmol, 1.0 equiv.) and 2-cyclopentyl-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (**2c,** 115 mg, 0.5 mmol) afforded the compound **3ac**, as a colorless liquid (27 mg, 0.128 mmol, 64%).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 8.04 (d, *J* = 8.4 Hz, 1H), 7.93 (dd, *J* = 8.3, 0.7 Hz, 1H), 7.66 (ddd, *J* = 8.3, 6.9, 1.3 Hz, 1H), 7.48 (ddd, *J* = 8.1, 7.0, 1.1 Hz, 1H), 7.17 (s, 1H), 2.30 – 2.37 (m, 1H), 2.67 (s, 3H), 2.14 – 2.19 (m, 2H), 1.84 – 1.91 (m, 4H), 1.72 – 1.78 (m, 2H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 166.0, 147.6, 144.2, 129.6, 129.0, 127.1, 125.5, 123.7, 120.8, 48.9, 33.7, 26.2, 18.9. The spectroscopic data obtained were in agreement with the reported data for the compound **3ac**.[20]

2-Cyclohexyl-4-methylquinoline (3ad)

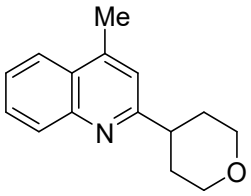


Following **GP3**, the starting materials Lepidine (**1a,** 27 µL, 0.2 mmol) and 2-cyclohexyl-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (**2d,** 122 mg, 0.5 mmol) afforded the compound **3ad**, as a colorless liquid (43 mg, 0.191 mmol, 95%).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 8.04 (d, *J* = 8.4 Hz, 1H), 7.94 (d, *J* = 8.3 Hz, 1H), 7.66 (ddd, *J* = 8.3, 6.9, 1.4 Hz, 1H), 7.49 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 7.16 (s, 1H), 2.87 (tt, *J* = 12.1, 3.4 Hz, 1H), 2.68 (s, 3H), 1.99 – 2.02 (m, 2H), 1.89 (dt, *J* = 12.8, 3.0 Hz, 2H), 1.77 – 1.81 (m, 1H), 1.62 (qd, *J* = 12.6, 3.1 Hz, 2H), 1.62 (qt, *J* = 12.8, 3.3 Hz, 2H), 1.62 (tt, *J* = 12.8, 3.6 Hz, 1H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 166.7, 147.8, 144.4, 129.7, 129.1, 127.2, 125.5, 123.7, 120.4, 47.8, 33.0,

26.7, 26.3, 19.0. The spectroscopic data obtained were in agreement with the reported data for the compound **3ad**.[20]

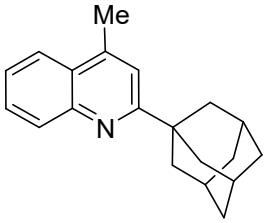
4-Methyl-2-(tetrahydro-2H-pyran-4-yl)quinoline (3ae)



Following **GP3**, the starting materials Lepidine (**1a,** 27 µL, 0.2 mmol) and 2-methyl-2-(tetrahydro-2H-pyran-4-yl)-2,3-dihydroquinazolin-4(1*H*)-one (**2e,** 123 mg, 0.5 mmol) afforded the compound **3ae**, as a colorless liquid (28 mg, 0.123 mmol, 62%).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 8.04 (dd, *J* = 8.4, 0.5 Hz, 1H), 7.95 (dd, *J* = 8.3, 0.8 Hz, 1H), 7.68 (ddd, *J* = 8.3, 6.9, 1.3 Hz, 1H), 7.51 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 7.18 (s, 1H), 4.13 (dd, *J* = 11.1, 4.0 Hz, 2H), 3.60 (td, *J* = 11.8, 2.1 Hz, 2H), 3.13 (tt, *J* = 11.9, 3.9 Hz, 1H), 2.70 (s, 3H), 1.98 – 2.06 (m, 2H), 1.90 – 1.93 (m, 2H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 164.4, 147.8, 144.8, 129.7, 129.3, 127.3, 125.8, 123.8, 120.0, 68.3, 44.5, 32.4, 19.0. The spectroscopic data obtained were in agreement with the reported data for the compound **3ae**.[22]

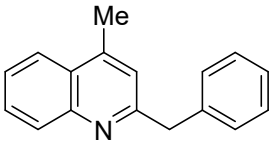
2-(Adamantan-1-yl)-4-methylquinoline (3af)



Following **GP3**, the starting materials Lepidine (**1a,** 27 µL, 0.2 mmol) and 2-(adamantan-1-yl)-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (**2f,** 148 mg, 0.5 mmol) afforded the compound **3af**, as a white solid (29 mg, 0.105 mmol, 52%).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 8.07 (d, *J* = 8.4 Hz, 1H), 7.94 (dd, *J* = 8.3, 0.8 Hz, 1H), 7.64 – 7.67 (m, 1H), 7.47 – 7.50 (m, 1H), 7.33 (s, 1H), 2.69 (s, 3H), 2.15 – 2.16 (m, 3H), 2.11 – 2.12 (m, 6H), 1.82 – 1.83 (m, 6H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 168.8, 147.7, 143.7, 130.1, 128.8, 126.9, 125.5, 123.6, 118.7, 42.0, 39.7, 37.1, 29.0, 19.1. The spectroscopic data obtained were in agreement with the reported data for the compound **3af**.[20]

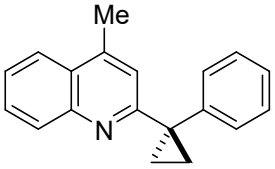
2-Benzyl-4-methylquinoline (3ag)



Following **GP3**, the starting materials Lepidine (**1a,** 27 µL, 0.2 mmol) and 2-benzyl-2-phenyl-2,3-dihydroquinazolin-4(1*H*)-one (**2g,** 157 mg, 0.5 mmol) afforded the compound **3ag**, as a colorless liquid (21 mg, 0.090 mmol, 45%).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 8.09 (d, *J* = 8.4 Hz, 1H), 7.94 (d, *J* = 8.3 Hz, 1H), 7.70 (t, *J* = 7.6 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.29 – 7.33 (m, 4H), 7.21 – 7.24 (m, 1H), 7.07 (s, 1H), 4.30 (s, 2H), 2.61 (s, 3H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 161.0, 147.8, 144.8, 139.5, 129.7, 129.4, 129.3, 128.8, 127.0, 126.6, 125.9, 123.8, 122.3, 77.4, 77.2, 76.9, 45.6, 18.9. The spectroscopic data obtained were in agreement with the reported data for the compound **3ag**.[23]

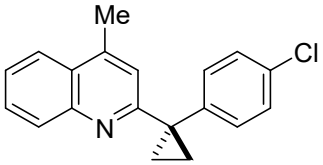
4-Methyl-2-(1-phenylcyclopropyl)quinoline (3ah)



Following **GP3**, the starting materials Lepidine (**1a,** 27 µL, 0.2 mmol) and (S)-2-methyl-2-(1-phenylcyclopropyl)-2,3-dihydroquinazolin-4(1*H*)-one (**2h,** 139 mg, 0.5 mmol) afforded the compound **3ah**, as a colorless liquid (47 mg, 0.181 mmol, 91%).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 8.04 (d, *J* = 8.5 Hz, 1H), 7.90 (d, *J* = 8.3 Hz, 1H), 7.67 (ddd, *J* = 8.4, 6.9, 1.3 Hz, 1H), 7.48 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 7.43 – 7.45 (m, 2H), 7.36 – 7.39 (m, 2H), 7.30 – 7.32 (m, 1H), 6.97 (s, 1H), 2.55 (s, 3H), 1.84 (dd, *J* = 6.2, 3.5 Hz, 2H), 1.38 (dd, *J* = 6.5, 3.8 Hz, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 163.9, 147.8, 144.0, 143.6, 130.3, 129.8, 129.1, 128.7, 126.8, 126.7, 125.4, 123.7, 122.1, 32.3, 18.8, 17.3. The spectroscopic data obtained were in agreement with the reported data for the compound **3ah**.[24]

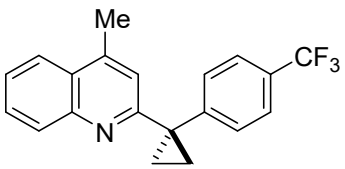
2-(1-(4-Chlorophenyl)cyclopropyl)-4-methylquinoline (3ai)



Following **GP3**, the starting materials Lepidine (**1a,** 27 µL, 0.2 mmol) and (S)-2-(1-(4-chlorophenyl)cyclopropyl)-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (**2i**, 156 mg, 0.5 mmol) afforded the compound **3ai**, as a white solid (55 mg, 0.187 mmol, 94%).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 8.01 (d, *J* = 8.5 Hz, 1H), 7.90 (dd, *J* = 8.4, 0.8 Hz, 1H), 7.64 – 7.68 (m, 1H), 7.48 – 7.50 (m, 1H), 7.31 – 7.36 (m, 4H), 6.91 (s, 1H), 2.56 (s, 3H), 1.82 (q, *J* = 3.9 Hz, 2H), 1.32 (q, *J* = 3.9 Hz, 2H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 163.2, 147.7, 143.9, 142.5, 132.5, 131.6, 129.8, 129.2, 128.8, 126.7, 125.6, 123.7, 121.8, 31.7, 18.8, 17.4; **HRMS (ESI):** m/z calc. for ($C_{19}H_{17}ClN$) $[M+H]^+$: 294.1045; found: 294.1043; **IR (ATR) (ν cm^{-1}):** 3096, 2973, 2939, 2863, 1607, 1561, 1500, 1454, 1411, 1354, 1270, 1165, 1100, 1025, 963, 809, 767, 703, 675, 613; **Melting Point:** 144 °C.

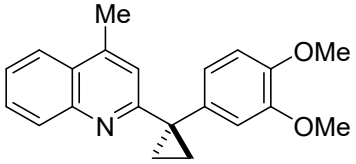
4-Methyl-2-(1-(4-(trifluoromethyl)phenyl)cyclopropyl)quinoline (3aj)



Following **GP3**, the starting materials Lepidine (**1a,** 27 µL, 0.2 mmol) and (S)-2-methyl-2-(1-(4-(trifluoromethyl)phenyl)cyclopropyl)-2,3-dihydroquinazolin-4(1*H*)-one (**2j,** 173 mg, 0.5 mmol) afforded the compound **3aj**, as a white solid (46 mg, 0.141 mmol, 70%).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 8.02 (d, *J* = 8.4 Hz, 1H), 7.92 (dd, *J* = 8.3, 0.8 Hz, 1H), 7.67 (ddd, *J* = 8.3, 6.9, 1.3 Hz, 1H), 7.60 (d, *J* = 8.2 Hz, 2H), 7.50 (d, *J* = 8.2 Hz, 2H), 7.48 – 7.51 (m, 1H), 6.91 (s, 1H), 2.57 (s, 3H), 1.85 (q, *J* = 4.0 Hz, 2H), 1.37 (q, *J* = 4.0 Hz, 2H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 130.3, 129.8, 129.3, 128.9 (q, *J* = 32.3 Hz), 126.8, 125.8, 125.6 (q, *J* = 3.8 Hz), 123.7, 123.4, 121.9, 32.20, 18.9, 17.4; **^{19}F NMR (471 MHz, $CDCl_3$)** δ (ppm) = – 62.33; **HRMS (ESI):** m/z calc. for ($C_{20}H_{17}F_3N_1^+$) $[M+H]^+$: 328.1308; found: 328.1308; **IR (ATR) (ν cm^{-1}):** 1609, 1415, 1333, 1145, 1071, 852, 808, 768, 712, 668, 640, 613; **Melting Point:** 123 °C.

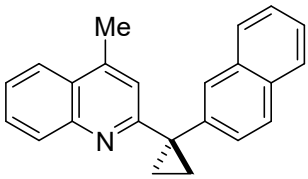
2-(1-(3,4-Dimethoxyphenyl)cyclopropyl)-4-methylquinoline (3ak)



Following **GP3**, the starting materials Lepidine (**1a,** 27 µL, 0.2 mmol) and (S)-2-(1-(3,4-dimethoxyphenyl)cyclopropyl)-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (**2k**, 169 mg, 0.5 mmol) afforded the compound **3ak**, as a white solid (56 mg, 0.175 mmol, 88%).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 8.00 (d, *J* = 8.4 Hz, 1H), 7.89 (d, *J* = 8.3 Hz, 1H), 7.65 (t, *J* = 7.6 Hz, 1H), 7.46 (t, *J* = 7.5 Hz, 1H), 7.00 – 7.02 (m, 1H), 6.94 – 6.97 (m, 2H), 6.88 (d, *J* = 8.2 Hz, 1H), 3.91 (s, 3H), 3.85 (s, 3H), 2.54 (s, 3H), 1.80 (q, *J* = 3.7 Hz, 2H), 1.33 (q, *J* = 3.7 Hz, 2H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 164.2, 149.0, 148.0, 147.7, 143.6, 136.5, 129.7, 129.1, 126.7, 125.4, 123.7, 122.4, 121.9, 113.9, 111.2, 56.1, 32.0, 18.9, 17.5; **HRMS (ESI):** m/z calc. for ($C_{21}H_{22}NO_2^+$) $[M+H]^+$: 320.1645; found: 320.1650; **IR (ATR) (ν cm^{-1}):** 3015, 2939, 2866, 1609, 1564, 1520, 1470, 1455, 1417, 1353, 1256, 1231, 1183, 1146, 1034, 963, 915, 864, 813, 765, 737, 652; **Melting Point:** 171 °C.

4-Methyl-2-(1-(naphthalen-2-yl)cyclopropyl)quinoline (3al)

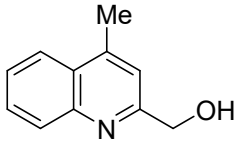


Following **GP-3**, the starting materials Lepidine (**1a,** 27 µL, 0.2 mmol) and (S)-2-methyl-2-(1-(naphthalen-2-yl)cyclopropyl)-2,3-dihydroquinazolin-4(1*H*)-one (**2l,** 164 mg, 0.5 mmol) afforded the compound **3al**, as a white solid (53 mg, 0.171 mmol, 86%).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 8.04 (d, *J* = 8.4 Hz, 1H), 7.83 – 7.90 (m, 5H), 7.65 – 7.69 (m, 1H), 7.54 (dd, *J* = 8.5, 1.4 Hz, 1H), 7.46 – 7.51 (m, 1H), 6.96 (s, 1H), 2.50 (s, 3H), 1.90 (q, *J* = 3.8 Hz, 2H), 1.46 (q, *J* = 3.8 Hz, 2H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 163.8, 147.8, 143.7, 141.4, 133.7, 132.6, 129.8, 129.1, 129.0, 128.5, 128.3, 127.9, 127.8, 126.7, 126.2, 125.9, 125.5, 123.7, 122.1, 32.4, 18.8, 17.4; **HRMS (ESI):** m/z calc. for ($C_{23}H_{20}N$) $[M+H]^+$: 310.1590; found: 310.1587;

IR (ATR) (ν cm^{-1}): 3076, 3020, 2979, 2942, 2870, 1739, 1693, 1608, 1565, 1513, 1455, 1417, 1351, 1271, 1162, 1089, 1033, 956, 901, 866, 823, 757, 706, 665; **Melting Point:** 153 °C.

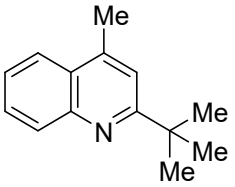
(4-Methylquinolin-2-yl)methanol (3am)



Following **GP3**, the starting materials Lepidine (**1a,** 27 µL, 0.2 mmol) and 2-(((tert-butyldimethylsilyl)oxy)methyl)-2-methyl-2,3-dihydroquinazolin-4(1H)-one (**2m,** 153 mg, 0.5 mmol) afforded the compound **3am**, as a colorless liquid (22 mg, 0.127 mmol, 64%), upon silyl-deprotection during reaction work-up.

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 8.06 (d, *J* = 8.4 Hz, 1H), 7.97 (d, *J* = 8.3 Hz, 1H), 7.69 – 7.72 (m, 1H), 7.53 – 7.57 (m, 1H), 7.12 (s, 1H), 4.87 (s, 2H), 2.69 (s, 3H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 158.8, 146.7, 145.2, 129.6, 129.3, 127.8, 126.2, 123.9, 119.1, 64.2, 18.9. The spectroscopic data obtained were in agreement with the reported data for the compound **3am**.[24]

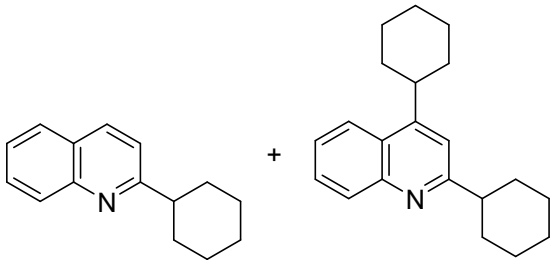
2-(*tert*-Butyl)-4-methylquinoline (3an)



Following **GP3**, the starting materials Lepidine (**1a,** 27 µL, 0.2 mmol) and 2-(tert-butyl)-2,3-dihydroquinazolin-4(1H)-one (**2n,** 102 mg, 0.5 mmol) afforded the compound **3an**, as a colorless liquid (35 mg, 0.176 mmol, 88%).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 8.06 (d, *J* = 8.4 Hz, 1H), 7.94 (d, *J* = 8.3 Hz, 1H), 7.66 (ddd, *J* = 8.2, 6.8, 1.2 Hz, 1H), 7.49 (ddd, *J* = 8.1, 6.8, 1.0 Hz, 1H), 7.35 (s, 1H), 2.69 (s, 3H), 1.46 (s, 9H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 169.1, 147.4, 143.8, 130.1, 128.8, 126.7, 125.5, 123.5, 119.0, 38.1, 30.3, 19.1. The spectroscopic data obtained were in agreement with the reported data for the compound **3an**.[20]

2,4-Dicyclohexylquinoline (3bd) & 2-Cyclohexylquinoline (3bd')

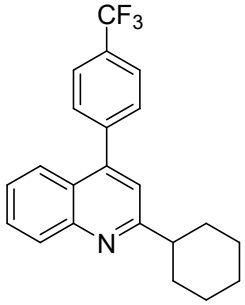


Following **GP3**, the starting materials Quinoline (**1b,** 24 µL, 0.2 mmol) and 2-cyclohexyl-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (**2d,** 122 mg, 0.5 mmol) afforded the compound **3bd** & **3bd'**, as a pale yellow liquid (**3bd** + **3bd' =** 28 mg, **3bd**:**3bd'** = 1:2; where, **3bd** = 0.035 mmol, 18% & **3bd'** = 0.070 mmol, 35%).

Following **GP3**, the starting materials Quinoline (**1b,** 24 µL, 0.2 mmol) and 2-cyclohexyl-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (**2d,** 49 mg, 0.2 mmol) afforded the compound **3bd** & **3bd'**, as a pale yellow liquid (**3bd** + **3bd' =** 16 mg, **3bd**:**3bd'** = 2:1; where, **3bd** = 0.045 mmol, 23% & **3bd'** = 0.022 mmol, 11%).

Compound **3bd** **^{1}H NMR (500 MHz, $CDCl_3$)** δ (ppm) = 8.06 (d, *J* = 8.8 Hz, 1H), 8.03 (d, *J* = 8.8 Hz, 1H), 7.62 – 7.65 (m, 1H), 7.45 – 7.49 (m, 1H), 7.20 (s, 1H), 3.27 – 3.32 (m, 1H), 2.85 – 2.92 (m, 1H), 1.77 – 2.03 (m, 10H), 1.34 – 1.68 (m, 10H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 166.8, 153.5, 148.2, 130.0, 128.7, 125.8, 125.3, 122.9, 115.9, 48.0, 39.1, 33.8, 33.0, 27.1, 26.7, 26.5, 26.3. The spectroscopic data obtained were in agreement with the reported data for the compound **3bd**.[25] Compound **3bd'**: **^{1}H NMR (500 MHz, $CDCl_3$)** δ (ppm) = 8.08 – 8.02 (m, 2H), 7.76 (dd, *J* = 8.1, 1.0 Hz, 1H), 7.67 (td, *J* = 7.7, 1.4 Hz, 1H), 7.45 – 7.48 (m, 1H), 7.32 (d, *J* = 8.5 Hz, 1H), 2.92 (tt, *J* = 12.1, 3.4 Hz, 1H), 1.32 – 2.03 (m, 10H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 167.0, 147.9, 136.4, 129.3, 129.1, 127.6, 127.1, 125.7, 119.7, 47.8, 33.0, 26.7, 26.2. The spectroscopic data obtained were in agreement with the reported data for the compound **3bd'**.[26]

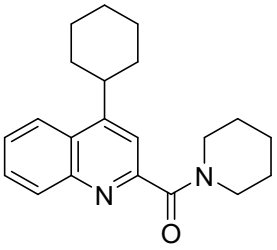
2-Cyclohexyl-4-(4-(trifluoromethyl)phenyl)quinoline (3cd)



Following **GP3**, the starting materials 4-(4-(trifluoromethyl)phenyl)quinoline (**1c,** 55 mg, 0.2 mmol) and 2-cyclohexyl-2-methyl-2,3-dihydroquinazolin-4(1H)-one (**2d,** 122 mg, 0.5 mmol)afforded the compound **3cd**, as a colorless viscous liquid (50 mg, 0.141 mmol, 70%).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 8.14 (d, *J* = 8.3 Hz, 1H), 7.79 (d, *J* = 8.1 Hz, 2H), 7.75 (d, *J* = 8.4 Hz, 1H), 7.68 – 7.72 (m, 1H), 7.63 (d, *J* = 8.0 Hz, 2H), 7.43 – 7.46 (m, 1H), 7.26 (s, 1H), 2.97 (tt, *J* = 12.0, 3.4 Hz, 1H), 2.06 – 2.08 (m, 2H), 1.89 – 1.92 (m, 2H), 1.78 – 1.81 (m, 1H), 1.62 – 1.70 (m, 2H), 1.45 – 1.53 (m, 2H), 1.28 – 1.38 (m, 1H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ (ppm) = 166.5, 148.4, 147.2, 142.4 (q, *J* = 1.3 Hz), 130.6 (q, *J* = 32.6 Hz), 130.1, 129.7, 129.5, 126.2, 125.6 (q, *J* = 3.7 Hz), 125.2, 125.2, 124.2 (q, *J* = 272.2 Hz), 120.0, 47.7, 33.0, 26.6, 26.2; **^{19}F NMR (471 MHz, $CDCl_3$)** δ (ppm) = – 62.53. The spectroscopic data obtained were in agreement with the reported data for the compound **3cd**.[27]

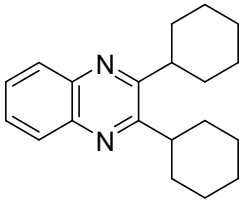
2,3-Dicyclohexylquinoxaline (3dd)



Following **GP3**, the starting materials (**1d** 48 mg, 0.2 mmol) and 2-cyclohexyl-2-methyl-2,3-dihydroquinazolin-4(1H)-one (**2d,** 122 mg, 0.5 mmol) afforded the compound **3dd**, as a viscous liquid (35 mg, 0.109 mmol, 54%).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 8.01 – 8.31 (m, 2H), 7.70 (t, *J* = 7.6 Hz, 1H), 7.58 (t, *J* = 7.7 Hz, 1H), 7.51 (s, 1H), 3.78 – 3.80 (m, 2H), 3.47 – 3.49 (m, 2H), 3.30 – 3.36 (m, 1H), 2.00 – 2.02 (m, 2H), 1.91 – 1.94 (m, 2H), 1.82 – 1.85 (m, 1H), 1.67 – 1.74 (m, 4H), 1.49 – 1.61 (m, 6H), 1.29 – 1.37 (m, 1H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 168.3, 154.8, 154.5, 147.2, 130.8, 129.4, 127.0, 126.7, 123.1, 116.7, 48.4, 43.4, 39.2, 33.6, 27.0, 26.6, 26.3, 25.7, 24.7; **HRMS (ESI):** m/z calc. for ($C_{21}H_{27}N_2O^+$) $[M+H]^+$: 323.2118; found: 323.2104; **IR (ATR) (ν cm^{-1}):** 2944, 2869, 1643, 1604, 1483, 1452, 1268, 1032, 772.

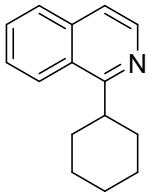
2,3-Dicyclohexylquinoxaline (3ed)



Following **GP3**, the starting materials quinoxaline (**1e,** 26 mg, 0.2 mmol) and 2-cyclohexyl-2-methyl-2,3-dihydroquinazolin-4(1H)-one (**2d,** 122 mg, 0.5 mmol) afforded the compound **3ed**, as a pale yellow solid (26 mg, 0.088 mmol, 44%).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 7.98 (dd, *J* = 6.3, 3.5 Hz, 2H), 7.62 (dd, *J* = 6.4, 3.4 Hz, 2H), 3.09 (tt, *J* = 11.1, 3.7 Hz, 2H), 1.91 – 1.95 (m, 4H), 1.85 – 1.89 (m, 5H), 1.80 – 1.83 (m, 5H), 1.44 – 1.52 (m, 4H), 1.37 – 1.43 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 159.8, 141.0, 128.8, 128.5, 41.9, 32.5, 26.9, 3.1. The spectroscopic data obtained were in agreement with the reported data for the compound **3ed**.[28]

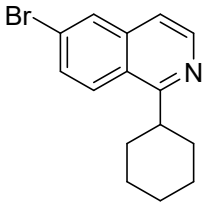
1-Cyclohexylisoquinoline (3fd)



Following **GP3**, the starting materials isoquinoline (**1f,** 24 µL, 0.2 mmol) and 2-cyclohexyl-2-methyl-2,3-dihydroquinazolin-4(1H)-one (**2d,** 122 mg, 0.5 mmol) afforded the compound **3fd**, as a colorless liquid (41 mg, 0.194 mmol, 97%).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 8.48 (d, *J* = 5.7 Hz, 1H), 8.22 (d, *J* = 8.4 Hz, 1H), 7.80 (d, *J* = 8.1 Hz, 1H), 7.64 (ddd, *J* = 8.1, 7.0, 1.1 Hz, 1H), 7.58 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1H), 7.48 (d, *J* = 5.7 Hz, 1H), 3.56 (tt, *J* = 11.7, 3.3 Hz, 1H), 1.92 – 2.00 (m, 4H), 1.79 – 1.87 (m, 3H), 1.49 – 1.58 (m, 2H), 1.34 – 1.44 (m, 1H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 165.8, 142.1, 136.5, 129.7, 127.7, 126.9, 126.4, 124.9, 119.0, 41.7, 32.7, 27.0, 26.4. The spectroscopic data obtained were in agreement with the reported data for the compound **3fd**.[22]

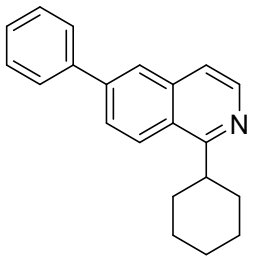
6-Bromo-1-cyclohexylisoquinoline (3gd)



Following **GP3**, the starting materials 6-bromoisoquinoline (**1g,** 42 mg, 0.2 mmol) and 2-cyclohexyl-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (**2d,** 122 mg, 0.5 mmol) afforded the compound **3gd**, as a yellow solid (35 mg, 0.121 mmol, 60%).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 8.50 (d, *J* = 5.7 Hz, 1H), 8.09 (d, *J* = 9.0 Hz, 1H), 7.99 (d, *J* = 1.9 Hz, 1H), 7.66 (dd, *J* = 9.0, 2.0 Hz, 1H), 7.40 (d, *J* = 5.7 Hz, 1H), 3.50 (tt, *J* = 11.7, 3.2 Hz, 1H), 1.92 – 1.96 (m, 4H), 1.78 – 1.86 (m, 3H), 1.47 – 1.57 (m, 2H), 1.36 – 1.43 (m, 1H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 166.1, 142.9, 137.8, 130.6, 129.8, 126.8, 124.8, 124.6, 118.1, 41.8, 32.7, 26.9, 26.3. The spectroscopic data obtained were in agreement with the reported data for the compound **3gd**.[29]

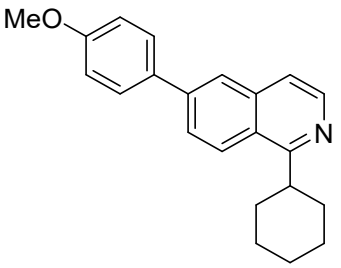
1-Cyclohexyl-6-phenylisoquinoline (3hd)



Following **GP3**, the starting materials 6-phenylisoquinoline (**1h,** 41 mg, 0.2 mmol) and 2-cyclohexyl-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (**2d,** 122 mg, 0.5 mmol) afforded the compound **3hd**, as a white solid (47 mg, 0.164 mmol, 82%).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 8.50 (d, *J* = 5.7 Hz, 1H), 8.29 (d, *J* = 8.8 Hz, 1H), 7.99 (d, *J* = 1.4 Hz, 1H), 7.84 (dd, *J* = 8.8, 1.7 Hz, 1H), 7.72 (d, *J* = 7.3 Hz, 2H), 7.50 – 7.54 (m, 3H), 7.43 (t, *J* = 7.4 Hz, 1H), 3.59 (tt, *J* = 11.7, 3.1 Hz, 1H), 1.94 – 2.02 (m, 4H), 1.82 – 1.89 (m, 3H), 1.51 – 1.60 (m, 2H), 1.39 – 1.45 (m, 1H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 165.8, 142.4, 142.4, 140.3, 137.0, 129.2, 128.2, 127.6, 126.7, 125.6, 125.5, 125.4, 119.3, 41.8, 32.7, 27.0, 26.4; **HRMS (ESI):** m/z calc. for ($C_{21}H_{22}N^+$) $[M+H]^+$: 288.1747; found: 288.1745; **IR (ATR) (ν cm^{-1}):** 3064, 2937, 2867, 1738, 1632, 1571, 1496, 1455, 1408, 1365, 1271, 1170, 1106, 1082, 1032, 997, 896, 836, 816, 760, 701; **Melting Point:** 72 °C.

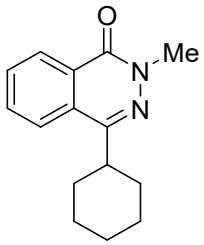
1-Cyclohexyl-6-(4-methoxyphenyl)isoquinoline (3id)



Following **GP3**, the starting materials 6-(4-methoxyphenyl)isoquinoline (**1i**, 47 mg, 0.2 mmol) and 2-cyclohexyl-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (**2d,** 122 mg, 0.5 mmol) afforded the compound **3id**, as a white solid (55 mg, 0.173 mmol, 87%).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 8.48 (d, *J* = 5.7 Hz, 1H), 8.26 (d, *J* = 8.9 Hz, 1H), 7.93 (d, *J* = 1.6 Hz, 1H), 7.80 (dd, *J* = 8.8, 1.8 Hz, 1H), 7.65 – 7.68 (m, 2H), 7.50 (d, *J* = 5.7 Hz, 1H), 7.02 – 7.05 (m, 2H), 3.88 (s, 3H), 3.57 (tt, *J* = 11.7, 3.2 Hz, 1H), 1.93 – 2.02 (m, 4H), 1.81 – 1.89 (m, 3H), 1.50 – 1.59 (m, 2H), 1.36 – 1.45 (m, 1H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 165.7, 159.9, 142.4, 141.8, 137.0, 132.7, 128.7, 126.4, 125.4, 125.2, 124.5, 119.2, 114.6, 55.5, 41.7, 32.7, 27.0, 26.4; **HRMS (ESI):** m/z calc. for ($C_{22}H_{24}NO^+$) $[M+H]^+$: 318.1852; found: 318.1850; **IR (ATR) (ν cm^{-1}):** 2940, 2865, 1616, 1571, 1524, 1498, 1466, 1291, 1256, 1187, 1118, 1032, 997, 895, 827, 794; **Melting Point:** 118 °C.

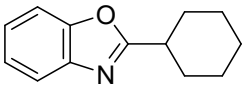
1-Chloro-4-cyclohexylphthalazine (3jd)



Following **GP3**, the starting materials 2-methylphthalazin-1(2H)-one (**1j**, 32 mg, 0.2 mmol) and 2-cyclohexyl-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (**2d,** 122 mg, 0.5 mmol) afforded the compound **3jd**, as a colorless liquid (30 mg, 0.124 mmol, 62%).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 8.48 (dd, *J* = 7.9, 0.7 Hz, 1H), 7.85 (d, *J* = 8.0 Hz, 1H), 7.76 – 7.80 (m, 1H), 7.71 – 7.74 (m, 1H), 3.83 (s, 3H), 3.10 (tt, *J* = 11.6, 3.1 Hz, 1H), 1.88 – 1.98 (m, 4H), 1.78 – 1.81 (m, 1H), 1.59 – 1.65 (m, 2H), 1.43 – 1.51 (m, 2H), 1.27 – 1.36 (m, 1H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 159.6, 150.0, 132.6, 130.9, 129.1, 128.2, 127.4, 124.0, 39.7, 39.6, 32.0, 26.8, 26.3; **HRMS (ESI):** m/z calc. for ($C_{15}H_{19}N_2O_1^+$) $[M+H]^+$: 243.1492; found: 243.1486; **IR (ATR) (ν cm^{-1}):** 2944, 2869, 1661, 1593, 1455, 1345, 1032, 785, 742, 699.

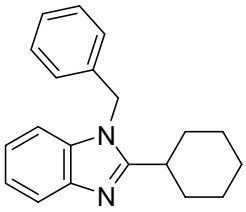
2-Cyclohexylbenzo[d]oxazole (3kd)



Following **GP3**, the starting materials benzo[d]oxazole (**1k,** 24 mg. 0.2 mmol) and 2-cyclohexyl-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (**2d,** 122 mg, 0.5 mmol) afforded the compound **3kd**, as an orange solid (26 mg, 0.129 mmol, 65%).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 7.67 – 7.68 (m, 1H), 7.46 – 7.48 (m, 1H), 7.27 – 7.29 (m, 2H), 2.95 (tt, *J* = 11.4, 3.6 Hz, 1H), 2.15 – 2.19 (m, 2H), 1.84 – 1.88 (m, 2H), 1.69 – 1.75 (m, 3H), 1.38 – 1.47 (m, 2H), 1.30 – 1.36 (m, 1H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 170.6, 150.7, 141.4, 124.5, 124.1, 119.7, 110.4, 38.1, 30.6, 25.9, 25.8. The spectroscopic data obtained were in agreement with the reported data for the compound **3kd**[30].

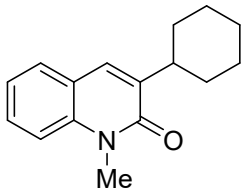
1-Benzyl-2-cyclohexyl-1H-benzo[d]imidazole (3ld)



Following **GP-3**, the starting materials 1-benzyl-1H-benzo[d]imidazole (**1l**, 42 mg,0.2 mmol) and 2-cyclohexyl-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (**2d,** 122 mg, 0.5 mmol) afforded the compound **3ld**, as a pale yellow solid (26 mg, 0.090 mmol, 45%).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 7.78 (d, *J* = 7.9 Hz, 1H), 7.21 – 7.32 (m, 4H), 7.17 – 7.18 (m, 2H), 7.04 (d, *J* = 7.2 Hz, 2H), 5.37 (s, 2H), 2.78 – 2.82 (m, 1H), 1.79 – 1.89 (m, 5H), 1.73 – 1.75 (m, 1H), 1.28 – 1.39 (m, 4H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 174.9, 159.5, 142.8, 136.5, 135.2, 129.1, 128.0, 126.2, 122.4, 122.1, 119.5, 109.8, 77.4, 77.2, 76.9, 46.9, 36.6, 32.1, 26.5, 25.9. The spectroscopic data obtained were in agreement with the reported data for the compound **3ld**.[31].

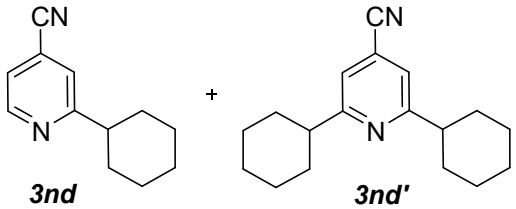
3-Cyclohexyl-1-methylquinolin-2(1*H*)-one (3md)



Following **GP3**, the starting materials 1-Methylquinolin-2(1*H*)-one (**1m**, 32 mg, 0.2 mmol) and 2-cyclohexyl-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (**2d,** 122 mg, 0.5 mmol) afforded the compound **3md**, as a white solid (21 mg, 0.087 mmol, 44%).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 7.47 – 7.53 (m, 3H), 7.32 – 7.33 (m, 1H), 7.19 – 7.22 (m, 1H), 3.74 (s, 3H), 2.98 (tt, *J* = 11.9, 3.0 Hz, 1H), 1.95 – 1.97 (m, 2H), 1.82 – 1.86 (m, 2H), 1.76 – 1.79 (m, 1H), 1.44 – 1.53 (m, 2H), 1.25 – 1.34 (m, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 162.4, 139.2, 138.8, 132.9, 129.4, 128.3, 122.0, 121.0, 113.9, 38.0, 32.7, 29.9, 26.9, 26.6. The spectroscopic data obtained were in agreement with the reported data for the compound **3md**.[32]

2-Cyclohexylisonicotinonitrile (3nd) & 2,6-Dicyclohexylisonicotinonitrile (3nd')



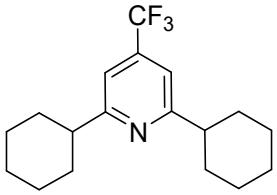
3nd ***3nd'***

Following **GP3**, the starting materials isonicotinonitrile (**1n,** 21 mg, 0.2 mmol) and 2-cyclohexyl-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (**2d,** 122 mg, 0.5 mmol) afforded the compound **3nd**, as a colorless liquid (18 mg, 0.097 mmol, 48%) and **3nd'**, as a colorless liquid (15 mg, 0.056 mmol, 28%).

Compound 3xc: ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 8.69 (d, *J* = 5.0 Hz, 1H), 7.38 (s, 1H), 7.33 (dd, *J* = 5.0, 1.4 Hz, 1H), 2.76 (tt, *J* = 11.9, 3.4 Hz, 1H), 1.93 – 1.96 (m, 2H), 1.85 – 1.89 (m, 2H), 1.75 – 1.78 (m, 1H), 1.47 – 1.55 (m, 2H), 1.37 – 1.46 (m, 2H), 1.26 – 1.33 (m, 1H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 168.3, 150.2, 123.0, 122.6, 120.8, 117.0, 46.5, 32.8, 26.5, 26.0. The spectroscopic data obtained were in agreement with the reported data for the compound **3nd**.[33]

Compound 3nd': ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 7.16 (s, 2H), 2.71 (tt, *J* = 11.6, 3.3 Hz, 2H), 1.92 – 1.96 (m, 4H), 1.83 – 1.87 (m, 4H), 1.73 – 1.77 (m, 2H), 1.36 – 1.51 (m, 8H), 1.23 – 1.32 (m, 2H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 167.4, 120.7, 119.8, 117.7, 46.5, 32.8, 26.5, 26.1. The spectroscopic data obtained were in agreement with the reported data for the compound **3nd'**.[20]

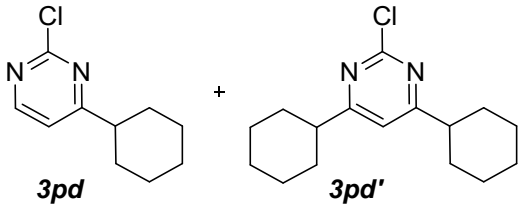
2,6-Dicyclohexyl-4-(trifluoromethyl)pyridine (3od)



Following **GP3**, the starting materials 4-(trifluoromethyl)pyridine (**1o,** 30 mg, 0.2 mmol) and 2-cyclohexyl-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (**2d,** 122 mg, 0.5 mmol) afforded the compound **3od**, as a colorless liquid (36 mg, 0.116 mmol, 58%).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 7.14 (s, 1H), 2.72 – 2.78 (m, 2H), 1.95 – 1.98 (m, 4H), 1.84 – 1.87 (m, 4H), 1.74 – 1.77 (m, 2H), 1.38 – 1.55 (m, 8H), 1.27 – 1.33 (m, 2H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ (ppm) = 167.3, 138.8 (q, *J* = 32.9 Hz), 123.5 (q, *J* = 273.1 Hz), 113.7 (q, *J* = 3.5 Hz), 46.7, 33.0, 26.6, 26.2; **^{19}F NMR (471 MHz, $CDCl_3$)** δ (ppm) = – 64.51. The spectroscopic data obtained were in agreement with the reported data for the compound **3od**.[34]

2-Chloro-4-cyclohexylpyrimidine (3pd) & 2-Chloro-4,6-dicyclohexylpyrimidine (3pd')

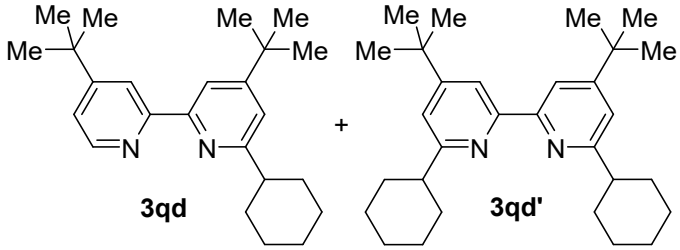


Following **GP3**, the starting materials 2-chloropyrimidine (**1p**, 23 mg, 0.2 mmol) and 2-cyclohexyl-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (**2d,** 122 mg, 0.5 mmol) afforded the compound **3pd**, as a colorless liquid (20 mg, 0.102 mmol, 51%) and **3pd'**, as a colorless liquid (8 mg, 0.029 mmol, 14%).

Compound 3pd: ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 8.48 (d, *J* = 5.1 Hz, 1H), 7.10 (d, *J* = 5.1 Hz, 1H), 2.66 (tt, *J* = 11.9, 3.4 Hz, 1H), 1.93 – 1.95 (m, 2H), 1.84 – 1.87 (m, 2H), 1.73 – 1.76 (m, 1H), 1.47 – 1.52 (m, 2H), 1.33 – 1.42 (m, 2H), 1.24 – 1.30 (m, 1H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 178.7, 161.3, 159.4, 117.2, 46.0, 32.0, 26.2, 25.8. The spectroscopic data obtained were in agreement with the reported data for the compound **3pd**.[35]

Compound 3pd': ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 6.92 (s, 1H), 2.62 (tt, *J* = 11.9, 3.4 Hz, 2H), 1.91 – 1.94 (m, 4H), 1.83 – 1.88 (m, 4H), 1.72 – 1.76 (m, 2H), 1.45 – 1.53 (m, 4H), 1.33 – 1.42 (m, 4H), 1.26 – 1.31 (m, 2H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 178.3, 160.8, 114.1, 46.1, 32.1, 26.3, 25.9. The spectroscopic data obtained were in agreement with the reported data for the compound **3pd'**.[36]

4,4'-Di-*tert*-butyl-6-cyclohexyl-2,2'-bipyridine (3qd) & 4,4'-Di-*tert*-butyl-6,6'-dicyclohexyl-2,2'-bipyridine (3qd')

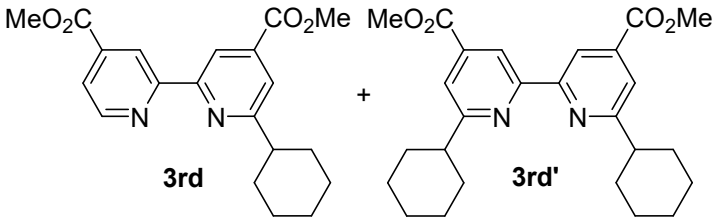


Following **GP3**, the starting materials 4,4'-di-tert-butyl-2,2'-bipyridine (**1q,** 54 mg, 0.2 mmol) and 2-cyclohexyl-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (**2d,** 122 mg, 0.5 mmol) afforded the compound **3qd**, as a white solid (44 mg, 0.116 mmol, 58%) and **3qd'**, as a white solid (10 mg, 0.116 mmol, 12%).

Compound 3qd: ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 8.57 (dd, *J* = 5.3, 0.4 Hz, 1H), 8.46 (d, *J* = 1.5 Hz, 1H), 8.17 (d, *J* = 1.7 Hz, 1H), 7.27 (dd, *J* = 5.2, 2.0 Hz, 1H), 7.15 (d, *J* = 1.7 Hz, 1H), 2.79 (tt, *J* = 11.8, 3.4 Hz, 1H), 2.02 – 2.05 (m, 2H), 1.87 – 1.91 (m, 2H), 1.76 – 1.82 (m, 2H), 1.59 – 1.67 (m, 2H), 1.41 – 1.50 (m, 2H), 1.39 (s, 9H), 1.37 (s, 9H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 165.9, 161.1, 160.8, 157.3, 155.6, 149.0, 120.6, 118.6, 118.0, 115.8, 46.8, 35.1, 35.1, 33.2, 30.9, 30.8, 26.8, 26.4. The spectroscopic data obtained were in agreement with the reported data for the compound **3qd**.[28]

Compound 3qd': ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 8.19 (d, *J* = 1.7 Hz, 2H), 7.11 (d, *J* = 1.7 Hz, 2H), 2.77 (tt, *J* = 11.8, 3.4 Hz, 2H), 2.00 – 2.05 (m, 4H), 1.86 – 1.90 (m, 4H), 1.76 – 1.78 (m, 2H), 1.57 – 1.65 (m, 4H), 1.40 – 1.49 (m, 4H), 1.37 (s, 18H), 1.28 – 1.34 (m, 2H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 165.7, 160.7, 156.5, 117.6, 116.0, 46.8, 35.1, 33.3, 30.9, 26.8, 26.4. The spectroscopic data obtained were in agreement with the reported data for the compound **3qd'**.[37]

4,4'-Di-*tert*-butyl-6-cyclohexyl-2,2'-bipyridine (3rd) & 4,4'-Di-*tert*-butyl-6,6'-dicyclohexyl-2,2'-bipyridine (3rd')



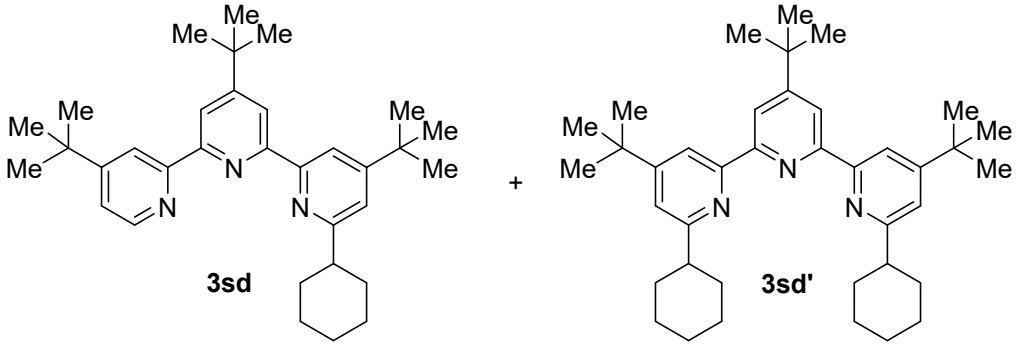
Following **GP3**, the starting materials dimethyl [2,2'-bipyridine]-4,4'-dicarboxylate (**1r,** 55 mg, 0.2 mmol) and 2-cyclohexyl-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (**2d,** 122 mg, 0.5 mmol) afforded the compound **3rd**, as a white solid (23 mg, 0.065 mmol, 32%) and **3rd'**, as a white solid (10 mg, 0.023 mmol, 11%).

Compound 3rd: ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 8.92 (s, 1H), 8.83 (d, *J* = 4.0 Hz, 1H), 8.79 (s, 1H), 8.64 (s, 1H), 7.88 (d, *J* = 4.2 Hz, 1H), 3.99 (s, 3H), 3.97 (s, 3H), 3.30 (tt, *J* = 12.0, 2.9 Hz, 1H), 1.88 – 1.96 (m, 4H), 1.79 – 1.81 (m, 1H), 1.51 – 1.59 (m, 2H), 1.41 – 1.49 (m, 2H), 1.30 – 1.36 (m, 1H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 167.3, 165.9, 156.8, 153.3, 150.2, 149.4, 142.5, 138.7, 138.2, 123.0, 120.5, 120.3, 52.9, 52.7, 38.9, 34.1, 27.0, 26.2. **HRMS (ESI):** m/z calc. for ($C_{20}H_{23}N_2O_4^+$) $[M+H]^+$: 355.1652; found: 355.1651; **IR (ATR) (ν cm^{-1}):** 2958, 2924, 2852, 1729,

1590, 1469, 1378, 1293, 1268, 1261, 1126, 1017, 969, 909, 863, 818, 796, 785, 735, 626; **Melting Point:** 149 °C.

Compound 3rd': ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 8.75 (s, 2H), 8.59 (s, 2H), 3.96 (s, 6H), 3.29 (tt, *J* = 11.8, 2.9 Hz, 2H), 1.87 – 1.95 (m, 8H), 1.78 – 1.80 (m, 2H), 1.50 – 1.57 (m, 4H), 1.40 – 1.48 (m, 4H), 1.27 – 1.35 (m, 2H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 167.4, 153.5, 149.3, 142.1, 138.2, 120.1, 52.7, 38.9, 34.1, 27.0, 26.2; **HRMS (ESI):** m/z calc. for ($C_{26}H_{33}N_2O_4^+$) $[M+H]^+$: 437.2435; found: 437.2441; **IR (ATR) (ν cm^{-1}):** 3271, 3191, 3000, 2981, 29622383, 2356, 2293, 1751, 1728, 1575, 1438, 1383, 1334, 1281, 1093, 1047, 978, 919, 878, 783, 733, 695, 633; **Melting Point:** 160 °C.

4,4',4''-Tri-*tert*-butyl-6-cyclohexyl-2,2':6',2''-terpyridine (3sd) & 4,4',4''-Tri-*tert*-butyl-6,6''-dicyclohexyl-2,2':6',2''-terpyridine (3sd')

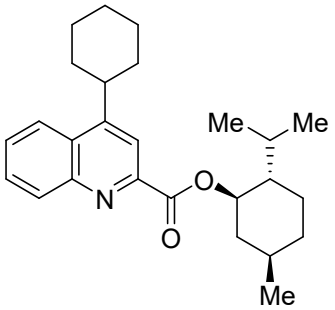


Following **GP3**, the starting materials 4,4',4''-tri-tert-butyl-2,2':6',2''-terpyridine (**1s,** 80 mg, 0.2 mmol) and 2-cyclohexyl-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (**2d,** 122 mg, 0.5 mmol) afforded the compound **3sd**, as a white solid (25 mg, 0.052 mmol, 26%) and **3sd'**, as a white solid (5 mg, 0.09 mmol, <5%).

Compound 3sd: ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 8.74 (d, *J* = 1.7 Hz, 1H), 8.61 (d, *J* = 5.2 Hz, 1H), 8.52 (d, *J* = 1.6 Hz, 1H), 8.49 (d, *J* = 1.5 Hz, 1H), 8.43 (d, *J* = 1.6 Hz, 1H), 7.32 (dd, *J* = 5.2, 2.0 Hz, 1H), 7.18 (d, *J* = 1.5 Hz, 1H), 2.82 (tt, *J* = 11.8, 3.3 Hz, 1H), 2.02 – 2.07 (m, 2H), 1.89 – 1.92 (m, 2H), 1.77 – 1.81 (m, 1H), 1.61 – 1.69 (m, 2H), 1.45 – 1.52 (m, 2H), 1.47 (s, 9H), 1.42 (s, 9H), 1.41 (s, 9H), 1.30 – 1.37 (m, 1H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 165.9, 162.0, 160.8, 160.8, 156.9, 156.3, 155.7, 155.3, 149.0, 120.9, 118.6, 118.2, 118.0, 117.8, 115.8, 46.8, 35.4, 35.1, 35.1, 33.3, 30.9, 30.8, 30.7, 26.8, 26.4.; **HRMS (ESI):** m/z calc. for ($C_{33}H_{46}N_3^+$) $[M+H]^+$: 484.3686; found: 484.3688; **IR (ATR) (ν cm^{-1}):** 2976, 2943, 2874, 1596, 1555, 1485, 1459, 1389, 1273, 912, 849, 807, 734, 675; **Melting Point:** 135 °C.

Compound 3sd': ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 8.49 (d, *J* = 1.8 Hz, 2H), 8.48 (s, 2H), 7.16 (d, *J* = 1.7 Hz, 2H), 2.80 (tt, *J* = 11.8, 3.4 Hz, 2H), 2.03 – 2.07 (m, 4H), 1.89 – 1.91 (m, 4H), 1.77 – 1.81 (m, 2H), 1.61 – 1.69 (m, 4H), 1.43 – 1.52 (m, 4H), 1.47 (s, 9H), 1.40 (s, 18H), 1.30 – 1.38 (m, 2H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 165.8, 161.5, 160.7, 156.1, 155.9, 117.9, 117.9, 115.9, 46.8, 35.4, 35.1, 33.3, 30.9, 30.8, 26.9, 26.4; **HRMS (ESI):** m/z calc. for ($C_{39}H_{56}N_3^+$) $[M+H]^+$: 566.4469; found: 566.4471; **IR (ATR) (ν cm^{-1}):** 27624327315997, 556, 1458, 1394, 1267, 1095, 1022, 911, 805, 735; **Melting Point:** 153 °C.

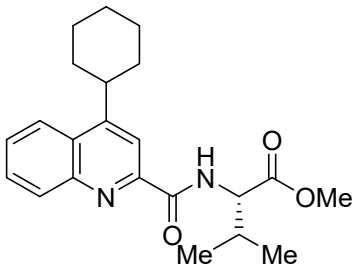
(*1R,2S,5R*)-2-isopropyl-5-methylcyclohexyl 4-cyclohexylquinoline-2-carboxylate (3td)



Following **GP-3**, the starting materials (*1R,2S,5R*)-2-isopropyl-5-methylcyclohexyl quinoline-2-carboxylate (**1t**, 62 mg, 0.2 mmol) and 2-cyclohexyl-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (**2d,** 122 mg, 0.5 mmol) afforded the compound **3td**, as a light yellow viscous liquid (57 mg, 0.145 mmol, 72%).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 8.32 (d, *J* = 8.4 Hz, 1H), 8.11 (d, *J* = 8.4 Hz, 1H), 8.02 (s, 1H), 7.73 (t, *J* = 7.6 Hz, 1H), 7.63 (t, *J* = 7.6 Hz, 1H), 5.09 (td, *J* = 10.8, 4.4 Hz, 1H), 3.36 (tt, *J* = 11.4, 2.9 Hz, 1H), 2.18 – 2.22 (m, 1H), 2.01 – 2.04 (m, 3H), 1.94 – 1.97 (m, 2H), 1.85 – 1.87 (m, 1H), 1.69 – 1.78 (m, 3H), 1.52 – 1.66 (m, 5H), 1.33 – 1.42 (m, 1H), 1.33 – 1.42 (m, 2H), 1.12 – 1.21 (m, 1H), 0.95 (d, *J* = 6.2 Hz, 3H), 0.93 (d, *J* = 6.7 Hz, 3H), 0.84 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 165.4, 154.9, 148.6, 148.1, 132.0, 129.5, 128.1, 128.0, 123.0, 117.4, 76.2, 47.1, 40.9, 39.3, 34.4, 33.7, 33.5, 31.7, 27.0, 27.0, 26.7, 26.3, 23.9, 22.2, 20.8, 16.8; **HRMS (ESI):** m/z calc. for ($C_{26}H_{36}NO_2^+$) $[M+H]^+$: 394.2741; found: 394.2741; **IR (ATR) (ν cm^{-1}):** 2942, 2870, 1746, 1720, 1599, 1569, 1516, 1465, 1374, 1350, 1273, 1249, 1219, 1160, 1119, 968, 803, 768, 741.

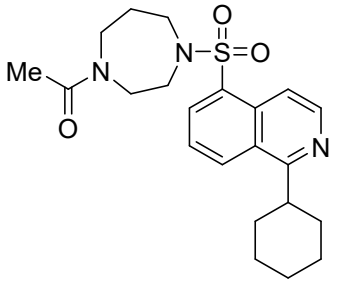
(*1R,2S,5R*)-2-isopropyl-5-methylcyclohexyl 4-cyclohexylquinoline-2-carboxylate (3ud)



Following **GP-3**, the starting materials methyl (quinoline-2-carbonyl)-*L*-valinate (**1u,** 57 mg, 0.2 mmol) and 2-cyclohexyl-2-methyl-2,3-dihydroquinazolin-4(1H)-one (**2d,** 122 mg, 0.5 mmol) afforded the compound **3ud**, as a viscous liquid (37 mg, 0.10 mmol, 50%).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 8.76 (d, *J* = 9.2 Hz, 1H), 8.20 (s, 1H), 8.18 (d, *J* = 8.4 Hz, 1H), 8.13 (d, *J* = 8.5 Hz, 1H), 7.72 – 7.75 (m, 1H), 7.61 – 7.64 (m, 1H), 4.79 (dd, *J* = 9.2, 5.3 Hz, 1H), 3.79 (s, 3H), 3.36 (tt, *J* = 11.5, 2.7 Hz, 1H), 2.33 – 2.39 (m, 1H), 1.93 – 2.03 (m, 4H), 1.83 – 1.86 (m, 1H), 1.60 – 1.68 (m, 2H), 1.50 – 1.55 (m, 2H), 1.31 – 1.40 (m, 1H), 1.06 (d, *J* = 6.8 Hz, 6H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 172.6, 165.1, 155.4, 149.2, 147.1, 131.2, 129.5, 128.2, 127.7, 123.2, 115.4, 57.7, 52.3, 39.4, 33.6, 33.6, 31.8, 27.1, 27.0, 26.4, 19.4, 18.2; **HRMS (ESI):** m/z calc. for ($C_{22}H_{29}N_2O_3^+$) $[M+H]^+$: 369.2173; found: 369.2168; **IR (ATR) (ν cm^{-1}):** 2980, 2944, 2865, 1753, 1690, 1563, 1512, 1462, 1380, 1267, 1215, 1168, 1087, 1057, 1023, 912, 800, 766, 735, 653.

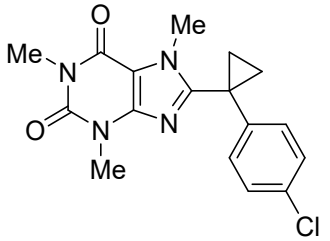
1-(4-((1-cyclohexylisoquinolin-5-yl)sulfonyl)-1,4-diazepan-1-yl)ethan-1-one (3vd)



Following **GP-3**, the starting materials 1-(4-(isoquinolin-5-ylsulfonyl)-1,4-diazepan-1-yl)ethan-1-one (**1v**, 67 mg, 0.2 mmol) and 2-cyclohexyl-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (**2d,** 122 mg, 0.5 mmol) afforded the compound **3vd**, as a white solid (40 mg, 0.096 mmol, 48%).

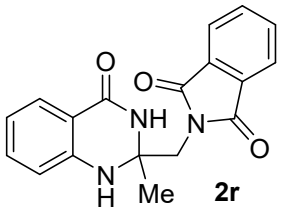
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 8.61 – 8.63 (m, 1H), 8.48 – 8.49 (m, 1H), 8.27 – 8.31 (m, 1H), 8.20 (d, *J* = 5.9 Hz, 1H), 7.63 – 7.67 (m, 1H), 3.32 – 3.72 (m, 9H), 2.03 – 2.09 (m, 3H), 1.92 – 2.00 (m, 6H), 1.75 – 1.86 (m, 3H), 1.48 – 1.56 (m, 2H), 1.34 – 1.42 (m, 1H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) (a mixture of rotamers) = 170.4, 170.3, 170.0, 166.9, 144.2, 144.1, 134.9, 132.6, 132.6, 132.3, 130.8, 130.7, 127.1, 125.3, 115.4, 115.3, 51.0, 50.2, 49.3, 48.4, 48.1, 47.8, 47.0, 44.6, 42.3, 42.2, 32.9, 29.1, 27.8, 26.9, 26.3, 21.7, 21.2. The spectroscopic data obtained were in agreement with the reported data for the compound **3vd**.[18]

8-(1-(4-Chlorophenyl)cyclopropyl)-1,3,7-trimethyl-3,7-dihydro-1H-purine-2,6-dione (3wi)

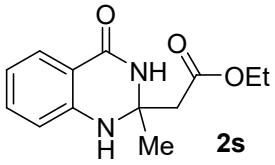


Following **GP-3**, the starting materials 1,3,7-trimethyl-3,7-dihydro-1H-purine-2,6-dione (**1w,** 39 mg, 0.2 mmol) and (S)-2-(1-(4-chlorophenyl)cyclopropyl)-2-methyl-2,3-dihydroquinazolin-4(1H)-one (**2i**, 156 mg, 0.5 mmol) afforded the compound **3wi**, as a semi-solid (32 mg, 0.093 mmol, 46%). Reaction temperature = 80 °C.

^{1}H NMR (500 MHz, DMSO-d6) δ (ppm) = 7.41 (d, *J* = 8.6 Hz, 2H), 7.10 (d, *J* = 8.6 Hz, 2H), 3.73 (s, 3H), 3.50 (s, 3H), 3.28 (s, 3H), 1.62 (dd, *J* = 7.1, 4.7 Hz, 2H), 1.53 (dd, *J* = 7.0, 4.8 Hz, 2H); **^{13}C NMR (125 MHz, DMSO-d6)** δ (ppm) = 154.5, 153.7, 151.0, 146.8, 140.1, 131.0, 128.7, 127.3, 107.2, 32.1, 29.5, 27.5, 21.6, 16.4; **HRMS (ESI):** m/z calc. for ($C_{17}H_{18}ClN_4O_2^+$) $[M+H]^+$: 345.1113; found: 345.1110; **IR (ATR) (ν cm^{-1}):** 3098, 3070, 2965, 2340, 2282, 2186, 2081, 1724, 1683, 1536, 1458, 1431, 1408, 1048, 985, 941, 802, 756, 726, 655, 619.



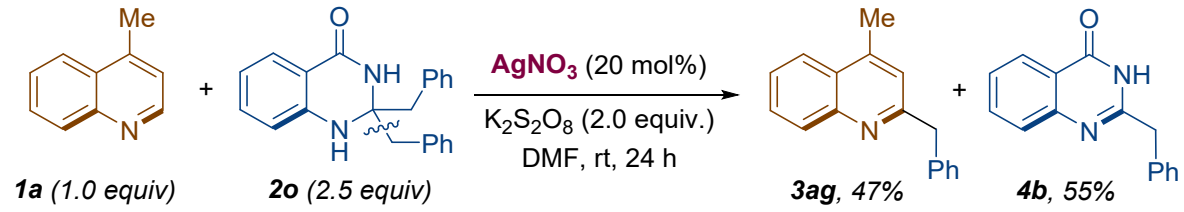
2r



2s

Figure S4: List of unsuccessful 2,3-Dihydroquinazolinone derivatives

4.2 C*sp*³-group transposition with concomitant alkaloid formation

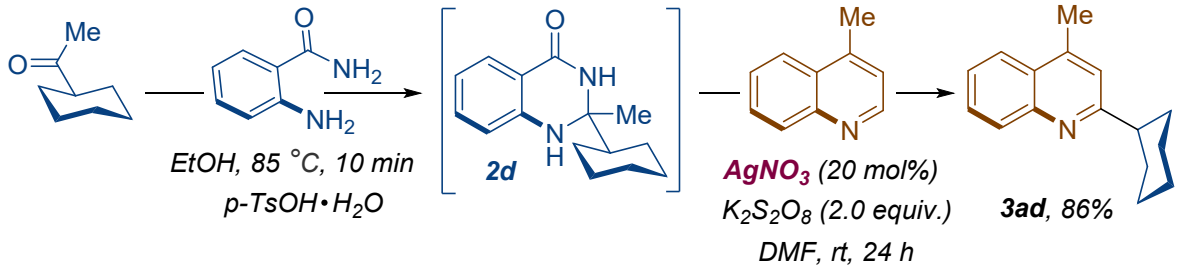


Following **GP3**, the starting materials Lepidine (**1a**, 0.2 mmol) and **2o** (0.5 mmol) afforded 2-benzyl-4-methylquinoline (**3ag**, 22 mg, 0.094 mmol, 47%) as a colorless liquid and 2-benzylquinazolin-4(3*H*)-one (**4b**, 65 mg, 0.275 mmol, 55%) as a white solid.

