

Electronic Supplementary Information

2-Pyridone assisted palladium catalyzed regioselective arylation of naphthamides

Jayprakash Prajapati, and Sourav Chatterjee*

Department of Chemistry, Ashoka University, Sonapat, Haryana-131029, India.

Email: sourav.chatterjee@ashoka.edu.in

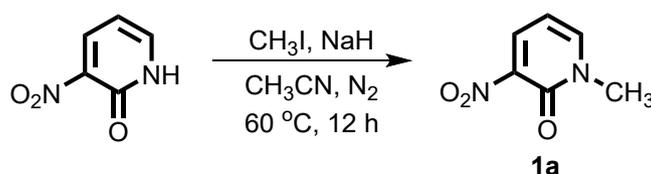
Table of Contents		
1	General information	S1
2	Experimental procedure for the N-alkylation of 3-nitro-2-pyridones (1a-d)	S1-S4
3	Typical experimental procedure for the synthesis of N-alkylated 3-amino-2-pyridones (2a-d)	S4-S5
4	Typical experimental procedure for the synthesis of N-(1-alkyl-2-oxo-1,2-dihydropyridin-3-yl)-1-naphthamides (3a-d)	S6-S7
5	Experimental procedure for the synthesis of N-(1-methyl-2-oxo-1,2-dihydropyridin-3-yl)-2-naphthamide (3e)	S8
6	Typical experimental procedure for the synthesis of N-(1-alkyl-2-oxo-1,2-dihydropyridin-3-yl)-2-phenyl-1-naphthamides (4a1-4d5)	S8-S17
7	Experimental procedure for the synthesis of N-(1-methyl-2-oxo-1,2-dihydropyridin-3-yl)-3-phenyl-2-naphthamide (4e1)	S17
8	¹ H NMR and ¹³ C NMR spectra	S17-S53
9	HPLC Analysis	S54-S60
10	X-ray single crystal analysis	S61-S62
11	Computational calculation	S63-S88
12	References	S88

1. General information:

Unless stated otherwise, all reactions were carried out in flame dried Schlenk tube under an atmosphere of nitrogen. All commercial solvents were used as such without further purification. The reaction products were purified by flash chromatography (Buchi, Pure C-815 Flash) using 200-300 mesh silica gel cartridges (Elegance Life Sciences, India). ^1H , and ^{13}C NMR spectra were recorded on a Bruker AVANCE III HD 400MHz NMR instrument (400 MHz and 101 MHz respectively). Data for ^1H NMR were recorded as follows: chemical shift (δ , ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, q = quartet or unresolved, coupling constant(s) in Hz, integration). Data for ^1H , and ^{13}C NMR are reported in terms of chemical shift (δ , ppm). Mass spectral data correspond to ESIMS and are given in m/z unit. ESI HRMS were done on Agilent's 6540 UHD Accurate-Mass Q-TOF MicroTM Mass Spectrometer. The X-ray diffraction measurements were carried out at 298K on a Bruker D8 VENTURE SC-XRD system. Analytical thin-layer chromatography (TLC) was carried out on Merck $20 \times 20\text{cm}$ silica gel 60-F₂₅₄ plates. HPLC analyses for the yield determination was carried out on Agilent 1260 Infinity II with DAD-detector using ZORBAX Eclipse Plus C18 HPLC column ($4.6\text{mm} \times 250\text{mm} \times 5\mu\text{m}$). Water/Methanol (25/75 v/v) were used as isocratic mobile phase with a flow rate 0.7 mL/min, 250 nm at 25 °C.

2. Experimental procedure for the N-alkylation of 3-nitro-2-pyridones (1a-d)

2.1 Typical procedure for the synthesis of (1-methyl-3-nitropyridin-2(1H)-one) (1a)

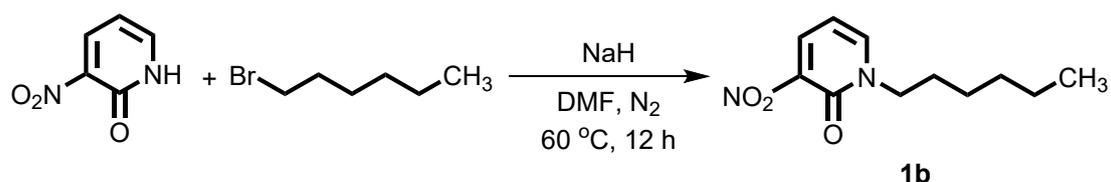


In a closed vessel, sodium hydride (1.979 g, 55-60% dispersion in mineral oil, 57.10 mmol) was washed with n-pentane (2 mL x 2 times) and was added CH_3CN (15 mL). 3-Nitro-2-oxopyridin-1(2H)-one (5 g, 35.69 mmol) was then added portion wise at $0\text{ }^\circ\text{C}$ and allowed to stir for 15 min followed by dropwise addition of iodomethane (4.46 mL, 71.38 mmol) at $0\text{ }^\circ\text{C}$ under an atmosphere of nitrogen. The reaction mixture was allowed to stir at $60\text{ }^\circ\text{C}$ temperature for 12 h. The progress of the reaction was monitored by TLC. The reaction mixture was washed with cold water and extracted with ethyl acetate (25 mL x 3). The combined organic layers washed with brine (30 mL) and dried over anhydrous MgSO_4 . The solvent was removed under reduced pressure. The residue was purified by flash column

chromatography on silica gel (230-400 mesh cartridge) eluting with 5 % methanol in DCM to give 1-methyl-3-nitropyridin-2(1H)-one (**1a**) (5.50 g, 80 %) as a yellow solid.

^1H NMR (400 MHz, CDCl_3) δ 8.31 (dd, $J = 7.70, 2.14$ Hz, 1H), 7.74 (dd, $J = 6.58, 2.12$ Hz, 1H), 6.30 (dd, $J = 7.69, 6.58$ Hz, 1H), 3.68 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 154.84, 144.95, 138.70, 103.30, 38.82. HRMS (ESI-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_6\text{H}_6\text{N}_2\text{O}_3$ 155.0457; Found 155.0430.

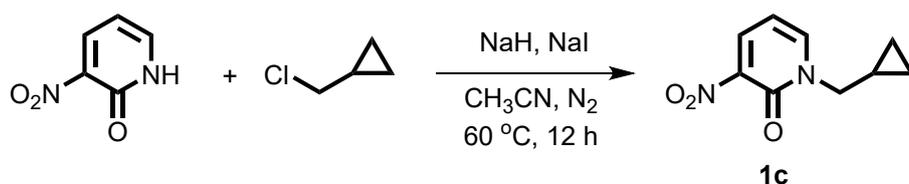
2.2 Typical procedure for the synthesis of (1-hexyl-3-nitropyridin-2(1H)-one) (**1b**)



Sodium hydride (0.79 g, 55-60 % dispersion in mineral oil, 22.84 mmol) was washed with n-pentane (1 mL x 2 times) and was added DMF (5 mL). 3-Nitro-2-oxopyridin-1(2H)-one (2 g, 14.27 mmol) was then added portion wise at 0 °C and allowed to stir for 15 min followed by dropwise addition of 1-bromohexane (2.2 mL, 15.70 mmol) at 0 °C under an atmosphere of nitrogen. The reaction mixture was then heated at 60 °C for 12 h. The progress of the reaction was monitored by TLC. The reaction mixture was washed with water and extracted with ethyl acetate (15 mL x 3). The combined organic layers washed with brine (10 mL) and dried over anhydrous MgSO_4 . The solvent was removed under reduced pressure. The residue was purified by flash column chromatography on silica gel (230-400 mesh cartridge) eluting with 25-30 % ethyl acetate in hexane to give 1-hexyl-3-nitropyridin-2(1H)-one (**1b**) (2.71 g, 85%) as dark red liquid.

^1H NMR (400 MHz, CDCl_3) δ 8.25 (dd, $J = 7.70, 2.08$ Hz, 1H), 7.76 (dd, $J = 6.58, 2.03$ Hz, 1H), 6.29 (dd, $J = 7.79, 6.59$ Hz, 1H), 4.06 – 3.93 (m, 2H), 1.71 (dt, $J = 14.72, 7.72$ Hz, 2H), 1.32 – 1.16 (m, 6H), 0.83 – 0.74 (m, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 154.32, 144.64, 138.54, 103.33, 77.48, 77.16, 76.84, 51.18, 31.14, 28.94, 26.08, 22.31, 13.84. HRMS (ESI-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{11}\text{H}_{16}\text{N}_2\text{O}_3$ 225.1239; Found 225.1183.

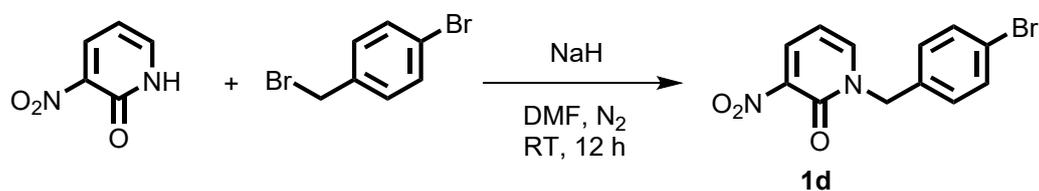
2.3 Typical procedure for the synthesis of (1-(cyclopropylmethyl)-3-nitropyridin-2(1H)-one) (**1c**)



Sodium hydride (0.87 g, 55-60 % dispersion in mineral oil, 25.12 mmol) was washed with n-pentane (2 mL x 2 times) and was added CH₃CN (15 mL). 3-Nitro-2-oxopyridin-1(2H)-one (2.2 g, 15.70 mmol) was then added portion wise at 0 °C and allowed to stir for 15 min followed by slow addition of (chloromethyl)cyclopropane (1.6 mL, 17.27 mmol) and NaI (2.4 g, 15.7 mmol) at 0 °C under an atmosphere of nitrogen. The reaction mixture was then heated at 60 °C for 12 h. The progress of the reaction was monitored by TLC. The reaction mixture was washed with water and extracted with ethyl acetate (25 mL x 3). The combined organic layers washed with brine (30 mL) and dried over anhydrous MgSO₄. The solvent was removed under reduced pressure. The residue was purified by flash column chromatography on silica gel (230-400 mesh cartridge) eluting with 75-80 % ethyl acetate in hexane to give 1-(cyclopropylmethyl)-3-nitropyridin-2(1H)-one (**1c**) (1.45 g, 48 %) as yellow crystalline solid.

¹H NMR (400 MHz, CDCl₃) δ 8.28 (dd, *J* = 7.68, 2.12 Hz, 1H), 7.89 (dd, *J* = 6.59, 2.15 Hz, 1H), 6.33 (dd, *J* = 7.71, 6.57 Hz, 1H), 3.88 (d, *J* = 7.27 Hz, 2H), 1.24 (pt, *J* = 7.62, 4.84 Hz, 1H), 0.59 (ddd, *J* = 8.17, 3.93, 2.59 Hz, 2H), 0.38 (dt, *J* = 6.32, 4.87 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 154.63, 144.25, 138.68, 138.46, 103.43, 55.00, 10.38, 4.17. HRMS (ESI-TOF) *m/z*: [M+H]⁺ Calcd for C₉H₁₀N₂O₃ 195.0770; Found 195.0752.

2.4 Typical procedure for the synthesis of (1-(4-bromobenzyl)-3-nitropyridin-2(1H)-one) (**1d**)



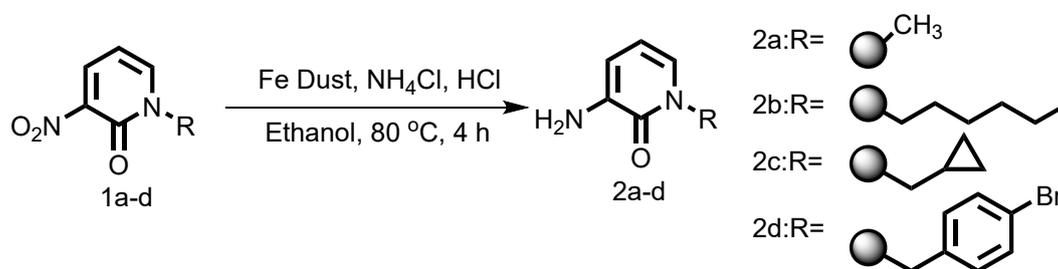
Sodium hydride (0.27 g, 55-60 % dispersion in mineral oil, 11.42 mmol) was washed with n-pentane (1 mL x 2 times) and was added DMF (5 mL). 3-Nitro-2-oxopyridin-1(2H)-one (1 g, 7.14 mmol) was then added portion wise at 0 °C and allowed to stir for 15 min followed by slow addition of 1-bromo-4-(bromomethyl)benzene (2.1 g, 8.6 mmol) at 0 °C under an atmosphere of nitrogen. The reaction mixture was allowed to stir at room temperature for 12 h. The progress of the reaction was monitored by TLC. The reaction mixture was washed with

water and extracted with ethyl acetate (5 mL x 3). The combined organic layers washed with brine (5 mL) and dried over anhydrous MgSO₄. The solvent was removed under reduced pressure. The residue was purified by flash column chromatography on silica gel (230-400 mesh cartridge) eluting with 30-35 % ethyl acetate in hexane to give 1-(4-bromobenzyl)-3-nitropyridin-2(1H)-one (**1d**) (1.7 g, 76 %) as yellow crystalline solid.

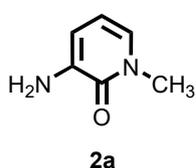
¹H NMR (400MHz, CDCl₃) δ 8.30 (dd, *J* = 7.66, 2.12 Hz, 1H), 7.72 (dd, *J* = 6.68, 2.13 Hz, 1H), 7.50 – 7.45 (m, 2H), 7.24 (d, *J* = 8.41 Hz, 2H), 6.32 (dd, *J* = 7.66, 6.66 Hz, 1H), 5.17 (s, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 154.58, 143.63, 139.20, 138.81, 133.83, 132.47, 130.43, 123.13, 103.86, 52.95. HRMS (ESI-TOF) *m/z*: [M+H]⁺ Calcd for C₁₂H₉BrN₂O₃ 308.9875; Found 308.9865.

3. Typical experimental procedure for the synthesis of N-alkylated 3-amino-2-pyridones (**2a-d**)

To a solution of **1a** (2.00 g, 12.98 mmol) in ethanol (10 mL), NH₄Cl (4.16 g, 77.86 mmol.), and Fe powder (4.35 g, 77.86 mmol.) were added and cooled. Conc. HCl (2.41 mL, 77.86 mmol) was then added to the reaction mixture dropwise under cold condition and further heated at 80 °C for 4 h. The progress of the reaction was monitored by TLC. After cooling to room temperature, the reaction mixture was treated with saturated sodium bicarbonate, filtered through a pad of celite under vacuum pressure, and washed with chloroform. It was further washed with water and the separated organic layer dried over anhydrous MgSO₄. The solvent was removed under reduced pressure. The crude residue was purified by flash column chromatography on silica gel (230-400 mesh cartridge) eluting with 5 % methanol in DCM to give 3-amino-1-methylpyridin-2(1H)-one (**2a**). The same protocol was followed for the synthesis of **2b-d**.



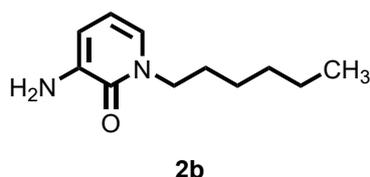
3.1 3-Amino-1-methylpyridin-2(1H)-one (**2a**)



Dark green liquid. 1.37 g (from 2.00 g **1a**; 95 % yield).

^1H NMR (400 MHz, CDCl_3) δ 6.63 (dd, $J = 6.82, 1.71$ Hz, 1H), 6.46 (dd, $J = 7.19, 1.73$ Hz, 1H), 5.97 (t, $J = 6.99$ Hz, 1H), 4.25 (s, 2H), 3.49 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 158.12, 137.69, 125.81, 112.15, 106.64, 37.39. HRMS (ESI-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_6\text{H}_8\text{N}_2\text{O}$ 125.0715; Found 125.0696.

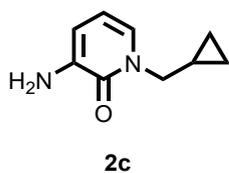
3.2 3-Amino-1-hexylpyridin-2(1H)-one (2b)



Dark brown solid. 2.0 g (from 2.60 g **1b**; 89 % yield).

^1H NMR (400 MHz, CDCl_3) δ 6.66 (dd, $J = 6.79, 1.73$ Hz, 1H), 6.48 (dd, $J = 7.10, 1.72$ Hz, 1H), 6.01 (t, $J = 6.93$ Hz, 1H), 4.21 (s, 2H), 3.94 – 3.86 (m, 2H), 1.71 (p, $J = 7.83$ Hz, 2H), 1.36 – 1.22 (m, 5H), 0.85 (d, $J = 7.00$ Hz, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ 157.70, 137.86, 125.26, 112.13, 106.61, 50.02, 31.49, 29.23, 26.42, 22.55, 14.05. HRMS (ESI-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{11}\text{H}_{18}\text{N}_2\text{O}$ 195.1497; Found 195.1465.

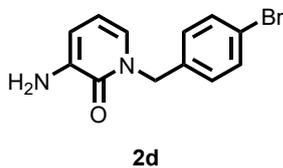
3.3 3-amino-1-(cyclopropylmethyl)pyridin-2(1H)-one (2c)



Brown oil. 0.610 g (from 0.966 g **1c**; 75 % yield).

^1H NMR (400 MHz, CDCl_3) δ 6.70 (dd, $J = 6.81, 1.69$ Hz, 1H), 6.45 (d, $J = 7.09$ Hz, 1H), 5.97 (t, $J = 6.95$ Hz, 1H), 4.25 (s, 2H), 3.73 (d, $J = 7.09$ Hz, 2H), 1.16 (dtd, $J = 15.90, 7.53, 3.97$ Hz, 1H), 0.53 – 0.41 (m, 2H), 0.29 (t, $J = 5.18$ Hz, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ 157.65, 137.72, 124.71, 112.05, 106.51, 53.55, 10.52, 3.72. HRMS (ESI-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_9\text{H}_{12}\text{N}_2\text{O}$ 165.1028; Found 165.1022.

3.4 3-Amino-1-(4-bromobenzyl)pyridin-2(1H)-one (2d)

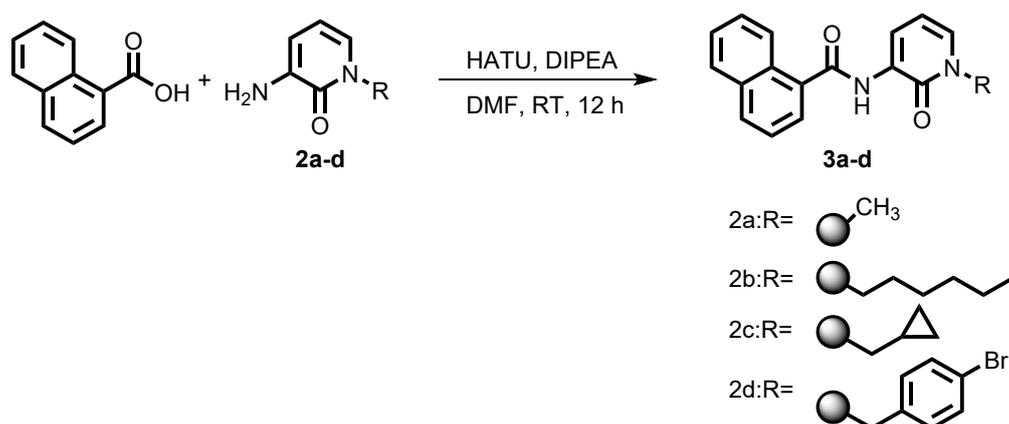


Yellow solid. 1.3 g (from 1.5 g **1d**; 96 % yield). ^1H NMR (400 MHz, CDCl_3) δ 7.41 – 7.35 (m, 2H), 7.14 – 7.07 (m, 2H), 6.66 (dd, $J = 6.85, 1.70$ Hz, 1H), 6.45 (dd, $J = 7.19, 1.71$ Hz, 1H), 6.00 (t, $J = 6.99$ Hz, 1H), 5.04 (s, 2H), 4.31 (s, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ 157.65, 137.98, 135.62, 131.71, 129.51, 124.55, 121.66, 112.02, 107.19, 51.75.

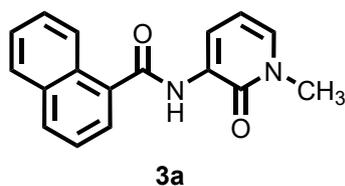
HRMS (ESI-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{12}\text{H}_{11}\text{BrN}_2\text{O}$ 279.0133; Found 279.0065.

4. Typical experimental procedure for the synthesis of N-(1-alkyl-2-oxo-1,2-dihydropyridin-3-yl)-1-naphthamides (3a-d)*

To a solution of 1-naphthoic acid (0.96 g, 5.56 mmol) in DMF (5 mL), were added DIPEA (1.21 mL, 6.95 mmol) and HATU (1.94 g, 5.10 mmol) at 0 °C. The reaction mixture was allowed to stirred for 10 min followed by addition of **2a** (0.58 g, 4.63 mmol) at 0 °C. It was further allowed to warm to room temperature and stirred for 12 h under an atmosphere of nitrogen. The progress of the reaction was monitored by TLC. Cold water was added, and the reaction mixture was extracted with ethyl acetate (15 mL x 3). The combined organic layers treated with brine, saturated sodium bicarbonate solution and dried over anhydrous MgSO₄. The solvent was removed under reduced pressure. The residue was purified by flash column chromatography on silica gel cartridge silica gel (230-400 mesh cartridge) eluting with 50-60 % ethyl acetate in hexane to give the N-(1-methyl-2-oxo-1,2-dihydropyridin-3-yl)-1-naphthamide (**3a**). The same protocol was followed for the synthesis of **3b-d** (*reaction performed at 60 °C for **3b**).



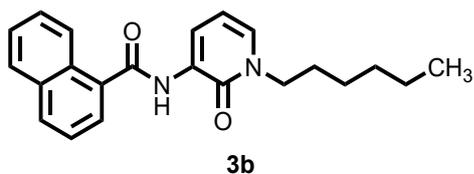
4.1 N-(1-methyl-2-oxo-1,2-dihydropyridin-3-yl)-1-naphthamide (**3a**)



Light pink solid. 1.18 g (from 580 mg **2a**; 91 % yield).

¹H NMR (400 MHz, CDCl₃) δ 8.99 (s, 1H), 8.65 (d, *J* = 7.39 Hz, 1H), 8.42 (d, *J* = 8.18 Hz, 1H), 7.97 (d, *J* = 8.25 Hz, 1H), 7.93 – 7.84 (m, 1H), 7.78 (d, *J* = 7.04 Hz, 1H), 7.65 – 7.41 (m, 3H), 7.13 – 6.99 (m, 1H), 6.32 (t, *J* = 7.08 Hz, 1H), 3.62 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 168.20, 133.97, 133.89, 131.52, 131.11, 130.35, 129.85, 128.56, 127.52, 126.66, 125.78, 125.45, 124.86, 122.54, 106.78, 37.96. HRMS (ESI-TOF) *m/z*: [M+H]⁺ Calcd for C₁₇H₁₄N₂O₂ 279.1134; Found 279.1060.

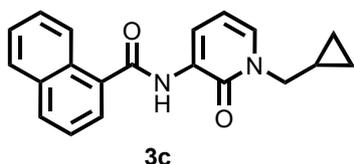
4.2 N-(1-hexyl-2-oxo-1,2-dihydropyridin-3-yl)-1-naphthamide (**3b**)



Light blue solid. 461 mg (from 381 mg **2b**; 68 % yield).

^1H NMR (400 MHz, CDCl_3) δ 9.03 (s, 1H), 8.63 (dd, $J = 7.45, 1.78$ Hz, 1H), 8.44 (d, $J = 8.22$ Hz, 1H), 7.96 (d, $J = 8.25$ Hz, 1H), 7.92 – 7.85 (m, 1H), 7.79 (dd, $J = 7.15, 1.20$ Hz, 1H), 7.61 – 7.47 (m, 2H), 7.03 (dd, $J = 6.92, 1.77$ Hz, 1H), 6.32 (t, $J = 7.13$ Hz, 1H), 3.98 (t, $J = 7.43$ Hz, 2H), 1.75 (q, $J = 7.40$ Hz, 2H), 1.39 – 1.28 (m, 9H), 0.92 – 0.84 (m, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 168.13, 157.45, 133.92, 133.84, 131.49, 130.40, 130.31, 129.82, 128.51, 127.48, 126.61, 125.74, 125.46, 124.80, 122.30, 106.66, 50.59, 31.48, 29.24, 26.39, 22.59, 14.10. HRMS (ESI-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{22}\text{H}_{24}\text{N}_2\text{O}_2$ 349.1916; Found 349.1912.

4.3 N-(1-(cyclopropylmethyl)-2-oxo-1,2-dihydropyridin-3-yl)-1-naphthamide (**3c**)



Off-white solid. 536 mg (from 530 mg **2c**; 52 % yield).

^1H NMR (400 MHz, CDCl_3) δ 9.05 (s, 1H), 8.65 (d, $J = 7.28$ Hz, 1H), 8.44 (d, $J = 8.30$ Hz, 1H), 7.99 – 7.75 (m, 3H), 7.60 – 7.43 (m, 3H), 7.13 (d, $J = 6.77$ Hz, 1H), 6.37 – 6.25 (m, 1H), 3.85 (d, $J = 4.40$ Hz, 2H), 1.24 (dt, $J = 12.99, 6.07$ Hz, 1H), 0.60 (d, $J = 7.58$ Hz, 2H), 0.39 (d, $J = 5.08$ Hz, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ 168.12, 157.56, 133.87, 133.84, 133.77, 131.41, 130.27, 130.05, 129.71, 128.47, 127.42, 126.57, 125.69, 125.41, 124.78, 122.45, 106.62, 54.30, 10.59, 4.04. HRMS (ESI-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{20}\text{H}_{18}\text{N}_2\text{O}_2$ 319.1447; Found 319.1437.

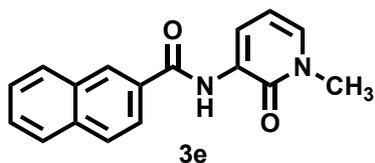
4.4 N-(1-(4-bromobenzyl)-2-oxo-1,2-dihydropyridin-3-yl)-1-naphthamide (**3d**)



Light blue solid. 466.1mg (from 436 mg **2d**, 69 % yield).

^1H NMR (400 MHz, CDCl_3) δ 9.10 (s, 1H), 8.74 (dd, $J = 7.36, 1.76$ Hz, 1H), 8.53 (d, $J = 8.21$ Hz, 1H), 8.05 (d, $J = 8.26$ Hz, 1H), 7.98 (d, $J = 7.17$ Hz, 1H), 7.92 – 7.83 (m, 1H), 7.71 – 7.51 (m, 5H), 7.25 (d, $J = 8.32$ Hz, 2H), 7.14 (dd, $J = 6.91, 1.81$ Hz, 1H), 6.42 (t, $J = 7.15$ Hz, 1H), 5.19 (s, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ 168.11, 157.55, 134.93, 133.86, 133.63, 132.12, 131.55, 130.23, 130.04, 129.97, 129.75, 128.51, 127.49, 126.63, 125.70, 125.36, 124.75, 122.49, 122.34, 107.22, 52.53. HRMS (ESI-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{23}\text{H}_{17}\text{BrN}_2\text{O}_2$ 433.0552; Found 433.0533.

5. Experimental procedure for the synthesis of N-(1-methyl-2-oxo-1,2-dihydropyridin-3-yl)-2-naphthamide (3e)

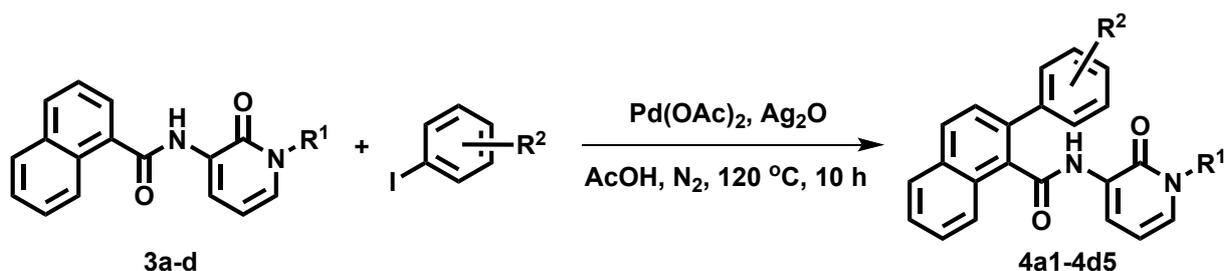


To a solution of 2-naphthoic acid (832 mg, 4.83 mmol) in DMF (5 mL), were added DIPEA (1.05 mL, 6.04 mmol) and HATU (1.68 g, 4.43 mmol) at 0 °C. The reaction mixture was allowed to stirred for 10 min followed by addition of **2a** (500 mg, 4.02 mmol) at 0 °C. It was further allowed to warm to room temperature and stirred for 12 h under an atmosphere of nitrogen. The progress of the reaction was monitored by TLC. Cold water was added, and the reaction mixture was extracted with ethyl acetate (15 mL x 3). The combined organic layers treated with brine, saturated sodium bicarbonate solution and dried over anhydrous MgSO₄. The solvent was removed under reduced pressure. The residue was purified by flash column chromatography on silica gel cartridge silica gel (230-400 mesh cartridge) eluting with 50-60 % ethyl acetate in hexane to give the N-(1-methyl-2-oxo-1,2-dihydropyridin-3-yl)-2-naphthamide (**3e**) (439.8 mg, 39 %) as light grey solid.

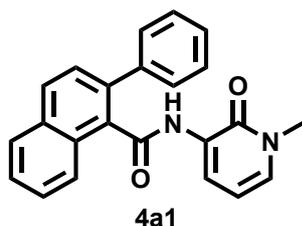
¹H NMR (400 MHz, CDCl₃) δ 9.38 (s, 1H), 8.61 – 8.53 (m, 1H), 8.44 (s, 1H), 8.00 – 7.81 (m, 4H), 7.56 (p, *J* = 6.66 Hz, 2H), 7.09 – 7.01 (m, 1H), 6.32 (t, *J* = 7.10 Hz, 1H), 3.64 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 135.12, 132.72, 131.05, 129.26, 128.86, 128.15, 128.02, 127.86, 127.03, 123.59, 122.69, 107.15, 38.04. HRMS (ESI-TOF) *m/z*: [M+H]⁺ Calcd for C₁₇H₁₄N₂O₂ 279.1134; Found 279.1122.

6. Typical experimental procedure for the synthesis of N-(1-alkyl-2-oxo-1,2-dihydropyridin-3-yl)-2-phenyl-1-naphthamides (4a1-4d5)

In a dry Schlenk reaction tube, Pd(OAc)₂ (4.03 mg, 10 mol%) in AcOH (1.5 mL) was taken and purged with nitrogen. **3a** (50 mg, 0.18 mmol), Ag₂O (83.26 mg, 0.36 mmol) and iodobenzene (73.3 mg, 0.36 mmol) gradually added to it under nitrogen. It was further allowed to heat at 120 °C and stirred for 10 h under an atmosphere of nitrogen. The progress of the reaction was monitored by TLC. Cold water was added, and the reaction mixture was extracted with ethyl acetate (15 mL x 3). The combined organic layers washed with brine and dried over anhydrous MgSO₄. The solvent was removed under reduced pressure. The residue was purified by flash column chromatography on silica gel cartridge silica gel (230-400 mesh cartridge) eluting with 75-80 % ethyl acetate in hexane to give the N-(1-methyl-2-oxo-1,2-dihydropyridin-3-yl)-2-phenyl-1-naphthamide (**4a1**). The same protocol was followed for the synthesis of other analogs (**4a2-4d5**).



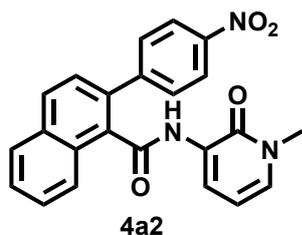
6.1 N-(1-methyl-2-oxo-1,2-dihydropyridin-3-yl)-2-phenyl-1-naphthamide (4a1)



Purification by flash column chromatography (ethyl acetate/hexane 75/25, v/v) afforded the title compound as a brown solid. 55 mg (from 50 mg **3a**; 86 % yield).

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.52 (d, $J = 7.68$ Hz, 1H), 8.43 (s, 1H), 8.12 – 7.84 (m, 3H), 7.73 – 7.46 (m, 5H), 7.46 – 7.35 (m, 2H), 7.34 – 7.27 (m, 1H), 6.95 (d, $J = 6.90$ Hz, 1H), 6.23 (q, $J = 7.95$ Hz, 1H), 3.48 (s, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 168.46, 157.51, 140.32, 137.08, 133.18, 132.61, 131.08, 130.36, 129.95, 129.41, 129.07, 129.04, 128.66, 128.64, 128.21, 127.77, 127.74, 127.61, 126.57, 125.47, 122.23, 106.49, 37.84. HRMS (ESI-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{23}\text{H}_{18}\text{N}_2\text{O}_2$ 355.1447; Found 355.1453.

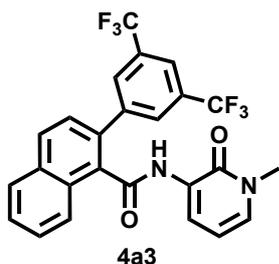
6.2 N-(1-methyl-2-oxo-1,2-dihydropyridin-3-yl)-2-(4-nitrophenyl)-1-naphthamide (4a2)



Purification by flash column chromatography (ethyl acetate/hexane 75/25; v/v) afforded the title compound as a yellow solid. 58.1 mg (from 50 mg **3a**; 81 % yield).

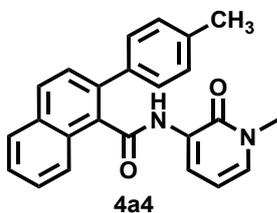
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.61 (s, 1H), 8.51 (dd, $J = 7.46, 1.78$ Hz, 1H), 8.22 (d, $J = 8.59$ Hz, 2H), 8.07 – 8.02 (m, 1H), 8.00 (d, $J = 8.49$ Hz, 1H), 7.93 – 7.88 (m, 1H), 7.74 (d, $J = 8.57$ Hz, 2H), 7.60 – 7.53 (m, 2H), 7.49 (d, $J = 8.51$ Hz, 1H), 6.99 (dd, $J = 6.89, 1.80$ Hz, 1H), 6.24 (t, $J = 7.15$ Hz, 1H), 3.47 (s, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 167.63, 157.50, 147.49, 147.06, 134.61, 133.81, 133.12, 131.55, 130.39, 130.21, 130.00, 129.08, 128.31, 128.09, 127.34, 126.70, 125.58, 123.85, 122.63, 106.51, 37.81. HRMS (ESI-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{23}\text{H}_{17}\text{N}_3\text{O}_4$ 400.1297; Found 400.1245.

6.3 2-(3,5-bis(trifluoromethyl)phenyl)-N-(1-methyl-2-oxo-1,2-dihydropyridin-3-yl)-1-naphthamide (4a3)



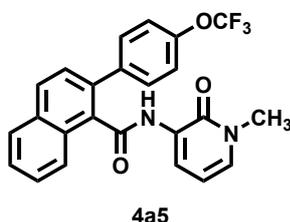
Purification by flash column chromatography (ethyl acetate/hexane 35/65; v/v) afforded the title compound as off-white solid. 50.3 mg (from 50 mg **3a**; 57 % yield). ¹H NMR (400 MHz, CDCl₃) δ 8.59 (s, 1H), 8.45 (d, *J* = 7.42 Hz, 1H), 8.19 – 7.70 (m, 6H), 7.70 – 7.42 (m, 3H), 6.99 (d, *J* = 6.87 Hz, 1H), 6.23 (t, *J* = 7.11 Hz, 1H), 3.50 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 167.45, 157.39, 142.19, 133.93, 133.56, 132.97, 132.27, 131.94, 131.61, 131.49, 131.27, 130.48, 130.02, 129.16, 129.12, 128.74, 128.20, 128.07, 127.33, 127.29, 126.53, 125.42, 124.57, 122.77, 121.86, 121.46, 121.42, 121.38, 106.33, 77.36, 37.71. HRMS (ESI-TOF) *m/z*: [M+H]⁺ Calcd for C₂₅H₁₆F₆N₂O₂ 491.1194; Found 491.1204.

6.4 N-(1-methyl-2-oxo-1,2-dihydropyridin-3-yl)-2-(p-tolyl)-1-naphthamide (**4a4**)



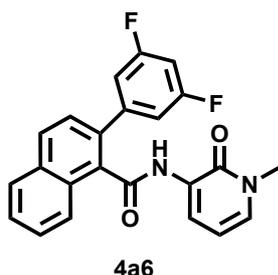
Purification by flash column chromatography (ethyl acetate/hexane 50/50; v/v) afforded the title compound as a pale red solid. 35.3 mg (from 50 mg **3a**; 53 % yield). ¹H NMR (400 MHz, CDCl₃) δ 8.55 (dd, *J* = 7.45, 1.79 Hz, 1H), 8.47 (s, 1H), 8.08 – 7.99 (m, 1H), 7.95 (d, *J* = 8.53 Hz, 1H), 7.91 – 7.84 (m, 1H), 7.56 – 7.44 (m, 5H), 7.18 (d, *J* = 7.79 Hz, 2H), 6.95 (dd, *J* = 6.95, 1.81 Hz, 1H), 6.23 (t, *J* = 7.13 Hz, 1H), 3.48 (s, 3H), 2.33 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 168.65, 157.54, 137.48, 137.36, 137.01, 132.98, 132.47, 131.06, 130.39, 129.86, 129.45, 129.40, 128.89, 128.17, 127.90, 127.53, 126.41, 125.37, 122.30, 106.54, 37.85, 21.33. HRMS (ESI-TOF) *m/z*: [M+H]⁺ Calcd for C₂₄H₂₀N₂O₂ 369.1603; Found 369.1608.

6.5 N-(1-methyl-2-oxo-1,2-dihydropyridin-3-yl)-2-(4-(trifluoromethoxy)phenyl)-1-naphthamide (**4a5**)



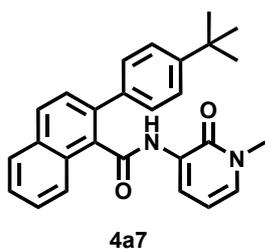
Purification by flash column chromatography (ethyl acetate/hexane 40/60; v/v) afforded the title compound as a grey solid. 22.2 mg (from 50 mg **3a**; 28 % yield). ¹H NMR (400 MHz, CDCl₃) δ 8.60 – 8.37 (m, 2H), 8.18 – 7.86 (m, 3H), 7.70 – 7.48 (m, 5H), 7.30 – 7.21 (m, 2H), 6.98 (d, *J* = 6.90 Hz, 1H), 6.25 (t, *J* = 7.19 Hz, 1H), 3.50 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 168.12, 157.44, 148.91, 139.05, 135.63, 133.43, 132.75, 131.26, 130.48, 130.30, 130.16, 129.19, 128.24, 127.82, 127.27, 126.84, 125.47, 122.27, 121.84, 121.08, 119.28, 106.44, 37.78. HRMS (ESI-TOF) *m/z*: [M+H]⁺ Calcd for C₂₄H₁₇F₃N₂O₃ 439.1270; Found 439.1275.

6.6 2-(3,5-difluorophenyl)-N-(1-methyl-2-oxo-1,2-dihydropyridin-3-yl)-1-naphthamide (4a6)



Purification by flash column chromatography (ethyl acetate/hexane 50/50; v/v) afforded the title compound as a yellow solid. 27.3 mg (from 50 mg **3a**; 38 % yield). ¹H NMR (400 MHz, CDCl₃) δ 8.64 – 8.46 (m, 2H), 8.05 – 7.86 (m, 3H), 7.55 (dd, *J* = 6.48, 3.18 Hz, 2H), 7.48 (d, *J* = 8.50 Hz, 1H), 7.20 – 7.07 (m, 2H), 6.99 (d, *J* = 6.85 Hz, 1H), 6.75 (tt, *J* = 8.94, 2.37 Hz, 1H), 6.25 (t, *J* = 7.14 Hz, 1H), 3.50 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 167.78, 164.23, 164.10, 161.75, 161.62, 143.49, 134.50, 133.46, 132.93, 131.41, 130.25, 130.15, 128.25, 127.95, 127.12, 126.87, 125.52, 122.67, 112.33, 112.25, 112.14, 112.07, 106.60, 103.58, 103.33, 103.08, 37.88. HRMS (ESI-TOF) *m/z*: [M+H]⁺ Calcd for C₂₃H₁₆F₂N₂O₂ 391.1258; Found 391.1260.

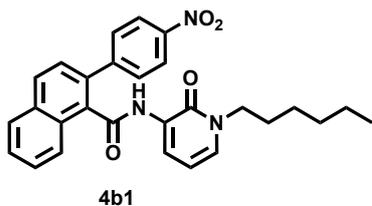
6.7 2-(4-(tert-butyl)phenyl)-N-(1-methyl-2-oxo-1,2-dihydropyridin-3-yl)-1-naphthamide (4a7)



Purification by flash column chromatography (ethyl acetate/hexane 50/50; v/v) afforded the title compound as a brown solid. 24 mg (from 50 mg **3a**; 33 % yield).

¹H NMR (400 MHz, CDCl₃) δ 8.52 (d, *J* = 7.42 Hz, 1H), 8.41 (s, 1H), 8.05 (d, *J* = 7.76 Hz, 1H), 7.95 (d, *J* = 8.61 Hz, 1H), 7.89 (d, *J* = 7.50 Hz, 1H), 7.61 – 7.46 (m, 5H), 7.39 (d, *J* = 8.02 Hz, 2H), 6.92 (d, *J* = 6.79 Hz, 1H), 6.21 (t, *J* = 7.19 Hz, 1H), 3.45 (s, 3H), 1.28 (s, 9H). ¹³C NMR (101 MHz, CDCl₃) δ 168.64, 157.43, 150.56, 137.32, 137.14, 133.02, 132.50, 130.91, 130.45, 129.89, 129.45, 128.70, 128.16, 127.79, 127.52, 126.39, 125.54, 125.39, 122.08, 106.44, 37.75, 34.64, 31.37. HRMS (ESI-TOF) *m/z*: [M+H]⁺ Calcd for C₂₇H₂₆N₂O₂ 411.2073; Found 411.2089.

6.8 N-(1-hexyl-2-oxo-1,2-dihydropyridin-3-yl)-2-(4-nitrophenyl)-1-naphthamide (4b1)

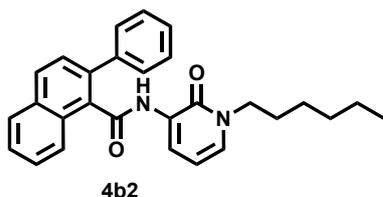


Purification by flash column chromatography (ethyl acetate/hexane 25/75; v/v) afforded the title compound as a yellow solid. 61.7 mg (from 50 mg **3b**; 92 % yield).

¹H NMR (400 MHz, CDCl₃) δ 8.55 – 8.43 (m, 2H), 8.27 – 8.18 (m, 2H), 8.11 – 8.05 (m, 1H), 8.00 (d, *J* = 8.52 Hz, 1H), 7.94 – 7.89 (m, 1H), 7.78 – 7.71 (m, 2H), 7.61 – 7.52 (m, 2H), 7.50

(d, $J = 8.52$ Hz, 1H), 6.96 (dd, $J = 6.93, 1.81$ Hz, 1H), 6.24 (t, $J = 7.13$ Hz, 1H), 3.83 (t, $J = 7.50$ Hz, 2H), 1.63 (t, $J = 7.30$ Hz, 2H), 1.26 (s, 6H), 0.88 – 0.81 (m, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 167.56, 156.90, 147.36, 147.04, 134.54, 133.74, 133.05, 130.80, 130.37, 130.16, 129.98, 129.03, 128.27, 128.05, 127.30, 126.65, 125.60, 123.81, 122.41, 106.40, 50.42, 31.34, 29.08, 26.27, 22.51, 14.03. HRMS (ESI-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{28}\text{H}_{27}\text{N}_3\text{O}_4$ 470.2080; Found 470.2075.

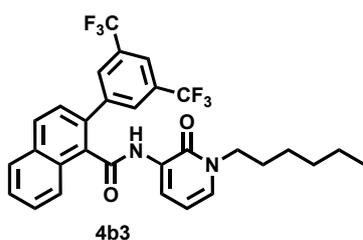
6.9 N-(1-hexyl-2-oxo-1,2-dihydropyridin-3-yl)-2-phenyl-1-naphthamide (4b2)



Purification by flash column chromatography (ethyl acetate/hexane 30/70; v/v) afforded the title compound as a brown solid. 40.7 mg (from 50 mg **3b**; 67 % yield). ^1H

NMR (400 MHz, CDCl_3) δ 8.50 (dd, $J = 7.39, 1.78$ Hz, 1H), 8.44 (s, 1H), 8.11 – 8.04 (m, 1H), 7.96 (d, $J = 8.50$ Hz, 1H), 7.93 – 7.86 (m, 1H), 7.62 – 7.50 (m, 5H), 7.38 (t, $J = 7.56$ Hz, 2H), 7.30 (d, $J = 7.23$ Hz, 1H), 6.92 (dd, $J = 6.90, 1.81$ Hz, 1H), 6.22 (t, $J = 7.12$ Hz, 1H), 3.84 (t, $J = 7.41$ Hz, 2H), 1.65 (p, $J = 7.54$ Hz, 2H), 1.27 (d, $J = 4.22$ Hz, 6H), 0.87 (t, $J = 6.65$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 168.44, 156.97, 140.36, 137.11, 133.20, 132.61, 130.39, 130.33, 129.94, 129.46, 129.07, 128.61, 128.18, 127.71, 127.58, 126.53, 125.54, 122.04, 106.41, 50.39, 31.46, 30.45, 29.83, 29.13, 26.31, 22.58, 14.10. HRMS (ESI-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{28}\text{H}_{28}\text{N}_2\text{O}_2$ 425.2229; Found 425.2233.

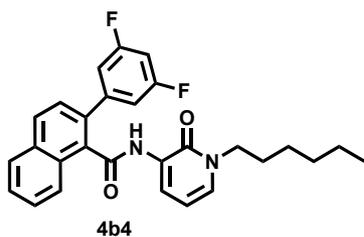
6.10 2-(3,5-bis(trifluoromethyl)phenyl)-N-(1-hexyl-2-oxo-1,2-dihydropyridin-3-yl)-1-naphthamid (4b3)



Purification by flash column chromatography (ethyl acetate/hexane 25/75; v/v) afforded the title compound as a yellow solid. 27.3 mg (from 50 mg **3b**; 34 % yield). ^1H NMR

(400 MHz, CDCl_3) δ 8.59 (s, 1H), 8.44 (d, $J = 7.44$ Hz, 1H), 8.06 (q, $J = 8.75$ Hz, 4H), 7.93 (d, $J = 4.69$ Hz, 1H), 7.82 (s, 1H), 7.63 – 7.47 (m, 3H), 6.97 (d, $J = 6.95$ Hz, 1H), 6.24 (t, $J = 7.24$ Hz, 1H), 3.87 (t, $J = 7.47$ Hz, 2H), 1.70 – 1.61 (m, 2H), 1.28 (d, $J = 7.93$ Hz, 6H), 0.88 (d, $J = 5.91$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 167.47, 156.99, 142.35, 134.04, 133.73, 133.09, 132.36, 132.03, 131.70, 130.87, 130.60, 130.15, 129.27, 129.23, 128.89, 128.30, 128.16, 127.42, 126.60, 125.61, 124.68, 122.61, 121.96, 121.46, 106.34, 50.46, 31.40, 29.82, 29.02, 26.26, 22.52, 14.04. HRMS (ESI-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{30}\text{H}_{26}\text{F}_6\text{N}_2\text{O}_2$ 561.1977; Found 561.1985.

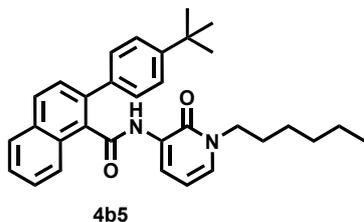
6.11 2-(3,5-difluorophenyl)-N-(1-hexyl-2-oxo-1,2-dihydropyridin-3-yl)-1-naphthamide (4b4)



Purification by flash column chromatography (ethyl acetate/hexane 25/75; v/v) afforded the title compound as a yellow solid. 33.9 mg (from 50 mg **3b**; 51 % yield). ¹H NMR (400 MHz, CDCl₃) δ 8.68 – 8.43 (m, 2H), 8.10 – 7.85 (m,

3H), 7.61 – 7.43 (m, 3H), 7.13 (dt, *J* = 6.58, 2.14 Hz, 2H), 6.97 (dd, *J* = 6.88, 1.81 Hz, 1H), 6.74 (tt, *J* = 8.88, 2.37 Hz, 1H), 6.24 (t, *J* = 7.12 Hz, 1H), 3.86 (t, *J* = 7.43 Hz, 2H), 1.67 (t, *J* = 7.29 Hz, 2H), 1.28 (s, 6H), 0.93 – 0.81 (m, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 167.58, 164.12, 163.99, 161.64, 161.51, 156.91, 143.43, 134.42, 133.39, 132.83, 130.56, 130.13, 130.07, 129.13, 128.13, 127.81, 126.98, 126.72, 125.49, 122.26, 112.24, 111.98, 106.31, 103.39, 103.14, 102.89, 50.30, 31.32, 29.01, 26.20, 22.44, 13.97. HRMS (ESI-TOF) *m/z*: [M+H]⁺ Calcd for C₂₈H₂₆F₂N₂O₂ 461.2041; Found 461.2048.

