Synthesis of quinazoin-4-ones through acid ion exchange resin mediated cascade reaction

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Supporting Information

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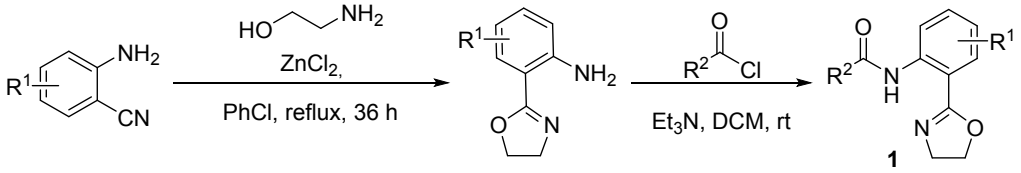
1. Procedures to synthesize starting materials 1

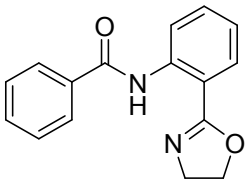


2-aminobenzonitrile(19.00 g, 250 mmol) and $ZnCl_2$(3.34 g, 25mmol) was added to a 500 mL three-necked flask, and then suspended in chlorobenzene (350 mL) under nitrogen. 2-aminoethanol (45 mL, 750 mmol) was added to the suspension via a syringe. The mixture was slowly heated to reflux until no gas was produced. After refluxing for 36 hours, the reaction mixture was cooled down to room temperature and the solvent was removed in a rotary evaporator. CH_2Cl_2 (250 mL) was added to the residue and washed with saturated $NaHCO_3$ (150 mL) and H_2O (150 mL). The aqueous fraction was extracted with CH_2Cl_2 (250 mL × 3). The combined organic phase was dried over Na_2SO_4, filtered and the solvent was removed in a rotary evaporator. The crude product was recrystallized from EA/PE to give the substituted 2-(4,5-dihydrooxazol-2-yl)anilines.

Substituted 2-(4,5-dihydrooxazol-2-yl)anilines (5 mmol) and acid chloride (5.5 mmol) were added to a 100 mL flask and then dissolved with DCM (20 mL). Et_3N (7.5 mmol) was taken to the vigorously stirred solution via a syringe. The reaction was stirred at room temperature for 10 h and quenched with saturated $NaHCO_3$. And then the mixture was extracted with EtOAc. Combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude product was further recrystallized from EA/PE to give the starting materials **1**.

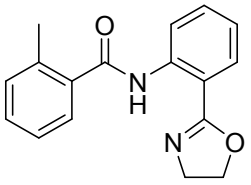
2. Characterization of starting materials 1

_N_-(2-(4,5-dihydrooxazol-2-yl)phenyl)benzamide (1a)



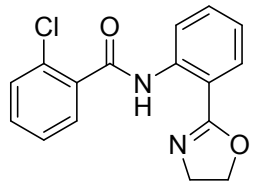
^{1}H NMR (500 MHz, $CDCl_3$) δ 13.02 (s, 1H), 8.97 (d, *J* = 8.5 Hz, 1H), 8.11 – 8.06 (m, 2H), 7.89 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.57 – 7.46 (m, 4H), 7.10 (td, *J* = 7.9, 1.1 Hz, 1H), 4.40 (t, *J* = 9.3 Hz, 2H), 4.18 (t, *J* = 9.6 Hz, 2H).

_N_-(2-(4,5-dihydrooxazol-2-yl)phenyl)-2-methylbenzamide (1b)



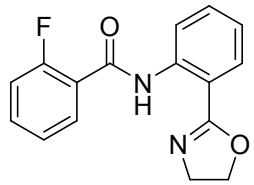
^{1}H NMR (500 MHz, $CDCl_3$) δ 12.58 (s, 1H), 8.95 (d, *J* = 8.5 Hz, 1H), 7.89 (d, *J* = 7.9 Hz, 1H), 7.63 (d, *J* = 7.8 Hz, 1H), 7.52 (t, *J* = 7.9 Hz, 1H), 7.36 (t, *J* = 7.5 Hz, 1H), 7.29 – 7.26 (m, 2H), 7.12 (t, *J* = 7.6 Hz, 1H), 4.36 (t, *J* = 9.5 Hz, 2H), 4.05 (t, *J* = 9.5 Hz, 2H), 2.57 (s, 3H).

2-Chloro-N-(2-(4,5-dihydrooxazol-2-yl)phenyl)benzamide (1c)



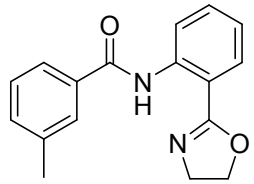
^{1}H NMR (500 MHz, $CDCl_3$) δ 12.70 (s, 1H), 8.93 (d, *J* = 8.4 Hz, 1H), 7.89 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.65 (dd, *J* = 7.4, 1.8 Hz, 1H), 7.55 – 7.50 (m, 1H), 7.46 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.41 – 7.33 (m, 2H), 7.14 (t, *J* = 7.6 Hz, 1H), 4.35 (dd, *J* = 12.8, 6.4 Hz, 2H), 4.03 (t, *J* = 9.5 Hz, 2H).

***N*-(2-(4,5-dihydrooxazol-2-yl)phenyl)-2-fluorobenzamide (1d)**



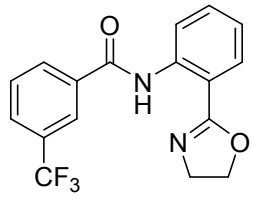
^{1}H NMR (500 MHz, $CDCl_3$) δ 12.81 (s, 1H), 8.91 (d, *J* = 8.4 Hz, 1H), 7.93 (td, *J* = 7.6, 1.6 Hz, 1H), 7.86 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.52 – 7.43 (m, 2H), 7.24 (t, *J* = 7.5 Hz, 1H), 4.33 (t, *J* = 9.5 Hz, 2H), 4.07 (t, *J* = 9.5 Hz, 2H).

***N*-(2-(4,5-dihydrooxazol-2-yl)phenyl)-3-methylbenzamide (1e)**



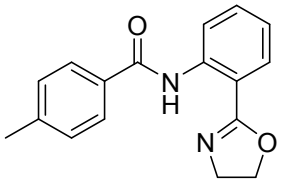
^{1}H NMR (500 MHz, $CDCl_3$) δ 12.98 (s, 1H), 8.96 (d, *J* = 8.5 Hz, 1H), 7.93 (s, 1H), 7.91 – 7.84 (m, 2H), 7.55 – 7.47 (m, 1H), 7.41 – 7.32 (m, 2H), 7.14 – 7.07 (m, 1H), 4.41 (t, *J* = 9.5 Hz, 2H), 4.20 (t, *J* = 9.4 Hz, 2H), 2.44 (s, 3H).

***N*-(2-(4,5-dihydrooxazol-2-yl)phenyl)-3-(trifluoromethyl)benzamide (1f)**



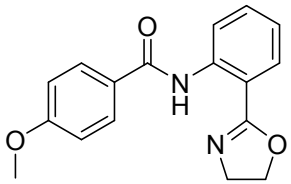
^{1}H NMR (500 MHz, $CDCl_3$) δ 13.30 (s, 1H), 8.45 (s, 1H), 8.31 (d, *J* = 7.8 Hz, 1H), 7.92 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.80 (d, *J* = 7.7 Hz, 1H), 7.65 (t, *J* = 7.8 Hz, 1H), 7.57 – 7.52 (m, 1H), 7.15 (t, *J* = 7.6 Hz, 1H), 4.45 (t, *J* = 9.4 Hz, 2H), 4.23 (t, *J* = 9.6 Hz, 2H).

_N_-(2-(4,5-dihydrooxazol-2-yl)phenyl)-4-methylbenzamide (1g)



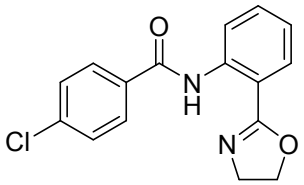
^{1}H NMR (500 MHz, $CDCl_3$) δ 12.96 (s, 1H), 8.96 (d, *J* = 8.5 Hz, 1H), 7.99 (d, *J* = 8.2 Hz, 2H), 7.89 (d, *J* = 7.1 Hz, 1H), 7.56 – 7.48 (m, 1H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.10 (t, *J* = 7.6 Hz, 1H), 4.40 (t, *J* = 9.3 Hz, 2H), 4.19 (t, *J* = 9.5 Hz, 2H), 2.42 (s, 3H).

_N_-(2-(4,5-dihydrooxazol-2-yl)phenyl)-4-methoxybenzamide (1h)



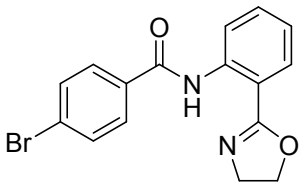
^{1}H NMR (500 MHz, $CDCl_3$) δ 12.90 (s, 1H), 8.95 (d, *J* = 8.5 Hz, 1H), 8.06 (d, *J* = 8.8 Hz, 2H), 7.93 – 7.84 (m, 1H), 7.54 – 7.45 (m, 1H), 7.09 (t, *J* = 7.6 Hz, 1H), 6.98 (d, *J* = 8.8 Hz, 2H), 4.40 (t, *J* = 9.5 Hz, 2H), 4.20 (t, *J* = 9.5 Hz, 2H), 3.87 (s, 3H).

4-Chloro-_N_-(2-(4,5-dihydrooxazol-2-yl)phenyl)benzamide (1i)



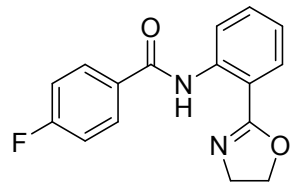
^{1}H NMR (500 MHz, $CDCl_3$) δ 13.03 (s, 1H), 8.92 (d, *J* = 8.4 Hz, 1H), 8.07 – 8.00 (m, 2H), 7.90 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.55 – 7.50 (m, 1H), 7.48 – 7.42 (m, 2H), 7.15 – 7.09 (m, 1H), 4.43 (dd, *J* = 14.4, 4.9 Hz, 2H), 4.19 (t, *J* = 9.6 Hz, 2H).

4-Bromo-N-(2-(4,5-dihydrooxazol-2-yl)phenyl)benzamide (1j)



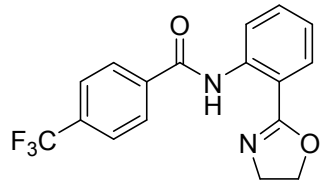
^{1}H NMR (500 MHz, $CDCl_3$) δ 13.03 (s, 1H), 8.92 (d, *J* = 8.4 Hz, 1H), 7.95 (d, *J* = 8.4 Hz, 2H), 7.89 (d, *J* = 7.7 Hz, 1H), 7.63 (d, *J* = 8.4 Hz, 2H), 7.52 (t, *J* = 7.5 Hz, 1H), 7.12 (t, *J* = 7.6 Hz, 1H), 4.42 (t, *J* = 9.5 Hz, 2H), 4.18 (t, *J* = 9.5 Hz, 2H).

***N*-(2-(4,5-dihydrooxazol-2-yl)phenyl)-4-fluorobenzamide (1k)**



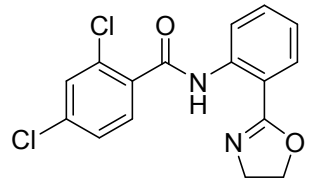
^{1}H NMR (500 MHz, $CDCl_3$) δ 13.01 (s, 1H), 10.70 – 10.68 (m, 1H), 8.93 (d, *J* = 8.4 Hz, 1H), 8.15 – 8.05 (m, 2H), 7.90 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.55 – 7.46 (m, 1H), 7.16 (t, *J* = 8.6 Hz, 2H), 7.11 (t, *J* = 7.3 Hz, 1H), 4.41 (t, *J* = 9.5 Hz, 2H), 4.19 (t, *J* = 9.5 Hz, 2H).

***N*-(2-(4,5-dihydrooxazol-2-yl)phenyl)-4-(trifluoromethyl)benzamide (1l)**



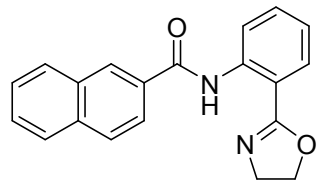
^{1}H NMR (500 MHz, $CDCl_3$) δ 13.15 (s, 1H), 8.93 (d, *J* = 8.4 Hz, 1H), 8.17 (d, *J* = 8.0 Hz, 2H), 7.86 (d, *J* = 7.8 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 2H), 7.50 (t, *J* = 7.8 Hz, 1H), 7.11 (t, *J* = 7.6 Hz, 1H), 4.38 (t, *J* = 9.4 Hz, 2H), 4.15 (t, *J* = 9.5 Hz, 2H).

2,4-Dichloro-N-(2-(4,5-dihydrooxazol-2-yl)phenyl)benzamide (1m)



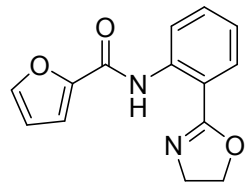
^{1}H NMR (500 MHz, $CDCl_3$) δ 12.75 (s, 1H), 8.88 (d, *J* = 8.4 Hz, 1H), 7.90 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.60 (d, *J* = 8.3 Hz, 1H), 7.55 – 7.51 (m, 1H), 7.49 (d, *J* = 2.0 Hz, 1H), 7.35 (dd, *J* = 8.3, 2.0 Hz, 1H), 7.15 (td, *J* = 7.9, 1.1 Hz, 1H), 4.38 (t, *J* = 9.6 Hz, 2H), 4.05 (t, *J* = 9.5 Hz, 2H).

***N*-(2-(4,5-dihydrooxazol-2-yl)phenyl)-2-naphthamide (1n)**



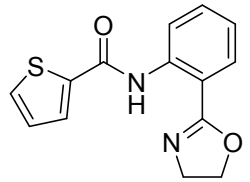
^{1}H NMR (500 MHz, $CDCl_3$) δ 13.17 (s, 1H), 9.00 (d, *J* = 8.4 Hz, 1H), 8.64 (s, 1H), 8.16 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.98 – 7.88 (m, 4H), 7.60 – 7.53 (m, 3H), 7.13 (td, *J* = 7.9, 1.1 Hz, 1H), 4.49 – 4.40 (m, 2H), 4.24 (dd, *J* = 14.3, 5.1 Hz, 2H).

***N*-(2-(4,5-dihydrooxazol-2-yl)phenyl)furan-2-carboxamide (1o)**



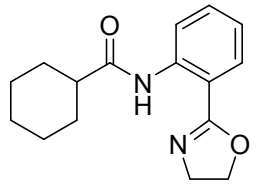
^{1}H NMR (500 MHz, $CDCl_3$) δ 13.05 (s, 1H), 8.85 (dd, *J* = 8.3, 3.8 Hz, 1H), 7.80 (ddd, *J* = 19.5, 16.8, 5.8 Hz, 2H), 7.58 – 7.40 (m, 2H), 7.15 – 6.95 (m, 2H), 4.37 (dd, *J* = 20.4, 10.3 Hz, 2H), 4.23 – 4.09 (m, 2H).

***N*-(2-(4,5-dihydrooxazol-2-yl)phenyl)thiophene-2-carboxamide (1p)**



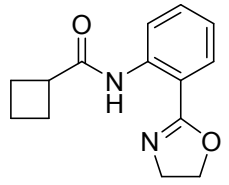
^{1}H NMR (500 MHz, $CDCl_3$) δ 13.08 (s, 1H), 8.86 (d, *J* = 8.5 Hz, 1H), 7.92 – 7.86 (m, 1H), 7.82 – 7.77 (m, 1H), 7.55 (d, *J* = 4.9 Hz, 1H), 7.52 – 7.47 (m, 1H), 7.15 (dd, *J* = 4.8, 3.9 Hz, 1H), 7.10 (t, *J* = 7.6 Hz, 1H), 4.43 (t, *J* = 9.4 Hz, 2H), 4.23 (t, *J* = 9.6 Hz, 2H).

***N*-(2-(4,5-dihydrooxazol-2-yl)phenyl)cyclohexanecarboxamide (1r)**



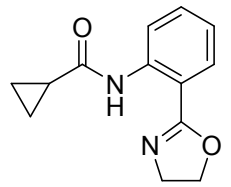
^{1}H NMR (500 MHz, $CDCl_3$) δ 12.11 (s, 1H), 8.78 (dd, *J* = 8.5, 0.8 Hz, 1H), 7.85 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.50 – 7.40 (m, 1H), 7.10 – 7.00 (m, 1H), 4.39 (t, *J* = 9.4 Hz, 2H), 4.17 (t, *J* = 9.6 Hz, 2H), 2.32 (ddd, *J* = 11.7, 7.6, 3.5 Hz, 1H), 2.01 (dd, *J* = 13.7, 1.9 Hz, 2H), 1.82 (d, *J* = 2.5 Hz, 2H), 1.74 – 1.68 (m, 1H), 1.58 (ddd, *J* = 24.7, 12.4, 3.1 Hz, 2H), 1.37 – 1.24 (m, 3H).

***N*-(2-(4,5-dihydrooxazol-2-yl)phenyl)cyclobutanecarboxamide (1s)**



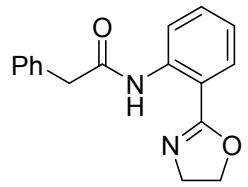
^{1}H NMR (500 MHz, $CDCl_3$) δ 12.10 (s, 1H), 8.78 (d, *J* = 8.5 Hz, 1H), 7.84 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.45 (dd, *J* = 11.5, 4.3 Hz, 1H), 7.10 – 7.00 (m, 1H), 4.38 (t, *J* = 9.4 Hz, 2H), 4.13 (dd, *J* = 20.0, 10.3 Hz, 2H), 3.26 (p, *J* = 8.6 Hz, 1H), 2.43 (dtd, *J* = 18.2, 9.2, 2.3 Hz, 2H), 2.33 – 2.20 (m, 2H), 2.07 – 1.85 (m, 2H).

***N*-(2-(4,5-dihydrooxazol-2-yl)phenyl)cyclopropanecarboxamide (1t)**



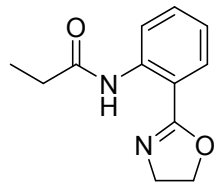
^{1}H NMR (500 MHz, $CDCl_3$) δ 12.41 (s, 1H), 8.73 (dd, *J* = 8.5, 0.7 Hz, 1H), 7.86 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.48 – 7.41 (m, 1H), 7.05 (td, *J* = 8.0, 1.1 Hz, 1H), 4.40 (dd, *J* = 14.4, 5.0 Hz, 2H), 4.17 (t, *J* = 9.6 Hz, 2H), 1.66 (tt, *J* = 7.9, 4.6 Hz, 1H), 1.15 – 1.06 (m, 2H), 0.90 – 0.82 (m, 2H).

***N*-(2-(4,5-dihydrooxazol-2-yl)phenyl)-2-phenylacetamide (1u)**



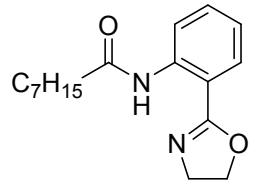
^{1}H NMR (500 MHz, $CDCl_3$) δ 12.11 (s, 1H), 8.76 (d, *J* = 8.5 Hz, 1H), 7.79 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.45 – 7.40 (m, 1H), 7.39 – 7.33 (m, 4H), 7.30 – 7.26 (m, 1H), 7.06 – 7.01 (m, 1H), 4.28 (td, *J* = 9.5, 2.1 Hz, 2H), 3.88 (td, *J* = 9.5, 1.6 Hz, 2H), 3.77 (s, 2H).

***N*-(2-(4,5-dihydrooxazol-2-yl)phenyl)propionamide (1w)**



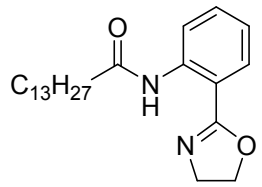
^{1}H NMR (500 MHz, $CDCl_3$) δ 12.15 (s, 1H), 8.76 (d, *J* = 8.4 Hz, 1H), 7.85 (d, *J* = 7.5 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.06 (t, *J* = 7.6 Hz, 1H), 4.38 (t, *J* = 9.5 Hz, 2H), 4.15 (t, *J* = 9.5 Hz, 2H), 2.47 (q, *J* = 7.6 Hz, 2H), 1.27 (t, *J* = 7.6 Hz, 3H).

***N*-(2-(4,5-dihydrooxazol-2-yl)phenyl)octanamide (1x)**



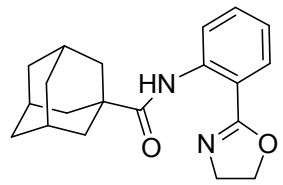
^{1}H NMR (500 MHz, $CDCl_3$) δ 12.15 (s, 1H), 8.76 (d, *J* = 8.4 Hz, 1H), 7.85 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.51 – 7.40 (m, 1H), 7.05 (t, *J* = 7.6 Hz, 1H), 4.37 (t, *J* = 9.5 Hz, 2H), 4.14 (t, *J* = 9.5 Hz, 2H), 2.42 (t, *J* = 7.6 Hz, 2H), 1.80 – 1.70 (m, 2H), 1.39 – 1.26 (m, 8H), 0.88 (t, *J* = 6.7 Hz, 3H).

***N*-(2-(4,5-dihydrooxazol-2-yl)phenyl)tetradecanamide (1y)**



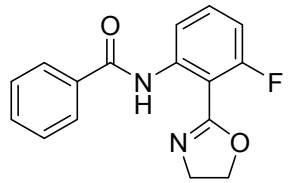
^{1}H NMR (500 MHz, $CDCl_3$) δ 12.15 (s, 1H), 8.76 (d, *J* = 8.3 Hz, 1H), 7.84 (d, *J* = 7.5 Hz, 1H), 7.44 (t, *J* = 7.4 Hz, 1H), 7.05 (t, *J* = 7.2 Hz, 1H), 4.37 (t, *J* = 9.2 Hz, 2H), 4.14 (t, *J* = 9.2 Hz, 2H), 2.42 (t, *J* = 7.3 Hz, 2H), 1.83 – 1.71 (m, 2H), 1.37 (s, 2H), 1.25 (s, 17H), 0.88 (t, *J* = 6.1 Hz, 4H).

(3r,5r,7r)-*N*-(2-(4,5-dihydrooxazol-2-yl)phenyl)adamantane-1-carboxamide (1z)



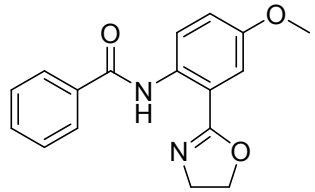
^{1}H NMR (500 MHz, $CDCl_3$) δ 12.12 (s, 1H), 8.81 (dd, *J* = 8.5, 0.7 Hz, 1H), 7.85 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.48 – 7.40 (m, 1H), 7.09 – 7.00 (m, 1H), 4.40 (t, *J* = 9.4 Hz, 2H), 4.18 (t, *J* = 9.5 Hz, 2H), 2.09 (s, 3H), 2.02 (d, *J* = 2.6 Hz, 6H), 1.75 (d, *J* = 13.8 Hz, 6H).

***N*-(2-(4,5-dihydrooxazol-2-yl)-3-fluorophenyl)benzamide (1aa)**



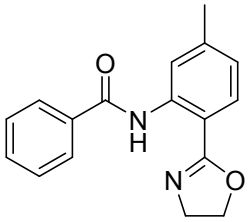
^{1}H NMR (500 MHz, $CDCl_3$) δ 13.01 (s, 1H), 8.74 (d, *J* = 8.5 Hz, 1H), 8.11 – 7.99 (m, 2H), 7.59 – 7.42 (m, 4H), 6.91 – 6.82 (m, 1H), 4.48 (t, *J* = 9.7 Hz, 2H), 4.14 (t, *J* = 9.7 Hz, 2H).

***N*-(2-(4,5-dihydrooxazol-2-yl)-4-methoxyphenyl)benzamide (1ab)**



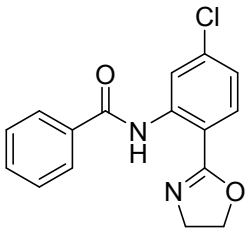
^{1}H NMR (500 MHz, $CDCl_3$) δ 12.79 (s, 1H), 8.91 (d, *J* = 9.2 Hz, 1H), 8.10 – 8.02 (m, 2H), 7.53 – 7.46 (m, 3H), 7.42 (d, *J* = 3.0 Hz, 1H), 7.09 (dd, *J* = 9.2, 3.0 Hz, 1H), 4.41 (t, *J* = 9.6 Hz, 2H), 4.20 (t, *J* = 9.4 Hz, 2H), 3.83 (s, 3H).

***N*-(2-(4,5-dihydrooxazol-2-yl)-5-methylphenyl)benzamide (1ac)**



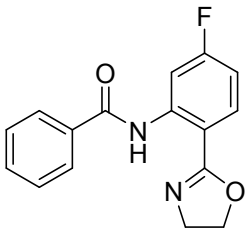
^{1}H NMR (500 MHz, $CDCl_3$) δ 13.00 (s, 1H), 8.82 (s, 1H), 8.10 (d, *J* = 7.9 Hz, 2H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.49 (dd, *J* = 14.3, 6.7 Hz, 3H), 6.91 (d, *J* = 7.9 Hz, 1H), 4.36 (t, *J* = 9.4 Hz, 2H), 4.15 (t, *J* = 9.4 Hz, 2H), 2.42 (s, 3H).

***N*-(5-chloro-2-(4,5-dihydrooxazol-2-yl)phenyl)benzamide (1ad)**



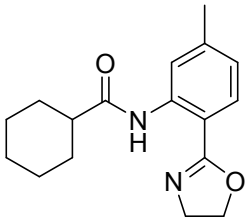
^{1}H NMR (500 MHz, $CDCl_3$) δ 13.07 (s, 1H), 9.07 (d, *J* = 1.9 Hz, 1H), 8.08 (d, *J* = 7.3 Hz, 2H), 7.81 (d, *J* = 8.5 Hz, 1H), 7.57 – 7.46 (m, 3H), 7.08 (dd, *J* = 8.5, 1.9 Hz, 1H), 4.42 (t, *J* = 9.5 Hz, 2H), 4.20 (t, *J* = 9.5 Hz, 2H).

***N*-(2-(4,5-dihydrooxazol-2-yl)-5-fluorophenyl)benzamide (1ae)**



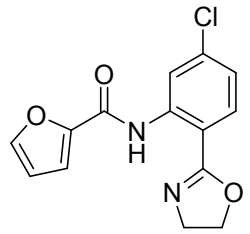
^{1}H NMR (500 MHz, $CDCl_3$) δ 13.01 (s, 1H), 8.75 (d, *J* = 8.5 Hz, 1H), 8.08 – 7.99 (m, 2H), 7.58 – 7.44 (m, 4H), 6.86 (ddd, *J* = 11.5, 8.3, 0.9 Hz, 1H), 4.49 (t, *J* = 9.8 Hz, 2H), 4.15 (t, *J* = 9.7 Hz, 2H), 3.75 (t, *J* = 5.7 Hz, 1H).

***N*-(2-(4,5-dihydrooxazol-2-yl)-5-methylphenyl)cyclohexanecarboxamide (1ag)**



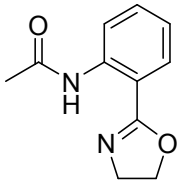
^{1}H NMR (500 MHz, $CDCl_3$) δ 12.08 (s, 1H), 8.64 (s, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), 6.90 – 6.81 (m, 1H), 4.36 (t, *J* = 9.5 Hz, 2H), 4.14 (t, *J* = 9.5 Hz, 2H), 2.37 (s, 3H), 2.31 (ddd, *J* = 11.6, 7.6, 3.5 Hz, 1H), 2.00 (dd, *J* = 13.5, 2.0 Hz, 2H), 1.87 – 1.79 (m, 2H), 1.74 – 1.67 (m, 1H), 1.58 (qd, *J* = 12.4, 3.1 Hz, 2H), 1.39 – 1.25 (m, 3H).

***N*-(5-chloro-2-(4,5-dihydrooxazol-2-yl)phenyl)furan-2-carboxamide (1ah)**



^{1}H NMR (500 MHz, $CDCl_3$) δ 13.05 (s, 1H), 8.96 (d, *J* = 2.1 Hz, 1H), 7.78 (d, *J* = 8.5 Hz, 1H), 7.57 (d, *J* = 0.8 Hz, 1H), 7.22 (d, *J* = 3.4 Hz, 1H), 7.06 (dd, *J* = 8.5, 2.1 Hz, 1H), 6.54 (dd, *J* = 3.5, 1.7 Hz, 1H), 4.41 (dd, *J* = 14.4, 4.9 Hz, 2H), 4.21 (t, *J* = 9.4 Hz, 2H).

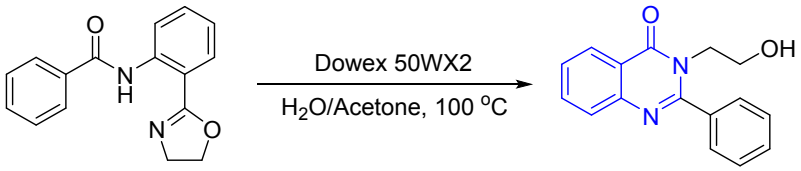
***N*-(2-(4,5-dihydrooxazol-2-yl)phenyl)acetamide (1aj)**



^{1}H NMR (500 MHz, $CDCl_3$) δ 12.17 (s, 1H), 8.72 (d, *J* = 8.4 Hz, 1H), 7.84 (d, *J* = 7.7 Hz, 1H), 7.45 (t, *J* = 7.7 Hz, 1H), 7.05 (t, *J* = 7.5 Hz, 1H), 4.36 (t, *J* = 9.4 Hz, 2H), 4.13 (t, *J* = 9.4 Hz, 2H), 3.60 – 3.58 (m, 1H), 2.21 (s, 3H).

3. Optimization of reaction conditions

The effect of ratios of mixed solvents on the reaction[a,b]

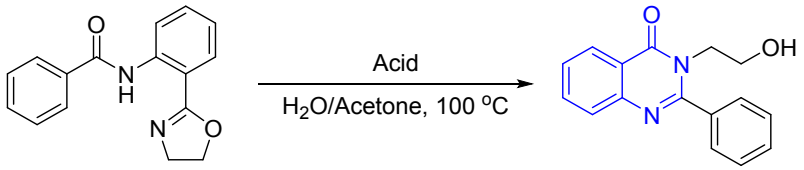


1a **2a**

Entry	H_2O/Acetone (v/v)	Yield [%][b]
1	19:1	45
2	14:1	72
3	9:1	83
4	4:1	82
5	1:1	85

[a] Reaction conditions: **1a** (0.3 mmol), dowex 50WX2 (150 mg), H_2O/Acetone (5.0 mL), 100 °C, 6 h, air. [b] Isolated yields.

The effect of strong acids on the reaction[a,b]



1a **2a**

Entry	Deviation from initial conditions	Yield [%][b]
1	none	83
2[c]	dowex 50WX2 was replaced with HCl	57
3[d]	dowex 50WX2 was replaced with H_2SO_4	45

[a] Reaction conditions: **1a** (0.3 mmol), dowex 50WX2 (150 mg), H_2O/Acetone (5.0 mL, v/v = 9:1), 100 °C, 6 h, air. [b] Isolated yields. [c] HCl (12 M) (0.3 mmol). [d] H_2SO_4 (18.4 M) (0.3 mmol).

4. X-ray Crystal Data for 2a

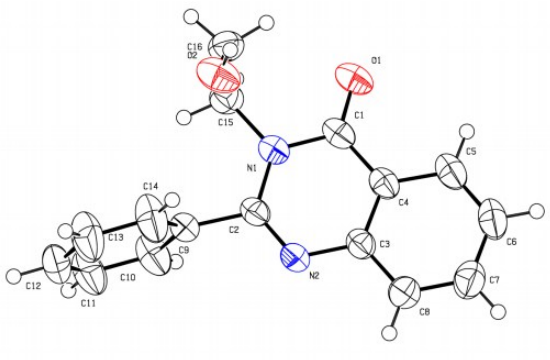
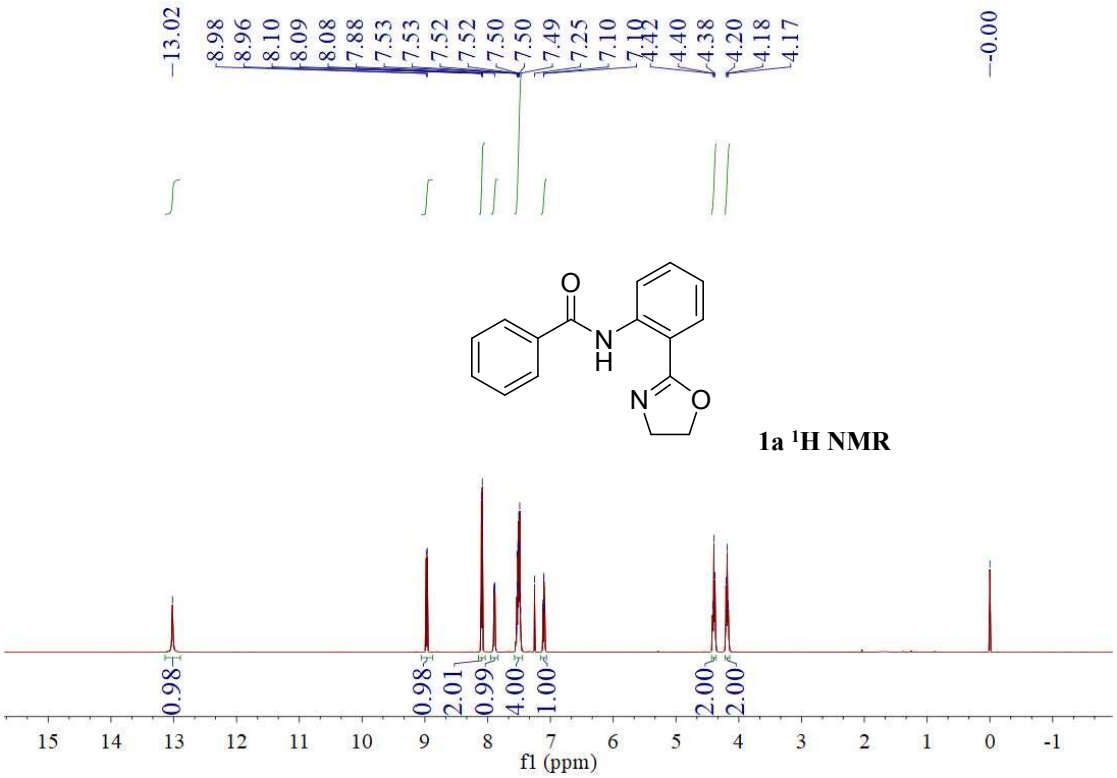


Figure 1 Single-crystal X-ray structure of **2a**. Ellipsoids are represented at 30% probability.

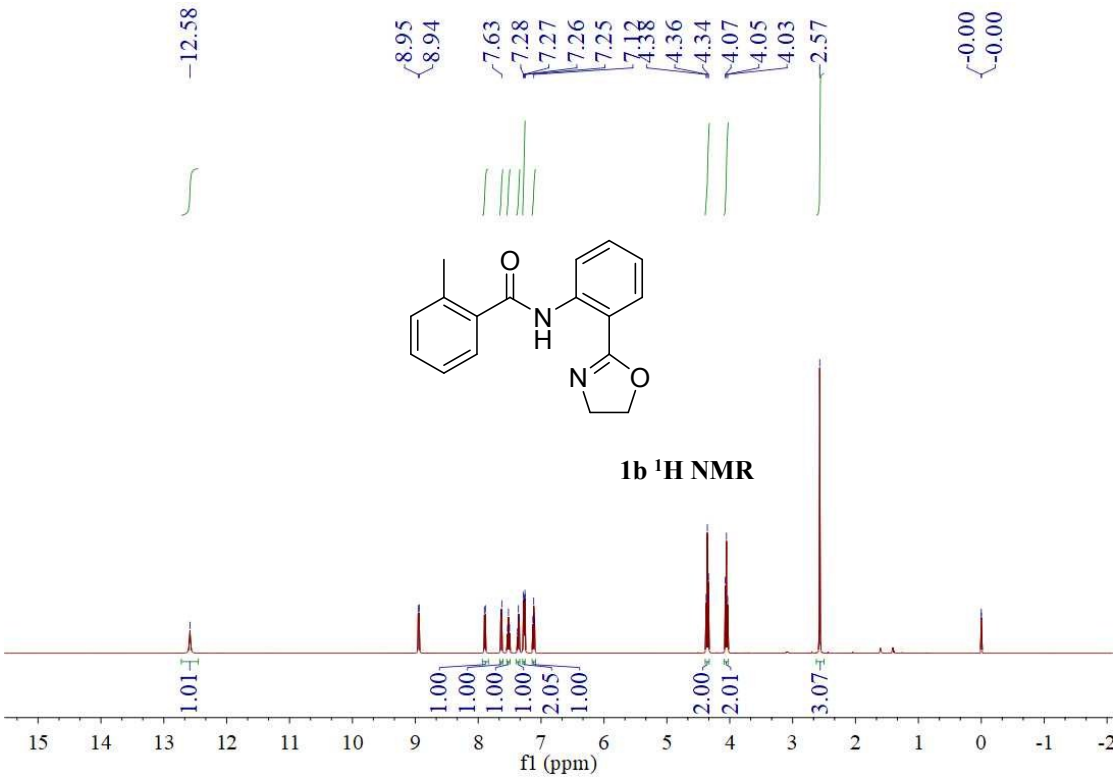
Table S1. Crystallographic data and structure refinement for **2a**

CCDC	1959603
Empirical formula	$C_{16}H_{14}N_2O_2$
Formula weight	266.29
Temperature K	296.15
Wavelength Å	0.71073
Crystal system	Triclinic
Space group	P-1
a, *b*, *c* Å	4.9529 (7), 11.1696 (16), 13.2334 (19)
α, β, γ °	112.6230 (10), 99.490 (2), 94.354 (2)
Volume Å^3	658.67 (16)
Z	2
Calculated density, Mg/m^3	1.343
F (000)	280
Theta range for data collection °	1.705 to 27.744
Limiting indices	-6<=h<=6, -14<=k<=13, -16<=l<=16
Reflections collected / unique	5331 / 2834 [R(int) = 0.0150]
Absorption correction	Semi-empirical from equivalents
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2834 / 0 / 181
Goodness of fit on F^2	1.064

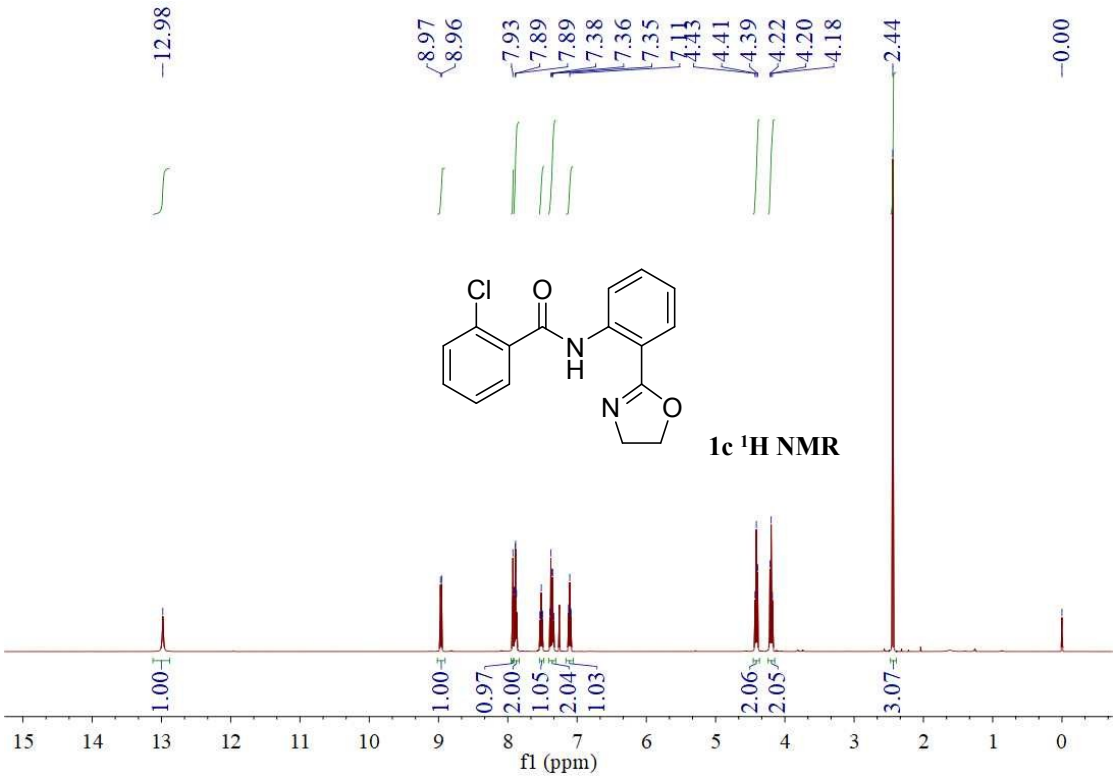
5. Copies of ^{1}H, ^{13}C and ^{19}F NMR Spectra



