Electronic Supplementary Material (ESI) for Green Chemistry.

Supporting Information

For

Sustainable Methine Sources for the Synthesis of Heterocycles under Metal- and Peroxide-Free Conditions

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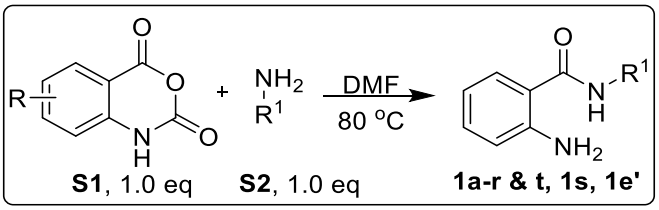
(1) General Information

^{1}H, ^{13}C and DEPT NMR spectra were recorded on a 400 MHz Varian Unity Plus or Varian Mercury plus spectrometer. The chemical shift (δ) values are reported in parts per million (ppm), and the coupling constants (J) are given in Hz. The spectra were recorded using $CDCl_3$ as a solvent. ^{1} H NMR chemical shifts are referenced to tetramethylsilane (TMS) (0 ppm). ^{13}C NMR was referenced to $CDCl_3$ (77.0 ppm) or DMSO-d_6 (39.51 ppm). The abbreviations used are as follows: s, singlet; d, doublet; t, triplet; q, quartet; dd, doublet of doublet; ddd, doublet of doublet of doublet; dt, doublet of triplets; td, triplet of doublet; m, multiplet. Mass spectra and high resolution mass spectra (HRMS) were measured using the ESI (FT-MS solariX) at National Sun Yat-Sen University, Kaohsiung, Taiwan. Melting points were determined on an EZ-Melt (Automated melting point apparatus). All products reported showed ^{1}H NMR spectra in agreement with the assigned structures. Reaction progress and product mixtures were routinely monitored by TLC using Merck TLC aluminum sheets (silica gel 60 F254). Column chromatography was carried out with 230–400 mesh silica gel 60 (Merck) and a mixture of hexane/ethyl acetate or hexane as an eluent. Preparative TLC was run on a Merck TLC aluminum sheets (silica gel 60 F254).

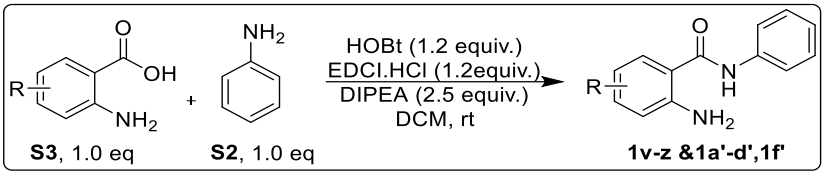
(2) Experimental Procedures

(i) General Experimental Procedure (A) for the Synthesis of 2-Amino-*N*-phenylbenzamides: [1]



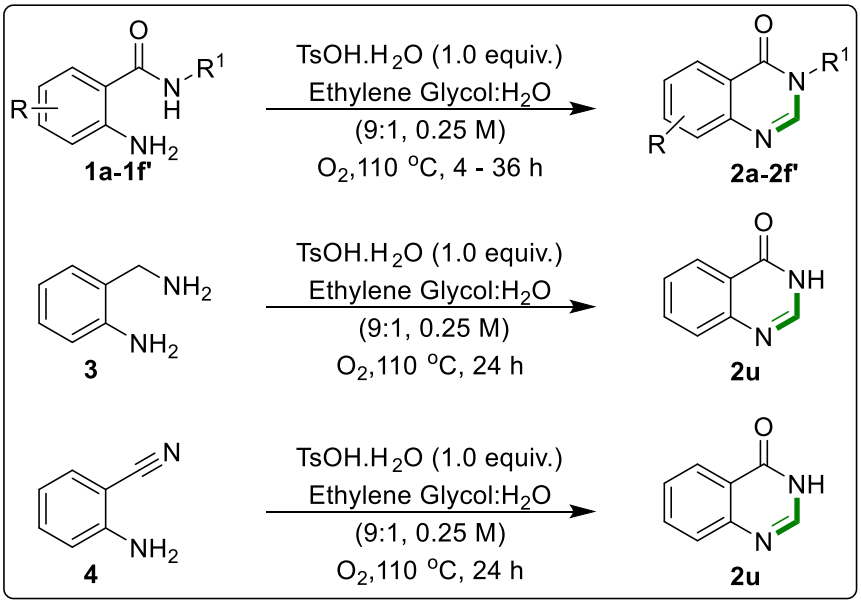
To a stirred solution of Isatoic anhydride (**S1**, 1.2 mol) in DMF (10 mL) was added aniline derivatives (**S2**, 1.2 mmol) and stirred at 80 °C for 8 ~ 24 h. After the completion of the reaction by TLC chromatogram, the reaction mixture was cooled to room temperature and diluted with ice water (60 mL) followed by extraction with ethyl acetate (3X20 mL). The obtained organic layer was partitioned between saturated brine solutions (20 mL) and dried over Na_2SO_4 followed by concentration under rotary vacuum. The obtained crude was purified using column chromatography by eluting 8-15% of ethylene acetate (EA)/hexane (HEX) to afford the pure 2-amino-*N*-phenylbenzamides **1a-r & t, 1s, 1e'** in 60%-80% yields.

(ii) General Experimental Procedure (B) for Synthesis of 2-Amino-*N*-phenylbenzamides:[2]



To a stirred solution of anthranilic acid (**S3**, 1.2 mmol) in dichloromethane (CH_2Cl_2) (3.0 mL) was added EDC.HCl (1.2 mmol), HOBt (1.2 mmol) and aniline derivatives (**S2**, 1.2 mmol) followed by the dropwise addition of DIPEA (2.5 mmol). The reaction mixture was allowed to stir at room temperature until the completion of reaction was monitored by TLC (24 ~ 36 h). After completion, the reaction mixture was diluted with ice water (10 mL) followed by the extraction with EA (3X20 mL). The combined organic layer was washed with 1N HC1 (15 mL) followed by saturated brine solution, dried over Na_2SO_4 and concentrated under rotary vacuum. The obtained crude was purified using column chromatography by eluting 8-15% of EA/HEX to afford the pure 2-amino-*N*-phenylbenzamides **1v-z & 1a'-d', 1f'**in 50%-65% yields.

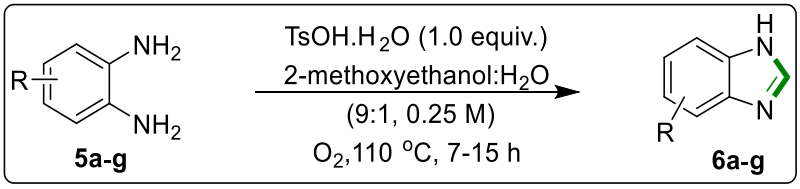
(iii) General Experimental Procedure (C) and Spectral Characterization for the Synthesis of Quinazolin-4(3*H*)-ones with Ethylene Glycol (EG) as "–CH-" Source



To an oven dried sealed tube was charged with **1a-1f' or 3 or 4** (0.15 mmol), ethylene glycol (EG): H_2O (9:1) (0.25 M) and TsOH. H_2O (0.15 mmol) and allowed to stir at 110° C until the completion of reaction (4 ~ 36 h) by TLC. After completion, the reaction mixture was cooled to room temperature and diluted with 5.0 mL of water. The water layer was extracted with (3X10 mL) of ethyl acetate and the combined ethyl acetate layer was given brine wash (1X10 mL). The final ethyl acetate layer was dried over sodium sulfate and concentrated

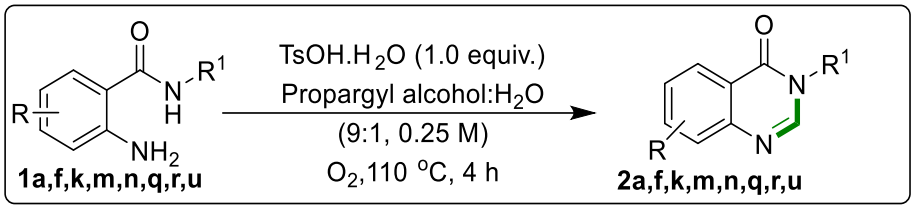
under reduced pressure to get the crude compound. The obtained crude was purified using column chromatography by eluting from hexane to 20% ethyl acetate/hexane to afford pure quinazolin-4(3*H*)-ones **2a-2f'** in 71%-96% yields.

(iv) General Experimental Procedure (D) and Spectral Characterization for the Synthesis of Benzimidazoles using 2-methoxyethanol as "-CH-" source



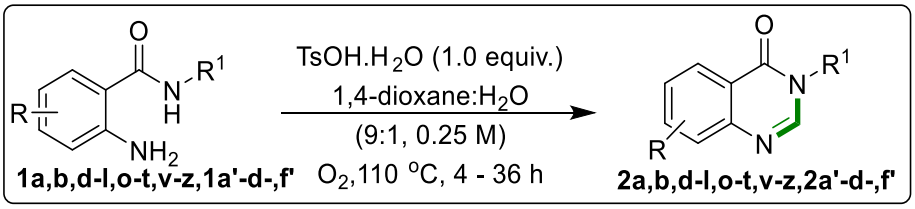
To an oven dried sealed tube was charged **5** (0.15 mmol), 2-methoxyethanol: H_2O (9:1) (0.25 M) and TsOH. H_2O (0.15 mmol) and allowed to stir at 110° C until the completion of reaction (8 ~ 16 h) by TLC. After completion, the reaction mixture was cooled to room temperature and diluted with 5.0 mL of water. The water layer was extracted with (3X10 mL) of ethyl acetate and the combined ethyl acetate layer was given brine wash (1X10 mL). The final ethyl acetate layer was dried over sodium sulfate and concentrated under reduced pressure to get the crude compound. The obtained crude was purified using column chromatography by eluting from hexane to 50 % ethyl acetate/hexane to afford pure benzimidazoles **6a-g** in 74%-87% yields.

(v) General Experimental Procedure (E) and Spectral Characterization for the Synthesis of Quinazolin-4(3*H*)-ones with Propargyl alcohol as "–CH-" Source



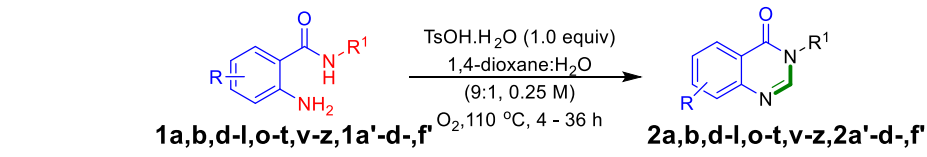
To an oven dried sealed tube was charged **1a-1u** (0.15 mmol), Propargyl alcohol (0.25 M) and TsOH. H_2O (0.15 mmol) and allowed to stir at 110° C until the completion of reaction (4 h) by TLC. After completion, the reaction mixture was cooled to room temperature and diluted with 5.0 mL of water. The water layer was extracted with (3X10 mL) of ethyl acetate and the combined ethyl acetate layer was given brine wash (1X10 mL). The final ethyl acetate layer was dried over sodium sulfate and concentrated under reduced pressure to get the crude compound. The obtained crude was purified using column chromatography by eluting from hexane to 20 % ethyl acetate/hexane to afford pure quinazolin-4(3*H*)-ones **2f, k, m, n, q, r, u** in 73%-96% yields.

(vi) General Experimental Procedure (F) and Spectral Characterization for the Synthesis of Quinazolin-4(3*H*)-ones with 1, 4-Dioxane as "–CH-" Source

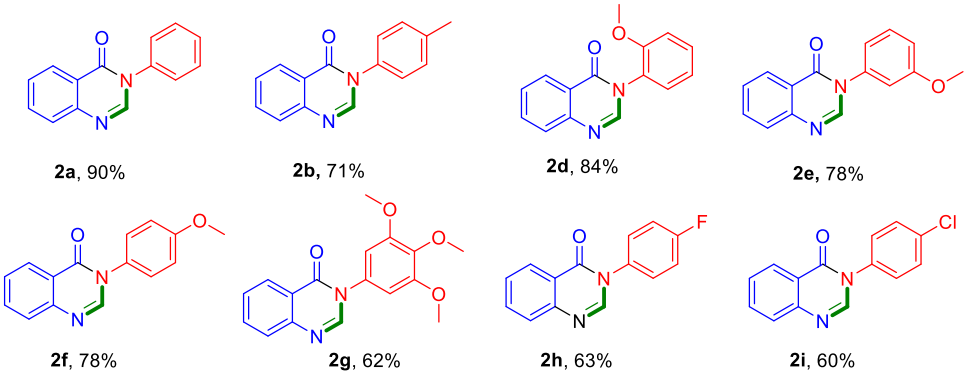


To an oven dried sealed tube was charged **1a-1f'** (0.15 mmol), 1, 4-dioxane (0.25 M) and TsOH. H_2O (0.15 mmol) and allowed to stir at 110 ^oC until the completion of reaction (4 ~ 36 h) by TLC. After completion, the reaction mixture was cooled to room temperature and diluted with 5.0 mL of water. The water layer was extracted with (3X10 mL) of ethyl acetate and the combined ethyl acetate layer was given brine wash (1X10 mL). The final ethyl acetate layer was dried over sodium sulfate and concentrated under reduced pressure to get the crude compound. The obtained crude was purified using column chromatography by eluting from hexane to 20 % ethyl acetate/hexane to afford pure quinazolin-4(3*H*)-ones **2a,b,d-l,o-t,v-z,2a'-d-,f'** in 53%-90% yields.

Scheme S1. Scope of *o*-amino benzamide derivatives with 1, 4-Dioxane [a,b]

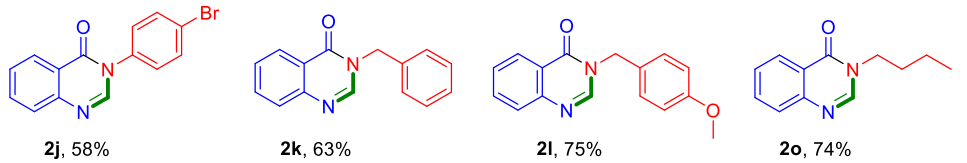


1a,b,d-l,o-t,v-z,1a'-d-,f' → **2a,b,d-l,o-t,v-z,2a'-d-,f'**

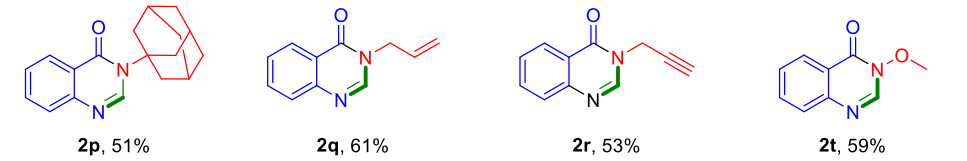


2a, 90% **2b**, 71% **2d**, 84% **2e**, 78%

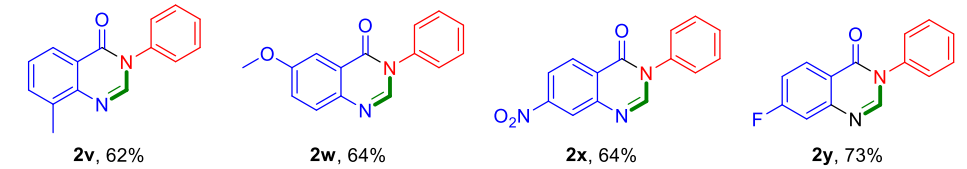
2f, 78% **2g**, 62% **2h**, 63% **2i**, 60%



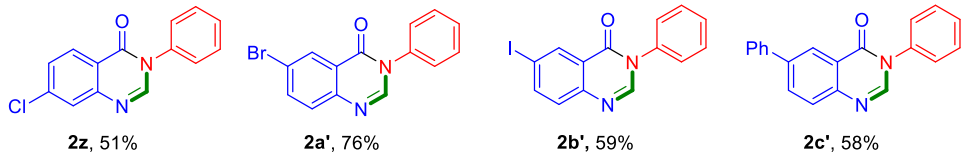
2j, 58% **2k**, 63% **2l**, 75% **2o**, 74%



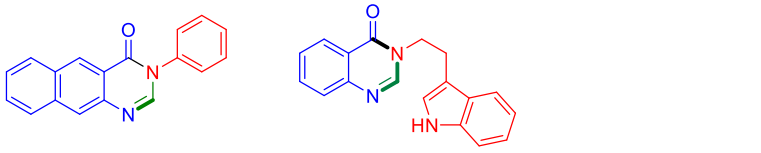
2p, 51% **2q**, 61% **2r**, 53% **2t**, 59%



2v, 62% **2w**, 64% **2x**, 64% **2y**, 73%



2z, 51% **2a'**, 76% **2b'**, 59% **2c'**, 58%



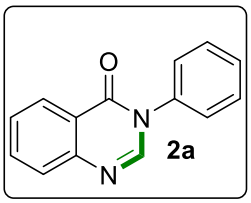
2d', 72% **2f'**, 53%

Precursors for rutaecarpine and evodiamine

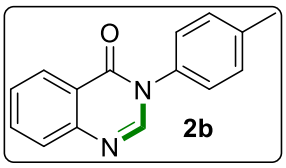
[a] Reaction conditions: Compound **1** (0.15 mmol), TsOH.H2O (1.0 equiv) and 1,4-Dioxane (0.25 M) were stirred at 110 °C in the presence of O_2 balloon for 4 – 36 h. [b] Isolated yields.

(3) Spectral Characterization

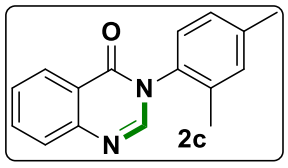
3-phenylquinazolin-4(3*H*)-one (**2a**):[3] The title compound was prepared according to the general procedure C on a 0.15 mmol scale to obtain as a white solid (32 mg, yield = 96%); Mp. 132-140 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.38 (ddd, *J* = 7.6, 1.2, 0.4 Hz, 1H), 8.14 (s, 1H), 7.82-7.77 (m, 2H), 7.58-7.54 (m, 3H), 7.52-7.50 (m, 1H), 7.45-7.42 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.75, 147.85, 146.06, 137.46, 134.58, 129.63, 129.10, 127.64, 127.56, 127.17, 126.98, 122.36.



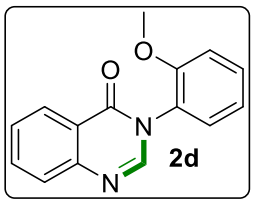
3-(*p*-tolyl)quinazolin-4(3*H*)-one (2b):[3] The title compound was prepared according to the general procedure C on a 0.15 mmol scale to obtain as a light yellow solid (31 mg, yield = 88%); Mp.172-174 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.36-8.34 (m, 1H), 8.10 (s, 1H), 7.78-7.73 (m, 2H), 7.53 (ddd, *J* = 8.0, 6.8, 1.6 Hz, 1H), 7.34-7.27 (m ,4H), 2.42 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz); δ 160.80, 147.84, 146.22, 139.14, 134.85, 134.42, 130.15, 127.49, 127.47, 127.09, 126.66, 122.33, 21.13.



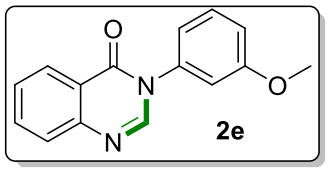
3-(2,4-dimethylphenyl)quinazolin-4(3*H*)-one (2c):[4] The title compound was prepared according to the general procedure C on a 0.15 mmol scale to obtain as a light brown solid (31 mg, yield = 82%); Mp.81-83 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.37 (ddd, *J* = 8.0, 2.0, 1.2 Hz, 1H) 7.98 (s, 1H), 7.82-7.76 (m, 2H), 7.54 (ddd, *J* = 8.0, 6.4, 1.2 Hz, 1H), 7.20-719 (m, 1H),7.14-7.11 (m,2H), 2.39 (s, 3H), 2.15 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.55, 148.05, 146.56, 139.74, 135.32, 134.44, 134.00, 131.96, 127.91, 127.50, 127.47, 127.12, 122.38, 21.09, 17.58.



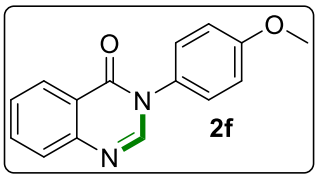
3-(2-methoxyphenyl)quinazolin-4(3*H*)-one (2d):[5] The title compound was prepared according to the general procedure C on a 0.15 mmol scale to obtain as alight yellow solid (34 mg, yield = 90%); Mp.144-146 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.38-8.36 (m, 1H), 7.98 (s, 1H), 7.82-7.76 (m, 2H), 7.54-7.46 (m, 2H), 7.35 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.13-7.08 (ddd, *J* = 10.4, 7.6, 1.2 Hz, 2H), 3.81 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.62, 154.62, 148.00, 147.15, 134.34, 130.89, 129.09, 127.44, 127.25, 127.12, 125.92, 122.64, 120.94, 112.21, 55.79.



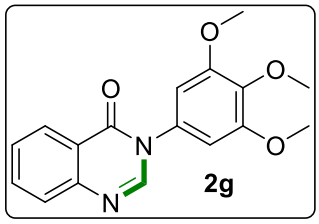
3-(3-methoxyphenyl)quinazolin-4(3*H*)-one (2e):[3] The title compound was prepared according to the general procedure C on a 0.15 mmol scale to obtain as a white solid (34 mg, yield = 90%); Mp.151-153 °C; ^{1}H NMR($CDCl_3$, 400 MHz) δ 8.39-8.36 (m, 1H), 8.13 (s, 1H), 7.81-7.78 (m, 2H), 7.56 (ddd, *J* =8.0, 6.8,1.2 Hz, 1H), 7.45 (t, *J* = 8.4 Hz, 1H), 7.04 (ddd, *J* = 8.4, 2.4, 0.4 Hz, 1H), 6.98-6.96 (m, 2H), 3.85 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.67, 160.39, 147.79, 146.03, 138.47, 134.55, 130.36, 127.61, 127.54, 127.15, 122.34, 119.06, 115.03, 112.80, 55.52.



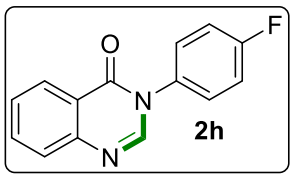
3-(4-methoxyphenyl)quinazolin-4(3*H*)-one (2f):[3] The title compound was prepared according to the general procedure C on a 0.15 mmol scale to obtain as a light yellow solid (35mg, yield = 93%); Mp.181-183 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.38 (ddd, *J* = 8.0, 0.4, 1.2 Hz, 1H), 8.11 (s, 1H), 7.82-7.75 (m, 2H), 7.54 (ddd, *J* = 8.0, 6.8, 1.6 Hz, 1H), 7.35-7.26 (m ,2H),7.06-7.03 (m ,2H), 3.87 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.93, 159.82, 147.81, 146.35, 134.39, 130.08, 128.05, 127.47, 127.44, 127.05, 122.28, 114.73, 55.51.



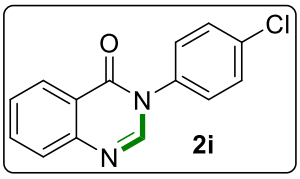
3-(3,4,5-trimethoxyphenyl)quinazolin-4(3*H*)-one (2g):[6] The title compound was prepared according to the general procedure C on a 0.15 mmol scale to obtain as a light yellow solid (38 mg, yield = 79%); Mp.139-141 °C;^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.36 (dd, *J* = 8.0, 1.2 Hz, 1H), 8.12 (s, 1H), 7.83-7.75 (m, 2H), 7.56 (ddd, *J* = 8.0, 6.8, 1.4 Hz, 1H), 6.62 (s, 2H), 3.88 (d, *J* = 9.2 Hz, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.84, 153.76, 147.74, 146.06, 138.42, 134.60, 132.95, 127.66, 127.53, 127.07, 122.21, 104.59, 60.86, 56.26.



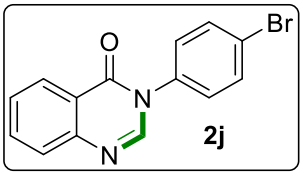
3-(4-fluorophenyl)quinazolin-4(3*H*)-one (2h):[3] The title compound was prepared according to the general procedure C on a 0.15 mmol scale to obtain as a white solid (30 mg, yield = 83%); Mp.199-201 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.36 (dd, *J* = 8.0, 1.2 Hz, 1H), 8.10 (s, 1H), 7.83-7.76 (m, 2H), 7.56 (ddd, *J* = 8.0, 6.8, 1.2 Hz, 1H), 7.43-7.40 (m, 2H), 7.27-7.22 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 163.84, 161.35 (d, J_F =248.2 Hz), 160.78, 147.81, 145.81, 134.69, 133.37 (d, J_F =3.0 Hz), 128.93, 128.84 (d, J_F =8.7 Hz), 127.77, 127.63, 127.15, 122.24, 116.78, 116.55, (d, J_F =23.2 Hz).



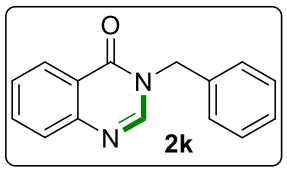
3-(4-chlorophenyl)quinazolin-4(3*H*)-one (2i):[5] The title compound was prepared according to the general procedure C on a 0.15 mmol scale to obtain as a white solid (33 mg, yield = 86%); Mp.138-140 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.36 (ddd, *J* = 7.6, 1.2, 0.4 Hz, 1H), 8.10 (s, 1H), 7.84-7.76 (m, 2H), 7.58-7.52 (m, 3H), 7.41-7.37 (m ,2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.55, 147.70, 145.50, 135.82, 135.09, 134.69, 129.80, 128.28, 127.77, 127.61, 127.11, 122.14.



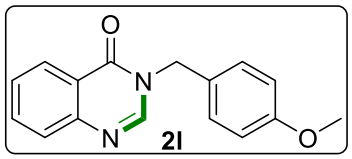
3-(4-bromophenyl)quinazolin-4(3*H*)-one (2j):[3] The title compound was prepared according to the general procedure C on a 0.15 mmol scale to obtain as a white solid (39 mg, yield = 87%); Mp.186-188 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.35 (ddd, *J* = 8.0, 1.4, 0.5 Hz, 1H), 8.07 (s, 1H), 7.80-7.77 (m, 2H), 7.68-7.66 (m, 2H), 7.55 (ddd, *J* = 8.0, 6.8, 1.2 Hz, 1H), 7.33-7.29 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.50, 147.72, 145.43, 136.37, 134.72, 132.81, 128.58, 127.80, 127.64, 127.14, 123.13, 122.17.



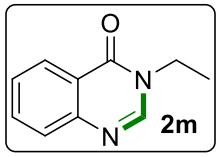
3-benzylquinazolin-4(3*H*)-one (2k):[3] The title compound was prepared according to the general procedure C on a 0.15 mmol scale to obtain as a white solid (31 mg, yield = 88%); Mp.114-116 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.33 (dd, *J* = 8.0 1.2, Hz, 1H), 8.11 (s, 1H), 7.78-7.69 (m, 2H), 7.51 (ddd, *J* = 8.8, 7.2, 1.2, Hz, 1H), 7.36-7.30 (m, 5H), 5.19 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.02, 147.99, 146.28, 135.68, 134.25, 128.98, 128.26, 127.95, 127.47, 127.33, 126.84, 122.17, 49.55.



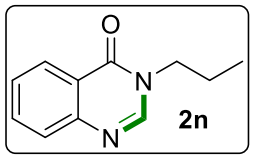
3-(4-methoxybenzyl)quinazolin-4(3*H*)-one (2l):[7] The title compound was prepared according to the general procedure C on a 0.15 mmol scale to obtain as a light yellow solid (32 mg, yield = 81%); Mp.123-125 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.31 (dd, *J* = 8.0, 1.2 Hz, 1H), 8.09 (s, 1H), 7.76-7.67 (m, 2H), 7.49 (ddd, *J* = 8.8, 6.8, 1.2 Hz, 1H), 7.31-7.29 (m, 2H), 6.88-6.85 (m, 2H), 5.12 (s, 2H), 3.77 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.04, 159.56, 147.98, 146.24, 134.20, 129.57, 127.77, 127.43, 127.28, 126.81, 122.19, 114.35, 55.27, 49.17.



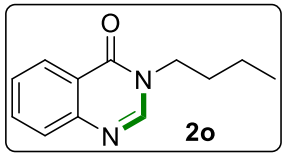
3-ethylquinazolin-4(3*H*)-one (2m):[8] The title compound was prepared according to the general procedure C on a 0.15 mmol scale to obtain as alight yellow solid (19 mg, yield = 73%); Mp.72-74 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.33 (ddd, *J* = 8.0, 1.6, 0.4 Hz, 1H), 8.06 (s, 1H), 7.78-7.70 (m, 2H), 7.51 (ddd, *J* = 8.0, 6.8, 1.2 Hz, 1H), 4.08 (q, *J* = 7.2 Hz, 2H), 1.43 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.86, 148.08, 146.21, 134.06, 127.32, 127.16, 126.57, 122.12, 42.05, 14.82.



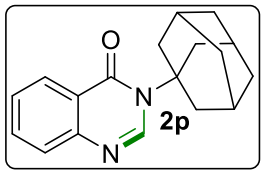
3-propylquinazolin-4(3*H*)-one (2n):[9] The title compound was prepared according to the general procedure C on a 0.15 mmol scale to obtain as a light brown solid (25 mg, yield = 89%); Mp.73-75 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.32 (ddd, *J* = 8.0, 1.2, 0.8 Hz, 1H), 8.03 (s, 1H), 7.78-7.69 (m, 2H), 7.50 (ddd, *J* = 8.0, 6.8, 1.2 Hz, 1H), 3.99-3.95 (m , 2H), 1.88-1.79 (m ,2H), 1.01 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.03, 148.06, 146.58, 134.10, 127.34, 127.18, 126.66, 122.14, 48.56, 22.61, 11.10.



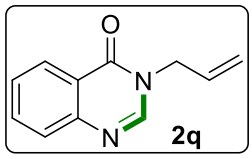
3-butylquinazolin-4(3*H*)-one (2o):[10] The title compound was prepared according to the general procedure C on a 0.15 mmol scale to obtain as a light brown solid (22 mg, yield = 71%); Mp.59-61 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.33 (dd, *J* = 8.0, 1.2 Hz, 1H) 8.04 (s, 1H), 7.78-7.70 (m, 2H), 7.51 (ddd, *J* = 8.0, 6.8, 1.2 Hz, 1H), 4.01 (t, *J* = 7.2 Hz, 2H), 1.83-1.75 (m, 2H), 1.45-1.40 (m, 2H) 0.99 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.01, 148.06, 146.53, 134.06, 127.33, 127.15, 126.63, 122.14, 46.75, 31.37, 19.84, 13.59.



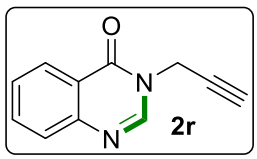
3-(adamantan-1-yl)quinazolin-4(3*H*)-one (2p): The title compound was prepared according to the general procedure C on a 0.15 mmol scale to obtain as a white solid (32 mg, yield = 76%); Mp.203-205 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.27 (dd, *J* = 6.2, 2.0 Hz, 2H), 7.74-7.70 (m, 1H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.48-7.44 (m, 1H), 2.46 (d, *J* = 2.4 Hz, 6H), 2.88 (s, 3H), 1.84-1.76 (m, 6H), 1.69 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 162.03, 146.93, 143.91, 133.88, 126.83, 126.69, 126.67, 123.15, 62.48, 39.87, 35.99, 29.99; HRMS (ESI): Calc'd for $[M+H]^+$ $C_{18}H_{21}N_2O$: 281.1649; found 281.1648.



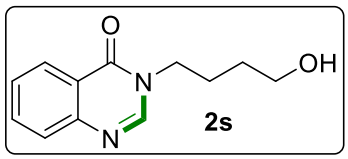
3-allylquinazolin-4(3*H*)-one (2q):[11] The title compound was prepared according to the general procedure C on a 0.15 mmol scale to obtain as a light brown solid (20 mg, yield = 73%); Mp. 54-56 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.33 (dd, *J* = 8.0, 1.6 Hz, 1H), 8.02 (s, 1H), 7.79-7.71 (m, 2H), 7.52 (ddd, *J* = 8.0, 6.8, 1.2 Hz, 1H), 6.05-5.95 (m, 1H), 5.32-5.25 (m, 2H), 4.65 (dt, *J* =1.6, 5.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.74, 147.97, 146.15, 134.22, 131.76, 127.40, 127.28, 126.72, 122.01, 118.80, 48.27.



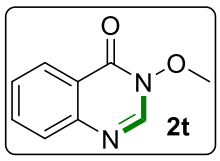
3-(prop-2-yn-1-yl) quinazolin-4(3*H*)-one (2r):[12] The title compound was prepared according to the general procedure C on a 0.15 mmol scale to obtain as a white solid (21 mg, yield = 77%); Mp.114-115 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.31 (dd, *J* = 0.8, 8.0 Hz, 2H), 7.78 (ddd, *J* = 1.6, 7.2, 8.4 Hz, 1H), 7.73 (dd, *J* = 1.2, 8.4 Hz, 1H), 7.52 (ddd, *J* = 8.4, 7.6, 1.6 Hz, 1H), 4.83 (d, *J* =2.8, 2H), 2.51 (t, *J* = 2.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.32, 147.83, 144.97, 134.46, 127.52, 127.48, 126.72, 126.60, 121.68, 75.08, 35.14.



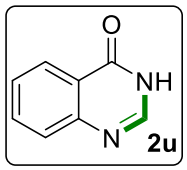
3-(2-hydroxyethyl) quinazolin-4(3*H*)-one (2s): The title compound was prepared according to the general procedure C on a 0.15 mmol scale to obtain as a white solid (26 mg, yield = 78%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.31 (ddd, *J* = 8.0, 1.6, 0.4 Hz, 1H), 8.06 (s, 1H), 7.77-770 (m, 2H), 7.52 (ddd, *J* = 8.4, 6.8, 1.6 Hz, 1H), 4.07 (t, *J* = 7.2 Hz, 2H), 3.73 (t, *J* = 6.0 Hz 2H), 1.94-1.90 (m, 2H), 1.76 (s, 1H), 1.69-1.64 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.12, 147.88, 146.53, 134.20, 127.27, 127.22, 126.56, 121.92, 61.85, 46.73, 29.26, 26.01:HRMS (ESI): Calc'd for $[M+H]^+$ $C_{12}H_{15}N_2O_2$: 219.11280; found 219.11304.



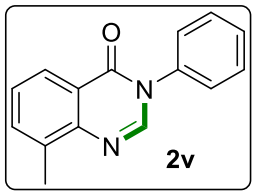
3-methoxyquinazolin-4(3*H*)-one (2t): The title compound was prepared according to the general procedure C on a 0.15 mmol scale to obtain as a light yellow solid (20 mg, yield = 75%); Mp.182-184 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.35 (ddd, *J* = 8.0, 1.2, 0.4 Hz, 1H), 8.26 (s, 1H), 7.79-7.74 (m, 2H), 7.55 (ddd, *J* = 8.0, 6.8, 1.2 Hz, 1H), 4.17 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 157.08, 147.03, 143.92, 134.37, 127.85, 127.45, 126.70, 123.52, 65.81; HRMS (ESI): Calc'd for $[M+H]^+$ $C_9H_9N_2O_2$: 177.0656; found 177.0658.



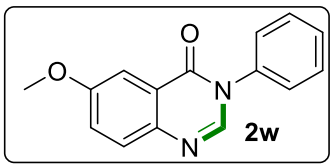
quinazolin-4(3*H*)-one(2u):[3] The title compound was prepared according to the general procedure C on a 0.15 mmol scale to obtain as a white solid (17 mg, yield = 78%); Mp.110-112 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 11.99 (s, 1H), 8.27 (ddd, *J* = 8.0, 1.6, 0.8 Hz, 1H), 8.02 (s,1H), 7.79-7.70 (m, 2 H), 7.50 (ddd, *J* = 8.4, 6.8, 1.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 162.28, 148.73, 144.06, 134.37, 127.36, 126.93, 126.14, 122.64, 39.95, 39.74, 39.53.



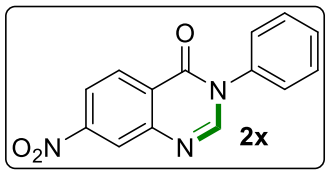
8-methyl-3-phenylquinazolin-4(3*H*)-one(2v):[13] The title compound was prepared according to the general procedure C on a 0.15 mmol scale to obtain as a light yellow solid (27 mg, yield = 77%); Mp.109-111 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.22 (ddd, *J* =8.0, 1.6, 0.8 Hz, 1H), 8.15 (s, 1H), 7.64 (ddd, *J* = 7.2, 1.6, 0.8 Hz, 1H), 7.57-7.53 (m, 2H), 7.50-7.47 (m, 1H), 7.45-7.41 (m, 3H), 2.66 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.06, 146.39, 144.81, 137.56, 135.97, 135.24, 129.91, 129.59, 128.99, 127.18, 126.94, 124.84, 122.31, 17.46.



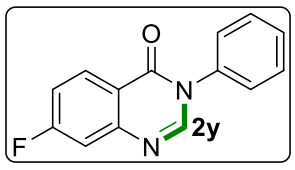
6-methoxy-3-phenylquinazolin-4(3*H*)-one (2w):[14] The title compound was prepared according to the general procedure C on a 0.15 mmol scale to obtain as a white solid (30 mg, yield = 79%); Mp.160-162 °C; Mp: C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.04 (s, 1H), 7.72 (dd, *J* = 8.0, 3.2 Hz, 2H), 7.58-7.54 (m, 2H), 7.52-7.50 (m, 1H), 7.44-7.38 (m, 3H), 3.94 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.61, 159.00, 143.96, 142.36, 137.61, 129.59, 129.11, 129.03, 128.91, 126.98, 125.22, 124.63, 106.59, 55.86.



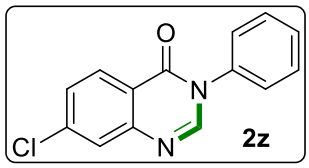
7-nitro-3-phenylquinazolin-4(3*H*)-one (2x): The title compound was prepared according to the general procedure C on a 0.15 mmol scale to obtain as a white solid (30 mg, yield = 74%); Mp.225-227 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.61 (d, *J* = 2 Hz, 1H),8.53 (dd, *J*=8.4, 0.4 Hz, 1H), 8.31 (dd, *J* = 8.8, 2.4 Hz, 1H), 8.23 (s, 1H), 7.59-7.53 (m, 3H), 7.44-7.42 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.54, 151.61, 148.47, 148.03, 136.72, 129.87, 129.63, 129.15, 126.75, 126.57, 123.24, 121.30; HRMS (ESI): Calc'd for $[M+H]^+$ $C_{14}H_{10}N_3O_3$: 268.0715; found 268.0716.



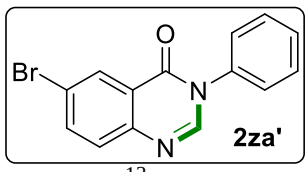
7-fluoro-3-phenylquinazolin-4(3*H*)-one (2y):[3] The title compound was prepared according to the general procedure C on a 0.15 mmol scale to obtain as a white solid (28 mg, yield = 78%); Mp.180-182 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.39(dd, *J* = 8.8, 6.0 Hz, 1H), 8.14 (s, 1H), 7.57-7.48 (m, 3H), 7.42-7.40 (m, 3H), 7.28-7.23 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.79, 165.26 (d, J_F =253.5 Hz), 160.03, 150.11, 149.98 (d, J_F =13 Hz), 147.26, 137.16, 130.00, 129.89, 129.68, 129.25, 129.14, 129.03, 126.92, 125.28, 123.63, 120.99, 119.87, 119.06, 116.48, 116.25 (d, J_F = 23.2 Hz), 113.15, 112.93(d, J_F = 21.8Hz).



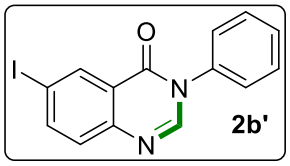
7-chloro-3-phenylquinazolin-4(3*H*)-one (2z):[3] The title compound was prepared according to the general procedure C on a 0.15 mmol scale to obtain as a white solid (35 mg, yield = 89%); Mp.186-188 °C; ^{1}H NMR($CDCl_3$, 400 MHz) δ 8.26 (d, *J* = 8.4 Hz, 1H), 8.13 (s, 1H), 7.76 (d, *J* = 2.0 Hz, 1H), 7.57-7.48 (m, 4H), 7.42-7.40 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.11, 148.79, 147.20, 140.78, 137.10, 129.67, 129.25, 128.60, 128.21, 127.14, 126.86, 120.79.



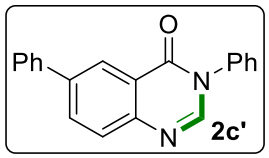
6-bromo-3-phenylquinazolin-4(3*H*)-one (2a'):[3] The title compound was prepared according to the general procedure C on a 0.15 mmol scale to obtain as a white solid (34 mg, yield = 76%); Mp.178-180 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.49 (d, *J* = 2.4 Hz, 1H), 8.12 (s, 1H), 7.88 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.64 (d, *J* = 8.4 Hz, 1H), 7.58-7.48 (m, 3H) , 7.42-7.40 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.56, 146.69, 146.38, 137.74, 137.15, 129.72, 129.69, 129.38, 129.29, 126.87, 123.75, 121.30.



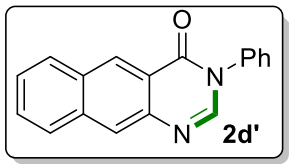
6-iodo-3-phenylquinazolin-4(3*H*)-one(2b'):[3] The title compound was prepared according to the general procedure C on a 0.15 mmol scale to obtain as a light yellow solid (38 mg, yield = 73%); Mp.166-168 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.68 (d, *J* = 2.0 Hz, 1H), 8.12 (s, 1H), 8.05 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.57-7.47 (m, 4H), 7.41-7.39 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.28, 147.13, 146.56, 143.34, 137.13, 135.91, 130.06, 129.70, 129.34, 129.27, 127.84, 126.85, 123.91, 92.24.



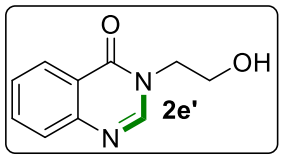
3,6-diphenylquinazolin-4(3*H*)-one (2c'): The title compound was prepared according to the general procedure C on a 0.15 mmol scale to obtain as a white solid (36 mg, yield = 80%); Mp.124-126°C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.59 (d, *J* = 2.4 Hz, 1H), 8.14 (s, 1H), 8.06 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.84 (d, *J* = 8.4 Hz, 1H), 7.71 (dd, *J* = 3.2, 1.6 Hz, 2H), 7.57 (dd, *J* = 8.8, 7.2 Hz, 2H), 7.52-7.40 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.80, 147.00, 145.96, 140.60, 139.43, 137.47, 133.47, 129.65, 129.12, 129.00, 128.08, 127.98, 127.23, 126.98, 125.02, 122.60, 77.31; HRMS (ESI): Calc'd for $[M+H]^+$ $C_{20}H_{15}N_2O$: 299.1179; found 299.1178.



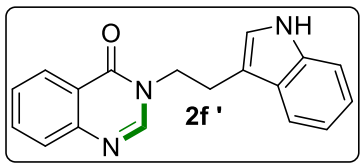
3-phenylbenzo[g]quinazolin-4(3*H*)-one (2d'): The title compound was prepared according to the general procedure C on a 0.15 mmol scale to obtain as a white solid (31mg, yield = 76%); Mp.224-226 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.98 (s, 1H), 8.26 (s, 1H), 8.12-8.08 (m, 2H), 8.03 (d, *J* = 8.4 Hz 1H), 7.66 (ddd, *J* = 8.0, 6.8, 1.2 Hz, 1H), 7.60-7.56 (m, 3H), 7.53-7.46 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.25, 145.35, 143.08, 137.60, 136.59, 131.95, 129.66, 129.42, 128.99, 128.87, 128.70, 128.09, 127.09, 126.68, 125.59, 120.81, 109.97; HRMS (ESI): Calc'd for $[M+H]^+$ $C_{18}H_{13}N_2O$: 273.1021; found 273.1022.



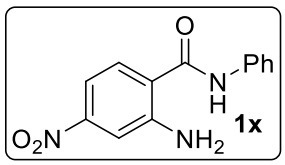
3-(2-hydroxyethyl) quinazolin-4(3*H*)-one (2e'):[10] The title compound was prepared according to the general procedure C on a 0.15 mmol scale to obtain as a white solid (24 mg, yield = 83%); Mp.154-155 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.07-8.05 (m, 2H), 7.65 (ddd, *J* = 8.4, 7.2, 1.6 Hz, 1H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.38-7.34 (m, 1H), 4.09 (t, *J* = 9.6 Hz, 2H), 3.97 (t, *J* = 10.0 Hz, 2H), 3.70 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.20, 147.51, 147.39, 134.29, 127.20, 126.77, 126.35, 121.54, 63.61, 60.06, 49.64.



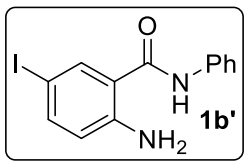
3-(2-(1H-indol-3-yl)ethyl)quinazolin-4(3*H*)-one (2f'):[15] The title compound was prepared according to the general procedure C on a 0.15 mmol scale to obtain as alight yellow solid (31mg, yield = 71%); Mp.162-164 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.36 (ddd, *J* = 8.0, 1.6, 0.4 Hz, 1H), 8.20 (s, 1H), 7.73 (ddd, *J* = 8.0, 6.8, 1.6 Hz, 1H), 7.66-7.62 (m, 2H), 7.53-7.50 (m, 2H), 7.36-7.33 (m, 1H), 7.20 (ddd, *J* = 8.0, 1.6, 0.4 Hz, 1H), 7.12 (ddd, *J* = 8.0, 7.2, 1.2 Hz, 1H), 6.86 (d, *J* = 2.4 Hz, 1H), 4.29 (t, *J* = 6.8 Hz, 2H), 3.26 (dd, *J* = 7.2, 6.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.08, 148.10, 146.69, 136.41, 134.11, 127.31, 127.09, 126.77, 126.60, 122.74, 122.34, 122.06, 119.72, 118.34, 111.47, 111.25, 47.51, 24.90.



