---Electronic supplementary information---

Aerobic primary and secondary amine oxidation cascade by a copper amine oxidase inspired catalyst

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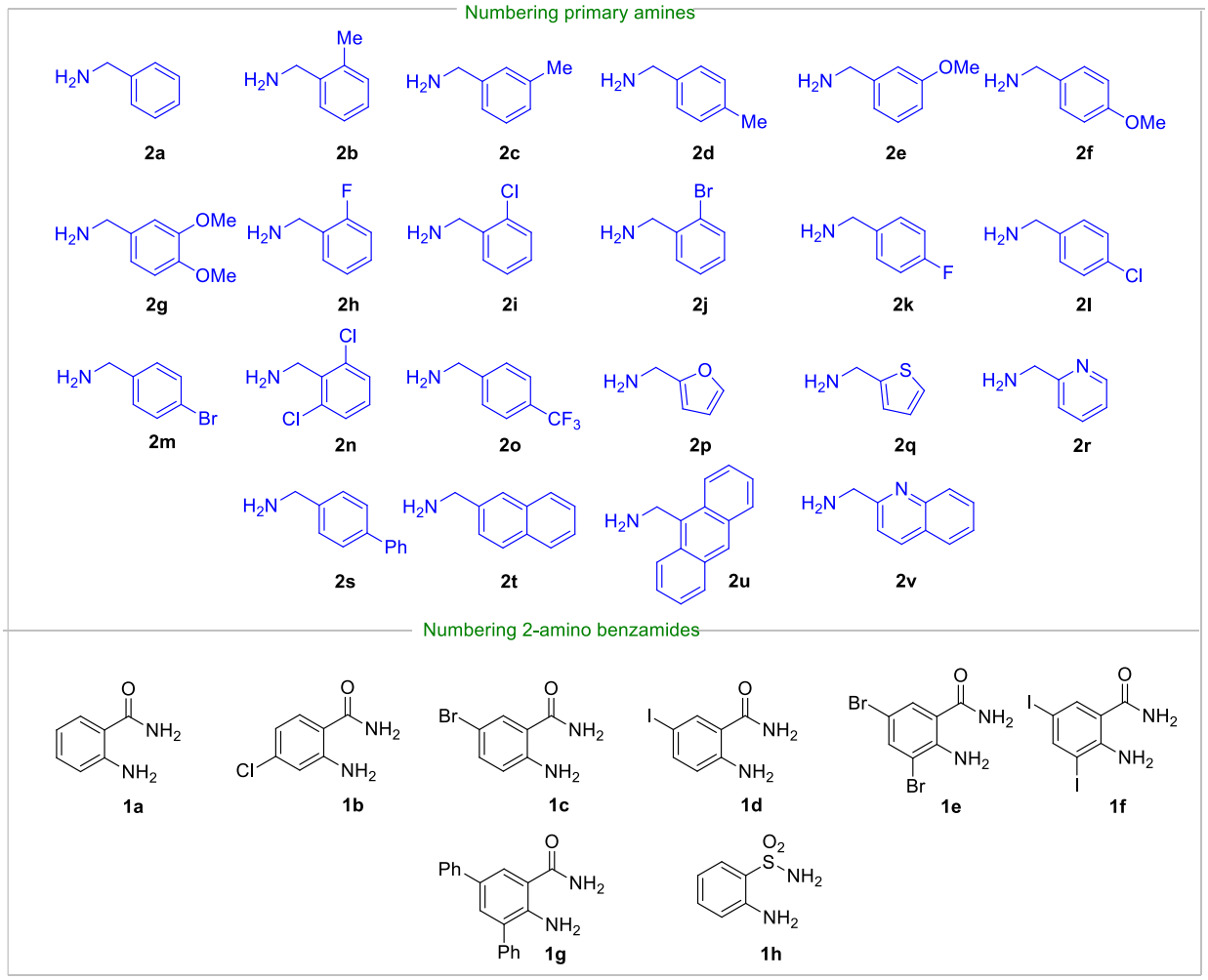
1. General information.

All experiments were carried out under an aerial condition in a round bottom flask. Solvents were dried using standard procedures before use. Products were purified by flash column chromatography on silica gel (100–200 mesh). ^{1}H NMR spectra were recorded on either JEOL-ECS400 or Bruker-AVANCE500 spectrometer at 278 K in $CDCl_3$ as well as DMSO-d_6 solvent. Signals are assigned as δ values in ppm using residual protonated solvent signals as the internal standard (^{1}H NMR: $CDCl_3$: δ 7.26 ppm and DMSO-d_6: δ 2.50 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet) and coupling constants in (Hz). ^{13}C NMR spectra were recorded on either JEOL-ECS400 or Bruker-AVANCE500 spectrometer with complete proton decoupling. Chemical shifts (δ) are reported in ppm with the solvent as the internal reference (^{13}C NMR: $CDCl_3$: δ 77.16 ppm and DMSO-d_6: δ 39.5 ppm). FT-IR spectra were recorded in a Perkin–Elmer FT–IR Spectrometer. Gas chromatography were recorded in the Thermo Fisher GC-MS spectrometer with appropriate internal standard. High-resolution mass spectra (HRMS) were recorded on a Bruker mass spectrometer. Benzylamines, metal salts, and other chemicals were purchased from Sigma-Aldrich, Alfa-Aesar, Spectrochem, Avra Synthesis and used without further purification. 2-Aminoaryl amides (**1b-1h**) were prepared according to the literature procedure.[1]

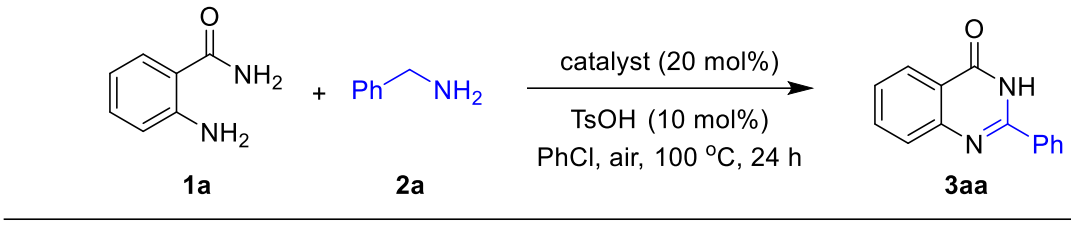
2. Numbering of starting materials.



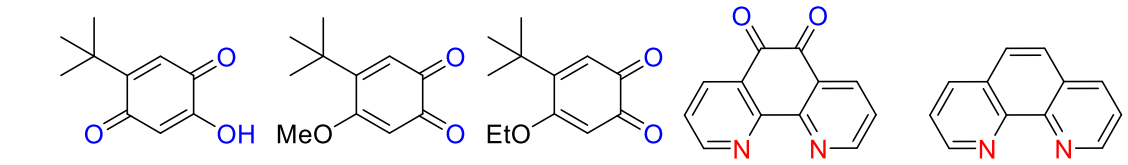
3. Reaction optimization.

Optimization for the 2-benzylquinazolin-4(3*H*)-one **3aa** by using 2-aminobenzamide **1a** and benzylamine **2a** as the model substrates.

