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Supporting Information

Palladium-catalysed C_{sp3}-H functionalization of unactivated 8- aminoquinoline amides in Deep Eutectic Solvents

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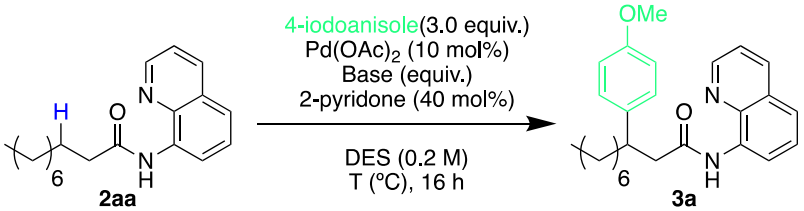
Materials and Methods

General

Melting points were obtained with a *Reichert Thermovar* apparatus. NMR spectra were recorded on a *Bruker AC- 300* (300 MHz for ^{1}H and 75 MHz for ^{13}C) using $CDCl_3$ as a solvent (unless otherwise stated). ^{1}H and ^{13}C chemical shifts are given in δ (parts per million) and coupling constants (*J*) in Hertz. FT-IR spectra were obtained on *a JASCO 4100LE (Pike Miracle ATR)* spectrophotometer. Mass spectra (EI) were obtained at 70 eV on a *Agilent Technologies* GC/MS-8890N, giving fragment ions in *m/z* with relative intensities (%) in parentheses. The mass spectrometry analyses of high resolution (HRMS) were performed in the Mass Spectrometry Unit of the Technical Services Research at the University of Alicante with a spectrometer *Agilent 7200* using Electronic Impact for ionization and Q-TOF for mass measurement. Thin layer chromatography (TLC) was carried out on *Schleicher&Schuell* F1400/LS 254 plates coated with a 0.2 mm layer of silica gel; detection by UV_{254} light. Column chromatography was performed using silica gel 60 of 40-63 mesh. All reagents were commercially available (*Acros, Aldrich, Fluorochem*) and were used as received.

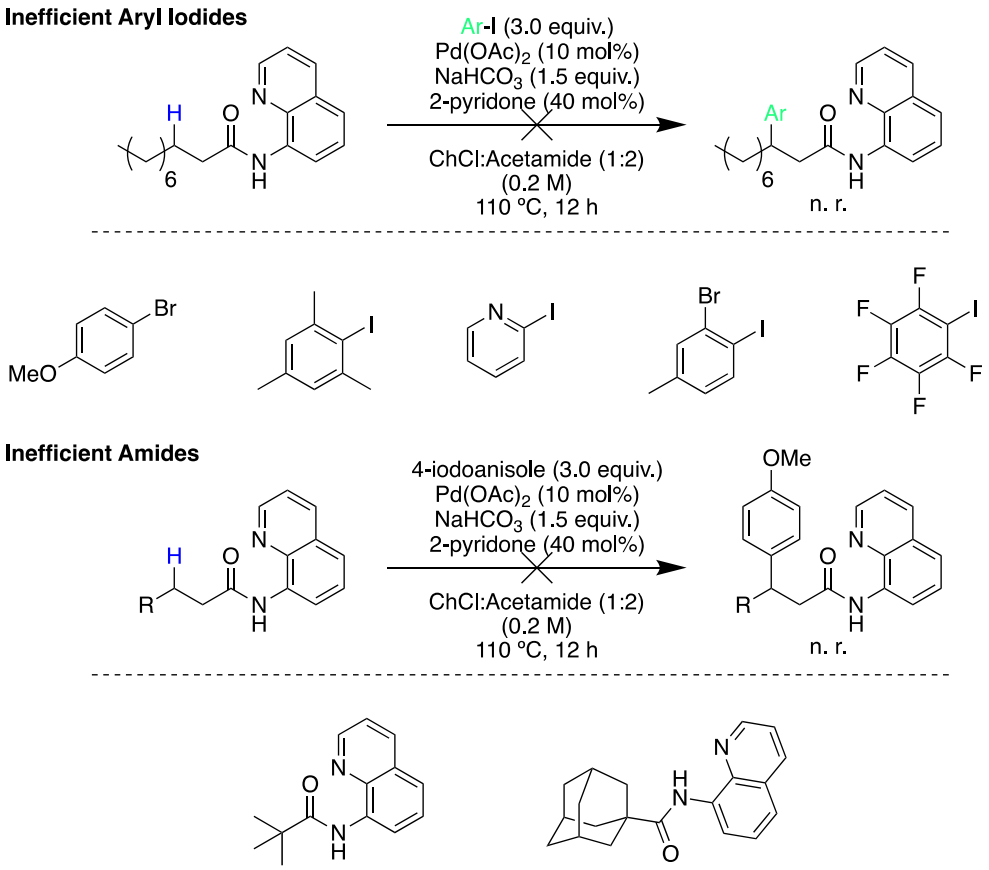
Optimisation studies



Entry	Solvent	Base (equiv.)	T (°C)	Conversion 3a (%)[a]
1	ChCl:Glycerol (1:2)	K_2CO_2 (1.5)	110	41
2	ChCl:Glycerol (1:2)	K_2CO_2 (1.5)	110	0[b]
3	AcChCl:Acetamide (1:2)	K_2CO_2 (1.5)	110	63
4	ChCl:Acetamide (1:2)	K_2CO_2 (1.5)	110	74
5	Ph_3PMeBr:Glycerol (1:2)	K_2CO_2 (1.5)	110	0
6	ChCl:Resorcinol (1:1)	K_2CO_2 (1.5)	110	3
7	ChCl:$(CH_2OH)_2$ (1:2)	K_2CO_2 (1.5)	110	23
8	Betaine:Glycerol (1:2)	K_2CO_2 (1.5)	110	47
9	ChCl:Urea (1:2)	K_2CO_2 (1.5)	110	12
10	Decanoic acid:Menthol (1:2)	K_2CO_2 (1.5)	110	0
11	AcChCl:Glycerol (1:2)	K_2CO_2 (1.5)	110	32
12	Betaine:Lactic Acid (1:2)	K_2CO_2 (1.5)	110	13
13	*L*-Carnitine:Urea (1:2)	K_2CO_2 (1.5)	110	28
14	ChCl:Acetamide (1:2)	NaOAc (1.5)	110	85
15	ChCl:Acetamide (1:2)	Na_2CO_3 (1.5)	110	87
16	ChCl:Acetamide (1:2)	K_3PO_4 (1.5)	110	70
17	ChCl:Acetamide (1:2)	^{t}BuOK (1.5)	110	3
18	ChCl:Acetamide (1:2)	Na_3PO_4 (1.5)	110	84
19	ChCl:Acetamide (1:2)	Ag_2CO_3 (1.5)	110	32
20	ChCl:Acetamide (1:2)	NaOH (1.5)	110	22
21	ChCl:Acetamide (1:2)	$NaHCO_3$ (1.5)	110	93 (88)[c]
23	ChCl:Acetamide (1:2)	$NaHCO_3$ (1.5)	110	74[d]
24	ChCl:Acetamide (1:2)	$NaHCO_3$ (1.5)	110	85[e]
26	ChCl:Acetamide (1:2)	$NaHCO_3$ (1.5)	110	93[f]
27	ChCl:Acetamide (1:2)	$NaHCO_3$ (2.0)	110	62
28	ChCl:Acetamide (1:2)	$NaHCO_3$ (3.0)	110	29
29	ChCl:Acetamide (1:2)	$NaHCO_3$ (1.5)	100	85
30	ChCl:Acetamide (1:2)	$NaHCO_3$ (1.5)	90	64
31	HFIP + 0.5 equiv. Betaine	$NaHCO_3$ (1.5)	110	34
32	K_2CO_3:Ethyleneglycol (1:10)	-	110	58
33	ChCl:Acetamide (1:2)	$NaHCO_3$ (1.5)	110	43[g]
34	ChCl:Acetamide (1:2)	$NaHCO_3$ (1.5)	110	85[h]
35	Betaine:HFIP (1:2)	$NaHCO_3$ (1.5)	110	100 (97)[c]
36	HFIP	$NaHCO_3$ (1.5)	110	55
37	Neat conditions	$NaHCO_3$ (1.5)	110	10
38	H_2O	$NaHCO_3$ (1.5)	110	45
39	*t*BuOH	$NaHCO_3$ (1.5)	110	5
40	PhMe	$NaHCO_3$ (1.5)	110	15

[a] Conversion determined by GC-MS. [b] Reaction performed with substrate **2ab**. [c]Isolated yield. [d] Reaction performed without ligand. [e] Reaction performed with 20 mol% of ligand. [f] Reaction performed with $PdCl_2$ instead of $Pd(OAc)_2$. [g] Reaction performed with 1.0 equiv of 4-iodoanisole. [h] Reaction performed with 2.0 equiv. of 4-iodoanisole.

Chart S1. Inefficient substrates.



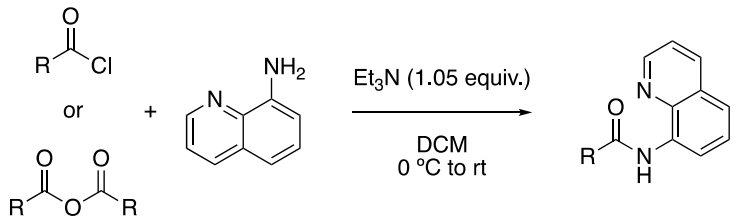
General procedures

Deep Eutectic Solvents preparation

DESs were prepared by mixing the corresponding components in the appropriate molar ratio and heating the mixture at 80 °C under Ar atmosphere until a clear solution was obtained. Since some of the components of DESs are very hygroscopic, they were always stored under Ar atmosphere, although the reactions employing DESs as solvents were carried out in opened to air reaction vessels.

Synthesis of starting materials

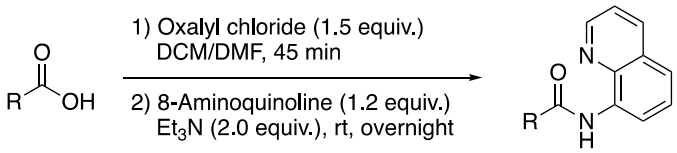
General procedure A:



For commercially available anhydrides or acid chlorides a literature procedure was adapted:[1] 8-aminoquinoline (1.0 equiv.) and Et_3N (1.05 equiv.) were dissolved in DCM. The solution was cooled to 0 °C the corresponding acid anhydride or acid chloride (1.05 equiv.) was slowly added. The mixture

was allowed to warm to room temperature and stirred overnight. The reaction was transferred to a separatory funnel and washed with water, $NaHCO_3$ (sat. aq.) and brine. The organic phase was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Products were purified by column chromatography using mixtures of hexane and ethyl acetate as eluent.

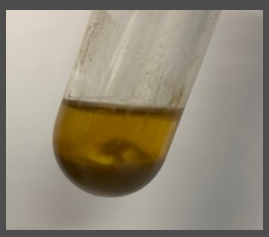
General procedure B:



For non-commercially available acid chlorides or anhydrides: The corresponding acid (1.0 equiv.) was placed in a Schlenk flask, and the system was evacuated and backfilled with Ar (x3). Dry DCM was added (concentration of acid 0.25 M) followed by dry DMF (20 µL/mmol of acid). The mixture was cooled to 0 ^oC and oxalyl chloride (1.5 equiv.) was slowly added. The reaction was allowed to warm to room temperature and stirred for 45 min. Then, volatiles were removed under reduced pressure. The resulting residue was redissolved in dry DCM under Ar atmosphere, cooled to 0 ^oC and 8-aminoquinoline (1.2 equiv.) was added. After stirring for 10 min, Et_3N (2.0 equiv.) was added, and the mixture was allowed to reach room temperature and was stirred overnight. The reaction was quenched by addition of saturated $NaHCO_3$ aqueous solution and extracted with DCM (x3). The combined organic phase was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Products were purified by column chromatography using mixtures of hexane and ethyl acetate as eluent.

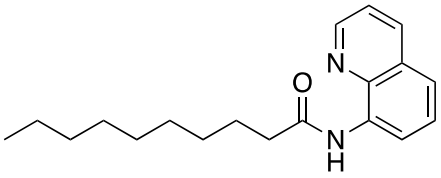
Arylation/Alkynylation reactions

General procedure C: $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), 2-pyridone (7.6 mg, 0.08 mmol), $NaHCO_3$ (25 mg, 0.30 mmol), and the corresponding amide (0.20 mmol) and aryl halide (0.60 mmol) were charged in a reaction vessel. Next, 1 mL of DES [ChCl:Acetamide (1:2) or Betaine:HFIP (1:2)] previously heated to 80 ^oC was added and the reaction was heated to 110 ^oC under air atmosphere and magnetic stirring for 12 h (in ChCl:Acetamide/1:2) or 2.5 h (in betaine:HFIP/1:2). Once the reaction was finished, it was quenched by addition of water (3.0 mL) and extracted with EtOAc (3x5 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. Arylated products were purified by column chromatography or preparative TLC using mixtures of hexanes and EtOAc.

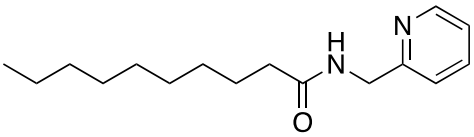


General Procedure for Recycling Experiments: reaction was performed according to general procedure C. Once the reaction was completed, the reaction mixture was cooled to room temperature, and 2-MeTHF (3 x 1 mL) was added to the reaction vessel for reactions performed in ChCl:acetamide (1:2). In the case of using Betaine:HFIP (1:2) as reaction media, PhMe was employed as extraction solvent. The biphasic mixture was stirred for 5 min and the upper phase, containing unreacted organic reagents and products, was separated by decantation and analysed by ^1H NMR using 1,2,4,5-tetramethylbenzene as internal standard. The eutectic mixture was dried under vacuum and was charged again with fresh amide, aryl iodide and sodium bicarbonate, repeating the process.

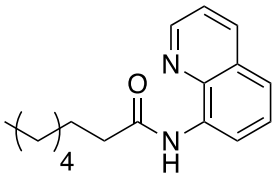
Characterisation data



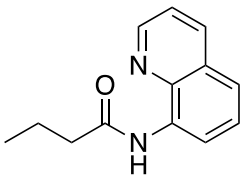
***N*-(quinolin-8-yl)decanamide (2aa):**[2] Prepared from general procedure B (2.44 g, 82% yield). Pale yellow solid. m.p. = 48-50 °C. R_f = 0.58 (hexane:EtOAc = 4:1). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.85 (s, 1H), 8.83 – 8.75 (m, 2H), 8.17 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.58 – 7.39 (m, 3H), 2.56 (t, *J* = 7.5 Hz, 2H), 1.87 – 1.75 (m, 2H), 1.48 – 1.20 (m, 12H), 0.91 – 0.81 (m, 3H). ^{13}C NMR ($CDCl_3$, 101 MHz): δ 172.1, 147.8, 138.0, 136.8, 134.4, 128.0, 127.6, 121.5, 121.4, 116.8, 38.3, 31.9, 29.5, 29.4, 29.3 (2C), 25.7, 22.7, 14.1. MS m/z 298 (M^+, 16%), 208 (12), 207 (53), 186 (100), 171 (64). IR (neat, cm^{-1}) $\tilde{\nu}$: 3340, 2923, 2850, 1681, 1523, 1477, 1165, 687.



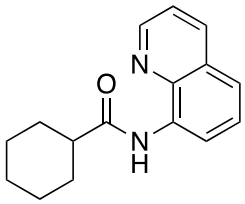
***N*-(pyridin-2-ylmethyl)decanamide (2ab):**[3] Compound synthetised following general procedure B, substituting 8-aminoquinoline by 2-picolylamine (2.23 g, 85% yield). Yellowish solid. m.p. = 41-43 °C. R_f = 0.45 (EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.50 (ddd, *J* = 4.9, 1.8, 1.1 Hz, 1H), 7.65 (td, *J* = 7.7, 1.8 Hz, 1H), 7.27 (dt, *J* = 7.7, 1.1 Hz, 1H), 7.19 (ddd, *J* = 7.7, 4.9, 1.1 Hz, 1H), 6.89 (s, 1H), 4.53 (d, *J* = 5.1 Hz, 2H), 2.27 – 2.22 (m, 2H), 1.63 (td, *J* = 10.1, 4.6 Hz, 2H), 1.31 – 1.20 (m, 10H), 0.84 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$, 101 MHz): δ 173.5, 156.87, 148.8, 137.2, 122.5, 122.5, 44.4, 36.8, 31.9, 29.5, 29.4, 29.4, 29.3, 3.8, 22.7, 14.2. MS m/z 262 (M^+, 28%), 205 (11), 177 (11), 163 (35), 151 (15), 150 (100). IR (neat, cm^{-1}) $\tilde{\nu}$: 3301, 2919, 2854, 1643, 1550, 1427, 717.



***N*-(quinolin-8-yl)octanamide (2b)**:[4] Obtained following general procedure A (2.48 g, 92% yield). Brown oil. R_f = 0.55 (hexane:EtOAc = 4:1). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.80 (s, 1H), 8.83 – 8.71 (m, 2H), 8.11 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.55 – 7.35 (m, 3H), 2.54 (t, *J* = 7.7 Hz, 2H), 1.80 (tt, *J* = 8.4, 6.2 Hz, 2H), 1.47 – 1.21 (m, 8H), 0.92 – 0.81 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.0, 148.0, 136.5, 134.6, 128.0, 127.5, 121.6, 121.4, 116.6, 38.3, 31.8, 29.3, 29.1, 25.7, 22.7, 14.1. MS m/z 270 (M^+, 24%), 207 (42), 199 (19), 187 (14), 186 (100), 171 (79). IR (neat, cm^{-1}) $\tilde{\nu}$: 3355, 2927, 2858, 1685, 1523, 1481, 1326, .729.

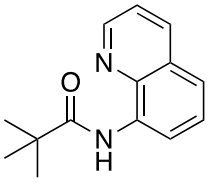


***N*-(quinolin-8-yl)butyramide (2c)**:[1] Obtained following general procedure A (1.93 g, 90% yield). Brown oil. R_f = 0.45 (hexane:EtOAc = 4:1). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.82 (s, 1H), 8.90 – 8.70 (m, 2H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.58 – 7.35 (m, 3H), 2.54 (dd, *J* = 7.9, 7.1 Hz, 2H), 1.94 – 1.77 (m, 2H), 1.05 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 171.9, 148.1, 138.3, 136.6, 134.6, 128.1, 127.6, 121.6, 121.5, 116.7, 40.2, 19.2, 13.9. MS m/z 214 (M^+, 25%), 171 (42), 145 (12), 144 (100). IR (neat, cm^{-1}) $\tilde{\nu}$: 3353, 2962, 1681, 1523, 1481, 1322, 1172, 790.

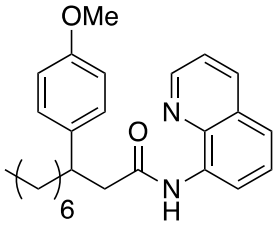


***N*-(quinolin-8-yl)cyclohexanecarboxamide (2d)**:[1] Obtained following general procedure A (1.65 g, 65% yield). Pale brown solid. m.p. = 60-62 °C. R_f = 0.56 (hexane:EtOAc = 4:1). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.94 (s, 1H), 8.82 (dt, *J* = 5.3, 1.5 Hz, 2H), 8.22-8.12 (m, 1H), 7.59 – 7.43 (m, 3H), 2.57 – 2.46 (m, 1H), 2.13 – 2.06 (m, 2H), 1.88 (dt, *J* = 12.7, 3.3 Hz, 2H), 1.75 (dtd, *J* = 10.9, 3.1, 1.6 Hz, 1H),

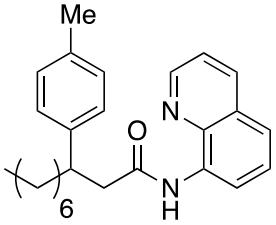
1.70 – 1.60 (m, 2H), 1.46 – 1.28 (m, 3H). ^{13}C NMR ($CDCl_3$, 101 MHz): δ 175.0, 147.9, 138.2, 136.7, 134.5, 128.0, 127.6, 121.5, 121.3, 116.8, 46.9, 29.8, 25.8, 25.6. MS m/z 254 (M^+, 37%), 208 (14), 172 (12), 171 (100). IR (neat, cm^{-1}) $\tilde{\nu}$: 3340, 2923, 2850, 1685, 1519, 1477, 1322, 1160.



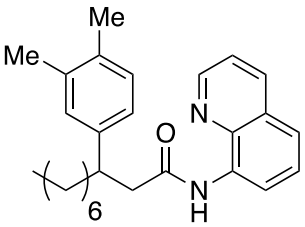
***N*-(quinolin-8-yl)pivalamide (2f)**:[5] Obtained following general procedure A (2.14 g, 94% yield). Yellow oil. R_f = 0.61 (hexane:EtOAc = 4:1). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.27 (s, 1H), 8.90 – 8.75 (m, 2H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.58 – 7.41 (m, 3H), 1.43 (s, 9H). ^{13}C NMR ($CDCl_3$, 101 MHz): δ 177.4, 148.3, 138.8, 136.6, 134.8, 128.1, 127.6, 121.6, 121.4, 116.5, 40.5, 27.9. MS m/z 228 (M^+, 42%), 172 (36), 171 (100), 144 (45), 143 (14), 117 (13), 116 (15). IR (neat, cm^{-1}) $\tilde{\nu}$: 3363, 2962, 1677, 1523, 1481, 1326, 1157.



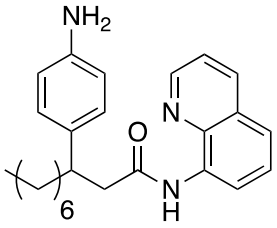
3-(4-methoxyphenyl)-*N*-(quinolin-8-yl)decanamide (3a): Obtained following general procedure C (78 mg, 97% yield). Pale brown solid. m.p. = 55-57 °C. R_f = 0.46 (hexane:EtOAc = 4:1). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.68 (s, 1H), 8.80 – 8.69 (m, 2H), 8.12 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.55 – 7.36 (m, 3H), 7.24 – 7.17 (m, 2H), 6.87 – 6.77 (m, 2H), 3.73 (s, 3H), 3.24 (dtd, *J* = 9.3, 7.3, 5.1 Hz, 1H), 2.90 – 2.73 (m, 2H), 1.71 (ddt, *J* = 23.0, 8.7, 4.8 Hz, 2H), 1.32 – 1.10 (m, 10H), 0.88 – 0.78 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.7, 158.1, 147.9, 136.5, 136.5, 134.5, 128.5, 128,0, 127.5, 121.6, 121.4, 116.65, 114,0, 55.2, 46.2, 42,0, 36.5, 31.9, 29.6, 29.3, 27.5, 22.7, 14.2. MS m/z 404 (M^+, 4%), 282 (12), 253 (15), 209 (13), 208 (20), 207 (100) 191 (11). HRMS calcd. for $C_{26}H_{32}N_2O_2$ (M^+): 404.2464, found: 404.2458. IR (neat, cm^{-1}) $\tilde{\nu}$: 3355, 2923, 2854, 1735, 1685, 1519, 1481, 1245, 1037.



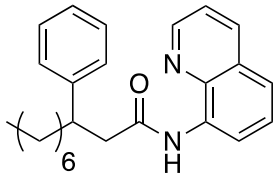
***N*-(quinolin-8-yl)-3-(*p*-tolyl)decanamide (3b):** Obtained following general procedure C (75 mg, 97% yield). Pale brown solid. m.p. = 40-42 °C. R_f = 0.48 (hexane:EtOAc = 4:1). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.71 (s, 1H), 8.80 – 8.69 (m, 2H), 8.13 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.57 – 7.36 (m, 3H), 7.19 (d, *J* = 8.2 Hz, 2H), 7.09 (d, *J* = 7.8 Hz, 2H), 3.26 (dtd, *J* = 9.4, 7.4, 5.1 Hz, 1H), 2.83 (dd, *J* = 7.4, 1.4 Hz, 2H), 2.28 (s, 3H), 1.81 – 1.62 (m, 2H), 1.32 – 1.12 (m, 10H), 0.84 (t, *J* = 6.7 Hz, 3H).^{13}C NMR ($CDCl_3$, 101 MHz): δ 170.8, 147.8, 141.5, 138.0, 135.9, 134.4, 129.3, 128.1, 127.6, 127.5, 121.6, 121.5, 46.0, 42.4, 36.4, 31.9, 29.7, 29.3, 27.6, 22.7, 21.1, 14.2. MS m/z 388 (M^+, 31%), 303 (23), 289 (11), 281 (37), 253(19), 208 (22), 207 (100), 191 (10), 186 (30), 171 (26), 159 (10). HRMS calcd. for $C_{26}H_{32}N_2O$ (M^+): 388.2515, found: 388.2514. IR (neat, cm^{-1}) $\tilde{\nu}$: 3359, 2923, 2858, 1685, 1523, 1481, 1326, 821.



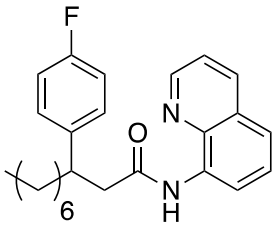
3-(3,4-dimethylphenyl)-*N*-(quinolin-8-yl)decanamide (3c): Obtained following general procedure C (77 mg, 96% yield).Pale brown solid. m.p. = 47-48 °C. R_f = 0.48 (hexane:EtOAc = 4:1). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.70 (s, 1H), 8.80 – 8.67 (m, 2H), 8.12 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.55 – 7.38 (m, 3H), 7.09 – 7.00 (m, 3H), 3.24 (dtd, *J* = 9.5, 7.4, 5.1 Hz, 1H), 2.83 (dd, *J* = 7.3, 0.9 Hz, 2H), 2.21 (s, 3H), 2.18 (s, 3H), 1.84 – 1.64 (m, 2H), 1.32 – 1.15 (m, 10H), 0.85 (t, *J* = 6.9 Hz, 3H).^{13}C NMR ($CDCl_3$, 101 MHz): δ 170.8, 147.9, 142.0, 136.6, 136.5, 134.5, 134.4, 129.8, 129.0, 127.5, 124.9, 121.5, 121.4, 116.7, 46.1, 42.3, 36.4, 31.9, 29.7, 29.3, 27.6, 22.7, 19.9, 19.4, 14.2. MS m/z 402 (M^+, 100%), 318 (14), 317 (57), 304 (19), 303 (33), 281 (12), 253 (11), 209 (13), 208 (20), 207 (90), 186 (60), 172 (19), 171 (61), 169 (10), 159 (13). HRMS calcd. for $C_{27}H_{34}N_2O_2$ (M^+): 402.2671, found: 402.2673. IR (neat, cm^{-1}) $\tilde{\nu}$: 3359, 2923, 2854, 1685, 1523, 1481, 1326, 821, 790.



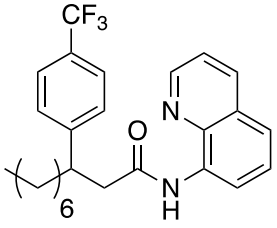
3-(4-aminophenyl)-*N*-(quinolin-8-yl)decanamide (3d): Obtained following general procedure C (65 mg, 83% yield).Red oil. R_f = 0.51 (hexane:EtOAc = 1:1). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.69 (s, 1H), 8.79-8.70 (m, 2H), 8.11 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.51 – 7.38 (m, 3H), 7.14 – 7.03 (m, 2H), 6.84 – 6.41 (m, 2H), 3.66 (br s, 2H), 3.18 (dtd, *J* = 9.5, 7.4, 5.1 Hz, 1H), 2.87 – 2.70 (m, 2H), 1.77 – 1.59 (m, 2H), 1.26 – 1.15 (m, 10H), 0.84 (t, *J* = 6.8 Hz, 3H).^{13}C NMR ($CDCl_3$, 101 MHz): δ 170.8, 148.1, 142.9, 138.4, 136.4, 135.8, 134.6, 128.5, 128-9, 127.5, 121.6, 121.4, 116.6, 116.4, 46.2, 42.0, 36.5, 31.9, 29.7, 29.3, 27.6, 22.7, 14.2. MS m/z 389 (M^+, 15%), 281 (29), 209 (13), 208 (21), 207 (100), 160 (10). HRMS calcd. for $C_{25}H_{31}N_3O$ (M^+): 389.2467, found: 389.2463. IR (neat, cm^{-1}) $\tilde{\nu}$: 3351, 2923, 2854, 1731, 1519, 1481, 1322, 825.



