Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Copper-Catalyzed Versatile C(sp^3)-H Arylation: Synthetic Scope and Regioselectivity Investigations

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Context

General methods.

Solvents were dried according to standard procedures. All purchased chemicals were used as received without further purification. All reactions were monitored by TLC with silica gel-coated plates. ^{1}H (400 MHz) NMR and ^{13}C (101 MHz) NMR spectra were recorded on a Varian spectrometer in $CDCl_3$ using tetramethylsilane (TMS) as internal standards. Mass spectra were measured with a HRMS-APCI instrument or a low-resolution MS instrument using ESI or EI ionization.

General procedure for the synthesis of compounds in Table 2

A dry reaction tube was charged with heteroaromatics (0.5 mmol, 1.0 equiv.), alkanes, F-TEDA-BF_4 (2.0 equiv.), CuBr (5 mol %) and H_2SO_4 (1.0 equiv.). CH_3CN (5 mL) was then added and the resulting mixture became a light yellow solution. The reaction was allowed to stir at 50 °C for 4 h. After the completion of the reaction (as indicated by TLC), the reaction mixture was quenched with satd. aq. $NaHCO_3$ (10 mL). The mixture was extracted with EtOAc twice. The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude products were purified on a silica gel column using hexane/EtOAc.

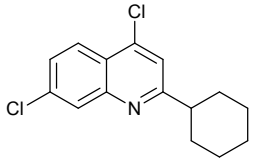
General procedure for the synthesis of compounds in Table 3

A dry reaction tube was charged with heteroaromatics (0.5 mmol, 1.0 equiv.), ethers (20.0 equiv.), F-TEDA-BF_4 (2.0 equiv.), CuBr (5 mol %). CH_3CN (5 mL) was then added and the resulting mixture became a light yellow solution. The reaction was allowed to stir at 50 °C for 4 h. After the completion of the reaction (as indicated by TLC), the reaction mixture was quenched with satd. aq. $NaHCO_3$ (10 mL). The mixture was extracted with EtOAc twice. The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude products were purified on a silica gel column using hexane/EtOAc.

General procedure for the synthesis of compounds in Table 5

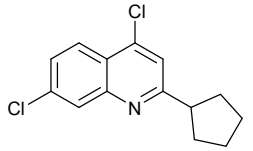
A dry reaction tube was charged with halogenated heteroaromatics (0.5 mmol, 1.0 equiv.), ethers (20.0 equiv.), F-TEDA-BF_4 (2.0 equiv.), CuBr (5 mol %) and TfOH (1.0 equiv.). CH_3CN (5 mL) was then added and the resulting mixture became a black solution. The reaction was allowed to stir at 50 °C for 4 h. After the completion of the reaction (as indicated by TLC), the reaction mixture was quenched with satd. aq. $NaHCO_3$ (10 mL). The mixture was extracted with EtOAc twice. The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude products were purified on a silica gel column using hexane/EtOAc.

Characterization of the products.



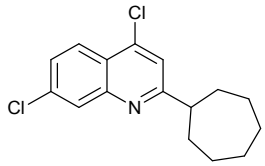
(3aa) 4,7-dichloro-2-cyclohexylquinoline

Colorless oil (90% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 − 8.09 (m, 2H), 7.54 − 7.51 (m, 1H), 7.42 (s, 1H), 2.93 − 2.85 (m, 1H), 2.04 (d, *J* = 11.9 Hz, 2H), 1.93 (d, *J* = 12.8 Hz, 2H), 1.82 (d, *J* = 12.5 Hz, 1H), 1.68 − 1.59 (m, 2H), 1.53 − 1.44 (m, 2H), 1.40 − 1.33 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.1, 149.0, 142.5, 136.2, 128.3, 127.5, 125.2, 123.6, 120.1, 47.3, 32.5 (2C), 26.4 (2C), 25.9; MS (ESI^+): $C_{15}H_{16}Cl_2N$ ($[M+H]^+$); calculated: 280.1, found: 280.1.



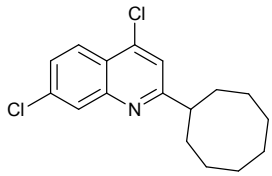
(3ab) 4,7-dichloro-2-cyclopentylquinoline

Colorless oil (82% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 − 8.09 (m, 2H), 7.54 (dd, *J* = 8.9, 1.9 Hz, 1H), 7.44 (s, 1H), 3.4 − 3.3 (m, 1H), 2.2 − 2.17 (m, 2H), 1.97 − 1.88 (m, 4H), 1.81 − 1.79 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.6, 148.9, 142.3, 136.1, 128.3, 127.4, 125.2, 123.5, 120.6, 48.5, 33.3 (2C), 25.9 (2C); MS (ESI^+): $C_{14}H_{14}Cl_2N$ ($[M+H]^+$); calculated: 266.1, found: 266.1.



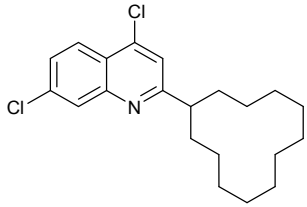
(3ac) 4,7-dichloro-2-cycloheptylquinoline

Colorless oil (88% yield).^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 − 8.08 (m, 2H), 7.52 (d, *J* = 8.9 Hz, 1H), 7.40 (s, 1H), 3.09 − 3.02 (m, 1H), 2.08 − 2.03 (m, 2H), 1.93 − 1.63 (m, 10H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.6, 148.9, 142.4, 136.2, 128.3, 127.4, 125.2, 123.5, 120.2, 49.2, 34.8 (2C), 28.0 (2C), 27.2 (2C); MS (ESI^+): $C_{16}H_{18}Cl_2N$ ($[M+H]^+$); calculated: 294.1, found: 294.2.



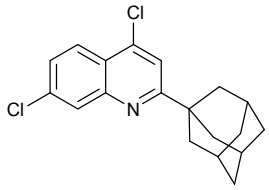
(3ad) 4,7-dichloro-2-cyclooctylquinoline

Colorless oil (72% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 − 8.10 (m, 2H), 7.54 (dd, *J* = 8.9, 1.4 Hz, 1H), 7.40 (s, 1H), 3.18 − 3.12 (m, 1H), 2.04 − 1.89 (m, 6H), 1.75 − 1.66 (m, 8H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.2, 148.8, 142.4, 136.2, 128.3, 127.4, 125.2, 123.4, 120.5, 47.3, 33.0 (2C), 26.6 (2C), 26.4, 25.9 (2C); MS (ESI^+): $C_{17}H_{20}Cl_2N$ ($[M+H]^+$); calculated: 308.1, found: 308.2.



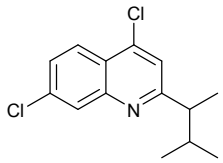
(3ae) 4,7-dichloro-2-cyclododecylquinoline

White solid (63% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 − 8.12 (m, 2H), 7.54 (dd, *J* = 9.0, 1.5 Hz, 1H), 7.41 (s, 1H), 3.18 − 3.12 (m, 1H), 1.97 − 1.89 (m, 2H), 1.78 − 1.70 (m, 2H), 1.60 − 1.32 (m, 18H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.4, 149.1, 142.2, 136.1, 128.5, 127.4, 125.2, 123.5, 120.9, 43.1, 30.0 (2C), 23.9 (4C), 23.6 (2C), 23.3, 22.8 (2C); HRMS (ESI$^+$): $C_{21}H_{28}Cl_2N$ ([M+H]$^+$); calculated: 364.1593, found: 364.1590.



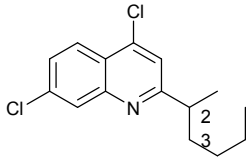
(3af) 2-adamantyl-4,7-dichloroquinoline

White solid (66% yield).^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 − 8.13 (m, 2H), 7.60 (s, 1H), 7.55 (dd, *J* = 8.9, 1.8 Hz, 1H), 2.23 – 2.17 (m, 3H), 2.15 − 2.09 (m, 6H), 1.90 − 1.83 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5, 148.9, 142.4, 135.9, 128.6, 127.5, 125.2, 123.3, 118.3, 41.6 (3C), 40.0, 36.7 (3C), 28.7 (3C); MS (ESI$^+$): $C_{19}H_{20}Cl_2N$ ([M+H]$^+$); calculated: 332.1, found: 332.2.



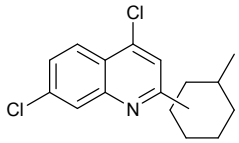
(3ak) 4,7-dichloro-2-(3-methylbutan-2-yl)quinolone

Colorless oil (25% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 − 8.11 (m, 2H), 7.55 (dd, *J* = 8.9, 1.8 Hz, 1H), 7.39 (s, 1H), 2.84 – 2.77 (m, 1H), 2.12 − 2.04 (m, 1H), 1.37 (d, *J* = 7.0 Hz, 3H), 1.04 (d, *J* = 6.7 Hz, 3H), 0.85 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.3, 149.0, 142.3, 136.2, 128.4, 127.5, 125.3, 123.6, 120.6, 49.6, 33.5, 21.4, 19.8, 17.3; HRMS (ESI$^+$): $C_{14}H_{16}Cl_2N$ ([M+H]$^+$); calculated: 268.0654, found: 268.0662.



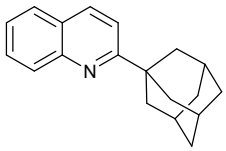
(3am) 4,7-dichloro-2-(hexan-2-yl)quinolone

Colorless oil (C2:C3=10:3, 53% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 – 8.10 (m, 2H), 7.53 (d, *J* = 9.0 Hz, 1H), 7.40 – 7.37 (m, 1H), 3.10 – 3.02 (m, 0.76H), 2.92 – 2.83 (m, 0.23H), 1.89 – 1.64 (m, 2H), 1.39 – 1.28 (m, 5H), 1.26 – 1.19 (m, 1H), 0.93 – 0.84 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.6, 167.6, 149.1, 149.1, 142.4, 142.3, 136.2, 136.1, 128.4, 127.5, 125.2, 123.6, 120.7, 120.1, 120.1, 50.2, 42.8, 37.4, 36.6, 29.8, 28.4, 22.7, 20.7, 20.5, 14.2, 14.0, 12.1; HRMS (ESI$^+$): $C_{15}H_{18}C_{l2}N$ ([M+H]$^+$); calculated: 282.0811, found: 282.0815.



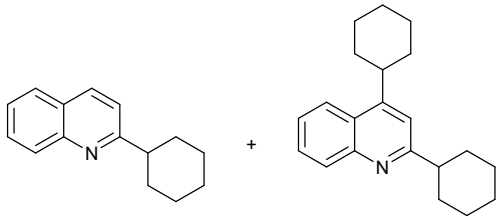
(3al) Methylcyclohexyl 4,7-dichloroquinoline

Colorless oil (68% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 – 8.07 (m, 2H), 7.51 – 7.48 (m, 1H), 7.44 – 7.37 (m, 1H), 3.19 –3.14 (m, 0.09H), 2.94 – 2.78 (m, 0.57H), 2.55 – 2.48 (m, 0.16H), 2.08 – 0.73 (m, 13H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.0, 167.9, 167.7, 149.1, 149.0, 149.0, 142.4, 142.4, 142.3, 136.1, 136.0, 128.3, 127.4, 125.2, 123.6, 123.5, 123.4, 120.6, 120.5, 120.4, 120.3, 120.2, 120.1, 54.9, 47.2, 46.9, 45.6, 41.0, 38.0, 36.5, 35.3, 35.1, 34.6, 33.8, 32.8, 32.5, 32.2, 32.1, 31.8, 31.5, 28.1, 27.7, 27.2, 26.4, 26.3, 26.2, 22.8, 22.6, 20.9, 20.6, 19.2, 18.8; HRMS (ESI$^+$): $C_{16}H_{18}Cl_2N$ ([M+H]$^+$); calculated: 294.0811, found: 294.0816.



(3bf) 2-adamantyl-quinoline

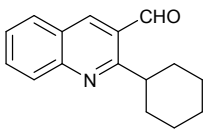
White solid (72% yield).^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 − 8.10 (m, 2H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.71 (t, *J* = 7.5 Hz, 1H), 7.55 – 7.49 (m, 2H), 2.21 − 2.14 (m, 9H), 1.91 – 1.86 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.0, 147.7, 135.8, 129.4, 128.9, 127.3, 126.6, 125.6, 117.8, 41.9 (3C), 39.8, 36.9 (3C), 28.9 (3C); MS (ESI$^+$): $C_{19}H_{22}N$ ([M+H]$^+$); calculated: 264.2, found: 264.2.



(3ma) 2-cyclohexylquinoline (major)

(3ma') 2,4-dicyclohexylquinoline (minor)

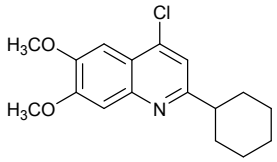
Colorless oil (**3ma**:**3ma'** = 7:3, 75% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 – 8.06 (m, 2.03H), 7.78 – 7.65 (m, 1.57H), 7.52 – 7.46 (m, 1.02H), 7.34 – 7.25 (m, 0.77H), 3.35 – 3.33 (m, 0.31H), 3.00 – 2.92 (m, 1H), 2.09 – 1.32 (m, 16H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.8, 166.6, 153.3, 148.1, 147.8, 136.2, 129.9, 129.2, 129.0, 128.6, 127.4, 127.0, 125.6, 125.6, 125.2, 122.8, 119.6, 115.8, 47.8, 47.6, 39.0, 33.6, 32.9, 32.8, 27.0, 26.6, 26.6, 26.3, 26.2, 26.1; MS (ESI$^+$): $C_{15}H_{18}N$ ([M+H]$^+$); calculated: 212.1, found: 212.1. MS (ESI$^+$): $C_{21}H_{28}N$ ([M+H]$^+$); calculated: 294.2, found: 294.2.



(3oa) 2-cyclohexylquinoline-3-carbaldehyde

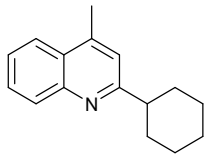
Colorless oil (79% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.47 (s, 1H), 8.60 (s, 1H), 8.12 (d, *J* = 8.5 Hz, 1H), 7.93 (d, *J* = 8.1 Hz, 1H), 7.83 (t, *J* = 7.5 Hz, 1H), 7.57 (t, *J* = 7.5 Hz, 1H), 3.75 – 3.70

(m, 1H), 2.01 – 1.83 (m, 7H), 1.60 – 1.51 (m, 2H), 1.46 – 1.36 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.2, 165.7, 149.5, 141.7, 132.2, 129.2, 129.0, 127.1, 126.7, 125.8, 42.2, 32.5 (2C), 26.6 (2C), 26.1; HRMS (ESI$^+$): $C_{16}H_{18}NO$ ([M+H]$^+$); calculated: 240.1383, found: 240.1389.



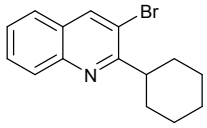
(3qa) 4-chloro-2-cyclohexyl-6,7-dimethoxyquinoline

White solid (45% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, *J* = 11.0 Hz, 2H), 7.31 (s, 1H), 4.07 (s, 3H), 4.06 (s, 3H), 2.89 – 2.83 (m, 1H), 2.06 – 2.03 (m, 2H), 1.94 – 1.91 (m, 2H), 1.83 – 1.80 (m, 1H), 1.66 – 1.33 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.7, 152.9, 150.0, 145.6, 140.6, 120.3, 117.8, 108.1, 101.2, 56.2, 56.1, 47.2, 32.9 (2C), 26.5 (2C), 26.0; HRMS (ESI$^+$): $C_{17}H_{21}ClNO_2$ ([M+H]$^+$); calculated: 306.1255, found: 306.1263.



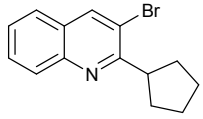
(3da) 2-cyclohexyl-4-methylquinoline

Colorless oil (54% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 8.4 Hz, 1H), 7.96 (d, *J* = 8.3 Hz, 1H), 7.70 − 7.66 (m, 1H), 7.53 − 7.49 (m, 1H), 7.19 (s, 1H), 2.90 (tt, *J* = 12.0, 3.4 Hz, 1H), 2.70 (s, 3H), 2.04 (dd, *J* = 13.2, 1.7 Hz, 2H), 1.93 − 1.89 (m, 2H), 1.83 − 1.79 (m, 1H), 1.70 − 1.60 (m, 2H), 1.55 − 1.44 (m, 2H), 1.41 − 1.33 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 147.6, 144.3, 129.5, 128.9, 127.0, 125.4, 123.6, 120.2, 47.6, 32.8 (2C), 26.6 (2C), 26.2, 18.9; MS (ESI$^+$): $C_{16}H_{20}N$ ([M+H]$^+$); calculated: 226.2, found: 226.2.



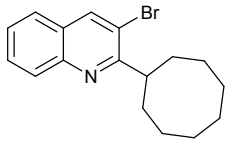
(3ea) 3-bromo-2-cyclohexylquinoline

Colorless oil (75% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (s, 1H), 8.08 (d, *J* = 8.8 Hz, 1H), 7.74 − 7.70 (m, 2H), 7.53 (t, *J* = 7.5 Hz, 1H), 3.40 (tt, *J* = 11.6, 3.2 Hz, 1H), 2.06 − 1.95 (m, 4H), 1.85 − 1.75 (m, 3H), 1.59 − 1.40 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.5, 146.6, 138.7, 129.4, 129.2, 127.9, 126.5, 126.4, 118.8, 44.5, 31.6 (2C), 26.6 (2C), 26.1; MS (ESI$^+$): $C_{15}H_{17}BrN$ ([M+H]$^+$); calculated: 290.1, found: 290.1.



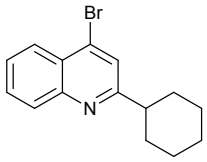
(3eb) 3-bromo-2-cyclopentylquinoline

Colorless oil (61% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (s, 1H), 8.06 (d, *J* = 8.8 Hz, 1H), 7.73 − 7.69 (m, 2H), 7.52 (t, *J* = 7.4 Hz, 1H), 3.90 – 3.82 (m, 1H), 2.19 − 2.05 (m, 4H), 1.99 − 1.91 (m, 2H), 1.84 − 1.78 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.0, 146.4, 138.5, 129.3, 129.2, 127.9, 126.4, 126.3, 119.5, 46.1, 32.1 (2C), 26.0 (2C); HRMS (ESI$^+$): $C_{14}H_{15}BrN$ ([M+H]$^+$); calculated: 276.0382, found: 276.0381.



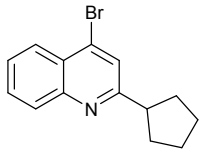
(3ed) 3-bromo-2-cyclooctylquinoline

Colorless oil (50% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (s, 1H), 8.07 (d, *J* = 8.7 Hz, 1H), 7.73 − 7.70 (m, 2H), 7.52 (t, *J* = 7.3 Hz, 1H), 3.76 − 3.70 (m, 1H), 2.11 − 1.98 (m, 4H), 1.92 − 1.90 (m, 2H), 1.75 − 1.71 (m, 8H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.5, 146.5, 138.8, 129.4, 129.1, 127.7, 126.4, 126.4, 118.7, 43.5, 32.3 (2C), 26.9, 26.7 (2C), 26.1 (2C); HRMS (ESI^+): $C_{17}H_{21}BrN$ ($[M+H]^+$); calculated: 318.0852, found: 318.0859.



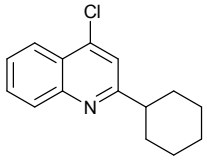
(3fa) 4-bromo-2-cyclohexylquinoline

Colorless oil (80% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8.3 Hz, 1H), 8.08 (d, *J* = 8.4 Hz, 1H), 7.75 (t, *J* = 7.6 Hz, 1H), 7.67 (s, 1H), 7.60 (t, *J* = 7.6 Hz, 1H), 2.92 (tt, *J* = 11.9, 3.3 Hz, 1H), 2.07 (d, *J* = 11.8 Hz, 2H), 1.94 (d, *J* = 12.9 Hz, 2H), 1.83 (d, *J* = 12.5 Hz, 1H), 1.66 (m, 2H), 1.55 − 1.45 (m, 2H), 1.42 − 1.34 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.7, 148.5, 134.2, 130.1, 129.4, 126.8, 126.5, 126.5, 123.7, 47.2, 32.7 (2C), 26.4 (2C), 26.0; MS (ESI^+): $C_{15}H_{17}BrN$ ($[M+H]^+$); calculated: 290.1, found: 290.2.



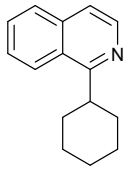
(3fb) 4-bromo-2-cyclopentylquinoline

Colorless oil (83% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8.3 Hz, 1H), 8.07 (d, *J* = 8.4 Hz, 1H), 7.74 (t, *J* = 7.7 Hz, 1H), 7.67 (s, 1H), 7.59 (t, *J* = 7.6 Hz, 1H), 3.42 − 3.34 (m, 1H), 2.24 − 2.18 (m, 2H), 1.97 − 1.88 (m, 4H), 1.81 − 1.79 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2, 148.4, 134.0, 130.1, 129.4, 126.8, 126.5, 126.4, 124.1, 48.4, 33.5 (2C), 26.0 (2C); HRMS (ESI^+): $C_{14}H_{15}BrN$ ($[M+H]^+$); calculated: 276.0382, found: 276.0387.



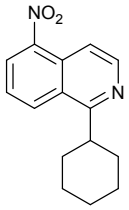
(3ga) 4-chloro-2-cyclohexylquinoline

Colorless oil (79% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.4 Hz, 1H), 8.07 (d, *J* = 8.5 Hz, 1H), 7.73 (t, *J* = 7.7 Hz, 1H), 7.56 (t, *J* = 7.6 Hz, 1H), 7.43 (s, 1H), 2.90 (tt, *J* = 12.0, 3.4 Hz, 1H), 2.05 − 2.02 (m, 2H), 1.92 − 1.89 (m, 2H), 1.81 − 1.78 (m, 1H), 1.67 − 1.57 (m, 2H), 1.53 − 1.42 (m, 2H), 1.39 − 1.30 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.8, 148.6, 142.6, 130.2, 129.3, 126.6, 125.1, 123.9, 119.8, 47.4, 32.7 (2C), 26.4 (2C), 26.0; MS (ESI^+): $C_{15}H_{17}ClN$ ($[M+H]^+$); calculated: 246.1, found: 246.1.



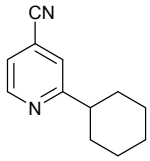
(3ca) 1-cyclohexyl *iso*-quinolin

Colorless oil (65% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (d, J = 5.7 Hz, 1H), 8.25 (d, J = 8.4 Hz, 1H), 7.83 (d, J = 8.0 Hz, 1H), 7.69 − 7.65 (m, 1H), 7.63 − 7.59 (m, 1H), 7.51 (d, J = 5.7 Hz, 1H), 3.59 (tt, J = 11.7, 3.2 Hz, 1H), 2.03 − 1.94 (m, 4H), 1.91 − 1.81 (m, 3H), 1.62 − 1.50 (m, 2H), 1.49 − 1.39 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.7, 141.8, 136.4, 129.6, 127.6, 126.8, 126.3, 124.8, 118.9, 41.5, 32.6 (2C), 26.9 (2C), 26.2; MS (ESI$^+$): $C_{15}H_{18}N$ ([M+H]$^+$); calculated: 212.1, found: 212.2.



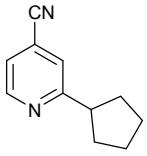
(3sa) 1-cyclohexyl-5-nitroisoquinoline

Colorless oil (56% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (d, J = 5.8 Hz, 1H), 8.58 (d, J = 8.5 Hz, 1H), 8.41 (d, J = 7.6 Hz, 1H), 8.19 (d, J = 6.0 Hz, 1H), 7.68 (t, J = 8.0 Hz, 1H), 3.60 − 3.54 (m, 1H), 1.96 − 1.83 (m, 7H), 1.59 − 1.34 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4, 145.9, 145.2, 131.3, 128.7, 127.2, 126.8, 125.1, 113.3, 42.2, 32.7 (2C), 26.7 (2C), 26.1; HRMS (ESI$^+$): $C_{15}H_{17}N_2O_2$ ([M+H]$^+$); calculated: 257.1285, found: 257.1294.



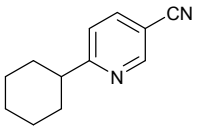
(3ha) 2-cyclohexylisonicotinonitrile

Colorless oil (47% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (d, J = 4.9 Hz, 1H), 7.39 (s, 1H), 7.34 – 7.33 (m, 1H), 2.77 (tt, J = 11.7, 3.4 Hz, 1H), 1.97 − 1.94 (m, 2H), 1.90 − 1.86 (m, 2H), 1.57 − 1.37 (m, 1H), 1.46 (m, 4H), 1.34 − 1.25 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.1, 150.0, 122.9, 122.4, 120.6, 116.9, 46.4, 32.6 (2C), 26.3 (2C), 25.8; MS (ESI$^+$): $C_{12}H_{15}N_2$ ([M+H]$^+$); calculated: 187.1, found: 187.1.



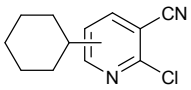
(3hb) 2-cyclopentylisonicotinonitrile

Colorless oil (49% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (d, J = 5.0 Hz, 1H), 7.41 (s, 1H), 7.34 – 7.32 (m, 1H), 3.28 – 3.20 (m, 1H), 2.15 − 2.07 (m, 2H), 1.91 − 1.71 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.5, 150.1, 123.5, 122.3, 120.4, 116.9, 47.8, 33.4 (2C), 25.8 (2C); MS (ESI$^+$): $C_{11}H_{13}N_2$ ([M+H]$^+$); calculated: 173.1, found: 173.1.



(3wa) 6-cyclohexylnicotinonitrile

Colorless oil (29% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (d, *J* = 1.6 Hz, 1H), 7.88 (dd, *J* = 8.2, 2.2 Hz, 1H), 7.30 (d, *J* = 8.8 Hz, 1H), 2.83 – 2.75 (m, 1H), 1.98 – 1.87 (m, 4H), 1.81 – 1.77 (m, 1H), 1.59 – 1.34 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 152.0, 139.4, 121.2, 117.1, 107.1, 46.8, 32.5 (2C), 26.3 (2C), 25.8; HRMS (ESI^+): $C_{12}H_{15}N_2$ ($[M+H]^+$); calculated: 187.1230, found: 187.1235.

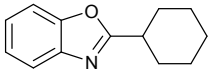


(3ta) 2-chloro-6-cyclohexylnicotinonitrile

(3ta') 2-chloro-4-cyclohexylnicotinonitrile

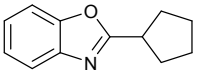
(3ta'') 2-chloro-4,6-dicyclohexylnicotinonitrile

Colorless oil (3ta:3ta':3ta'' = 5:4:7, 80%yield). **C6-substituted:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.9 Hz, 1H), 7.25 (d, *J* = 8.0 Hz, 1H), 2.82 – 2.74 (m, 1H), 1.98 – 1.88 (m, 4H), 1.81 – 1.78 (m, 1H), 1.59 – 1.29 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.9, 152.0, 142.6, 119.6, 115.1, 107.6, 46.5, 32.2 (2C), 26.1 (2C), 25.7; HRMS (ESI^+): $C_{12}H_{14}ClN_2$ ($[M+H]^+$); calculated: 221.0840, found: 221.0846. **C4-substituted:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, *J* = 5.3 Hz, 1H), 7.29 (d, *J* = 5.3 Hz, 1H), 3.03 – 2.97 (m, 1H), 1.96 – 1.83 (m, 5H), 1.57 – 1.26 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.8, 153.3, 152.1, 120.0, 113.9, 110.3, 43.1, 32.8 (2C), 26.1 (2C), 25.6; HRMS (ESI^+): $C_{12}H_{14}ClN_2$ ($[M+H]^+$); calculated: 221.0840, found: 221.0843. **C4,6-disubstituted:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09 (s, 1H), 2.98 – 2.93 (m, 1H), 2.76 – 2.69 (m, 1H), 1.95 – 1.76 (m, 10H), 1.59 – 1.26 (m, 10H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 163.6, 152.5, 117.2, 114.5, 107.3, 46.6, 43.1, 32.8 (2C), 32.3 (2C), 26.2 (2C), 26.2 (2C), 25.7, 25.6; HRMS (ESI^+): $C_{18}H_{24}ClN_2$ ($[M+H]^+$); calculated: 303.1623, found: 303.1628.



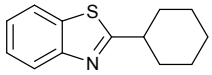
(3ia) 2-cyclohexylbenzo[*d*]oxazole

Colorless oil (82% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 − 7.71 (m, 1H), 7.51 − 7.49 (m, 1H), 7.32 − 7.30 (m, 2H), 2.99 (tt, *J* = 11.3, 3.5 Hz, 1H), 2.22 − 2.19 (m, 2H), 1.92 − 1.88 (m, 2H), 1.80 − 1.70 (m, 3H), 1.52 − 1.34 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.4, 150.6, 141.3, 124.3, 123.9, 119.6, 110.2, 37.9, 30.5 (2C), 25.8, 25.6 (2C); MS (ESI^+): $C_{13}H_{16}NO$ ($[M+H]^+$); calculated: 202.1, found: 202.1.



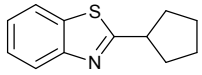
(3ib) 2-cyclopentylbenzo[*d*]oxazole

Colorless oil (71% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 − 7.70 (m, 1H), 7.51 − 7.48 (m, 1H), 7.34 − 7.29 (m, 2H), 3.46 – 3.38 (m, 1H), 2.20 (td, *J* = 12.1, 7.3 Hz, 2H), 2.08 (td, *J* = 15.0, 7.7 Hz, 2H), 1.94 − 1.85 (m, 2H), 1.81 − 1.71 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.6, 150.8, 141.3, 124.3, 124.0, 119.5, 110.2, 38.9, 31.4 (2C), 25.7 (2C); MS (ESI^+): $C_{12}H_{14}NO$ ($[M+H]^+$); calculated: 188.1, found: 188.1.



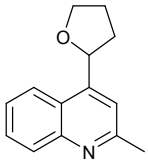
(3ja) 2-cyclohexylbenzo[*d*]thiazole

Colorless oil (60% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.1 Hz, 1H), 7.88 (d, *J* = 7.9 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 1H), 7.37 (t, *J* = 7.5 Hz, 1H), 3.15 (tt, *J* = 11.6, 3.5 Hz, 1H), 2.26 − 2.33 (m, 2H), 1.95 − 1.91 (m, 2H), 1.82 − 1.79 (m, 1H), 1.74 − 1.64 (m, 2H), 1.54 − 1.43 (m, 2H), 1.41 − 1.33 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.6, 153.1, 134.5, 125.8, 124.5, 122.6, 121.5, 43.4, 33.4 (2C), 26.1 (2C), 25.8; MS (ESI$^+$): $C_{13}H_{16}NS$ ([M+H]$^+$); calculated: 218.1, found: 218.1.



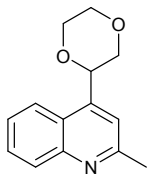
(3jb) 2-cyclopentylbenzo[*d*]thiazole

Colorless oil (56% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.1 Hz, 1H), 7.87 (d, *J* = 7.9 Hz, 1H), 7.48 (t, *J* = 7.7 Hz, 1H), 7.37 (t, *J* = 7.6 Hz, 1H), 3.63 − 3.55 (m, 1H), 2.34 − 2.27 (m, 2H), 2.04 − 1.86 (m, 4H), 1.82 − 1.76 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.1, 153.2, 134.8, 125.8, 124.5, 122.5, 121.5, 44.8, 34.0 (2C), 25.6 (2C); MS (ESI$^+$): $C_{12}H_{14}NS$ ([M+H]$^+$); calculated: 204.1, found: 204.0.



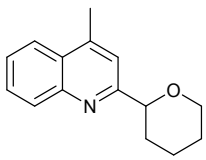
(3kg) 2-methyl-4-(tetrahydrofuran-2-yl)quinoline

Colorless oil (60% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.4 Hz, 1H), 7.86 (d, *J* = 8.4 Hz, 1H), 7.68 (t, *J* = 7.6 Hz, 1H), 7.51 − 7.46 (m, 2H), 5.58 (t, *J* = 7.1 Hz, 1H), 4.27 − 4.22 (m, 1H), 4.08 − 4.02 (m, 1H), 2.76 (s, 3H), 2.66 − 2.57 (m, 1H), 2.14 − 1.96 (m, 2H), 1.89 − 1.81 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.0, 149.3, 147.9, 129.4, 128.9, 125.4, 123.8, 123.0, 117.2, 76.8, 68.9, 33.8, 26.0, 25.5; MS (ESI$^+$): $C_{14}H_{16}NO$ ([M+H]$^+$); calculated: 214.1, found: 214.1.



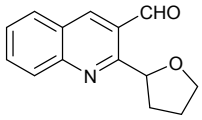
(3kh) 4-(1,4-dioxan-2-yl)-2-methylquinoline

Colorless oil (51% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 8.4 Hz, 1H), 7.98 (d, *J* = 8.4 Hz, 1H), 7.71 (t, *J* = 7.6 Hz, 1H), 7.56 – 7.53 (m, 2H), 5.38 (dd, *J* = 9.8, 2.0 Hz, 1H), 4.16 (dd, *J* = 11.8, 2.2 Hz, 1H), 4.10 – 4.05 (m, 2H), 3.94 – 3.91 (m, 1H), 3.87 – 3.80 (m, 1H), 3.52 – 3.47 (m, 1H), 2.79 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.1, 147.8, 143.6, 129.6, 129.2, 126.0, 123.6, 122.4, 119.1, 74.2, 72.0, 67.4, 66.6, 25.5; MS (ESI$^+$): $C_{14}H_{16}NO_2$ ([M+H]$^+$); calculated: 230.1, found: 230.1.



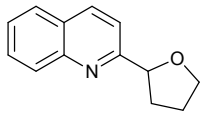
(3li) 4-methyl-2-(tetrahydro-*2H*-pyran-2-yl)quinoline

Colorless oil (63% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 8.4 Hz, 1H), 8.01 (d, *J* = 8.3 Hz, 1H), 7.72 (t, *J* = 7.5 Hz, 1H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.51 (s, 1H), 4.66 (dd, *J* = 11.1, 1.9 Hz, 1H), 4.26 (dd, *J* = 11.2, 3.4 Hz, 1H), 3.77 – 3.71 (m, 1H), 2.75 (s, 3H), 2.15 (d, *J* = 13.0 Hz, 1H), 2.03 – 2.02 (m, 1H), 1.87 – 1.63 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.1, 147.1, 145.1, 129.6, 129.1, 127.5, 125.8, 123.6, 118.8, 81.6, 68.9, 32.8, 25.9, 23.7, 18.8; MS (ESI^+): $C_{15}H_{18}NO$ ($[M+H]^+$); calculated: 228.1, found: 228.1.



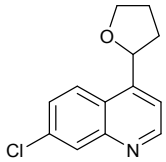
(3yg) 2-(tetrahydrofuran-2-yl)quinoline-3-carbaldehyde

Colorless oil (50% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.60 (s, 1H), 8.71 (s, 1H), 8.20 (d, *J* = 8.5 Hz, 1H), 7.99 (d, *J* = 8.1 Hz, 1H), 7.88 (t, *J* = 7.6 Hz, 1H), 7.65 (t, *J* = 7.5 Hz, 1H), 5.75 (t, *J* = 6.9 Hz, 1H), 4.20 (dd, *J* = 14.8, 7.2 Hz, 1H), 4.07 (dd, *J* = 14.8, 7.3 Hz, 1H), 2.58 – 2.46 (m, 2H), 2.18 – 2.09 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.4, 160.6, 148.7, 140.7, 132.3, 129.5, 129.0, 128.1, 127.4, 126.5, 80.0, 69.0, 31.1, 25.8; HRMS (ESI^+): $C_{14}H_{14}NO_2$ ($[M+H]^+$); calculated: 228.1019, found: 228.1022.



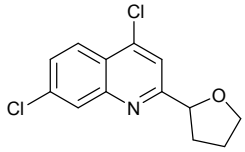
(3mg) 2-(tetrahydrofuran-2-yl)quinoline

Colorless oil (23% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.5 Hz, 1H), 8.09 (d, *J* = 8.5 Hz, 1H), 7.79 (d, *J* = 8.1 Hz, 1H), 7.70 (t, *J* = 7.6 Hz, 1H), 7.61 (d, *J* = 8.5 Hz, 1H), 7.50 (t, *J* = 7.5 Hz, 1H), 5.21 (t, *J* = 7.0 Hz, 1H), 4.18 (dd, *J* = 14.4, 7.0 Hz, 1H), 4.05 (dd, *J* = 14.5, 7.3 Hz, 1H), 2.57 – 2.49 (m, 1H), 2.14 – 1.98 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.5, 147.5, 136.7, 129.4, 129.0, 127.6, 127.4, 126.0, 118.0, 82.0, 69.2, 33.4, 25.9; MS (ESI^+): $C_{13}H_{14}NO$ ($[M+H]^+$); calculated: 200.1, found: 200.1.



(3ag) 7-chloro-4-(tetrahydrofuran-2-yl)quinoline

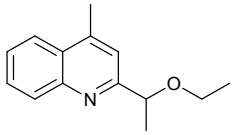
Colorless oil (75% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (d, *J* = 4.5 Hz, 1H), 8.16 (d, *J* = 1.8 Hz, 1H), 7.90 (d, *J* = 9.0 Hz, 1H), 7.58 – 7.52 (m, 2H), 5.59 (t, *J* = 7.1 Hz, 1H), 4.25 (dd, *J* = 13.6, 7.5 Hz, 1H), 4.08 (dd, *J* = 15.1, 7.3 Hz, 1H), 2.63 (td, *J* = 14.2, 7.6 Hz, 1H), 2.18 – 2.01 (m, 2H), 1.91 – 1.83 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.5, 149.6, 148.6, 134.8, 129.1, 127.3, 124.6, 124.0, 116.7, 76.6, 69.0, 33.9, 25.9. HRMS (ESI^+): $C_{13}H_{13}ClNO$ ($[M+H]^+$); calculated: 234.0680, found: 234.0674.



(3ag') 4,7-dichloro-2-(tetrahydrofuran-2-yl)quinoline

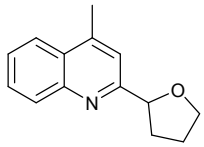
Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, *J* = 8.9 Hz, 1H), 8.07 (d, *J* = 1.7 Hz, 1H), 7.72 (s, 1H), 7.55 (dd, *J* = 8.9, 1.9 Hz, 1H), 5.16 – 5.12 (m, 1H), 4.17 (dd, *J* = 14.5, 6.8 Hz, 1H),

4.06 (dd, J = 14.1, 7.3 Hz, 1H), 2.57 – 2.46 (m, 1H), 2.13 – 1.96 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.2, 148.7, 143.3, 136.5, 128.3, 128.0, 125.5, 124.1, 118.5, 81.3, 69.4, 33.2, 25.9; HRMS (ESI^+): $C_{13}H_{12}Cl_2NO$ ($[M+H]^+$); calculated: 268.0290, found: 268.0284.