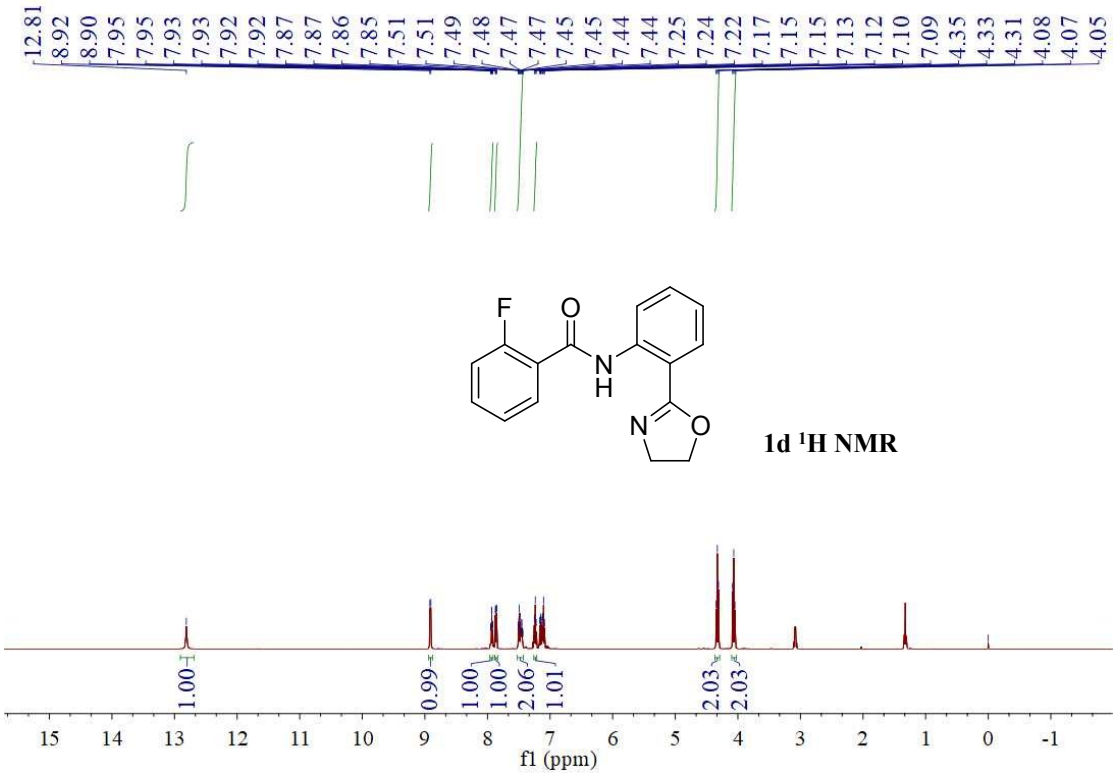
1a ^{1}H NMR



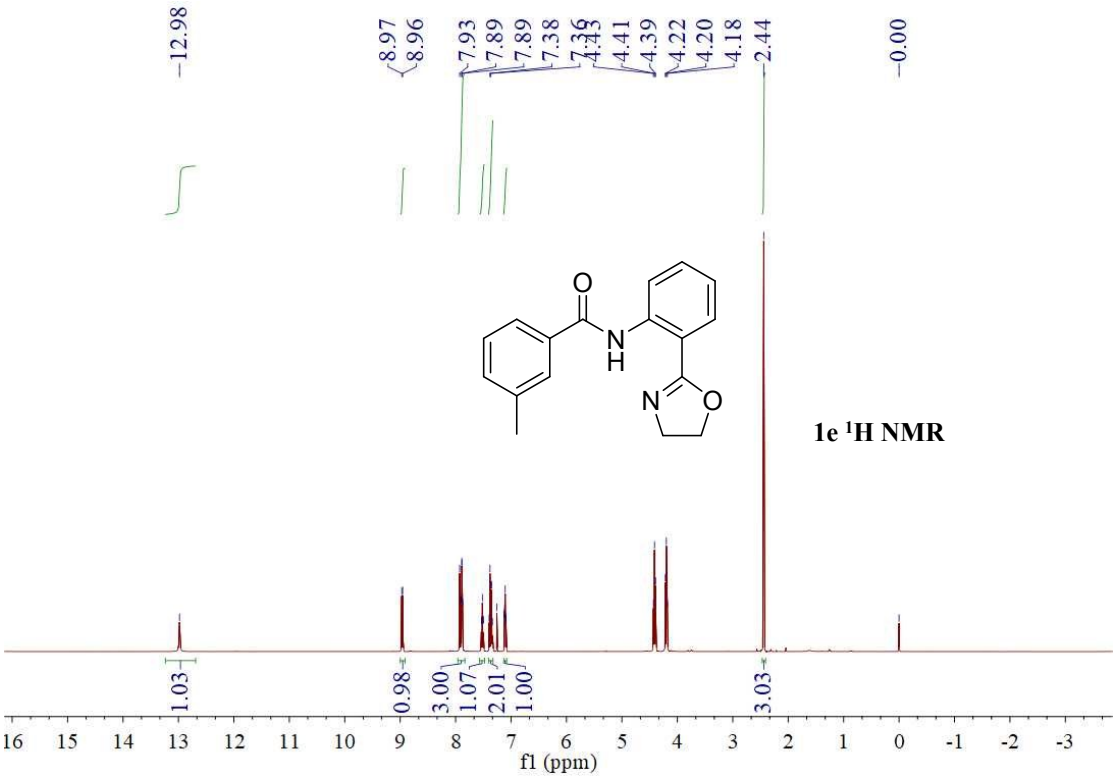
1b ^{1}H NMR

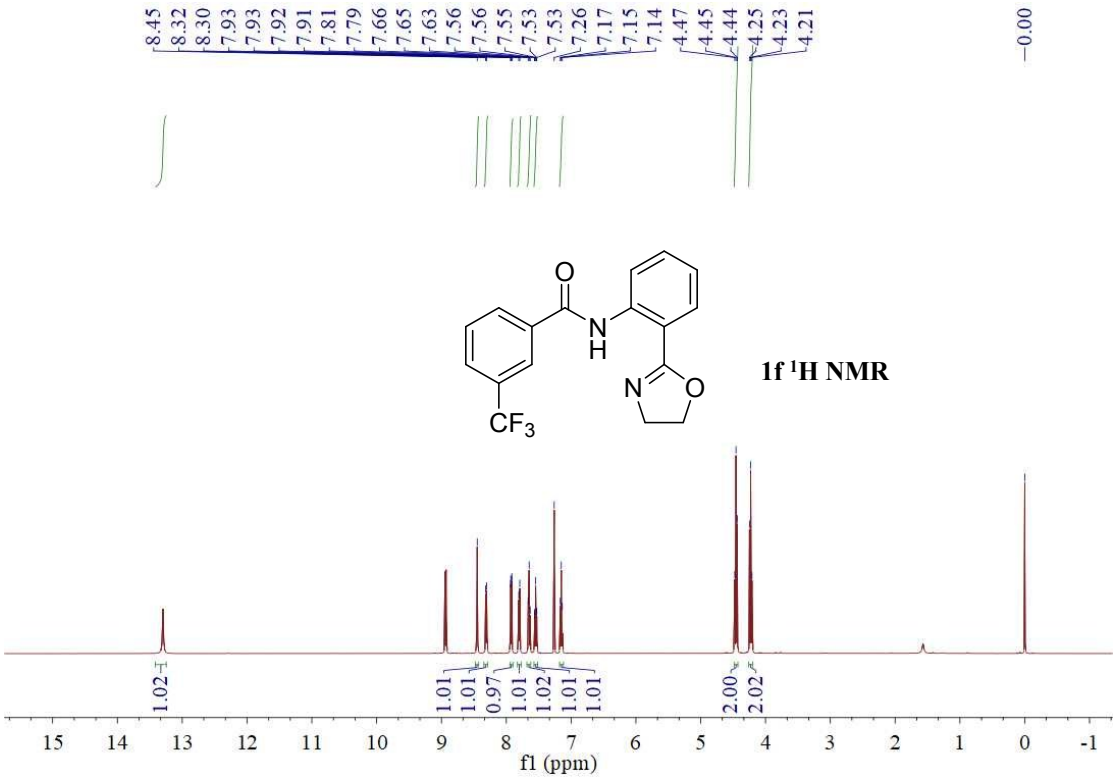


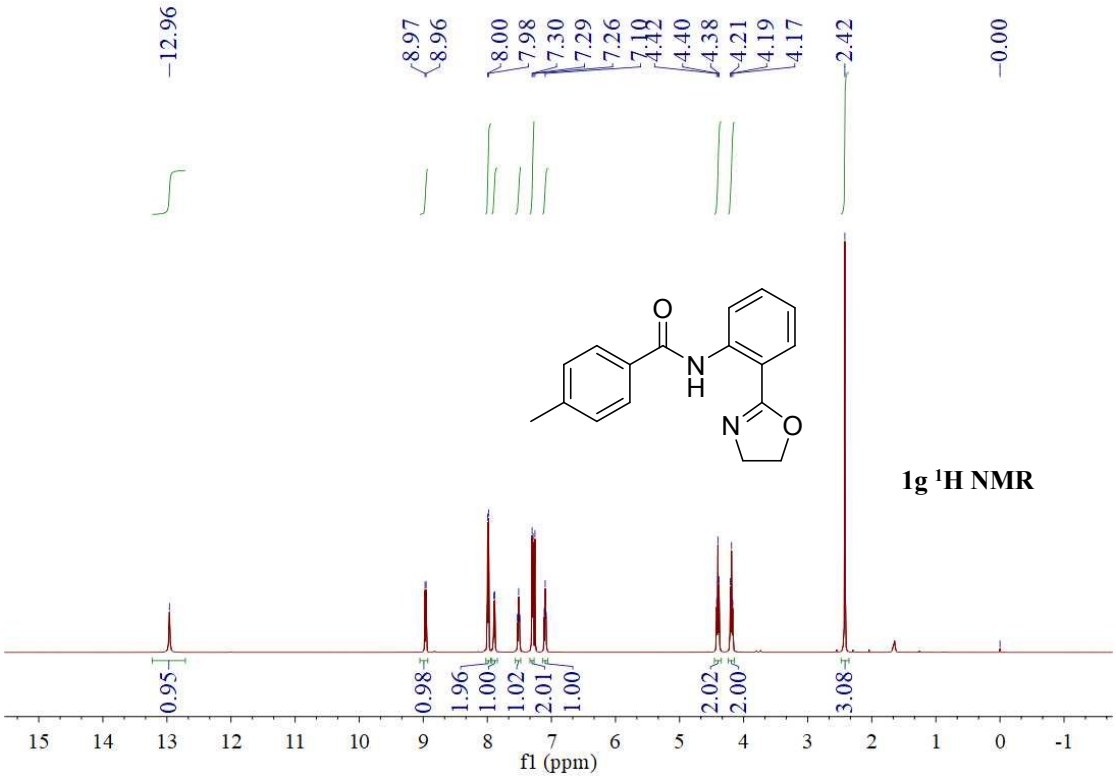
1c ^{1}H NMR

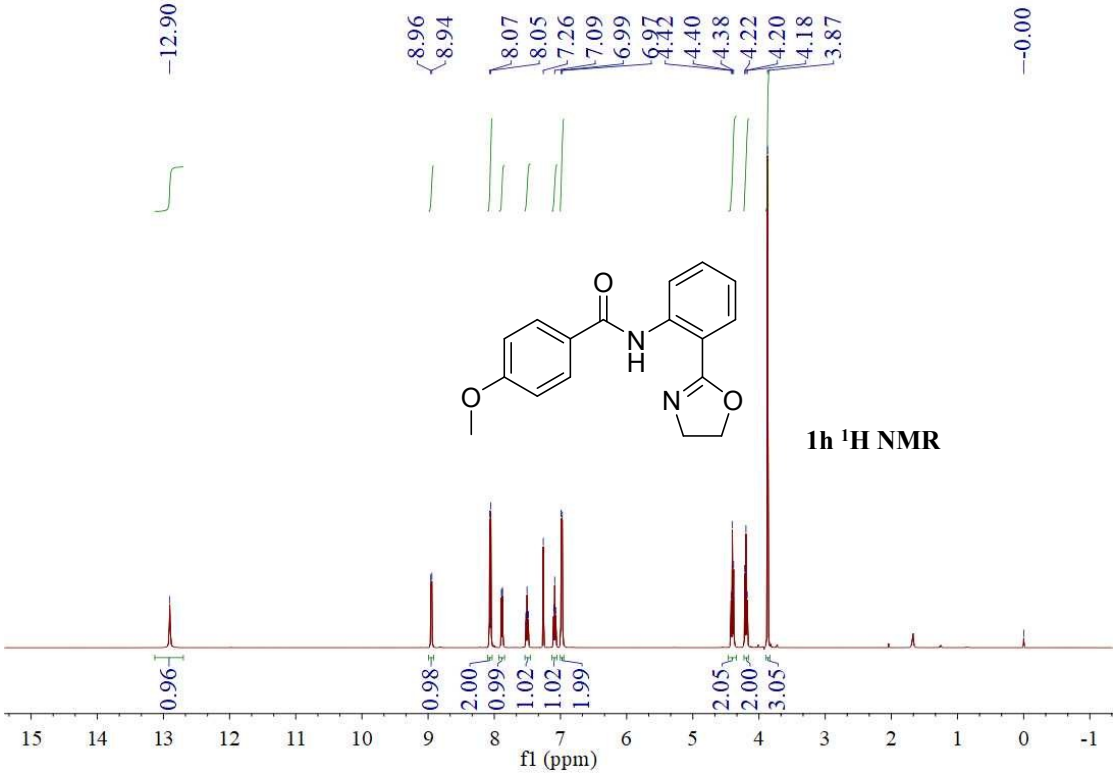


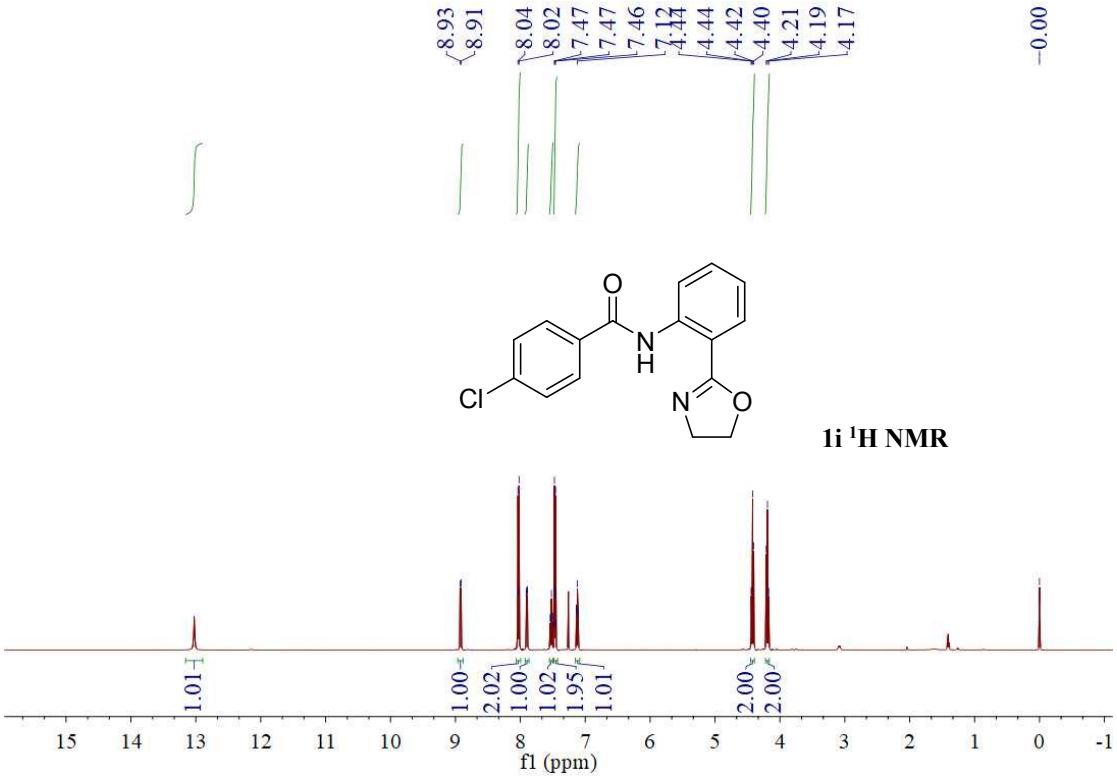
1d ^{1}H NMR


12.98
8.97
8.96
7.93
7.89
7.89
7.38
4.41
4.39
4.22
4.20
4.18
2.44
0.00
O
N
H
N
O
1e ¹H NMR
1.03
0.98
3.00
1.07
2.01
1.00
3.03
fl (ppm)

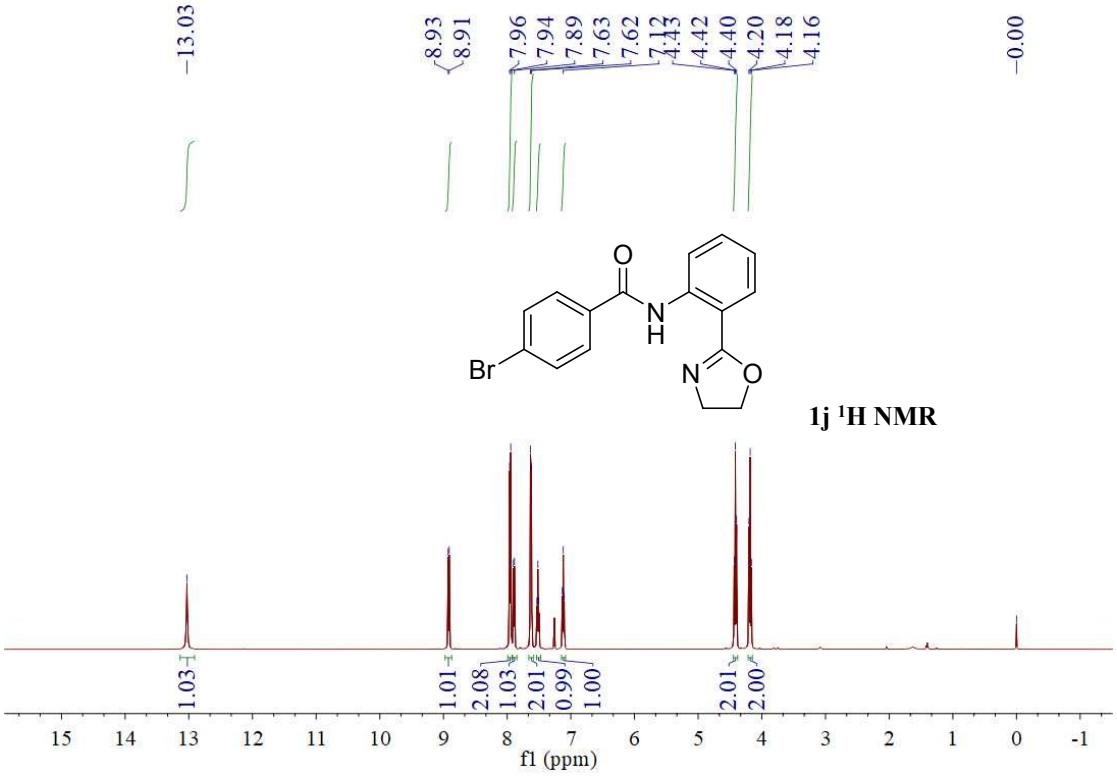

8.45
8.32
8.30
7.93
7.93
7.92
7.91
7.81
7.79
7.66
7.65
7.63
7.56
7.56
7.55
7.53
7.53
7.26
7.17
7.15
7.14
4.47
4.45
4.44
4.25
4.23
4.21
0.00
O
N
H
N
O
CF3
1f ¹H NMR
1.02
1.01
1.01
0.97
1.01
1.02
1.01
1.01
2.00
2.02
fl (ppm)


12.96
8.97
8.96
8.00
7.98
7.30
7.29
7.26
7.10
4.42
4.40
4.38
4.21
4.19
4.17
2.42
0.00
O
N
H
N
O
1g ¹H NMR
0.95
0.98
1.96
1.00
1.02
2.01
1.00
2.02
2.00
3.08
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)

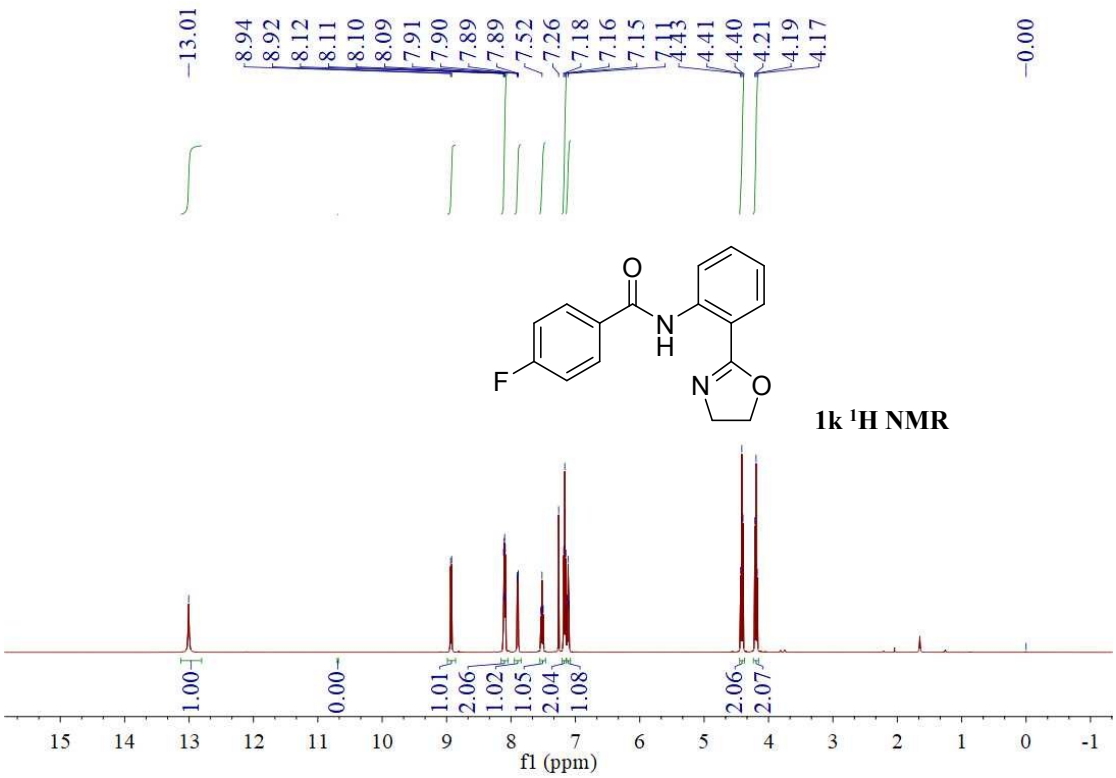

12.90
8.96
8.94
8.07
8.05
7.26
7.09
6.99
6.97
6.95
4.40
4.38
4.22
4.20
4.18
3.87
0.00
O
N
H
O
N
O
1h ¹H NMR
0.96
0.98
2.00
0.99
1.02
1.02
1.99
2.05
2.00
3.05
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)



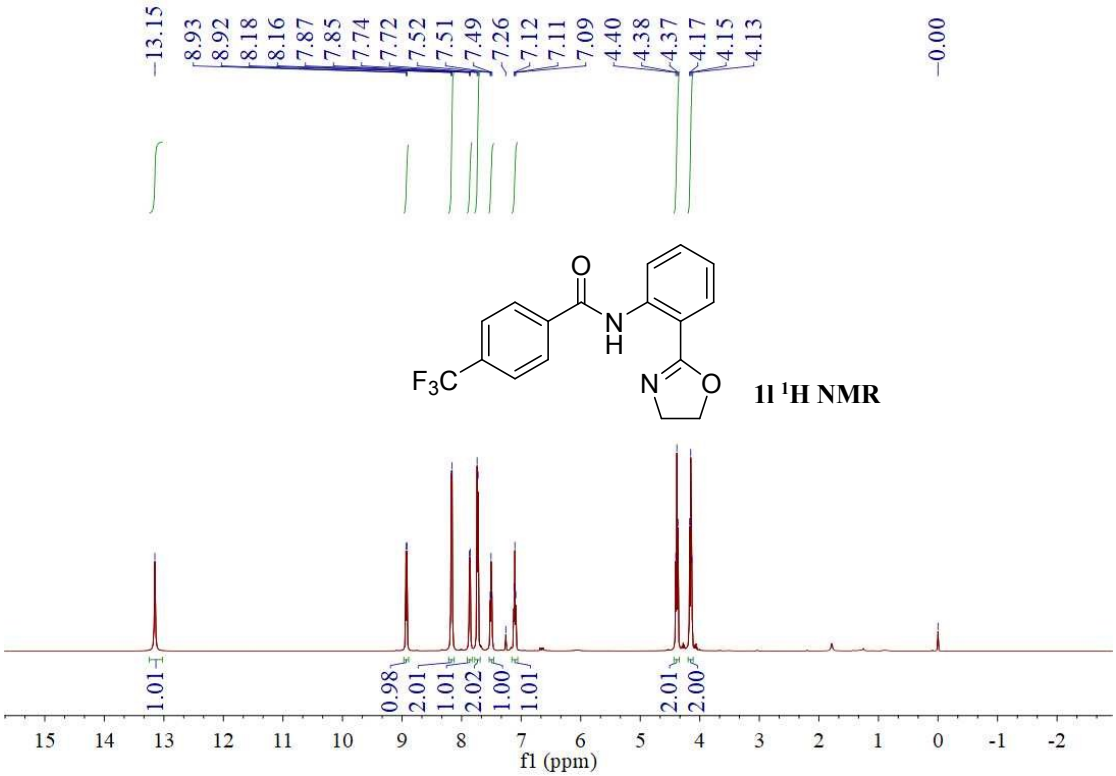
1i ^{1}H NMR



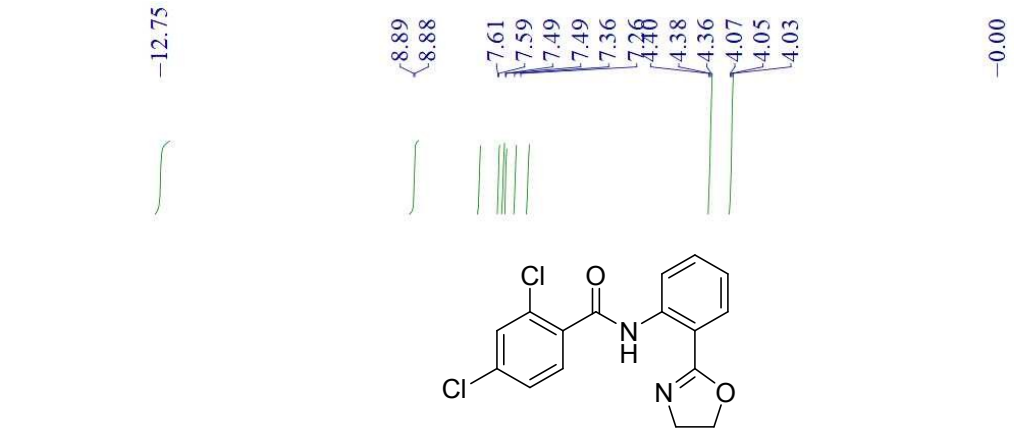
1j ^{1}H NMR



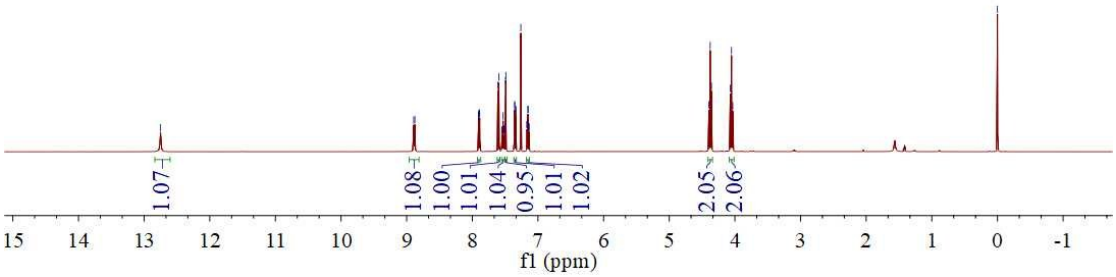
1k ^{1}H NMR

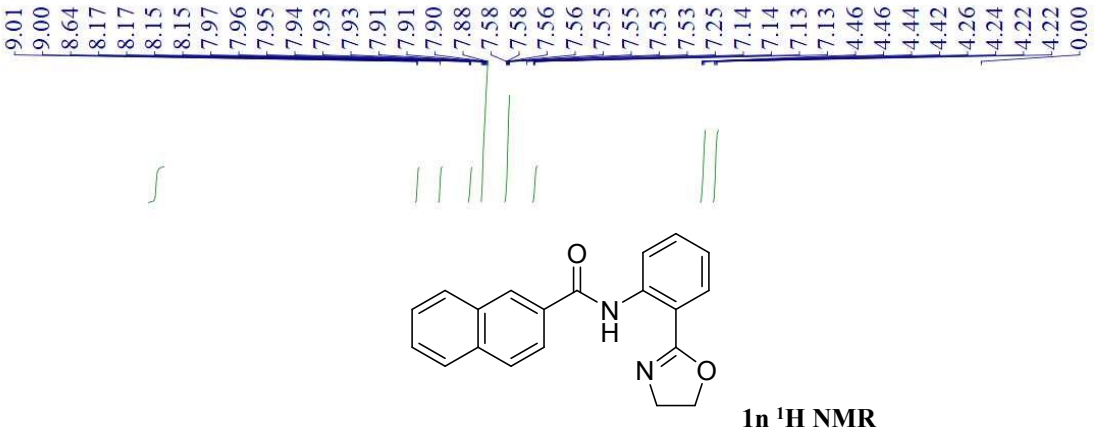


1l ^{1}H NMR

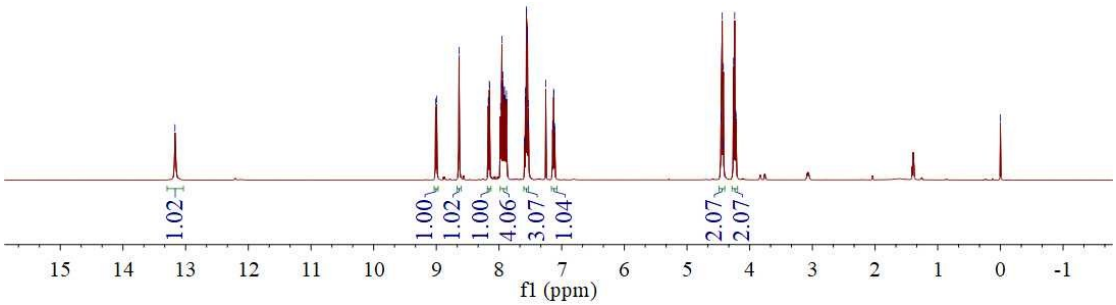


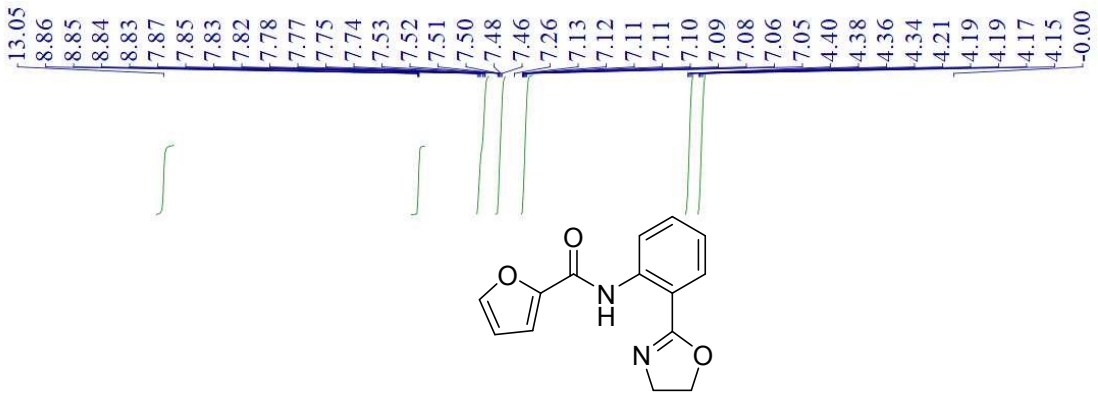
1m ^{1}H NMR



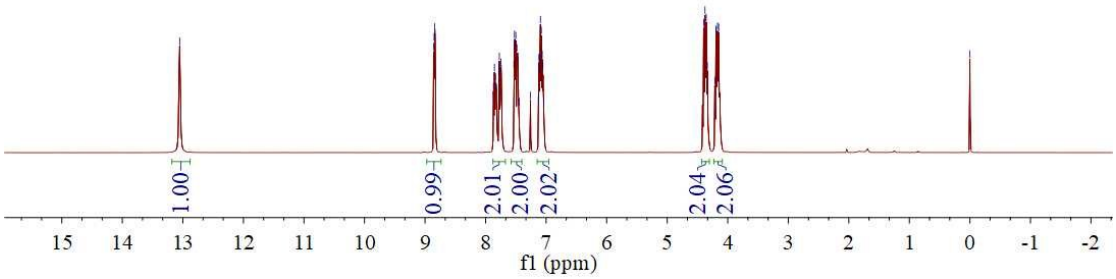


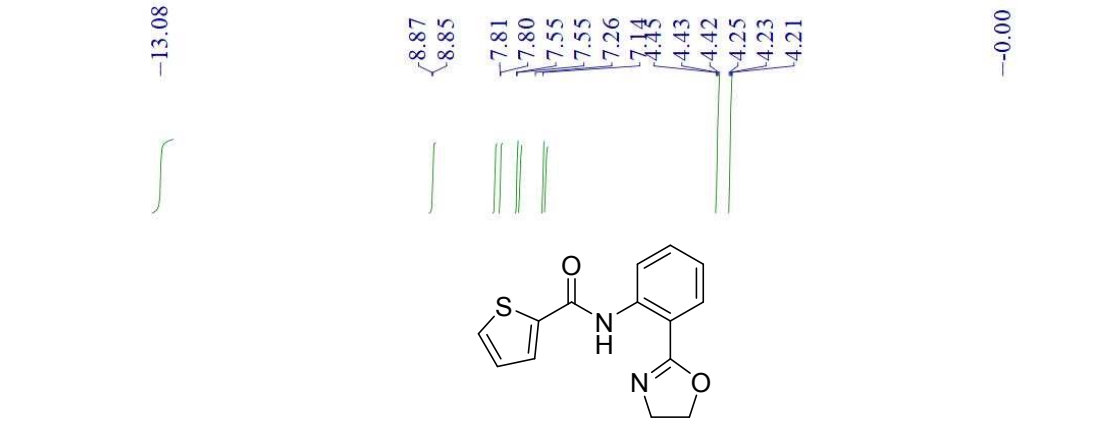
1n ^{1}H NMR



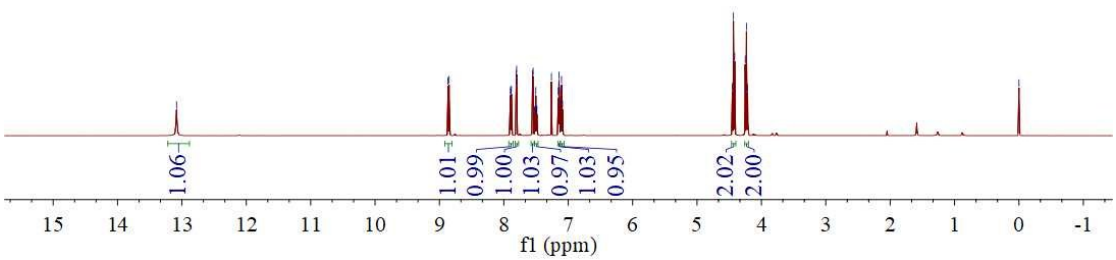


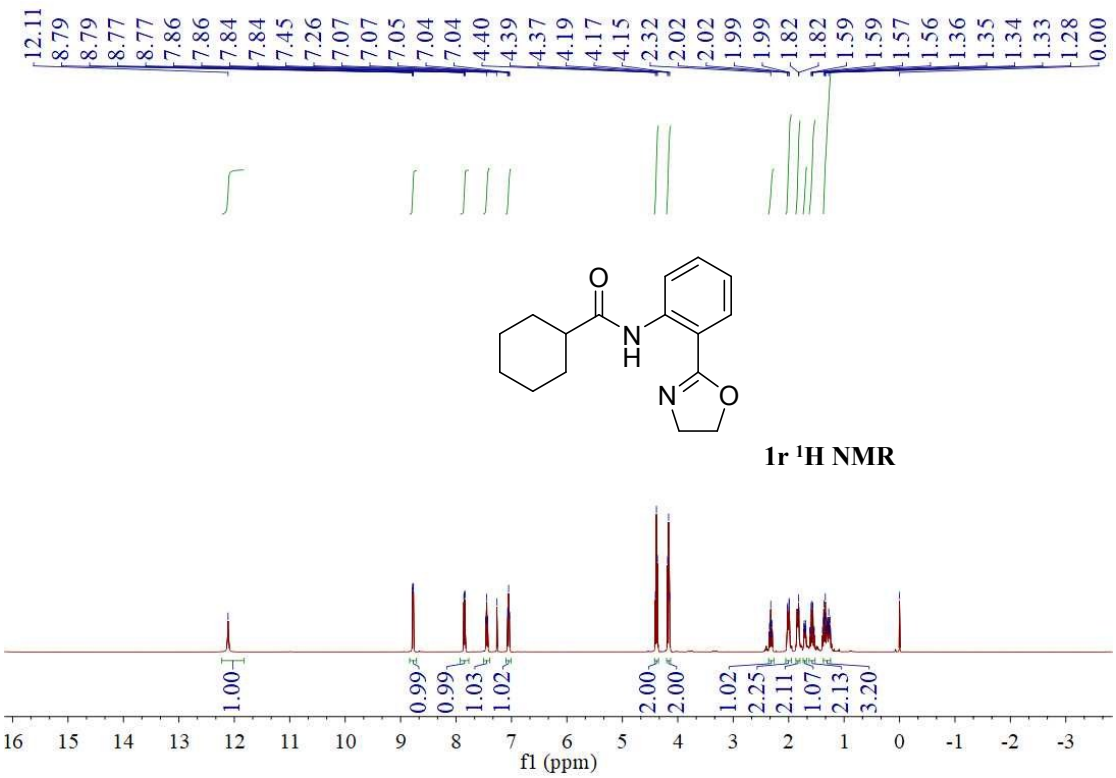
1o ^{1}H NMR



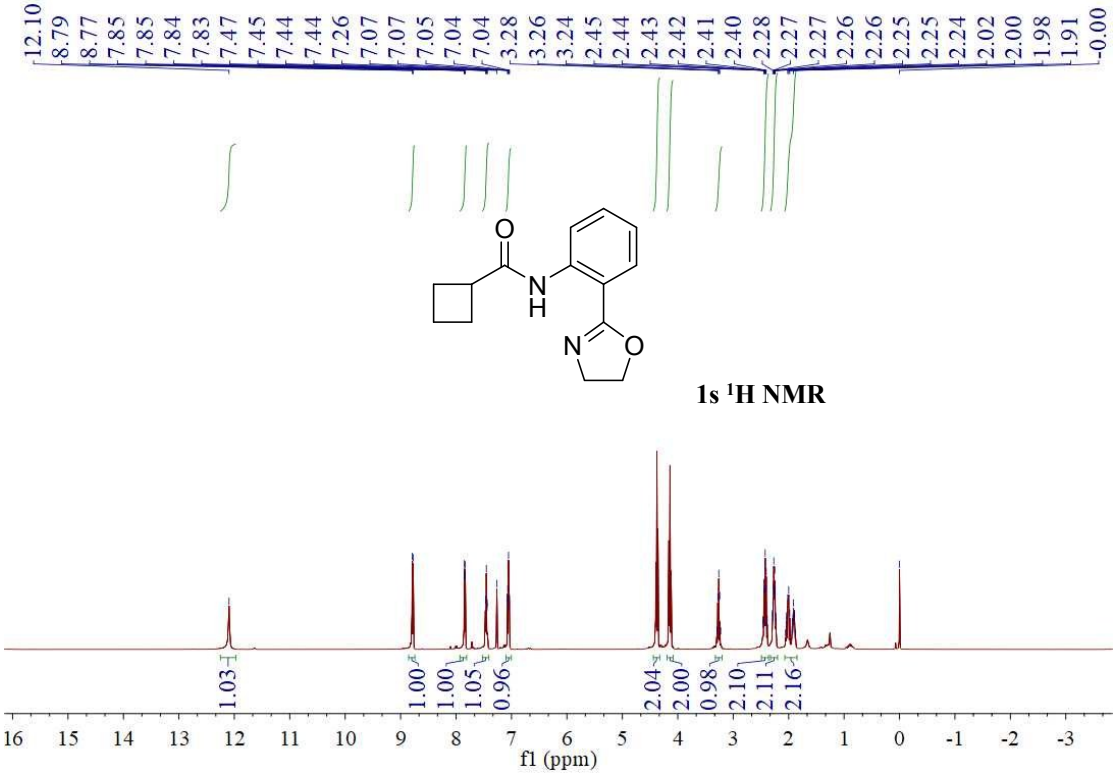


1p ^{1}H NMR





1r ^{1}H NMR



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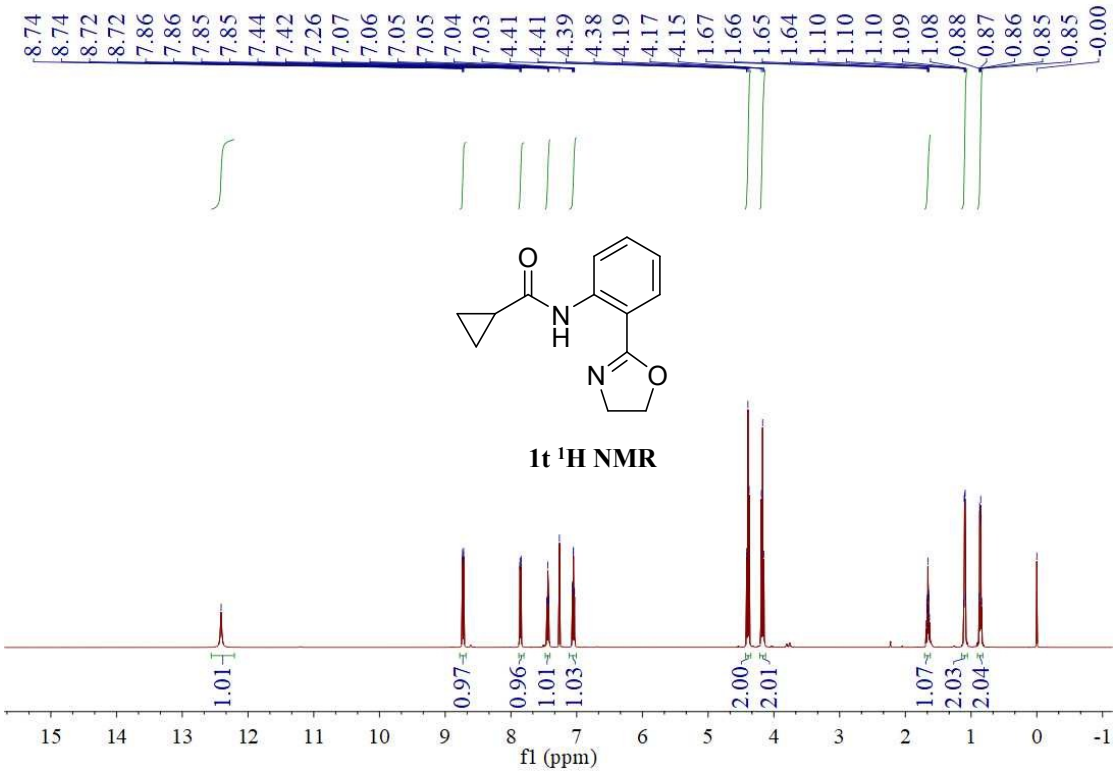

