Electronic Supplementary Information

Copper(I)-Catalyzed Tandem Synthesis of 2-Acylquinolines from 2-Ethynylanilines and Glyoxals

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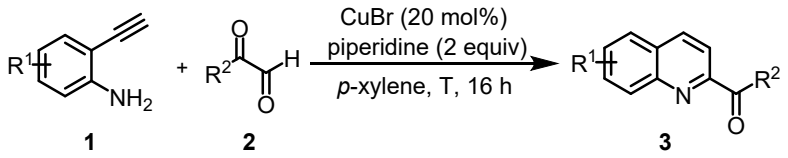
1. General Information

General. Unless otherwise noted, all reactions were carried out in a flame-dried, sealed Schlenk reaction tube under an atmosphere of nitrogen with magnetic stirring. Analytical thin-layer chromatography (TLC) was performed on glass plates coated with 0.25 mm 230-400 mesh silica gel containing a fluorescent indicator. Visualization was accomplished by exposure to a UV lamp. All the products in this article are compatible with standard silica gel chromatography. Column chromatography was performed on silica gel (300-400 mesh) using standard methods.

Structural Analysis. ^{1}H NMR and proton decoupled ^{13}C NMR spectra were recorded on Bruker Avance 500 MHz spectrometers at ambient temperature. NMR standards were used as follows: ^{1}H NMR: δ = 7.26 ppm ($CDCl_3$). ^{13}C NMR: δ = 77.16 ppm ($CDCl_3$). All ^{13}C NMR signals are singlets unless noted otherwise. IR spectra were recorded on a Bruker Alpha FT-IR spectrophotometer. High-resolution mass spectra were recorded on a Thermo Fisher Scientific Ultimate 3000-Q-Exactive instrument.

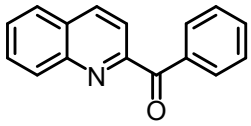
Materials. Solvents were distilled under nitrogen from calcium hydride or sodium/benzophenone. Reagents from commercial suppliers (*J&K*, Energy, Sigma-Aldrich, Alfa Aesar, Acros Organics, Strem Chemicals, TCI, Bidepharm) were used without further purification.

2. Synthesis and Characterization of 2-Acylquinolines



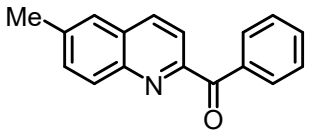
General procedure: A pre-dried 10 mL Schlenk tube was charged with *o*-ethynylanilines **1** (0.2 mmol, 1.0 eq.), glyoxals **2** (0.3 mmol, 1.5 eq.), piperidine (0.4 mmol, 2.0 eq.) and CuBr (0.04 mmol, 5.8 mg, 20 mol%) under an atmosphere of N_2. Dried *p*-xylene (0.8 mL, 0.25 M) was added via syringe in sequence. The reaction mixture was stirred at the indicated temperature for 16 h under an atmosphere of N_2. After cooling to room temperature, the mixture was directly transferred to a column and purified by flash chromatography on silica gel using PE/EA to give the analytical pure products **3**.

Characterization data:



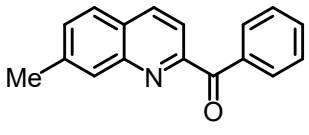
3aa

Phenyl(quinolin-2-yl)methanone (3aa), white solid (35.0 mg, 75% yield). PE/EA = 40:1, R_f = 0.20. **Reported compound.**[1] **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.35 (d, J = 8.4 Hz, 1H), 8.30-8.16 (m, 3H), 8.11 (d, J = 8.4 Hz, 1H), 7.91 (d, J = 8.0 Hz, 1H), 7.83-7.75 (m, 1H), 7.72-7.59 (m, 2H), 7.52 (t, J = 8.0 Hz, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 193.9, 154.8, 146.9, 137.2, 136.3, 133.2, 131.6, 130.7, 130.2, 129.0, 128.5, 128.3, 127.8, 120.9.



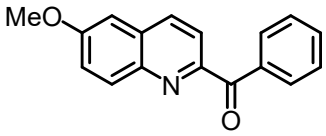
3ab

(6-Methylquinolin-2-yl)(phenyl)methanone (3ab), white solid (35.2 mg, 71% yield). PE/EA = 40:1, R_f = 0.20. **Reported compound.**[2] **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.24 (d, J = 8.0 Hz, 3H), 8.08 (d, J = 8.4 Hz, 1H), 7.66 (s, 1H), 7.64-7.58 (m, 2H), 7.51 (t, J = 7.6 Hz, 2H), 2.58 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 194.0, 154.0, 145.5, 138.9, 136.4, 133.1, 132.6, 131.6, 130.4, 129.1, 128.2, 126.6, 121.0, 21.9.



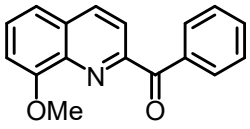
3ac

(7-Methylquinolin-2-yl)(phenyl)methanone (3ac), white solid (32.0 mg, 65% yield). PE/EA = 40:1, R_f = 0.20. **Reported compound.**[2] **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.28 (d, J = 8.4 Hz, 1H), 8.26-8.19 (m, 2H), 8.04 (d, J = 8.4 Hz, 1H), 7.98 (s, 1H), 7.79 (d, J = 8.4 Hz, 1H), 7.62 (t, J = 7.4 Hz, 1H), 7.54-7.45 (m, 3H), 2.58 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 194.1, 154.8, 147.1, 140.6, 136.8, 136.4, 133.1, 131.6, 130.9, 129.6, 128.2, 127.4, 127.1, 120.1, 22.0.



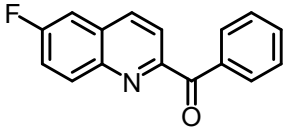
3ad

(6-Methoxyquinolin-2-yl)(phenyl)methanone (3ad), white solid (32.2 mg, 61% yield). PE/EA = 10:1, R_f = 0.20. **Reported compound.**[2] **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.28-8.18 (m, 3H), 8.14-8.05 (m, 2H), 7.61 (t, J = 7.5 Hz, 1H), 7.51 (t, J = 7.5 Hz, 2H), 7.42 (dd, J = 9.2 Hz, 2.7 Hz, 1H), 7.14 (d, J = 2.7 Hz, 1H), 3.98 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 193.8, 159.5, 152.5, 142.9, 136.6, 135.7, 133.0, 132.2, 131.6, 130.5, 128.2, 123.3, 121.5, 105.0, 55.8.



3ae

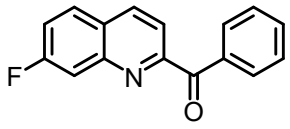
(8-Methoxyquinolin-2-yl)(phenyl)methanone (3ae), white solid (43.6 mg, 83% yield). PE/EA = 10:1, R_f = 0.20. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.42-8.33 (m, 2H), 8.30 (d, J = 8.5 Hz, 1H), 8.13 (d, J = 8.5 Hz, 1H), 7.63-7.55 (m, 2H), 7.50 (t, J = 7.6 Hz, 2H), 7.46 (d, J = 7.8 Hz, 1H), 7.11 (d, J = 7.8 Hz, 1H), 4.06 (s, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 193.2, 156.4, 153.5, 138.8, 137.0, 136.3, 133.1, 132.0, 130.2, 129.0, 128.2, 121.5, 119.4, 108.5, 56.4. **HRMS** (ESI, m/z) Calculated for $C_{17}H_{14}NO_2$ $[M + H]^+$: 264.1019, found: 264.1012. **IR** (film): ν (cm^{-1}) 3068, 2935, 2834, 1655, 1596, 1560, 1500, 1447, 1323, 1257, 1155, 1104, 946, 842, 717, 684, 615.



3af

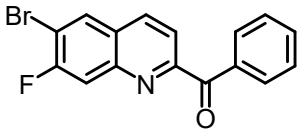
(6-Fluoroquinolin-2-yl)(phenyl)methanone (3af), white solid (36.2 mg, 69% yield). PE/EA = 40:1, R_f = 0.20. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.29 (d, J = 8.5 Hz, 1H), 8.26-8.17 (m, 3H), 8.14 (d, J = 8.5 Hz, 1H), 7.63 (t, J = 7.5 Hz, 1H), 7.60-7.47 (m, 4H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 193.6, 161.8 (d, J = 252.0 Hz), 154.2 (d, J = 3.2 Hz), 143.9, 136.6 (d, J = 5.5 Hz), 136.2, 133.3 (d, J = 9.5 Hz), 133.2, 131.5, 129.9 (d, J = 10.2 Hz), 128.3, 121.7, 120.7 (d, J = 26.2 Hz), 110.9 (d, J = 22.0 Hz).

HRMS (ESI, m/z) Calculated for $C_{16}H_{11}FNO$ $[M + H]^+$: 252.0819, found: 252.0814. **IR** (film): ν (cm^{-1}) 2962, 1654, 1470, 1259, 1222, 1074, 1014, 791, 718, 684, 628.



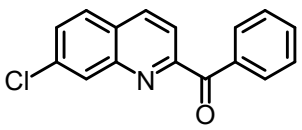
3ag

(7-Fluoroquinolin-2-yl)(phenyl)methanone (3ag), white solid (36.3 mg, 72% yield). PE/EA = 40:1, R_f = 0.20. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.35 (d, J = 8.5 Hz, 1H), 8.25-8.15 (m, 1H), 8.07 (d, J = 8.5 Hz, 1H), 7.91 (dd, J = 9.0, 6.0 Hz, 1H), 7.83 (dd, J = 9.0, 6.0 Hz, 1H), 7.83 (dd, J = 9.9, 2.4 Hz, 1H), 7.68-7.59 (m, 1H), 7.52 (t, J = 7.8 Hz, 2H), 7.46 (td, J = 8.8, 2.5 Hz, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 193.7, 163.5 (d, J = 251.5 Hz), 155.8, 147.8 (d, J = 12.6 Hz), 137.2, 136.1, 133.4, 131.5, 129.8 (d, J = 10.0 Hz), 128.3, 126.0, 120.3 (d, J = 2.6 Hz), 119.2 (d, J = 25.7 Hz), 114.2 (d, J = 20.6 Hz). **HRMS** (ESI, m/z) Calculated for $C_{16}H_{11}FNO$ $[M + H]^+$: 252.0819, found: 252.0815. **IR** (film): ν (cm^{-1}) 3068, 3023, 1656, 1323, 1208, 1156, 904, 867, 850, 717, 684, 618.



3ah

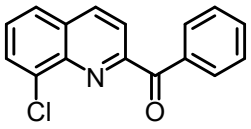
(6-Bromo-7-fluoroquinolin-2-yl)(phenyl)methanone(3ah), white solid (46.6 mg, 71% yield). PE/EA = 40:1, R_f = 0.20. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.28 (d, J = 8.5 Hz, 1H), 8.23-8.15 (m, 3H), 8.10 (d, J = 8.5 Hz, 1H), 7.90 (d, J = 9.2 Hz, 1H), 7.64 (t, J = 7.4 Hz, 1H), 7.52 (t, J = 7.8 Hz, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 193.4, 159.4 (d, J = 252.8 Hz), 155.9, 146.7 (d, J = 11.8 Hz), 136.2, 135.9, 133.5, 132.2, 131.5, 128.4, 126.8, 121.2 (d, J = 2.6 Hz), 115.3 (d, J = 21.8 Hz), 112.9 (d, J = 24.6 Hz). **HRMS** (ESI, m/z) Calculated for $C_{16}H_{10}BrFNO$ $[M + H]^+$: 329.9924, found: 329.9919. **IR** (film): ν (cm^{-1}) 3072, 2961, 1725, 1655, 1598, 1507, 1434, 1323, 1207, 1158, 983, 905, 849, 774, 719, 683, 623.



3ai

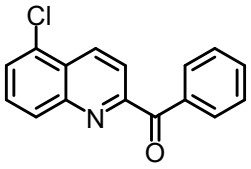
(7-Chloroquinolin-2-yl)(phenyl)methanone (3ai), white solid (38.6 mg, 72% yield). PE/EA = 40:1, R_f = 0.20. **Reported compound.**[3] **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.27 (d, J = 8.5 Hz, 1H), 8.24-8.18 (m, 2H), 8.14 (d, J = 8.7 Hz, 2H), 7.90 (d, J = 2.2 Hz, 1H), 7.72 (dd, J = 9.0, 2.3 Hz, 1H), 7.64 (t, J

= 7.4 Hz, 1H), 7.64 (t, *J* = 7.8 Hz, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$): *δ* 193.5, 155.0, 145.2, 136.3, 136.1, 134.5, 133.3, 132.2, 131.5, 131.3, 129.6, 128.3, 126.5, 121.9.



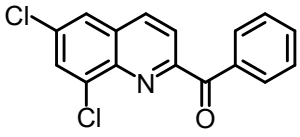
3aj

(8-Chloroquinolin-2-yl)(phenyl)methanone (3aj), white solid (43.0 mg, 81% yield). PE/EA = 40:1, R_f = 0.20. **^{1}H NMR** (500 MHz, $CDCl_3$): *δ* 8.76 (d, *J* = 8.7 Hz, 1H), 8.27-8.17 (m, 3H), 8.13 (d, *J* = 8.3 Hz, 1H), 7.77-7.67 (m, 2H), 7.64 (t, *J* = 7.5 Hz, 1H), 7.52 (t, *J* = 7.8 Hz, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$): *δ* 193.5, 155.4, 147.5, 136.0, 134.3, 133.4, 131.6, 131.5, 129.9, 129.8, 128.5, 128.4, 127.1, 121.8. **HRMS** (ESI, m/z) Calculated for $C_{16}H_{11}ClNO$ $[M + H]^+$: 268.0524, found: 268.0520. **IR** (film): *ν* (cm^{-1}) 3067, 2961, 1658, 1323, 1207, 1156, 904, 850, 786, 717, 684.



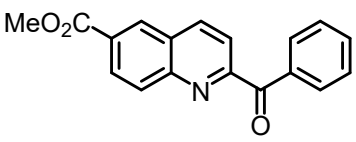
3ak

(5-Chloroquinolin-2-yl)(phenyl)methanone (3ak), white solid (40.0 mg, 75% yield). PE/EA = 40:1, R_f = 0.20. **Reported compound.**[3] **^{1}H NMR** (500 MHz, $CDCl_3$): *δ* 8.75 (d, *J* = 8.8 Hz, 1H), 8.28-8.15 (m, 3H), 8.12 (d, *J* = 8.2 Hz, 1H), 8.66-8.76 (m, 2H), 7.63 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.8 Hz, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$): *δ* 193.4, 155.3, 147.5, 136.0, 134.2, 133.4, 131.6, 131.5, 129.9, 129.8, 128.4, 128.3, 127.1, 121.7.



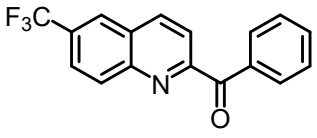
3al

(6,8-Dichloroquinolin-2-yl)(phenyl)methanone (3al), white solid (42.1 mg, 70% yield). PE/EA = 40:1, R_f = 0.20. **^{1}H NMR** (500 MHz, $CDCl_3$): *δ* 8.54-8.45 (m, 2H)), 8.28 (s, 2H), 7.88 (d, *J* = 2.1 Hz, 1H), 7.81 (d, *J* = 2.1 Hz, 1H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.53 (t, *J* = 7.6 Hz, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$): *δ* 191.9, 154.8, 141.8, 136.8, 136.4, 135.9, 134.0, 133.4, 132.1, 131.0, 130.4, 128.3, 125.5, 122.7. **HRMS** (ESI, m/z) Calculated for $C_{16}H_{10}Cl_2NO$ $[M + H]^+$: 302.0134, found: 302.0131. **IR** (film): *ν* (cm^{-1}) 3068, 2962, 1656, 1593, 1322, 1156, 866, 850, 786, 718, 684.



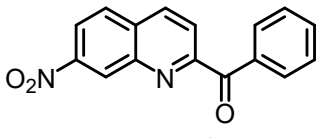
3am

Methyl 2-benzoylquinoline-6-carboxylate (3am), white solid (38.0 mg, 65% yield). PE/EA = 10:1, R_f = 0.20. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.66 (d, J = 1.2 Hz, 1H), 8.45 (d, J = 8.5 Hz, 1H), 8.36 (dd, J = 8.8, 1.6 Hz, 1H), 8.29-8.19 (m, 3H), 8.15 (d, J = 8.5 Hz, 1H), 7.64 (t, J = 7.4 Hz, 1H), 7.53 (t, J = 7.8 Hz, 2H), 4.02 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 193.6, 166.5, 156.7, 148.7, 138.6, 135.9, 133.5, 131.6, 130.9, 130.8, 129.8, 129.7, 128.4, 128.1, 121.6, 52.7. **HRMS** (ESI, m/z) Calculated for $C_{18}H_{14}NO_3$ $[M + H]^+$: 292.0968, found: 292.0962. **IR** (film): ν (cm^{-1}) 3071, 3023, 2960, 1727, 1659, 1593, 1507, 1433, 1323, 1156, 981, 904, 850, 717, 684, 619.



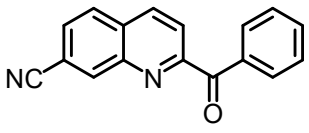
3an

Phenyl(6-(trifluoromethyl)quinolin-2-yl)methanone (3an), white solid (38.0 mg, 65% yield). PE/EA = 40:1, R_f = 0.20. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.45 (d, J = 8.5 Hz, 1H), 8.32 (d, J = 8.9 Hz, 1H), 8.27-8.15 (m, 4H), 7.95 (dd, J = 8.9, 1.8 Hz, 1H), 7.65 (t, J = 7.5 Hz, 1H), 7.53 (t, J = 7.8 Hz, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 193.4, 156.7, 147.8, 138.2, 135.8, 133.5, 131.9, 131.5, 130.2 (q, J = 32.9 Hz), 128.4, 127.9, 125.9 (q, J = 3.0 Hz), 125.7 (q, J = 4.2 Hz), 123.9 (q, J = 272.2 Hz), 122.1. **HRMS** (ESI, m/z) Calculated for $C_{17}H_{11}F_3NO$ $[M + H]^+$: 302.0787, found: 302.0781. **IR** (film): ν (cm^{-1}) 2960, 1727, 1660, 1323, 1258, 1156, 905, 850, 717, 684, 618.



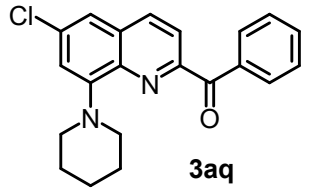
3ao

(7-Nitroquinolin-2-yl)(phenyl)methanone (3ao), pale yellow solid (34.0 mg, 61% yield). PE/EA = 10:1, R_f = 0.20. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.87 (d, J = 2.4 Hz, 1H), 8.61-8.50 (m, 2H), 8.34 (d, J = 9.3 Hz, 1H), 8.28-8.18 (m, 3H), 7.71-7.63 (m, 1H), 7.59-7.50 (m, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 193.1, 157.9, 148.8, 146.8, 139.2, 135.6, 133.7, 132.5, 131.5, 128.5, 127.8, 124.4, 123.7, 122.7. **HRMS** (ESI, m/z) Calculated for $C_{16}H_{11}N_2O_3$ $[M + H]^+$: 279.0764, found: 279.0759. **IR** (film): ν (cm^{-1}) 3072, 2960, 2923, 1726, 1656, 1322, 1258, 1156, 715, 682, 619.



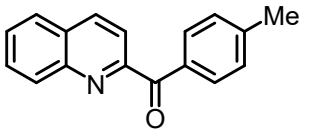
3ap

2-Benzoylquinoline-7-carbonitrile (3ap), pale yellow solid (23.0 mg, 45% yield). PE/EA = 10:1, R_f = 0.20. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.42 (d, J = 8.5 Hz, 1H), 8.32 (s, 1H), 8.29 (d, J = 8.7 Hz, 1H), 8.20 (d, J = 8.4 Hz, 3H), 7.92 (dd, J = 8.8, 1.3 Hz, 1H), 7.66 (t, J = 7.4 Hz, 1H), 7.53 (t, J = 7.7 Hz, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 193.1, 157.3, 147.7, 137.7, 135.6, 134.0, 133.7, 132.1, 131.5, 130.9, 128.5, 128.2, 122.5, 118.3, 112.2. **HRMS** (ESI, m/z) Calculated for $C_{17}H_{11}N_2O$ [M + H]$^+$: 259.0866, found: 259.0862. **IR** (film): ν (cm^{-1}) 3072, 2960, 2922, 1726, 1659, 1594, 1507, 1434, 1323, 1258, 1157, 1096, 982, 903, 842, 786, 717, 686, 619.



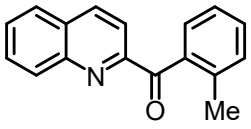
3aq

(6-Chloro-8-(piperidin-1-yl)quinolin-2-yl)(phenyl)methanone (3aq), orange solid (45 mg, 64% yield). PE/EA = 40:1, R_f = 0.20. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.22-8.12 (m, 4H), 7.60 (t, J = 7.4 Hz, 1H), 7.49 (t, J = 7.6 Hz, 2H), 7.40 (d, J = 2.0 Hz, 1H), 7.05 (d, J = 1.8 Hz, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 194.0, 152.8, 151.0, 139.8, 137.1, 136.9, 135.2, 132.5, 131.2, 128.0, 121.6, 118.8, 117.8, 53.6, 26.2, 24.5. **HRMS** (ESI, m/z) Calculated for $C_{21}H_{20}ClN_2O$ [M + H]$^+$: 351.1259, found: 351.1254. **IR** (film): ν (cm^{-1}) 3072, 2922, 2851, 2814, 1726, 1660, 1593, 1449, 1318, 1290, 1240, 1156, 1091, 960, 868, 685, 619.



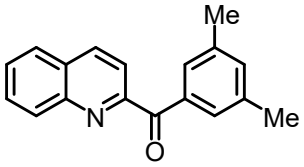
3ar

Quinolin-2-yl(p-tolyl)methanone (3ar), white solid (34.1 mg, 69% yield). PE/EA = 40:1, R_f = 0.20. **Reported compound.**[4] **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.33 (d, J = 8.5 Hz, 1H), 8.20 (d, J = 8.5 Hz, 1H), 8.15 (d, J = 8.2 Hz, 2H), 8.08 (d, J = 8.5 Hz, 1H), 7.90 (d, J = 8.1 Hz, 1H), 7.81-7.75 (m, 1H), 7.70-7.61 (m, 1H), 7.32 (d, J = 8.2 Hz, 2H), 2.46 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 193.6, 155.2, 146.8, 144.1, 137.2, 133.7, 131.7, 130.6, 130.2, 129.04, 128.96, 128.4, 127.8, 121.0, 21.9.



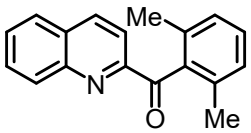
3as

Quinolin-2-yl(o-tolyl)methanone (3as), white solid (24.2 mg, 49% yield). PE/EA = 40:1, R_f = 0.20. **Reported compound.**[4] **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.34 (d, J = 8.5 Hz, 1H), 8.22-8.08 (m, 2H), 7.90 (d, J = 8.1 Hz, 1H), 7.78-7.72 (m, 1H), 7.69-7.69 (m, 1H), 7.60 (d, J = 7.7 Hz, 1H) 7.45 (td, J = 7.5, 1.1 Hz, 1H), 7.33 (d, J = 7.7 Hz, 1H), 7.28 (t, J = 7.5 Hz, 1H), 2.44 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 197.7, 154.9, 147.2, 138.7, 137.3, 137.2, 131.4, 131.2, 130.9, 130.2, 129.2, 128.7, 127.7, 125.1, 120.4, 21.0.



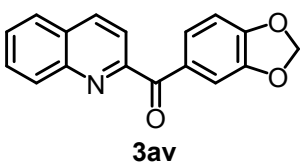
3at

(3,5-Dimethylphenyl)(quinolin-2-yl)methanone (3at), white solid (41.8 mg, 80% yield). PE/EA = 40:1, R_f = 0.20. **Reported compound.**[4] **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.34 (d, J = 8.5 Hz, 1H), 8.22 (d, J = 8.5 Hz, 1H), 8.05 (d, J = 8.5 Hz, 1H), 7.91 (d, J = 8.2 Hz, 1H), 7.84-7.74 (m, 3H), 7.66 (t, J = 7.5 Hz, 1H), 7.26 (s, 1H), 2.39 (s, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 194.6, 155.3, 146.9, 137.9, 137.1, 136.3, 135.0, 130.7, 130.2, 129.2, 129.0, 128.4, 127.8, 120.9, 21.4.



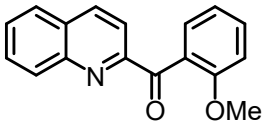
3au

(2,6-Dimethylphenyl)(quinolin-2-yl)methanone (3au), colourless liquid (12.0 mg, 23% yield). PE/EA = 40:1, R_f = 0.20. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.33 (d, J = 8.5 Hz, 1H), 8.19 (d, J = 8.5 Hz, 1H), 8.10 (d, J = 8.5 Hz, 1H), 7.88 (d, J = 7.8 Hz, 1H), 7.76-7.69 (m, 1H), 7.68-7.61 (m, 1H), 7.27 (t, J = 7.6 Hz, 1H), 7.10 (d, J = 7.6 Hz, 2H), 2.16 (s, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 201.5, 153.7, 147.9, 140.1, 137.4, 134.8, 131.3, 130.1, 129.6, 128.95, 128.92, 127.7, 127.6, 119.4, 19.9. **HRMS** (ESI, m/z) Calculated for $C_{18}H_{16}NO$ $[M + H]^+$: 262.1226, found: 262.1224. **IR** (film): ν (cm^{-1}) 3063, 2922, 1669, 1592, 1460, 1308, 1208, 1164, 1110, 960, 918, 841, 768, 719, 618.



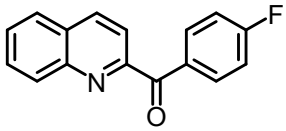
3av

Benzo[d][1,3]dioxol-5-yl(quinolin-2-yl)methanone (3av), white solid (43.2 mg, 78% yield). PE/EA = 10:1, R_f = 0.20. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.33 (d, J = 8.5 Hz, 1H), 8.21(d, J = 8.5 Hz, 1H), 8.04 (d, J = 8.5 Hz, 1H), 7.95-7.87 (m, 2H), 7.83-7.74 (m, 2H), 7.65 (t, J = 7.4 Hz, 1H), 6.91 (d, J = 8.2 Hz, 1H), 6.07 (s, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 191.9, 155.3, 152.2, 147.9, 146.7, 137.2, 130.7, 130.6, 130.2, 128.9, 128.8, 128.4, 127.8, 121.1, 111.1, 108.0, 102.0. **HRMS** (ESI, m/z) Calculated for $C_{17}H_{12}NO_3$ $[M + H]^+$: 278.0812, found: 278.0805. **IR** (film): v (cm^{-1}) 3068, 2919, 1646, 1447, 1314, 1250, 1091, 1030, 928, 841, 760, 619.



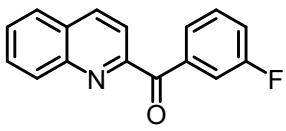
3aw

(2-Methoxyphenyl)(quinolin-2-yl)methanone (3aw), white solid (29.0 mg, 55% yield). PE/EA = 10:1, R_f = 0.20. **Reported compound.**[5] **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.29 (d, J = 8.5 Hz, 1H), 8.10 (d, J = 8.5 Hz, 1H), 8.06 (d, J = 8.5 Hz, 1H), 7.87 (d, J = 8.0 Hz, 1H), 7.75-7.69 (m, 1H), 7.66 (dd, J = 7.5, 1.5 Hz, 1H), 7.61 (t, J = 7.5 Hz, 1H), 7.56-7.49 (m, 1H), 7.09 (t, J = 7.5 Hz, 1H), 7.01 (d, J = 8.4 Hz, 1H), 3.60 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 196.4, 159.0, 155.3, 147.3, 136.8, 133.1, 131.1, 130.7, 129.9, 129.2, 128.3, 128.2, 127.7, 120.6, 119.9, 112.1, 55.9.



3ax

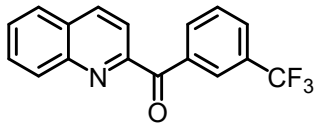
(4-fluorophenyl)(quinolin-2-yl)methanone (3ax), white solid (24.0 mg, 48%). PE/EA = 40:1, R_f = 0.20. **Reported compound.**[6] **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.42-8.29 (m, 3H), 8.20 (d, J = 8.5 Hz, 1H), 8.12 (d, J = 8.5 Hz, 1H), 7.92 (d, J = 8.25 Hz, 1H), 7.80 (t, J = 7.5 Hz, 1H), 7.67 (t, J = 7.5 Hz, 1H), 7.19 (t, J = 8.5 Hz, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 192.2, 166.0 (d, J = 255.2 Hz), 154.6, 146.8, 137.4, 134.4 (d, J = 9.2 Hz), 132.6 (d, J = 3.0 Hz), 130.6, 130.3, 129.1, 128.7, 127.8, 120.9, 115.4 (d, J = 21.5 Hz).



3ay

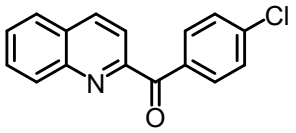
(3-Fluorophenyl)(quinolin-2-yl)methanone (3ay), white solid (20.1 mg, 40% yield). PE/EA = 40:1, R_f = 0.20. **Reported compound.**[6] **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.36 (d, J = 8.5 Hz, 1H), 8.21 (d, J = 8.5 Hz, 1H), 8.14 (d, J = 8.25 Hz, 1H), 8.06 (d, J = 7.8 Hz, 1H), 8.04-7.97 (m, 1H), 7.92 (d, J =

8.2 Hz, 1H), 7.86-7.76 (m, 1H), 7.73-7.64 (m, 1H), 7.53-7.46 (m ,1H), 7.38-7.29 (m, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 192.4, 162.5 (d, J = 246.8 Hz), 154.2, 146.8, 138.3 (d, J = 6.7 Hz), 137.4, 130.7, 130.4, 129.9 (d, J = 7.9 Hz), 129.2, 128.8, 127.8, 127.4 (d, J = 2.8 Hz), 120.9, 120.1 (d, J = 21.3 Hz), 118.4 (d, J = 23.0 Hz).



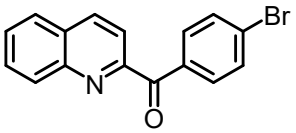
3az

Quinolin-2-yl(3-(trifluoromethyl)phenyl)methanone (3az), white solid (14.0 mg, 26% yield). PE/EA = 40:1, R_f = 0.20. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.63 (s, 1H), 8.47 (d, J = 7.8 Hz, 1H), 8.39 (d, J = 8.5 Hz, 1H), 8.23-8.16 (m, 2H), 7.93 (d, J = 8.0 Hz, 1H), 7.88 (d, J = 7.8 Hz, 1H), 7.84-7.79 (m ,1H), 7.73-7.63 (m, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 192.2, 153.8, 146.9, 137.5, 136.9, 134.8, 130.8 (q, J = 32.7 Hz), 130.7, 130.5, 129.4 (q, J = 3.5 Hz), 129.3, 129.0, 128.8, 128.7(q, J = 4.0 Hz), 127.3, 124.0 (q, J = 272.4 Hz), 120.8. **HRMS** (ESI, m/z) Calculated for $C_{17}H_{11}F_3NO$ $[M + H]^+$: 302.0787, found: 302.0782. **IR** (film): ν (cm^{-1}): 3055, 2960, 1667, 1591, 1429, 1339, 1279, 1154, 1072, 930, 842, 765, 688, 621.



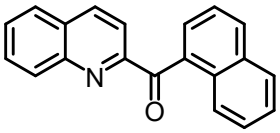
3ba

(4-Chlorophenyl)(quinolin-2-yl)methanone (3ba), white solid (19.2 mg, 36% yield). PE/EA = 40:1, R_f = 0.20. **Reported compound.**[4] **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.35 (d, J = 8.5 Hz, 1H), 8.28-8.21 (m, 2H), 8.19 (d, J = 8.5 Hz, 1H), 8.13 (d, J = 8.5 Hz, 1H), 7.91 (d, J = 8.1 Hz, 1H), 7.83-7.75 (m, 1H), 7.71-7.63 (m, 1H), 7.53-7.46 (m, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 192.5, 154.3, 146.8, 139.7, 137.4, 134.6, 133.1, 130.6, 130.4, 129.1, 128.8, 128.6, 127.8, 120.9.



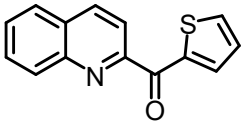
3bb

(4-Bromophenyl)(quinolin-2-yl)methanone (3bb), white solid (42.2 mg, 68% yield). PE/EA = 40:1, R_f = 0.20. **Reported compound.**[4] **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.35 (d, J = 8.5 Hz, 1H), 8.25-8.08 (m, 4H), 7.91 (d, J = 8.2 Hz, 1H), 7.83-7.75 (m, 1H), 7.73-7.62 (m, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 192.7, 154.3, 146.8, 137.4, 135.1, 133.2, 133.6, 130.7, 130.4, 129.1, 128.8, 128.5, 127.8, 120.9.



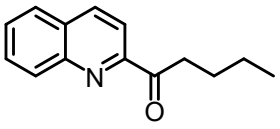
3bc

Naphthalen-1-yl(quinolin-2-yl)methanone (3bc), white solid (18.0 mg, 32% yield). PE/EA = 40:1, R_f = 0.20. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.50-8.41 (m, 1H), 8.37 (d, J = 8.5 Hz, 1H), 8.24 (d, J = 8.5 Hz, 1H), 8.15-8.03 (m, 2H), 7.98-7.83 (m, 3H), 7.77-7.71 (m ,1H), 7.65 (t, J = 7.4 Hz, 1H), 7.59-7.49 (m, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 196.8, 155.4, 147.2, 137.2, 134.4, 134.1, 132.6, 131.7, 131.4, 130.9, 130.2, 129.2, 128.7, 128.6, 127.7, 126.4, 126.1, 124.3, 120.8. **HRMS** (ESI, m/z) Calculated for $C_{20}H_{14}NO$ $[M + H]^+$: 284.1070, found: 284.1062. **IR** (film): v (cm^{-1}) 3048, 2961, 1651, 1307, 1258, 1052, 1018, 919, 806, 761, 607.



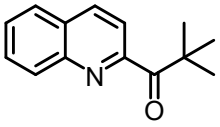
3bd

Quinolin-2-yl(thiophen-2-yl)methanone (3bd), white solid (28.2 mg, 59% yield). PE/EA = 40:1, R_f = 0.20. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.51 (dd, J = 3.8, 1.1 Hz, 1H), 8.36-8.24 (m, 3H), 7.91 (d, J = 8.1 Hz, 1H), 7.84-7.78 (m, 2H), 7.70-7.64 (m, 1H), 7.25-7.21 (m, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 183.7, 153.6, 146.8, 139.9, 137.3, 136.96, 136.95, 130.4, 130.3, 129.4, 128.8, 127.9, 127.6, 119.9. **HRMS** (ESI, m/z) Calculated for $C_{14}H_{10}NOS$ $[M + H]^+$: 240.0478, found: 240.0474. **IR** (film): v (cm^{-1}) 3099, 2961, 1635, 1501, 1463, 1406, 1355, 1309, 1218, 1037, 918, 837, 765, 714, 618.



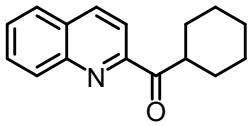
3be

1-(Quinolin-2-yl)pentan-1-one (3be), pale yellow liquid (22.2 mg, 52% yield). PE/EA = 50:1, R_f = 0.20. **Reported compound.**[7] **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.25 (d, J = 8.5 Hz, 1H), 8.19 (d, J = 8.5 Hz, 1H), 8.12 (d, J = 8.5 Hz, 1H), 7.86 (d, J = 8.0 Hz, 1H), 7.80-7.75 (m, 1H), 7.67-7.60 (m, 1H), 3.40 (t, J = 7.5 Hz, 2H), 1.82-1.72 (m, 2H), 1.54-1.40 (m, 2H), 0.98 (t, J = 7.4 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 202.9, 153.3, 147.3, 137.0, 130.7, 130.0, 129.76, 128.6, 127.8, 118.3, 37.3, 26.5, 22.7, 14.2.