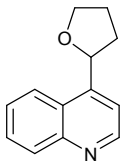
(3nj) 2-(1-ethoxyethyl)-4-methylquinoline

Colorless oil (40% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, J = 8.4 Hz, 1H), 8.03 (d, J = 8.3 Hz, 1H), 7.74 (t, J = 7.5 Hz, 1H), 7.58 (t, J = 7.5 Hz, 1H), 7.49 (s, 1H), 4.72 (q, J = 6.6 Hz, 1H), 3.59 – 3.43 (m, 2H), 2.77 (s, 3H), 1.58 (d, J = 6.6 Hz, 3H), 1.27 (t, J = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.0, 147.1, 145.3, 129.5, 129.2, 127.6, 125.0, 123.7, 118.3, 79.7, 64.6, 22.6, 19.0, 15.5; MS (ESI^+): $C_{14}H_{18}NO$ ($[M+H]^+$); calculated: 216.1, found: 216.1.



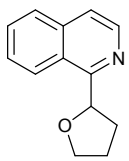
(3ng) 4-methyl-2-(tetrahydrofuran-2-yl)quinoline

Colorless oil (57% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, J = 8.4 Hz, 1H), 8.01 (d, J = 8.2 Hz, 1H), 7.72 (t, J = 7.6 Hz, 1H), 7.56 (t, J = 7.6 Hz, 1H), 7.48 (s, 1H), 5.18 (t, J = 6.9 Hz, 1H), 4.22 (dd, J = 13.9, 5.8 Hz, 1H), 4.08 (dd, J = 14.6, 7.0 Hz, 1H), 2.75 (s, 3H), 2.59 – 2.52 (m, 1H), 2.16 – 2.03 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.0, 147.3, 145.0, 129.5, 129.1, 127.4, 125.8, 123.7, 118.6, 82.0, 69.2, 33.3, 26.0, 18.9; MS (ESI^+): $C_{14}H_{16}NO$ ($[M+H]^+$); calculated: 214.1, found: 214.1.



(3mg') 4-(tetrahydrofuran-2-yl)quinoline

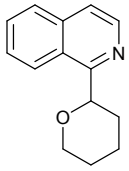
Colorless oil (42% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (d, J = 4.5 Hz, 1H), 8.16 (d, J = 8.4 Hz, 1H), 7.93 (d, J = 8.4 Hz, 1H), 7.72 (t, J = 8.0 Hz, 1H), 7.58 – 7.55 (m, 2H), 5.63 (t, J = 7.1 Hz, 1H), 4.26 – 4.23 (m, 1H), 4.09 – 4.03 (m, 1H), 2.63 (td, J = 14.3, 7.6 Hz, 1H), 2.14 – 1.96 (m, 2H), 1.91 – 1.82 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.4, 149.6, 148.0, 130.1, 129.0, 126.3, 125.5, 123.2, 116.4, 76.7, 69.0, 33.9, 26.0. MS (ESI^+): $C_{13}H_{14}NO$ ($[M+H]^+$); calculated: 200.1, found: 200.1.



(3cg) 1-(tetrahydrofuran-2-yl)isoquinoline

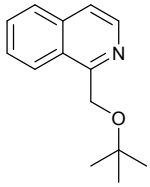
Colorless oil (52% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, J = 5.7 Hz, 1H), 8.38 (d, J = 8.4 Hz, 1H), 7.86 (d, J = 8.1 Hz, 1H), 7.71 (t, J = 7.2 Hz, 1H), 7.63 (dd, J = 15.3, 7.0 Hz, 2H), 5.76 (t,

J = 7.1 Hz, 1H), 4.23 (dd, *J* = 14.5, 7.4 Hz, 1H), 4.11 – 4.05 (m, 1H), 2.61 – 2.52 (m, 1H), 2.49 – 2.40 (m, 1H), 2.27 – 2.12 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.6, 141.5, 136.5, 129.8, 127.3, 127.1, 126.6, 125.3, 120.5, 79.1, 69.0, 30.8, 26.1; MS (ESI^+): $C_{13}H_{14}NO$ ($[M+H]^+$); calculated: 200.1, found: 200.1.



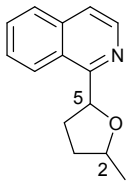
(3ui) 1-(tetrahydro-*2H*-pyran-2-yl)isoquinoline

Colorless oil (67% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (d, *J* = 5.6 Hz, 1H), 8.34 (d, *J* = 8.3 Hz, 1H), 7.78 (d, *J* = 7.9 Hz, 1H), 7.64 – 7.53 (m, 3H), 5.17 (dd, *J* = 11.0, 2.2 Hz, 1H), 4.28 – 4.24 (m, 1H), 3.77 (td, *J* = 11.6, 2.1 Hz, 1H), 2.16 – 1.96 (m, 3H), 1.92 – 1.72 (m, 2H), 1.66 – 1.63 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.6, 141.7, 136.6, 129.7, 127.3, 127.0, 126.0, 125.2, 120.5, 79.2, 69.4, 31.1, 25.9, 23.9; MS (ESI^+): $C_{14}H_{16}NO$ ($[M+H]^+$); calculated: 214.1, found: 214.1.



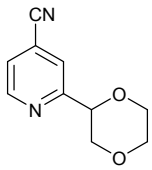
(3cn) 1-(*tert*-butoxymethyl)isoquinoline

Colorless oil (48% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, *J* = 5.7 Hz, 1H), 8.41 (d, *J* = 8.3 Hz, 1H), 7.81 (d, *J* = 8.1 Hz, 1H), 7.69 – 7.58 (m, 3H), 5.05 (s, 2H), 1.40 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.3, 141.7, 136.5, 129.9, 127.6, 127.1, 127.0, 126.2, 120.9, 74.3, 65.8, 27.7 (3C); HRMS (ESI^+): $C_{14}H_{18}NO$ ($[M+H]^+$); calculated: 216.1383, found: 216.1386.



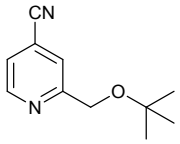
(3co) 1-(5-methyltetrahydrofuran-2-yl)isoquinoline

Colorless oil (60% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, *J* = 5.5 Hz, 1H), 8.46 – 8.36 (m, 1H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.68 – 7.56 (m, 3H), 5.91 – 5.63 (m, 1H), 4.50 – 4.27 (m, 1H), 2.73 – 2.56 (m, 1H), 2.48 – 2.20 (m, 2H), 1.87 – 1.67 (m, 1H), 1.40 (d, *J* = 5.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.1, 159.1, 141.6, 136.6, 136.5, 129.7, 127.2, 127.2, 127.0, 127.0, 126.9, 126.6, 125.7, 125.3, 120.6, 120.3, 80.0, 78.4, 76.8, 76.0, 34.0, 33.2, 31.3, 30.3, 21.4, 21.1; HRMS (ESI^+): $C_{14}H_{16}NO$ ($[M+H]^+$); calculated: 214.1226, found: 214.1234.



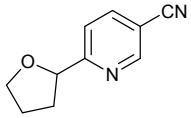
(3hh) 2-(1,4-dioxan-2-yl)isonicotinonitrile

Colorless oil (47% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (d, *J* = 4.9 Hz, 1H), 7.79 (s, 1H), 7.47 (d, *J* = 4.3 Hz, 1H), 4.83 – 4.80 (m, 1H), 4.26 – 4.23 (m, 1H), 4.05 – 3.95 (m, 2H), 3.88 – 3.85 (m, 1H), 3.78 – 3.71 (m, 1H), 3.50 – 3.45 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.0, 149.8, 124.0, 122.4, 121.1, 116.4, 77.0, 70.8, 66.8, 66.3; HRMS (ESI$^+$): $C_{10}H_{11}N_2O_2$ ([M+H]$^+$); calculated: 191.0815, found: 191.0820.



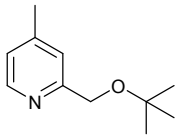
(3hn) 2-(*tert*-butoxymethyl)isonicotinonitrile

Colorless oil (35% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (d, *J* = 4.8 Hz, 1H), 7.77 (s, 1H), 7.40 (d, *J* = 4.6 Hz, 1H), 4.64 (s, 2H), 1.32 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.4, 149.5, 123.2, 122.7, 120.8, 116.8, 74.2, 64.5, 27.5 (3C); HRMS (ESI$^+$): $C_{11}H_{15}N_2O$ ([M+H]$^+$); calculated: 191.1179, found: 191.1176.



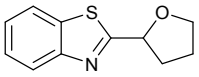
(3wg) 6-(tetrahydrofuran-2-yl)nicotinonitrile

Colorless oil (40% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (s, 1H), 7.97 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.64 (d, *J* = 8.2 Hz, 1H), 5.10 – 5.07 (m, 1H), 4.15 – 4.10 (m, 1H), 4.06 – 4.00 (m, 1H), 2.55 – 2.45 (m, 1H), 2.09 – 1.82 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.8, 151.8, 139.8, 119.7, 116.8, 108.0, 80.8, 69.3, 33.0, 25.7; HRMS (ESI$^+$): $C_{10}H_{11}N_2O$ ([M+H]$^+$); calculated: 175.0866, found: 175.0869.



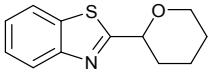
(3xn) 2-(*tert*-butoxymethyl)-4-methylpyridine

Colorless oil (14% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, *J* = 4.8 Hz, 1H), 7.36 (s, 1H), 7.02 (d, *J* = 4.5 Hz, 1H), 4.61 (s, 2H), 2.40 (s, 3H), 1.35 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.7, 148.3, 147.9, 123.0, 122.0, 73.8, 65.1, 27.6 (3C), 21.2. HRMS (ESI$^+$): $C_{11}H_{18}NO$ ([M+H]$^+$); calculated: 180.1383, found: 180.1388.



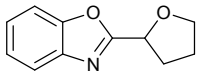
(3jg) 2-(tetrahydrofuran-2-yl)benzo[*d*]thiazole

Colorless oil (55% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.1 Hz, 1H), 7.96 (d, *J* = 7.9 Hz, 1H), 7.54 (t, *J* = 7.3 Hz, 1H), 7.44 (t, *J* = 7.5 Hz, 1H), 5.43 (dd, *J* = 7.7, 5.5 Hz, 1H), 4.24 (dd, *J* = 14.7, 6.7 Hz, 1H), 4.08 (dd, *J* = 15.1, 7.2 Hz, 1H), 2.64 – 2.56 (m, 1H), 2.40 – 2.32 (m, 1H), 2.15 – 2.08 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.3, 153.6, 134.7, 125.9, 124.8, 122.8, 121.8, 78.8, 69.4, 33.4, 25.7; MS (ESI$^+$): $C_{11}H_{12}NOS$ ([M+H]$^+$); calculated: 206.1, found: 206.1.



(3pi) 2-(tetrahydro-*2H*-pyran-2-yl)benzo[*d*]thiazole

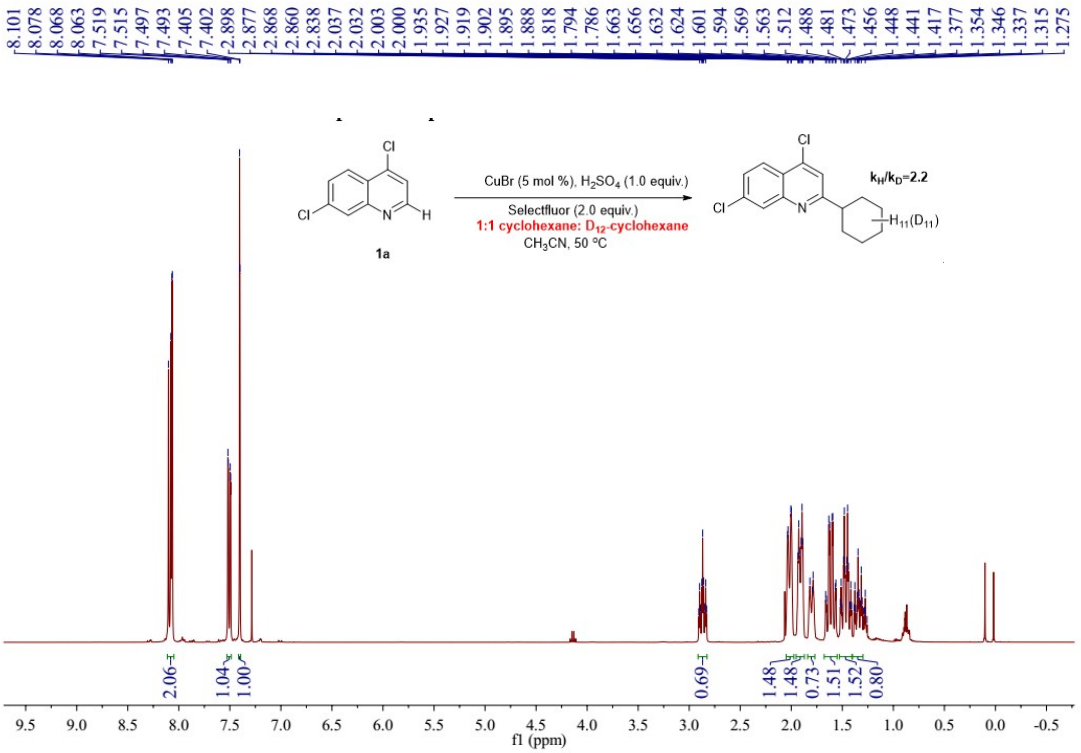
Colorless oil (73% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.1 Hz, 1H), 7.91 (d, *J* = 8.0 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 1H), 7.38 (t, *J* = 7.5 Hz, 1H), 4.82 – 4.79 (m, 1H), 4.24 – 4.20 (m, 1H), 3.74 – 3.68 (m, 1H), 2.31 – 2.29 (m, 1H), 2.05 – 1.99 (m, 1H), 1.83 – 1.63 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.8, 153.0, 134.7, 125.8, 124.8, 123.0, 121.7, 77.9, 68.9, 32.4, 25.6, 23.0; MS (ESI^+): $C_{12}H_{14}NOS$ ($[M+H]^+$); calculated: 220.1, found: 220.1.

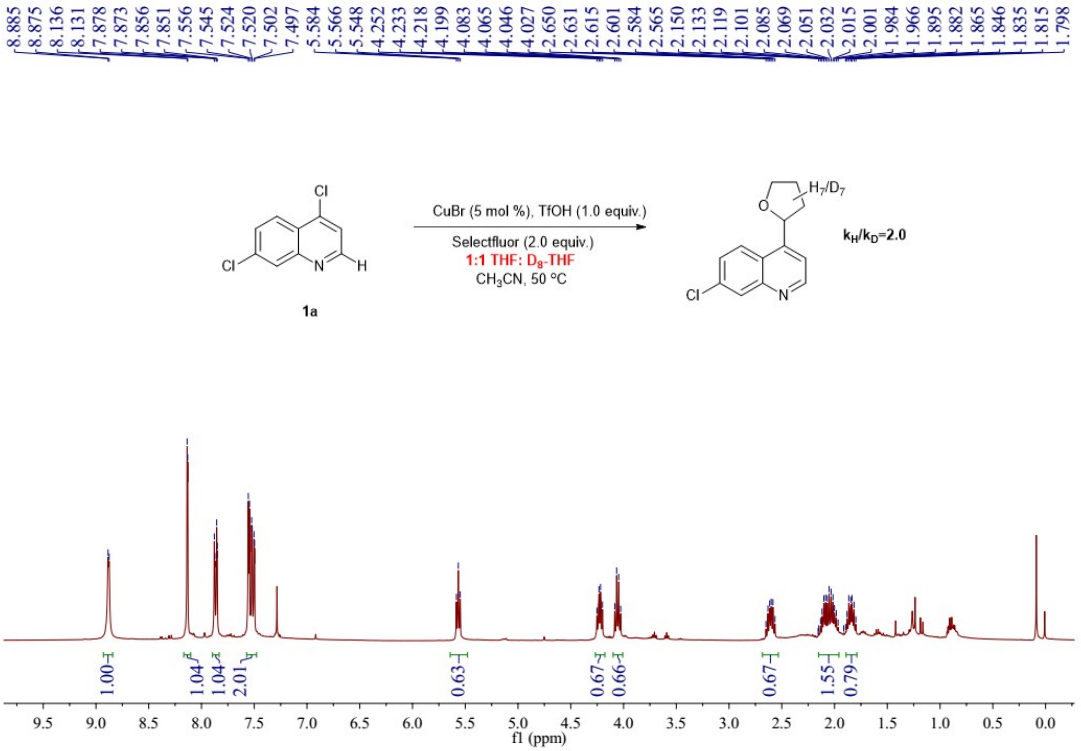


(3rg) 2-(tetrahydrofuran-2-yl)benzo[*d*]oxazole

Colorless oil (75% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 – 7.72 (m, 1H), 7.56 – 7.54 (m, 1H), 7.37 – 7.32 (m, 2H), 5.23 (t, *J* = 6.7 Hz, 1H), 4.15 (dd, *J* = 14.7, 7.3 Hz, 1H), 4.04 (dd, *J* = 14.1, 7.6 Hz, 1H), 2.43 (q, *J* = 7.2 Hz, 2H), 2.20 (tt, *J* = 14.0, 7.1 Hz, 1H), 2.09 (tt, *J* = 14.2, 7.3 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2, 150.9, 140.8, 125.1, 124.3, 120.2, 110.7, 73.9, 69.3, 30.7, 25.8; MS (ESI^+): $C_{11}H_{12}NO_2$ ($[M+H]^+$); calculated: 190.1, found: 190.1.

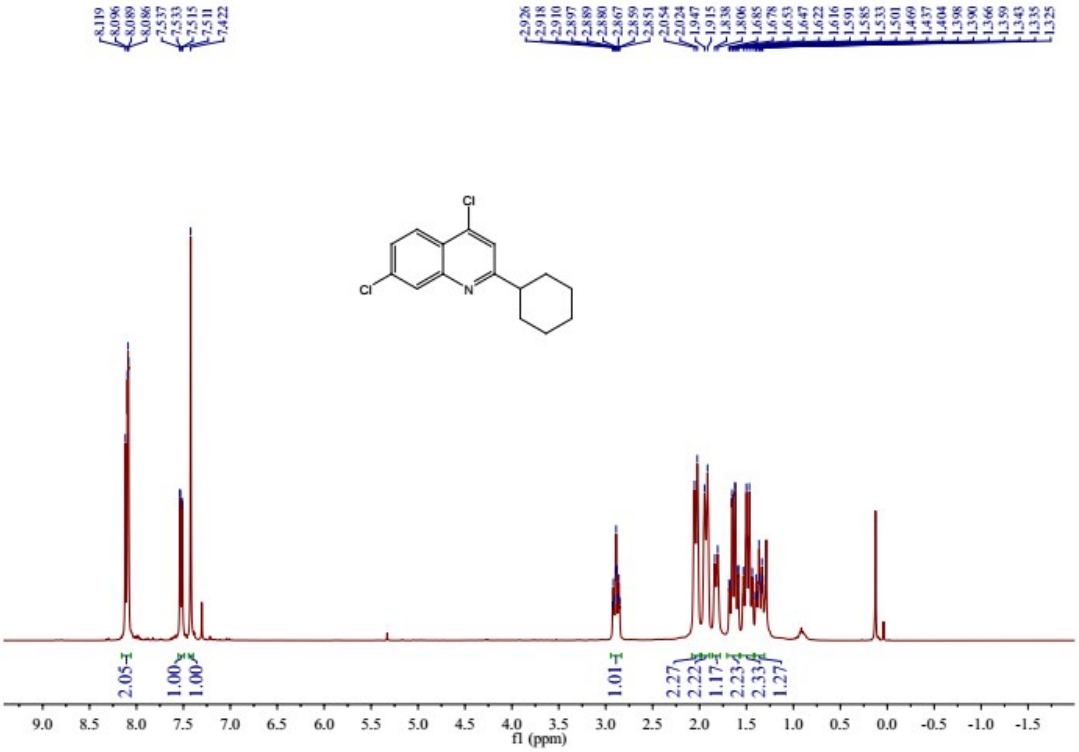
Kinetic isotope e□ect experiments

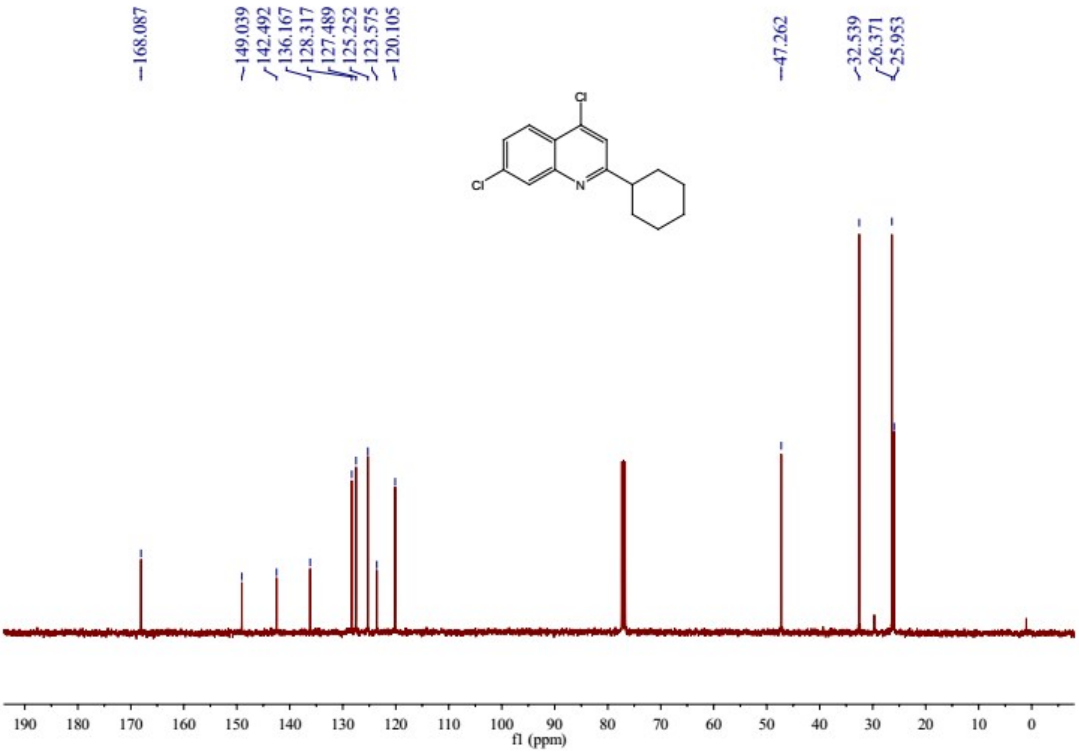




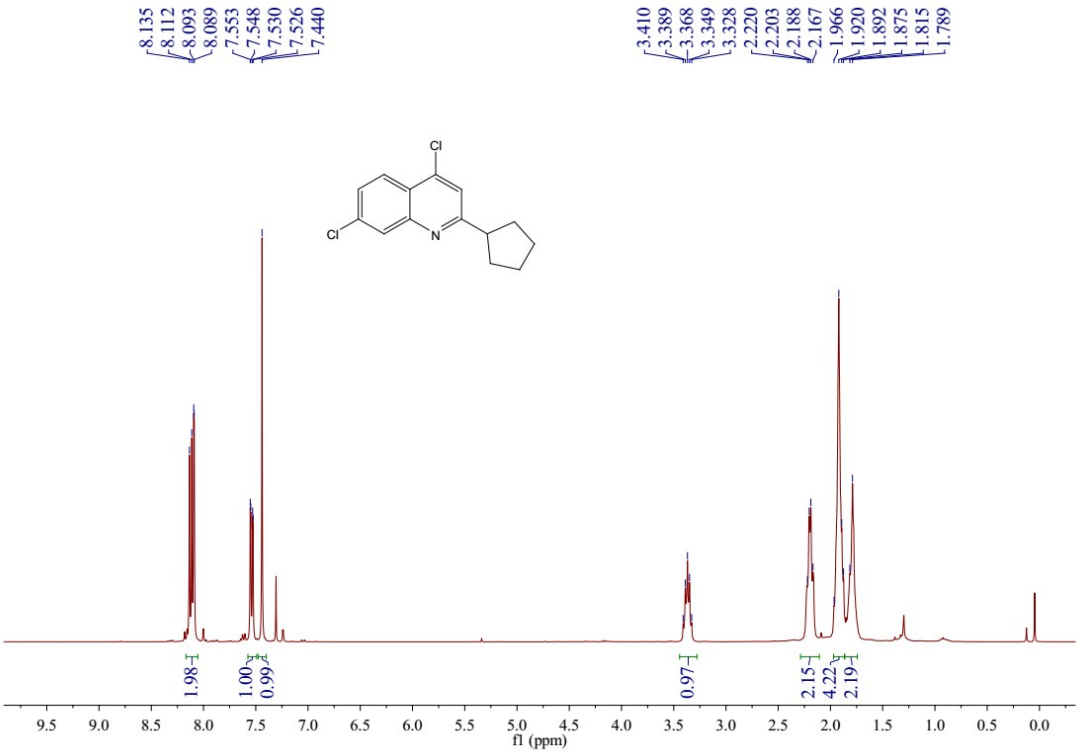
NMR spectra for the products

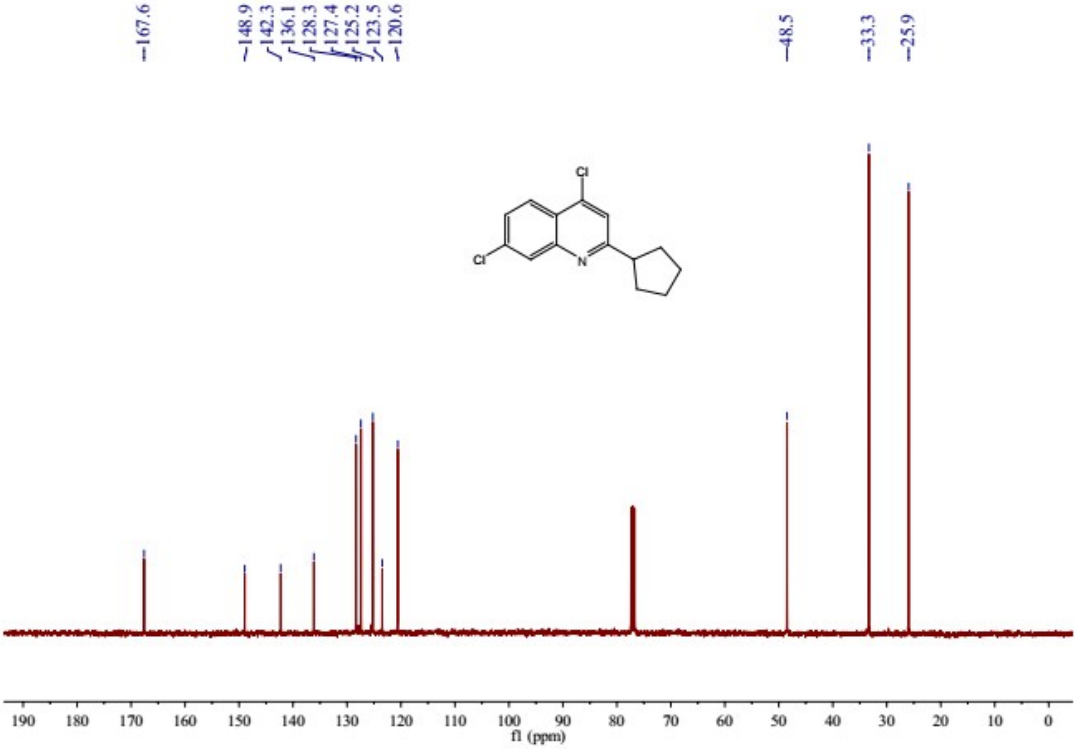
(3aa) 4,7-dichloro-2-cyclohexylquinoline



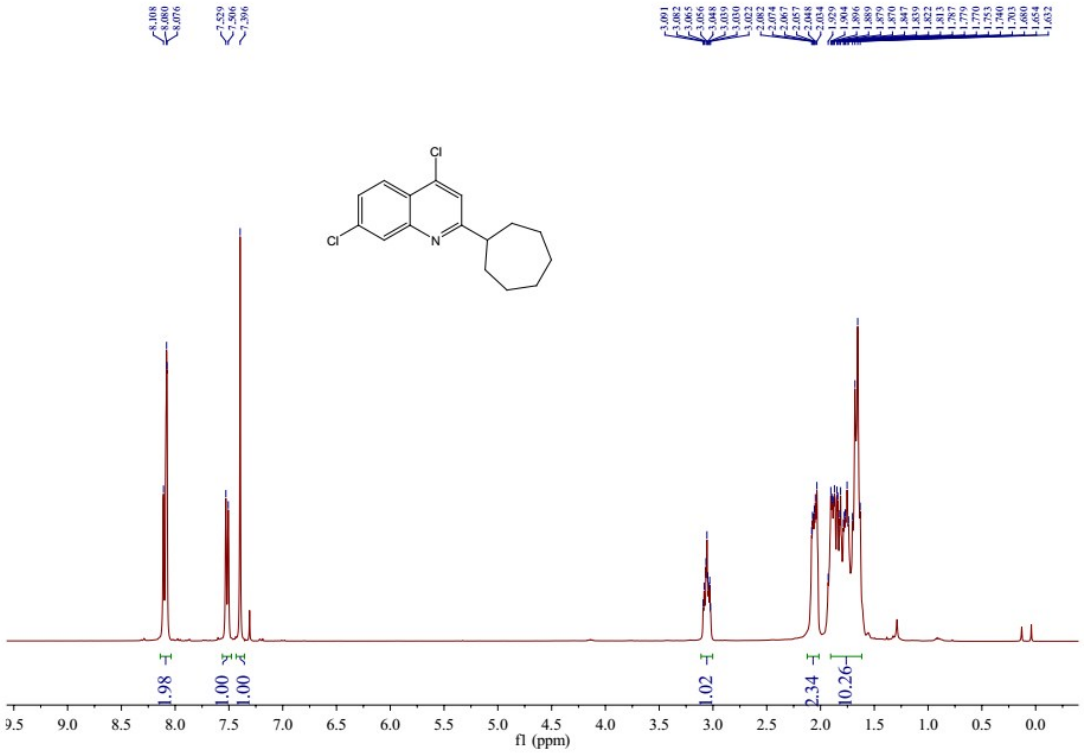


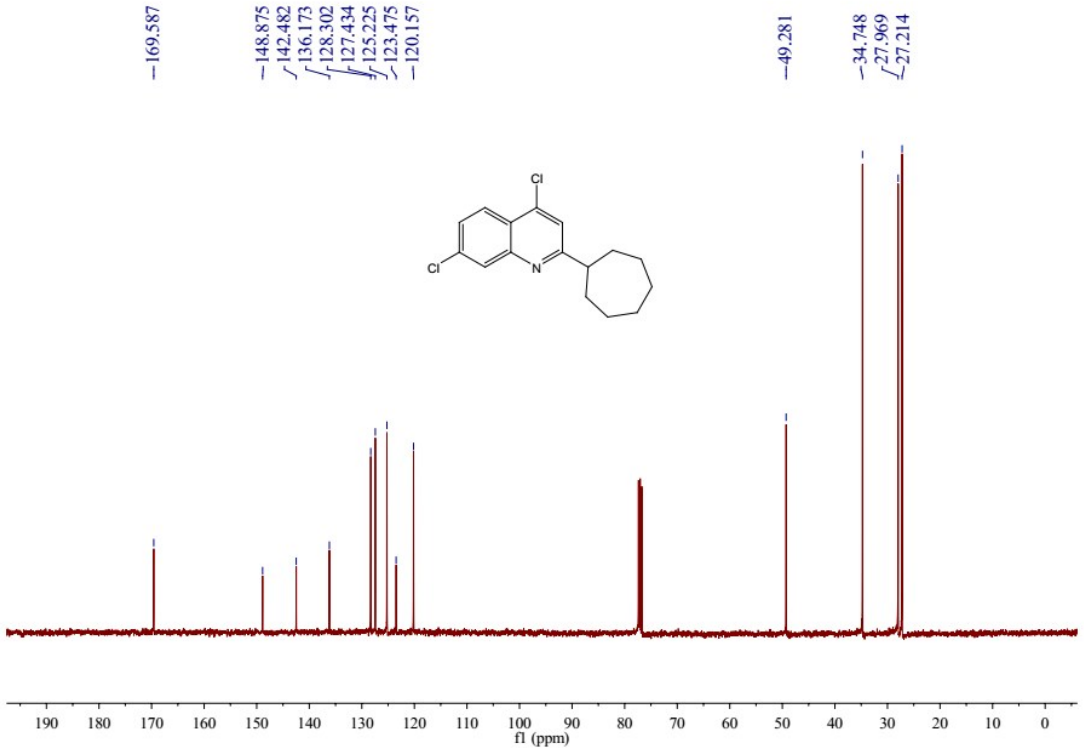
(3ab) 4,7-dichloro-2-cyclopentylquinoline



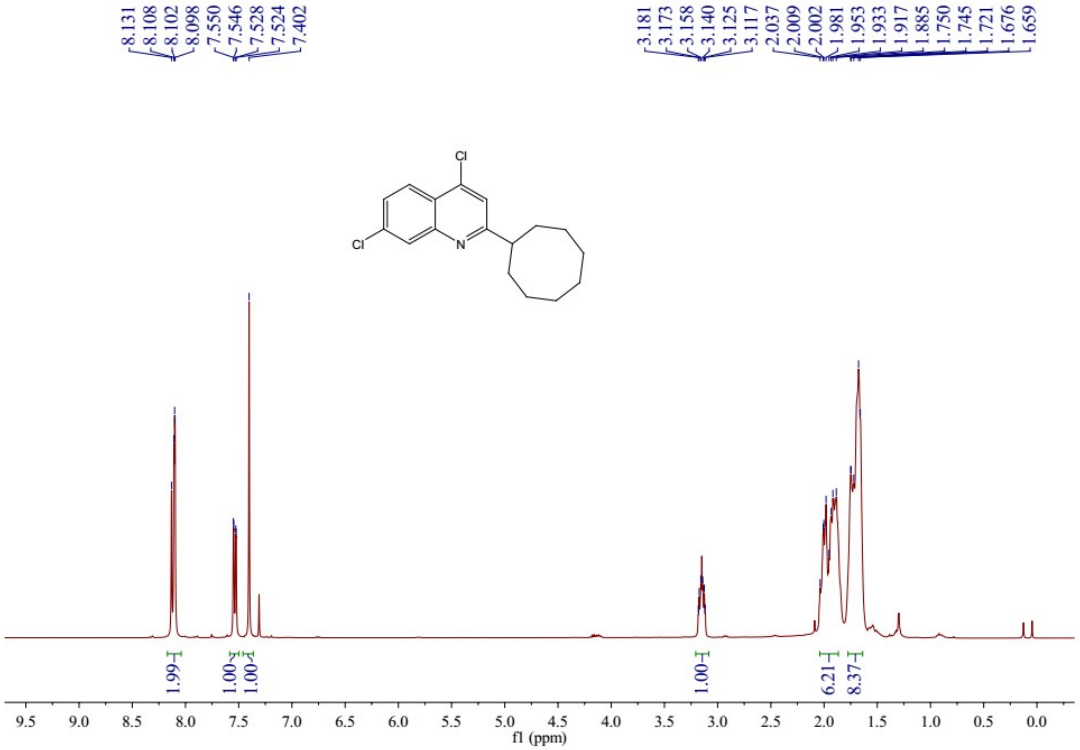


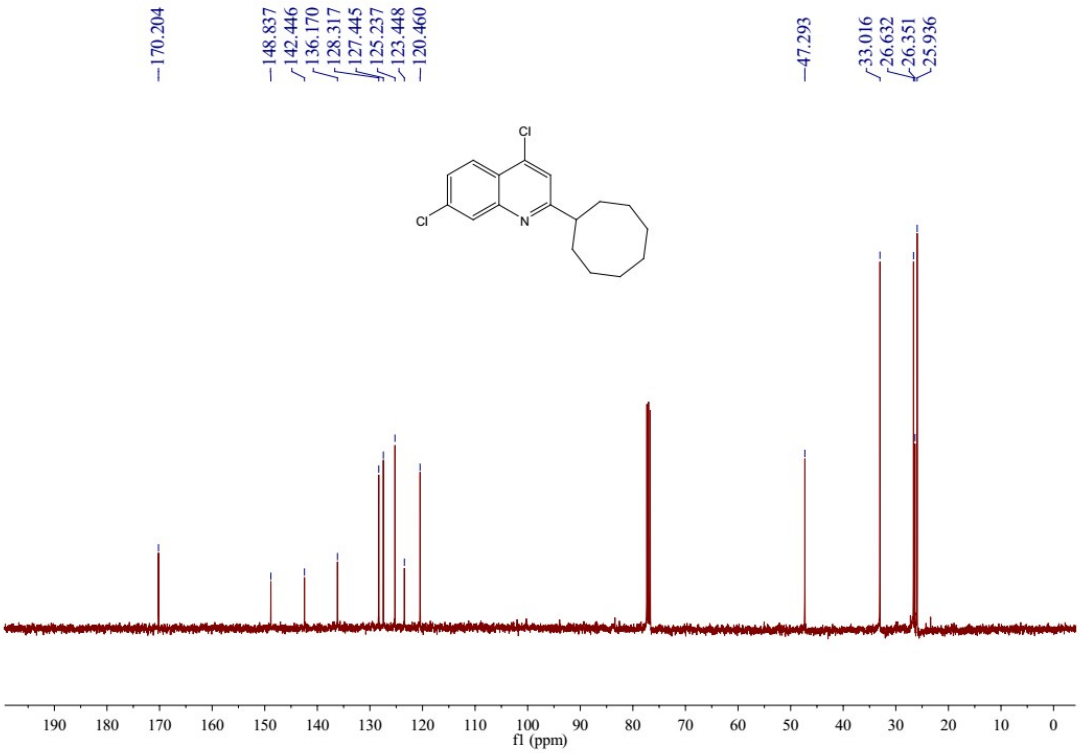
(3ac) 4,7-dichloro-2-cycloheptylquinoline