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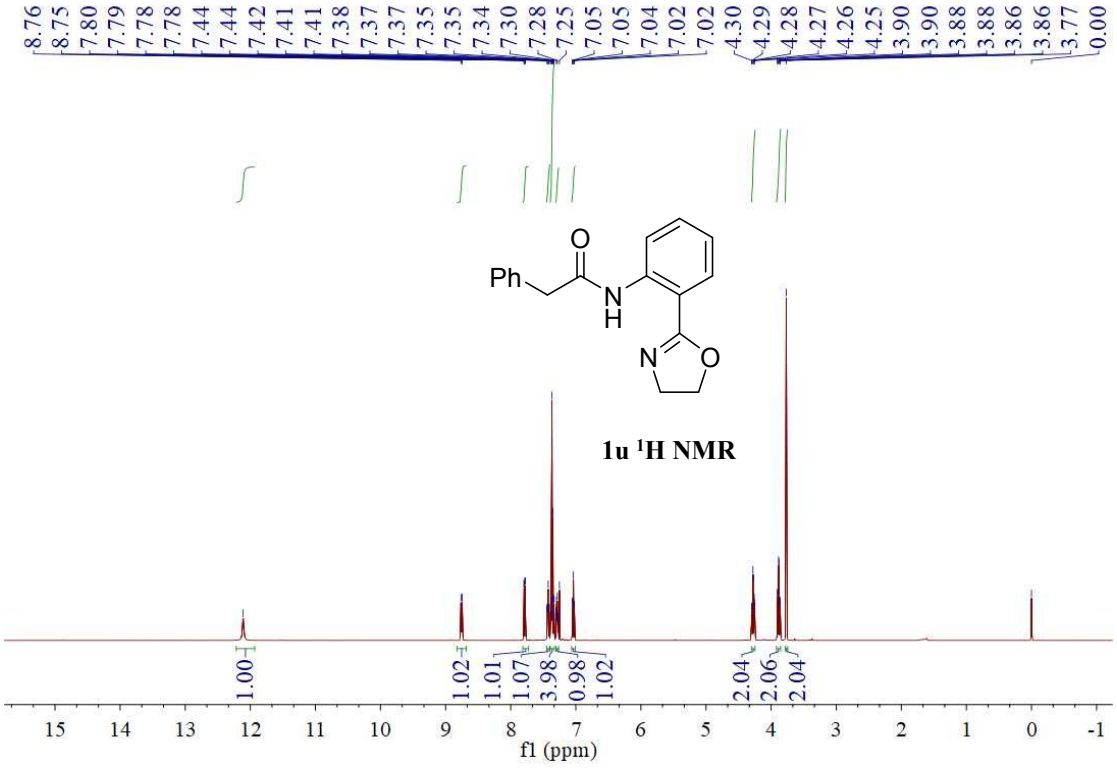
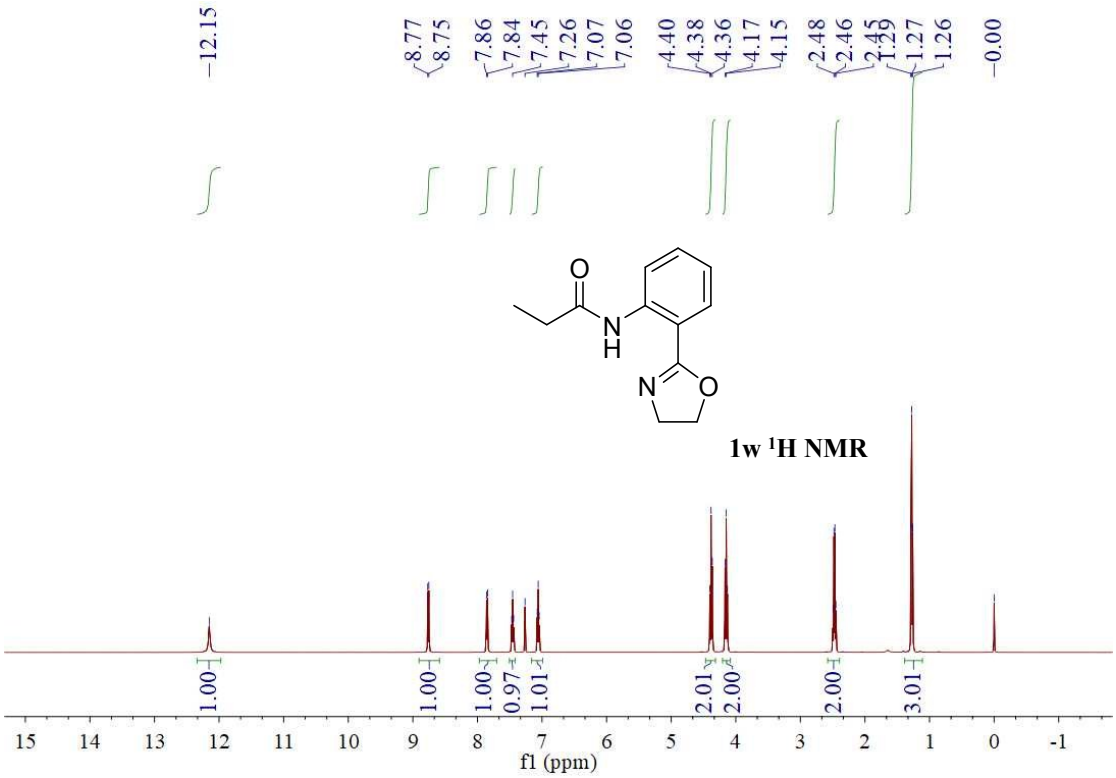


1u ^{1}H NMR



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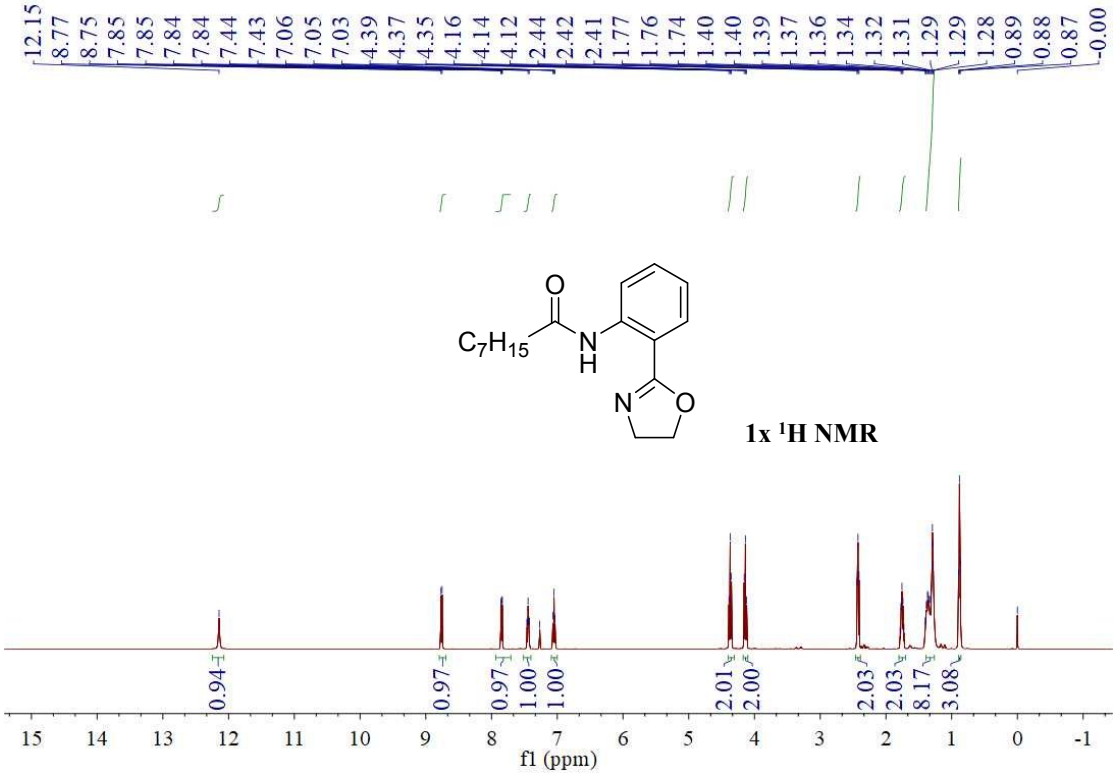
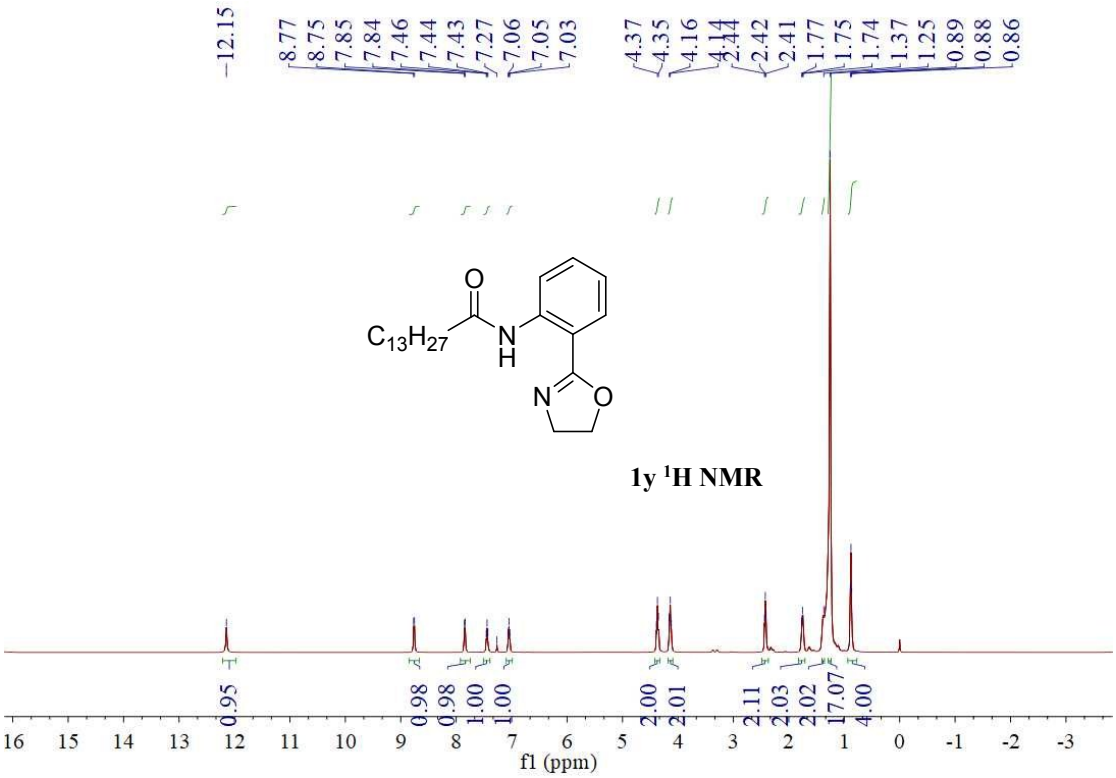


1x ^{1}H NMR



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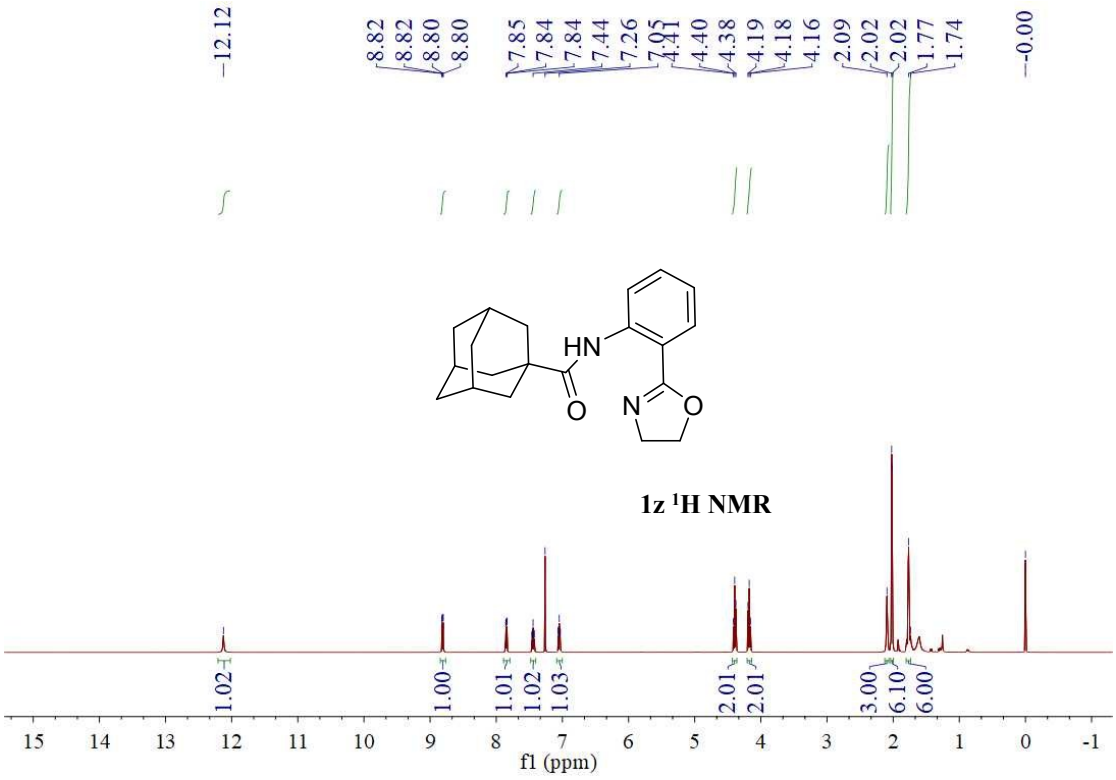

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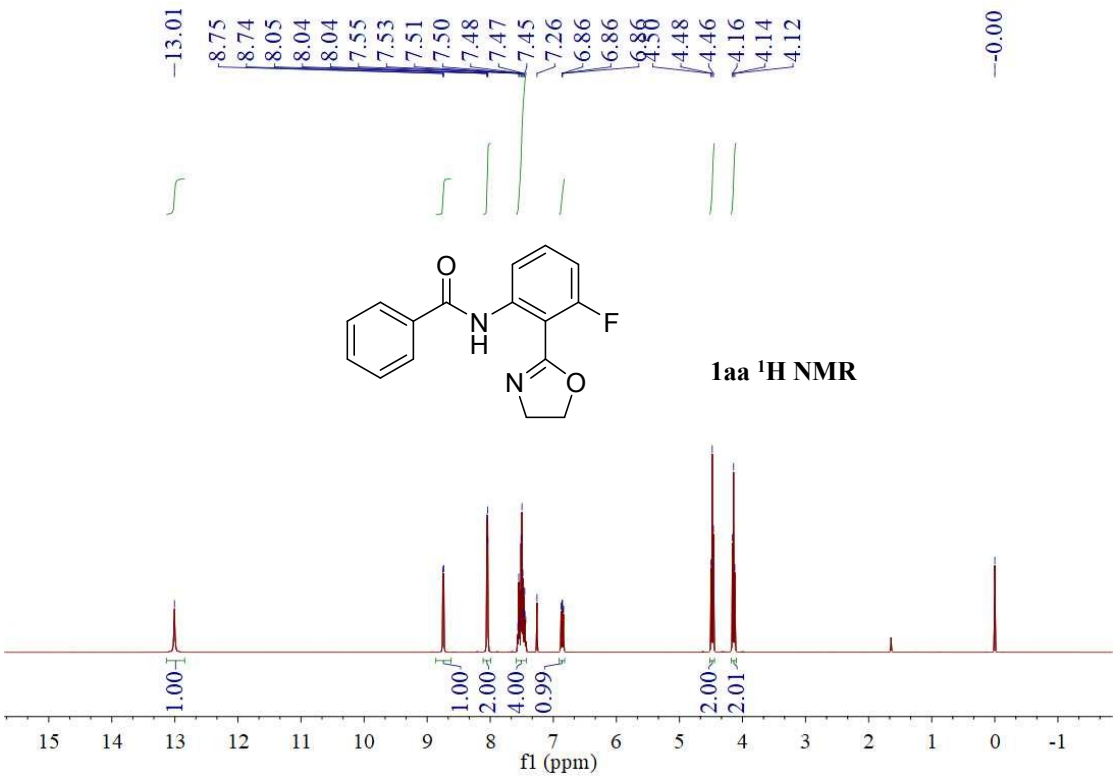

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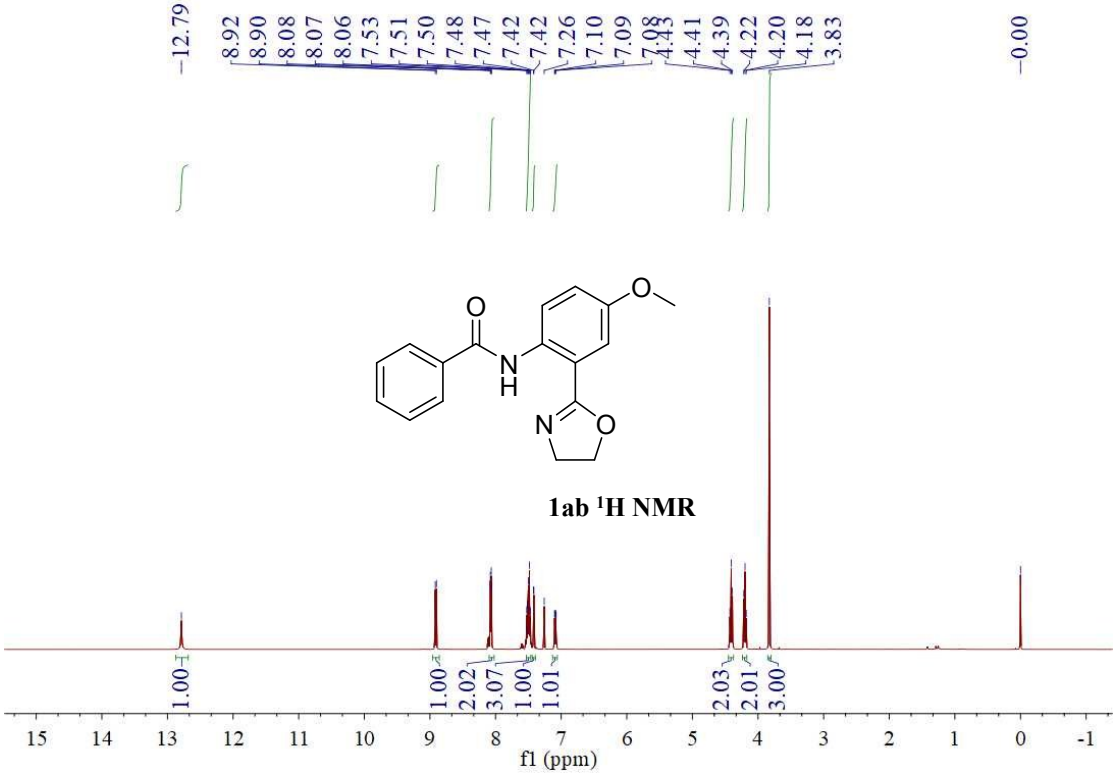
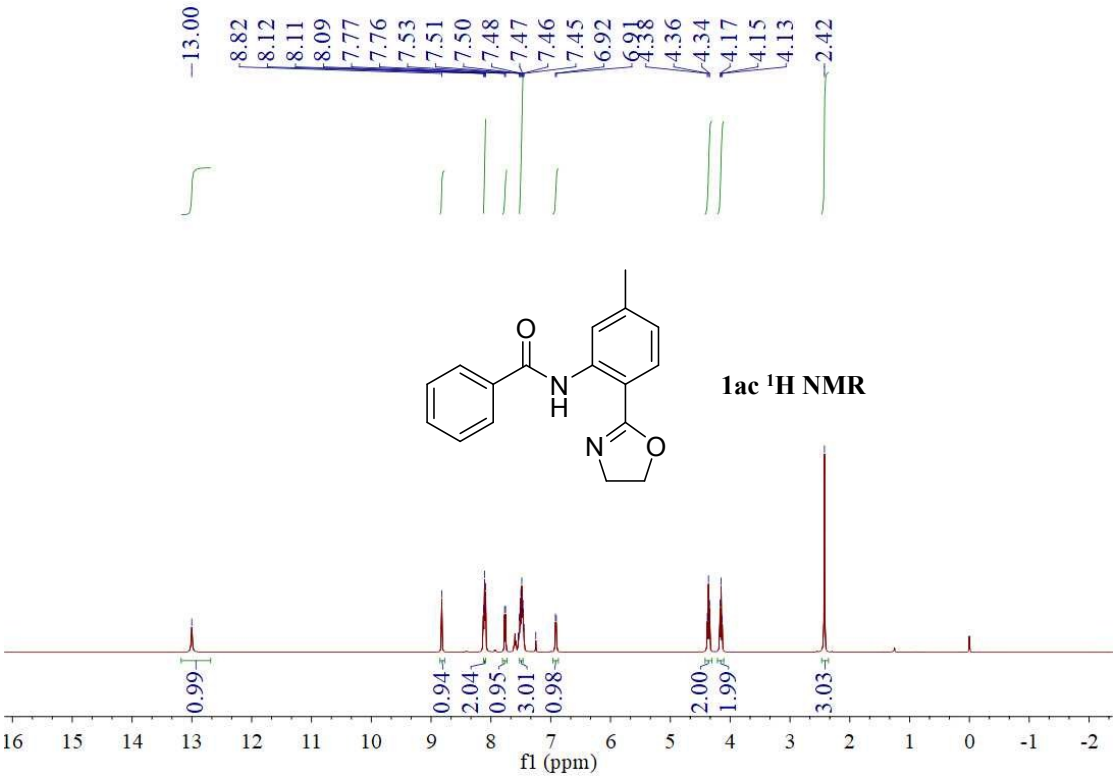


1ab ^{1}H NMR



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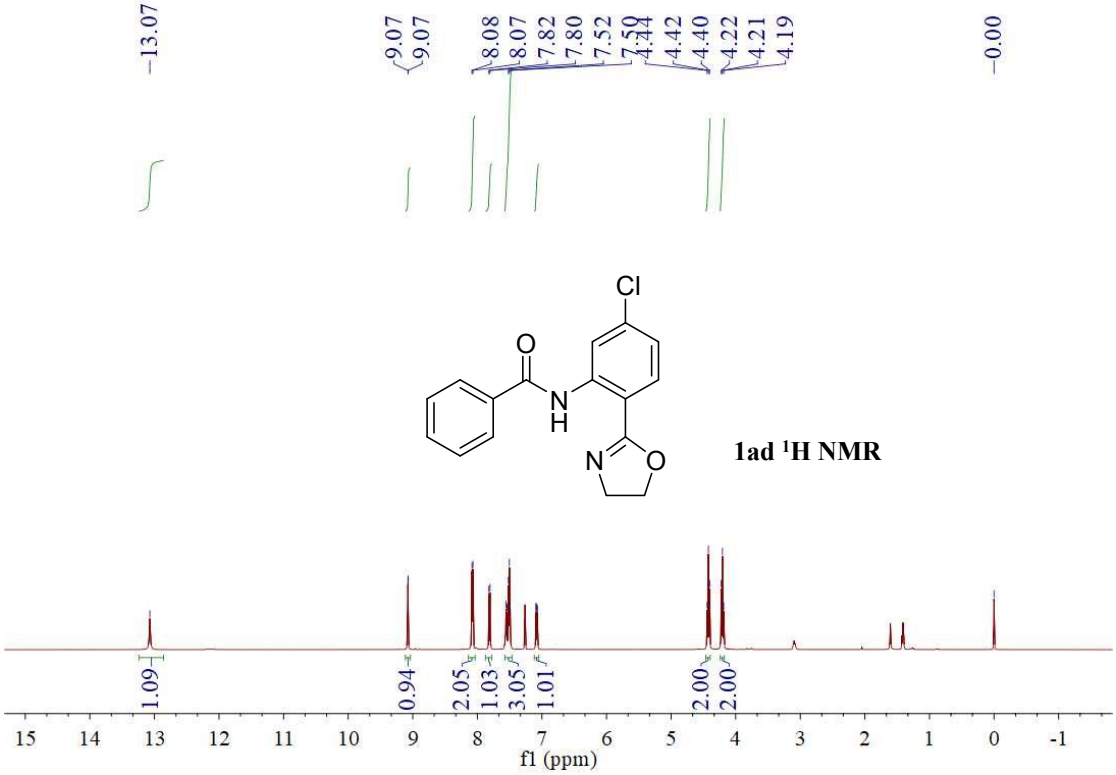
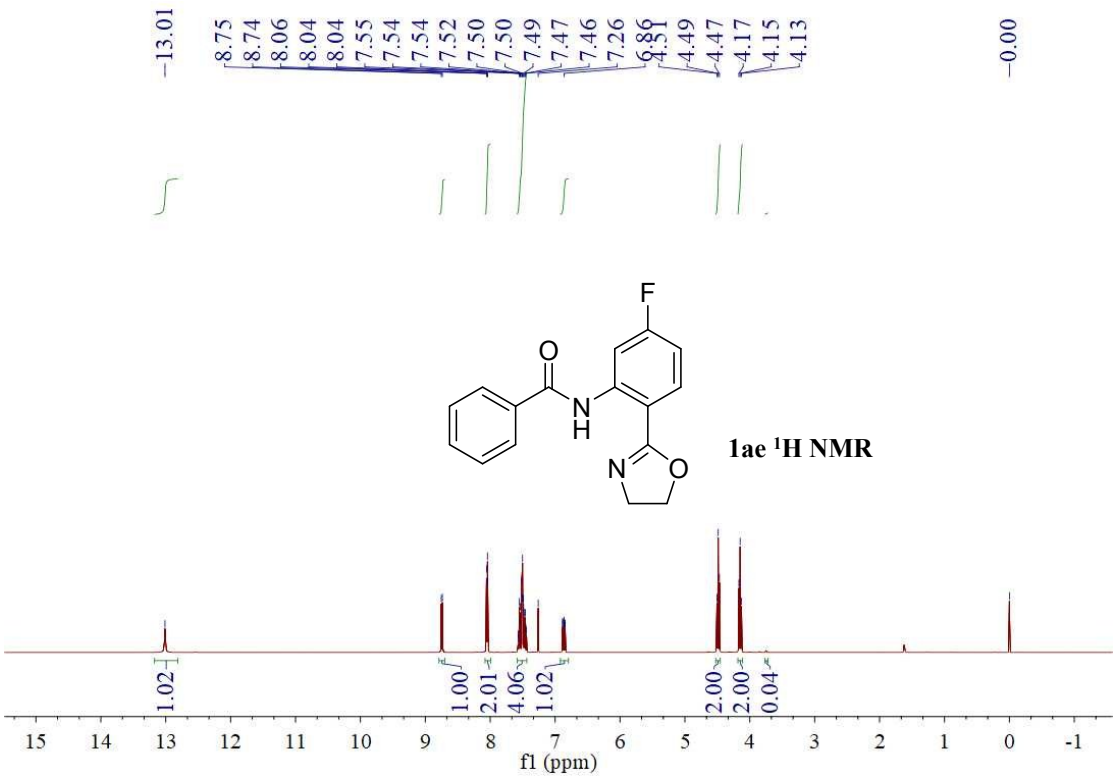


1ad ^{1}H NMR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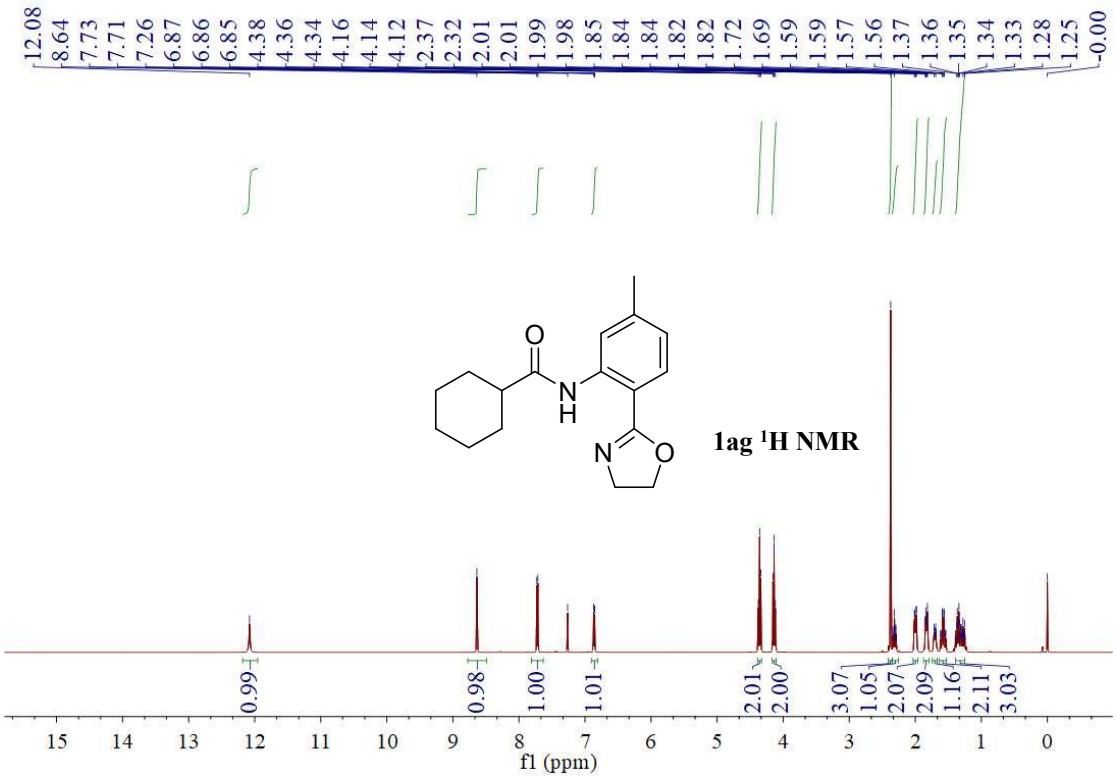
8.74
8.06
8.04
8.04
7.55
7.54
7.54
7.52
7.50
7.50
7.49
7.47
7.46
7.26
6.86
6.85
4.49
4.47
4.17
4.15
4.13
0.00
F
O
N
H
N
O
1ae ¹H NMR
1.02
1.00
2.01
4.06
1.02
2.00
2.00
0.04
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)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7.73
7.71
7.26
6.87
6.86
6.85
4.38
4.36
4.34
4.16
4.14
4.12
2.37
2.32
2.01
2.01
1.99
1.98
1.85
1.84
1.84
1.82
1.82
1.72
1.69
1.59
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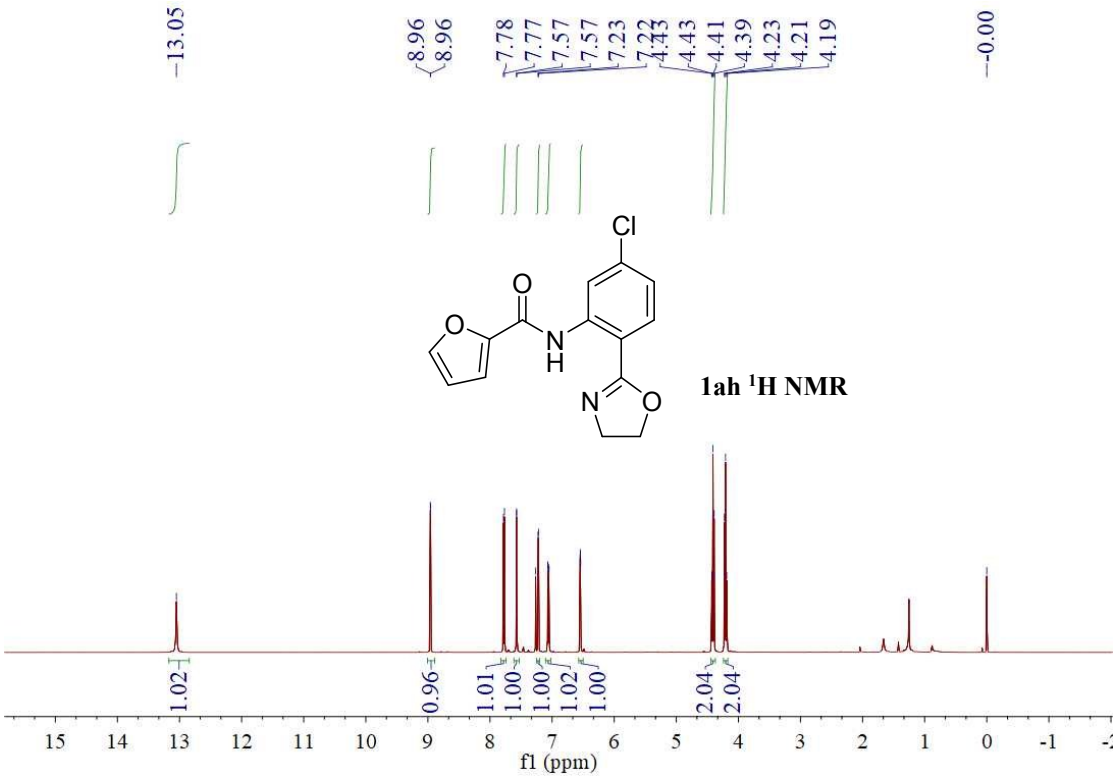
1.35
1.34
1.33
1.28
1.25
0.00
O
N
H
N
O
1ag ¹H NMR
0.99
0.98
1.00
1.01
2.01
2.00
3.07
1.05
2.07
2.09
1.16
2.11
3.03
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)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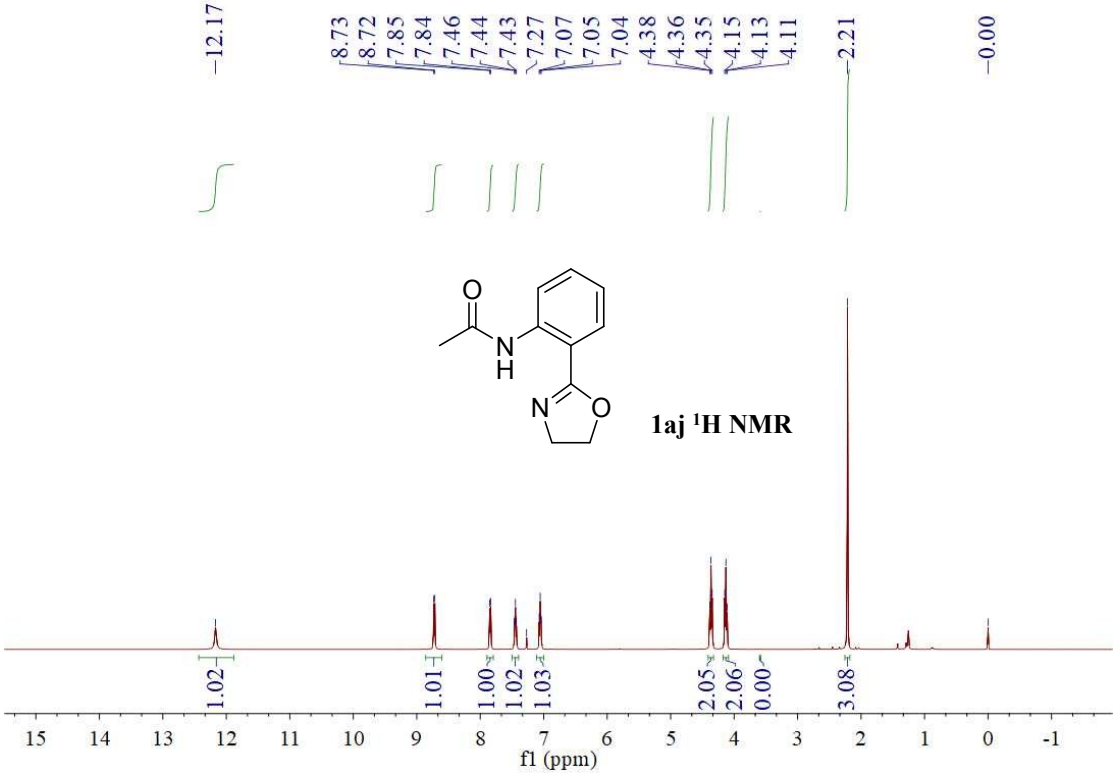
8.96
8.96
7.78
7.77
7.57
7.57
7.23
7.22
4.43
4.41
4.39
4.23
4.21
4.19
0.00
Cl
O
O
N
H
N
O
1ah ^{1}H NMR
1.02
0.96
1.01
1.00
1.00
1.02
1.00
2.04
2.04
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)


