Electronic Supplementary Material (ESI) for ChemComm.

Supplementary information for

Pyridine N-oxides as HAT reagents for photochemical C-H functionalization of electron-deficient heteroarenes

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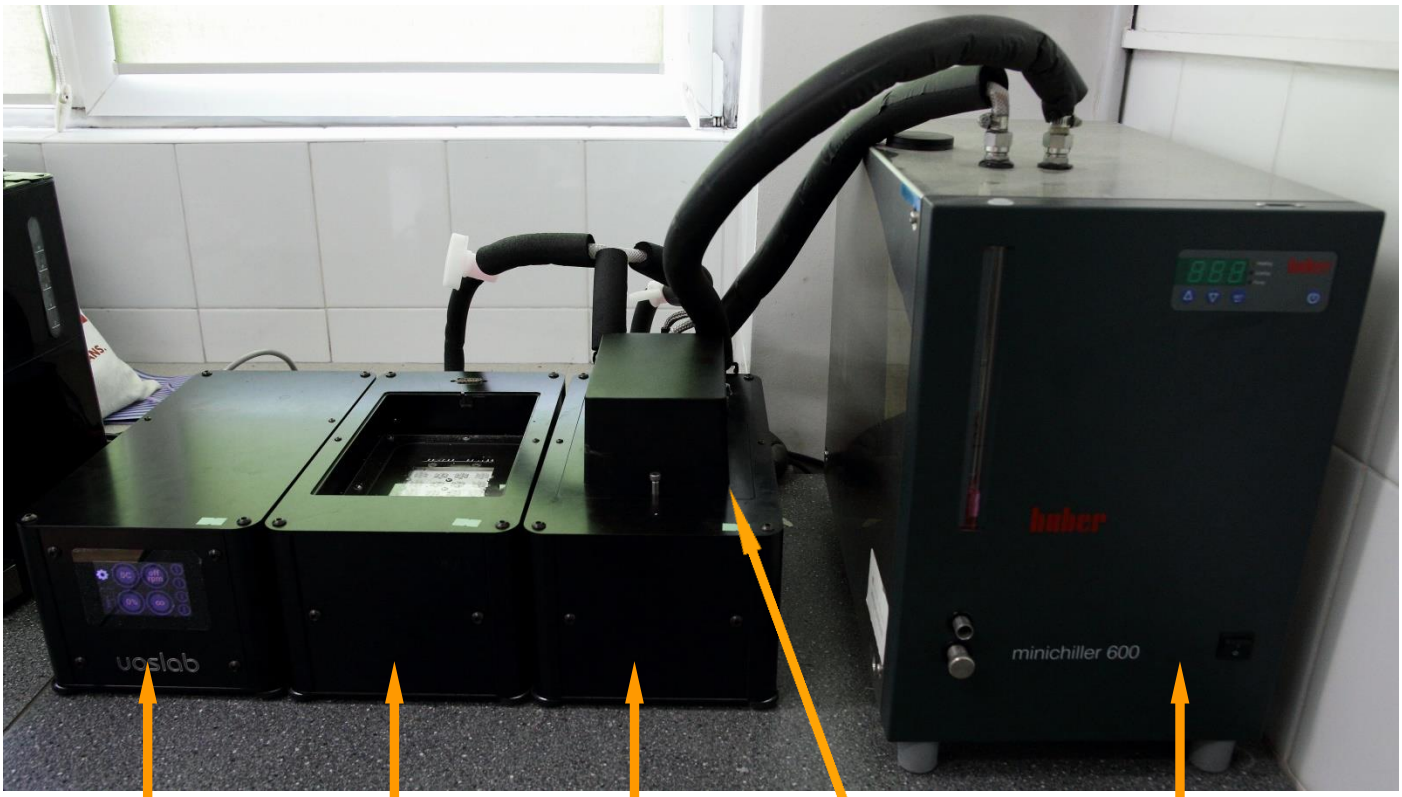
1 General information

All solvents and commercially available reagents were purchased as reagent grade and were used without further purification, unless otherwise stated. Reactions were monitored by thin layer chromatography (TLC), using 0.20 mm Merck silica plates (60F-254) and visualised using UV-light. Colum chromatography was performed on Merck silica gel 60 (230-400 mesh). Yields refer to spectroscopically (^{1}H NMR) homogeneous materials.

NMR spectra were recorded on Bruker 400 MHz, Bruker 500 MHz or Varian 500 MHz apparatus and calibrated using residual undeuterated solvent ($CHCl_3$ – 7.26 ppm ^{1}H NMR, 77.16 ppm ^{13}C NMR) or TMS as an internal reference. Low-resolution mass spectra (LRMS) were recorded on an Applied Biosystems API 365 mass spectrometer using electrospray ionization (ESI) technique. High-resolution mass spectra (HRMS) were recorded on a Waters SYNAPT G2-S HDMS instrument using electrospray ionization (ESI) with time of flight detector (TOF). Elemental analyses (C, H, N) are performed using a PERKIN-ELMER 240 Elemental Analyzer. Gas chromatography coupled with a flame ionization detector (GC-FID) was performed on an Shimadzu GCMS-QP2010 SE with helium as the carrier gas and Zebron ZB 5MSi column. GC yields were determined using dodecane as an internal standard. UV-Vis experiments were performed on Agilent Cary 60 UV-Vis Spectrophotometer. Photochemical reactions were conducted in commercially available UOSlab MiniPhoto photoreactor.



power source/controller unit
maximum electrical power:
600W

LED blocks:
left: mixed wavelength: 525, 365, 405, 660 nm
right: single wavelength: 455 nm

vial holder
(for 24 10 mL vials)

chiller

2 General procedures

2.1 GP-1: General procedure for alkylation of lepidine with radical precursors using $Zn(OTf)_2$ as an activating agent

In a 10 mL crimp-top vial equipped with a stirring bar, a solution of 109 mg of $Zn(OTf)_2$ (0.30 mmol) in 2.5 mL of HPLC-grade acetonitrile is prepared. Then 26 µL (28.6 mg, 0.20 mmol) of lepidine and 27 µL (0.25 mmol) of 2,6-lutidine *N*-oxide is added, the vial is crimped and the solution is deoxygenated via argon flow in a ultrasonic bath for 10 minutes. After deoxygenation, a radical precursor is added with a Hamilton syringe. The top of the vial is then secured with parafilm, and the reaction mixture is irradiated for 16 hours at 405 nm with UOSlab MiniPhoto photoreactor set to 100% power. After irradiation the reaction mixture is diluted with brine, extracted 3 times with dichloromethane and dried over Na_2SO_4. After evaporation of the solvent a crude product is purified using column chromatography.

2.2 GP-1': General procedure for alkylation of lepidine with radical precursors using $Zn(OTf)_2$ as an activating agent in anhydrous conditions

To a 10 mL crimp-top vial equipped with a stirring bar, 109 mg of $Zn(OTf)_2$ (0.30 mmol) is added, then the vial is sealed and air is evacuated using vacuum pump and bacfilled with argon 3 times. Then 2.5 mL of anhydrous acetonitrile, 26 µL (28.6 mg, 0.20 mmol) of lepidine and 27 µL (0.25 mmol) of 2,6-lutidine *N*-oxide and the solution is deoxygenated via argon flow in a ultrasonic bath for 10 minutes. After deoxygenation, a radical precursor is added with a Hamilton syringe. The top of the vial is then secured with parafilm, and the reaction mixture is irradiated for 16 hours at 405 nm with UOSlab MiniPhoto photoreactor set to 100% power. After irradiation the reaction mixture is diluted with brine, extracted 3 times with dichloromethane and dried over Na_2SO_4. After evaporation of the solvent a crude product is purified using column chromatography.

2.3 GP-2: General procedure for alkylation of lepidine with radical precursors using TFA as an activating agent

In a 10 mL crimp-top vial equipped with a stirring bar, a solution of 26 µL (28.6 mg, 0.20 mmol) of lepidine and 27 µL (0.25 mmol) of 2,6-lutidine *N*-oxide in 2.5 mL of HPLC-grade acetonitrile is prepared. Then 47 µL (0.6 mmol) of TFA is added, the vial is crimped and the solution is deoxygenated via argon flow in a ultrasonic bath for 10 minutes. After deoxygenation, a radical precursor is added with a Hamilton syringe. The top of the vial is then secured with parafilm, and the reaction mixture is irradiated for 16 hours at 405 nm with UOSlab MiniPhoto photoreactor set to 100% power. After irradiation the reaction mixture is diluted with aqueous $NaHCO_3$, extracted 3 times with dichloromethane and dried over Na_2SO_4. After evaporation of the solvent a crude product is purified using column chromatography.

2.4 GP-3: General procedure for alkylation of electron-deficient heteroarenes with cyclohexane using TFA as an activating agent

In a 10 mL crimp-top vial equipped with a stirring bar, a solution electron-deficient heteroarene (0.20 mmol) and 27 µL (0.25 mmol) of 2,6-lutidine *N*-oxide in 2.5 mL of HPLC-grade acetonitrile is prepared. Then 47 µL (0.6 mmol) of TFA is added, the vial is crimped and the solution is deoxygenated via argon flow in a ultrasonic bath for 10 minutes. After deoxygenation 215 µL (2 mmol) of cyclohexane is added with a Hamilton syringe. The top of the vial is then secured with parafilm, and the reaction mixture is irradiated for 16 hours at 405 nm with UOSlab MiniPhoto photoreactor set to 100% power. After irradiation the reaction mixture is diluted with aqueous $NaHCO_3$, extracted 3 times with dichloromethane and dried over Na_2SO_4. After evaporation of the solvent a crude product is purified using column chromatography.

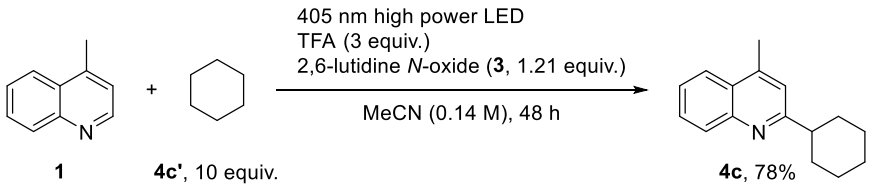
2.5 GP-4: General procedure for alkylation of electron-deficient heteroarenes with cycloheaxane using $Zn(OTf)_2$ as an activating agent

In a 10 mL crimp-top vial equipped with a stirring bar, a solution of 109 mg of $Zn(OTf)_2$ (0.30 mmol) in 2.5 mL of HPLC-grade acetonitrile is prepared. Then electron-deficient heteroarene (0.20 mmol) and 27 µL (0.25 mmol) of 2,6-lutidine *N*-oxide is added, the vial is crimped and the solution is deoxygenated via argon flow in a ultrasonic bath for 10 minutes. After deoxygenation 215 µL (2 mmol) of cyclohexane is added with a Hamilton syringe. The top of the vial is then secured with parafilm, and the reaction mixture is irradiated for 48 hours at 405 nm with UOSlab MiniPhoto photoreactor set to 100% power. After irradiation the reaction mixture is diluted with brine, extracted 3 times with dichloromethane and dried over Na_2SO_4. After evaporation of the solvent a crude product is purified using column chromatography.

2.6 GP-5: General procedure for alkylation of electron-deficient heteroarenes with cyclohexane using an increased amount of TFA as an activating agent

In a 10 mL crimp-top vial equipped with a stirring bar, a solution electron-deficient heteroarene (0.20 mmol) and 27 µL (0.25 mmol) of 2,6-lutidine *N*-oxide in 2.5 mL of HPLC-grade acetonitrile is prepared. Then 94 µL (1.2 mmol) of TFA is added, the vial is crimped and the solution is deoxygenated via argon flow in a ultrasonic bath for 10 minutes. After deoxygenation 215 µL (2 mmol) of cyclohexane is added with a Hamilton syringe. The top of the vial is then secured with parafilm, and the reaction mixture is irradiated for 16 hours at 405 nm with UOSlab MiniPhoto photoreactor set to 100% power. After irradiation the reaction mixture is diluted with aqueous $NaHCO_3$, extracted 3 times with dichloromethane and dried over Na_2SO_4. After evaporation of the solvent a crude product is purified using column chromatography.

3 Reaction scale-up

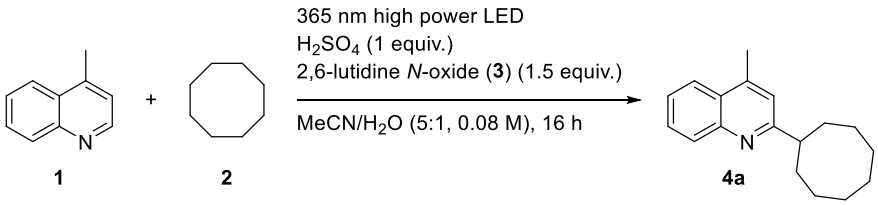


1 **4c'**, 10 equiv. **4c**, 78%

In a 10 mL crimp-top vial equipped with a stirring bar, a solution of 130 µL (146.3 mg, 1.02 mmol) of lepidine and 138 µL (151,9 mg, 1.23 mmol) of 2,6-lutidine *N*-oxide in 7.0 mL of HPLC-grade acetonitrile is prepared. Then 235 µL (3.0 mmol) of TFA is added, the vial is crimped and the solution is deoxygenated via argon flow in a ultrasonic bath for 15 minutes. After deoxygenation, a 1mL (10 mmol) of cyclohexane is added with a syringe. The top of the vial is then secured with parafilm, and the reaction mixture is irradiated for 48 hours at 405 nm with UOSlab MiniPhoto photoreactor set to 100% power. After irradiation the reaction mixture is diluted with aqueous $NaHCO_3$, extracted 4 times with dichloromethane and dried over Na_2SO_4. After evaporation of the solvent a crude product is purified using column chromatography (eluent: 7% ethyl acetate/hexane). The product **4c** is obtained as 175.6 mg (0.78 mmol 76% yield) of a colourless oil.

4 Detailed optimisation of the reaction conditions

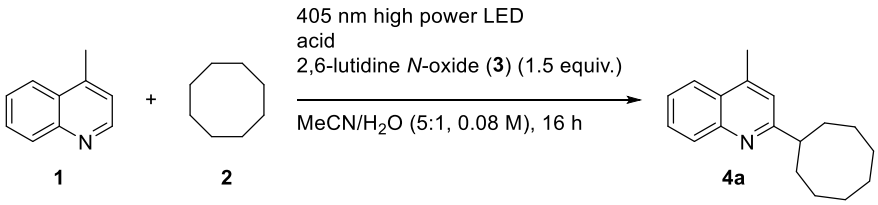
Table S1 Initial optimization and background experiments.



entry	deviation from listed conditions	yield (GC) /%
1	none	30
2	no acid	traces
3	no irradiation	traces
4	thermal activation (60 °C)	traces
5	no *N*-oxide	traces
6	not degassed (open to air)	25
7	prolonged irradiation (24h)	32
8	**irradiated at 405 nm**	**37**
9	irradiated at 455 nm	traces

Reaction conditions: lepidine (**1**) 0.2 mmol, cyclooctane (**2**) 1.0 mmol, H_2SO_4 0.2 mmol, 2,6-lutidine *N*-oxide (**3**) 0.3 mmol in 2.5 mL of MeCN/H_2O (5:1) irradiated with high power LEDs for 16 h, yield determined by GC.

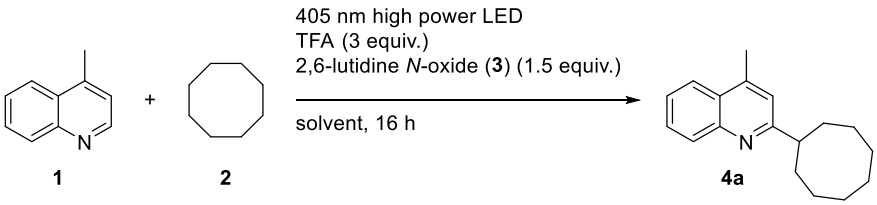
Table S2 Screening and optimization of the amount of acid.



entry	acid	amount	yield (GC) /%
1	H_2SO_4	1 equiv.	37
2	H_2SO_4	2 equiv.	70
3	H_2SO_4	4 equiv.	75
4	H_2SO_4	3 equiv.	76
5	HCl (36%)	3 equiv.	57
6	acetic acid	3 equiv.	12
7	formic acid	3 equiv.	9
8	oxalic acid	3 equiv.	65
9	H_3PO_4	3 equiv.	38
10	HBF_4	3 equiv.	75
11	*p*-toluenesulphonic acid	3 equiv.	30
12	chloroacetic acid	3 equiv.	22
13	TFA	3 equiv.	78
14	**TFA, no H_2O added**	**3 equiv.**	**79**

Reaction conditions: lepidine (**1**) 0.2 mmol, cyclooctane (**2**) 1.0 mmol, acid, 2,6-lutidine *N*-oxide (**3**) 0.3 mmol in 2.5 mL of MeCN/H_2O (5:1) irradiated at 405 nm with high power LEDs for 16 h, yield determined by GC.

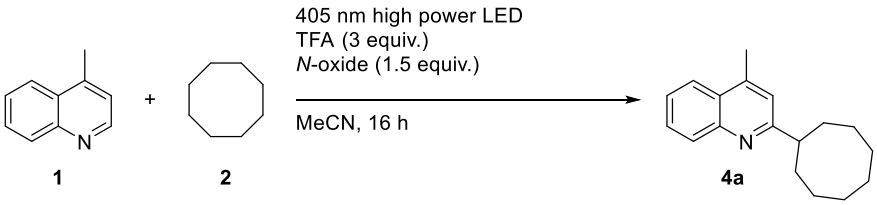
Table S3 Solvent and concentration screening.



entry	solvent	concentration /M	yield (GC) /%
1	methanol	0.08	traces
2	acetone	0.08	52
3	dichloromethane	0.08	42
4	dichloroethane	0.08	61
5	dimethylformamide	0.08	traces (different product)
6	dimethylsulfoxide	0.08	traces (different product)
7	CD_3CN	0.08	74
8	**acetonitrile**	**0.08**	**79**
9	acetonitrile	0.2	67
10	acetonitrile	0.04	73

Reaction conditions: lepidine (**1**) 0.2 mmol, cyclooctane (**2**) 1.0 mmol, TFA (3 equiv.), 2,6-lutidine *N*-oxide (**3**) 0.3 mmol in solvent irradiated at 405 nm with high power LEDs for 16 h, yield determined by GC.

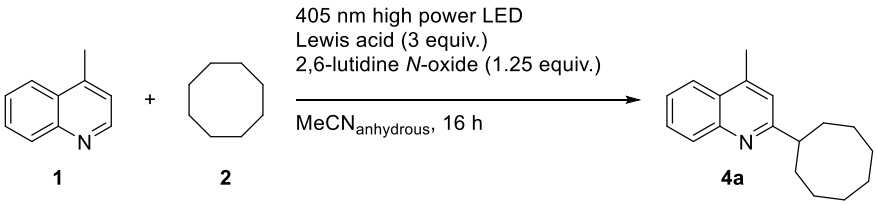
Table S4 Screening of *N*-oxides



entry	*N*-oxide	yield (GC) /%
1	2-picoline-	74
2	4-picoline-	60
3	4-nitropyridine-	8
4	*N*-methylmorpholine-	traces
5	2,4,5-trimethylpyridine-	40
6	4-cyanopyridine-	17 (side products)
7	4-methyoxypyridine-	15
8	3-(methoxycarbonyl)-	28
9	isoquinoline-	10 (side product)
10	2-cyano,6-methoxypyridine-	55
11	2,6-lutidine-	79
12	2,6-lutidine-; 2 equiv.	65
13	**2,6-lutidine-; 1.25 equiv.**	**78**

Reaction conditions: lepidine (**1**) 0.2 mmol, cyclooctane (**2**) 1.0 mmol, TFA (3 equiv.), *N*-oxide 0.3 mmol in 2.5 mL of MeCN irradiated at 405 nm with high power LEDs for 16 h, yield determined by GC.

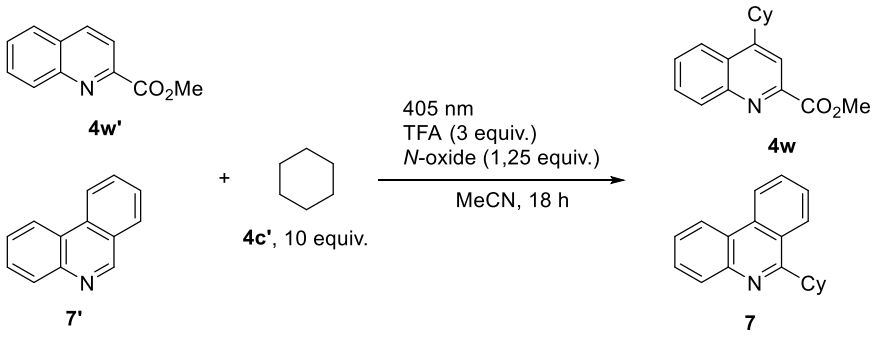
Table S5 Screening of an alternative activating agent –Lewis acid



entry	*N*-oxide	yield (GC) /%
1	$LiBF_4$	20
2	$MgCl_2$	traces
3	$ZnCl_2$	traces
4	$Zn(OAc)_2$	traces
5	$Sc(OTf)_3$	73
6	$Al(OTf)_3$	traces
7	$Fe(OTf)_2$	traces
8	$AlCl_3$	77
9	$Zn(OTf)_2$	79
10	$Zn(OTf)_2$, HPLC MeCN	79
11	$Zn(OTf)_2$, HPLC MeCN, 2 equiv.	78
12	**$Zn(OTf)_2$, HPLC MeCN, 1.5 equiv.**	**81**
13	$Zn(OTf)_2$, HPLC MeCN, 1.25 equiv.	69

Reaction conditions: lepidine (**1**) 0.2 mmol, cyclooctane (**2**) 1.0 mmol, Lewis acid (3 equiv.), 2,6-lutidine *N*-oxide 0.25 mmol in 2.5 mL of MeCN irradiated at 405 nm with high power LEDs for 16 h, yield determined by GC.

Table S6 Additional screening of *N*-oxides for selected substrates **4w**' and **7'**

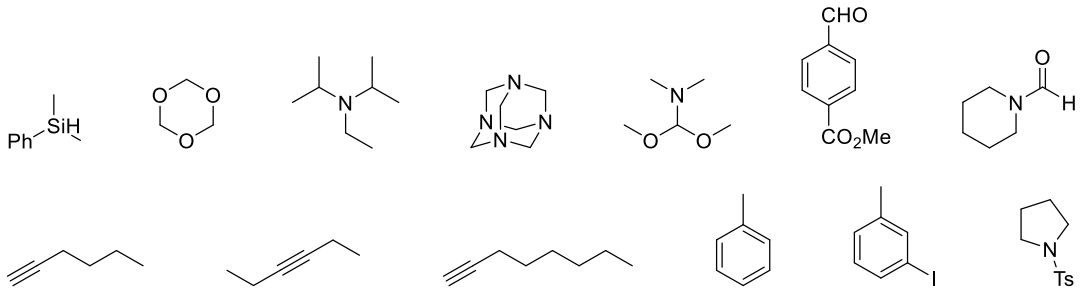


entry	*N*-oxide	yield **4w** /%	yield **7** /%
1	2,6-lutidine-	25	21
2	2-cyano-6-mehtylpyridine-	33	41
3	3-(methoxycarbonyl)-	21	32
4	isoquinoline-	13	24
5	lepidine-	26	25
6	2,4,6-trimethylpyridine	23	7

Reaction conditions: heteroarene 0.1 mmol, cyclohexane 1.0 mmol, trifluoracetic acid 0.3 mmol, *N*-oxide 0.125 mmol in 1.5 mL of MeCN irradiated with 405 nm LED for 18 hours, yield determined by GC.

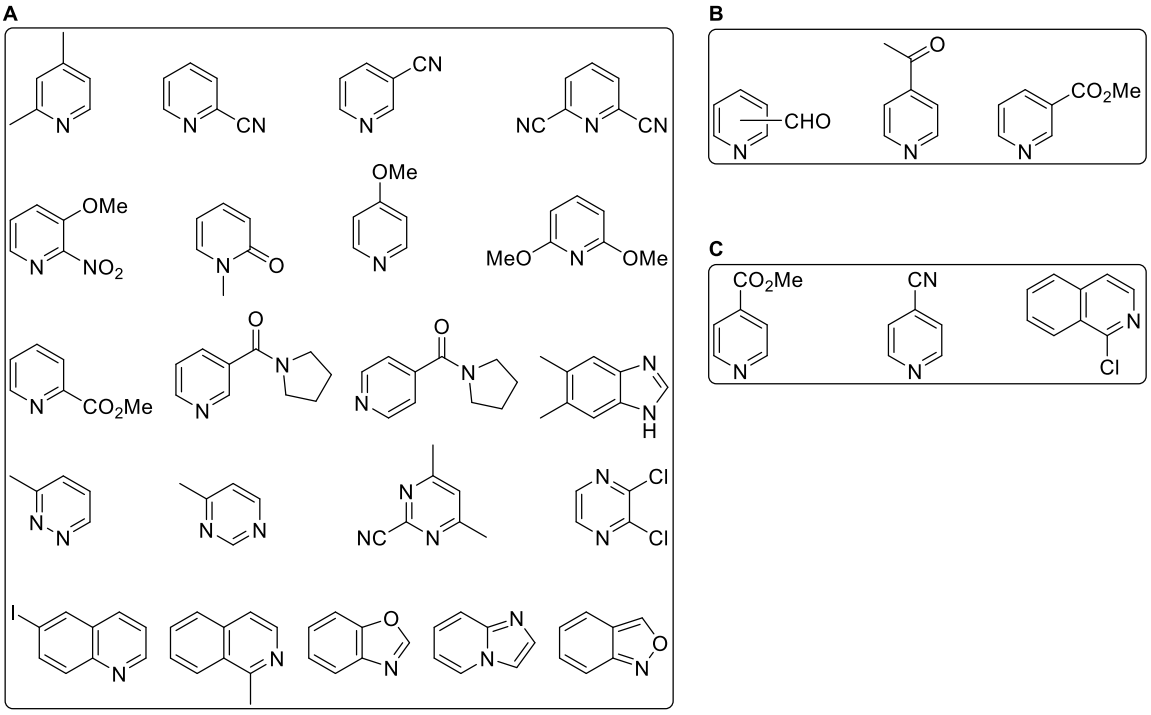
5 Unsuccessful substrates

5.1 Radical precursors



Scheme S1 Unsuccessful radical precursors

5.2 Heteroaromatic compounds



Scheme S2 Unsuccessful heteroaromatic substrates: **A** – low or no conversion of substrate, **B** – full conversion of substrate, complex mixture of products formed. **C** – low conversion and a mixture of products formed.

6 Mechanistic studies

6.1 UV-Vis Experiments

Electron donor-acceptor (EDA) complex formation between 2,6-lutidine *N*-oxide (**3**) and lepidine is postulated, therefore a series of UV-Vis spectra measurements were performed.

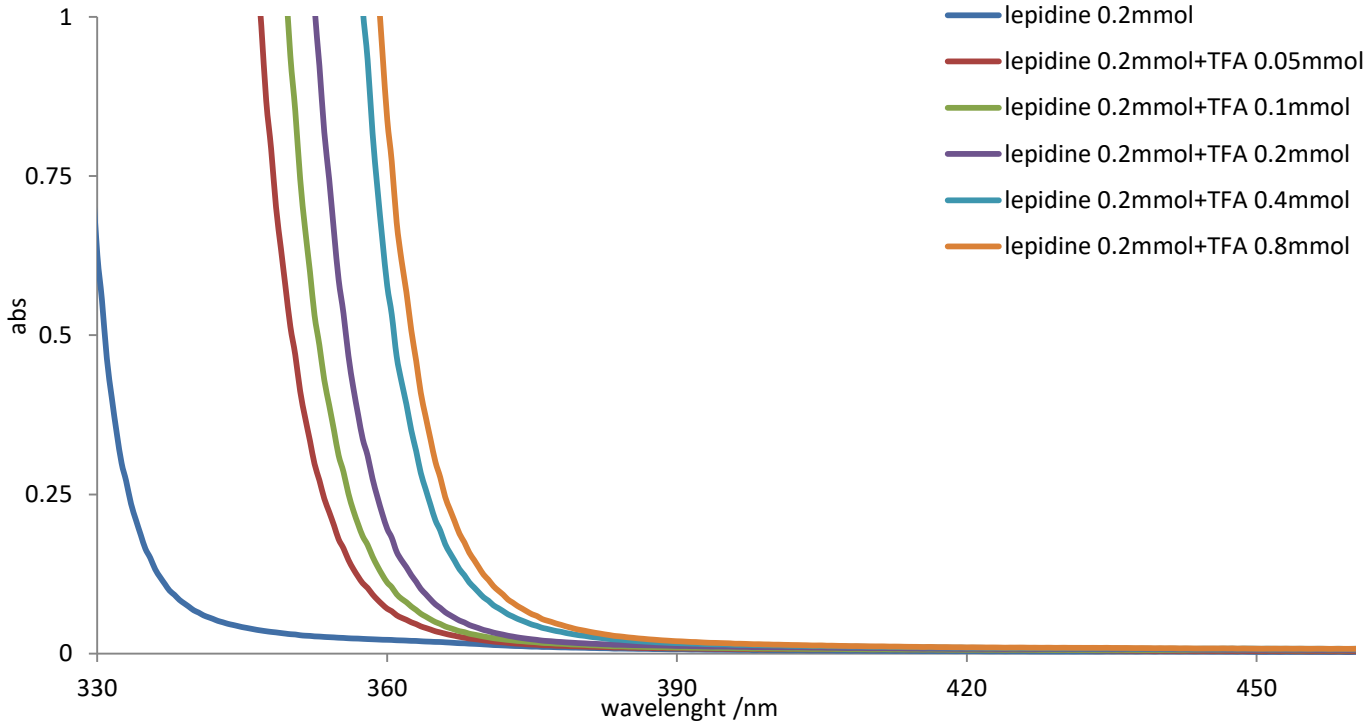


Figure S1 UV-Vis spectra of lepidine (**1**, 0.2 mmol) in acetonitrile (2.5 mL) in the presence of varying amount of TFA.

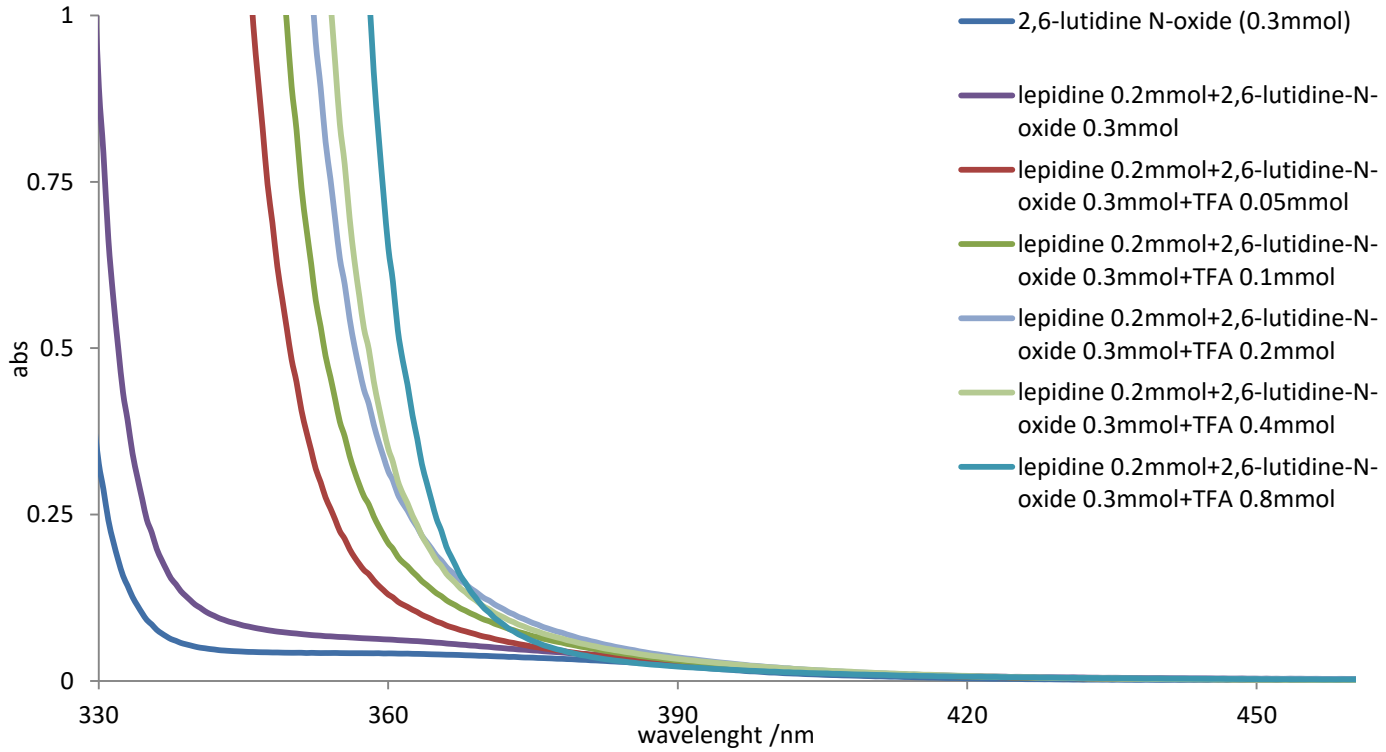


Figure S2 UV-Vis spectra of 2,6-lutidine *N*-oxide (**3**, 0.3 mmol) in acetonitrile (2.5 mL) in the presence lepidine (**1**, 0.2 mmol) and varying amount of TFA.

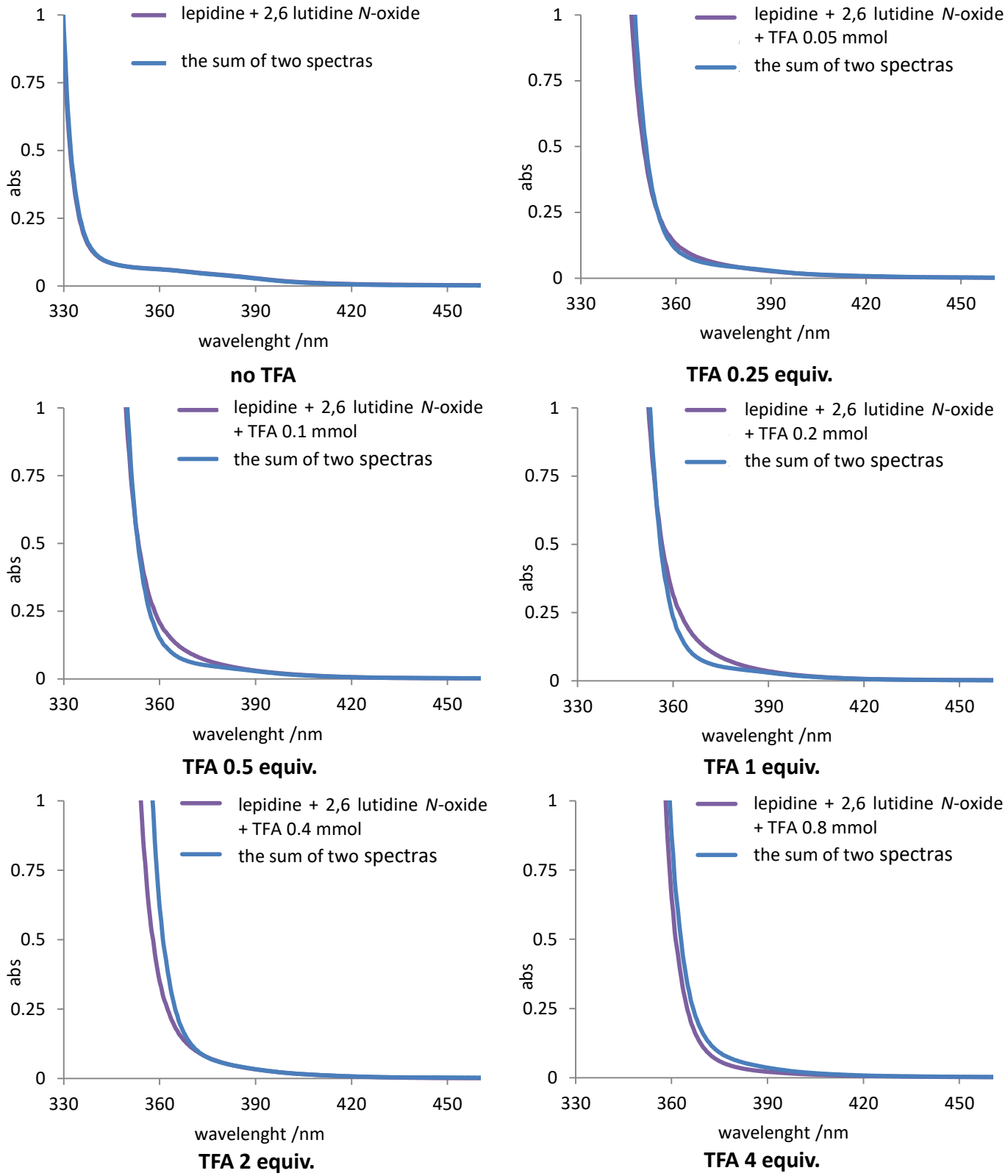


Figure S3 UV-Vis sprectras of mixtures of lepidine (**1**, 0.08 M) and 2,6-lutidine *N*-oxide (**3**, 0.12 M) in the presence of varying amount of TFA collated with a mathematical sum of the spectra of the mixture components.

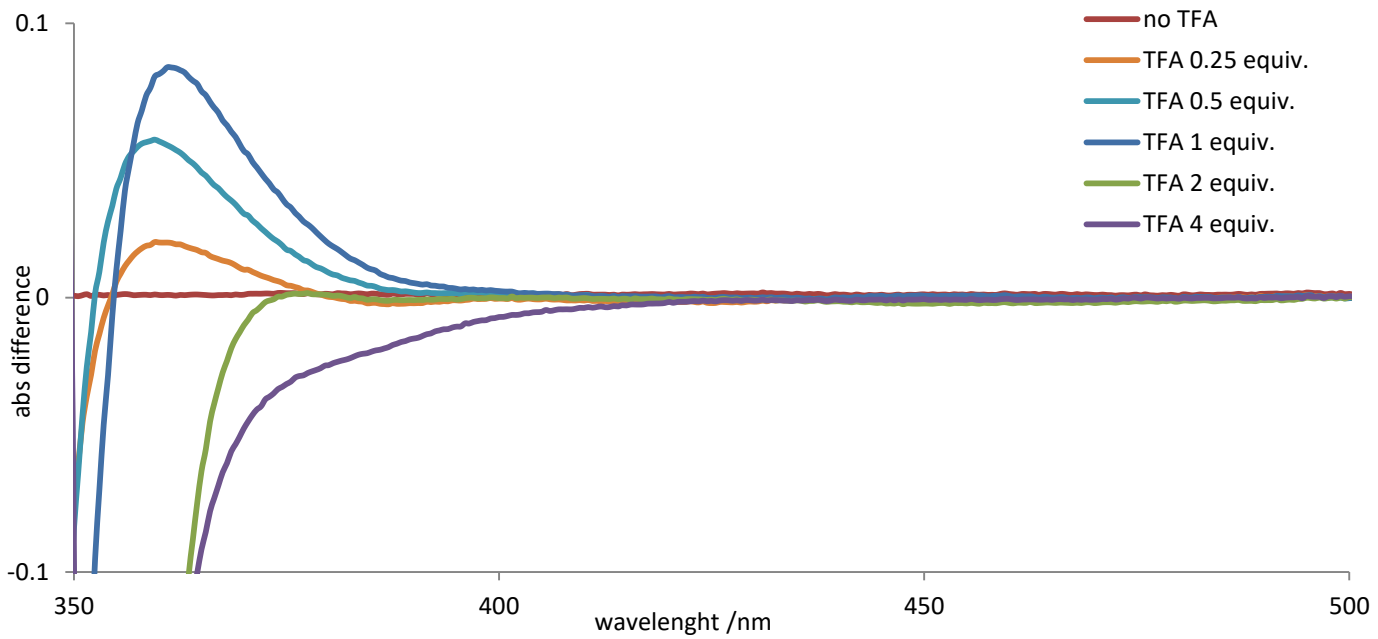


Figure S4 Difference between absorption of the mixture of 2,6-lutidine *N*-oxide (**3**, 0.3 mmol) and lepidine (**1**, 0.2 mmol) in the presence of varying amount of TFA and the sum of the absorption of 2,6-lutidine *N*-oxide (**3**, 0.3 mmol) and lepidine (**1**, 0.2 mmol) in the presence of varying amount of TFA.

On the Figure S3 a gradual increase in absorption of the mixture of 2,6-lutidine *N*-oxide (**3**) and lepidine (**1**) is pronounced upon addition of TFA up to 1 equiv. in comparison to the sum of absorption of the components. This increase around 375 nm suggests the formation of EDA complex between protonated lepidine and 2,6-lutidine *N*-oxide (**3**). Upon further addition of TFA this new band diminishes, which is probably caused by the protonation of the *N*-oxide and subsequent decomposition of the complex. To better visualize the absorption increase we substracted the sum of the spectra of the components from the spectra of the EDA complex (Figure S4). A similar experiment was conducted for the pair of phenanthridine (**7'**) and 2-cyano,6-methylpyridine *N*-oxide (Figure S5). In this case the absorption increase was also visible, however its maximum observed in the presence of only 0.25 equiv. of TFA.