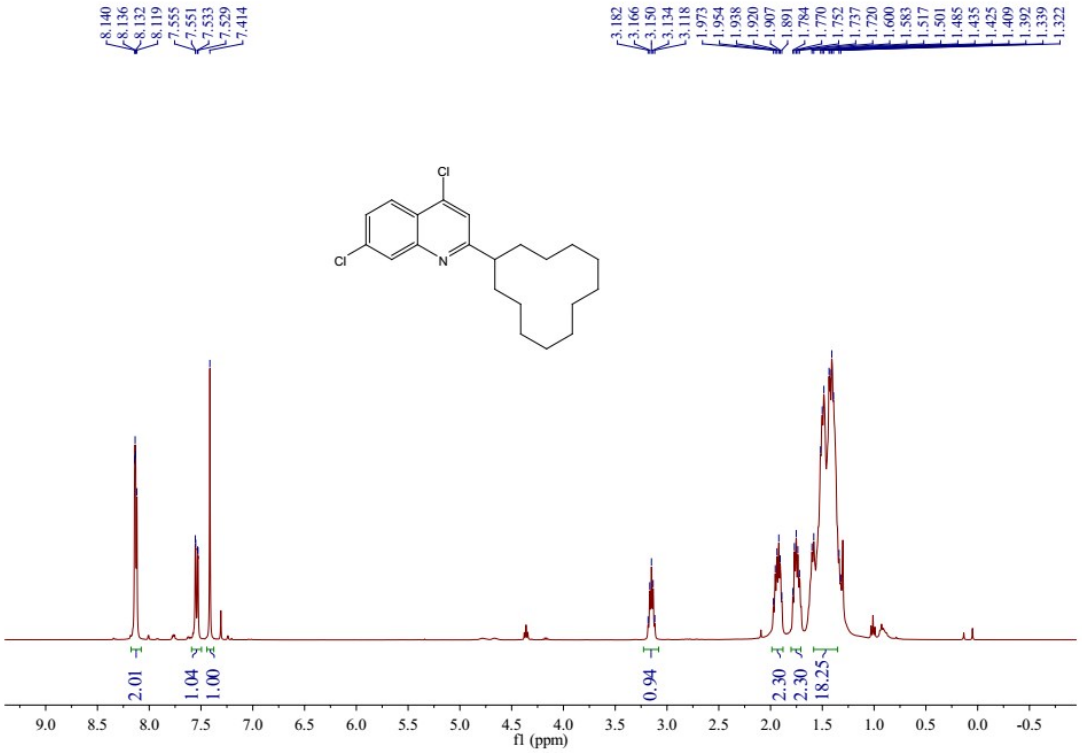


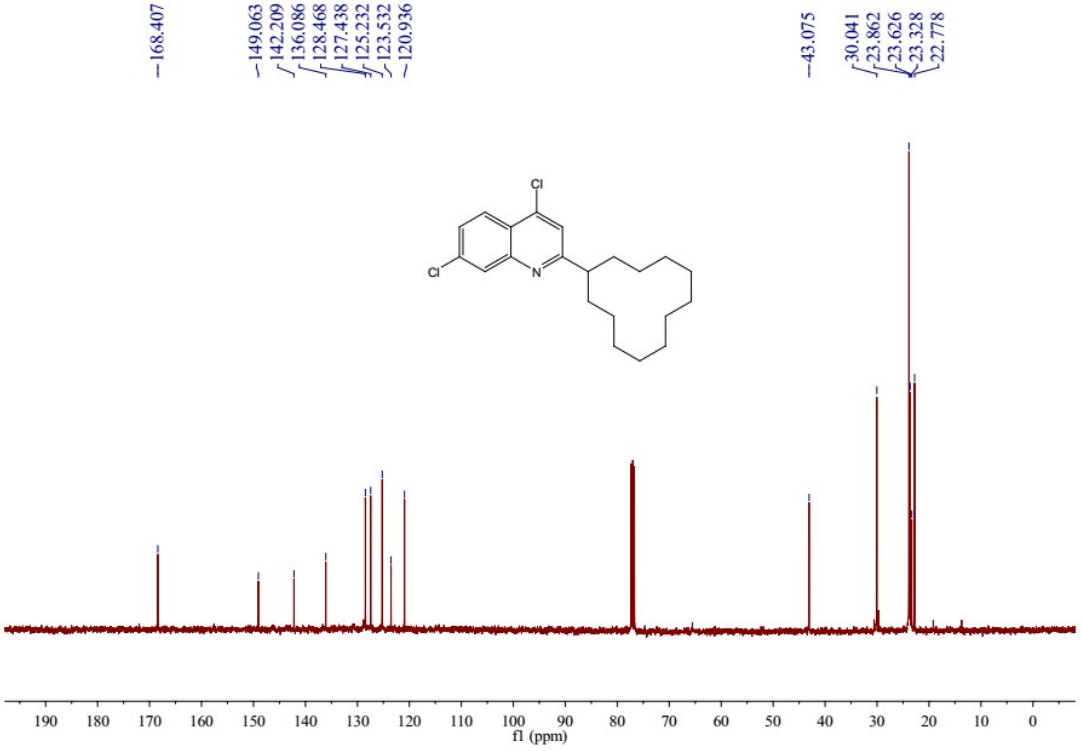
(3ad) 4,7-dichloro-2-cyclooctylquinoline



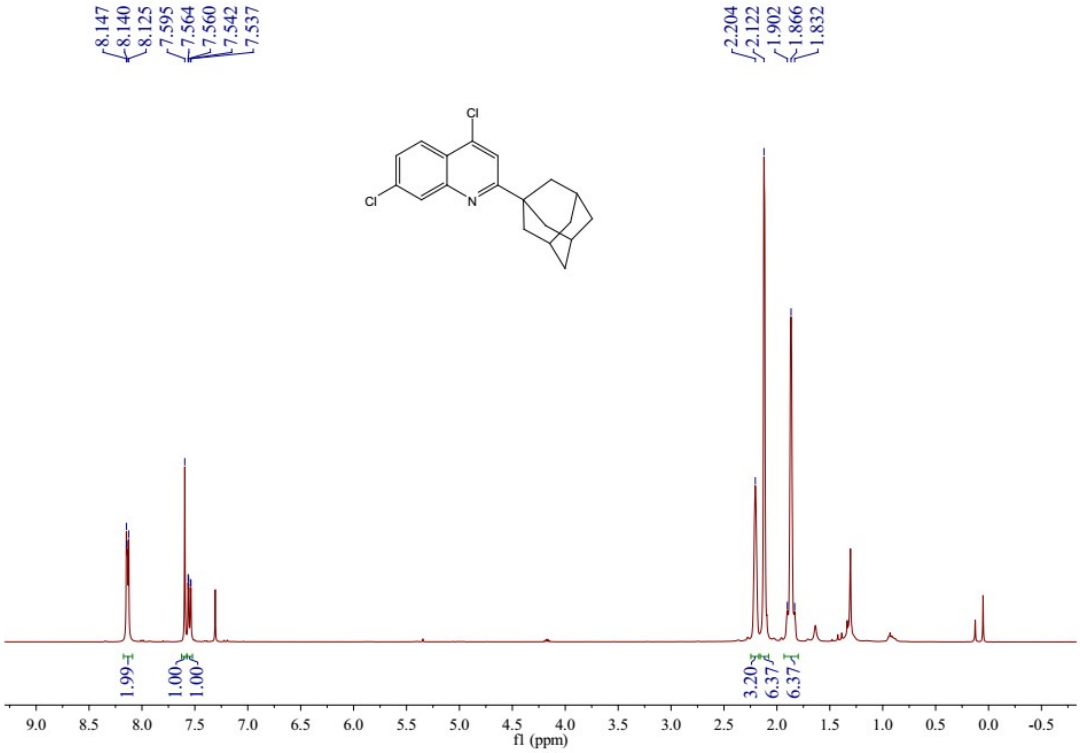


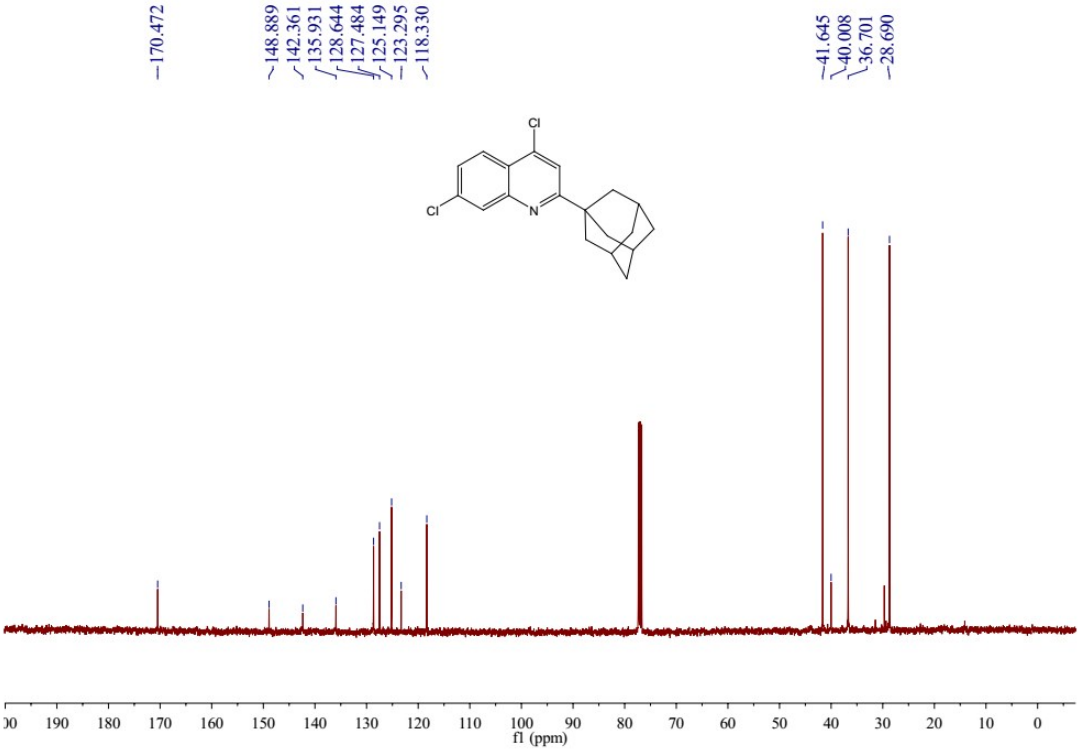
(3ae) 4,7-dichloro-2-cyclododecylquinoline



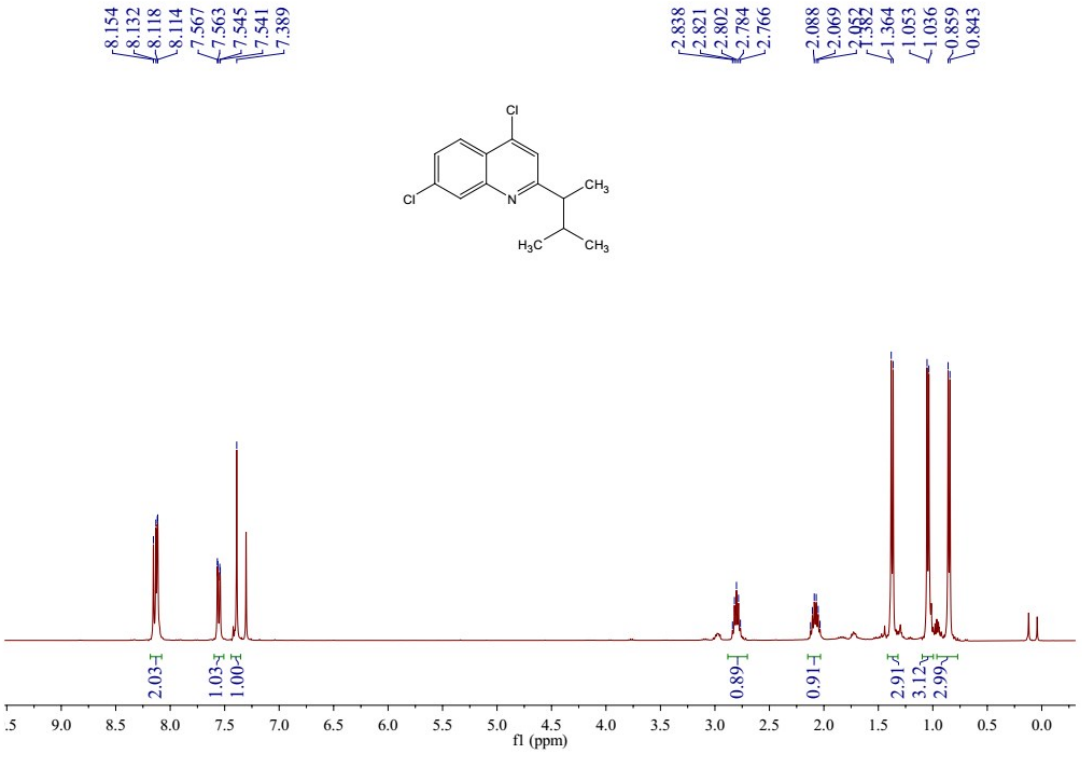


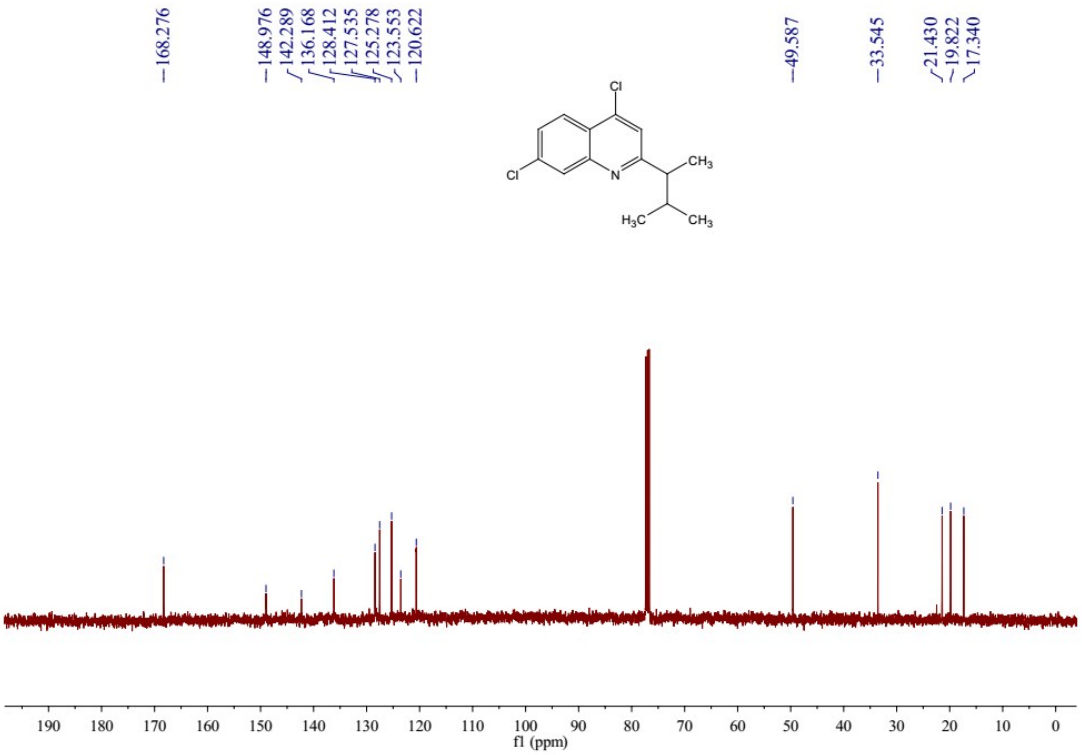
(3af) 2-adamantyl-4,7-dichloroquinoline



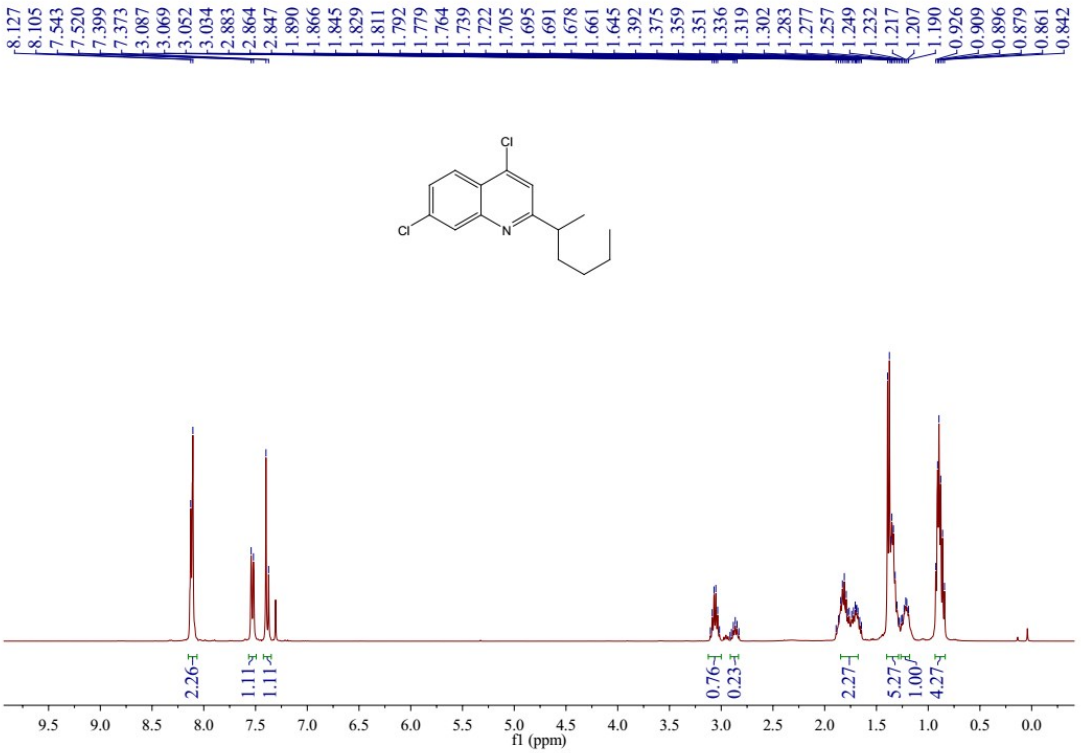


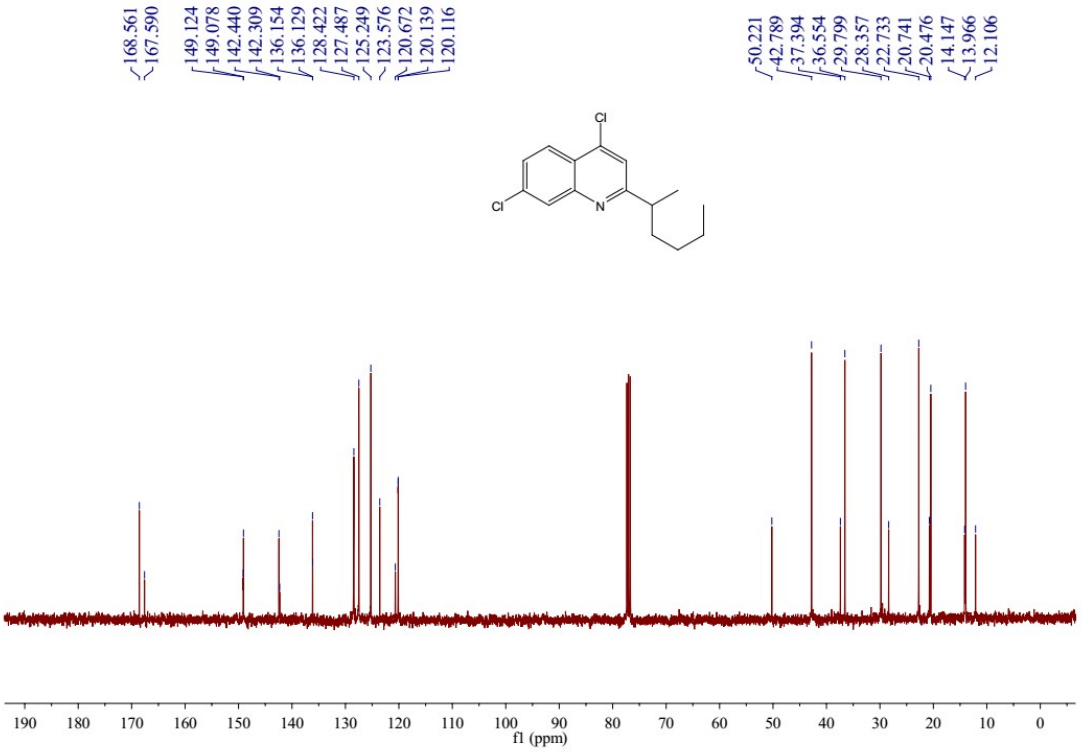
(3ak) 4,7-dichloro-2-(3-methylbutan-2-yl)quinolone



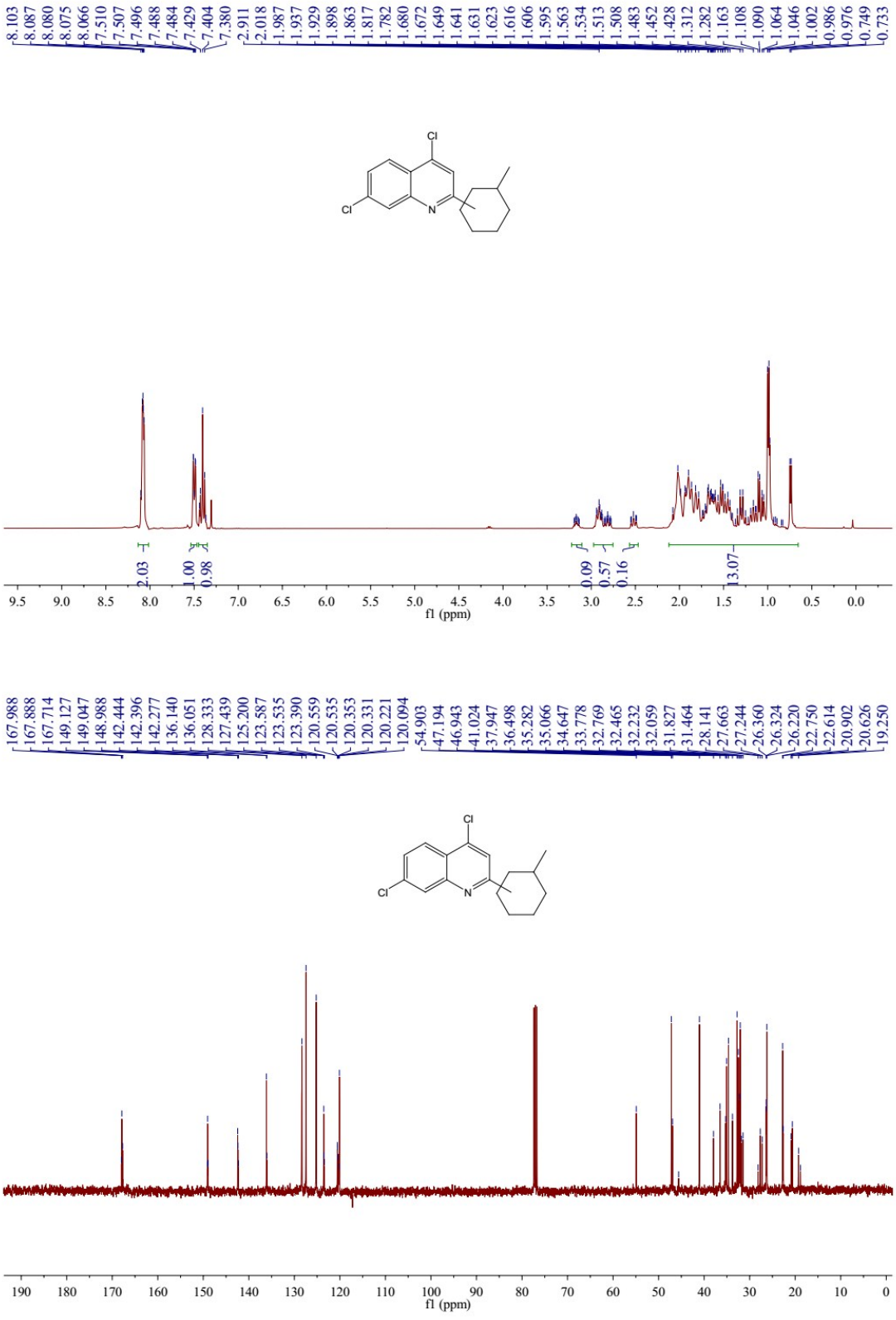


(3am) 4,7-dichloro-2-(hexan-2-yl)quinolone

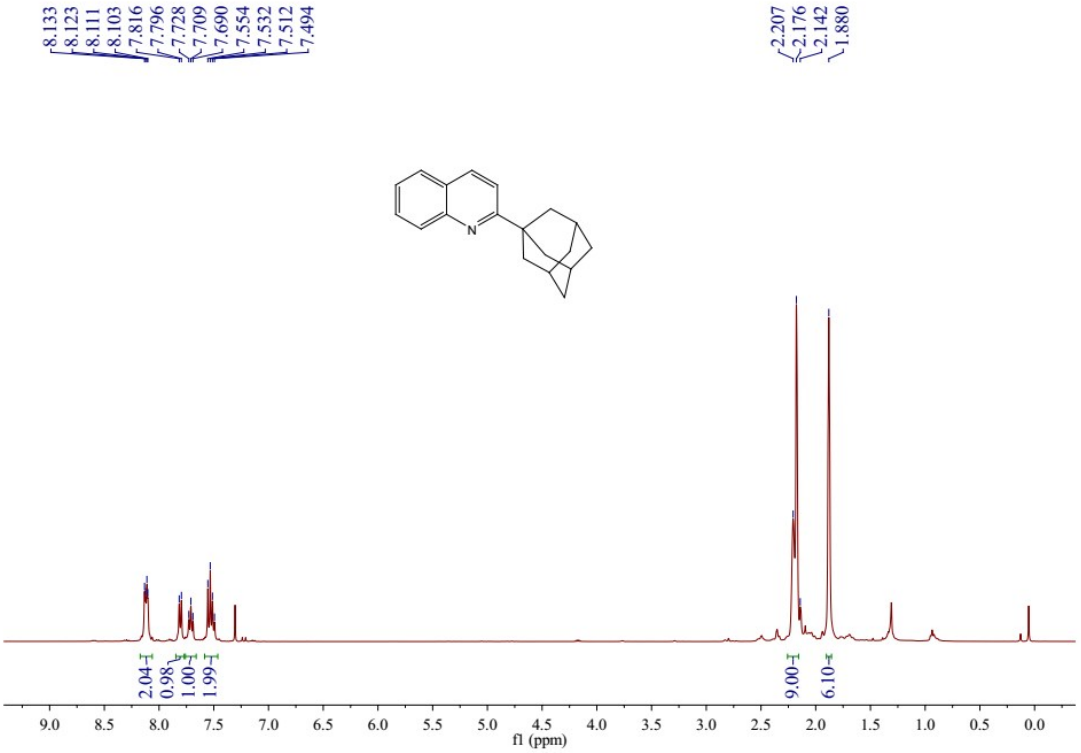


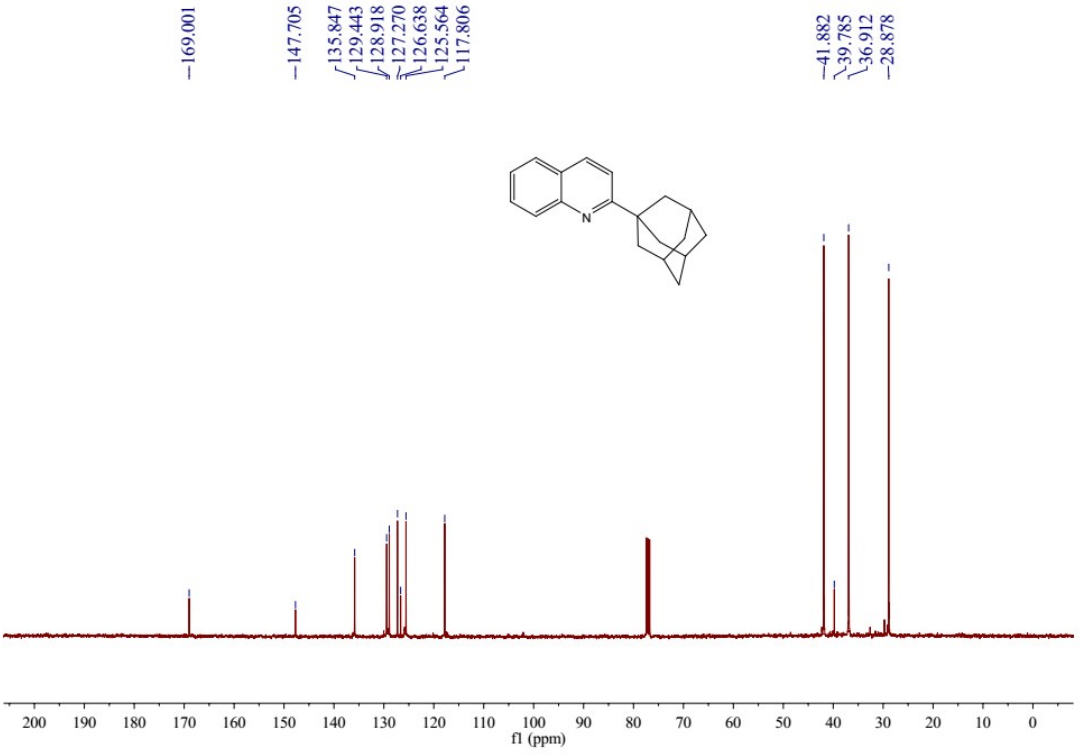


(3al) Methylcyclohexyl 4,7-dichloroquinoline



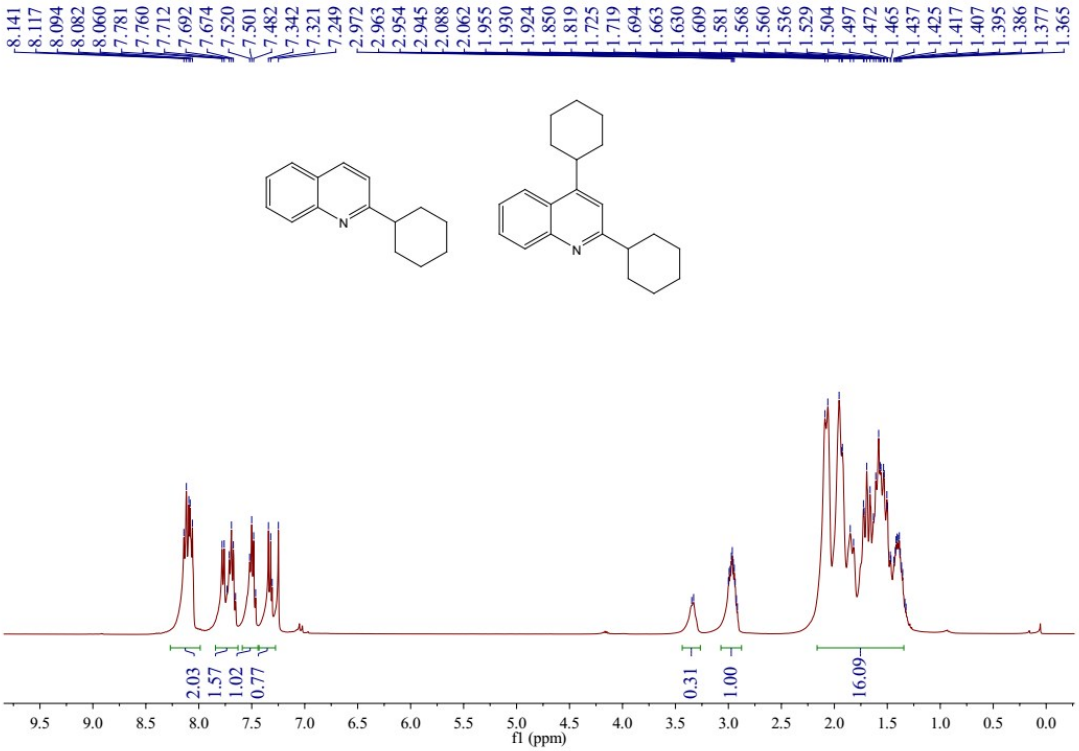
(3bf) 2-adamantyl-quinoline

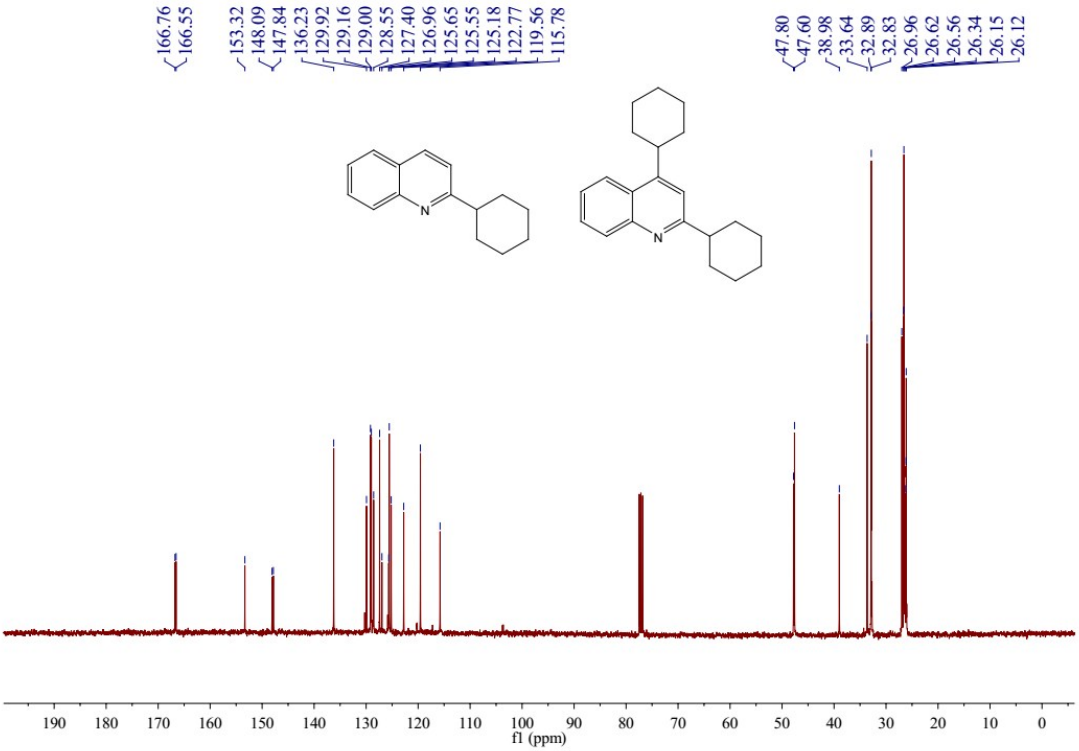




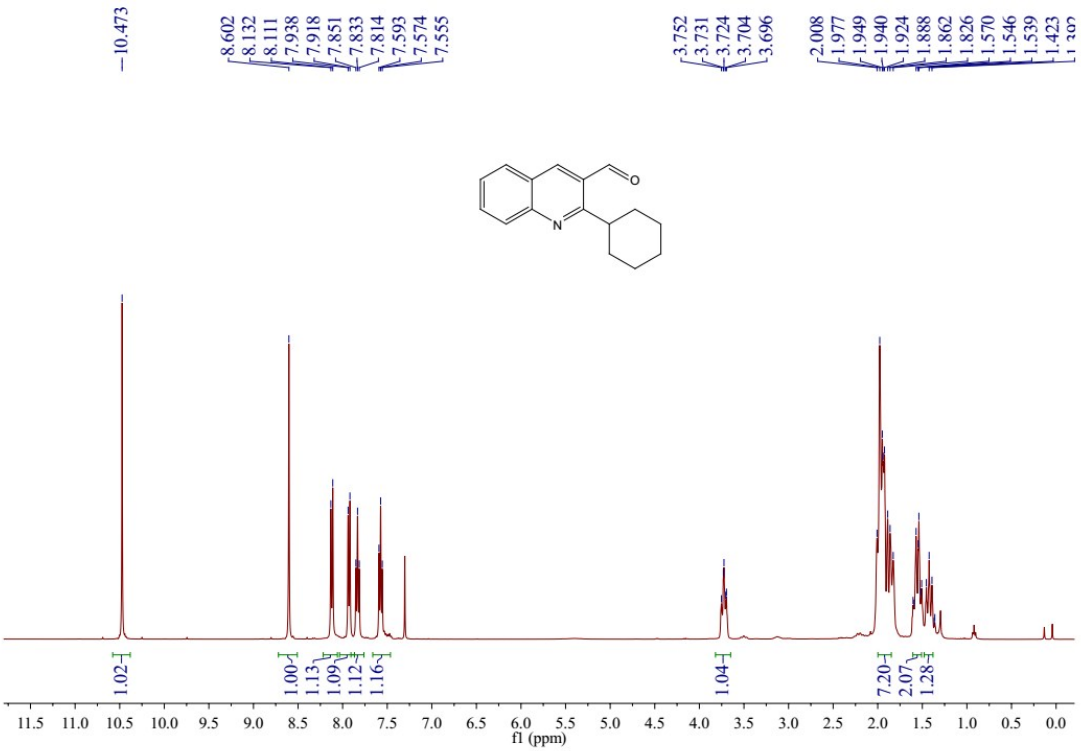
(3ma) 2-cyclohexylquinoline (major)

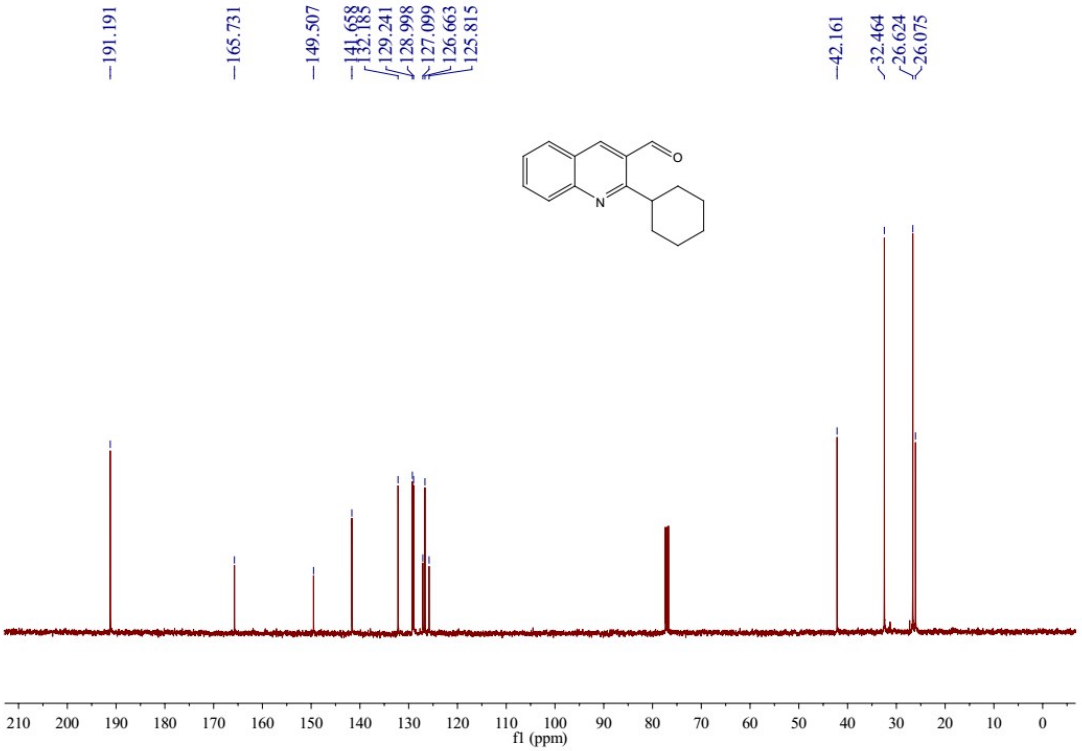
(3ma') 2,4-dicyclohexylquinoline (minor)