Table S1. Effect of catalyst.[a]



1a **2a** **3aa**

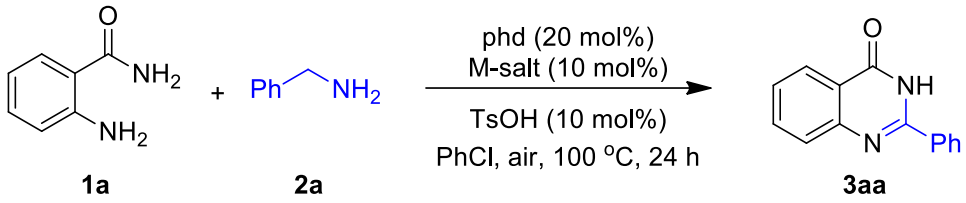


Catalyst = **Q1** **Q2** **Q3** **phd** **phen**

Entry	Catalyst	Yield of **3aa** (%)[b]
1.	Q1	40
2.	Q2	39
3.	Q3	40
4.	**phd**	**53**
5.	phen	trace
6.	-	trace

[a] Reaction conditions: **1a** (0.1 mmol, 1.0 equiv), **2a** (0.15 mmol, 1.5 equiv), catalyst (20 mol%), TsOH (10 mol%) in chlorobenzene (0.5 mL), 100 °C, 24 h, air. [b] Isolated yield.

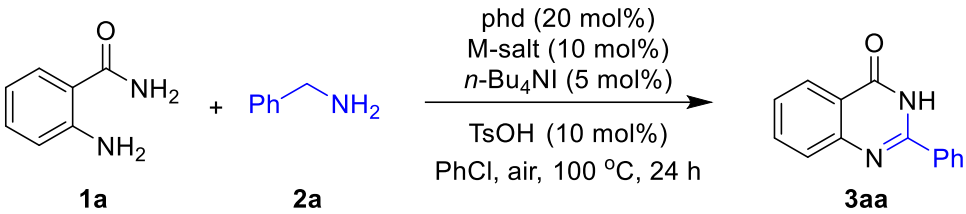
Table S2a. Effect of M-salts[a]



Entry	Metal salts	Yield of **3aa** (%)[b]
1.	$Sc(OTf)_3$	18
2.	$FeCl_3$	63
3.	$AlCl_3$	32
4.	$MnBr_2$	21
5.	$RuCl_3$	50
6.	$CoCl_2$	32
7.	$NiBr_2$	20
8.	$ZnCl_2$	40
9.	CuCl	83
10.	-	53

[a] Reaction conditions: **1a** (0.1 mmol, 1.0 equiv), **2a** (0.15 mmol, 1.5 equiv), phd (20 mol%), M-salt (10 mol%), TsOH (10 mol%) in chlorobenzene (0.5 mL), 100 °C, 24 h, air. [b] GC yields with *n*-decane as an internal standard.

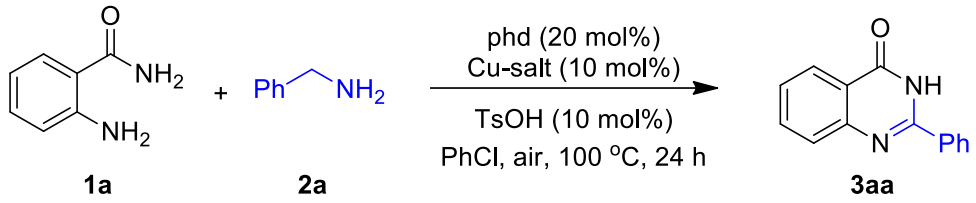
Table S2b. Effect of M-salts and additional Bu_4NI[a]



Entry	Metal salts	Yield of **3aa** (%)[b]
1.	$Sc(OTf)_3$	15
2.	$FeCl_3$	40
3.	$AlCl_3$	20
4.	$MnBr_2$	25
5.	$RuCl_3$	50
6.	$CoCl_2$	38
7.	$NiBr_2$	24
8.	$ZnCl_2$	50
9.	CuCl	85
10.	-	5

[a] Reaction conditions: **1a** (0.1 mmol, 1.0 equiv), **2a** (0.15 mmol, 1.5 equiv), phd (20 mol%), M-salt (10 mol%), *n*-Bu_4NI (5 mol%), TsOH (10 mol%) in chlorobenzene (0.5 mL), 100 °C, 24 h, air. [b] GC yields with *n*-decane as an internal standard.

Table S3. Effect of Cu-salts [a]

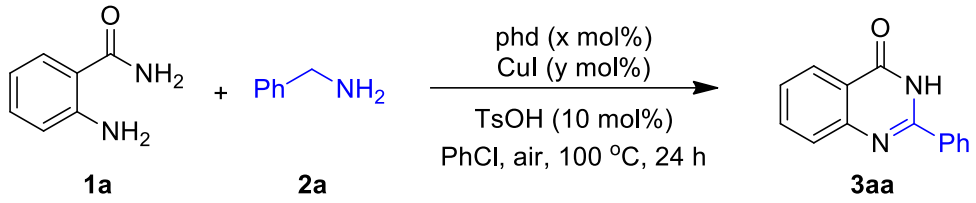


1a 2a 3aa

Entry	Cu-salts	Yield of **3aa** (%)[b]
1.	CuCl	83
2.	CuBr	66
3.	**CuI**	**91**
4.	CuCN	21
5.	$CuCl_2$	75
6.	Cu $(OAc)_2$	62
7.	Cu $(OTf)_2$	91
8.	CuO	45
9.	$Cu(phd)_2I$	94
10.	$Cu(phd)_2PF_6$	92
11.	$Cu(phd)_2BF_4$	88
12.	-	53

[a] Reaction conditions: **1a** (0.1 mmol, 1.0 equiv), **2a** (0.15 mmol, 1.5 equiv), phd (20 mol%), Cu-salt (10 mol%), (TsOH 10 mol%) in chlorobenzene (0.5 mL), 100 °C, 24 h, air. [b] GC yields with *n*-decane as an internal standard.

Table S4. Effect of catalyst and Cu-salt loading [a]

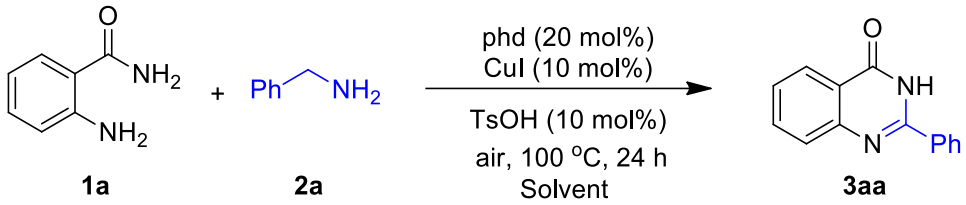


1a 2a 3aa

Entry	CuI (y mol %) and phd (x mol %)	Yield of **3aa** (%)[b]
1.	**10 and 20**	**94**
2.	5 and 10	85
3.	2 and 5	72
4.	-	n.r.

[a] Reaction conditions: **1a** (0.1 mmol, 1.0 equiv), **2a** (0.15 mmol, 1.5 equiv), phd, Cu-salt, TsOH (10 mol%) in chlorobenzene (0.5 mL), 100 °C, 24 h, air. [b] Isolated yields. n.r. = no reaction.

Table S5. Effect of solvent [a]

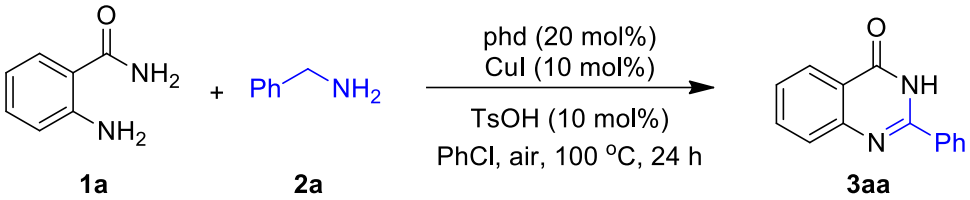


1a 2a 3aa

Entry	Solvent (0.5 mL)	Yield of **3aa** (%)[b]
1.	Toluene	72
2.	Acetonitrile	58
3.	**Chlorobenzene**	**94**

[a] Reaction conditions: **1a** (0.1 mmol, 1.0 equiv), **2a** (0.15 mmol, 1.5 equiv), phd (20 mol%), Cu-salt (10 mol%), TsOH (10 mol%) in a solvent (0.5 mL), 100 ˚C, 24 h, air. [b] Isolated yields.