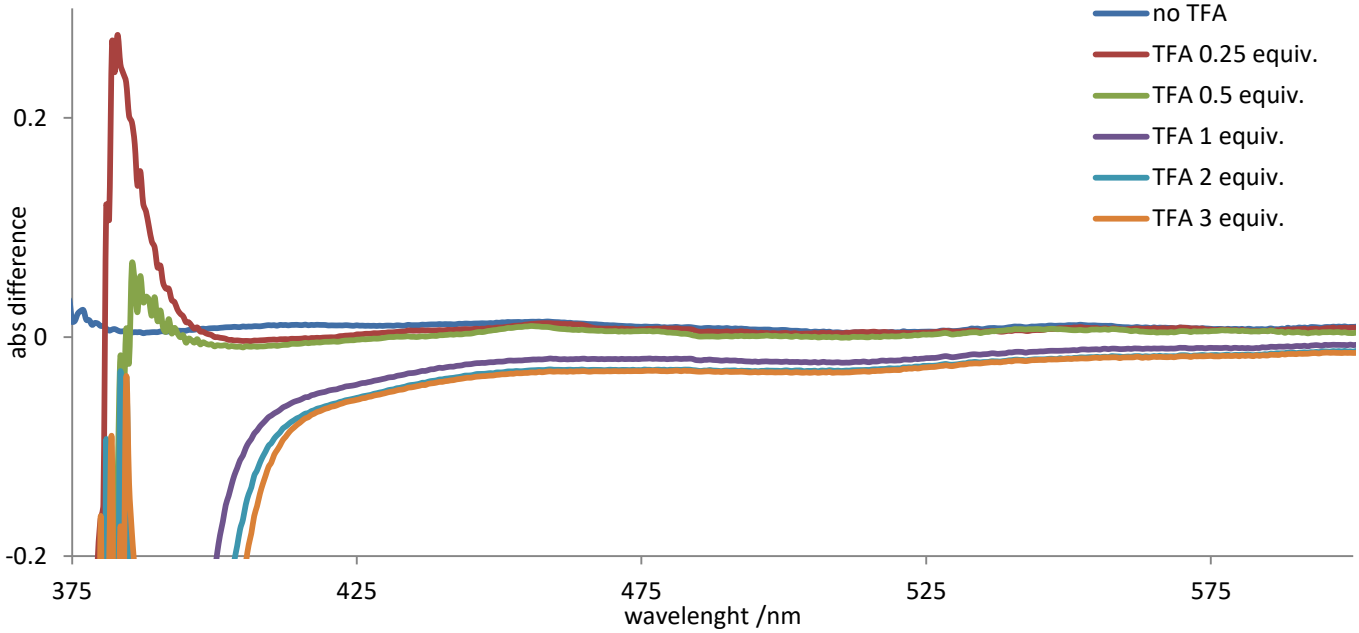
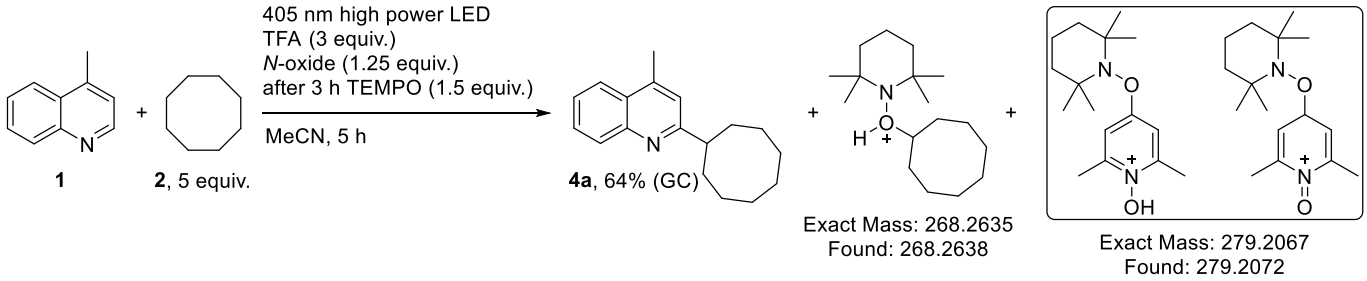


Figure S5 Difference between absorbtion of the mixture of 2-cyano,6-methylpyridine *N*-oxide (0.15 mmol) and phenanthridine (**7'**, 0.1 mmol) in the presence of varying amount of TFA and the sum of the absorption of 2-cyano,6-methylpyridine *N*-oxide (0.15 mmol)and and phenanthridine (**7'**, 0.1 mmol)in the presence of varying amount of TFA.

6.2 Reaction in the presence of the radical trap

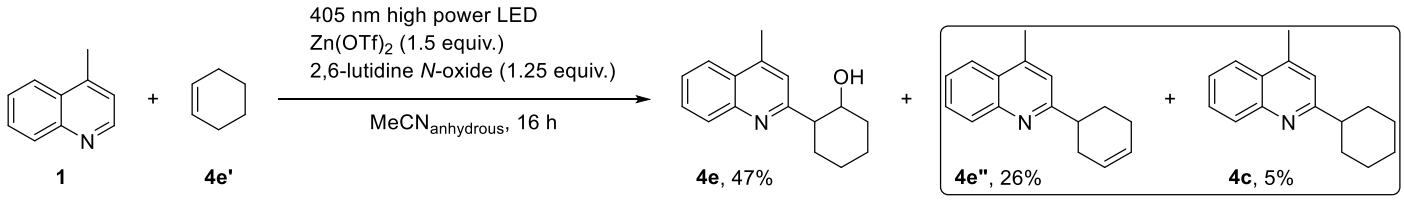


Scheme S3 Radical trapping experiments.

The reaction was set up according to a slightly modified general procedure GP-2: 1.5 equiv. (0.3 mmol, 48.9 mg) of TEMPO as a solution in 0.5 mL of MeCN was added to the reaction mixture after 3 hours of irradiation. Then the septum was sealed with parafilm and irradiation was continued for 2 hours. After the irradiation an internal standard (dodecane) was added and GC and MS samples were prepared. Reaction performed in the presence of TEMPO from the start yielded only 9% of **4a**.

6.3 Reaction with alkenes

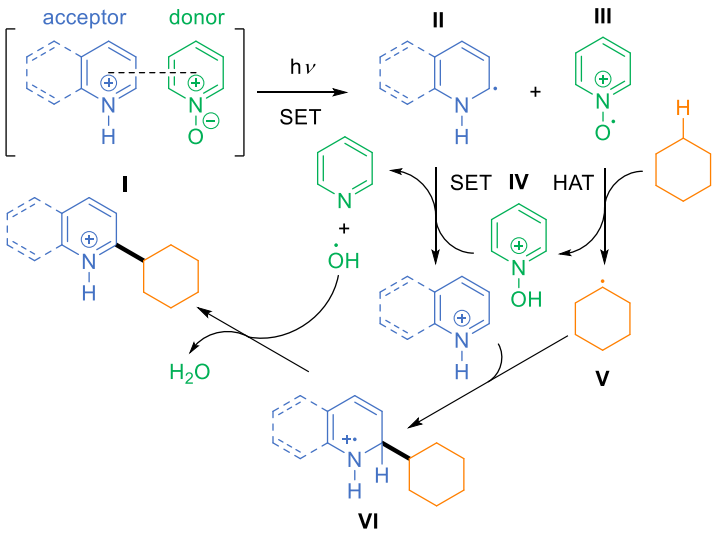
When cyclohexene (**4e'**) was subjected to GP-1 hydroxylated compound **4e** formed as a main product (51%). In the reaction mixture a siginificant amount of **4e"** has been also detected by the GC-MS analysis. We wondered whether the oxygen atom in **4e** originates from 2,6-lutidine *N*-oxide (**3**) or from the traces of water present in the reaction mixture. To exclude the latter, the reaction with cyclohexene (**4e'**) was set up in anhydrous conditions (GP-1').



Scheme S4 Reaction with cyclohexane performed in anhydrous conditions.

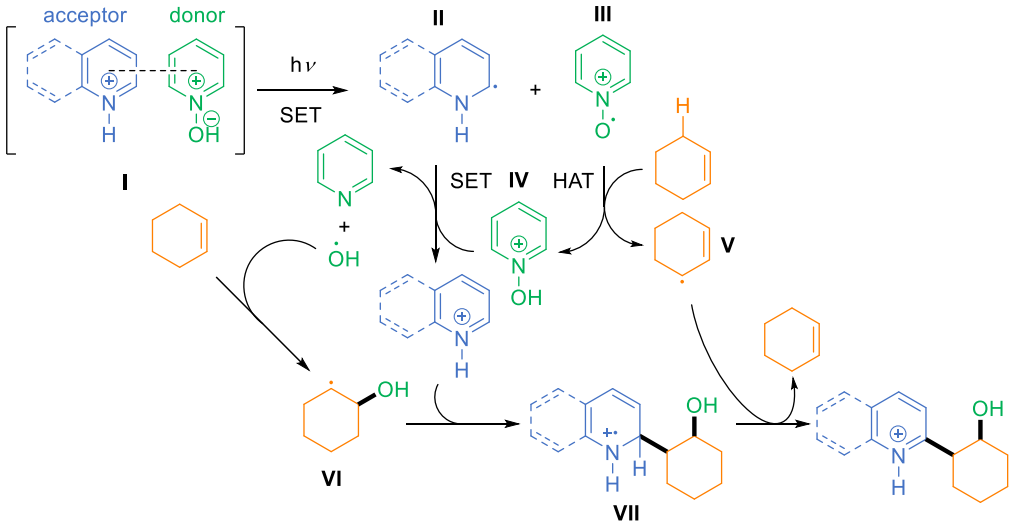
Expectedly in anhydrous conditions the yield of product **4e** remained at the same level (Scheme S2). The Regioselectivity of the formation of **4e"** suggests that product **4e** has to be formed via a different pathway, rather than by the hydroxylation of compound **4e"** (see Scheme S6).

6.4 Mechanistic proposal



Scheme S5 Mechanistic proposal.

The reaction starts from the formation of an EDA complex **I** between protonated lepidine and the *N*-oxide (confirmed by UV-Vis studies). After irradiation, radical **II** derived from lepidine and *N*-oxyl radical cation **III** (captured with TEMPO) is formed. The hydrogen atom is abstracted from a substrate to give corresponding radical **V** (captured with TEMPO), which then reacts with the protonated lepidine. The resultant radical adduct **VI**, after hydrogen atom abstraction, gives the final product in its protonated form. The reaction requires an overstoichiometric amount of *N*-oxide, and no traces of the reduced product is observed, which imposes the SET process between protonated *N*-oxide **VI** and lepidine-derived radical **II**. In addition the formation of hydroxylated products **4e** and **4f** in the reaction with alkenes conducted under anhydrous conditions, corroborates the formation of the hydroxyl radical in the reaction mixture.

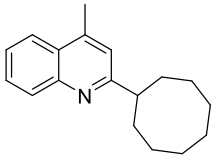


Scheme S6 Plausible pathway for the formation of **4e**.

For cyclohexene (**4e'**), the formation of hydroxylated product **4e** can be justified with the following mechanistic pathway. The radical **V** is formed in a similar way to the one described on Scheme S5, however, due to its greater stability, it is less prone to react with the protonated substrate. Instead, the hydroxyl radical formed from the *N*oxide combines with the substrate giving radical **VI,** which reacts with the protonated heterocycle, leading to **VII**. Radical **V** then abstracts the hydrogen from **VII** giving the final product.

7 Characterization of products

2-cyclooctyl-4-methylquinoline (4a)



4a

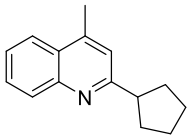
Synthesized according to the general procedure GP-1 using 5 equiv. (1mmol) of cyclooctane. The product was obtained as 38.3 mg of a colourless oil after purification via column chromatography using 7% ethyl acetate/hexane as an eluent. The spectroscopic data are consistent with previously reported in the literature.[1]

Rf (10% ethyl acetate/hexane) = 0.41

δ_H (400 MHz, Chloroform-*d*) 8.08 – 8.01 (1 H, m), 7.93 (1 H, dd, *J* 8.3, 1.4 Hz), 7.65 (1 H, ddd, *J* 8.4, 6.8, 1.5 Hz), 7.48 (1 H, ddd, *J* 8.2, 6.9, 1.3 Hz), 7.12 (1 H, d, *J* 1.1 Hz), 3.11 (1 H, tt, *J* 9.8, 3.6 Hz), 2.67 (3 H, d, *J* 1.0 Hz), 2.13 – 1.53 (14 H, m).

δ_C (101 MHz, Chloroform-*d*) 168.9, 147.6, 144.3, 129.7, 129.0, 127.0, 125.4, 123.6, 120.8, 47.7, 33.6, 26.8, 26.6, 26.3, 18.9.

2-cyclopentyl-4-methylquinoline (4b)



4b

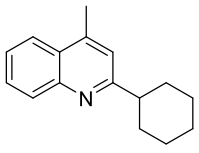
Synthesized according to the general procedure GP-1 using 10 equiv. (2 mmol) of cyclopentane. The product was obtained as 33.4 mg of a colourless oil after purification via column chromatography using 7% ethyl acetate/hexane as an eluent. The spectroscopic data are consistent with previously reported in the literature.[1]

Rf (10% ethyl acetate/hexane) = 0.35

δ_H (400 MHz, Chloroform-*d*) 8.04 (1 H, dd, *J* 8.5, 1.2 Hz), 7.93 (1 H, dd, *J* 8.3, 1.4 Hz), 7.65 (1 H, ddd, *J* 8.4, 6.9, 1.5 Hz), 7.48 (1 H, ddd, *J* 8.3, 6.9, 1.3 Hz), 7.17 (1 H, d, *J* 1.1 Hz), 3.42 – 3.27 (1 H, m), 2.67 (3 H, d, *J* 1.0 Hz), 2.25 – 2.08 (2 H, m), 1.99 – 1.82 (4 H, m), 1.81 – 1.66 (2 H, m).

δ_C (101 MHz, Chloroform-*d*) 166.0, 147.7, 144.1, 129.7, 129.0, 127.1, 125.4, 123.6, 120.8, 48.9, 33.7, 26.2, 18.9.

2-cyclohexyl-4-methylquinoline (4c)



4c

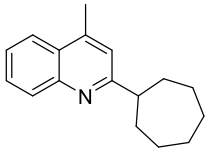
Synthesized according to the general procedure GP-1 using 10 equiv. (2 mmol) of cyclohexane. The product was obtained as 39.3 mg of a colourless oil after purification via column chromatography using 7% ethyl acetate/hexane as an eluent. The spectroscopic data are consistent with previously reported in the literature.[1]

Rf (10% ethyl acetate/hexane) = 0.37

δ_H (400 MHz, Chloroform-*d*) 8.05 (1 H, dd, *J* 8.4, 1.3 Hz), 7.93 (1 H, dd, *J* 8.4, 1.4 Hz), 7.66 (1 H, ddd, *J* 8.4, 6.8, 1.5 Hz), 7.48 (1 H, ddd, *J* 8.2, 6.8, 1.3 Hz), 7.16 (1 H, d, *J* 1.2 Hz), 2.88 (1 H, tt, *J* 12.0, 3.5 Hz), 2.67 (3 H, d, *J* 1.0 Hz), 2.11 – 1.96 (2 H, m), 1.89 (2 H, dt, *J* 12.7, 3.3 Hz), 1.79 (1 H, dddd, *J* 12.9, 5.0, 3.2, 1.6 Hz), 1.63 (2 H, qd, *J* 12.5, 3.2 Hz), 1.47 (2 H, qt, *J* 12.5, 3.2 Hz), 1.34 (1 H, qt, *J* 13.1, 3.5).

δ_C (101 MHz, Chloroform-*d*) 166.6, 147.8, 144.3, 129.7, 129.0, 127.2, 125.5, 123.7, 120.4, 47.7, 33.0, 26.7, 26.3, 18.9.

2-cycloheptyl-4-methylquinoline (4d)



4d

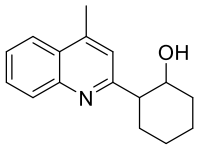
Synthesized according to the general procedure GP-1 using 10 equiv. (2 mmol) of cycloheptane. The product was obtained as 37.8 mg of a colourless oil after purification via column chromatography using 7% ethyl acetate/hexane as an eluent. The spectroscopic data are consistent with previously reported in the literature.[1]

Rf (10% ethyl acetate/hexane) = 0.36

δ_H (400 MHz, Chloroform-*d*) 8.04 (1 H, dd, *J* 8.4, 1.2 Hz), 7.93 (1 H, dd, *J* 8.3, 1.4 Hz), 7.65 (1 H, ddd, *J* 8.4, 6.8, 1.4 Hz), 7.48 (1 H, ddd, *J* 8.2, 6.8, 1.3 Hz), 7.13 (1 H, d, *J* 1.1 Hz), 3.03 (1 H, tt, *J* 10.5, 3.5 Hz), 2.67 (3 H, d, *J* 1.0 Hz), 2.10 – 1.97 (2 H, m), 1.93 – 1.56 (10 H, m).

δ_C (101 MHz, Chloroform-*d*) 168.2, 147.6, 144.4, 129.6, 129.0, 127.1, 125.4, 123.6, 120.4, 49.7, 35.2, 28.1, 27.6, 18.9.

2-(4-methylquinolin-2-yl)cyclohexan-1-ol (4e)



4e

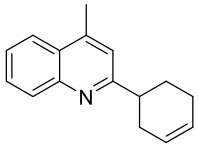
Synthesized according to the general procedure GP-1' using 10 equiv. (2 mmol) of cyclohexene. The product was obtained as 22.7 mg of a colourless oil after purification via column chromatography using 20-25% ethyl acetate/hexane as an eluent. The spectroscopic data are consistent with previously reported in the literature.[2]

Rf (20% ethyl acetate/hexane) = 0.10

δ_H (400 MHz, Chloroform-*d*) 8.02 (1 H, dt, *J* 8.3, 0.9 Hz), 7.95 (1 H, dd, *J* 8.6, 1.4 Hz), 7.67 (1 H, ddd, *J* 8.4, 6.9, 1.5 Hz), 7.52 (1 H, ddd, *J* 8.3, 6.9, 1.3 Hz), 7.21 (1 H, d, *J* 1.1 Hz), 4.58 (1 H, s), 4.22 – 4.00 (1 H, m), 2.81 (1 H, ddd, *J* 12.0, 9.6, 3.7 Hz), 2.68 (3 H, d, *J* 1.0 Hz), 2.28 – 2.10 (2 H, m), 1.96 – 1.73 (2 H, m), 1.62 – 1.36 (4 H, m).

δ_C (101 MHz, Chloroform-*d*) 163.9, 147.1, 145.0, 129.6, 129.3, 127.1, 126.0, 123.7, 121.2, 72.8, 52.8, 34.3, 31.5, 26.3, 25.0, 19.0.

2-(cyclohex-3-en-1-yl)-4-methylquinoline (4e")



4e"

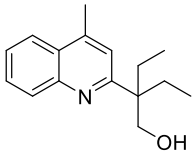
Synthesized according to the general procedure GP-1' using 10 equiv. (2 mmol) of cyclohexene. The product was obtained as 13.8 mg of a colourless oil (5:1 mixture with **4c**) after purification via column chromatography using 10% ethyl acetate/hexane as an eluent. The spectroscopic data are consistent with previously reported in the literature.[3]

Rf (10% ethyl acetate/hexane) = 0.34

δ_H (500 MHz, Chloroform-*d*) 8.12 – 8.00 (1 H, m), 7.95 (1 H, ddd, *J* 7.7, 6.1, 1.4 Hz), 7.66 (1 H, dddd, *J* 8.4, 6.7, 5.1, 1.4 Hz), 7.49 (1 H, dtd, *J* 7.6, 6.5, 1.3 Hz), 7.22 – 7.13 (1 H, m), 5.88 – 5.75 (2 H, m), 3.22 – 3.07 (1 H, m), 2.69 (3 H, dd, *J* 4.1, 1.0 Hz), 2.50 – 2.15 (4 H, m), 2.12 – 2.04 (1 H, m), 1.98 – 1.88 (1 H, m).

δ_C (126 MHz, $CDCl_3$) 166.1, 147.9, 144.5, 129.7, 129.1, 127.1, 126.6, 125.6, 123.7, 120.6, 43.3, 31.5, 28.8, 25.8, 19.0.

2-ethyl-2-(4-methylquinolin-2-yl)butan-1-ol (4f)



4f

Synthesized according to the general procedure GP-1' using 10 equiv. (2 mmol) of 3-methylenepentane. The product was obtained as 25.1 mg of a colourless oil after purification via column chromatography using 12-20% ethyl acetate/hexane as an eluent.

Rf (20% ethyl acetate/hexane) = 0.35

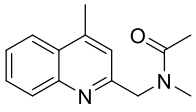
δ_H (400 MHz, Chloroform-*d*) 8.00 (1 H, dt, *J* 8.4, 0.9 Hz), 7.96 (1 H, dd, *J* 8.4, 1.4 Hz), 7.67 (1 H, ddd, *J* 8.4, 6.9, 1.4 Hz), 7.52 (1 H, ddd, *J* 8.3, 6.9, 1.3 Hz), 7.21 (1 H, d, *J* 1.1 Hz), 5.43 (1 H, s), 4.04 (2 H, s), 2.71 (3 H, d, *J* 1.0 Hz), 1.98 – 1.71 (4 H, m), 0.84 (6 H, t, *J* 7.6).

δ_C (101 MHz, Chloroform-*d*) 167.3, 146.5, 144.4, 129.5, 129.1, 126.6, 125.9, 123.5, 120.3, 66.9, 47.9, 29.4, 19.0, 8.8.

HRMS (ESI): m/z: [M+H$^+$] Calc. for $C_{16}H_{22}NO^+$: 244.1696; Found: 244.1703.

Elemental analyisis: Calc. for $C_{16}H_{21}NO$: C, 78.65; H, 9.08; N, 5.73; Found: C, 78.87; H, 8.72; N, 5.55%.

***N*-methyl-*N*-((4-methylquinolin-2-yl)methyl)acetamide (4g)**



4g

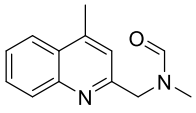
Synthesized according to the general procedure GP-2 using 10 equiv. (2 mmol) of dimethylacetamide. The product was obtained as 32.9 mg of a colourless oil after purification via column chromatography using 2-5% methanol/dichloromethane as an eluent. The spectroscopic data are consistent with previously reported in the literature.[4]

Rf (5% methanol/dichloromethane) = 0.44

δ_H (400 MHz, Chloroform-*d*) 8.03 (1 H, dt, *J* 8.5, 1.7 Hz), 7.96 (1 H, ddd, *J* 11.2, 8.3, 1.4 Hz), 7.69 (1 H, dddd, *J* 11.6, 8.4, 6.9, 1.4 Hz), 7.53 (1 H, dddd, *J* 10.6, 8.3, 6.9, 1.3 Hz), 7.16 (1 H, dd, *J* 49.4, 1.1 Hz), 4.78 (2 H, d, *J* 39.3 Hz), 3.04 (3 H, d, *J* 1.7 Hz), 2.68 (3 H, dd, *J* 16.5, 1.0 Hz), 2.19 (3 H, d, *J* 4.9).

δ_C (101 MHz, Chloroform-*d*) 171.5, 171.0, 157.8, 156.9, 147.9, 147.5, 146.0, 145.3, 129.8, 129.7, 129.3, 127.6, 127.5, 126.5, 126.2, 123.9, 123.8, 120.8, 118.8, 57.0, 53.4, 36.2, 34.5, 21.9, 21.8, 19.0, 18.8.

***N*-methyl-*N*-((4-methylquinolin-2-yl)methyl)formamide (4h)**



4h

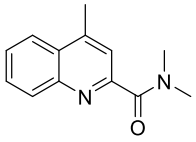
Synthesized according to the general procedure GP-2 using 10 equiv. (2 mmol) of dimethylformamide. The product was obtained as 22.3 mg of a colourless oil after purification via column chromatography using 2-5% methanol/dichloromethane as an eluent. The spectroscopic data are consistent with previously reported in the literature.[5]

Rf (5% methanol/dichloromethane) = 0.43

δ_H (400 MHz, Chloroform-*d*) 8.30 (1 H, d, *J* 57.6 Hz), 8.05 (1 H, dt, *J* 8.5, 2.0 Hz), 8.02 – 7.94 (1 H, m), 7.71 (1 H, dddd, *J* 9.9, 8.4, 6.9, 1.4 Hz), 7.56 (1 H, dddd, *J* 9.7, 8.2, 6.9, 1.3 Hz), 7.17 (1 H, dd, *J* 34.6, 1.2 Hz), 4.71 (2 H, d, *J* 58.3 Hz), 2.93 (3 H, d, *J* 40.3 Hz), 2.69 (3 H, dd, *J* 12.5, 1.0).

δ_C (101 MHz, Chloroform-*d*) 163.4, 162.9, 156.5, 156.1, 147.8, 147.6, 146.0, 145.6, 129.8, 129.8, 129.5, 127.6, 126.7, 126.4, 123.9, 123.8, 120.7, 119.5, 56.0, 50.6, 34.8, 30.2, 19.0, 18.8.

***N,N,*4-trimethylquinoline-2-carboxamide (4i)**



4i

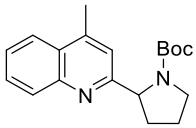
Synthesized according to the general procedure GP-2 using 10 equiv. (2 mmol) of dimethylformamide. The product was obtained as 7.3 mg of a yellow oil after purification via column chromatography using 2-5% methanol/dichloromethane as an eluent. The spectroscopic data are consistent with previously reported in the literature.[6]

Rf (5% methanol/dichloromethane) = 0.48

δ_H (500 MHz, Chloroform-*d*) 8.09 (1 H, dd, *J* 8.4, 1.3 Hz), 8.01 (1 H, dd, *J* 8.4, 1.4 Hz), 7.73 (1 H, ddd, *J* 8.4, 6.8, 1.4 Hz), 7.60 (1 H, ddd, *J* 8.3, 6.8, 1.3 Hz), 7.56 – 7.51 (1 H, m), 3.17 (6 H, d, *J* 14.4 Hz), 2.78 – 2.68 (3 H, m).

δ_C (126 MHz, Chloroform-*d*) 169.4, 154.1, 146.6, 145.8, 130.3, 129.8, 128.2, 127.3, 123.8, 121.2, 39.2, 35.9, 18.9.

***tert*-butyl 2-(4-methylquinolin-2-yl)pyrrolidine-1-carboxylate (4j)**



4j

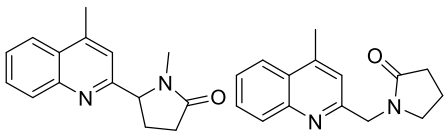
Synthesized according to the general procedure GP-2 using 5 equiv. (1 mmol) of 1-Boc-pyrrolidine. The product was obtained as 37.5 mg of a colourless oil after purification via column chromatography using 2-5% methanol/dichloromethane as an eluent. The spectroscopic data are consistent with previously reported in the literature.[7]

Rf (5% methanol/dichloromethane) = 0.59

δ_H (400 MHz, Chloroform-*d*) 8.02 (1 H, d, *J* 8.4 Hz), 7.96 (1 H, d, *J* 8.6 Hz), 7.66 (1 H, t, *J* 7.9 Hz), 7.55 – 7.37 (1 H, m), 7.14 (1 H, s), 5.25 – 4.86 (1 H, m), 3.91 – 3.49 (2 H, m), 2.67 (3 H, s), 2.55 – 2.35 (1 H, m), 2.22 – 1.78 (3 H, m), 1.46 (3 H, s), 1.11 (6 H, s).

δ_C (101 MHz, Chloroform-*d*) 164.0, 154.8, 147.5, 144.6, 129.6, 129.2, 127.2, 125.8, 123.7, 118.4, 79.5, 63.7, 47.4, 34.7, 28.3, 23.7, 18.9.

1-methyl-5-(4-methylquinolin-2-yl)pyrrolidin-2-one (4k) and **1-((4-methylquinolin-2-yl)methyl)pyrrolidin-2-one (4l)**



4k **4l**

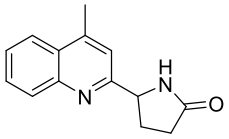
Synthesized according to the general procedure GP-2 using 10 equiv. (2 mmol) of 1-methylpyrrolidin-2-one. A mixture of regioisomeric products (**4k**:**4l** 3.7:1) was obtained as 36.0 mg of a yellowish solid after purification via column chromatography using 2-5% methanol/dichloromethane as an eluent. The spectroscopic data are consistent with previously reported in the literature.[4]

Rf (5% methanol/dichloromethane) = 0.43

δ_H (500 MHz, Chloroform-*d*) 8.09 – 8.01 (1.28 H, m), 8.01 – 7.93 (1.41 H, m), 7.77 – 7.64 (1.38 H, m), 7.59 – 7.50 (1.35 H, m), 7.20 (0.27 H, d, *J* 1.1 Hz), 7.09 (1.00 H, d, *J* 1.1 Hz), 4.83 – 4.76 (1.01 H, m), 4.70 (0.60 H, s), 3.46 – 3.37 (0.67 H, m), 2.75 (3.17 H, d, *J* 0.9 Hz), 2.71 (3.31 H, d, *J* 1.0 Hz), 2.66 (1.33 H, d, *J* 1.0 Hz), 2.65 – 2.44 (3.75 H, m), 2.07 – 1.95 (1.79 H, m).

δ_C (126 MHz, Chloroform-*d*) 175.9, 175.3, 160.7, 157.0, 147.7, 147.5, 146.2, 145.5, 129.8, 129.7, 129.7, 129.4, 127.7, 127.6, 126.6, 126.3, 123.9, 123.8, 120.6, 118.2, 66.7, 49.4, 47.4, 30.9, 30.1, 28.7, 26.4, 19.1, 18.8, 18.0.

5-(4-methylquinolin-2-yl)pyrrolidin-2-one (4m)



4m

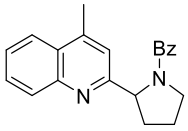
Synthesized according to the general procedure GP-2 using 10 equiv. (2 mmol) of pyrrolidin-2-one The product was obtained as 35.7 mg of a colourless oil after purification via column chromatography using 2-5% methanol/dichloromethane as an eluent. The spectroscopic data are consistent with previously reported in the literature.[8]

Rf (5% methanol/dichloromethane) = 0.37

δ_H (400 MHz, Chloroform-*d*) 8.01 (1 H, dd, *J* 8.6, 1.3 Hz), 7.95 (1 H, dd, *J* 8.5, 1.4 Hz), 7.68 (1 H, ddd, *J* 8.4, 6.9, 1.5 Hz), 7.53 (1 H, ddd, *J* 8.3, 6.9, 1.3 Hz), 7.24 (1 H, d, *J* 1.1 Hz), 6.81 (1 H, s), 4.97 (1 H, dd, *J* 8.1, 6.2 Hz), 2.77 – 2.62 (4 H, m), 2.58 – 2.39 (2 H, m), 2.16 (1 H, dddd, *J* 12.7, 9.4, 7.7, 6.2).

δ_C (101 MHz, Chloroform-*d*) 178.7, 161.2, 147.5, 146.0, 129.8, 129.7, 127.6, 126.4, 123.8, 118.2, 59.8, 30.3, 29.1, 19.0.

(2-(4-methylquinolin-2-yl)pyrrolidin-1-yl)(phenyl)methanone (4n)



4n

Synthesized according to the general procedure GP-2 using 5 equiv. (1 mmol) of phenyl(pyrrolidin-1-yl)methanone The product was obtained as 44.3 mg of a off-white solid after purification via column chromatography using 2-5% methanol/dichloromethane as an eluent. A mixture of rotamers.

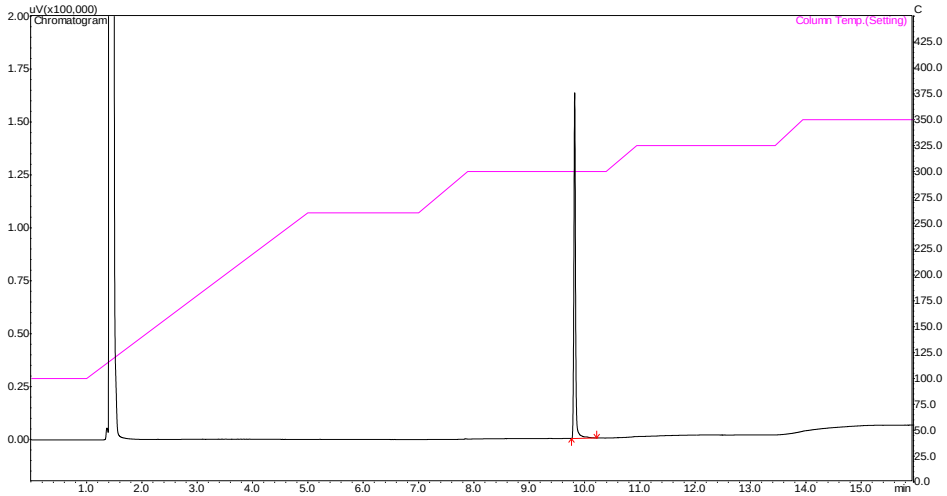
Rf (5% methanol/dichloromethane) = 0.52

δ_H (500 MHz, Chloroform-*d*) 8.09 – 7.90 (2.01 H, m), 7.70 – 7.29 (5.74 H, m), 7.19 – 7.00 (2.28 H, m), 5.52 (0.59 H, t, *J* 7.0 Hz), 5.11 (0.41 H, dd, *J* 7.9, 2.9 Hz), 4.11 – 3.93 (1.04 H, m), 3.88 (0.60 H, dt, *J* 10.4, 7.3 Hz), 3.67 (0.72 H, ddd, *J* 11.1, 7.4, 5.1 Hz), 2.68 (3.00 H, d, *J* 13.7 Hz), 2.54 – 2.38 (1.28 H, m), 2.26 (0.85 H, dq, *J* 13.3, 7.0 Hz), 2.11 – 1.88 (2.39 H, m).

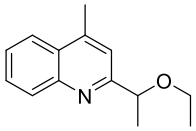
δ_C (126 MHz, Chloroform-*d*) 171.2, 170.0, 162.2, 162.0, 147.9, 147.6, 145.2, 144.7, 137.2, 130.1, 129.9, 129.8, 129.5, 129.5, 129.0, 128.4, 128.3, 128.1, 127.5, 127.3, 126.7, 126.2, 125.8, 123.7, 119.8, 118.9, 65.4, 63.0, 51.1, 47.5, 34.8, 32.7, 25.5, 22.3, 19.1, 19.0.

HRMS (ESI): m/z: $[M+H^+]$ Calc. for $C_{21}H_{21}N_2O^+$: 317.1648; Found: 317.1656

GC (FID) purity: >95%



2-(1-ethoxyethyl)-4-methylquinoline (4o)



4o

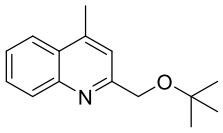
Synthesized according to the general procedure GP-1 using 10 equiv. (2 mmol) of diethyl ether The product was obtained as 31.5 mg of a colourless oil after purification via column chromatography using 18% ethyl acetate/hexane as an eluent. The spectroscopic data are consistent with previously reported in the literature.[9]

Rf (20% ethyl acetate/hexane) = 0.33

δ_H (500 MHz, Chloroform-*d*) 8.06 (1 H, dt, *J* 8.5, 0.9 Hz), 7.98 (1 H, dd, *J* 8.3, 1.5 Hz), 7.69 (1 H, ddd, *J* 8.3, 6.8, 1.4 Hz), 7.54 (1 H, ddd, *J* 8.3, 6.9, 1.3 Hz), 7.44 (1 H, d, *J* 1.2 Hz), 4.67 (1 H, q, *J* 6.6 Hz), 3.47 (2 H, ddq, *J* 45.7, 9.4, 7.0 Hz), 2.73 (3 H, d, *J* 1.0 Hz), 1.53 (3 H, d, *J* 6.6 Hz), 1.23 (3 H, t, *J* 7.0).

δ_C (126 MHz, Chloroform-*d*) 164.2, 147.4, 145.3, 129.7, 129.3, 127.8, 126.1, 123.8, 118.4, 79.9, 64.8, 22.8, 19.1, 15.6.

2-(*tert*-butoxymethyl)-4-methylquinoline (4p)



4p

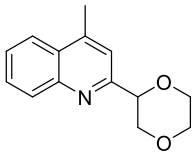
Synthesized according to the general procedure GP-1 using 10 equiv. (2 mmol) of methyl-*tert*-butyl ether. The product was obtained as 31.2 mg of a yellow oil after purification via column chromatography using 18% ethyl acetate/hexane as an eluent. The spectroscopic data are consistent with previously reported in the literature.[10]

Rf (20% ethyl acetate/hexane) = 0.32

δ_H (400 MHz, Chloroform-*d*) 8.02 (1 H, dd, *J* 8.5, 1.3 Hz), 7.96 (1 H, dd, *J* 8.3, 1.4 Hz), 7.67 (1 H, ddd, *J* 8.4, 6.8, 1.5 Hz), 7.54 – 7.46 (2 H, m), 4.72 (2 H, s), 2.71 (3 H, d, *J* 1.0 Hz), 1.34 (9 H, s).

δ_C (101 MHz, Chloroform-*d*) 160.5, 147.4, 144.8, 129.5, 129.2, 127.6, 125.9, 123.8, 120.2, 74.1, 66.2, 27.8, 18.9.

2-(1,4-dioxan-2-yl)-4-methylquinoline (4q)



4q

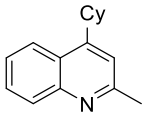
Synthesized according to the general procedure GP-1 using 10 equiv. (2 mmol) of 1,4-dioxane. The product was obtained as 32.1 mg of a colourless oil after purification via column chromatography using 20% ethyl acetate/hexane as an eluent. The spectroscopic data are consistent with previously reported in the literature.[1]

Rf (20% ethyl acetate/hexane) = 0.18

δ_H (400 MHz, Chloroform-*d*) 8.07 (1 H, dt, *J* 8.5, 1.0 Hz), 7.97 (1 H, dd, *J* 8.4, 1.4 Hz), 7.69 (1 H, ddd, *J* 8.4, 6.8, 1.4 Hz), 7.53 (1 H, ddd, *J* 8.3, 6.8, 1.3 Hz), 7.46 (1 H, d, *J* 1.1 Hz), 4.89 (1 H, dd, *J* 10.1, 2.9 Hz), 4.24 (1 H, dd, *J* 11.6, 3.0 Hz), 4.07 – 3.92 (2 H, m), 3.88 – 3.72 (2 H, m), 3.64 (1 H, dd, *J* 11.6, 10.1 Hz), 2.71 (3 H, d, *J* 1.0).

δ_C (101 MHz, Chloroform-*d*) 158.0, 147.4, 145.3, 129.9, 129.4, 127.8, 126.3, 123.8, 119.2, 78.9, 71.2, 67.2, 66.6, 19.0.

4-cyclohexyl-2-methylquinoline (4r)



4r

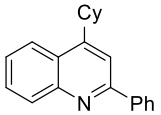
Synthesized according to the general procedure GP-3. The product was obtained as 30.7 mg of a colourless oil after purification via column chromatography using 15% ethyl acetate/hexane as an eluent. The spectroscopic data are consistent with previously reported in the literature.[1]

Rf (20% ethyl acetate/hexane) = 0.25

δ_H (400 MHz, Chloroform-*d*) 8.02 (2 H, dd, *J* 8.3, 1.4 Hz), 7.64 (1 H, ddd, *J* 8.2, 6.8, 1.4 Hz), 7.47 (1 H, ddd, *J* 8.4, 6.9, 1.4 Hz), 7.16 (1 H, s), 3.29 (1 H, tt, *J* 8.4, 3.6 Hz), 2.71 (3 H, s), 2.08 – 1.89 (4 H, m), 1.89 – 1.78 (1 H, m), 1.62 – 1.46 (4 H, m), 1.41 – 1.27 (1 H, m).

δ_C (101 MHz, Chloroform-*d*) 158.8, 153.2, 148.2, 129.6, 128.7, 125.2, 125.1, 122.8, 118.3, 38.8, 33.6, 26.9, 26.3, 25.5.

4-cyclohexyl-2-phenylquinoline (4s)



4s

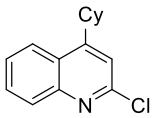
Synthesized according to the general procedure GP-3. The product was obtained as 35.1 mg of a off-white solid after purification via column chromatography using 4% ethyl acetate/hexane as an eluent. The spectroscopic data are consistent with previously reported in the literature.[11]

Rf (10% ethyl acetate/hexane) = 0.41

δ_H (500 MHz, Chloroform-*d*) 8.22 (1 H, d, *J* 8.4 Hz), 8.16 (2 H, dd, *J* 7.3, 1.8 Hz), 8.10 (1 H, d, *J* 8.3 Hz), 7.76 (1 H, s), 7.71 (1 H, ddd, *J* 8.3, 6.7, 1.4 Hz), 7.60 – 7.50 (3 H, m), 7.50 – 7.41 (1 H, m), 3.39 (1 H, tt, *J* 11.5, 3.1 Hz), 2.19 – 2.04 (2 H, m), 2.04 – 1.93 (2 H, m), 1.93 – 1.80 (1 H, m), 1.75 – 1.51 (4 H, m), 1.47 – 1.32 (1 H, m).

δ_C (126 MHz, Chloroform-*d*) 157.5, 154.2, 148.7, 140.3, 130.8, 129.3, 129.2, 128.9, 127.8, 126.1, 126.0, 123.0, 115.7, 39.3, 33.8, 27.1, 26.5.

2-chloro-4-cyclohexylquinoline (4t)



4t

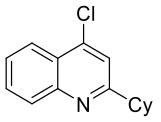
Synthesized according to the general procedure GP-3. The product was obtained as 8.9 mg of a colourless oil after purification via column chromatography using 10-50% ethyl acetate/hexane as an eluent. The spectroscopic data are consistent with previously reported in the literature.[12]

Rf (40% ethyl acetate/hexane) = 0.67

δ_H (400 MHz, Chloroform-*d*) 8.03 (2 H, ddd, *J* 8.5, 6.9, 1.3 Hz), 7.70 (1 H, ddd, *J* 8.4, 6.9, 1.5 Hz), 7.56 (1 H, ddd, *J* 8.4, 6.9, 1.4 Hz), 7.26 (1 H, s), 3.39 – 3.21 (1 H, m), 2.14 – 1.74 (5 H, m), 1.68 – 1.44 (4 H, m), 1.44 – 1.28 (1 H, m).

δ_C (101 MHz, Chloroform-*d*) 157.1, 151.3, 148.4, 130.1, 129.7, 126.7, 125.8, 123.3, 118.9, 39.3, 33.6, 27.0, 26.3.

4-chloro-2-cyclohexylquinoline (4u)



4u

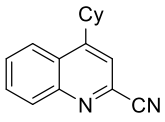
Synthesized according to the general procedure GP-3. The product was obtained as 16.7 mg of a colourless oil after purification via column chromatography using 7-35% ethyl acetate/hexane as an eluent. The spectroscopic data are consistent with previously reported in the literature.[13]

Rf (40% ethyl acetate/hexane) = 0.68

δ_H (500 MHz, Chloroform-*d*) 8.17 (1 H, dd, *J* 8.4, 1.4 Hz), 8.05 (1 H, dd, *J* 8.5, 1.1 Hz), 7.72 (1 H, ddd, *J* 8.4, 6.9, 1.5 Hz), 7.56 (1 H, ddd, *J* 8.2, 6.8, 1.2 Hz), 7.42 (1 H, s), 2.89 (1 H, tt, *J* 12.0, 3.5 Hz), 2.11 – 1.97 (2 H, m), 1.90 (2 H, dp, *J* 10.1, 3.4 Hz), 1.79 (1 H, dddd, *J* 13.6, 5.0, 3.2, 1.6 Hz), 1.61 (2 H, qd, *J* 12.5, 3.3 Hz), 1.46 (2 H, qt, *J* 12.8, 3.4 Hz), 1.33 (1 H, qt, *J* 12.9, 3.6).

