

Supporting Information

Orthogonal Selectivity in C–H Olefination: Synthesis of Branched Vinylarene with Unactivated Aliphatic Substitution

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1. General information:

Reagent information:

Unless otherwise stated, all the reactions were carried out in screw cap reaction tube with magnetic stirring under air atmosphere. All the palladium salts were purchased from Alfa Aesar and used directly for the reaction. Copper fluoride and copper carbonate were brought from Sigma-Aldrich Co. ^tBuOH was brought from Spectrochem and used directly. α,β -alkenyl carboxylic acids were purchased from either Sigma-Aldrich Co. or Alfa Aesar and used without further purification. Neocuproine was purchased from Sigma-Aldrich Co. Phenyl acetic acid derivatives were brought from Sigma-Aldrich Co. All the other reagents were purchased from commercial source and used as received. For column chromatography silica gel (60-120 mesh and 100-200 mesh) was supplied from SRL Co. During elution petroleum ether and ethyl acetate mixture was used. Thin layer chromatography was performed on EMD Chemicals Si 60 F₂₅₄. TLC plates (silica gel 60F₂₅₄) were supplied from MERCK.

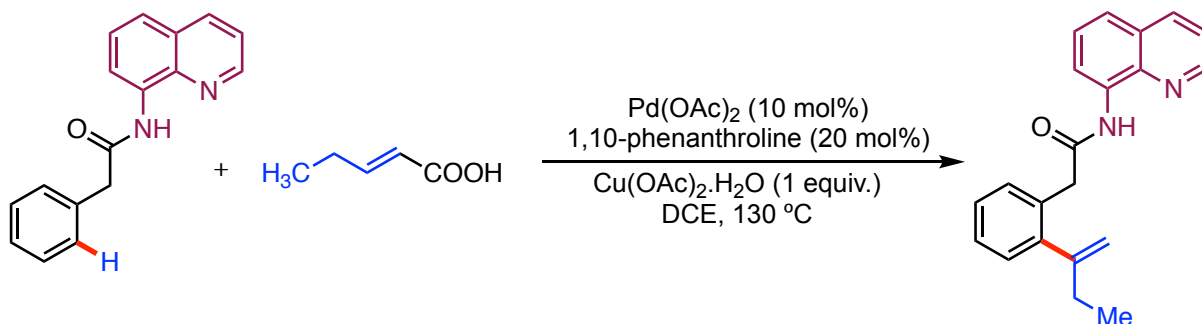
Analytical information:

¹H NMR, ¹³C NMR spectroscopy, Gas chromatography mass spectra (GCMS) or HRMS were used to characterize all the isolated compounds. Copies of the ¹H NMR, ¹³C NMR spectra were attached in this supporting information. All NMR spectra were recorded on a BRUKER 400 MHz or BRUKER 500 MHz instrument. All ¹H NMR spectra are reported in parts per million (ppm) downfield of TMS and were measured relative to residual CHCl₃ (7.26 ppm). All ¹³C NMR spectra were reported in ppm relative to CDCl₃ (77.23 ppm) and were obtained with proton decoupling. Coupling constants, J, are reported in Hertz. All GC analyses were performed on a Agilent 7890A GC system connected with a FID detector using a J & W DB-1 column (10 m, 0.1 mm I.D.). All GCMS analyses were done by Agilent 7890A GC system connected with 5975C inert XL EI/CI MSD (with triple axis detector).

2. Experimental section:

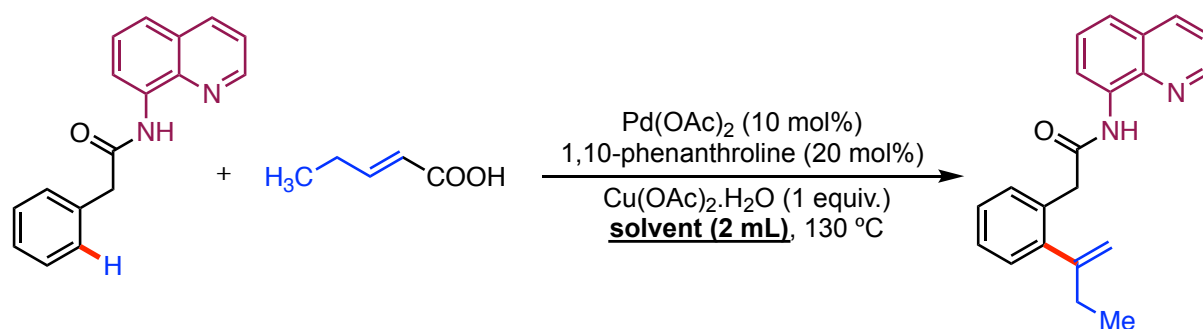
2.1 Optimization details

Initial reaction condition:



Branched olefinated product was obtained in 12% yield in the above mentioned condition. Then, optimization study was carried out by varying different parameters. Unless otherwise stated, 0.125 mmol of amide along with 0.25 mmol of 2-pentenoic acid were used for optimization purpose.

Table S1: Optimization of solvents



Entry	Solvent	Yield (%)
1	DCE	12
2	1,4-dioxane	13
3	THF	13
4	Cyclohexane	21
5	Benzene	23
6	Isobutyl benzene	18
7	<i>p</i> -xylene	1
8	<i>m</i> -xylene	18
9	Mesitylene	14
10	TFT	17
11	^tBuOH	44
12	$\text{CF}_3\text{CH}_2\text{OH}$	12
13	Isopropanol	7
14	HFIP	11
15	NMP	17

Table S2: Ligand optimization

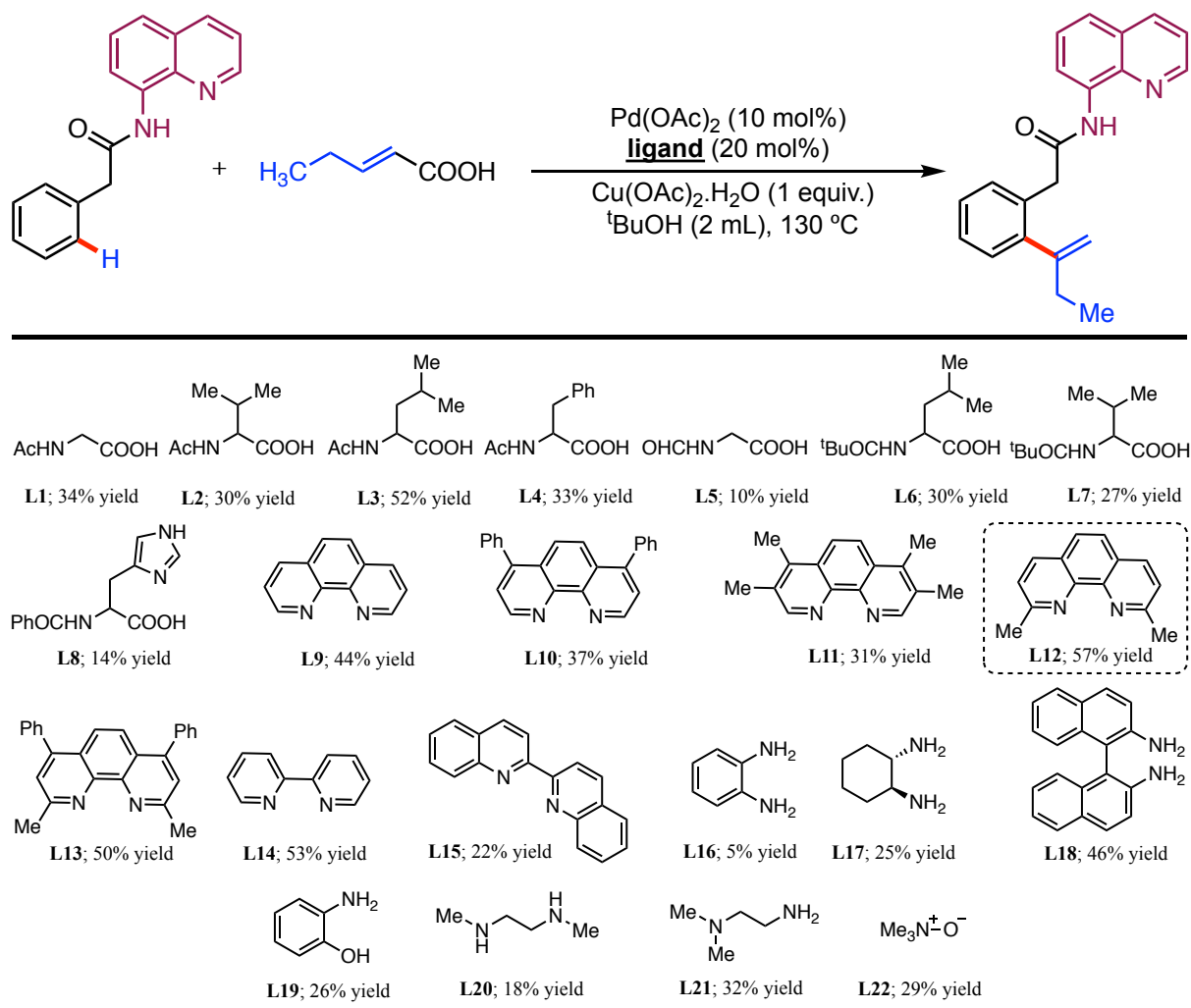


Table S3 and S4: Oxidant optimization

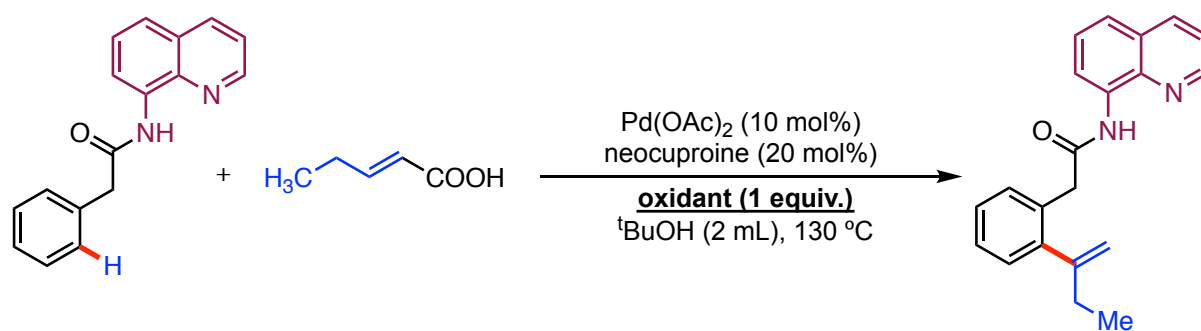


Table S3

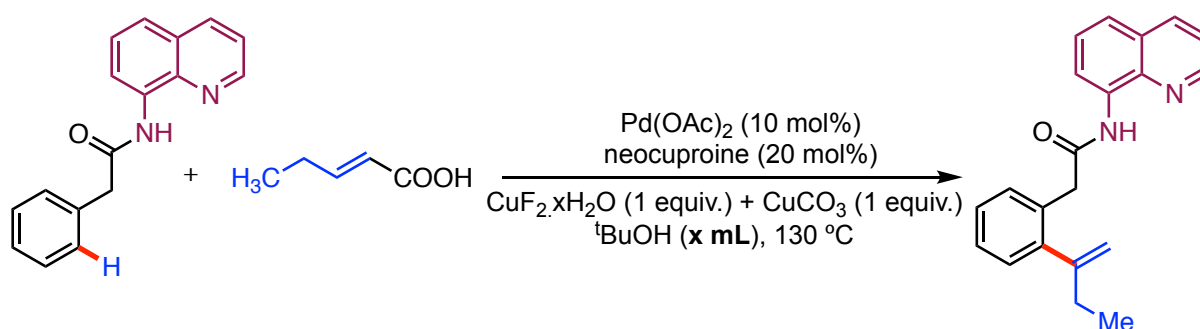
Entry	Oxidant	Yield (%)
1	$\text{CuF}_2 \cdot x\text{H}_2\text{O}$	72
2	CuBr	22
3	Cu	19

4	Cu ₂ O	17
5	CuSCN	8
6	CuCO₃	73
7	CuO	70
8	Cu(acac) ₂	45
9	Cu(OAc) ₂ ·H ₂ O	57
10	AgOAc	8
11	Benzoquinone	16

Table S4

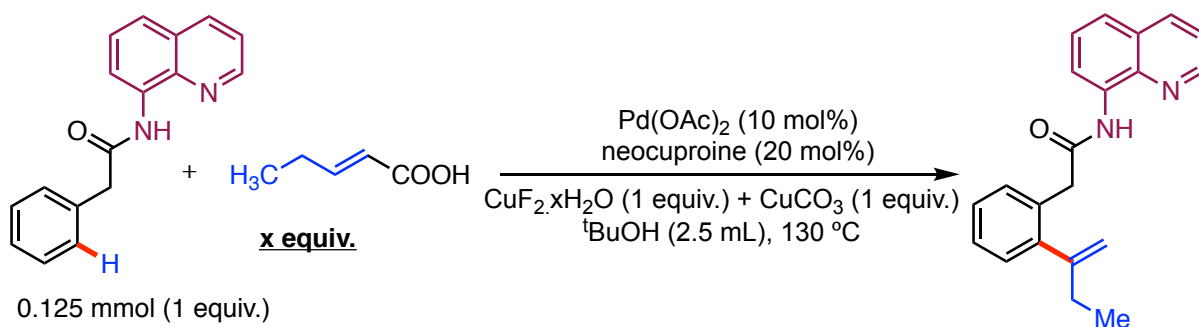
Entry	Oxidant	Yield (%)
1	CuF ₂ ·xH ₂ O (1.5 equiv.)	70
2	CuF ₂ ·xH ₂ O (2.0 equiv.)	61
3	CuCO ₃ (1.5 equiv.)	62
4	CuCO ₃ (2.0 equiv.)	50
5	CuF₂·xH₂O (1.0 equiv.) + CuCO₃ (1.0 equiv.)	80
6	CuF ₂ ·xH ₂ O (0.5 equiv.) + CuCO ₃ (0.5 equiv.)	75
7	CuF ₂ ·xH ₂ O (0.5 equiv.) + CuO (0.5 equiv.)	66
8	CuCO ₃ (0.5 equiv.) + CuO (0.5 equiv.)	63

Table S5: Optimization: Amount of Solvent



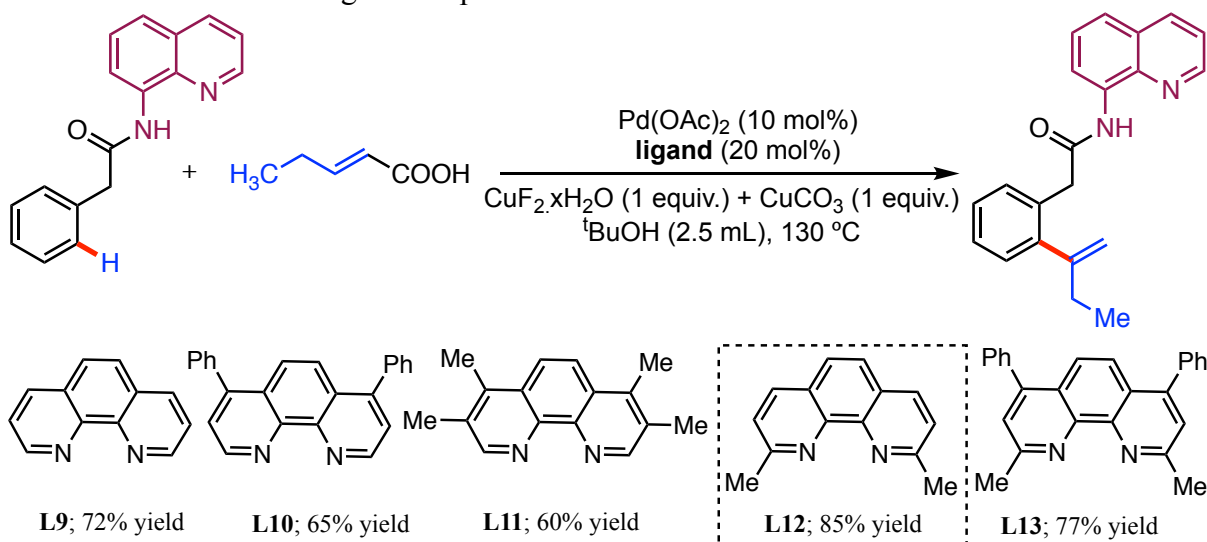
Entry	Solvent amount	Yield (%)
1	0.5	31
2	1.0	51
3	1.5	64
4	2.0	85
5	2.5	85
6	3.0	77

Table S6: Optimization: Amount of α,β-alkenyl carboxylic acids



Entry	2-pentenoic acid amount (equiv.)	Yield (%)
1	1.0	53
2	1.5	60
3	2.0	85
4	2.5	82
5	3.0	81
6	4.0	75

Table S7: Effect of bi-dentate ligand in optimized condition



2.2. General procedure A: Branched selective olefination of phenyl acetic acid derivatives

In a clean, oven-dried screw cap reaction tube containing magnetic stir-bar, phenyl acetic acid derivative (0.1 mmol), Pd(OAc)₂ (10 mol%, 0.01 mmol), neocuproine (20 mol%, 0.02 mmol), copper (II) carbonate basic (1 equiv, 0.1 mmol), copper (II) fluoride (1 equiv, 0.1 mmol) were weighed. α , β -unsaturated alkenyl carboxylic acid (2 equiv, 0.2 mmol) was transferred through micro pipette. Common laboratory syringe was used to introduce *t*-BuOH (2 mL) into the reaction mixture. Then the tube was placed in a preheated oil bath at 130 °C and the reaction were stirred (at 1000 rpm) vigorously for 24 h. After detaching the reaction, it was cooled to room temperature and filtered through celite pad using ethyl acetate (30 mL). Solvent was removed in rotatory evaporator. Desired compound was extracted using EtOAc-saturated NaHCO₃ and combined organic layer was dried over Na₂SO₄. Finally, it was concentrated in reduced pressure and was purified by column chromatography through silica gel (100-200 mesh

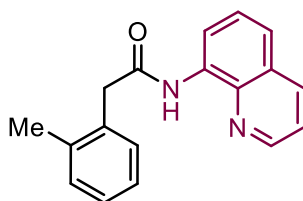
size) using PET-ether / ethyl acetate as eluent.

General procedure B: Sequential synthesis of bis-alkenylated products

Hetero-diolefination of branched olefinated derivatives was prepared by using literature method.¹ In a clean, oven-dried screw cap reaction tube containing magnetic stir-bar, branched olefinated derivative (0.1 mmol), Pd(OAc)₂ (10 mol%, 0.01 mmol), 2-amino phenol (20 mol%, 0.02 mmol), benzoquinone (1 equiv, 0.1 mmol) and sodium hydrogen carbonate (1 equiv, 0.1 mmol) were added. The cap was fitted with a rubber septum and the reaction tube was evacuated and back filled with oxygen three times. The corresponding olefin derivative (2 equiv, 0.2 mmol) was transferred through micro syringe and then 2 mL of DCE was added into the reaction mixture. Then the tube was placed in a preheated oil bath at 100 °C and the reaction were stirred vigorously for 24 h. After detaching the reaction, it was cooled to room temperature and filtered through celite pad using ethyl acetate (3*10 mL). Solvent was removed in rotatory evaporator. Desired compound was extracted using ethyl acetate-saturated NaHCO₃ and combined organic layer was dried over Na₂SO₄. Finally, it was concentrated in reduced pressure and was purified by column chromatography through silica gel (100-200 mesh size) using PET-ether / ethyl acetate as eluent.

2.3. Characterization data

Representative starting materials



Starting material for entry 3i, 3j and 3s

Rf: 0.5 (eluent:10% EtOAc/90% hexane)

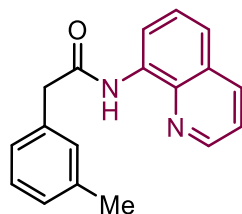
Isolation: Silica gel column (eluent: 5% EtOAc/95% hexane)

Appearance: light yellow solid

Yield: 98%

¹H NMR (400 MHz, CDCl₃) δ: 9.86 (s, 1H), 8.75 (dd, J = 7.3, 1.7 Hz, 1H), 8.64 (dd, J = 4.2, 1.7 Hz, 1H), 8.11 (dd, J = 8.3, 1.7 Hz, 1H), 7.54 – 7.46 (m, 2H), 7.40 – 7.35 (m, 2H), 7.28 (dd, J = 5.0, 4.0 Hz, 3H), 3.91 (s, 2H), 2.41 (s, 3H).

^{13}C NMR (101 MHz, CDCl_3) δ : 169.59, 148.39, 137.49, 136.37, 134.61, 133.42, 130.99, 130.81, 128.05, 127.99, 127.54, 126.83, 121.76, 121.71, 116.49, 43.52, and 19.94.



Starting material for entry 3m

Rf: 0.5 (eluent: 10% EtOAc/90% hexane)

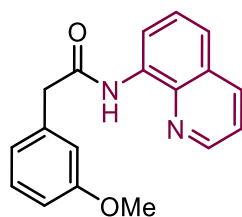
Isolation: Silica gel column (eluent: 5% EtOAc/95% hexane)

Appearance: yellow solid

Yield: 82%

^1H NMR (400 MHz, CDCl_3) δ : 9.94 (s, 1H), 8.77 (dd, J = 7.3, 1.4 Hz, 1H), 8.70 (dd, J = 4.2, 1.6 Hz, 1H), 8.11 (dd, J = 8.3, 1.5 Hz, 1H), 7.54 – 7.44 (m, 2H), 7.40 (dd, J = 8.3, 4.2 Hz, 1H), 7.29 (dd, J = 13.5, 6.0 Hz, 2H), 7.24 (d, J = 7.6 Hz, 1H), 7.15 (d, J = 7.4 Hz, 1H), 3.86 (s, 2H), 2.39 (s, 3H).

^{13}C NMR (101 MHz, CDCl_3) δ : 169.82, 148.33, 138.83, 138.64, 136.40, 134.76, 134.59, 130.45, 129.04, 128.25, 128.03, 127.51, 126.71, 121.74, 121.70, 116.52, 45.50, and 21.59.



Starting material for entry 3q and 3r

Rf: 0.45 (eluent: 10% EtOAc/90% hexane)

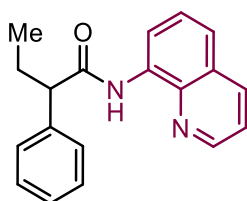
Isolation: Silica gel column (eluent: 6% EtOAc/94% hexane)

Appearance: white solid

Yield: 76%

^1H NMR (400 MHz, CDCl_3) δ : 9.95 (s, 1H), 8.75 (dd, J = 7.2, 1.8 Hz, 1H), 8.70 (dd, J = 4.2, 1.7 Hz, 1H), 8.12 (dd, J = 8.3, 1.7 Hz, 1H), 7.54 – 7.46 (m, 2H), 7.41 (dd, J = 8.3, 4.2 Hz, 1H), 7.35 – 7.30 (m, 1H), 7.05 – 6.98 (m, 2H), 6.88 (ddd, J = 8.3, 2.6, 0.8 Hz, 1H), 3.87 (s, 2H), 3.84 (s, 3H).

^{13}C NMR (101 MHz, CDCl_3) δ : 148.38, 136.45, 136.34, 134.62, 131.49, 130.23, 127.56, 122.09, 121.81, 121.75, 116.58, 115.08, 113.44, 55.49, and 45.70.



Starting material for entry 3aa

Rf: 0.5 (eluent:10% EtOAc/90% hexane)

Isolation: Silica gel column (eluent: 5% EtOAc/95% hexane)

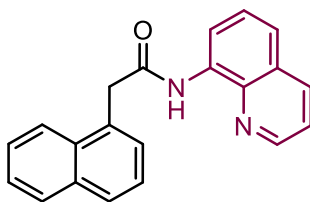
Appearance: light brown crystalline solid

Yield: 96%

¹H NMR (400 MHz, CDCl₃) δ: 9.92 (s, 1H), 8.79 (dd, *J* = 7.4, 1.5 Hz, 1H), 8.74 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.10 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.48 (qd, *J* = 8.0, 3.9 Hz, 1H), 7.42 – 7.34 (m, 1H), 7.29 (dt, *J* = 4.1, 1.7 Hz, 1H), 3.63 (t, *J* = 7.6 Hz, 1H), 2.43 – 2.25 (m, 1H), 2.05 – 1.91 (m, 1H), 1.01 (t, *J* = 7.4 Hz, 1H).

¹³C NMR (101 MHz, CDCl₃) δ: 172.33, 148.31, 140.01, 138.62, 136.43, 134.74, 129.01, 128.25, 128.05, 127.53, 127.45, 121.70, 121.60, 116.51, 56.94, 26.80, and 12.61.

Literature report¹



Starting material for entry 3ab

Rf: 0.5 (eluent:10% EtOAc/90% hexane)

Isolation: Silica gel column (eluent: 5% EtOAc/95% hexane)

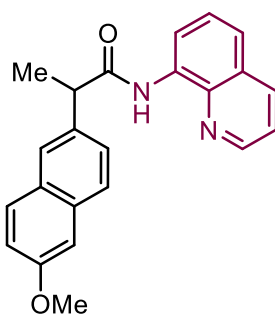
Appearance: white solid

Yield: 72%

¹H NMR (400 MHz, CDCl₃) δ: 9.93 (s, 1H), 8.74 (dd, *J* = 7.5, 1.5 Hz, 1H), 8.52 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.16 (dd, *J* = 12.7, 5.3 Hz, 1H), 8.05 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.89 (dd, *J* = 9.1, 8.0 Hz, 2H), 7.62 (d, *J* = 6.2 Hz, 1H), 7.57 – 7.41 (m, 6H), 7.32 (dd, *J* = 8.3, 4.2 Hz, 1H), 4.35 (s, 2H).

¹³C NMR (101 MHz, CDCl₃) δ: 169.63, 148.26, 138.61, 136.28, 134.54, 134.29, 132.52, 131.29, 128.96, 128.65, 128.57, 127.98, 127.47, 126.92, 126.23, 125.91, 124.18, 121.72, 121.64, 116.43, and 43.48.

Literature report¹



Starting material for entry 3ad

Rf: 0.45 (eluent:10% EtOAc/90% hexane)

Isolation: Silica gel column (eluent: 6% EtOAc/94% hexane)

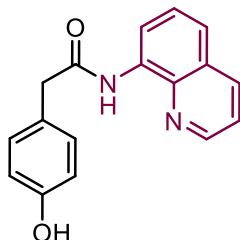
Appearance: white solid

Yield: 63%

¹H NMR (400 MHz, CDCl₃) δ: 9.97 (s, 1H), 8.77 (dd, *J* = 7.5, 1.4 Hz, 1H), 8.65 – 8.60 (m, 1H), 8.22 (d, *J* = 8.8 Hz, 1H), 8.09 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.89 (t, *J* = 5.7 Hz, 1H), 7.79

(d, J = 9.0 Hz, 1H), 7.69 (dd, J = 8.8, 1.8 Hz, 1H), 7.48 (ddd, J = 10.3, 8.3, 4.8 Hz, 2H), 7.37 (dd, J = 8.3, 4.3 Hz, 1H), 7.30 (d, J = 9.0 Hz, 1H), 4.10 (q, J = 7.1 Hz, 1H), 4.02 (s, 3H), 1.76 (dd, J = 6.9, 3.2 Hz, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ : 172.72, 152.70, 148.23, 138.44, 137.33, 136.63, 134.54, 131.35, 129.88, 128.12, 128.07, 127.76, 127.58, 126.59, 124.55, 121.76, 121.70, 116.69, 114.15, 57.15, 48.54, and 18.87.



Starting material for entry 3x

Rf: 0.35 (eluent: 10% EtOAc/90% hexane)

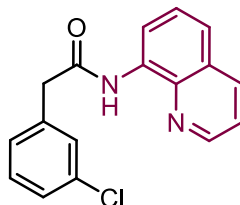
Isolation: Silica gel column (eluent: 8% EtOAc/92% hexane)

Appearance: grey solid

Yield: 53%

^1H NMR (500 MHz, DMSO) δ : 10.15 (s, 1H), 9.36 (s, 1H), 8.89 (dd, J = 4.2, 1.6 Hz, 1H), 8.62 (d, J = 6.9 Hz, 1H), 8.41 (dd, J = 8.3, 1.6 Hz, 1H), 7.66 (dd, J = 7.0, 6.1 Hz, 1H), 7.63 (dd, J = 8.3, 4.2 Hz, 1H), 7.57 (t, J = 8.0 Hz, 1H), 7.22 (d, J = 8.4 Hz, 1H), 6.76 (t, J = 5.7 Hz, 1H), 3.81 (s, 1H).

^{13}C NMR (126 MHz, DMSO) δ : 170.69, 156.69, 149.34, 138.48, 137.07, 134.95, 130.85, 128.27, 127.43, 126.20, 122.60, 122.32, 116.77, 115.78, 60.25, and 43.41.



Starting material for entry 3p and 3y

Rf: 0.5 (eluent: 10% EtOAc/90% hexane)

Isolation: Silica gel column (eluent: 5% EtOAc/95% hexane)

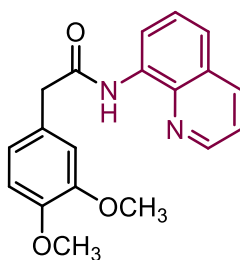
Appearance: white solid

Yield: 60%

^1H NMR (500 MHz, CDCl_3) δ : 9.93 (s, 1H), 8.75 – 8.72 (m, 2H), 8.14 (dd, J = 8.3, 1.7 Hz, 1H), 7.54 – 7.49 (m, 2H), 7.46 – 7.42 (m, 2H), 7.34 – 7.30 (m, 3H), 3.87 (s, 2H).

^{13}C NMR (126 MHz, CDCl_3) δ : 168.79, 148.48, 138.67, 136.83, 136.52, 134.44, 130.34, 129.89, 128.11, 127.93, 127.76, 127.56, 122.00, 121.84, 116.68, and 44.99.

Literature report¹



Starting material for entry 3ag and 3ah

Rf: 0.4 (eluent: 10% EtOAc/90% hexane)

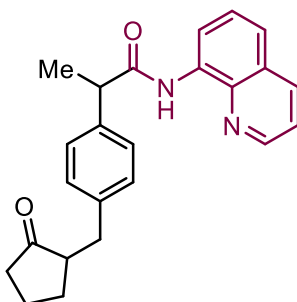
Isolation: Silica gel column (eluent: 6% EtOAc/94% hexane)

Appearance: white solid

Yield: 75%

¹H NMR (500 MHz, CDCl₃) δ: 9.95 (s, 1H), 8.75 (dd, *J* = 7.4, 1.5 Hz, 1H), 8.69 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.12 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.53 – 7.46 (m, 2H), 7.40 (dd, *J* = 8.3, 4.2 Hz, 1H), 6.97 (dd, *J* = 6.0, 2.0 Hz, 2H), 6.93 – 6.88 (m, 1H), 3.92 (s, 3H), 3.89 (s, 3H), 3.83 (s, 2H).

¹³C NMR (126 MHz, CDCl₃) δ: 170.00, 149.60, 148.65, 148.35, 138.69, 136.50, 134.58, 128.10, 127.55, 127.38, 122.01, 121.83, 121.73, 116.65, 112.87, 111.89, 56.19, 56.13, and 45.18.



Starting material for entry 3ae

Rf: 0.6 (eluent: 10% EtOAc/hexane)

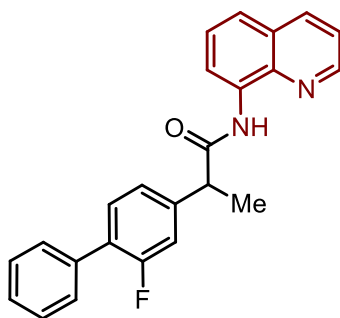
Isolation: Silica gel column (eluent: 5% EtOAc/hexane)

Appearance: solid

Yield: 89%

¹H NMR (500 MHz, CDCl₃) δ 9.86 (s, 1H), 8.74 (d, *J* = 7.5 Hz, 1H), 8.62 (d, *J* = 3.1 Hz, 1H), 8.01 (t, *J* = 13.3 Hz, 1H), 7.42 (t, *J* = 7.9 Hz, 1H), 7.37 (d, *J* = 7.6 Hz, 2H), 7.30 (dd, *J* = 8.0, 4.1 Hz, 1H), 7.14 (d, *J* = 7.8 Hz, 2H), 3.88 (q, *J* = 6.9 Hz, 1H), 3.09 (dt, *J* = 11.0, 5.5 Hz, 1H), 2.48 (dd, *J* = 13.7, 9.7 Hz, 1H), 2.26 (dd, *J* = 18.9, 8.0 Hz, 2H), 2.07 – 1.97 (m, 2H), 1.64 (d, *J* = 7.1 Hz, 4H), 1.48 (ddd, *J* = 16.2, 11.5, 5.1 Hz, 1H).

¹³C NMR (126 MHz, CDCl₃) δ 177.28, 172.79, 148.02, 138.87, 138.29, 136.17, 134.38, 129.37, 127.75, 127.69, 127.18, 121.46, 116.21, 77.49, 77.23, 76.97, 50.90, 50.88, 48.10, 44.87, 38.08, 35.09, 29.05, 29.03, 20.44, 18.57.



Starting material for entry 3af

Rf: 0.55 (eluent: 10% EtOAc/hexane)

Isolation: Silica gel column (eluent: 8% EtOAc/hexane)

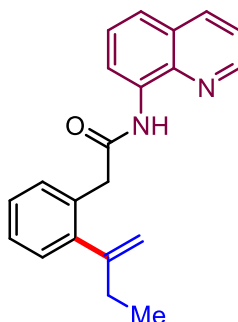
Appearance: solid

Yield: 86%

^1H NMR (500 MHz, CDCl_3) δ 10.01 (s, 1H), 8.79 (t, J = 10.4 Hz, 1H), 8.77 – 8.70 (m, 1H), 8.11 (d, J = 7.1 Hz, 1H), 7.58 – 7.50 (m, 3H), 7.50 – 7.31 (m, 8H), 3.98 (q, J = 6.8 Hz, 1H), 1.74 (d, J = 6.6 Hz, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ 172.05 (s), 159.9 (d, $^1J_{\text{FC}}$ = 249.4 Hz), 142.6, 138.5, 136.4, 135.6, 134.4, 131.2 (d, $^4J_{\text{FC}}$ = 3.78 Hz), 129.0, 128.5, 128.1 (d, $^3J_{\text{FC}}$ = 13.8 Hz), 127.7, 127.4, 123.8, 121.72 (d, J = 7.2 Hz), 116.4, 115.4 (d, $^2J_{\text{FC}}$ = 23.9 Hz), 48.2, 18.7.

Olefinated product



(Scheme 2, entry 3a)

Rf: 0.55 (eluent: 10% EtOAc/90% hexane)

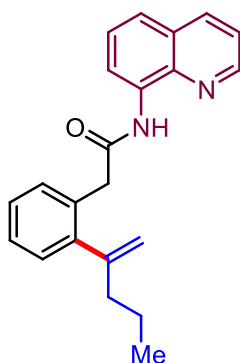
Isolation: Silica gel column (eluent: 5% EtOAc/95% hexane)

Appearance: colorless liquid

Yield: 76%

^1H NMR (400 MHz, CDCl_3) δ : 9.84 (s, 1H), 8.75 (dd, J = 7.4, 1.2 Hz, 1H), 8.65 (dd, J = 4.2, 1.6 Hz, 1H), 8.10 (dd, J = 8.3, 1.6 Hz, 1H), 7.53 – 7.45 (m, 3H), 7.38 (dd, J = 8.3, 4.2 Hz, 1H), 7.34 – 7.30 (m, 2H), 7.22 – 7.19 (m, 1H), 5.26 (d, J = 1.6 Hz, 1H), 5.01 (s, 1H), 3.91 (s, 2H), 2.38 (q, J = 7.4 Hz, 2H), 1.06 (t, J = 7.4 Hz, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ : 170.23, 150.74, 148.25, 144.25, 138.67, 136.33, 134.68, 131.81, 130.74, 129.18, 128.04, 127.62, 127.53, 127.35, 121.67, 121.65, 116.45, 114.07, 42.82, 31.46, and 12.45.



(Scheme 2, entry 3b)

Rf: 0.55 (eluent:10% EtOAc/90% hexane)

Isolation: Silica gel column (eluent: 5% EtOAc/95% hexane)

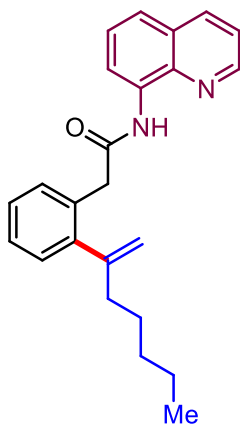
Appearance: colorless liquid

Yield: 83%

¹H NMR (500 MHz, CDCl₃) δ: 9.85 (s, 1H), 8.75 (dd, *J* = 7.5, 1.0 Hz, 1H), 8.66 (dd, *J* = 4.1, 1.4 Hz, 1H), 8.12 (d, *J* = 7.6 Hz, 1H), 7.51 (t, *J* = 7.8 Hz, 1H), 7.49 – 7.44 (m, 2H), 7.40 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.34 – 7.28 (m, 2H), 7.21 – 7.18 (m, 1H), 5.25 (d, *J* = 1.4 Hz, 1H), 5.01 (s, 1H), 3.92 (s, 2H), 2.33 (t, *J* = 7.7 Hz, 2H), 1.45 (dq, *J* = 14.8, 7.4 Hz, 2H), 0.86 (t, *J* = 7.3 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃) δ: 170.31, 149.25, 148.16, 144.17, 136.53, 134.64, 131.82, 130.78, 129.25, 128.33, 128.10, 127.62, 127.34, 121.70, 121.66, 116.67, 115.22, 42.84, 40.78, 21.06, and 14.01.

HRMS (ESI): [M-H]⁺ calculated for C₂₂H₂₃N₂O: 331.1805, found: 331.1806.



(Scheme 2, entry 3d)

Rf: 0.55 (eluent:10% EtOAc/90% hexane)

Isolation: Silica gel column (eluent: 5% EtOAc/95% hexane)

Appearance: colorless liquid

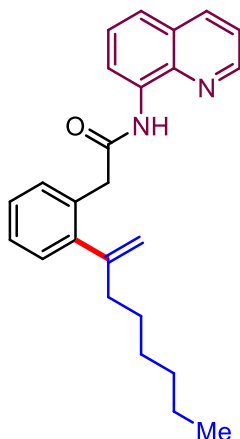
Yield: 78%

¹H NMR (500 MHz, CDCl₃) δ: 9.83 (s, 1H), 8.74 (d, *J* = 7.5 Hz, 1H), 8.66 – 8.62 (m, 1H), 8.10 (d, *J* = 8.3 Hz, 1H), 7.50 (t, *J* = 7.8 Hz, 1H), 7.46 (d, *J* = 8.3 Hz, 2H), 7.38 (dd, *J* = 7.8, 3.8 Hz, 1H), 7.35 – 7.28 (m, 2H), 7.20 (d, *J* = 7.1 Hz, 1H), 5.24 (s, 1H), 5.00 (s, 1H),

3.91 (s, 2H), 2.35 – 2.31 (m, 2H), 1.45 – 1.35 (m, 2H), 1.16 (dd, $J = 14.1, 6.6$ Hz, 4H), 0.77 (t, $J = 6.6$ Hz, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ : 170.27, 149.51, 148.26, 144.23, 138.68, 136.36, 134.68, 131.79, 130.83, 129.26, 128.06, 127.63, 127.56, 127.38, 121.67, 116.48, 115.03, 42.90, 38.64, 31.78, 27.59, 22.63, and 14.17.

HRMS (ESI): $[\text{M}-\text{H}]^+$ calculated for $\text{C}_{24}\text{H}_{27}\text{N}_2\text{O}$: 359.2118, found: 359.2115.



(Scheme 2, entry 3e)

Rf: 0.6 (eluent: 10% EtOAc/90% hexane)

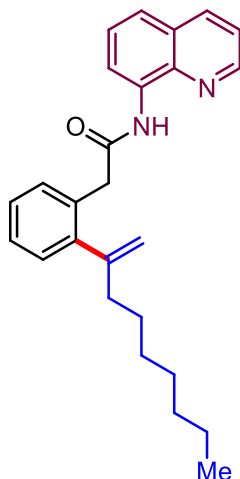
Isolation: Silica gel column (eluent: 4% EtOAc/96% hexane)

Appearance: colorless liquid

Yield: 81%

^1H NMR (500 MHz, CDCl_3) δ : 9.85 (s, 1H), 8.75 (dd, $J = 7.5, 1.4$ Hz, 1H), 8.65 (dd, $J = 4.2, 1.6$ Hz, 1H), 8.12 (dd, $J = 8.3, 1.4$ Hz, 1H), 7.53 – 7.49 (m, 1H), 7.46 (ddd, $J = 4.6, 4.2, 1.5$ Hz, 2H), 7.39 (dd, $J = 8.3, 4.2$ Hz, 1H), 7.35 – 7.29 (m, 2H), 7.21 – 7.18 (m, 1H), 5.24 (d, $J = 1.6$ Hz, 1H), 5.00 – 4.98 (m, 1H), 3.92 (s, 2H), 2.36 – 2.30 (m, 2H), 1.38 (dt, $J = 15.4, 7.6$ Hz, 2H), 1.24 – 1.07 (m, 6H), 0.77 (t, $J = 7.1$ Hz, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ : 170.32, 149.52, 148.16, 144.22, 138.52, 134.60, 131.77, 130.85, 129.25, 128.33, 128.09, 127.87, 127.62, 127.38, 121.71, 121.66, 116.67, 115.01, 42.86, 38.70, 31.83, 29.29, 27.90, 22.76, and 14.22.



(Scheme 2, entry 3f)

Rf: 0.6 (eluent:10% EtOAc/90% hexane)

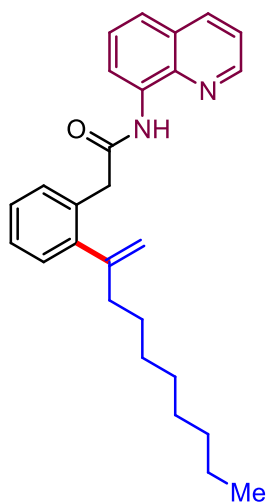
Isolation: Silica gel column (eluent: 4% EtOAc/96% hexane)

Appearance: colorless liquid

Yield: 82%

¹H NMR (500 MHz, CDCl₃) δ: 9.85 (s, 1H), 8.75 (dd, *J* = 7.5, 1.4 Hz, 1H), 8.65 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.12 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.53 – 7.49 (m, 1H), 7.46 (ddd, *J* = 4.6, 4.2, 1.5 Hz, 2H), 7.39 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.35 – 7.29 (m, 2H), 7.21 – 7.18 (m, 1H), 5.24 (d, *J* = 1.6 Hz, 1H), 5.00 – 4.98 (m, 1H), 3.92 (s, 2H), 2.36 – 2.30 (m, 2H), 1.38 (dt, *J* = 15.4, 7.6 Hz, 2H), 1.24 – 1.05 (m, 8H), 0.77 (t, *J* = 7.1 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃) δ: 170.32, 149.52, 148.16, 144.22, 138.52, 134.60, 131.77, 130.85, 129.25, 128.33, 128.09, 127.87, 127.62, 127.38, 121.71, 121.66, 116.67, 115.01, 42.86, 38.70, 31.83, 29.29, 27.90, 22.76, and 14.22.



(Scheme 2, entry 3g)

Rf: 0.6 (eluent:10% EtOAc/90% hexane)

Isolation: Silica gel column (eluent: 4% EtOAc/96% hexane)

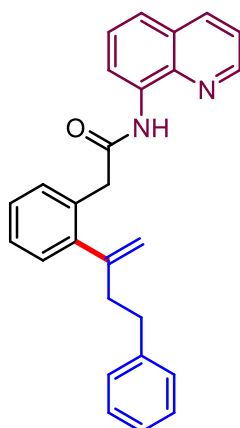
Appearance: colorless liquid

Yield: 80%

¹H NMR (500 MHz, CDCl₃) δ: 9.83 (s, 1H), 8.75 (dd, *J* = 7.5, 1.4 Hz, 1H), 8.64 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.10 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.48 (ddd, *J* = 11.0, 8.6, 4.9 Hz, 4H), 7.38 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.33 – 7.30 (m, 2H), 7.21 – 7.18 (m, 1H), 5.24 (dd, *J* = 3.1, 1.4 Hz, 1H), 5.01 – 4.99 (m, 1H), 3.92 (s, 2H), 2.35 – 2.31 (m, 2H), 1.42 – 1.35 (m, 2H), 1.20 (dt, *J* = 14.6, 6.9 Hz, 4H), 1.15 – 1.08 (m, 6H), 0.84 (dd, *J* = 9.3, 5.1 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃) δ: 170.27, 149.52, 148.25, 144.21, 138.65, 136.36, 134.65, 131.76, 130.85, 129.26, 128.04, 127.62, 127.55, 127.38, 121.67, 116.47, 115.01, 42.88, 38.70, 32.01, 29.63, 29.57, 29.42, 27.95, 22.81, and 14.29.

HRMS (ESI): [M-H]⁺ calculated for C₂₇H₃₃N₂O: 401.2587, found: 401.2586.



(Scheme 2, entry 3h)

Rf: 0.5 (eluent: 10% EtOAc/90% hexane)

Isolation: Silica gel column (eluent: 5% EtOAc/95% hexane)

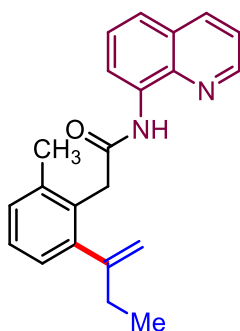
Appearance: white solid

Yield: 65%

¹H NMR (500 MHz, CDCl₃) δ: 9.85 (s, 1H), 8.75 (dd, *J* = 7.4, 1.5 Hz, 1H), 8.62 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.11 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.53 – 7.45 (m, 3H), 7.39 – 7.36 (m, 1H), 7.35 – 7.30 (m, 2H), 7.24 – 7.21 (m, 1H), 7.20 – 7.15 (m, 2H), 7.14 – 7.09 (m, 1H), 7.06 – 7.03 (m, 2H), 5.34 – 5.31 (m, 1H), 5.07 – 5.05 (m, 1H), 3.91 (s, 2H), 2.77 – 2.71 (m, 2H), 2.68 (ddd, *J* = 8.1, 6.0, 5.1 Hz, 2H).

¹³C NMR (126 MHz, CDCl₃) δ: 170.23, 148.57, 148.19, 143.70, 141.83, 134.56, 131.91, 130.98, 129.23, 128.46, 128.44, 128.11, 127.80, 127.65, 127.47, 125.98, 121.75, 121.69, 115.73, 42.86, 40.12, and 34.24.

HRMS (ESI): [M-H]⁺ calculated for C₂₇H₂₅N₂O: 393.1961, found: 393.1959.



(Scheme 2, entry 3i)

Rf: 0.5 (eluent: 10% EtOAc/90% hexane)

Isolation: Silica gel column (eluent: 5% EtOAc/95% hexane)

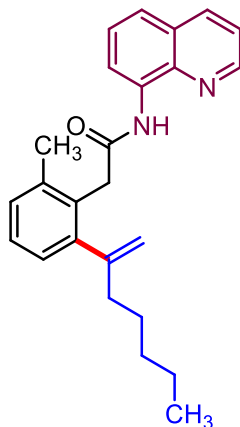
Appearance: liquid

Yield: 71%

¹H NMR (400 MHz, CDCl₃) δ: 9.78 (s, 1H), 8.73 (dt, *J* = 8.1, 4.0 Hz, 1H), 8.60 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.10 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.51 (dd, *J* = 10.3, 5.4 Hz, 1H), 7.46 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.37 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.24 (d, *J* = 7.5 Hz, 1H), 7.19 (d, *J* =

7.2 Hz, 1H), 7.09 (d, $J = 7.4$ Hz, 1H), 5.20 (d, $J = 1.7$ Hz, 1H), 5.05 – 5.02 (m, 1H), 3.94 (s, 2H), 2.40 – 2.32 (m, 5H), 1.05 (t, $J = 7.4$ Hz, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ : 170.05, 151.50, 148.28, 145.13, 138.76, 138.31, 136.28, 134.71, 130.35, 129.59, 128.06, 127.54, 127.34, 127.07, 121.66, 121.62, 116.48, 113.79, 40.27, 31.70, 20.53, and 12.49.



(Scheme 2, entry 3j)

Rf: 0.55 (eluent: 10% EtOAc/90% hexane)

Isolation: Silica gel column (eluent: 4% EtOAc/96% hexane)

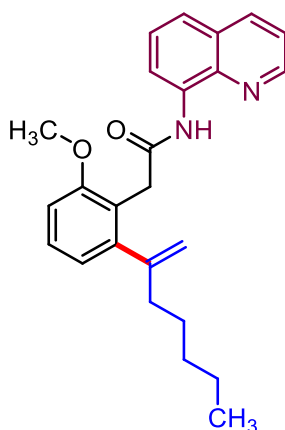
Appearance: liquid

Yield: 74%

^1H NMR (500 MHz, CDCl_3) δ : 9.78 (s, 1H), 8.74 (dd, $J = 7.5, 1.4$ Hz, 1H), 8.59 (dd, $J = 4.2, 1.7$ Hz, 1H), 8.09 (dd, $J = 8.3, 1.6$ Hz, 1H), 7.53 – 7.48 (m, 1H), 7.47 – 7.44 (m, 1H), 7.36 (dd, $J = 8.3, 4.2$ Hz, 1H), 7.23 (d, $J = 7.5$ Hz, 1H), 7.19 (d, $J = 6.9$ Hz, 1H), 7.10 – 7.06 (m, 1H), 5.19 (dd, $J = 3.1, 1.4$ Hz, 1H), 5.05 – 5.02 (m, 1H), 3.95 (s, 2H), 2.39 (s, 3H), 2.34 – 2.28 (m, 2H), 1.44 – 1.37 (m, 2H), 1.24 – 1.12 (m, 4H), 0.79 – 0.74 (m, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ : 170.05, 150.22, 148.25, 145.05, 138.73, 138.31, 136.27, 134.67, 130.31, 129.58, 128.04, 127.53, 127.33, 127.13, 121.63, 121.61, 116.46, 114.75, 40.27, 38.88, 31.78, 27.60, 22.63, 20.52, and 14.15.

HRMS (ESI): $[\text{M}-\text{H}]^+$ calculated for $\text{C}_{25}\text{H}_{29}\text{N}_2\text{O}$: 373.2274, found: 373.2273.



(Scheme 2, entry 3k)

Rf: 0.5 (eluent:10% EtOAc/90% hexane)

Isolation: Silica gel column (eluent: 5% EtOAc/95% hexane)

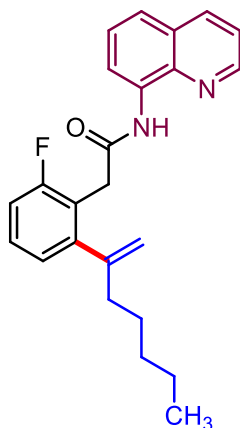
Appearance: liquid

Yield: 70%

¹H NMR (400 MHz, CDCl₃) δ: 10.18 (s, 1H), 8.76 (dd, *J* = 7.6, 1.5 Hz, 1H), 8.68 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.10 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.47 (ddd, *J* = 12.0, 9.7, 4.8 Hz, 2H), 7.38 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.28 (d, *J* = 8.0 Hz, 1H), 6.92 – 6.86 (m, 1H), 6.83 (dd, *J* = 7.7, 1.1 Hz, 1H), 5.24 (dd, *J* = 3.3, 1.5 Hz, 1H), 5.02 – 4.95 (m, 1H), 3.93 (s, 3H), 3.92 (s, 2H), 2.39 – 2.33 (m, 2H), 1.45 – 1.35 (m, 2H), 1.25 – 1.18 (m, 4H), 0.79 (t, *J* = 7.1 Hz, 3H).

¹³C NMR (101 MHz, CDCl₃) δ: 170.53, 157.85, 149.17, 148.07, 146.02, 138.83, 136.32, 135.25, 128.09, 128.02, 127.64, 121.54, 121.51, 121.23, 121.03, 116.57, 114.99, 109.06, 55.91, 38.73, 37.50, 31.81, 27.58, 22.69, and 14.22.

HRMS (ESI): [M-H]⁺ calculated for C₂₅H₂₉N₂O₂: 389.2224, found: 389.2223.



(Scheme 2, entry 3l)

Rf: 0.5 (eluent:10% EtOAc/90% hexane)

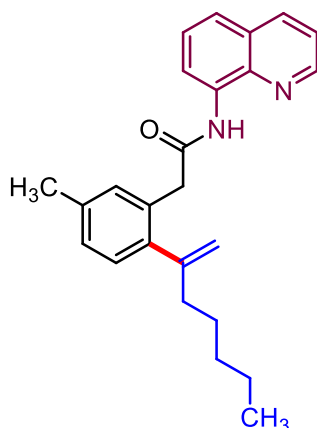
Isolation: Silica gel column (eluent: 5% EtOAc/95% hexane)

Appearance: liquid

Yield: 53%

¹H NMR (500 MHz, CDCl₃) δ: 9.85 (s, 1H), 8.75 – 8.67 (m, 2H), 8.13 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.54 – 7.46 (m, 2H), 7.41 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.17 (ddd, *J* = 14.4, 9.0, 4.3 Hz, 2H), 6.99 (td, *J* = 8.4, 2.7 Hz, 1H), 5.26 (d, *J* = 1.5 Hz, 1H), 5.00 – 4.98 (m, 1H), 3.88 (s, 2H), 2.33 – 2.27 (m, 2H), 1.40 – 1.35 (m, 2H), 1.23 – 1.14 (m, 4H), 0.78 (t, *J* = 7.1 Hz, 3H).

¹³C NMR (101 MHz, CDCl₃) δ: 169.08, 161.91 (d, *J* = 247.4 Hz), 148.31, 146.62, 146.58, 138.66, 136.42, 134.81, 134.58, 132.99, 128.73, 128.64, 128.07, 127.59, 124.66, 124.63, 121.72, 121.22, 119.88, 119.73, 116.70, 116.61, 115.61, 114.21, 113.98, 38.52, 36.02, 31.73, 27.55, 22.63, and 14.17.



(Scheme 2, entry 3m)

Rf: 0.55 (eluent: 10% EtOAc/90% hexane)

Isolation: Silica gel column (eluent: 4% EtOAc/96% hexane)

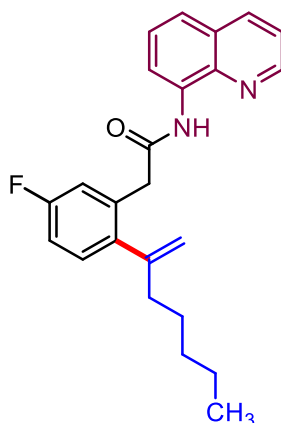
Appearance: liquid

Yield: 68%

¹H NMR (500 MHz, CDCl₃) δ: 9.86 (s, 1H), 8.75 (dd, *J* = 7.5, 1.4 Hz, 1H), 8.68 – 8.64 (m, 1H), 8.11 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.53 – 7.45 (m, 2H), 7.39 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.29 (s, 1H), 7.13 – 7.07 (m, 2H), 5.23 (t, *J* = 4.6 Hz, 1H), 5.01 – 4.97 (m, 1H), 3.88 (s, 2H), 2.38 (s, 3H), 2.34 – 2.29 (m, 2H), 1.42 – 1.35 (m, 2H), 1.23 – 1.14 (m, 4H), 0.77 (t, *J* = 7.1 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃) δ: 170.38, 149.45, 148.24, 141.25, 138.73, 137.22, 136.34, 134.73, 131.61, 131.41, 129.13, 128.11, 128.06, 127.55, 121.66, 121.63, 116.49, 114.95, 42.84, 38.75, 31.79, 27.62, 22.63, 21.28, 14.17.

HRMS (ESI): [M-H]⁺ calculated for C₂₅H₂₈N₂NaO: 395.2094, found: 395.2089.



(Scheme 2, entry 3n)

Rf: 0.5 (eluent: 10% EtOAc/90% hexane)

Isolation: Silica gel column (eluent: 5% EtOAc/95% hexane)

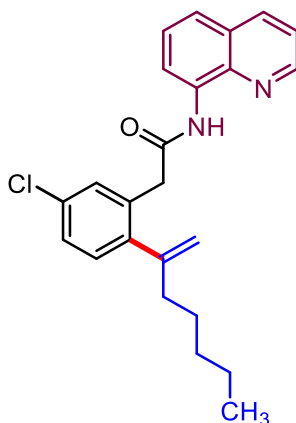
Appearance: liquid

Yield: 49%

¹H NMR (500 MHz, CDCl₃) δ: 9.87 (s, 1H), 8.73 (dt, *J* = 8.7, 4.3 Hz, 1H), 8.69 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.16 – 8.11 (m, 1H), 7.54 – 7.47 (m, 2H), 7.41 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.18 (dd, *J* = 9.6, 2.6 Hz, 1H), 7.15 (dd, *J* = 8.5, 5.9 Hz, 1H), 7.00 (td, *J* = 8.4, 2.7 Hz, 1H), 5.26 (d, *J* = 1.5 Hz, 1H), 4.99 (s, 1H), 3.89 (s, 2H), 2.33 – 2.28 (m, 2H), 1.38 (dd, *J* = 14.2, 6.4 Hz, 2H), 1.23 – 1.14 (m, 4H), 0.78 (t, *J* = 7.0 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃) δ: 169.47, 161.95 (d, *J* = 245.7 Hz), 148.63, 148.30, 140.05, 140.03, 138.57, 136.52, 135.58, 134.48, 134.02, 133.96, 132.59, 130.71, 130.64, 128.09, 127.58, 121.86, 121.76, 117.40, 117.23, 116.63, 115.66, 114.39, 114.22, 42.72, 38.71, 31.75, 27.53, 22.64, and 14.17.

HRMS (ESI): [M-H]⁺ calculated for C₂₄H₂₆N₂O: 377.2024, found: 377.2022.



(Scheme 2, entry 3o)

Rf: 0.5 (eluent: 10% EtOAc/90% hexane)

Isolation: Silica gel column (eluent: 5% EtOAc/95% hexane)

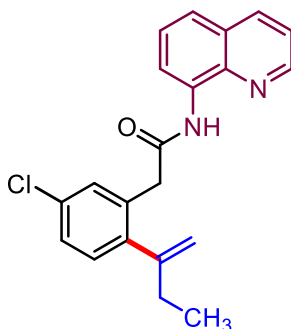
Appearance: liquid

Yield: 57%

¹H NMR (500 MHz, CDCl₃) δ: 9.87 (s, 1H), 8.74 – 8.65 (m, 2H), 8.13 (d, *J* = 8.3 Hz, 1H), 7.54 – 7.46 (m, 3H), 7.42 (ddd, *J* = 8.2, 4.1, 1.8 Hz, 1H), 7.27 (d, *J* = 9.4 Hz, 1H), 7.12 (dd, *J* = 8.2, 1.5 Hz, 1H), 5.26 (s, 1H), 5.00 (s, 1H), 3.87 (d, *J* = 1.2 Hz, 2H), 2.31 (t, *J* = 7.6 Hz, 2H), 1.37 (dd, *J* = 14.1, 7.3 Hz, 2H), 1.20 (dd, *J* = 9.2, 6.3 Hz, 4H), 0.78 (dd, *J* = 7.0, 5.5 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃) δ: 169.34, 148.44, 148.38, 142.55, 138.63, 136.43, 134.47, 133.77, 133.14, 130.67, 130.46, 128.06, 127.54, 127.50, 121.85, 121.78, 116.53, 115.68, 42.51, 38.53, 31.73, 27.51, 22.62, 14.17.

HRMS (ESI): [M-H]⁺ calculated for C₂₄H₂₆ClN₂O: 393.1728, found: 393.1727.



(Scheme 2, entry 3p)

Rf: 0.5 (eluent:10% EtOAc/90% hexane)

Isolation: Silica gel column (eluent: 5% EtOAc/95% hexane)

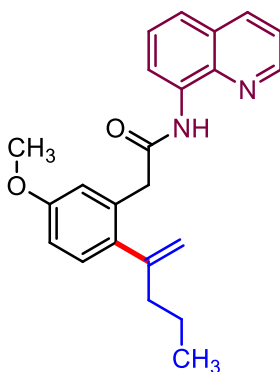
Appearance: liquid

Yield: 60%

¹H NMR (500 MHz, CDCl₃) δ: 9.86 (s, 1H), 8.71 (tt, *J* = 7.3, 3.8 Hz, 2H), 8.15 – 8.11 (m, 1H), 7.50 (ddd, *J* = 13.5, 9.0, 2.4 Hz, 3H), 7.42 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.27 (dd, *J* = 7.6, 1.6 Hz, 2H), 7.14 – 7.11 (m, 1H), 5.29 – 5.25 (m, 1H), 5.00 (d, *J* = 1.4 Hz, 1H), 3.86 (s, 2H), 2.38 – 2.30 (m, 2H), 1.05 (t, *J* = 7.4 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃) δ: 169.34, 149.71, 148.39, 142.61, 138.64, 136.47, 133.81, 133.17, 130.61, 130.41, 128.33, 128.08, 127.56, 127.51, 121.86, 121.80, 116.57, 114.74, 42.46, 31.40, and 12.40.

HRMS (ESI): [M-H]⁺ calculated for C₂₁H₂₀ClN₂O: 351.1259, found: 351.1256.



(Scheme 2, entry 3q)

Rf: 0.5 (eluent:10% EtOAc/90% hexane)

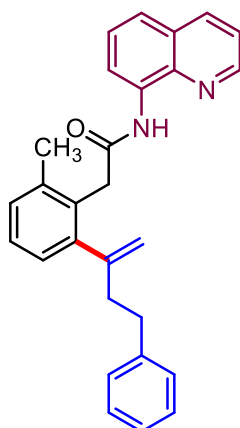
Isolation: Silica gel column (eluent: 5% EtOAc/95% hexane)

Appearance: liquid

Yield: 65%

¹H NMR (400 MHz, CDCl₃) δ: 9.87 (s, 1H), 8.74 (dt, *J* = 7.1, 3.5 Hz, 1H), 8.66 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.11 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.53 – 7.45 (m, 2H), 7.39 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.12 (d, *J* = 8.5 Hz, 1H), 7.01 (d, *J* = 2.7 Hz, 1H), 6.86 (dd, *J* = 8.5, 2.7 Hz, 1H), 5.24 (dd, *J* = 3.3, 1.5 Hz, 1H), 5.02 – 4.95 (m, 1H), 3.89 (s, 2H), 3.83 (s, 3H), 2.31 (t, *J* = 7.6 Hz, 2H), 1.42 (dt, *J* = 6.5, 4.9 Hz, 2H), 0.86 (dd, *J* = 8.6, 6.1 Hz, 3H).

¹³C NMR (101 MHz, CDCl₃) δ: 170.07, 158.91, 148.86, 148.26, 138.72, 136.55, 136.35, 134.71, 133.06, 130.32, 128.05, 127.55, 121.70, 121.68, 116.49, 115.42, 115.37, 113.56, 55.55, 43.14, 41.03, 21.11, 14.05.



(Scheme 2, entry 3r)

Rf: 0.5 (eluent: 10% EtOAc/90% hexane)

Isolation: Silica gel column (eluent: 5% EtOAc/95% hexane)

Appearance: brown sticky liquid

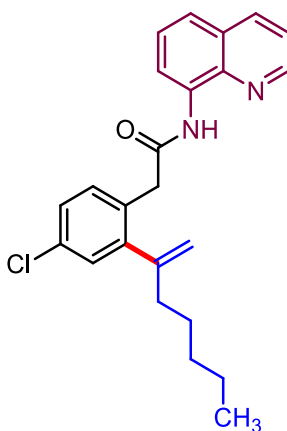
Yield: 59%

¹H NMR (500 MHz, CDCl₃) δ: 9.80 (s, 1H), 8.77 – 8.71 (m, 1H), 8.58 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.09 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.49 (dt, *J* = 8.2, 7.6 Hz, 2H), 7.35 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.25 (m, 1H), 7.21 (d, *J* = 7.2 Hz, 1H), 7.18 – 7.08 (m, 4H), 7.04 (d, *J* = 7.1 Hz, 2H), 5.27 (d, *J* = 1.1 Hz, 1H), 5.09 (s, 1H), 3.94 (s, 2H), 2.78 – 2.70 (m, 2H), 2.70 – 2.64 (m, 2H), 2.40 (s, 3H).

¹³C NMR (126 MHz, CDCl₃) δ: 169.94, 149.32, 148.32, 144.52, 141.85, 138.70, 138.42, 136.30, 134.62, 130.42, 129.77, 128.45, 128.40, 128.04, 127.53, 127.43, 127.14, 125.94, 121.68, 116.48, 115.47, 40.38, 40.22, 34.27, and 20.57.

DEPT-135 NMR (101 MHz, CDCl₃) δ: (aromatic C-H): 148.12, 136.10, 129.57, 128.25, 128.20, 127.33, 127.24, 126.94, 125.74, 121.47, 116.28; (C=CH₂): 115.27; (CH₂): 40.18, 40.02, 34.08; and (CH₃) 20.37.

HRMS (ESI): [M-Na]⁺ calculated for C₂₈H₂₆N₂NaO: 429.1937, found: 429.1938.



(Scheme 2, entry 3s)

Rf: 0.5 (eluent: 10% EtOAc/90% hexane)

Isolation: Silica gel column (eluent: 5% EtOAc/95% hexane)

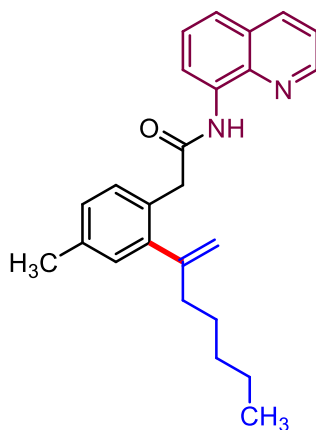
Appearance: liquid

Yield: 62%

¹H NMR (500 MHz, CDCl₃) δ: 9.82 (s, 1H), 8.72 (dd, *J* = 7.2, 1.7 Hz, 1H), 8.69 (dt, *J* = 4.3, 2.1 Hz, 1H), 8.12 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.53 – 7.47 (m, 1H), 7.43 – 7.37 (m, 2H), 7.32 – 7.27 (m, 2H), 7.19 (d, *J* = 2.2 Hz, 1H), 5.26 (d, *J* = 1.4 Hz, 1H), 5.01 (s, 1H), 3.86 (s, 2H), 2.34 – 2.27 (m, 2H), 1.44 – 1.34 (m, 2H), 1.23 – 1.14 (m, 4H), 0.78 (t, *J* = 7.0 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃) δ: 169.64, 148.37, 145.84, 138.59, 136.43, 134.49, 133.08, 132.16, 130.44, 129.07, 128.64, 128.05, 127.65, 127.53, 121.83, 121.77, 116.50, 115.74, 42.15, 38.34, 31.71, 27.49, 22.60, 14.15.

HRMS (ESI): [M-H]⁺ calculated for C₂₄H₂₆ClN₂O: 393.1728, found: 393.1729.



(Scheme 2, entry 3t)

Rf: 0.55 (eluent: 10% EtOAc/90% hexane)

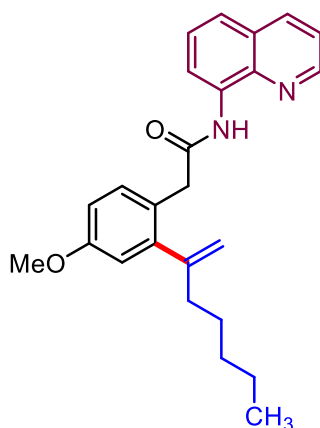
Isolation: Silica gel column (eluent: 4% EtOAc/96% hexane)

Appearance: liquid

Yield: 70%

¹H NMR (500 MHz, CDCl₃) δ: 9.83 (s, 1H), 8.74 (dt, *J* = 9.0, 4.5 Hz, 1H), 8.67 – 8.63 (m, 1H), 8.10 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.52 – 7.44 (m, 2H), 7.38 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.35 (d, *J* = 7.8 Hz, 1H), 7.14 (d, *J* = 7.8 Hz, 1H), 7.01 (s, 1H), 5.22 (t, *J* = 4.8 Hz, 1H), 4.98 (d, *J* = 0.8 Hz, 1H), 3.87 (s, 2H), 2.37 (s, 3H), 2.35 – 2.29 (m, 2H), 1.40 (ddd, *J* = 15.4, 9.3, 5.8 Hz, 2H), 1.21 – 1.14 (m, 4H), 0.78 (t, *J* = 7.0 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃) δ: 170.54, 149.62, 148.24, 144.06, 138.67, 136.94, 136.33, 134.71, 130.69, 129.79, 128.72, 128.37, 128.03, 127.55, 121.65, 121.60, 116.44, 114.73, 42.51, 38.62, 31.80, 29.91, 27.57, 22.64, 21.34, and 14.18.