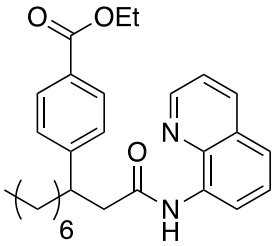
***N*-(quinolin-8-yl)-3-(*p*-tolyl)decanamide (3e):** Obtained following general procedure C (73 mg, 97% yield).White solid. m.p. = 40-41 °C. R_f = 0.45 (hexane:EtOAc = 4:1). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.70 (s, 1H), 8.81 – 8.69 (m, 2H), 8.13 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.56 – 7.39 (m, 3H), 7.32 – 7.28 (m, 4H), 7.21 – 7.11 (m, 1H), 3.36 – 3.21 (m, 1H), 2.85 (dd, *J* = 7.4, 1.6 Hz, 2H), 1.85 – 1.62 (m, 2H), 1.30 – 1.09 (m, 10H), 0.83 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$, 101 MHz): δ 170.6, 148.0, 144.5, 138.2, 136.6, 134.5, 128.6, 128.0, 127.7, 127.6, 126.5, 121.6, 121.5, 116.7, 46.0, 42.7, 36.4, 31.9, 29.7, 29.3, 27.6, 22.7, 14.2. MS m/z 374 (M^+, 38%), 341 (11), 289 (43), 282 (14), 281 (37), 276 (17), 275 (18), 253 (21), 209 (13), 208 (21), 207 (100), 191 (11), 187 (12), 186 (89), 172 (12), 171 (54). HRMS calcd. for $C_{25}H_{30}N_2O$ (M^+): 374.2358, found: 374.2350. IR (neat, cm^{-1}) $\tilde{\nu}$: 3355, 2923, 2854, 1685, 1523, 1481, 1384, 1326, 698.



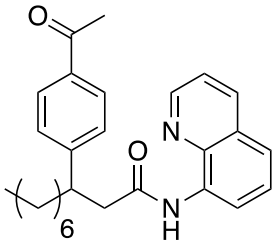
3-(4-fluorophenyl)-*N*-(quinolin-8-yl)decanamide (**3f):** Obtained following general procedure C (74 mg, 94% yield).Brown oil. R_f = 0.42 (hexane:EtOAc = 4:1). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.70 (s, 1H), 8.80-8.67 (m, 2H), 8.17 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.54 – 7.39 (m, 7H), 3.45 – 3.30 (m, 1H), 2.97 – 2.78 (m, 2H), 1.83 – 1.64 (m, 2H), 1.29 – 1.15 (m, 10H), 0.90 – 0.78 (t, *J* = 6.8 Hz, 3H). ^{19}F NMR ($CDCl_3$, 282 MHz): δ -117.0. ^{13}C NMR ($CDCl_3$, 101 MHz): δ 170.3, 161.5 (d, *J* = 243.7 Hz), 147.7, 140.0 (d, *J* = 3.3 Hz), 137.8, 136.8, 134.2, 128.9 (d, *J* = 7.9 Hz), 128.0, 127.5, 121.5, 116.9, 115.3 (d, *J* = 21.1 Hz), 45.9, 42.0, 36.4, 31.8, 29.5, 29.2, 27.4, 22.6, 14.1. MS m/z 292 (M^+, 45%), 307 (52), 294 (22), 281 (18), 253 (10), 207 (48), 187 (14), 171 (70), 163 (13). HRMS calcd. for $C_{25}H_{29}FN_2O$ (M^+): 392.2264, found: 392.2258. IR (neat, cm^{-1}) $\tilde{\nu}$: 3351, 2927, 2857, 1685, 1523, 1484, 1326, 1222, 829.



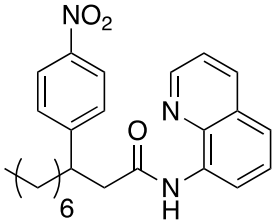
***N*-(quinolin-8-yl)-3-(4-(trifluoromethyl)phenyl)decanamide (3g):** Obtained following general procedure C (84 mg, 95% yield).Brown solid. m.p. = 44-46 °C. R_f = 0.40 (hexane:EtOAc = 4:1). ^{1}H NMR ($CDCl_3$, 300 MHz): 9.70 (s, 1H), 8.79-8.67 (m, 2H), 8.17 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.54 – 7.39 (m, 7H), 3.45 – 3.30 (m, 1H), 2.97 – 2.78 (m, 2H), 1.83 – 1.64 (m, 2H), 1.29 – 1.15 (m, 10H), 0.90 – 0.78 (t, *J* = 6.8 Hz, 3H). ^{19}F NMR ($CDCl_3$, 282 MHz): δ -62.35.^{13}C NMR ($CDCl_3$, 101 MHz): δ 170.1, 148.8, 147.8, 137.2, 134.1, 128.8 (q, *J* = 31.8), 128.2, 128.1, 127.7, 125.6 (q, *J* = 3.6 Hz), 124.4 (q, *J* = 271.8 Hz), 121.8, 121.6, 117.3, 45.5, 42.6, 36.2, 31.9, 29.6, 29.3, 27.5, 22.7, 14.2. MS m/z 442 (M^+, 35%), 358 (11), 357 (49), 344 (26), 343 (17), 207 (17), 187 (14), 172 (14), 171 (68). HRMS calcd. for $C_{26}H_{29}F_3N_2O_2$ (M^+): 442.2232, found: 442.2227. IR (neat, cm^{-1}) $\tilde{\nu}$: 3351, 2927, 2858, 1685, 1527, 1481, 1322, 1160, 1118, 829.



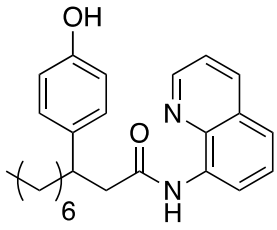
Ethyl 4-(1-oxo-1-(quinolin-8-ylamino)decan-3-yl)benzoate (3h): Obtained following general procedure C (87 mg, 97% yield).Yellow oil. R_f = 0.39 (hexane:EtOAc = 4:1). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.70 (s, 1H), 8.76 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.72 (dd, *J* = 7.0, 2.0 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 8.02 – 7.95 (m, 2H), 7.56 – 7.42 (m, 3H), 7.42 – 7.35 (m, 2H), 4.35 (q, *J* = 7.1 Hz, 2H), 3.39 (dtd, *J* = 9.5, 7.4, 5.3 Hz, 1H), 2.95 – 2.79 (m, 2H), 1.82 (tt, *J* = 10.3, 5.0 Hz, 1H), 1.73 (tt, *J* = 9.3, 4.5 Hz, 1H), 1.37 (t, *J* = 7.1 Hz, 3H), 1.33 – 1.11 (m, 10H), 0.85 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$, 101 MHz): δ 170.1, 166.7, 149.9, 148.0, 138.1, 136.6, 134.3, 123.0, 128.8, 128.0, 127.7, 127.5, 121.6, 116.8, 60.9, 45.5, 42.8, 36.2, 31.9, 29.6, 29.2, 27.5, 22.7, 14.5, 14.2. MS m/z 446 (M^+, 7%), 253 (11), 209 (13), 208 (21), 207 (100), 186 (23), 171 (20). HRMS calcd. For $C_{28}H_{34}N_2O_3$ (M^+) 446.2569, found: 446.2567. IR (neat, cm^{-1}) $\tilde{\nu}$: 3351, 2927, 2858, 1708, 1608, 1523, 1272, 1106, 787.



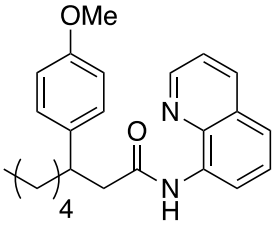
3-(4-acetylphenyl)-*N*-(quinolin-8-yl)decanamide (3i): Obtained following general procedure C (80 mg, 96% yield). Orange oil. R_f = 0.20 (hexane:EtOAc = 4:1). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.72 (s, 1H), 8.74 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.70 (dd, *J* = 6.4, 2.6 Hz, 1H), 8.16 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.93 – 7.85 (m, 2H), 7.54 – 7.34 (m, 5H), 3.38 (p, *J* = 7.5 Hz, 1H), 2.98 – 2.77 (m, 2H), 2.52 (s, 3H), 1.86 – 1.67 (m, 2H), 1.21 (d, *J* = 14.4 Hz, 19H), 0.81 (t, *J* = 6.8 Hz, 3H).^{13}C NMR ($CDCl_3$, 101 MHz): δ 197.9, 170.1, 150.3, 147.6, 137.5, 137.2, 135.5, 133.9, 128.7, 128.0, 127.9, 127.6, 121.7, 121.5, 117.3, 45.2, 42.6, 36.1, 31.8, 29.5, 29.1, 27.4, 26.6, 22.6, 14.1. MS m/z 416 (M^+, 8%), 331 (15), 281 (27), 253 (13), 209 (13), 208 (20), 207 (100), 186 (30), 171 (26). HRMS calcd. for $C_{27}H_{32}N_2O_2$ (M^+): 416.2464, found: 416.2455. IR (neat, cm^{-1}) $\tilde{\nu}$: 3351, 2923, 2857, 1681, 1604, 1523, 1481, 1265, 829, 790.



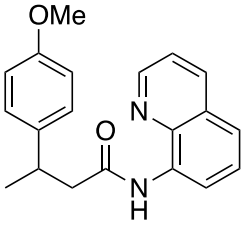
3-(4-nitrophenyl)-*N*-(quinolin-8-yl)decanamide (**3j):** Obtained following general procedure C (72 mg, 83% yield). Brown oil. R_f = 0.54 (hexane:EtOAc = 4:1). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.66 (s, 1H), 8.74 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.70 – 8.62 (m, 1H), 8.18 – 8.11 (m, 3H), 7.51 – 7.41 (m, 5H), 3.44 (tt, *J* = 9.0, 5.9 Hz, 1H), 3.01 – 2.77 (m, 2H), 1.86 – 1.61 (m, 2H), 1.32 – 1.11 (m, 10H), 0.84 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$, 101 MHz): δ 169.6, 152.5, 147.9, 146.8, 137.9, 137.0, 134.1, 128.6, 128.1, 127.6, 124.0, 121.9, 121.7, 117.1, 45.2, 42.7, 36.2, 31.9, 29.6, 29.2, 27.5, 22.7, 14.2. MS m/z 419 (M^+, 3%), 281 (12), 153 (11), 209 (13), 208 (21), 207 (100), 186 (15), 171 (13). HRMS calcd. For $C_{25}H_{29}N_3O_4$ (M^+): 435.2158, found: 435.2201. IR (neat, cm^{-1}) $\tilde{\nu}$: 3347, 2927, 2858, 1685, 1519, 1484, 1342, 1160.



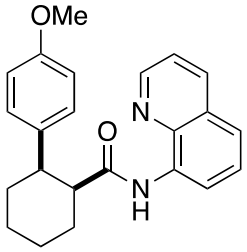
3-(4-hydroxyphenyl)-*N*-(quinolin-8-yl)decanamide (3k): Obtained following general procedure C (68 mg, 87% yield). Yellow oil. R_f = 0.21 (hexane:EtOAc = 4:1). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.71 (s, 1H), 8.76 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.68 (dd, *J* = 6.2, 2.9 Hz, 1H), 8.11 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.49 – 7.43 (m, 2H), 7.41 (dd, *J* = 8.3, 4.3 Hz, 1H), 7.15 – 7.04 (m, 2H), 6.79 – 6.69 (m, 2H), 5.91 (br. s, 1H), 3.24 – 3.12 (m, 1H), 2.79 (qd, *J* = 14.5, 7.5 Hz, 2H), 1.76 – 1.65 (m, 1H), 1.68 – 1.56 (m, 1H), 1.28 – 1.12 (m, 10H), 0.83 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$, 101 MHz): δ 171.3, 154.7, 148.1, 138.2, 136.7, 135.8, 134.2, 128.6, 128.1, 127.5, 121.8, 121.7, 117.1, 115.6, 46.2, 42.2, 36.7, 31.9, 29.6, 29.3, 27.5, 22.7, 14.2. MS m/z 390 (M^+, 19%), 305 (11), 253 (11), 207 (100), 186 (14), 171 (20), 161 (11). HRMS calcd. For $C_{25}H_{30}N_2O_2$ (M^+): 390.2307, found: 390.2318. IR (neat, cm^{-1}) $\tilde{\nu}$: 3340. 2923, 2854, 1666, 1523, 1484, 1226, 1160, 825.



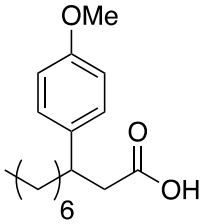
3-(4-methoxyphenyl)-*N*-(quinolin-8-yl)octanamide. (4a):[6] Obtained following general procedure C (74 mg, 98% yield).Brown solid. m.p. = 59-61 °C. R_f = 0.39 (hexane:EtOAc = 4:1). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.69 (s, 1H), 8.85 – 8.64 (m, 2H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.57 – 7.39 (m, 3H), 7.24 – 7.13 (m, 2H), 6.87 – 6.75 (m, 2H), 3.73 (s, 3H), 3.24 (dtd, *J* = 9.4, 7.4, 5.2 Hz, 1H), 2.91 – 2.74 (m, 2H), 1.80 – 1.62 (m, 2H), 1.29 – 1.14 (m, 6H), 0.87 – 0.76 (m, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.8, 158.1, 147.9, 138.0, 136.8, 136.5, 134.4, 128.6, 128.1, 127.6, 121.6, 121.5, 116.9, 114.0, 55.3, 46.2, 42.0, 36.5, 31.9, 27.2, 22.7, 14.2. MS m/z 376 (M^+, 38%), 341 (17), 327 (11), 319 (12), 282 (11), 281 (36), 253 (25), 209 (14), 208 (22), 207 (100), 191 (12), 186 (15), 175 (22), 171 (26), 161 (11). IR (neat, cm^{-1}) $\tilde{\nu}$: 3355, 2927, 2857, 1685, 1519, 1481, 1245, 825.



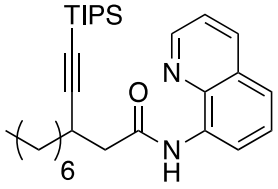
3-(4-methoxyphenyl)-*N*-(quinolin-8-yl)butanamide (**4b**):[1] Obtained following general procedure C (62 mg, 97% yield).Brown solid. m.p. = 65-66 °C. R_f = 0.34 (hexane:EtOAc = 4:1). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.84 (s, 1H), 8.84 – 8.75 (m, 2H), 8.30 – 8.17 (m, 1H), 7.58 – 7.45 (m, 3H), 7.32 – 7.24 (m, 2H), 6.89 – 6.81 (m, 2H), 3.76 (s, 3H), 3.47 (h, *J* = 7.1 Hz, 1H), 2.90 (dd, *J* = 14.4, 7.0 Hz, 1H), 2.80 (dd, *J* = 14.4, 7.9 Hz, 1H), 1.40 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR ($CDCl_3$, 101 MHz): δ 170.8, 158.2, 147.5, 138.2, 134.2, 128.2, 127.9, 121.7, 121.6, 114.1, 55.3, 47.2, 36.3, 22.2. MS m/z 320 (M^+, 21%), 281 (30), 253 (12), 209 (13), 208 (21), 207 (100), 191 (10). IR (neat, cm^{-1}) $\tilde{\nu}$: 3355, 2962, 1685, 1519, 1481, 1245, 825.



2-(4-methoxyphenyl)-*N*-(quinolin-8-yl)cyclohexane-1-carboxamide (4c):[1] Obtained following general procedure C (49 mg, 68% yield).Brown solid. m.p. = 68-70 °C. R_f = 0.61 (hexane:EtOAc = 4:1). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.33 (s, 1H), 8.73 – 8.60 (m, 2H), 8.12 (d, *J* = 8.3 Hz, 1H), 7.54 – 7.34 (m, 3H), 7.29 – 7.19 (m, 2H), 6.75 – 6.62 (m, 2H), 3.58 (s, 3H), 3.16 – 3.05 (m, 1H), 3.01 (dt, *J* = 11.9, 4.1 Hz, 1H), 2.47 (qd, *J* = 12.1, 3.6 Hz, 1H), 2.24 (dd, *J* = 13.0, 3.4 Hz, 1H), 2.15 – 1.94 (m, 2H), 1.93 – 1.74 (m, 2H), 1.63 (dd, *J* = 8.7, 4.1 Hz, 1H), 1.53 – 1.43 (m, 1H). ^{13}C NMR ($CDCl_3$, 101 MHz): δ 173.5, 158.0, 147.4, 137.6, 137.2, 136.8, 134.4, 128.8, 128.1, 127.7, 121.3, 121.2, 117.0, 113.8, 55.1, 49.0, 45.1, 29.8, 27.4, 26.3, 22.0. MS m/z 360 (M^+, 11%), 281 (36), 253 (17), 209 (13), 208 (22), 207 (100). IR (neat, cm^{-1}) $\tilde{\nu}$: 3351, 2923, 2854, 1685, 1520, 1481, 1245, 825.

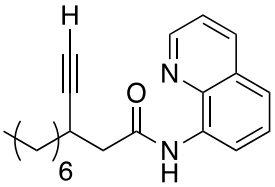


3-(4-methoxyphenyl)decanoic acid (5a): Obtained in a 0.2 mmol reaction scale (42 mg, 75%). Brown oil. R_f = 0.60 (hexane:EtOAc = 1:1). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.09 (d, *J* = 8.6 Hz, 2H), 6.83 (d, *J* = 8.6 Hz, 2H), 3.79 (s, 3H), 3.01 (dtd, *J* = 9.0, 7.4, 5.4 Hz, 1H), 2.66 – 2.51 (m, 2H), 1.60 (dddd, *J* = 21.0, 17.6, 8.2, 5.1 Hz, 2H), 1.27 – 1.13 (m, 10H), 0.85 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$, 101 MHz): δ 178.6, 158.3, 136.1, 128.4, 114.0, 55.3, 41.9, 41.2, 36.5, 31.9, 29.6, 29.3, 27.4, 22.8, 14.2. MS m/z 278 (M^+, 38%), 220 (10), 219 (52), 180 (25), 179 (100). HRMS calcd. for $C_{17}H_{26}O_3$ (M^+): 278.1882, found: 278.1877. IR (neat, cm^{-1}) $\tilde{\nu}$: 2924, 2854, 1704, 1511, 1345, 1037, 825.

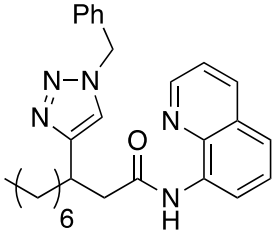


***N*-(quinolin-8-yl)-3-((triisopropylsilyl)ethynyl)decanamide.** (**6):** Obtained in a 0.2 mmol reactio scale (59 mg, 62% yield). Yellow oil. R_f = 0.60 (hexane:EtOAc = 4:1). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.89 (s, 1H), 8.86 – 8.76 (m, 2H), 8.17 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.58 – 7.42 (m, 3H), 3.20 – 3.07 (m, 1H), 2.72 (qd, *J* = 14.1, 7.4 Hz, 2H), 1.70 – 1.46 (m, 4H), 1.33 – 1.22 (m, 8H), 0.94

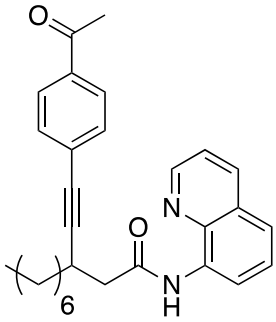
– 0.75 (m, 24H). ^{13}C NMR ($CDCl_3$, 101 MHz): δ 169.7, 147.7, 137.9, 136.8, 134.3, 128.0, 127.6, 121.6, 121.5, 117.2, 110.5, 82.1, 77.4, 77.0, 76.7, 44.3, 34.9, 31.8, 30.1, 29.2, 27.2, 22.7, 18.5, 14.1, 11.2. MS m/z 449 (M^+, 1%), 282 (11), 181 (37), 253 (19), 209 (14), 208 (22), 207 (100). HRMS calcd. for $C_{30}H_{46}N_2OSi$ (M^+): 478.3379, found: 478.3368. IR (neat, cm^{-1}) $\tilde{\nu}$: 3351, 2927, 2858, 1685, 1527, 1481, 1326, 790.



3-ethynyl-*N*-(quinolin-8-yl)decanamide (7): Prepared **a**ccording to the published protocol,[7] compound **6** was charged in round bottom flask, (0.06 mmol, 28 mg) and THF was added (0.1 M). Hydrated TBAF (0.072 mmol, 20.1 mg, 1.2 equiv.) was added. The reaction was allowed to stir at rt. After 2 h, the reaction mixture was concentrated under reduced pressure. Column chromatography of the residue furnished the desired product (16 mg, 86%). Yellow oil. R_f = 0.52 (hexane:EtOAc = 4:1). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.97 (s, 1H), 8.84 – 8.78 (m, 2H), 8.18 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.58 – 7.44 (m, 3H), 3.10 – 3.01 (m, 1H), 2.81-2.68 (m, 2H), 2.13 (d, *J* = 2.4 Hz, 1H), 1.67 – 1.42 (m, 4H), 1.39 – 1.19 (m,8H), 0.91 – 0.84 (m, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz): δ 169.4, 147.9, 138.2, 136.6, 134.4, 128.0, 127.5, 121.6, 121.5, 116.9, 86.4, 70.2, 43.8, 34.6, 31.8, 29.3, 29.2, 28.6, 27.2, 22.6, 14.1. MS m/z 322 (M^+, 6%), 282 (12), 253 (10), 223 (11), 209 (13), 208 (21), 207 (100). HRMS calcd. for $C_{21}H_{26}N_2O$ (M^+): 322.2045, found: 322.2044. IR (neat, cm^{-1}) $\tilde{\nu}$: 2927, 2858, 1681, 1527, 1484, 906, 728.



3-(1-benzyl-1*H*-1,2,3-triazol-4-yl)-*N*-(quinolin-8-yl)decanamide (8): Obtained in a 0.2 mmol reaction scale (59 mg, 65% yield). White solid. m.p. = 67-69 °C. R_f = 0.52 (hexane:EtOAc = 1:1). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.83 (s, 1H), 8.78 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.67 (dd, *J* = 5.1, 3.9 Hz, 1H), 8.17 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.52 – 7.41 (m, 3H), 7.28 (s, 1H), 7.23 – 7.03 (m, 5H), 5.42 (s, 2H), 3.47 (ddd, *J* = 8.5, 6.1, 2.4 Hz, 1H), 3.08 – 2.88 (m, 2H), 1.90 – 1.72 (m, 2H), 1.24 (d, *J* = 5.6 Hz, 10H), 0.85 (t, *J* = 6.5 Hz, 3H). ^{13}C NMR ($CDCl_3$, 101 MHz): δ 170.6, 150.6, 148.3, 138.4, 136.4, 135.0, 134.5, 129.0, 128.5, 128.0, 127.8, 127.5, 121.7, 121.6, 121.5, 116.6, 54.0, 43.9, 35.0, 34.0, 31.9, 29.5, 29.3, 27.4, 22.7, 14.2. MS m/z 455 (M^+, 3%), 312 (11), 311 (53), 283 (10), 269 (22), 185 (27), 170 (18), 144 (12), 143 (39), 90 (100). HRMS calcd. for $C_{28}H_{33}N_5O$ (M^+): 455.2685, found: 455.2686. IR (neat, cm^{-1}) $\tilde{\nu}$: 2923, 2854, 1708, 1523, 1245, 1172.

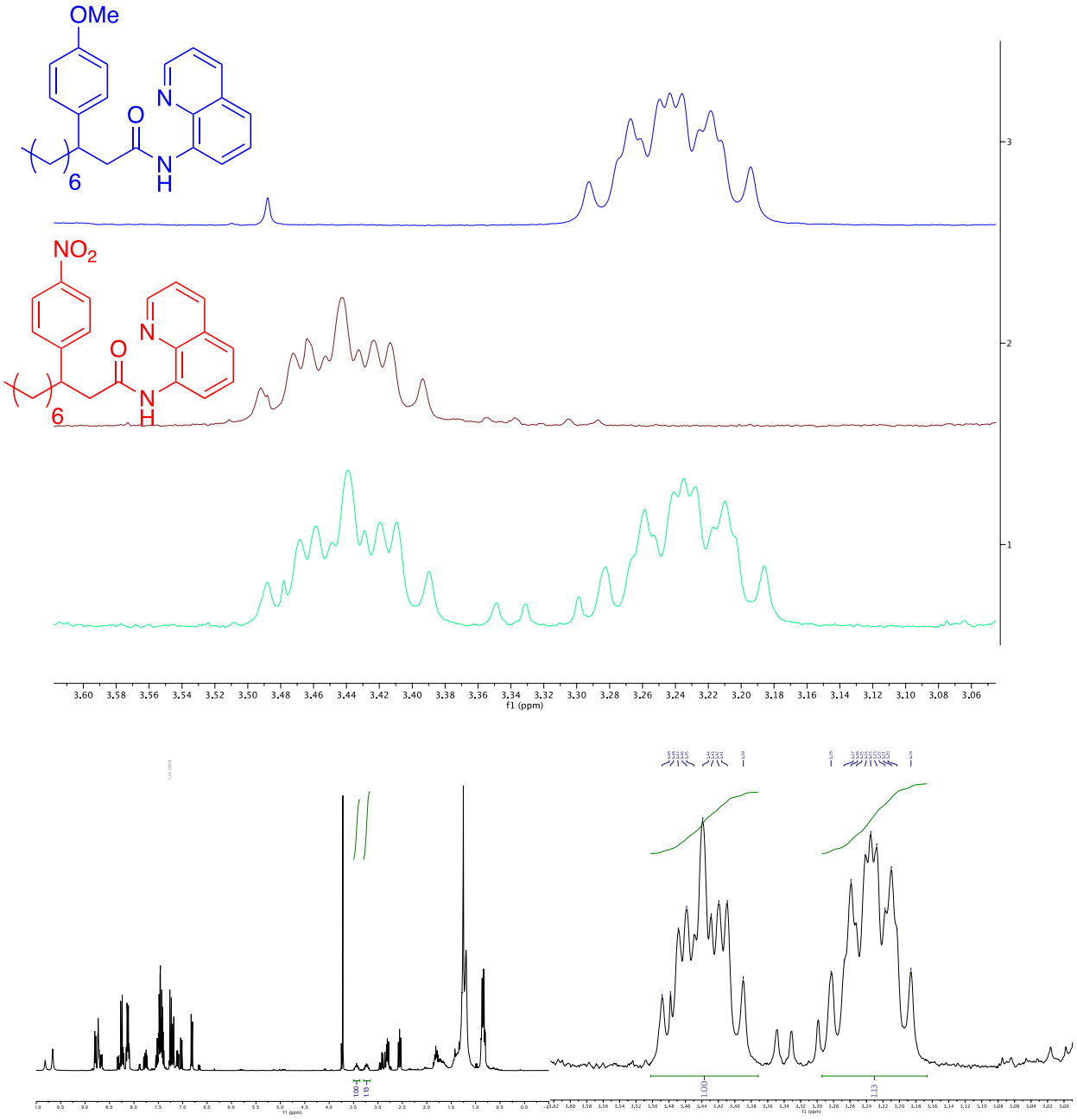


3-((4-acetylphenyl)ethynyl)-*N*-(quinolin-8-yl)decanamide (9): Obtained in a 0.2 mmol reaction scale (40 mg, 45% yield). Yellow oil. R_f = 0.30 (hexane:EtOAc = 4:1). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.03 (s, 1H), 8.82 (dd, *J* = 7.3, 1.7 Hz, 1H), 8.63 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.86 – 7.69 (m, 2H), 7.55 – 7.50 (m, 2H), 7.43 – 7.37 (m, 3H), 3.28 (ddd, *J* = 13.8, 8.2, 5.8 Hz, 1H), 2.89 – 2.75 (m, 2H), 2.55 (s, 3H), 1.69 – 1.59 (m, 2H), 1.34 – 1.24 (m, 10H), 0.89 – 0.85 (m, 3H). ^{13}C NMR ($CDCl_3$, 101 MHz): δ 197.3, 169.5, 148.0, 138.3, 136.5, 135.8, 134.4, 131.8, 128.7, 128.0, 127.5, 121.6, 121.5, 116.8, 95.7, 82.3, 43.9, 34.8, 31.8, 29.7, 29.3, 29.2, 27.4, 26.5, 22.6, 14.1. MS m/z 440 (M^+, 2%), 281 (13), 253 (10), 209 (13), 208 (21), 207 (100). HRMS calcd. for $C_{29}H_{32}N_2O_2$ (M^+): 440.2464, found: 440.2456. IR (neat, cm^{-1}) $\tilde{\nu}$: 3347, 2923, 2854, 1685, 1527, 1261, 1172, 964.