δ_C (126 MHz, Chloroform-*d*) 167.0, 148.9, 142.7, 130.3, 129.5, 126.7, 125.3, 124.0, 119.9, 47.5, 32.8, 26.6, 26.2.

4-cyclohexylquinoline-2-carbonitrile (4v)



4v

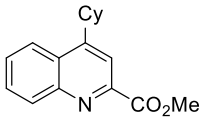
Synthesized according to the general procedure GP-3. The product was obtained as 9.0 mg of a yellowish solid after purification via column chromatography using 15% ethyl acetate/hexane as an eluent. The spectroscopic data are consistent with previously reported in the literature.[12]

Rf (20% ethyl acetate/hexane) = 0.50

δ_H (500 MHz, Chloroform-*d*) 8.14 (2 H, ddd, *J* 14.6, 8.6, 1.3 Hz), 7.80 (1 H, ddd, *J* 8.4, 6.8, 1.4 Hz), 7.69 (1 H, ddd, *J* 8.4, 6.8, 1.4 Hz), 7.57 (1 H, s), 3.36 (1 H, ddd, *J* 11.5, 8.3, 3.2 Hz), 2.04 – 1.94 (4 H, m), 1.90 – 1.84 (1 H, m), 1.60 – 1.50 (4 H, m), 1.41 – 1.30 (1 H, m).

δ_C (126 MHz, Chloroform-*d*) 155.8, 148.5, 133.9, 131.1, 130.6, 129.1, 127.6, 123.3, 120.1, 118.1, 39.2, 33.6, 26.8, 26.2.

methyl 4-cyclohexylquinoline-2-carboxylate (4w)



4w

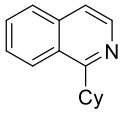
Synthesized according to the general procedure GP-3. The product was obtained as 16.1 mg of a yellow oil after purification via column chromatography using 20% ethyl acetate/hexane as an eluent. The spectroscopic data are consistent with previously reported in the literature.[14]

Rf (20% ethyl acetate/hexane) = 0.20

δ_H (400 MHz, Chloroform-*d*) 8.30 (1 H, ddq, *J* 8.6, 1.8, 0.8 Hz), 8.13 (1 H, ddd, *J* 8.5, 2.0, 1.2 Hz), 8.09 (1 H, d, *J* 1.6 Hz), 7.74 (1 H, ddt, *J* 8.4, 7.0, 1.5 Hz), 7.64 (1 H, ddq, *J* 8.4, 6.8, 1.5 Hz), 4.07 (3 H, d, *J* 1.5 Hz), 3.36 (1 H, tt, *J* 11.4, 2.8 Hz), 2.08 – 1.90 (4 H, m), 1.90 – 1.80 (1 H, m), 1.74 – 1.46 (4 H, m), 1.44 – 1.29 (1 H, m).

δ_C (101 MHz, Chloroform-*d*) 166.5, 155.2, 148.0, 148.0, 131.8, 129.7, 128.3, 128.2, 123.1, 117.6, 53.2, 39.3, 33.6, 27.0, 26.3.

1-cyclohexylisoquinoline (5a)



5a

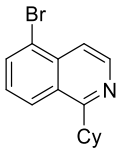
Synthesized according to the general procedure GP-3. The product was obtained as 30.9 mg of a colourless oil after purification via column chromatography using 7% ethyl acetate/hexane as an eluent. The spectroscopic data are consistent with previously reported in the literature.[13]

Rf (10% ethyl acetate/hexane) = 0.33

δ_H (400 MHz, Chloroform-*d*) 8.48 (1 H, d, *J* 5.7 Hz), 8.23 (1 H, d, *J* 8.4 Hz), 7.65 (1 H, ddd, *J* 8.1, 6.8, 1.3 Hz), 7.58 (1 H, ddd, *J* 8.3, 6.8, 1.4 Hz), 7.47 (1 H, dd, *J* 5.7, 0.9 Hz), 3.56 (1 H, tt, *J* 11.6, 3.3 Hz), 2.05 – 1.76 (7 H, m), 1.62 – 1.47 (2 H, m), 1.41 (1 H, tt, *J* 12.7, 3.3).

δ_C (101 MHz, Chloroform-*d*) 165.8, 142.1, 136.5, 129.6, 127.7, 126.9, 126.4, 124.9, 119.0, 41.7, 32.7, 27.0, 26.4.

5-bromo-1-cyclohexylisoquinoline (5b)



5b

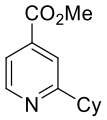
Synthesized according to the general procedure GP-4. The product was obtained as 26.7 mg of a white solid after purification via column chromatography using 7% ethyl acetate/hexane as an eluent. The spectroscopic data are consistent with previously reported in the literature.[11]

Rf (10% ethyl acetate/hexane) = 0.45

δ_H (400 MHz, Chloroform-*d*) 8.58 (1 H, d, *J* 5.9 Hz), 8.20 (1 H, d, *J* 8.5 Hz), 7.93 (1 H, dd, *J* 7.5, 1.0 Hz), 7.85 (1 H, dd, *J* 6.0, 1.0 Hz), 7.42 (1 H, dd, *J* 8.6, 7.4 Hz), 3.61 – 3.49 (1 H, m), 2.02 – 1.75 (8 H, m), 1.62 – 1.45 (2 H, m), 1.38 (1 H, qt, *J* 12.8, 3.3).

δ_C (101 MHz, Chloroform-*d*) 166.2, 143.5, 135.6, 133.5, 127.6, 127.2, 124.6, 122.7, 117.8, 41.9, 32.8, 27.0, 26.3.

methyl 2-cyclohexylisonicotinate (6a)



6a

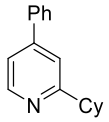
Synthesized according to the general procedure GP-5. The product was obtained as 15.3 mg of a colourless oil after purification via column chromatography using 18-40% ethyl acetate/hexane as an eluent. The spectroscopic data are consistent with previously reported in the literature.[15]

Rf (40% ethyl acetate/hexane) = 0.50

δ_H (400 MHz, Chloroform-*d*) 8.67 (1 H, dd, *J* 5.0, 0.9 Hz), 7.71 (1 H, s), 7.63 (1 H, dd, *J* 5.1, 1.6 Hz), 3.94 (3 H, s), 2.79 (1 H, tt, *J* 11.9, 3.5 Hz), 2.04 – 1.92 (2 H, m), 1.92 – 1.82 (1 H, m), 1.82 – 1.70 (1 H, m), 1.64 – 1.49 (2 H, m), 1.42 (2 H, qt, *J* 12.5, 2.9 Hz), 1.36 – 1.21 (1 H, m).

δ_C (101 MHz, Chloroform-*d*) 167.9, 166.2, 149.9, 137.9, 120.5, 120.4, 52.7, 46.7, 33.0, 26.6, 26.1.

2-cyclohexyl-4-phenylpyridine (6b)



6b

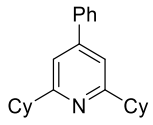
Synthesized according to the general procedure GP-5. The product was obtained as 22.3 mg of a colourless oil after purification via column chromatography using 30-40% ethyl acetate/hexane as an eluent. The spectroscopic data are consistent with previously reported in the literature.[16]

Rf (40% ethyl acetate/hexane) = 0.48

δ_H (400 MHz, Chloroform-*d*) 8.57 (1 H, dd, *J* 5.2, 0.8 Hz), 7.67 – 7.59 (2 H, m), 7.52 – 7.39 (3 H, m), 7.36 (1 H, dd, *J* 1.8, 0.8 Hz), 7.31 (1 H, dd, *J* 5.1, 1.8 Hz), 2.77 (1 H, tt, *J* 11.9, 3.4 Hz), 2.10 – 1.94 (2 H, m), 1.94 – 1.83 (2 H, m), 1.77 (1 H, dddt, *J* 12.9, 5.0, 3.3, 1.6 Hz), 1.60 (2 H, qd, *J* 12.4, 2.9 Hz), 1.52 – 1.27 (3 H, m).

δ_C (101 MHz, Chloroform-*d*) 167.2, 149.6, 148.9, 139.0, 129.1, 128.9, 127.2, 119.3, 119.2, 46.9, 33.2, 26.8, 26.3.

2,6-dicyclohexyl-4-phenylpyridine (6c)



6c

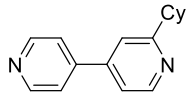
Synthesized according to the general procedure GP-5. The product was obtained as 15.3 mg of a white solid after purification via column chromatography using 10-15% ethyl acetate/hexane as an eluent. The spectroscopic data are consistent with previously reported in the literature.[16]

Rf (20% ethyl acetate/hexane) = 0.71

δ_H (400 MHz, Chloroform-*d*) 7.67 – 7.58 (2 H, m), 7.54 – 7.37 (3 H, m), 7.17 (2 H, s), 2.76 (2 H, tt, *J* 11.8, 3.4 Hz), 2.10 – 1.97 (4 H, m), 1.87 (4 H, dt, *J* 12.7, 3.2 Hz), 1.81 – 1.71 (2 H, m), 1.62 – 1.39 (8 H, m), 1.38 – 1.26 (2 H, m).

δ_C (101 MHz, Chloroform-*d*) 166.4, 149.1, 139.8, 129.0, 128.6, 127.3, 116.1, 46.9, 33.3, 26.8, 26.4.

2-cyclohexyl-4,4'-bipyridine (6d)



6d

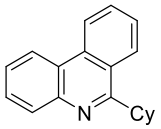
Synthesized according to the general procedure GP-5. The product was obtained as 15.7 mg of a yellowish oil after purification via column chromatography using 50-80% ethyl acetate/hexane as an eluent. The spectroscopic data are consistent with previously reported in the literature.[6]

Rf (ethyl acetate) = 0.23

δ_H (400 MHz, Chloroform-*d*) 8.76 – 8.66 (2 H, m), 8.62 (1 H, d, *J* 5.1 Hz), 7.57 – 7.46 (2 H, m), 7.36 (1 H, d, *J* 1.8 Hz), 7.31 (1 H, dd, *J* 5.1, 1.8 Hz), 2.77 (1 H, tt, *J* 11.9, 3.4 Hz), 2.10 – 1.93 (2 H, m), 1.87 (2 H, dt, *J* 12.9, 3.4 Hz), 1.81 – 1.70 (1 H, m), 1.58 (2 H, qd, *J* 12.4, 3.1 Hz), 1.42 (2 H, qt, *J* 12.6, 3.2 Hz), 1.30 (1 H, tt, *J* 12.6, 3.3).

δ_C (101 MHz, Chloroform-*d*) 167.6, 150.5, 149.9, 146.2, 145.9, 121.5, 118.8, 118.8, 46.7, 32.9, 26.5, 26.0.

6-cyclohexylphenanthridine (7)



7

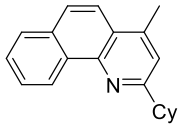
Synthesized according to the general procedure GP-3. The product was obtained as 11.0 mg of a colourless oil after purification via column chromatography using 5% ethyl acetate/hexane as an eluent. The spectroscopic data are consistent with previously reported in the literature.[13]

Rf (10% ethyl acetate/hexane) = 0.51

δ_H (500 MHz, Chloroform-*d*) 8.72 – 8.61 (1 H, m), 8.54 (1 H, dd, *J* 8.3, 1.4 Hz), 8.32 (1 H, d, *J* 8.3 Hz), 8.14 (1 H, dd, *J* 8.2, 1.3 Hz), 7.81 (1 H, ddd, *J* 8.2, 6.9, 1.3 Hz), 7.75 – 7.65 (2 H, m), 7.60 (1 H, td, *J* 7.5, 7.0, 1.4 Hz), 3.62 (1 H, ddt, *J* 11.3, 6.6, 3.3 Hz), 2.15 – 2.04 (2 H, m), 2.03 – 1.89 (4 H, m), 1.89 – 1.80 (1 H, m), 1.66 – 1.52 (2 H, m), 1.52 – 1.38 (1 H, m).

δ_C (126 MHz, Chloroform-*d*) 165.4, 144.1, 133.2, 130.1, 130.0, 128.5, 127.2, 126.3, 125.8, 124.9, 123.5, 122.7, 121.9, 42.2, 32.5, 27.0, 26.5.

2-cyclohexyl-4-methylbenzo[h]quinoline (8)



8

Synthesized according to the general procedure GP-3. The product was obtained as 30.8 mg of a white solid after purification via column chromatography using 7% ethyl acetate/hexane as an eluent.

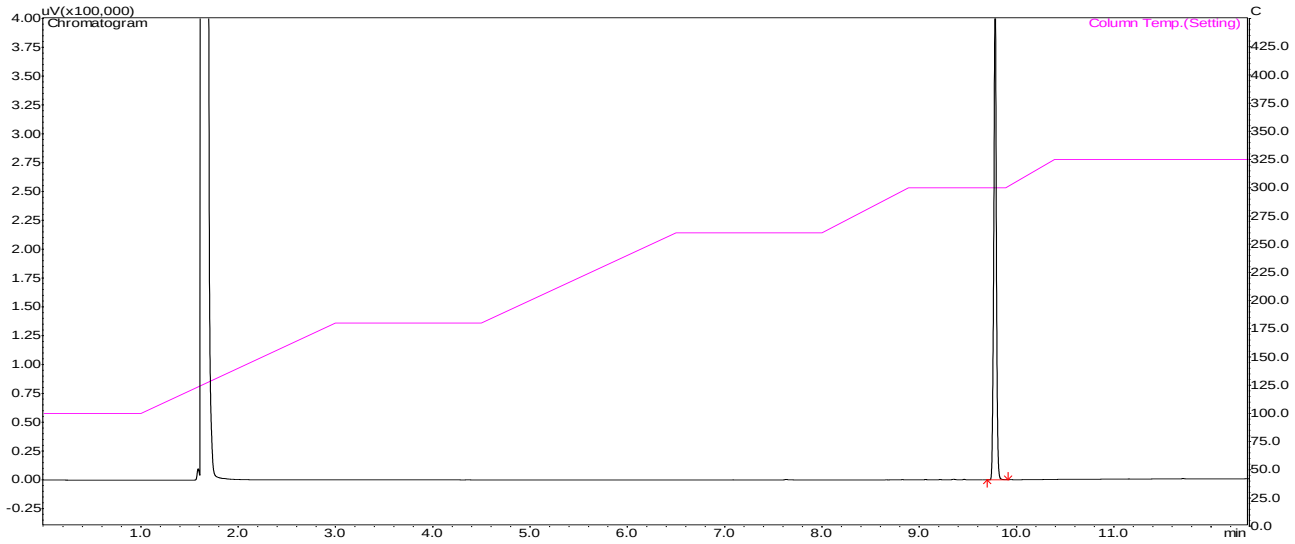
Rf (10% ethyl acetate/hexane) = 0.56

δ_H (400 MHz, Chloroform-*d*) 9.43 (1 H, dd, *J* 8.0, 1.8 Hz), 7.93 – 7.83 (2 H, m), 7.77 (1 H, d, *J* 9.1 Hz), 7.74 – 7.62 (2 H, m), 7.26 – 7.24 (1 H, m), 2.95 (1 H, tt, *J* 11.8, 3.5 Hz), 2.73 (3 H, d, *J* 0.9 Hz), 2.17 – 2.07 (2 H, m), 1.94 (2 H, dt, *J* 12.5, 3.3 Hz), 1.87 – 1.69 (3 H, m), 1.60 – 1.31 (3 H, m).

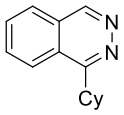
δ_C (101 MHz, Chloroform-*d*) 165.1, 145.7, 143.9, 133.5, 132.2, 127.7, 127.6, 126.7, 126.3, 125.2, 124.2, 121.5, 121.4, 47.2, 33.2, 26.8, 26.5, 19.3.

HRMS (ESI): m/z: [M+H$^+$] Calc. for $C_{20}H_{22}N^+$: 276.1747; Found: 276.1757

GC (FID) purity: >95%



1-cyclohexylphthalazine (9a)



9a

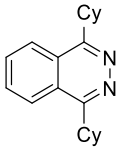
Synthesized according to the general procedure GP-3. The product was obtained as 14.4 mg of a yellowish solid after purification via column chromatography using 4% methanol/dichloromethane as an eluent. The spectroscopic data are consistent with previously reported in the literature.[9]

Rf (5% methanol/dichloromethane) = 0.50

δ_H (400 MHz, Chloroform-*d*) 9.38 (1 H, d, *J* 0.9 Hz), 8.31 – 8.04 (1 H, m), 8.01 – 7.75 (3 H, m), 3.50 (1 H, tt, *J* 11.2, 3.8 Hz), 2.14 – 1.89 (6 H, m), 1.82 (1 H, dddd, *J* 12.6, 6.0, 3.0, 1.3 Hz), 1.63 – 1.29 (3 H, m).

δ_C (101 MHz, Chloroform-*d*) 163.6, 150.3, 132.3, 131.7, 127.3, 126.8, 125.1, 123.6, 40.9, 32.5, 27.0, 26.3.

1,4-dicyclohexylphthalazine (9b)



9b

Synthesized according to the general procedure GP-3. The product was obtained as 7.0 mg of a off-white solid after purification via column chromatography using 4% methanol/dichloromethane as an eluent. The spectroscopic data are consistent with previously reported in the literature.[9]

Rf (5% methanol/dichloromethane) = 0.79

δ_H (400 MHz, Chloroform-*d*) 8.16 (2 H, dt, *J* 6.6, 3.3 Hz), 7.84 (2 H, dq, *J* 6.5, 3.5 Hz), 3.46 (2 H, tt, *J* 11.5, 3.7 Hz), 2.13 – 1.89 (12 H, m), 1.88 – 1.74 (2 H, m), 1.61 – 1.45 (4 H, m), 1.45 – 1.32 (2 H, m).

δ_C (101 MHz, Chloroform-*d*) 161.9, 131.2, 125.1, 124.4, 40.6, 32.5, 27.1, 26.4.

4-cyclohexylquinazoline (10)

10

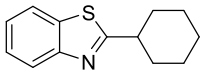
Synthesized according to the general procedure GP-3 with irradiation time prolonged to 48 hours. The product was obtained as 8.1 mg of a yellowish oil after purification via column chromatography using 25-50% ethyl acetate/hexane as an eluent. The spectroscopic data are consistent with previously reported in the literature.[17]

Rf (40% ethyl acetate/hexane) = 0.40

δ_H (400 MHz, Chloroform-*d*) 9.25 (1 H, s), 8.18 (1 H, d, *J* 8.4 Hz), 8.04 (1 H, d, *J* 8.5 Hz), 7.86 (1 H, ddd, *J* 8.4, 6.8, 1.4 Hz), 7.62 (1 H, dd, *J* 8.4, 6.9 Hz), 3.56 (1 H, tt, *J* 11.6, 3.3 Hz), 2.03 – 1.90 (4 H, m), 1.90 – 1.74 (2 H, m), 1.52 (2 H, qt, *J* 12.2, 3.7 Hz), 1.40 (1 H, tt, *J* 12.8, 3.2).

δ_C (101 MHz, Chloroform-*d*) 175.2, 154.9, 150.3, 133.4, 129.5, 127.4, 124.3, 123.4, 41.4, 32.2, 26.7, 26.2.

2-cyclohexylbenzothiazole (11)



11

Synthesized according to the general procedure GP-3. The product was obtained as 11.6 mg of a colourless oil after purification via column chromatography using 7% ethyl acetate/hexane as an eluent. The spectroscopic data are consistent with previously reported in the literature.[6]

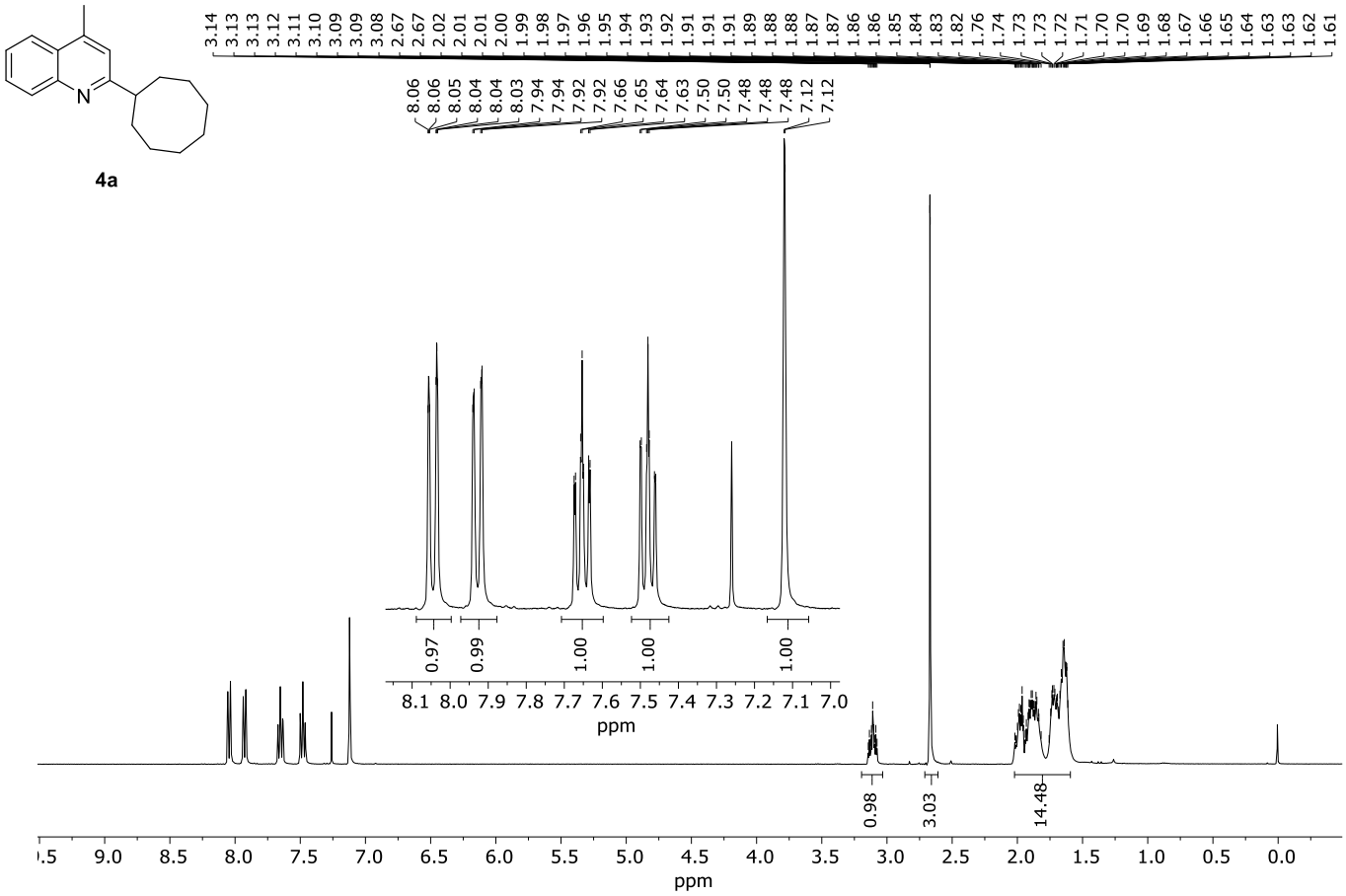
Rf (10% ethyl acetate/hexane) = 0.41

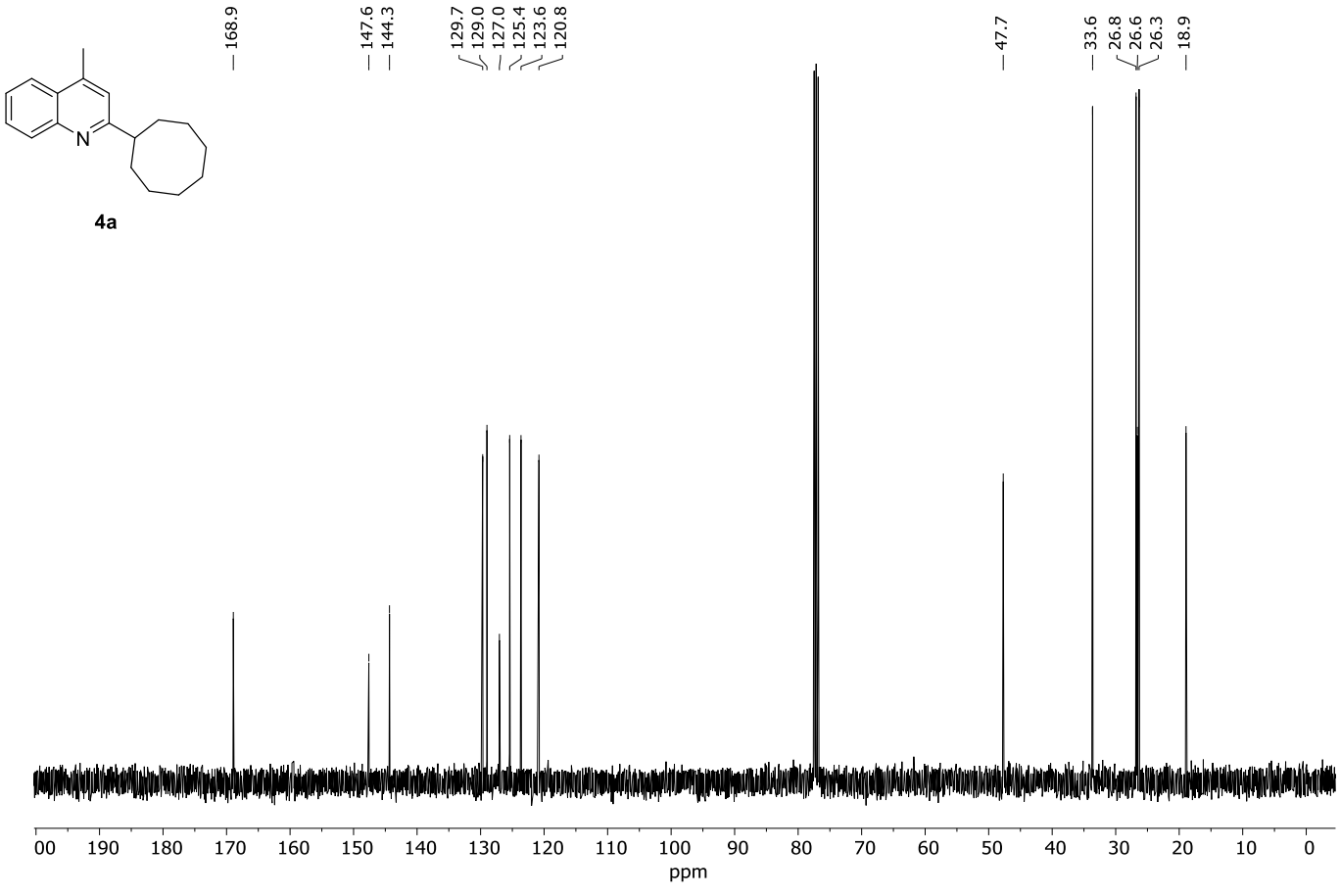
δ_H (500 MHz, Chloroform-*d*) 7.97 (1 H, dd, *J* 8.2, 0.8 Hz), 7.85 (1 H, dd, *J* 7.9, 0.5 Hz), 3.11 (1 H, tt, *J* 11.7, 3.6 Hz), 2.28 – 2.13 (2 H, m), 1.96 – 1.82 (2 H, m), 1.82 – 1.72 (1 H, m), 1.65 (2 H, qd, *J* 12.3, 3.5 Hz), 1.45 (2 H, qt, *J* 12.7, 3.4 Hz), 1.32 (1 H, qt, *J* 12.8, 3.5 Hz).

δ_C (126 MHz, $CDCl_3$) 177.7, 153.3, 134.7, 125.9, 124.6, 122.7, 121.7, 43.6, 33.6, 26.2, 26.0.

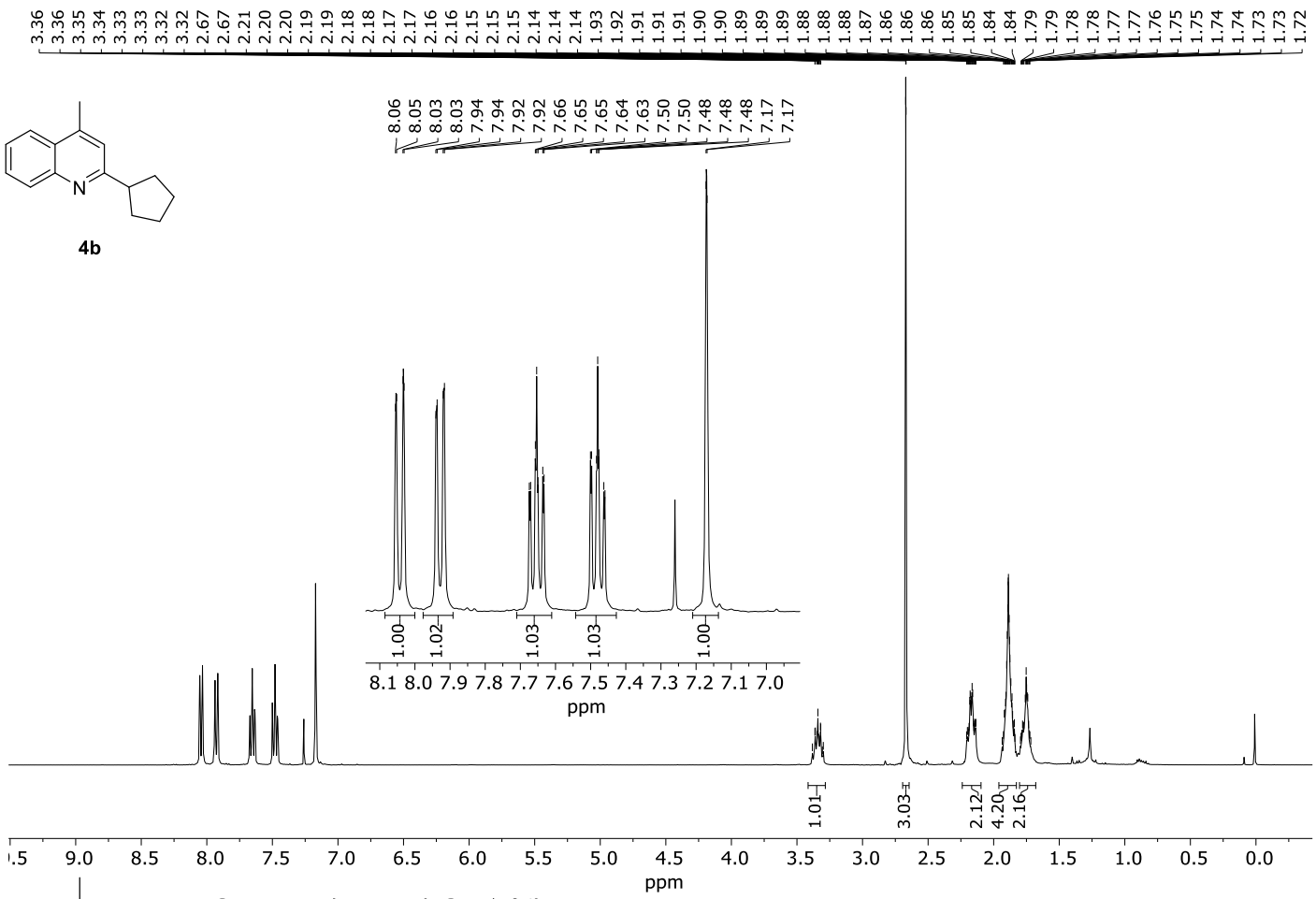
8 NMR spectra of products

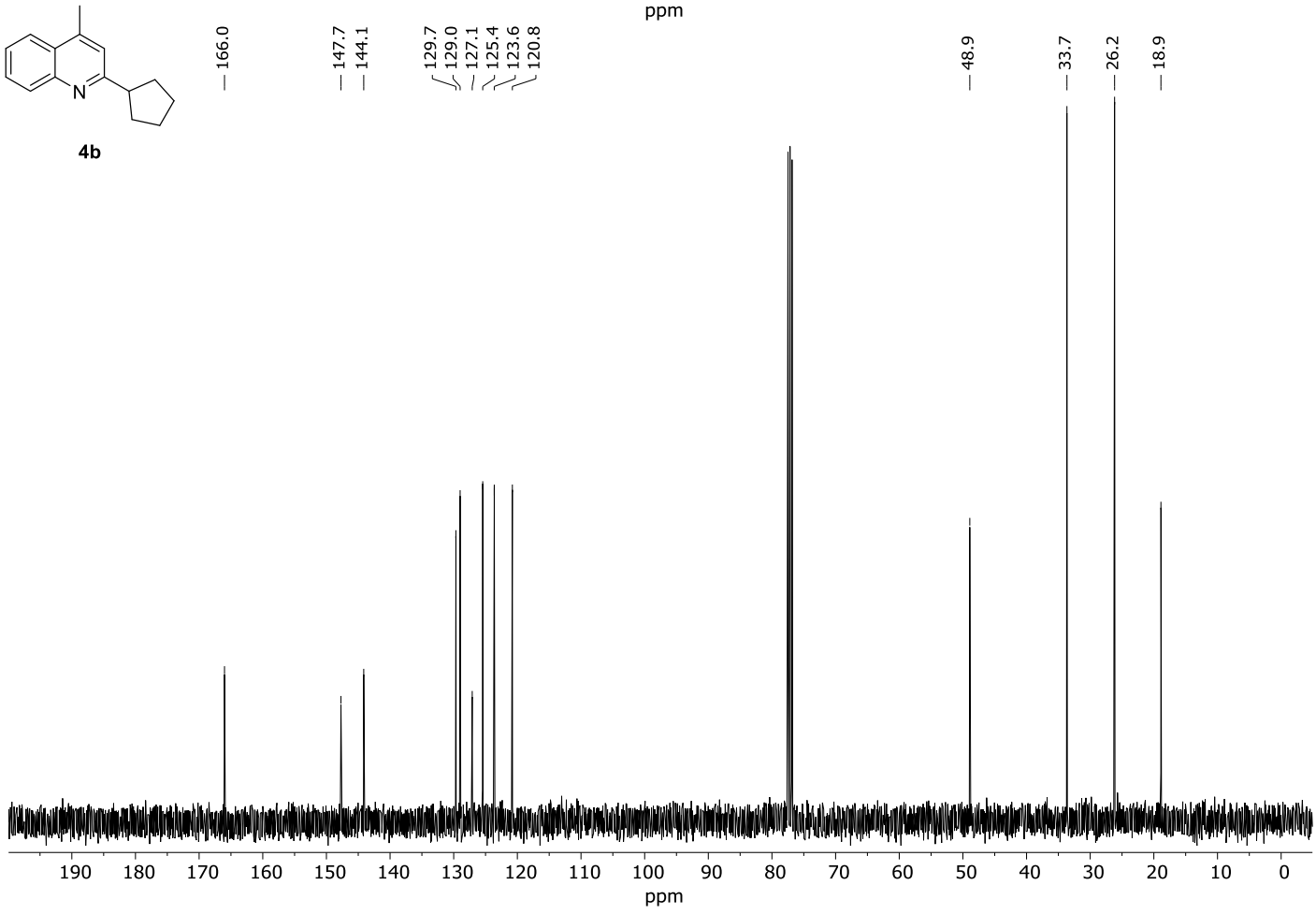
8.1 2-cyclooctyl-4-methylquinoline (4a)



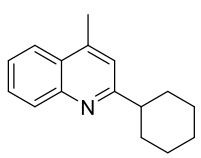


8.2 2-cyclopentyl-4-methylquinoline (4b)

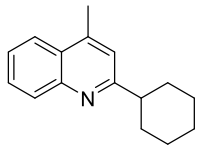




8.3 2-cyclohexyl-4-methylquinoline (4c)