2-Benzyl-4-methylquinoline (3ag): ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 8.09 (d, *J* = 8.4 Hz, 1H), 7.94 (d, *J* = 8.3 Hz, 1H), 7.70 (t, *J* = 7.6 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.29 – 7.33 (m, 4H), 7.21 – 7.24 (m, 1H), 7.07 (s, 1H), 4.30 (s, 2H), 2.61 (s, 3H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 161.0, 147.8, 144.8, 139.5, 129.7, 129.4, 129.3, 128.8, 127.0, 126.6, 125.9, 123.8, 122.3, 77.4, 77.2, 76.9, 45.6, 18.9. The spectroscopic data obtained were in agreement with the reported data for the compound **3ag**.[23]

2-Benzylquinazolin-4(3*H*)-one (4b): ^{1}H NMR (500 MHz, DMSO-d6) δ (ppm) = 12.42 (s, 1H), 8.07 (d, *J* = 7.9 Hz, 1H), 7.77 (t, *J* = 7.7 Hz, 1H), 7.60 (d, *J* = 8.1 Hz, 1H), 7.46 (t, *J* = 7.5 Hz, 1H), 7.37 – 7.39 (m, 2H), 7.32 (t, *J* = 7.5 Hz, 2H), 7.24 (t, *J* = 7.2 Hz, 1H), 3.93 (s, 2H); **^{13}C NMR (126 MHz, DMSO-d6)** δ (ppm) = 161.9, 156.0, 148.9, 136.6, 134.4, 128.9, 128.5, 126.9, 126.8, 126.2, 125.7, 120.7, 40.8. The spectroscopic data obtained were in agreement with the reported data for the compound **4b**.[38]

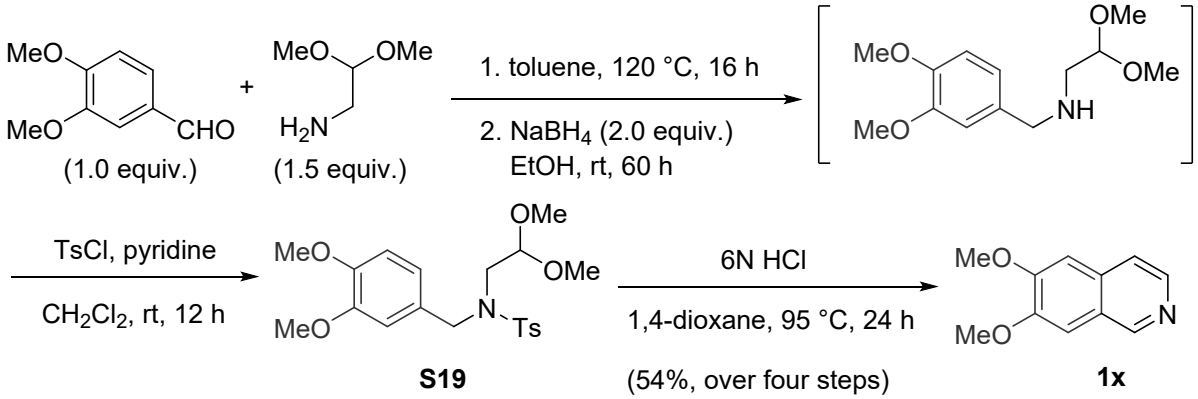
4.3 Scale-Up Telescopic Approach for the Alkylation of *N*-heteroarene



In a heat gun-dried Schlenk tube equipped with a Teflon-coated stirring bar, anthranilamide (341 mg, 2.5 mmol, 1.0 equiv.), ketone (344 µL, 2.5 mmol, 1.0 equiv.) and *p*-toluenesulfonic acid (95 mg, 0.5 mmol, 0.2 equiv.) were dissolved in absolute ethanol (1 mL). The resulting mixture was heated at 85 ºC for 10 min. After cooling down to room temperature, the reaction mixture was concentrated under reduced pressure, affording the crude residue. Afterward, $AgNO_3$ (34 mg, 0.2 mmol, 0.2 equiv.), $K_2S_2O_8$ (541 mg, 2.0 mmol, 2.0 equiv.), Lepidine (1.0 mmol, 1.0 equiv.) and DMF (10 mL) were added to the crude residue in the Schlenk tube under inert atmosphere. The solution was stirred at room temperature for 24 h under dark condition. The reaction was quenched by the addition of brine solution (10 mL) and then extracted with ethyl acetate (3×10 mL). The combined organic layers were

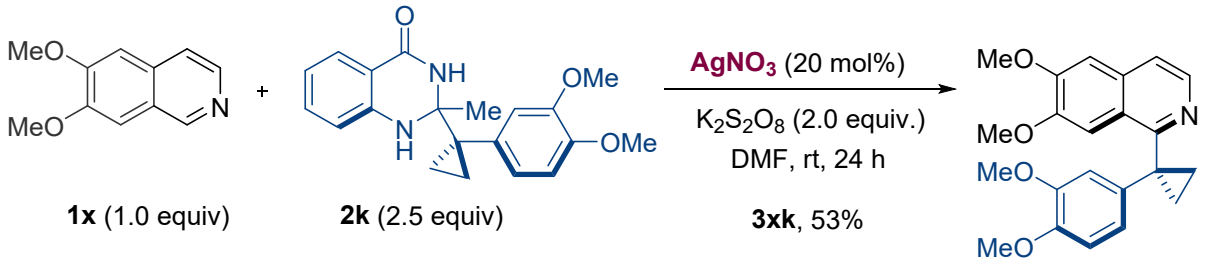
washed once again with water (10 ml), followed by brine (10 ml) and the solvents were removed under reduced pressure. The crude reaction mixture was purified by flash column chromatography through Silica gel (eluent: petroleum ether/ethyl acetate) to afford pure product **3ad** (194 mg, 0.861 mmol, 86%) as colorless liquid.

4.4 Synthesis of Papaverine Analogue (3xk)



Following a modified procedure reported by Knochel and co-workers,[39] in a round bottom flask equipped with a Teflon-coated stirring bar and Dean-Stark apparatus, 3,4-dimethoxybenzaldehyde (2.77 g, 16.67 mmol, 1.0 equiv.) and 2,2-dimethoxyethan-1-amine (2.75 mL, 25.36 mmol, 1.5 equiv.) were dissolved in toluene (50 mL). The reaction mixture was refluxed at 120 °C for 16 h. After cooling the reaction to room temperature, the solvent was removed under reduced pressure. The resulting yellow liquid was dissolved in dichloromethane and then washed with water followed by drying over anhydrous sodium sulfate. The removal of solvent obtained the crude product that was directly used in next step. Sodium borohydride (1.26 g, 33.34 mmol, 2.0 equiv.) was added to the solution of the crude product in absolute ethanol (17 mL). The resulting solution was stirred at room temperature for 60 h. The reaction was quenched with water and extracted with dichloromethane. The combined organic layers were washed with brine solution, dried over anhydrous sodium sulfate and concentrated under reduced pressure to obtain the crude product (3.97 g, 15.55 mmol) as a yellow liquid. The crude mixture from previous step was dissolved in dichloromethane (31 mL). The reaction mixture was cooled at 0 °C and then pyridine (1.76 mL, 21.85 mmol, 1.4 equiv.) followed by tosyl chloride (3.85 g, 20.2 mmol, 1.3 equiv.) was added to the solution. The resulting reaction mixture was warmed up to room temperature and stirred at room temperature for 12 h. The reaction mixture was quenched with aq. $NaHCO_3$ solution, extracted with dichloromethane, dried over anhydrous sodium sulfate and concentrated under reduced pressure. The crude mixture was purified by flash column chromatography through silica (eluent = petroleum ether/ethyl acetate) to afford pure *N*-(3,4-dimethoxybenzyl)-*N*-(2,2-dimethoxyethyl)-4-methylbenzenesulfonamide (**S19**, 4.85 g, 11.84 mmol, 71%) as a white solid. **^{1}H NMR (500 MHz, $CDCl_3$)** δ (ppm) = 7.73 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 1H), 7.72 – 7.76 (m, 2H), 6.66 (d, *J* = 1.3 Hz, 1H), 4.40 (s, 2H), 4.35 (t, *J* = 5.3 Hz, 1H), 3.84 (s, 3H), 3.84 (s, 3H), 3.25 (s, 6H), 3.20 (d, *J* = 5.3 Hz, 2H), 2.42 (s, 3H).; **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 149.2, 148.7, 143.4, 137.8, 129.8, 128.6, 127.3, 121.3, 111.5, 110.8, 104.1, 56.0, 55.8, 54.7, 52.4, 48.5, 21.6. The spectroscopic data obtained were in agreement with the reported data for the compound **S19**.[41]

In a round bottom flask equipped with a Teflon-coated stirring bar and condenser, 6N HCl (5.5 mL) was added dropwise to the solution of *N*-(3,4-dimethoxybenzyl)-*N*-(2,2-dimethoxyethyl)-4-methylbenzenesulfonamide (4.85 g, 11.84 mmol, 1.0 equiv.) in 1,4-dioxane (70 mL). The resulting mixture was heated at 95 °C for 24 h. After cooling down to room temperature, the reaction was quenched with water and extracted with diethyl ether followed by dichloromethane. The aqueous layer was treated with 10% NaOH solution until pH > 10. Then, the aqueous layer was extracted with diethyl ether followed by dichloromethane. The combined organic layers were washed with brine, dried over anhydrous sodium sulfate and concentrated under reduced pressure. The crude mixture was purified by flash column chromatography through silica (eluent = ethyl acetate) to afford pure 6,7-dimethoxyisoquinoline (**1x**, 1.7 g, 8.98 mmol, 76%) as a white solid. **^{1}H NMR (500 MHz, $CDCl_3$)** δ (ppm) = 9.05 (s, 1H), 8.37 (d, *J* = 5.7 Hz, 1H), 7.53 (d, *J* = 5.7 Hz, 1H), 7.21 (s, 1H), 7.07 (s, 1H), 4.04 (s, 3H), 4.03 (s, 3H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 153.2, 150.4, 149.5, 141.3, 132.7, 124.7, 119.4, 105.3, 104.5, 56.1, 56.1. The spectroscopic data obtained were in agreement with the reported data for the compound **1x**.[41]

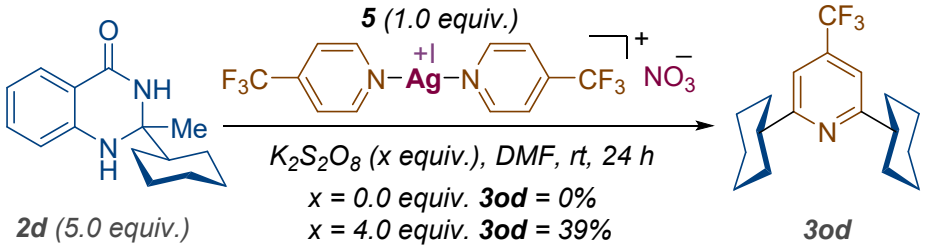


1x (1.0 equiv) **2k** (2.5 equiv) **3xk**, 53%

In a heat gun-dried Schlenk tube equipped with a Teflon-coated stirring bar, *N*-Heteroarene **1** (0.2 mmol, 1.0 equiv.), 2,3-Dihydroquinazolinone substrate (**2**) (0.5 mmol, 2.5 equiv.), $AgNO_3$ (0.04 mmol, 0.2 equiv.) and $K_2S_2O_8$ (0.4 mmol, 2.0 equiv.) were dissolved in dry DMF (2 m) under inert atmosphere. The reaction mixture was stirred at room temperature for 24 h under dark condition. The reaction was quenched by the addition of brine solution (2 mL) and then extracted with ethyl acetate (3×5 mL). The combined organic layers were washed once again with water (5 ml), followed by brine (5 ml) and the solvents were removed under reduced pressure. The crude reaction mixture was purified by flash column chromatography through Silica gel (eluent: petroleum ether/ethyl acetate) to afford pure product **3xk** (39 mg, 0.107 mmol, 53%) as yellow oil. **^{1}H NMR (500 MHz, $CDCl_3$)** δ (ppm) = 8.39 (d, *J* = 5.6 Hz, 1H), 7.61 (s, 1H), 7.44 (d, *J* = 5.6 Hz, 1H), 7.04 (s, 1H), 7.78 – 7.82 (m, 2H), 6.72 (d, *J* = 8.3 Hz, 1H), 3.99 (s, 3H), 3.88 (s, 3H), 3.80 (s, 3H), 3.72 (s, 3H), 1.53 – 1.55 (m, 2H), 1.48 – 1.51 (m, 2H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 160.0, 152.5, 149.6, 149.0, 147.5, 140.8, 137.1, 133.7, 123.8, 119.1, 118.4, 111.0, 111.0, 105.3, 105.3, 77.4, 77.2, 76.9, 56.1, 56.0, 56.0, 56.0, 30.2, 15.3; **HRMS (ESI):** m/z calc. for ($C_{17}H_{18}ClN_4O_2^+$) $[M+H]^+$: 345.1113; found: 345.1110; **IR (ATR) (ν cm^{-1}):** 2954, 1519, 1482, 1259, 1155, 1033, 913, 866, 816.

5 Mechanistic Investigation:

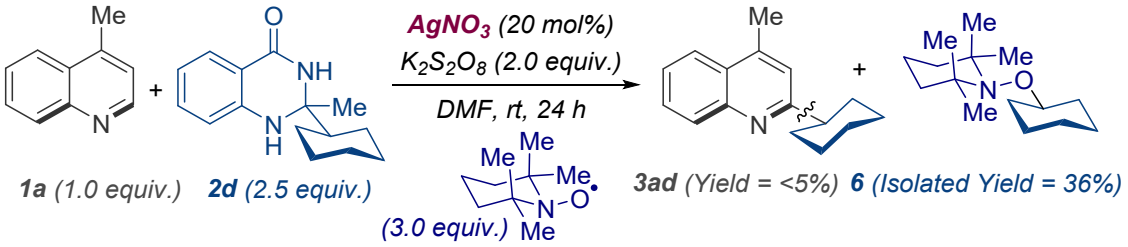
5.1 Reactions with well-defined Silver complex



Reaction without $K_2S_2O_8$: In a heat gun-dried Schlenk tube equipped with a Teflon-coated stirring bar, Bis(4-(trifluoromethyl)pyridine)silver(I) nitrate ([Ag(4-CF_3-Py)$_2$]NO_3) (**5**, 49.4 mg, 0.1 mmol, 1.0 equiv.), and 2-Cyclohexyl-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (**2d**, 122 mg, 0.5 mmol, 5.0 equiv.) were dissolved in dry DMF (1 mL) under inert atmosphere. The reaction mixture was stirred at room temperature for 24 h under dark condition. The reaction was quenched by the addition of brine solution (2 mL) followed by aq. $NaHCO_3$ solution (2 mL) and then extracted with ethyl acetate (3×5 mL). The combined organic layers were washed once again with water (5 ml), followed by brine (5 ml) and the solvents were removed under reduced pressure. No product **3od** was detected, while the reaction was performed in the absence of $K_2S_2O_8$.

Reaction with $K_2S_2O_8$ (4.0 equiv.): In a heat gun-dried Schlenk tube equipped with a Teflon-coated stirring bar, Bis(4-(trifluoromethyl)pyridine)silver(I) nitrate ([Ag(4-CF_3-Py)$_2$]NO_3) (**5**, 49.4 mg, 0.1 mmol, 1.0 equiv.), 2-Cyclohexyl-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (**2d**, 122 mg, 0.5 mmol, 5.0 equiv.), and $K_2S_2O_8$ (108 mg, 0.4 mmol, 4.0 equiv.) were dissolved in dry DMF (1 mL) under inert atmosphere. The reaction mixture was stirred at room temperature for 24 h under dark condition. The reaction was quenched by the addition of brine solution (2 mL) followed by aq. $NaHCO_3$ solution (2 mL) and then extracted with ethyl acetate (3×5 mL). The combined organic layers were washed once again with water (5 ml), followed by brine (5 ml) and the solvents were removed under reduced pressure. The purification of the crude mixture by flash column chromatography through Silica gel (eluent: petroleum ether/ethyl acetate) afforded pure product **3od** (24 mg, 0.077 mmol, 39%).

5.2 Radical Trapping Experiment with TEMPO



In a heat gun-dried Schlenk tube equipped with a Teflon-coated stirring bar, lepidine (**1a**, 0.2 mmol, 1.0 equiv.), 2-cyclohexyl-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (**2d**) (0.5 mmol, 2.5 equiv.), $AgNO_3$ (0.04 mmol, 0.2 equiv.), $K_2S_2O_8$ (0.4 mmol, 2.0 equiv.) and TEMPO (0.6 mmol, 3.0 equiv.) were dissolved in dry DMF (2 mL) under inert atmosphere. The reaction mixture was stirred at room temperature for 24 h under dark condition. The reaction was quenched by the addition of brine (2

mL) followed by aq. $NaHCO_3$ solution (2 mL) and then extracted with ethyl acetate (3×5 mL). The combined organic layers were washed once again with water (5 ml), followed by brine (5 ml) and the solvents were removed under reduced pressure. HRMS analysis of the crude reaction mixture identified 1-(cyclohexyloxy)-2,2,6,6-tetramethylpiperidine (Cyclohexyl-TEMPO) (**6**) (Figure 5).

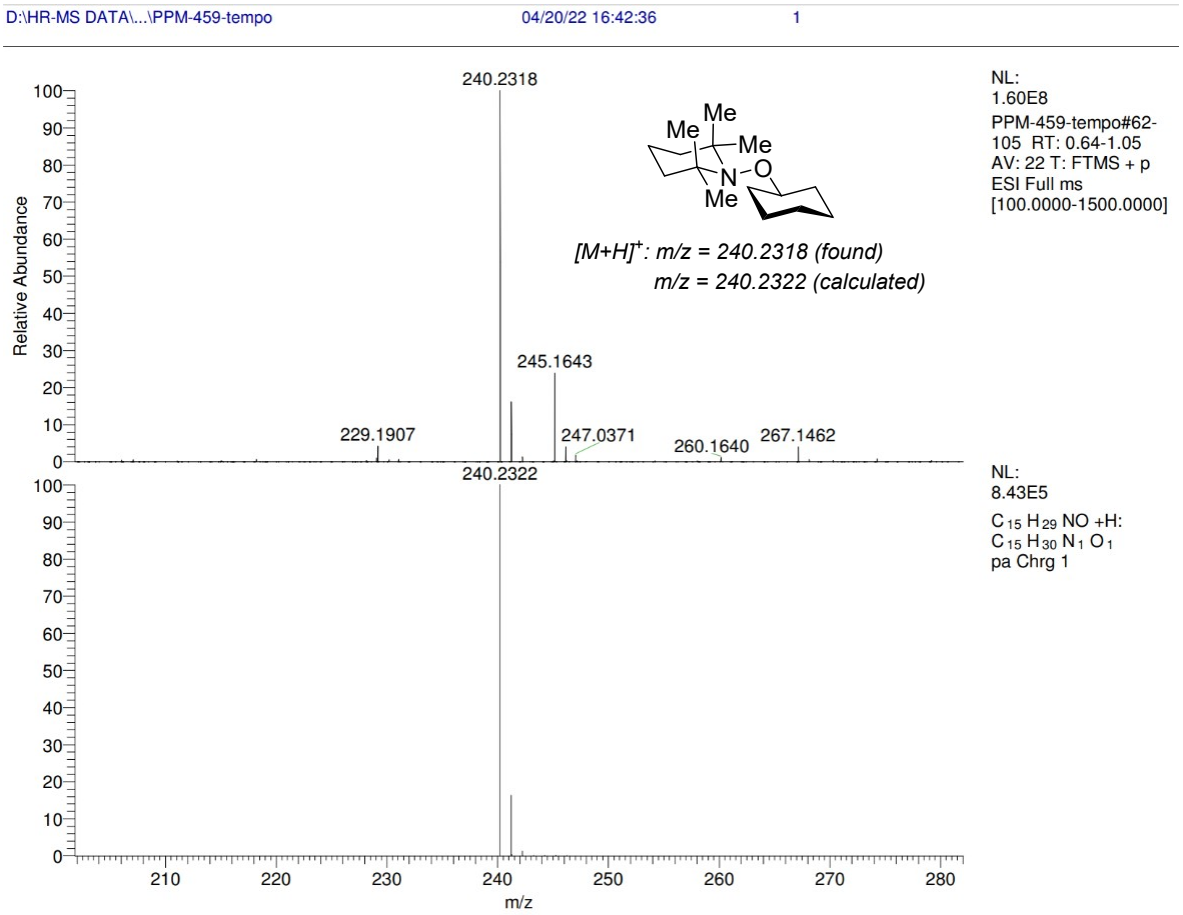
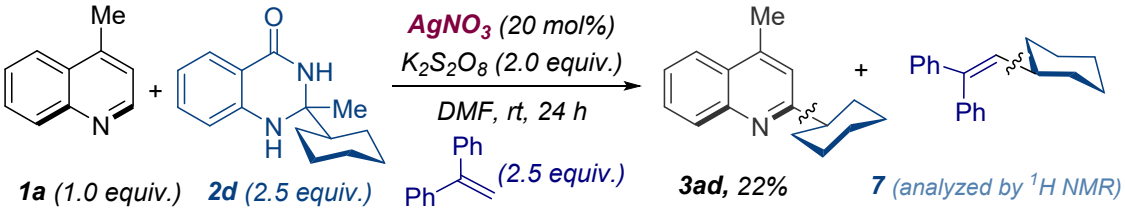


Figure S5: Detection of 1-(Cyclohexyloxy)-2,2,6,6-tetramethylpiperidine (**6**) adduct in the crude reaction mixture of radical trapping experiment using TEMPO by HRMS analysis.

The purification of the crude mixture by flash column chromatography through Silica gel (eluent: petroleum ether/ethyl acetate) afforded pure product **3ad** as colorless liquid (2 mg, 0.009 mmol, <5%) and **6** as colorless liquid (43 mg, 0.178 mmol, 36%, with respect to **2c**).

Compound 6: **^{1}H NMR (500 MHz, $CDCl_3$)** δ (ppm) = 3.55 – 3.61 (m, 1H), 2.01 – 2.06 (m, 2H), 1.71 – 1.76 (m, 2H), 1.44 – 1.53 (m, 6H), 1.10 – 1.25 (m, 18H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 81.9, 59.8, 40.4, 34.6, 33.1, 26.1, 25.2, 20.4, 17.5. The spectroscopic data obtained were in agreement with the reported data for the compound **6**.[40]

Radical Inhibition Experiment with Ethene-1,1-diyldibenzene



In a heat gun-dried Schlenk tube equipped with a Teflon-coated stirring bar, Lepidine (**1a**, 0.2 mmol, 1.0 equiv.), 2-Cyclohexyl-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (**2d**, 0.5 mmol, 2.5 equiv.), $AgNO_3$ (0.04 mmol, 0.2 equiv.), $K_2S_2O_8$ (0.4 mmol, 2.0 equiv.) and Ethene-1,1-diyldibenzene (0.5 mmol, 2.5 equiv.) were dissolved in dry DMF (2 mL) under inert atmosphere. The reaction mixture was stirred at room temperature for 24 h under dark condition. The reaction was quenched by the addition of brine (2 mL) followed by aq. $NaHCO_3$ solution (2 mL) and then extracted with ethyl acetate (3×5 mL). The combined organic layers were washed once again with water (5 ml), followed by brine (5 ml) and the solvents were removed under reduced pressure. ^{1}H NMR analysis of the crude reaction mixture identified (2-cyclohexylethene-1,1-diyl)dibenzene (**7**) (Scheme S6).[41] The purification of the crude mixture by flash column chromatography through Silica gel (eluent: petroleum ether/ethyl acetate) afforded pure product **3ad** as colorless liquid (8 mg, 0.043 mmol, 22%).

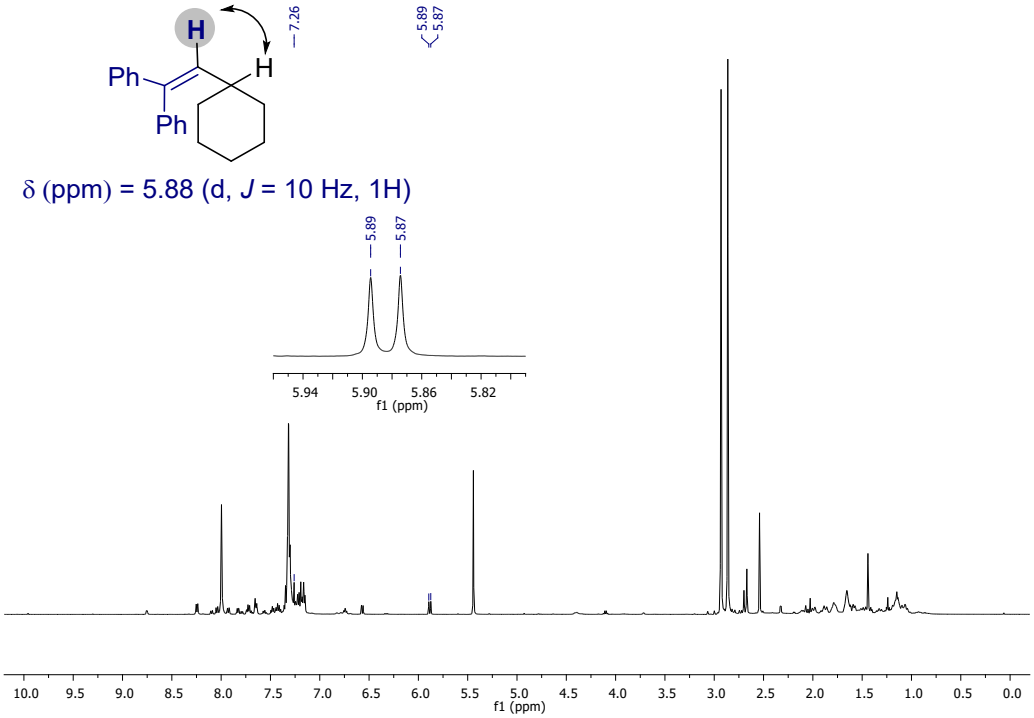
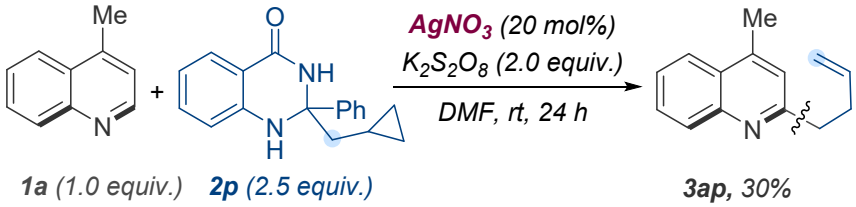


Figure S6: Detection of (2-cyclohexylethene-1,1-diyl)dibenzene (**7**) in the crude reaction mixture of radical inhibition experiment using ethene-1,1-diyldibenzene by ^{1}H NMR analysis.

5.3 Radical Clock Experiment



In a heat gun-dried Schlenk tube equipped with a Teflon-coated stirring bar, lepidine (**1a**, 13.5 µL, 0.1 mmol, 1.0 equiv.), 2-(cyclopropylmethyl)-2-phenyl-2,3-dihydroquinazolin-4(1*H*)-one (**2p**, 70 mg, 0.25 mmol, 2.5 equiv.), $AgNO_3$ (3.4 mg, 0.02 mmol, 0.2 equiv.), and $K_2S_2O_8$ (54 mg, 0.2 mmol, 2.0 equiv.) were dissolved in dry DMF (1 m) under inert atmosphere. The reaction mixture was stirred at room temperature for 24 h under dark condition. The reaction was quenched by the addition of brine solution (1 mL) followed by aq. $NaHCO_3$ solution (1 mL) and then extracted with ethyl acetate

(3×5 mL). The combined organic layers were washed once again with water (5 ml), followed by brine (5 ml) and the solvents were removed under reduced pressure. The purification of the crude mixture by flash column chromatography through Silica gel (eluent: petroleum ether/ethyl acetate) afforded pure product 2-(but-3-en-1-yl)-4-methylquinoline (**3ap**, 6 mg, 0.03 mmol, 30%).

Compound 3ao: ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 8.04 (d, *J* = 8.4 Hz, 1H), 7.96 (d, *J* = 8.3 Hz, 1H), 7.66 – 7.69 (m, 1H), 7.49 – 7.52 (m, 1H), 7.15 (s, 1H), 5.93 (ddt, *J* = 16.8, 10.2, 6.6 Hz, 1H), 5.09 (dd, *J* = 17.1, 1.6 Hz, 1H), 4.99 (d, *J* = 10.2 Hz, 1H), 3.02 (dd, *J* = 8.8, 7.1 Hz, 2H), 2.68 (s, 3H), 2.58 (dt, *J* = 7.7, 6.7 Hz, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ (ppm) = 161.9, 147.9, 144.5, 138.0, 129.5, 129.2, 127.0, 125.7, 123.8, 122.3, 115.3, 38.6, 34.0, 18.9. The spectroscopic data obtained were in agreement with the reported data for the compound **3ao**.[20]

5.4 Measurement of Cyclic Voltammetry of Dihydroquinazolin-4(1*H*)-ones (2a, 2q, 2r, & 2s)

On an electrochemical workstation from CH Instruments, Inc., cyclic voltammetry was carried out. Glassy carbon working electrode, graphite rod auxiliary electrode, and Ag wire pseudo-reference electrode were used to record CV. Before any experiment, the chemical was completely degassed by Ar gas bubbling and sonicated with 0.05 M NBu_4PF_6/DMF supporting electrolyte solution. As an internal benchmark, Ferrocene was introduced, and all potential was indicated by V vs. Fc/Fc+.

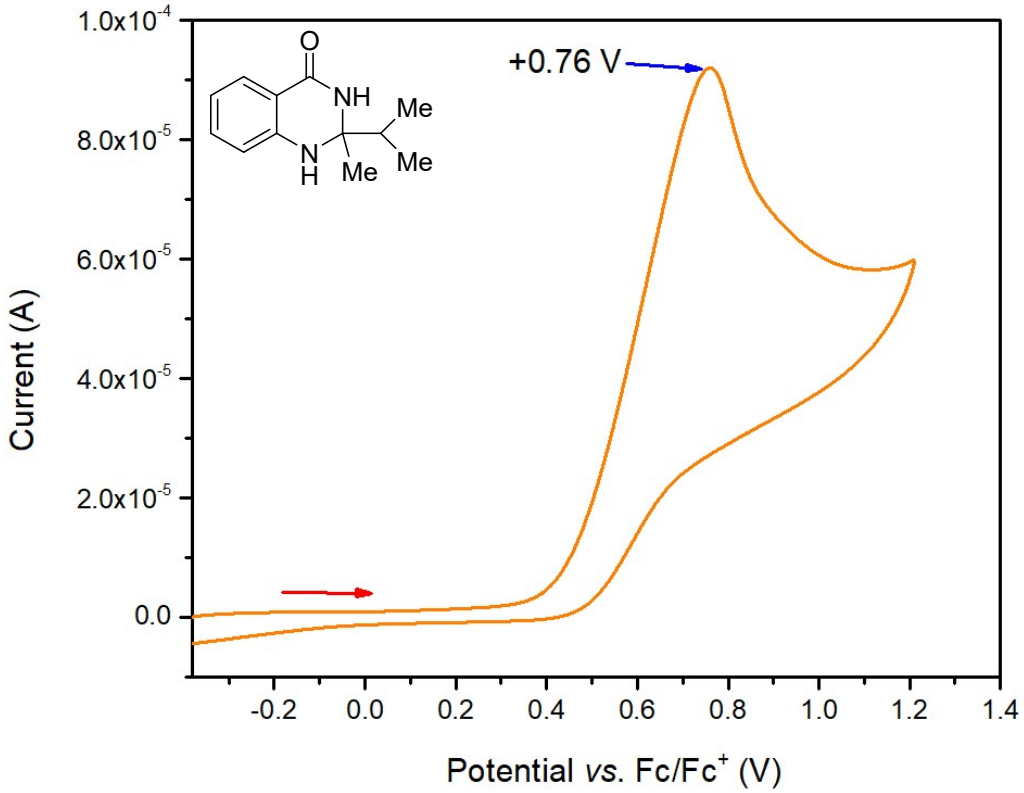


Figure S7: Cyclic Voltammogram of 2-isopropyl-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (**2a**) in DMF at a scan rate of 0.1 mV.s^{-1}.

Compound 2a: E^{ox} = + 0.76 V vs Fc^+/Fc

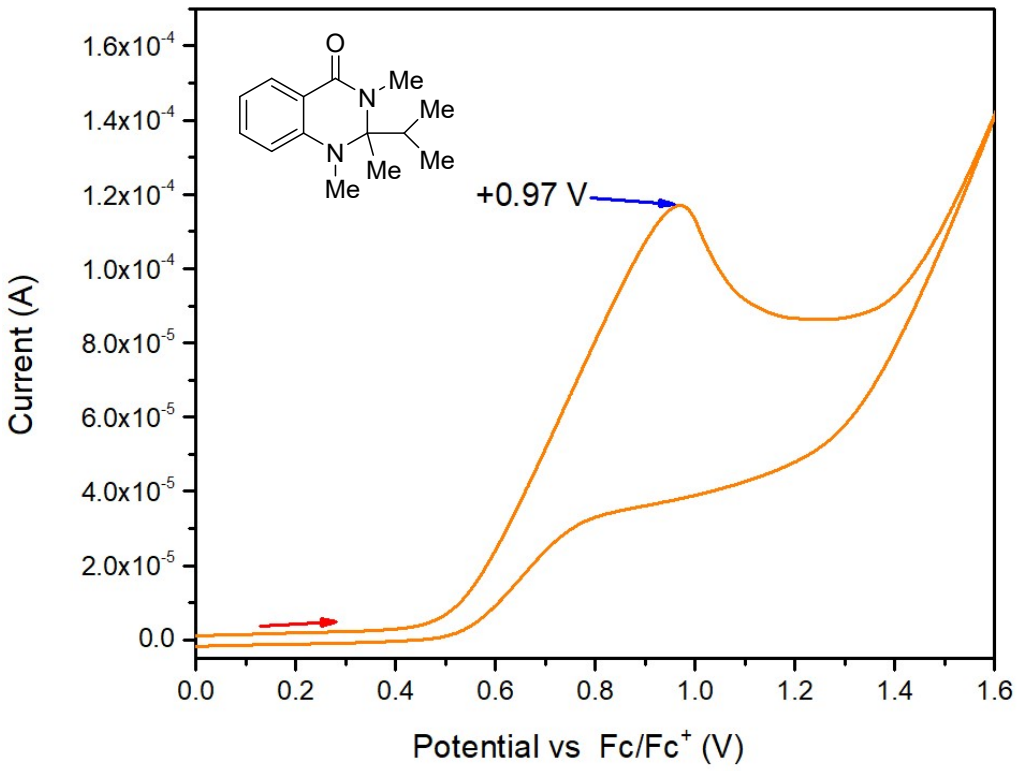
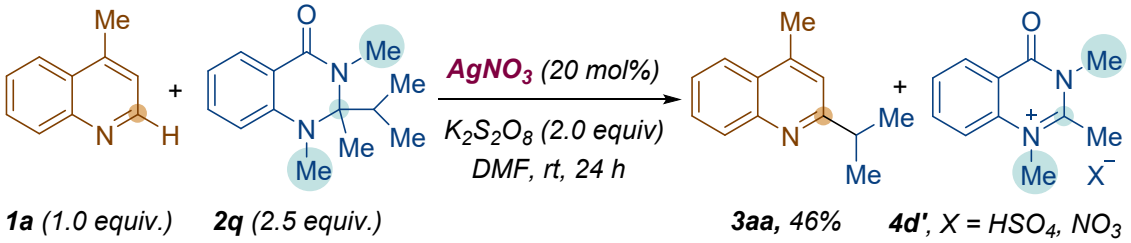


Figure S8: Cyclic Voltammogram of 3-butyl-2-isopropyl-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (**2q**) in DMF at a scan rate of 0.1 $mV.s^{-1}$.

Compound 2q: E^{ox} = + 0.97 V vs Fc^{+}/Fc

5.5 Reaction with *N*-Substituted Dihydroquinazolin-4(1*H*)-one

Reaction with 3-butyl-2-isopropyl-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (2q)



In a heat gun-dried Schlenk tube equipped with a Teflon-coated stirring bar, Lepidine (**1a**, 0.2 mmol,1.0 equiv.), 2-isopropyl-1,2,3-trimethyl-2,3-dihydroquinazolin-4(1*H*)-one (**2q**) (0.5 mmol, 2.5 equiv.), $AgNO_3$ (0.04 mmol, 0.2 equiv.), and $K_2S_2O_8$ (0.4 mmol, 2.0 equiv.) were dissolved in dry DMF (2 mL) under inert atmosphere. The reaction mixture was stirred at room temperature for 24 h under dark condition. The reaction was quenched by the addition of brine solution (2 mL) followed by aq. $NaHCO_3$ solution (2 mL) and then extracted with ethyl acetate (3×5 mL). The combined organic layers were washed once again with water (5 ml), followed by brine (5 ml) and the solvents were removed under reduced pressure. The purification of the crude mixture by flash column chromatography through Silica gel (eluent: petroleum ether/ethyl acetate) afforded pure product **3aa** (17 mg, 0.092 mmol, 46%) and **4d'** was detected by HRMS analysis of crude reaction mixture (Figure S9).

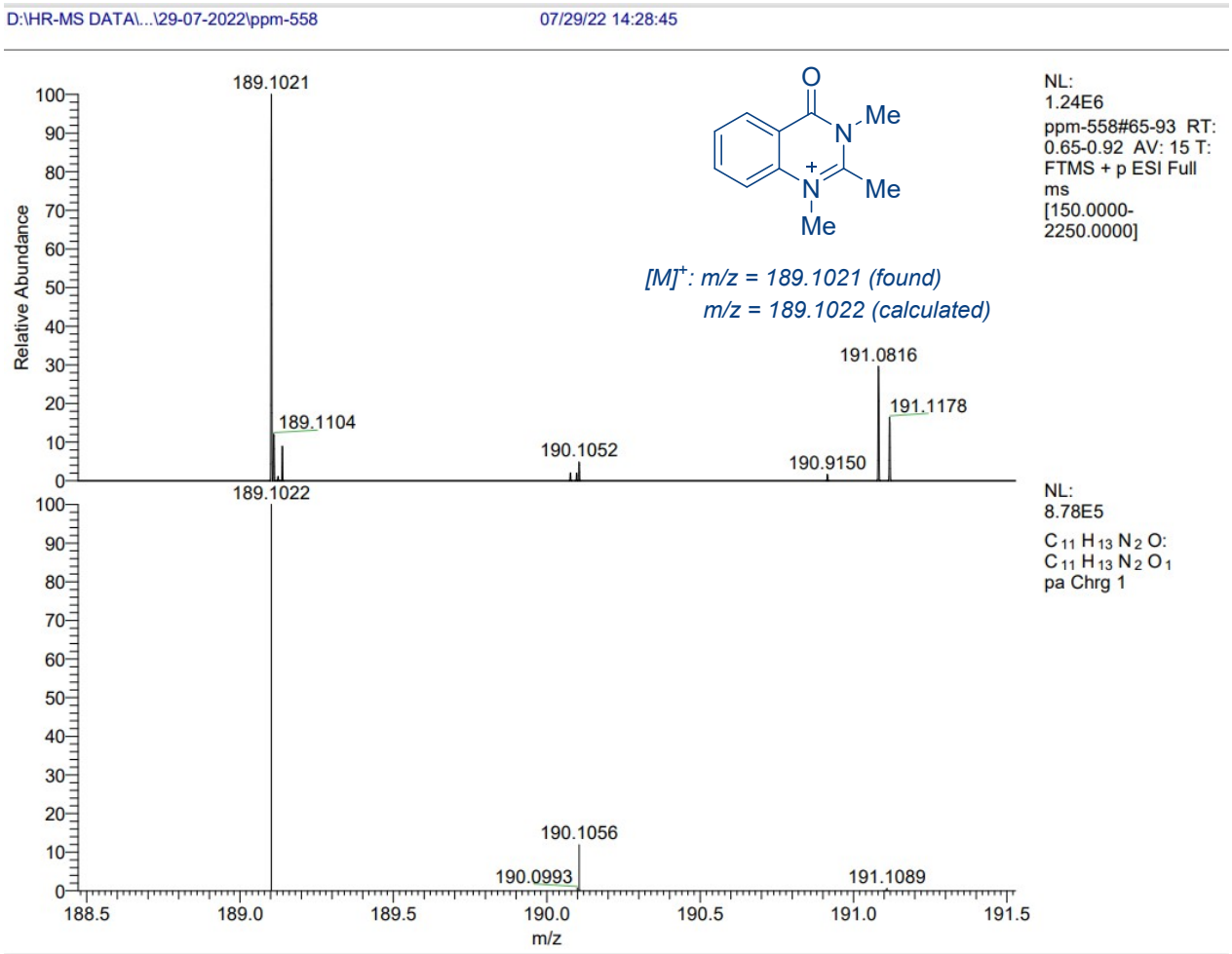


Figure S9: Detection of byproduct (**4d'**) in the crude reaction mixture of by HRMS analysis.

References

[1] H. Maekawa, Y. Yamamoto, H. Shimada, K. Y. I. Nishiguchi, *Tetrahedron Lett.* **2004**, *45*, 3869–3872.

[2] A. N. Baumann, F. Schüppel, M. Eisold, A. Kreppel, R. de Vivie-Riedle, D. Didier, *J. Org. Chem.* **2018**, *83*, 4905−4921.

[3] M. S. Davey, R. Malde, R. C. Mykura, A. T. Baker, T. E. Taher, C. S. Le Duff, B. E. Willcox**,** Y. Mehellou, *J. Med. Chem.* **2018**, *61*, 2111–2117.

[4] X. Y. Lv, R. Abrams, R. Martin, *Nat. Commun.* **2022**, doi: 10.1038/s41467-022-29984-0.

[5] W. Luo, Y. Fang, L. Zhang, T. Xu, Y. Liu, Y. Li, X. Jin, J. Bao, X. Wu, Z. Zhang, *Eur. J. Org. Chem*. **2020**, *2020*, 1778-1781.

[6] S. -C. Lee, L. -Y. Li, Z. -N. Tsai, Y. -H. Lee, Y. -T. Tsao, P.-G. Huang, C. -K. Cheng, H. -B. Lin, T. -W. Chen, C. -H. Yang, C. -C. Chiu, H.-H. Liao, *Org. Lett.* **2022**, *24*, 85–89.

[7] M. Kamlar, R. Reiberger, M. Nigríni, I. Císařová, J. Veselý, *Beilstein J. Org. Chem.* **2021,** *17,* 2433–2440.

[8] L. Wang, X.-F. Wang, M.-W. Xue, S.-R. Duan, T. Li, Z.-Z. Yu, D. -L. Zhang, *Chin. J. Struc. Chem.* **2022**, *41*, 55-61.

[9] K. Revathy, A. Lalitha, *J. Iran Chem. Soc.* **2015**, *12*, 2045-2049.

[10] N. Kausar, I. Roy, D. Chattopadhyay, A. R. Das, *RSC Adv.* **2016**, *6*, 22320-22330.

[11] Y. Liu, B. Shi, Z. Liu, R. Gao, C. Huang, H. Alhumade, S. Wang, X. Qi**,** A. Lei**,** *J. Am. Chem. Soc.* **2021**, *143*, 20863–20872.

[12] T. Gonec, P. Bobal, J. Sujan, M. Pesko, J. Guo, K. Kralova, L. Pavlacka, L. Vesely, E. Kreckova, J. Kos, A. Coffey, P. Kollar, A. Imramovsky, L. Placek , J. Jampilek, *Molecules* **2012**, *17*, 613-644.

[13] N. Jha, R. P. Singh, P. Saxena, M. Kapur**,** *Org. Lett.* **2021**, *22*, 8694–8698.

[14] M. P. Huestis, *J. Org. Chem.* **2016**, *24*, 12545–12552.

[15] G.-L. Gao, C. Yang, W. Xia, *Chem. Commun.* **2017**, *53*, 1041-1044.

[16] T. Hartman, R. Cibulka, *Org. Lett.* **2016**, *15*, 3710–3713.

[17] V. V. Menon, E. Fazal, Y. S. Mary, C. Y. Panicker, S. Armakovic, S. J. Armakovic, S. Nagarajan, C. V. Alsenoy, *J. Mol. Struct.* **2017**, *1127*, 124-137.

[18] R. A. Garza-Sanchez, A. Tlahuext-Aca, G. Tavakoli, F. Glorius**,** *ACS Catal.* **2017***, 7,* 4057−4061.

[19] J. D. Galloway, D. N. Mai, R. D. Baxter, *J. Org. Chem.* **2019**, *84*, 12131-12137.

[20] X. –Y. Zhang, W.-Z. Weng, H. Liang, H. Yang, B. Zhang, *Org. Lett.* **2018**, *20*, 4686-4690.

[21] G. Xu, L. Wang, M. Li, M. Tao, W. Zhang *Green Chem.* **2017,** *19***,** 5818-5830.

[22] T. McCalluma, L. Barriault, *Chem. Sci.* **2016,** *7*, 4754-4758.

[23] S. Zhong, G. -J. Deng, Z. Dai, H. Huang, *Org. Chem. Front.* **2021**, *8*, 4419-4425.

[24] Z. Li, X. Weng, S. Xia, J. Jin, *Org. Lett.* **2019**, *11*, 4259-4265.

[25] G. Deng, C. -J. Li, *Org. Lett.* **2009**, *11*, 1171-1174.

[26] J. C. Lewis, R. R. Bergman, J. A. Ellman, *J. Am. Chem. Soc.* **2007**, *129*, 5332-5333.

[27] Y. Liu, B. Shi, Z. Liu, R. Gao, C. Huang, H Alhumade, S. Wang, X. Qi**,** A. Lei**,** *J. Am. Chem. Soc.* **2021**, *143*, 20863–20872.

[28] X. Shao, X. Wu, C. Zhu, *Org. Lett.* **2020**, *22*, 7450-7454.

[29] C. Huang, J.-H. Wang, J. Qiao, X.-W. Fan, B. Chen, C.-H. Tung, L.-Z. Wu, *J. Org. Chem.* **2019**, *84*, 12904–12912.

[30] C. Yu, X. Guo, Z. Xi, M. Muzzio, Z. Yin, B. Shen, J. Li, C. T. Seto, S. Sun, *J. Am. Chem. Soc.* **2017**, *139*, 5712–5715.

[31] P.-Y. Xin, H.-Y. Niu, G.-R. Qu, R.-F. Ding, H.-M. Guo, *Chem. Commun.* **2012**, *48*, 6717-6719.

[32] L. Liu, N. Pan, W. Sheng, L. Su, L. Liu, J. Dong, Y. Zhou, S.-F. Yin *Adv. Synth. Catal.* **2019***, 361,* 4126-4132.

[33] F. Rammal, D. Gao, S. Boujnah, A. −C. Gaumont, A. A. Hussein, S. Lakhdar, *Org. Lett.* **2020**, 22, 7671–7675.

[34] G. –X. Li, C. A. Morales-Rivera, Y. Wang, F. Gao, G. He, P. Liu, G. Chen, *Chem. Sci.* **2016**, *7*, 6407-6412.

[35] X.-L. Lyu, S.-S. Huang, H.-J. Song, Y.-X. Liu, Q.-M. Wang *Org. Lett.* **2019**, *21*, 5728–5732.

[36] C. -Y. Huang, J. Li, C.-J. Li, *Nat. Commun.* **2021**, *12*, 4010.

[37] C. -Y. Huang, J. Li, W. Liu, C.-J. Li, *Chem. Sci.* **2019**, *10*, 5018-5024.

[38] A. J. A. Watson, A. C. Maxwell, J. M. J. Williams, *Org. Biomol. Chem.* **2012**, *10*, 240-243.

[39] A. Metzger, M. A. Schade, P. Knochel, *Org. Lett.* **2008**, *10*, 1107-1110.

[40] S. Sumino, I. Ryu, *Org. Lett.* **2016**, *18*, 52-55.

[41] S. Jin, G. C. Haug, V. T. Nguyen, C. F.-Hansen, H. D. Arman, O. V. Larionov**,** *ACS Catal.* **2019**, *9*, 9764–9774.

7 NMR Spectra

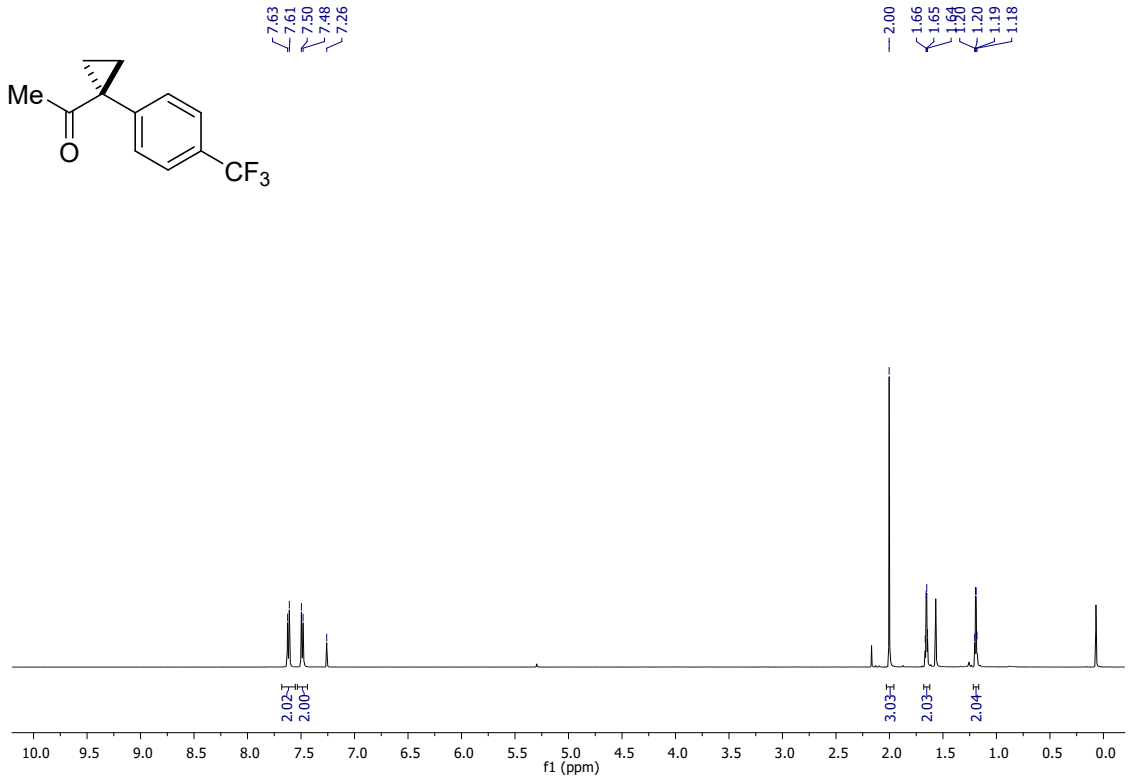


Figure S10: ^{1}H NMR spectrum of **S12** (500 MHz, $CDCl_3$)

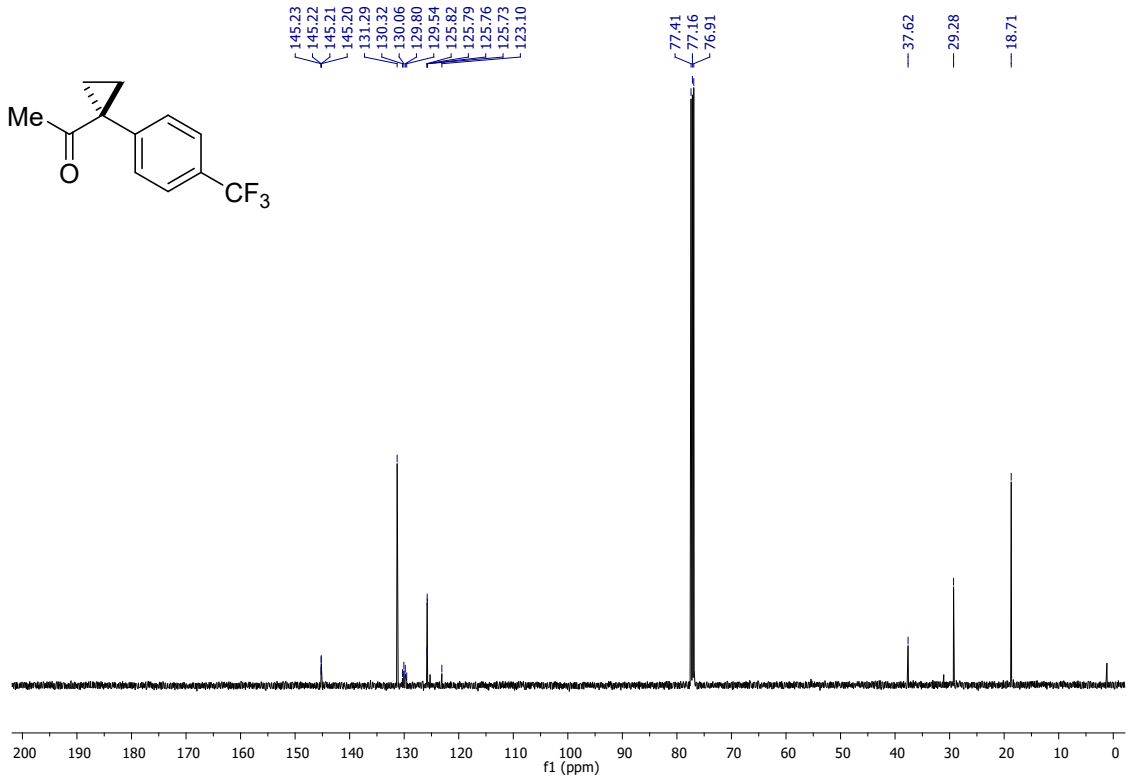


Figure S11: $^{13}C\{^{1}H\}$ NMR spectrum of **S12** (126 MHz, $CDCl_3$)

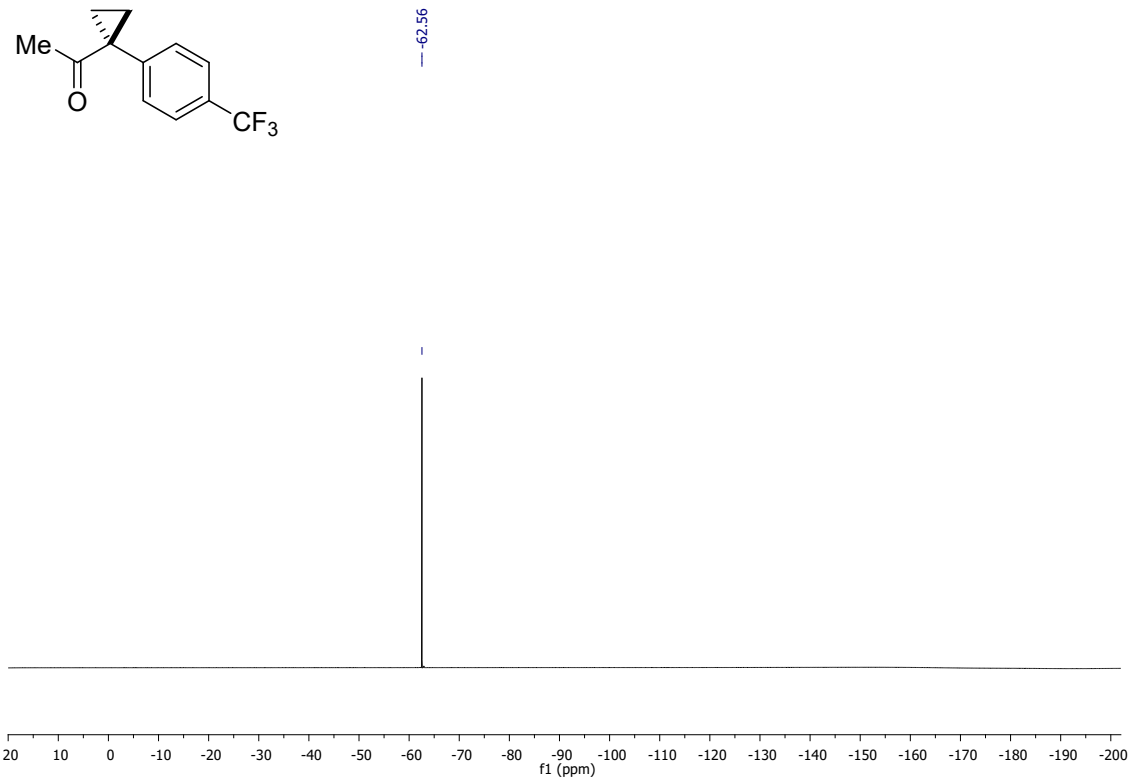


Figure S12: ^{19}F NMR spectrum of **S12** (471 MHz, $CDCl_3$)

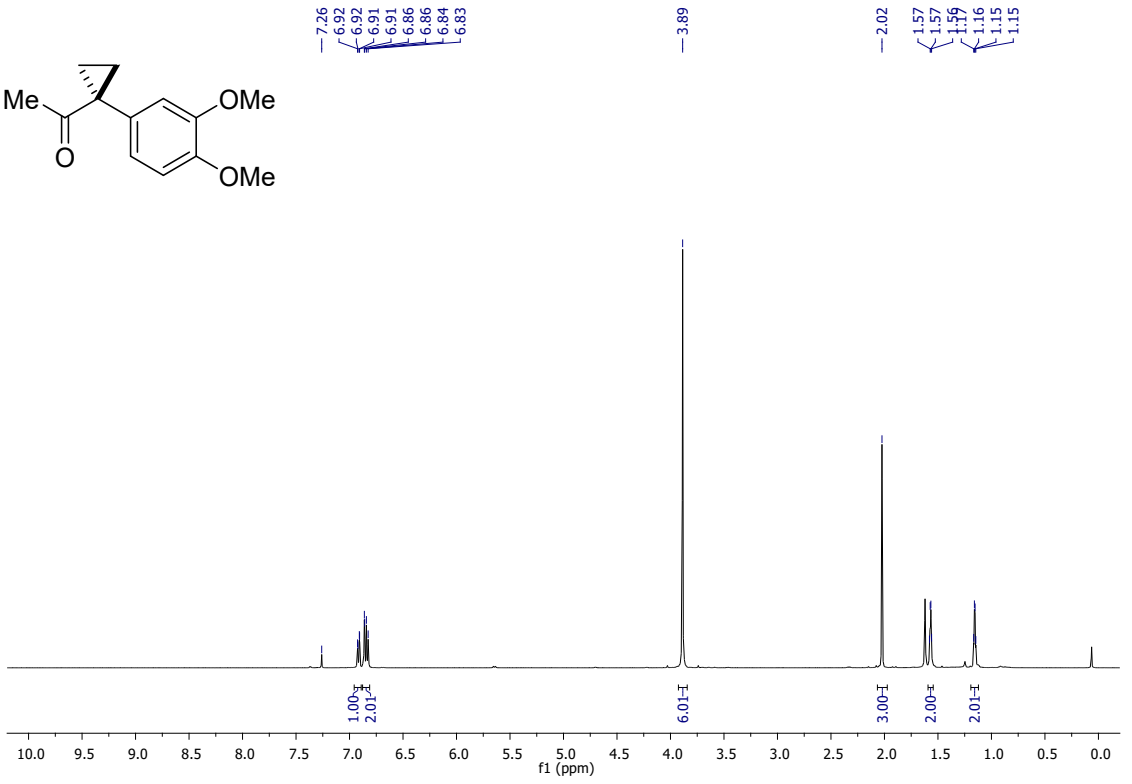


Figure S13: ^{1}H NMR spectrum of **S13** (500 MHz, $CDCl_3$)

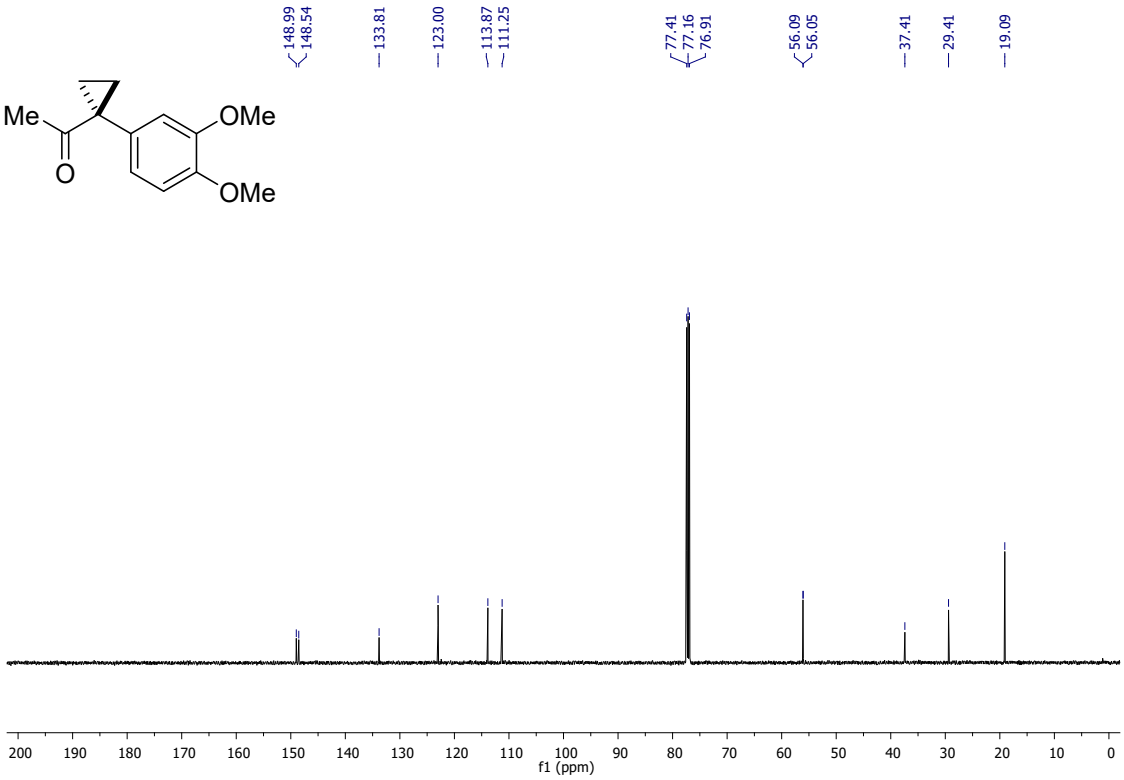


Figure S14: $^{13}C\{^{1}H\}$ NMR spectrum of **S13** (126 MHz, $CDCl_3$)