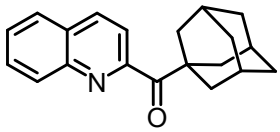
3bf

2,2-Dimethyl-1-(quinolin-2-yl)propan-1-one (3bf), purple liquid (37.0 mg, 86% yield). PE/EA = 50:1, R_f = 0.20. **Reported compound.**[8] **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.23 (d, J = 8.5 Hz, 1H), 8.15 (d, J = 8.5 Hz, 1H), 7.99 (d, J = 8.6 Hz, 1H), 7.84 (d, J = 8.2 Hz, 1H), 7.78-7.73 (m, 1H), 7.64-7.59 (m, 1H), 1.56 (s, 9H). **^{13}C NMR** (125 MHz, $CDCl_3$): 207.4, 154.1, 146.5, 136.6, 130.6, 129.8, 128.9, 128.3, 127.7, 120.3, 44.6, 27.9.



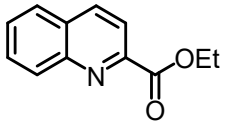
3bg

Cyclohexyl(quinolin-2-yl)methanone (3bg), pale yellow liquid (37.5 mg, 78% yield). PE/EA = 50:1, R_f = 0.20. **Reported compound.**[8] **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.26 (d, J = 8.5 Hz, 1H), 8.21 (d, J = 8.5 Hz, 1H), 8.11 (d, J = 8.5 Hz, 1H), 7.86 (d, J = 8.0 Hz, 1H), 7.81-7.74 (m, 1H), 7.67-7.61 (m, 1H), 4.21-4.09 (m, 1H), 2.03-1.95 (m, 2H), 1.89-1.82 (m, 2H), 1.80-1.73 (m, 1H), 1.56-1.44 (m, 4H), 1.35-1.26 (m, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 205.6, 152.8, 147.3, 137.0, 130.8, 130.0, 129.6, 128.5, 127.8, 118.9, 43.9, 29.2, 26.3, 26.0.



3bh

((3r,5r,7r)-adamantan-1-yl)(quinolin-2-yl)methanone (3bh), white solid (50.0 mg, 86% yield). PE/EA = 40:1, R_f = 0.20. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.22 (d, J = 8.5 Hz, 1H), 8.16 (d, J = 8.5 Hz, 1H), 7.88 (d, J = 8.6 Hz, 1H), 7.83 (d, J = 8.1 Hz, 1H), 7.76 (t, J = 7.4 Hz, 1H), 7.61 (t, J = 7.4 Hz, 1H), 2.34 (d, J = 1.7 Hz, 6H), 2.11 (s, 3H), 1.82 (m, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 206.9, 154.8, 146.5, 136.6, 130.6, 129.8, 128.8, 128.2, 127.7, 120.3, 47.3, 38.9, 37.0, 28.5. **HRMS** (ESI, m/z) Calculated for $C_{20}H_{22}NO$ $[M + H]^+$: 292.1696, found: 292.1690. **IR** (film): ν (cm^{-1}) 3048, 2961, 1651, 1307, 1258, 1052, 1018, 919, 806, 761, 607.



3bi

Ethyl quinoline-2-carboxylate (3bi), colourless liquid (22.2 mg, 55% yield). PE/EA = 5:1, R_f = 0.20. **Reported compound.**[1] **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.30 (t, J = 8.5 Hz, 2H), 8.18 (d, J = 8.5 Hz, 1H), 7.87 (J = 8.1 Hz, 1H), 7.81-7.74 (m, 1H), 7.67-7.60 (m, 1H), 4.56 (q, J = 7.2 Hz, 2H), 1.48

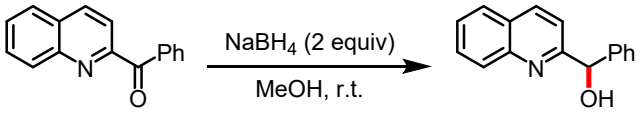
(t, J = 7.2 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 165.6, 148.4, 147.7, 137.4, 130.9, 130.3, 129.4, 128.7, 127.6, 121.1, 62.4, 14.5.

3. Large-Scale Experiment and Synthetic Applications

(a) 10-Fold scale experiment

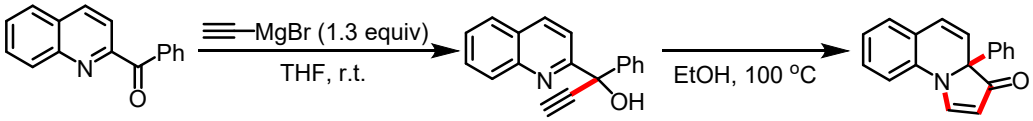
A pre-dried 50 mL Schlenk tube was charged with *o*-ethynylanilines **1a** (234.4 mg, 2.0 mmol, 1.0 eq.), glyoxals **2a** (456.3 mg, 3.0 mmol, 1.5 eq.), piperidine (340.4 mg, 0.4 mmol, 2.0 eq.) and CuBr (58.0 mg, 0.4 mmol, 20 mol%) under an atmosphere of N_2. Dried *p*-xylene (8.0 mL, 0.25 M) was added via syringe in sequence. The reaction mixture was stirred at 120 °C for 20 h under an atmosphere of N_2. After cooling to room temperature, the mixture was directly transferred to a column and purified by flash chromatography on silica gel using PE/EA as eluent to give the analytical pure product **3aa** (298.0 mg, 64% yield).

(b) Synthetic transformation of products



3aa **4**

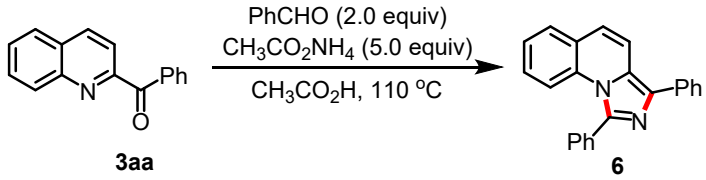
Phenyl(quinolin-2-yl)methanone **3aa** (46.6 mg, 0.2 mmol, 1.0 equiv) was dissolved in 2.0 mL of MeOH and then $NaBH_4$ (15.2 mg, 0.4 mmol, 2.0 equiv) was added slowly. After the insoluble mixture disappeared, the reaction was quenched slowly with 5.0 mL of H_2O and the mixture was extracted with EtOAc for three times. The pooled organics were dried over anhydrous Na_2SO_4, and concentrated and purified by silica gel chromatography using PE/EA to afford the product **4** (colourless oil, 46.0 mg, 98% yield). PE/EA = 5:1, R_f = 0.30. **Reported compound.**[9] **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.15 (d, J = 8.5 Hz, 1H), 8.06 (d, J = 8.5 Hz, 1H), 7.80 (d, J = 8.1 Hz, 1H), 7.78-7.72 (m, 1H), 7.61-7.51 (m, 1H), 7.46-7.38 (m, 2H), 7.37-7.31 (m, 2H), 7.31-7.26 (m, 1H), 7.19 (d, J = 8.5 Hz, 1H), 6.09 (bs, 1H), 5.88 (s, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 160.6, 146.1, 142.9, 137.2, 130.1, 128.9, 128.8, 128.1, 127.7, 127.65, 127.61, 126.8, 119.4, 75.3.



3aa **S1** **5**

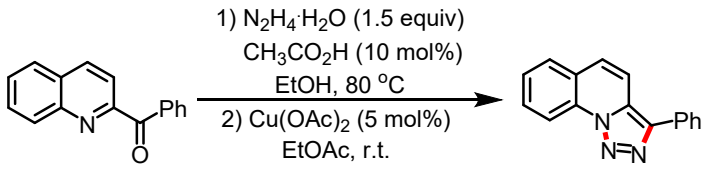
Phenyl(quinolin-2-yl)methanone **3aa** (46.6 mg, 0.2 mmol, 1.0 equiv) was dissolved in 1.0 mL of dry THF and the resulting solution was cooled to 0 °C under an N_2 atmosphere. Ethynylmagnesium bromide (0.5 M, 0.26 mmol, 1.3 equiv) was added dropwise and the reaction mixture was stirred at 0 °C for 1 h and then at room temperature for 2 h. The reaction was quenched with sat. NH_4Cl and the

mixture was extracted with EtOAc for three times. The pooled organics were washed with brine, dried over anhydrous Na_2SO_4, and concentrated to afford a brown syrup which was purified by silica gel chromatography using PE/EA (20:1, R_f = 0.20) to give yellow oil product **S1** (47.0 mg, 91% yield). Then, a solution of **S1** (46.6 mg, 0.18 mmol) in 1.0 mL of absolute EtOH was heated at 100 °C for 2 h. The crude reaction mixture was concentrated in vacuo and the resulting residue was purified by silica gel chromatography using PE/EA (5:1, R_f = 0.20). to afford the product **5** (yellow solid, 41.4 mg, 89% yield). **Reported compound.**[10] **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.30 (d, J = 3.6 Hz, 1H), 7.46-7.36 (m, 2H), 7.33-7.18 (m, 5H), 7.11 (dd, J = 7.5, 1.2 Hz, 1H), 7.06 (td, J = 7.5, 1.2 Hz, 1H), 6.56 (d, J = 9.5 Hz, 1H), 6.51 (d, J = 9.5 Hz, 1H), 5.25 (d, J = 3.7 Hz, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 200.9, 163.1, 139.1, 136.4, 129.6, 128.9, 128.1, 128.0, 127.2, 126.8, 125.8, 124.9, 124.7, 116.9, 98.9, 71.1.



3aa **6**

A mixture of phenyl(quinolin-2-yl)methanone **3aa** (46.6 mg, 0.2 mmol, 1.0 eq.) and benzaldehyde (42.5 mg, 0.4 mmol, 2.0 eq.), and ammonium acetate (77.2 mg, 1.0 mmol, 5.0 eq.) in glacial acetic acid (1.0 mL) was stirred at 110 °C under inert atmosphere. After 20 h, the reaction mixture was cooled to room temperature and the acetic acid was removed by evaporation under reduced pressure. The obtained solid was dissolved in a saturated aqueous solution of Na_2CO_3 and the mixture extracted with DCM. The collected organic layer was separated, dried and the solvent evaporated under vacuum. The obtained crude product was purified via silica gel column chromatography using PE/EA (10:1, R_f = 0.20) as eluent to give desired product **6** (white solid, 56.0 mg, 88% yield). **Reported compound.**[11] **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.92 (d, J = 7.4 Hz, 1H), 7.76-7.66 (m, 3H), 7.63 (d, J = 7.6, 1H), 7.59-7.52 (m, 3H), 7.52-7.42 (m, 3H), 7.38-7.28 (m, 2H), 7.21-7.14 (m, 1H), 7.08 (d, J = 9.5 Hz, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 142.3, 134.6, 133.9, 133.8, 132.6, 129.9, 129.6, 129.0, 128.8, 128.6, 127.6, 127.1, 126.6, 125.9, 125.3, 122.2, 117.65, 117.63.

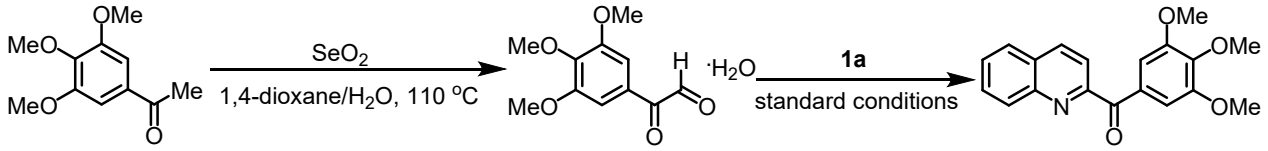


3aa **7**

Hydrazine monohydrate (15.0 mg, 0.30 mmol, 1.5 eq.) and acetic acid (1.2 mg, 0.02 mmol, 0.1 eq.) were added to a solution of phenyl(quinolin-2-yl)methanone **3aa** (46.6 mg, 0.20 mmol, 1.0 eq.) in 0.6 mL of EtOH at room temperature and the reaction mixture was heated at 80 °C for 6 h. After cooling to room temperature, EtOAc (3.0 mL) and $Cu(OAc)_2$ (2.0 mg, 0.01 mmol, 0.05 eq.) were

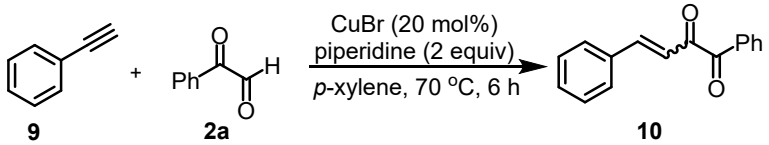
added. After stirring at the room temperature for the 8 h, the resulting mixture was diluted with EtOAc (10 mL). The organic phase was washed with H_2O (5 mL) and then dried over anhydrous Na_2SO_4. Concentration under reduced pressure and successive purification by column chromatography on silica gel (PE/EA = 20:1, R_f = 0.20) gave the desired product **7** (white solid, 30.0 mg, 61% yield). **Reported compound.**[12] **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.83 (d, J = 8.4 Hz, 1H), 7.99 (d, J = 7.2 Hz, 2H), 7.85 (d, J = 7.9 Hz, 1H), 7.83-7.74 (m, 2H), 7.61 (t, J = 7.3 Hz, 1H), 7.59-7.50 (m, 3H), 7.42 (t, J = 7.4 Hz, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 140.1, 132.2, 131.5, 130.3, 129.2, 128.6, 128.6, 128.5, 128.2, 17.3, 127.1, 124.1, 116.5, 115.4.

(c) Synthesis of pharmaceutical molecules



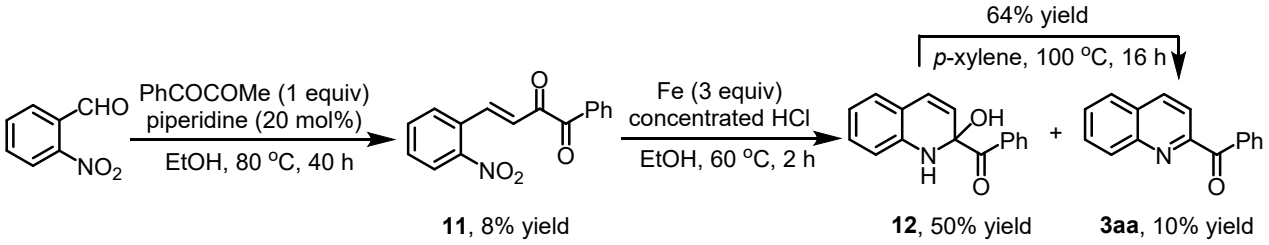
Into a dry flask were added SeO_2 (166.5 mg, 1.5 mmol, 1.5 eq.), 1,4-dioxane (2.0 mL) and H_2O (0.2 mL), and the reaction mixture was stirred at 50 °C until SeO_2 dissolved completely. Then 1-(3,4,5-trimethoxyphenyl)ethan-1-one **8** (210.0 mg, 1.0 mmol, 1.0 eq.) was added and the reaction mixture was stirred at 110 °C for 20 h. After cooling to room temperature, the reaction mixture was directly purified by flash column chromatography on silica gel (PE/EA = 1:1, R_f = 0.20) to give white solid **S2** (218.0 mg, 90% yield). According to the **General procedure** for synthesis of 2-acylquinolines under standard conditions, purification by flash column chromatography on silica gel (PE/EA = 5:1, R_f = 0.20) gave **3bg** (white solid, 44.0 mg, 70% yield). **Reported compound.**[13] **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.36 (d, J = 8.5 Hz, 1H), 8.19 (d, J = 8.5 Hz, 1H), 8.11 (d, J = 8.5 Hz, 1H), 7.92 (d, J = 8.5 Hz, 1H), 7.85-7.76 (m, 1H), 7.71-7.65 (m, 1H), 7.64 (s, 2H), 3.97 (s, 3H), 3.91 (s, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 192.2, 155.0, 152.9, 146.8, 142.9, 137.3, 131.1, 130.5, 130.4, 129.0, 128.6, 127.9, 121.2, 109.4, 61.1, 56.4.

4. Control Experiments



A pre-dried 10 mL Schlenk tube was charged with ethynylbenzene **1** (20.4 mg, 0.2 mmol, 1.0 eq.), glyoxals **2a** (40.2 mg, 0.3 mmol, 1.5 eq.), piperidine (34 mg, 0.4 mmol, 2.0 eq.) and CuBr (0.04 mmol, 5.8 mg, 0.2 eq.) under an atmosphere of N_2. Dried *p*-xylene (0.8 mL, 0.25 M) was added via

syringe in sequence. The reaction mixture was stirred at 70 °C for 6 h under an atmosphere of N_2. After cooling to room temperature, the mixture was directly transferred to a column and purified by flash chromatography on silica gel (PE/EA = 40:1, R_f = 0.20) to give pale yellow oil **10** (24.0 mg, 51% yield, *E*:*Z* = 96:4). **Reported compound.**[14] **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.04 (d, *J* = 7.5 Hz, 2H), 7.72 (d, *J* = 16.4 Hz, 2H), 7.66 (t, *J* = 7.5 Hz, 1H), 7.62-7.56 (m, 2H), 7.52 (t, *J* = 7.8 Hz, 2H), 7.47-7.39 (m, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 193.4, 192.9, 149.0, 134.8, 134.1, 132.9, 131.7, 130.3, 129.2, 129.03, 129.01, 122.5.



To a 50 mL round bottom flask was added a mixture of 2-nitrobenzaldehyde (755.5 mg, 5.0 mmol, 1.0 eq.), 1-phenylpropane-1,2-dione (741.0 mg, 5.0 mmol, 1.0 eq.) and absolute ethanol (5 mL, 1 M) under an atmosphere of N_2. Then piperidine (85.1 mg, 1.0 mmol, 0.2 eq.) was added into the above reaction mixture and the reaction was refluxed at 80 °C for 40 h with stirring. After the reaction mixture was cooled to room temperature, the solvent was removed in a rotatory evaporator and the residue was extracted with DCM. The organic extracts were collected and washed with water and dried over anhydrous Na_2SO_4. The solvent was removed in a rotatory evaporator and the crude product was purified through a silica gel column (PE/EA = 10:1, R_f = 0.20) to give yellow solid **11** (113.5 mg, 8% yield). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.20 (d, *J* = 16.2 Hz, 1H), 8.11-8.04 (m, 3H), 7.76-7.73 (m, 1H), 7.73-7.65 (m, 2H), 7.63-7.58 (m, 1H), 7.54 (m, 2H), 7.10 (d, *J* = 16.2 Hz, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 192.6, 191.6, 148.7, 143.9, 135.1, 134.0, 132.7, 131.4, 130.63, 130.56, 129.5, 129.2, 126.7, 125.4. **HRMS** (ESI, m/z) Calculated for $C_{16}H_{12}NO_4$ $[M + H]^+$: 282.0761, found: 282.0757. **IR** (film): ν (cm^{-1}) 3067, 1667, 1597, 1519, 1449, 1343, 1259, 1118, 849, 684, 717, 698, 682, 653, 585. To a solution of **11** (113.5 mg, 0.4 mmol, 1.0 eq.) in absolute ethanol (2.0 mL, 0.2 M) was added Fe powder (67.2 mg, 1.2 mmol, 3.0 eq.) and concentrated HCl (0.2 mL, 37% aqueous solution). The reaction mixture was heated at 60 °C and monitored by TLC. Upon completion, the mixture was cooled to room temperature, and added into saturated Na_2CO_3 aqueous solution (2.0 mL). The mixture was extracted with EtOAc for three times, and the organic layers were collected and dried over Na_2SO_4, then concentrated in vacuo. The residue was purified by silica gel column chromatography (PE/EA = 10:1, R_f = 0.20) to give **3aa** (9.5 mg, 10% yield) and colorless oil **12** (50.2 mg, 50% yield). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.15 (d, *J* = 8.4 Hz, 1H), 8.06 (d, *J* = 8.5 Hz, 1H), 7.80 (d, *J* = 8.1 Hz, 1H), 7.78-7.73 (m, 1H), 7.59-7.53 (m, 1H), 7.46-7.38 (m, 2H), 7.38-7.31 (m, 2H), 7.31-7.26 (m, 1H), 7.19 (d, *J* = 8.5 Hz, 1H), 6.08 (bs, 1H), 5.87 (s, 1H). **^{13}C NMR** (125

MHz, $CDCl_3$): δ 160.6, 146.1, 142.9, 137.2, 130.1, 129.0, 128.8, 128.2, 127.7, 127.65, 127.61, 126.8, 119.4, 75.3. **HRMS** (ESI, m/z) Calculated for $C_{16}H_{12}NO_4$ $[M + H]^+$: 252.1019, found: 252.1016. **IR** (film): ν (cm^{-1}) 3351, 3060, 1598, 1505, 1048, 2026, 816, 751, 725, 698, 616, 441. The solution of **12** (50.2 mg, 0.2 mmol) in *p*-xylene was heated at 100 °C for 16 h. After cooling to room temperature, the reaction was directly purified by flash column chromatography on silica gel (PE/EA = 30:1, R_f = 0.20) to give **3aa** (29.8 mg, 64% yield).

5. References

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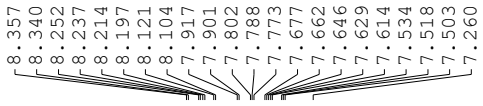
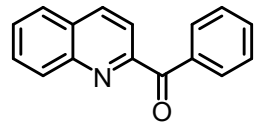
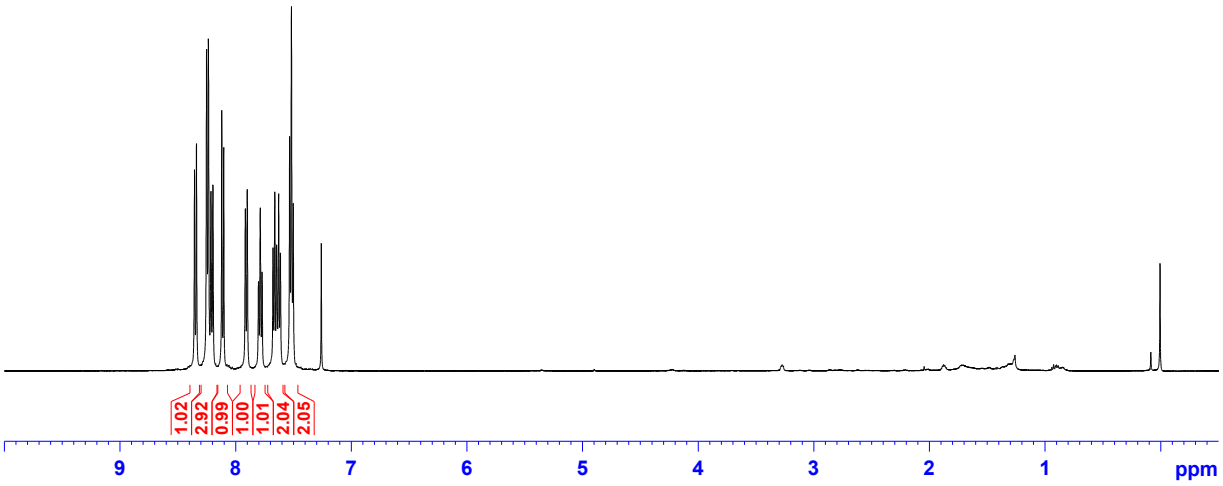
6. NMR Spectra

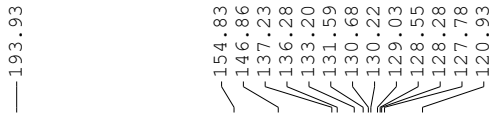


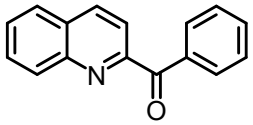


3aa

^{1}H NMR (500 MHz, $CDCl_3$)

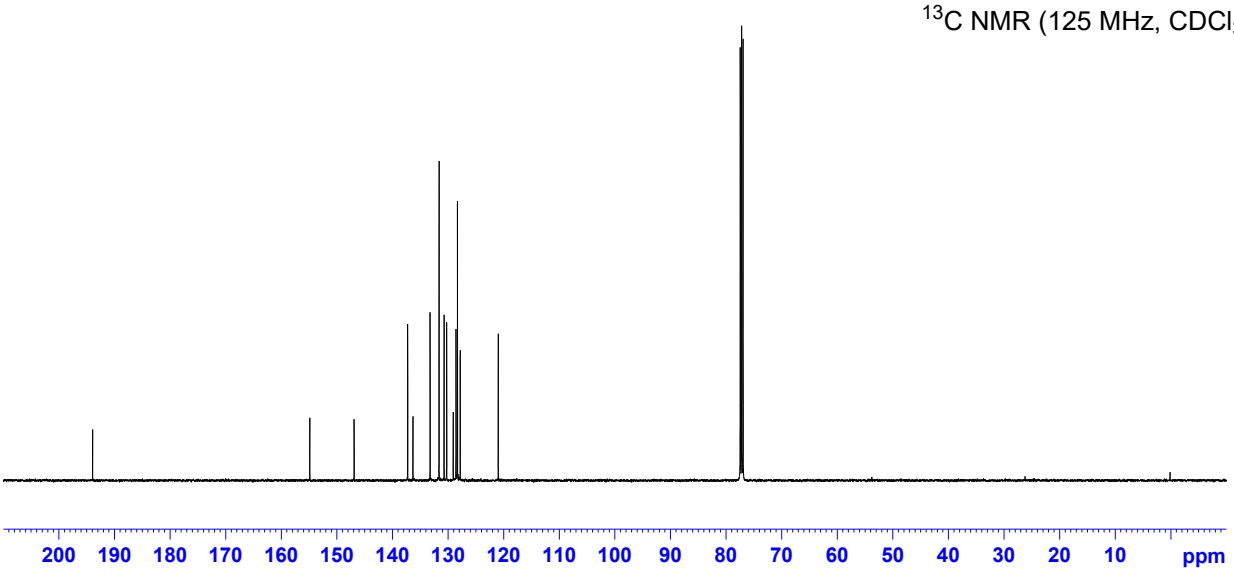


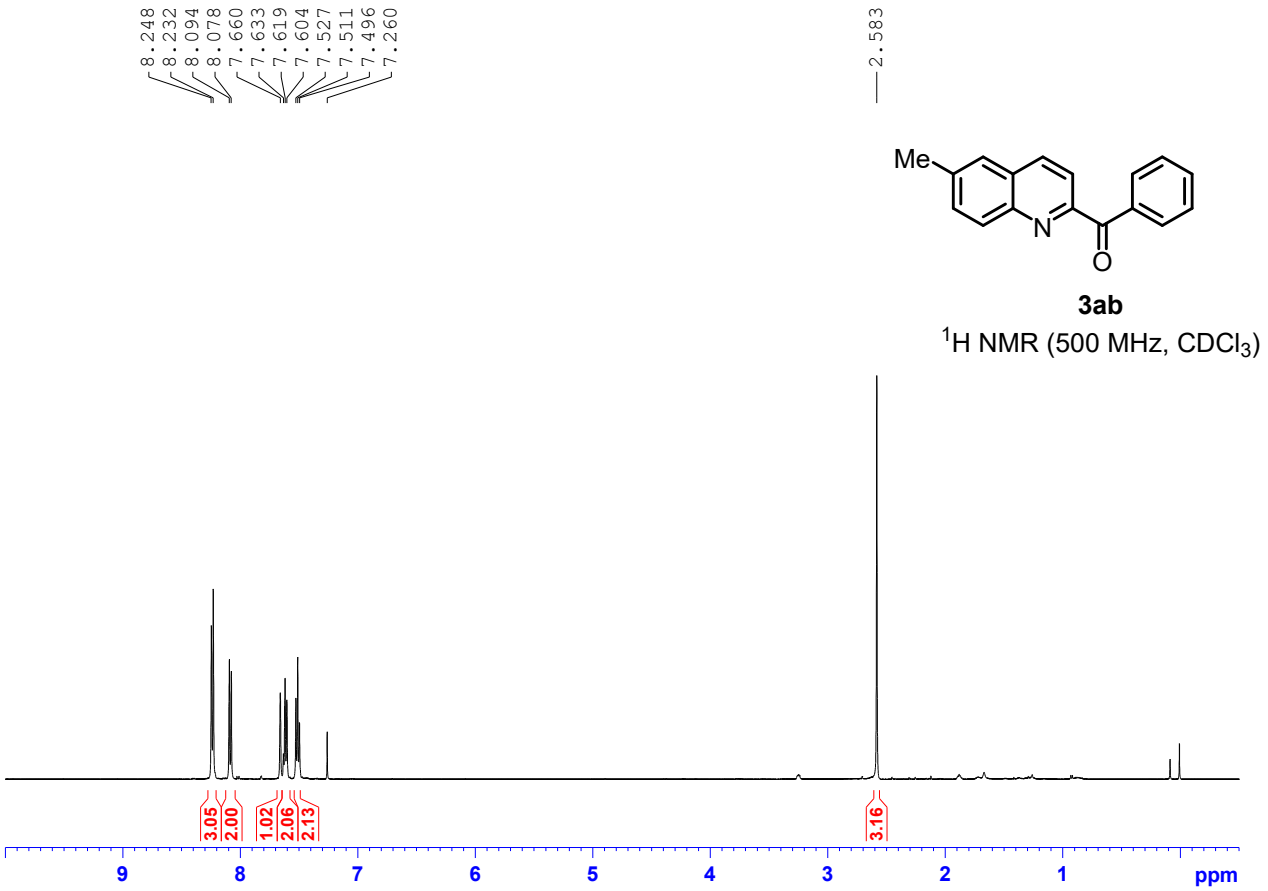




3aa

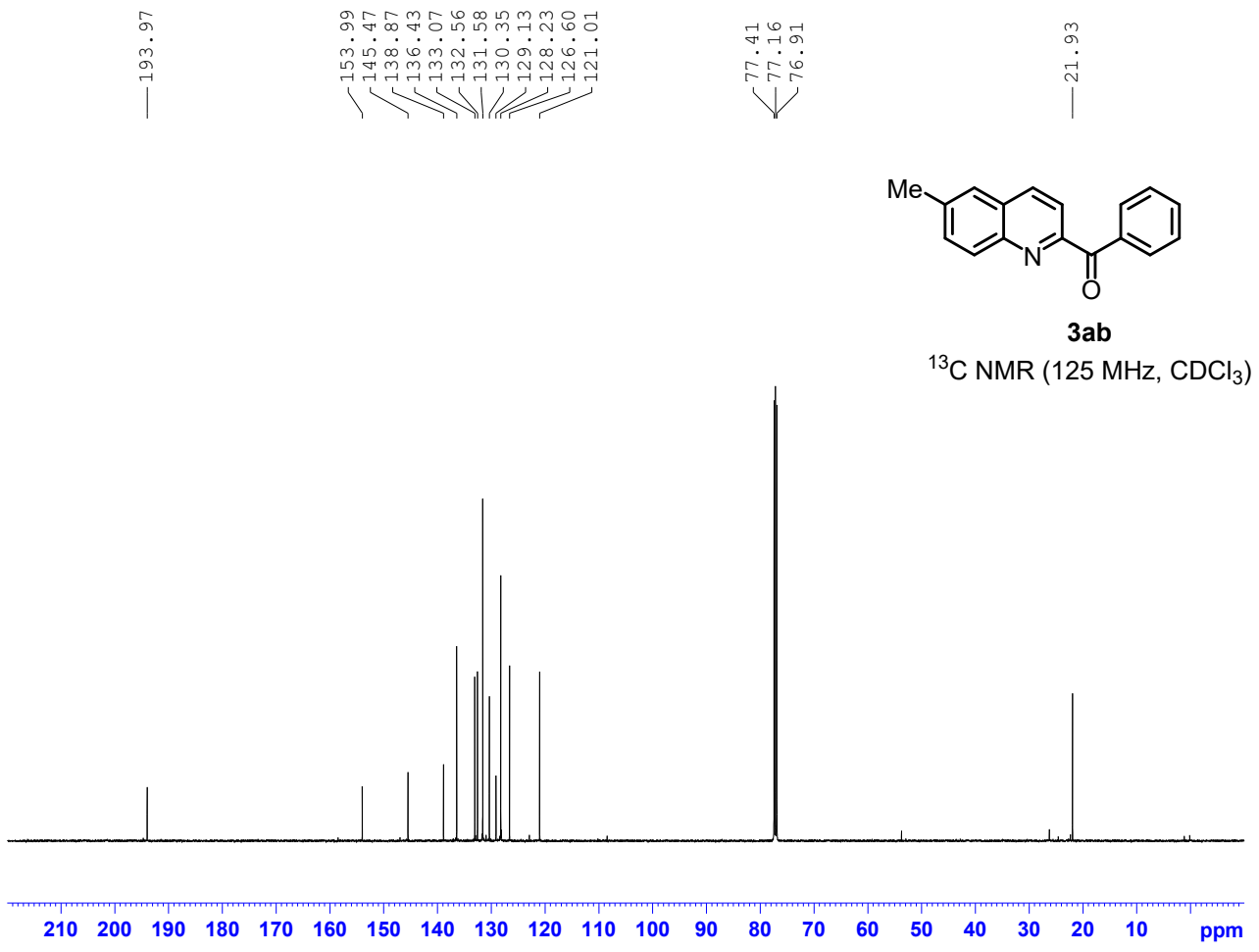
^{13}C NMR (125 MHz, $CDCl_3$)





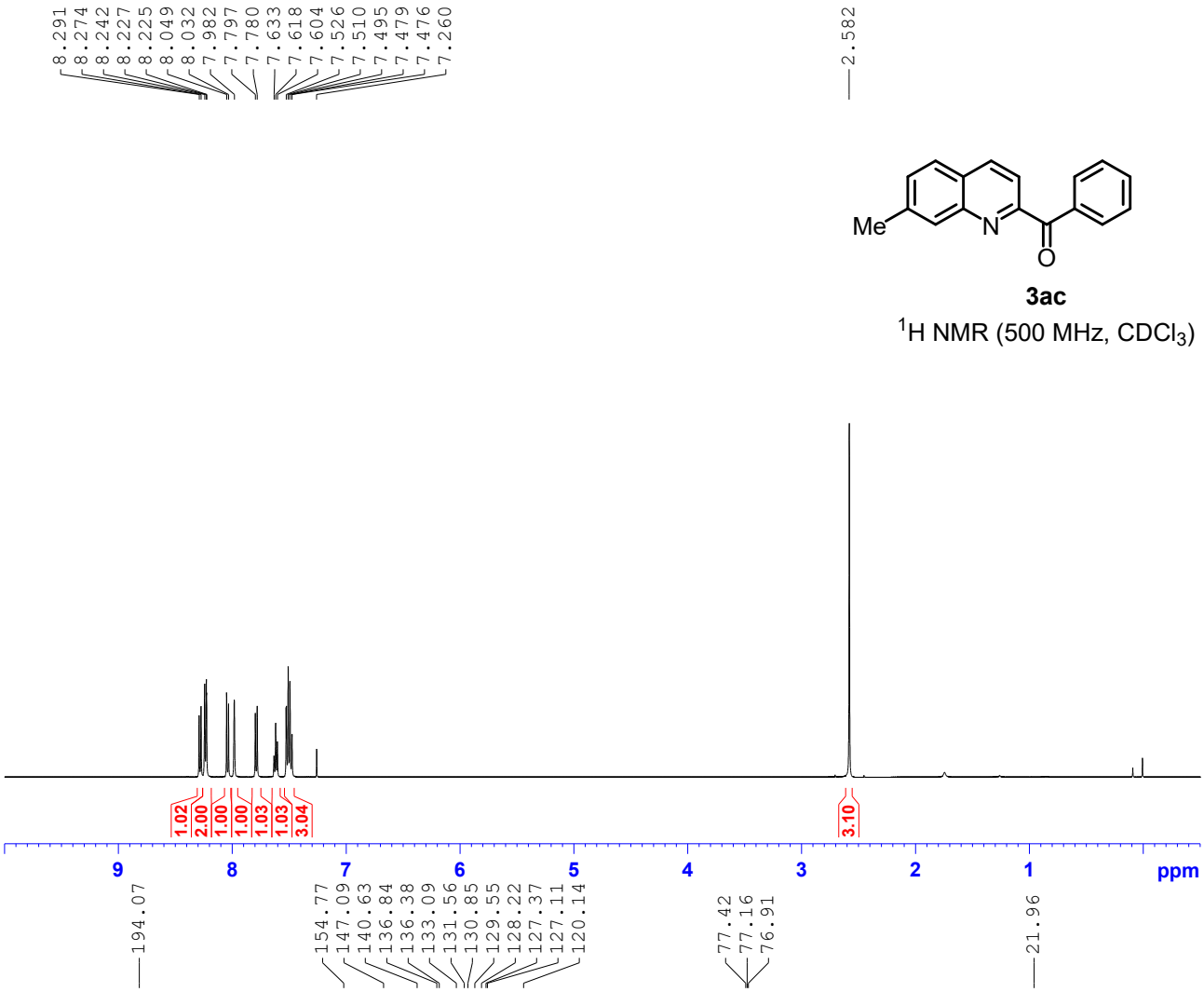
3ab

^{1}H NMR (500 MHz, $CDCl_3$)