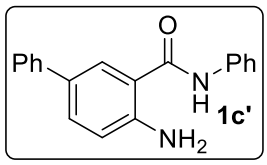
2-amino-4-nitro-*N*-phenylbenzamide (1x): The title compound was prepared according to the general procedure B on a 1.2 mmol scale to obtain as a yellow solid (205 mg, yield = 66%); Mp.161-163 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.80 (s, 1H), 7.62-7.56 (m, 3H), 7.55 (d, *J* = 2.0 Hz, 1H), 7.49 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.41 (ddd, *J* = 7.6, 4.0, 2.0 Hz, 2H), 7.21 (ddd, *J* = 7.2, 2.4, 1.2 Hz, 1H), 5.79 (s, 2H); ^{13}C NMR ($CDCl_3$,100 MHz) δ 165.97, 150.33, 149.41, 137.09, 129.18, 128.32, 125.22, 120.79, 120.71, 111.56, 110.76; HRMS (ESI): Calc'd for $[M+H]^+$ $C_{13}H_{12}N_3O_3$: 258.0872; found 258.0873.



2-amino-5-iodo-*N*-phenylbenzamide (1b'): The title compound was prepared according to the general procedure B on a 1.2 mmol scale to obtain as a light yellow solid (300 mg, yield = 72%); Mp.158-160 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.74-7.72 (m, 2H), 7.56-7.54 (m, 2H), 7.47 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.39-7.35 (m, 2H), 7.16(ddd, *J* = 8.4, 2.4, 1.2 Hz, 1H), 6.50 (d, *J* = 8.4 Hz, 1H), 5.50 (s, 2H), ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.16, 148.32, 140.86, 137.42, 135.47, 129.03, 124.76, 120.67, 119.44, 118.53, 77.31; HRMS (ESI): Calc'd for $[M+H]^+$ $C_{13}H_{12}IN_2O$: 338.9991; found 338.9988.

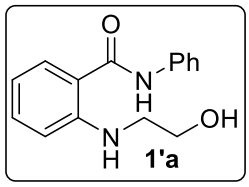


4-amino-*N*-phenyl-[1,1'-biphenyl]-3-carboxamide (1c'): The title compound was prepared according to the general procedure B on a 1.2 mmol scale to obtain as a light yellow solid (220 mg, yield = 63%); Mp.179-180 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.65 (d, *J* = 2.4 Hz, 1H), 7.57-7.47 (m, 5H), 7.42-7.36 (m, 4H), 7.35-7.28 (m, 2H), 7.14 (t, *J* =7.6 Hz, 1H), 6.75 (d, *J* =

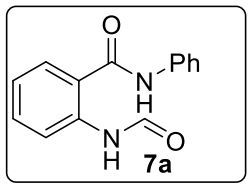


8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.58, 148.04, 140.27, 137.75, 131.37, 130.24, 129.95, 129.03, 128.97, 128.77, 128.67, 126.62, 126.40, 126.25, 125.77, 124.47, 120.58, 117.86, 116.64; HRMS (ESI): Calc'd for $[M+H]^+$ $C_{19}H_{17}N_2O$: 289.1335; found 289.1335.

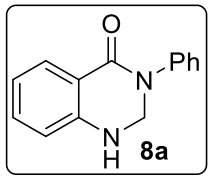
2-((2-hydroxyethyl)amino)-*N*-phenylbenzamide (1'a):[19] The title compound was prepared according to the literature procedure on a 0.94 mmol scale to obtain as a yellow liquid (190 mg, yield = 78%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.84 (ddd, *J* = 8.0, 1.6, 0.4 Hz, 1H), 7.29-7.25 (m, 1H), 7.22-7.17 (m, 2H), 6.75 -6.71 (m, 1H), 6.69 -6.62 (m, 4H), 5.71(s, 2H), 4.49-4.46 (m, 2H), 4.08 (s, 1H), 3.54-3.48 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ δ168.02, 150.56, 147.63, 134.29, 131.13, 129.31, 117.83, 116.69, 116.26, 112.94, 110.34, 62.98, 42.99; HRMS (ESI): Calc'd for $[M^+H]^+$ $C_{15}H_{17}N_2O_2$: 257.12845; found 257.12838.



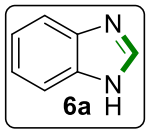
2-formamido-*N*-phenylbenzamide (7a):[20] The title compound was prepared according to the literature procedure on a 0.94 mmol scale to obtain as a white solid (170 mg, yield = 75%); Mp.159-161 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.60 (s,1H), 8.46-8.43 (m, 2H), 8.33 (d, *J* = 2.0 Hz, 1H), 7.65 -7.58 (m, 3H), 7.43-7.38 (m, 3H), 7.21 (ddd, *J* = 8.4, 2.0, 0.8 Hz, 1H), 7.12 (dt, *J* = 7.6, 1.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.04, 159.63, 137.83, 137.27, 132.60, 129.15, 126.99, 125.18, 123.65, 122.34, 121.58, 120.65. HRMS (ESI): Calc'd for $[M^+Na]^+$ $C_{14}H_{12}N_2NaO_2$: 263.07910; found 263.07922.



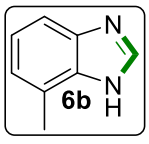
3-phenyl-2,3-dihydroquinazolin-4(1*H*)-one (8a):[21] The title compound was prepared according to the literature procedure on a 1.2 mmol scale to obtain as a White solid (200 mg, yield = 72%); Mp.164-166 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.04 (d, *J* = 8.0, 1.6 Hz, 1H), 7.42-7.33 (m, 5H), 7.27-2-7.23 (m, 1H), 6.95 (ddd, *J* = 8.0, 7.6, 1.2 Hz, 1H), 6.77-6.75 (m, 1H), 4.99 (s, 2H), 4.49(bs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 163.22, 147.48, 140.89, 133.51, 129.38, 129.00, 126.43, 125.00, 120.17, 118.20, 115.34, 62.10.



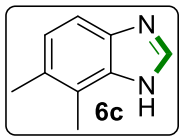
3-phenylquinazolin-4(3*H*)-one (6a):[16] The title compound was prepared according to the general procedure D on a 0.15 mmol scale to obtain as a white solid (15 mg, yield = 82%); Mp.173-174 °C; ^{1}H NMR ($CDCl_3$+ DMSO-d_6, 400 MHz) δ 8.08 (s, 1H), 7.65 (dt, *J* = 6.0, 3.2 Hz, 2H), 7.27-7.22 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 140.76,137.62,121.87, 115.06.



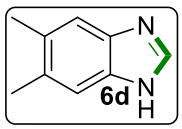
6-methyl-1*H*-benzo[*d*]imidazole (6b):[16] The title compound was prepared according to the general procedure D on a 0.15 mmol scale to obtain as alight yellow solid (17 mg, yield = 84%);Mp.127-128 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.09 (s, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.20 (t, *J* = 7.6 Hz, 1H), 7.10 (d, *J* = 7.2 Hz, 1H), 5.73 (s, 1H), 2.62 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.99, 137.72, 136.52, 126.01, 123.23, 122.97, 112.37, 17.01.



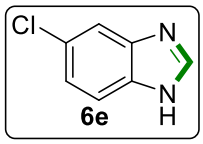
6,7-dimethyl-1*H*-benzo[*d*]imidazole(6c):[17] The title compound was prepared according to the general procedure D on a 0.15 mmol scale to obtain as alight yellow solid (19 mg, yield = 87%); Mp.193-194 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.03 (s, 1H), 7.83 (s, 1H), 7.39 (d, *J* = 7.2 Hz, 1H), 7.09 (d, *J* = 8.0 Hz, 1H), 2.52 (s, 3H), 2.39 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 140.30, 137.81, 135.84, 129.73, 124.66, 122.96, 112.08, 19.08, 13.69.



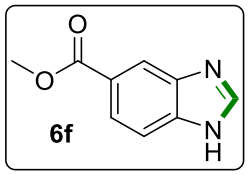
5,6-dimethyl-1*H*-benzo[*d*]imidazole (6d):[16] The title compound was prepared according to the general procedure D on a 0.15 mmol scale to obtain as alight yellow solid (17 mg, yield = 77%); Mp.198-199 °C;^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.00 (s, 1H), 7.73 (s, 1H), 7.42 (s, 2H), 2.35 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.93, 136.12, 131.84, 115.43, 20.31.



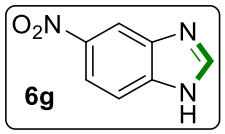
5-chloro-1*H*-benzo[*d*]imidazole (6e):[16] The title compound was prepared according to the general procedure D on a 0.15 mmol scale to obtain as alight yellow solid (20 mg, yield = 87%); Mp.112-113 °C; ^{1}H NMR ($CDCl_3$+DMSO-d_6, 400 MHz) δ 8.07 (s, 1H), 7.64 (d, *J* = 1.6 Hz, 1H), 7.56 (d, *J* = 8.8 Hz, 1H), 7.23 (dd, *J* = 8.8, 2.0 Hz, 1H); ^{13}C NMR (DMSO, 100 MHz) δ ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.84, 138.40, 136.53, 128.09, 123.05, 116.32, 115.23.



methyl 1*H*-benzo[*d*]imidazole-5-carboxylate (6f):[16] The title compound was prepared according to the general procedure D on a 0.15 mmol scale to obtain as alight yellow solid (23 mg, yield = 88%); Mp.133-134 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.40 (d, *J* =0.8 Hz, 1H), 8.17 (s, 1H), 7.98 (dd, *J* = 8.8, 1.6 Hz, 1H), 7.66 (d, *J* = 8.4 Hz, 1H), 3.94 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.56, 143.12, 124.27, 123.76,118.160, 114.818, 51.94.

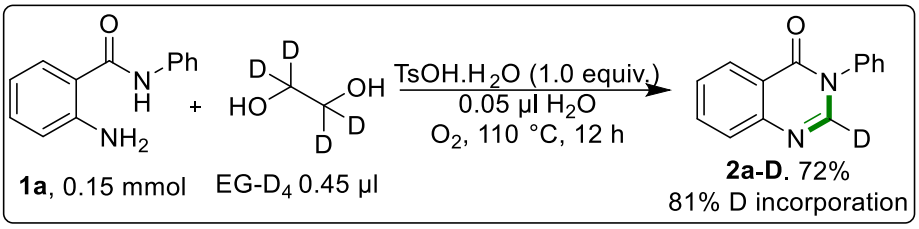


5-nitro-1*H*-benzo[*d*]imidazole (6g):[16] The title compound was prepared according to the general procedure D on a 0.15 mmol scale to obtain as a dark brown solid (18 mg, yield = 74%); Mp. 202-203 °C;^{1}H NMR ($CDCl_3$+DMSO-d_6, 400 MHz) δ 8.56 (d, *J* = 1.6 Hz, 1H), 8.23 (s, 1H), 8.14 (dd, *J* = 9.2, 2.4 Hz, 1H), 7.71 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR ($CDCl_3$+DMSO, 100 MHz) δ 145.29, 142.67, 117.35, 113.73, 62.99, 57.86.

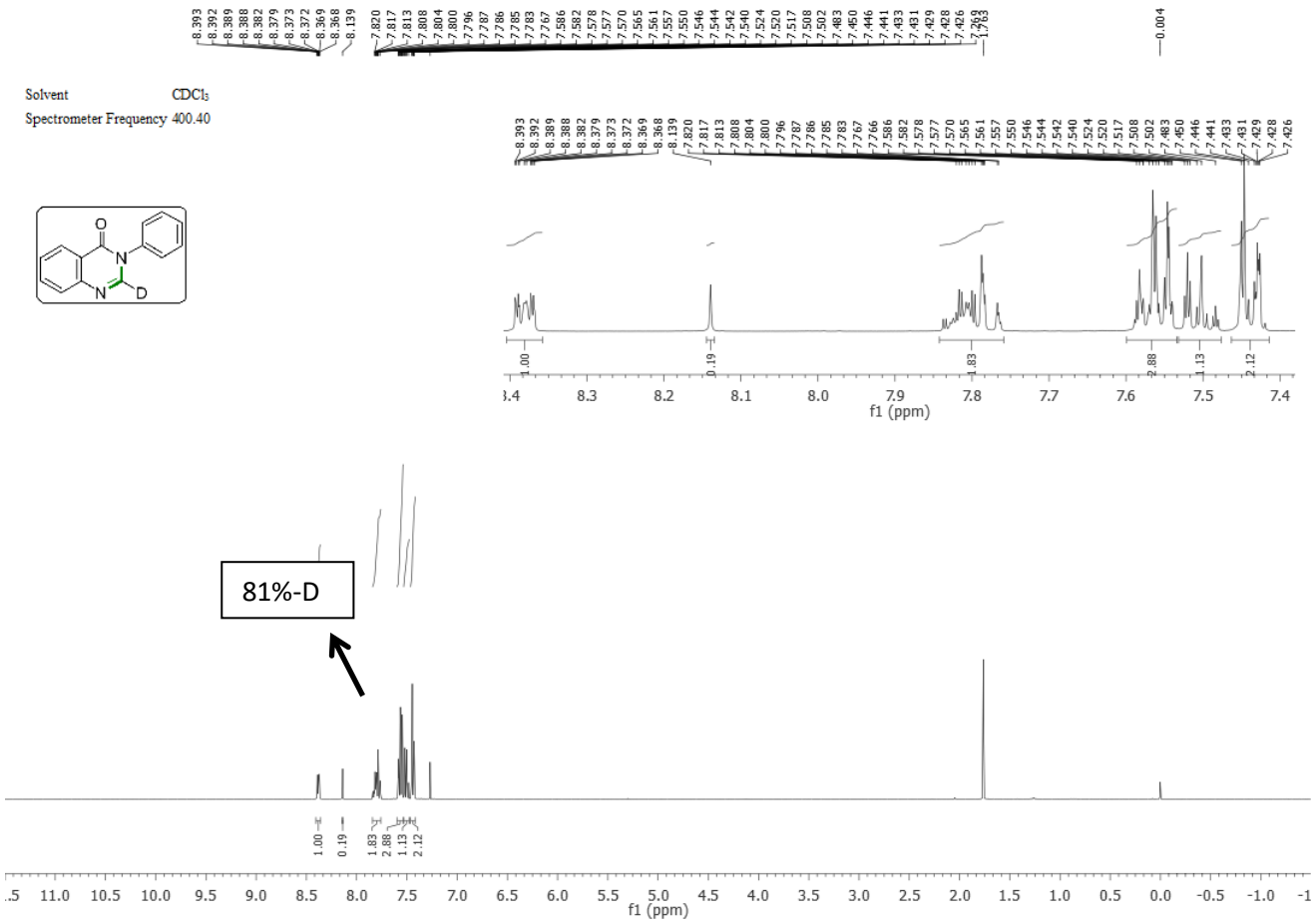


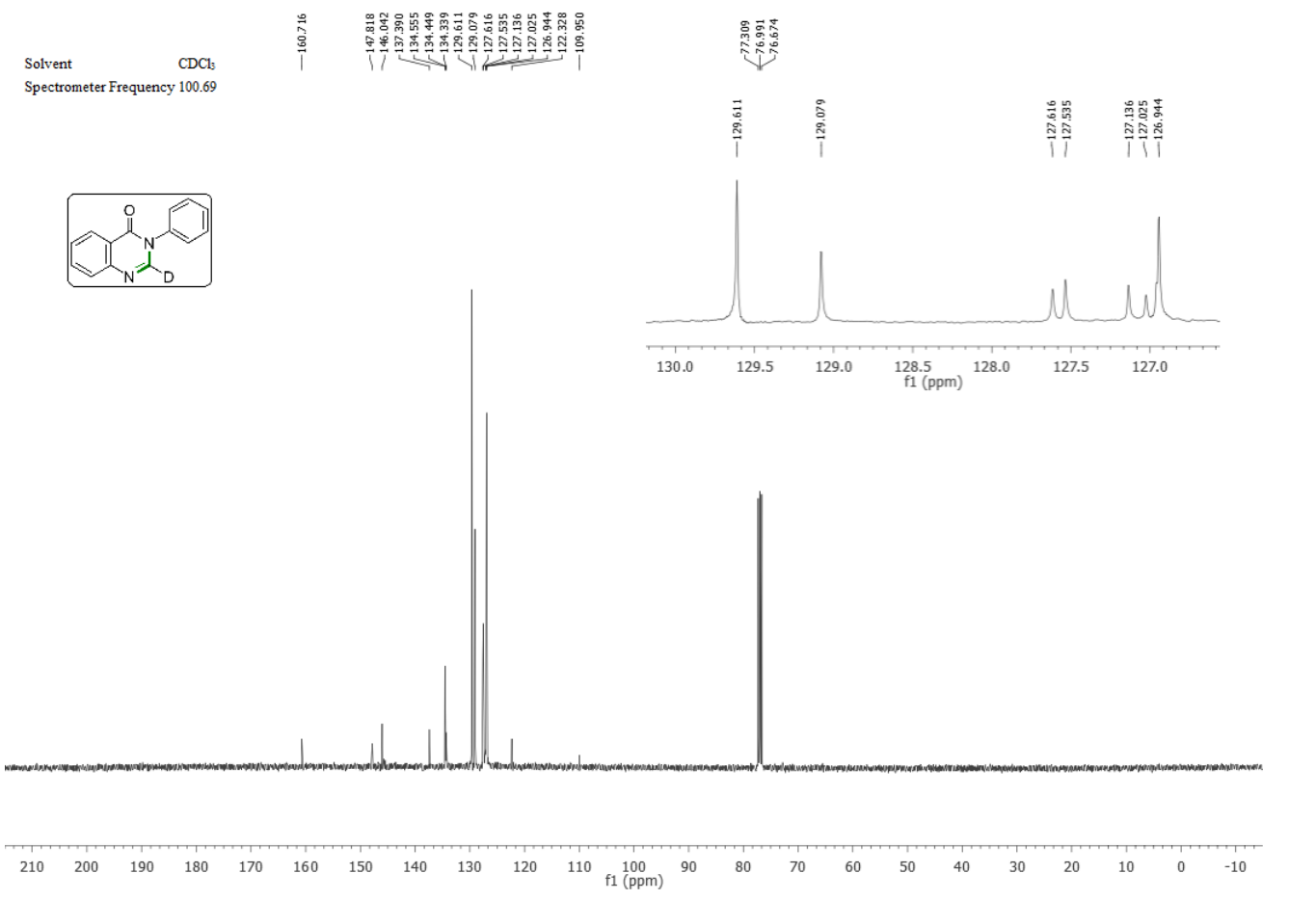
(4) Kinetic Studies

(a) Reaction with Deuterated Ethylene Glycol

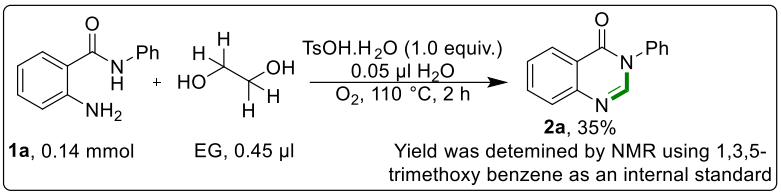


To an oven dried sealed tube was charged **1a** (30 mg, 0.14 mmol), EG D_4: H_2O (9:1) and TsOH. H_2O (0.15 mmol) and allowed to stir at 110 ^oC for 12 h. Then the reaction mixture was cooled to room temperature and diluted with 5.0 mL of water. The water layer was extracted with (3X10 mL) of ethyl acetate and the combined ethyl acetate layer was given brine wash (1X10 mL). The final ethyl acetate layer was dried over sodium sulfate and concentrated under reduced pressure to get the crude compound. The obtained crude was purified using column chromatography by eluting from hexane to 20% ethyl acetate/hexane to afford pure quinazolin-4(3*H*)-ones **2a** in 72% as a white solid (22 mg); Mp.137-138 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.39- 8.36 (m, 1H), 8.13 (s, 0.21H), 7.82-7.76 (m, 2H), 7.58-7.54 (m, 3H), 7.52-7.48 (m, 1H), 7.45-7.42 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.72, 147.82, 146.04, 137.39, 134.55, 134.45, 134.34, 129.61, 129.08, 127.62, 127.53, 127.14, 127.02, 126.94, 122.33, 109.95; HRMS (ESI): Calc'd for $[M+H]^+$ $C_{14}H_{10}DN_2O$: 224.0930; found 224.0928.

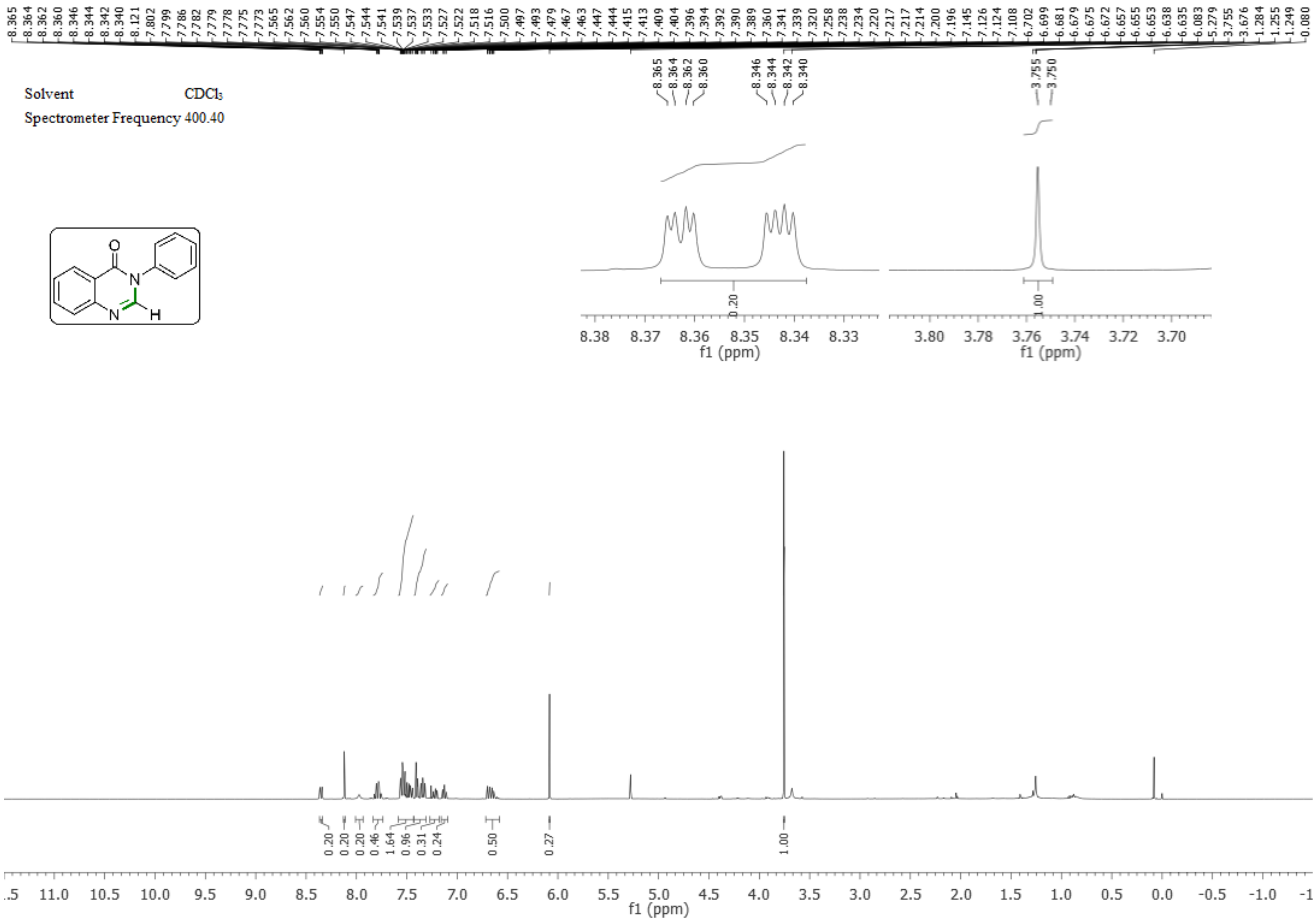

Solvent CDCl3
Spectrometer Frequency 400.40
81%-D
f1 (ppm)

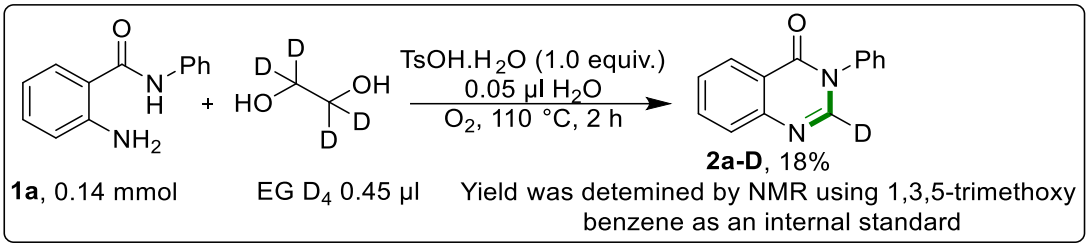

Solvent CDCl3
Spectrometer Frequency 100.69
f1 (ppm)

(b) Procedure for Parallel KIE Experiment:

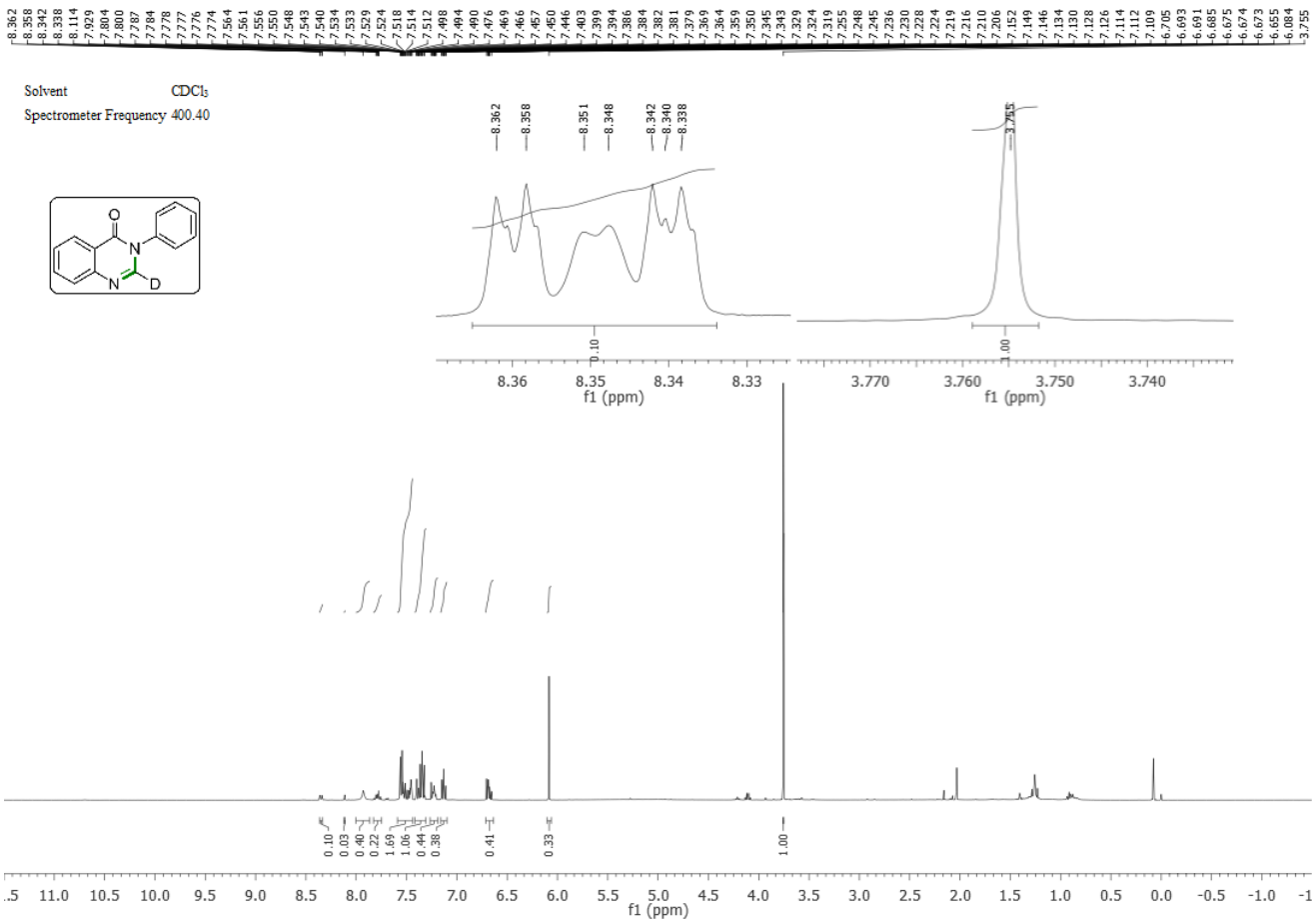


To an oven dried sealed tube was charged **1a** (30 mg, 0.14 mmol), ethylene glycol (EG): H_2O (9:1) and TsOH. H_2O (0.15 mmol) and allowed to stir at 110^o C for 2 h. Then the reaction mixture was cooled to room temperature and diluted with 5.0 mL of water. The water layer was extracted with (3X10 mL) of ethyl acetate and the combined ethyl acetate layer was given brine wash (1X10 mL). The final ethyl acetate layer was dried over sodium sulfate and concentrated under reduced pressure to get the crude compound. The yield of the compound was determined by using 1, 3, 5-trimethoxy benzene (4.6 mg) as an internal standard.



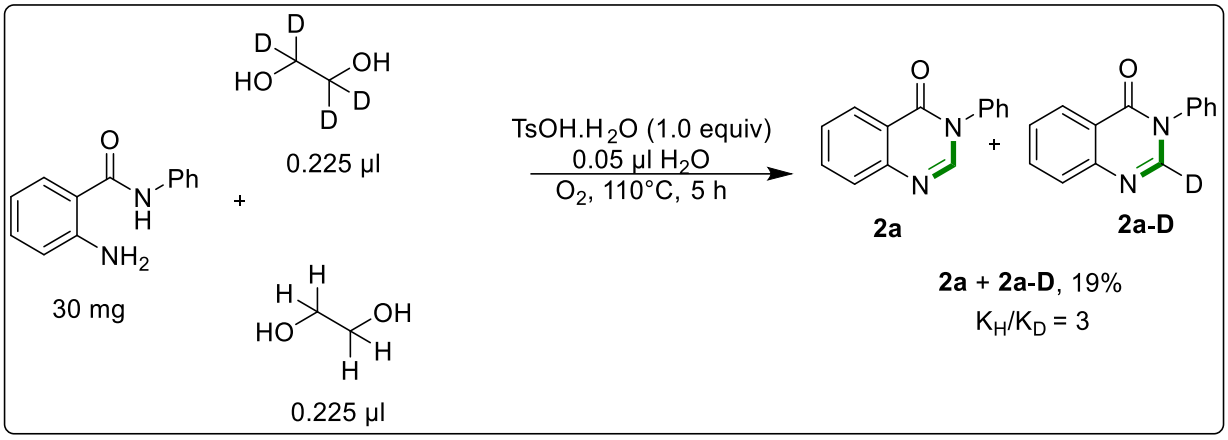


To an oven dried sealed tube was charged **1a** (30 mg, 0.14 mmol), ethylene glycol (EG): H_2O (9:1) and TsOH. H_2O (0.15 mmol) and allowed to stir at 110 ^oC for 2 h. Then the reaction mixture was cooled to room temperature and diluted with 5.0 mL of water. The water layer was extracted with (3X10 mL) of ethyl acetate and the combined ethyl acetate layer was given brine wash (1X10 mL). The final ethyl acetate layer was dried over sodium sulfate and concentrated under reduced pressure to get the crude compound. The yield of the compound was determined by using 1, 3, 5-trimethoxy benzene (4.7 mg) as an internal standard.

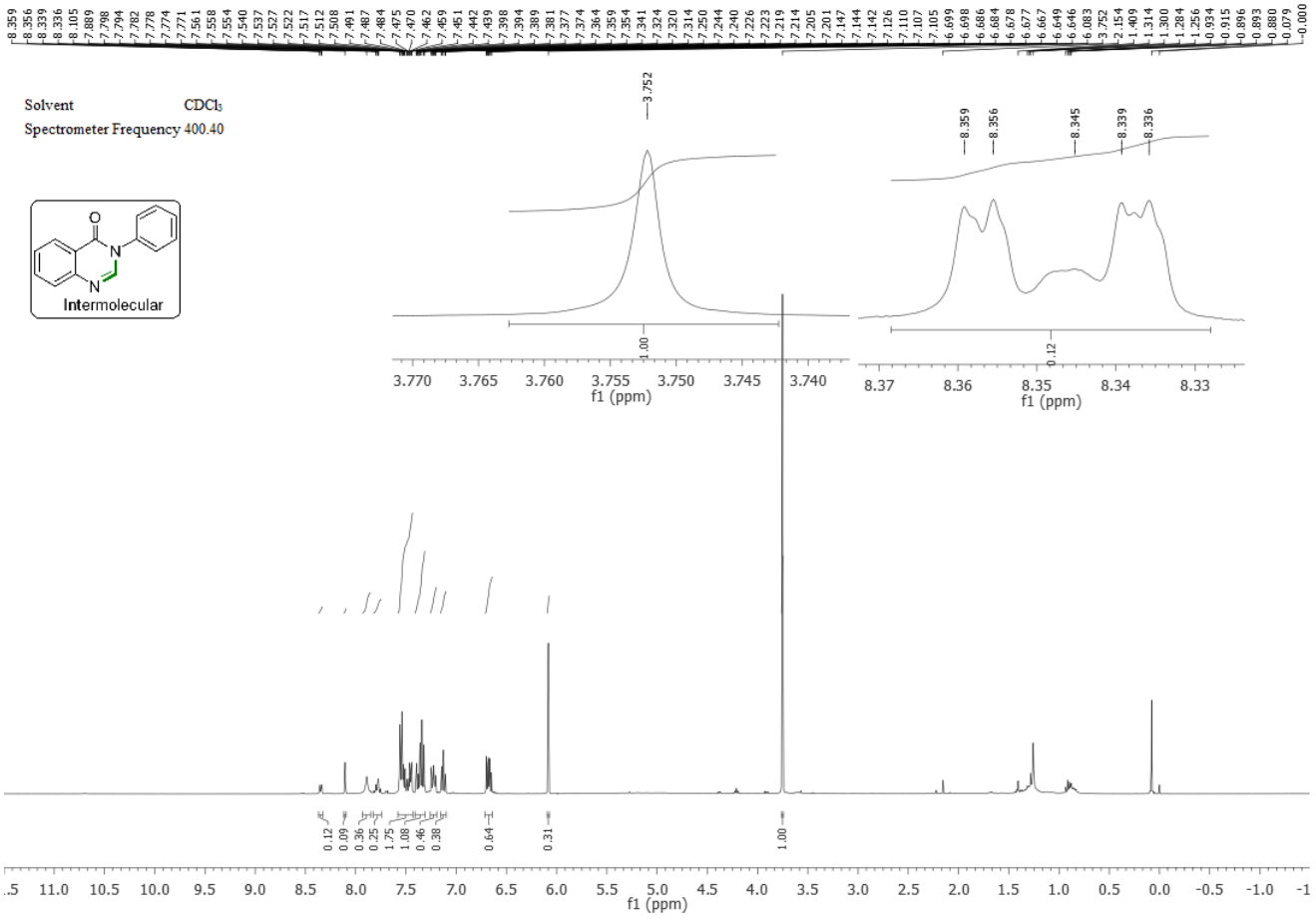


Parallel KIE ratio K_H/K_D= **1.94**

(c) Competitive KIE Experiment:

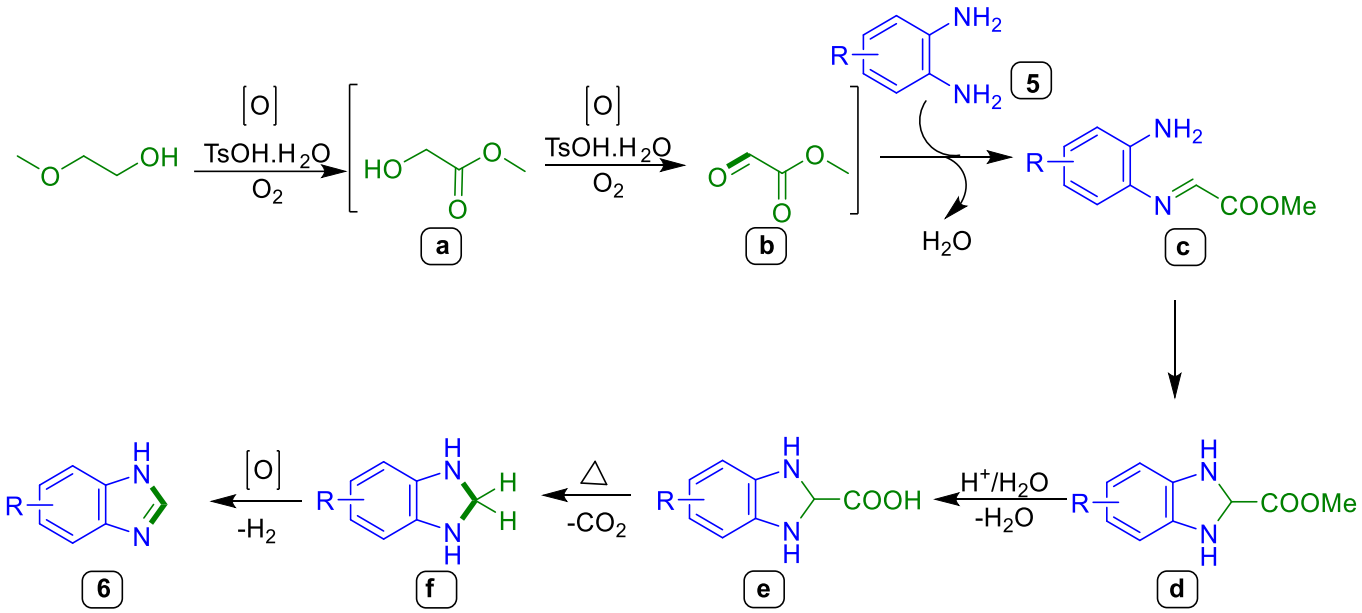


To an oven dried sealed tube was charged **1a** (30 mg, 0.14 mmol), EG + EG-D_4 (1:1): H_2O (9:1) and TsOH. H_2O (0.15 mmol) and allowed to stir at 110 ^oC for 5 h. Then the reaction mixture was cooled to room temperature and diluted with 5.0 mL of water. The water layer was extracted with (3X10 mL) of ethyl acetate and the combined ethyl acetate layer was given brine wash (1X10 mL). The final ethyl acetate layer was dried over sodium sulfate and concentrated under reduced pressure to get the crude compound. The yield of the compound was determined by using 1, 3, 5-trimethoxy benzene (4.2 mg) as an internal standard.



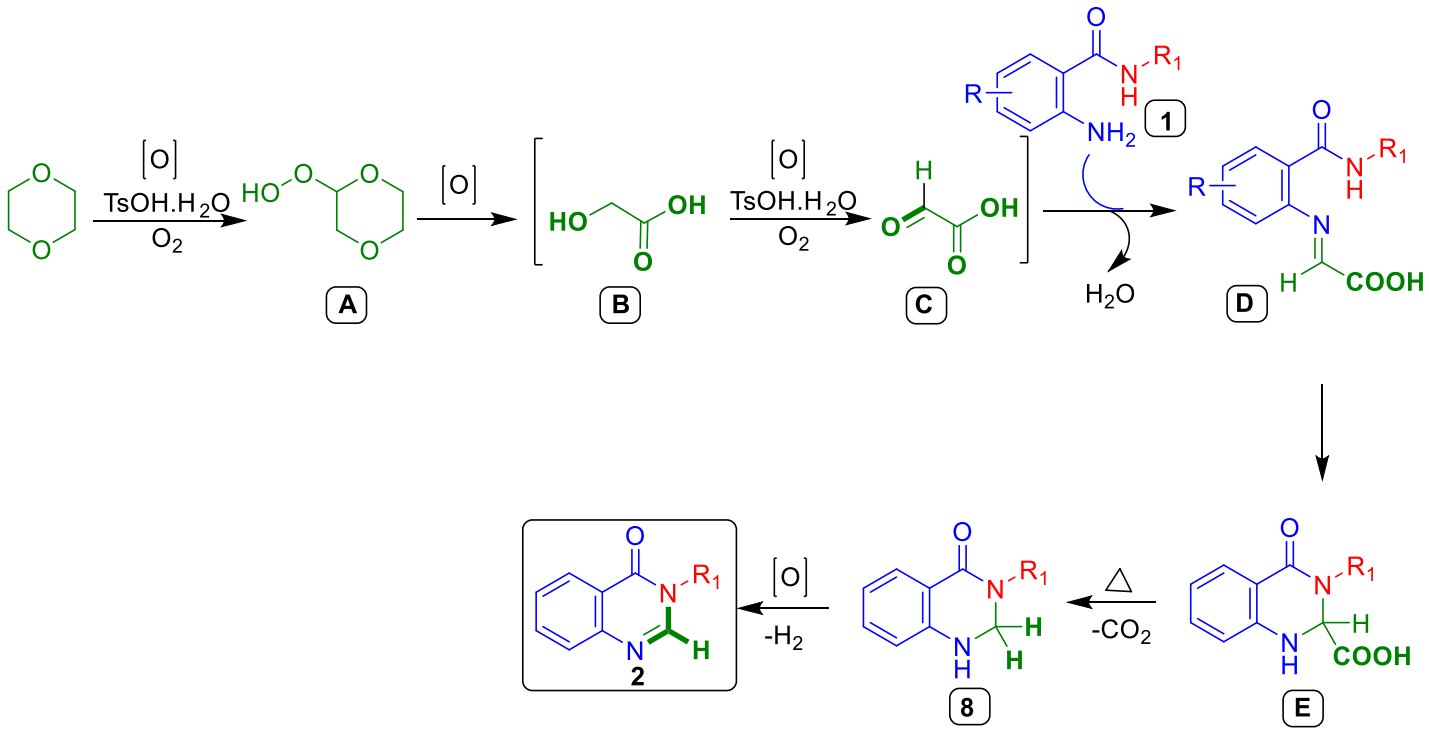
(5) Plausible reaction mechanism using 2-methoxy ethanol as methine source for the synthesis of benzimidazole:

Initial oxidation of 2-methoxy Ethanol with $TsOH.H_2O$ under O_2 atmosphere generated the methyl oxoacetate intermediate **b** via the formation of Methyl glycolate intermediate **a**. Then the compound **b** underwent condensation reaction with compound **5** to form the imine intermediate **c**. Intramolecular annulation of intermediate **c** resulted in the formation of methyl 2,3-dihydro-1*H*-benzo[*d*]imidazole-2-carboxylate **d** followed by hydrolysis to get **e**. Thermal decarboxylation of **e** resulted in penultimate product **f**. Aerobic oxidation of compound **f** gave the desired 1*H*-benzo[*d*]imidazole derivatives.



(6) Plausible reaction mechanism using Dioxane as Methine Source for the synthesis of 4(3*H*)-quinazolinones:

Initial oxidation of 1,4-dioxane with $TsOH.H_2O$ under O_2 atmosphere generated the 2-hydroperoxy-1, 4-dioxane intermediate **A**. It is known that under O_2 condition intermediate **A** will cleave to several fragments such as 1,4-dioxane-2-one, glycolic acid, glyoxylic acid and formic acid.[18] Then the Glyoxylic acid **C** underwent condensation reaction with compound **1** to form the imine intermediate **D**. Intramolecular annulation of intermediate **D** resulted in the formation of 4-oxo-1,2,3,4-tetrahydroquinazoline-2-carboxylic acid **E**. Thermal decarboxylation of **E** resulted in penultimate product **8**. Aerobic oxidation of compound **8** gave the desired 4(3*H*)-quinazolinones derivatives.



7) X-Ray Analysis Data

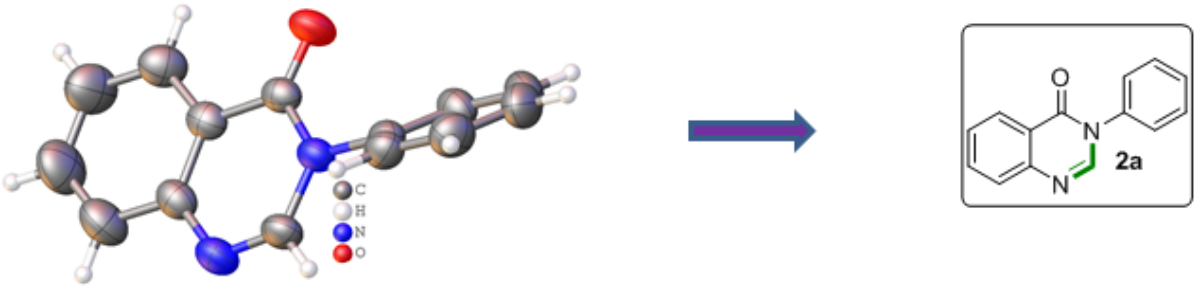


Table S1. Crystal data and structure refinement for **2a**.