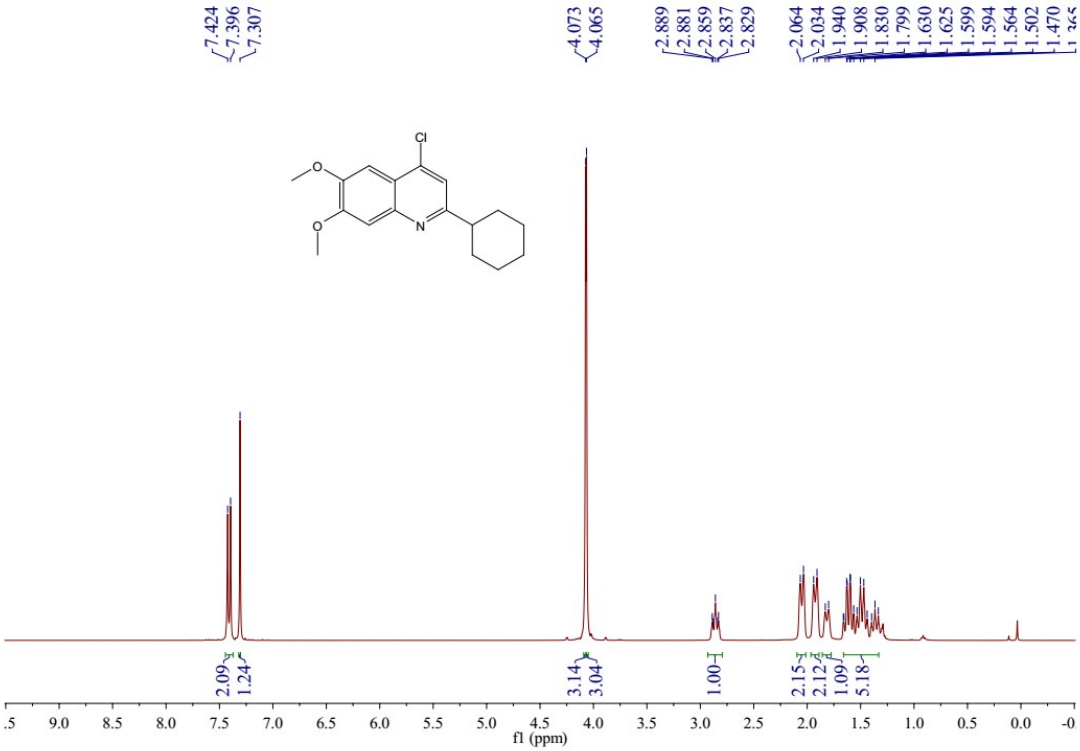


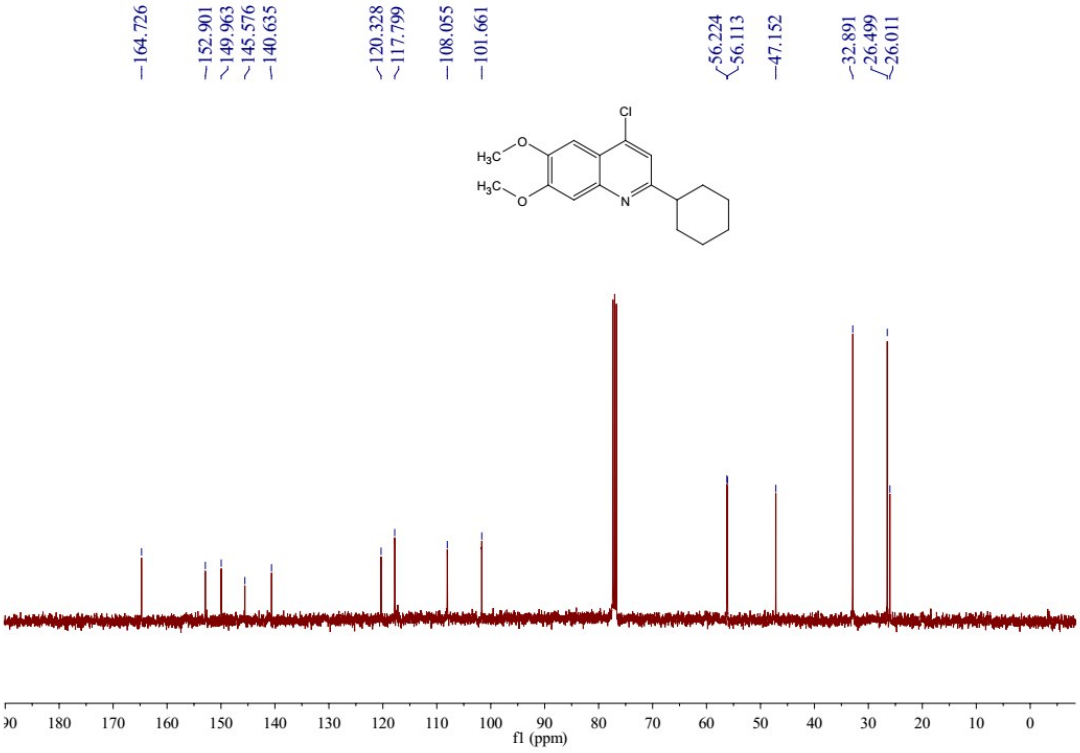
(3oa) 2-cyclohexylquinoline-3-carbaldehyde



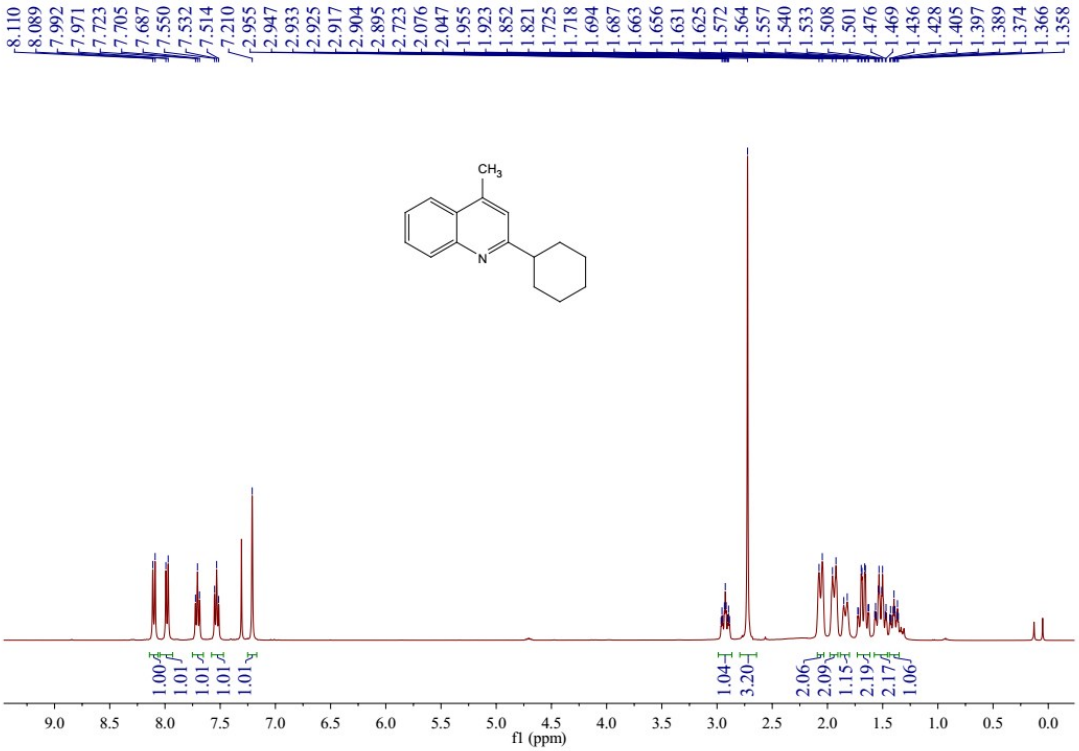


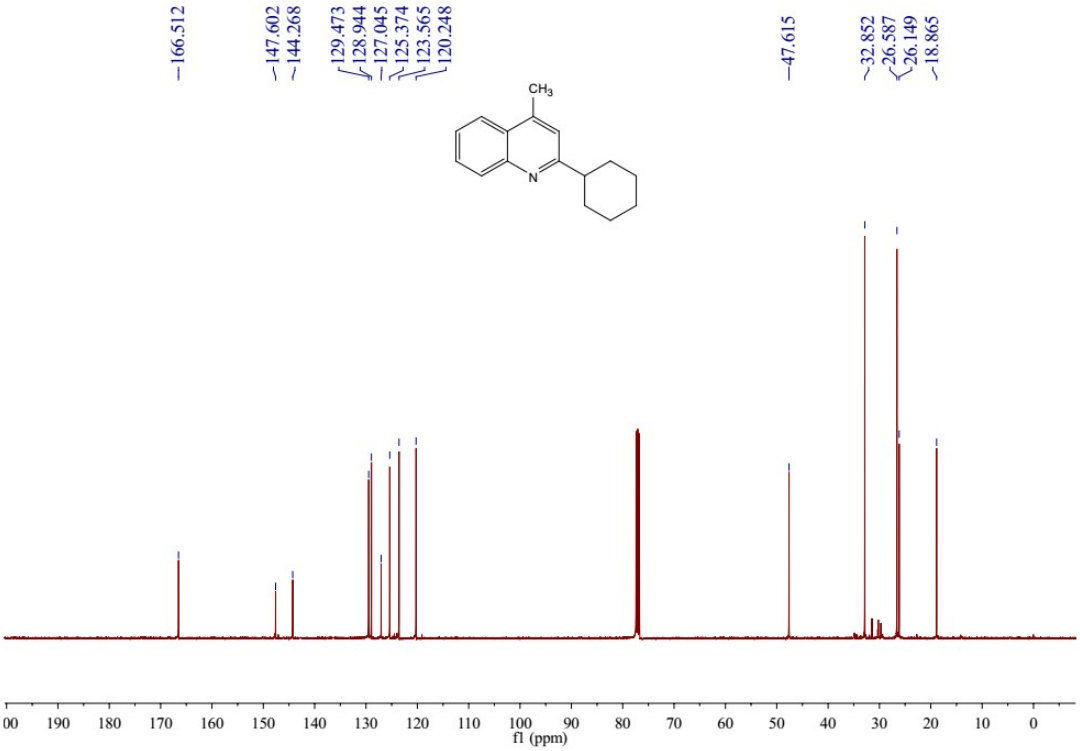
(3qa) 4-chloro-2-cyclohexyl-6,7-dimethoxyquinoline