3ab

^{13}C NMR (125 MHz, $CDCl_3$)

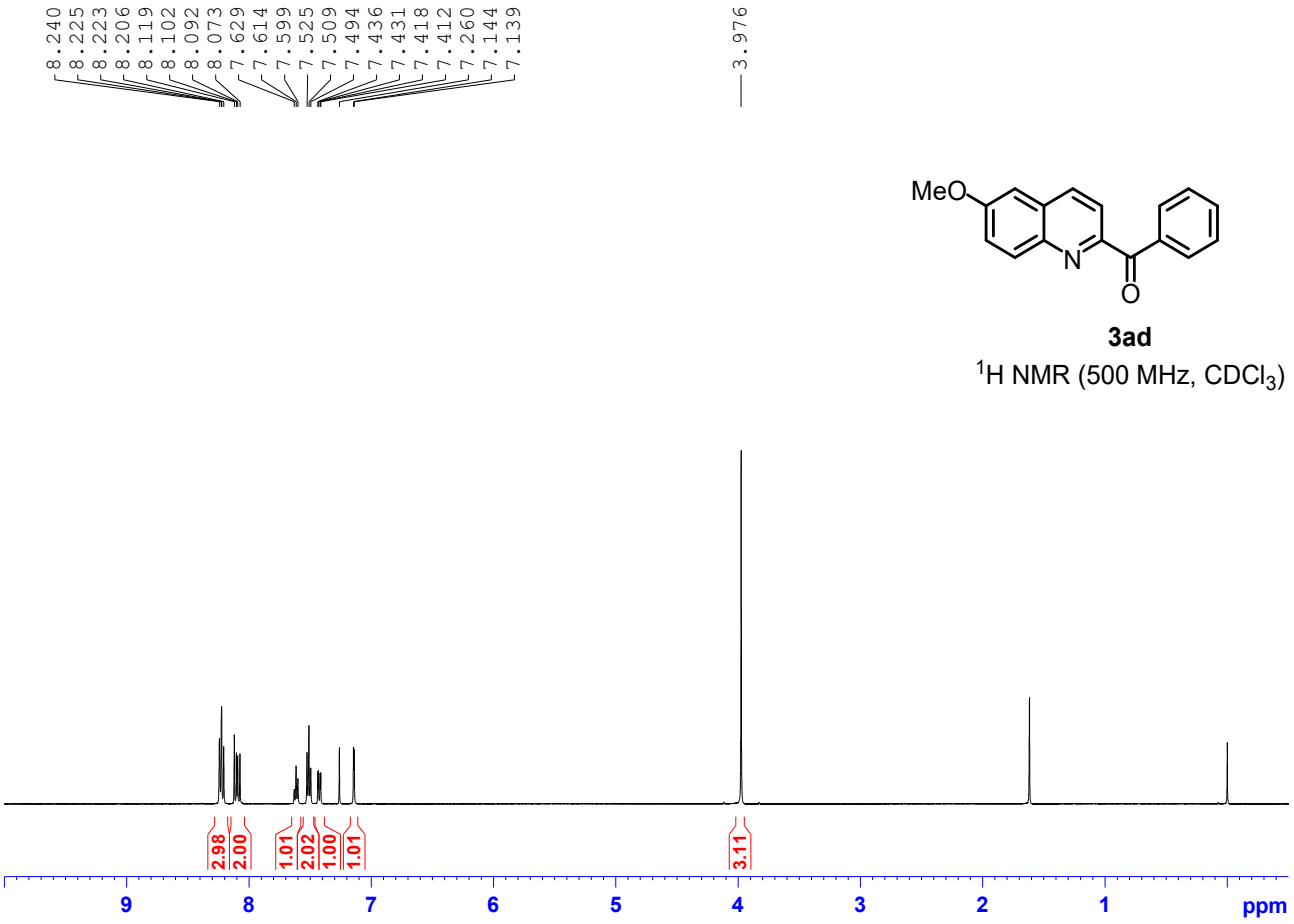


3ac

^{1}H NMR (500 MHz, $CDCl_3$)

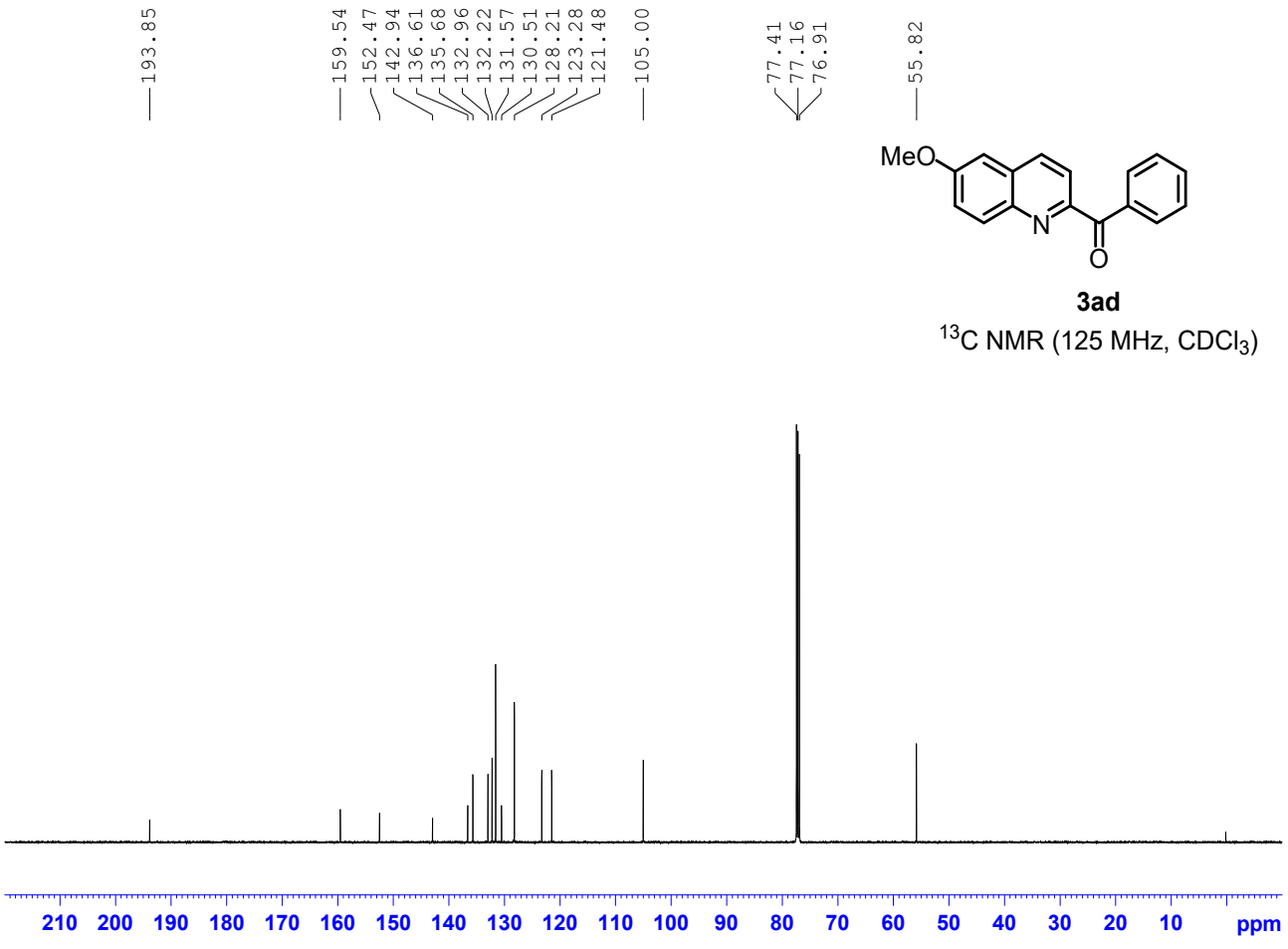
3ac

^{113}C NMR (125 MHz, $CDCl_3$)



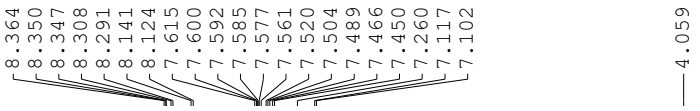
3ad

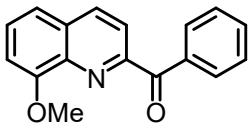
^{1}H NMR (500 MHz, $CDCl_3$)



3ad

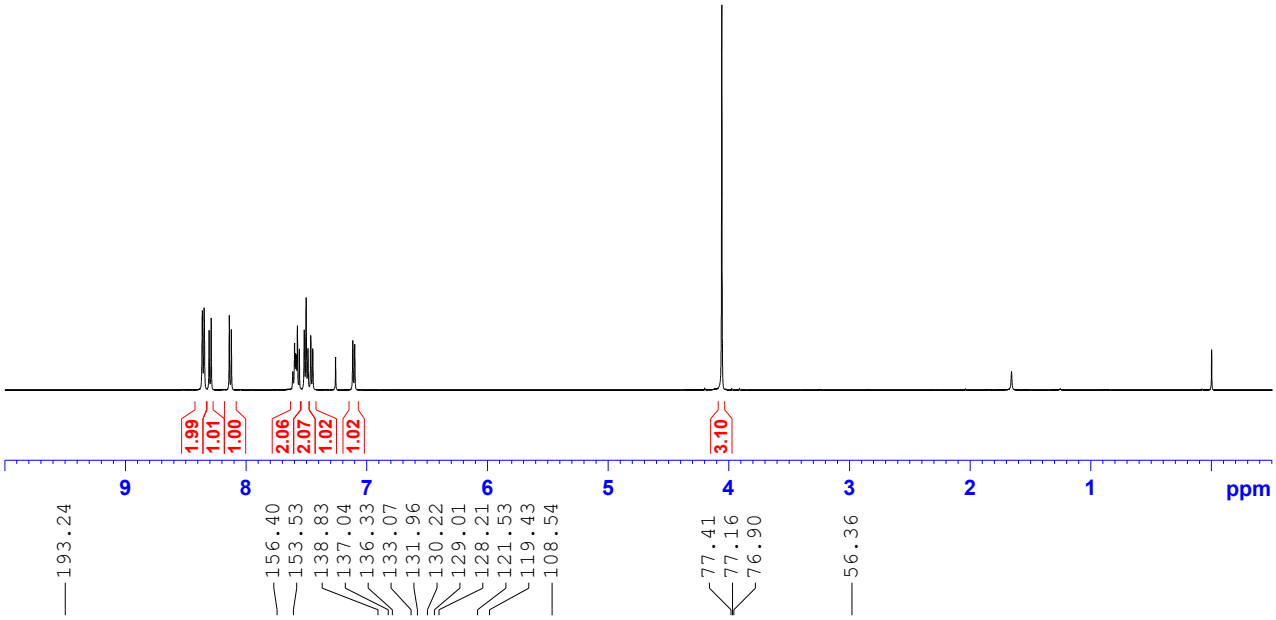
^{13}C NMR (125 MHz, $CDCl_3$)

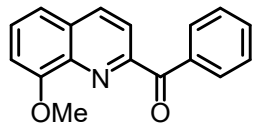




3ae

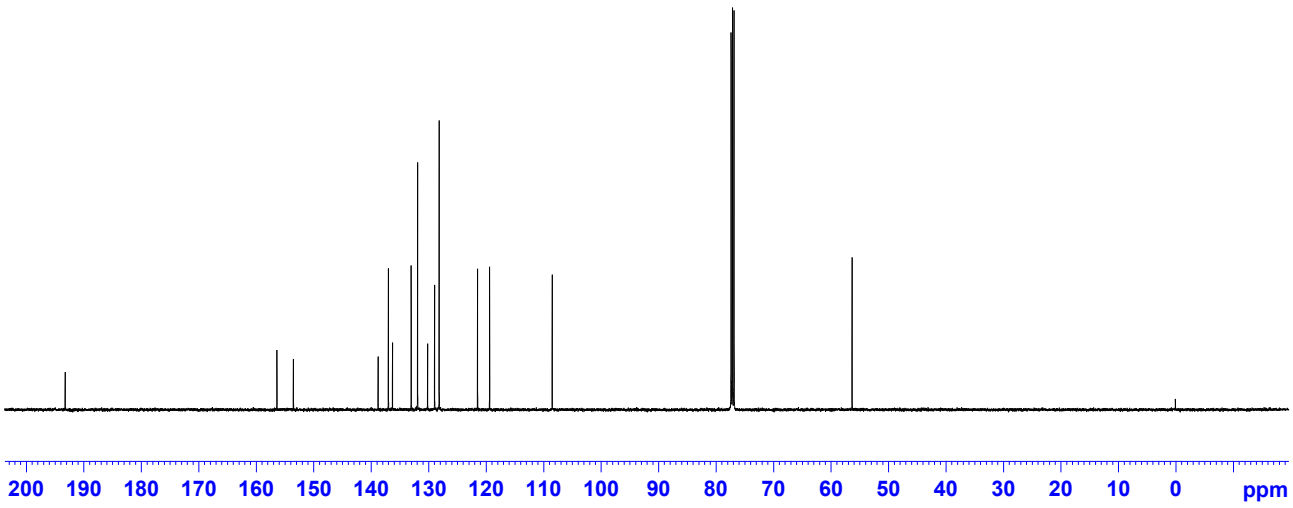
^{1}H NMR (500 MHz, $CDCl_3$)

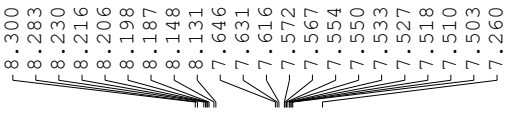


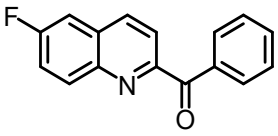


3ae

^{13}C NMR (125 MHz, $CDCl_3$)

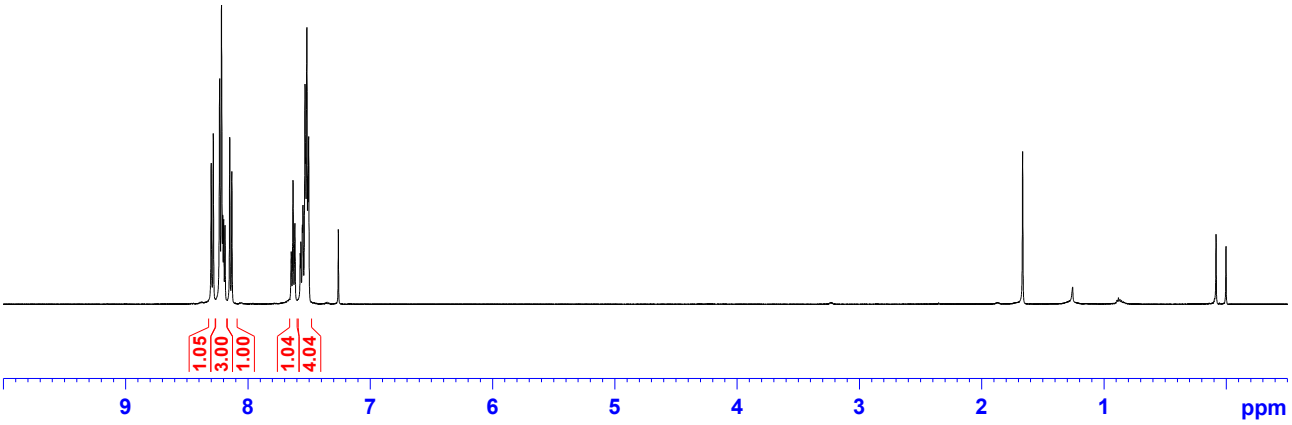


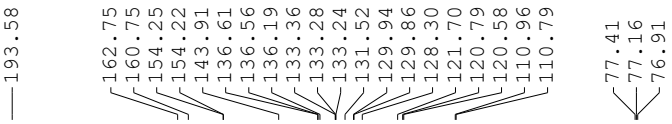


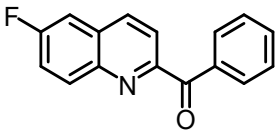


3af

^{1}H NMR (500 MHz, $CDCl_3$)

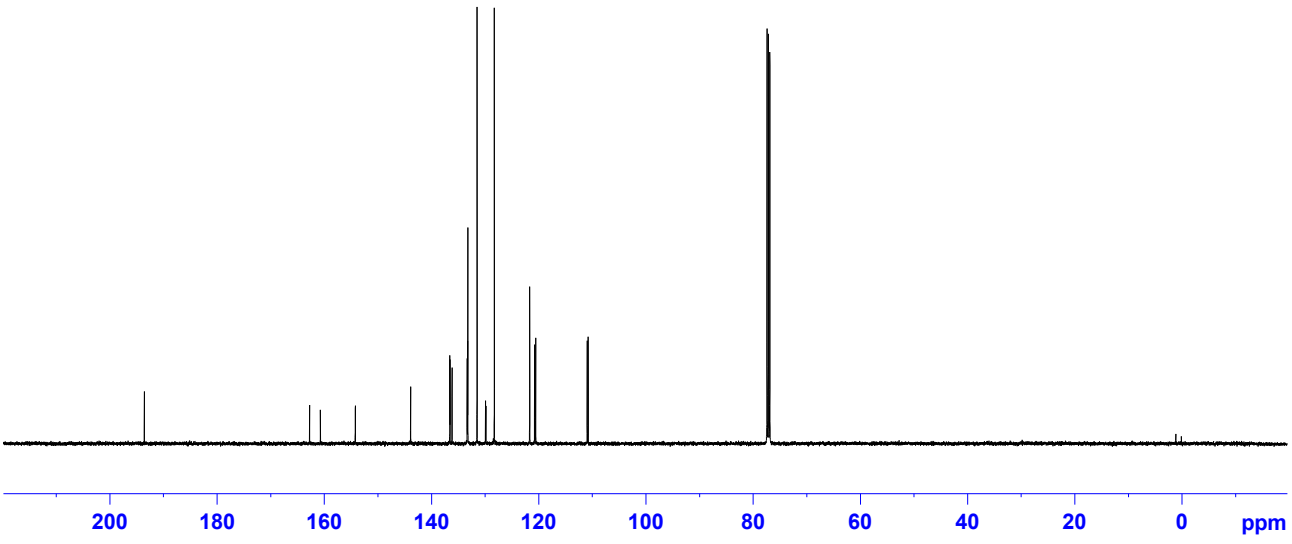


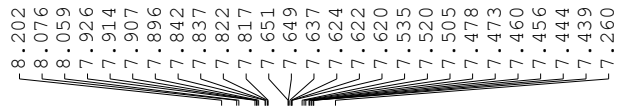


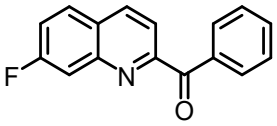


3af

^{13}C NMR (125 MHz, $CDCl_3$)

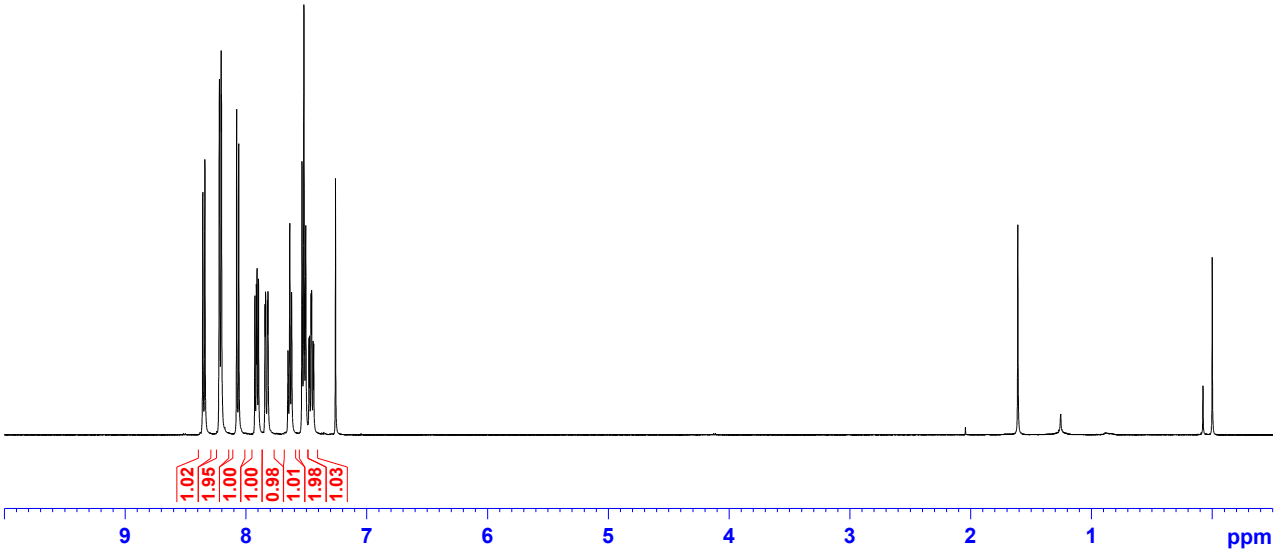


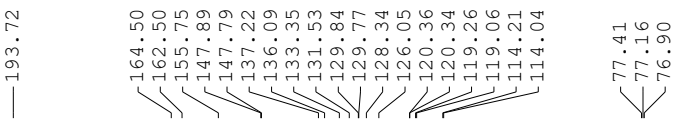


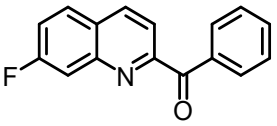


3ag

^{1}H NMR (500 MHz, $CDCl_3$)

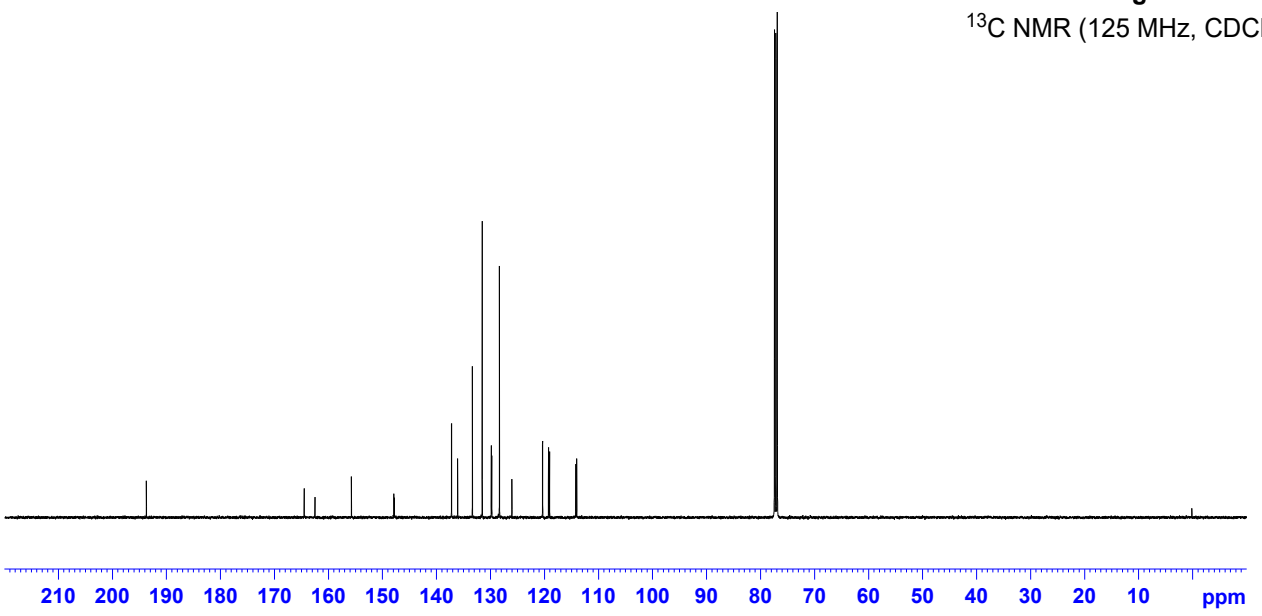


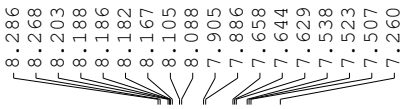


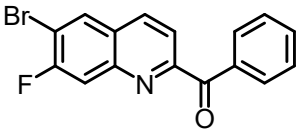


3ag

^{13}C NMR (125 MHz, $CDCl_3$)

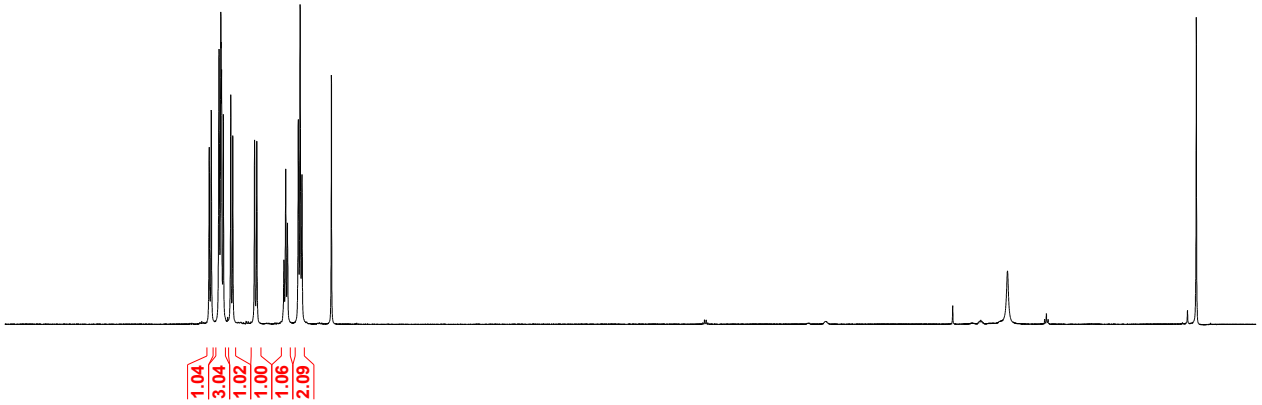


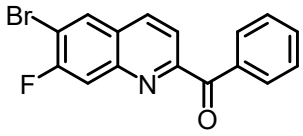




3ah

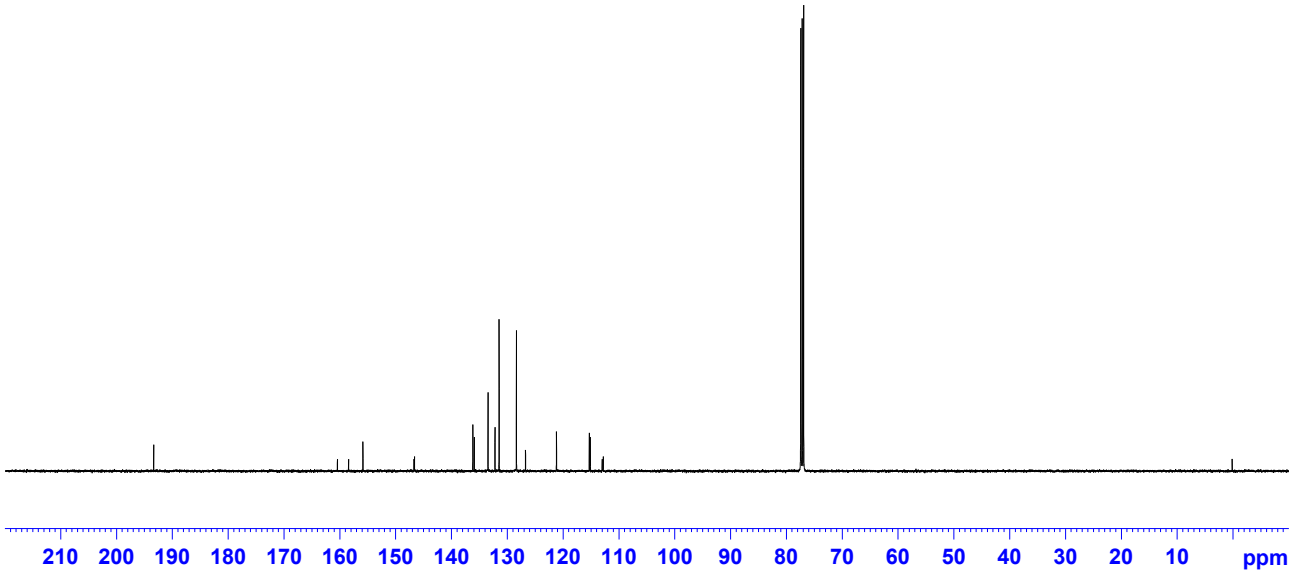
^{1}H NMR (500 MHz, $CDCl_3$)

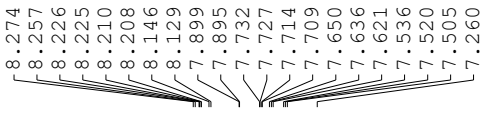


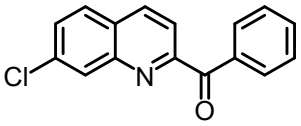


3ah

^{13}C NMR (125 MHz, $CDCl_3$)

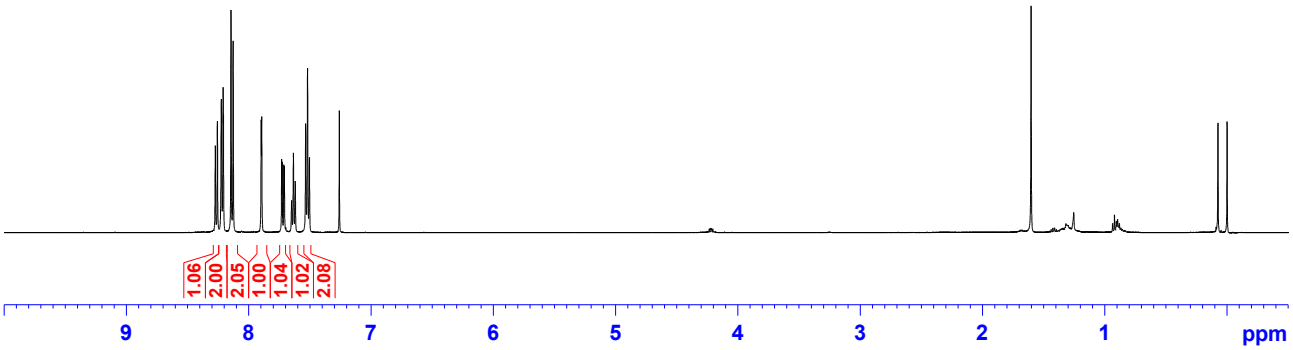


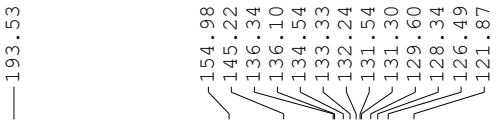


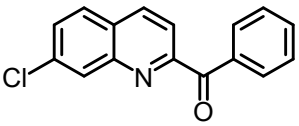


3ai

^{1}H NMR (500 MHz, $CDCl_3$)

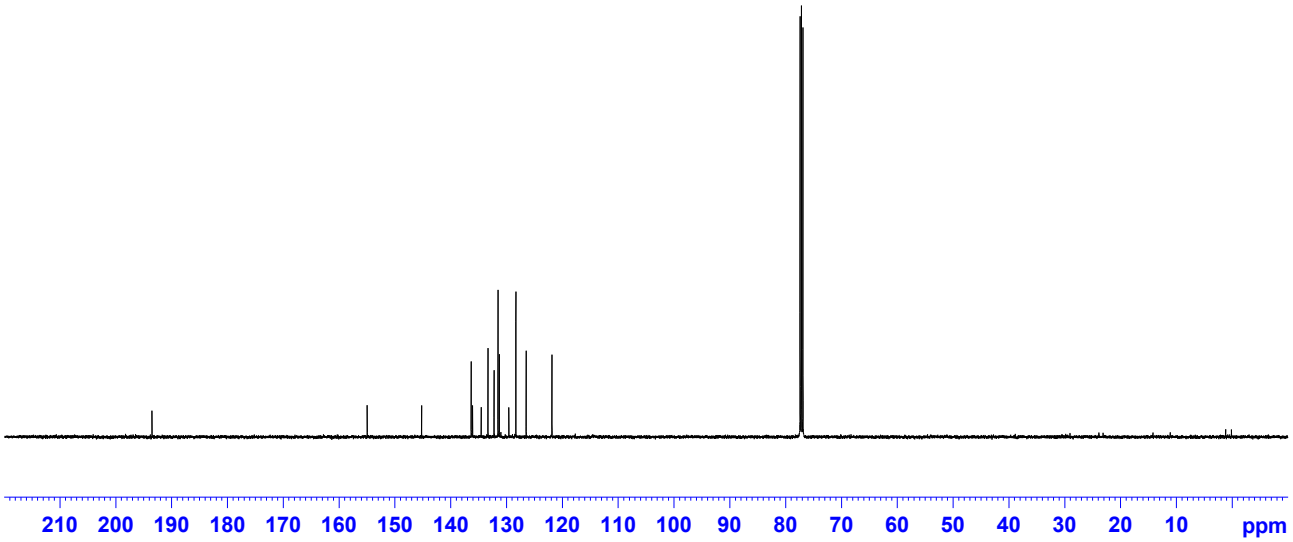


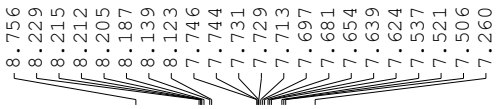


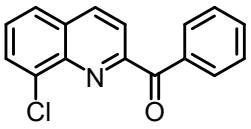


3ai

^{13}C NMR (125 MHz, $CDCl_3$)

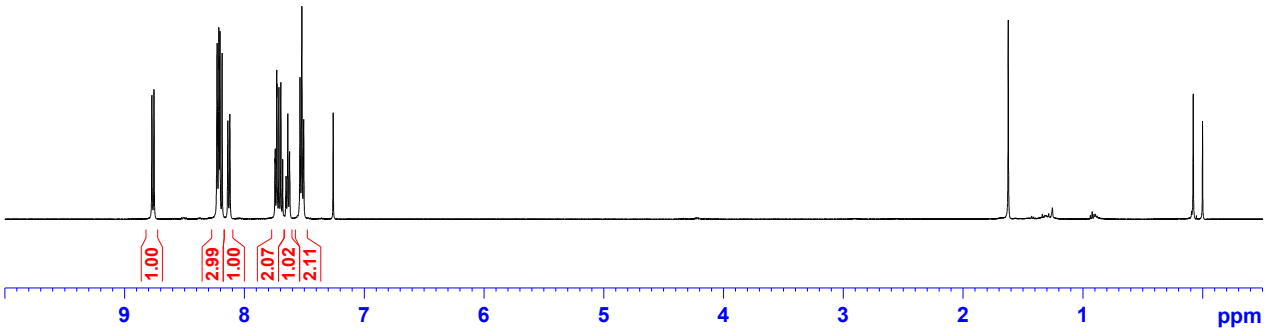


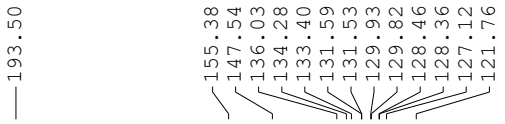


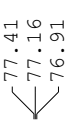


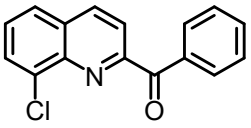
3aj

^{1}H NMR (500 MHz, $CDCl_3$)



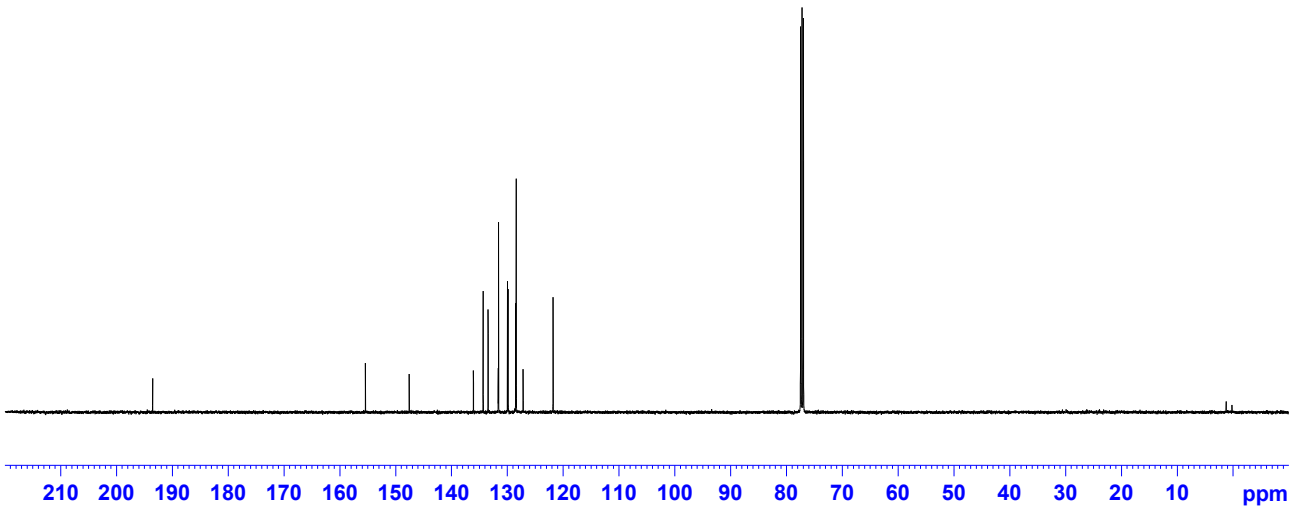


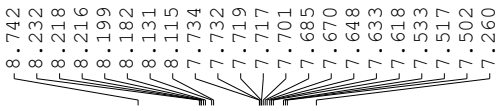


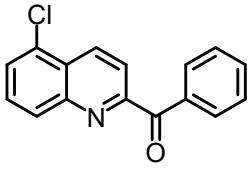


3aj

^{13}C NMR (125 MHz, $CDCl_3$)