Identification code	**2a**	
Empirical formula	$C_{14}H_{10}N_2O$	
Formula weight	222.24	
Temperature	297(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 21/c	
Unit cell dimensions	a = 12.1056(8) Å	a= 90°.
	b = 7.8020(5) Å	b= 97.574(5)°.
	c = 11.6256(6) Å	g = 90°.
Volume	1088.43(11) $Å^3$	
Z	4	
Density (calculated)	1.356 Mg/m^3	
Absorption coefficient	0.088 mm^{-1}	
F(000)	464	
Crystal size	0.53 x 0.40 x 0.24 mm^3	
Theta range for data collection	3.11 to 29.18°.	
Index ranges	-9<=h<=16, -8<=k<=10, -15<=l<=15	
Reflections collected	5091	
Independent reflections	2537 [R (int) = 0.0291]	
Completeness to theta = 26.00°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00000 and 0.93253	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2537 / 0 / 154	
Goodness-of-fit on F^2	1.012	
Final R indices [I>2sigma (I)]	R1 = 0.0537, wR2 = 0.1163	
R indices (all data)	R1 = 0.0957, wR2 = 0.1399	
Largest diff. peak and hole	0.154 and -0.209 $e.Å^{-3}$	

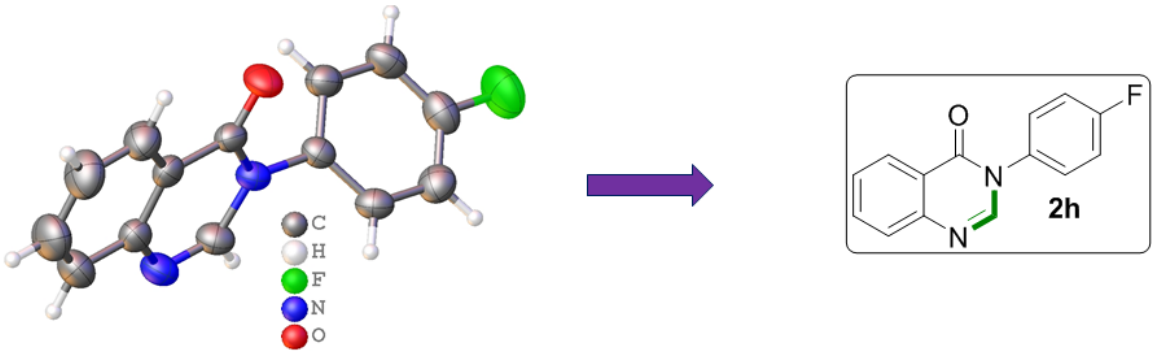


Table S2. Crystal data and structure refinement for **2h**.

Identification code	**2h**	
Empirical formula	$C_{14}H_9FNO$	
Formula weight	240.23	
Temperature	297(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 21/c	
Unit cell dimensions	a = 12.4895(9) Å	a= 90°.
	b = 7.7667(5) Å	b= 96.718(6)°.
	c = 11.5802(6) Å	g = 90°.
Volume	1115.59(12) $Å^3$	
Z	4	
Density (calculated)	1.430 Mg/m^3	
Absorption coefficient	0.104 mm^{-1}	
F(000)	496	
Crystal size	0.42 x 0.38 x 0.37 mm^3	
Theta range for data collection	3.09 to 29.12°.	
Index ranges	-11<=h<=16, -10<=k<=10, -15<=l<=9	
Reflections collected	5038	
Independent reflections	2592 [R(int) = 0.0629]	
Completeness to theta = 26.00°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00000 and 0.77825	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2592 / 0 / 163	
Goodness-of-fit on F^2	1.028	
Final R indices [I>2sigma(I)]	R1 = 0.0659, wR2 = 0.1548	
R indices (all data)	R1 = 0.0998, wR2 = 0.1854	
Largest diff. peak and hole	0.249 and -0.296 $e.Å^{-3}$	

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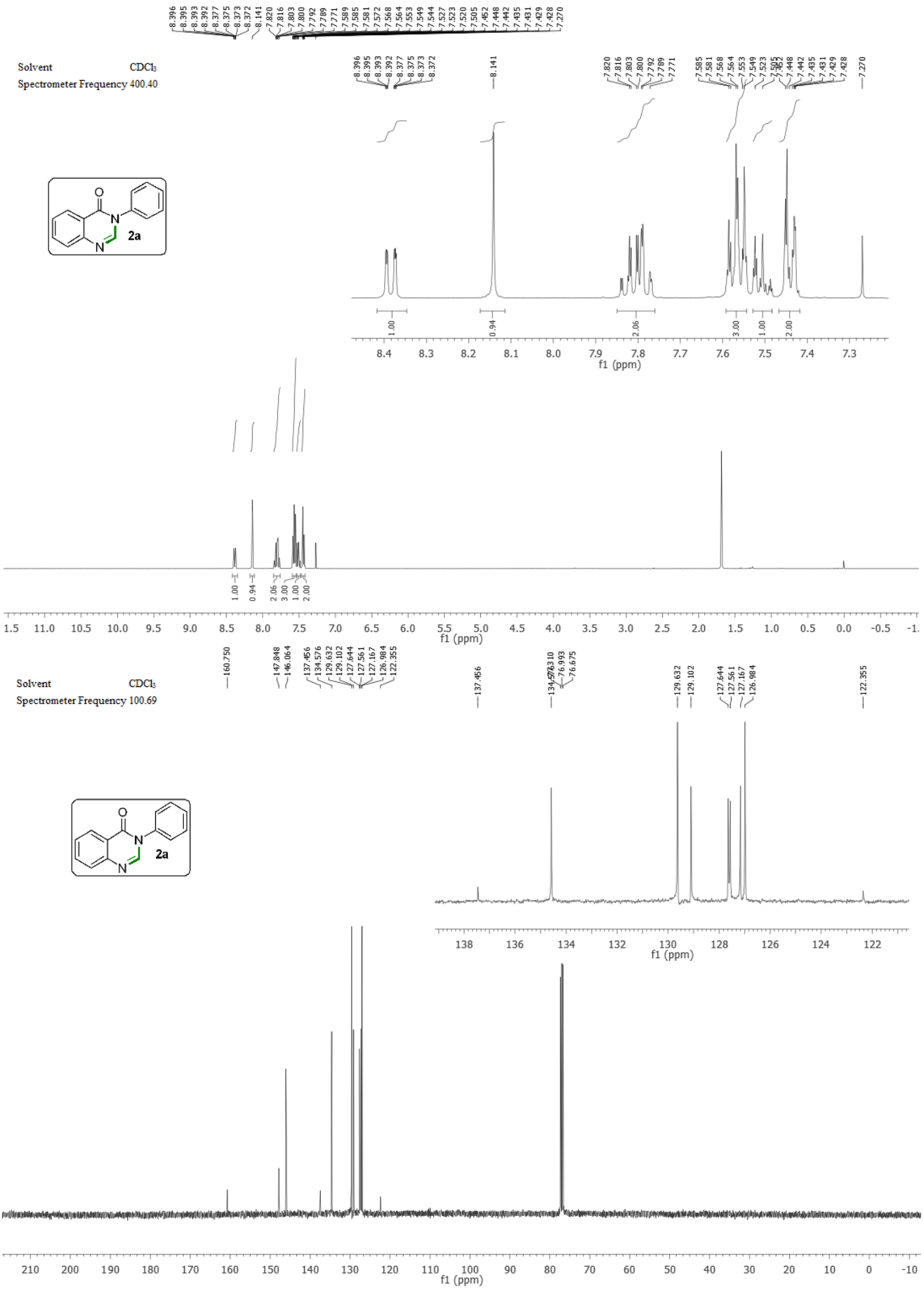
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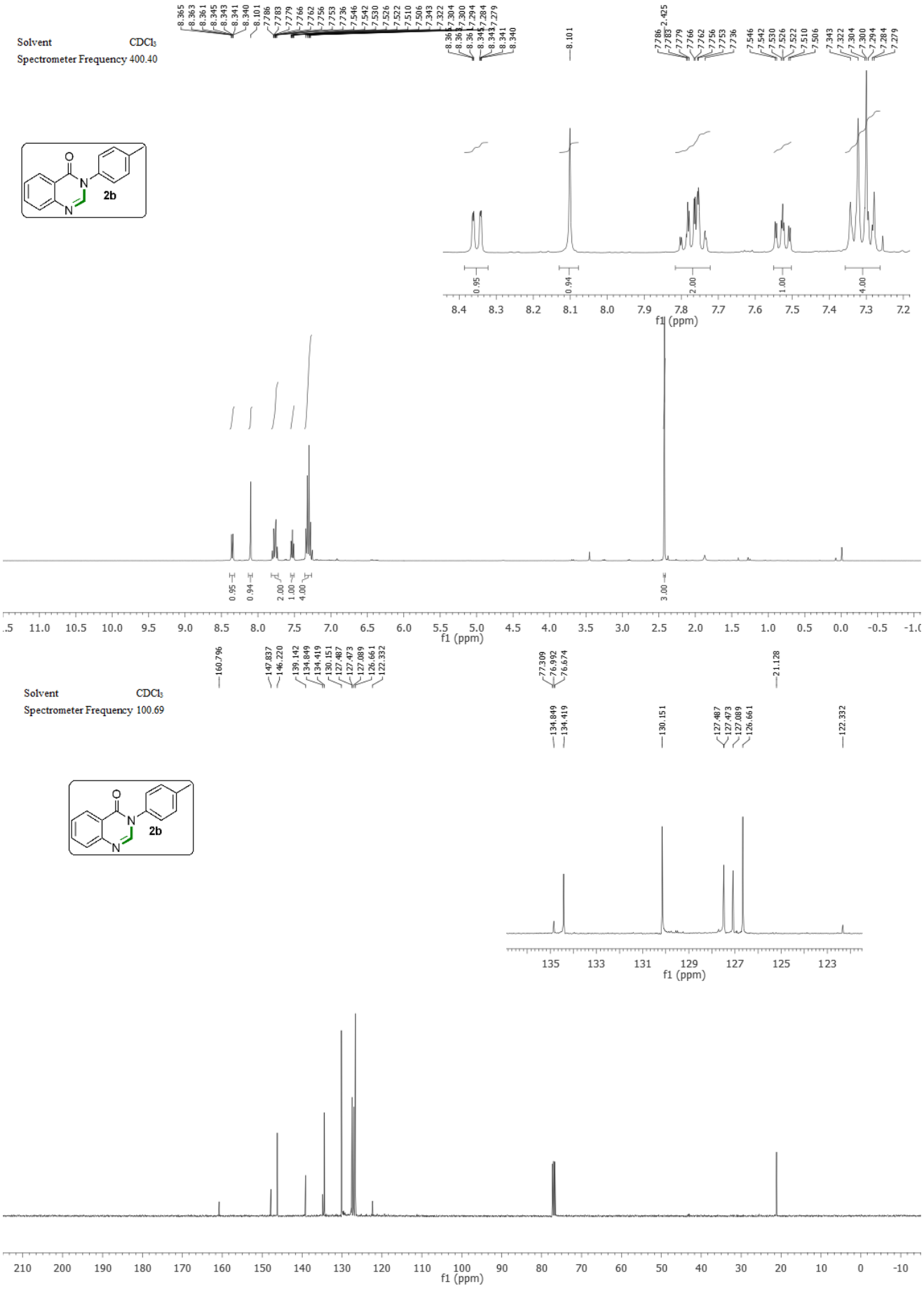
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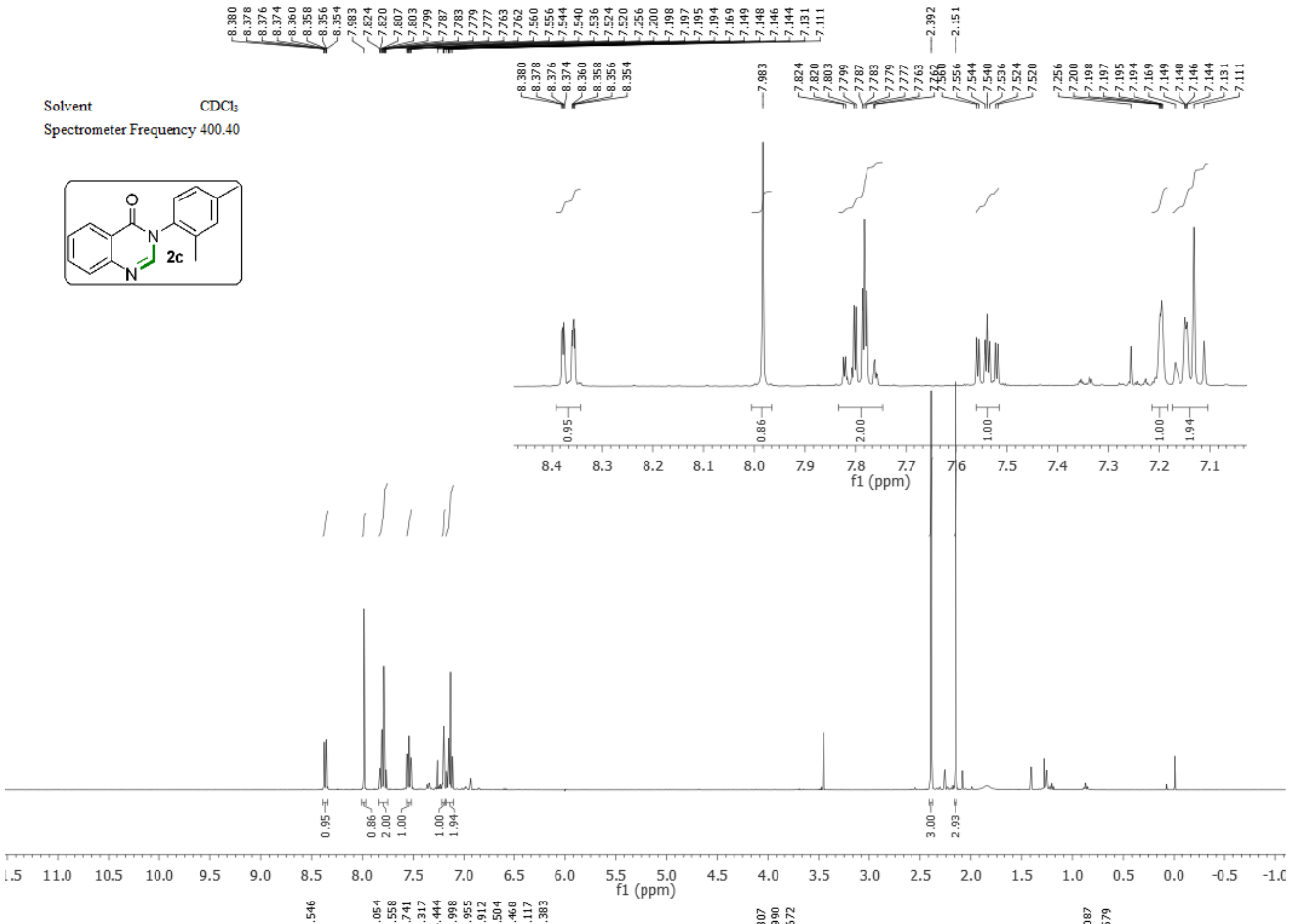
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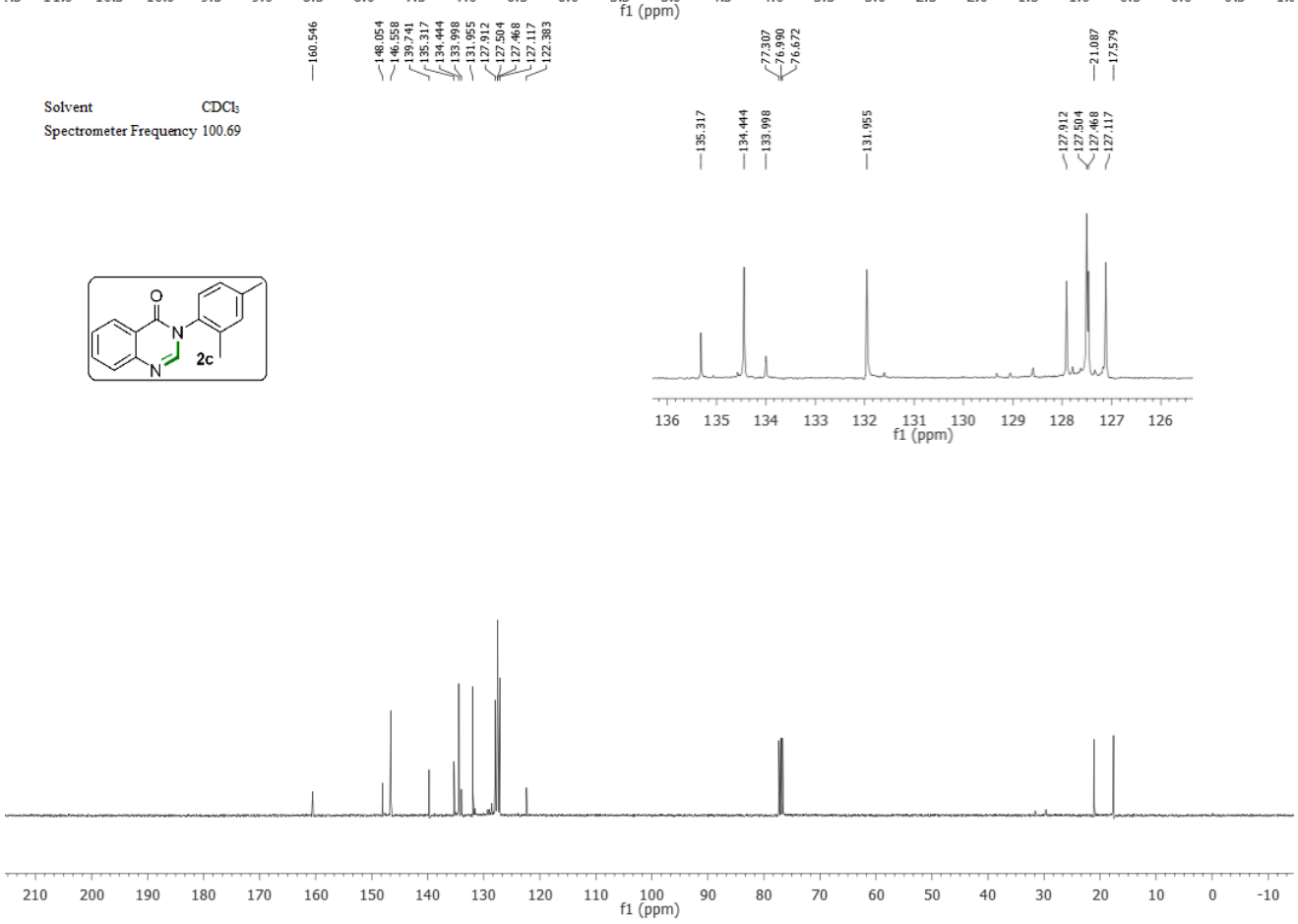
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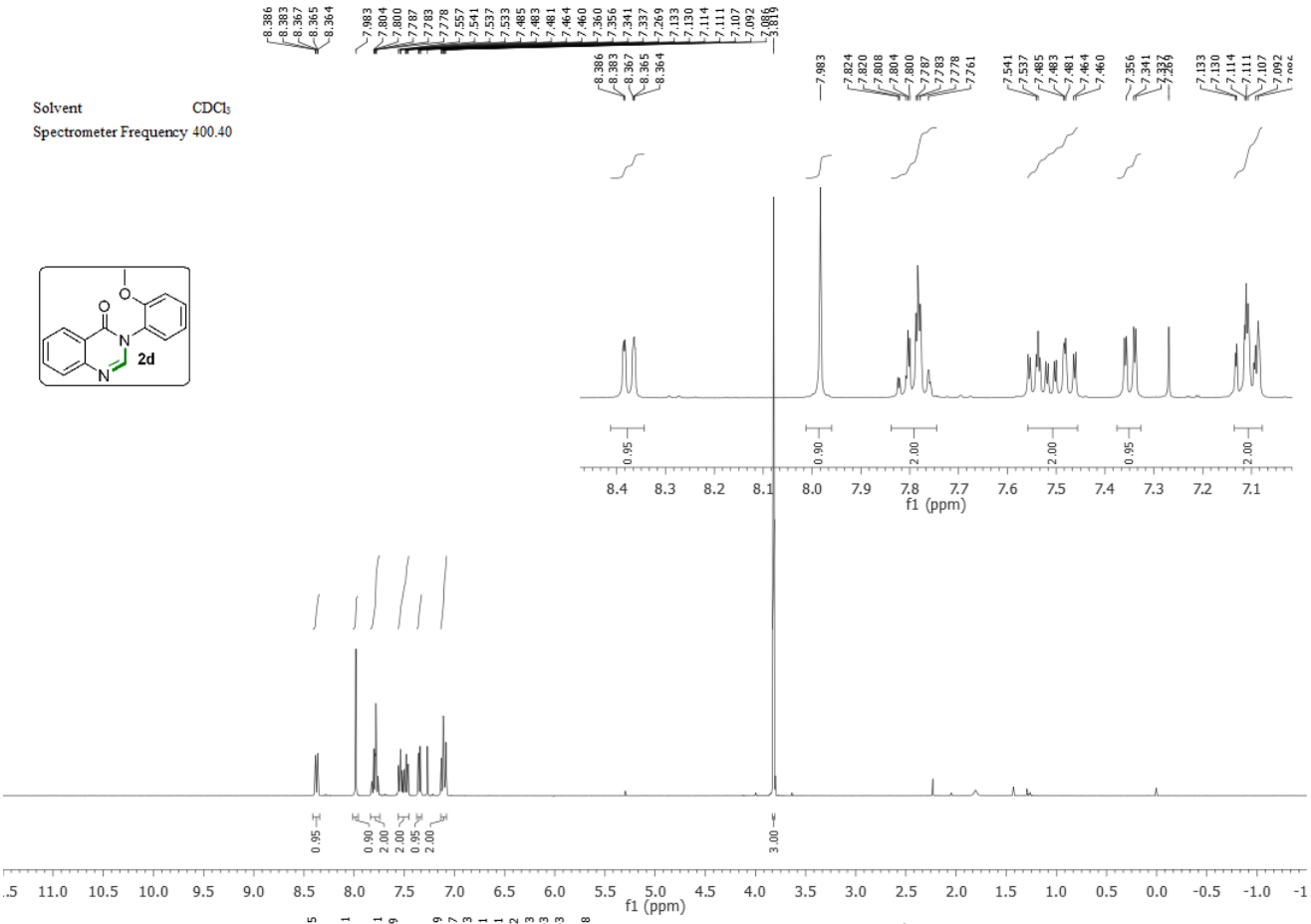
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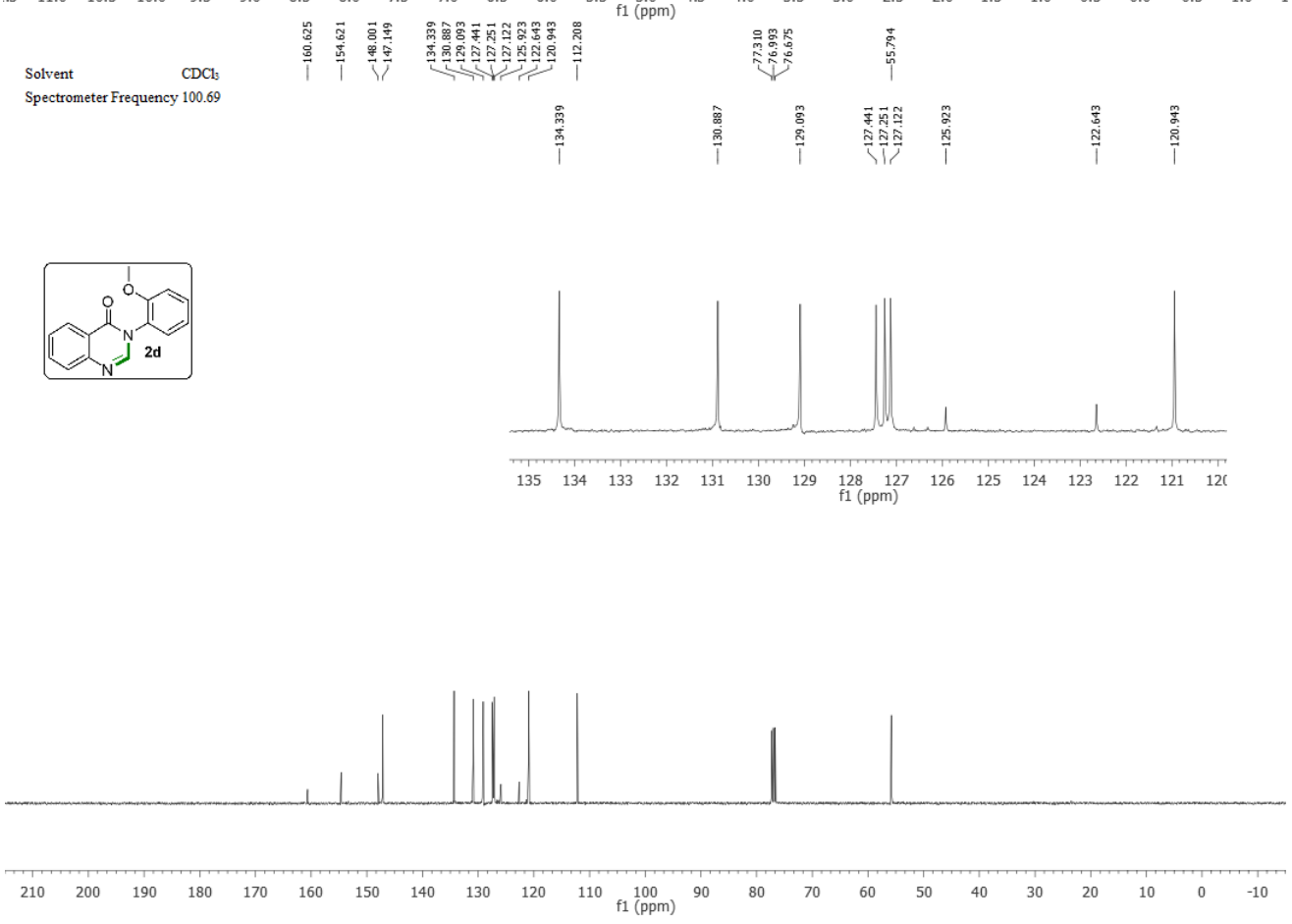
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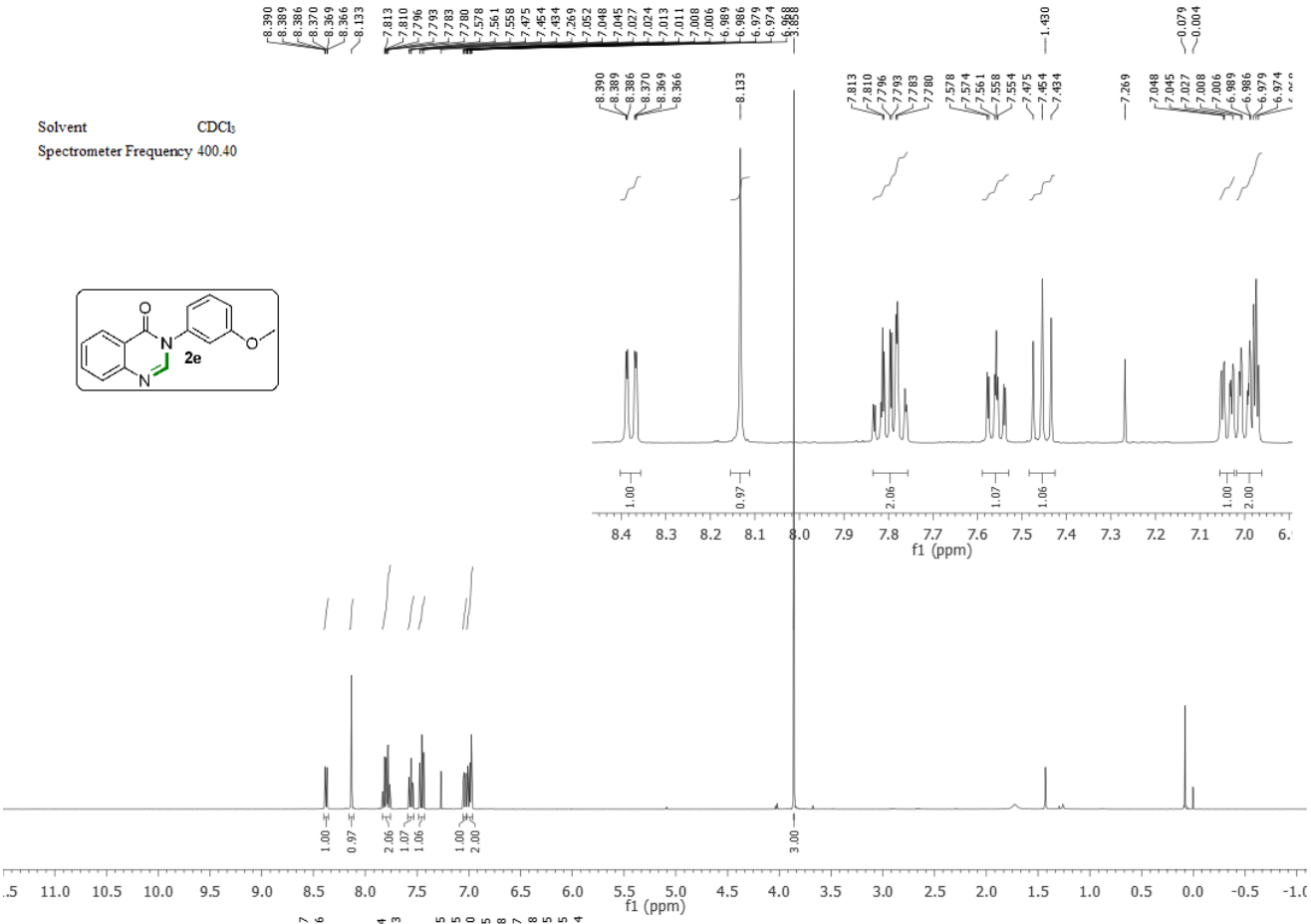
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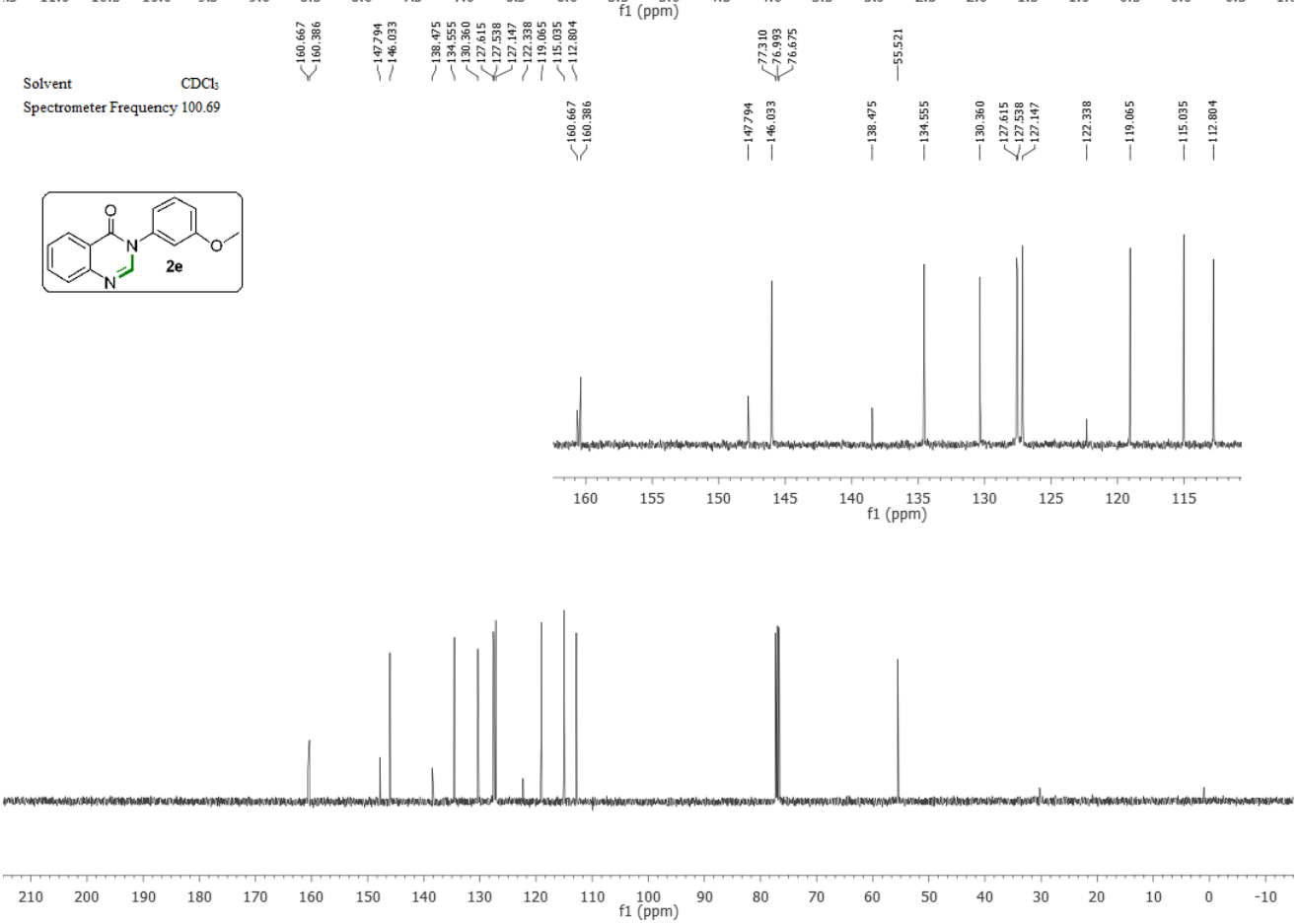
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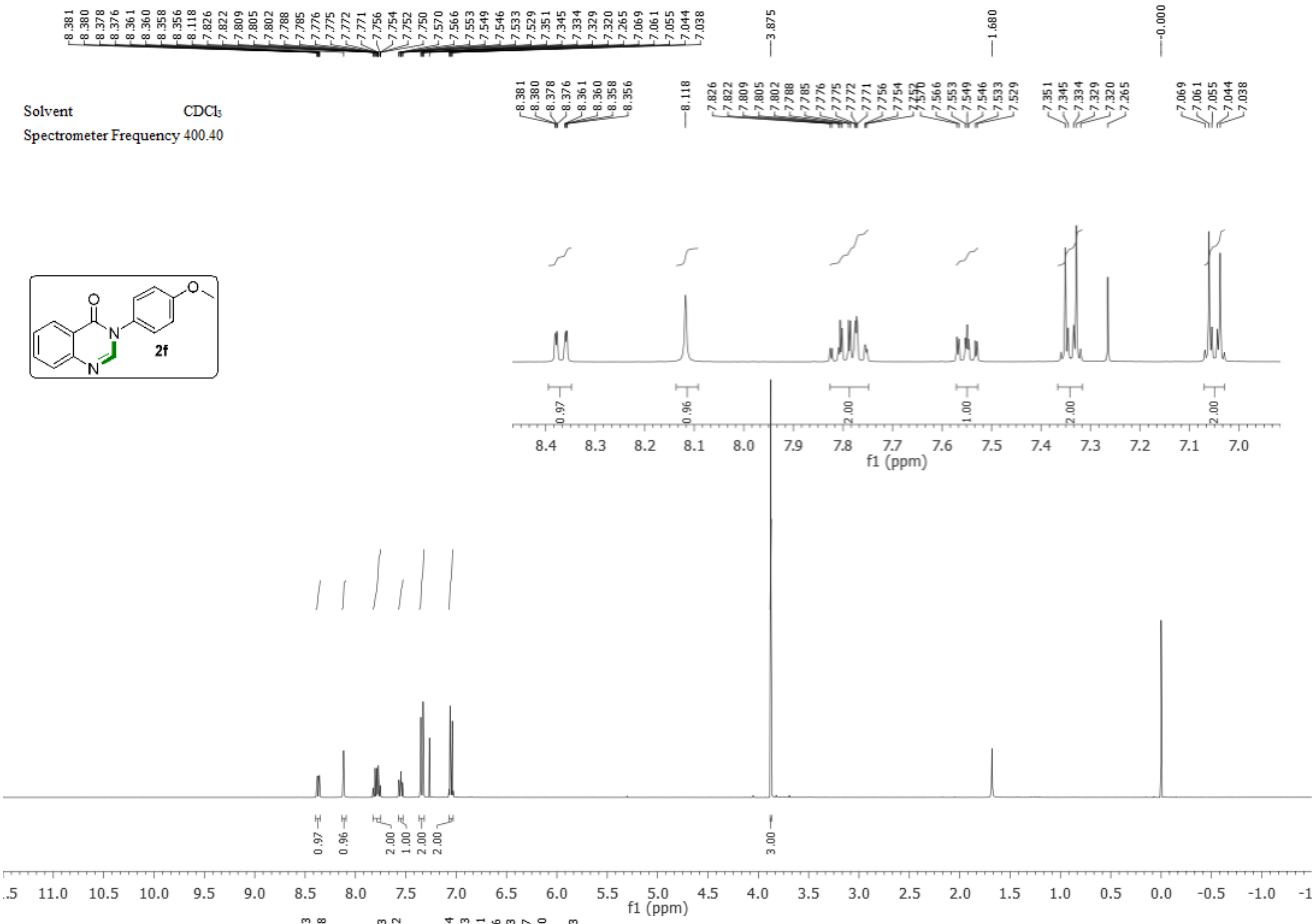
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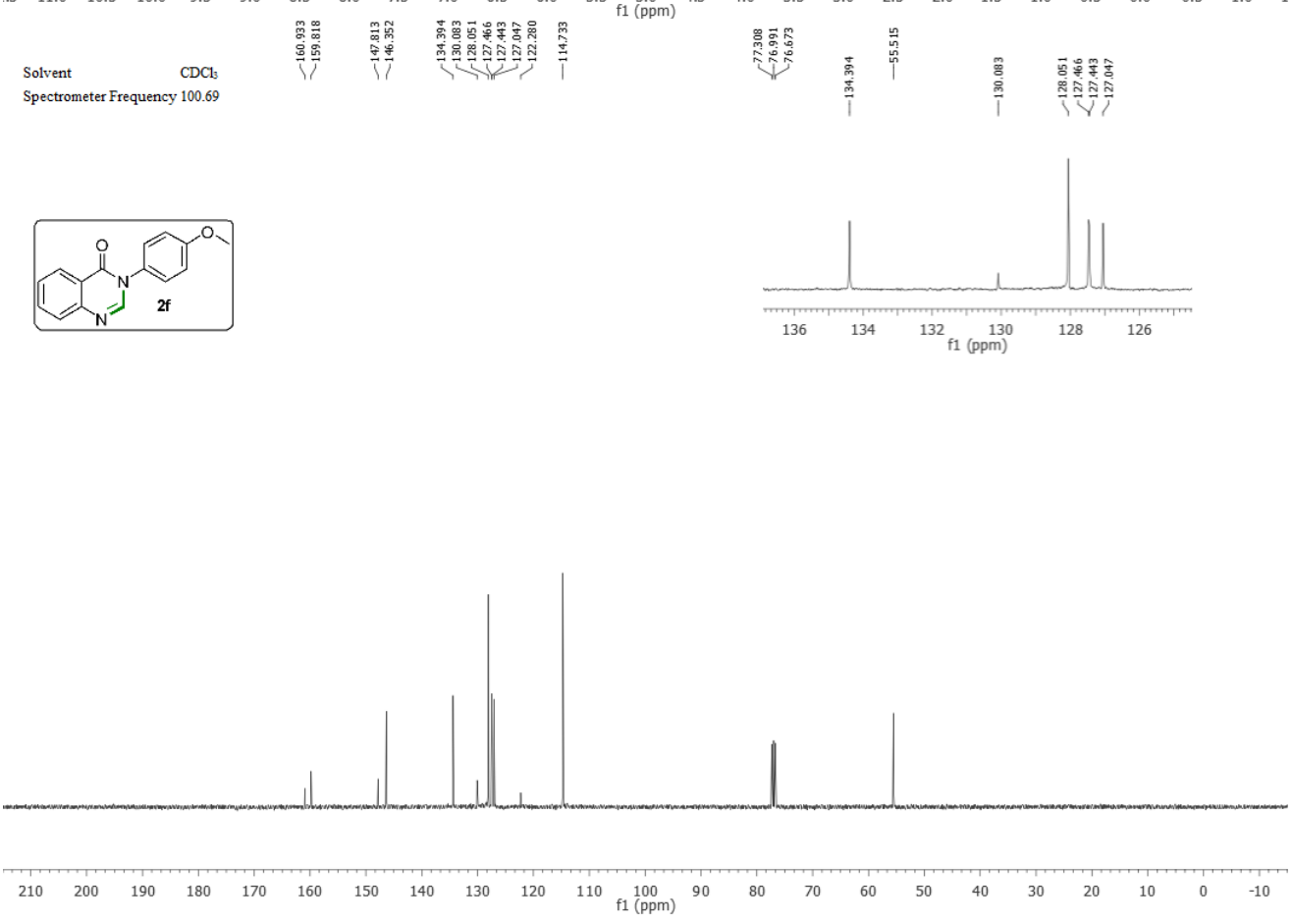
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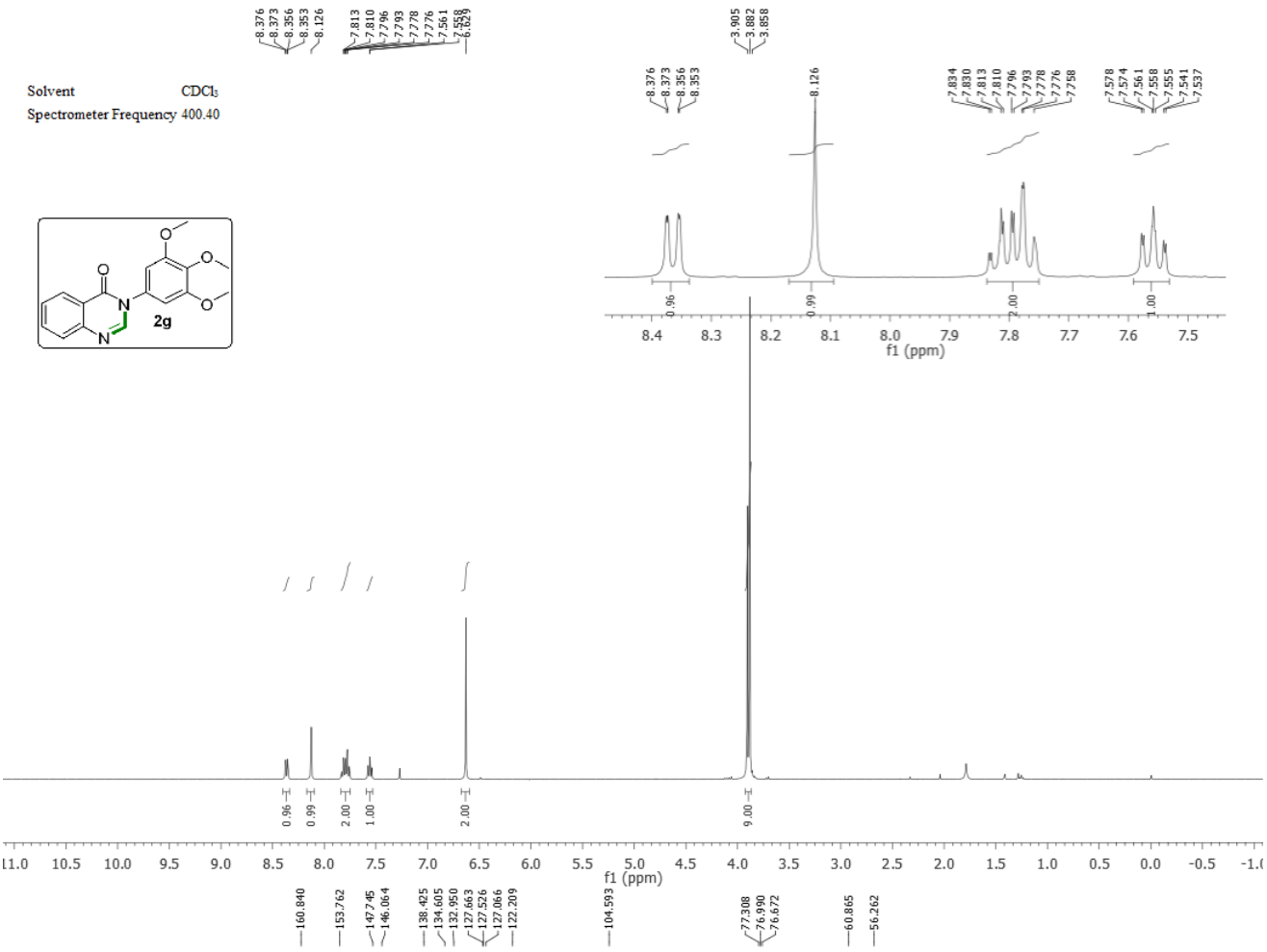
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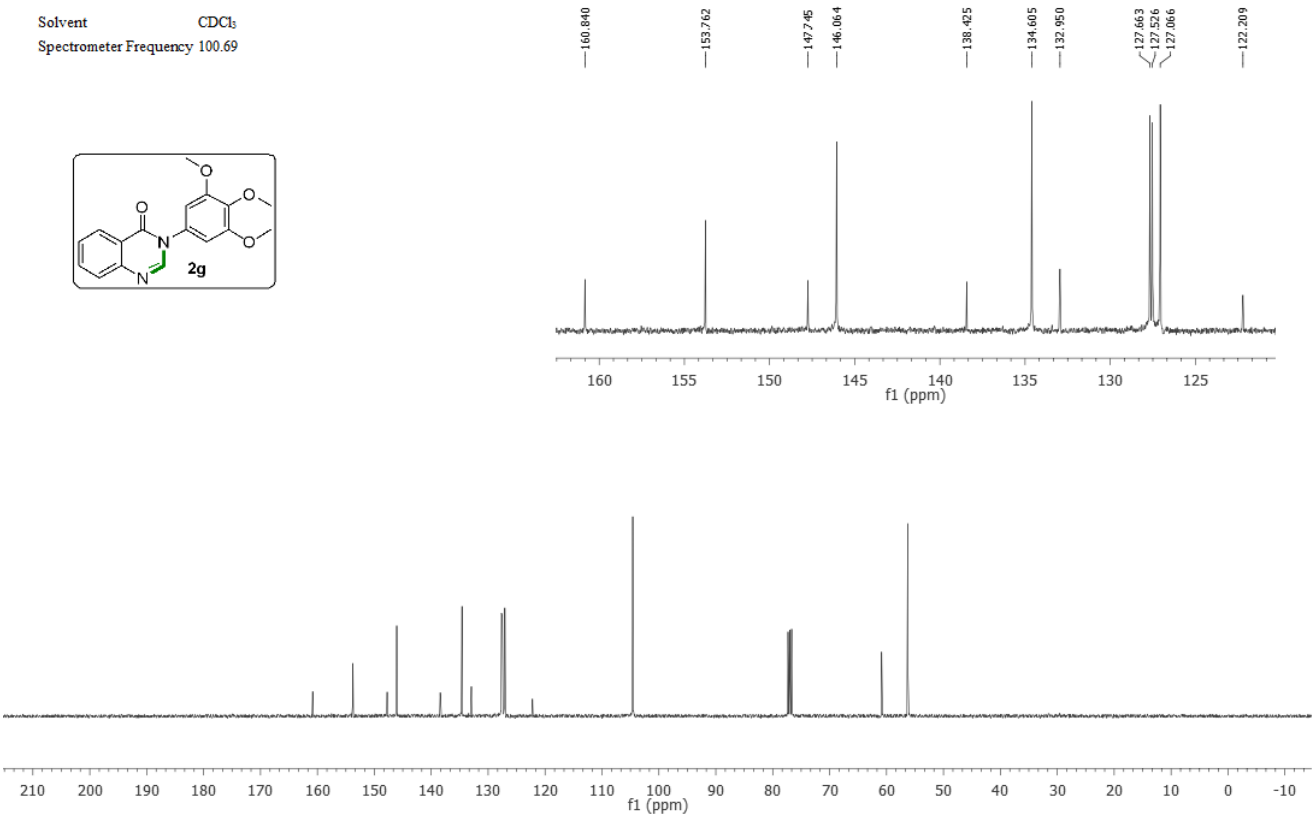
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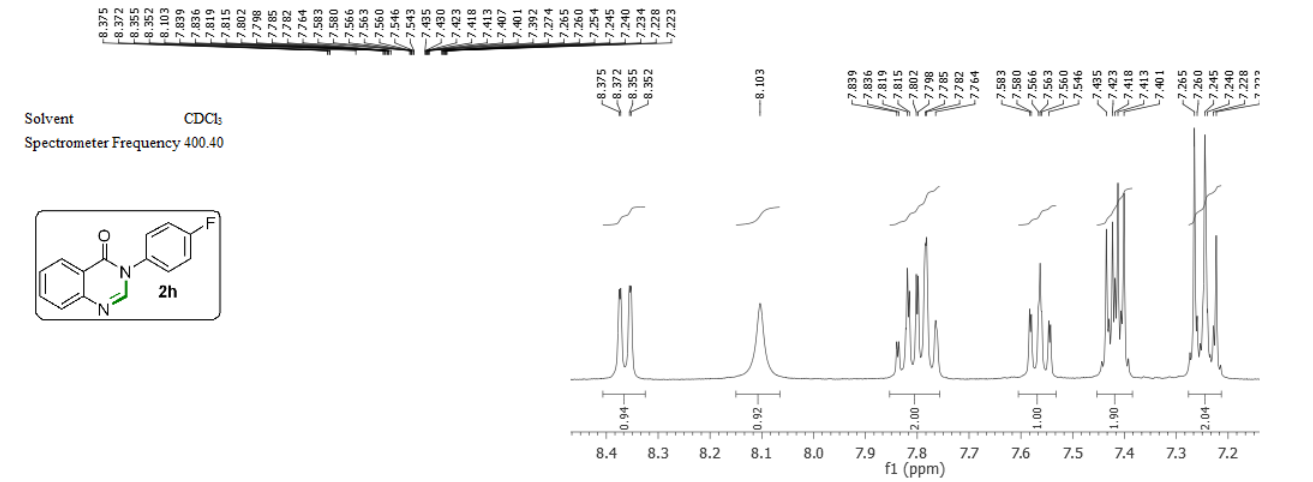
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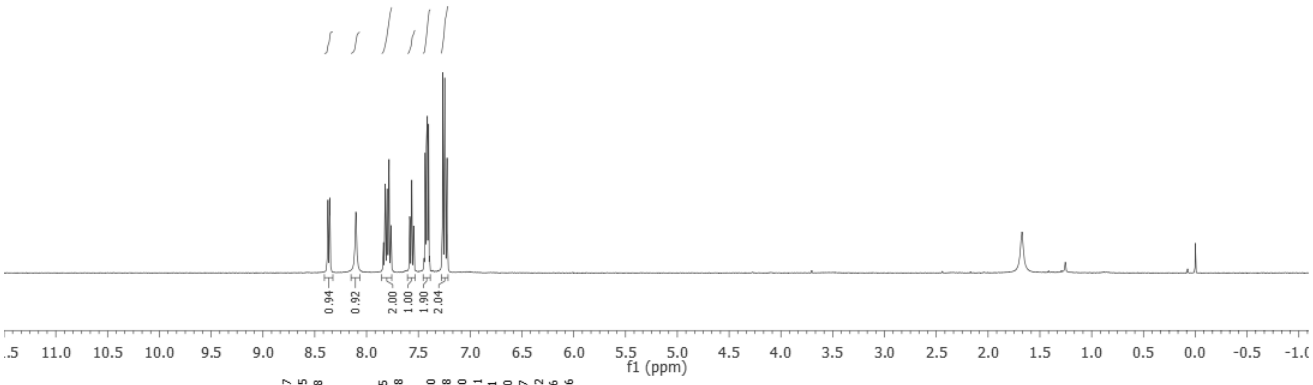
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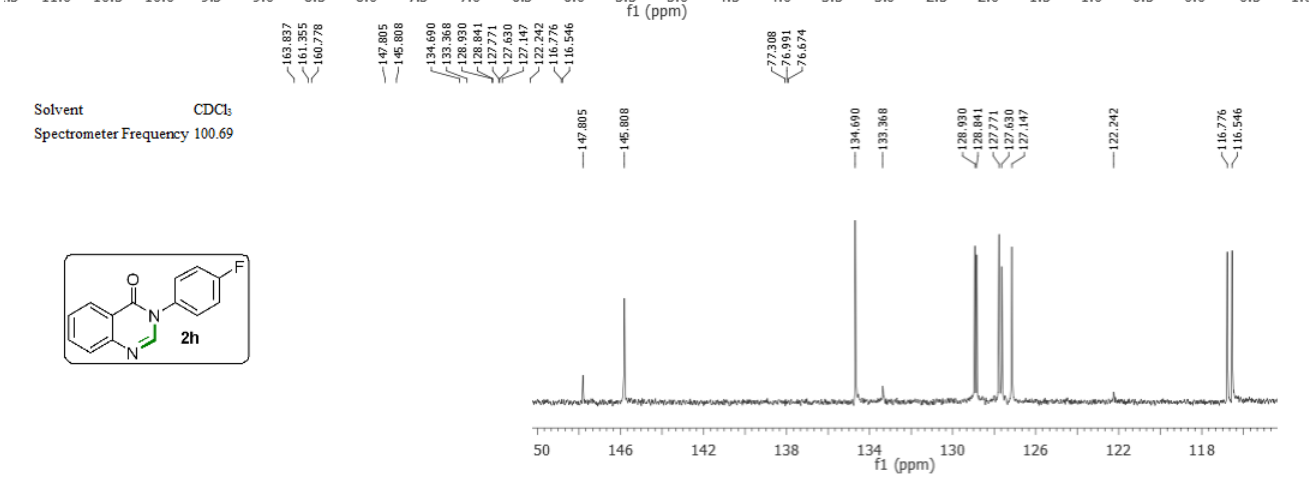
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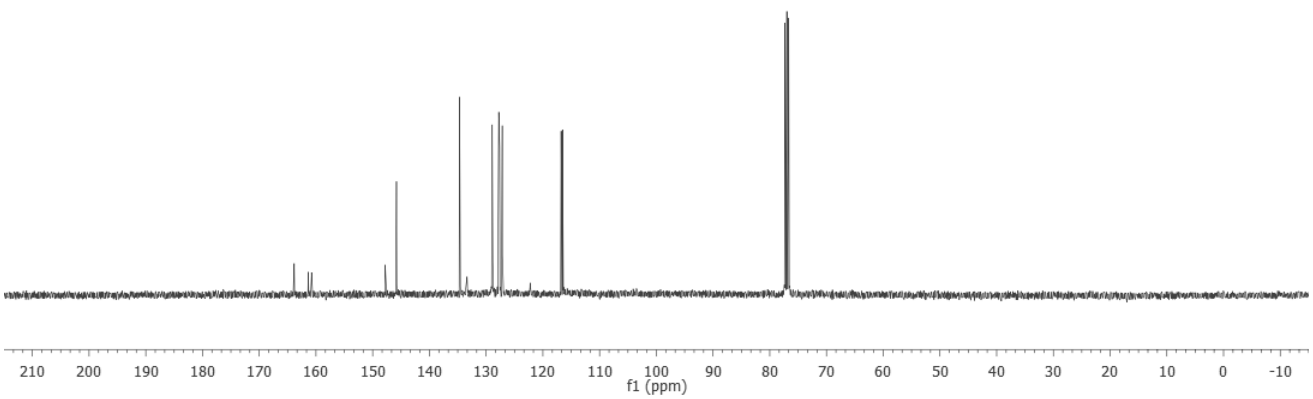
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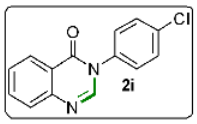