Competitive experiment

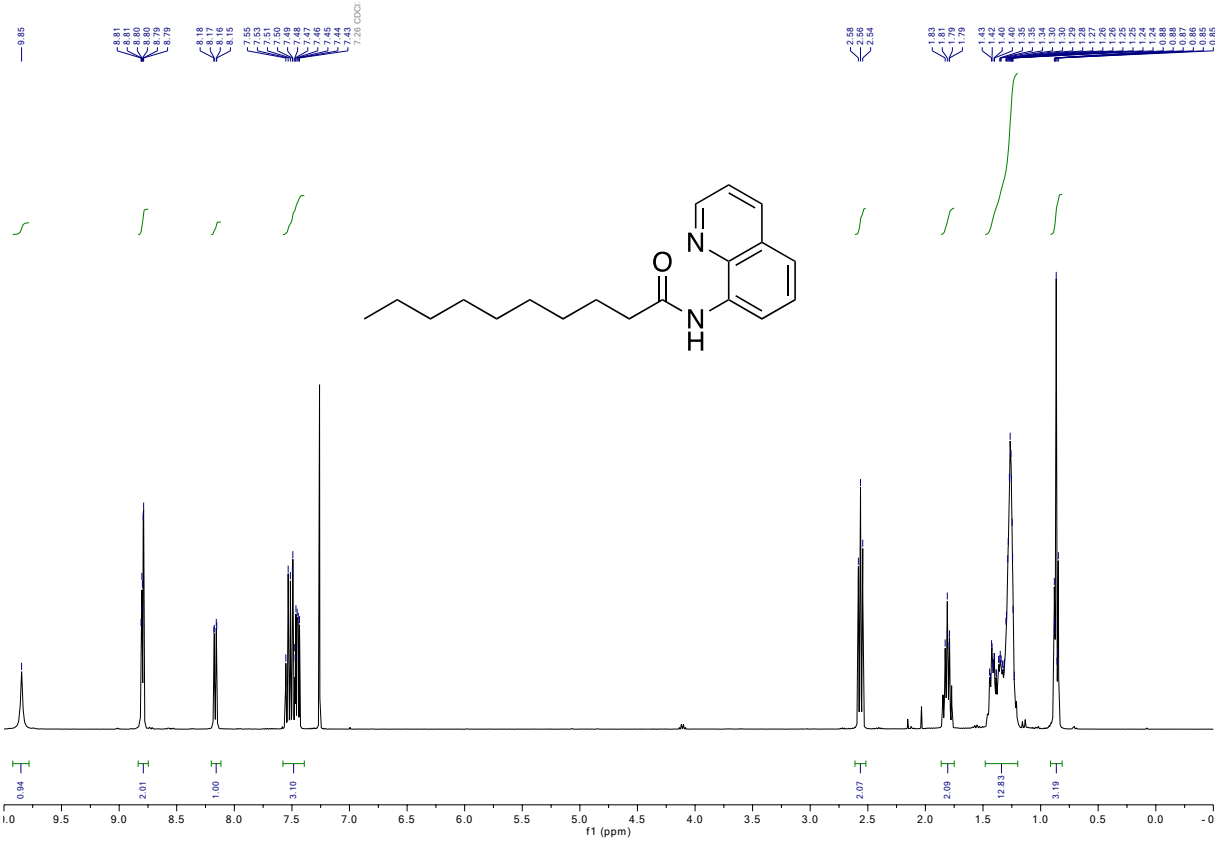
Amide **2aa** (59.7 mg, 0.20 mmol), $Pd(OAc)_2$ (4.5 mg, 20 µmol), $NaHCO_3$ (25 mg, 0.30 mmol), 2-pyridone (7.6 mg, 80 µmol), 4-iodoanisole (72 mg, 0.3 mmol) and 1-iodo-4-nitrobenzene (75 mg, 0.3 mmol) were placed in a reaction vial equipped with a stirring bar. The mixture ChCl:acetamide (1:2, 1 mL) was then added, and the mixture was heated at 110 °C for 12 h under air atmosphere. The reaction was then cooled to rt and quenched by addition of water. The crude mixture was extracted with EtOAc (x3),

dried over $MgSO_4$ and concentrated *in vacuo*. Products were isolated by preparative-TLC affording a mixture of the starting material **2aa**, and the two corresponding arylated products **3a** and **3j**, observing a product ratio of 1.0:1.1 (**3j**:**3a)**.

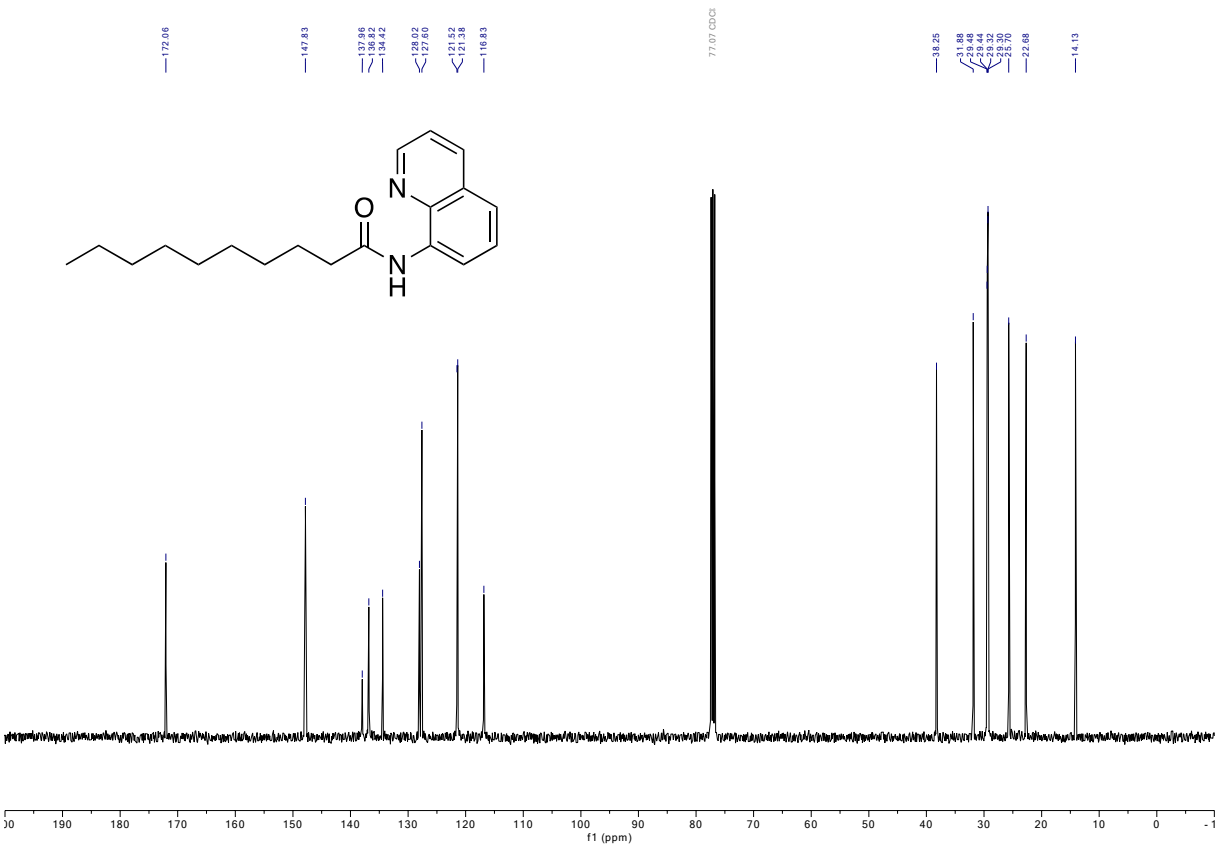


NMR Spectra

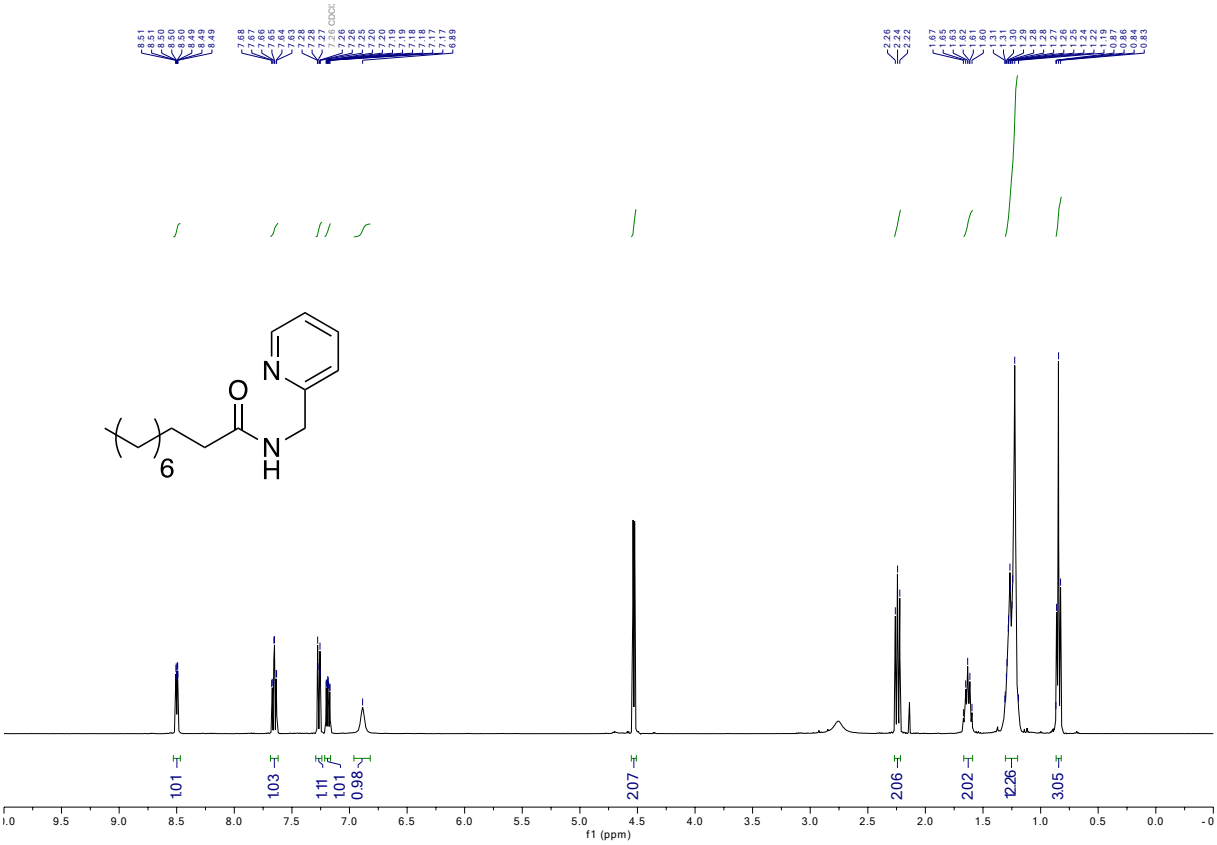
^{1}H NMR: (400 MHz, $CDCl_3$) of **2aa**



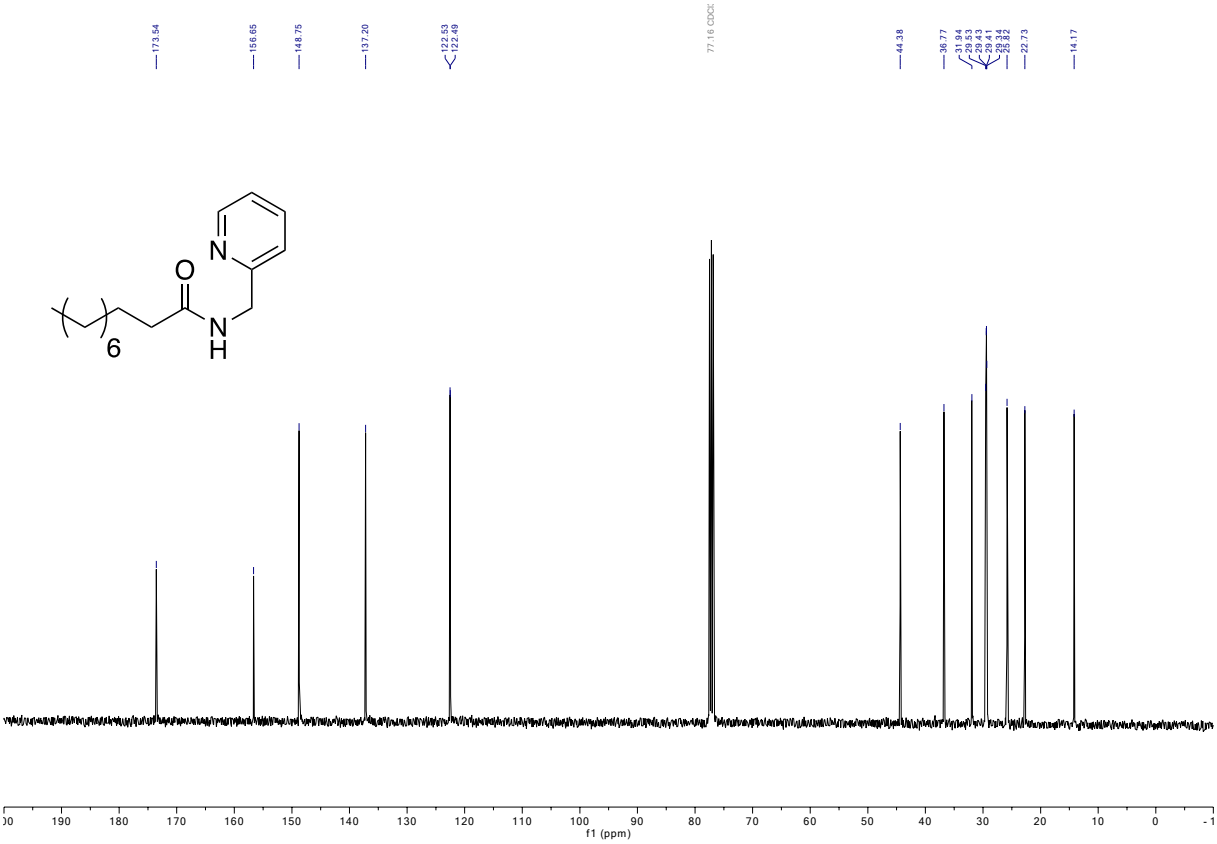
$^{13}C\{^{1}H\}$ NMR: (101 MHz, $CDCl_3$) of **2aa**


172.06
147.83
137.96
136.82
134.42
128.02
127.60
121.52
121.38
116.83
77.07 CDCl
38.25
31.88
29.48
29.44
29.32
29.30
25.70
22.68
14.13
O
N
N
H
f1 (ppm)

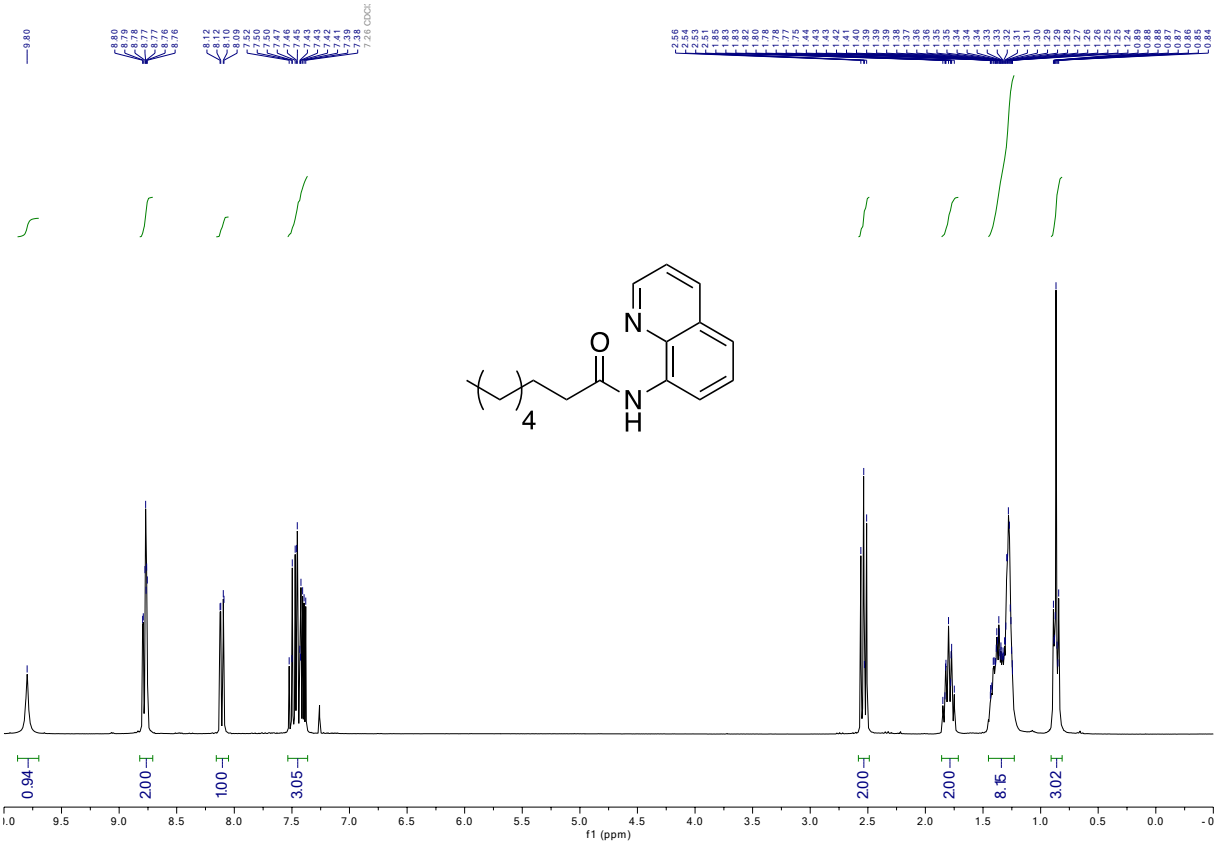
^{1}H NMR: (400 MHz, $CDCl_3$) of **2ab**



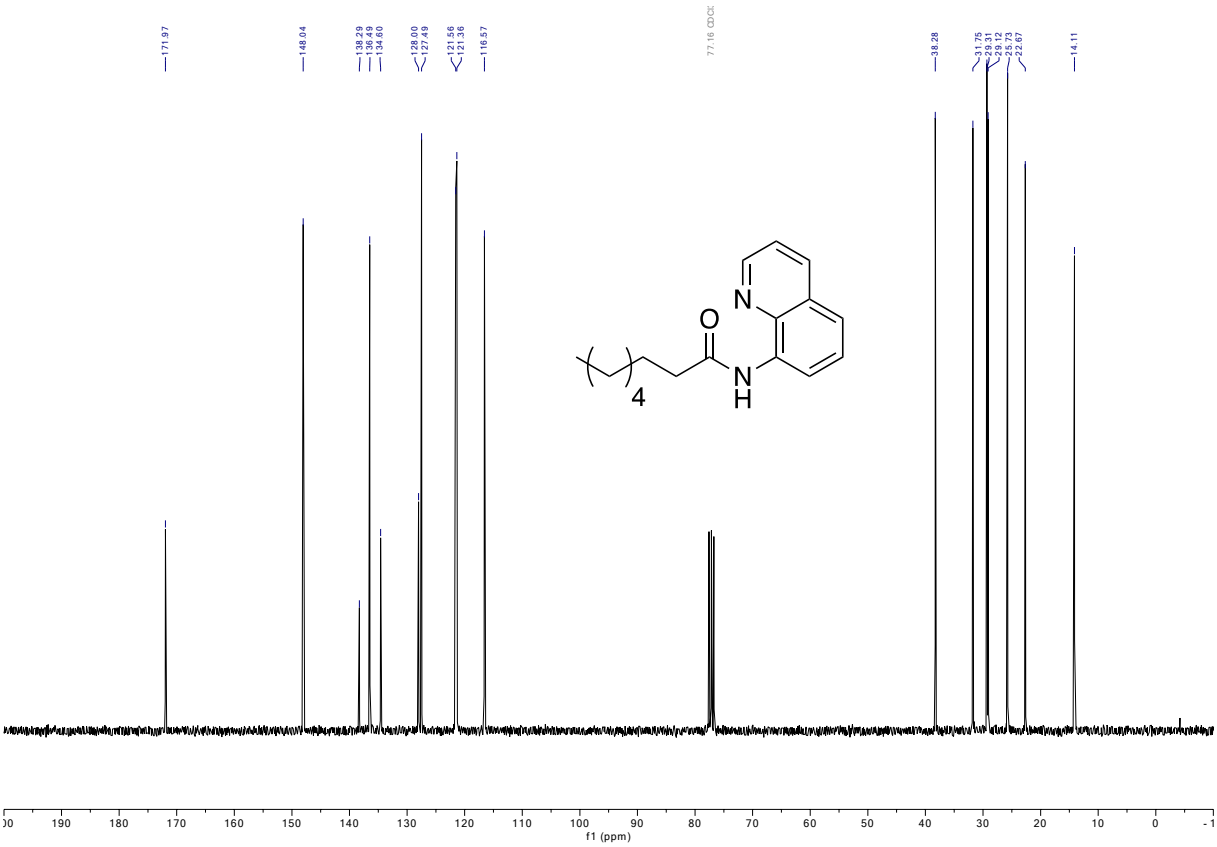
^{13}C{^{1}H} NMR: (101 MHz, $CDCl_3$) of **2ab**



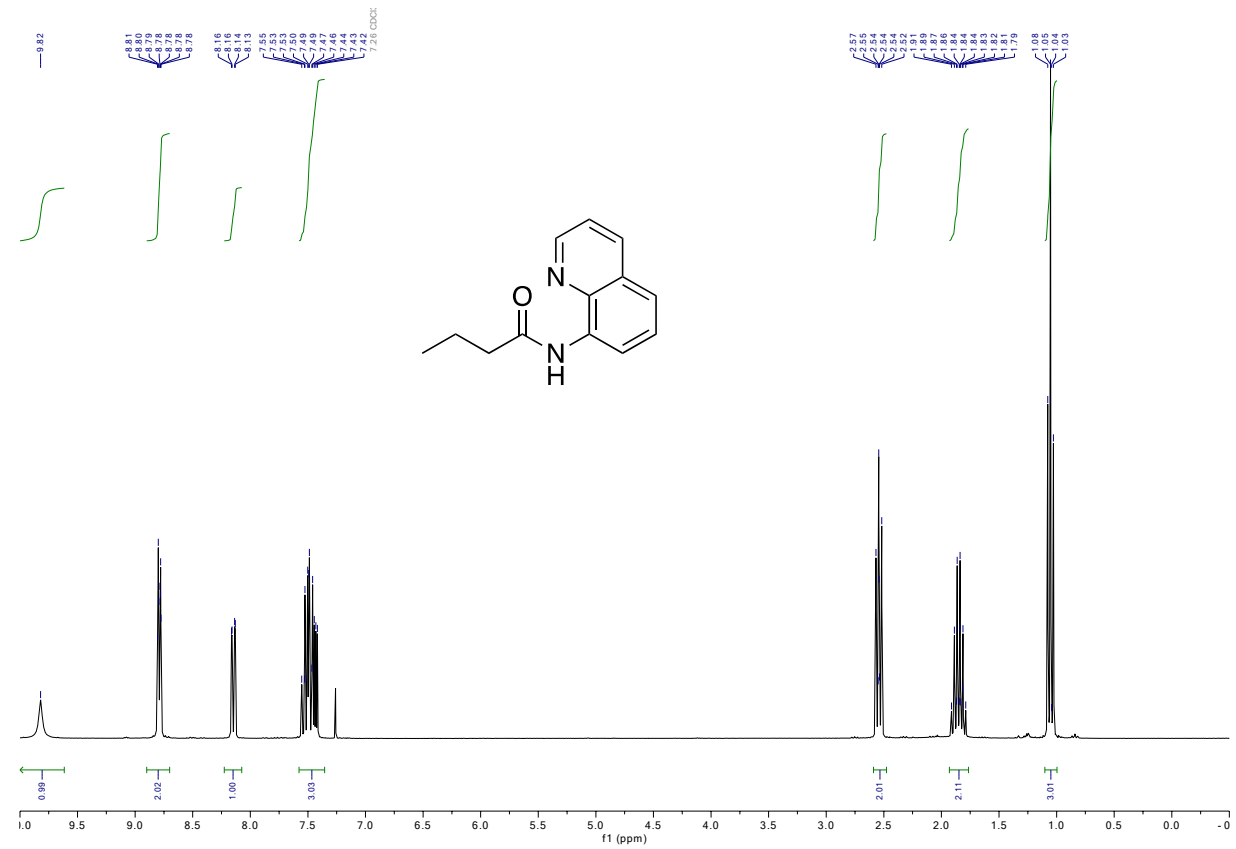
^{1}H NMR: (300 MHz, $CDCl_3$) of **2b**



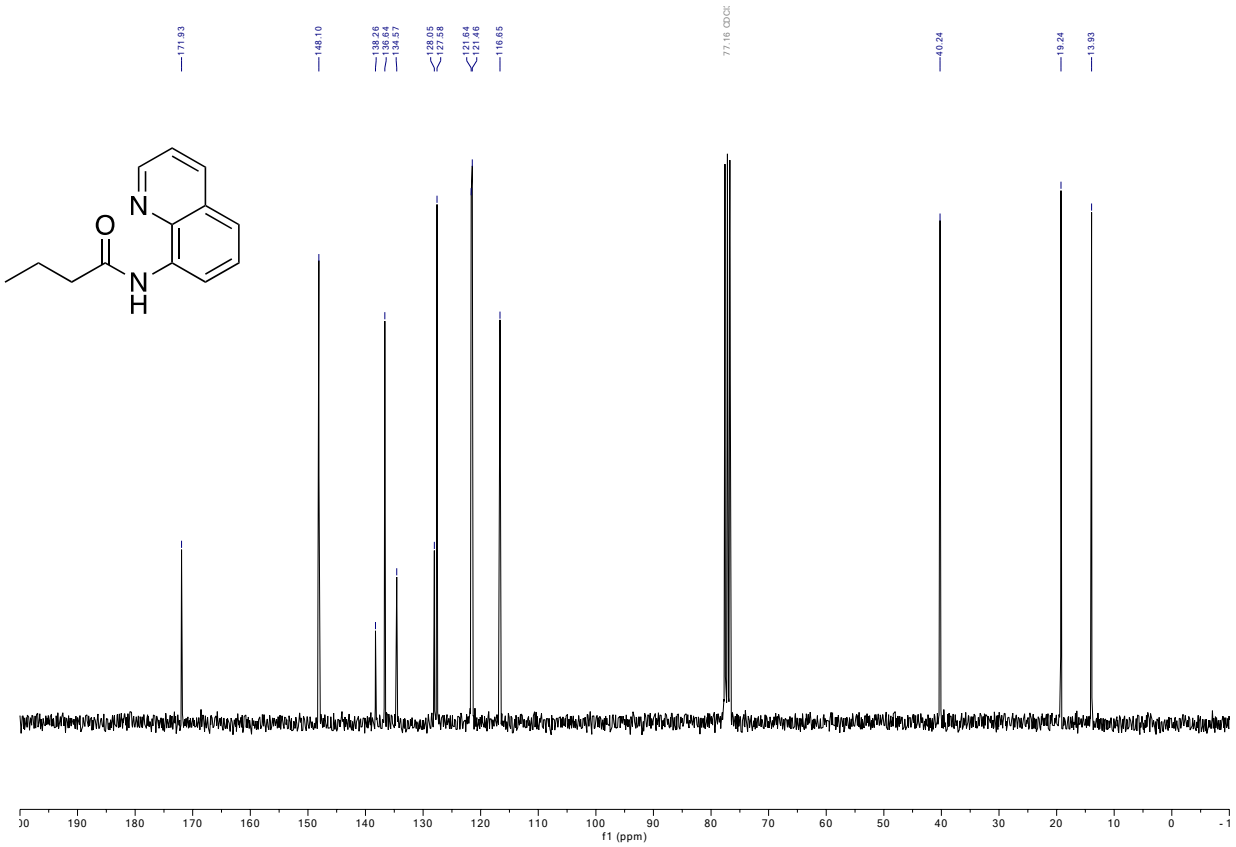
^{13}C{^{1}H} NMR: (101 MHz, $CDCl_3$) of **2b**