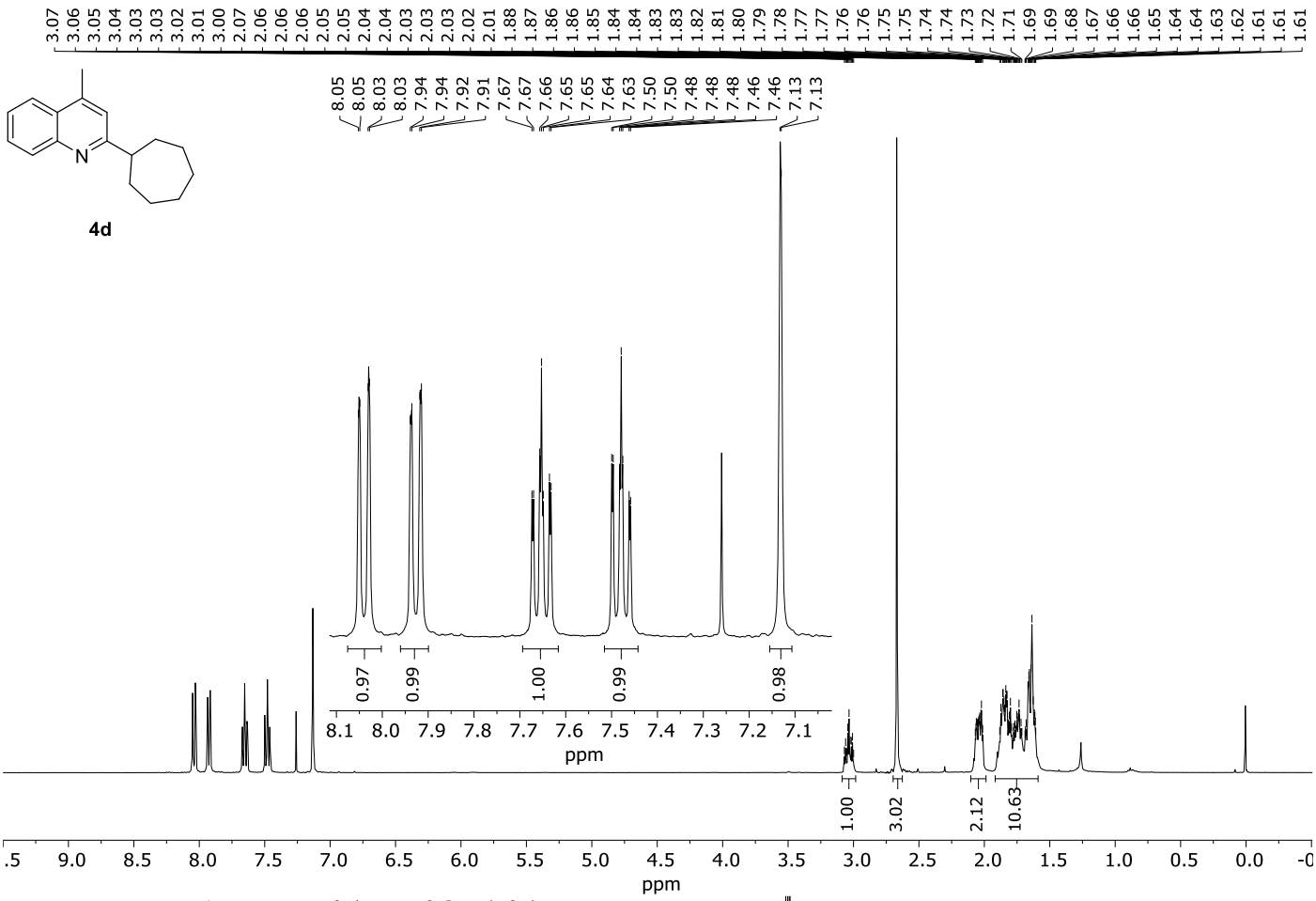


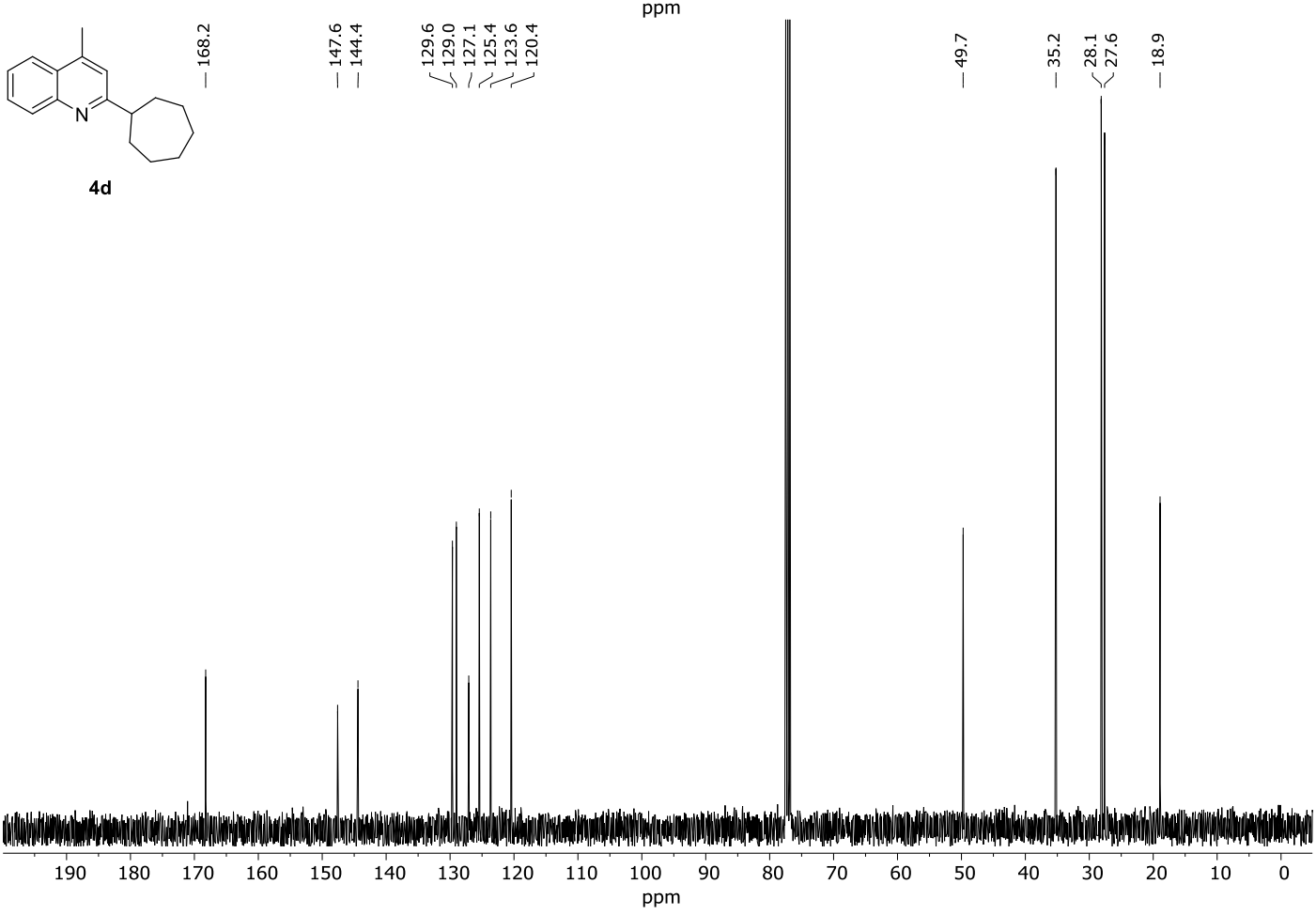
4c



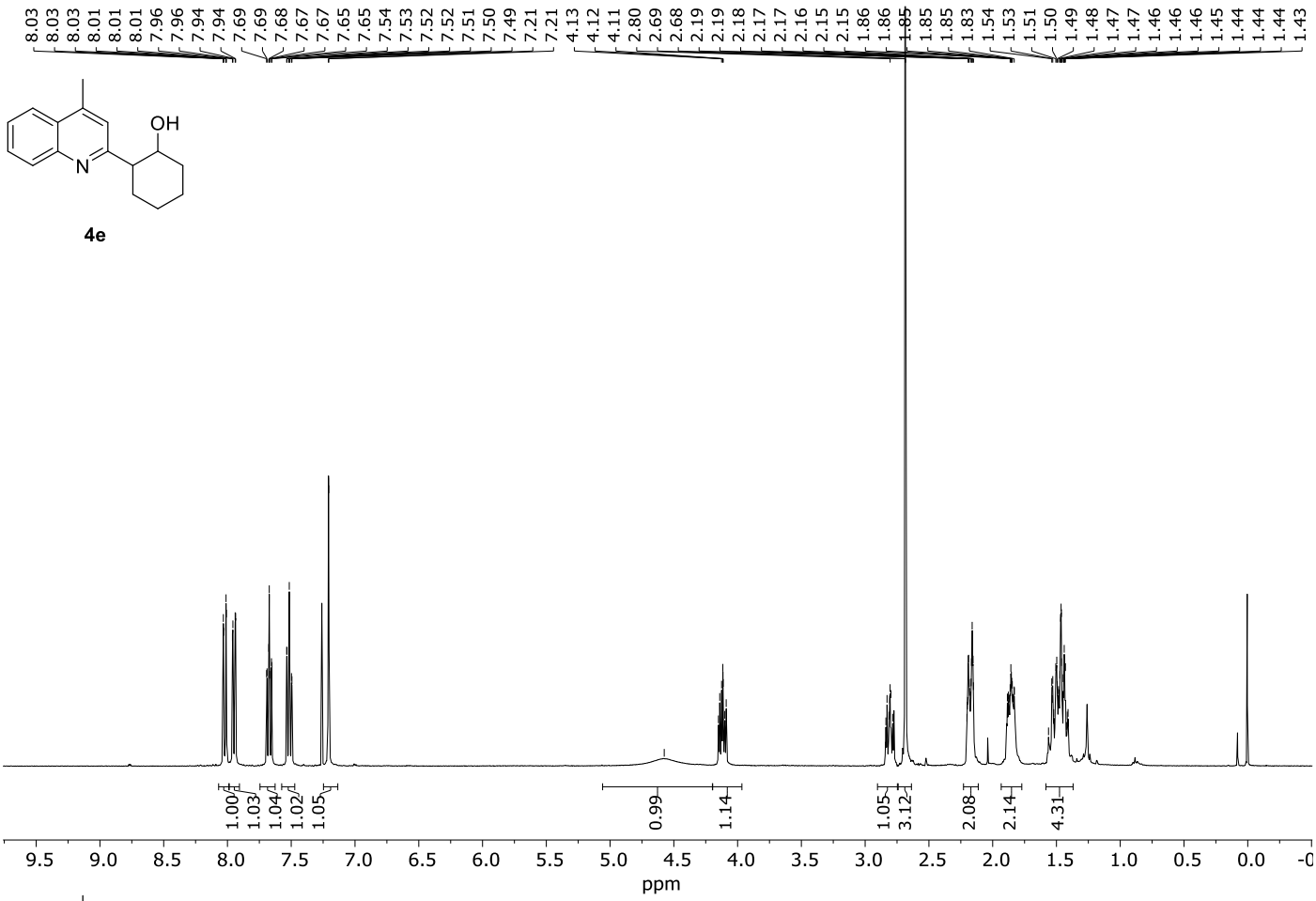
4c

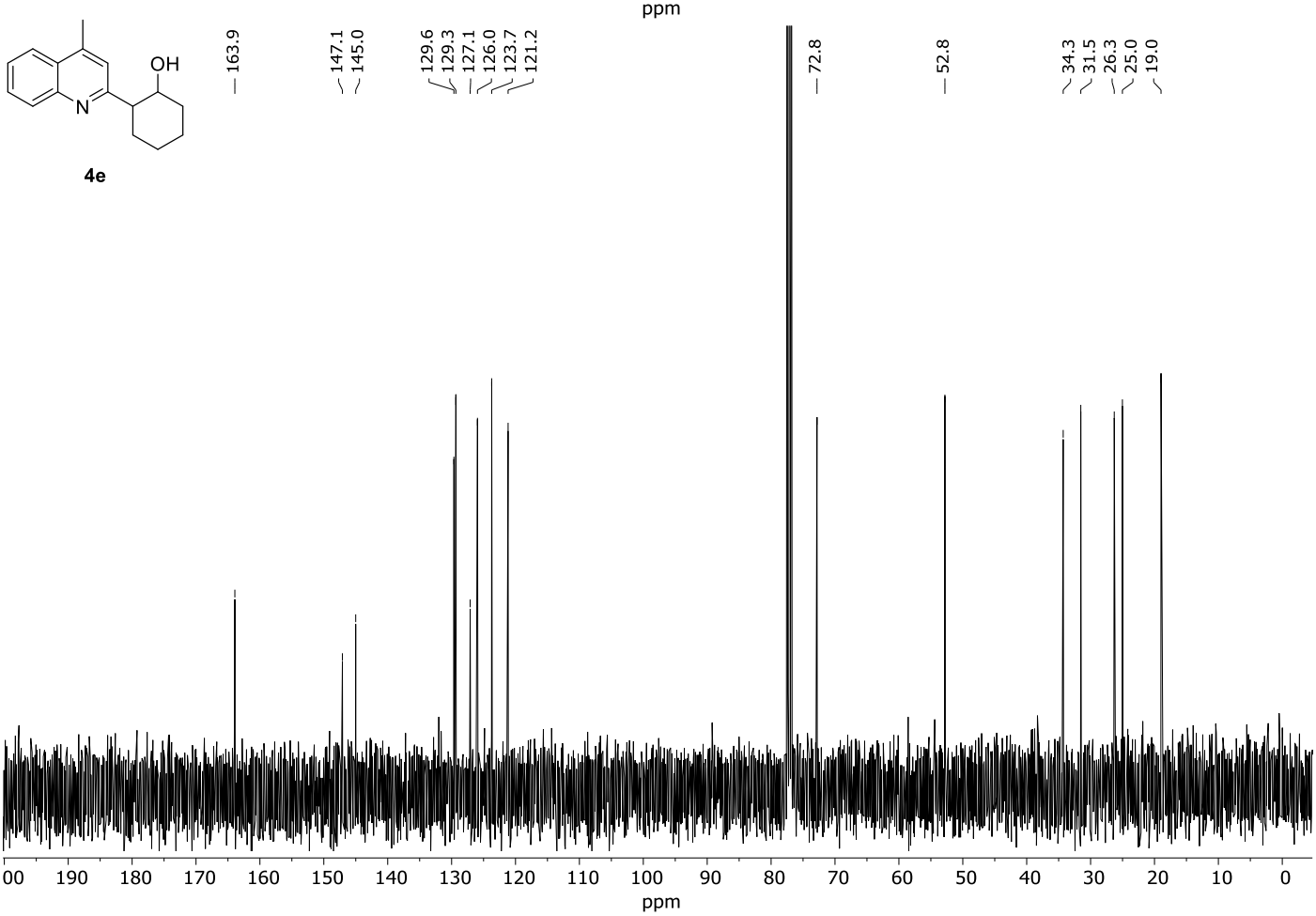
8.4 2-cycloheptyl-4-methylquinoline (4d)



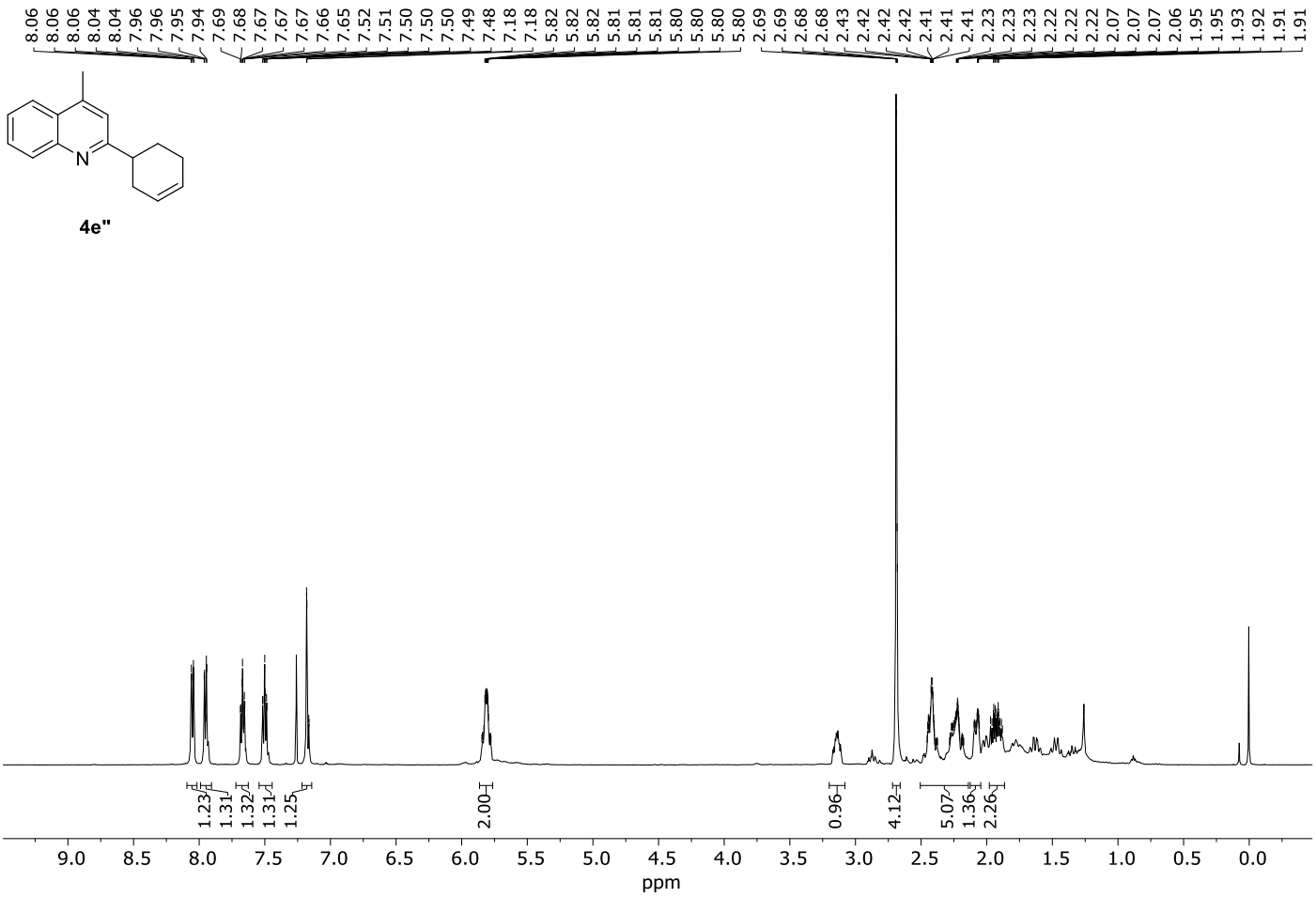


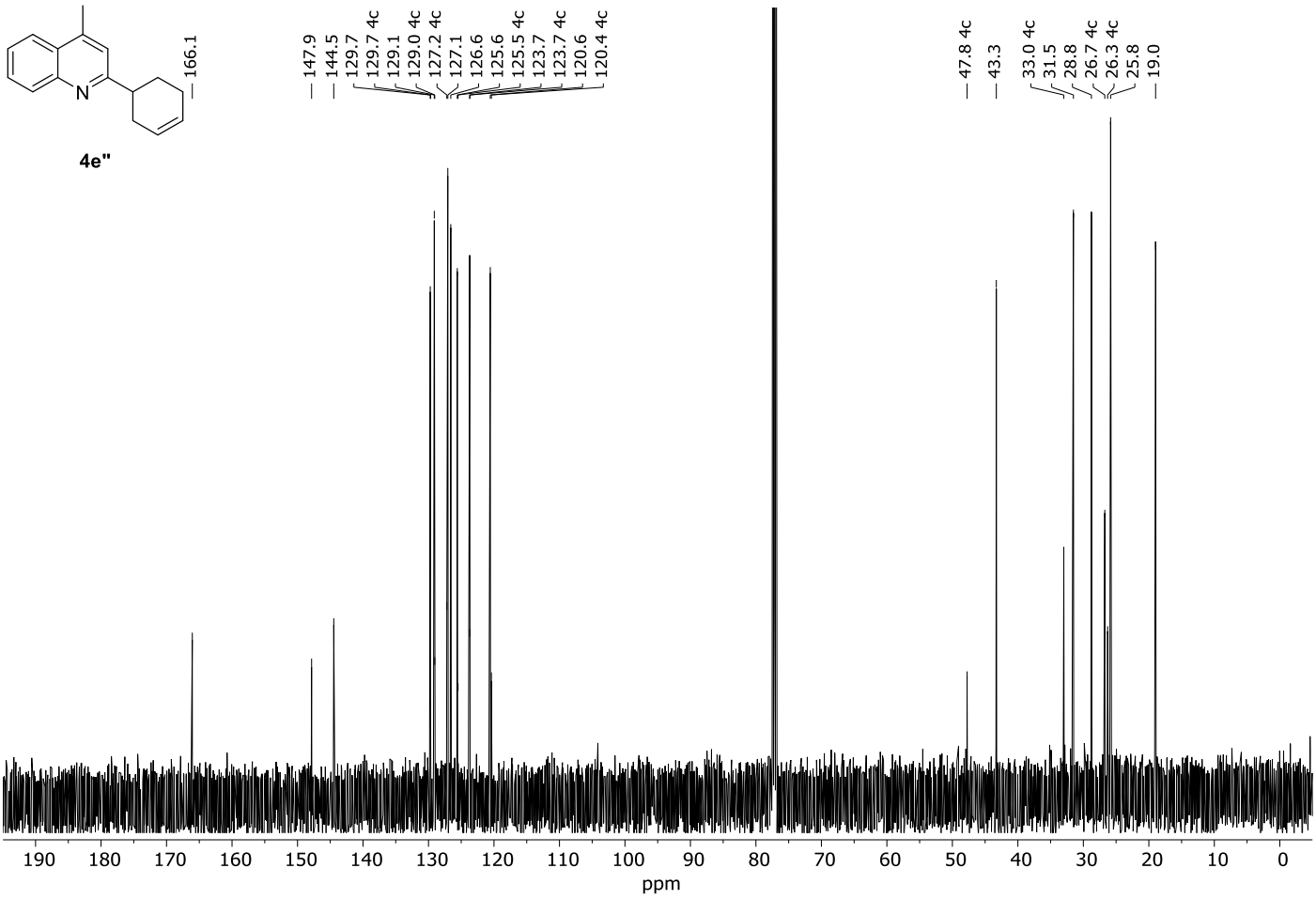
8.5 2-(4-methylquinolin-2-yl)cyclohexan-1-ol (4e)



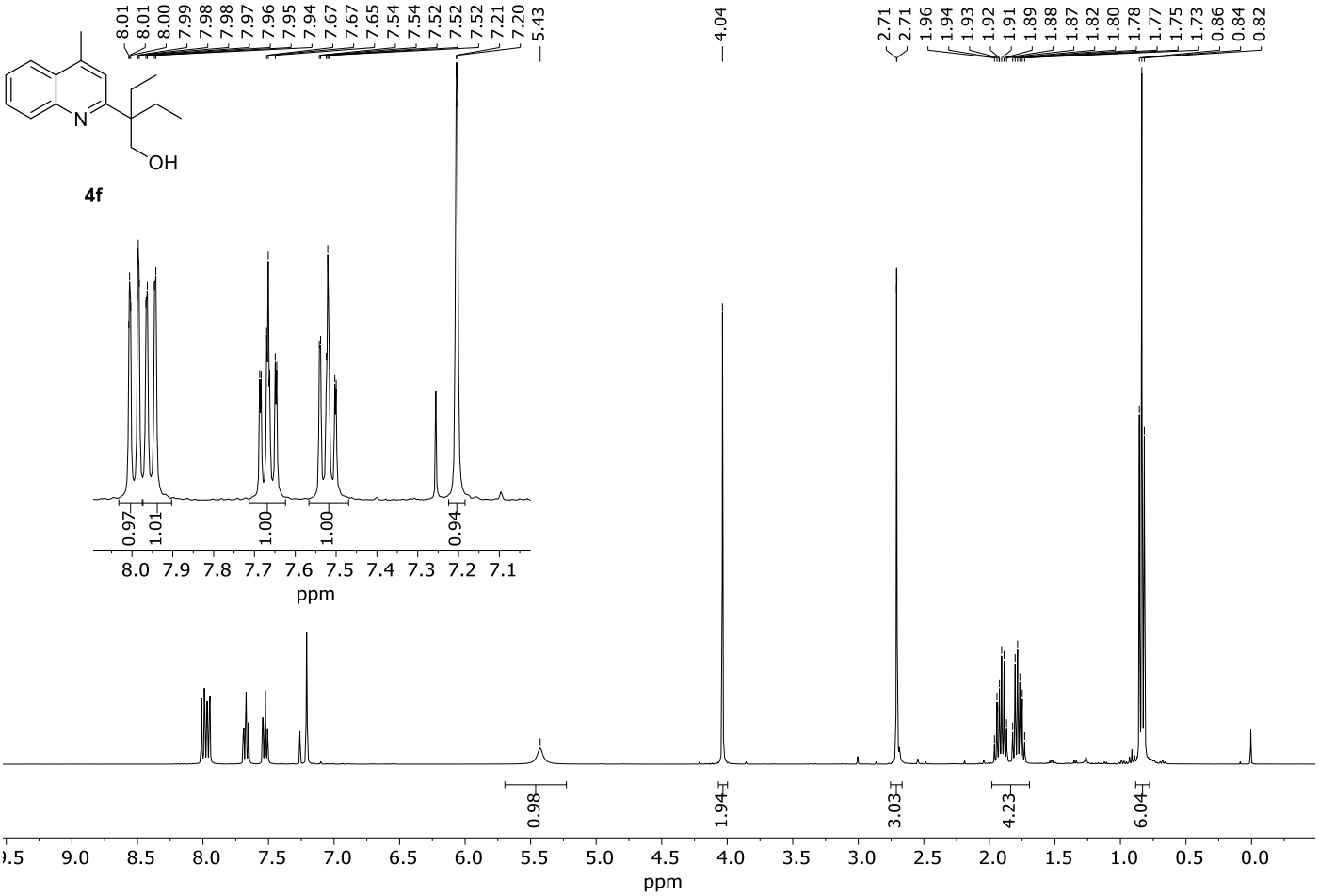


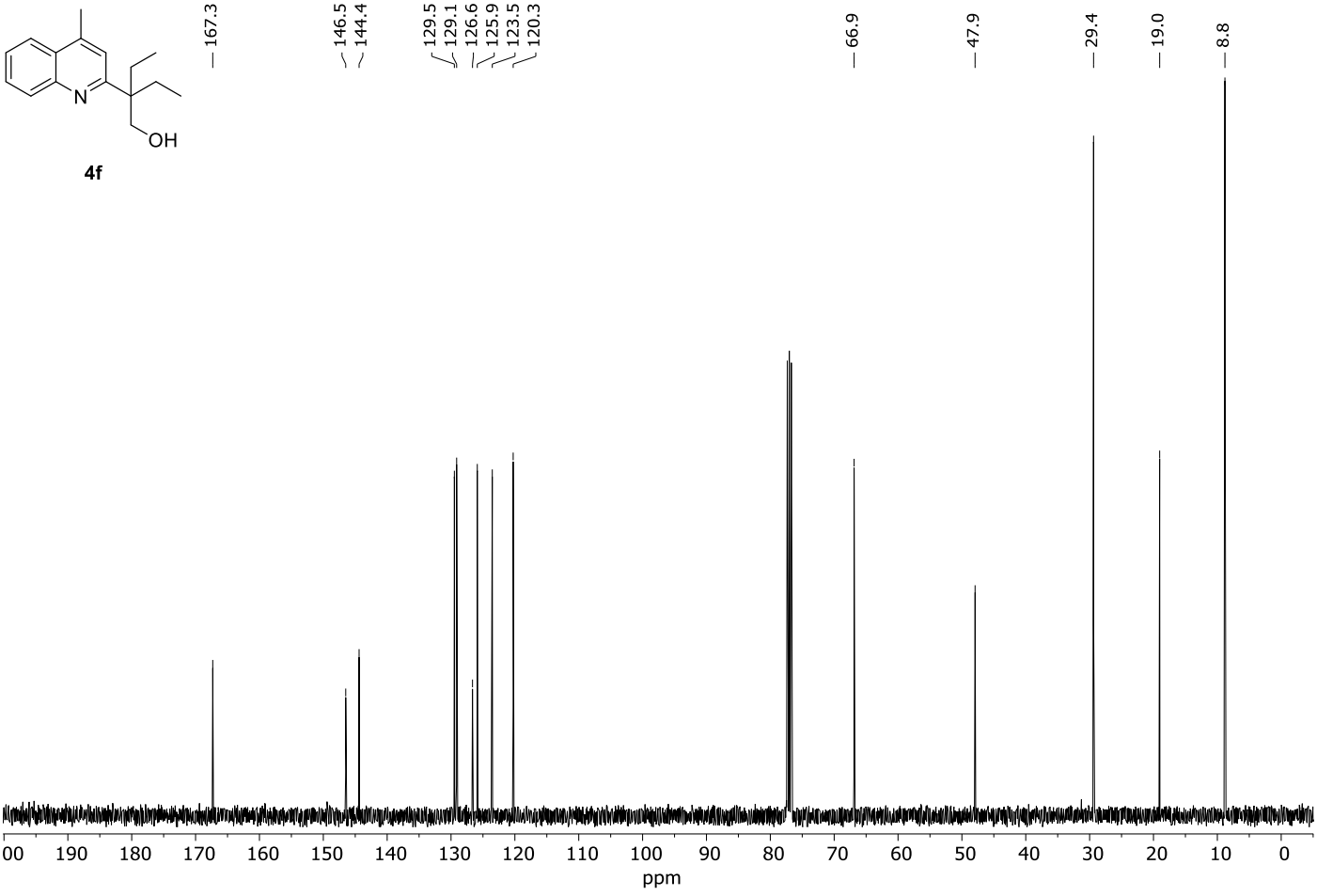
8.6 2-(cyclohex-3-en-1-yl)-4-methylquinoline (4e")



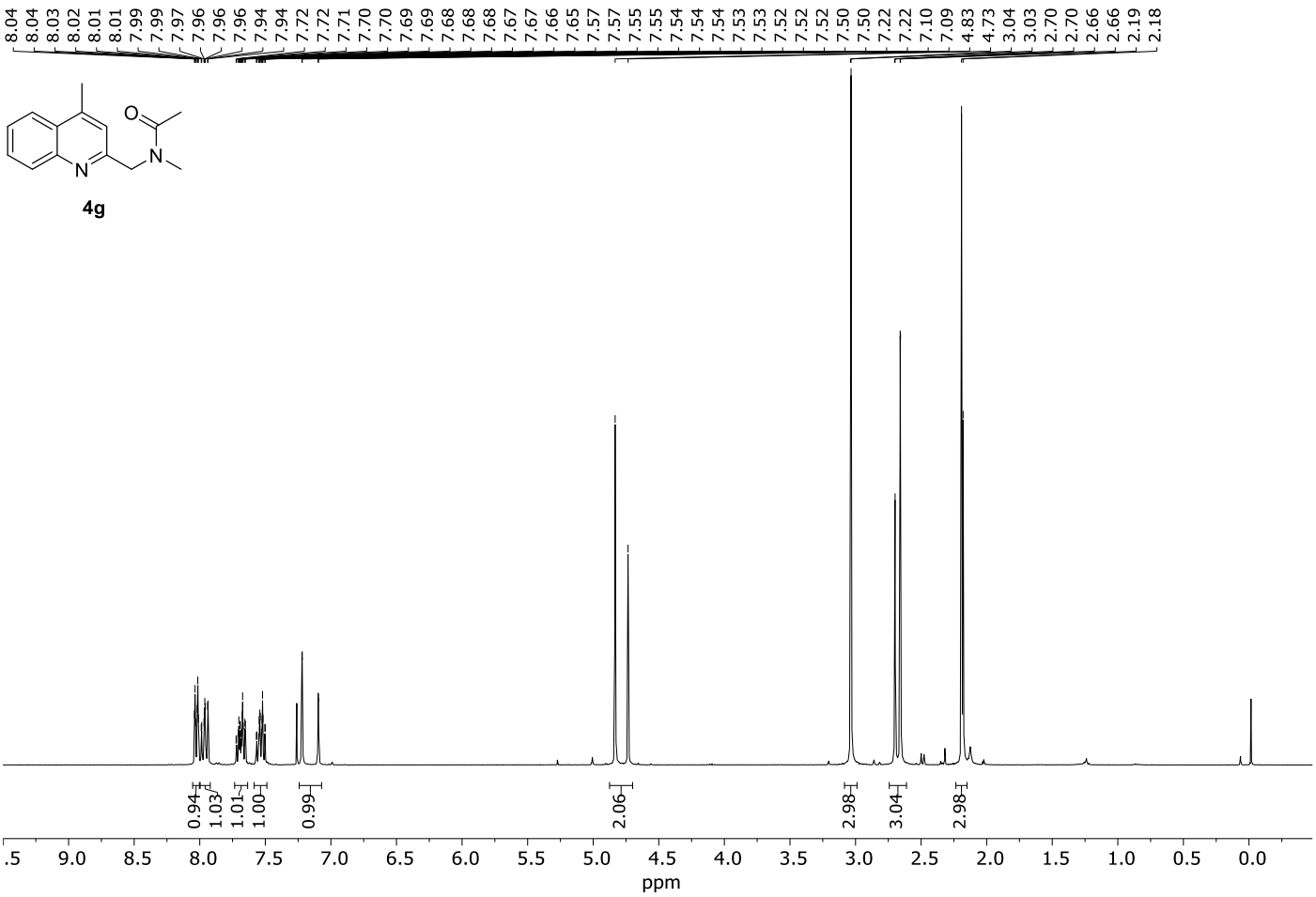


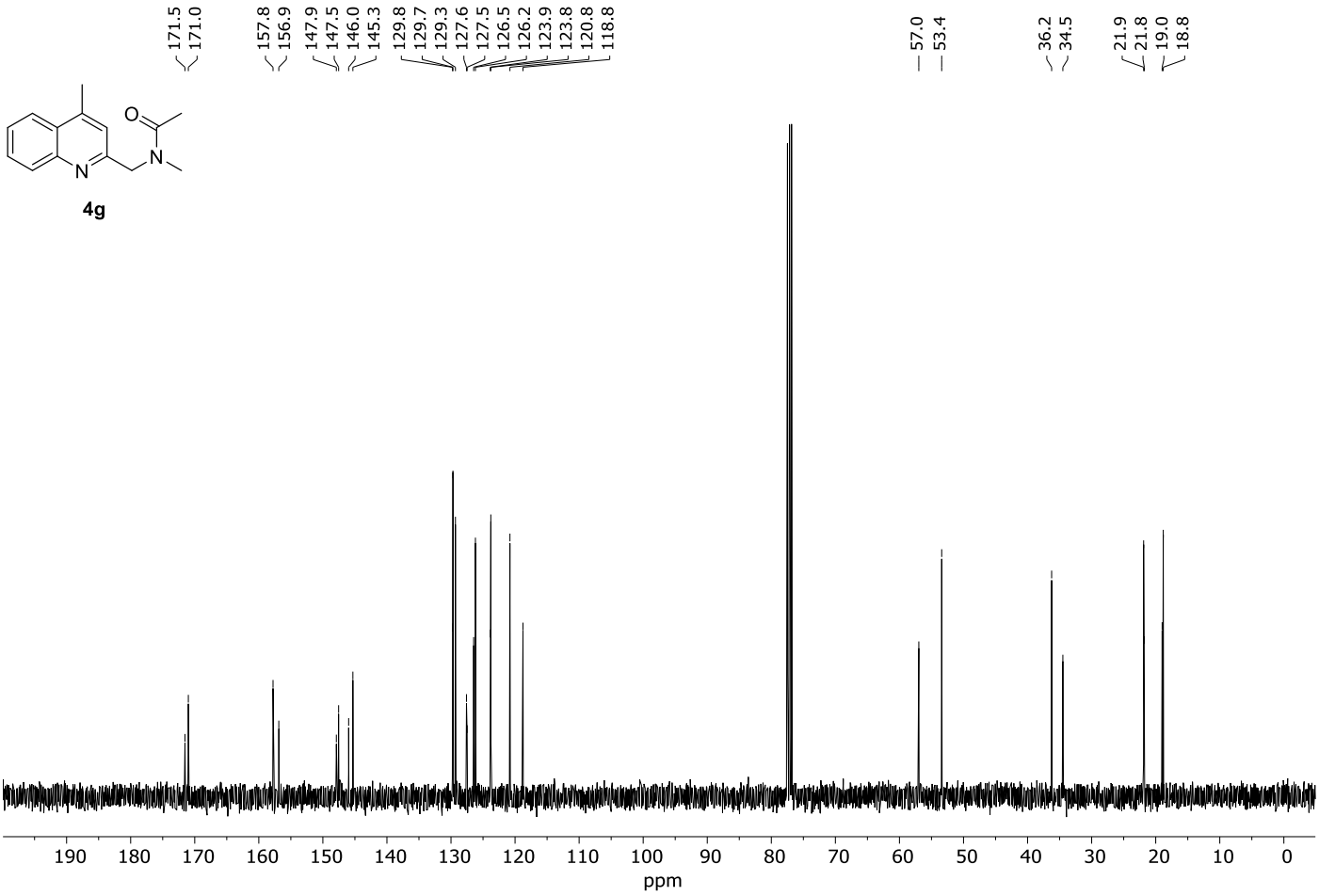
8.7 2-ethyl-2-(4-methylquinolin-2-yl)butan-1-ol (4f)



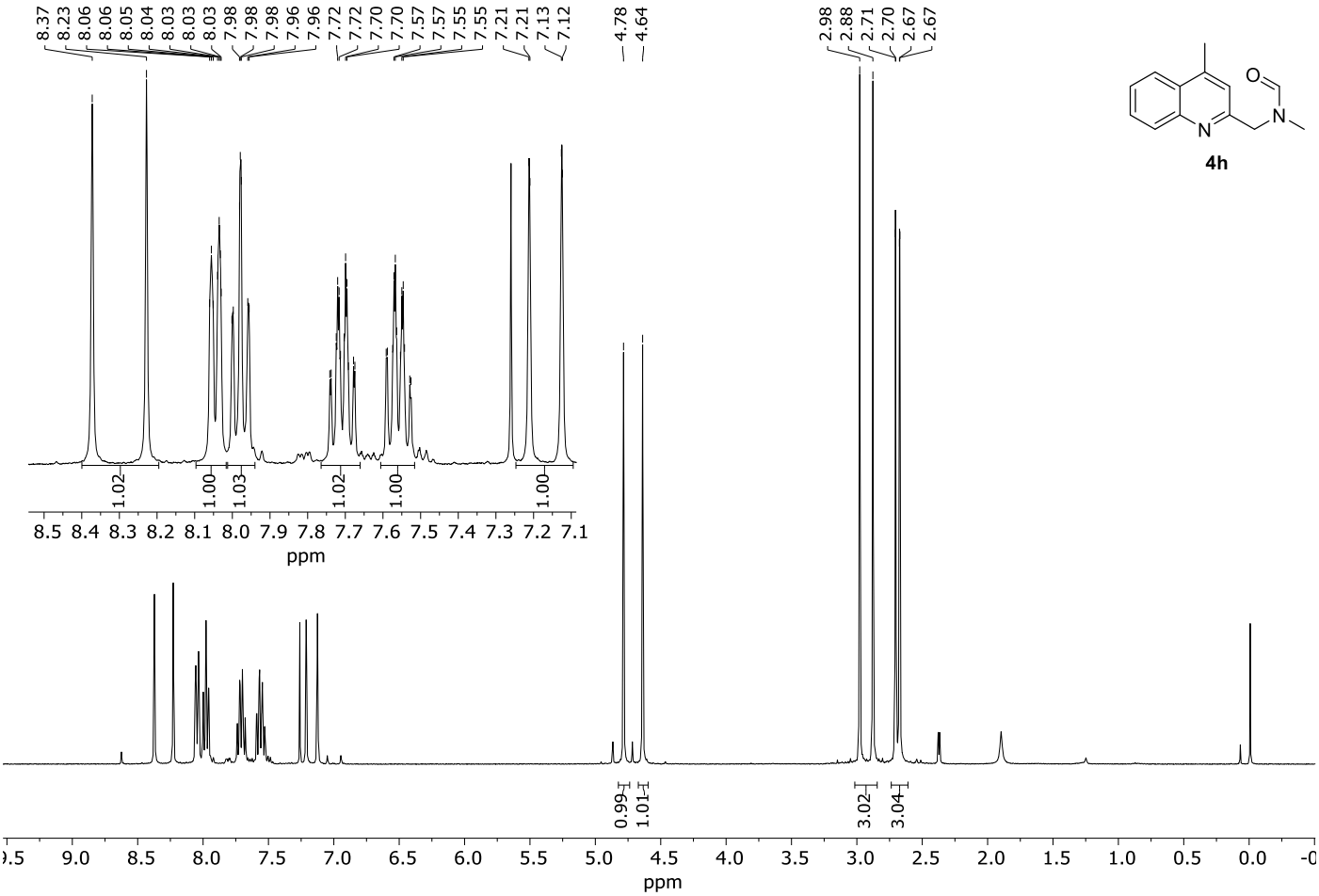


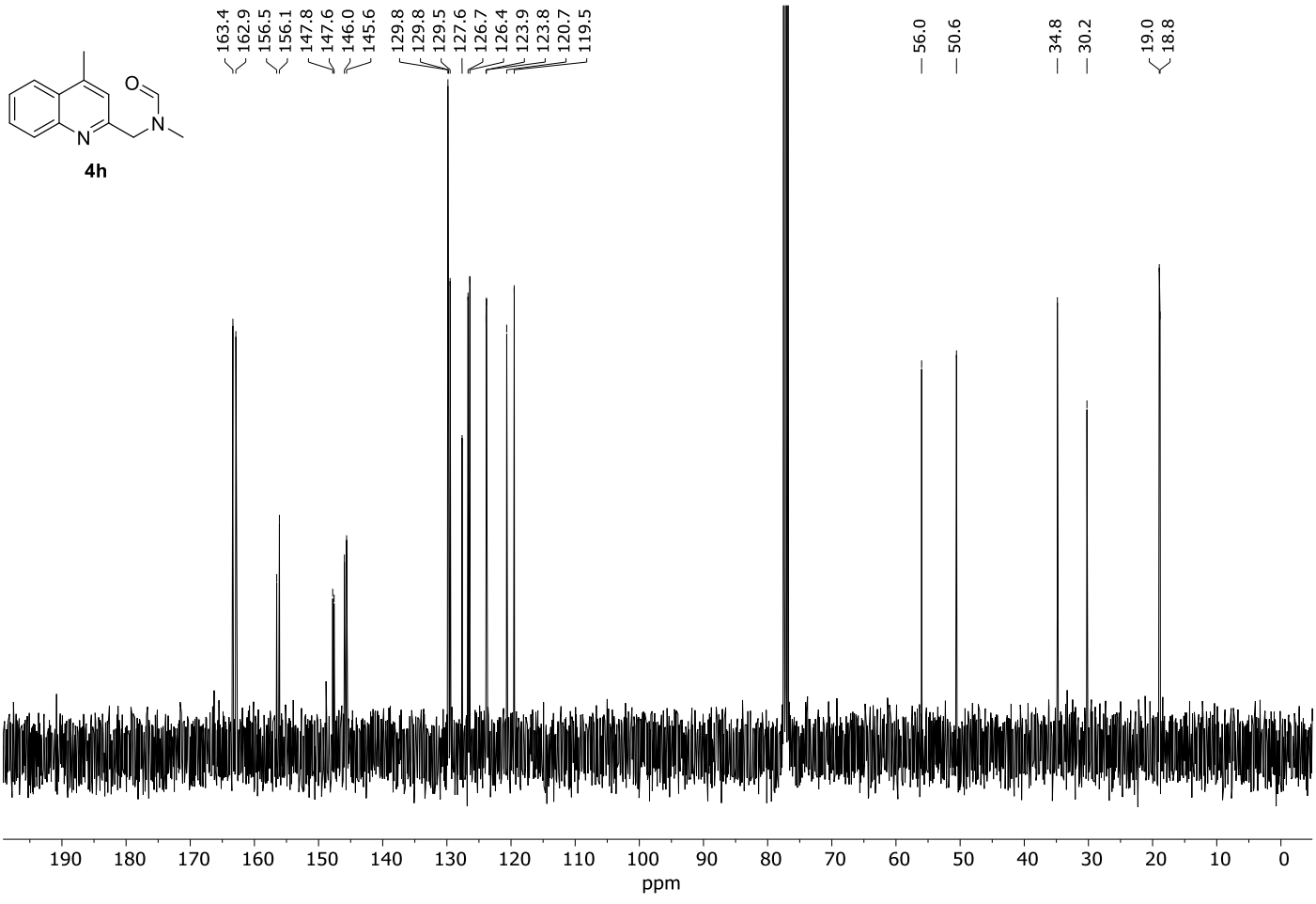
8.8 N-methyl-N-((4-methylquinolin-2-yl)methyl)acetamide (4g)



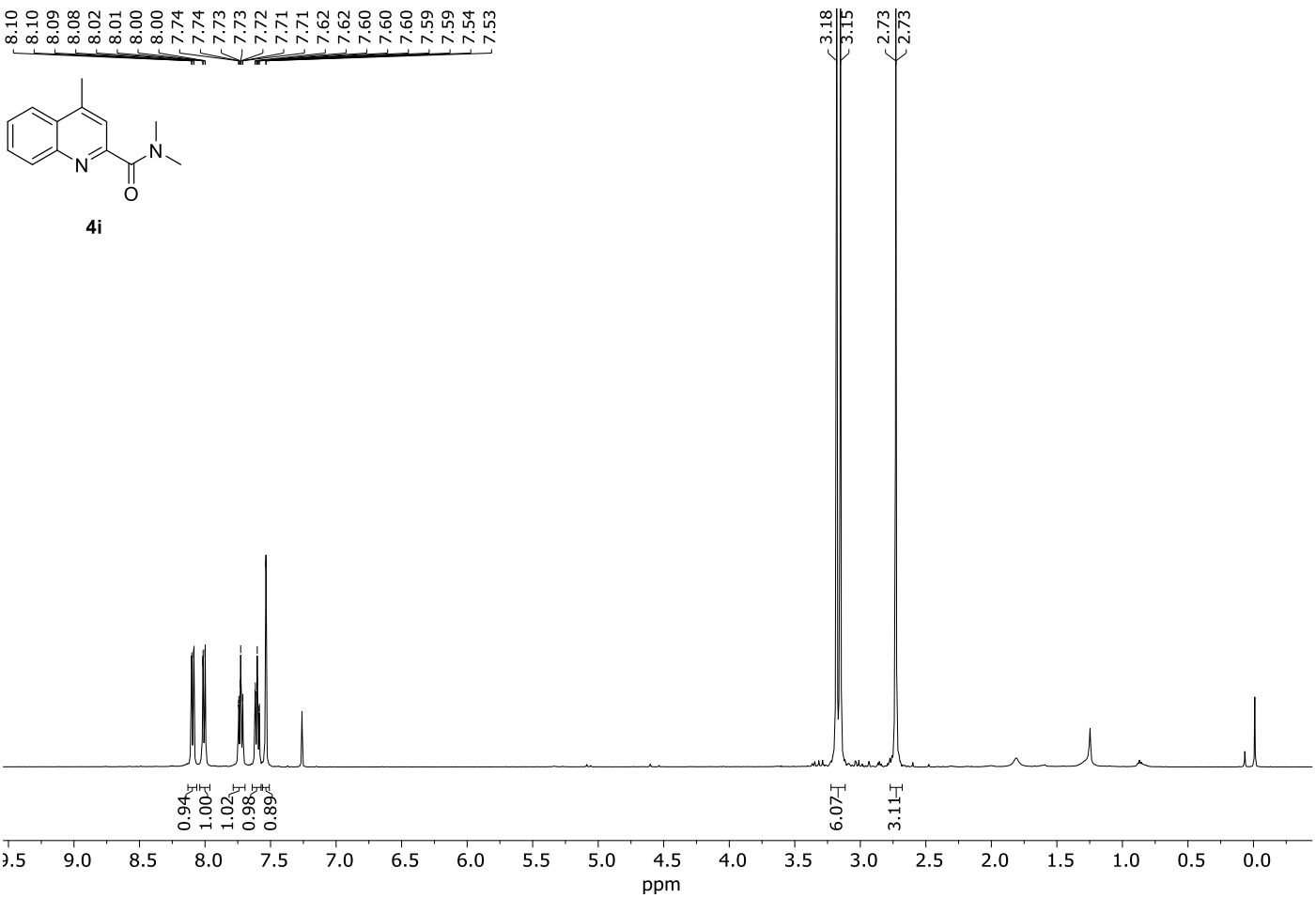


8.9 N-methyl-N-((4-methylquinolin-2-yl)methyl)formamide (4h)

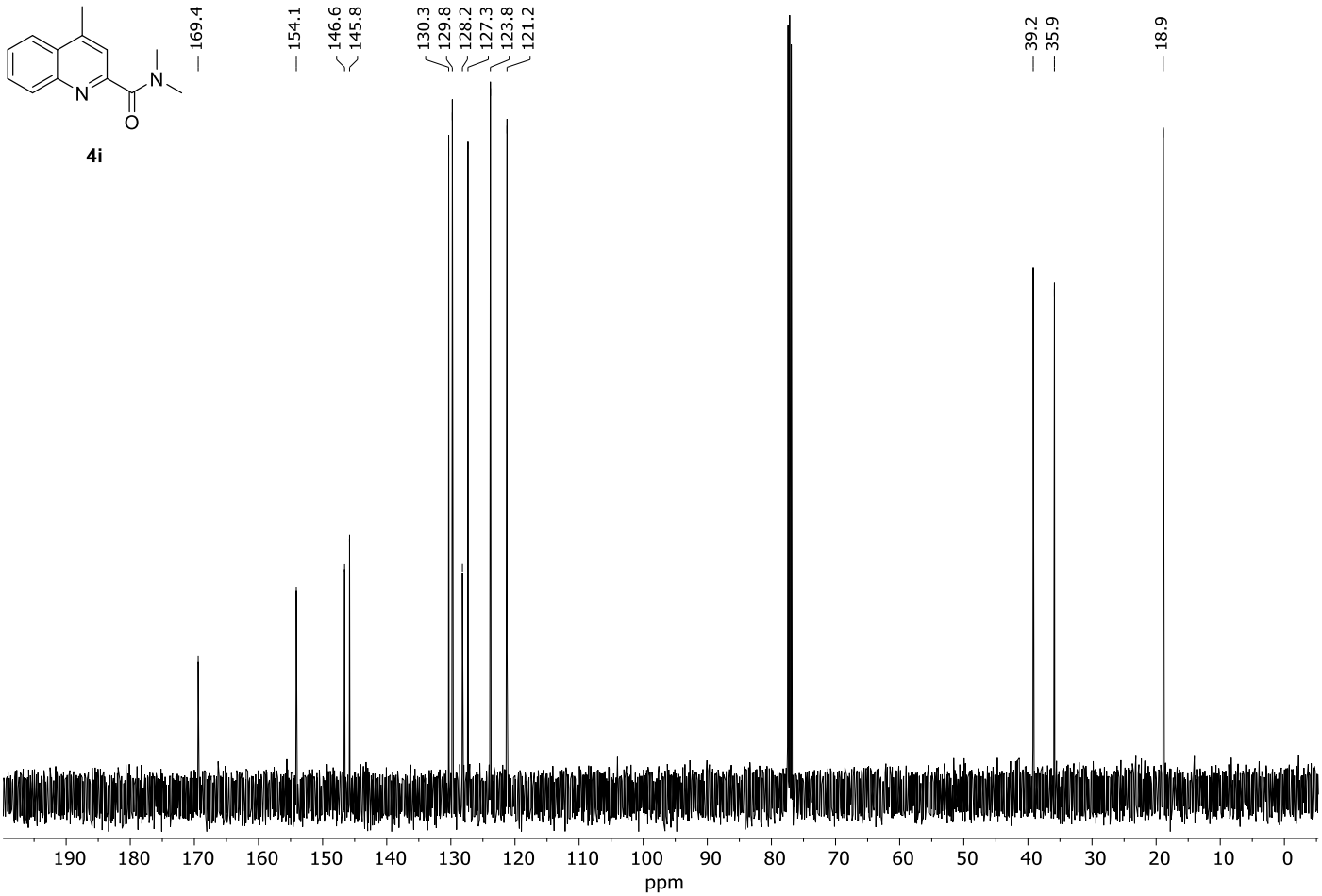




8.10 N,N,4-trimethylquinoline-2-carboxamide (4i)

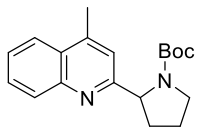


4i

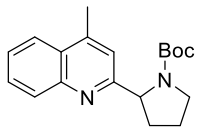


4i

8.11 tert-butyl 2-(4-methylquinolin-2-yl)pyrrolidine-1-carboxylate (4j)