Table S6. Effect of solvent concentration [a]

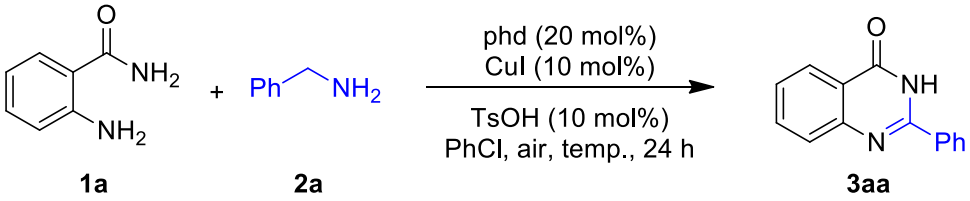


1a 2a 3aa

Entry	PhCl (x mL)	Yield of **3aa** (%)[b]
1.	**0.5**	**94**
2.	1.0	73
3.	1.5	67

[a] Reaction conditions: **1a** (0.1 mmol, 1.0 equiv), **2a** (0.15 mmol, 1.5 equiv), phd (20 mol%), Cu-salt (10 mol%), (TsOH 10 mol%) in chlorobenzene (0.5 mL), 100 ˚C, 24 h, air. [b] Isolated yields.

Table S7. Effect of temperature [a]

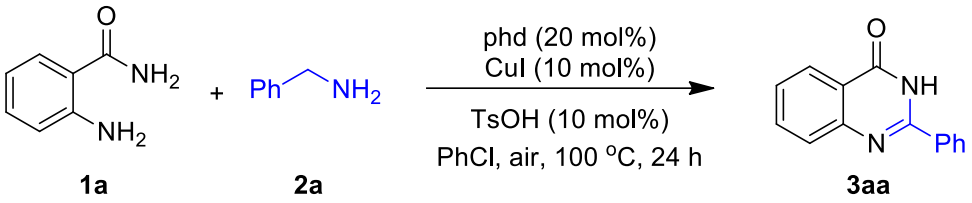


1a 2a 3aa

Entry	Temperature (˚C)	Yield of **3aa** (%)[b]
1.	**100**	**94**
2.	80	22
3.	60	n.r

[a] Reaction conditions: **1a** (0.1 mmol, 1.0 equiv), **2a** (0.15 mmol, 1.5 equiv), phd (20 mol%), Cu-salt (10 mol%), (TsOH 10 mol%) in chlorobenzene (0.5 mL), temperature, 24 h, air. [b] Isolated yields. n.r. = no reaction.

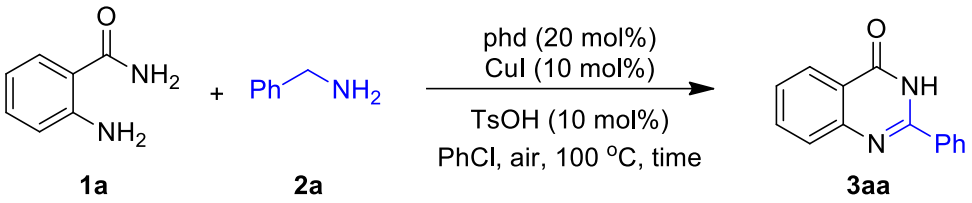
Table S8. Effect of the concentration of benzylamine [a]



Entry	**2a** (x equiv)	Yield of **3aa** (%)[b]
1.	1.2	75
2.	**1.5**	**94**

[a] Reaction conditions: **1a** (0.1 mmol, 1.0 equiv), **2a**, phd (20 mol%), Cu-salt (10 mol%), (TsOH 10 mol%) in chlorobenzene (0.5 mL), 100 ˚C, 24 h, air. [b] Isolated yields.

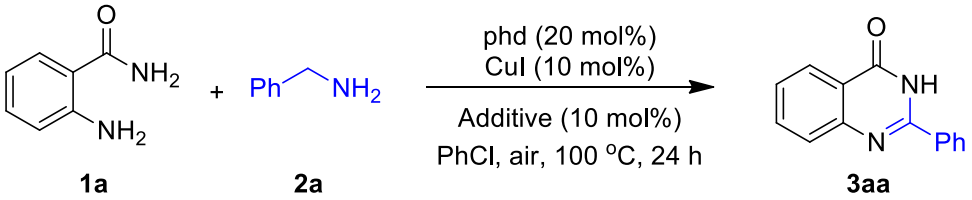
Table S9. Effect of reaction time [a]



Entry	Time (h)	Yield of **3aa** (%)[b]
1.	36	95
2.	**24**	**94**
3.	20	75

[a] Reaction conditions: **1a** (0.1 mmol, 1.0 equiv), **2a** (0.15 mmol, 1.5 equiv), phd (20 mol%), Cu-salt (10 mol%), TsOH (10 mol%) in chlorobenzene (0.5 mL), 100 ˚C, time, air. [b] Isolated yields.

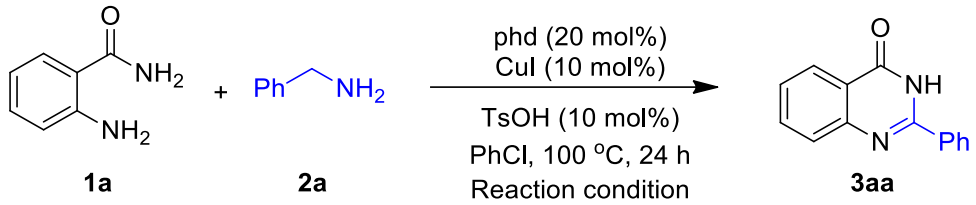
Table S10. Effect of additive [a]



Entry	Additive	Yield of **3aa** (%)[b]
1.	**TsOH**	**94**
2.	Na_2HPO_4	39
3.	$TsOH•H_2O$	90
4.	-	63

[a] Reaction conditions: **1a** (0.1 mmol, 1.0 equiv), **2a** (0.15 mmol, 1.5 equiv), phd (20 mol%), Cu-salt (10 mol%), additive, in chlorobenzene (0.5 mL), 100 ˚C, 24 h, air. [b] Isolated yields.

Table S11. Effect of reaction condition [a]

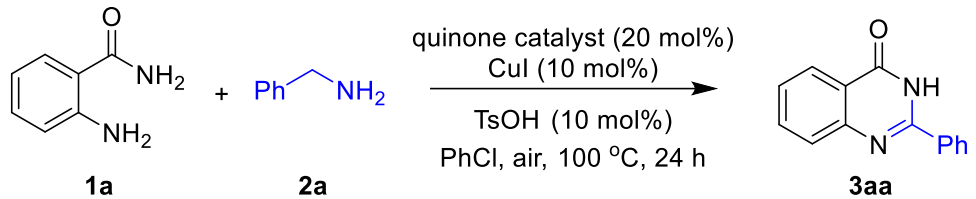


1a 2a 3aa

Entry	Reaction condition	Yield (%)[b]
1.	**Open-air**	**94**
2.	O_2 Balloon (1 atm)	90
3.	Under Ar or N_2 (1 atm)	trace

[a] Reaction conditions: **1a** (0.1 mmol, 1.0 equiv), **2a** (0.15 mmol, 1.5 equiv), phd (20 mol%), Cu-salt (10 mol%), TsOH (10 mol%) in chlorobenzene (0.5 mL), 100 °C, 24 h, air. [b] Isolated yields.