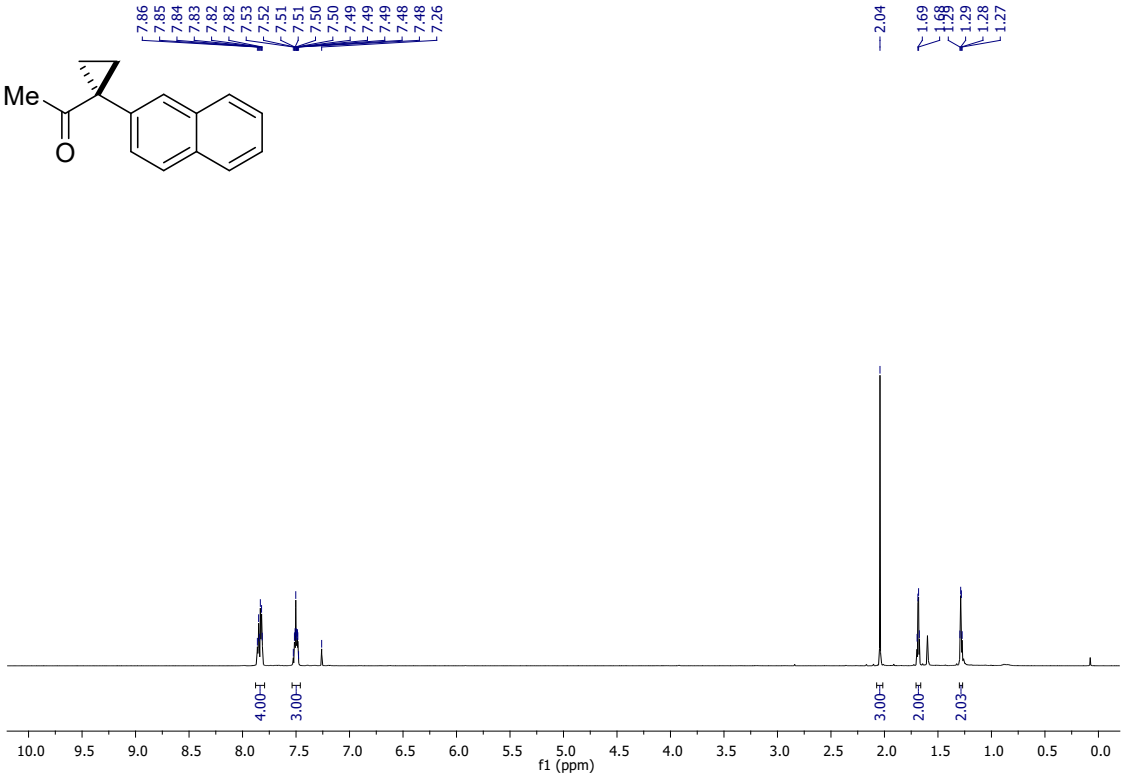


Figure S15: ^{1}H NMR spectrum of **S14** (500 MHz, $CDCl_3$)

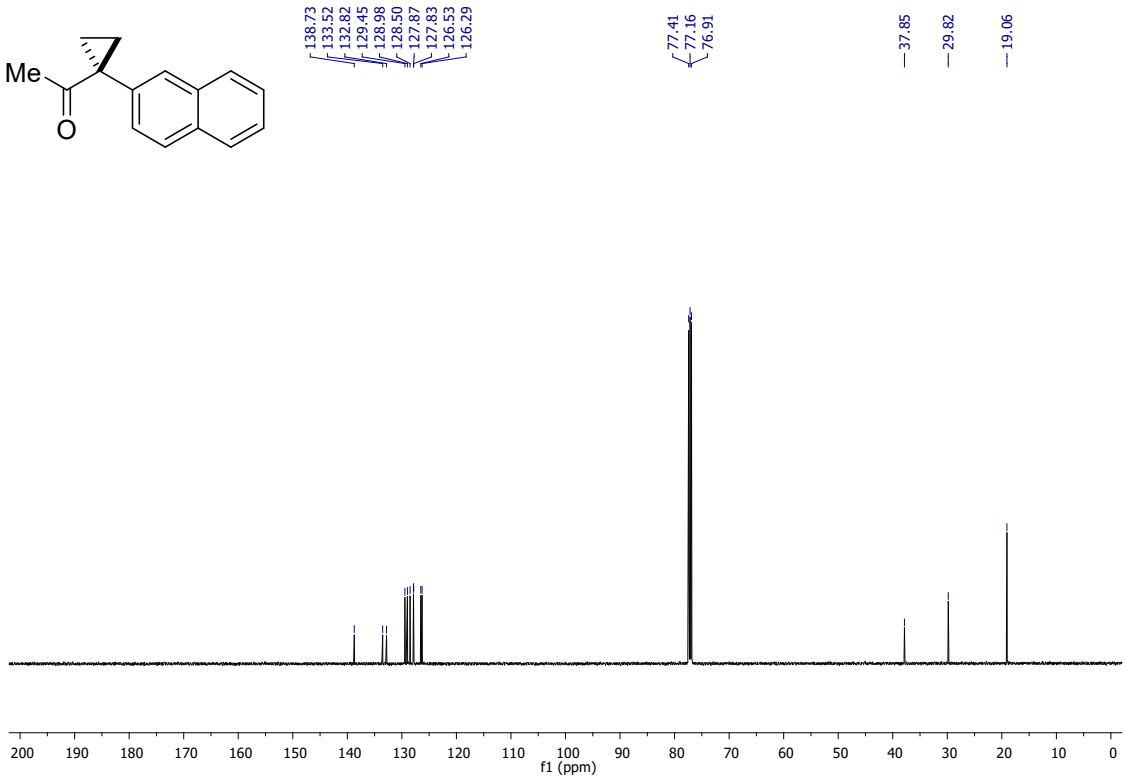


Figure S16: $^{13}C\{^{1}H\}$ NMR spectrum of **S14** (126 MHz, $CDCl_3$)

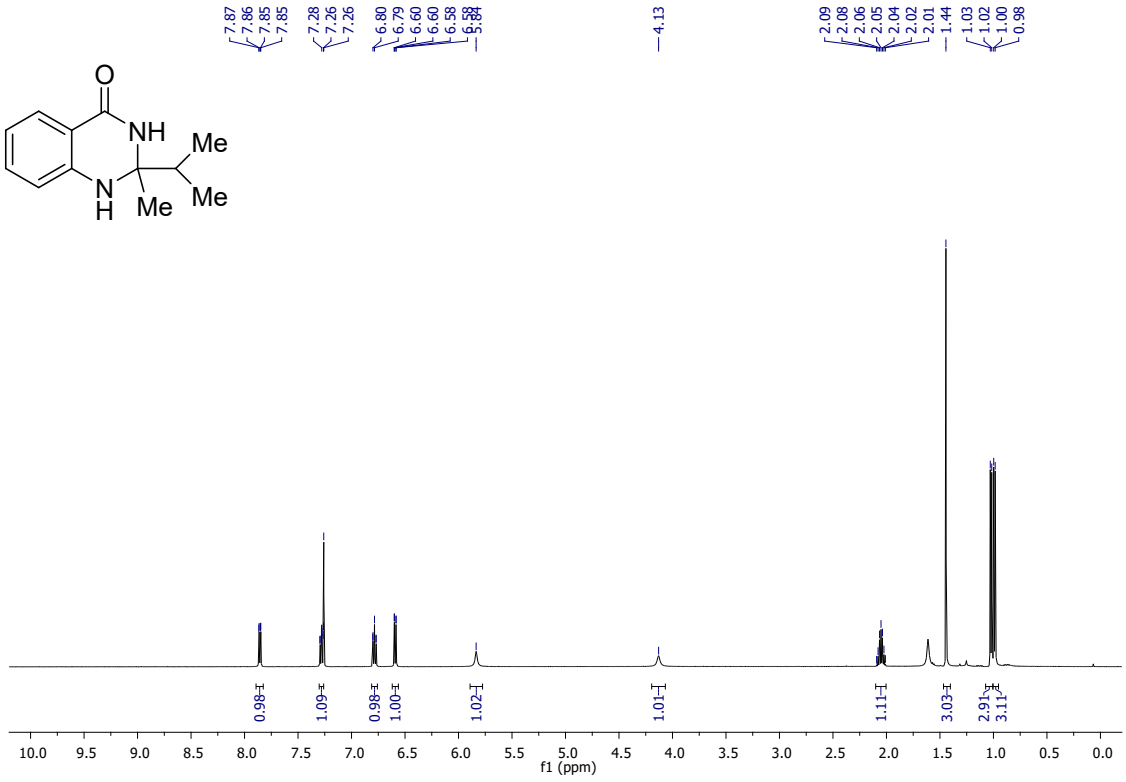


Figure S17: ^{1}H NMR spectrum of **2a** (500 MHz, $CDCl_3$)

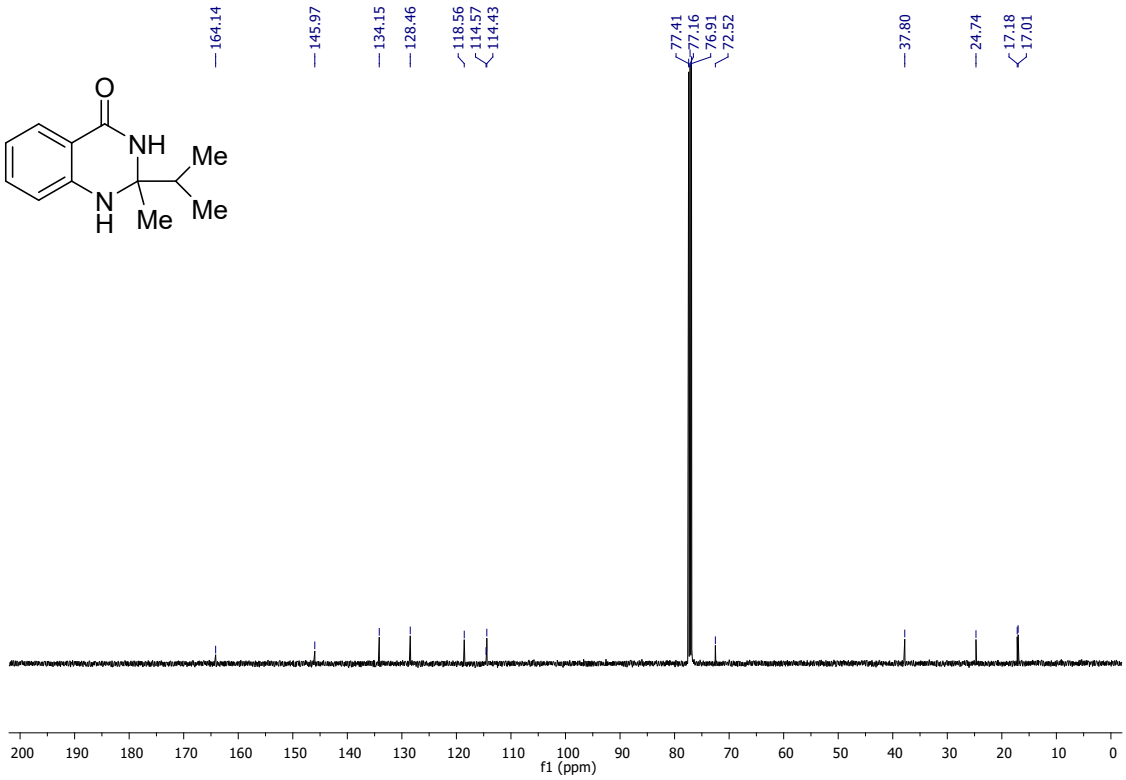


Figure S18: $^{13}C\{^{1}H\}$ NMR spectrum of **2a** (126 MHz, $CDCl_3$)

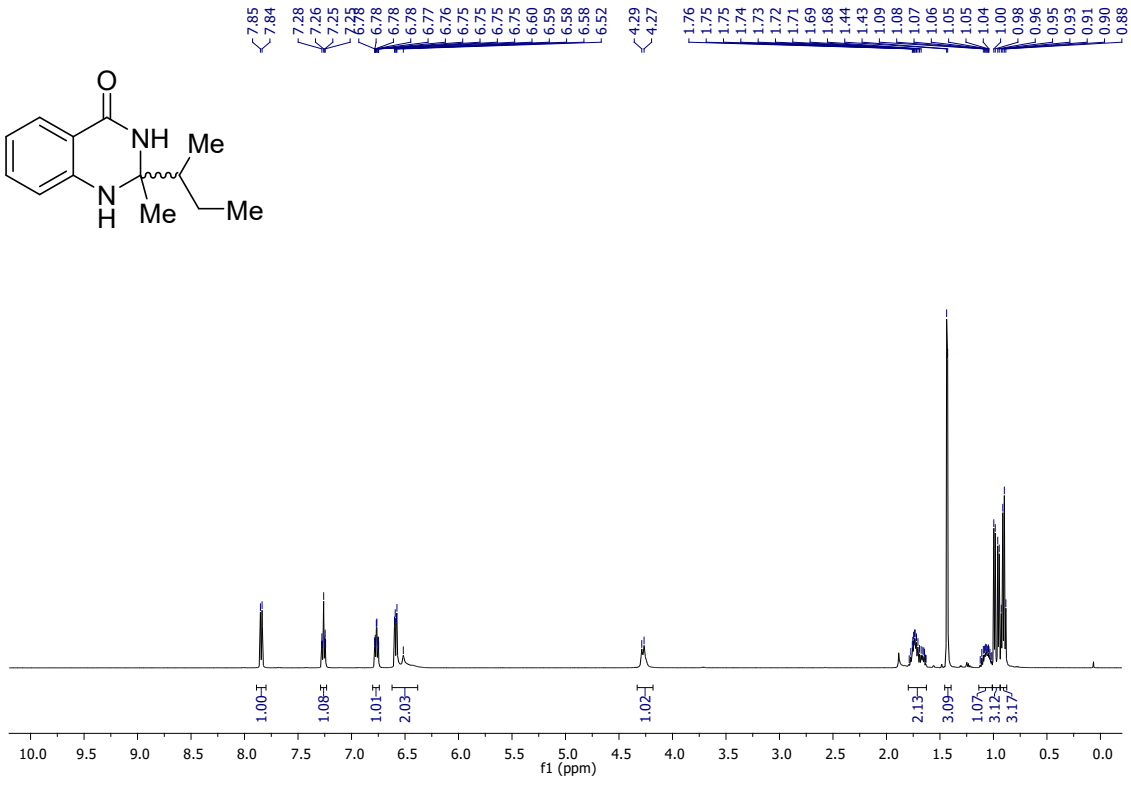


Figure S19: ^{1}H NMR spectrum of **2b** (500 MHz, $CDCl_3$)

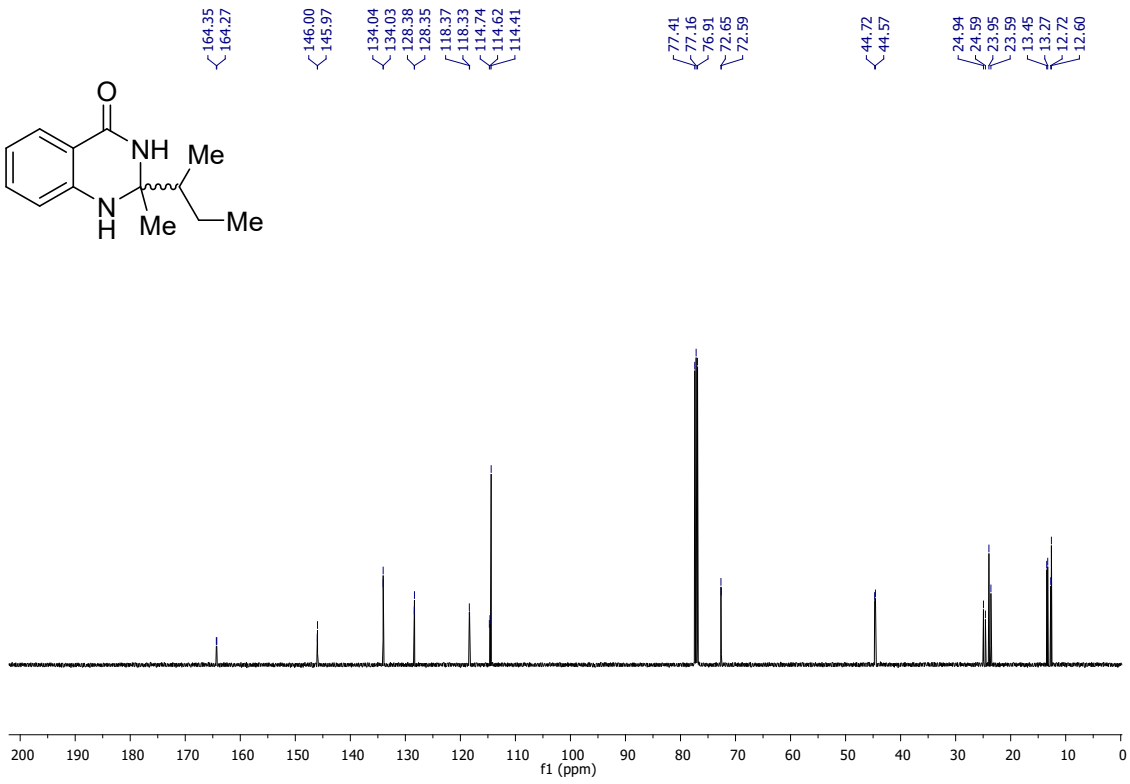


Figure S20: $^{13}C\{^{1}H\}$ NMR spectrum of **2b** (126 MHz, $CDCl_3$)

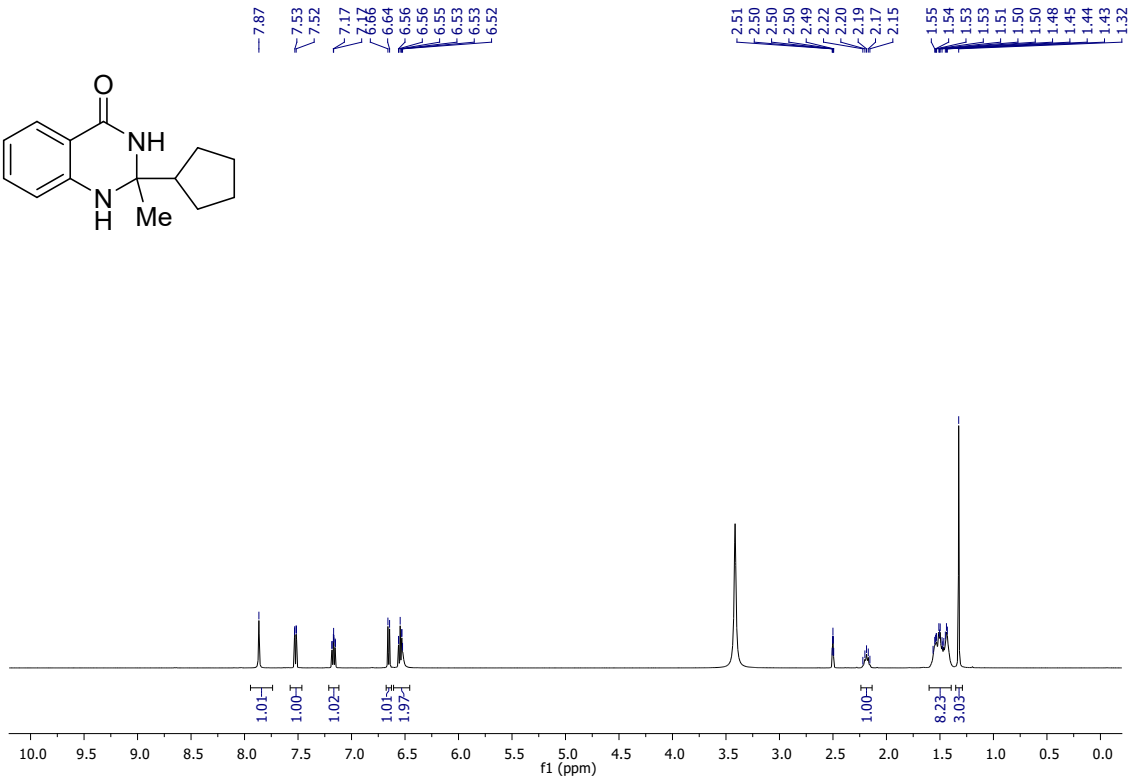


Figure S21: ^{1}H NMR spectrum of **2c** (500 MHz, DMSO-d6)

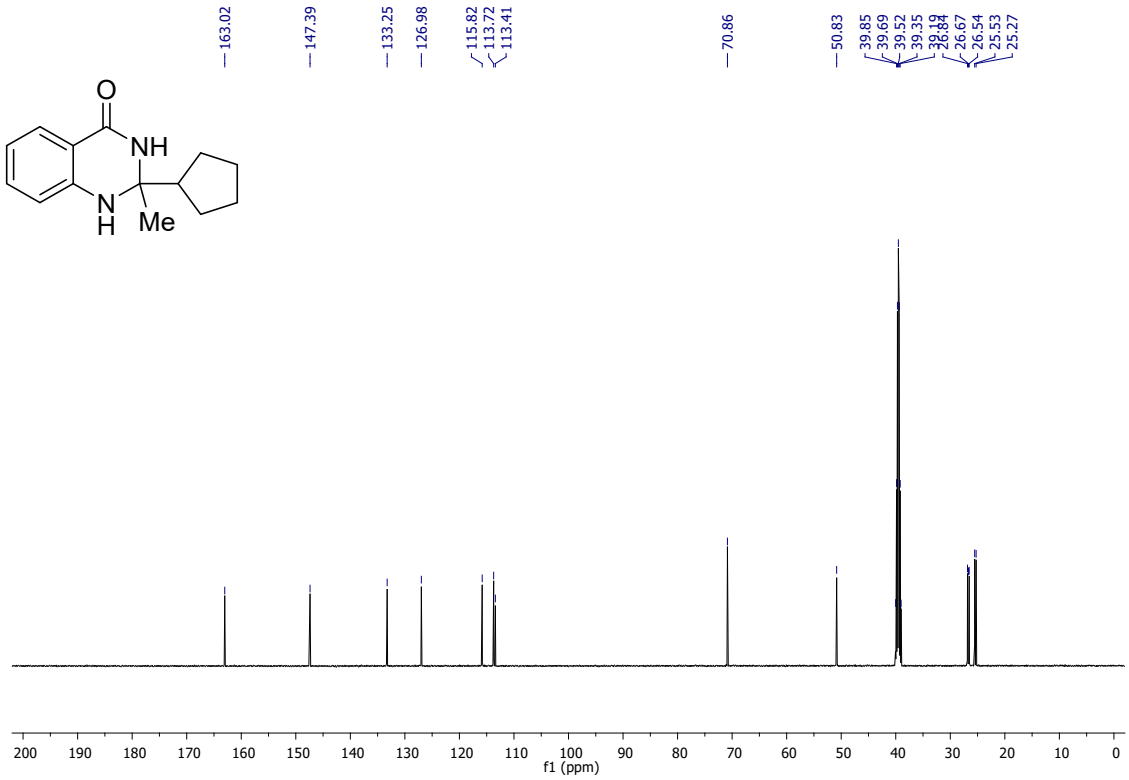


Figure S22: $^{13}C\{^{1}H\}$ NMR spectrum of **2c** (126 MHz, DMSO-d_6)

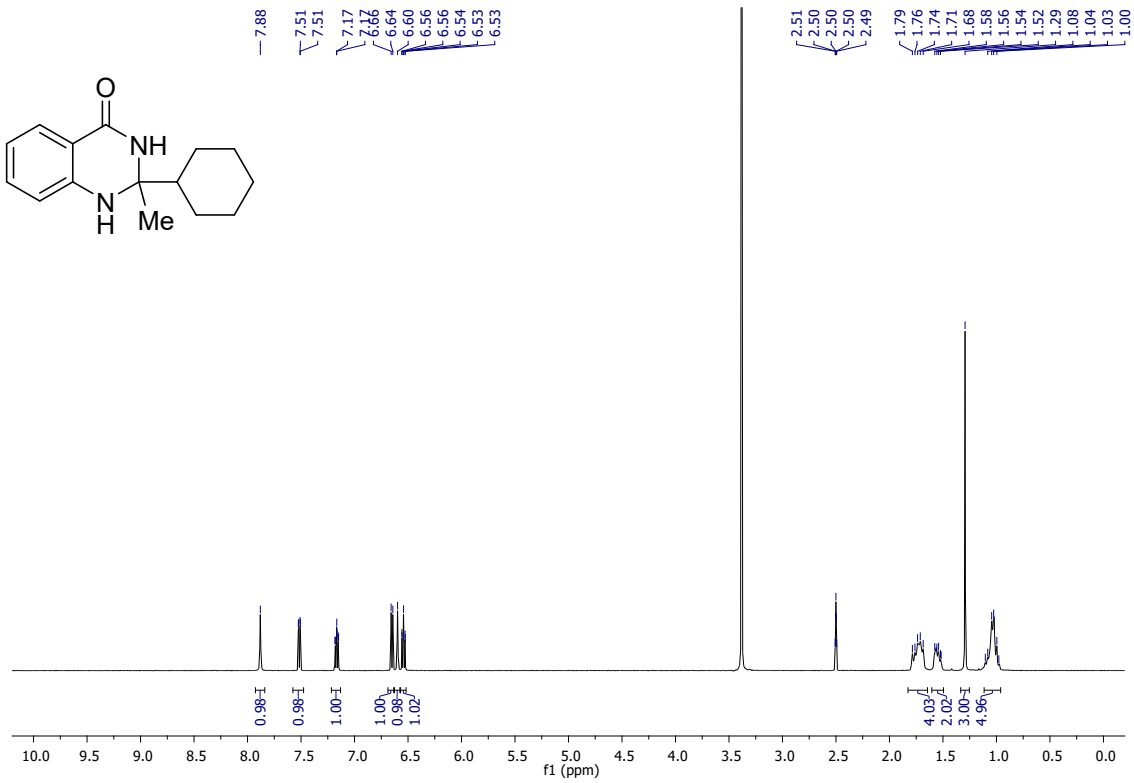


Figure S23: ^{1}H NMR spectrum of **2d** (500 MHz, DMSO-d6)

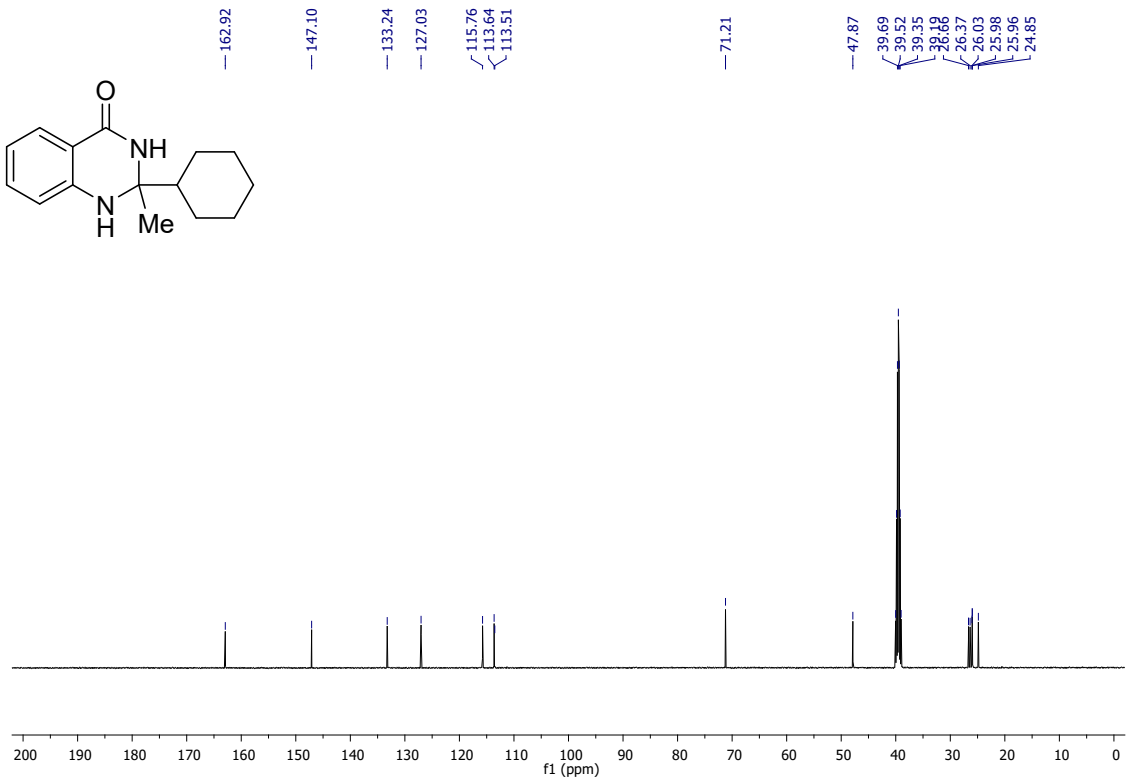


Figure S24: $^{13}C\{^{1}H\}$ NMR spectrum of **2d** (126 MHz, DMSO-d_6)

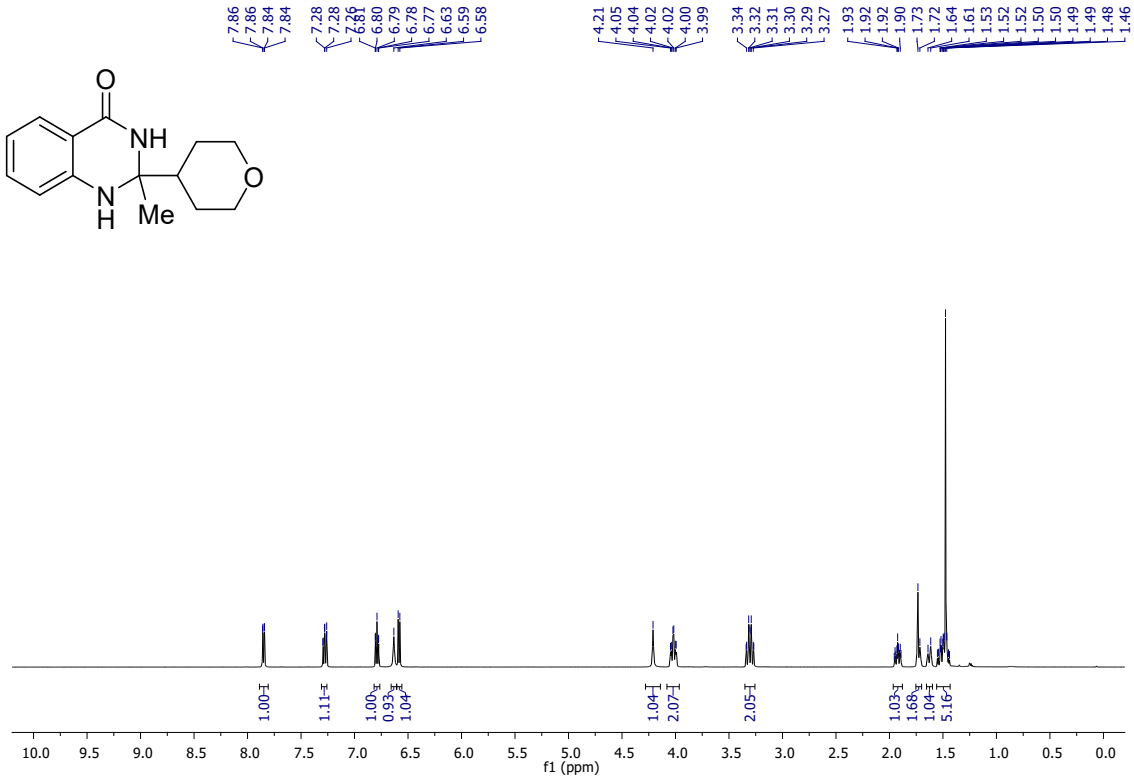


Figure S25: ^{1}H NMR spectrum of **2e** (500 MHz, $CDCl_3$)

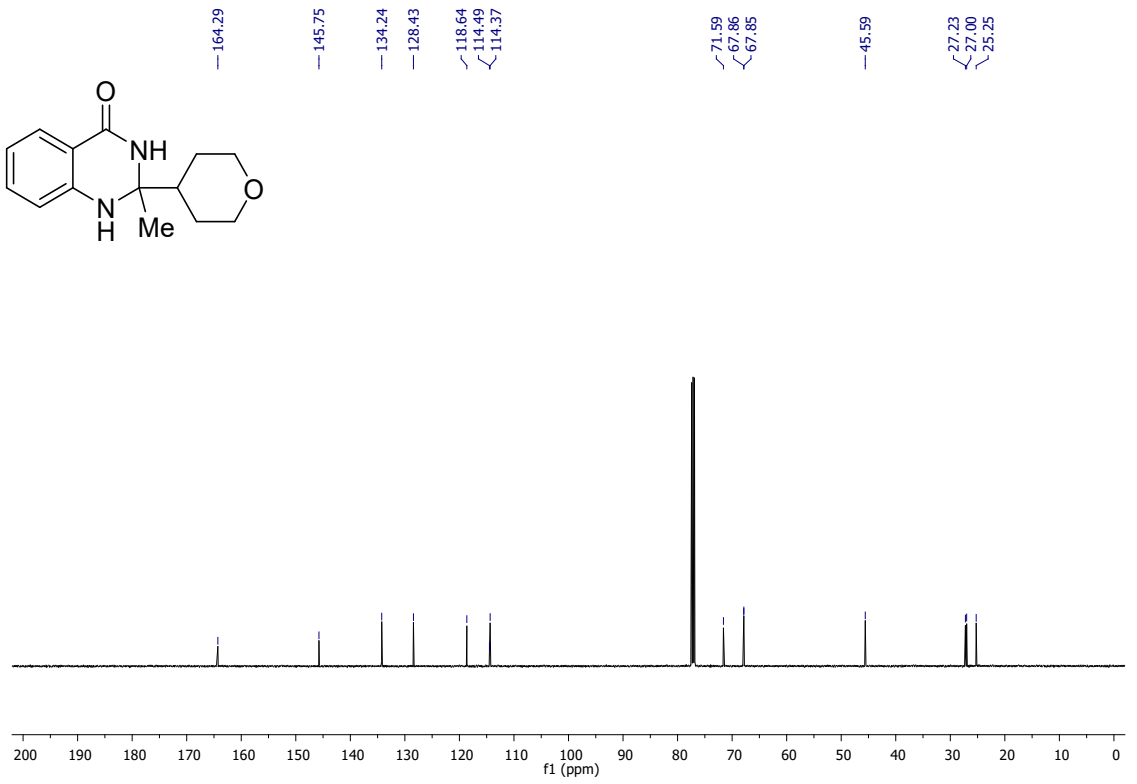


Figure S26: $^{13}C\{^{1}H\}$ NMR spectrum of **2e** (126 MHz, $CDCl_3$)

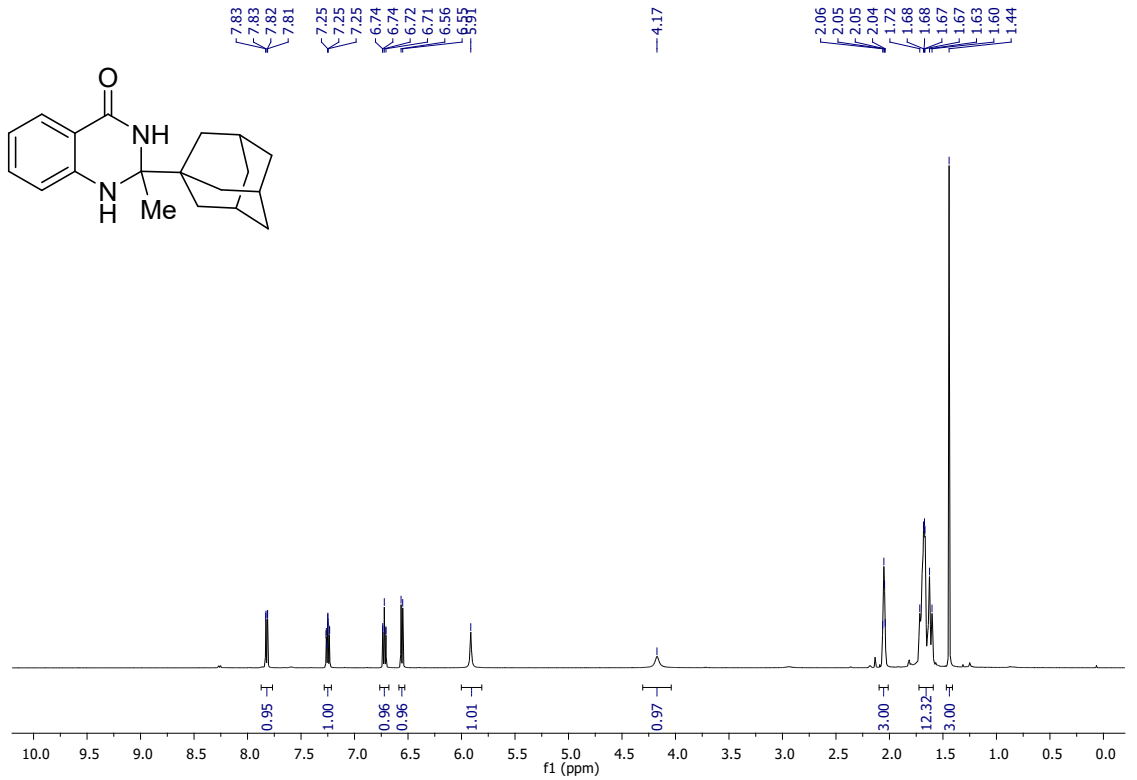


Figure S27: ^{1}H NMR spectrum of **2f** (500 MHz, $CDCl_3$)

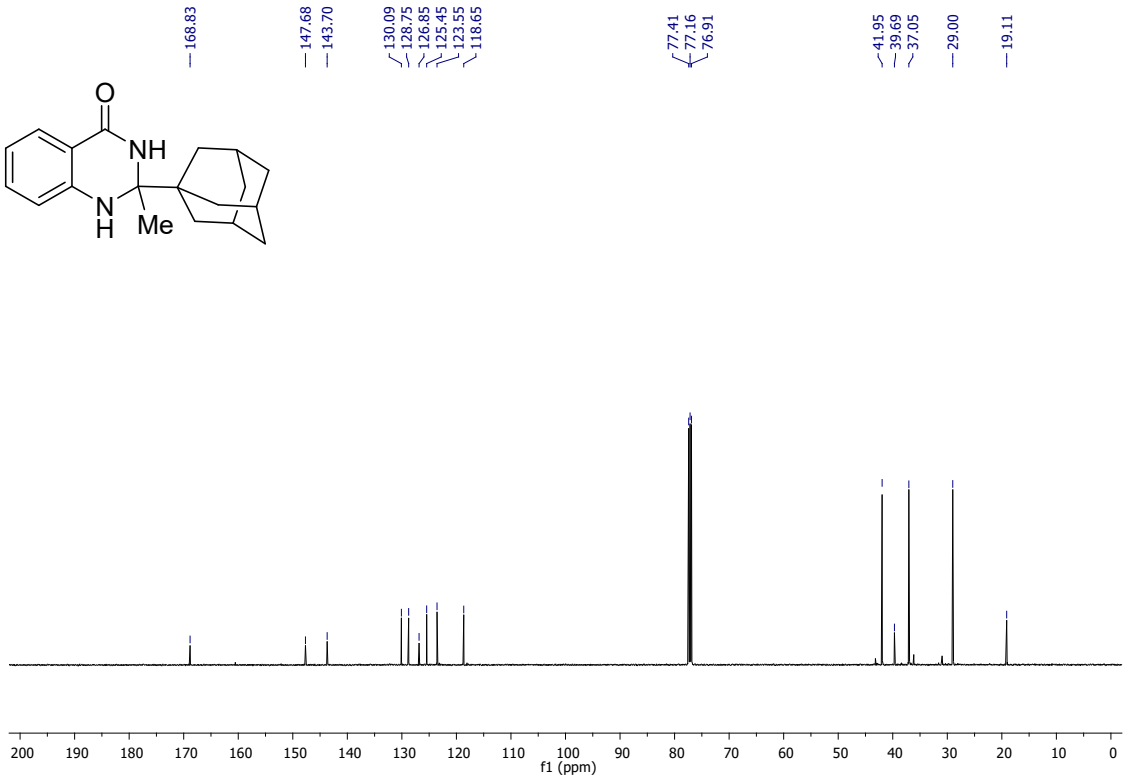


Figure S28: $^{13}C\{^{1}H\}$ NMR spectrum of **2f** (126 MHz, $CDCl_3$)

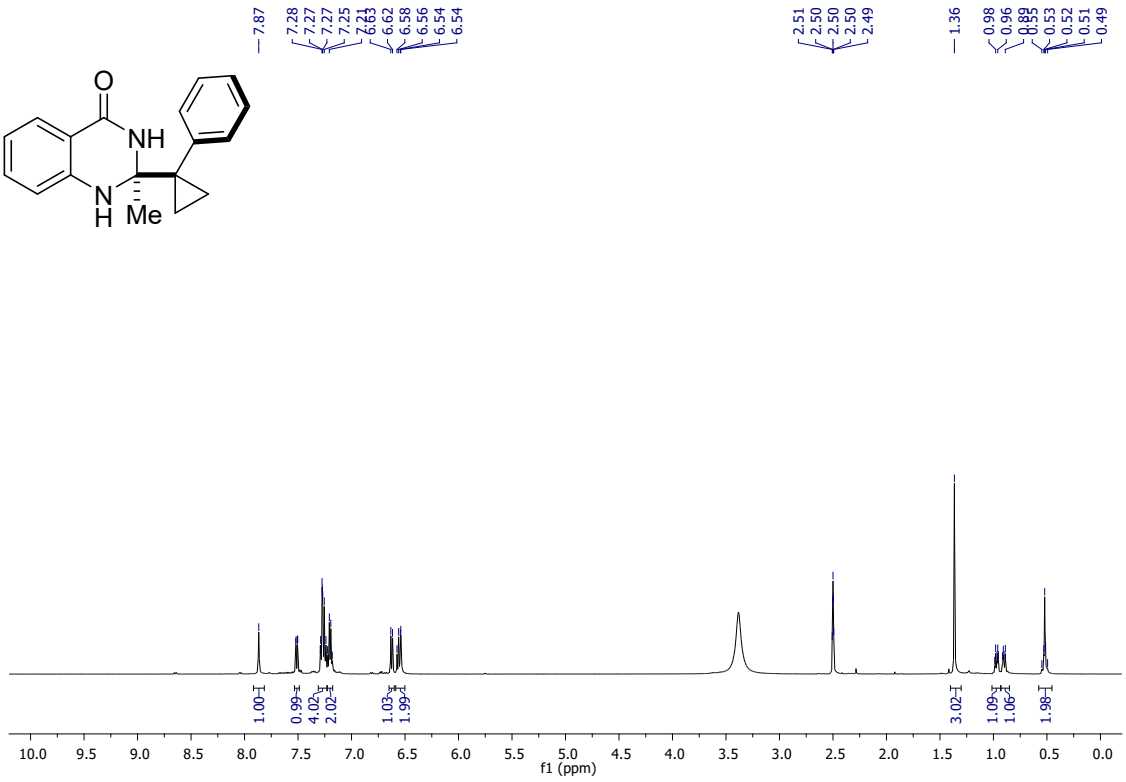


Figure 29: ^{1}H NMR spectrum of **2h** (500 MHz, DMSO-d6)

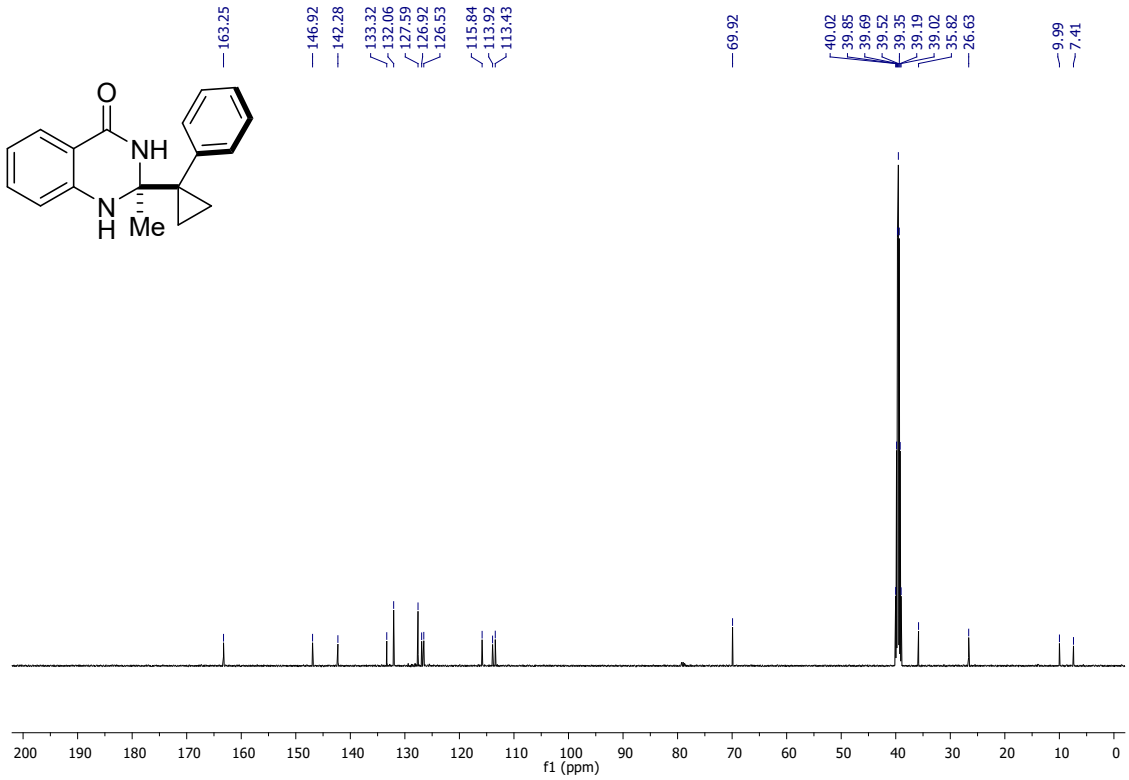


Figure S30: $^{13}C\{^{1}H\}$ NMR spectrum of **2h** (126 MHz, DMSO-d_6)

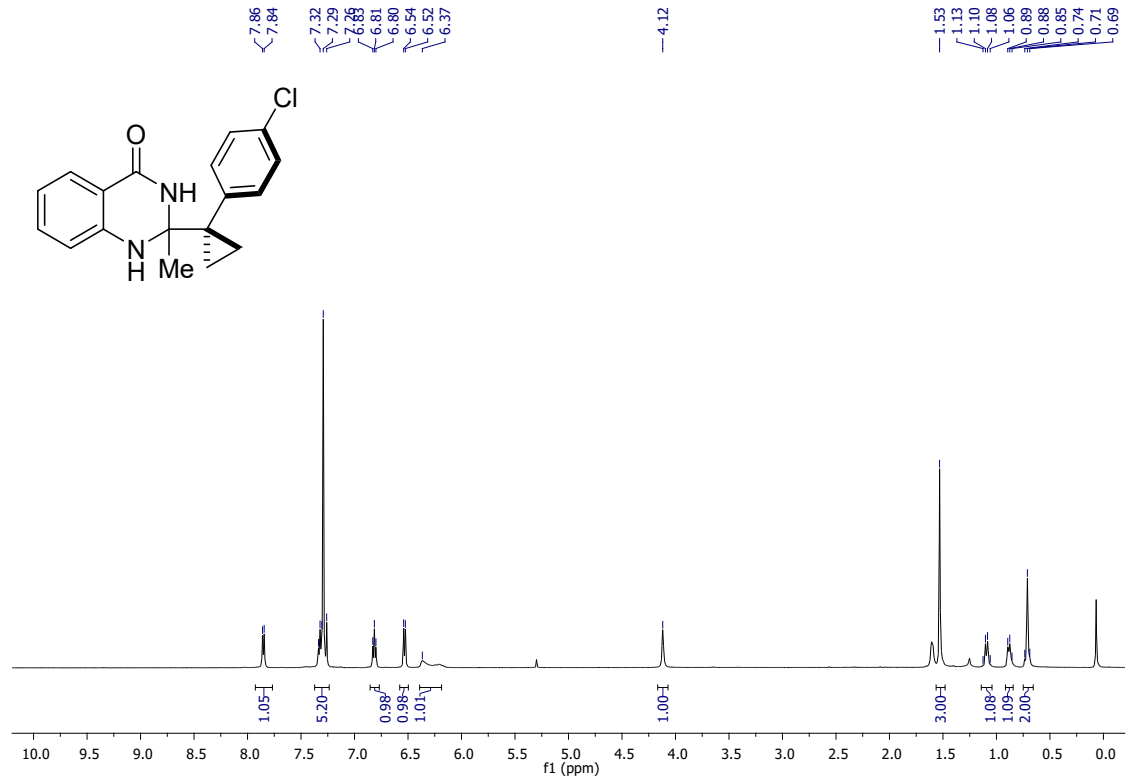


Figure S31: ^{1}H NMR spectrum of **2i** (500 MHz, $CDCl_3$)

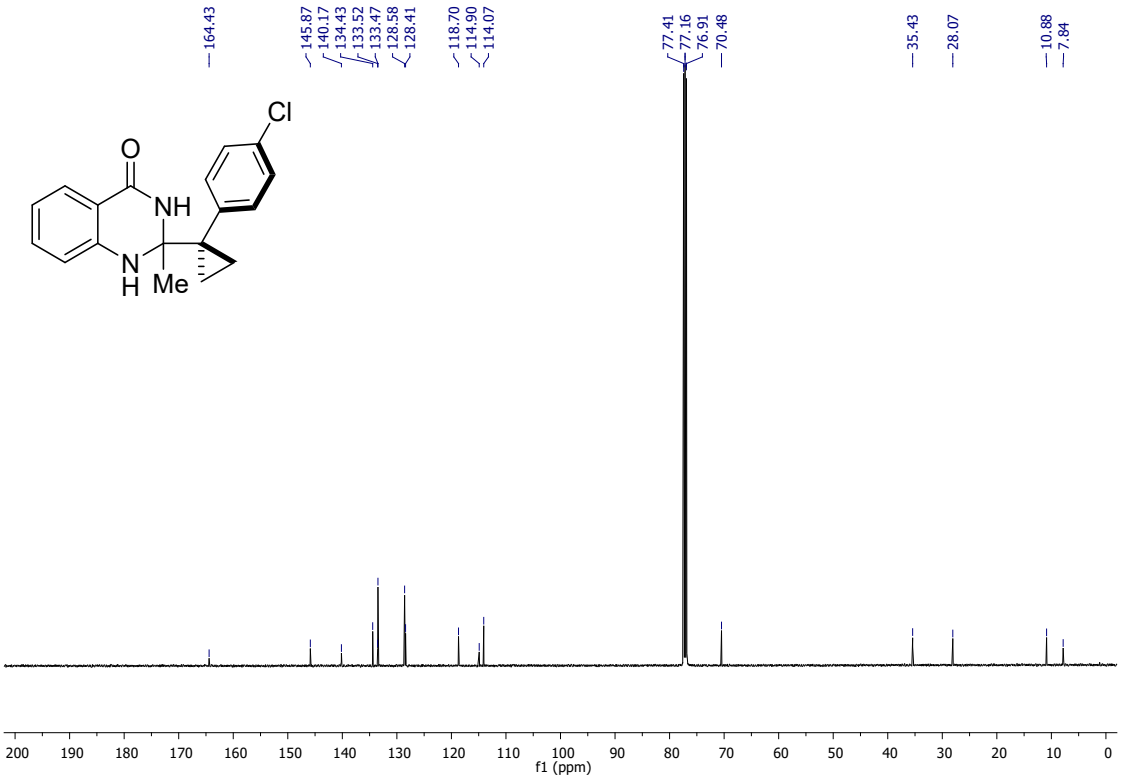


Figure S32: $^{13}C\{^{1}H\}$ NMR spectrum of **2i**(126 MHz, $CDCl_3$)

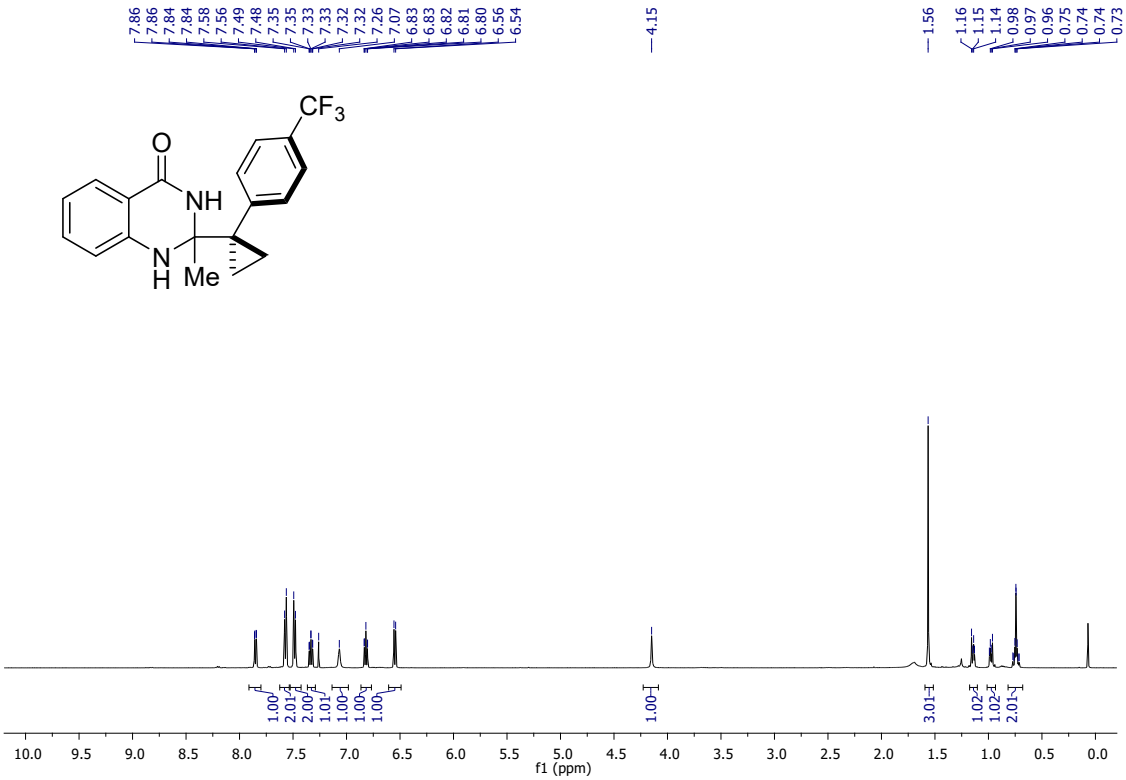


Figure S33: ^{1}H NMR spectrum of **2j** (500 MHz, $CDCl_3$)

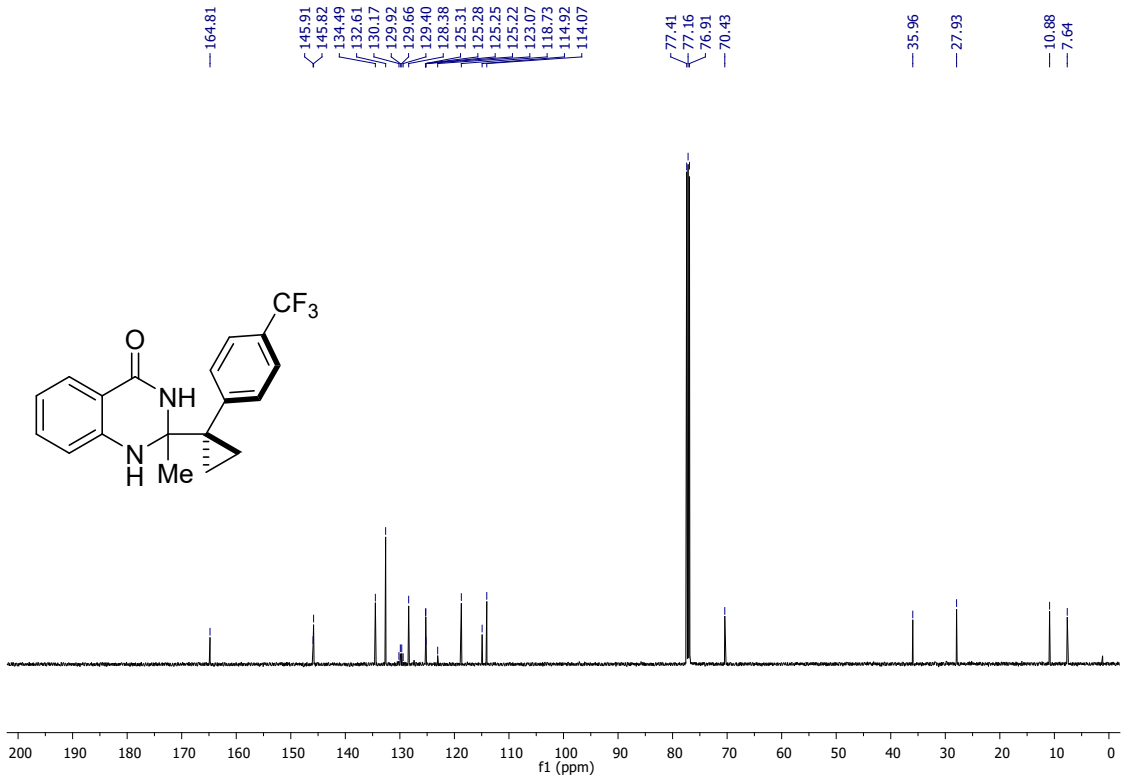


Figure S34: $^{13}C\{^{1}H\}$ NMR spectrum of **2j** (126 MHz, $CDCl_3$)

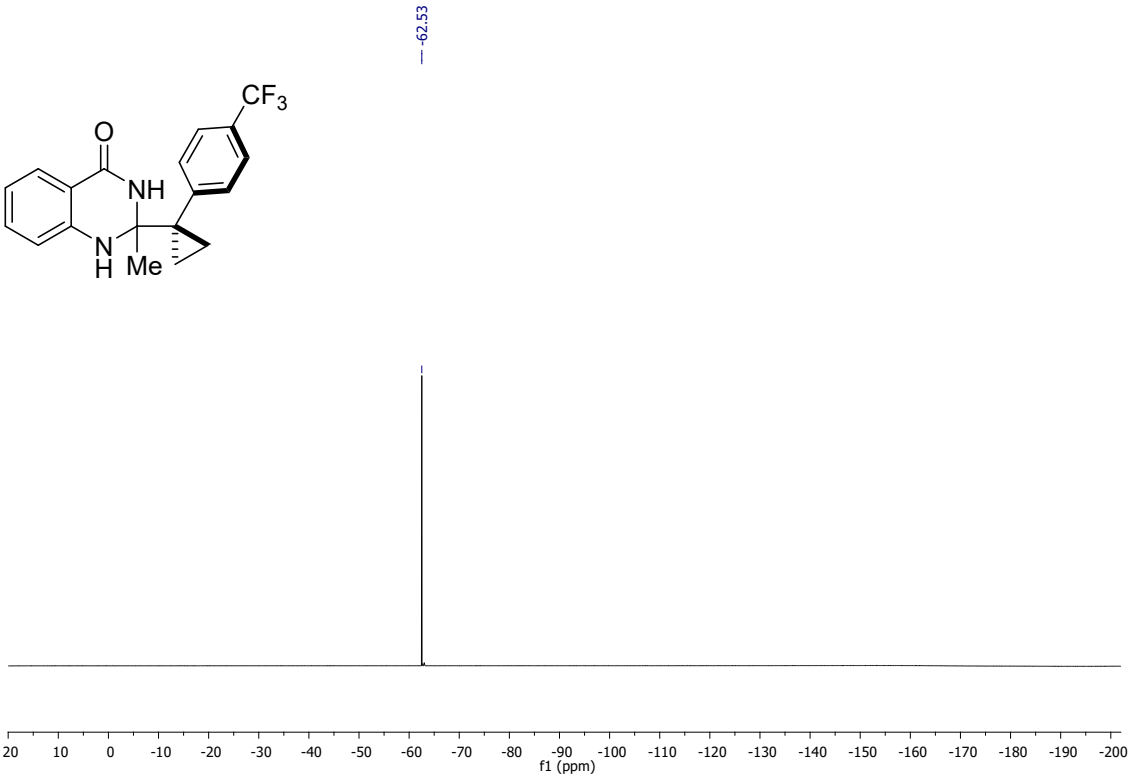


Figure S35: ^{19}F NMR spectrum of **2j** (471 MHz, $CDCl_3$)

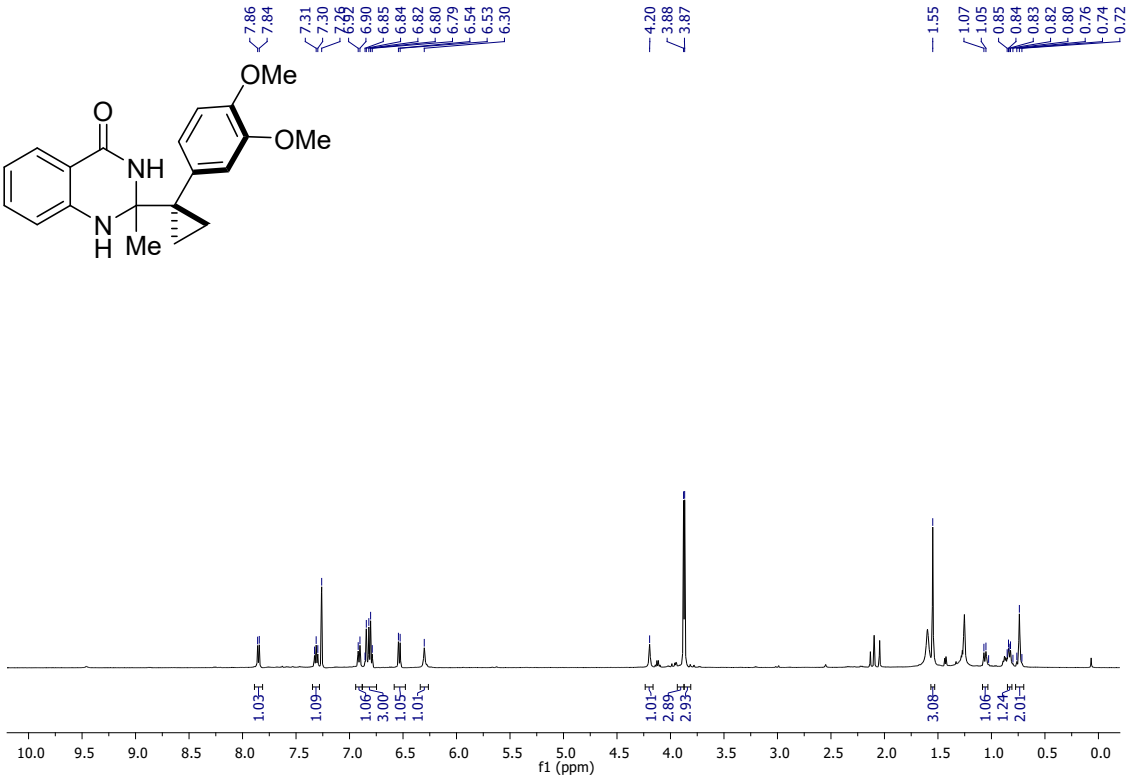


Figure S36: ^{1}H NMR spectrum of **2k** (500 MHz, $CDCl_3$)