12.17
8.73
8.72
7.85
7.84
7.46
7.44
7.43
7.27
7.07
7.05
7.04
4.38
4.36
4.35
4.15
4.13
4.11
2.21
0.00
O
N
H
N
O
1aj ^{1}H NMR
1.02
1.01
1.00
1.02
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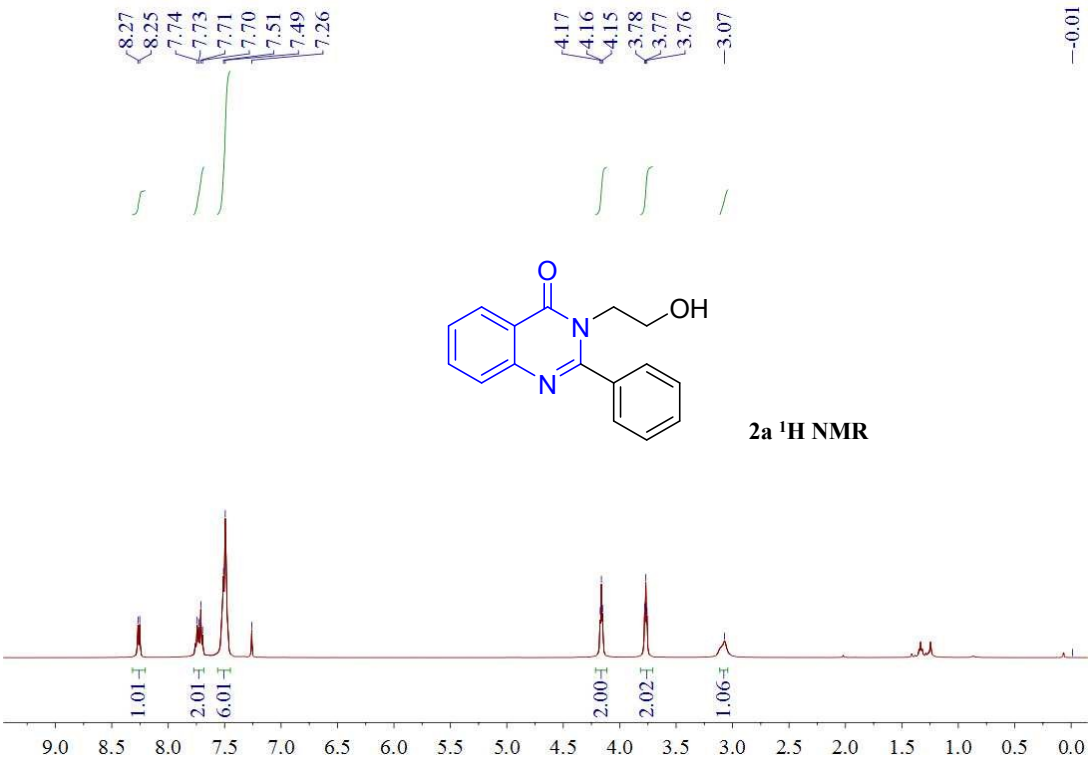
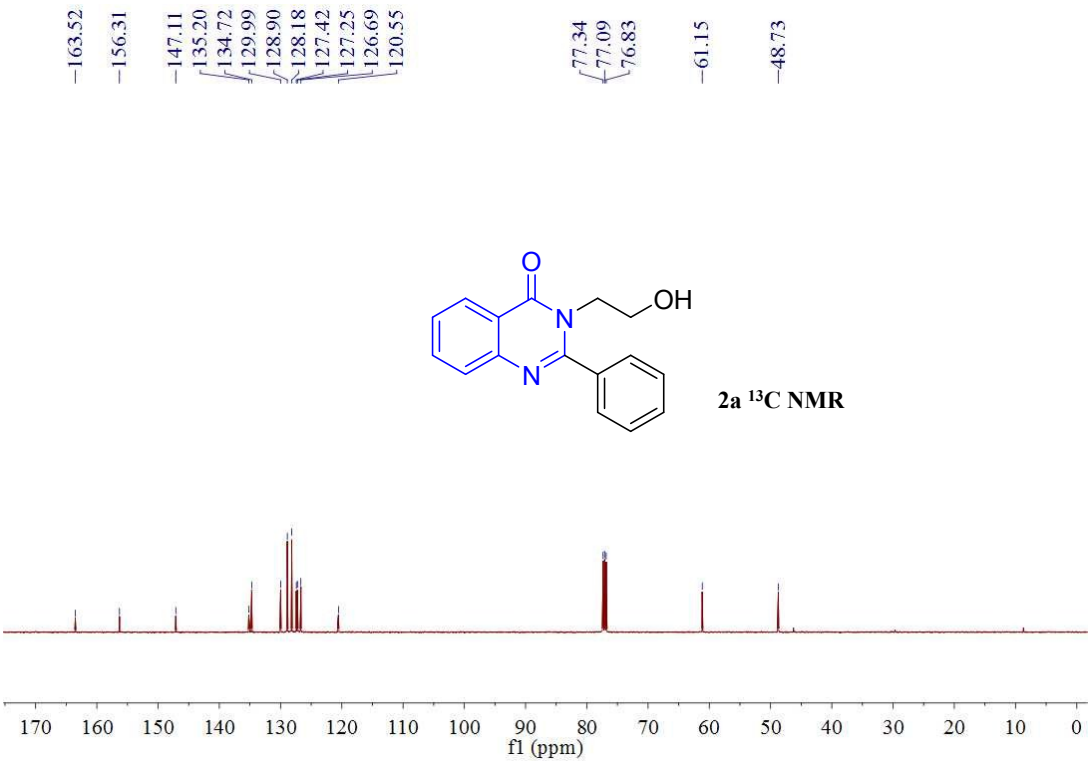
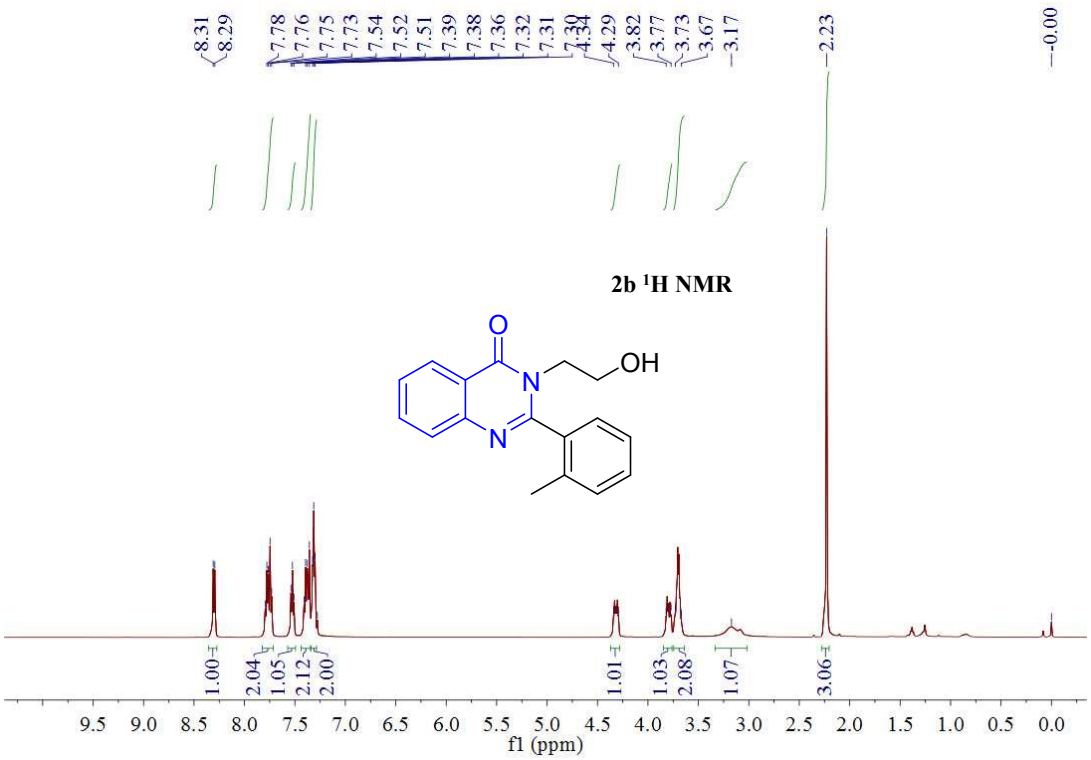
2.05
2.06
0.00
3.08
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)



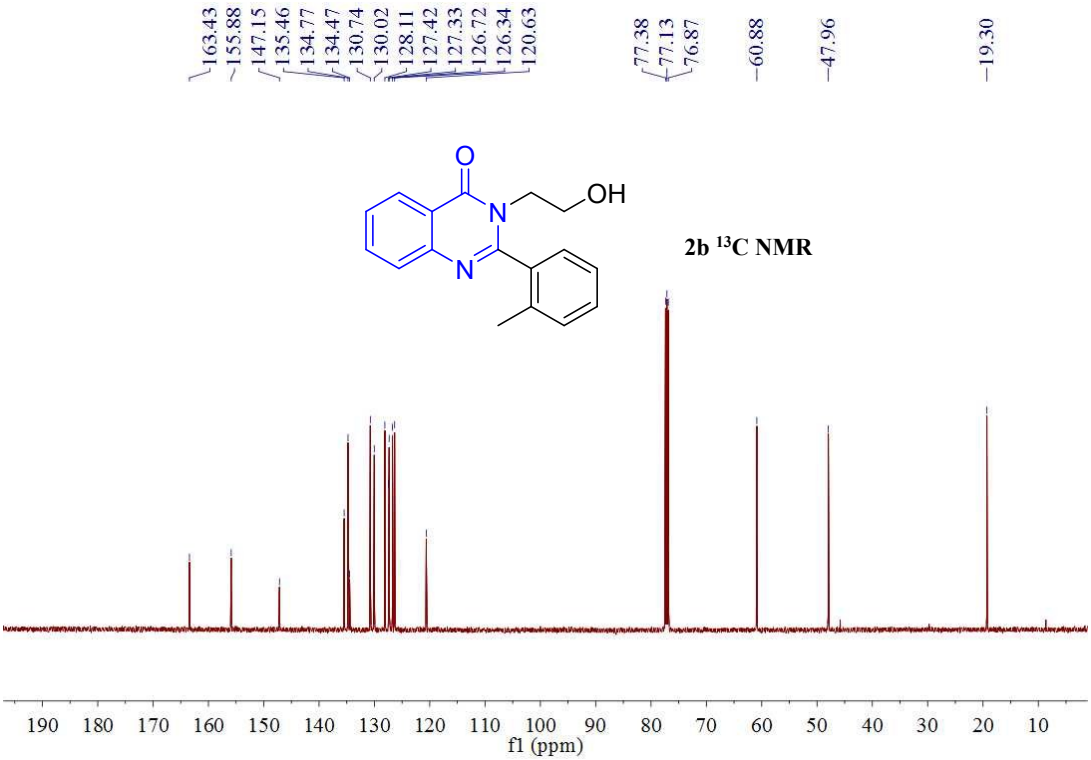
2a ^{1}H NMR



2a ^{13}C NMR



2b ^{1}H NMR



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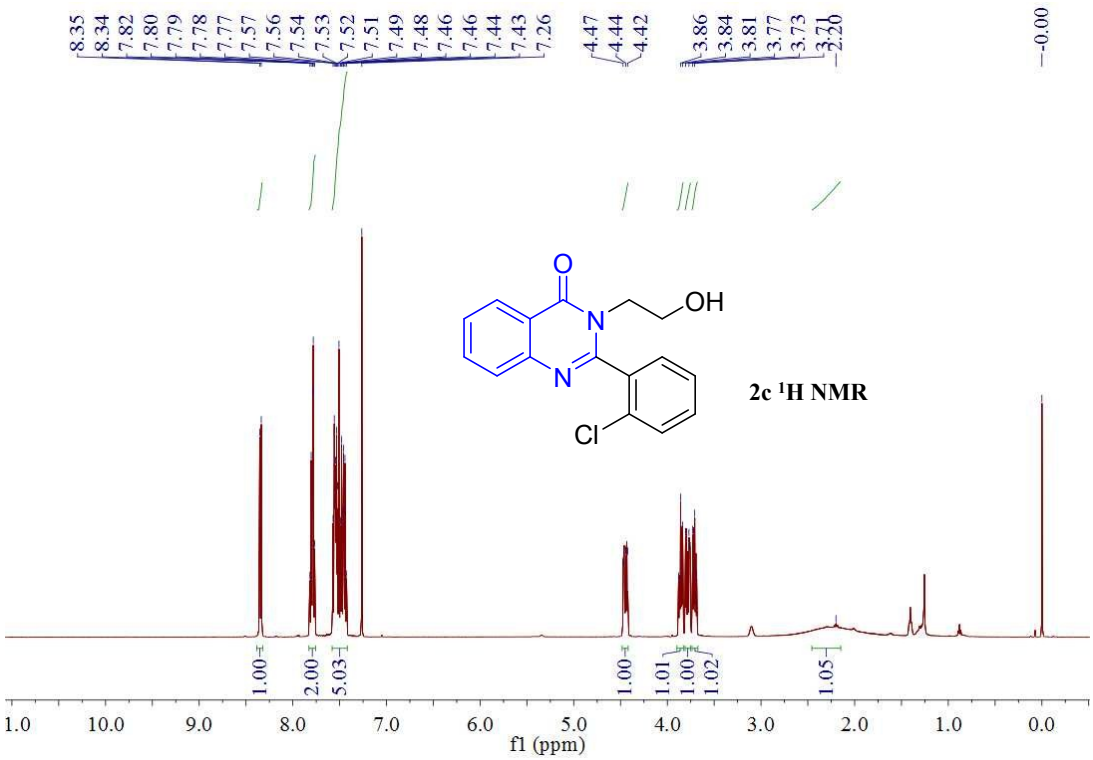
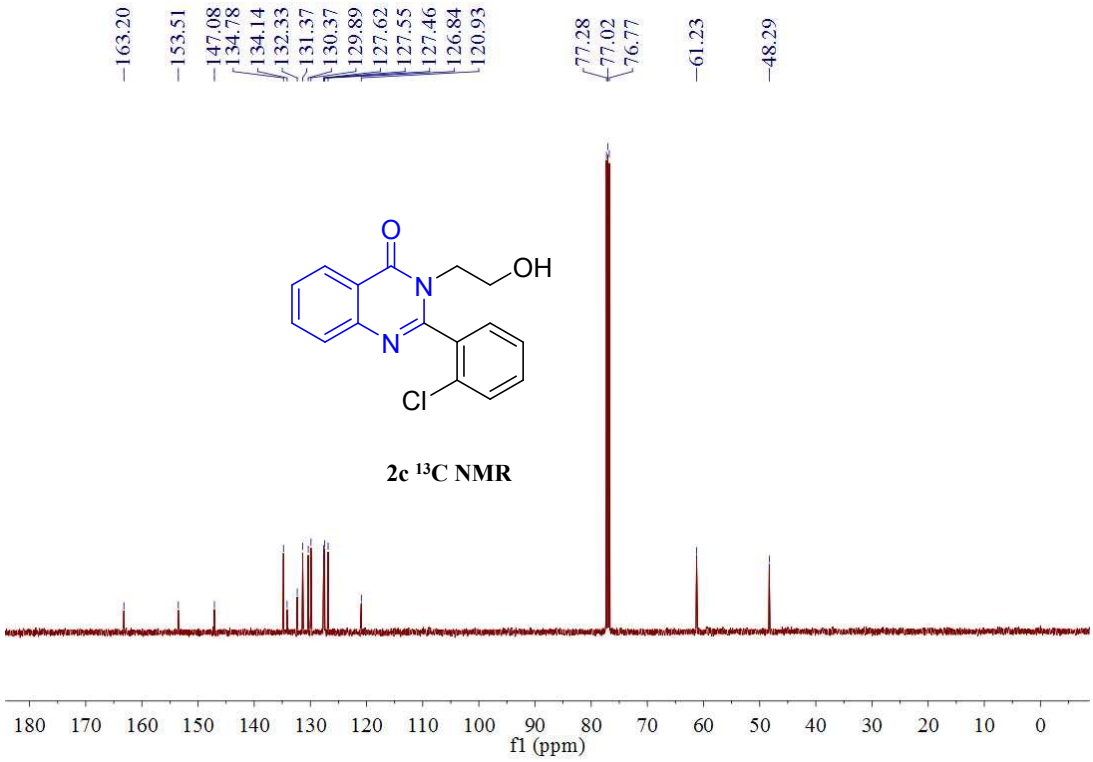


2c ^{1}H NMR



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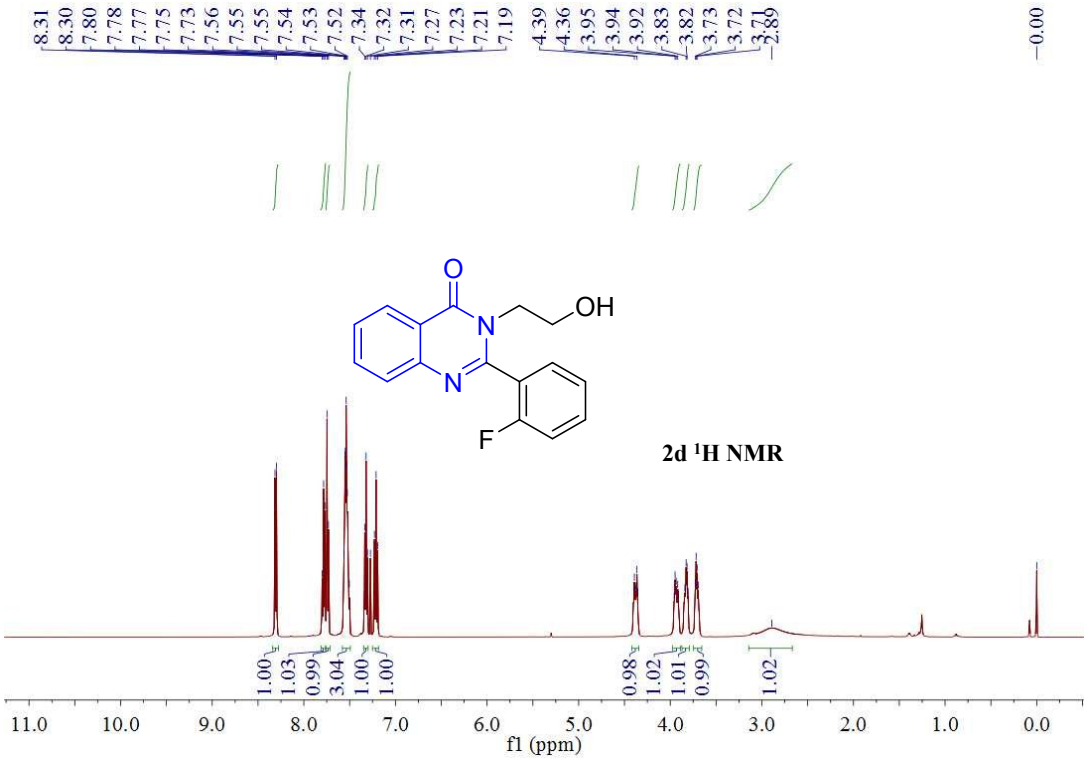
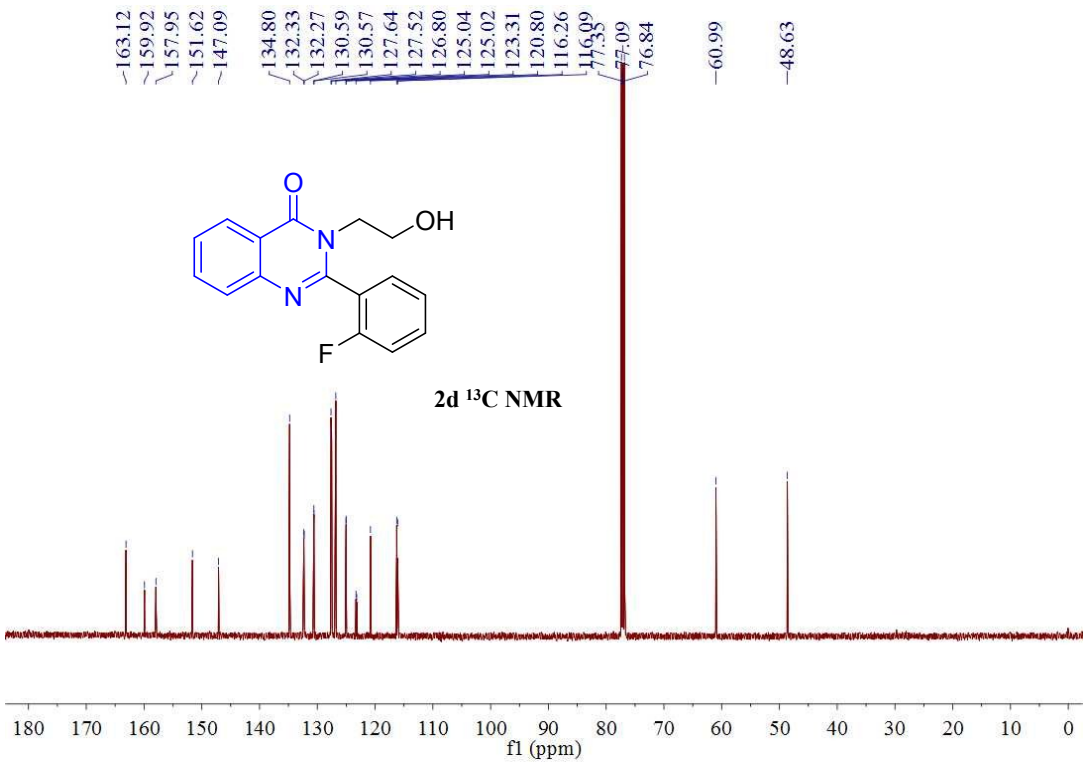


2d ^{1}H NMR



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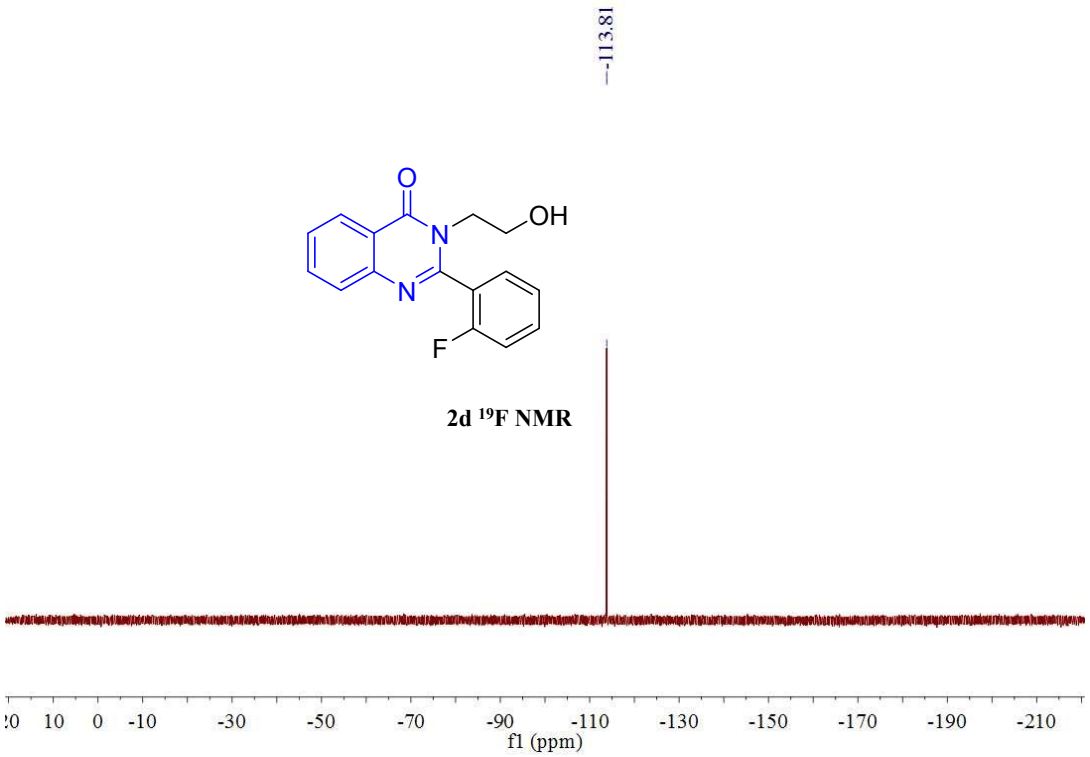
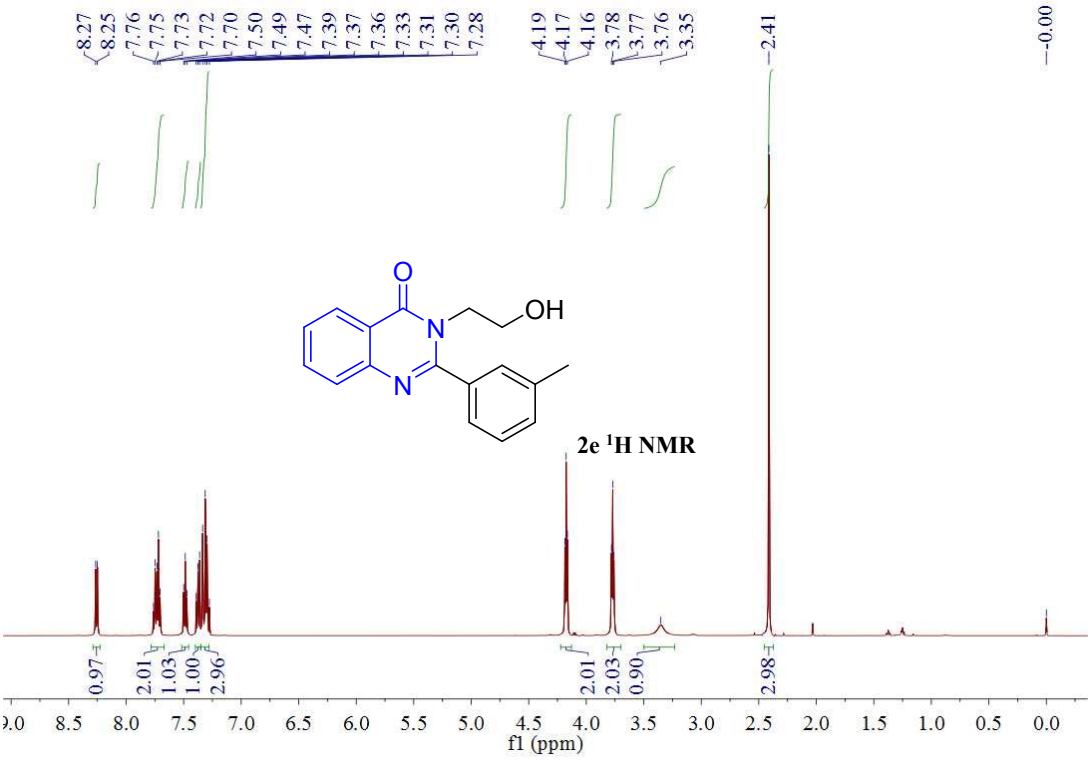
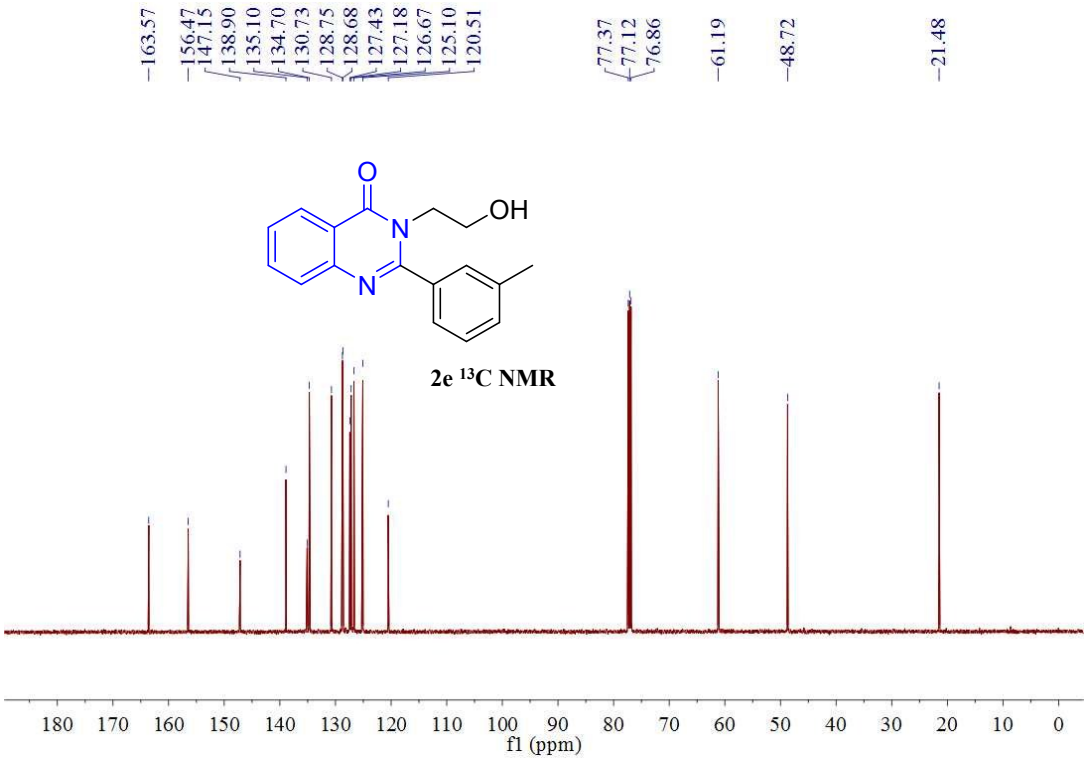


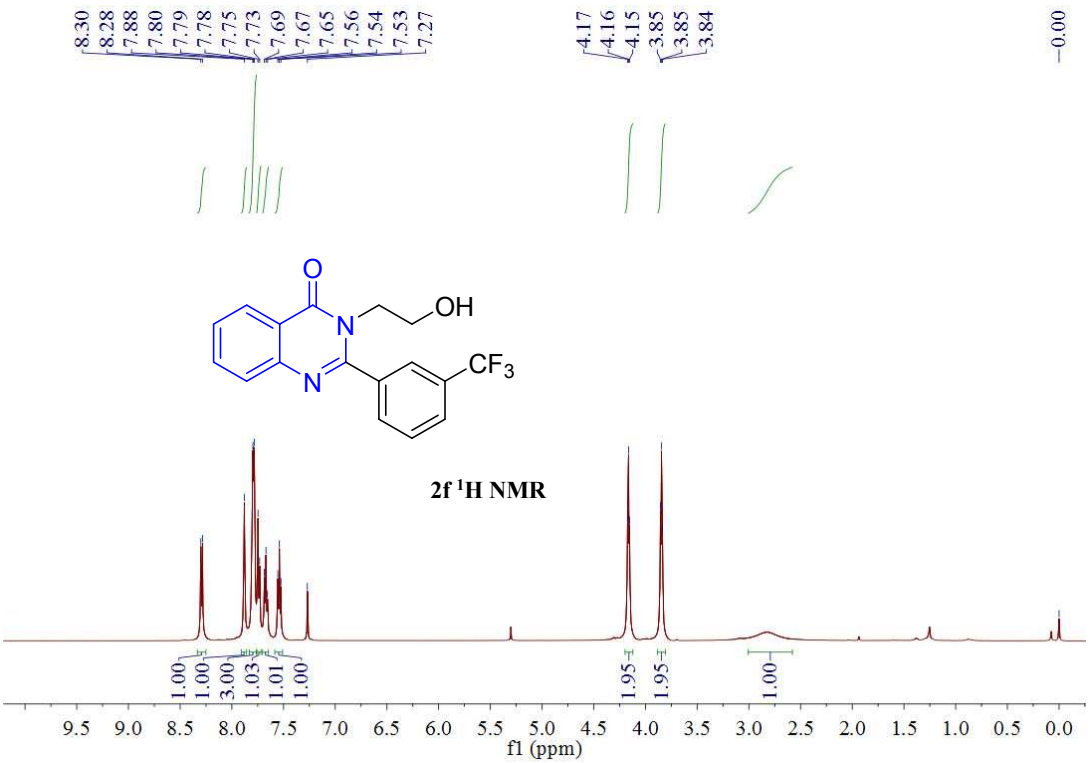
2d ^{19}F NMR



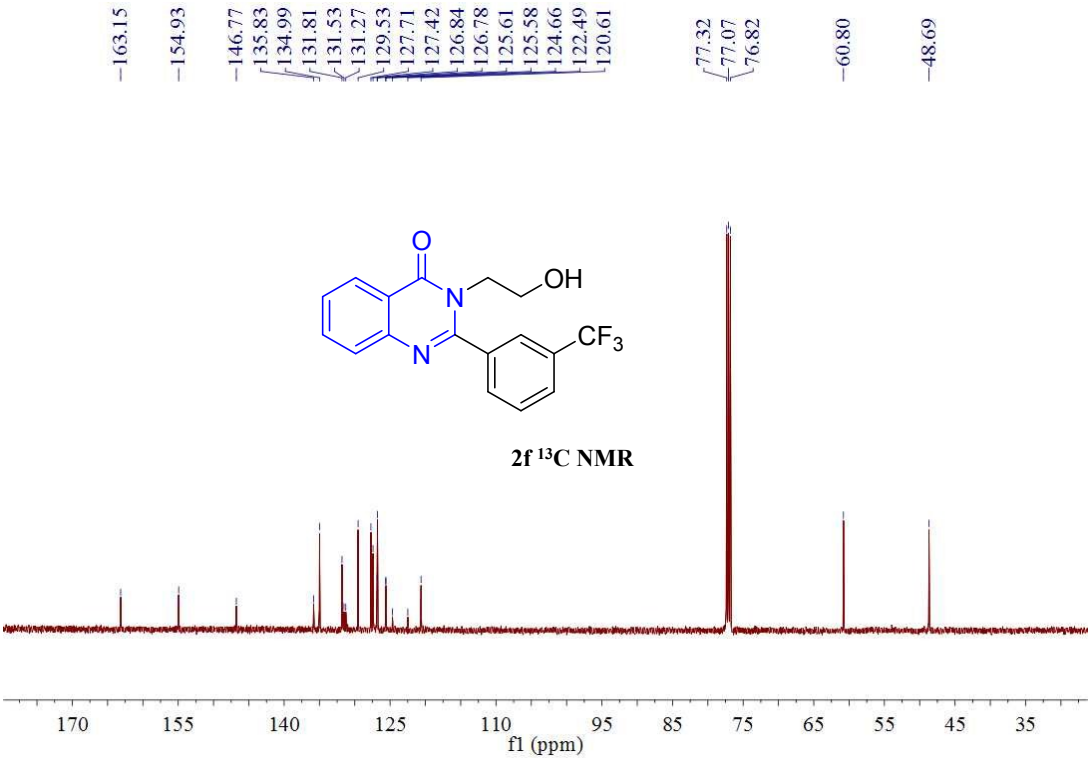
2e ^{1}H NMR



2e ^{13}C NMR



2f ^{1}H NMR



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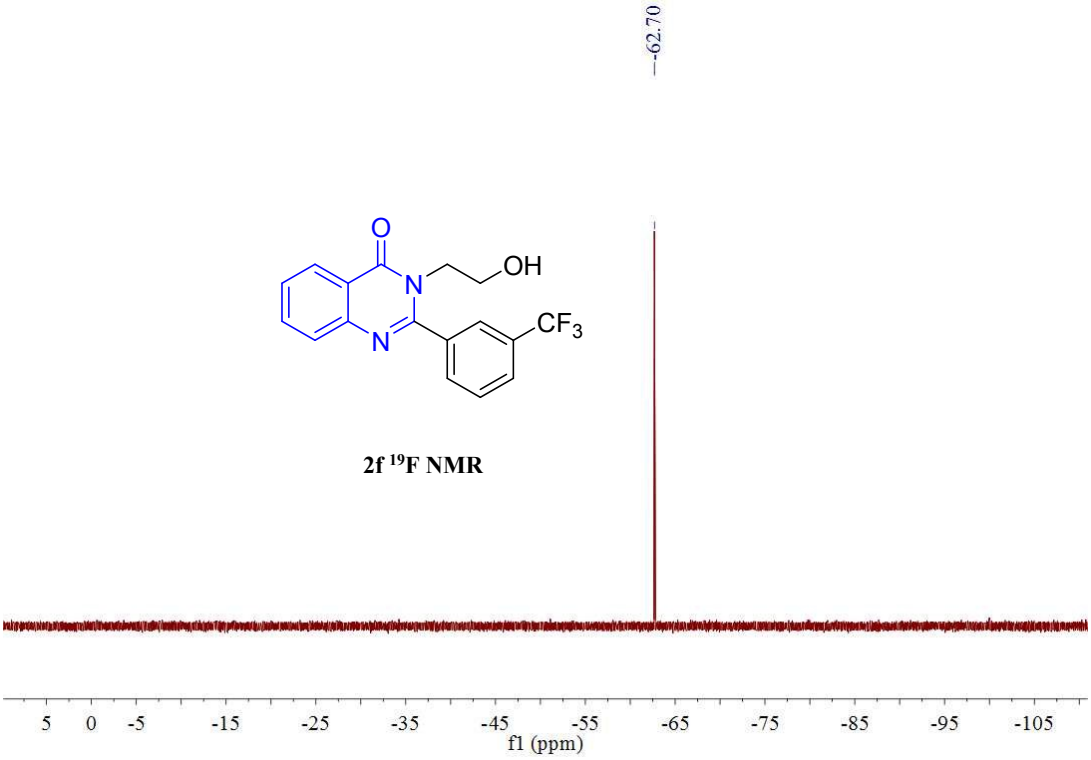
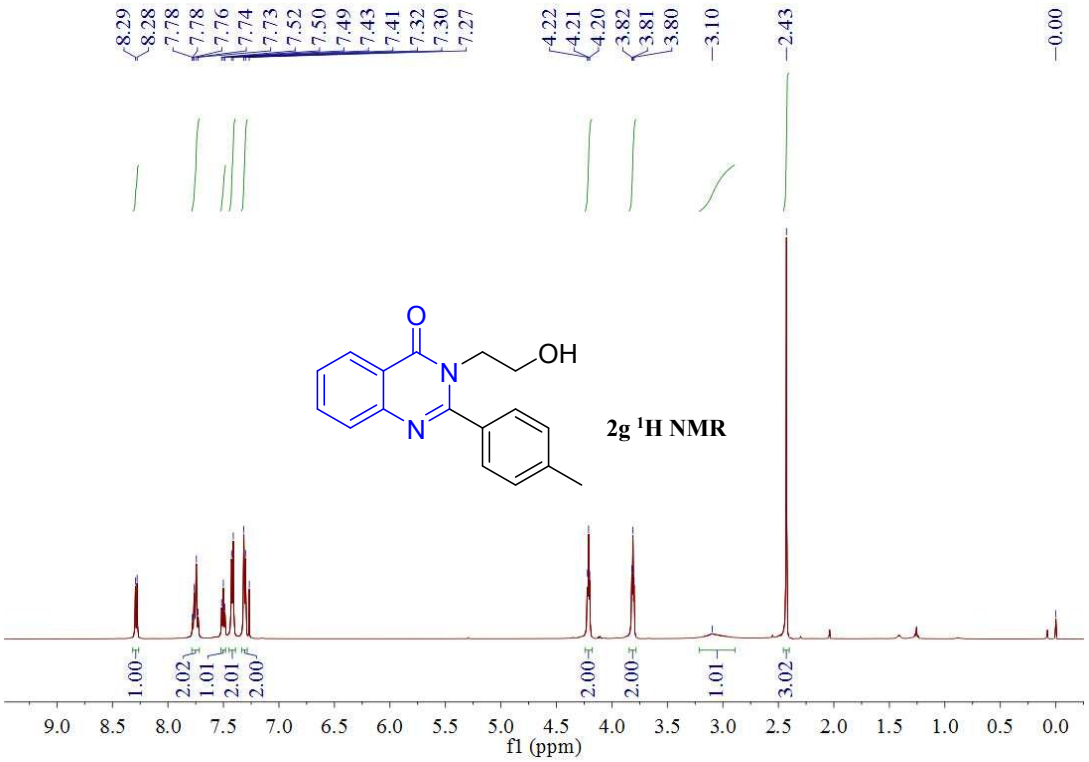