Table S12. Effect of quinone catalyst.[a]



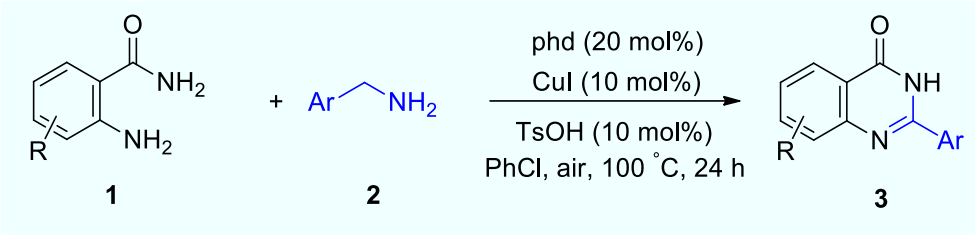
1a 2a 3aa

Entry	Catalyst	Yield of **3aa** (%)[b]
1.	Q1	73
2.	Q2	73
3.	Q3	75
4.	**phd**	**94**
5	none	50

[a] Reaction conditions: **1a** (0.1 mmol, 1.0 equiv), **2a** (0.15 mmol, 1.5 equiv), quinone (20 mol%), CuI (10 mol%), (TsOH 10 mol%) in chlorobenzene (0.5 mL), 100 °C, 24 h, air. [b] Isolated yields.

4. Biomimicking synthesis and characterization of 3.

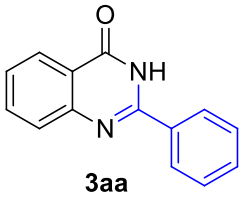
4.1 General procedure



In a 5 mL round bottom flask, 2-aminobenzylamide **1** (0.1 mmol, 1 equiv), CuI (1.9 mg, 10 mol%), phd (4.2 mg, 20 mol%), TsOH (1.7 mg, 10 mol%) in chlorobenzene (0.5 mL) were stirred at room temperature in open air. Then amine **2** (0.15 mmol, 1.5 equiv) was added and the mixture was placed in a preheated oil bath at 100 °C for 24 h. After completion of the reaction, mixture was quenched with 2 mL water and extracted with dichloromethane (3 x 5 mL). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated. The residue was purified by column chromatography over silica gel (100-200 mesh) with hexane/ethyl acetate as eluent to obtain compound **3**.

4.2 Characterization data:

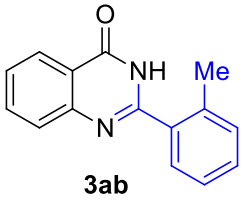
2-phenylquinazolin-4(3*H*)-one (3aa) [2]



3aa

Analytical TLC on silica gel, 8:2 hexane/ethylacetate R_f = 0.40; Yield 94% (21 mg, 0.094 mmol). **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 10.92 (s, 1H), 8.33 (d, *J* = 7.9 Hz, 1H), 8.21-8.18 (m, 2H), 7.86 – 7.79 (m, 2H), 7.61 – 7.57 (m, 3H), 7.51 (t, *J* = 7.3 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)**: δ 164.1, 151.9, 149.7, 135.1, 133.0, 131.8, 129.2, 128.2, 127.6, 127.0, 126.5, 121.0. **IR (neat / cm^{-1}):** 3437, 2920, 2850, 1664, 1602, 1559, 1480, 1470, 767, 693.

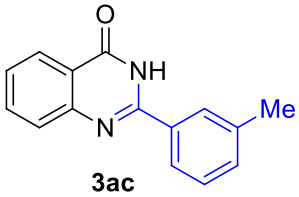
2-(o-tolyl)quinazolin-4(3*H*)-one (3ab) [2]



3ab

Analytical TLC on silica gel, 8:2 hexane/ethylacetate R_f = 0.40; Yield 97% (23 mg, 0.097 mmol). **^{1}H NMR (400 MHz, $CDCl_3$)** : δ 10.78 (s, 1H), 8.27 (d, *J* = 7.9 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 2H), 7.57 (d, *J* = 7.1 Hz, 1H), 7.53 – 7.49 (m, 1H), 7.43 (t, *J* = 7.4 Hz, 1H), 7.36 – 7.32 (m, 2H), 2.53 (s, 3H).**^{13}C NMR (101 MHz, $CDCl_3$)**: δ 163.4, 153.6, 149.2, 137.0, 135.1, 133.7, 131.6, 130.7, 128.9, 128.0, 127.2, 126.5, 126.4, 120.8, 20.2. **IR (neat / cm^{-1}):** 3437, 2919, 2850, 1726, 1684, 1611, 1594, 1242, 759, 721.

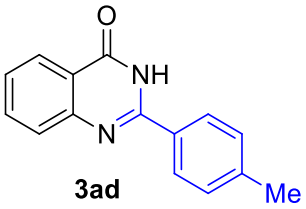
2-(m-tolyl)quinazolin-4(3*H*)-one(3ac) [2]



3ac

Analytical TLC on silica gel, 8:2 hexane/ethylacetate R_f = 0.40; Yield 97% (53 mg, 0.097 mmol).**^{1}H NMR (400 MHz, $CDCl_3$):** δ 11.77 (s, 1H), 8.33 (d, *J* = 7.9 Hz, 1H), 8.11 (s, 1H), 8.05 (d, *J* = 7.7 Hz, 1H), 7.86 – 7.78 (m, 2H), 7.52 – 7.44 (m, 2H), 7.39 (d, *J* = 7.6 Hz, 1H), 2.52 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 164.1, 152.1, 149.7, 139.0, 135.0, 132.9, 132.6, 129.1, 128.2, 128.1, 126.8, 126.4, 124.7, 121.0, 21.7. **IR (neat / cm^{-1}):** 3435, 2920, 2850, 1681, 1638, 1611, 765, 716, 682**.**

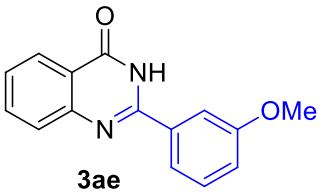
2-(p-tolyl)quinazolin-4(3*H*)-one (3ad) [2]



3ad

Analytical TLC on silica gel, 8:2 hexane/ethylacetate R_f = 0.40; Yield of R^3= H, 93% (22 mg, 0.093 mmol), R^3= CH_3, 76% (18 mg, 0.076 mmol).**^{1}H NMR (400 MHz, $CDCl_3$):** δ 11.59 (s, 1H), 8.33 (d, *J* = 8.3 Hz, 1H), 8.16 (d, *J* = 8.2 Hz, 2H), 7.84 – 7.77 (m, 2H), 7.51-7.47 (m, 1H), 7.38 (d, *J* = 8.1 Hz, 2H), 2.46 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 164.1, 152.0, 149.8, 142.3, 135.0, 130.1, 129.9, 128.0, 127.5, 126.7, 126.5, 120.9, 21.7. **IR (neat / cm^{-1}):** 3435, 2920, 2850, 1639, 1561, 768, 728, 686, 636.

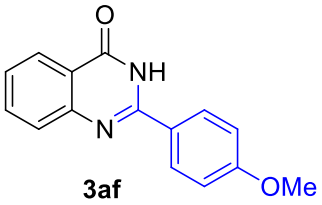
2-(3-methoxyphenyl)quinazolin-4(3*H*)-one (3ae) [3]



3ae

Analytical TLC on silica gel, 8:2 hexane/ethylacetate R_f = 0.35; Yield of R^3= H, 63% (16 mg, 0.063 mmol), R^3= CH_3, 70% (16 mg, 0.070 mmol). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 11.46 (s, 1H), 8.32 (d, *J* = 7.8 Hz, 1H), 7.86 – 7.79 (m, 4H), 7.53-7.47 (m, 2H), 7.13 (d, *J* = 8.5 Hz, 1H), 3.97 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 163.9, 160.3, 151.7, 149.6, 135.1, 134.3, 130.3, 128.2, 128.0, 126.5, 121.1, 119.7, 118.4, 112.3, 55.7. **IR (neat / cm^{-1}):** 3435, 2920, 2850, 1638, 1309, 854,767, 720, 681.