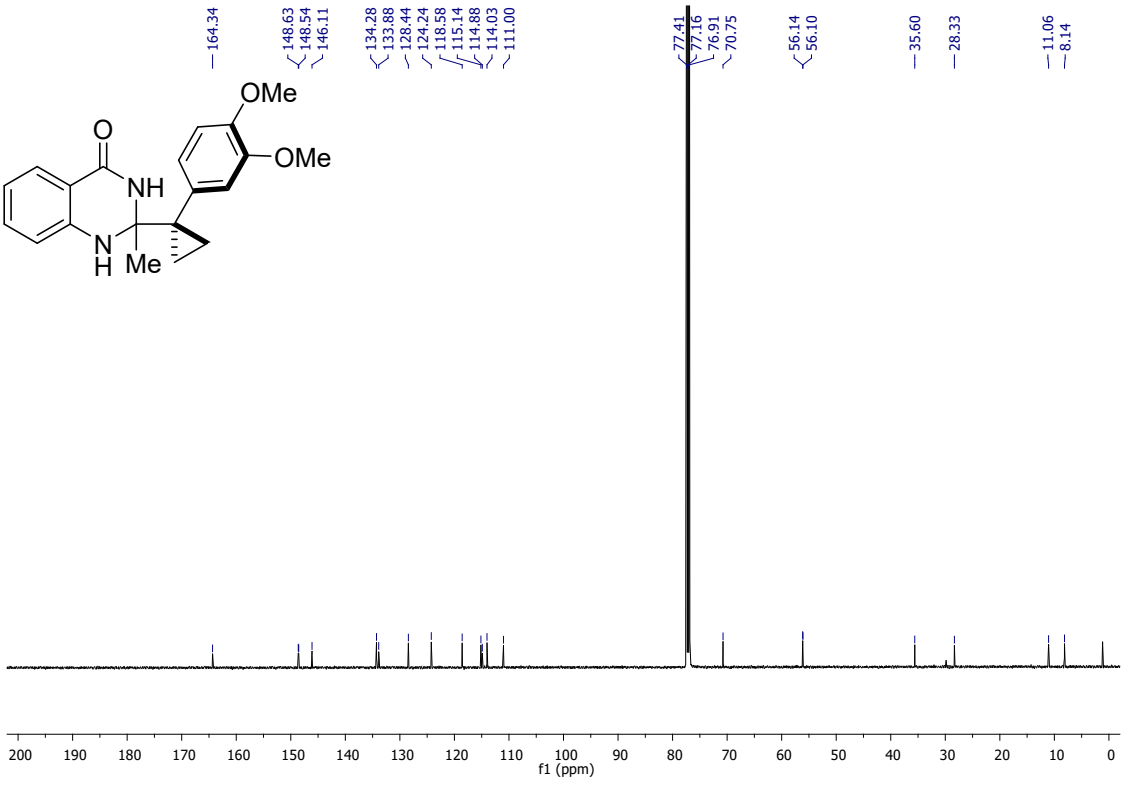


Figure S37: $^{13}C\{^{1}H\}$ NMR spectrum of **2k** (126 MHz, $CDCl_3$)

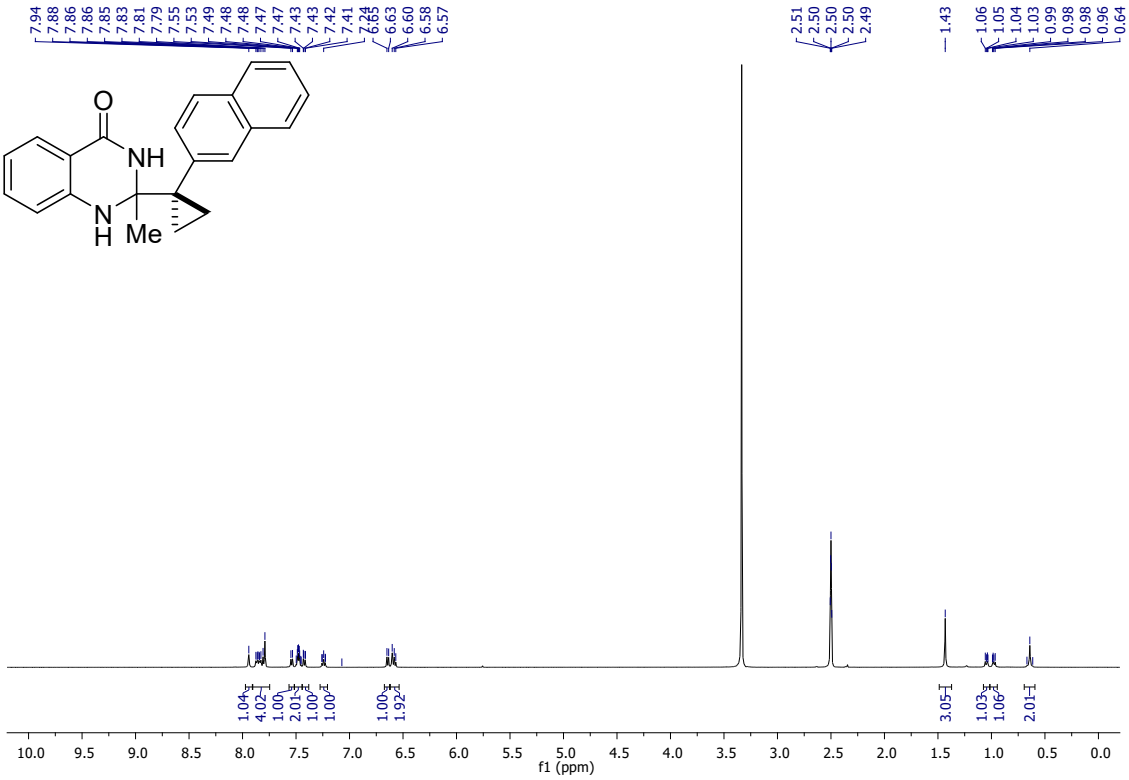


Figure S38: ^{1}H NMR spectrum of **2l** (500 MHz, DMSO-d6)

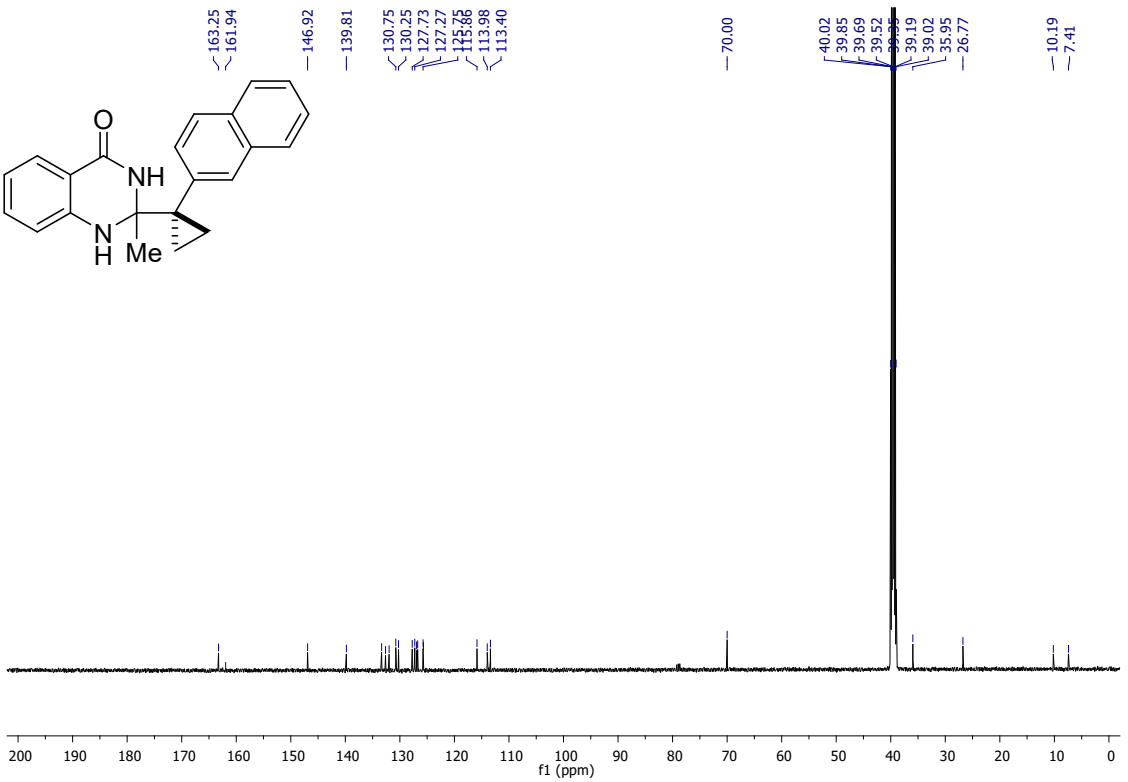


Figure S39: $^{13}C\{^{1}H\}$ NMR spectrum of **2l** (126 MHz, DMSO-d_6)

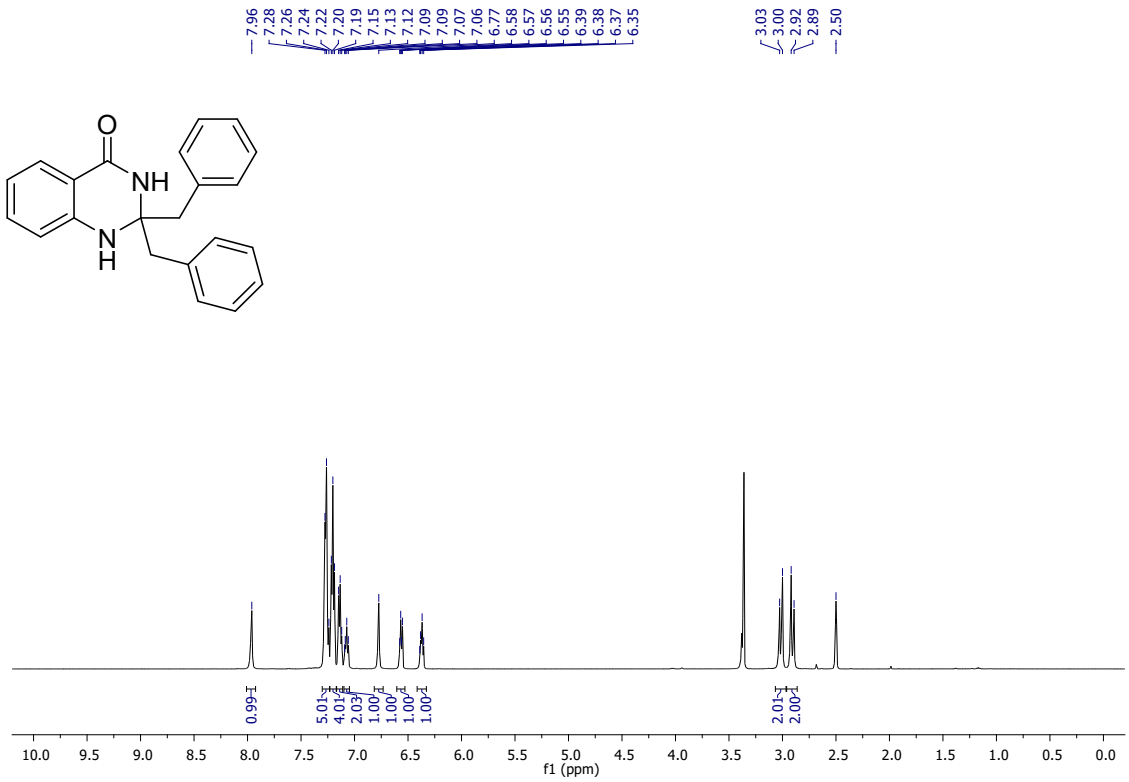


Figure S40: ^{1}H NMR spectrum of **2o** (500 MHz, DMSO-d6)

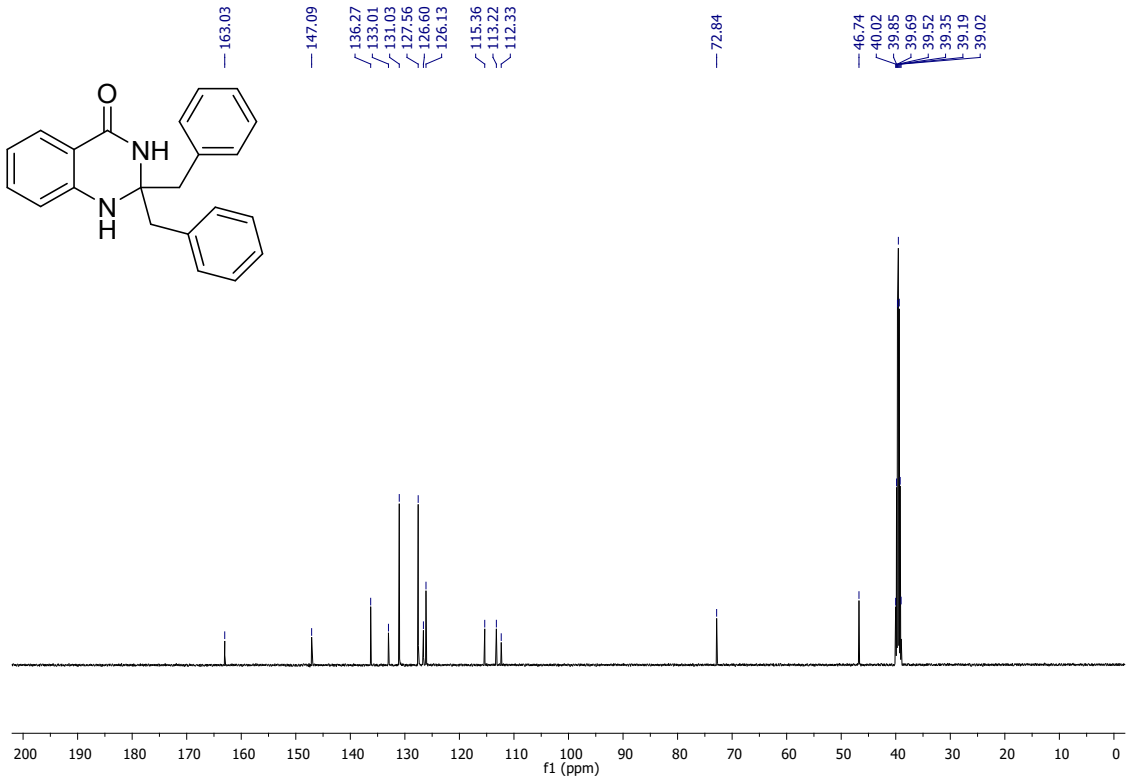


Figure S41: $^{13}C\{^{1}H\}$ NMR spectrum of **2o** (126 MHz, DMSO-d_6)

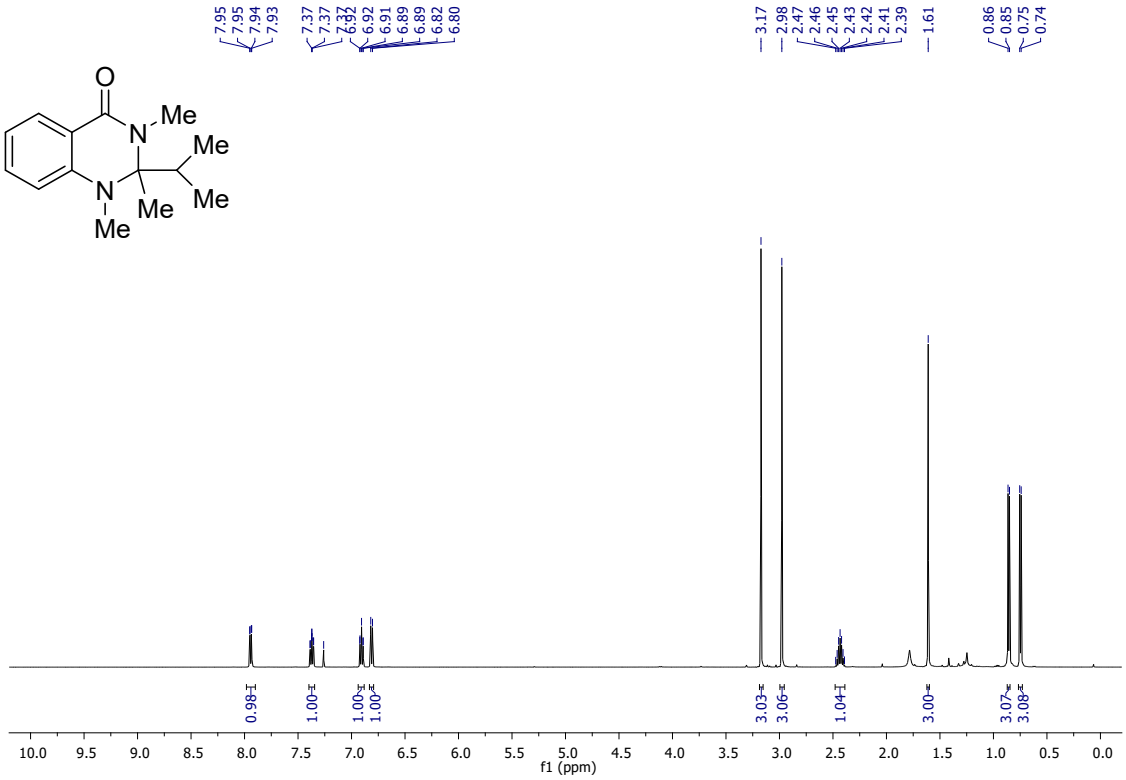


Figure S42: ^{1}H NMR spectrum of **2s** (500 MHz, $CDCl_3$)

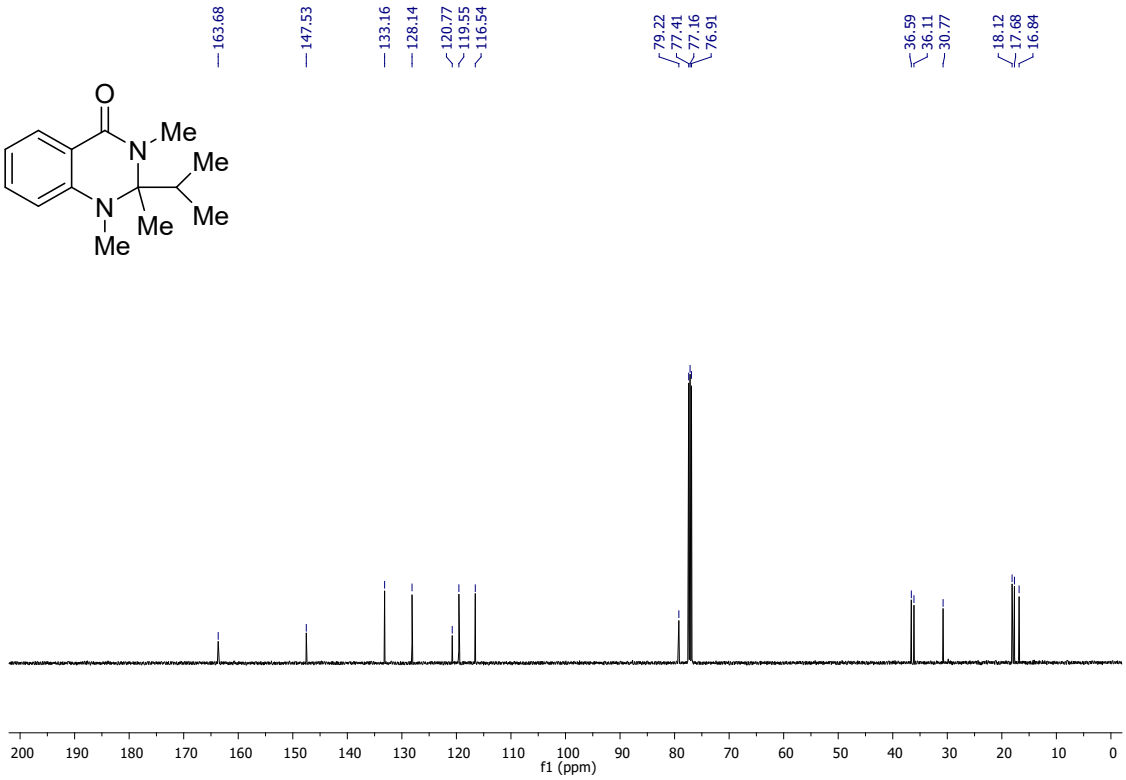


Figure S43: $^{13}C\{^{1}H\}$ NMR spectrum of **2s** (126 MHz, $CDCl_3$)

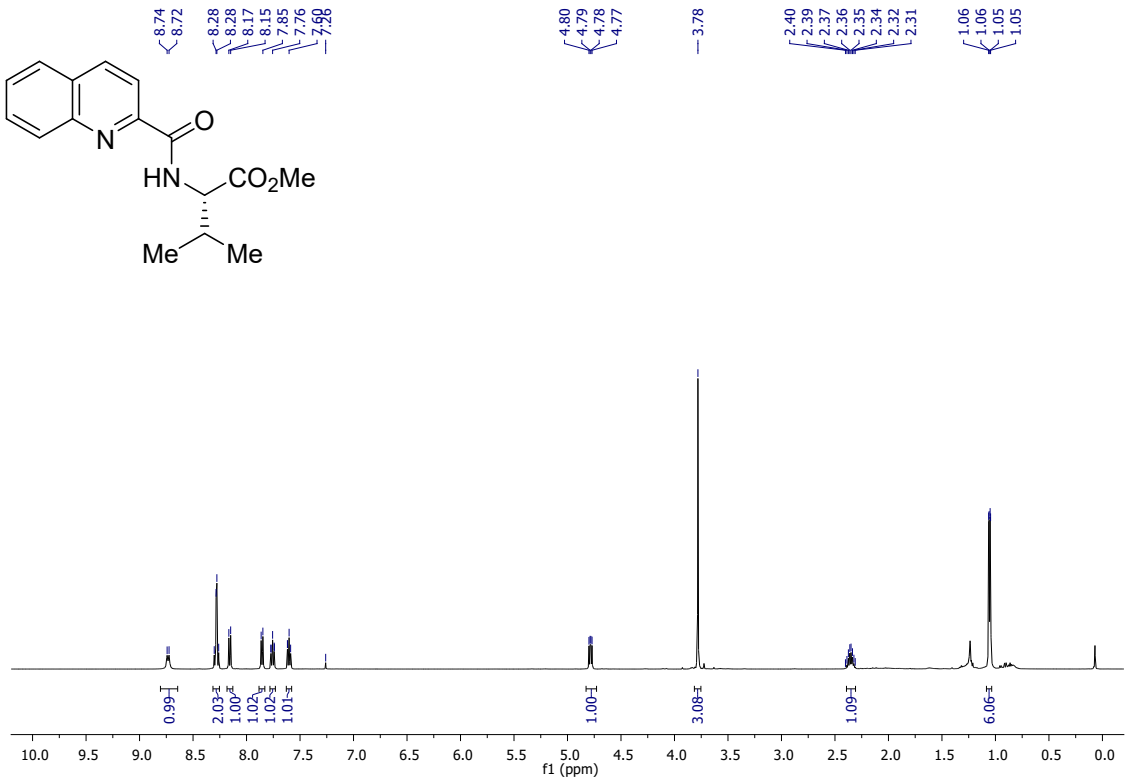


Figure S44: ^{1}H NMR spectrum of **1u** (500 MHz, $CDCl_3$)

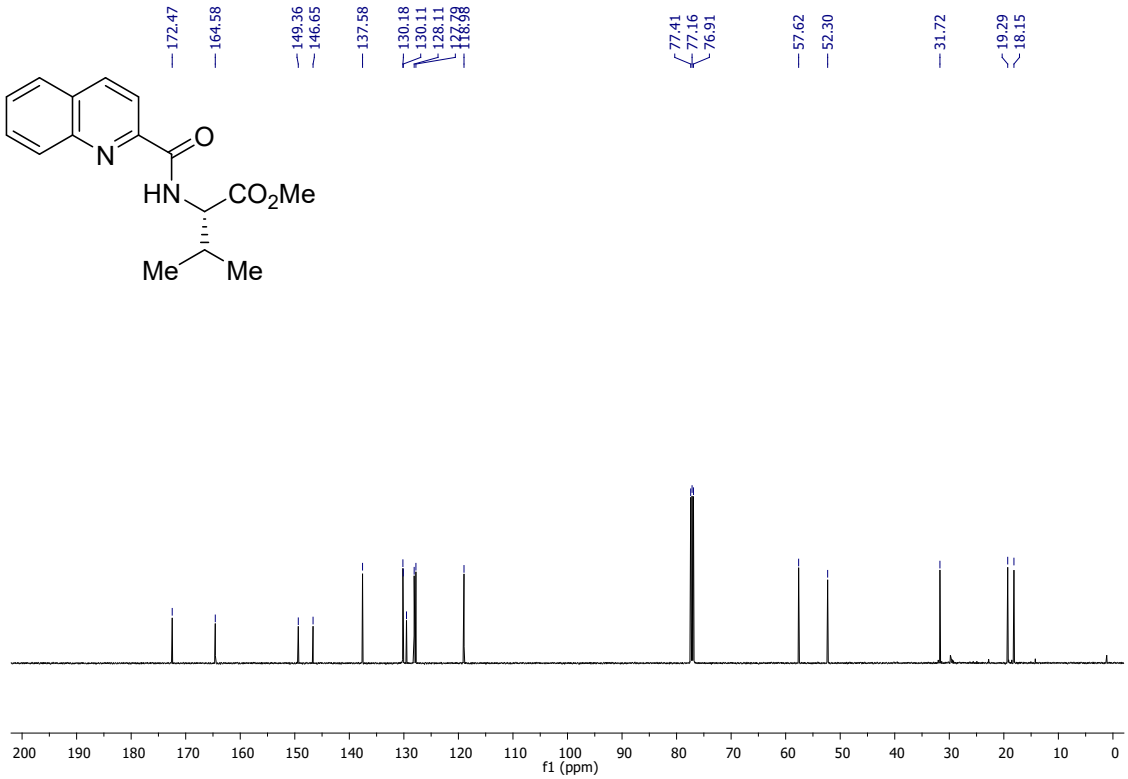


Figure S45: $^{13}C\{^{1}H\}$ NMR spectrum of **1u** (126 MHz, $CDCl_3$)

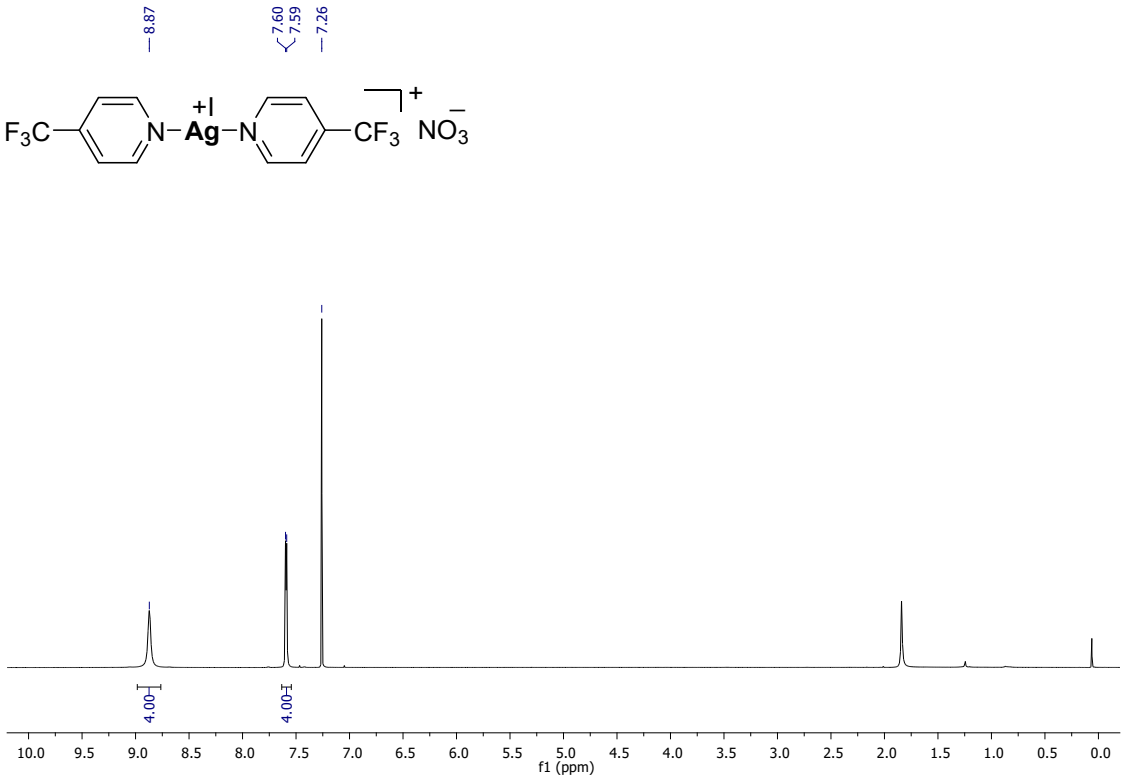


Figure S46: ^{1}H NMR spectrum of **5** (500 MHz, $CDCl_3$)

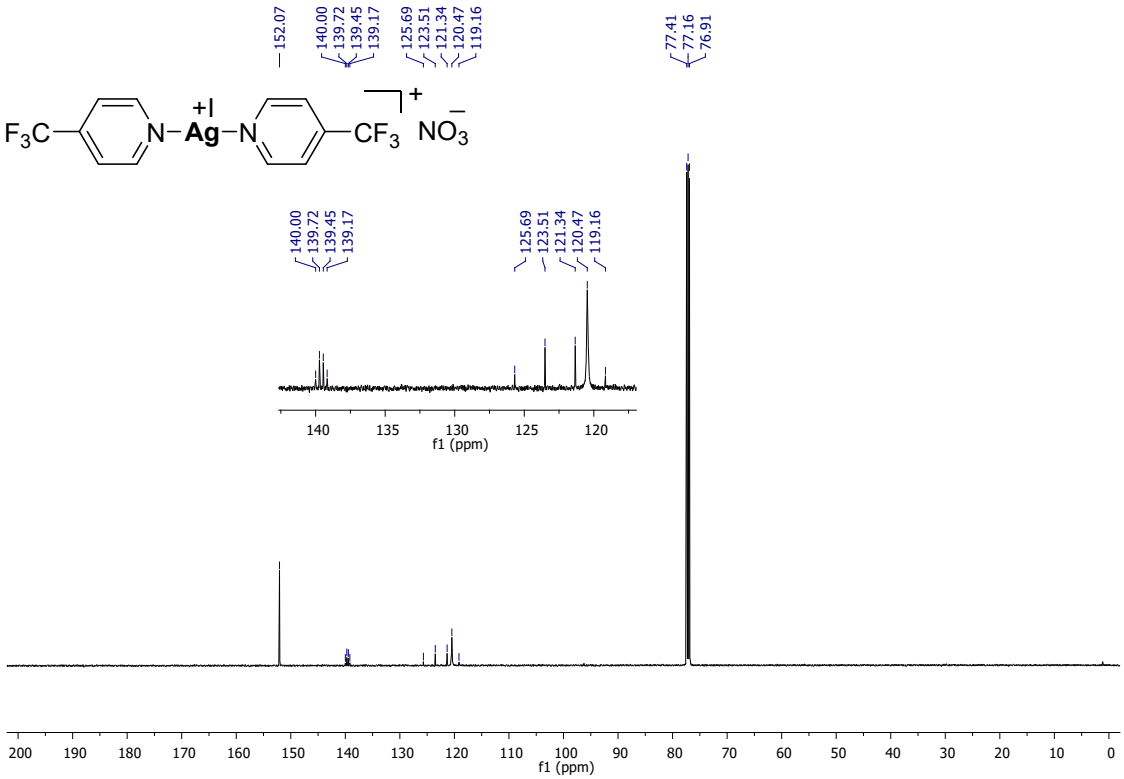


Figure S47: $^{13}C\{^{1}H\}$ NMR spectrum of **5** (126 MHz, $CDCl_3$)

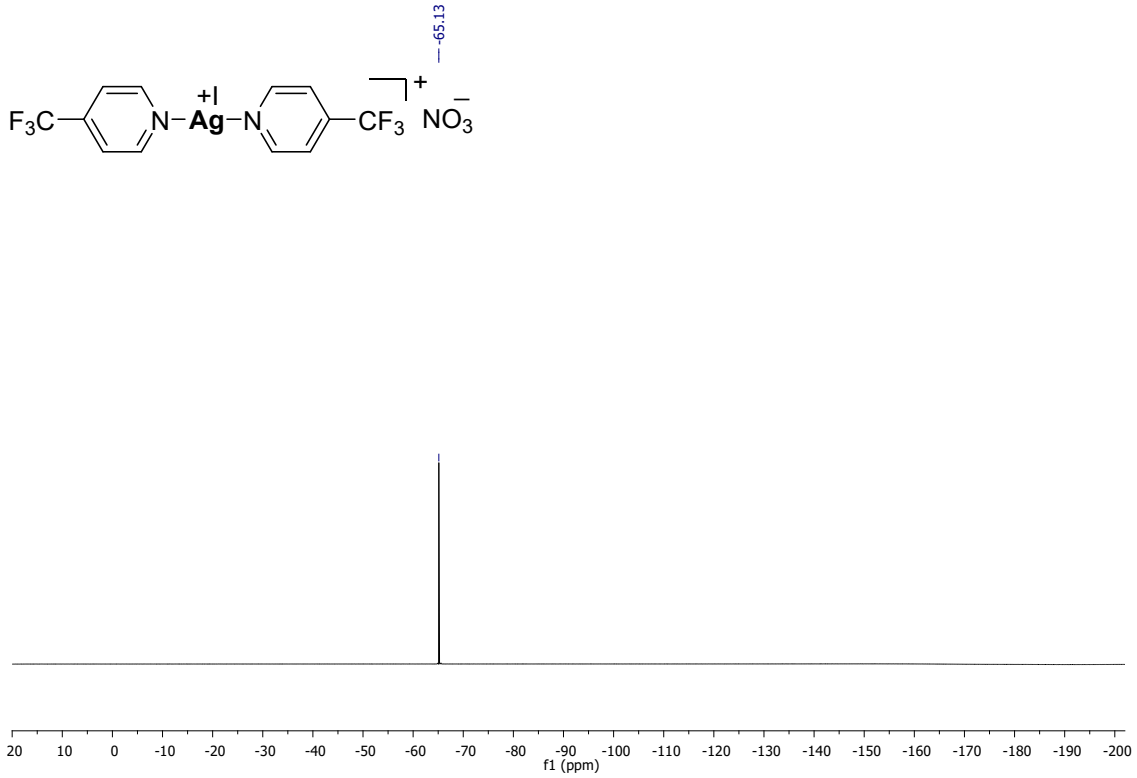


Figure S48: ^{19}F NMR spectrum of **5** (471 MHz, $CDCl_3$)

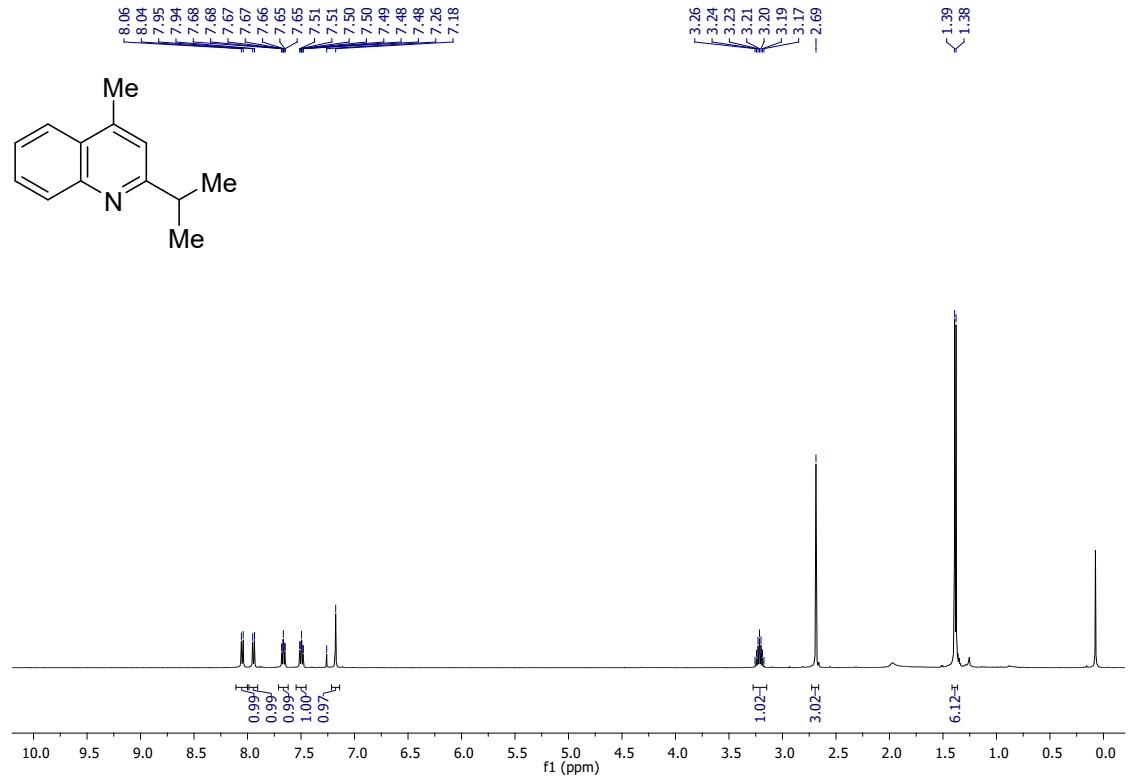


Figure S49: ^{1}H NMR spectrum of **3aa** (500 MHz, $CDCl_3$)

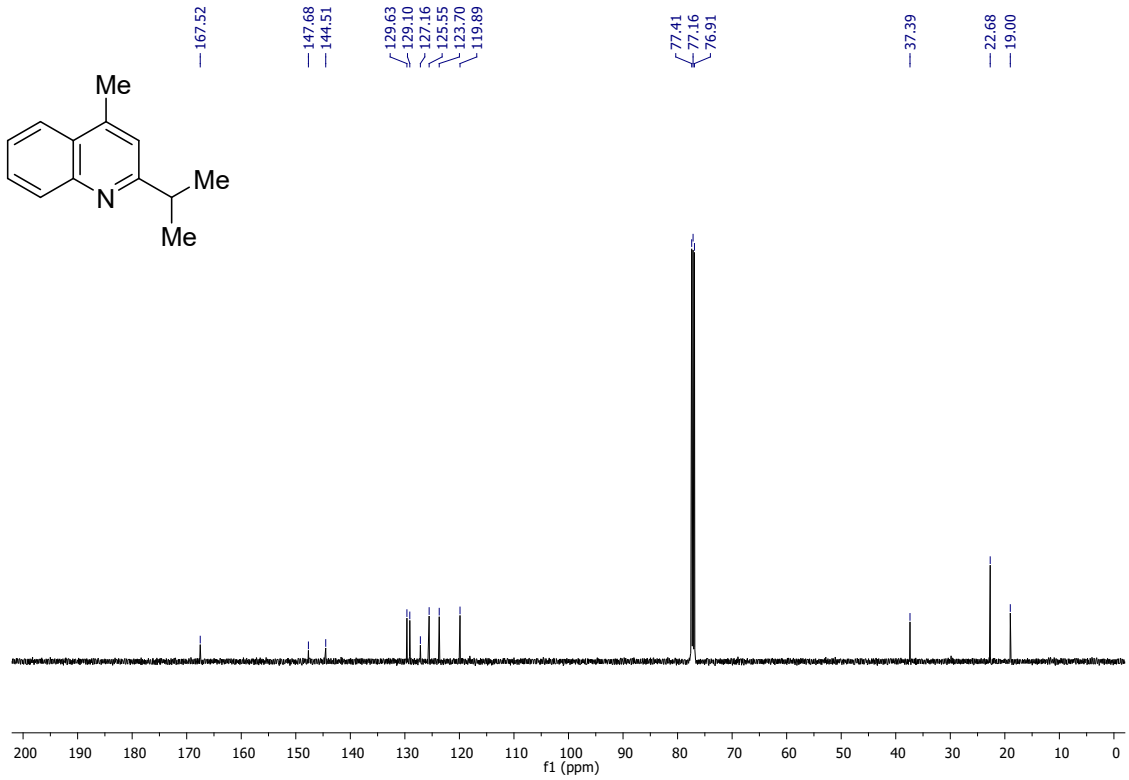


Figure S50: $^{13}C\{^{1}H\}$ NMR spectrum of **3aa** (126 MHz, $CDCl_3$)

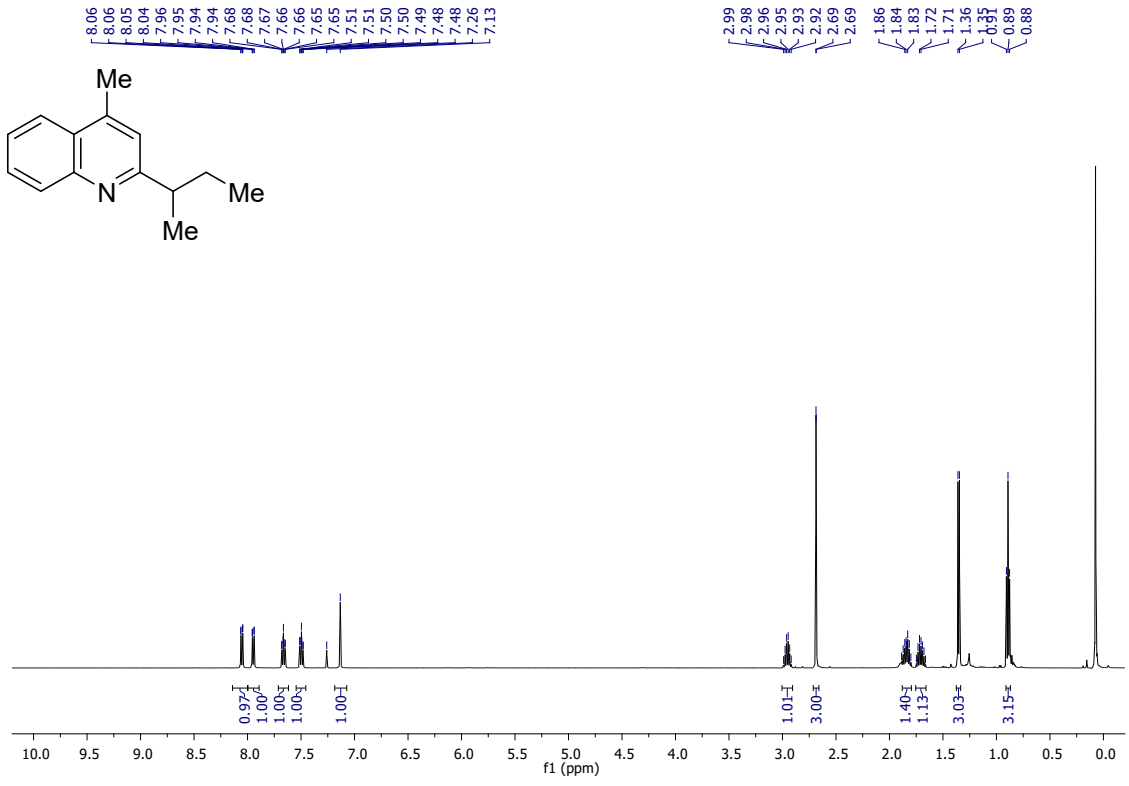


Figure S51: ^{1}H NMR spectrum of **3ab** (500 MHz, $CDCl_3$)

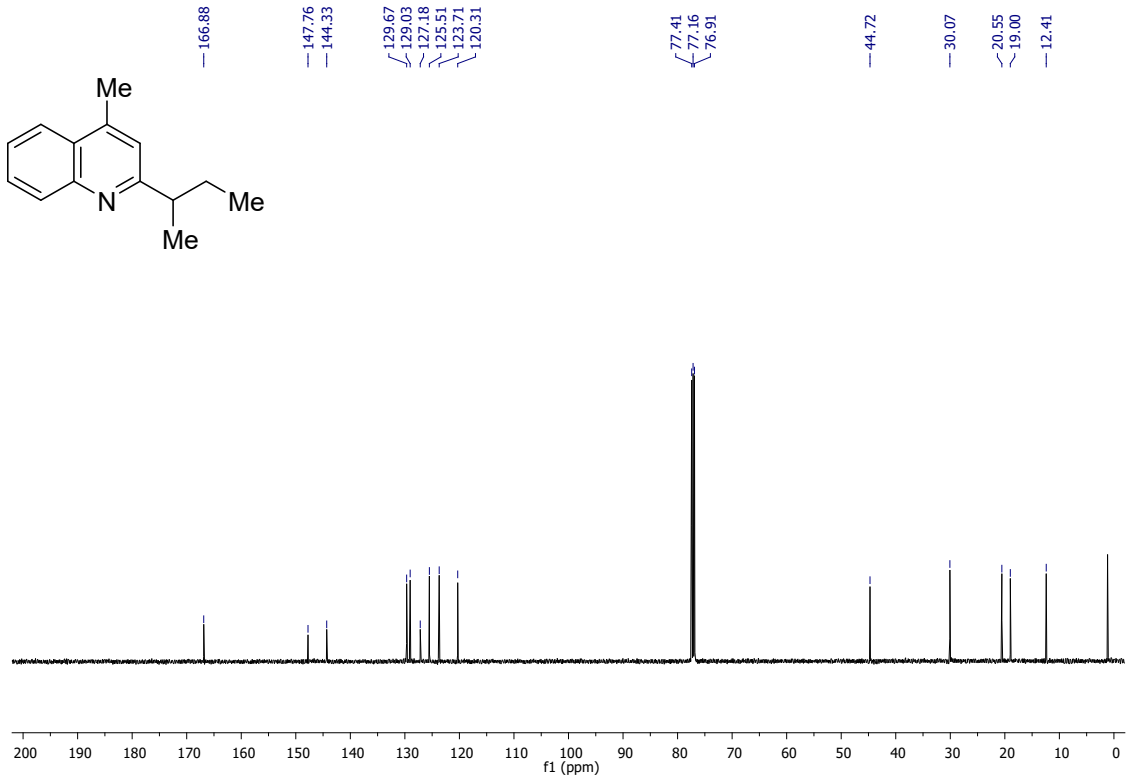


Figure S52: $^{13}C\{^{1}H\}$ NMR spectrum of **3ab** (126 MHz, $CDCl_3$)

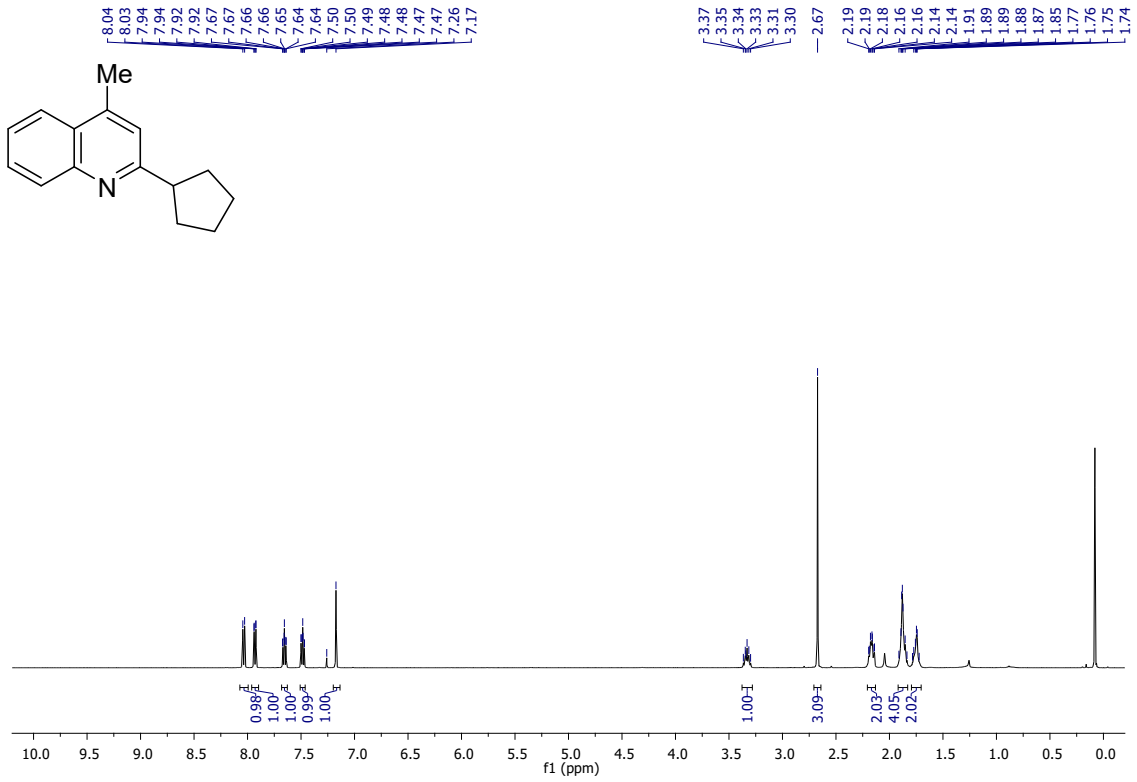


Figure S53: ^{1}H NMR spectrum of **3ac** (500 MHz, $CDCl_3$)

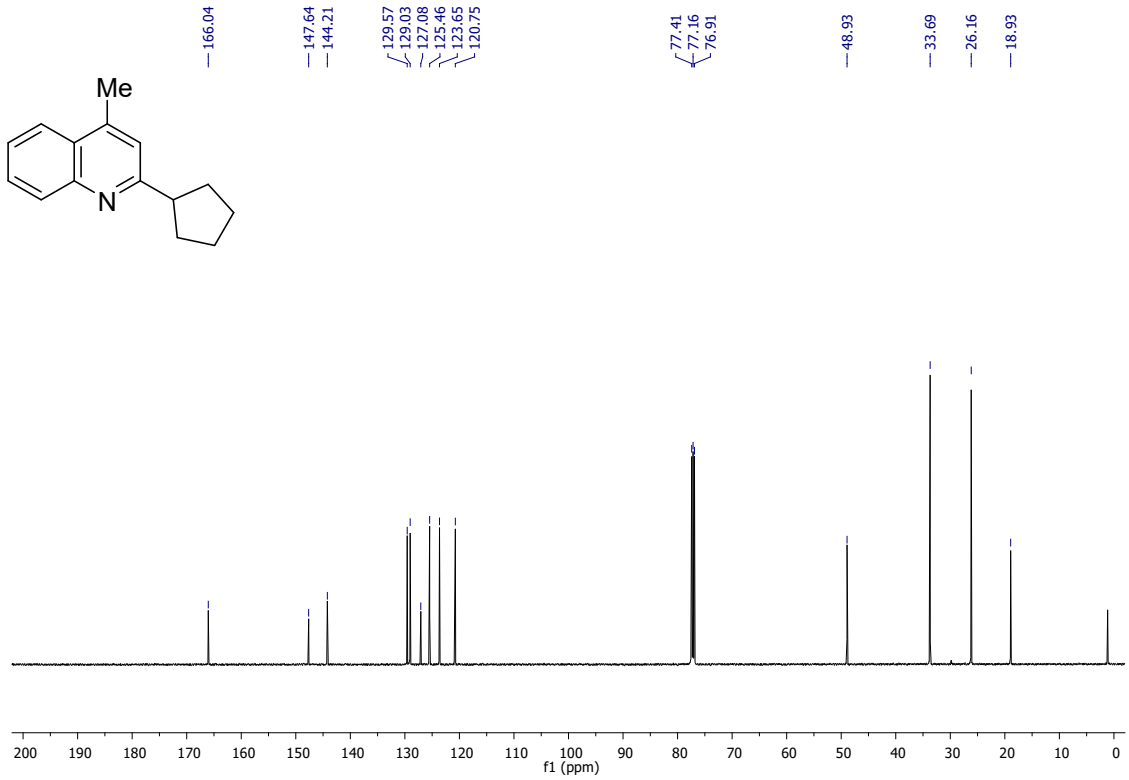


Figure S54: $^{13}C\{^{1}H\}$ NMR spectrum of **3ac** (126 MHz, $CDCl_3$)

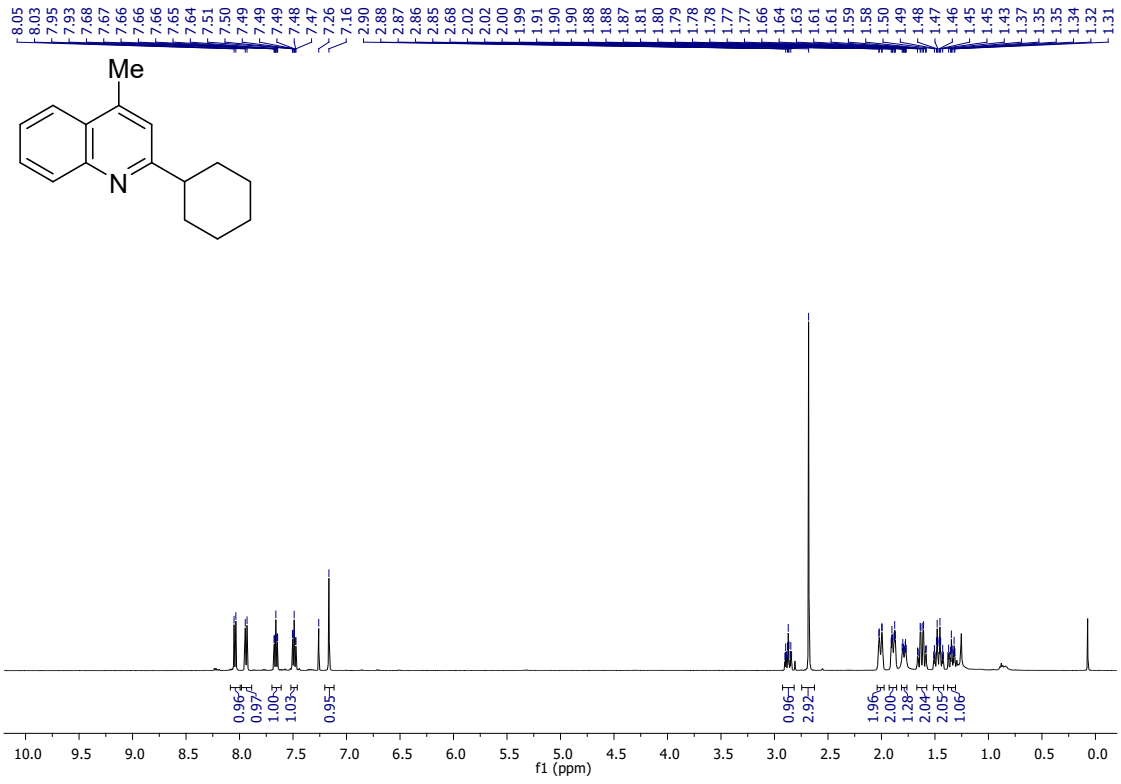


Figure S55: ^{1}H NMR spectrum of **3ad** (500 MHz, $CDCl_3$)

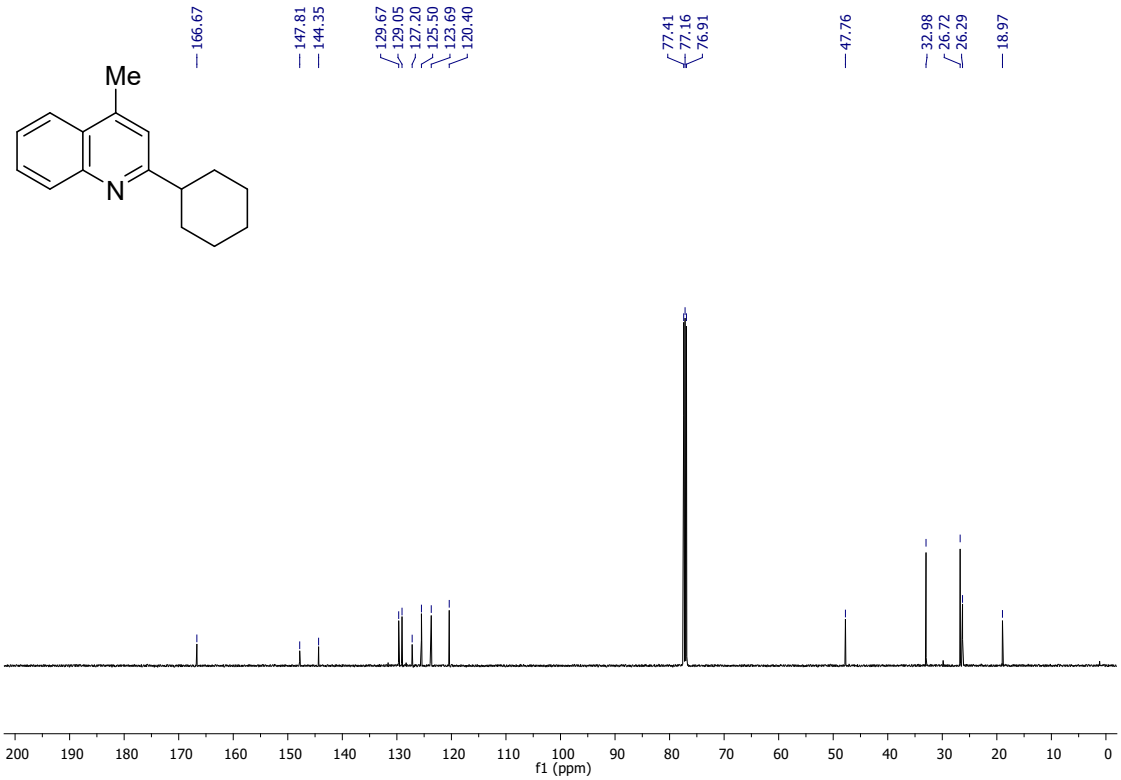


Figure S56: $^{13}C\{^{1}H\}$ NMR spectrum of **3ad** (126 MHz, $CDCl_3$)

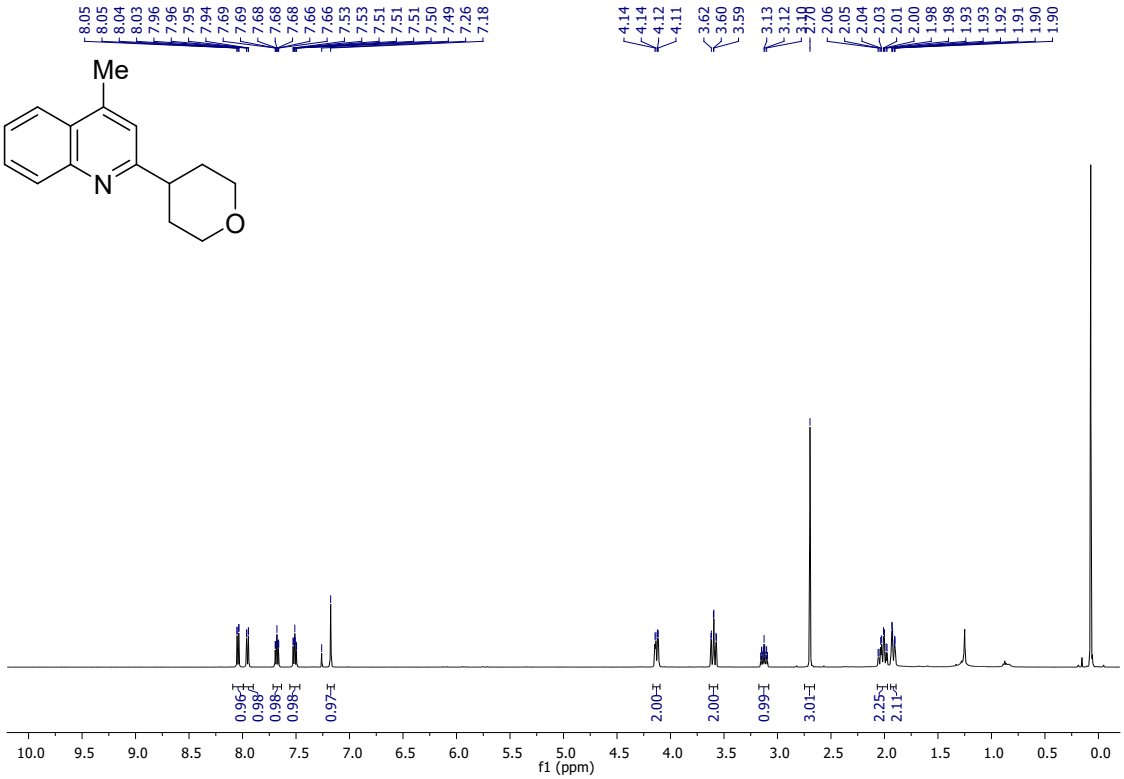


Figure S57: ^{1}H NMR spectrum of **3ae** (500 MHz, $CDCl_3$)

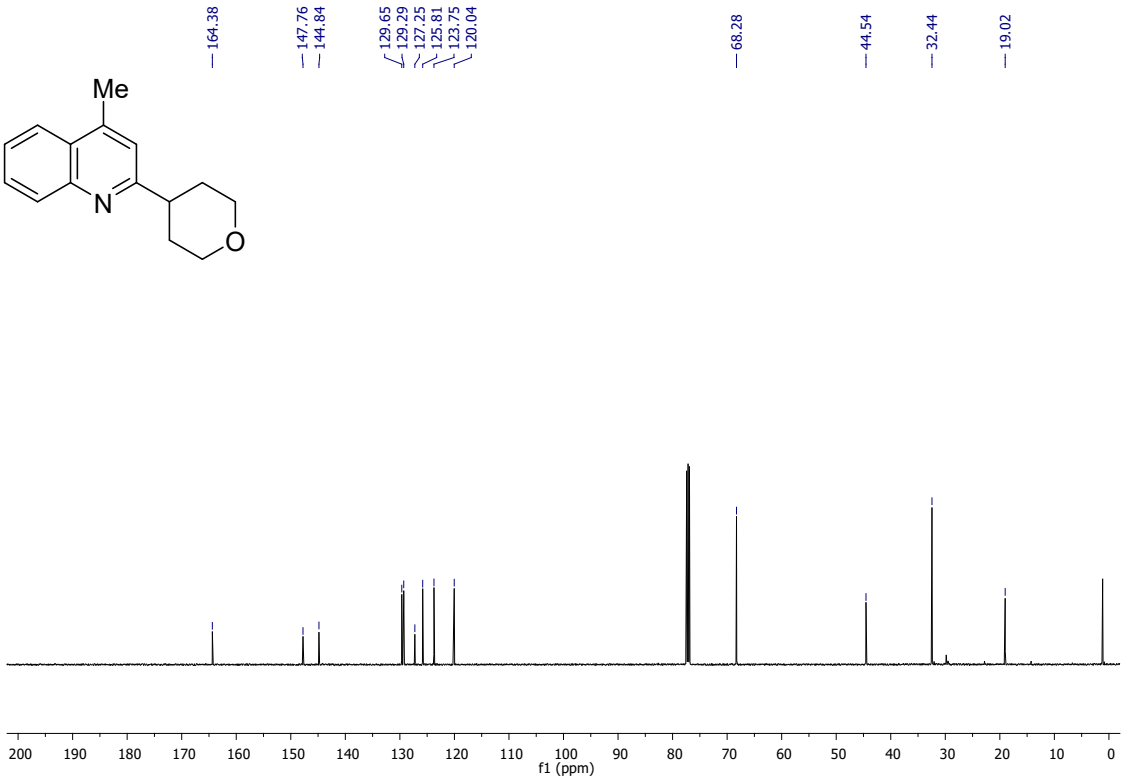


Figure S58: $^{13}C\{^{1}H\}$ NMR spectrum of **3ae** (126 MHz, $CDCl_3$)