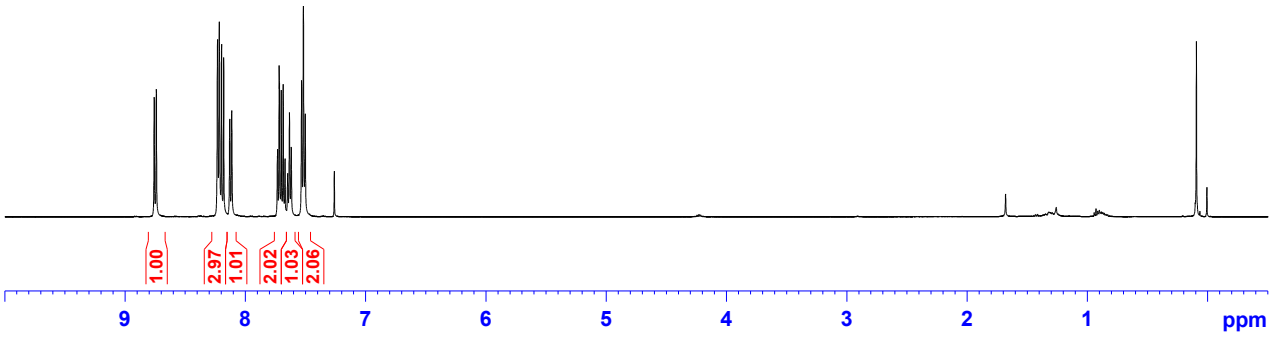


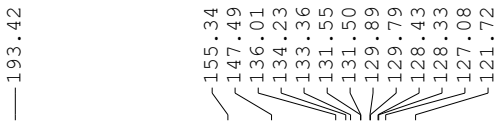


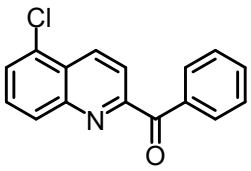


3ak

^{1}H NMR (500 MHz, $CDCl_3$)

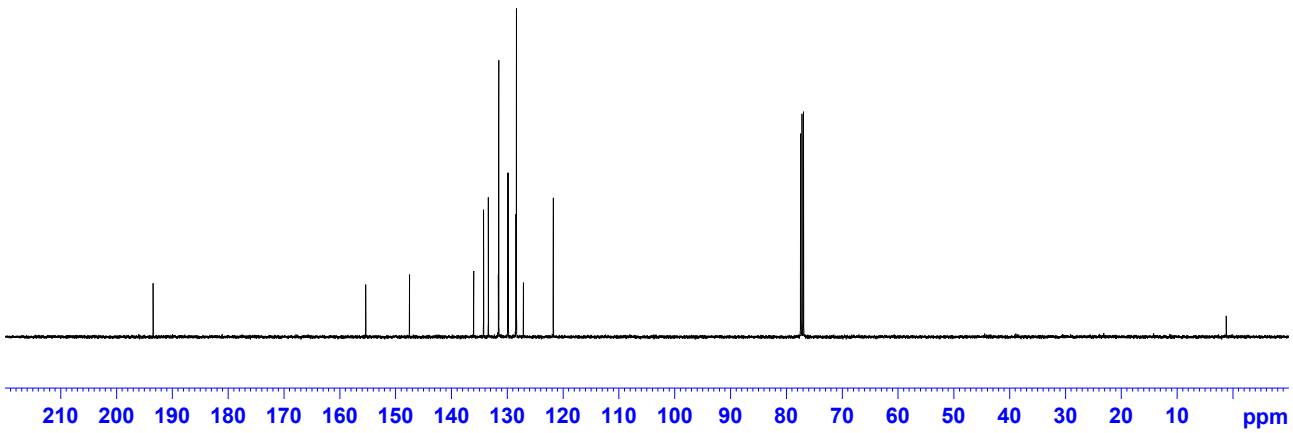


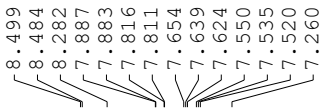


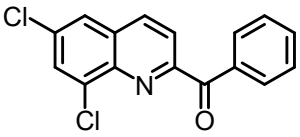


3ak

^{13}C NMR (125 MHz, $CDCl_3$)

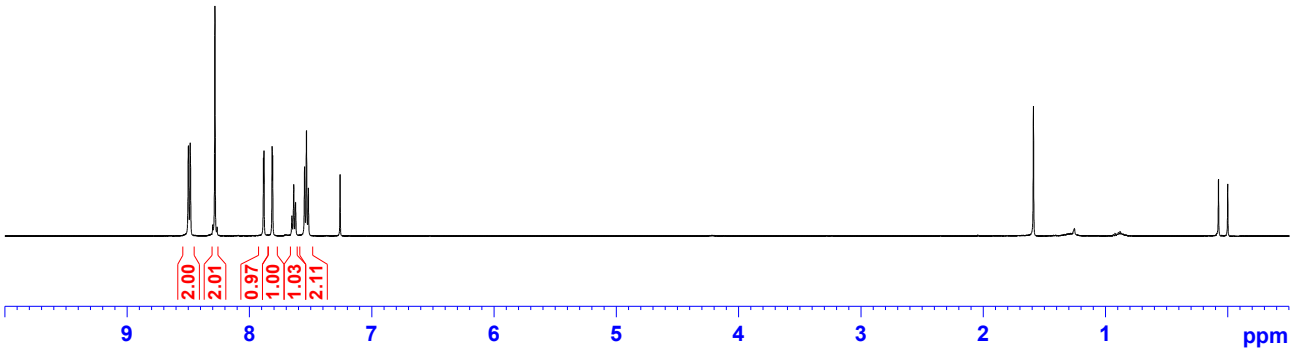


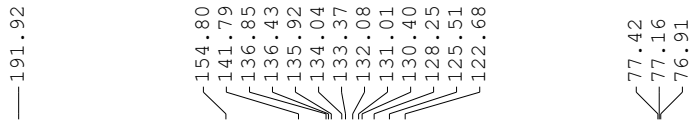


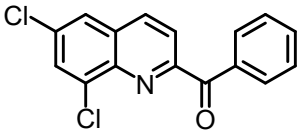


3al

^{1}H NMR (500 MHz, $CDCl_3$)

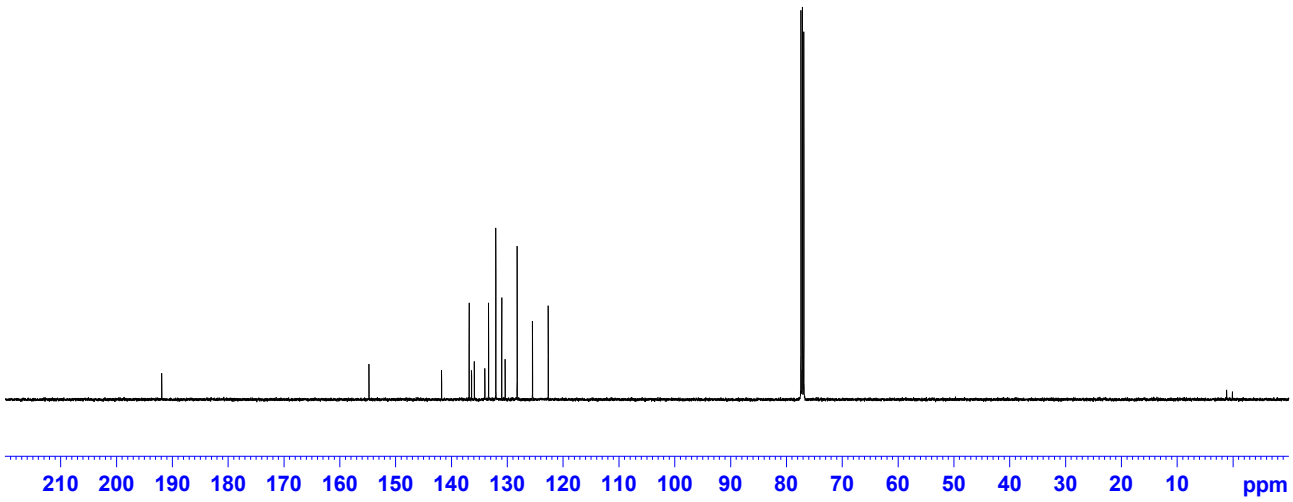


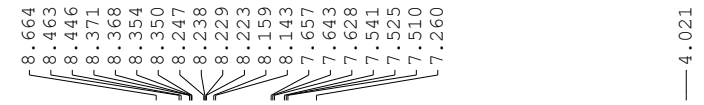


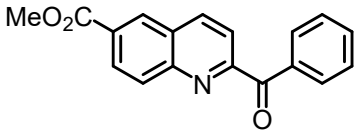


3al

^{13}C NMR (125 MHz, $CDCl_3$)

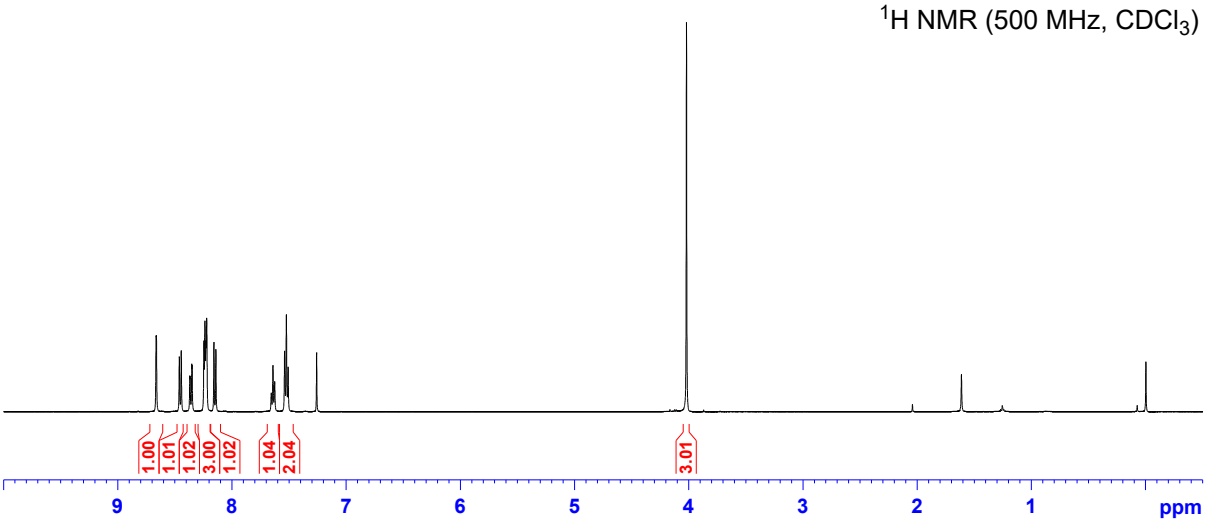


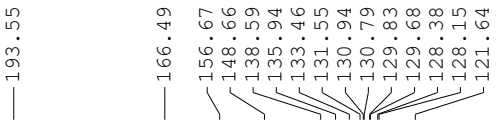


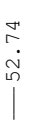


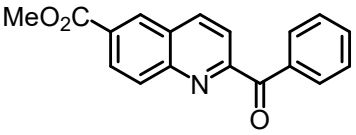
3am

^{1}H NMR (500 MHz, $CDCl_3$)



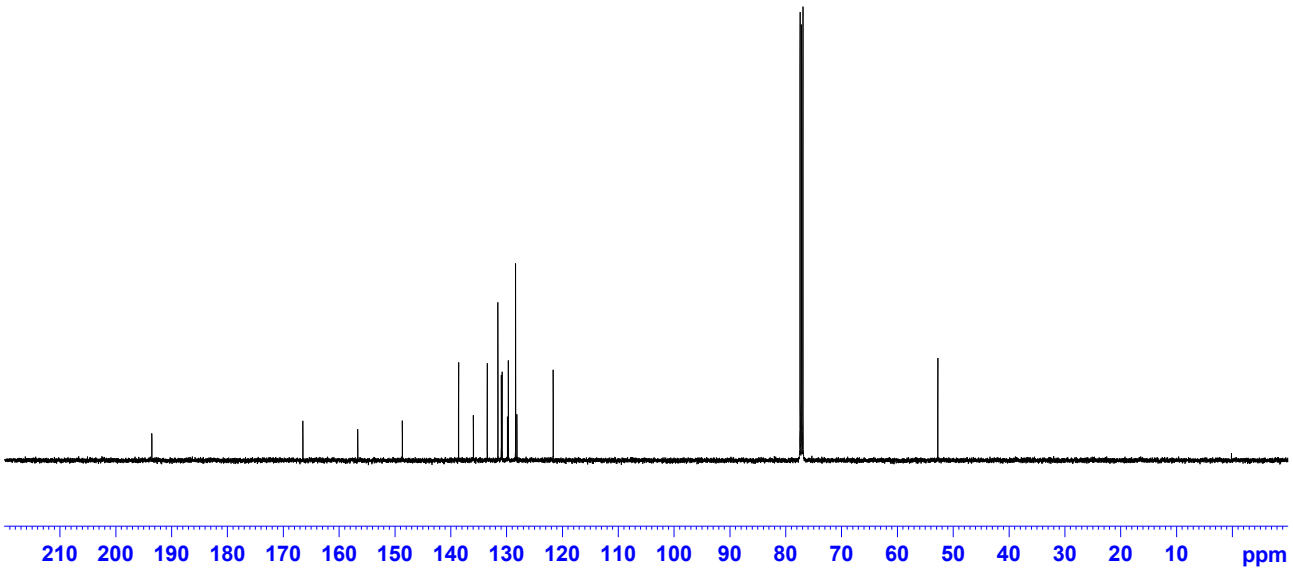


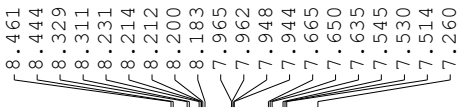


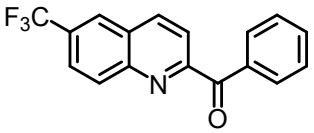


3am

^{13}C NMR (125 MHz, $CDCl_3$)

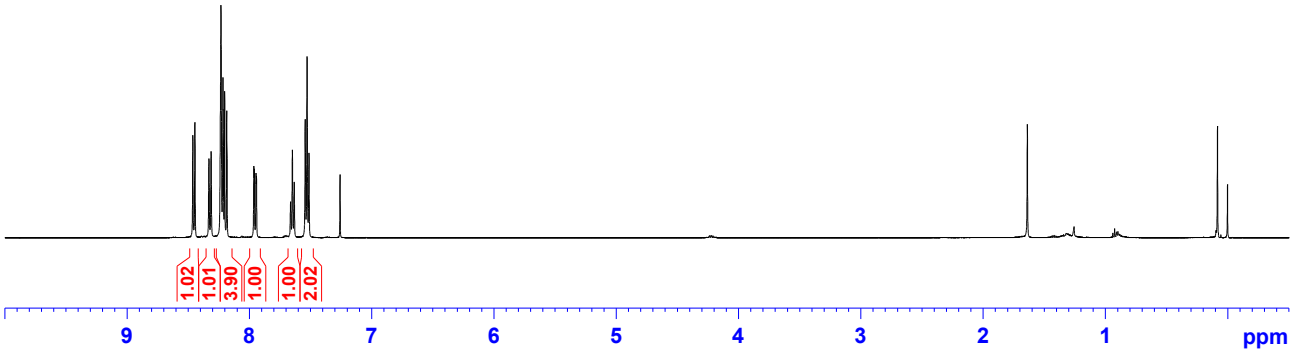


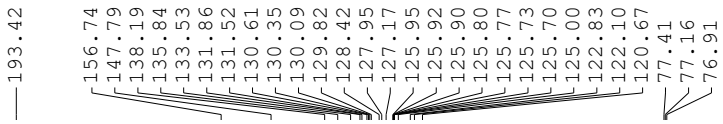


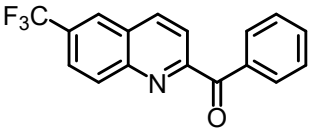


3an

^{1}H NMR (500 MHz, $CDCl_3$)

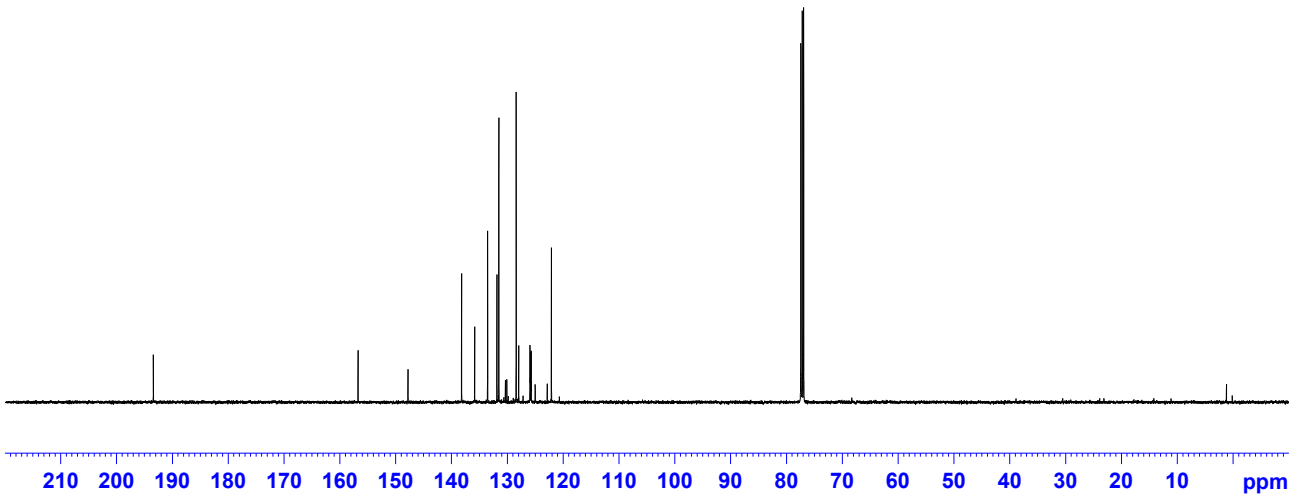


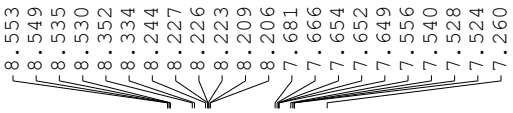


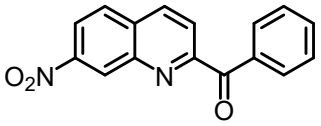


3an

^{13}C NMR (125 MHz, $CDCl_3$)

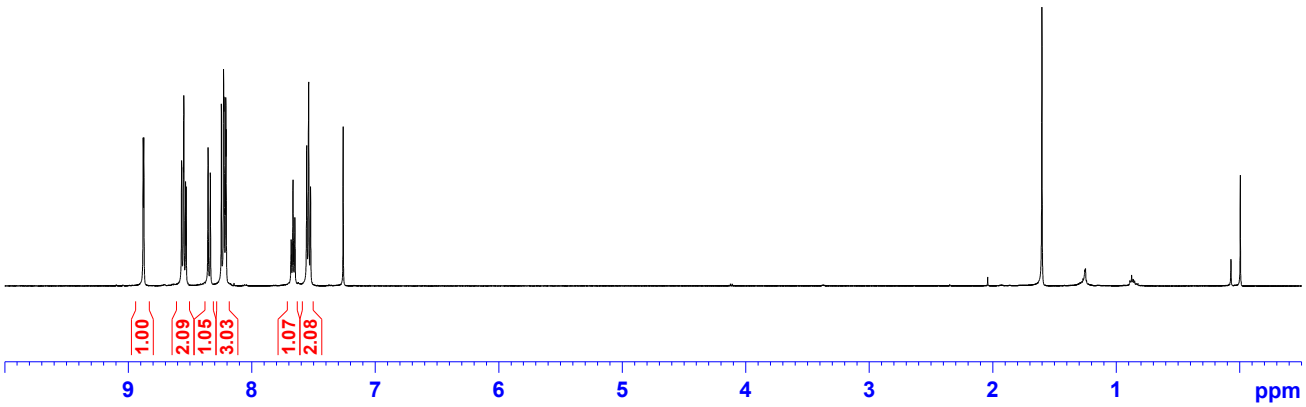


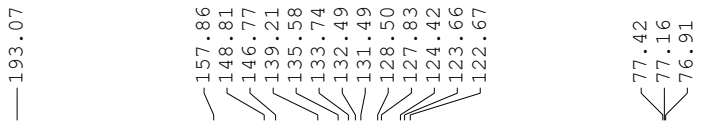


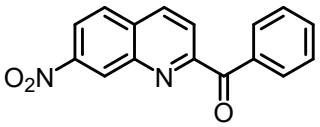


3ao

^{1}H NMR (500 MHz, $CDCl_3$)

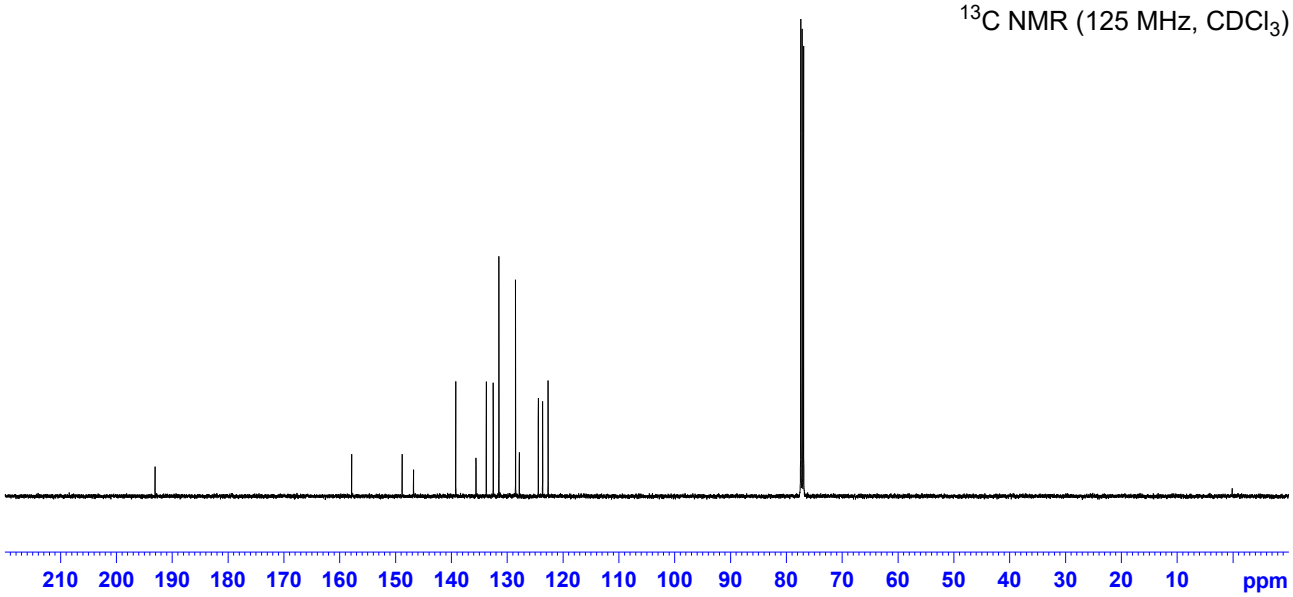


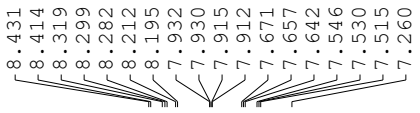


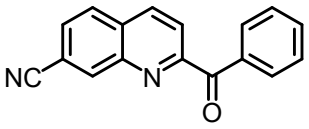


3ao

^{13}C NMR (125 MHz, $CDCl_3$)

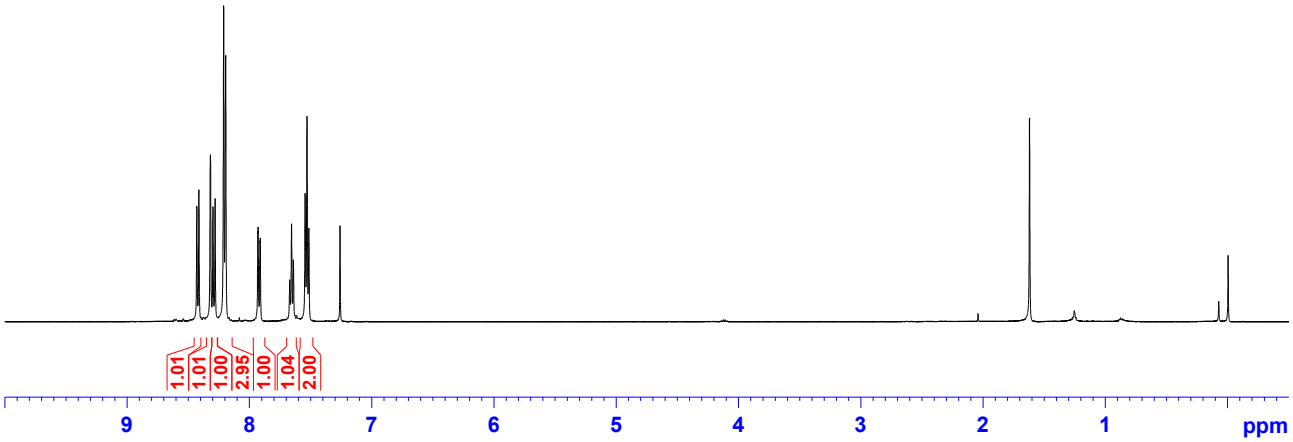


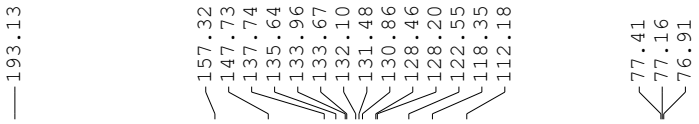


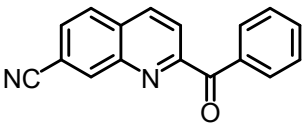


3ap

^{1}H NMR (500 MHz, $CDCl_3$)

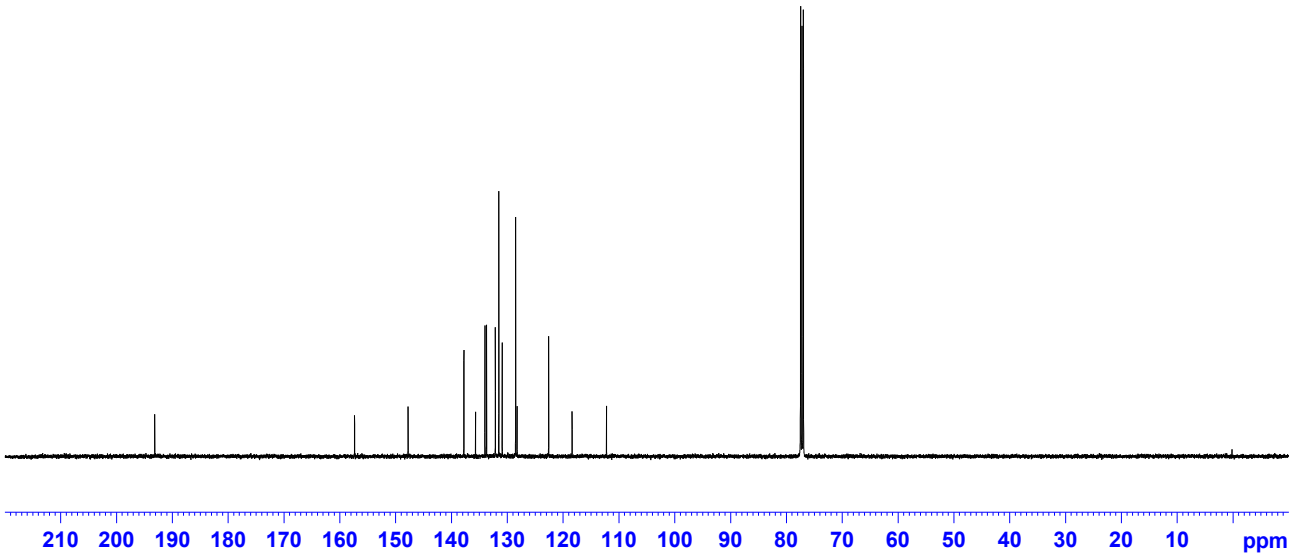


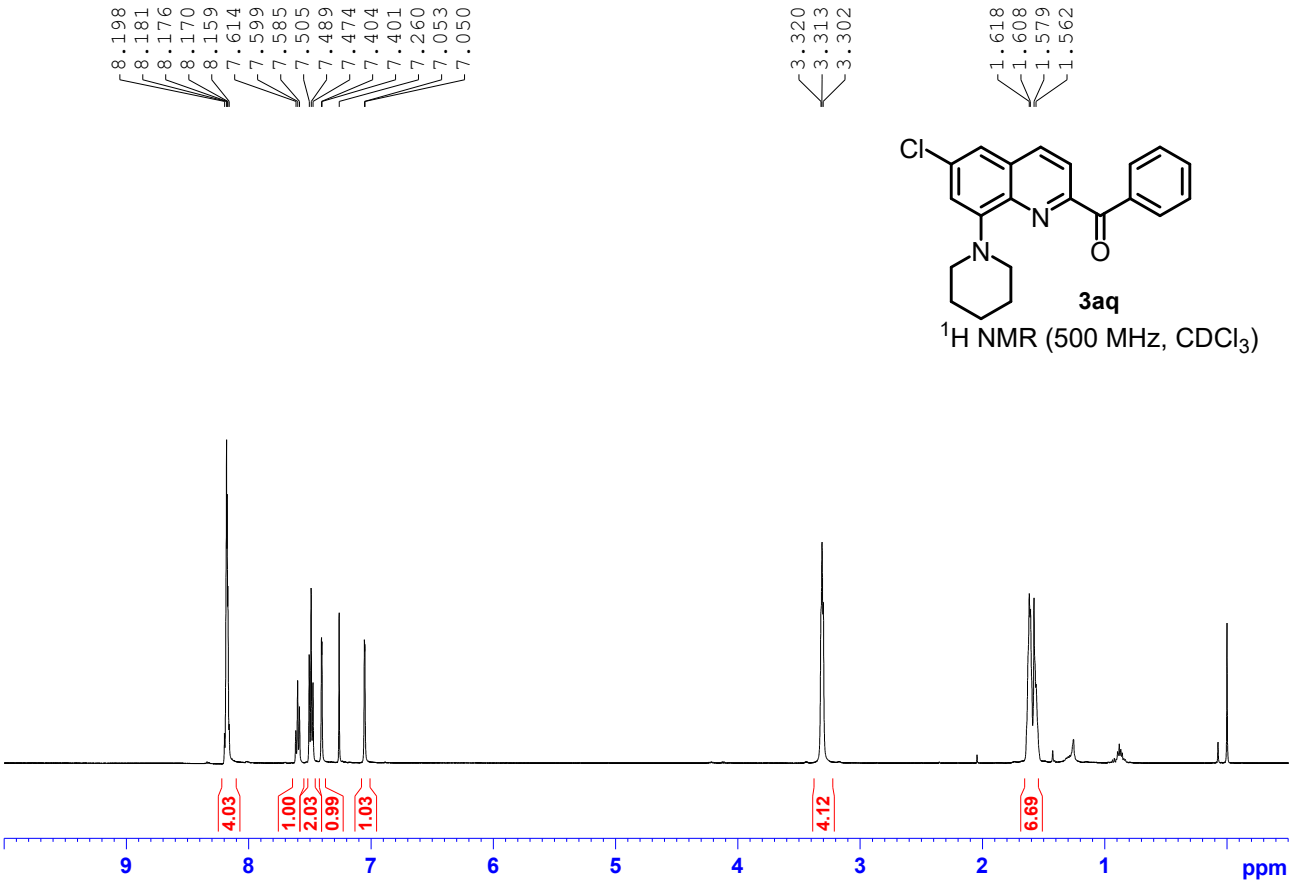




3ap

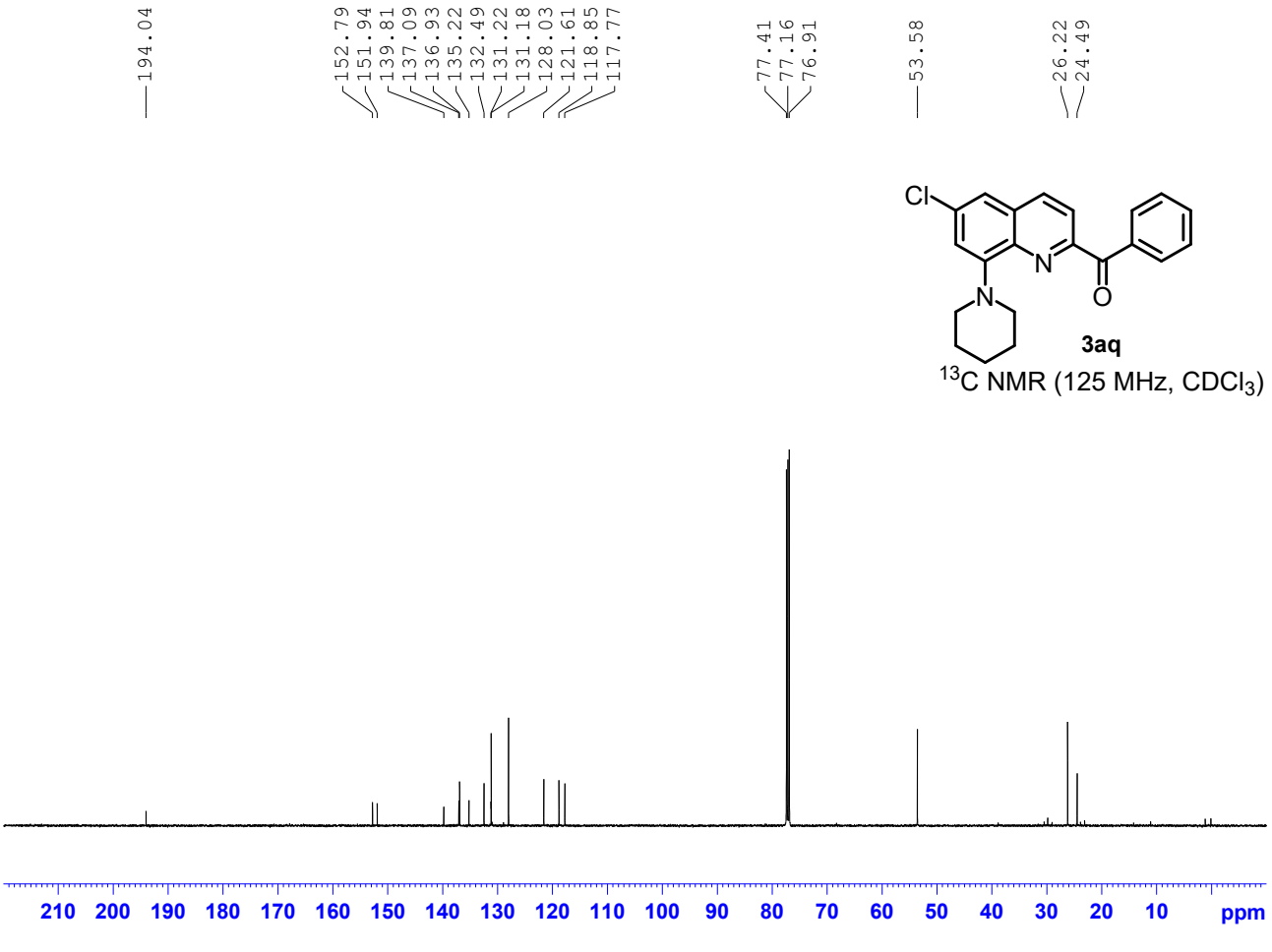
^{13}C NMR (125 MHz, $CDCl_3$)