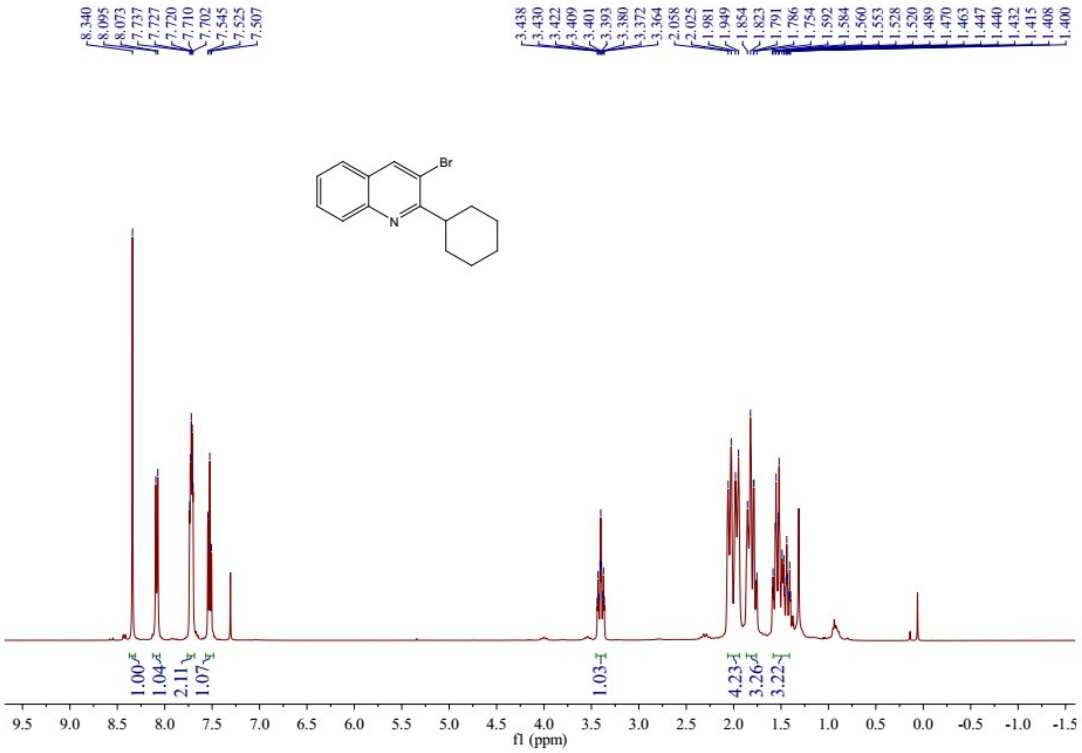


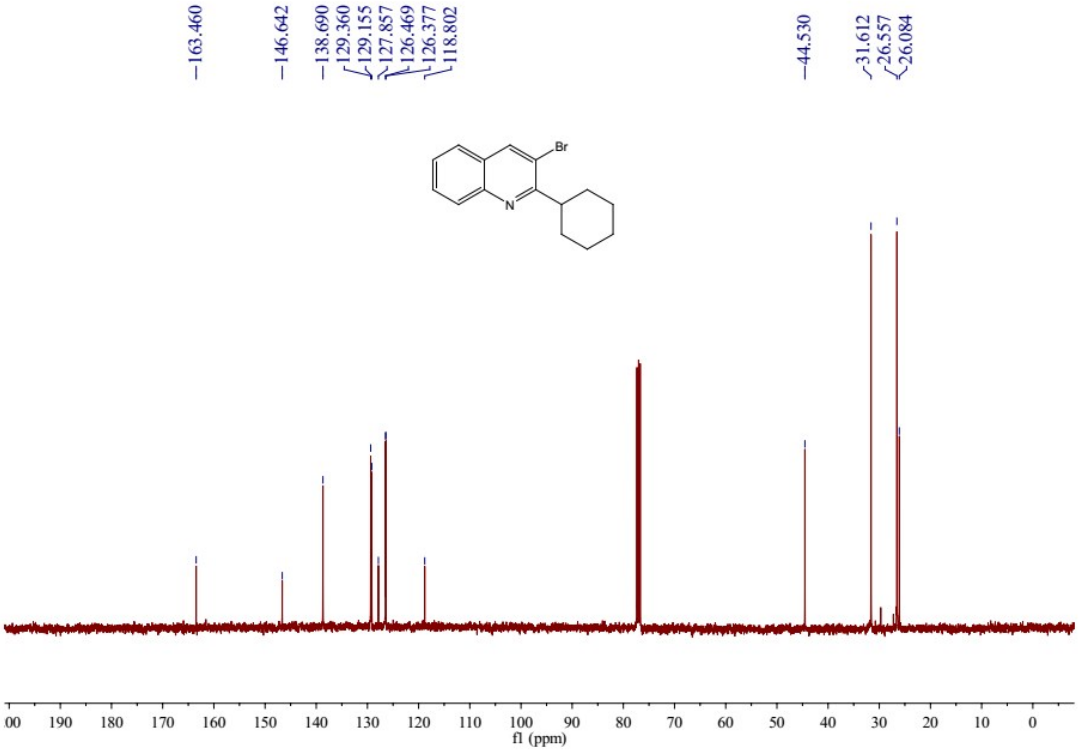
(3da) 2-cyclohexyl-4-methylquinoline



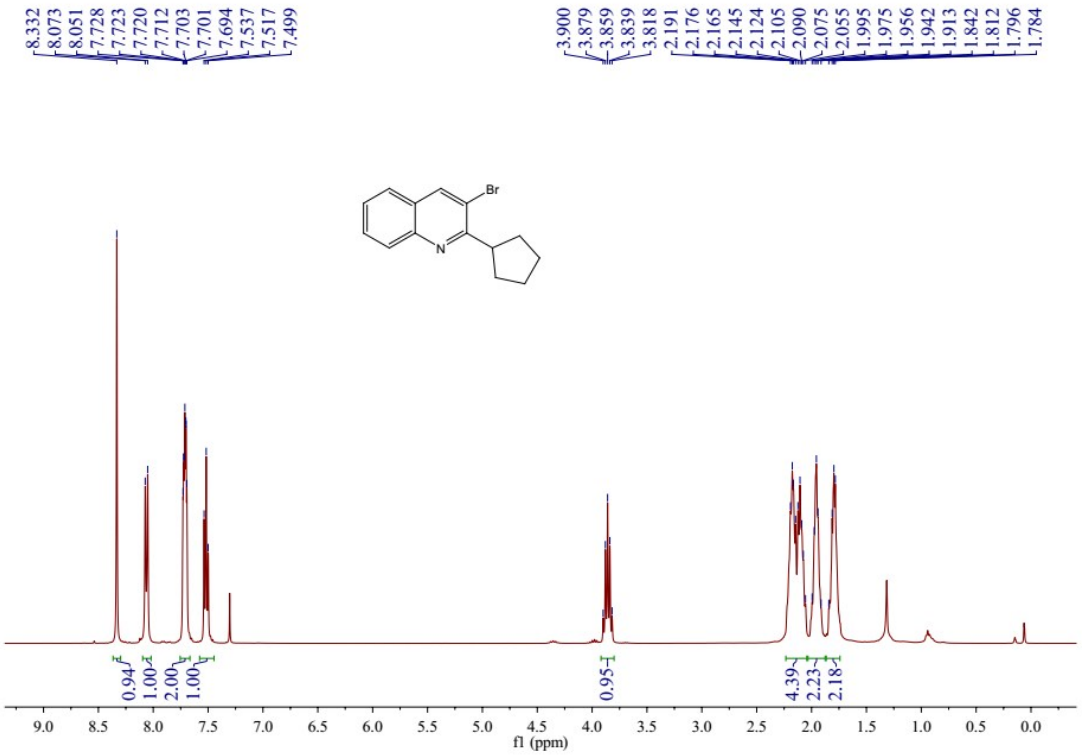


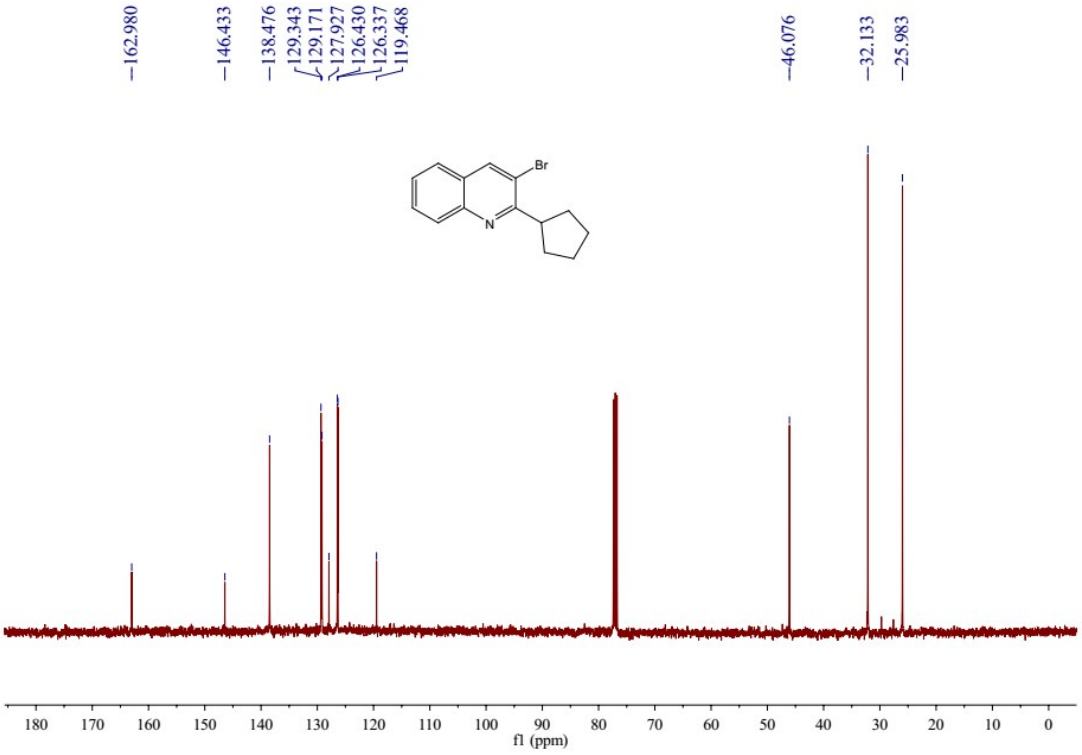
(3ea) 3-bromo-2-cyclohexylquinoline



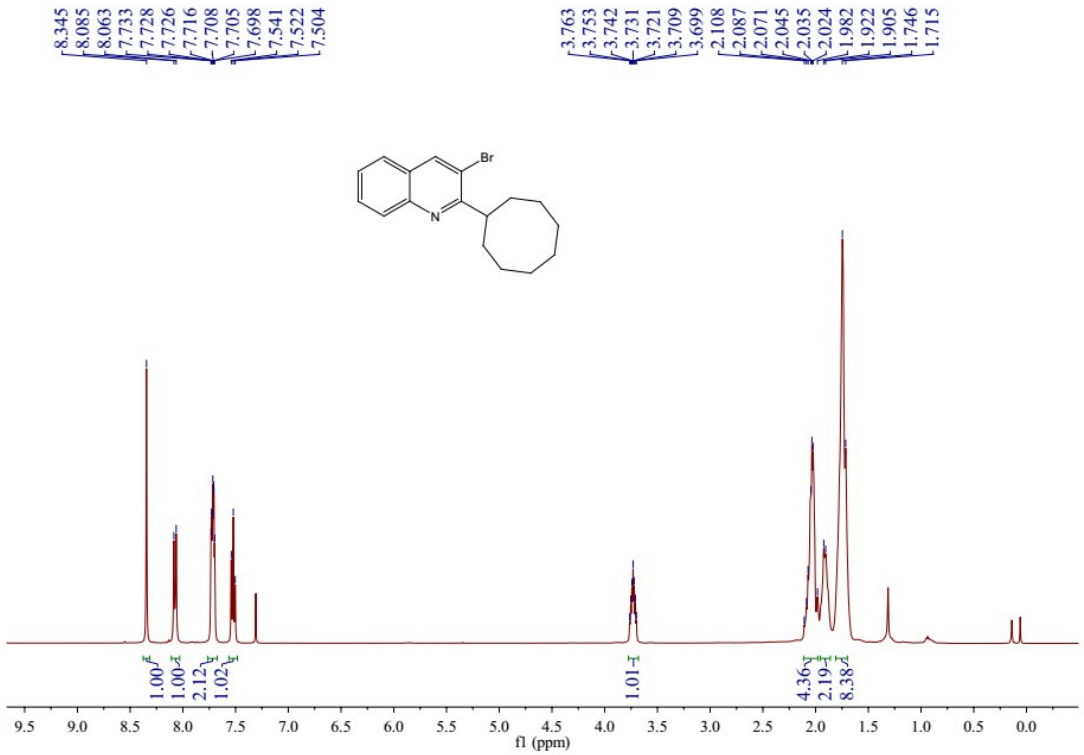


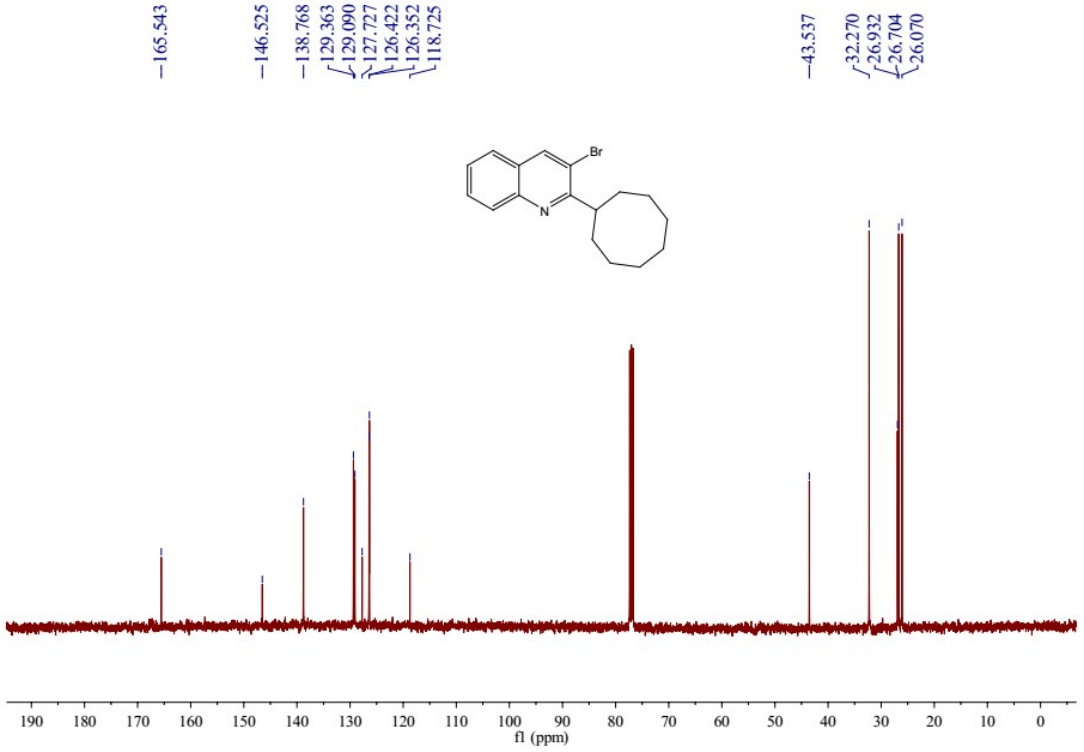
(3eb) 3-bromo-2-cyclopentylquinoline



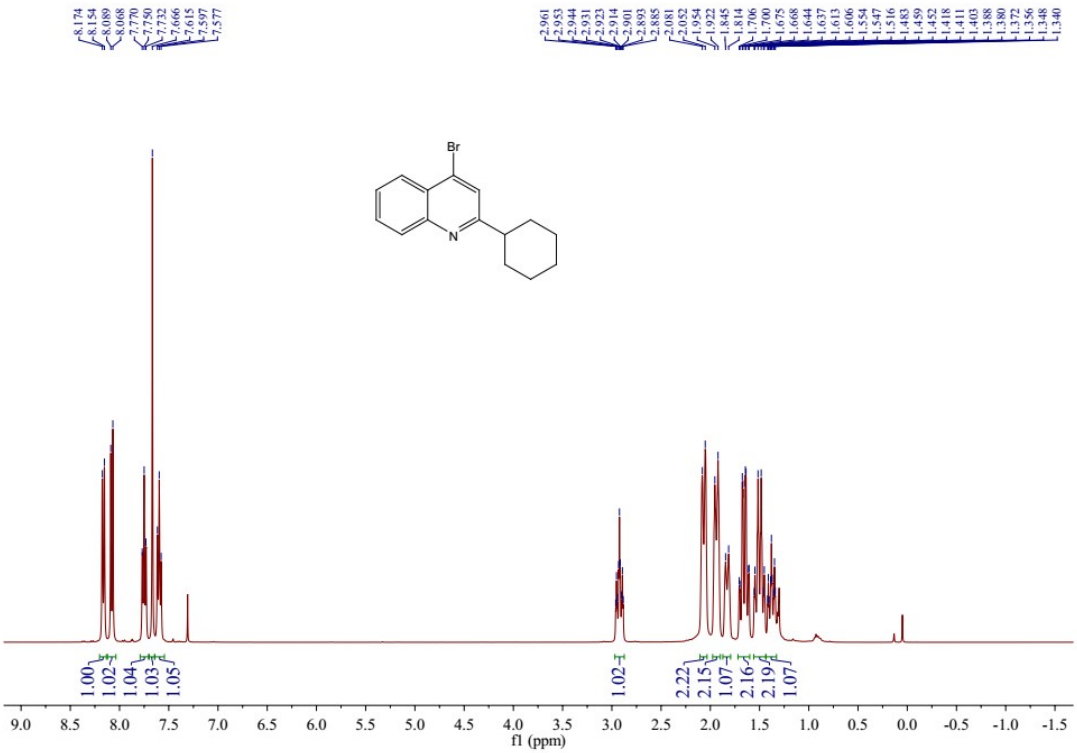


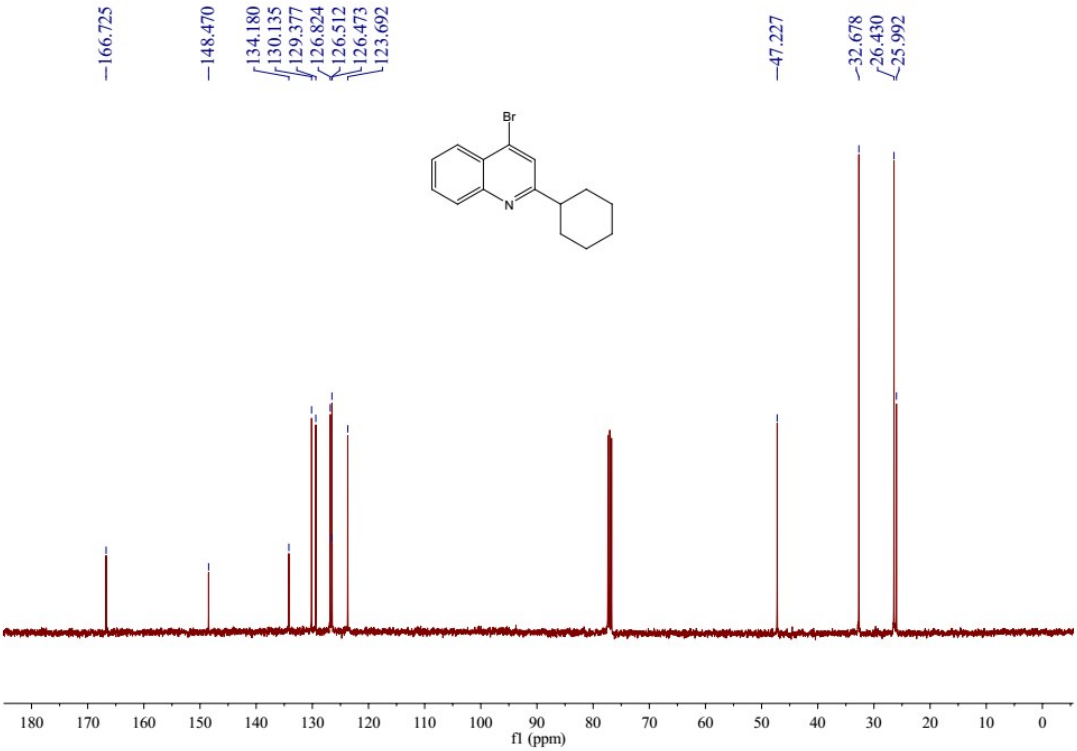
(3ed) 3-bromo-2-cyclooctylquinoline



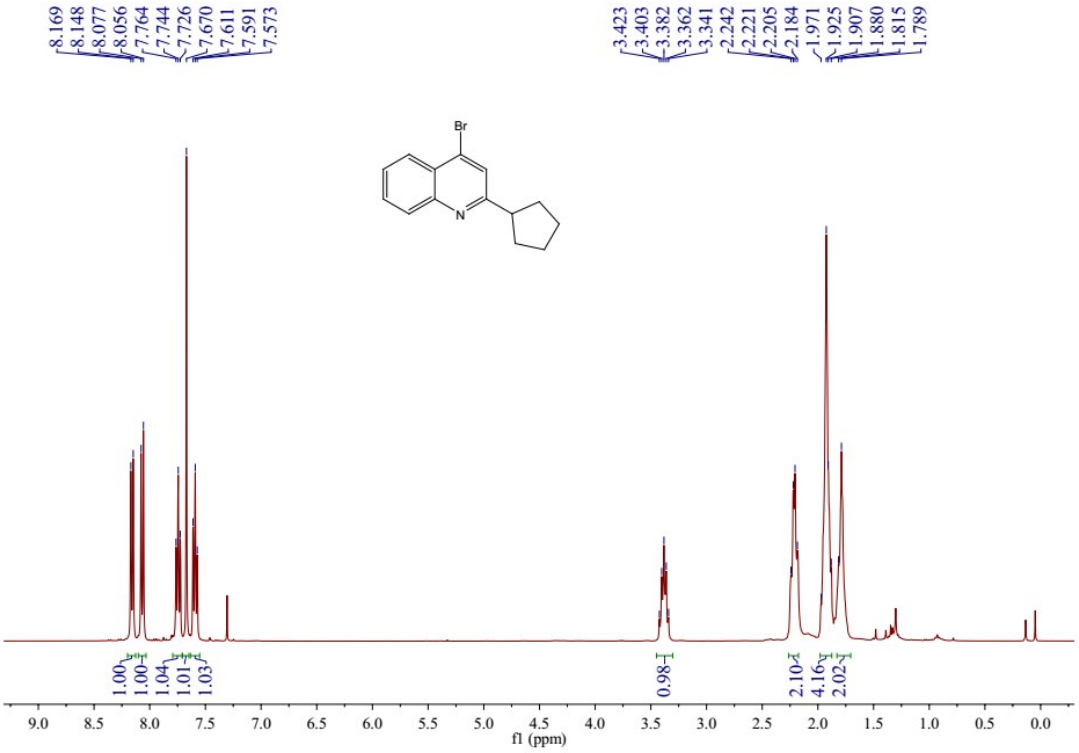


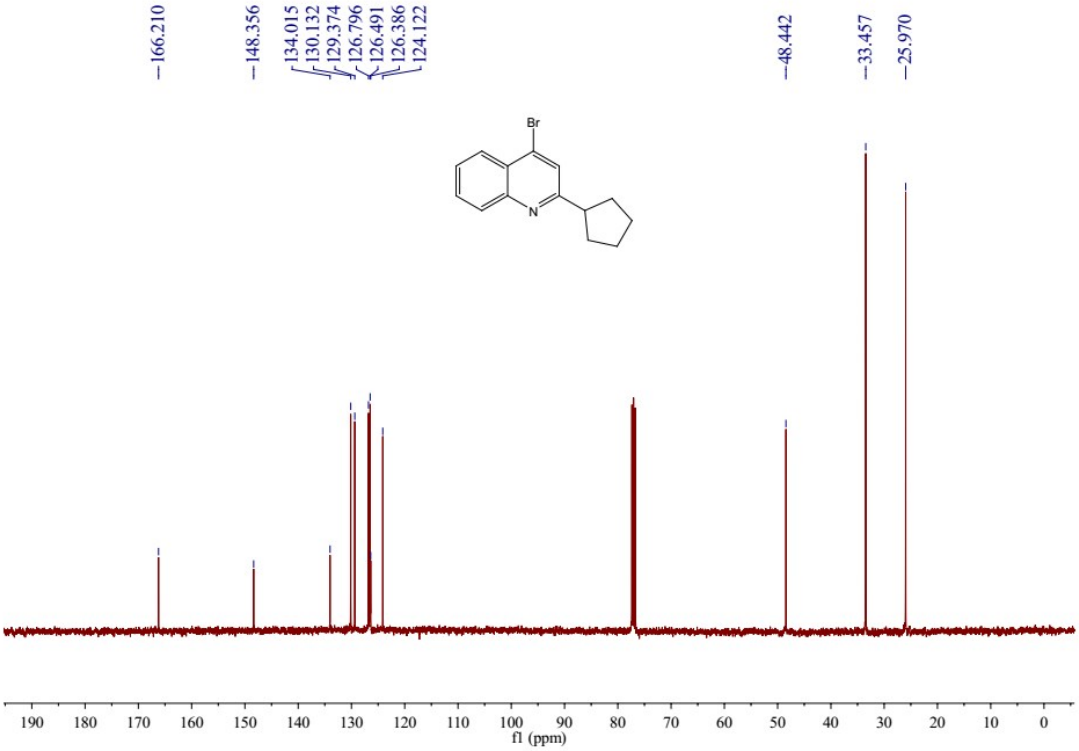
(3fa) 4-bromo-2-cyclohexylquinoline



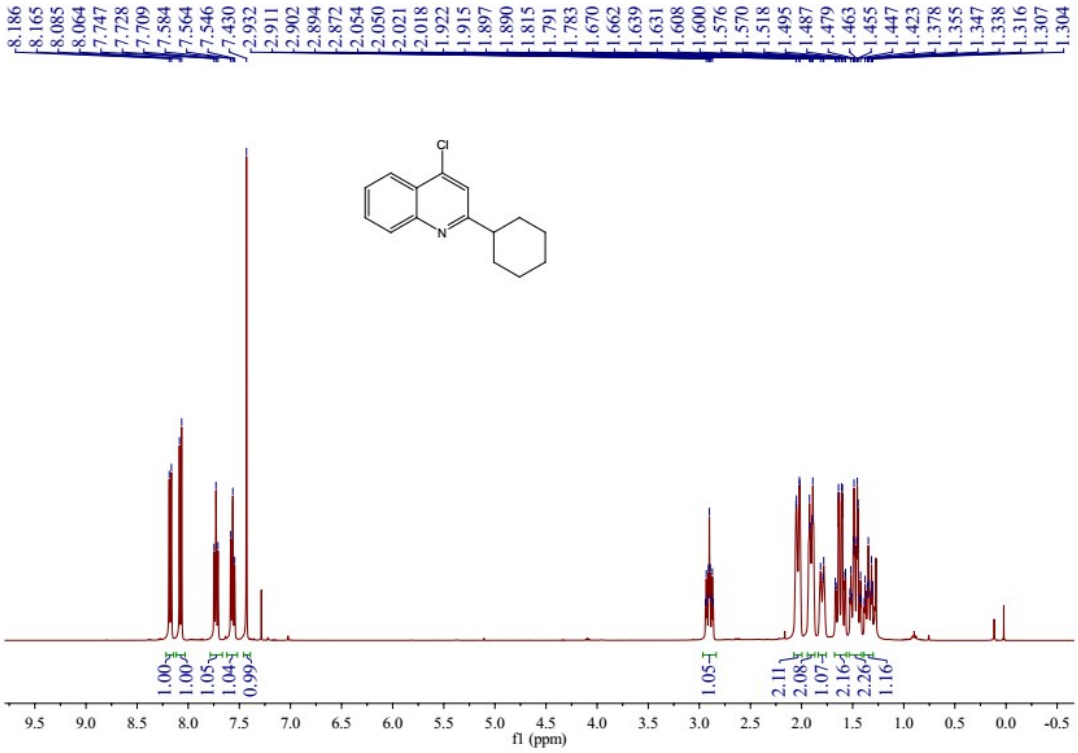


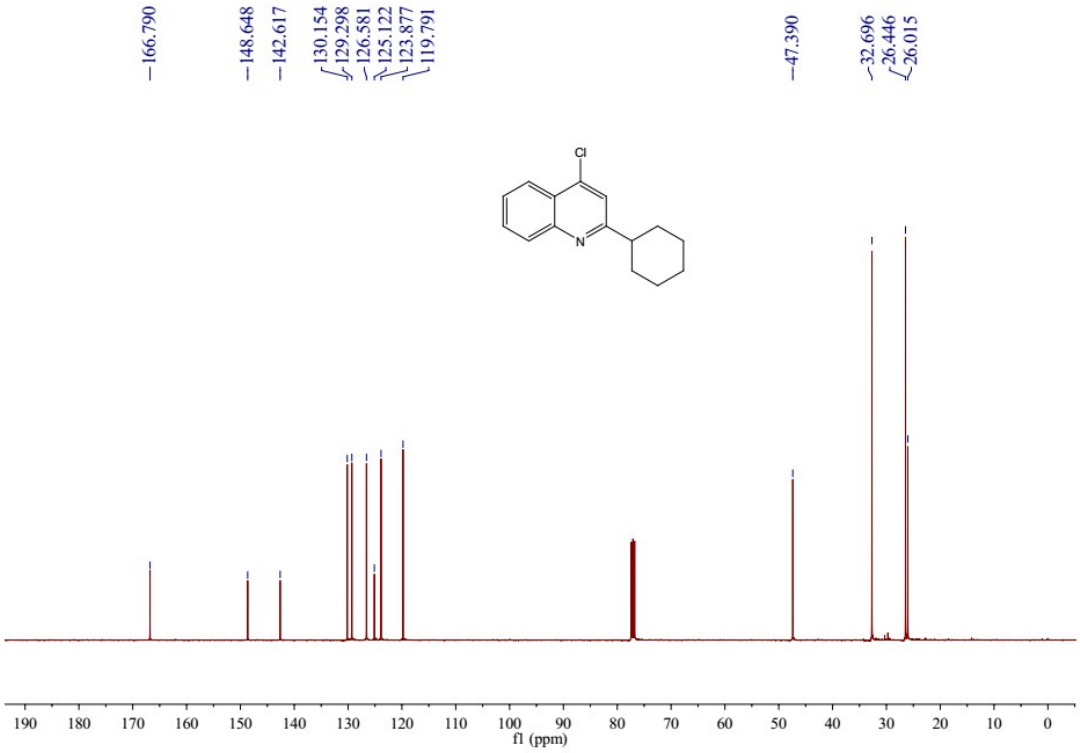
(3fb) 4-bromo-2-cyclopentylquinoline



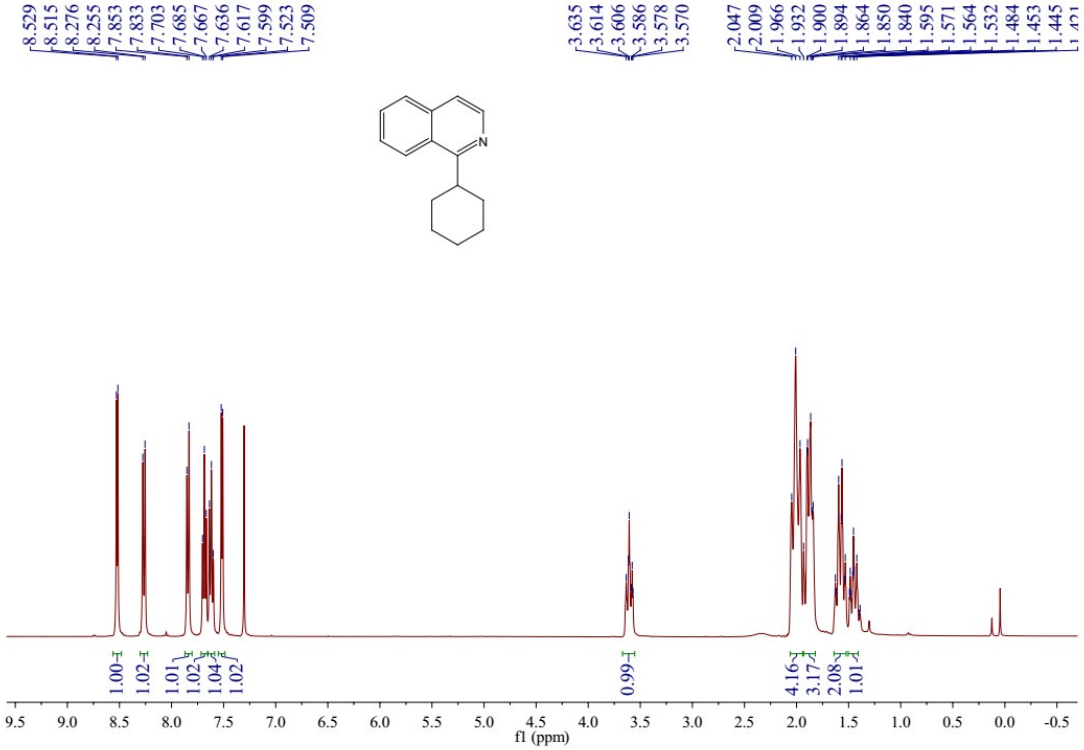


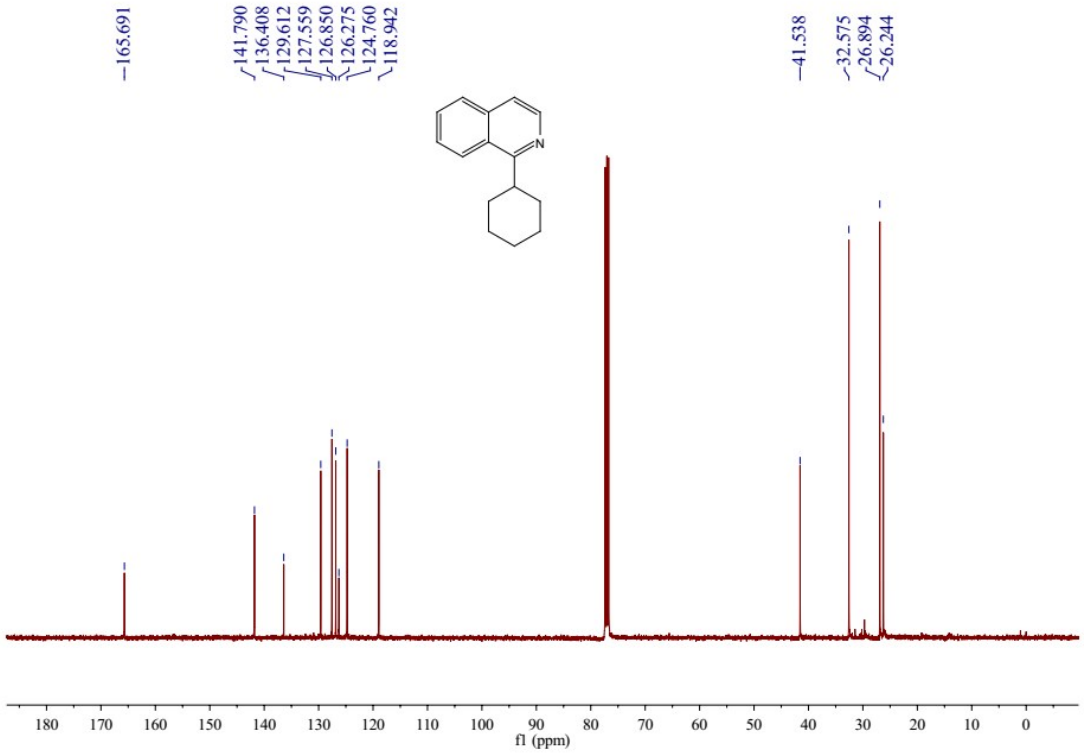
(3ga) 4-chloro-2-cyclohexylquinoline



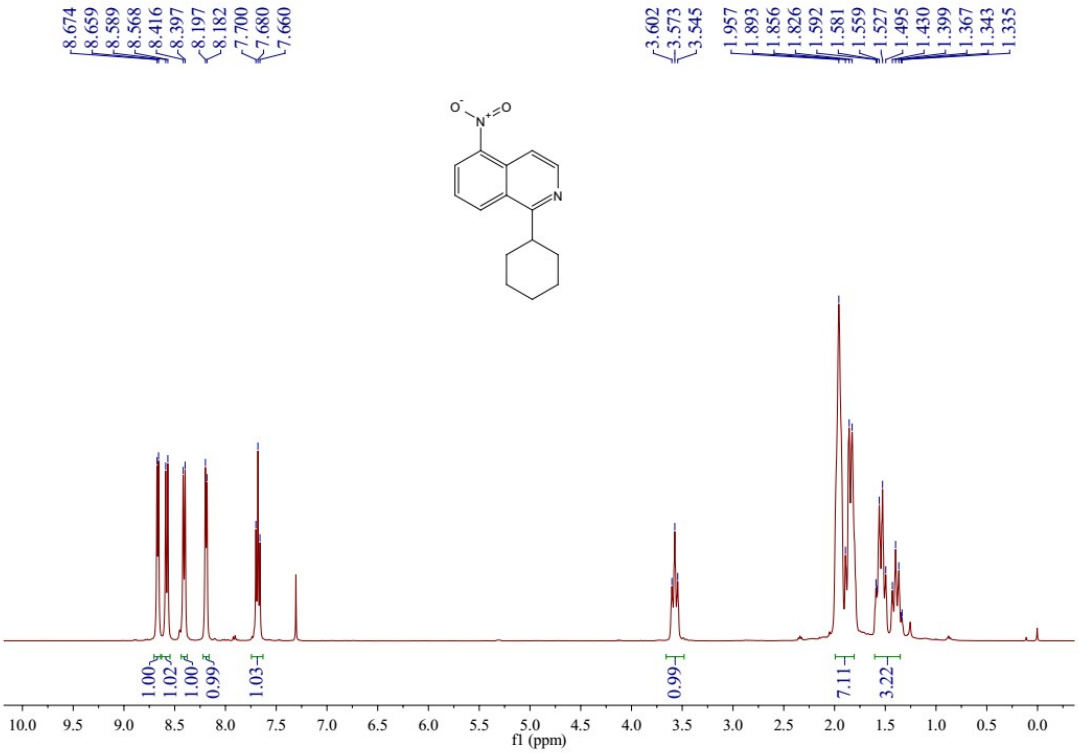


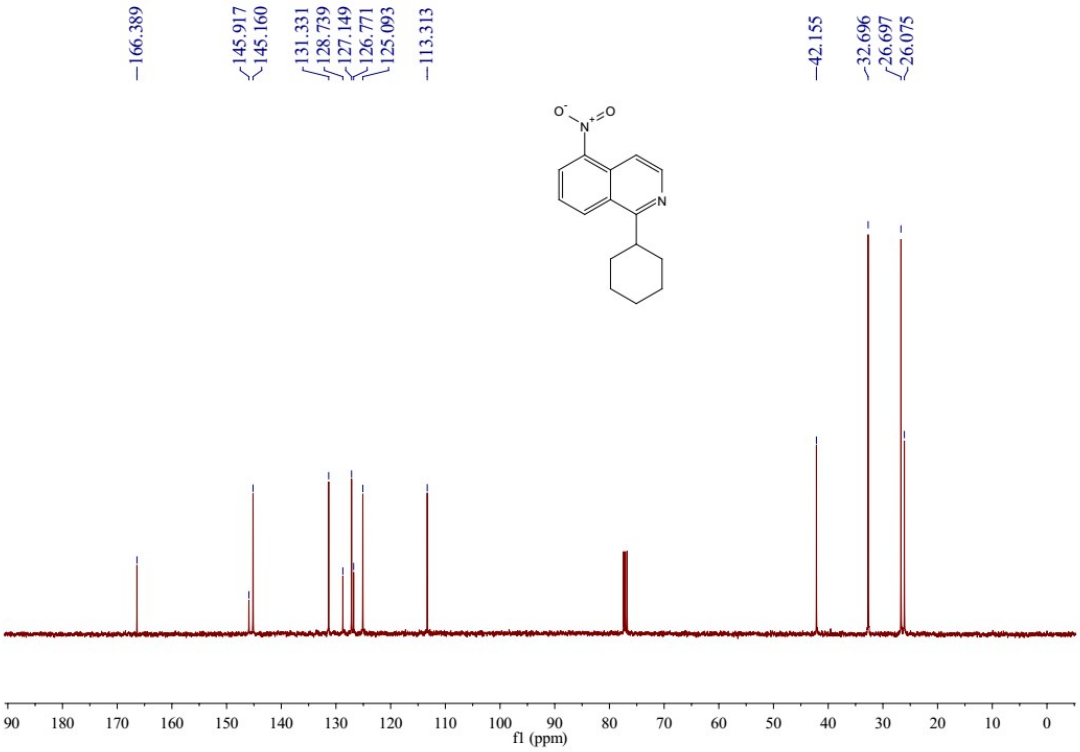
(3ca) 1-cyclohexyl *iso*-quinolin



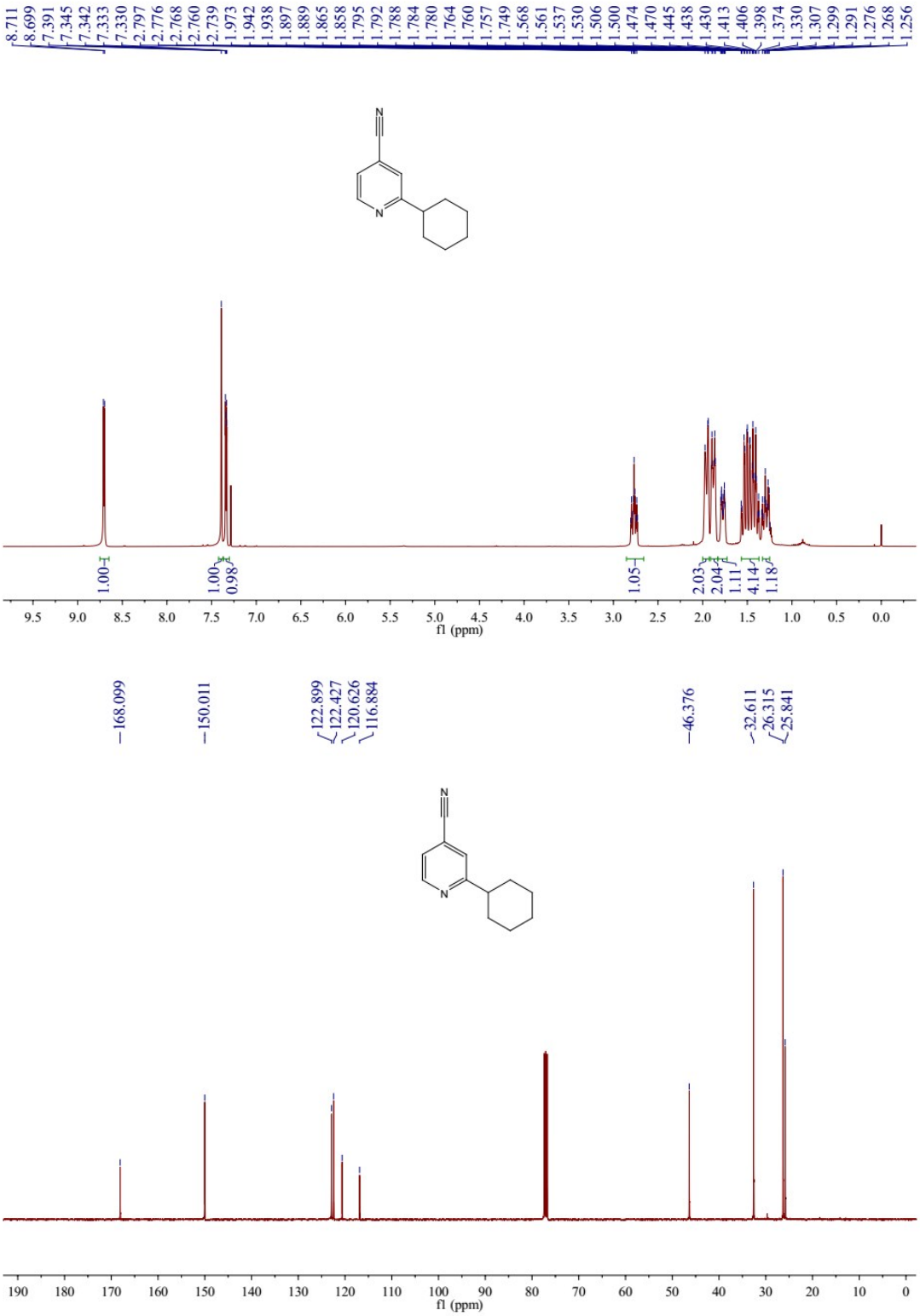


(3sa) 1-cyclohexyl-5-nitroisoquinoline

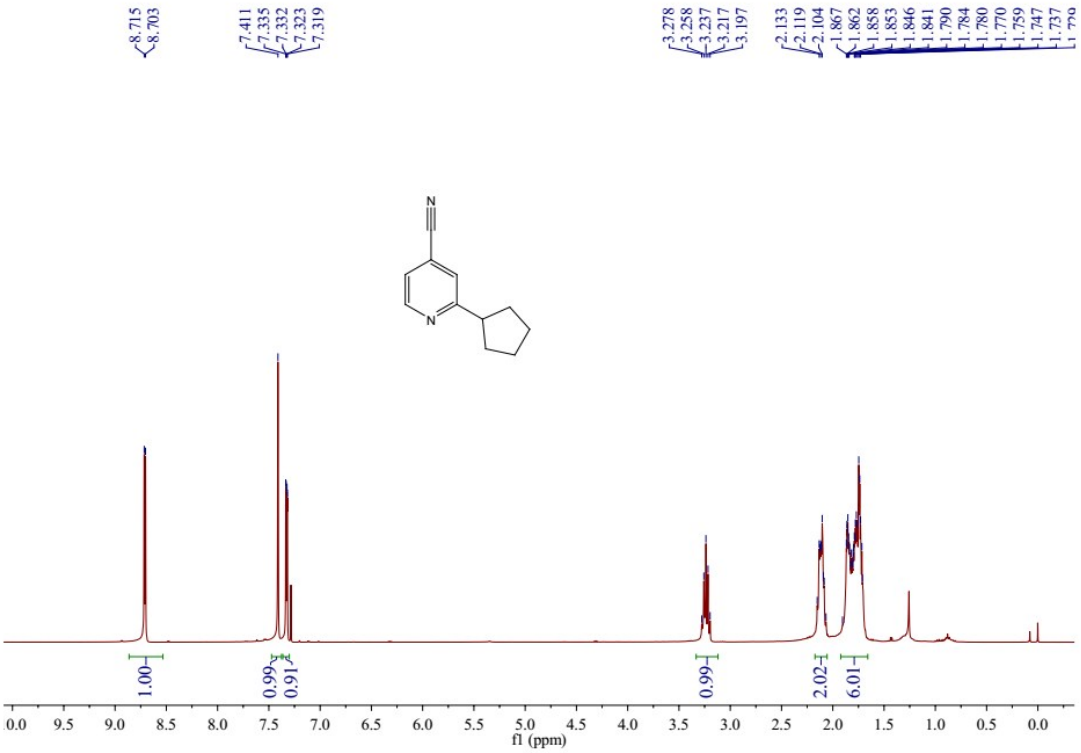


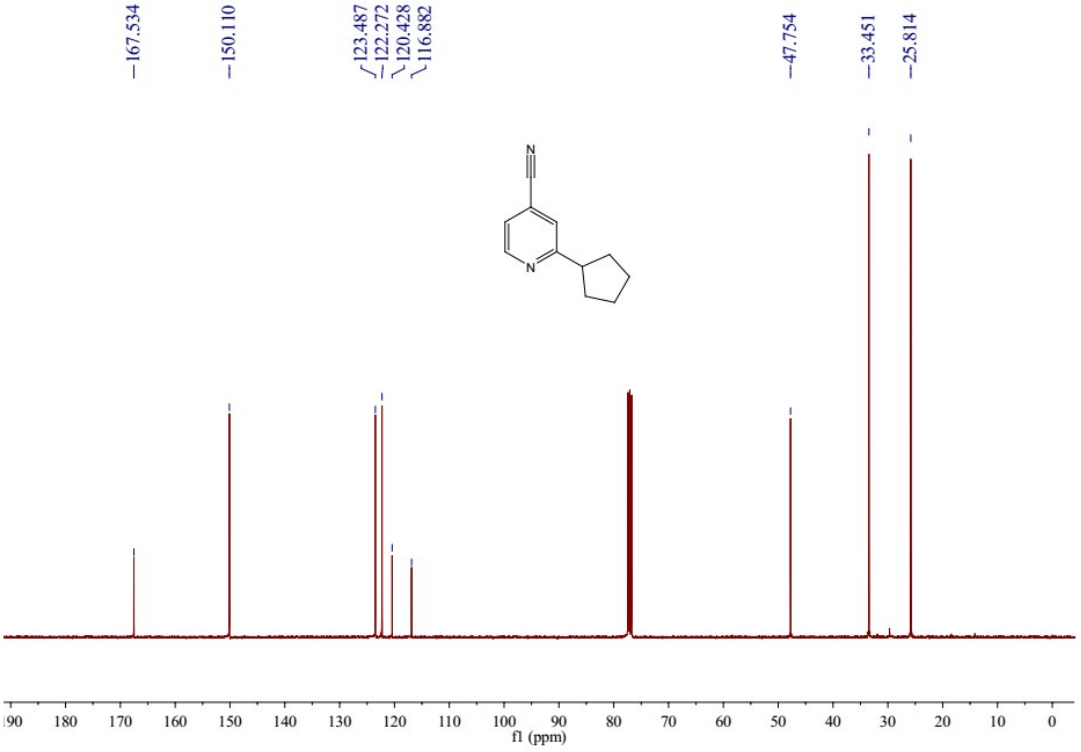


(3ha) 2-cyclohexylisonicotinonitrile

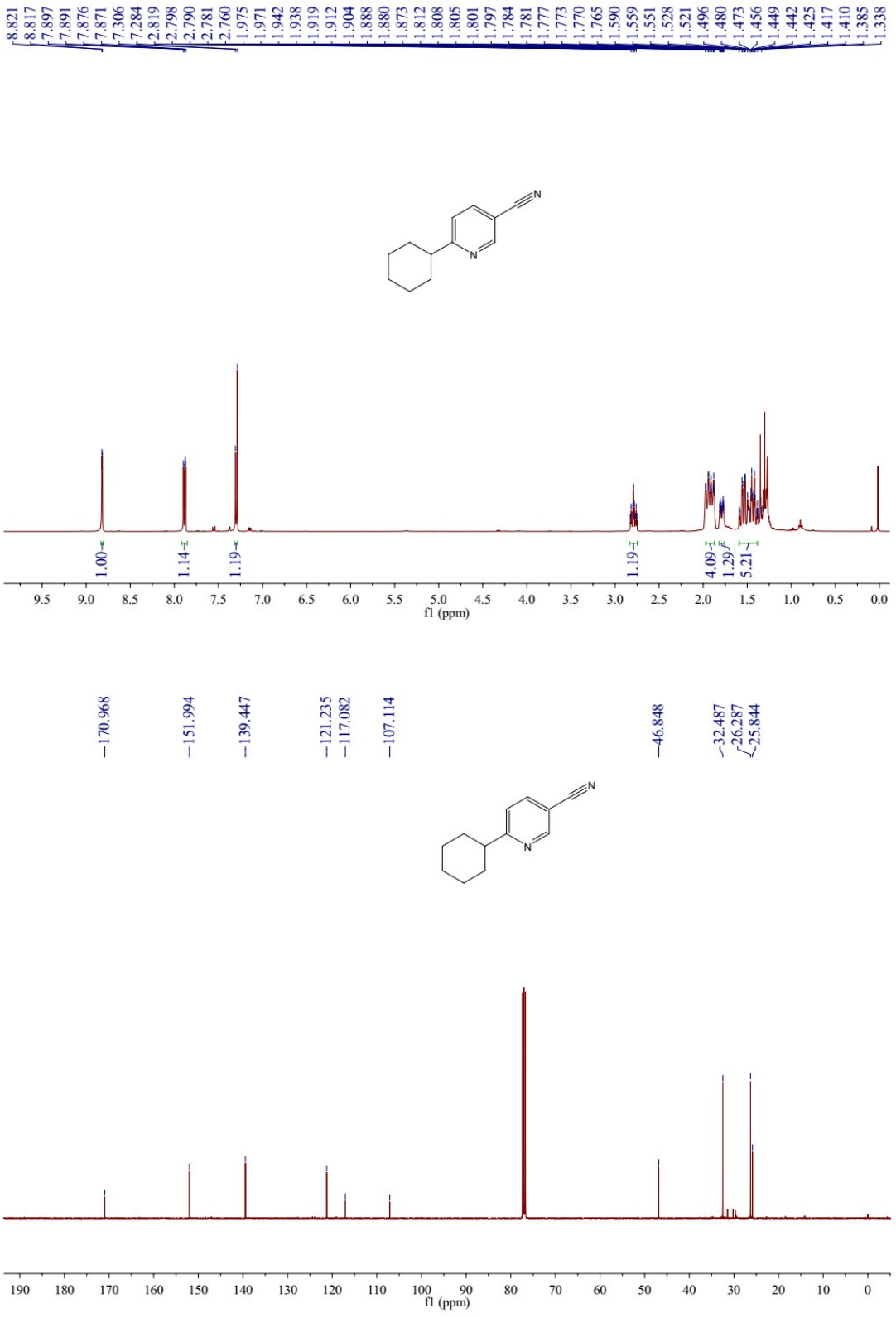


(3hb) 2-cyclopentylisonicotinonitrile

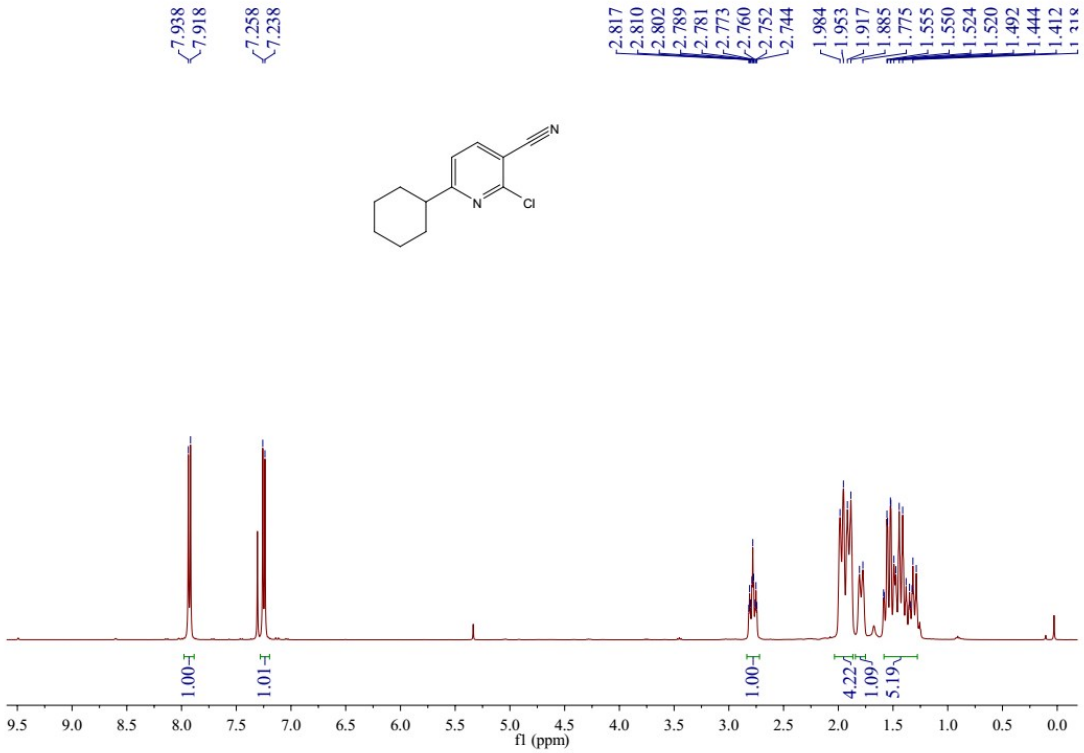


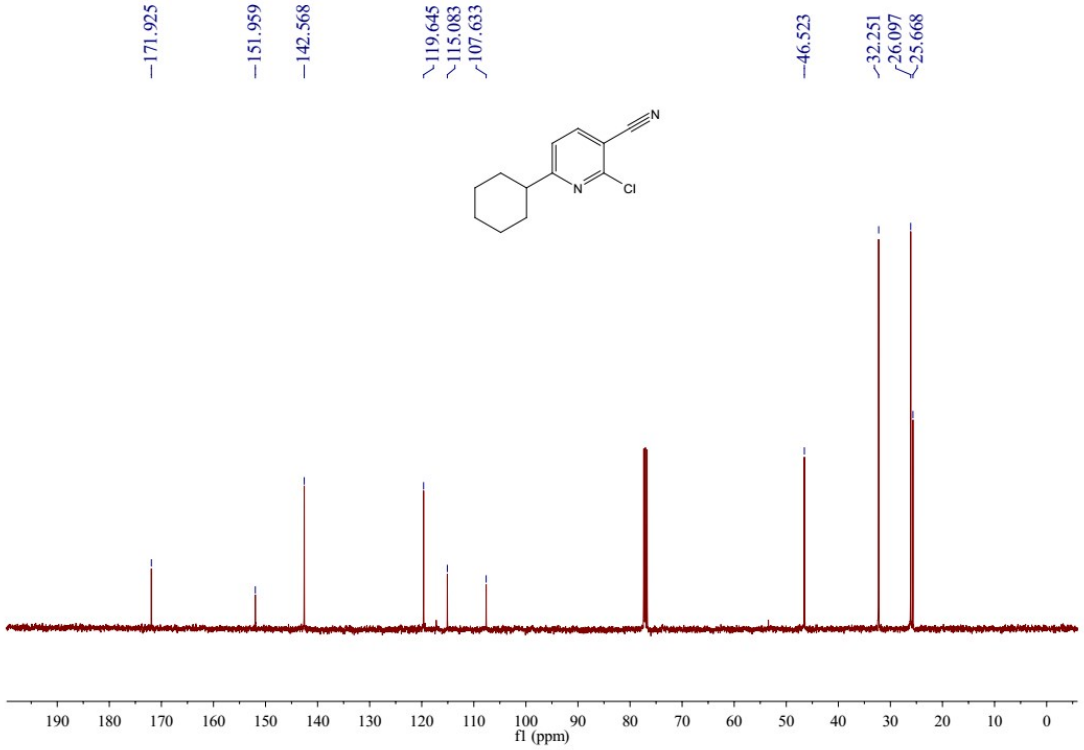


(3wa) 6-cyclohexylnicotinonitrile

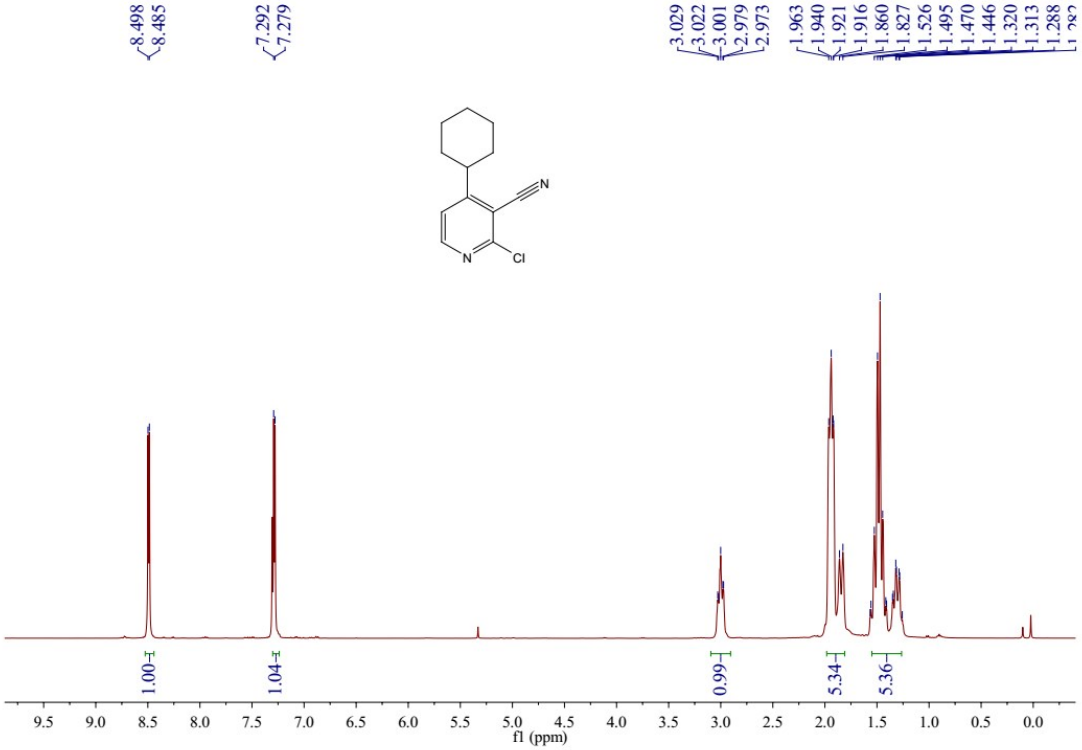


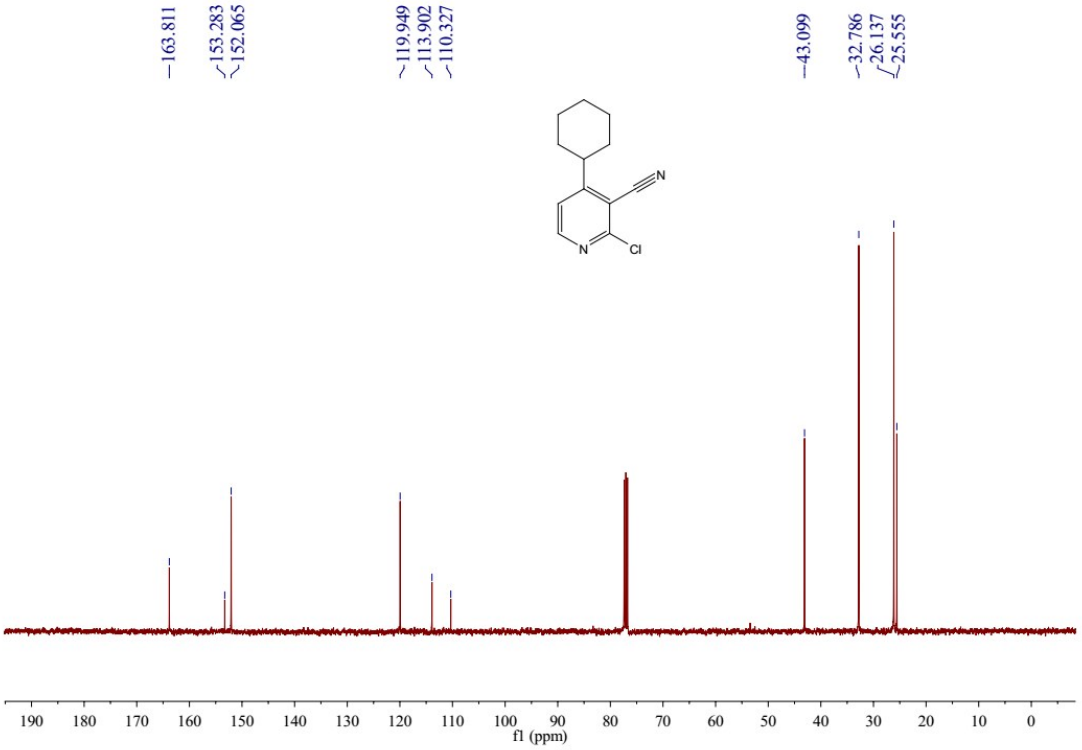
(3ta) 2-chloro-6-cyclohexylnicotinonitrile



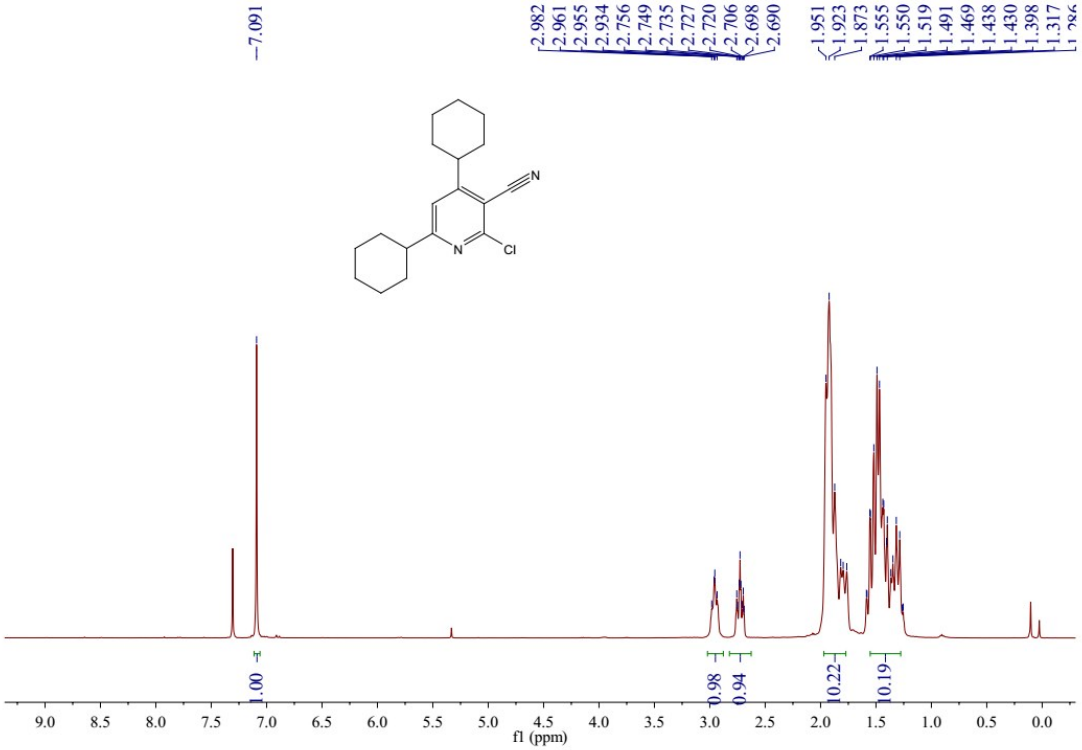


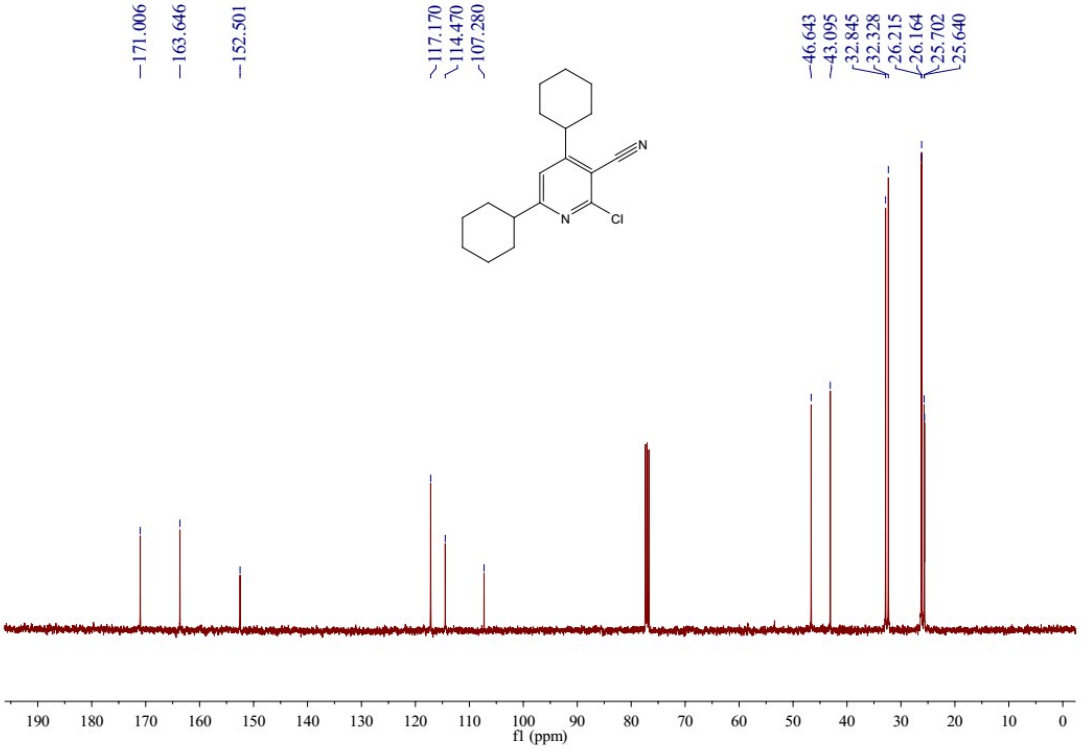
(3ta') 2-chloro-4-cyclohexylnicotinonitrile