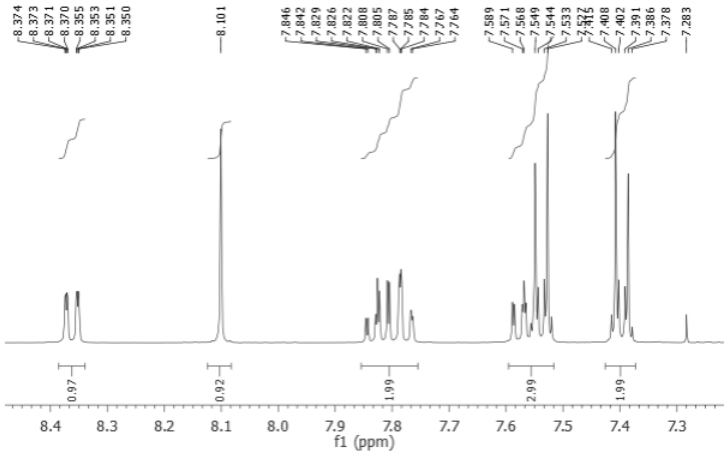

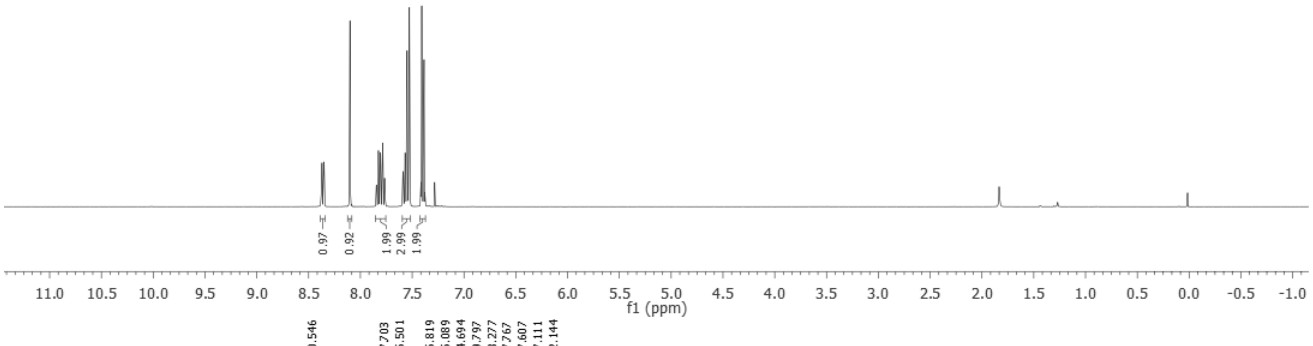

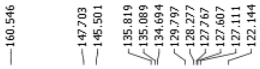

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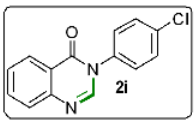

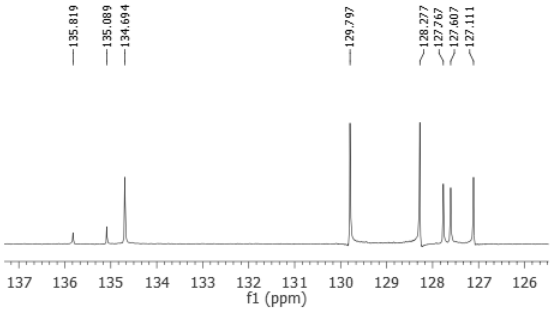

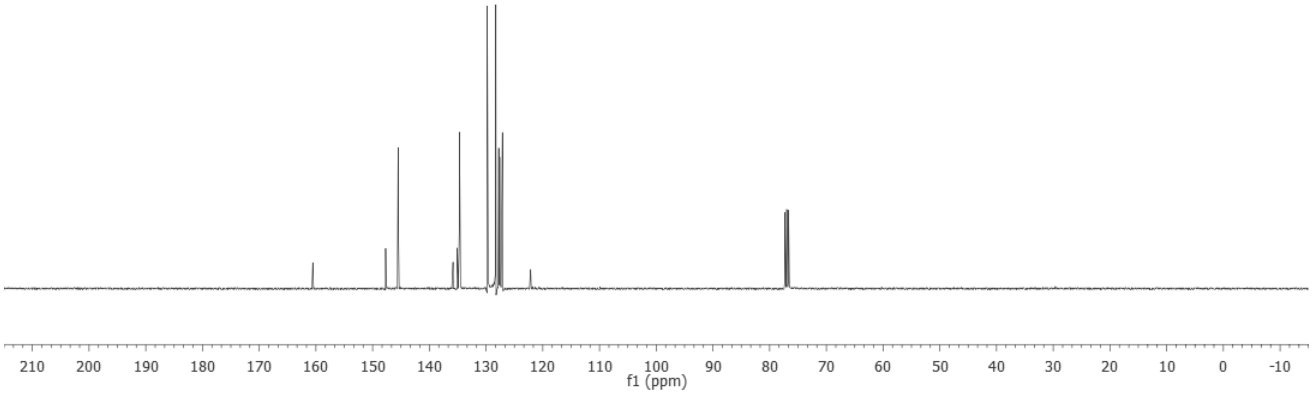

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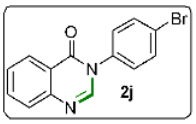

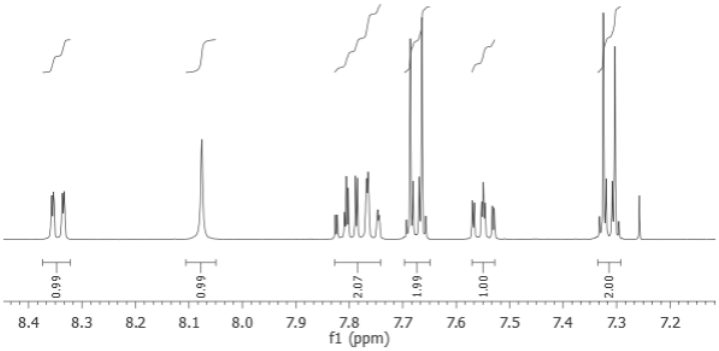

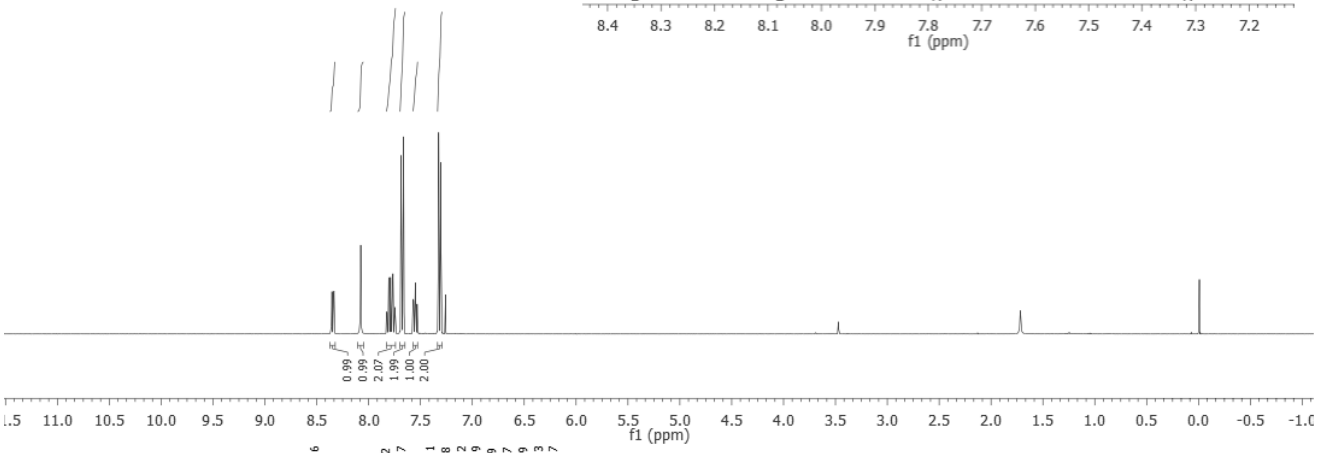

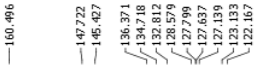

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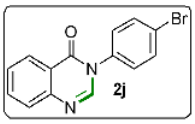

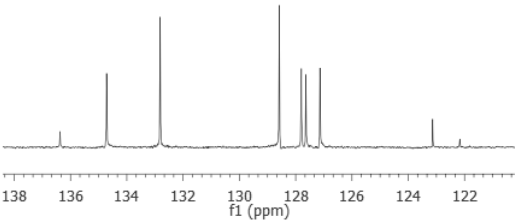

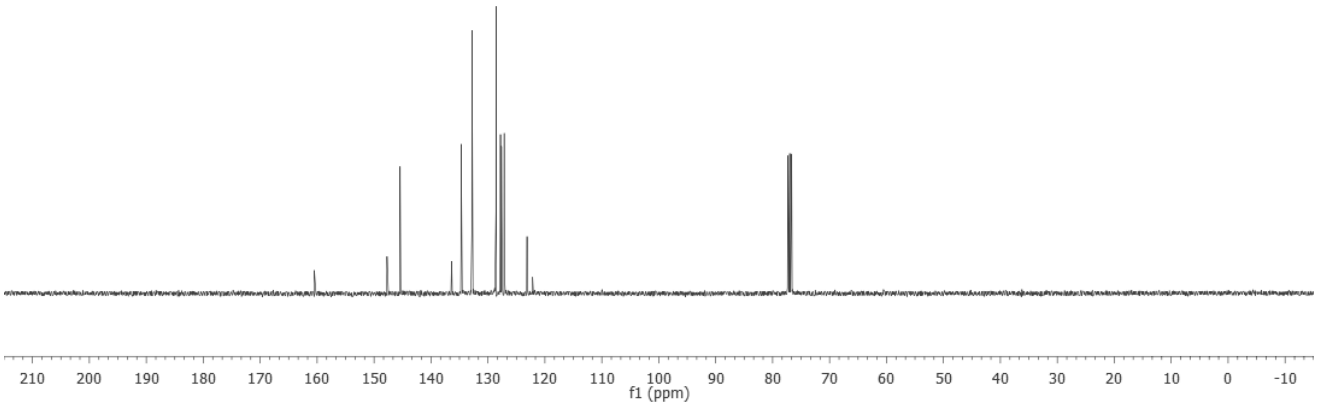

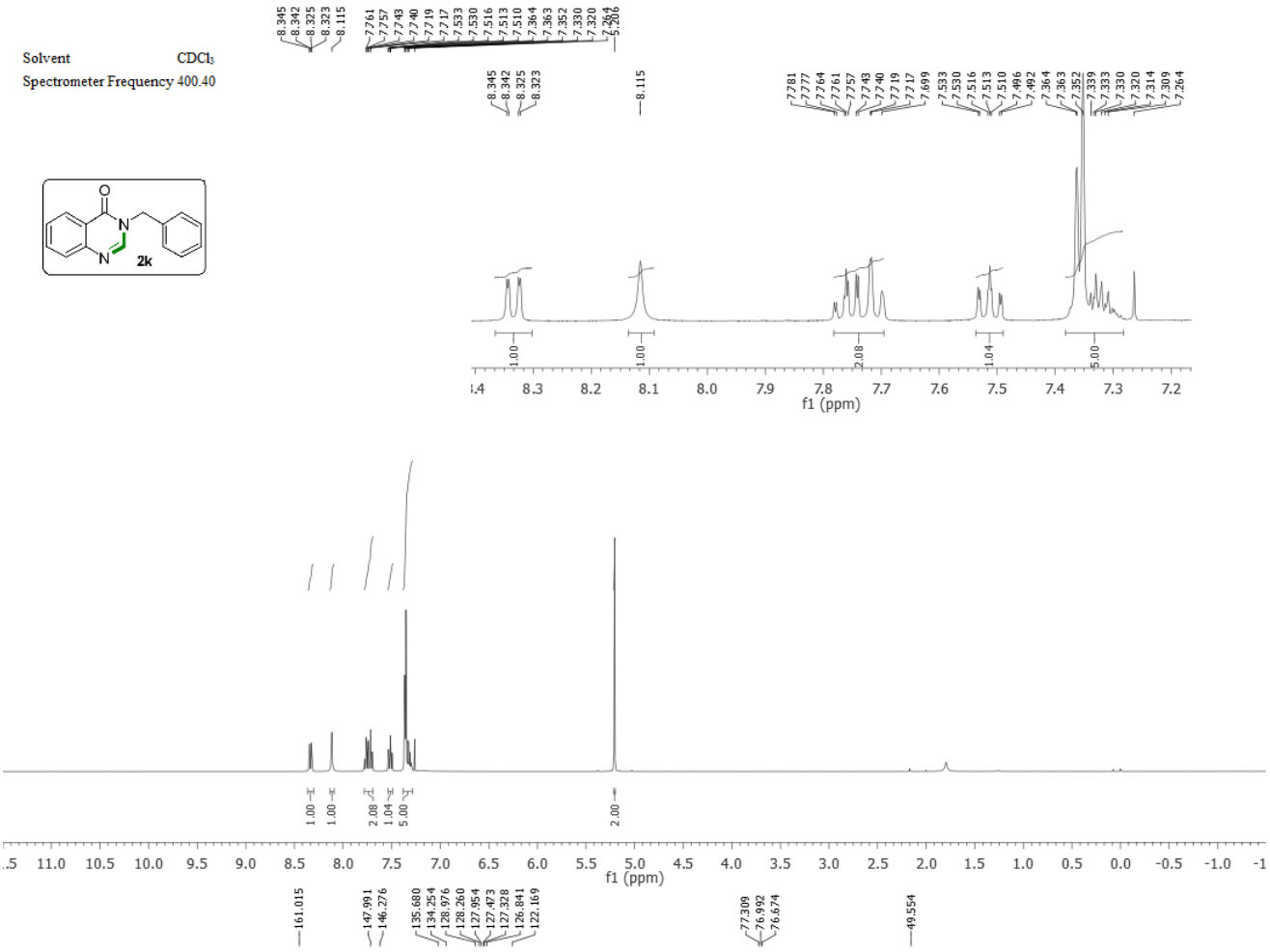
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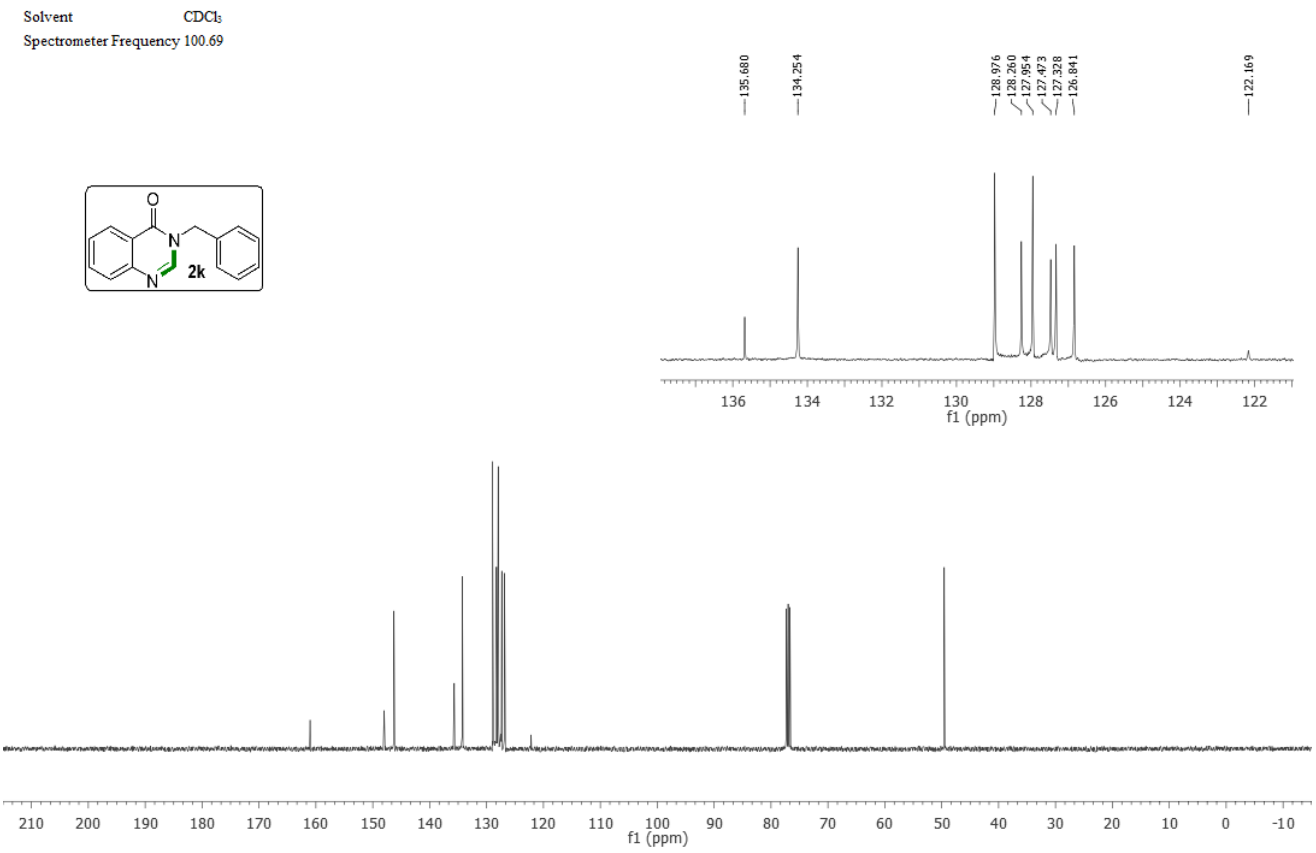
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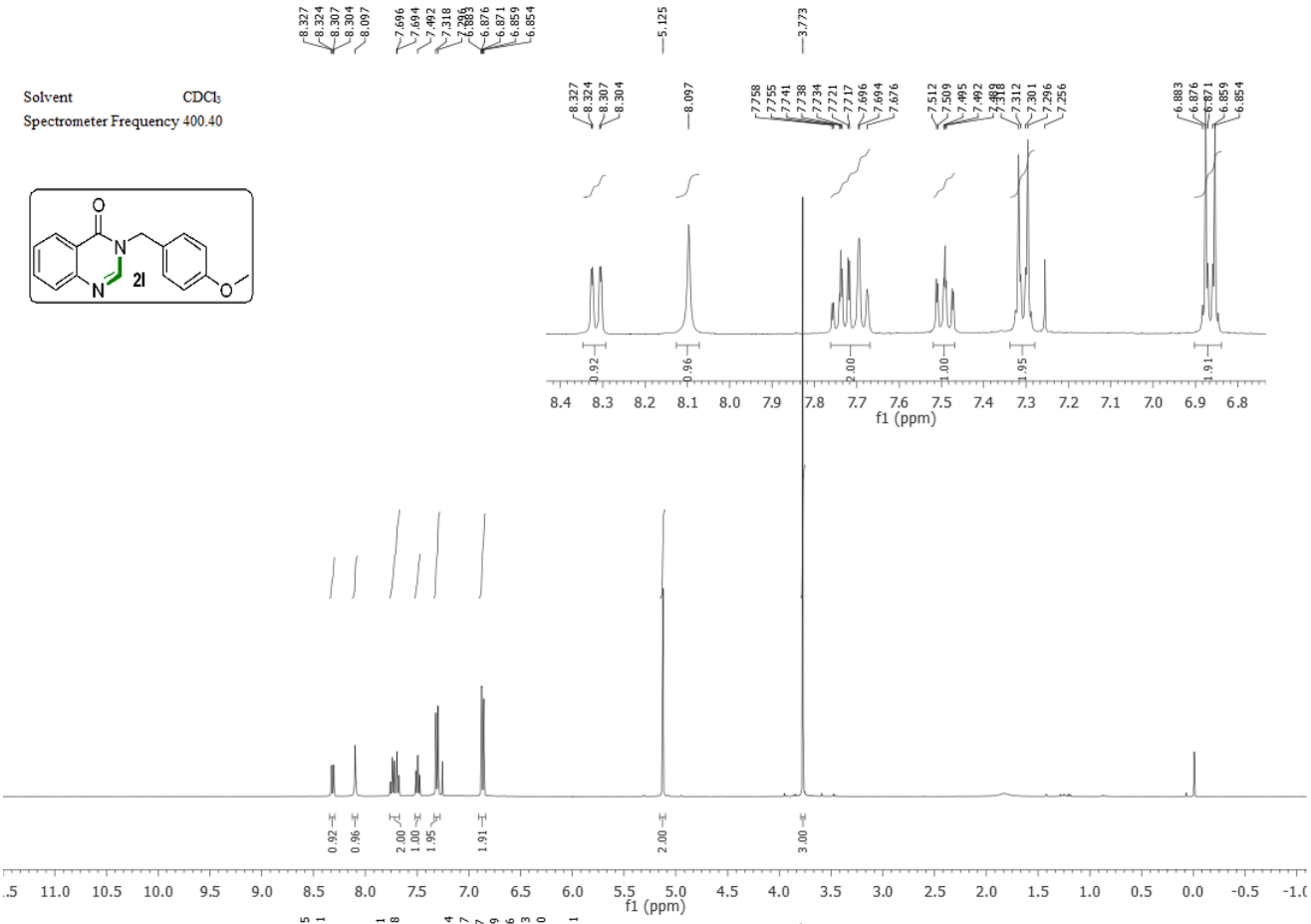
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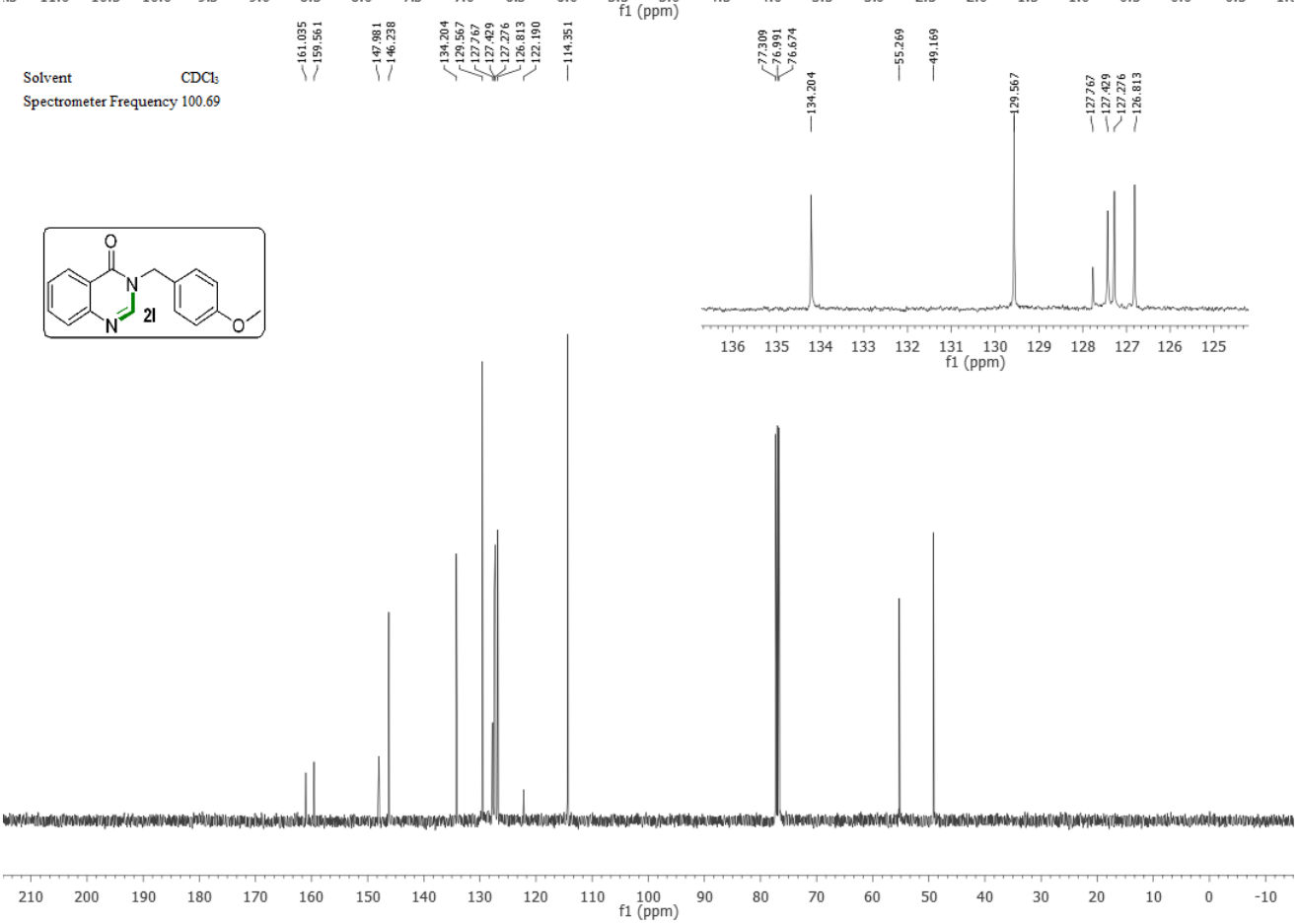
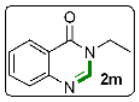
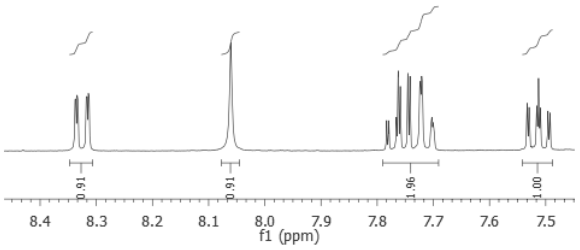
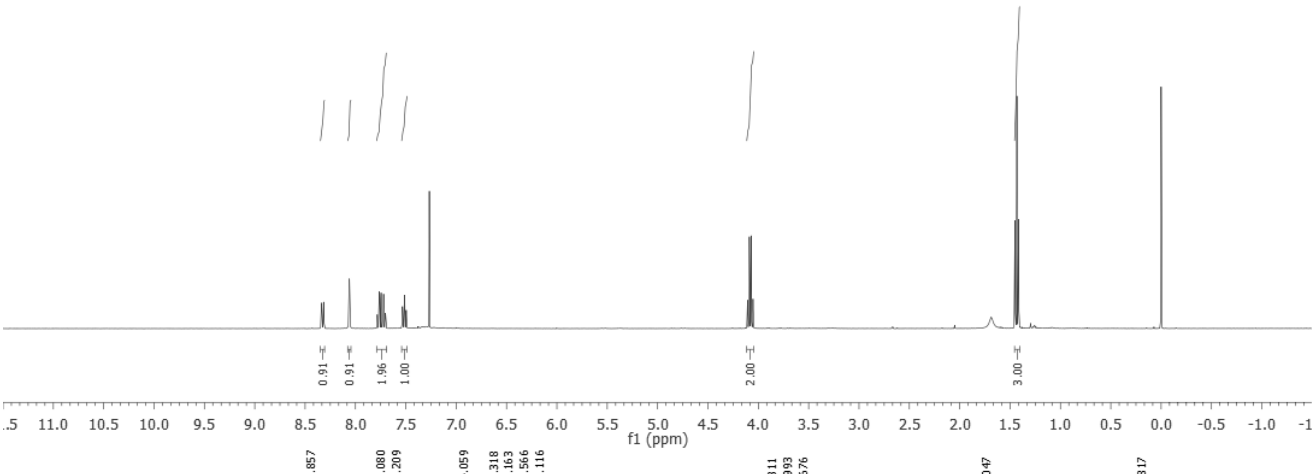

Solvent CDCl3
Spectrometer Frequency 100.69
2l
f1 (ppm)