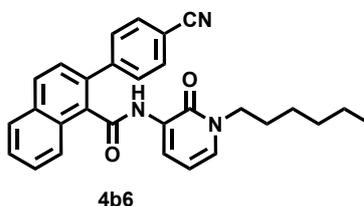
6.12 2-(4-(tert-butyl)phenyl)-N-(1-hexyl-2-oxo-1,2-dihydropyridin-3-yl)-1-naphthamide (4b5)



Purification by flash column chromatography (ethyl acetate/hexane 20/80; v/v) afforded the title compound as a brown solid. 11.2 mg (from 50 mg **3b**; 16 % yield).

¹H NMR (400 MHz, CDCl₃) δ 8.77 (dd, *J* = 7.47, 1.78 Hz, 1H), 8.66 (s, 1H), 8.37 – 8.31 (m, 1H), 8.22 (d, *J* = 8.52 Hz, 1H), 8.16 (dd, *J* = 7.02, 2.28 Hz, 1H), 7.82 (d, *J* = 8.36 Hz, 2H), 7.77 (d, *J* = 8.02 Hz, 2H), 7.65 (d, *J* = 8.15 Hz, 2H), 7.53 (s, 1H), 7.19 (dd, *J* = 6.87, 1.81 Hz, 1H), 6.49 (t, *J* = 7.12 Hz, 1H), 4.10 (t, *J* = 7.51 Hz, 2H), 1.93 – 1.88 (m, 2H), 1.55 (s, 9H), 1.52 (s, 6H), 1.15 – 1.11 (m, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 168.60, 156.93, 150.57, 137.36, 137.18, 133.06, 132.54, 130.48, 130.17, 129.91, 129.53, 128.73, 128.18, 127.78, 127.52, 126.39, 125.53, 125.48, 121.85, 106.38, 50.36, 34.65, 31.46, 31.40, 30.45, 29.84, 29.21, 26.37, 22.59, 14.10. HRMS (ESI-TOF) *m/z*: [M+H]⁺ Calcd for C₂₃H₁₇BrN₂O₂ 481.2855; Found 481.2869.

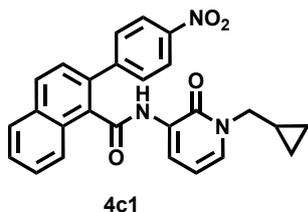
6.13 2-(4-cyanophenyl)-N-(1-hexyl-2-oxo-1,2-dihydropyridin-3-yl)-1-naphthamide (4b6)



Purification by flash column chromatography (ethyl acetate/hexane 35/65; v/v) afforded the title compound as a light brown solid. 14.1 mg (from 50 mg **3b**; 22 % yield).

^1H NMR (400 MHz, CDCl_3) δ 8.51 – 8.39 (m, 2H), 8.10 – 8.03 (m, 1H), 8.00 (d, $J = 8.46$ Hz, 1H), 7.95 – 7.89 (m, 1H), 7.68 (d, $J = 2.94$ Hz, 4H), 7.61 – 7.54 (m, 2H), 7.51 – 7.45 (m, 1H), 6.98 (d, $J = 6.73$ Hz, 1H), 6.24 (t, $J = 7.12$ Hz, 1H), 3.86 (t, $J = 7.52$ Hz, 2H), 1.66 (t, $J = 7.32$ Hz, 2H), 1.27 (d, $J = 11.66$ Hz, 6H), 0.86 (t, $J = 6.36$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 167.53, 156.83, 144.99, 134.88, 133.54, 132.91, 132.29, 130.64, 130.29, 130.12, 129.70, 129.00, 128.17, 127.92, 127.13, 126.59, 125.51, 122.16, 111.46, 106.29, 50.35, 31.28, 29.04, 26.21, 22.45, 13.95. HRMS (ESI-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{29}\text{H}_{27}\text{N}_3\text{O}_2$ 450.2182; Found 450.2175.

6.14 N-(1-(cyclopropylmethyl)-2-oxo-1,2-dihydropyridin-3-yl)-2-(4-nitrophenyl)-1-naphthamide (4c1)

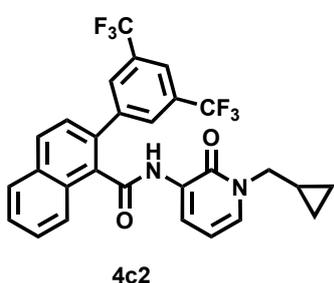


Purification by flash column chromatography (DCM 100%) afforded the title compound as a red solid. 19.9 mg (from 50 mg **3c**; 29 % yield).

^1H NMR (400 MHz, CDCl_3) δ 8.66 (d, $J = 7.38$ Hz, 1H), 8.37 (d, $J = 7.78$ Hz, 2H), 8.27 – 8.19 (m, 1H), 8.15 (d, $J = 8.60$ Hz, 1H), 8.10 – 8.02 (m, 1H), 7.89 (d, $J = 8.13$ Hz, 2H), 7.76 – 7.68 (m, 2H), 7.65 (d, $J = 8.46$ Hz, 1H), 7.25 (d, $J = 6.71$ Hz, 1H), 6.35 (s, 1H), 3.91 (s, 2H), 1.41 (d, $J = 11.23$ Hz, 2H), 1.02 (t, $J = 6.88$ Hz, 1H), 0.71 (d, $J = 7.17$ Hz, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ 167.43, 147.36, 146.98, 134.54, 133.71, 133.02, 130.28, 130.20, 130.16, 129.93, 129.89, 128.18, 127.96, 127.21, 126.55, 125.56, 124.05, 123.71, 122.29, 106.44, 53.98, 10.45, 3.87. HRMS (ESI-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{26}\text{H}_{21}\text{N}_3\text{O}_4$ 440.1610; Found 440.1595.

6.16 2-(3,5-bis(trifluoromethyl)phenyl)-N-(1-(cyclopropylmethyl)-2-oxo-1,2-dihydropyridin-3-yl)-1-naphthamide (4c2)

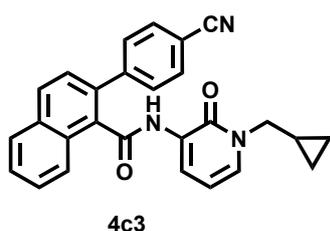
Purification by flash column chromatography (DCM 100%) afforded the title compound as a yellow solid. 32.2 mg (from 50 mg **3c**; 39 % yield).



^1H NMR (400 MHz, CDCl_3) δ 8.61 (s, 1H), 8.45 (dd, $J = 7.39$, 1.79 Hz, 1H), 8.11 – 8.00 (m, 4H), 7.97 – 7.90 (m, 1H), 7.81 (s, 1H), 7.64 – 7.49 (m, 3H), 7.10 (dd, $J = 6.99$, 1.80 Hz, 1H), 6.26 (t, $J = 7.14$ Hz, 1H), 3.76 (d, $J = 7.14$ Hz, 2H), 1.16 (ddt, $J =$

10.56, 7.61, 3.83 Hz, 1H), 0.63 – 0.52 (m, 2H), 0.33 (q, $J = 5.35$ Hz, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ 167.39, 157.06, 142.24, 133.96, 133.61, 132.99, 132.25, 131.92, 131.58, 131.25, 130.47, 130.40, 130.06, 129.17, 129.13, 128.75, 128.18, 128.04, 127.31, 126.51, 125.52, 124.58, 122.71, 121.86, 121.38, 106.27, 54.12, 10.38, 3.86. HRMS (ESI-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{28}\text{H}_{20}\text{F}_6\text{N}_2\text{O}_2$ 531.1507; Found 531.1523.

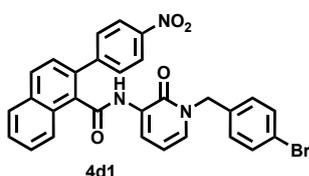
6.17 2-(4-cyanophenyl)-N-(1-(cyclopropylmethyl)-2-oxo-1,2-dihydropyridin-3-yl)-1-naphthamide (4c3)



Purification by flash column chromatography (DCM 100%) afforded the title compound as a colourless crystalline solid. 15.6 mg (from 50 mg **3c**; 23 % yield).

^1H NMR (400 MHz, CDCl_3) δ 8.54 – 8.37 (m, 2H), 8.13 – 8.04 (m, 1H), 8.01 (d, $J = 8.50$ Hz, 1H), 7.96 – 7.88 (m, 1H), 7.78 – 7.63 (m, 4H), 7.62 – 7.53 (m, 2H), 7.49 (d, $J = 8.47$ Hz, 1H), 6.27 (t, $J = 7.14$ Hz, 1H), 4.12 (q, $J = 7.13$ Hz, 1H), 3.75 (d, $J = 7.13$ Hz, 2H), 1.14 (d, $J = 7.19$ Hz, 1H), 0.66 – 0.54 (m, 2H), 0.34 (t, $J = 5.21$ Hz, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ 167.64, 157.11, 145.13, 135.02, 133.67, 133.04, 132.42, 130.43, 130.41, 130.27, 129.82, 129.08, 128.29, 128.04, 127.25, 126.71, 125.65, 122.40, 118.93, 111.57, 106.38, 60.52, 54.23, 31.72, 29.83, 22.78, 21.18, 14.33, 14.25, 10.55, 4.03. HRMS (ESI-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{27}\text{H}_{21}\text{N}_3\text{O}_2$ 420.1712; Found 420.1721.

6.18 N-(1-(4-bromobenzyl)-2-oxo-1,2-dihydropyridin-3-yl)-2-(4-nitrophenyl)-1-naphthamide (4d1)

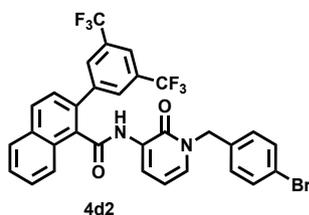


Purification by flash column chromatography (ethyl acetate/hexane 45/55; v/v) afforded the title compound as a yellow solid. 61.7 mg (from 50 mg **3d**; 96 % yield).

^1H NMR (400 MHz, CDCl_3) δ 8.54 – 8.40 (m, 2H), 8.24 (d, $J = 8.49$ Hz, 2H), 8.10 – 7.99 (m, 2H), 7.97 – 7.89 (m, 1H), 7.75 (d, $J = 8.39$ Hz, 2H), 7.62 – 7.54 (m, 2H), 7.51 (d, $J = 8.49$ Hz, 1H), 7.43 (d, $J = 8.11$ Hz, 2H), 7.07 (d, $J = 8.15$ Hz, 2H), 6.99 (dd, $J = 6.94, 1.77$ Hz, 1H), 6.26 (t, $J = 7.17$ Hz, 1H), 4.99 (s, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ 167.63, 157.13, 147.44, 147.03, 134.73, 134.60, 133.64, 133.09, 132.19, 130.49, 130.32, 130.16, 130.03, 129.82, 129.34, 128.34, 128.14, 127.39, 126.66, 125.57, 123.86, 122.60,

122.51, 107.06, 52.44. HRMS (ESI-TOF) m/z : $[M+H]^+$ Calcd for $C_{29}H_{20}BrN_3O_4$ 554.0715; Found 554.0703.

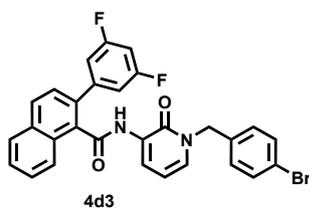
6.19 2-(3,5-bis(trifluoromethyl)phenyl)-N-(1-(4-bromobenzyl)-2-oxo-1,2-dihydropyridin-3-yl)-1-naphthamide (4b2)



Purification by flash column chromatography (ethyl acetate/hexane 35/65; v/v) afforded the title compound as a yellow solid. 106.5 mg (from 100 mg **3d**; 72 % yield).

1H NMR (400 MHz, $CDCl_3$) δ 8.53 (s, 1H), 8.46 (d, $J = 7.36$ Hz, 1H), 8.11 – 8.01 (m, 4H), 7.97 – 7.90 (m, 1H), 7.80 (s, 1H), 7.64 – 7.49 (m, 3H), 7.45 (d, $J = 7.97$ Hz, 2H), 7.09 (d, $J = 7.99$ Hz, 2H), 7.01 (d, $J = 7.59$ Hz, 1H), 6.26 (t, $J = 7.15$ Hz, 1H), 5.01 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.40, 142.19, 134.72, 133.76, 133.65, 132.99, 132.03, 131.94, 131.61, 130.59, 130.27, 130.02, 129.70, 129.17, 129.12, 128.23, 128.11, 127.37, 126.48, 125.46, 124.55, 122.71, 122.33, 121.84, 121.39, 106.91, 52.35. HRMS (ESI-TOF) m/z : $[M+H]^+$ Calcd for $C_{31}H_{19}BrF_6N_2O_2$ 645.0612; Found. 645.0594

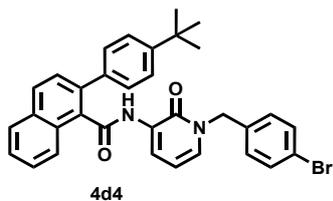
6.20 N-(1-(4-bromobenzyl)-2-oxo-1,2-dihydropyridin-3-yl)-2-(3,5-difluorophenyl)-1-naphthamide (4d3)



Purification by flash column chromatography (ethyl acetate/hexane 40/60; v/v) afforded the title compound as a yellow solid. 38.0 mg (from 50 mg **3d**; 60 % yield).

1H NMR (400 MHz, $CDCl_3$) δ 8.56 – 8.42 (m, 2H), 8.08 – 8.01 (m, 1H), 7.98 (d, $J = 8.55$ Hz, 1H), 7.94 – 7.86 (m, 1H), 7.61 – 7.52 (m, 2H), 7.46 (dd, $J = 11.79, 8.26$ Hz, 3H), 7.11 (t, $J = 6.76$ Hz, 4H), 7.00 (dd, $J = 6.92, 1.78$ Hz, 1H), 6.77 – 6.68 (m, 1H), 6.27 (t, $J = 7.14$ Hz, 1H), 5.02 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.63, 164.12, 163.99, 161.64, 161.51, 157.09, 143.38, 143.29, 134.79, 134.49, 133.22, 132.83, 132.04, 130.23, 130.07, 130.04, 129.78, 129.40, 128.17, 127.87, 127.03, 126.70, 125.44, 122.49, 122.32, 112.24, 112.17, 112.05, 111.98, 106.98, 103.42, 103.17, 102.92, 52.33. HRMS (ESI-TOF) m/z : $[M]^+$ Calcd for $C_{29}H_{19}BrF_2N_2O_2$ 545.0676; Found 545.0661.

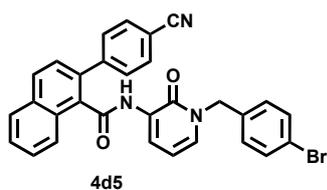
6.21 N-(1-(4-bromobenzyl)-2-oxo-1,2-dihydropyridin-3-yl)-2-(4-(tert-butyl)phenyl)-1-naphthamide (4d4)



Purification by flash column chromatography (ethyl acetate/hexane 35/65; v/v) afforded the title compound as a yellow solid. 17.8 mg (from 50 mg **3d**; 27 % yield).

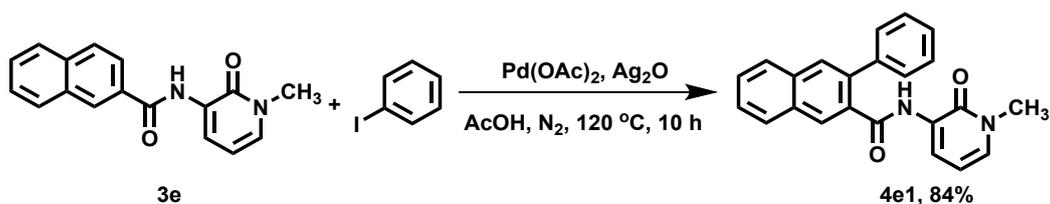
^1H NMR (400 MHz, CDCl_3) δ 8.53 (dd, $J = 7.39, 1.78$ Hz, 1H), 8.38 (s, 1H), 8.12 – 8.03 (m, 1H), 7.95 (d, $J = 8.52$ Hz, 1H), 7.89 (dd, $J = 6.74, 2.47$ Hz, 1H), 7.59 – 7.47 (m, 5H), 7.41 (dd, $J = 11.11, 8.15$ Hz, 4H), 7.08 (d, $J = 8.12$ Hz, 2H), 6.93 (dd, $J = 7.05, 1.83$ Hz, 1H), 6.23 (t, $J = 7.15$ Hz, 1H), 4.98 (s, 2H), 1.28 (s, 9H). ^{13}C NMR (101 MHz, CDCl_3) δ 168.55, 157.01, 150.52, 137.19, 137.03, 134.86, 132.80, 132.40, 132.03, 130.30, 129.86, 129.74, 129.66, 129.58, 128.62, 128.09, 127.67, 127.45, 126.32, 125.43, 125.27, 122.26, 121.96, 106.91, 52.06, 34.54, 31.28. HRMS (ESI-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{23}\text{H}_{17}\text{BrN}_2\text{O}_2$ 565.1491; Found 565.1468.

6.22 N-(1-(4-bromobenzyl)-2-oxo-1,2-dihydropyridin-3-yl)-2-(4-cyanophenyl)-1-naphthamide (4d5)



Purification by flash column chromatography (ethyl acetate/hexane 50/50; v/v) afforded the title compound as a light orange solid. 52.2 mg (from 50 mg **3d**; 85 % yield). ^1H NMR (400 MHz, CDCl_3) δ 8.51 (dd, $J = 7.45, 1.80$ Hz, 1H), 8.43 (s, 1H), 8.10 – 8.03 (m, 1H), 7.99 (d, $J = 8.51$ Hz, 1H), 7.96 – 7.88 (m, 1H), 7.82 (d, $J = 8.08$ Hz, 2H), 7.66 (d, $J = 7.99$ Hz, 2H), 7.59 – 7.54 (m, 2H), 7.51 (d, $J = 8.44$ Hz, 1H), 7.43 (d, $J = 8.30$ Hz, 2H), 7.06 (d, $J = 8.16$ Hz, 2H), 6.96 (dd, $J = 7.01, 1.82$ Hz, 1H), 6.25 (t, $J = 7.18$ Hz, 1H), 4.98 (s, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ 169.02, 167.96, 157.02, 144.01, 135.67, 134.70, 133.16, 132.73, 132.30, 132.07, 130.15, 130.00, 129.69, 129.40, 129.23, 128.16, 127.77, 127.66, 127.05, 126.87, 125.39, 122.36, 122.29, 106.99, 52.26. HRMS (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{30}\text{H}_{20}\text{BrN}_3\text{O}_2$ 533.0739; Found 534.089.

7. Experimental procedure for the synthesis of N-(1-methyl-2-oxo-1,2-dihydropyridin-3-yl)-3-phenyl-2-naphthamide (4e1)

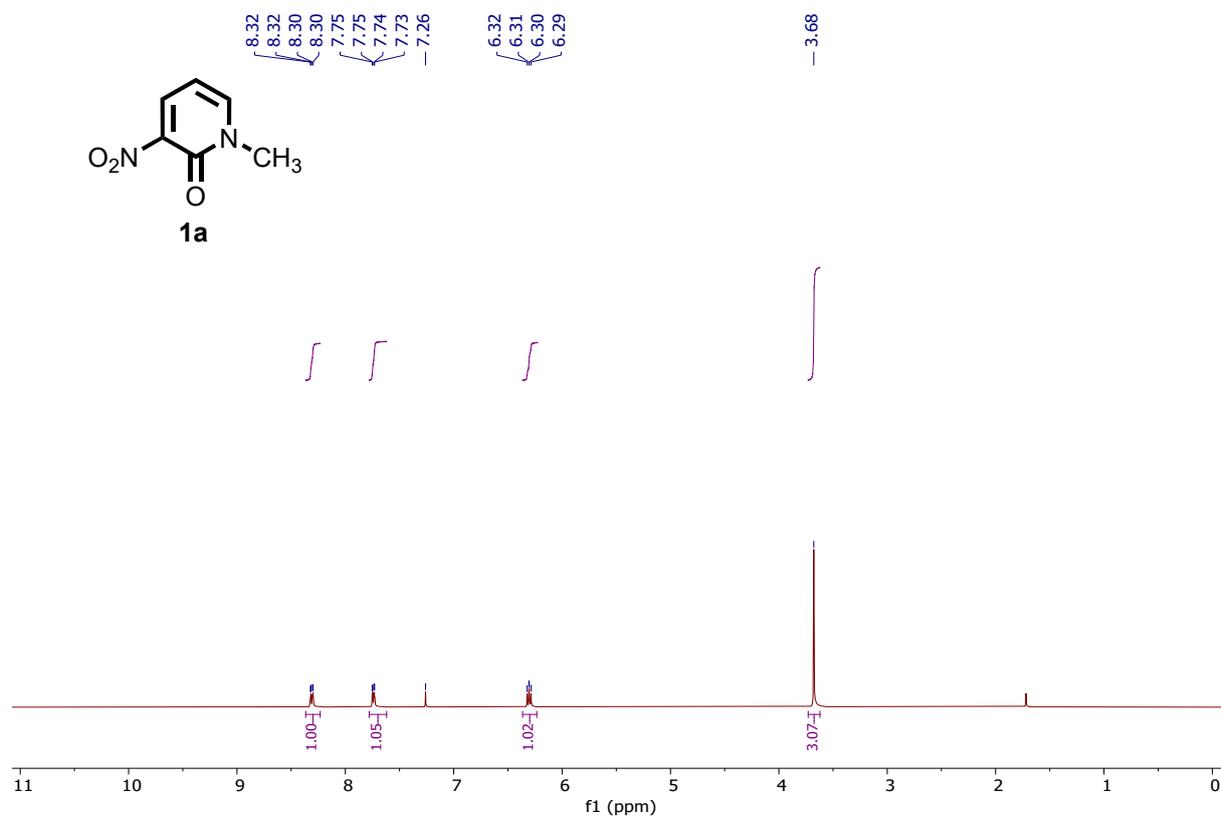


In a dry Schlenk reaction tube, Pd(OAc)₂ (8.06 mg, 10 mol%) in AcOH (2 mL) was taken and purged with nitrogen. **3e** (100 mg, 0.36 mmol), Ag₂O (166.53 mg, 0.72 mmol) and iodobenzene (80.11 mg, 0.72 mmol) gradually added to it under nitrogen. It was further allowed to heat at 120 °C and stirred for 10 h under an atmosphere of nitrogen. The progress of the reaction was monitored by TLC. Cold water was added, and the reaction mixture was extracted with ethyl acetate (15 mL x 3). The combined organic layers washed with brine and dried over anhydrous MgSO₄. The solvent was removed under reduced pressure. The residue was purified by flash column chromatography on silica gel cartridge silica gel (230-400 mesh cartridge) eluting with 90-100 % DCM in hexane to give the N-(1-methyl-2-oxo-1,2-dihydropyridin-3-yl)-3-phenyl-2-naphthamide (**4e1**) as a light orange solid. 52.2 mg (from 50 mg **3e**; 85 % yield).

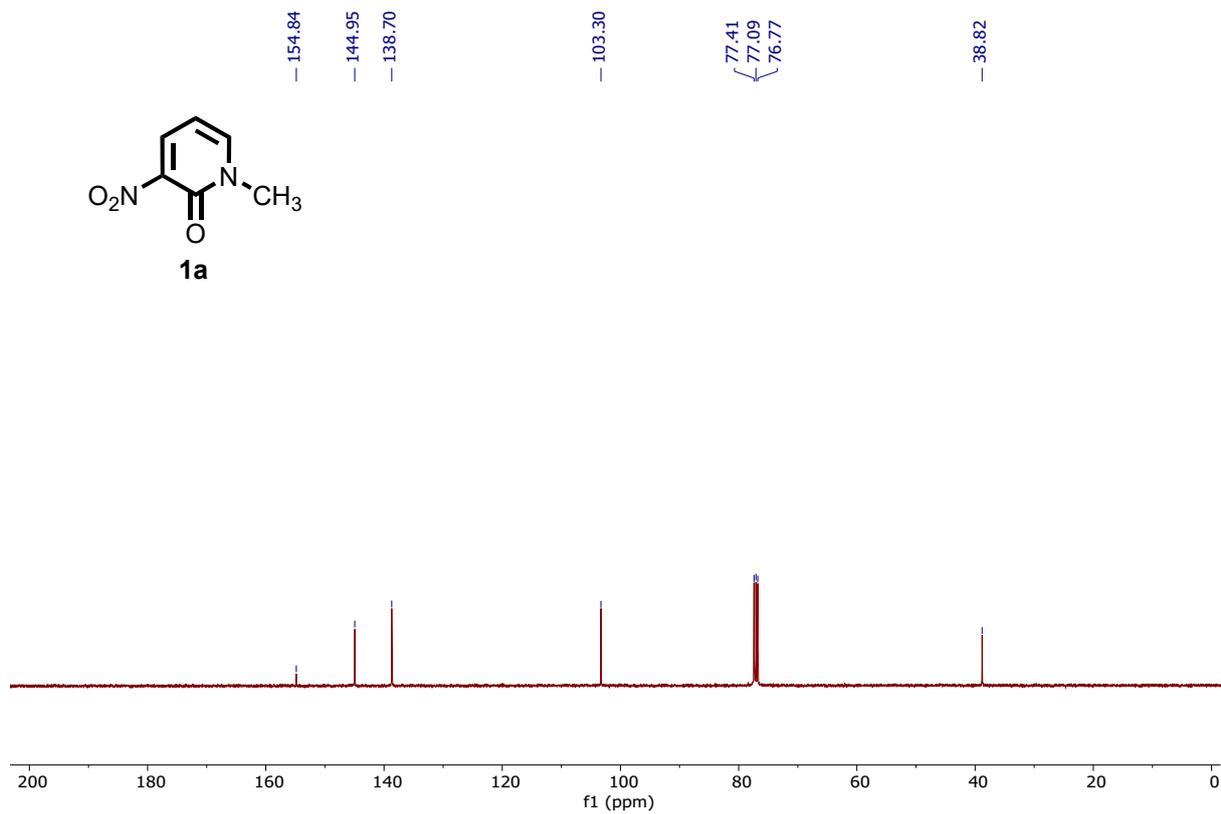
¹H NMR (400 MHz, CDCl₃) δ 8.67 (s, 1H), 8.43 (dd, *J* = 7.42, 1.81 Hz, 1H), 8.22 (s, 1H), 7.96 – 7.83 (m, 3H), 7.63 – 7.49 (m, 4H), 7.41 (t, *J* = 7.47 Hz, 2H), 7.34 (t, *J* = 7.44 Hz, 1H), 6.94 (dd, *J* = 6.90, 1.86 Hz, 1H), 6.20 (t, *J* = 7.14 Hz, 1H), 3.51 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 168.24, 157.53, 140.18, 137.36, 134.04, 133.97, 131.77, 130.76, 129.83, 129.41, 129.34, 128.88, 128.84, 128.60, 128.56, 128.41, 127.87, 127.59, 126.86, 122.07, 106.51, 37.80. HRMS (ESI-TOF) *m/z*: [M+H]⁺ Calcd for C₂₃H₁₈N₂O₂ 355.1447; Found 355.1433.

8. ^1H NMR and ^{13}C NMR spectra

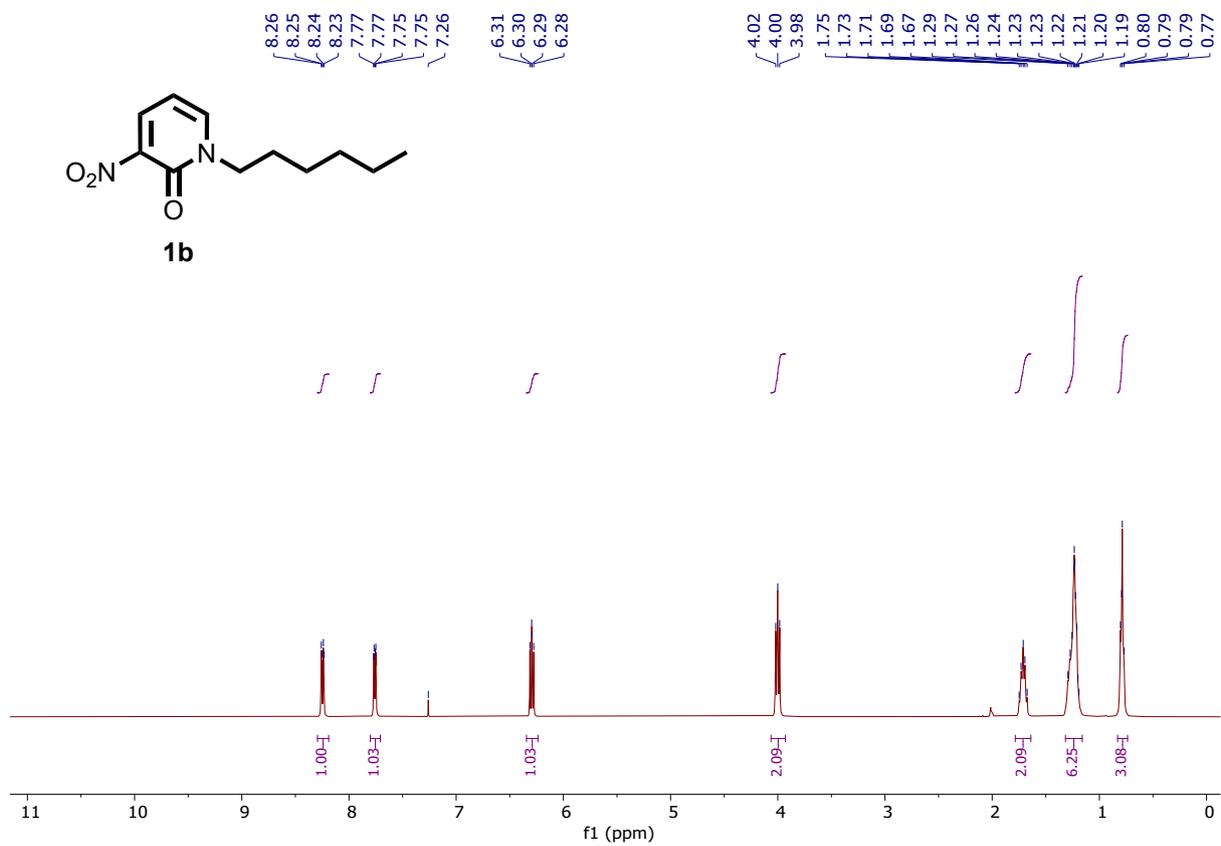
^1H NMR of **1a** in CDCl_3 (400MHz)



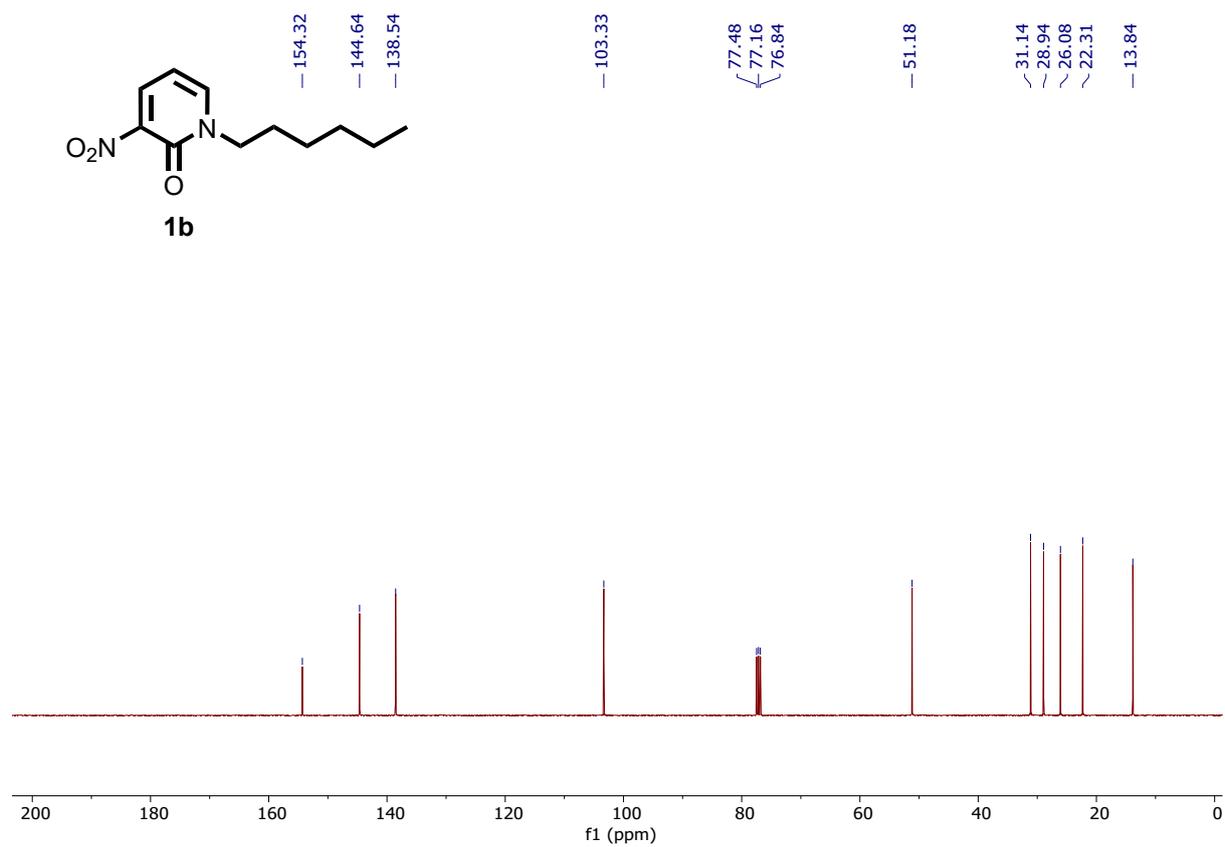
^{13}C NMR of **1a** in CDCl_3 (400MHz)



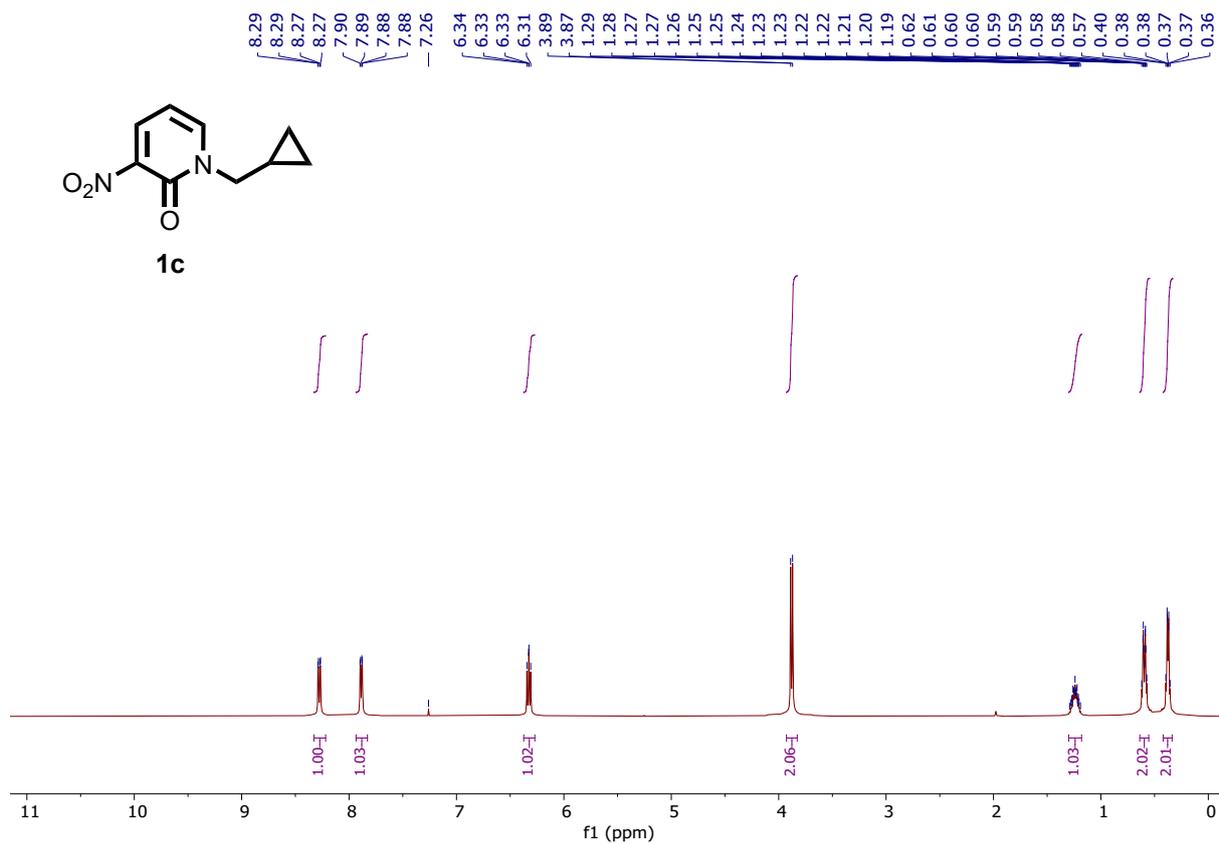
¹H NMR of **1b** in CDCl₃ (400MHz)



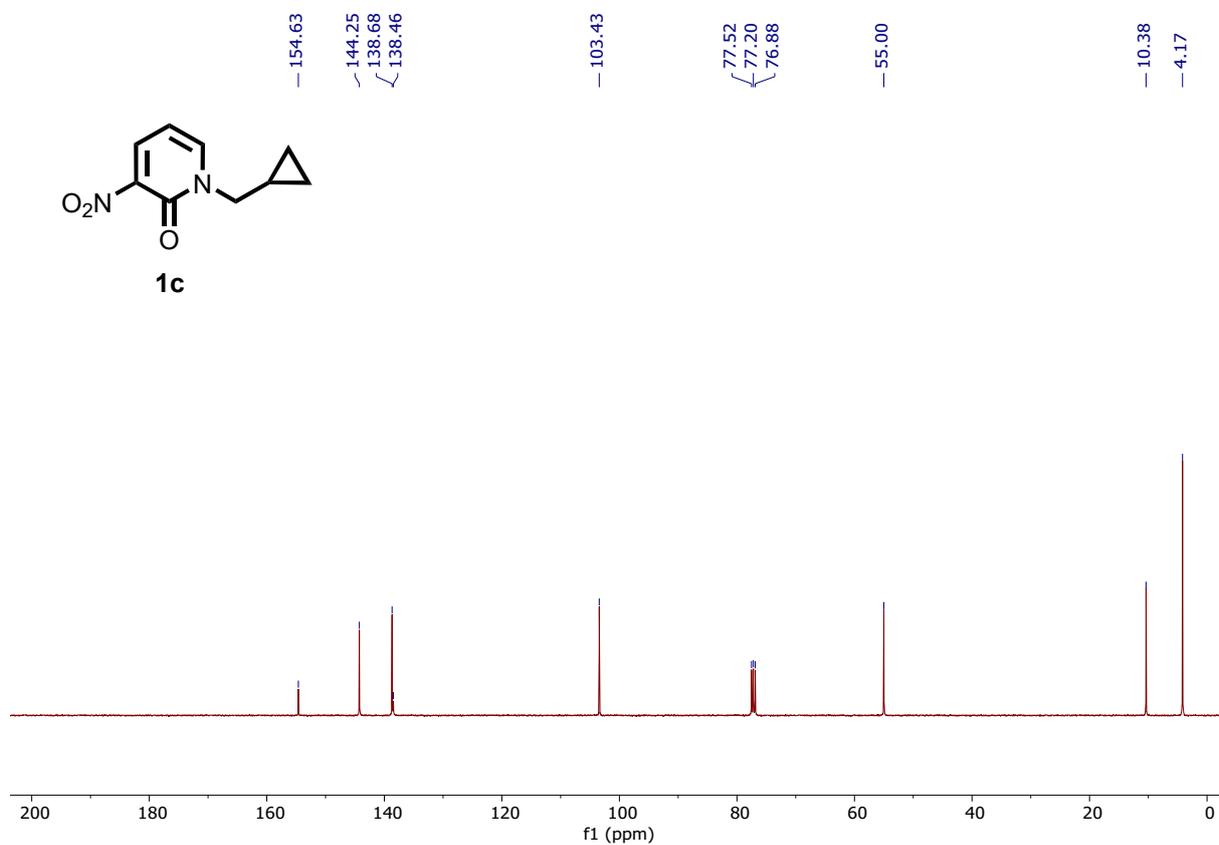
^{13}C NMR of **1b** in CDCl_3 (400MHz)



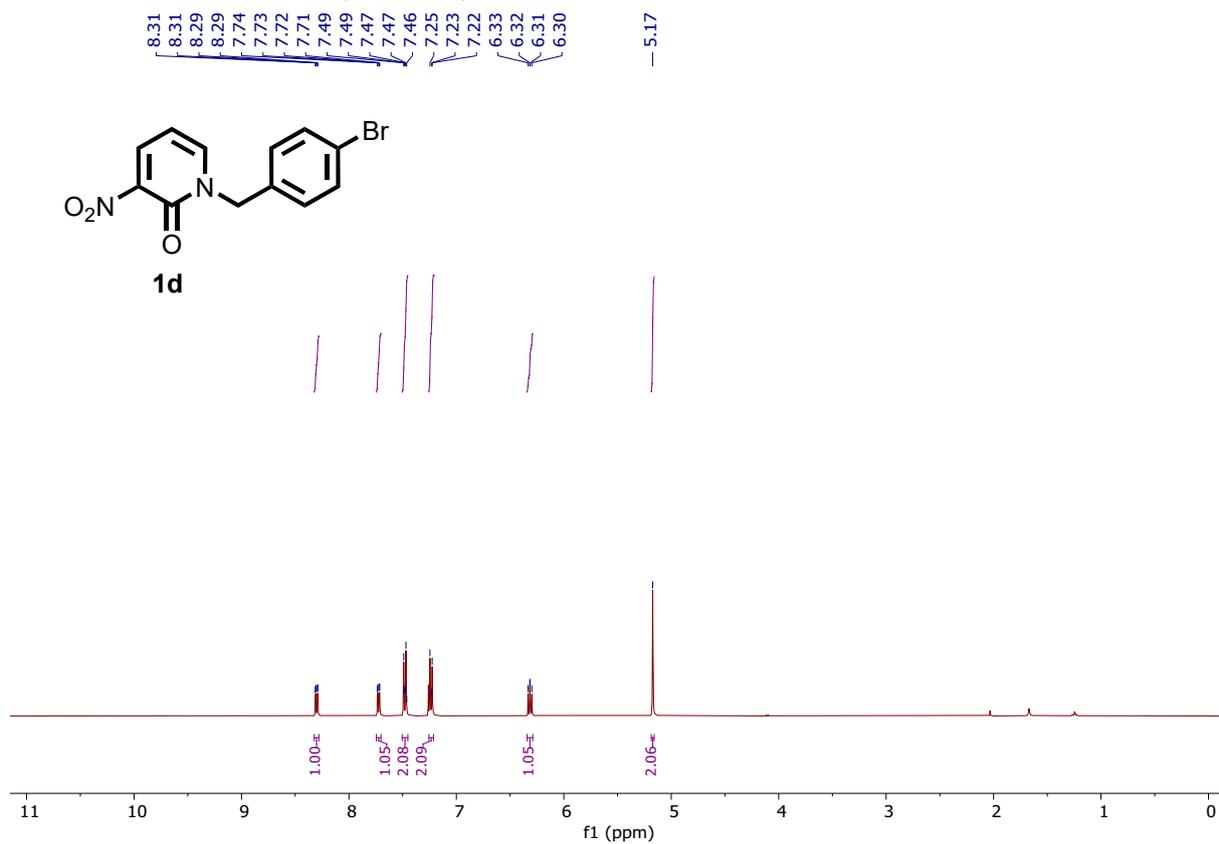
^1H NMR of **1c** in CDCl_3 (400MHz)



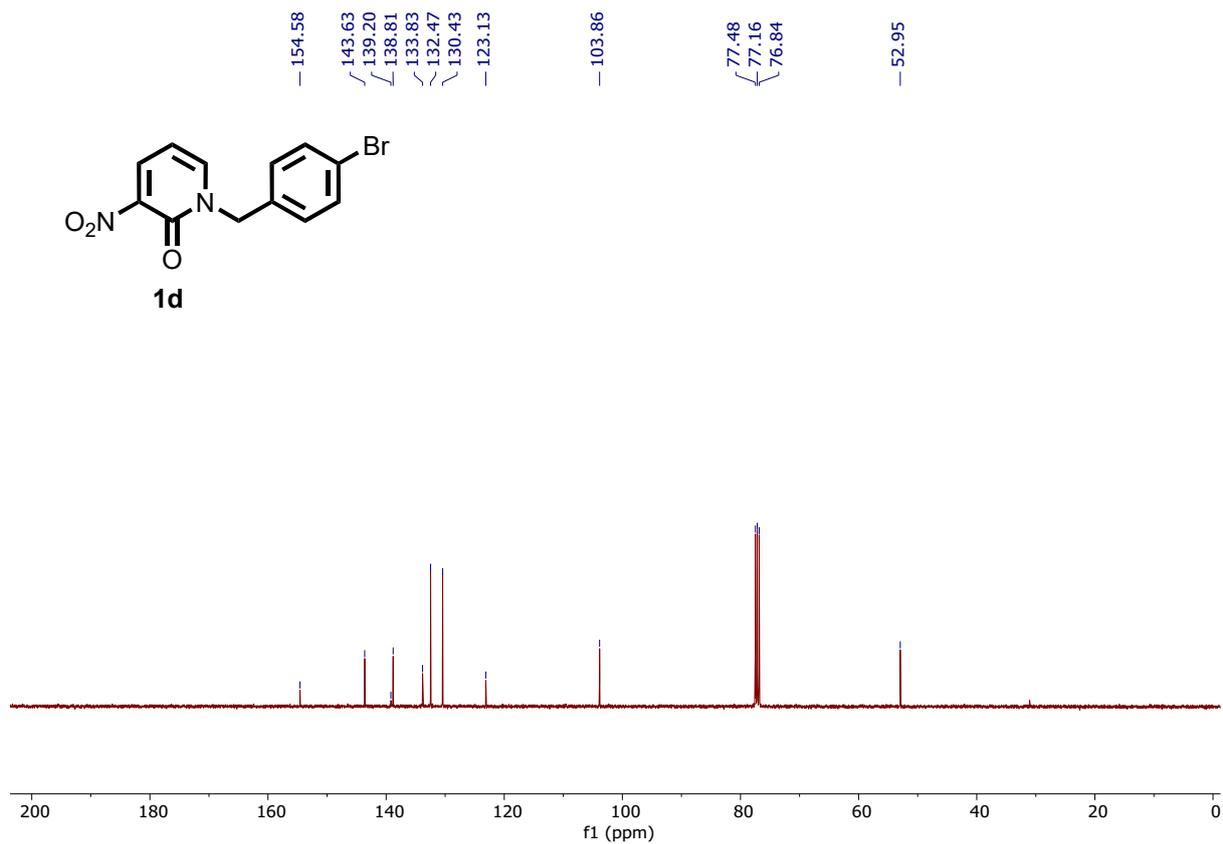
¹³C NMR of **1c** in CDCl₃ (400MHz)