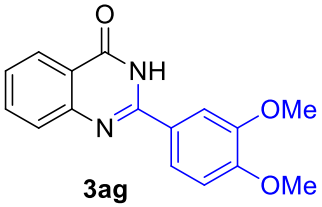
2-(4-methoxyphenyl) quinazolin-4(3*H*)-one (3af) [2]



3af

Analytical TLC on silica gel, 8:2 hexane/ethylacetate R_f = 0.35; Yield 99% (25 mg, 0.099 mmol). **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 11.43 (s, 1H), 8.32 (d, *J* = 7.7 Hz, 1H), 8.22 (d, *J* = 8.7 Hz, 2H), 7.80-7.78 (m, 2H), 7.51-7.46 (m,1H), 7.08 (d, *J* = 9.0 Hz, 2H), 3.92 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)**: δ 164.0, 162.6, 151.6, 149.9, 135.0, 129.2, 127.9, 126.5, 125.3, 120.7, 114.6, 55.7. **IR (neat / cm^{-1}):** 3436, 2920, 2850, 1676, 1634, 1484, 1248, 764, 686.

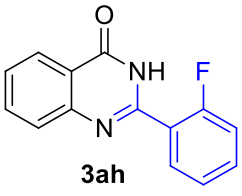
2-(3,4-dimethoxyphenyl)quinazolin-4(3*H*)-one (3ag) [4]



3ag

Analytical TLC on silica gel, 8:2 hexane/ethylacetate R_f = 0.20; Yield 99% (28 mg, 0.099 mmol).**^{1}H NMR (400 MHz, DMSO-d_6):** ^{1}H NMR (400 MHz, DMSO-D6) δ 12.43 (s, 1H), 8.13 (d, *J* = 7.9 Hz, 1H), 7.87 (d, *J* = 8.5 Hz, 1H), 7.81 (t, *J* = 7.6 Hz, 2H), 7.71 (d, *J* = 7.8 Hz, 1H), 7.48 (t, *J* = 7.1 Hz, 1H), 7.11 (d, *J* = 8.6 Hz, 1H), 3.88 (s, 3H), 3.85 (s, 3H). **^{13}C NMR (101 MHz, DMSO-d_6):** δ 162.4, 151.9, 151.6, 148.9, 148.6, 134.6, 127.3, 126.2, 125.9, 124.7, 121.2, 120.7, 111.4, 110.7, 55.7. **IR (neat / cm^{-1}):** 3400, 2922, 2858,2257, 2129, 1649, 1047, 1025, 996, 827, 766, 690.

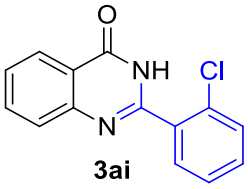
2-(2-fluorophenyl)quinazolin-4(3*H*)-one (3ah) [5]



3ah

Analytical TLC on silica gel, 8:2 hexane/ethylacetate R_f = 0.35; Yield 75% (18 mg, 0.075 mmol). **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 10.04 (s, 1H), 8.37 – 8.29 (m, 2H), 7.82 – 7.77 (m, 2H), 7.57 – 7.49 (m, 2H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.24 – 7.21 (m, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)**: δ162.2 (d, *J* = 18.3 Hz), 162.0, 149.1, 148.4, 135.0, 133.7, 131.5, 128.2, 127.4, 126.7, 125.4, 121.4, 120.2 (d, *J* = 8.7 Hz), 116.8 (d, *J* = 23.4 Hz). **^{19}F NMR (376 MHz, $CDCl_3$):** δ -115.3. **IR (neat / cm^{-1}):** 3436, 2920, 2850, 1695, 1681, 1655, 1602, 1482, 1455, 1386, 761, 739.

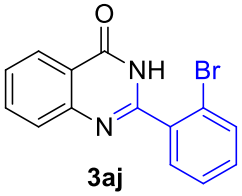
2-(2-chlorophenyl)quinazolin-4(3*H*)-one (3ai) [3]



3ai

Analytical TLC on silica gel, 8:2 hexane/ethylacetate R_f = 0.35; Yield 97% (25 mg, 0.097 mmol).**^{1}H NMR (500 MHz, $CDCl_3$):** δ 11.02 (s, 1H), 8.23 (d, *J* = 7.9 Hz, 1H), 7.80 – 7.77 (m, 3H), 7.52 – 7.40 (m, 4H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 162.7, 151.3, 149.1, 135.0, 133.0, 132.3, 132.0, 131.5, 130.6, 128.1, 127.5, 127.4, 126.6, 121.2. **IR (neat / cm^{-1}):** 3436, 2922, 2855, 1666, 1472, 765, 732.

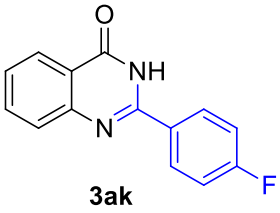
2-(2-bromophenyl)quinazolin-4(3*H*)-one (3aj) [5]



3aj

Analytical TLC on silica gel, 8:2 hexane/ethylacetate R_f = 0.40; Yield of R^3= H, 83% (25 mg, 0.083 mmol), R^3= CH_3, 66% (20 mg, 0.066 mmol). **^{1}H NMR (500 MHz, DMSO-d_6):** δ 12.64 (s, 1H), 8.19 (d, *J* = 7.9 Hz, 1H), 7.85 (t, *J* = 7.6 Hz, 1H), 7.77 (d, *J* = 7.9 Hz, 1H), 7.72 (d, *J* = 8.1 Hz, 1H), 7.64 (d, *J* = 7.5 Hz, 1H), 7.59-7.52 (m, 2H), 7.48 (t, *J* = 7.7 Hz, 1H). **^{13}C NMR (101 MHz, DMSO-d_6):** δ 162.0, 153.7, 148.9, 136.0, 135.3, 133.1, 132.3, 131.1, 128.2, 127.9, 127.7, 126.3, 121.5, 121.3. **IR (neat / cm^{-1}):** 3400, 2945, 1658, 1472, 1304, 1255, 1025, 996, 765.

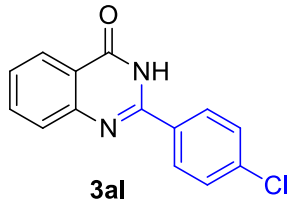
2-(4-fluorophenyl)quinazolin-4(3*H*)-one (3ak) [2]



3ak

Analytical TLC on silica gel, 8:2 hexane/ethylacetate R_f = 0.35; Yield 92% (22 mg, 0.092 mmol). **^{1}H NMR (400 MHz, DMSO-d_6):** δ 12.56 (s, 1H), 8.30 – 8.19 (m, 2H), 8.14 (d, *J* = 7.6 Hz, 1H), 7.83 (t, *J* = 7.2 Hz, 1H), 7.72 (d, *J* = 7.9 Hz, 1H), 7.51 (t, *J* = 7.2 Hz, 1H), 7.38 (t, *J* = 8.4 Hz, 2H). **^{13}C NMR (101 MHz, DMSO-d_6)**: δ 165.2(d, *J* = 251.34 Hz), 162.5, 151.4, 148.6, 134.6, 130.4 (d, *J* = 8.8 Hz), 129.2, 127.4, 126.6, 125.9, 120.9, 115.6 (d, *J* = 21.9 Hz). **^{19}F NMR (376 MHz, $CDCl_3$)** δ -109.0. **IR (neat / cm^{-1}):** 3400, 2920, 2850,2254, 2128, 1661, 1049, 1025, 1003, 825, 764, 684, 632.