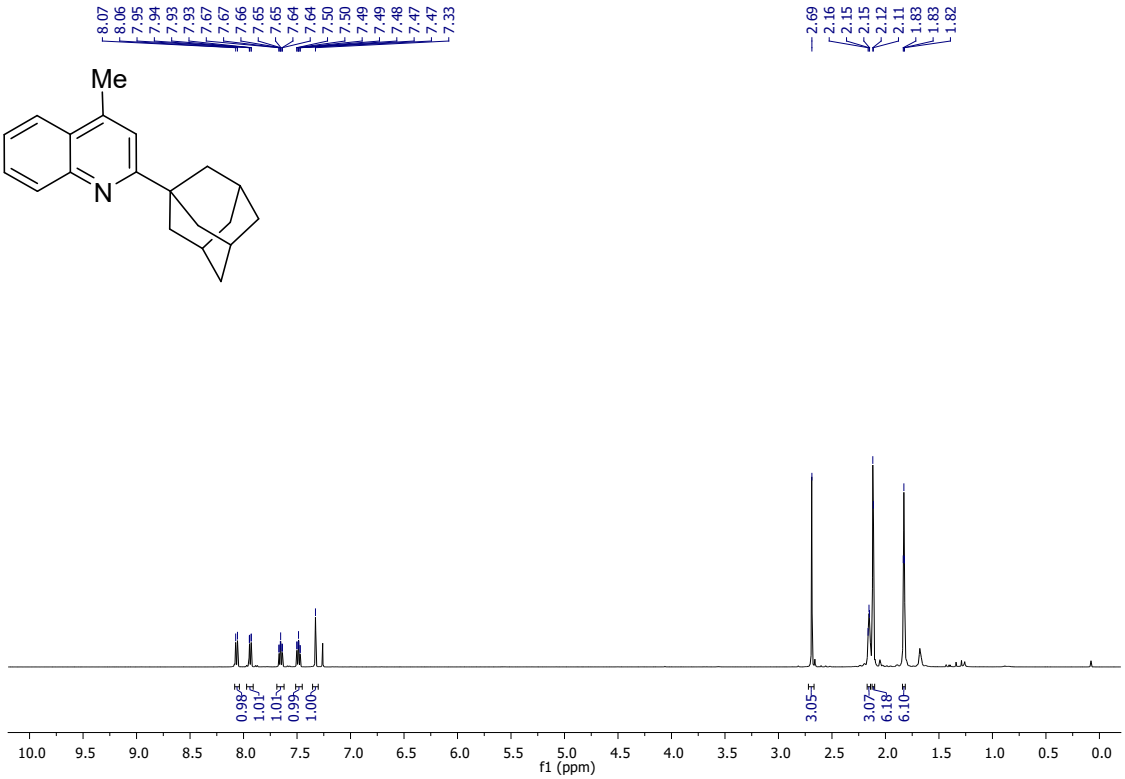


Figure S59: ^{1}H NMR spectrum of **3af** (500 MHz, $CDCl_3$)

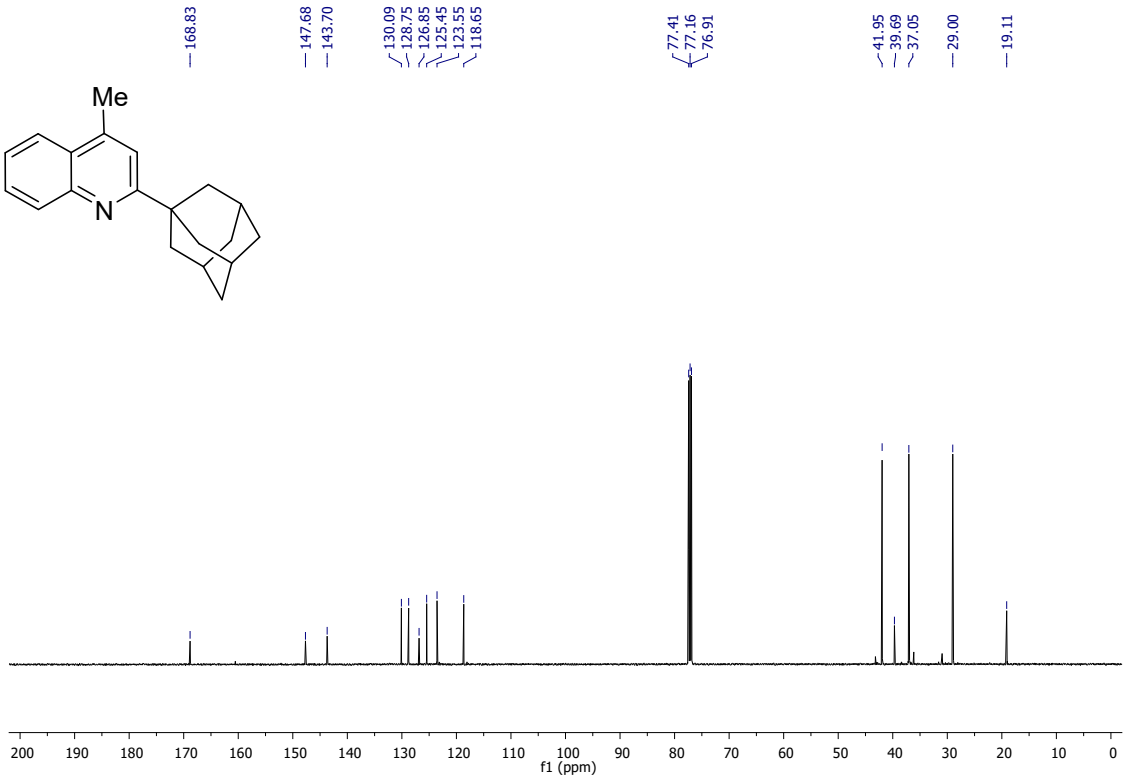


Figure S60: $^{13}C\{^{1}H\}$ NMR spectrum of **3af** (126 MHz, $CDCl_3$)

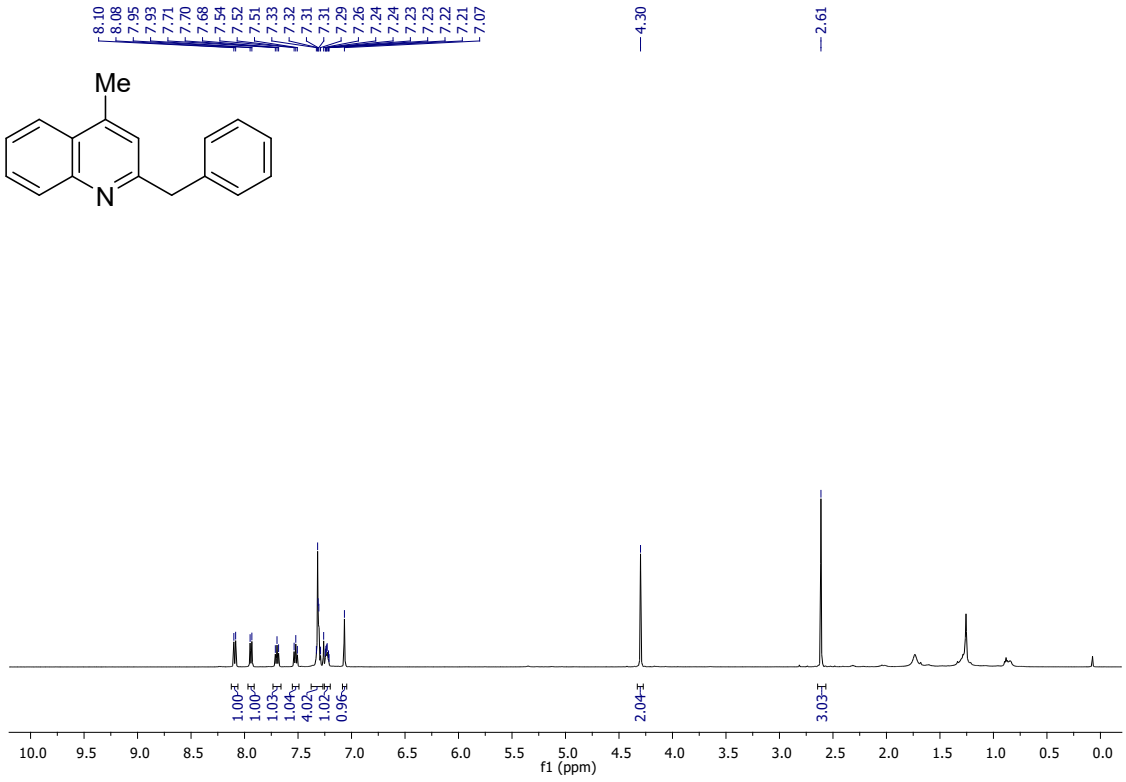


Figure S61: ^{1}H NMR spectrum of **3ag** (500 MHz, $CDCl_3$)

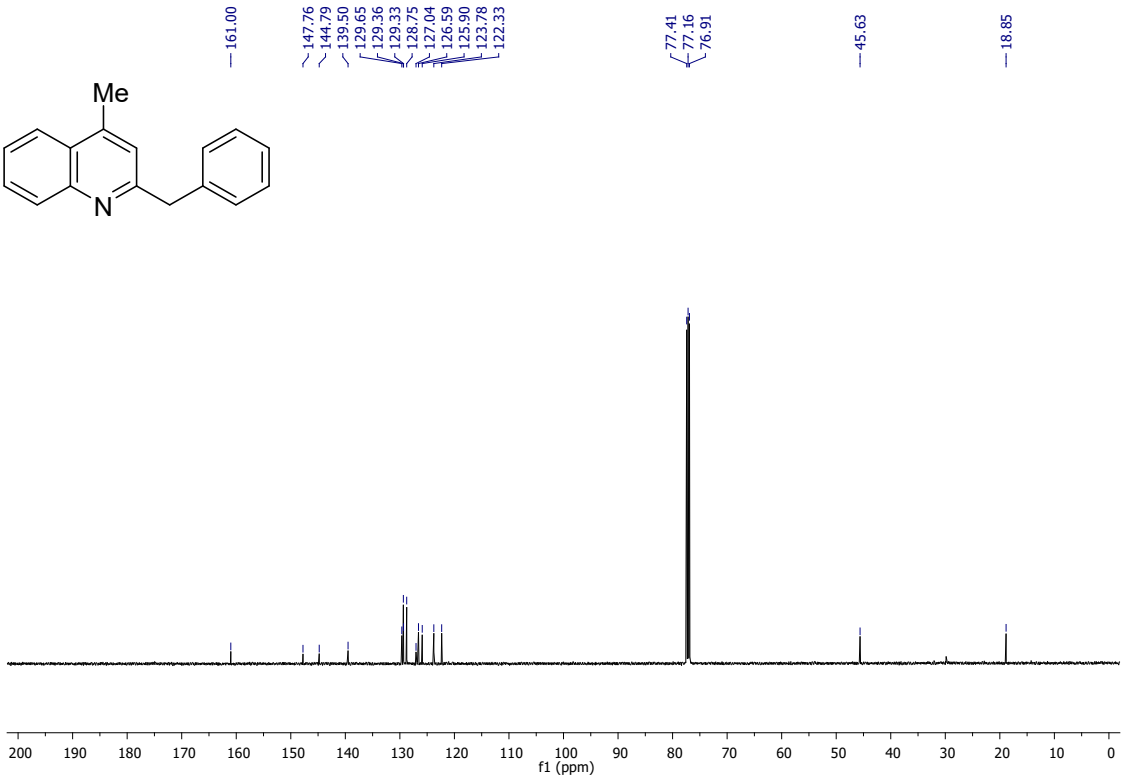


Figure S62: $^{13}C\{^{1}H\}$ NMR spectrum of **3ag** (126 MHz, $CDCl_3$)

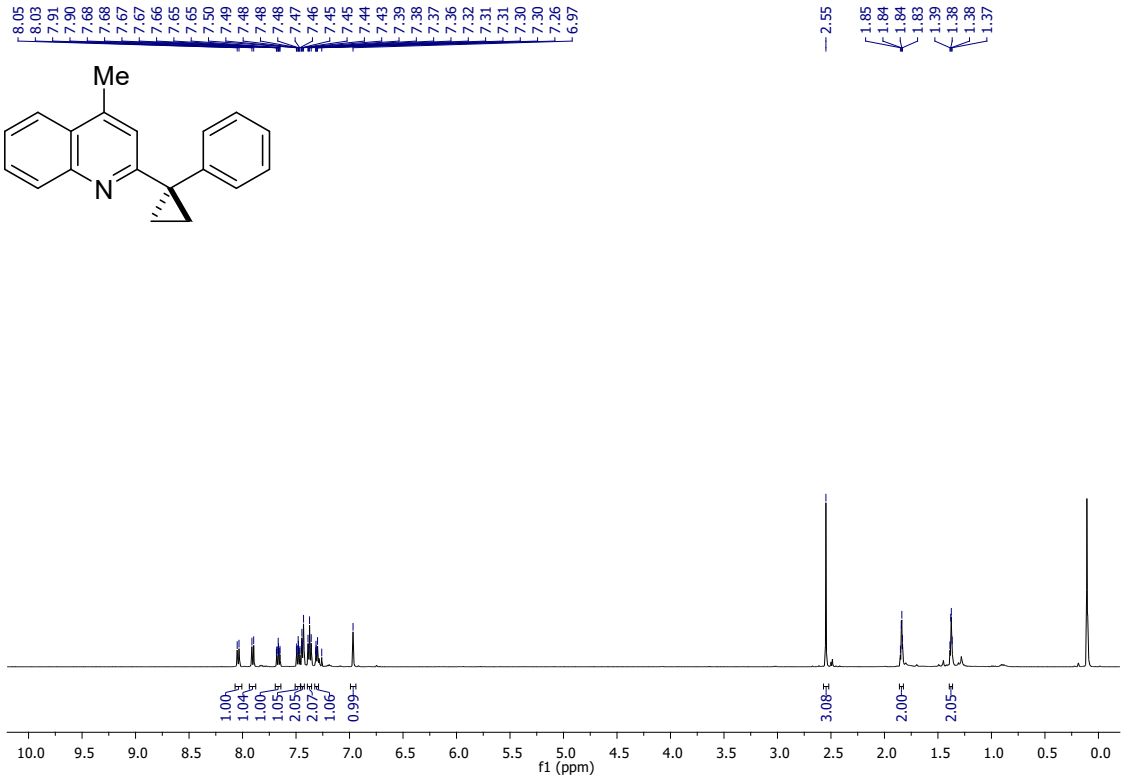


Figure S63: ^{1}H NMR spectrum of **3ah** (500 MHz, $CDCl_3$)

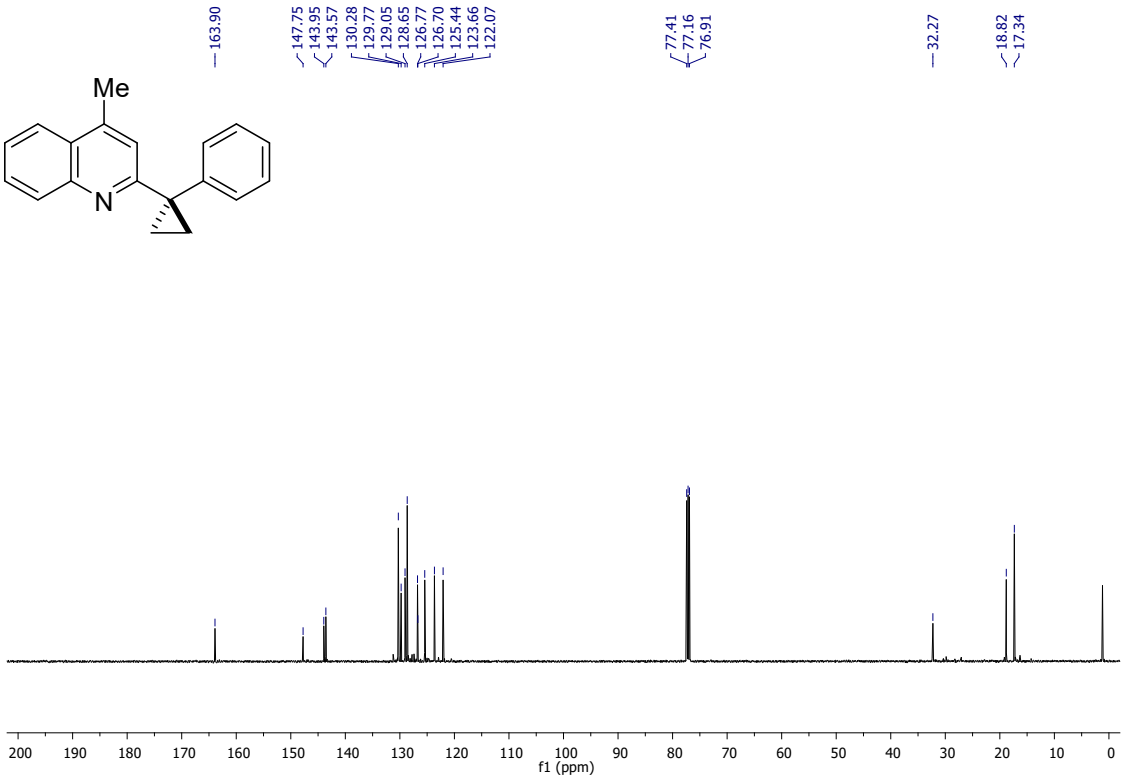


Figure S64: $^{13}C\{^{1}H\}$ NMR spectrum of **3ah** (126 MHz, $CDCl_3$)

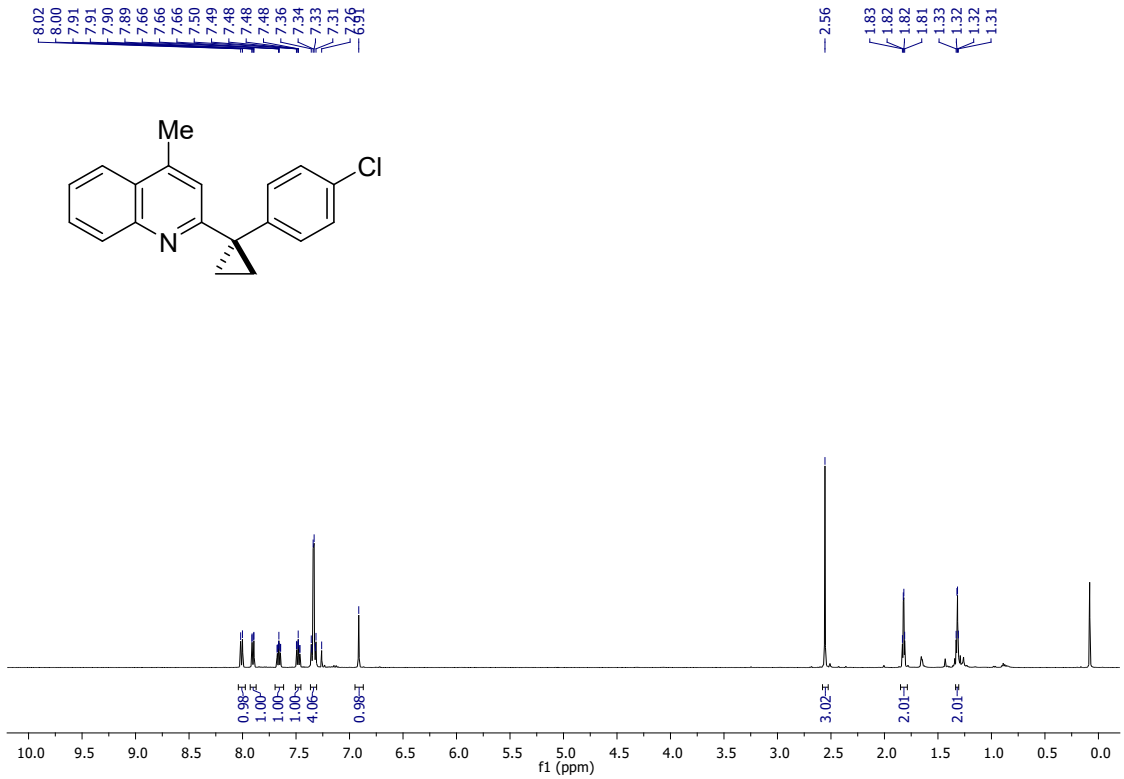


Figure S65: ^{1}H NMR spectrum of **3ai** (500 MHz, $CDCl_3$)

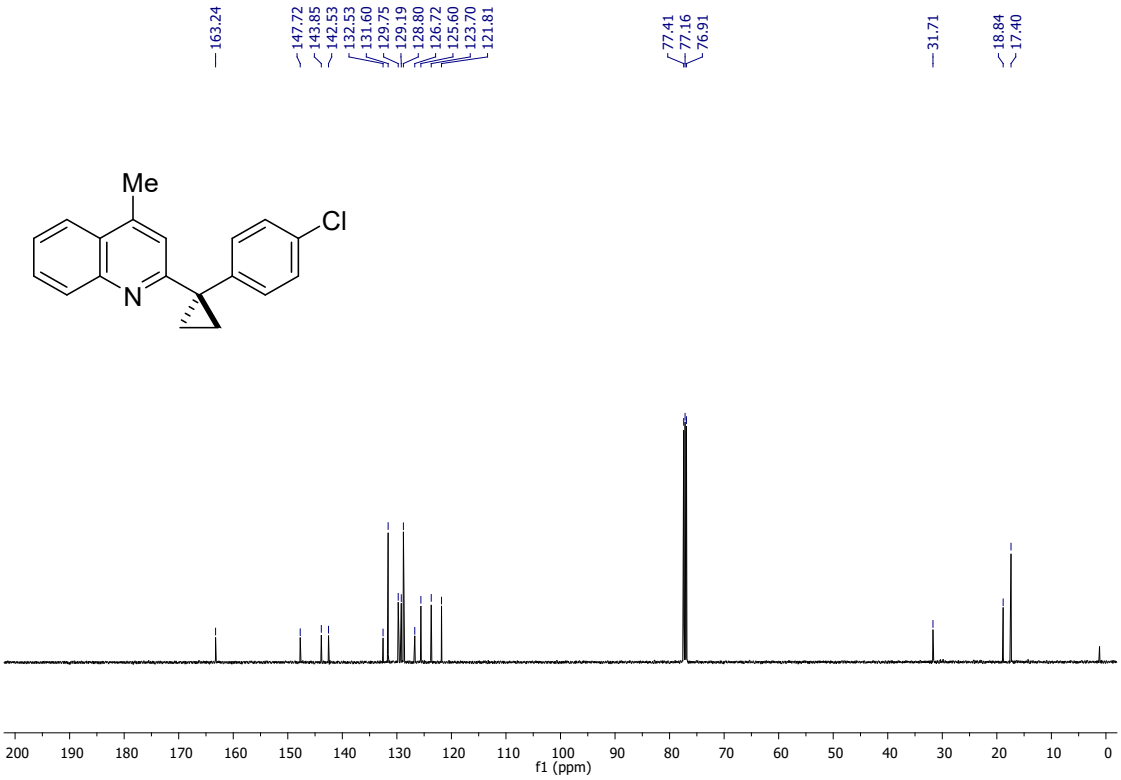


Figure S66: $^{13}C\{^{1}H\}$ NMR spectrum of **3ai** (126 MHz, $CDCl_3$)

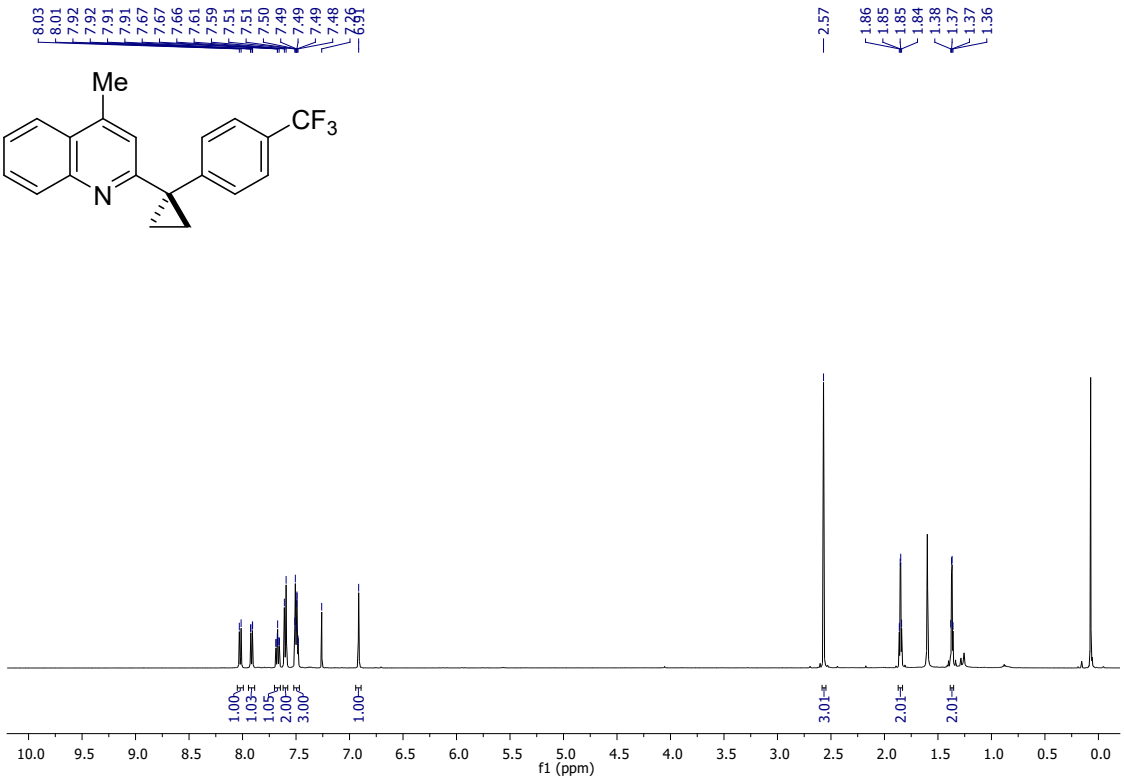


Figure S67: ^{1}H NMR spectrum of **3aj** (500 MHz, $CDCl_3$)

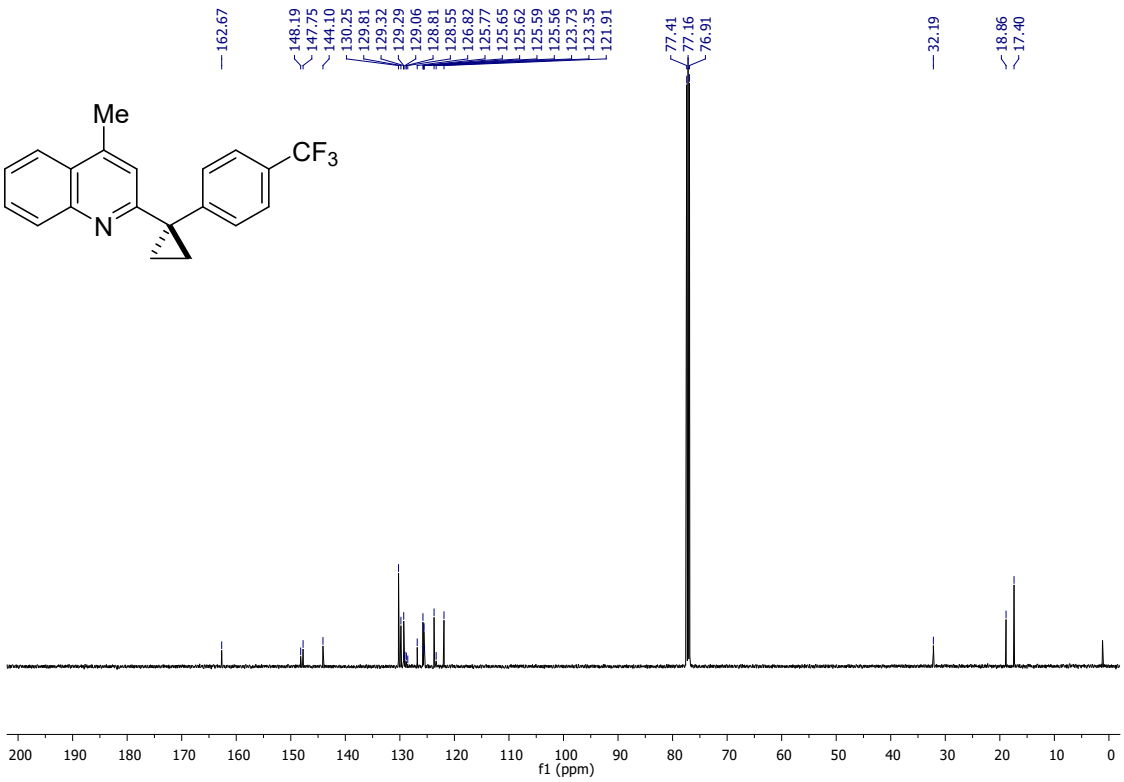


Figure S68: $^{13}C\{^{1}H\}$ NMR spectrum of **3aj** (126 MHz, $CDCl_3$)

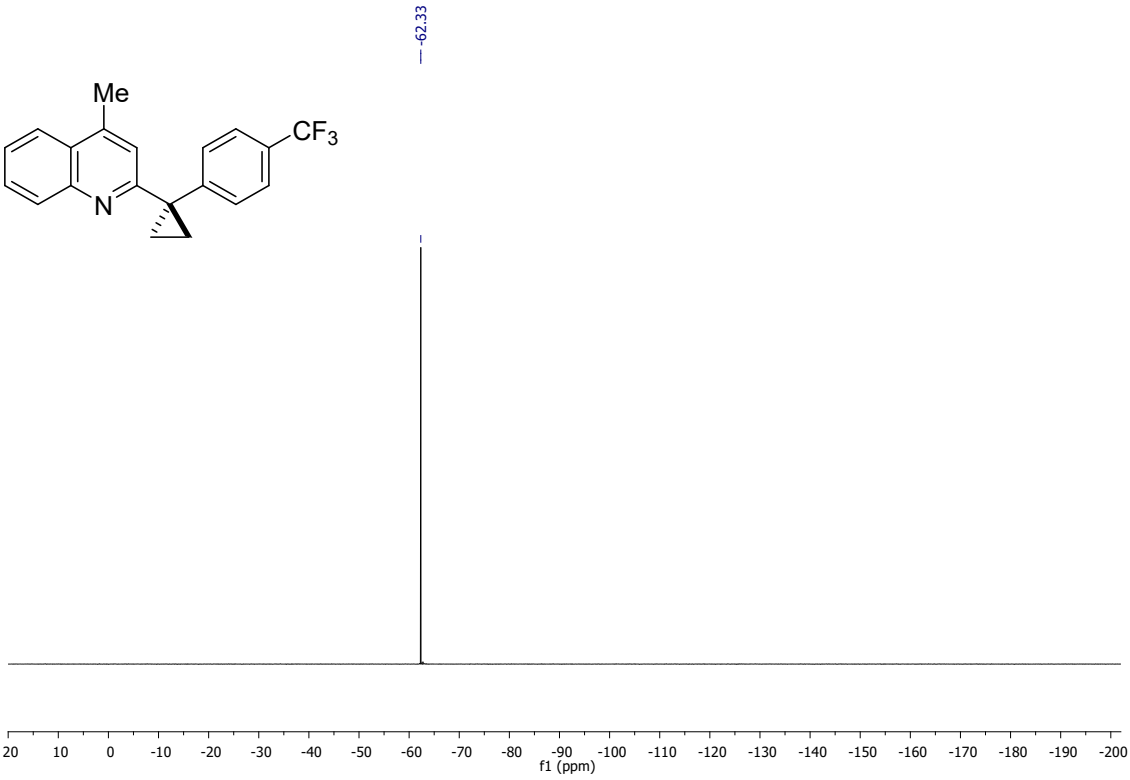


Figure S69: ^{19}F NMR spectrum of **3aj** (471 MHz, $CDCl_3$)

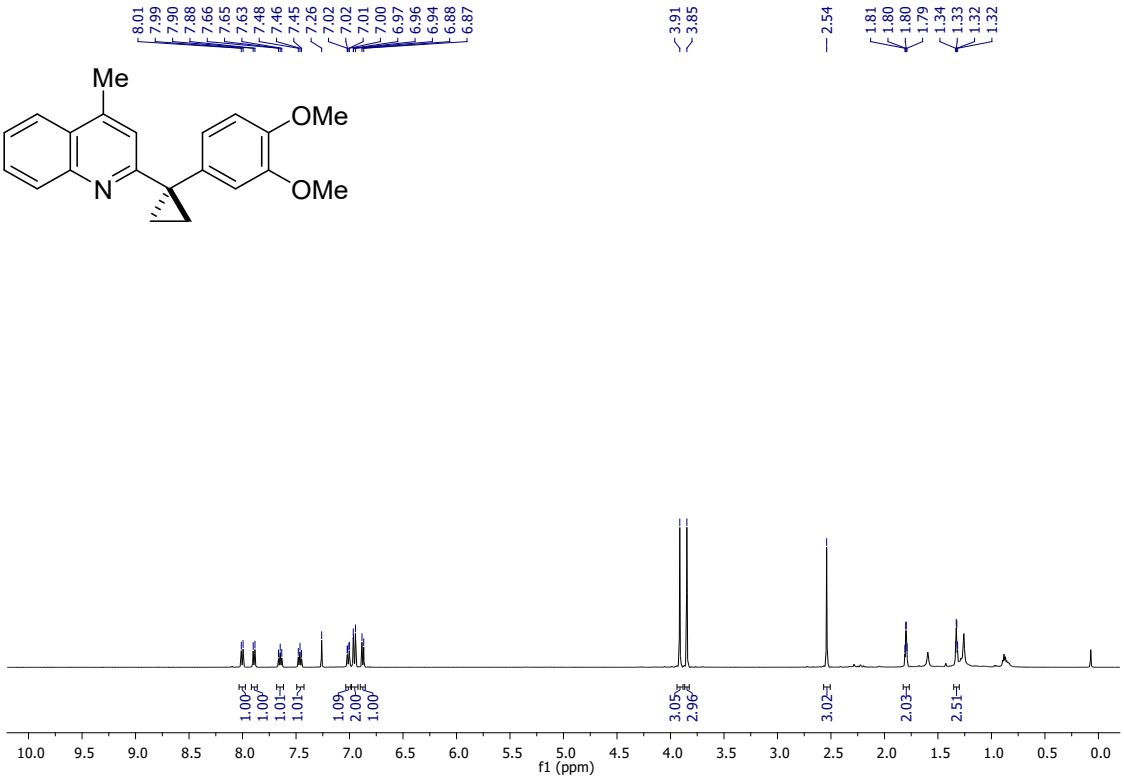


Figure S70: ^{1}H NMR spectrum of **3ak** (500 MHz, $CDCl_3$)

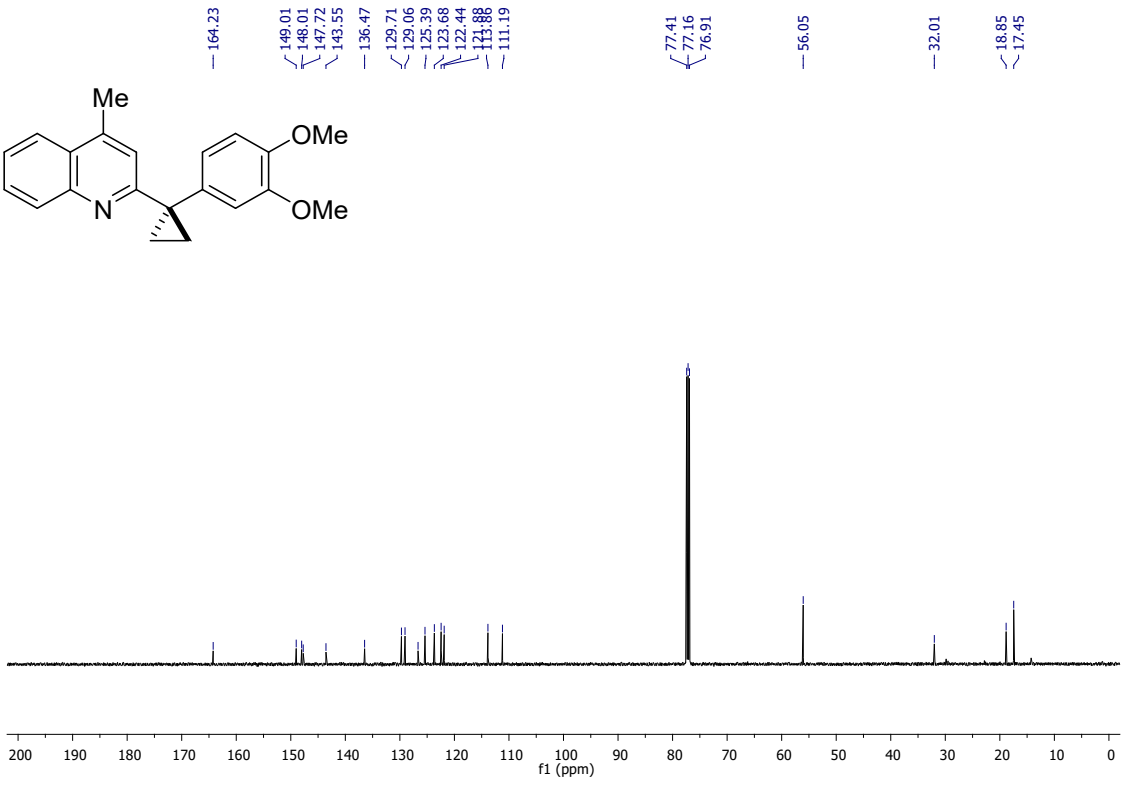


Figure S71: $^{13}C\{^{1}H\}$ NMR spectrum of **3ak** (126 MHz, $CDCl_3$)

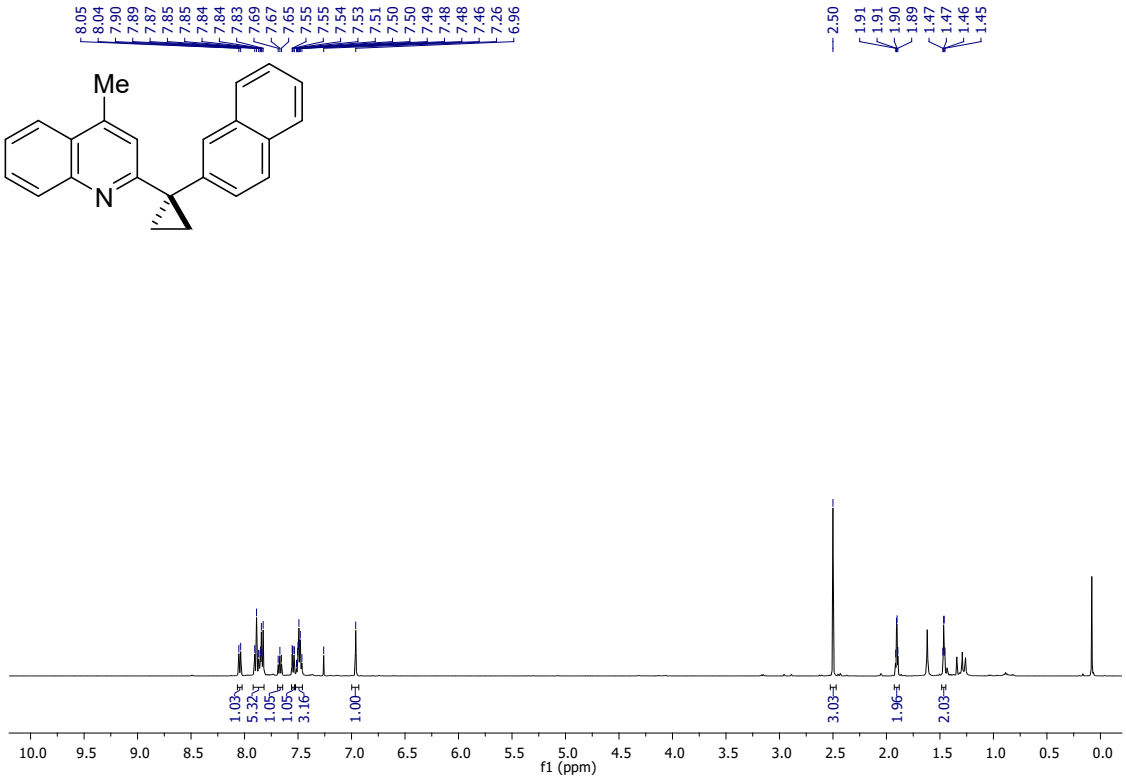


Figure S72: ^{1}H NMR spectrum of **3al** (500 MHz, $CDCl_3$)

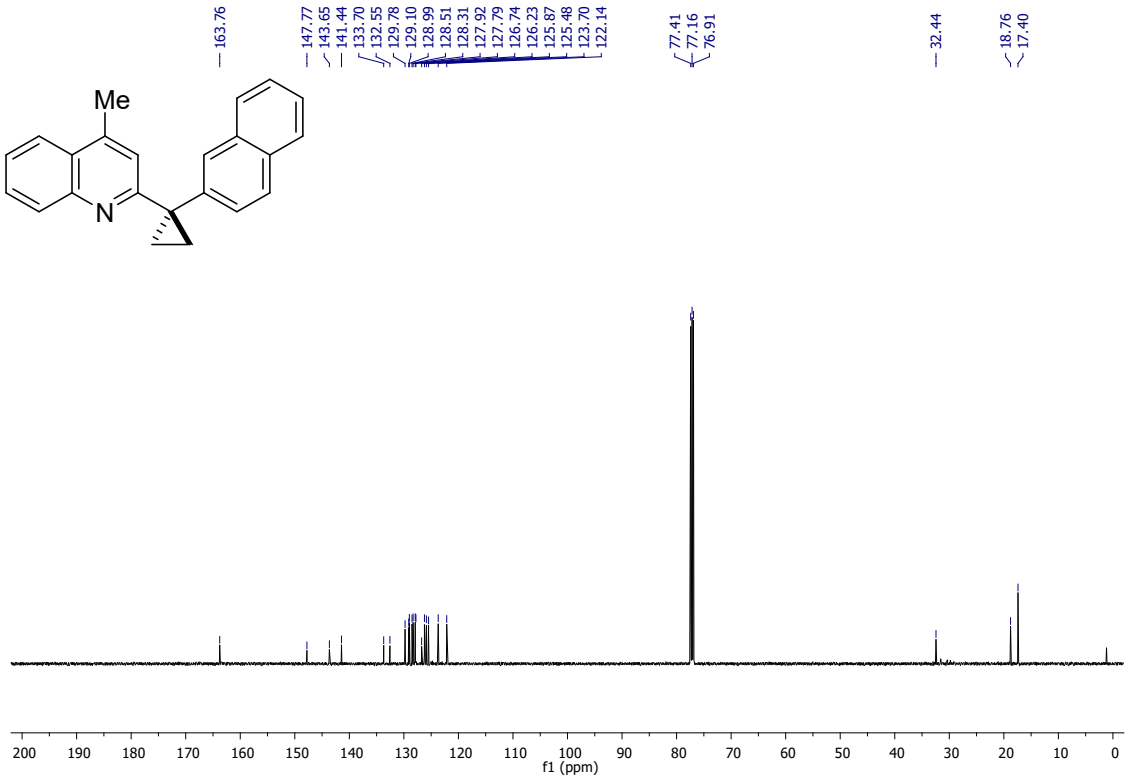


Figure S73: $^{13}C\{^{1}H\}$ NMR spectrum of **3al** (126 MHz, $CDCl_3$)

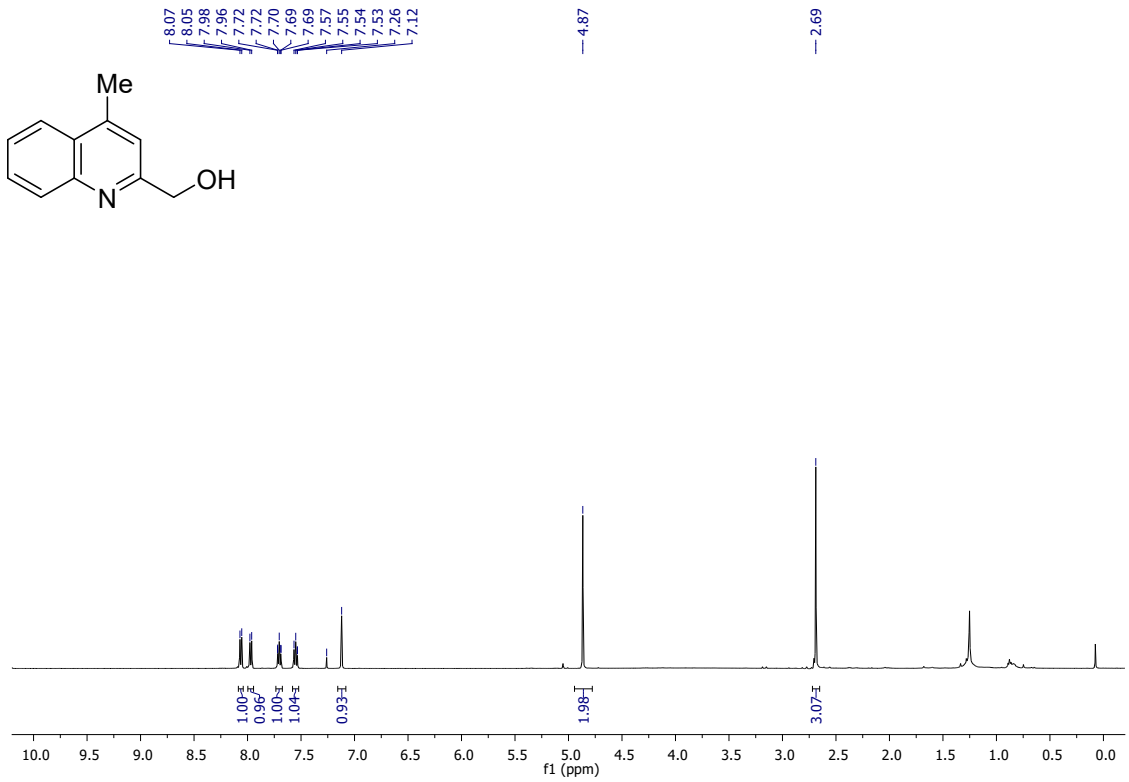


Figure S74: ^{1}H NMR spectrum of **3am** (500 MHz, $CDCl_3$)

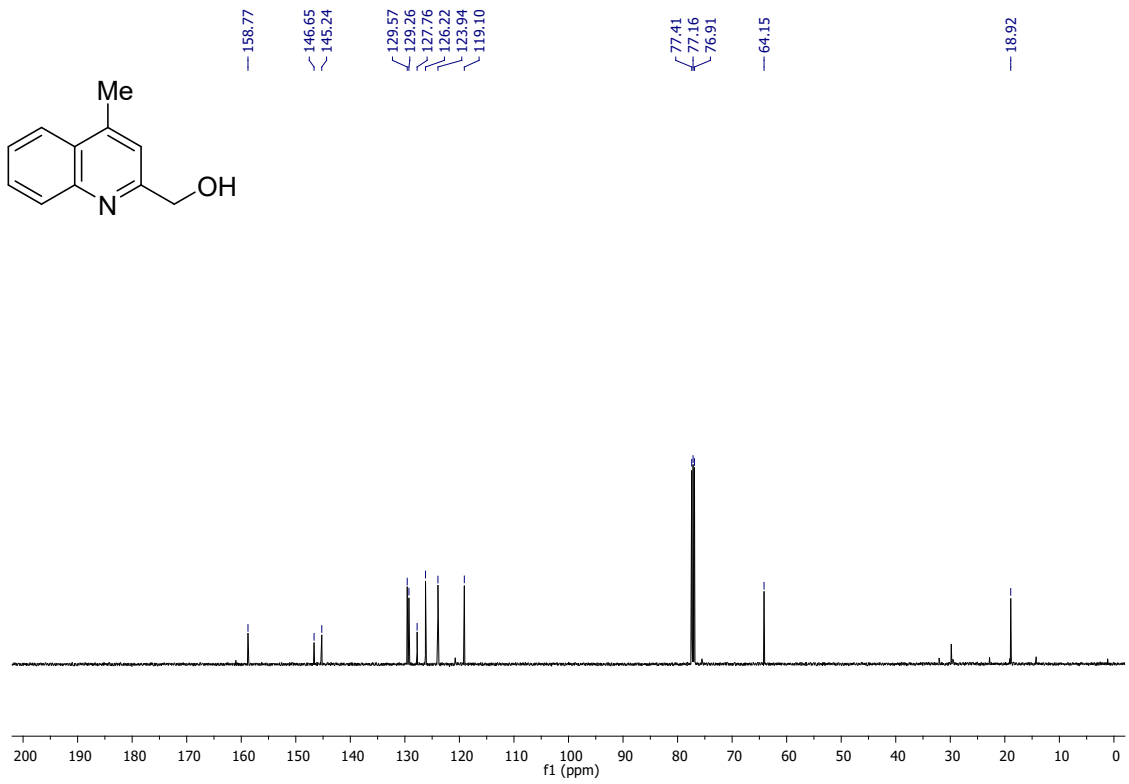


Figure S75: $^{13}C\{^{1}H\}$ NMR spectrum of **3am** (126 MHz, $CDCl_3$)

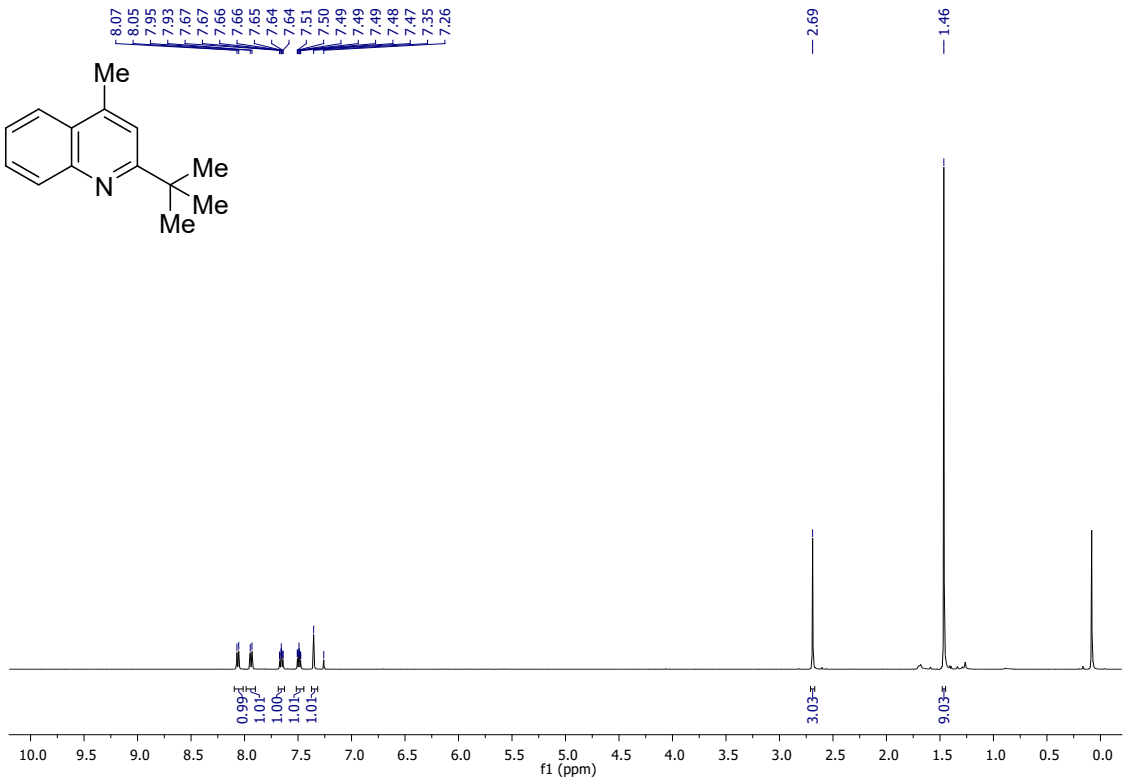


Figure S76: ^{1}H NMR spectrum of **3an** (500 MHz, $CDCl_3$)

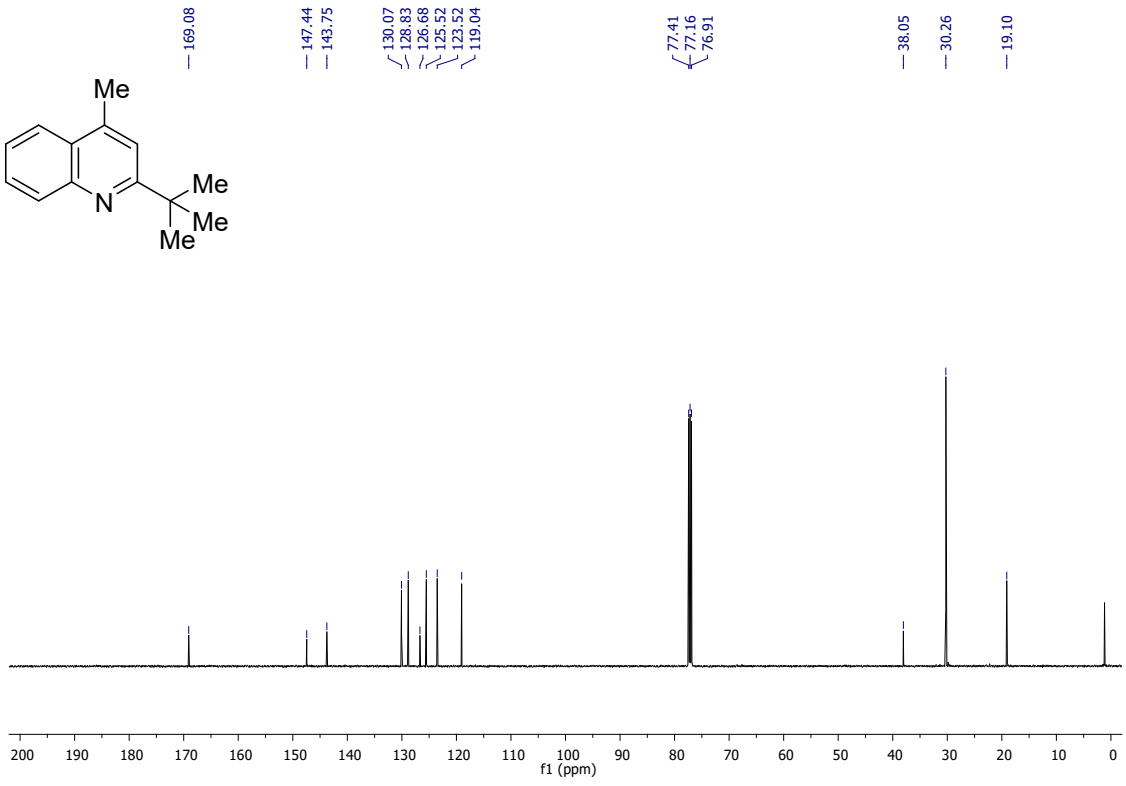


Figure S77: $^{13}C\{^{1}H\}$ NMR spectrum of **3an** (126 MHz, $CDCl_3$)

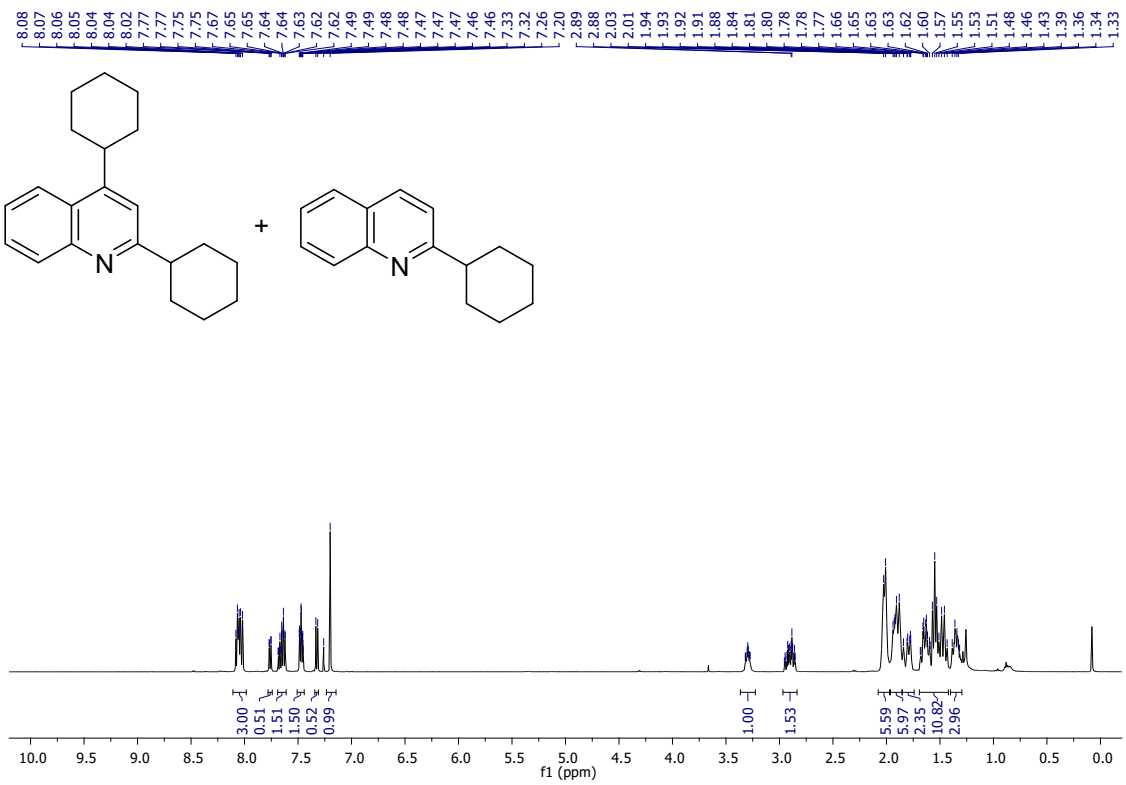


Figure S78: ^{1}H NMR spectrum of **3bd, 3bd'** (500 MHz, $CDCl_3$)

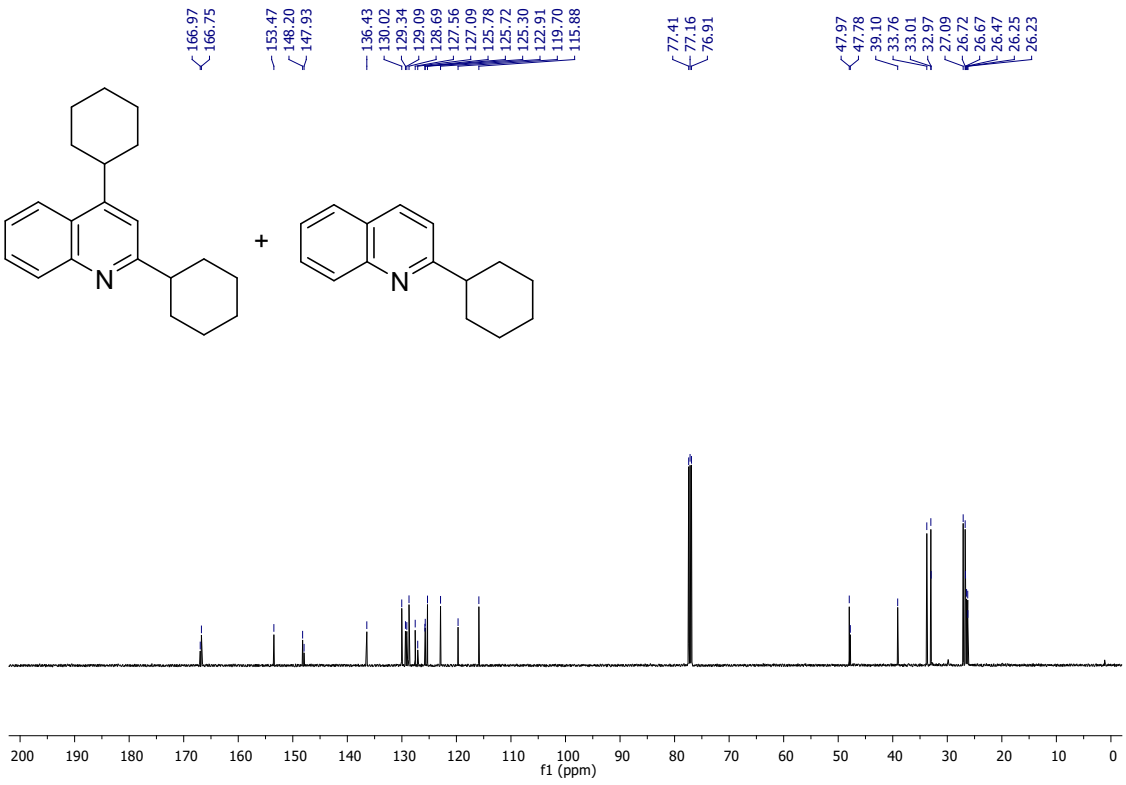


Figure S79: $^{13}C\{^{1}H\}$ NMR spectrum of **3bd, 3bd'** (126 MHz, $CDCl_3$)

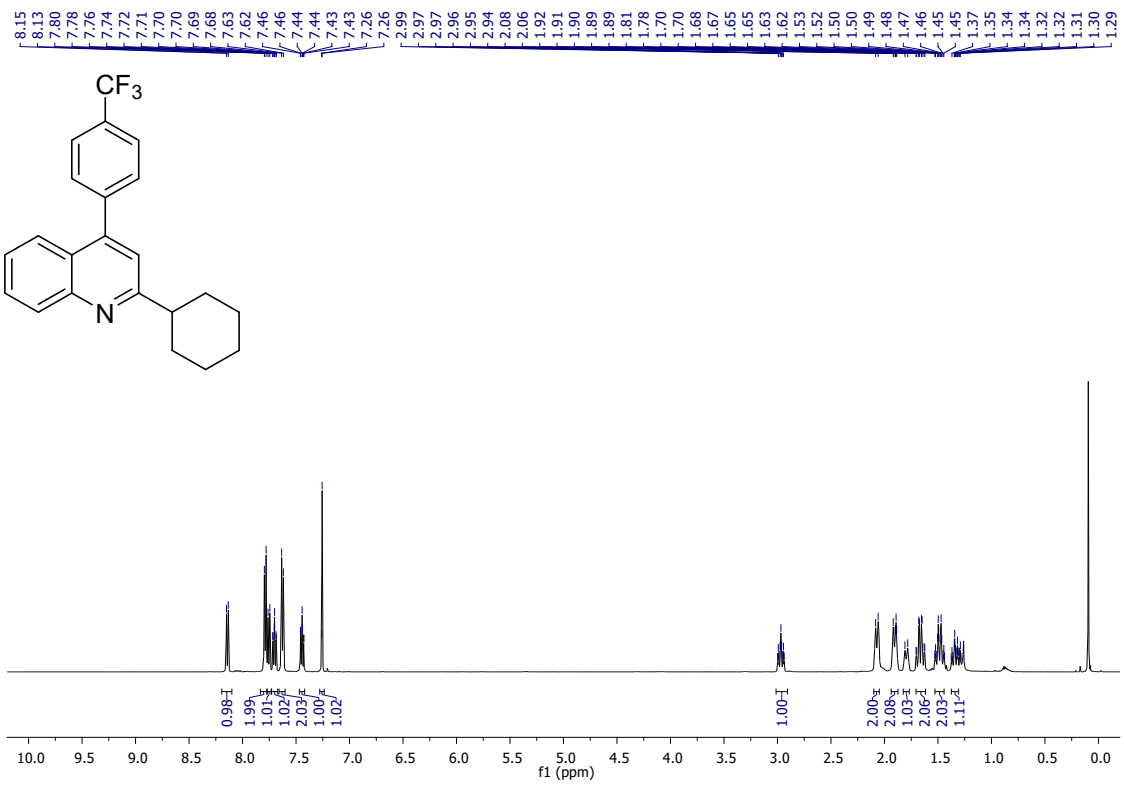


Figure S80: ^{1}H NMR spectrum of **3cd** (500 MHz, $CDCl_3$)