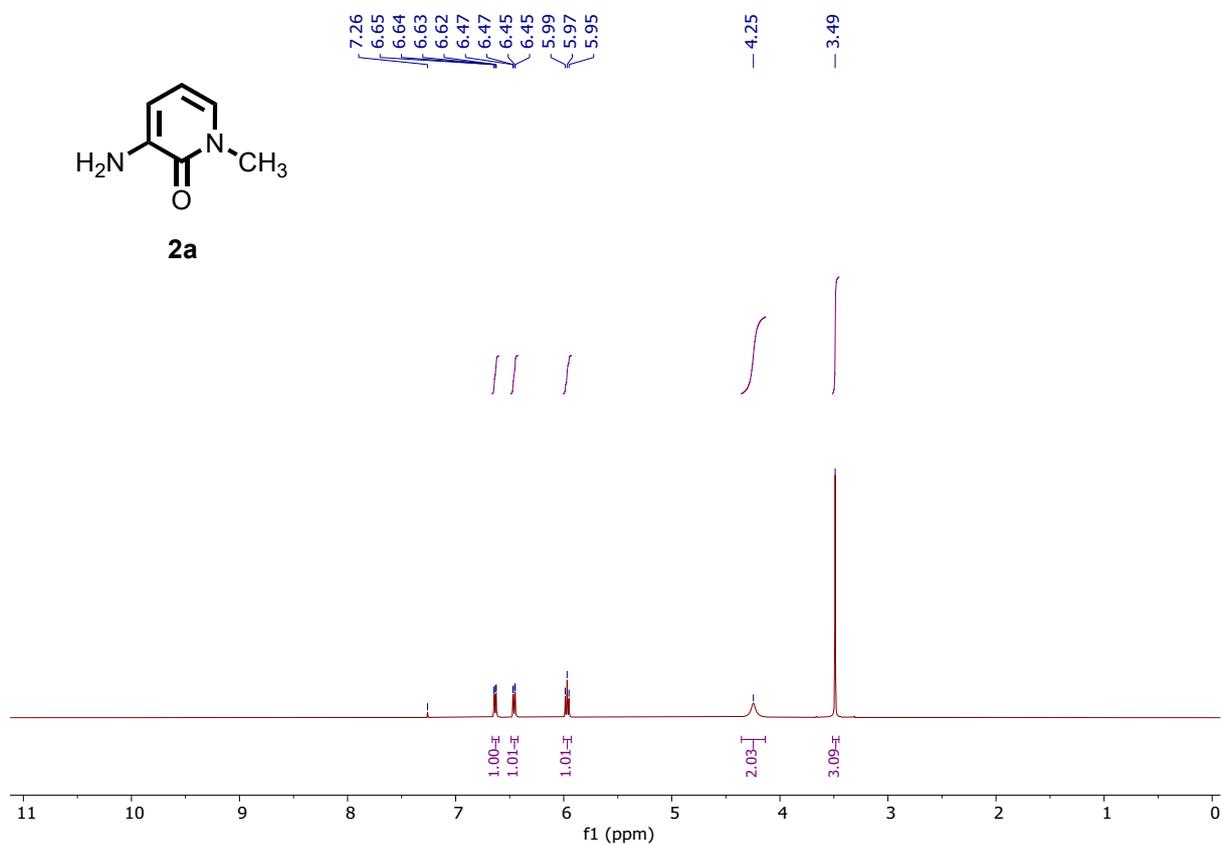
¹H NMR of **1d** in CDCl₃ (400MHz)



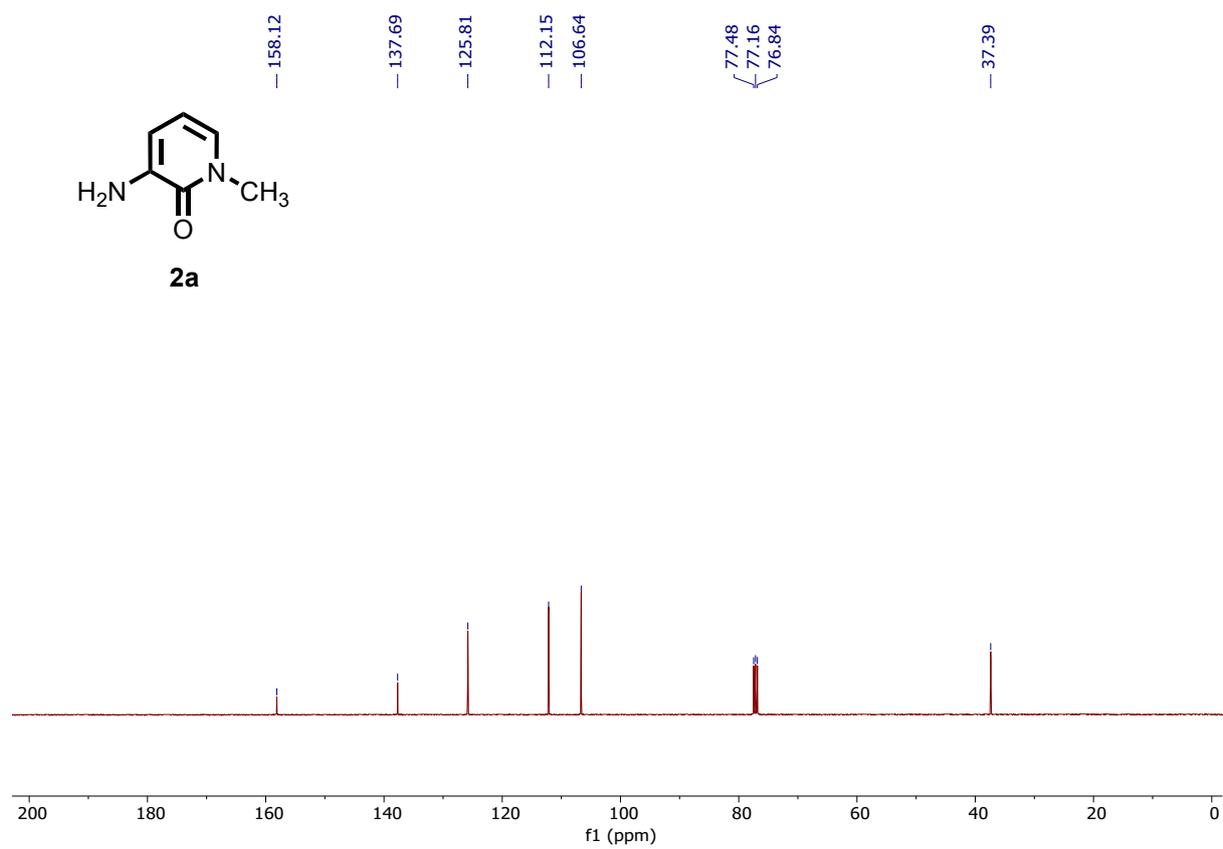
¹³C NMR of **1d** in CDCl₃ (400MHz)



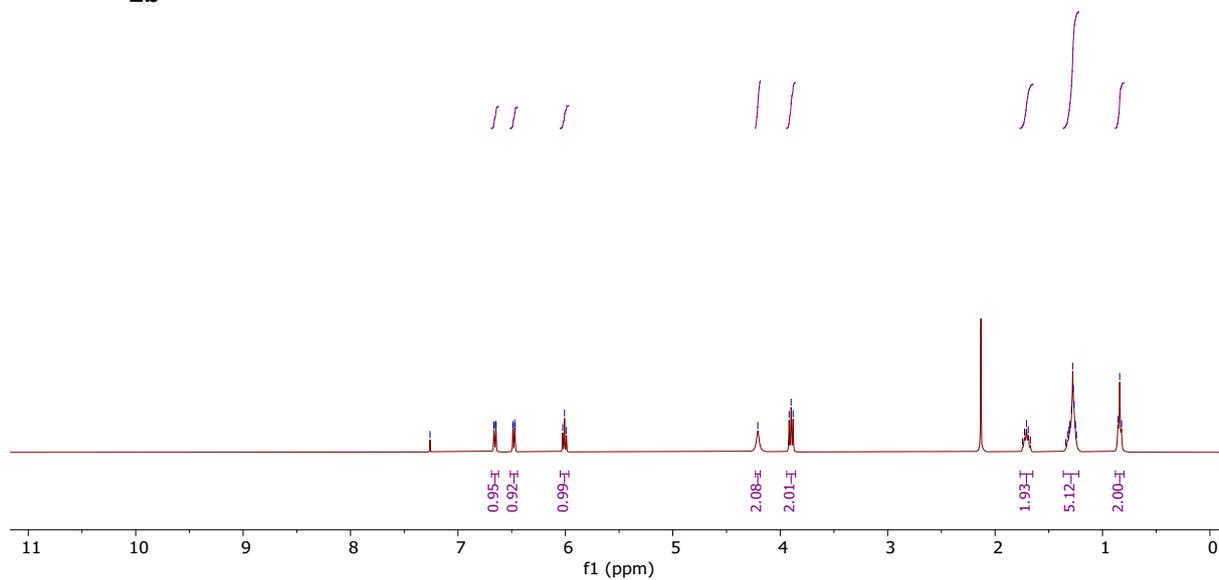
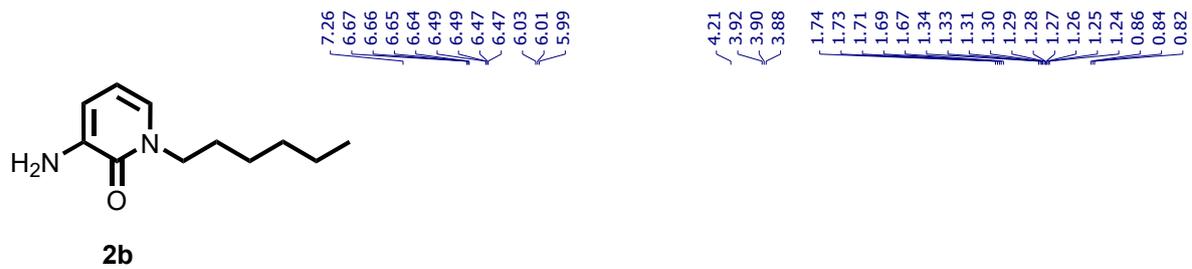
¹H NMR of **2a** in CDCl₃ (400MHz)



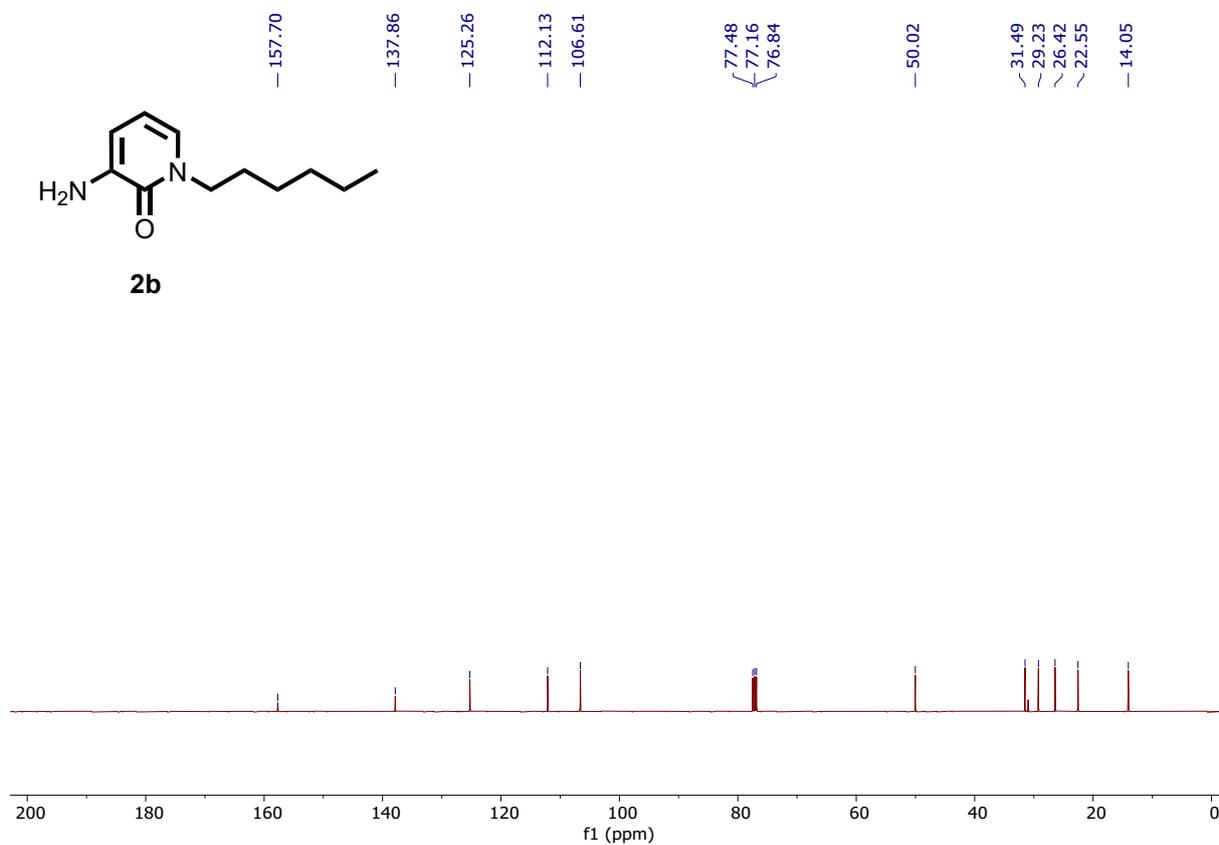
^{13}C NMR of **2a** in CDCl_3 (400MHz)



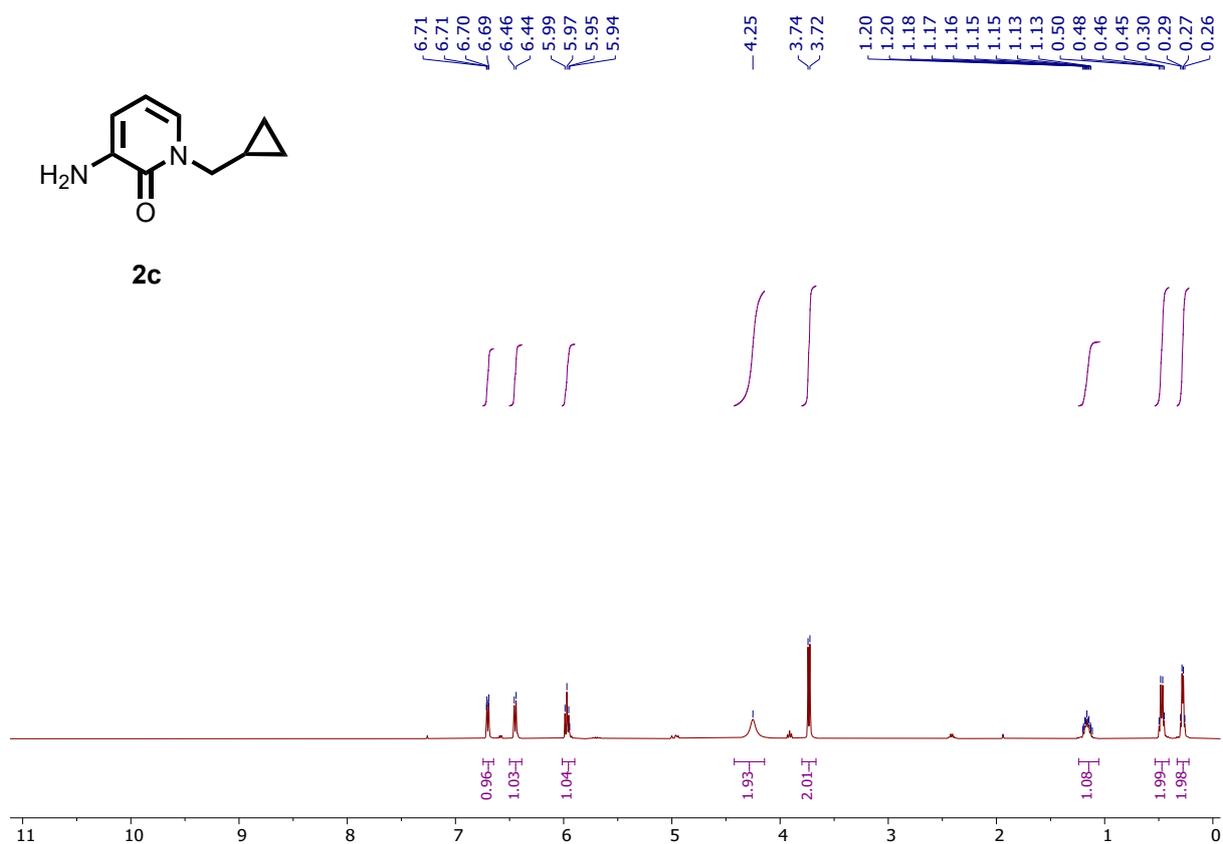
^1H NMR of **2b** in CDCl_3 (400MHz)



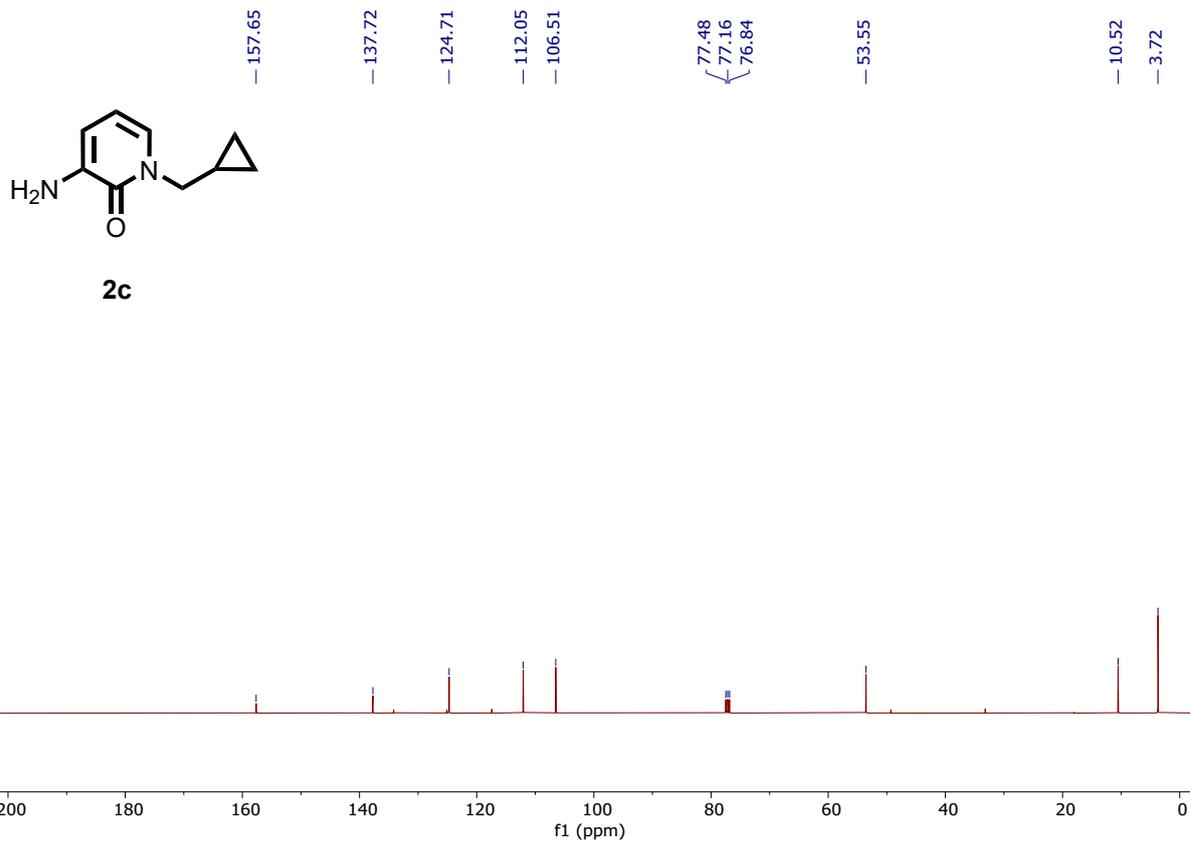
¹³C NMR of **2b** in CDCl₃ (400MHz)



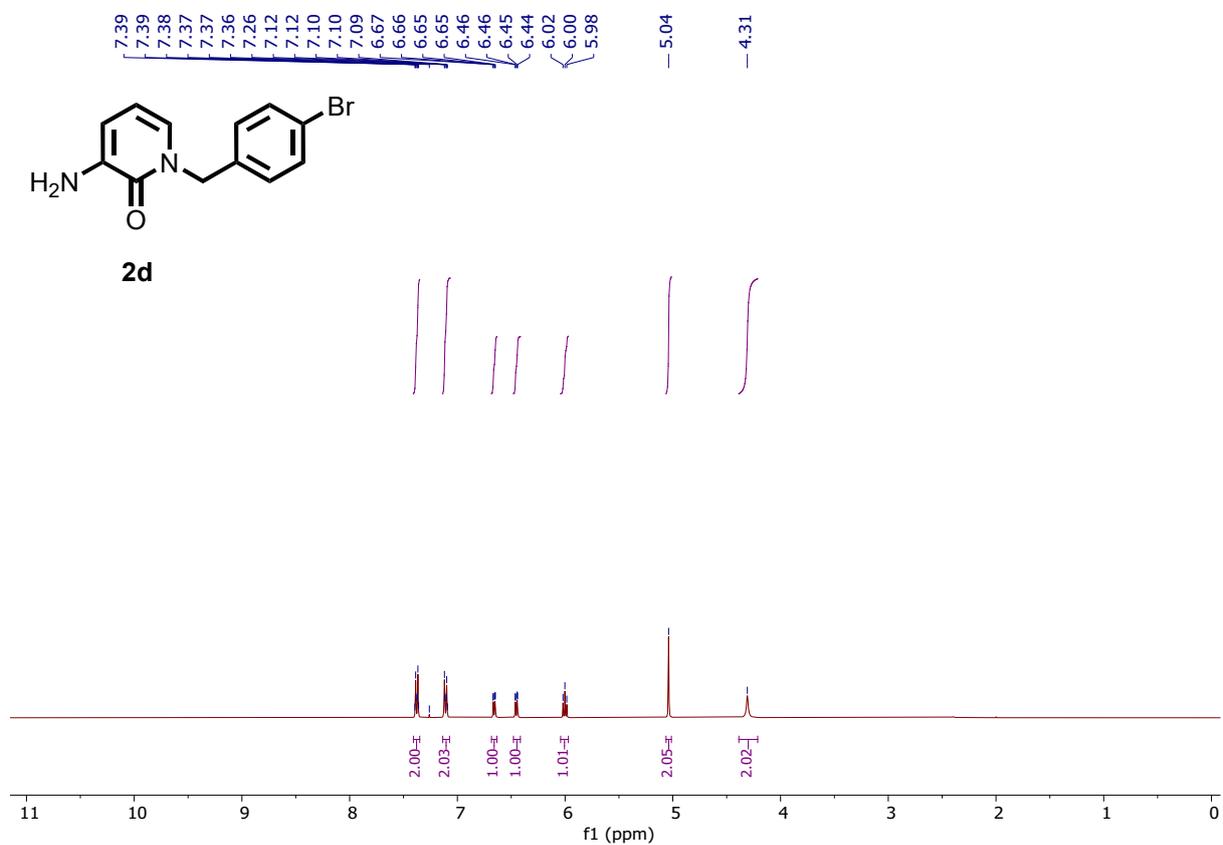
^1H NMR of **2c** in CDCl_3 (400MHz)



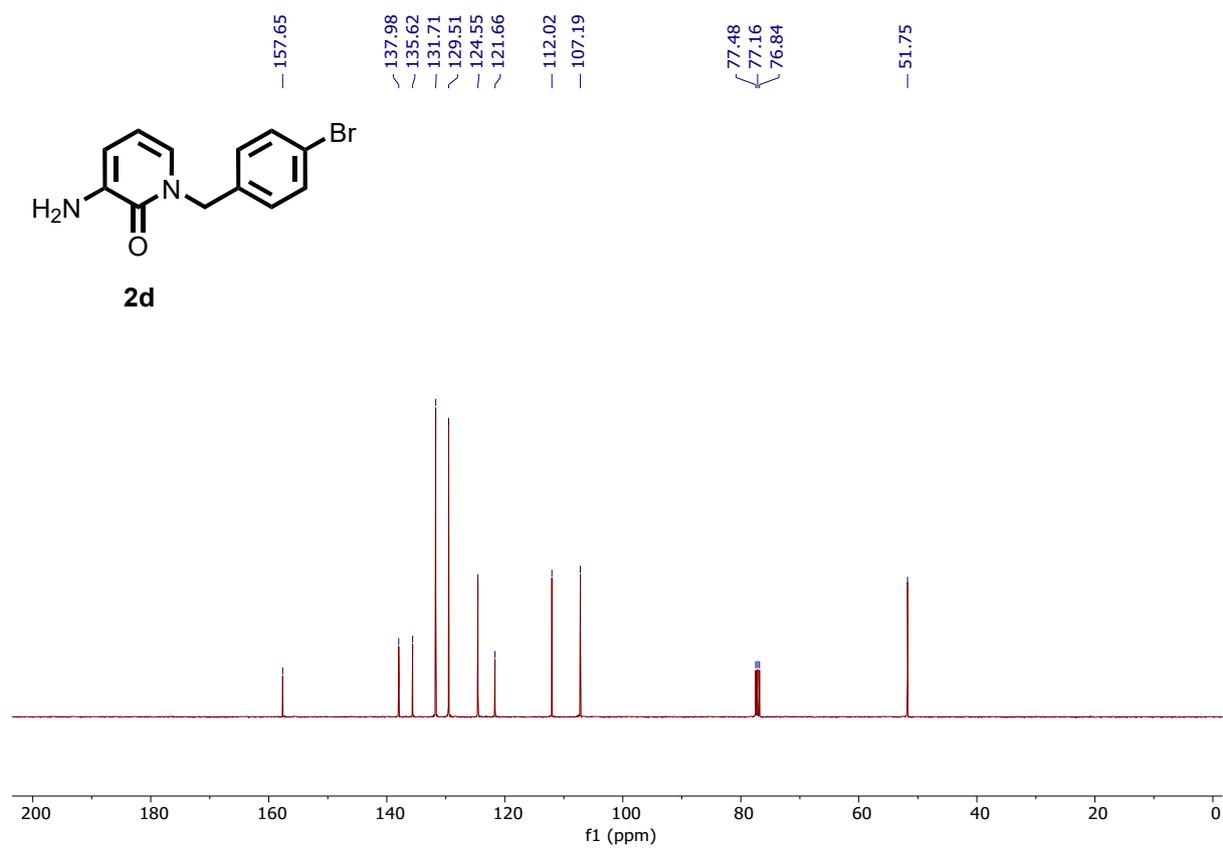
^{13}C NMR of **2c** in CDCl_3 (400MHz)



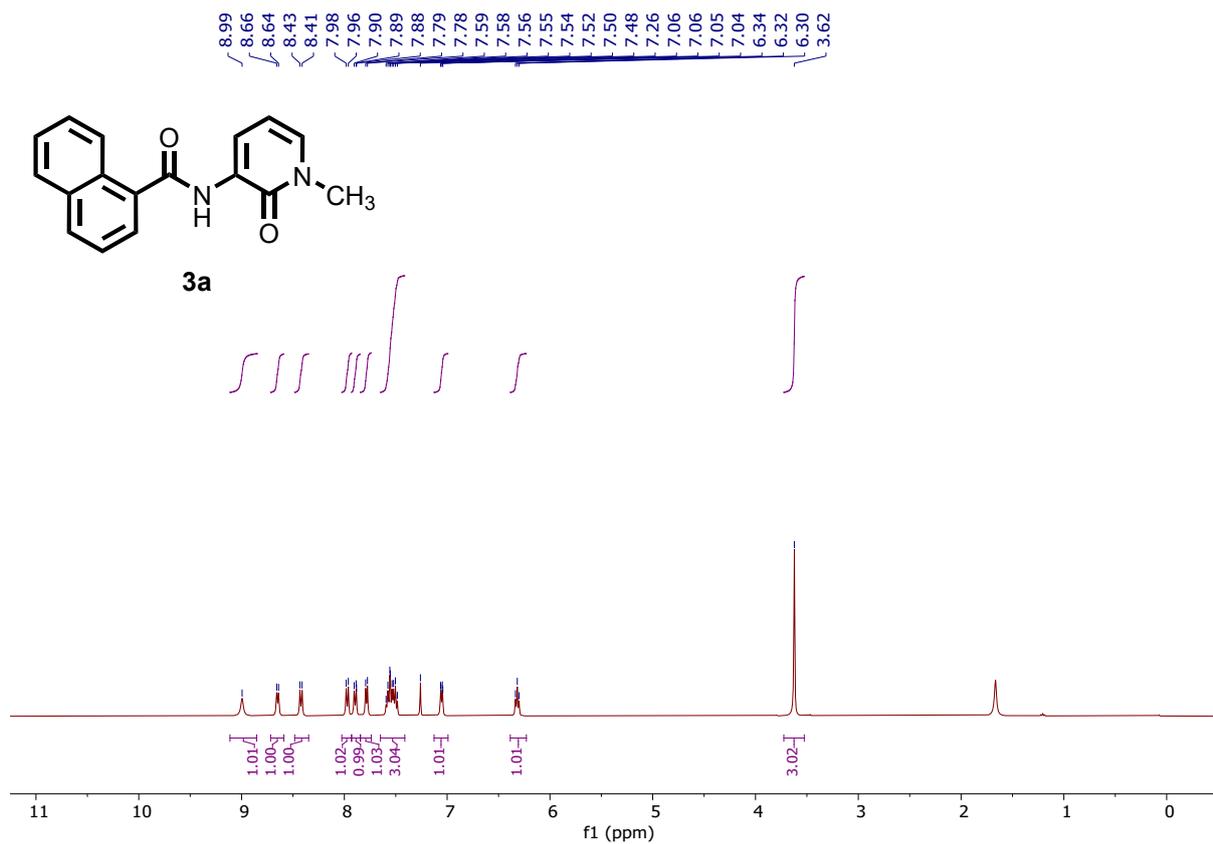
¹H NMR of **2d** in CDCl₃ (400MHz)



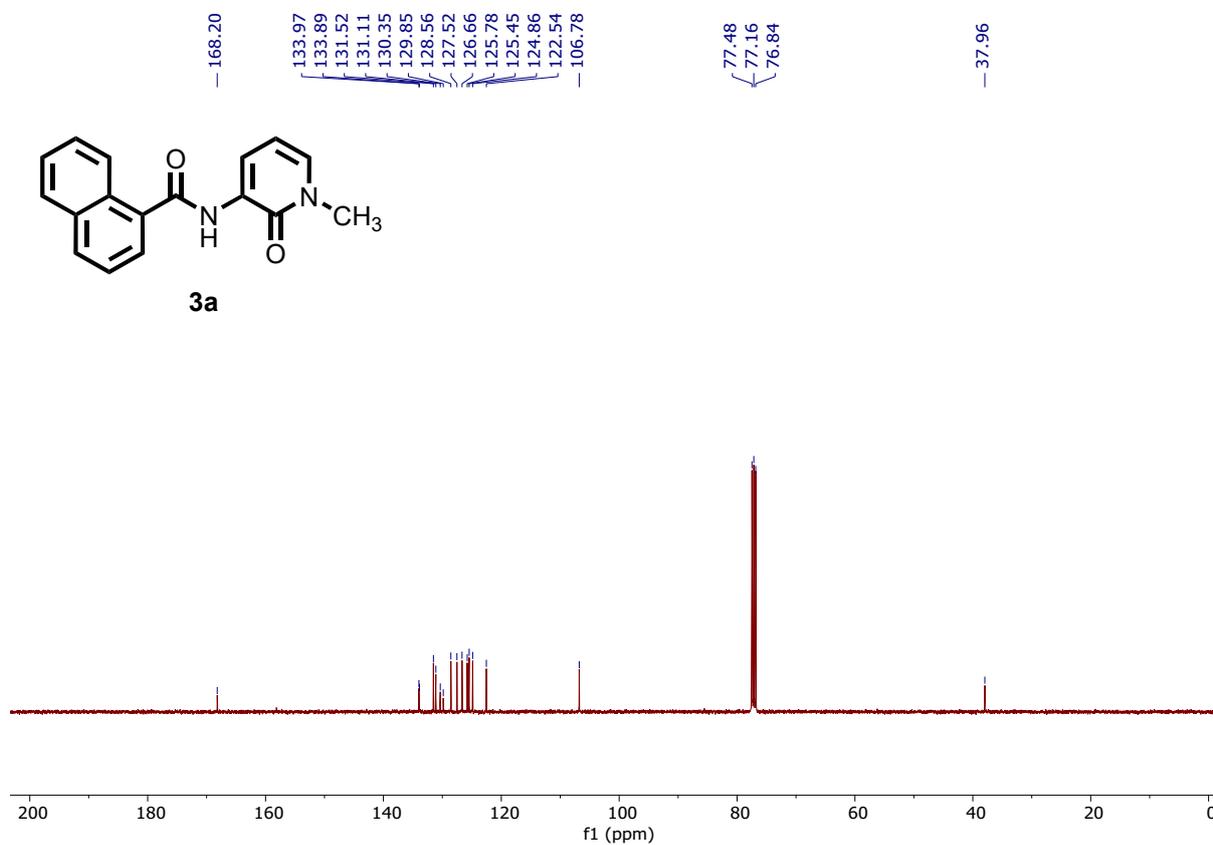
^{13}C NMR of **2d** in CDCl_3 (400MHz)



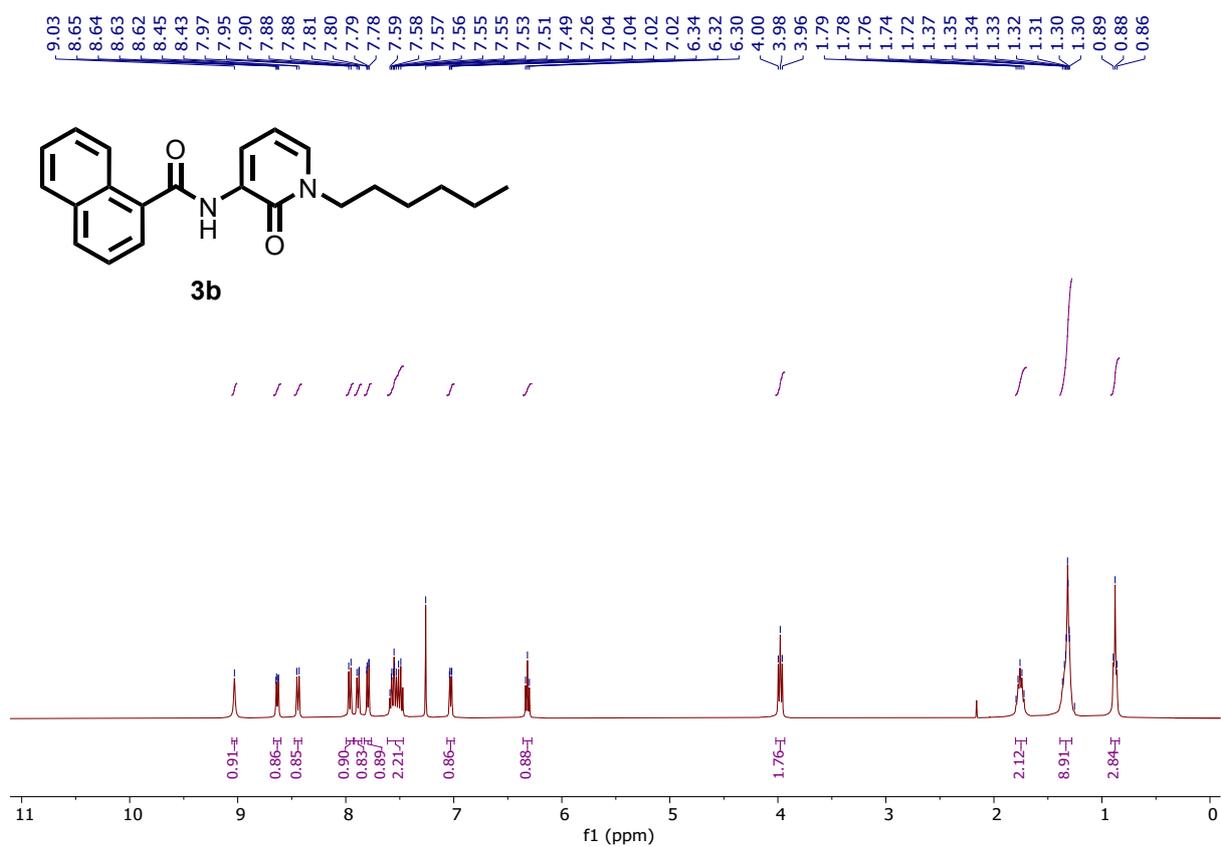
^1H NMR of **3a** in CDCl_3 (400MHz)



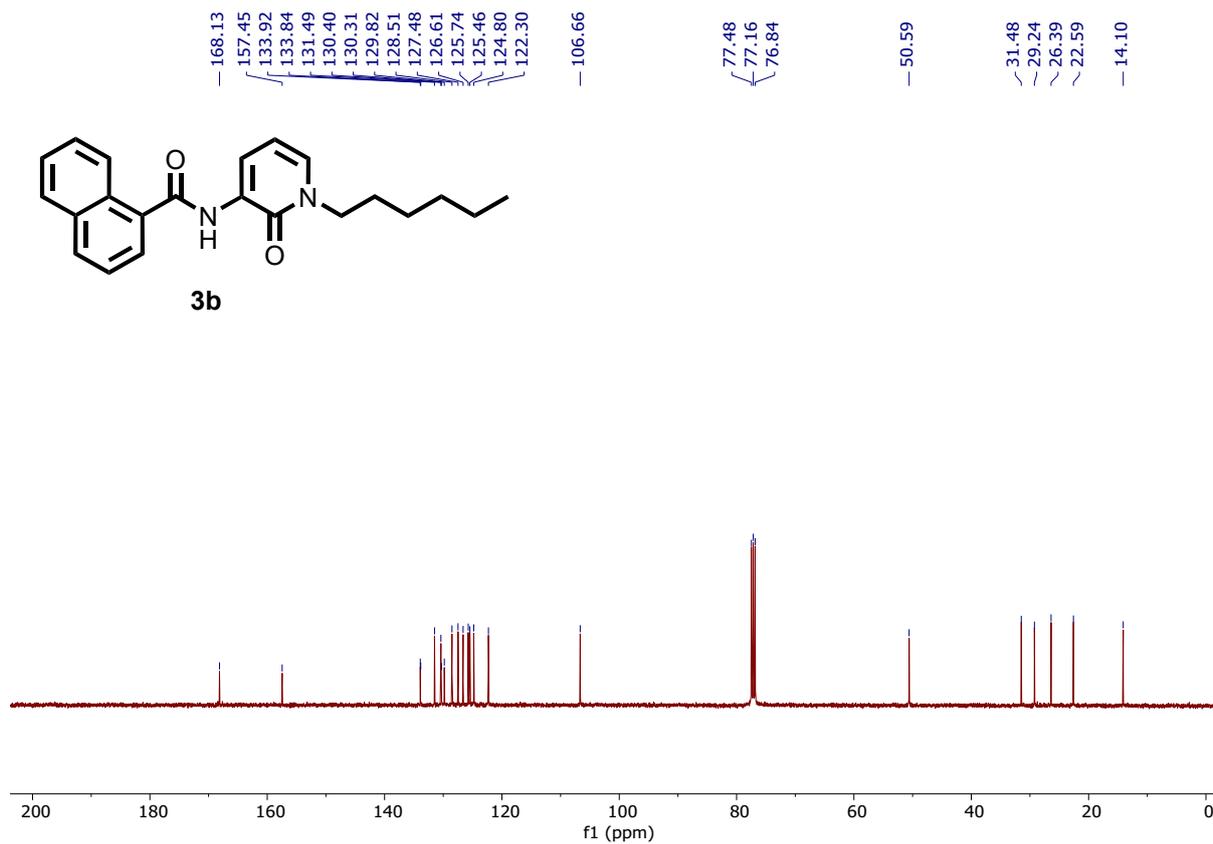
¹³C NMR of 3a in CDCl₃ (400MHz)



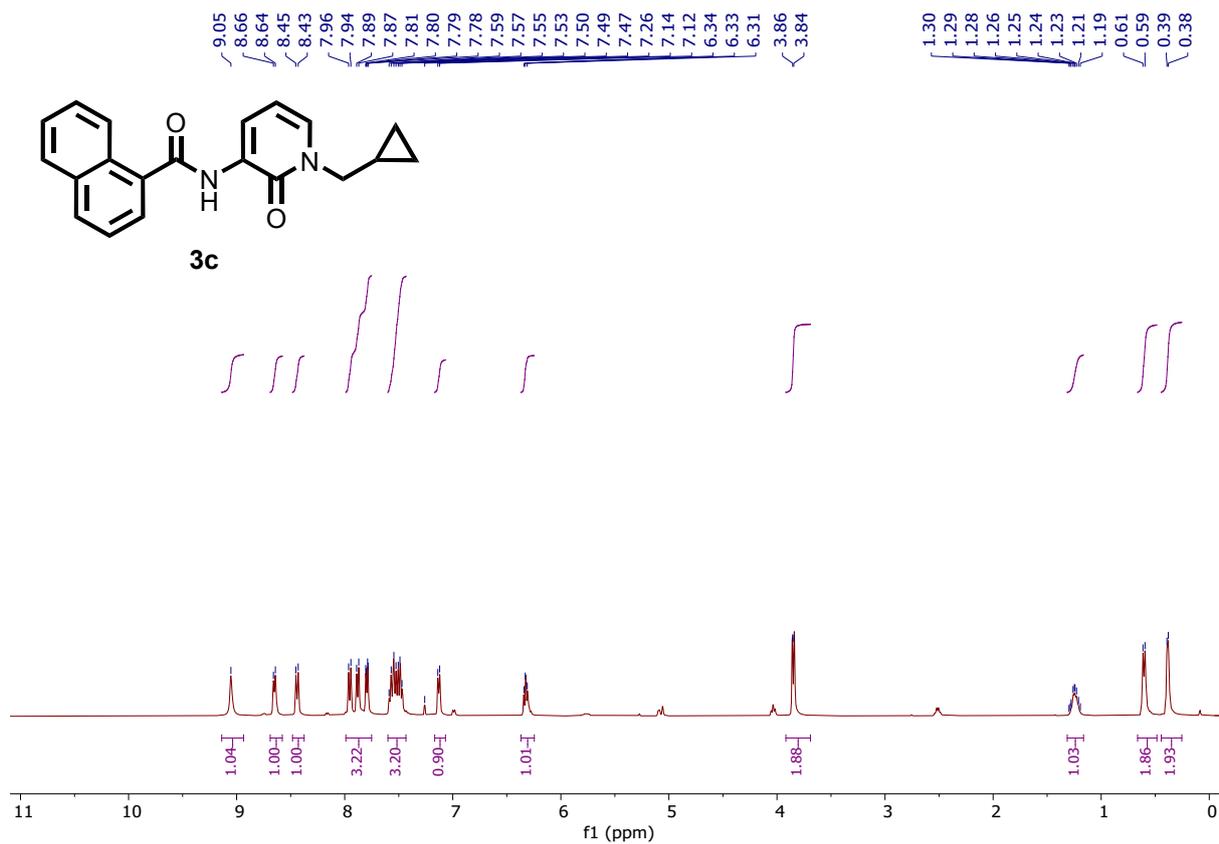
^1H NMR of **3b** in CDCl_3 (400MHz)



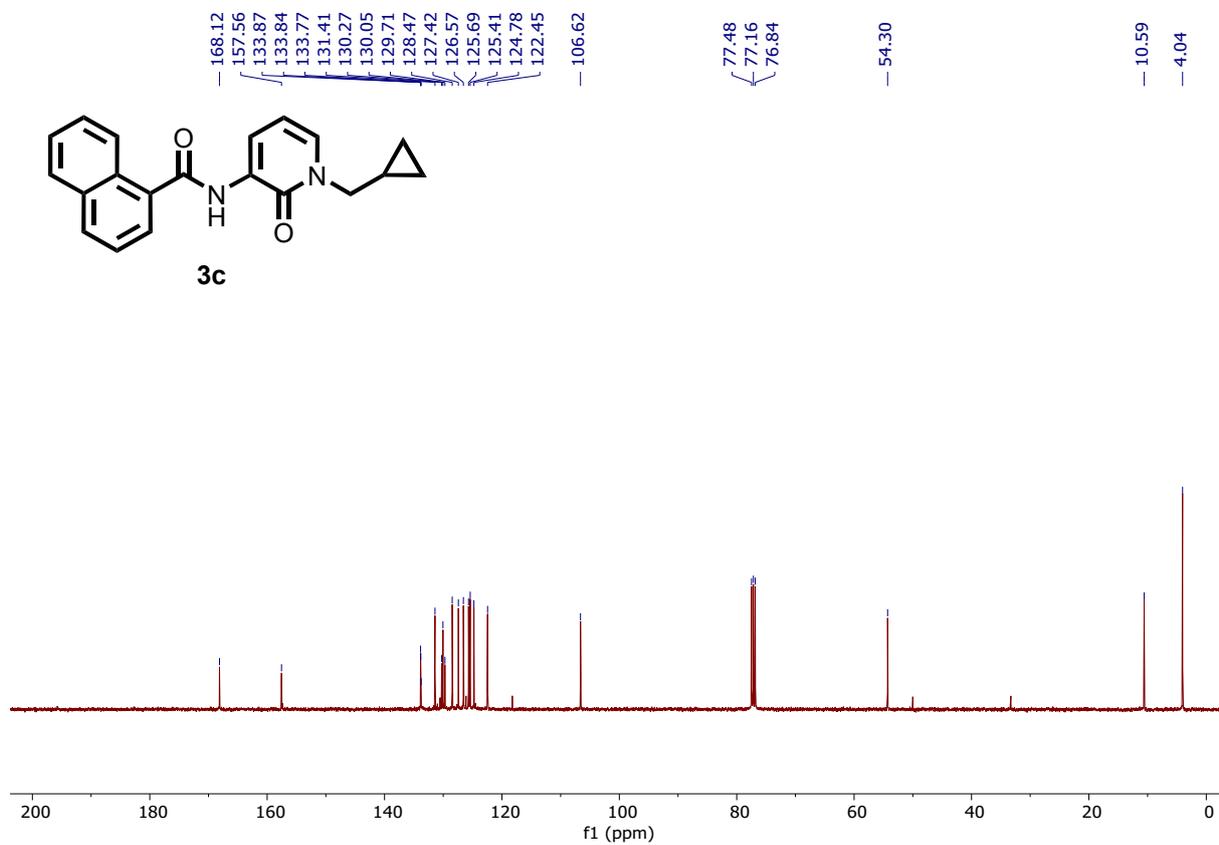
^{13}C NMR of **3b** in CDCl_3 (400MHz)



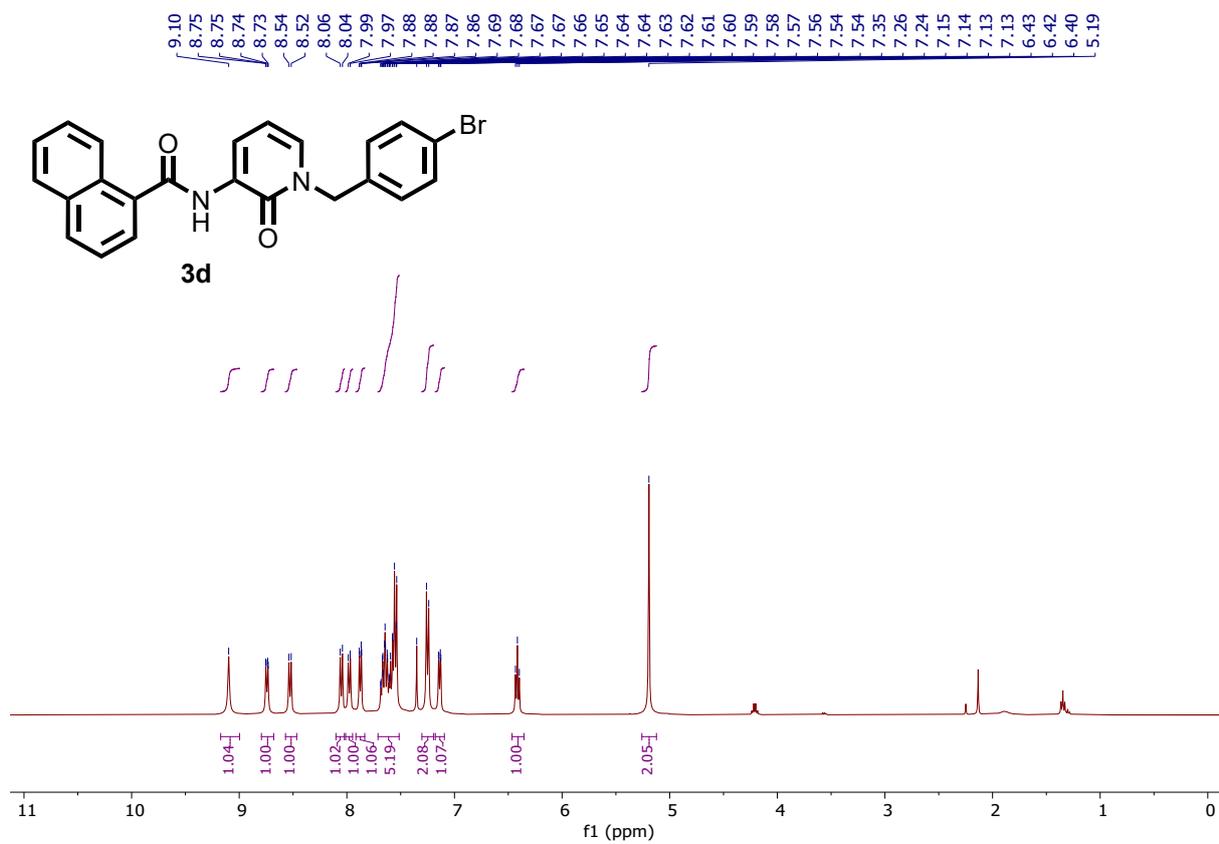
¹H NMR of **3c** in CDCl₃ (400MHz)