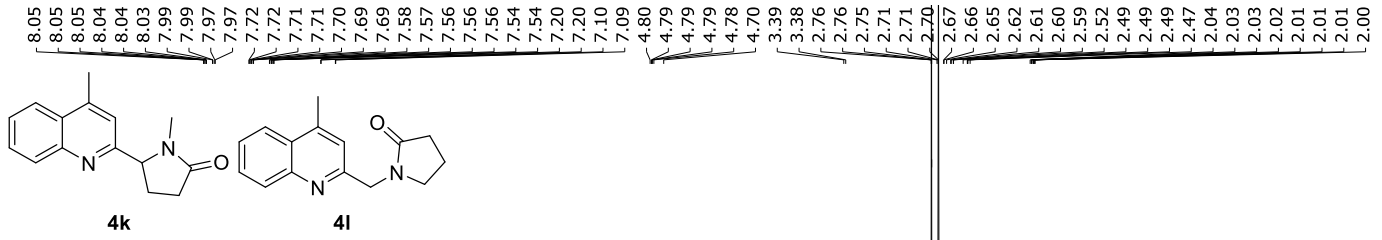


4j

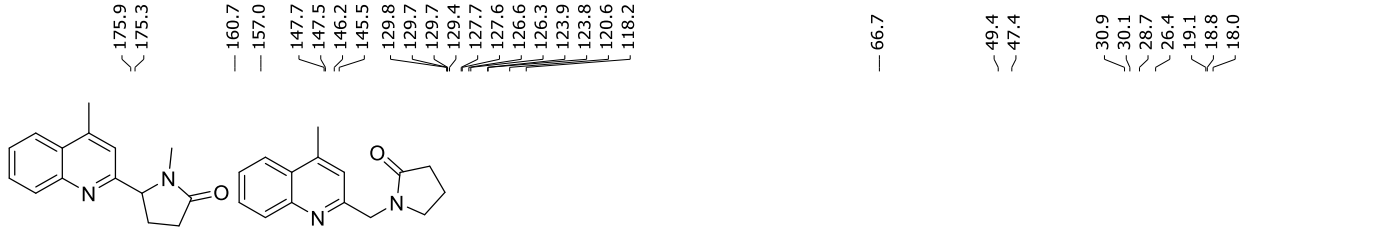


4j

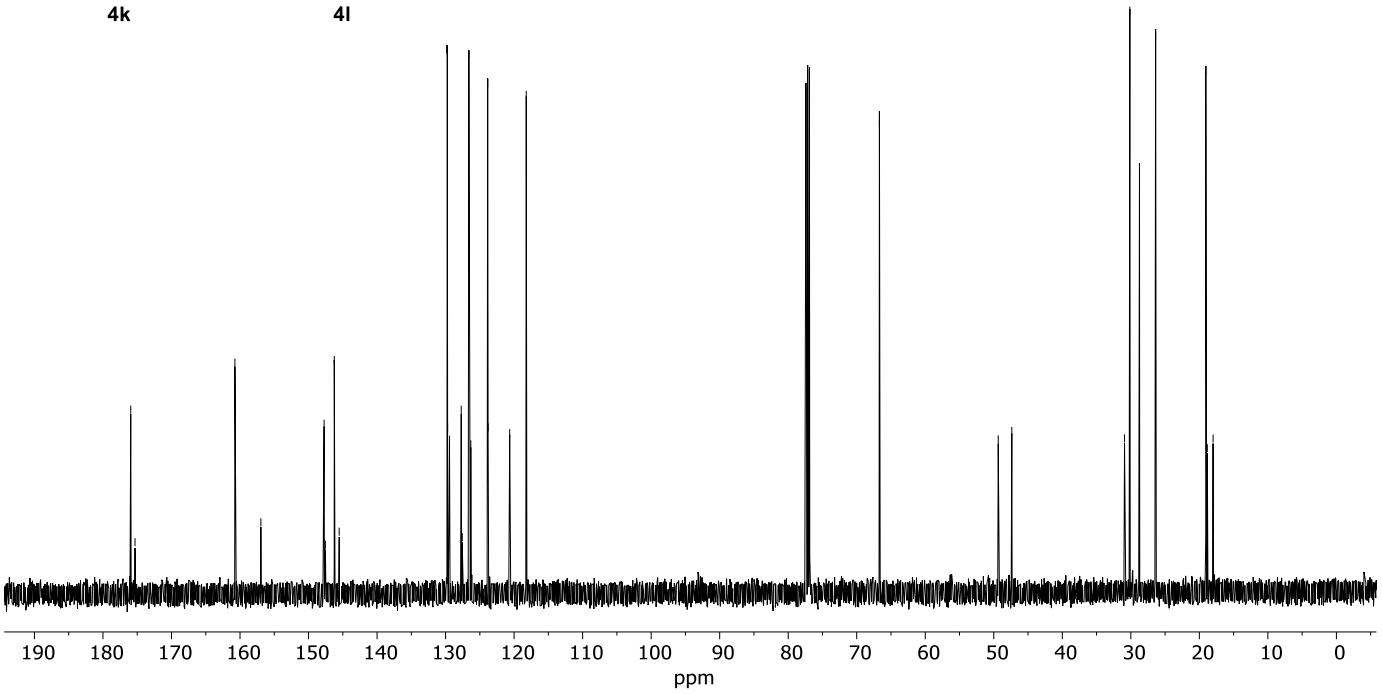
8.12 1-methyl-5-(4-methylquinolin-2-yl)pyrrolidin-2-one (4k) and 1-((4-methylquinolin-2-yl)methyl)pyrrolidin-2-one (4l)



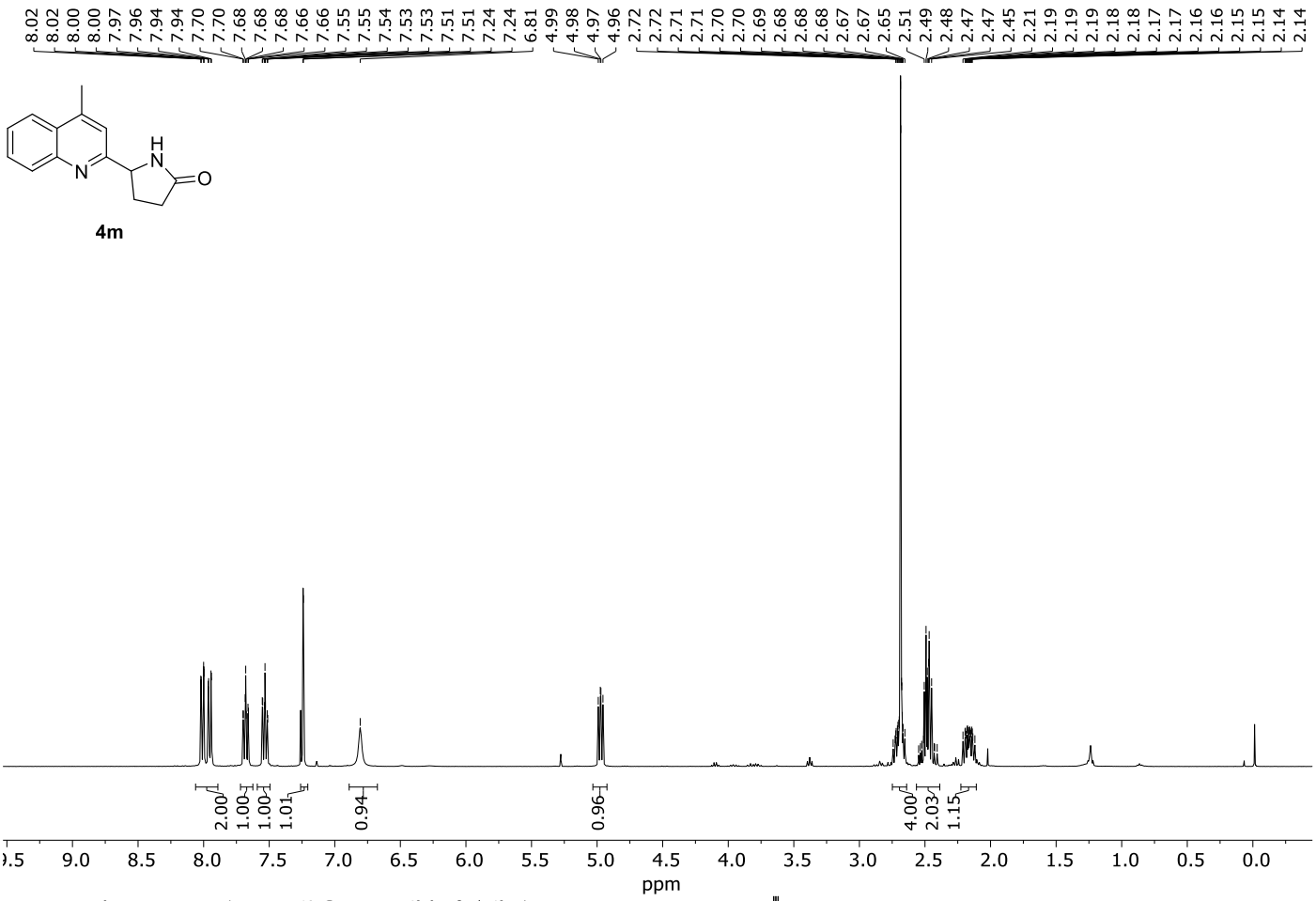
4k **4l**

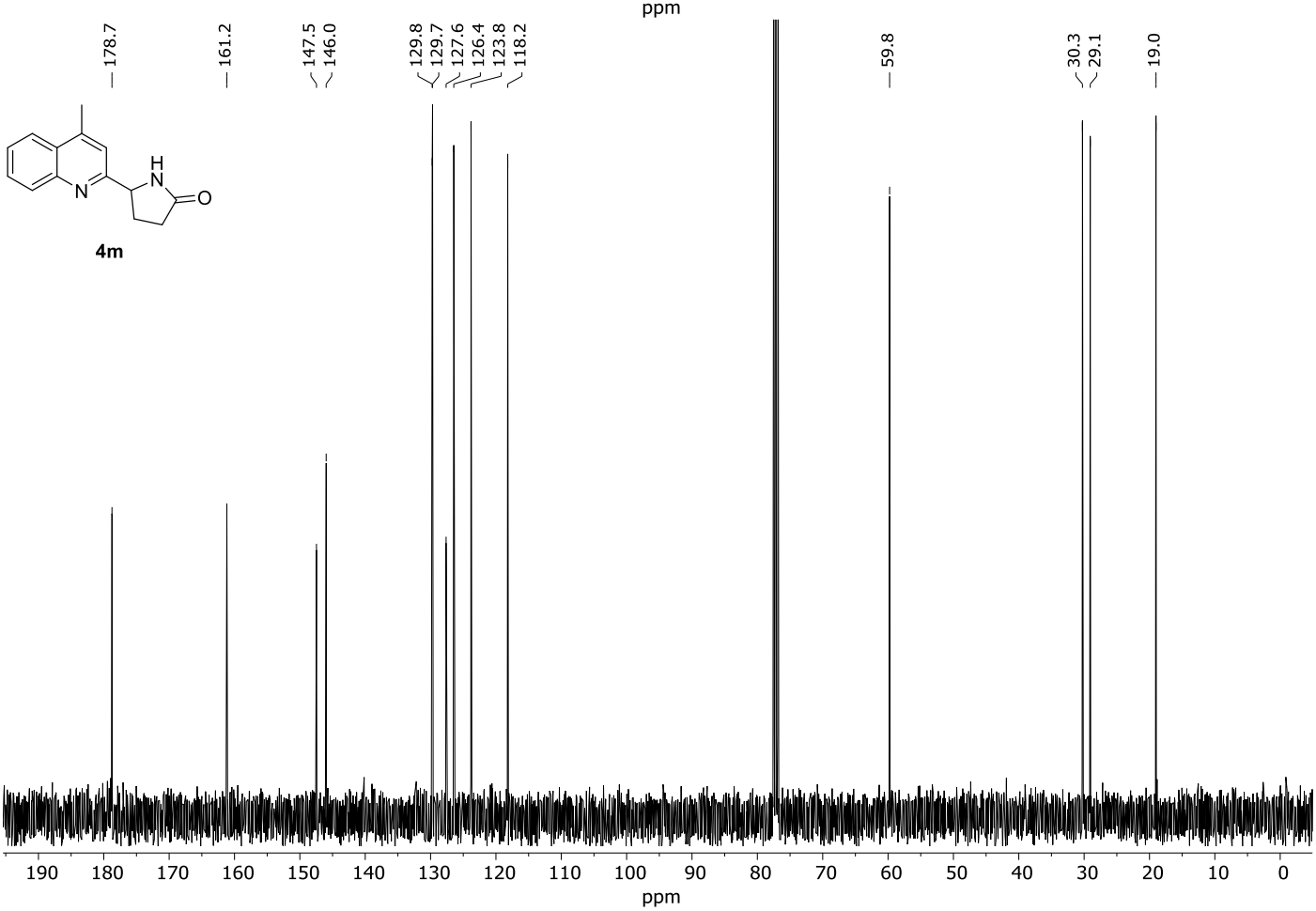


4k **4l**

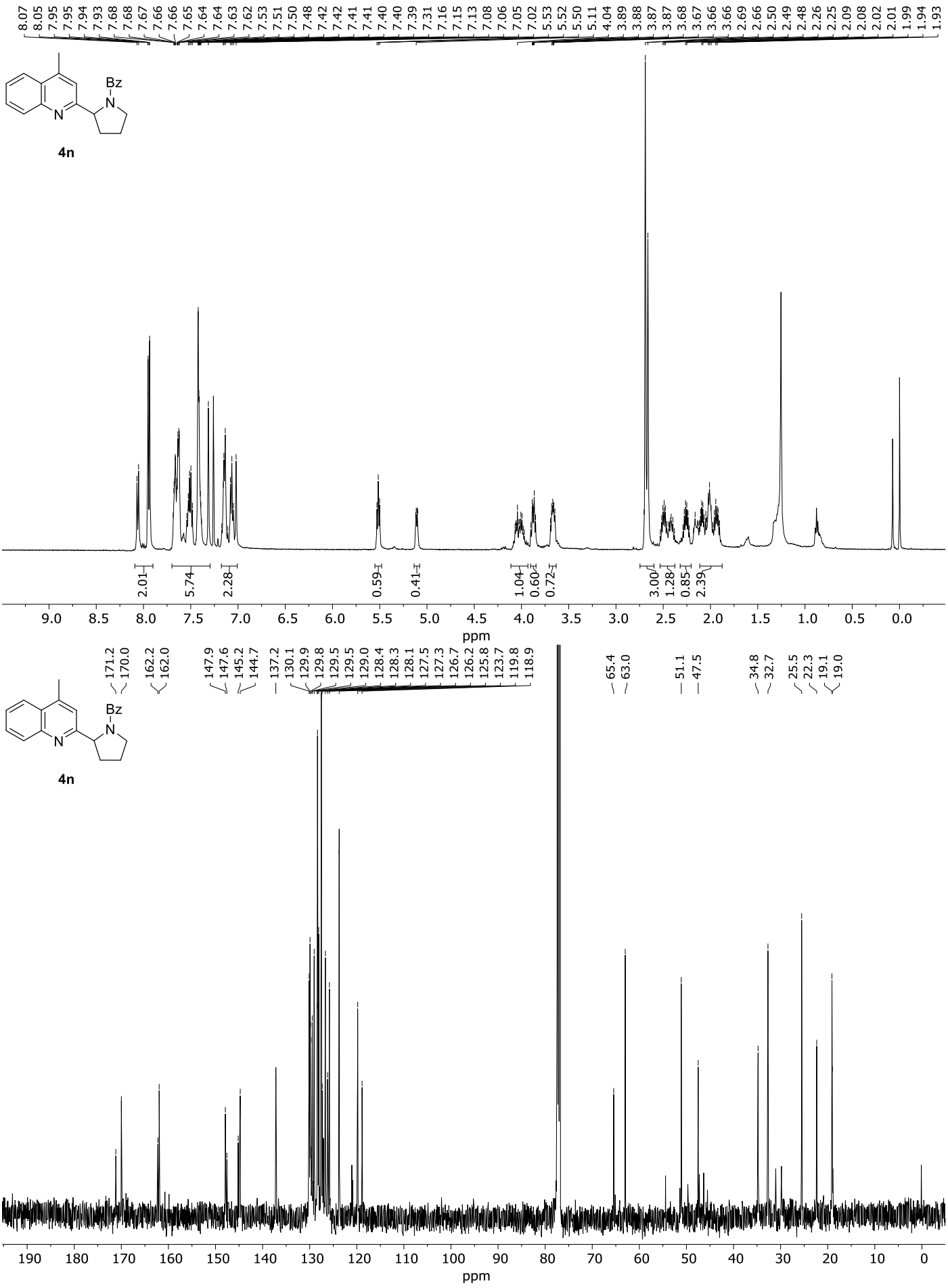


8.13 5-(4-methylquinolin-2-yl)pyrrolidin-2-one (4m)

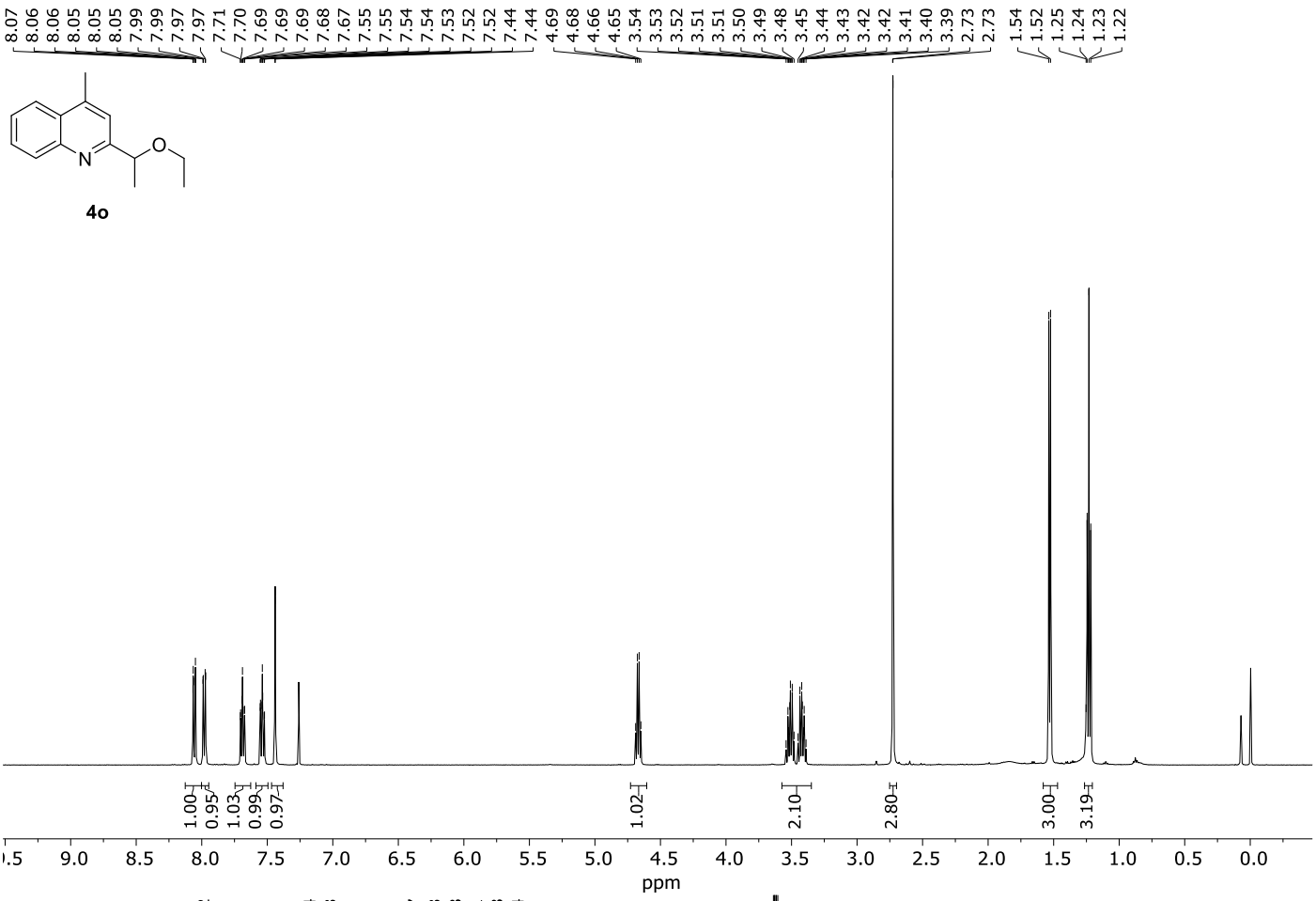


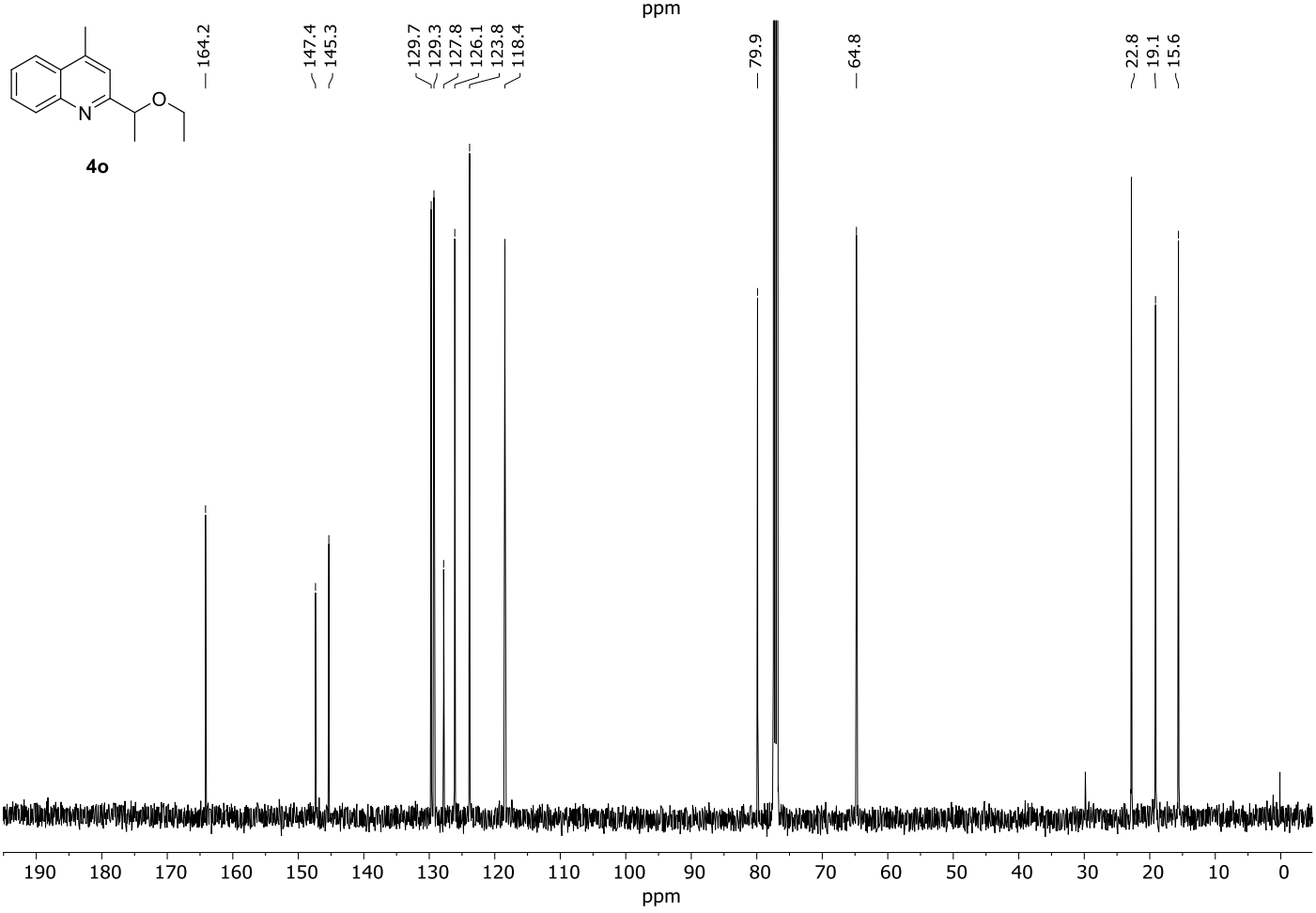


8.14 (2-(4-methylquinolin-2-yl)pyrrolidin-1-yl)(phenyl)methanone (4n)

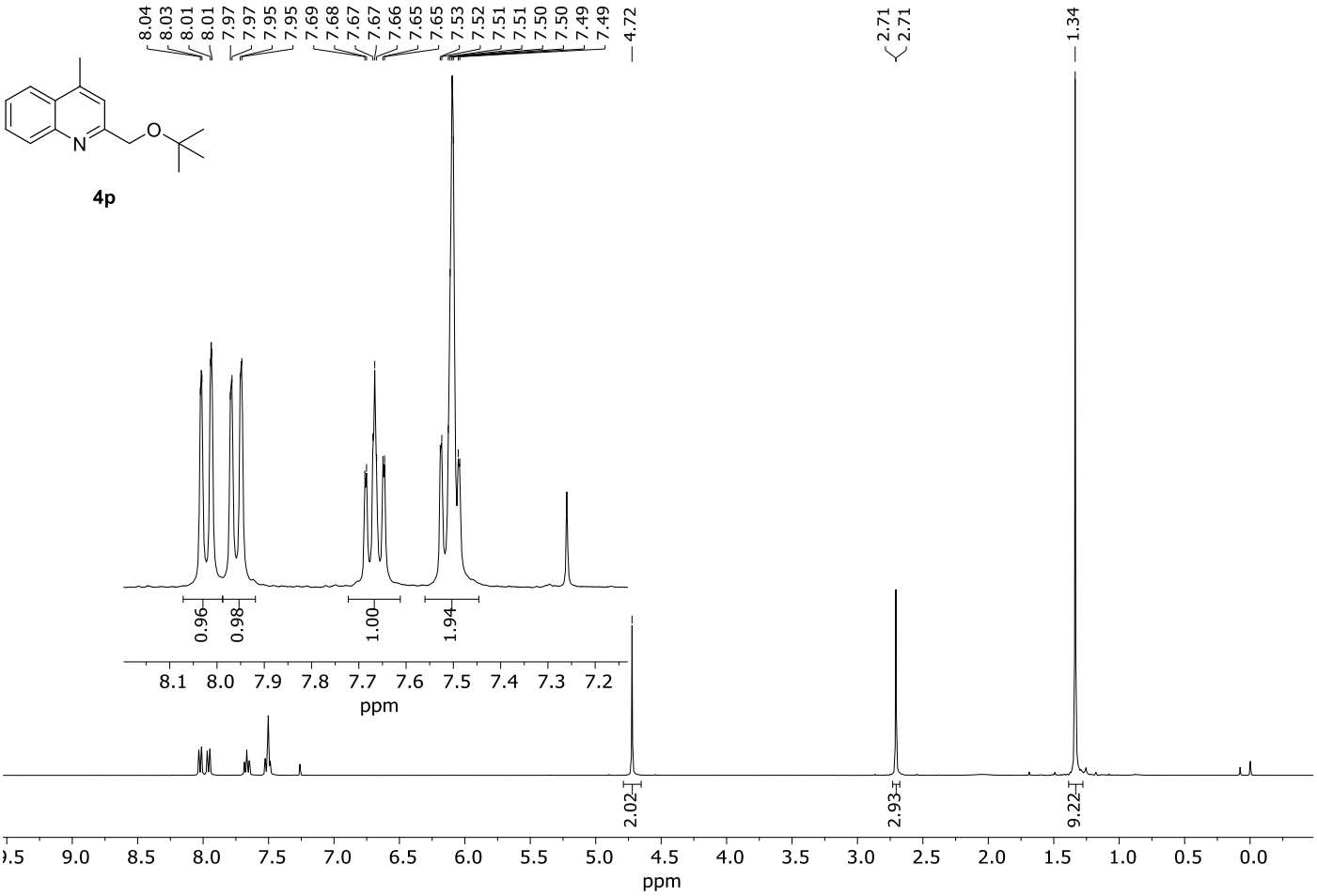


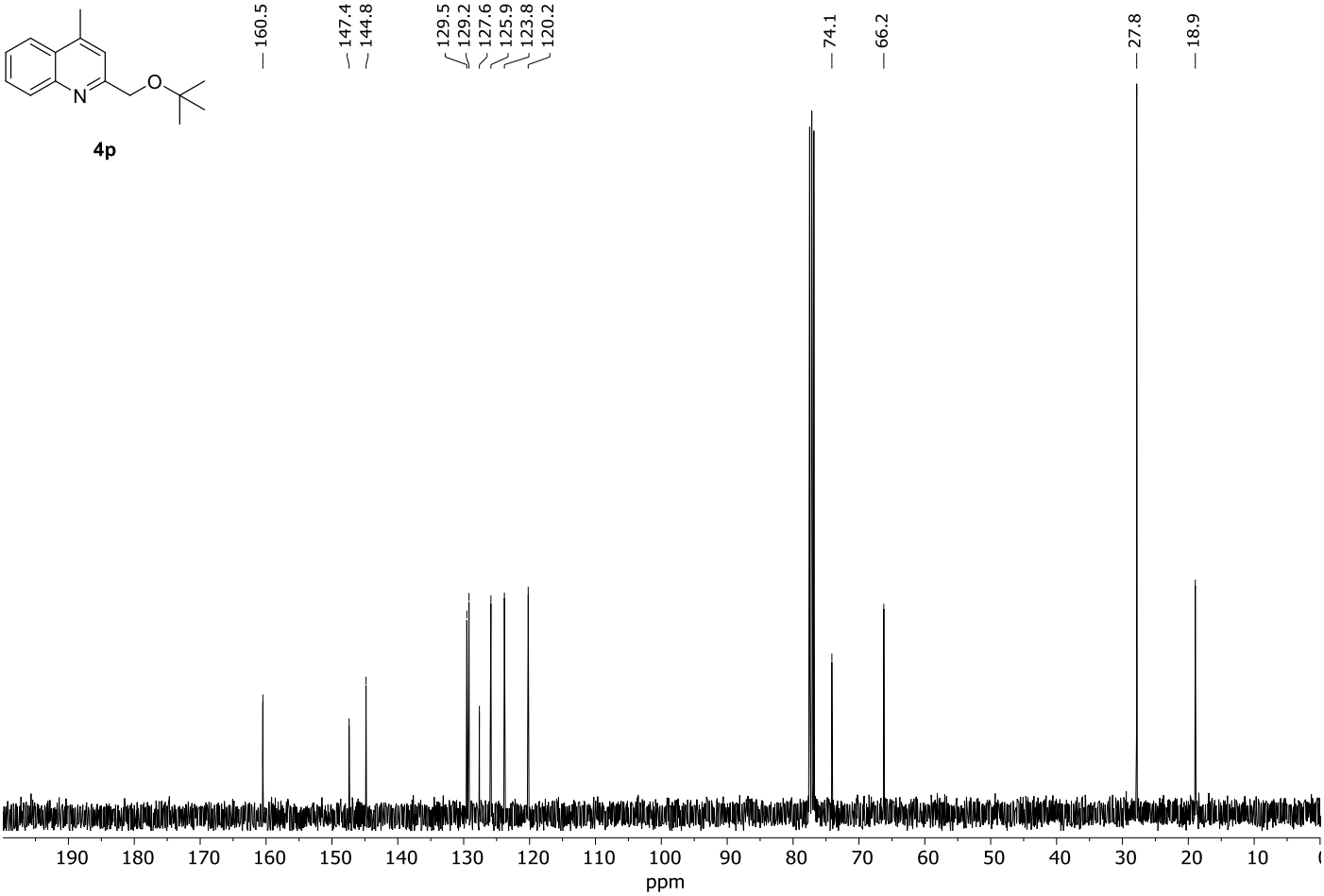
8.15 2-(1-ethoxyethyl)-4-methylquinoline (4o)



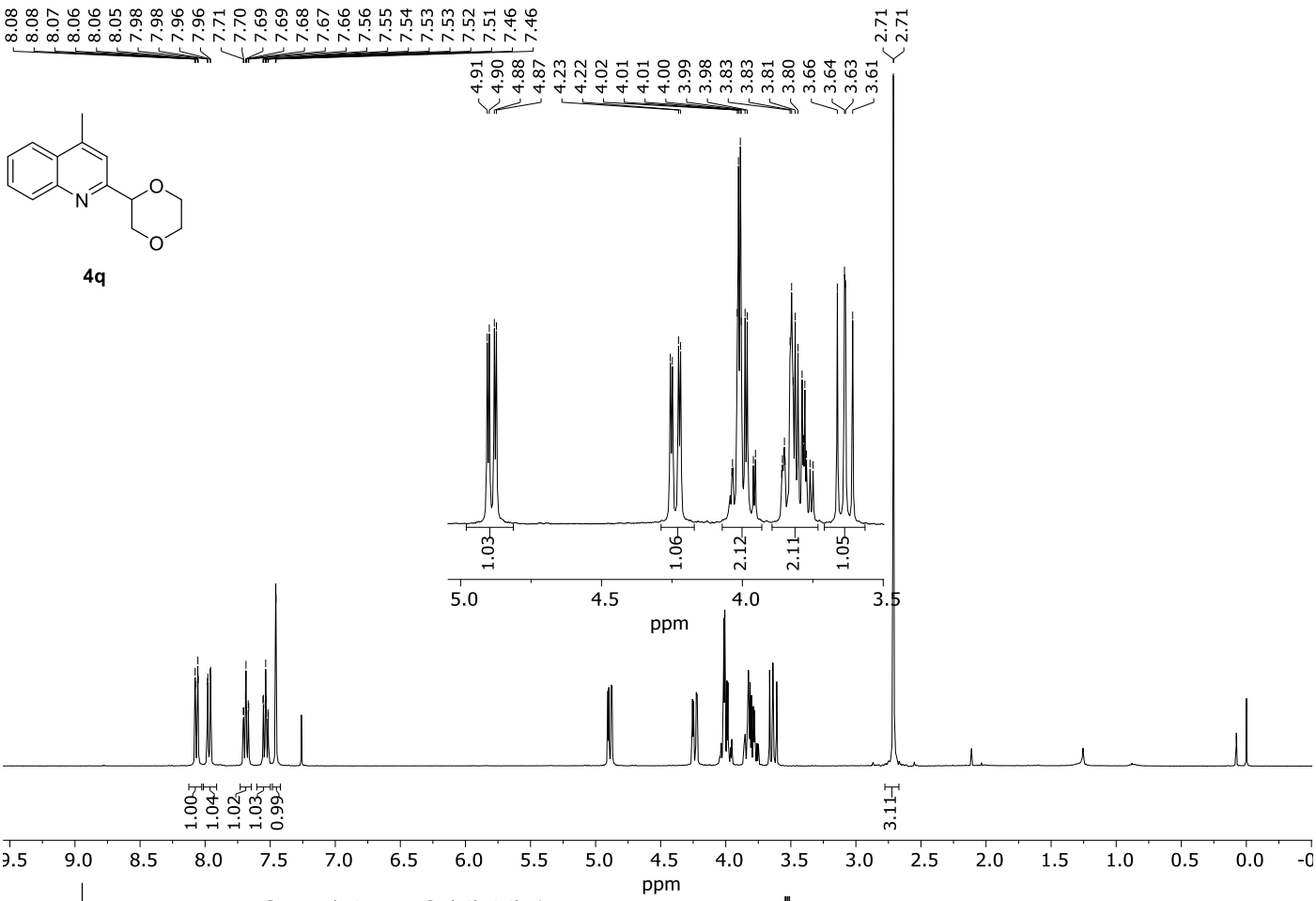


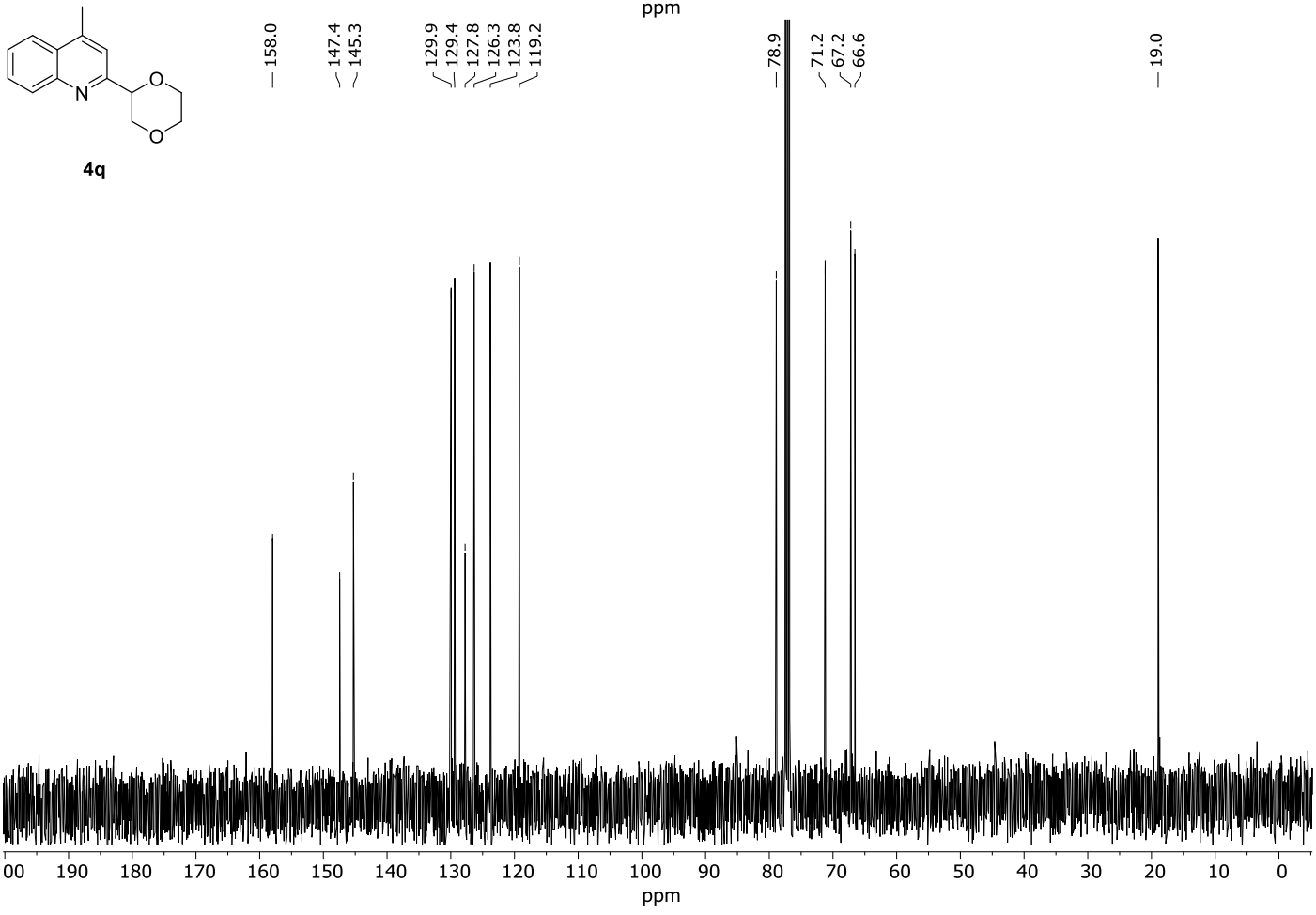
8.16 2-(tert-butoxymethyl)-4-methylquinoline (4p)