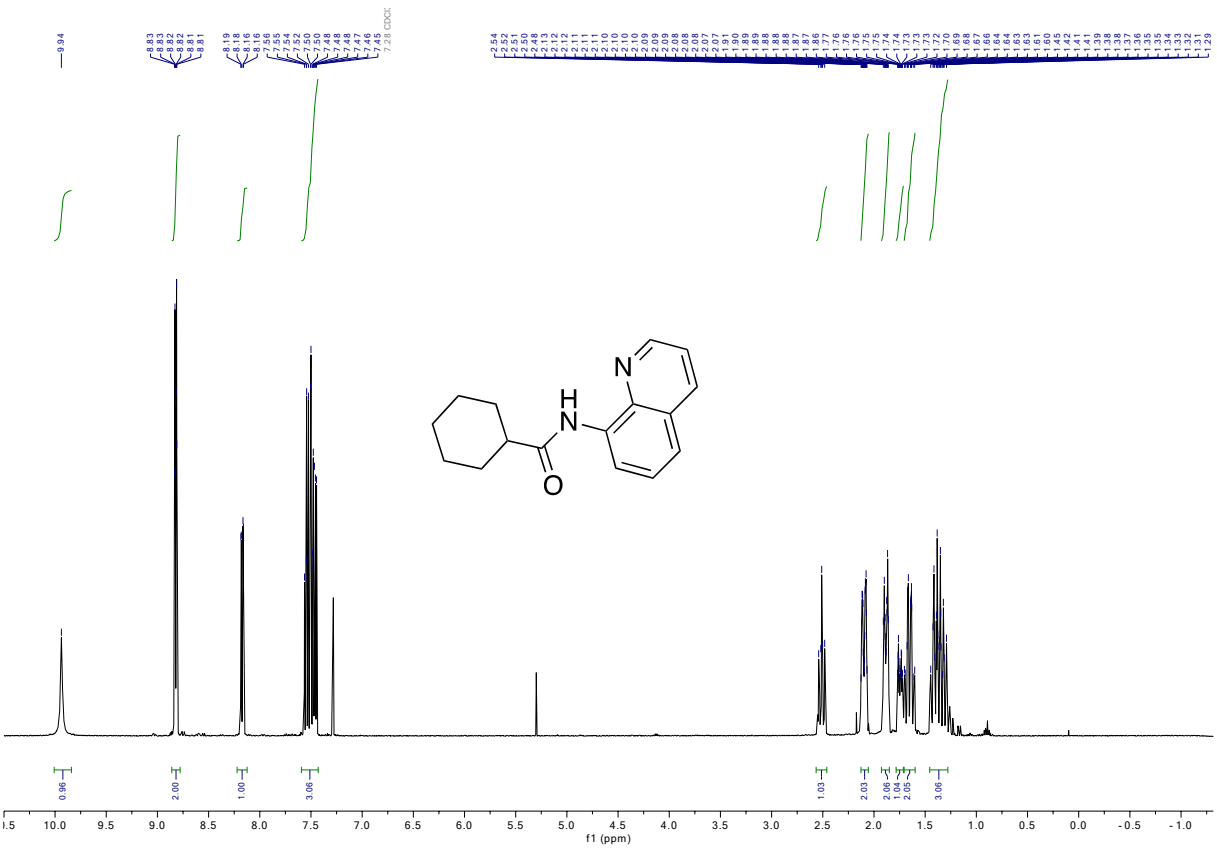
^{1}H NMR: (300 MHz, $CDCl_3$) of **2c**



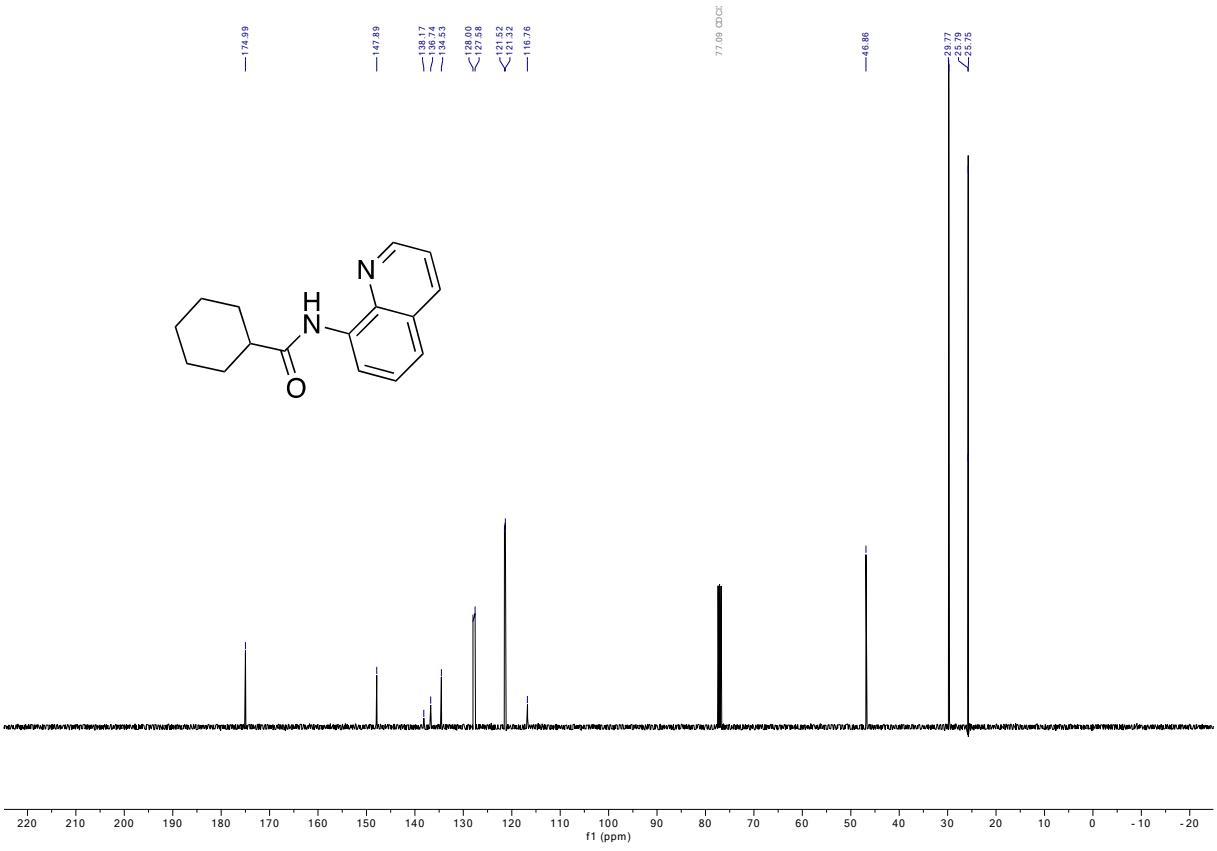
^{13}C{^{1}H} NMR: (75 MHz, $CDCl_3$) of **2c**



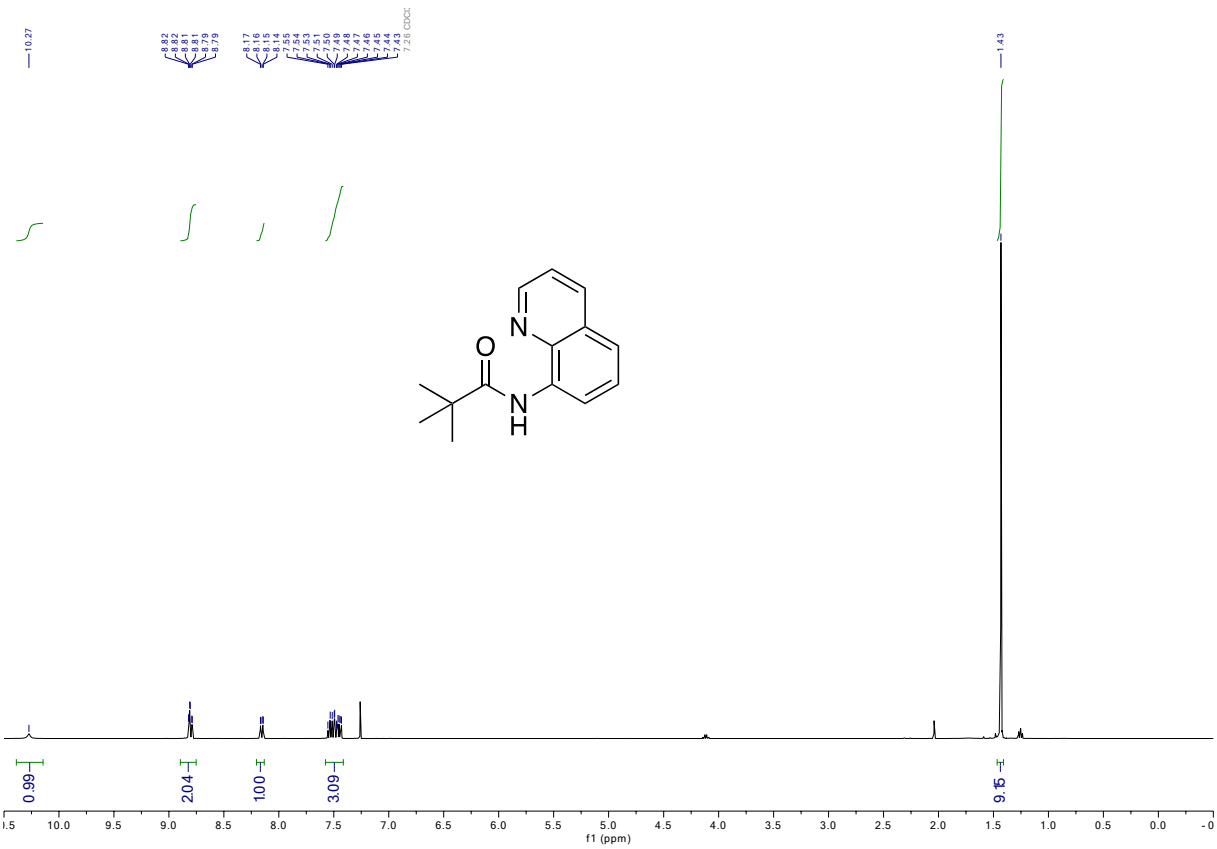
^{1}H NMR: (400 MHz, $CDCl_3$) of **2d**



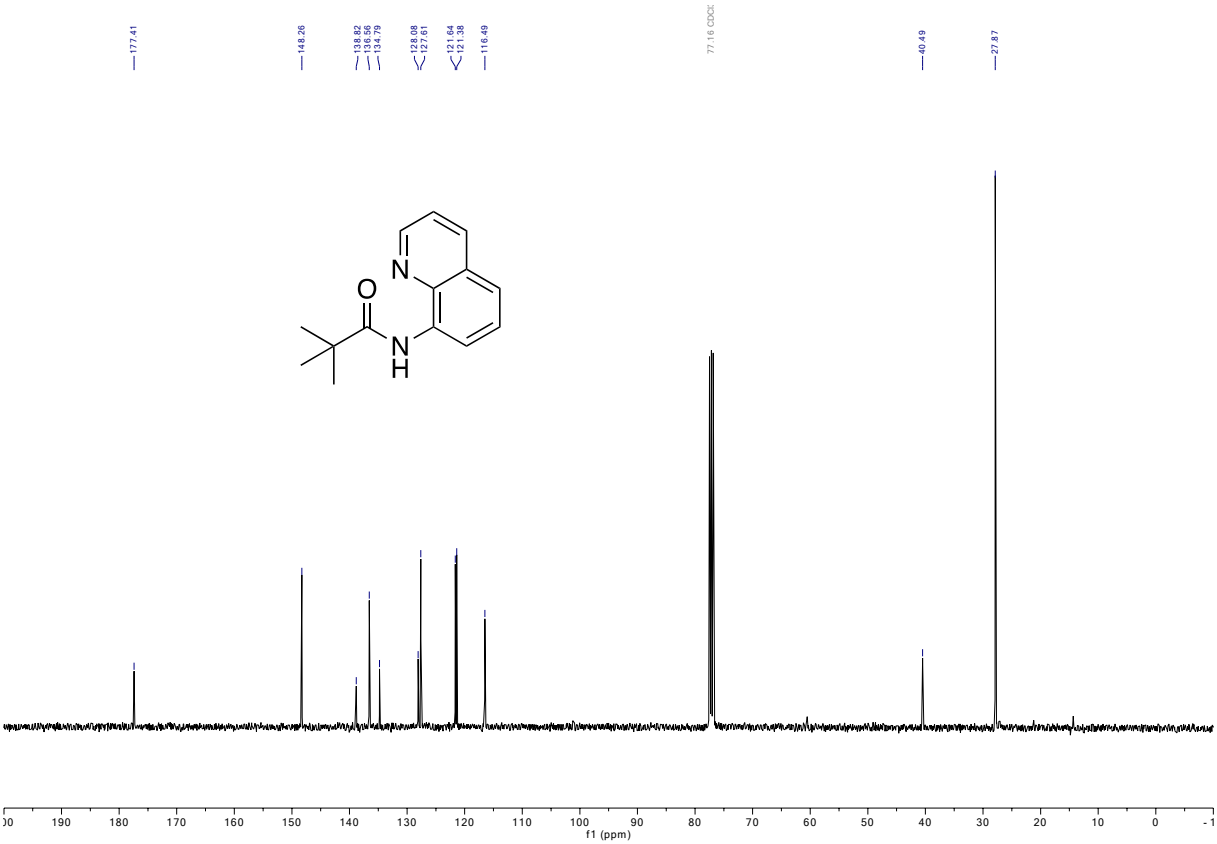
^{13}C{^{1}H} NMR: (101 MHz, $CDCl_3$) of **2d**



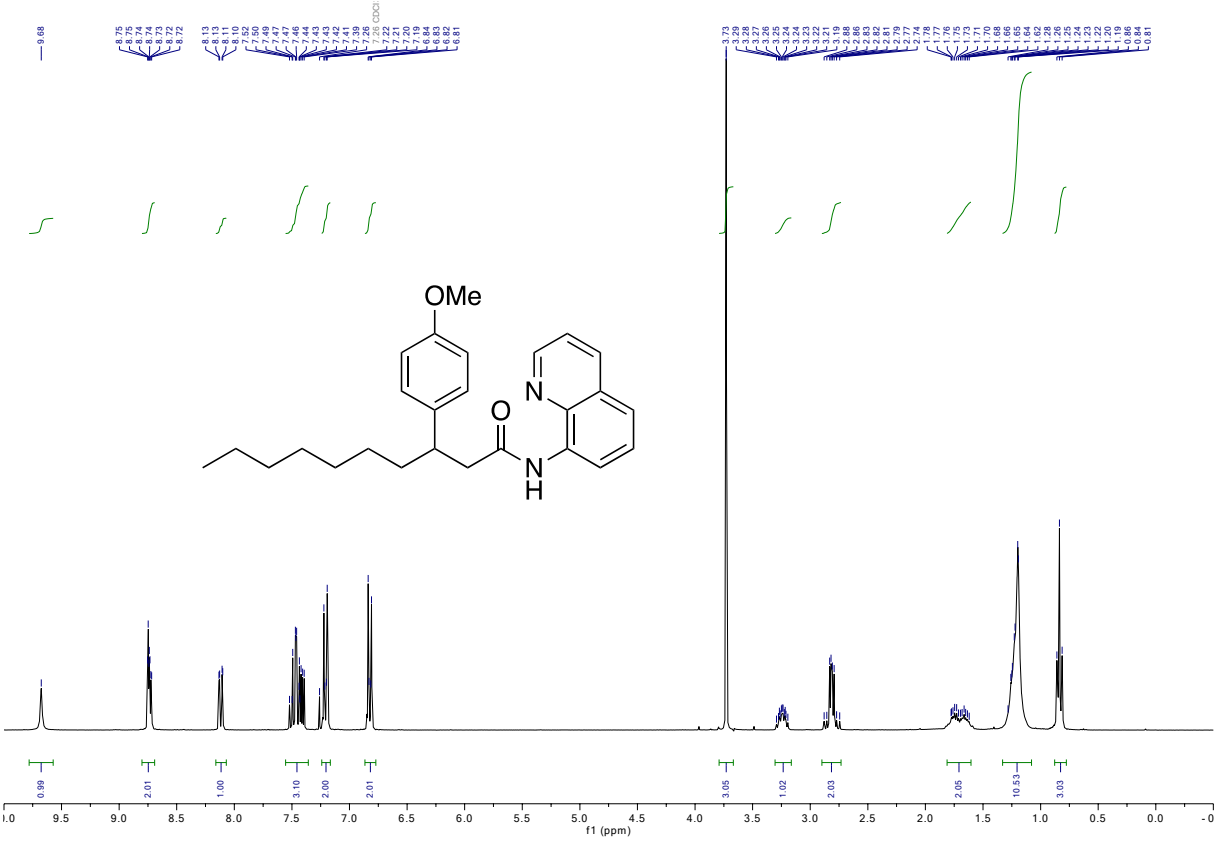
^{1}H NMR: (400 MHz, $CDCl_3$) of **2f**



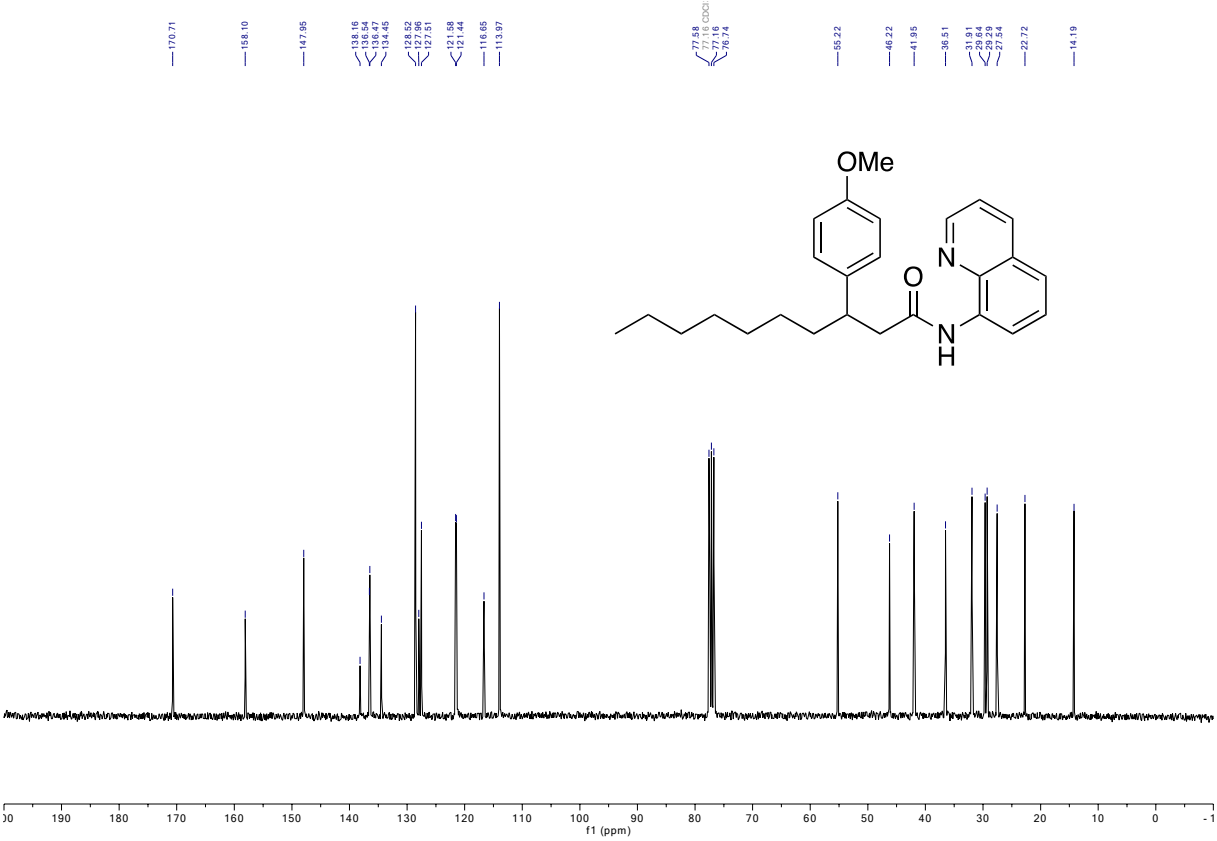
^{13}C{^{1}H} NMR: (101 MHz, $CDCl_3$) of **2f**



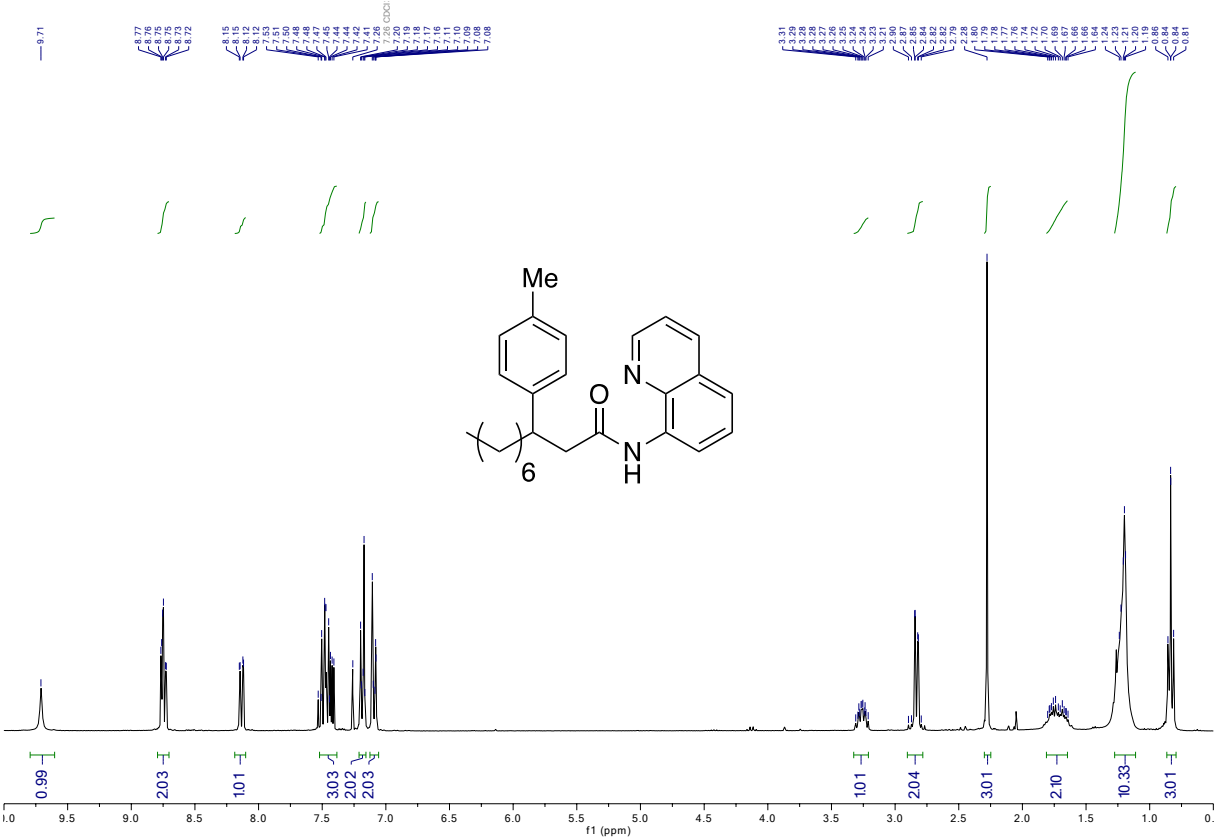
^{1}H NMR: (300 MHz, $CDCl_3$) of **3a**



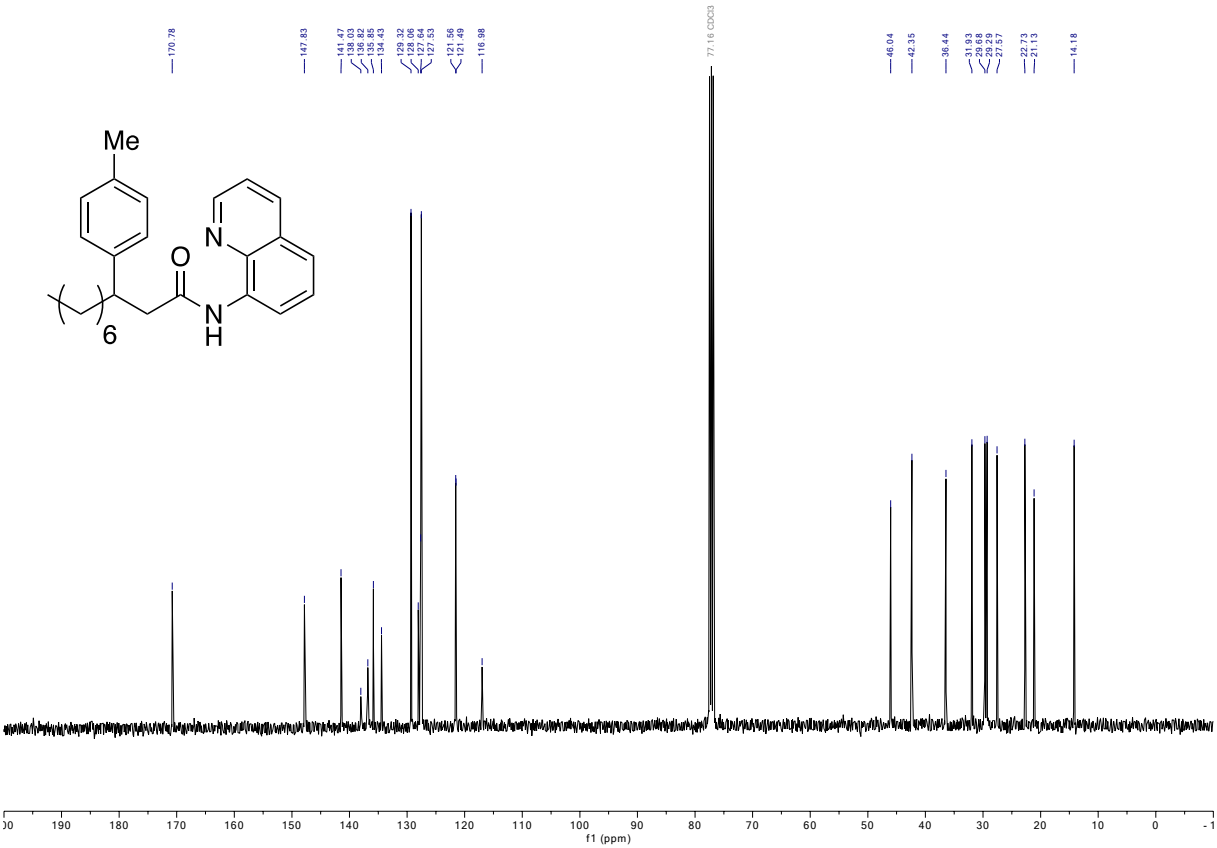
$^{13}C\{^{1}H\}$ NMR: (75 MHz, $CDCl_3$) of **3a**



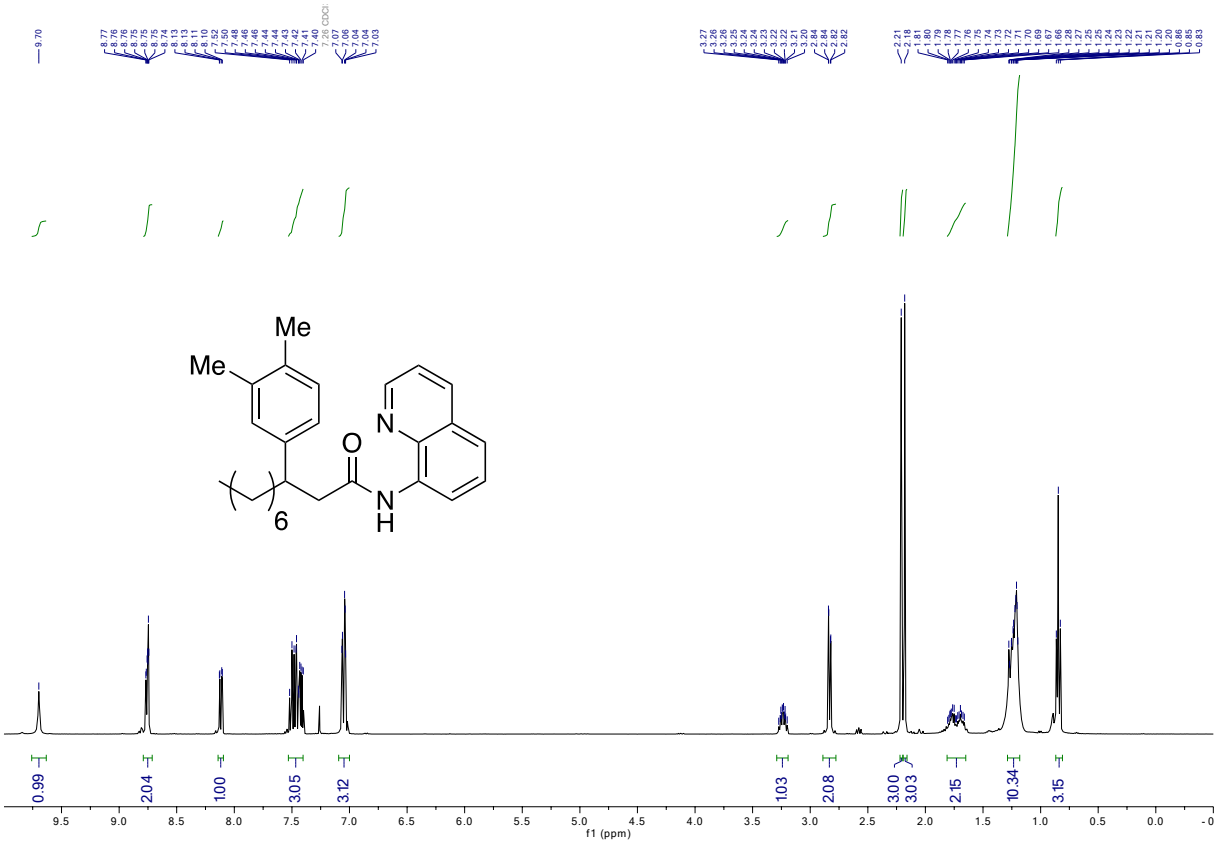
^{1}H NMR: (300 MHz, $CDCl_3$) of **3b**