Solvent CDCl3

Spectrometer Frequency 400.40

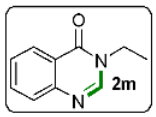


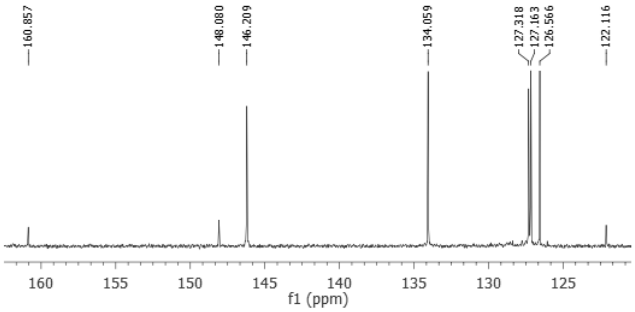


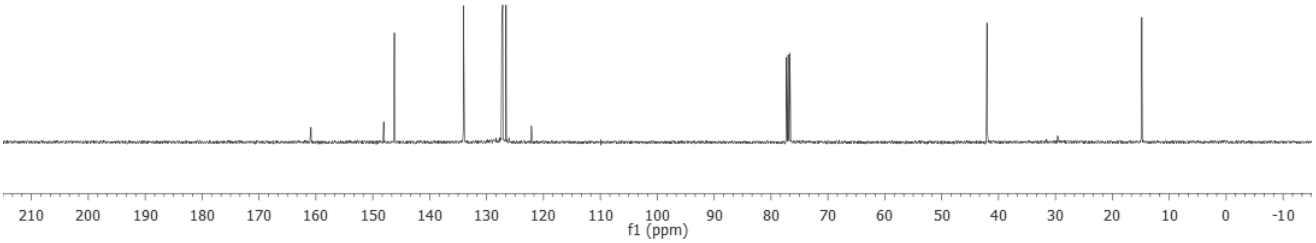


Solvent CDCl3

Spectrometer Frequency 100.69

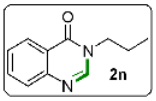


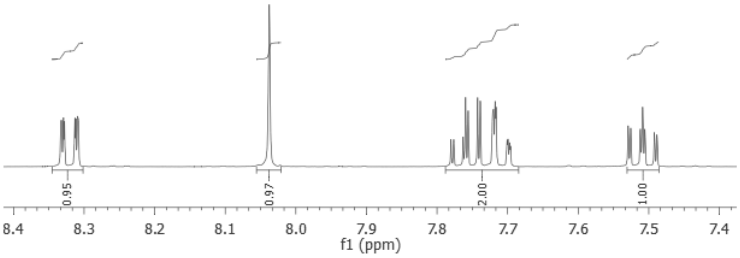


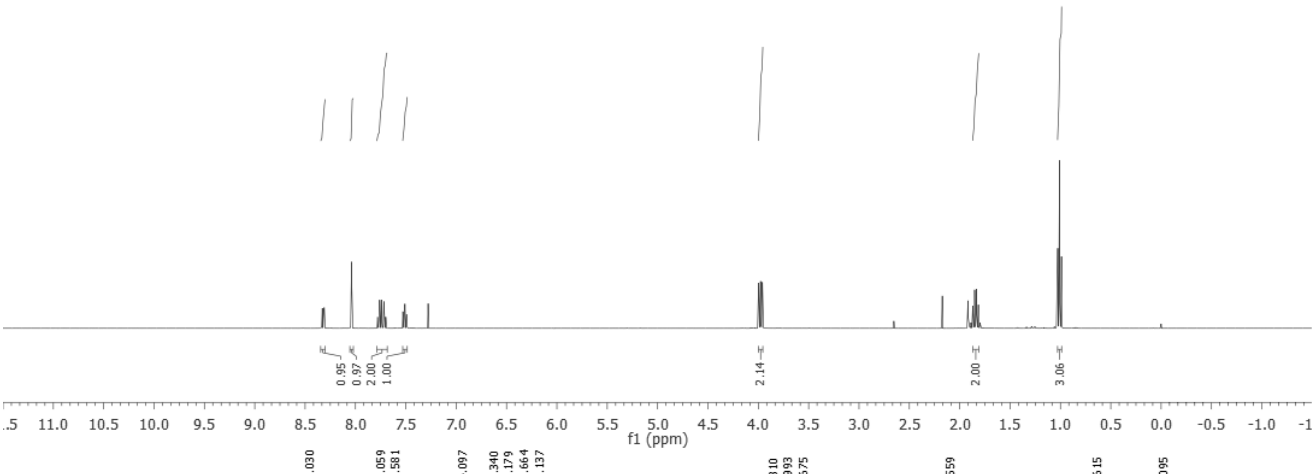


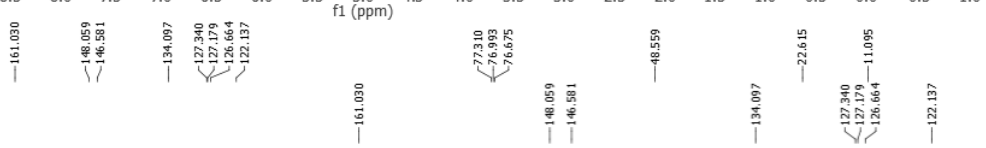
Solvent CDCl3

Spectrometer Frequency 400.40



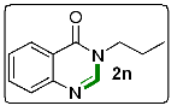


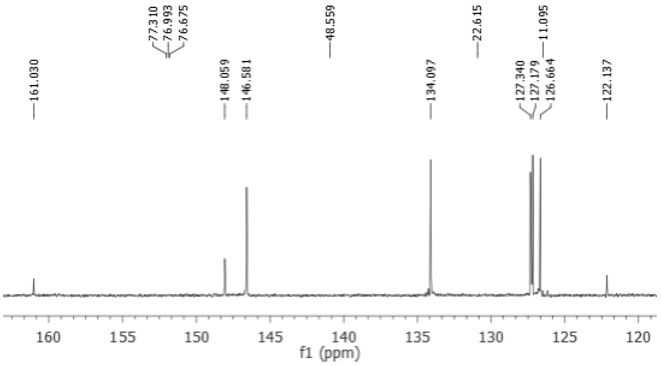


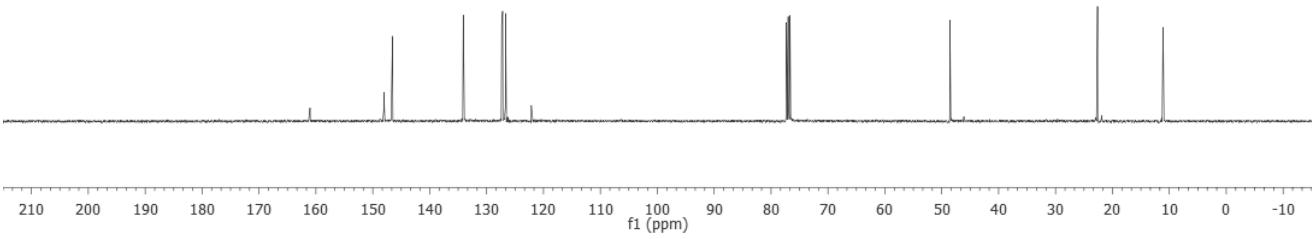


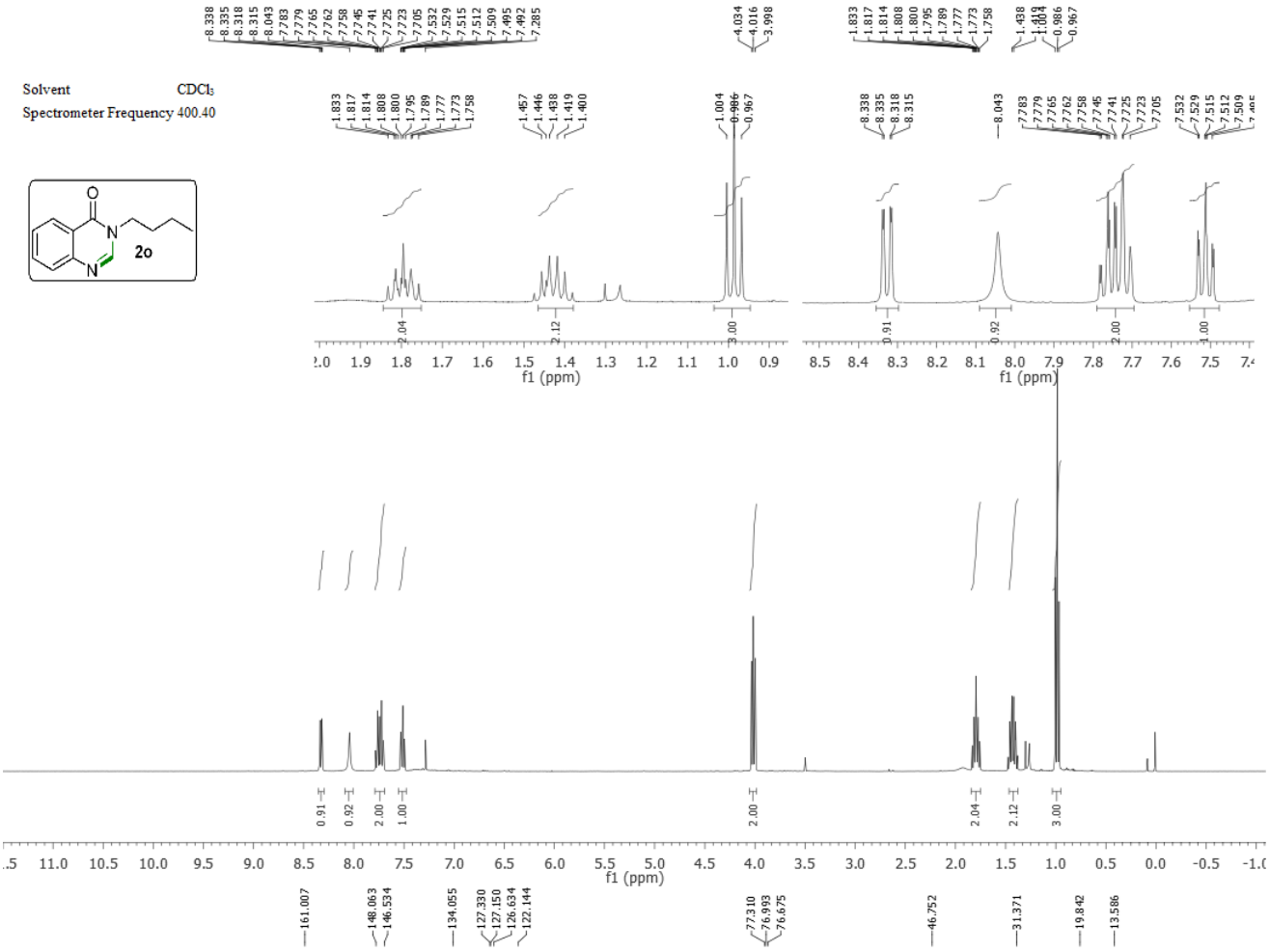
Solvent CDCl3

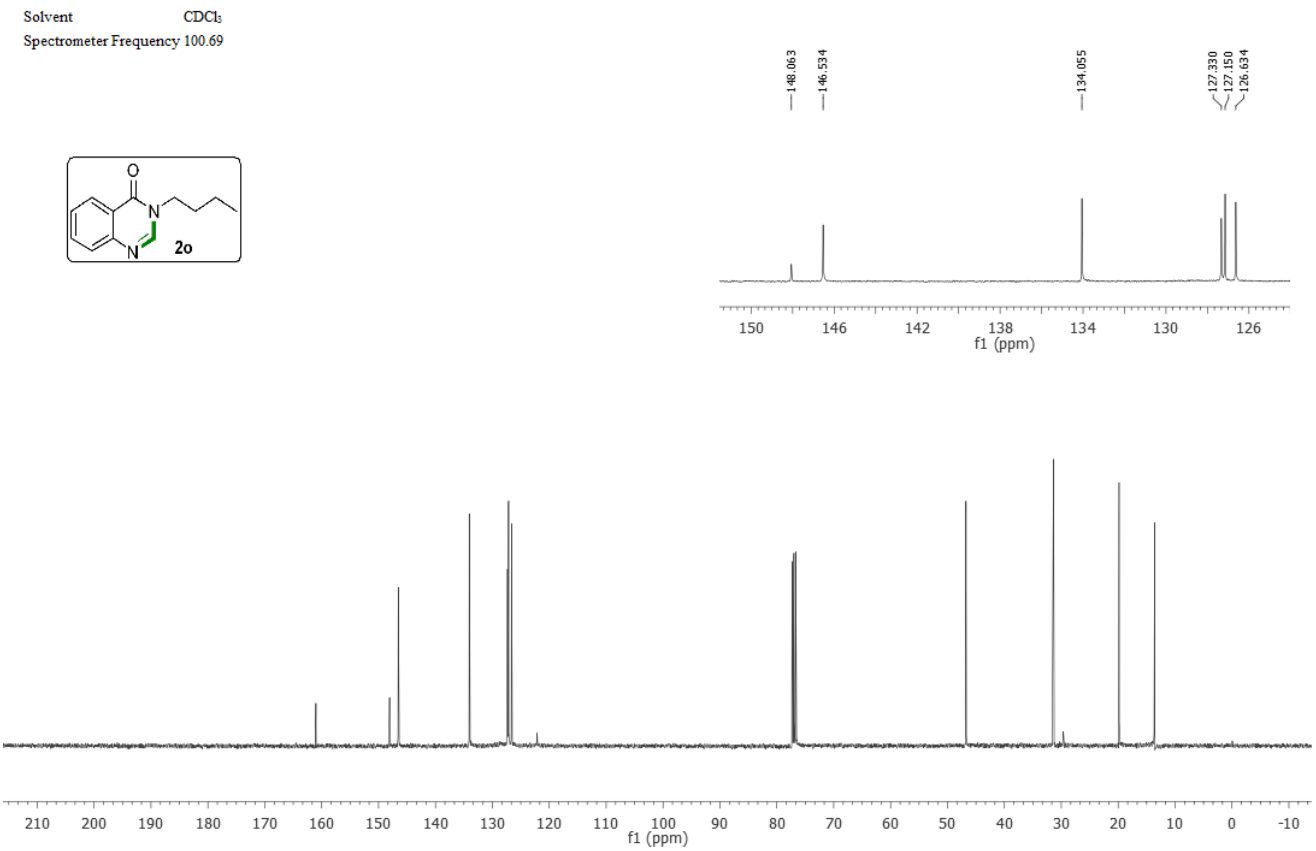
Spectrometer Frequency 100.69

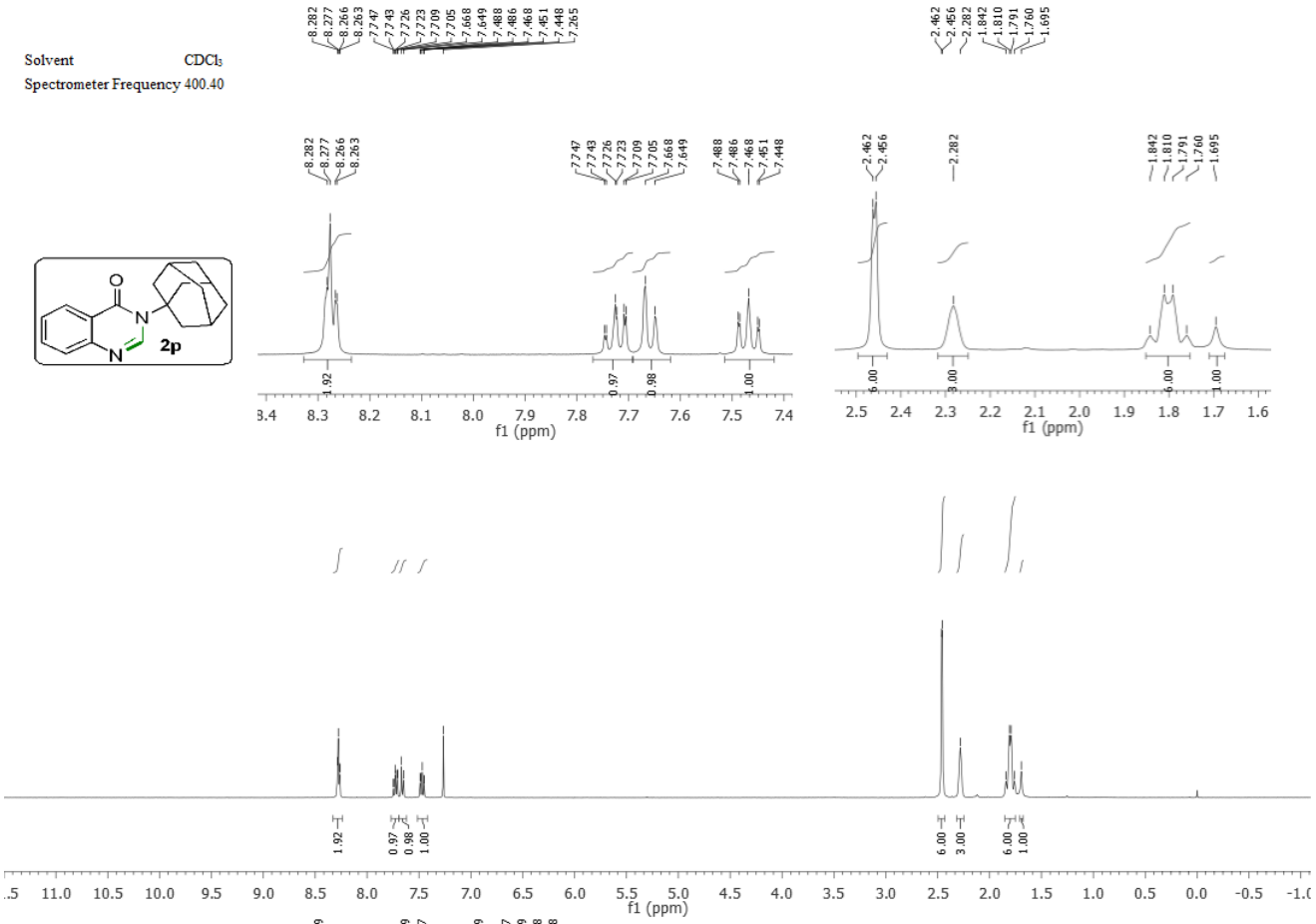


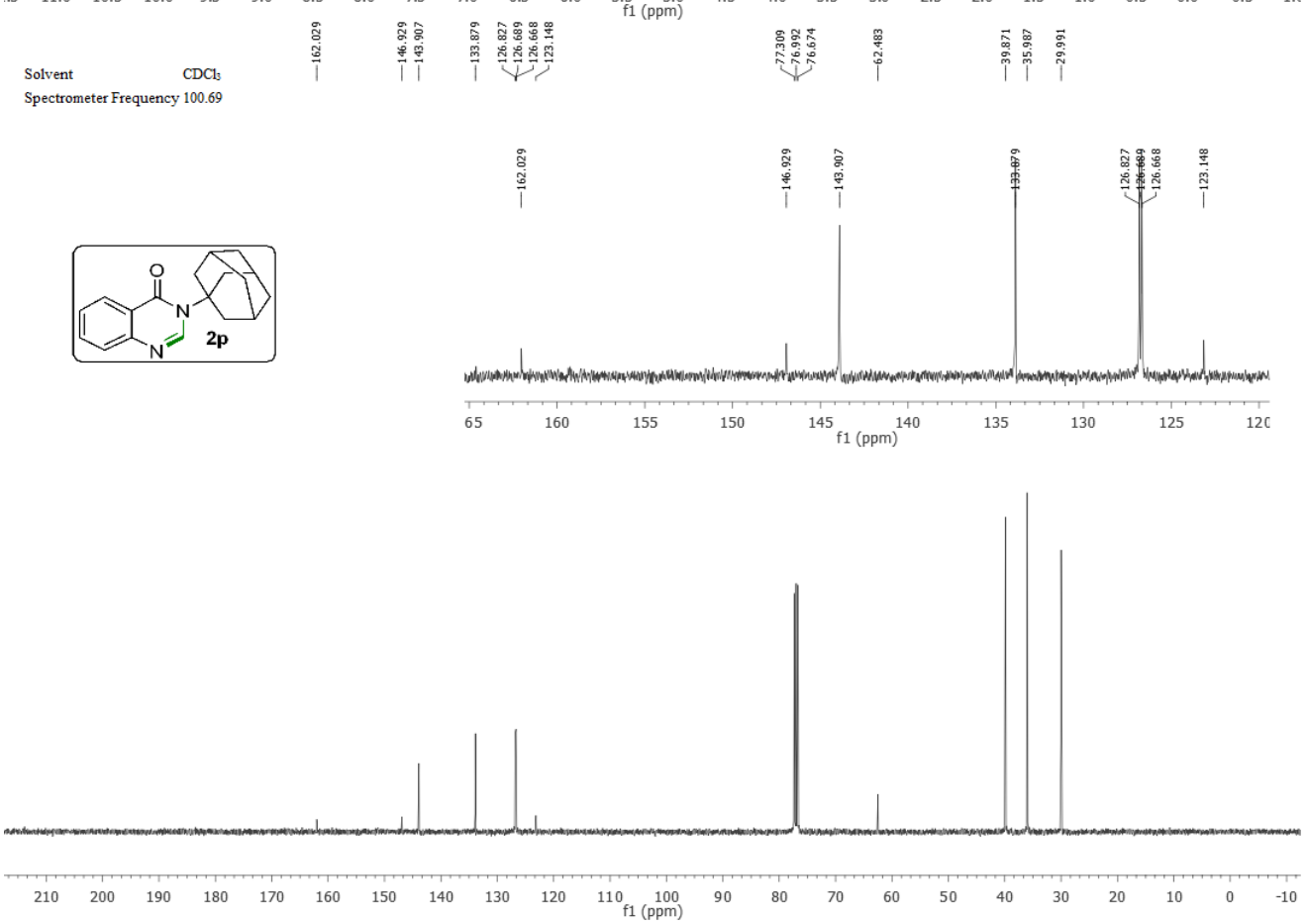


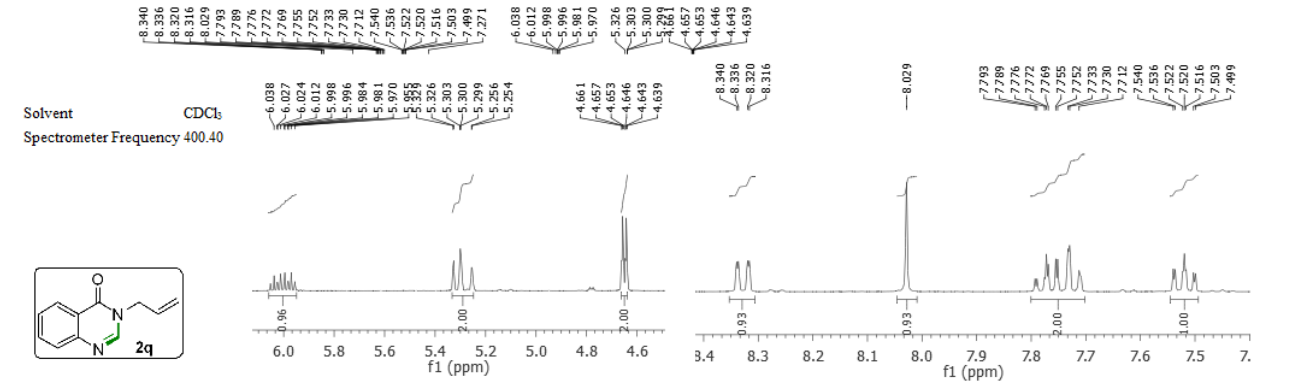


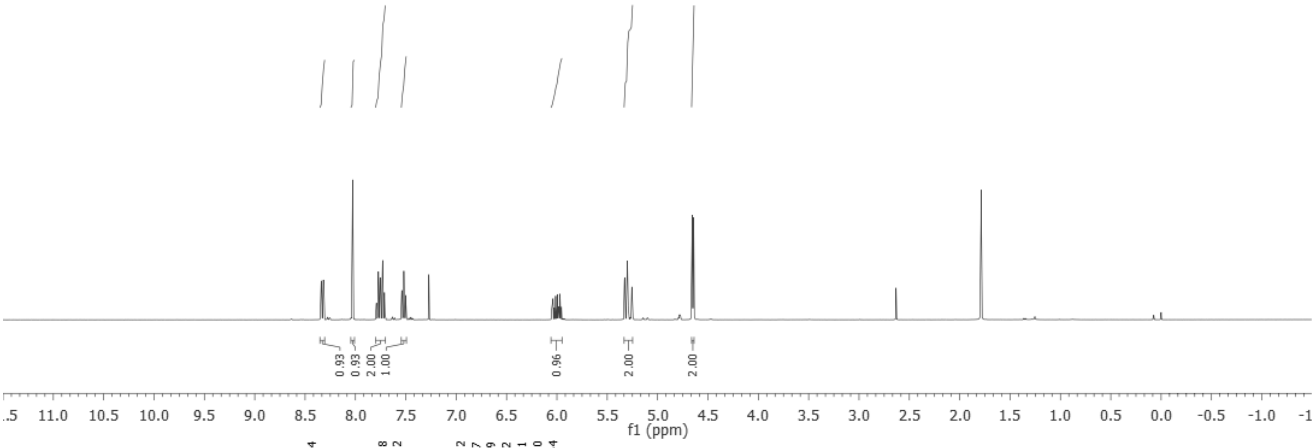

Solvent CDCl3
Spectrometer Frequency 400.40
2o
f1 (ppm)

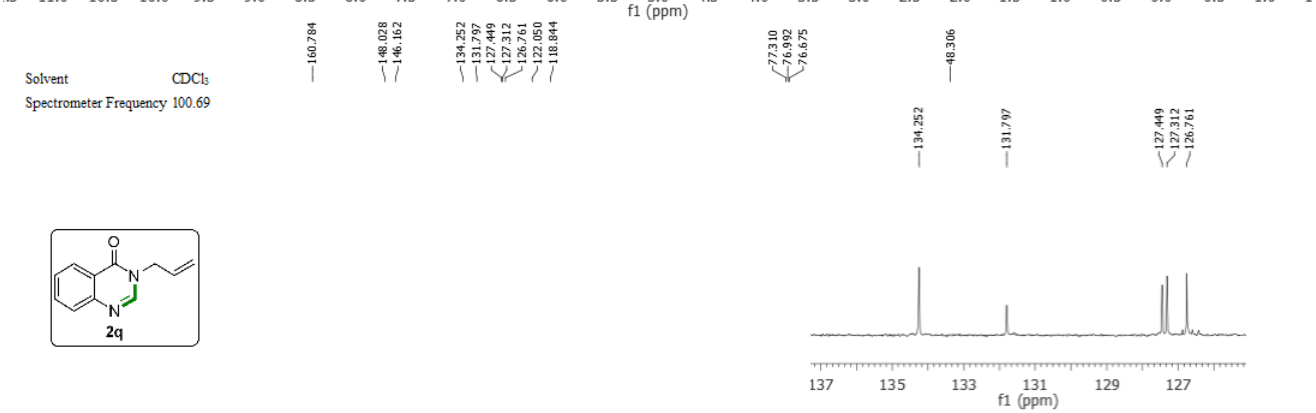

Solvent CDCl3
Spectrometer Frequency 100.69
2o
f1 (ppm)

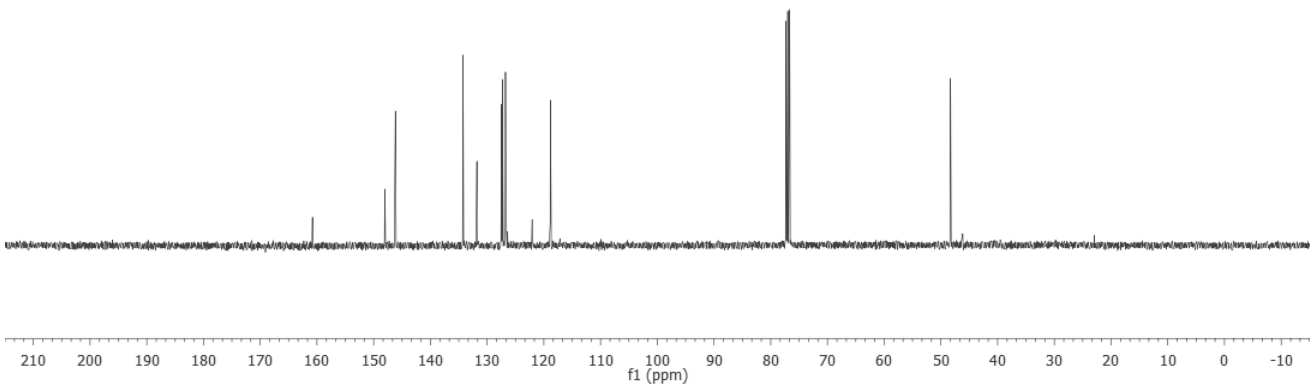

Solvent CDCl3
Spectrometer Frequency 400.40
2p
f1 (ppm)


Solvent CDCl3
Spectrometer Frequency 100.69
2p
f1 (ppm)


Solvent CDCl3
Spectrometer Frequency 400.40
2q
f1 (ppm)

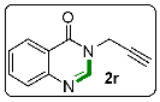

f1 (ppm)

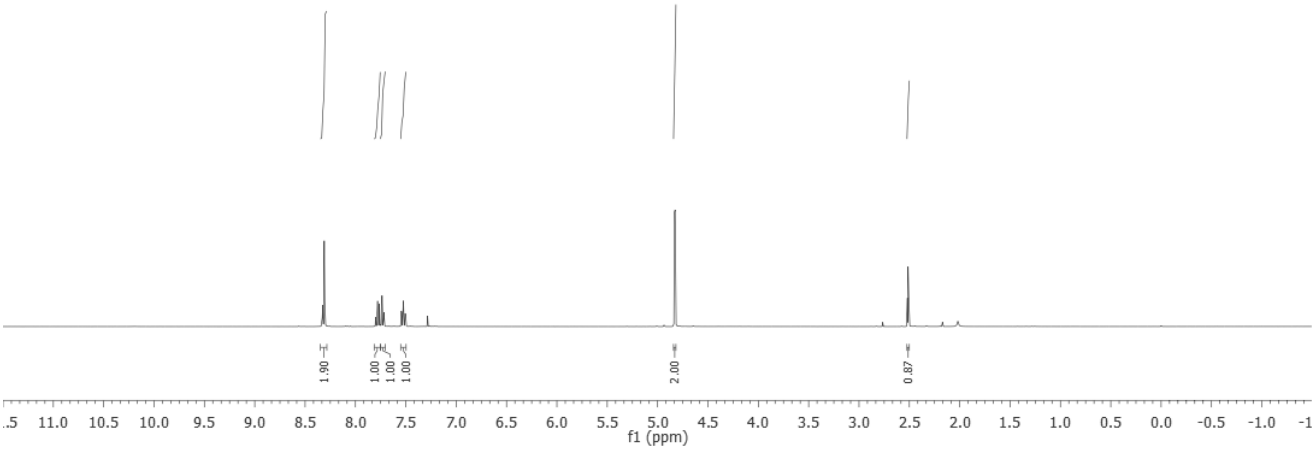

Solvent CDCl3
Spectrometer Frequency 100.69
2q
f1 (ppm)


f1 (ppm)

Solvent CDCl3

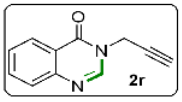
Spectrometer Frequency 400.40

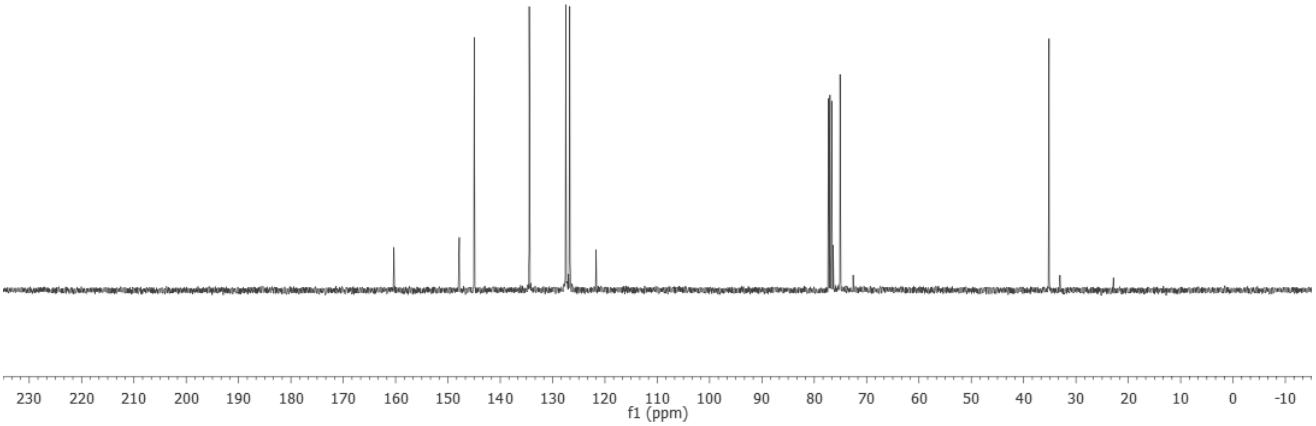


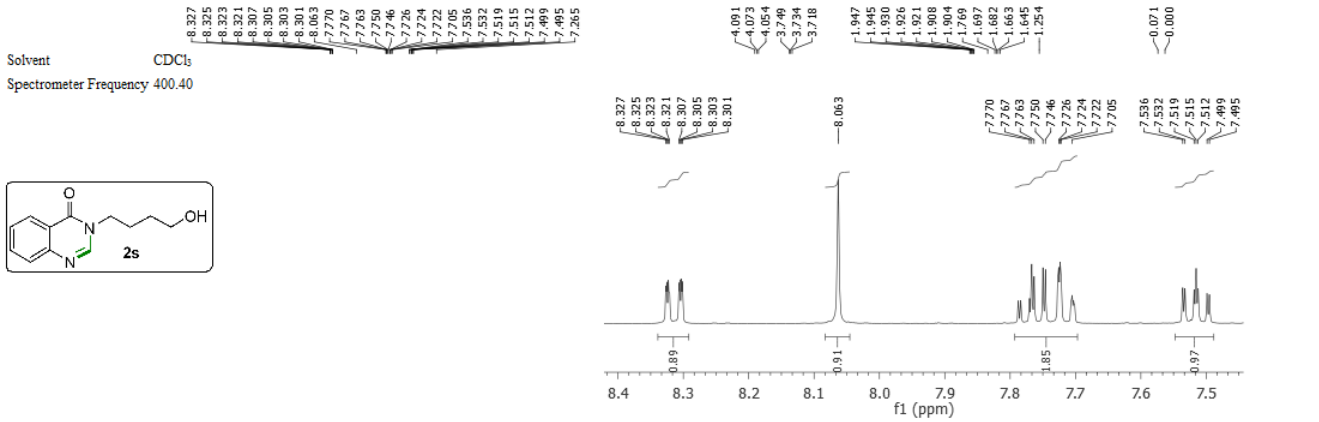


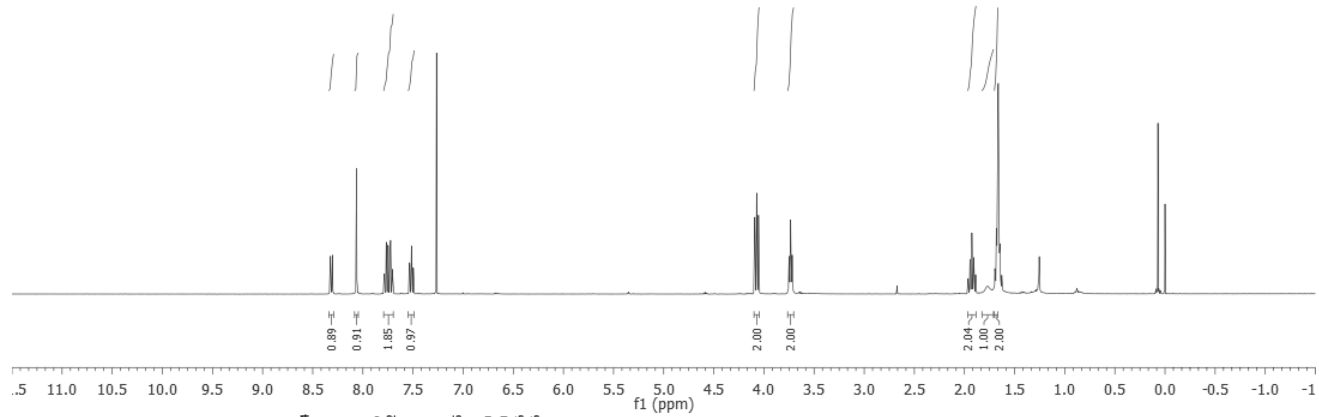
Solvent CDCl3

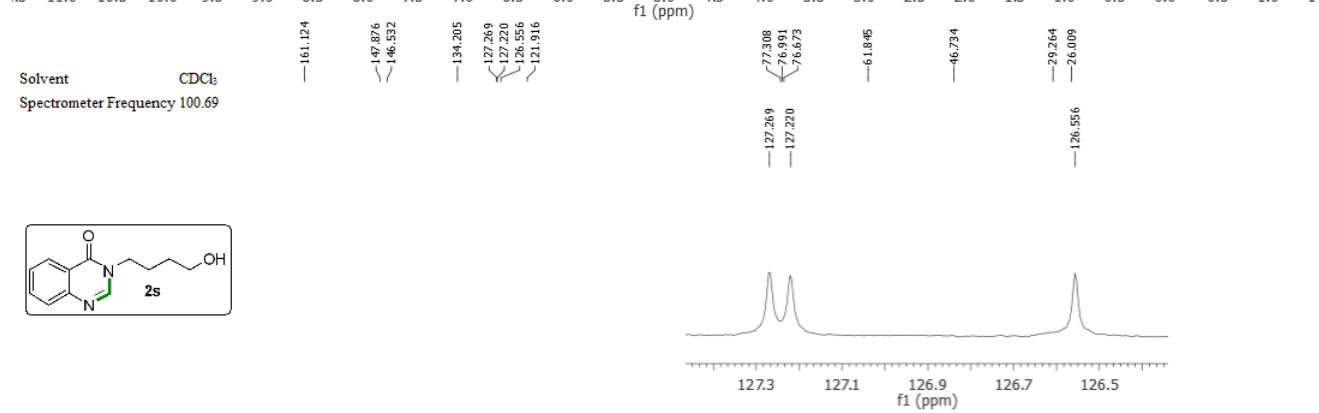
Spectrometer Frequency 100.69

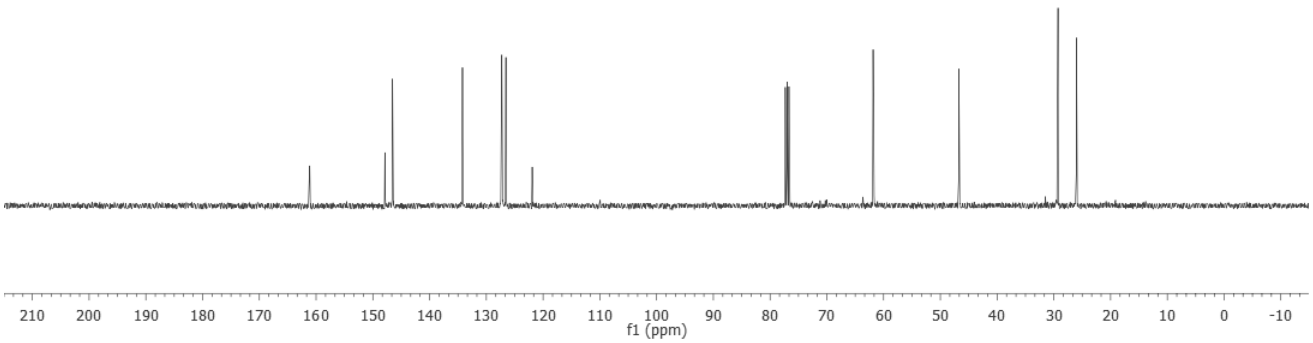


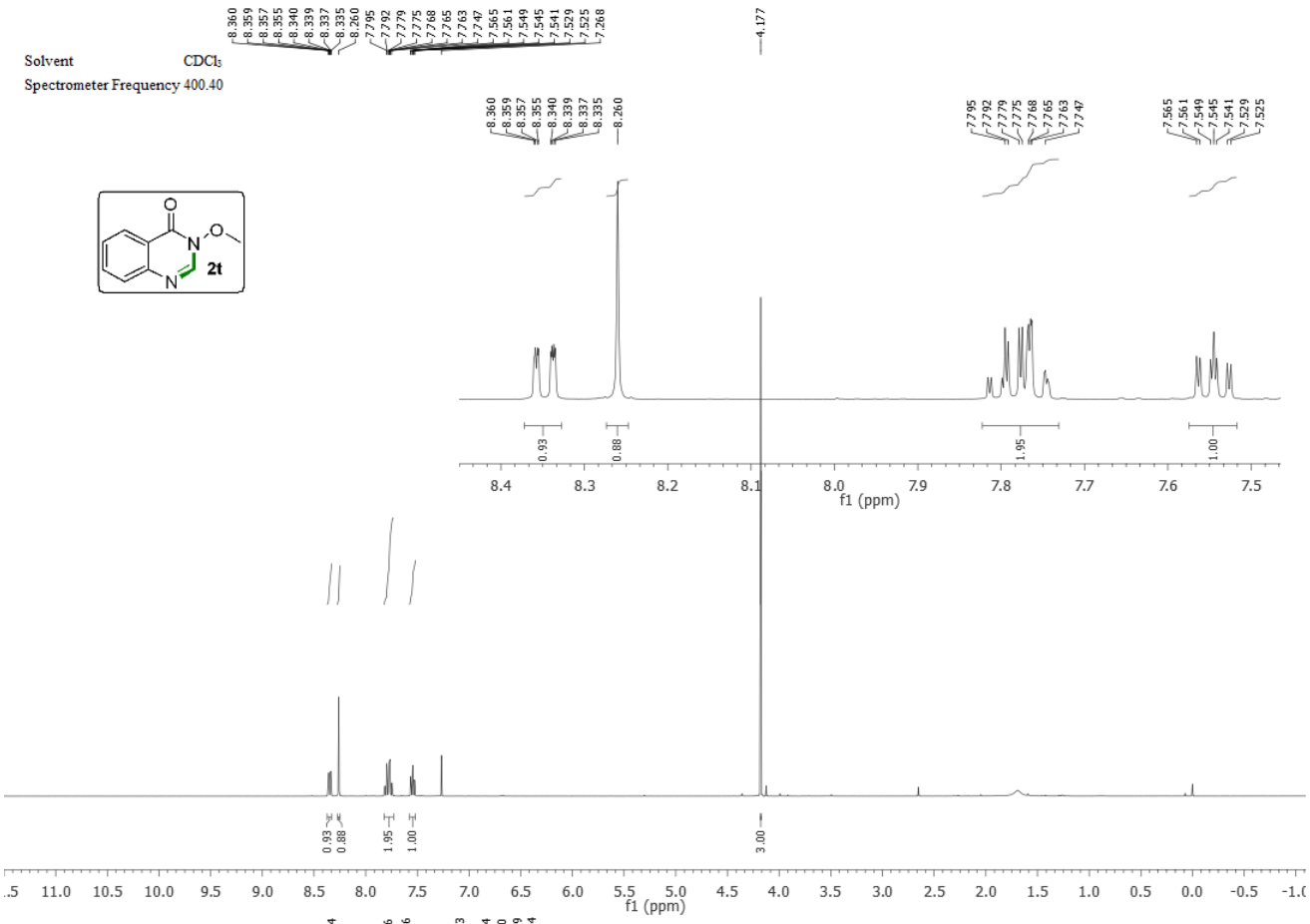


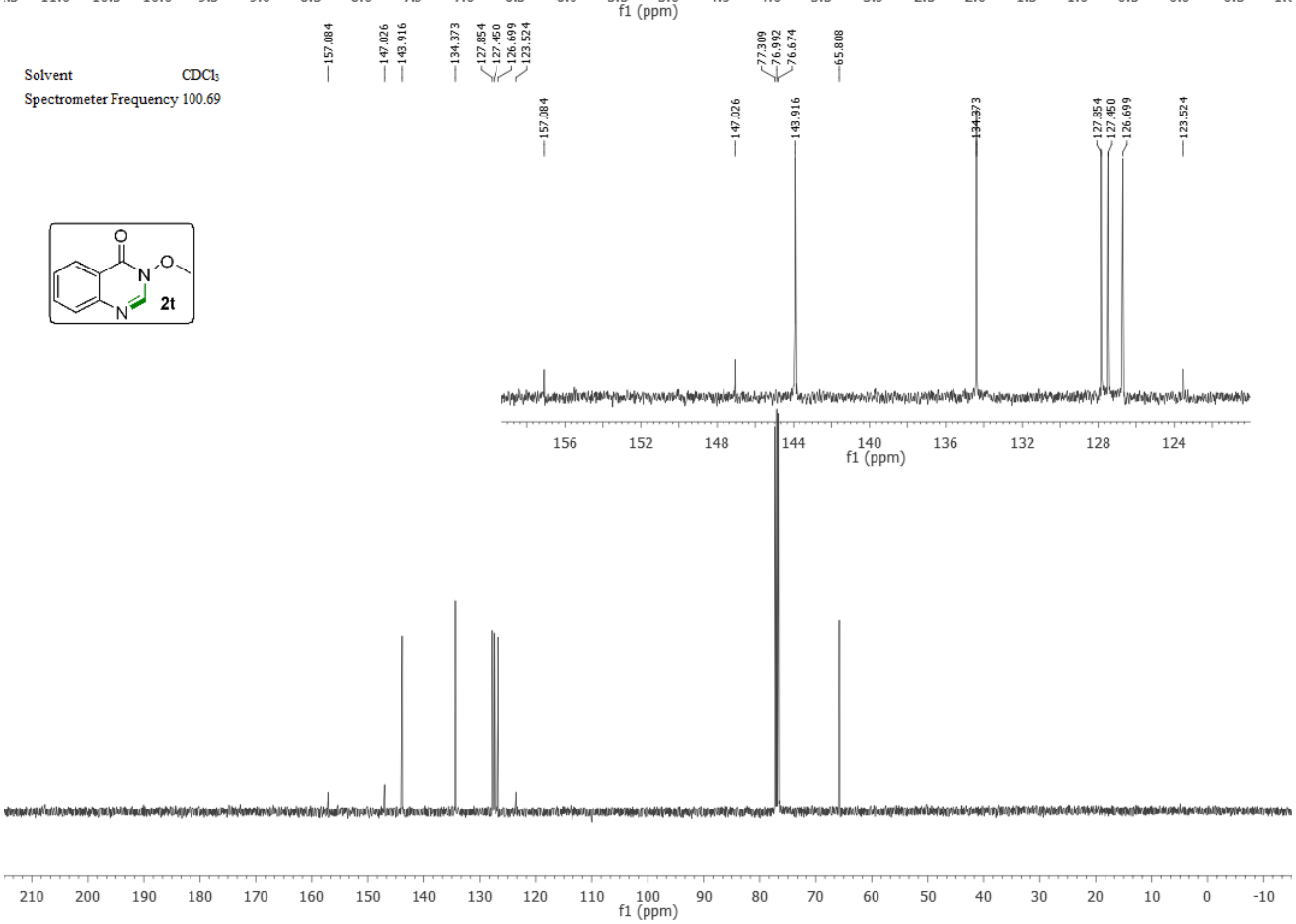

Solvent CDCl3
Spectrometer Frequency 400.40
2s
f1 (ppm)

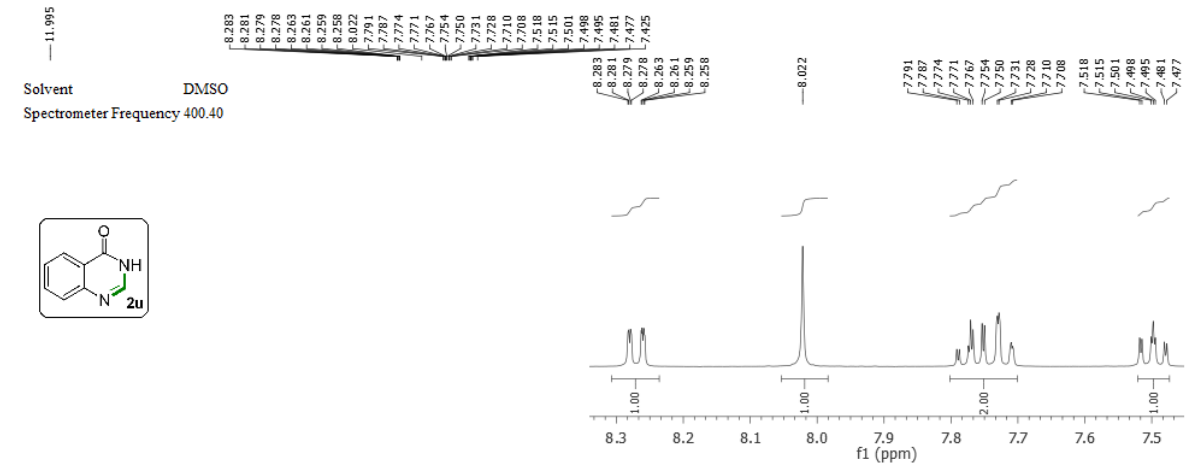

f1 (ppm)

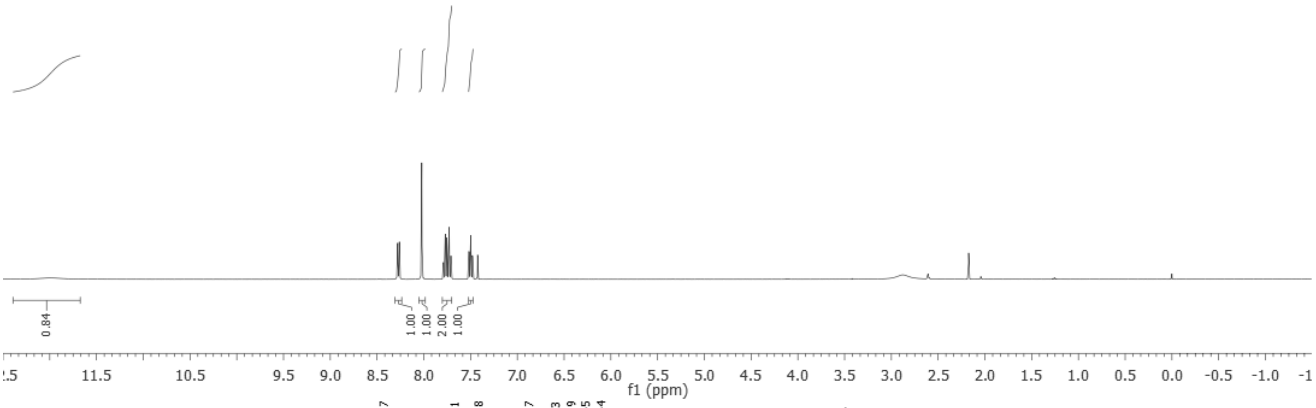

Solvent CDCl3
Spectrometer Frequency 100.69
2s
f1 (ppm)

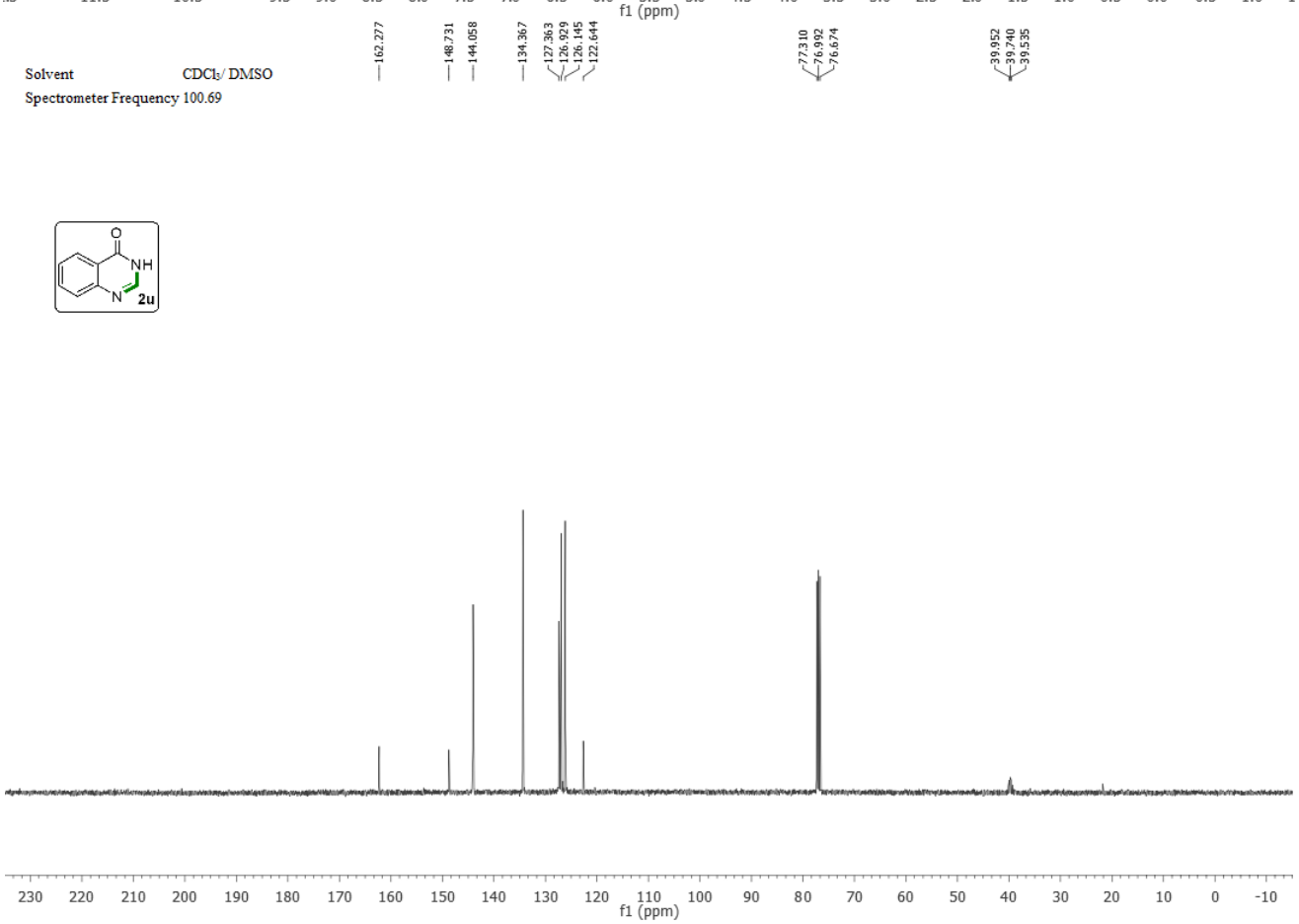

f1 (ppm)


Solvent CDCl3
Spectrometer Frequency 400.40
2t
f1 (ppm)

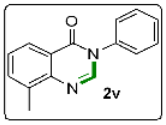

Solvent CDCl3
Spectrometer Frequency 100.69
2t
f1 (ppm)

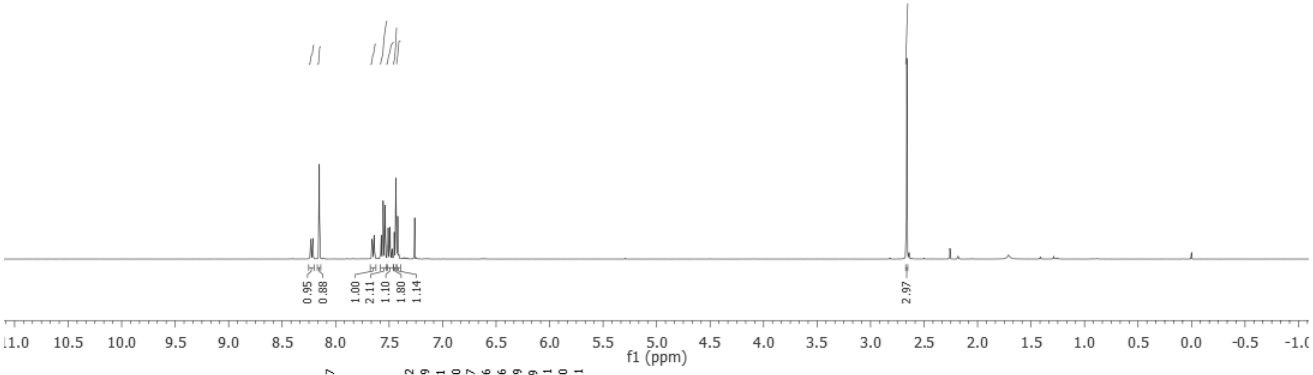

11.995
8.283
8.281
8.279
8.278
8.263
8.261
8.259
8.258
8.022
7.791
7.787
7.774
7.771
7.767
7.754
7.750
7.731
7.728
7.710
7.708
7.518
7.515
7.501
7.498
7.495
7.481
7.477
7.425
Solvent DMSO
Spectrometer Frequency 400.40
2u
1.00
1.00
2.00
1.00
f1 (ppm)