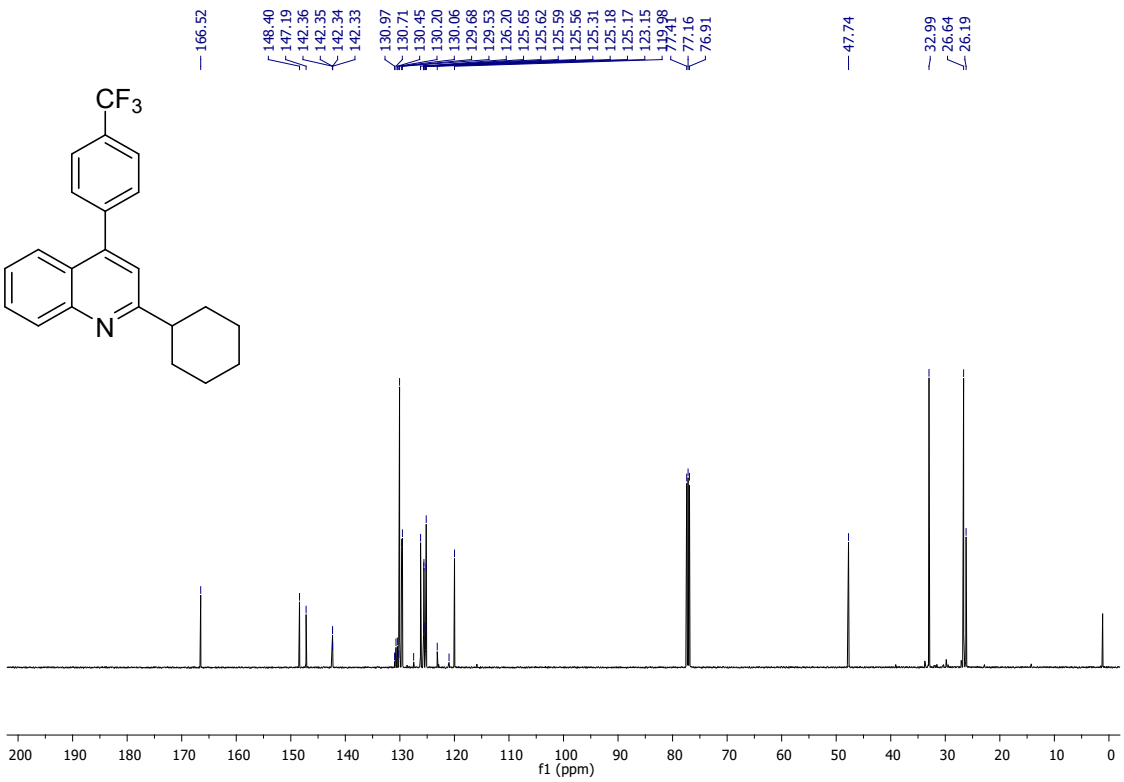


Figure S81: $^{13}C\{^{1}H\}$ NMR spectrum of **3cd** (126 MHz, $CDCl_3$)

Figure S82: ^{19}F NMR spectrum of **3cd** (471 MHz, $CDCl_3$)

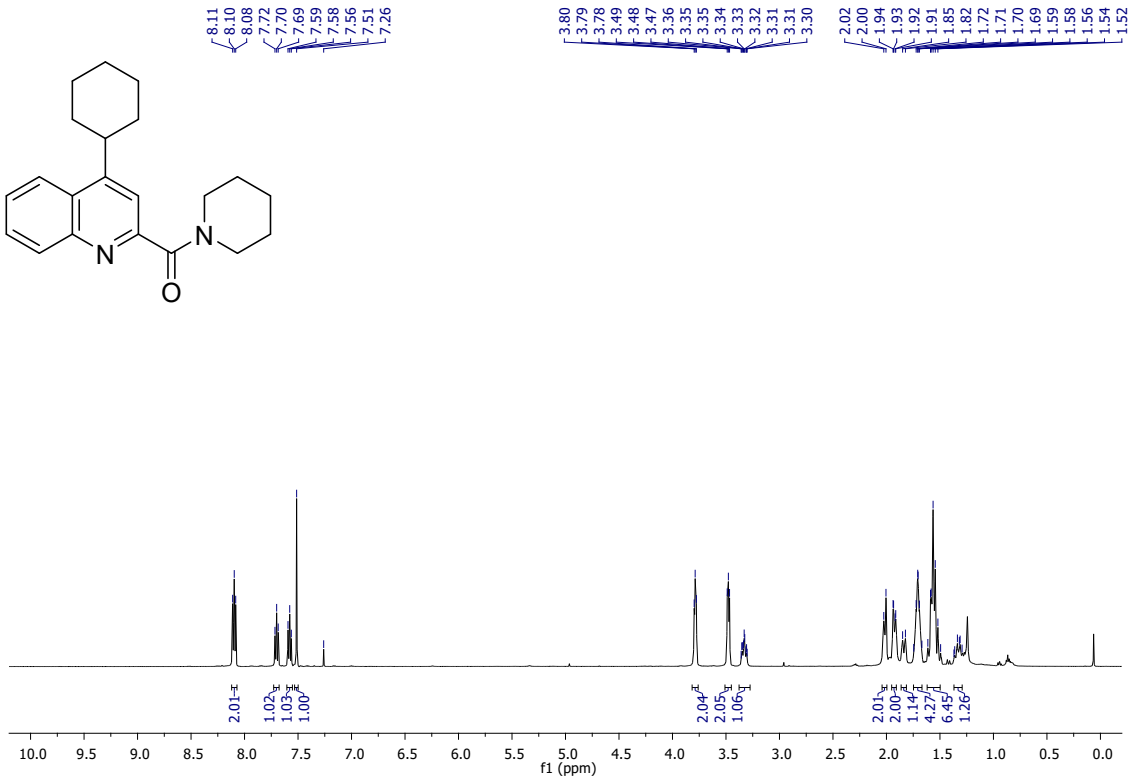


Figure S83: ^{1}H NMR spectrum of **3dd** (500 MHz, $CDCl_3$)

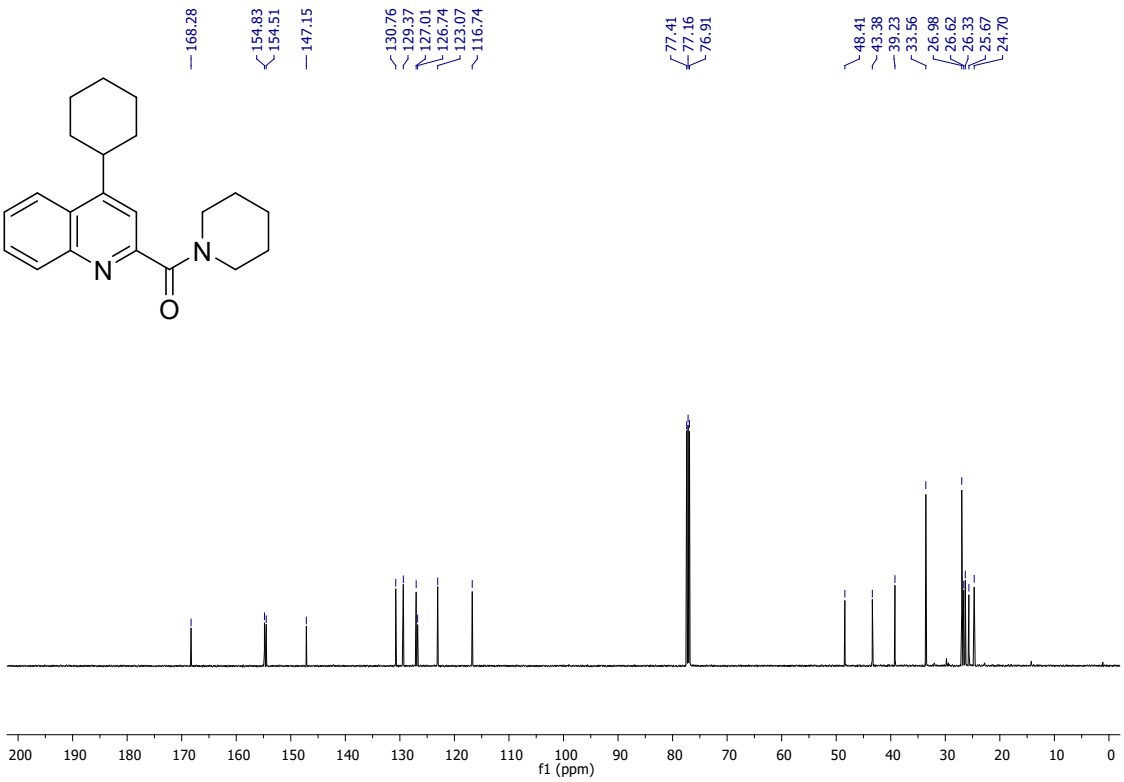


Figure S84: $^{13}C\{^{1}H\}$ NMR spectrum of **3dd** (126 MHz, $CDCl_3$)

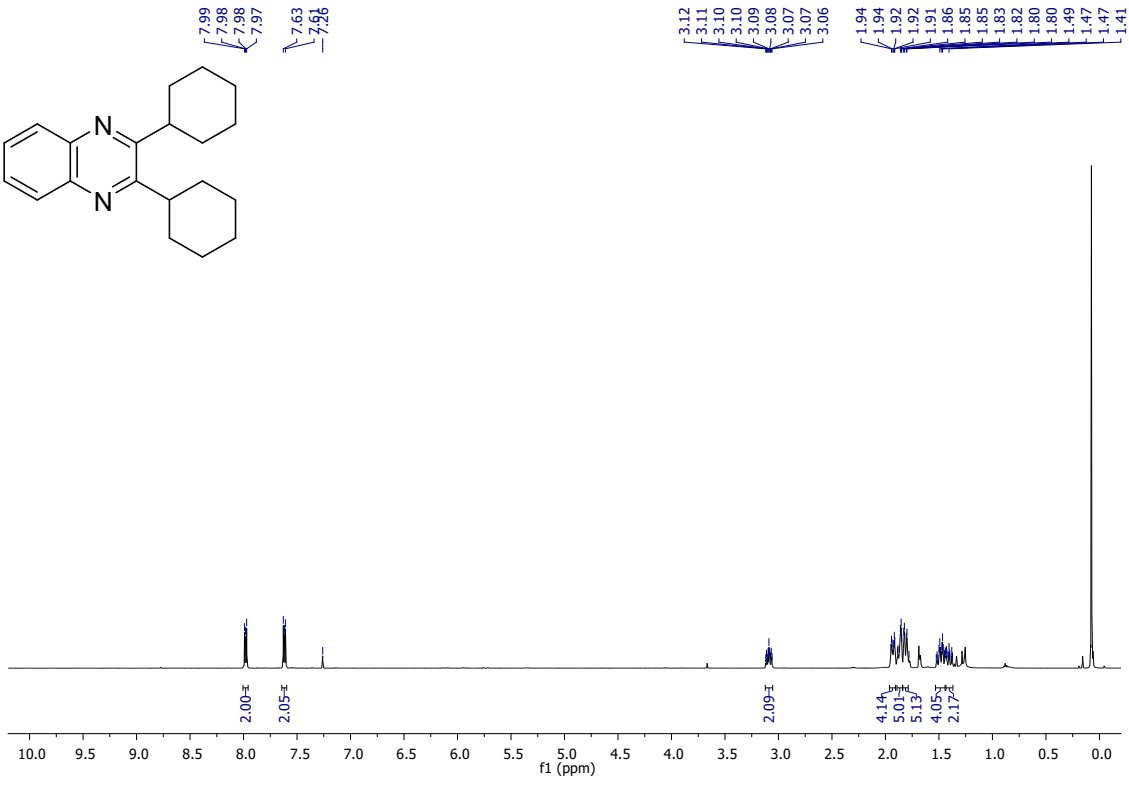


Figure S85: ^{1}H NMR spectrum of **3ed** (500 MHz, $CDCl_3$)

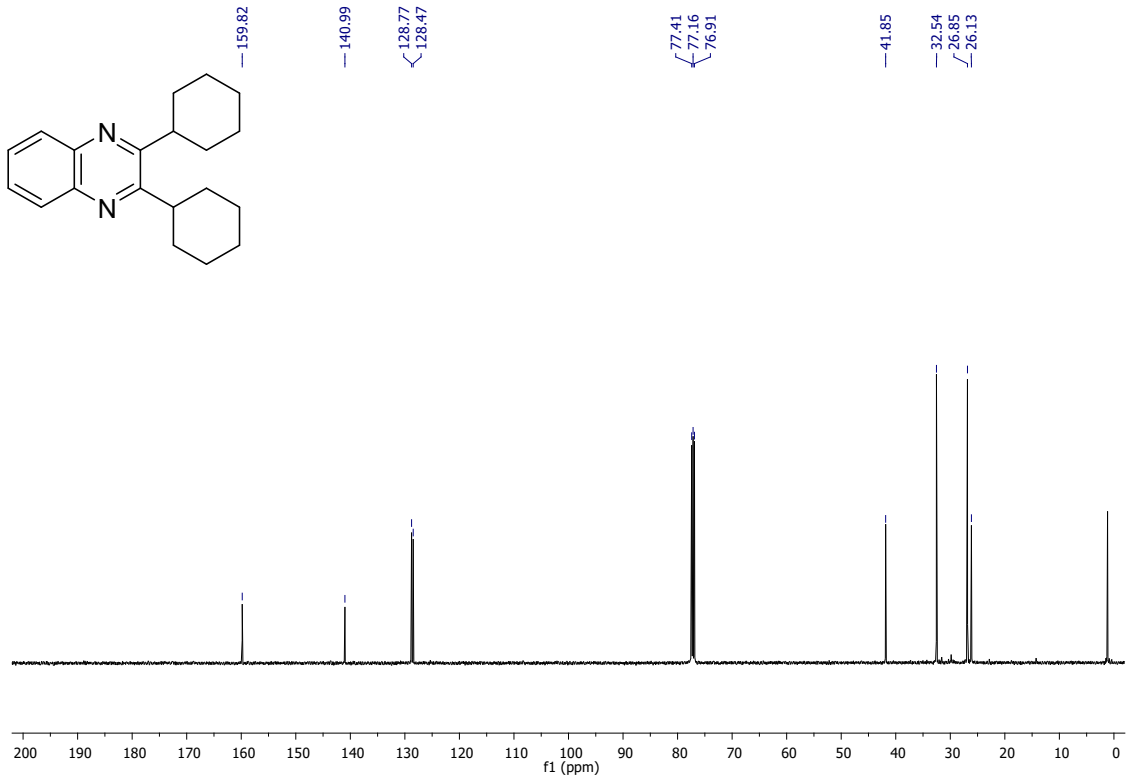


Figure S86: $^{13}C\{^{1}H\}$ NMR spectrum of **3ed** (126 MHz, $CDCl_3$)

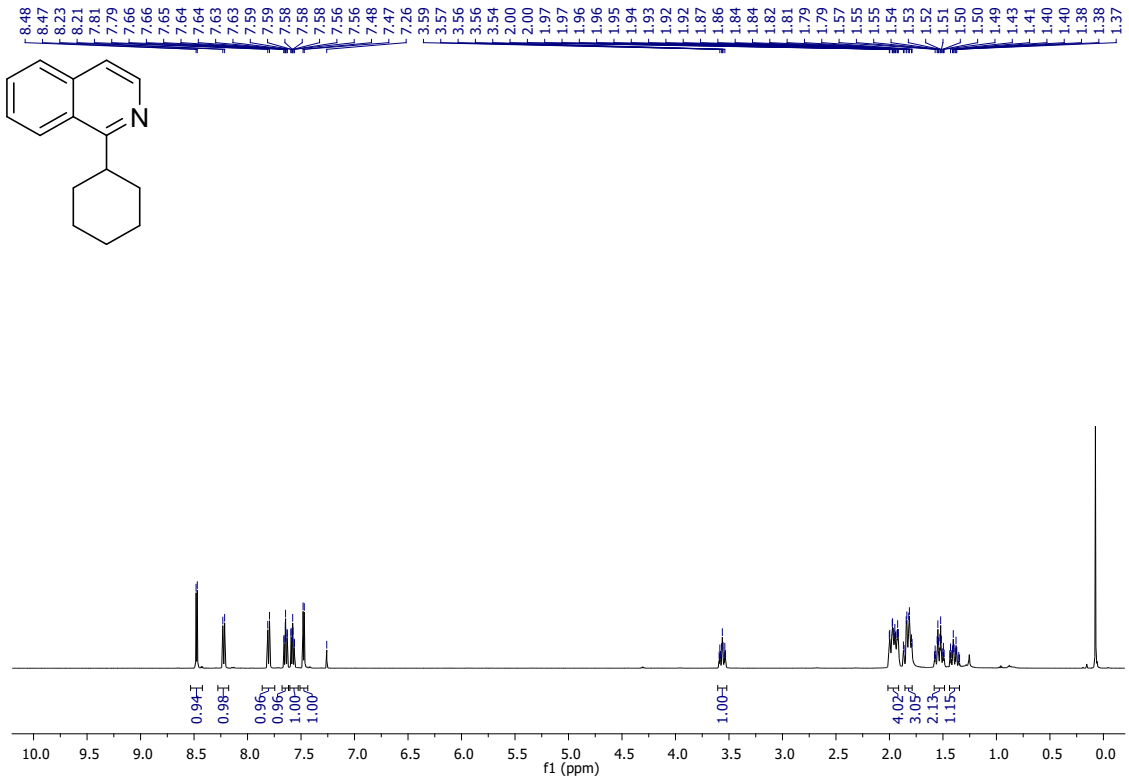


Figure S87: ^{1}H NMR spectrum of **3fd** (500 MHz, $CDCl_3$)

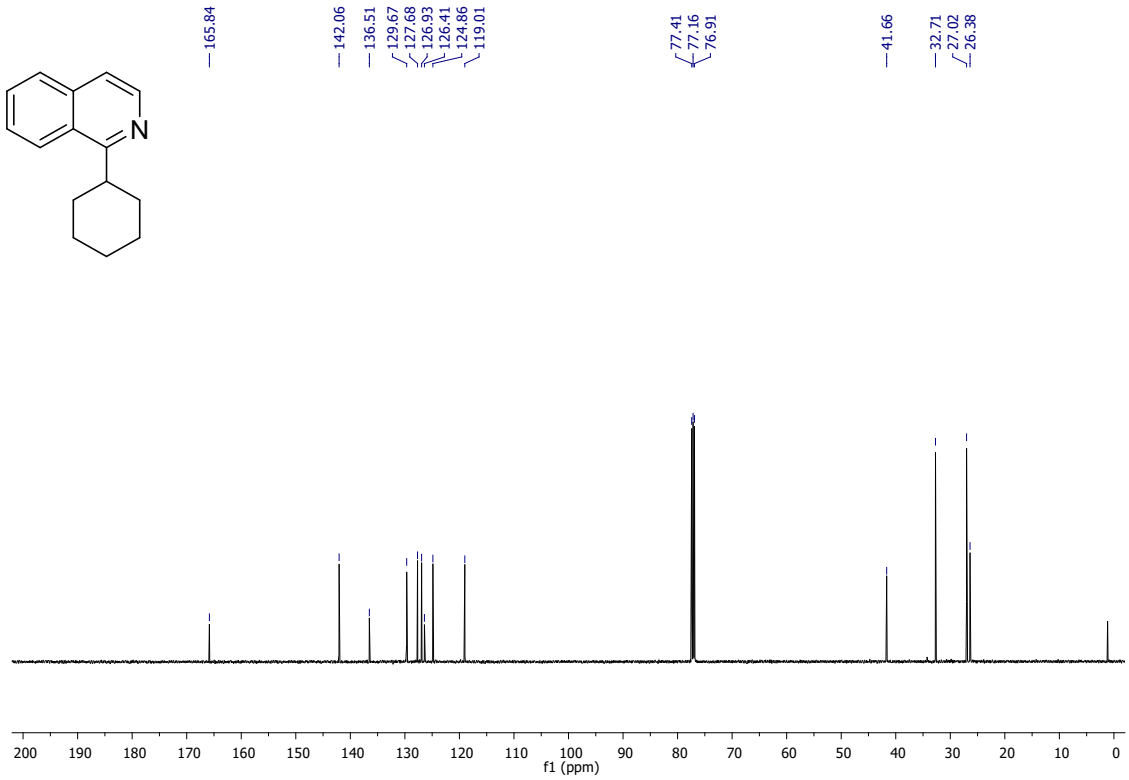


Figure S88: $^{13}C\{^{1}H\}$ NMR spectrum of **3fd** (126 MHz, $CDCl_3$)

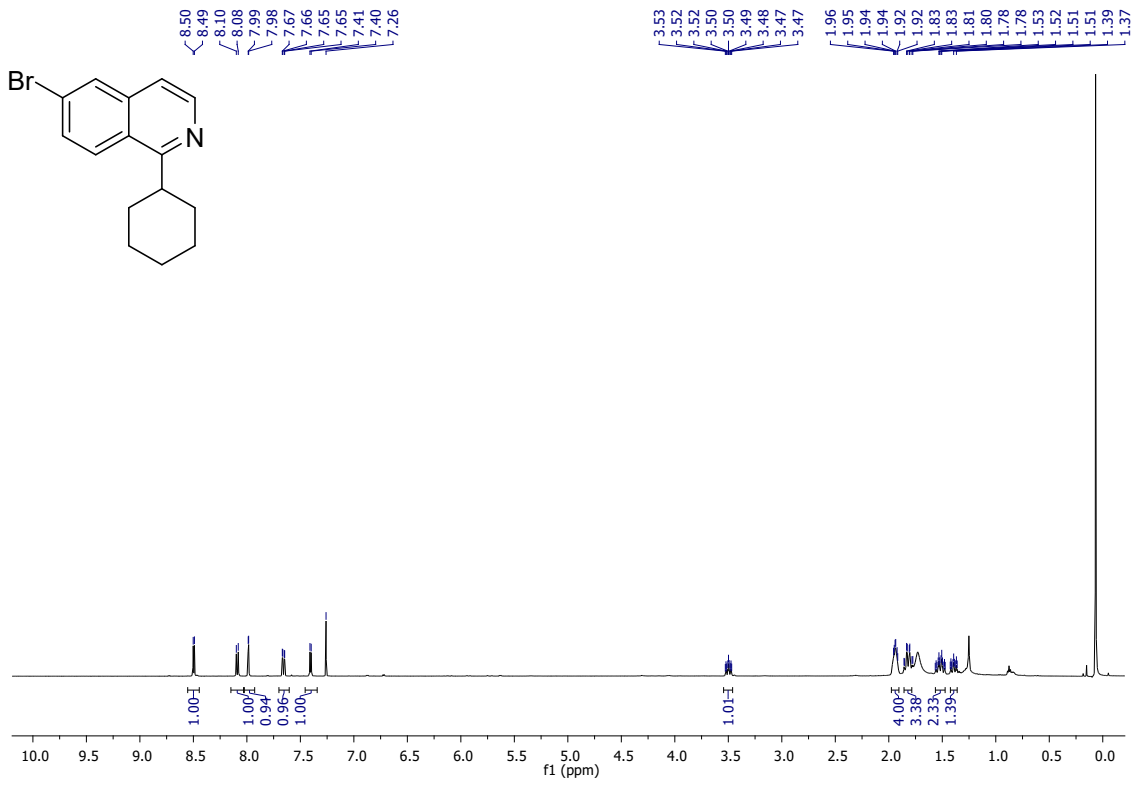


Figure S89: ^{1}H NMR spectrum of **3gd** (500 MHz, $CDCl_3$)

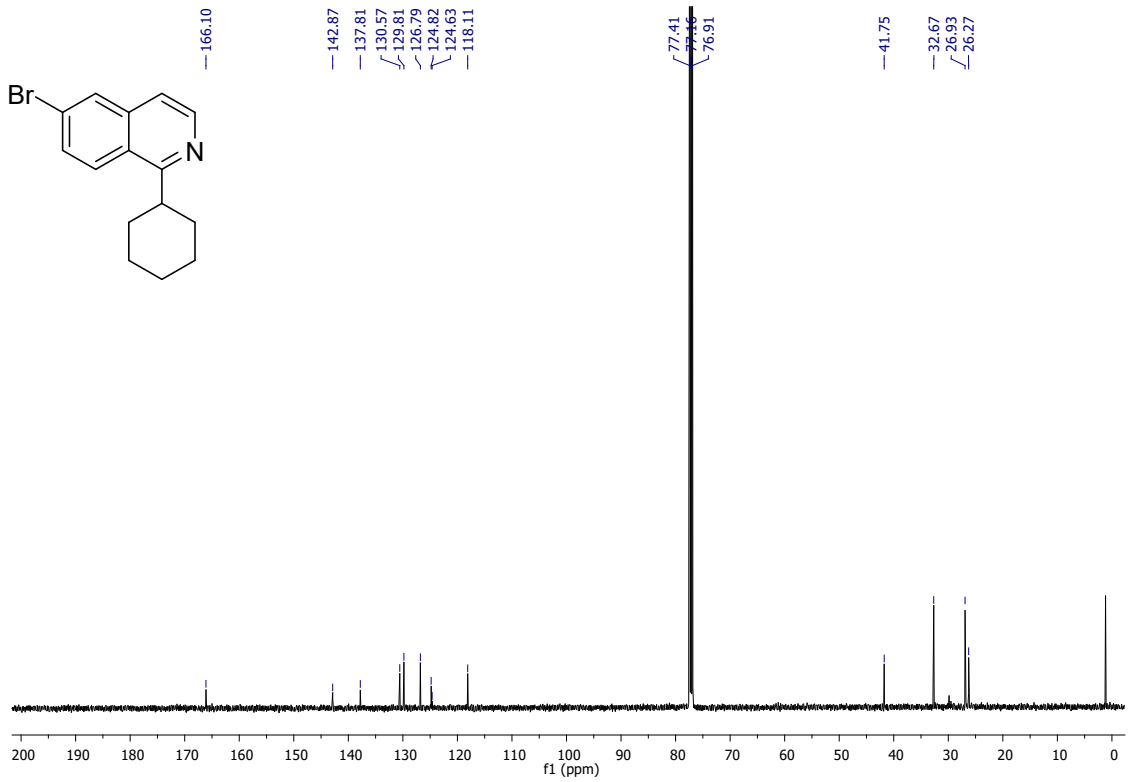


Figure S90: $^{13}C\{^{1}H\}$ NMR spectrum of **3gd** (126 MHz, $CDCl_3$)

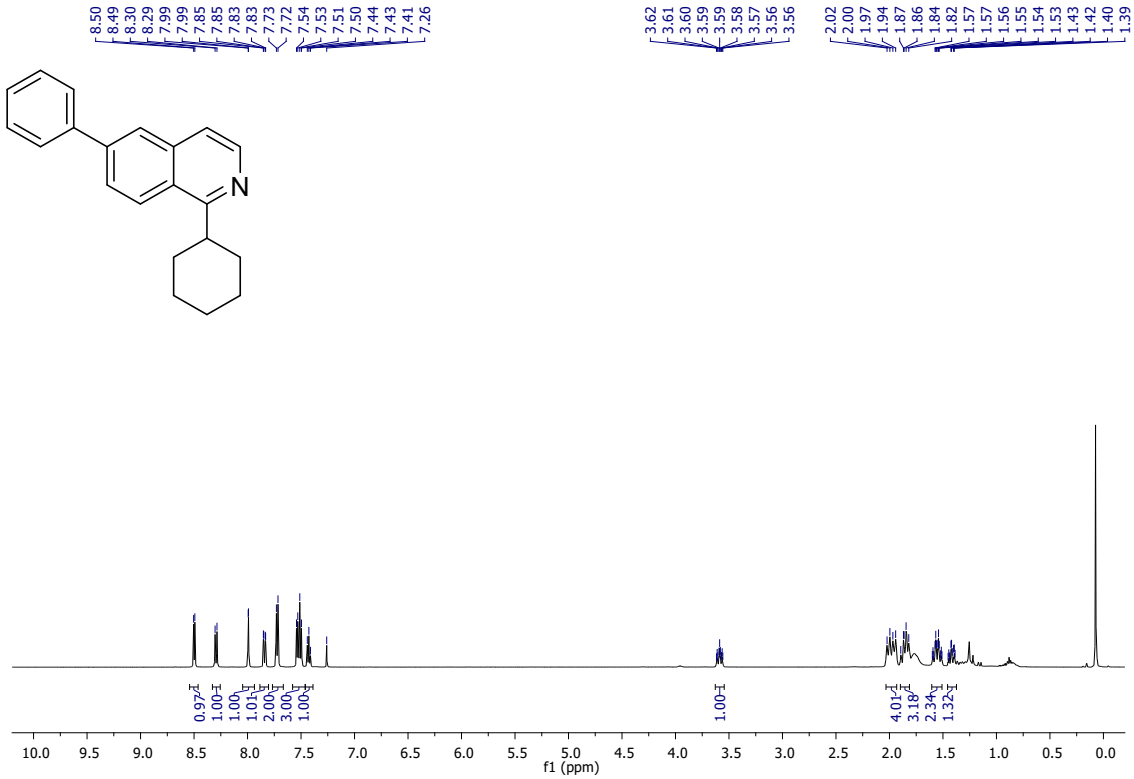


Figure S91: ^{1}H NMR spectrum of **3hd** (500 MHz, $CDCl_3$)

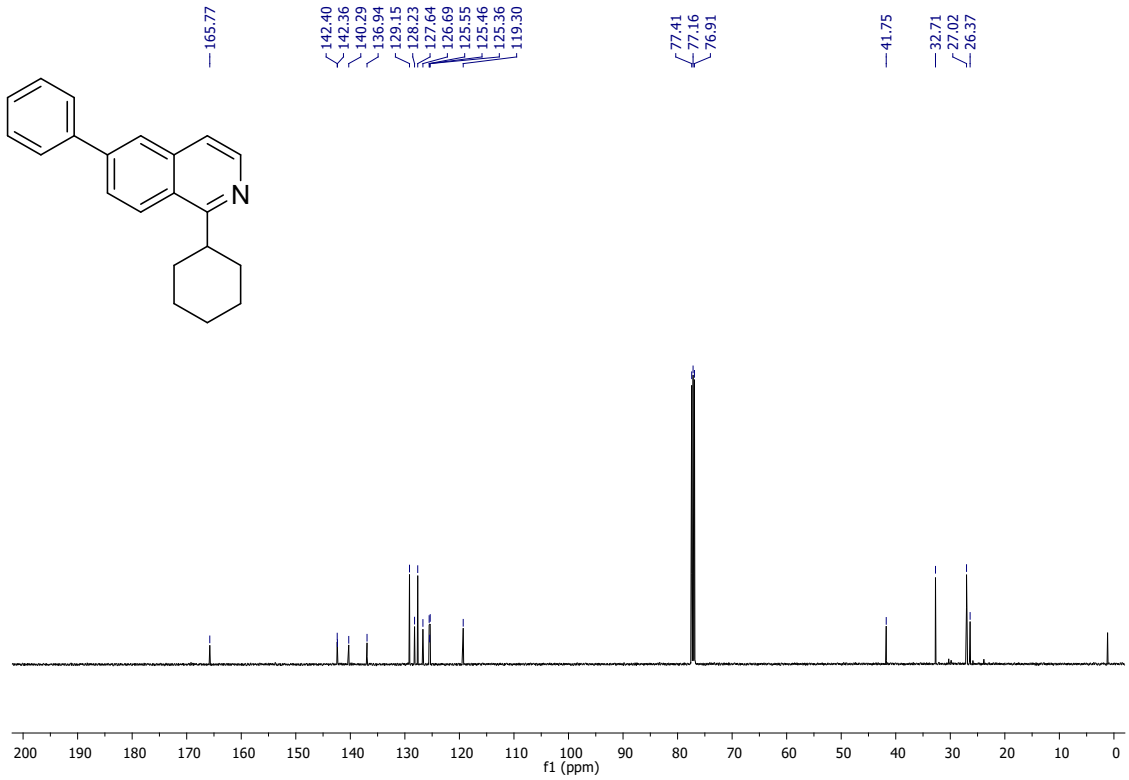


Figure S92: $^{13}C\{^{1}H\}$ NMR spectrum of **3hd** (126 MHz, $CDCl_3$)

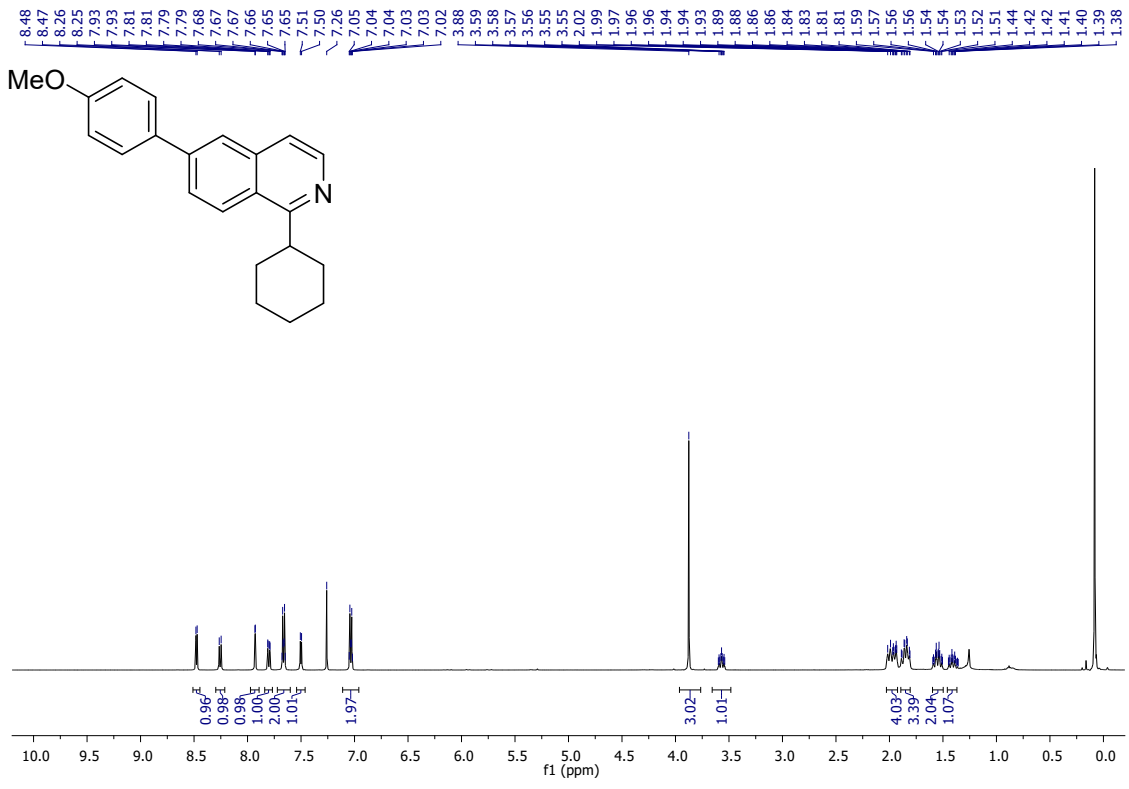


Figure S93: ^{1}H NMR spectrum of **3id** (500 MHz, $CDCl_3$)

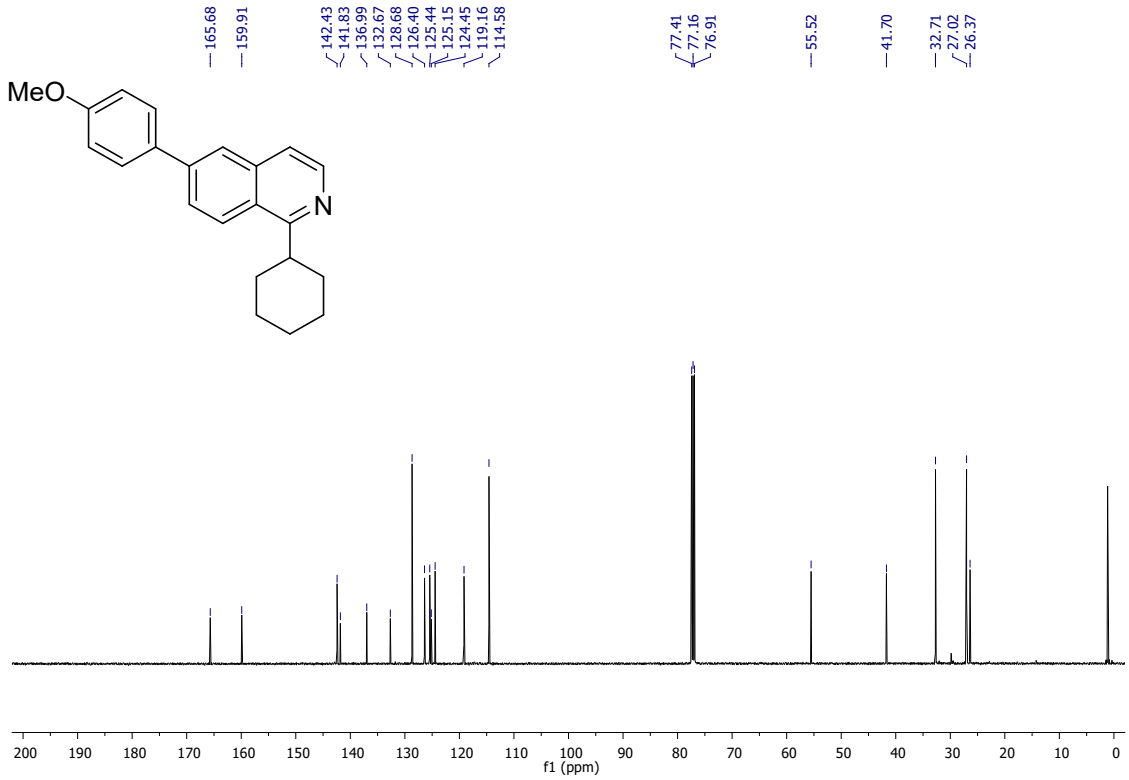


Figure S94: $^{13}C\{^{1}H\}$ NMR spectrum of **3id** (126 MHz, $CDCl_3$)

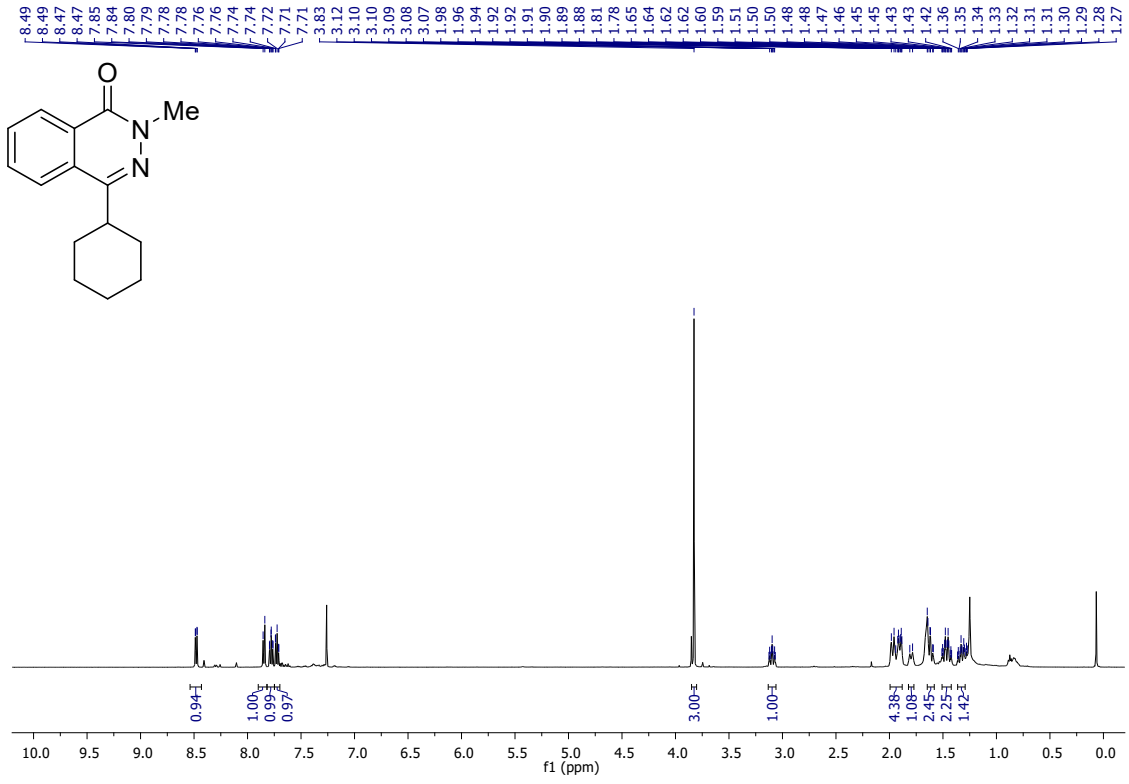


Figure S95: ^{1}H NMR spectrum of **3jd** (500 MHz, $CDCl_3$)

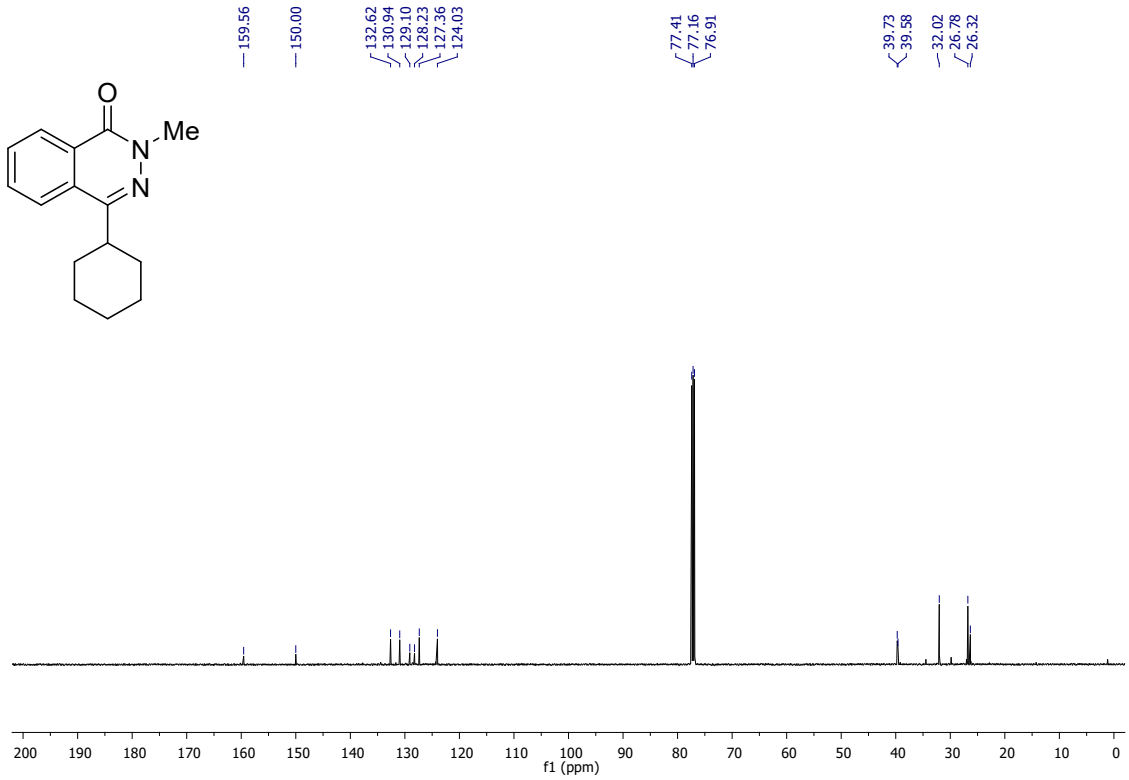


Figure S96: $^{13}C\{^{1}H\}$ NMR spectrum of **3jd** (126 MHz, $CDCl_3$)

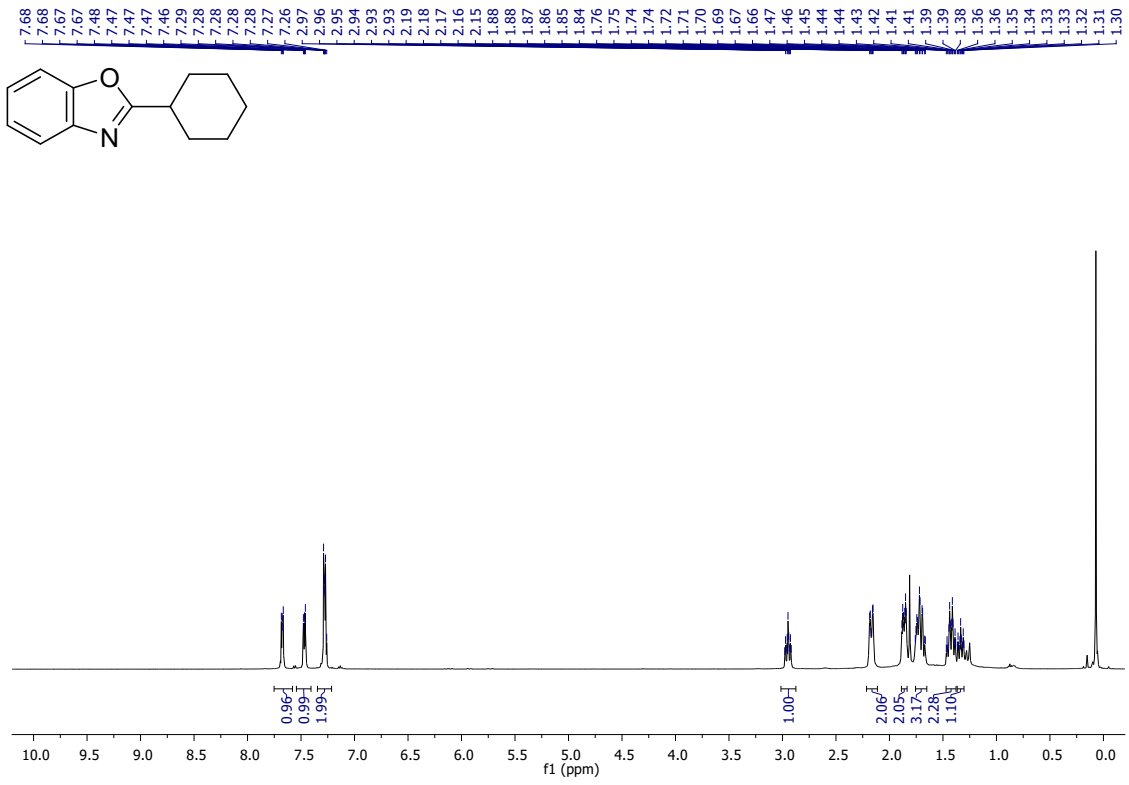


Figure S97: ^{1}H NMR spectrum of **3kd**(500 MHz, $CDCl_3$)

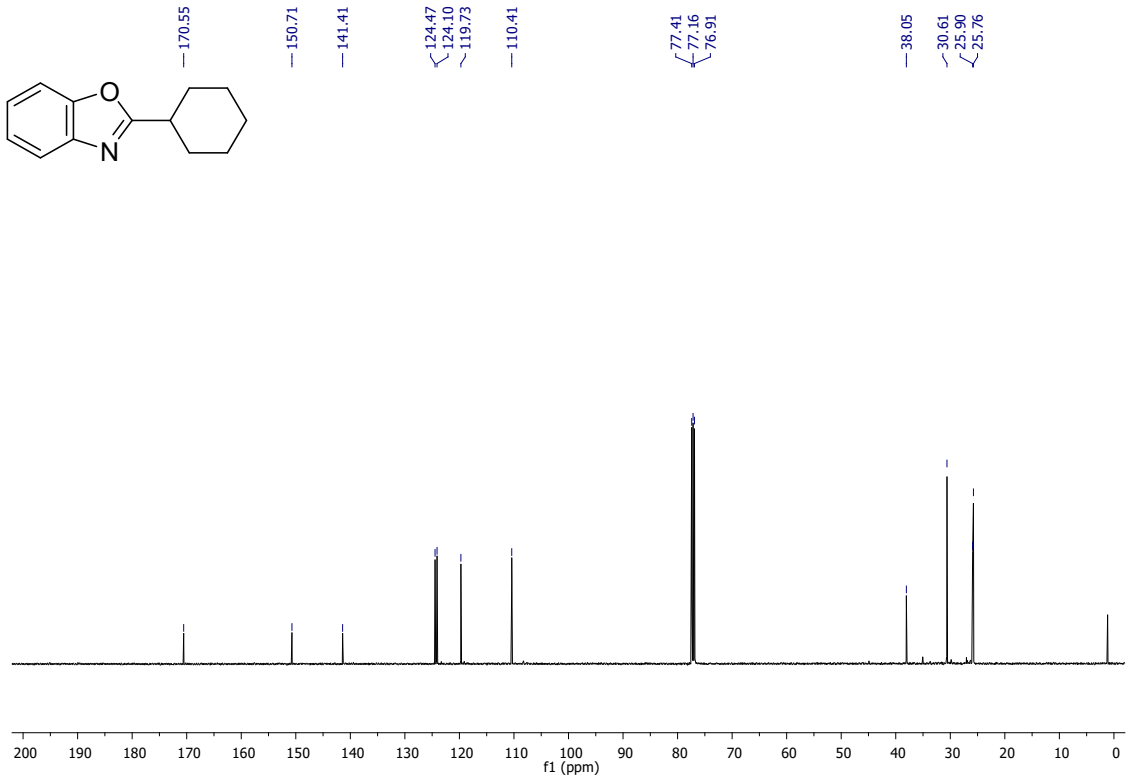


Figure S98: $^{13}C\{^{1}H\}$ NMR spectrum of **3kd** (126 MHz, $CDCl_3$)

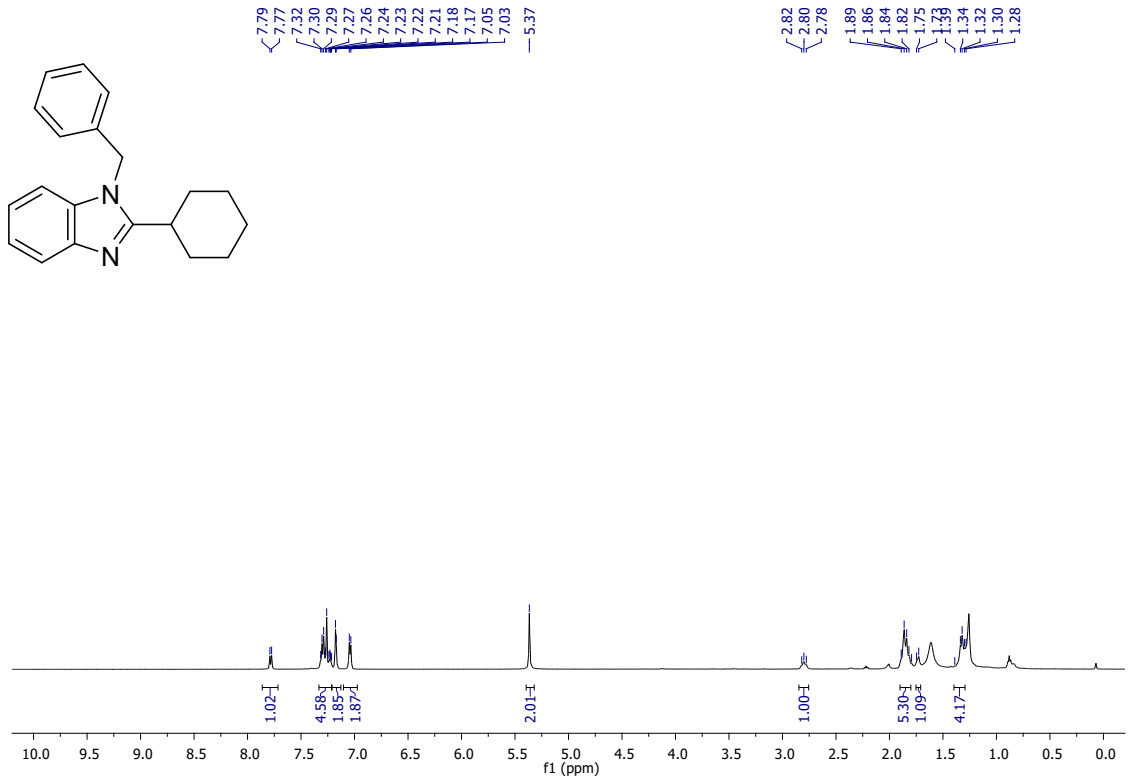


Figure S99: ^{1}H NMR spectrum of **3ld** (500 MHz, $CDCl_3$)

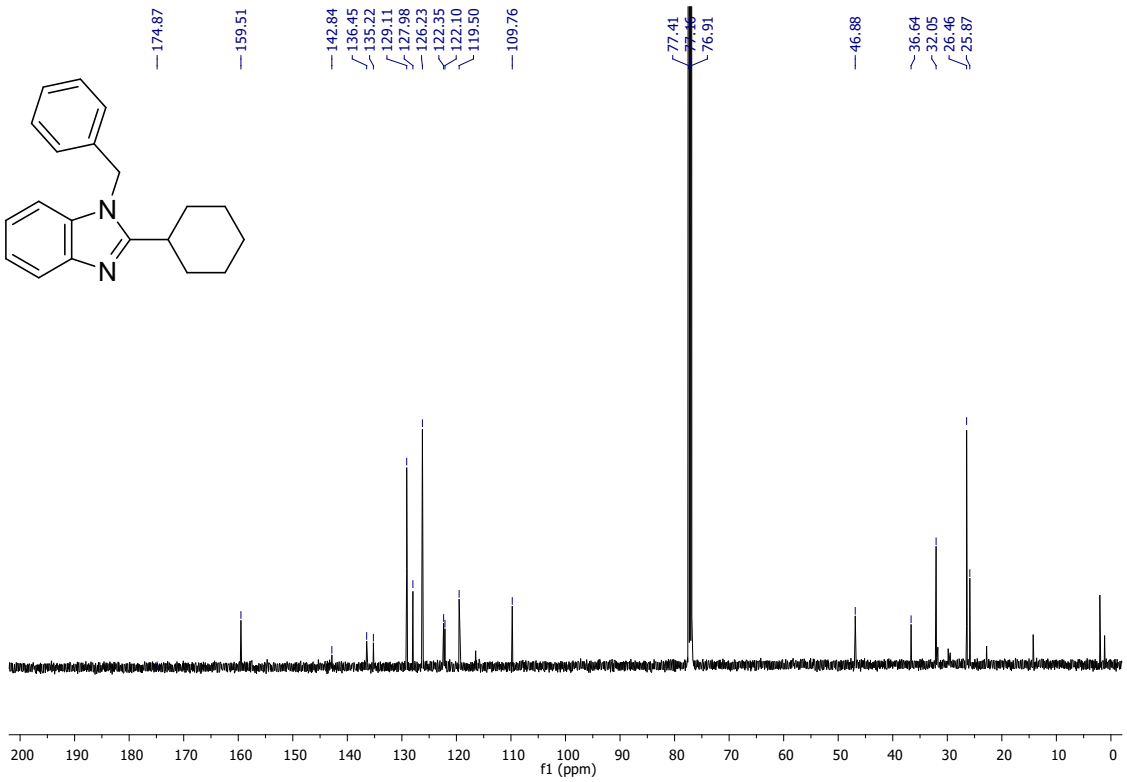


Figure S100: $^{13}C\{^{1}H\}$ NMR spectrum of **3ld** (126 MHz, $CDCl_3$)

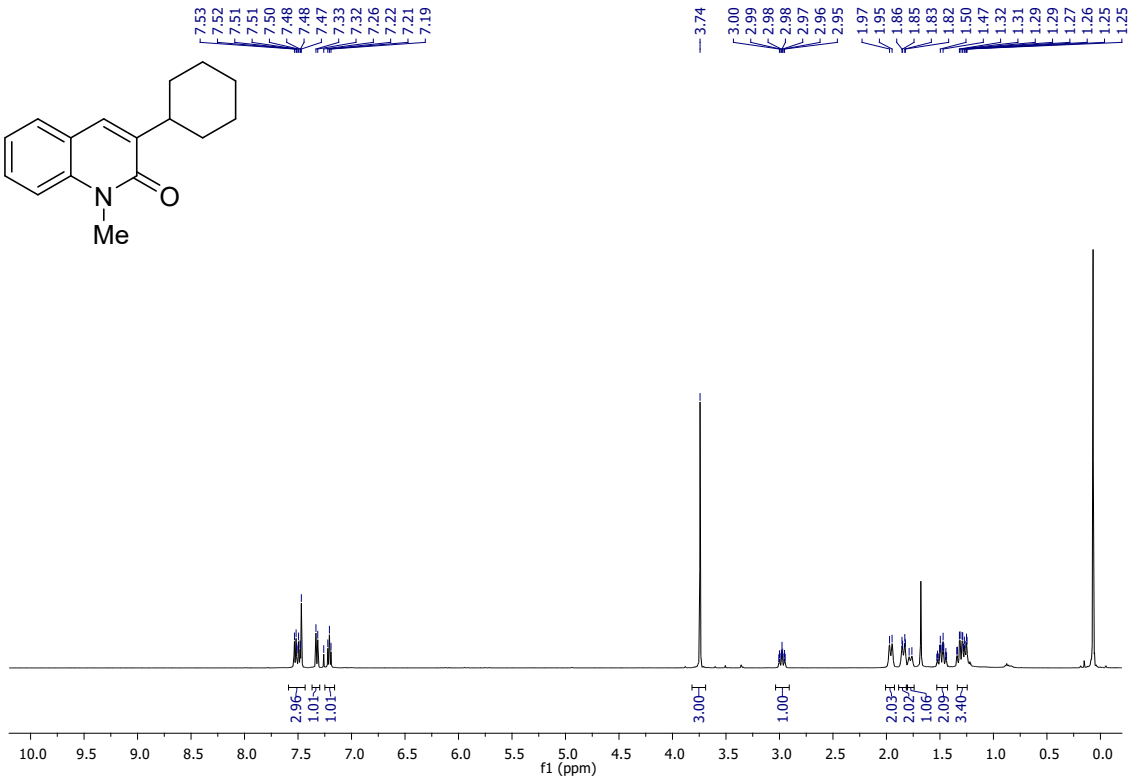


Figure S101: ^{1}H NMR spectrum of **3md** (500 MHz, $CDCl_3$)

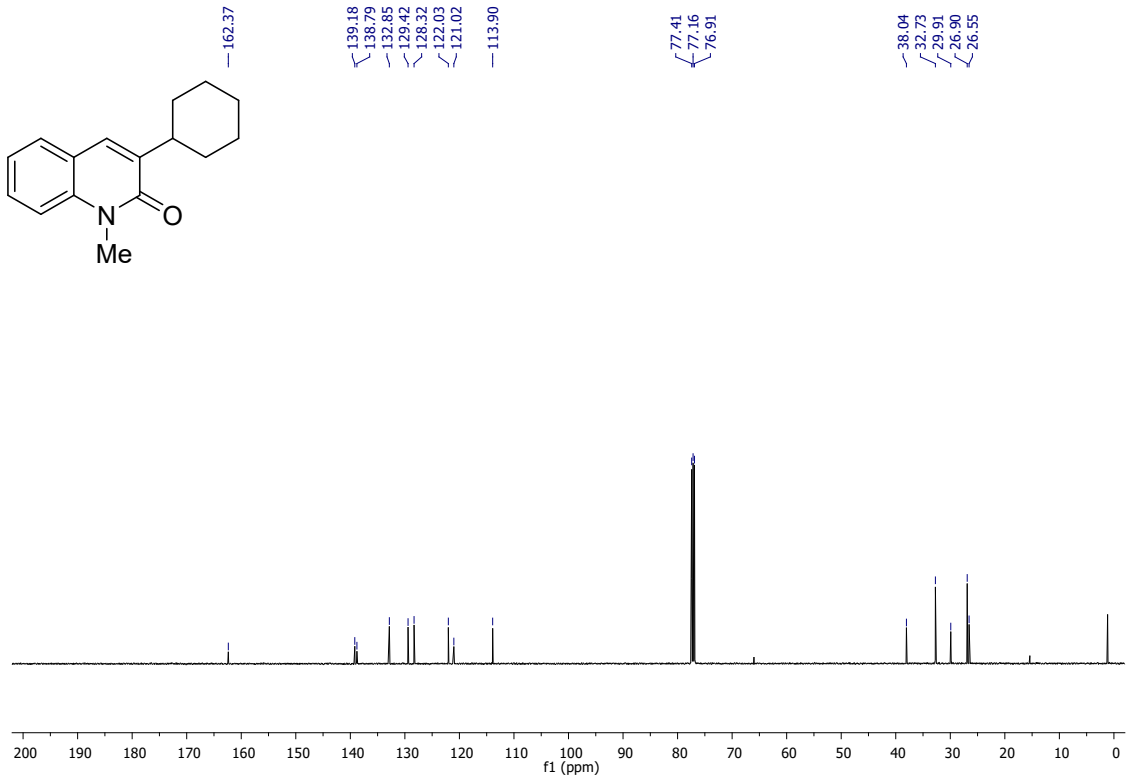


Figure S102: $^{13}C\{^{1}H\}$ NMR spectrum of **3md** (126 MHz, $CDCl_3$)

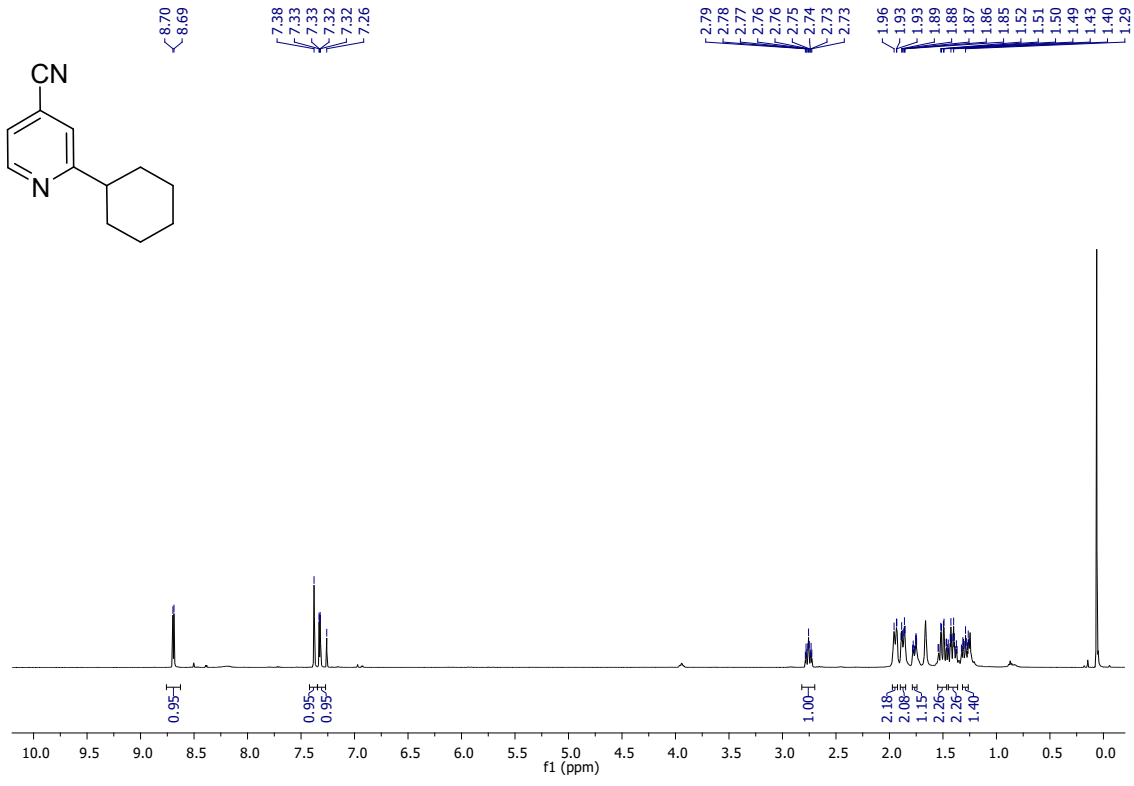


Figure S103: ^{1}H NMR spectrum of **3nd** (500 MHz, $CDCl_3$)