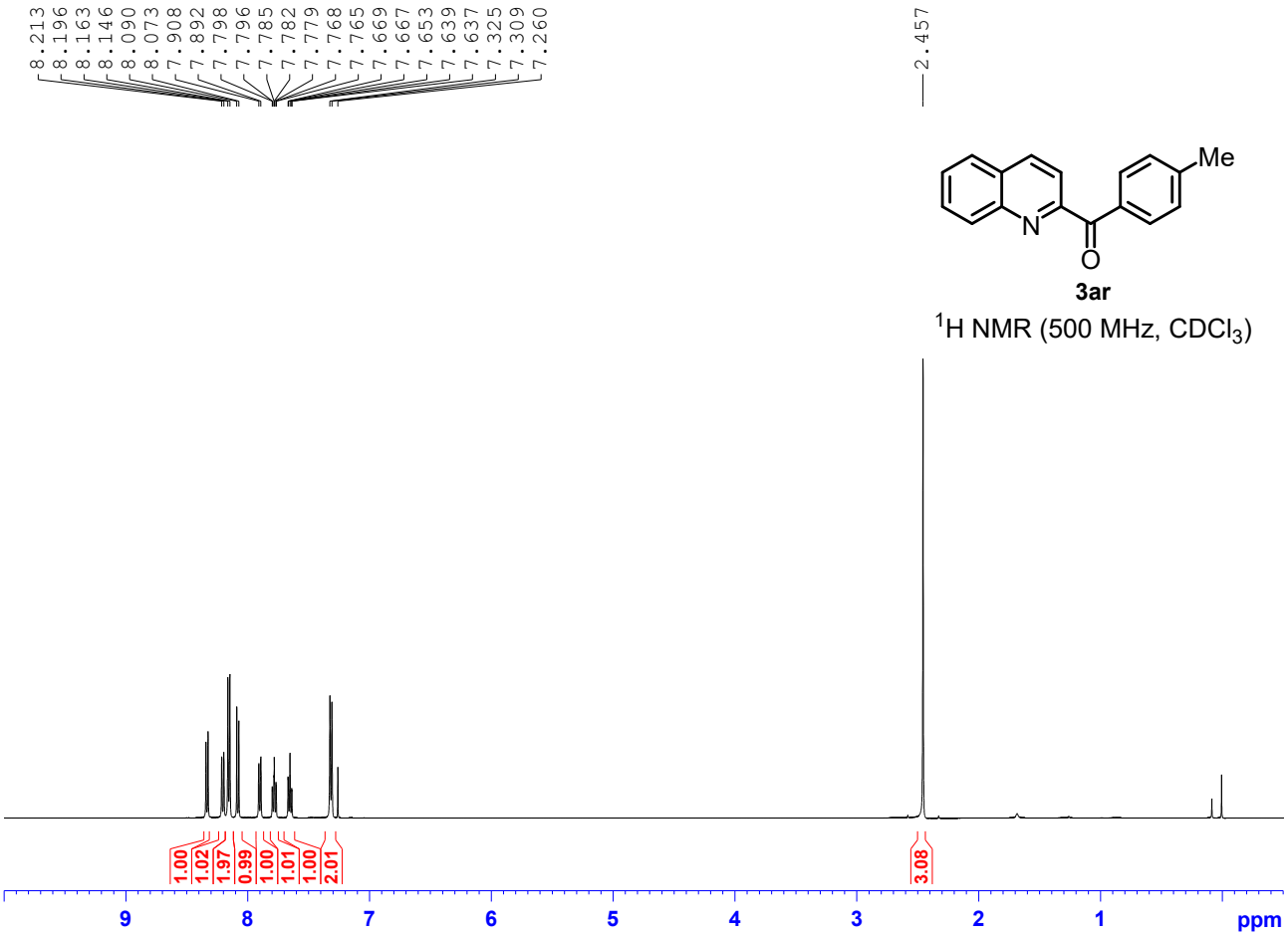
3aq

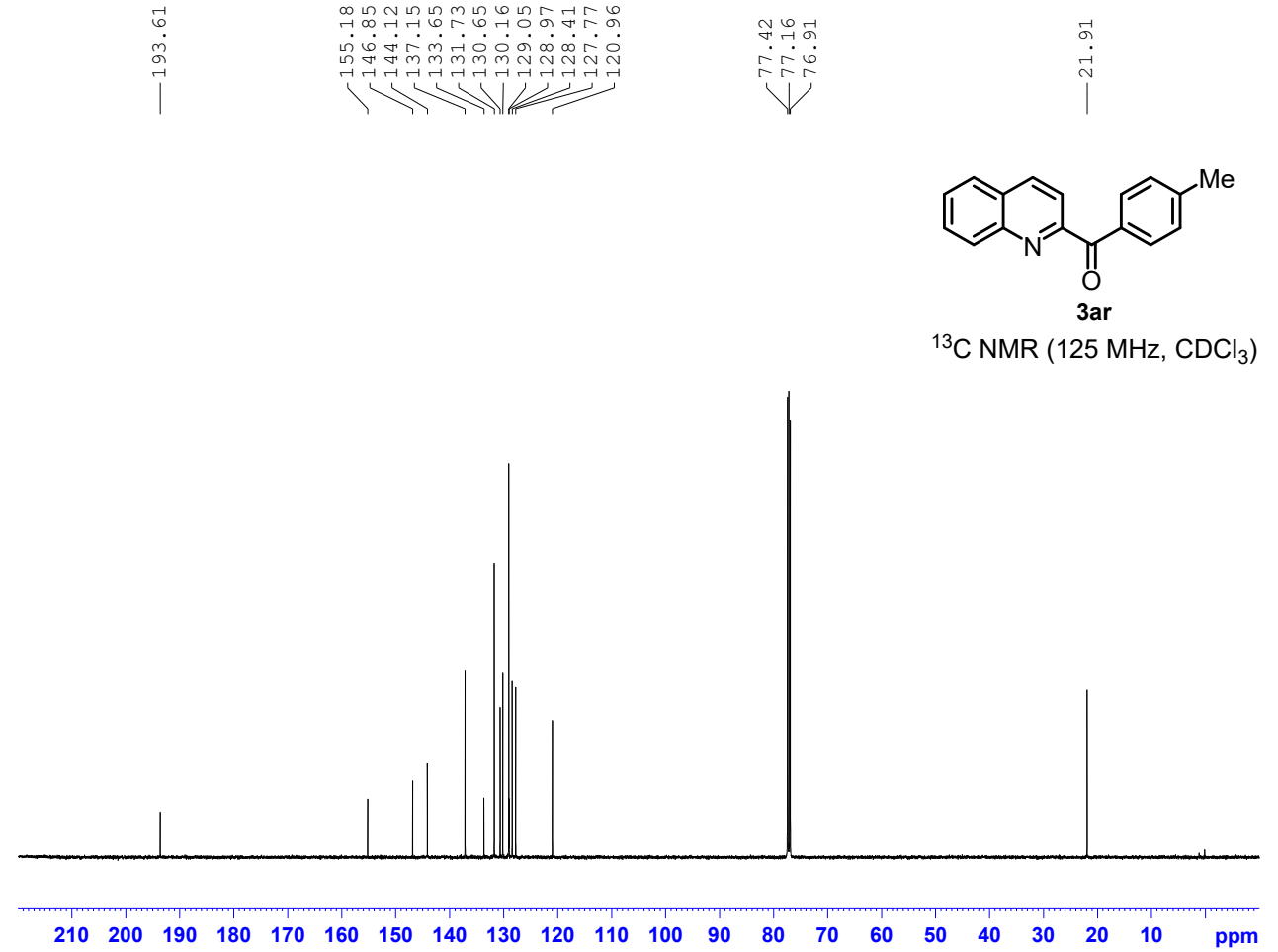
^{1}H NMR (500 MHz, $CDCl_3$)

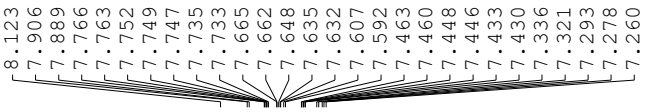


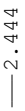
3aq

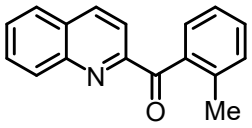
^{13}C NMR (125 MHz, $CDCl_3$)


8.213
8.196
8.163
8.146
8.090
8.073
7.908
7.892
7.798
7.796
7.785
7.782
7.779
7.768
7.765
7.669
7.667
7.653
7.639
7.637
7.325
7.309
7.260
2.457
Me
N
O
3ar
1H NMR (500 MHz, CDCl3)
1.00
1.02
1.97
0.99
1.00
1.01
1.00
2.01
3.08
9
8
7
6
5
4
3
2
1
ppm


193.61
155.18
146.85
144.12
137.15
133.65
131.73
130.65
130.16
129.05
128.97
128.41
127.77
120.96
77.42
77.16
76.91
21.91
Me
N
O
3ar
13C NMR (125 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

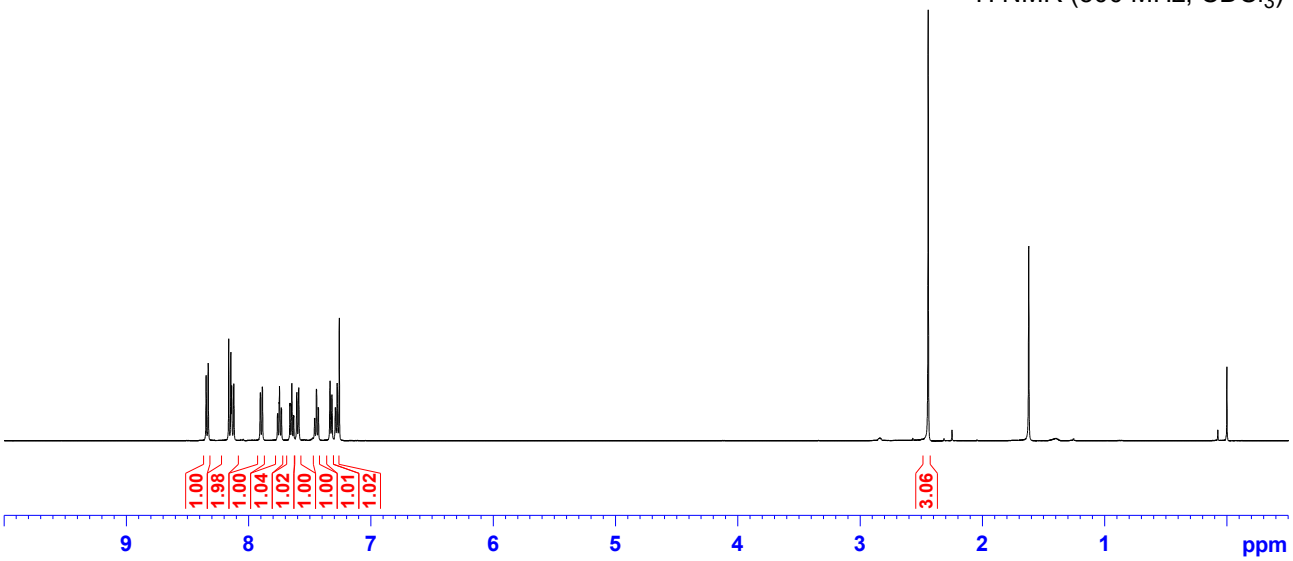


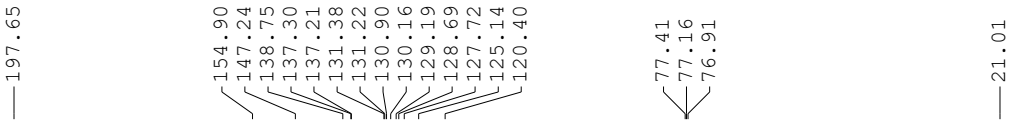


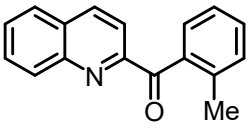


3as

^{1}H NMR (500 MHz, $CDCl_3$)

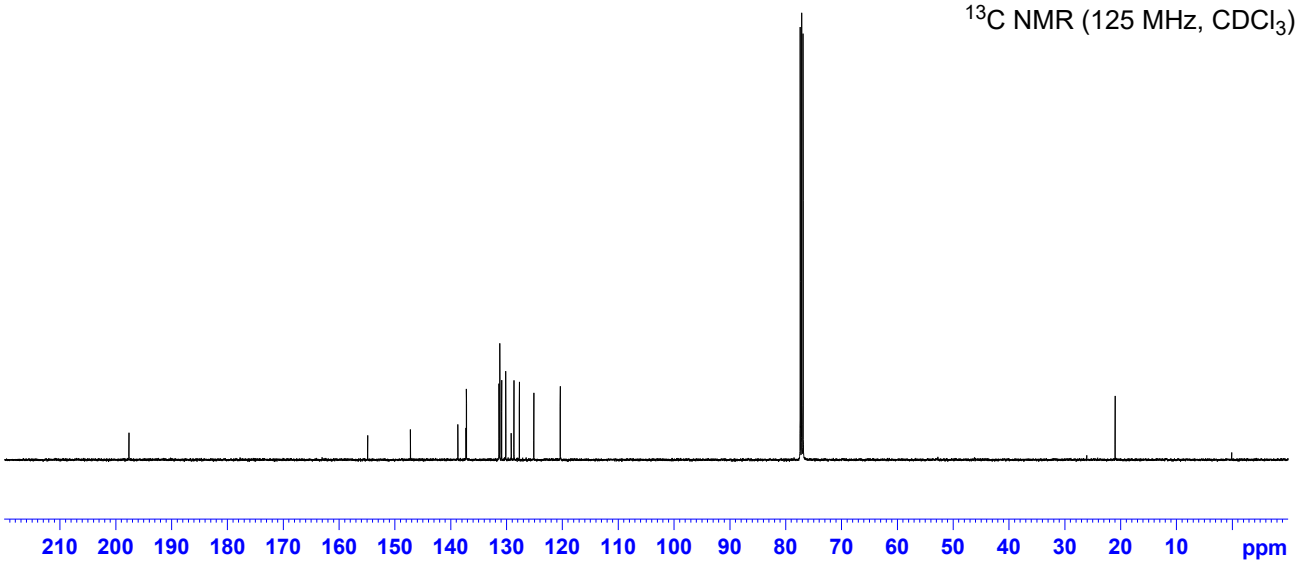


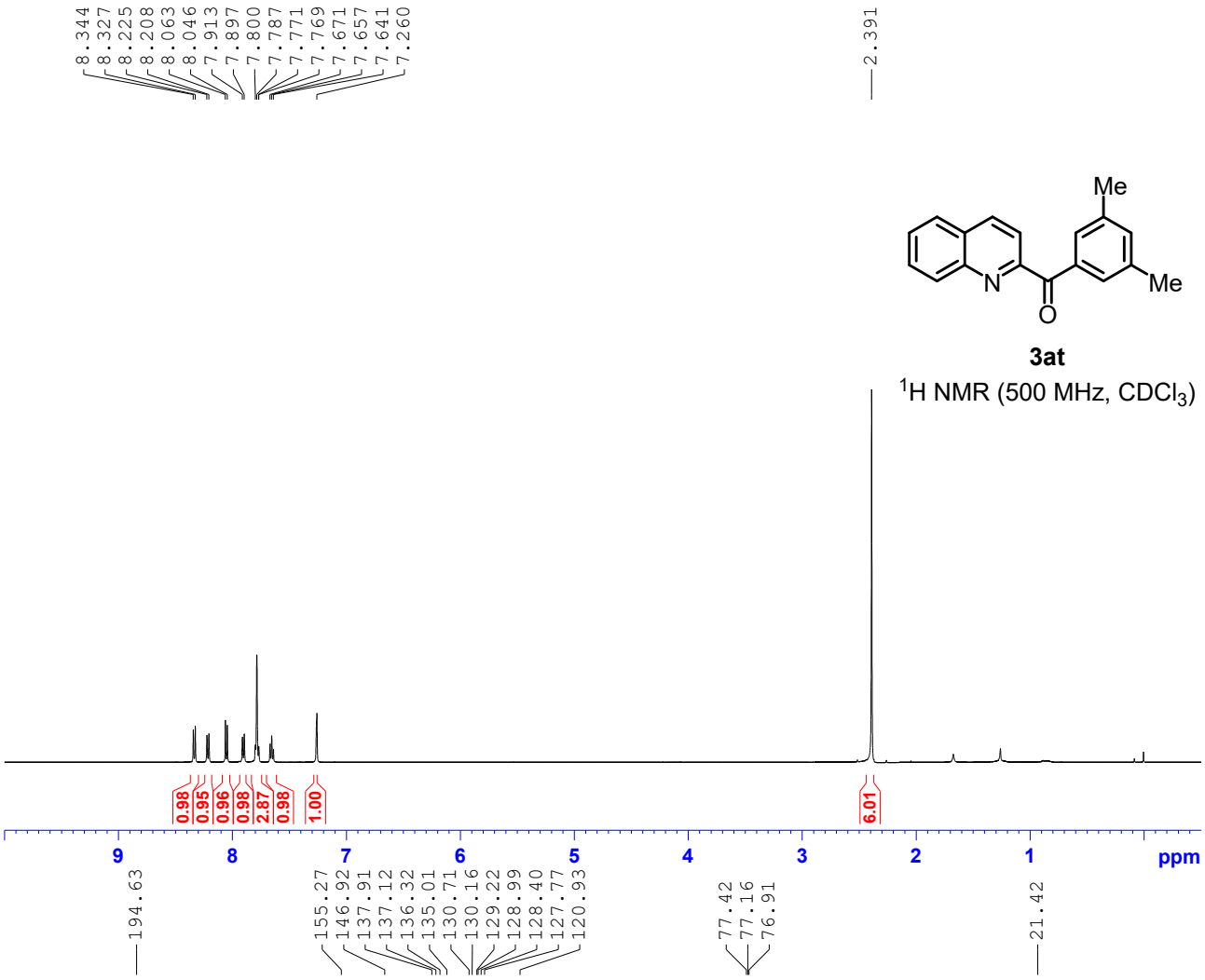




3as

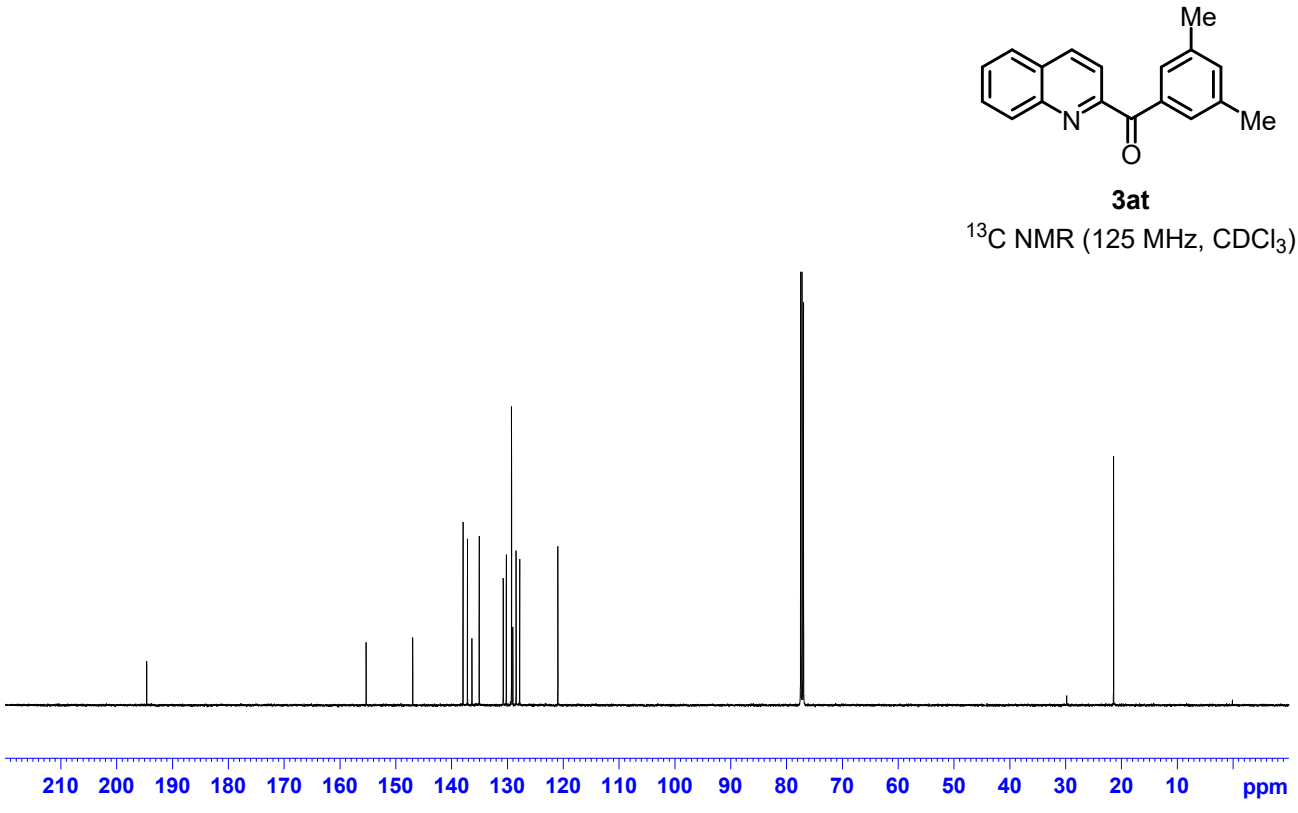
^{13}C NMR (125 MHz, $CDCl_3$)





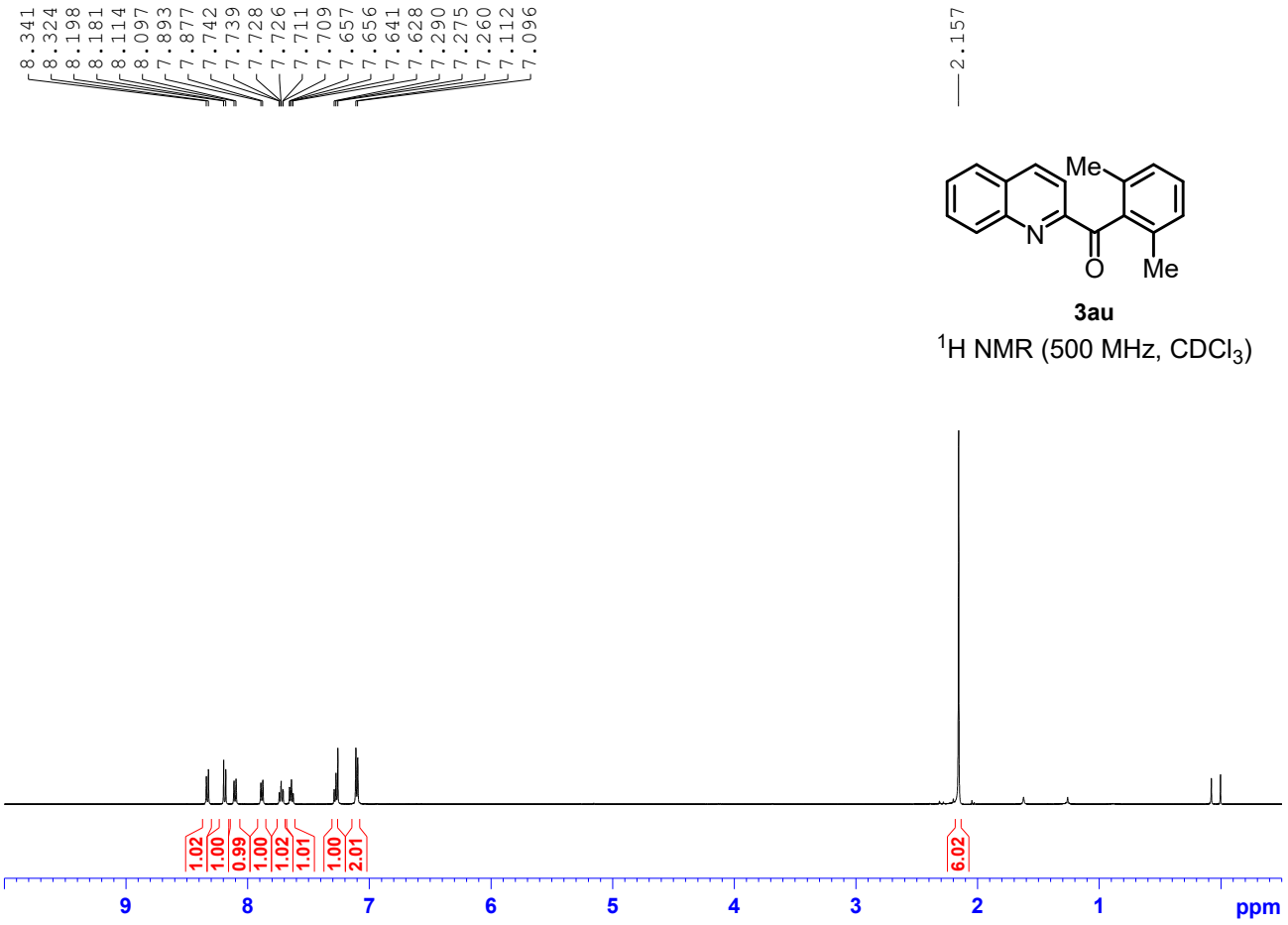
3at

^{1}H NMR (500 MHz, $CDCl_3$)



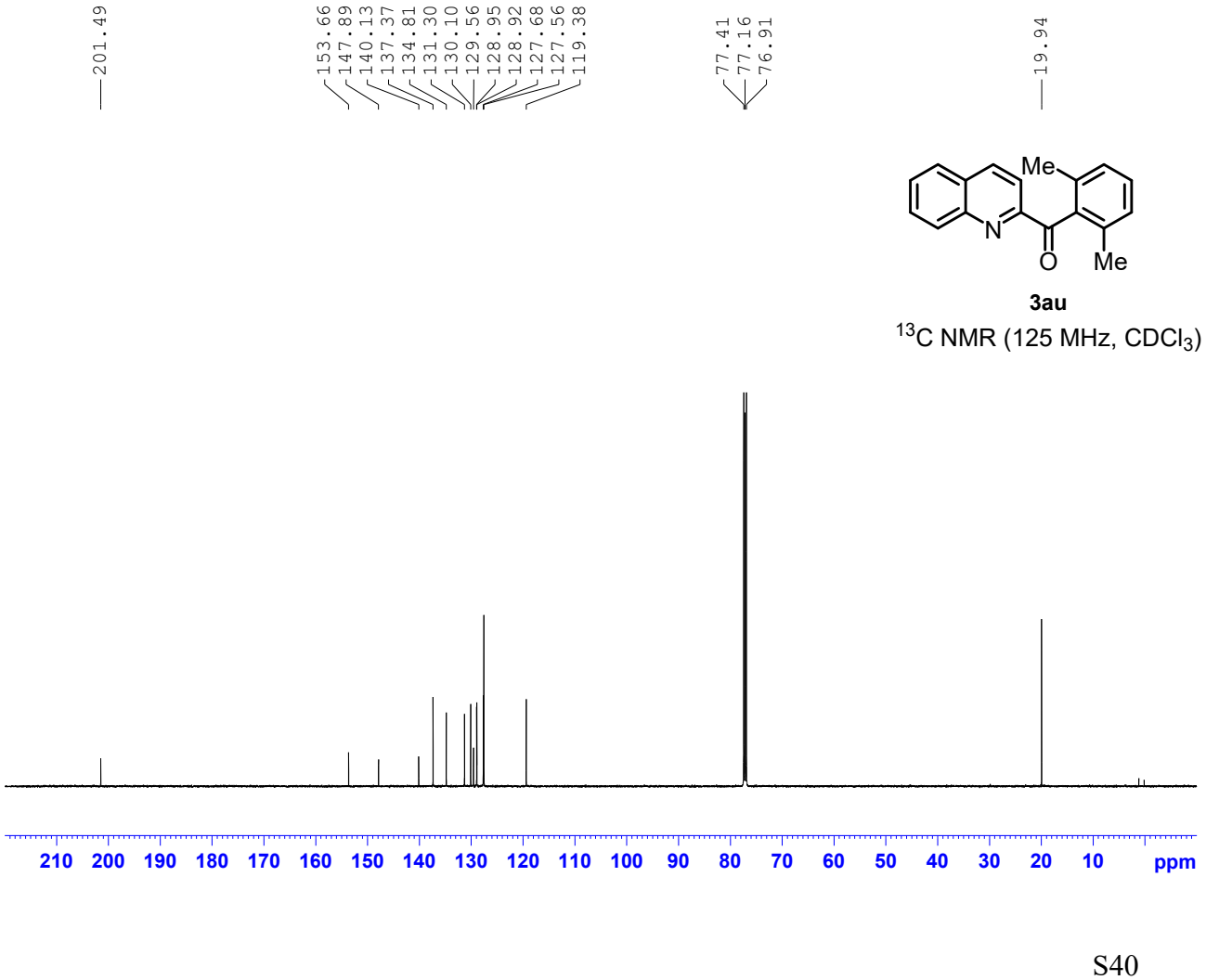
3at

^{13}C NMR (125 MHz, $CDCl_3$)



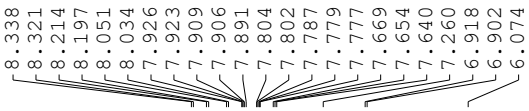
3au

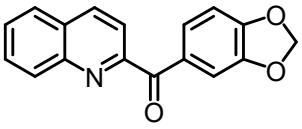
^{1}H NMR (500 MHz, $CDCl_3$)



3au

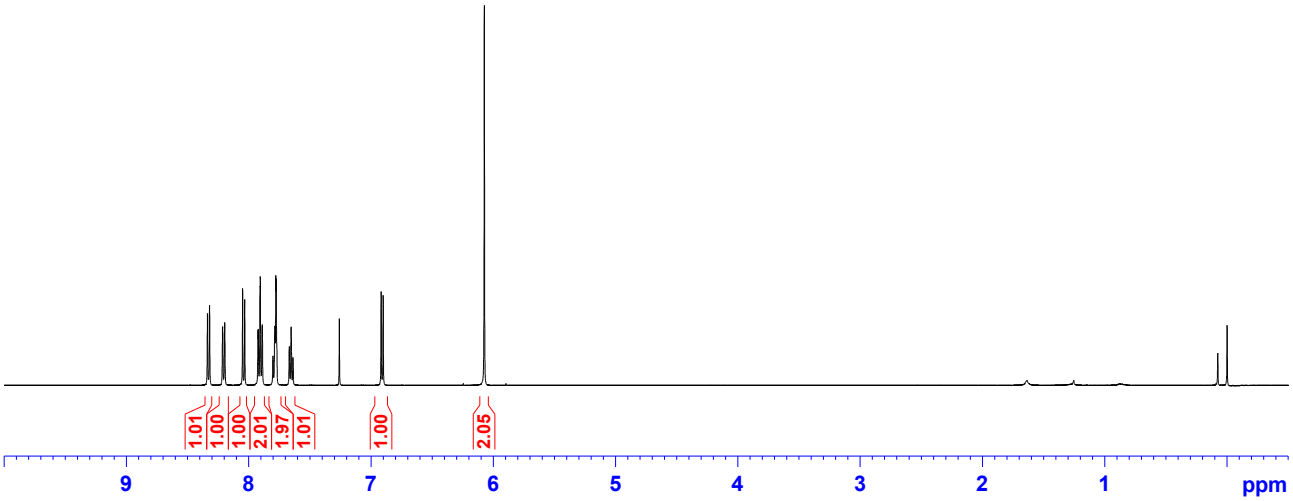
^{13}C NMR (125 MHz, $CDCl_3$)

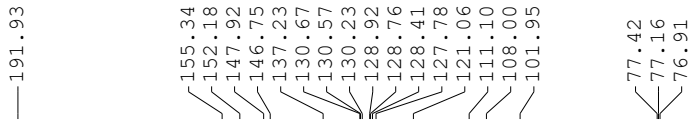


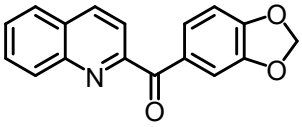


3av

^{1}H NMR (500 MHz, $CDCl_3$)

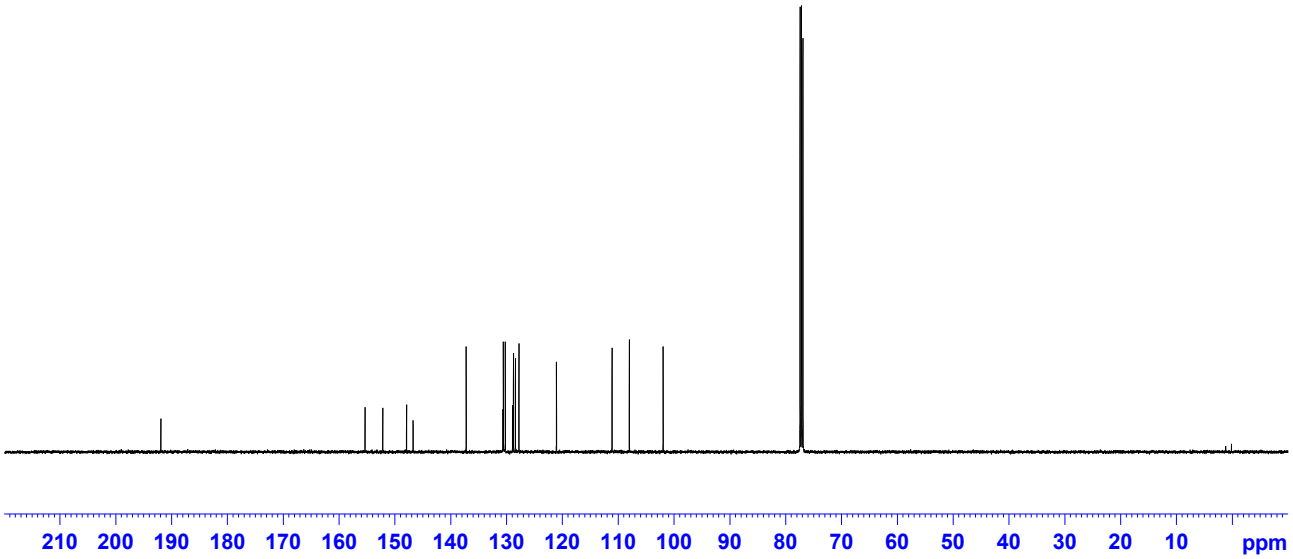


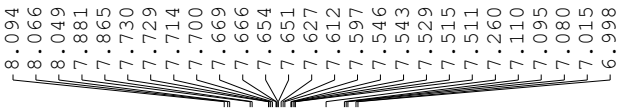


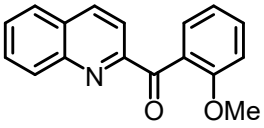


3av

^{13}C NMR (125 MHz, $CDCl_3$)

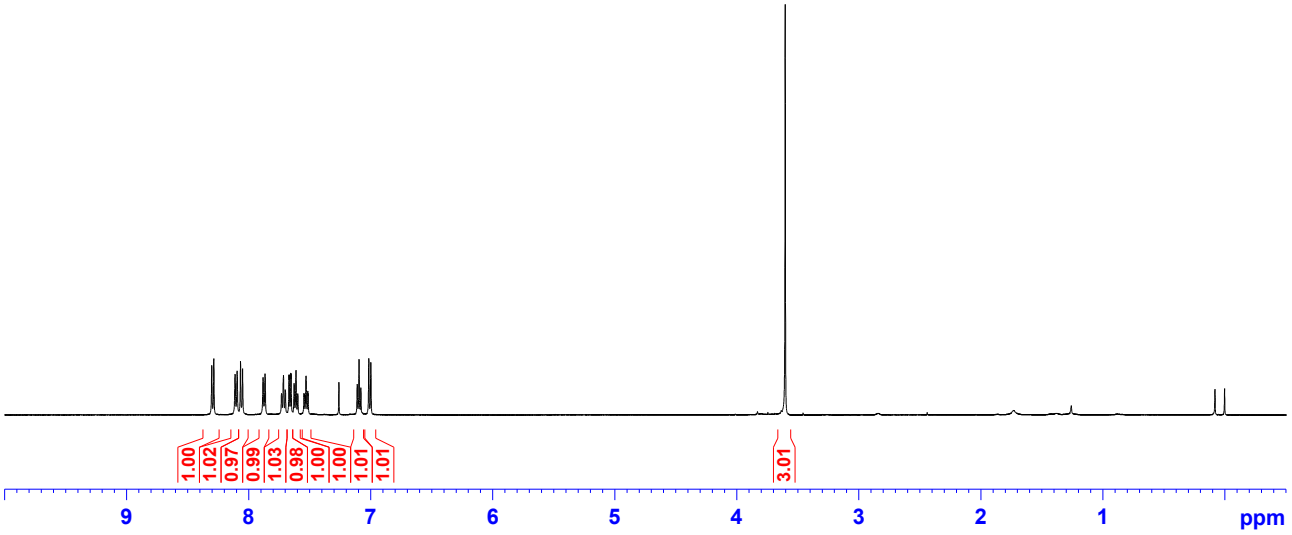


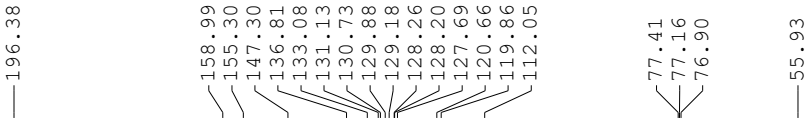


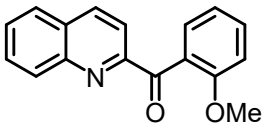


3aw

^{1}H NMR (500 MHz, $CDCl_3$)