(Scheme 2, entry 3u)

Rf: 0.3 (eluent: 10% EtOAc/90% hexane)

Isolation: Silica gel column (eluent: 5% EtOAc/95% hexane)

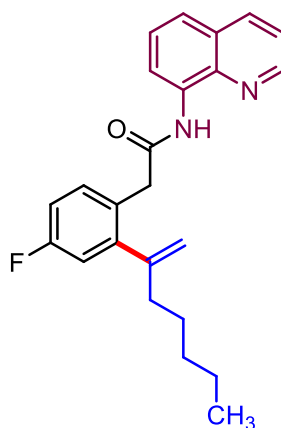
Appearance: semi solid

Yield: 73%

¹H NMR (500 MHz, CDCl₃) δ: 9.85 (s, 1H), 8.77 – 8.74 (m, 1H), 8.66 (dd, *J* = 4.1, 1.4 Hz, 1H), 8.12 (d, *J* = 7.9 Hz, 1H), 7.55 – 7.45 (m, 2H), 7.41 – 7.36 (m, 2H), 6.88 (dd, *J* = 8.5, 2.8 Hz, 1H), 6.74 (d, *J* = 2.7 Hz, 1H), 5.22 (d, *J* = 1.5 Hz, 1H), 5.00 (d, *J* = 0.6 Hz, 1H), 3.84 (d, *J* = 2.8 Hz, 5H), 2.35 – 2.29 (m, 2H), 1.41 – 1.38 (m, 1H), 1.20 – 1.13 (m, 4H), 0.76 (t, *J* = 5.9 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃) δ: 170.68, 158.67, 149.38, 148.09, 145.43, 134.54, 133.59, 131.87, 130.75, 128.02, 127.57, 123.93, 121.60, 121.58, 114.86, 114.69, 112.96, 77.16, 55.48, 42.02, 38.42, 31.71, 29.84, 27.51, 22.56, 14.11.

HRMS (ESI): [M-H]⁺ calculated for C₂₅H₂₈N₂O₂: 388.2010, found: 388.2005.



(Scheme 2, entry 3v)

Rf: 0.5 (eluent: 10% EtOAc/90% hexane)

Isolation: Silica gel column (eluent: 5% EtOAc/95% hexane)

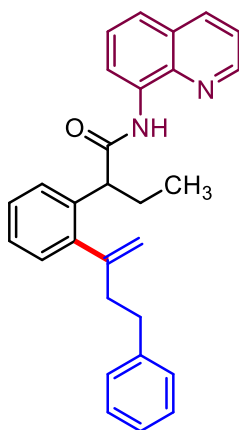
Appearance: liquid

Yield: 55%

¹H NMR (500 MHz, CDCl₃) δ: 9.82 (s, 1H), 8.73 (dd, *J* = 7.3, 1.4 Hz, 1H), 8.67 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.12 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.52 – 7.46 (m, 2H), 7.43 – 7.38 (m, 2H), 7.06 – 7.00 (m, 1H), 6.92 (dd, *J* = 9.5, 2.7 Hz, 1H), 5.26 (d, *J* = 1.4 Hz, 1H), 5.01

(s, 1H), 3.87 (s, 2H), 2.33 – 2.28 (m, 2H), 1.41 (d, $J = 10.6$ Hz, 1H), 1.36 (d, $J = 7.6$ Hz, 1H), 1.23 – 1.12 (m, 4H), 0.77 (t, $J = 7.0$ Hz, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ : 170.01, 161.94 (d, $J = 246.9$ Hz), 148.77, 148.54, 148.33, 146.24, 146.18, 138.60, 136.42, 134.51, 132.49, 132.42, 128.50, 128.05, 127.64, 127.53, 127.44, 122.10, 121.79, 121.74, 116.67, 116.47, 116.00, 115.83, 115.57, 115.43, 115.26, 114.57, 114.41, 42.03, 38.32, 31.71, 27.51, 22.59, and 14.14.



(Scheme 3, entry 3w)

Rf: 0.5 (eluent: 10% EtOAc/90% hexane)

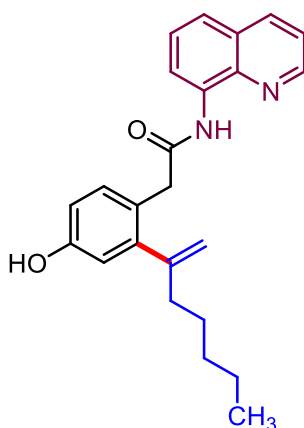
Isolation: Silica gel column (eluent: 5% EtOAc/95% hexane)

Appearance: white solid

Yield: 54%

^1H NMR (400 MHz, CDCl_3) δ : 9.88 (s, 1H), 8.77 (dd, $J = 7.5, 1.5$ Hz, 1H), 8.55 (dd, $J = 4.2, 1.5$ Hz, 1H), 8.09 (dd, $J = 8.3, 1.7$ Hz, 1H), 7.61 (dd, $J = 7.9, 1.1$ Hz, 1H), 7.52 – 7.43 (m, 2H), 7.35 (dd, $J = 8.3, 4.2$ Hz, 1H), 7.30 (td, $J = 7.6, 1.5$ Hz, 1H), 7.25 – 7.20 (m, 3H), 7.16 (ddd, $J = 7.6, 4.0, 1.7$ Hz, 4H), 5.50 (d, $J = 1.5$ Hz, 1H), 5.19 (s, 1H), 3.92 (dd, $J = 8.0, 7.0$ Hz, 1H), 2.91 – 2.84 (m, 2H), 2.76 (dd, $J = 9.9, 5.7$ Hz, 2H), 2.44 – 2.30 (m, 1H), 1.93 – 1.81 (m, 1H), 0.98 (t, $J = 7.4$ Hz, 3H).

^{13}C NMR (101 MHz, CDCl_3) δ : 172.59, 149.18, 148.20, 143.23, 141.93, 138.61, 137.16, 136.34, 134.91, 129.05, 128.55, 128.04, 127.95, 127.56, 127.35, 126.85, 126.09, 121.66, 121.49, 116.45, 115.98, 51.82, 40.91, 34.43, 27.33, and 12.91.



(Scheme 2, entry 3x)

Rf: 0.4 (eluent: 10% EtOAc/90% hexane)

Isolation: Silica gel column (eluent: 6% EtOAc/94% hexane)

Appearance: liquid

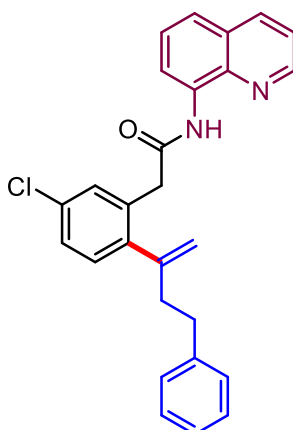
Yield: 43%

¹H NMR (400 MHz, CDCl₃) δ: 9.87 (s, 1H), 8.74 (dd, *J* = 7.1, 1.8 Hz, 1H), 8.68 – 8.64 (m, 1H), 8.10 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.52 – 7.45 (m, 2H), 7.38 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.26 (s, 1H), 6.78 (dd, *J* = 8.3, 2.7 Hz, 1H), 6.70 (d, *J* = 2.7 Hz, 1H), 5.19 (d, *J* = 1.6 Hz, 1H), 4.99 – 4.94 (m, 1H), 3.82 (d, *J* = 7.0 Hz, 2H), 2.31 – 2.22 (m, 2H), 1.36 (tt, *J* = 20.3, 10.1 Hz, 2H), 1.19 – 1.07 (m, 4H), 0.74 (t, *J* = 7.1 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃) δ: 171.23, 155.29, 149.26, 148.37, 145.65, 138.67, 136.39, 134.49, 132.12, 128.06, 127.52, 123.41, 121.85, 121.70, 116.64, 116.12, 114.87, 114.83, 63.90, 42.09, 38.41, 31.76, 27.58, 22.60, and 14.15.

HRMS (ESI): [M-H]⁺ calculated for C₂₄H₂₇N₂O₂: 375.2067, found: 375.2071.

X-ray: CCDC 1841319



(Scheme 2, entry 3y)

Rf: 0.45 (eluent: 10% EtOAc/90% hexane)

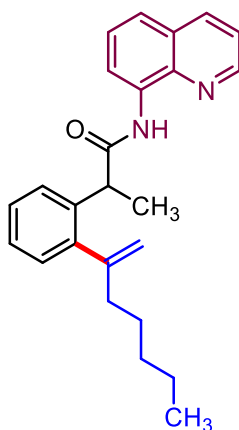
Isolation: Silica gel column (eluent: 6% EtOAc/94% hexane)

Appearance: brown sticky liquid

Yield: 49%

¹H NMR (500 MHz, CDCl₃) δ: 9.87 (s, 1H), 8.73 (dd, *J* = 7.1, 1.8 Hz, 1H), 8.68 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.12 (dt, *J* = 11.2, 5.6 Hz, 1H), 7.54 – 7.48 (m, 3H), 7.41 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.29 (dd, *J* = 8.2, 2.2 Hz, 1H), 7.19 (dd, *J* = 10.0, 4.5 Hz, 2H), 7.15 – 7.11 (m, 2H), 7.06 – 7.04 (m, 2H), 5.34 (d, *J* = 1.4 Hz, 1H), 5.06 (s, 1H), 3.85 (s, 2H), 2.75 – 2.70 (m, 2H), 2.69 – 2.63 (m, 2H).

¹³C NMR (126 MHz, CDCl₃) δ: 169.24, 148.43, 147.51, 142.05, 141.55, 138.63, 136.45, 134.46, 133.91, 133.35, 130.83, 130.43, 128.50, 128.46, 128.08, 127.60, 127.56, 126.09, 121.89, 121.81, 116.58, 116.44, 42.50, 39.96, and 34.16.



(Scheme 2, entry 3z)

Rf: 0.55 (eluent: 10% EtOAc/90% hexane)

Isolation: Silica gel column (eluent: 4% EtOAc/96% hexane)

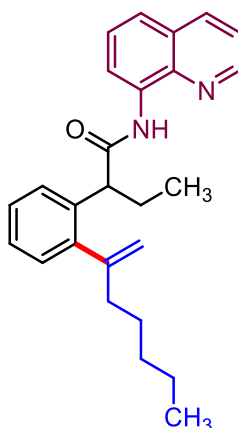
Appearance: solid

Yield: 58%

¹H NMR (500 MHz, CDCl₃) δ: 9.81 (s, 1H), 8.74 (d, *J* = 7.6 Hz, 1H), 8.66 (d, *J* = 2.9 Hz, 1H), 8.10 (d, *J* = 8.0 Hz, 1H), 7.56 – 7.47 (m, 2H), 7.44 (d, *J* = 8.0 Hz, 1H), 7.38 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.28 (t, *J* = 7.6 Hz, 1H), 7.22 (t, *J* = 7.4 Hz, 1H), 7.15 (d, *J* = 7.5 Hz, 1H), 5.38 (s, 1H), 5.17 (s, 1H), 4.19 (q, *J* = 7.0 Hz, 1H), 2.48 – 2.35 (m, 2H), 1.62 (d, *J* = 6.9 Hz, 5H), 1.52 (dt, *J* = 15.2, 7.6 Hz, 2H), 1.29 (ddd, *J* = 18.1, 12.7, 5.1 Hz, 5H), 0.85 (t, *J* = 7.0 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃) δ: 173.40, 149.99, 148.05, 143.30, 138.54, 136.43, 134.90, 129.05, 128.05, 127.87, 127.59, 127.26, 126.87, 121.64, 121.44, 116.41, 115.12, 44.11, 39.21, 31.84, 27.63, 22.72, 19.34, and 14.25.

HRMS (ESI): [M-Na]⁺ calculated for C₂₅H₂₈N₂NaO: 395.2094, found: 395.2087.



(Scheme 2, entry 3aa)

Rf: 0.55 (eluent: 10% EtOAc/90% hexane)

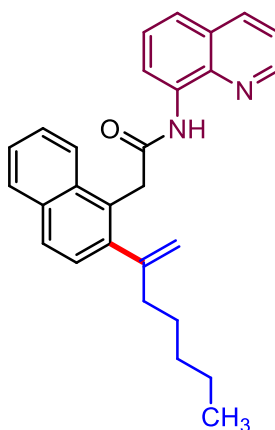
Isolation: Silica gel column (eluent: 4% EtOAc/96% hexane)

Appearance: solid

Yield: 59%

¹H NMR (500 MHz, CDCl₃) δ: 9.87 (s, 1H), 8.77 (dd, *J* = 7.6, 1.2 Hz, 1H), 8.71 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.10 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.61 – 7.58 (m, 1H), 7.51 – 7.43 (m, 2H), 7.39 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.28 (td, *J* = 7.7, 1.3 Hz, 1H), 7.20 (td, *J* = 7.5, 1.2 Hz, 1H), 7.12 (dd, *J* = 7.6, 1.2 Hz, 1H), 5.42 (d, *J* = 1.4 Hz, 1H), 5.14 (s, 1H), 3.92 (t, *J* = 7.5 Hz, 1H), 2.44 – 2.33 (m, 3H), 1.91 – 1.81 (m, 1H), 1.57 – 1.48 (m, 2H), 1.38 – 1.27 (m, 4H), 1.02 – 0.95 (m, 3H), 0.85 (t, *J* = 7.0 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃) δ: 172.73, 150.05, 148.10, 143.74, 138.64, 137.03, 136.37, 134.95, 129.01, 128.05, 127.74, 127.56, 127.23, 126.72, 121.66, 121.46, 116.46, 115.30, 51.75, 39.29, 31.86, 27.60, 27.26, 22.74, 14.25, 12.88.



(Scheme 2, entry 3ab)

Rf: 0.5 (eluent: 10% EtOAc/90% hexane)

Isolation: Silica gel column (eluent: 5% EtOAc/95% hexane)

Appearance: liquid

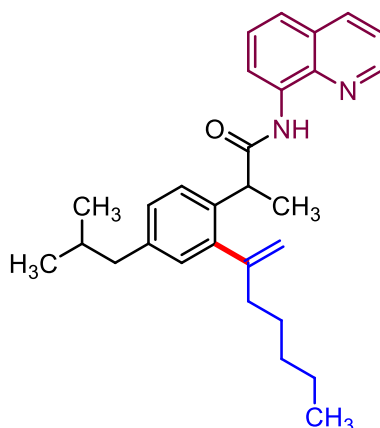
Yield: 47%

¹H NMR (400 MHz, CDCl₃) δ: 9.82 (s, 1H), 8.73 (dt, *J* = 4.8, 2.4 Hz, 1H), 8.48 – 8.43 (m, 1H), 8.14 (d, *J* = 8.6 Hz, 1H), 8.04 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.85 (dd, *J* = 10.7, 8.5

Hz, 2H), 7.54 – 7.37 (m, 5H), 7.30 (dd, $J = 8.3, 4.2$ Hz, 1H), 5.36 (d, $J = 1.6$ Hz, 1H), 5.27 – 5.24 (m, 1H), 4.40 (s, 2H), 2.47 – 2.42 (m, 2H), 1.47 (dt, $J = 11.2, 7.5$ Hz, 2H), 1.31 – 1.17 (m, 4H), 0.80 (t, $J = 7.1$ Hz, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ : 170.38, 150.20, 147.89, 142.68, 136.53, 136.51, 136.43, 134.52, 133.16, 133.01, 128.73, 128.00, 127.97, 127.57, 127.28, 127.14, 127.01, 125.77, 124.65, 121.62, 121.53, 115.45, 39.91, 38.98, 31.85, 27.60, 22.67, and 14.19.

HRMS (ESI): $[\text{M}-\text{H}]^+$ calculated for $\text{C}_{28}\text{H}_{29}\text{N}_2\text{O}$: 409.2274, found: 409.2275.



(Scheme 2, entry 3ac)

R_f: 0.55 (eluent: 10% EtOAc/90% hexane)

Isolation: Silica gel column (eluent: 4% EtOAc/96% hexane)

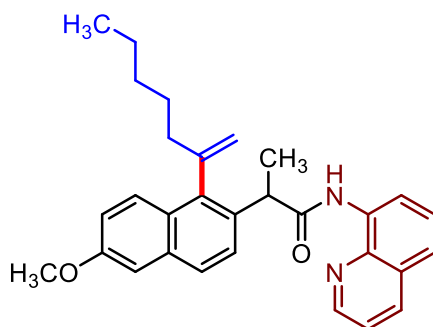
Appearance: solid

Yield: 54%

^1H NMR (400 MHz, CDCl_3) δ : 9.79 (s, 1H), 8.75 (dt, $J = 8.7, 4.3$ Hz, 1H), 8.61 (dd, $J = 4.2, 1.7$ Hz, 1H), 8.08 (dd, $J = 8.3, 1.6$ Hz, 1H), 7.49 (dd, $J = 10.3, 5.5$ Hz, 1H), 7.44 – 7.41 (m, 2H), 7.36 (dd, $J = 8.3, 4.2$ Hz, 1H), 7.08 (dd, $J = 8.0, 1.8$ Hz, 1H), 6.93 (d, $J = 1.8$ Hz, 1H), 5.34 (d, $J = 1.7$ Hz, 1H), 5.13 (d, $J = 1.8$ Hz, 1H), 4.15 (q, $J = 7.1$ Hz, 1H), 2.45 (d, $J = 7.2$ Hz, 2H), 2.40 (td, $J = 7.3, 3.5$ Hz, 2H), 1.86 (dp, $J = 13.5, 6.8$ Hz, 1H), 1.61 (d, $J = 7.2$ Hz, 3H), 1.53 – 1.44 (m, 2H), 1.33 – 1.21 (m, 4H), 0.91 (d, $J = 6.6$ Hz, 6H), 0.83 (t, $J = 7.1$ Hz, 3H).

^{13}C NMR (101 MHz, CDCl_3) δ : 173.74, 150.21, 148.05, 143.05, 140.27, 138.69, 136.28, 135.64, 135.01, 129.79, 128.69, 128.04, 127.56, 127.01, 121.61, 121.35, 116.27, 114.85, 45.22, 43.91, 39.22, 31.81, 30.40, 27.64, 22.70, 22.58, 19.26, and 14.20.

HRMS (ESI): $[\text{M}-\text{H}]^+$ calculated for $\text{C}_{29}\text{H}_{37}\text{N}_2\text{O}$: 429.2900, found: 429.2900.



(Scheme 2, entry 3ad)

Rf: 0.55 (eluent: 10% EtOAc/90% hexane)

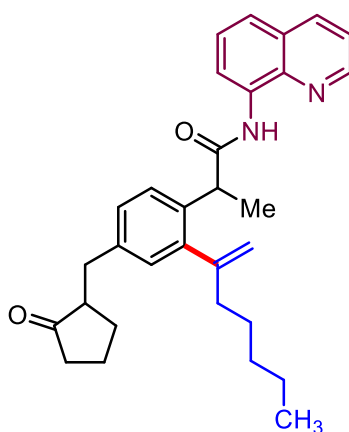
Isolation: Silica gel column (eluent: 5% EtOAc/95% hexane)

Yield: 53%

¹H NMR (400 MHz, CDCl₃) δ: 9.86 (s, 1H), 8.73 (dd, *J* = 7.5, 1.3 Hz, 1H), 8.60 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.07 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.97 (d, *J* = 11.5 Hz, 2H), 7.75 (d, *J* = 9.0 Hz, 1H), 7.52 – 7.40 (m, 2H), 7.36 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.25 (t, *J* = 4.5 Hz, 2H), 5.49 (d, *J* = 1.4 Hz, 1H), 5.29 (s, 1H), 4.26 (q, *J* = 7.0 Hz, 1H), 4.01 (s, 3H), 2.57 – 2.43 (m, 2H), 1.71 (d, *J* = 7.0 Hz, 3H), 1.56 (dd, *J* = 15.2, 7.6 Hz, 2H), 1.38 – 1.27 (m, 4H), 0.85 (t, *J* = 7.1 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃) δ: 173.27, 152.86, 150, 148.16, 143.44, 138.60, 136.41, 136.03, 134.87, 130.90, 129.25, 128.12, 128.06, 127.55, 126.59, 123.34, 121.71, 121.56, 116.61, 116.41, 115.89, 113.95, 57.24, 44.04, 39.20, 31.82, 27.65, 22.75, 19.81, and 14.28.

DEPT-135 (126 MHz, CDCl₃) δ: (aromatic C-H): 147.93, 136.18, 127.89, 127.32, 126.36, 123.11, 121.48, 121.33, 116.17; (C=CH₂): 115.65; (aromatic C-H): 113.72; (-OCH₃): 57.00; (*sp*³-C-H): 43.80; (CH₂): 38.97, 31.59, 27.42; 22.51; (CH-CH₃): 19.58; and (CH₂-CH₃): 14.05.



(Scheme 2, entry 3ae)

Rf: 0.15 (eluent: 10% EtOAc/hexane)

Isolation: Silica gel column (eluent: 8% EtOAc/hexane)

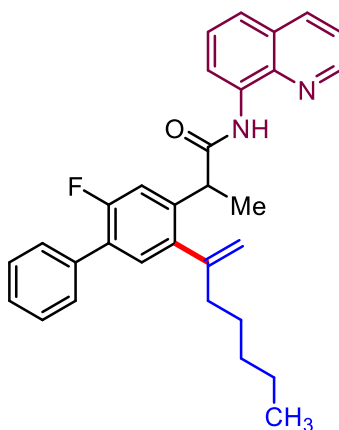
Appearance: liquid

Yield: 62%

¹H NMR (500 MHz, CDCl₃) δ 9.78 (s, 1H), 8.74 (d, *J* = 7.4 Hz, 2H), 8.65 (d, *J* = 3.6 Hz, 2H), 8.09 (dd, *J* = 8.3, 1.4 Hz, 2H), 7.49 – 7.42 (m, 5H), 7.38 (dd, *J* = 8.3, 4.2 Hz, 2H), 7.09 (d, *J* = 8.7 Hz, 2H), 6.94 (s, 1H), 5.84 (s, 2H), 5.80 (s, 2H), 5.36 (s, 2H), 5.14 (s, 2H), 4.14 (q, *J* = 7.0 Hz, 2H), 3.13 (dd, *J* = 13.8, 3.8 Hz, 2H), 2.22 (q, *J* = 6.9 Hz, 6H), 1.59 (t, *J* = 7.4 Hz, 7H), 1.34 – 1.28 (m, 21H), 0.87 (dd, *J* = 9.5, 4.8 Hz, 12H).

¹³C NMR (126 MHz, CDCl₃) δ 220.49, 220.47, 173.51, 171.86, 152.55, 149.94, 148.03, 143.38, 138.66, 138.59, 138.56, 136.36, 134.93, 129.46, 129.43, 128.42, 128.37, 128.05, 127.58, 127.37, 127.34, 121.64, 121.43, 120.80, 116.36, 115.09, 115.04, 51.22, 51.15, 43.85, 39.18, 39.15, 38.40, 38.38, 35.41, 32.47, 32.13, 31.80, 31.49, 29.90, 29.56, 29.42, 29.41, 27.75, 27.63, 22.89, 22.71, 22.61, 20.74, 19.30, 14.31, 14.21, 14.13, 1.22.

HRMS (ESI): [M+H]⁺ calculated for C₃₁H₃₇N₂O₂: 469.2850, found: 469.2849.



(Scheme 2, entry 3af)

Rf: 0.3 (eluent: 10% EtOAc/hexane)

Isolation: Silica gel column (eluent: 5% EtOAc/hexane)

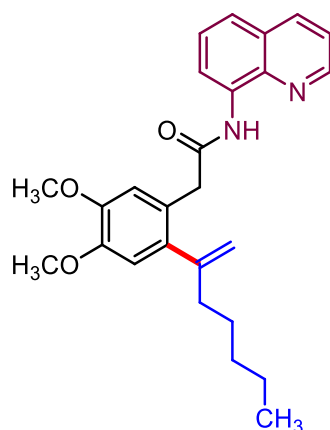
Appearance: liquid

Yield: 59%

¹H NMR (400 MHz, CDCl₃) δ 9.89 (s, 1H), 8.80 – 8.67 (m, 2H), 8.12 (d, *J* = 8.0 Hz, 1H), 7.57 – 7.51 (m, 3H), 7.51 – 7.46 (m, 1H), 7.42 (d, *J* = 7.2 Hz, 2H), 7.39 – 7.35 (m, 2H), 7.22 (d, *J* = 7.9 Hz, 1H), 5.42 (s, 1H), 5.21 (s, 1H), 4.19 (d, *J* = 6.6 Hz, 1H), 2.42 (d, *J* = 6.9 Hz, 2H), 1.68 – 1.62 (m, 4H), 1.58 – 1.49 (m, 3H), 1.29 (s, 5H), 0.89 – 0.83 (m, 4H).

¹³C NMR (101 MHz, CDCl₃) δ 172.6, 159.2 (d, ¹*J*_{FC} = 248.46 Hz), 149.0, 148.2, 139.9, 139.8, 139.4, 138.6, 138.5, 136.5, 136.4, 135.7, 134.8, 134.7, 131.0 (d, ³*J*_{FC} = 4.0 Hz), 129.2 (d, ⁴*J*_{FC} = 3.0 Hz), 128.6, 127.8, 127.6, 127.6, 121.7, 121.6, 116.5, 115.8, 115.59, 114.8 (d, ²*J*_{FC} = 24.2 Hz), 44.1, 39.2, 31.8, 29.9, 27.6, 22.7, 19.4, 14.2.

HRMS (ESI): [M+Na]⁺ calculated for C₃₁H₃₁N₂OFNa: 489.2313, found: 489.2309.



(Scheme 2, entry 3ag)

Rf: 0.45 (eluent: 10% EtOAc/90% hexane)

Isolation: Silica gel column (eluent: 5% EtOAc/95% hexane)

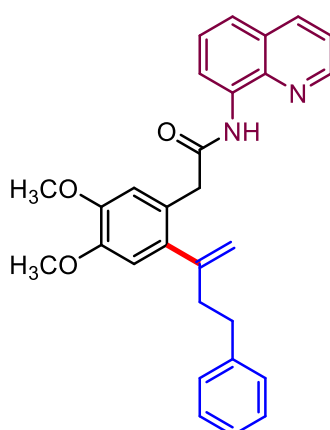
Appearance: liquid

Yield: 78%

¹H NMR (500 MHz, CDCl₃) δ: 9.89 (s, 1H), 8.73 (dt, *J* = 8.4, 4.2 Hz, 1H), 8.66 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.11 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.48 (ddd, *J* = 10.1, 8.2, 4.7 Hz, 2H), 7.39 (dd, *J* = 8.3, 4.2 Hz, 1H), 6.95 (d, *J* = 13.8 Hz, 1H), 6.71 (s, 1H), 5.24 (d, *J* = 1.5 Hz, 1H), 5.01 (d, *J* = 1.5 Hz, 1H), 3.91 (s, 3H), 3.90 (s, 3H), 3.84 (s, 2H), 2.35 – 2.29 (m, 2H), 1.43 – 1.36 (m, 2H), 1.22 – 1.13 (m, 4H), 0.78 (t, *J* = 7.0 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃) δ: 170.53, 149.25, 148.35, 148.30, 148.08, 138.73, 136.70, 136.36, 134.68, 128.07, 127.53, 123.83, 121.70, 116.48, 115.17, 113.41, 112.21, 56.20, 56.19, 42.59, 38.80, 31.79, 27.62, 22.65, and 14.18.

HRMS (ESI): [M-H]⁺ calculated for C₂₆H₃₁N₂O₃: 419.2329, found: 419.2328.



(Scheme 2, entry 3ah)

Rf: 0.4 (eluent: 10% EtOAc/90% hexane)

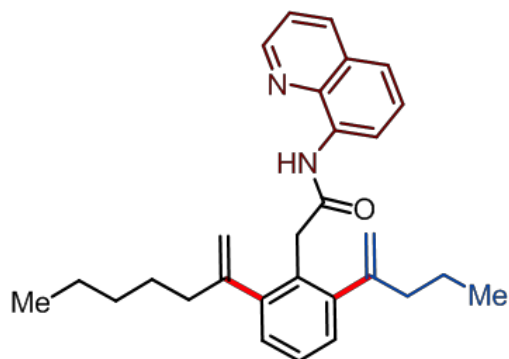
Isolation: Silica gel column (eluent: 6% EtOAc/94% hexane)

Appearance: yellow liquid

Yield: 63%

¹H NMR (500 MHz, CDCl₃) δ: 9.90 (s, 1H), 8.75 (d, *J* = 7.3 Hz, 1H), 8.63 (d, *J* = 2.9 Hz, 1H), 8.16 – 8.03 (m, 1H), 7.50 (dt, *J* = 16.1, 7.9 Hz, 2H), 7.38 (dd, *J* = 8.0, 4.0 Hz, 1H), 7.15 (dt, *J* = 29.6, 7.0 Hz, 3H), 7.06 (d, *J* = 7.3 Hz, 2H), 6.98 (s, 1H), 6.69 (s, 1H), 5.33 (s, 1H), 5.07 (s, 1H), 3.92 (s, 3H), 3.89 (s, 3H), 3.83 (s, 2H), 2.74 (d, *J* = 8.4 Hz, 2H), 2.69 (d, *J* = 8.4 Hz, 2H).

¹³C NMR (126 MHz, CDCl₃) δ: 170.43, 148.47, 148.34, 148.31, 148.14, 141.80, 138.71, 136.38, 136.16, 134.65, 128.49, 128.45, 128.08, 127.54, 126.02, 123.95, 121.72, 116.52, 115.92, 113.51, 112.17, 56.20, 42.60, 40.17, and 34.31.



(Scheme 3, entry 4a)

Rf: 0.6 (eluent:10% EtOAc/90% hexane)

Isolation: Silica gel column (eluent: 5% EtOAc/hexane)

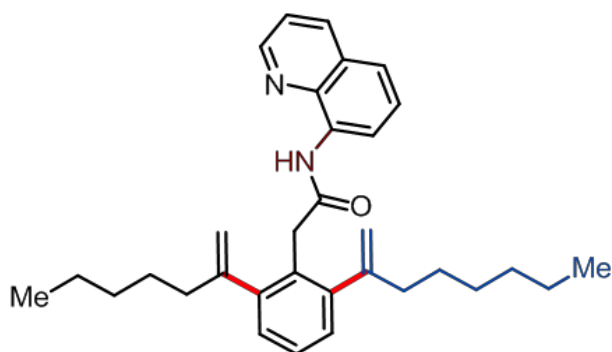
Appearance: liquid

Yield: 56%

Synthesized by following General rocedure A

¹H NMR (400 MHz, CDCl₃) δ 9.69 (s, 1H), 8.70 (dd, *J* = 7.4, 1.3 Hz, 1H), 8.57 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.09 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.49 – 7.43 (m, 2H), 7.36 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.30 (d, *J* = 7.7 Hz, 1H), 7.11 (d, *J* = 7.6 Hz, 2H), 5.15 – 5.14 (2H), 4.98 (2H), 3.93 (s, 2H), 2.33 – 2.25 (m, 4H), 1.41 – 1.34 (m, 4H), 1.15 – 1.12 (m, 4H), 0.74 (t, *J* = 7.1 Hz, 6H).

¹³C NMR (101 MHz, CDCl₃) δ 170.6, 149.9, 148.1, 145.2, 136.2, 134.6, 128.5, 128.0, 127.9, 127.5, 127.0, 121.5, 121.4, 116.2, 114.8, 40.2, 38.4, 31.7, 27.5, 22.6, 14.0.



(Scheme 3, entry 4b)

Rf: 0.6 (eluent:10% EtOAc/90% hexane)

Isolation: Silica gel column (eluent: 5% EtOAc/hexane)

Appearance: liquid

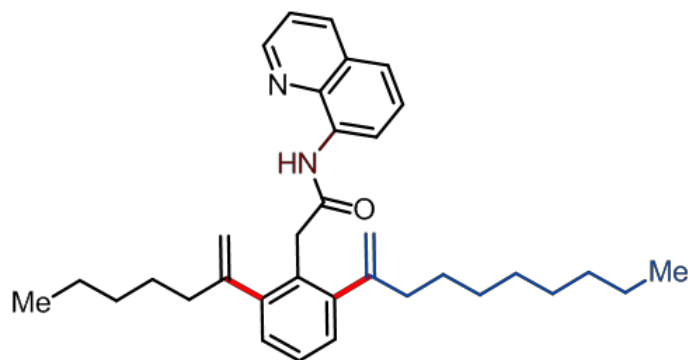
Yield: 52%

Synthesized by following General rocedure A

¹H NMR (500 MHz, CDCl₃) δ 9.69 (s, 1H), 8.70 (d, *J* = 7.5 Hz, 1H), 8.57 (dd, *J* = 4.1, 1.5 Hz, 1H), 8.09 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.49 – 7.43 (m, 2H), 7.36 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.29 (t, *J* = 7.6 Hz, 1H), 7.11 (d, *J* = 7.6 Hz, 2H), 5.15 – 5.14 (2H), 4.98 (s, 2H), 3.94 (s, 2H), 2.30 – 2.27 (m, 4H), 1.37 (dd, *J* = 15.2, 7.5 Hz, 4H), 1.17 – 1.11 (m, 8H), 1.06 (td, *J* = 8.6, 4.6 Hz, 2H), 0.75 (dd, *J* = 11.7, 4.7 Hz, 6H).

¹³C NMR (126 MHz, CDCl₃) δ 170.6, 149.9, 148.1, 145.2, 138.6, 136.2, 134.6, 128.5, 128.0, 127.9, 127.5, 127.0, 121.5, 121.4, 116.2, 114.8, 40.2, 38.5, 38.4, 31.8, 31.7, 27.8, 27.5, 22.7, 22.6, 14.2, 14.1.

HRMS (ESI): [M-Na]⁺ calculated for C₃₂H₄₀N₂NaO: 491.3033, found: 491.3030.



(Scheme 3, entry 4c)

Rf: 0.65 (eluent:10% EtOAc/90% hexane)

Isolation: Silica gel column (eluent:3% EtOAc/hexane)

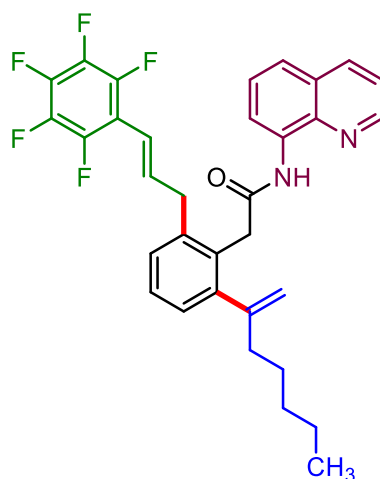
Appearance: liquid

Yield: 61% **Synthesized by following General rocedure A**

¹H NMR (500 MHz, CDCl₃) δ 9.69 (s, 1H), 8.70 (d, *J* = 7.5 Hz, 1H), 8.57 (dd, *J* = 4.1, 1.5 Hz, 1H), 8.09 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.50 – 7.43 (m, 2H), 7.36 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.29 (t, *J* = 7.6 Hz, 1H), 7.11 (d, *J* = 7.6 Hz, 2H), 5.14 (s, 2H), 4.98 (s, 2H), 3.94 (s, 2H), 2.30 – 2.25 (m, 4H), 1.37 (dd, *J* = 14.9, 7.6 Hz, 6H), 1.15 – 1.09 (m, 10H), 0.88 (s, 2H), 0.83 (d, *J* = 7.3 Hz, 3H), 0.74 (t, *J* = 6.9 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 170.6, 149.9, 149.8, 148.1, 145.2, 138.6, 136.2, 134.6, 128.5, 128.1, 128.0, 127.5, 127.0, 121.5, 121.4, 116.2, 114.8, 40.2, 38.5, 38.4, 31.9, 31.7, 29.6, 29.5, 29.3, 27.9, 27.5, 22.7, 22.5, 14.2, 14.1.

HRMS (ESI): [M-K]⁺ calculated for C₃₄H₄₄KN₂O: 535.3085, found: 535.3084.



(Scheme 3, entry 6a)

Rf: 0.35 (eluent: 10% EtOAc/hexane)

Isolation: Silica gel column (eluent: 5% EtOAc/hexane)

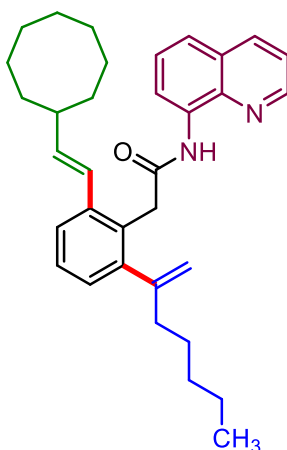
Appearance: liquid

Yield: 53%

Synthesized by following General rocedure B

¹H NMR (500 MHz, CDCl₃) δ 9.63 (s, 1H), 8.74 – 8.62 (m, 3H), 8.55 – 8.46 (m, 3H), 8.08 (dd, *J* = 8.3, 1.5 Hz, 3H), 7.52 – 7.44 (m, 5H), 7.35 – 7.29 (m, 4H), 7.17 – 7.12 (m, 3H), 6.87 – 6.76 (m, 3H), 6.06 (dd, *J* = 14.9, 7.5 Hz, 2H), 5.21 (s, 1H), 4.98 (s, 2H), 3.96 (s, 2H), 3.47 (d, *J* = 6.0 Hz, 4H), 2.33 – 2.27 (m, 5H), 1.37 (ddd, *J* = 25.0, 15.7, 7.0 Hz, 18H), 1.17 (dt, *J* = 9.3, 7.2 Hz, 11H), 0.74 (t, *J* = 7.0 Hz, 8H).

¹³C NMR (126 MHz, CDCl₃) δ 169.5, 149.7, 148.0, 145.2, 138.50 – 138.3 (m), 136.16, 134.45, 130.78, 129.2–129.1 (m), 128.74, 127.8, 127.6–127.5 (m), 125.9, 121.5, 116.4, 115.1, 40.0, 38.8, 32.1, 31.7, 29.9, 29.6, 27.5, 26.0, 22.9, 22.6, 14.3, 14.1.



(Scheme 3, entry 6b)

Rf: 0.4 (eluent: 10% EtOAc/hexane)

Isolation: Silica gel column (eluent: 5% EtOAc/hexane)

Appearance: liquid

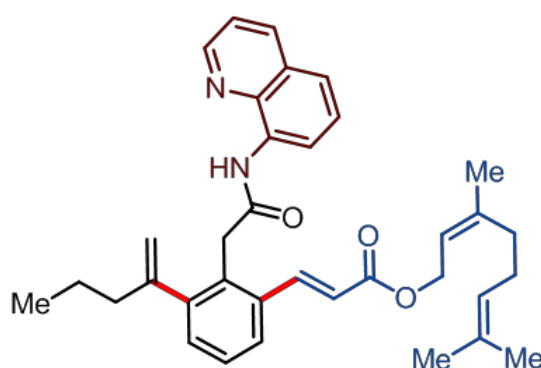
Yield: 49%

Synthesized by following General procedure B

¹H NMR (500 MHz, CDCl₃) δ 9.78 (s, 1H), 8.70 (dd, *J* = 7.1, 1.6 Hz, 1H), 8.64 (dd, *J* = 4.1, 1.4 Hz, 1H), 8.13 – 8.08 (m, 1H), 8.05 (s, 1H), 7.59 (d, *J* = 7.4 Hz, 1H), 7.48 (dd, *J* = 6.3, 4.5 Hz, 1H), 7.40 – 7.31 (m, 2H), 7.24 (d, *J* = 0.7 Hz, 1H), 6.38 (d, *J* = 15.7 Hz, 1H), 5.23 (s, 1H), 5.00 (s, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 4.08 (s, 2H), 2.34 – 2.28 (m, 2H), 1.49 – 1.11 (m, 17H), 0.93 – 0.86 (m, 2H), 0.76 (t, *J* = 5.7 Hz, 2H).

¹³C NMR (126 MHz, CDCl₃) δ 169.16, 166.80, 149.40, 148.23, 145.63, 142.44, 138.61, 136.37, 135.62, 134.51, 131.10, 130.82, 128.01, 127.71, 127.53, 126.19, 121.73, 121.67, 121.58, 116.63, 115.38, 60.68, 38.68, 31.74, 27.49, 22.62, 14.37, 14.15.

HRMS (ESI): [M+K]⁺ calculated for C₂₉H₃₂N₂O₃K: 495.2045, found: 495.2044.



(Scheme 3, entry 6c)

Rf: 0.40 (eluent: 10% EtOAc/90% hexane)

Isolation: Silica gel column (eluent: 5% EtOAc/hexane)

Appearance: liquid

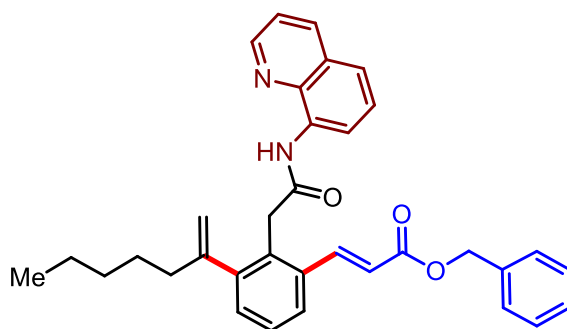
Yield: 69%

Synthesized by following General procedure A

¹H NMR (500 MHz, CDCl₃) δ 9.76 (s, 1H), 8.70 (d, *J* = 7.1 Hz, 1H), 8.64 (d, *J* = 2.8 Hz, 1H), 8.09 (dd, *J* = 21.1, 11.9 Hz, 2H), 7.57 (d, *J* = 7.8 Hz, 1H), 7.52 – 7.45 (m, 2H), 7.38 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.34 (t, *J* = 7.7 Hz, 1H), 7.23 (d, *J* = 7.4 Hz, 1H), 6.38 (d, *J* = 15.7 Hz, 1H), 5.32 (t, *J* = 6.9 Hz, 1H), 5.23 (s, 1H), 5.06 (t, *J* = 6.3 Hz, 1H), 5.00 (s, 1H), 4.60 (d, *J* = 7.1 Hz, 2H), 4.07 (s, 2H), 2.29 (t, *J* = 7.5 Hz, 2H), 2.08 – 2.01 (m, 4H), 1.71 (s, 3H), 1.64 (s, 3H), 1.56 (s, 3H), 1.44 (dd, *J* = 15.1, 7.5 Hz, 2H), 0.85 (t, *J* = 7.3 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 168.9, 166.7, 149.1, 148.2, 145.5, 142.6, 142.5, 138.6, 136.3, 135.6, 134.5, 132.3, 131.1, 130.8, 127.9, 127.6, 127.5, 126.1, 123.7, 121.6, 121.5, 119.3, 116.6, 115.5, 61.3, 40.7, 39.4, 32.3, 26.7, 25.8, 23.6, 20.9, 17.8, 13.9.

HRMS (ESI): [M-H]⁺ calculated for C₃₅H₄₁N₂O₃: 537.3112, found: 537.3112.



(Scheme 3, entry 6d)

Rf: 0.35 (eluent: 10% EtOAc/90% hexane)

Isolation: Silica gel column (eluent: 5% EtOAc/hexane)

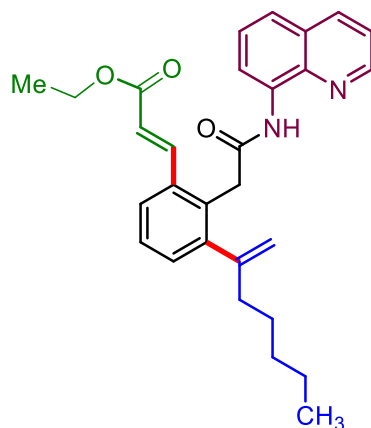
Appearance: white solid

Yield: 54%

Synthesized by following General procedure A

^1H NMR (400 MHz, CDCl_3) δ 9.76 (s, 1H), 8.70 (dd, J = 6.8, 2.2 Hz, 1H), 8.63 (dd, J = 4.2, 1.6 Hz, 1H), 8.17 – 8.08 (m, 2H), 7.59 (d, J = 6.9 Hz, 1H), 7.52 – 7.45 (m, 2H), 7.40 – 7.36 (m, 1H), 7.35 – 7.26 (m, 6H), 7.23 (dd, J = 7.6, 1.1 Hz, 1H), 6.43 (d, J = 15.7 Hz, 1H), 5.24 (d, J = 1.5 Hz, 1H), 5.16 (s, 2H), 5.01 (s, 1H), 4.07 (s, 2H), 2.31 (dd, J = 13.3, 5.8 Hz, 2H), 1.44 – 1.37 (m, 2H), 1.20 – 1.16 (m, 2H), 0.88 (dd, J = 8.6, 4.9 Hz, 2H), 0.76 (t, J = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, CDCl_3) δ 168.95, 166.49, 149.34, 148.17, 145.61, 143.01, 138.58, 136.30, 136.17, 135.47, 134.50, 131.15, 130.88, 128.62, 128.23, 128.21, 127.97, 127.66, 127.50, 126.13, 121.62, 121.06, 116.57, 115.36, 77.16, 66.37, 39.39, 38.63, 31.69, 29.85, 27.44, 22.57, 14.09



(Scheme 3, entry 6e)

Rf: 0.15 (eluent: 10% EtOAc/hexane)

Isolation: Silica gel column (eluent: 10% EtOAc/hexane)

Appearance: liquid

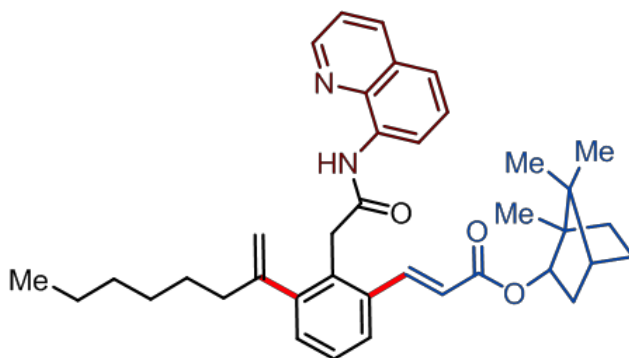
Yield: 65%

Synthesized by following General procedure A

^1H NMR (500 MHz, CDCl_3) δ 9.78 (s, 1H), 8.71 (dd, J = 6.9, 2.0 Hz, 1H), 8.64 (dd, J = 3.9, 1.3 Hz, 1H), 8.11 (dd, J = 8.3, 1.6 Hz, 1H), 8.07 (d, J = 15.7 Hz, 1H), 7.59 (d, J = 6.2 Hz, 1H),

7.49 (s, 1H), 7.47 (d, $J = 2.1$ Hz, 1H), 7.40 – 7.32 (m, 2H), 7.25 – 7.22 (m, 1H), 6.38 (d, $J = 15.7$ Hz, 1H), 5.23 (d, $J = 1.4$ Hz, 1H), 5.01 (s, 1H), 4.16 (q, $J = 7.1$ Hz, 2H), 4.08 (s, 2H), 2.34 – 2.28 (m, 2H), 1.39 (dt, $J = 7.4, 5.8$ Hz, 3H), 1.31 (dd, $J = 6.8, 3.5$ Hz, 2H), 1.27 – 1.20 (m, 6H), 0.76 (t, $J = 7.0$ Hz, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ 169.1, 166.8, 152.5, 149.4, 148.2, 145.6, 142.4, 138.6, 136.3, 135.6, 134.5, 131.1, 130.8, 128.0, 127.7, 127.5, 126.2, 121.7, 121.7, 121.6, 116.6, 115.4, 77.2, 60.7, 39.4, 38.7, 31.7, 31.5, 29.9, 27.5, 22.6, 14.4, 14.1.



(Scheme 3, entry 6f)

Rf: 0.5 (eluent: 10% EtOAc/90% hexane)

Isolation: Silica gel column (eluent: 5% EtOAc/hexane)

Appearance: liquid

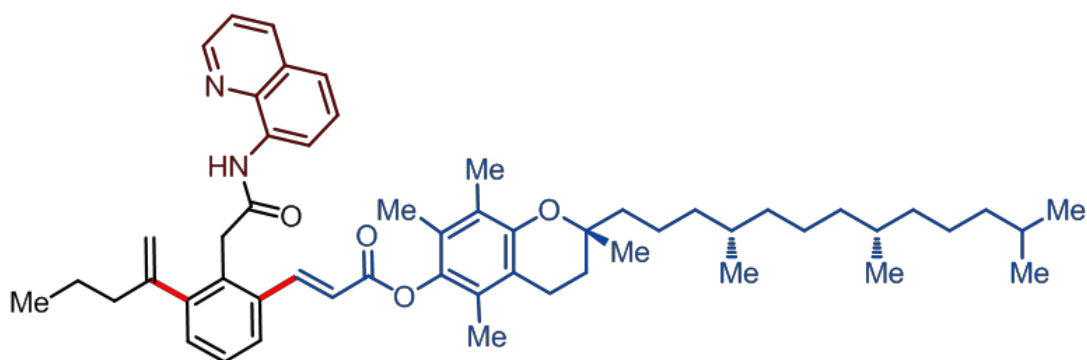
Yield: 46%

Synthesized by following General procedure A

^1H NMR (400 MHz, CDCl_3) δ 9.77 (s, 1H), 8.70 (td, $J = 6.7, 2.1$ Hz, 1H), 8.68 – 8.62 (m, 1H), 8.11 (dd, $J = 8.3, 1.6$ Hz, 1H), 7.99 (d, $J = 15.7$ Hz, 1H), 7.61 – 7.58 (m, 1H), 7.47 (dd, $J = 8.5, 6.5$ Hz, 2H), 7.40 – 7.36 (m, 1H), 7.33 (d, $J = 7.7$ Hz, 1H), 7.23 (dd, $J = 7.6, 1.1$ Hz, 1H), 6.34 (d, $J = 15.7$ Hz, 1H), 5.23 (s, 1H), 5.00 (s, 1H), 4.67 (dd, $J = 7.6, 3.8$ Hz, 1H), 4.06 (s, 2H), 2.32 (dd, $J = 16.2, 8.4$ Hz, 2H), 1.75 – 1.67 (m, 3H), 1.47 (d, $J = 3.8$ Hz, 2H), 1.39 (d, $J = 7.9$ Hz, 2H), 1.18 – 1.05 (m, 6H), 0.88 (s, 5H), 0.77 (t, $J = 6.9$ Hz, 3H), 0.69 (d, $J = 2.5$ Hz, 6H).

^{13}C NMR (101 MHz, CDCl_3) δ 168.8, 166.2, 149.4, 148.2, 145.6, 141.9, 138.6, 136.3, 135.6, 134.5, 130.9, 130.7, 127.9, 127.6, 127.5, 126.0, 122.1, 121.6, 116.6, 115.3, 81.2, 48.9, 47.0, 45.1, 39.4, 38.9, 38.7, 33.8, 31.8, 29.8, 29.2, 27.8, 27.4, 22.7, 20.1, 19.9, 14.1, 11.4.

HRMS (ESI): $[\text{M-K}]^+$ calculated for $\text{C}_{38}\text{H}_{46}\text{KN}_2\text{O}_3$: 617.3140, found: 617.3144.



(Scheme 3, entry 6g)

Rf: 0.5 (eluent: 10% EtOAc/90% hexane)

Isolation: Silica gel column (eluent: 5% EtOAc/hexane)

Appearance: liquid

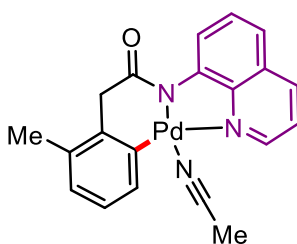
Yield: 73%

Synthesized by following General procedure A

¹H NMR (500 MHz, CDCl₃) δ 9.82 (s, 1H), 8.70 (d, *J* = 7.2 Hz, 1H), 8.62 (d, *J* = 2.8 Hz, 1H), 8.30 (d, *J* = 15.7 Hz, 1H), 8.09 (d, *J* = 8.2 Hz, 1H), 7.69 (d, *J* = 7.7 Hz, 1H), 7.51 – 7.44 (m, 2H), 7.41 – 7.33 (m, 2H), 7.28 (d, *J* = 7.6 Hz, 1H), 6.59 (d, *J* = 15.7 Hz, 1H), 5.27 (s, 1H), 5.05 (s, 1H), 4.13 (s, 2H), 2.51 (t, *J* = 6.5 Hz, 2H), 2.33 (t, *J* = 7.6 Hz, 2H), 2.02 (s, 3H), 1.85 (s, 3H), 1.81 (s, 3H), 1.58 – 1.43 (m, 8H), 1.43 – 1.33 (m, 6H), 1.26 (s, 3H), 1.21 (s, 3H), 1.15 – 1.11 (m, 3H), 0.89 – 0.83 (m, 20H).

¹³C NMR (126 MHz, CDCl₃) δ 168.9, 165.2, 149.4, 149.1, 148.1, 145.6, 143.7, 140.5, 138.5, 136.2, 135.3, 134.5, 131.4, 131.0, 127.9, 127.7, 127.4, 126.9, 126.1, 125.2, 122.9, 121.6, 121.5, 120.6, 117.3, 116.5, 115.6, 75.1, 40.8, 39.5, 37.6, 37.5, 37.5, 37.4, 32.93, 32.92, 32.87, 32.85, 28.1, 24.96, 24.95, 24.6, 22.9, 22.8, 20.9, 20.7, 19.9, 19.8, 13.9, 12.9, 12.1, 11.9.

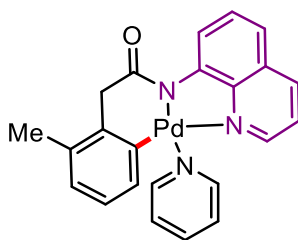
HRMS (ESI): [M-H]⁺ calculated for C₅₄H₇₃N₂O₄: 813.5565, found: 813.5551.



(Scheme 4, entry C2)

¹H NMR (500 MHz, CD₃CN) δ 8.67 (ddd, *J* = 8.9, 6.2, 1.3 Hz, 1H), 8.42 (dd, *J* = 8.4, 1.5 Hz, 1H), 7.56 (dd, *J* = 8.3, 4.7 Hz, 1H), 7.51 (d, *J* = 7.9 Hz, 1H), 7.43 (dd, *J* = 8.1, 1.1 Hz, 1H), 7.16 (d, *J* = 7.4 Hz, 1H), 6.81 (d, *J* = 7.1 Hz, 1H), 6.75 (t, *J* = 7.2 Hz, 1H), 3.92 (s, 1H), 2.30 (s, 2H), 1.95 (s, 1H).

¹³C NMR (126 MHz, CD₃CN) δ 175.01, 150.63, 148.33, 145.25, 144.10, 139.62, 134.86, 133.84, 130.47, 129.33, 127.50, 125.14, 123.19, 122.42, 119.87, 49.09, 21.19.



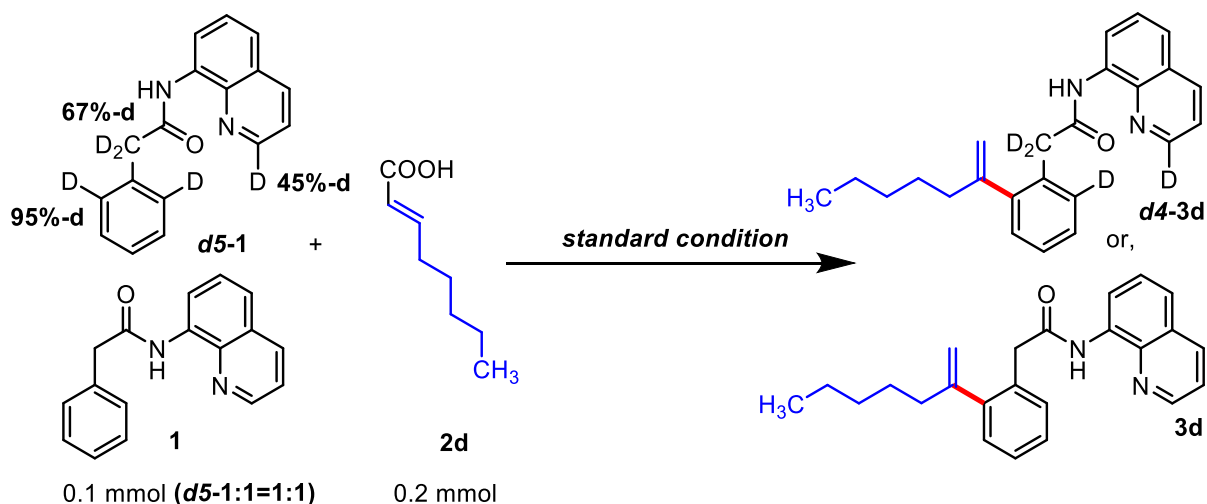
C3: complex formation with pyridine

^1H NMR (500 MHz, CDCl_3) δ 8.92 – 8.88 (m, 1H), 8.71 (t, J = 3.4 Hz, 1H), 8.23 (dd, J = 8.3, 1.5 Hz, 1H), 7.96 (tt, J = 7.8, 1.6 Hz, 1H), 7.61 (dd, J = 4.7, 1.5 Hz, 1H), 7.57 (t, J = 8.0 Hz, 1H), 7.51 (ddd, J = 7.7, 4.9, 1.4 Hz, 1H), 7.37 – 7.31 (m, 1H), 7.30 – 7.26 (m, 1H), 6.81 (d, J = 7.3 Hz, 1H), 6.57 (t, J = 7.0 Hz, 1H), 6.20 (d, J = 7.5 Hz, 1H), 4.23 (s, 1H), 2.42 (s, 2H).

^{13}C NMR (126 MHz, CDCl_3) δ 174.86, 153.26, 149.62, 147.65, 145.15, 144.37, 139.81, 138.47, 138.40, 133.60, 132.80, 129.41, 127.08, 126.16, 124.50, 124.32, 120.75, 118.79, 48.67, 21.73.

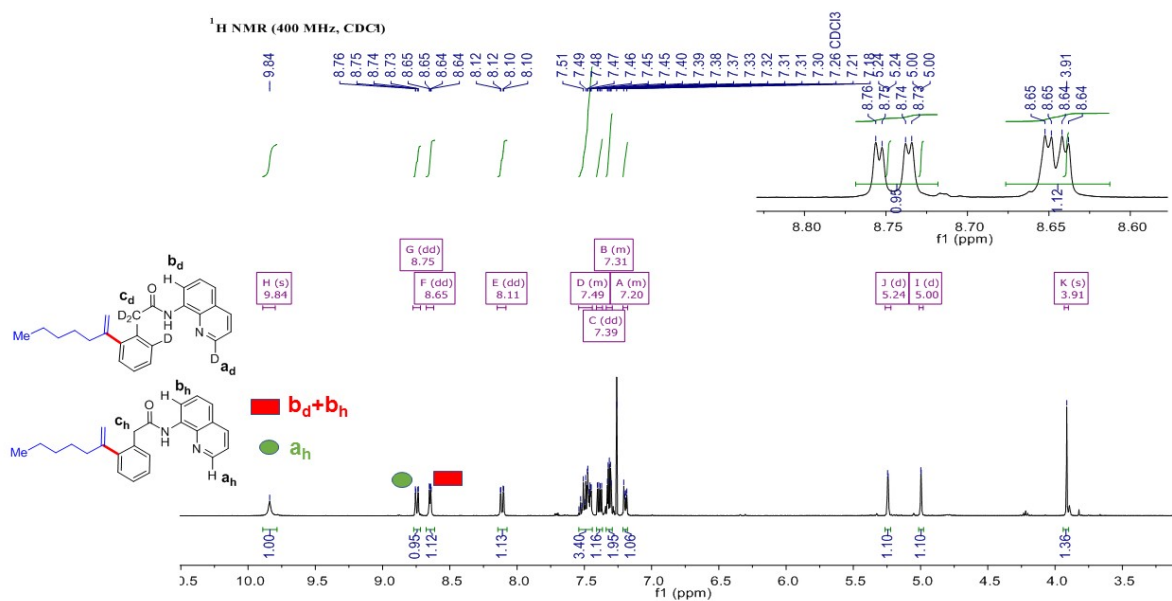
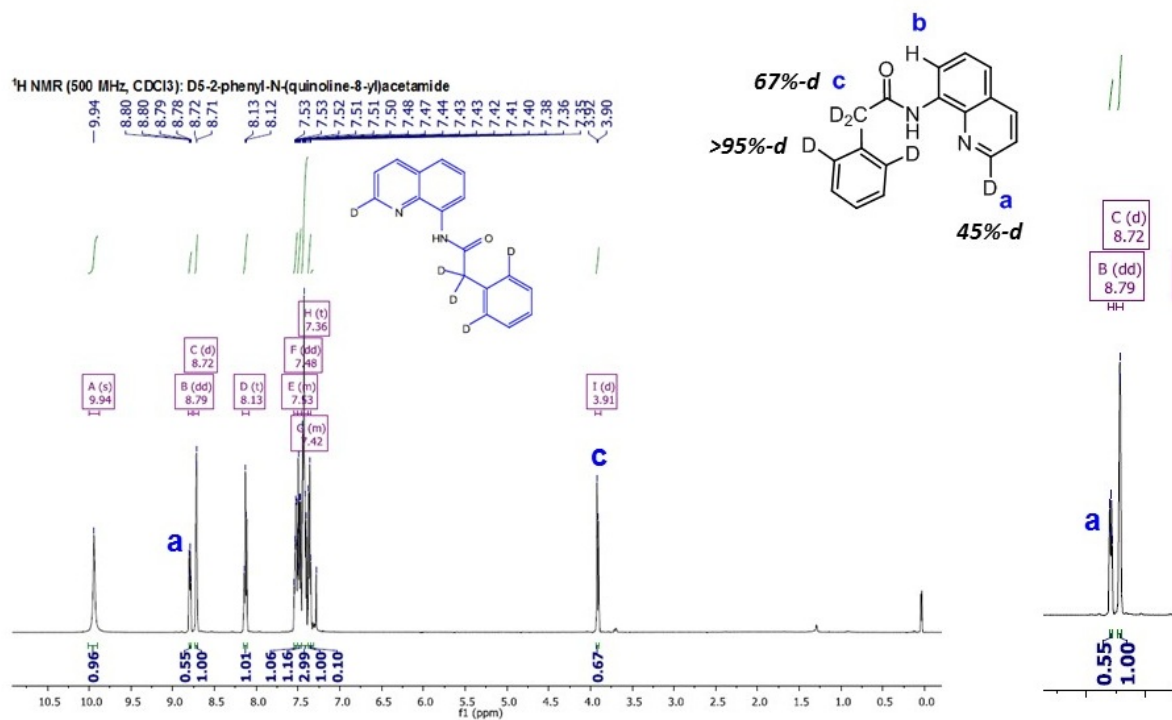
2.4. Mechanistic investigation

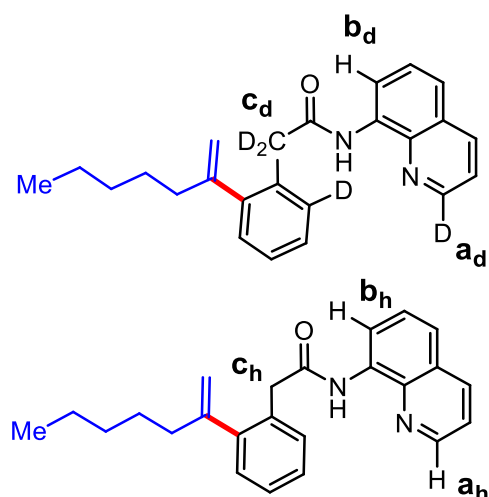
Labelling Experiment: determination of product distribution (3d/ d_4 -3d):



Procedure: In a clean, oven-dried screw cap reaction tube containing magnetic stir-bar, 2-phenyl-N-(quinolin-8-yl)acetamide (0.05 mmol), **d5-1** (0.05 mmol), $\text{Pd}(\text{OAc})_2$ (10 mol%, 0.01 mmol), neocuproine (20 mol%, 0.02 mmol), copper (II) carbonate basic (1 equiv, 0.1 mmol), copper (II) fluoride (1 equiv, 0.1 mmol) were weighed. Then, α , β -unsaturated octenoic acid (2 equiv, 0.2 mmol) was transferred through micro pipette. Common laboratory syringe was used to introduce *t*-BuOH (2 mL) into the reaction mixture. Finally, the tube was placed in a preheated oil bath at 130 °C and the reaction was stirred (at 850 rpm) vigorously for 24 h. After detaching the reaction, it was cooled to room temperature and filtered through celite pad using ethyl acetate (30 mL). Excess solvent was removed in rotatory evaporator and desired compound was purified by column chromatography through silica gel (100-200 mesh size) using PET-ether / ethyl acetate as eluent.

¹H NMR of deuterated starting material:





Value for $b_d + b_h = 1.12$

Value for $a_h = 0.95$ (ideal case)

One proton integration for deuterated compound = $(1.12 - 0.95) = 0.17$ (ideal case)

But, actual contribution is 45%-d (a_d)

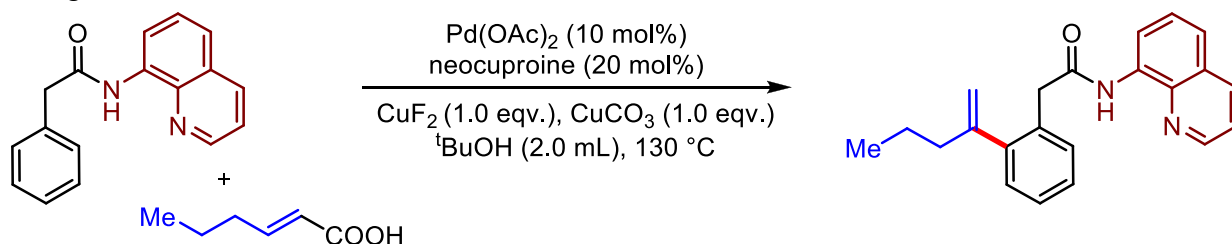
So, one proton integration for deuterated compound = $0.17 \times (100/45) = 0.37$

One proton integration for deuterated compound = $(1 - 0.37) = 0.63$

As a result, $P_H/P_D = 0.63/0.37 = 1.7$

Kinetic experiment:

Kinetic study was performed by monitoring the reaction of 2-phenyl-N-(quinolin-8-yl)acetamide with 2-hexenoic acid. Standard reaction protocol was followed for all the reactions. Amount of product in each reaction was measured by gas chromatography using *n*-decane as internal standard.