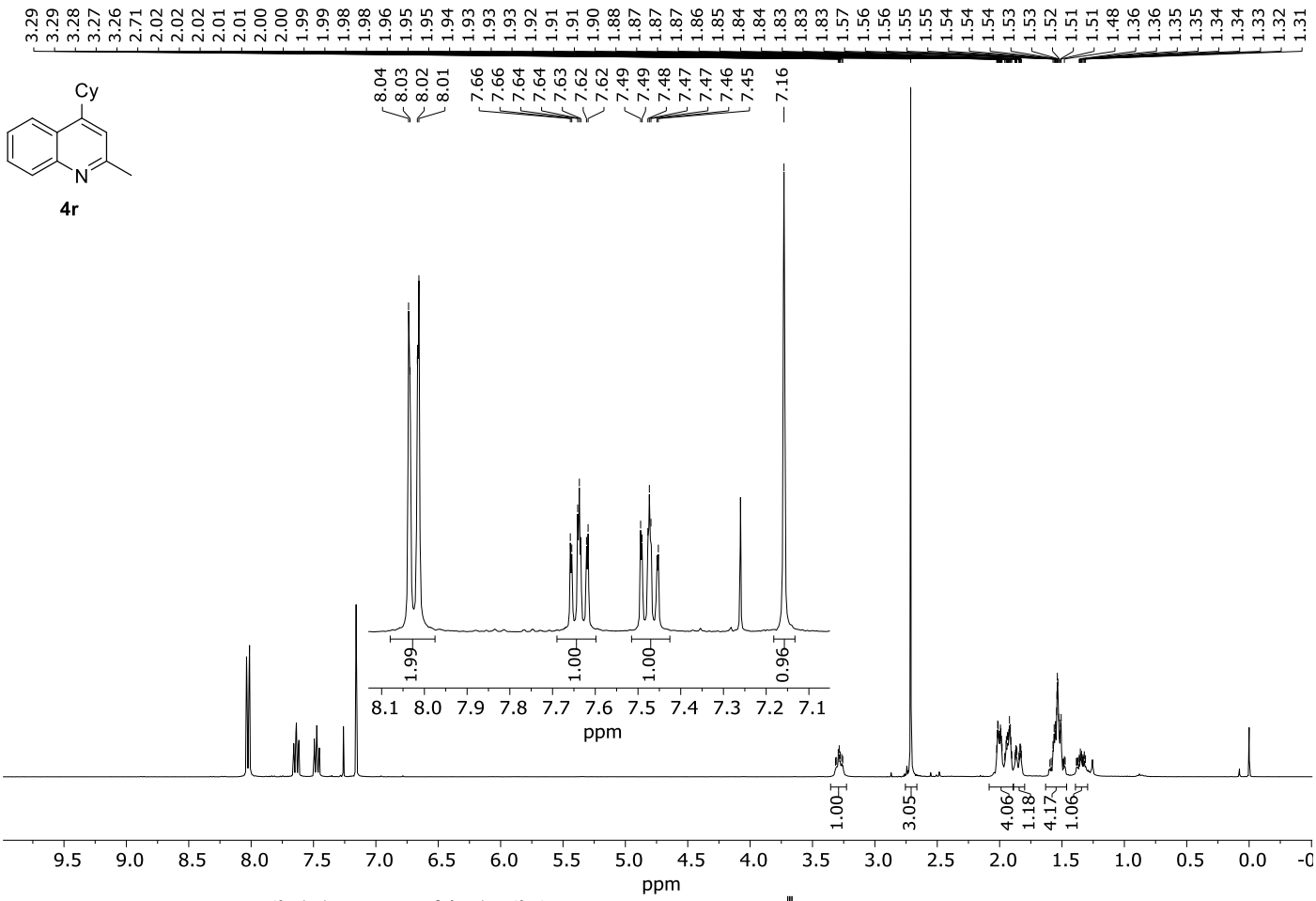
8.17 2-(1,4-dioxan-2-yl)-4-methylquinoline (4q)

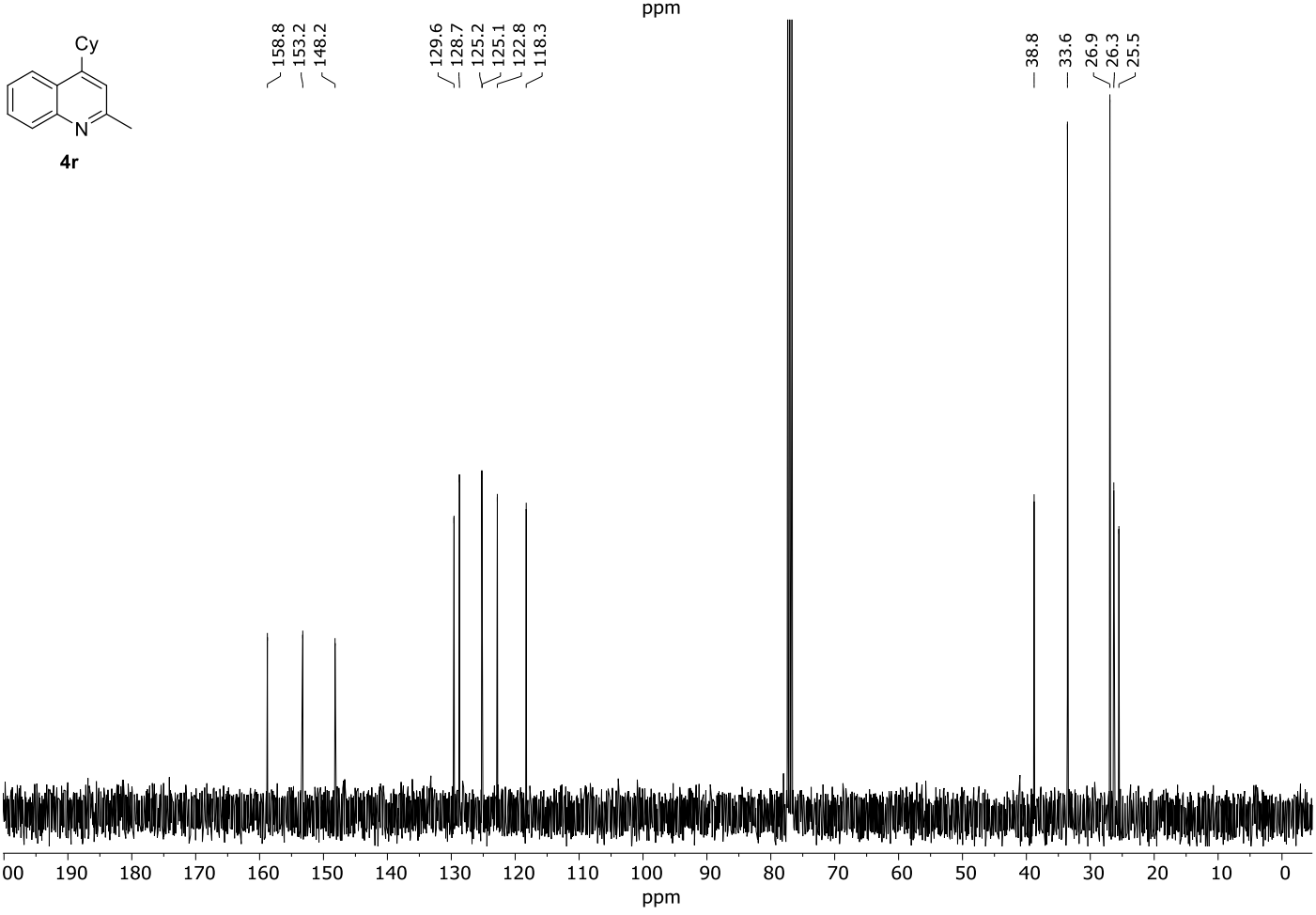




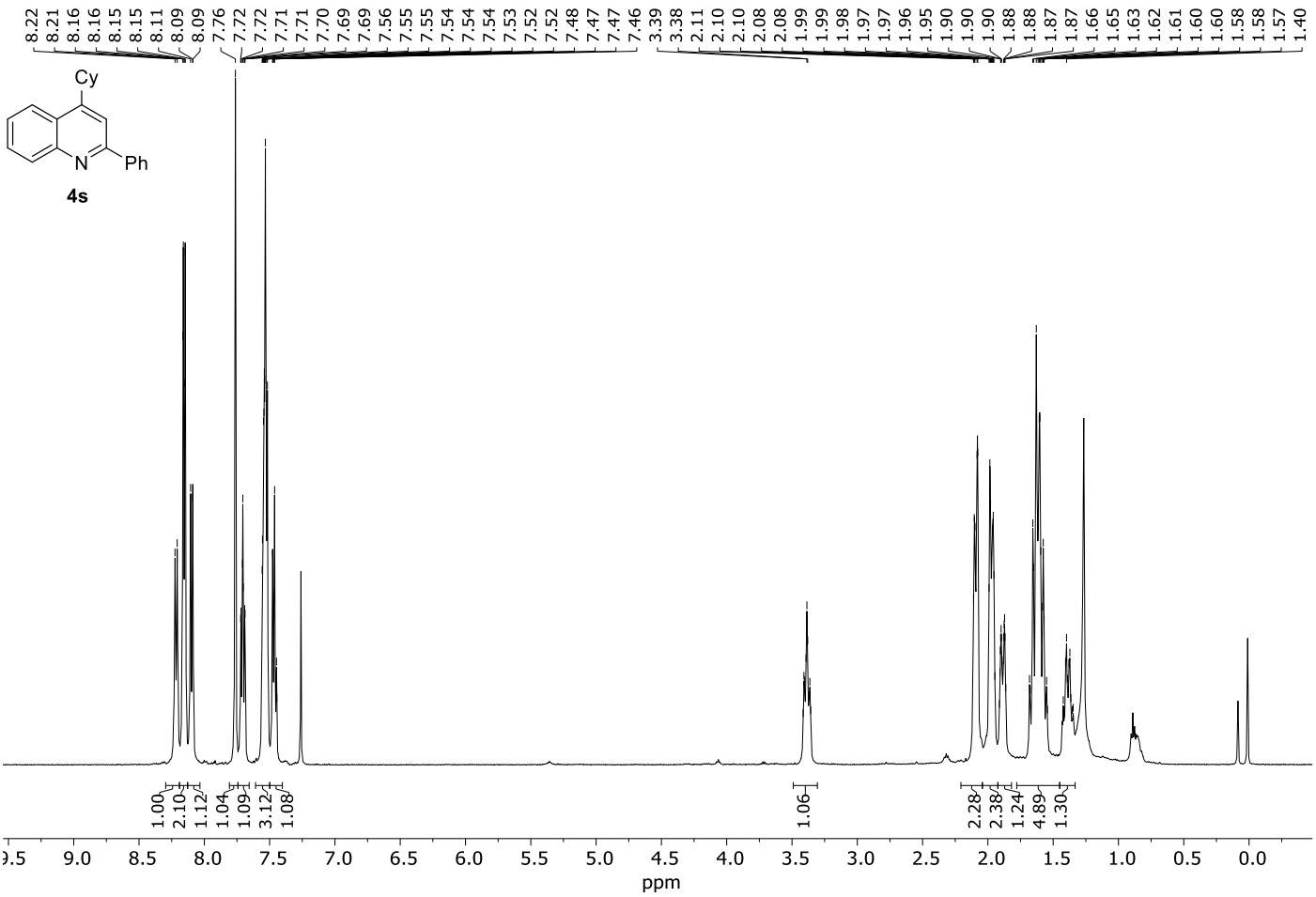
4q

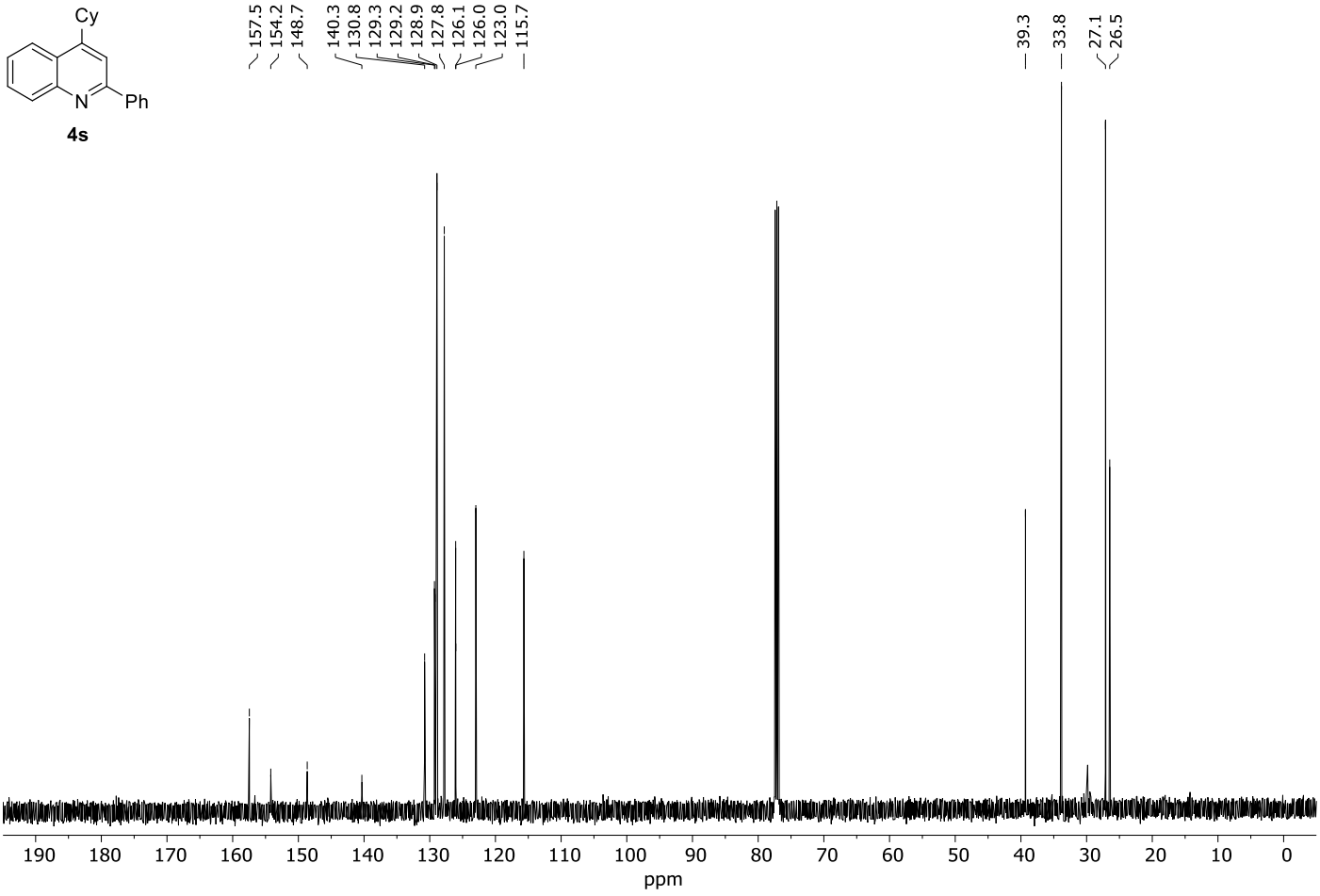
8.18 4-cyclohexyl-2-methylquinoline (4r)



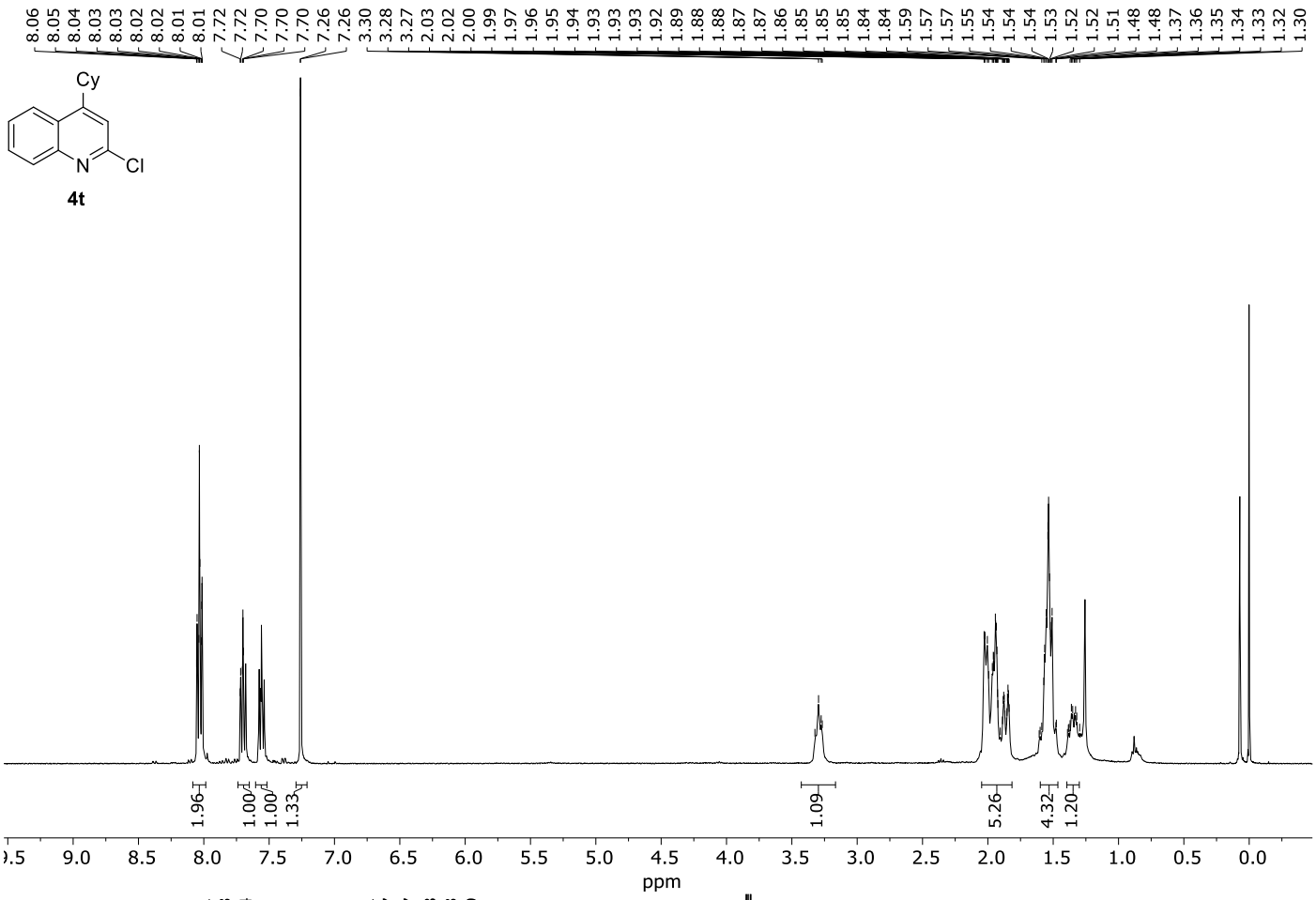


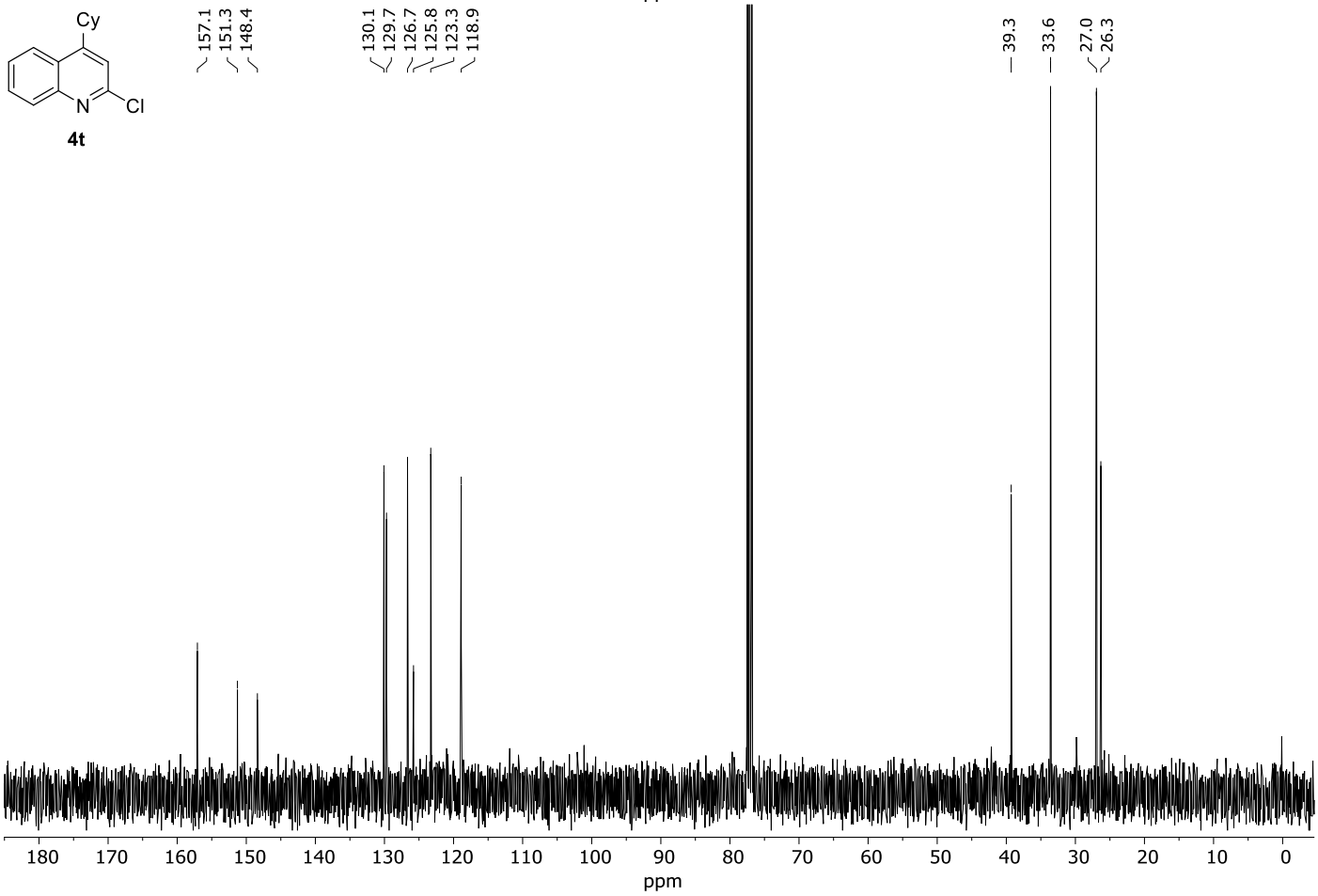
8.19 4-cyclohexyl-2-phenylquinoline (4s)



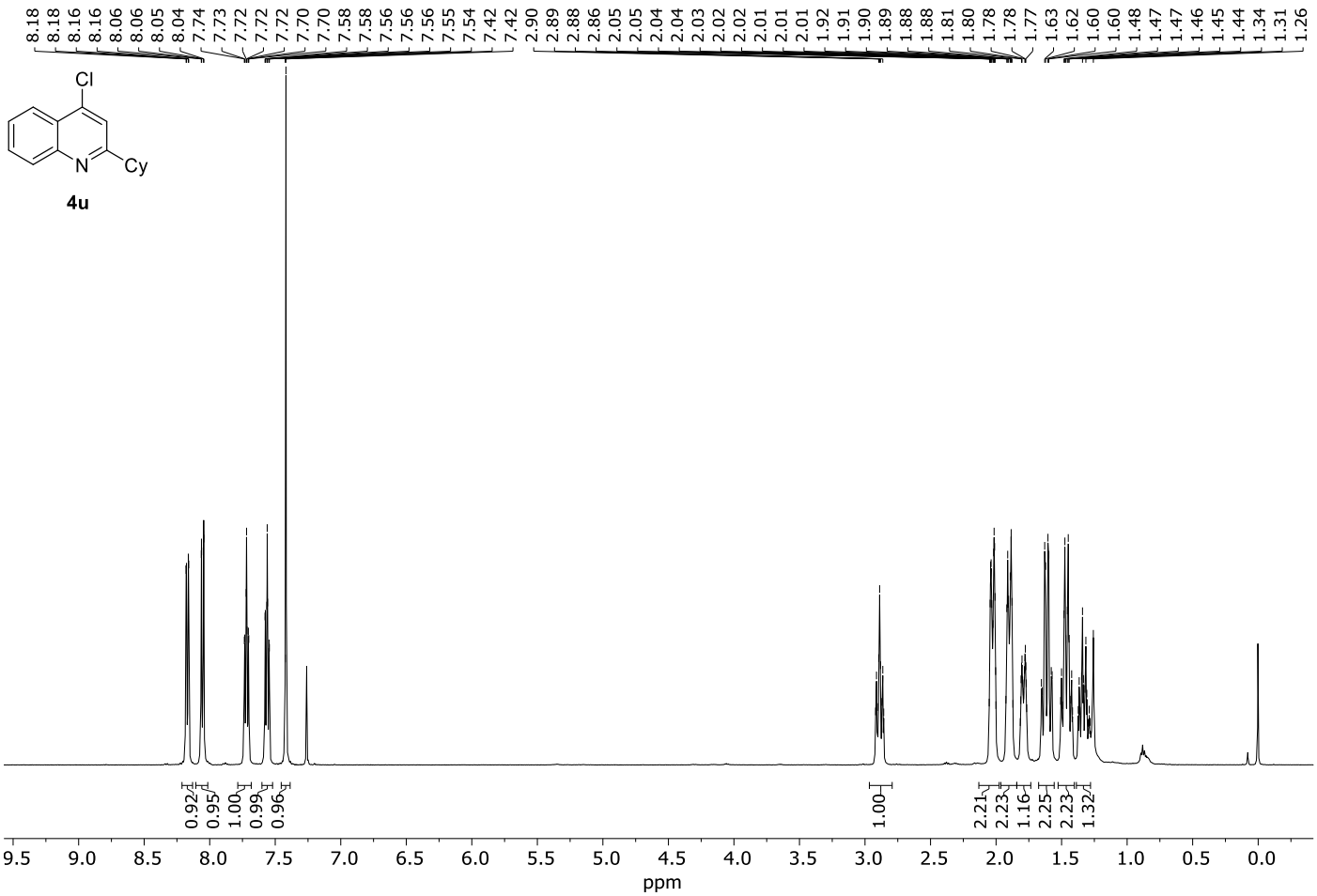


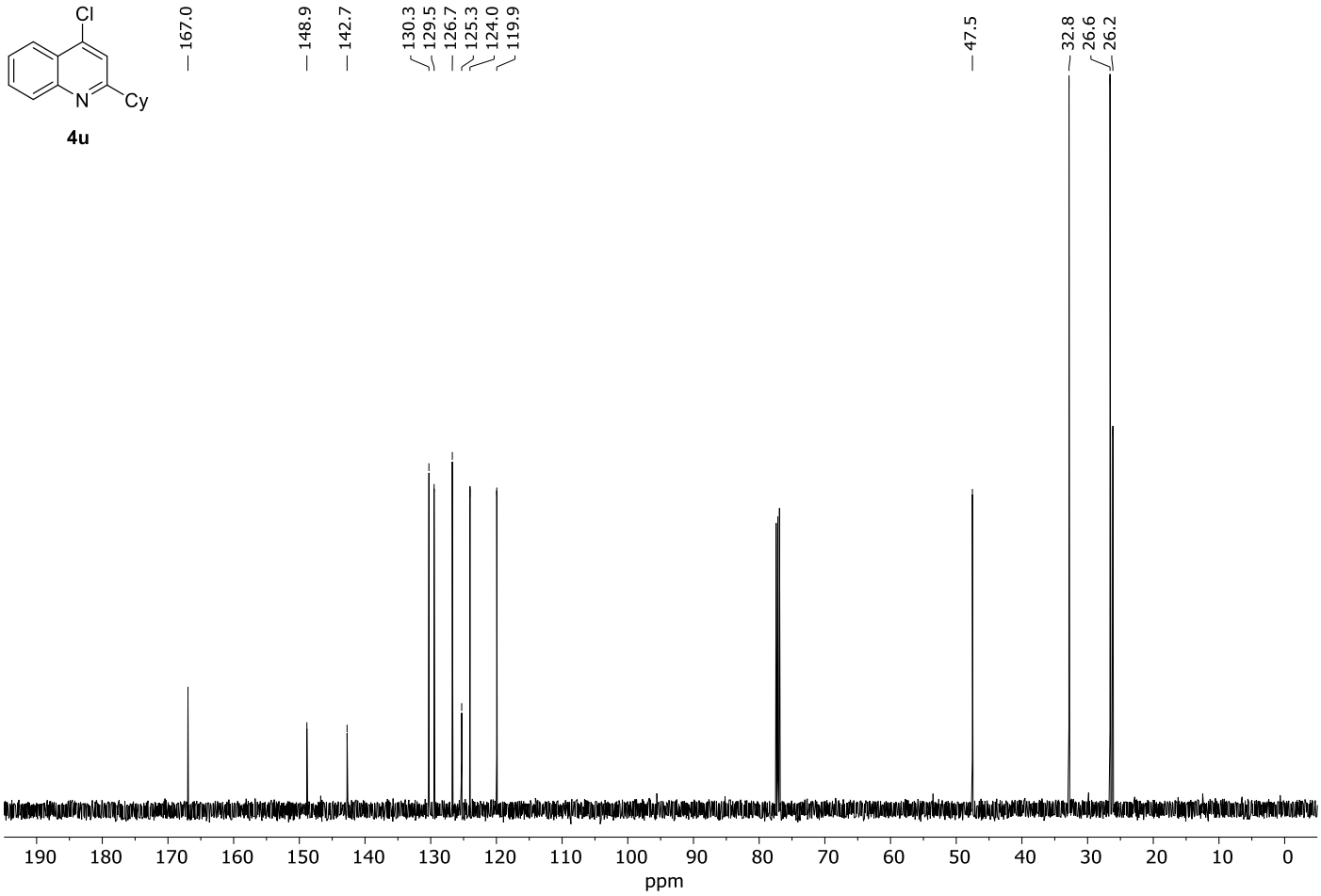
8.20 2-chloro-4-cyclohexylquinoline (4t)



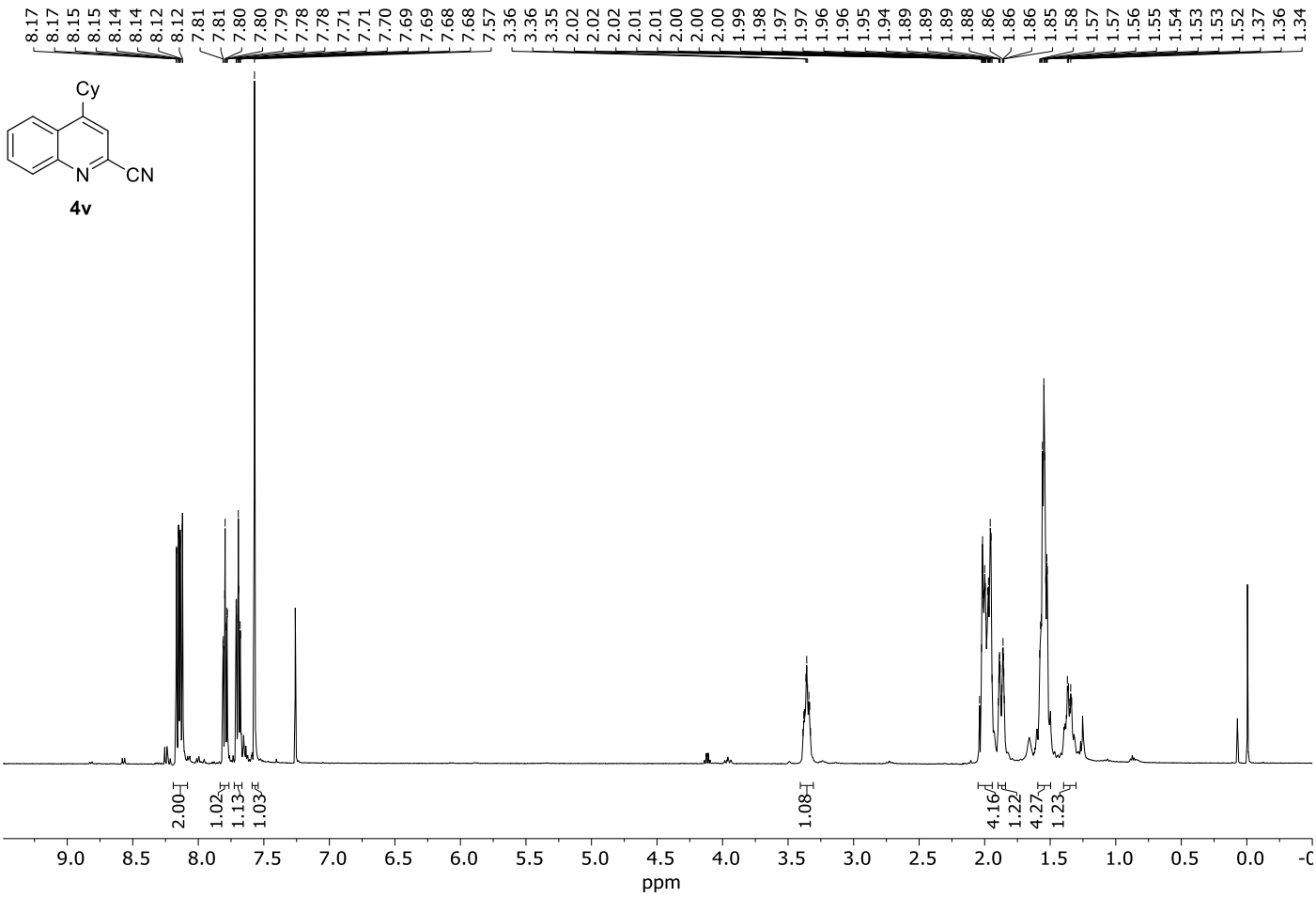


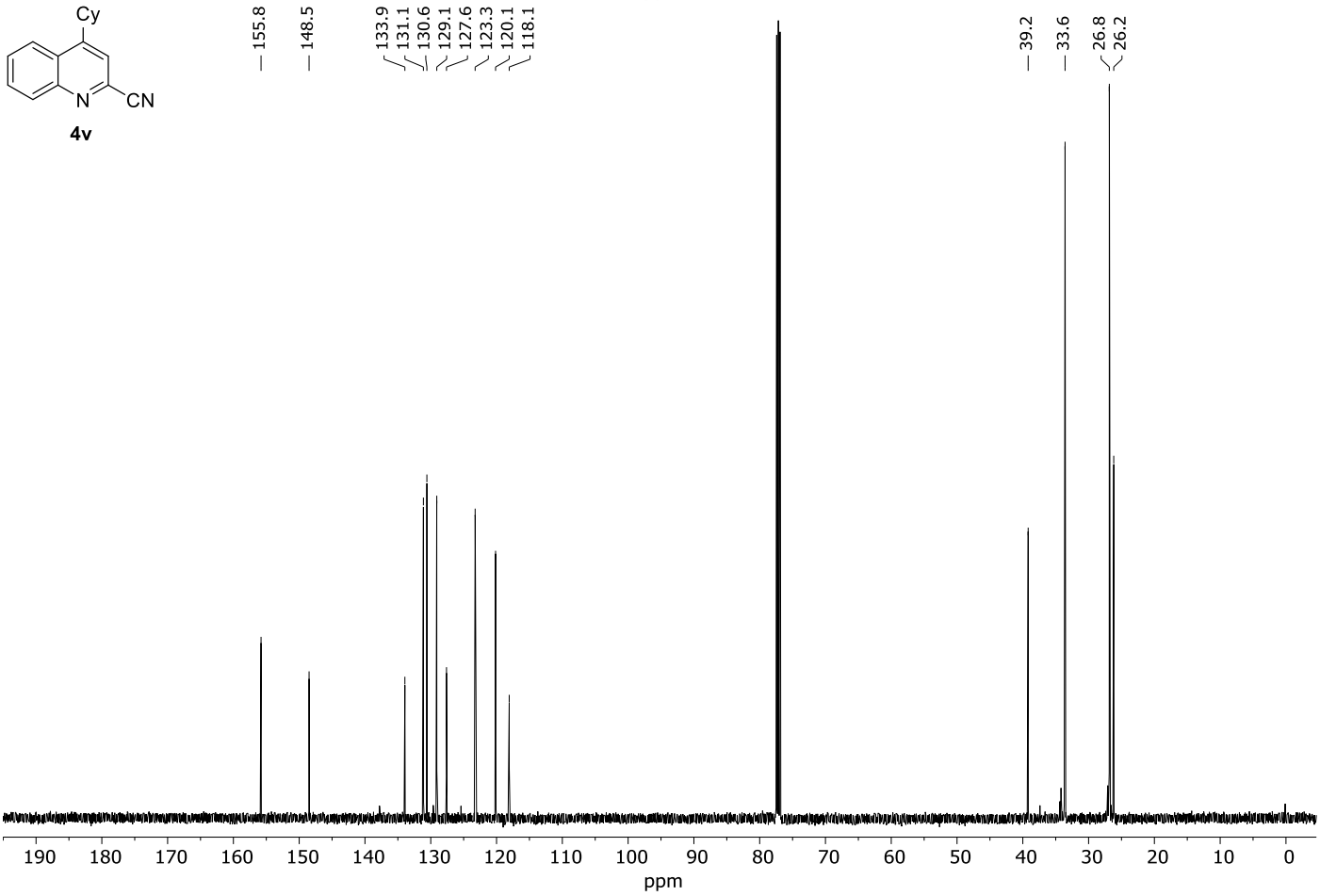
8.21 4-chloro-2-cyclohexylquinoline (4u)



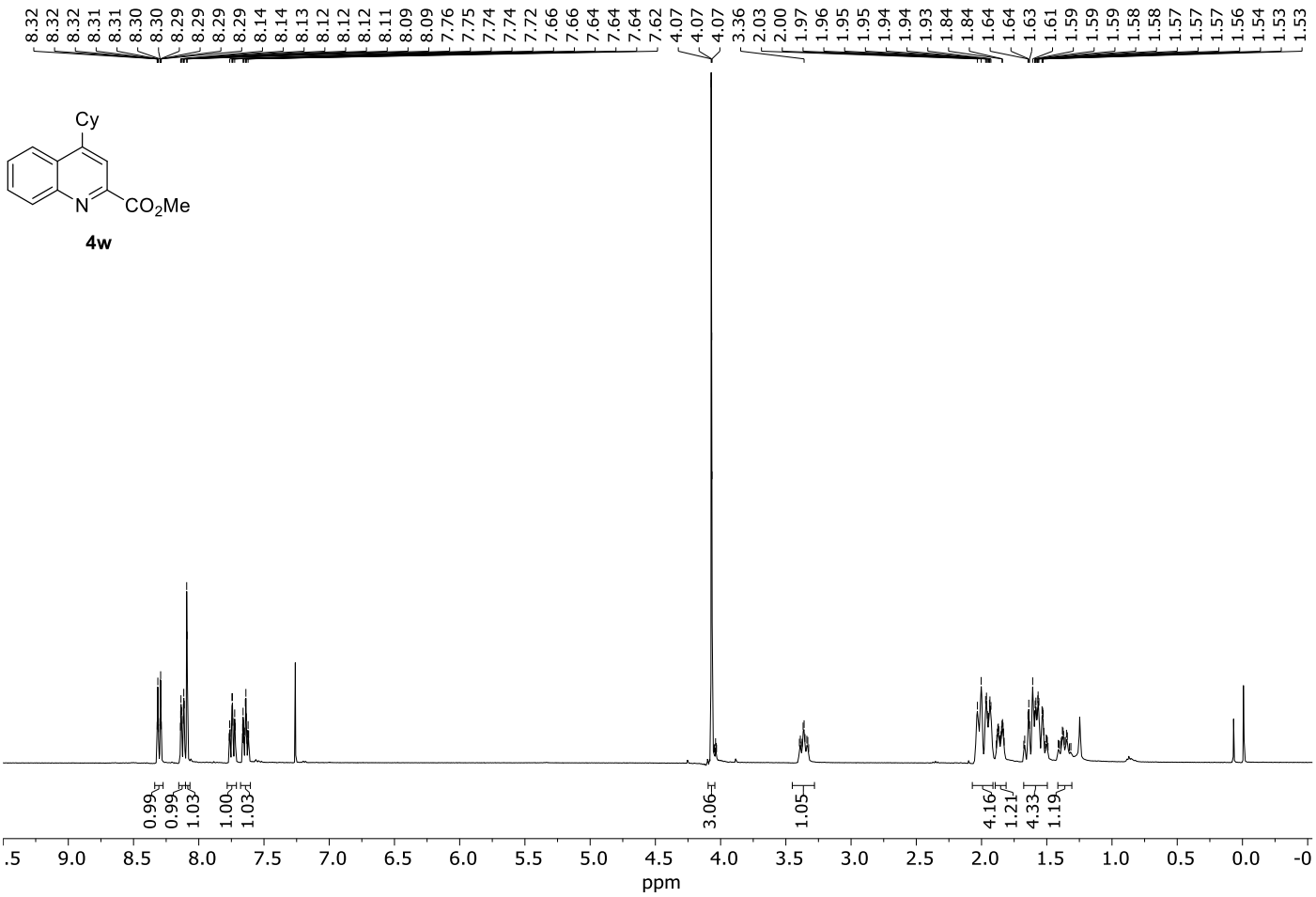


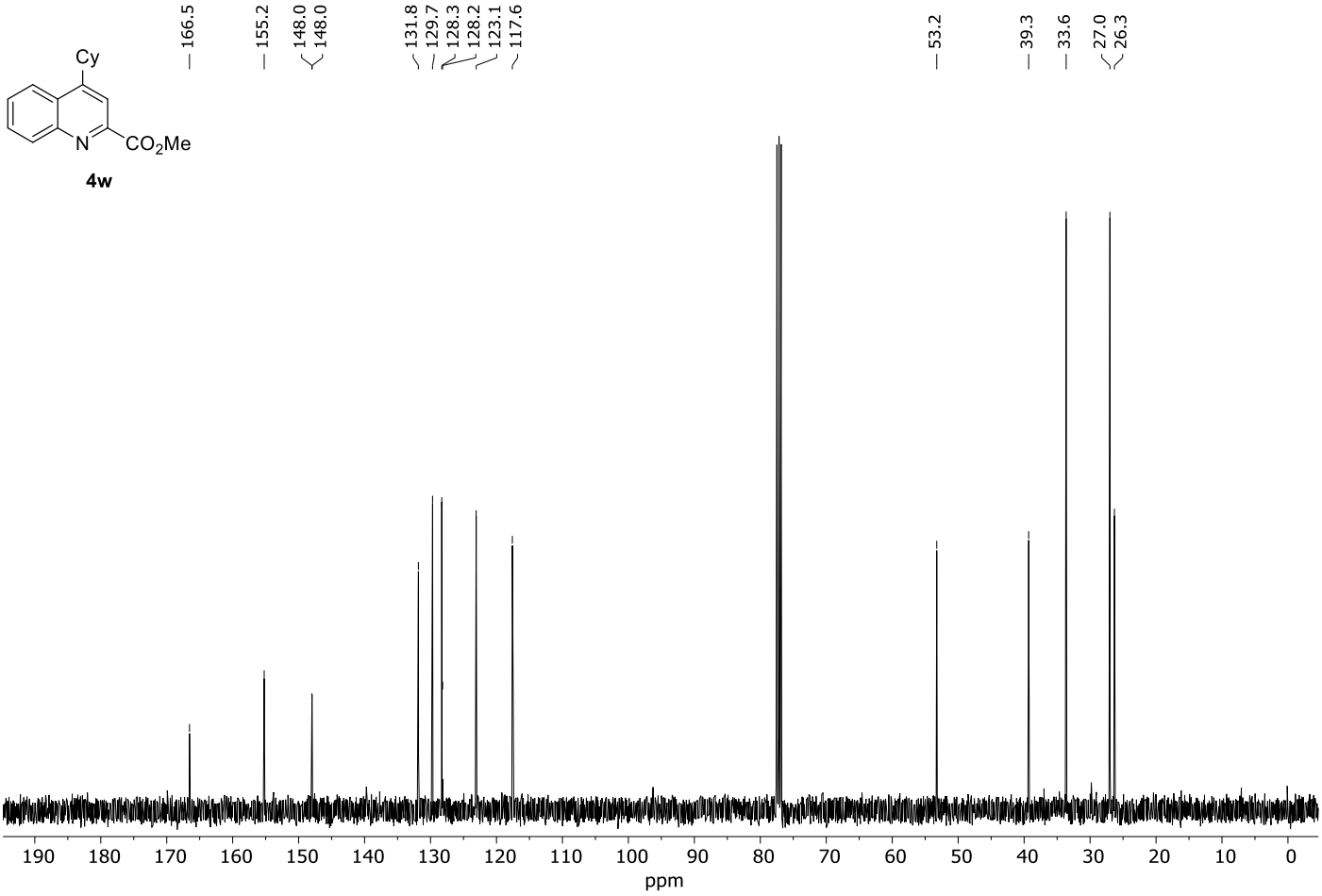
8.22 4-cyclohexylquinoline-2-carbonitrile (4v)