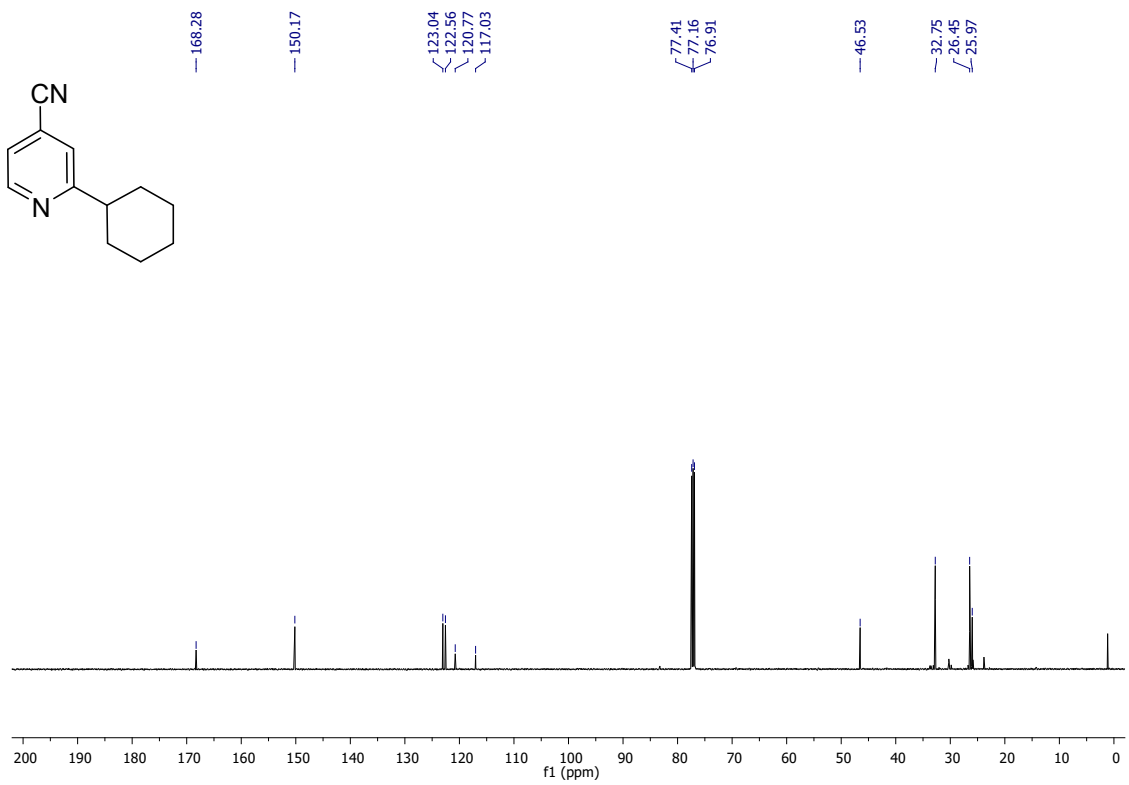


Figure S104: $^{13}C\{^{1}H\}$ NMR spectrum of **3nd** (126 MHz, $CDCl_3$)

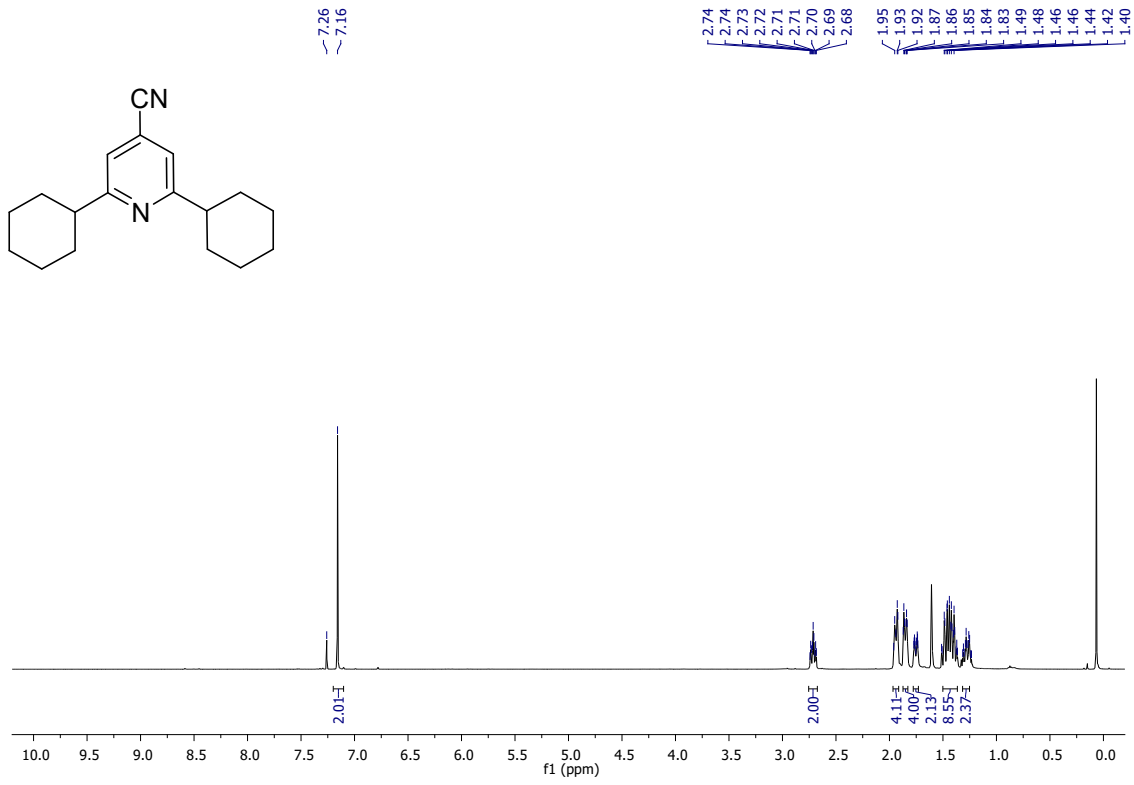


Figure S105: ^{1}H NMR spectrum of **3nd'** (500 MHz, $CDCl_3$)

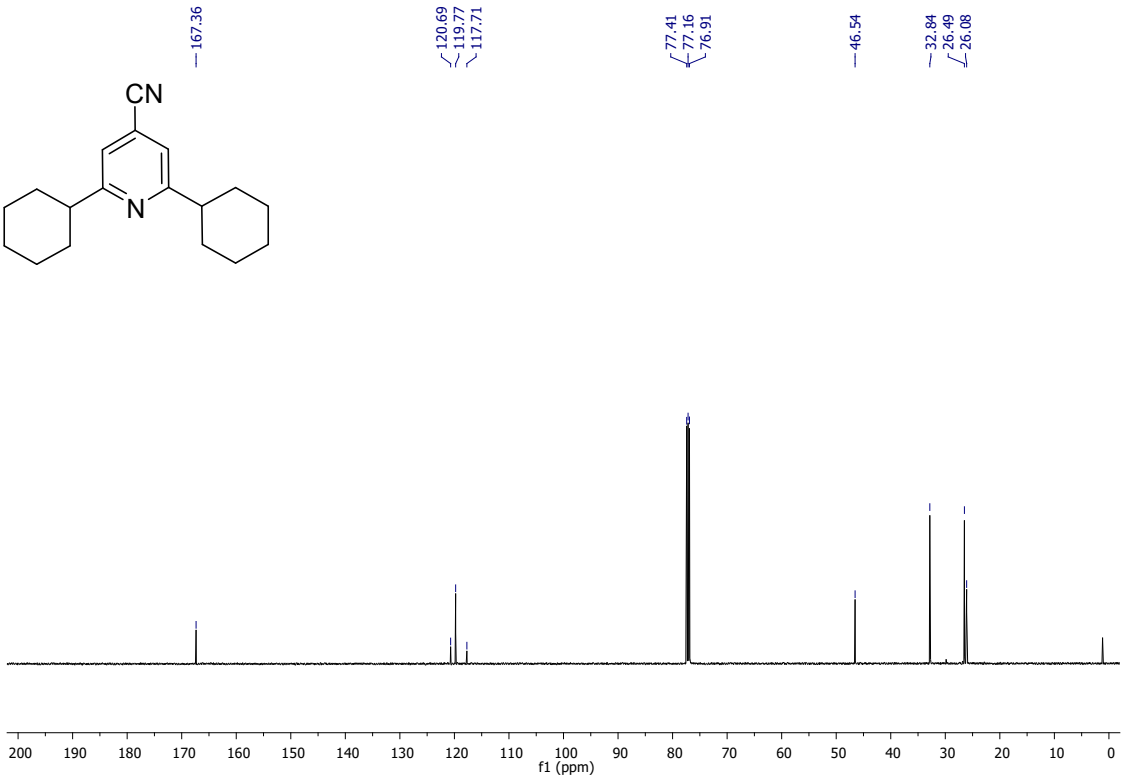


Figure S106: ^{1}H NMR spectrum of **3nd'** (500 MHz, $CDCl_3$)

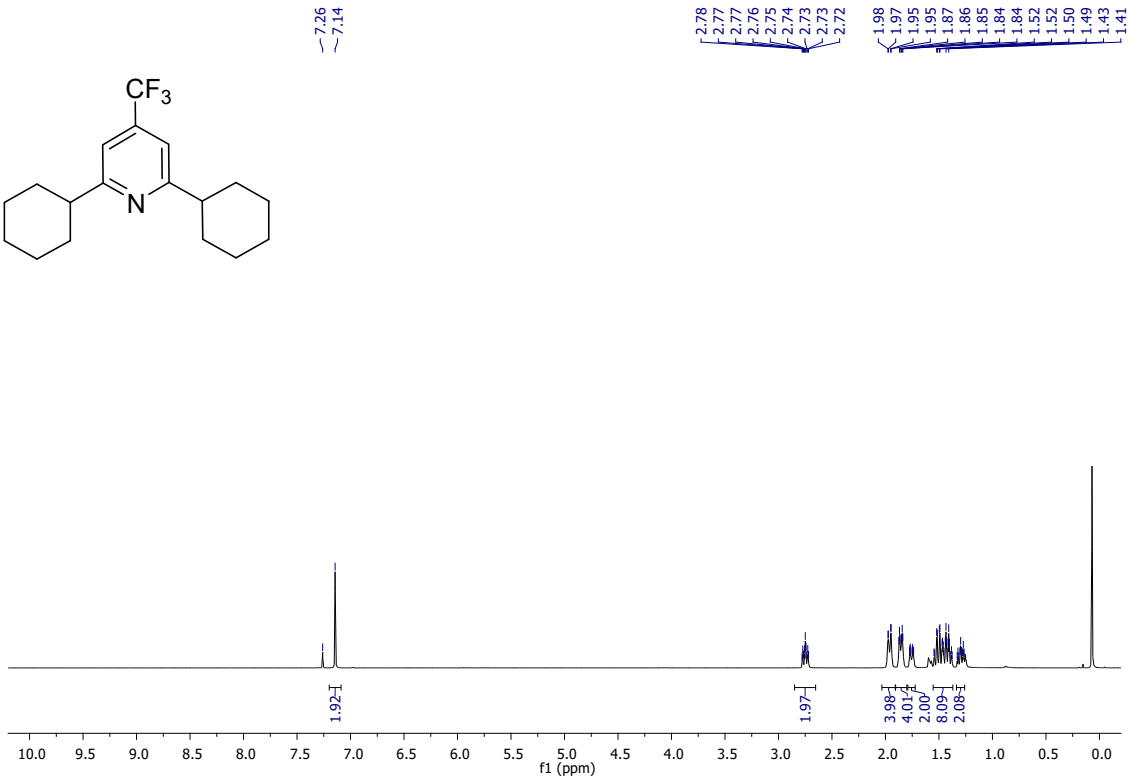


Figure S107: ^{1}H NMR spectrum of **3od** (500 MHz, $CDCl_3$)

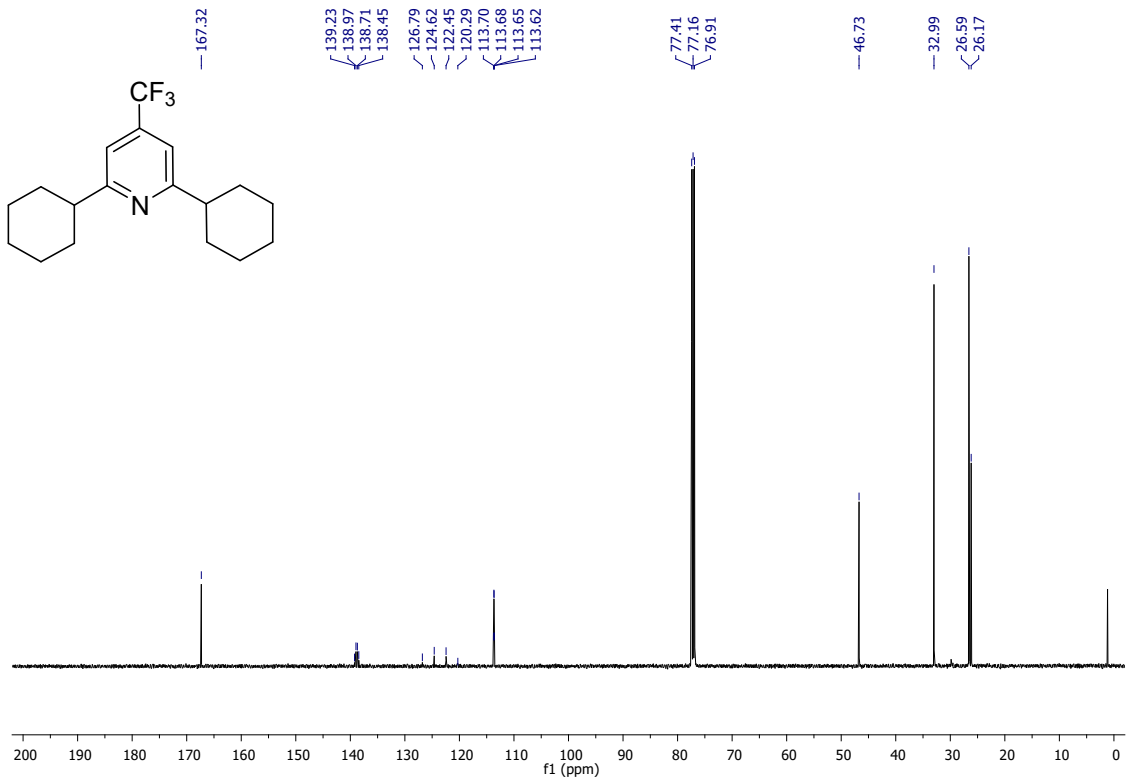


Figure S108: $^{13}C\{^{1}H\}$ NMR spectrum of **3od** (126 MHz, $CDCl_3$)

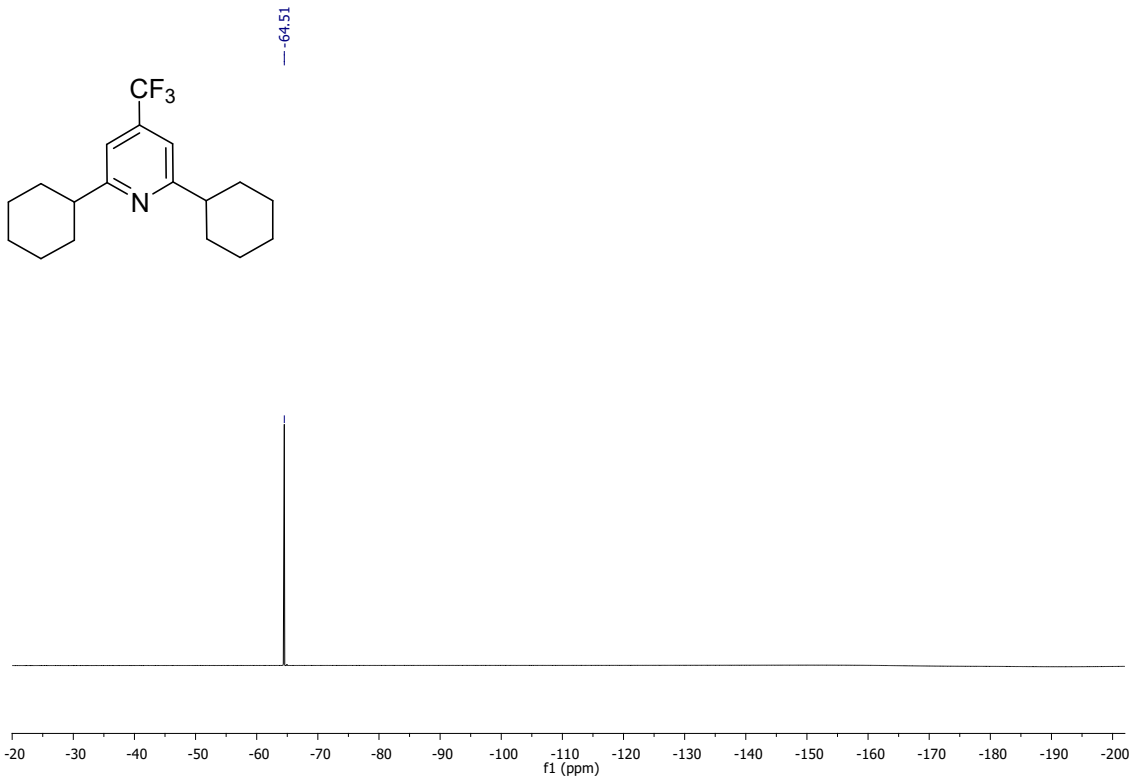


Figure S109: ^{19}F NMR spectrum of **3od** (471 MHz, $CDCl_3$)

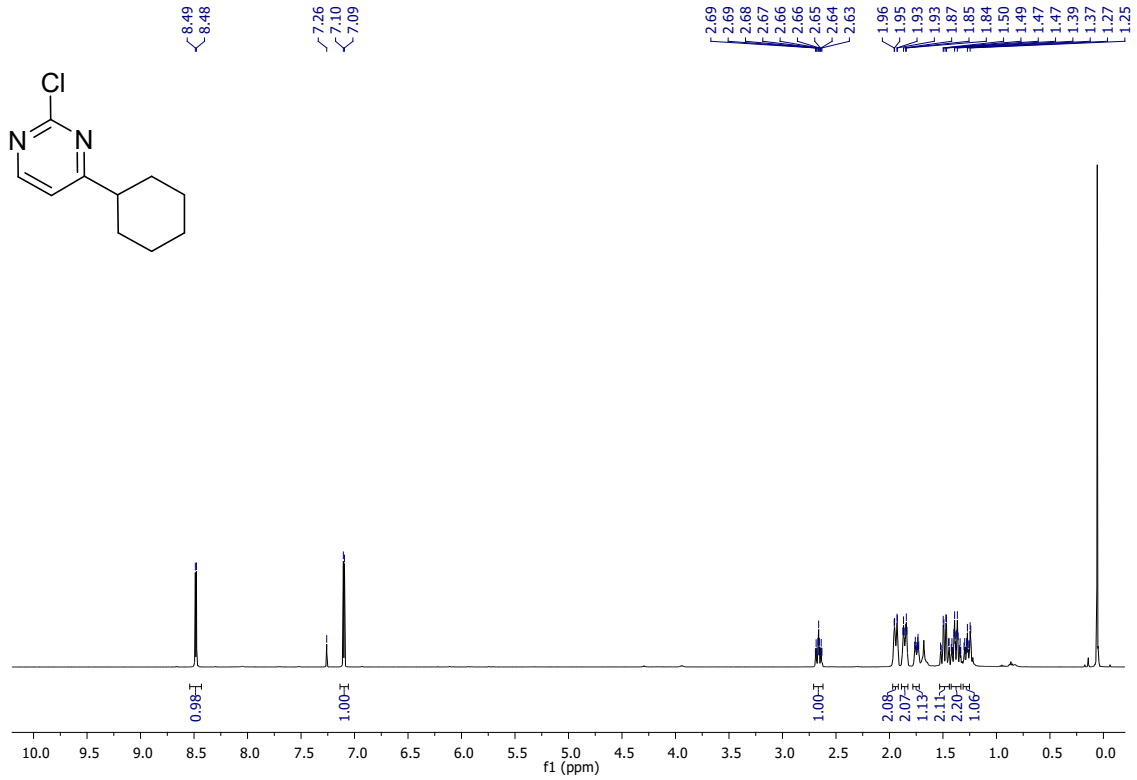


Figure S110: ^{1}H NMR spectrum of **3pd** (500 MHz, $CDCl_3$)

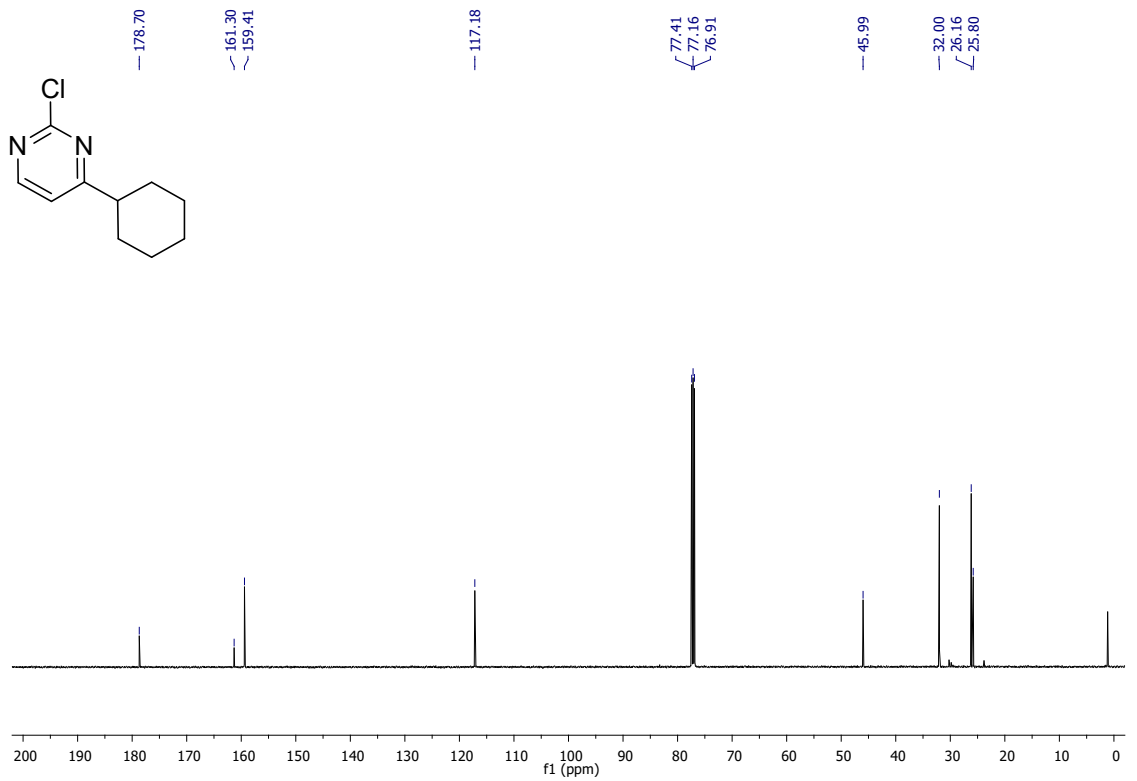


Figure S111: $^{13}C\{^{1}H\}$ NMR spectrum of **3pd** (126 MHz, $CDCl_3$)

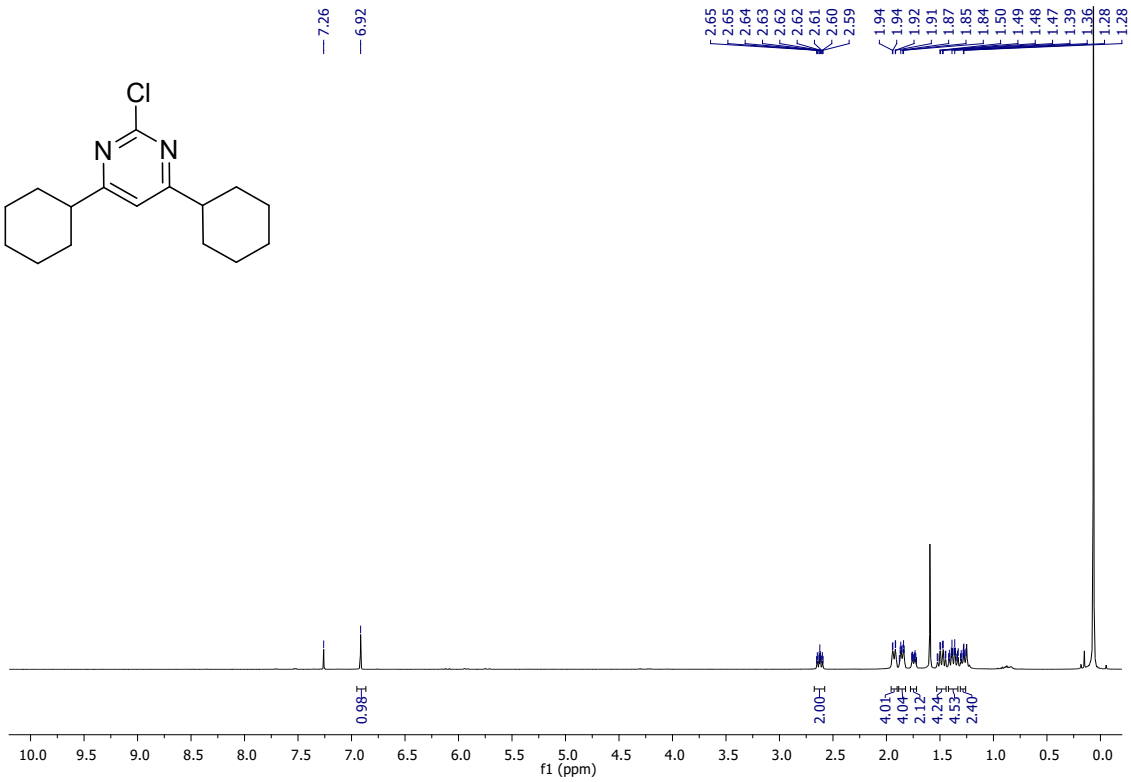


Figure S112: ^{1}H NMR spectrum of **3pd'** (500 MHz, $CDCl_3$)

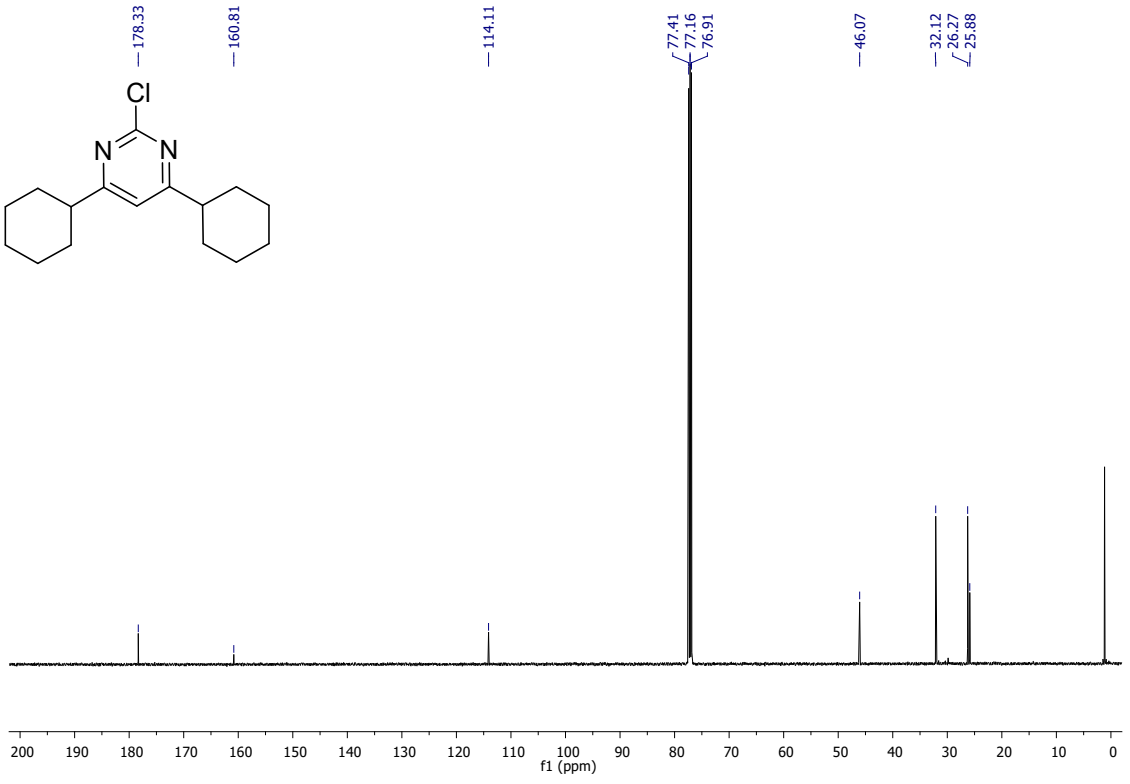


Figure S113: $^{13}C\{^{1}H\}$ NMR spectrum of **3pd'** (126 MHz, $CDCl_3$)

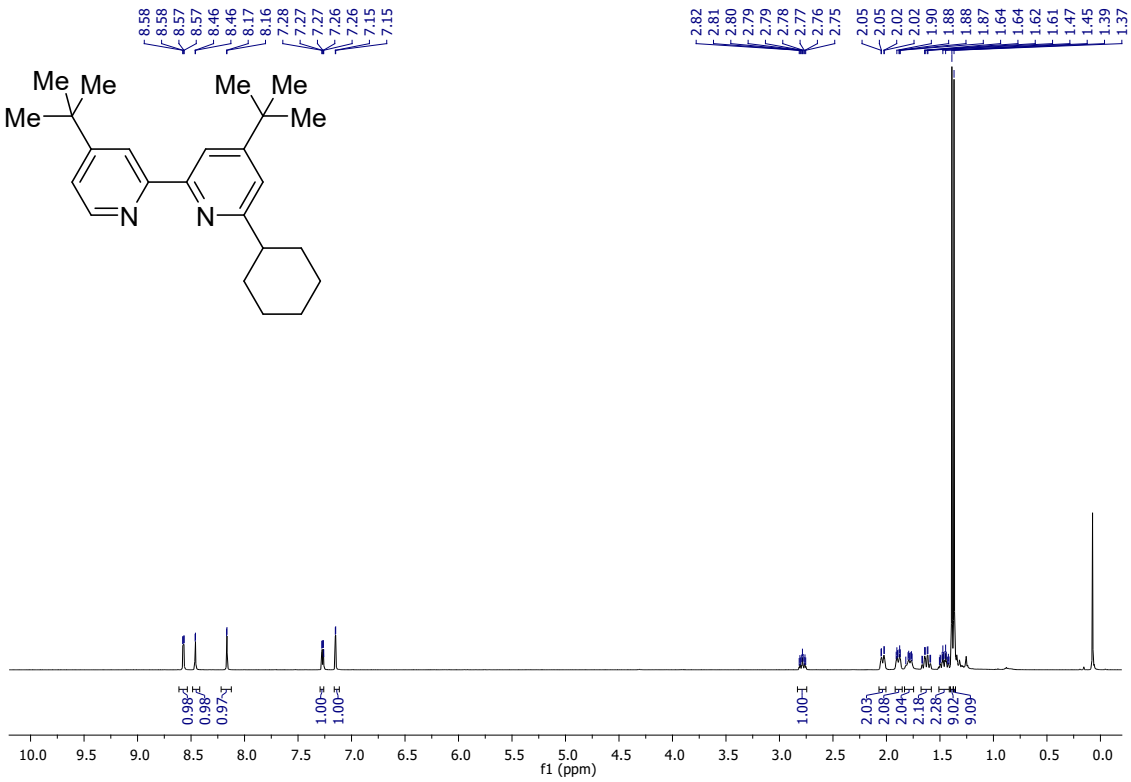


Figure S114: ^{1}H NMR spectrum of **3qd** (500 MHz, $CDCl_3$)

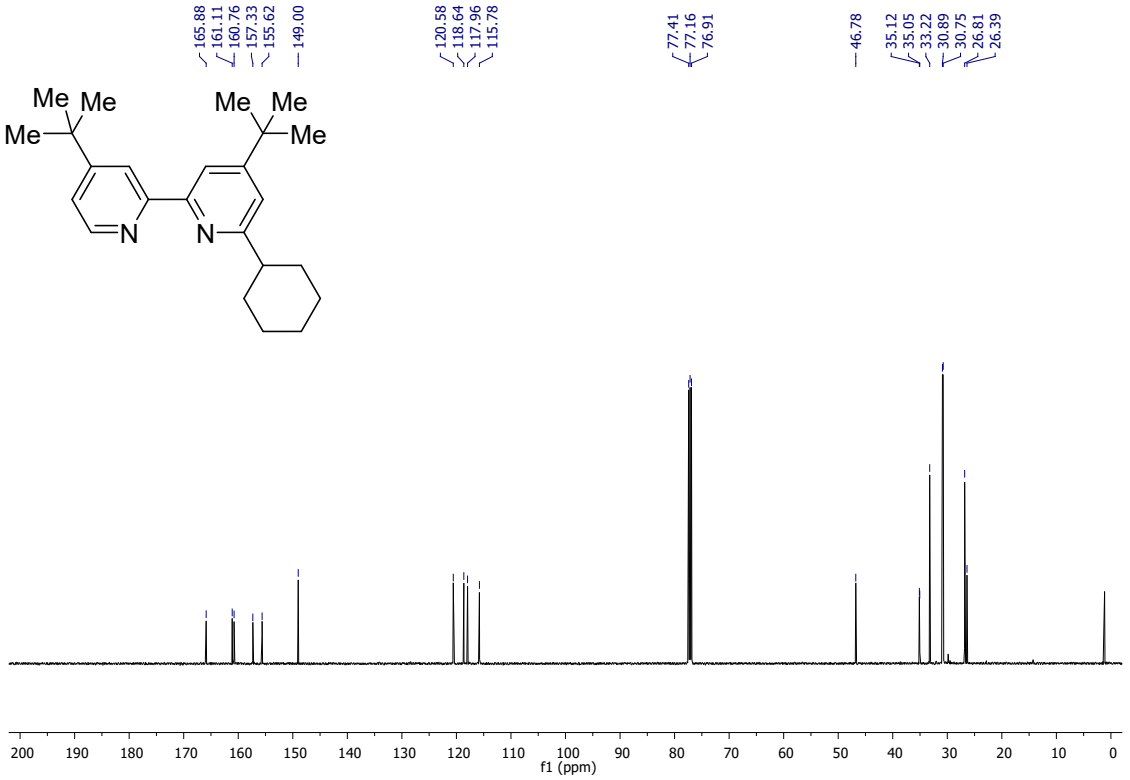


Figure S115: $^{13}C\{^{1}H\}$ NMR spectrum of **3qd** (126 MHz, $CDCl_3$)

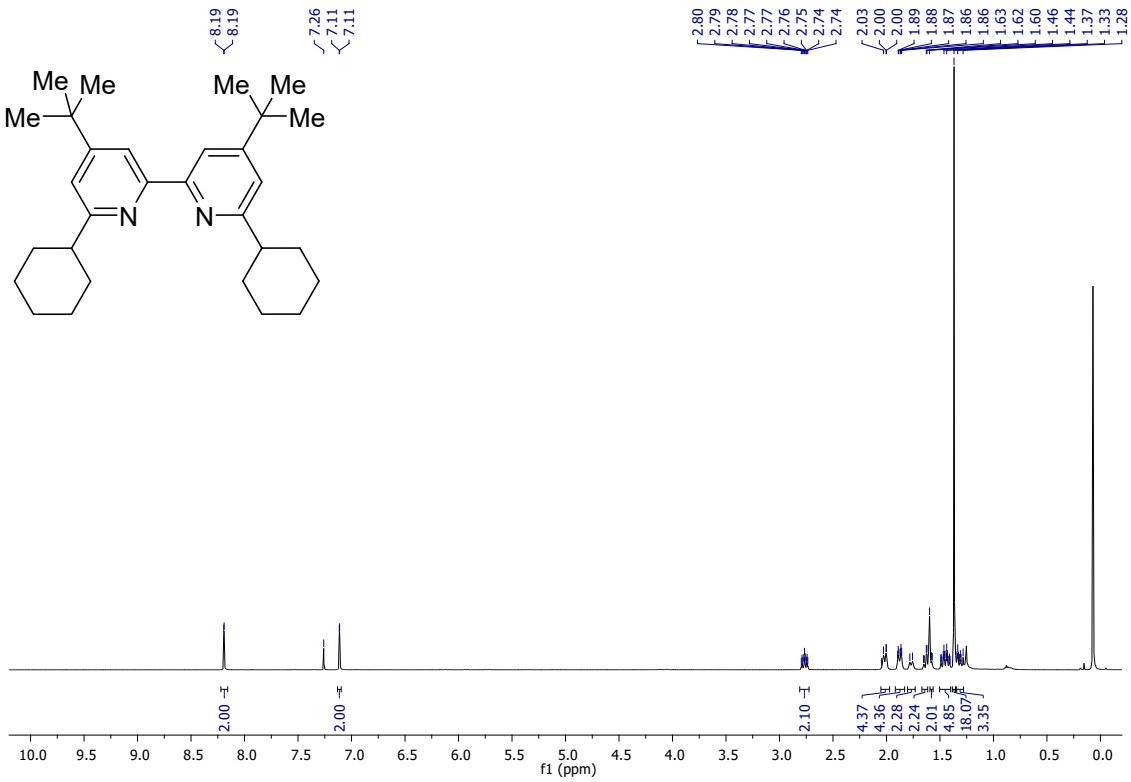


Figure S116: ^{1}H NMR spectrum of **3qd'** (500 MHz, $CDCl_3$)

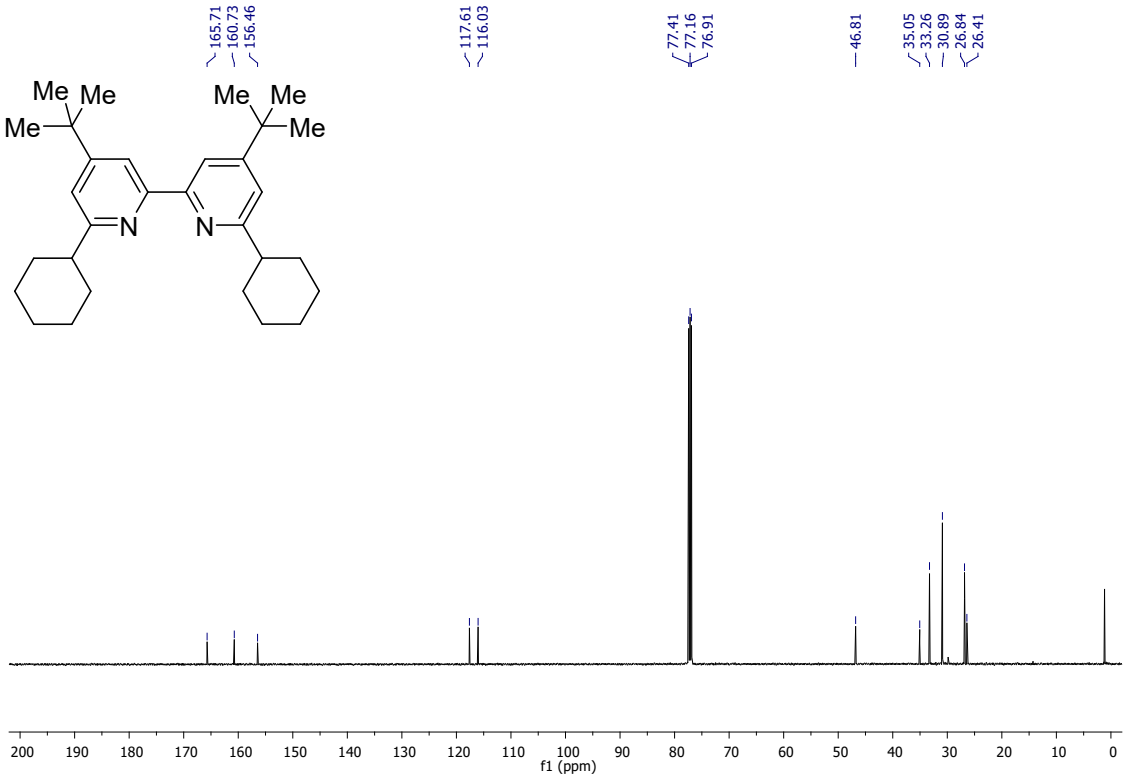


Figure S117: $^{13}C\{^{1}H\}$ NMR spectrum of **3qd'** (126 MHz, $CDCl_3$)

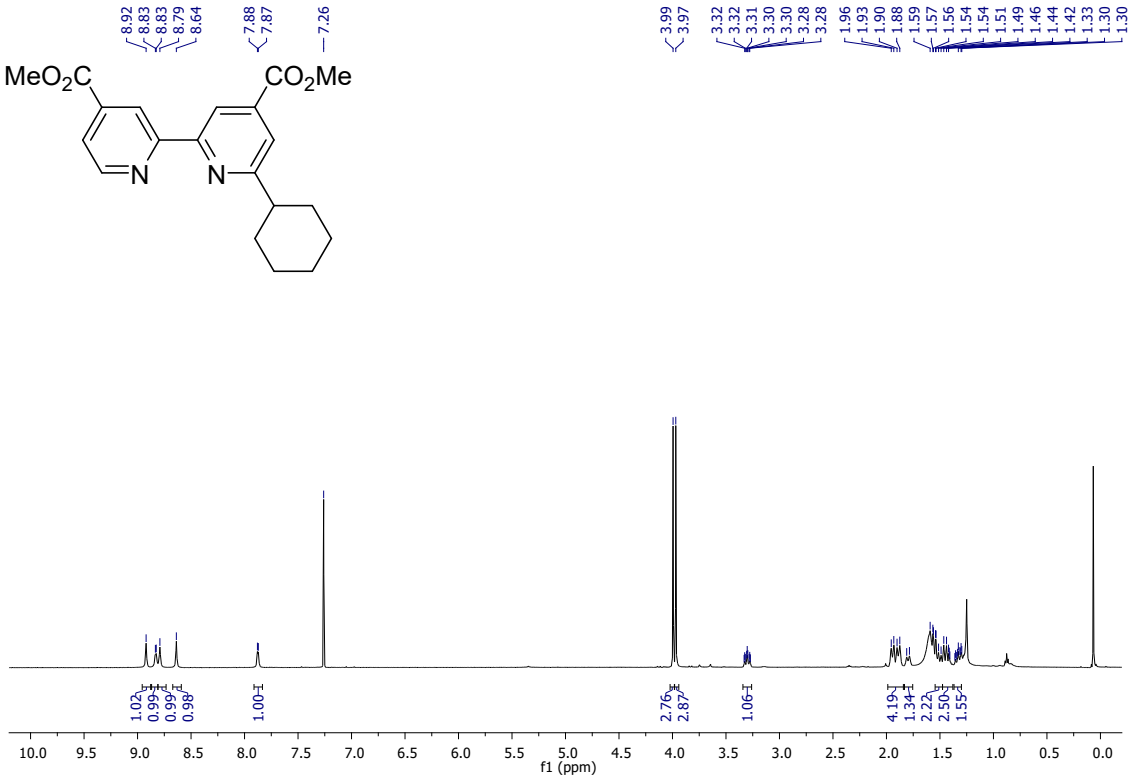


Figure S118: ^{1}H NMR spectrum of **3rd** (500 MHz, $CDCl_3$)

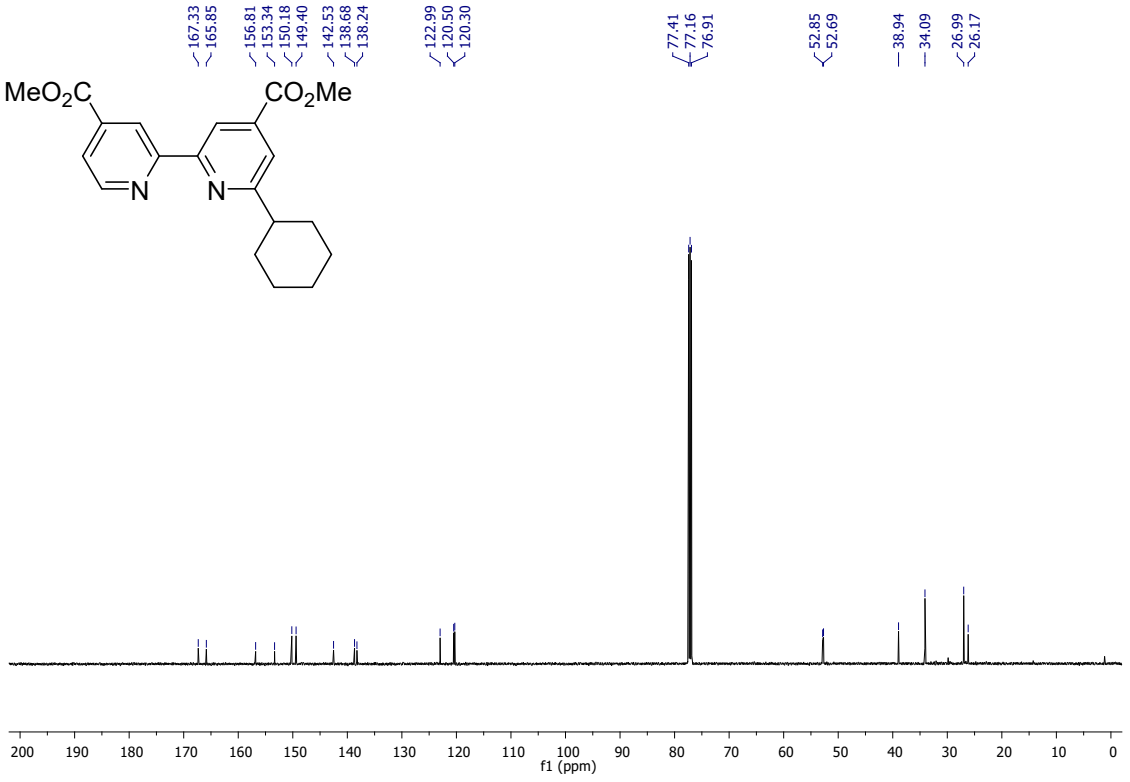


Figure S119: $^{13}C\{^{1}H\}$ NMR spectrum of **3rd** (126 MHz, $CDCl_3$)

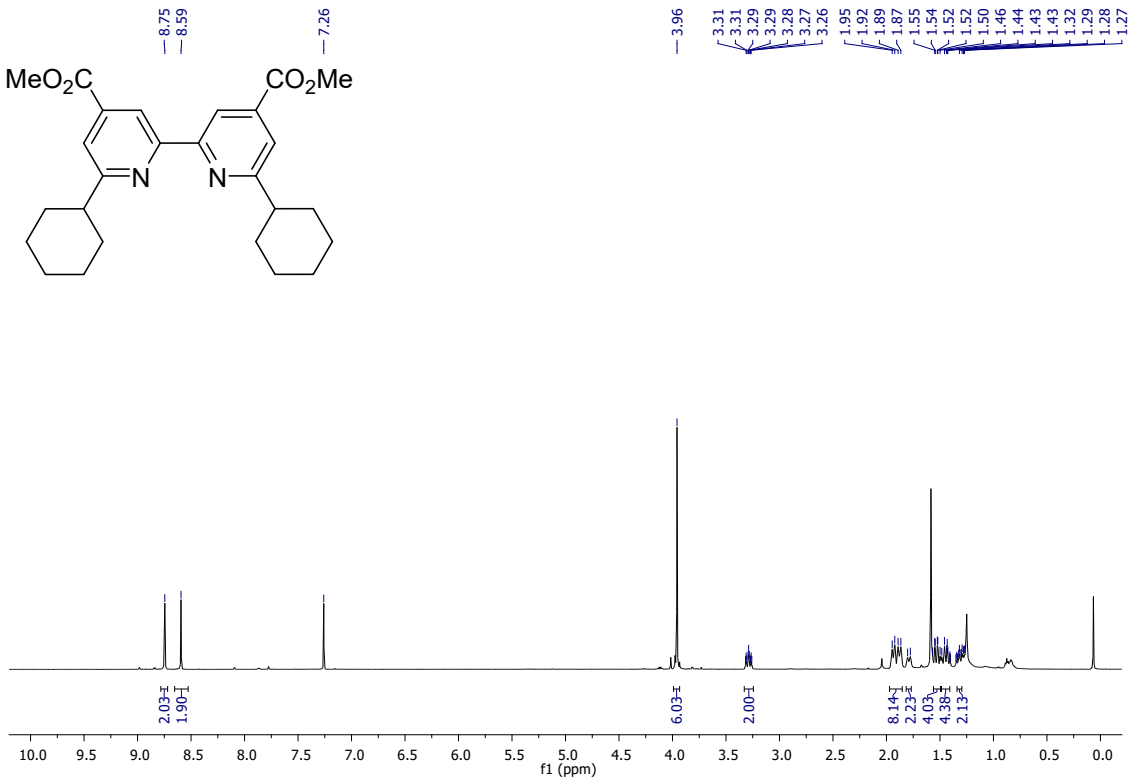


Figure S120: ^{1}H NMR spectrum of **3rd'** (500 MHz, $CDCl_3$)

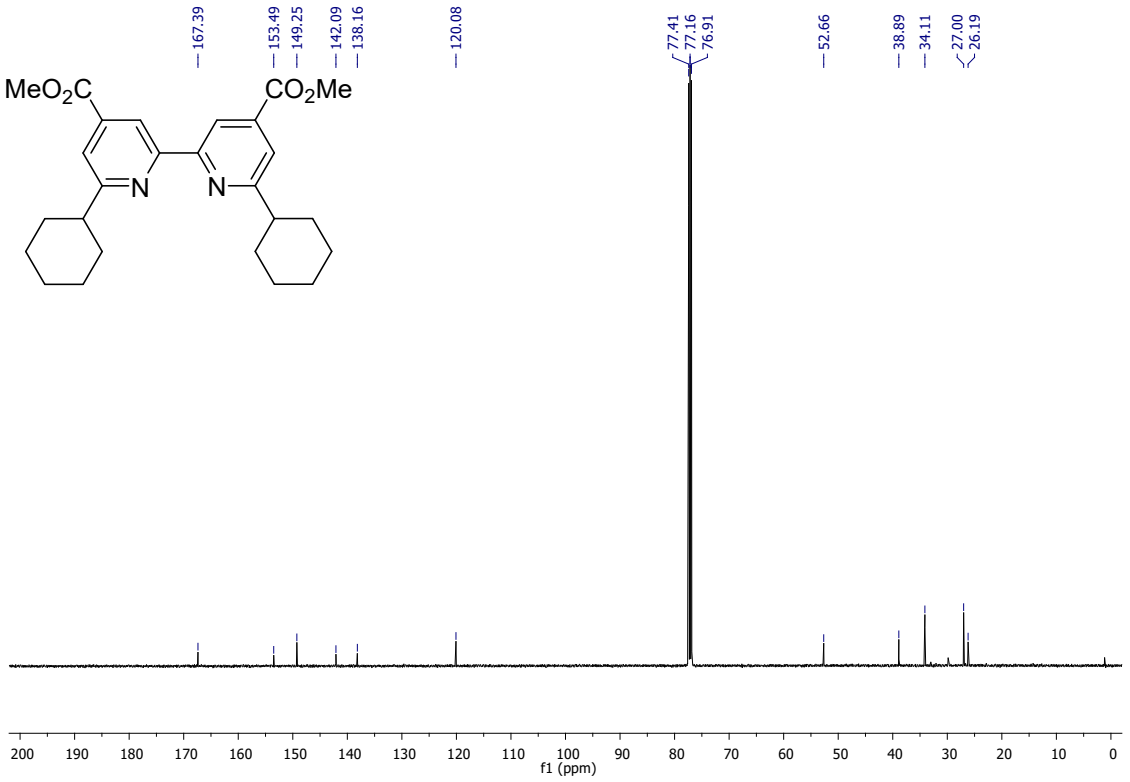


Figure S121: $^{13}C\{^{1}H\}$ NMR spectrum of **3rd'** (126 MHz, $CDCl_3$)

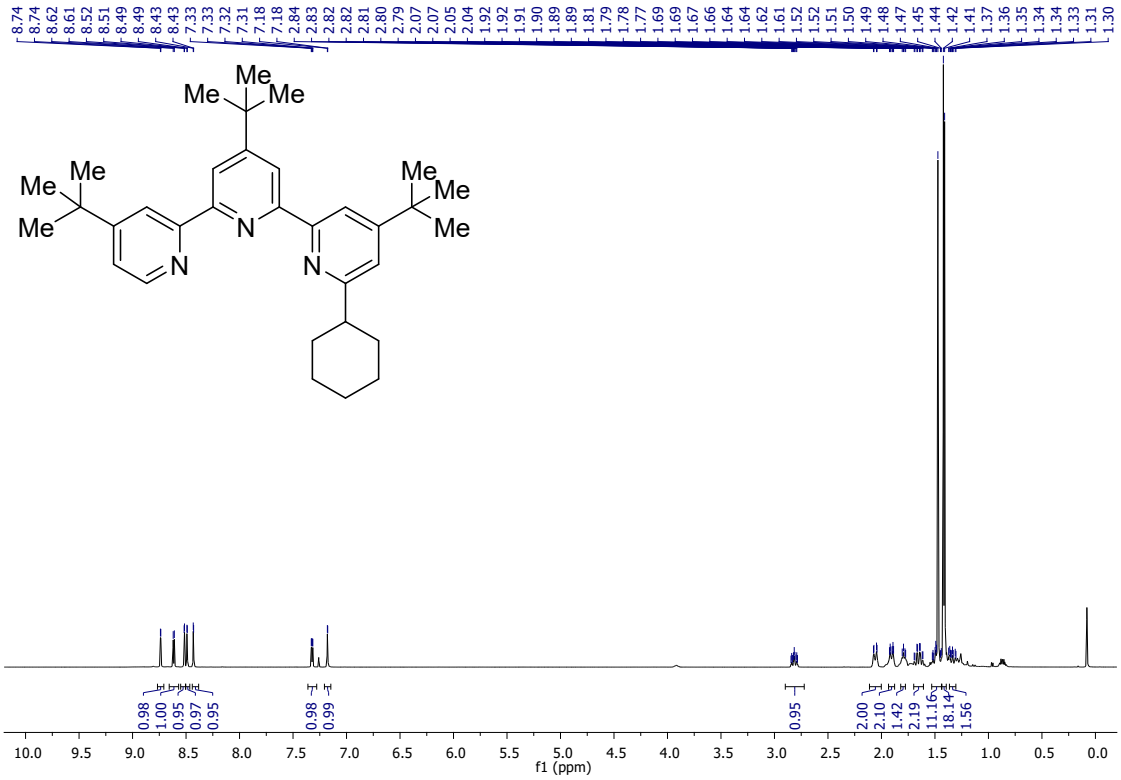


Figure S122: ^{1}H NMR spectrum of **3sd** (500 MHz, $CDCl_3$)

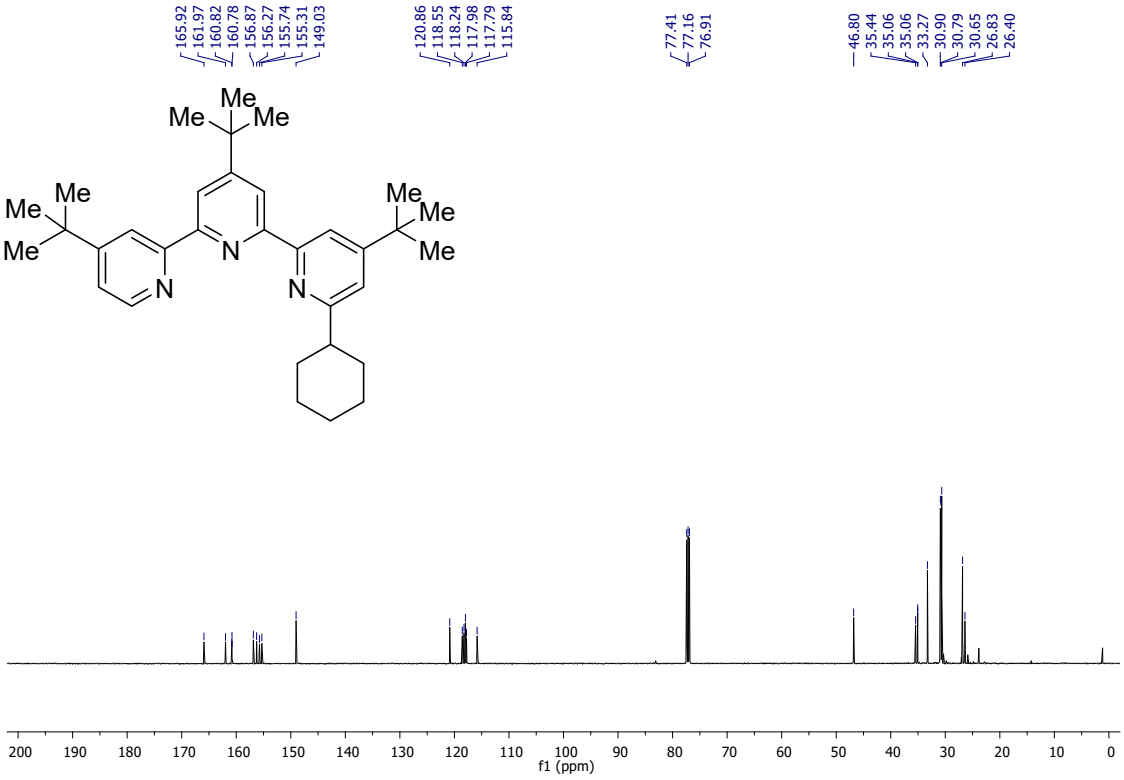


Figure S123: $^{13}C\{^{1}H\}$ NMR spectrum of **3sd** (126 MHz, $CDCl_3$)

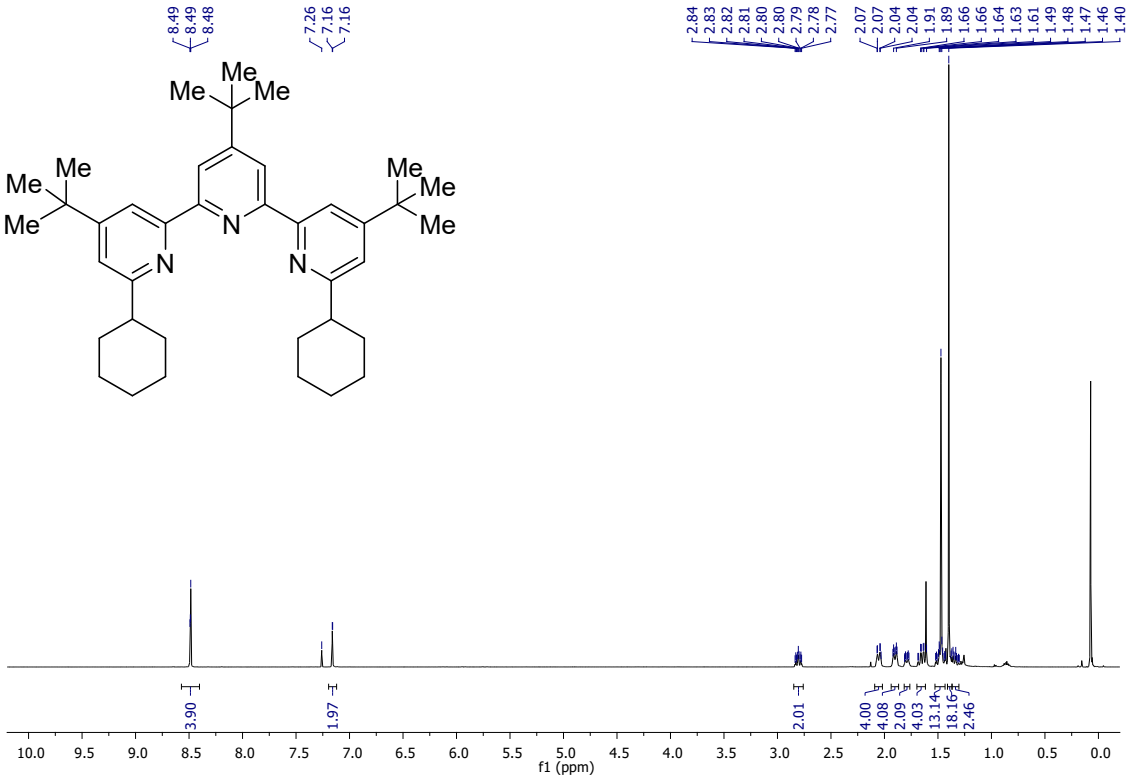


Figure S124: ^{1}H NMR spectrum of **3sd'** (500 MHz, $CDCl_3$)

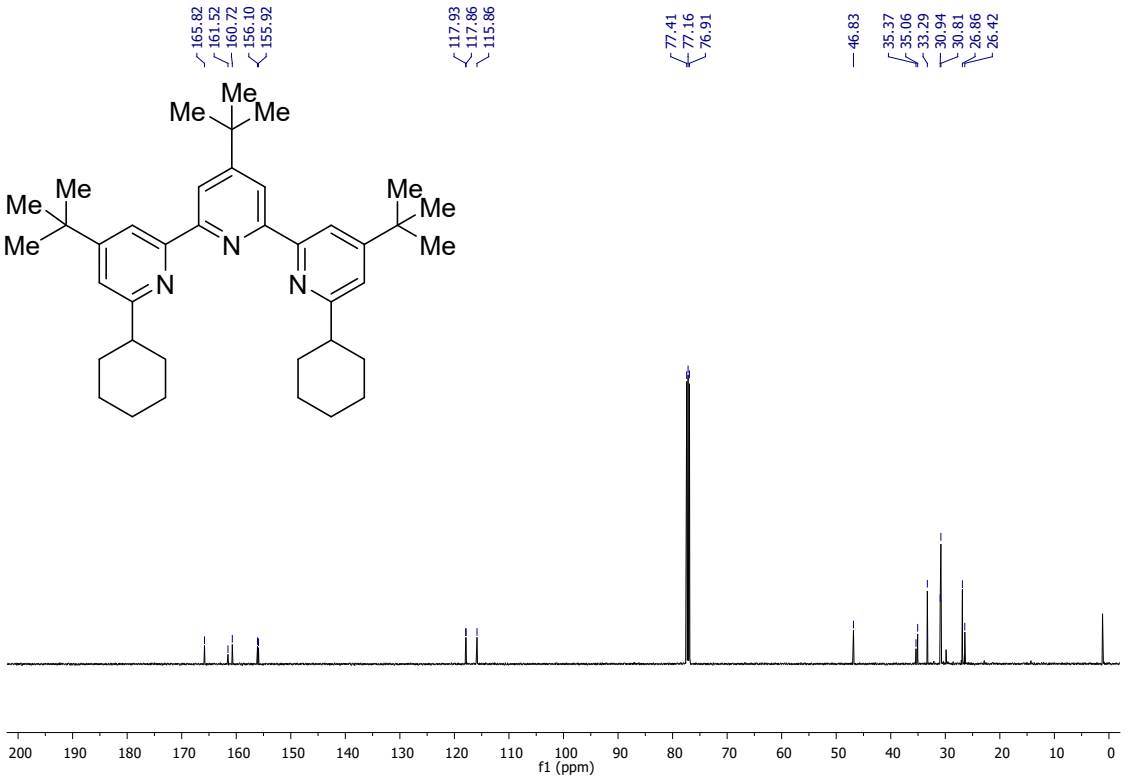


Figure S125: $^{13}C\{^{1}H\}$ NMR spectrum of **3sd'** (126 MHz, $CDCl_3$)