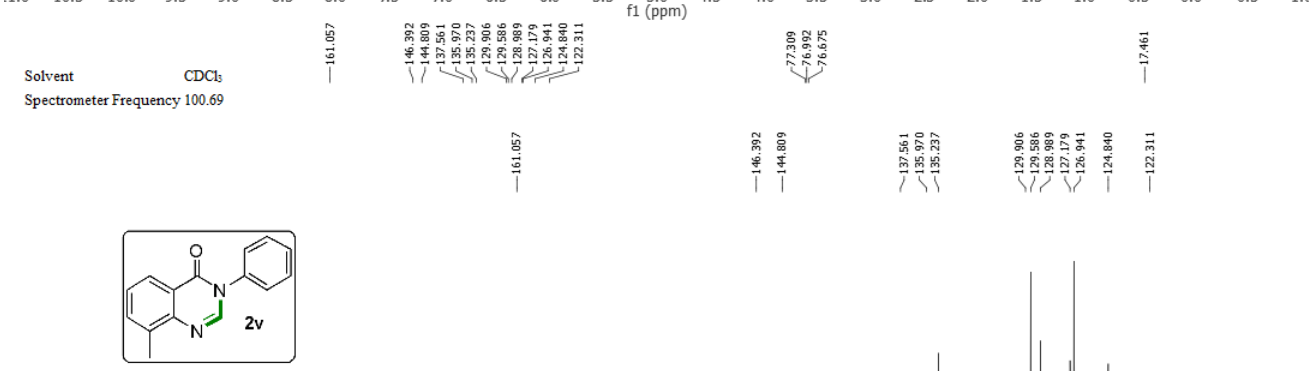

0.84
1.00
1.00
2.00
1.00
f1 (ppm)


162.277
148.731
144.058
134.367
127.363
126.929
126.145
122.644
77.310
76.992
76.674
39.952
39.740
39.535
Solvent CDCl3/ DMSO
Spectrometer Frequency 100.69
2u
f1 (ppm)


Solvent CDCl3
Spectrometer Frequency 400.40

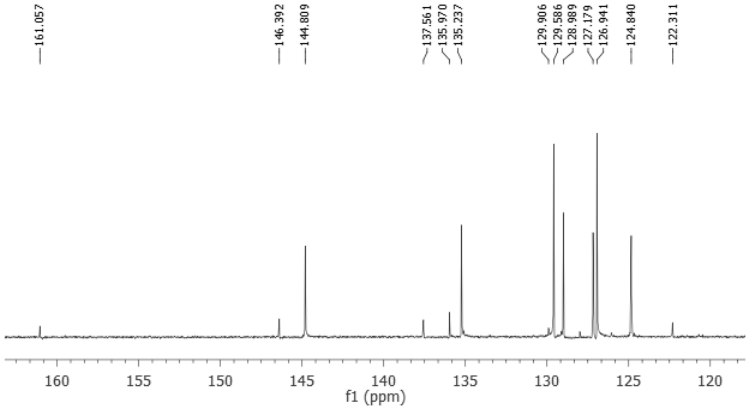

2v

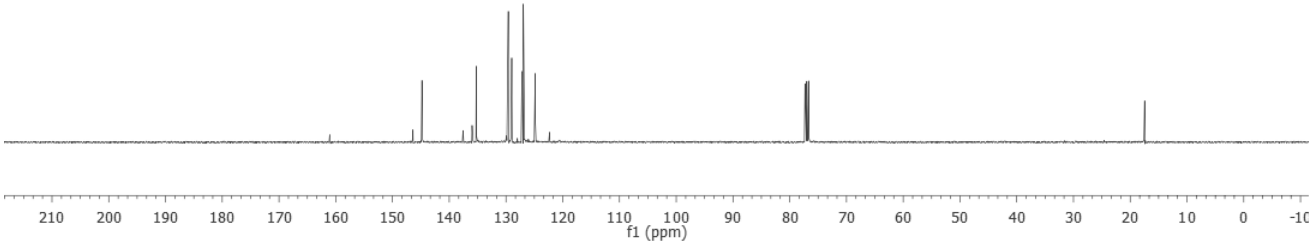

f1 (ppm)

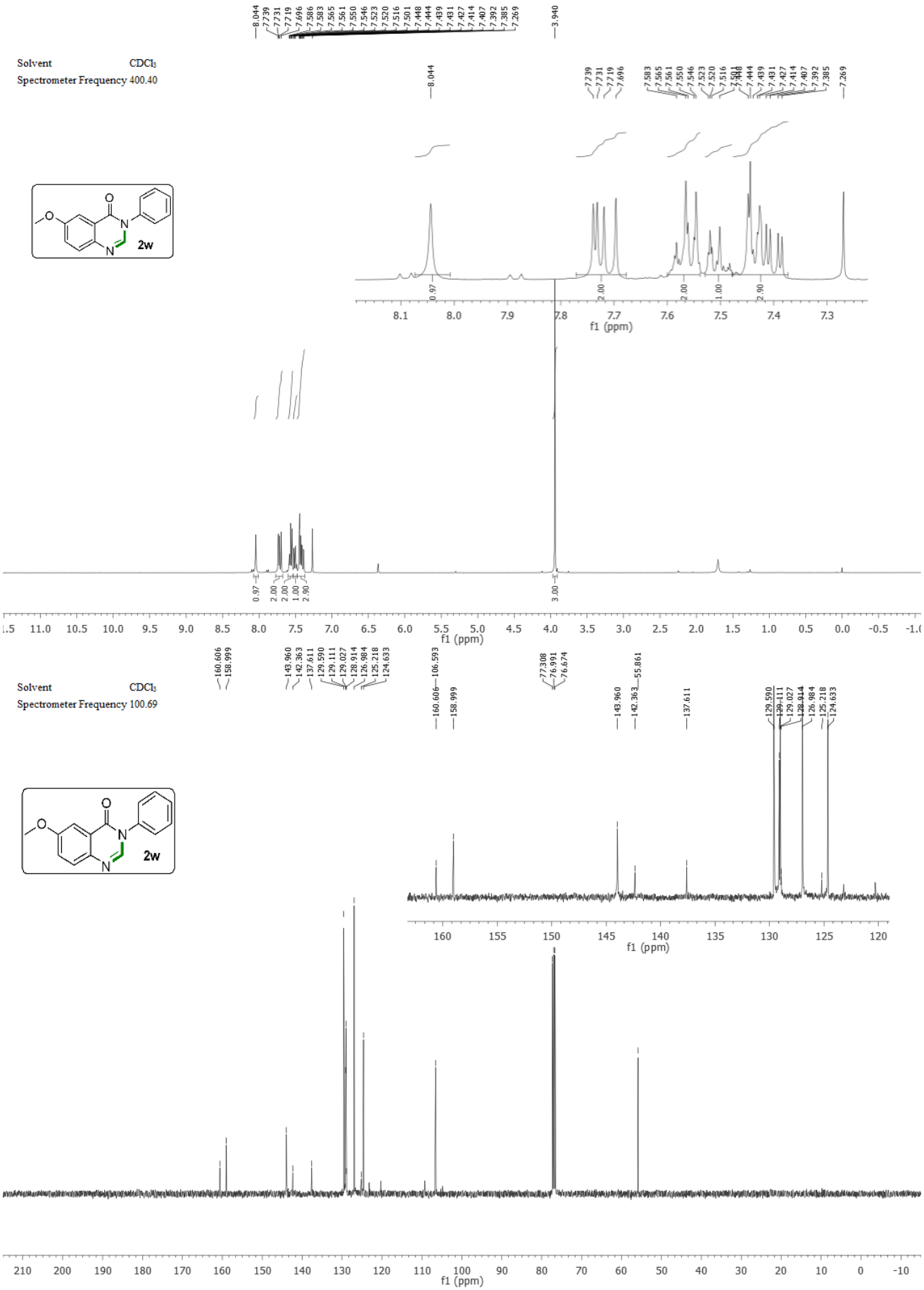

f1 (ppm)

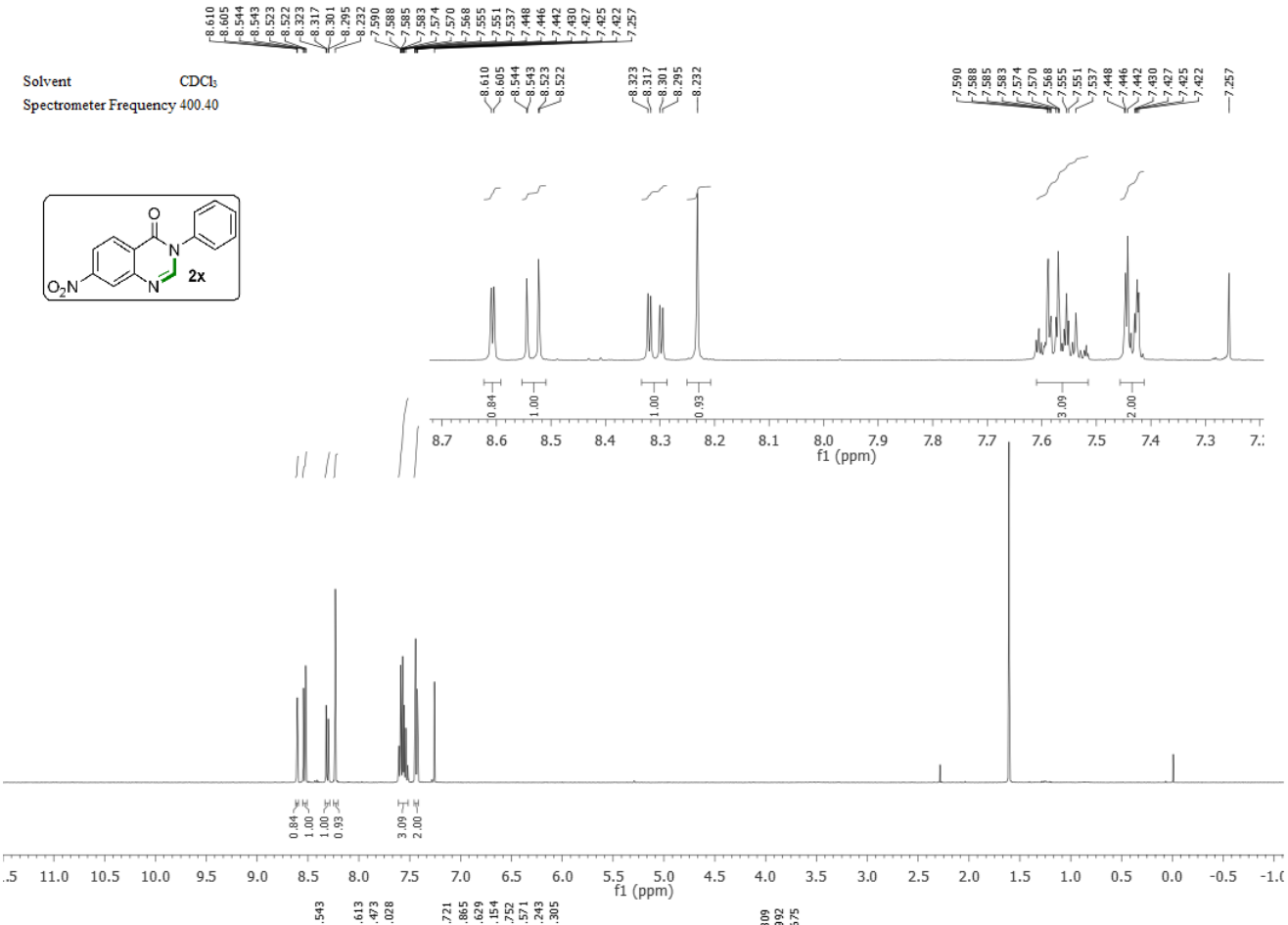
Solvent CDCl3
Spectrometer Frequency 100.69

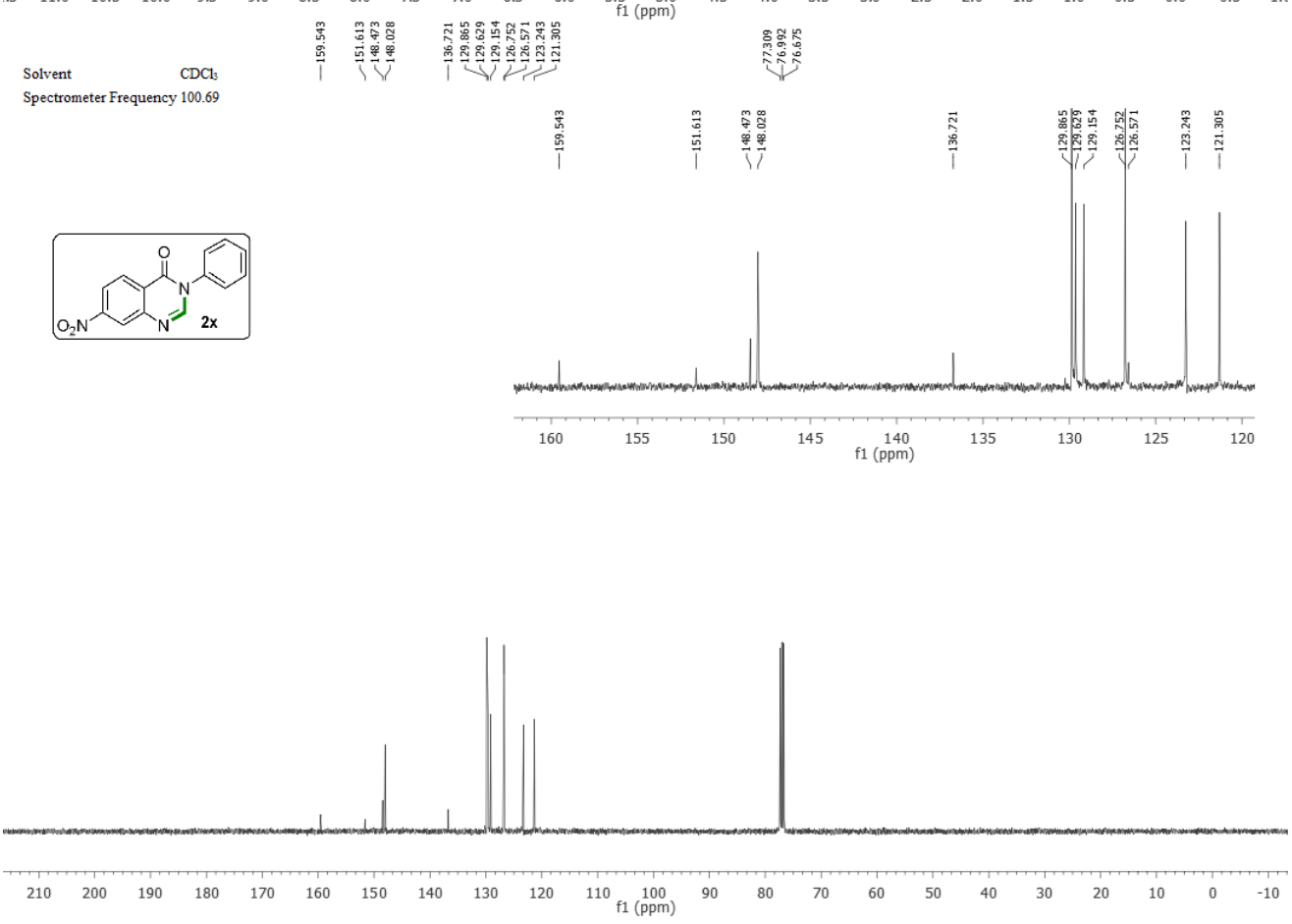
2v


f1 (ppm)

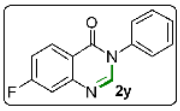

f1 (ppm)

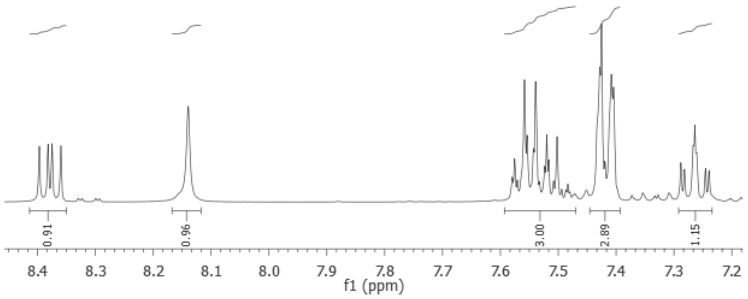

Solvent CDCl3
Spectrometer Frequency 400.40
2w
f1 (ppm)
Solvent CDCl3
Spectrometer Frequency 100.69
2w
f1 (ppm)

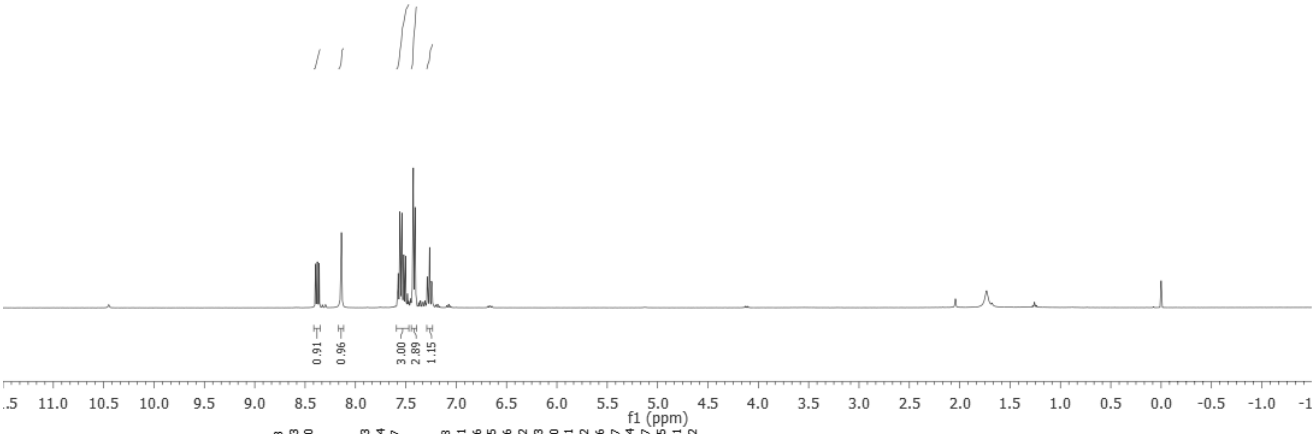

Solvent CDCl3
Spectrometer Frequency 400.40
2x
f1 (ppm)


Solvent CDCl3
Spectrometer Frequency 100.69
2x
f1 (ppm)

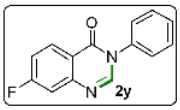
Solvent CDCl3
Spectrometer Frequency 400.40

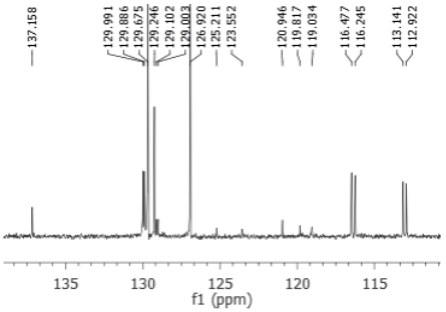


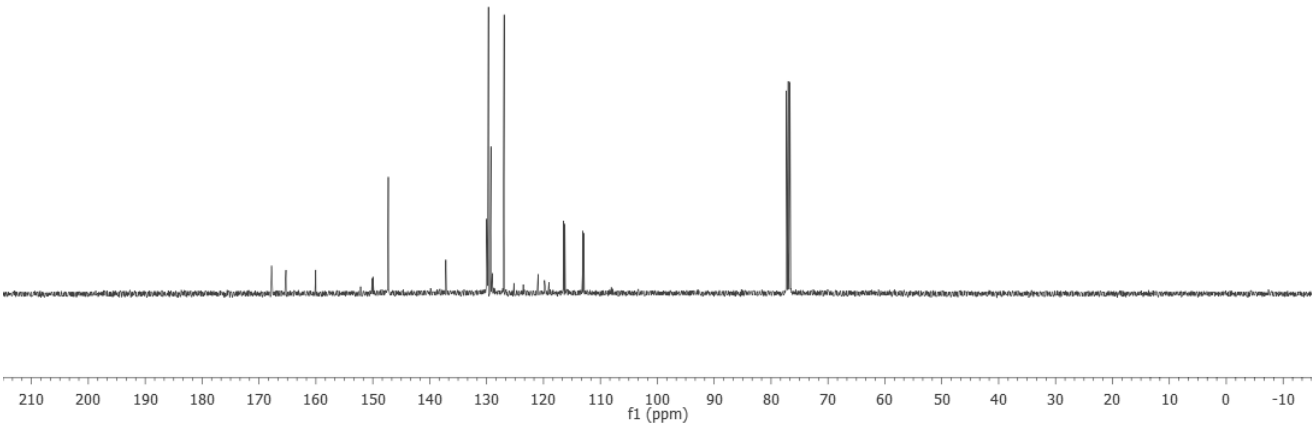


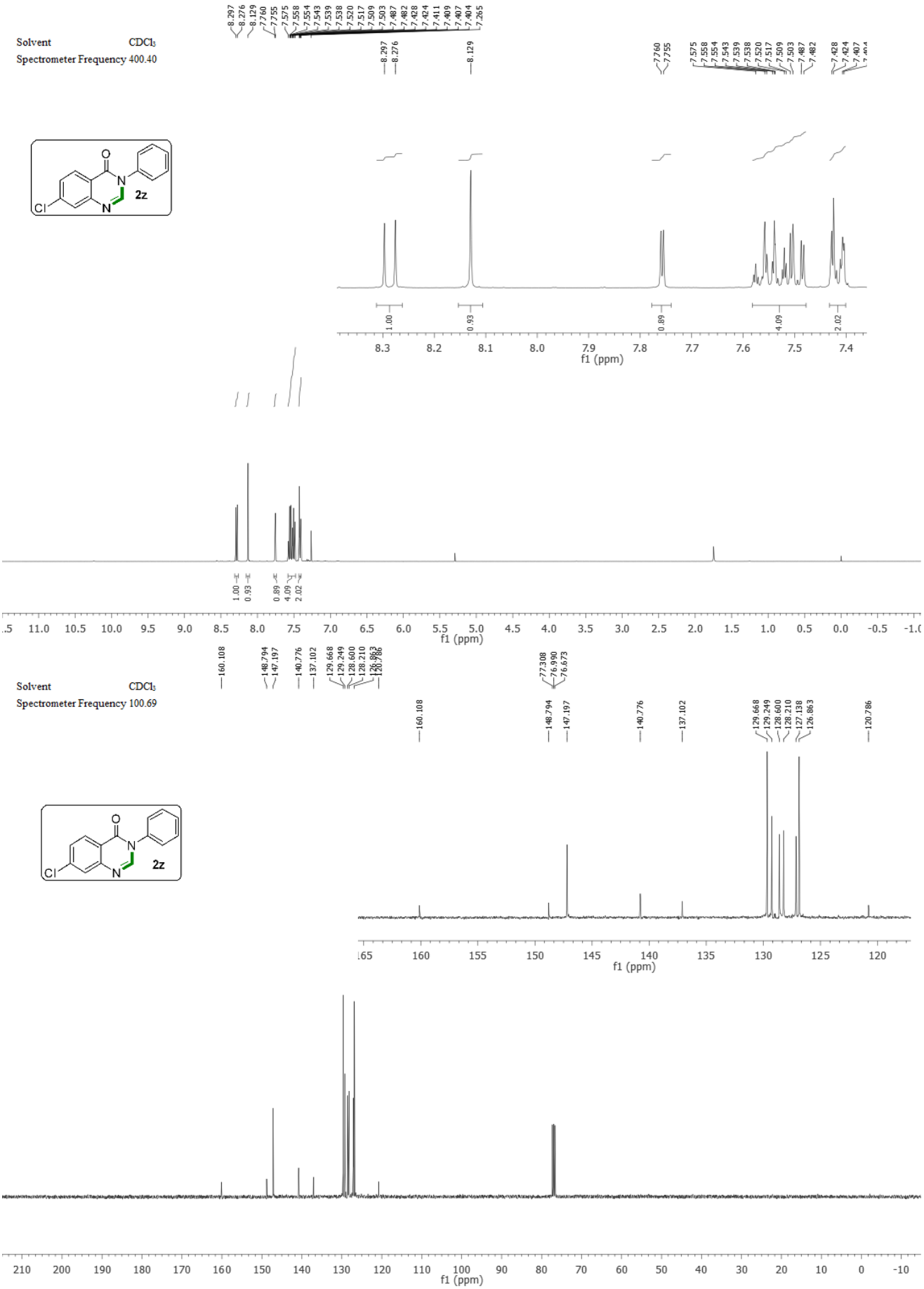


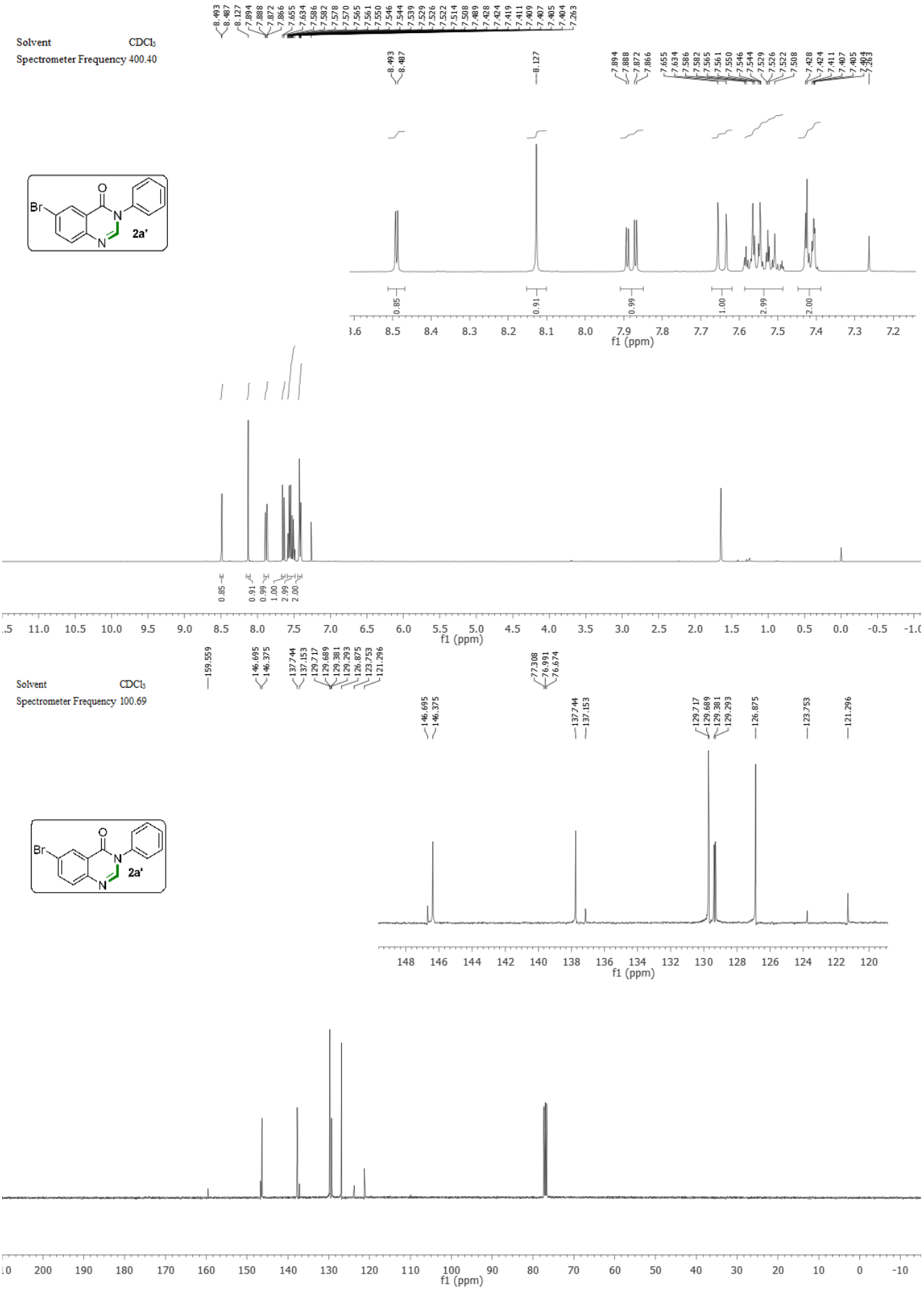
Solvent CDCl3
Spectrometer Frequency 100.69

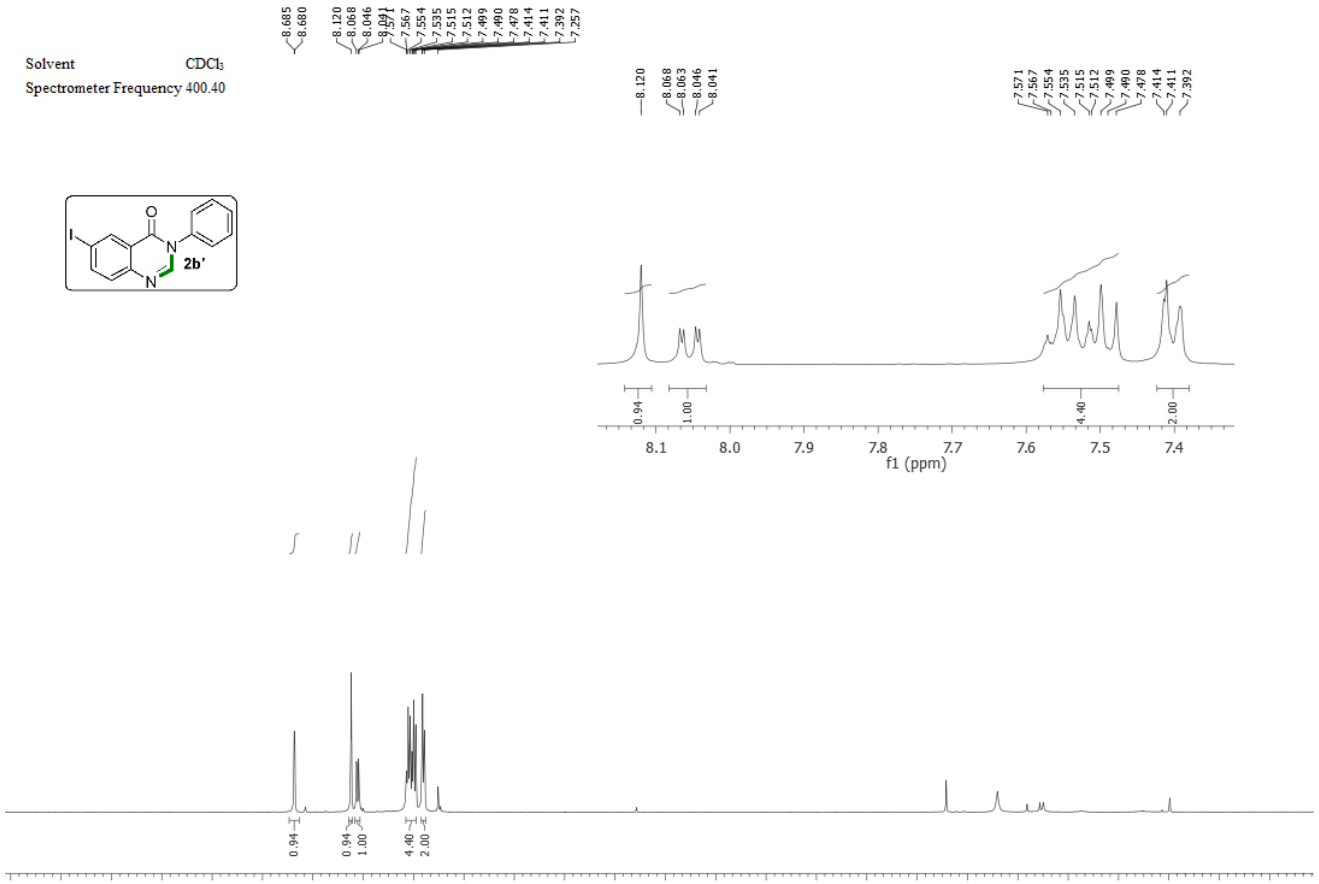


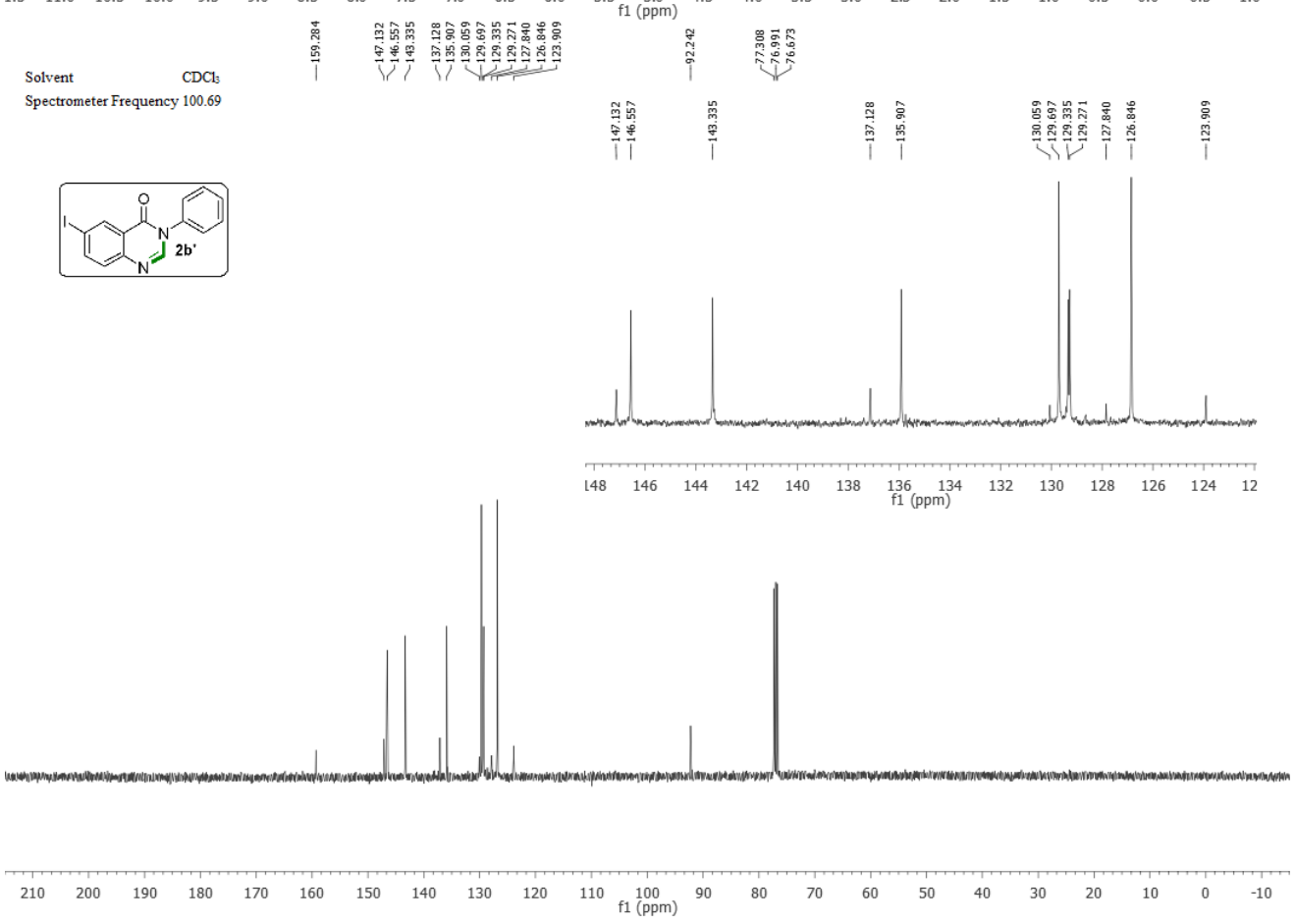


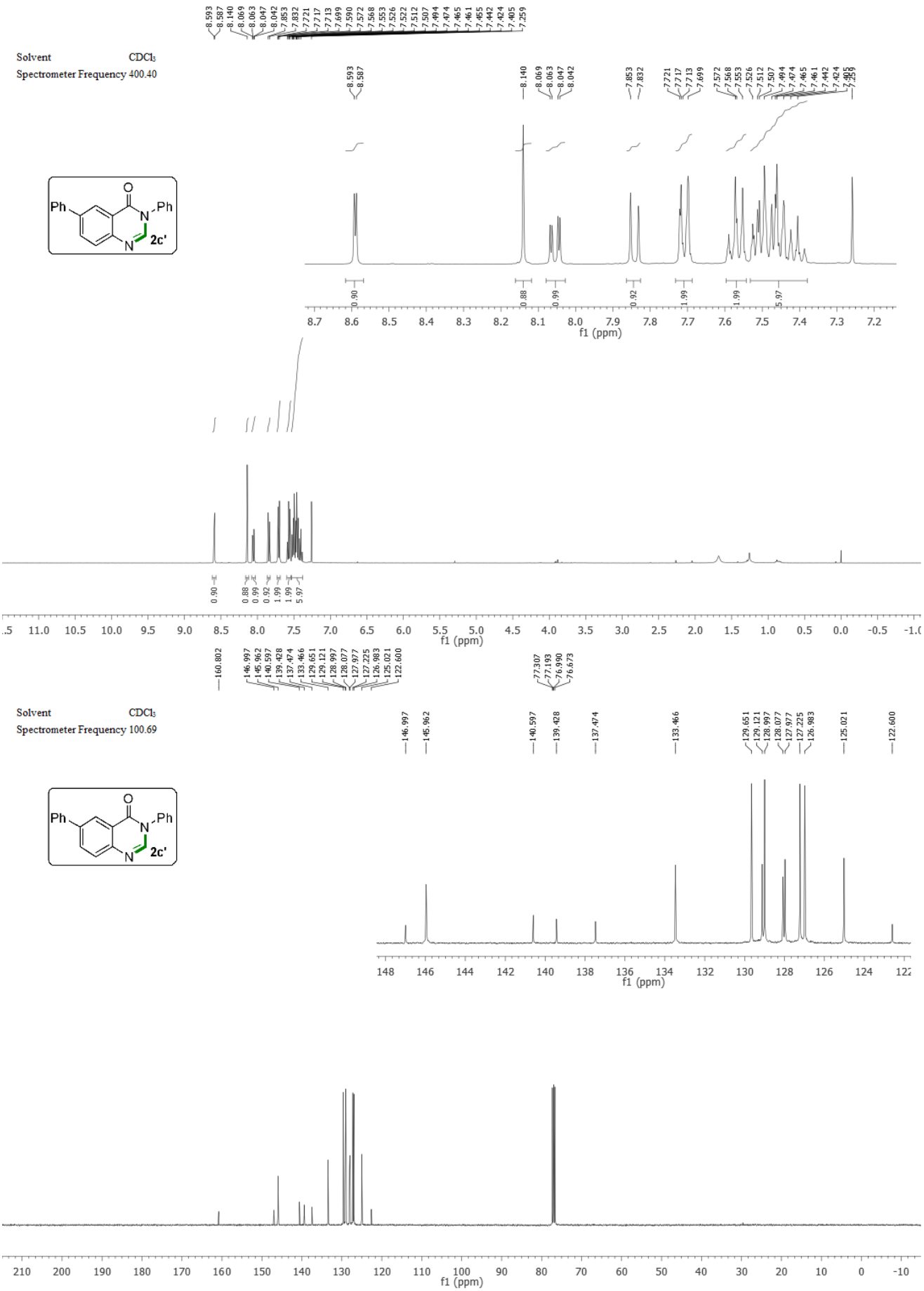


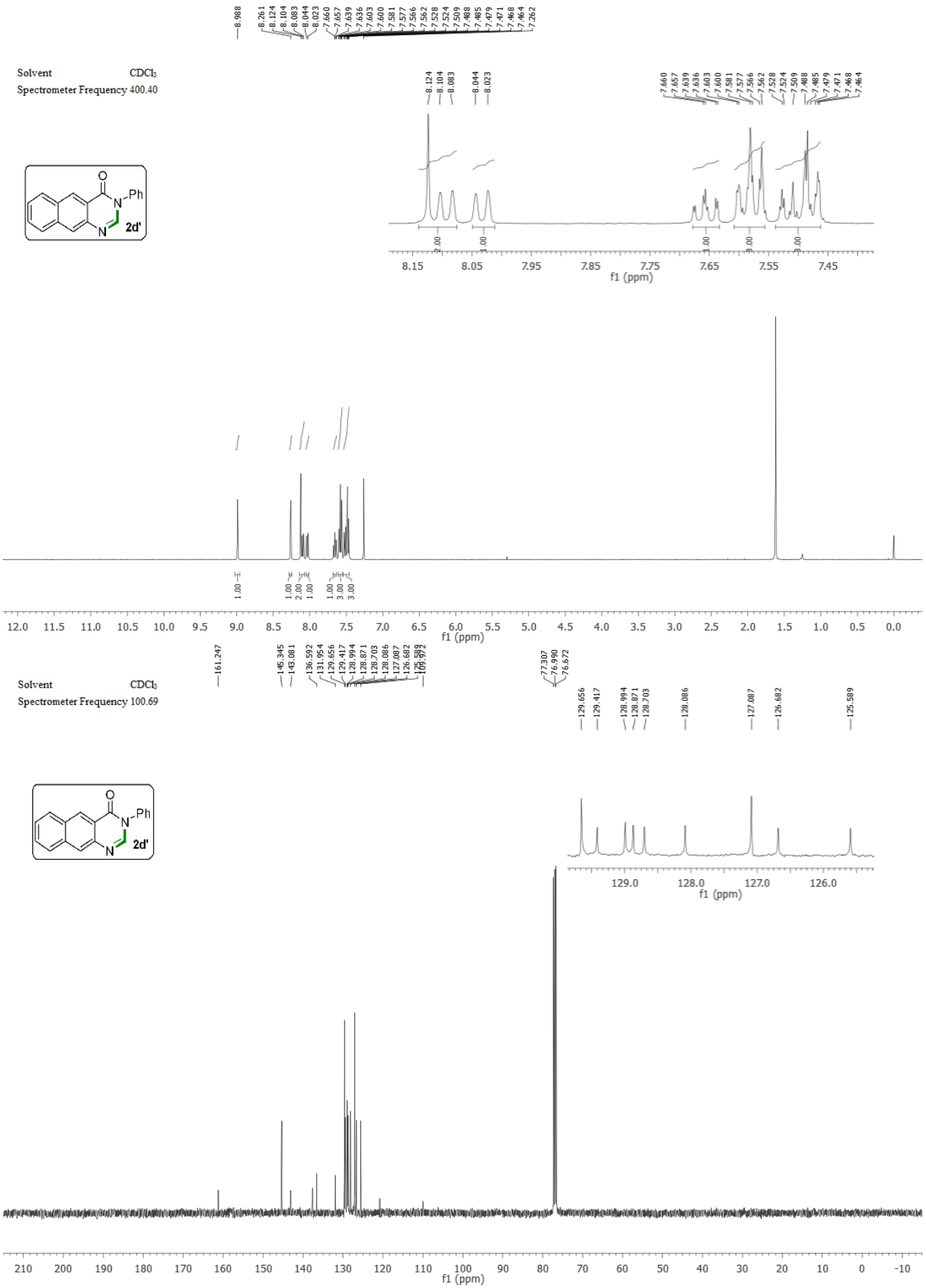

Solvent CDCl3
Spectrometer Frequency 400.40
2z
f1 (ppm)
Solvent CDCl3
Spectrometer Frequency 100.69
2z
f1 (ppm)


Solvent CDCl3
Spectrometer Frequency 400.40
2a'
f1 (ppm)
Solvent CDCl3
Spectrometer Frequency 100.69
2a'
f1 (ppm)


Solvent CDCl3
Spectrometer Frequency 400.40
2b'
f1 (ppm)