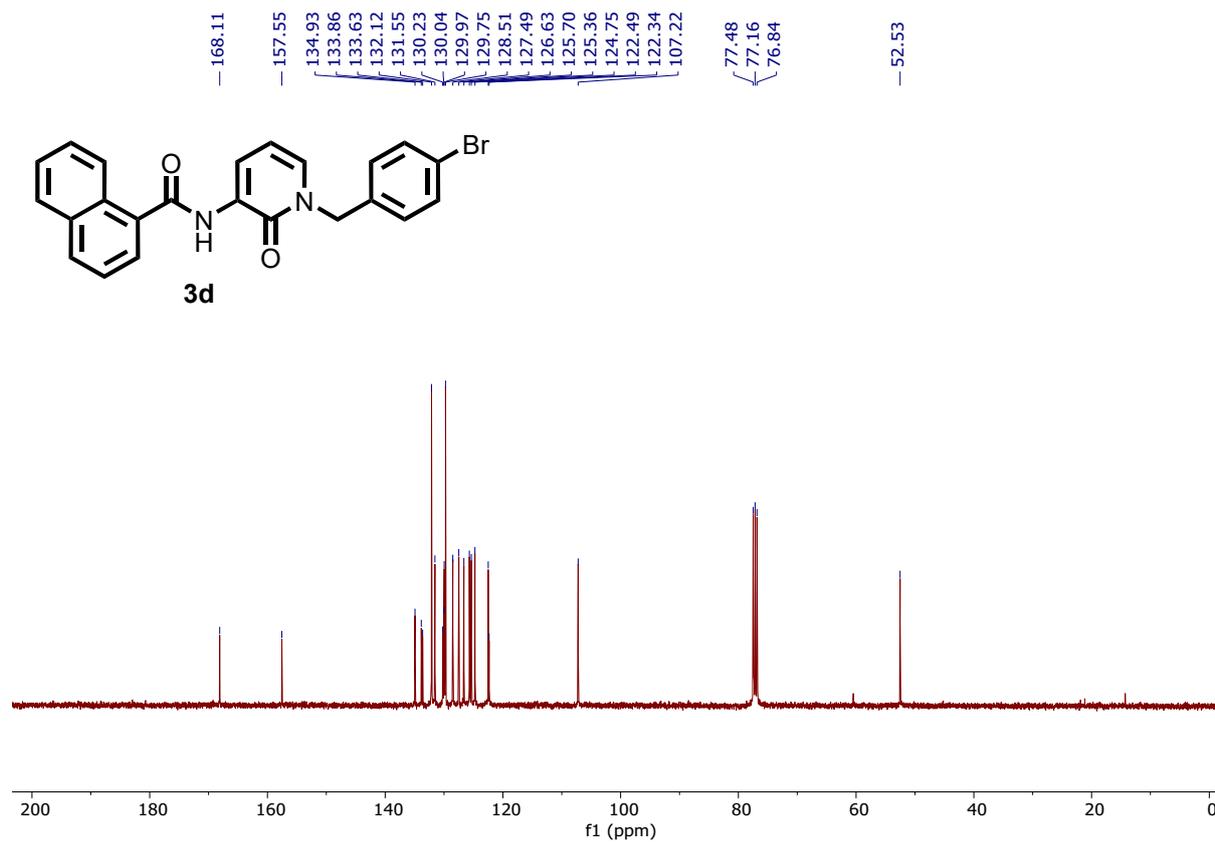
NMR of **3c** in CDCl₃ (400MHz)



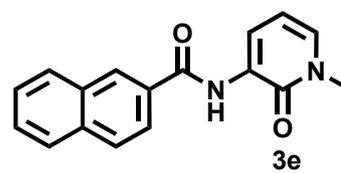
^1H NMR of **3d** in CDCl_3 (400MHz)

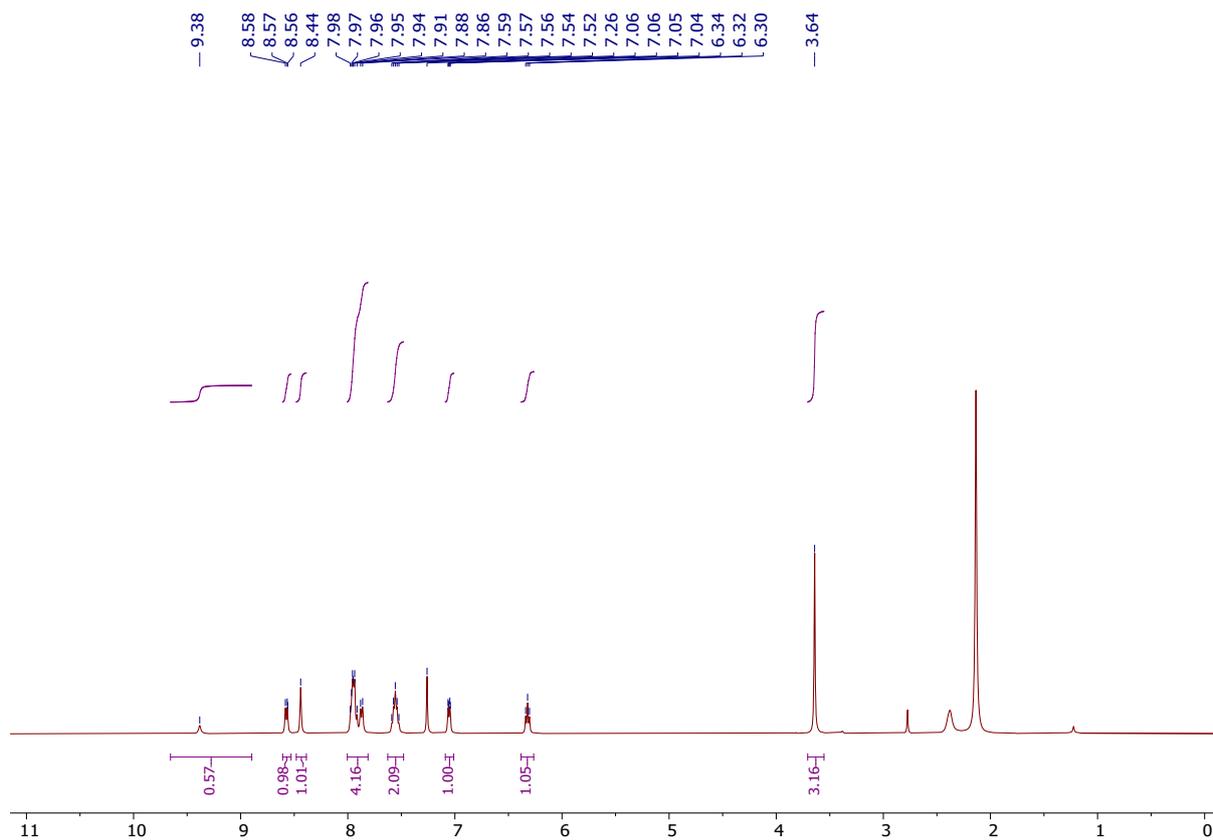


^{13}C NMR of **3d** in CDCl_3 (400MHz)

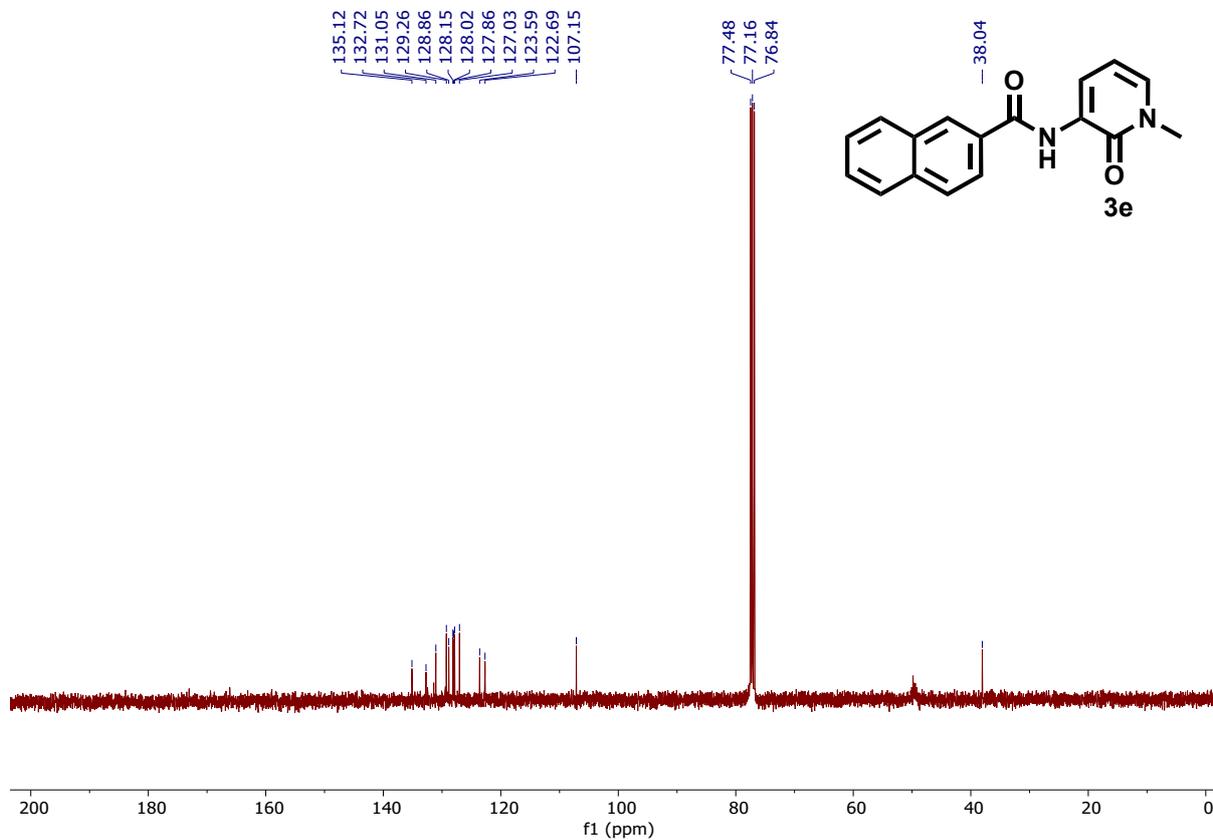


¹H NMR of **3e** in CDCl₃ (400MHz)

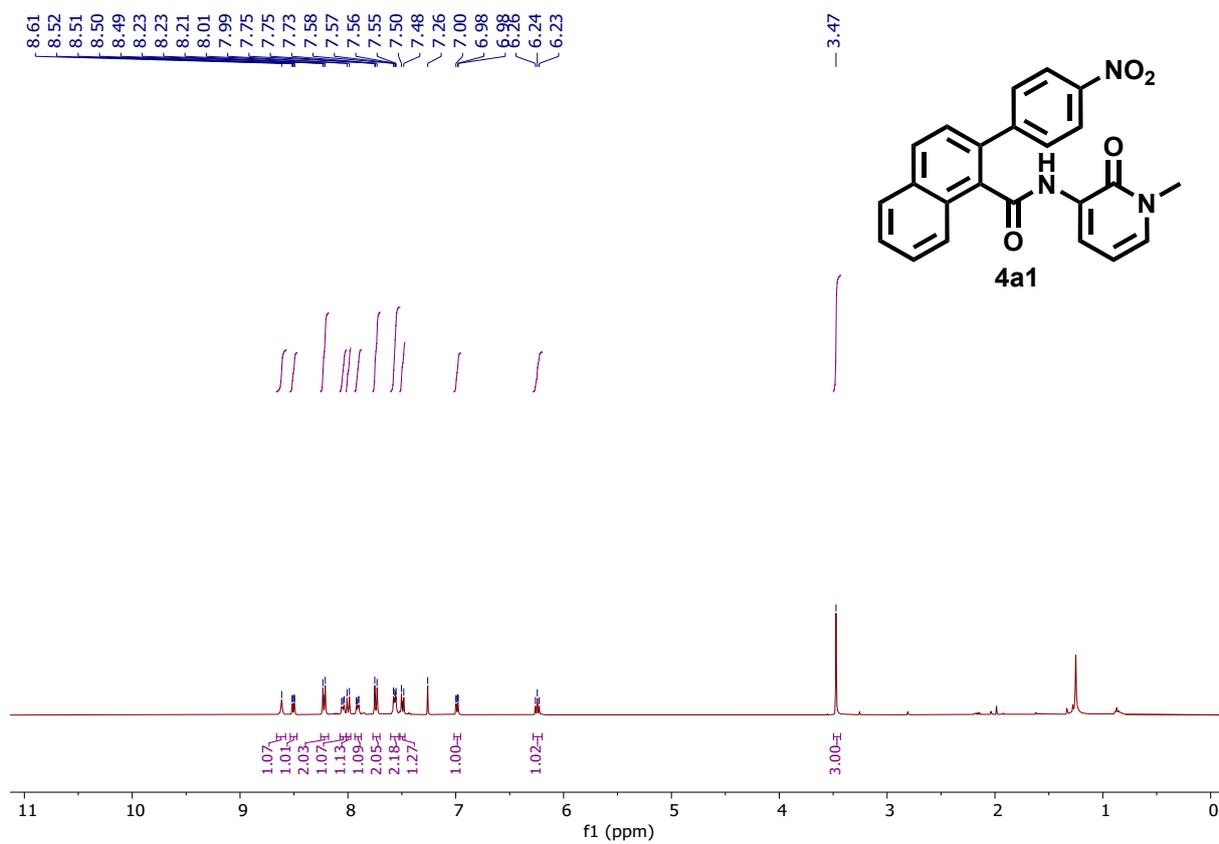




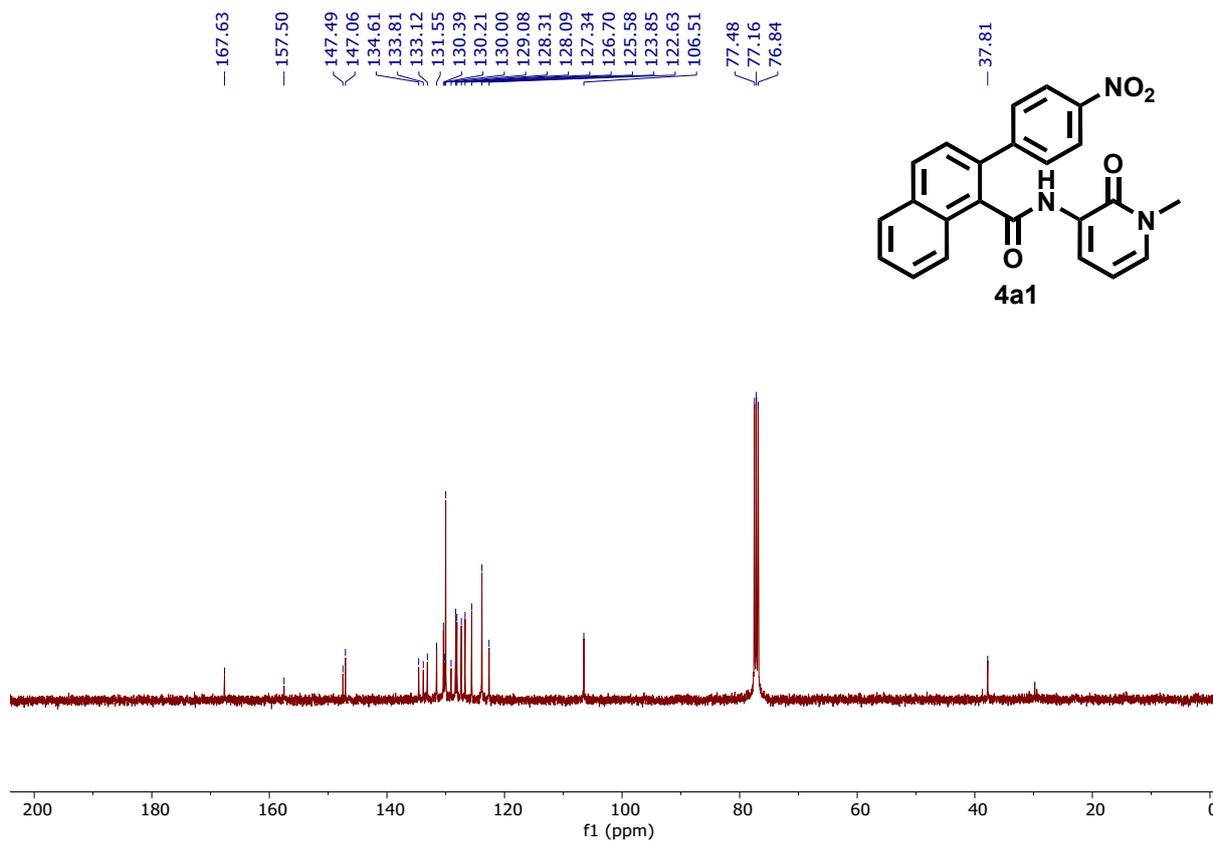
^{13}C NMR of **3e** in CDCl_3 (400MHz)



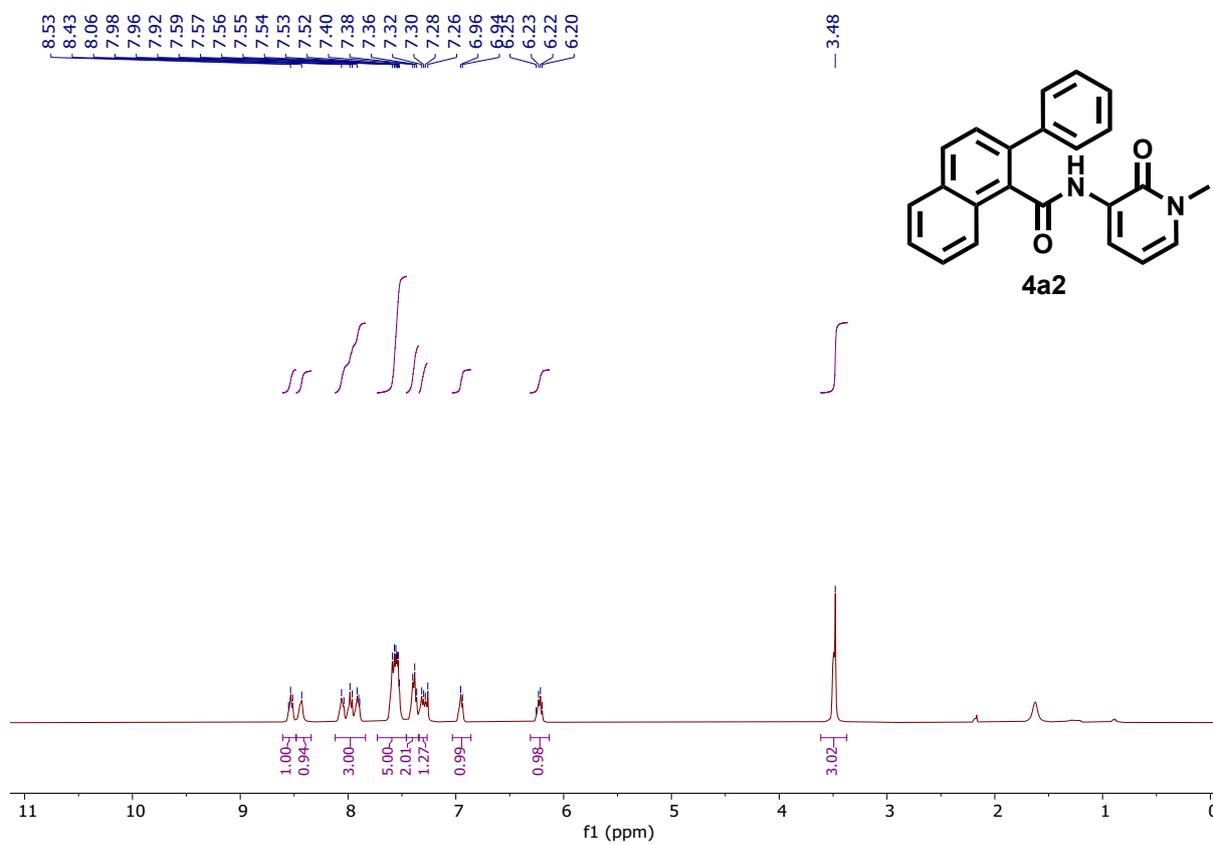
^1H NMR of **4a1** in CDCl_3 (400MHz)



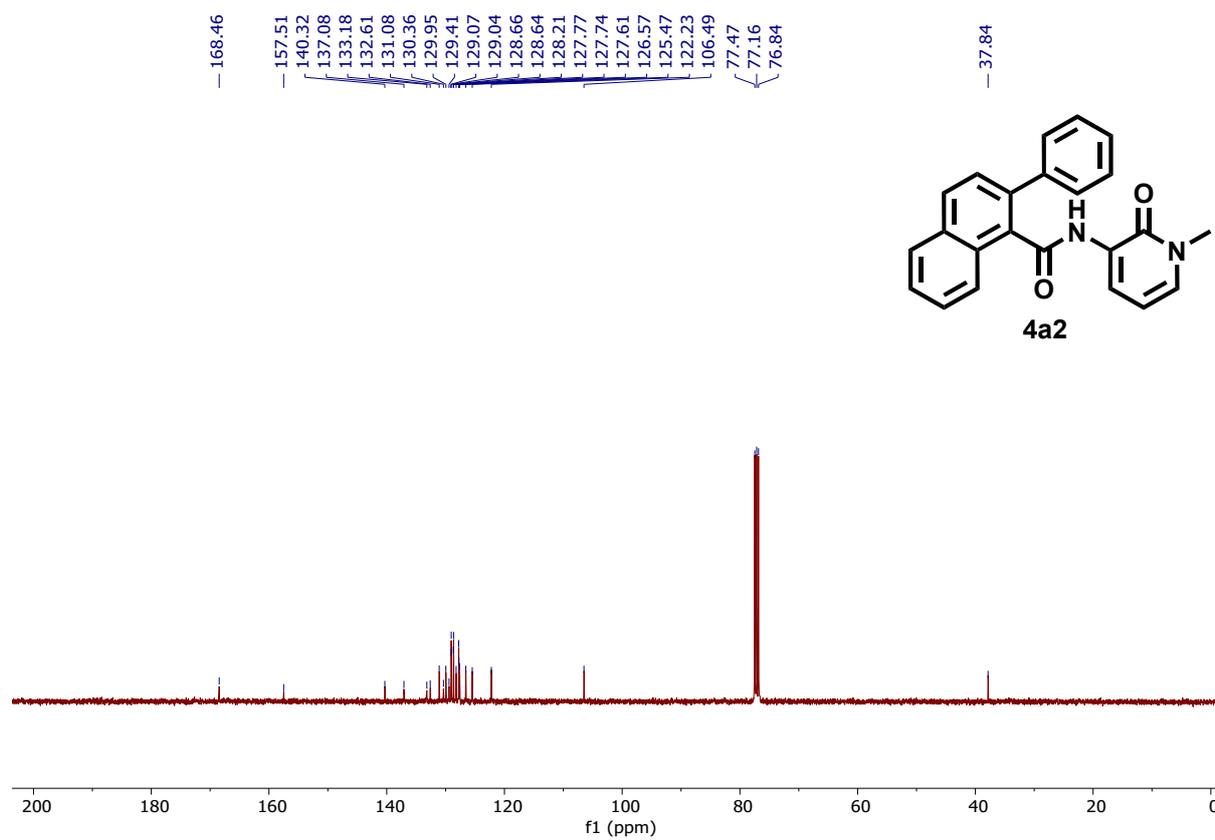
^{13}C NMR of **4a1** in CDCl_3 (400MHz)



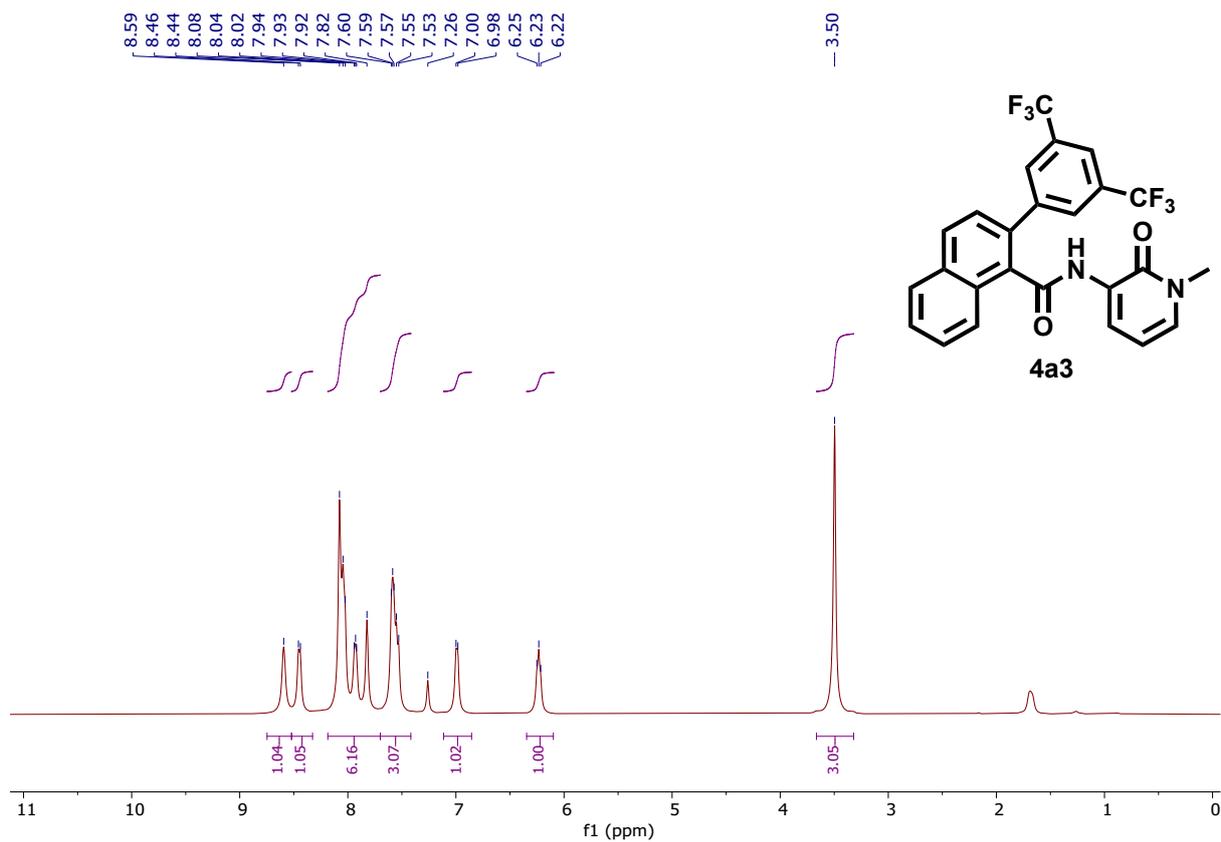
¹H NMR of **4a2** in CDCl₃ (400 MHz)



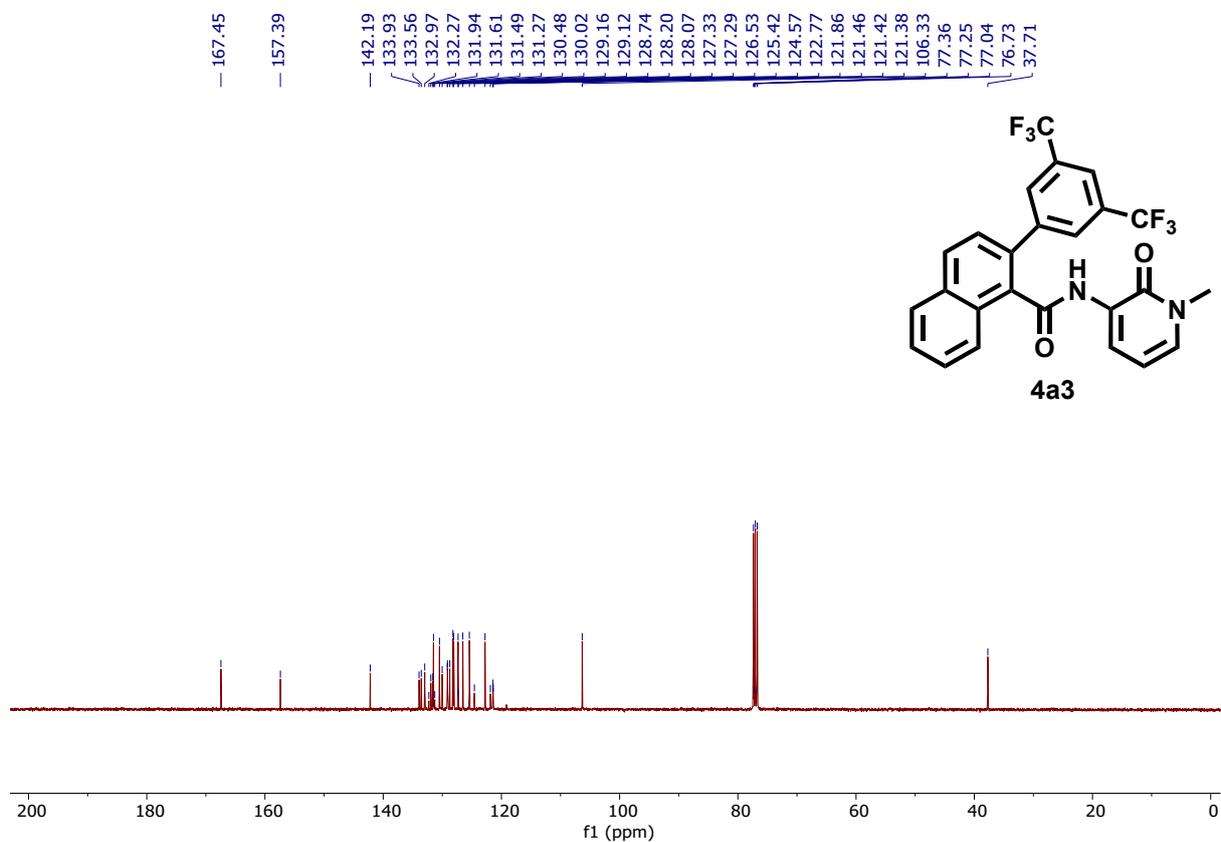
^{13}C NMR of **4a2** in CDCl_3 (400MHz)



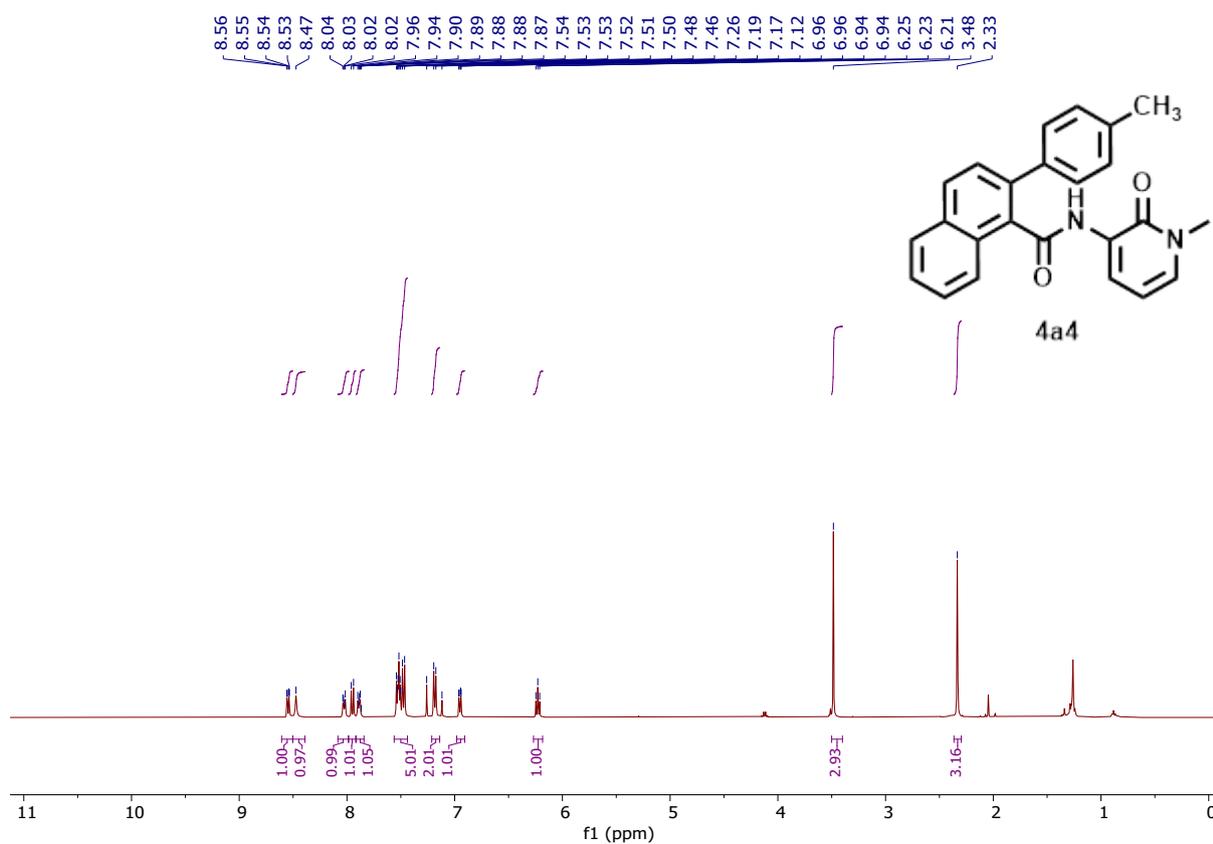
^1H NMR of **4a3** in CDCl_3 (400MHz)



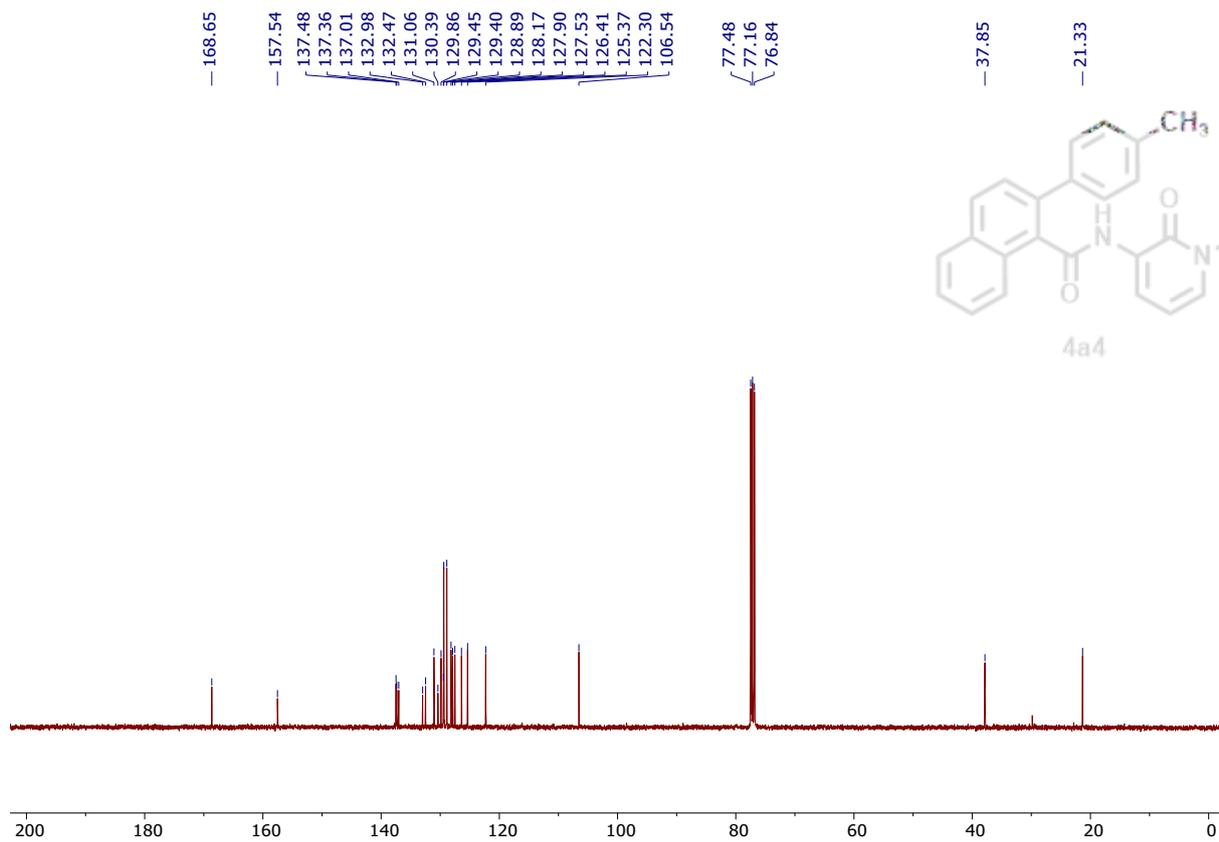
¹³C NMR of **4a3** in CDCl₃ (400MHz)



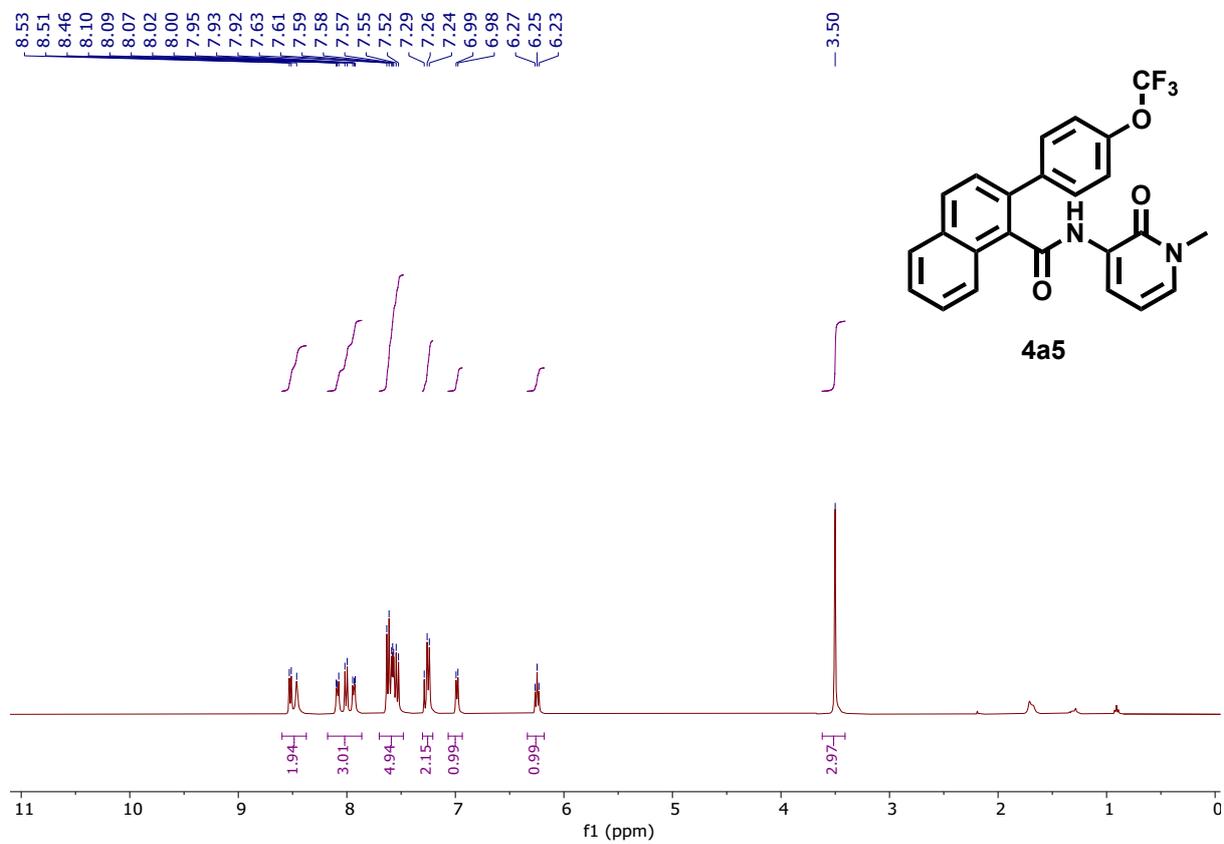
^1H NMR of **4a4** in CDCl_3 (400MHz)



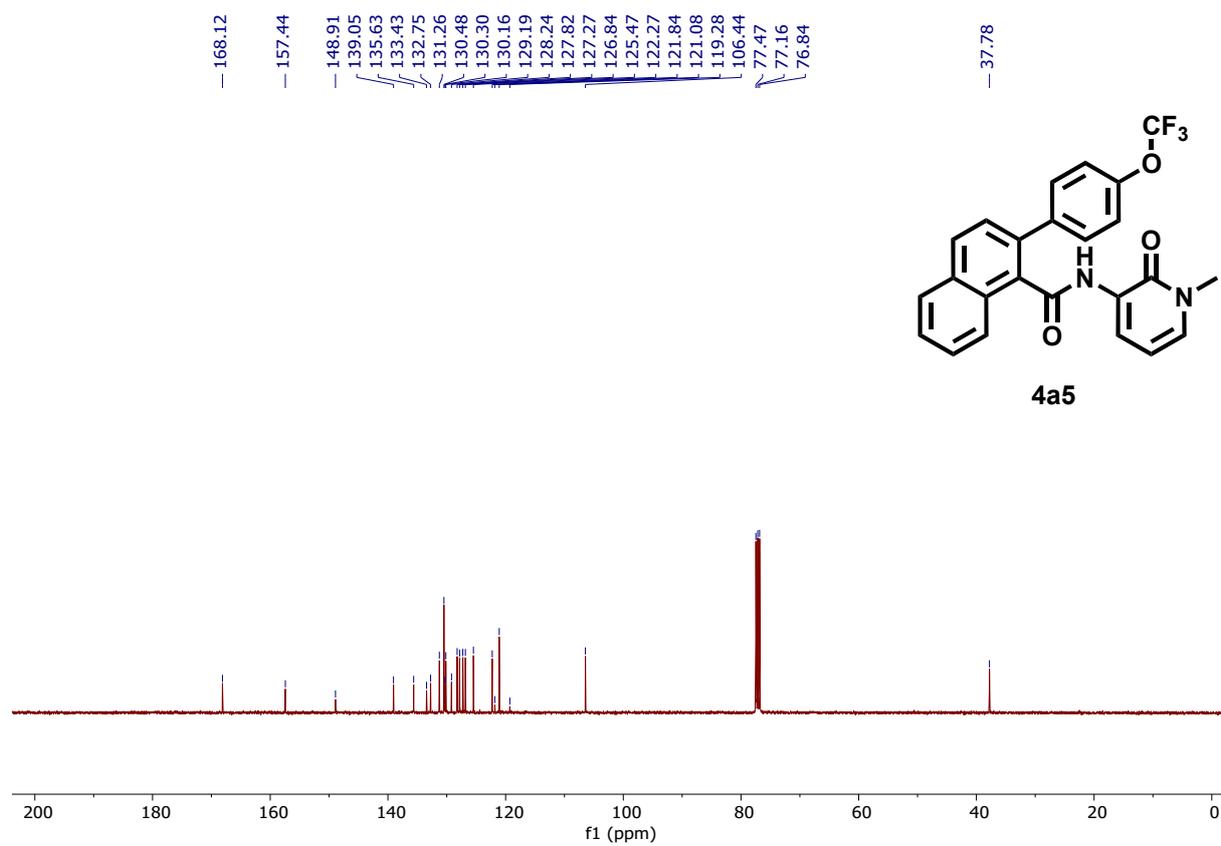
^{13}C NMR of **4a4** in CDCl_3 (400MHz)



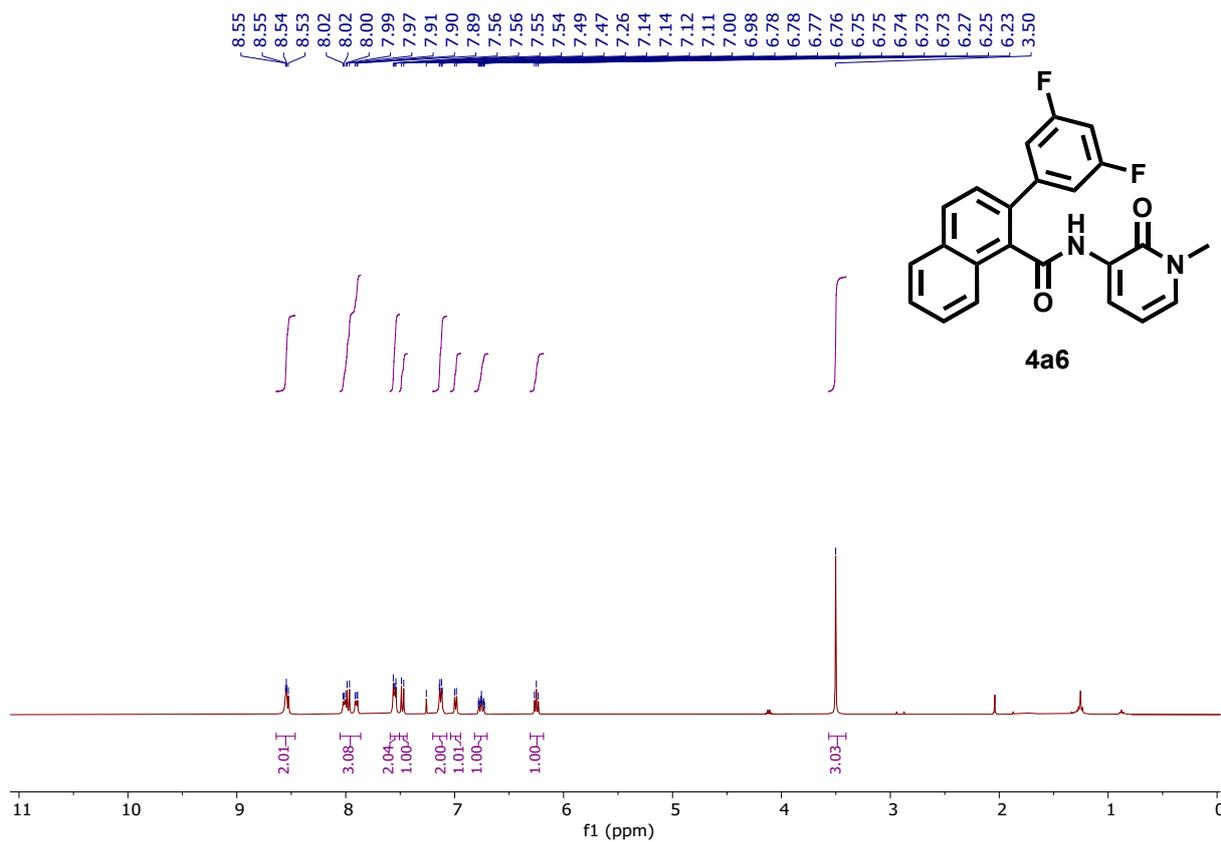
¹H NMR of **4a5** in CDCl₃ (400MHz)



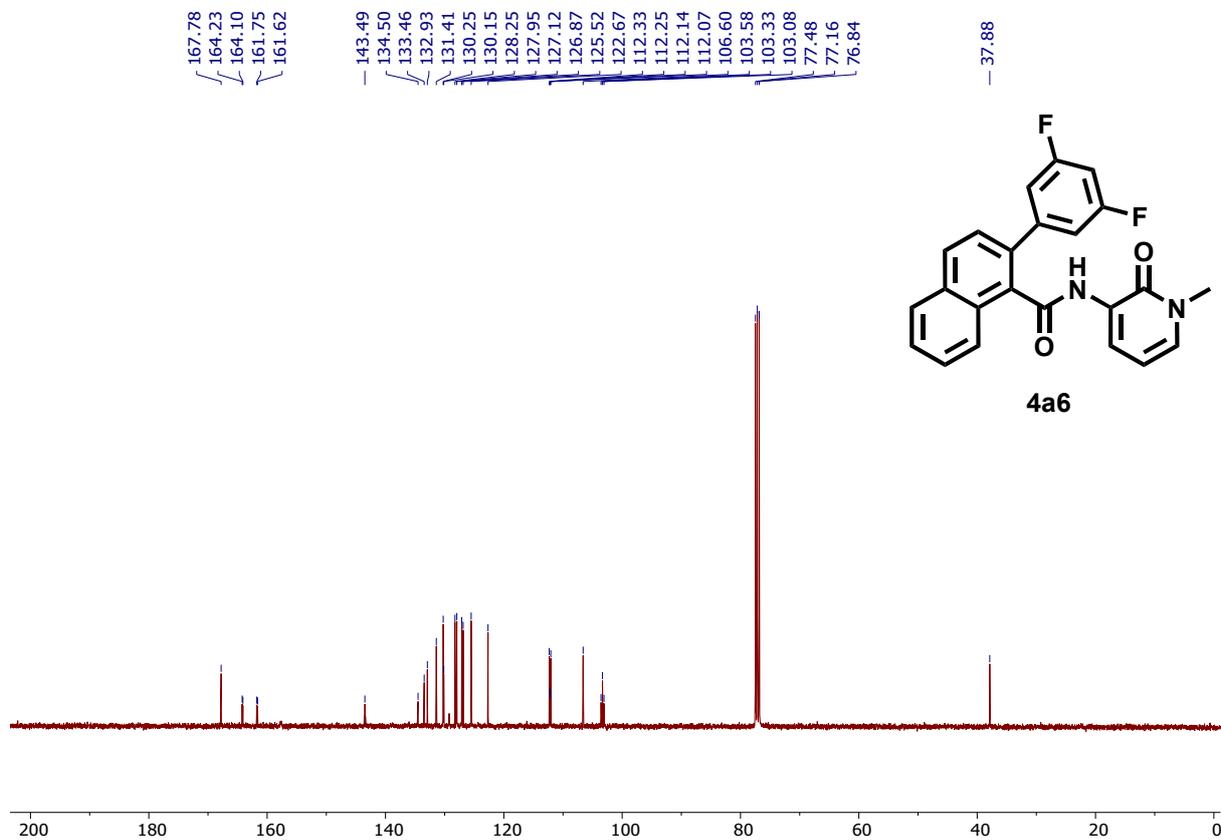
^{13}C NMR of **4a5** in CDCl_3 (400MHz)