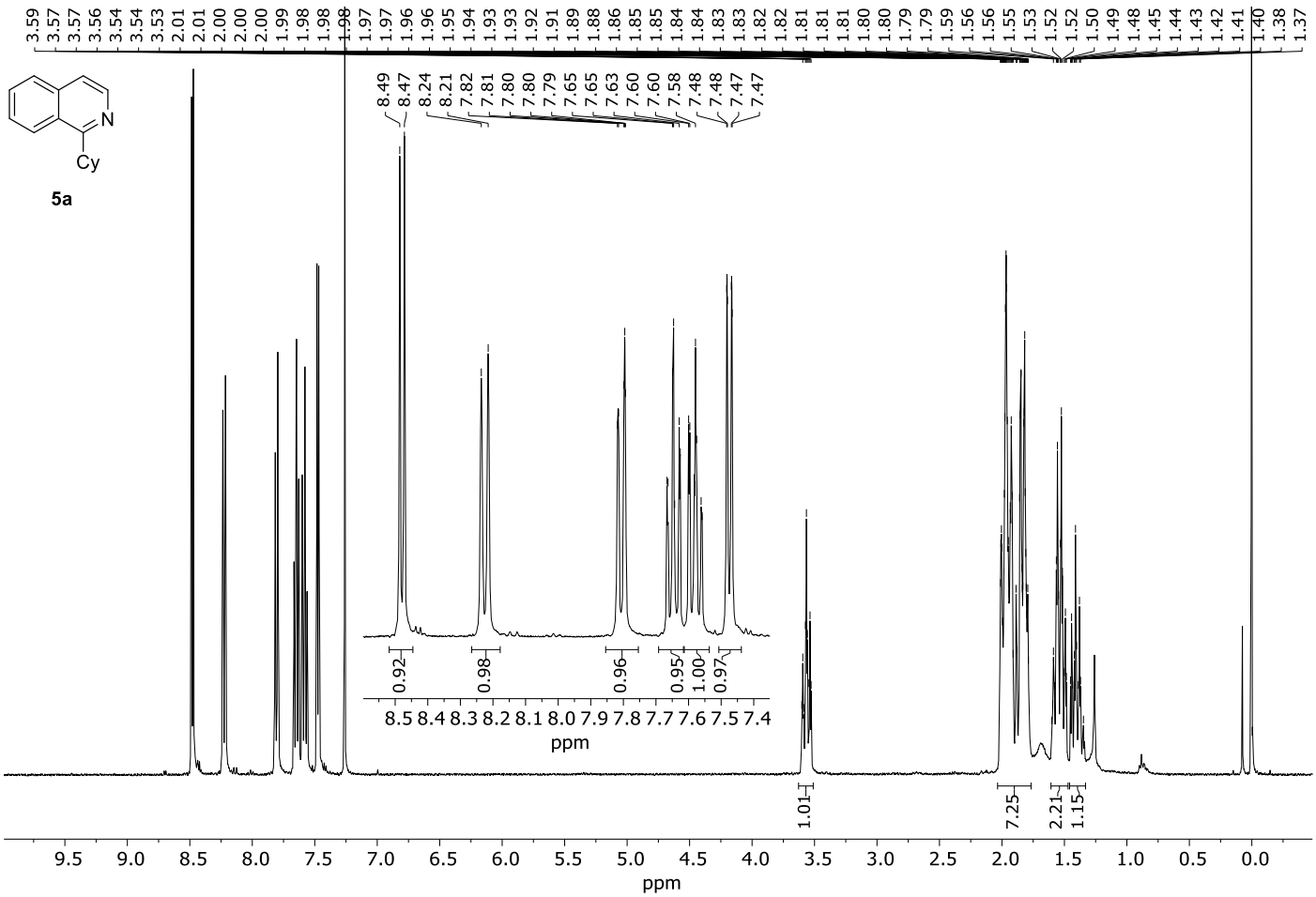


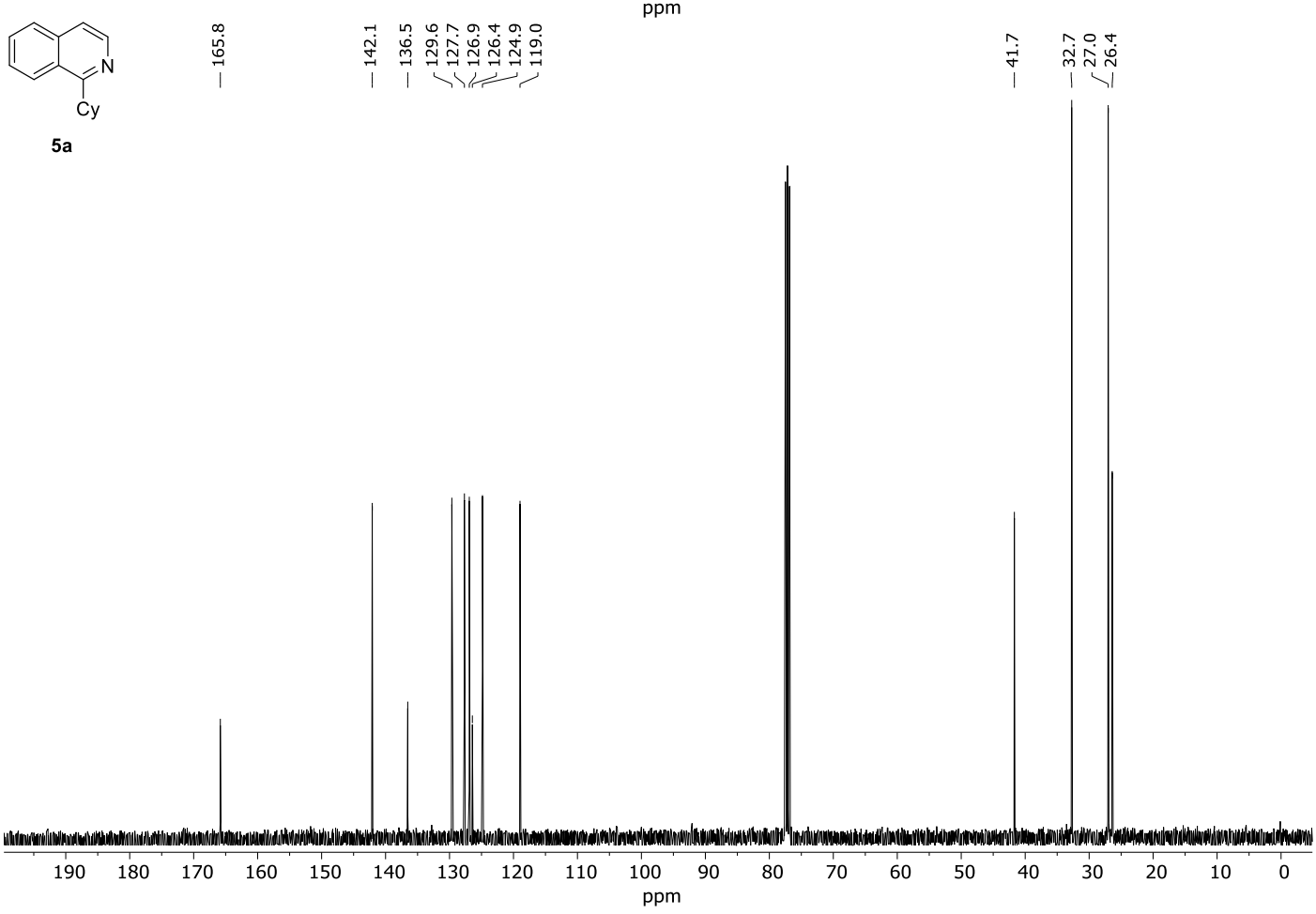
8.23 methyl 4-cyclohexylquinoline-2-carboxylate (4w)



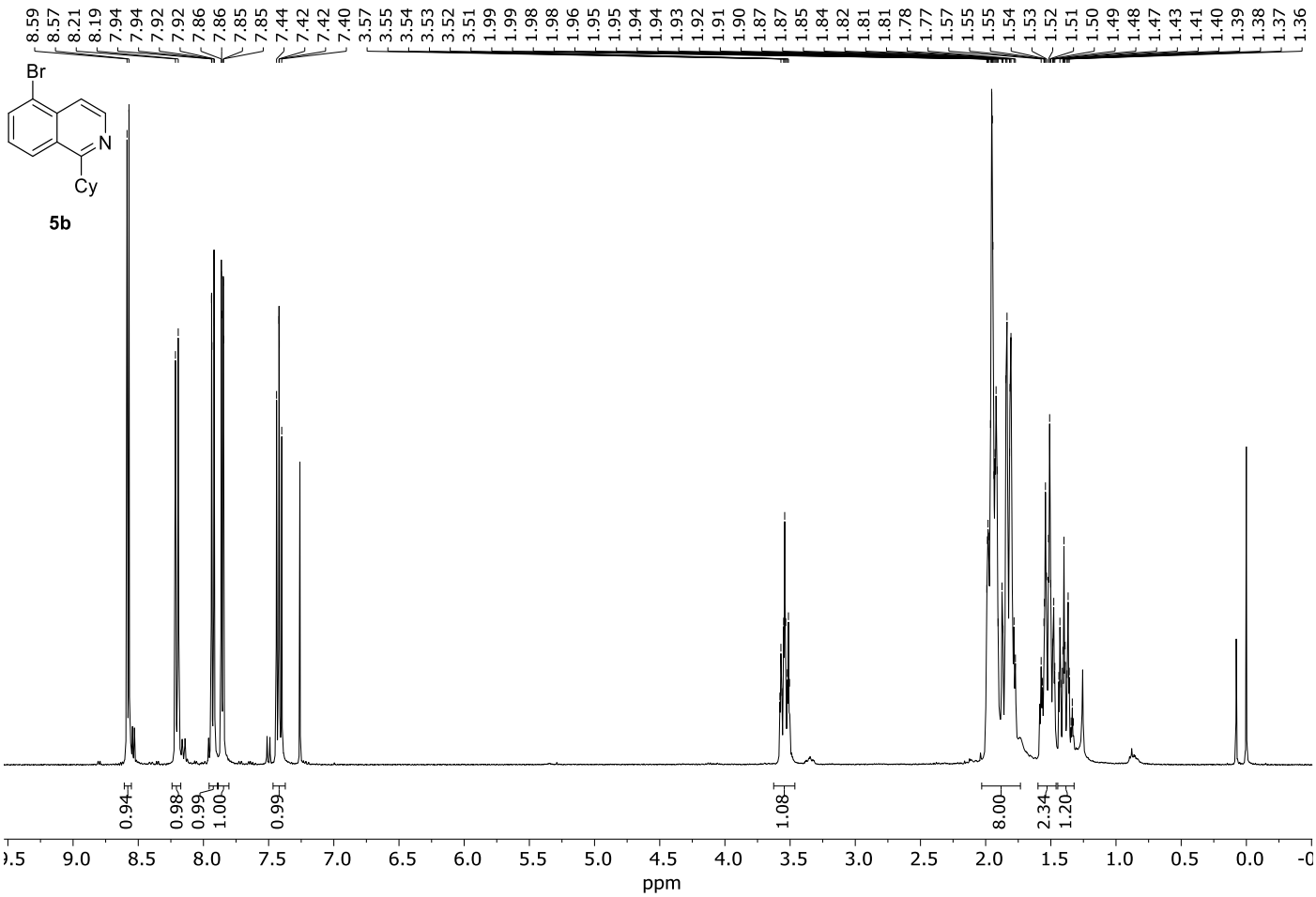


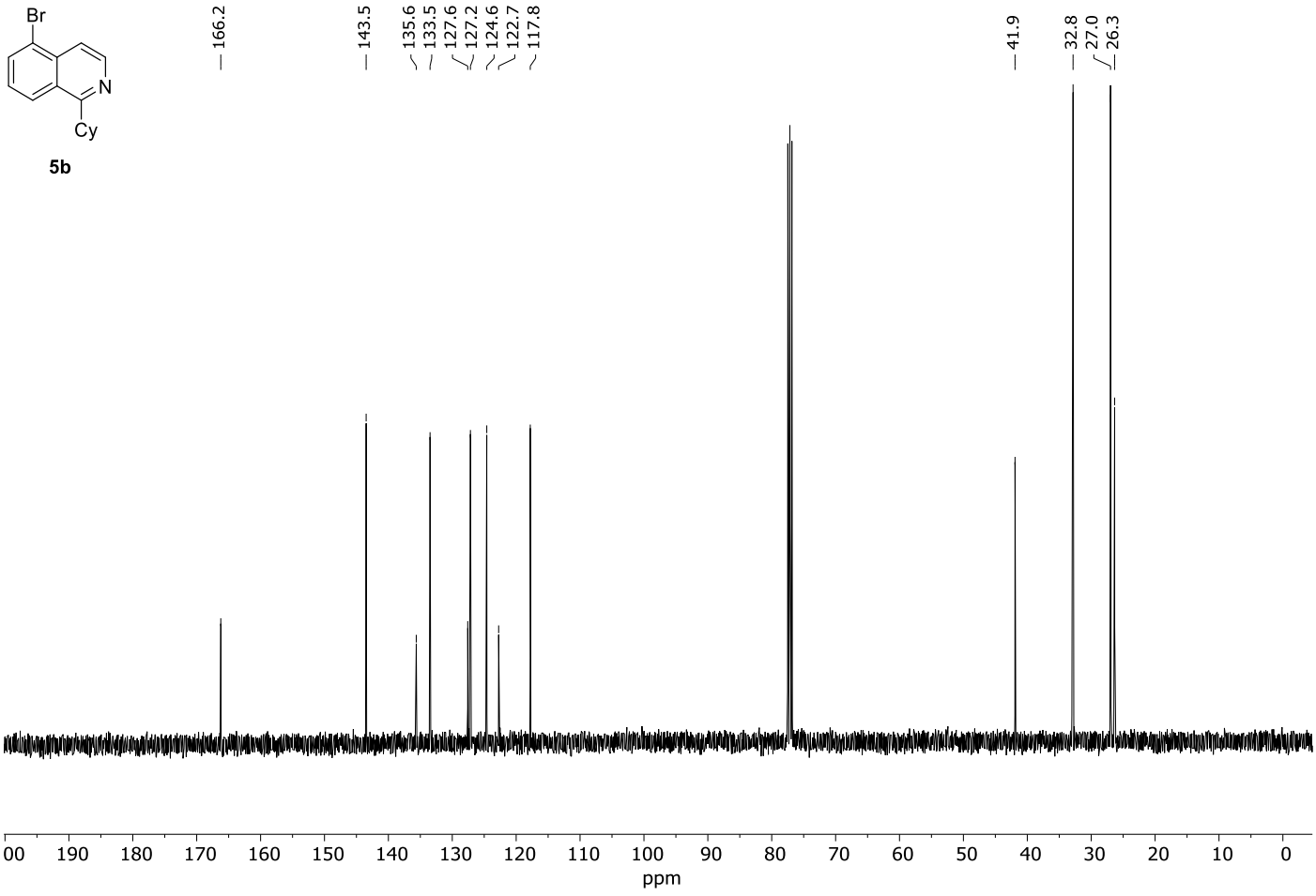
8.24 1-cyclohexylisoquinoline (5a)



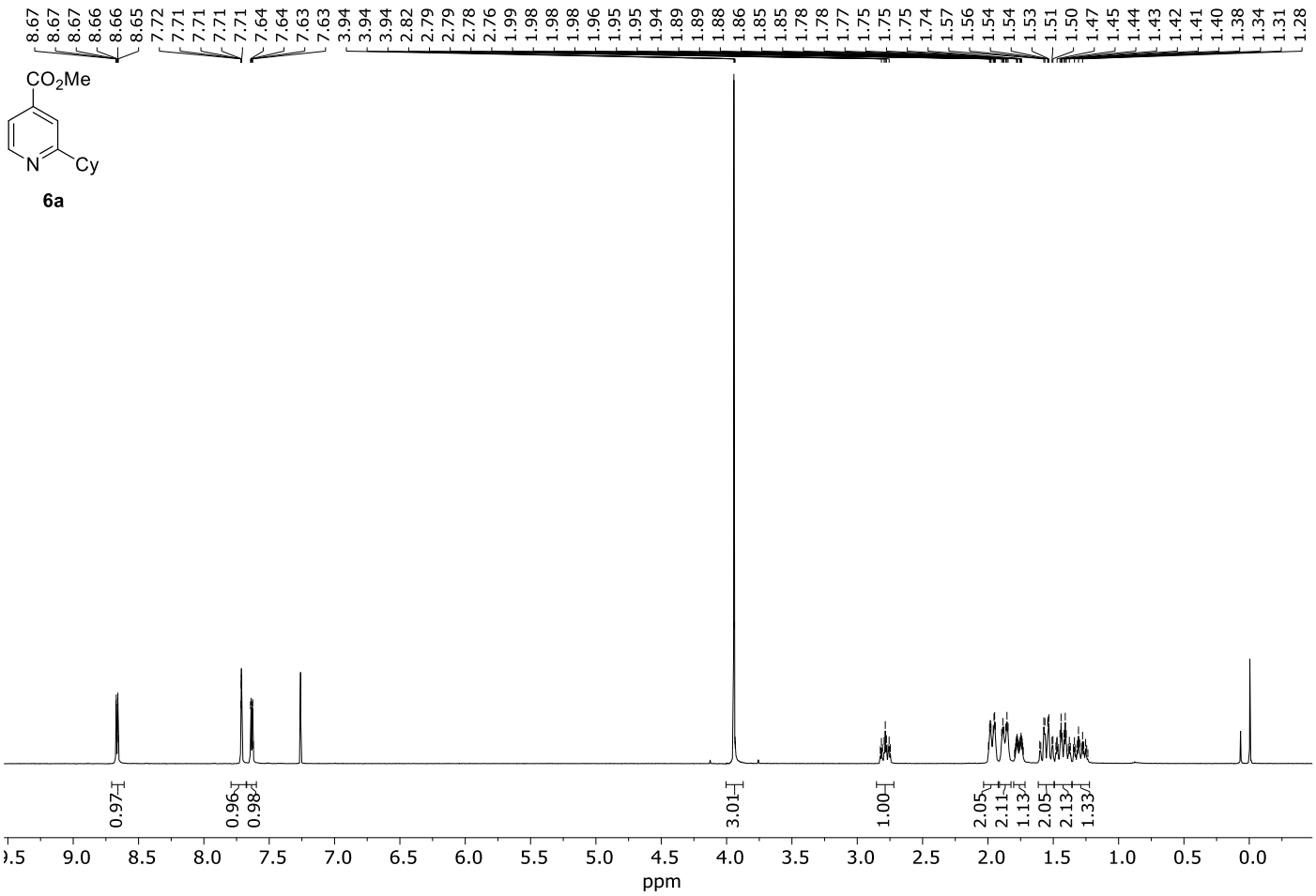


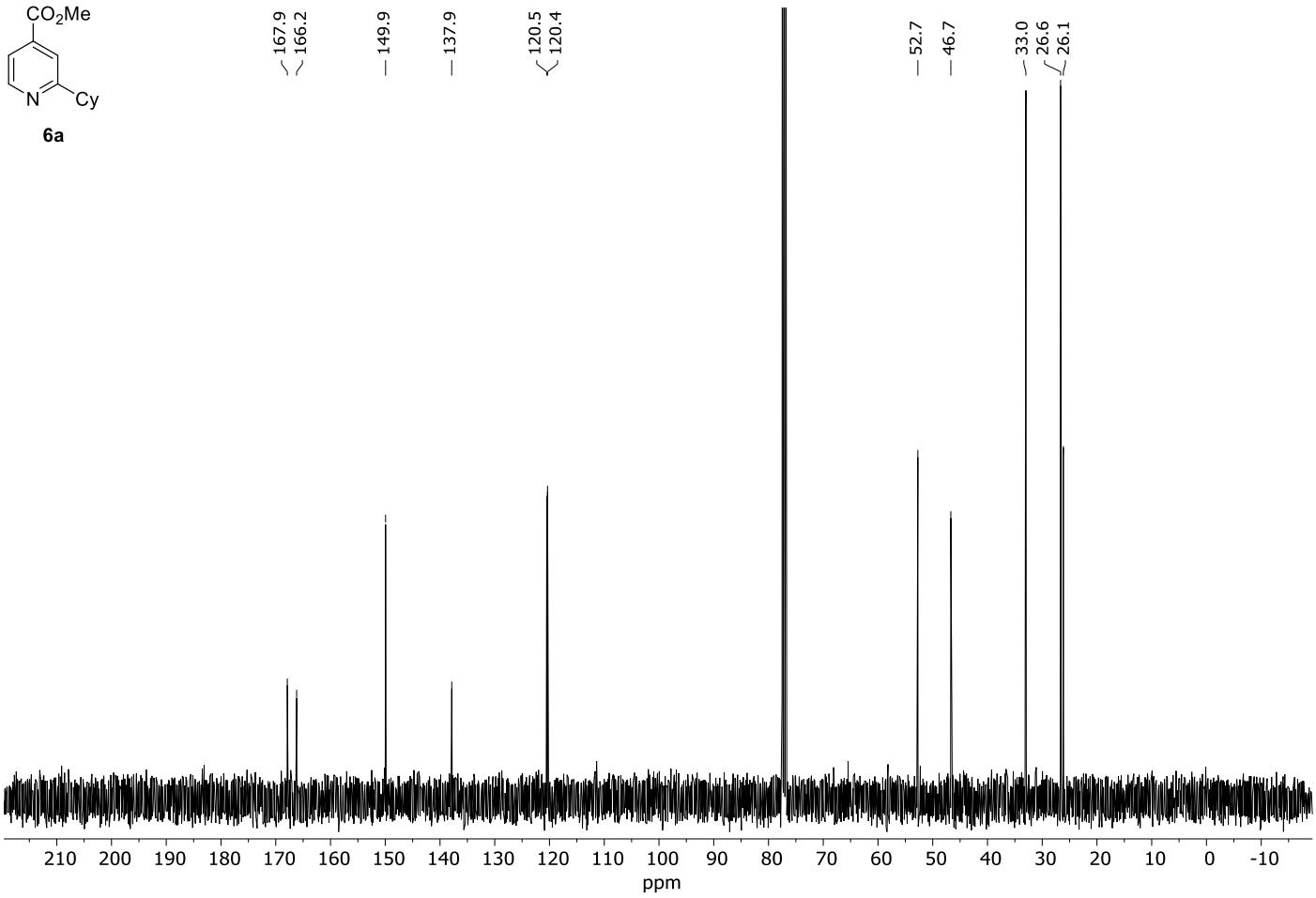
8.25 5-bromo-1-cyclohexylisoquinoline (5b)



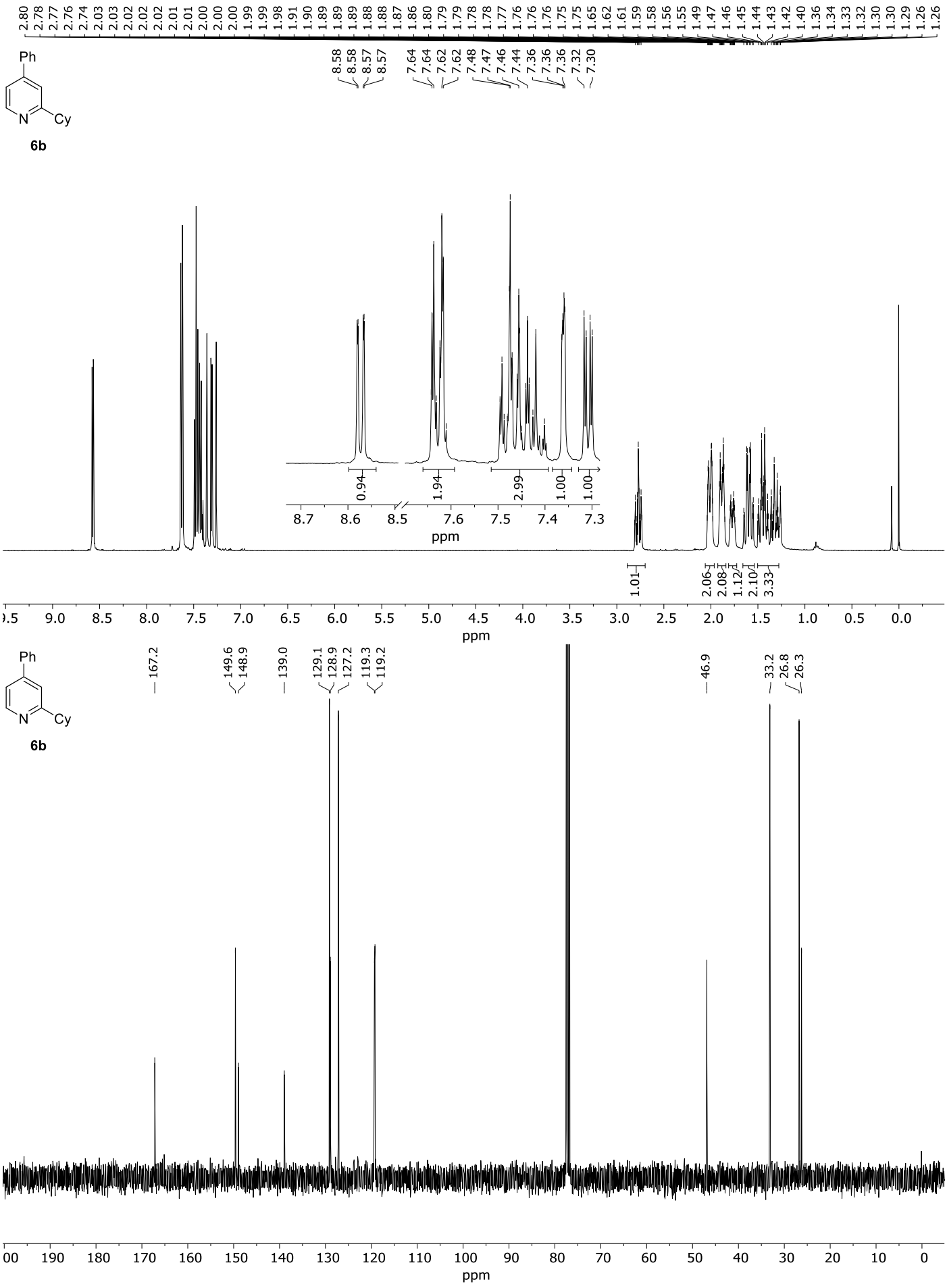


8.26 methyl 2-cyclohexylisonicotinate (6a)

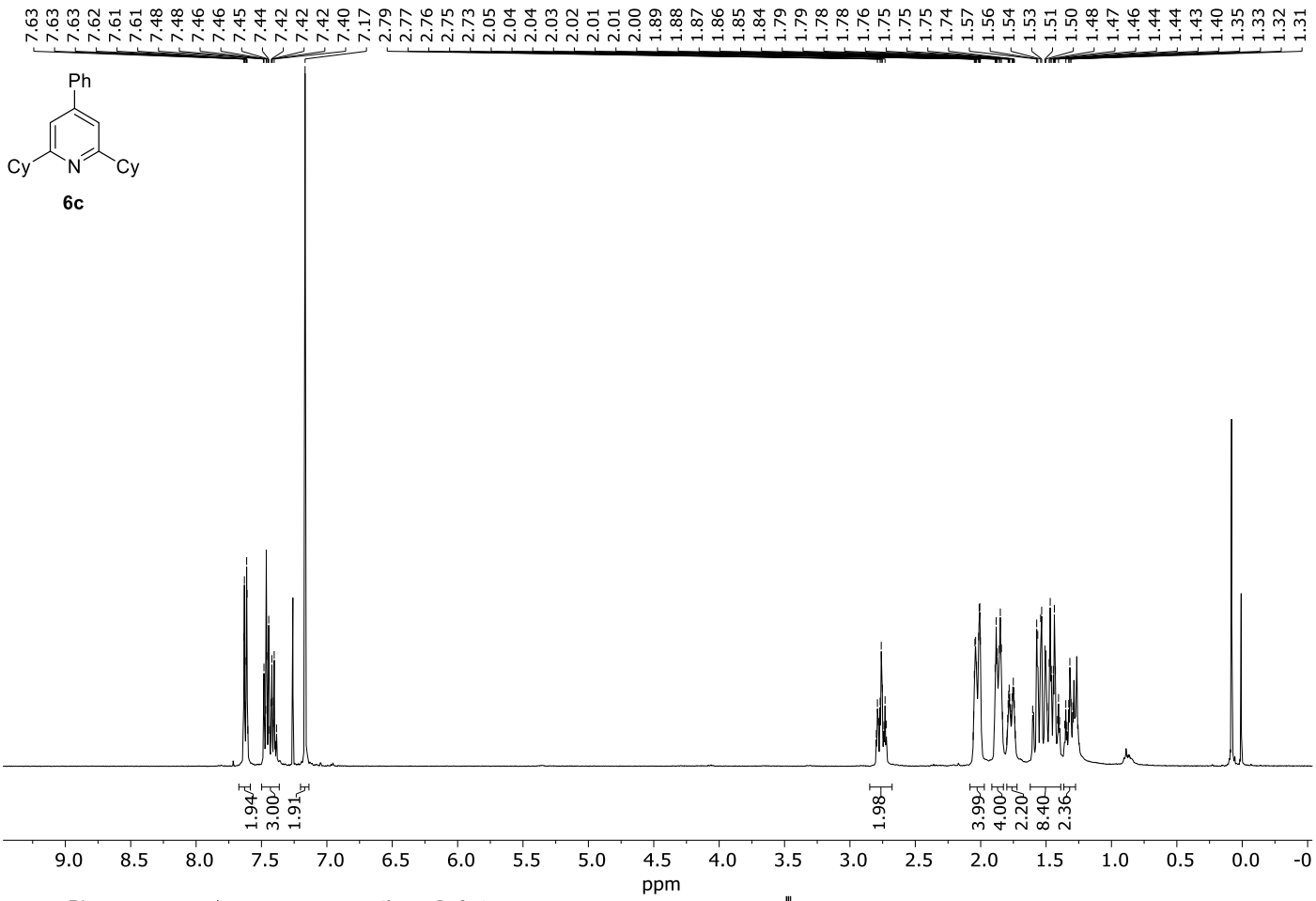


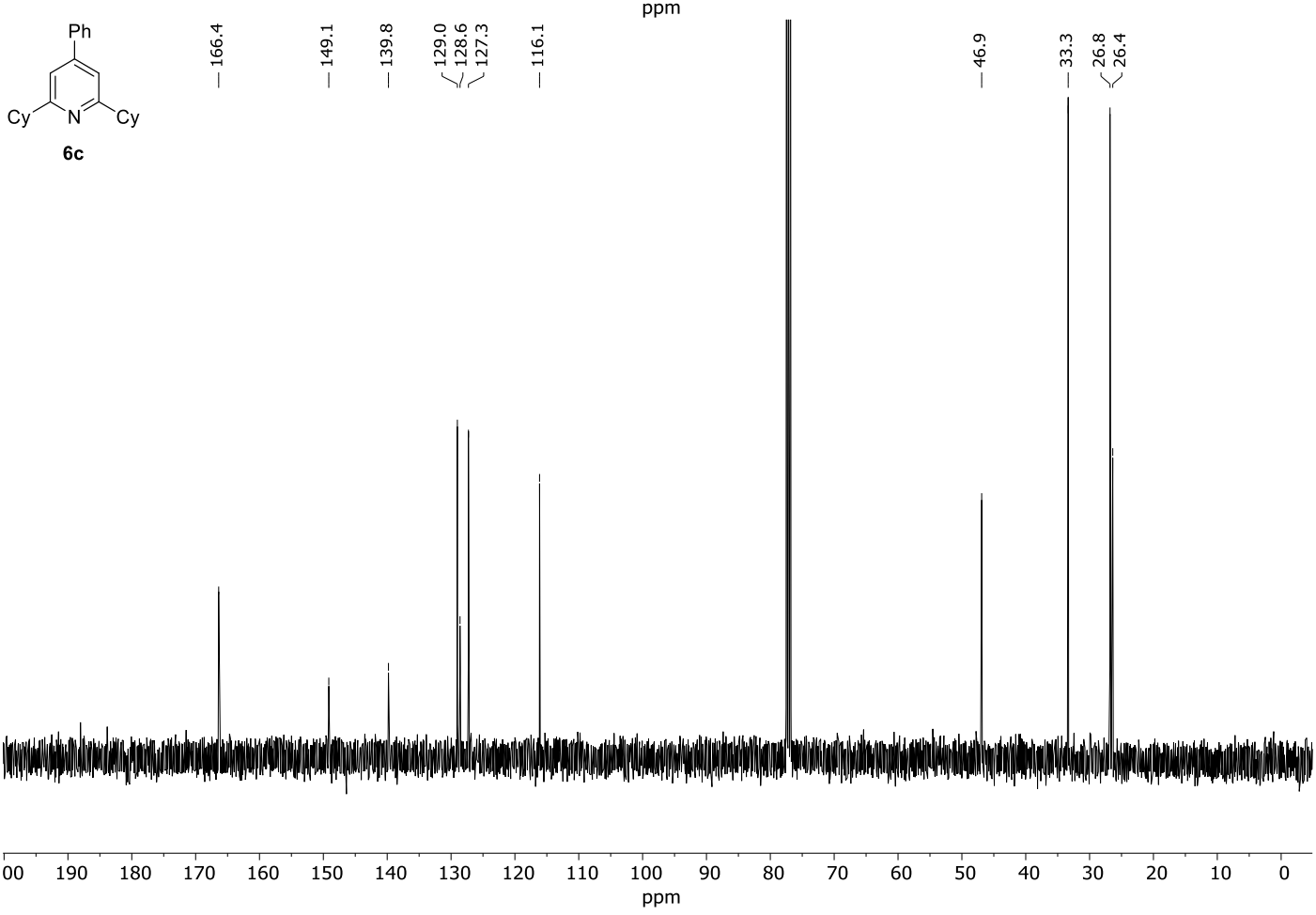


8.27 2-cyclohexyl-4-phenylpyridine (6b)

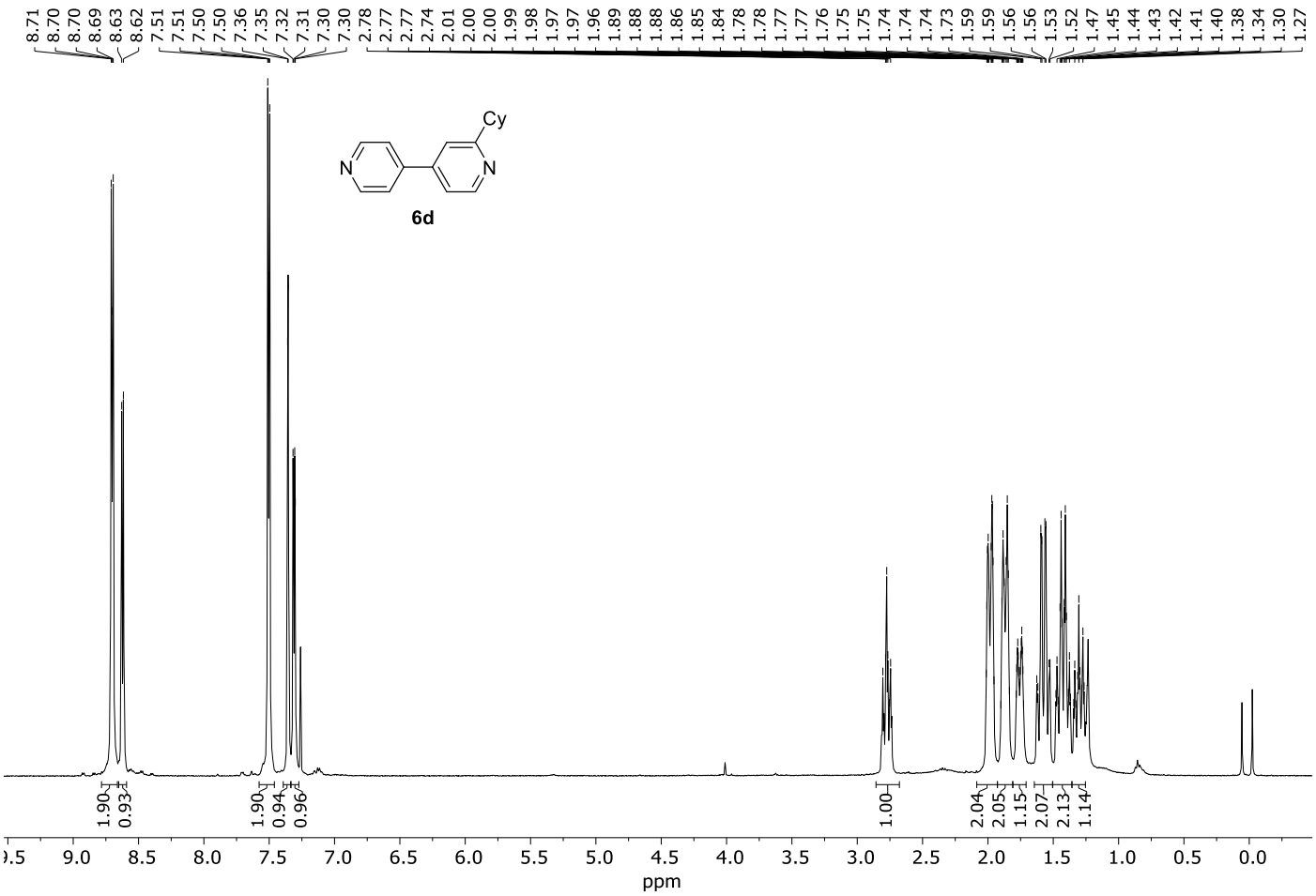


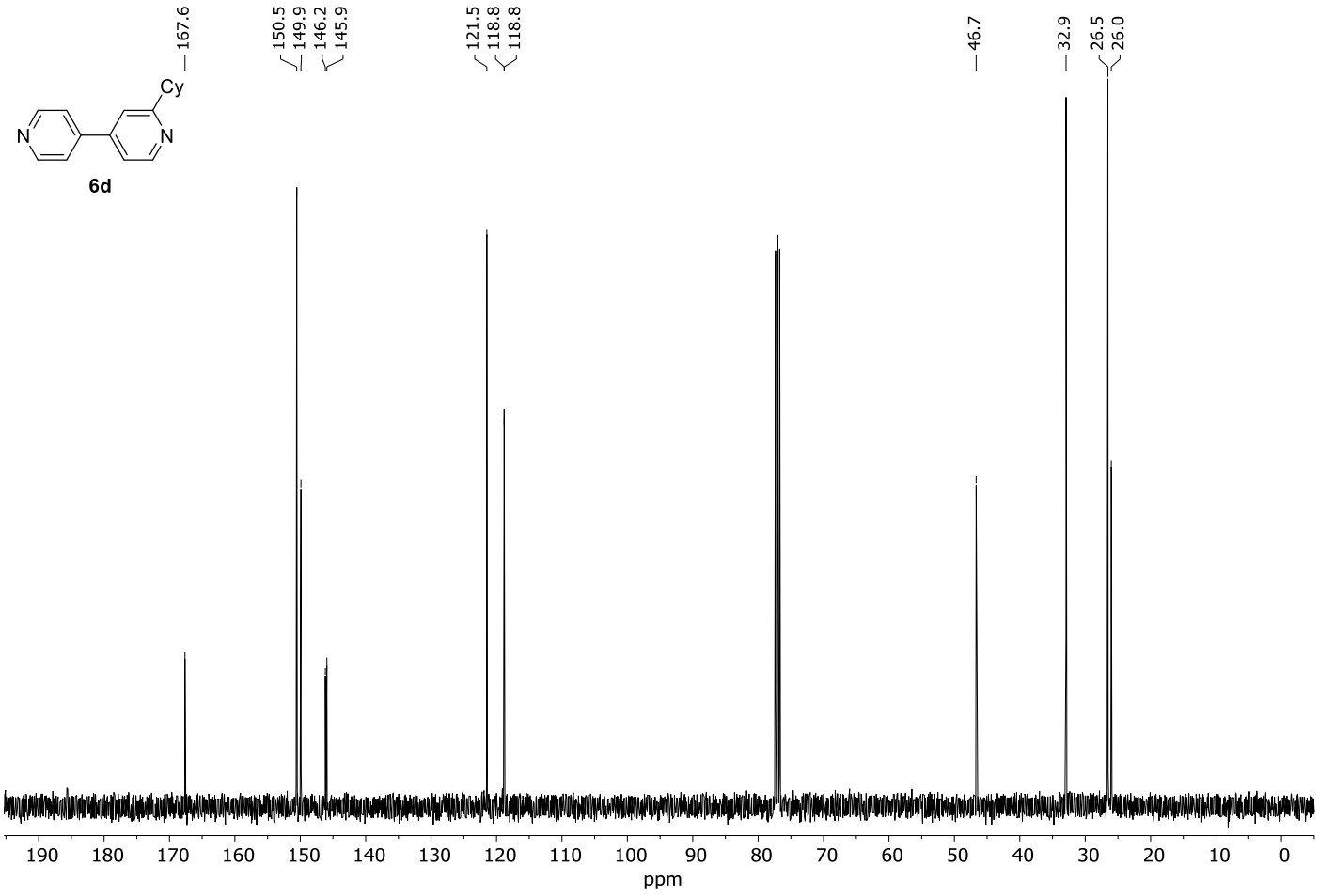
8.28 2,6-dicyclohexyl-4-phenylpyridine (6c)