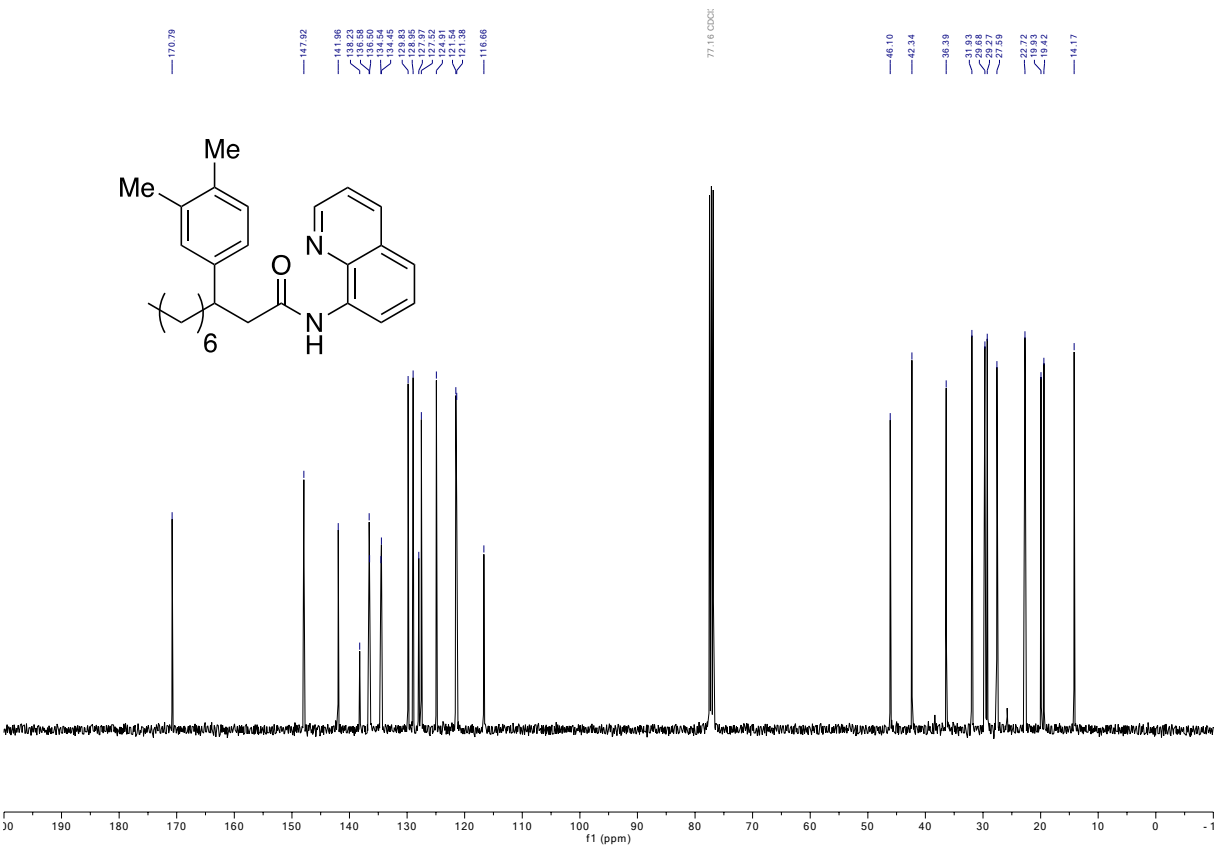
^{13}C{^{1}H} NMR: (101 MHz, $CDCl_3$) of **3b**



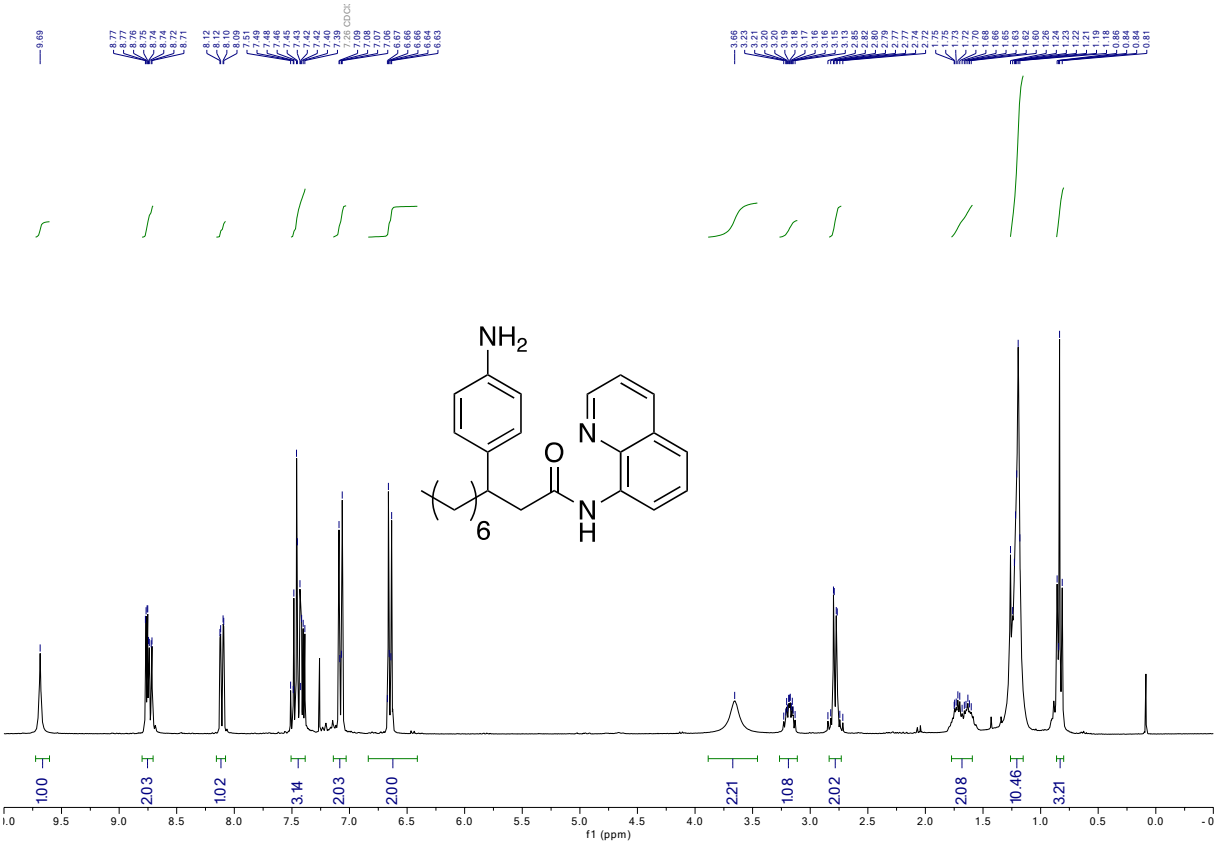
^{1}H NMR: (400 MHz, $CDCl_3$) of **3c**



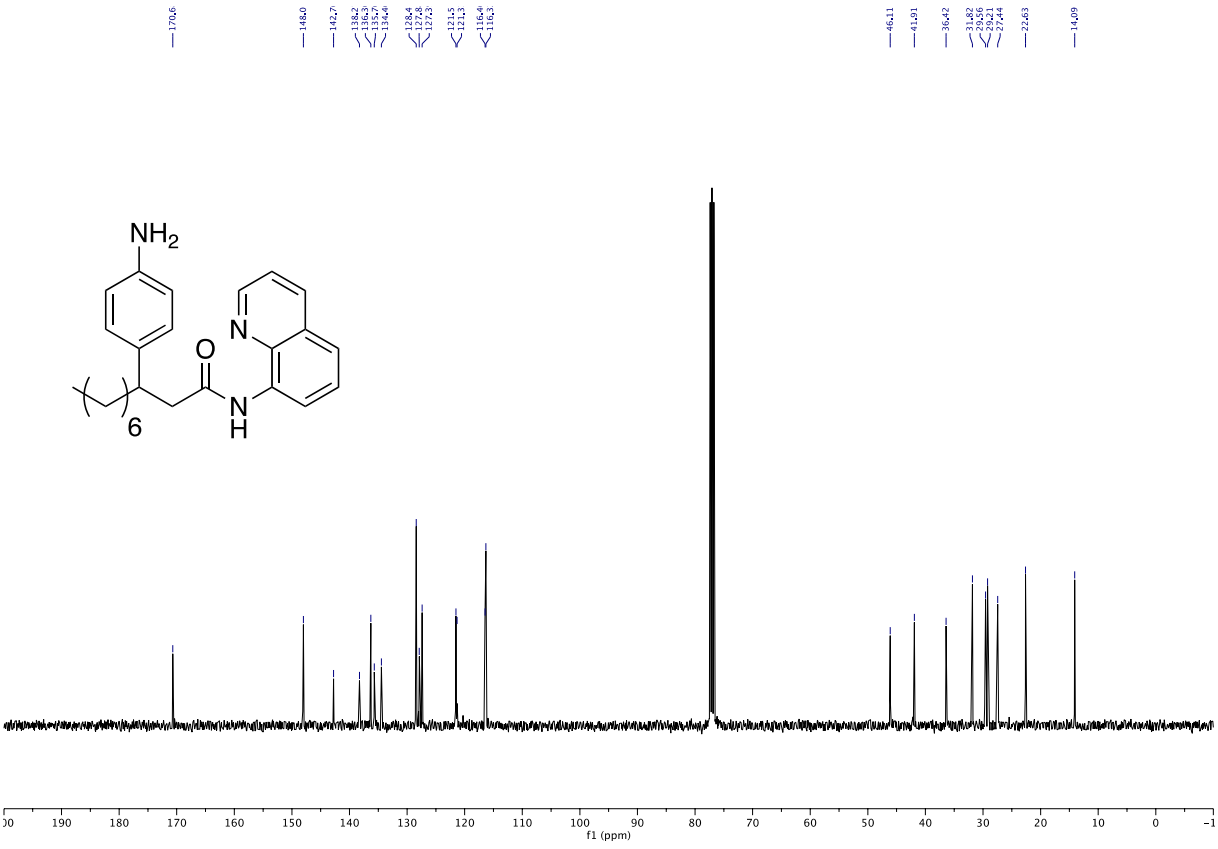
^{13}C{^{1}H} NMR: (101 MHz, $CDCl_3$) of **3c**



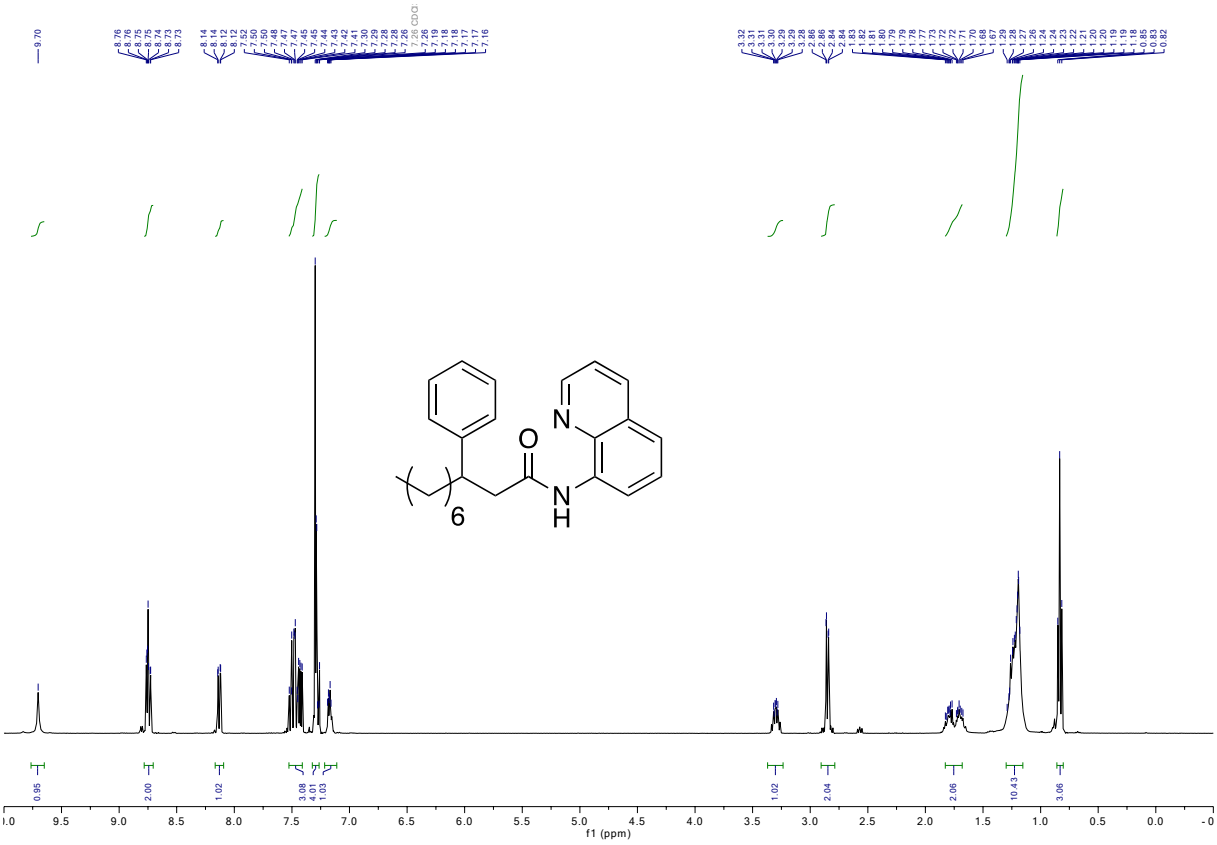
^{1}H NMR: (300 MHz, $CDCl_3$) of **3d**



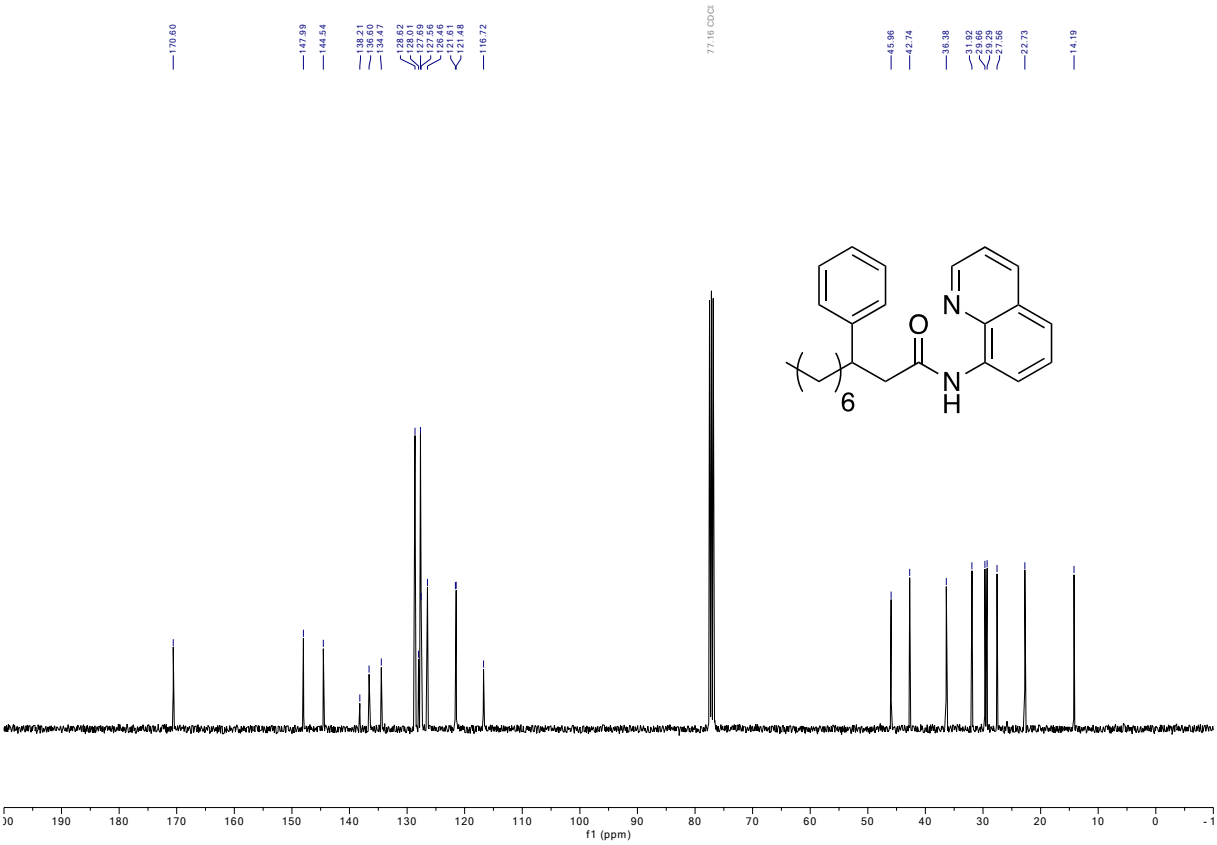
^{13}C{^{1}H} NMR: (101 MHz, $CDCl_3$) of **3d**



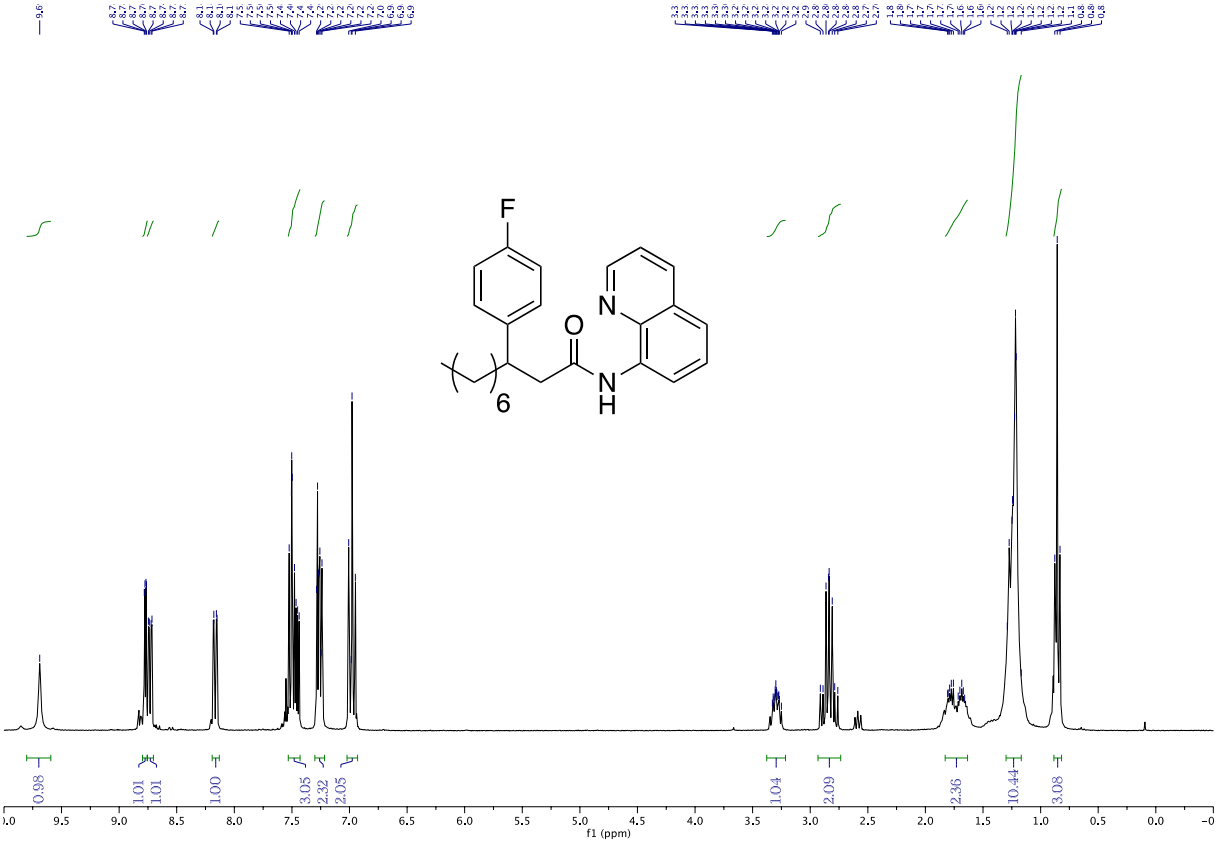
^{1}H NMR: (400 MHz, $CDCl_3$) of **3e**



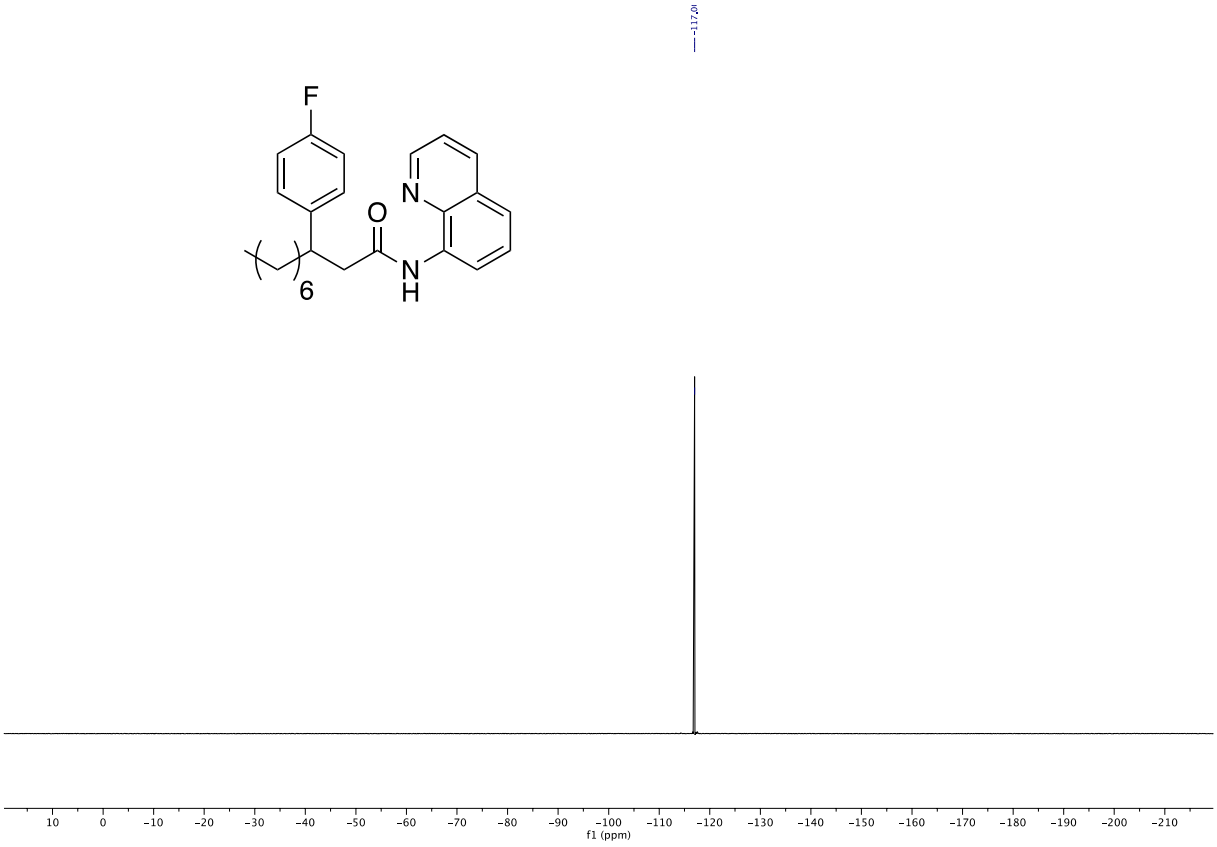
$^{13}C\{^{1}H\}$ NMR: (101 MHz, $CDCl_3$) **3e**


170.60
147.99
144.54
138.21
136.60
134.47
128.62
128.01
127.69
127.55
126.46
121.61
121.48
116.72
77.16 CDCl
45.96
42.74
36.38
31.92
29.66
29.29
27.56
22.73
14.19
N
O
N
H
6
f1 (ppm)

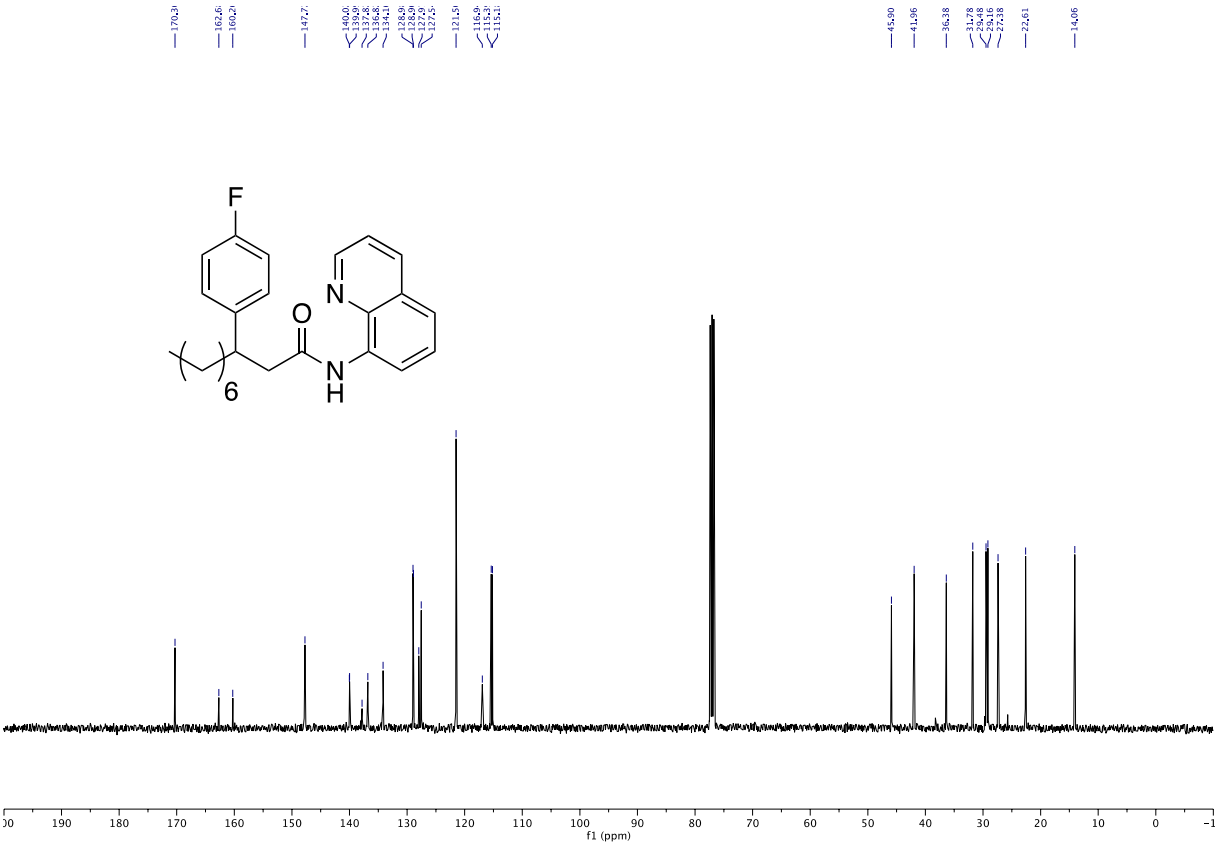
^{1}H NMR: (300 MHz, $CDCl_3$) of **3f**