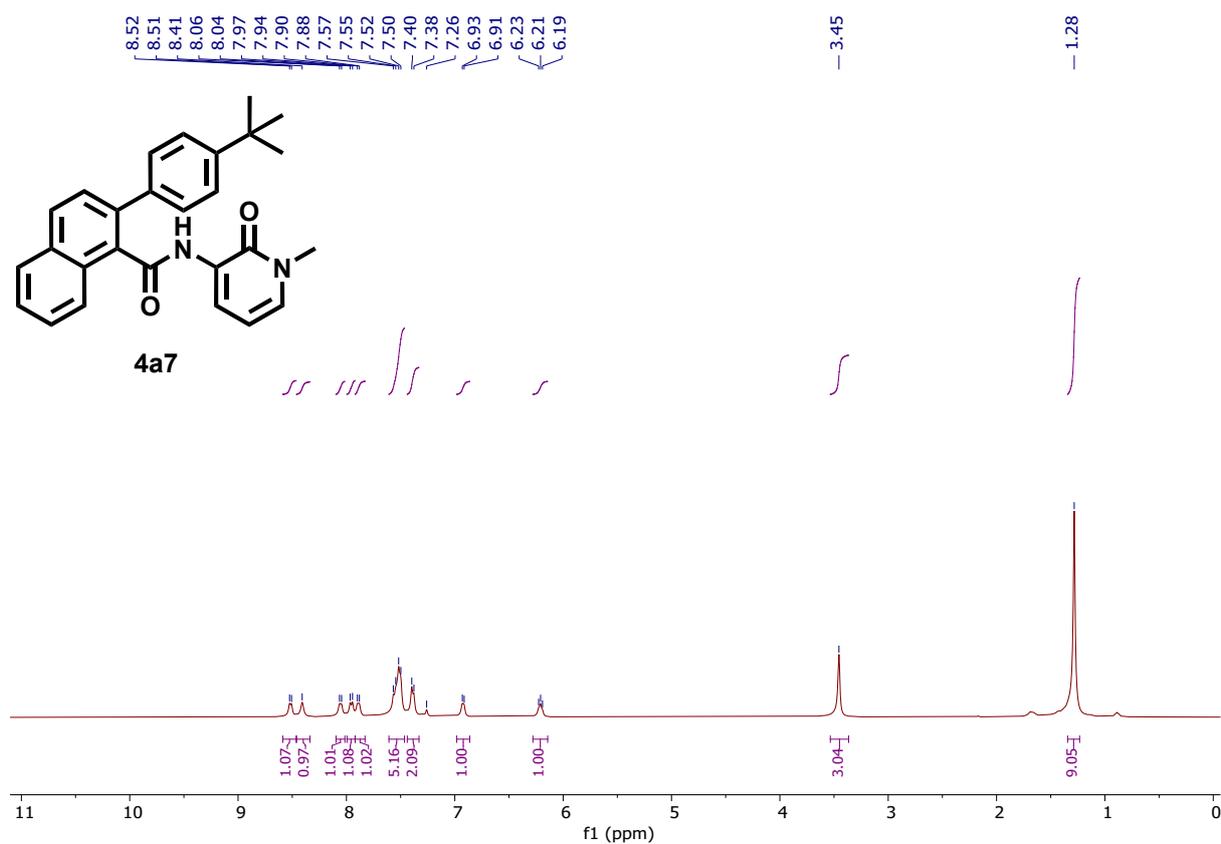
^1H NMR of **4a6** in CDCl_3 (400MHz)



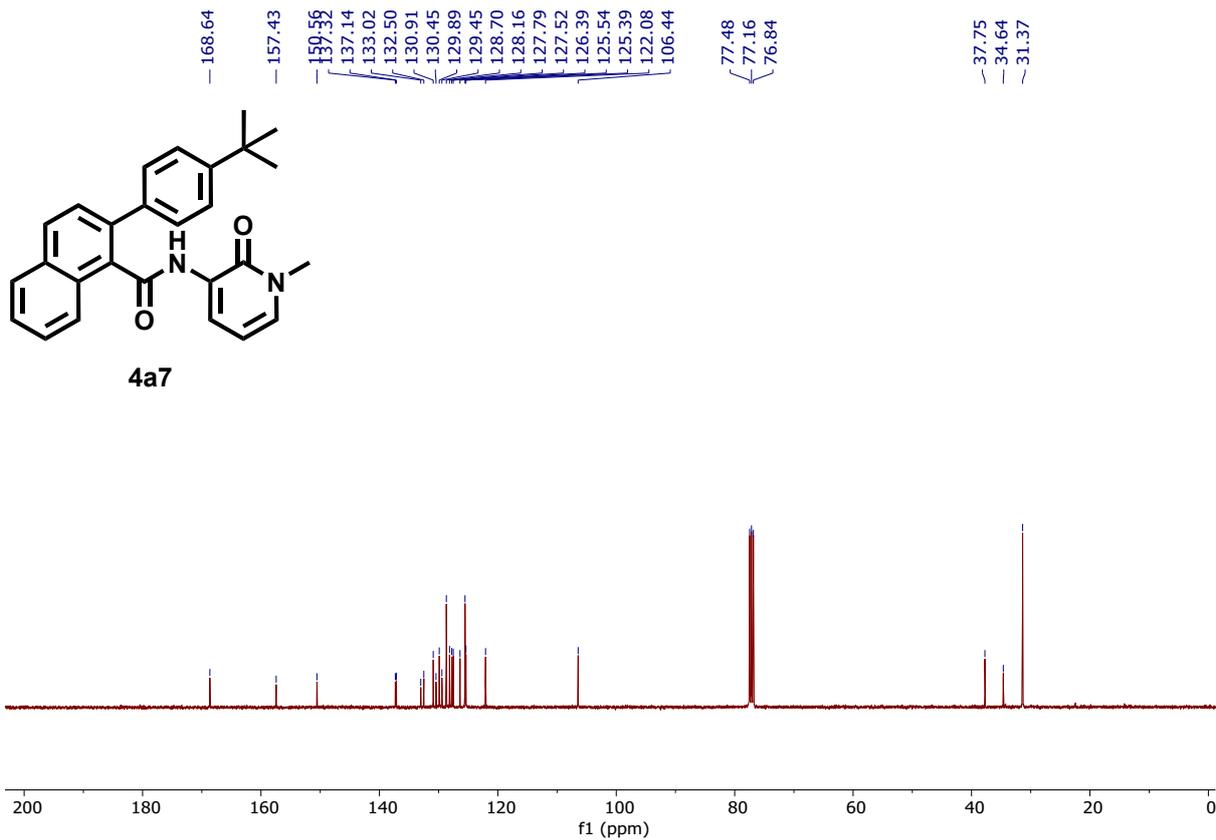
¹³C NMR of **4a6** in CDCl₃ (400MHz)



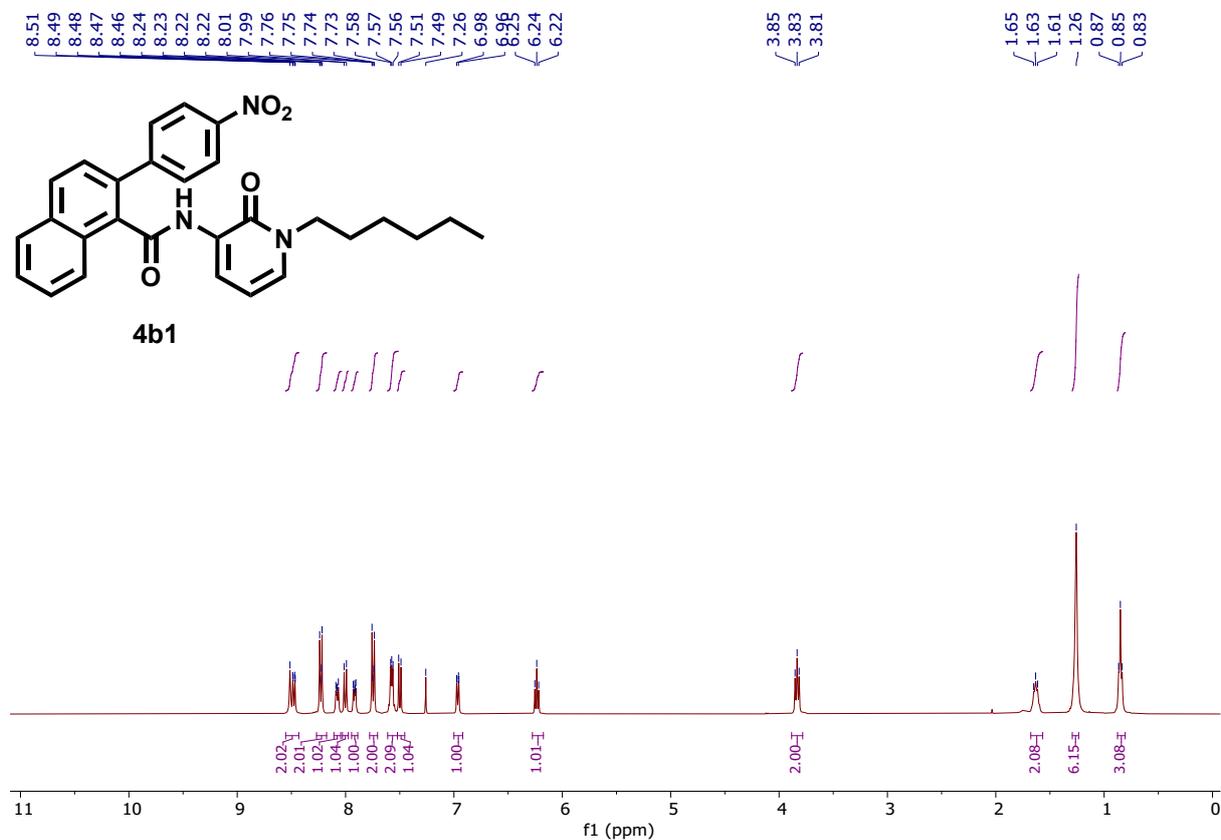
^1H NMR of **4a7** in CDCl_3 (400MHz)



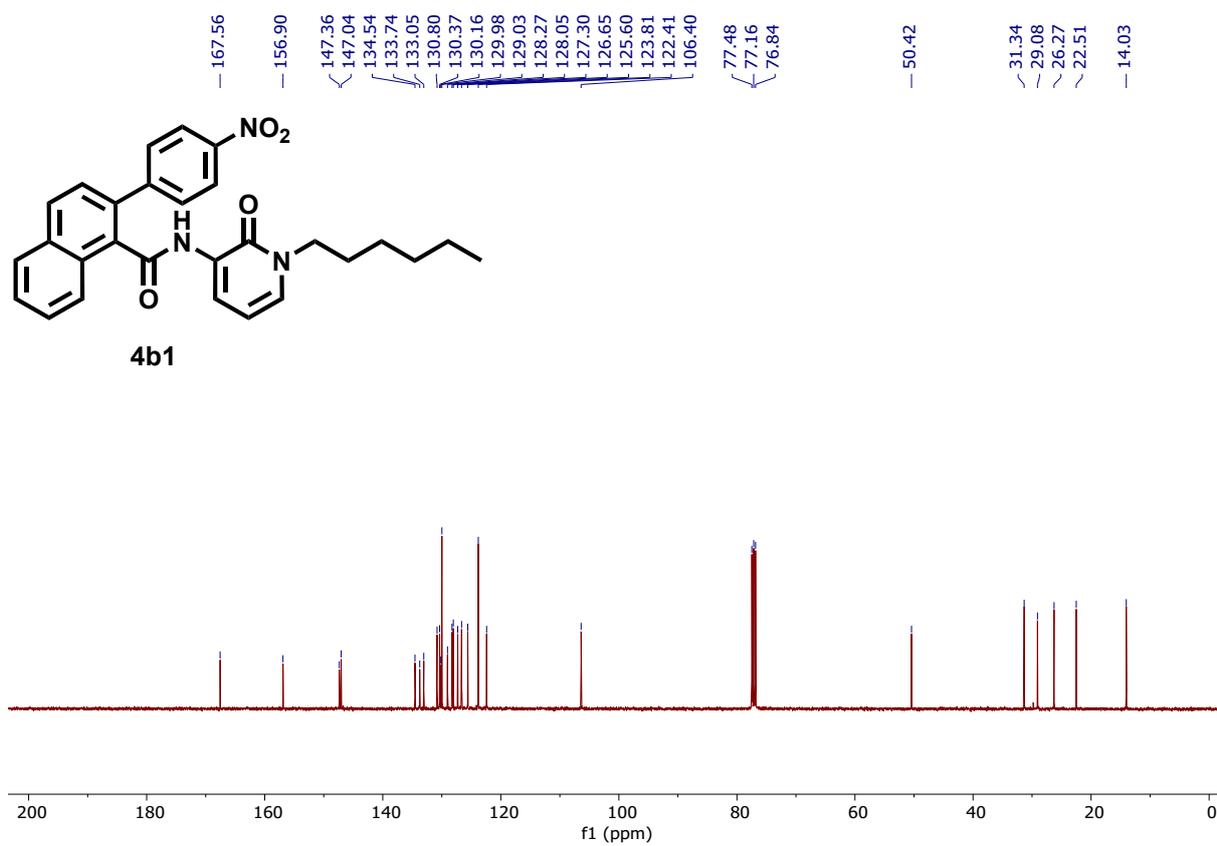
^{13}C NMR of **4a7** in CDCl_3 (400MHz)



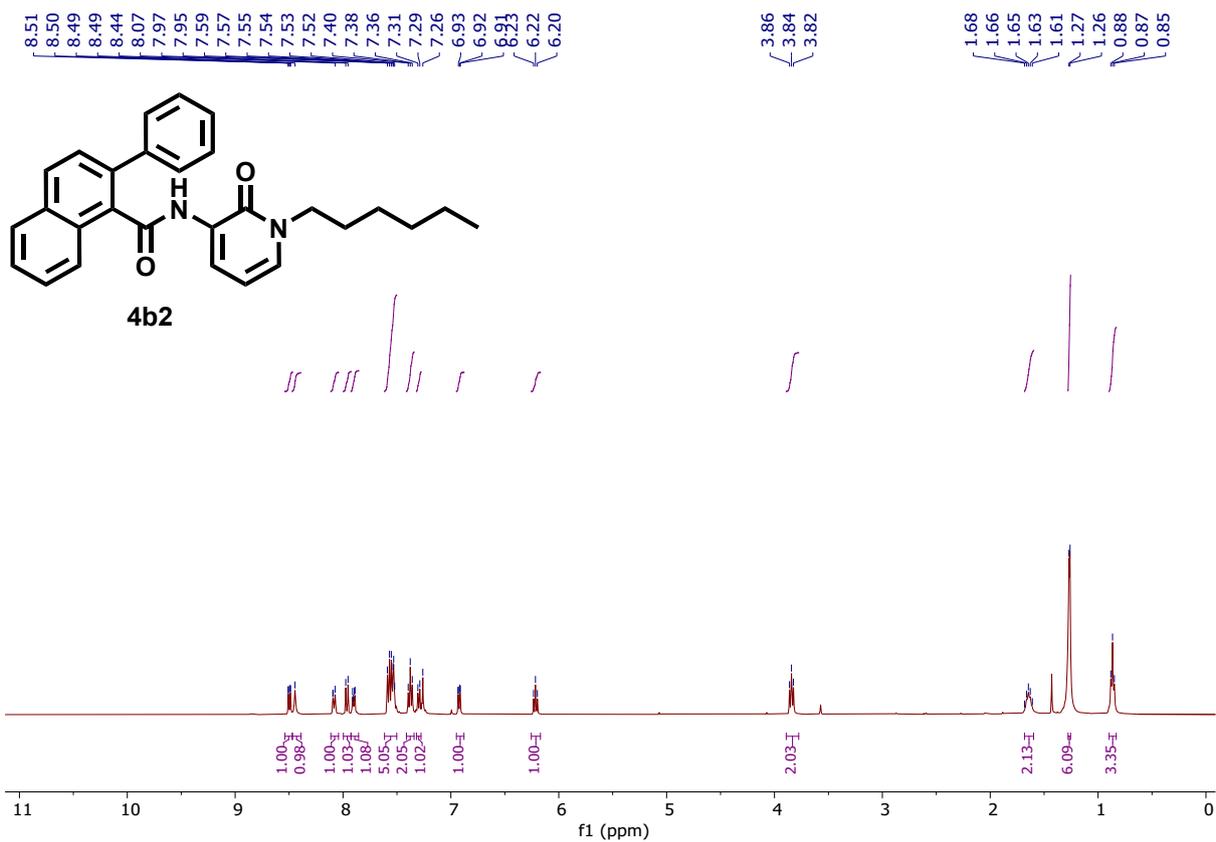
¹H NMR of 4b1 in CDCl₃ (400MHz)



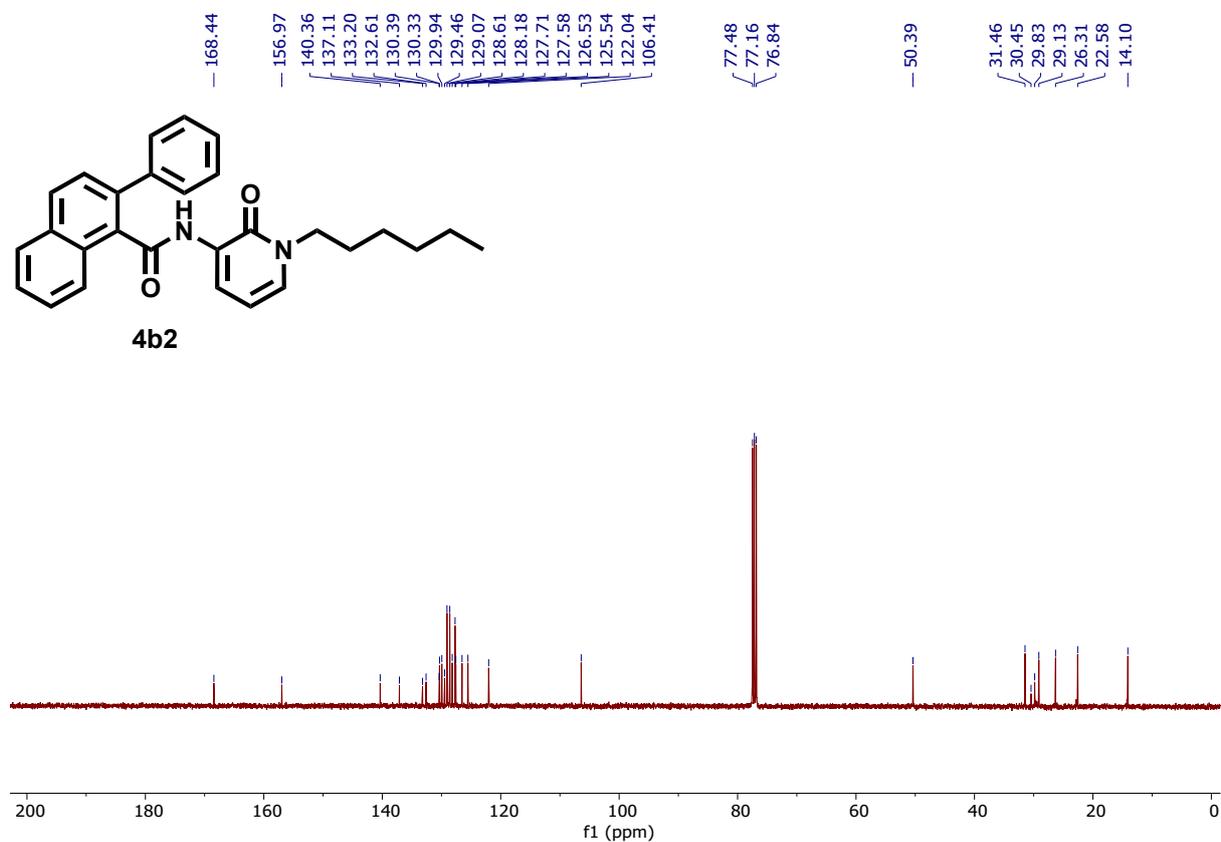
^{13}C NMR of **4b1** in CDCl_3 (400MHz)



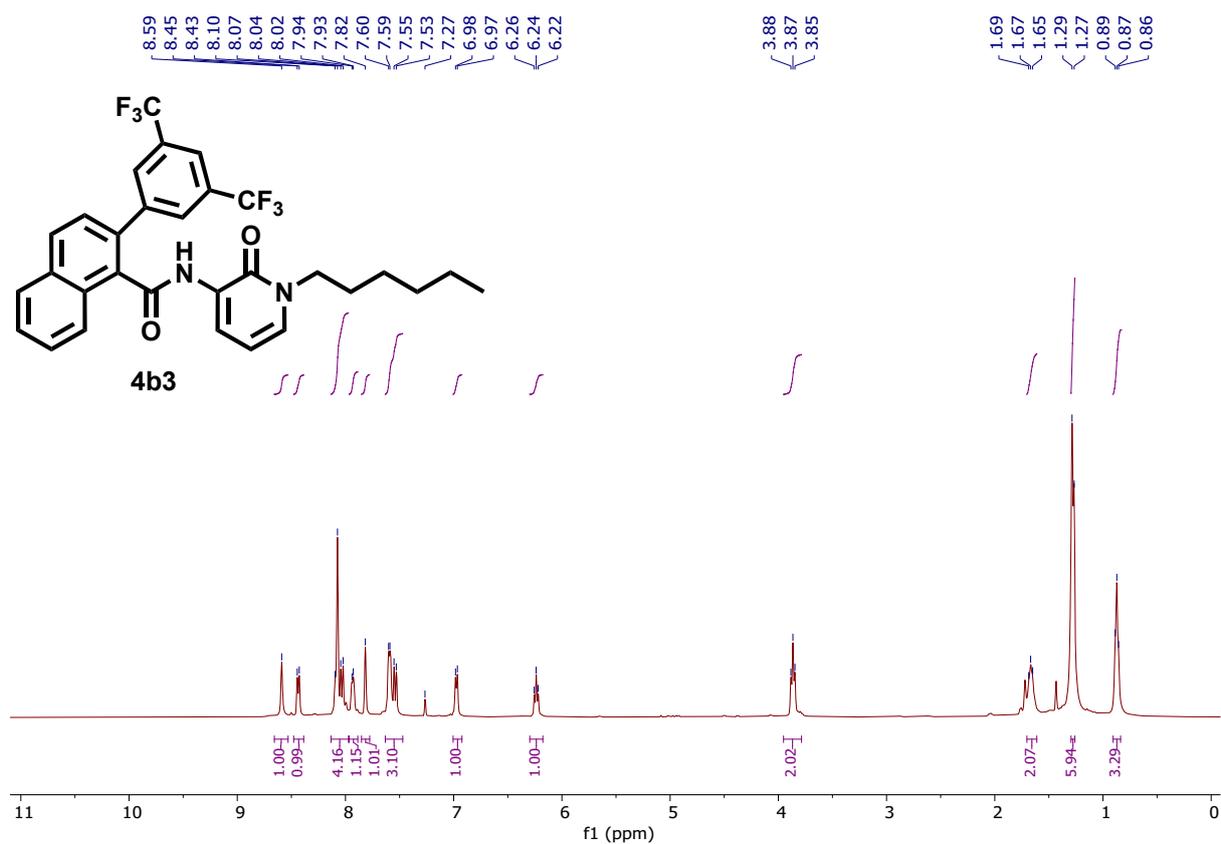
^1H NMR of **4b2** in CDCl_3 (400MHz)



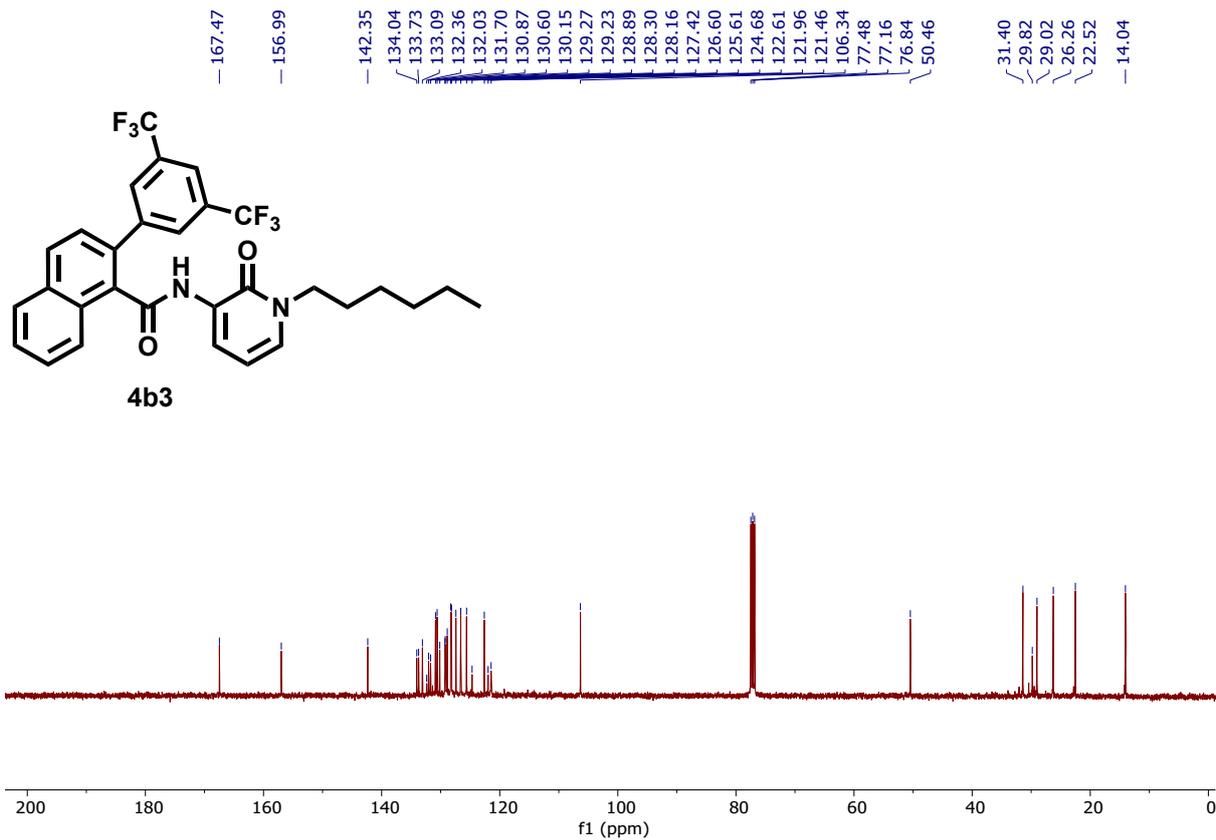
¹³C NMR of 4b2 in CDCl₃ (400MHz)



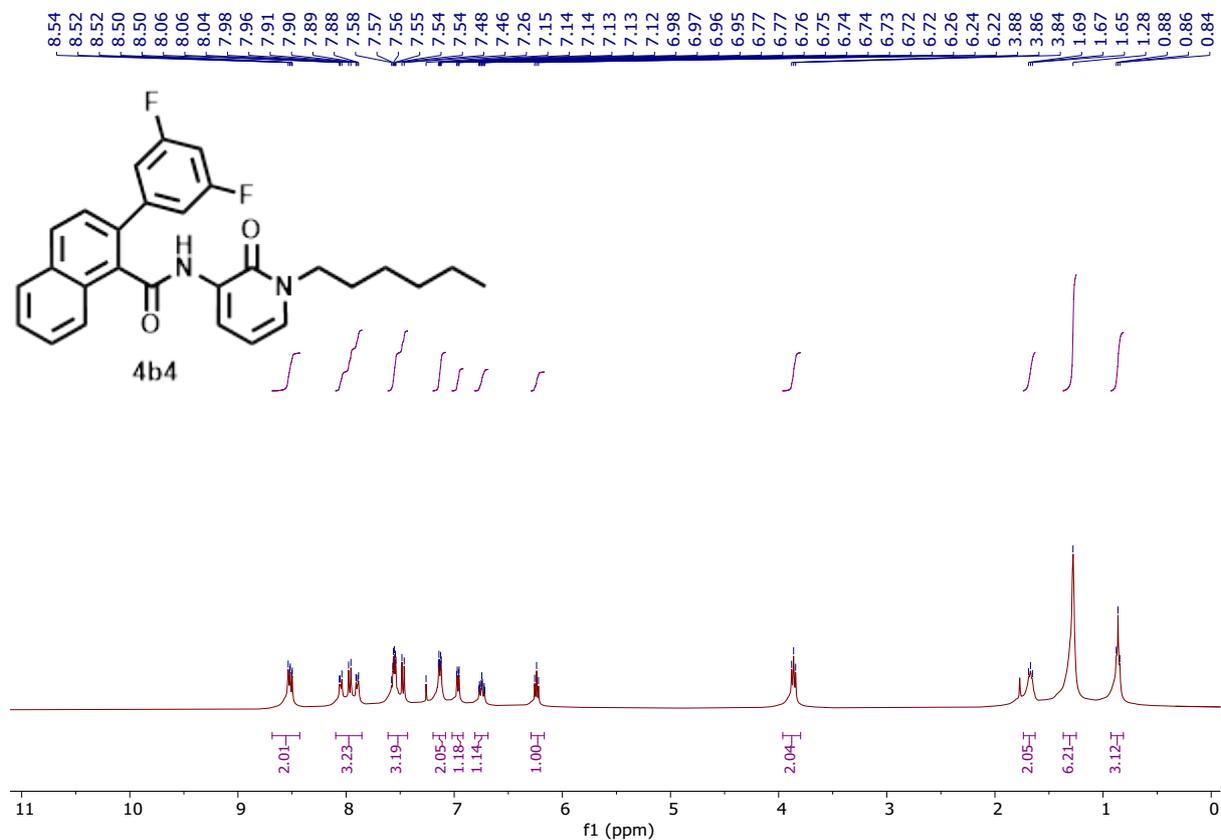
^1H NMR of **4b3** in CDCl_3 (400MHz)



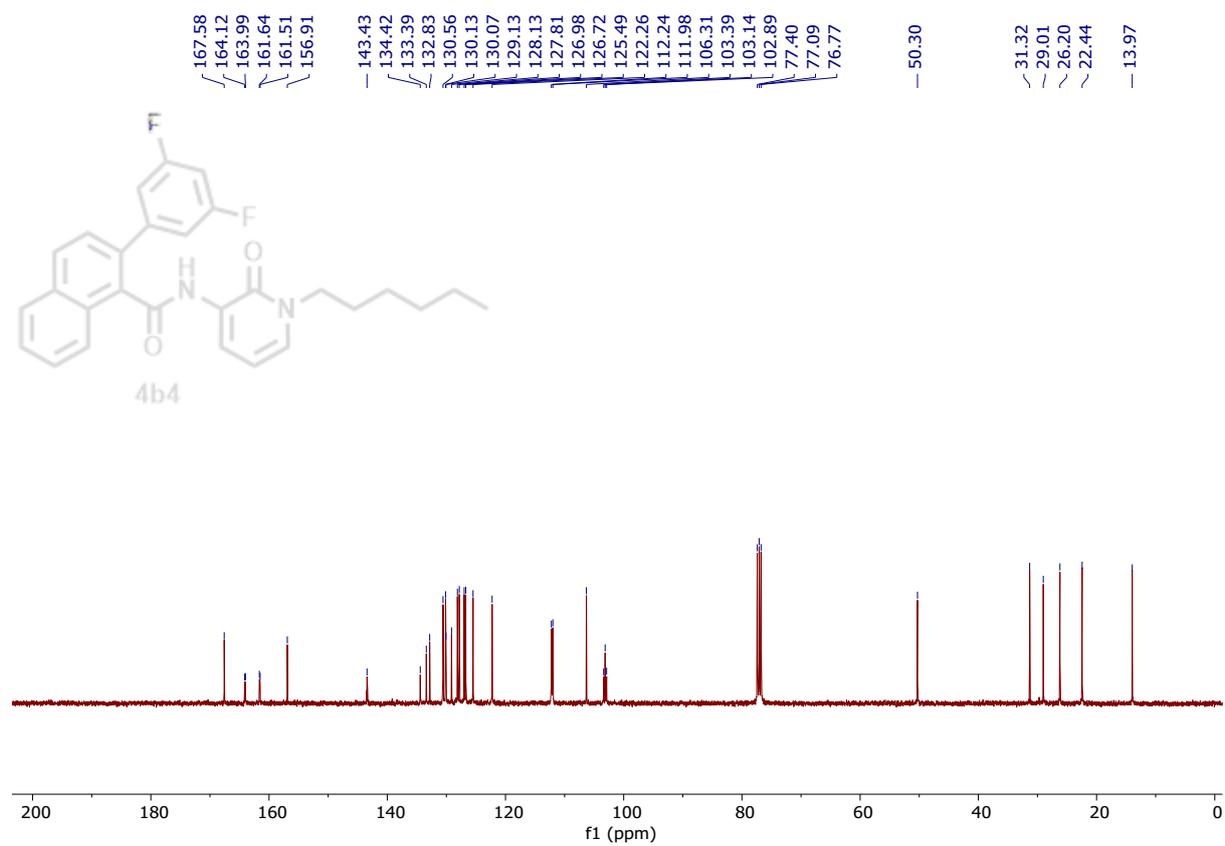
^{13}C NMR of **4b3** in CDCl_3 (400MHz)



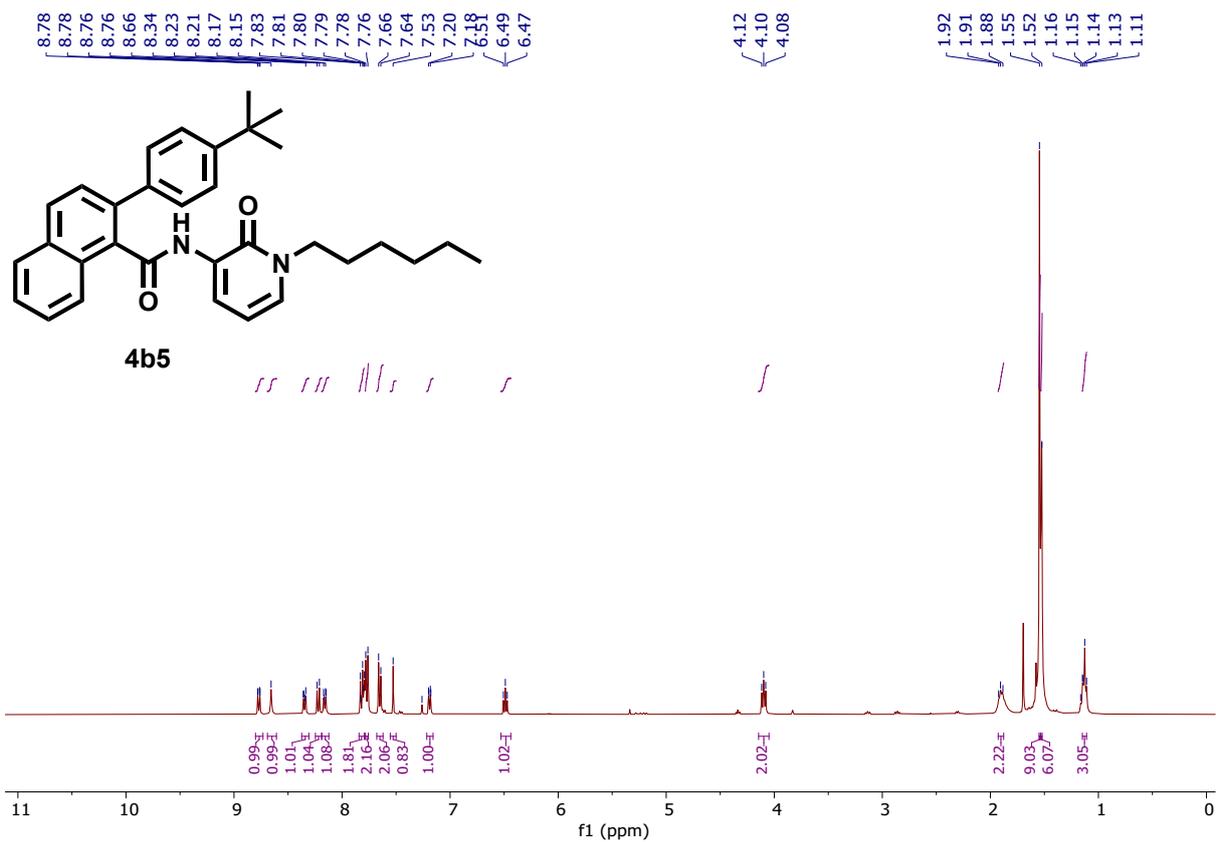
¹H NMR of **4b4** in CDCl₃ (400MHz)



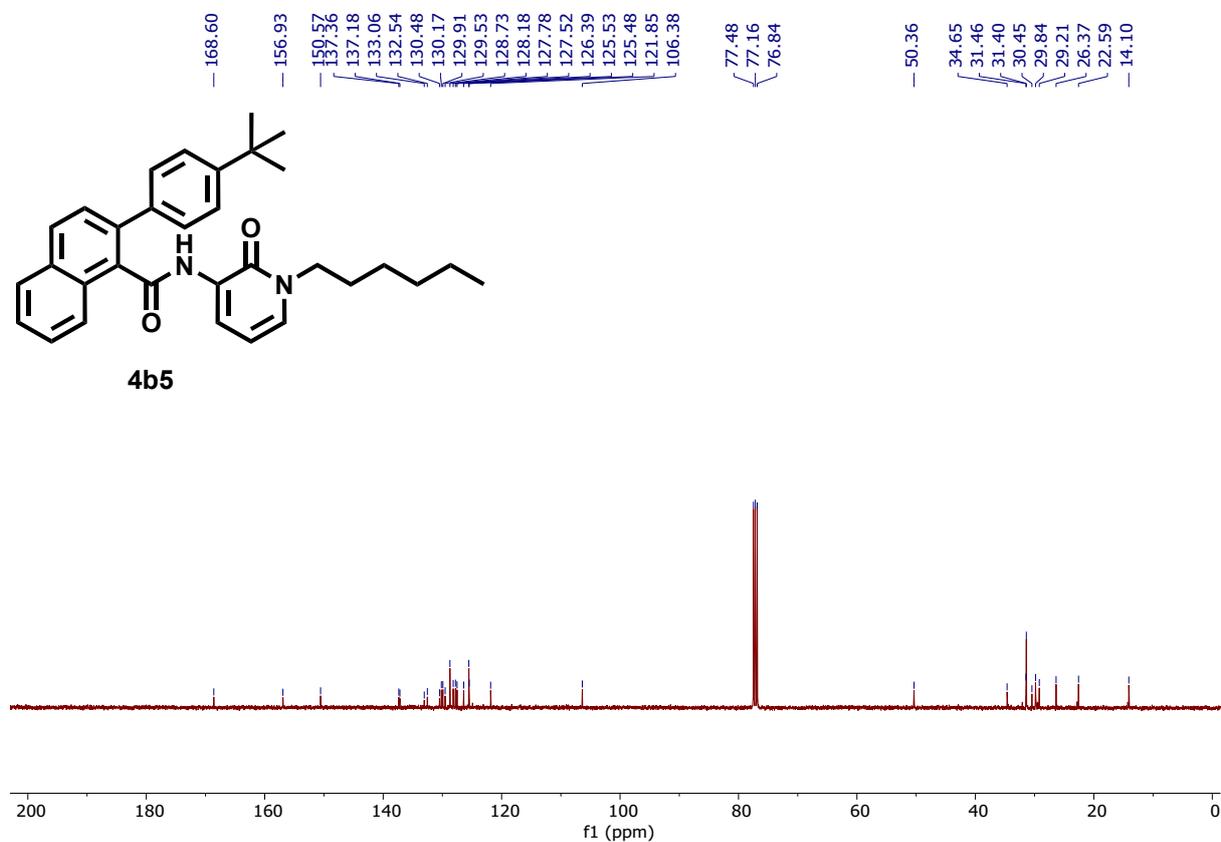
^{13}C NMR of **4b4** in CDCl_3 (400MHz)



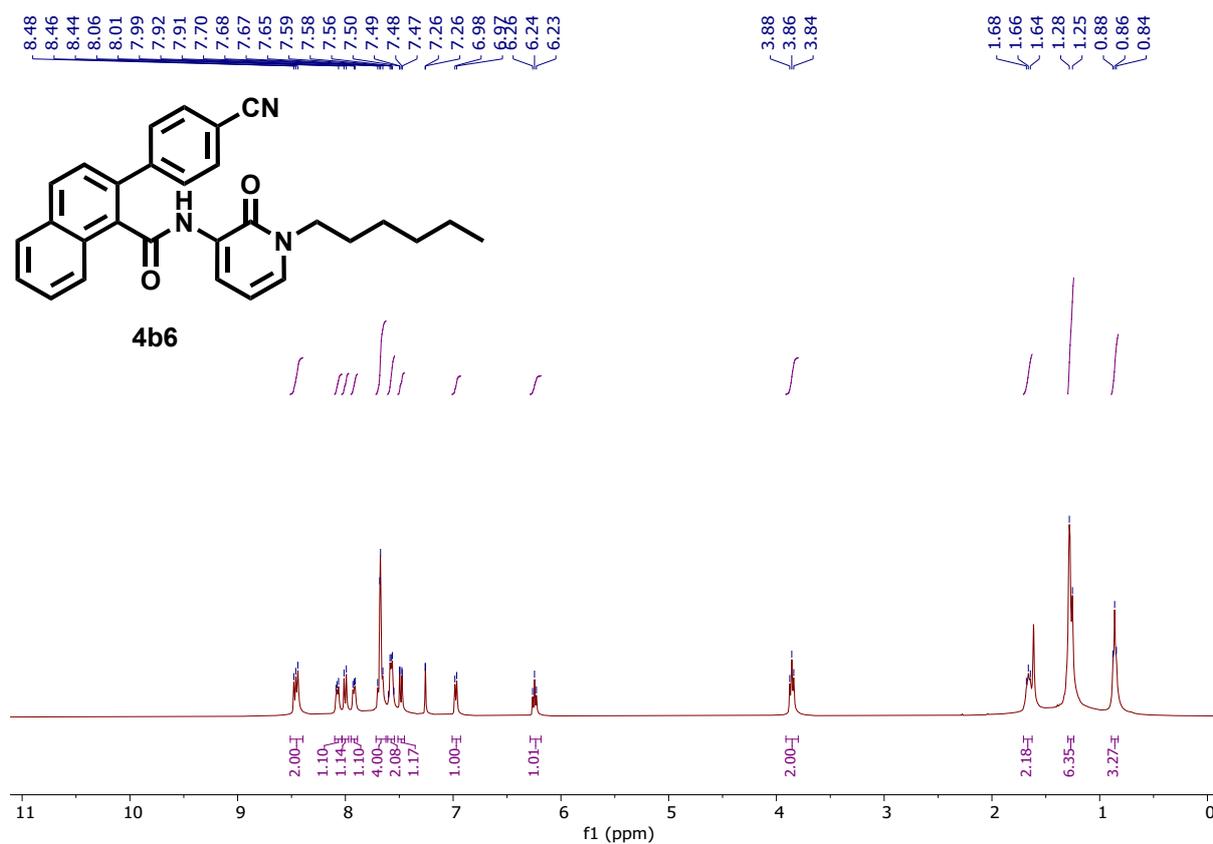
^1H NMR of **4b5** in CDCl_3 (400MHz)



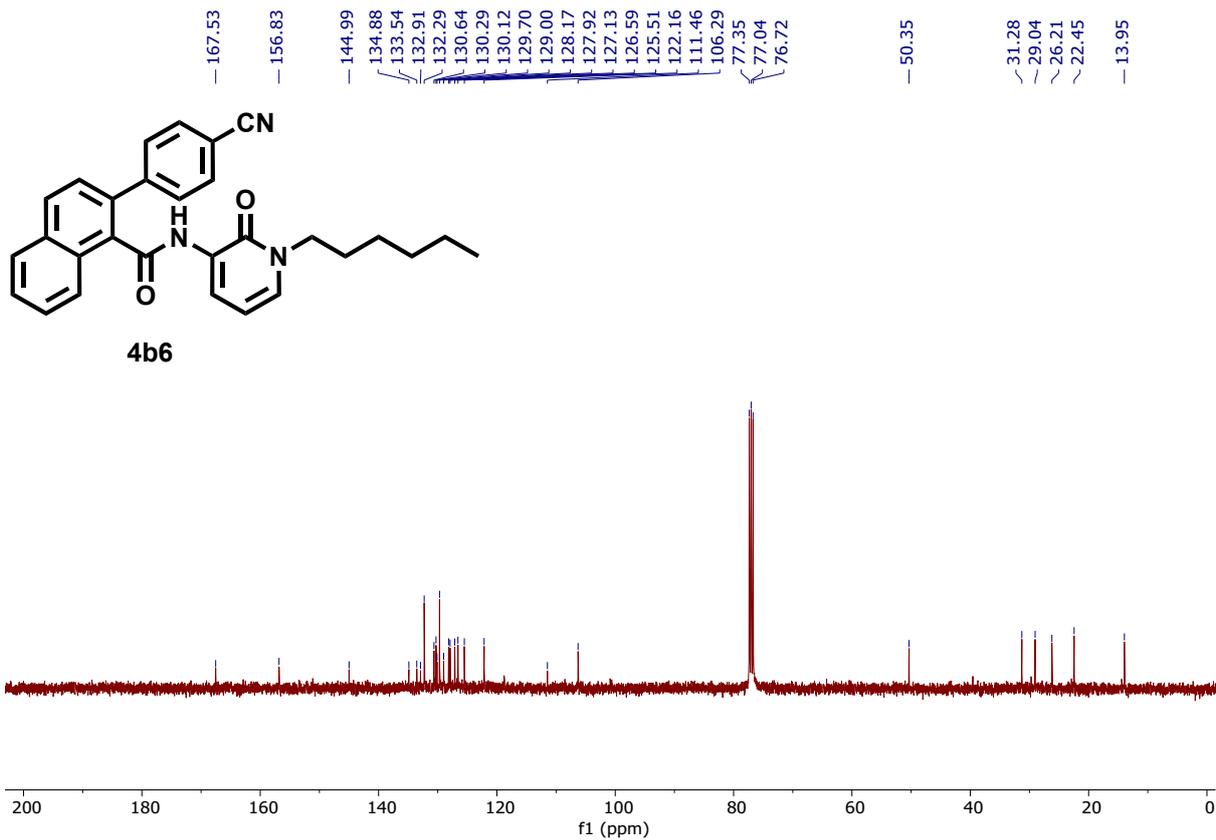
¹³C NMR of 4b5 in CDCl₃ (400MHz)