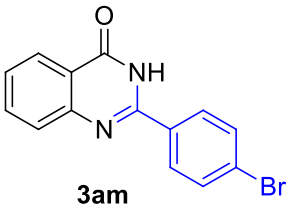
2-(4-chlorophenyl)quinazolin-4(3*H*)-one (3al) [2]



3al

Analytical TLC on silica gel, 8:2 hexane/ethylacetate R_f = 0.35; Yield 78% (20 mg, 0.078 mmol). **^{1}H NMR (400 MHz, DMSO-d_6):** δ 12.61 (s, 1H), 8.21 (d, *J* = 8.7 Hz, 2H), 8.16 (d, *J* = 7.9 Hz, 1H), 7.85 (t, *J* = 7.6 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.63 (d, *J* = 8.6 Hz, 2H), 7.54 (t, *J* = 7.6 Hz, 1H). **^{13}C NMR (101 MHz, DMSO-d_6)**: δ 162.2, 151.4, 148.6, 136.3, 134.7, 131.6, 129.6, 128.7, 127.6, 126.8, 125.9, 121.0**.** **IR (neat / cm^{-1}):** 3416, 2920, 2850, 2256, 2129, 1651, 1478, 1048, 1025, 999, 826, 765.

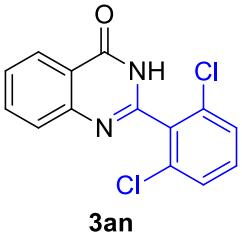
2-(4-bromophenyl)quinazolin-4(3H)-one (3am) [2]



3am

Analytical TLC on silica gel, 8:2 hexane/ethylacetate R_f = 0.35; Yield of R^3= H, 80% (24 mg, 0.080 mmol), R^3= CH_3, 70% (21 mg, 0.070 mmol).**^{1}H NMR (500 MHz, DMSO-d_6):** δ 8.14 (d, *J* = 7.8 Hz, 1H), 8.07 (d, *J* = 8.2 Hz, 2H), 7.84 (t, *J* = 7.6 Hz, 1H), 7.77 – 7.72 (m, 3H), 7.54 (t, *J* = 7.5 Hz, 1H). **^{13}C NMR (101 MHz, DMSO-d_6):** δ 162.7, 152.0, 149.0, 135.4, 132.3, 132.2, 130.3, 128.0, 127.5, 126.4, 125.8, 121.3. **IR (neat / cm^{-1}):** 3435, 2945, 1660, 1644, 1336, 1025, 995, 699.

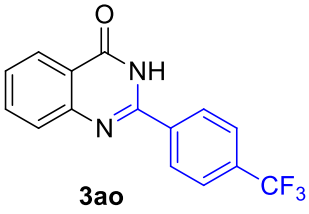
2-(2,6-dichlorophenyl)quinazolin-4(3*H*)-one (3an) [4]



3an

Analytical TLC on silica gel, 8:2 hexane/ethylacetate R_f = 0.30; Yield 82% (24 mg, 0.082 mmol).**^{1}H NMR (400 MHz, $CDCl_3$):** δ 11.42 (s, 1H), 8.16 (d, *J* = 7.9 Hz, 1H), 7.84 – 7.80 (m, 2H), 7.56 – 7.50 (m, 1H), 7.45 – 7.37 (m, 3H).). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 163.4, 149.2, 148.9, 135.1, 134.7, 132.7, 131.8, 128.5, 128.2, 127.7, 126.6, 121.4. **IR (neat / cm^{-1}):** 3132, 3030, 2785, 1680, 1608, 1469, 1431, 791, 731.

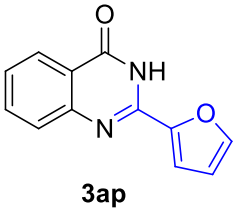
2-(4-(trifluoromethyl)phenyl)quinazolin-4(3*H*)-one (3ao) [2]



3ao

Analytical TLC on silica gel, 8:2 hexane/ethylacetate R_f = 0.30; Yield 58% (17 mg, 0.058 mmol). **^{1}H NMR (400 MHz, DMSO-d$_6$)**: δ 12.75 (s, 1H), 8.38 (d, *J* = 8.3 Hz, 2H), 8.18 (d, *J* = 7.9 Hz, 1H), 7.93 (d, *J* = 8.4 Hz, 2H), 7.90 – 7.85 (m, 1H), 7.78 (d, *J* = 7.9 Hz, 1H), 7.57 (t, *J* = 7.4 Hz, 1H). **^{13}C NMR (101 MHz, DMSO-d$_6$)**: δ 162.1, 151.1, 148.4, 136.6, 134.7, 131.5 (q, *J* = 31.33 Hz), 128.7, 128.1, 127.7, 127.1, 125.9 (d, JC-F = 3.43 Hz), 122.7 (q, JC-F = 272.7, 121.2. **^{19}F NMR (376 MHz, DMSO-d$_6$)**: δ -61.24 (s). **IR (neat / cm^{-1}):** 3412, 2925, 2854, 2257, 2129, 1680, 1449, 1047, 1025, 998, 827, 776.

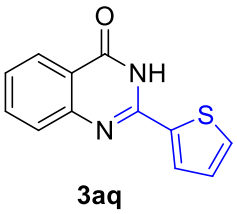
2-(furan-2-yl)quinazolin-4(3*H*)-one (3ap) [2]



3ap

Analytical TLC on silica gel, 8:2 hexane/ethylacetate R_f = 0.30; Yield 84% (18 mg, 0.084 mmol).**^{1}H NMR (400 MHz, CDCl$_3$):** δ 10.69 (s, 1H), 8.31 (d, *J* = 7.9 Hz, 1H), 7.78 (d, *J* = 3.7 Hz, 2H), 7.67 (d, *J* = 1.7 Hz, 1H), 7.53 (d, *J* = 3.4 Hz, 1H), 7.50-7.46 (m, 1H), 6.67-6.66 (m, 1H). **^{13}C NMR (101 MHz, CDCl$_3$):** δ 162.6, 149.4, 146.4, 145.7, 143.6, 135.2, 127.9, 127.0, 126.7, 121.2, 114.1, 113.1 **IR (neat / cm^{-1}):** 3436, 2919, 2851, 1627, 1605, 1552, 1459, 1021, 772.

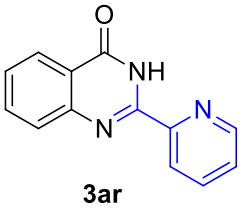
2-(thiophen-2-yl)quinazolin-4(3H)-one (3aq) [2]



3aq

Analytical TLC on silica gel, 8:2 hexane/ethylacetate R_f = 0.30; Yield 84% (19 mg, 0.084 mmol**^{1}H NMR (500 MHz, CDCl$_3$):** δ 12.09 (s, 1H), 8.28 (d, *J* = 7.3 Hz, 1H), 8.17 (s, 1H), 7.72 (s, 2H), 7.54 (s, 1H), 7.42 (d, *J* = 0.6 Hz, 1H), 7.19 (s, 1H). **^{13}C NMR (126 MHz, CDCl$_3$) δ** 164.0, 149.7, 147.5, 137.7, 135.2, 131.5, 128.6, 128.5, 127.9, 126.7, 126.6, 120.8. **IR (neat / cm^{-1}):** 3436, 1664, 1613, 847, 769, 713.