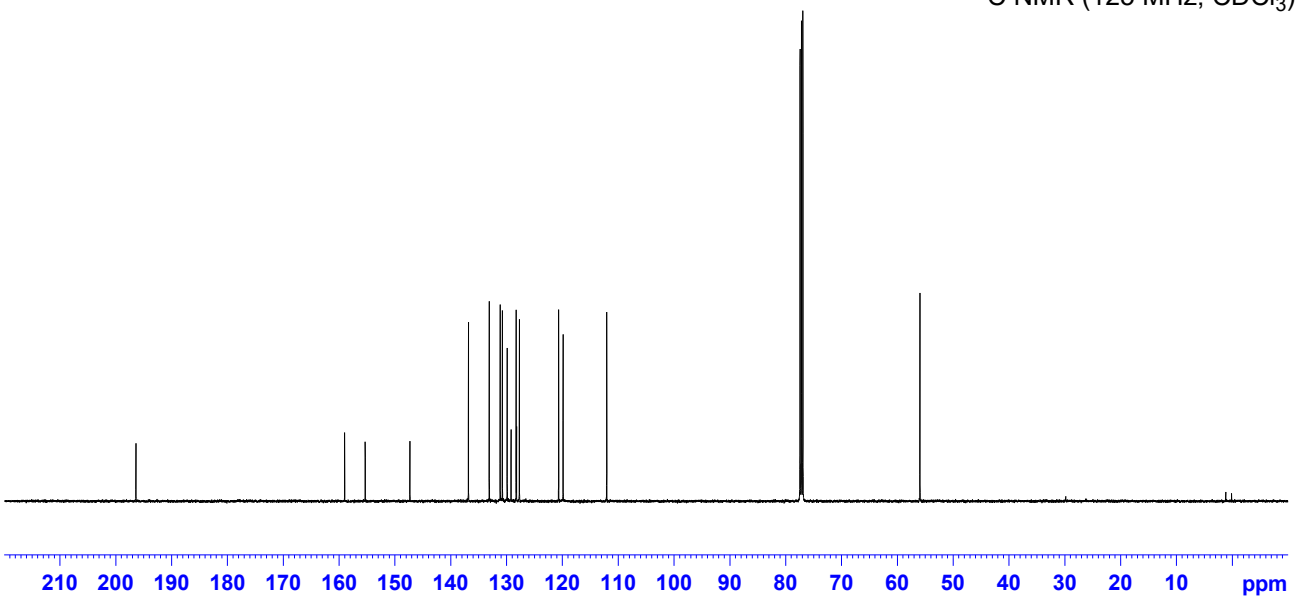


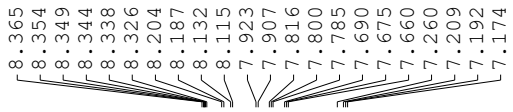


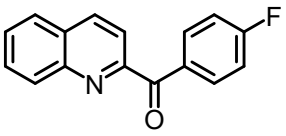


3aw

^{13}C NMR (125 MHz, $CDCl_3$)

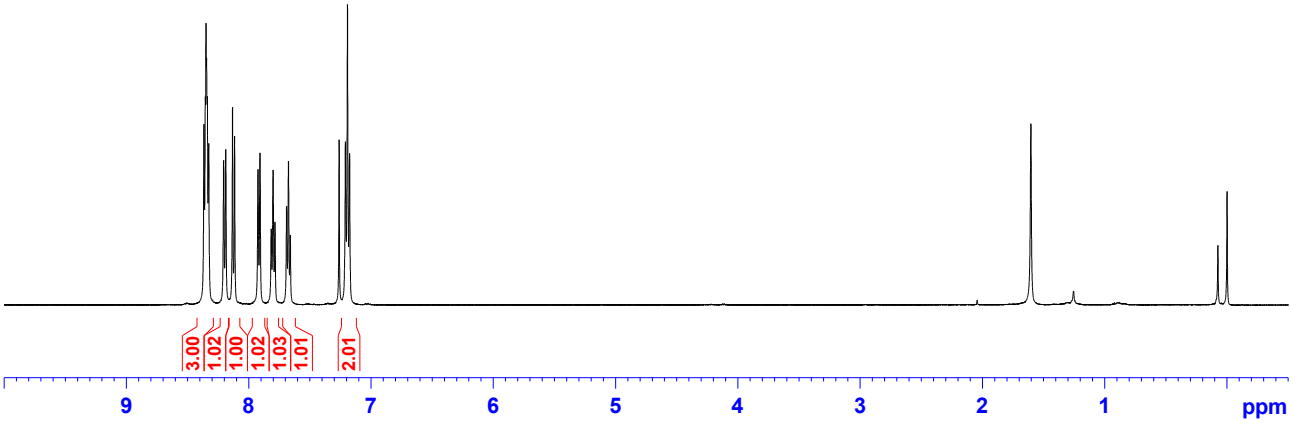


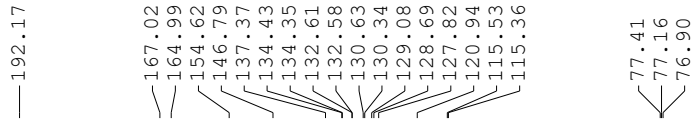


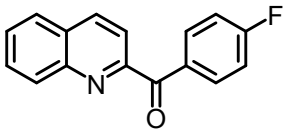


3ax

^{1}H NMR (500 MHz, $CDCl_3$)

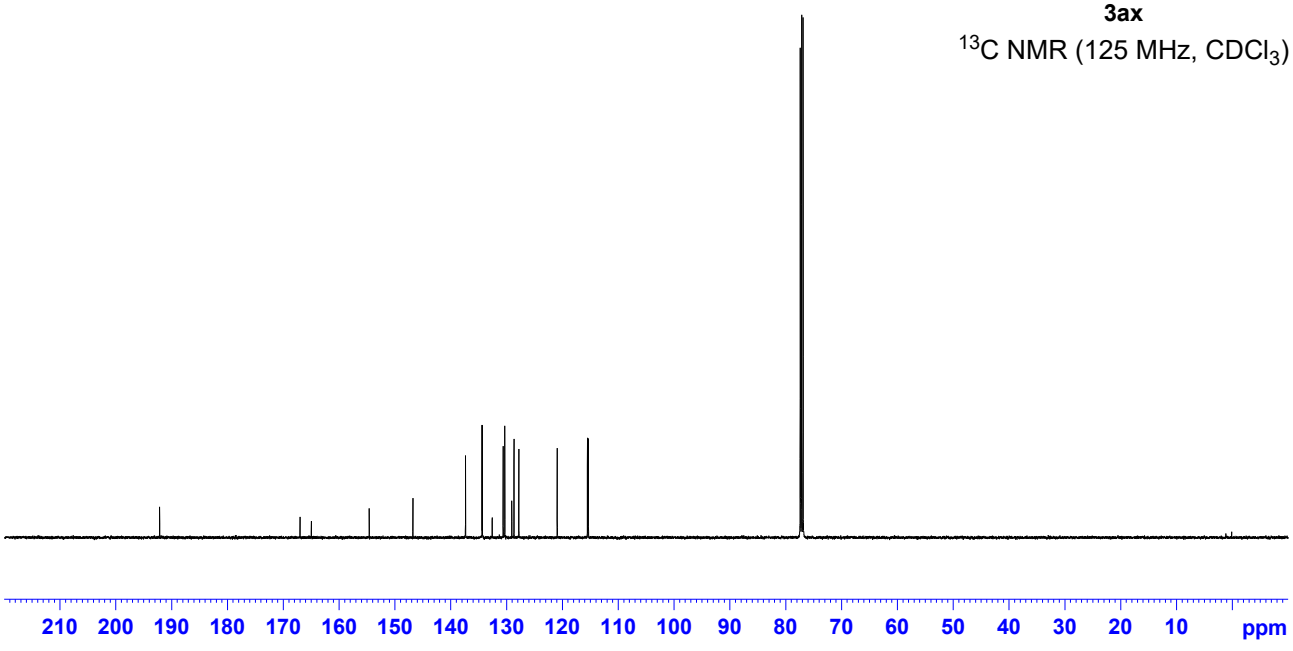


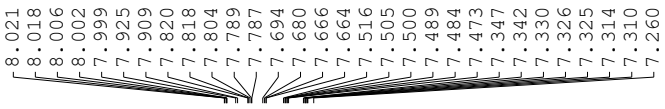


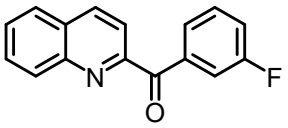


3ax

^{13}C NMR (125 MHz, $CDCl_3$)

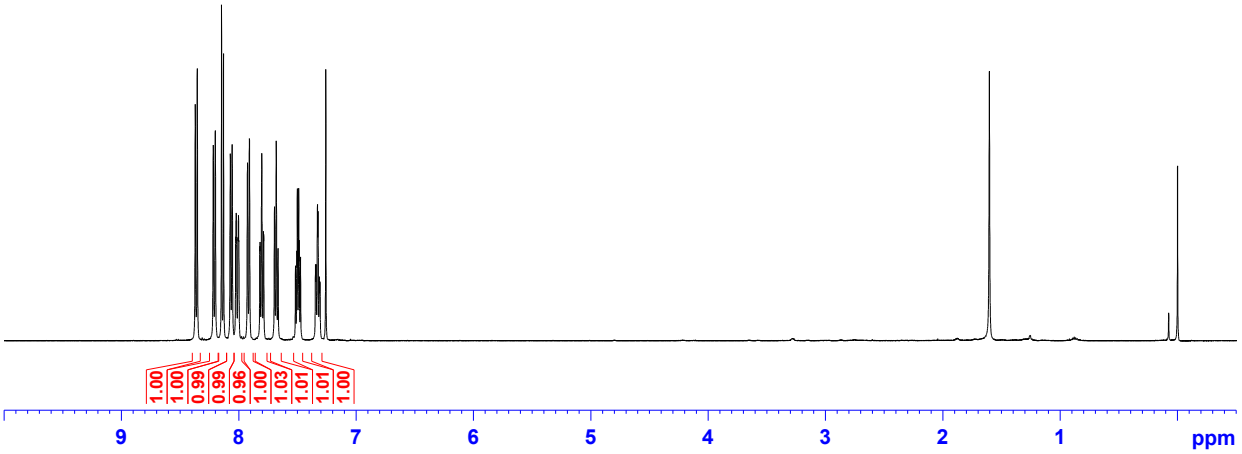


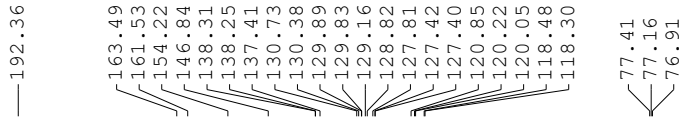


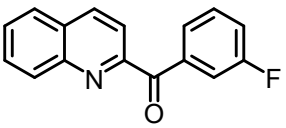


3ay

^{1}H NMR (500 MHz, $CDCl_3$)

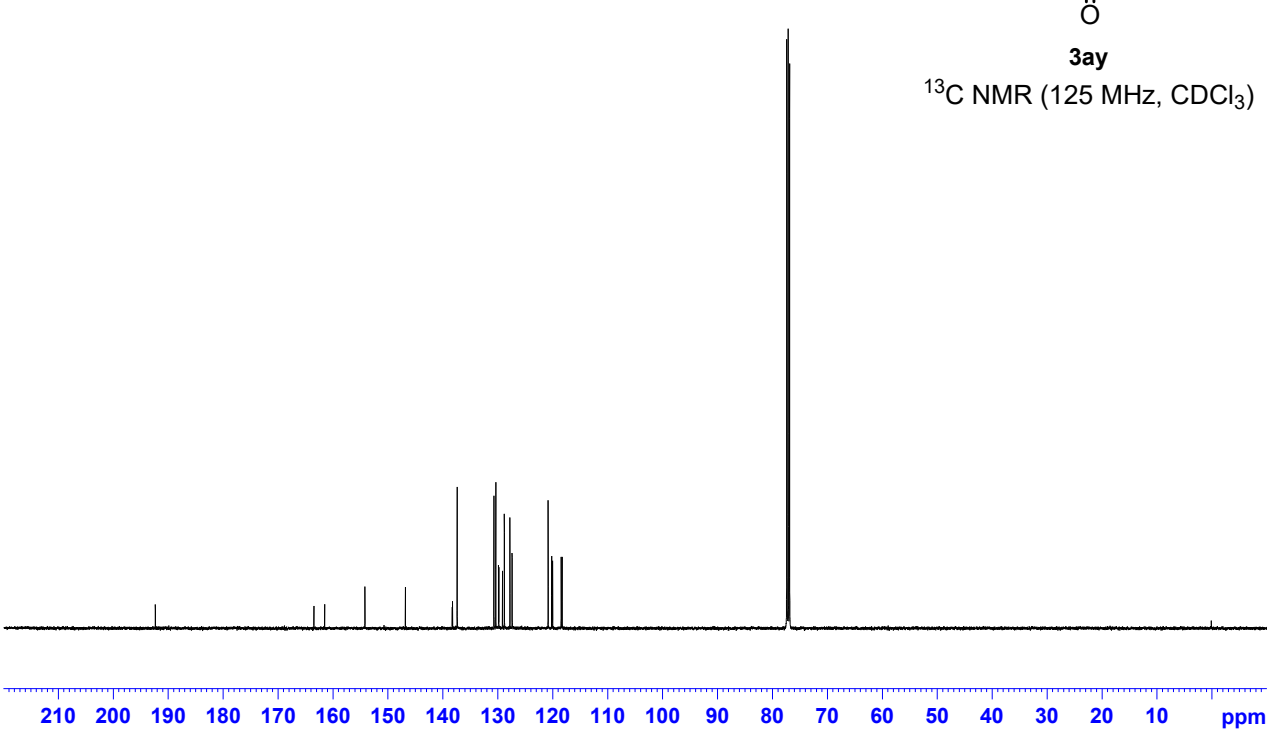


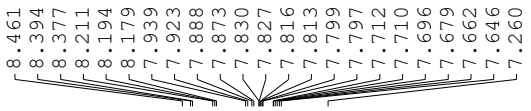


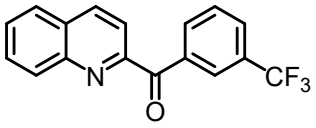


3ay

^{13}C NMR (125 MHz, $CDCl_3$)

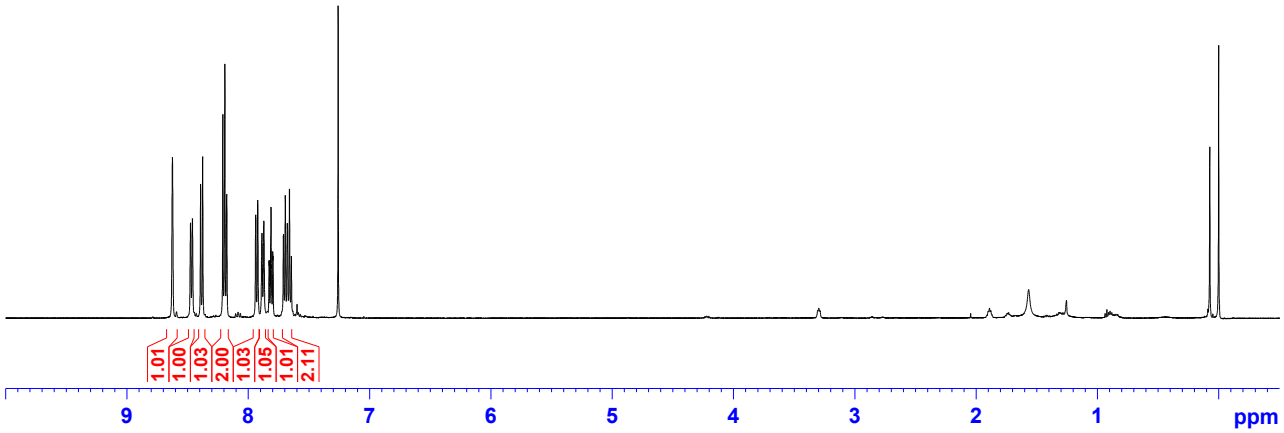


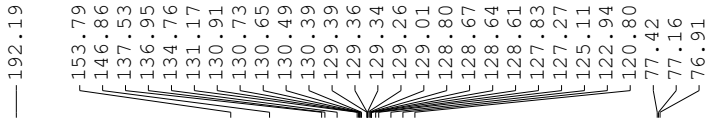


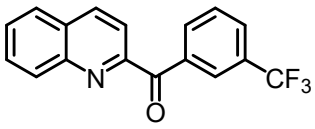


3az

^{1}H NMR (500 MHz, $CDCl_3$)

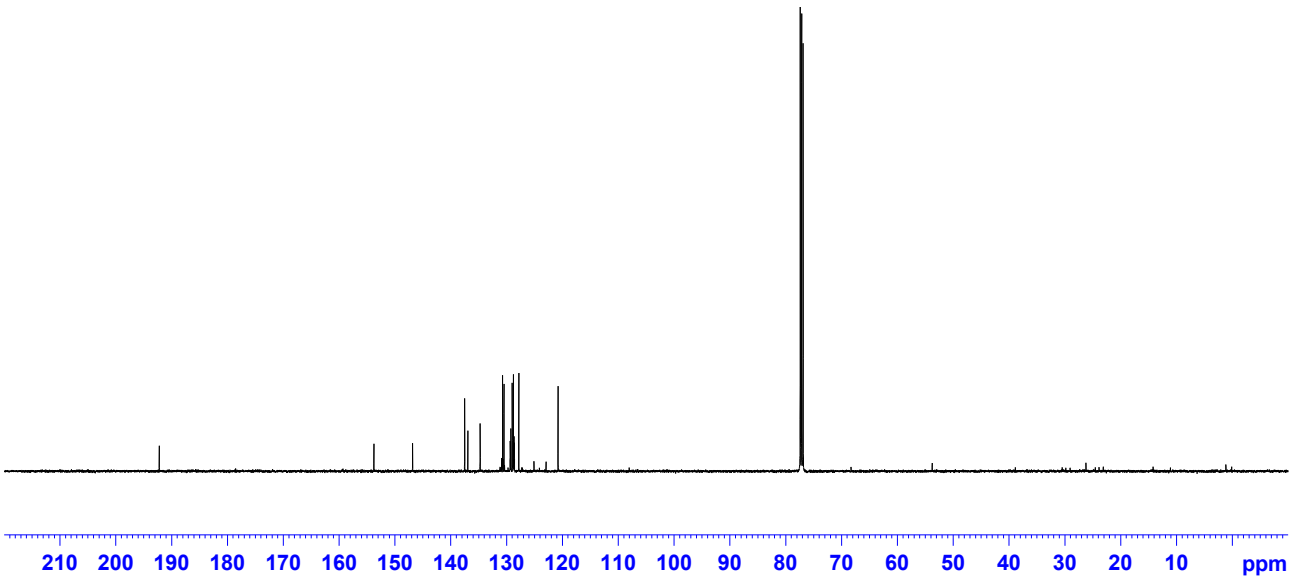


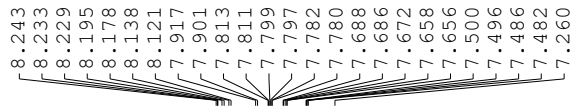


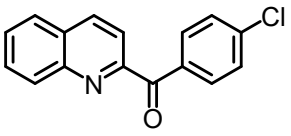


3az

^{13}C NMR (125 MHz, $CDCl_3$)

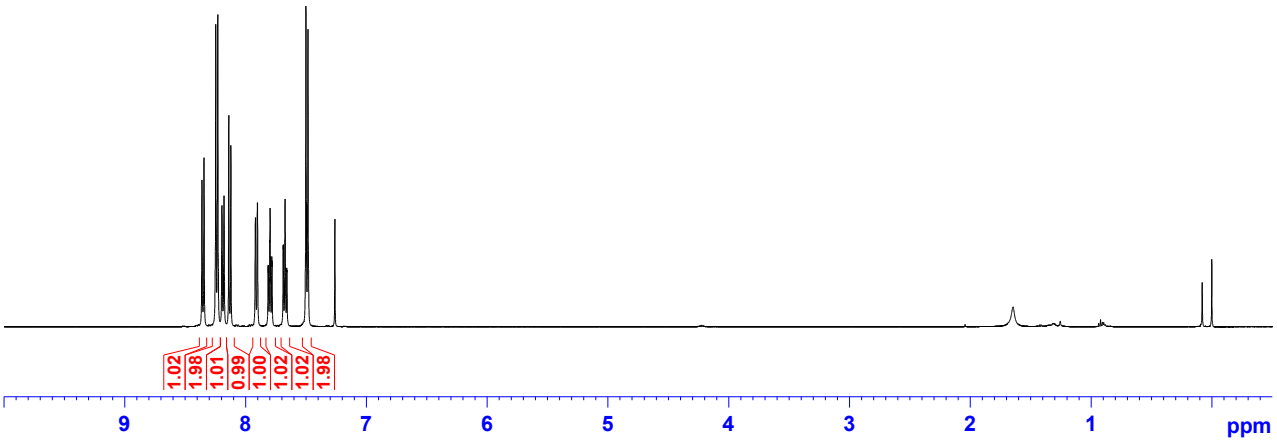


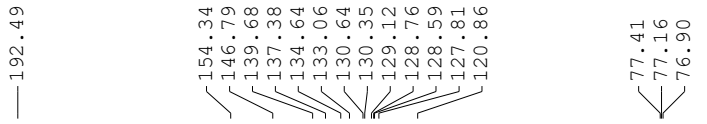


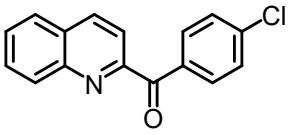


3ba

^{1}H NMR (500 MHz, $CDCl_3$)

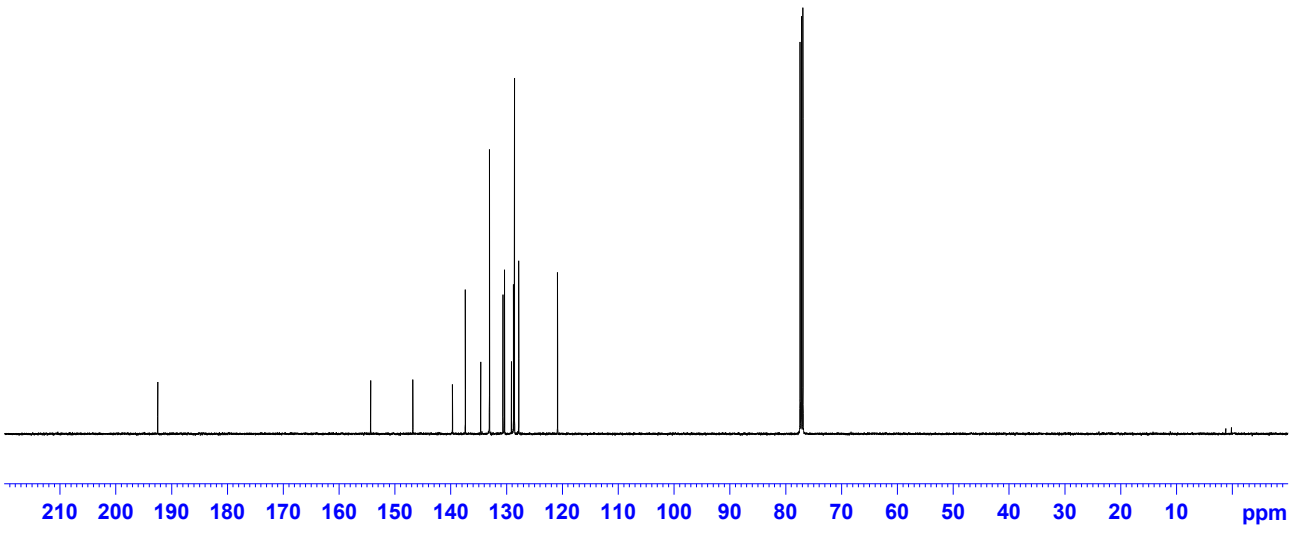


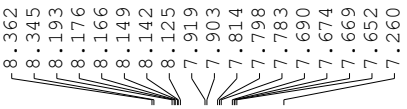


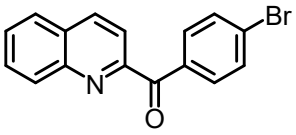


3ba

^{13}C NMR (125 MHz, $CDCl_3$)

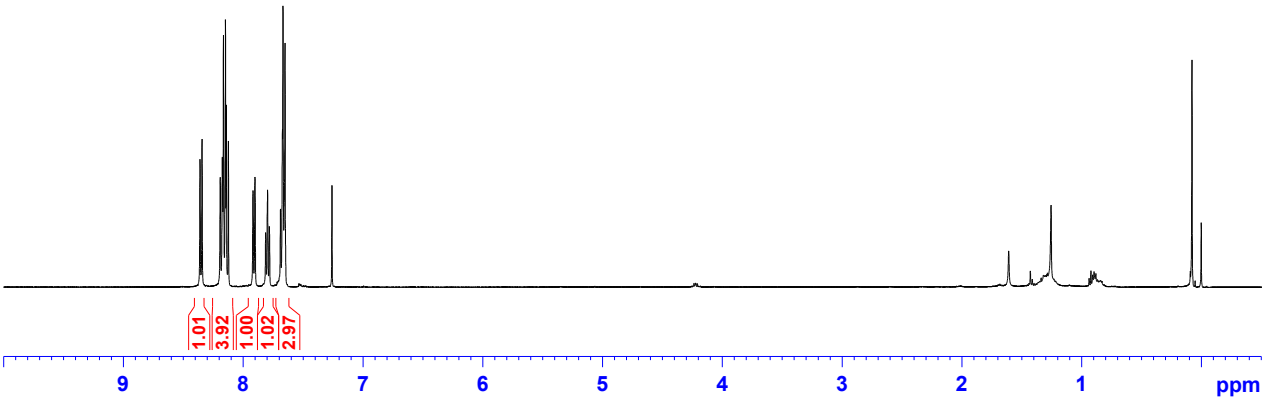


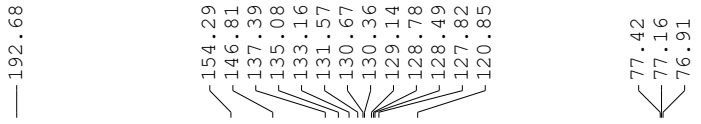


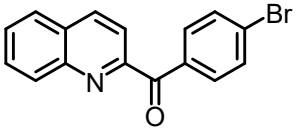


3bb

^{1}H NMR (500 MHz, $CDCl_3$)

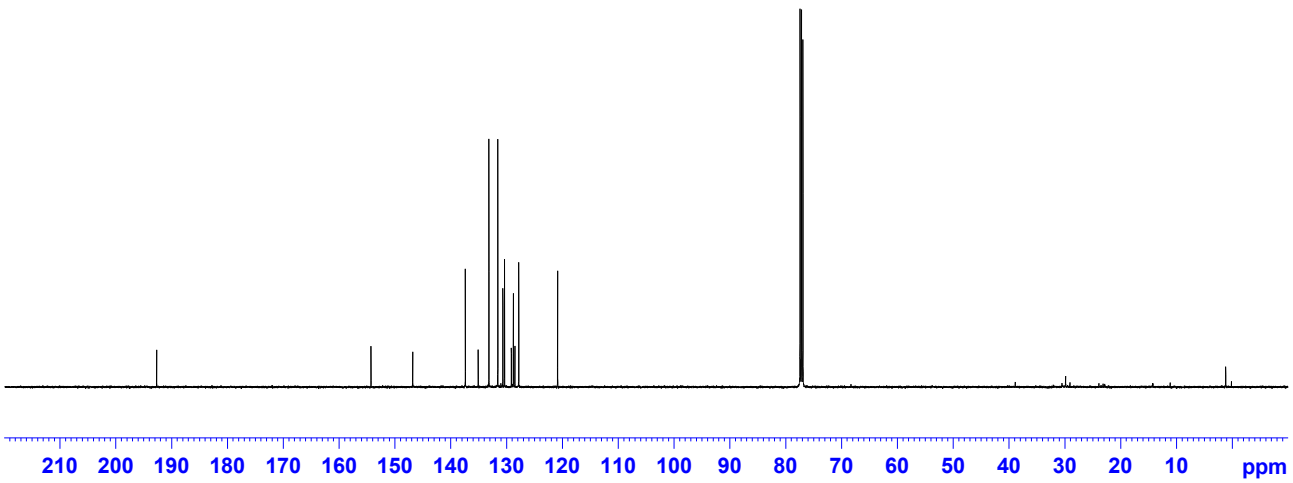


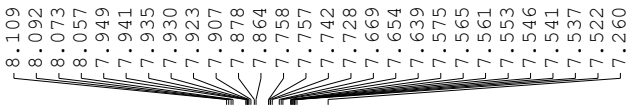


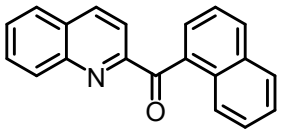


3bb

^{13}C NMR (125 MHz, $CDCl_3$)

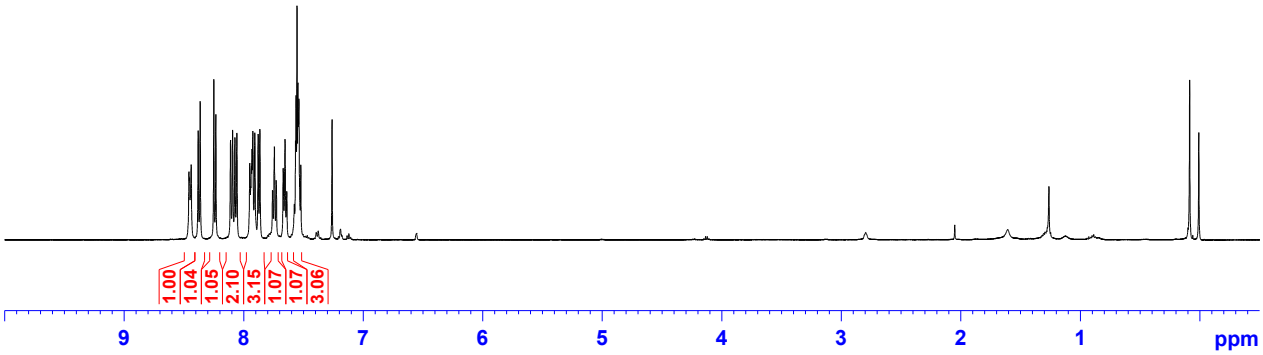


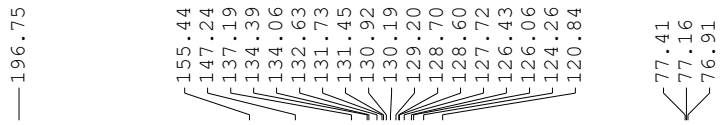


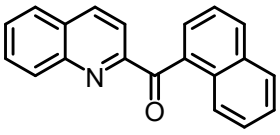


3bc

^{1}H NMR (500 MHz, $CDCl_3$)

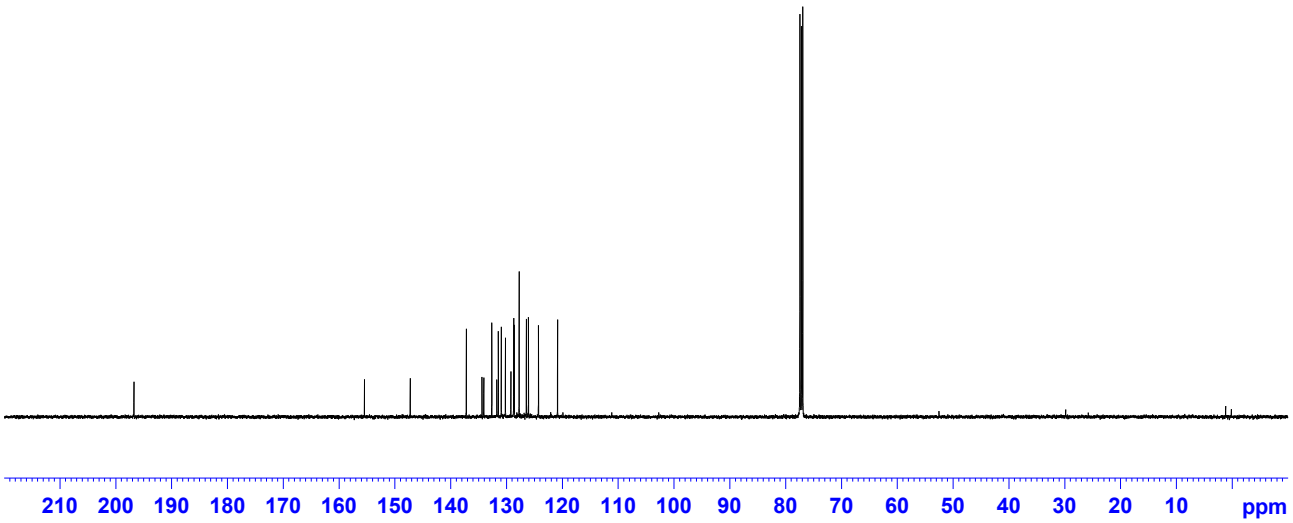


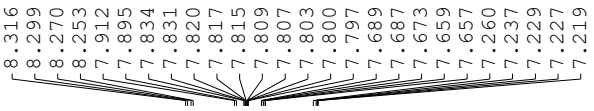


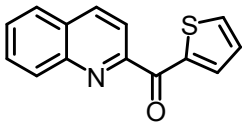


3bc

^{13}C NMR (125 MHz, $CDCl_3$)

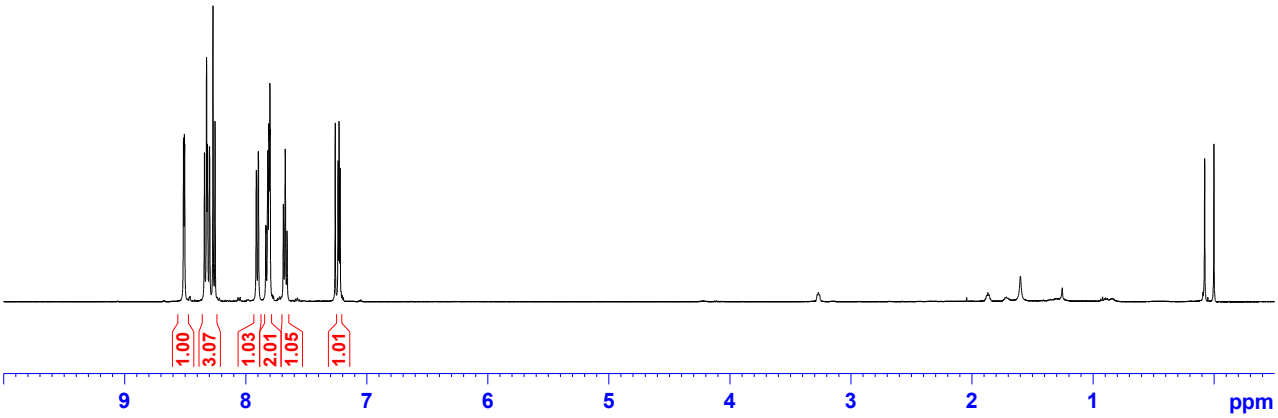


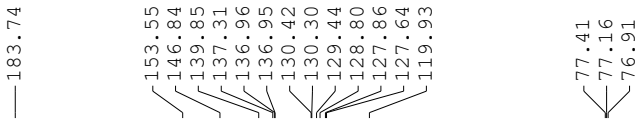


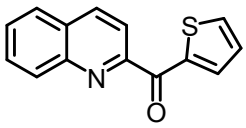


3bd

^{1}H NMR (500 MHz, $CDCl_3$)