Reagent	SET-1	SET-2	SET-3	SET-4
Amide	0.05 mmol	0.1 mmol	0.2 mmol	0.25 mmol
Olefin	0.2 mmol	0.2 mmol	0.2 mmol	0.2 mmol
Pd(OAc) ₂	10 mol%	10 mol%	10 mol%	10 mol%
Neocuproine	20 mol%	20 mol%	20 mol%	20 mol%
CuF ₂ & CuCO ₃	1 equiv.	1 equiv.	1 equiv.	1 equiv.
<i>t</i> -BuOH	2 mL	2 mL	2 mL	2 mL

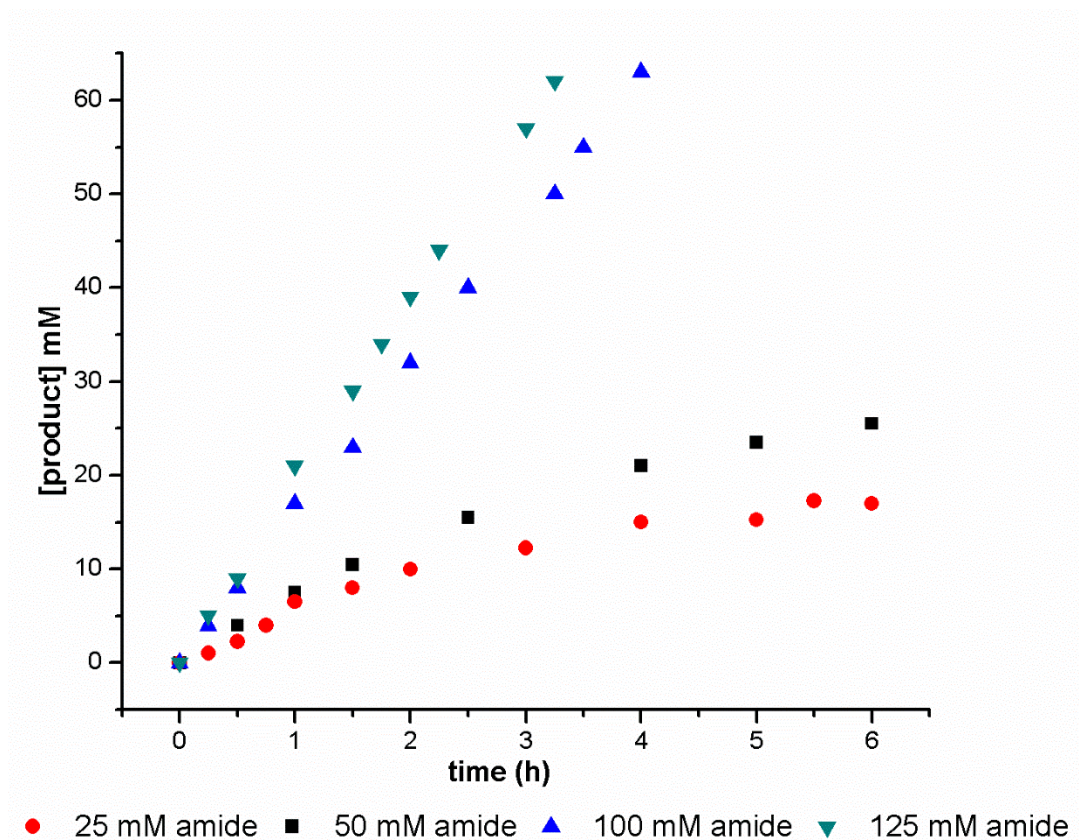


Figure S1. Product concentration (mM) vs time (h) plot

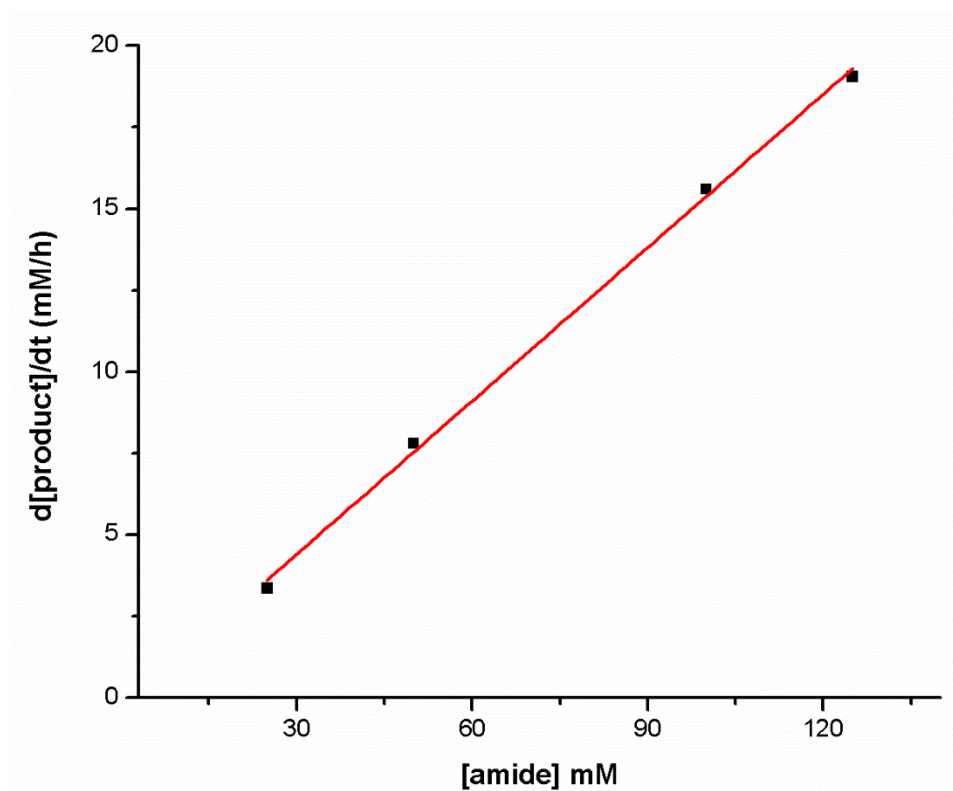


Figure S2. Initial amide concentration (mM) vs rate of product formation (mM/h) plot

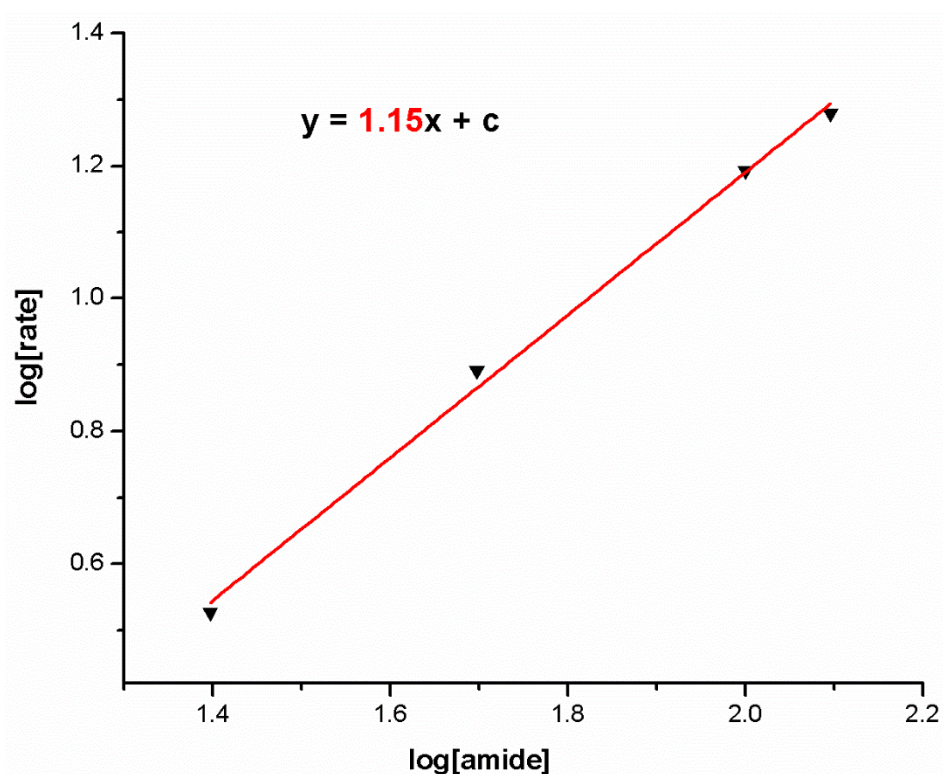


Figure S3. Logarithm plot of initial amide concentration vs rate of product formation

Fig 3 shows the logarithmic plot of initial concentration against the rate of the reaction, furnishing a straight line with a slope of 1.15. **So, order with respect to amide coupling partner is ~1.**

Reagent	SET-5	SET-6	SET-7
Amide	0.1 mmol	0.1 mmol	0.1 mmol
Olefin	0.15 mmol	0.3 mmol	0.4 mmol
Pd(OAc) ₂	10 mol%	10 mol%	10 mol%
Neocuproine	20 mol%	20 mol%	20 mol%
CuF ₂ & CuCO ₃	1 equiv.	1 equiv.	1 equiv.
<i>t</i> -BuOH	2 mL	2 mL	2 mL

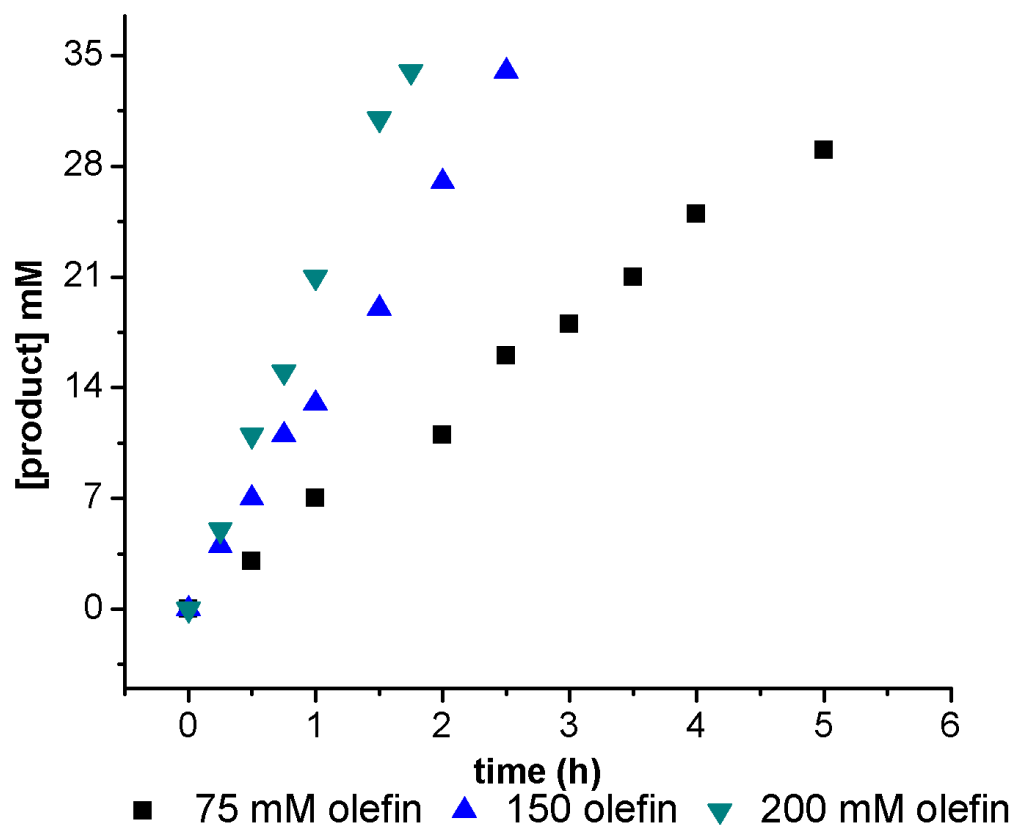


Figure S4. Product concentration (mM) vs time (h) plot

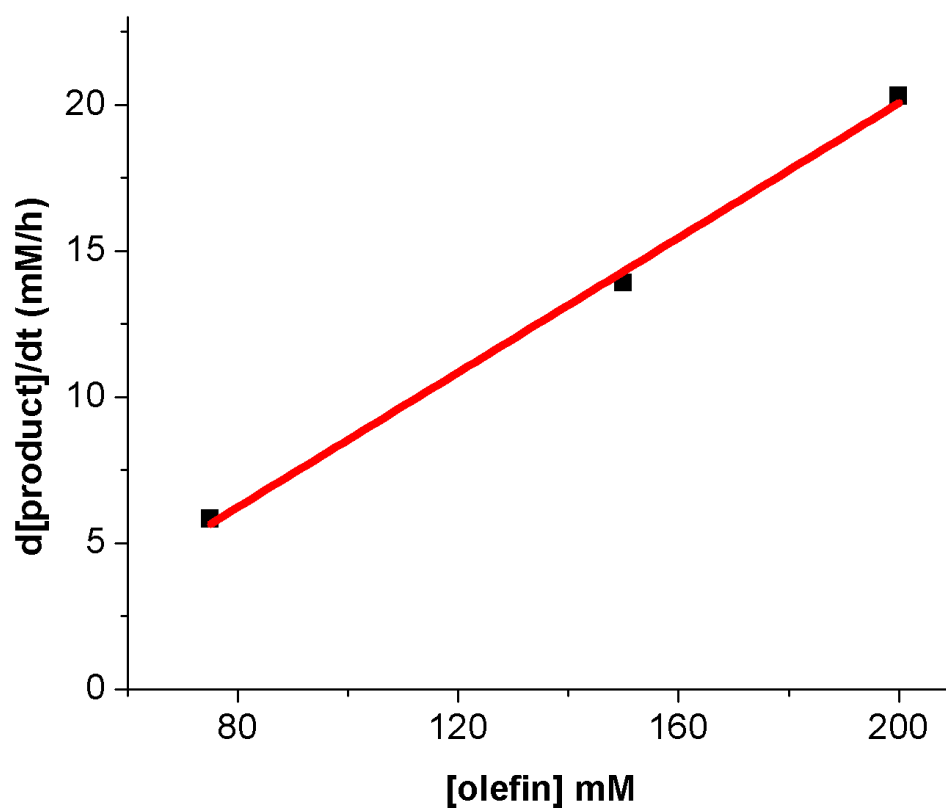


Figure S5. Initial olefin concentration (mM) vs rate of product formation (mM/h) plot

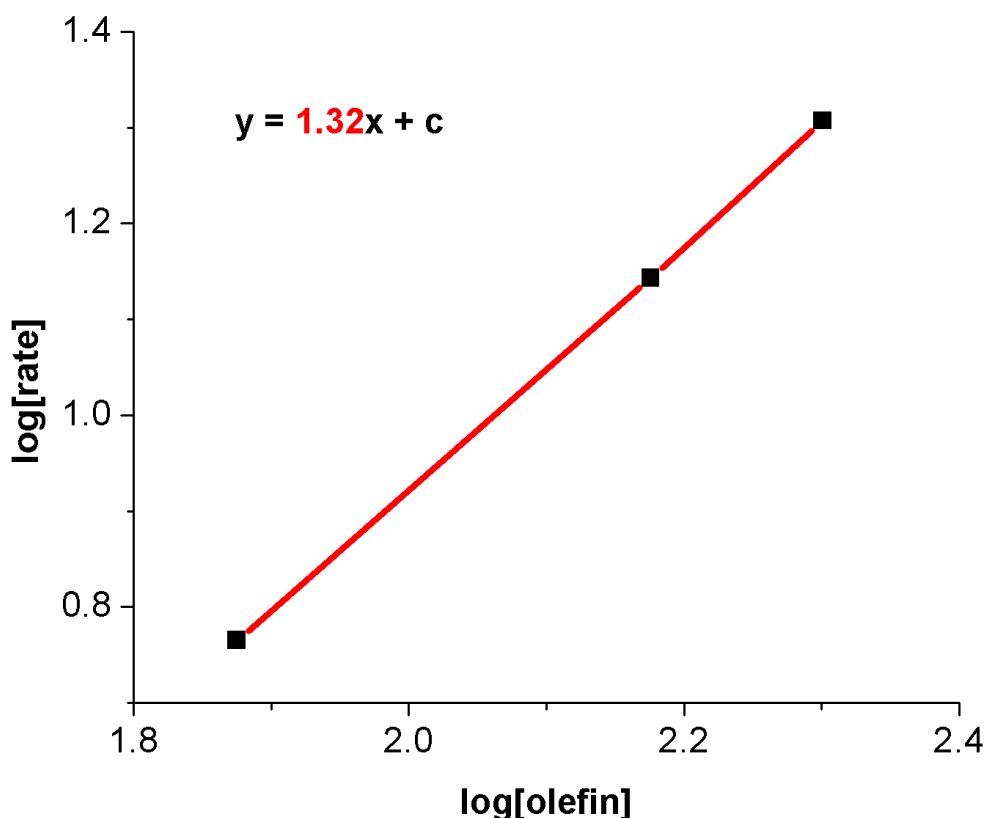
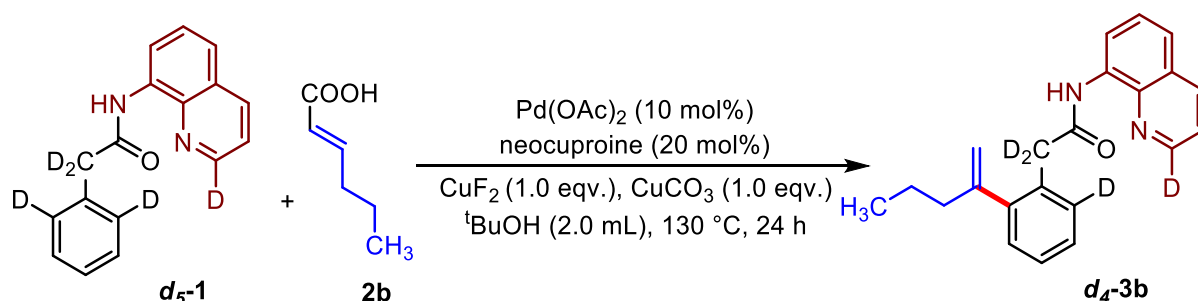


Figure S6. Logarithm plot of initial amide concentration vs rate of product formation
Logarithmic plot of initial concentration against the rate of the reaction furnishing a straight line with a slope of 1.32 (~1). **So, the reaction is first order with respect to olefin coupling partner.**

Kinetic isotope effect: Kinetic isotope effect study was performed by monitoring the reaction of 2-phenyl-N-(quinolin-8-yl)acetamide derivative (non-deuterated and deuterated) with 2-hexenoic acid. All the reactions were performed under the standard reaction condition. Amount of product formation in each reaction was measured by ^1H NMR spectroscopy using 1,3,5-trimethoxy benzene as internal standard.



SET-8:

Reagent	Amount
Amide	0.05 mmol

Olefin	0.2 mmol
Pd(OAc) ₂	10 mol%
Neocuproine	20 mol%
CuF ₂ & CuCO ₃	1 equiv
<i>t</i> -BuOH	2 mL

Initial rate for SET-8 (R_D) = k_D [amide]^x [olefin]^y.....(f) [k_D = rate constant]
Following the reaction kinetics for the **SET-8** we got the following plot:

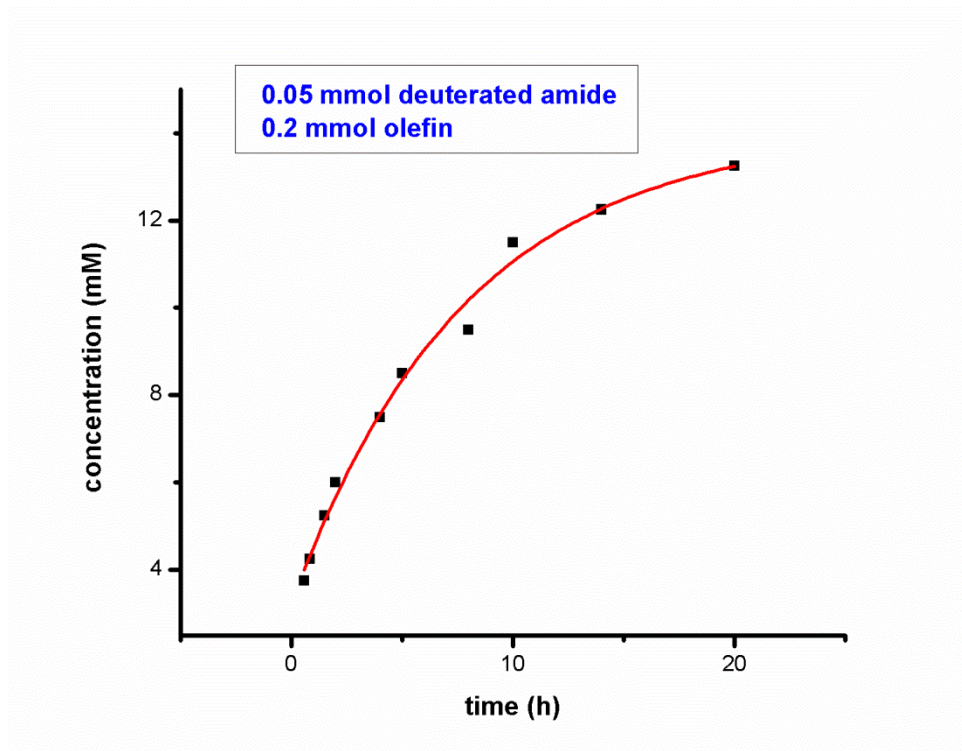
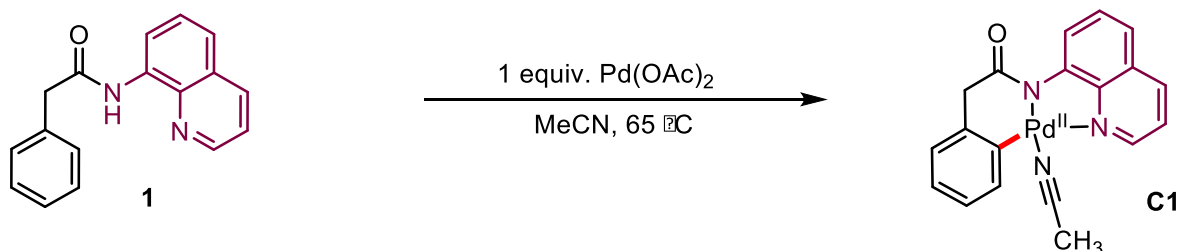


Figure S7. Concentration (mM) vs time (h) plot for run 4

$$\begin{aligned}
 (R_D) &= k_D [\text{amide}]^x [\text{olefin}]^y \\
 \text{or, } 2.368 &= k_D [0.05]^x [0.2]^y \dots\dots\dots(g) \\
 \text{From SET-1 we get, } (R_H) &= k_H [\text{amide}]^x [\text{olefin}]^y \\
 \text{or, } 3.36 &= k_H [0.05]^x [0.2]^y \dots\dots\dots(h) \\
 \text{Comparing eq. (g) and (h)} \\
 k_H / k_D &= 3.36/2.368 \\
 \text{or, } k_H / k_D &= 1.42 \\
 \text{So, kinetic isotope effect value is 1.4}
 \end{aligned}$$

Intermediate synthesis (C1):



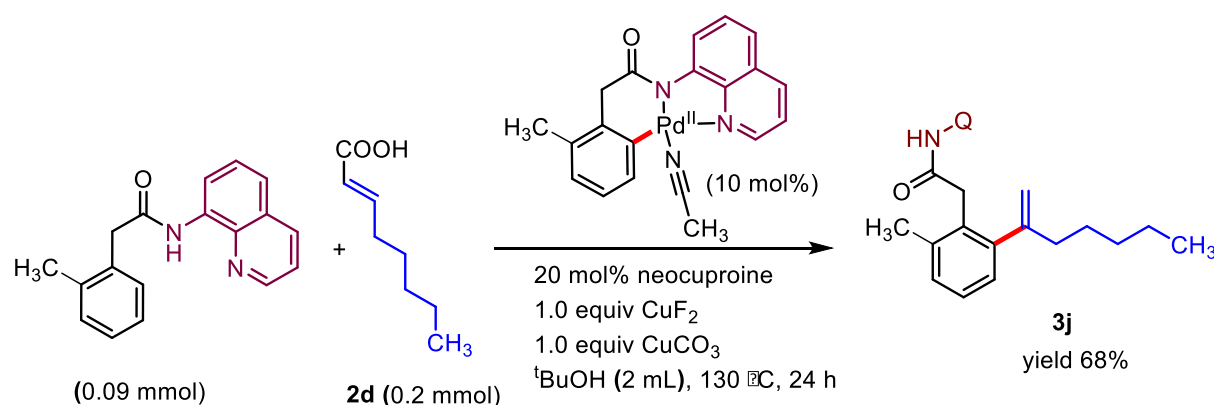
A clean, oven-dried screw cap reaction tube with previously placed magnetic stir-bar was charged with 2-phenyl-N-(quinolin-8-yl)acetamide (1 mmol, 262mg). In this tube,

palladium acetate (1 mmol, 1 equiv) was added into the reaction tube. Then 4 mL dry acetonitrile was transferred to this reaction mixture by common laboratory syringe. The reaction mixture was vigorously stirred (800 rpm on Heidolph MR Hei-Standard stirrer) for 5 h in a preheated oil bath of 65 °C. Insoluble part of the reaction mixture was filtered out by using acetonitrile. Finally, the clean solution was evaporated and again diluted with minimum amount of acetonitrile. The complex was recrystallized from acetonitrile (85% yield). ESI-MS and NMR of the metal complex was recorded in acetonitrile.

Characterization data for the above complex matched with the previously reported literature data.²

Follow the section 2.7 for the preparation of **C2**

Catalytic competence:



In a clean, oven-dried screw cap reaction tube containing magnetic stir-bar, *o*-tolyl acetamide of 8-amino quinoline (0.09 mmol), aryl palladium complex (10 mol%, 0.01 mmol), neocuproine (20 mol%, 0.02 mmol), copper (II) carbonate basic (1 equiv, 0.1 mmol), copper (II) fluoride (1 equiv, 0.1 mmol) were weighed. Then, 2-octenoic acid (2 equiv, 0.2 mmol) was transferred through micro pipette. Solvent was introduced in the reaction medium by common laboratory syringe. Then the tube was placed in a preheated oil bath at 130 °C and the reaction were stirred (at 850 rpm) vigorously for 24 h. After detaching the reaction, it was cooled to room temperature and filtered through celite pad using ethyl acetate (30 mL). Excess solvent was removed in rotatory evaporator and the desired compound was extracted using EtOAc-saturated NaHCO₃ and combined organic layer was dried over Na₂SO₄. Finally, it was concentrated in reduced pressure and was purified by column chromatography through silica gel (100-200 mesh size) using PET-ether / ethyl acetate as eluent.

¹H NMR study:

In a clean oven-dried vial (20 mL volume), 0.025 mmol of aryl-palladium complex (**C1**) was added. Then, 2-pentenoic acid (0.025 mmol, 1 equiv) was added into the reaction tube followed by 2 mL of CDCl₃ was transferred into the reaction mixture by common laboratory syringe. The reaction mixture was vigorously stirred (600 rpm on Heidolph MR Hei-Standard stirrer) for 24 h in room temperature. In a regular

interval, 200 μL of reaction mixture was taken out from the medium and diluted with additional solvent. This solution was utilized for recording the NMR spectra.

Cu and ligand complex formation study:

For this study, all the experiments were performed following the general procedure described in section 2.2. For all other cases except standard condition, reaction has been performed without amide and olefin. Other notable deviations from standard condition were listed below:

1. Copper salts were not utilized.
2. Palladium-catalyst was not used in the case.





<i>Reaction-1</i>	<i>Reaction-2</i>	<i>Reaction-3</i>	<i>Reaction-4</i>
$\text{Pd}(\text{OAc})_2$ neocuproine 	neocuproine CuF_2 CuCO_3 	$\text{Pd}(\text{OAc})_2$ neocuproine $\text{CuF}_2 + \text{CuCO}_3$ 	standard reaction mixture 

Figure S8. Cu-ligand complexation studies

Cu and ligand complex formation study by UV-vis spectroscopy:

For this study, all the experiments were performed following the general procedure described in section 2.2. For all the cases, reaction has been performed without amide and olefin. 20 μL of reaction mixture was taken out from the medium and diluted with 980 μL additional solvent. This solution was utilized for recording the spectra.

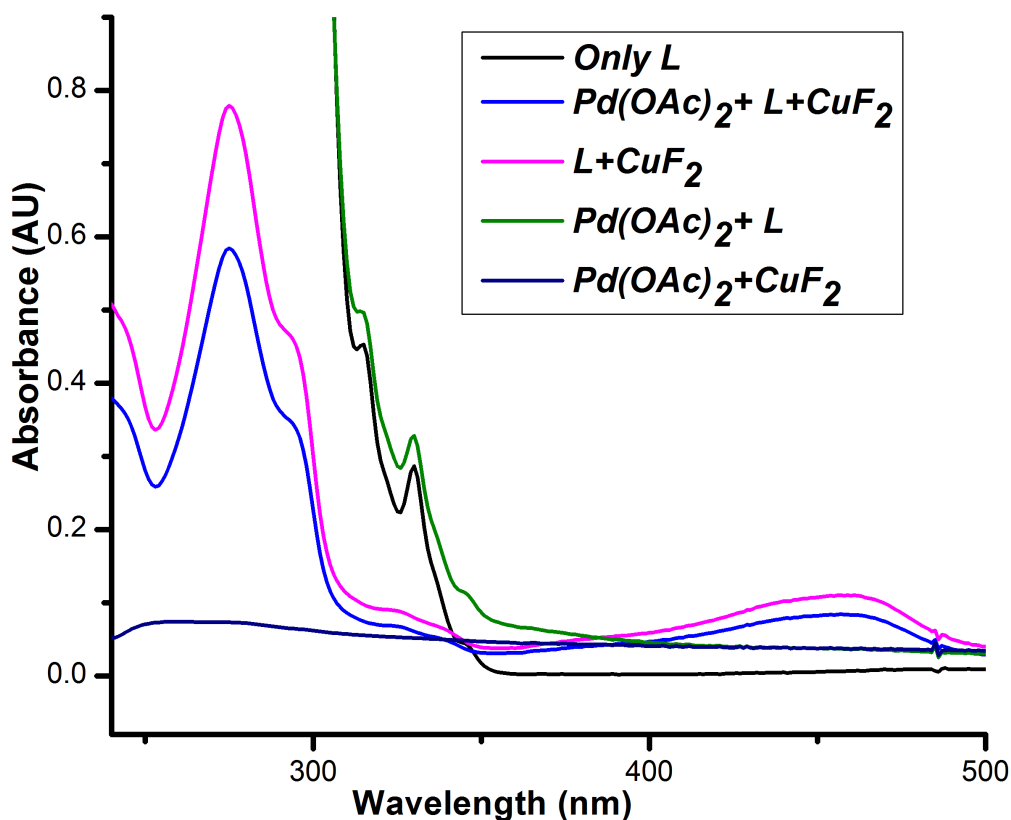


Figure S9. UV-Vis study

IR study: Following the above described procedure, reaction was monitored in a regular time interval. For the IR study, we used acetonitrile solvent instead of deuterated chloroform. From the reaction medium, 5 μL of solution was used for recording IR spectra.

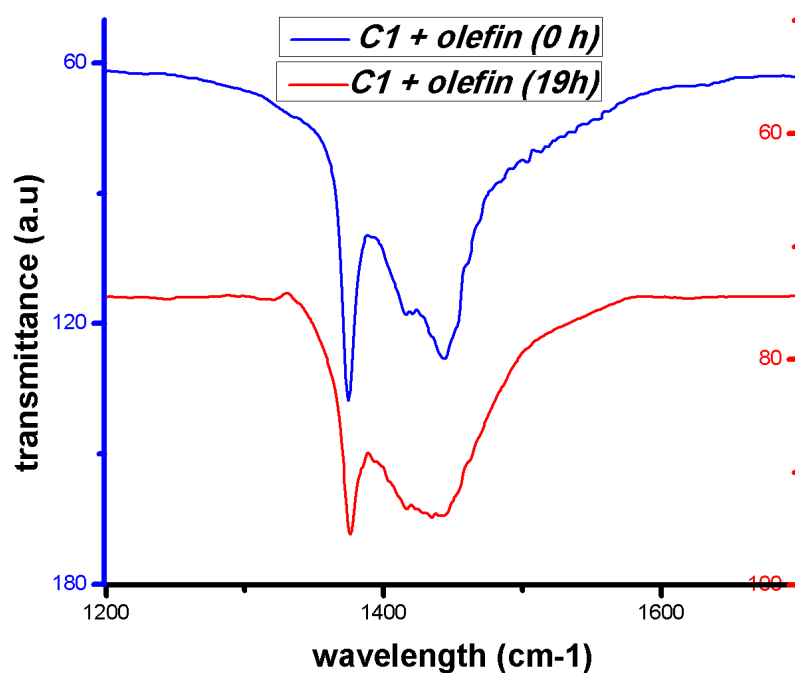


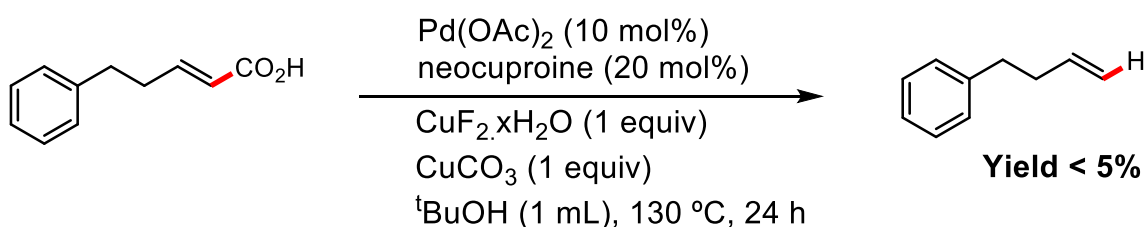
Figure S10. IR study

Synthesis of Cu-neocuproine complex:

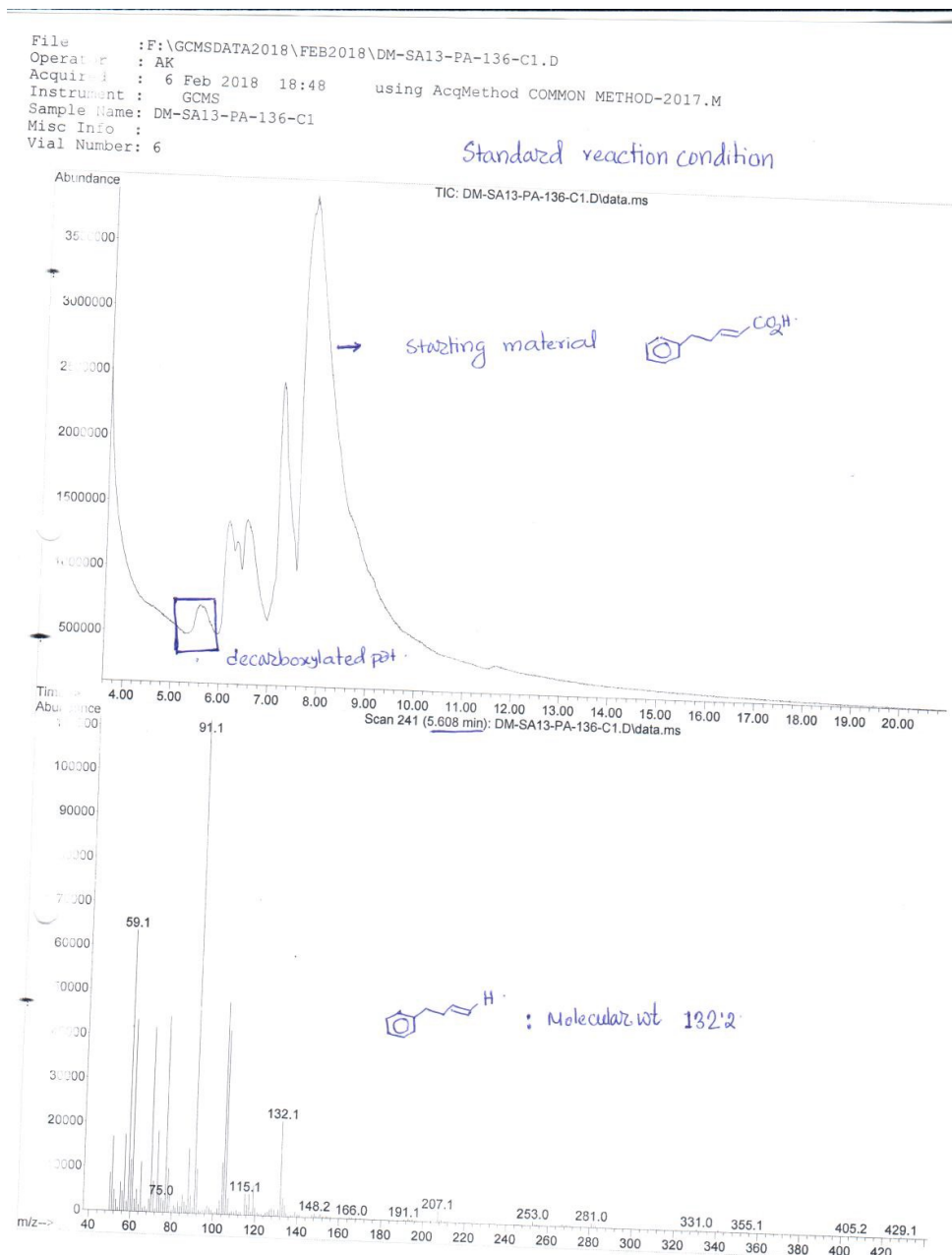
[Cu(neocuproine)₂Cl] complex was synthesized in gm scale by following literature reported procedure.³

Decarboxylation Study:

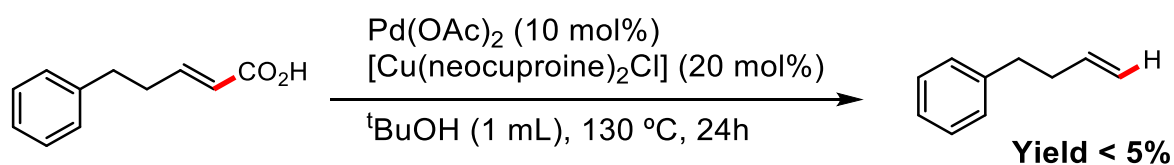
Condition 1: In a clean, oven-dried screw cap reaction tube containing magnetic stir-bar, 5-phenyl-2-pentenoic acid (0.05 mmol), palladium acetate (10 mol%, 0.01 mmol), neocuproine (20 mol%, 0.02 mmol), copper (II) carbonate basic (1 equiv, 0.1 mmol), copper (II) fluoride (1 equiv, 0.1 mmol) were weighed. Then, 1 mL of ^tBuOH solvent was introduced in the reaction medium and it was placed in a preheated oil bath (130 °C) for vigorous stirring (850 rpm). After 24 h, the reaction was cooled to room temperature and filtered through celite pad using minimum amount of ethyl acetate. After removing excess solvent, it was used directly for GC-MS analysis.



GC-MS spectra

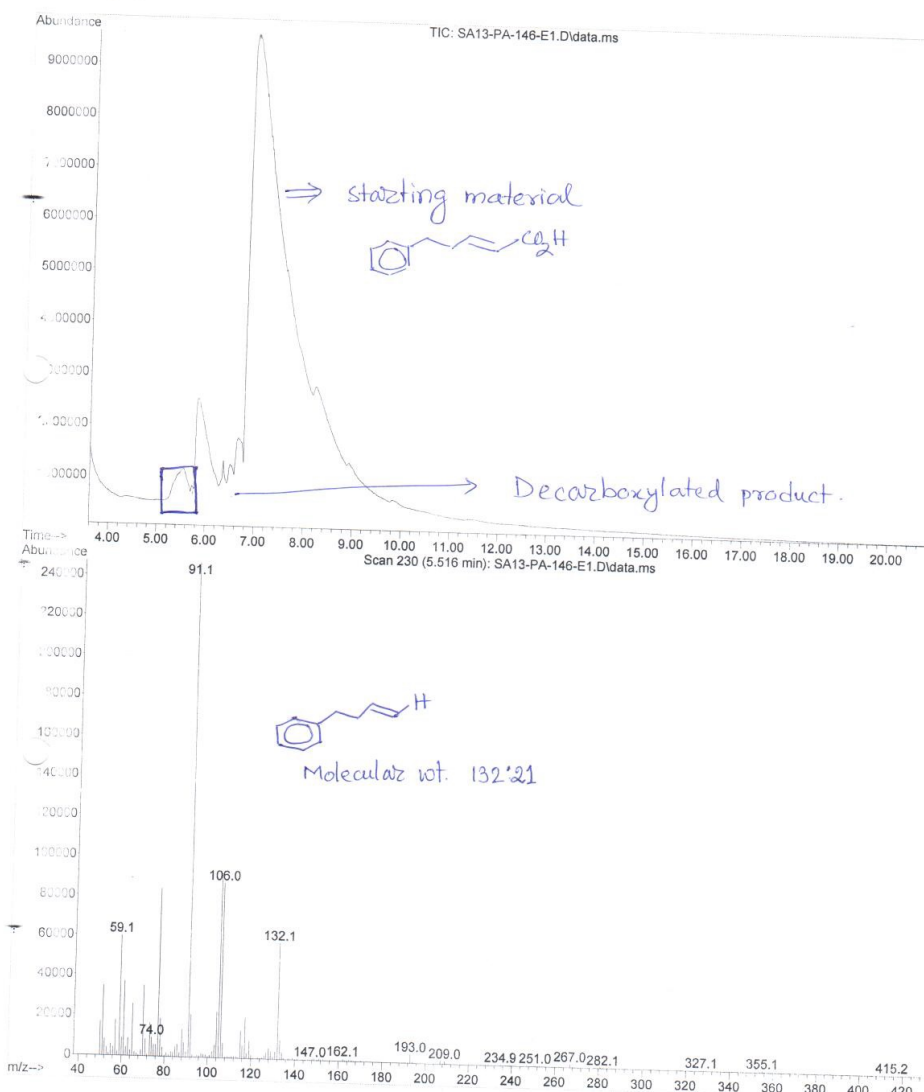


Condition 2: In a clean, oven-dried screw cap reaction tube containing magnetic stir-bar, 5-phenyl-2-pentenoic acid (0.05 mmol), palladium acetate (10 mol%, 0.01 mmol), [Cu(neocuproine)₂Cl] (20 mol%, 0.02 mmol) were weighed. Subsequently, 1 mL of *t*BuOH solvent was added in the reaction tube and it was placed in a heated oil bath (130 °C) for vigorous stirring (850 rpm). After 24 h, the reaction was cooled to room temperature and filtered through celite pad using minimum amount of ethyl acetate. After removing excess solvent, it was used directly for GC-MS analysis.



GC-MS spectra

File :F:\GCMSDATA2018\MAR 2018\SA13-PA-146-E1.D
 Operator : SRD
 Acquired : 22 Mar 2018 19:33 using AcqMethod COMMON METHOD-2017.M
 Instrument : GCMS
 Sample Name: SA13-PA-146-E1
 Misc Info :
 Vial Number: 1



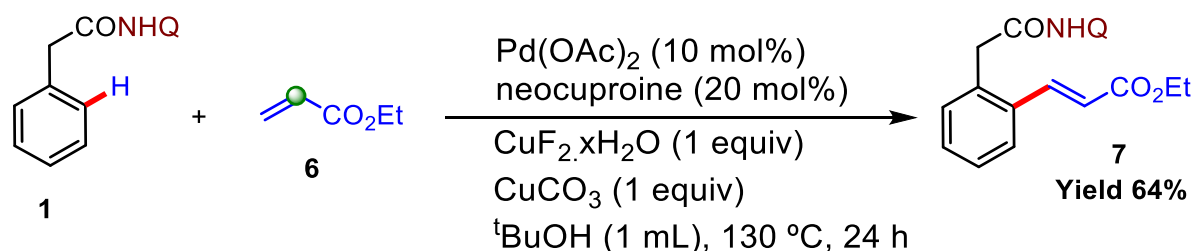
Role of Copper salts in the reaction:

Reaction without Cu(II)-salts: In a clean, oven-dried screw cap reaction tube containing magnetic stir-bar, phenyl acetamide of 8-amino quinoline (0.1 mmol), palladium acetate (10 mol%, 0.01 mmol), neocuproine (20 mol%, 0.02 mmol) were weighed. Then, 2-octenoic acid (2 equiv, 0.2 mmol) was transferred through micro pipette. Solvent was introduced in the reaction medium by common laboratory syringe. Then the tube was placed in a preheated oil bath at 130 °C and the reaction were stirred (at 850 rpm) vigorously for 24 h. After detaching the reaction, it was cooled to room temperature and filtered through celite pad using ethyl acetate (5 mL). Excess solvent was removed in rotatory evaporator and the reaction mixture was directly used for GC analysis.

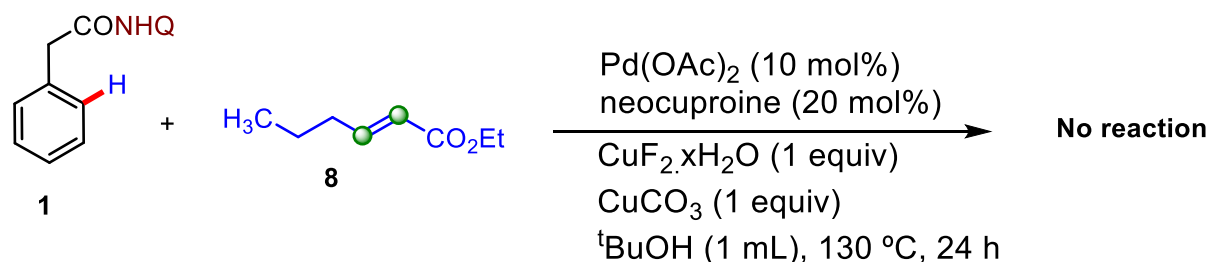
Reaction with Cu(I)-salt: In an oven-dried screw cap reaction tube containing magnetic stir-bar, phenyl acetamide of 8-amino quinoline (0.1 mmol), palladium

acetate (10 mol%, 0.01 mmol), neocuproine (20 mol%, 0.02 mmol), CuI (2 equiv, 0.2 mmol) were weighed. Then, 2-octenoic acid (2 equiv, 0.2 mmol) was transferred through micro pipette. Solvent was introduced in the reaction medium by common laboratory syringe. Then the tube was placed in a preheated oil bath at 130 °C and the reaction were stirred (at 850 rpm) vigorously for 24 h. After detaching the reaction, it was cooled to room temperature and filtered through celite pad using minimum amount of ethyl acetate (30 mL). Excess solvent was removed in rotatory evaporator and the reaction mixture was directly used for GC analysis.

Feasibility of olefination reaction with terminal and internal olefin:



Above experiment was performed following the general procedure described in section 2.2. Yield of the olefinated product was 64%. Characterization data for the isolated compound was matched with the literature reported data.⁴



Above experiment was performed following the general procedure described in section 2.2. Reaction mixture was analyzed by proton NMR and GC-MS.

Radical quenching experiments with TEMPO

In a clean, oven-dried screw cap reaction tube containing magnetic stir-bar, phenyl acetic acid derivative **1a** (0.1 mmol), Pd(OAc)₂ (10 mol%, 0.01 mmol), neocuproine (20 mol%, 0.02 mmol), copper (II) carbonate basic (1 equiv, 0.1 mmol), copper (II) fluoride (1 equiv, 0.1 mmol) and TEMPO (0.15 mmol) were weighed. 2 equiv of *trans*-2-octenoic acid (0.2 mmol) was transferred through micro pipette. Common laboratory syringe was used to introduce *t*-BuOH (2 mL) into the reaction mixture. Then the tube was placed in a preheated oil bath at 130 °C and the reaction was stirred (at 1000 rpm) vigorously for 24 h. Upon completion of the reaction, it was cooled to room temperature and filtered through celite pad using ethyl acetate (30 mL). Solvent was removed under reduced pressure. Then the reaction mixture was extracted with EtOAc (10 mL x 3) and saturated NaHCO₃. The combined organic layer was dried over anhydrous Na₂SO₄. Then the solvent was evaporated under reduced pressure. The crude product was then purified by column chromatography through silica gel (100-200 mesh size) using PET-

ether / ethyl acetate as eluent to afford olefinated product **3d** in 31% yield.

2.5. Computational Details:

All calculations were performed using Gaussian 16 suite of the quantum chemical program.⁵ Geometry optimizations were performed at the density functional theory (DFT) level employing ω B97xD functional in conjunction with 6-31G(d) basis set for the main group elements (H, C, N, O) and Lanl2DZ basis set and associated pseudopotential for Pd and Cu. Analytical frequency calculations were performed on the optimized geometries to verify the local minima with no imaginary frequency and first-order saddle points with one imaginary frequency. For the transition state structures, intrinsic reaction coordinate (IRC) calculations were performed to confirm whether the located transition state connects the appropriate minima. More accurate energy calculations were performed employing M06L functional, for which the main group elements (H, C, N, O) were described using 6-311++G(d,p) basis set and Pd and Cu were described with Stuttgart/Dresden SDD basis set and associated pseudopotential. Single point energy calculations were performed accounting implicit solvation effect with *tert*-butanol solvent invoked through the conductor-like polarizable continuum model (CPCM). The M06L functional has been reported to give good agreement with experiment for the Pd-catalyzed reactions.⁶

Terminal vs. Internal Olefin

The ester analogues can undergo 1,2-migratory insertion followed by β -hydride elimination and reductive elimination to form linear olefination products. Our computational results with ethyl 2-propenoate, a *terminal* olefin substrate, show that the 1,2-migratory insertion step is rate-determining with a free energy barrier of $\Delta G^\ddagger = 18.5$ kcal/mol (Figure S14). The overall reaction possesses a substantial net thermodynamic driving force of $\Delta G_{\text{rxn}} = -10.2$ kcal/mol (**B**→**I6**). On the other hand, a negligible net driving force ($\Delta G_{\text{rxn}} = -0.9$ kcal/mol) is observed for ethyl 2-hexenoate, an *internal* olefin substrate (Figure S15). We reason that electron-donating alkyl ($-\text{CH}_3\text{CH}_2\text{CH}_2$) substitution in the olefinic moiety for *internal* esters weaken the Pd^0 -olefin coordination in the final reductive elimination process, making the overall process thermodynamically unfavorable. Additionally, an energy decomposition analysis (EDA, Figure S16) for the 1,2-migratory insertion step shows that the olefin distortion ($E_{\text{dist(olefin)}}$) is the governing energy-component that dictates the differential reactivity between the terminal and internal olefin. The internal olefin has to undergo greater distortion compared to the terminal one, which makes it inert toward the olefination process. This explains why no product was obtained from the *internal* ester substrate.

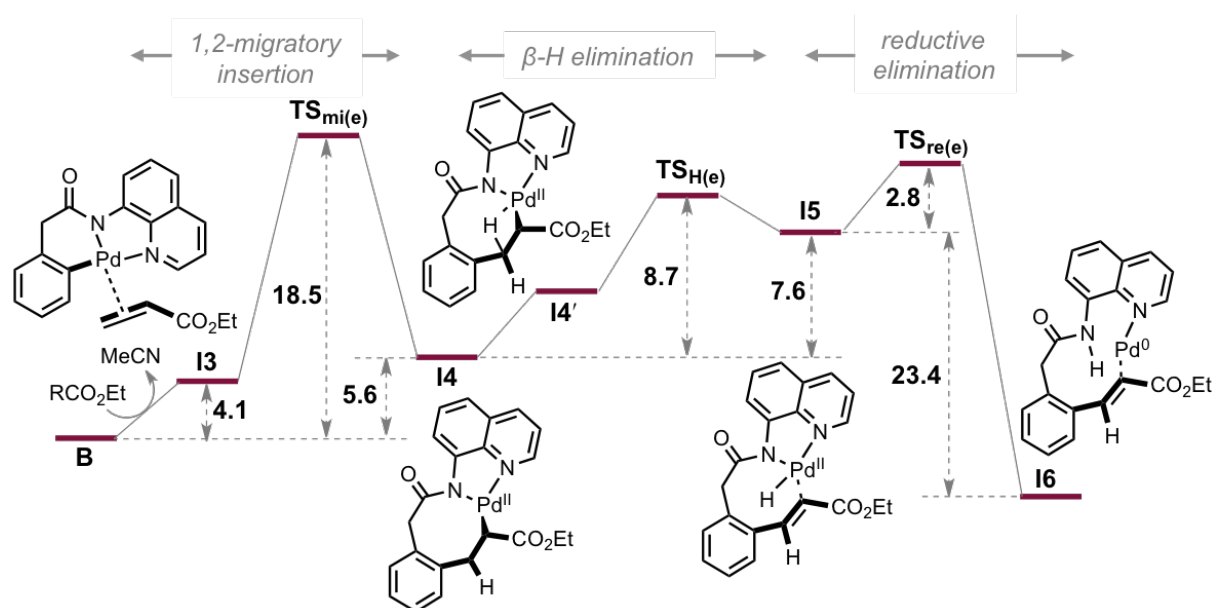


Figure S11. Gibbs Free energy profile ($\Delta\Delta G$ values in kcal/mol) for the formation for linear olefinated product using a *terminal* olefin.

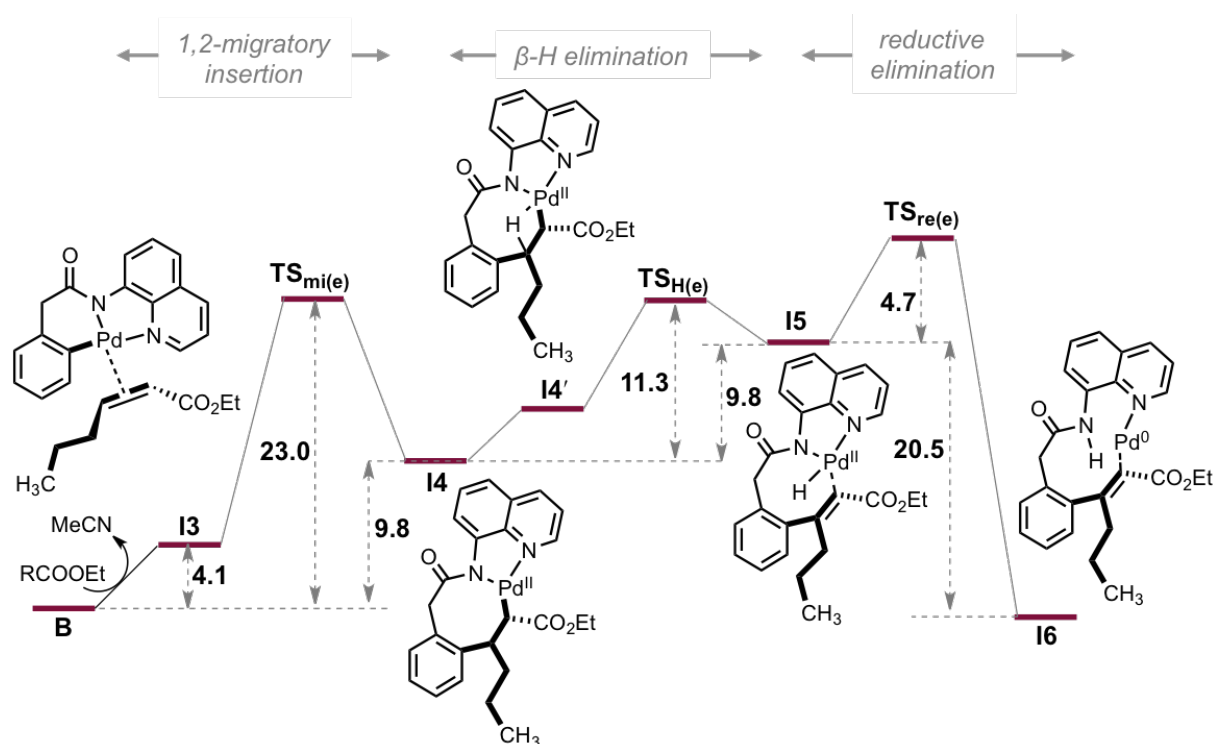


Figure S12. Gibbs Free energy profile ($\Delta\Delta G$ values in kcal/mol) for the formation for linear olefinated product using an *internal* olefin.

1,2-migratory insertion step

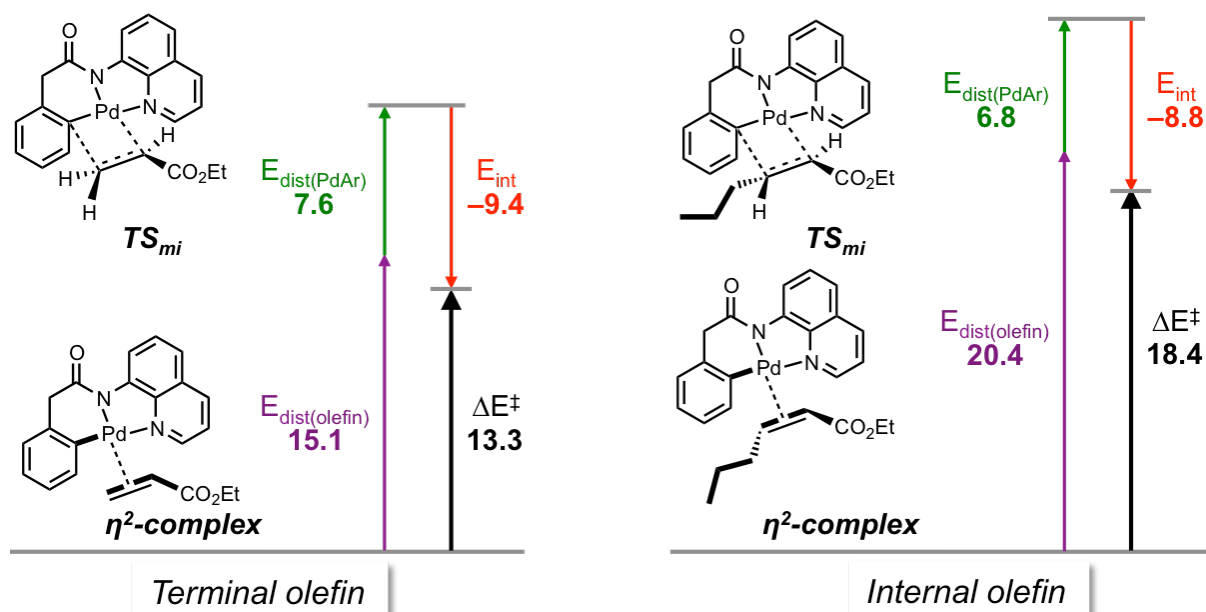


Figure S13. Distortion-interaction analysis on the 1,2 migratory insertion step for the terminal and internal olefin.

Promotional Effect of Cu-Complex on the 1,2-migratory insertion step

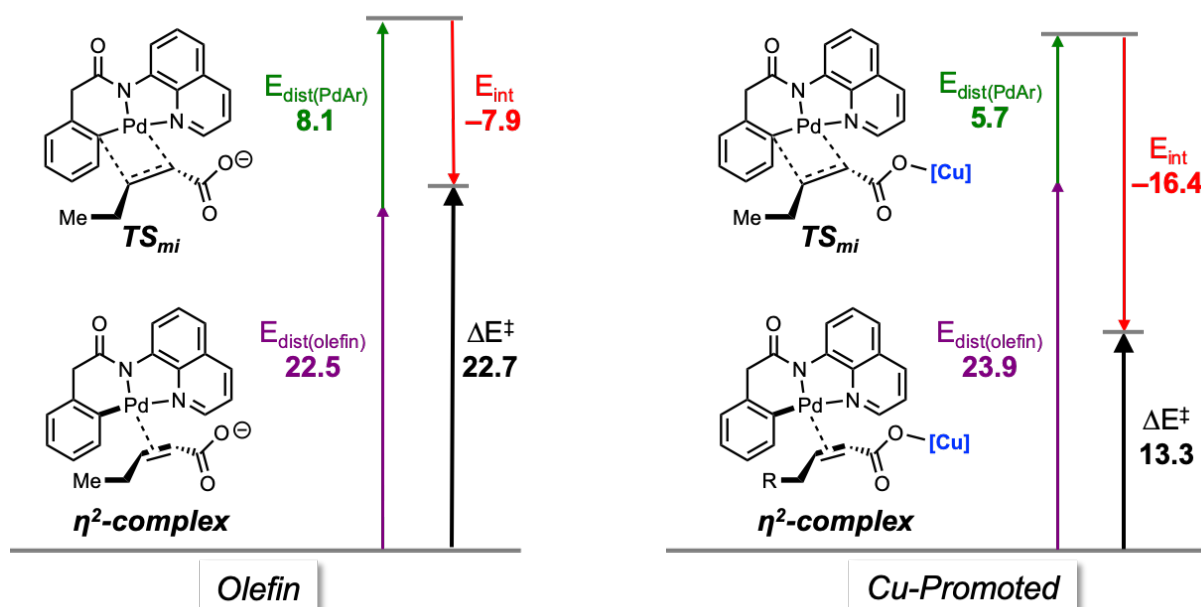


Figure S14. Distortion-interaction analysis on the 1,2 migratory insertion step for the unsaturated carboxylic acid to understand the promotional effect of Cu^I (neocuproine) complex.

2.6. X-ray crystallographic data

Synthesis of C2: To the stirring solution of Pd(OPiv)₂ (100 mg) in CH₃CN+MeOH (1:1) mixture, amide derivatives in CH₃CN (95 mg) was added dropwise. The reaction mixture was stirred at 60°C for 4 h. Orange red supernatant was filtered, dried and further recrystallised from CH₃CN to afford the desired complex (yield: 82%).

Synthesis of C3: To the solution of Pd(OAc)₂ (75 mg) in CH₃CN, amide derivative (97 mg) in CH₃CN was added dropwise with stirring. Reaction mixture was heated at 60°C for 30 min followed by addition of an equivalent of pyridine. After 4 h, the yellow supernatant was cooled to room temperature, filtered, dried and further recrystallized from CH₃CN to afford the desired complex (yield 92%).

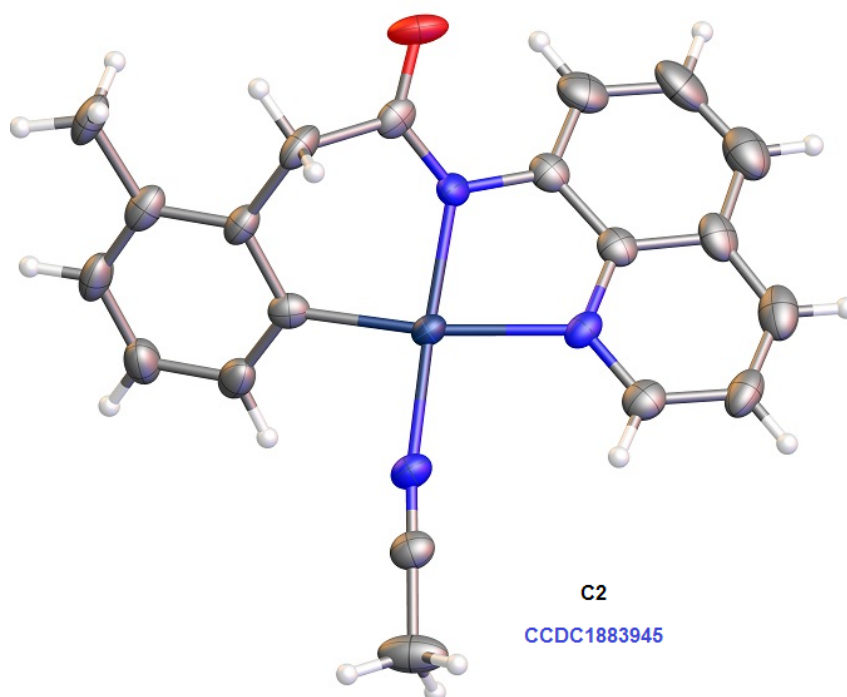


Figure S15. X-ray structure of **C2**

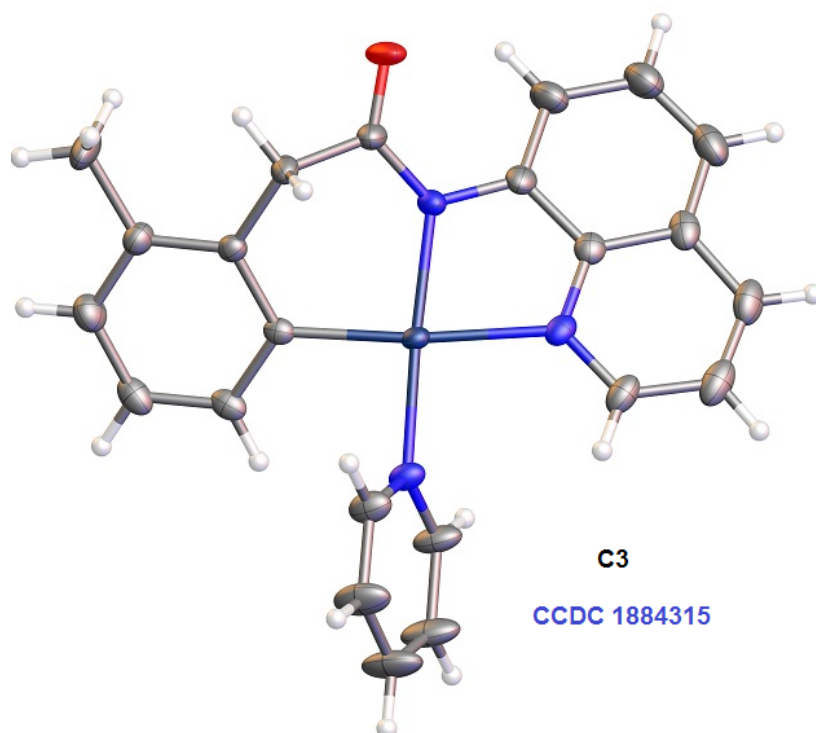


Figure S16. X-ray structure of C3

Crystal Data of C2 (CCDC 1883945) and C3 (CCDC 1884315)

Identification code	C2	C3
Formula	C ₂₀ H ₁₇ N ₃ OPd	C _{9.20} N _{1.20} O _{0.40} Pd _{0.40}
Formula weight(g/mol)	421.77	176.26
Temperature/K	150 K	150 K
Crystal system	Hexagonal	Triclinic
Space group	P 65	P -1
a/Å	22.1057(8)	9.6348(3)
b/Å	22.1057(8)	10.7198(3)
c/Å	6.7305(3)	11.5837(3)
α/°	90	105.639(2)
β/°	90	103.125(2)
γ/°	120	104.695(3)
Volume/Å ³	2848.3(2)	1056.87(6)
Z	6	5
P _{calc} /g/cm ³	1.475	1.385
μ/mm ⁻¹	0.988	0.892
F(000)	1272	426
Crystal size/mm ³	0.205 x 0.048 x 0.033	0.118 x 0.094 x 0.09
Radiation	MoKα (λ = 0.71073)	MoKα (λ = 0.71073)
2θ range for data collection/°	2.82 to 24.99	2.93 to 25.00

Index ranges	-26<=h<=26, -26<=k<=26, -8<=l<=8	-11<=h<=11, -12<=k<=12, -13<=l<=11
Reflections collected / unique	18452/ 3222 [R(int) = 0.0964]	8831/ 3701 [R(int) = 0.0630]
Data / restraints / parameters	3180 / 55 / 228	3701/ 0/ 253
Goodness-of-fit on F ²	1.051	1.224
Final R indices [I>2σ(I)]	R1 = 0.0425, wR2 = 0.0810	R1 = 0.0426, wR2 = 0.1244
R indices (all data)	R1 = 0.0526, wR2 = 0.0878	R1 = 0.0505, wR2 = 0.1391
Largest diff. peak and hole/ e Å ⁻³	0.550 and -0.346	1.136 and -1.134

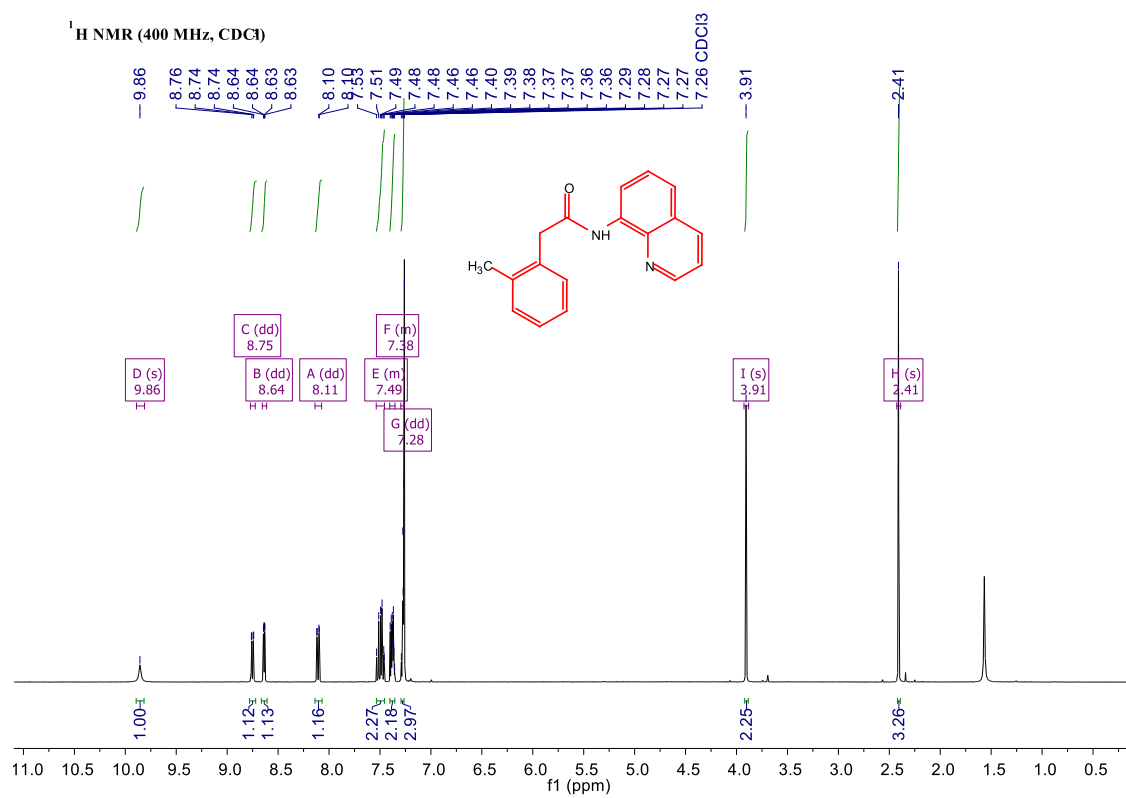
2.7 References

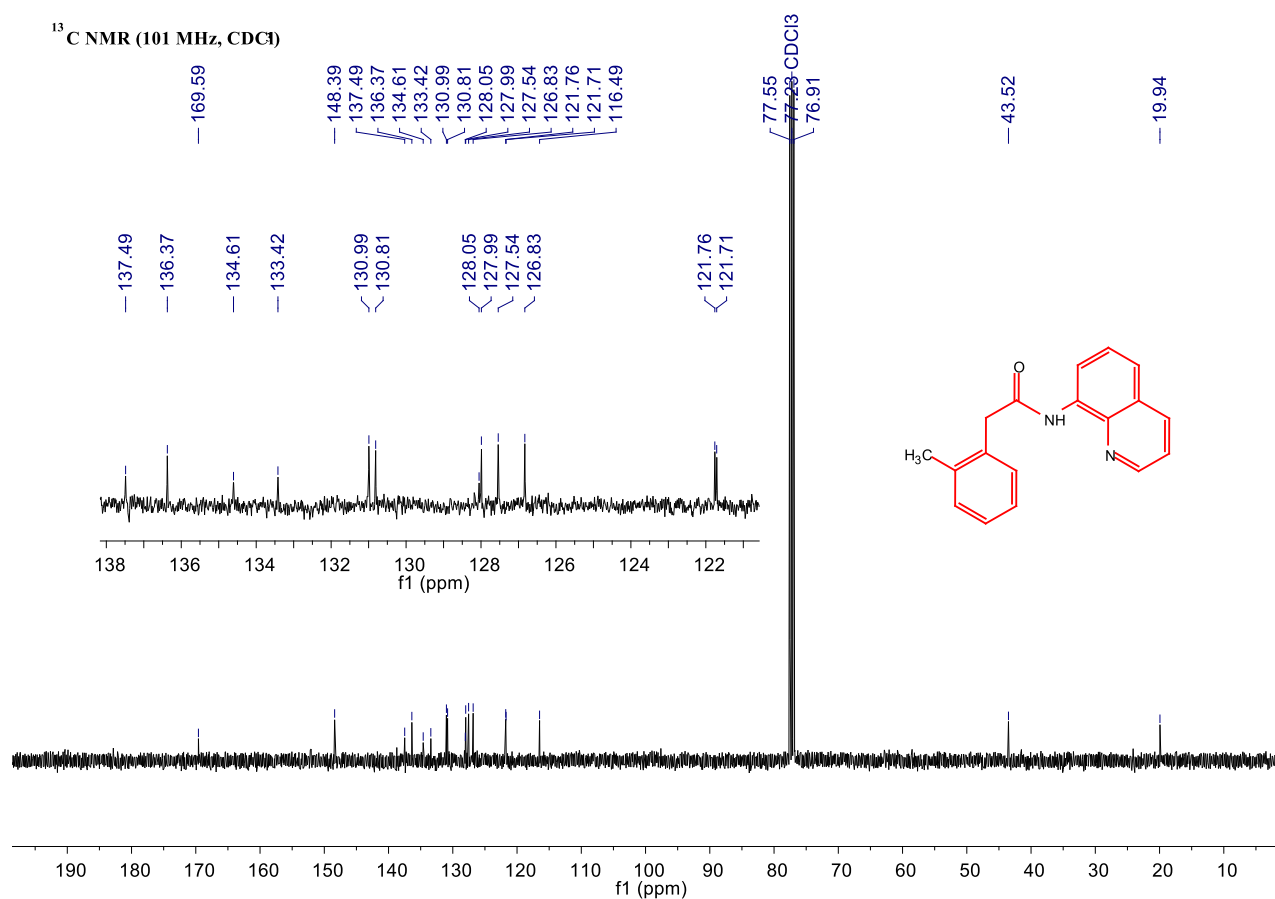
- (1) Deb, A.; Bag, S.; Kancharla, R.; Maiti, D. Palladium-Catalyzed Aryl C–H Olefination with Unactivated, Aliphatic Alkenes. *J. Am. Chem. Soc.* **2014**, *136*, 13602-13605.
- (2) Deb, A.; Hazra, A.; Peng, Q.; Paton, R. S.; Maiti, D. Detailed Mechanistic Studies on Palladium-Catalyzed Selective C–H Olefination with Aliphatic Alkenes: A Significant Influence of Proton Shuttling. *J. Am. Chem. Soc.* **2017**, *139*, 763-775.
- (3) Pallenberg, A. J.; Koenig, K. S.; Barnhart, D. M. Synthesis and characterization of some copper (I) phenanthroline complexes. *Inorg. Chem.* **1995**, *34*, 2833-2840.
- (4) Hu, Q.; Liu, X.; Wang, G.; Wang, F.; Li, Q.; Zhang, W. Ag₁Pd₁ Nanoparticles–Reduced Graphene Oxide as a Highly Efficient and Recyclable Catalyst for Direct Aryl C–H Olefination. *Chem. Eur. J.* **2017**, *23*, 17659 – 17662.
- (5) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Petersson, G. A.; Nakatsuji, H.; Li, X.; Caricato, M.; Marenich, A. V.; Bloino, J.; Janesko, B. G.; Gomperts, R.; Mennucci, B.; Hratchian, H. P.; Ortiz, J. V.; Izmaylov, A. F.; Sonnenberg, J. L.; Williams-Young, D.; Ding, F.; Lipparini, F.; Egidi, F.; Goings, J.; Peng, B.; Petrone, A.; Henderson, T.; Ranasinghe, D.; Zakrzewski, V. G.; Gao, J.; Rega, N.; Zheng, G.; Liang, W.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Throssell, K.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M. J.; Heyd, J. J.; Brothers, E. N.; Kudin, K. N.; Staroverov, V. N.; Keith, T. A.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A. P.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Millam, J. M.; Klene, M.; Adamo, C.; Cammi, R.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Farkas, O.; Foresman, J. B.; Fox, D. J. *Gaussian 16, Revision A.03*; Gaussian, Inc., Wallingford, CT, **2016**.
- (6) Sperger, T.; Sanhueza, I. A.; Kalvet, I.; Schoenebeck, F. Computational Studies of Synthetically Relevant Homogeneous Organometallic Catalysis Involving Ni, Pd, Ir, and Rh: An Overview of Commonly Employed DFT Methods and Mechanistic Insights. *Chem. Rev.* **2015**, *115*, 9532-9586.