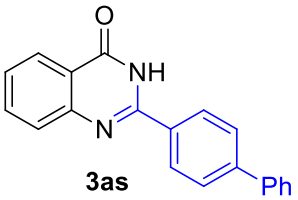
2-(pyridin-2-yl)quinazolin-4(3*H*)-one (3ar) [2]



3ar

Analytical TLC on silica gel, 8:2 hexane/ethylacetate R_f = 0.30; Yield 44% (10 mg, 0.044 mmol).**^{1}H NMR (400 MHz, CDCl$_3$):** δ 10.96 (s, 1H), 8.68 (d, *J* = 5.0 Hz, 1H), 8.60 (d, *J* = 7.9 Hz, 1H), 8.36 (d, *J* = 7.9 Hz, 1H), 7.93 (t, *J* = 7.9 Hz, 1H), 7.85 – 7.77 (m, 2H), 7.55 – 7.47 (m, 2H). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 161.6, 149.3, 149.1, 148.9, 148.6, 137.7, 134.7, 128.2, 127.5, 126.9, 126.4, 122.7, 122.2 **IR (neat / cm^{-1}):** 3436, 2924, 2852, 1634, 1472, 768, 739, 688, 615.

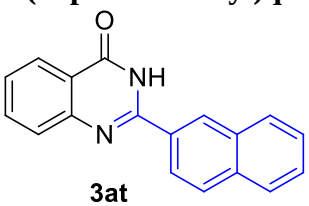
2-([1,1'-biphenyl]-4-yl)quinazolin-4(*3H*)-one (3as) [6]



3as

Analytical TLC on silica gel, 8:2 hexane/ethylacetate R_f = 0.30; Yield 94% (28 mg, 0.094 mmol). **^{1}H NMR (500 MHz, DMSO-D6)**: δ 8.33 – 8.10 (m, 1H), 7.86 – 7.66 (m, 4H), 7.62 – 7.30 (m, 7H), 7.24 (d, *J* = 8.0 Hz, 1H), 5.53 (s, 1H). **IR (neat / cm^{-1}):** 3438, 2915, 2851, 1664, 1602, 1559, 1480, 1470, 767, 693.

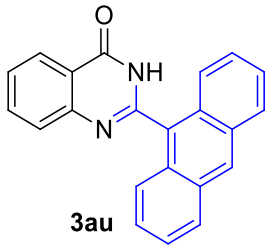
2-(naphthalen-2-yl)quinazolin-4(3*H*)-one (3at) [2]



3at

Analytical TLC on silica gel, 8:2 hexane/ethylacetate R_f = 0.35; Yield 78% (21 mg, 0.078 mmol). **^{1}H NMR (500 MHz, DMSO-d$_6$):** δ 12.66 (s, 1H), 8.83 (s, 1H), 8.31 (d, *J* = 8.6 Hz, 1H), 8.19 (d, *J* = 7.9 Hz, 1H), 8.10 – 7.97 (m, 3H), 7.91 – 7.83 (m, 1H), 7.80 (d, *J* = 7.8 Hz, 1H), 7.67-7.62 (m 2H), 7.55 (t, *J* = 7.5 Hz, 1H). **^{13}C NMR (101 MHz, DMSO-d$_6$)**: δ 162.8, 152.8, 149.3, 135.2, 134.7, 132.8, 130.5, 129.5, 128.7, 128.6, 128.5, 128.2, 128.1, 127.5, 127.2, 126.4, 125.0, 121.6. **IR (neat / cm^{-1}):** 3436, 2922, 2856, 1638, 1305, 817, 769, 743.

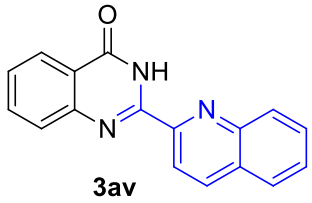
2-(anthracen-9-yl)quinazolin-4(3*H*)-one (3au) [5]



3au

Analytical TLC on silica gel, 8:2 hexane/ethylacetate R_f = 0.30; Yield 68% (22 mg, 0.068 mmol).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.92 (s, 1H), 8.51 (s, 1H), 8.17 (d, *J* = 7.6 Hz, 1H), 8.01 – 7.95 (m, 2H), 7.87 – 7.78 (m, 4H), 7.56 – 7.51 (m, 1H), 7.46 – 7.41 (m, 4H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 162.3, 152.3, 149.1, 135.1, 131.2, 129.9, 129.7, 128.8, 128.1, 127.6, 127.5, 127.3, 126.7, 125.7, 124.7, 121.3. **IR (neat / cm^{-1}):** 3436, 2920, 2850, 1646, 1466, 1439, 770, 732, 667, 653.

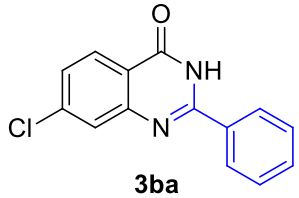
2-(quinolin-2-yl)quinazolin-4(3*H*)-one (3av) [7]



3av

Analytical TLC on silica gel, 8:2 hexane/ethylacetate R_f = 0.30; Yield 84% (23 mg, 0.084 mmol). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 11.23 (s, 1H), 8.67 (d, *J* = 8.6 Hz, 1H), 8.38 (t, *J* = 7.7 Hz, 2H), 8.17 (d, *J* = 8.5 Hz, 1H), 7.90 (t, *J* = 8.7 Hz, 2H), 7.82 (t, *J* = 7.8 Hz, 2H), 7.66 (t, *J* = 7.2 Hz, 1H), 7.55 (t, *J* = 7.2 Hz, 1H).). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 161.0, 148.7, 148.5, 147.6, 146.3, 137.2, 134.1, 130.0, 129.2, 128.8, 127.8, 127.8, 127.3, 127.1, 126.3, 122.2, 118.0. **IR (neat / cm^{-1}):** 2945, 1684, 1634, 1422, 1327, 841, 741.

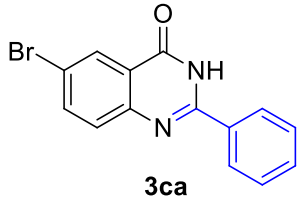
7-chloro-2-phenylquinazolin-4(3*H*)-one (3ba) [2]



3ba

Analytical TLC on silica gel, 8:2 hexane/ethylacetate R_f = 0.25; Yield of R^3= H, 78% (20 mg, 0.078 mmol) and R^3= CH_3, 74% (19 mg, 0.074 mmol). **^{1}H NMR (500 MHz, DMSO-d_6):** δ 8.12 (d, *J* = 8.5 Hz, 1H), 8.10 (d, *J* = 7.6 Hz, 2H), 7.76 (s, 1H), 7.60 (t, *J* = 7.2 Hz, 1H), 7.54 (t, *J* = 8.2 Hz, 3H). **^{13}C NMR (101 MHz, DMSO-d_6):** δ 162.2, 154.3, 150.2, 139.8, 132.6, 132.3, 129.5, 128.4, 128.3, 127.4, 126.9, 120.0. **IR (neat / cm^{-1}):** 3401, 1649, 1451, 1025, 998, 827, 765.

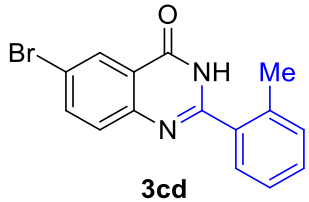
6-bromo-2-phenylquinazolin-4(3*H*)-one (3ca) [2]



3ca

Analytical TLC on silica gel, 8:2 hexane/ethylacetate R_f = 0.25; Yield 70% (21 mg, 0.070 mmol). **^{1}H NMR (400 MHz, DMSO-d_6)** δ 8.16 (d, *J* = 2.4 Hz, 1H), 8.07 (s, 1H), 8.05 (d, *J* = 1.7 Hz, 1H), 7.91 (dd, *J* = 8.7, 2.4 Hz, 1H), 7.64 (d, *J* = 8.7 Hz, 1H), 7.58 – 7.47 (m, 4H). **13C NMR (126 MHz, DMSO-d_6)** δ 161.6, 153.4, 148.0, 138.0, 132.7, 132.1, 129.2, 129.1, 128.3, 128.2, 122.8, 119.4. **IR (neat / cm^{-1}):** 3400, 1651, 1463, 1025, 996, 827, 766.