2f ^{19}F NMR



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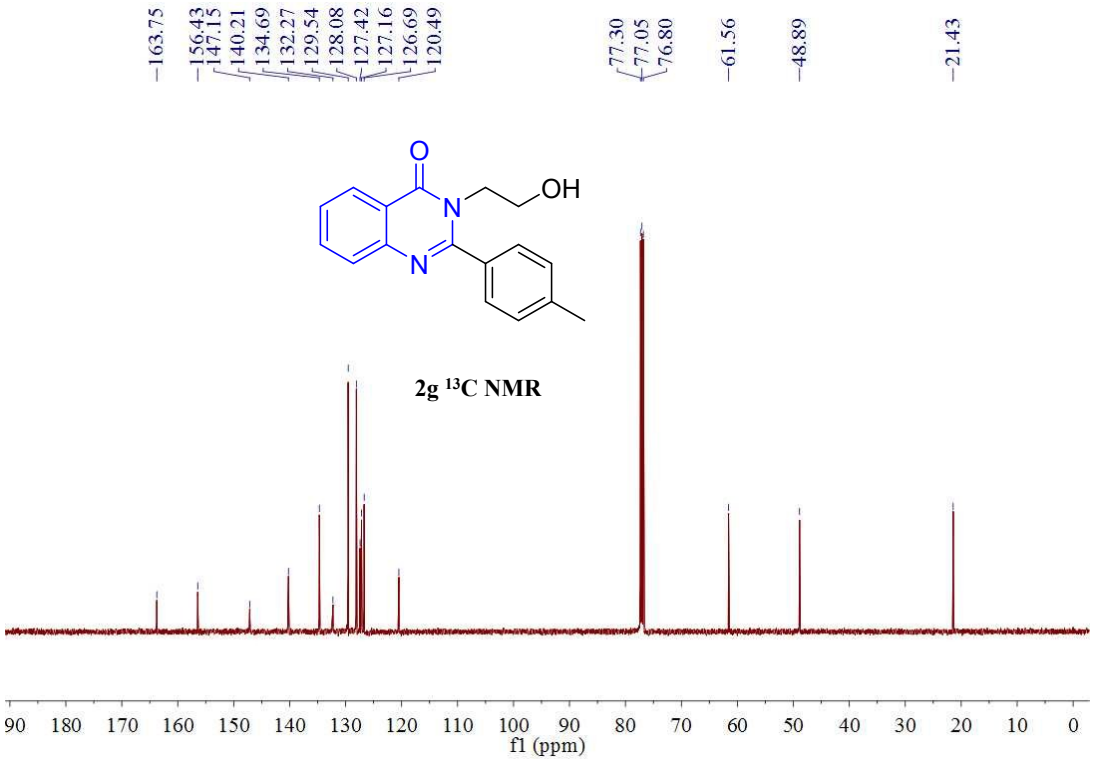
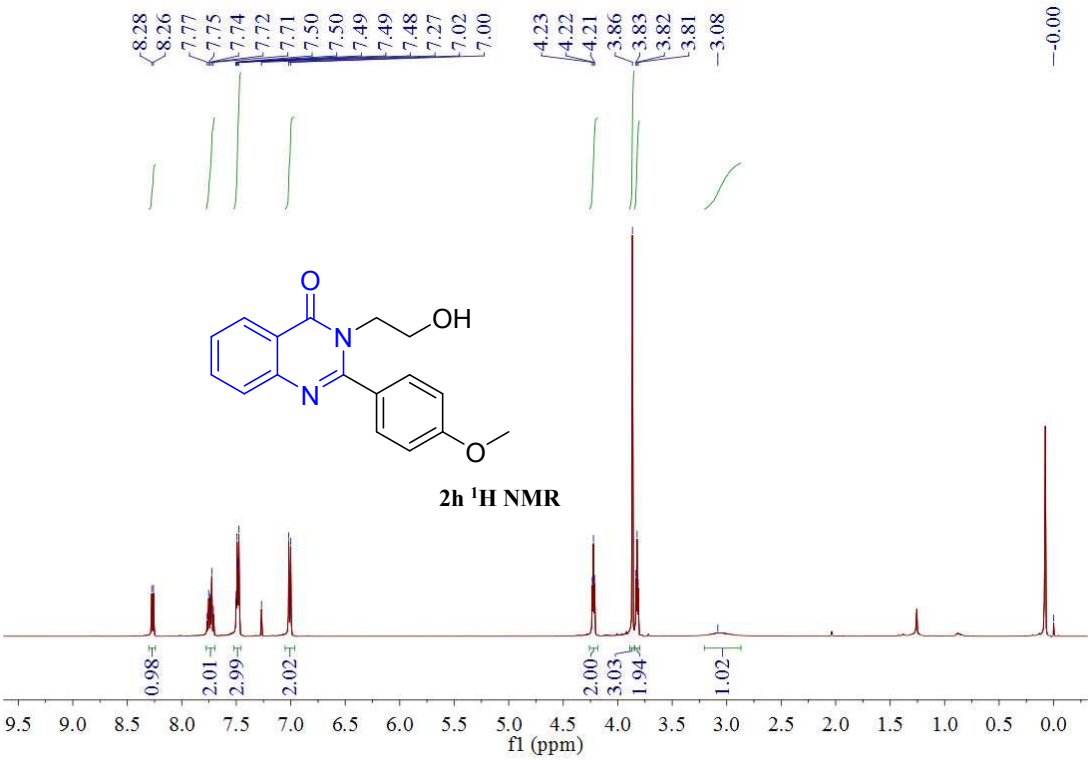
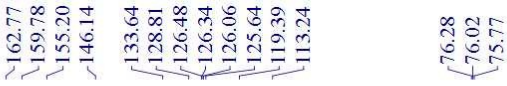
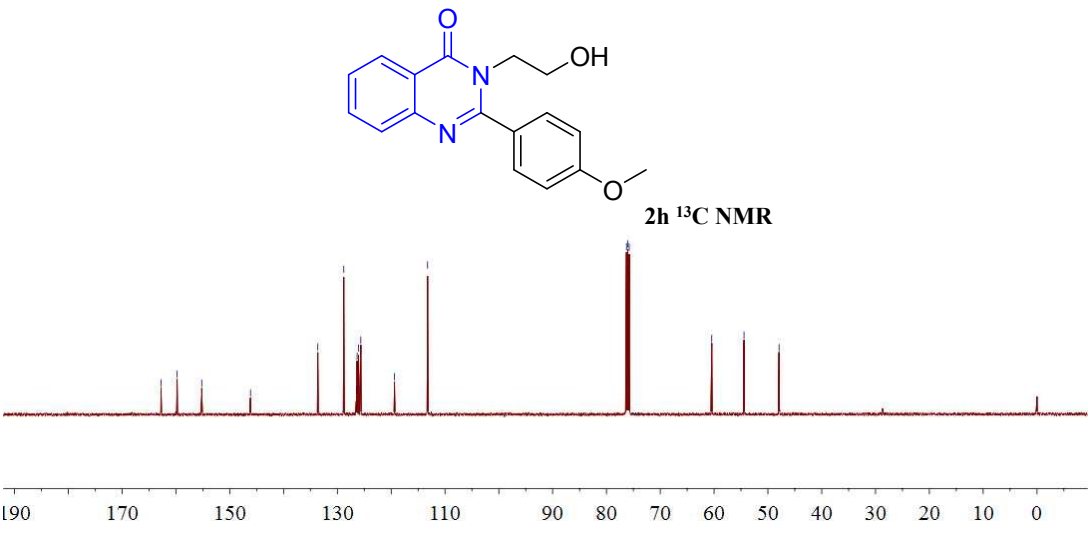


2g ^{13}C NMR



2h ^{1}H NMR





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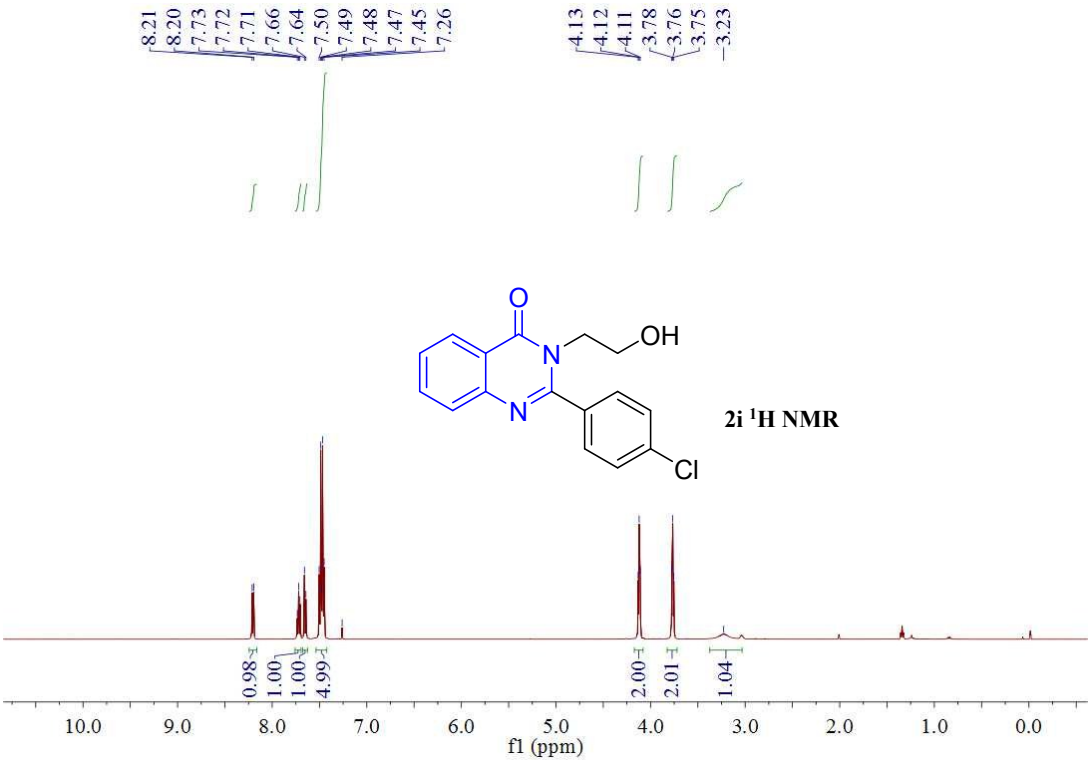

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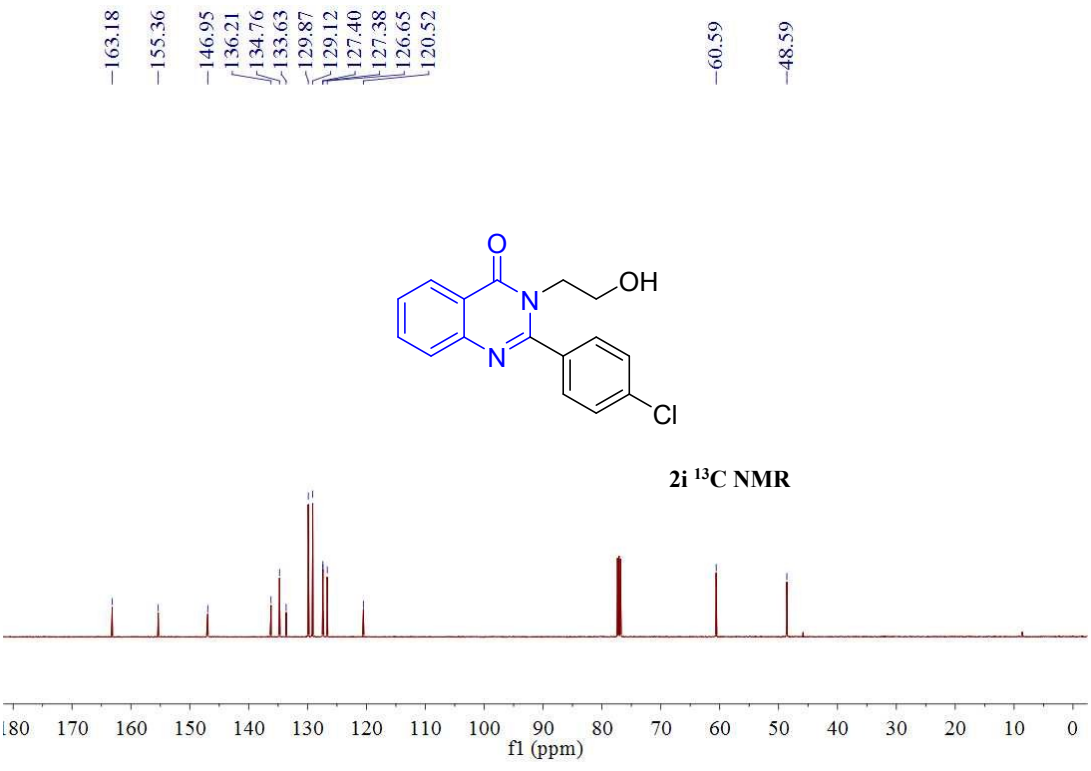

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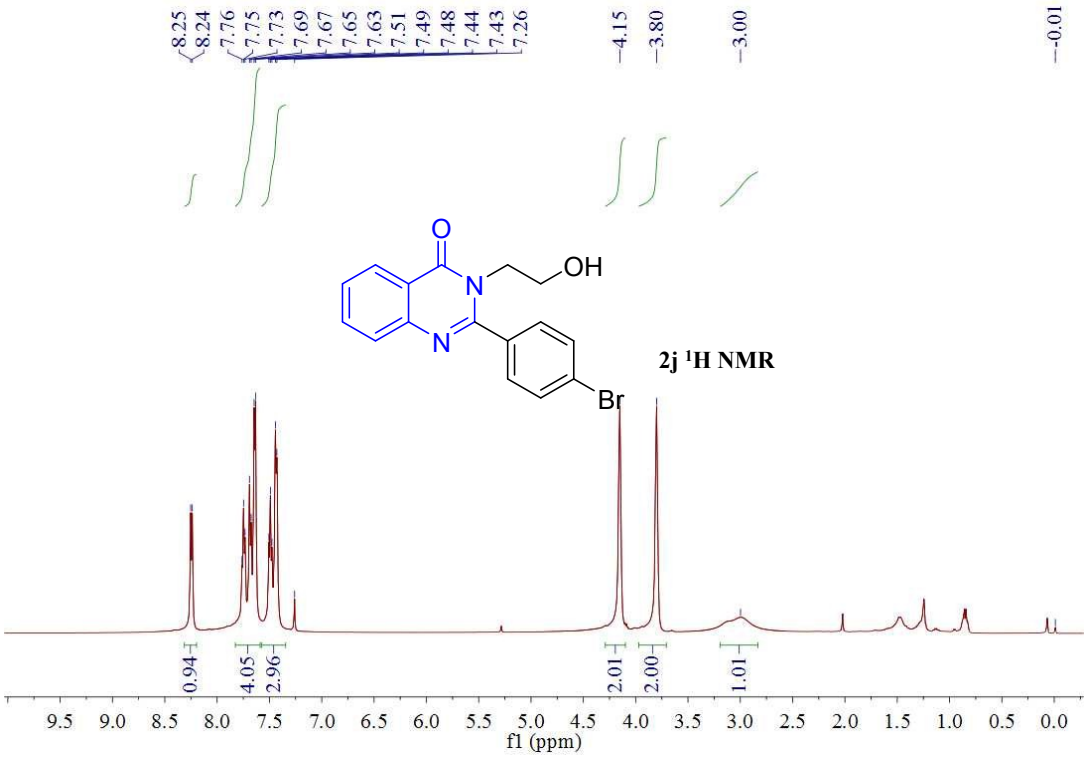

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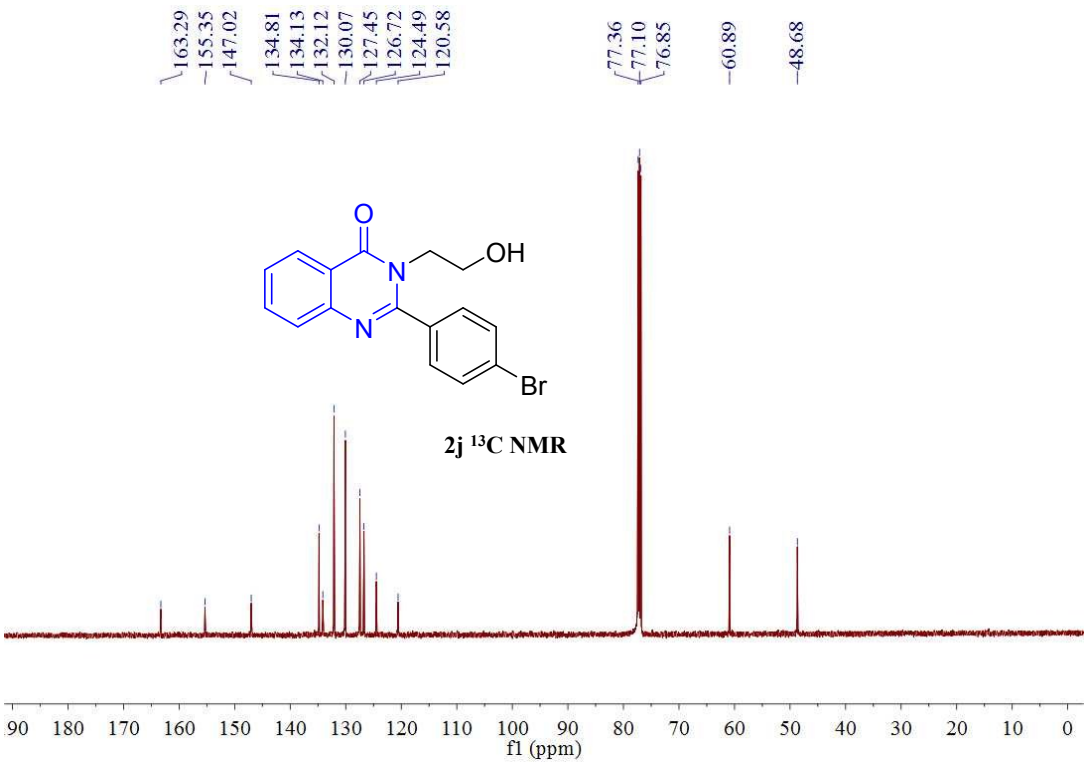

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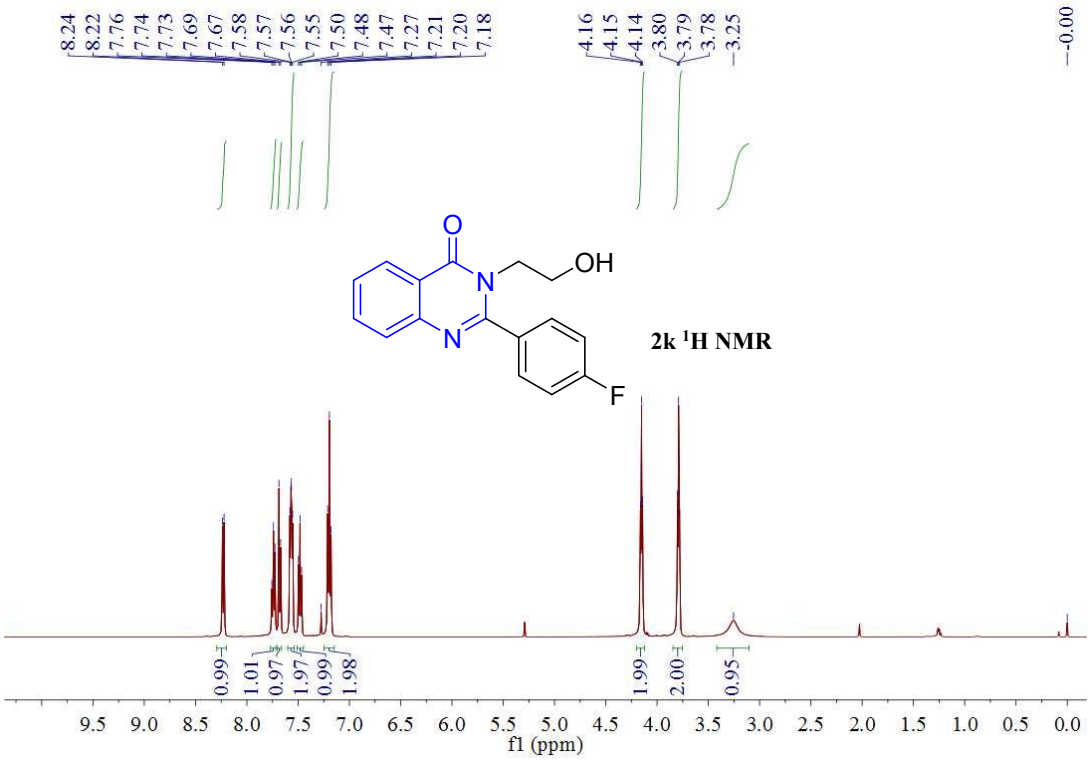
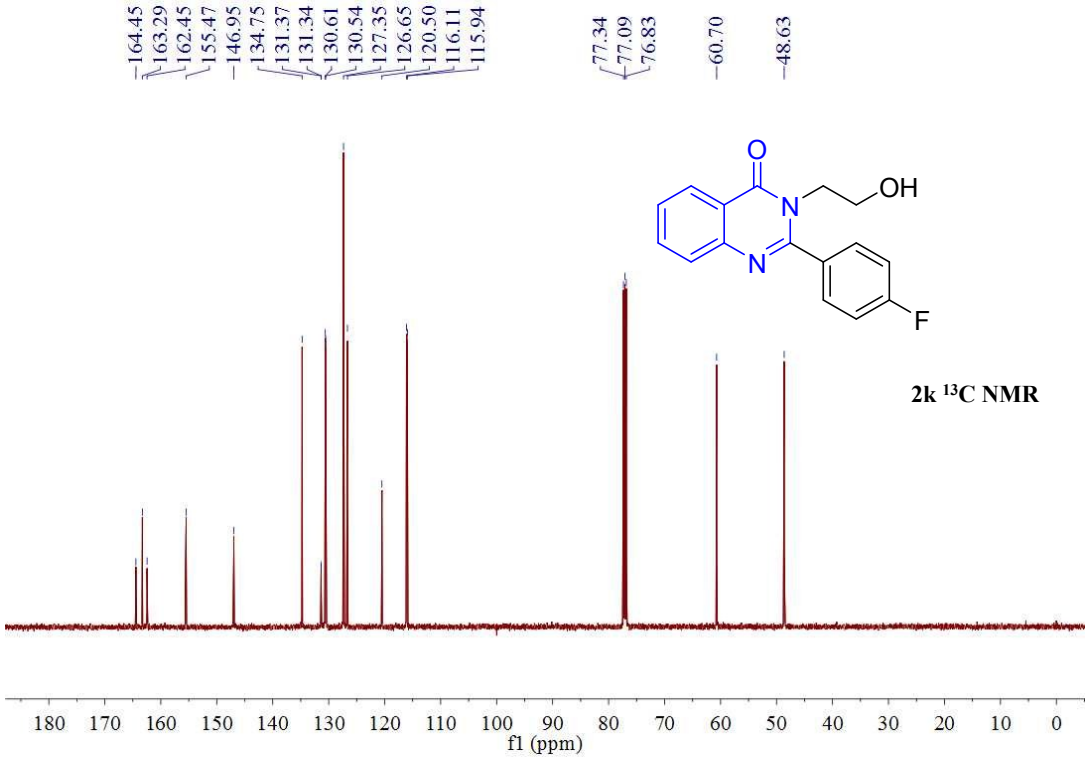


2k ^{1}H NMR



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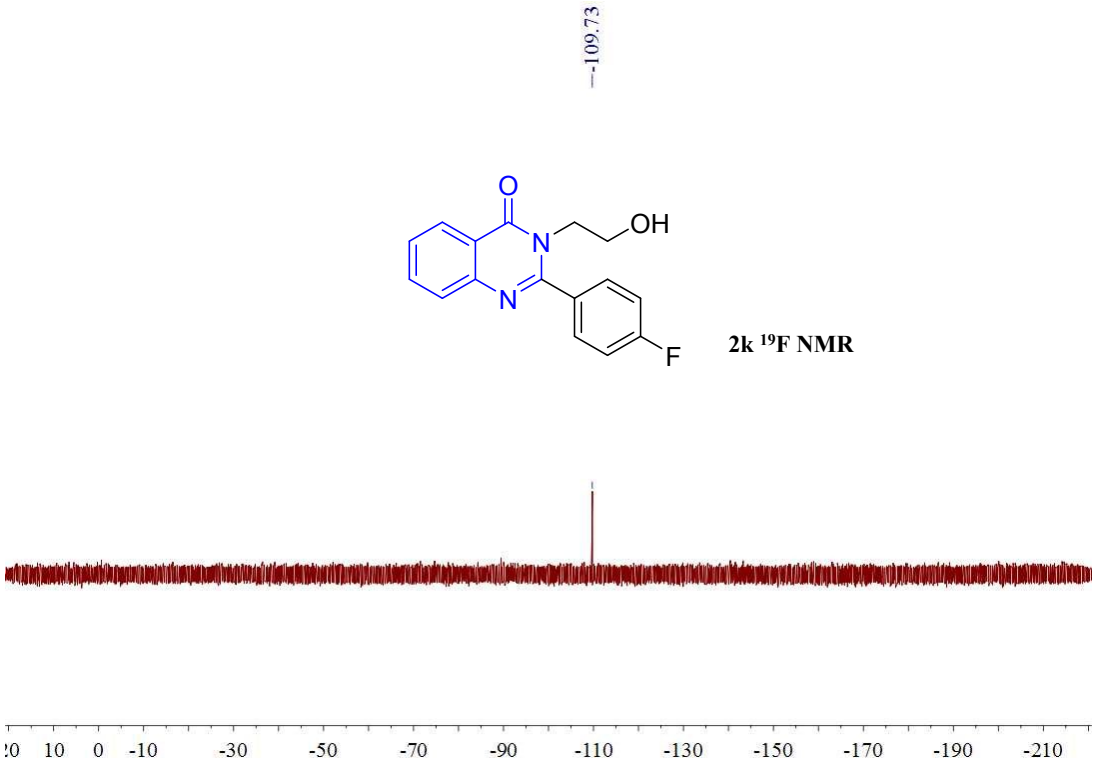
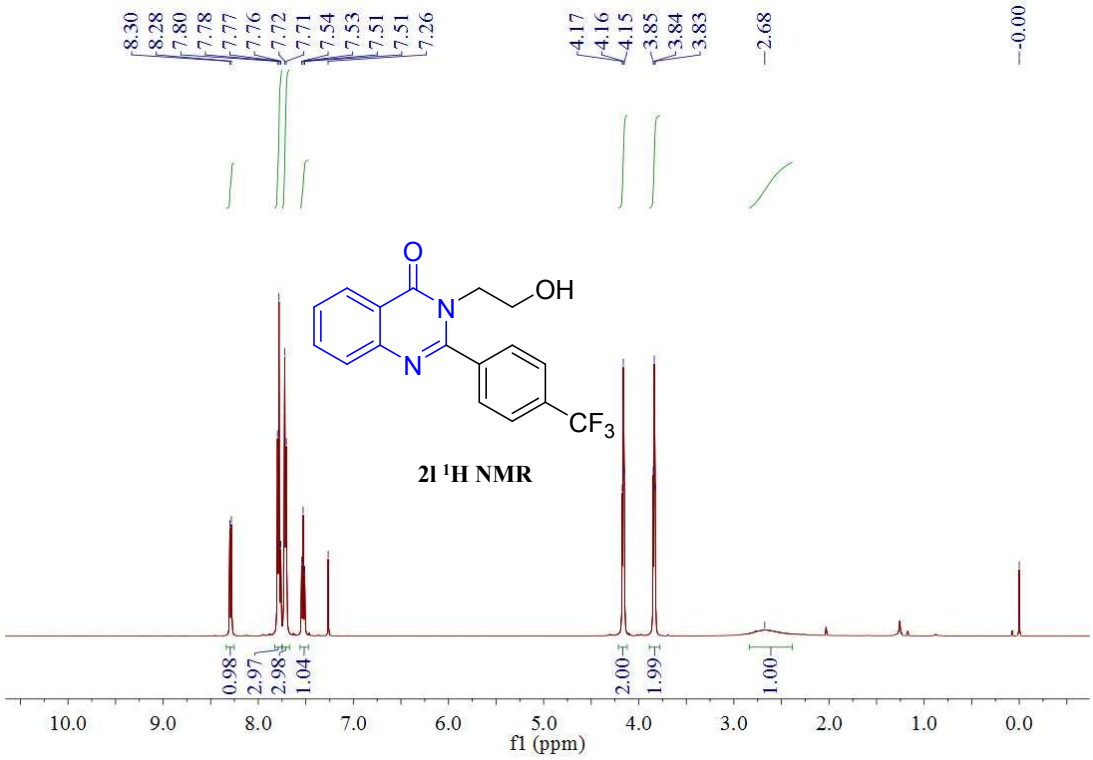
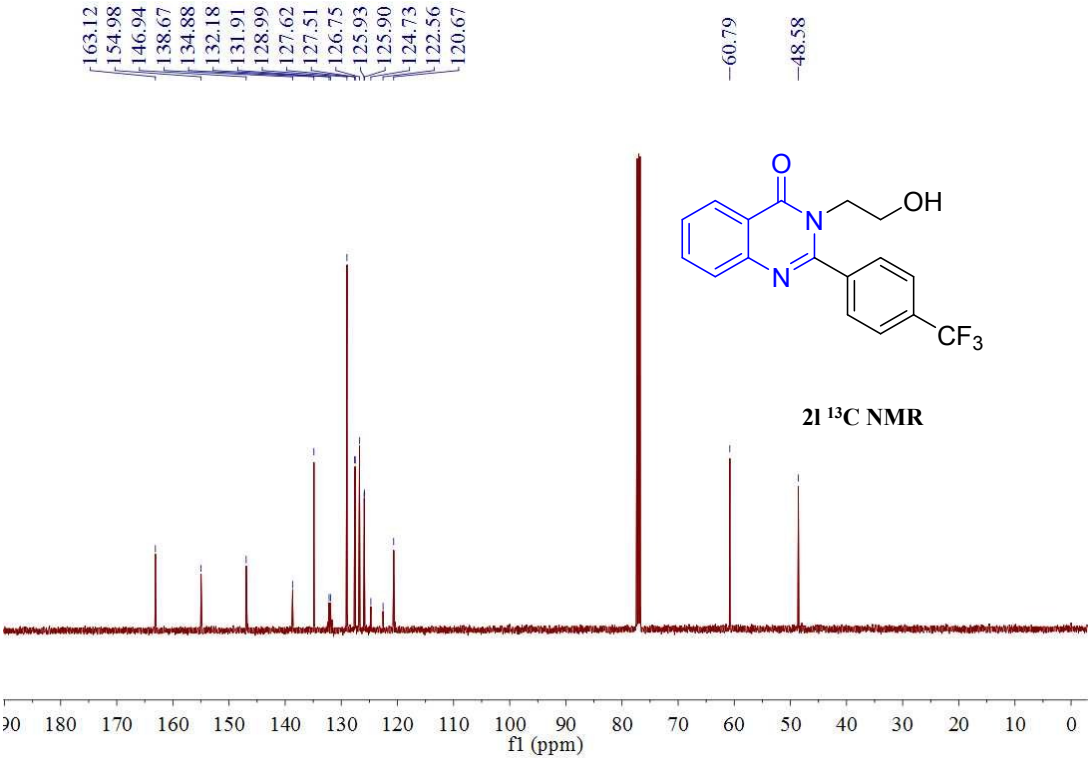


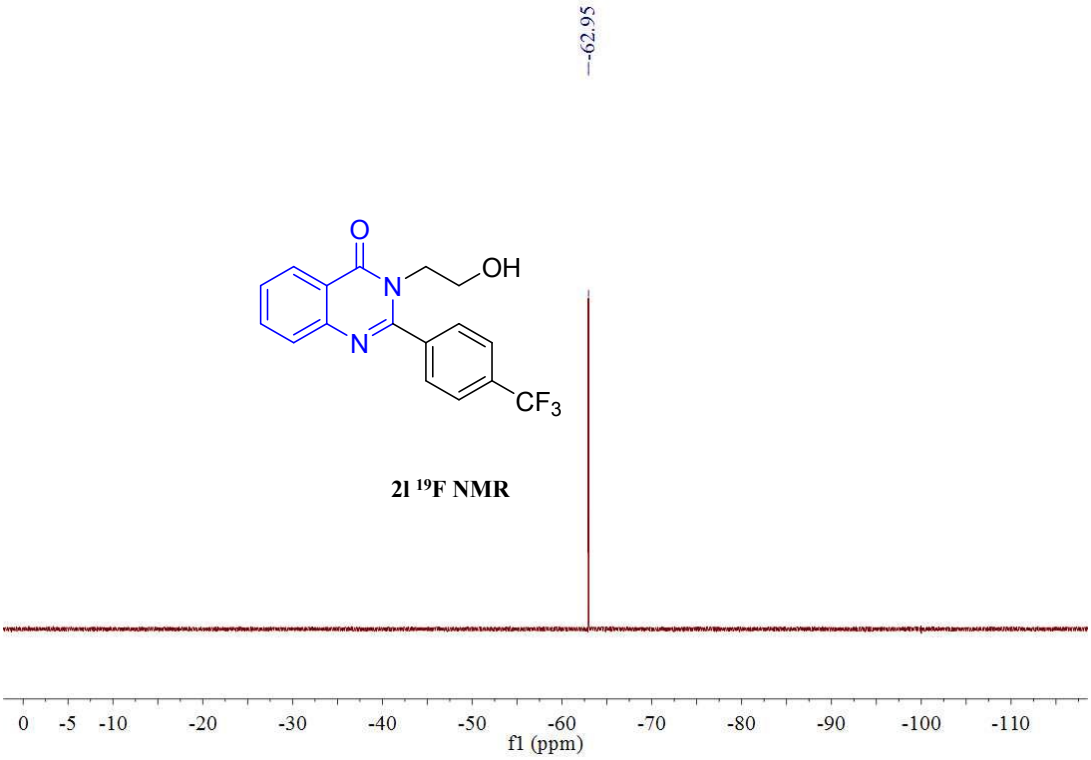
2k ^{19}F NMR



2l ^{1}H NMR



2l ^{13}C NMR



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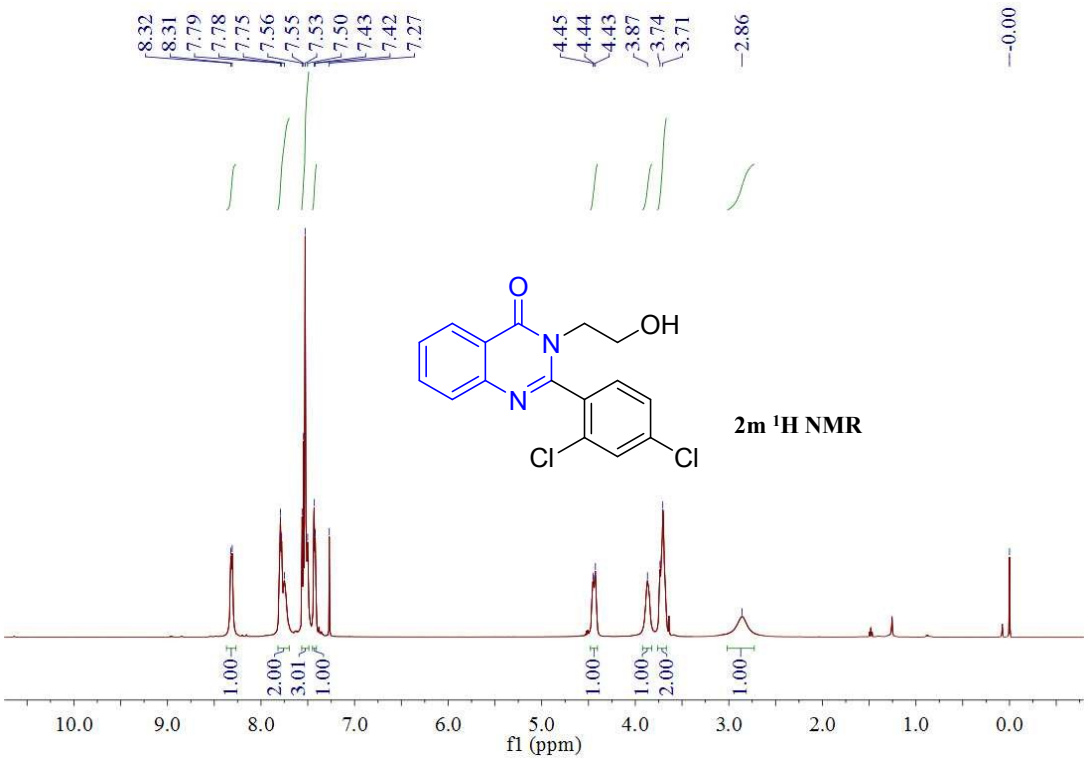

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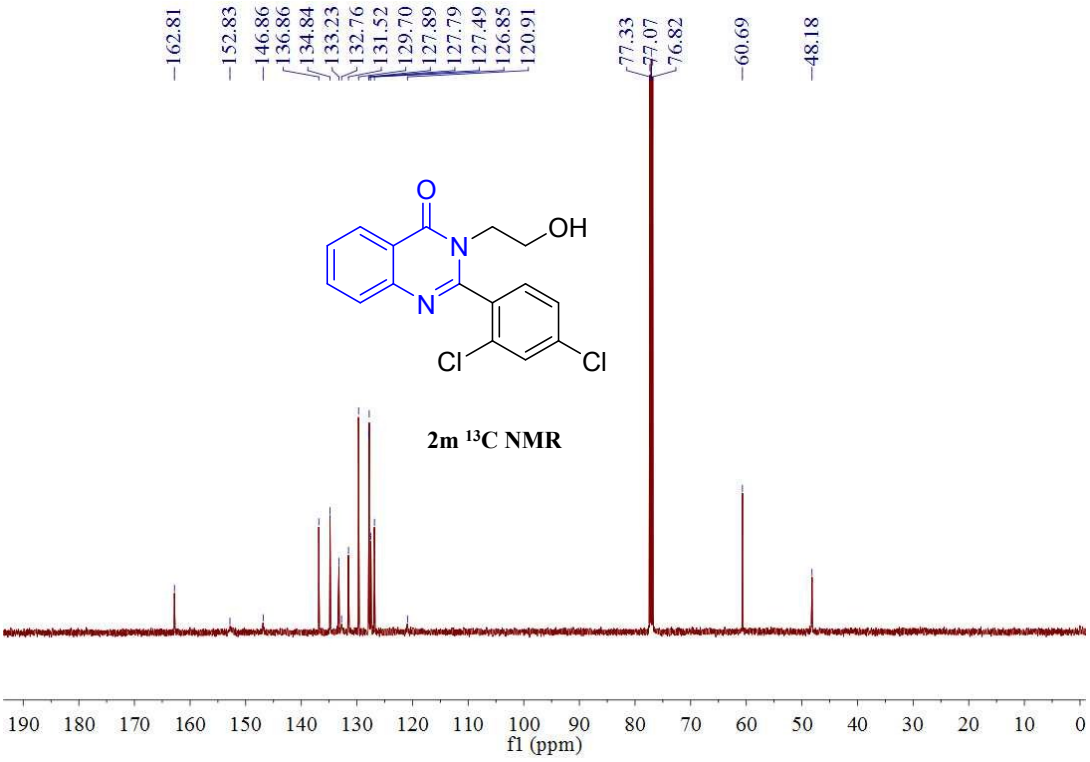
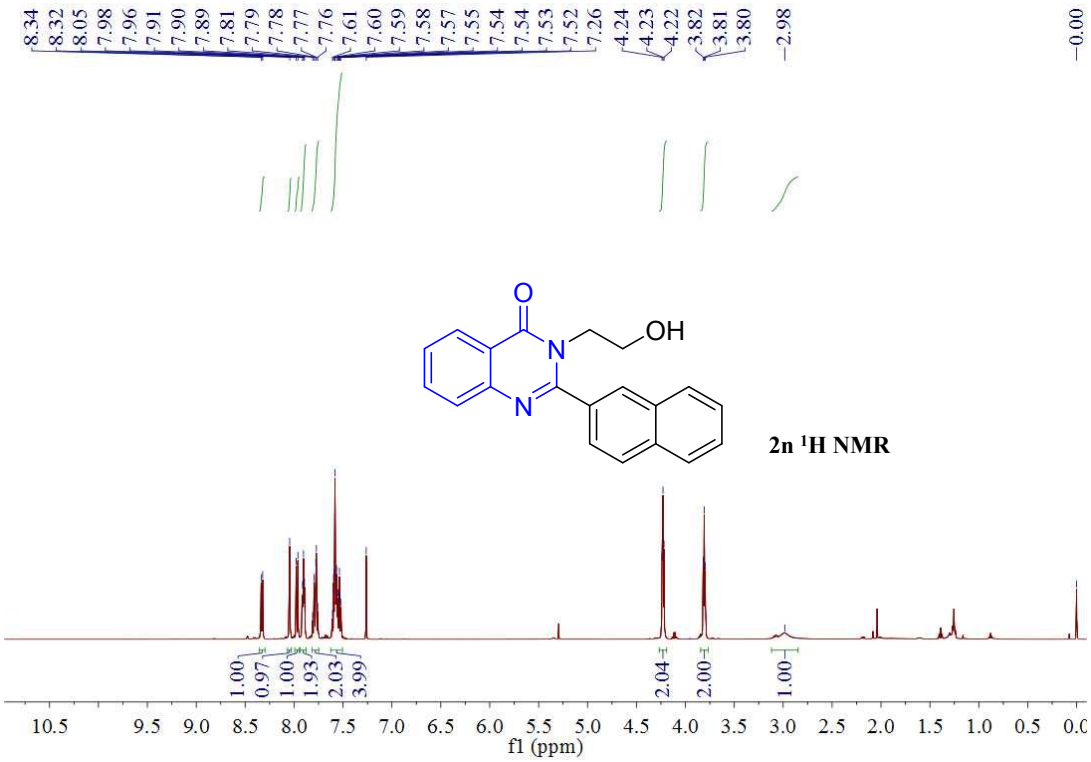
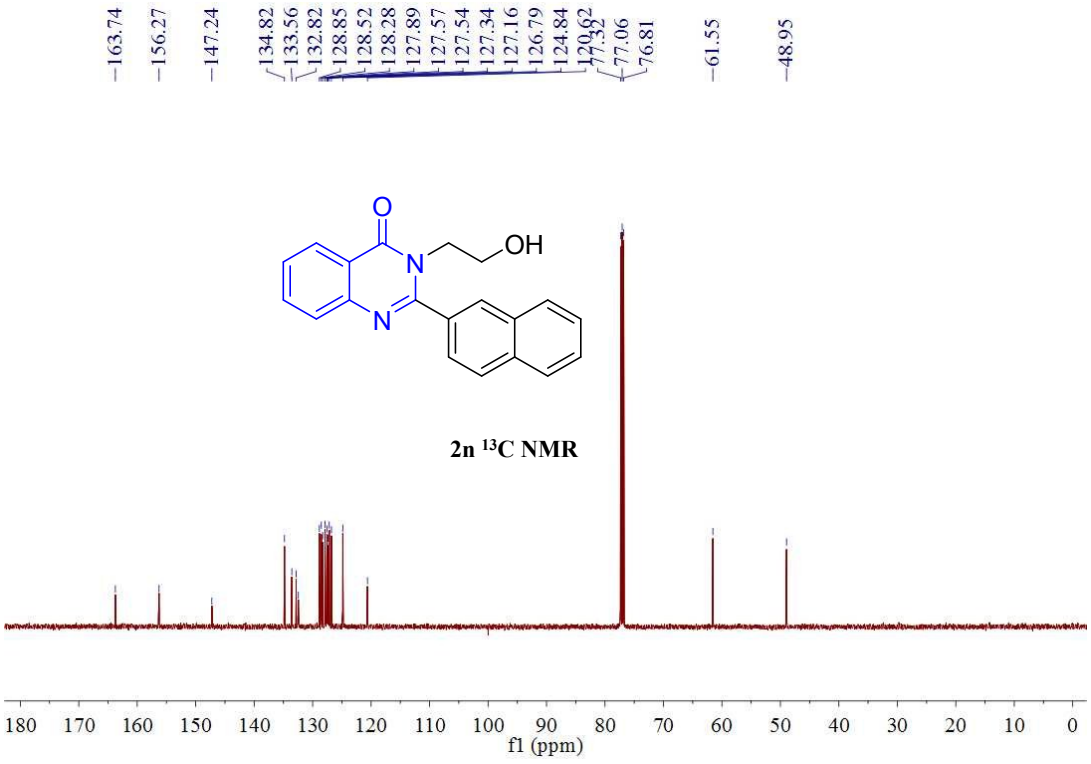