NMR Spectra

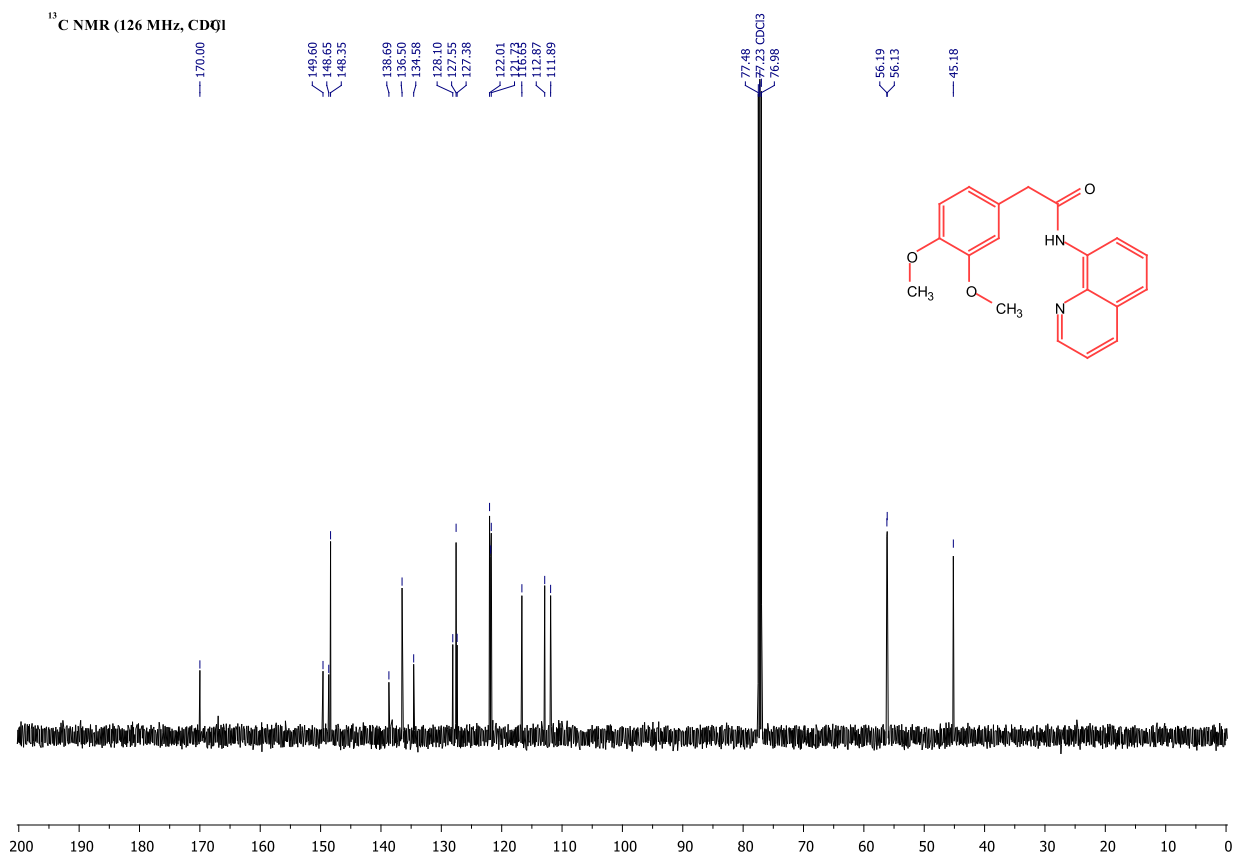
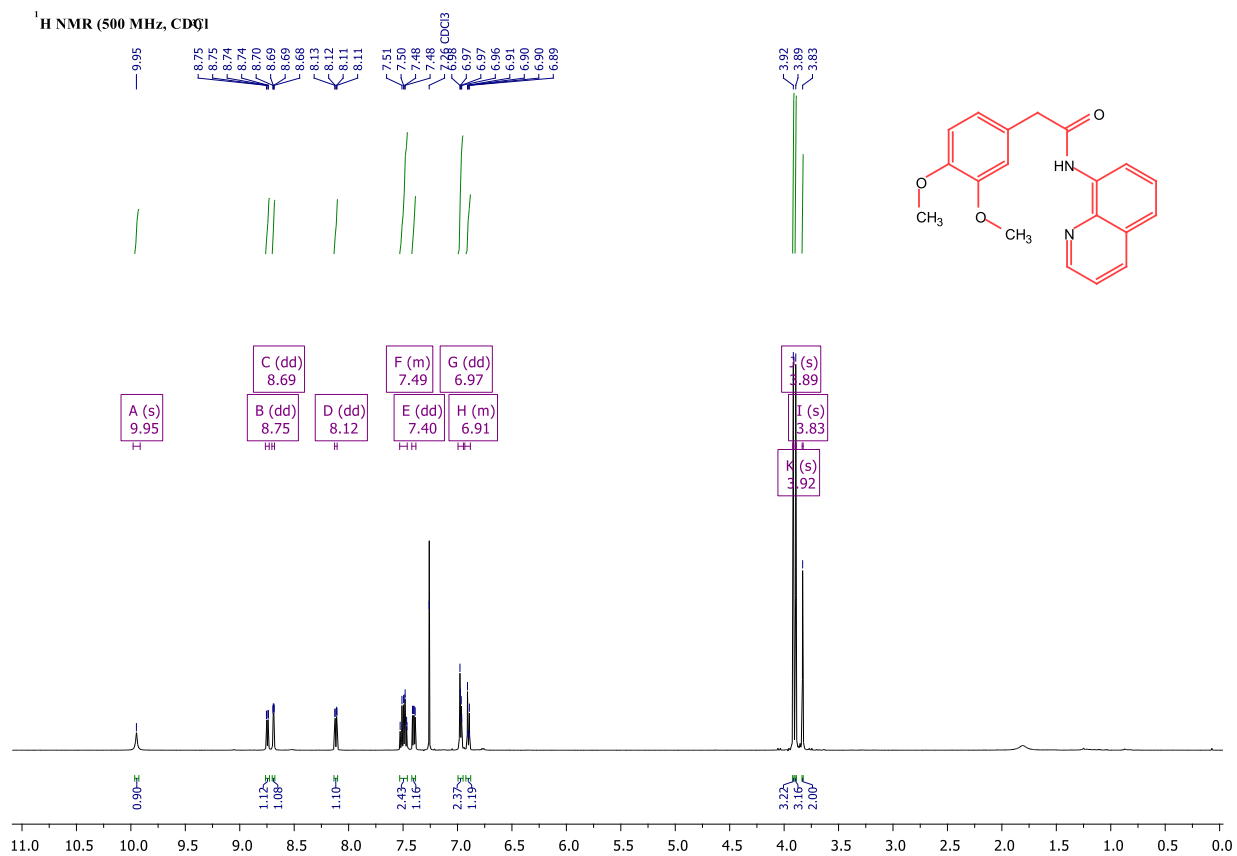
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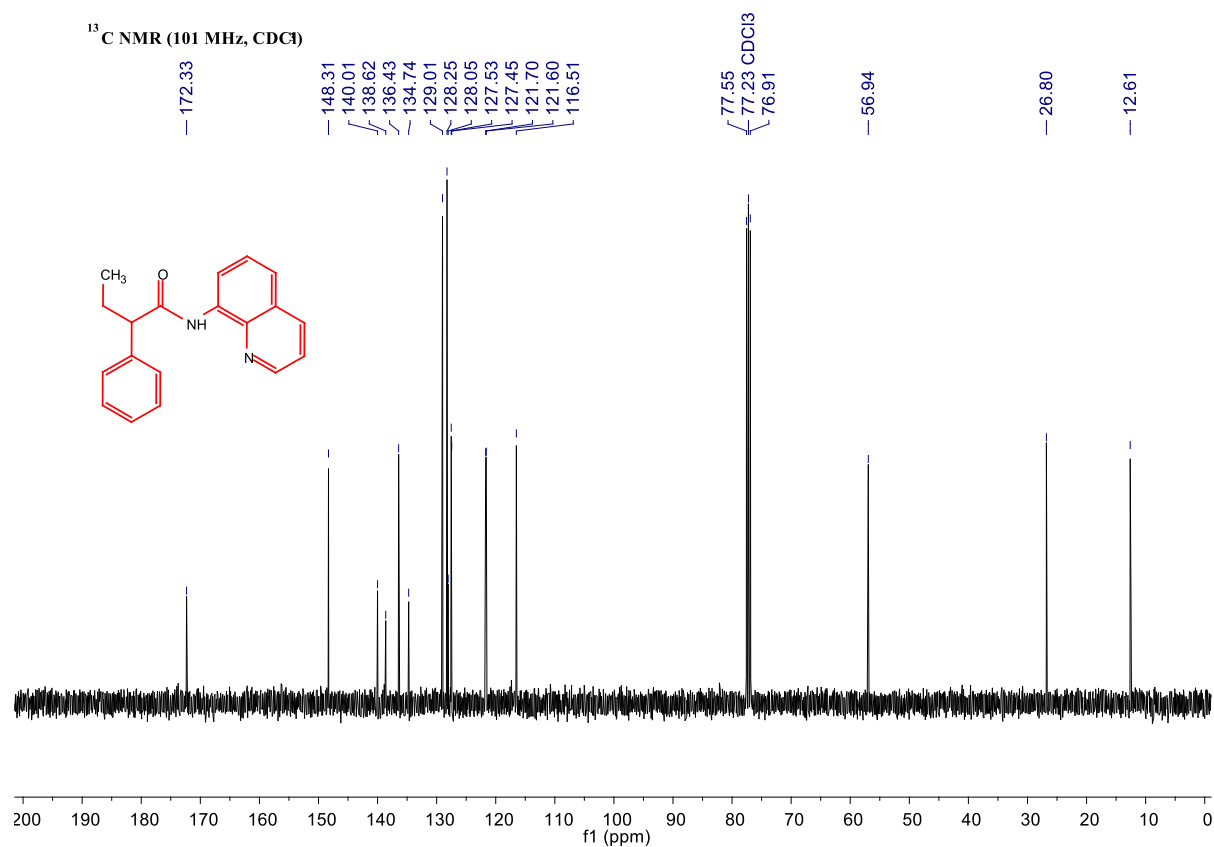
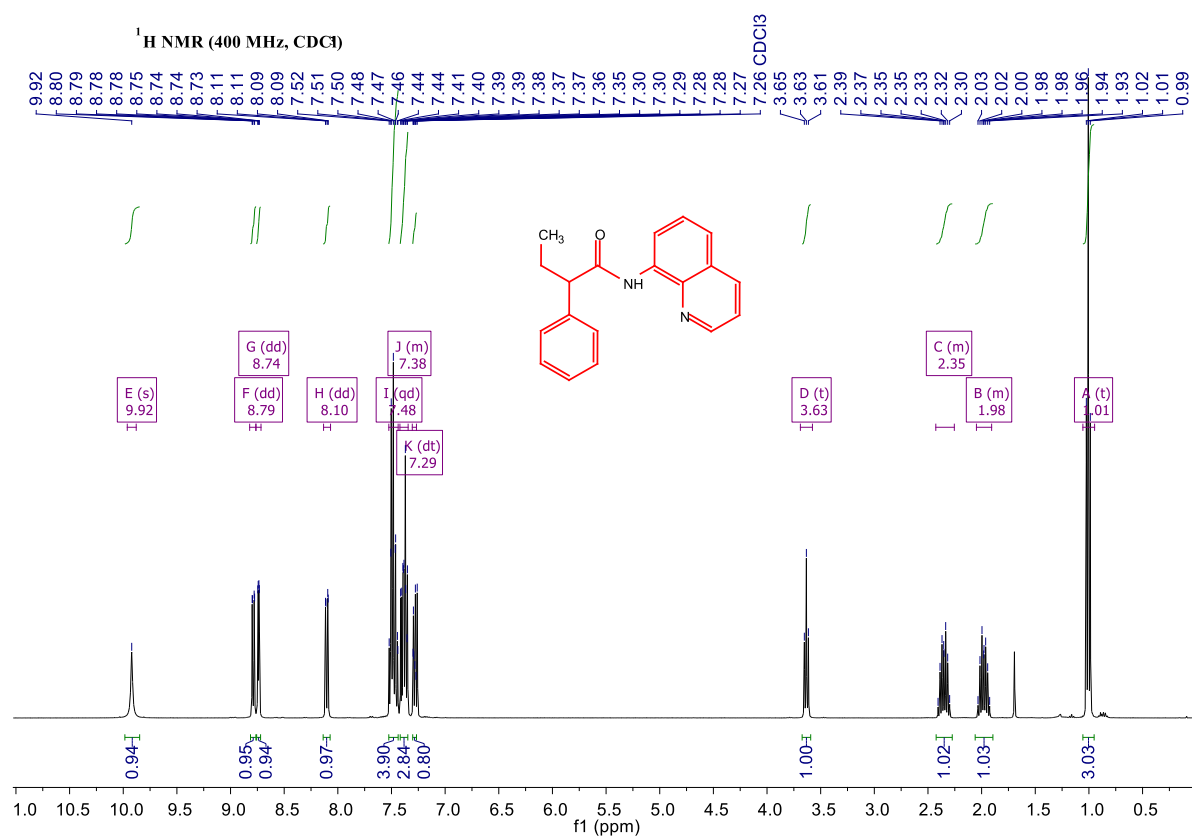




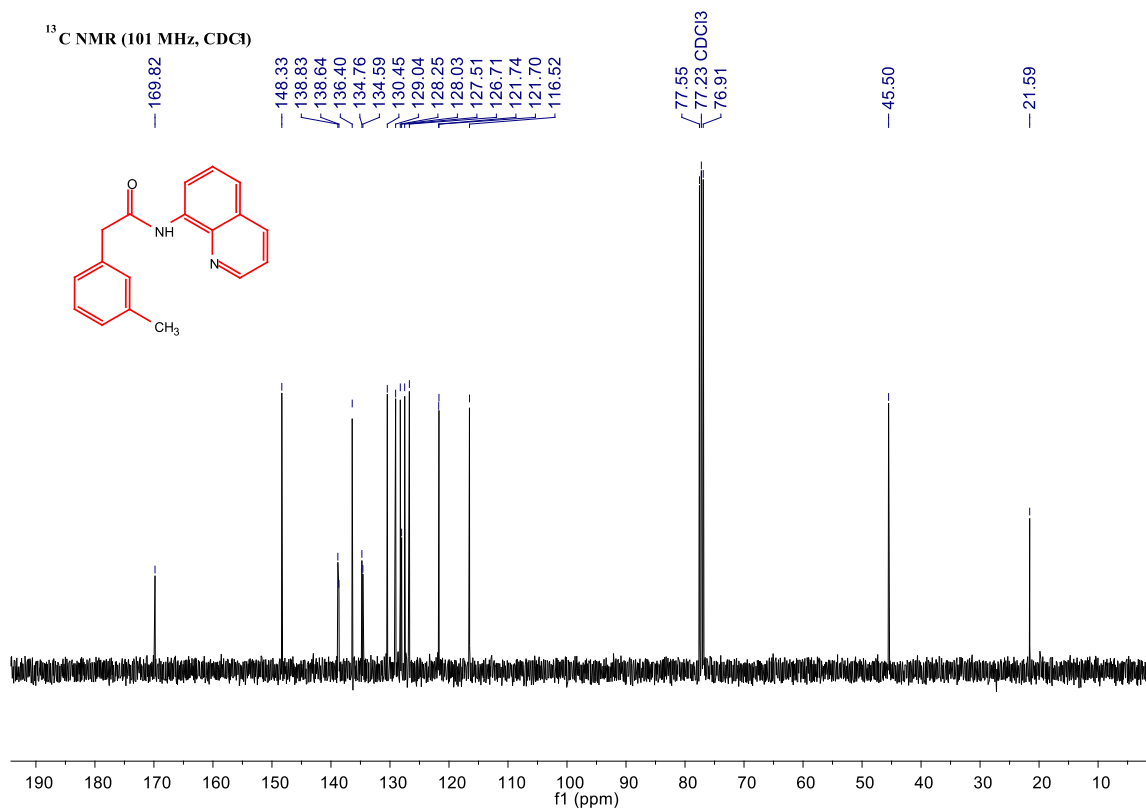
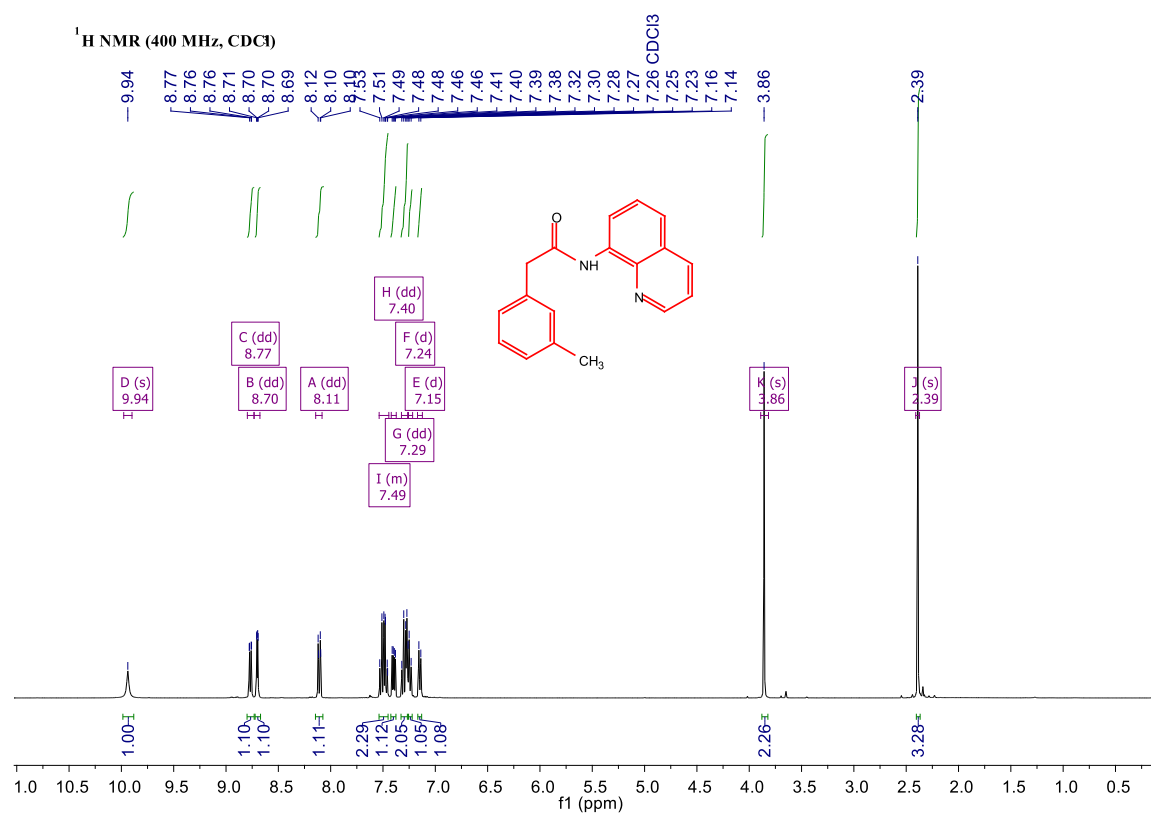
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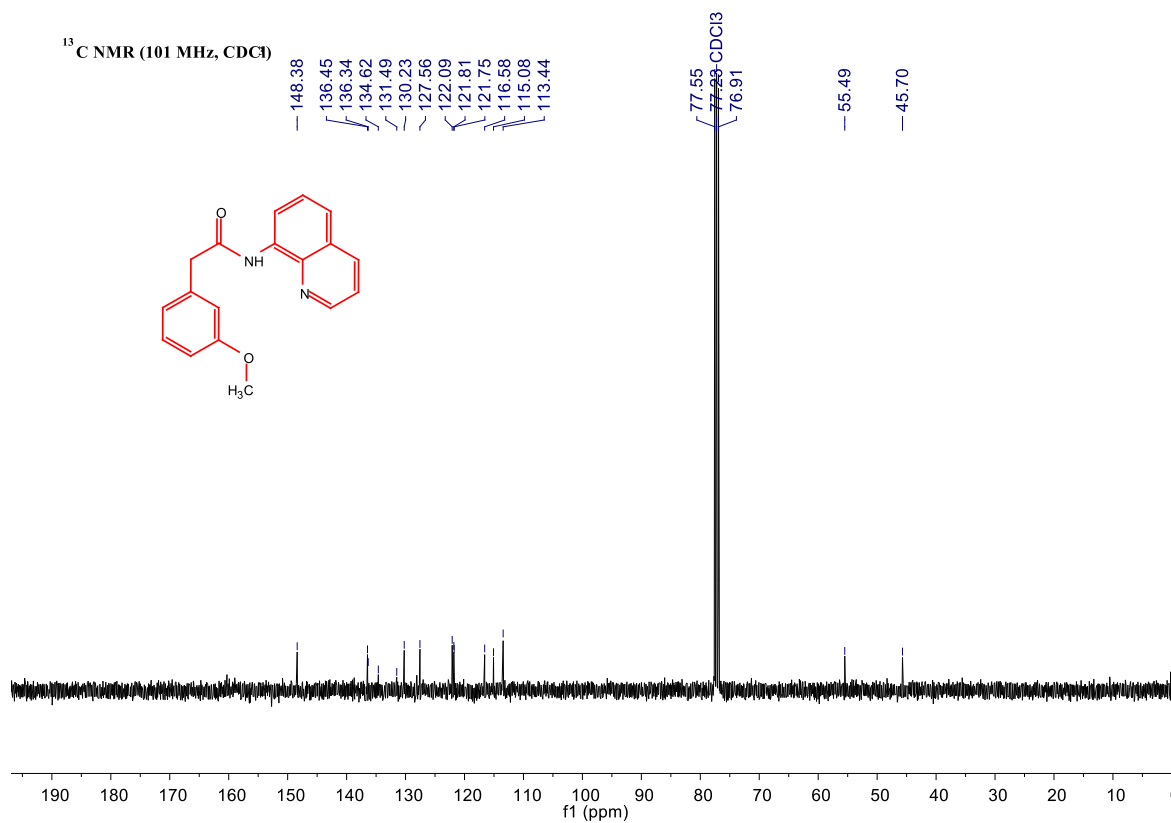
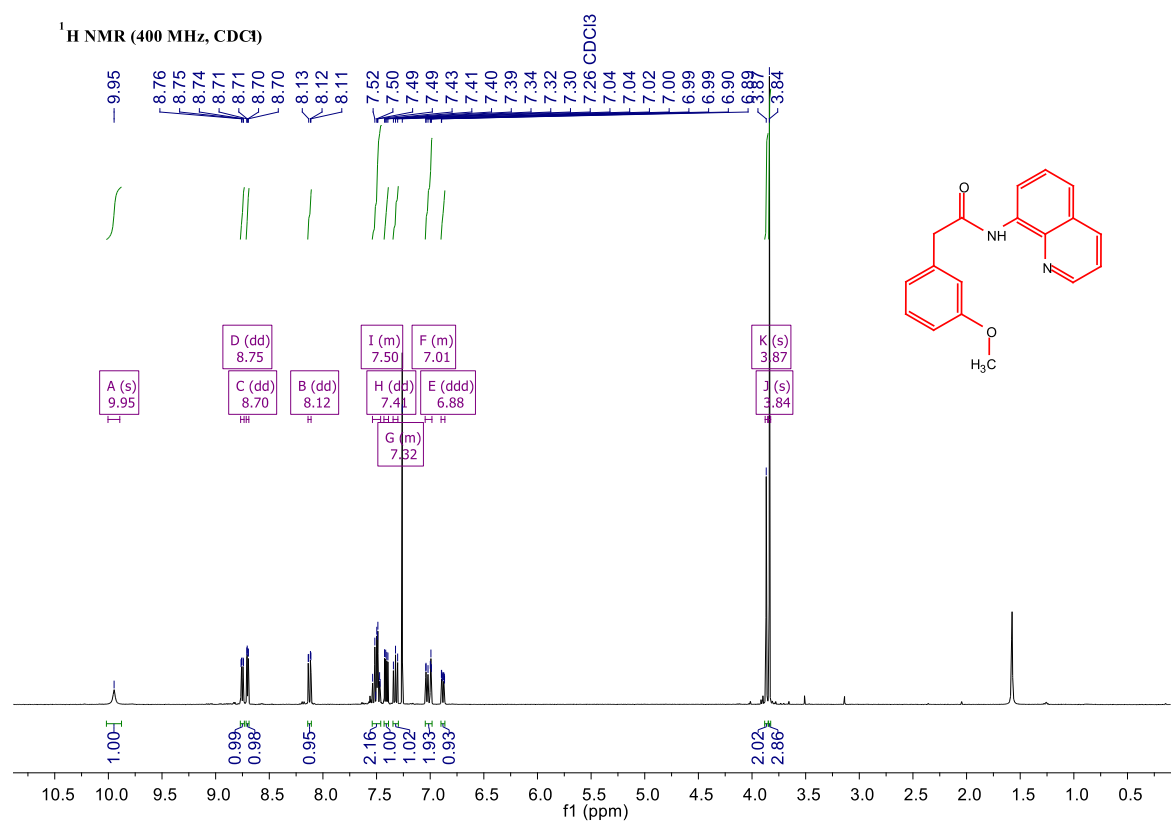
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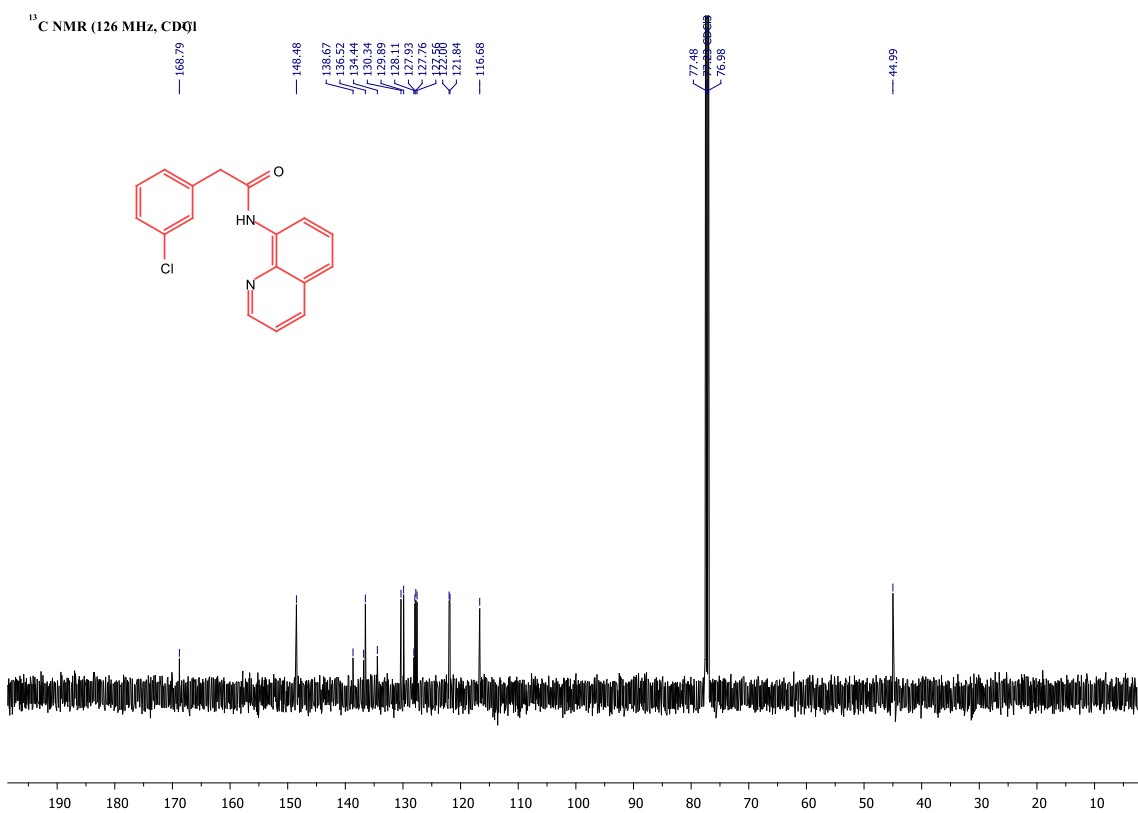
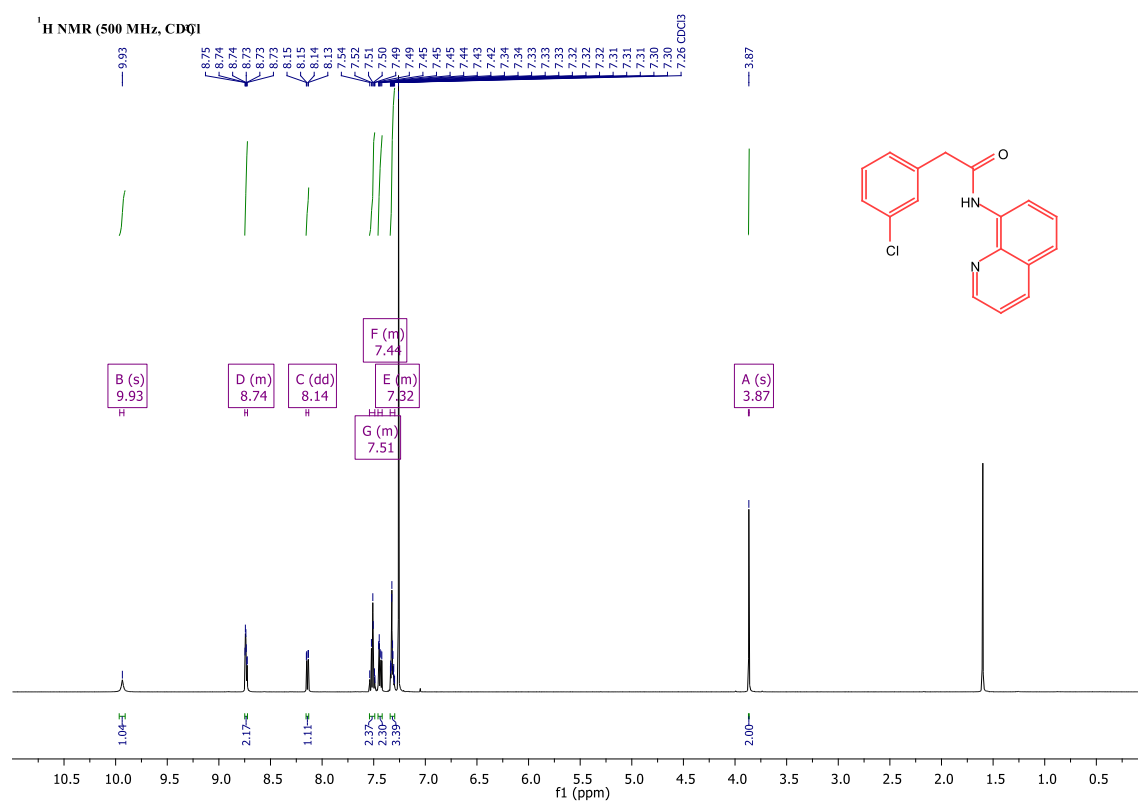
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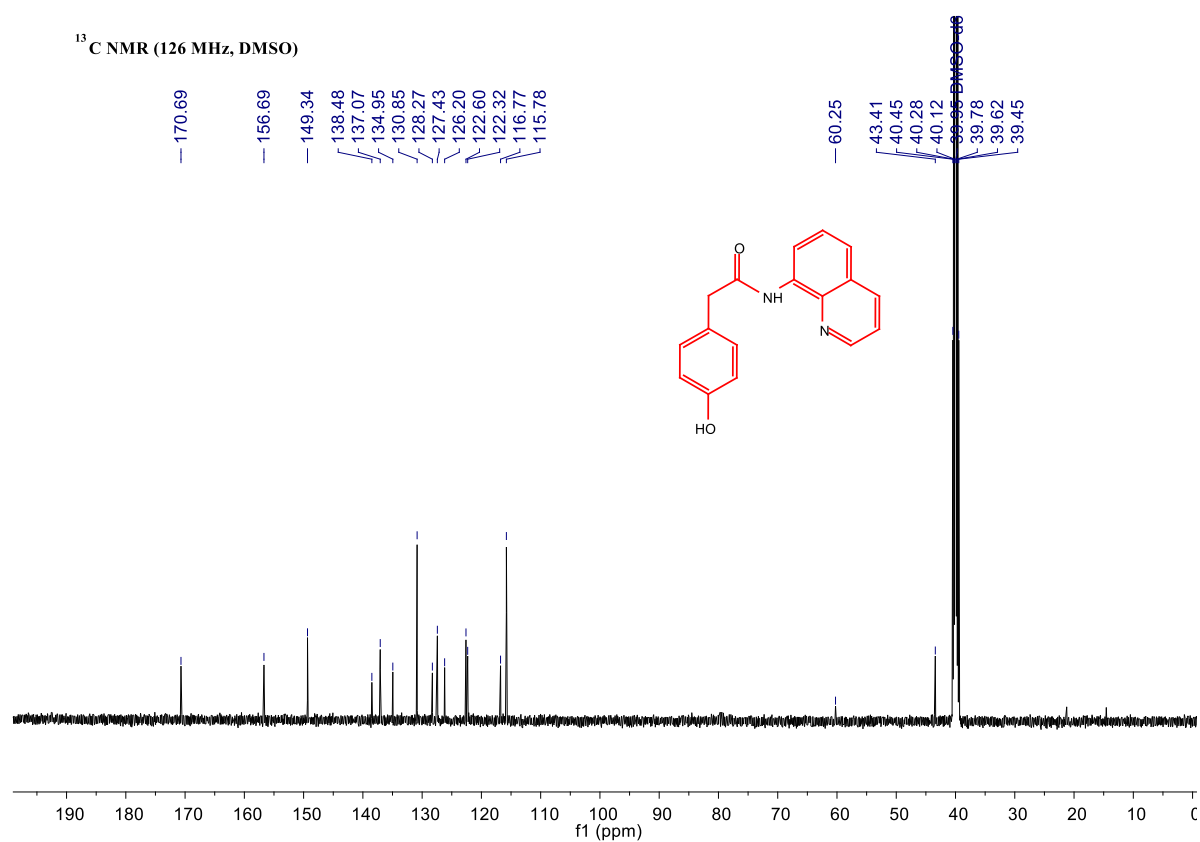
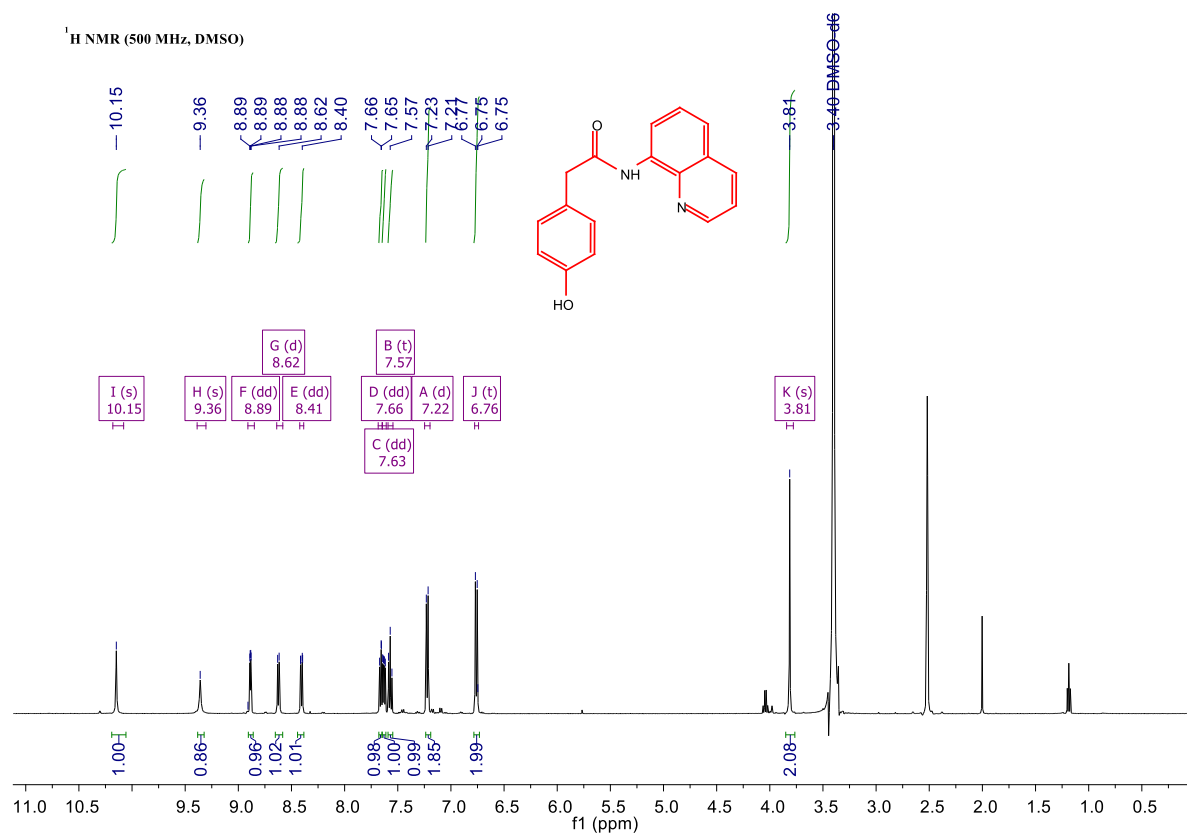
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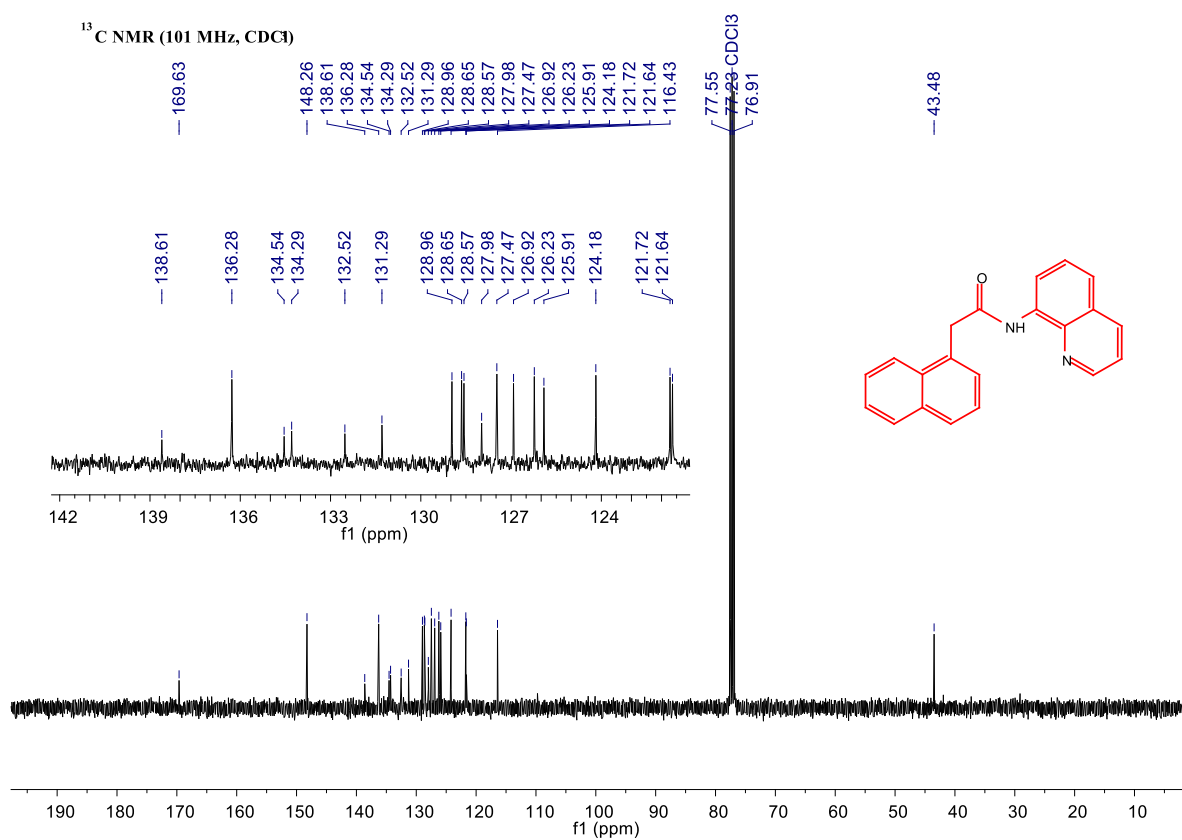
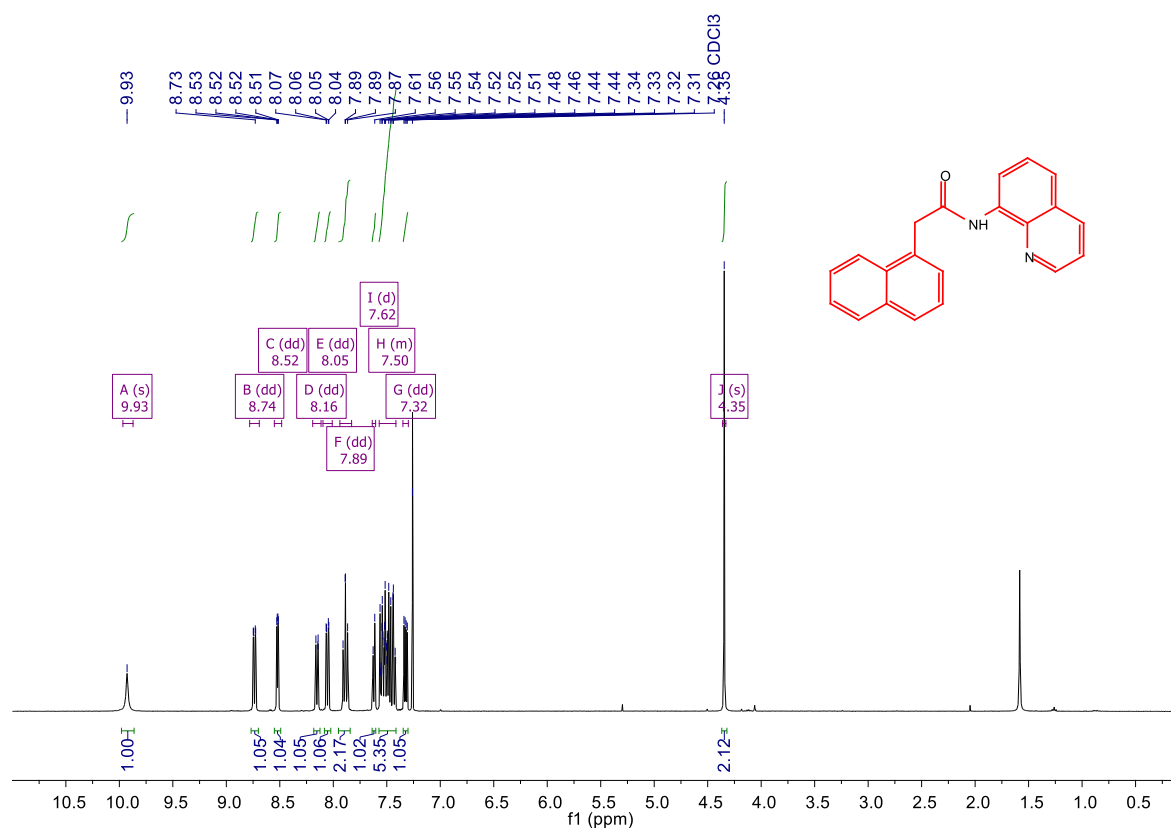
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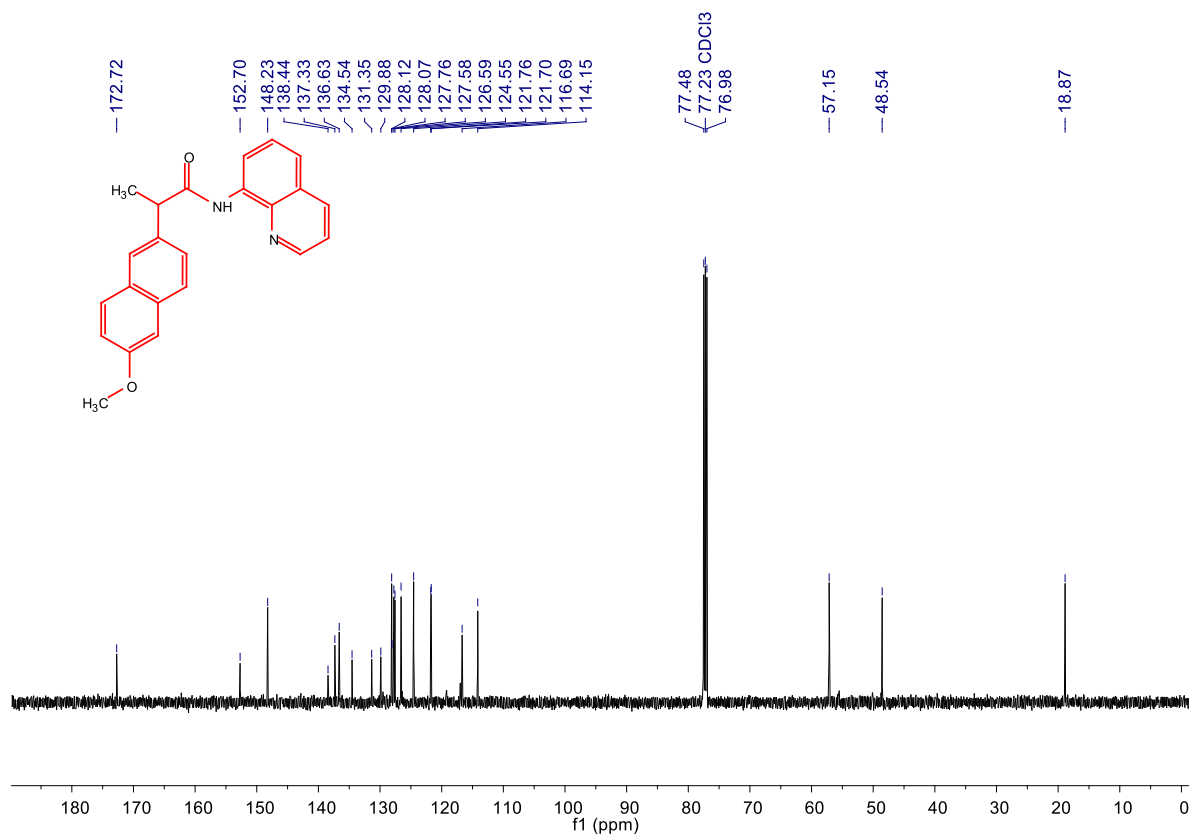
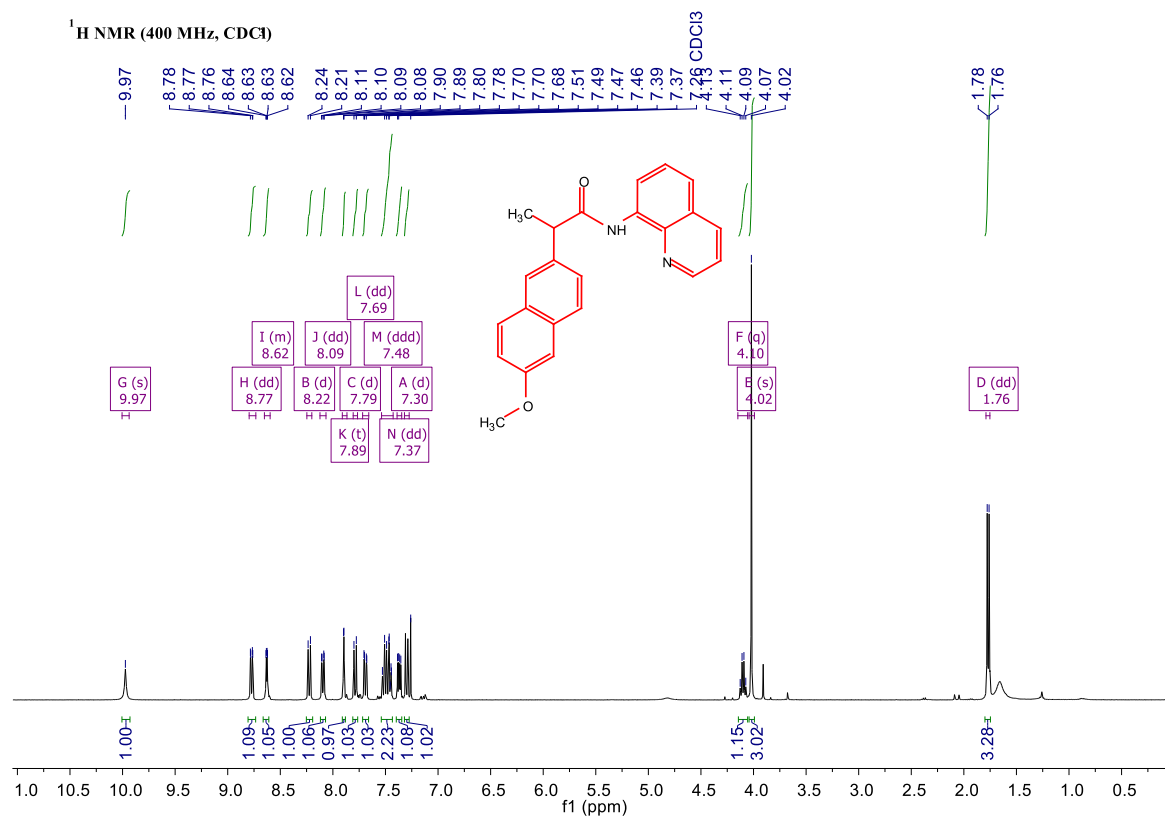
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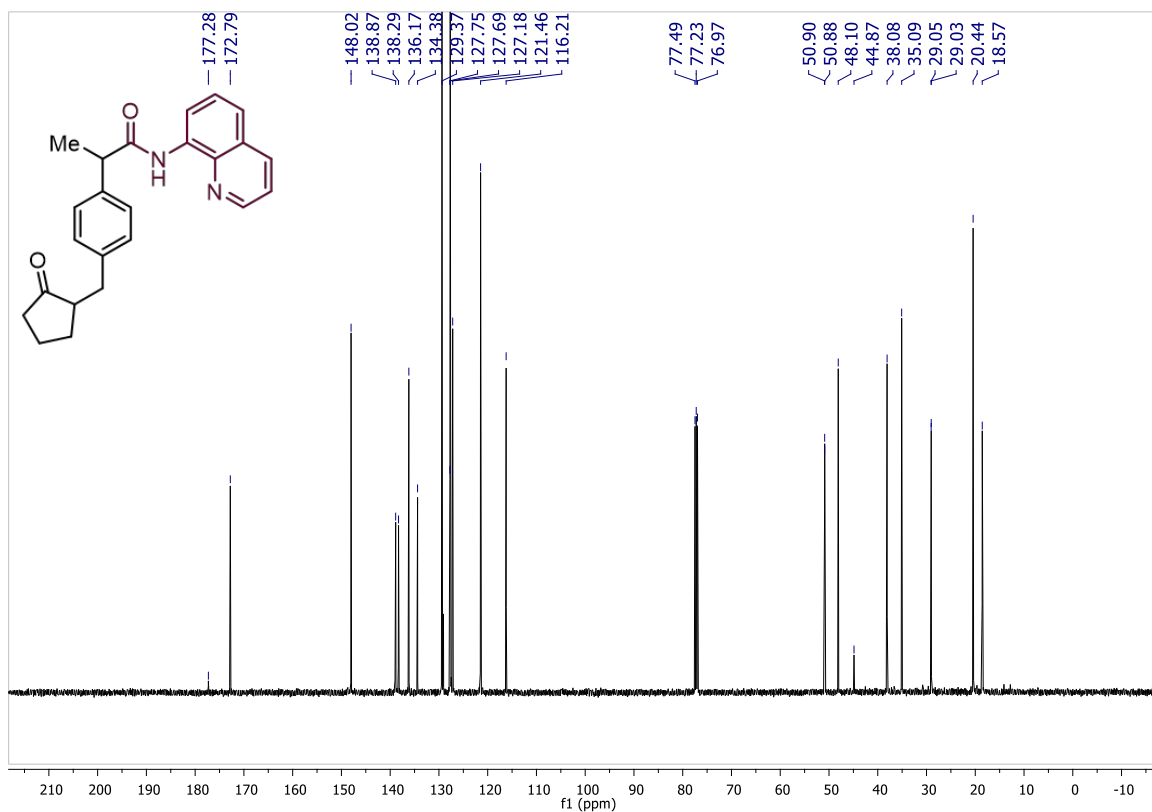
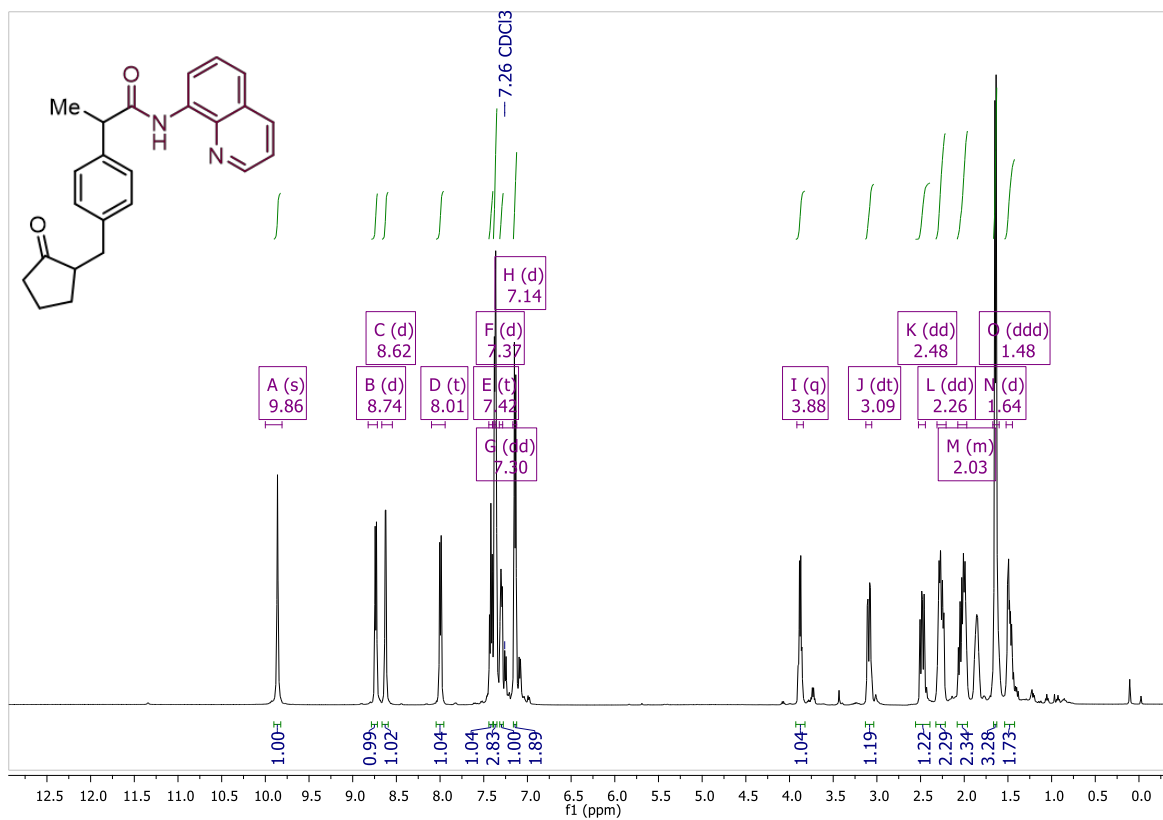
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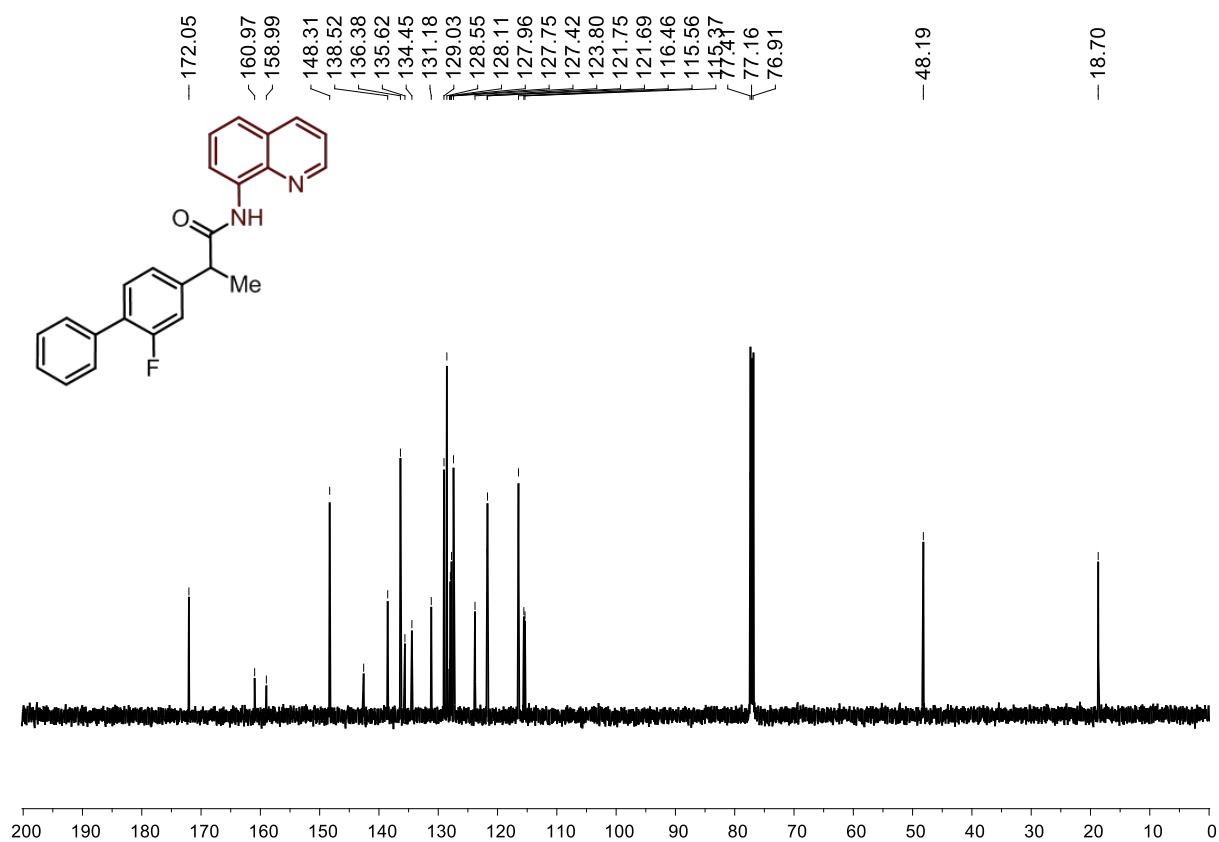
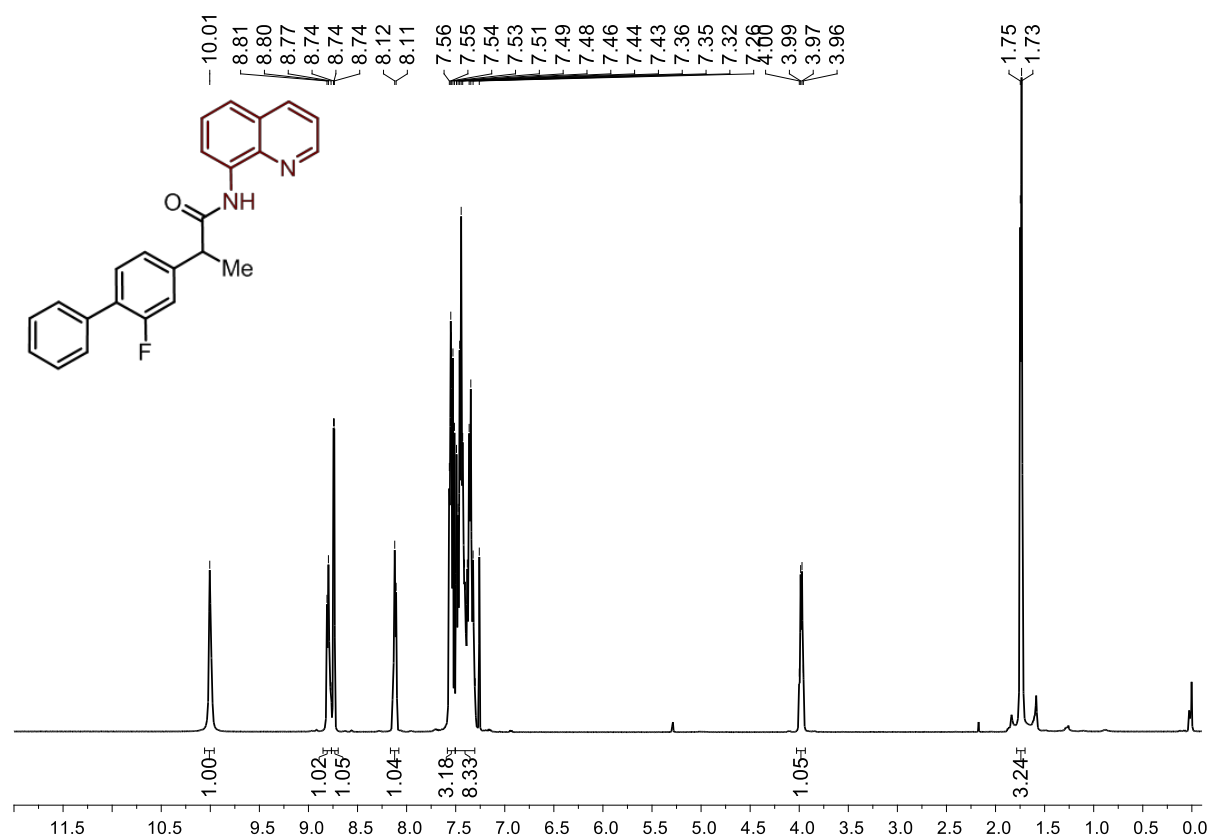
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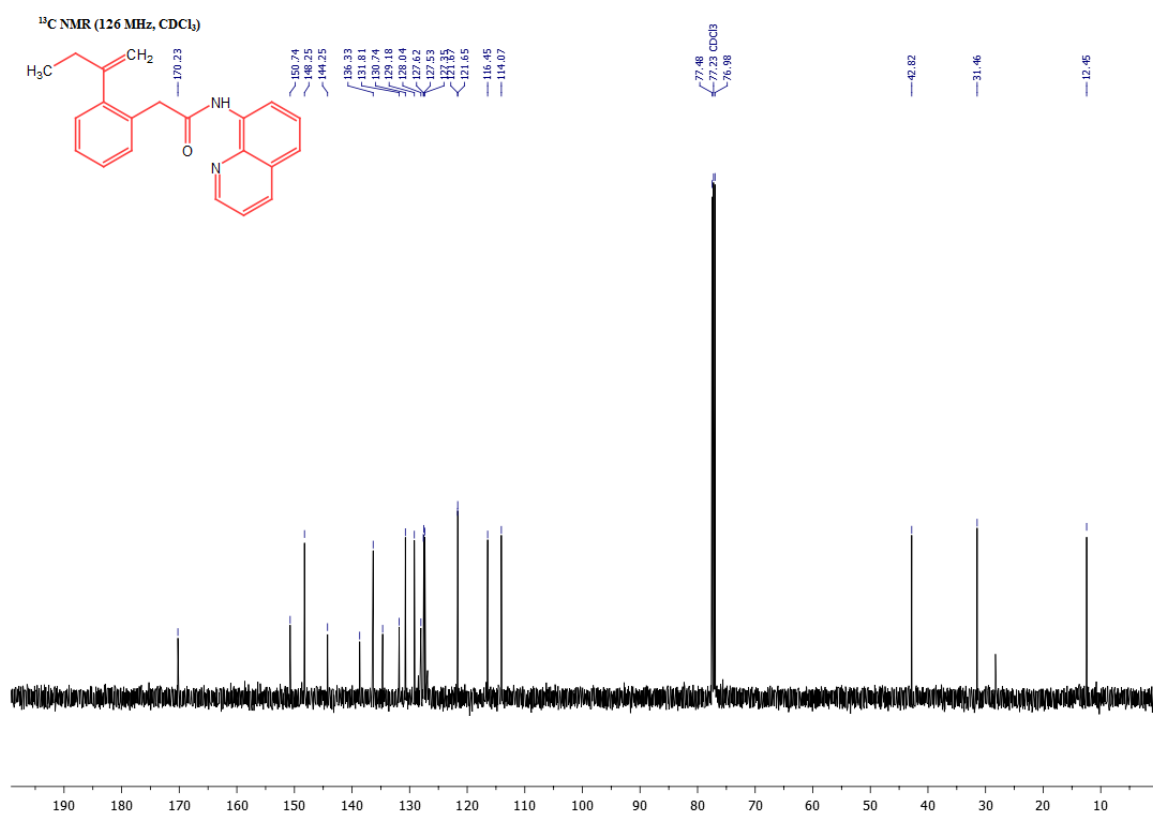
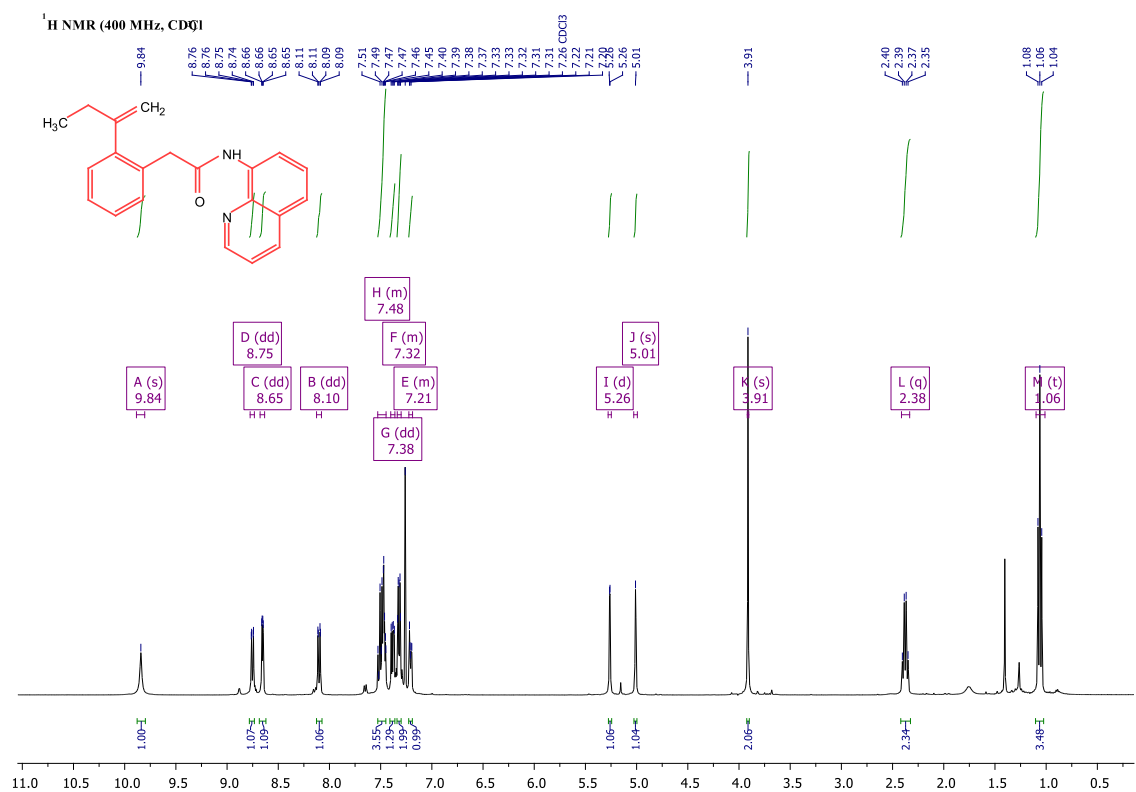
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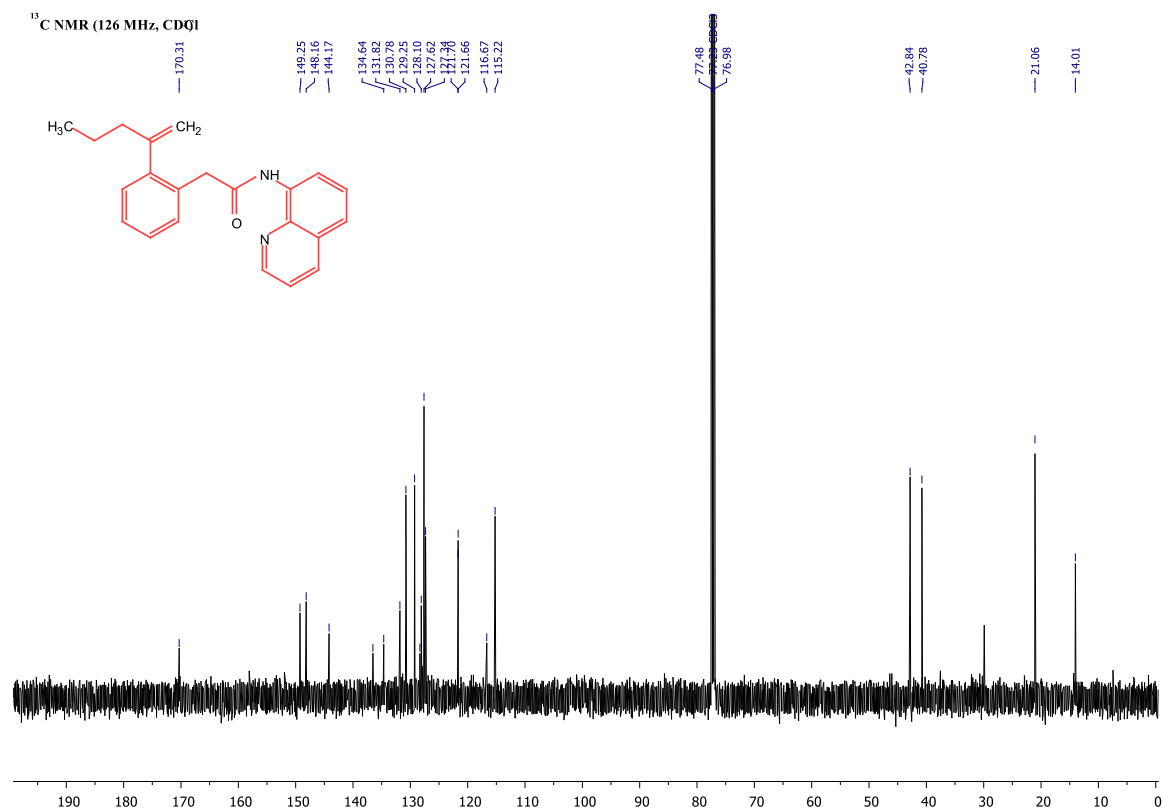
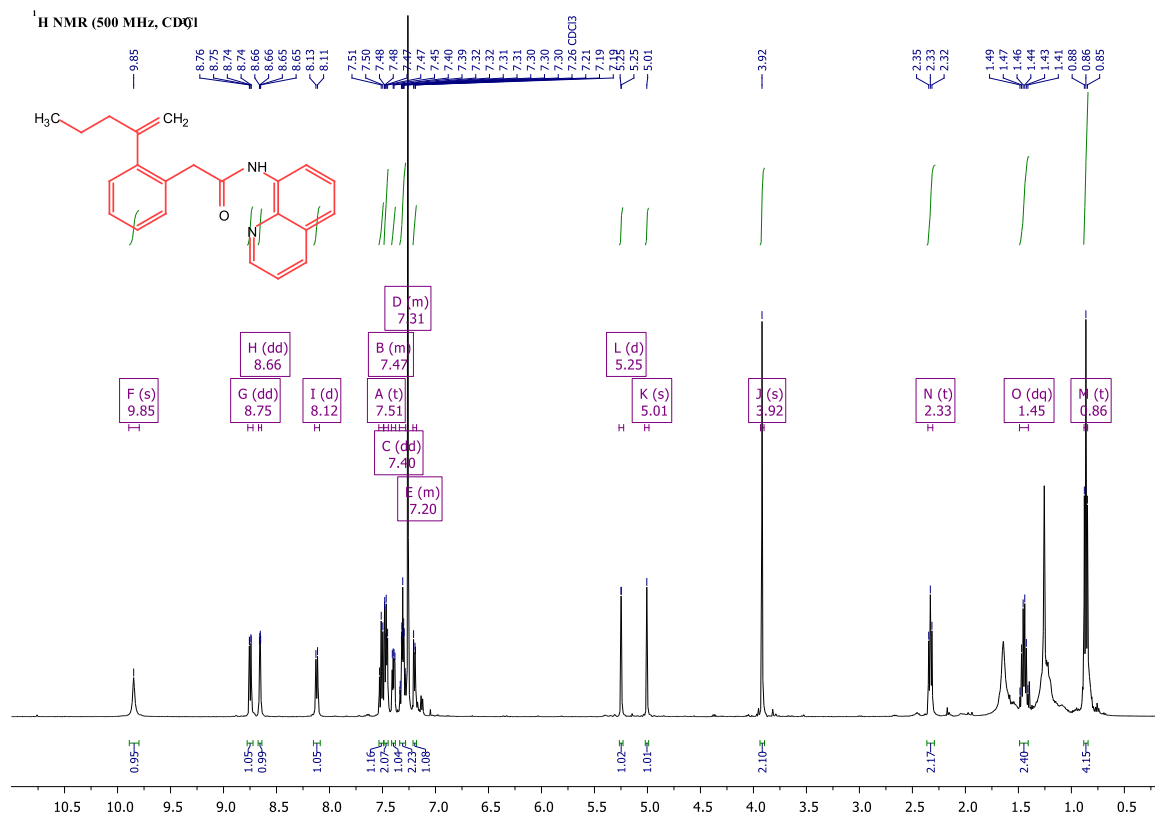
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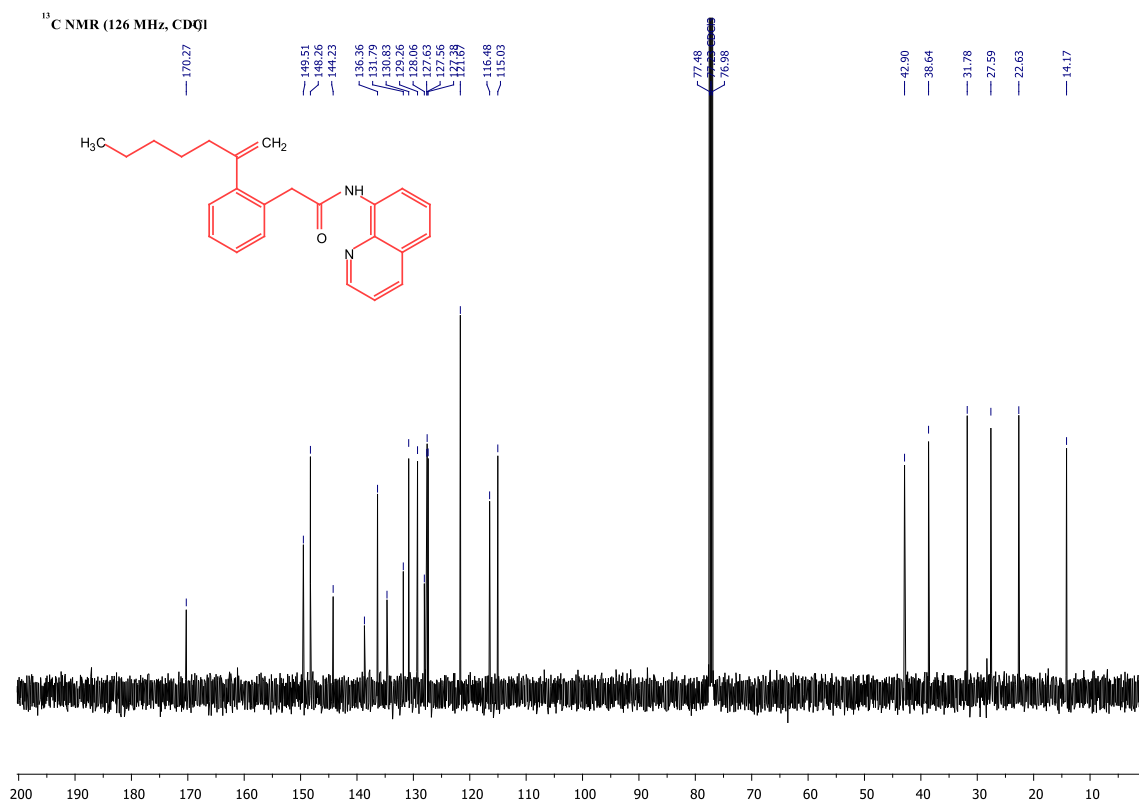
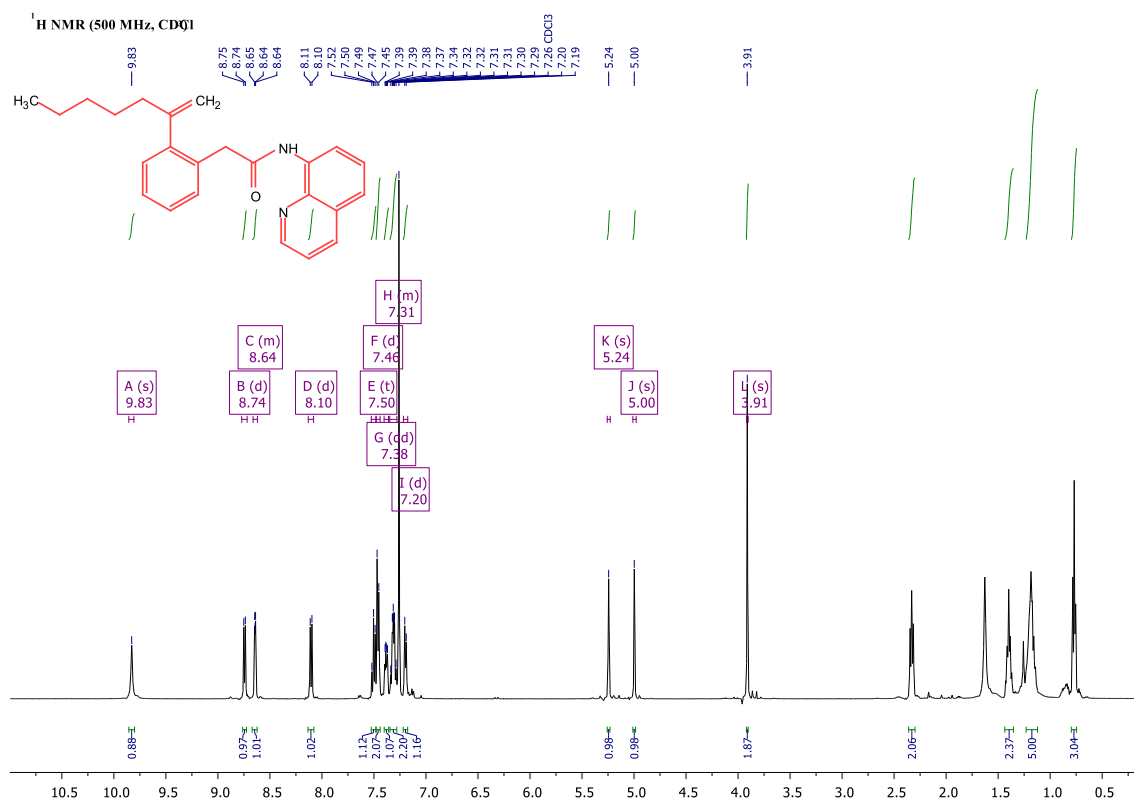
Olefinated product: Scheme 2, entry 3a:



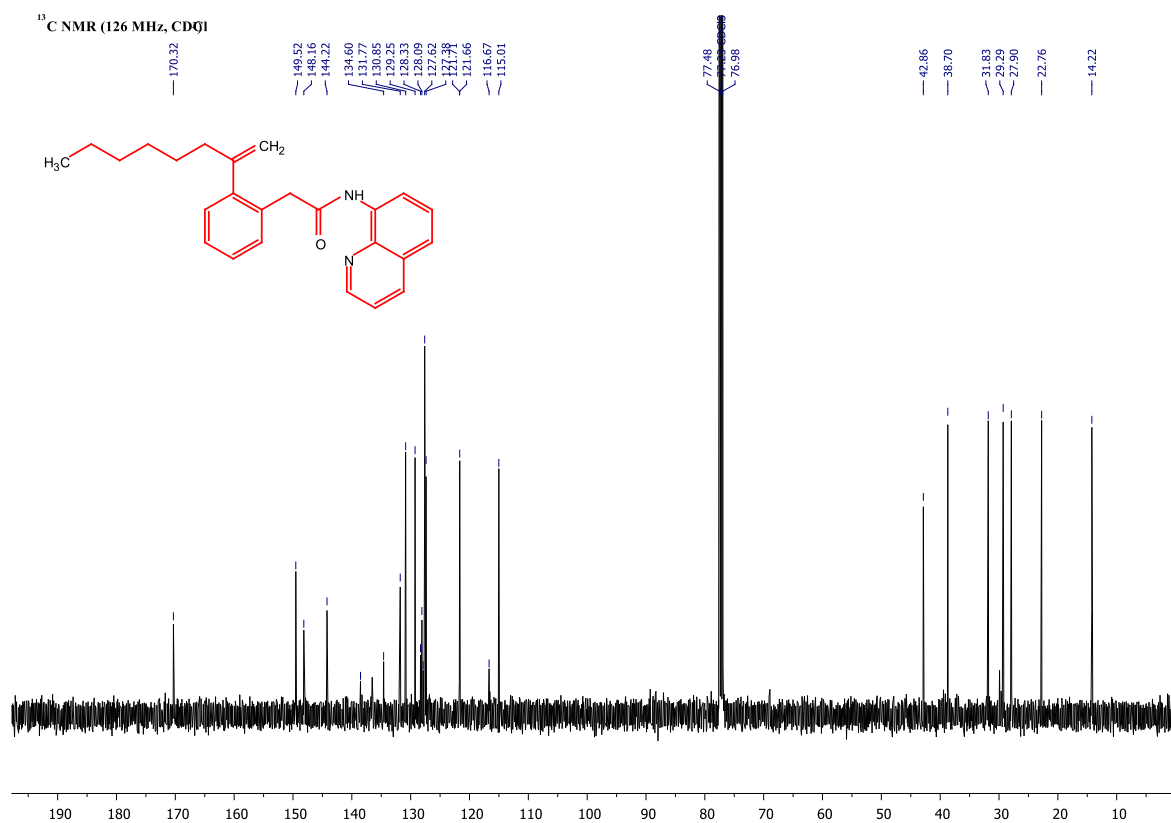
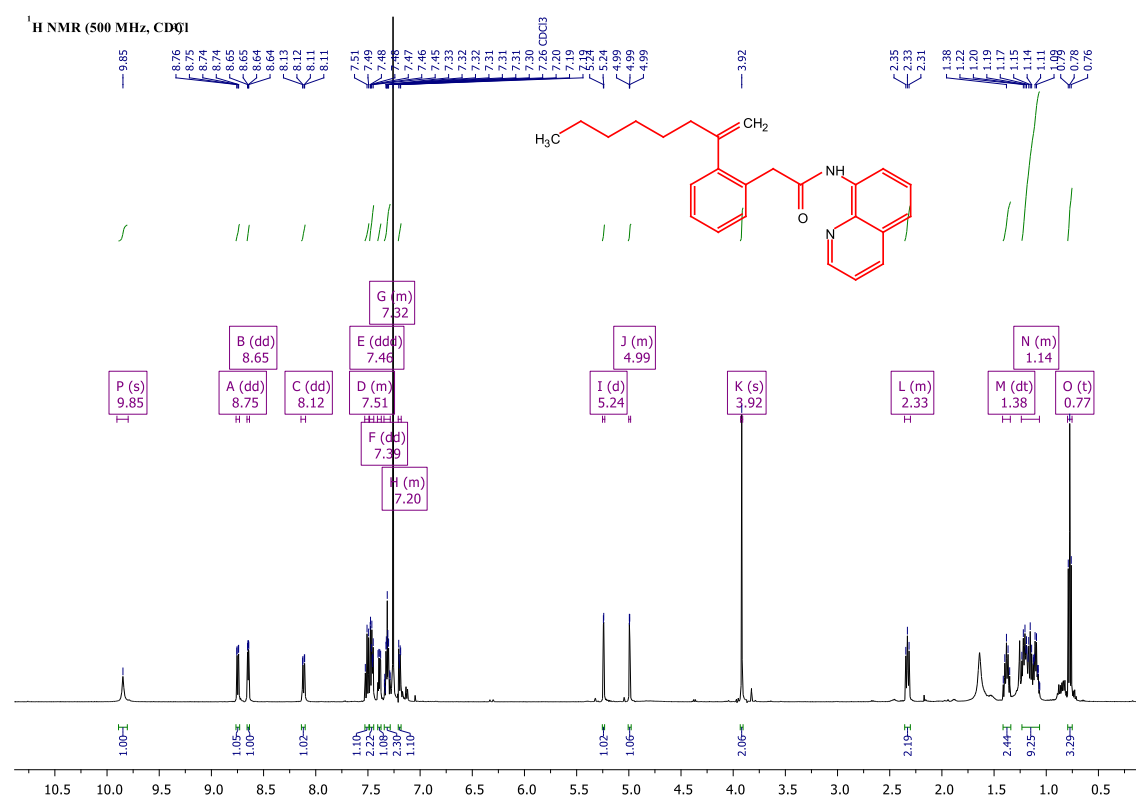
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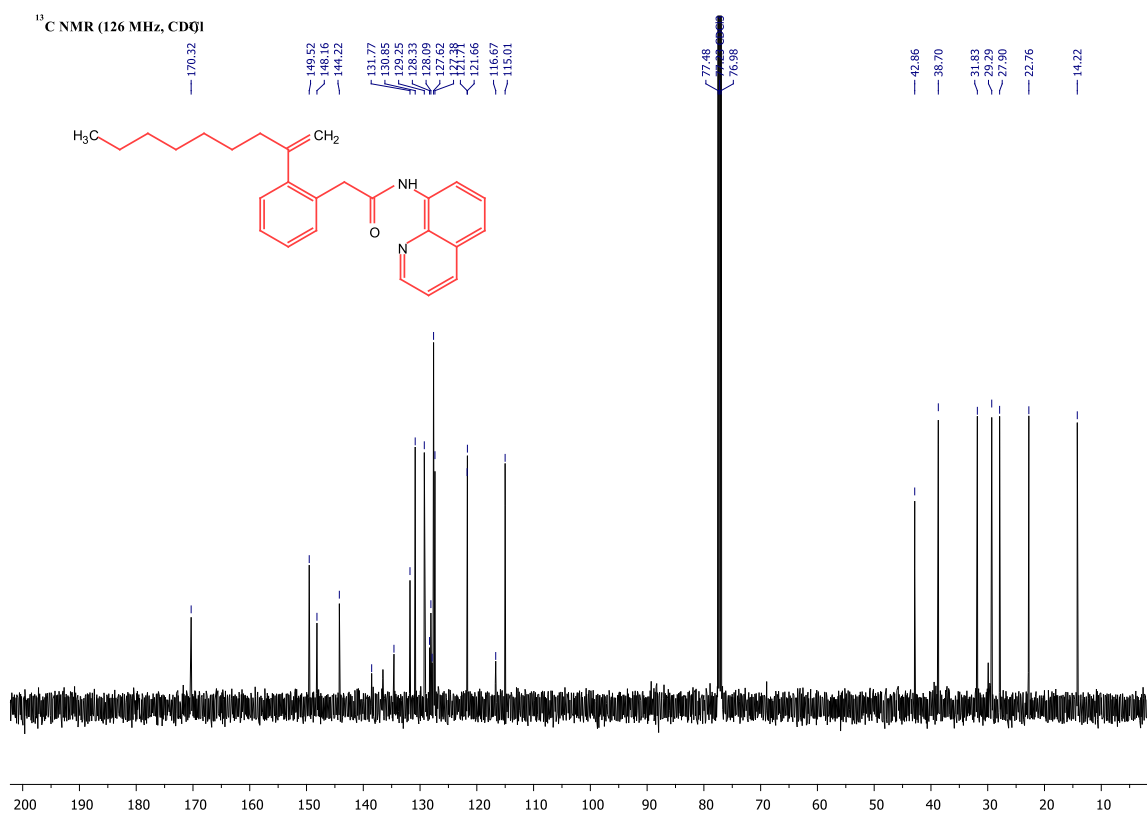
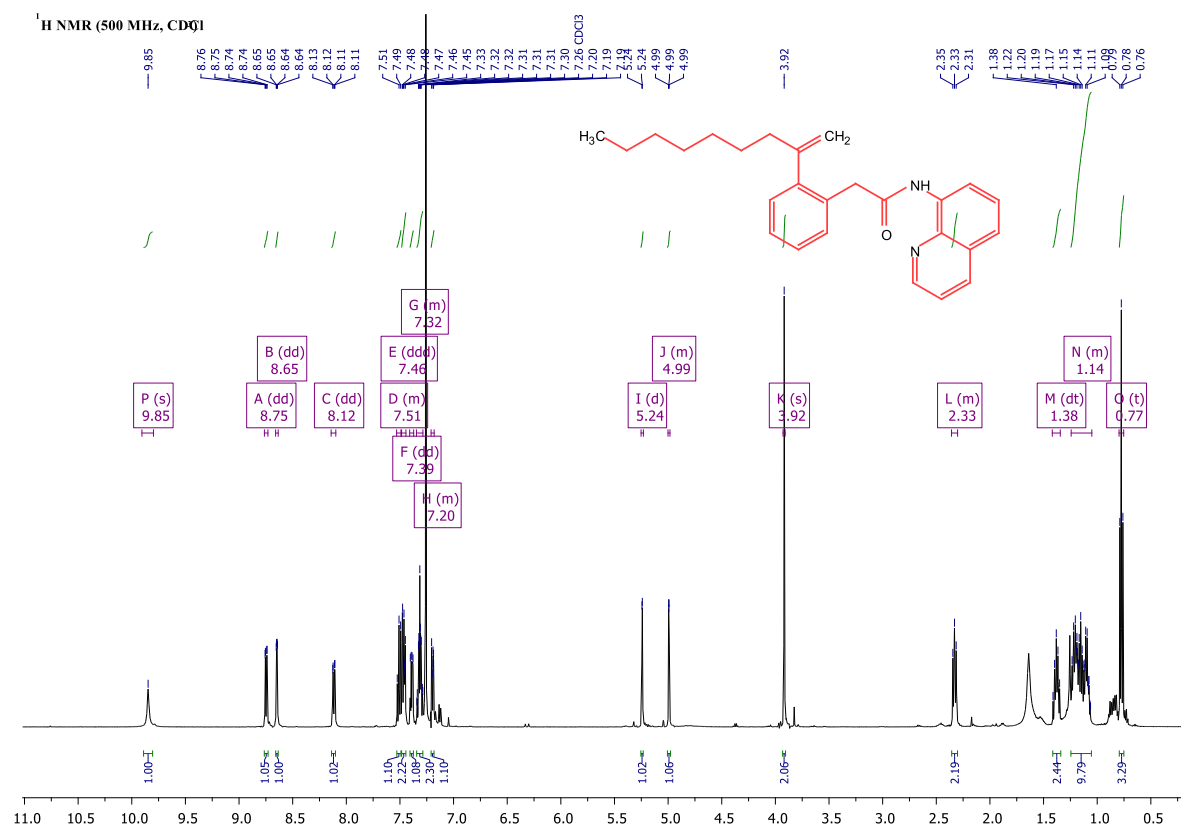
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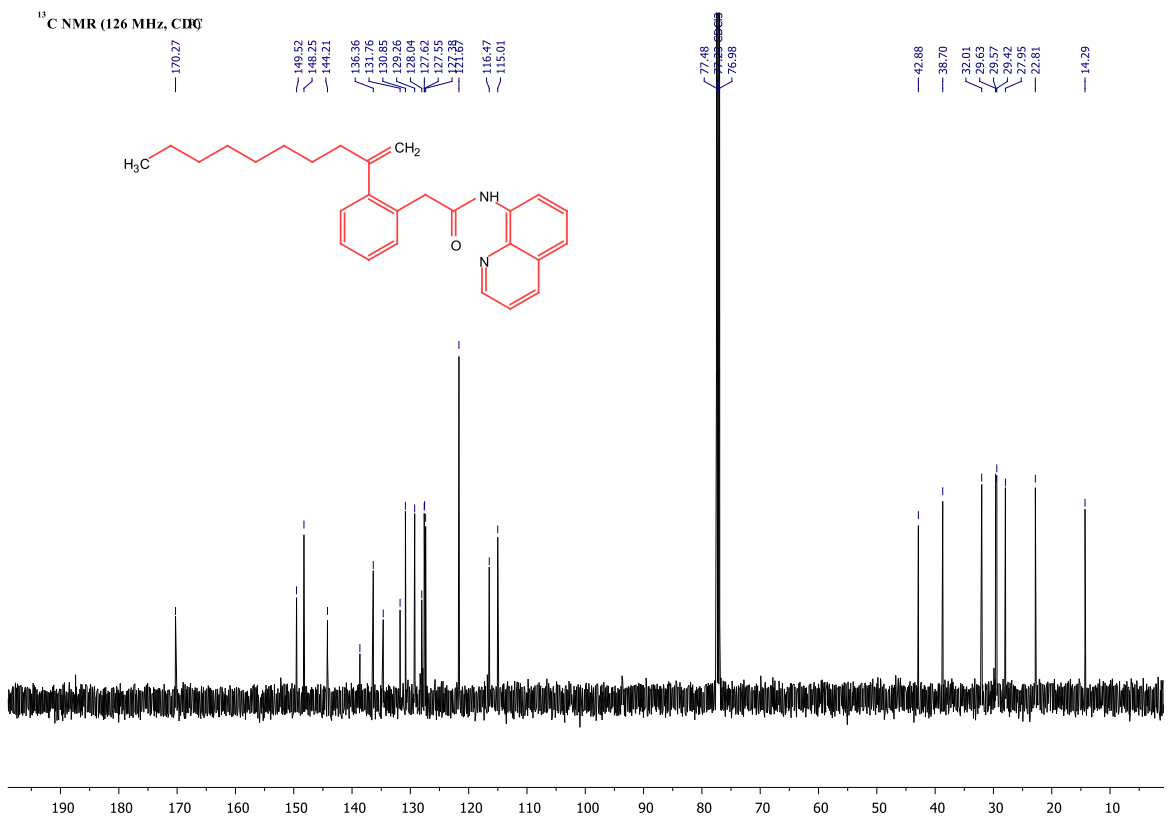
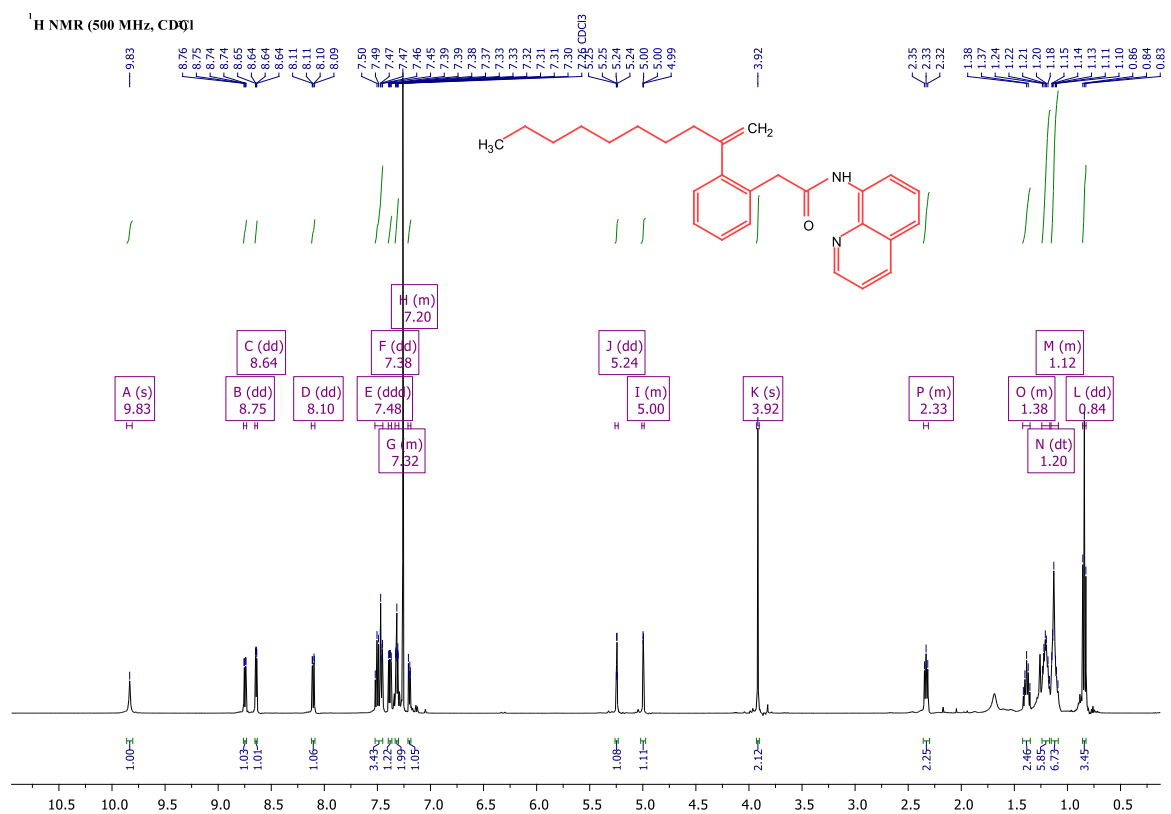
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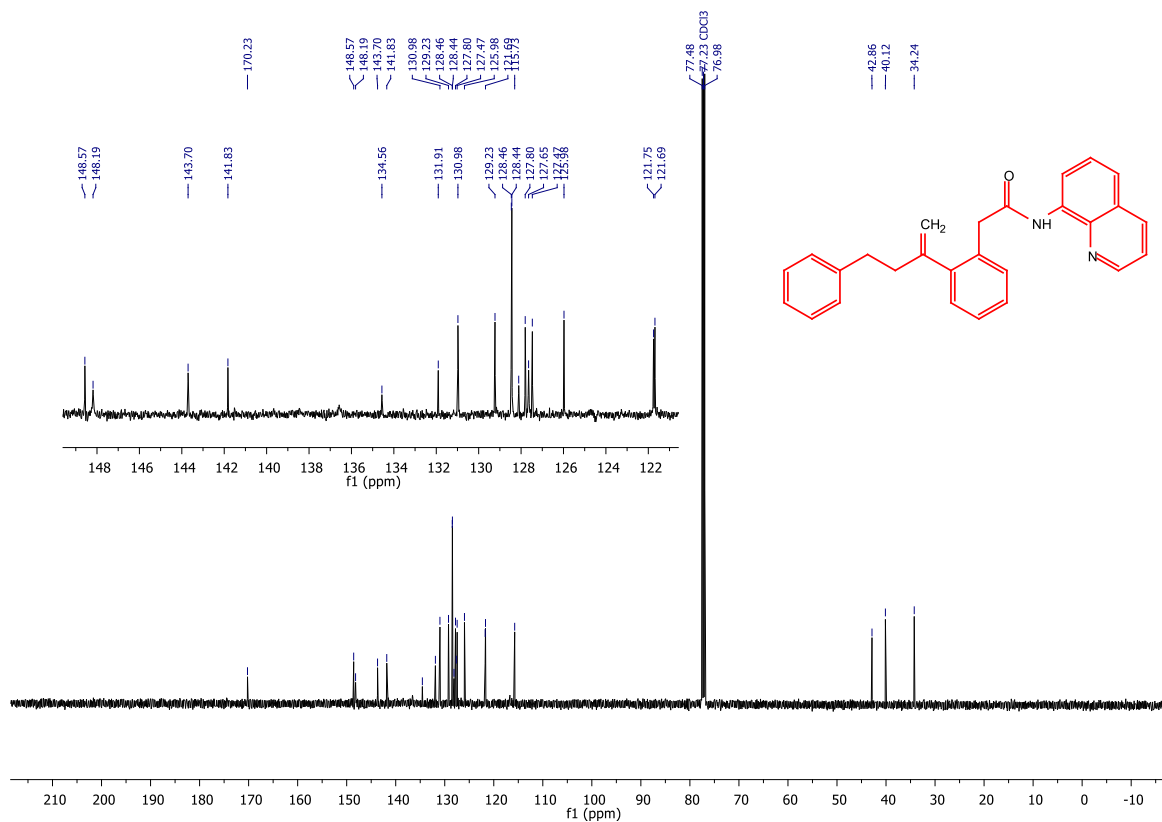
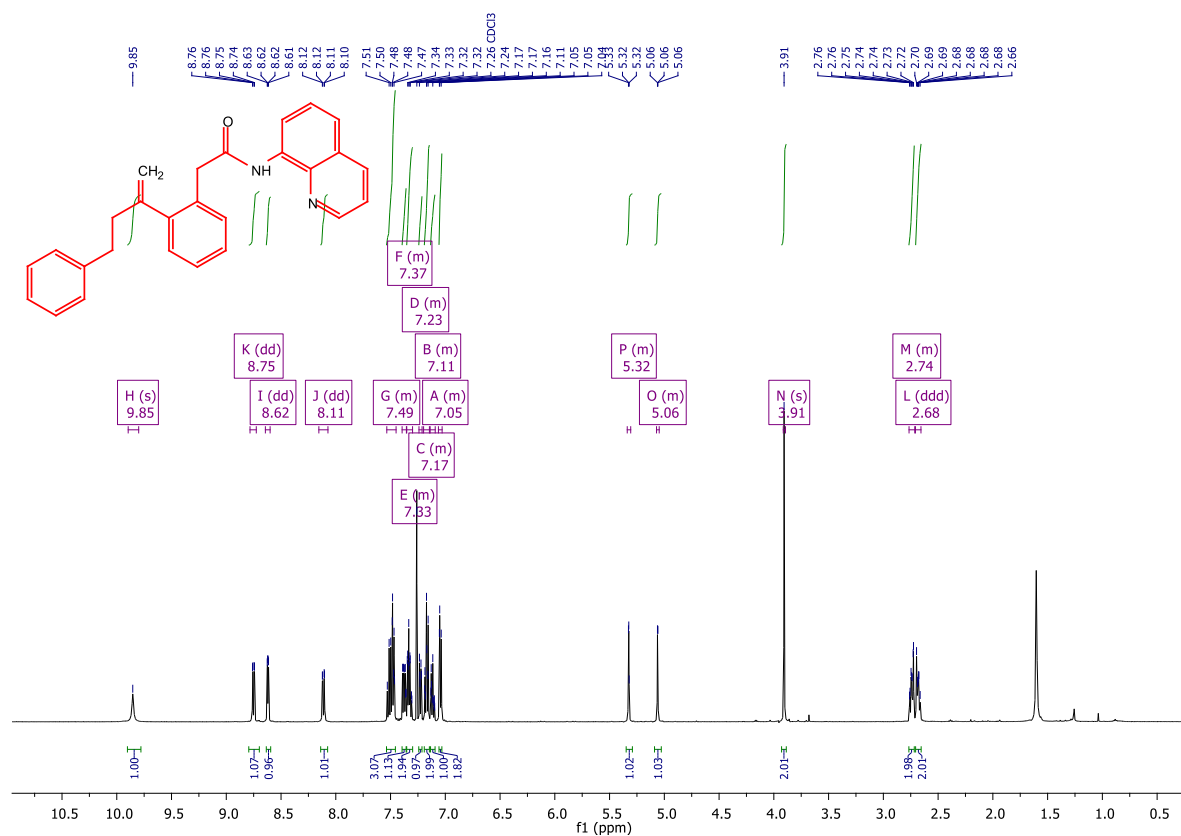
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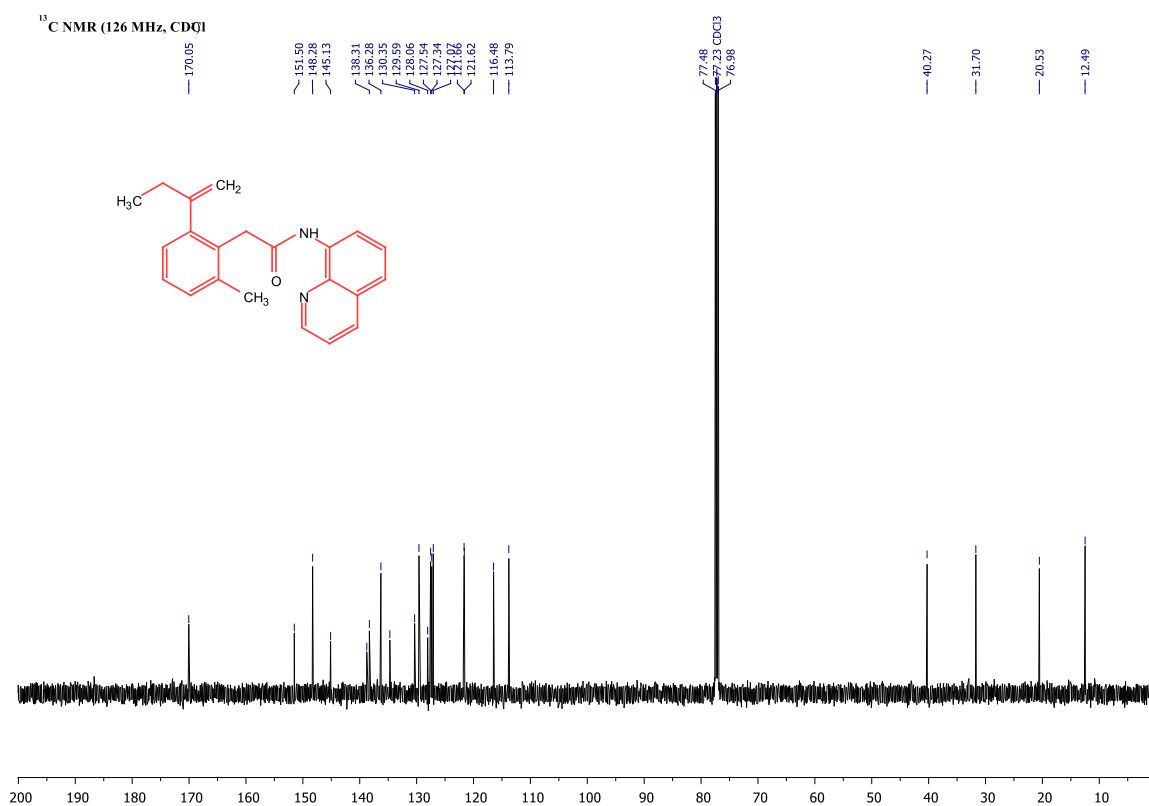
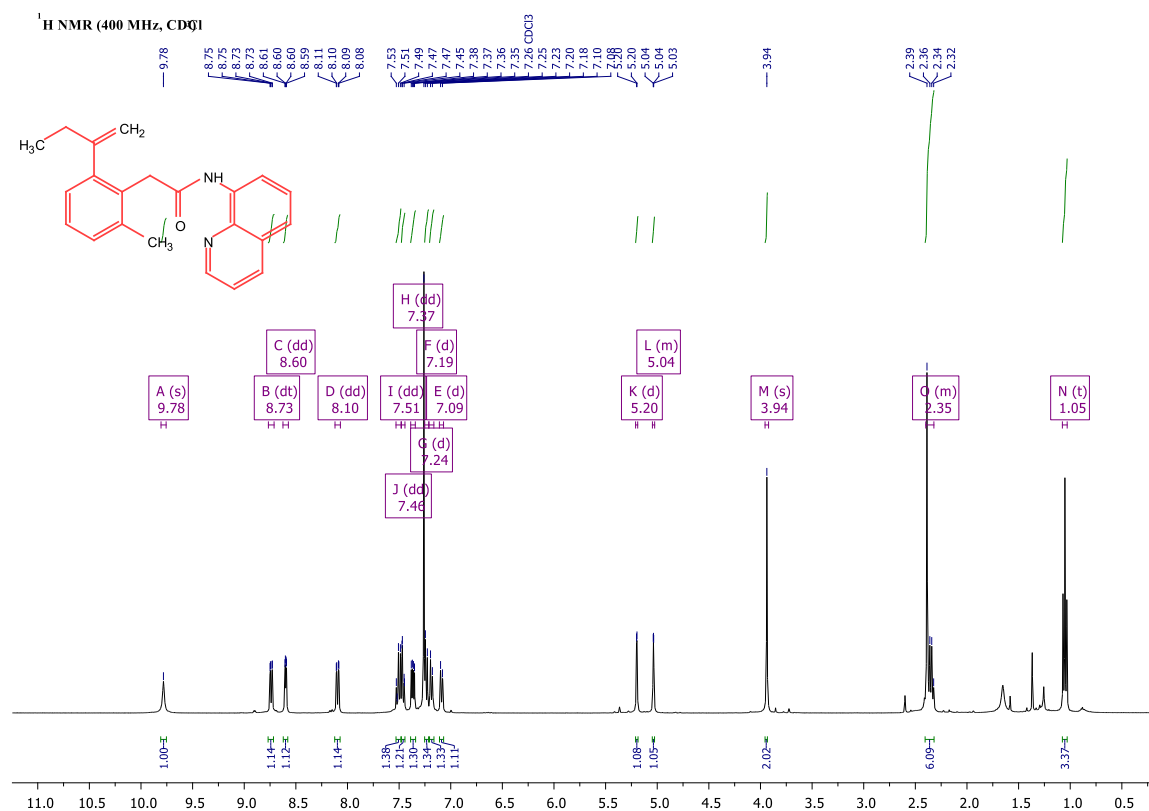
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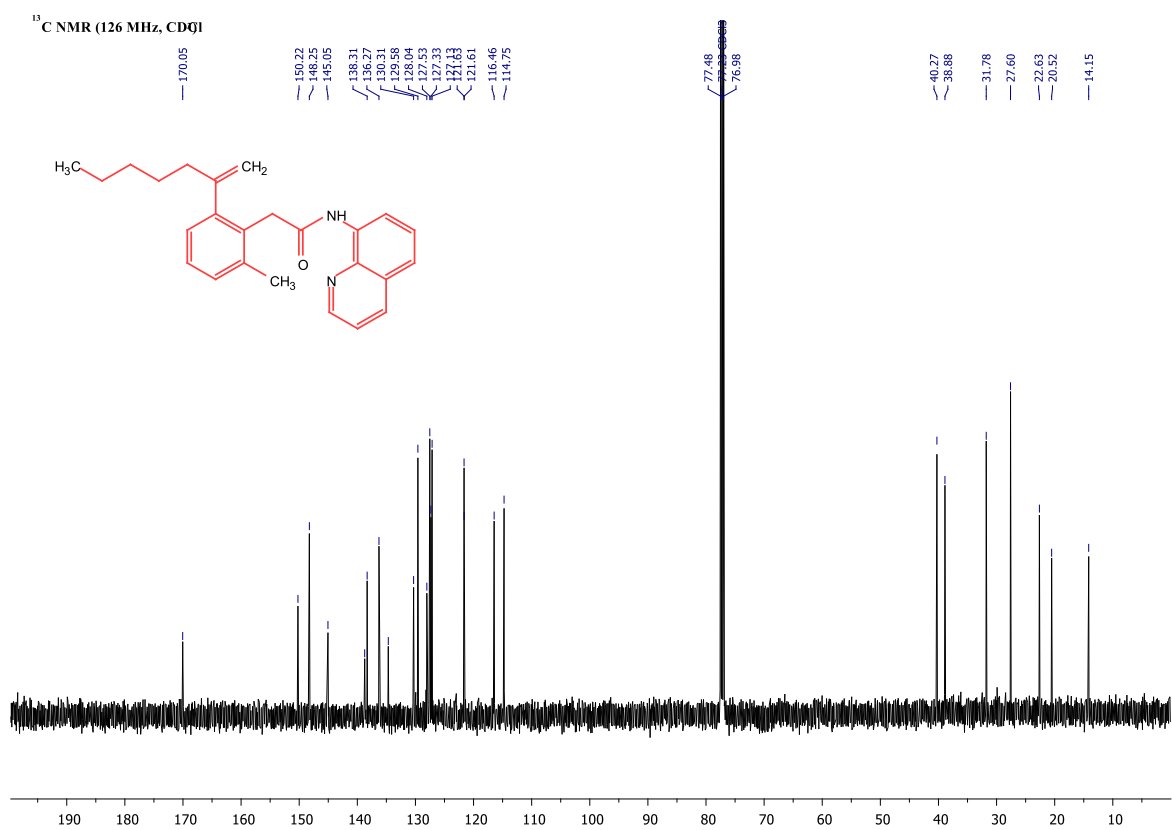
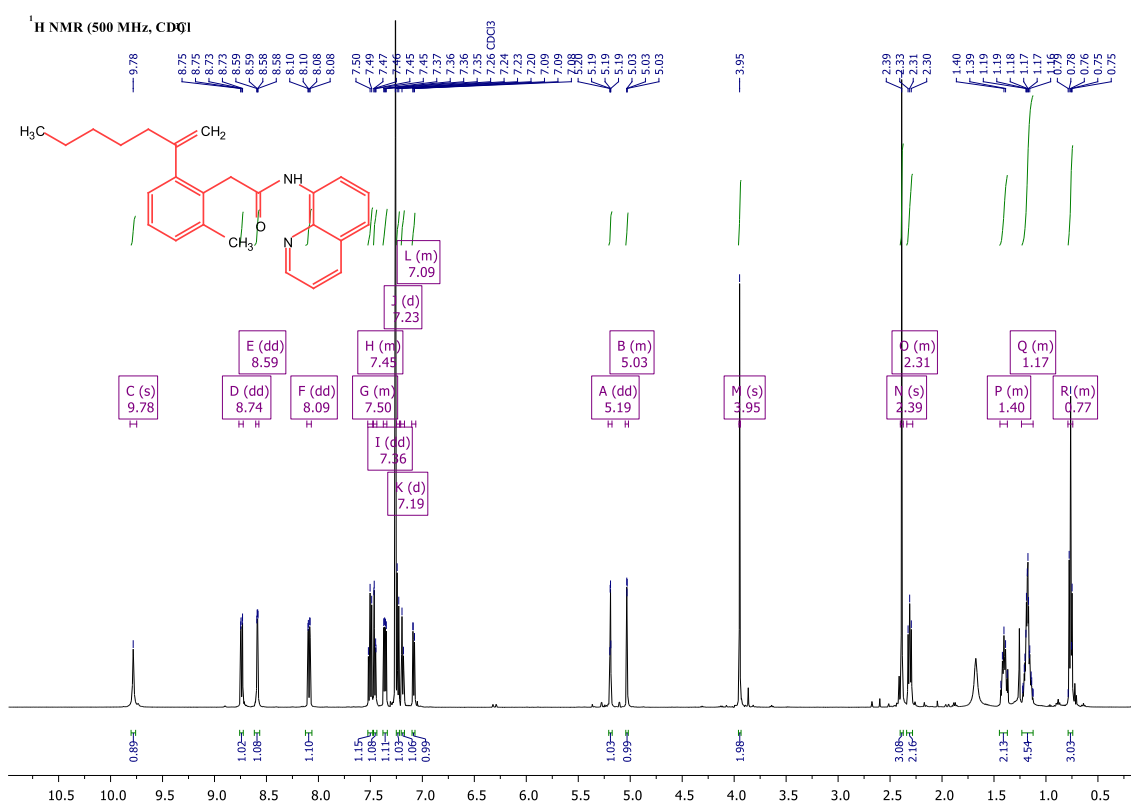
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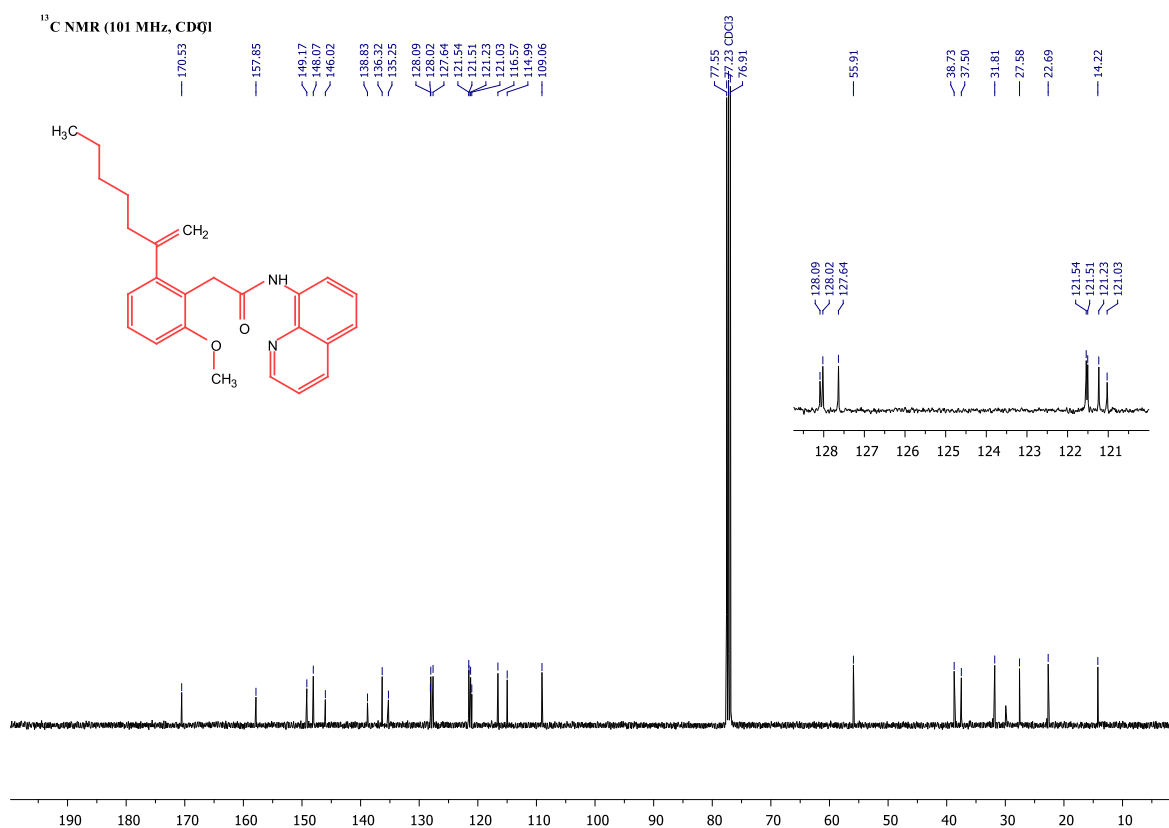
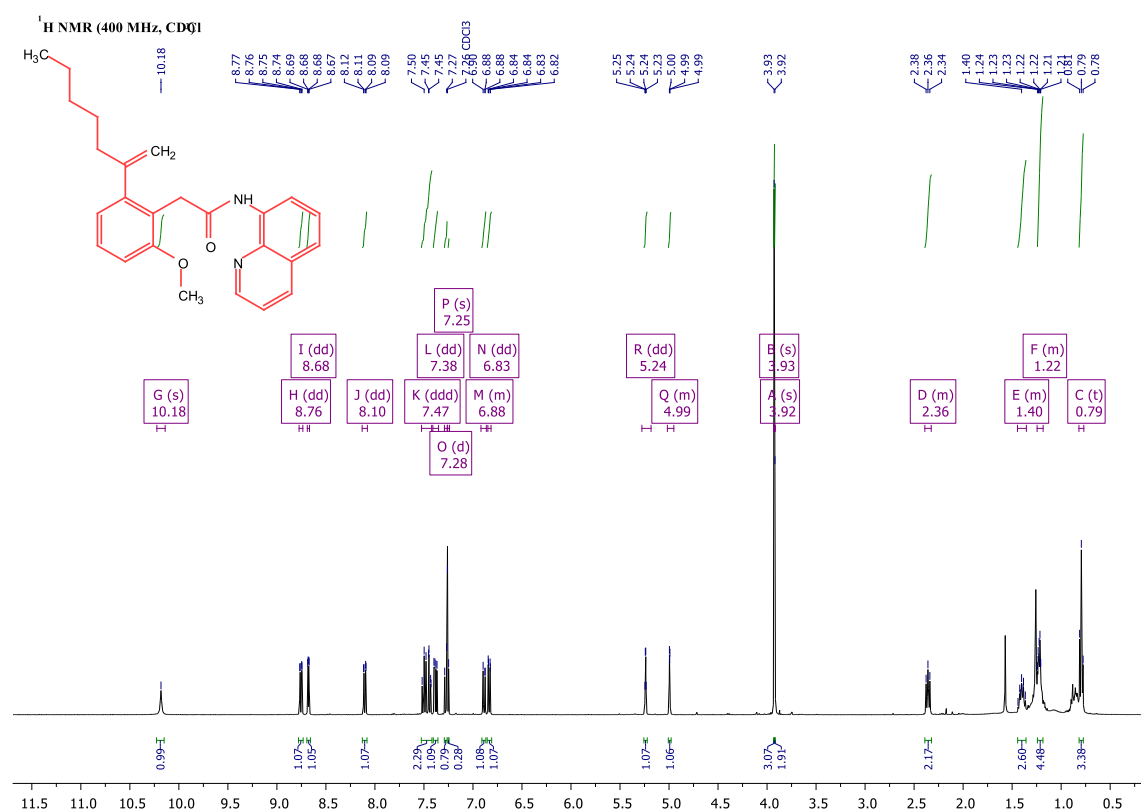
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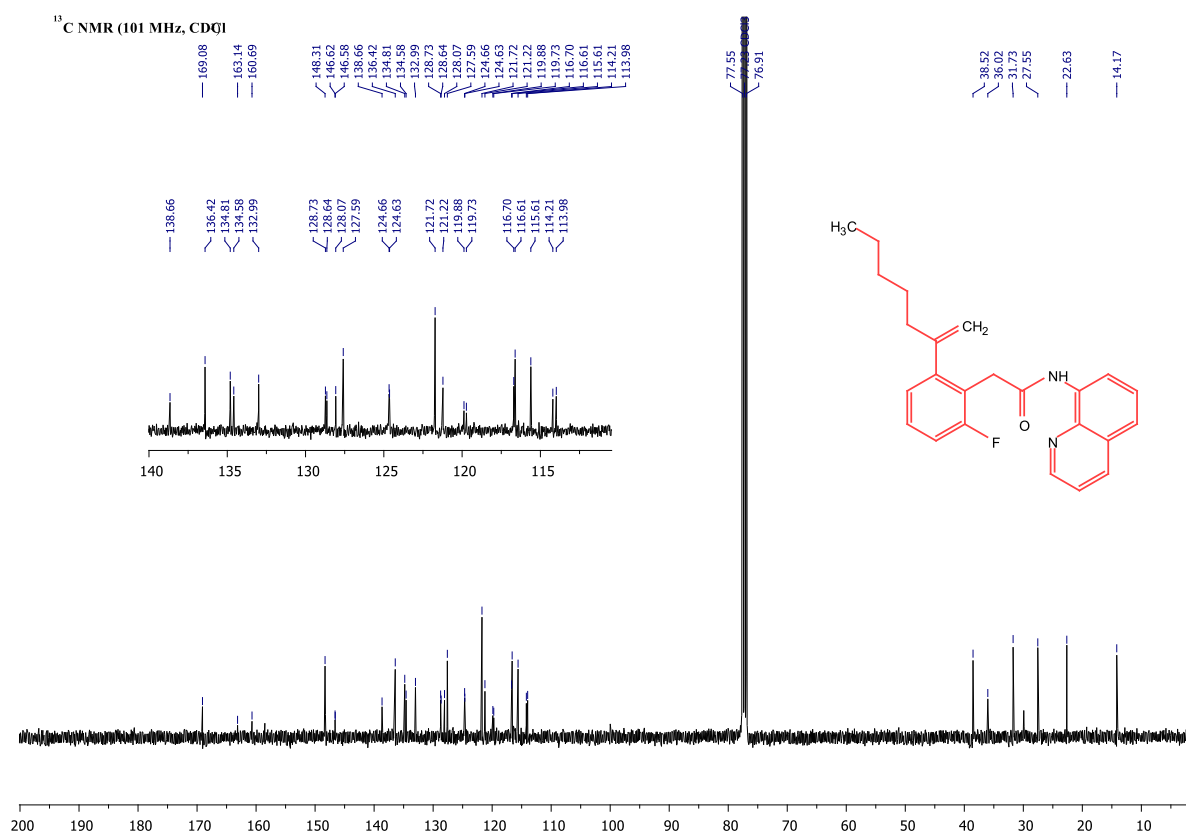
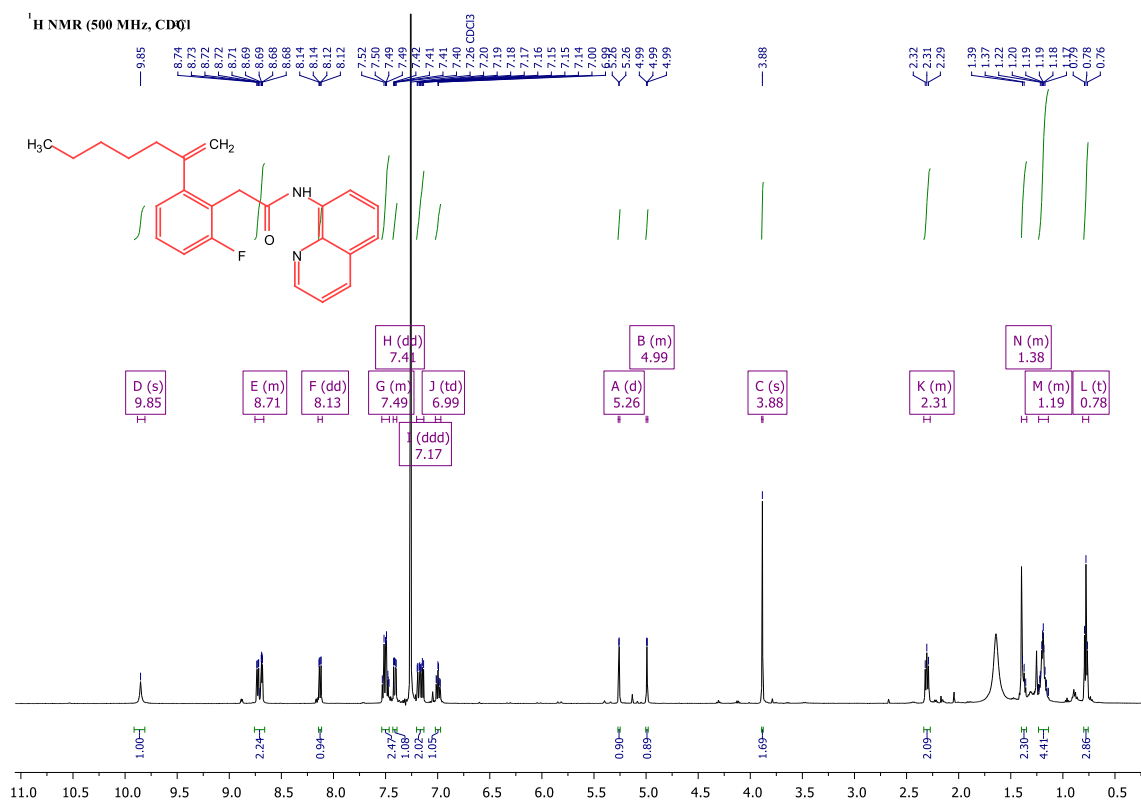
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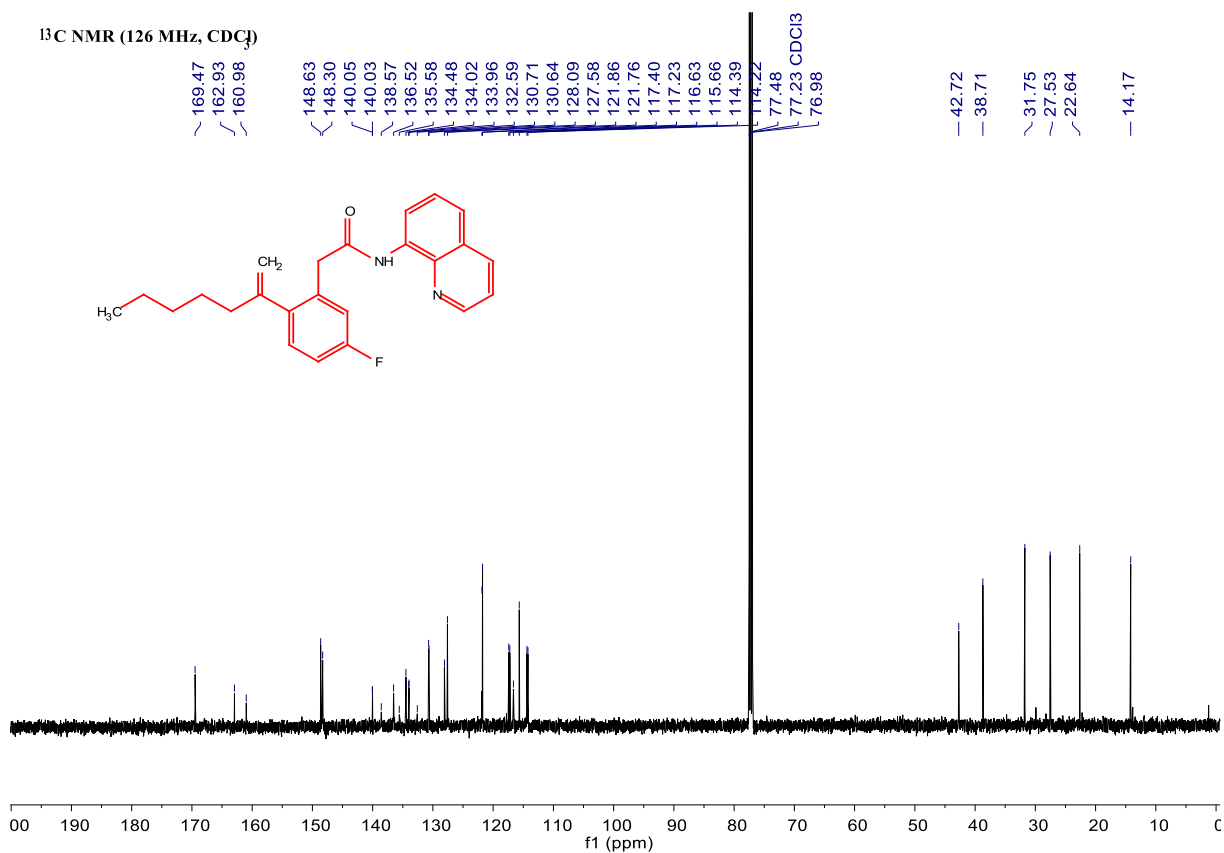
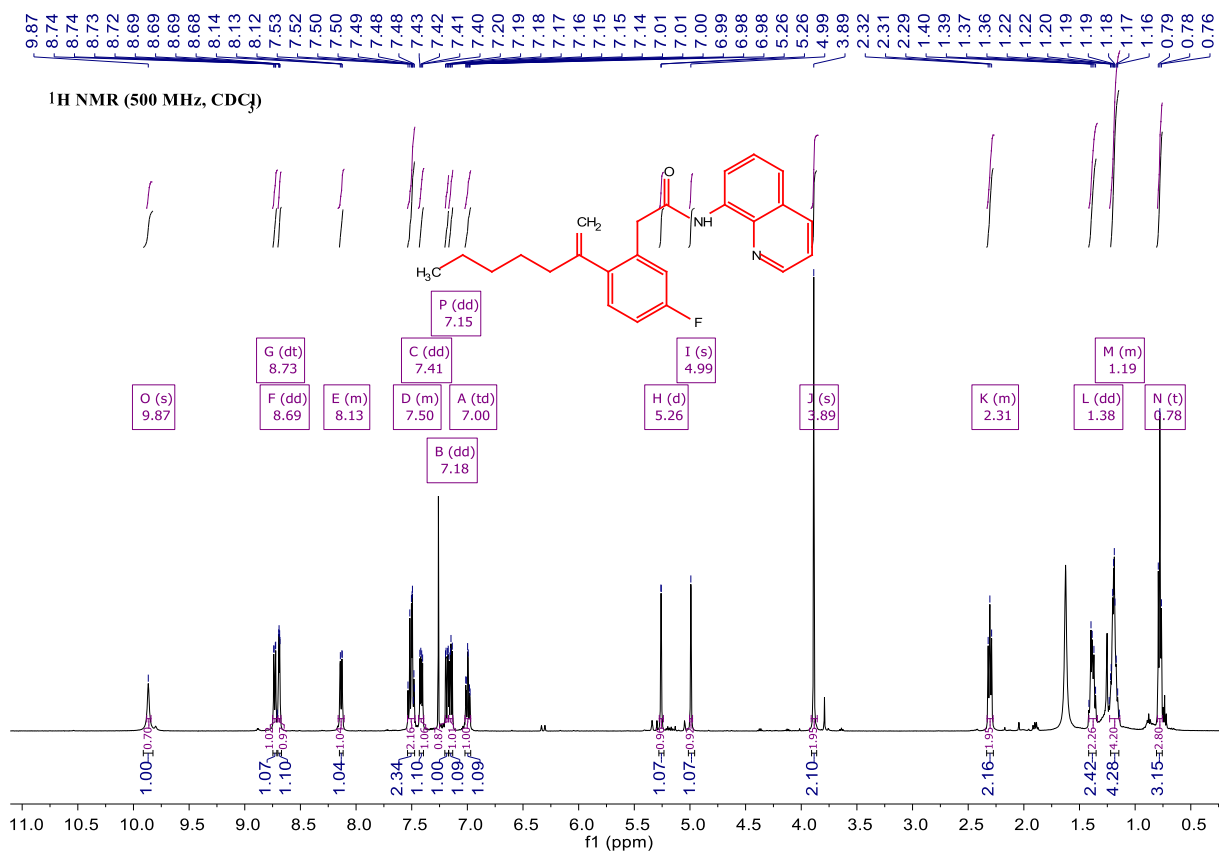
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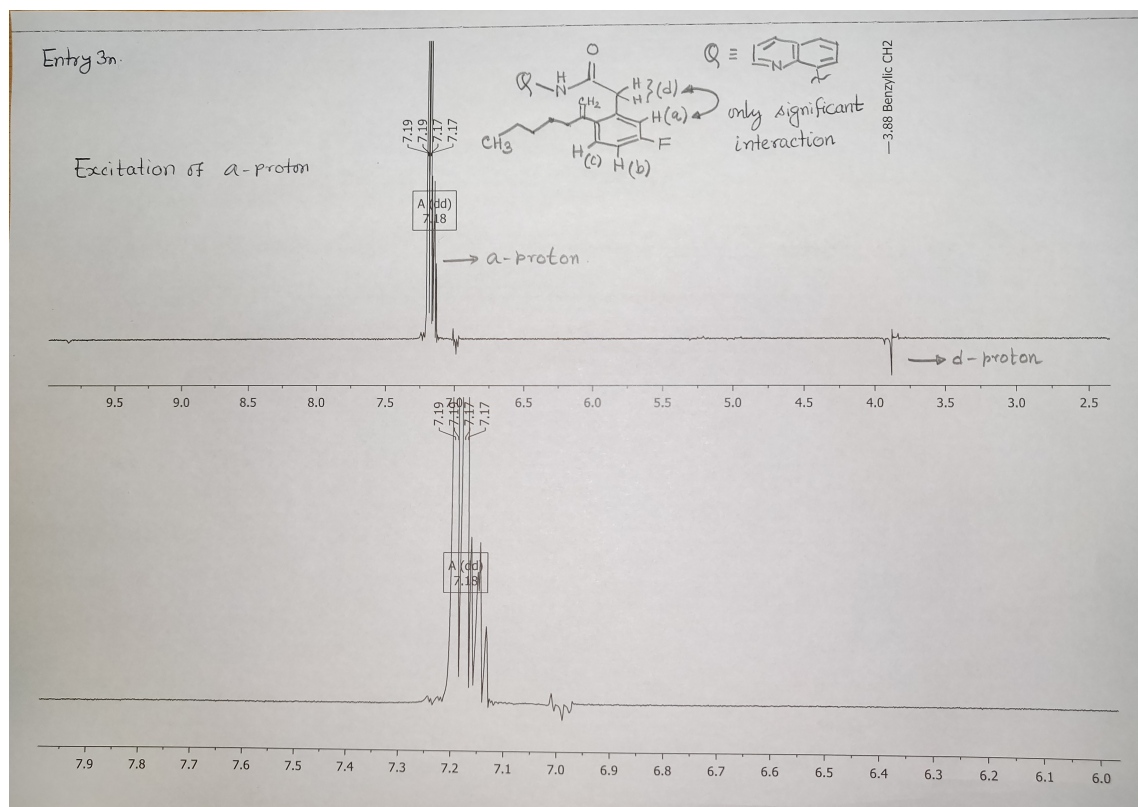
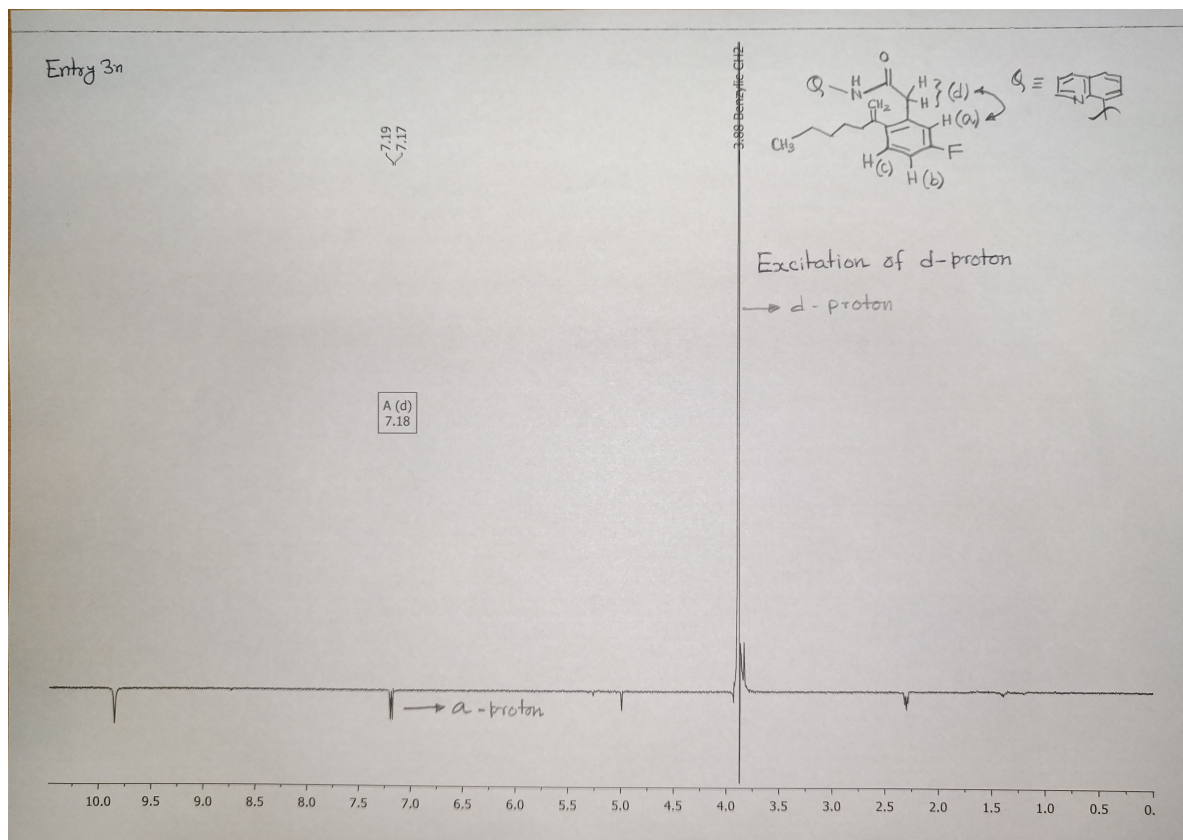