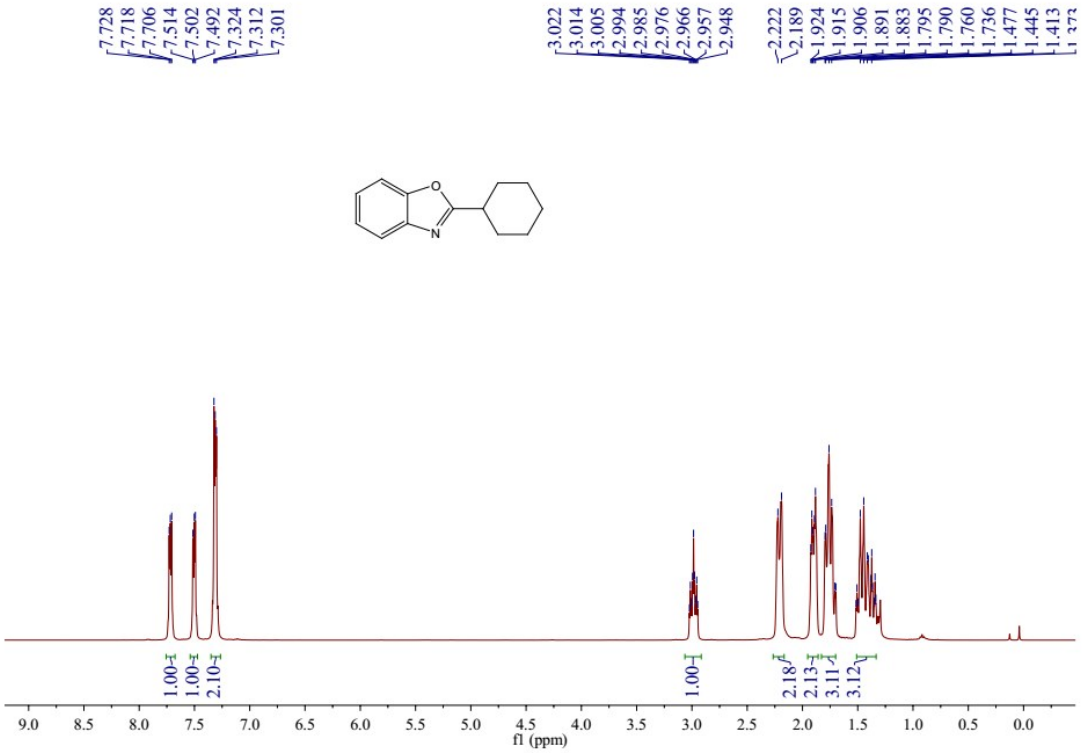


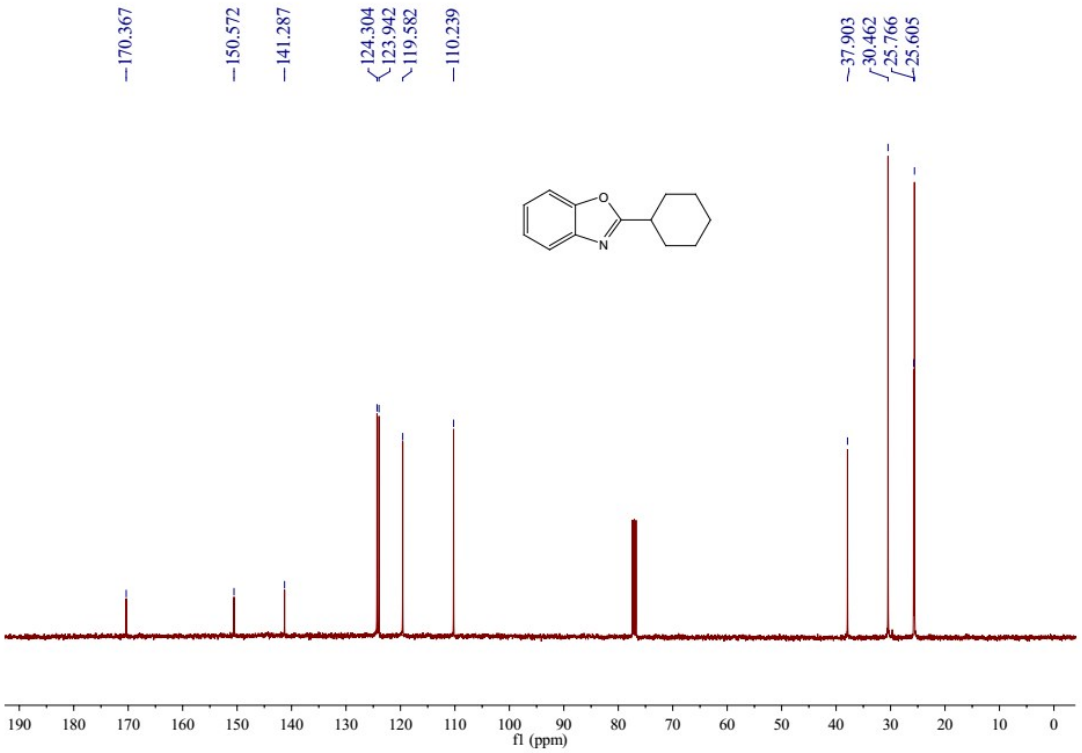
(3ta'') 2-chloro-4,6-dicyclohexylnicotinonitrile



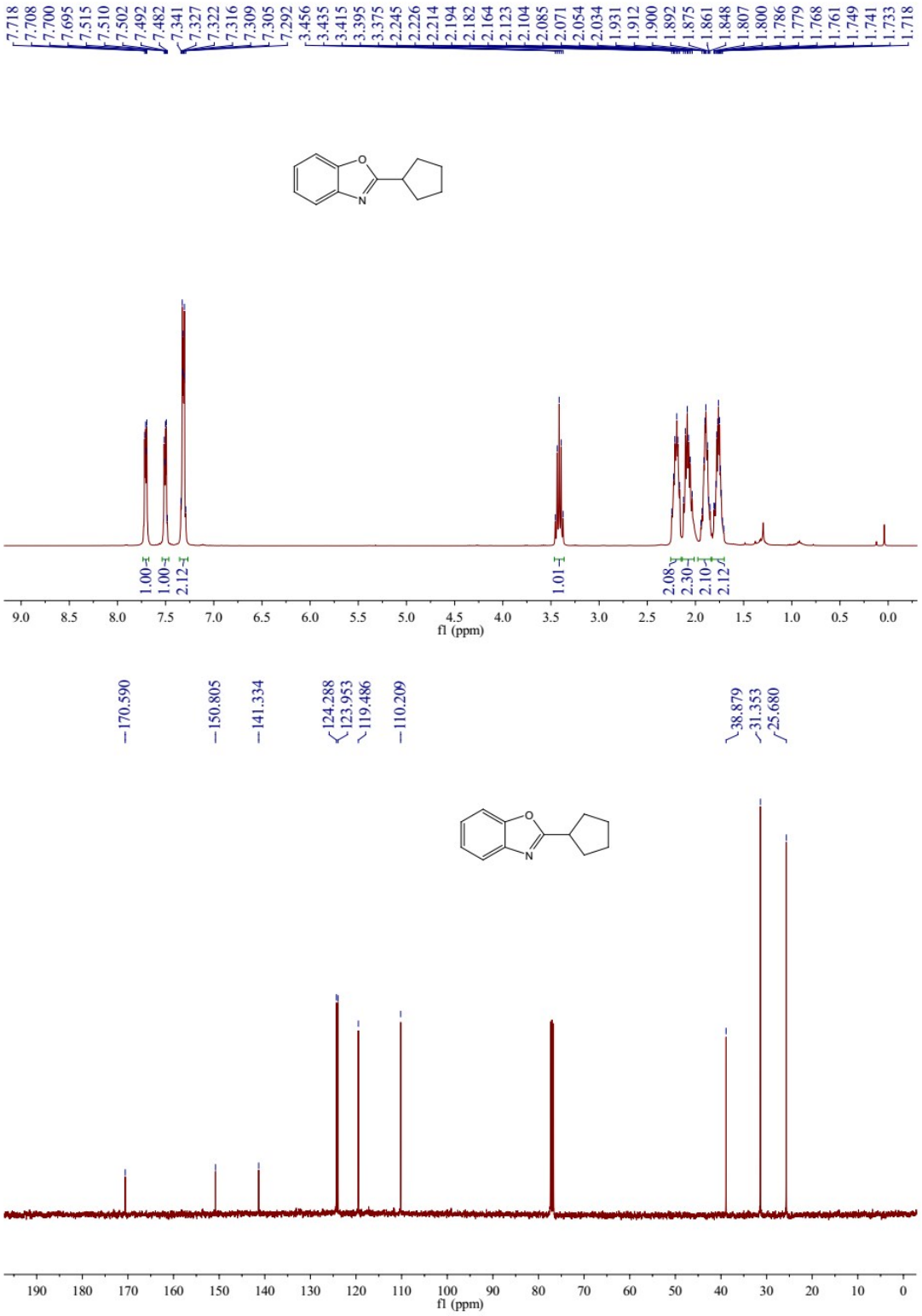


(3ia) 2-cyclohexylbenzo[*d*]oxazole

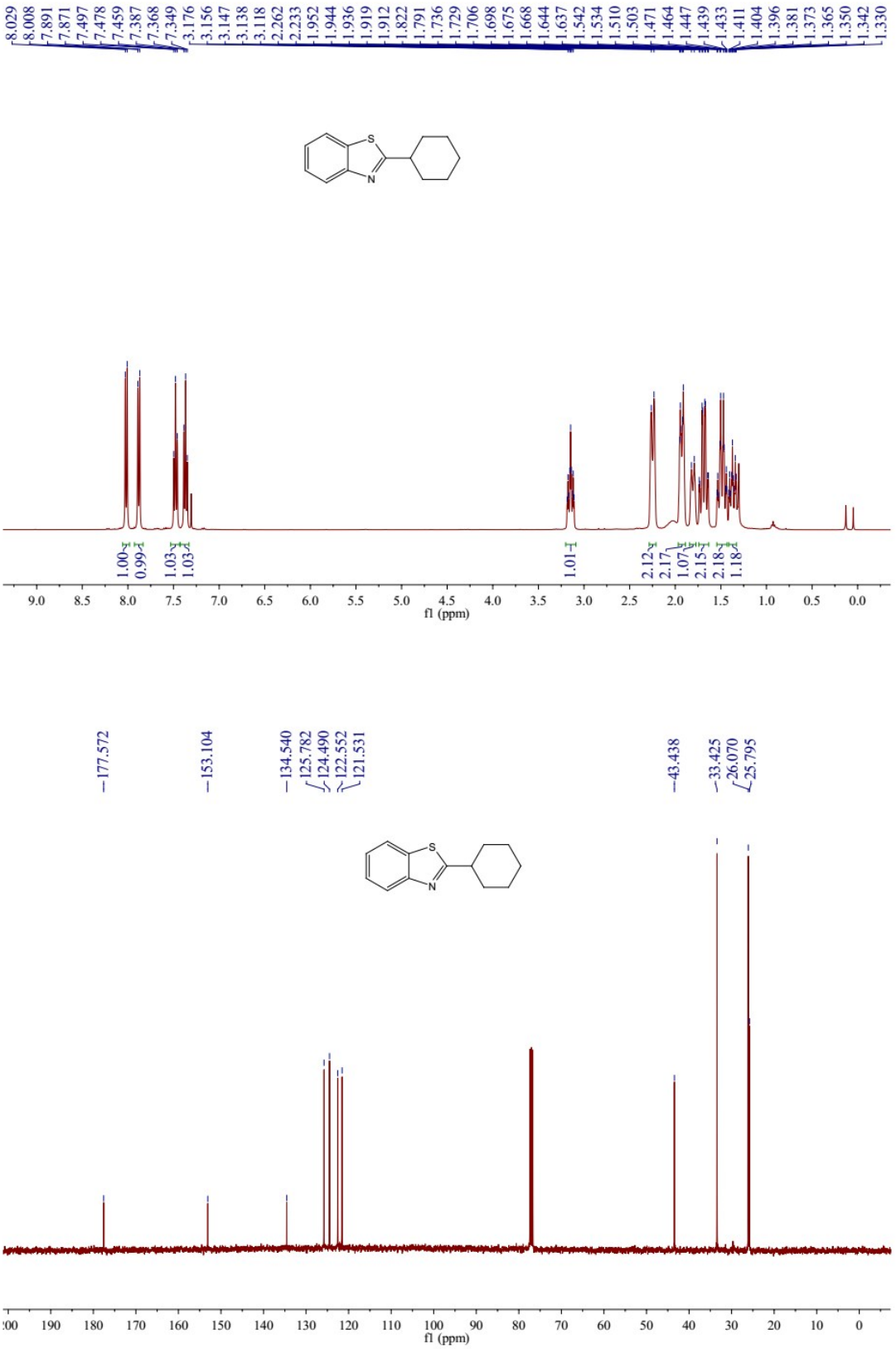




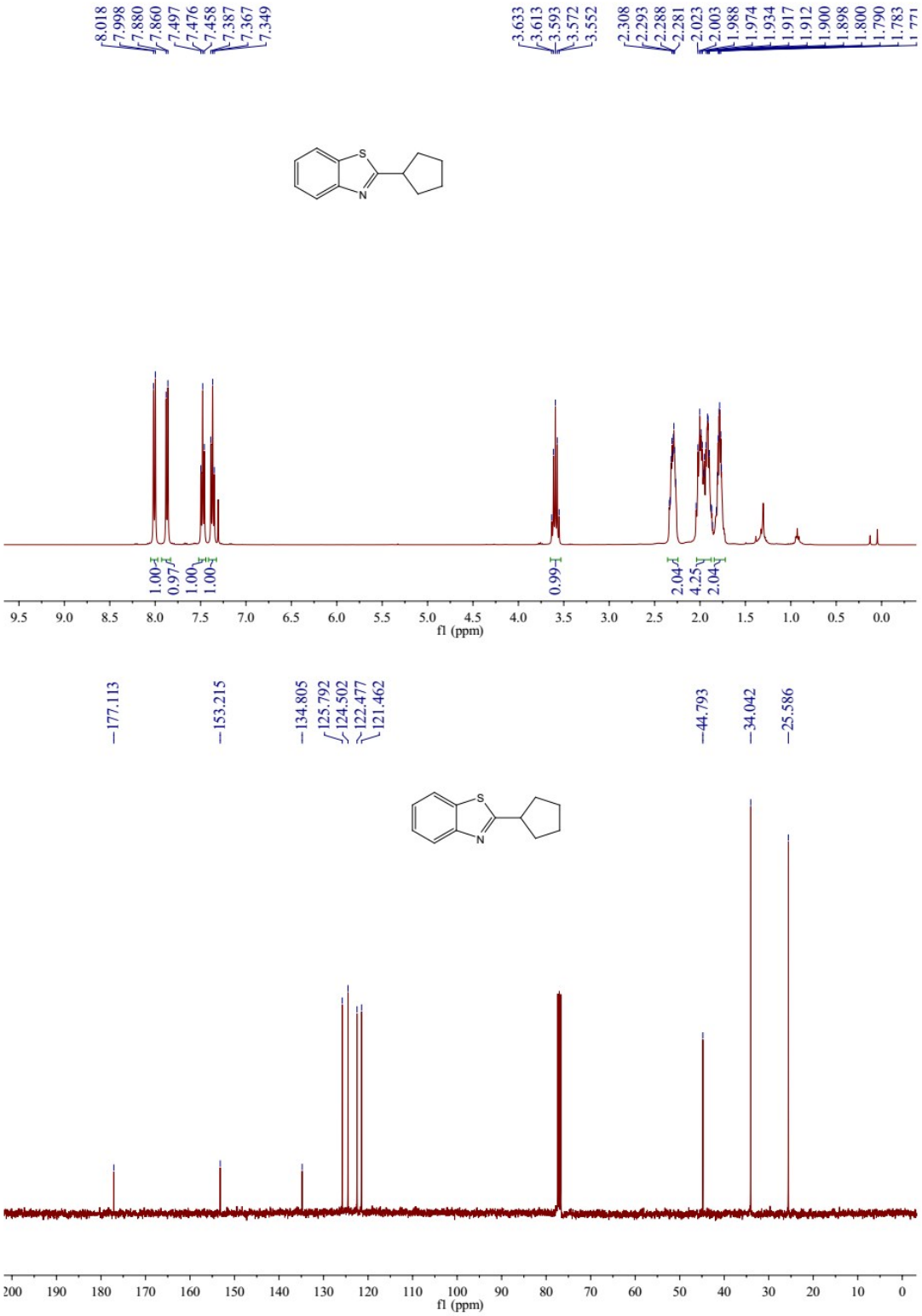
(3ib) 2-cyclopentylbenzo[*d*]oxazole



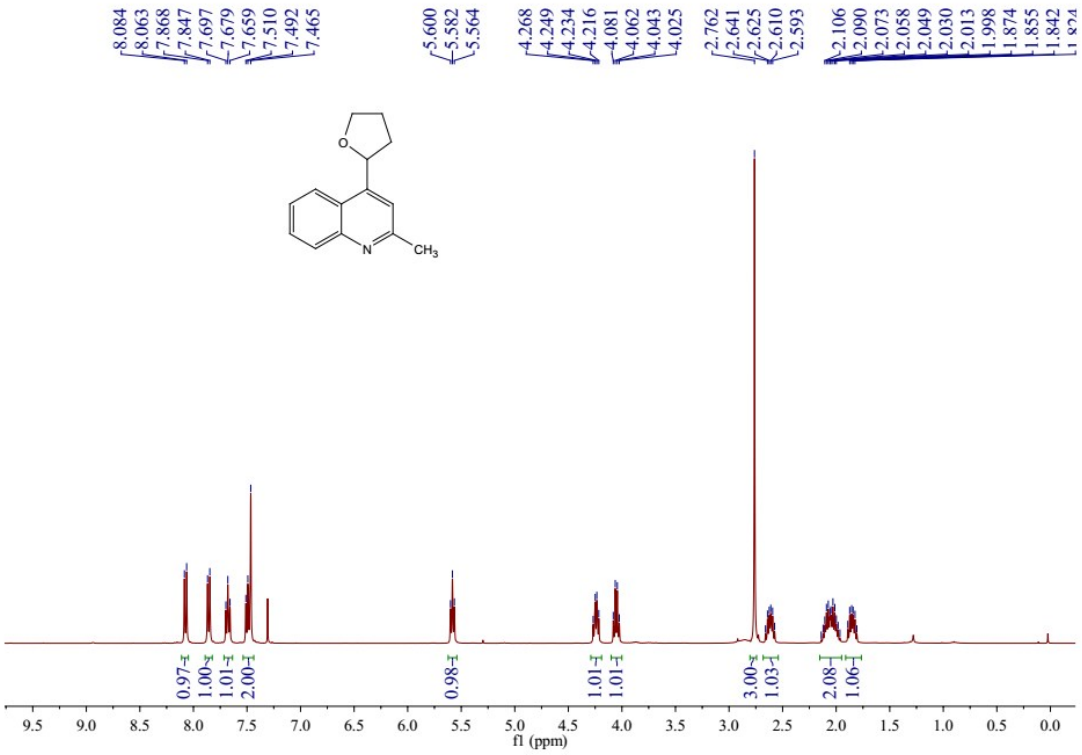
(3ja) 2-cyclohexylbenzo[*d*]thiazole

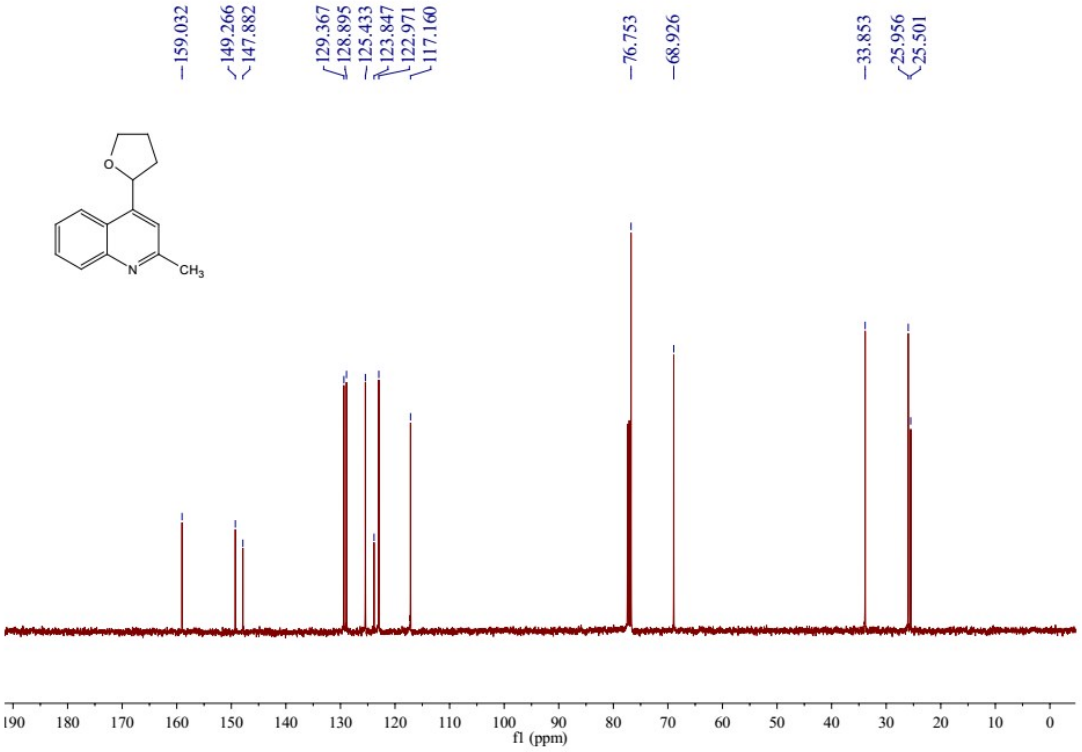


(3jb) 2-cyclopentylbenzo[*d*]thiazole

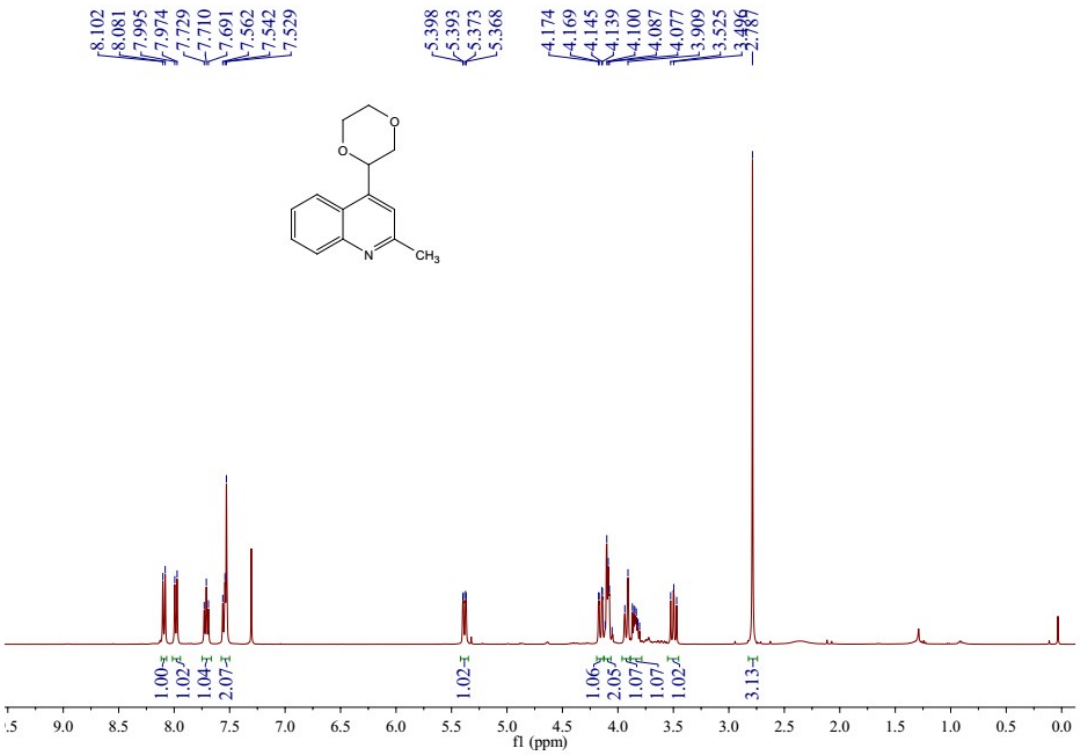


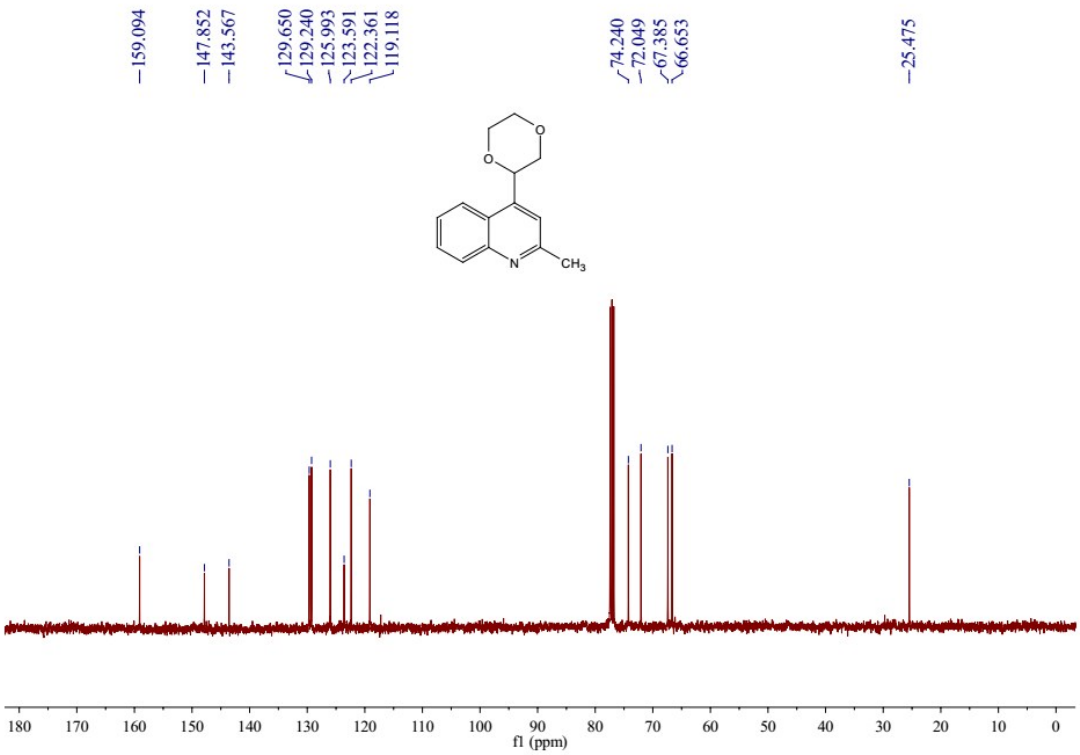
(3kg) 2-methyl-4-(tetrahydrofuran-2-yl)quinolone



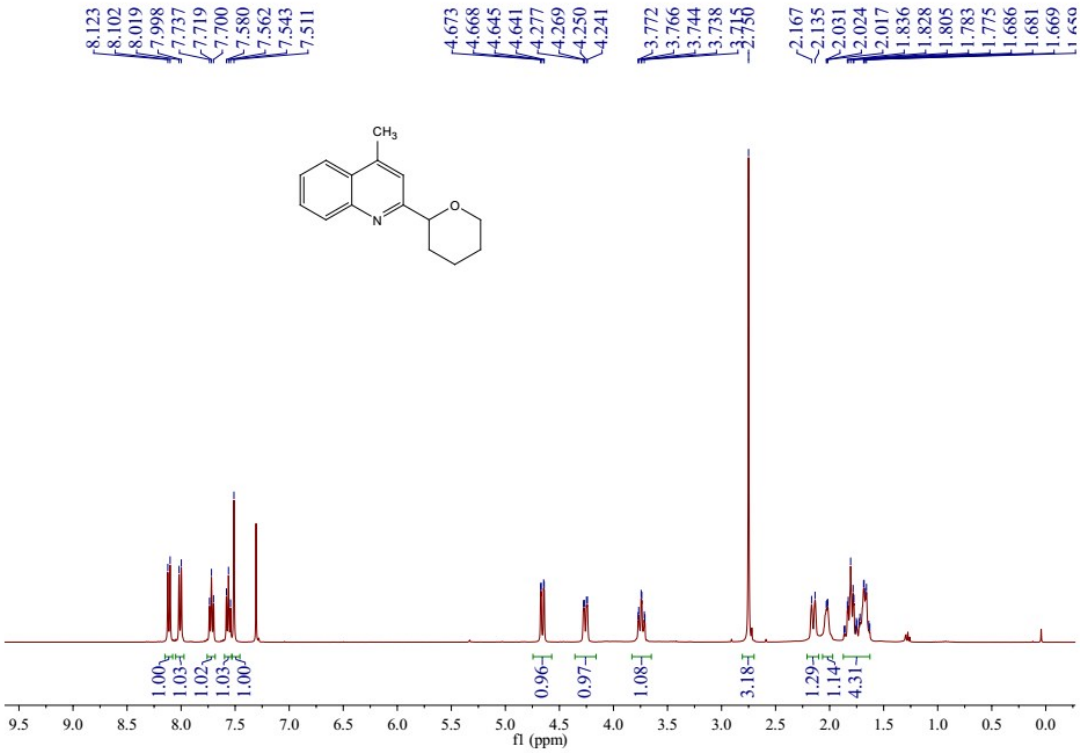


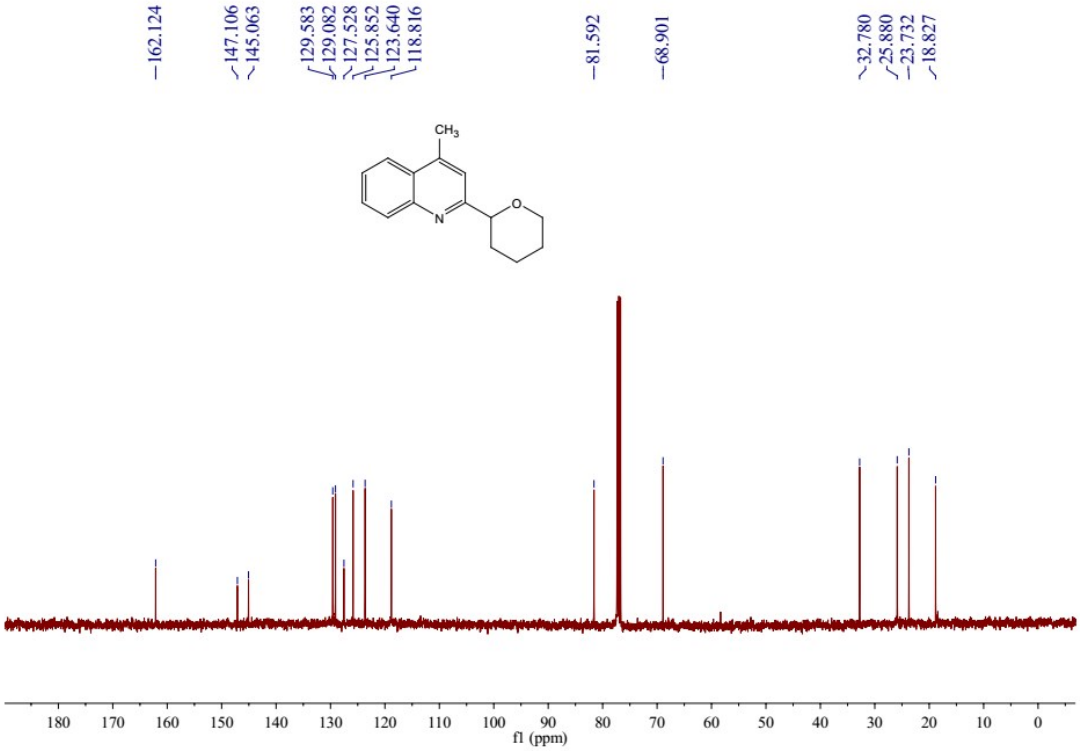
(3kh) 4-(1,4-dioxan-2-yl)-2-methylquinoline



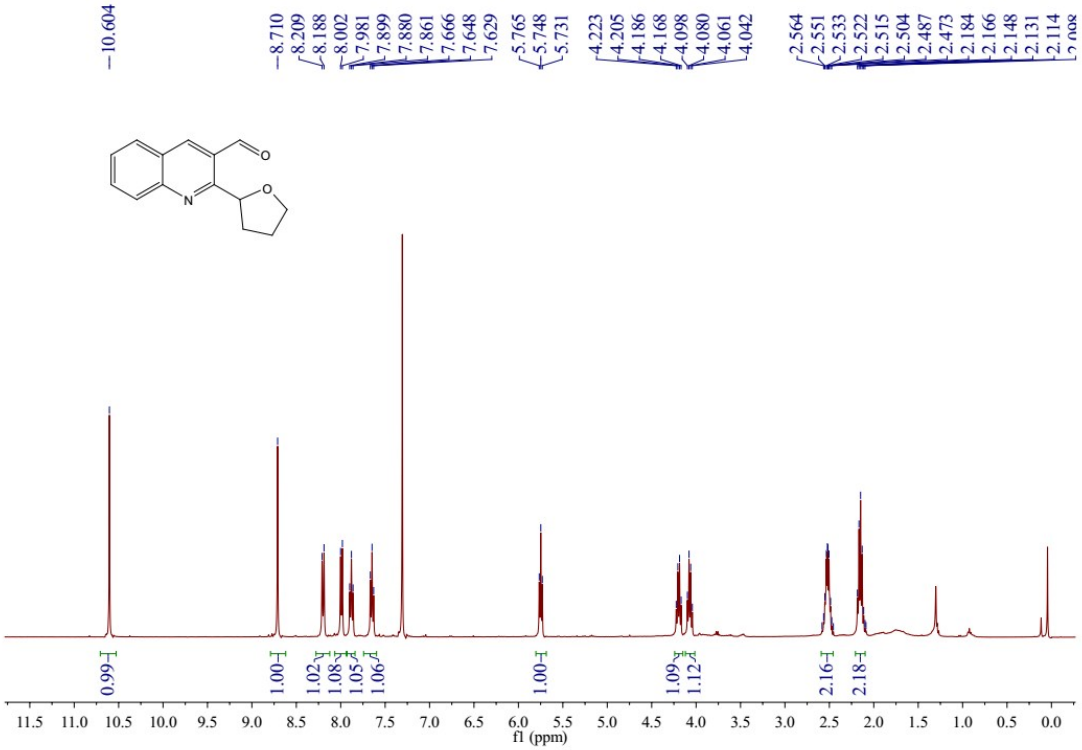


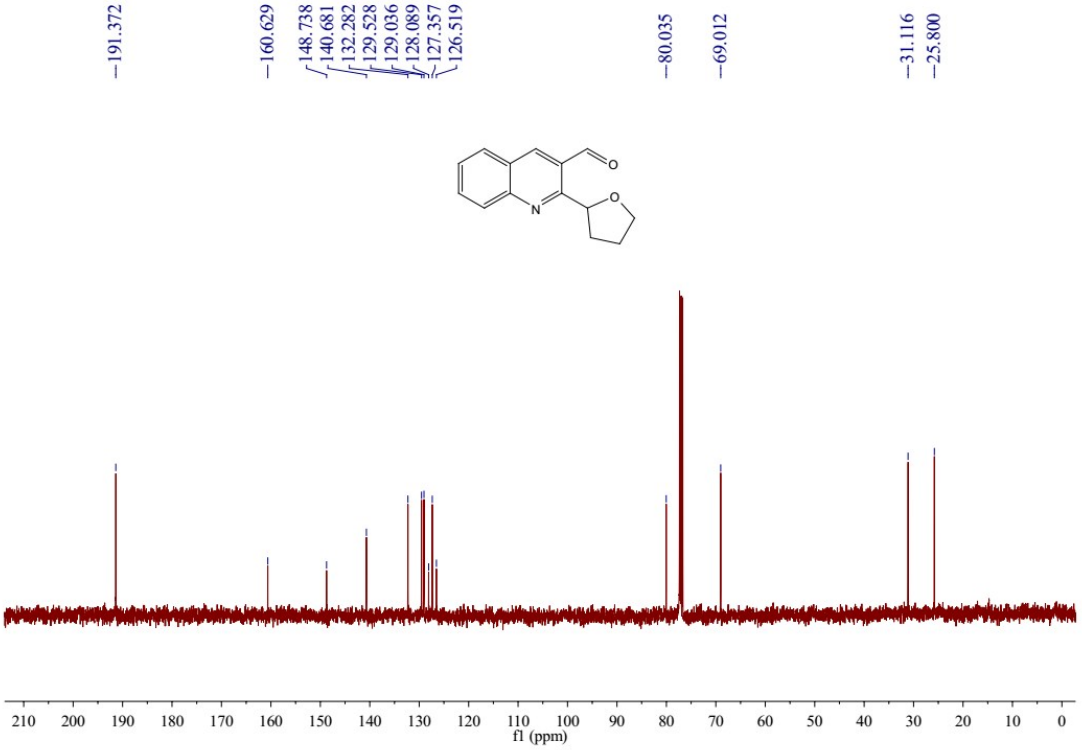
(3li) 4-methyl-2-(tetrahydro-*2H*-pyran-2-yl)quinoline