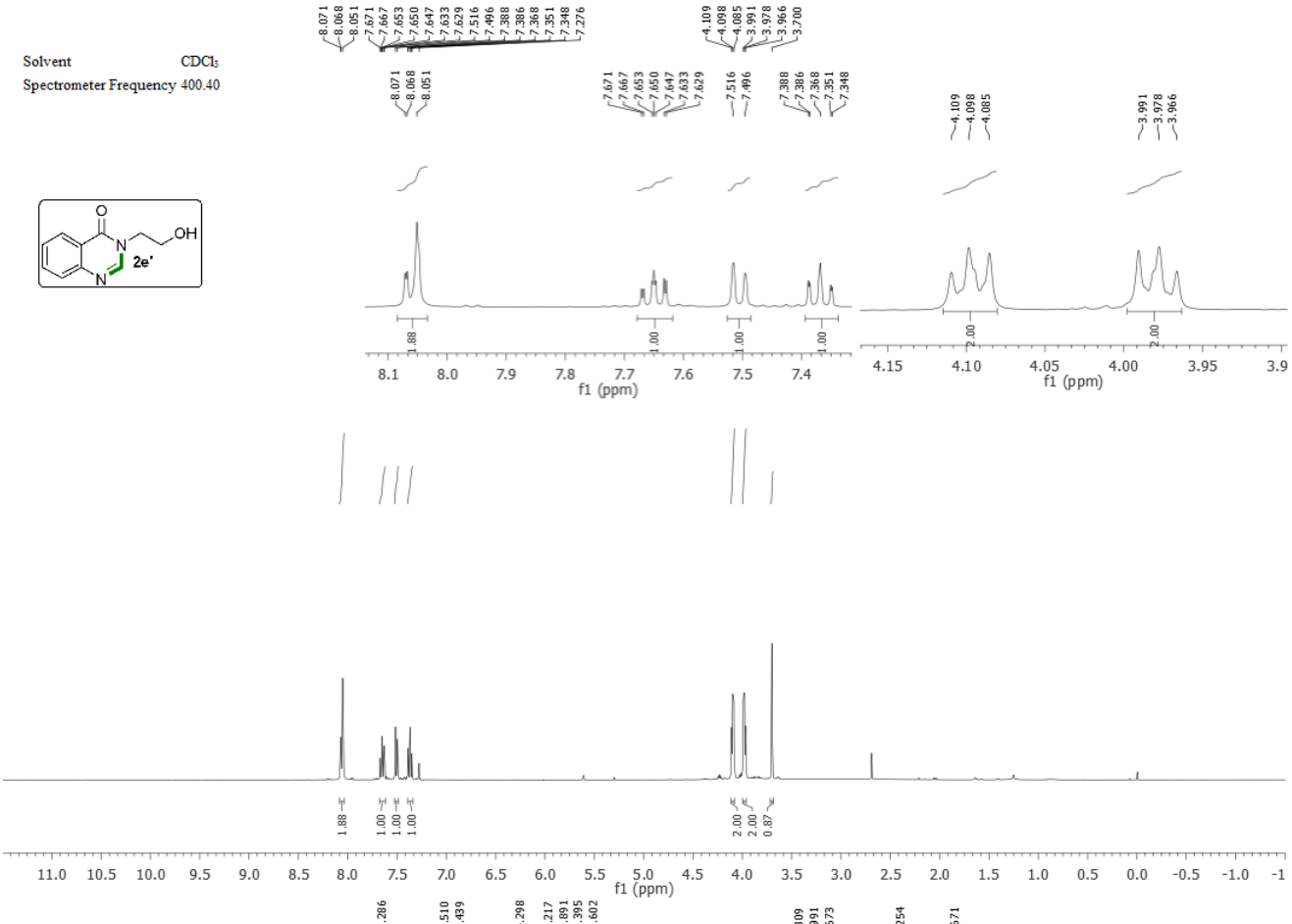

Solvent CDCl3
Spectrometer Frequency 100.69
2b'
f1 (ppm)


Solvent CDCl3
Spectrometer Frequency 400.40
Ph
Ph
N
N
O
2c'
f1 (ppm)
Solvent CDCl3
Spectrometer Frequency 100.69
Ph
Ph
N
N
O
2c'
f1 (ppm)
f1 (ppm)


Solvent CDCl3
Spectrometer Frequency 400.40
2d'
f1 (ppm)
Solvent CDCl3
Spectrometer Frequency 100.69
2d'
f1 (ppm)

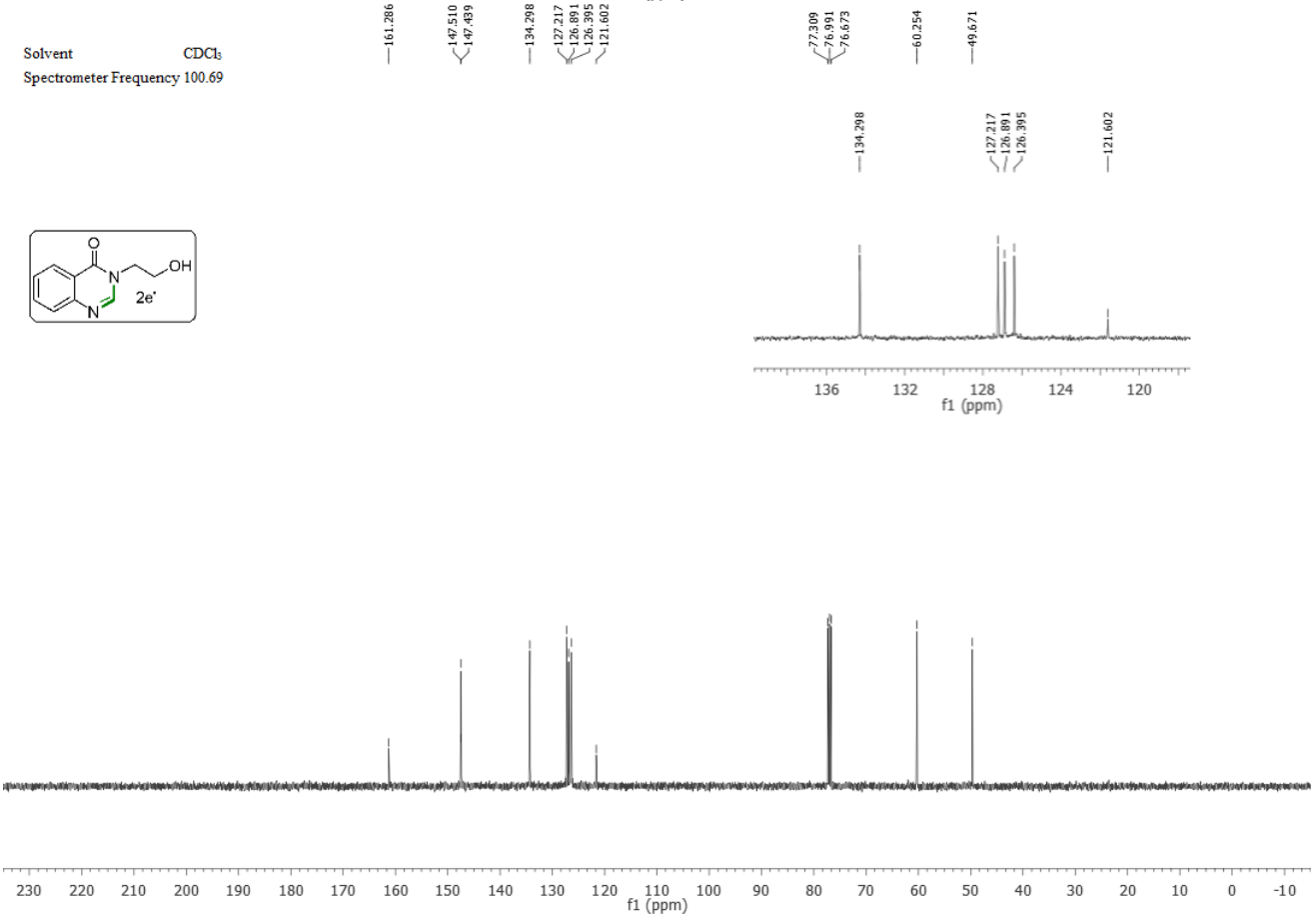
Solvent CDCl3

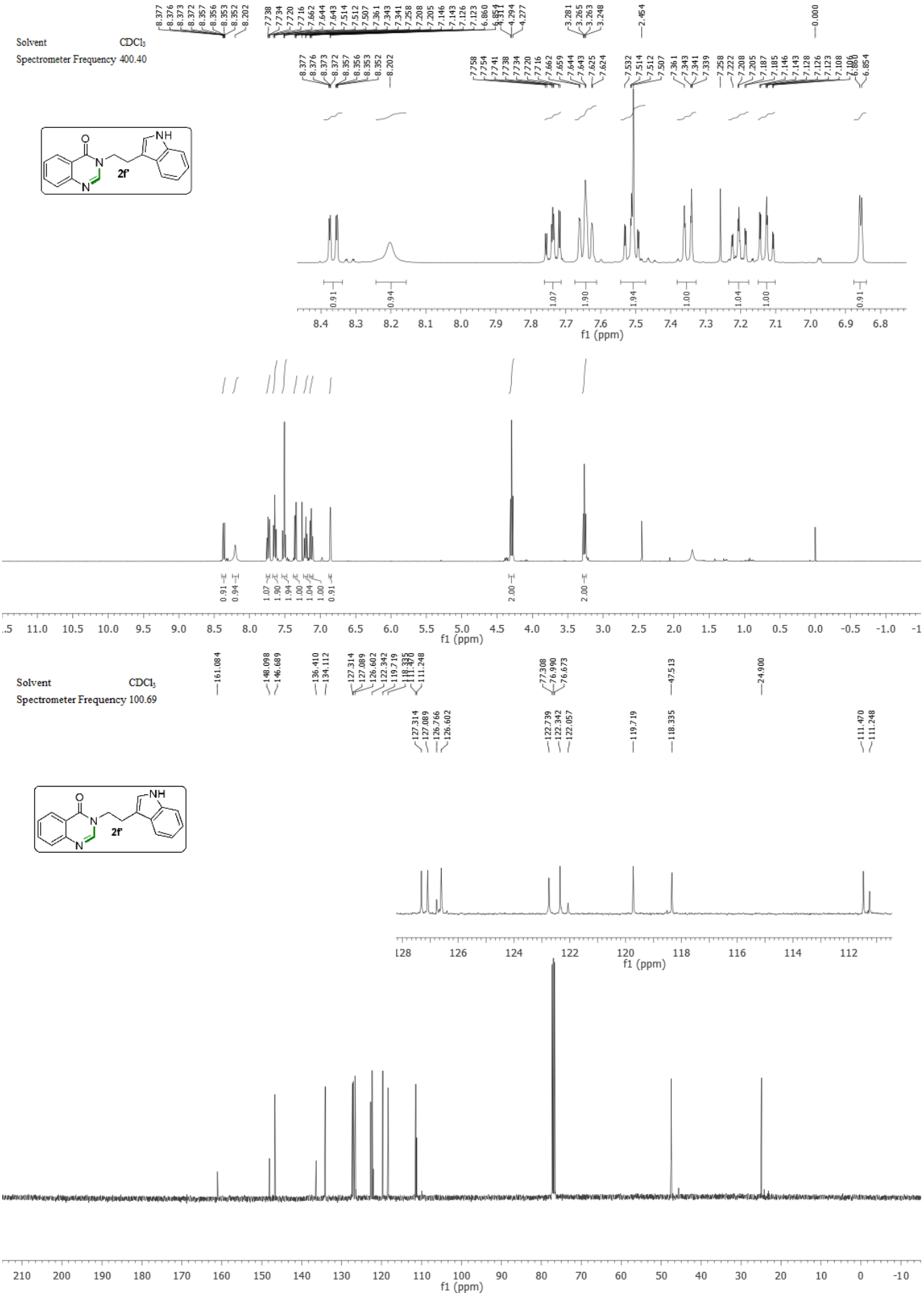
Spectrometer Frequency 400.40



Solvent CDCl3

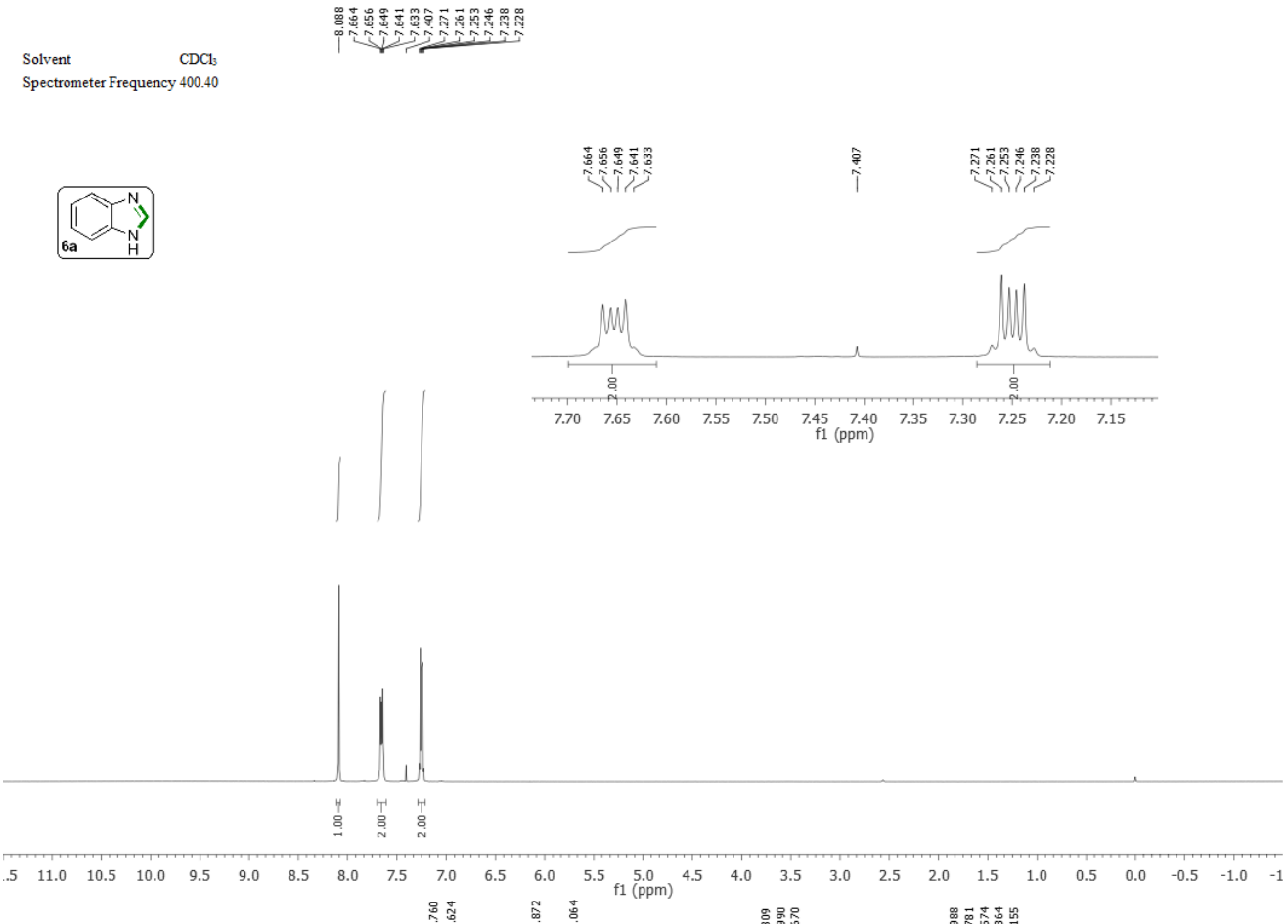
Spectrometer Frequency 100.69




Solvent CDCl3
Spectrometer Frequency 400.40
2f'
f1 (ppm)
Solvent CDCl3
Spectrometer Frequency 100.69
2f'
f1 (ppm)

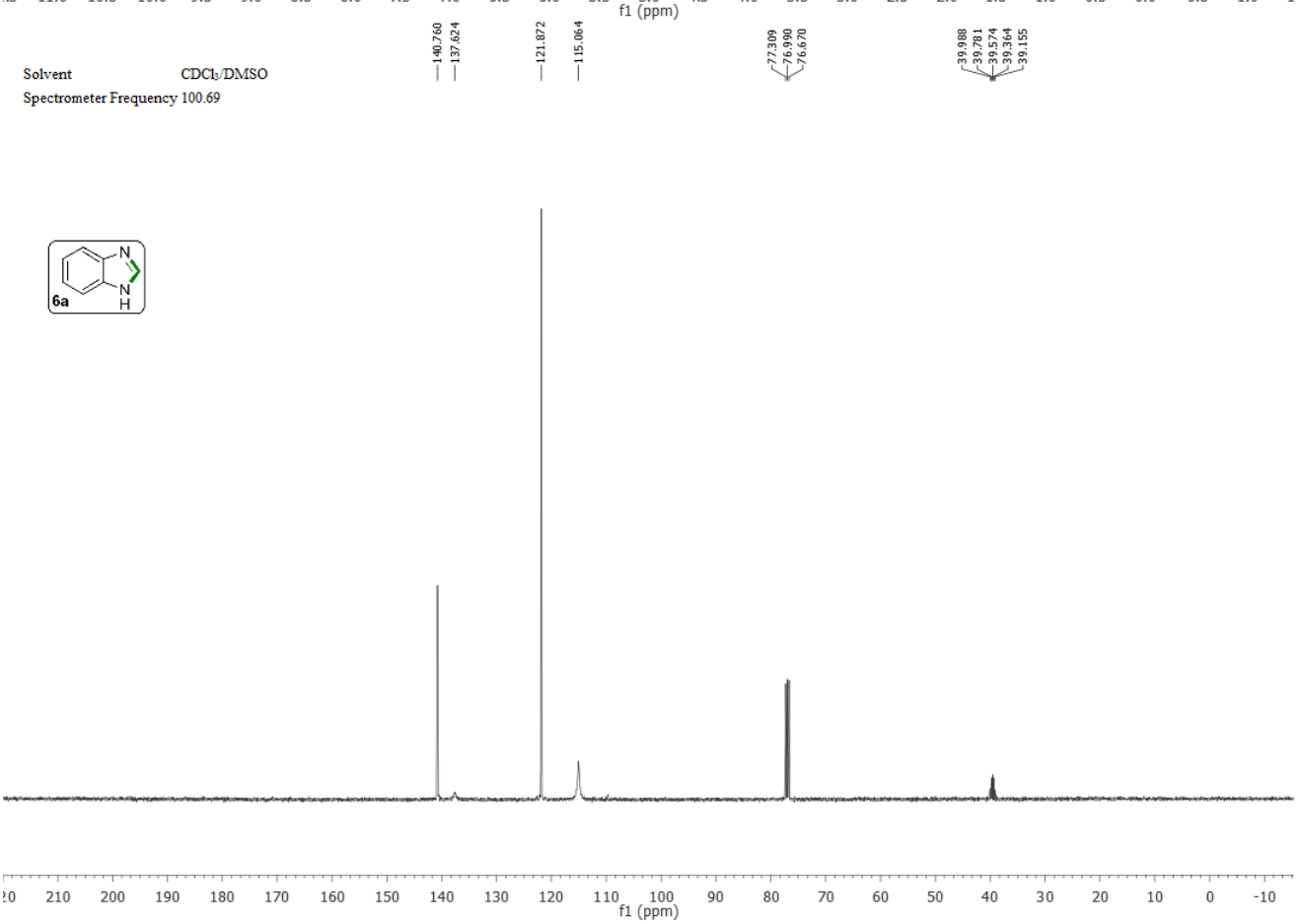
Solvent $CDCl_3$

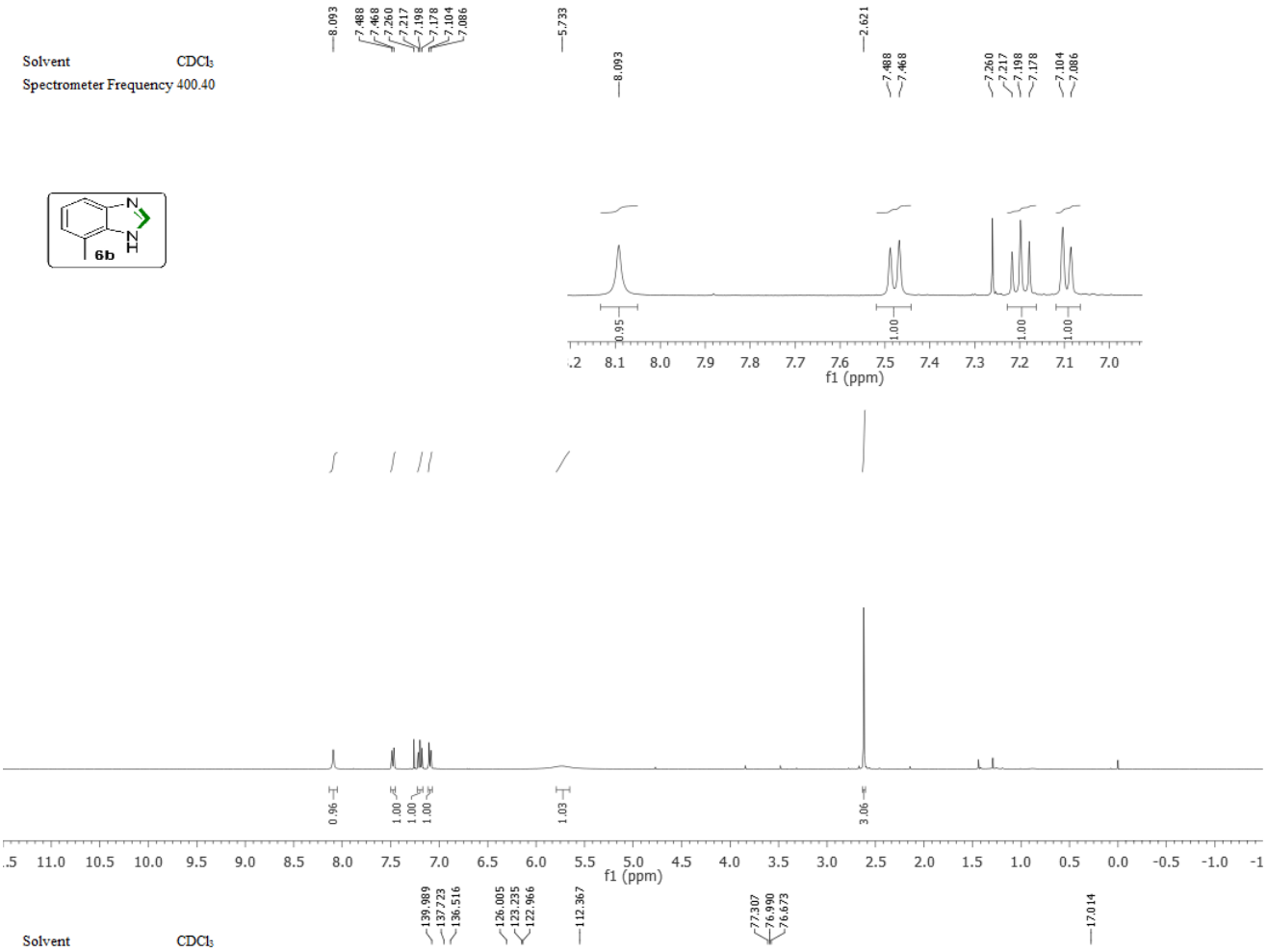
Spectrometer Frequency 400.40

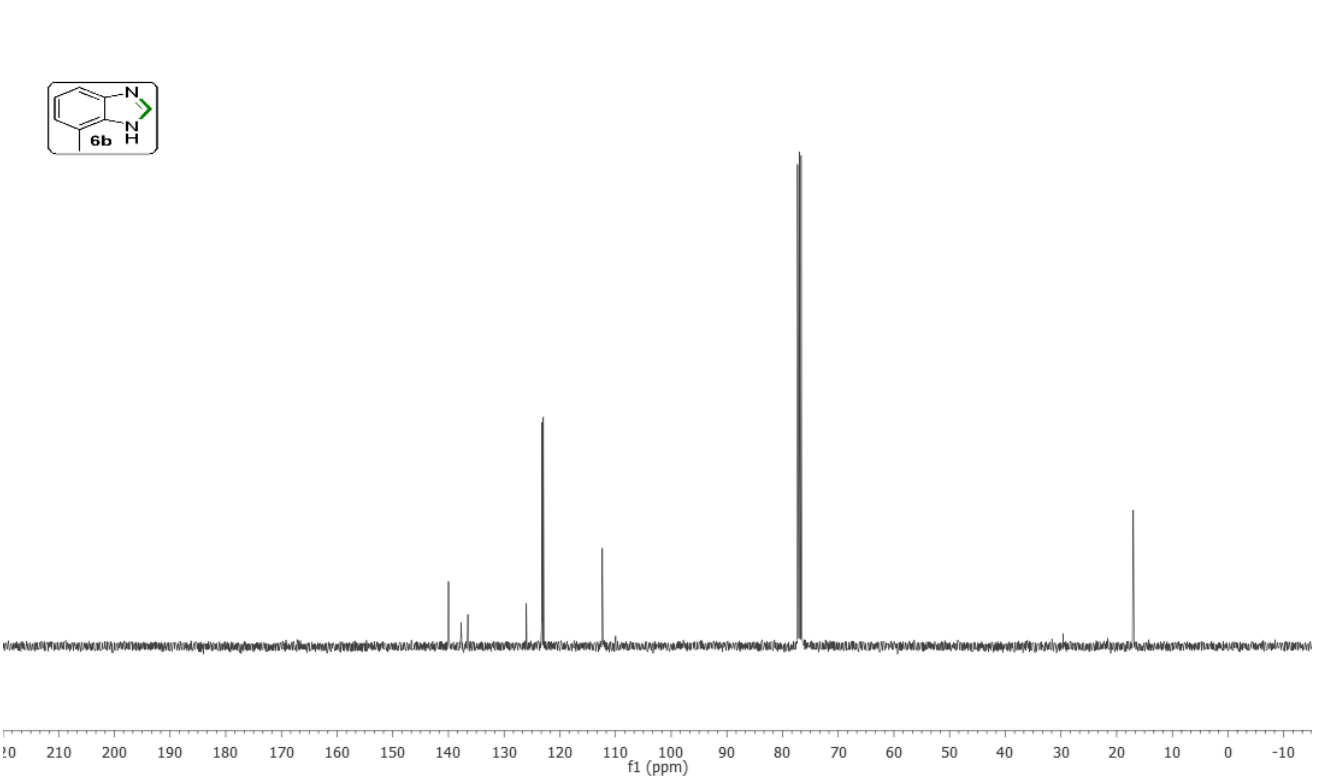


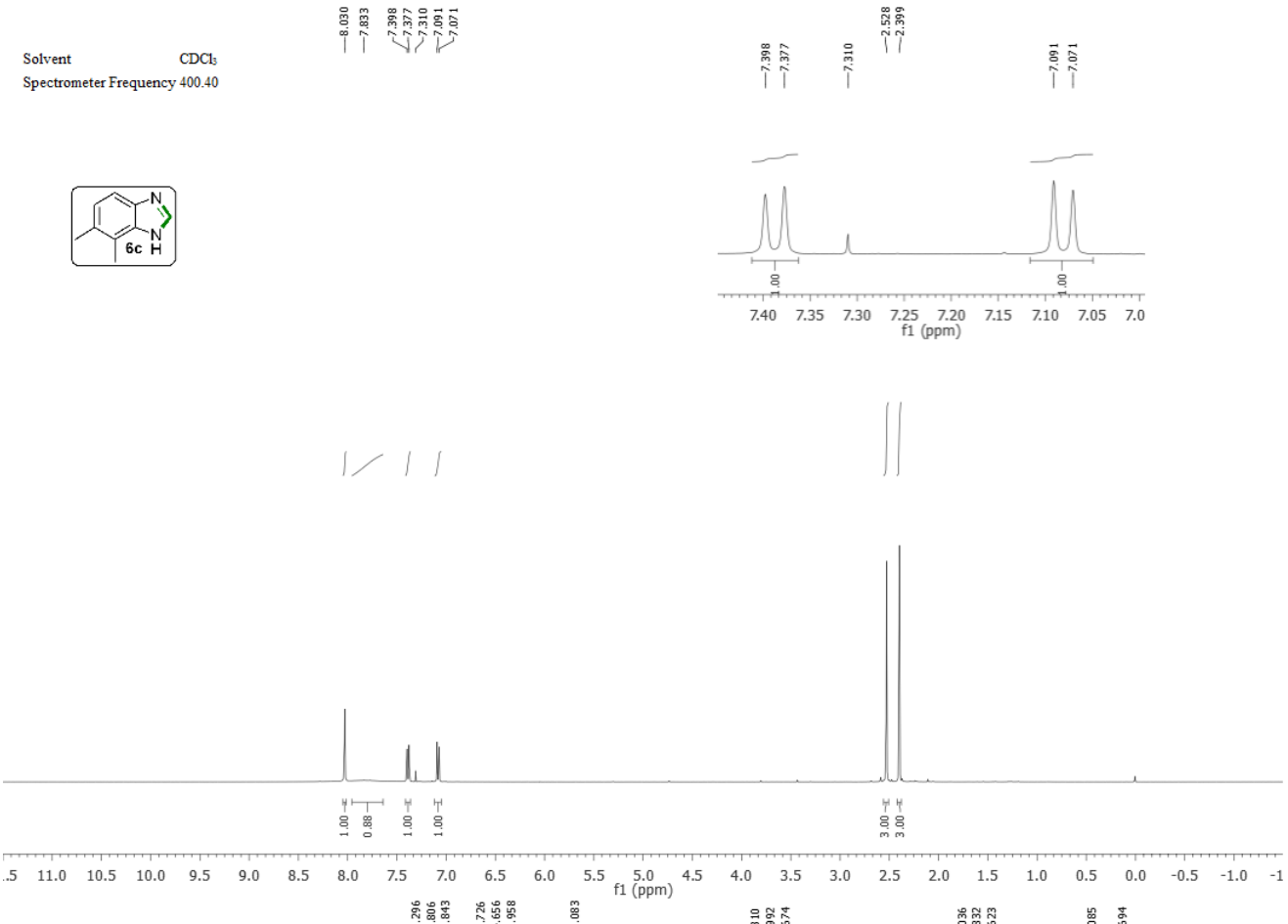
Solvent $CDCl_3$/DMSO

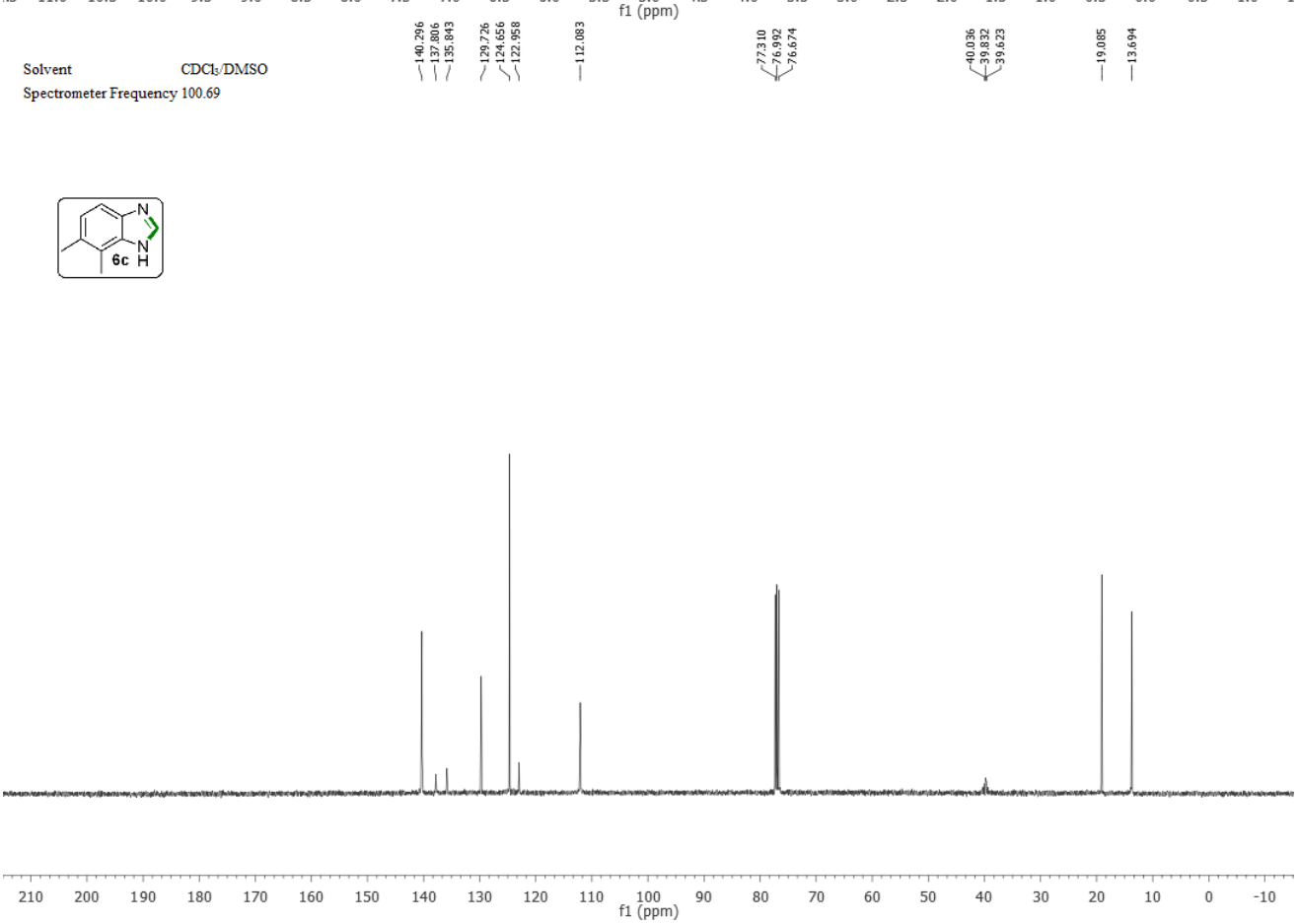
Spectrometer Frequency 100.69

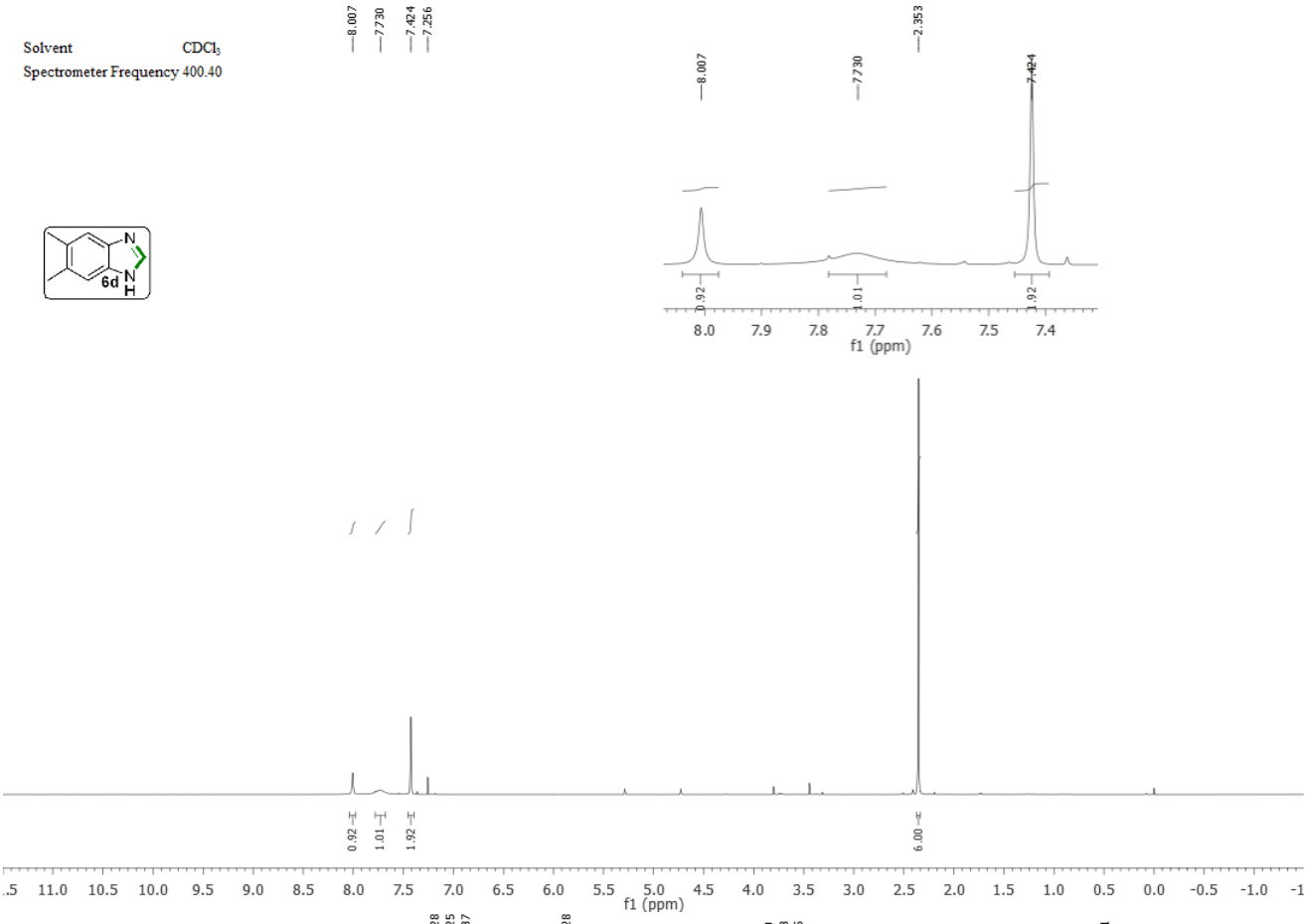


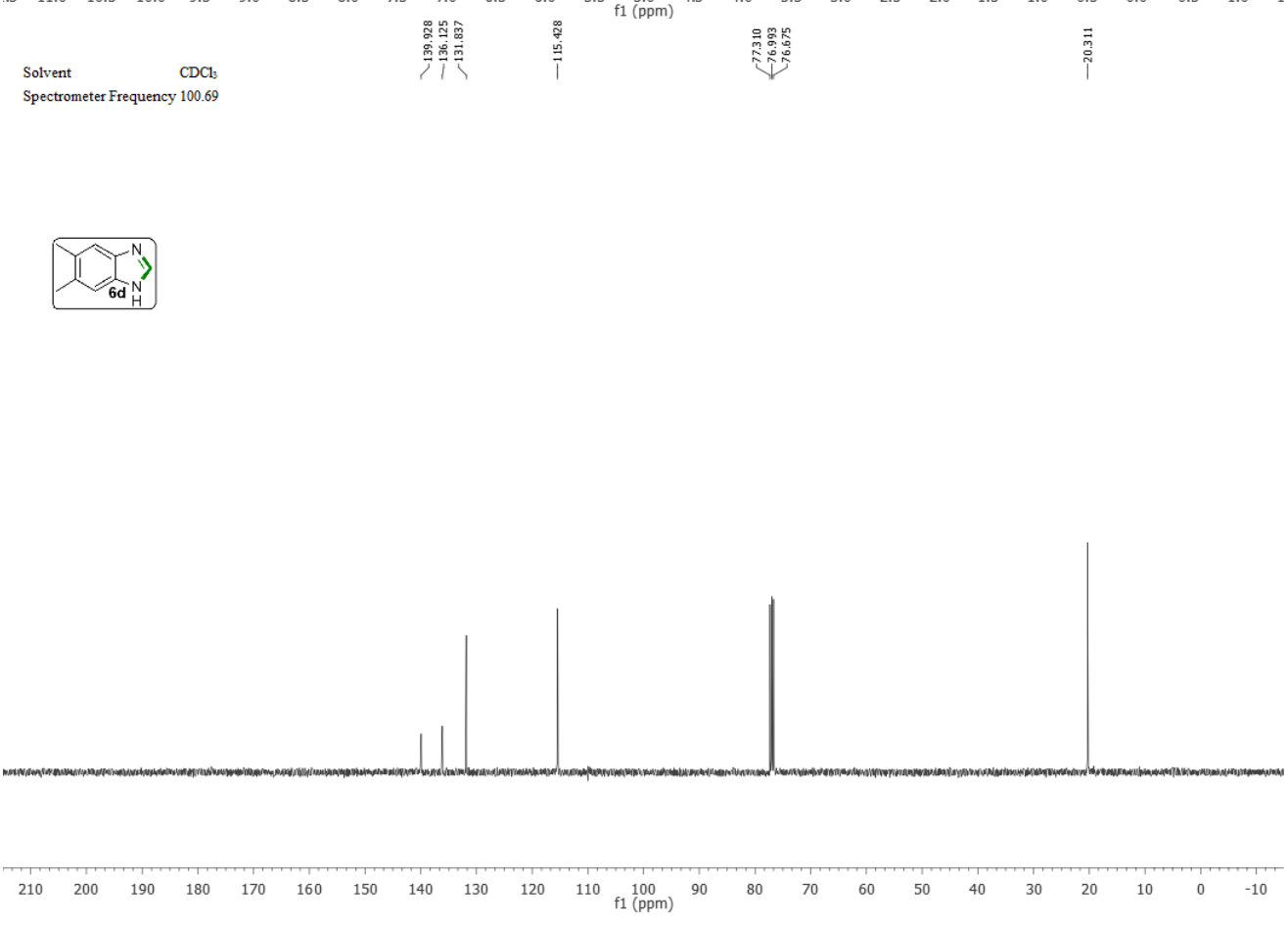

8.093
7.488
7.468
7.260
7.217
7.198
7.178
7.104
7.086
5.733
2.621
Solvent CDCl3
Spectrometer Frequency 400.40
6b
f1 (ppm)
0.96
1.00
1.00
1.00
1.03
3.06

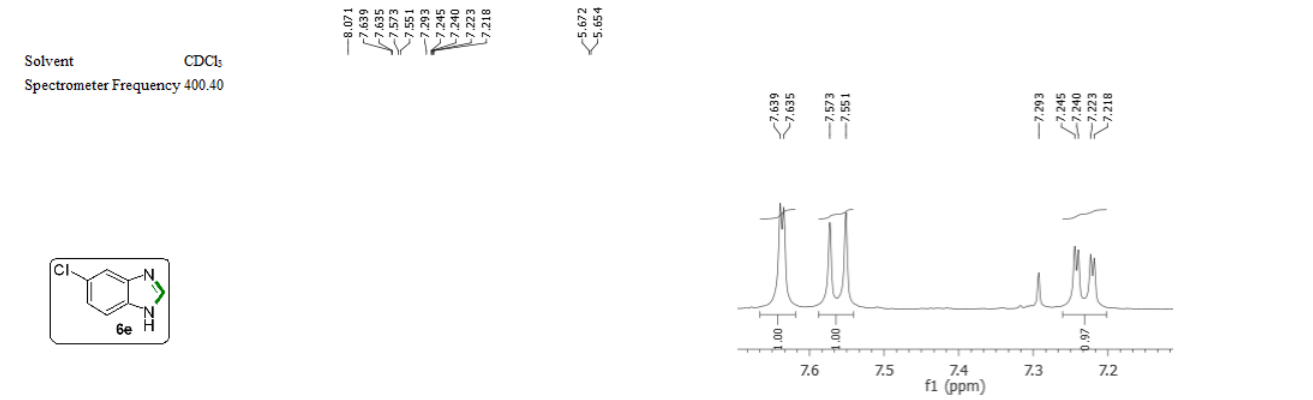

139.989
137.723
136.516
126.005
123.235
122.966
112.367
77.307
76.990
76.673
17.014
Solvent CDCl3
Spectrometer Frequency 100.69
6b
f1 (ppm)

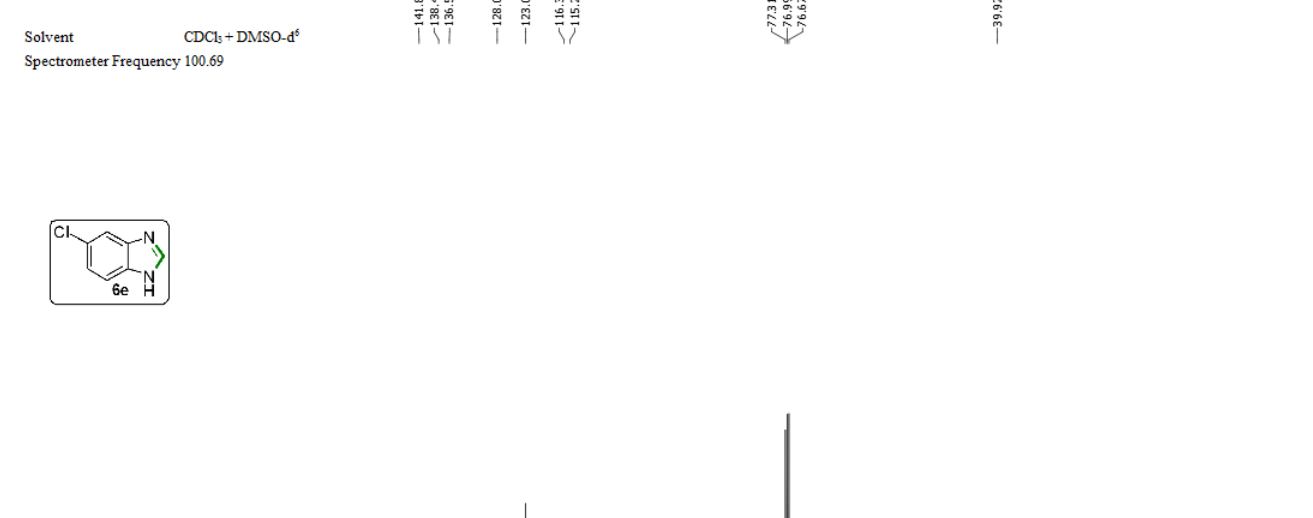

8.030
7.833
7.398
7.377
7.310
7.091
7.071
2.528
2.399
Solvent CDCl3
Spectrometer Frequency 400.40
6c H
1.00
0.88
1.00
1.00
3.00
3.00
f1 (ppm)


140.296
137.806
135.843
129.726
124.656
122.958
112.083
77.310
76.992
76.674
40.036
39.832
39.623
19.085
13.694
Solvent CDCl3/DMSO
Spectrometer Frequency 100.69
6c H
f1 (ppm)


Solvent CDCl3
Spectrometer Frequency 400.40
8.007
7.730
7.424
7.256
2.353
6d
f1 (ppm)