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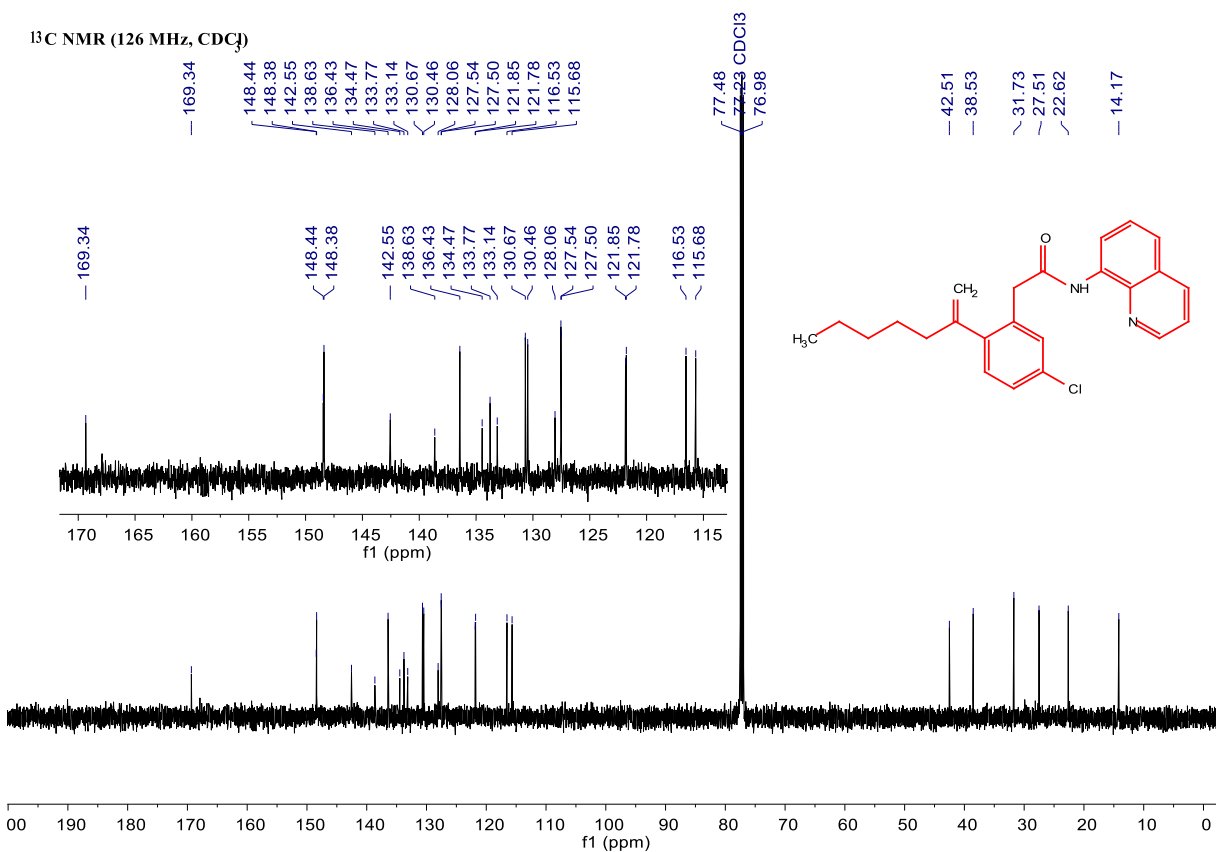
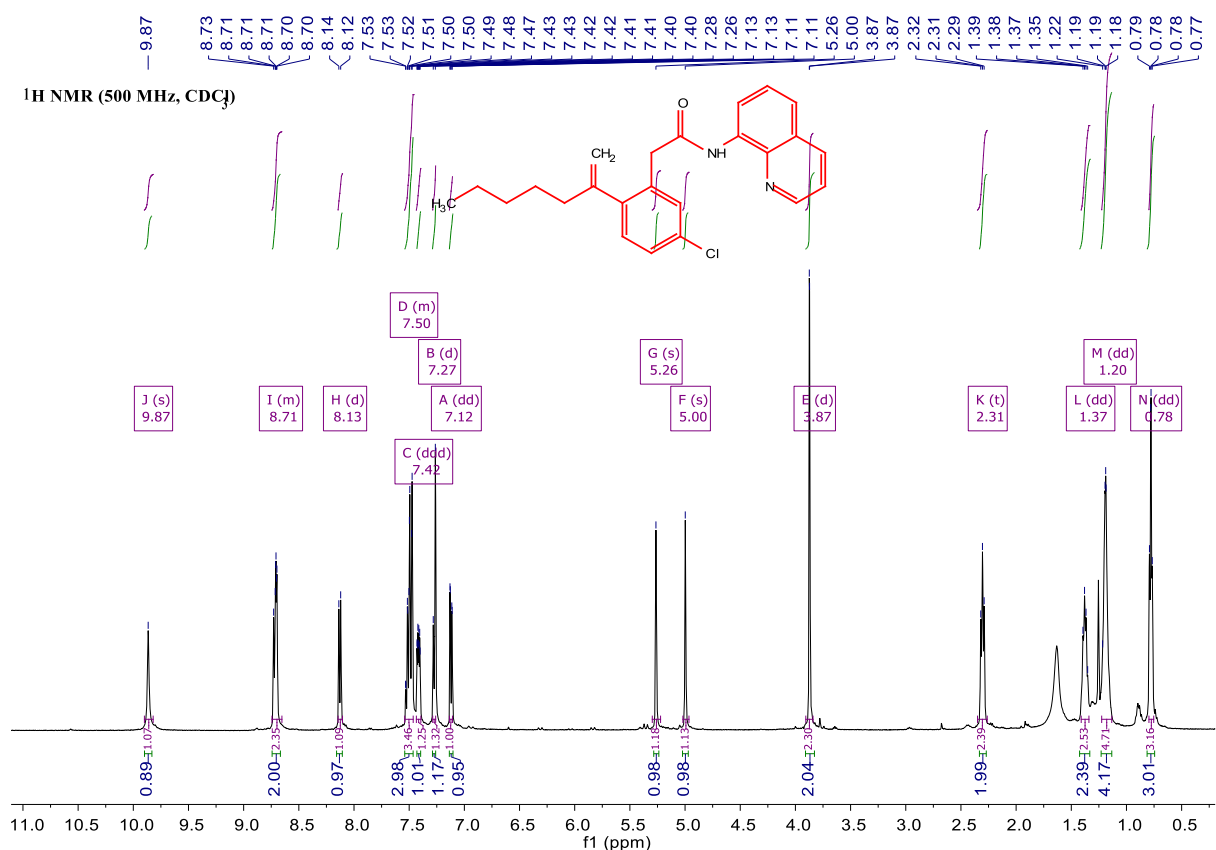


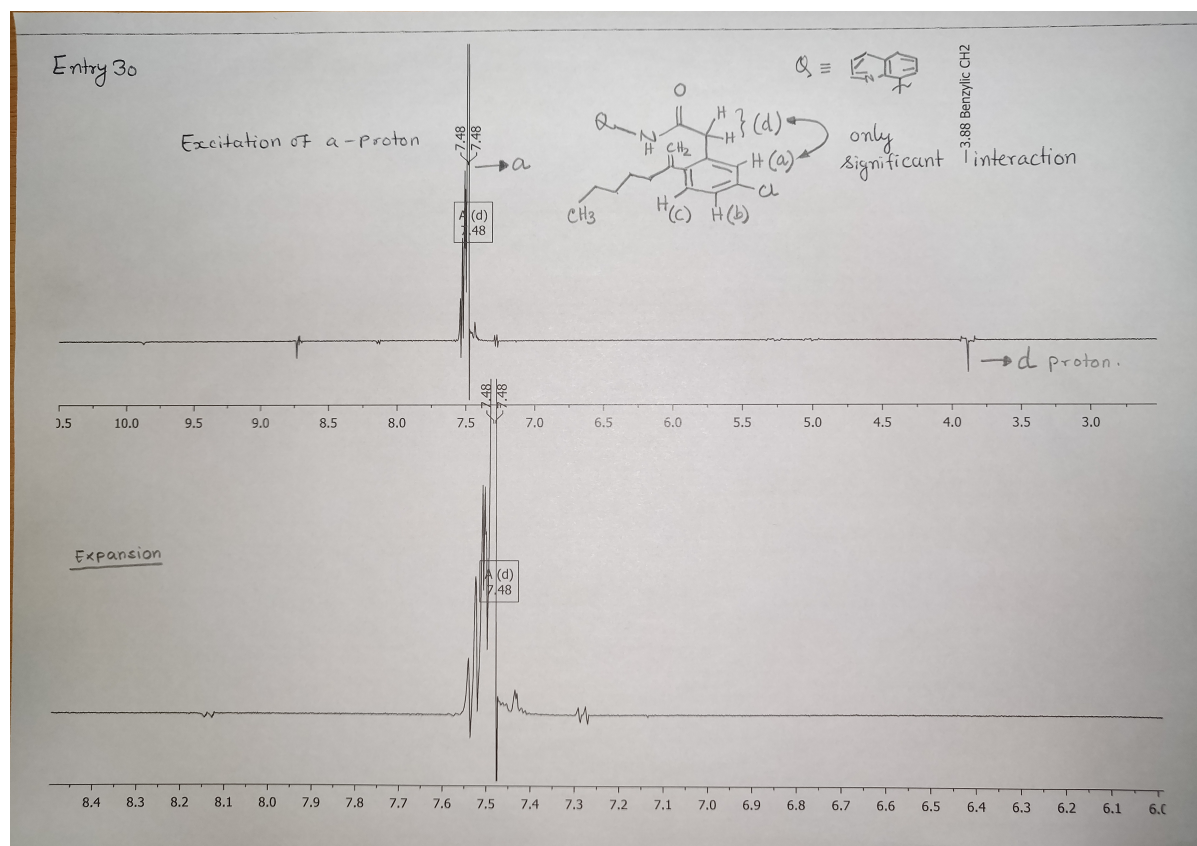
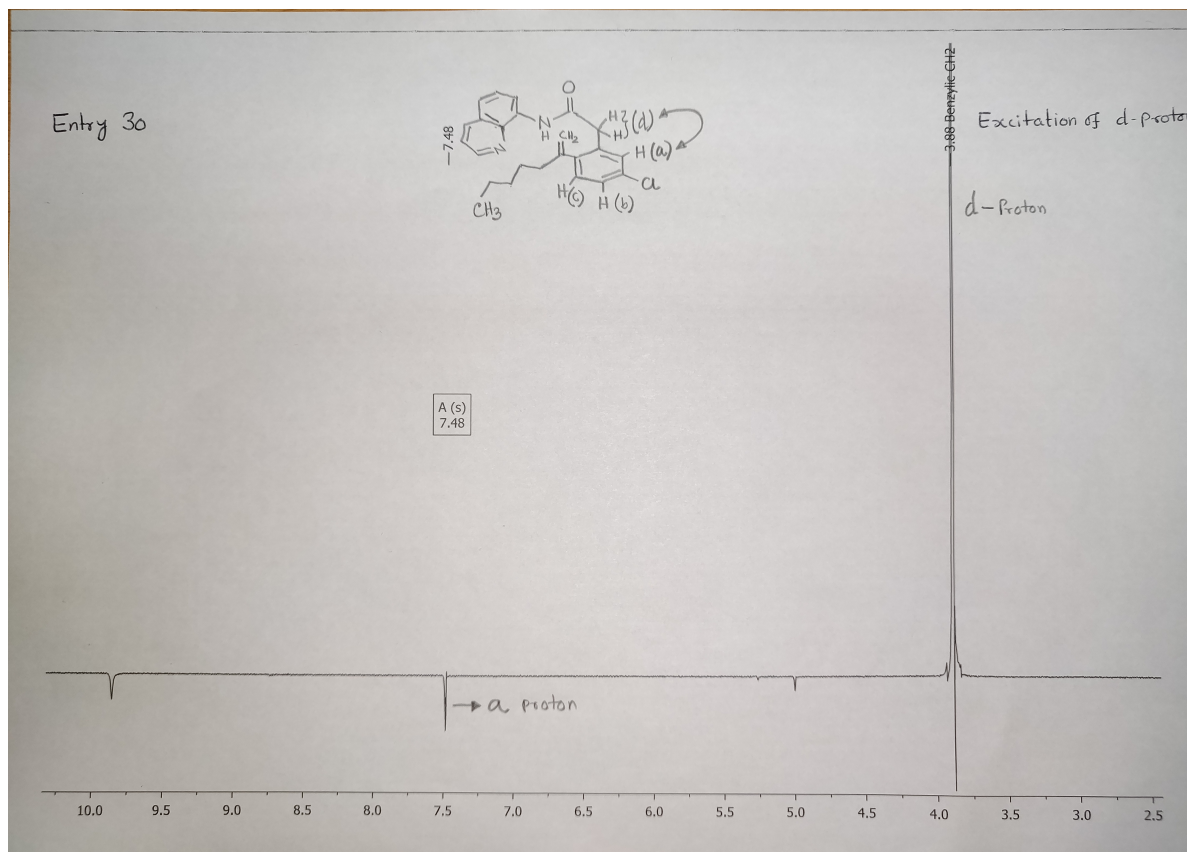
Scheme 2, entry 3m:



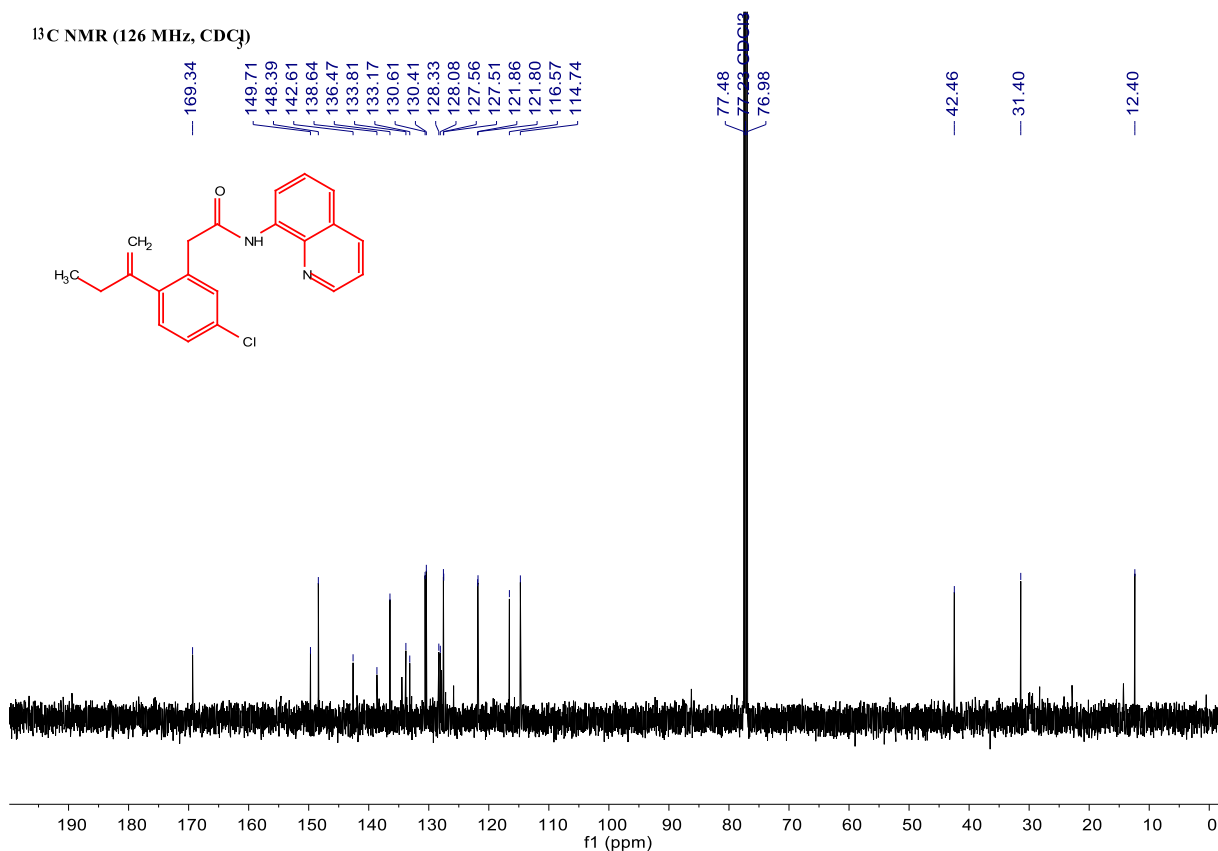
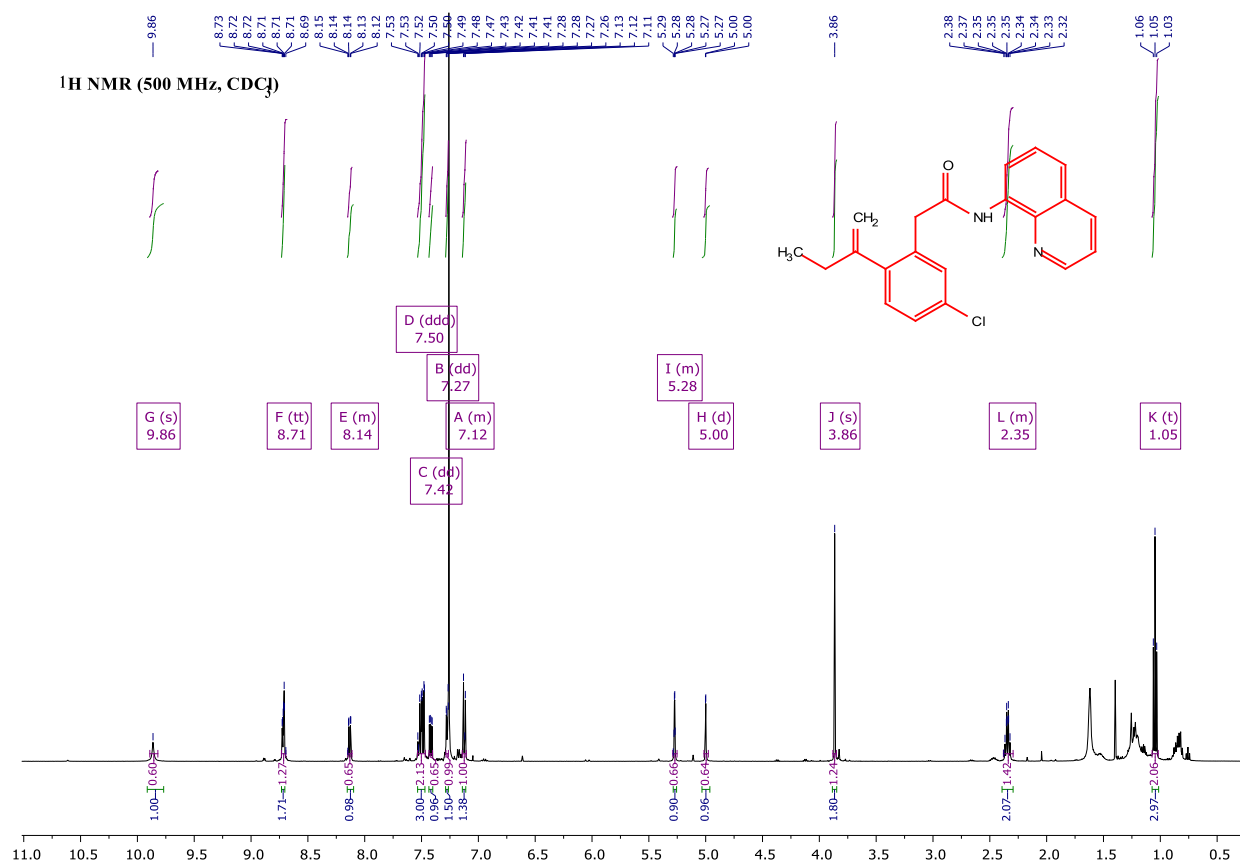


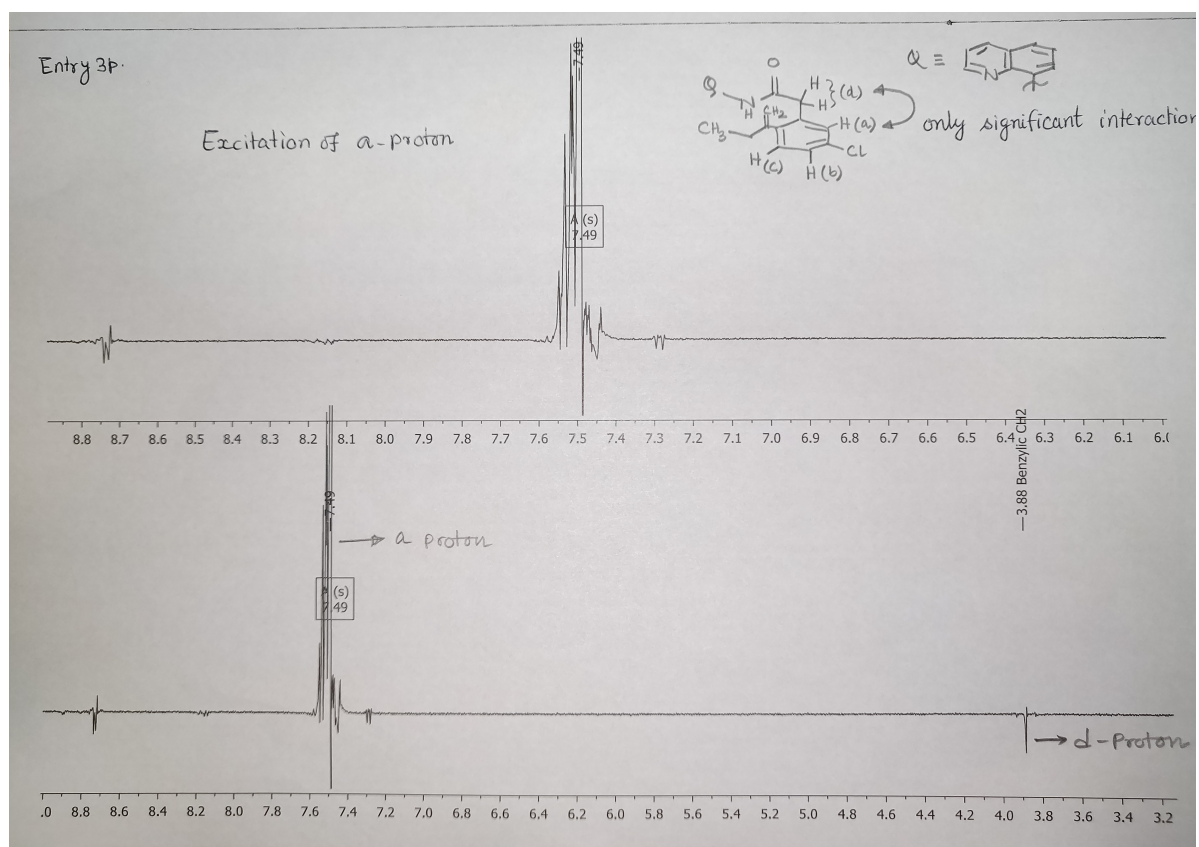
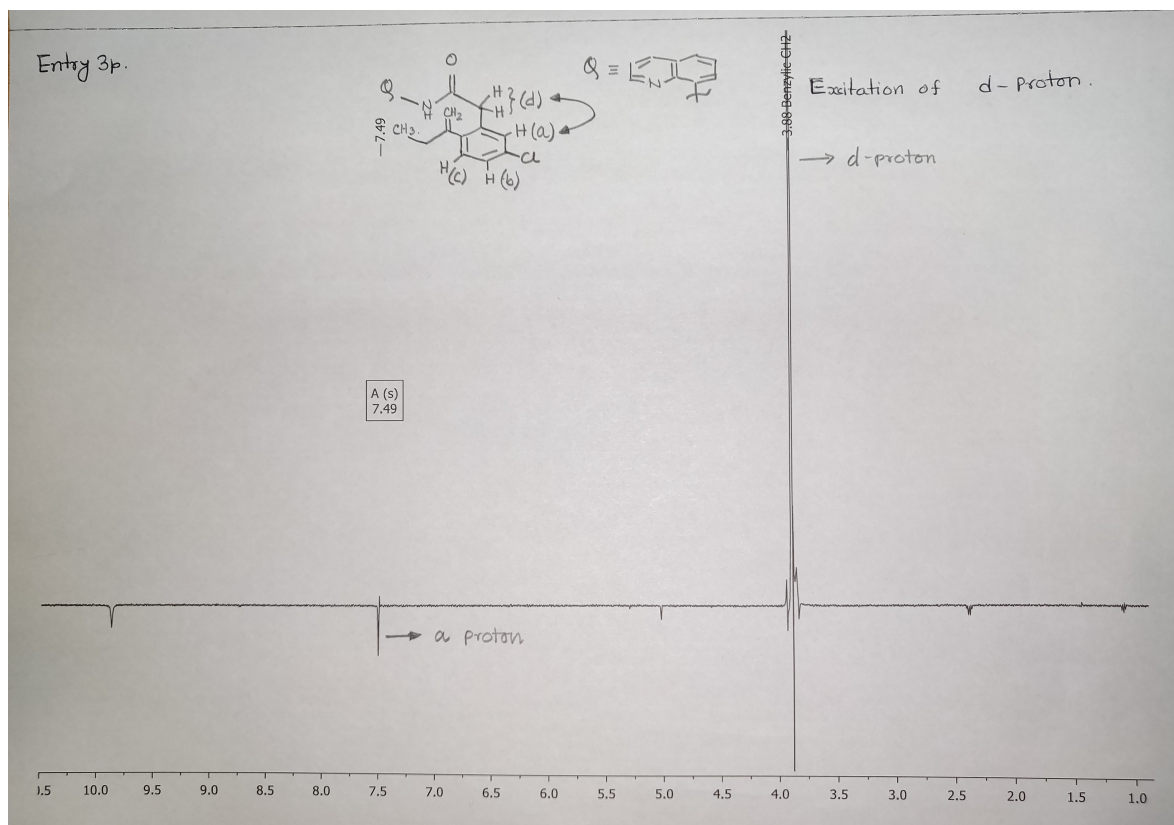
Scheme 2, entry 3o:



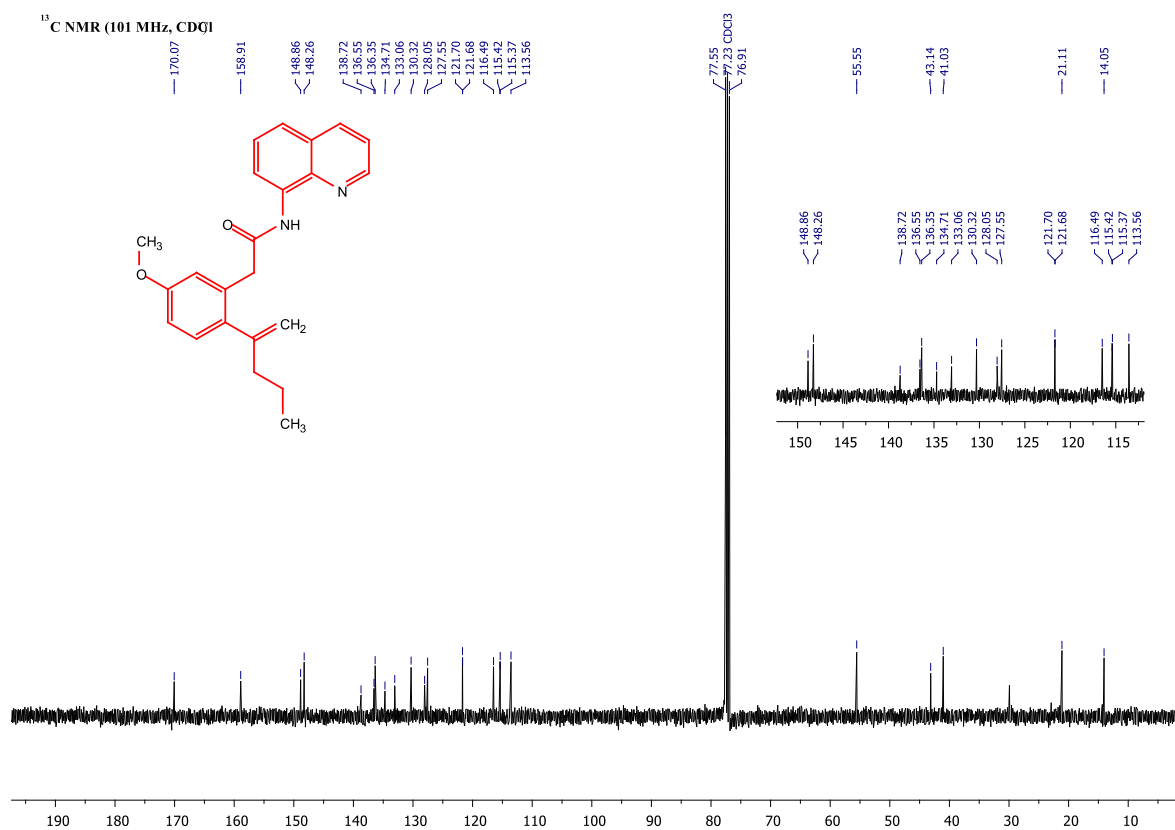
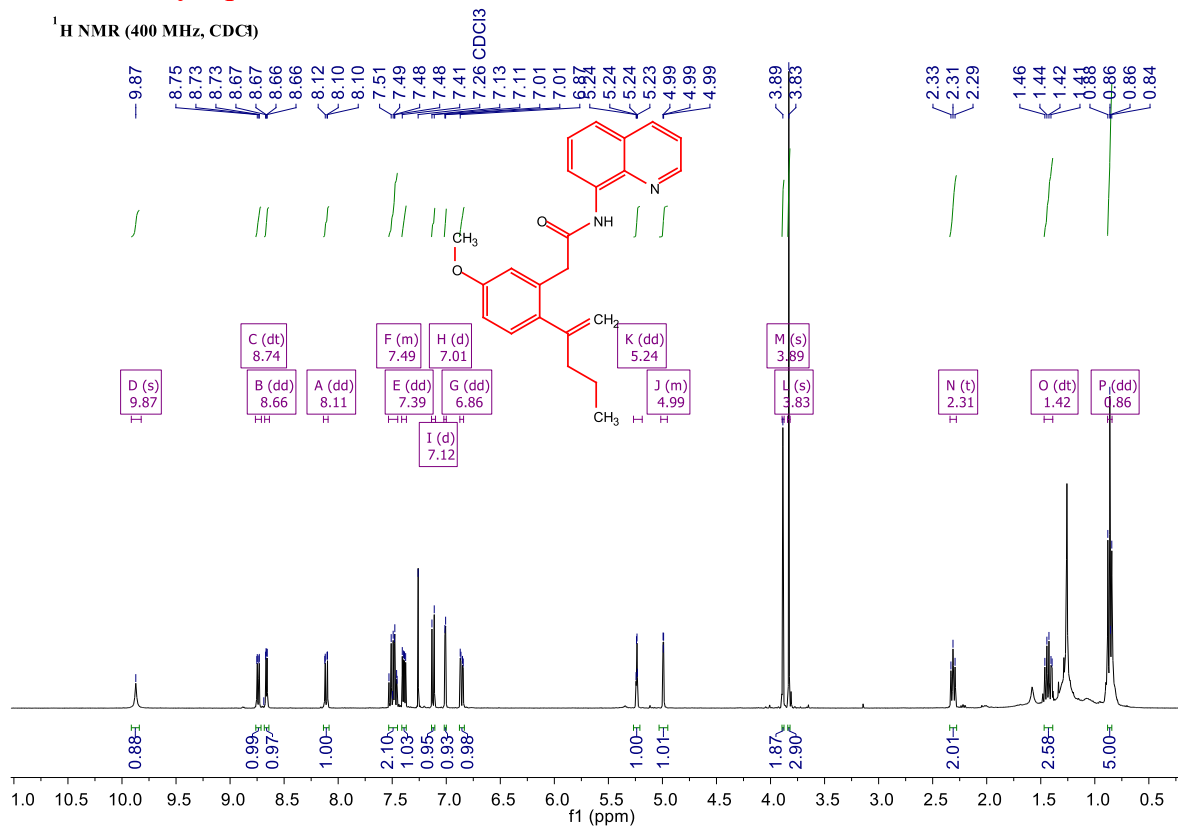


Scheme 2, entry 3p:

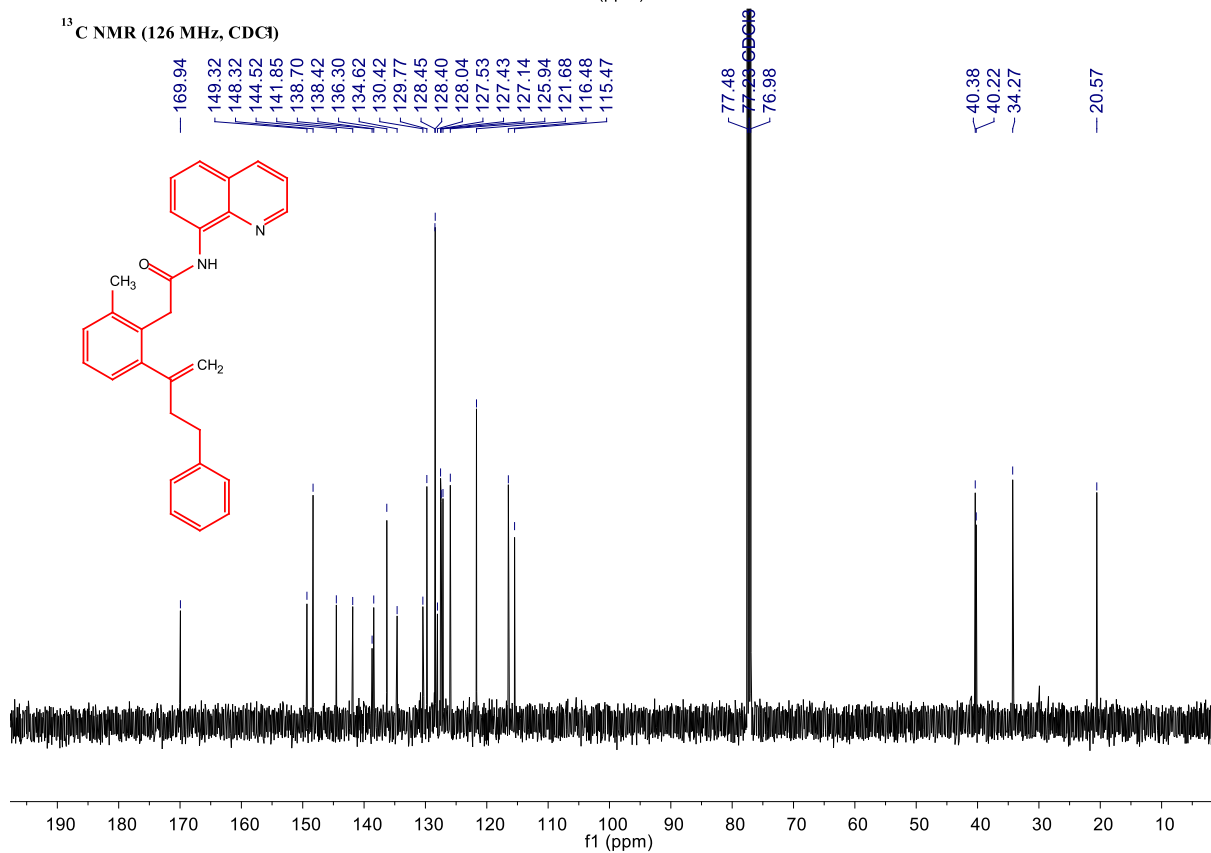
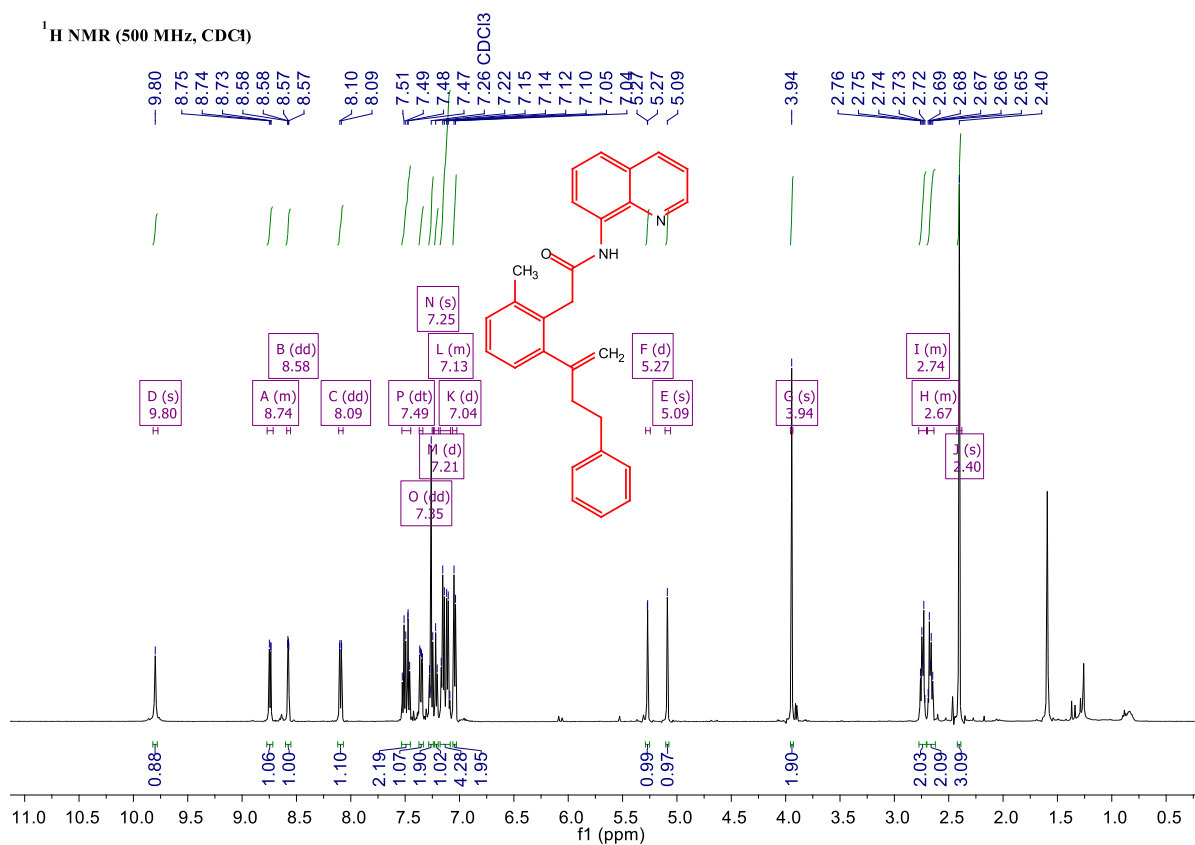


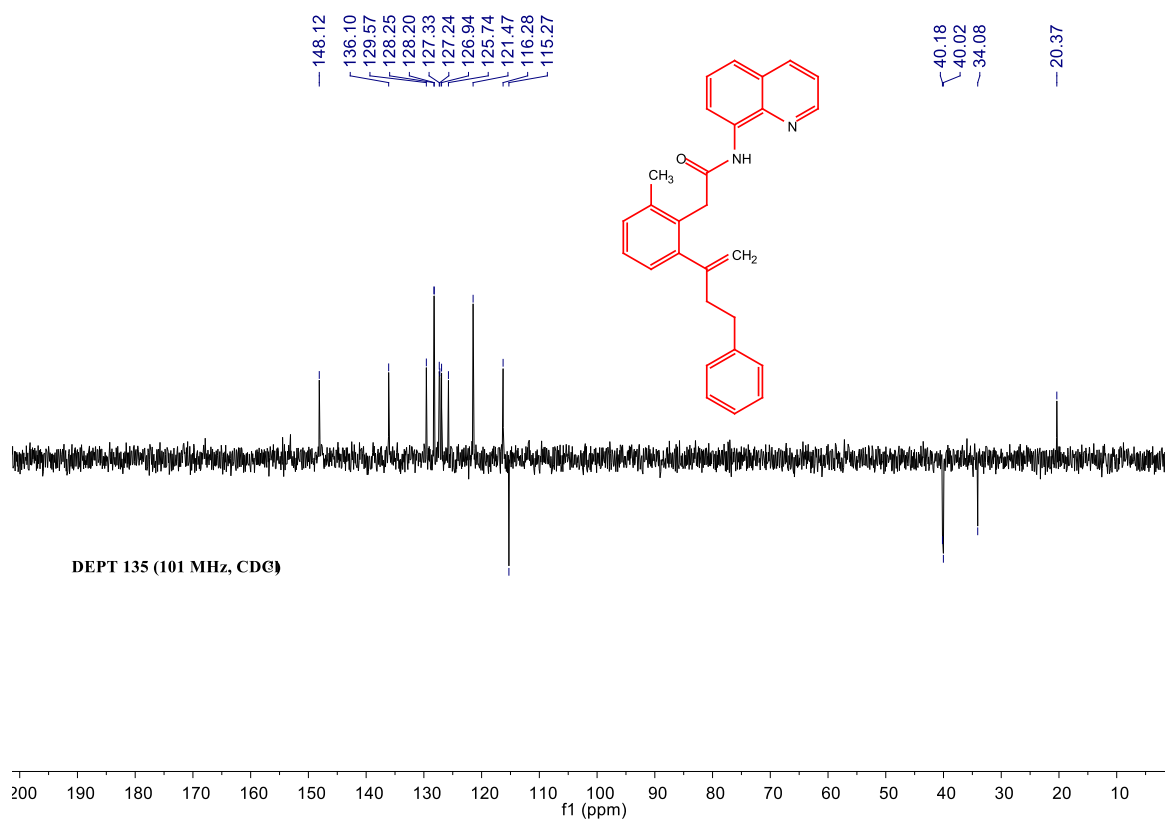


Scheme 2, entry 3q:

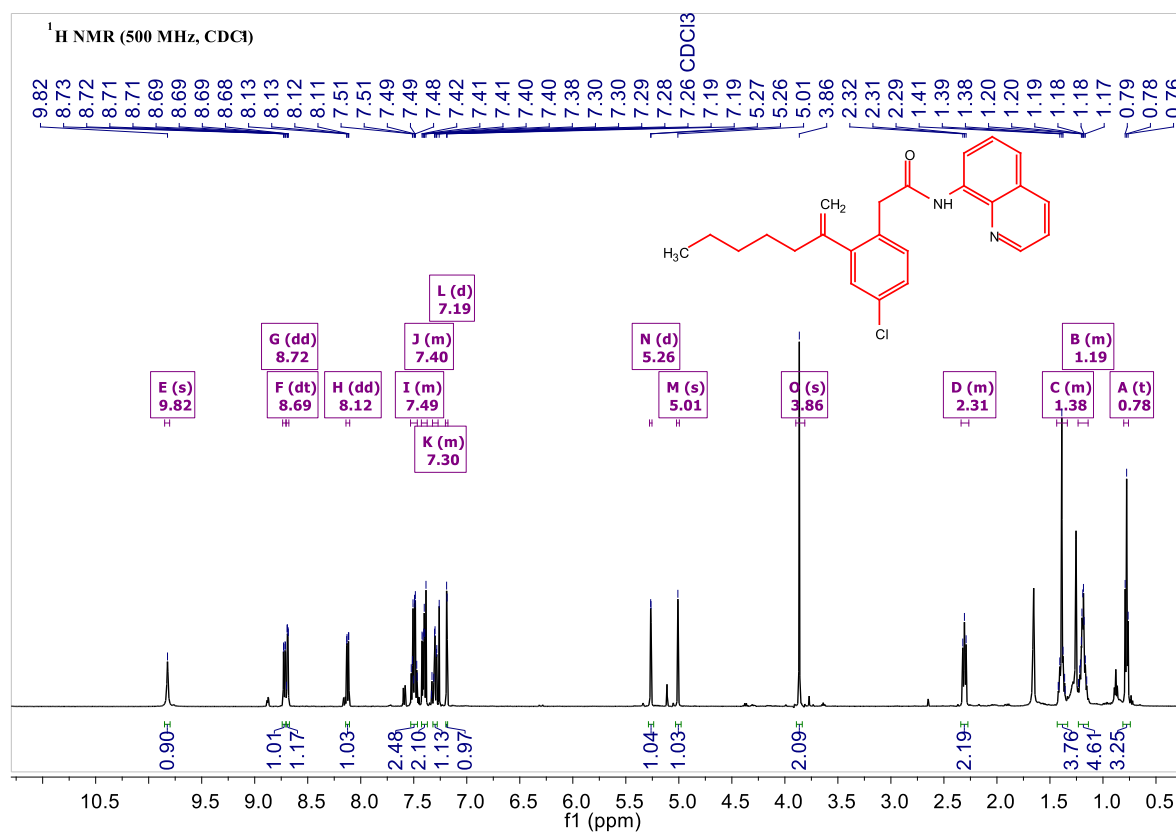


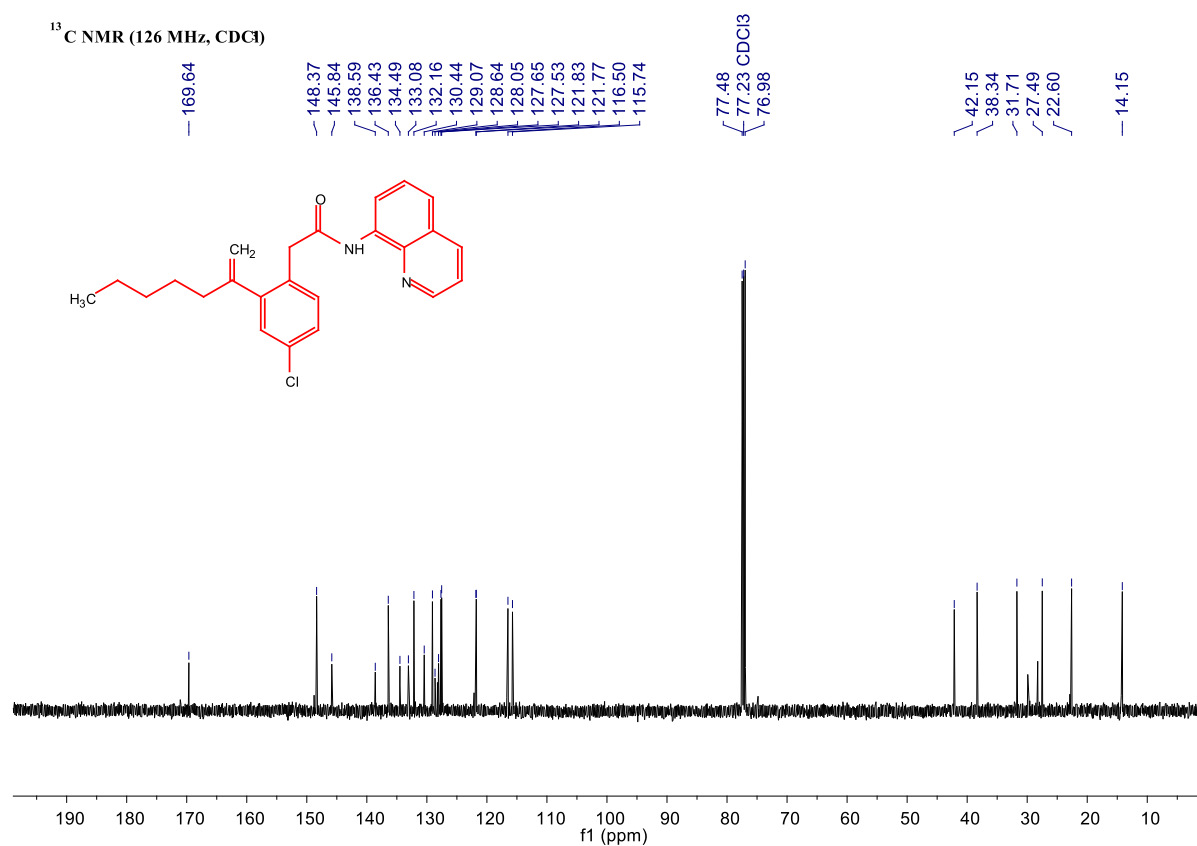
Scheme 2, entry 3r:



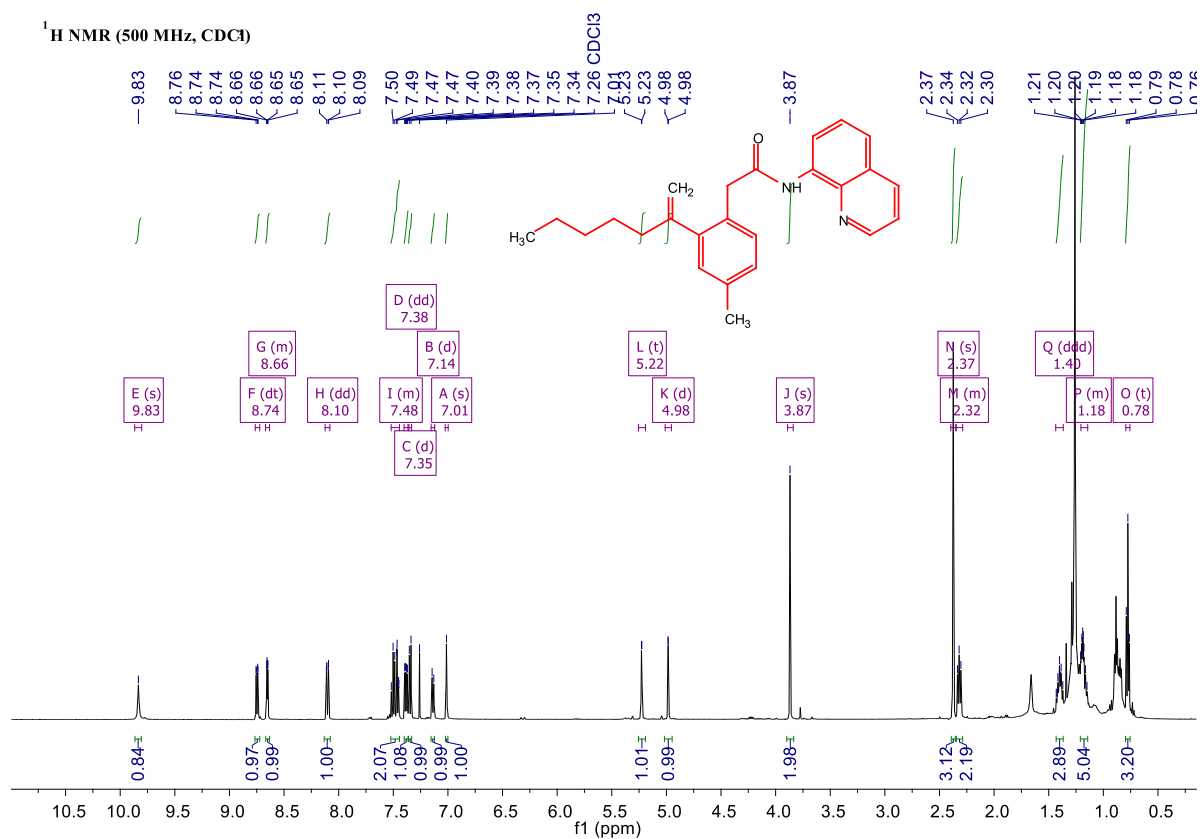


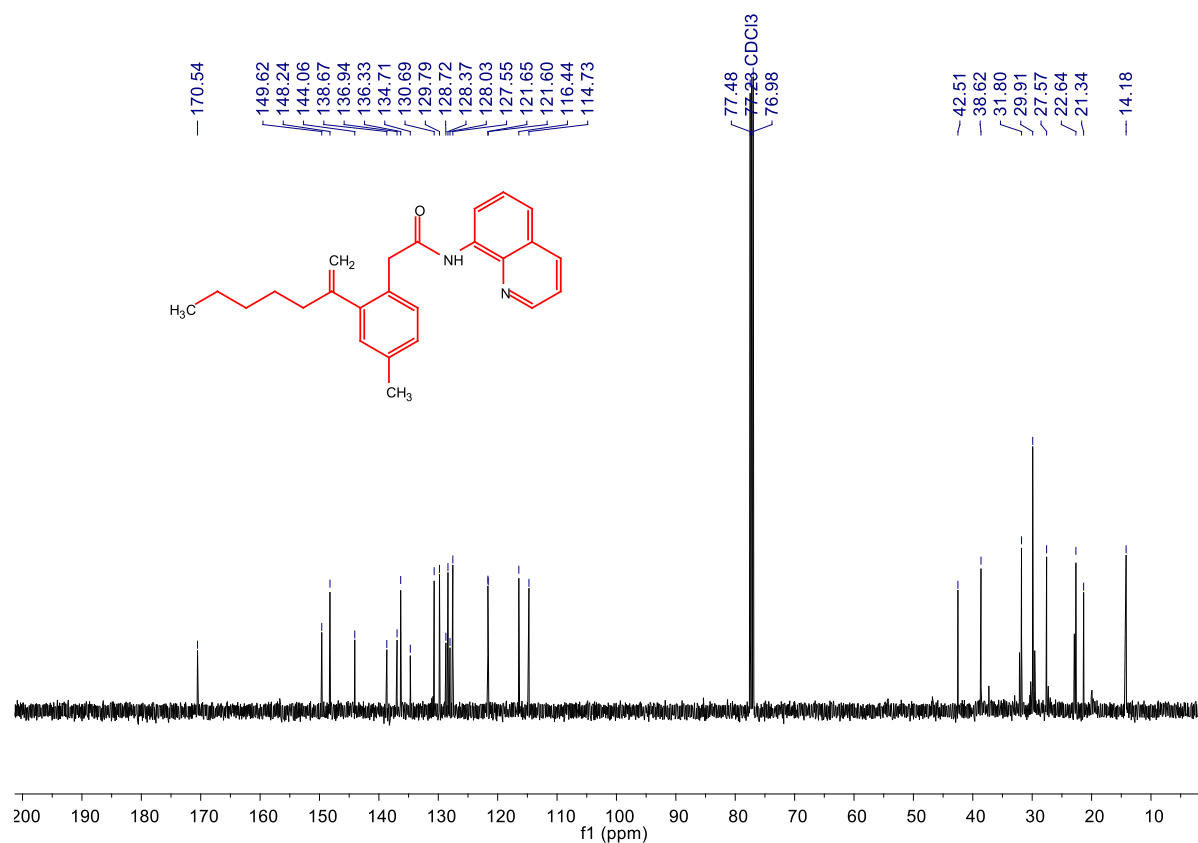
Scheme 2, entry 3s:



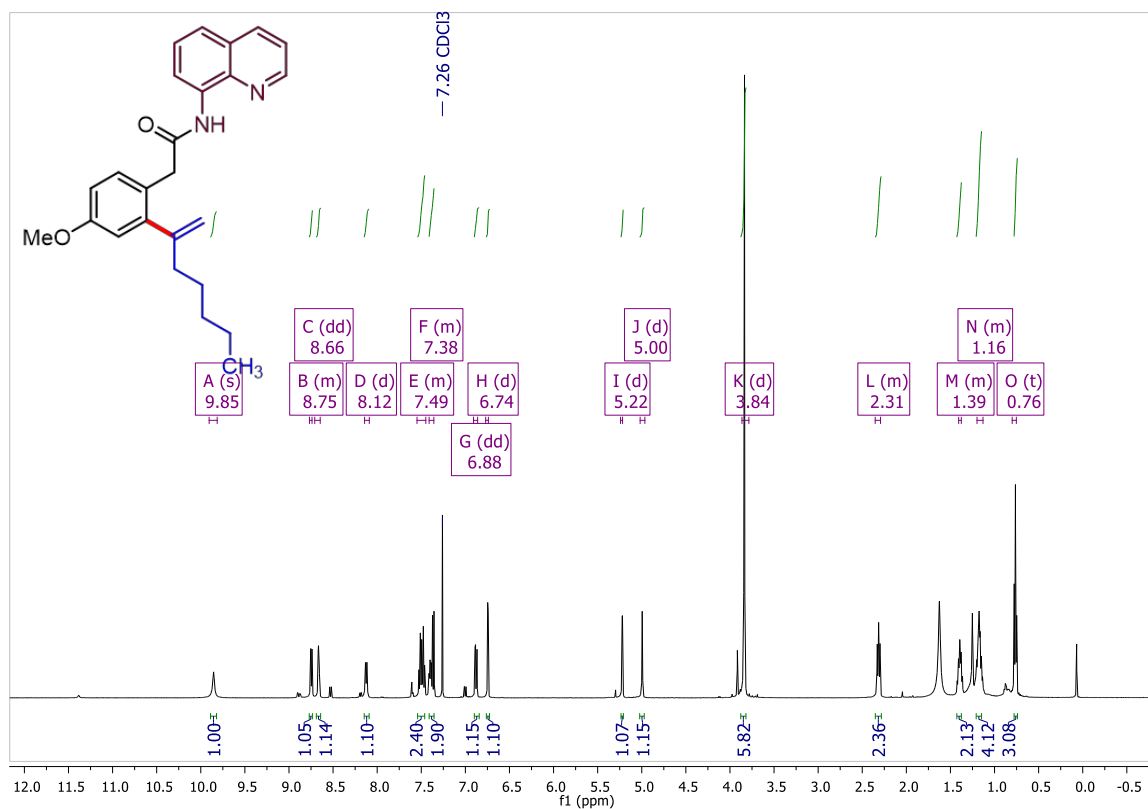


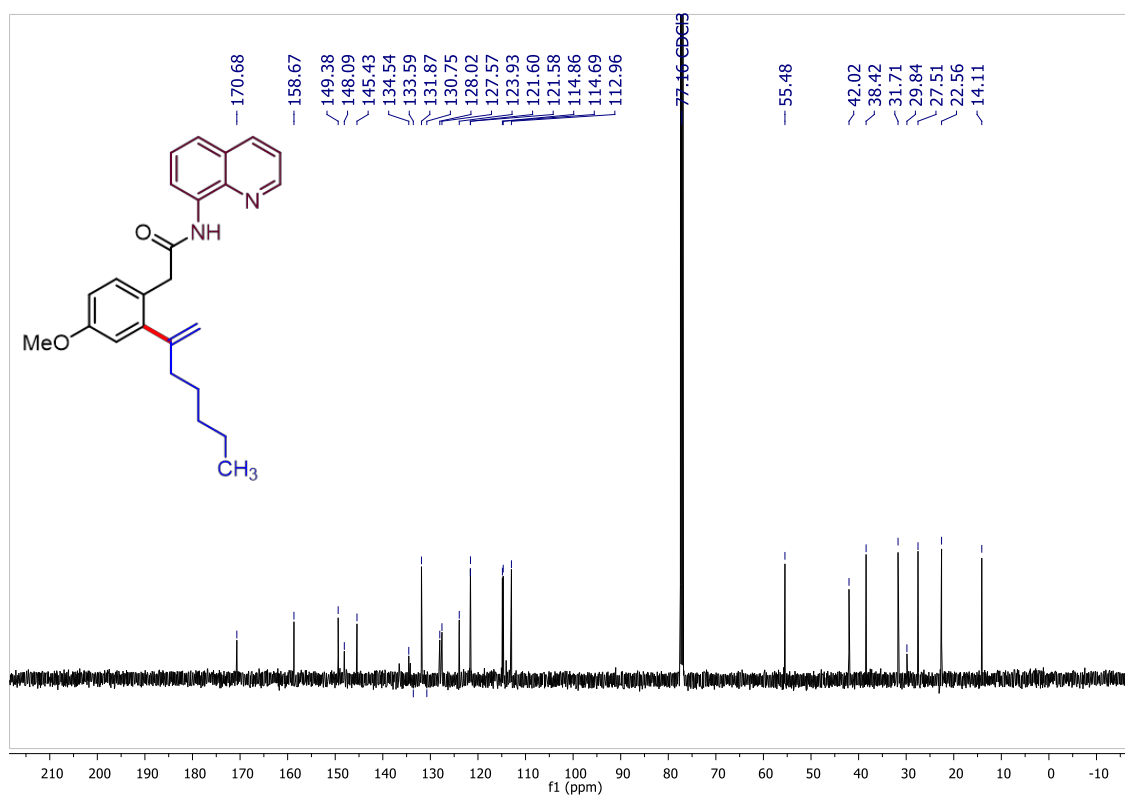
Scheme 2, entry 3t:



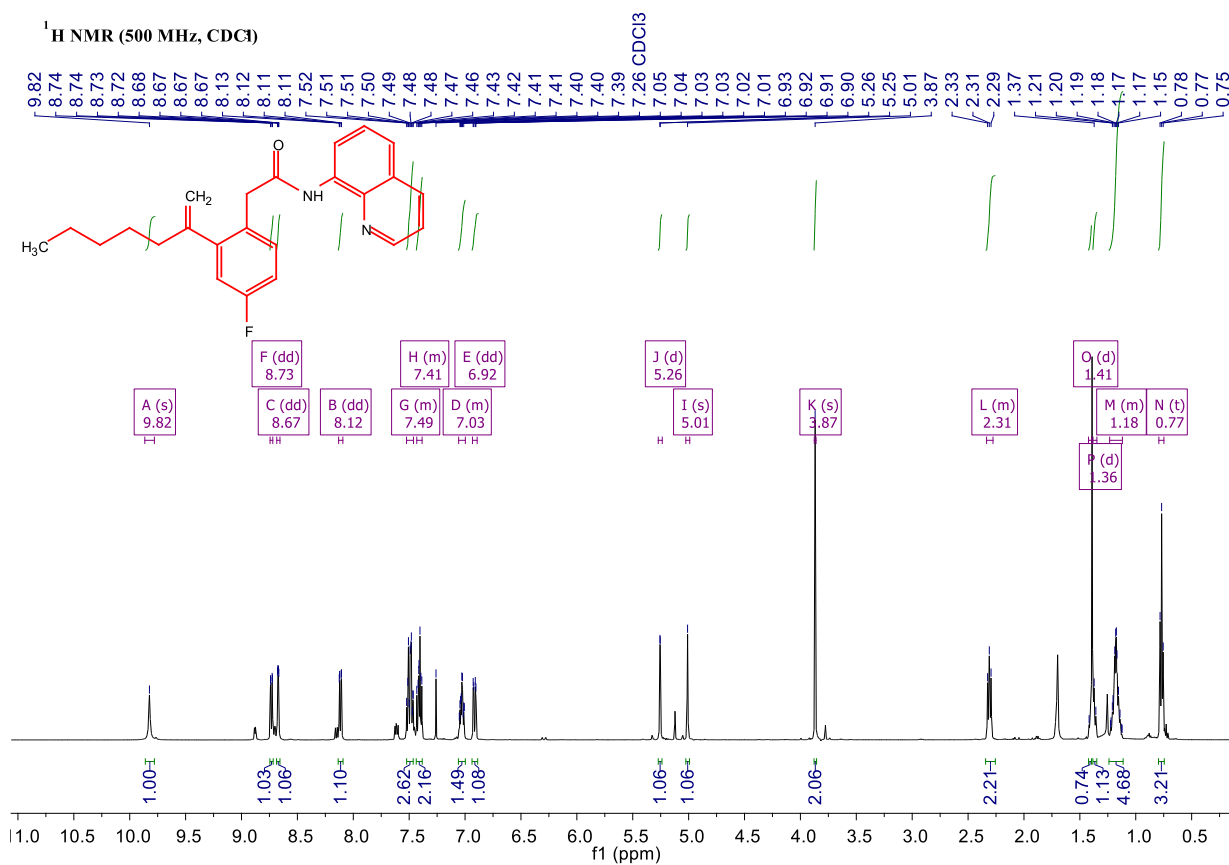


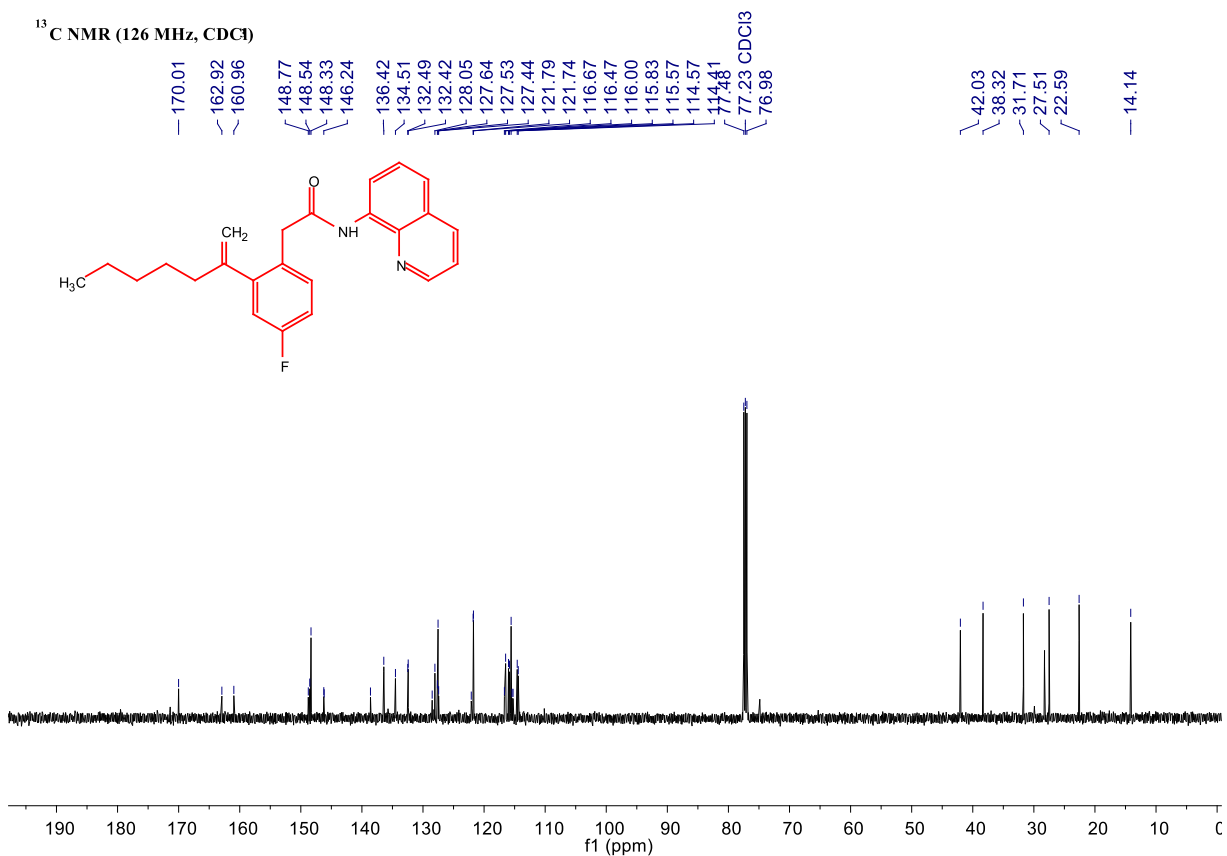
Scheme 2, entry 3u:



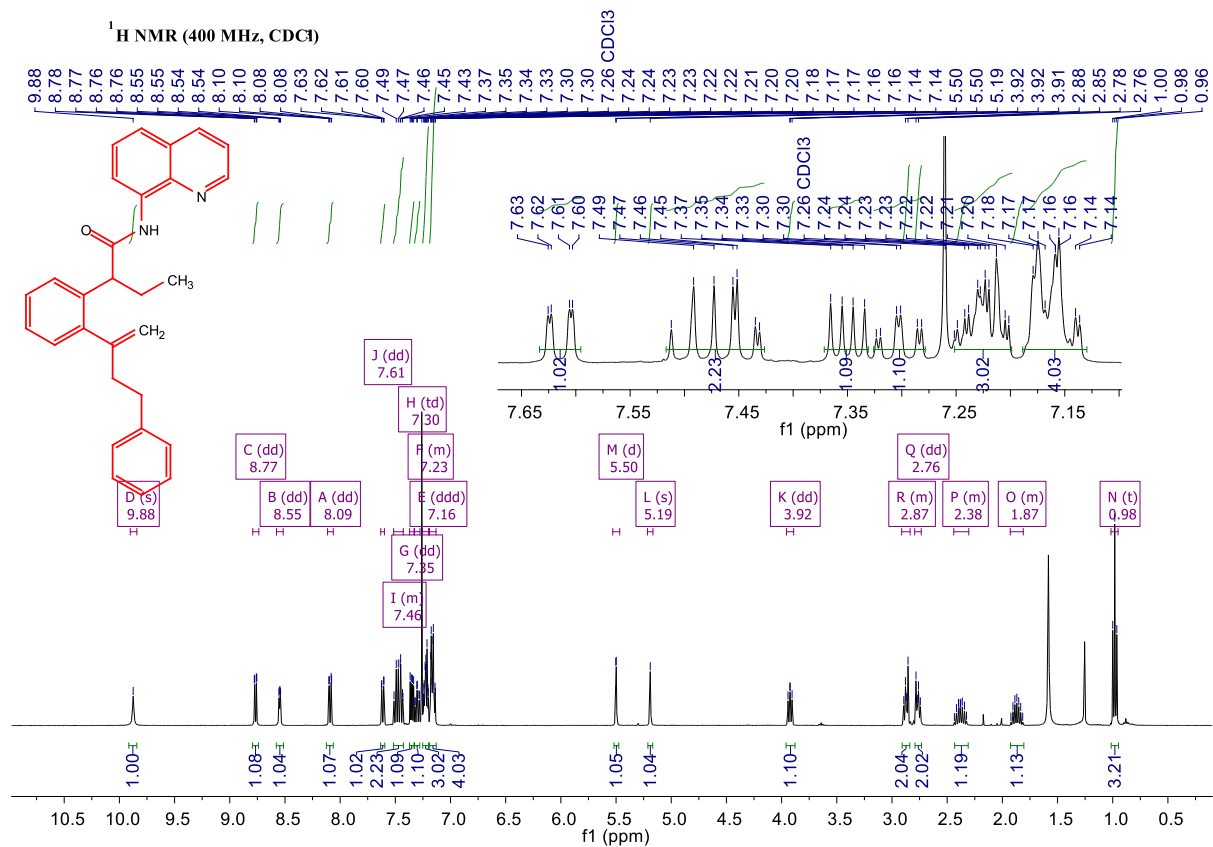


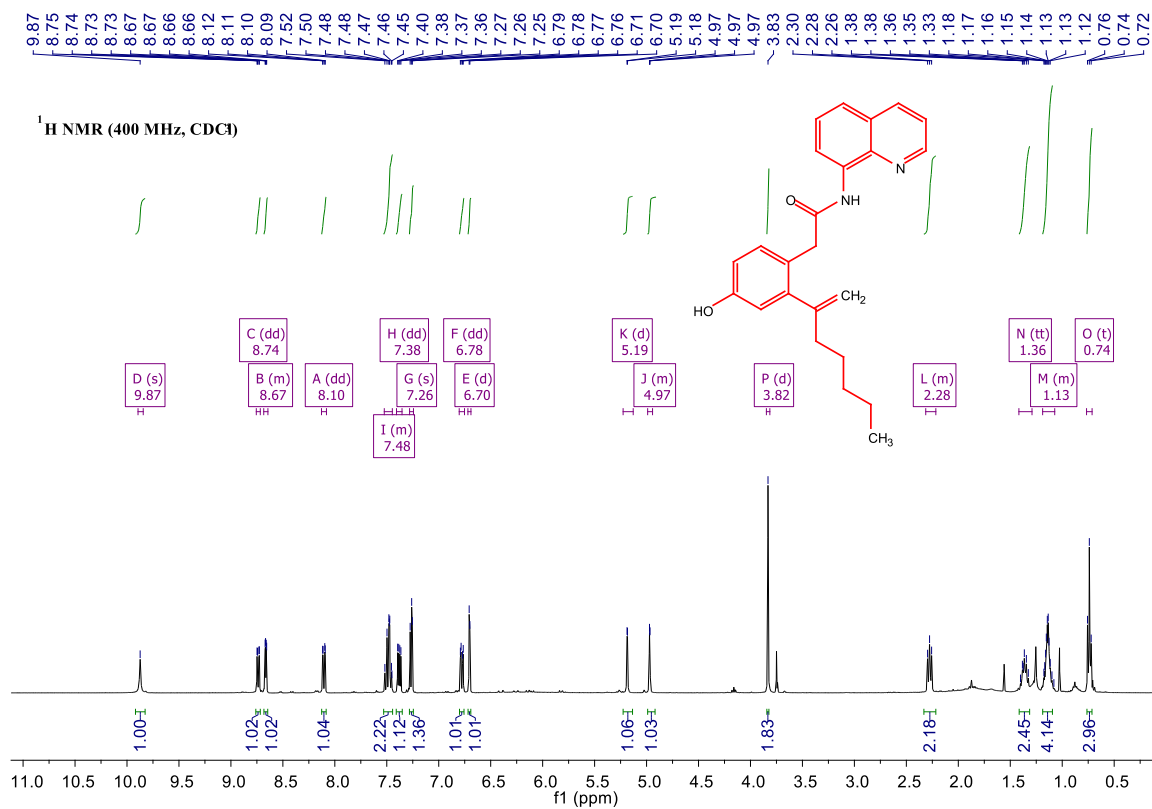
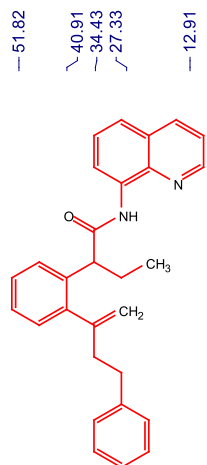
Scheme 2, entry 3v:

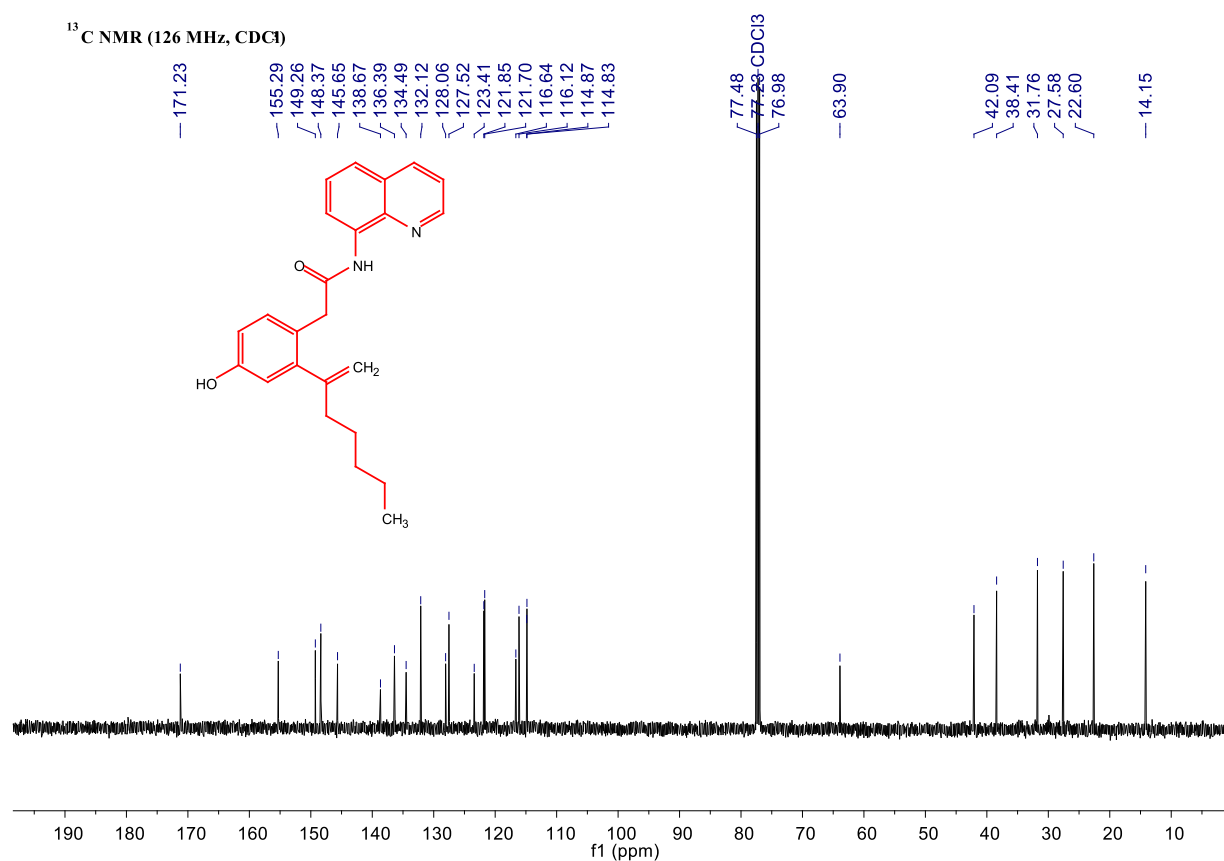




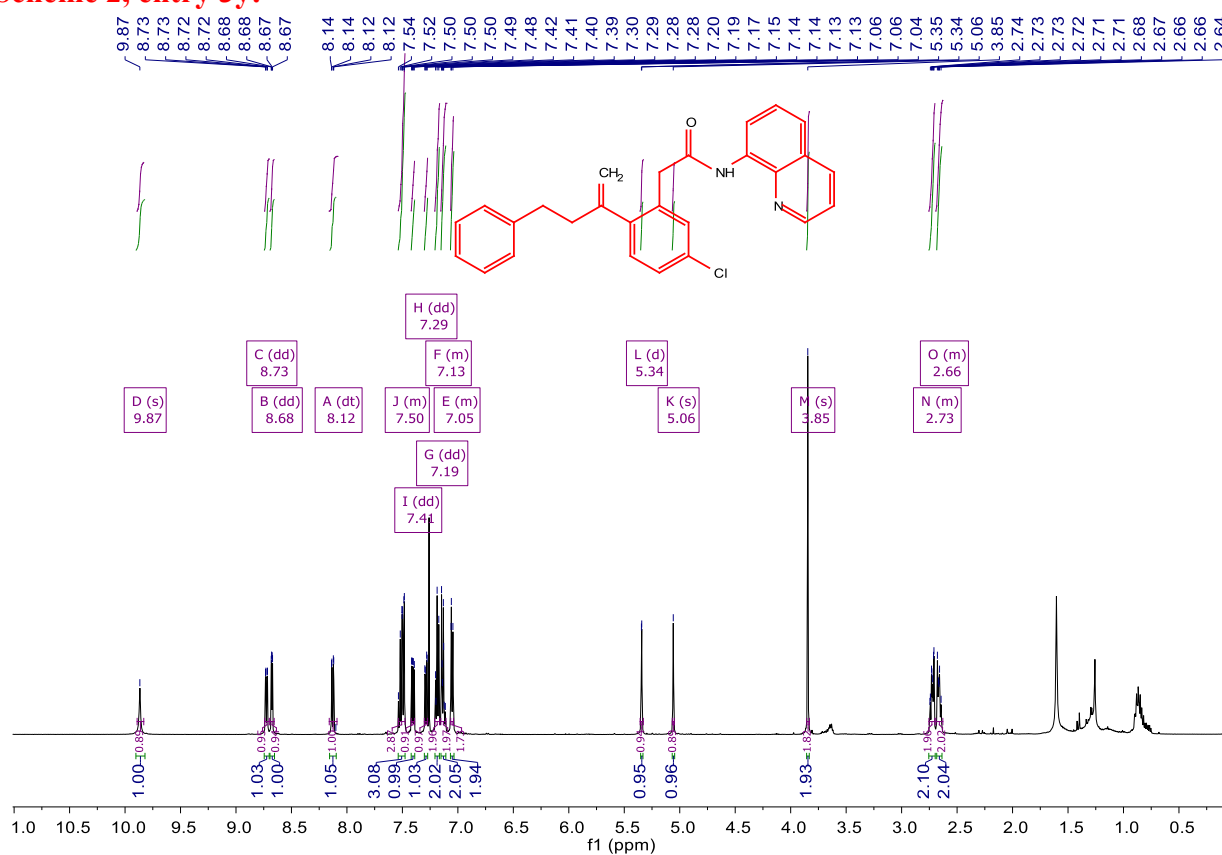
Scheme 2, entry 3w:

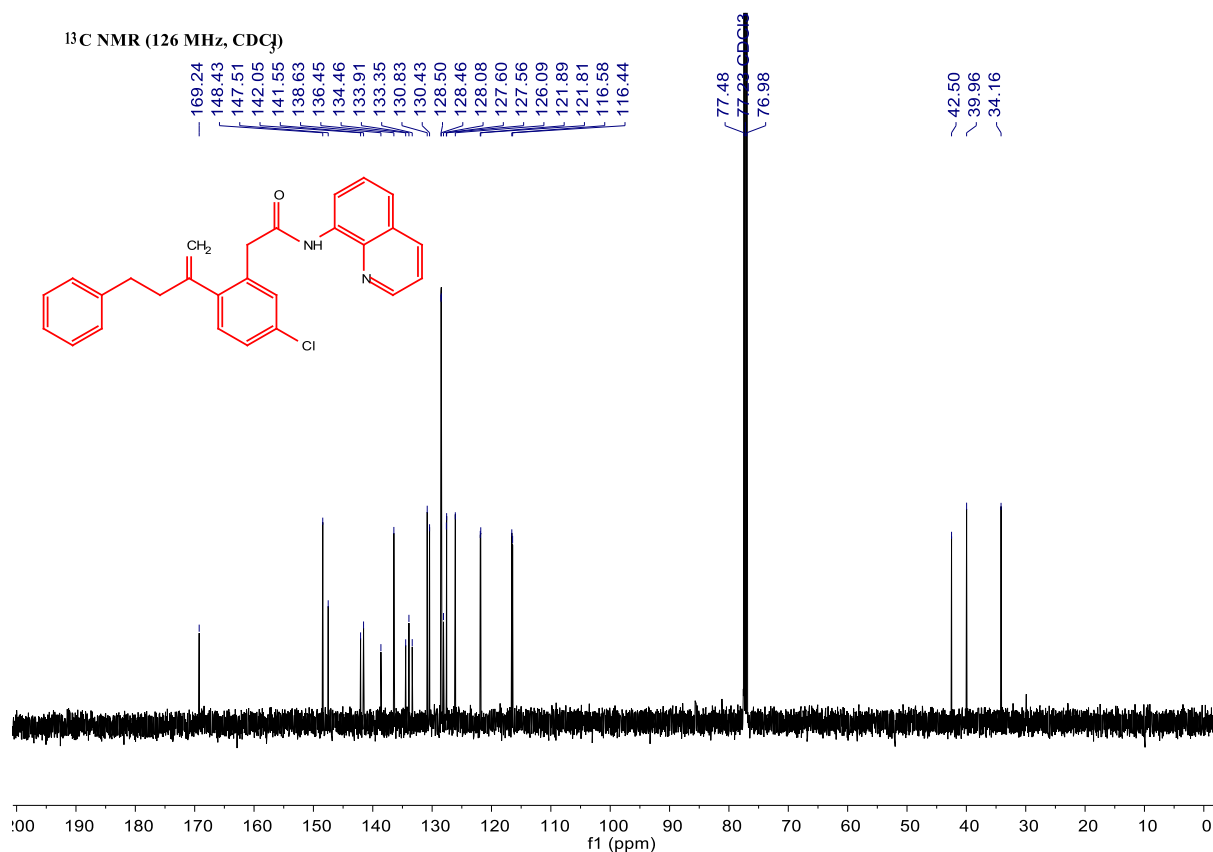




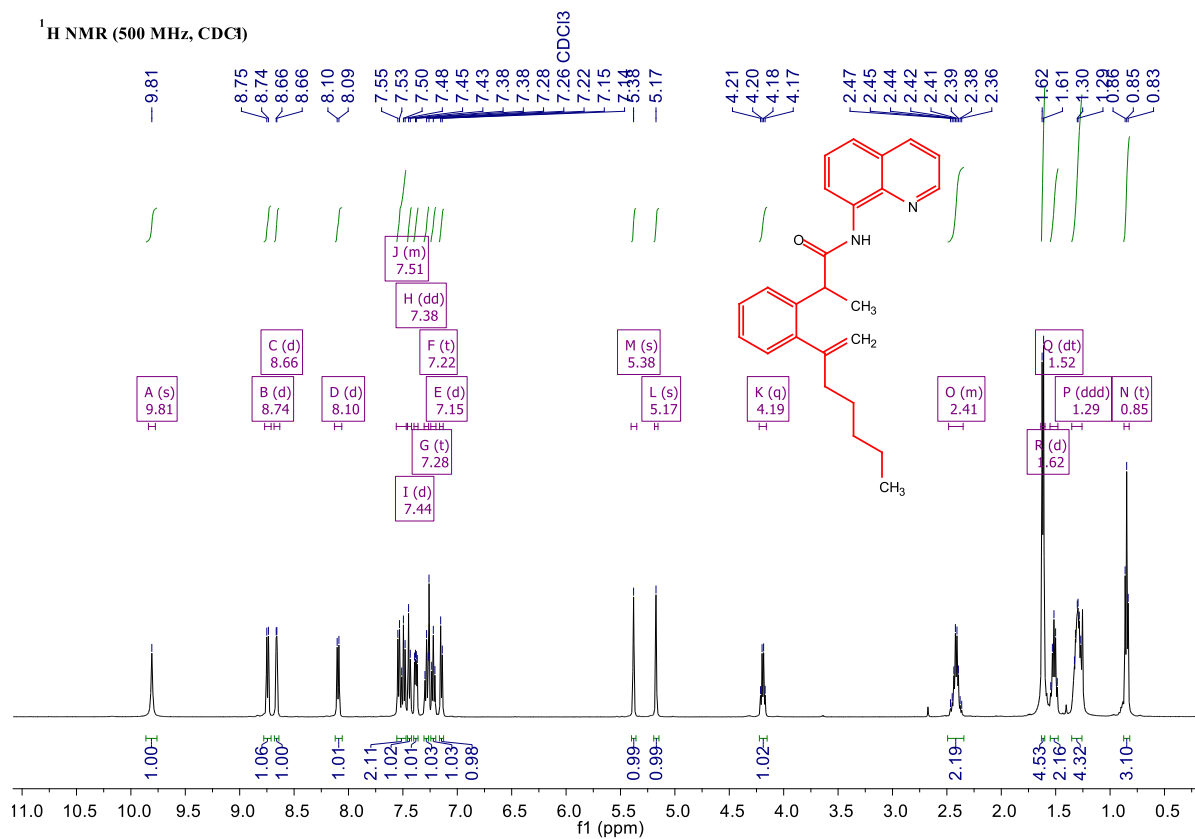


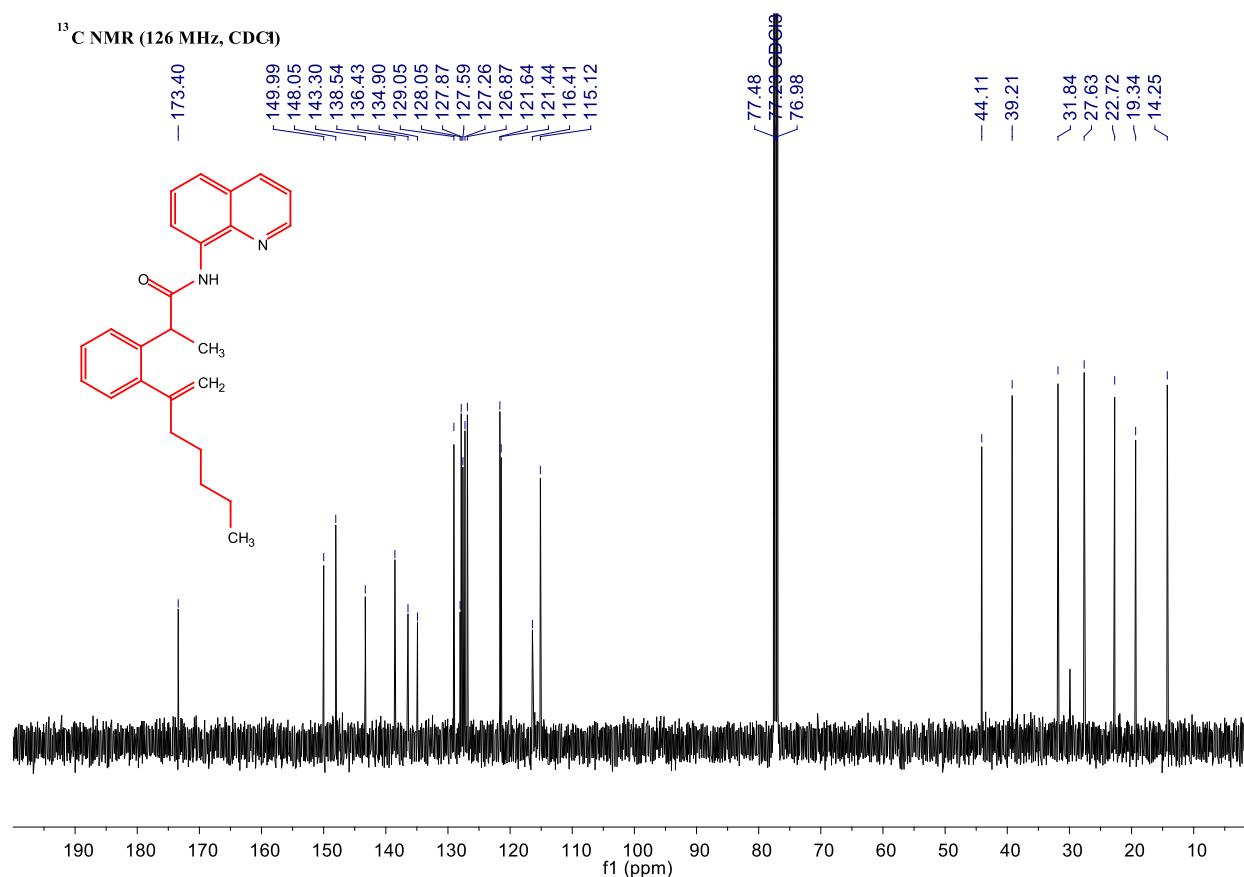
Scheme 2, entry 3y:



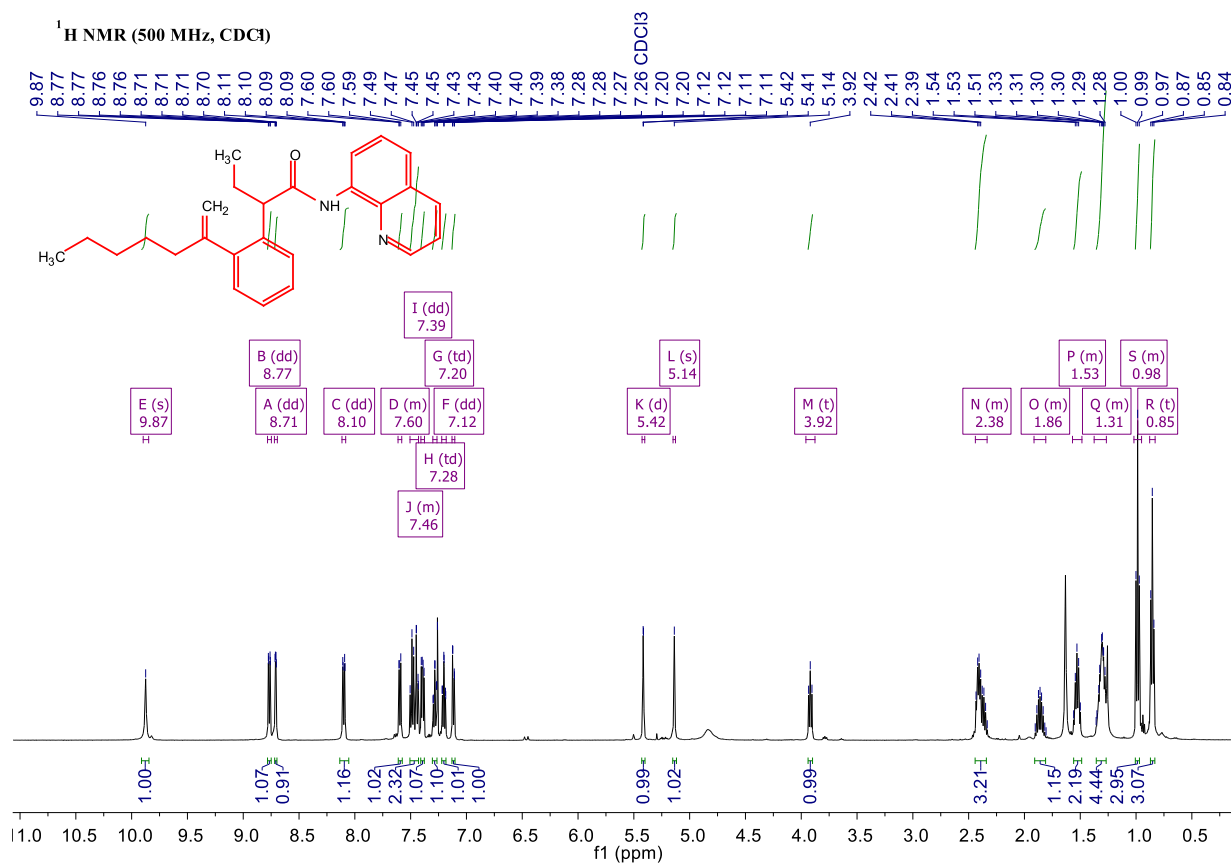


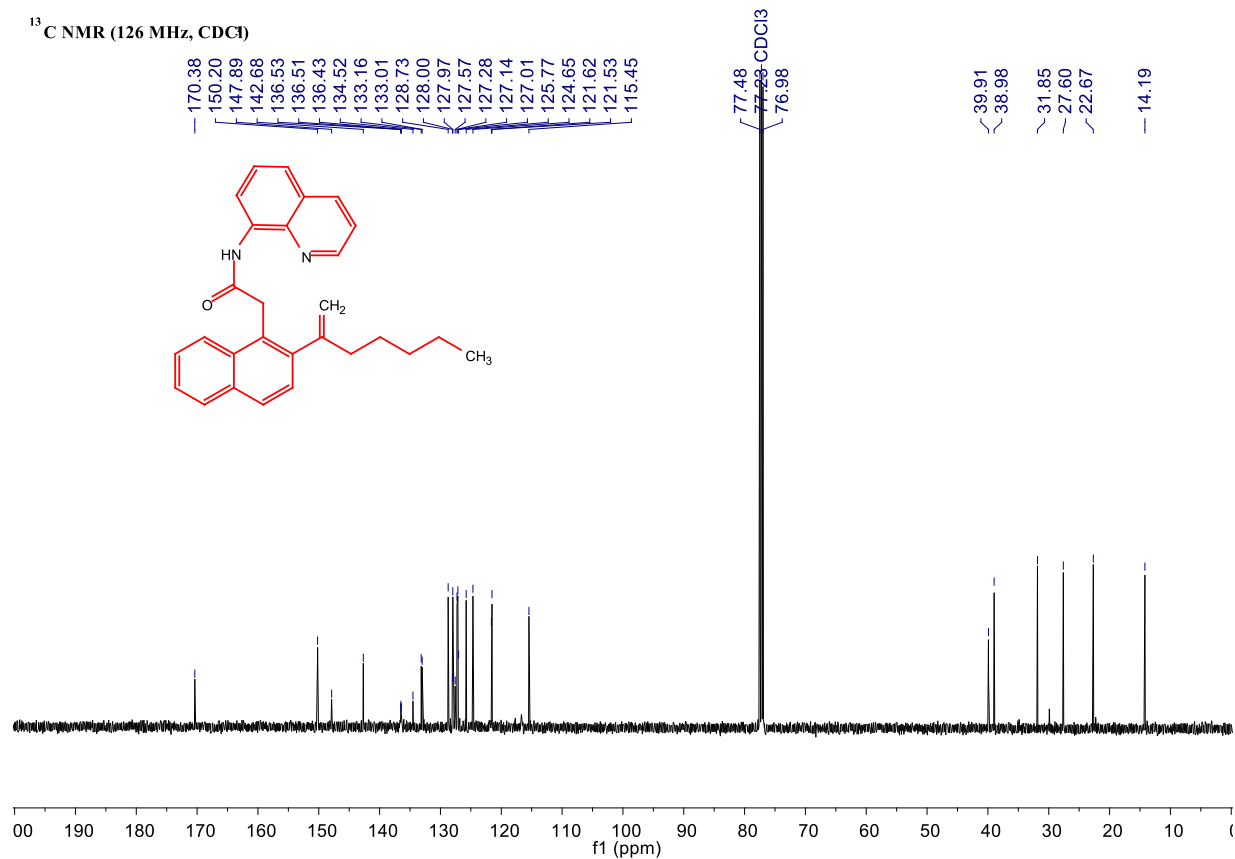
Scheme 2, entry 3z:



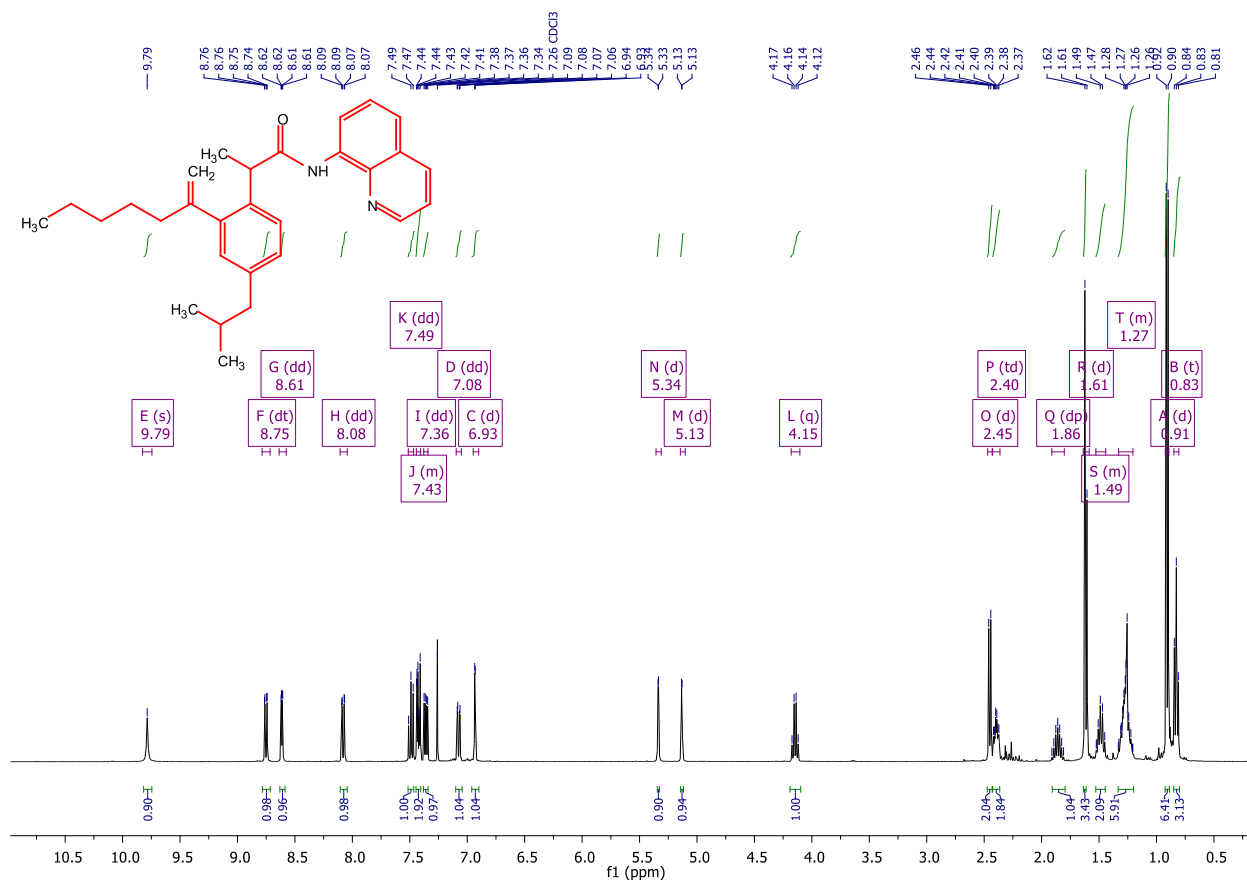


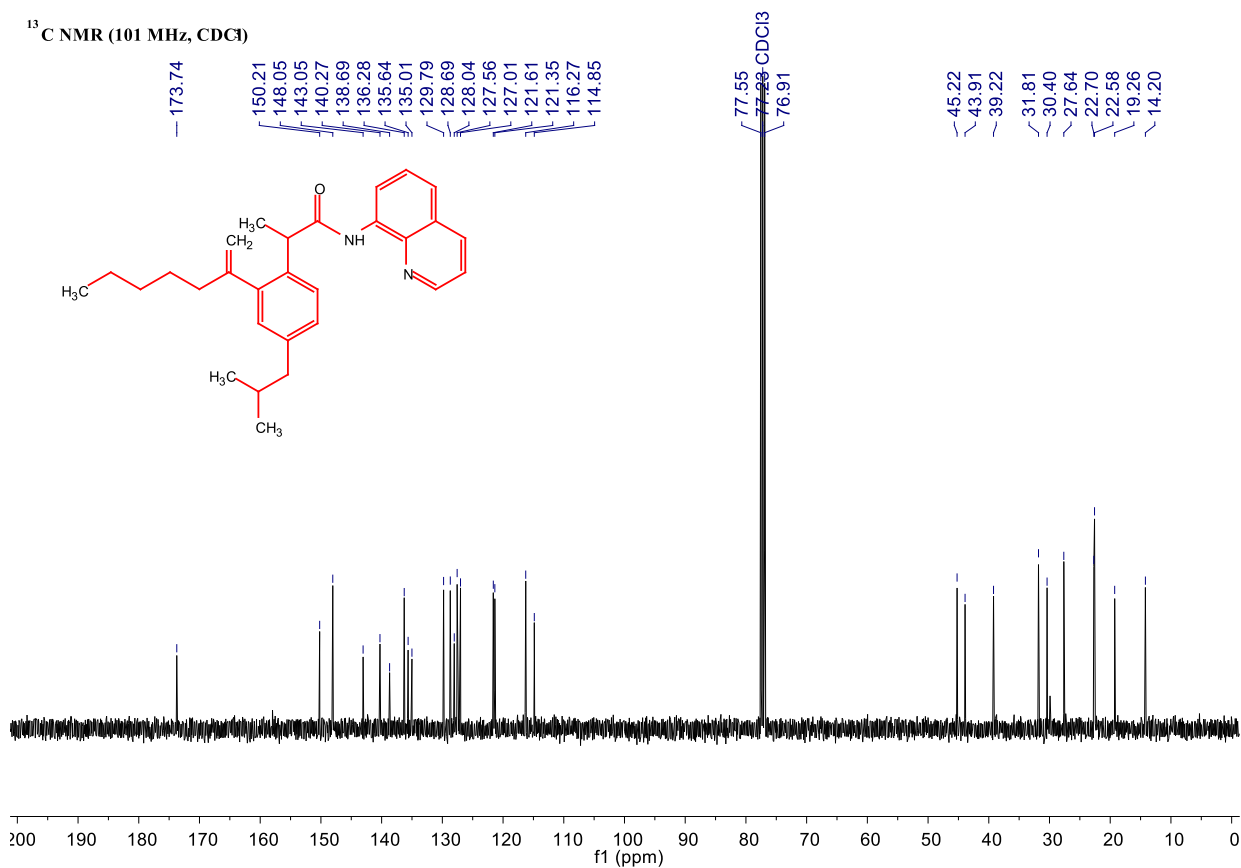
Scheme 2, entry 3aa:



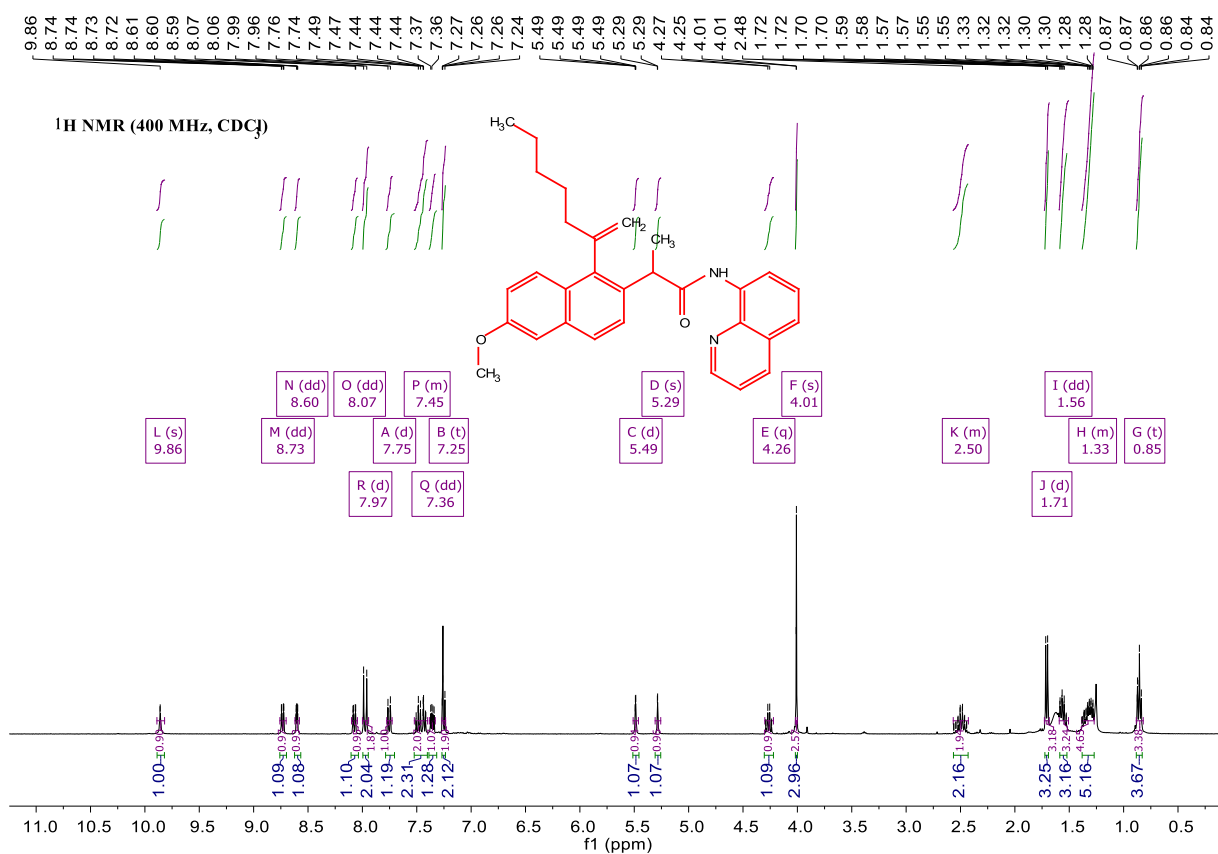


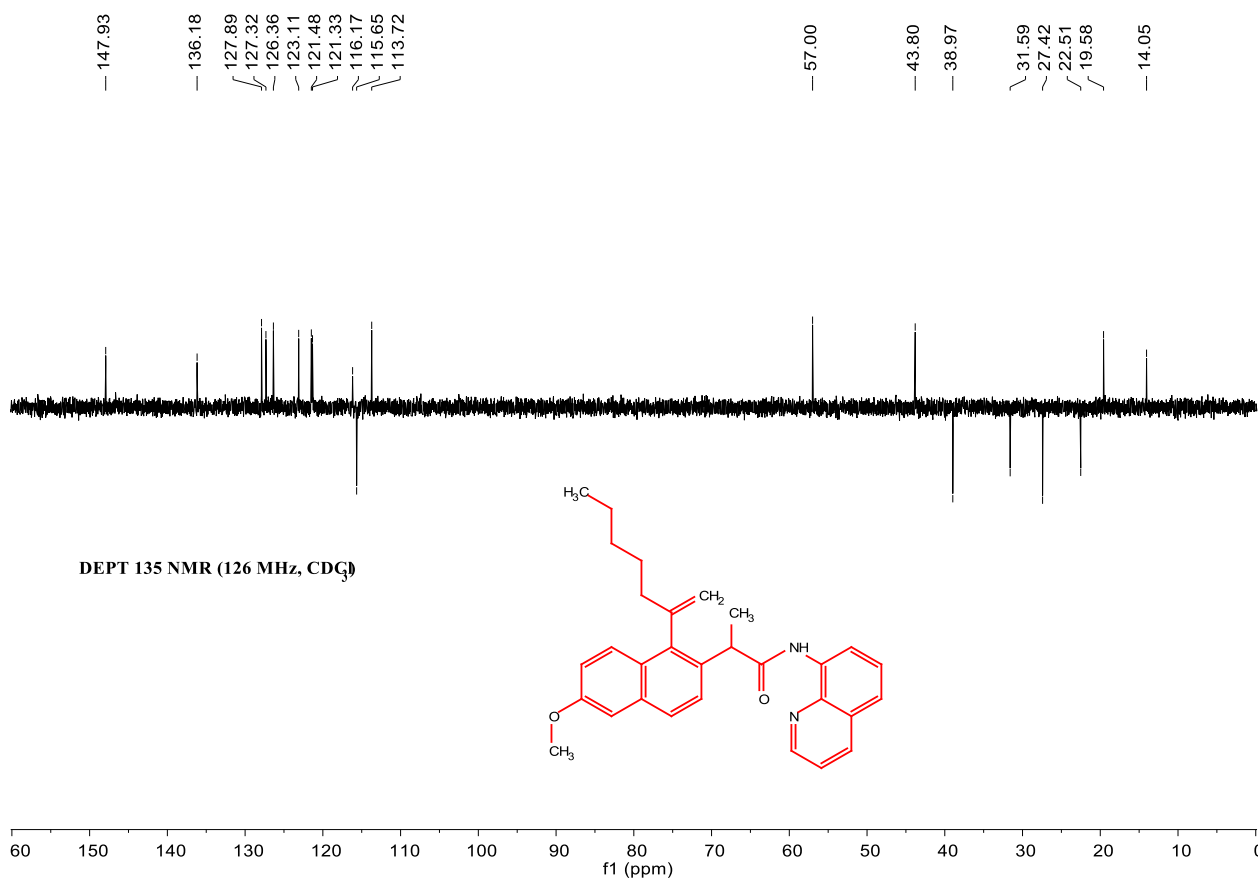
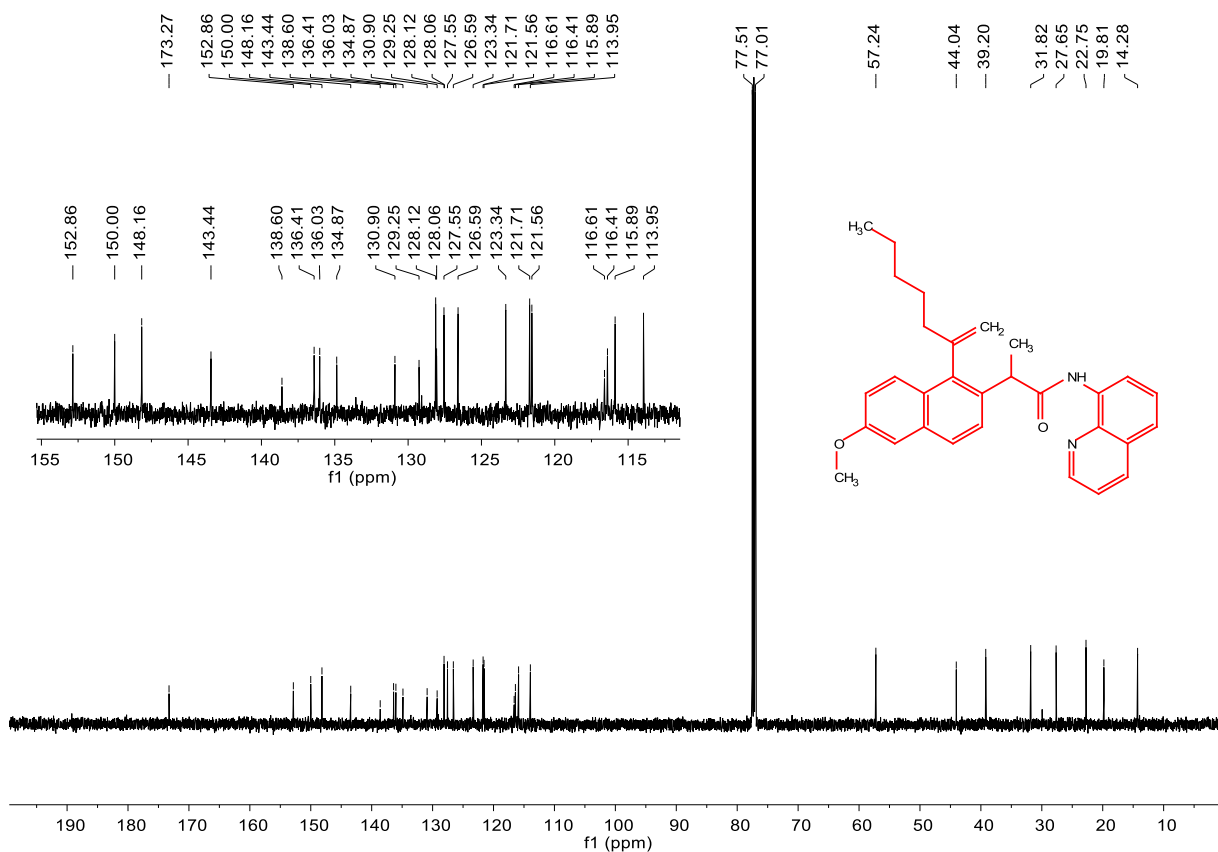
Scheme 2, entry 3ac:



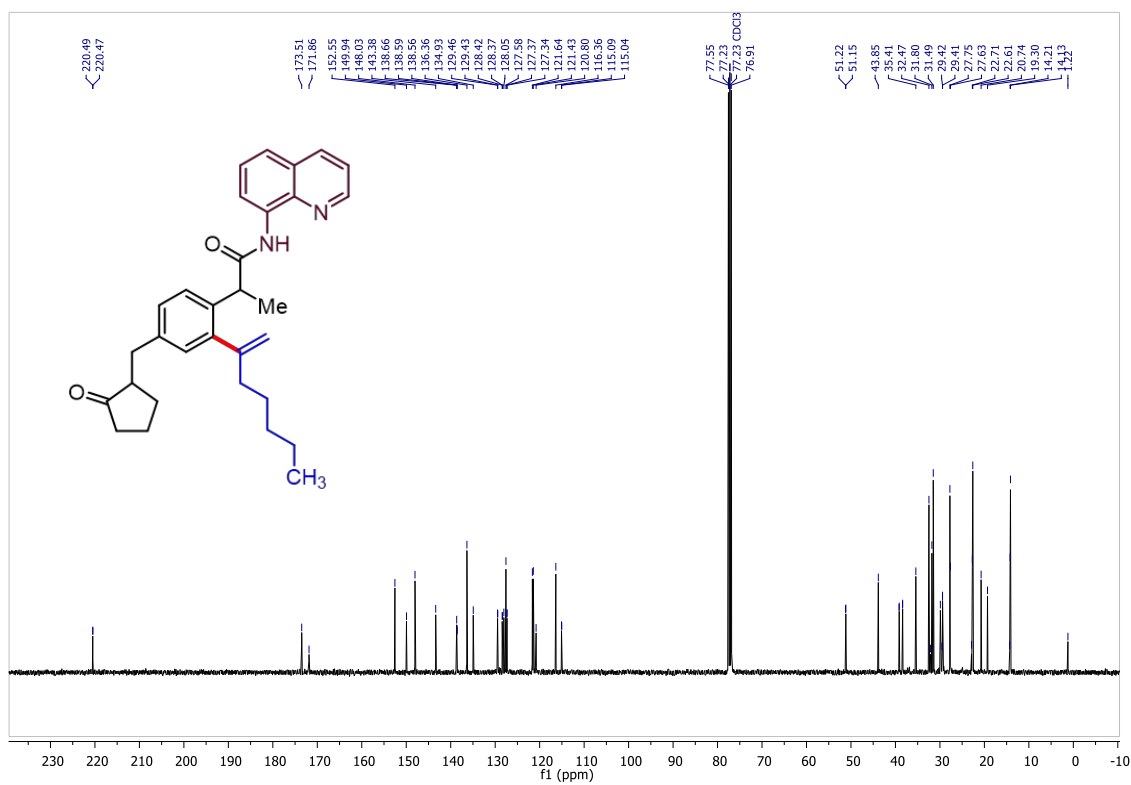
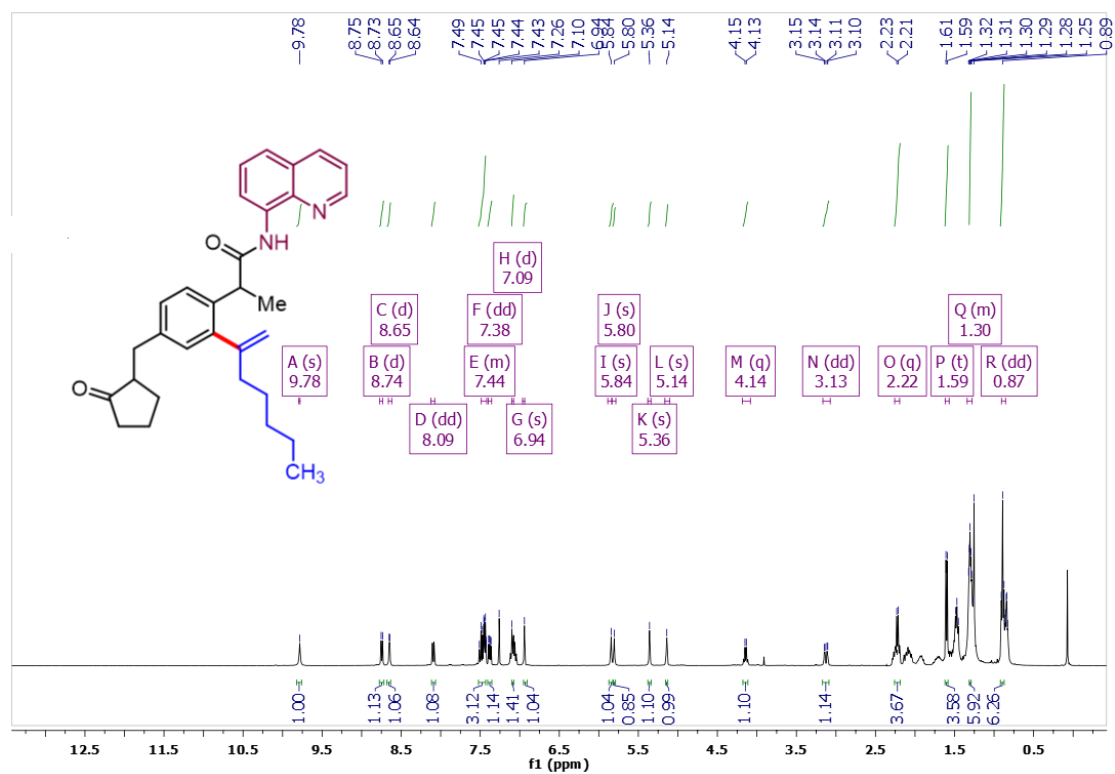


Scheme 2, entry 3ad:

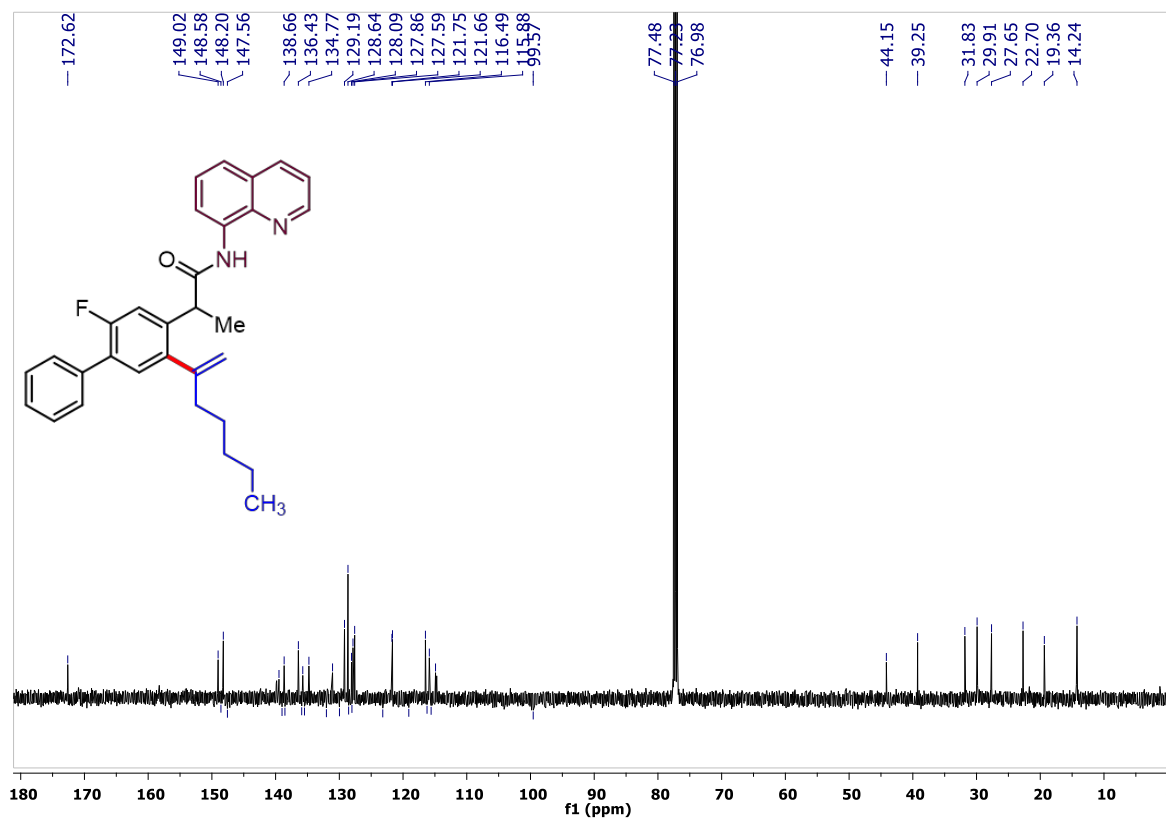
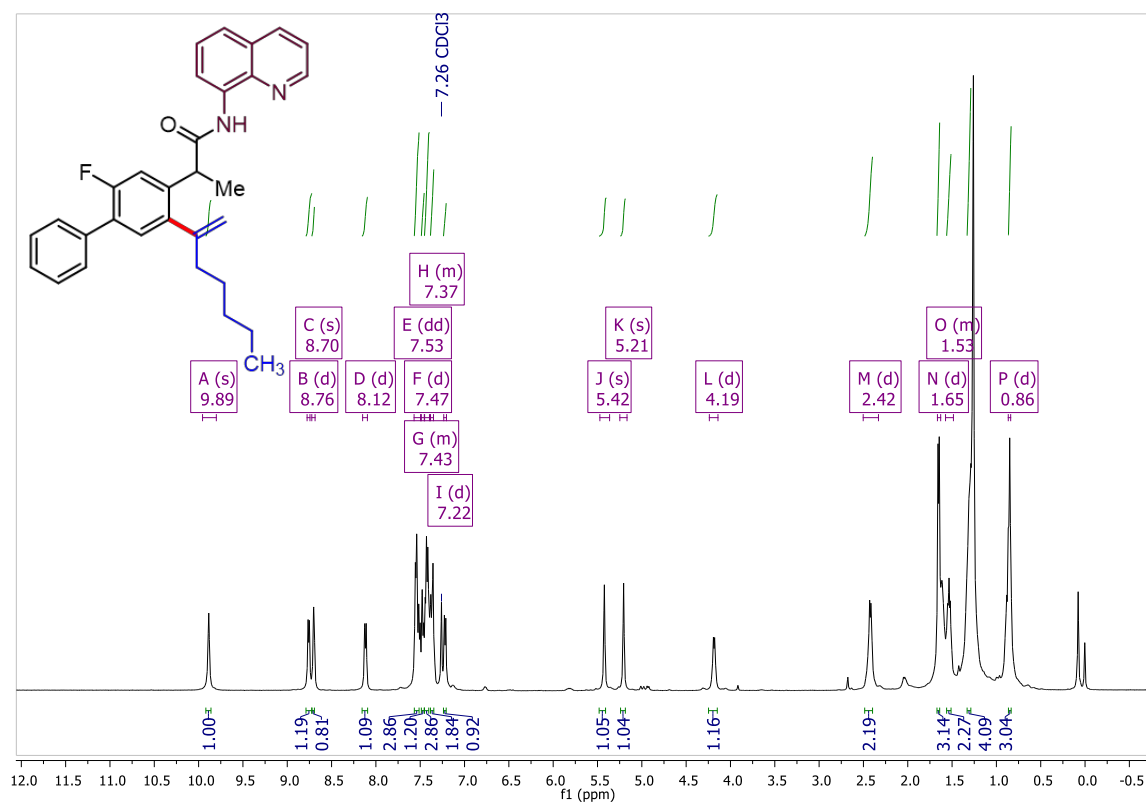