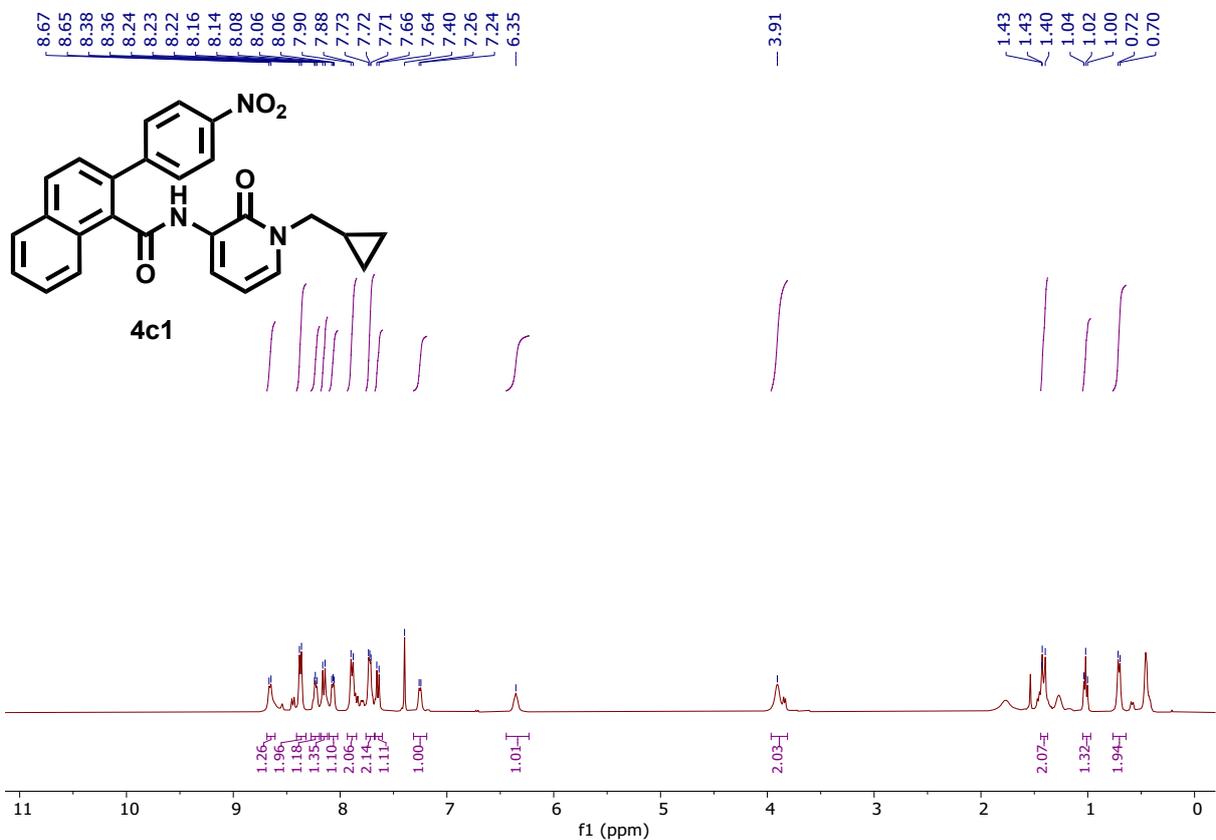
^1H NMR of **4b6** in CDCl_3 (400MHz)



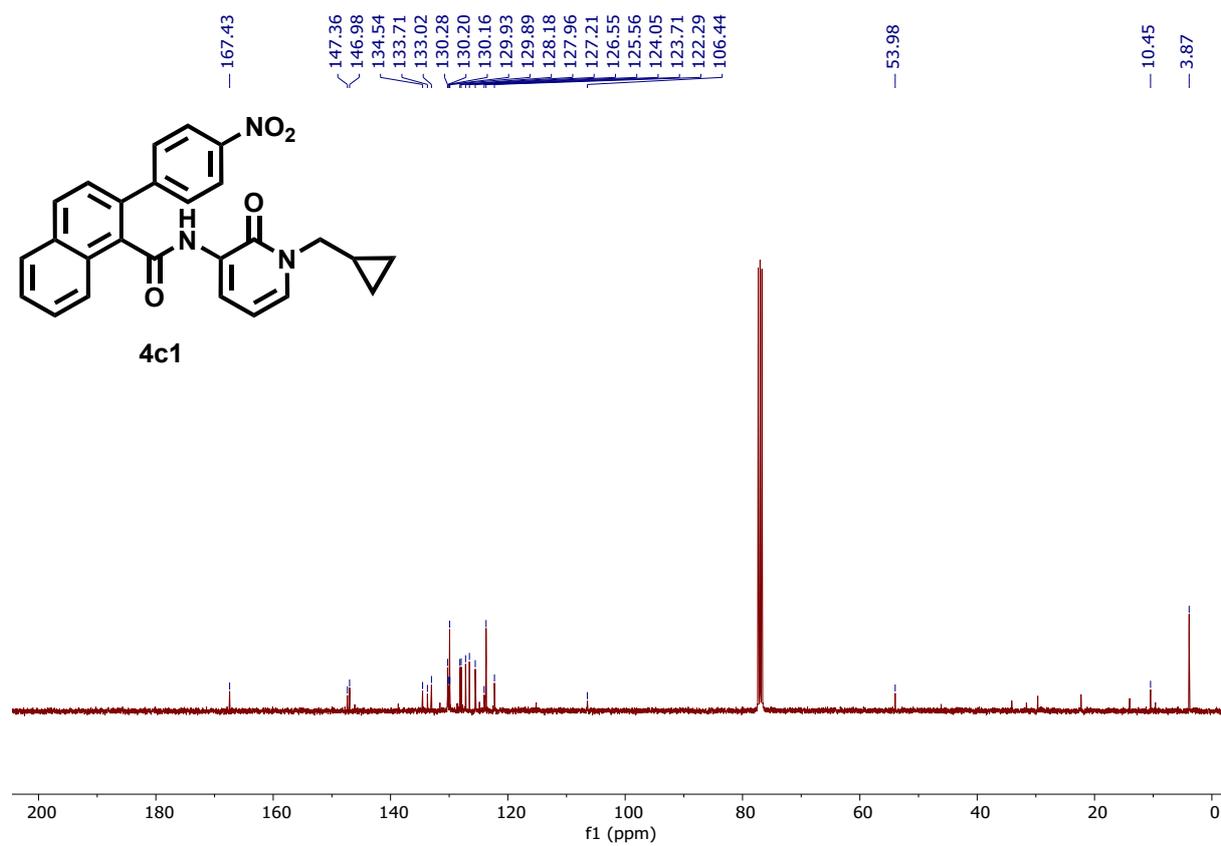
^{13}C NMR of **4b6** in CDCl_3 (400MHz)



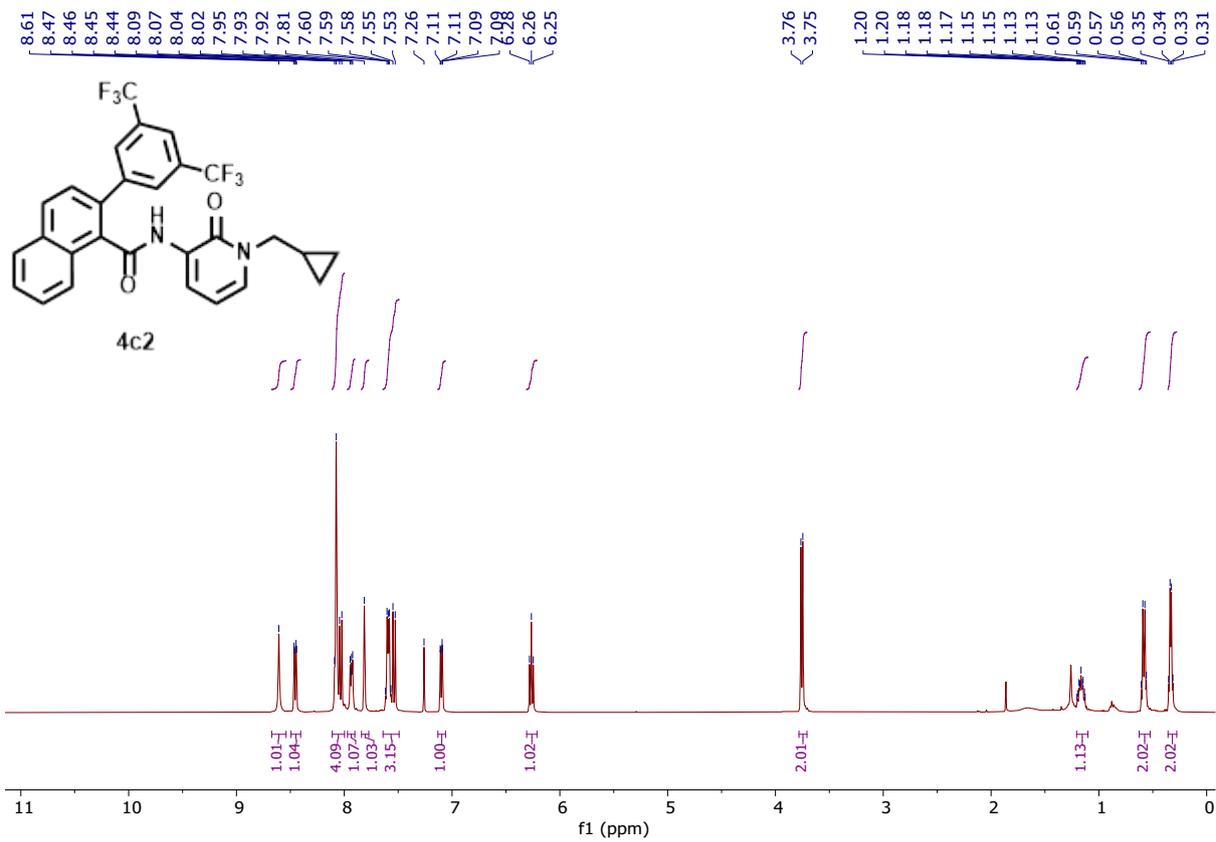
¹H NMR of **4c1** in CDCl₃ (400MHz)



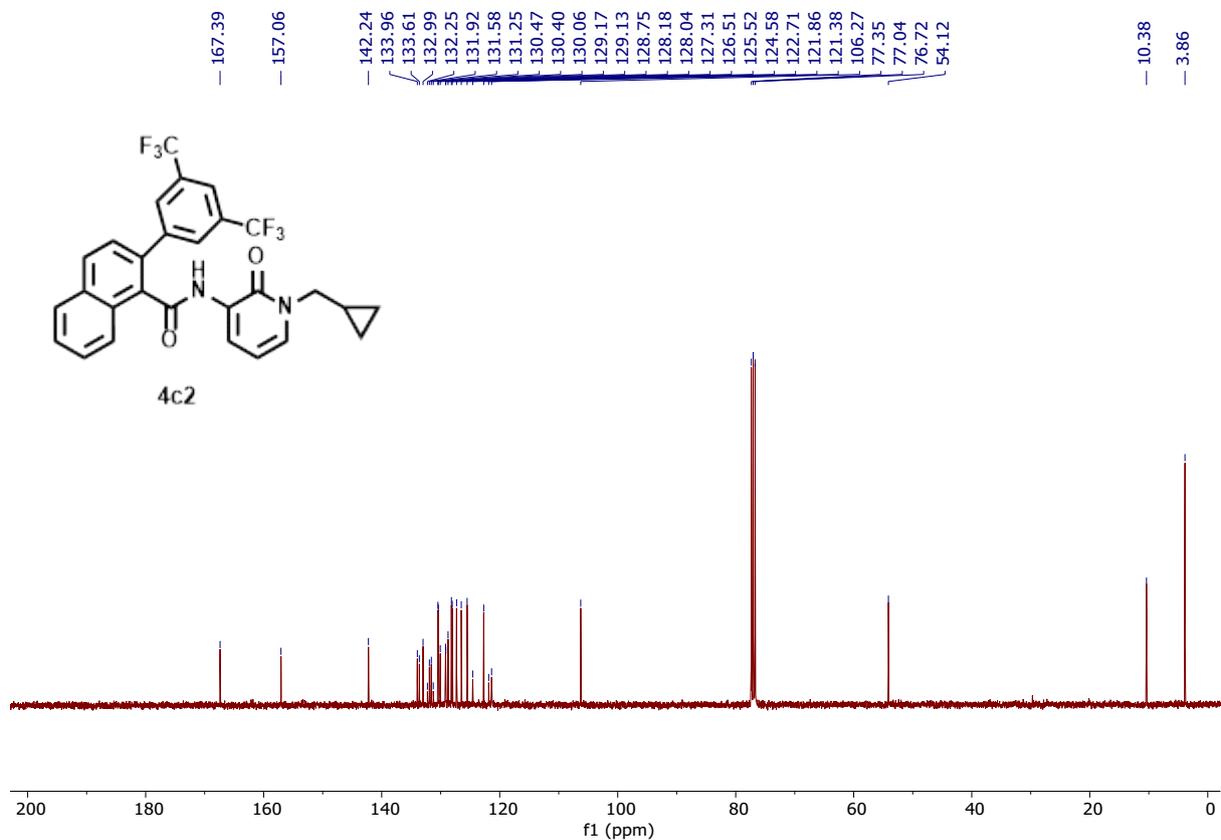
^{13}C NMR of **4c1** in CDCl_3 (400MHz)



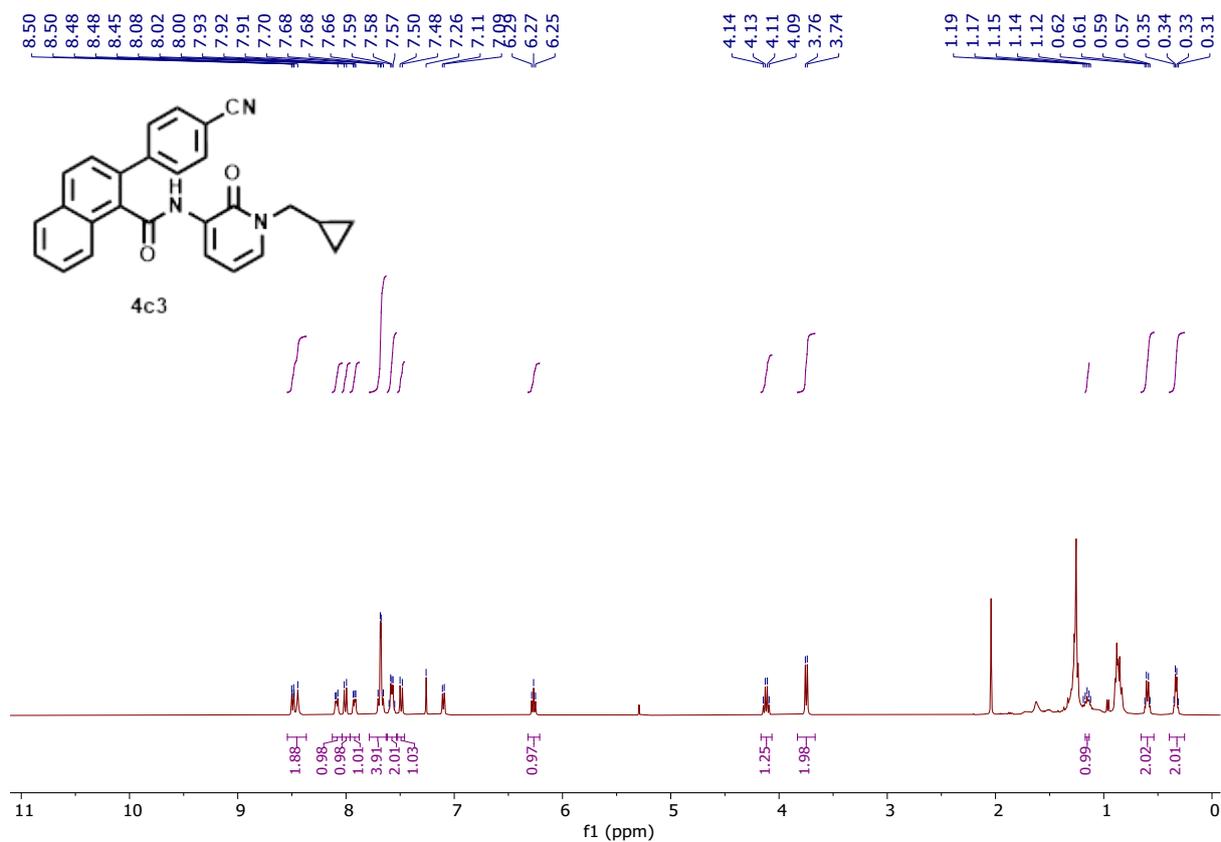
^1H NMR of **4c2** in CDCl_3 (400MHz)



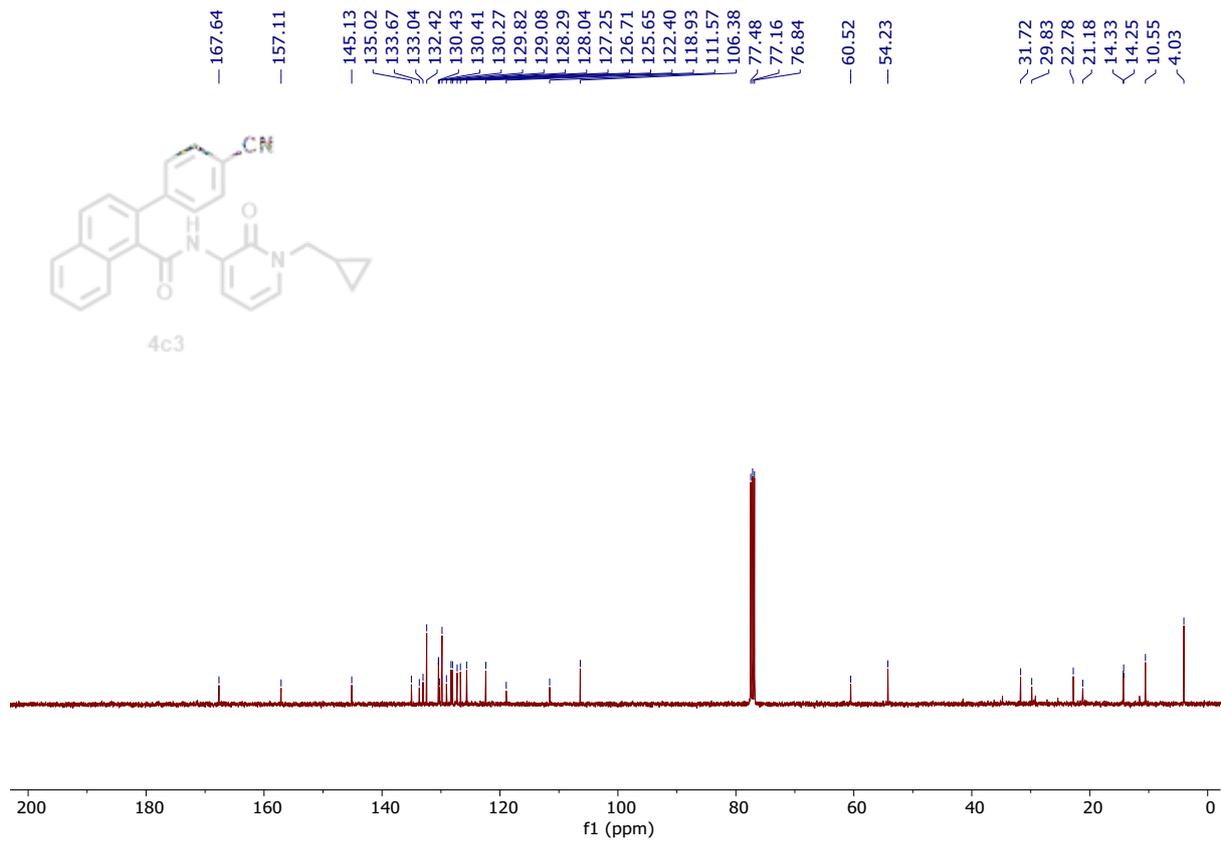
¹³C NMR of 4c2 in CDCl₃ (400MHz)



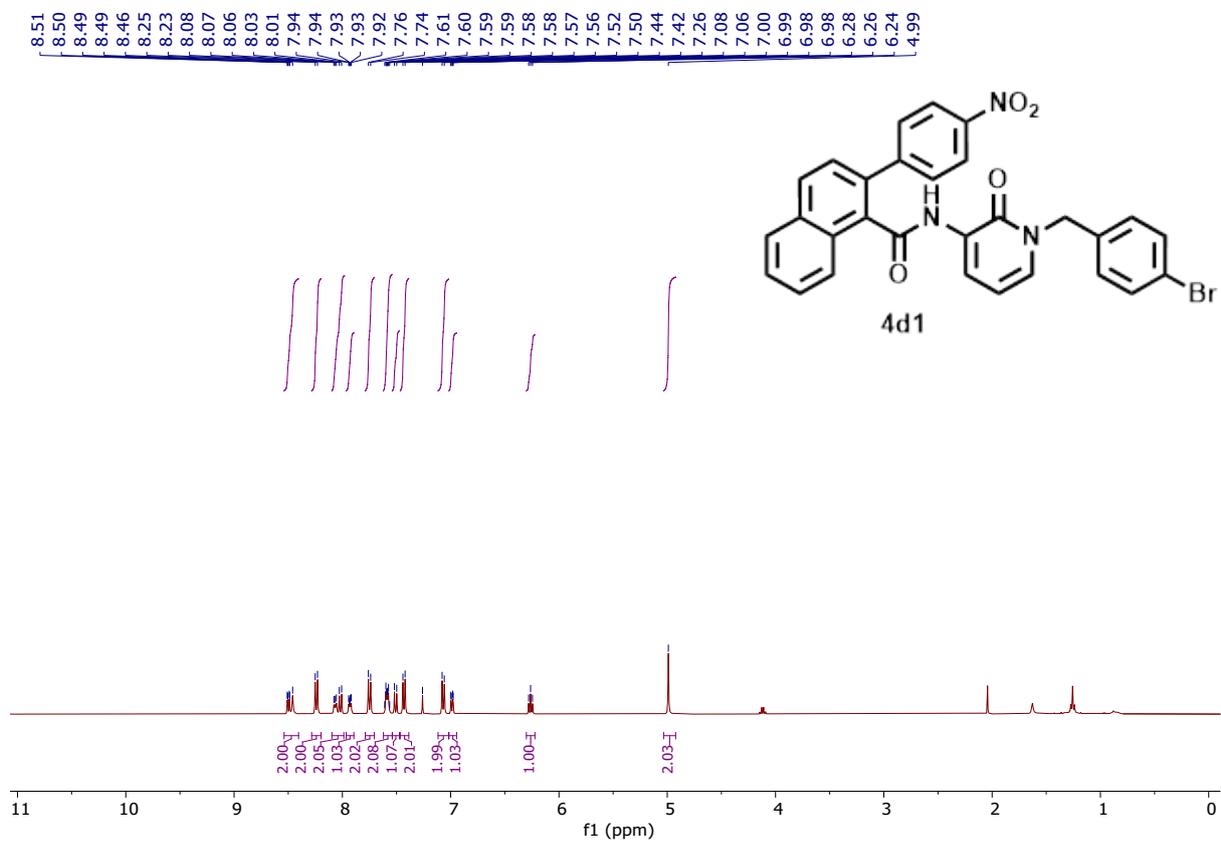
^1H NMR of **4c3** in CDCl_3 (400MHz)



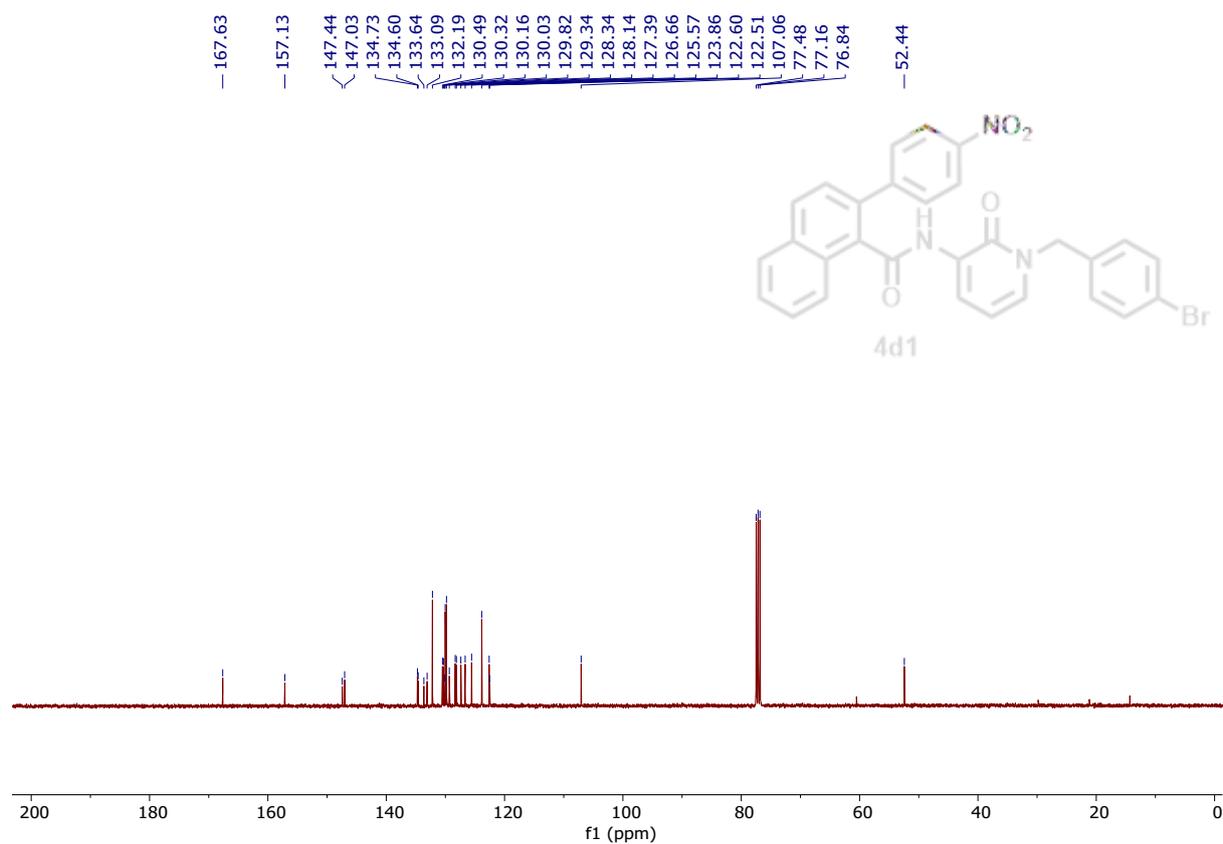
^{13}C NMR of **4c3** in CDCl_3 (400MHz)



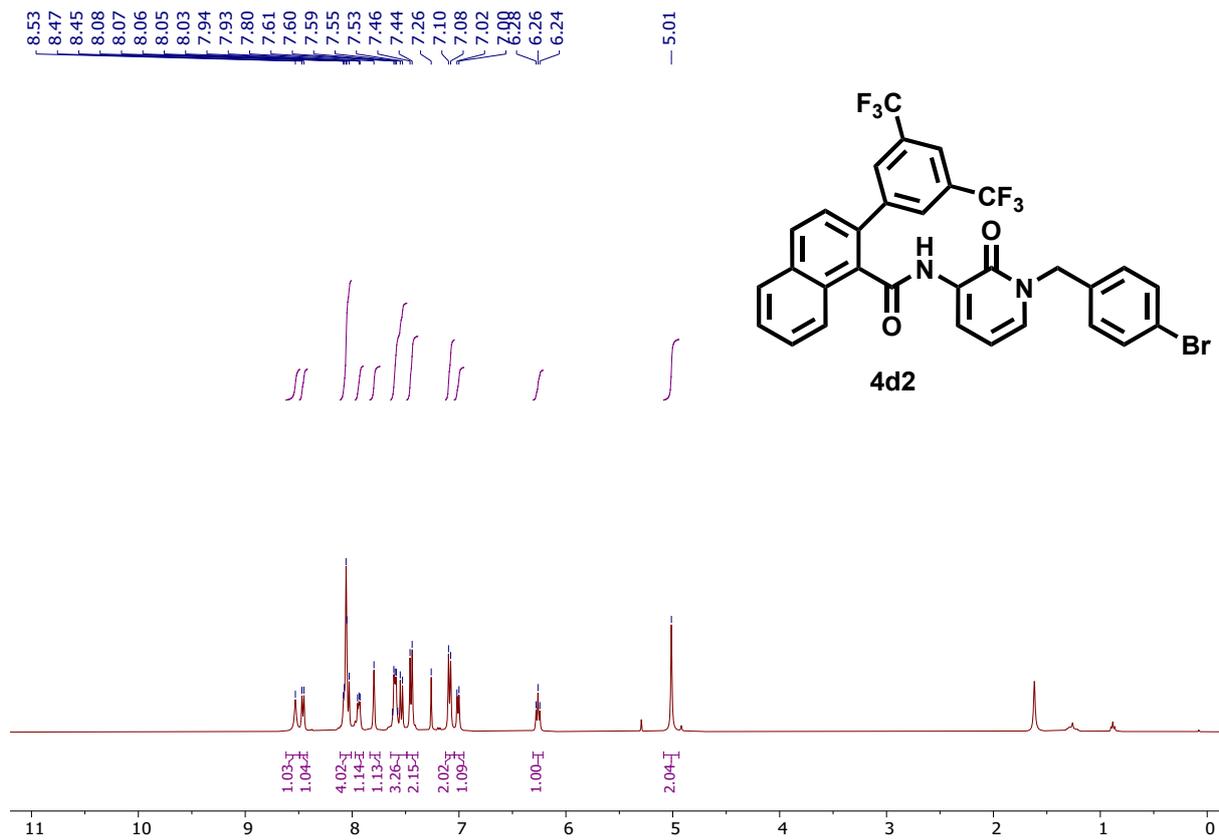
¹H NMR of 4d1 in CDCl₃ (400MHz)



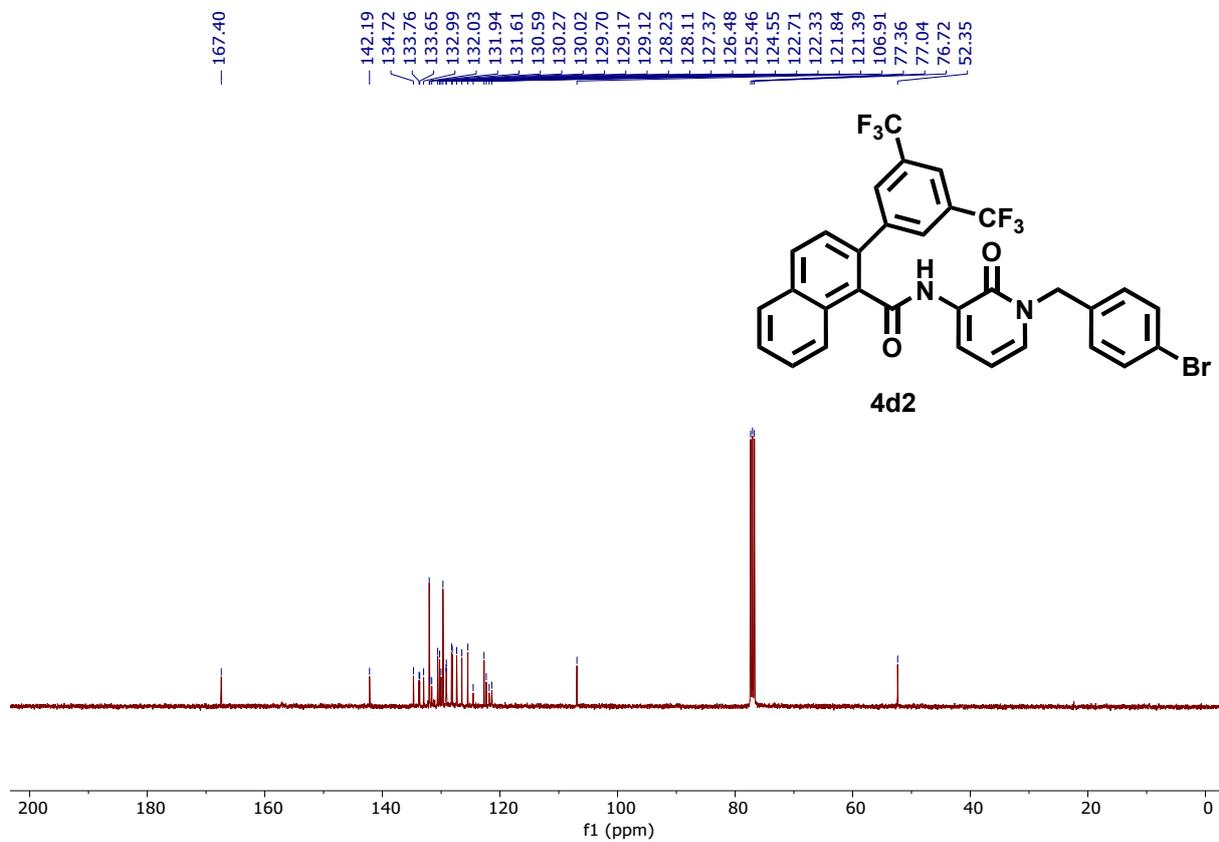
^{13}C NMR of **4d1** in CDCl_3 (400MHz)



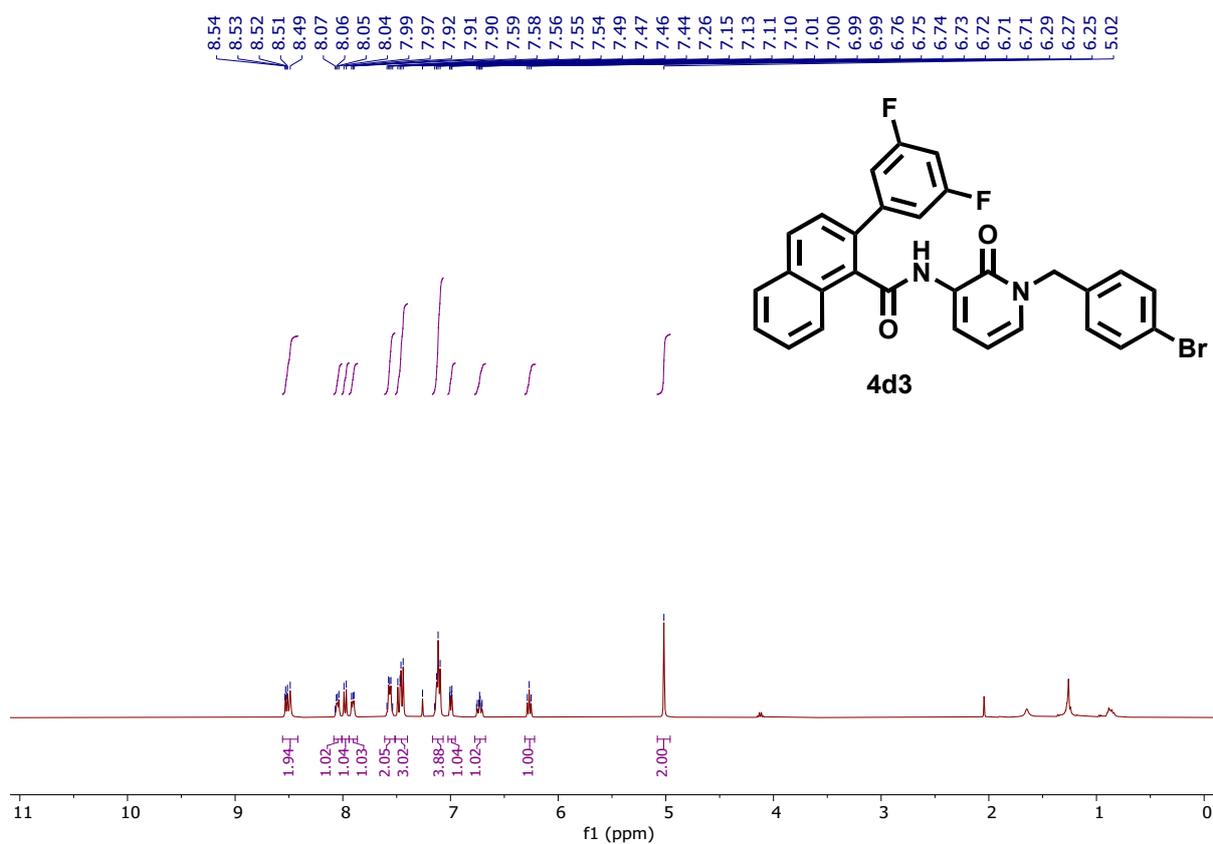
^1H NMR of **4d2** in CDCl_3 (400MHz)



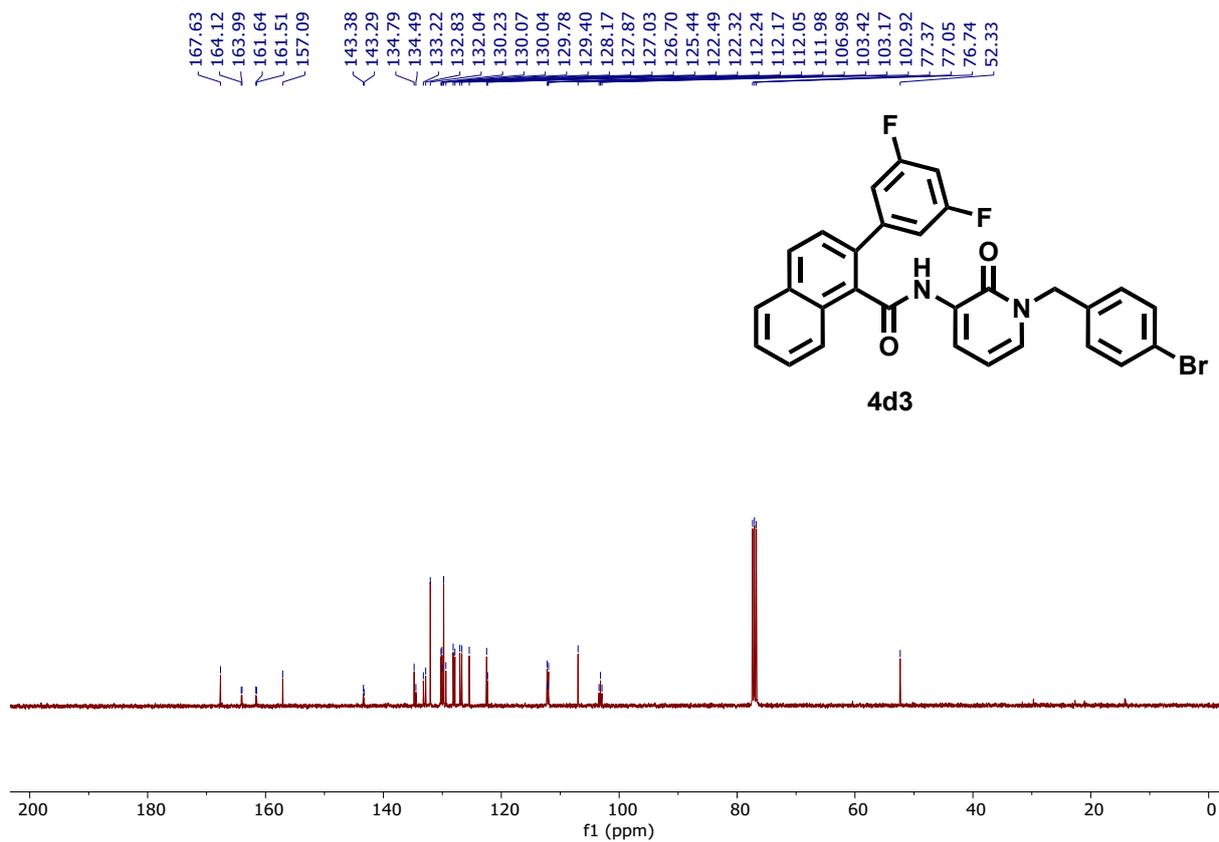
¹³C NMR of **4d2** in CDCl₃ (400 MHz)



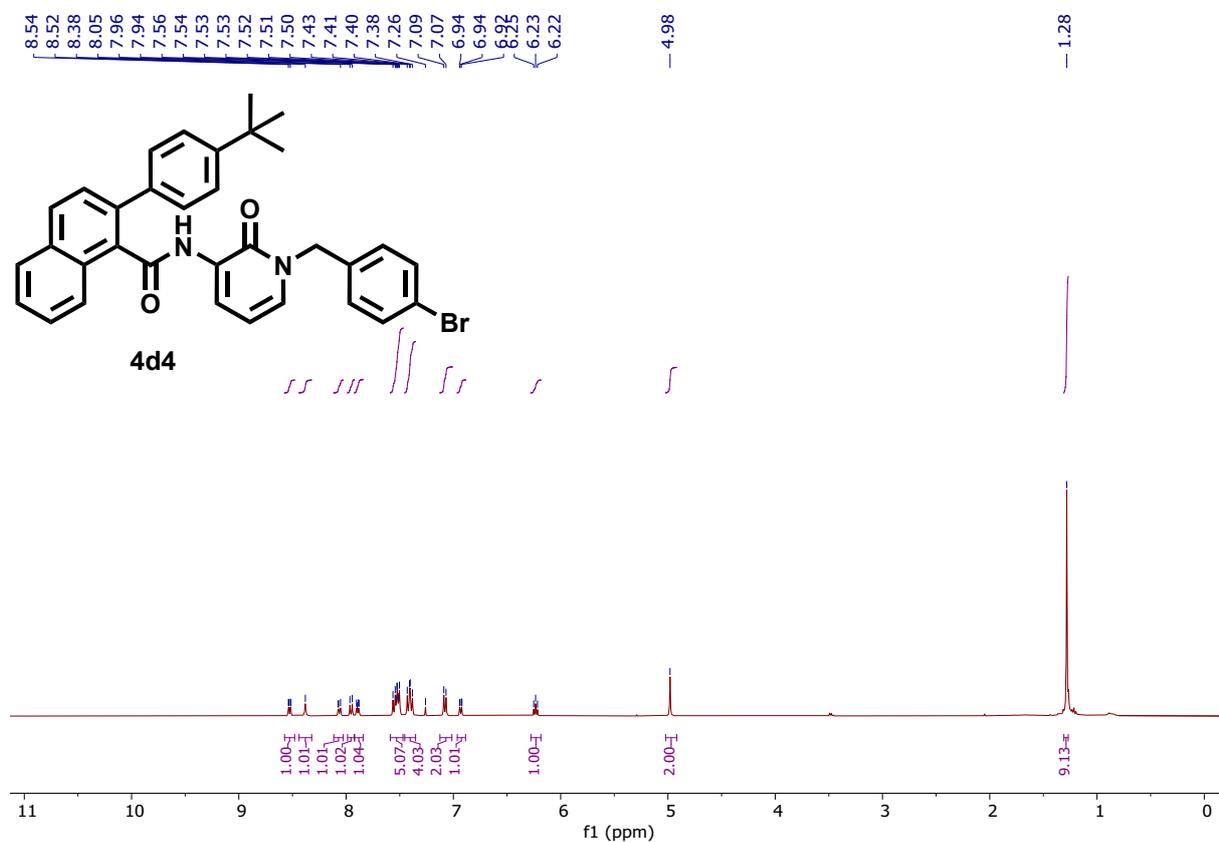
^1H NMR of **4d3** in CDCl_3 (400MHz)



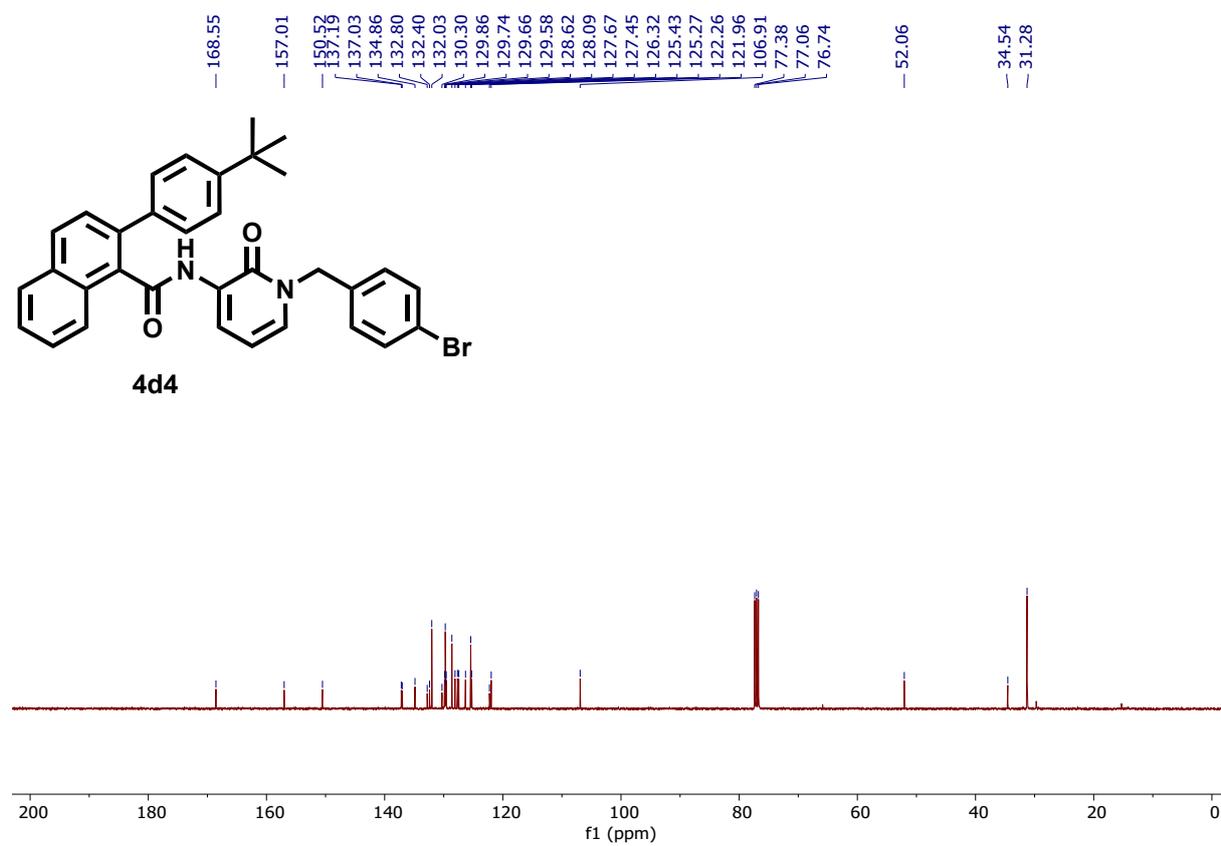
^{13}C NMR of **4d3** in CDCl_3 (400MHz)



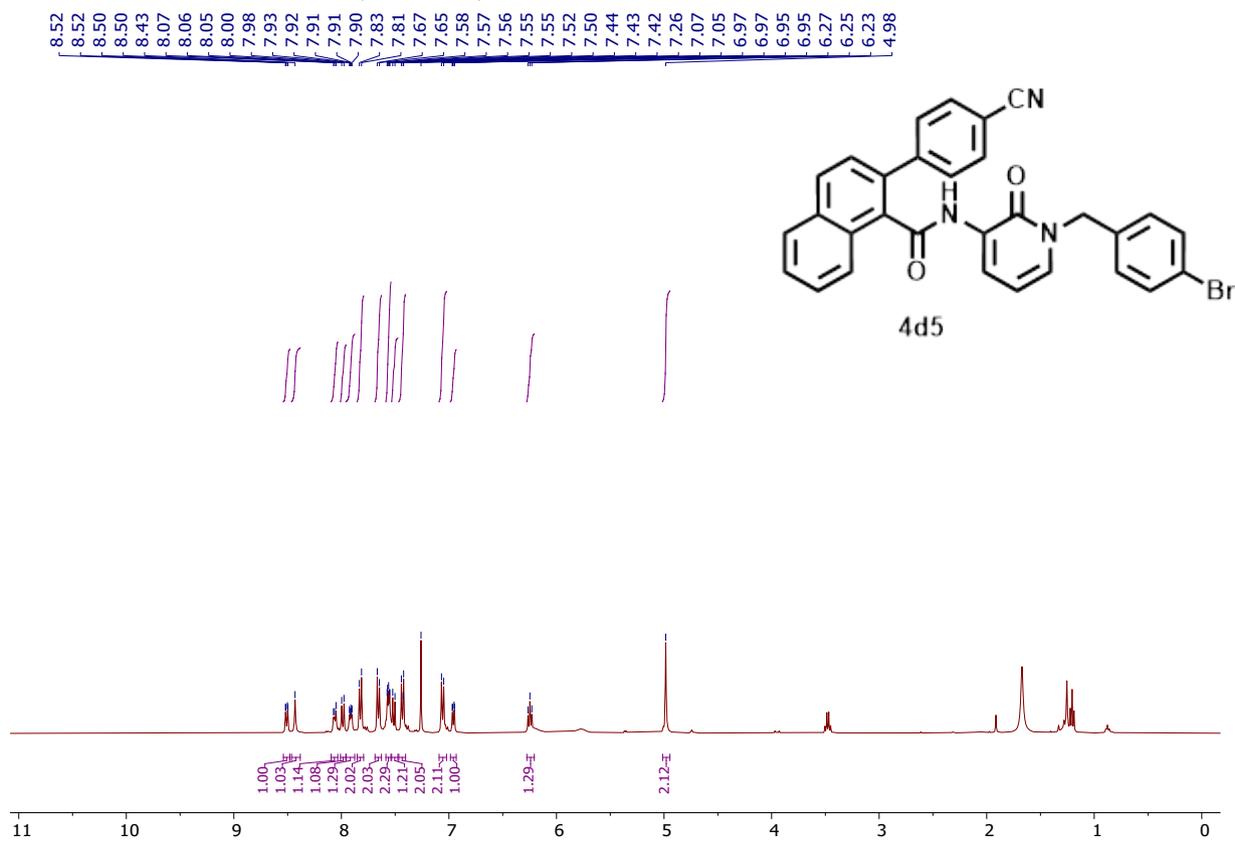
¹H NMR of **4d4** in CDCl₃ (400MHz)