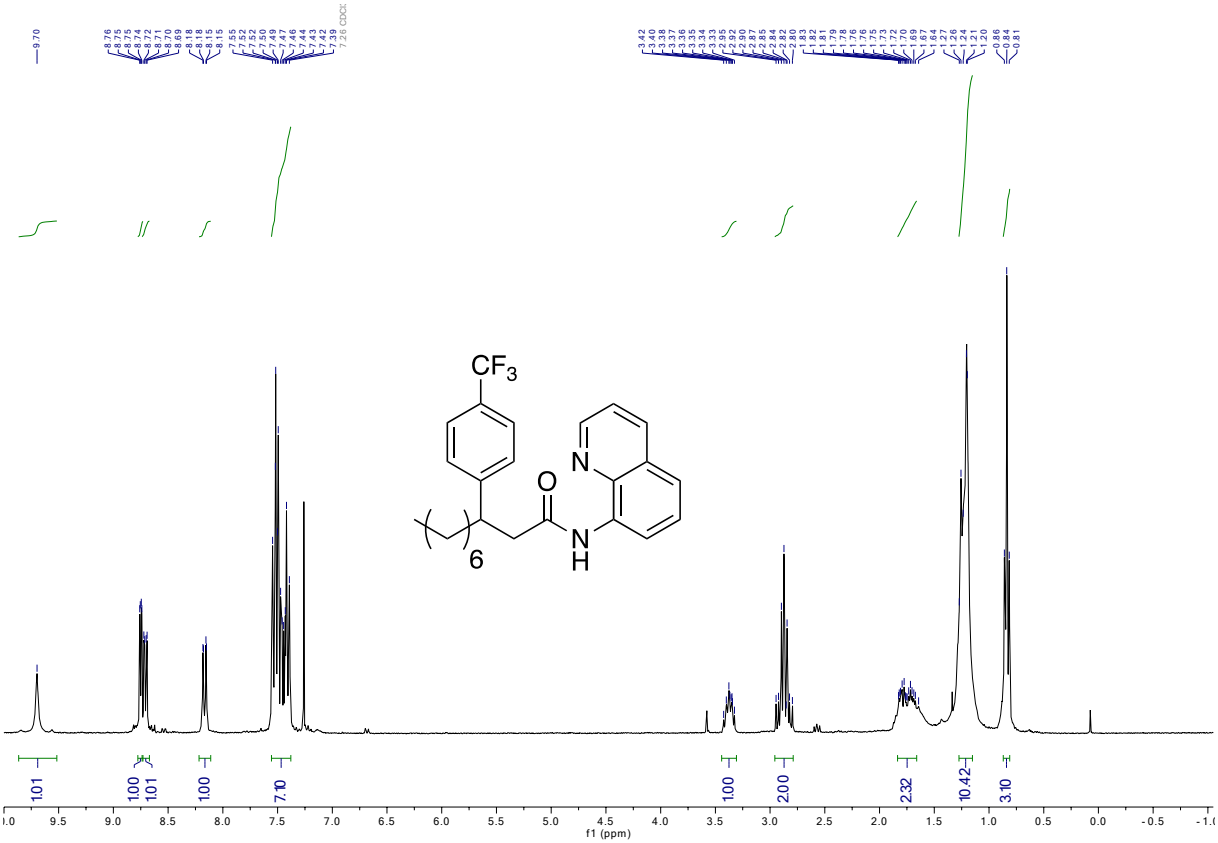
^{19}F NMR: (282 MHz, $CDCl_3$) of **3f**



$^{13}C\{^{1}H\}$ NMR: (101 MHz, $CDCl_3$) of **3f**

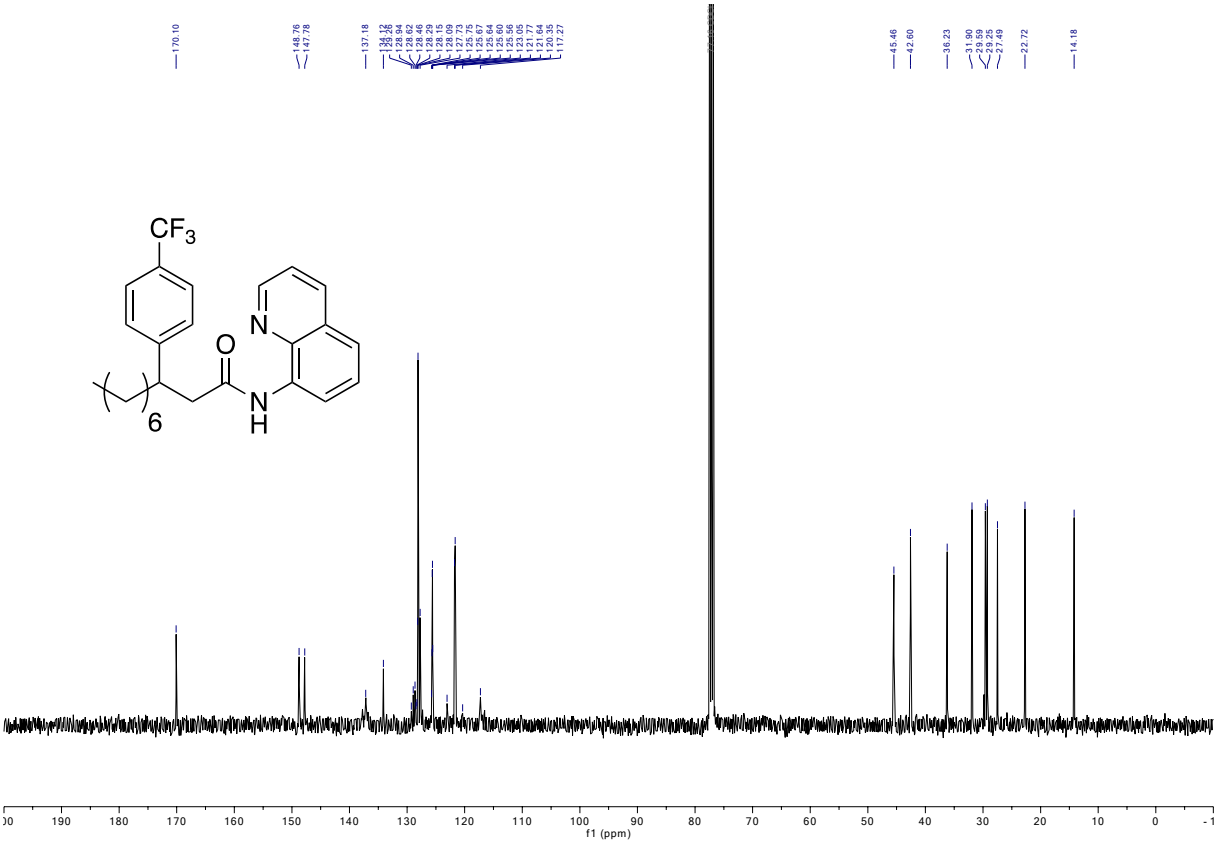


^{1}H NMR: (300 MHz, $CDCl_3$) of **3g**

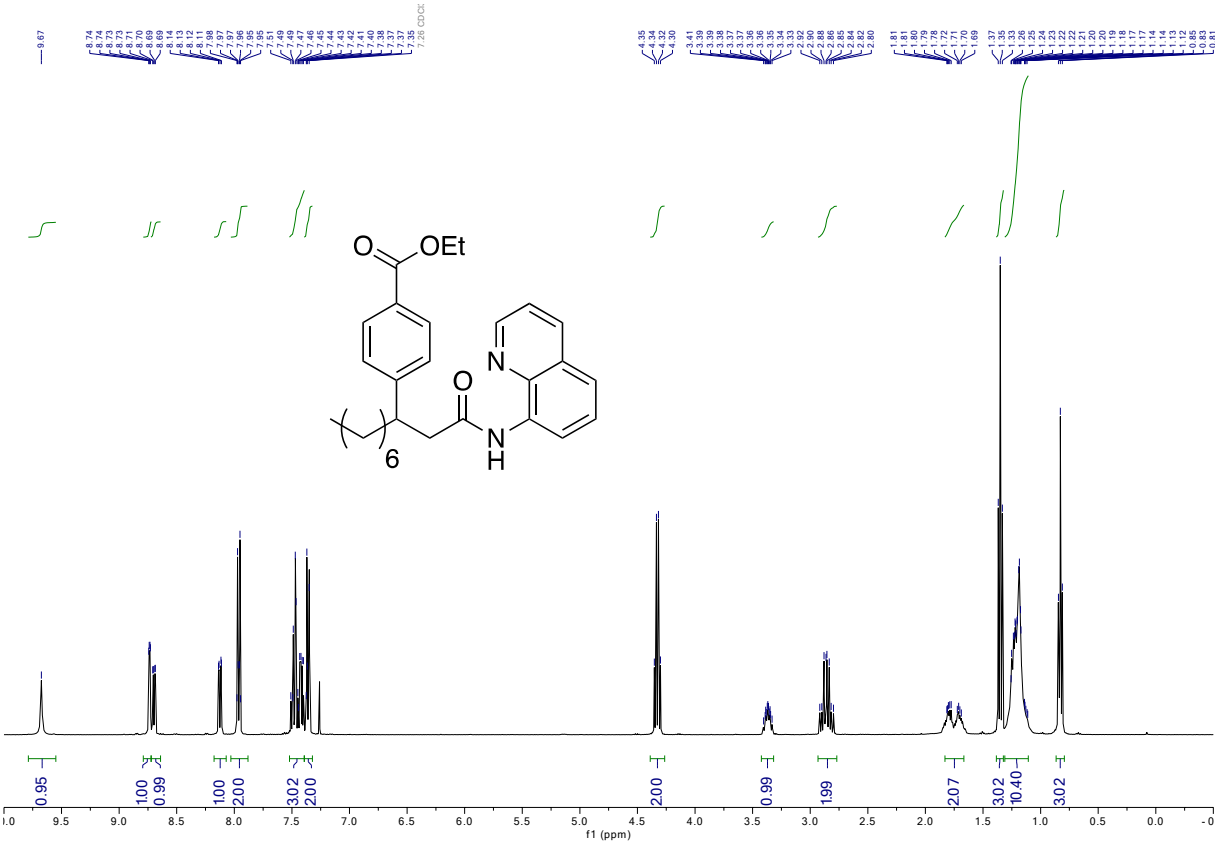


^{19}F NMR: (282 MHz, $CDCl_3$) of **3g**

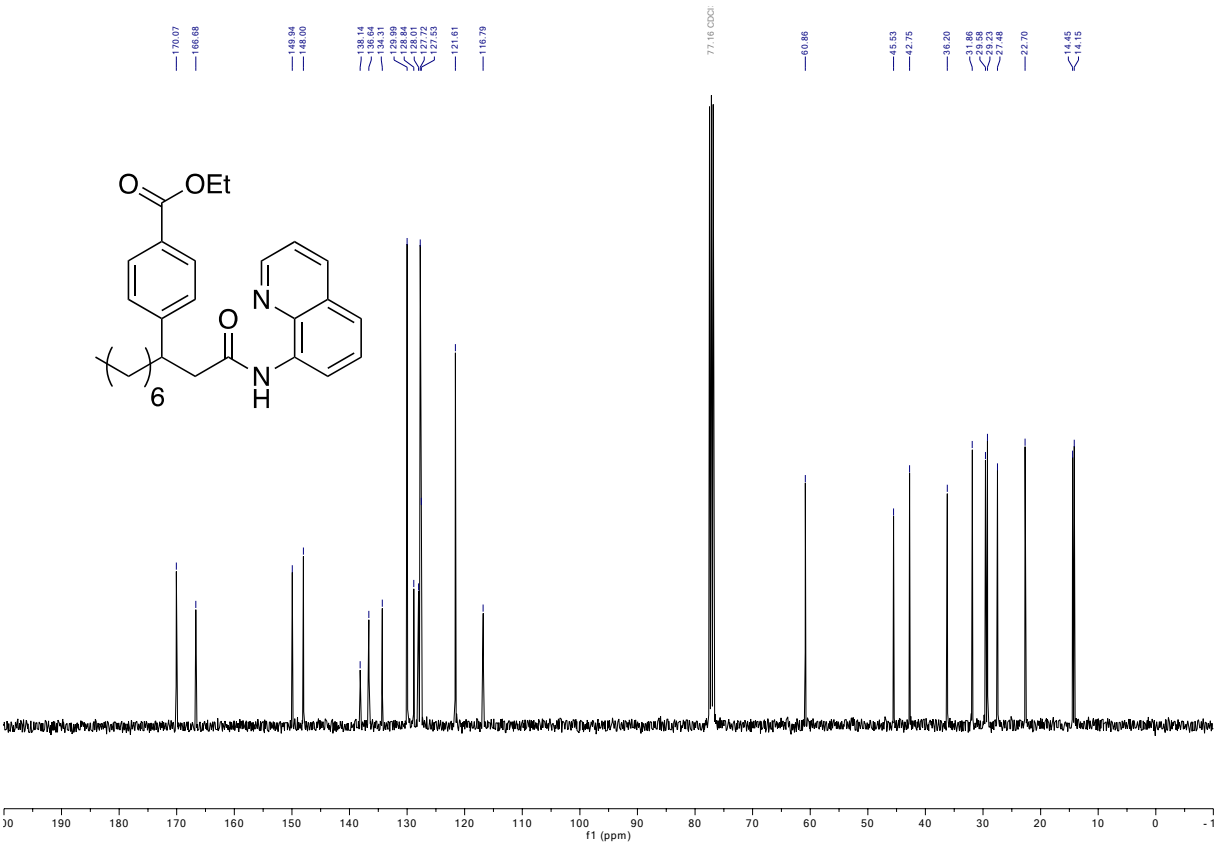
$^{13}C\{^1H\}$ NMR: (101 MHz, $CDCl_3$) of **3g**



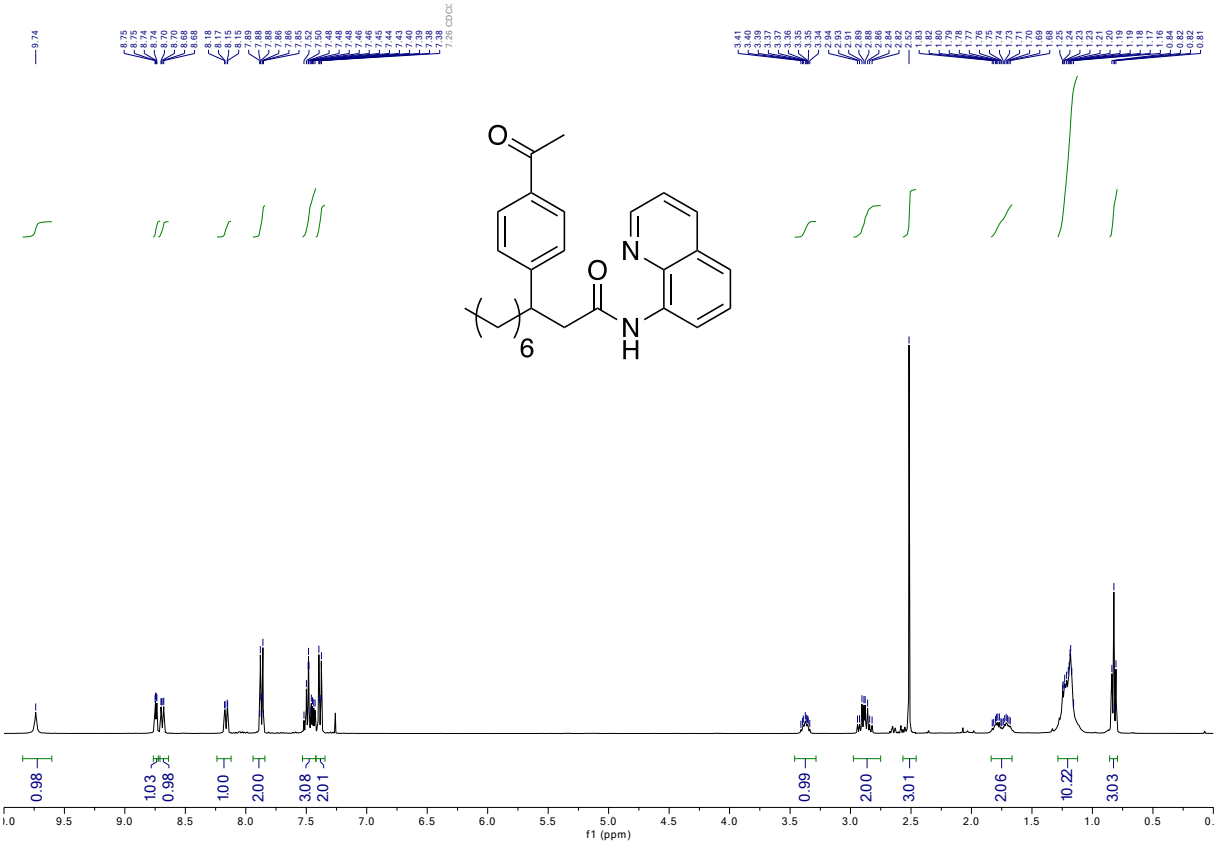
^{1}H NMR: (400 MHz, $CDCl_3$) of **3h**



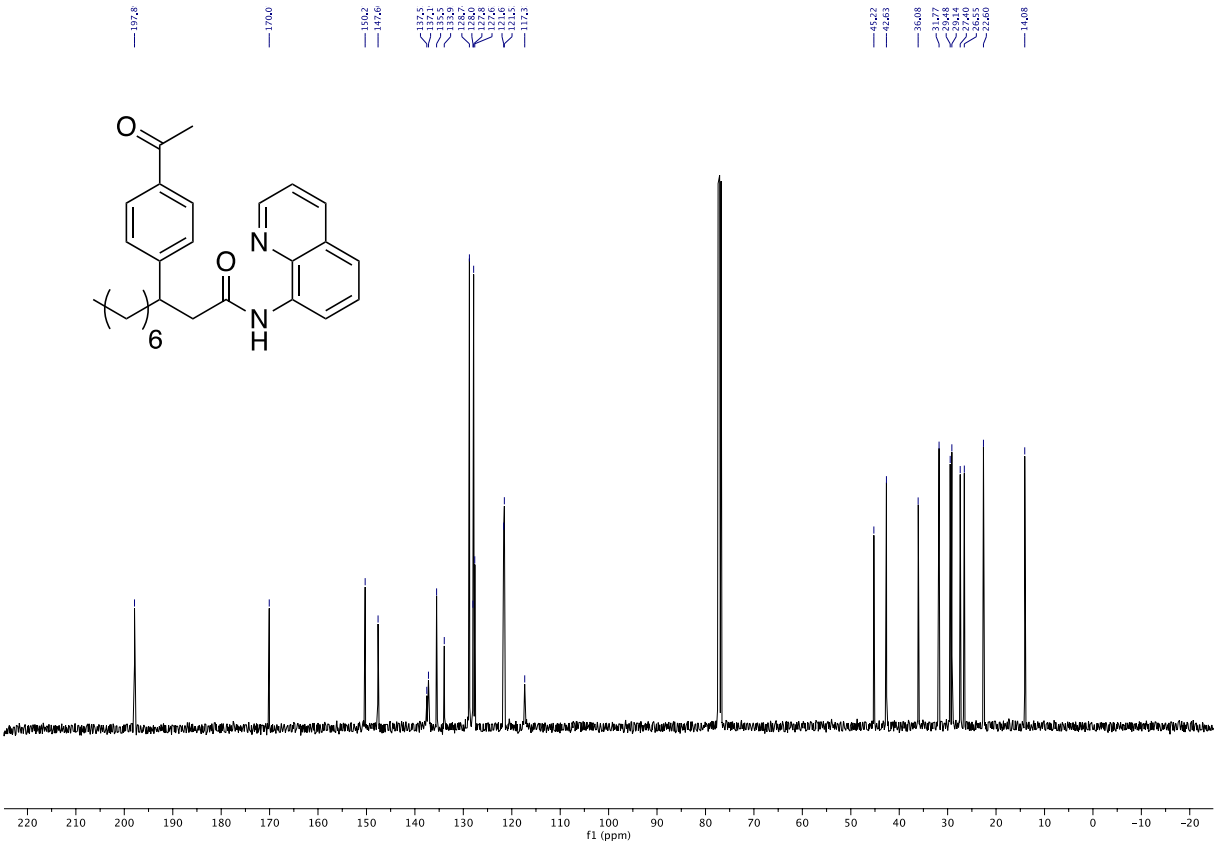
^{13}C{^{1}H} NMR: (101 MHz, $CDCl_3$) of **3h**



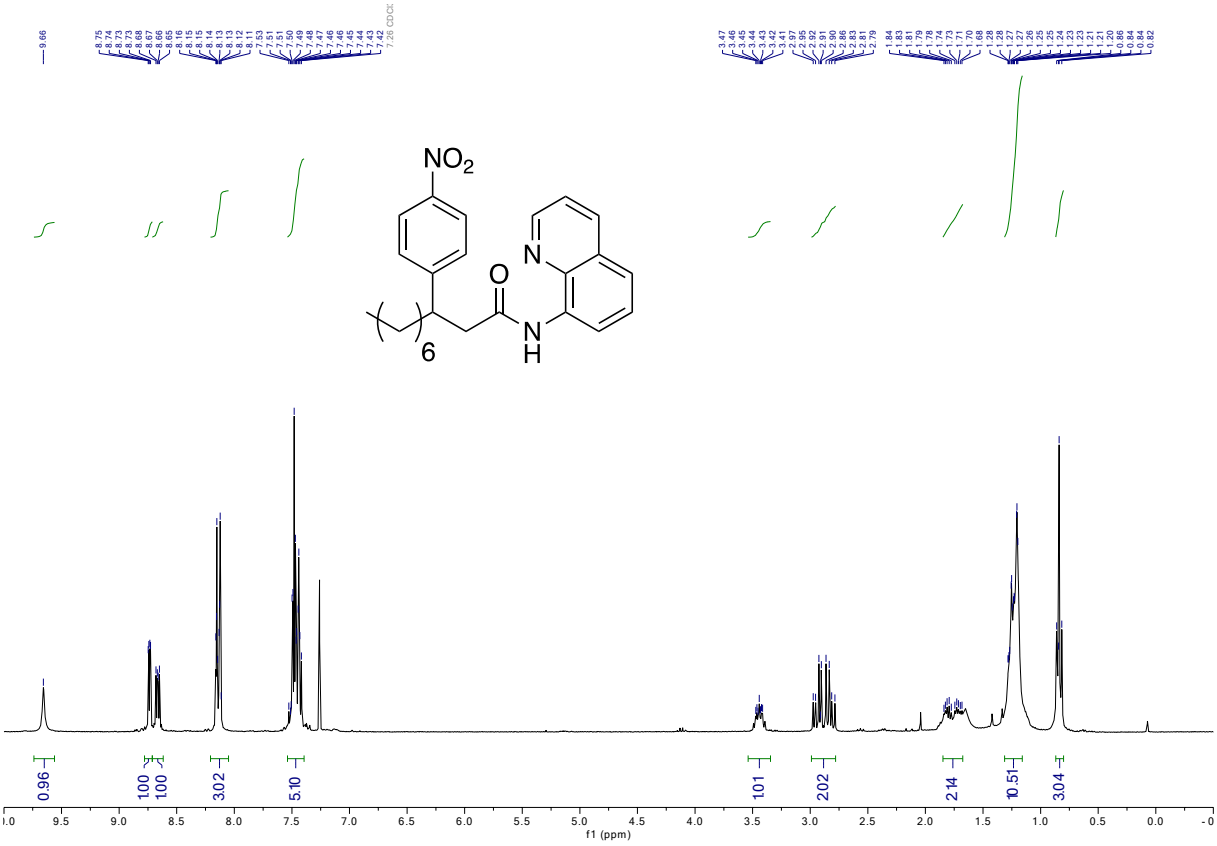
^{1}H NMR: (300 MHz, $CDCl_3$) of **3i**



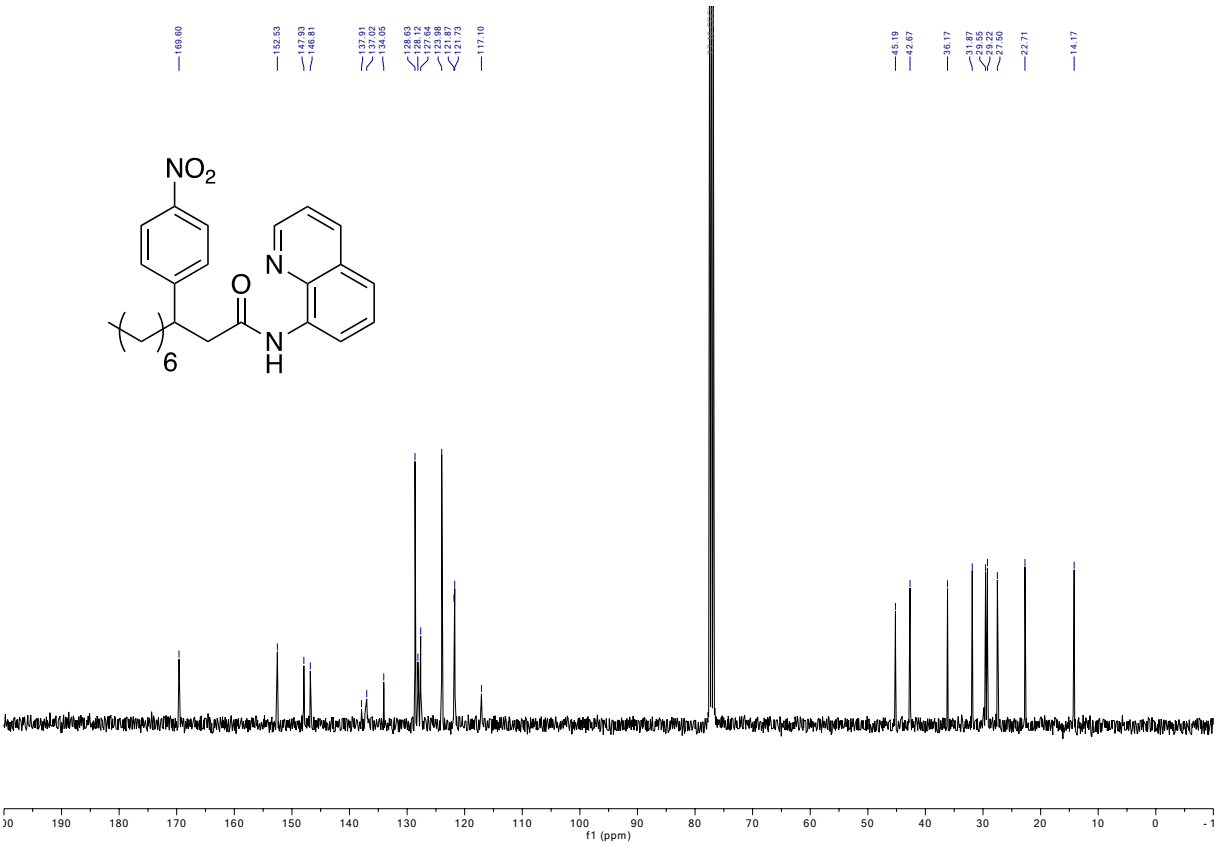
^{13}C{^{1}H} NMR: (101 MHz, $CDCl_3$) of **3i**



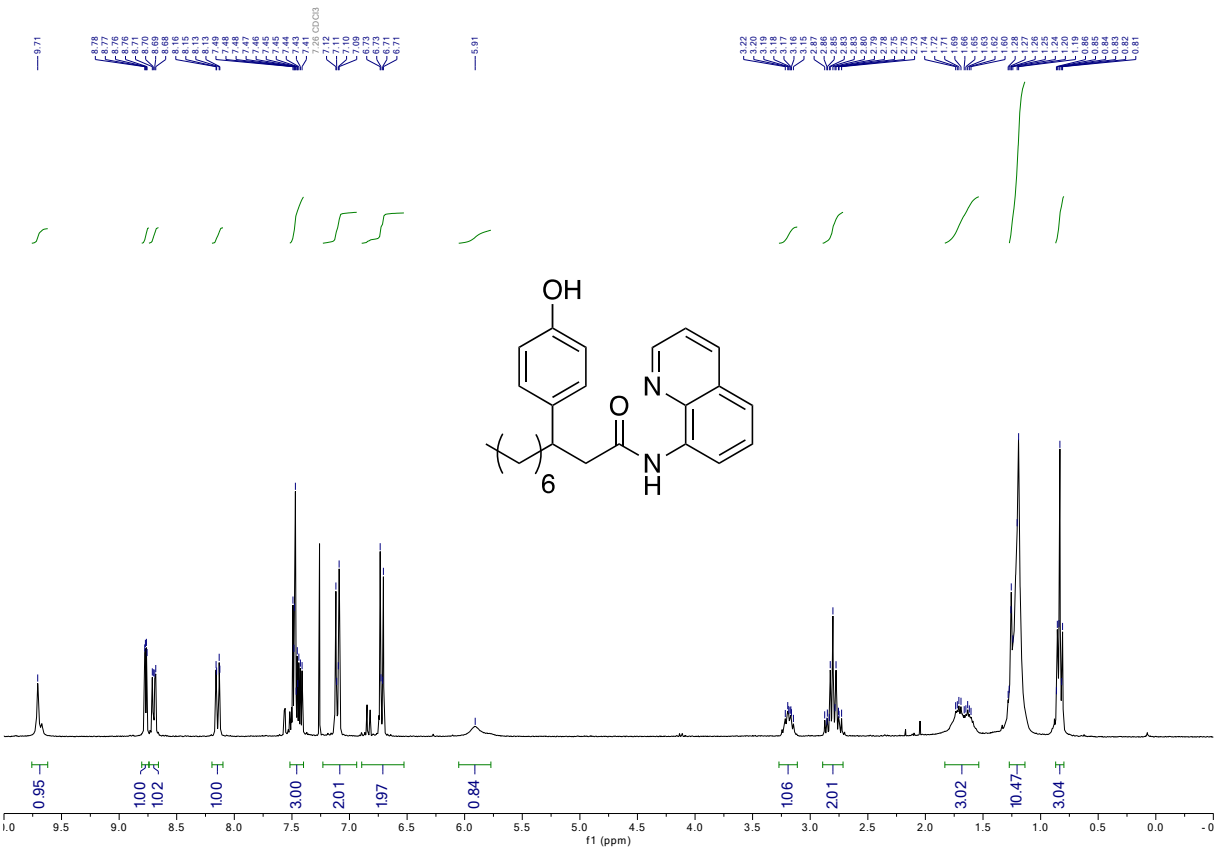
^{1}H NMR: (300 MHz, $CDCl_3$) of **3j**