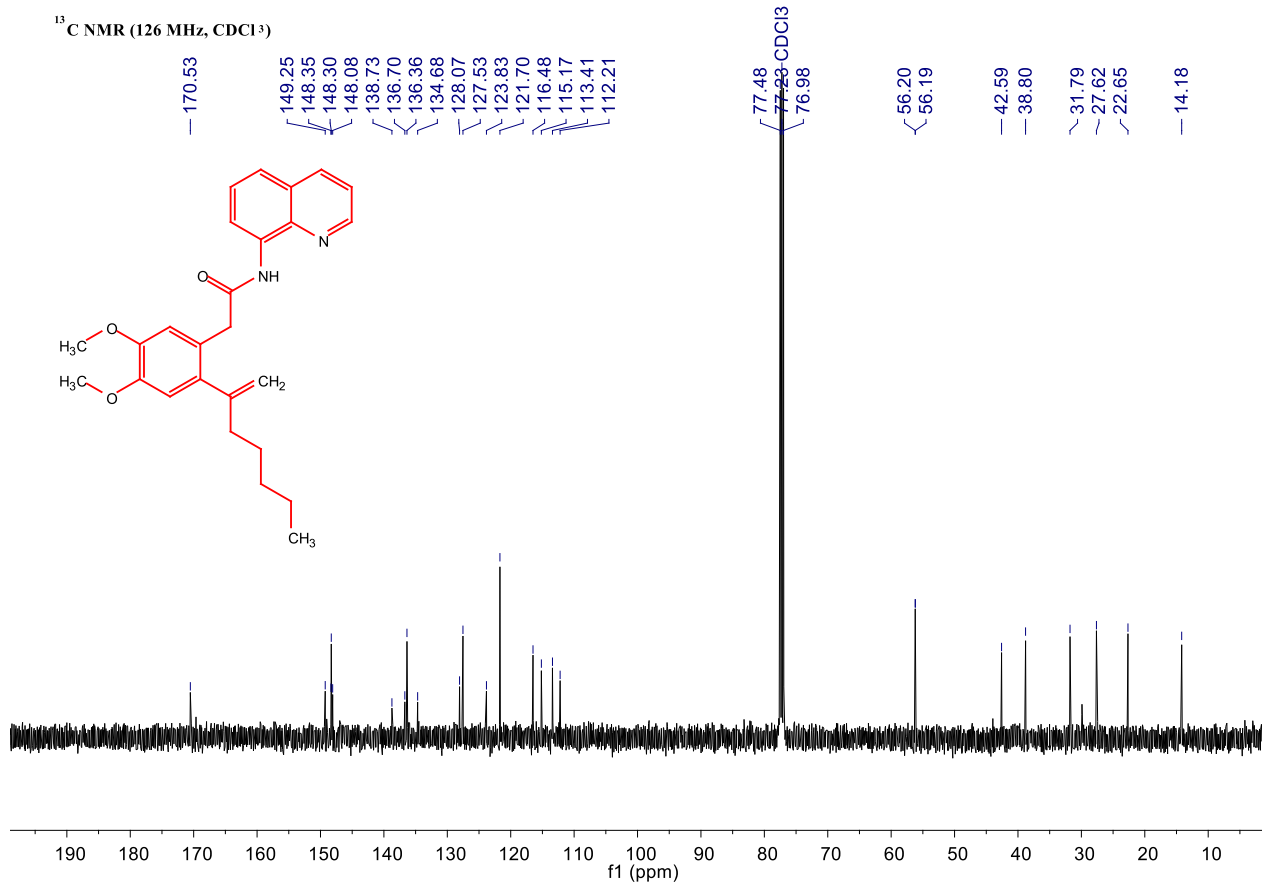
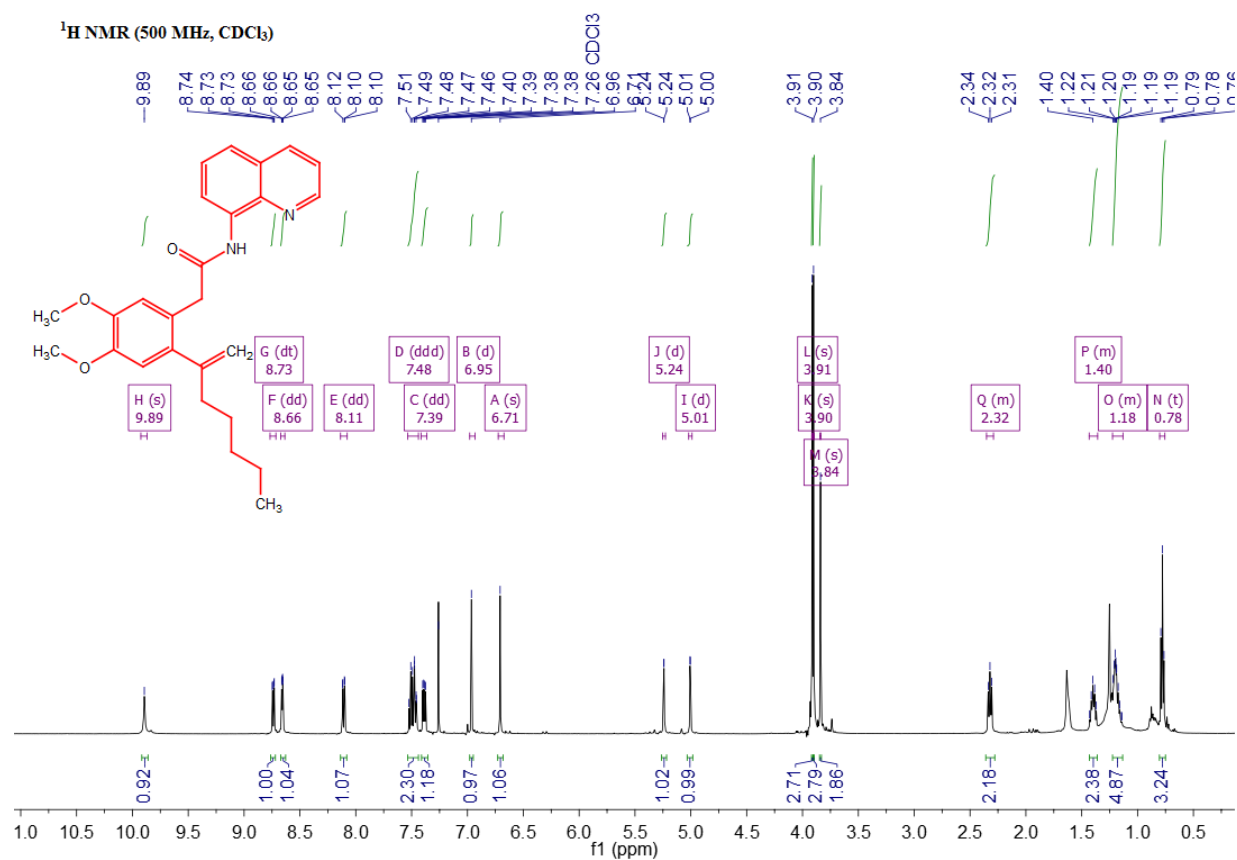
Scheme 2, entry 3ae



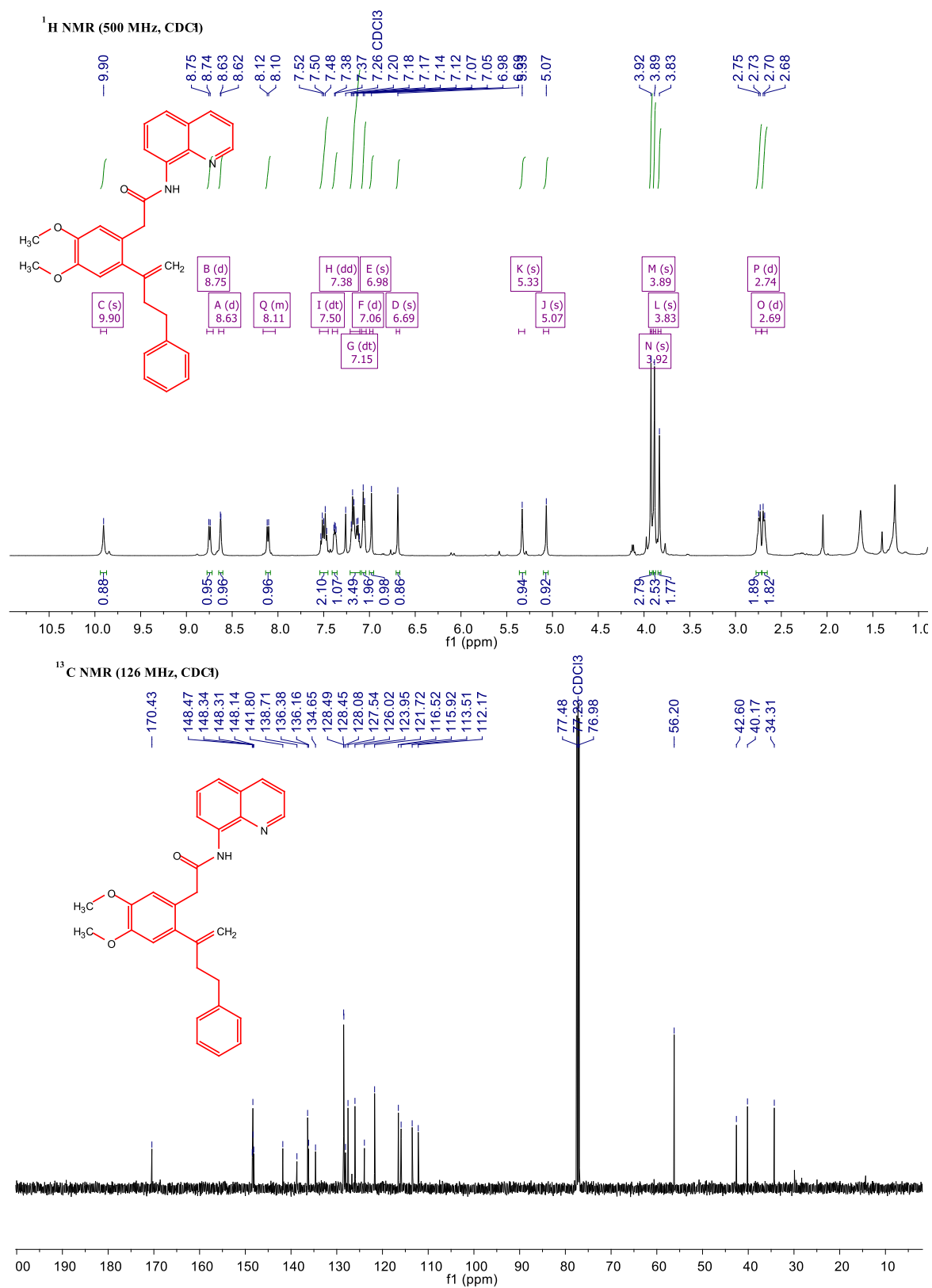
Scheme 2, entry 3af



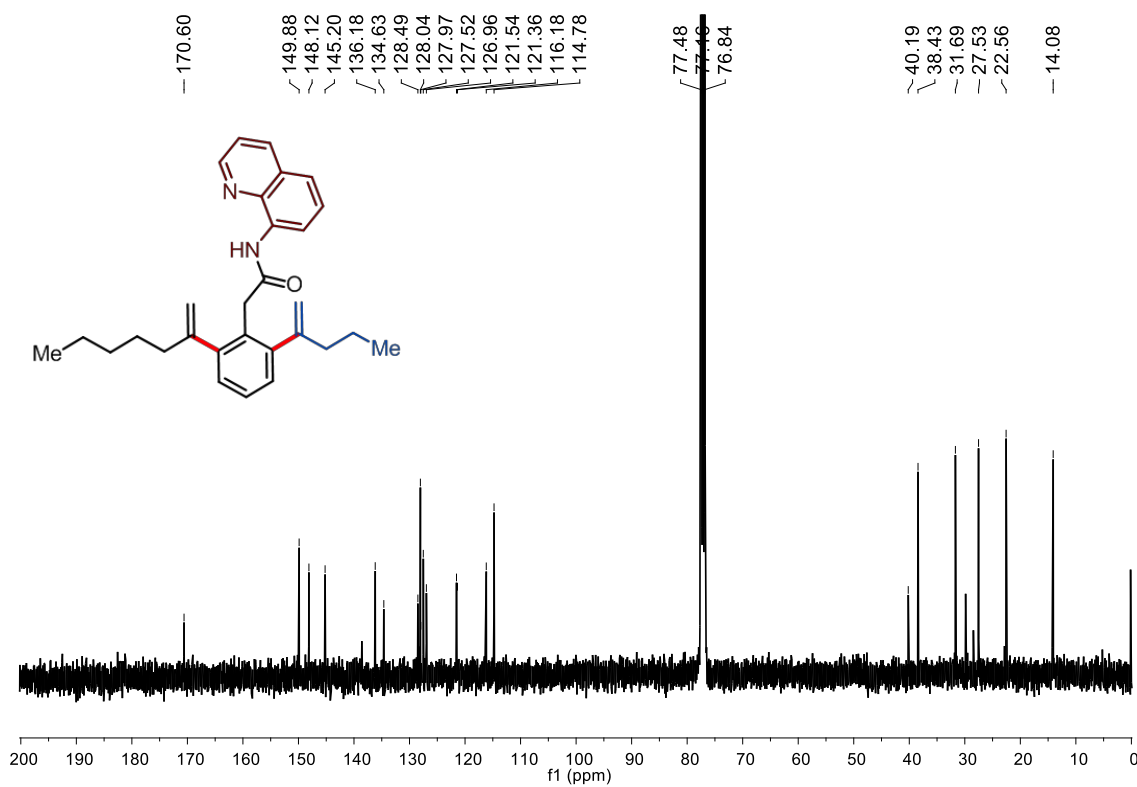
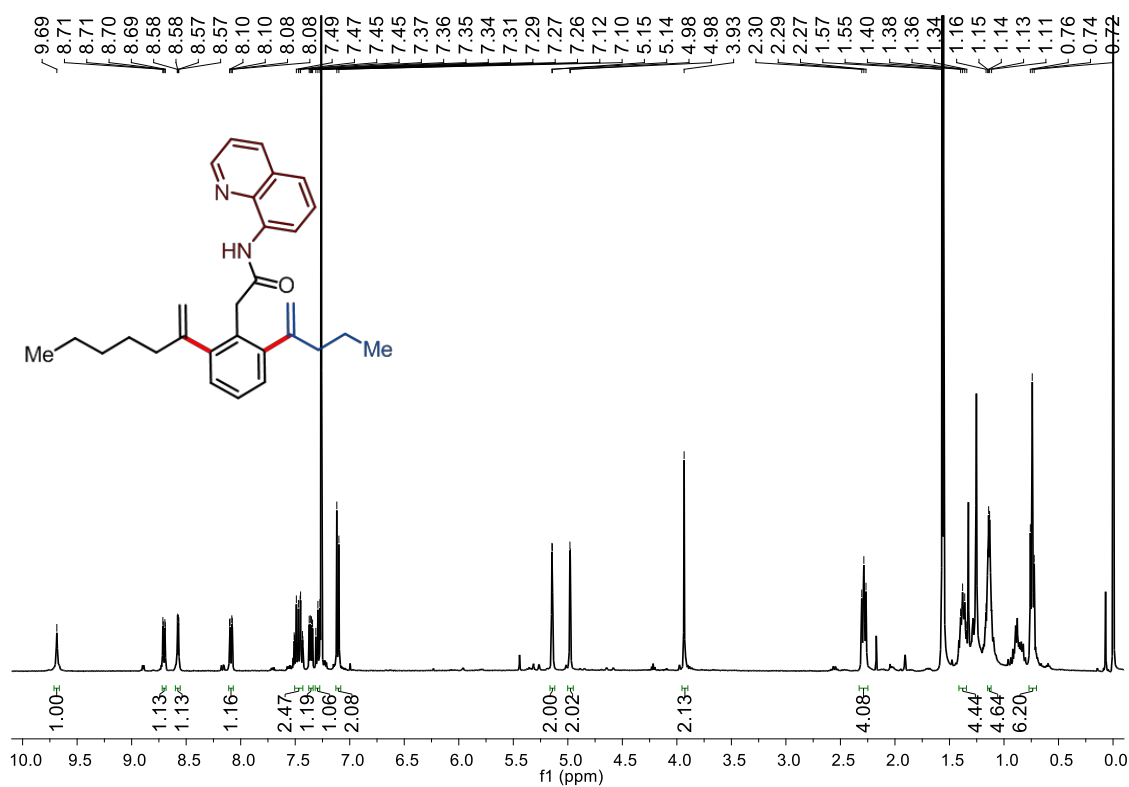
Scheme 2, entry 3ag:



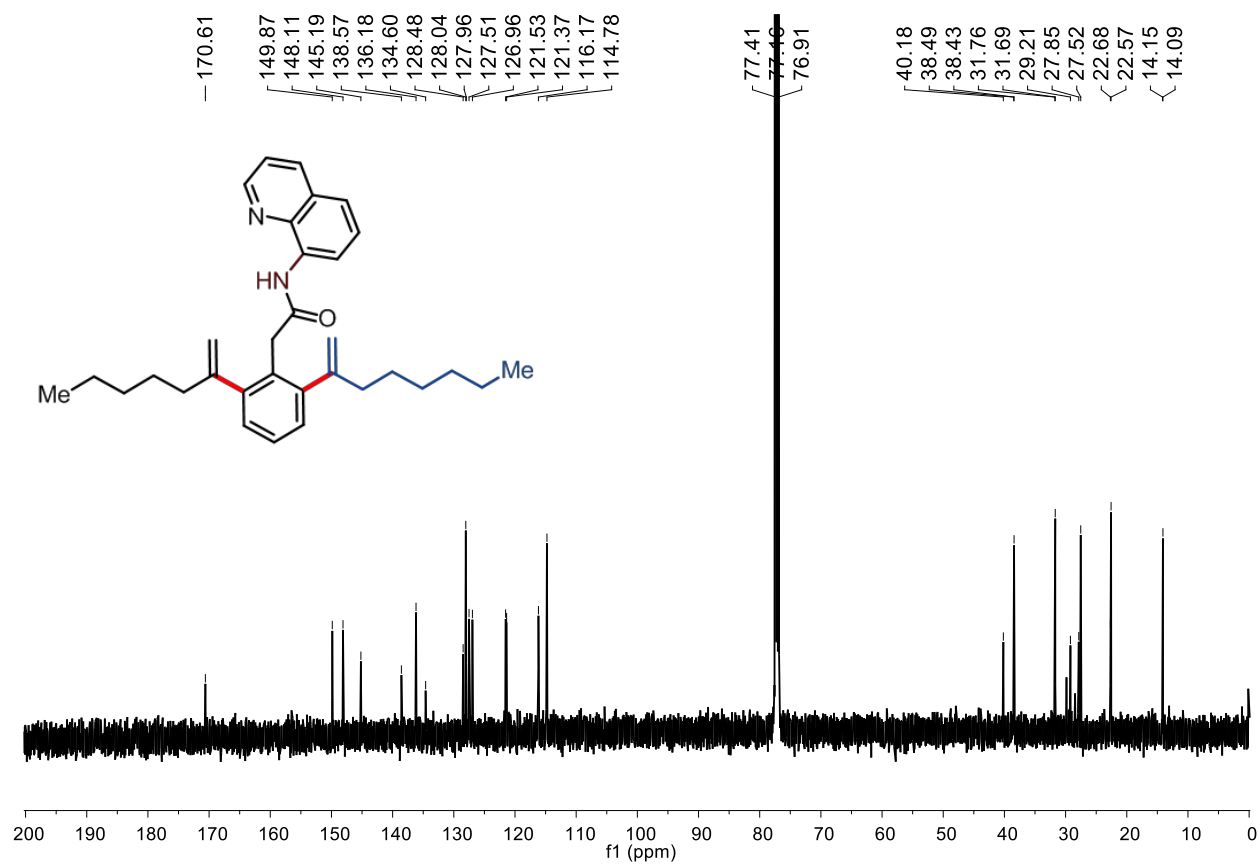
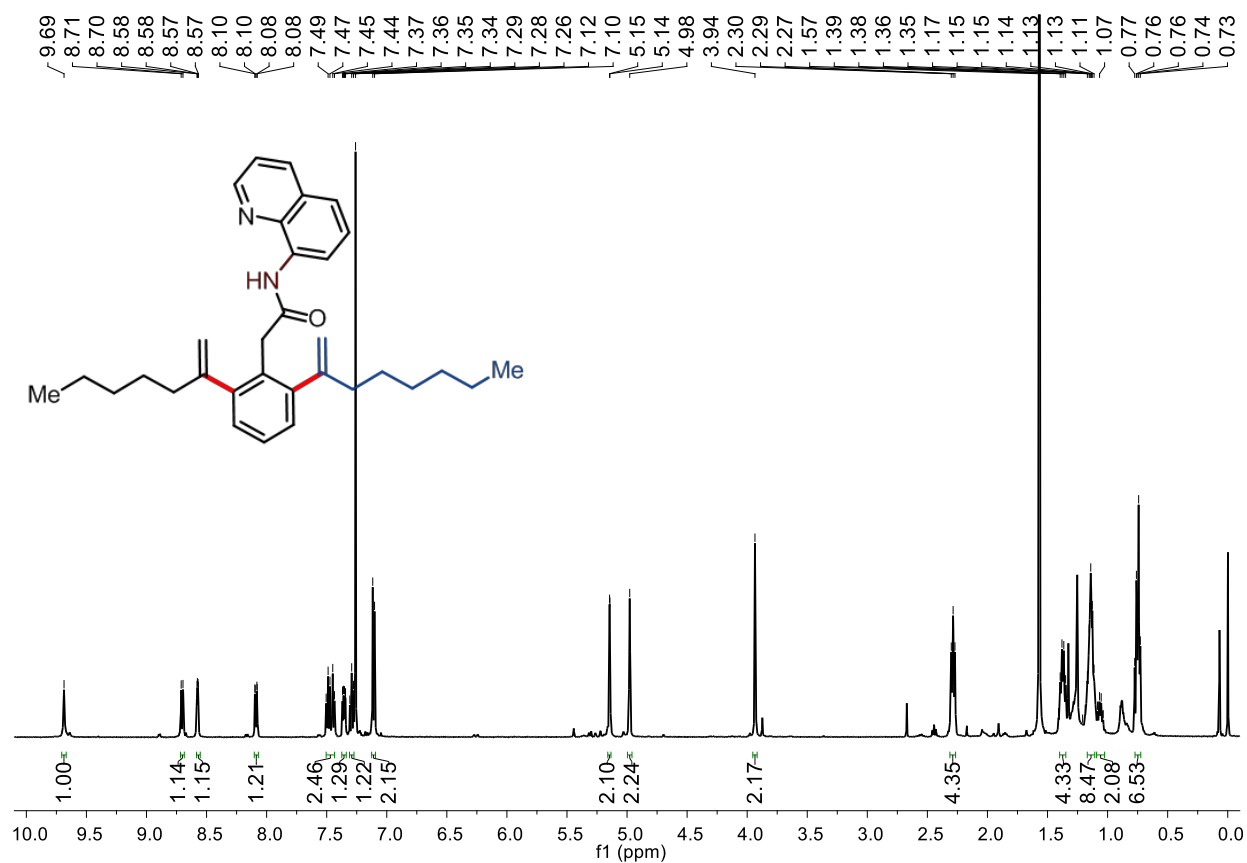
Scheme 2, entry 3ah:



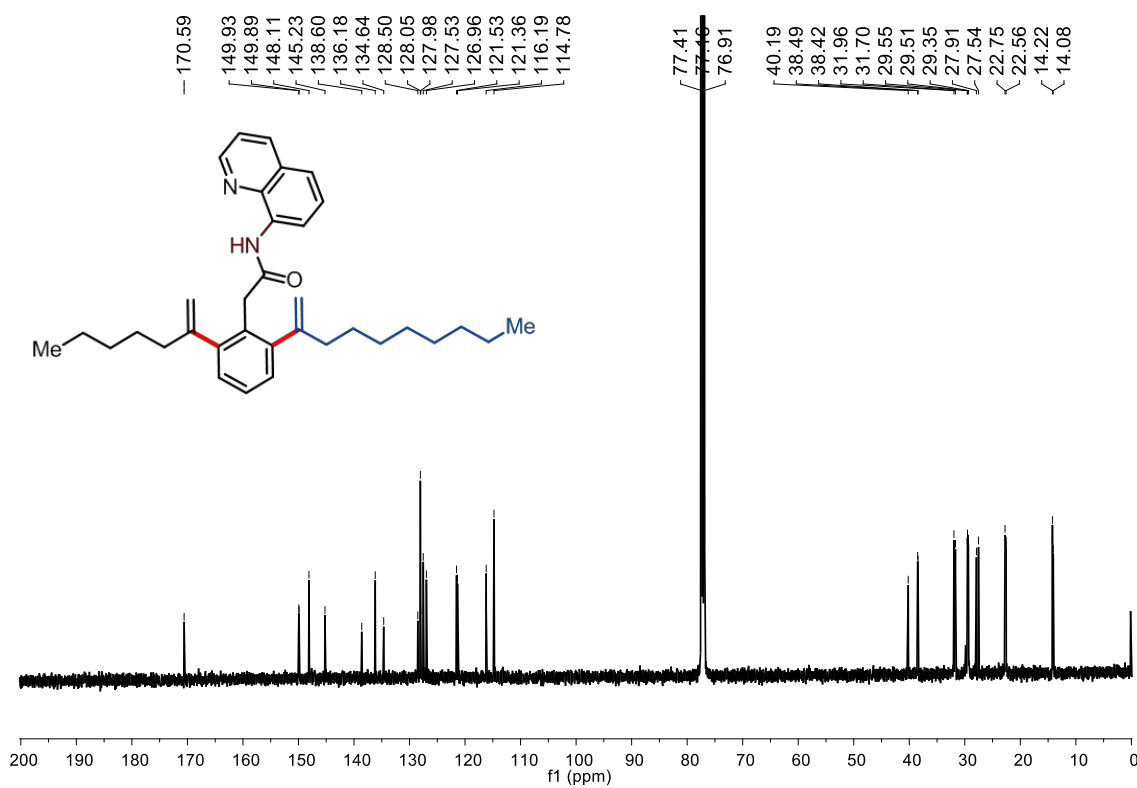
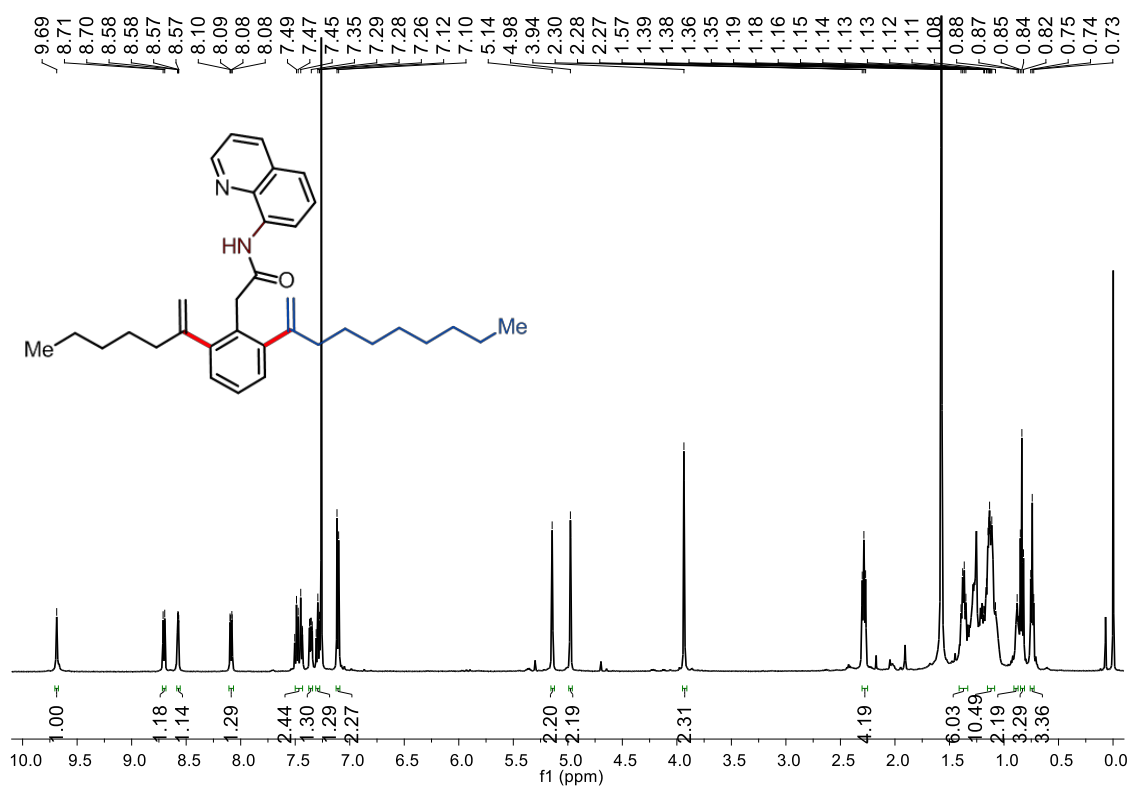
Scheme 3, entry 4a



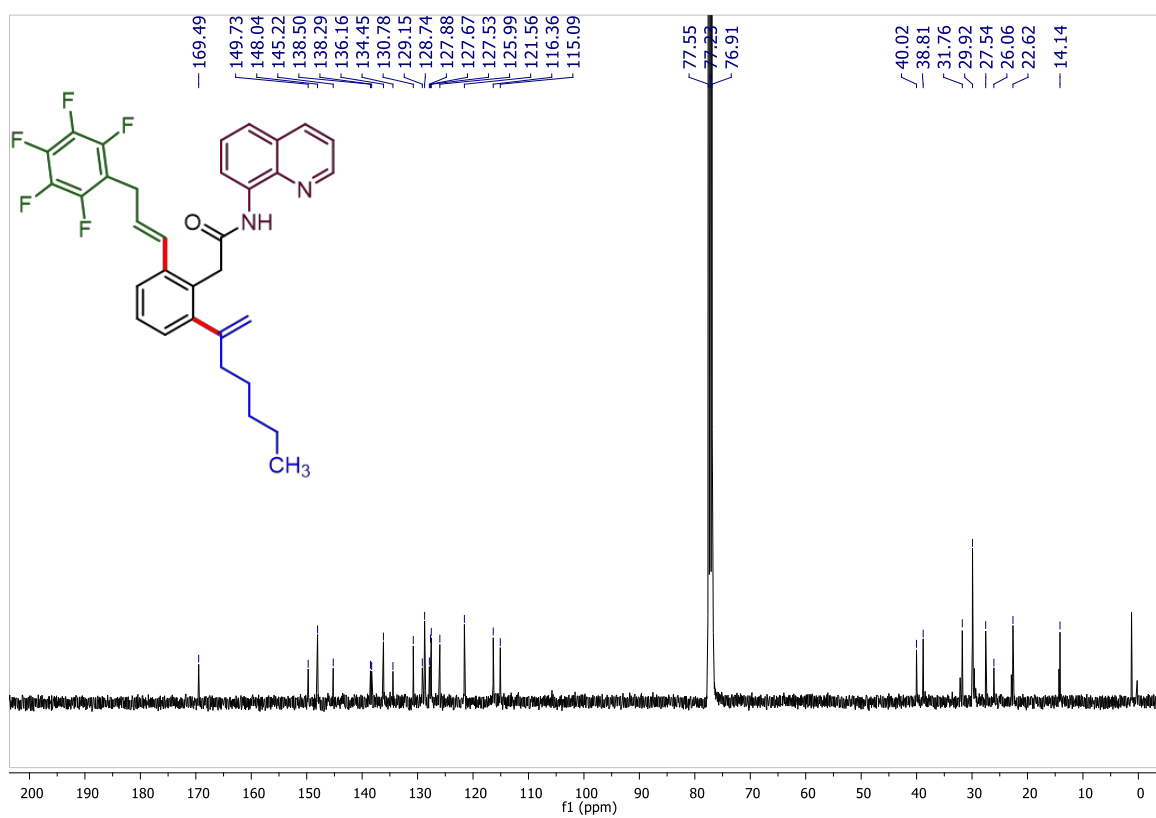
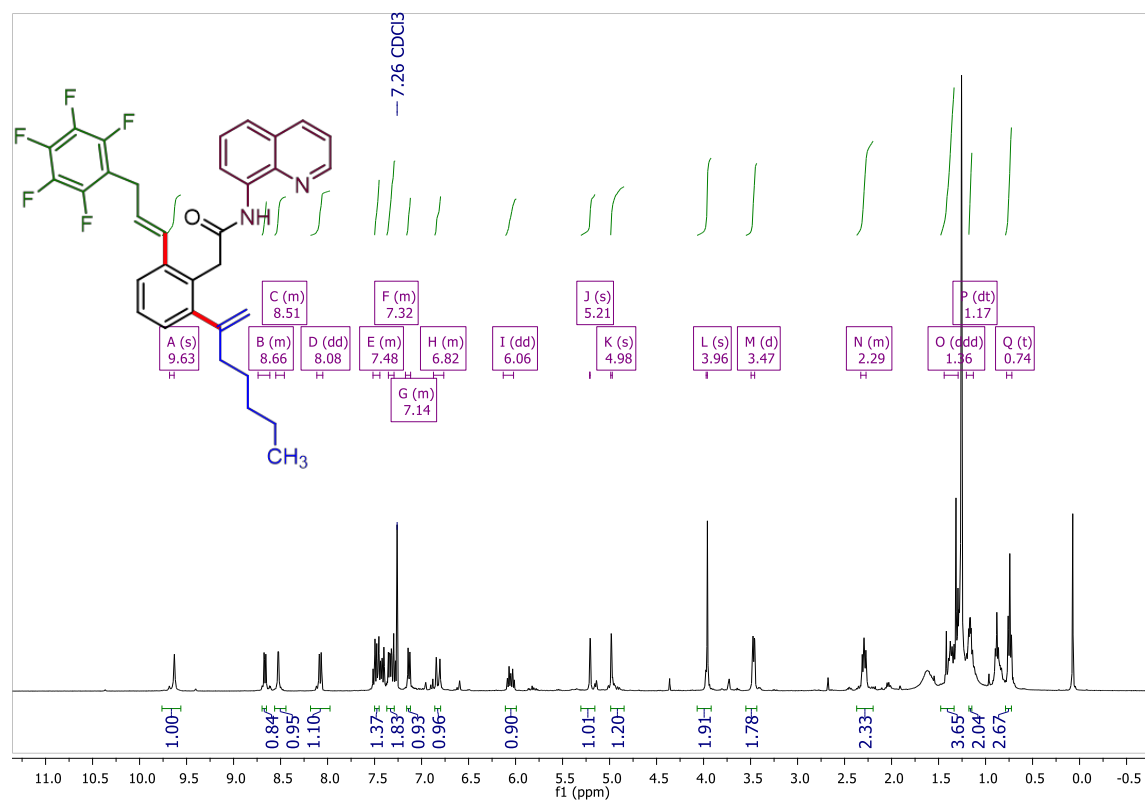
Scheme 3, entry 4b



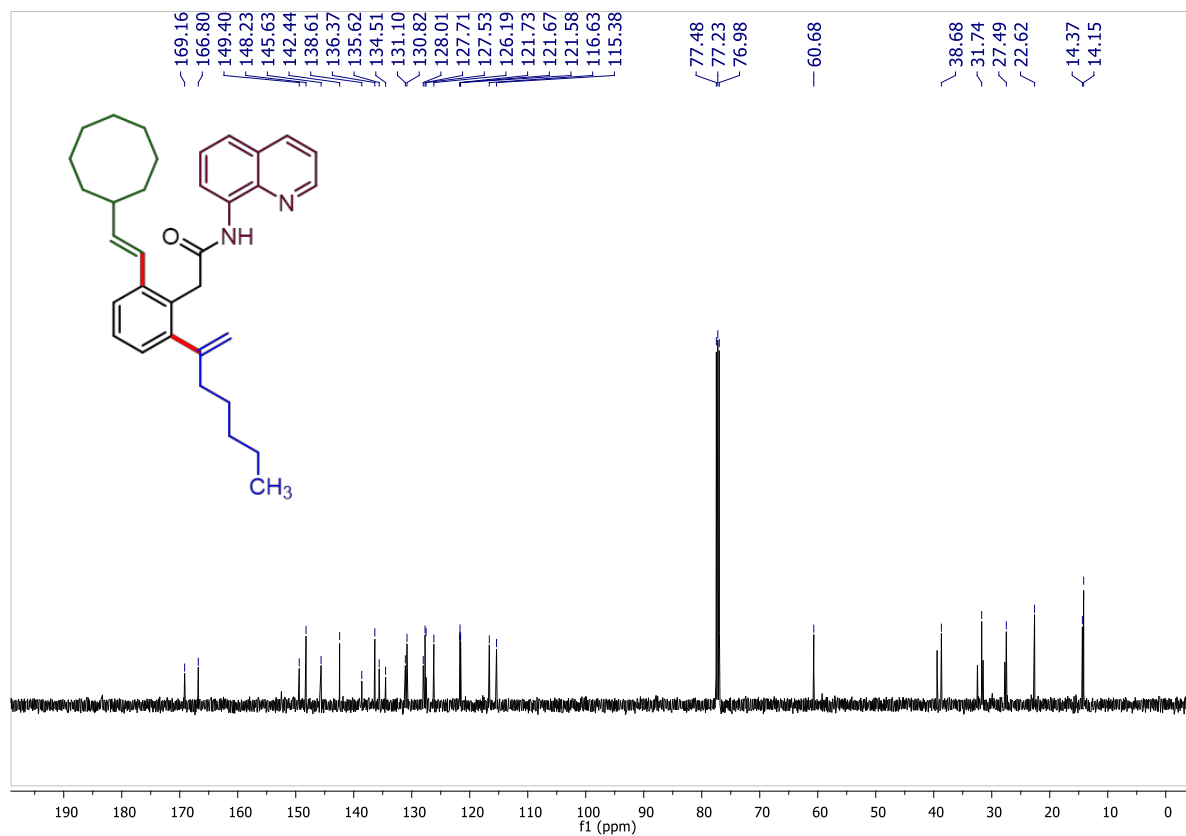
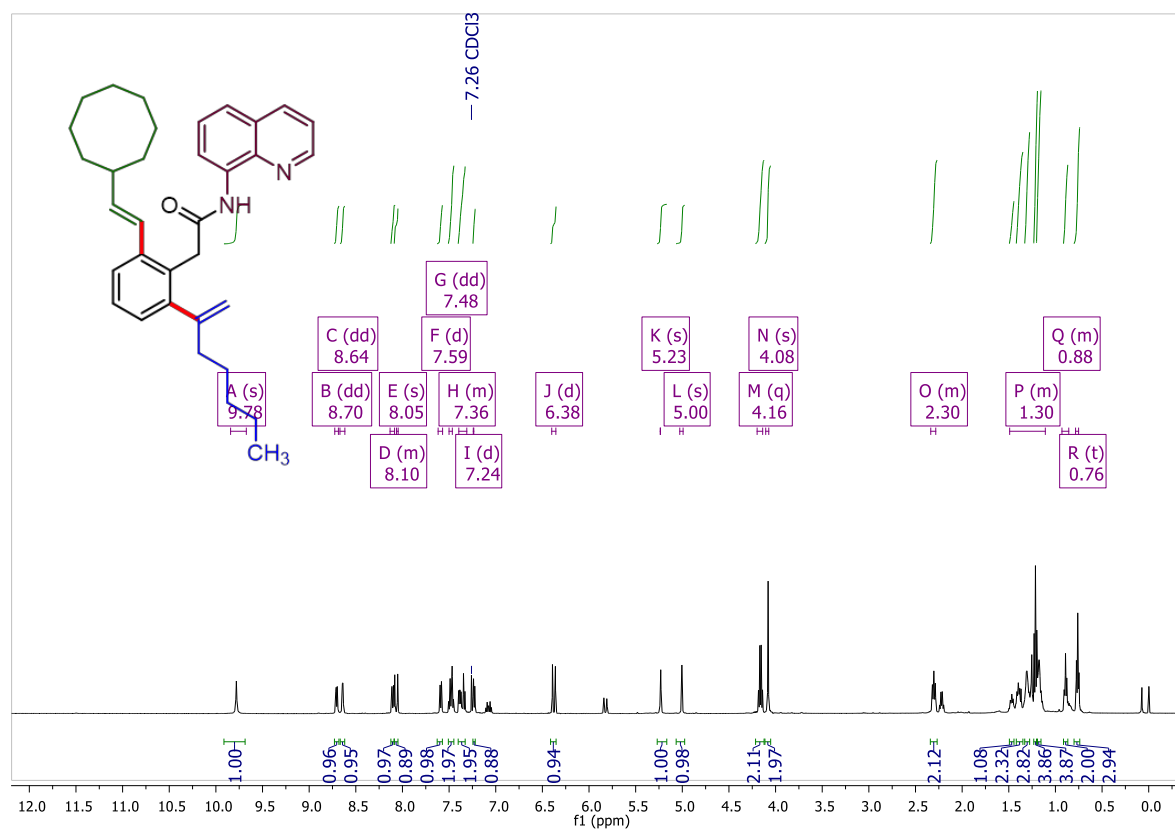
Scheme 3, entry 4c



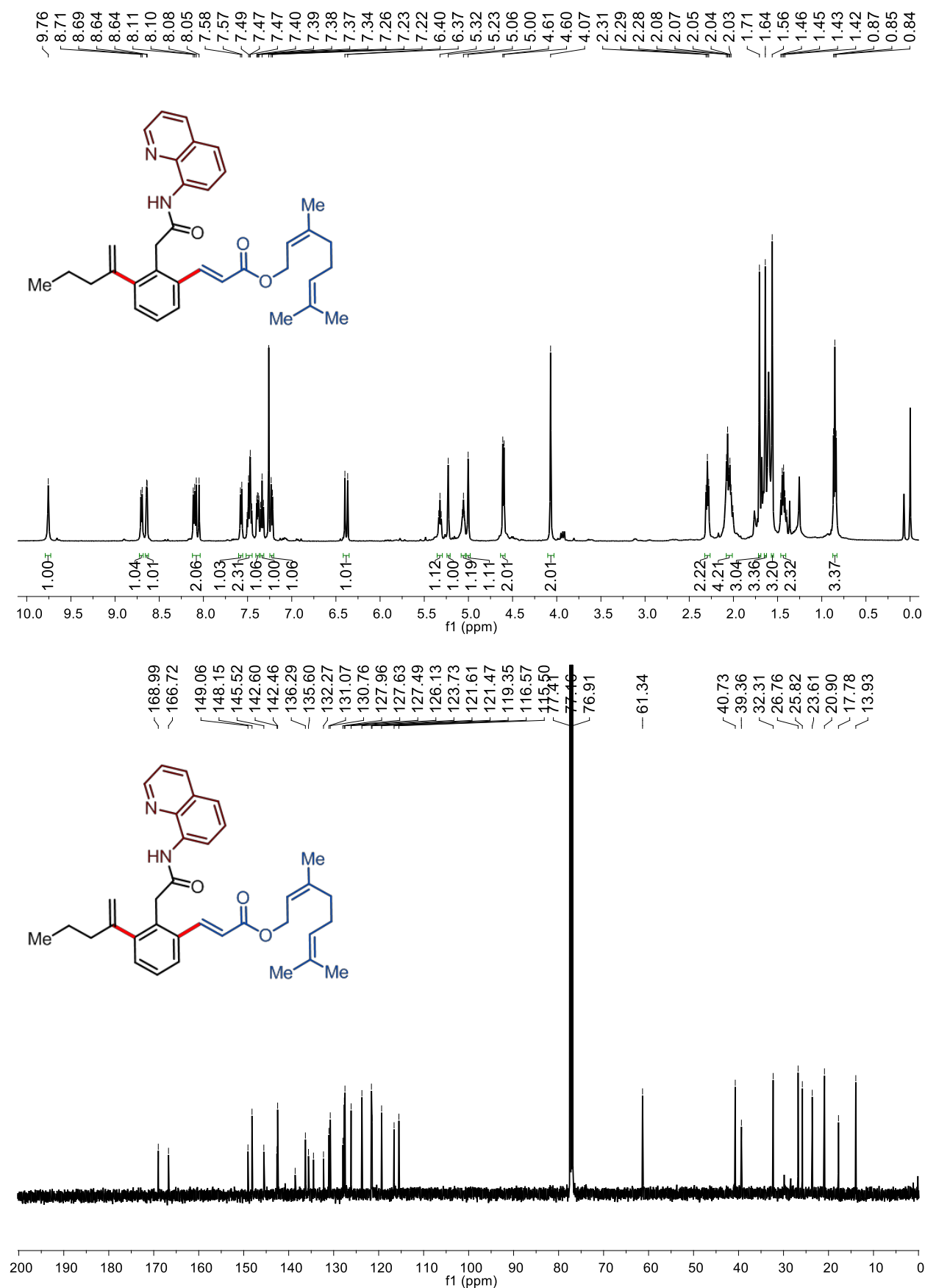
Scheme 3, entry 6a



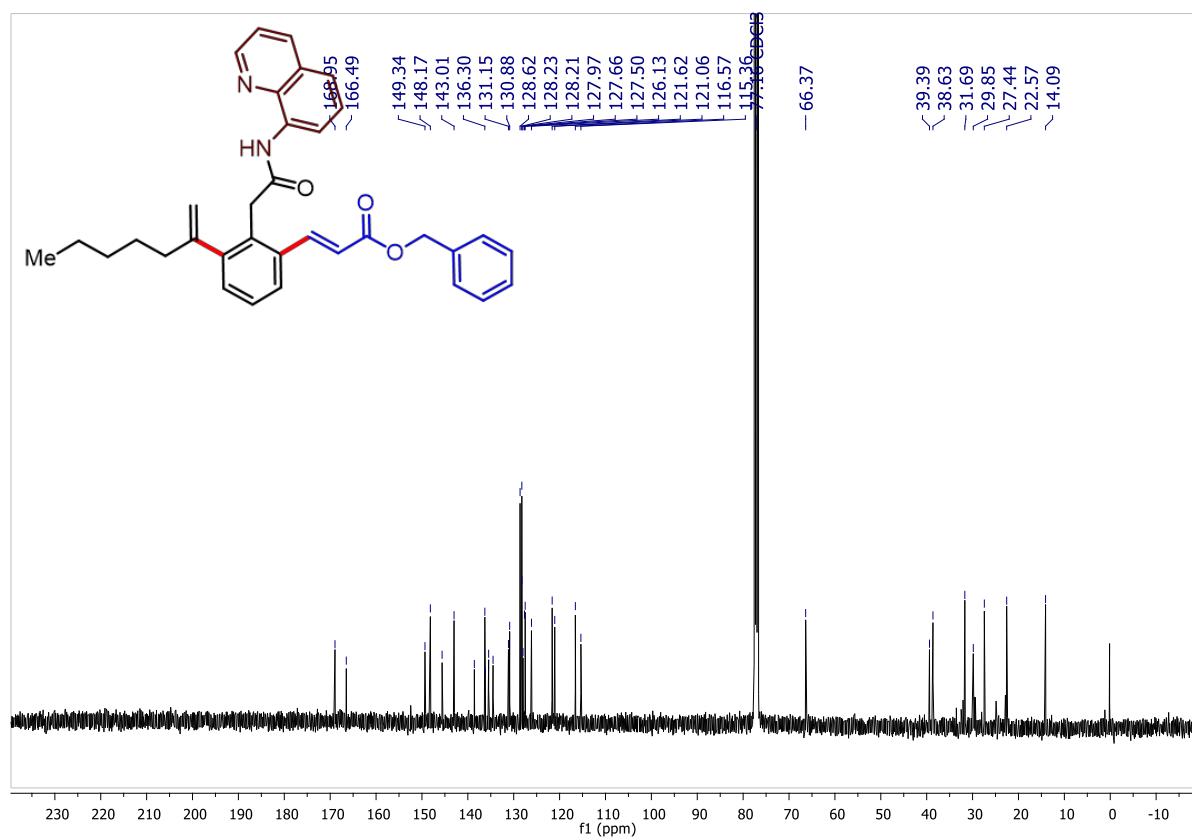
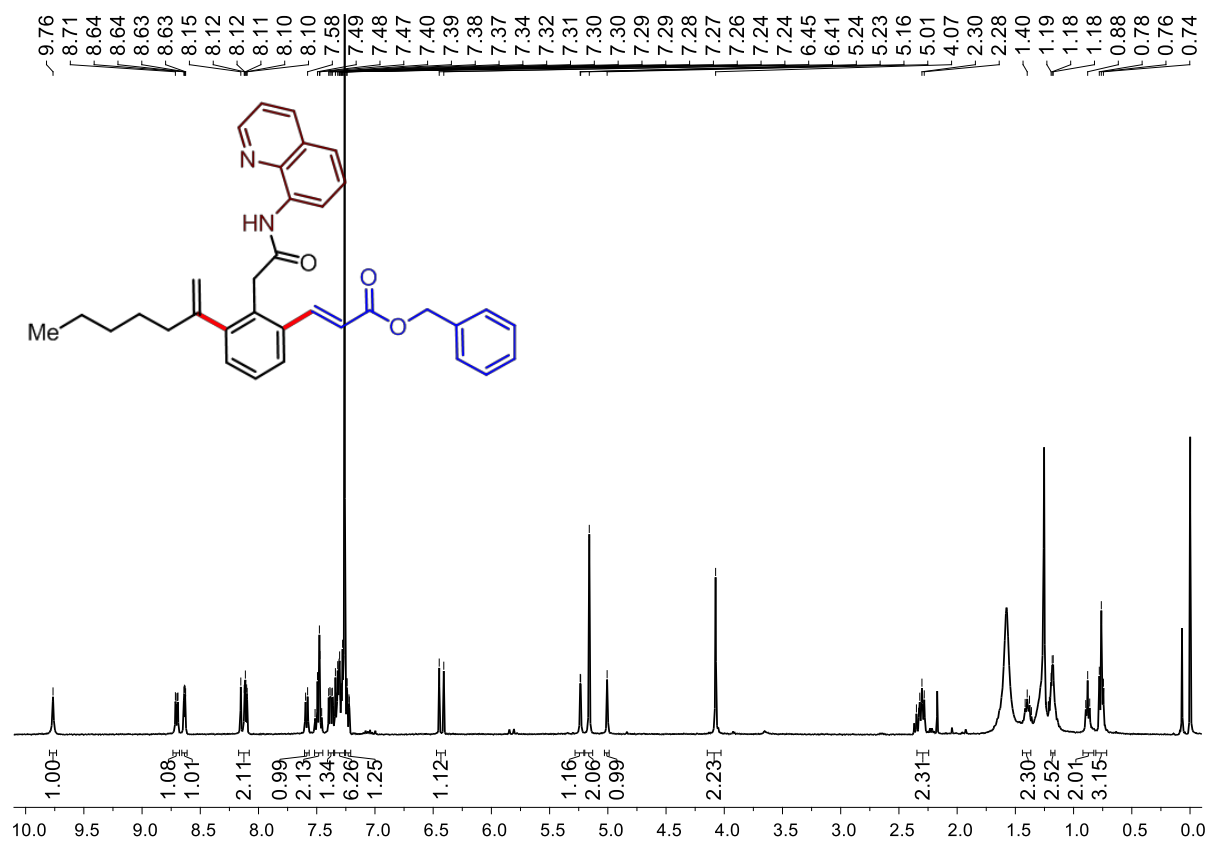
Scheme 3, entry 6b



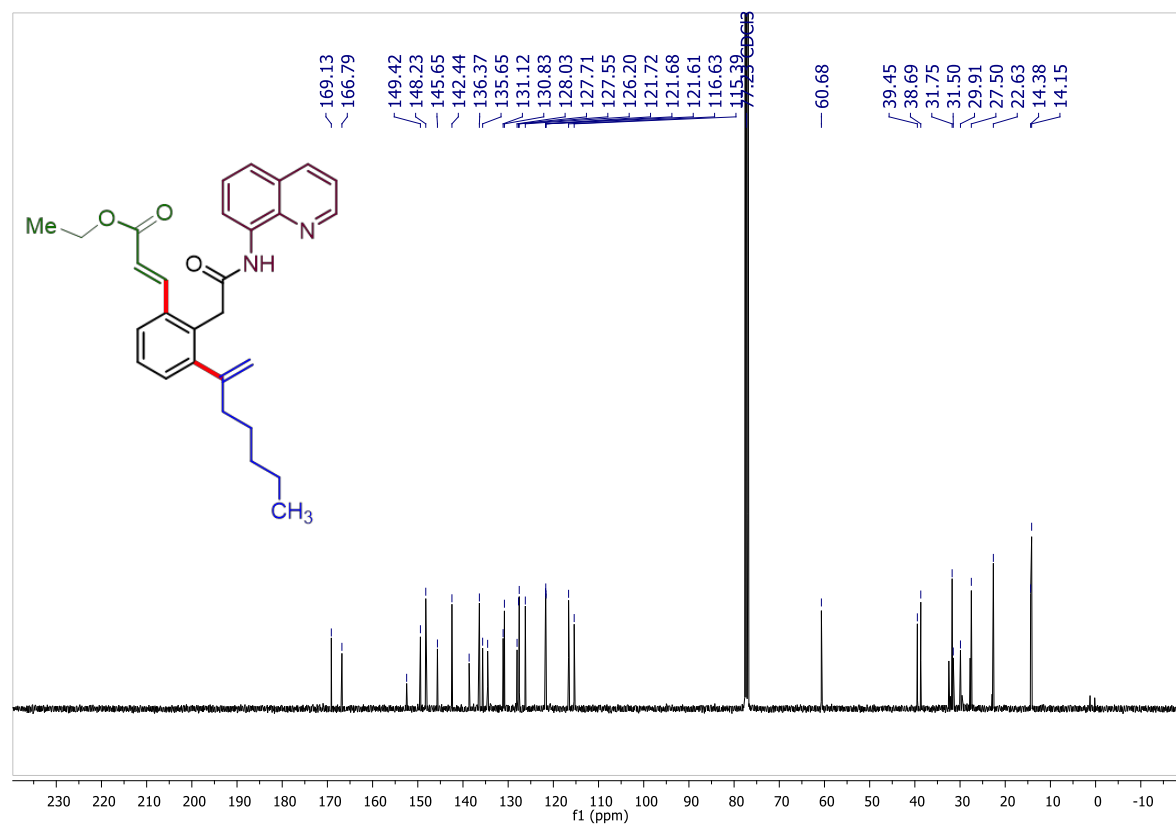
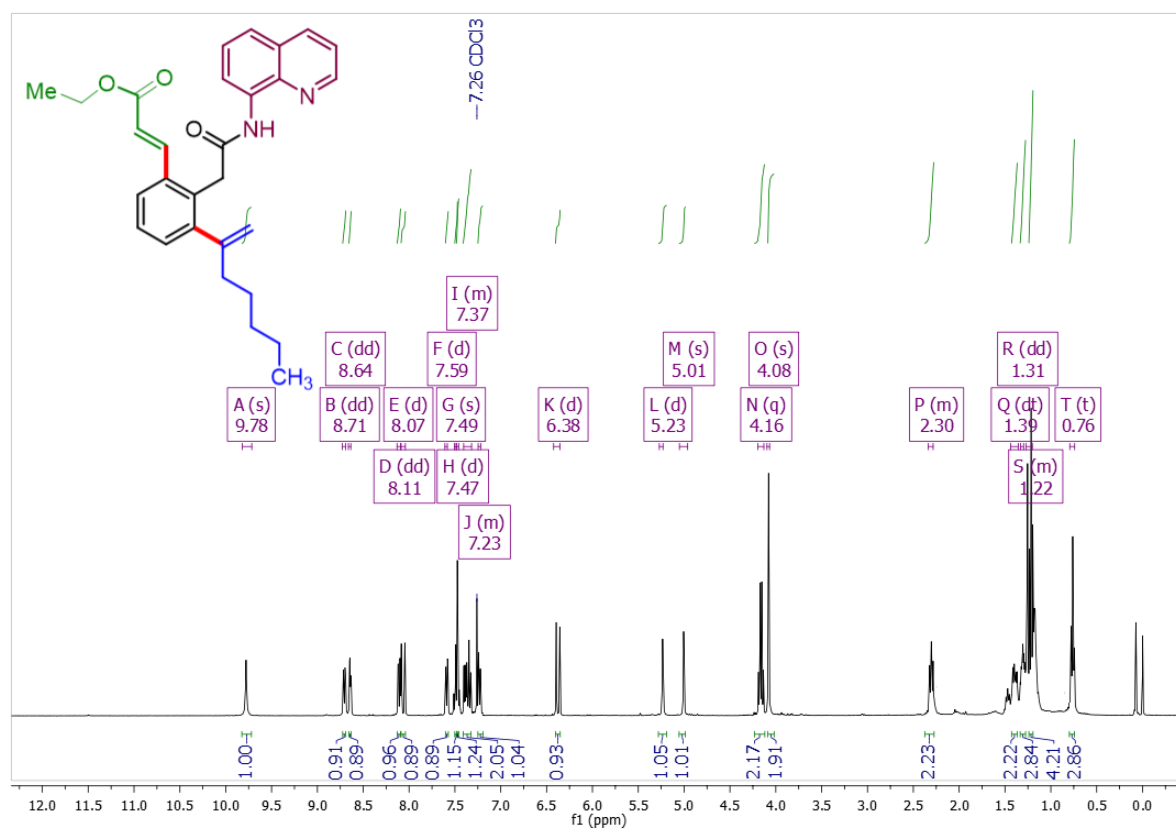
Scheme 3, entry 6c



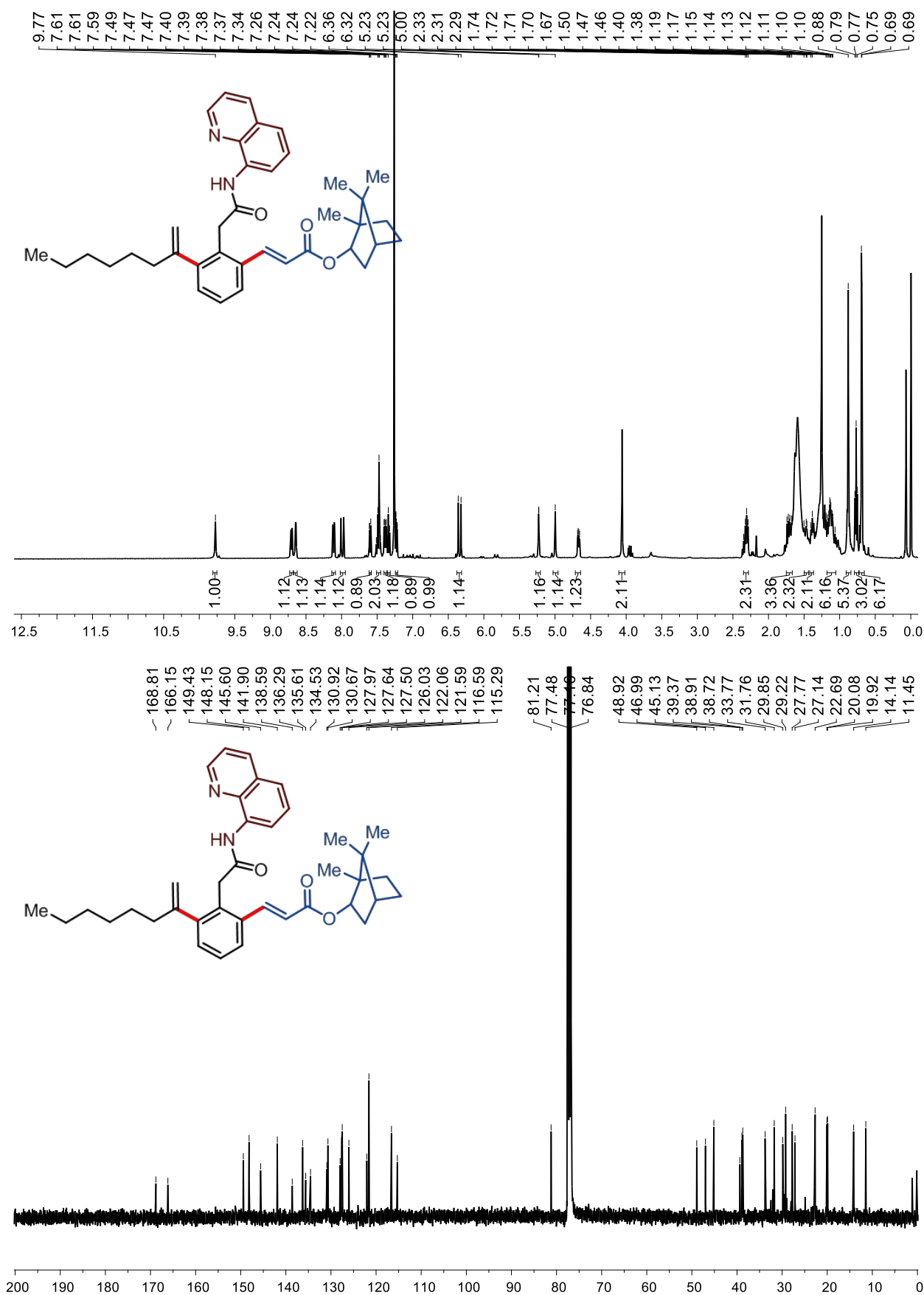
Scheme 3, entry 6d



Scheme 3, entry 6e



Scheme 3, entry 6f



The figure displays the chemical structure of compound 10 and its corresponding ¹H and ¹³C NMR spectra. The chemical structure is a complex molecule featuring a quinoxaline ring system, a benzene ring, a furan ring, and a long alkyl chain with multiple methyl groups. The ¹H NMR spectrum (top) shows peaks from 0.84 to 9.82 ppm, with integration values provided below the baseline. The ¹³C NMR spectrum (bottom) shows peaks from 11.90 to 168.96 ppm. The chemical structure is color-coded: red for the quinoxaline and benzene rings, blue for the furan ring and alkyl chain, and green for the methyl groups.

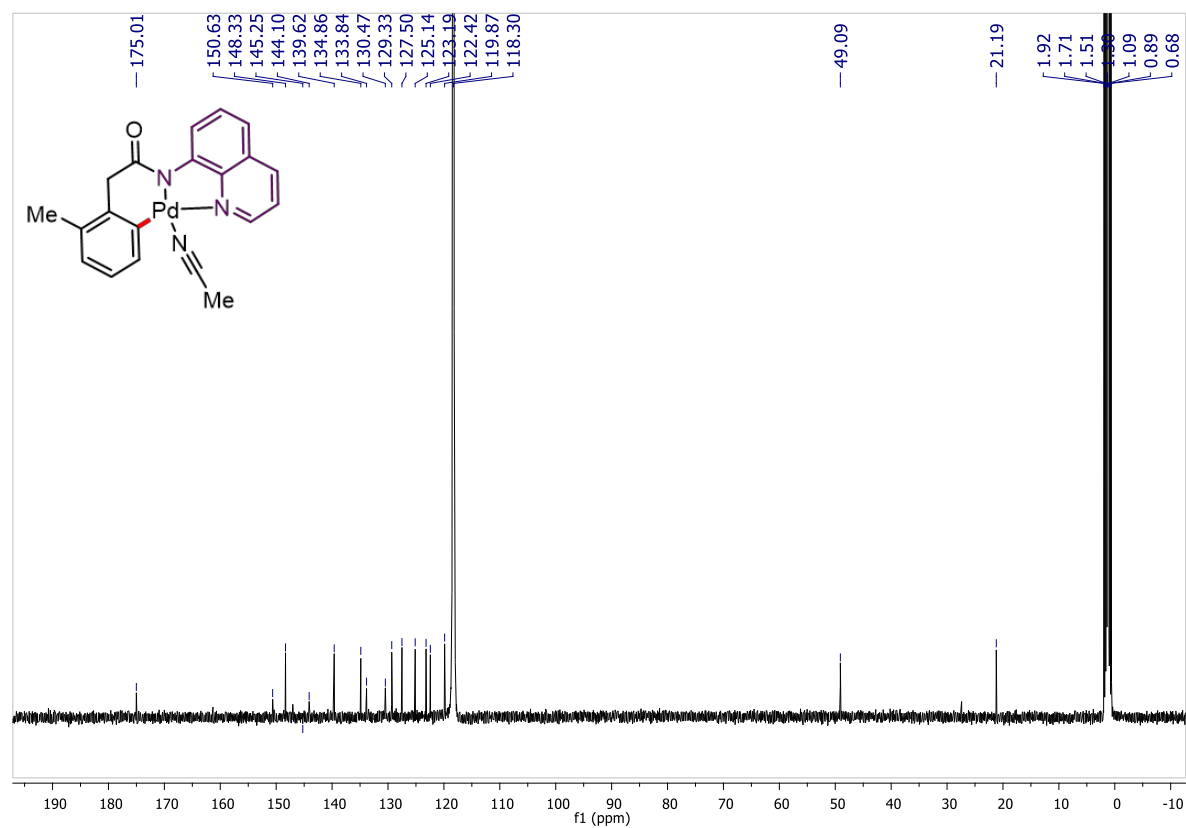
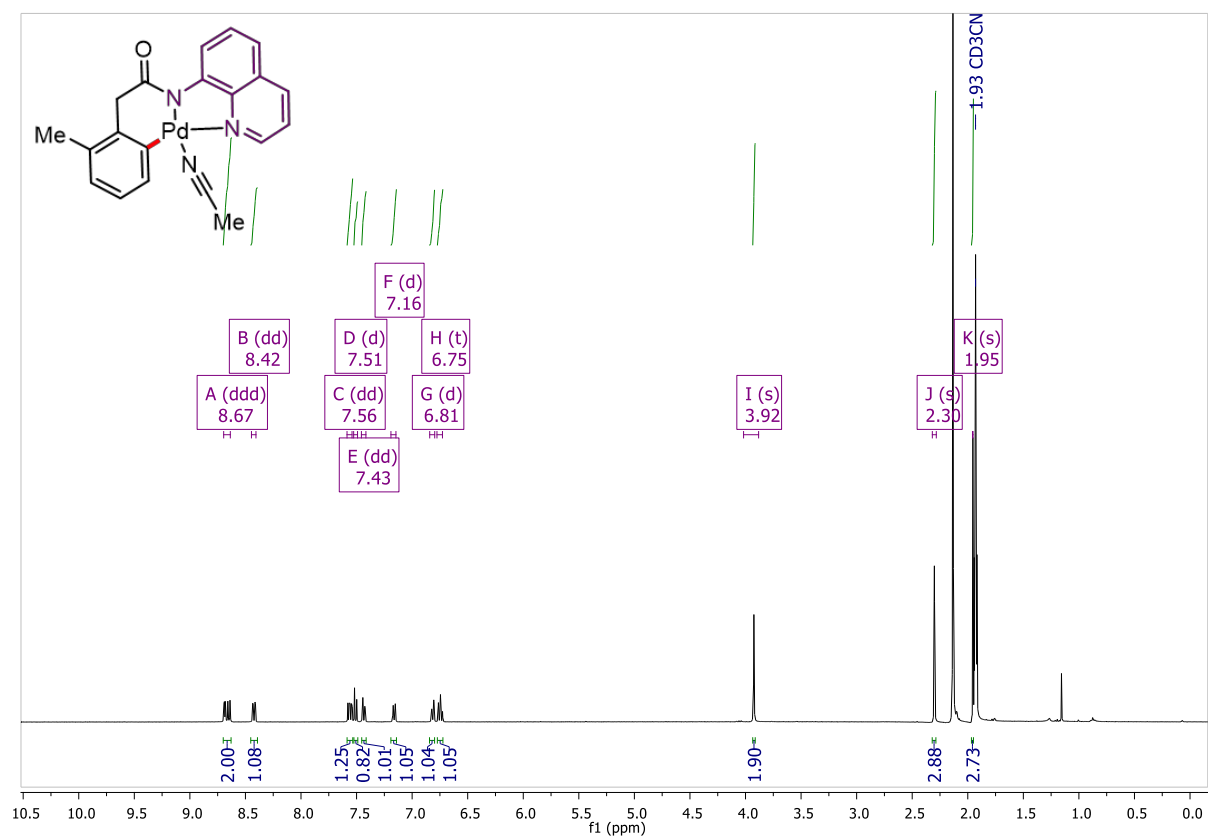
¹H NMR Spectrum (Top):

- Chemical Shift Range: 0.84 to 9.82 ppm.
- Integration Values: 1.00, 1.08, 1.08, 1.04, 1.03, 1.05, 2.14, 2.10, 1.00, 1.01, 1.05, 1.02, 2.01, 2.17, 2.25, 3.32, 3.14, 3.27, 8.31, 6.64, 3.33, 3.42, 3.56, 20.46.

¹³C NMR Spectrum (Bottom):

- Chemical Shift Range: 11.90 to 168.96 ppm.

Scheme 4, Complex C2



Complex C3