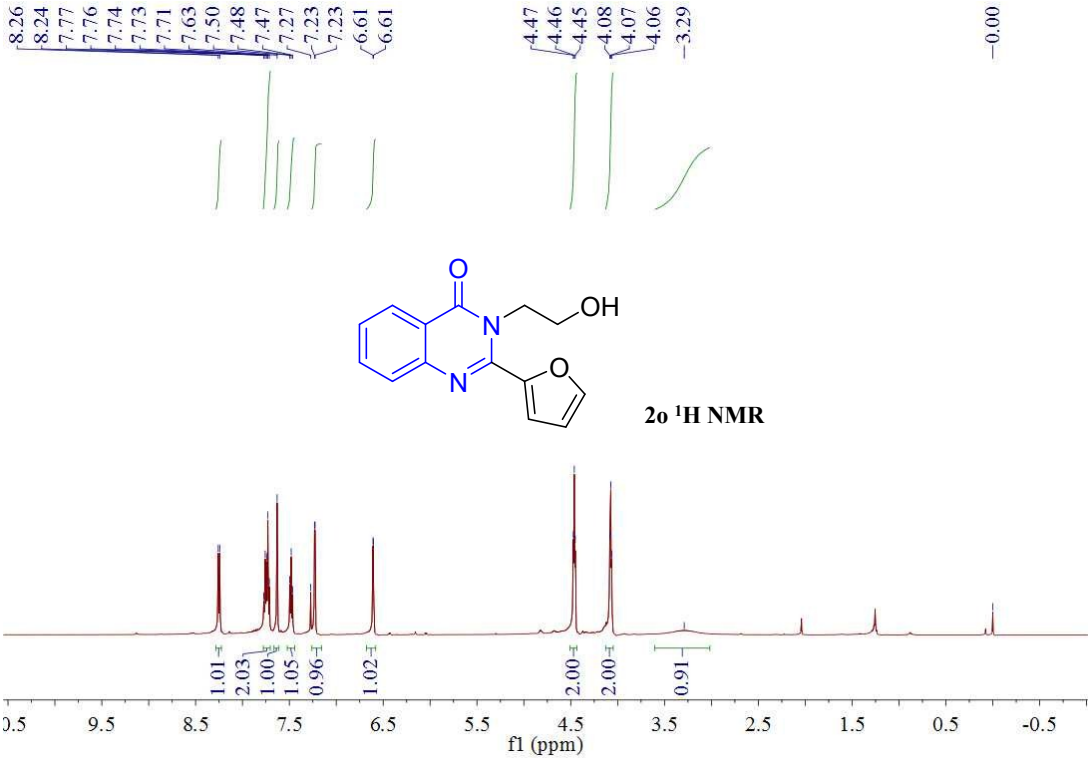
2m ^{13}C NMR



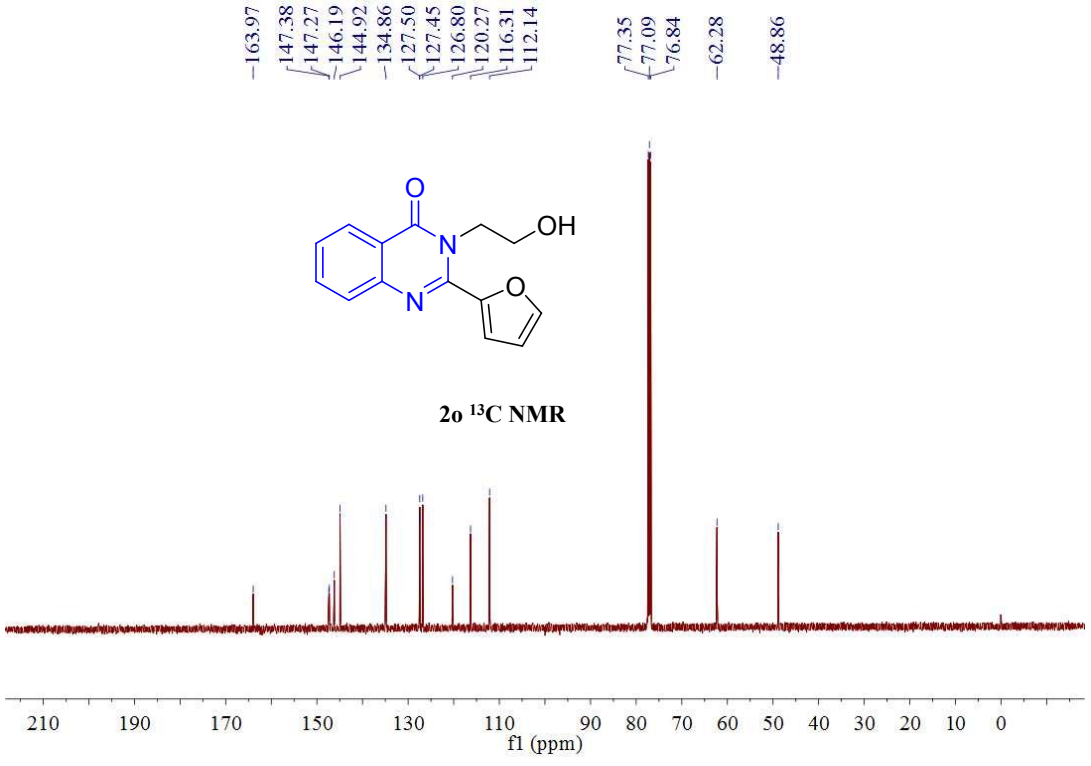
2n ^{1}H NMR



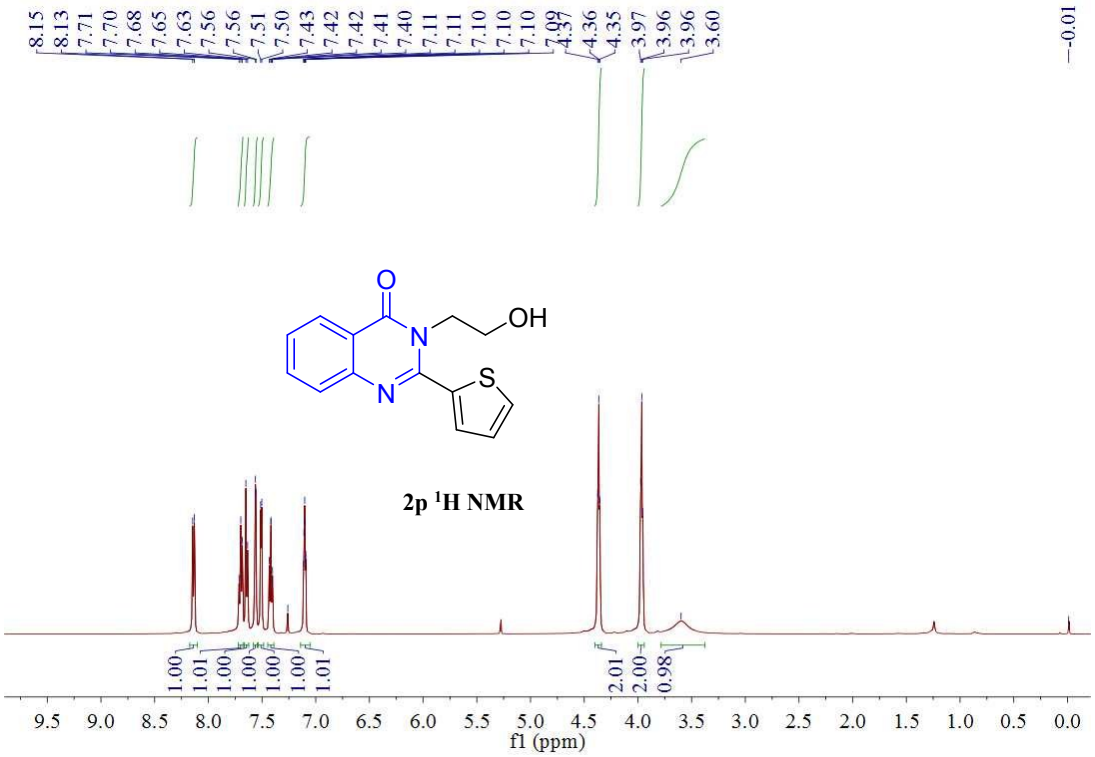
2n ^{13}C NMR



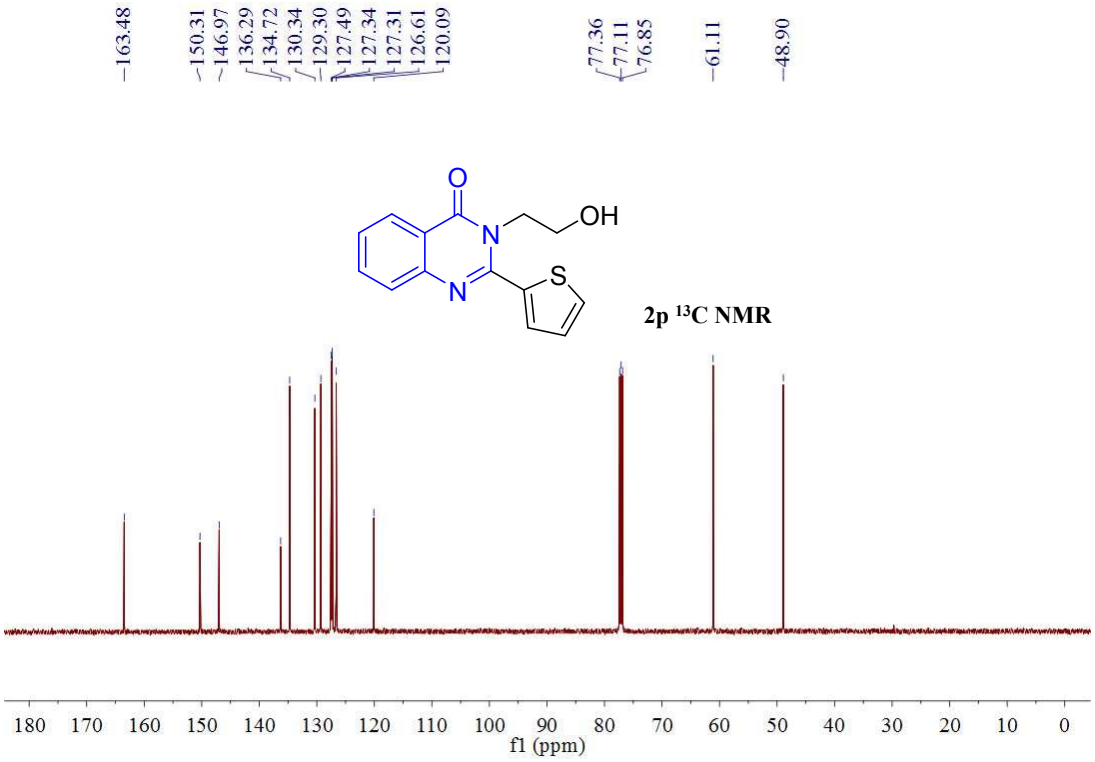
2o ^{1}H NMR



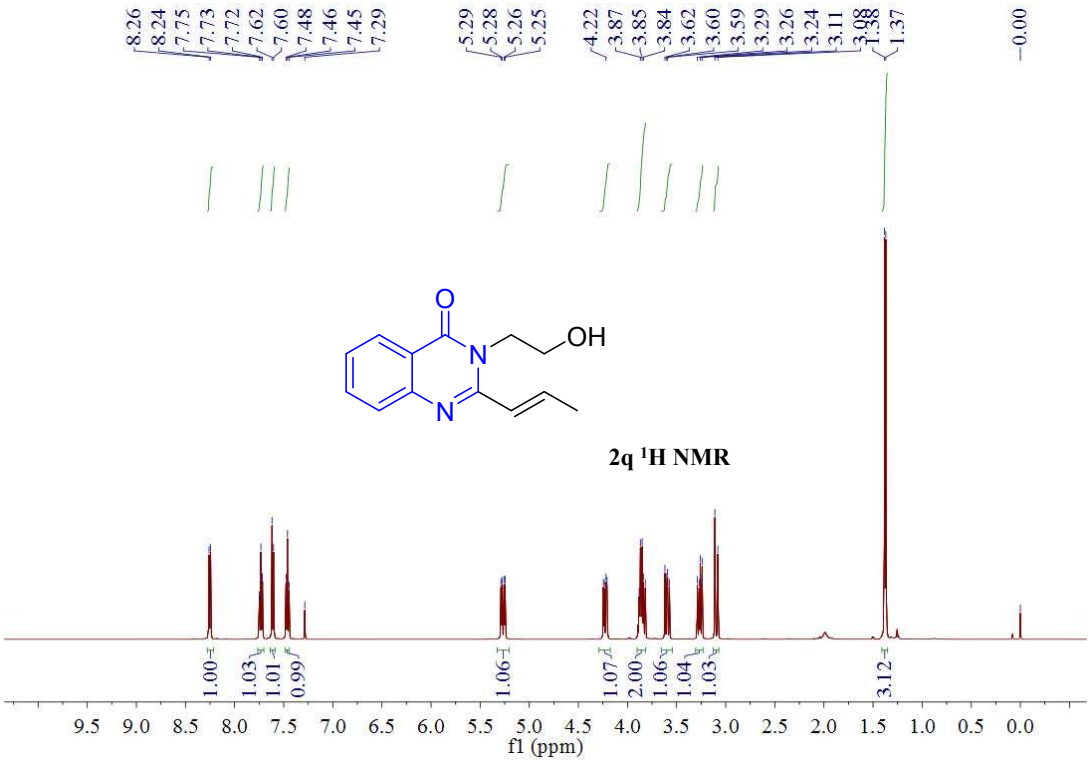
2o ^{13}C NMR



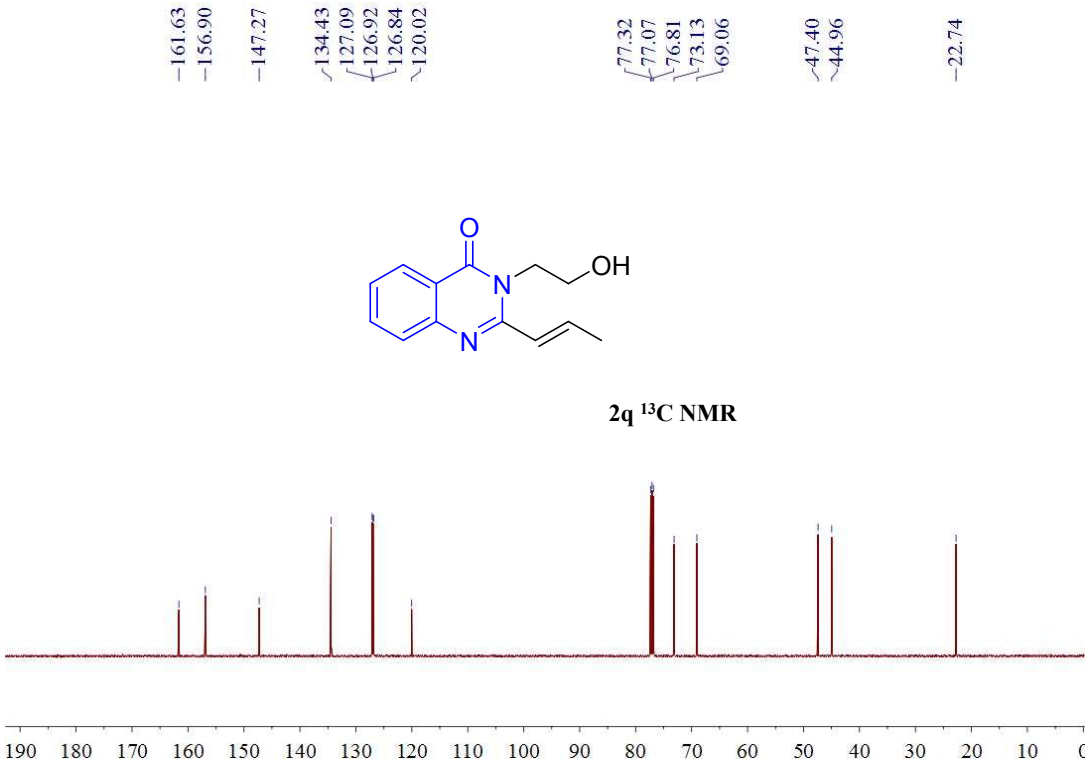
2p ^{1}H NMR



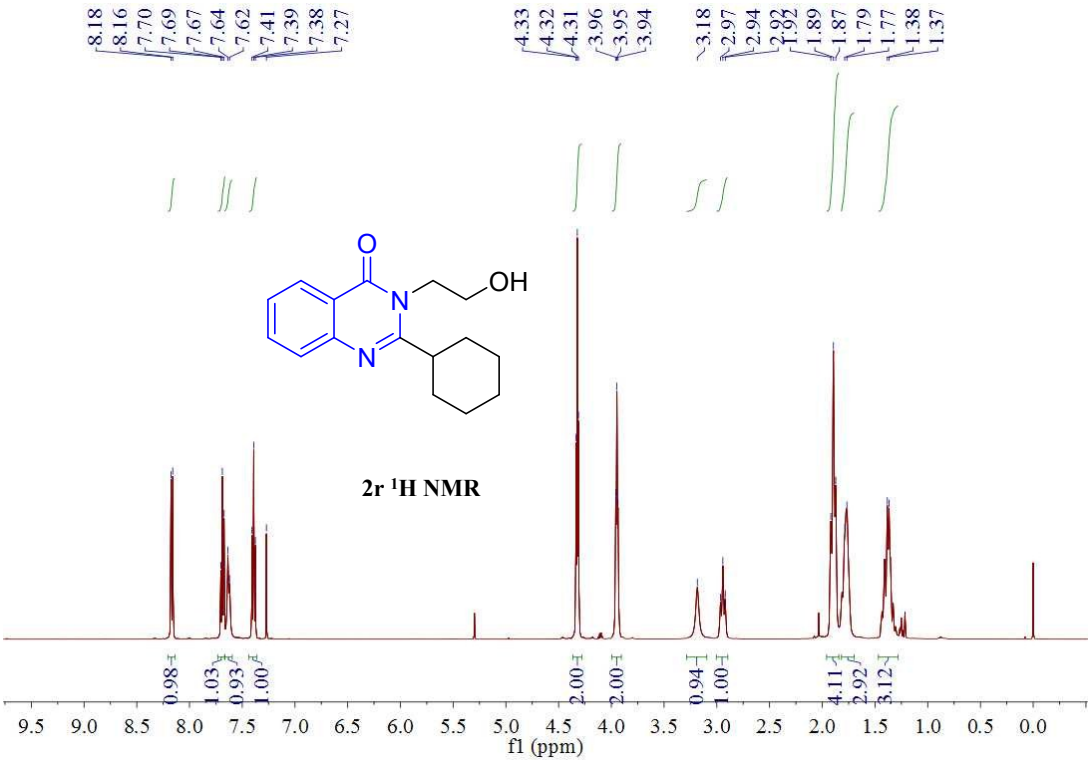
2p ^{13}C NMR



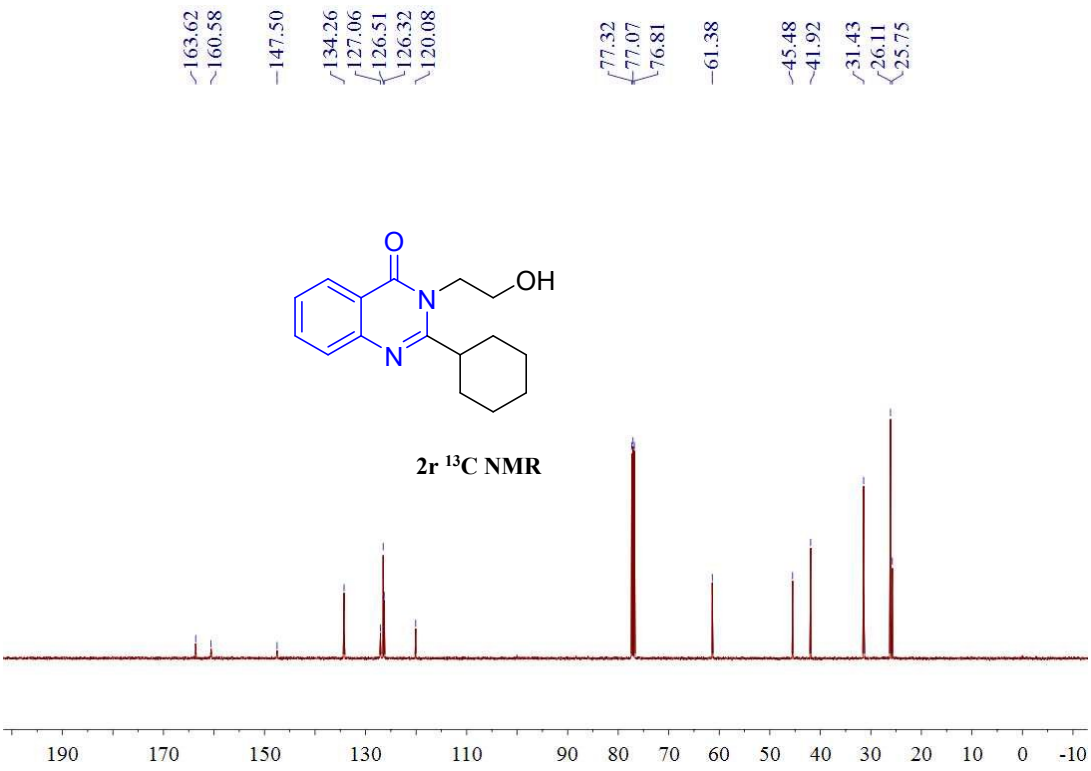
2q ^{1}H NMR



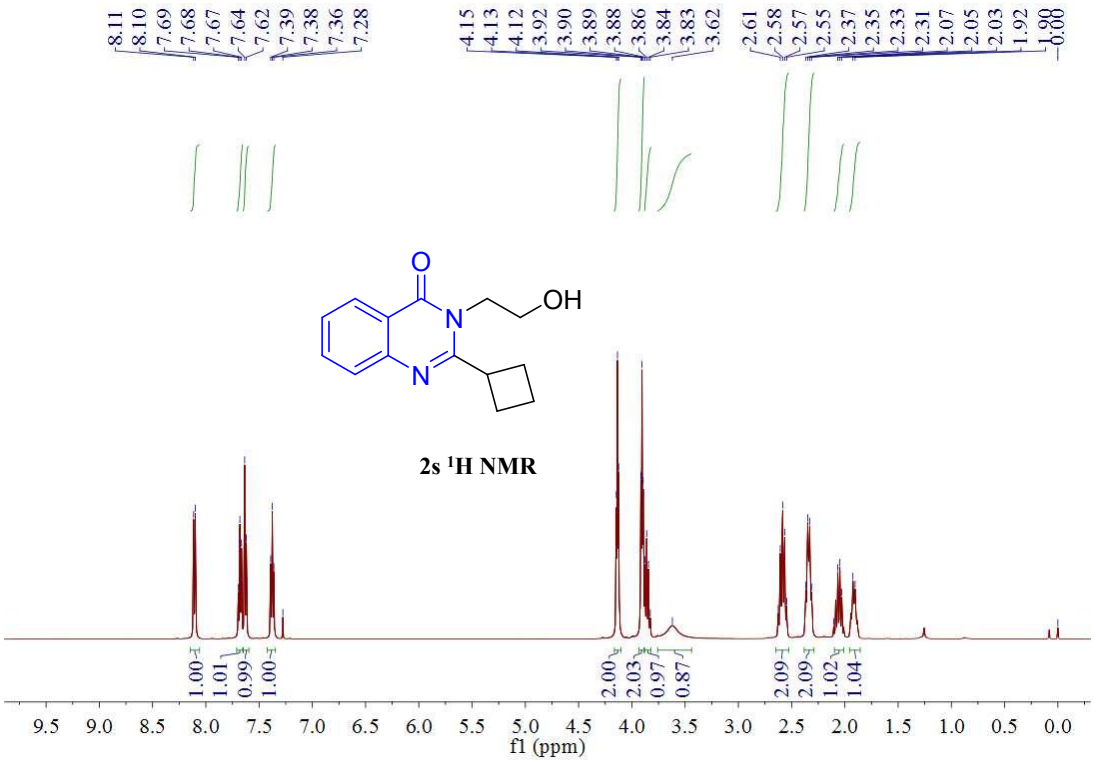
2q ^{13}C NMR



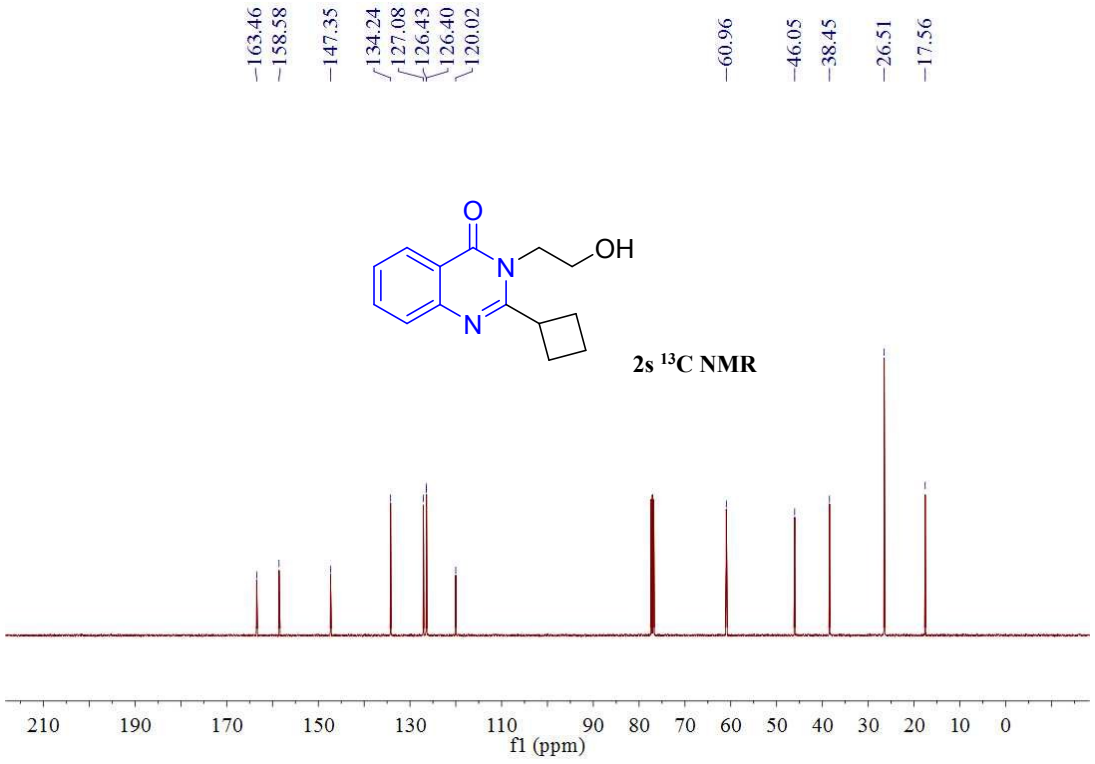
2r ^{1}H NMR



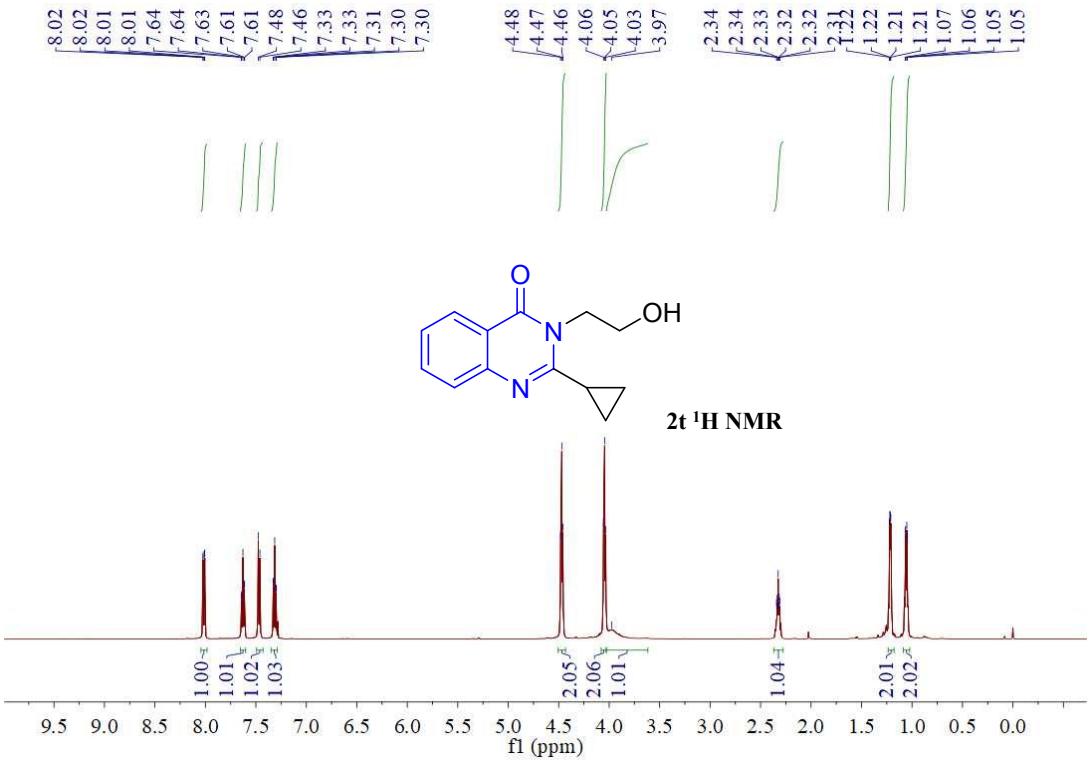
2r ^{13}C NMR



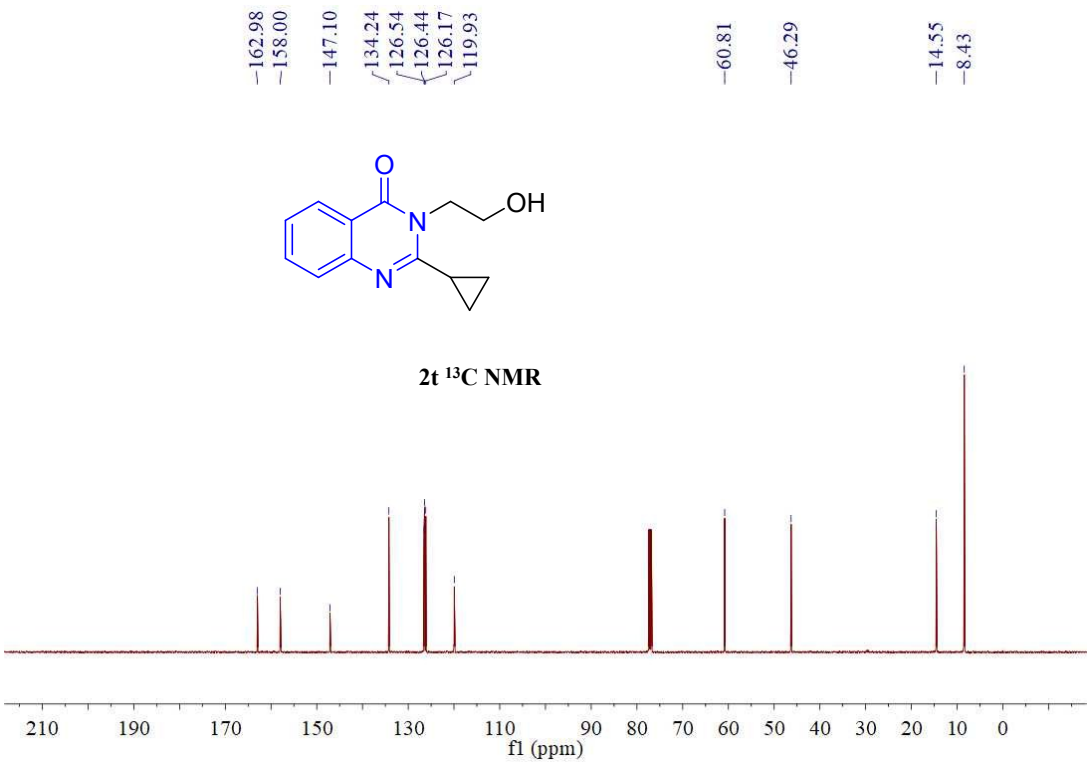
2s ^{1}H NMR



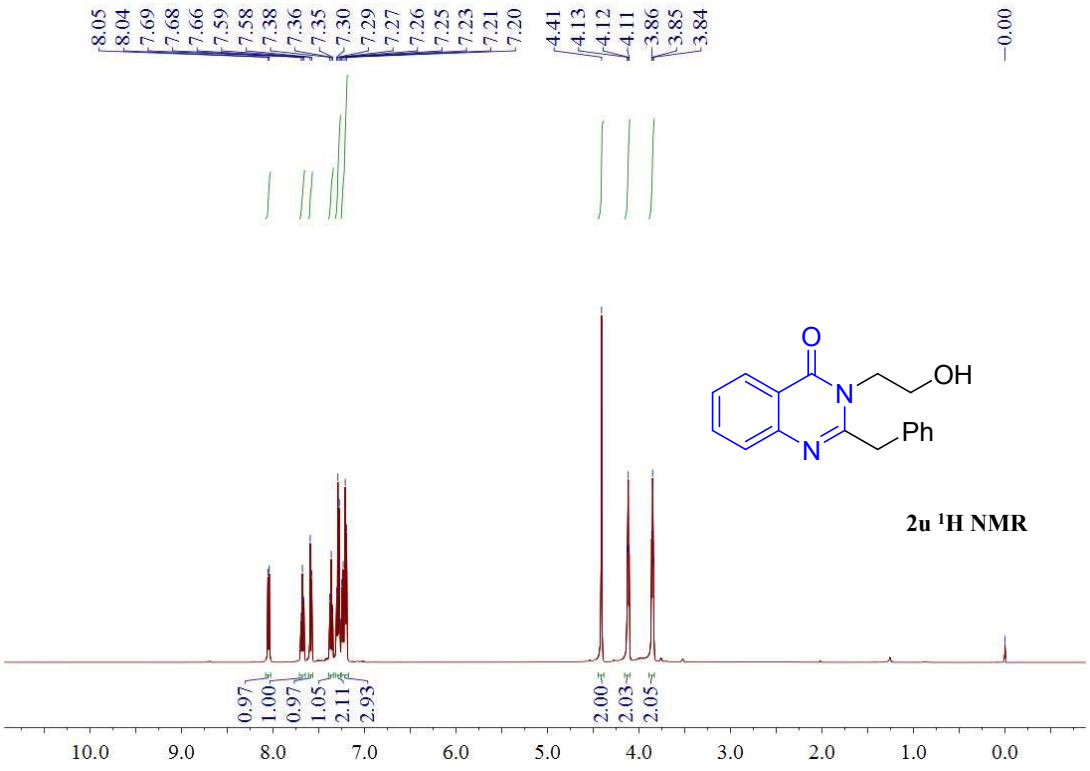
2s ^{13}C NMR



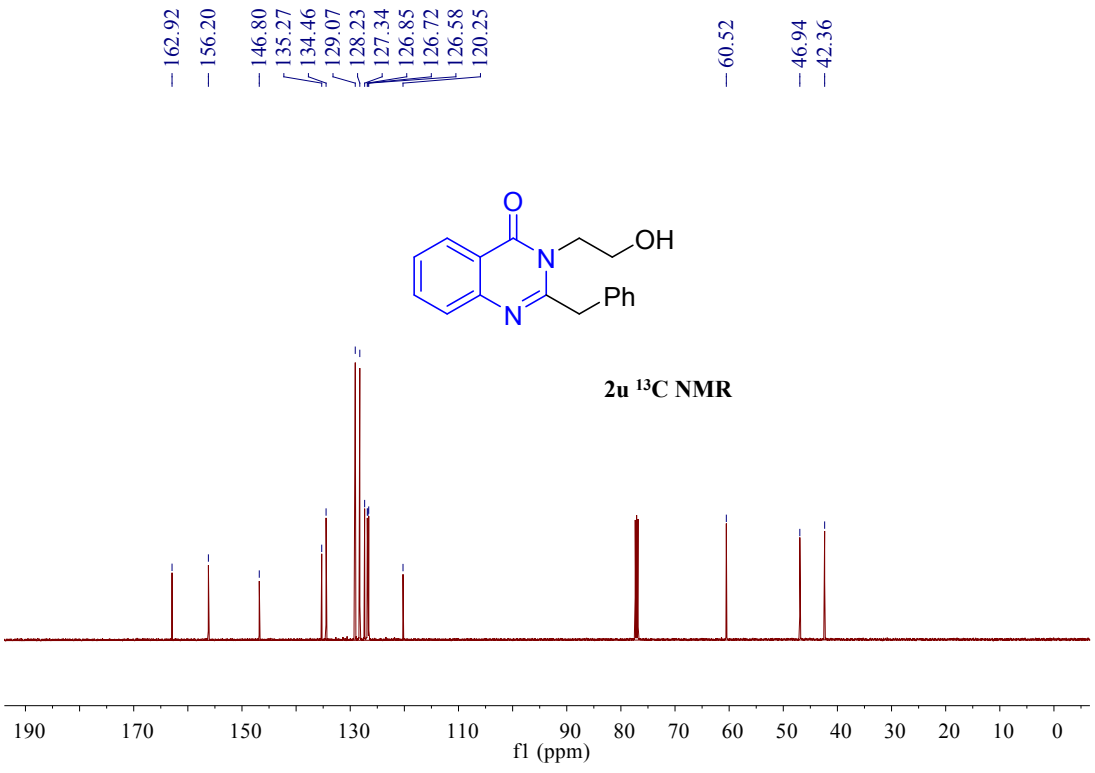
2t ^{1}H NMR



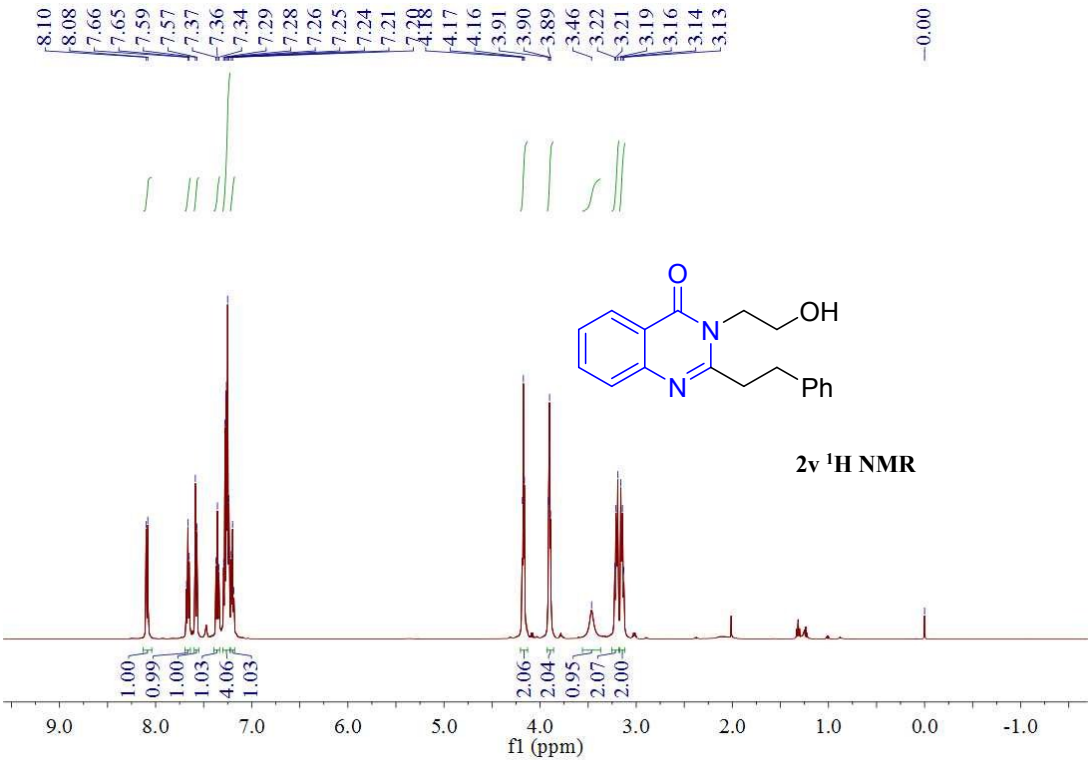
2t ^{13}C NMR



2u ^{1}H NMR



2u ^{13}C NMR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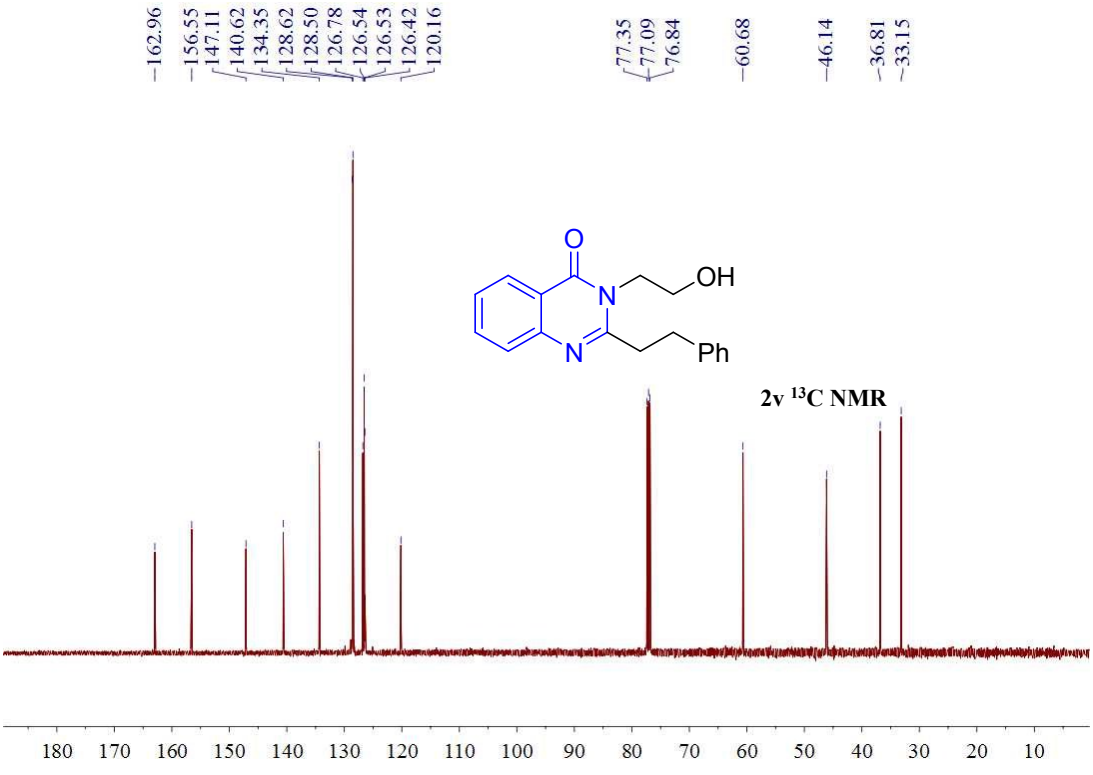
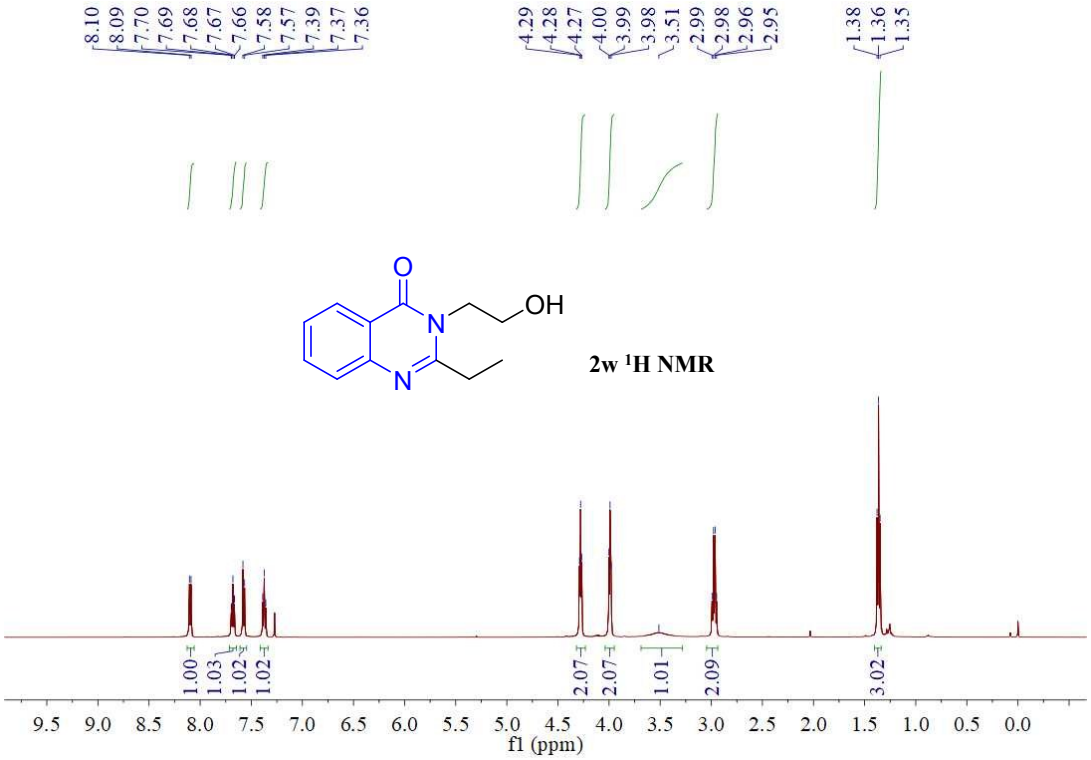
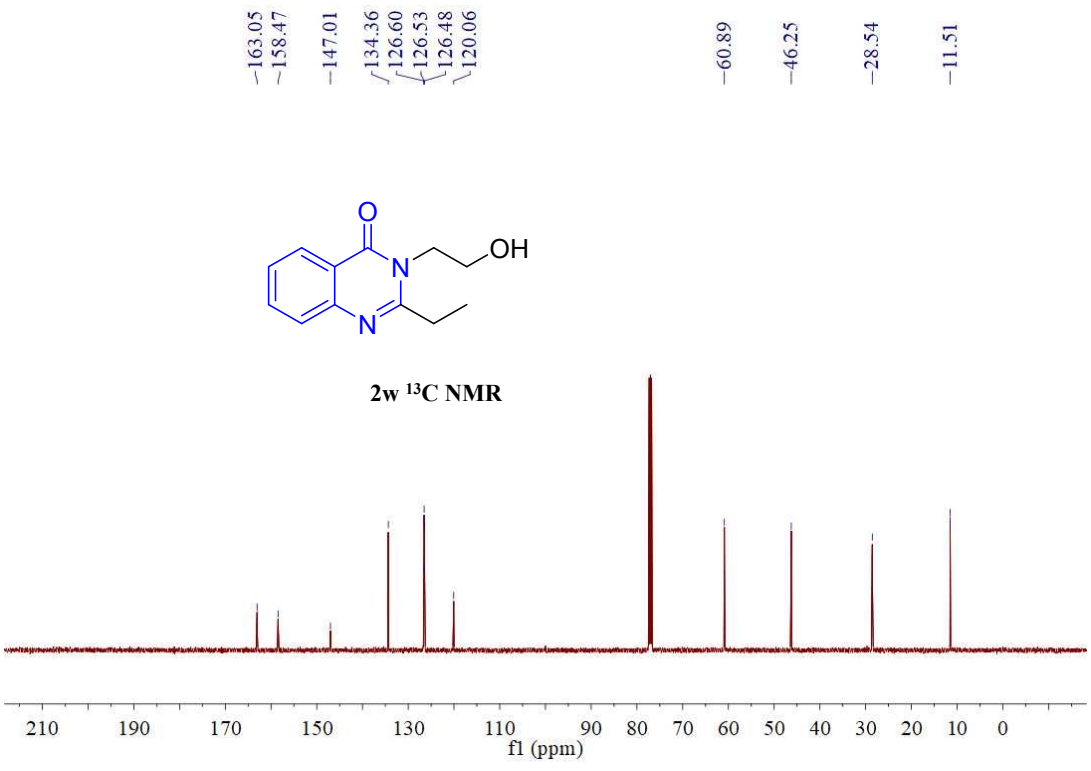
8.08
7.66
7.65
7.59
7.57
7.37
7.36
7.34
7.29
7.28
7.26
7.25
7.24
7.21
4.18
4.17
4.16
3.91
3.90
3.89
3.46
3.22
3.21
3.19
3.16
3.14
3.13
0.00
O
N
OH
N
Ph
2v ^{1}H NMR
1.00
0.99
1.00
1.03
4.06
1.03
2.06
2.04
0.95
2.07
2.00
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
f1 (ppm)

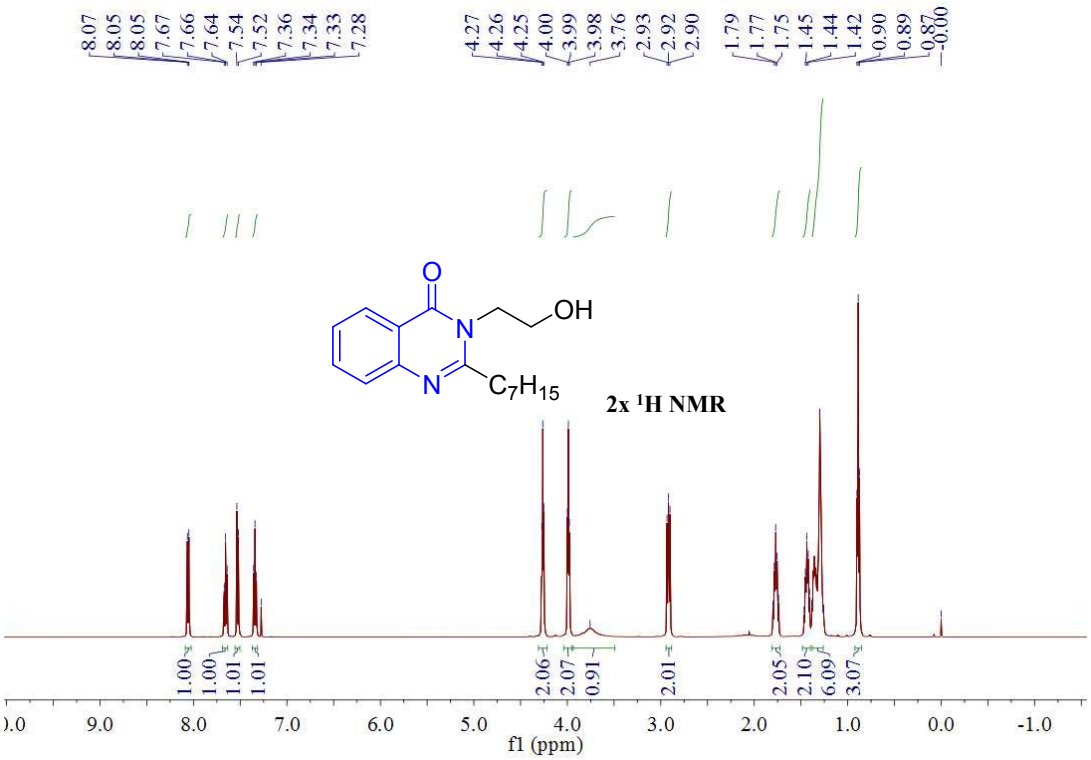

162.96
156.55
147.11
140.62
134.35
128.62
128.50
126.78
126.54
126.53
126.42
120.16
77.35
77.09
76.84
60.68
46.14
36.81
33.15
O
N
OH
N
Ph
2v ^{13}C NMR
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10