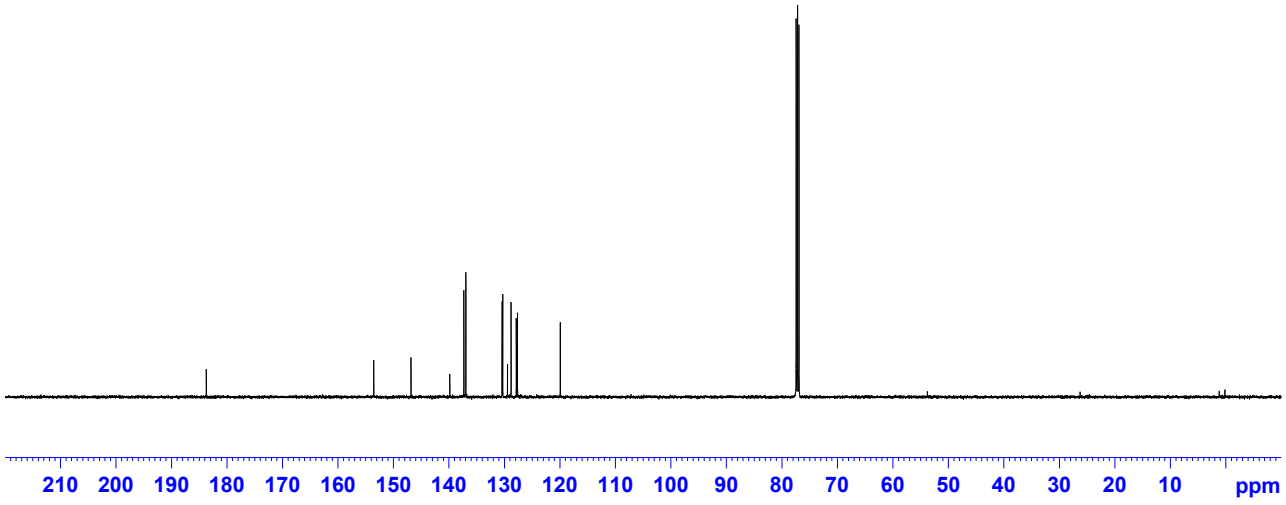


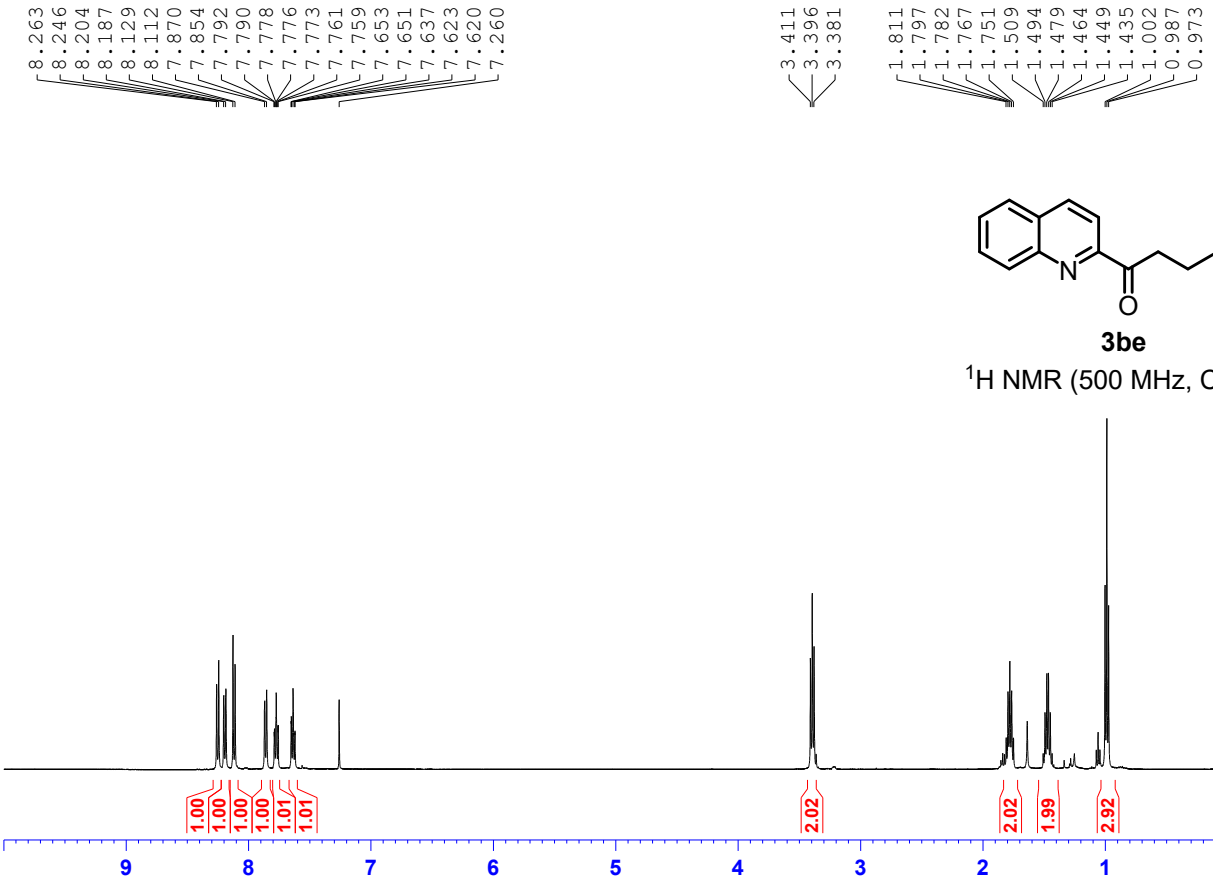


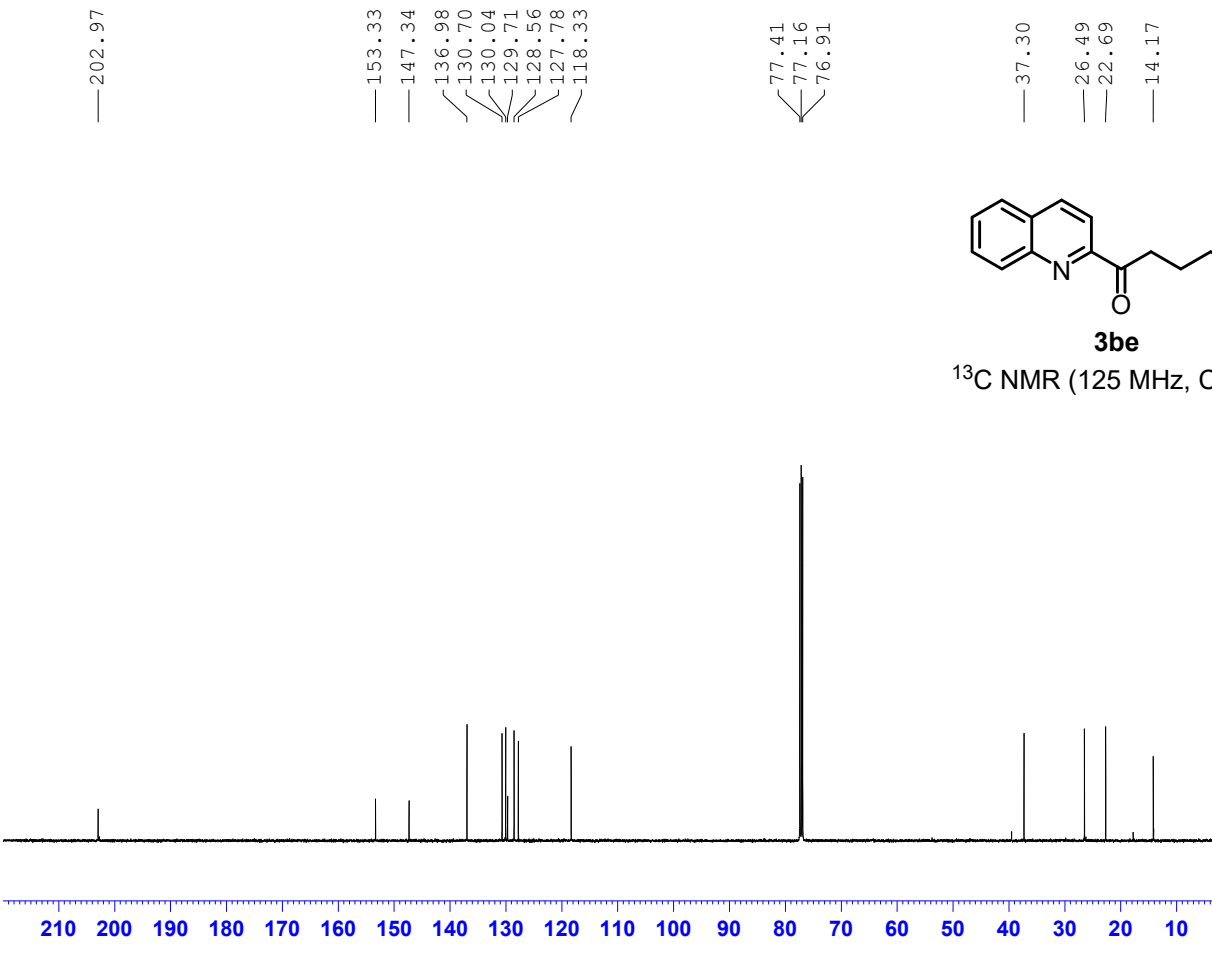


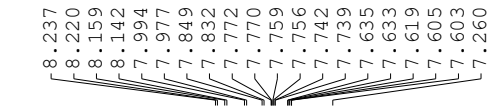
3bd

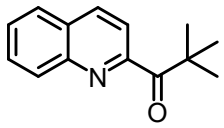
^{13}C NMR (125 MHz, $CDCl_3$)




8.263
8.246
8.204
8.187
8.129
8.112
7.870
7.854
7.792
7.790
7.778
7.776
7.773
7.761
7.759
7.653
7.651
7.637
7.623
7.620
7.260
3.411
3.396
3.381
1.811
1.797
1.782
1.767
1.751
1.509
1.494
1.479
1.464
1.449
1.435
1.002
0.987
0.973
N
O
3be
1H NMR (500 MHz, CDCl3)
1.00
1.00
1.00
1.00
1.01
1.01
2.02
2.02
1.99
2.92
9
8
7
6
5
4
3
2
1
ppm

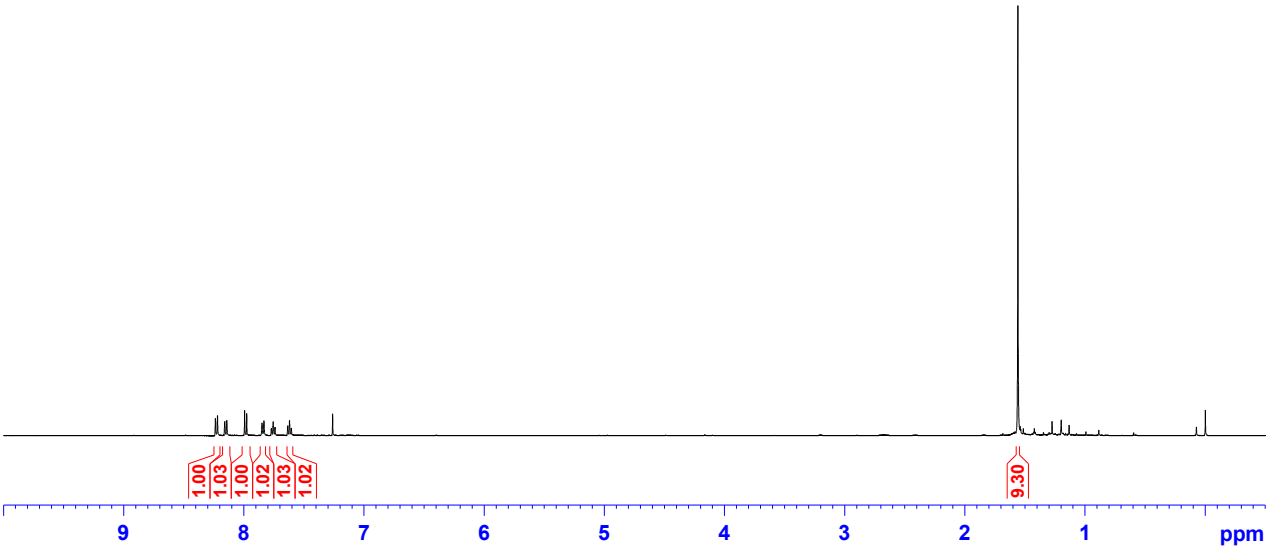

202.97
153.33
147.34
136.98
130.70
130.04
129.71
128.56
127.78
118.33
77.41
77.16
76.91
37.30
26.49
22.69
14.17
N
O
3be
13C NMR (125 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

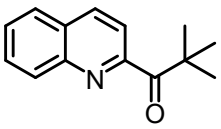




3bf

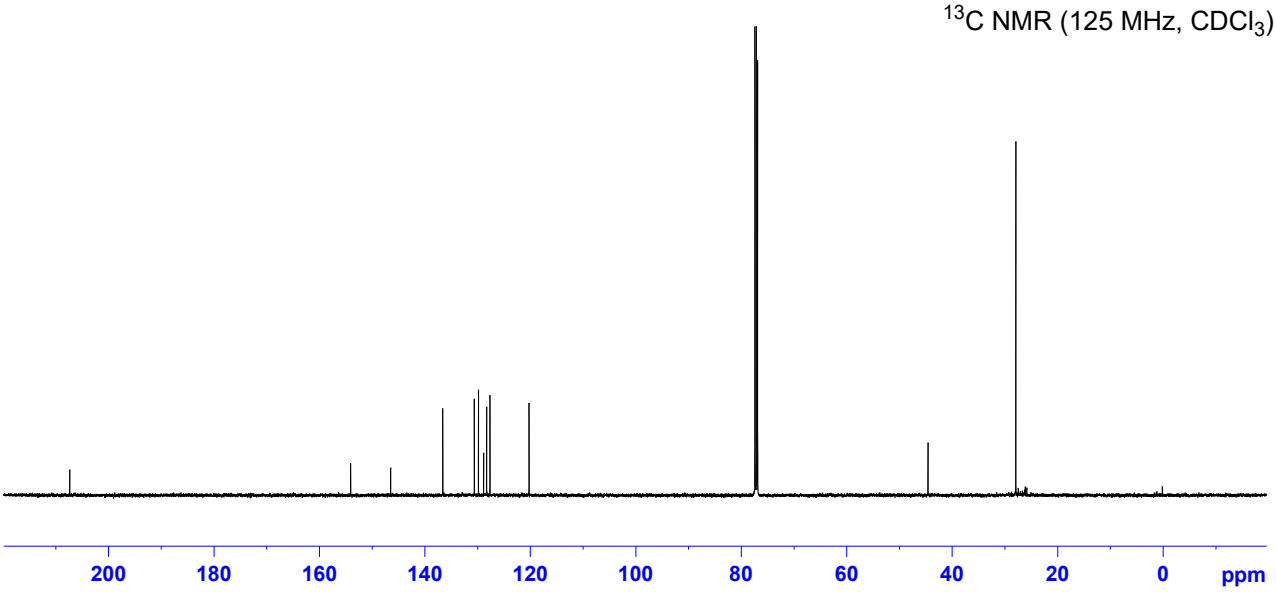
^{1}H NMR (500 MHz, $CDCl_3$)

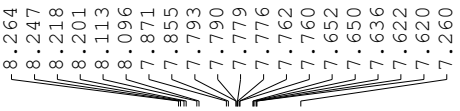


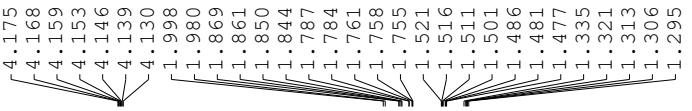


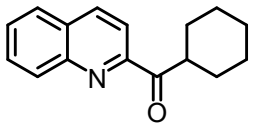
3bf

^{13}C NMR (125 MHz, $CDCl_3$)



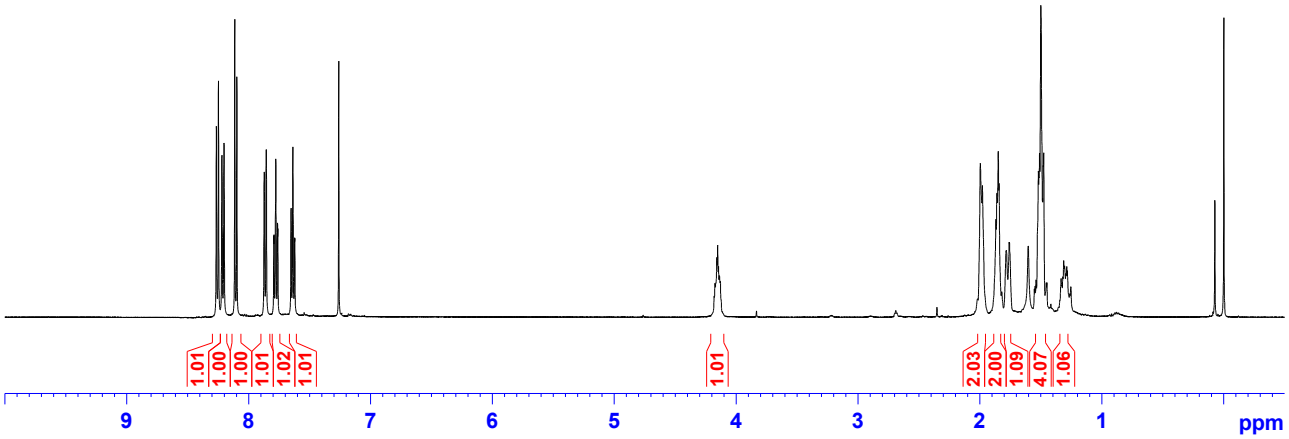


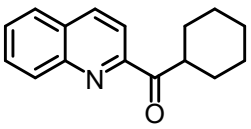




3bg

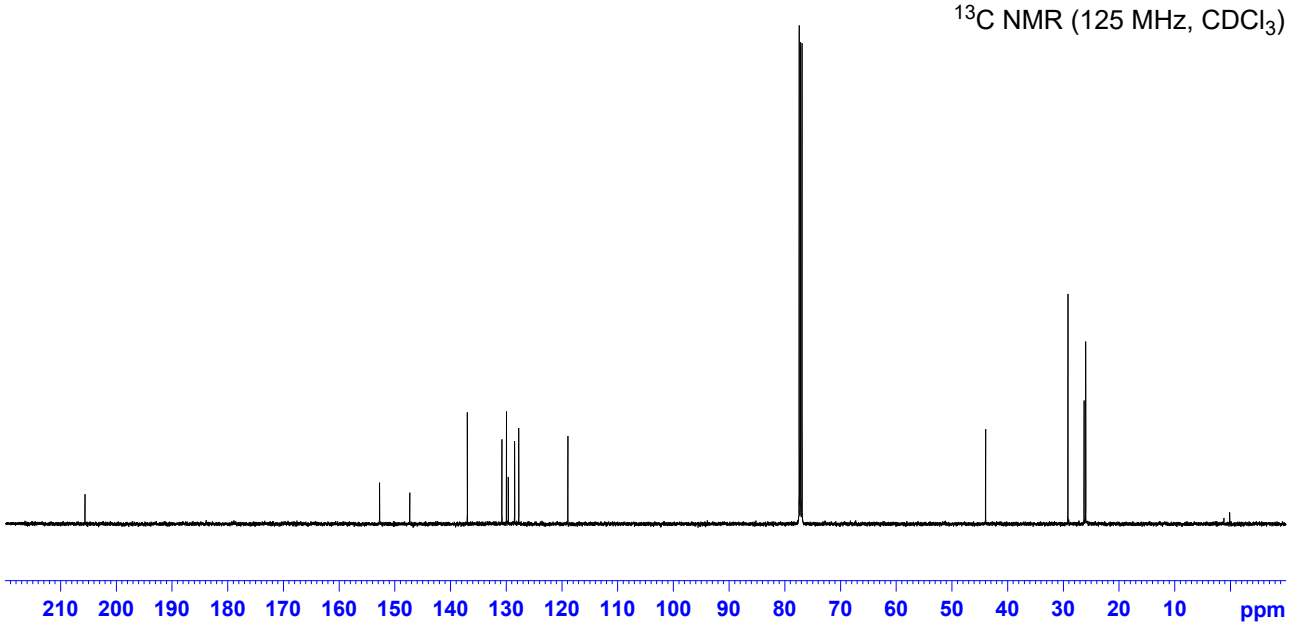
^{1}H NMR (500 MHz, $CDCl_3$)

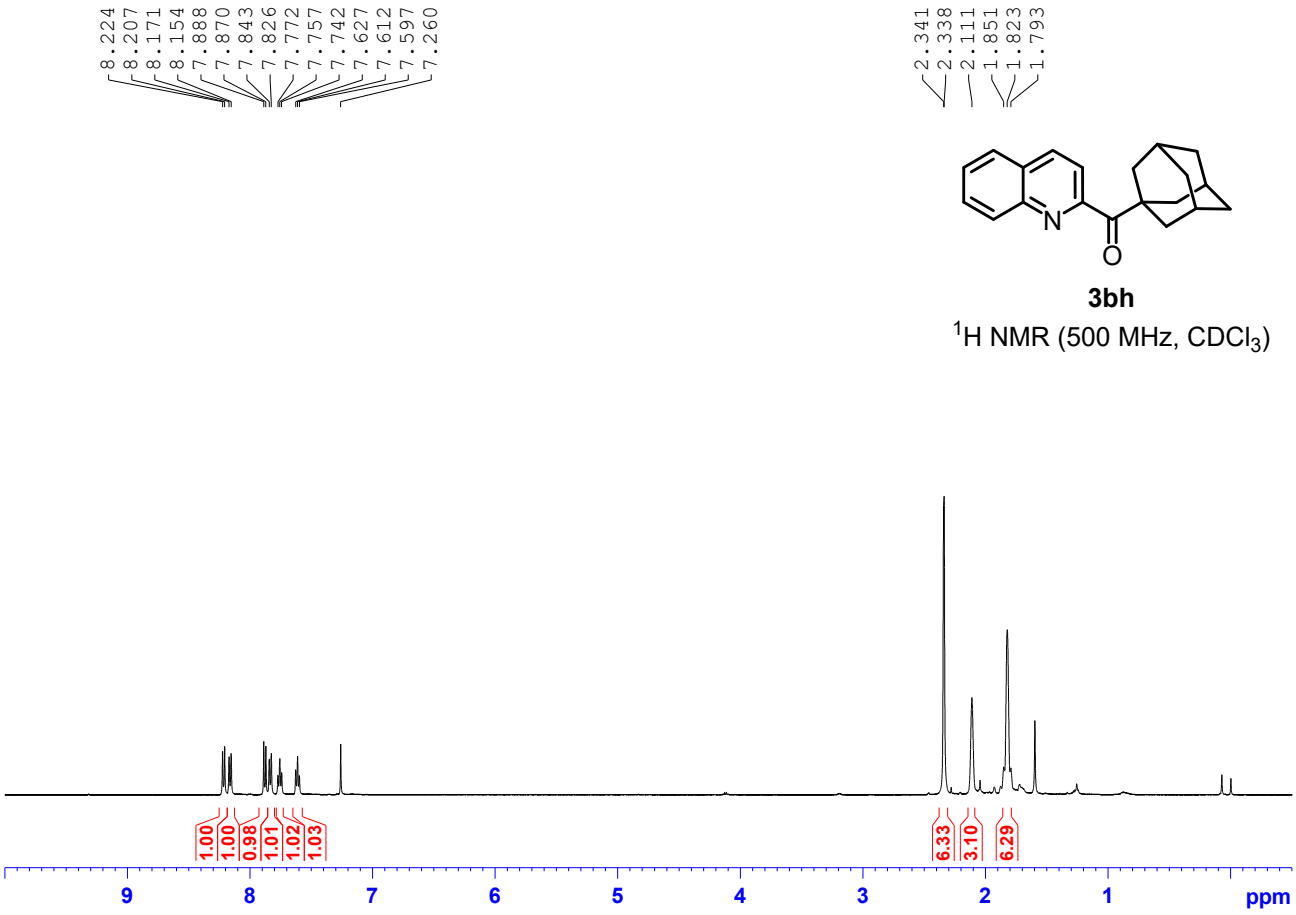




3bg

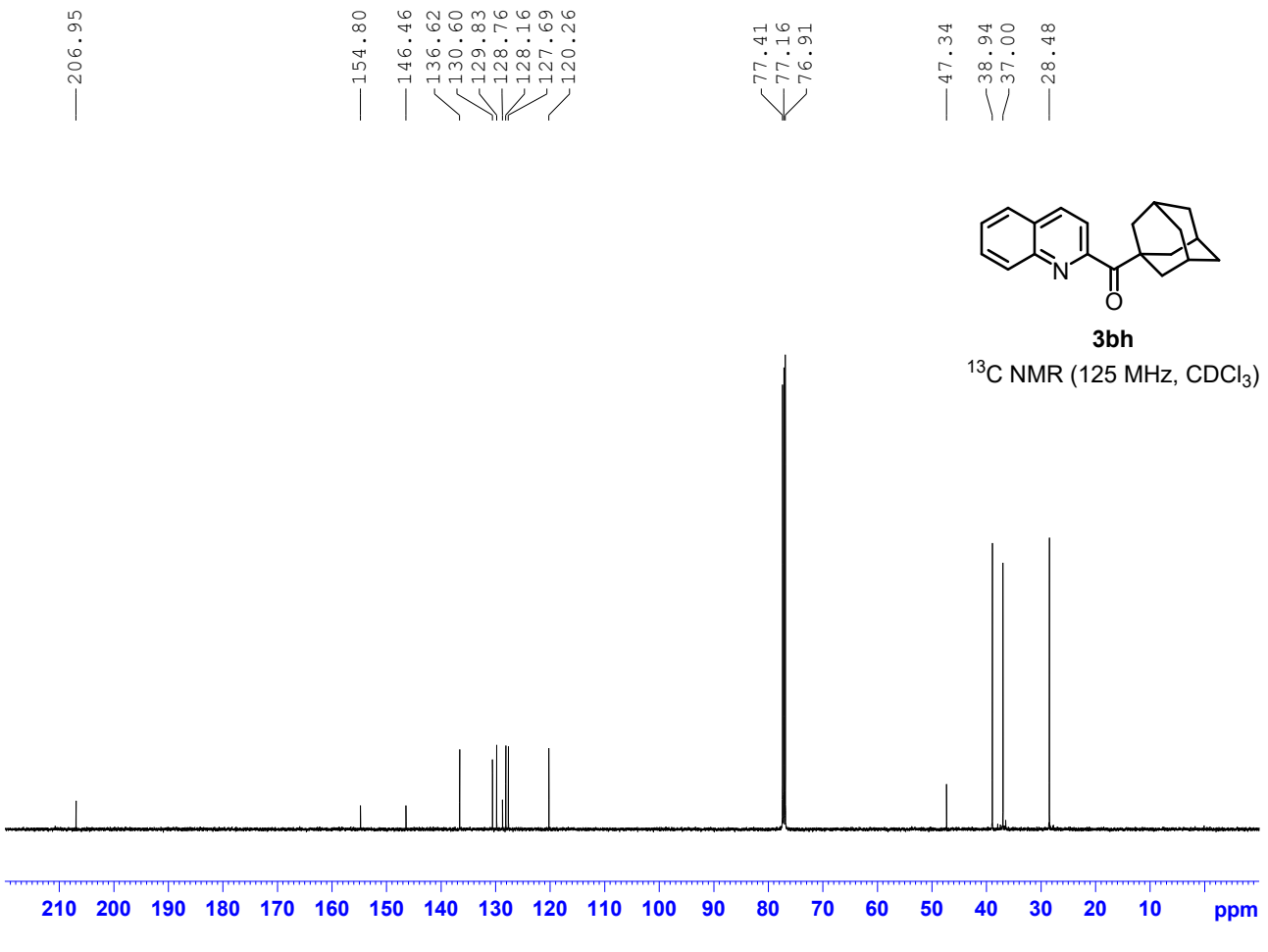
^{13}C NMR (125 MHz, $CDCl_3$)





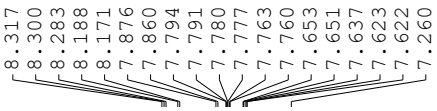
3bh

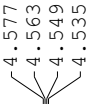
^{1}H NMR (500 MHz, $CDCl_3$)

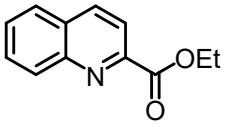


3bh

^{13}C NMR (125 MHz, $CDCl_3$)

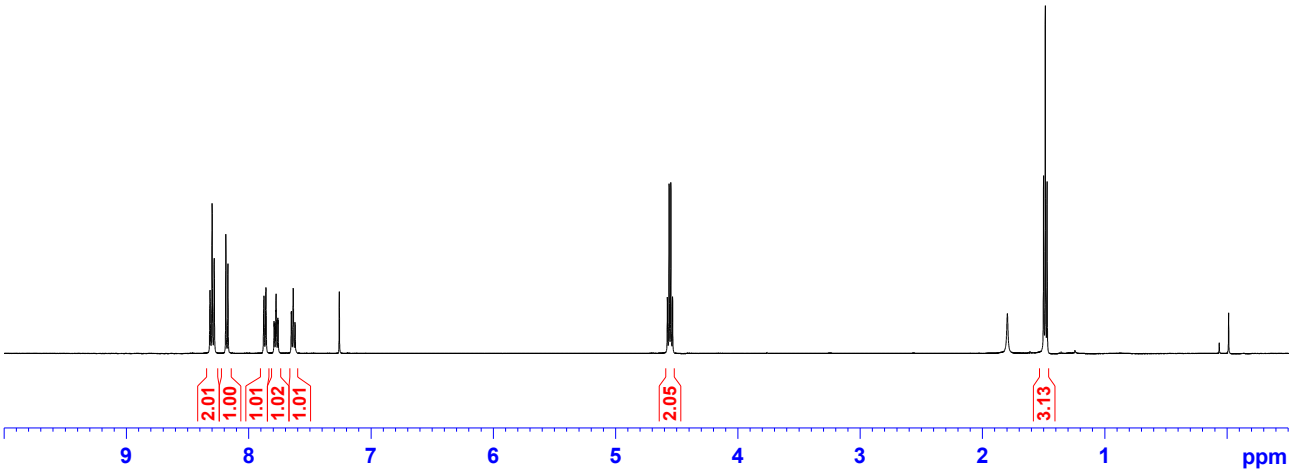


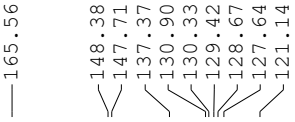


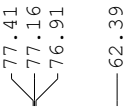


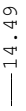
3bi

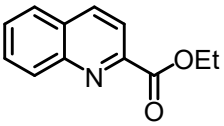
^{1}H NMR (500 MHz, $CDCl_3$)





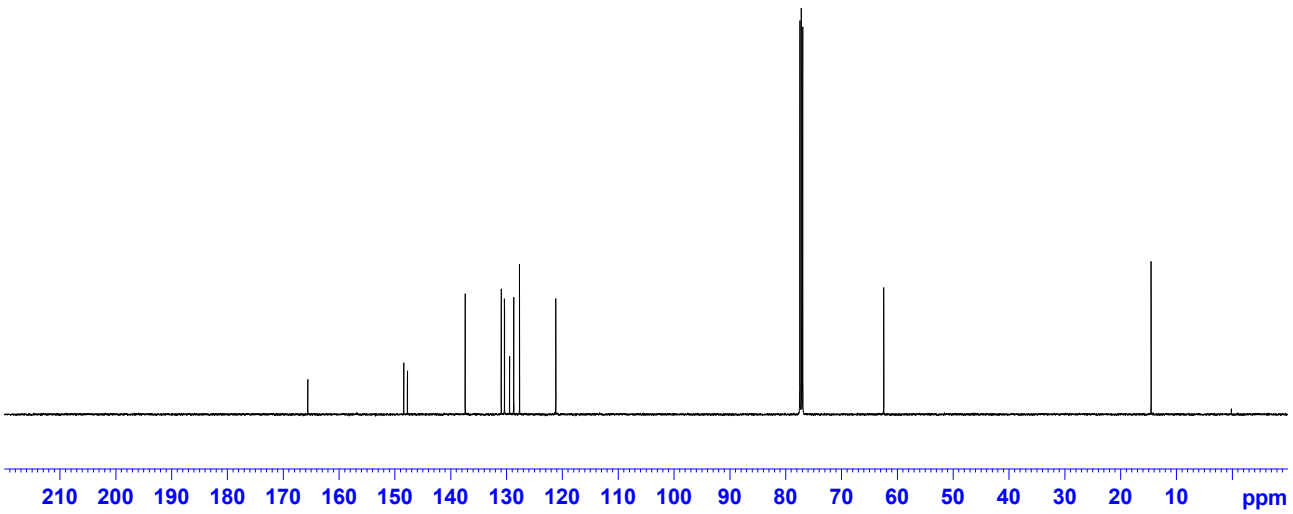


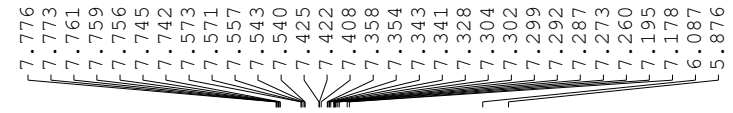


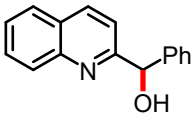


3bi

^{13}C NMR (125 MHz, $CDCl_3$)

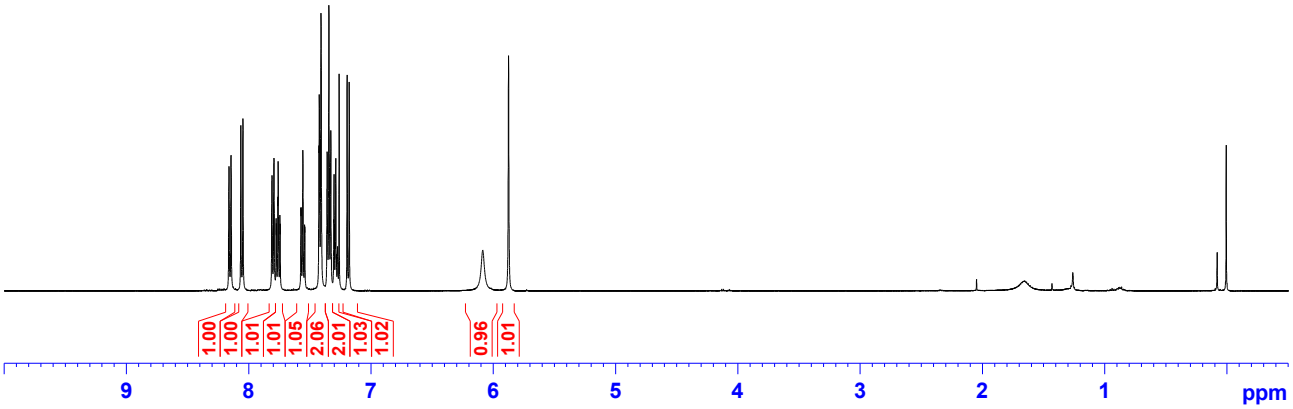


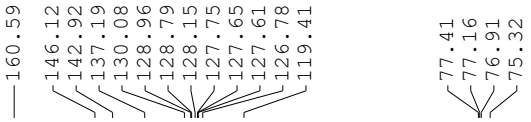


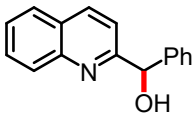


4

^{1}H NMR (500 MHz, $CDCl_3$)