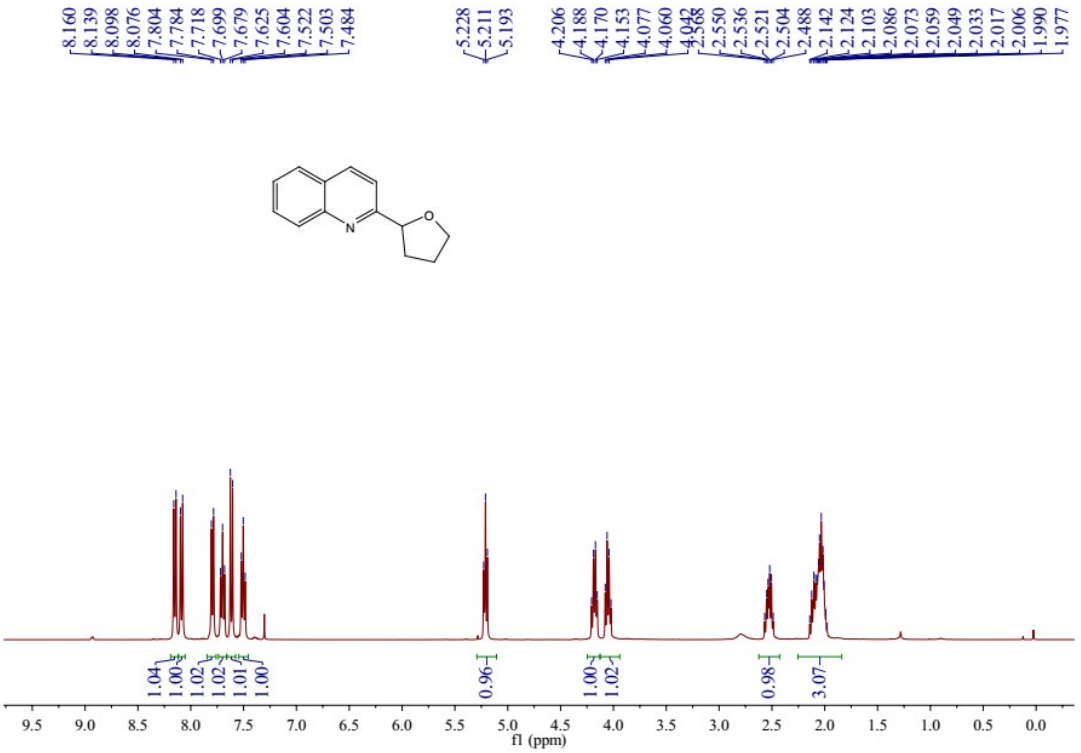


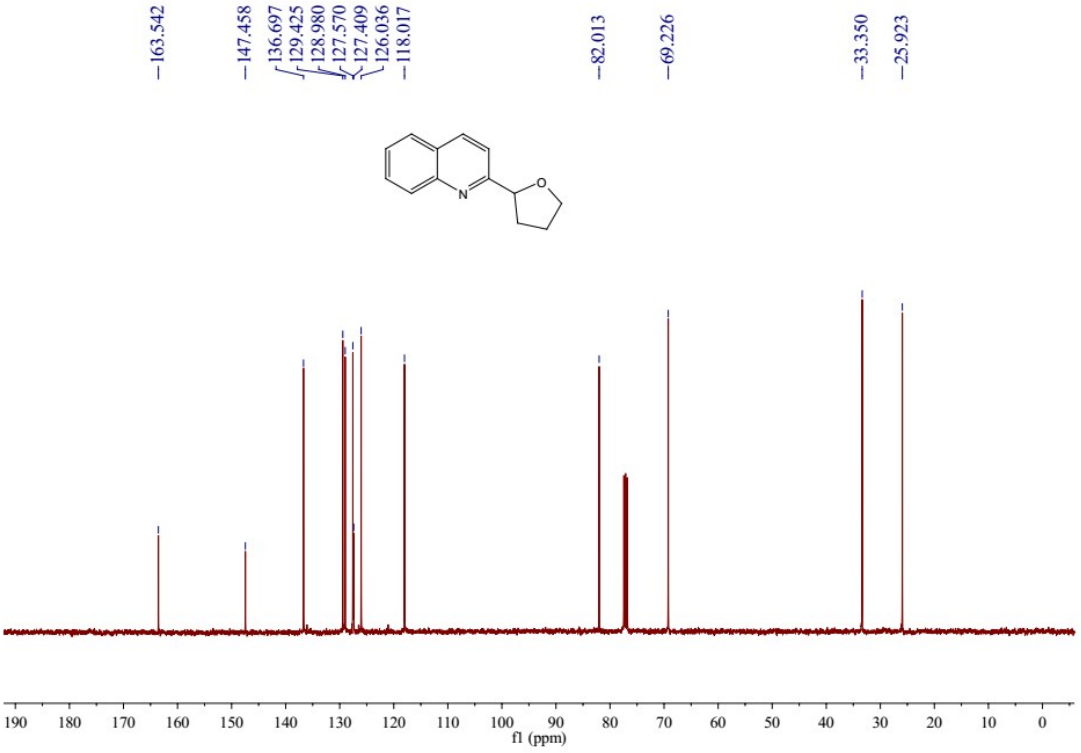
(3yg) 2-(tetrahydrofuran-2-yl)quinoline-3-carbaldehyde



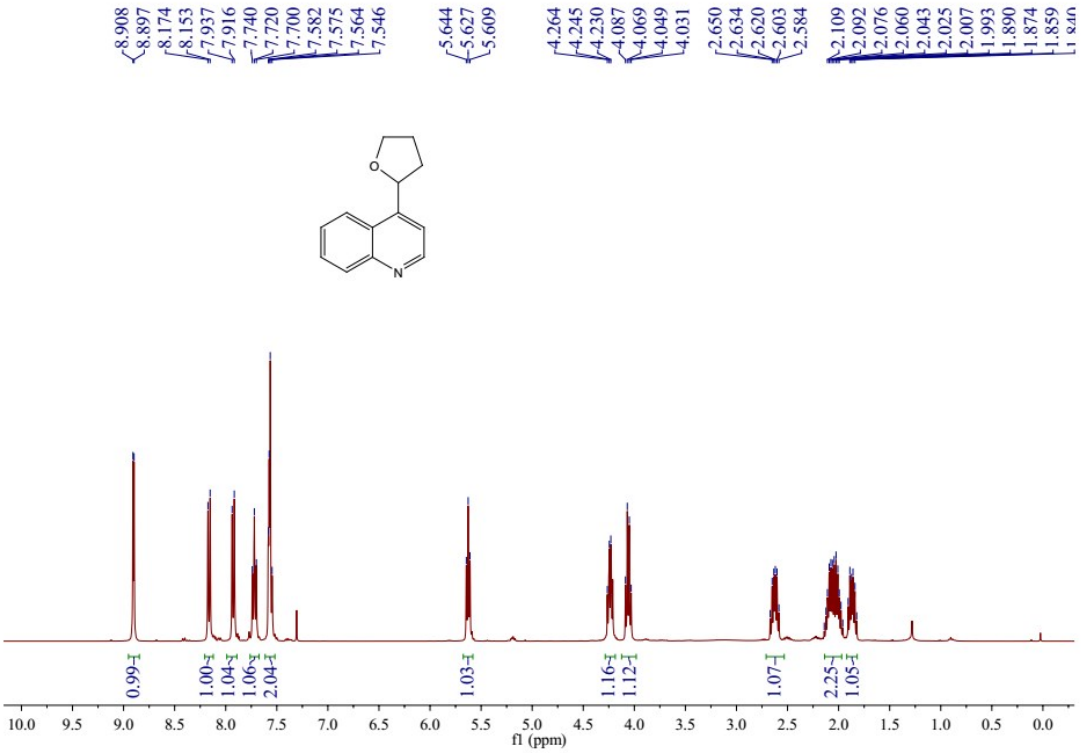


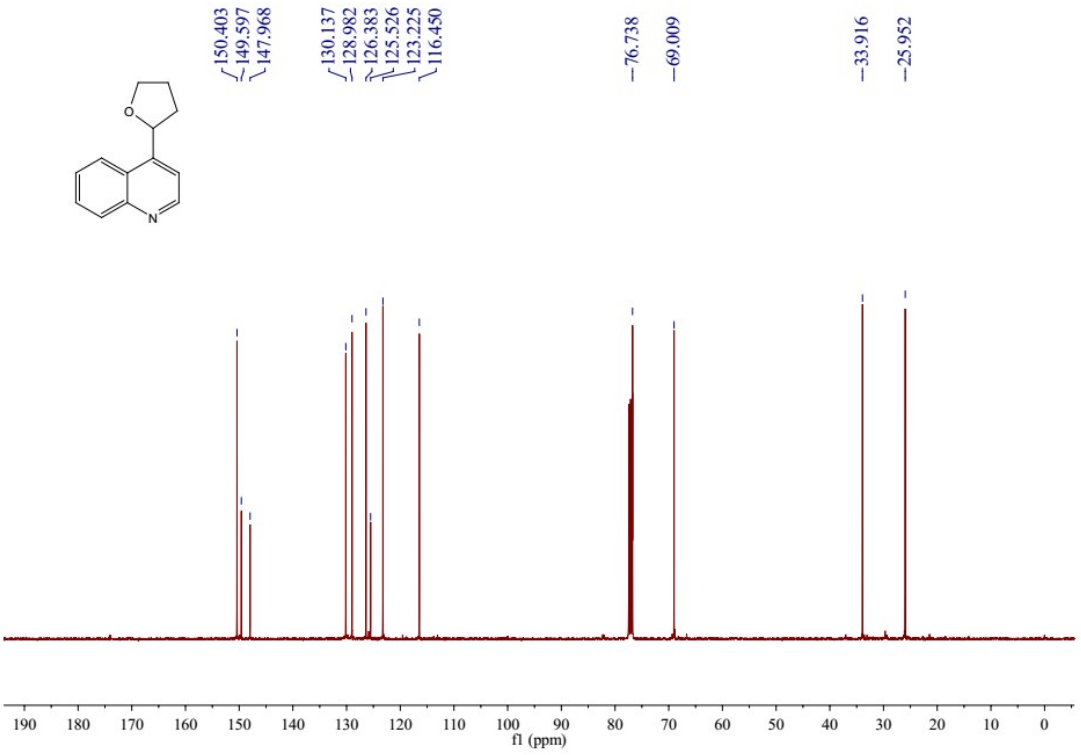
(3mg) 2-(tetrahydrofuran-2-yl)quinoline



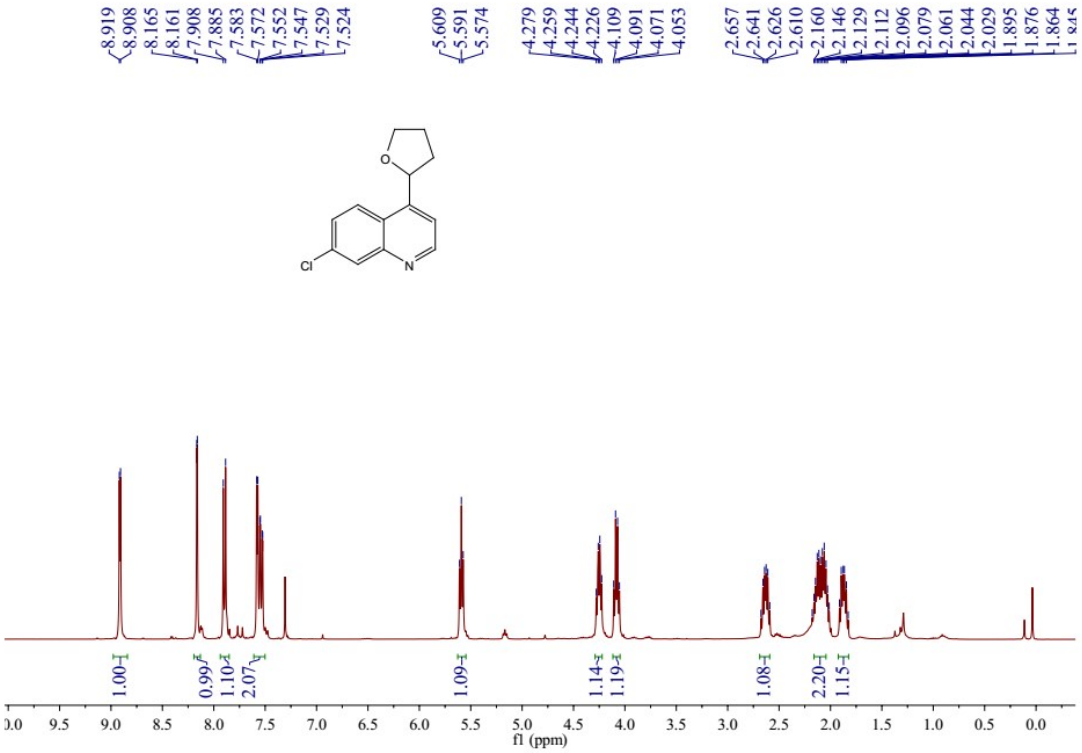


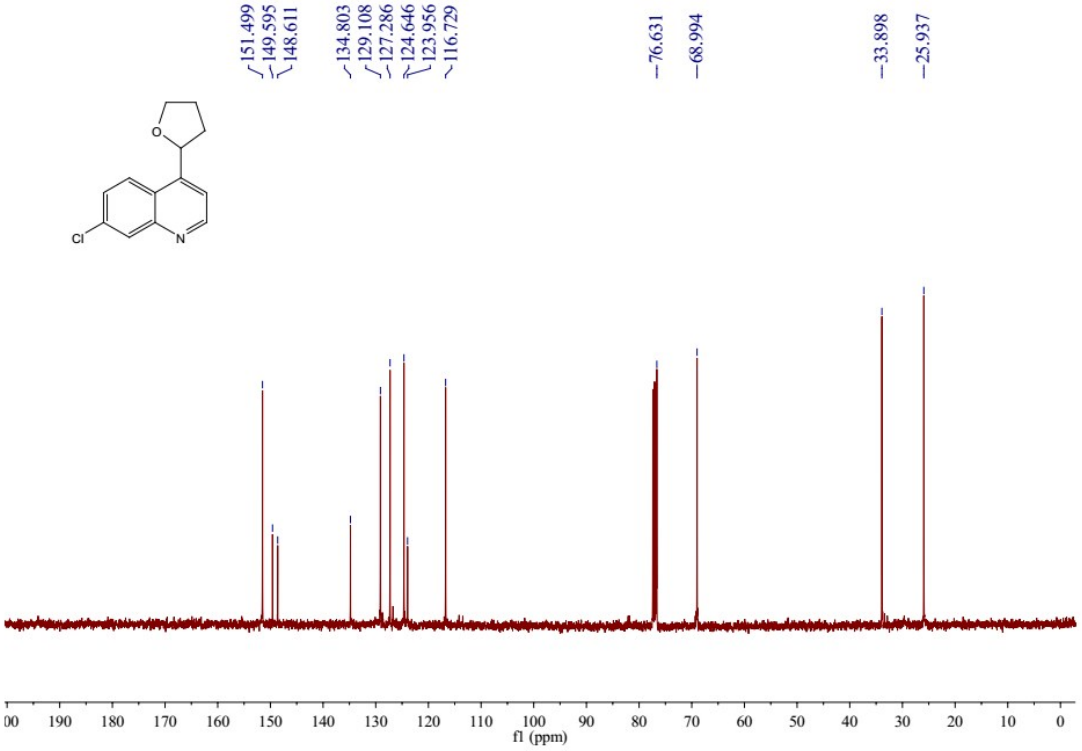
(3mg') 4-(tetrahydrofuran-2-yl)quinoline



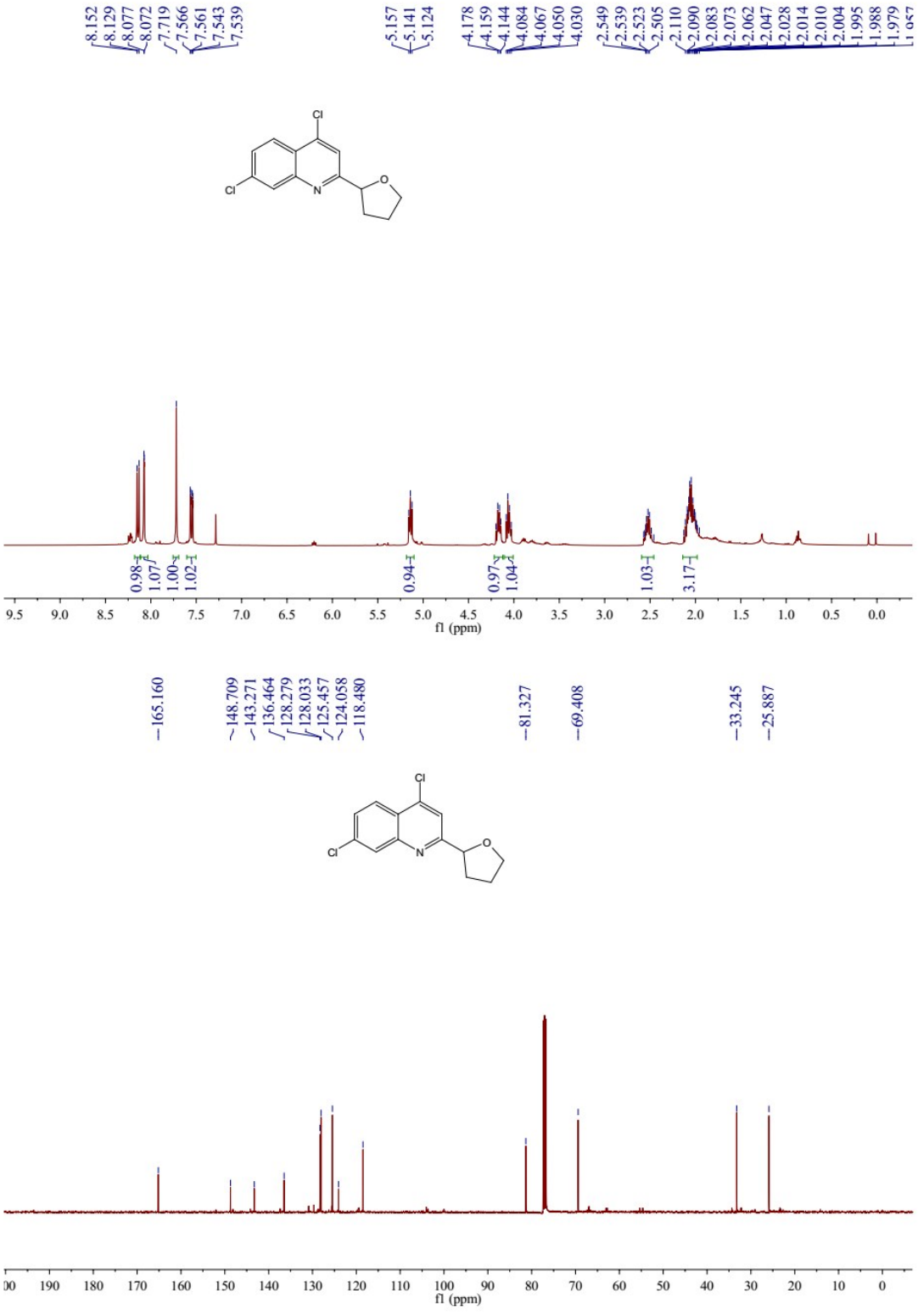


(3ag) 7-chloro-4-(tetrahydrofuran-2-yl)quinolone

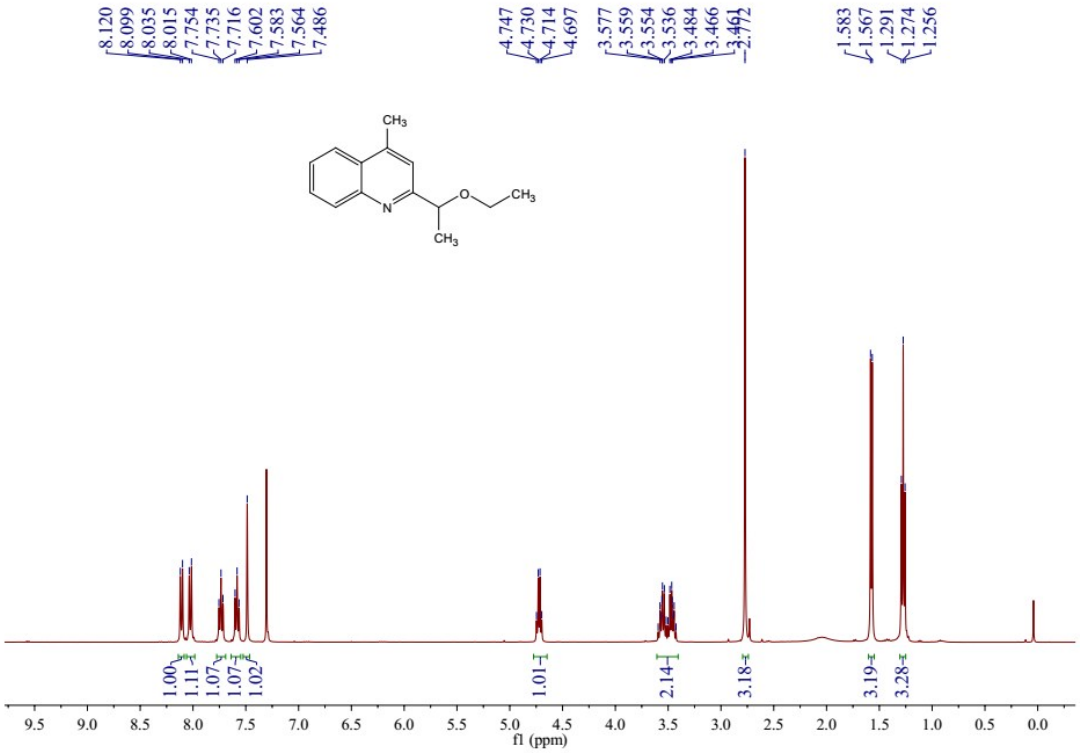


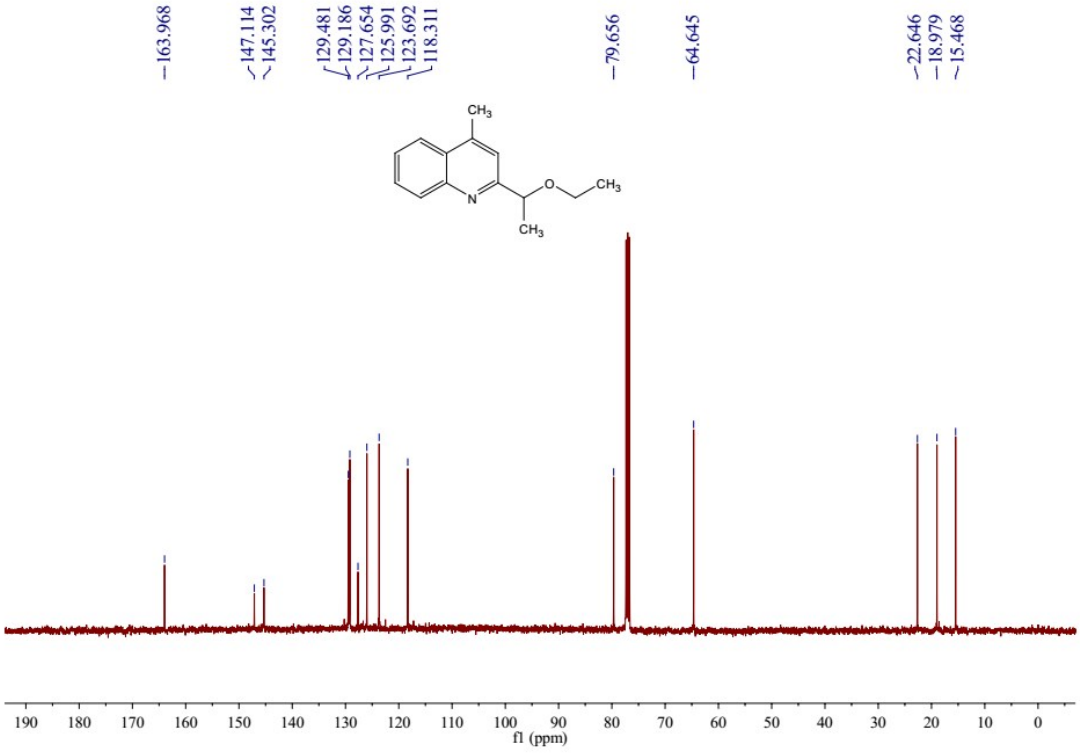


(3ag') 4,7-dichloro-2-(tetrahydrofuran-2-yl)quinoline

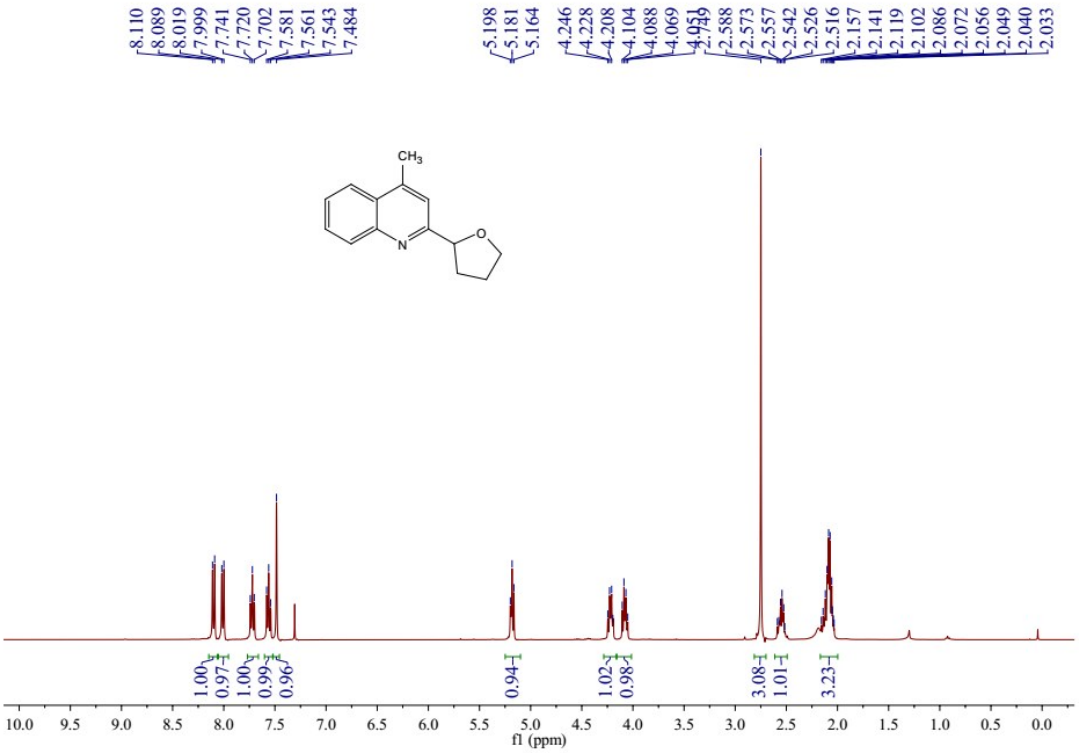


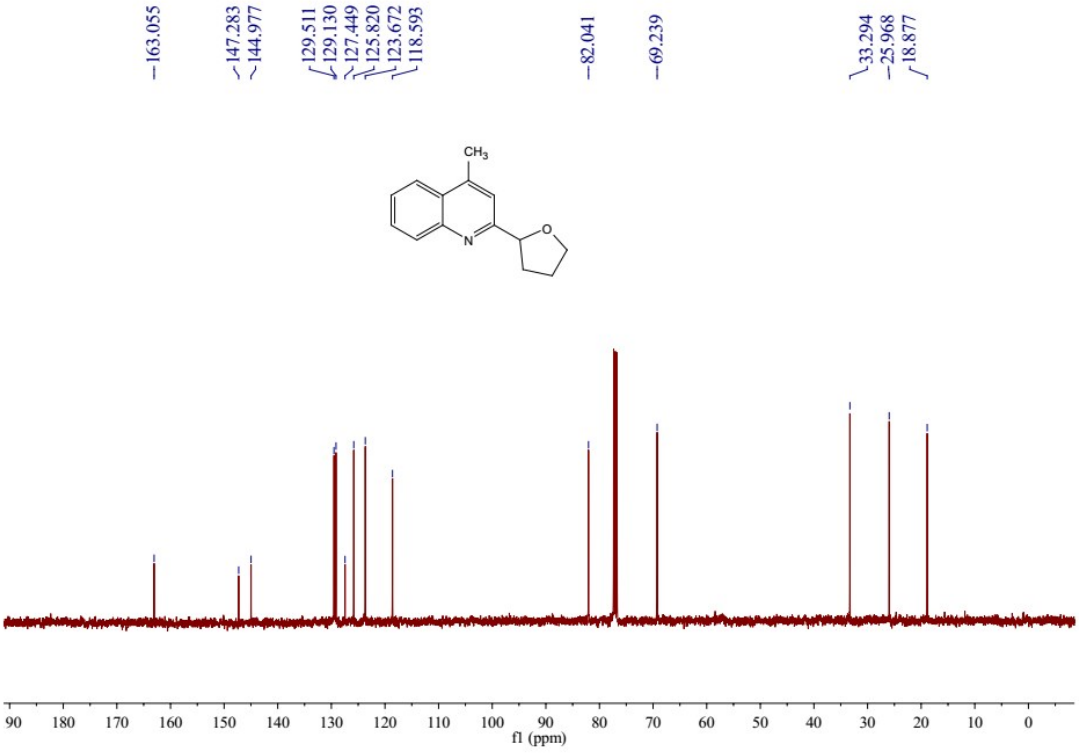
(3nj) 2-(1-ethoxyethyl)-4-methylquinoline