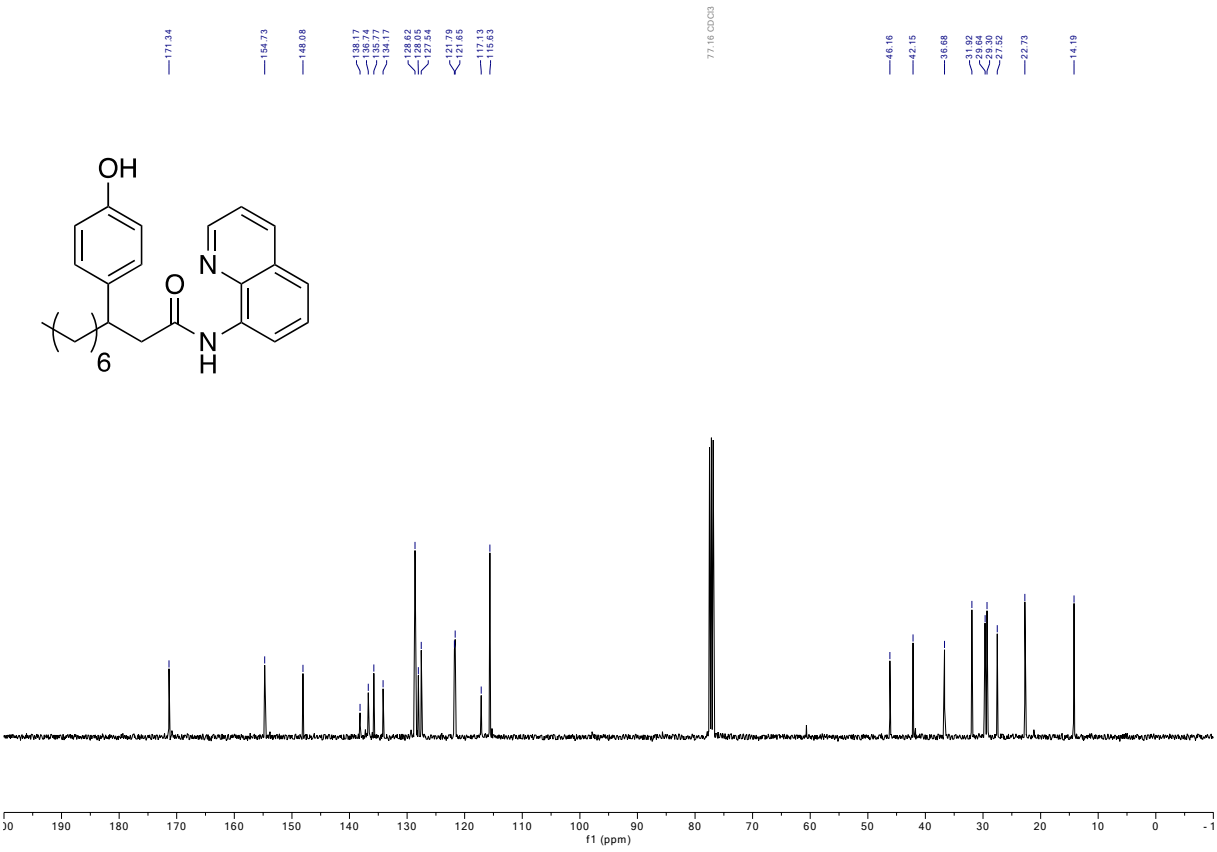
^{13}C{^{1}H} NMR: (101 MHz, $CDCl_3$) of **3j**



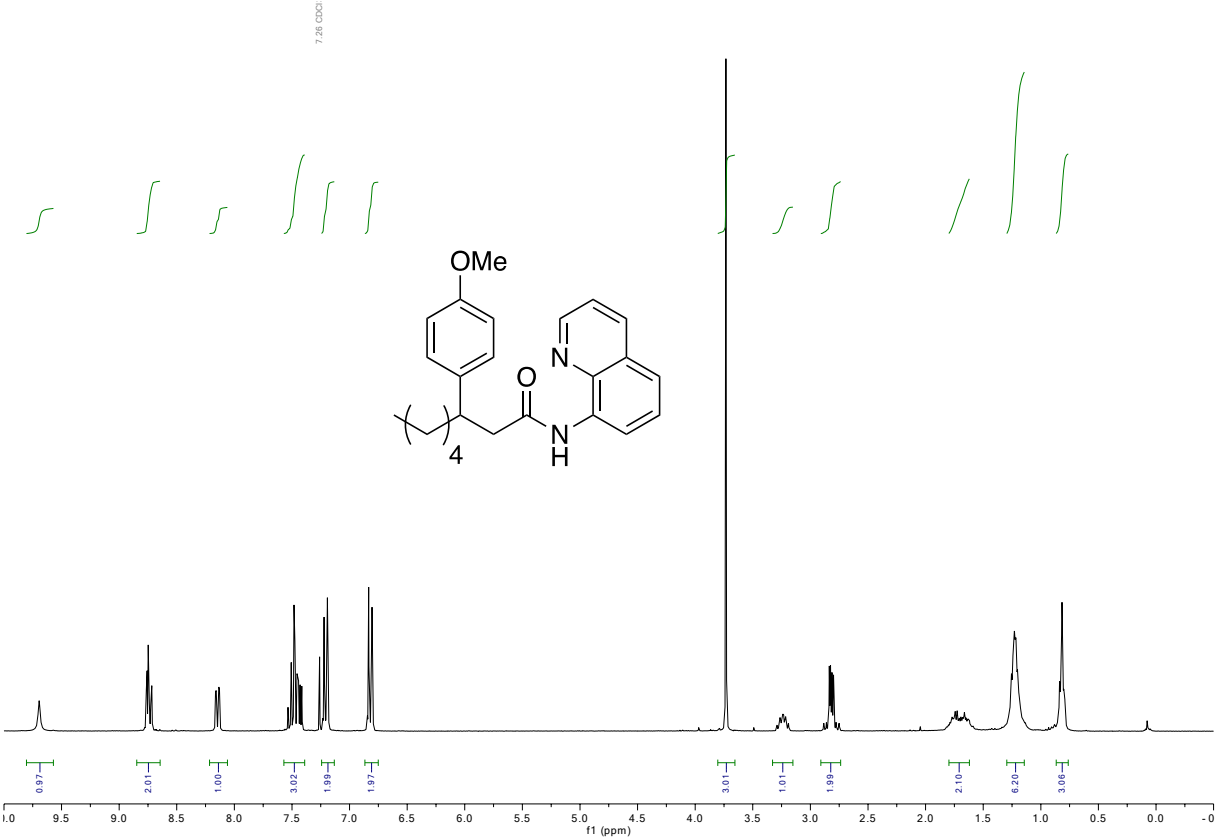
^{1}H NMR: (400 MHz, $CDCl_3$) of **3k**



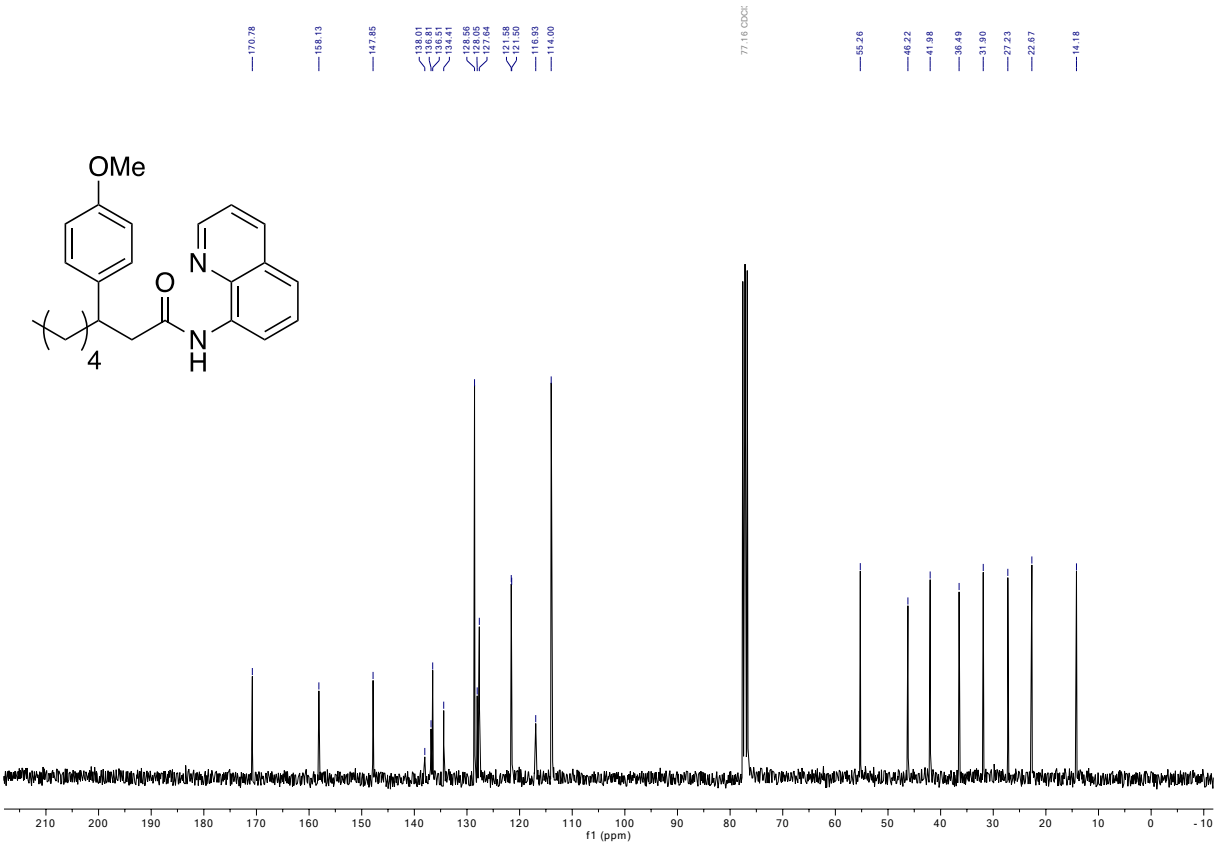
$^{13}C\{^{1}H\}$ NMR: (101 MHz, $CDCl_3$) of **3k**


171.34
154.73
148.08
138.17
136.74
135.77
134.17
128.62
129.65
127.54
121.79
121.65
117.13
115.63
77.16 CDCl3
46.16
42.15
36.68
31.92
29.64
29.30
27.52
22.73
14.19
OH
O
N
H
6
f1 (ppm)

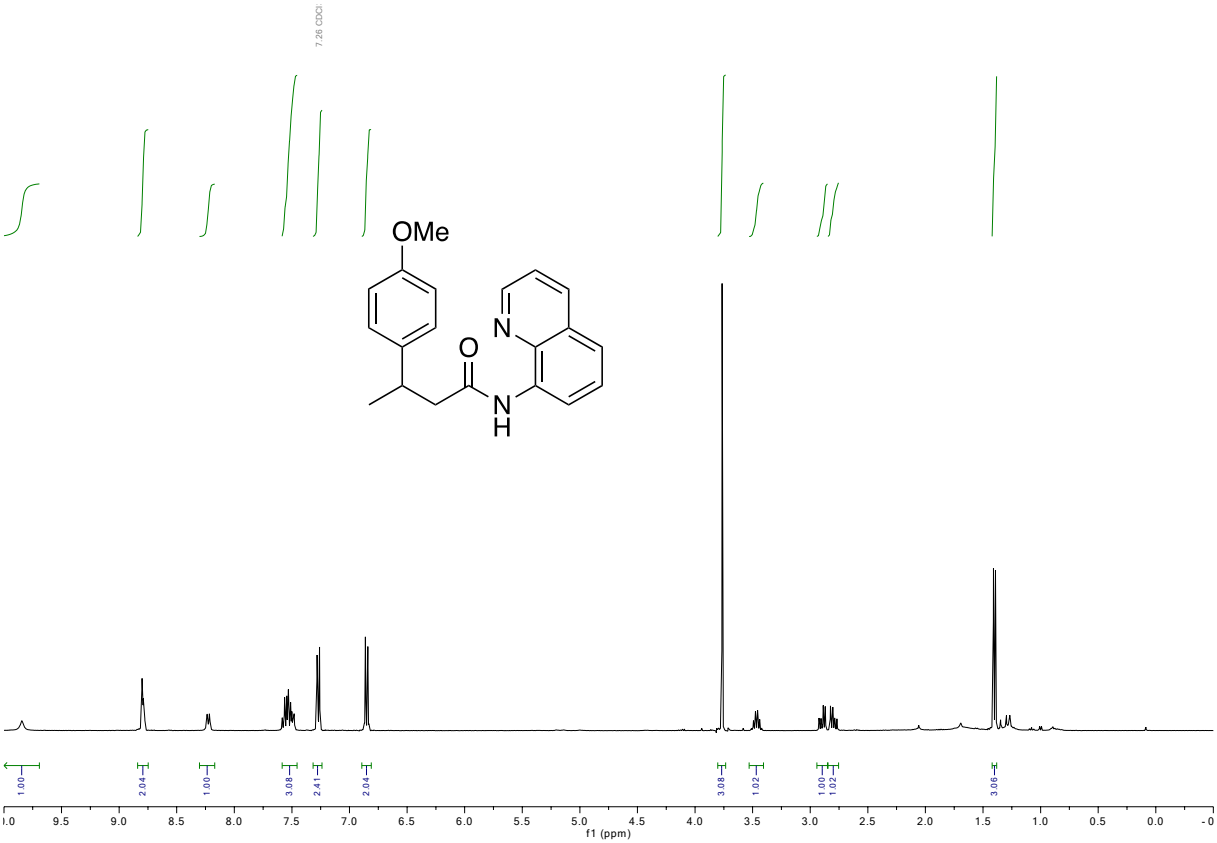
^{1}H NMR: (300 MHz, $CDCl_3$) of **4a**



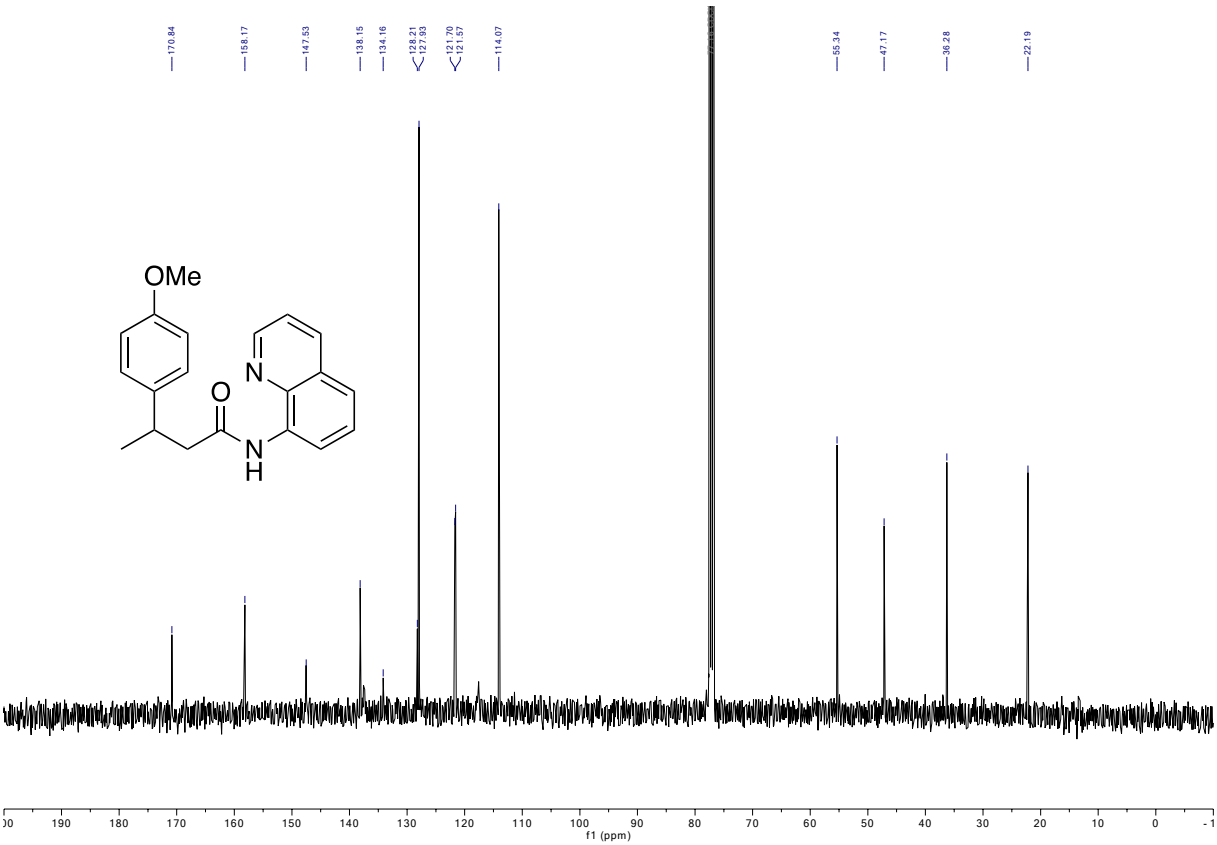
^{13}C{^{1}H} NMR: (75 MHz, $CDCl_3$) of **4a**



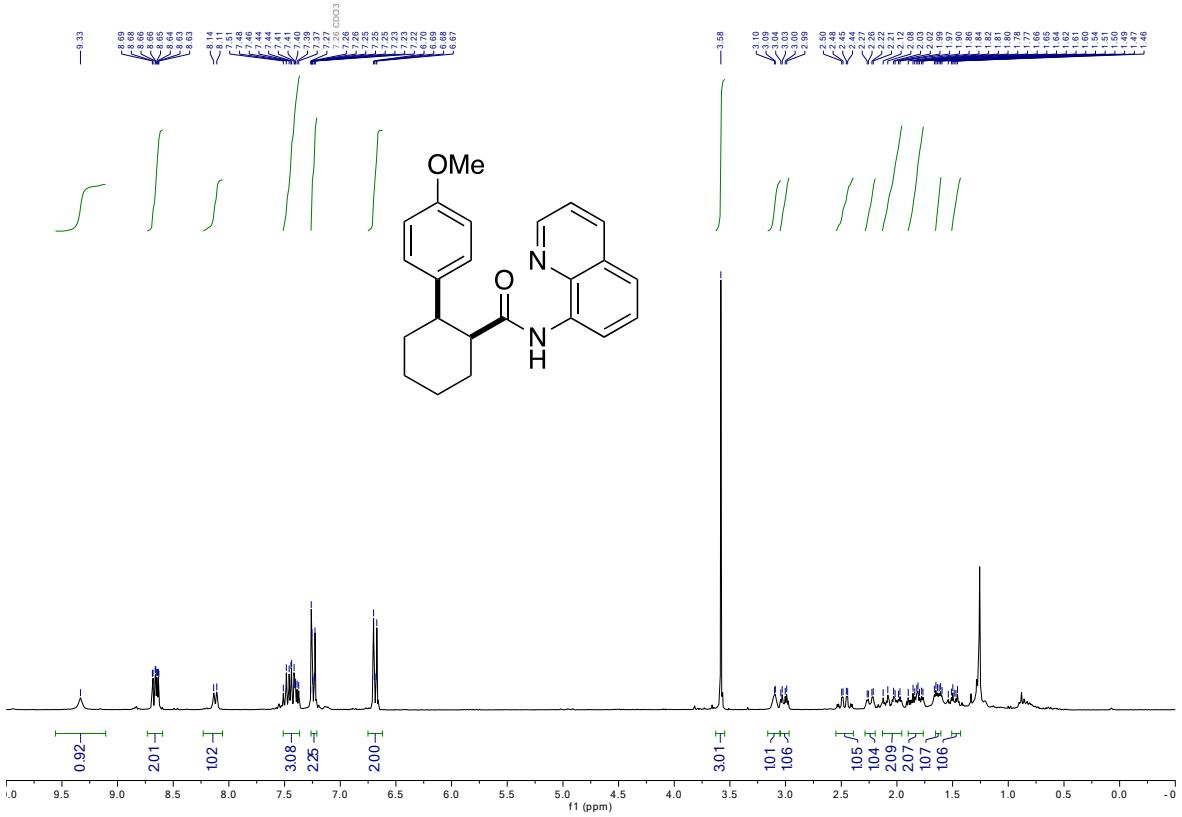
^{1}H NMR: (400 MHz, $CDCl_3$) of **4b**



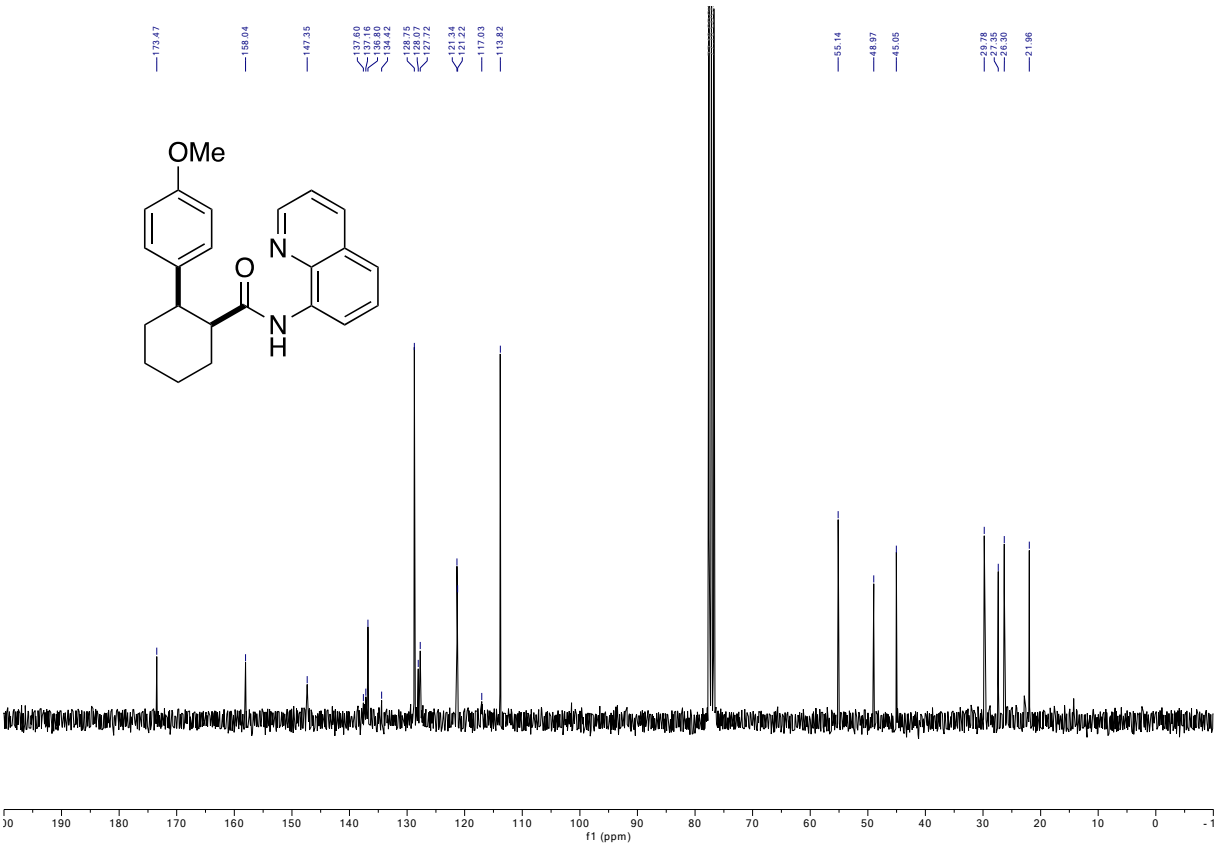
^{13}C{^{1}H} NMR: (101 MHz, $CDCl_3$) of **4b**



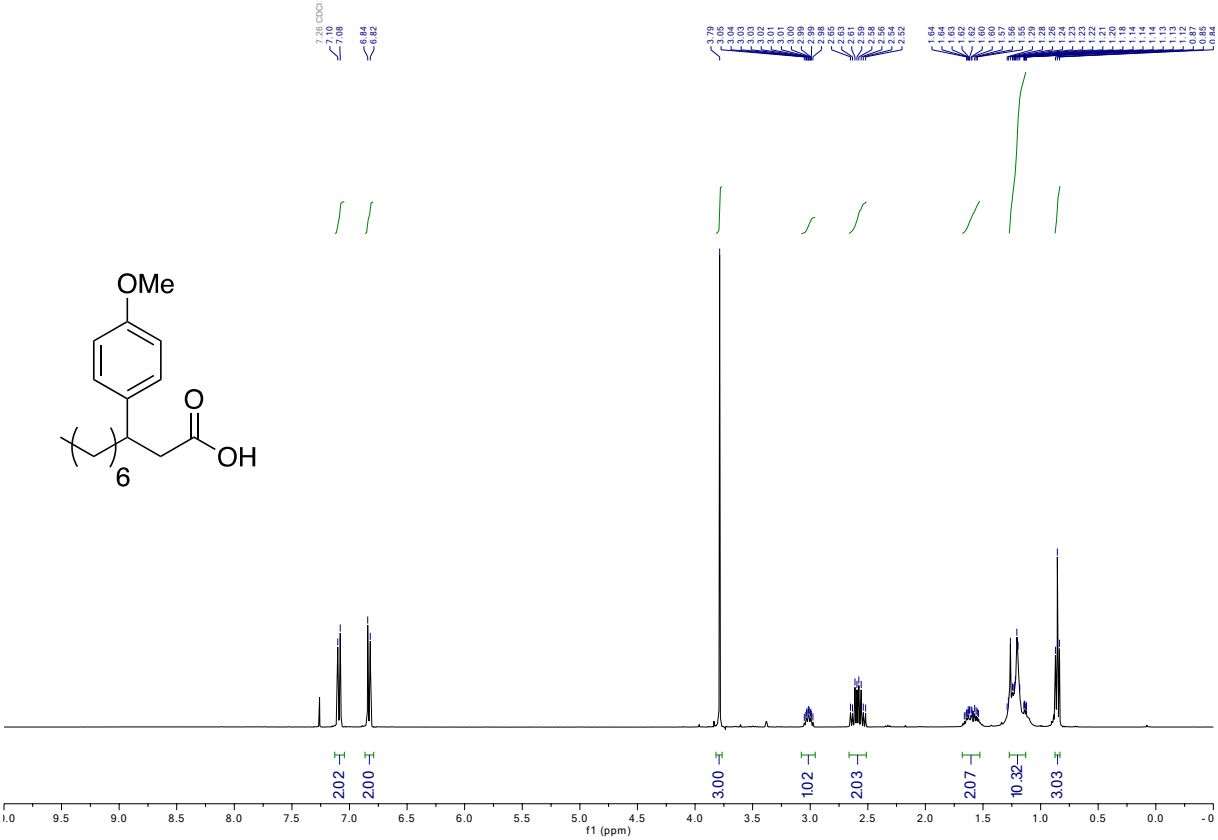
^{1}H NMR: (300 MHz, $CDCl_3$) of **4c**