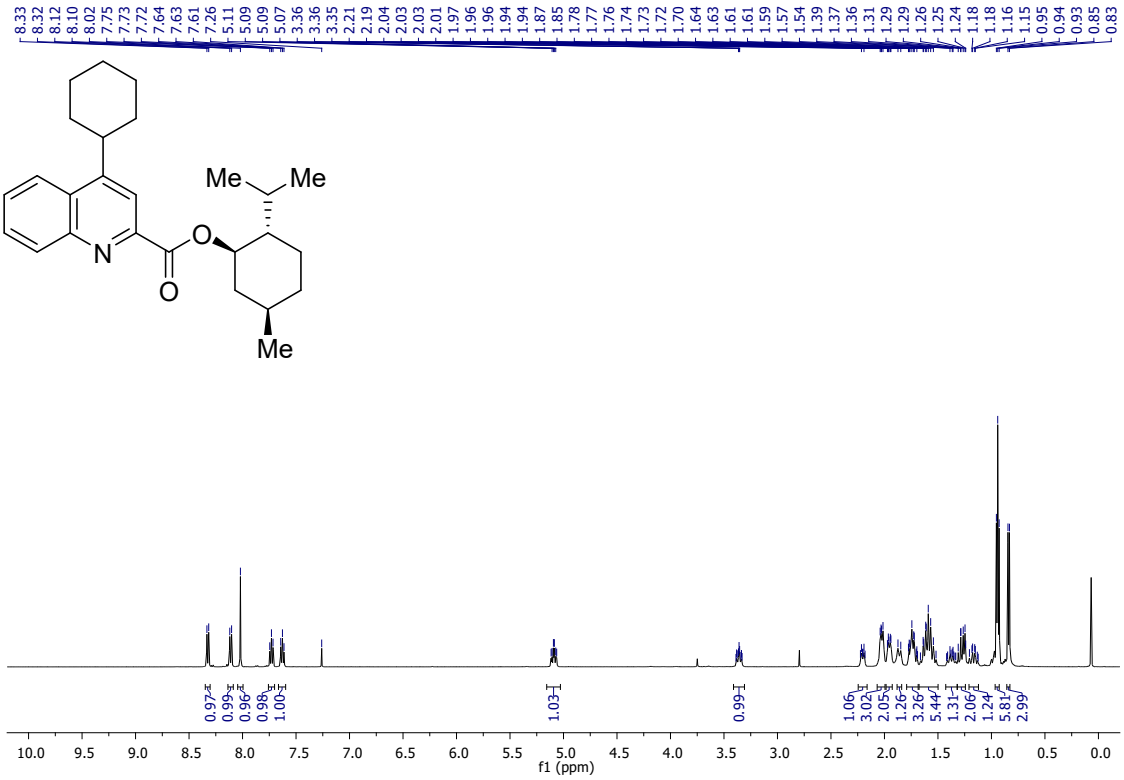


Figure S126: ^{1}H NMR spectrum of **3td** (500 MHz, $CDCl_3$)

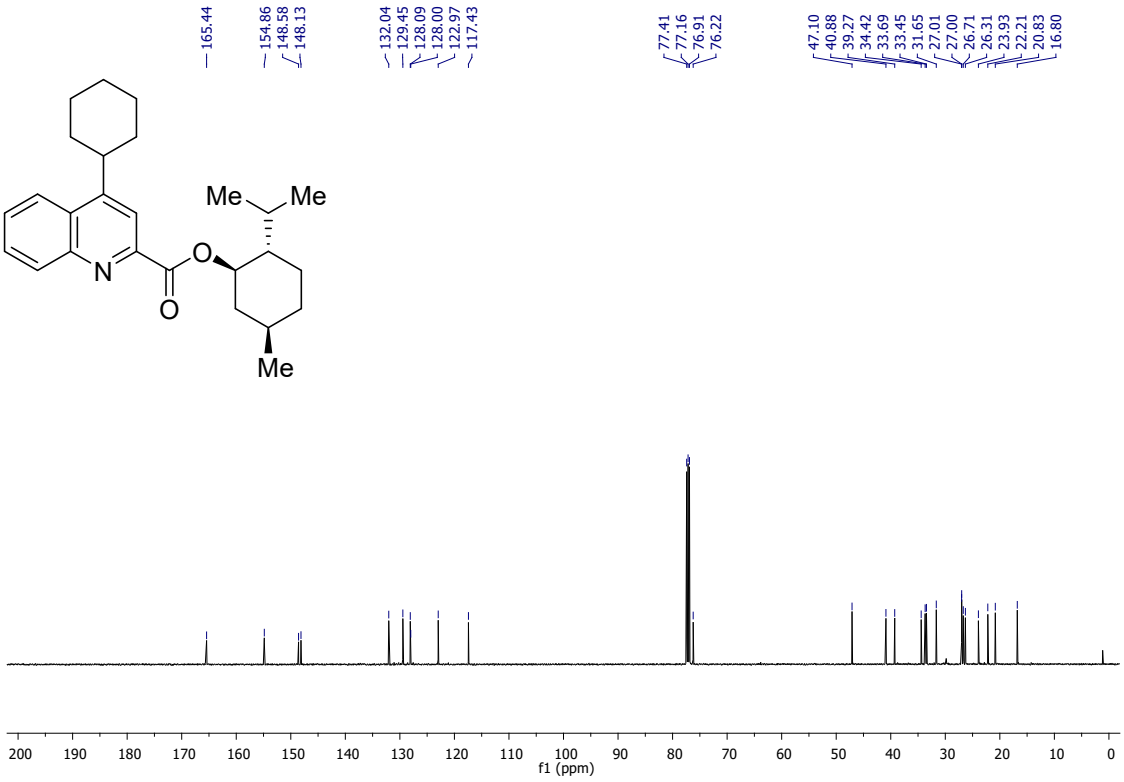


Figure S127: $^{13}C\{^{1}H\}$ NMR spectrum of **3td** (126 MHz, $CDCl_3$)

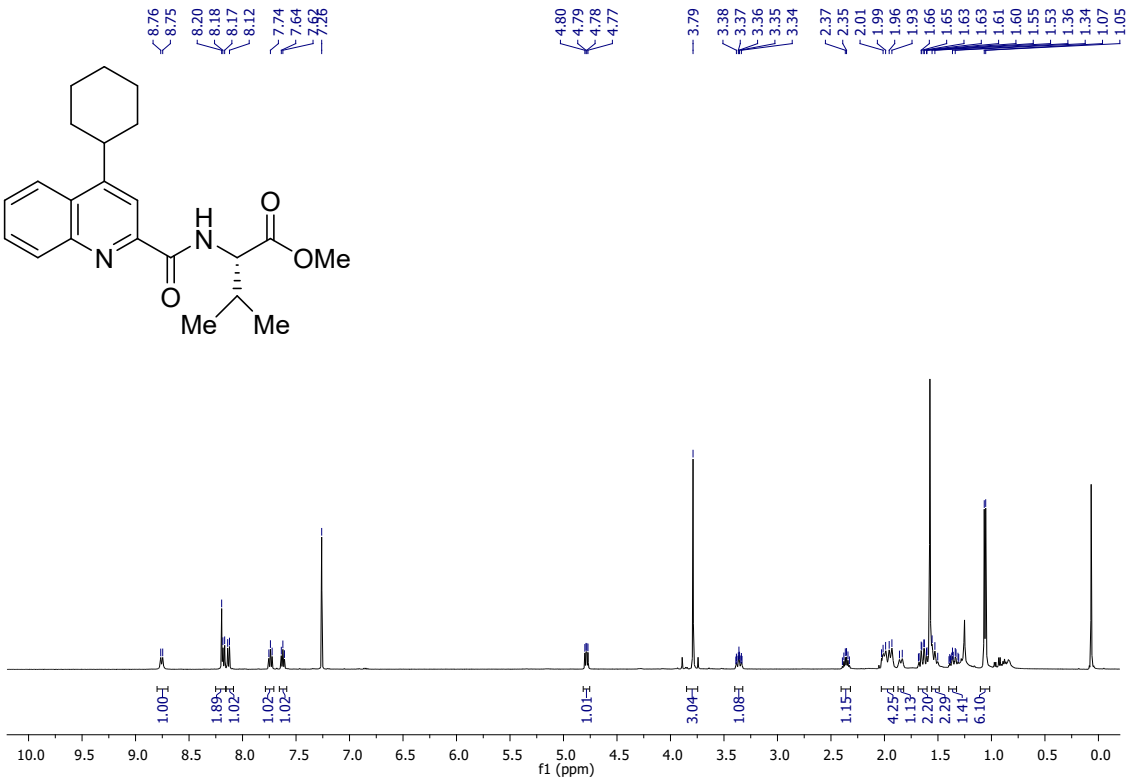


Figure S128: ^{1}H NMR spectrum of **3ud** (500 MHz, $CDCl_3$)

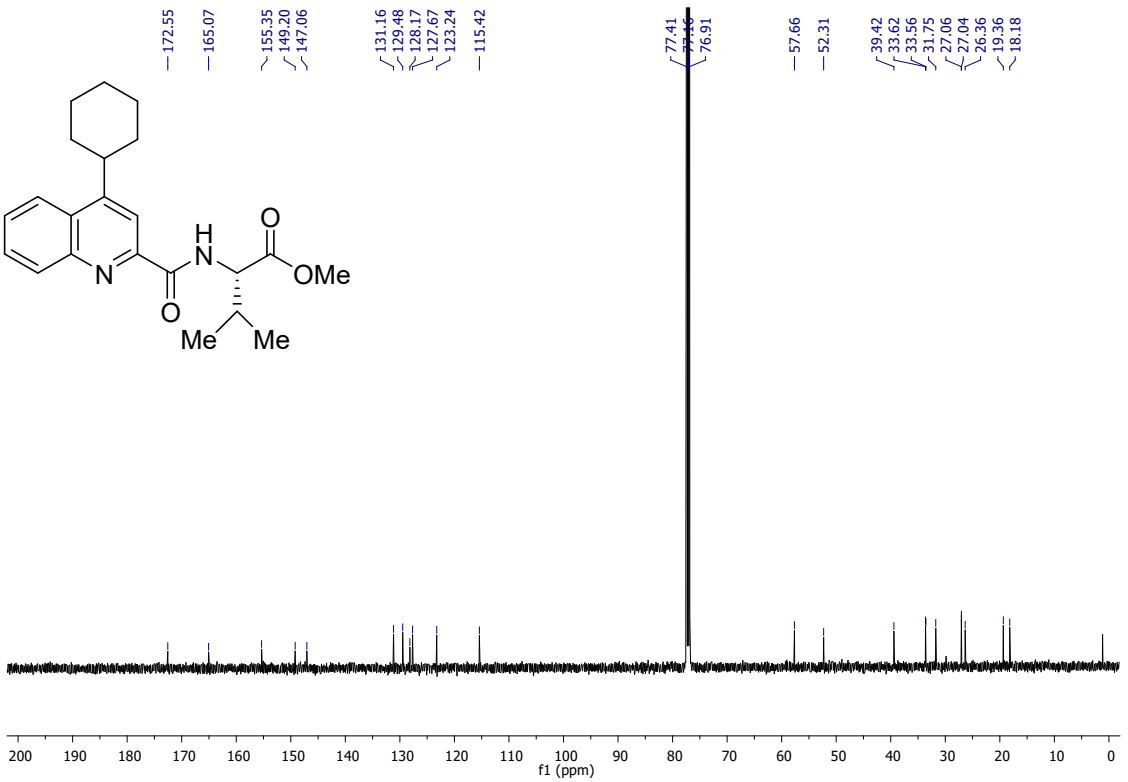


Figure S129: $^{13}C\{^{1}H\}$ NMR spectrum of **3ud** (126 MHz, $CDCl_3$)

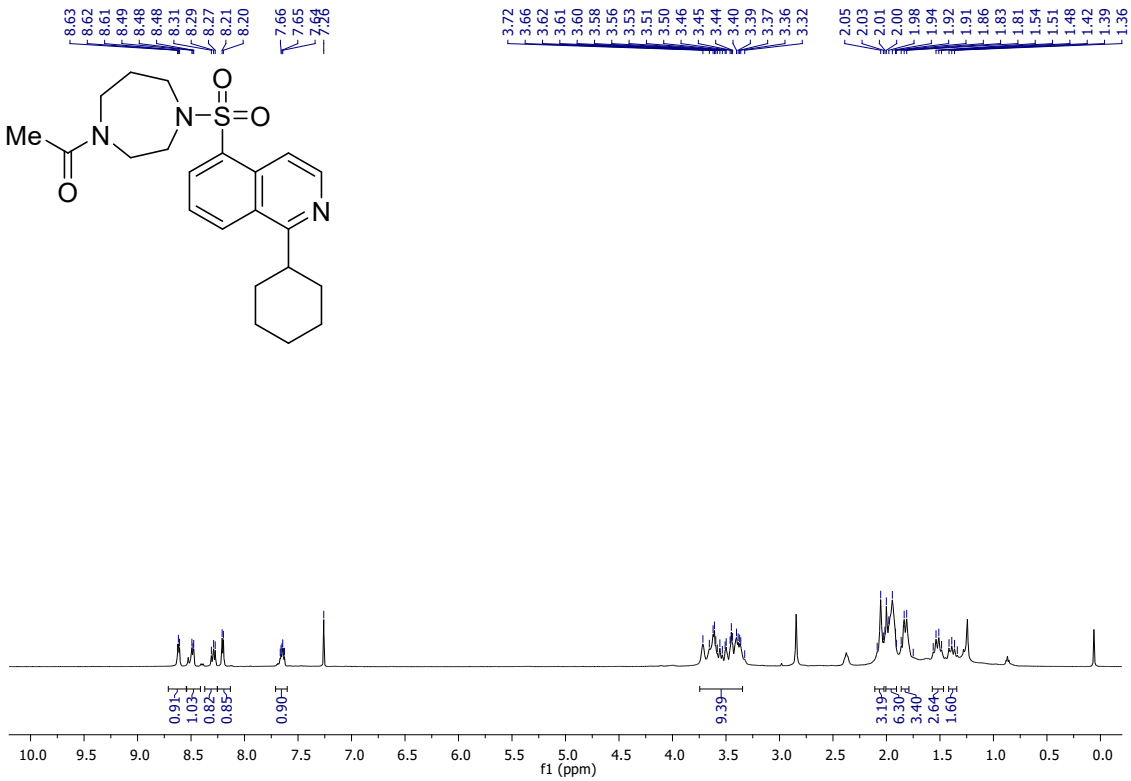


Figure S130: ^{1}H NMR spectrum of **3vd** (500 MHz, $CDCl_3$)

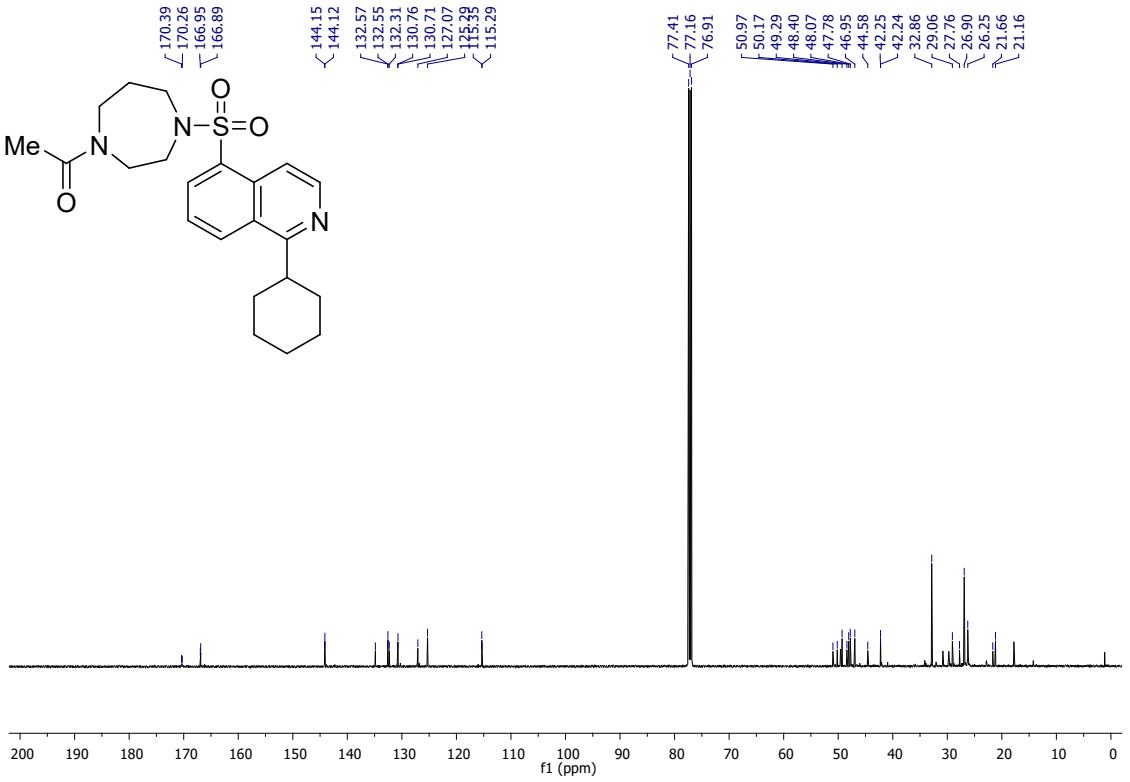


Figure S131: $^{13}C\{^{1}H\}$ NMR spectrum of **3vd** (126 MHz, $CDCl_3$)

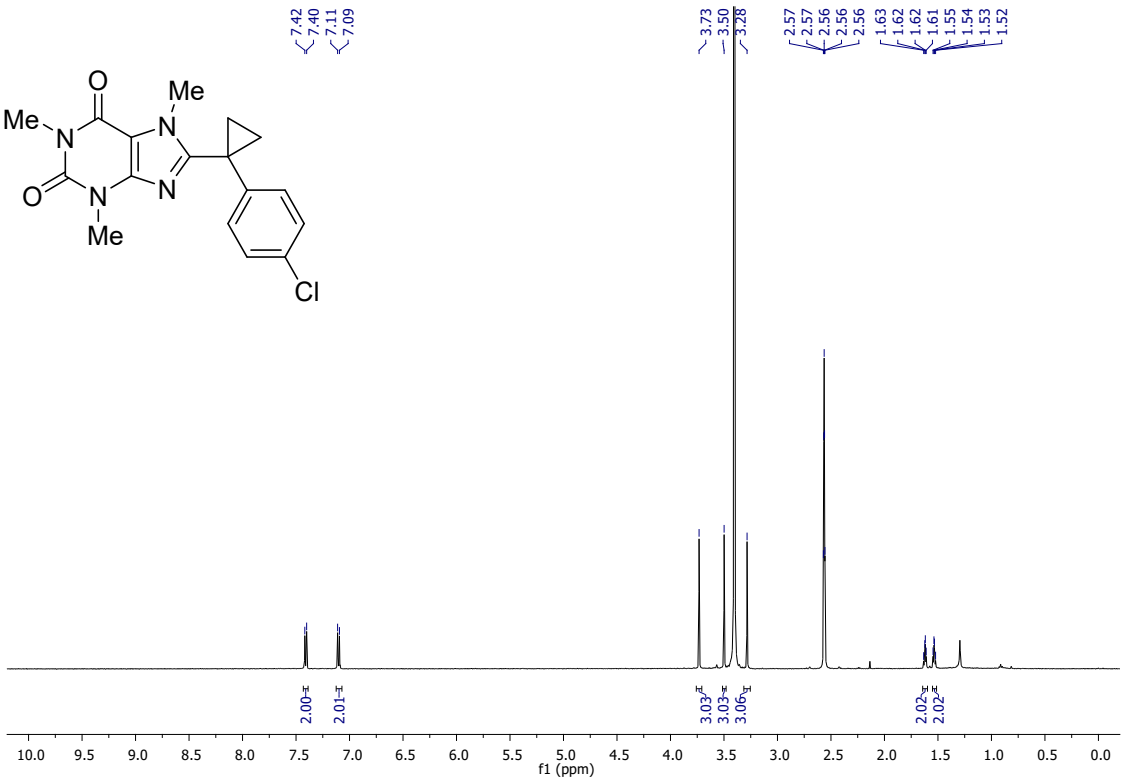


Figure S132: ^{1}H NMR spectrum of **3wi** (500 MHz, DMSO-d6)

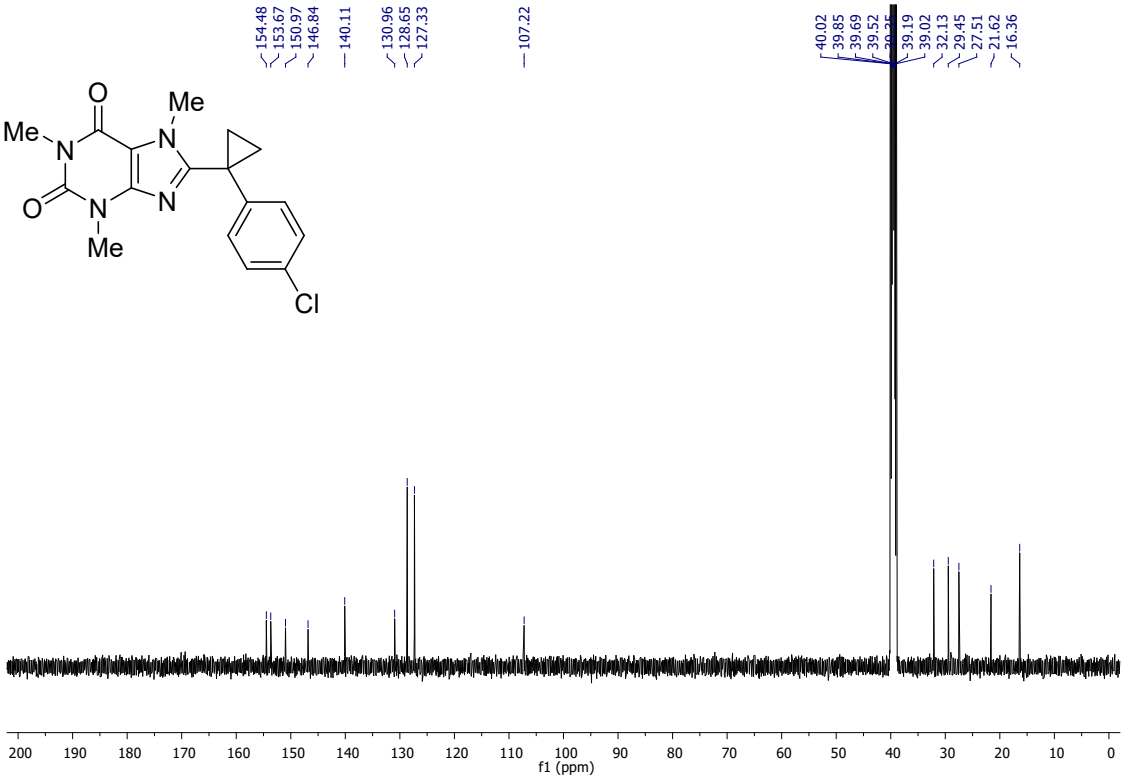


Figure S133: ^{13}C{^{1}H} NMR spectrum of **3wi** (126 MHz, DMSO-d_6)

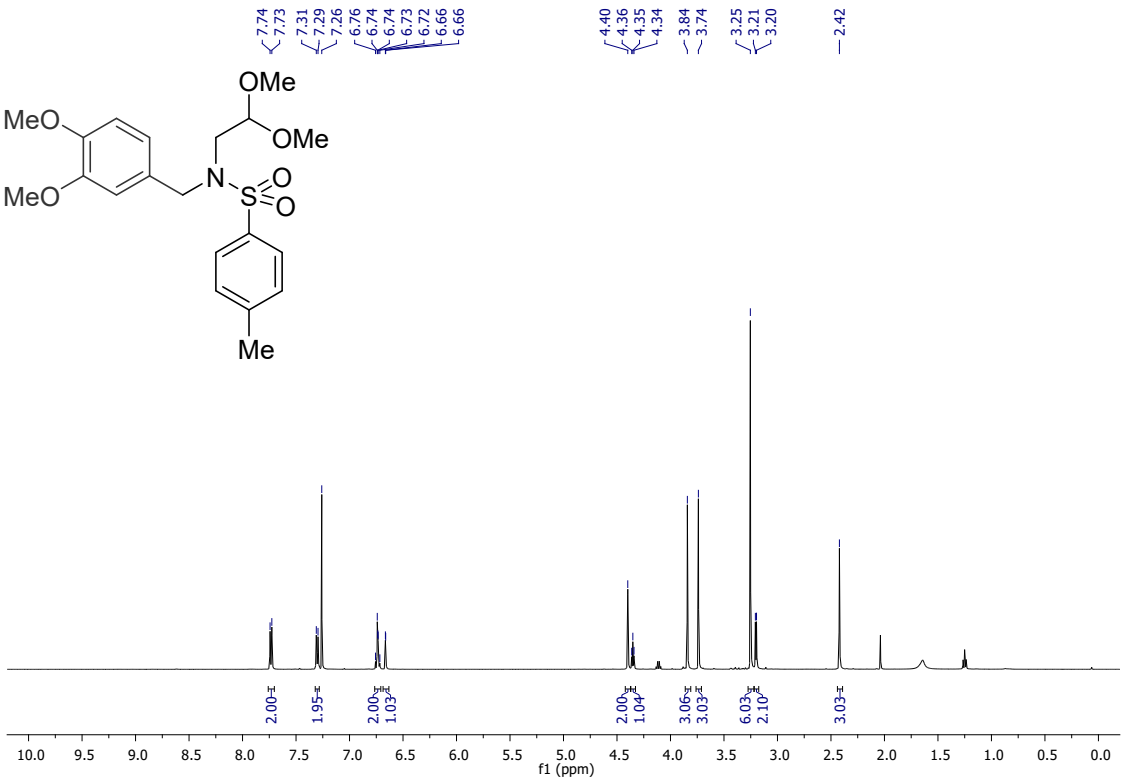


Figure S134: ^{1}H NMR spectrum of **S19** (500 MHz, $CDCl_3$)

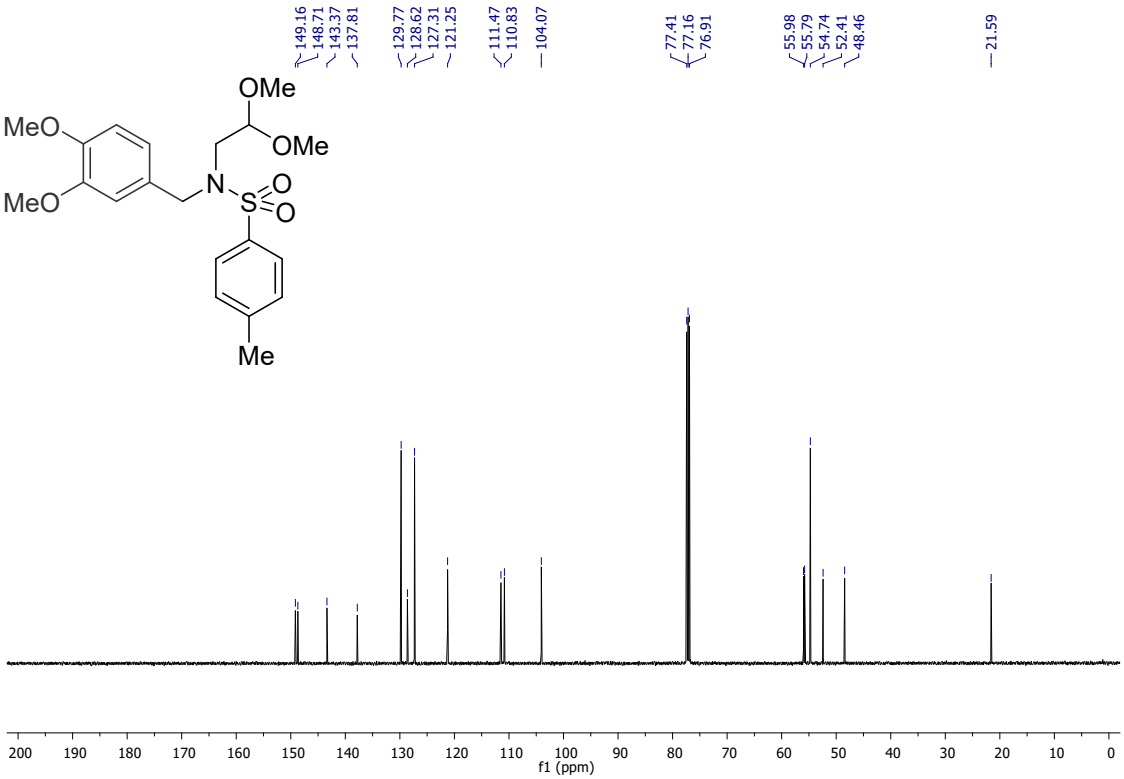


Figure S135: $^{13}C\{^{1}H\}$ NMR spectrum of **S19** (126 MHz, $CDCl_3$)

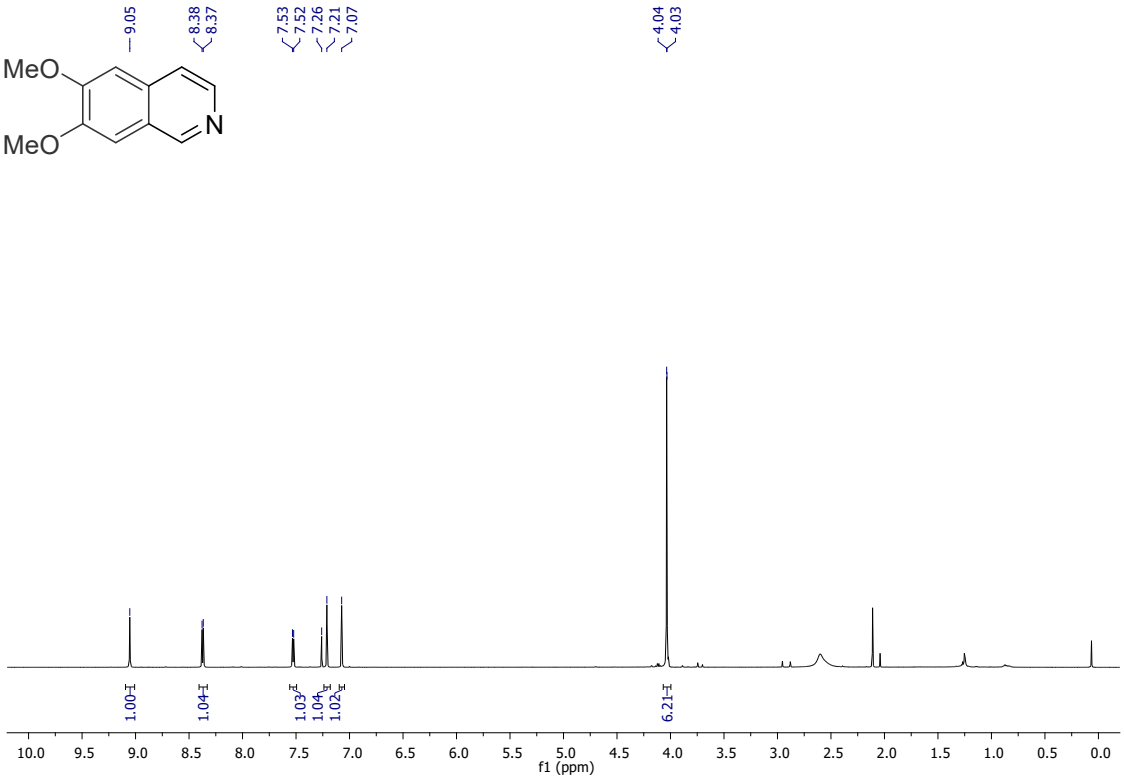


Figure S136: ^{1}H NMR spectrum of **1x** (500 MHz, $CDCl_3$)

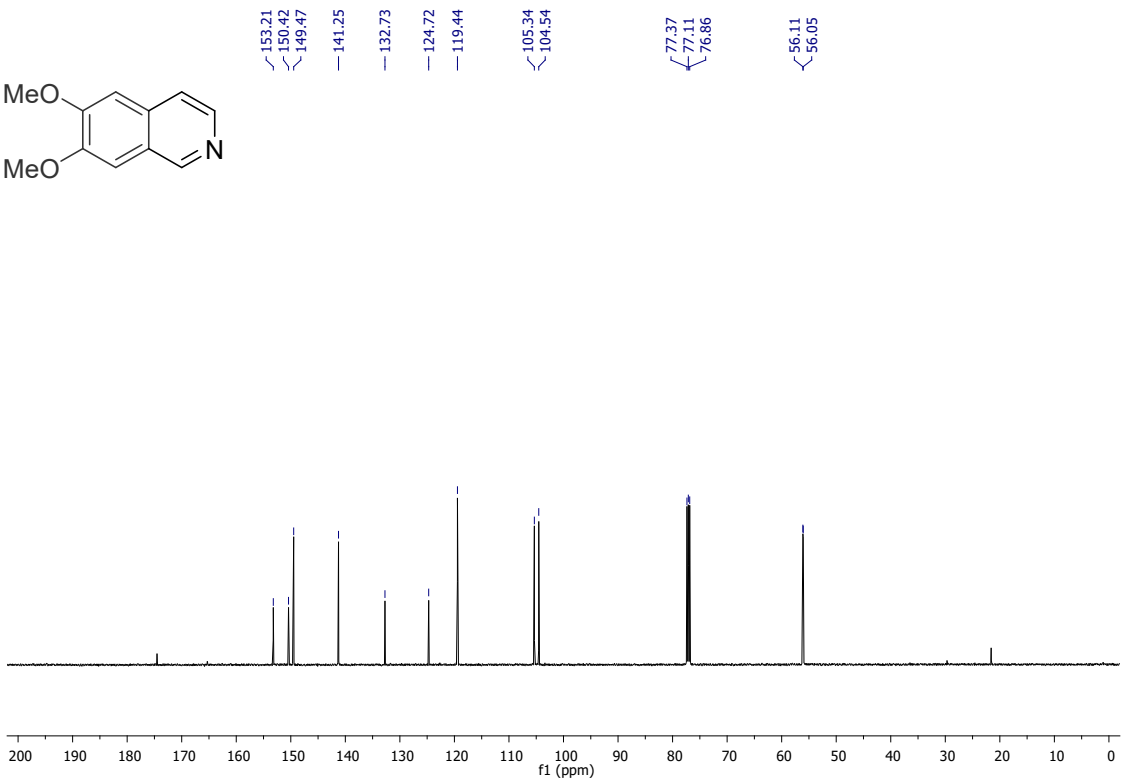


Figure S137: $^{13}C\{^{1}H\}$ NMR spectrum of **1x** (126 MHz, $CDCl_3$)

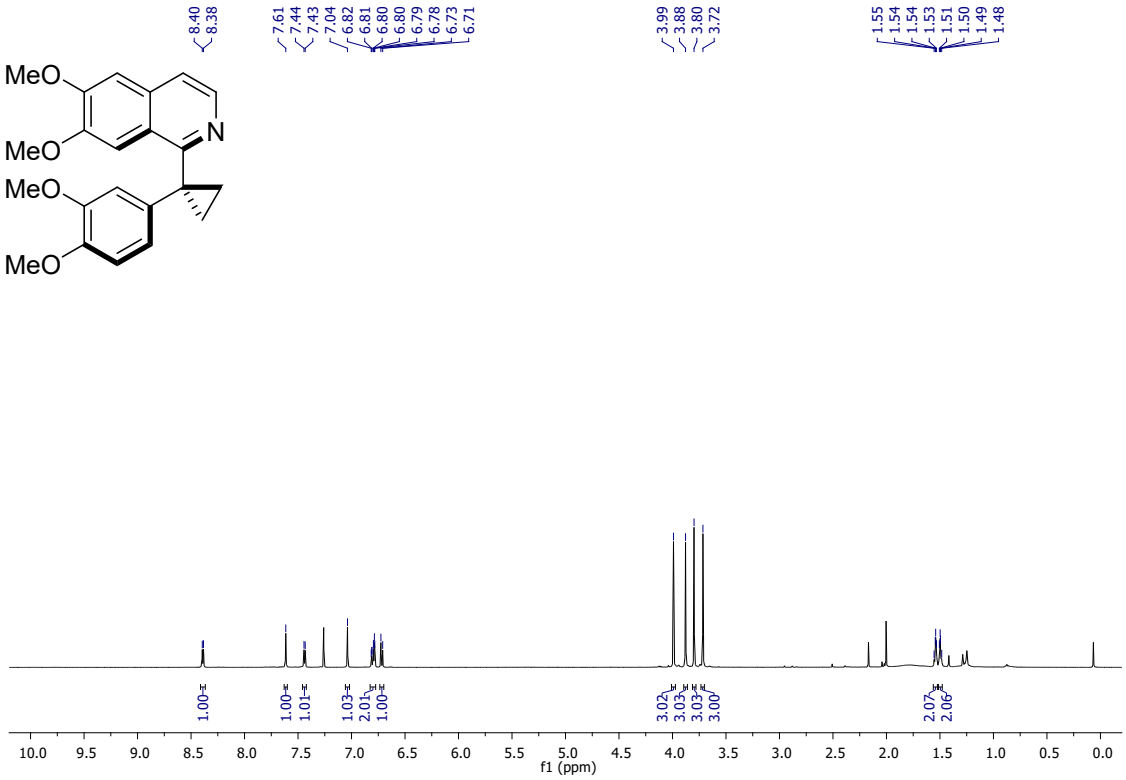


Figure S138: ^{1}H NMR spectrum of **3xk** (500 MHz, $CDCl_3$)

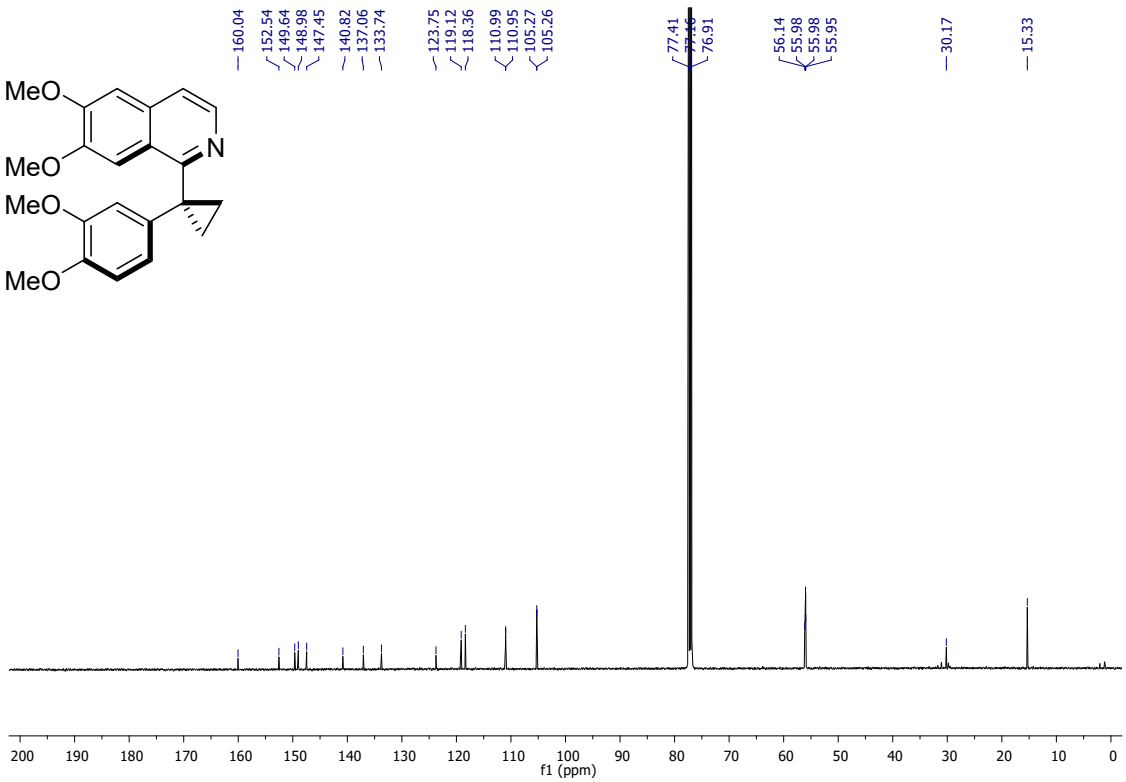


Figure S139: $^{13}C\{^{1}H\}$ NMR spectrum of **3xk** (126 MHz, $CDCl_3$)

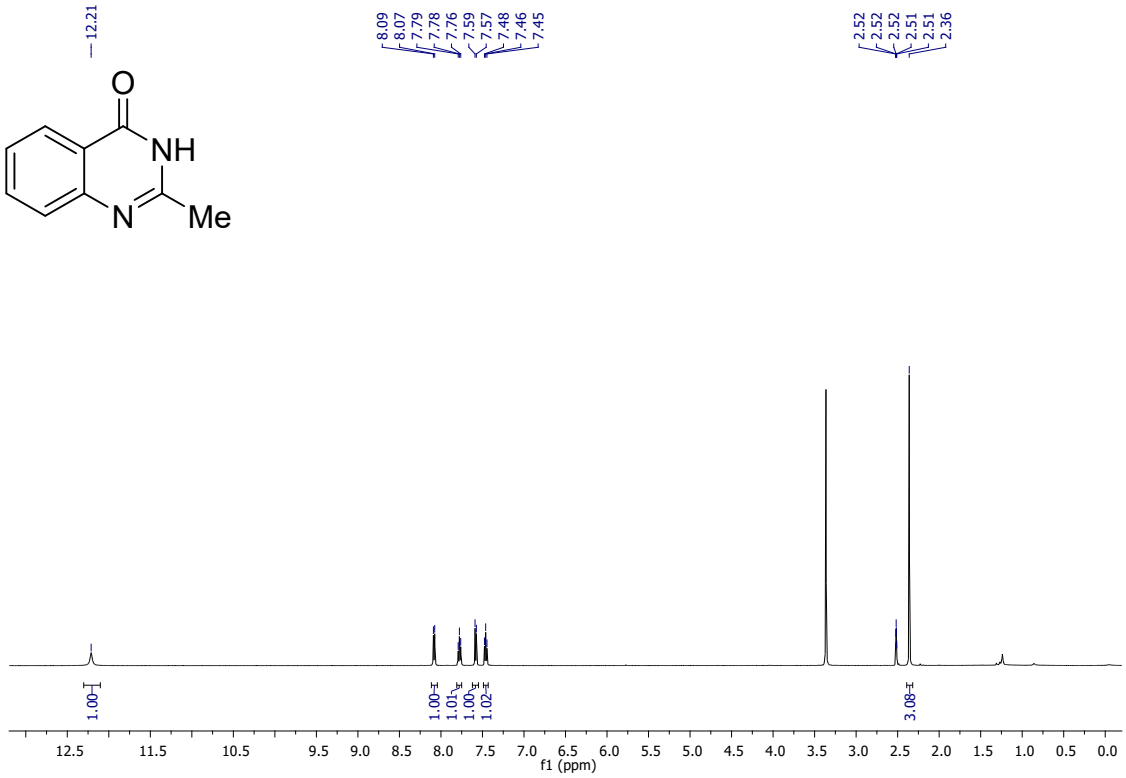


Figure S140: ^{1}H NMR spectrum of **4a** (500 MHz, DMSO-d6)

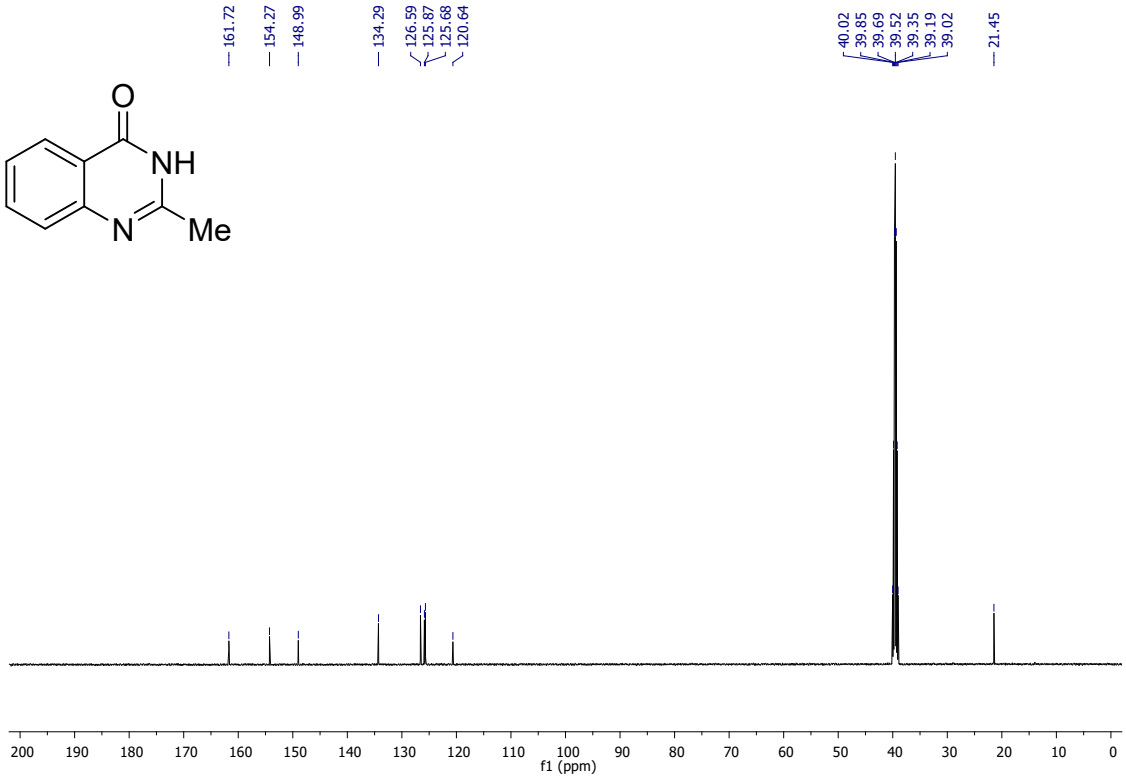


Figure S141: ^{13}C{^{1}H} NMR spectrum of **4a** (126 MHz, DMSO-d_6)

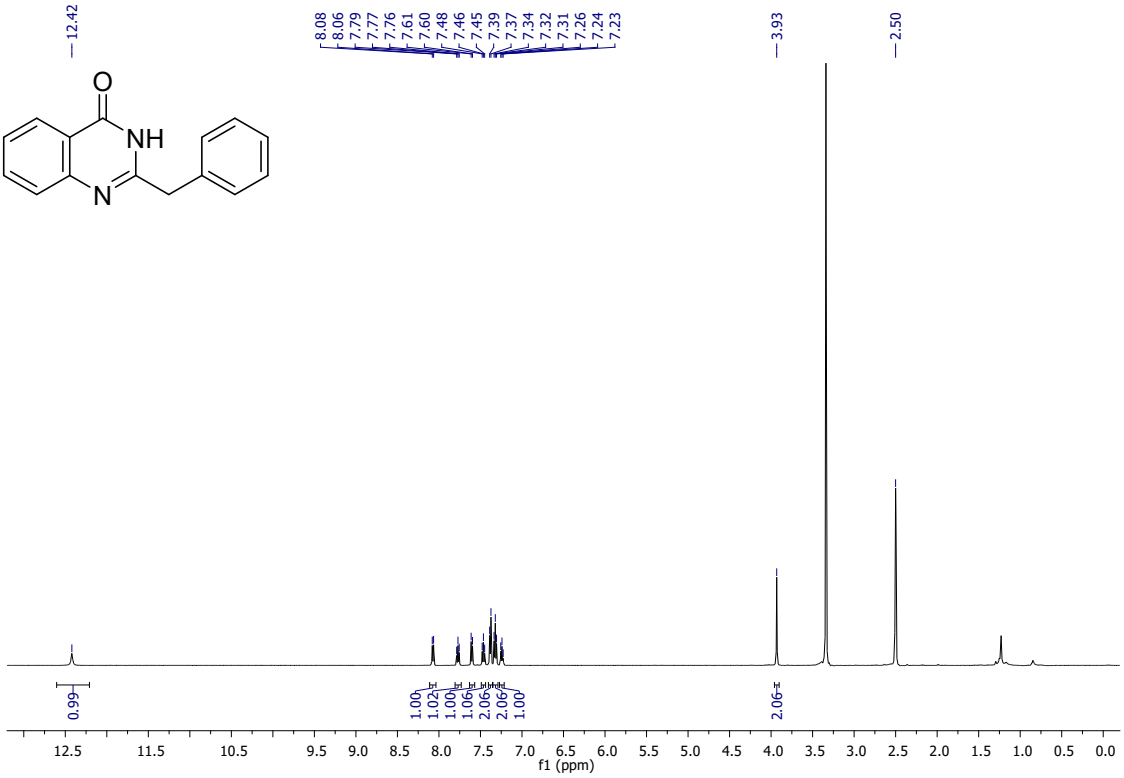


Figure S142: ^{1}H NMR spectrum of **4b** (500 MHz, DMSO-d6)

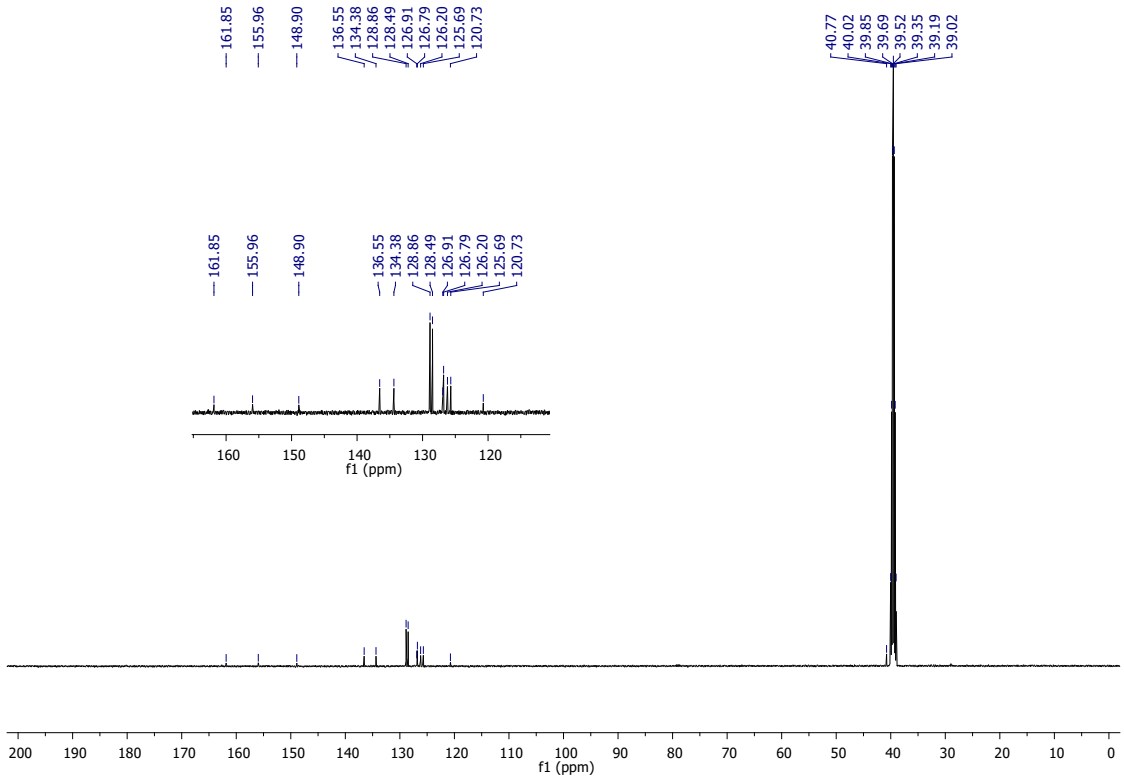


Figure S143: $^{13}C\{^{1}H\}$ NMR spectrum of **4b** (126 MHz, DMSO-d_6)

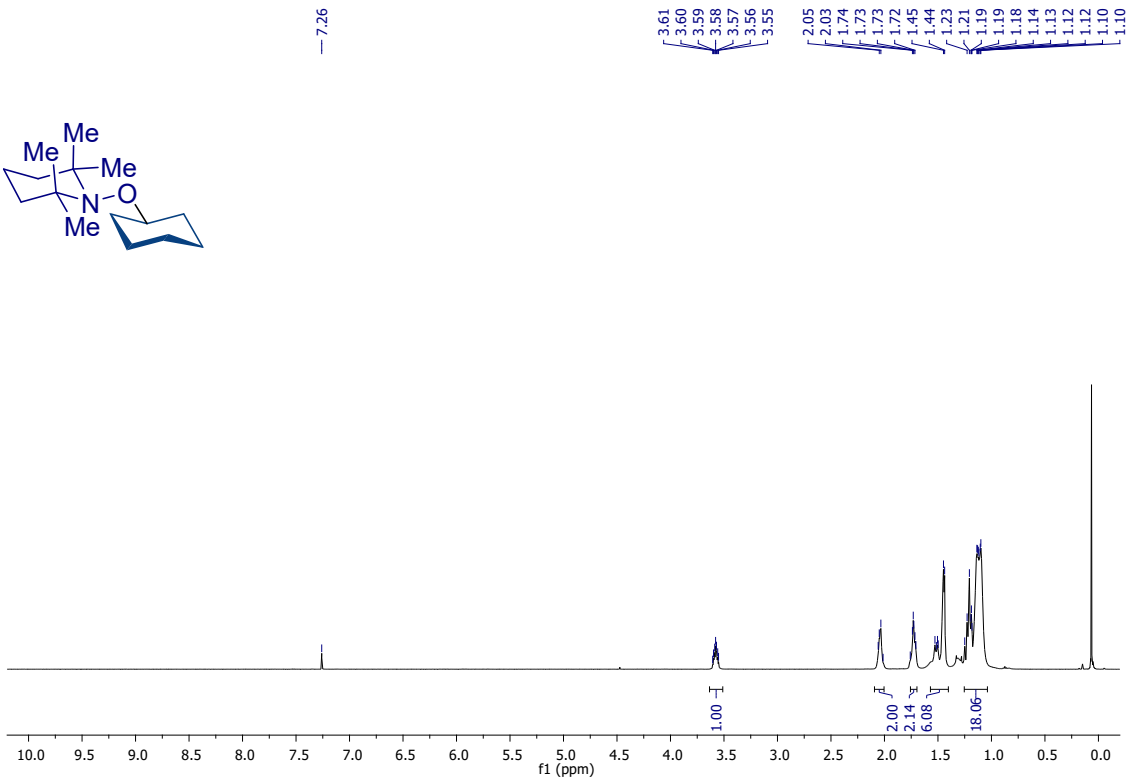


Figure S144: ^{1}H NMR spectrum of **6** (500 MHz, $CDCl_3$)

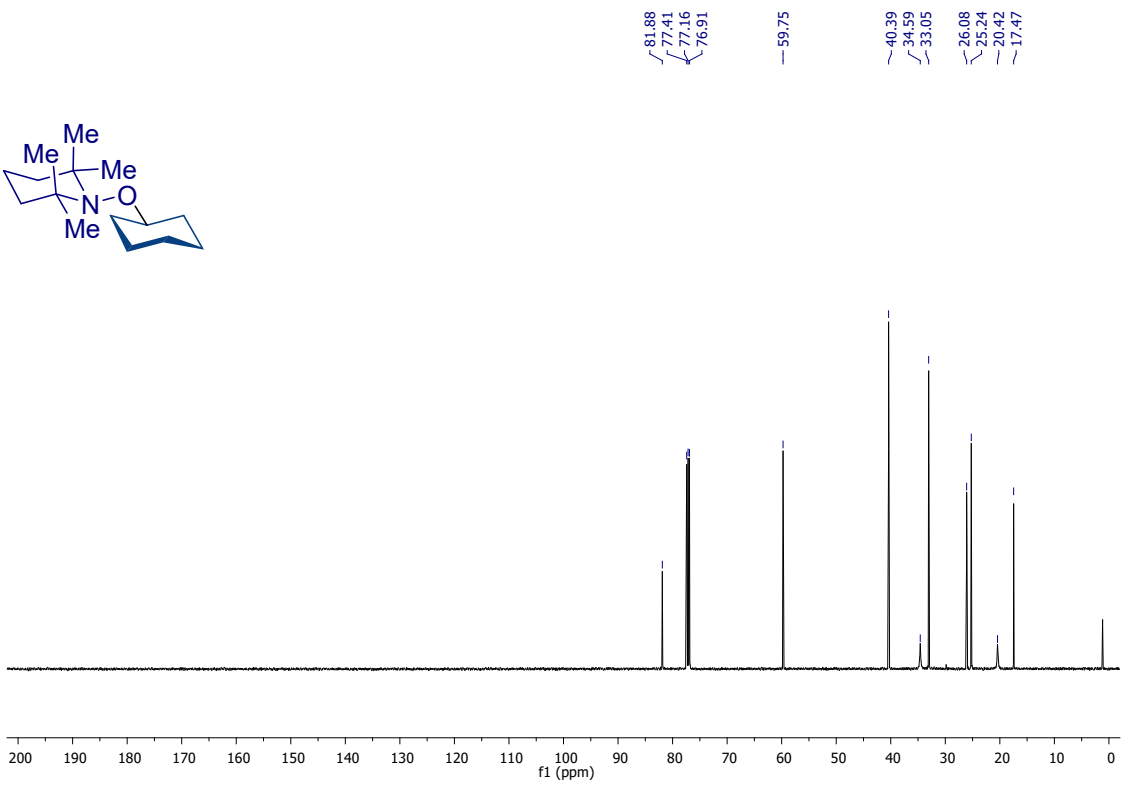


Figure S145: $^{13}C\{^{1}H\}$ NMR spectrum of **6** (126 MHz, $CDCl_3$)

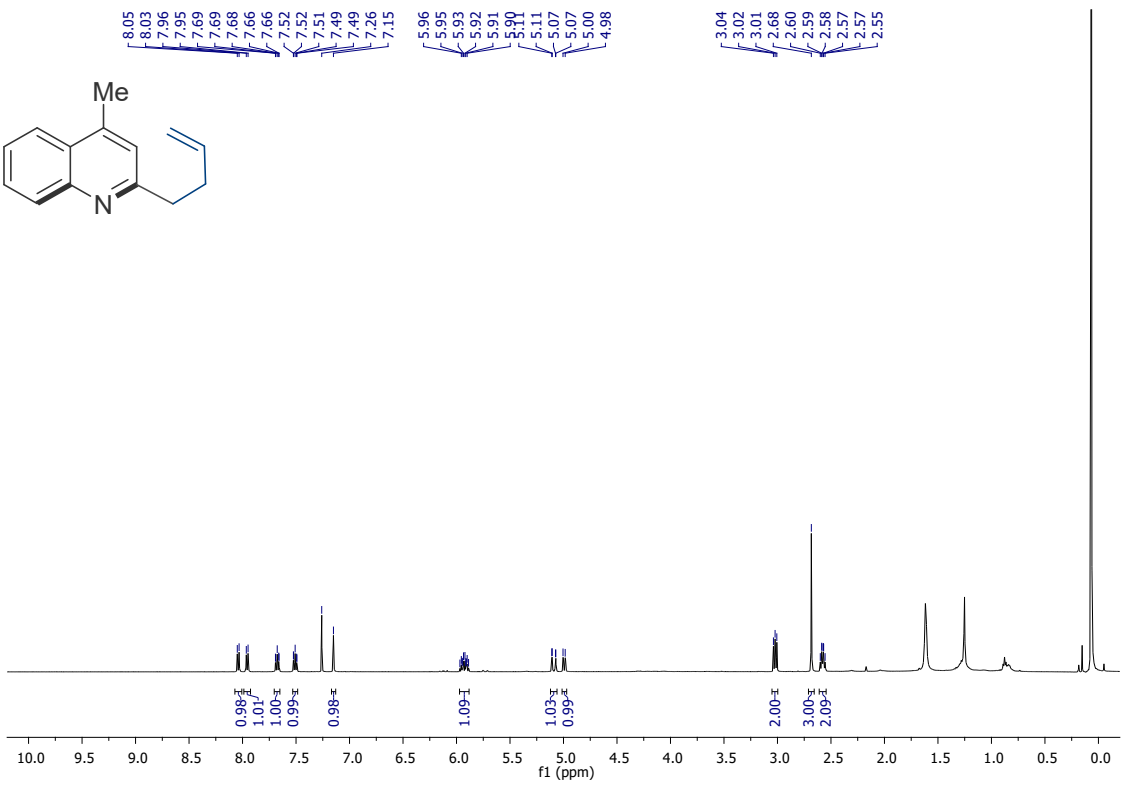


Figure S146: ^{1}H NMR spectrum of **3ap** (500 MHz, $CDCl_3$)

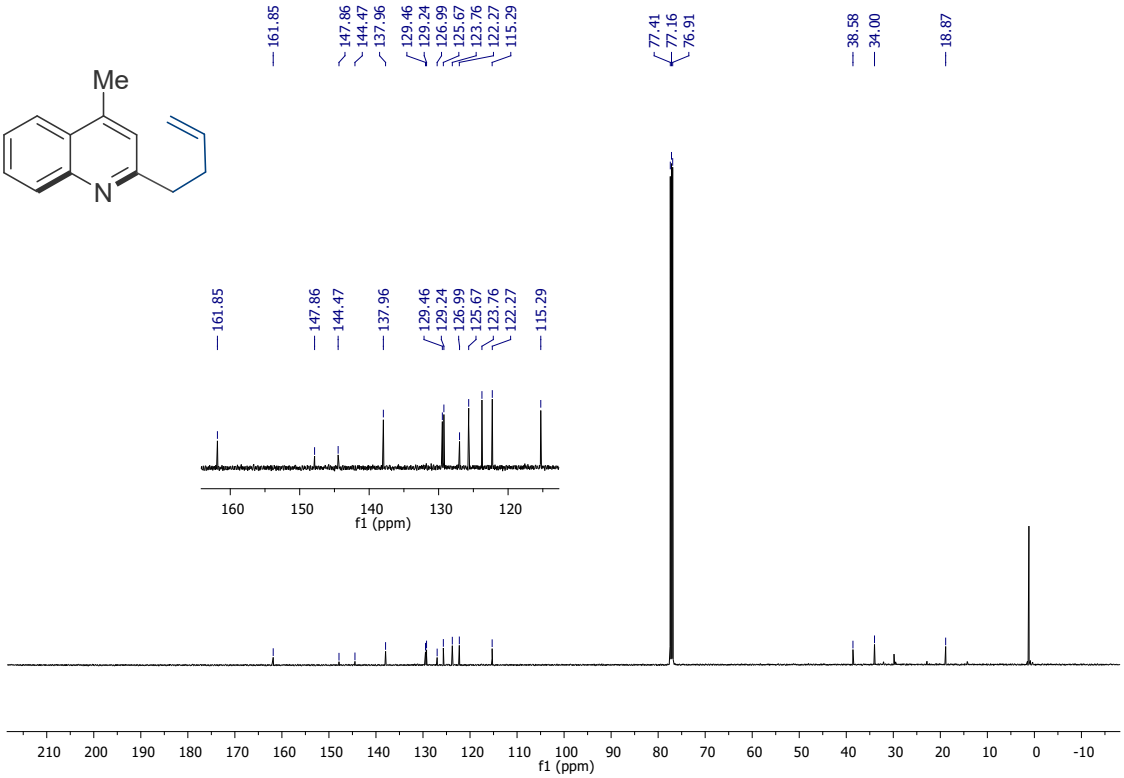


Figure S147: $^{13}C\{^{1}H\}$ NMR spectrum of **3ap** (126 MHz, $CDCl_3$)