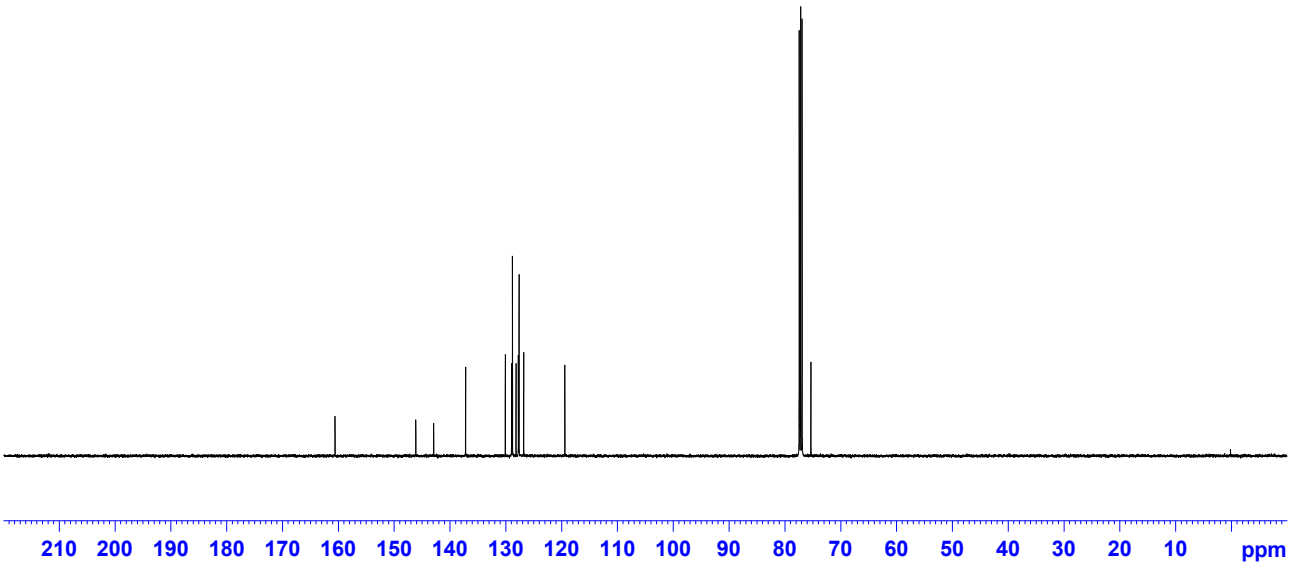


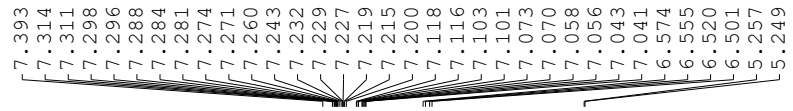


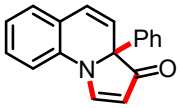


4

^{13}C NMR (125 MHz, $CDCl_3$)

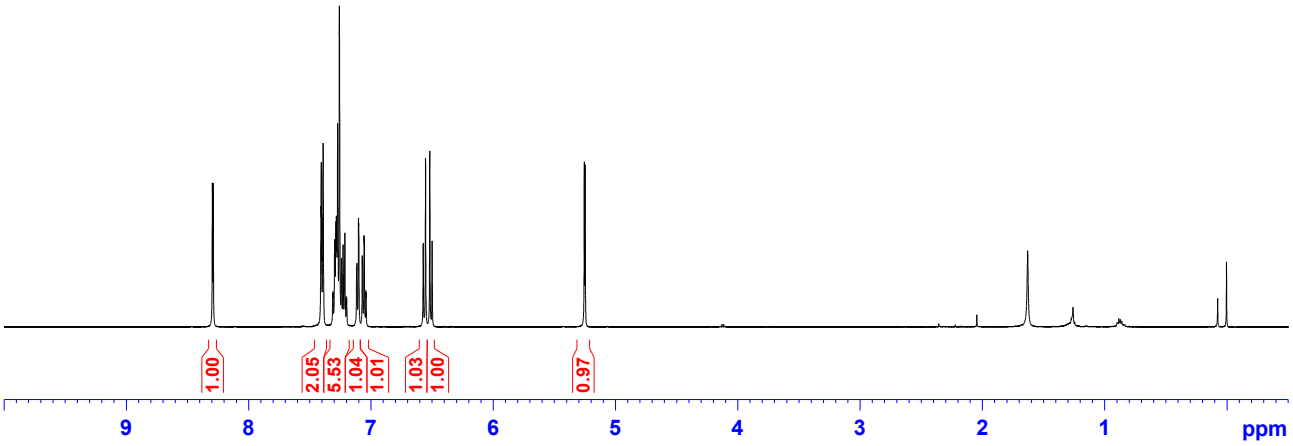


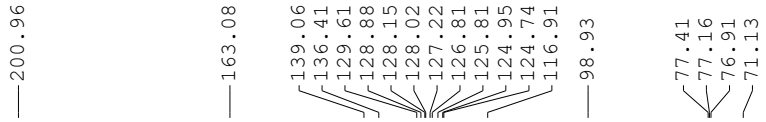


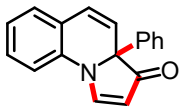


5

^{1}H NMR (500 MHz, $CDCl_3$)

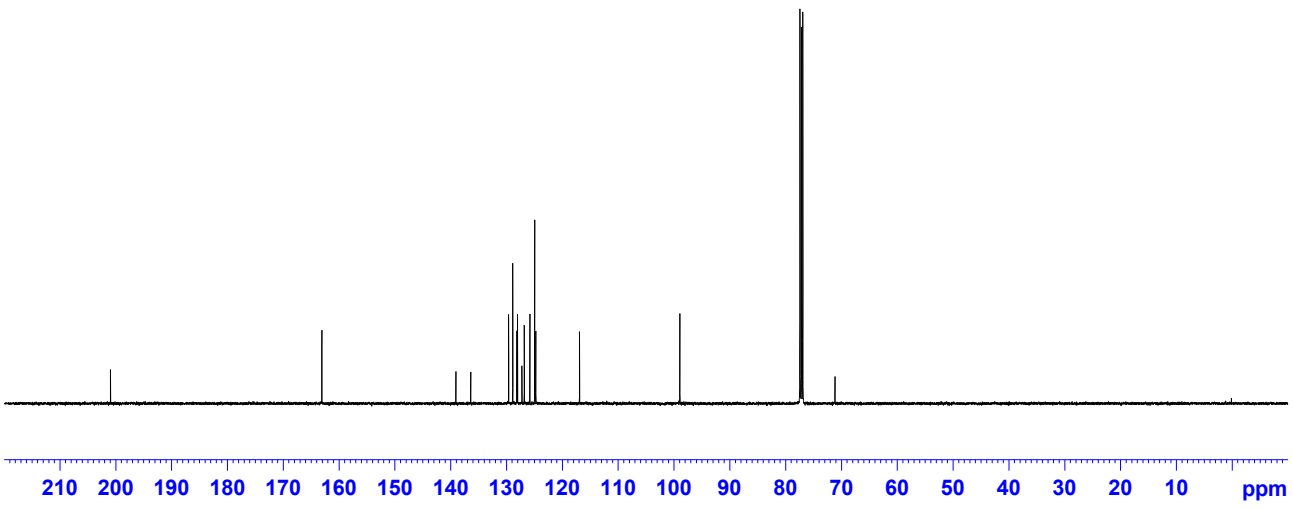


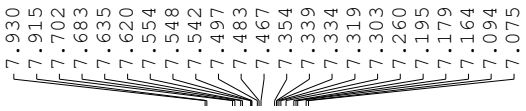


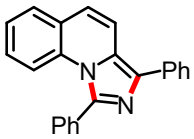


5

^{13}C NMR (125 MHz, $CDCl_3$)

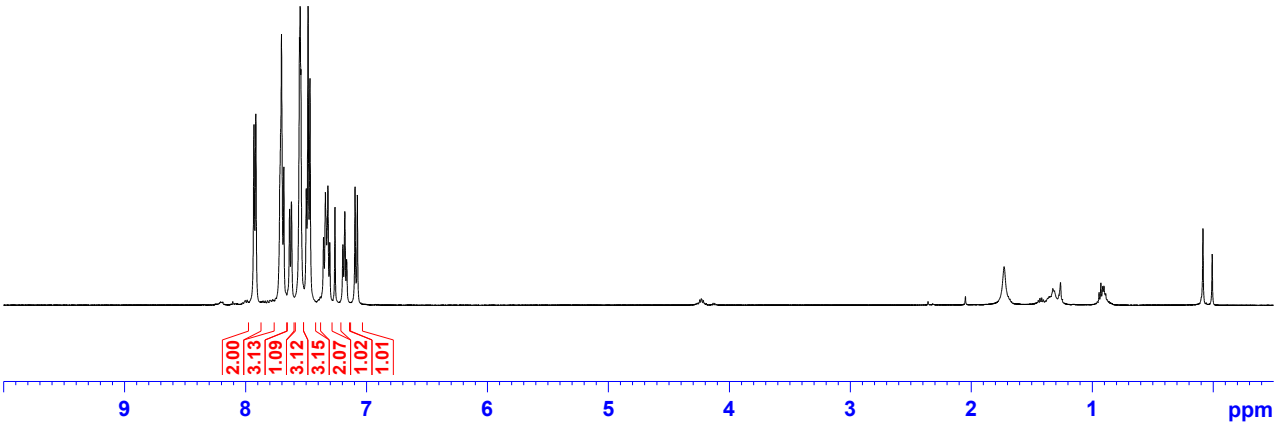


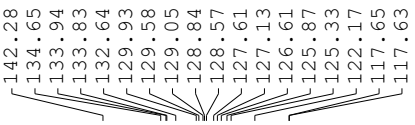


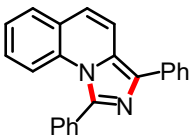


6

^{1}H NMR (500 MHz, $CDCl_3$)

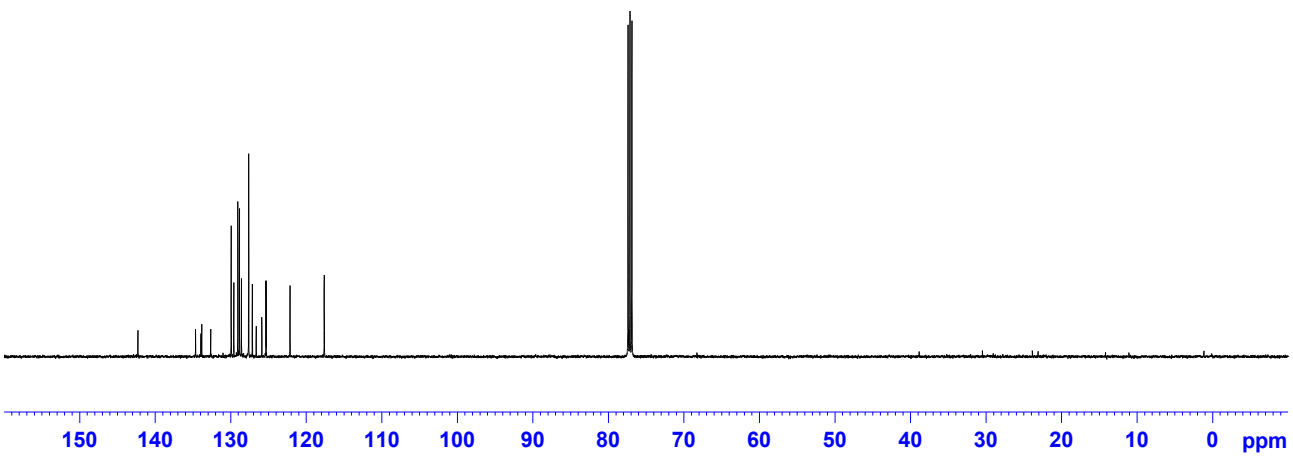


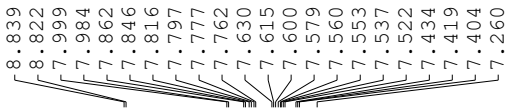


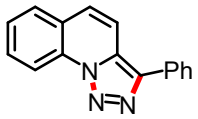


6

^{13}C NMR (125 MHz, $CDCl_3$)

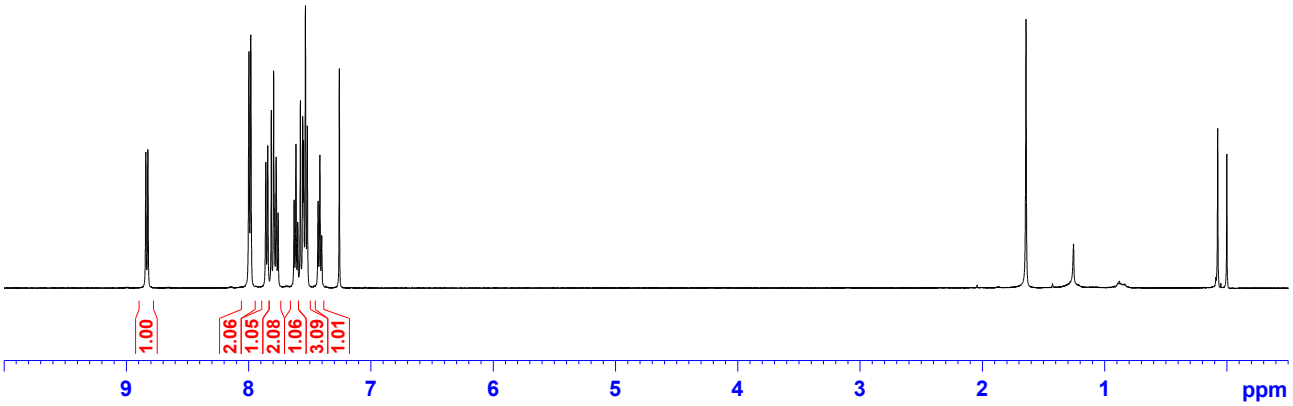


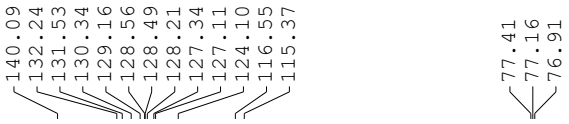


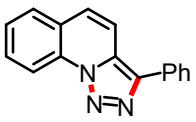


7

^{1}H NMR (500 MHz, $CDCl_3$)

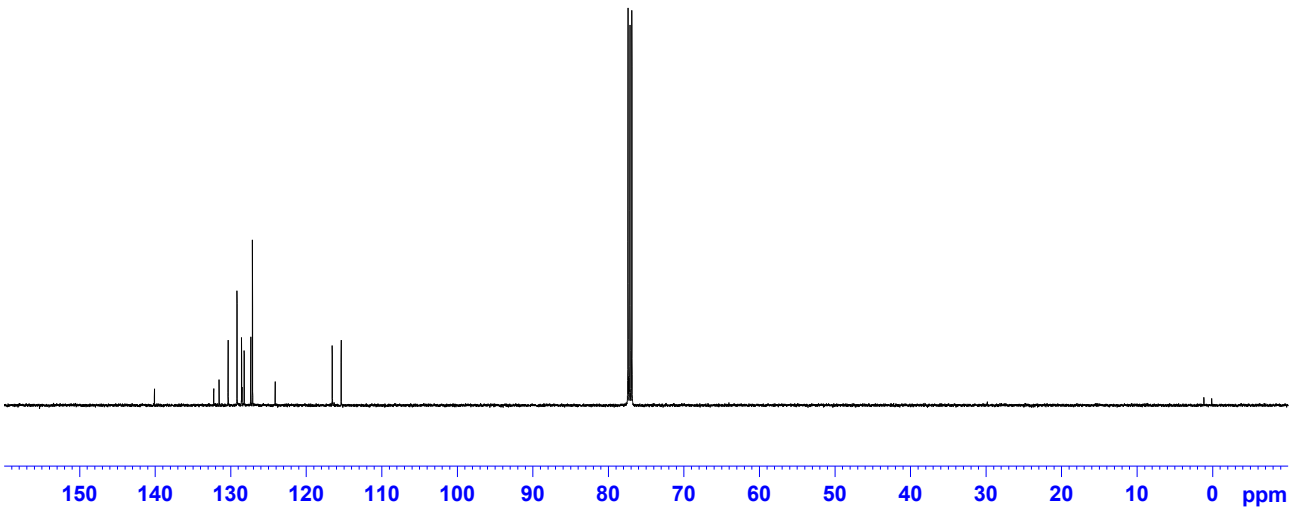


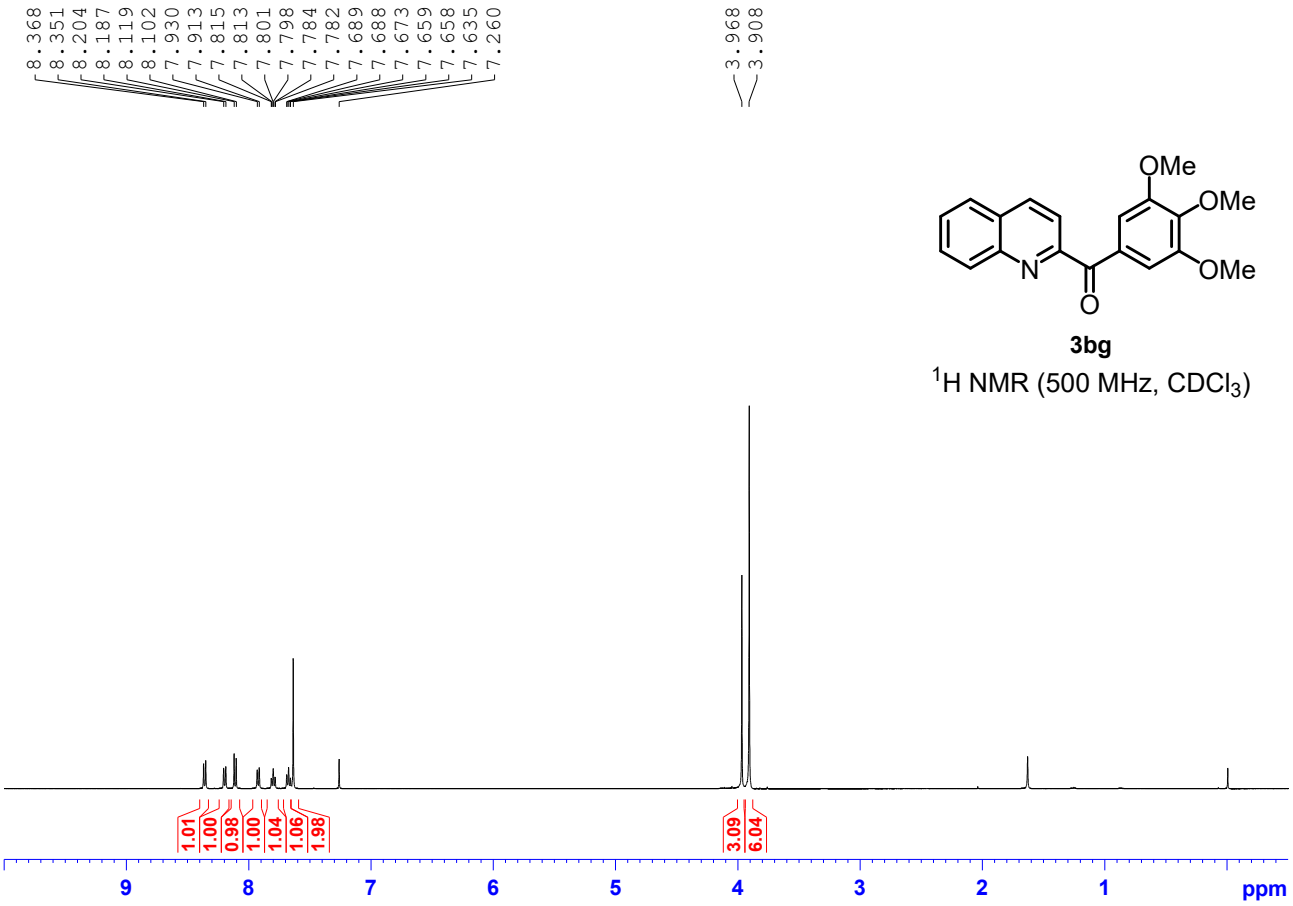




7

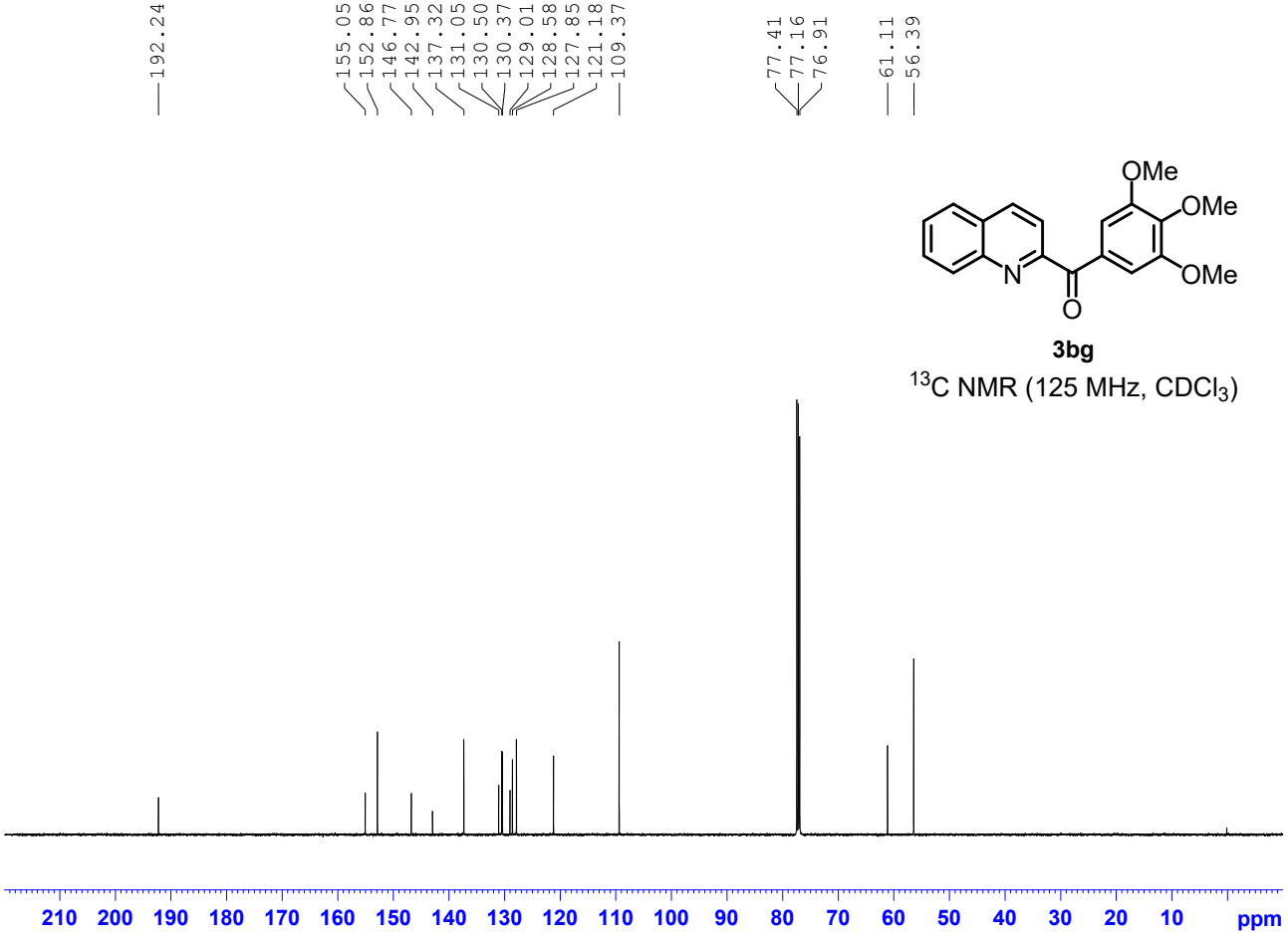
^{13}C NMR (125 MHz, $CDCl_3$)





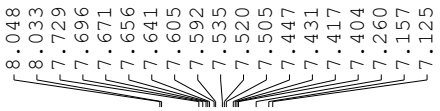
3bg

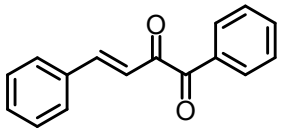
^{1}H NMR (500 MHz, $CDCl_3$)



3bg

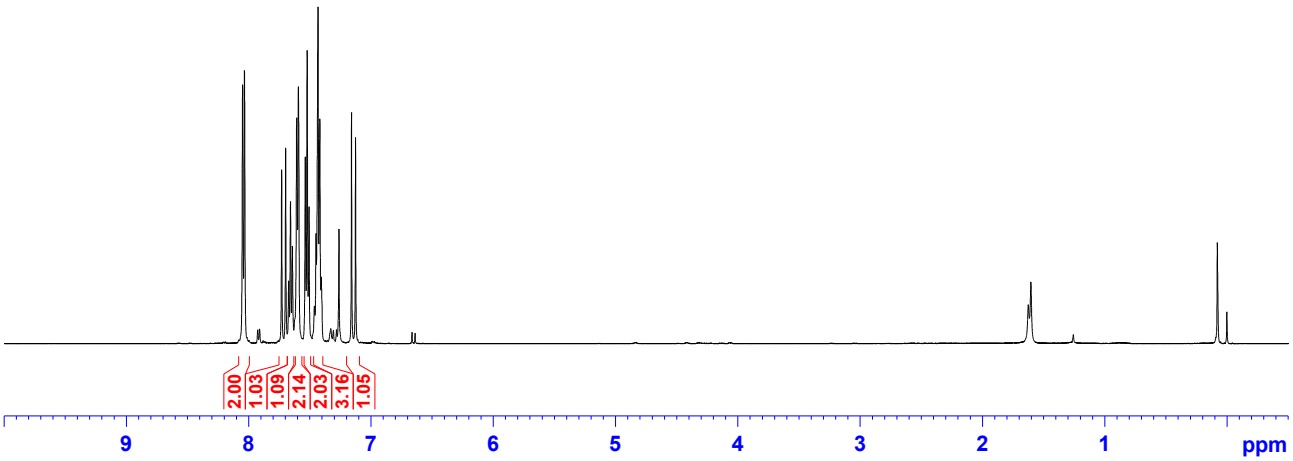
^{13}C NMR (125 MHz, $CDCl_3$)

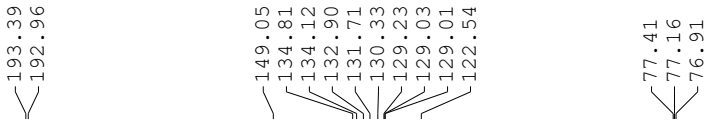


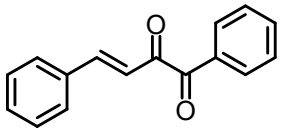


10

^{1}H NMR (500 MHz, $CDCl_3$)

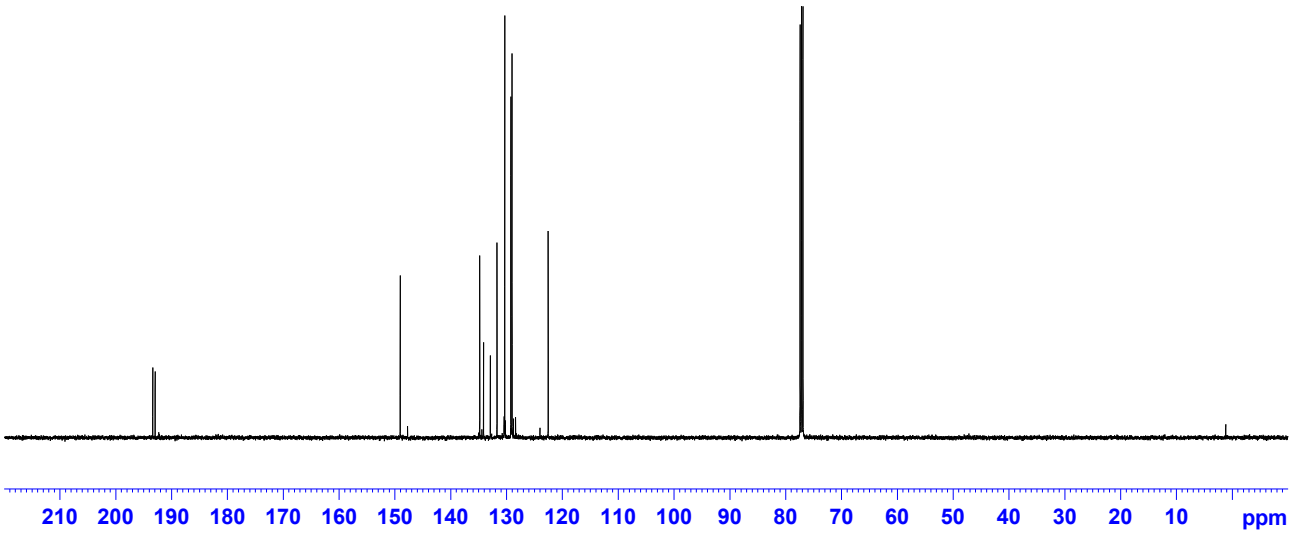


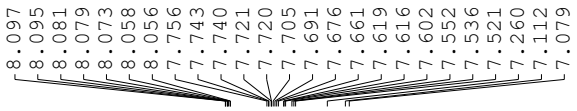


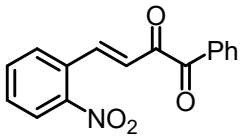


10

^{13}C NMR (125 MHz, $CDCl_3$)

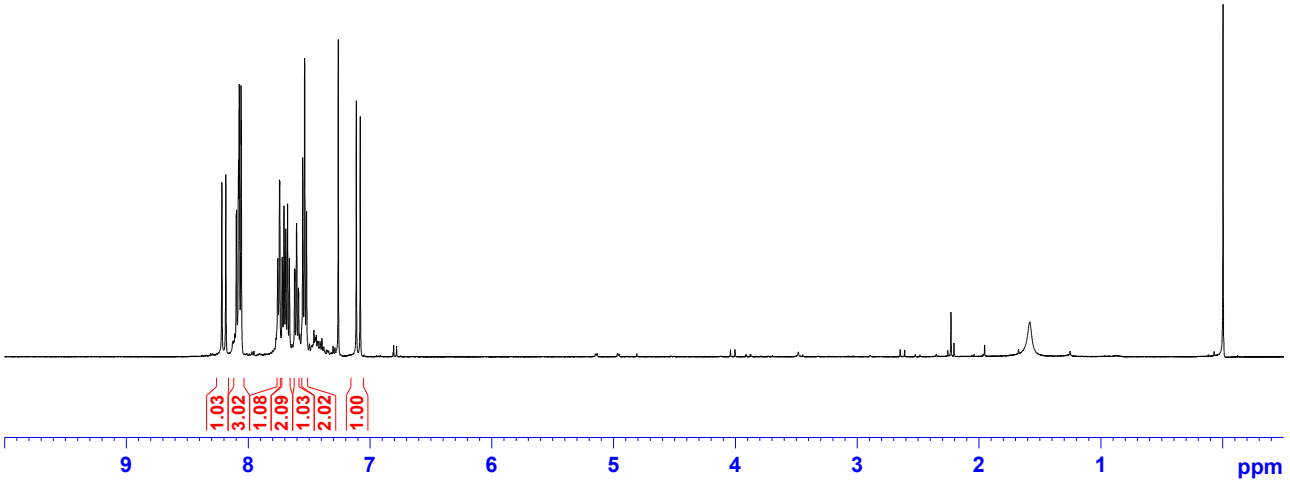


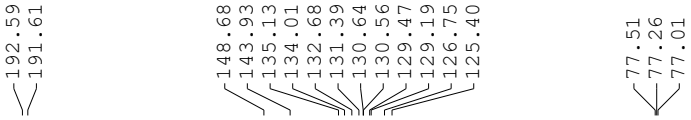


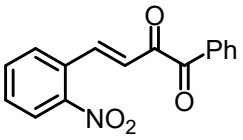


11

^{1}H NMR (500 MHz, $CDCl_3$)

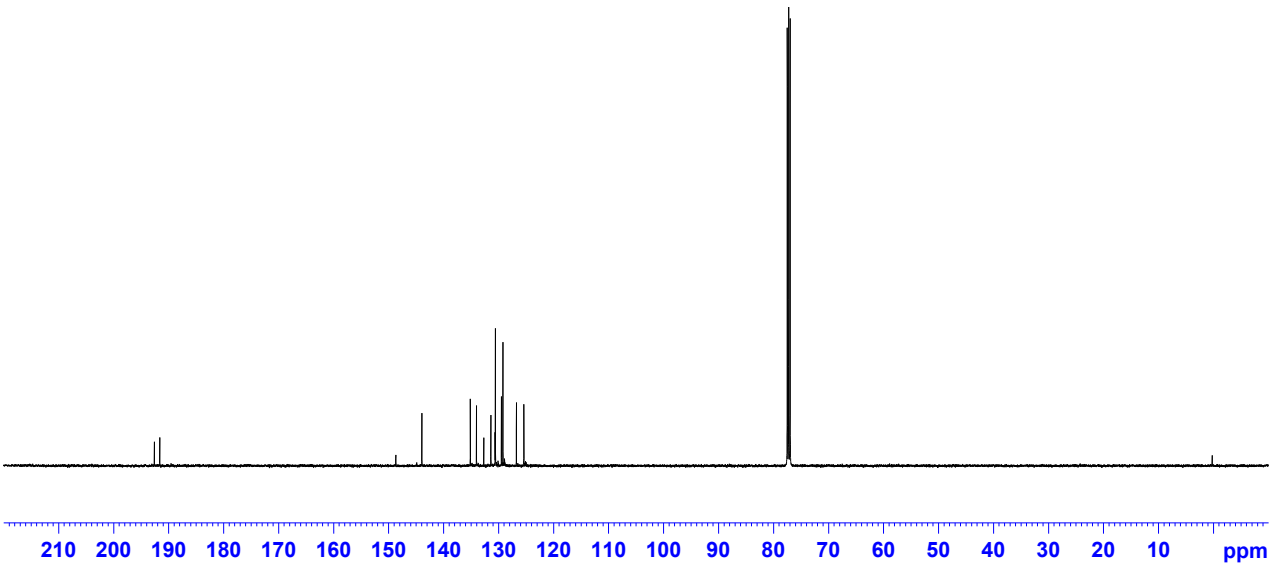


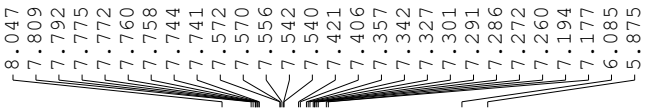


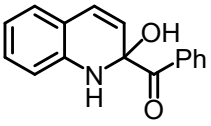


11

^{13}C NMR (125 MHz, $CDCl_3$)

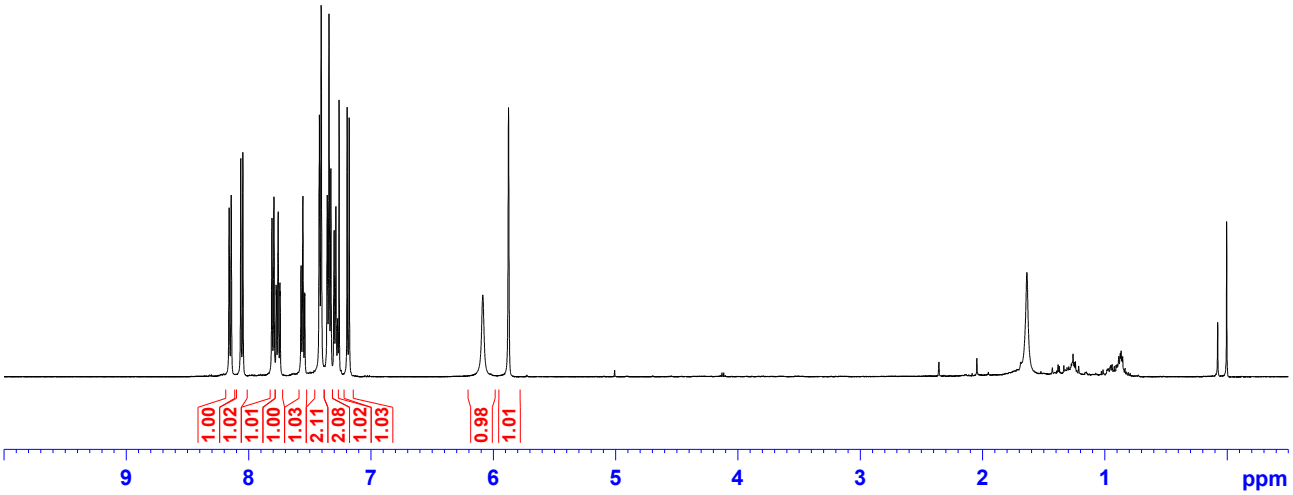


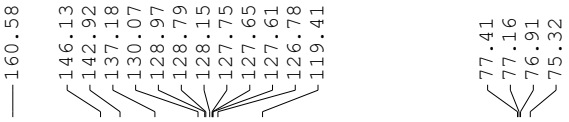


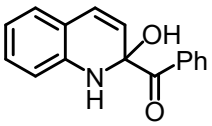


12

^{1}H NMR (500 MHz, $CDCl_3$)







12

^{13}C NMR (125 MHz, $CDCl_3$)