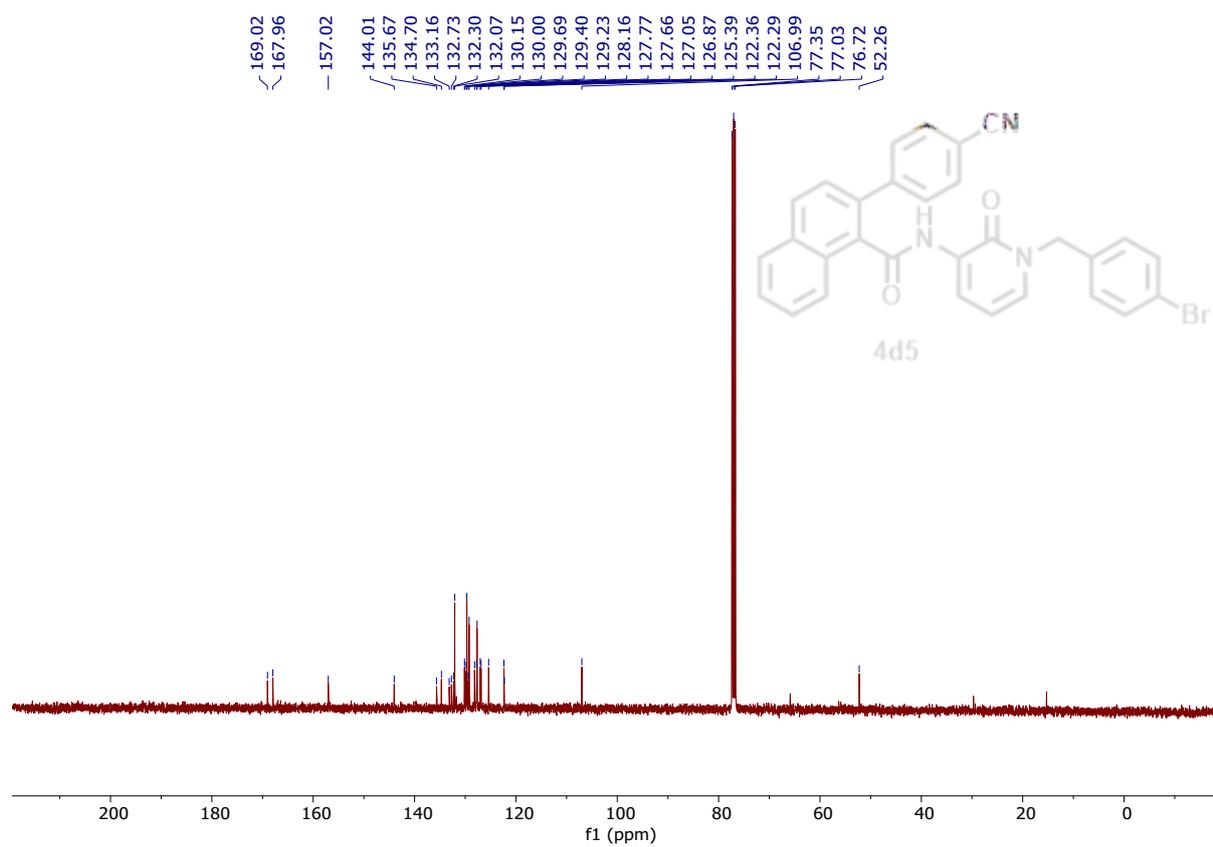
^{13}C NMR of **4d4** in CDCl_3 (400MHz)



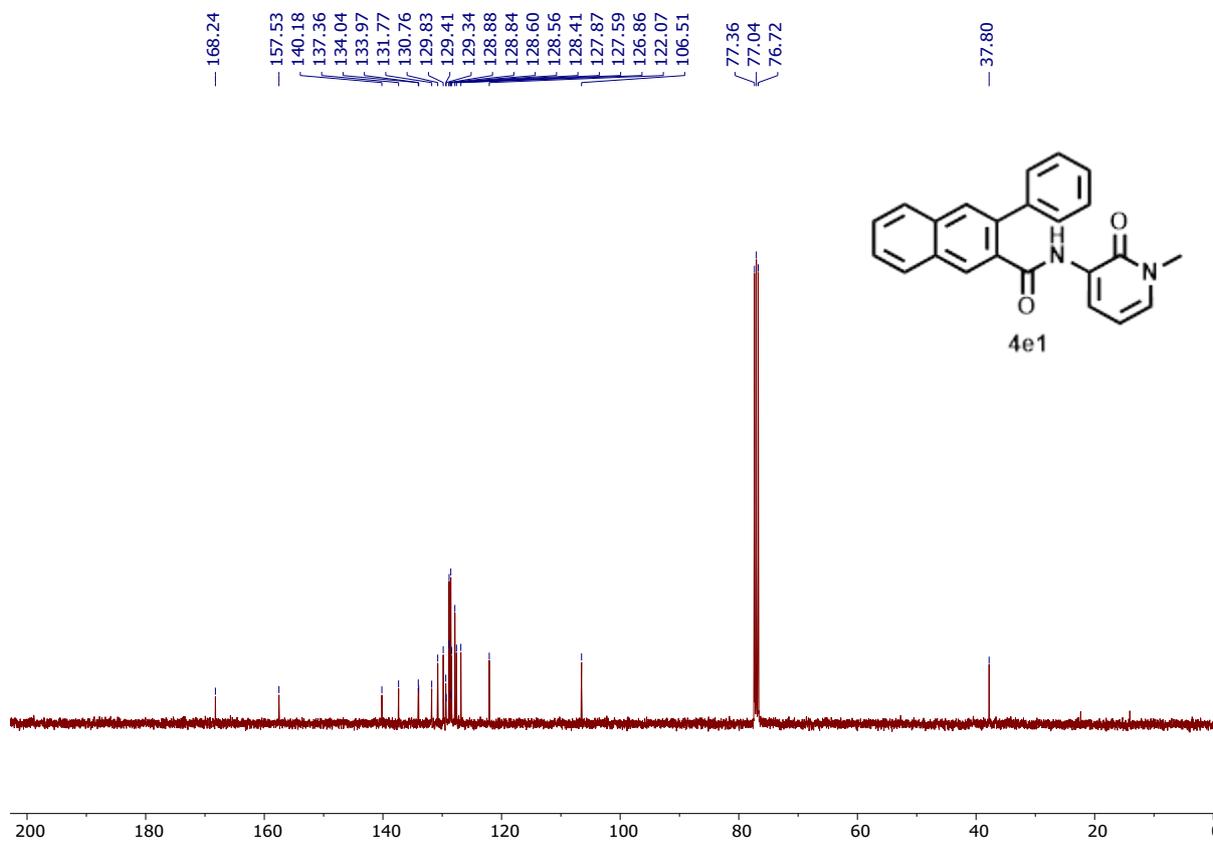
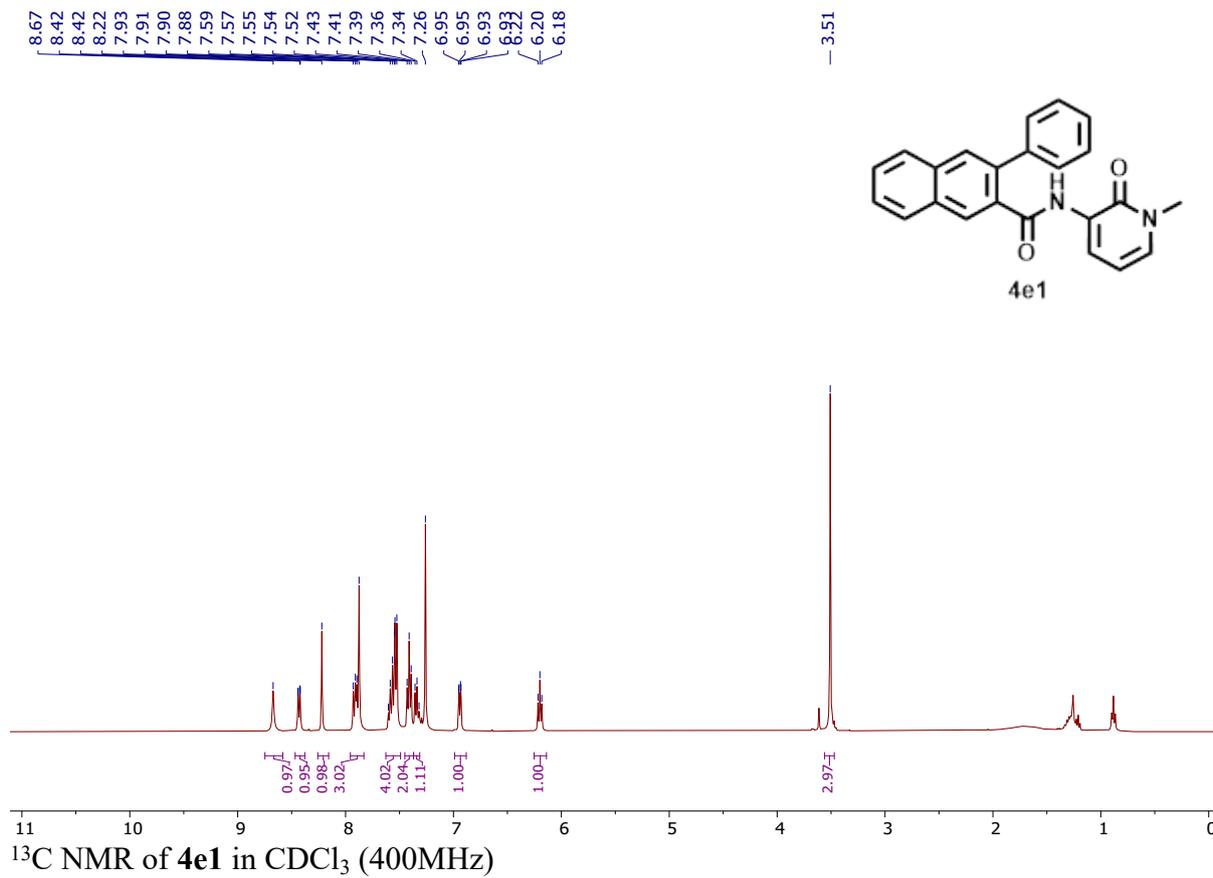
^1H NMR of **4d5** in CDCl_3 (400MHz)



^{13}C NMR of **4d5** in CDCl_3 (400MHz)

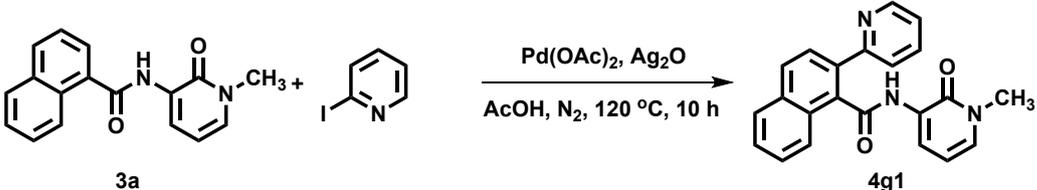
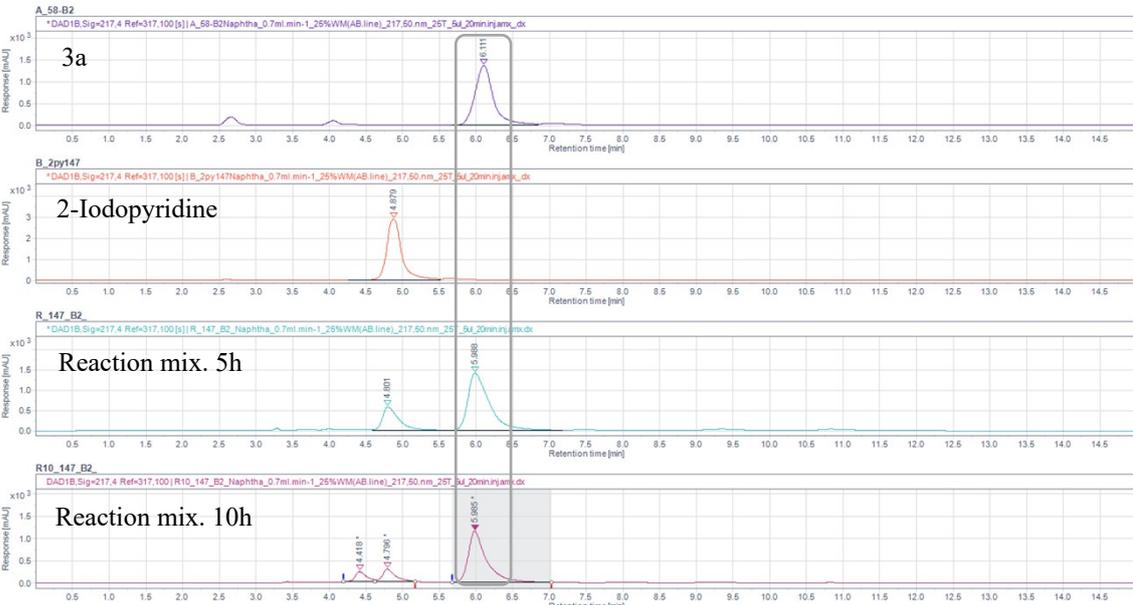
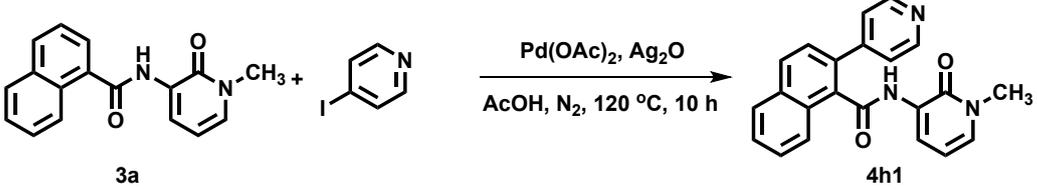


^1H NMR of **4e1** in CDCl_3 (400MHz)



9. HPLC Analysis

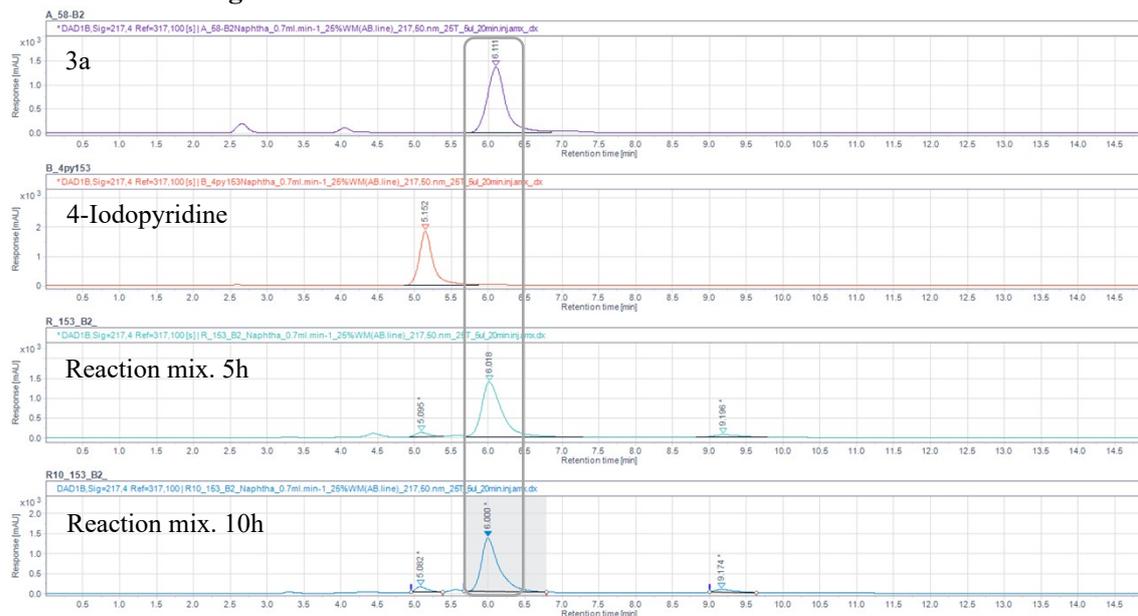
Table S1. HPLC analysis of the reaction of **3a** with 2-Iodo-pyridine, 4-Iodo-pyridine, 5-Iodo-1*H*-indole and 5-Iodo-1*H*-imidazole using identical reaction condition. HPLC chromatogram of the crude reaction mixture after 5h and 10h were recorded as below. The chromatography results and observations are tabulated below.

1	<p>Reaction:</p>  <p style="text-align: center;">3a 4g1</p>	
<p>HPLC Acquisition Method: Column: ZORBAX Eclipse Plus C18 (4.6mm × 250mm × 5μm). Solvent System: Water/Methanol (25/75 v/v) Mode: Isocratic Flow Rate: 0.7 mL/min Run Time: 15min Absorption Wavelength: 217nm (DAD-detector) Column Temperature: 25°C</p>		<p>Observation: HPLC analyses were performed after 5h and 10h of reaction. After 10h of reaction, the starting material 3a (retention time: 6.11 min) and 2-iodopyridine (retention time: 4.88 min) had remained unconsumed with a very trace non isolable peak observed at retention time 4.42 min.</p>
<p>HPLC Chromatogram:</p> 		
2	<p>Reaction:</p>  <p style="text-align: center;">3a 4h1</p>	
<p>HPLC Acquisition Method:</p>		<p>Observation:</p>

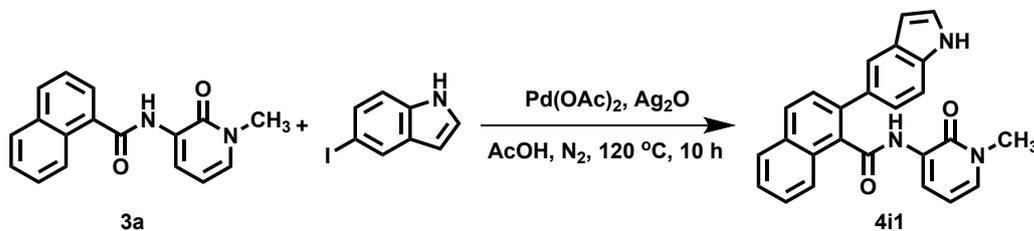
Column: ZORBAX Eclipse Plus C18 (4.6mm × 250mm × 5µm).
 Solvent System: Water/Methanol (25/75 v/v)
 Mode: Isocratic
 Flow Rate: 0.7 mL/min
 Run Time: 15min
 Absorption Wavelength: 217nm (DAD-detector)
 Column Temperature: 25°C

HPLC analyses were performed after 5h and 10h of reaction. In both the cases we observed identical chromatogram. The starting material **3a** (retention time: 6.11 min) and 4-iodopyridine (retention time: 5.15 min) had remained unconsumed with a very trace non isolable peak observed at retention time 9.17 min.

HPLC Chromatogram:



3 Reaction:



HPLC Acquisition Method:

Column: ZORBAX Eclipse Plus C18 (4.6mm × 250mm × 5µm).
 Solvent System: Water/Methanol (25/75 v/v)
 Mode: Isocratic
 Flow Rate: 0.7 mL/min
 Run Time: 15min
 Absorption Wavelength: 217nm (DAD-detector)
 Column Temperature: 25°C

Observation:

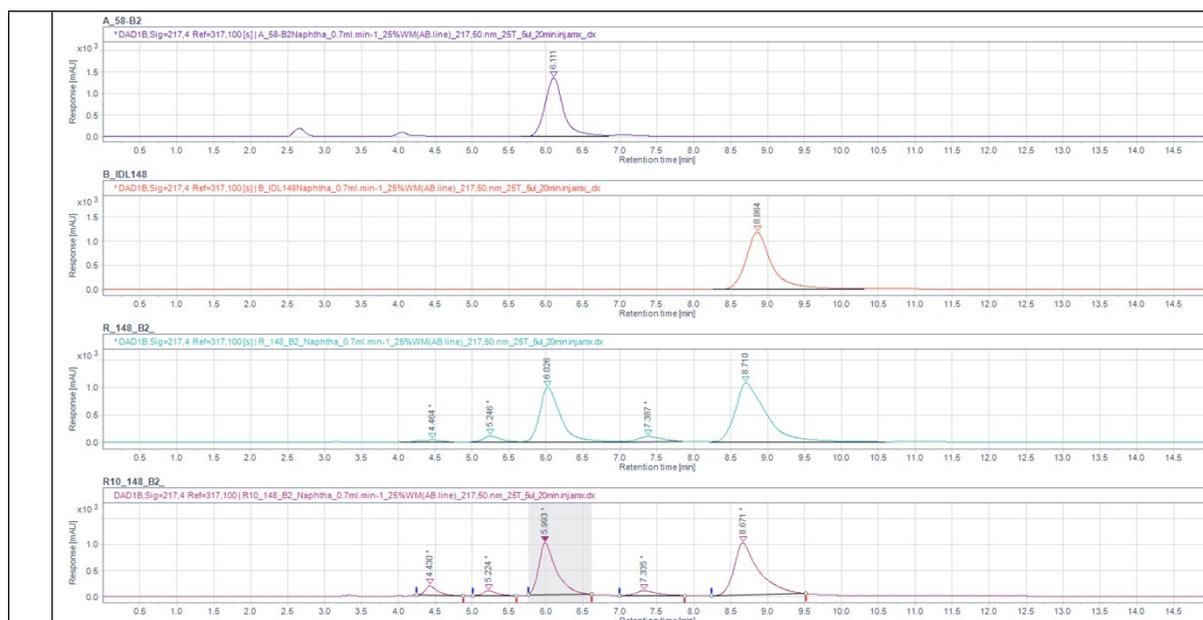
HPLC analyses were performed after 5h and 10h of reaction. In both the cases we observed similar chromatogram. The starting material **3a** (retention time: 6.11 min) and 5-iodoindole (retention time: 8.86 min) had remained unconsumed with a very trace non isolable peaks observed at retention times 4.43 min, 5.22 min, and 7.34 min.

HPLC Chromatogram:

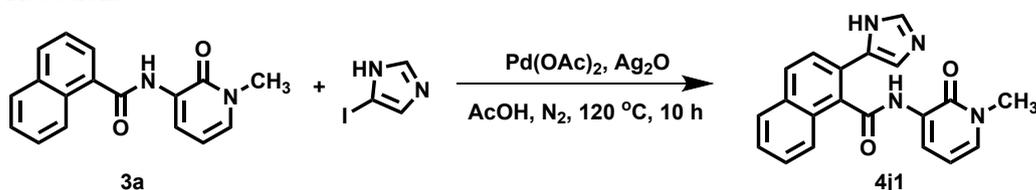
3a

5-Iodo-1H-indole

Reaction mix. 5h



4 Reaction:



HPLC Acquisition Method:

Column: ZORBAX Eclipse Plus C18 (4.6mm × 250mm × 5µm).
 Solvent System: Water/Methanol (25/75 v/v)
 Mode: Isocratic
 Flow Rate: 0.7 mL/min
 Run Time: 15min
 Absorption Wavelength: 217nm (DAD-detector)
 Column Temperature: 25°C

Observation:

HPLC analyses were performed after 5h and 10h of reaction. In both the cases we observed similar chromatogram. The starting material **3a** (retention time: 6.11 min) remained unconsumed with no formation of any new measurable product. Additionally, we did not observe any unconsumed 5-iodo-1*H*-imidazole (retention time: 4.05 min) after 5h or 10h of reaction, presumably because of its involvement in stable coordination with palladium.

HPLC Chromatogram:

3a

5-Iodo-1*H*-imidazole

Reaction mix. 5h

Reaction mix. 10h



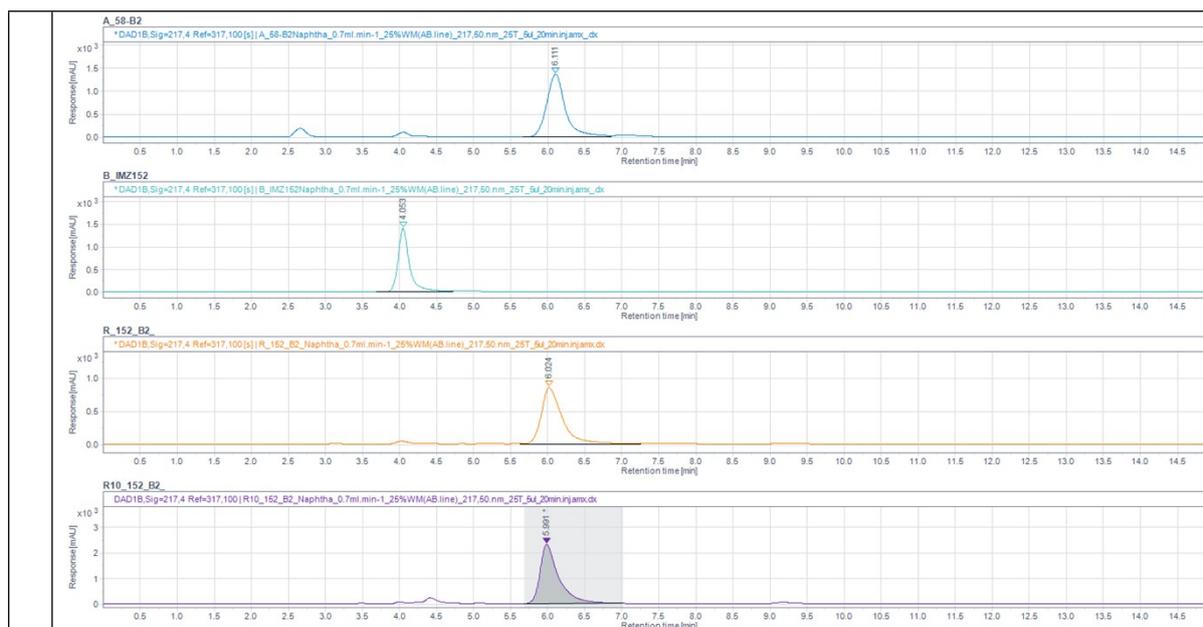


Table S2. HPLC analysis of the crude reaction mixture for the products of lower yields. To identify the reasons for a few lower yielded reactions, such as for the products **4b5** (16%), **3b6** (21%) and **4c3** (23%), we performed HPLC analysis of the crude reaction mixture after 10h and compared the HPLC retention time with the isolated standard sample. The chromatography results and observations are tabulated below.

<p>1 Reaction:</p> <p>3b + 4-tert-Butyl iodobenzene $\xrightarrow[\text{AcOH, N}_2, 120\text{ }^\circ\text{C, 10 h}]{\text{Pd(OAc)}_2, \text{Ag}_2\text{O}}$ 4b5</p>	
<p>HPLC Acquisition Method:</p> <p>Column: ZORBAX Eclipse Plus C18 (4.6mm × 250mm × 5μm). Solvent System: Water/Methanol (25/75 v/v) Mode: Isocratic Flow Rate: 0.7 mL/min Run Time: 15min Absorption Wavelength: 217nm (DAD-detector) Column Temperature: 25°C</p>	<p>Observation:</p> <p>HPLC analysis of the crude reaction mixture after 10h of reaction shows complete conversion of naphthamide (3b) and formation of 4b5 (retention time: 6.28 min) along with a few by-products.</p>
<p>HPLC Chromatogram:</p>	

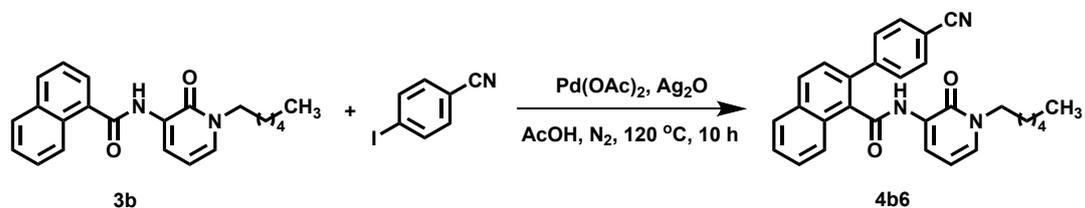
3b

4-tert-Butyl iodobenzene

Pure (4b5)



2 Reaction:



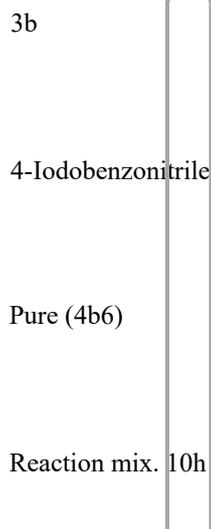
HPLC Acquisition Method:

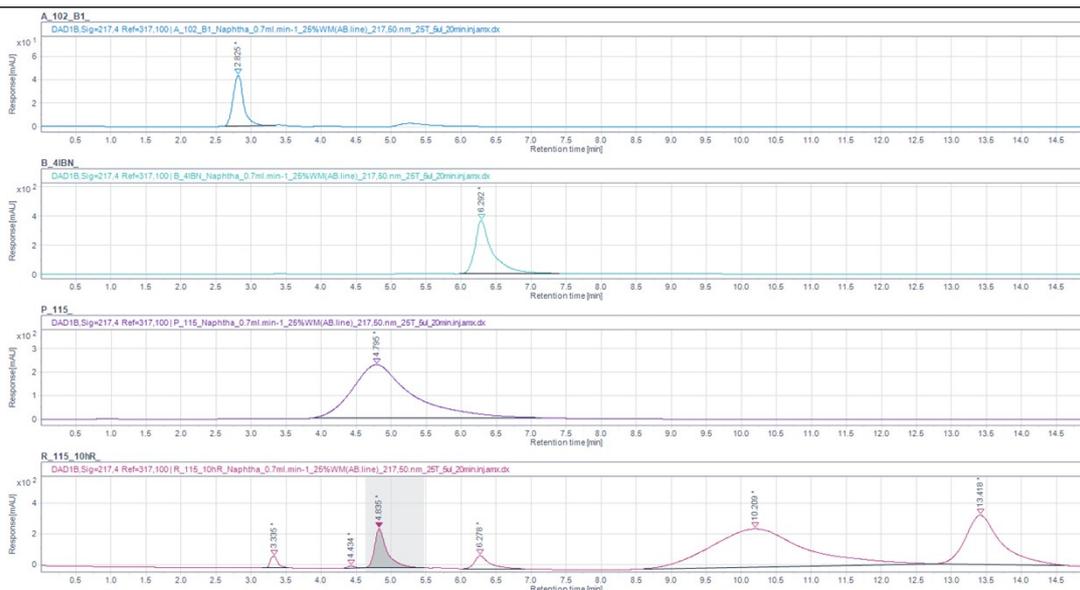
Column: ZORBAX Eclipse Plus C18 (4.6mm × 250mm × 5µm).
 Solvent System: Water/Methanol (25/75 v/v)
 Mode: Isocratic
 Flow Rate: 0.7 mL/min
 Run Time: 15min
 Absorption Wavelength: 217nm (DAD-detector)
 Column Temperature: 25°C

Observation:

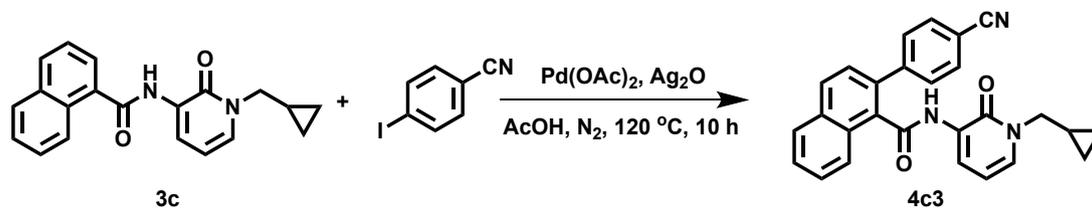
HPLC analysis of the crude reaction mixture after 10h of reaction shows complete conversion of naphthamide (**3b**) and formation of **4b6** (retention time: 4.83 min) along with a few by-products.

HPLC Chromatogram:





3 Reaction:



HPLC Acquisition Method:

Column: ZORBAX Eclipse Plus C18 (4.6mm × 250mm × 5µm).
 Solvent System: Water/Methanol (25/75 v/v)
 Mode: Isocratic
 Flow Rate: 0.7 mL/min
 Run Time: 15min
 Absorption Wavelength: 217nm (DAD-detector)
 Column Temperature: 25°C

Observation:

HPLC analysis of the crude reaction mixture after 10h of reaction shows complete conversion of naphthamide (3b) and formation of 4c3 (retention time: 9.51 min) along with a few by-products.

HPLC Chromatogram:

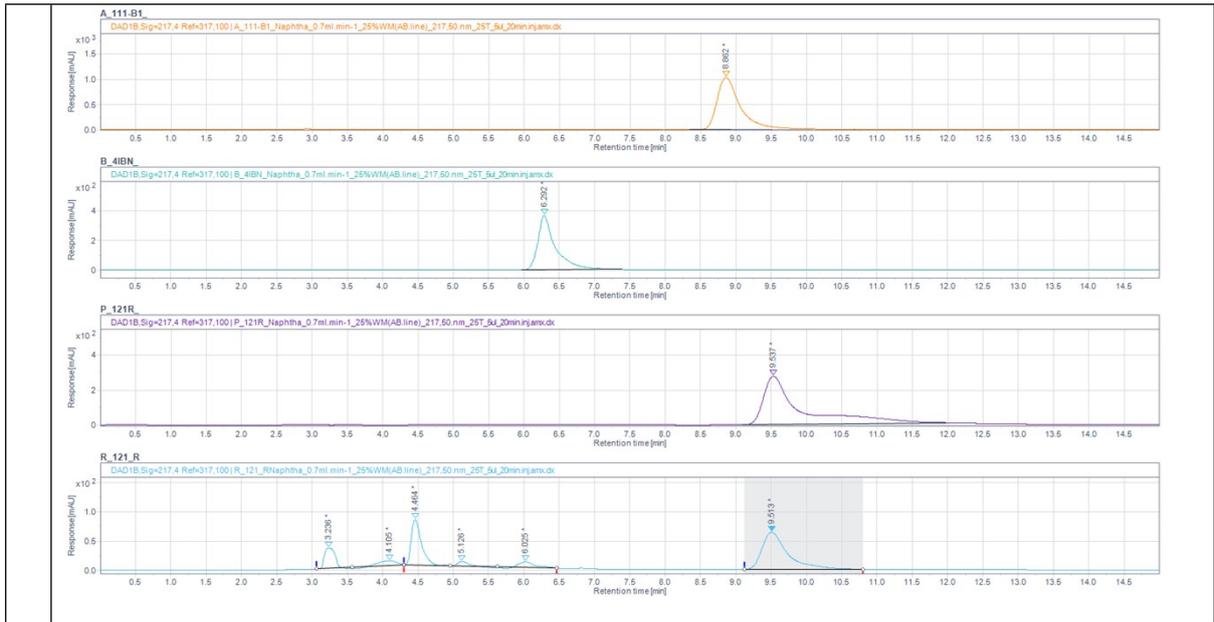
3c

4-Iodobenzonitrile

Pure (4c3)

Reaction mix. 10h

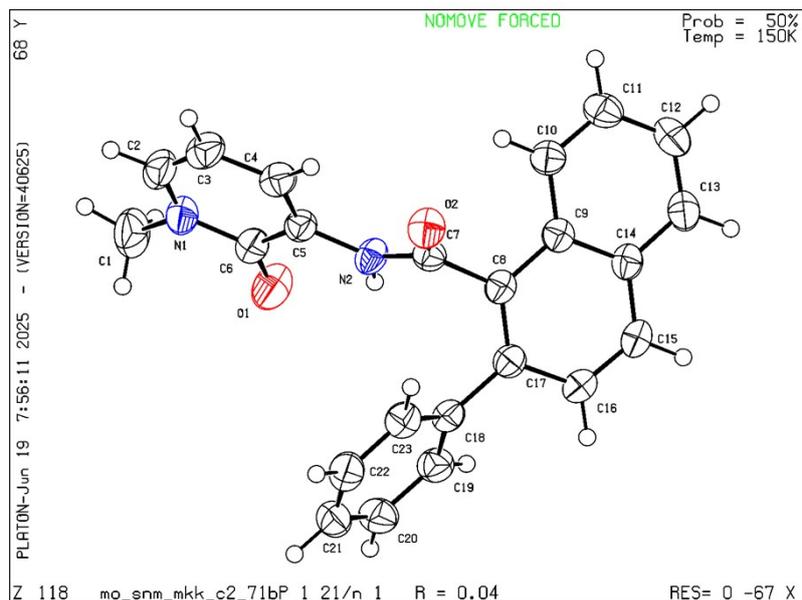




10. X-ray single crystal analysis

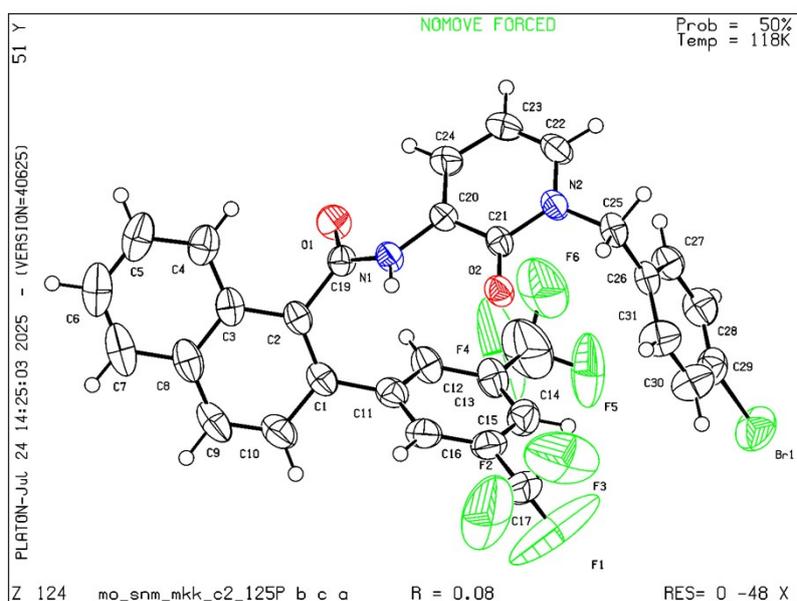
10.1 Crystal data and structure refinement for molecule 4a1.

Identification code	4a1
Empirical formula	C ₂₃ H ₁₈ N ₂ O ₂
Formula weight	354.39
Temperature/K	150.00
Crystal system	monoclinic
Space group	P2 ₁ /n
a/Å	8.9065(15)
b/Å	17.848(4)
c/Å	11.126(2)
α/°	90
β/°	91.918(6)
γ/°	90
Volume/Å ³	1767.5(6)
Z	4
ρ _{calc} /cm ³	1.332
μ/mm ⁻¹	0.086
F(000)	744.0
Crystal size/mm ³	0.11 × 0.08 × 0.04
Radiation	MoKα (λ = 0.71073)
2θ range for data collection/°	4.316 to 54.31
Index ranges	-10 ≤ h ≤ 11, -22 ≤ k ≤ 22, -13 ≤ l ≤ 14
Reflections collected	26844
Independent reflections	3907 [R _{int} = 0.0612, R _{sigma} = 0.0378]
Data/restraints/parameters	3907/0/249
Goodness-of-fit on F ²	1.111
Final R indexes [I ≥ 2σ (I)]	R ₁ = 0.0438, wR ₂ = 0.1034
Final R indexes [all data]	R ₁ = 0.0632, wR ₂ = 0.1268
Largest diff. peak/hole / e Å ⁻³	0.19/-0.28



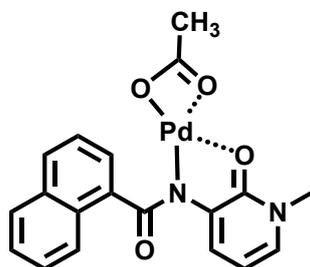
10.2 Crystal data and structure refinement for molecule 4b2.

Identification code	4b2
Empirical formula	$C_{31}H_{19}BrF_6N_2O_2$
Formula weight	645.39
Temperature/K	118.00
Crystal system	orthorhombic
Space group	Pbca
a/Å	16.923(2)
b/Å	17.004(2)
c/Å	19.383(2)
$\alpha/^\circ$	90
$\beta/^\circ$	90
$\gamma/^\circ$	90
Volume/Å ³	5577.8(12)
Z	8
$\rho_{\text{calc}}/\text{cm}^3$	1.537
μ/mm^{-1}	1.546
F(000)	2592.0
Crystal size/mm ³	0.12 × 0.08 × 0.05
Radiation	MoK α ($\lambda = 0.71073$)
2 θ range for data collection/ $^\circ$	3.994 to 54.688
Index ranges	-21 ≤ h ≤ 21, -21 ≤ k ≤ 21, -24 ≤ l ≤ 24
Reflections collected	163058
Independent reflections	6260 [$R_{\text{int}} = 0.0847$, $R_{\text{sigma}} = 0.0267$]
Data/restraints/parameters	6260/0/404
Goodness-of-fit on F ²	1.061
Final R indexes [$I \geq 2\sigma(I)$]	$R_1 = 0.0656$, $wR_2 = 0.1826$
Final R indexes [all data]	$R_1 = 0.0938$, $wR_2 = 0.2087$
Largest diff. peak/hole / e Å ⁻³	0.96/-0.80



11. Computational calculation

11.1 Optimized structure with a constraint dihedral angle



To confirm role of the 2-pyridone in catalytic cycle we extended our study to theoretical calculation to study the stability of palladium intermediate complex at different dihedral angle (Pd-N-C-CO) 0° , 90° , 180° , 270° . we conducted computational calculation using Orca 4.2.0 at restricted HF using def2-SVP basis set through the SMD(CH₃COOH) solvent-correction to get the relative Gibbs free energy profile for Pd intermediates.¹⁻⁶

Coordinated for the optimized structure and Gibbs free energy respect to constraint dihedral angle of possible intermediates.

1. For dihedral angle 0°

Final Gibbs free energy = -1263.14087538 Eh

C	-0.79579003579597	1.56496058319602	-4.21073751429866
C	-1.60773580768873	0.41087823404362	-4.01907365155132
C	-1.93229266051808	-0.00379971804513	-2.70663577966132
C	-1.40709061637794	0.74284562406499	-1.60228227100507
C	-0.62290393751356	1.83557253966694	-1.82722999964853
C	-0.31891447445384	2.26006516606161	-3.14441091266580
C	-1.80577992646437	0.41777175793823	-0.18325451820535
N	-0.80561372382532	0.13253376691919	0.67209337602320
O	-2.98022297842450	0.47377778154636	0.10887584713992
C	-1.03567847026656	0.08506290669590	2.05717643119772
C	-2.14571666606189	0.43863948205776	2.77100086625757
C	-2.15523795945103	0.32364545227446	4.18879773023622
C	-1.06806927827040	-0.14374783297654	4.82945447741936
N	0.05148311261141	-0.49906500006209	4.12742289705620
C	0.10400632529324	-0.39677800473625	2.79507916779484

O	1.16690300033863	-0.71015556635379	2.20103011557351
C	1.23837731809974	-0.99492442302239	4.83105638125725
C	-2.74686360537463	-1.16261842276430	-2.54325889248770
C	-3.20054884326434	-1.85731060033441	-3.62517025799095
C	-2.87534681418436	-1.43783478168311	-4.93939804319125
C	-2.10107665934533	-0.33311769274068	-5.12803801367952
Pd	1.08576196574287	-0.50679579612457	0.19756016584891
O	2.95259714375545	-1.17400373288095	-0.43858079485438
C	2.63209857061663	-1.03157840659083	-1.64467731650678
O	1.48989207233931	-0.60485727866669	-1.88913778877424
C	3.60788991522801	-1.35037654880836	-2.73038602689565
H	-0.56475544504895	1.87868756801012	-5.22067354584311
H	-0.23021605215181	2.39738062314138	-0.98993405675516
H	0.29554247335688	3.13857918142661	-3.29113804487429
H	-3.02301794181700	0.79693435660360	2.26527317766414
H	-3.03386271884802	0.60277009038532	4.75067107606946
H	-1.01242629396420	-0.26288012915356	5.89940805395268
H	2.07925318576606	-0.33168046818965	4.64971674861600
H	1.48656595353486	-1.99174098816106	4.47865196208331
H	1.01711678250285	-1.02548835780218	5.89154312277609
H	-3.01385989790348	-1.48766765759608	-1.54896031897243
H	-3.81690907984736	-2.73535009322704	-3.48197805259751
H	-3.24507015907807	-1.99803608269899	-5.78836764966376
H	-1.84713734803784	-0.00541795983257	-6.12804973444938
H	3.12432027270763	-1.32275156407527	-3.70265857562556
H	4.04445912228575	-2.33094037084607	-2.54718380447839
H	4.41047938979830	-0.61252364665955	-2.69742661229028

2. For dihedral angle 90°

Final Gibbs free energy = -1263.11613061 Eh

C	-0.84125055417454	1.54287452128752	-4.36813430417947
C	-1.84847437437976	0.54229475180872	-4.16799562257825
C	-2.27476808373432	0.22731440255258	-2.85994913990246
C	-1.66629535311954	0.92335569779494	-1.75523173238373
C	-0.69887809637624	1.88256185883548	-1.98695519219252

C	-0.28648833608923	2.19501550170815	-3.32076819131404
C	-2.06932892988250	0.66753935692211	-0.31072434402003
N	-1.00855876460707	0.21202246368885	0.34588263501456
O	-3.18447814354479	0.86700524768653	0.09745005237680
C	-0.99272801781587	0.07223300705191	1.74491145599980
C	-1.14704777035011	-1.11530298514618	2.36928675556022
C	-1.09548011968653	-1.20500460174013	3.79401433240377
C	-0.89105128124834	-0.07294208516775	4.49285676629682
N	-0.72792944545243	1.13693907512482	3.88351309520370
C	-0.75401545871223	1.29099537256293	2.51778050198106
O	-0.58434223252509	2.38177055675009	2.01818923872659
C	-0.50080919713324	2.33779748802204	4.68178251152875
C	-3.28005358179291	-0.75737296043715	-2.67755539061858
C	-3.82392637250758	-1.39742221753806	-3.75531920679659
C	-3.39282573727931	-1.08692853132470	-5.06435184044541
C	-2.42903081672874	-0.13987036509684	-5.26631467007149
Pd	0.51888608641216	0.05749561593474	-0.88884639740465
O	2.23999662254996	-0.31229438713662	-2.01235691367214
C	2.75027275820418	-0.99712117909409	-1.09203291519982
O	2.09748143369333	-1.13941872340711	-0.04035224643410
C	4.09299280697404	-1.62651986700084	-1.27802318010944
H	-0.53586647457679	1.77258196112143	-5.38012526775662
H	-0.34785370918483	2.49996264908844	-1.16809800679785
H	0.46196242818325	2.95971943186781	-3.47327250679966
H	-1.31232326515897	-2.00590822568050	1.77767165859660
H	-1.22009692954978	-2.14863683339213	4.30239397983592
H	-0.84474358085325	-0.06317740349556	5.57119877092485
H	-1.27891040157555	3.07101841388002	4.48470129776688
H	0.46232954092608	2.77757304770342	4.43413978047627
H	-0.51586475342147	2.06760882027180	5.73242880258181
H	-3.62304612922523	-0.99021326062728	-1.68060133018366
H	-4.59175701655898	-2.14495639380061	-3.60778272209452
H	-3.83229007225829	-1.60230446331236	-5.90807920653344
H	-2.09749064293261	0.10160616390682	-6.26738744802160

H	4.44435170216026	-2.06925004598634	-0.35047866329586
H	4.79603803246583	-0.87420950660811	-1.63259161340874
H	4.00761765086709	-2.39594612957879	-2.04611117305964

3. For dihedral angle 180°

Final Gibbs free energy = -1263.10191599 Eh

C	2.34367483647332	3.65736941762015	-1.34450042467421
C	2.52652739427450	2.50526591650961	-2.17701900669910
C	2.14379774881979	1.22857822699708	-1.71036270043859
C	1.55028536297532	1.13206754099373	-0.38696711279620
C	1.39918305795739	2.27925093281185	0.37858337974257
C	1.79816734239090	3.55639954276049	-0.10983567386288
C	1.15596499671598	-0.20013204659300	0.23463650938528
N	-0.04719628593234	-0.05391107221822	0.83820992674098
O	1.80528998461436	-1.19584770092823	0.07575414654928
C	-0.69360730682530	-1.20793125511639	1.32742867471788
C	-1.96205832021021	-1.53147888858255	0.99470290906870
C	-2.56263821463525	-2.75065921215165	1.44621649466470
C	-1.81857265867878	-3.59463550632938	2.17783890213940
N	-0.53458783883637	-3.28861828658718	2.53584372004598
C	0.07066857644869	-2.09537894335240	2.22037961682208
O	1.13741623517628	-1.81000825859084	2.71079405596204
C	0.21888715676920	-4.19898105671252	3.39146563636998
C	2.33329343181455	0.11018703763082	-2.56145930219326
C	2.87670176894509	0.26991050232018	-3.80697264465770
C	3.26021850944558	1.54557784493694	-4.26994895314482
C	3.08776000970624	2.63964588141777	-3.47046469354678
Pd	-0.78274540897382	1.35811049863724	-0.38572640445787
O	-1.66783926712851	2.75058011929824	-1.64279390779964
C	-2.81030461346110	2.25486407012892	-1.48226750624205
O	-2.91251615883960	1.26788543501031	-0.72815317275966
C	-3.99981004736790	2.85750966781807	-2.15468877621655
H	2.65654952183699	4.62050786724658	-1.72486148137483
H	1.06469626861164	2.19374477728873	1.40284233324989
H	1.67289002955879	4.42471844236095	0.52073930395422