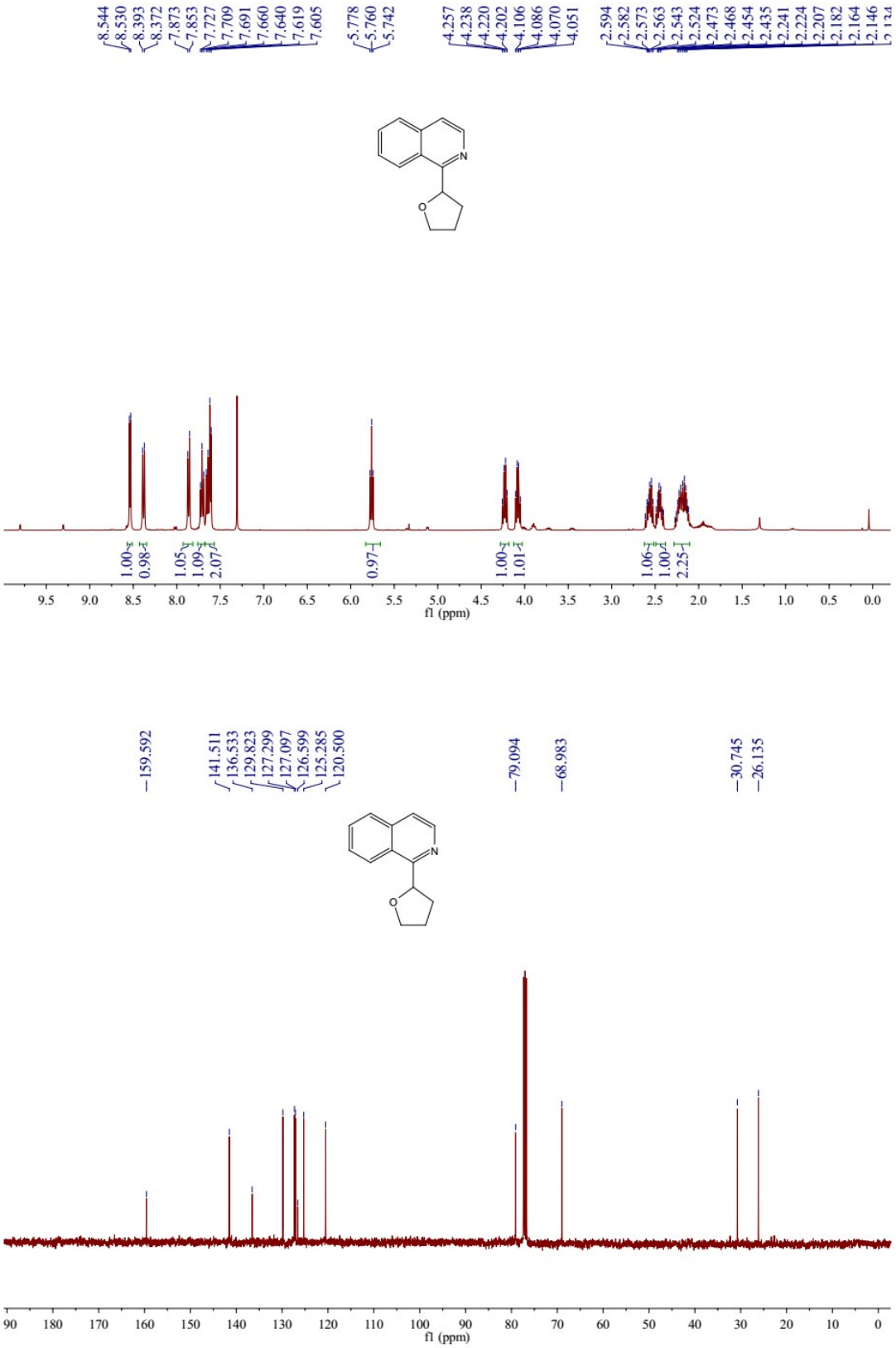


(3ng) 4-methyl-2-(tetrahydrofuran-2-yl)quinoline

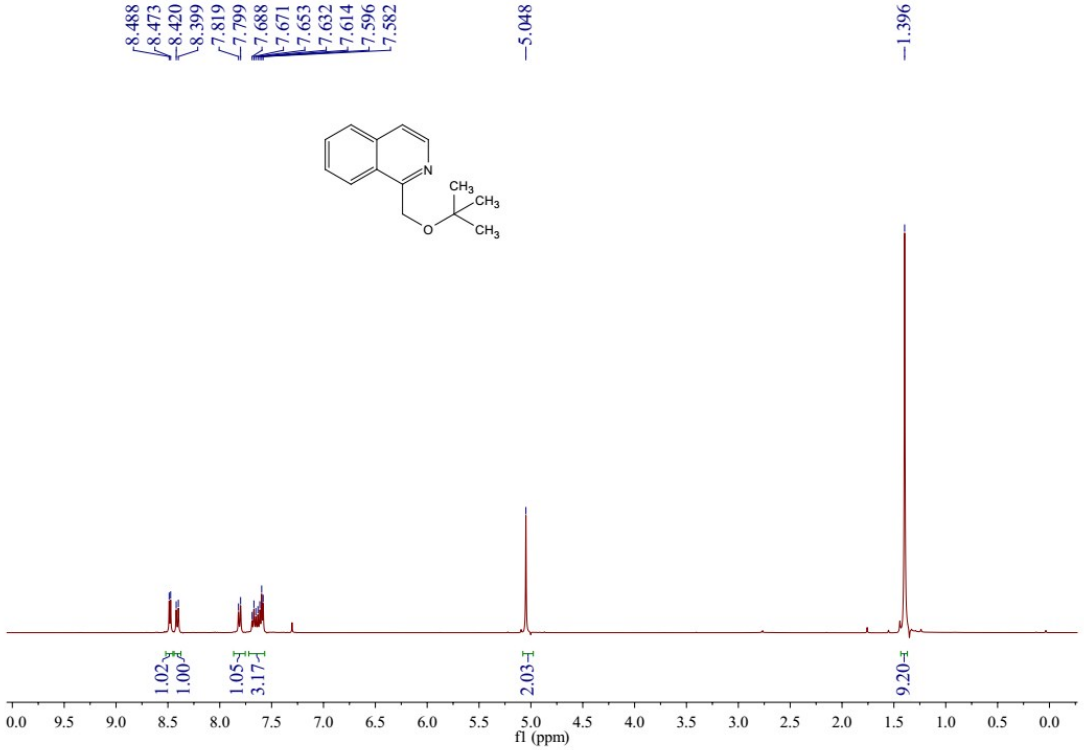


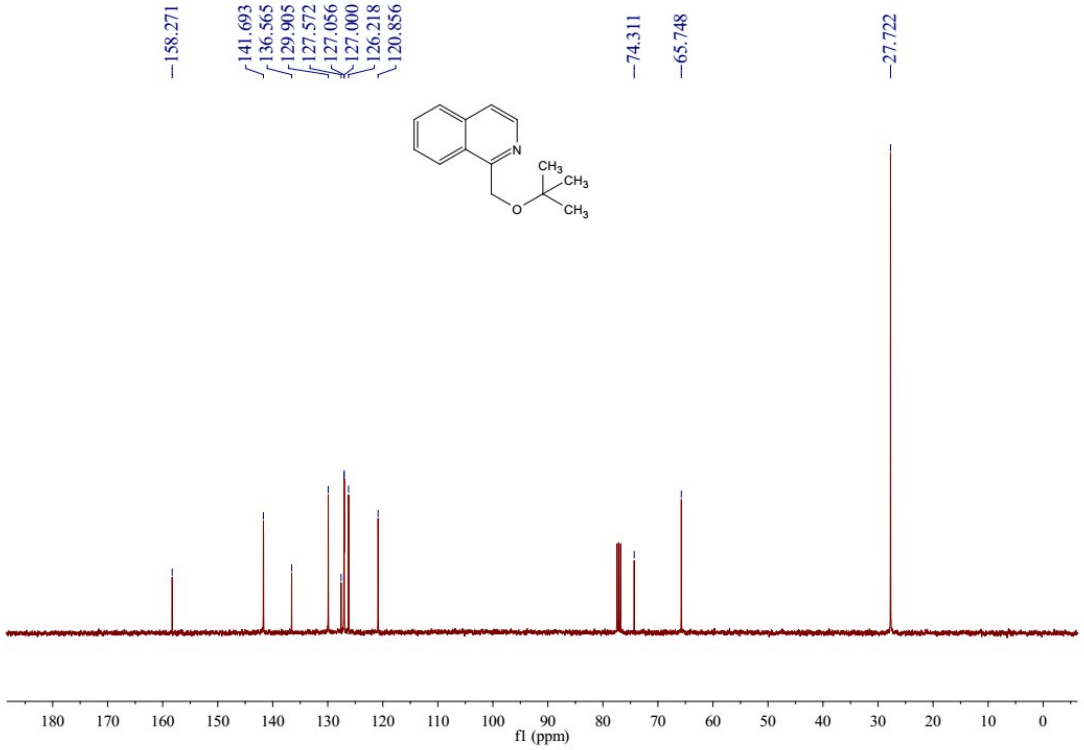


(3cg) 1-(tetrahydrofuran-2-yl)isoquinoline

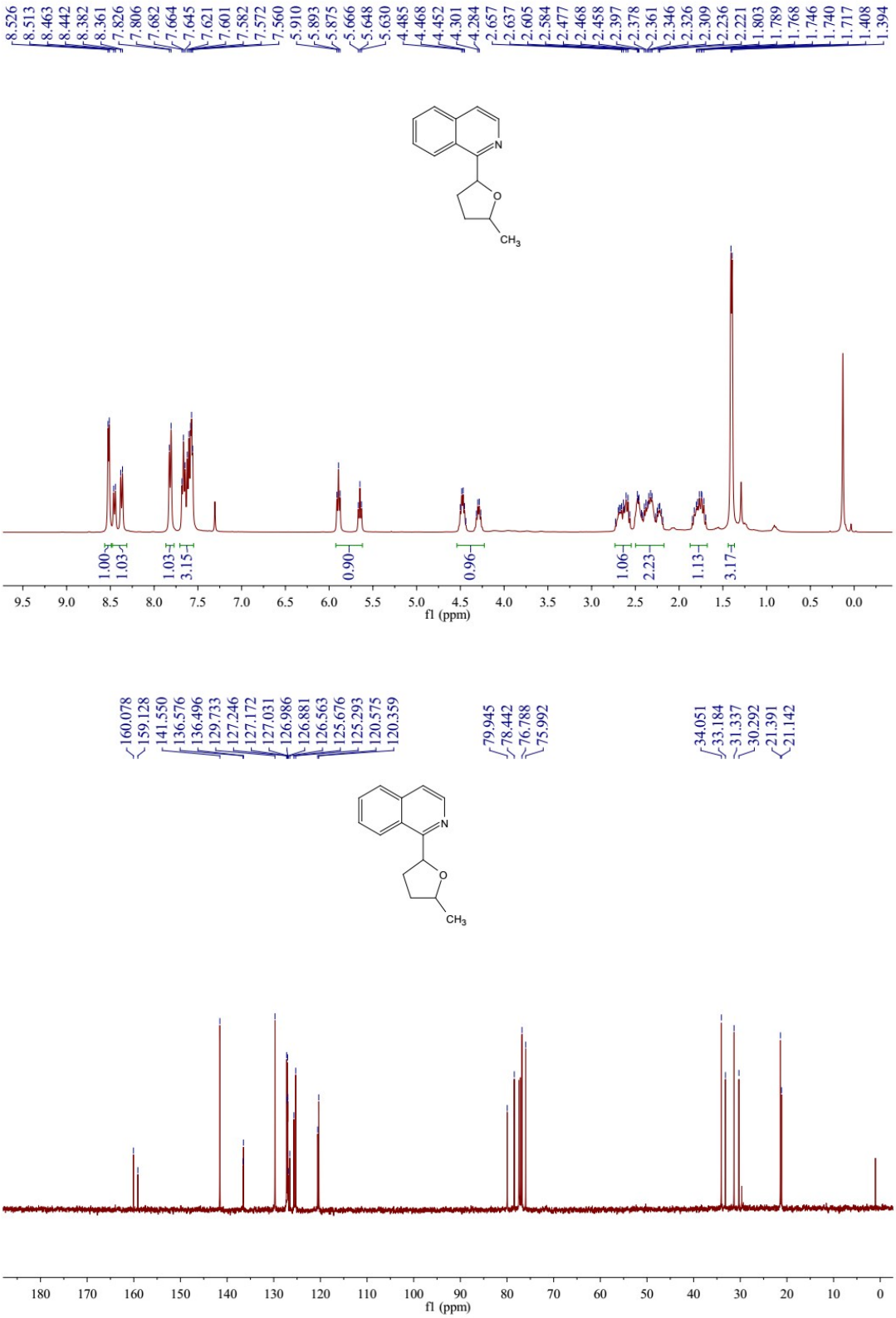


(3cn) 1-(*tert*-butoxymethyl)isoquinoline

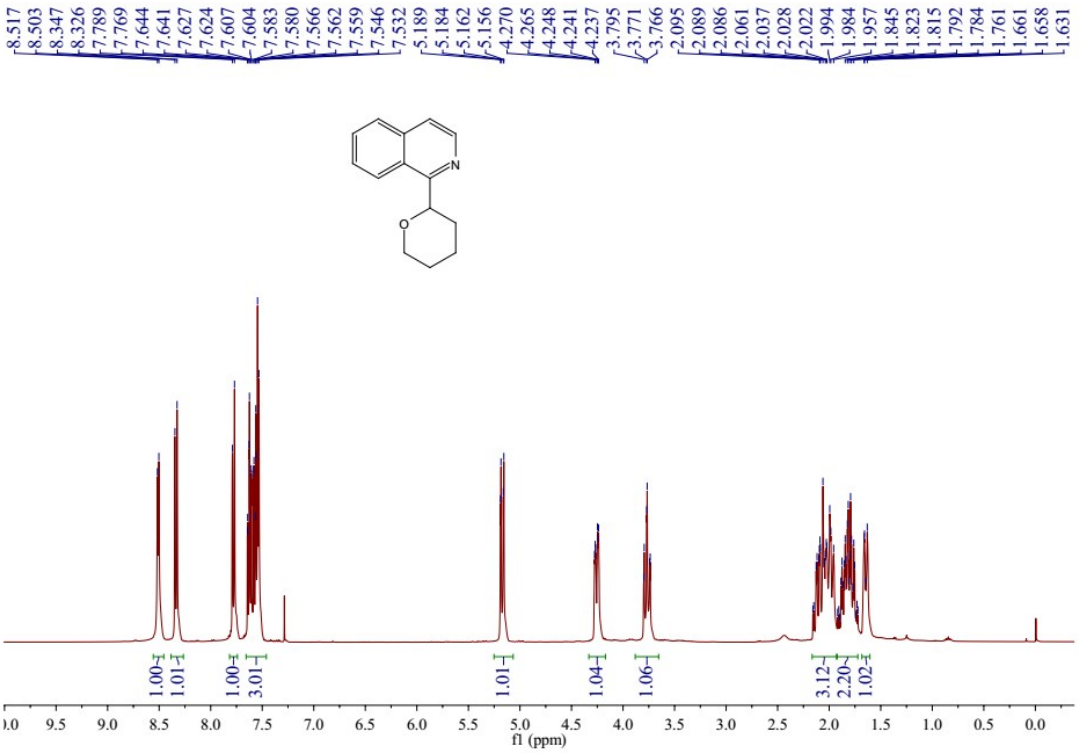


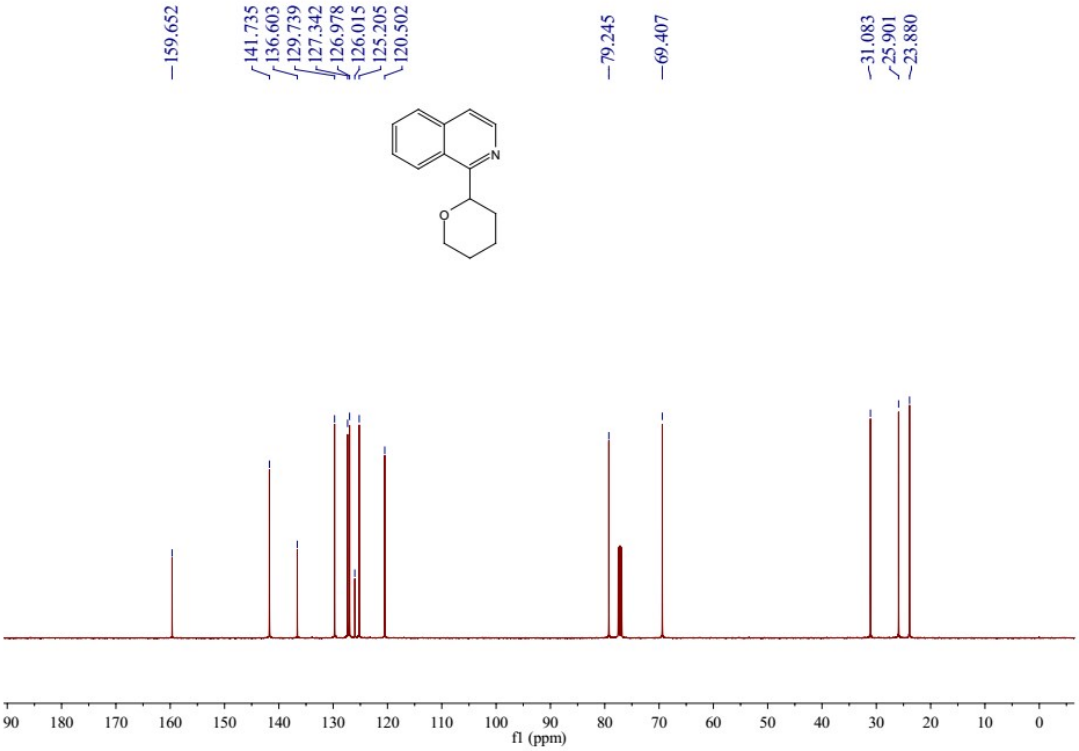


(3co) 1-(5-methyltetrahydrofuran-2-yl)isoquinoline

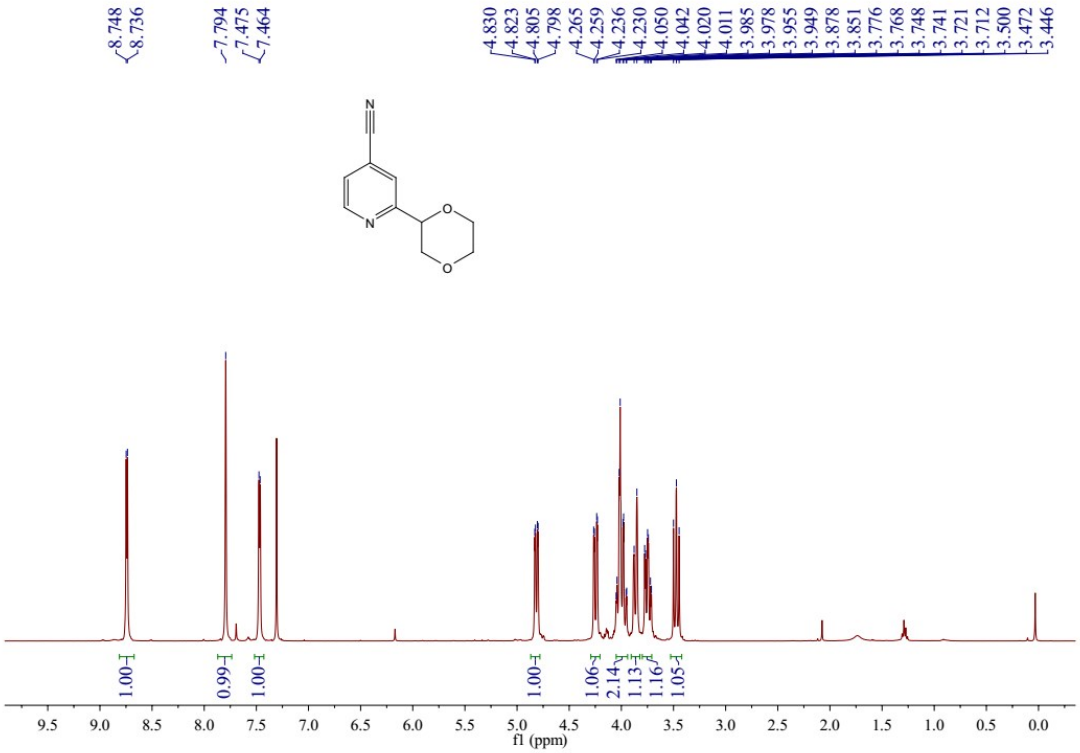


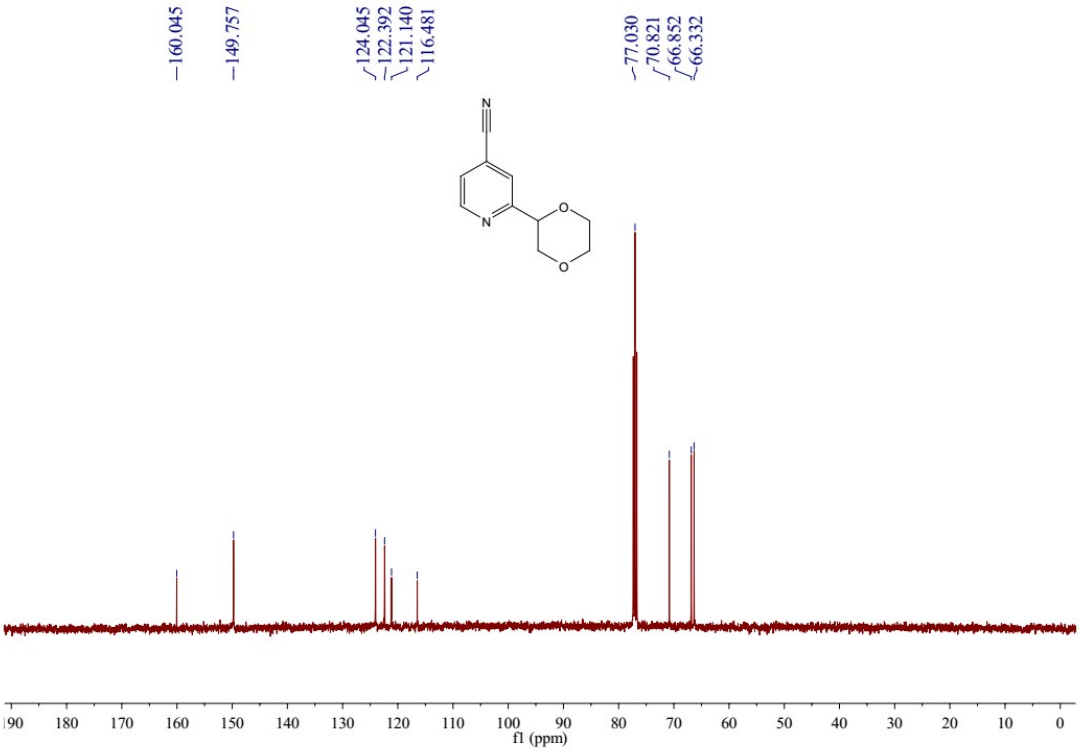
(3ui) 1-(tetrahydro-*2H*-pyran-2-yl)isoquinoline



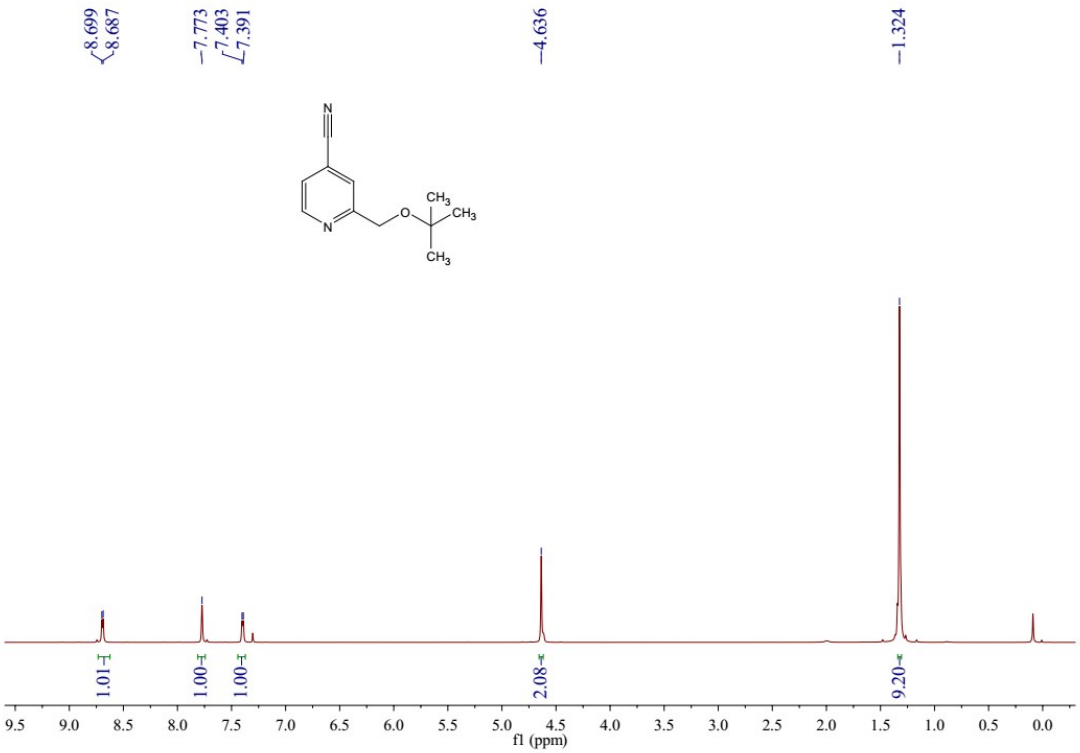


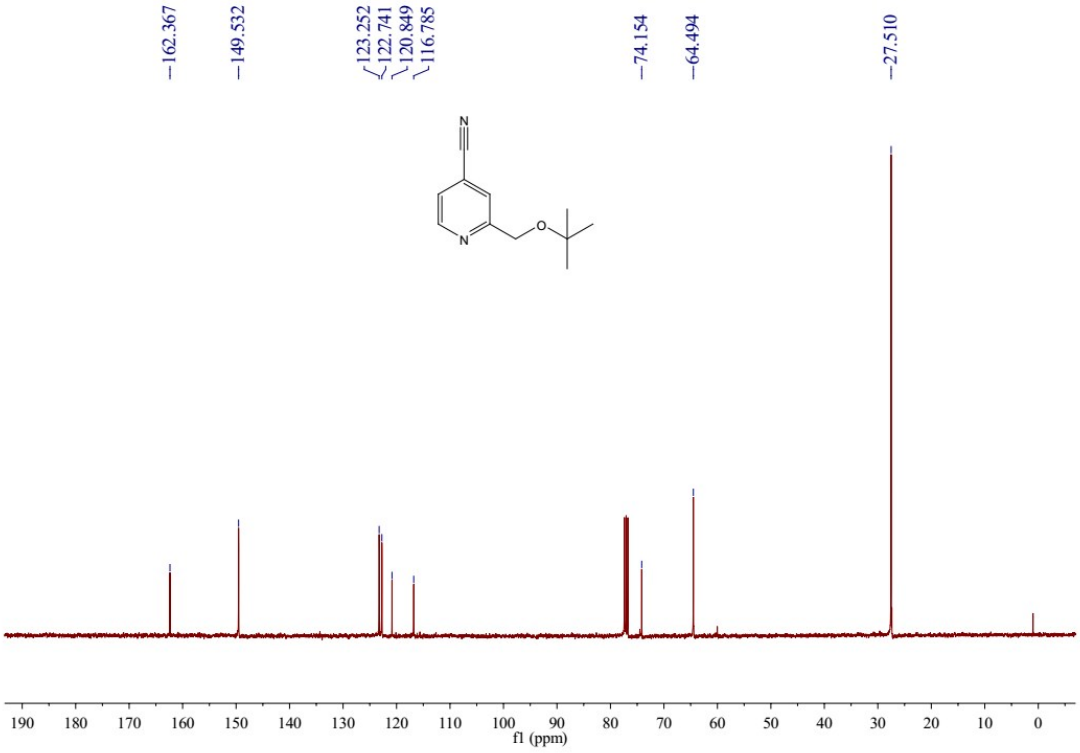
(3hh) 2-(1,4-dioxan-2-yl)isonicotinonitrile



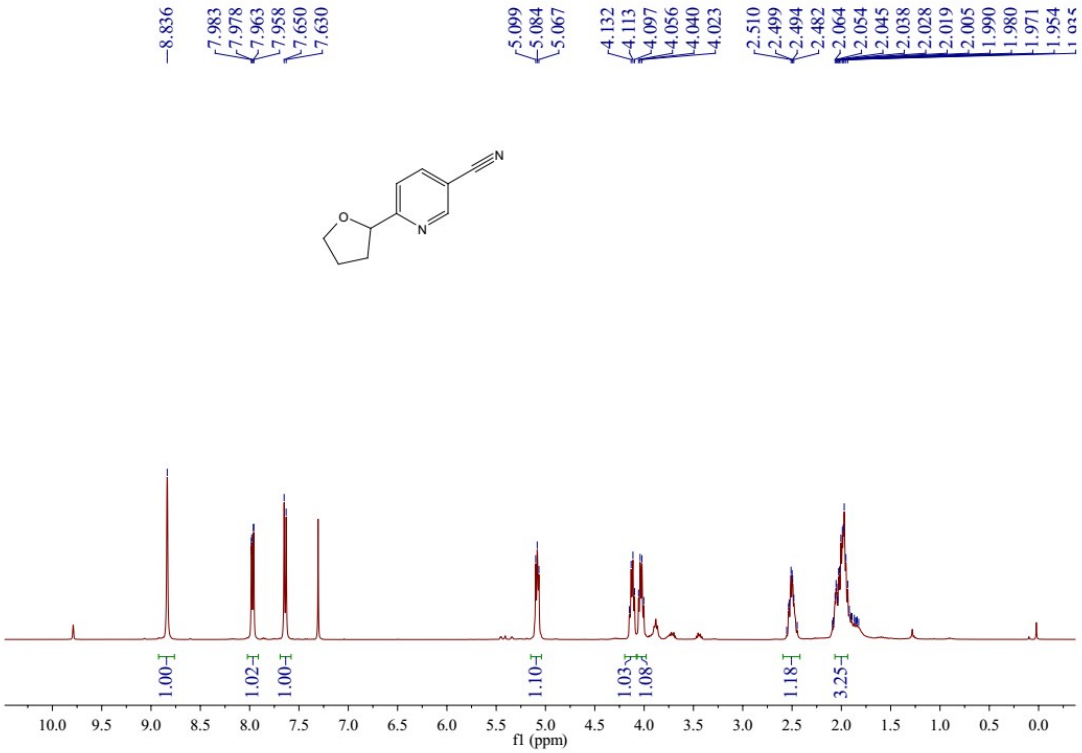


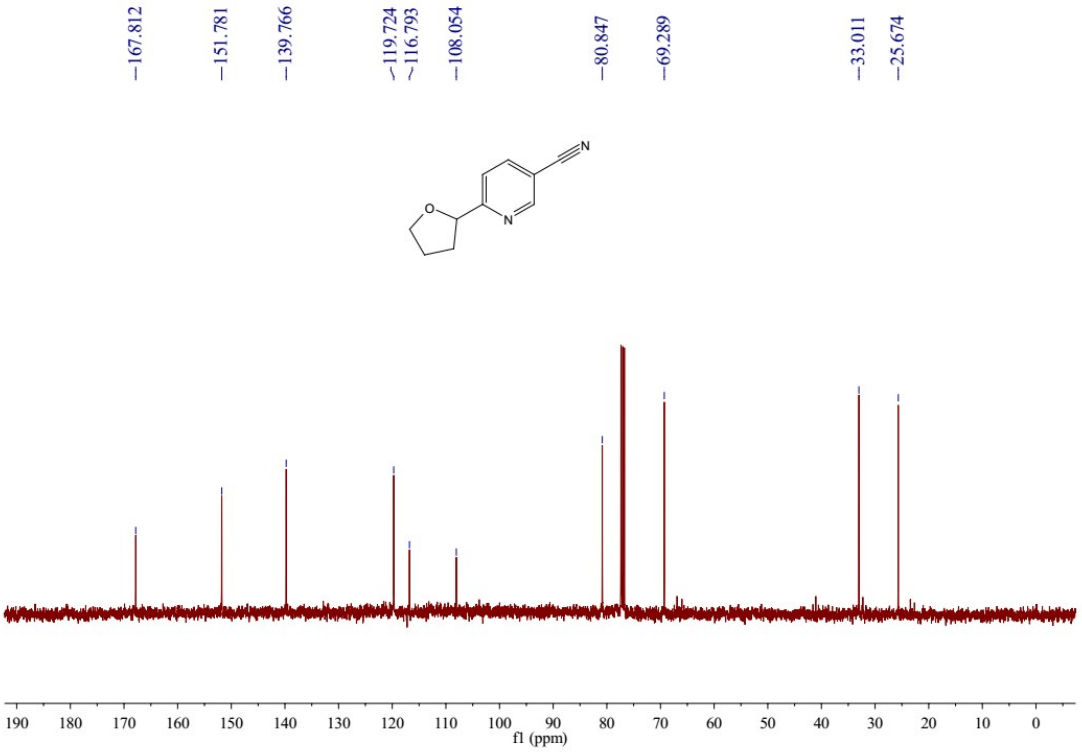
(3hn) 2-(*tert*-butoxymethyl)isonicotinonitrile



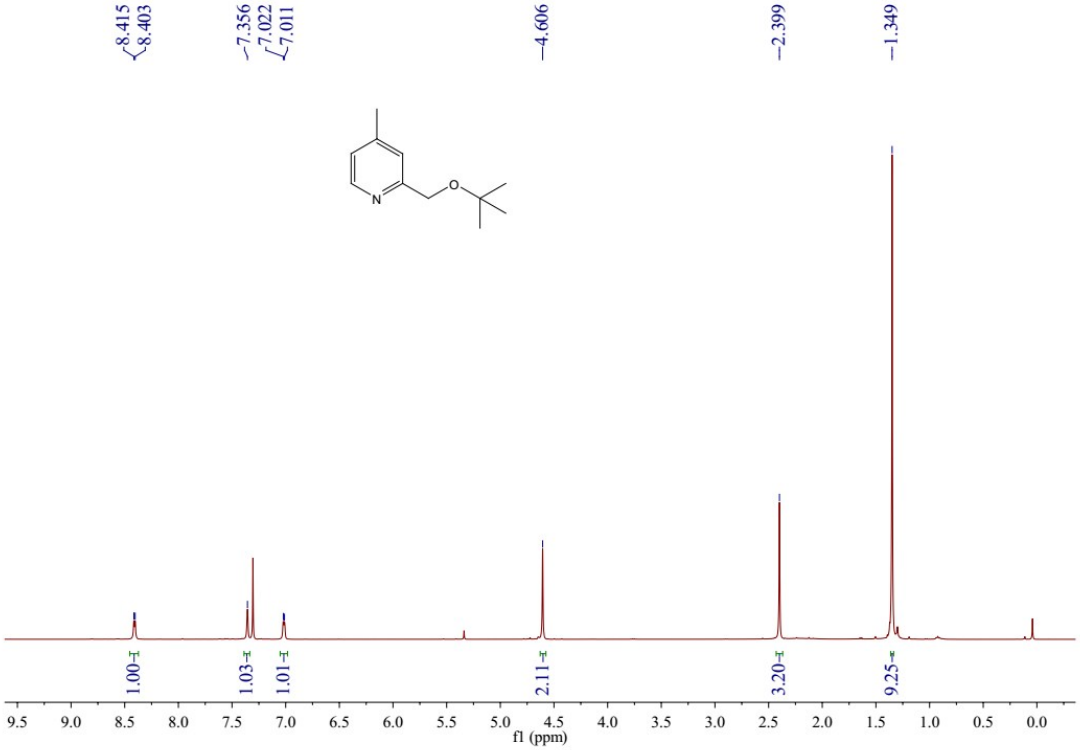


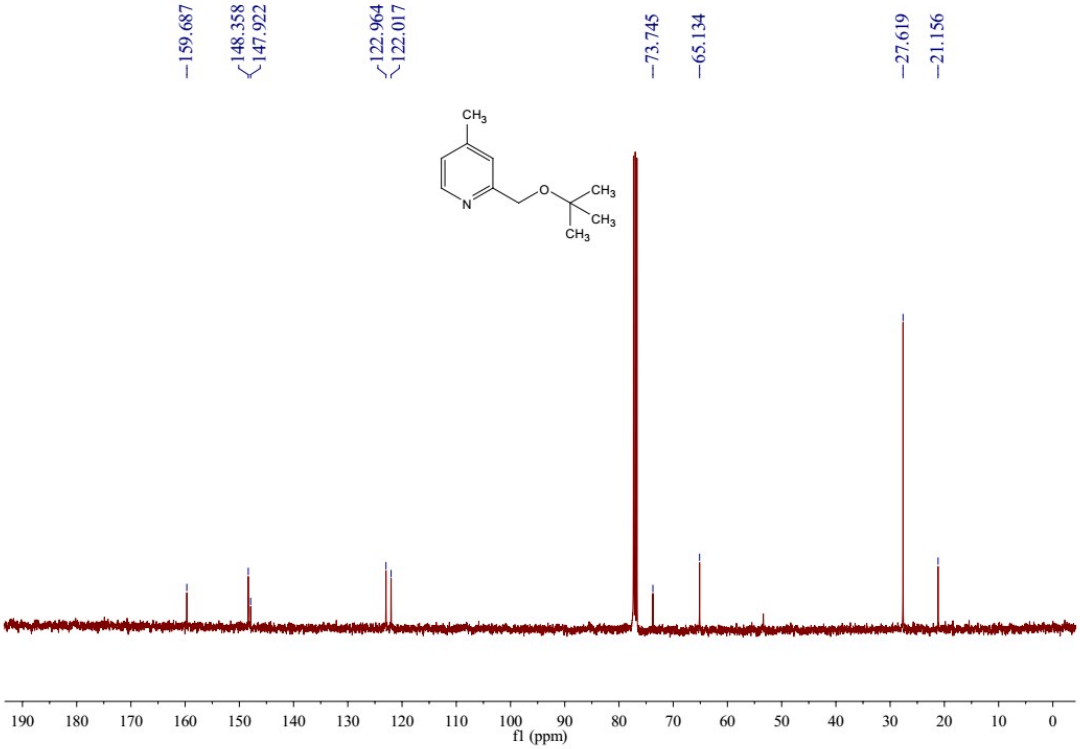
(3wg) 6-(tetrahydrofuran-2-yl)nicotinonitrile



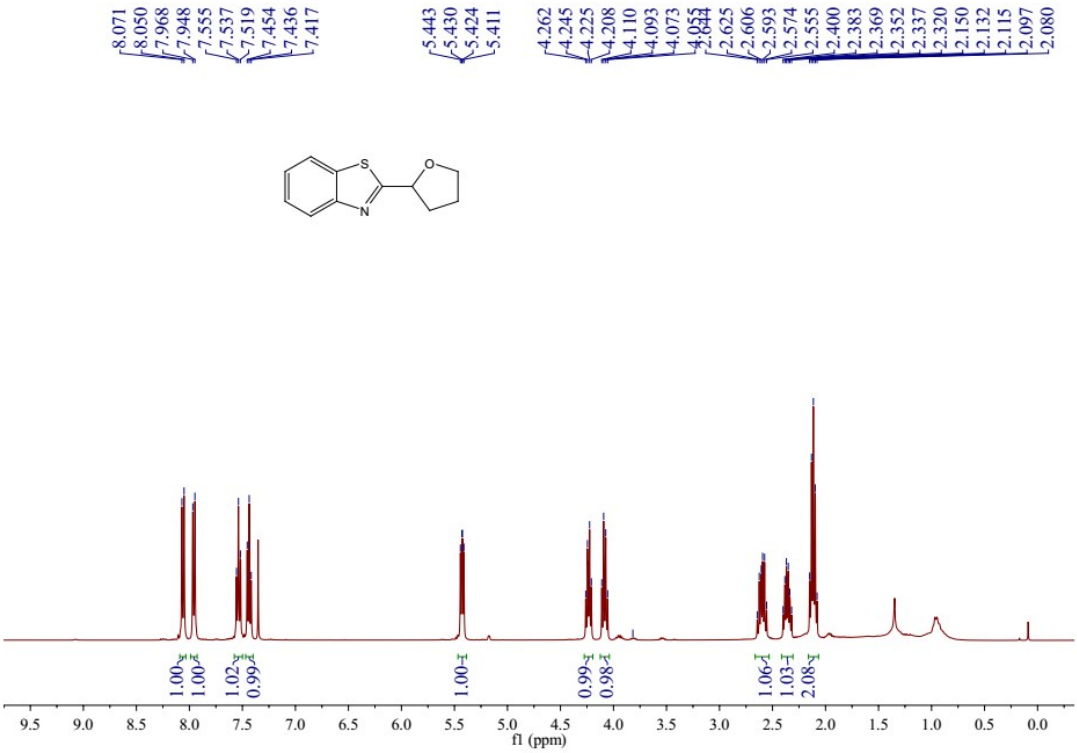


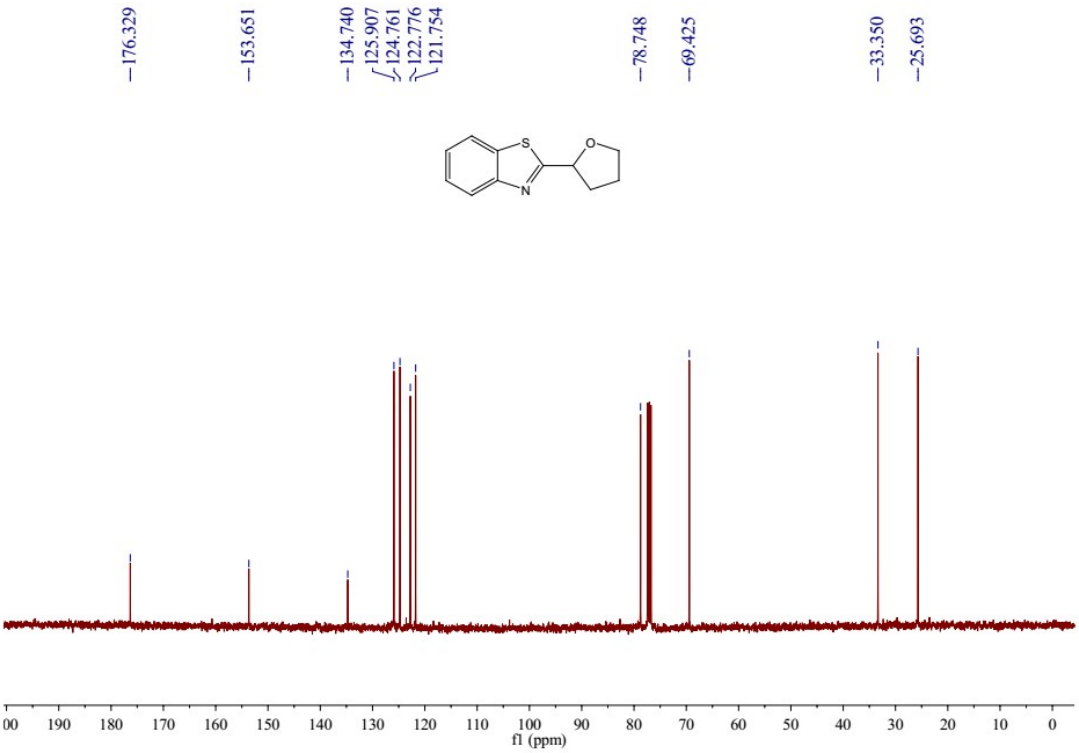
(3xn) 2-(*tert*-butoxymethyl)-4-methylpyridine



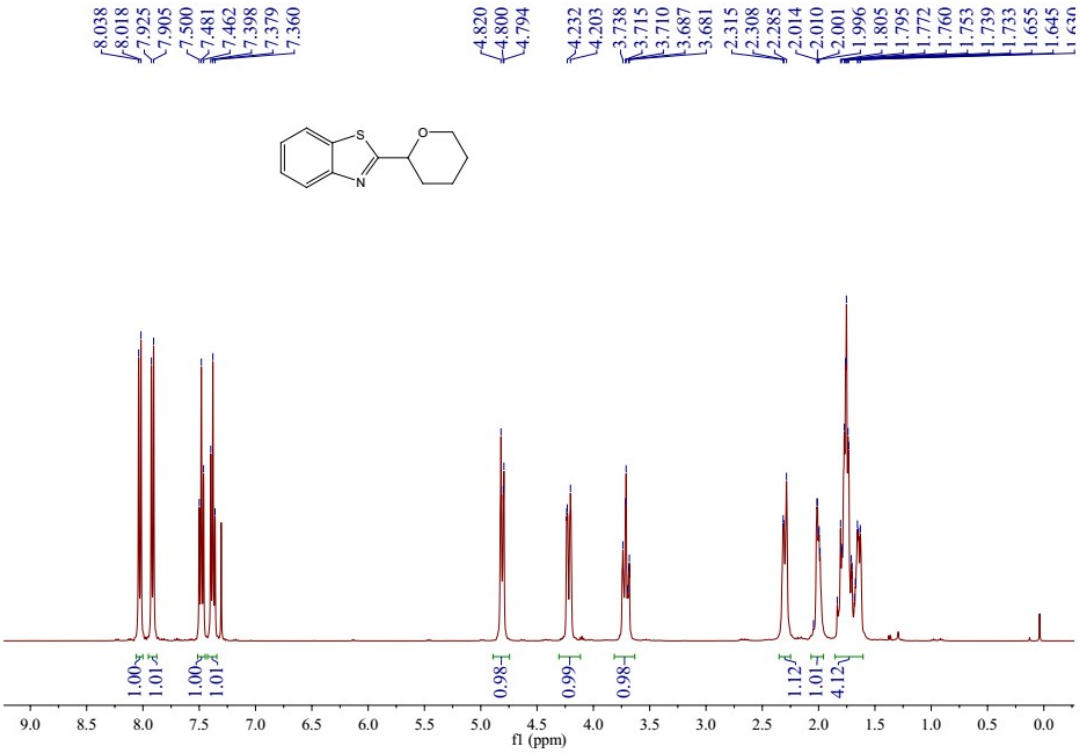


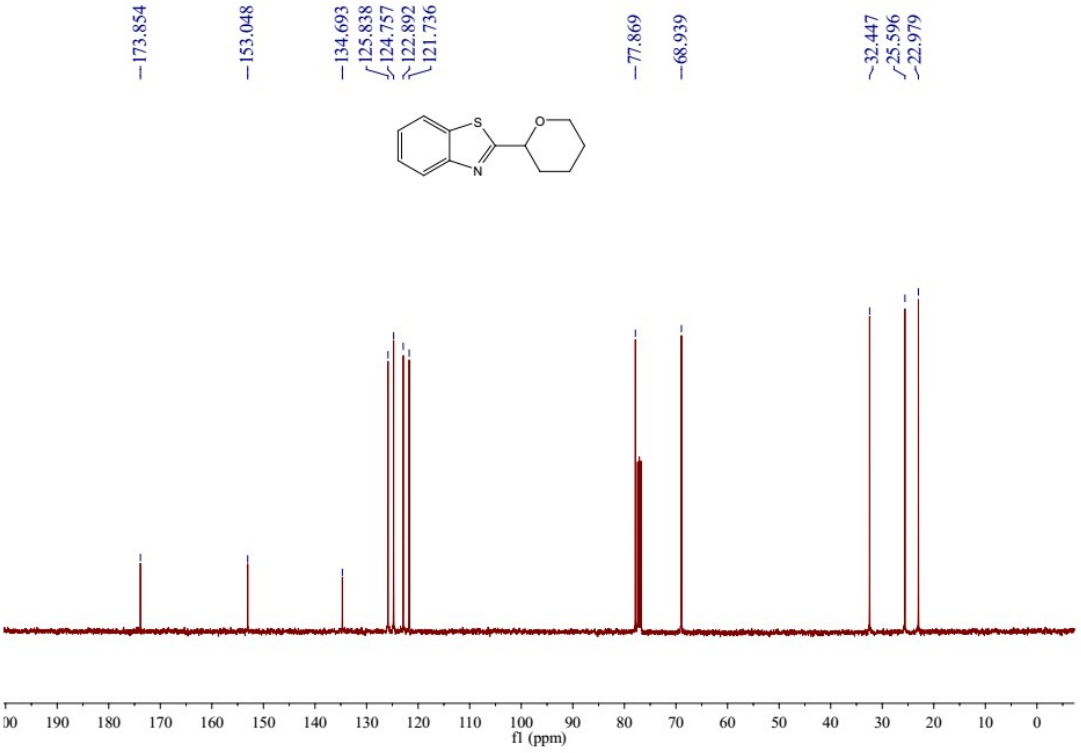
(3jg) 2-(tetrahydrofuran-2-yl)benzo[*d*]thiazole





(3pi) 2-(tetrahydro-*2H*-pyran-2-yl)benzo[*d*]thiazole





(3rg) 2-(tetrahydrofuran-2-yl)benzo[*d*]oxazole