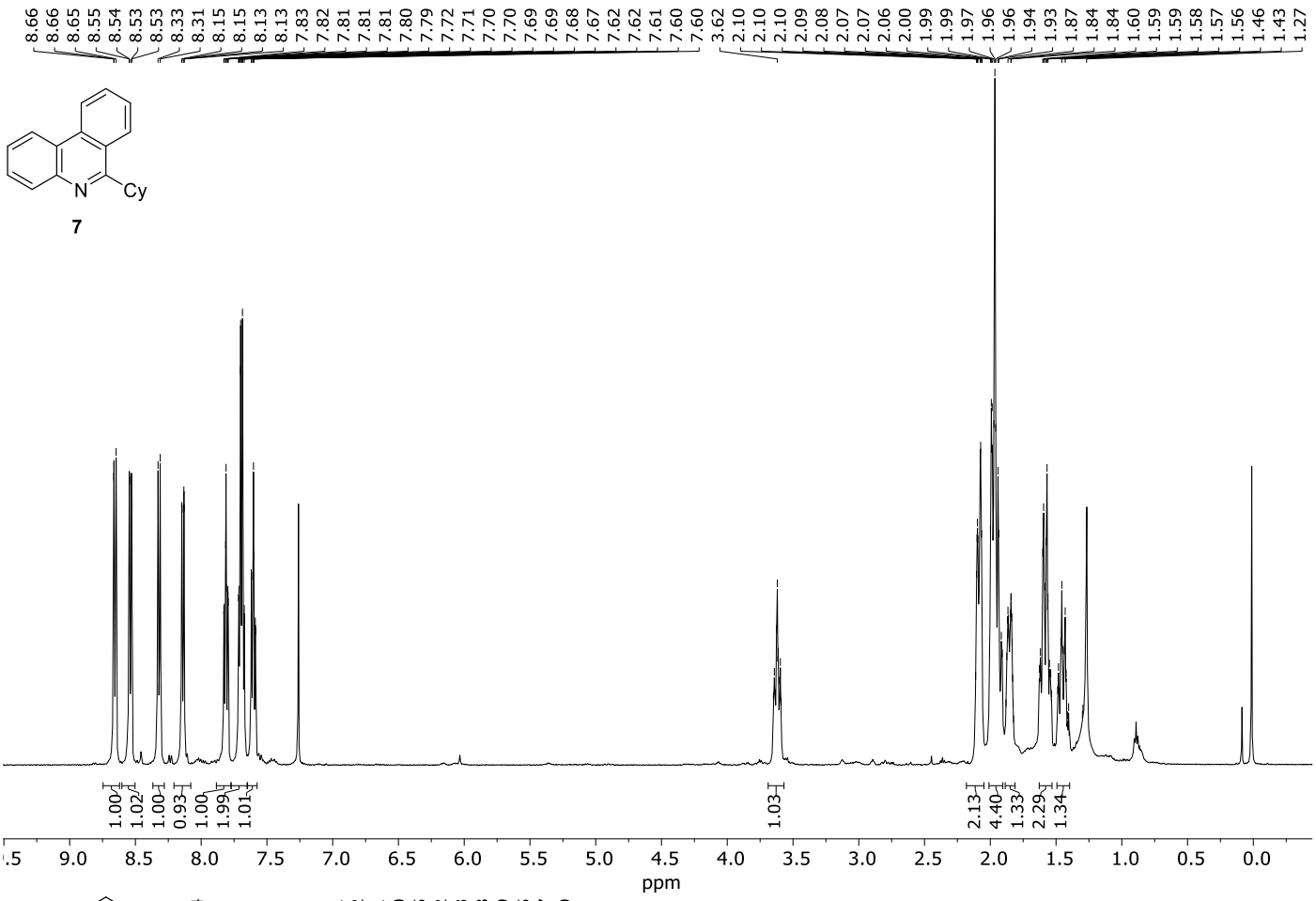


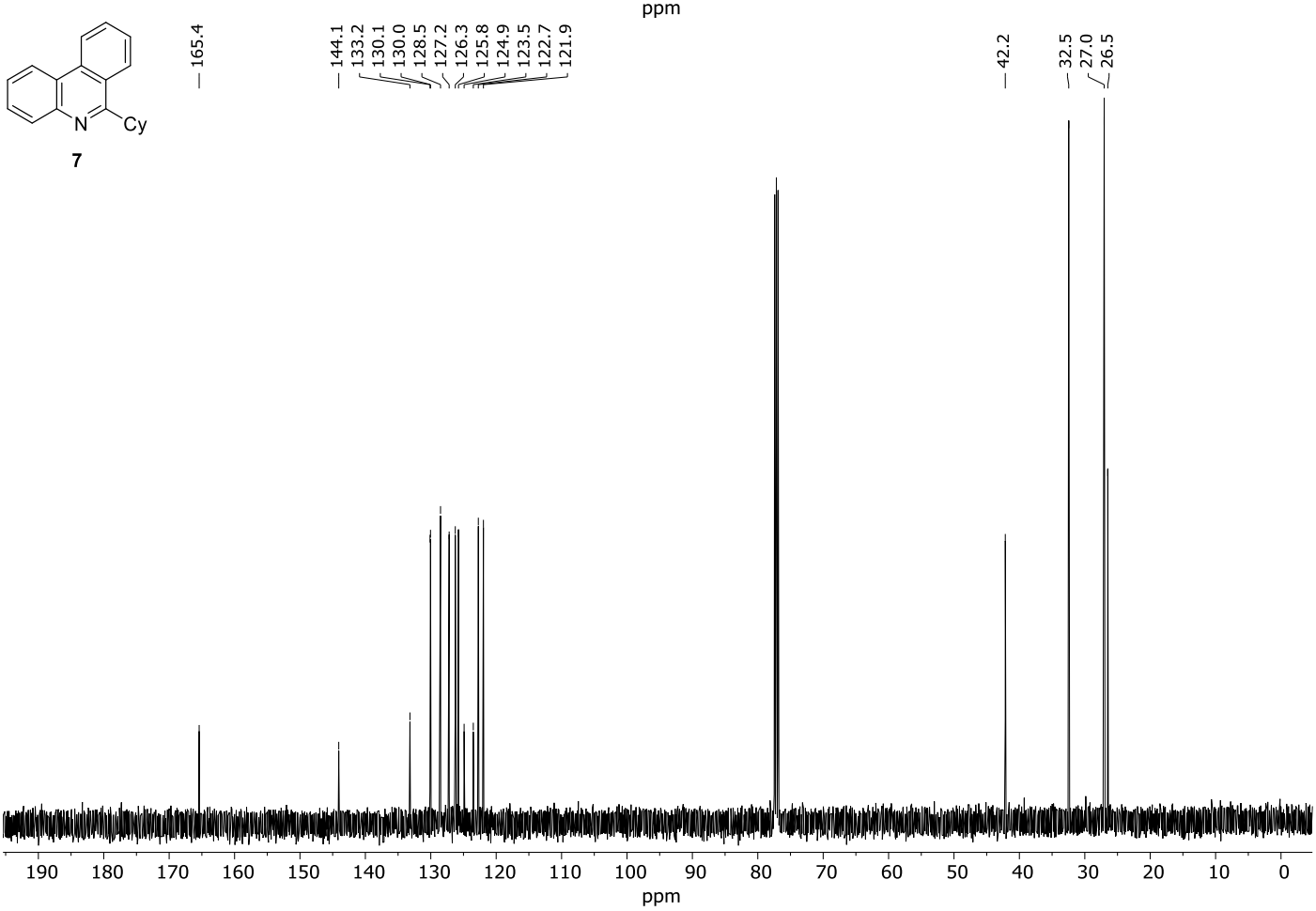
8.29 2-cyclohexyl-4,4'-bipyridine (6d)



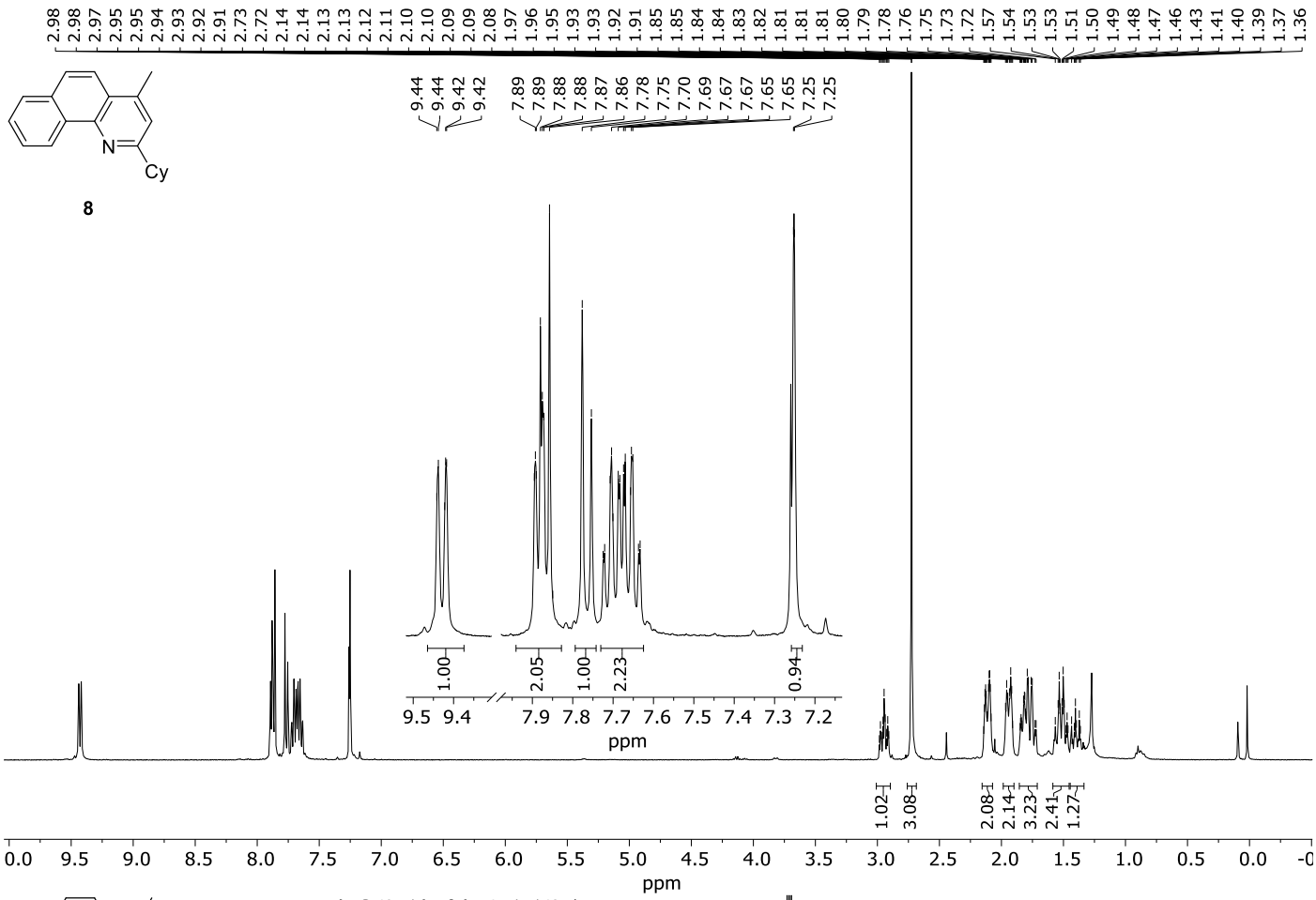


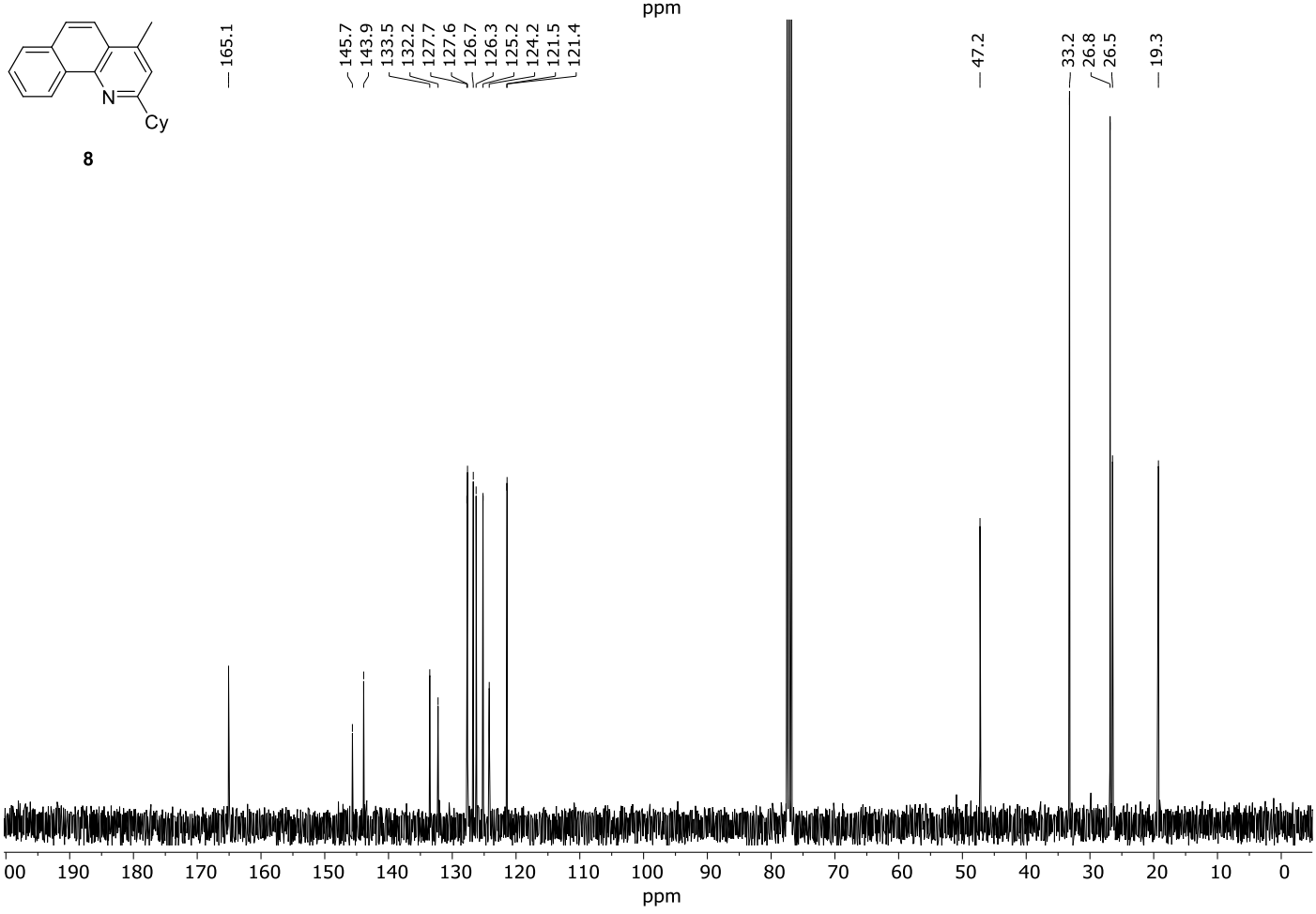
8.30 6-cyclohexylphenanthridine (7)



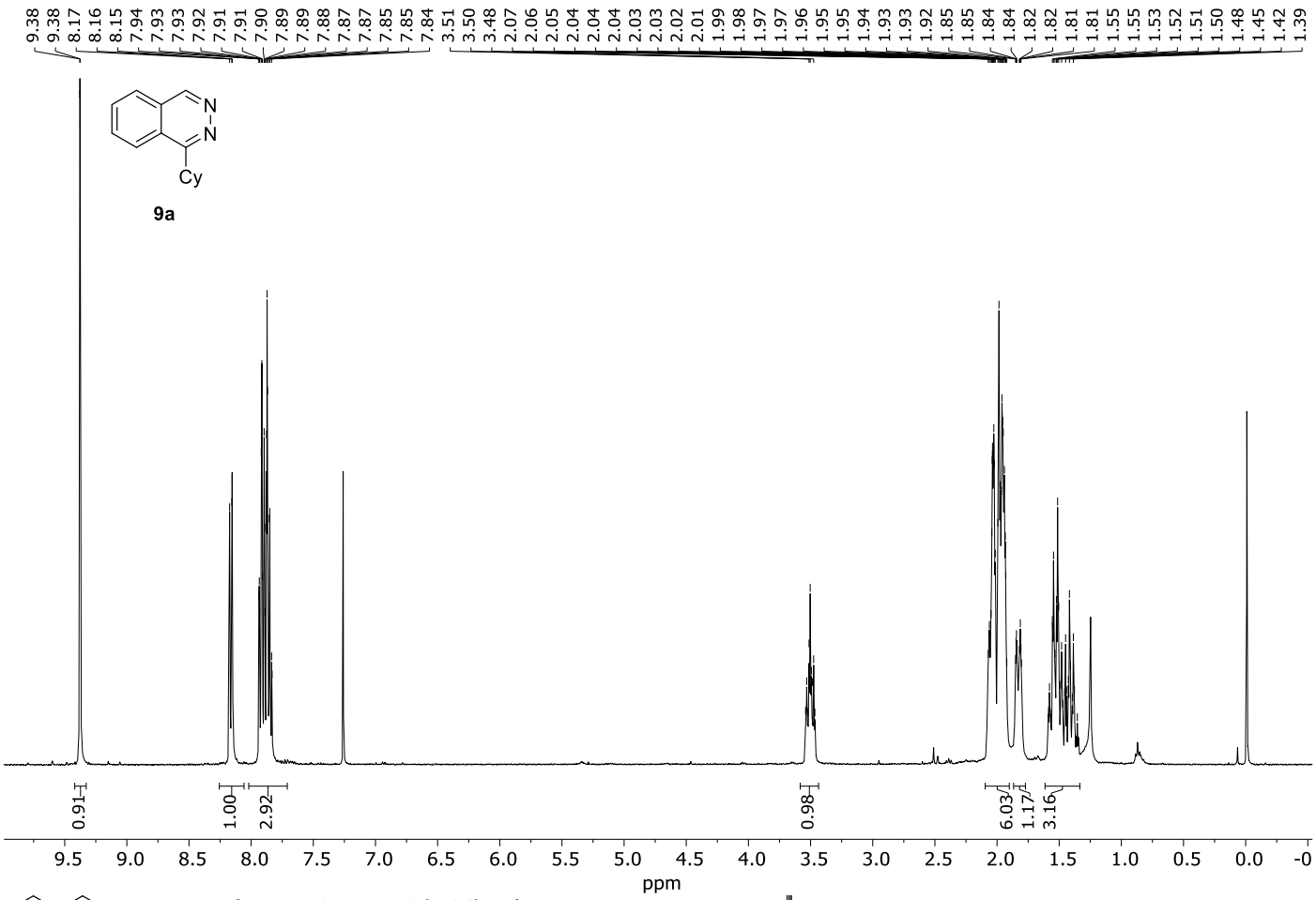


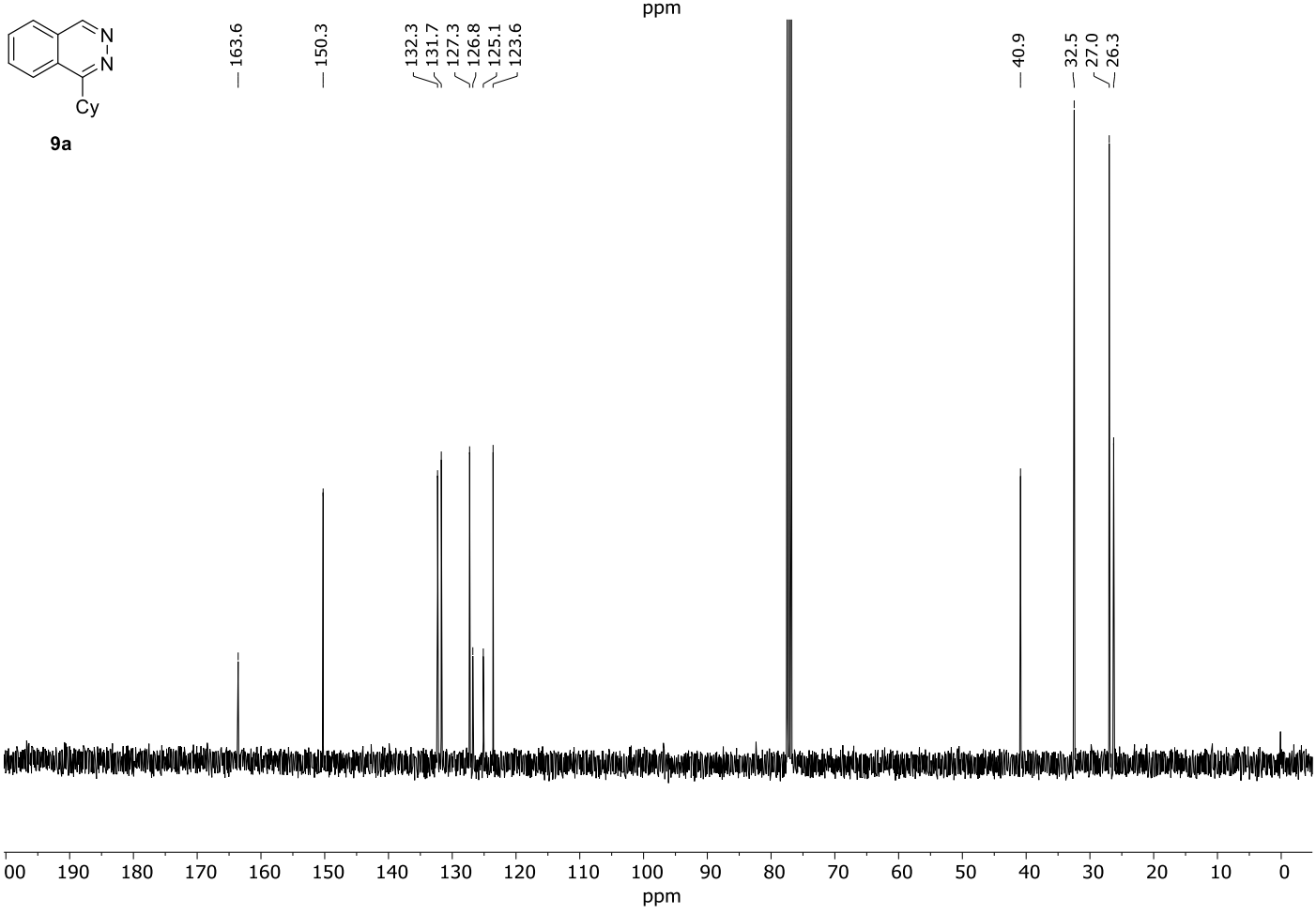
8.31 2-cyclohexyl-4-methylbenzo[h]quinoline (8)



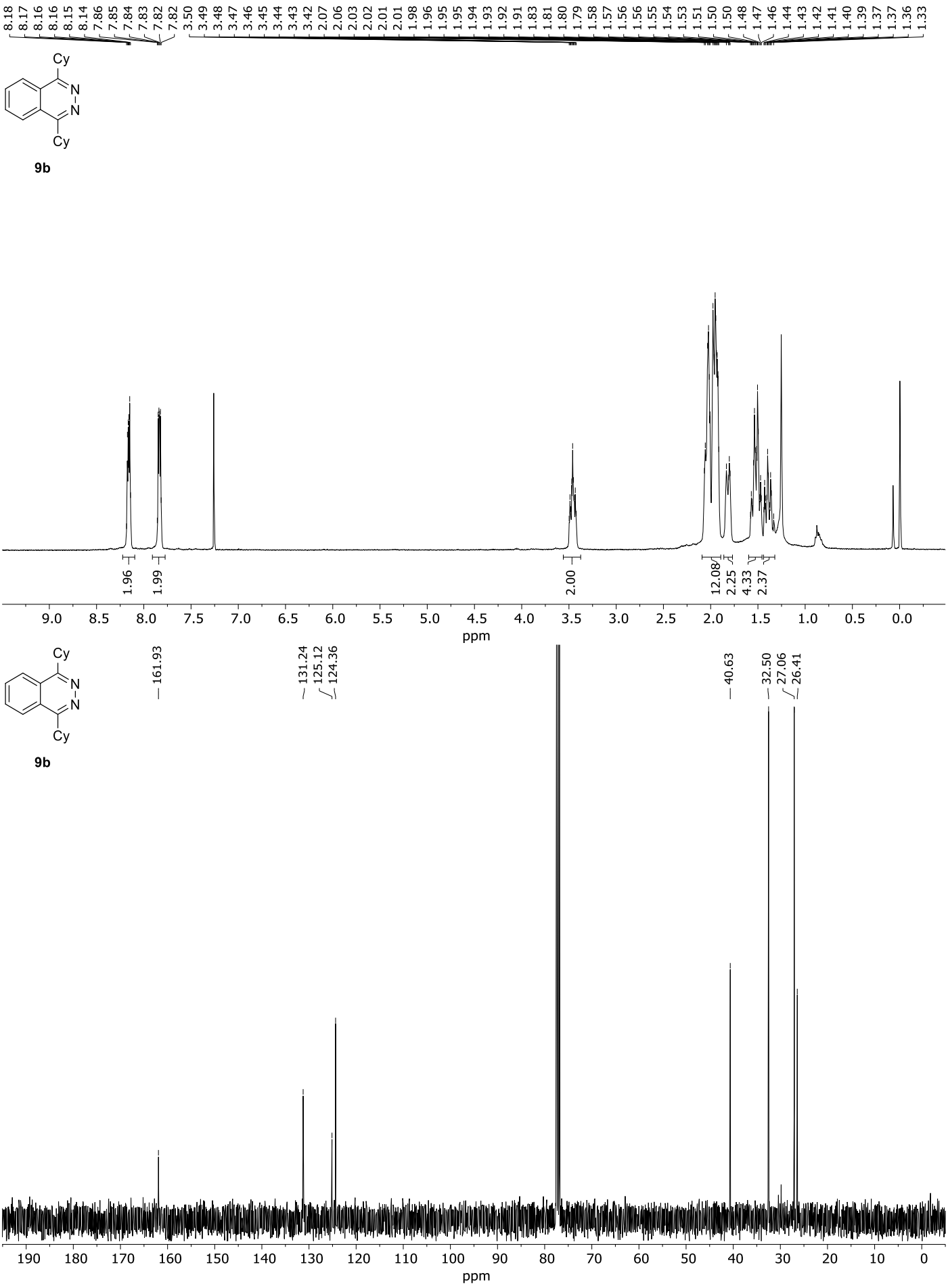


8.32 1-cyclohexylphthalazine (9a)

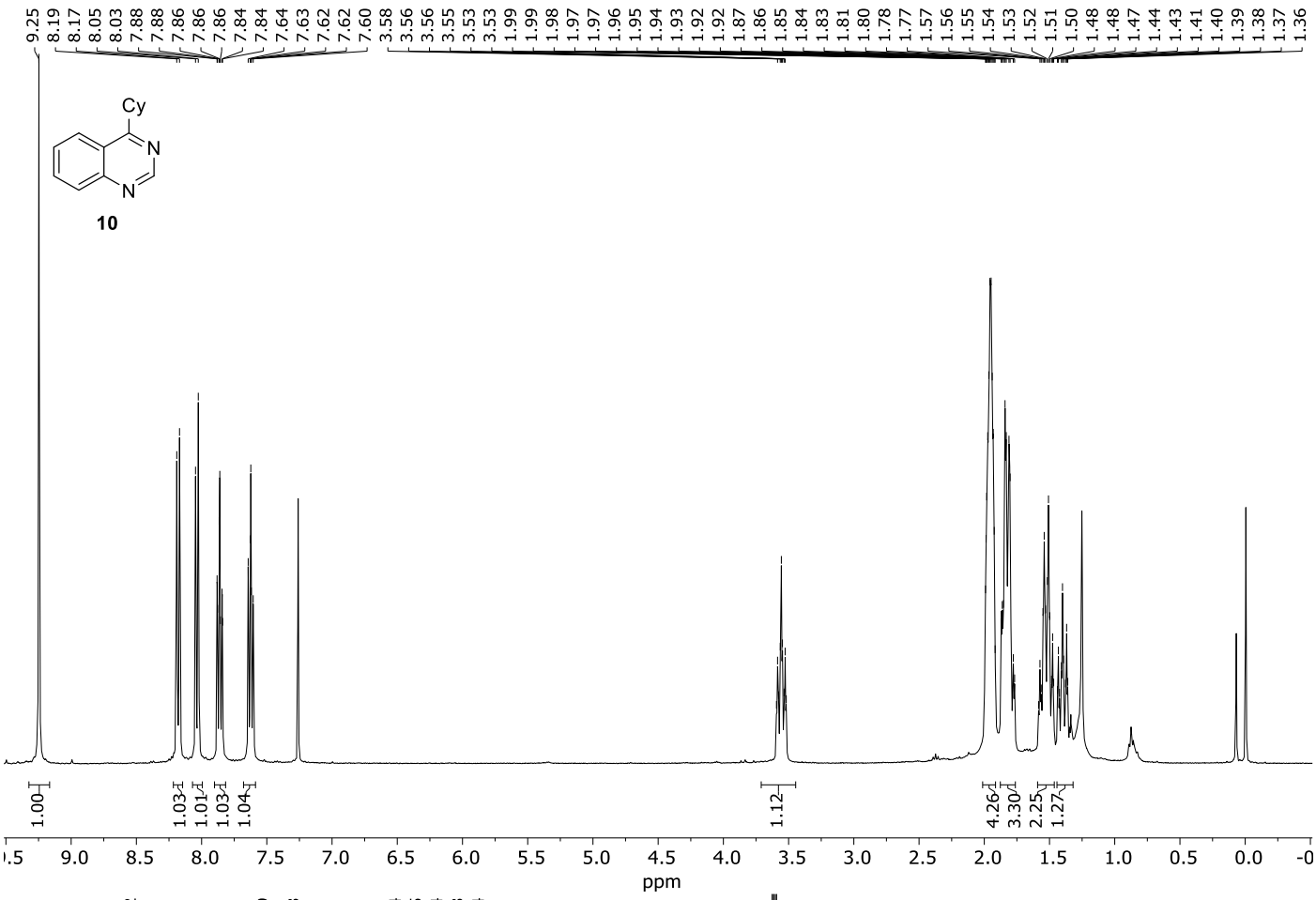


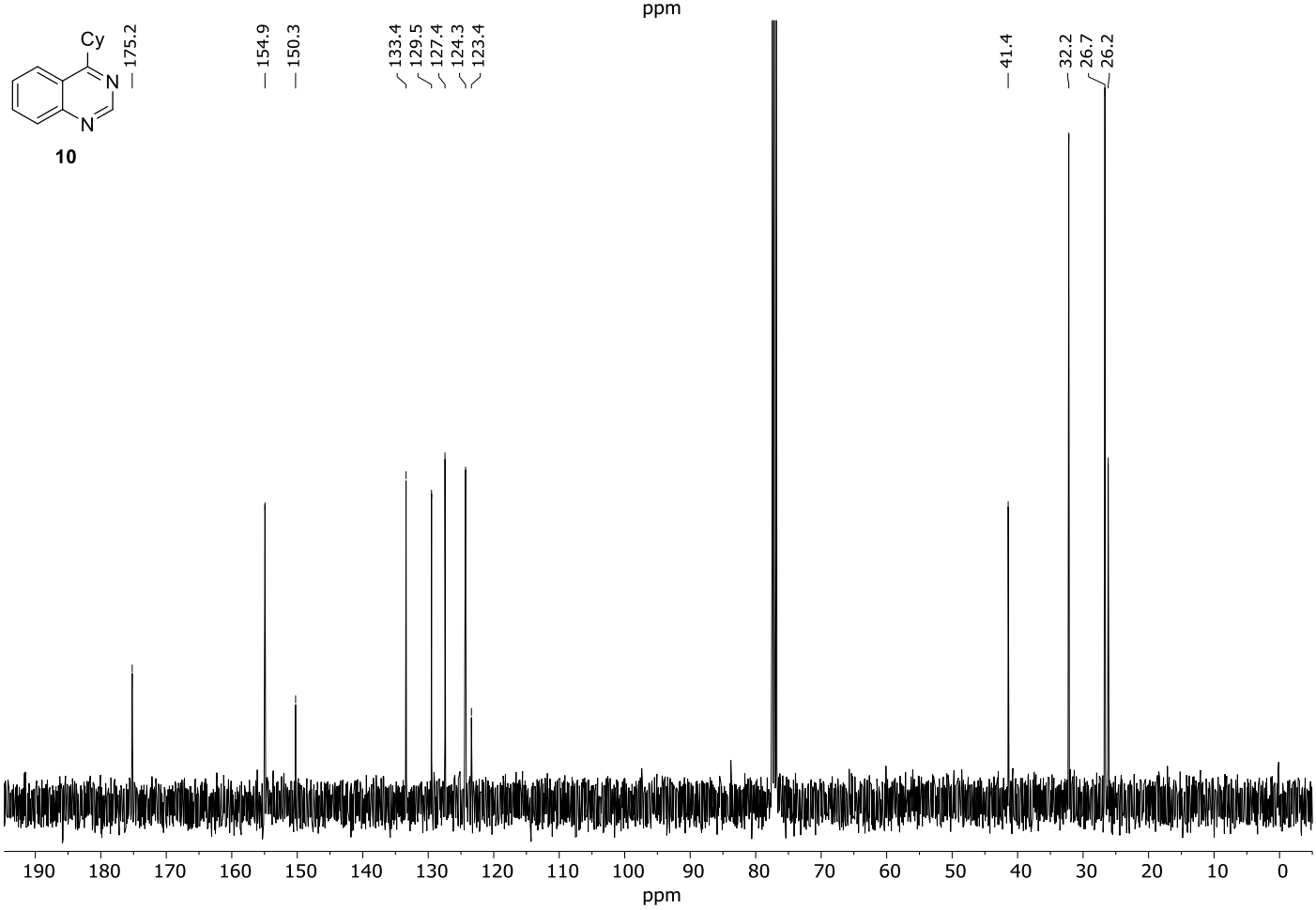


8.33 1,4-dicyclohexylphthalazine (9b)

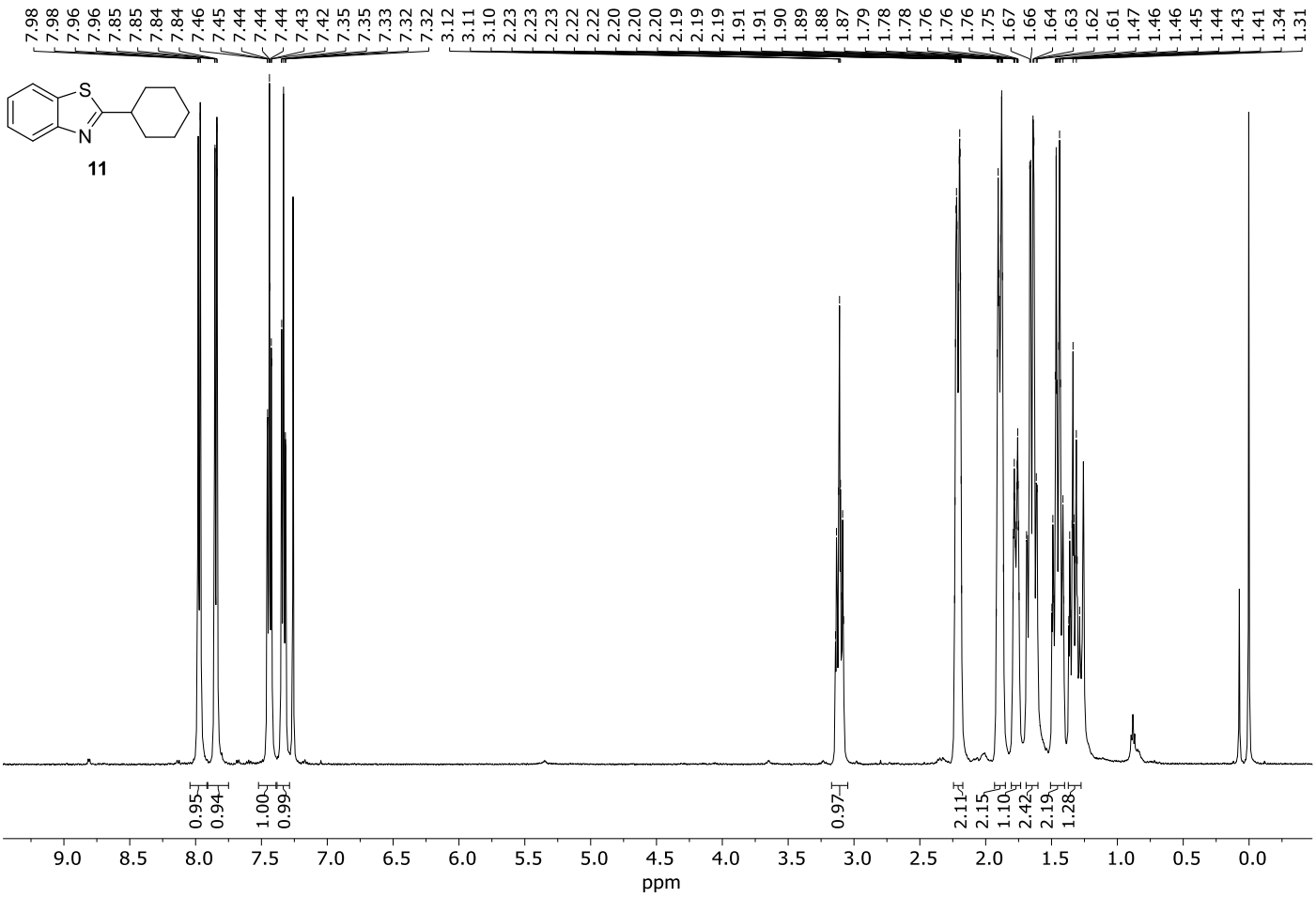


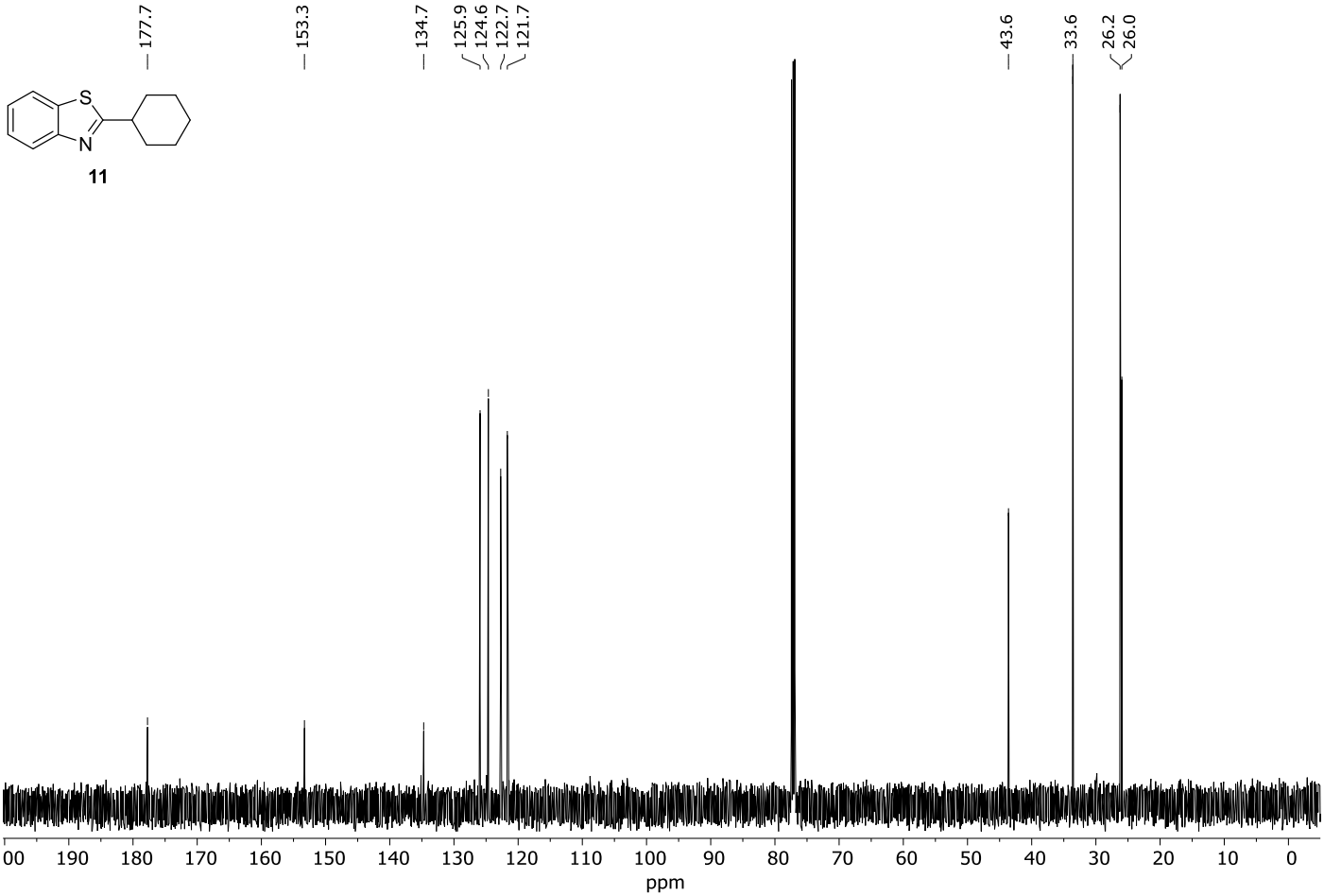
8.34 4-cyclohexylquinazoline (10)





8.35 2-cyclohexylbenzothiazole (11)





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