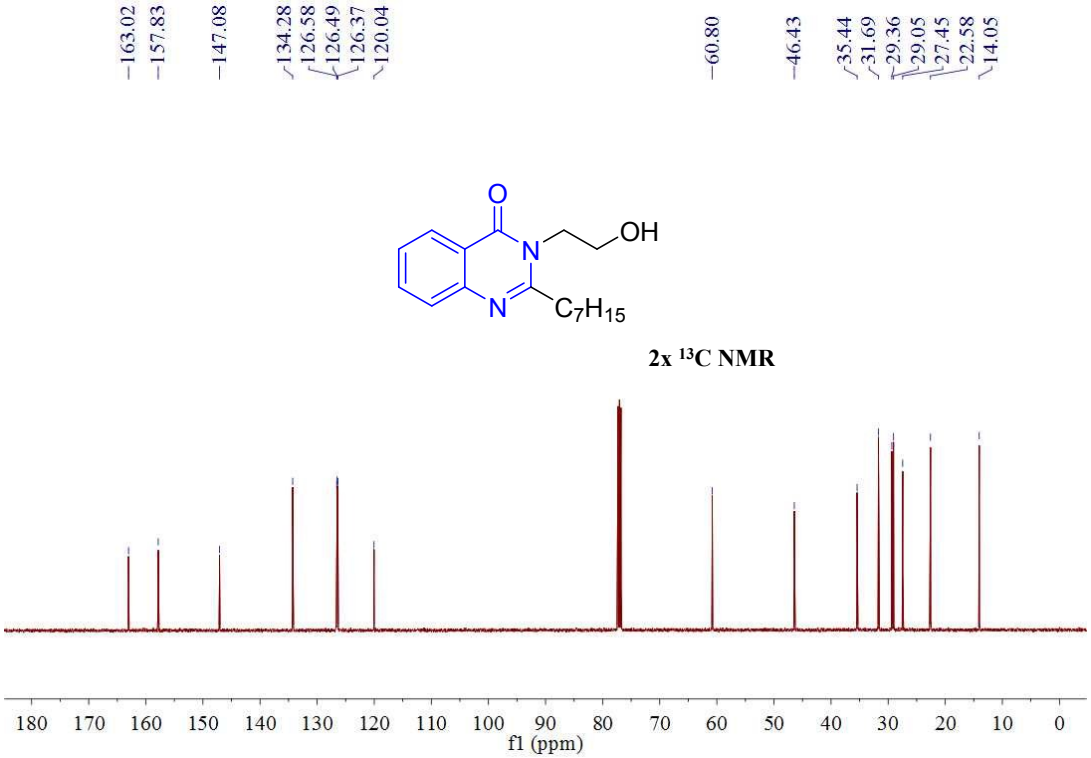
2w ^{1}H NMR



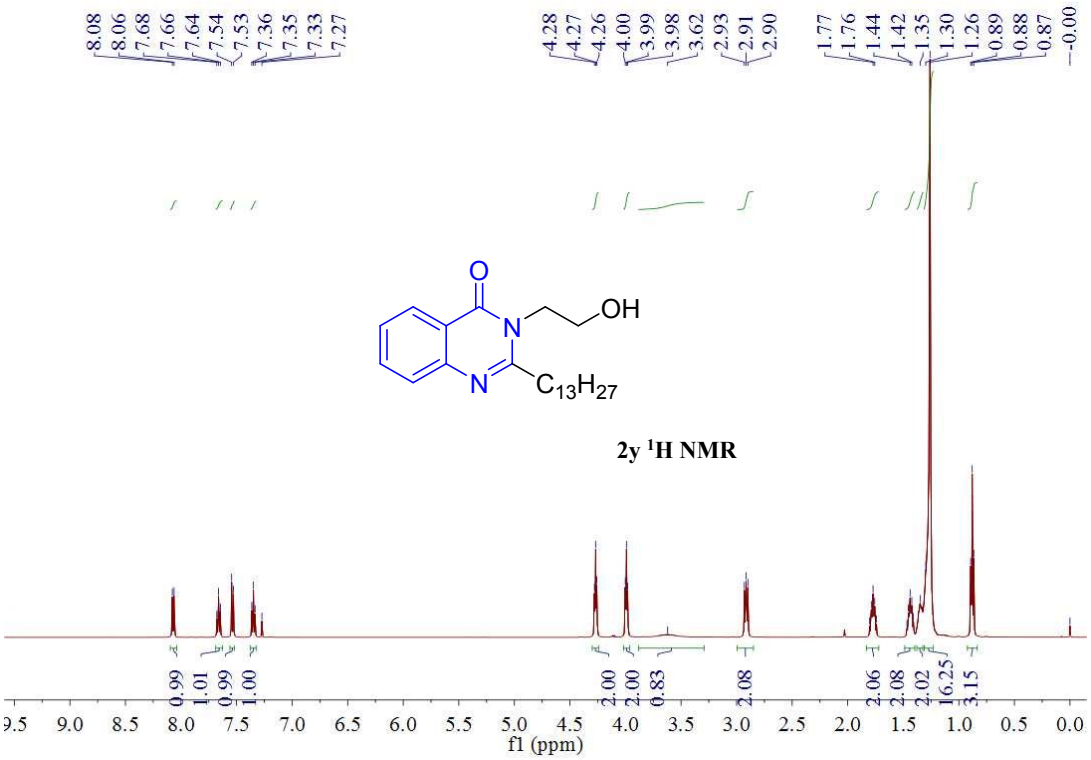
2w ^{13}C NMR



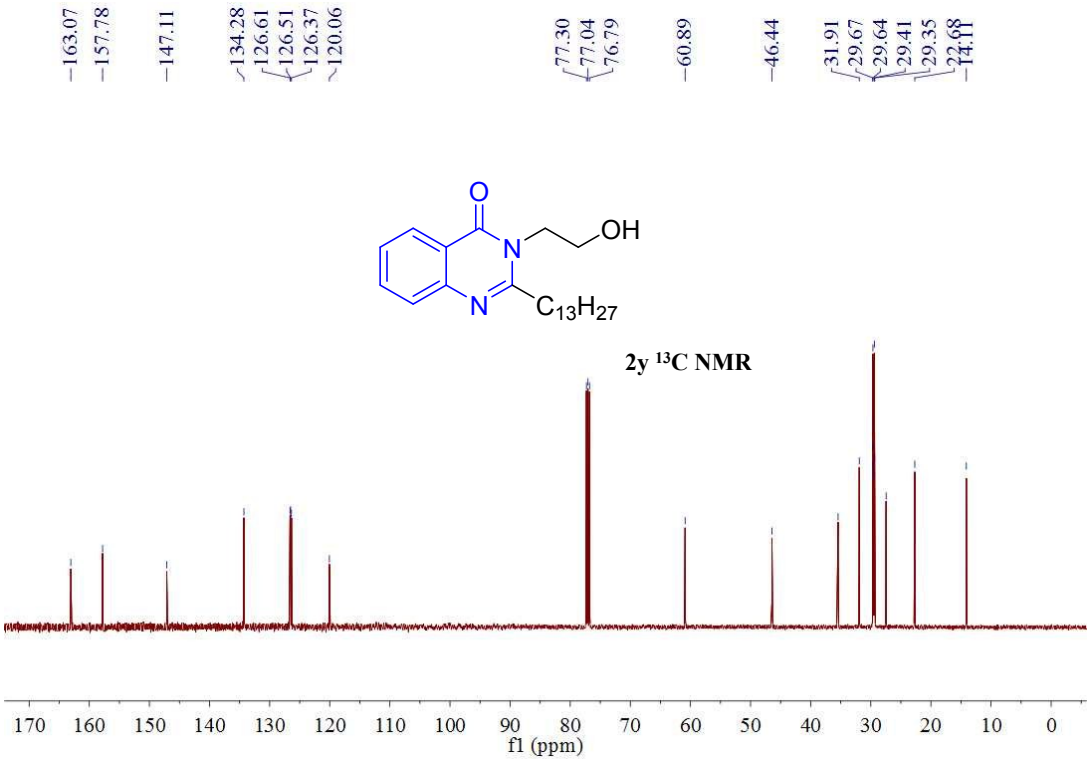
2x ^{1}H NMR



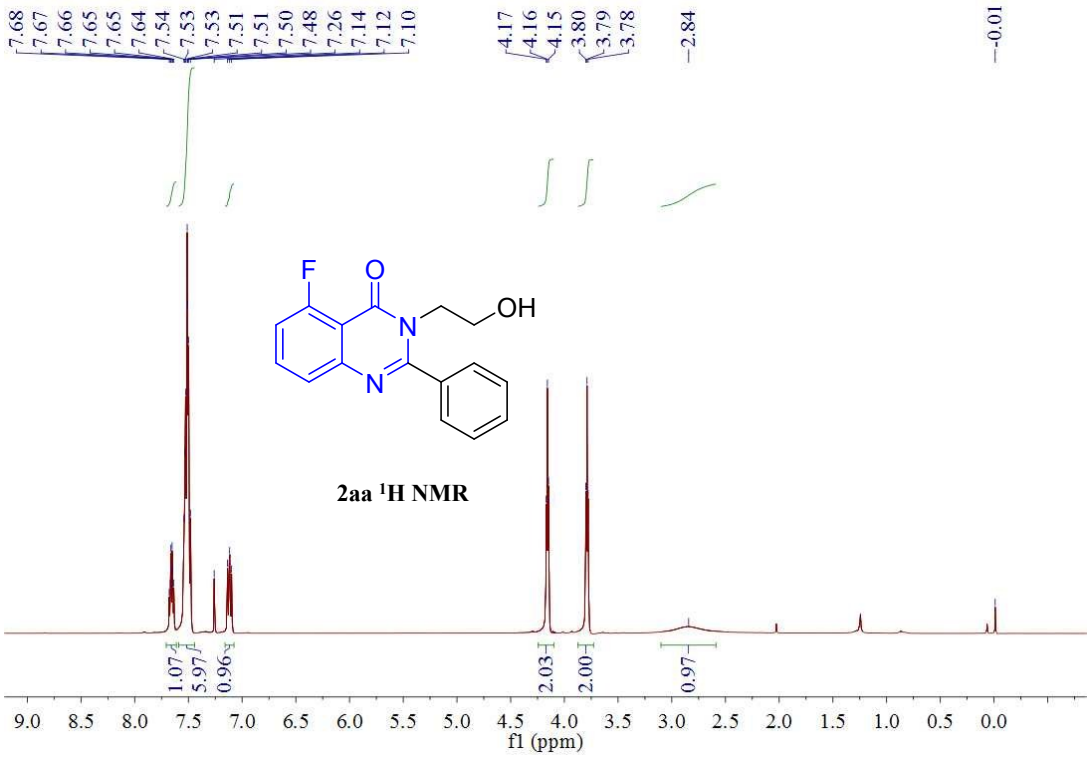
2x ^{13}C NMR



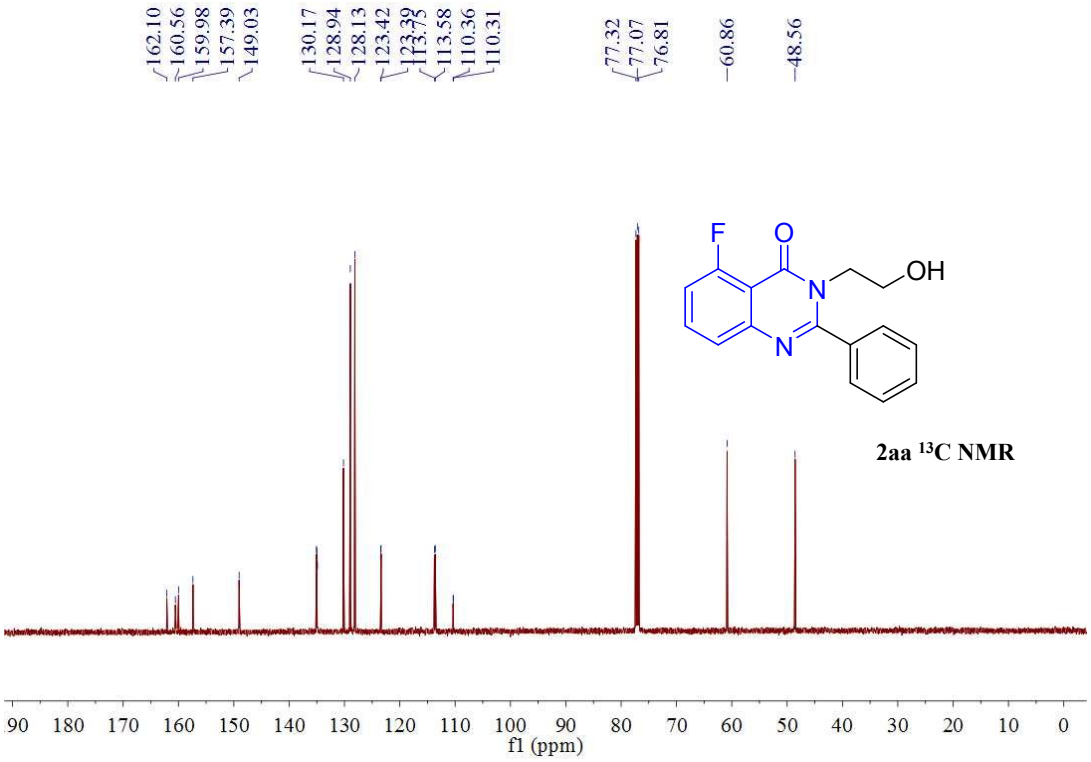
2y ^{1}H NMR



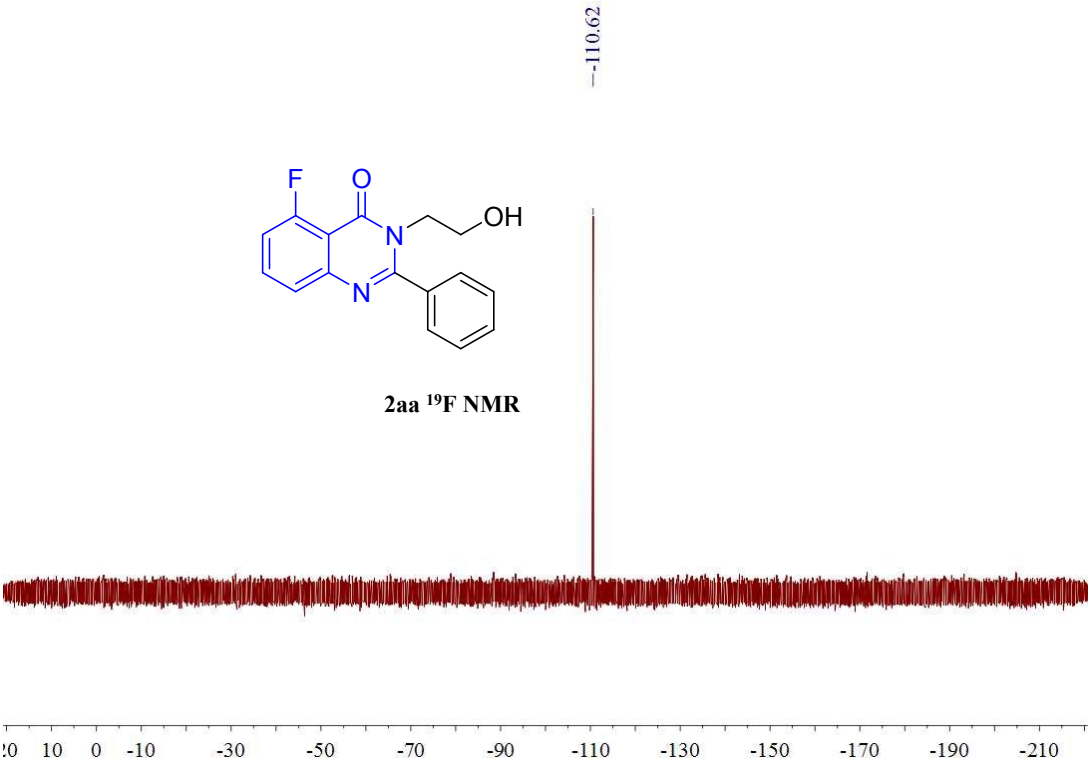
2y ^{13}C NMR



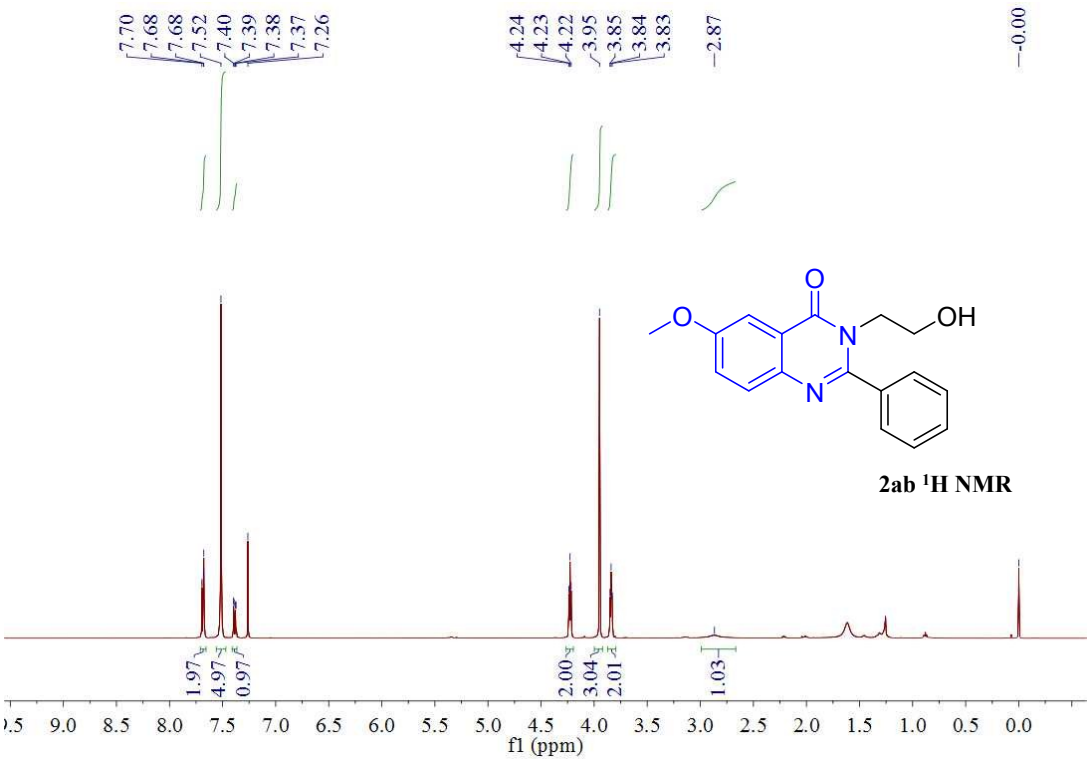
2aa ^{1}H NMR



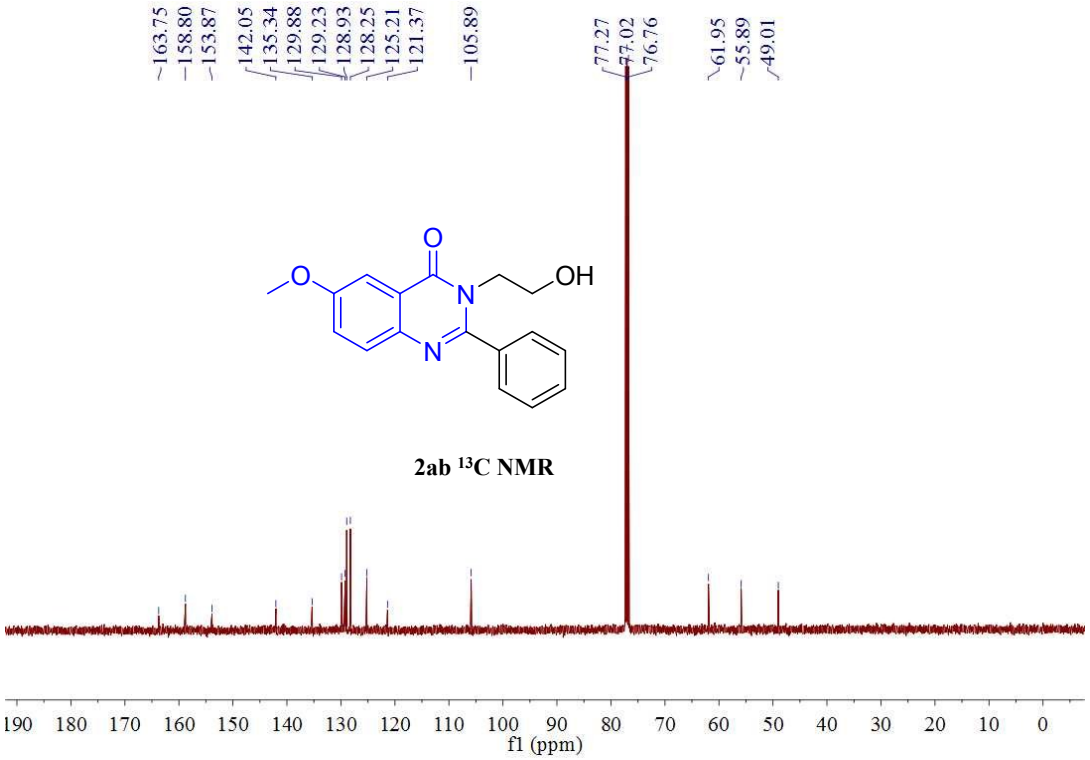
2aa ^{13}C NMR



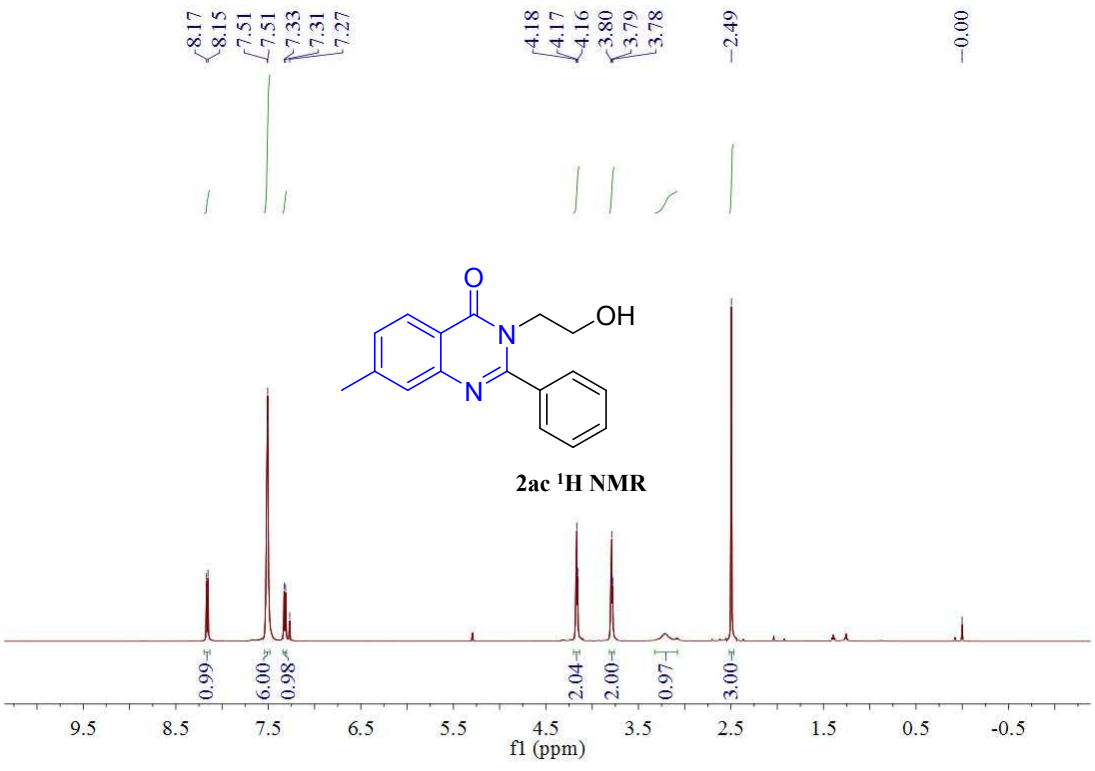
2aa ^{19}F NMR



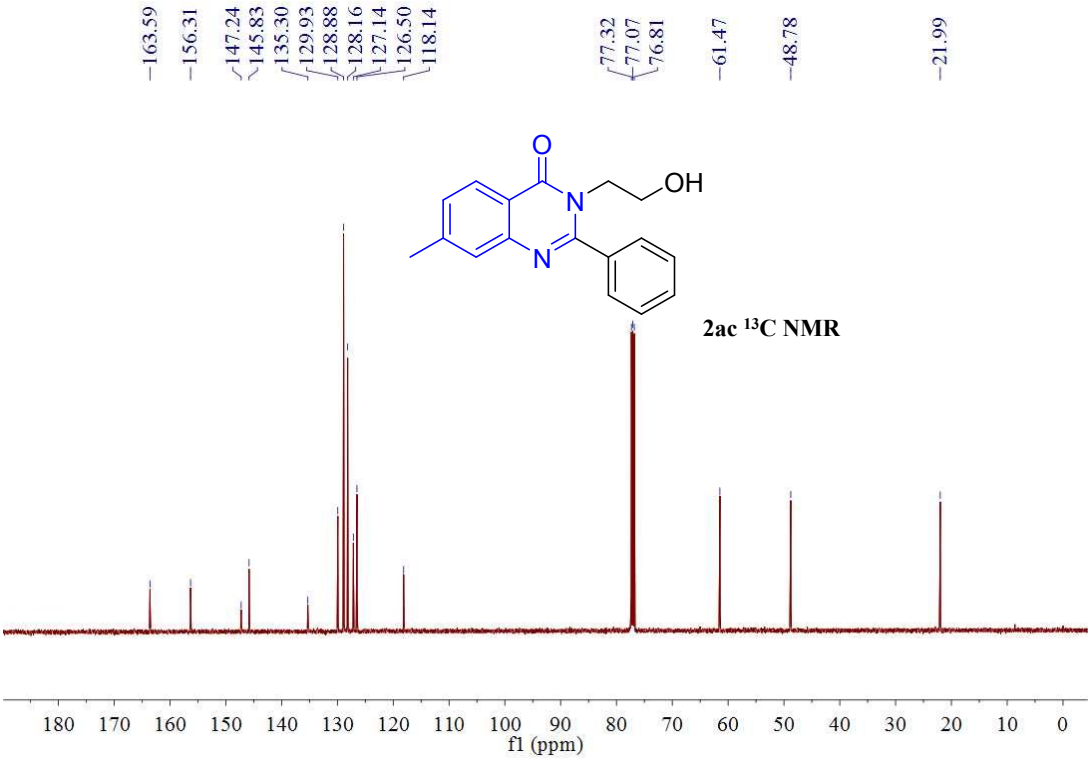
2ab ^{1}H NMR



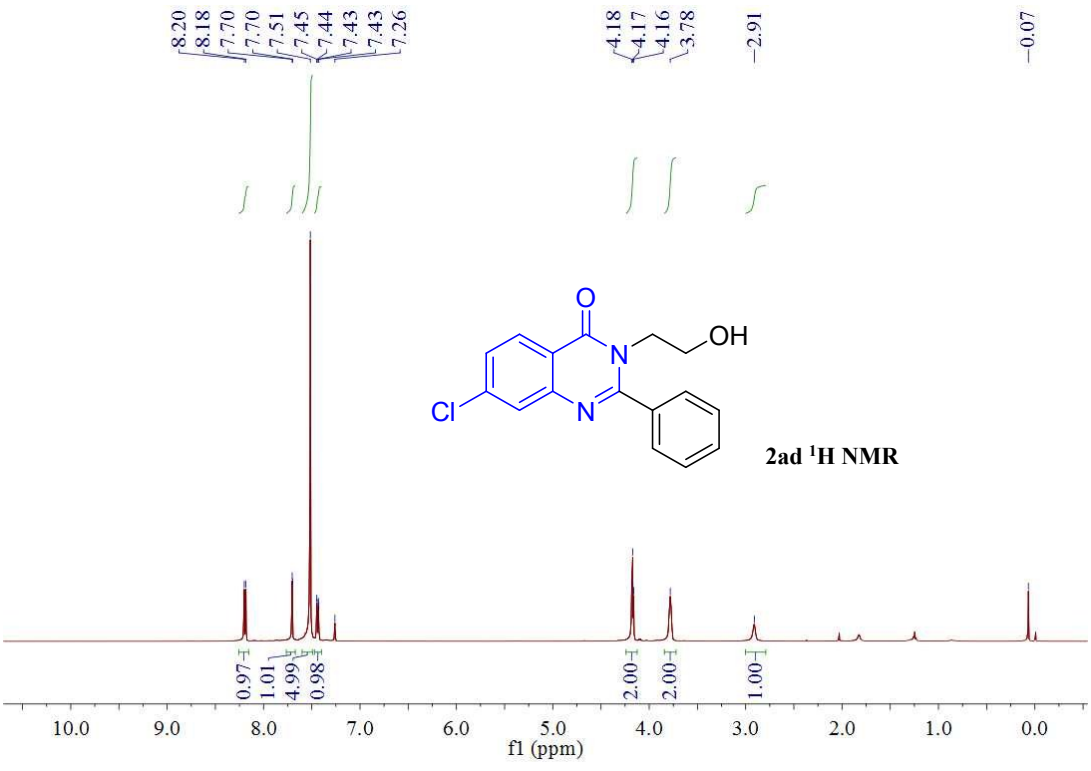
2ab ^{13}C NMR



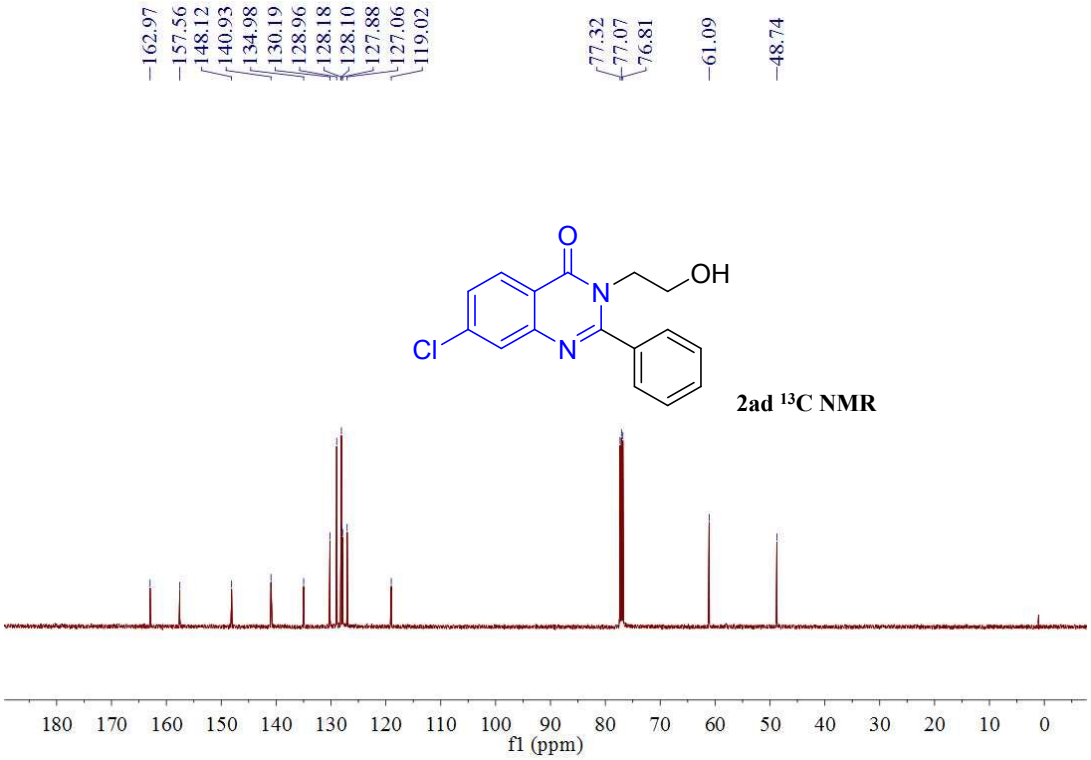
2ac ^{1}H NMR



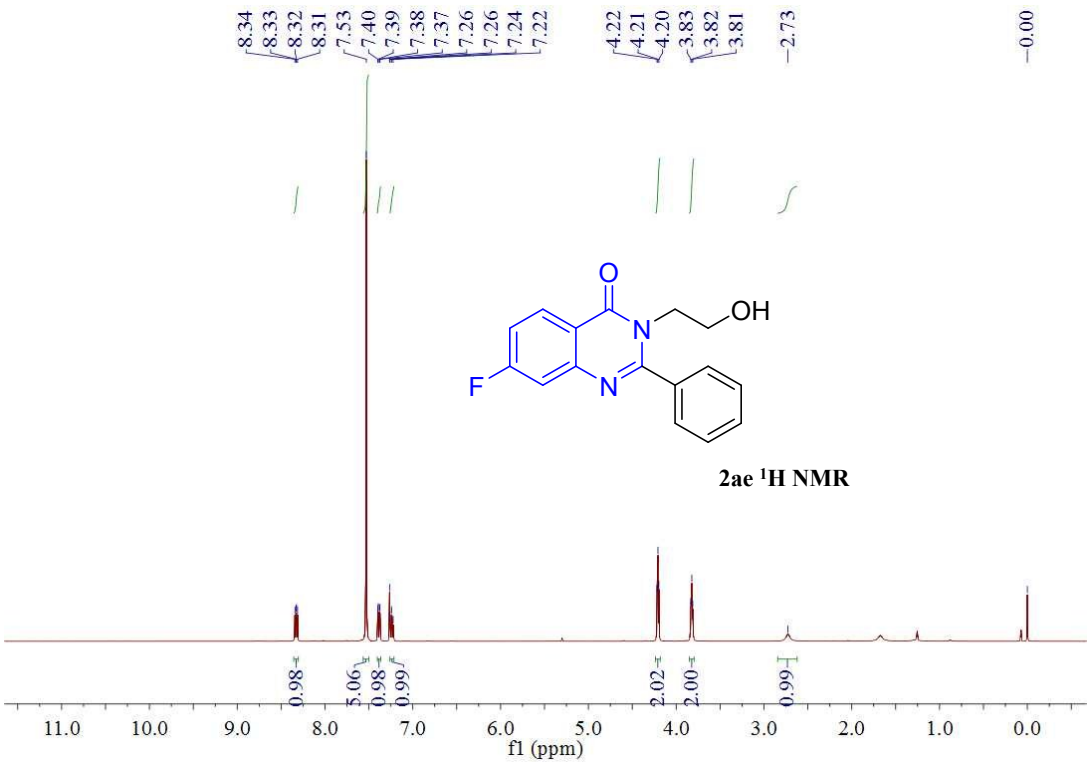
2ac ^{13}C NMR



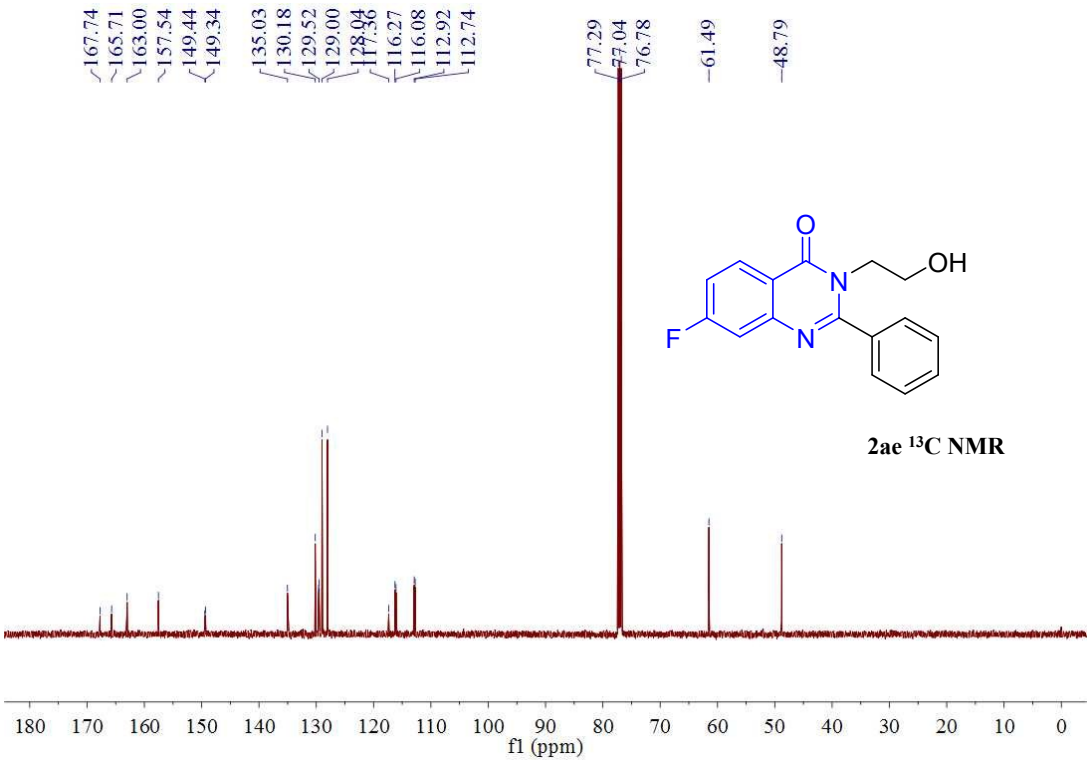
2ad ^{1}H NMR



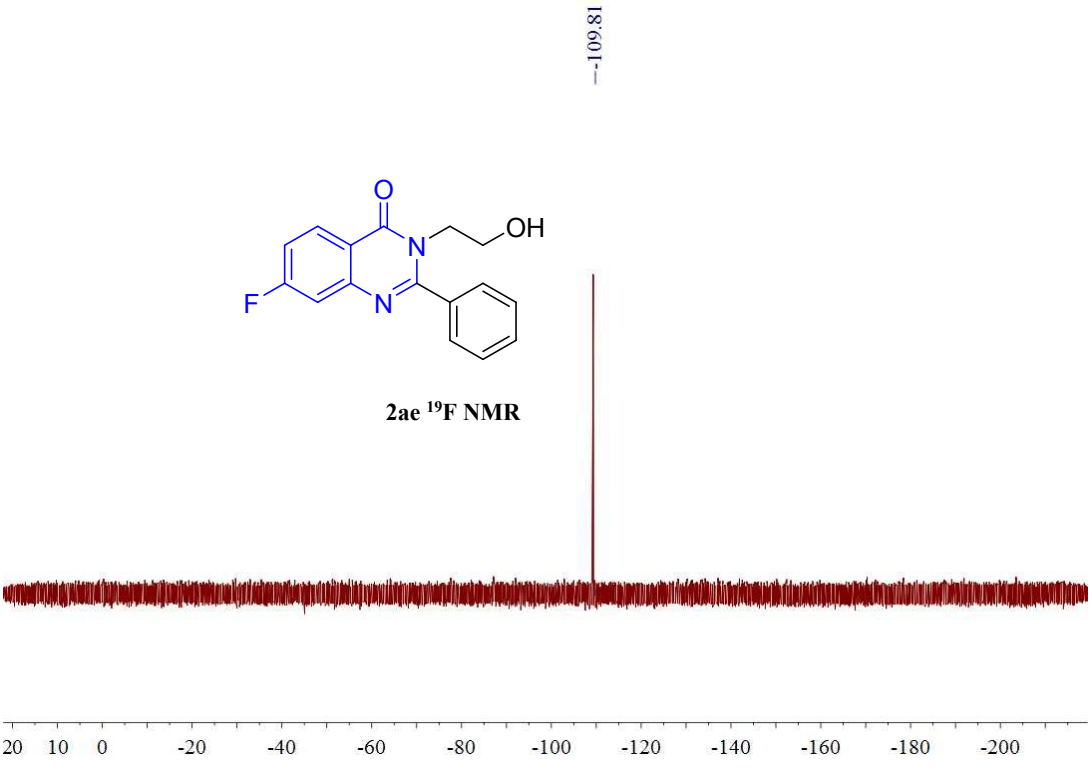
2ad ^{13}C NMR



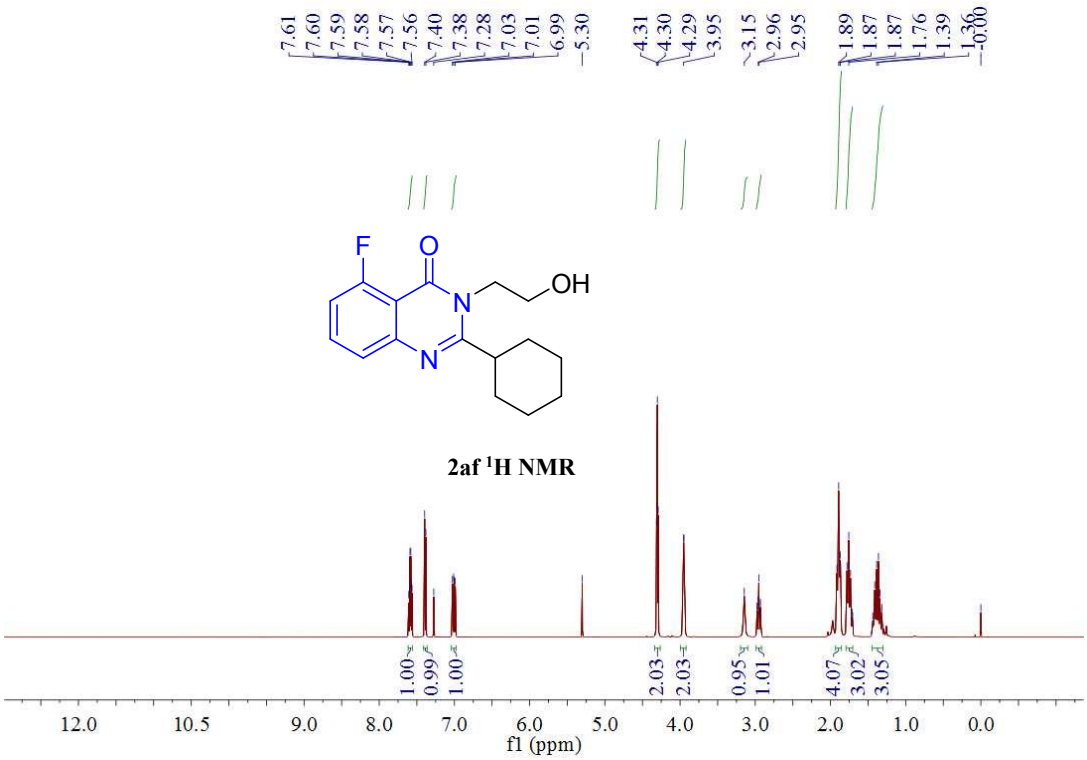
2ae ^{1}H NMR