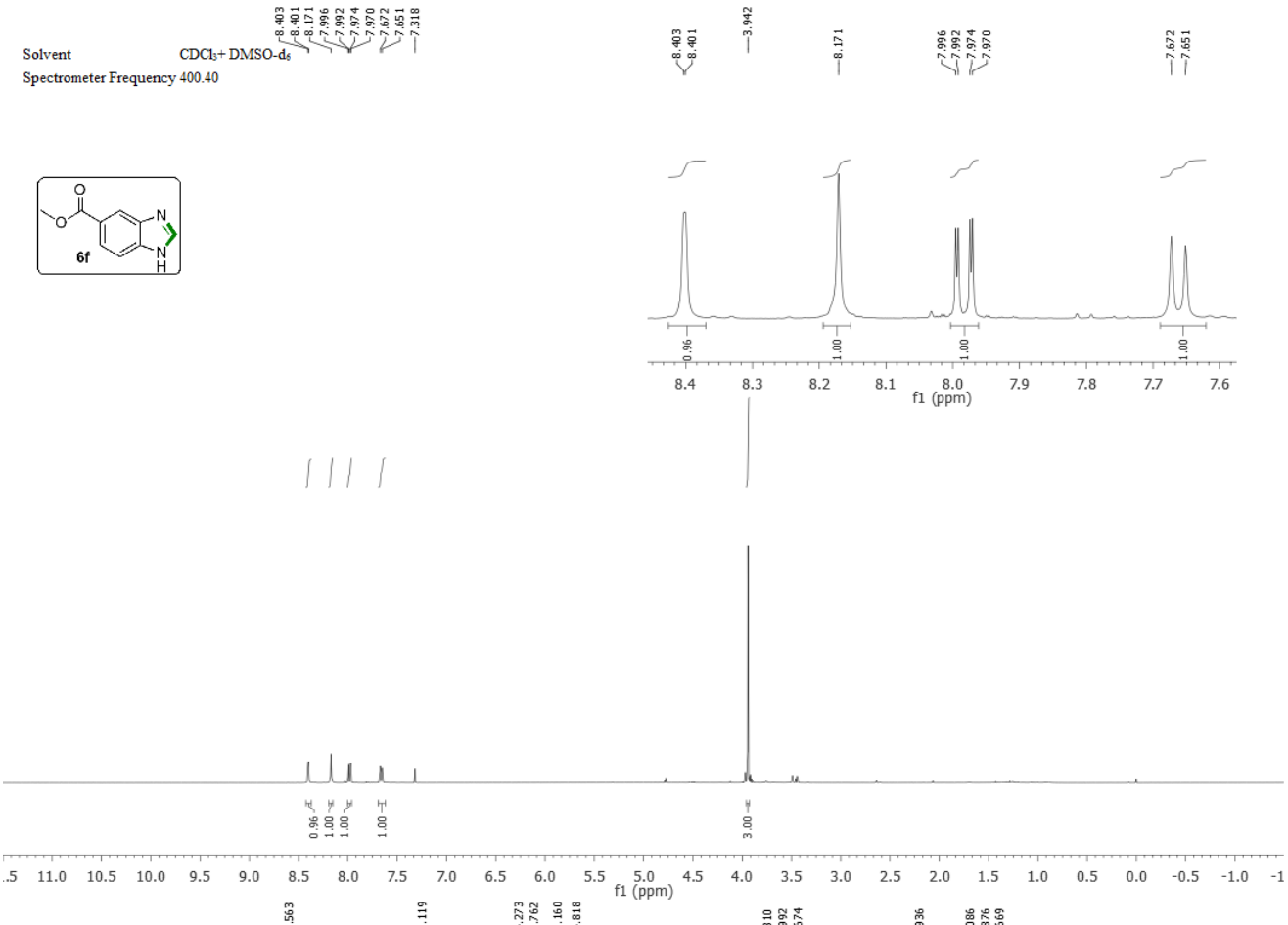

Solvent CDCl3
Spectrometer Frequency 100.69
139.928
136.125
131.837
115.428
77.310
76.993
76.675
20.311
6d
f1 (ppm)


8.071
7.639
7.635
7.573
7.551
7.293
7.245
7.240
7.223
7.218
5.672
5.654
Solvent CDCl3
Spectrometer Frequency 400.40
6e
1.00
1.00
0.97
f1 (ppm)
1.00
1.00
0.97
1.01
f1 (ppm)


141.844
138.402
136.526
128.085
123.052
116.322
115.229
77.310
76.992
76.675
39.923
Solvent CDCl3 + DMSO-d6
Spectrometer Frequency 100.69
6e
f1 (ppm)

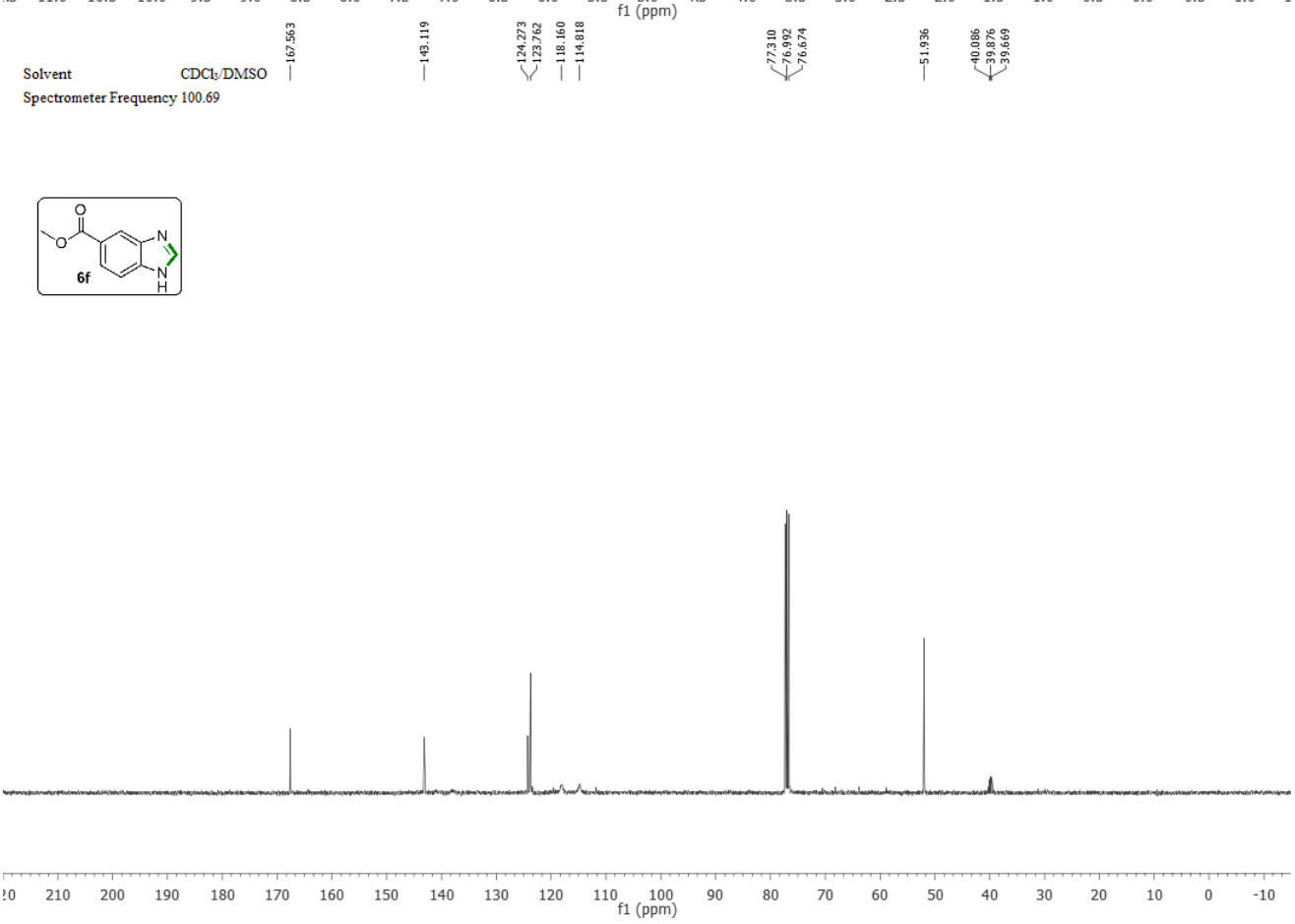
Solvent $CDCl_3$+ DMSO-d_6

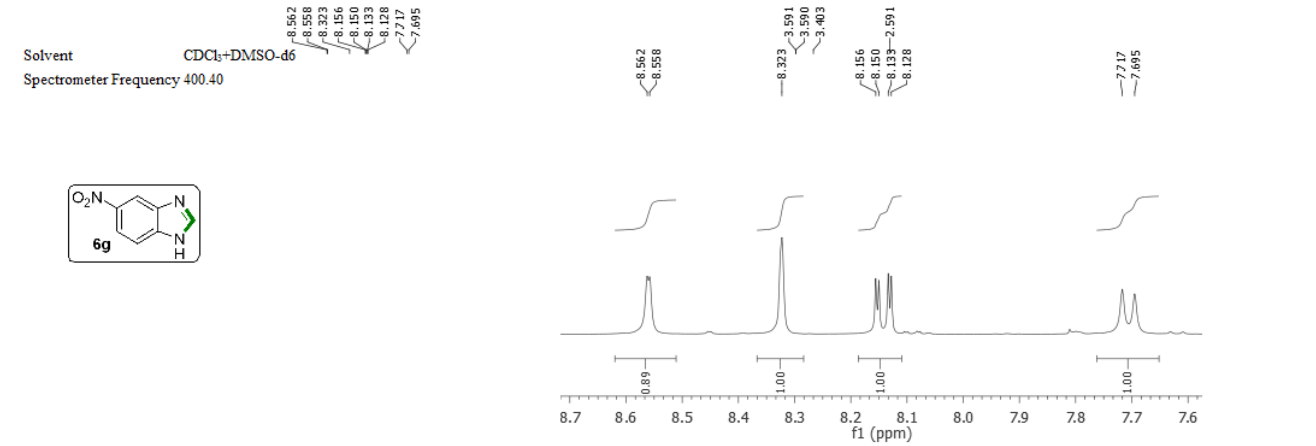
Spectrometer Frequency 400.40

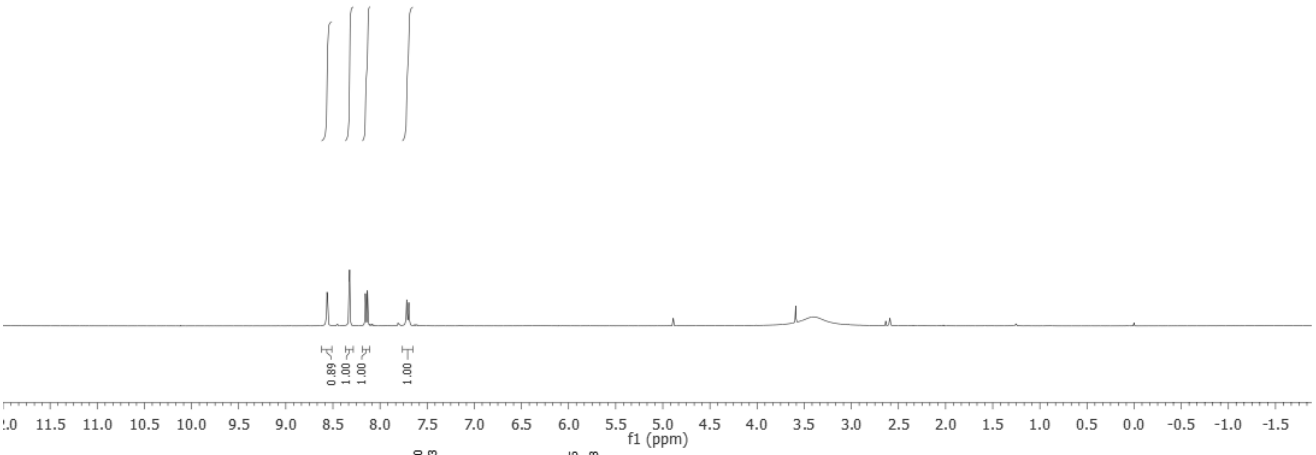


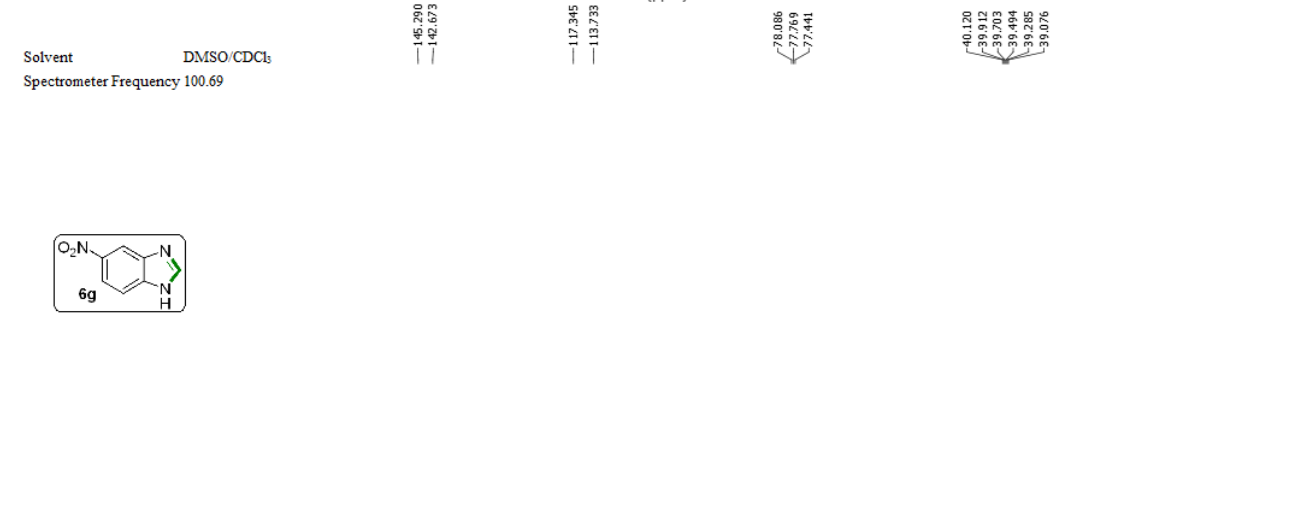
Solvent $CDCl_3$/DMSO

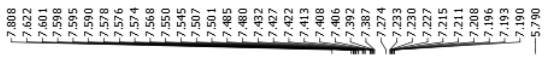
Spectrometer Frequency 100.69




8.562
8.558
8.323
8.156
8.150
8.133
8.128
7.717
7.695
Solvent CDCl3+DMSO-d6
Spectrometer Frequency 400.40
3.591
3.590
3.403
2.591
6g
0.89
1.00
1.00
1.00
f1 (ppm)

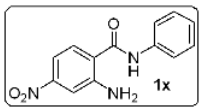

0.89
1.00
1.00
1.00
f1 (ppm)

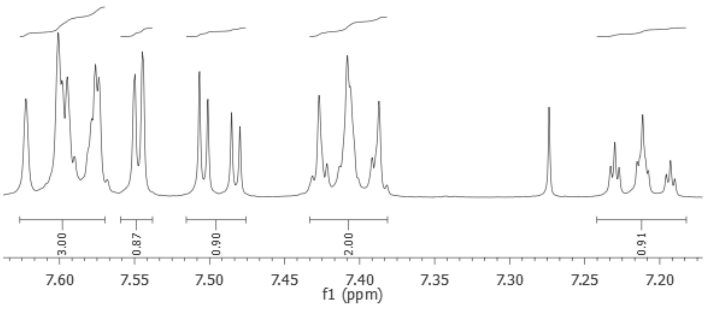

145.290
142.673
117.345
113.733
78.086
77.769
77.441
40.120
39.912
39.703
39.494
39.285
39.076
Solvent DMSO/CDCl3
Spectrometer Frequency 100.69
6g
f1 (ppm)

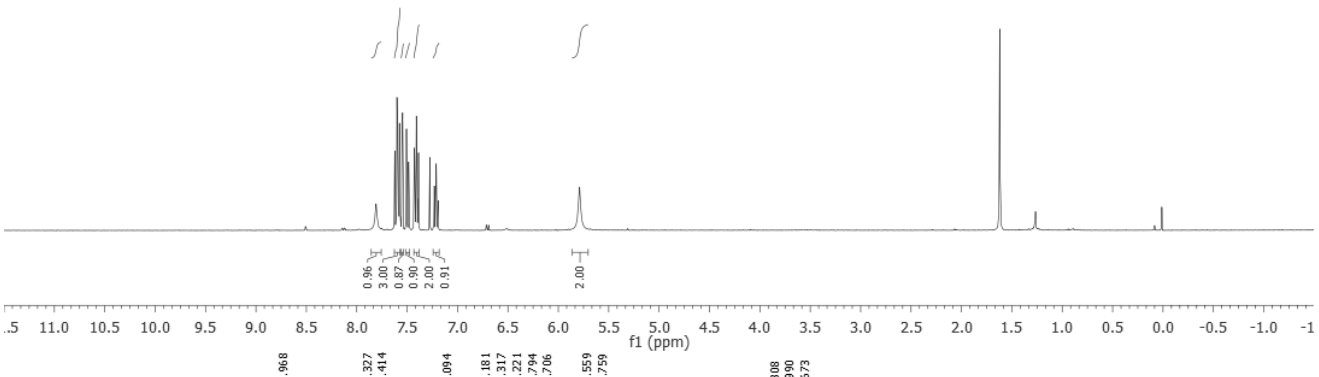


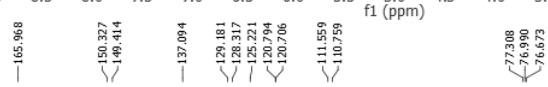
Solvent $CDCl_3$

Spectrometer Frequency 400.40



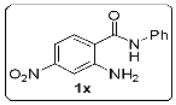


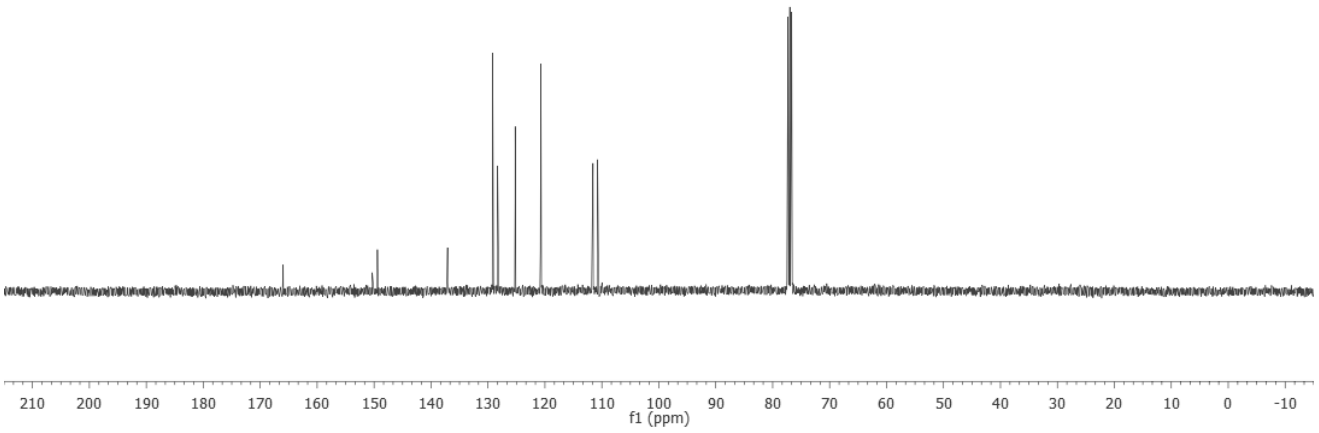


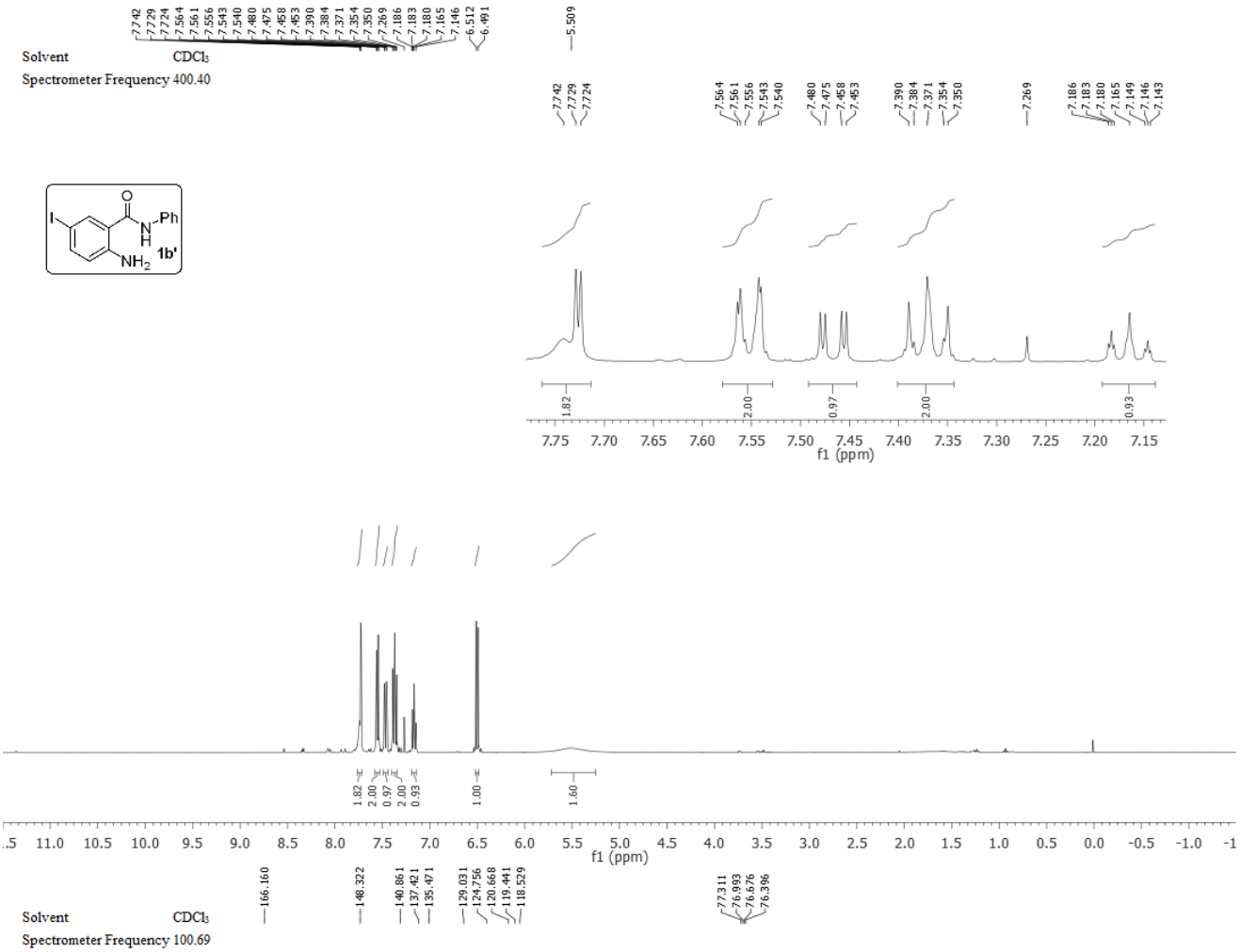


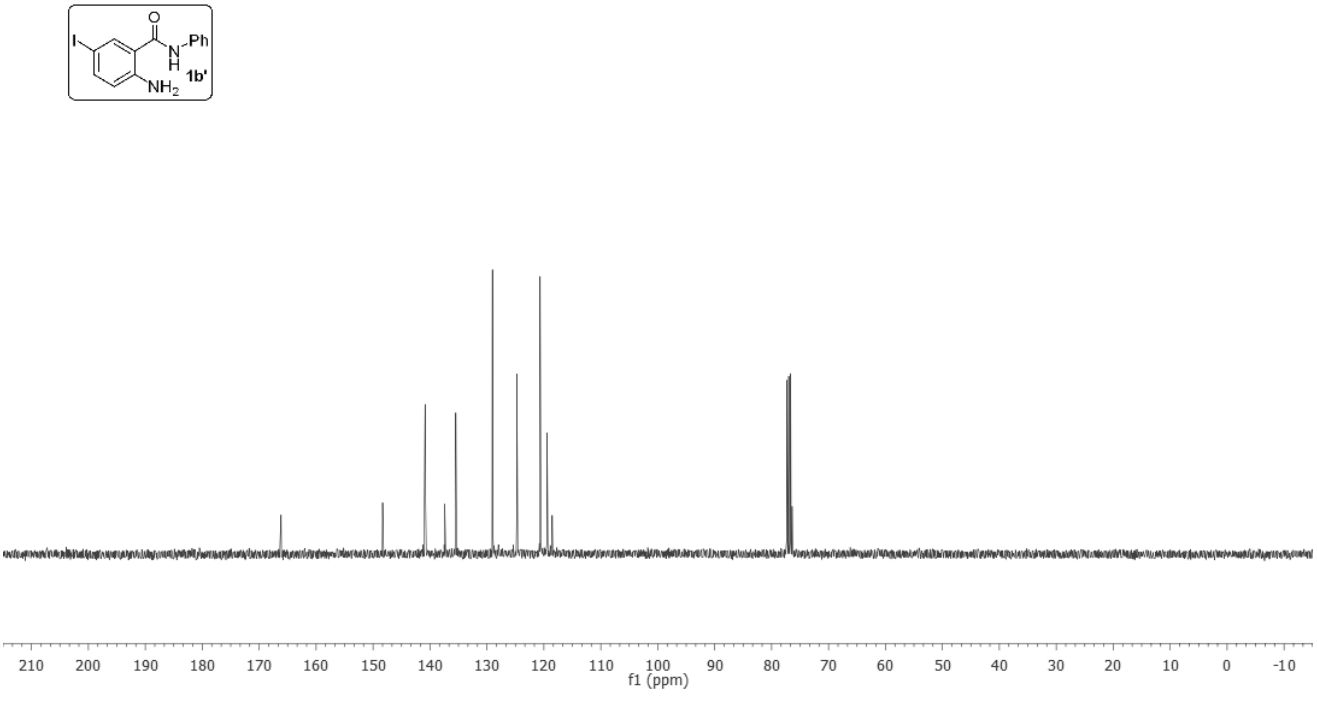
Solvent $CDCl_3$

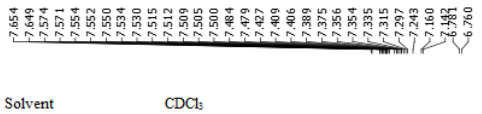
Spectrometer Frequency 100.69





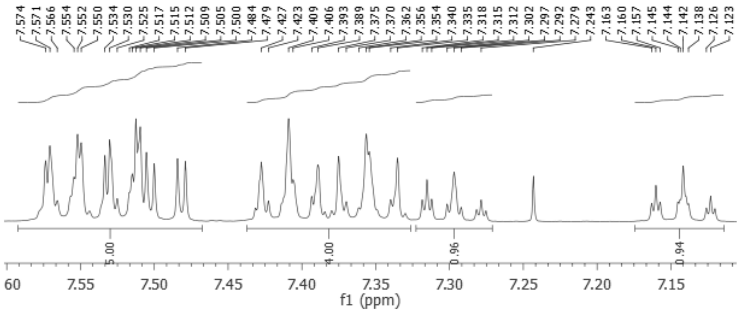

7.742
7.729
7.724
7.564
7.561
7.556
7.543
7.540
7.480
7.475
7.468
7.463
7.390
7.384
7.371
7.354
7.350
7.269
7.186
7.183
7.180
7.165
7.146
6.512
6.491
5.509
Solvent CDCl3
Spectrometer Frequency 400.40
1b'
1.82
2.00
0.97
2.00
0.93
1.00
1.60
f1 (ppm)

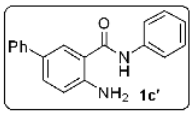

166.160
148.322
140.861
137.421
135.471
129.031
124.756
120.668
119.441
118.529
77.311
76.993
76.676
76.396
Solvent CDCl3
Spectrometer Frequency 100.69
1b'
f1 (ppm)

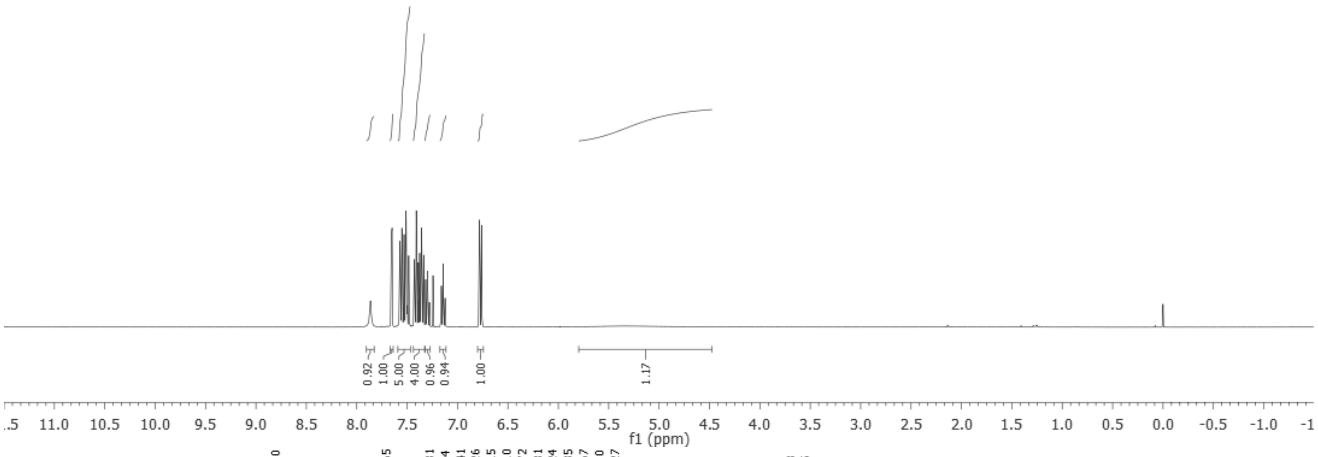


Solvent CDCl3

Spectrometer Frequency 400.40

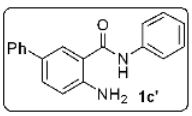


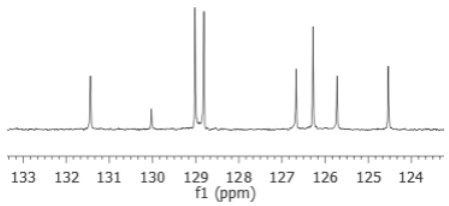


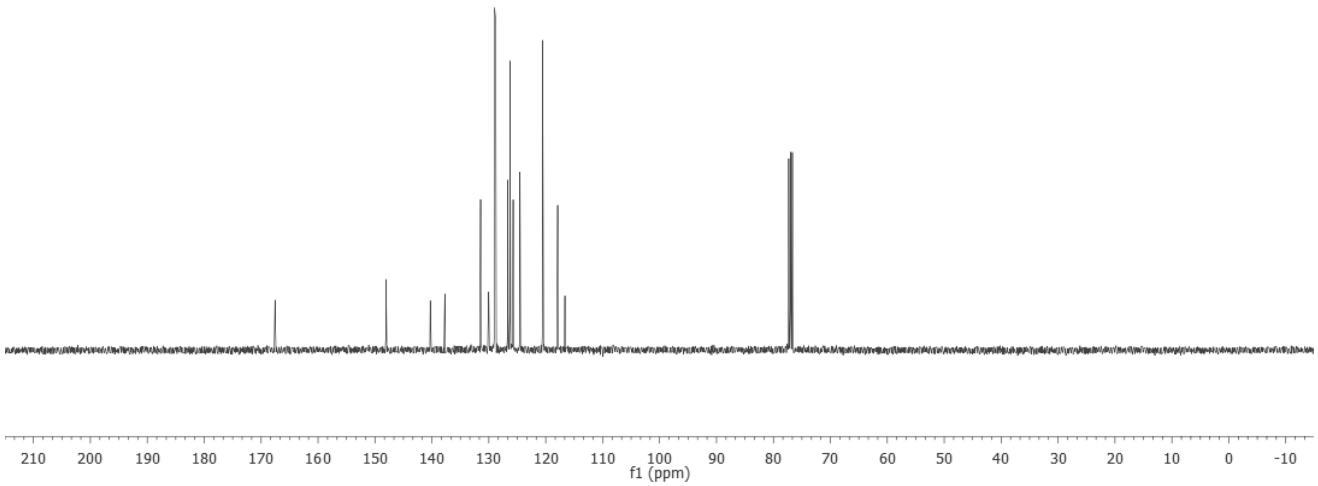


Solvent CDCl3

Spectrometer Frequency 100.69

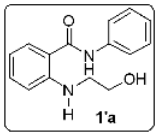




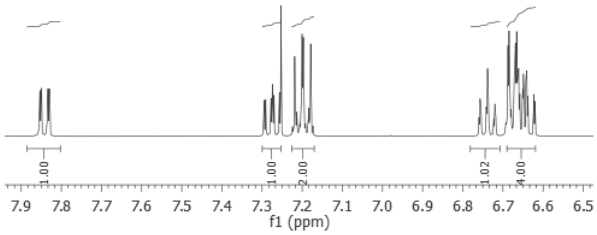


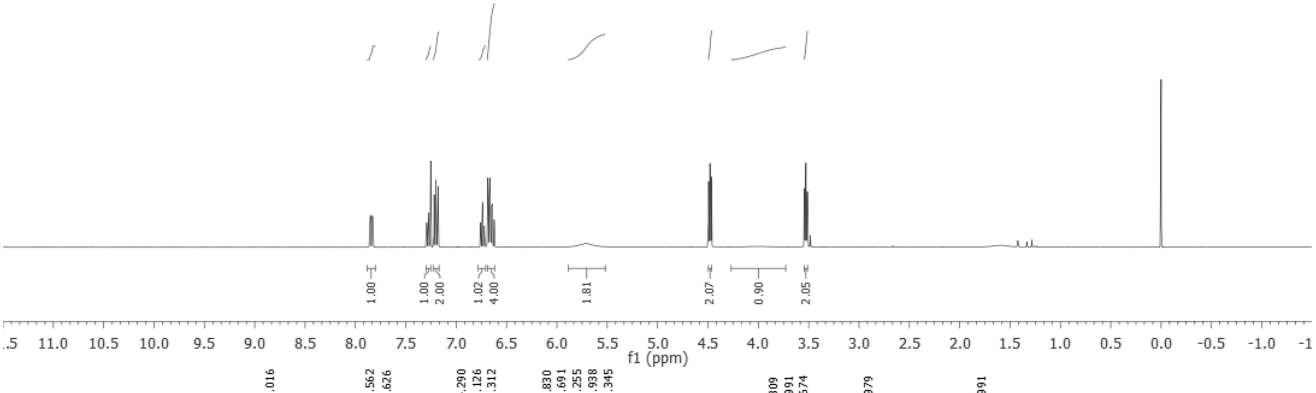
Solvent $CDCl_3$

Spectrometer Frequency 400.40



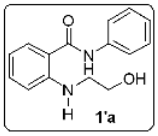
1'a



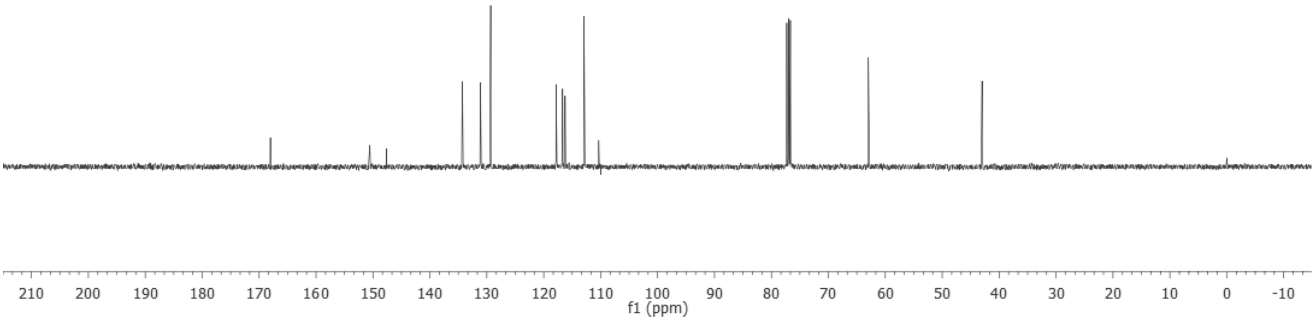


Solvent $CDCl_3$

Spectrometer Frequency 100.69

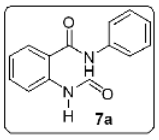


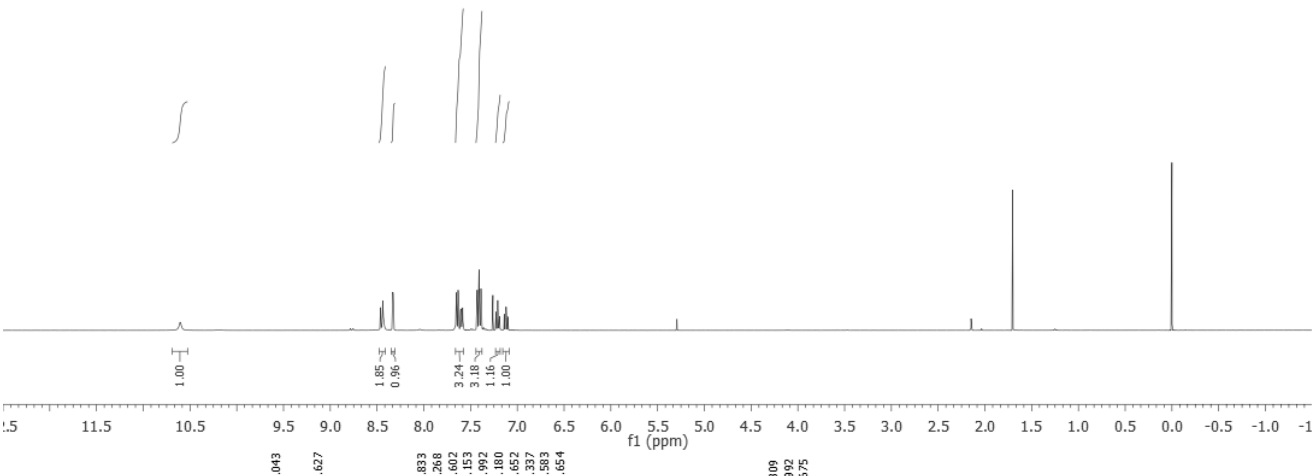
1'a



Solvent CDCl3

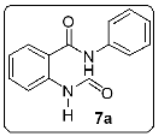
Spectrometer Frequency 400.40

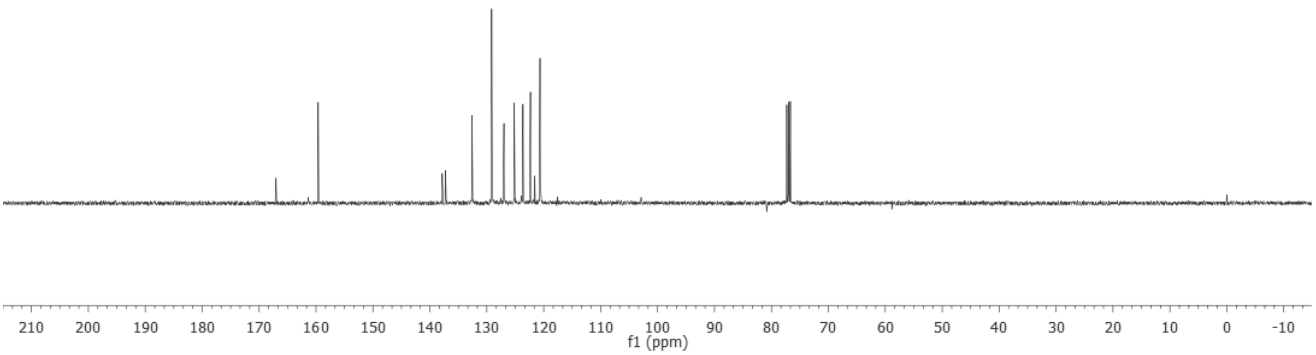


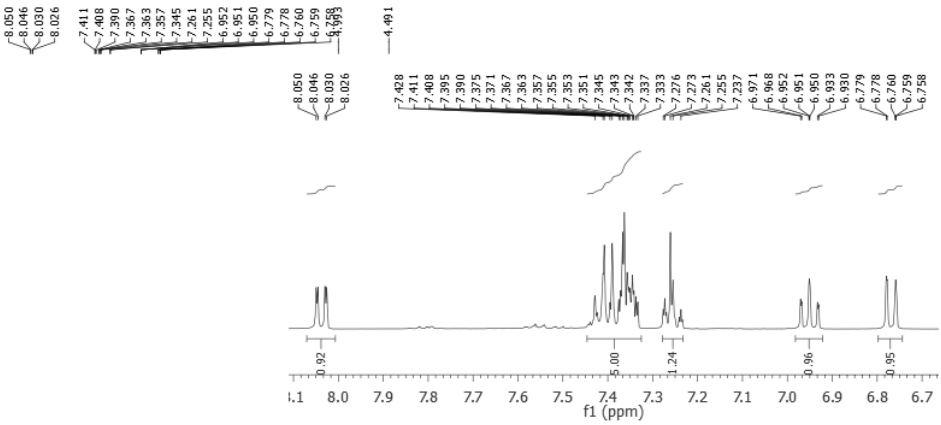


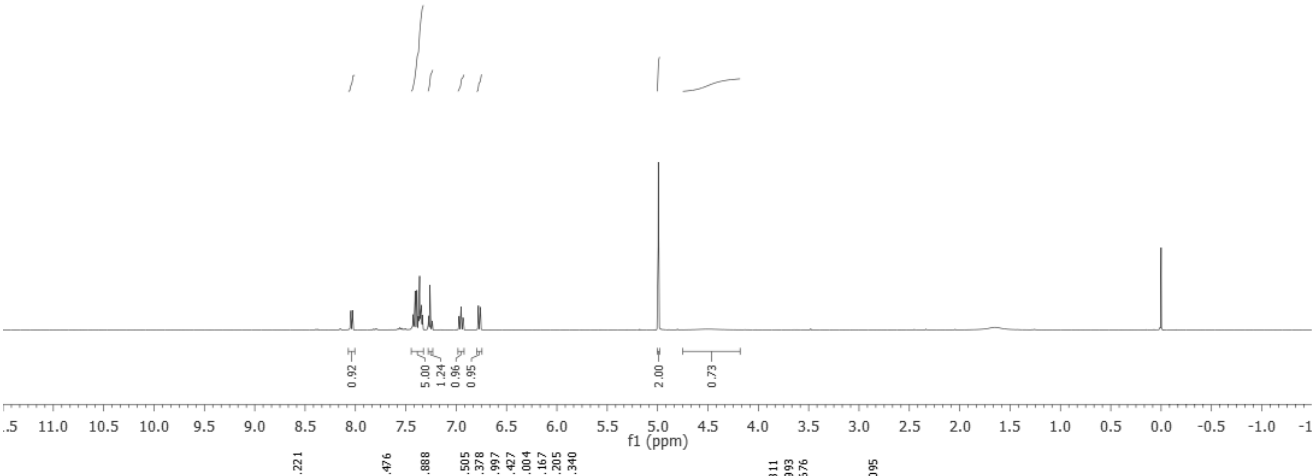
Solvent CDCl3

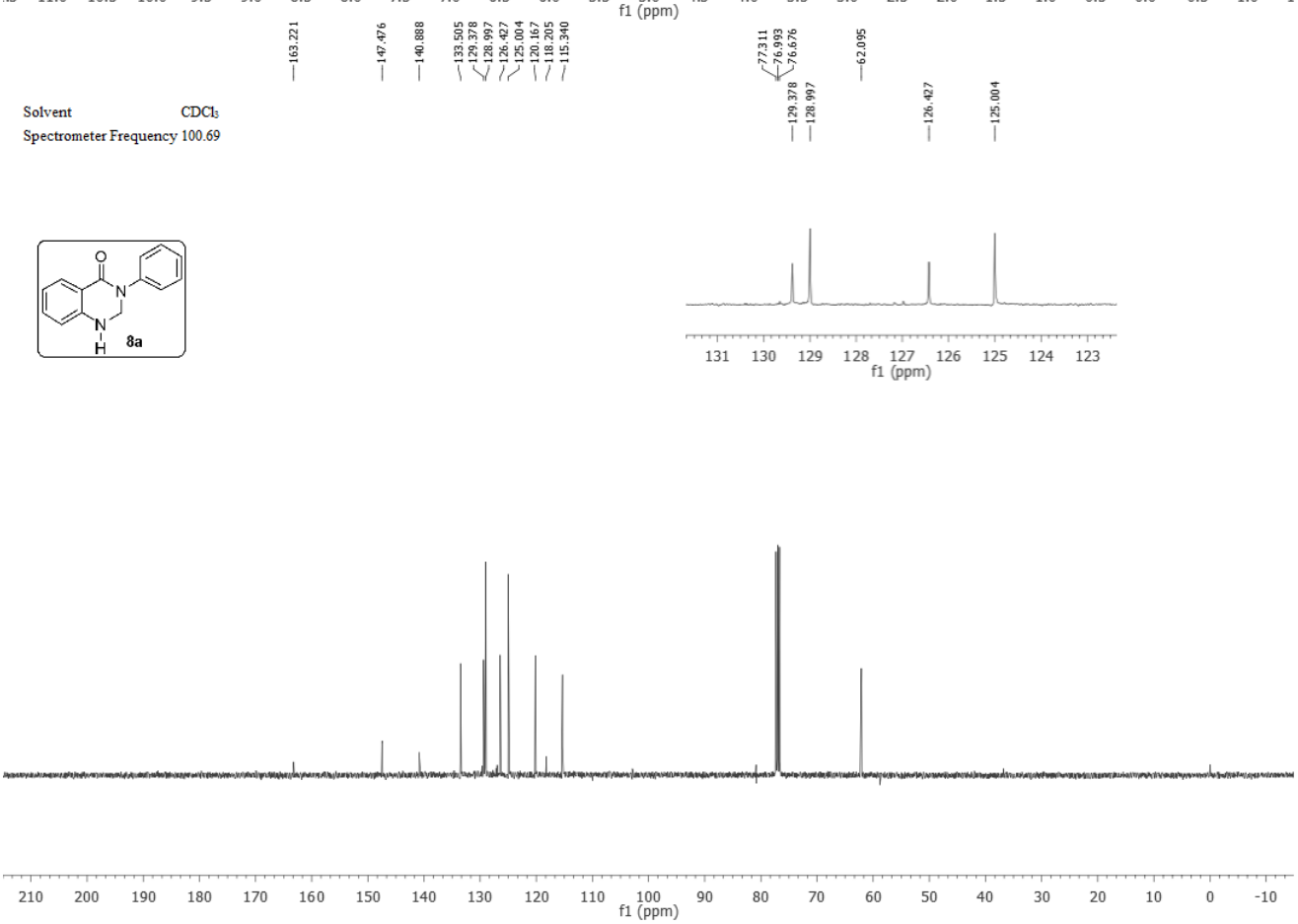
Spectrometer Frequency 100.69






Solvent CDCl3
Spectrometer Frequency 400.40
8a
f1 (ppm)


f1 (ppm)


Solvent CDCl3
Spectrometer Frequency 100.69
8a
f1 (ppm)
f1 (ppm)