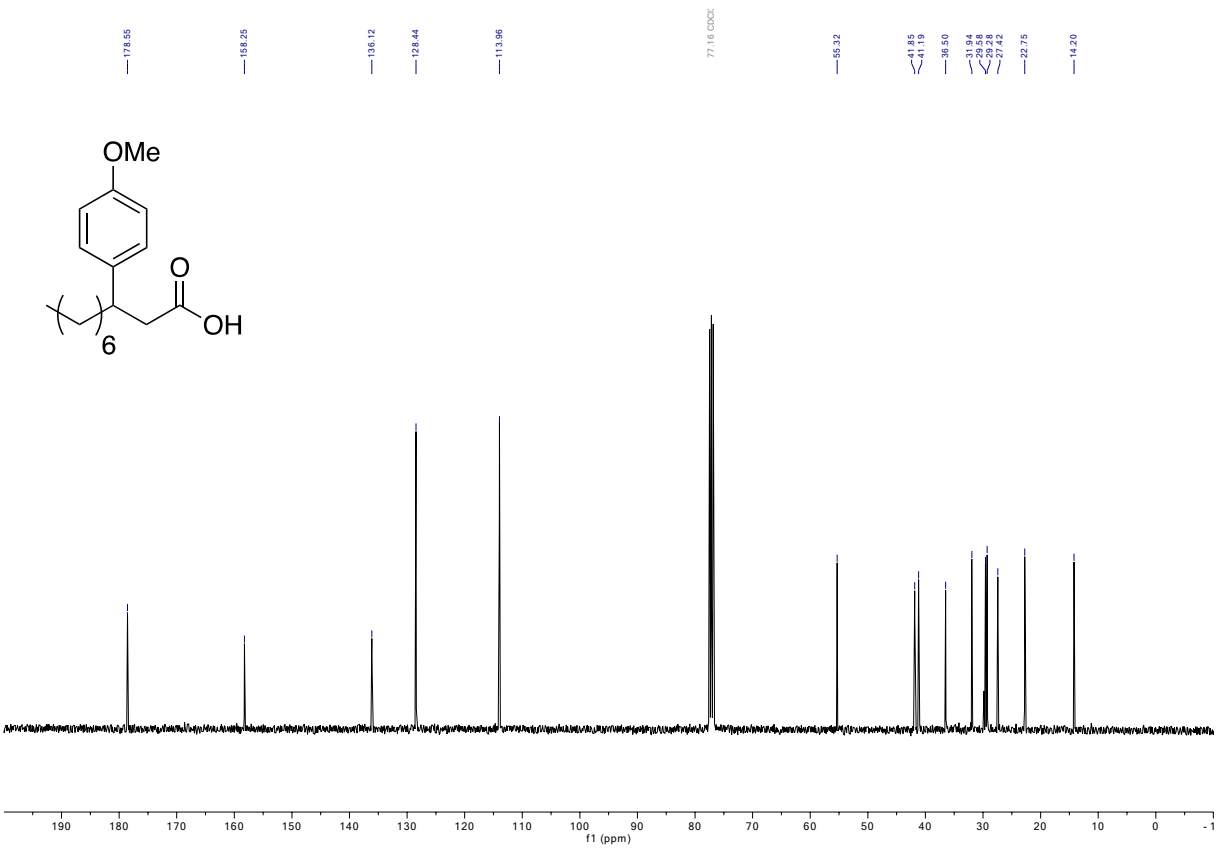
$^{13}C\{^{1}H\}$ NMR: (101 MHz, $CDCl_3$) of **4c**



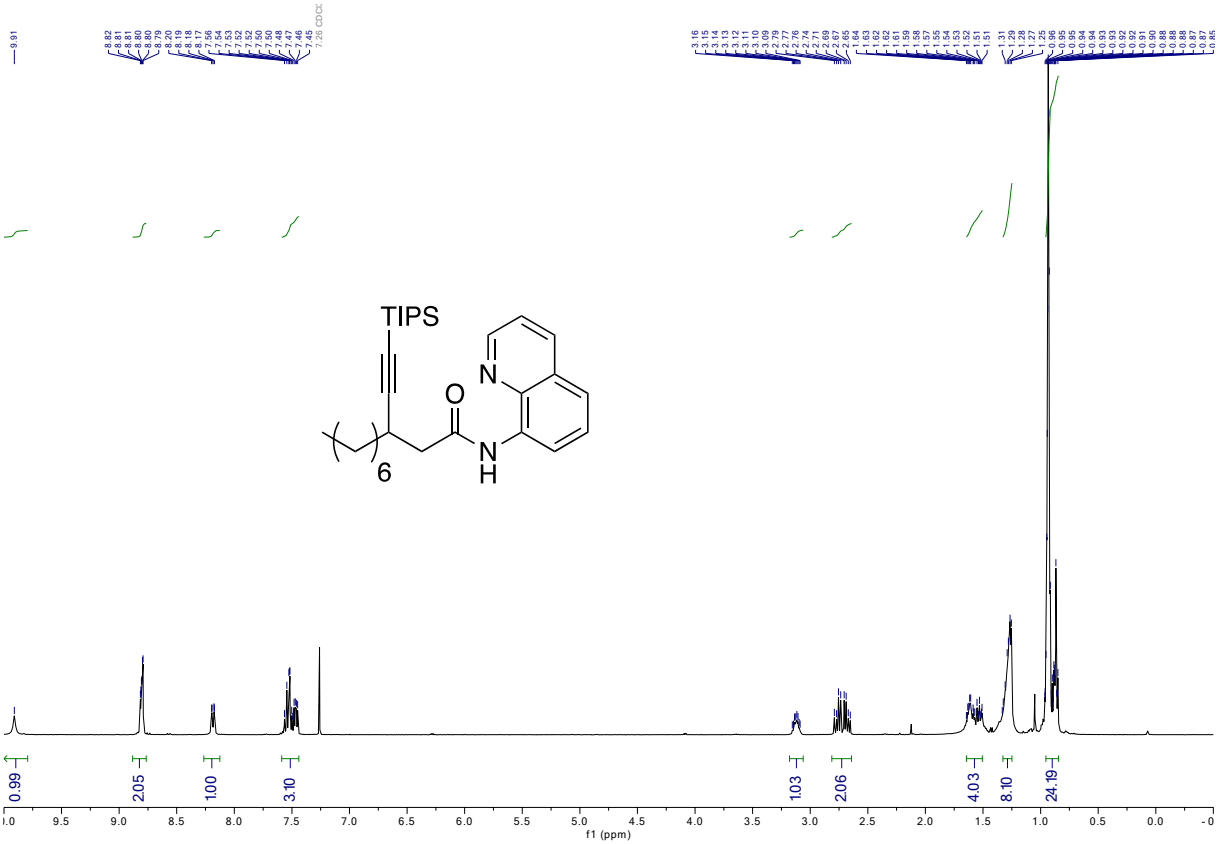
^{1}H NMR: (400 MHz, $CDCl_3$) of **5a**



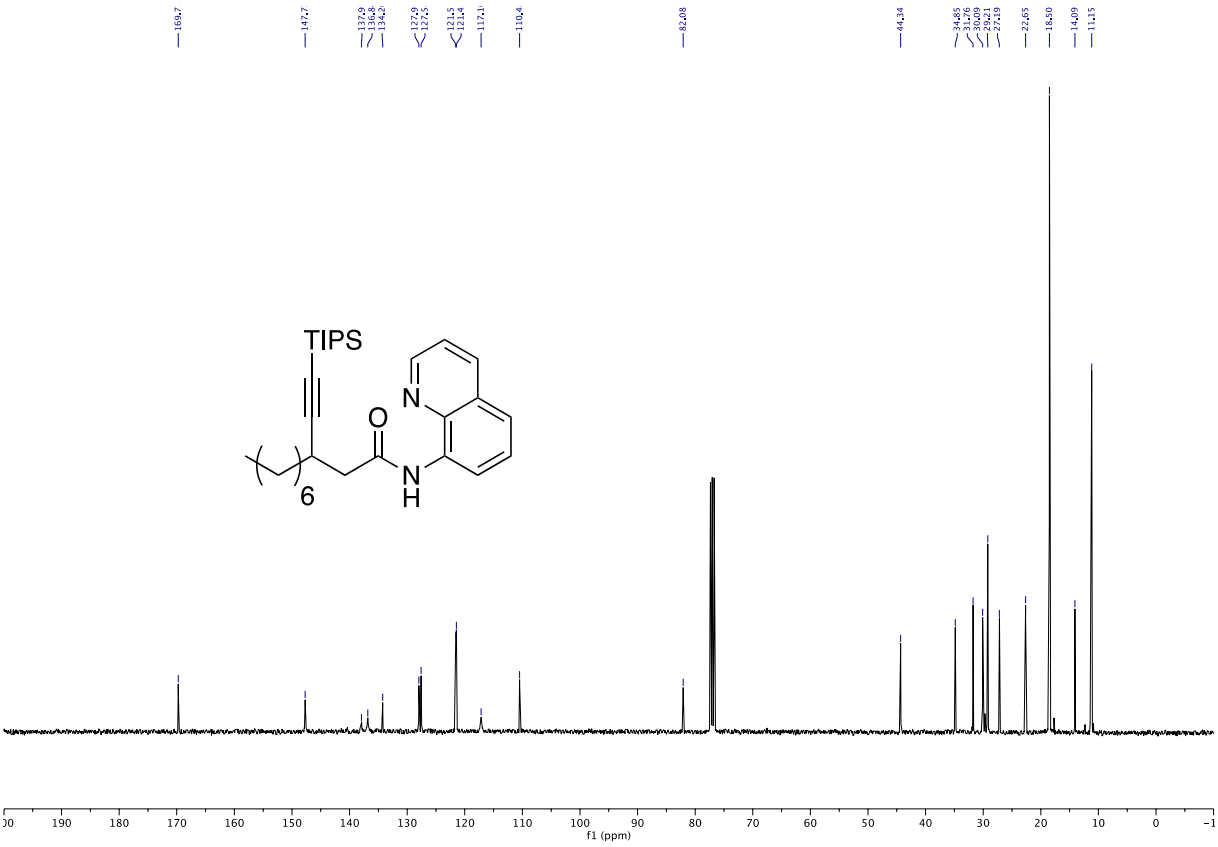
^{13}C{^{1}H} NMR: (101 MHz, $CDCl_3$) of **5a**



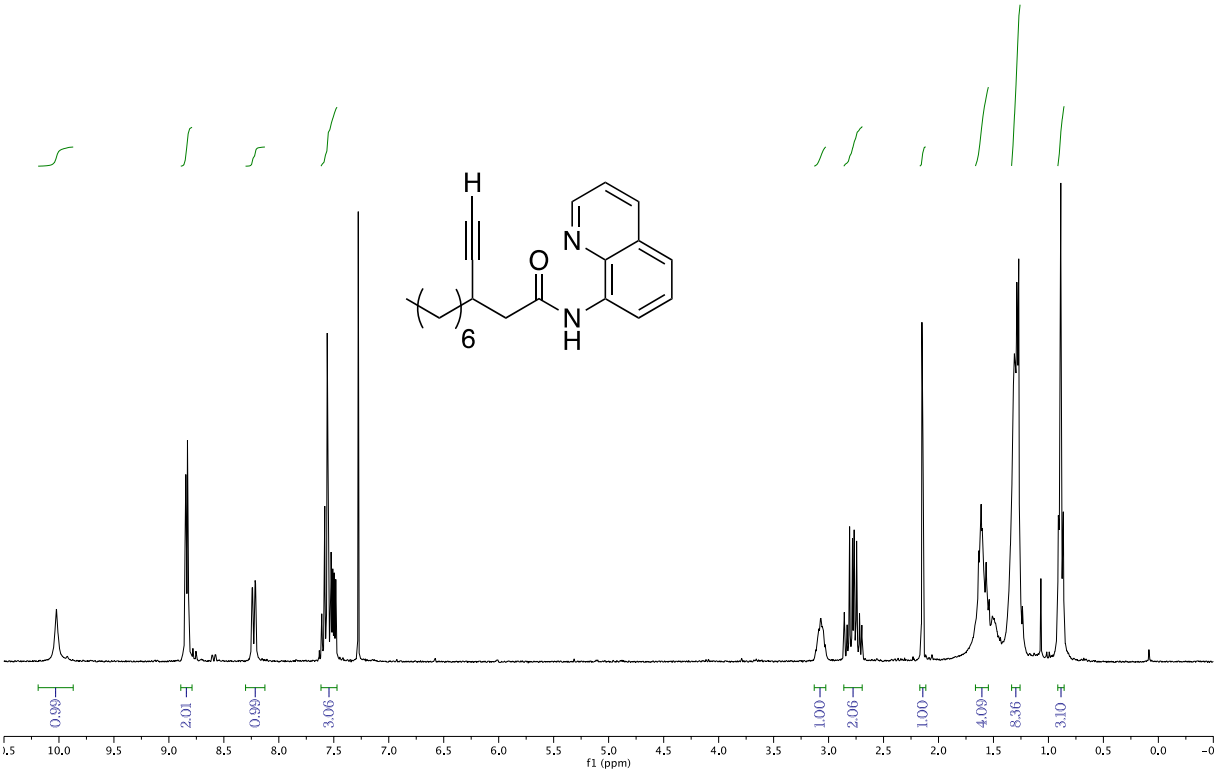
^{1}H NMR: (300 MHz, $CDCl_3$) of **6**



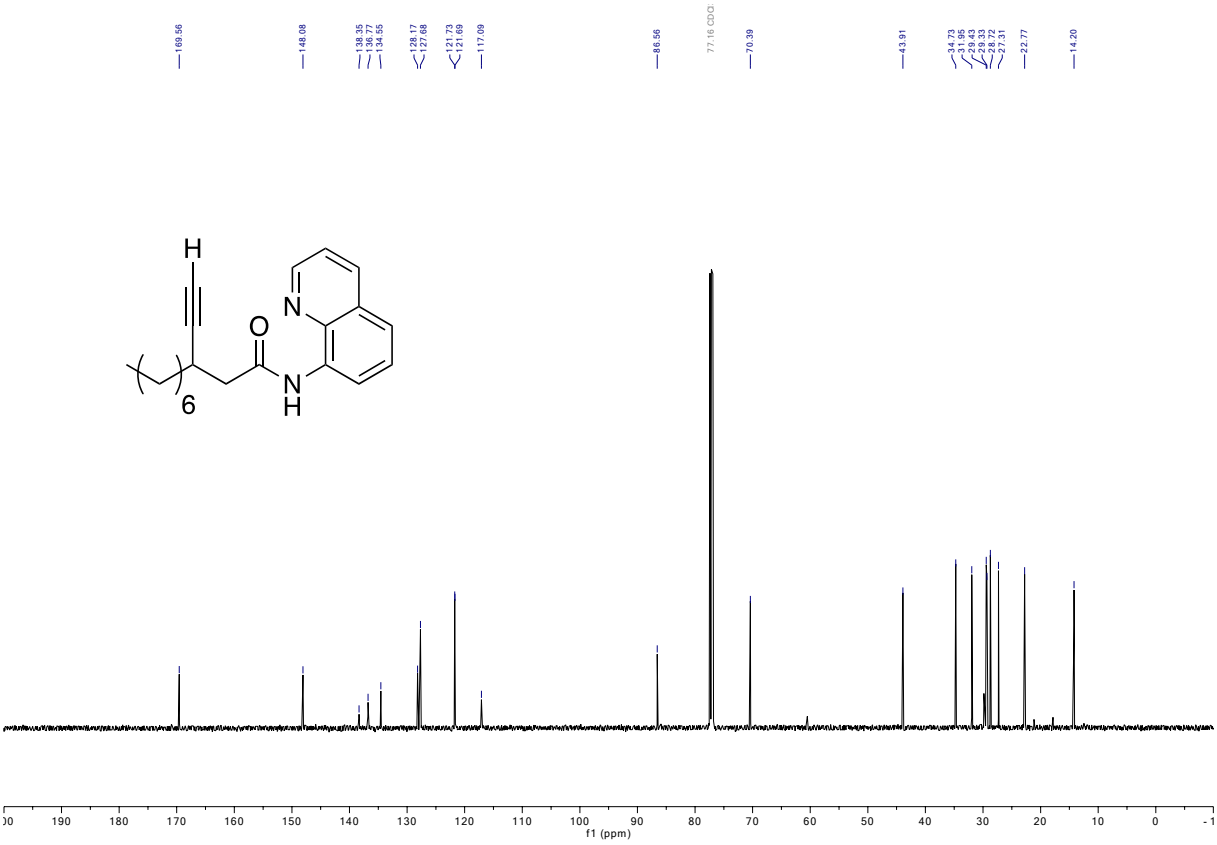
^{13}C{^{1}H} NMR: (101 MHz, $CDCl_3$) of **6**



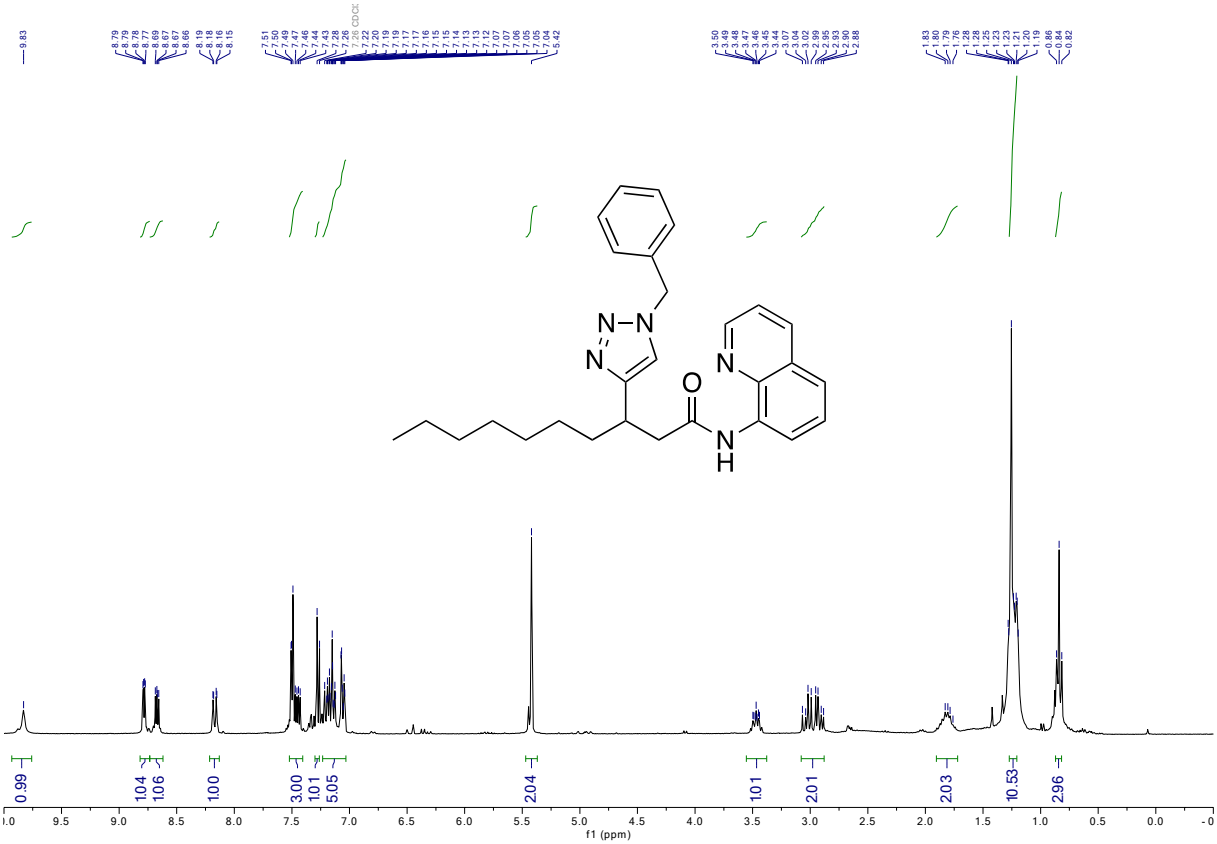
^{1}H NMR: (500 MHz, $CDCl_3$) of **7**



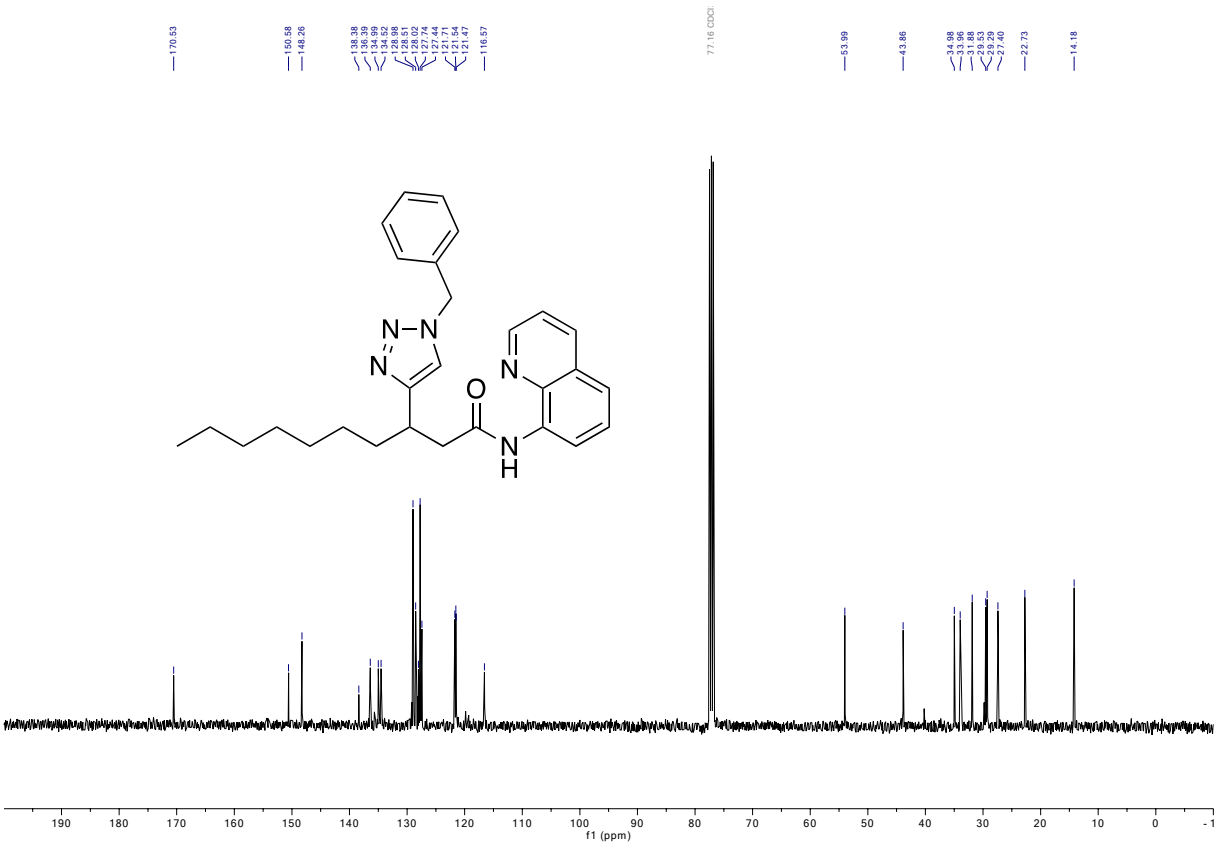
^{13}C{^{1}H} NMR: (126 MHz, $CDCl_3$) of **7**



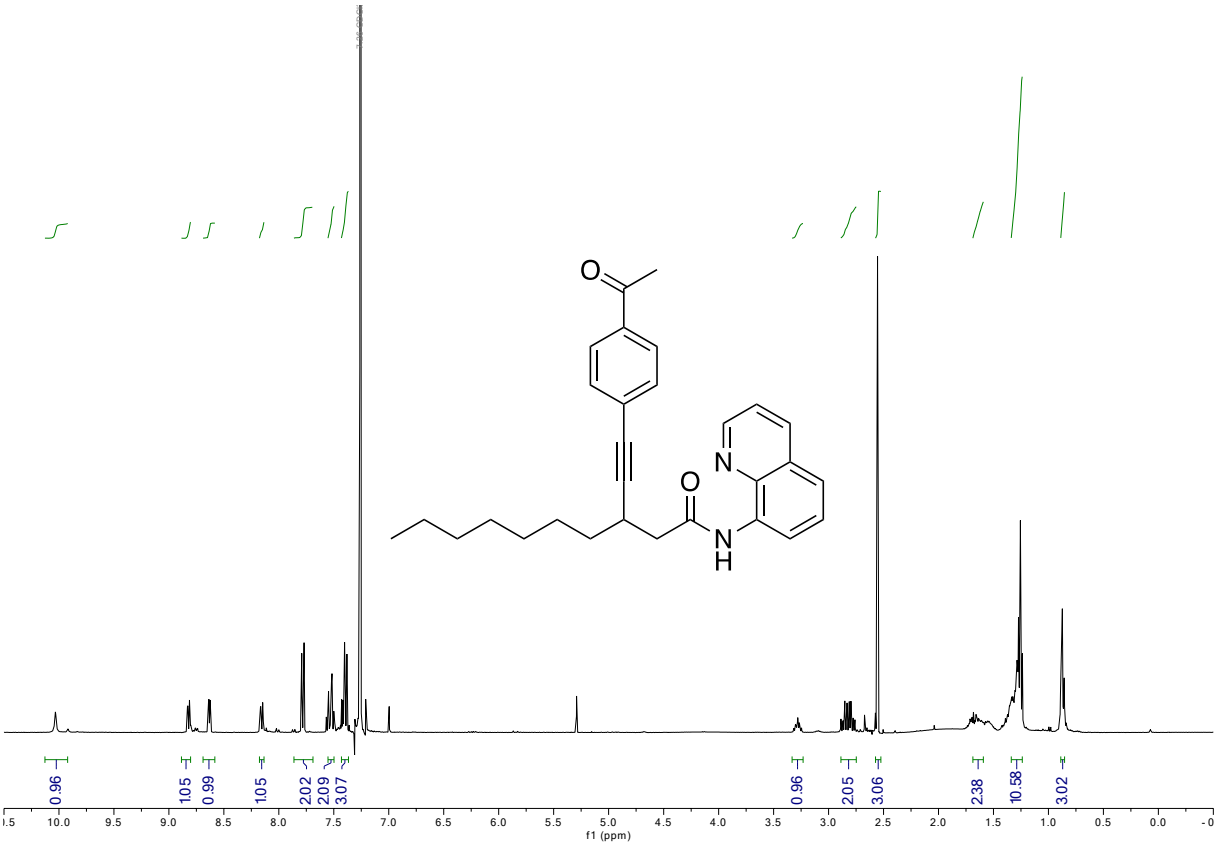
^{1}H NMR: (300 MHz, $CDCl_3$) of **8**



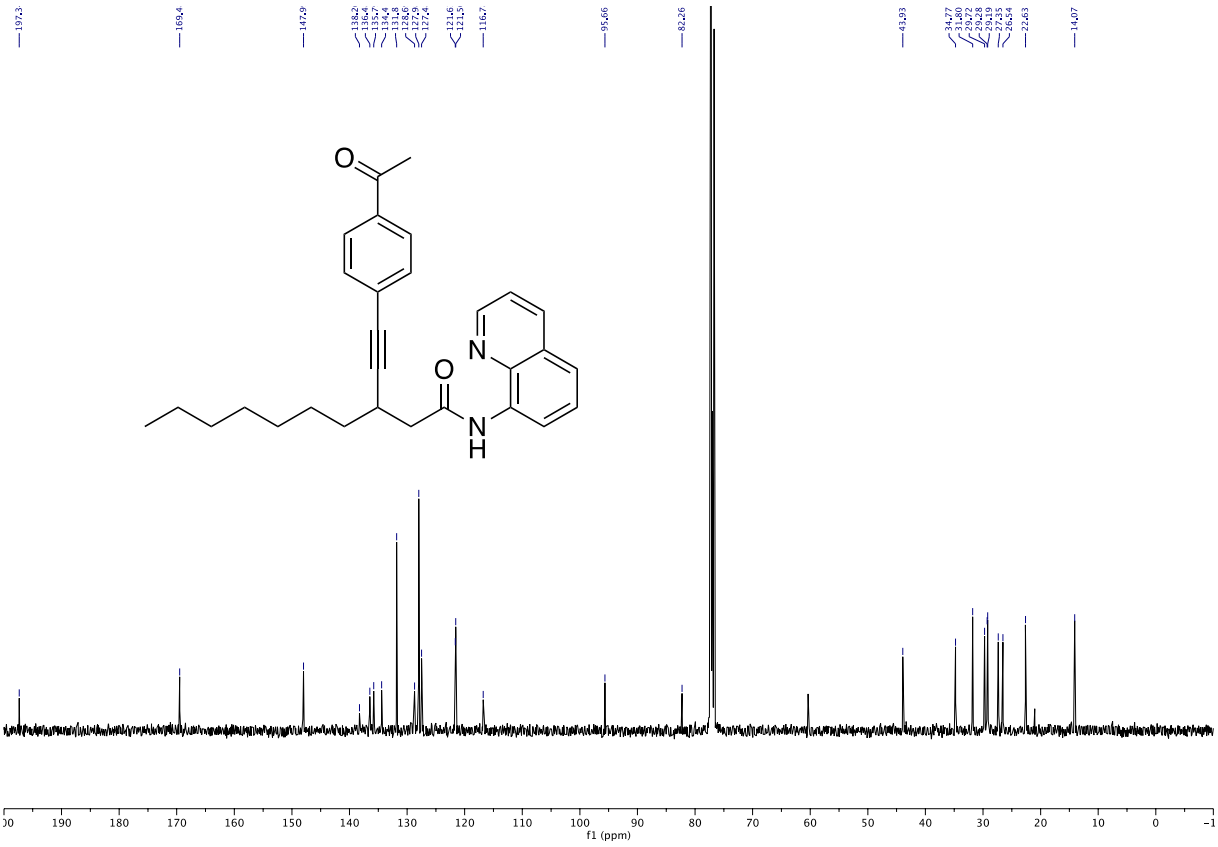
$^{13}C\{^{1}H\}$ NMR: (101 MHz, $CDCl_3$) of **8**



^{1}H NMR: (400 MHz, $CDCl_3$) of **9**



$^{13}C\{^{1}H\}$ NMR: (101 MHz, $CDCl_3$) of **9**



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