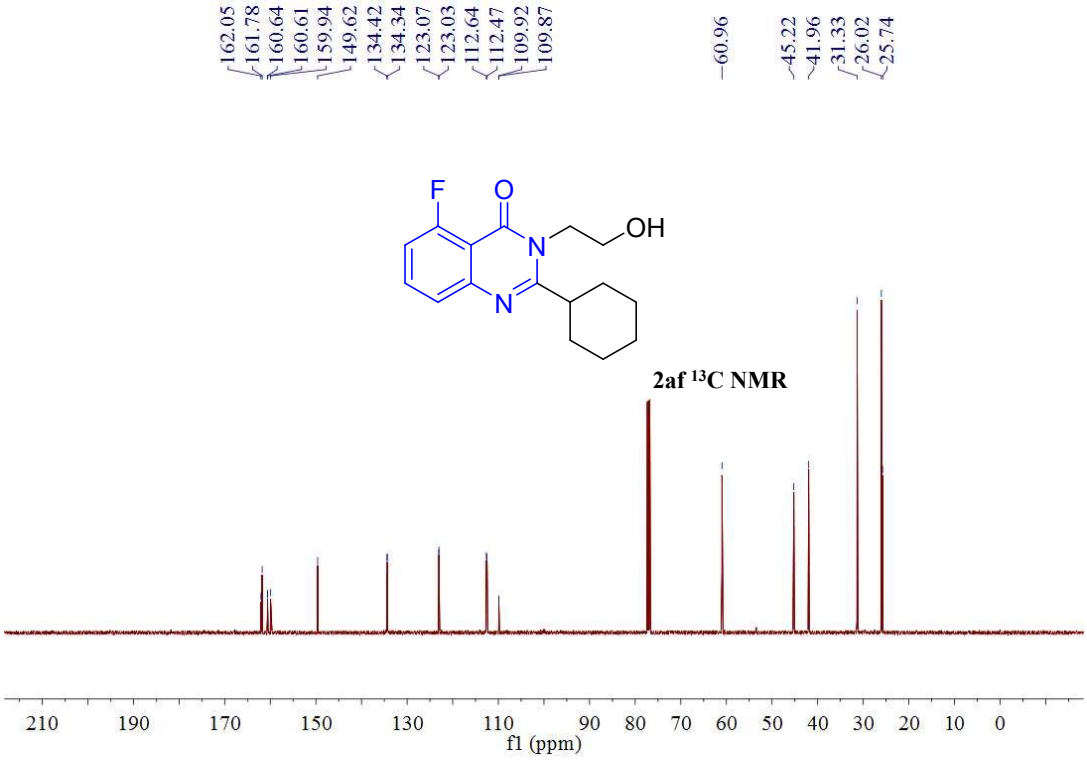
2ae ^{13}C NMR



2ae ^{19}F NMR



2af ^{1}H NMR



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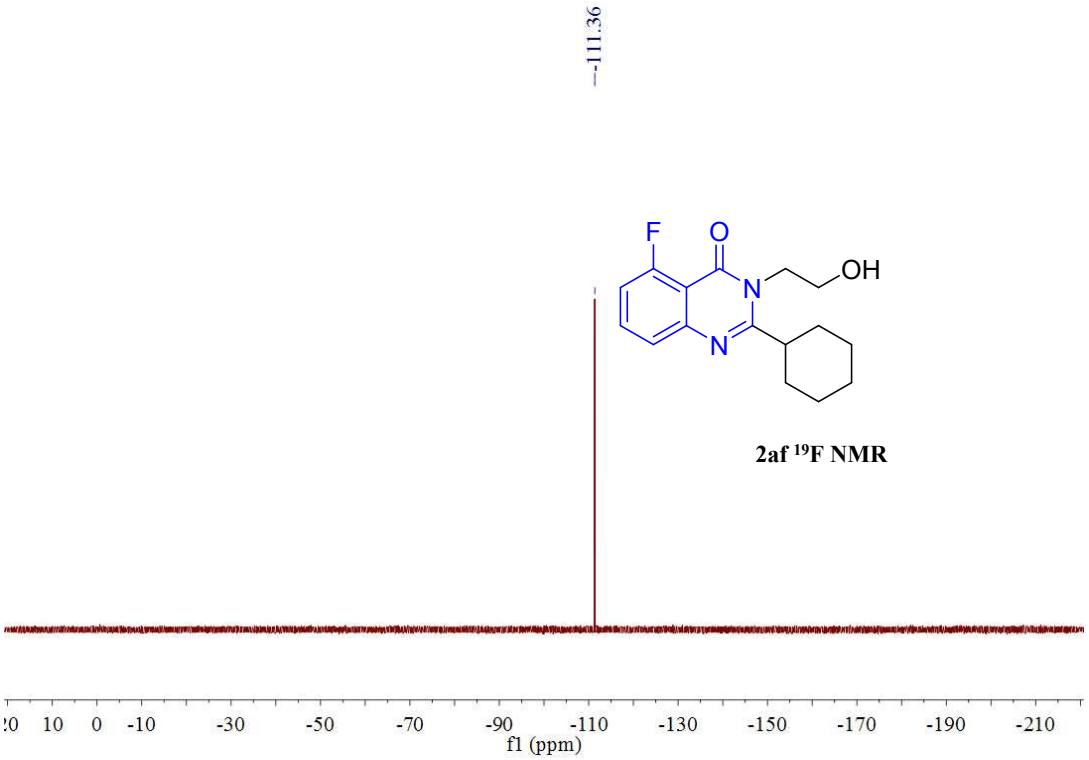
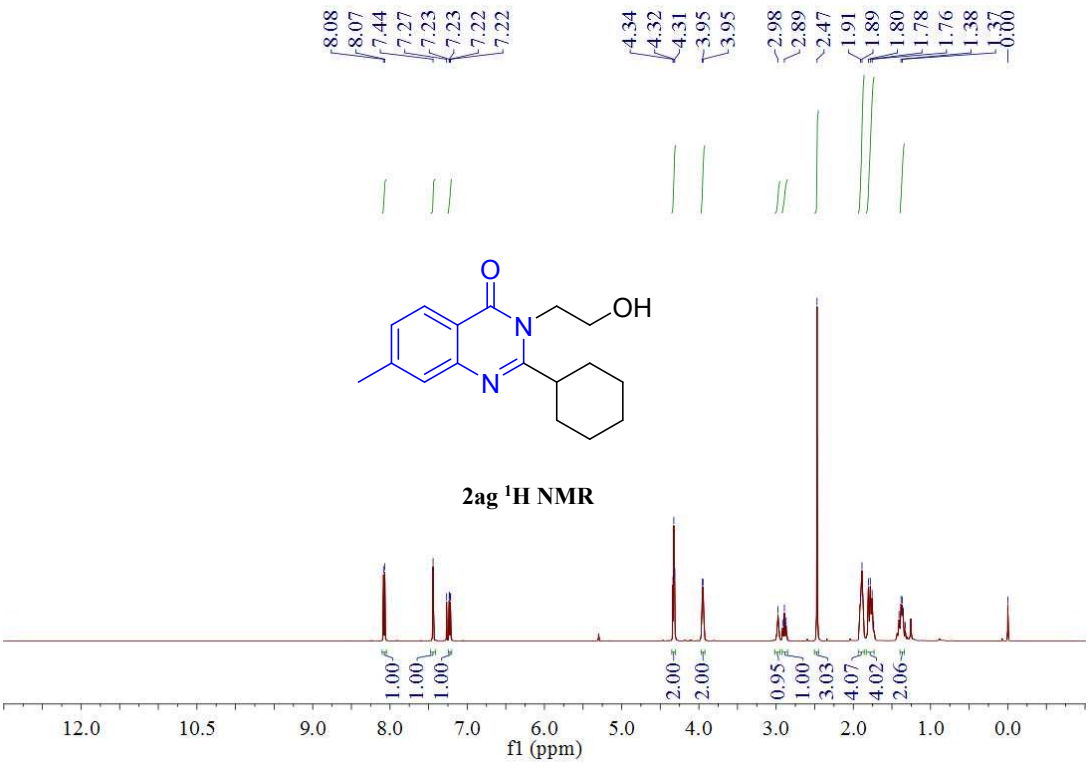
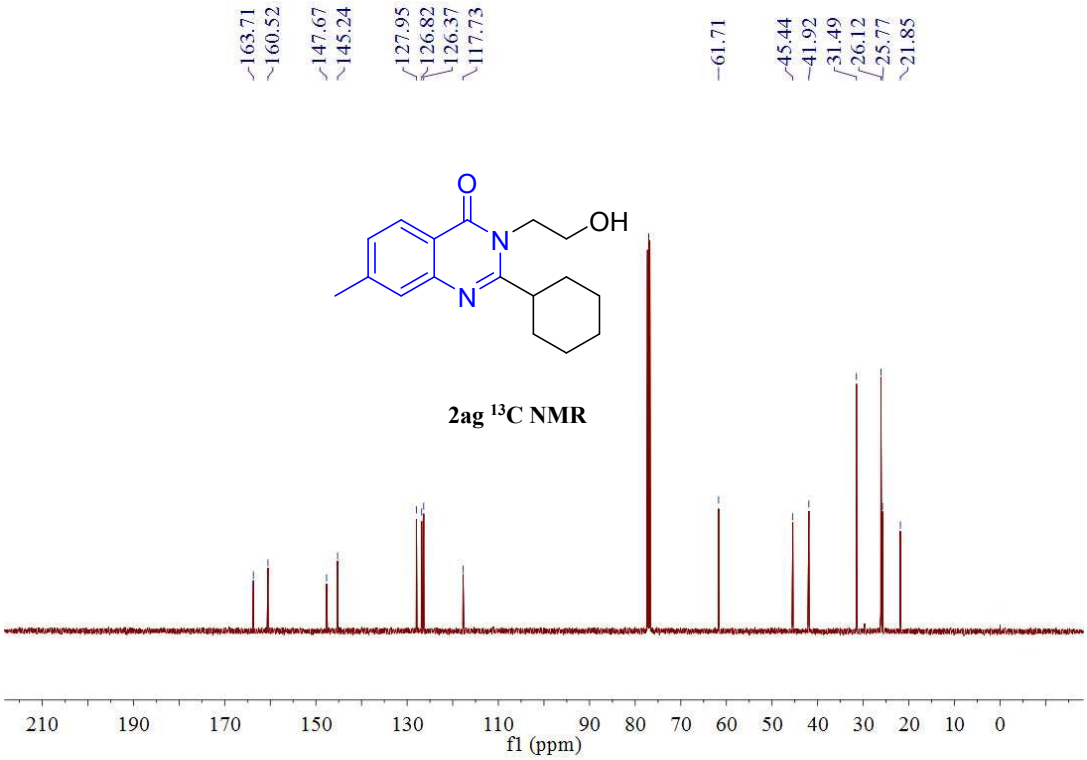


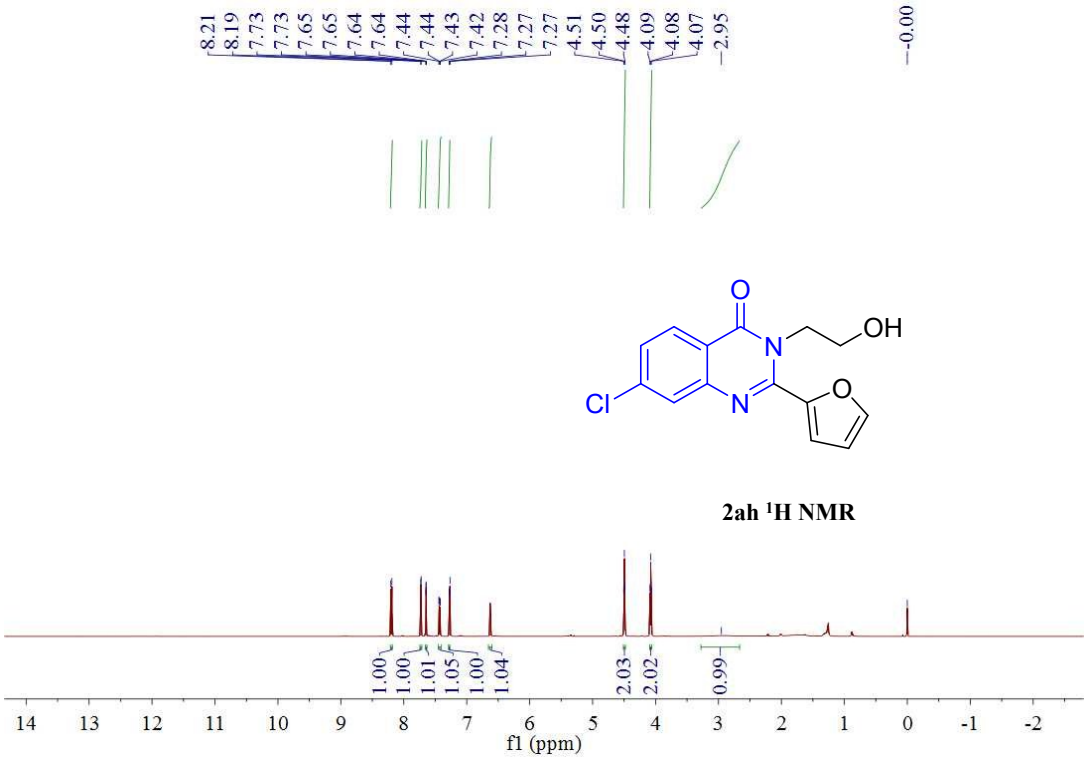
2af ^{19}F NMR



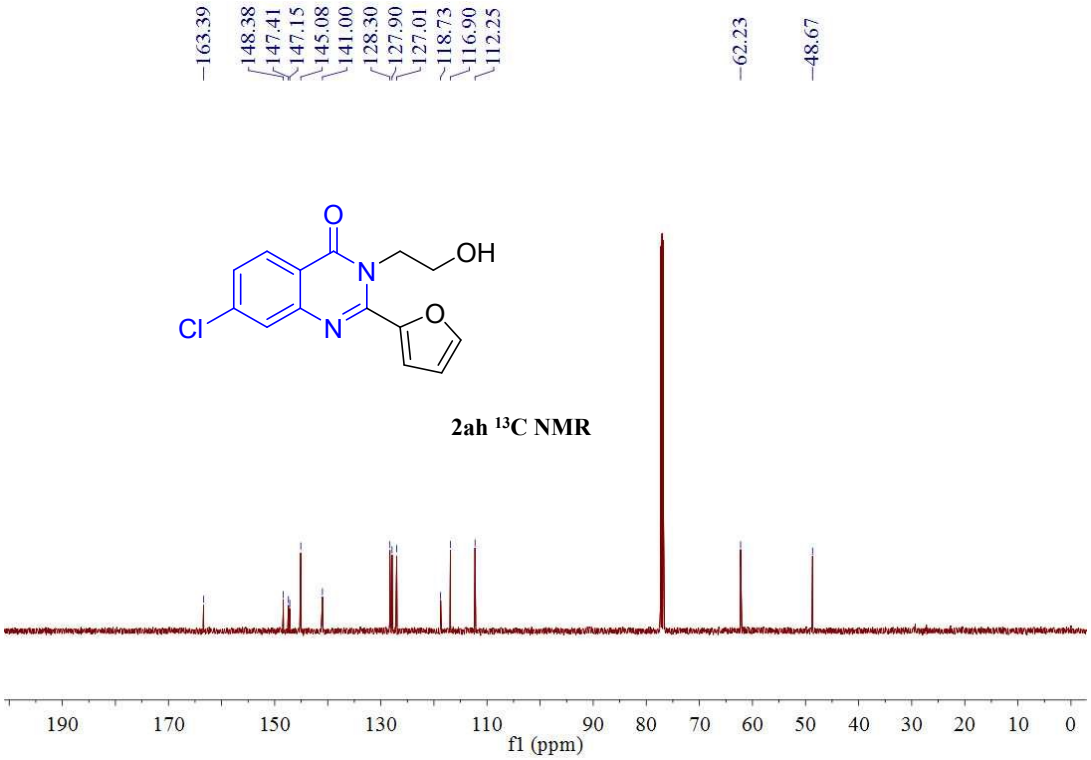
2ag ^{1}H NMR



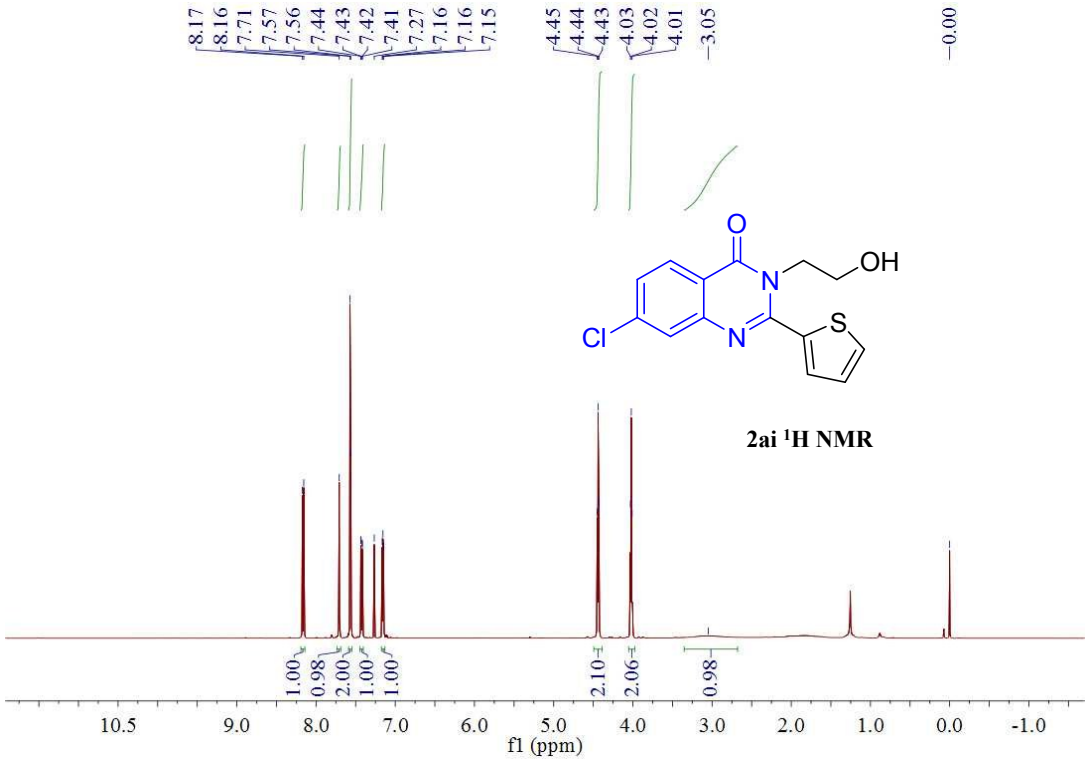
2ag ^{13}C NMR



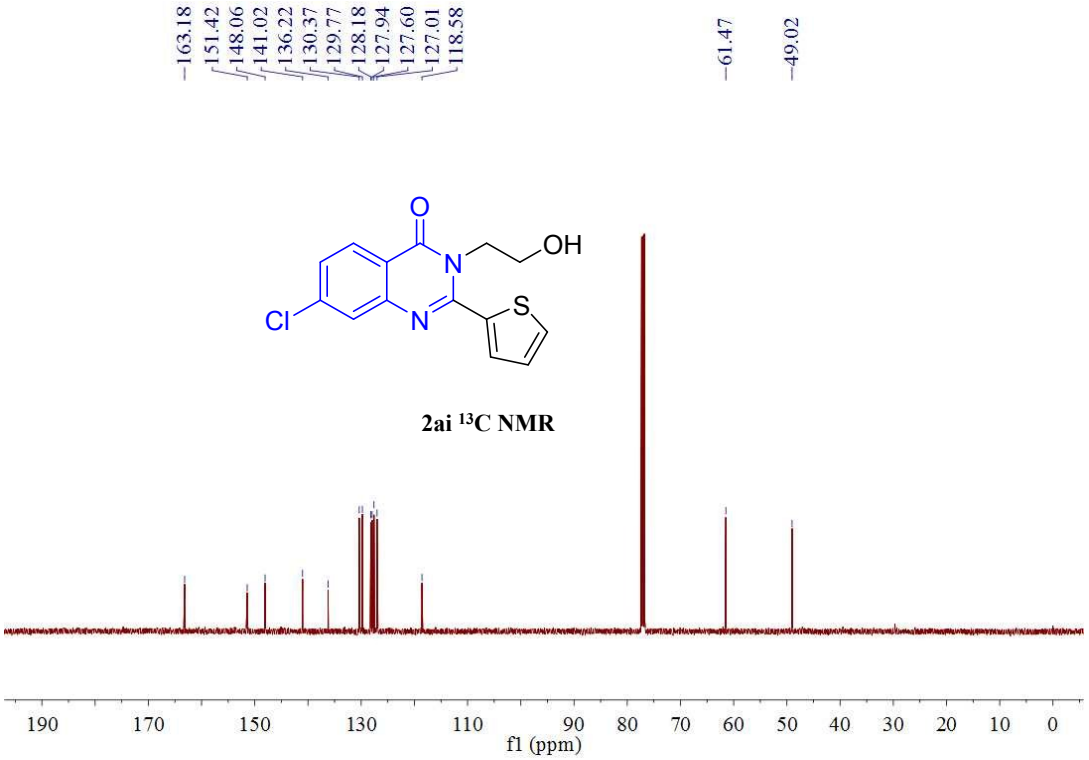
2ah ^{1}H NMR



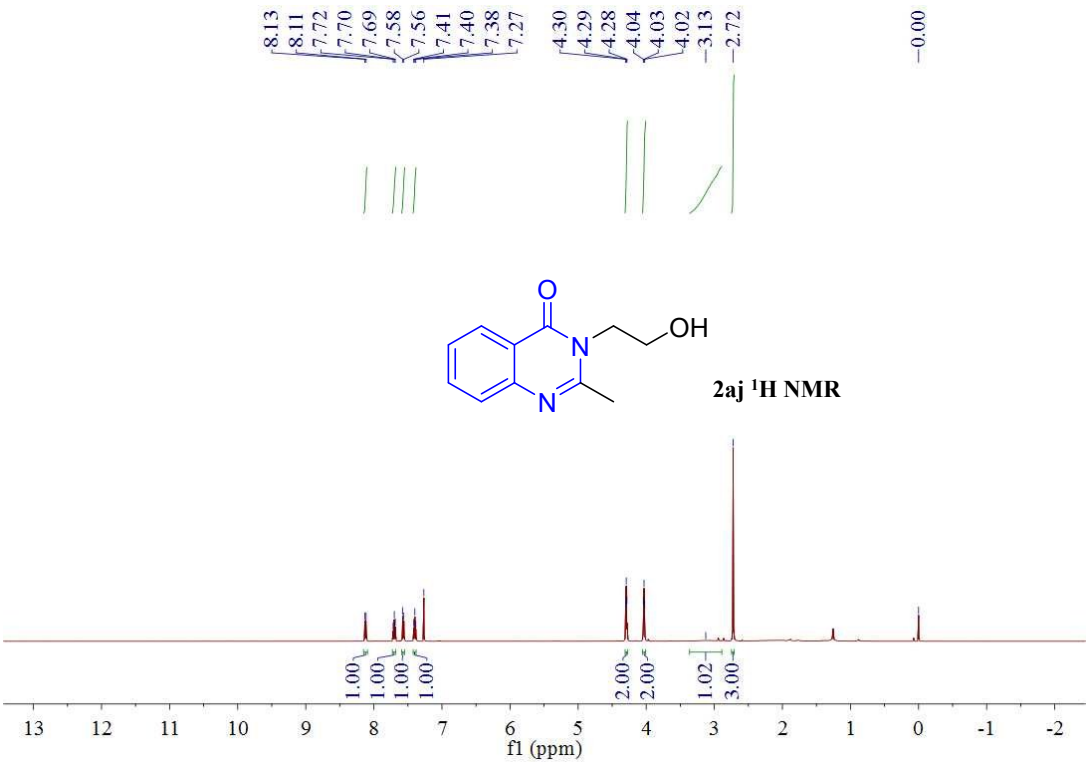
2ah ^{13}C NMR



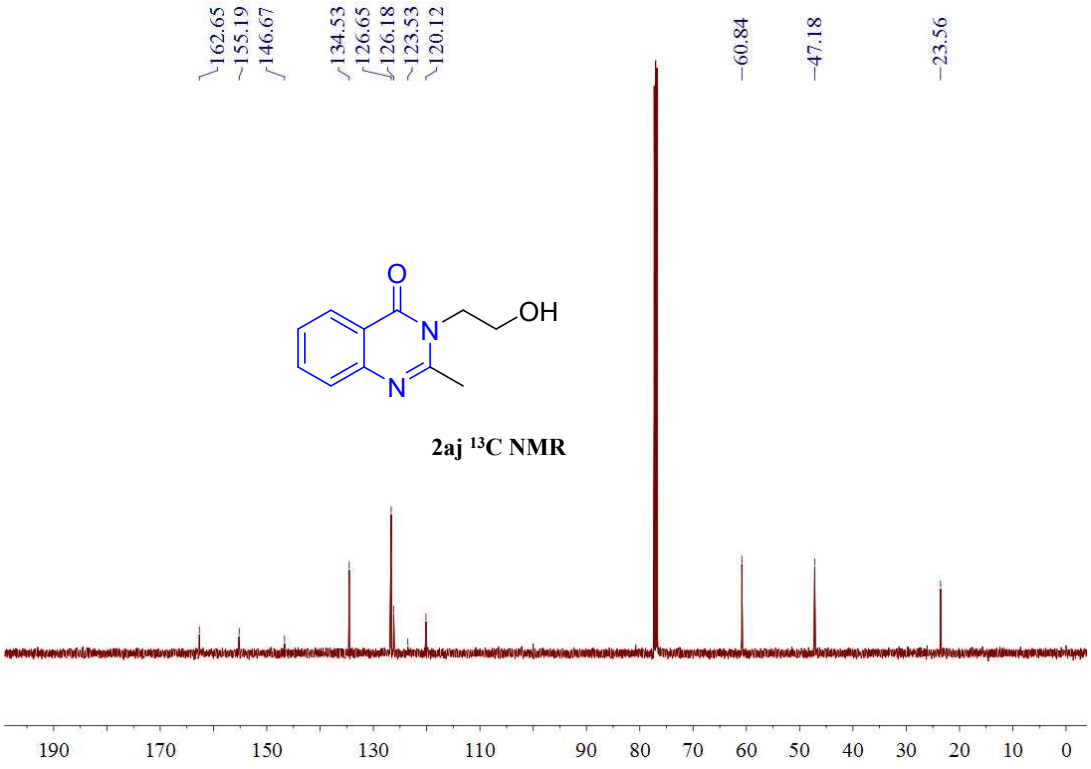
2ai ^{1}H NMR



2ai ^{13}C NMR



2aj ^{1}H NMR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155.19
146.67
134.53
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120.12
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47.18
23.56
O
N
N
OH
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0

2aj ^{13}C NMR