H	-2.53614002459401	-0.87331327822110	0.35832379609016
H	-3.57622792450324	-3.00339930989166	1.17486051258468
H	-2.18867382354489	-4.54701672909326	2.52525472504304
H	0.36027223214901	-3.76677742006055	4.38024534522604
H	-0.33009543774523	-5.13091769558479	3.47887738724890
H	1.19524757871745	-4.39470812450633	2.95690426925372
H	2.05531768528326	-0.87199166699813	-2.21825014647984
H	3.01534525908310	-0.59366526213474	-4.44366917308918
H	3.68872186148160	1.65346239551433	-5.25731830738138
H	3.37502114854711	3.62395133784465	-3.81537501470613
H	-4.82445325829982	2.15088319533535	-2.18151392045215
H	-4.29922355935464	3.73585252655598	-1.58024381797362
H	-3.73295205886516	3.18106940661491	-3.15835363391296

4. For dihedral angle 270°

Final Gibbs free energy = -1263.11609442 Eh

C	-0.89449000429539	1.52454205297569	-4.33291113292284
C	-1.86529708638629	0.50261060159434	-4.06966751984874
C	-2.24686471633195	0.22147515152786	-2.74019625403904
C	-1.63619063016994	0.98197677139300	-1.67655979507062
C	-0.69949955813697	1.95489772863741	-1.97123643528149
C	-0.32873531546266	2.22763603468594	-3.32546536946409
C	-2.01026106938766	0.75856273397077	-0.21987954377822
N	-0.90370925001812	0.45702120161001	0.45643989144837
O	-3.13878515396661	0.85695896683350	0.18565097061729
C	-0.95439256164988	0.01108006718419	1.78867334636165
C	-0.45028448367363	0.72984897555521	2.81482299110966
C	-0.50280637728550	0.23282156955305	4.15315952053104
C	-1.07498289190698	-0.96771904604796	4.36040368222634
N	-1.58624065451239	-1.71395749458881	3.33890632940136
C	-1.54538359479990	-1.30666874444726	2.02622676011538
O	-1.97272984761104	-2.02108154483223	1.14700136190215
C	-2.18161731578794	-3.01921027819966	3.60855755472001
C	-3.20224074040315	-0.79910969001024	-2.49591785156930
C	-3.74803436363914	-1.49675105156811	-3.53672986194501

C	-3.36943093703059	-1.21267420129558	-4.86735862819891
C	-2.44879990383586	-0.23727099402374	-5.12800895370313
Pd	0.55637368165851	0.16660493256804	-0.83511138580593
O	2.22788149716552	-0.29255193653368	-2.00456049876362
C	2.75915306700858	-0.94103947862343	-1.07009687627119
O	2.14721540483396	-1.01180260529928	0.01302121282128
C	4.07830759227154	-1.61332153761068	-1.27422748260066
H	-0.62334782740469	1.72595462668055	-5.36059451918432
H	-0.34268231911983	2.61367001300043	-1.18908964975571
H	0.39476426806950	3.00532072753214	-3.52557310075524
H	-0.00702975439619	1.69614662022815	2.61375633637870
H	-0.10537457246510	0.80137926558124	4.97969179529675
H	-1.15824547204197	-1.40337035523804	5.34449726521693
H	-1.61572525688687	-3.80240371339741	3.10934964976936
H	-3.20567887314039	-3.04471509489432	3.24517447521655
H	-2.17330338888136	-3.19310968739026	4.67941661609872
H	-3.49683160525573	-1.02031043035607	-1.48165986426702
H	-4.47583311160131	-2.27290454145078	-3.34145781399758
H	-3.81128296610279	-1.77322397895252	-5.68053427762701
H	-2.15280369703128	-0.01860512670707	-6.14533834097141
H	4.44717206480395	-2.03191736185487	-0.34222755493896
H	4.79034892992406	-0.89424709270716	-1.67677914504167
H	3.94828570488356	-2.40705890508229	-2.01063805342973

11.2 Optimized structure of Intermediates and Transition States of reaction coordinates

we conducted computational calculation using Orca 6.1.0, Geometry optimization and frequency calculation were performed at the B3LYP/def2-TZVP level of theory through the SMD(CH₃COOH) solvent-correction to get the relative Gibbs free energy. Transition state calculations were performed using the “OptTS” keyword, further the transition state was confirmed when the frequencies were analysed and found to have one imaginary frequency indicating the first saddle point. Spin contamination was minimized by confirming the $\langle S^2 \rangle$ to be within the 10% range in the expected value. Tight self-consistent field (SCF) criteria was adopted to confirm the reliability of the output structures.¹⁻⁶

Coordinated for the optimized structure and Gibbs free energy of reaction co-ordinates

Pd(OAc)₂

Final Gibbs free energy = -584.8017068 Eh

Pd	-0.56751278243331	0.31802798433678	-0.03155065883557
O	-2.54330905562067	-0.09403867801726	-0.42640519175411
O	-1.04414874254191	-1.65084621471735	-0.39550628463119
O	1.40830958307573	0.73020809356996	0.36312407645718
O	-0.09056293118531	2.28739861595276	0.33232023852291
C	-3.30519197720493	-2.33471266008588	-0.92231699929172
C	2.17107309243641	2.97075436688562	0.85761142221765
C	-2.26787828595131	-1.33234033125075	-0.56380458742171
C	1.13309824045031	1.96862475932738	0.50023092876053
H	-3.44298487378705	-2.31975640765431	-2.00670927593964
H	-4.25417910703834	-2.07476941629983	-0.45476959430810
H	-2.98836102660578	-3.33202209157355	-0.62280960691749
H	2.30988105086665	2.95603268192332	1.94187555733592
H	1.85429835815794	3.96809750652304	0.55815314229052
H	3.11953790618158	2.71038576368007	0.38924470461484

Iodobenzene

Final Gibbs free energy = -529.23504689 Eh

I	-1.52356663366660	3.26948800894303	-0.00000402982409
C	-5.83411167436840	2.58751763622541	-0.00000097689618
C	-5.95776680356014	1.20170848432302	-0.00000210621290
C	-4.81657354714264	0.40577710470574	-0.00000012385605
C	-3.55082245690070	0.98707396649551	-0.00000011713487
C	-3.44521222374417	2.37341776875653	0.00000062264863
C	-4.57520932838026	3.18354047415238	0.00000145926342
H	-2.66670573198377	0.36414978225972	0.00000067446356
H	-6.93902824372699	0.74411864427981	-0.00000189000450
H	-4.90404631102066	-0.67379944396237	0.00000311877065
H	-4.48403475229123	4.26122550635777	0.00000449365176
H	-6.71732229321442	3.21448206746344	-0.00000112486942

AcOH

Final Gibbs free energy = -229.04413232 Eh

O	-0.81788450547744	0.22832292607921	-0.31815198452868
O	1.21048974681965	1.16866341751647	-0.17009217025702
C	-0.73022980032267	2.57875858379721	0.01788709668664
C	0.00612103423965	1.28258303165430	-0.16239168088196
H	-0.27279733454377	-0.56999682442792	-0.42792376790862
H	-0.44315823591828	3.01179004262582	0.97725914344178
H	-1.80842685338342	2.44682156321462	-0.01917683343582
H	-0.41421405141373	3.27115725954028	-0.76360980311632

Ag₂O

Final Gibbs free energy = -369.16581487 Eh

Ag	0.68945189163391	1.13568639195974	0.00000000000000
Ag	2.63585947161896	3.53170907825967	0.00000000000000
O	2.69428863674713	1.49470452978058	0.00000000000000

HI

Final Gibbs free energy = -298.32481037 Eh

I	-4.17934343902284	3.51380000000000	0.00000000000000
H	-2.56125656097716	3.51380000000000	0.00000000000000

AgI

Final Gibbs free energy = -444.76928067 Eh

I	-5.01326303156891	2.38870000000000	0.00000000000000
Ag	-2.38193696843109	2.38870000000000	0.00000000000000

H₂O

Final Gibbs free energy = -76.43162824 Eh

O	-2.52855059683440	3.14303160042714	0.41460979284545
H	-3.49301218121200	3.11814739553187	0.42196568583635
H	-2.27183722195358	2.45422100404098	-0.21027547868180

Reactant (3a + Pd(OAc)₂)

Final Gibbs free energy = -1500.60137841 Eh

C	-3.63887041289565	1.34943016045885	-0.06543668376306
C	-3.73774164732460	0.22175521120205	-0.91746816247109
C	-2.57903795894941	-0.57676711184161	-1.17182999005726
C	-1.34521636550481	-0.18472577490375	-0.55598469840636
C	-1.29261103657320	0.93435711370747	0.24841463841388
C	-2.44417781308857	1.70066594374686	0.50519768865743

C	-0.13804958387399	-1.04209534029264	-0.66730519017867
N	1.11916076480249	-0.36532990964717	-0.91500480279423
O	-0.14519449859288	-2.24613431654337	-0.55798735701662
C	2.29274902612690	-1.08019558244303	-0.45470530598153
C	2.71979157307369	-1.07221451707803	0.84299716450266
C	3.84019880386957	-1.84124292264126	1.20385847922311
C	4.45379775160896	-2.60020312560895	0.25054437167092
N	4.02438946010691	-2.61058288326817	-1.03992690645649
C	2.96233624615927	-1.84882902006467	-1.44375123889719
O	2.62620754842347	-1.84904315130457	-2.67135752096984
C	4.71384275613553	-3.42092958784307	-2.05467581011023
C	-2.70665541629563	-1.68295011364828	-2.04858998767881
C	-3.91431716218128	-1.98757688395298	-2.62670272389647
C	-5.05965885082817	-1.20848675953407	-2.36137080448612
C	-4.96937033414431	-0.12573176472364	-1.52611348911182
H	-4.53032173046068	1.93574097057552	0.12446513046142
H	-0.36465200415905	1.22324516803077	0.72312412047078
H	-2.37543246715367	2.56272425504322	1.15589773225570
H	2.19677775738930	-0.48365237242608	1.58649290780380
H	4.21193823465632	-1.84920168692816	2.21708242431744
H	5.30904084901003	-3.22449285977992	0.46156678508877
H	4.01127345428726	-4.12515867376344	-2.49611875517045
H	5.10409626725222	-2.77006627210883	-2.83469362890933
H	5.52506010778227	-3.95526729647226	-1.57109747736829
H	-1.84463523823875	-2.29677463492658	-2.26481774565583
H	-3.98778510272624	-2.83581467595528	-3.29621890279966
H	-6.00440599092902	-1.46525818480933	-2.82367706682856
H	-5.83884224777527	0.48793028140814	-1.32192997331807
H	1.11949422680388	0.65586932826652	-0.75196751609413
Pd	1.36417020472611	-0.26374539382071	-3.03539987375564
O	0.24638118805613	1.37751429303741	-3.35485850195230
C	0.37164388331504	2.38791380259253	-2.55679791203829
O	1.00359479809260	2.37968691952150	-1.49047023959644
O	1.65528246995509	-0.35697725879767	-5.01665398613765

C	2.69580147866492	0.24894724532138	-5.50932826519488
O	3.52647806069709	0.87360203857406	-4.85422825058540
C	-0.31800389804699	3.64490407287317	-3.04049006084346
H	-1.22826394743052	3.40775312992175	-3.58910928162019
H	-0.53812394376553	4.30105495778226	-2.20061771967305
H	0.35991158050532	4.16594598934478	-3.72196731297993
C	2.79148073145367	0.13184816727144	-7.01974218392508
H	2.02914853340944	0.76852766108731	-7.47431263671932
H	3.77310701330022	0.45519646948647	-7.36008727732556
H	2.60117829127447	-0.89227242412591	-7.34115714209834

TS-1

Final Gibbs free energy = -1500.59499577 Eh

Pd	1.23038080213036	0.08380206409502	-1.45302902487825
O	3.52568889078518	2.93491783879381	0.40553583696043
O	2.54394507863143	1.50239826907327	-0.94073785615263
O	-1.21832003912737	0.81670501240810	-3.16563836103404
O	-0.25850464724507	1.41593444960171	-1.22335043227435
O	2.75867415414802	-1.24529311079408	-1.83583690157243
O	0.03771071701607	-3.09734929893294	-0.55271890689055
N	3.27087361342418	-2.93913092938770	-3.27365737080103
N	0.05045500907905	-1.51839499335073	-2.21880313075058
C	1.83786840774280	1.58514309801366	1.39906600994798
C	2.68907078427986	2.04995923561897	0.23358339526436
C	-2.05169407204288	2.73787220817217	-1.99538159310513
C	-1.12706396709201	1.55379492098375	-2.17430169529133
C	-3.85276606495402	-0.94709908863757	2.45658778296162
C	-2.91013645238157	-1.11225680519055	3.43763304061796
C	-1.59438312410153	-1.48278028961298	3.09136567641457
C	-1.24310920347890	-1.68747707580889	1.77979581404751
C	4.69078340274426	-2.75316134634851	-2.93749442010215
C	2.35495301763584	-2.13499553199237	-2.65261321364258
C	2.89031712992614	-3.86589897441324	-4.19269700350340
C	1.58019521323180	-4.04513995505826	-4.53084885879424
C	0.60076919845642	-3.26675289413635	-3.89048636433127

C	0.98559518231795	-2.33368916650084	-2.96945337970061
C	-0.55785266678988	-2.18899542537489	-1.08118267105452
C	-4.17469026813223	-1.13392467818457	-1.24466379583934
C	-2.86192384335595	-1.48521090002060	-1.60733138353739
C	-1.88824356921948	-1.69108743324269	-0.65193918305618
C	-2.19267781284771	-1.52951830481367	0.73978943982487
C	-3.52420296018795	-1.14561975908640	1.09266304502099
C	-4.49481016597015	-0.96556935825215	0.07654706141290
H	1.12429018424431	0.80884565371086	1.13333117522923
H	1.29944417784130	2.44343079582436	1.80394209723203
H	2.50060386221174	1.21369104474233	2.18293571347907
H	-1.55119240094700	3.62648163340298	-2.38850838623123
H	-2.26686166669297	2.91258485633929	-0.94263455681200
H	-2.97288494984171	2.58417550634654	-2.55367456916317
H	-4.86537022968533	-0.65497988651176	2.70805803668414
H	-3.16965380555668	-0.95514727779205	4.47718586184392
H	-0.85081463619495	-1.60596554966885	3.86901118501402
H	-0.23067777248057	-1.97774847879107	1.54111281398509
H	4.84008450553032	-2.94388764947911	-1.87648299935118
H	4.98489402419109	-1.72960887774507	-3.16081285751138
H	5.27565049420694	-3.44971189033577	-3.52931492655628
H	3.69104481499468	-4.43969929104205	-4.63374682677307
H	1.31334588148182	-4.78472444081175	-5.27053045657075
H	-0.44808672293604	-3.40818526671707	-4.12068847290152
H	-0.58816556203255	-0.93855339279815	-2.78662000022007
H	-4.92197316647660	-0.99849972097980	-2.01551681763338
H	-2.63649663318735	-1.62094229381208	-2.65691390815319
H	-5.50166755329309	-0.68725017150198	0.36496424824894

INT-1

Final Gibbs free energy = -1271.58077001 Eh

C	-1.55987593023241	2.01055367744512	2.58772773936969
C	-2.34338653404126	1.40864678667031	1.57225986115654
C	-1.69612281595267	0.81809243193834	0.44227364215250
C	-0.27049583916987	0.83780243123892	0.38539440480170

C	0.45236696764111	1.41769689749238	1.40177396415288
C	-0.19238713237315	2.01537908211169	2.50415902416033
C	0.45688699403114	0.36064790650252	-0.84105630592470
N	1.34999737100389	-0.65302498293843	-0.67692342680253
O	0.25148965316601	0.94077029892780	-1.91300640969711
C	2.27577539113502	-0.99442456462817	-1.67336466199646
C	2.46500688984646	-0.44031997978221	-2.92896892551170
C	3.50484275636720	-0.90793923453419	-3.75299704198392
C	4.32520859127821	-1.90684337726836	-3.32661009081974
N	4.14356236174336	-2.46555800353235	-2.09407486373309
C	3.15266886098868	-2.04682594061557	-1.26830435267914
O	3.03336107072298	-2.61415918983532	-0.12097396541855
C	5.02469931592440	-3.54591107412281	-1.62868703084539
C	-2.50194966394395	0.21354592677229	-0.55657368543863
C	-3.86974774274849	0.19334169035217	-0.44449707397410
C	-4.50734878081807	0.77969404566467	0.67045569474753
C	-3.75882684928928	1.37445568850017	1.65374815936367
Pd	1.43635312187527	-1.93708333838836	0.89031467096968
O	-0.15386165825467	-1.65414724301227	2.20456558830588
O	1.32964059221723	-3.19866768524846	2.54341756403466
C	0.26790875775704	-2.60752653988351	2.93351311884806
C	-0.42784253163972	-3.00547131298755	4.19004551867318
H	-2.06180589795523	2.46451151566889	3.43467243239239
H	1.53423735104952	1.42907753245932	1.34928082615680
H	0.40138403239465	2.47693362212613	3.28363364501864
H	1.81654812347928	0.34733665961980	-3.27109171728778
H	3.65742413030043	-0.47873828029088	-4.73250479842672
H	5.13808213984391	-2.30868595845499	-3.91129912415811
H	5.77020491428951	-3.73075569708299	-2.39525690991410
H	5.50947236390116	-3.24892853490618	-0.70074698757380
H	4.44021000549104	-4.44698271738607	-1.45059930594942
H	-2.02782250565016	-0.23112530429520	-1.42118639675535
H	-4.46657644217999	-0.27549710324294	-1.21774712790913
H	-5.58810608286352	0.75725844345477	0.74539001054430

H	-4.23997024645040	1.82568821650326	2.51420042425897
H	-1.40935300817331	-2.54004821455086	4.24808418233578
H	-0.51990990677512	-4.09115623004473	4.23319017879806
H	0.17479781206363	-2.68478234641608	5.04309955255819

TS-2

Final Gibbs free energy = -1271.58431215 Eh

Pd	0.34551871624445	1.99772227460239	-0.10670441926196
O	0.83868037090446	3.85305078536161	2.43006664983120
O	-0.23685084356033	3.95953374470911	0.47024051843939
O	2.21158508366880	2.49895290953202	-1.10854950101007
O	0.37468685282109	-2.03437089642989	-0.54336631479204
N	3.93013418443577	1.46213563910021	-2.19990176786633
N	0.91334073329495	0.19618024439552	-0.64626391353503
C	-0.19483568761944	5.90407949773380	1.86817047129748
C	0.13029368187119	4.49317237364590	1.51681996976020
C	-4.32553391524693	-1.45824877041282	2.06468802761511
C	-4.29537195453452	-2.81868101331814	1.90042758614274
C	-3.19885797052629	-3.41510803940481	1.24261638257653
C	-2.15958178726300	-2.65410217900345	0.76453049670504
C	4.59256677586803	2.75450392264180	-2.43335242522907
C	2.73821946700136	1.42022773143566	-1.53096947632811
C	4.54324588246004	0.33331048091639	-2.67588981101422
C	3.97873691748908	-0.88910230338233	-2.49734143201093
C	2.74992784349283	-1.00574400588968	-1.81792883806137
C	2.11756210669191	0.12239766243153	-1.33051003029920
C	0.11108301342112	-0.85676498847673	-0.28681965934998
C	-2.29776611123322	1.56523999898897	1.29359070420944
C	-1.18668338980169	0.99710041039823	0.63962471908910
C	-1.10916863234406	-0.37915108798150	0.44460605212691
C	-2.15351003896170	-1.24060466183761	0.91578659817049
C	-3.27151245892213	-0.64079332389398	1.58411965415988
C	-3.31303539909535	0.76339447066251	1.75332188267178
H	0.70727670716423	6.41823870870814	2.20029220841606
H	-0.90228156863648	5.90387174560558	2.70094670786371

H	-0.63313874726218	6.41137663091379	1.01375252148033
H	-5.16103216741708	-0.98185604013278	2.56576992155016
H	-5.10576614301252	-3.43444028590226	2.27105358395803
H	-3.17571354230196	-4.49088712508211	1.11177860608678
H	-1.32794409968413	-3.12329258987573	0.26343956937655
H	5.57995311661259	2.73938069987506	-1.97476882230002
H	3.99516921586597	3.54317667275520	-1.99319614064226
H	4.69024428234749	2.91937400770102	-3.50549923125293
H	5.48132302824683	0.49206880836758	-3.18569870209406
H	4.47873279052374	-1.76769359000788	-2.87867995866529
H	2.29597751095628	-1.97178777050750	-1.67334937216166
H	-2.36160807401172	2.63782878134814	1.42974035088375
H	-4.16978645740408	1.20073536361486	2.25523895577956
H	0.98695232745646	2.92790991609391	2.13733325768430

INT-2

Final Gibbs free energy = -1042.53332468 Eh

C	-3.31739672148504	1.22405096814649	2.35425495113264
C	-3.07021555808042	-0.13475895096104	2.66727629541584
C	-1.85582508454586	-0.75739717989184	2.22707123642274
C	-0.93202965151908	0.03780356995668	1.47647739705361
C	-1.21835582197162	1.36605496922655	1.19414272613390
C	-2.41328011800864	1.96508761516694	1.63246363720672
C	0.37604374033230	-0.45064809874851	0.93860764190541
N	1.03416798333204	0.54816384976836	0.25693482310774
O	0.83530373917347	-1.58531628599666	1.06645451022329
C	2.26392759092177	0.47206636539738	-0.38340916385300
C	3.09796001377300	-0.62593713299577	-0.48074145734345
C	4.31686499633988	-0.52413773022661	-1.17829089780142
C	4.67605827629208	0.65329968723796	-1.75670910532435
N	3.85977893538440	1.74740515696326	-1.66636543544595
C	2.66464496377472	1.71630328604044	-1.00585005533812
O	1.95781692938175	2.77422130924552	-0.96612178461546
C	4.25516358243881	3.01279281034466	-2.29683459067568
C	-1.65050347907397	-2.12140831226402	2.56471996215999

C	-2.58628058833323	-2.81948139822009	3.28906773261428
C	-3.78016836917717	-2.20322155048473	3.71908908793692
C	-4.01239545046796	-0.88754340876641	3.41208792697560
Pd	0.15731461471871	2.29665254082434	0.15583464209925
H	-4.24230134534700	1.67517380751162	2.69656721957282
H	-2.62580047413045	3.00424277614444	1.40535652901960
H	2.80804695518476	-1.55534436598786	-0.02009958586205
H	4.97353992267295	-1.37845067266390	-1.25955948637730
H	5.59472010373769	0.79586990379268	-2.30425234082329
H	5.22057235260919	2.87049672696640	-2.77238037229963
H	3.51323374984539	3.30287452974292	-3.03863022289961
H	4.32378580740892	3.79581989253828	-1.54377312140962
H	-0.74163486044862	-2.60395650779898	2.24178798155188
H	-2.40437655252980	-3.85908680426115	3.53423395849673
H	-4.50738711338988	-2.76952185163546	4.28813464906740
H	-4.92491306881309	-0.39980951411190	3.73527471197250

TS-3

Final Gibbs free energy = -1571.74675397 Eh

C	1.67352625011696	2.18696709950132	-2.70075329185381
C	1.98271982744661	3.10511626731492	-1.65615689603300
C	1.68374581502768	2.74161262841563	-0.30254600165236
C	0.95510889371130	1.53986579896573	-0.10797946170805
C	0.48518759526286	0.78402745487659	-1.15892466505525
C	0.94322793823788	1.04409118359972	-2.46770789924831
C	0.42630766421218	1.01773840224173	1.18137136870128
N	-0.94208178017948	0.80307012224288	1.03454924389437
O	1.10715277254079	0.71196587608758	2.15358664840048
C	-1.71091114406469	0.37857522694559	2.11560321394326
C	-1.63959260202997	0.76938007550258	3.43771512431620
C	-2.67873747445192	0.41904131608060	4.32607514556491
C	-3.75919106622514	-0.27752773807381	3.88124276438816
N	-3.81737948627696	-0.71099853513809	2.57970612015016
C	-2.80308269796697	-0.47520388006348	1.70001947845359
O	-2.82728541699110	-0.97120139857156	0.53572074003904

C	-4.94193623796232	-1.55371571254296	2.14320814040600
C	2.06281832794631	3.62130752463696	0.73447117975266
C	2.62185467589369	4.84622246777151	0.44221821283737
C	2.80604686543329	5.25485730893091	-0.89194560492928
C	2.49540050976309	4.39405024635038	-1.92206145975878
Pd	-0.87827472853516	-0.58204849063913	-0.53788850475498
I	-3.23337629051600	-2.33613283569134	-3.69322888912759
H	2.05574622734894	2.38605221955067	-3.69606187713245
H	0.69341956764608	0.41503509403654	-3.31276125156404
H	-0.77367694614445	1.31767945154335	3.77688810073216
H	-2.67007106576420	0.79827726507304	5.33846804526844
H	-4.58451765361035	-0.57307604507204	4.50961960903173
H	-4.57730017004894	-2.34360569214326	1.49413364308560
H	-5.41314928086641	-1.98083112374972	3.02447537547619
H	-5.67279862595679	-0.94732491563062	1.60929935940259
H	1.91220846539107	3.34769193892287	1.77102275149744
H	2.94182440205483	5.48231783130155	1.25880148646645
H	3.13377203728791	6.26298689180389	-1.11394271297544
H	2.60304956633676	4.71505088198044	-2.95174255385012
C	-1.80913769863423	-2.84937011832911	-2.21457734417669
C	-0.59967713698007	-2.09291076411958	-2.14215270164709
C	-2.09970755255788	-3.84823703269149	-1.31688132969281
C	0.30363149811233	-2.43753746877168	-1.09349552600723
H	-0.22025640836559	-1.73062849828536	-3.08962619101588
C	-1.15384428645689	-4.20444798993458	-0.33693895491501
H	-3.01491261310032	-4.41689415249112	-1.41238419103172
C	0.03609950649311	-3.51870869583503	-0.23141215846277
H	1.31612876651742	-2.07128610242498	-1.13471893958791
H	-1.37763860339324	-5.04117494409814	0.31279562654137
H	0.85727904429872	-3.90518450938016	0.35829756783087

INT-3

Final Gibbs free energy = -1571.75500317 Eh

C	-3.75852537753886	0.29750287006339	1.27000864595669
C	-3.55416049904642	-1.08191110242496	1.49906571819973

C	-2.33873541666250	-1.70027838739125	1.06096608320465
C	-1.36449185826263	-0.88081325547406	0.39723424847507
C	-1.61822559667439	0.46882763237217	0.21296085746962
C	-2.81041109212482	1.06821279500244	0.64413707455962
C	-0.07686918111402	-1.40671008738099	-0.15917244350432
N	0.63138020719882	-0.41914070083443	-0.79883556102602
O	0.30260444350294	-2.57284601528747	-0.10431461556358
C	1.83310852420080	-0.56147585191271	-1.48032501891447
C	2.64599015189229	-1.67904404293802	-1.54884682856699
C	3.81044818625968	-1.64792371356986	-2.33516007754027
C	4.14500427518604	-0.51723198368459	-3.01800251908415
N	3.36244491308383	0.59770575725283	-2.94098853891001
C	2.21865390657130	0.62914470527539	-2.19610113254443
O	1.53804242186831	1.70513333649737	-2.15229369601867
C	3.73284576767029	1.81505296002497	-3.67567454563107
C	-2.17546009201931	-3.08809590704217	1.31541722634770
C	-3.15190965999452	-3.80782011417230	1.96005280600712
C	-4.34803222270292	-3.19419175117083	2.38640740211185
C	-4.54090053346817	-1.85721427845878	2.15836362764712
Pd	-0.15481759205627	1.41522976200145	-0.79225263493921
C	0.65244263732956	1.97875869186311	0.99212854879287
I	-1.25436502258270	3.77990334312171	-1.37420886744486
C	2.00006682930963	1.70804428364017	1.15595912313751
C	2.62845218484245	2.12781857351858	2.33087181214181
C	1.91030688315068	2.79381631964412	3.31548254490379
C	0.55604286948902	3.04504618194296	3.12781736773131
C	-0.08926505778403	2.63502533186467	1.96049119275696
H	-4.68598584081966	0.75052501721923	1.60155062852220
H	-2.99083412513244	2.12095472263856	0.48425170613478
H	2.37274289497812	-2.57231348635788	-1.01255821838207
H	4.44552122913173	-2.51898836017154	-2.40749868217391
H	5.02296504115897	-0.43399615946918	-3.63987629174755
H	4.66030076126538	1.62413326317298	-4.20636790687165
H	2.94492124480588	2.07227916989285	-4.38090769141666

H	3.86500811803600	2.63994712223482	-2.97839829923014
H	-1.26804806581602	-3.57372801772987	0.99659012407555
H	-2.99922868582175	-4.86449381250980	2.14438946541131
H	-5.10700211333773	-3.77948352964041	2.89078193580201
H	-5.45321403370272	-1.36817921777558	2.47920540448589
H	2.58106065936242	1.18375918724523	0.41209954880712
H	3.68300693636070	1.91861135360063	2.46326715657208
H	2.40191312109101	3.11403133405979	4.22546826591467
H	-0.01649603961228	3.56609460589803	3.88572558912044
H	-1.13862610147173	2.84529145534924	1.83223946522052

TS-4

Final Gibbs free energy = -1800.76976451 Eh

C	-0.66941063973607	-1.62155814082931	1.65881111404608
C	-1.22706371759236	-2.81780800112528	2.02457206598368
C	-0.56931134752431	-3.63100554428516	2.97371321501658
C	0.60250410513650	-3.20979554453576	3.51742207722883
N	1.16497707971200	-2.01406195262031	3.15910949482765
C	0.58180288518736	-1.19282083506870	2.23162600154826
N	-1.16934451667716	-0.73802765789347	0.68735573589335
C	-1.28451493031199	-1.16995798140799	-0.62113359013725
C	-0.85658791744902	-0.12323327315674	-1.58313591466799
O	-1.60188893072749	-2.32013846434285	-0.90326780667276
O	1.12461046066016	-0.09853793069207	1.89585230442551
C	-0.28878869979825	1.00241539636600	-1.02046990489382
C	0.35670780239193	1.97875854262456	-1.79285295008505
C	0.39405918011727	1.82351862538347	-3.15704987154690
C	-0.21753911803242	0.72076758378551	-3.79801254260302
C	-0.85886368134229	-0.28365676532795	-3.00782383933208
C	-0.20410523778866	0.59892701642812	-5.20966000886866
C	-0.80410169946212	-0.46800522549226	-5.82700993713221
C	-1.44349880329966	-1.45664854913956	-5.05073117010139
C	-1.47017936103331	-1.37342013672827	-3.67924352092266
C	-4.81302797113279	3.13268721314480	0.08224596722743
C	-3.68370774988024	3.73590844149763	-0.46049399993042

C	-2.41914535316556	3.18343804026911	-0.25943873896221
C	-2.29224179864854	2.02531864265053	0.49790047817569
C	-3.41406765021343	1.40645631323548	1.03669955663289
C	-4.67468349001342	1.96927767843624	0.82959905341475
I	0.75319422786924	3.52692347882017	1.51481148987486
Pd	-0.51655478543545	1.15369119674768	0.97569422749855
O	-1.26370898004377	0.96955735860178	3.24585039455016
C	-1.12442744394549	1.44485712025563	4.36398119628393
O	-0.36736673174579	2.50120084180098	4.62289011642220
H	0.02657444506129	2.85109463663130	3.78679746969893
C	2.44276354983617	-1.62521445723413	3.77620705679949
C	-1.81610710412863	0.90102784697734	5.57540150803312
H	-2.16150730393328	-3.13391514993121	1.58529664721549
H	-0.98987099302001	-4.57761107596524	3.27909648150344
H	1.15133053345372	-3.77711784615940	4.25443427807286
H	0.81207575318397	2.84395627305996	-1.33601469543900
H	0.89044998295552	2.57185947687154	-3.76468740757940
H	0.28722249452780	1.36957802610228	-5.79219621415396
H	-0.79234110173877	-0.55319227215149	-6.90689413986263
H	-1.92287390386880	-2.29413963146444	-5.54339657033313
H	-1.95855827515565	-2.13878966610311	-3.09763427189954
H	-5.79289477515364	3.56497346966094	-0.07859196455043
H	-3.77531489035832	4.64389409622369	-1.04446329040755
H	-1.55837919547296	3.67109723971877	-0.69107917566401
H	-3.32587851044825	0.49995358579484	1.61666549346340
H	-5.54519034036501	1.48464151440031	1.25531618642279
H	2.65144489680210	-0.59188780632401	3.52543109387204
H	2.35748585060953	-1.73444384908562	4.85485445317825
H	3.24228861678492	-2.26224975517803	3.39963118051038
H	-2.19293270402357	-0.09782849851258	5.37466965890245
H	-1.14078228425613	0.89613203668563	6.43044990789825
H	-2.65472792736638	1.55905531858051	5.81629262112458

INT-4

Final Gibbs free energy = -1502.43943601 Eh

C	-3.56073908200185	-0.09464806953412	-0.41872359897220
C	-3.63531151851206	-1.46575737553538	-0.75873460620984
C	-2.46134616125143	-2.15383043872469	-1.20926797771911
C	-1.23746180100330	-1.41122627615876	-1.29252095004550
C	-1.23208095765705	-0.07804697776959	-0.92853944352161
C	-2.37734721998819	0.59826809353039	-0.49565177825147
C	0.05566139613331	-1.96149957173684	-1.81218048666659
N	1.02274881023494	-0.98671008295907	-1.87063638728364
O	0.23891225691299	-3.11671312956649	-2.18601302621325
C	2.31342140087913	-1.12915415040298	-2.36665693261456
C	2.95357111894620	-2.29033866751665	-2.75807094569224
C	4.26198257740520	-2.22704383276499	-3.27012501628642
C	4.89926454652565	-1.02745789120591	-3.37044168586633
N	4.28281154162244	0.12327765627150	-2.97208232759669
C	3.01239059109892	0.12835593294160	-2.46975851087227
O	2.49344196069930	1.23078780606199	-2.10650229379681
C	4.97884845544471	1.41278551809631	-3.07891252519586
C	-2.58527888798127	-3.52716727269300	-1.54736005945818
C	-3.79310956460875	-4.17274915377080	-1.44236765971885
C	-4.94589912519322	-3.49215961866559	-0.99806337935911
C	-4.86421297585139	-2.16584945470751	-0.66401768909425
Pd	0.53173516701578	0.81317647139044	-1.20335511913935
C	0.95040609073475	0.42058336757861	0.74022384046944
C	2.06895257977707	-0.34801222343247	1.00959226769089
C	2.44115060050263	-0.53169282568471	2.34358784400110
C	1.69457949667508	0.03327642677209	3.36936729867482
C	0.56917791775442	0.79193949064654	3.06615306100454
C	0.18313536011809	0.99107800678425	1.74073870783322
O	-0.19507272038409	2.67952414007117	-0.85453121209068
O	1.71671978723110	3.58063578614285	-0.09150035692827
C	0.55233917679313	3.67437255910990	-0.45820783499027
C	-0.16856352723437	5.01035772087223	-0.50497825532819
H	-4.46161115304857	0.40983793645386	-0.08820571152300
H	-2.33131200368457	1.64702259195745	-0.23869472926484

H	2.44283916634461	-3.23583696726533	-2.67975523633133
H	4.76962661380625	-3.12620104560359	-3.58721301927434
H	5.90078931967692	-0.91593372395586	-3.75558691517874
H	5.97789042632647	1.23103675378937	-3.46255127423274
H	4.43383394575393	2.07047186451316	-3.75388158135224
H	5.03273504154452	1.88188463720196	-2.09882003051464
H	-1.71250676950875	-4.05975276087704	-1.88823077819503
H	-3.86107895996236	-5.22152261557628	-1.70506491881176
H	-5.88920062187319	-4.01904666940806	-0.92248770414197
H	-5.74041501543087	-1.62832647554361	-0.32072190857902
H	2.66370471411924	-0.79996593451139	0.23056734939725
H	3.31997611962149	-1.12517841469984	2.56469480680728
H	1.98763532010694	-0.11729094389785	4.40087559957626
H	-0.02125425729465	1.23925630901863	3.85629083327531
H	-0.68641768953855	1.59036607786924	1.52046526457730
H	0.38979914558453	5.75733126703236	0.05554681160639
H	-0.24762174103484	5.33275091955997	-1.54604711138777
H	-1.18029889234651	4.92127523050256	-0.10965270721474

INT-5

Final Gibbs free energy = -1502.45490889 Eh

C	-1.57811131423792	2.29316682302163	-1.48977528388474
C	-1.98620781903133	0.96334199936043	-1.23333989663540
C	-1.08074007849062	0.08101327323726	-0.56839842169376
C	0.21164374190197	0.56318874259289	-0.19275876271352
C	0.57312883726246	1.88364313624148	-0.42057093947431
C	-0.34968964771716	2.73605783693478	-1.08598050725487
C	1.10753429610401	-0.35433493117693	0.61593178887186
N	1.72262794137001	-1.40916308433286	-0.00171737990912
O	1.19946455336016	-0.15188782651546	1.81912995570237
C	1.67260967188585	-1.73204162478150	-1.36824594050336
C	1.54612592127035	-0.89393370598167	-2.45700004247532
C	1.46844332160213	-1.43432729825089	-3.75347581692807
C	1.54154524878654	-2.78129288099511	-3.93866492807745

N	1.71654623584714	-3.61567510816997	-2.87228762698261
C	1.82308499057955	-3.13187016076280	-1.60934157976307
O	2.07526485523115	-3.94482059082673	-0.64932140487994
C	1.83761393736355	-5.06717895224334	-3.07201089578851
C	-1.52659561448502	-1.23616235548456	-0.27931122592453
C	-2.78091489525648	-1.65673273982332	-0.64485196037533
C	-3.66329419278220	-0.78677074409729	-1.32064293562476
C	-3.27128794402315	0.49603808424508	-1.60489681221657
Pd	2.51318944623744	-2.93135706607009	1.04728152070151
C	3.10033787156982	1.85330754499690	-0.24437027885508
C	4.29390659854036	2.44783996174717	0.14899022553658
C	4.28515522523979	3.67383035647548	0.80528420991912
C	3.07034428762942	4.30240385731478	1.06417990696892
C	1.87870416621718	3.71006330059851	0.66531073586657
C	1.87179744902028	2.47254536856289	0.00659634867308
O	3.03031341454306	-2.18437066544567	2.78871947707217
O	4.76069595866647	-1.01125191382254	1.97188241361009
C	4.05499926831229	-1.37650106403169	2.90241505009620
C	4.28033637153535	-0.90679959107506	4.32415312729663
H	-2.25783602399705	2.96136091217826	-2.00553424162982
H	-0.05513302390636	3.75736519975043	-1.28924370519488
H	1.49325535683582	0.17582567184471	-2.33430349226288
H	1.35113317387464	-0.78525086942302	-4.60869884240376
H	1.48262166728238	-3.25675818439816	-4.90531669384763
H	1.65599305878868	-5.28268076776783	-4.11997601134212
H	2.83671587024750	-5.39560021501054	-2.79030817141288
H	1.10574982227033	-5.58220122102424	-2.45351719622165
H	-0.87366731232779	-1.91982925481453	0.24642976820828
H	-3.09908788113786	-2.66435380607714	-0.40794258007625
H	-4.64931807933247	-1.13298476156109	-1.60389115068070
H	-3.94402466777023	1.17924270584205	-2.11037040119993
H	3.13851044775719	0.90266556202919	-0.75720968795333
H	5.23162856126284	1.94722997588740	-0.05663463225959
H	5.21536648615121	4.13427757821800	1.11412229795884

H	3.04897764464911	5.25376436742915	1.58145269684571
H	0.93986900798867	4.20329350589725	0.88500395279234
H	5.29010832001396	-0.51656687633436	4.43533321257294
H	3.56508738117263	-0.10940495093898	4.54059798527334
H	4.10577808612415	-1.71227255316826	5.03745477247927

TS-5

Final Gibbs free energy = -1731.50905833 Eh

C	-3.98202961148608	2.86015755889779	0.62874233030955
C	-3.242125444485667	2.62741723663693	1.81204802046830
C	-2.21432198912761	1.63622306185679	1.80469647715454
C	-1.97019694771505	0.91720498766013	0.59193045440351
C	-2.73412080801099	1.13920232563201	-0.54246497480051
C	-3.73875000307897	2.13934821600371	-0.50706683441713
C	-0.88700797664838	-0.11751090084533	0.57842047900033
N	0.28079113566316	0.19282756309260	-0.21847875483493
O	-0.92379182074322	-1.14260654277408	1.21268405439285
C	1.09022894151627	-0.95030684003507	-0.59179232269250
C	0.81115165774327	-1.76000198938389	-1.65633699128430
C	1.62463999615925	-2.88044197880225	-1.90168898928036
C	2.65683183433892	-3.14586096326688	-1.04993062591478
N	2.93792089864431	-2.33535869843437	0.00569077685193
C	2.20339201456691	-1.20798843217340	0.25264256827567
O	2.54752933827842	-0.43581444444775	1.20460252507543
C	4.07247116747909	-2.62613663618155	0.89516330826385
C	-1.47351273557086	1.42967869067678	2.99623091529250
C	-1.74454738813835	2.15453894288225	4.12916576878118
C	-2.76711312323828	3.12622803638328	4.13612425108078
C	-3.49709827619969	3.35749377739232	2.99908147475175
Pd	1.60017870092185	1.38041307809391	0.98039058126732
C	-2.82963797984162	-1.05759919476111	-1.74891992110037
C	-2.78315386702098	-1.81176955844920	-2.91794450646000
C	-2.50586327321873	-1.19789447283177	-4.13528129722456
C	-2.28042315514824	0.17594699054913	-4.17848326098276
C	-2.33690522466921	0.93215649026854	-3.01359186912211

C	-2.60560520146051	0.32384255853860	-1.78180936648579
O	0.76780608061612	3.17500048402562	0.61041397209539
C	0.32831675360152	3.45076371089191	-0.57240723505388
O	0.24849251727594	2.64541096071445	-1.51292118378477
C	-0.11958618637195	4.88402953849339	-0.76310145113333
H	0.12767146473232	0.90786066929709	-0.95604830000288
O	3.01894693774560	2.37958808962613	1.98923369810023
O	2.24800458966773	1.57530641445465	3.93928620766461
C	3.03894854770126	2.24912424603840	3.28434387843134
C	4.16839372199094	3.00884876092192	3.95759625339310
H	-4.75971568422857	3.61526182434604	0.63797462228725
H	-4.33448105701753	2.30640065671803	-1.39549133475993
H	-0.03409727964944	-1.54597103305550	-2.29766591453136
H	1.43656842258838	-3.53742888914088	-2.73721048192710
H	3.30683348925459	-3.99991973045362	-1.16725331904492
H	4.51720314610165	-3.56592366777004	0.58394251859015
H	4.80347780053063	-1.82232111198095	0.82750681327723
H	3.71802794265020	-2.70004755415806	1.92089412838145
H	-0.67981337583232	0.69590226190986	3.02109171813732
H	-1.16263776745231	1.98098024480380	5.02542879561859
H	-2.96894840334552	3.68867722140358	5.03919044986255
H	-4.28252603960336	4.10449738670365	2.98951293870563
H	-3.06550679475342	-1.54074342156003	-0.80906867893393
H	-2.97141381901607	-2.87753286605759	-2.87537454944914
H	-2.46919505913076	-1.78405671492499	-5.04533876075635
H	-2.06075267793707	0.66062570476602	-5.12187562008197
H	-2.15060204799216	1.99772648483755	-3.05186063328464
H	0.41831432974277	5.31121197256081	-1.61065384635363
H	-1.18283431411427	4.88987091161652	-1.00923746930012
H	0.05191754309718	5.48691929550484	0.12546293406452
H	3.78442551074861	3.51292373573728	4.84448387394763
H	4.92294393331795	2.28886002151289	4.28281285690170
H	4.63407868594345	3.73067703003872	3.28971187816978

Product (4a1)

Final Gibbs free energy = -1146.7298919 Eh

O	1.38276755726816	-0.57240875577627	2.26904127851997
O	1.19146590521776	0.98378488900493	-2.37604552333425
N	3.53459208609776	-1.20700042961813	1.82714895369307
N	0.95301521807526	0.30199622773962	-0.21276403877818
C	-2.14213317598767	-0.77811235328120	-0.70864568297866
C	0.08155486467924	-2.64740019685685	-3.14204610926402
C	0.59433595857598	-3.65995495326226	-2.33823931259428
C	0.24156527792755	-3.71173593553856	-0.99243938321309
C	-0.61782542786715	-2.76004573739005	-0.45737684174034
C	-1.13552963022586	-1.73165243565369	-1.25418675658221
C	-0.77464075733685	-1.69171851165729	-2.60534655394266
C	-0.99933576568196	2.72775414541836	-1.57341359216394
C	-4.37381905080327	0.79221811827410	0.01714310528935
C	-4.37580330257342	-0.55443266308088	0.25888491257704
C	-3.27100311028095	-1.33077255532599	-0.13161408487149
C	3.66555216634935	-1.65808891261398	3.21473270082332
C	2.31721499700704	-0.66668434673298	1.45578280353385
C	4.58539585452955	-1.32558864375379	0.96073745978748
C	4.48018543047160	-0.91114532516161	-0.32920241096800
C	3.26789137219147	-0.34796575706045	-0.78748062530538
C	2.21002764353640	-0.22622397236729	0.07477301730452
C	0.49456644395853	0.83901204194774	-1.37801486021276
C	-2.18614891040137	3.44934027244733	-1.35715389835229
C	-0.90965770090767	1.37938075899590	-1.29678940141207
C	-2.06310972723476	0.65032969653466	-0.85363789152493
C	-3.23839047813000	1.41993066613877	-0.54938620980413
C	-3.26944123720972	2.81099806621382	-0.81783759362193
H	0.34342571597172	-2.60099719474808	-4.19224687802312
H	1.26324452537159	-4.40248877148965	-2.75632995144543
H	0.63865591230228	-4.49371980703587	-0.35632929985651
H	-0.88075206577914	-2.80406584574274	0.59242205622367
H	-1.17822204542804	-0.91716454111470	-3.24543298082770
H	-0.11547038789198	3.24579599698181	-1.92324626606816

H	-5.23909863218105	1.40057694367546	0.25184195000123
H	-5.23900746425837	-1.03564674994848	0.70178206856410
H	-3.32629631578506	-2.40737904128022	-0.02813897561024
H	2.93251601051554	-2.43611108424693	3.42286359881112
H	3.48954467109682	-0.82547259579080	3.89416609483205
H	4.66929718821620	-2.04727200327657	3.35898740916900
H	5.48419713343095	-1.76214667436209	1.36985304612963
H	5.32435660739636	-1.01646017141665	-0.99485208174002
H	3.16989943530902	-0.01483770652548	-1.80810332717997
H	0.32650450615752	0.27556809086801	0.58294407565210
H	-2.21937289773764	4.50870584435628	-1.5775555884160
H	-4.17639139795174	3.35839691351287	-0.58965644065408

12. References

1. Neese, F., Software update: the ORCA program system, version 6.0, *WIREs Comput. Molec. Sci.* 2025 15(1), e70019, doi.org/10.1002/wcms.7019
2. Garcia-Rates, M.; Neese, F., Effect of the Solute Cavity on the Solvation Energy and its Derivatives within the Framework of the Gaussian Charge Scheme, *J. Comput. Chem.* 2020 41, 922-939, doi.org/10.1002/jcc.26139
3. Garcia-Rates, M.; Neese, F., Efficient implementation of the analytical second derivatives of hartree-fock and hybrid DFT energies within the framework of the conductor-like polarizable continuum model, *J. Comput. Chem.* 2019 40, 1816-1828, doi.org/10.1002/jcc.25833
4. Bykov, D.; Petrenko, T.; Izsak, R.; Kossmann, S.; Becker, U.; Valeev, E.; Neese, F., Efficient implementation of the analytic second derivatives of Hartree-Fock and hybrid DFT energies: a detailed analysis of different approximations, *Molec. Phys.* 2015 113, 1961-1977, doi.org/10.1080/00268976.2015.1025114
5. Neese, F.; Wennmohs, F.; Hansen, A.; Becker, U., Efficient, approximate and parallel Hartree-Fock and hybrid DFT calculations. A 'chain-of-spheres' algorithm for the Hartree-Fock exchange, *Chem. Phys.* 2009 356(1-3), 98-109, doi.org/10.1016/j.chemphys.2008.10.036
6. Helmich-Paris, B.; de Souza, B.; Neese, F.; Izsak, R., An improved chain of spheres for exchange algorithm, *J. Chem. Phys.* 2021 155(10), 104109, doi.org/10.1063/5.0058766