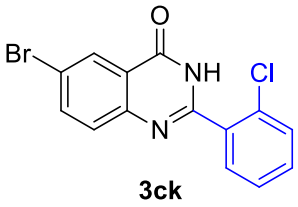
6-bromo-2-(o-tolyl)quinazolin-4(3*H*)-one (3cd)



3cd

Analytical TLC on silica gel, 8:2 hexane/ethylacetate R_f = 0.40; Yield 79% (25 mg, 0.079 mmol**). ^{1}H NMR (400 MHz, DMSO-d_6)** δ 8.22 (d, *J* = 2.4 Hz, 1H), 7.97 (dd, *J* = 8.7, 2.4 Hz, 1H), 7.64 (d, *J* = 8.7 Hz, 1H), 7.48 – 7.40 (m, 2H), 7.36 – 7.29 (m, 2H), 2.35 (s, 3H).**^{13}C NMR (101 MHz, DMSO-d_6)** δ 161.2, 155.4, 147.9, 137.8, 136.5, 134.1, 131.0, 130.6, 130.0, 129.4, 128.3, 126.2, 122.8, 119.5, 19.8. **IR (neat / cm^{-1}):** 3400, 1651, 1463, 1025, 826, 765. HRMS(ESI$^+$) calcd for $C_{15}H_{12}BrN_2O$ $[M + H]^+$, 315.0128; found, 315.0128.

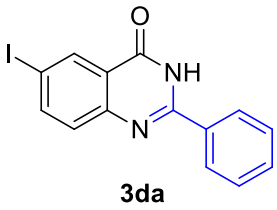
6-bromo-2-(2-chlorophenyl)quinazolin-4(3*H*)-one (3ck)



3ck

Analytical TLC on silica gel, 8:2 hexane/ethylacetate R_f = 0.40; Yield 73% (26 mg, 0.073 mmol). **^{1}H NMR (400 MHz, DMSO-d$_6$)** δ 8.22 (s, 1H), 7.97 (dd, *J* = 8.6, 2.3 Hz, 1H), 7.65 (d, *J* = 8.7 Hz, 1H), 7.61 (d, *J* = 8.1 Hz, 1H), 7.59 – 7.53 (m, 2H), 7.48 (t, *J* = 8.7 Hz, 2H). **^{13}C NMR (126 MHz, DMSO-D6**δ 160.6, 152.9, 147.5, 137.7, 133.4, 132.1, 131.5, 131.0, 129.9, 129.8, 128.1, 127.5, 122.8, 119.8. **IR (neat / cm^{-1}):** 3400, 1644, 1469, 1025, 828, 766. HRMS(ESI$^+$) calcd for $C_{14}H_9BrClN_2O$ [M + H]$^+$, 334.9581; found, 334.9576.

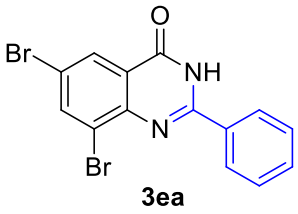
6-iodo-2-phenylquinazolin-4(3*H*)-one (3da) [1c]



3da

Analytical TLC on silica gel, 8:2 hexane/ethylacetate R_f = 0.25; Yield 63% (22 mg, 0.063 mmol). **^{1}H NMR (500 MHz, DMSO-d$_6$)** δ 8.19 (d, *J* = 2.3 Hz, 5H), 8.10 (s, 6H), 8.08 (d, *J* = 1.4 Hz, 1H), 7.94 (dd, *J* = 8.7, 2.4 Hz, 6H), 7.67 (d, *J* = 8.7 Hz, 6H), 7.58 (d, *J* = 7.2 Hz, 7H), 7.53 (t, *J* = 7.4 Hz, 15H). **^{13}C NMR (101 MHz, DMSO-d$_6$)** δ 161.5, 153.2, 147.8, 138.0, 132.7, 132.1, 130.2, 129.1, 128.4, 128.2, 122.8, 119.5. **IR (neat / cm^{-1}):** 3404, 1658, 1480, 1050, 996, 823, 734.

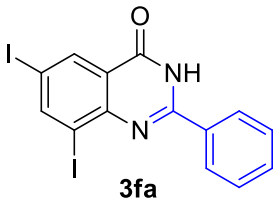
6,8-dibromo-2-phenylquinazolin-4(3*H*)-one (3ea) [8]



3ea

Analytical TLC on silica gel, 8:2 hexane/ethylacetate R_f = 0.25; Yield 66% (25 mg, 0.066 mmol). **^{1}H NMR (400 MHz, DMSO-d$_6$)** δ 8.33 (d, *J* = 2.2 Hz, 1H), 8.19 (d, *J* = 2.3 Hz, 2H), 8.17 (d, *J* = 1.6 Hz, 1H), 7.63 – 7.60 (m, 1H), 7.56 (dd, *J* = 11.4, 4.5 Hz, 3H). **^{13}C NMR (126 MHz, DMSO-d6):** δ 161.4, 153.8, 145.8, 140.2, 132.6, 132.5, 129.6, 128.4, 128.3, 124.0, 123.9, 119.1. **IR (neat / cm^{-1}):** 3400, 1651, 1454, 1025, 826, 765.

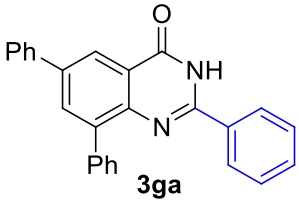
6,8-diiodo-2-phenylquinazolin-4(3*H*)-one (3fa) [9]



3fa

Analytical TLC on silica gel, 8:2 hexane/ethylacetate R_f = 0.25; Yield 54% (26 mg, 0.054 mmol) **^{1}H NMR (500 MHz, DMSO-d$_6$)** δ 8.61 (d, *J* = 1.9 Hz, 1H), 8.37 (d, *J* = 1.9 Hz, 1H), 8.22 (d, *J* = 8.5 Hz, 2H), 7.64 – 7.61 (m, 1H), 7.59-7.56 (m, 2H). **^{13}C NMR (126 MHz, DMSO-d$_6$)** δ 161.5, 154.0, 146.0, 140.4, 132.7, 132.6, 129.4, 128.5, 128.4, 124.2, 124.0, 119.3.
IR (neat / cm^{-1}): 3400, 1651, 1453, 1025, 826, 765.

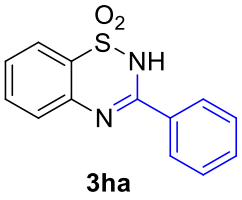
2,6,8-triphenylquinazolin-4(3*H*)-one (3ga) [1a]



3ga

Analytical TLC on silica gel, 8:2 hexane/ethylacetate R_f = 0.25; Yield 45% (17 mg, 0.045 mmol). **^{1}H NMR (400 MHz, CDCl$_3$):**
δ 9.79 (s, 1H), 8.59 (d, *J* = 2.0 Hz, 1H), 8.13 (d, *J* = 2.1 Hz, 1H), 8.01 (d, *J* = 8.1 Hz, 2H), 7.78 (t, *J* = 7.5 Hz, 4H), 7.55-7.53 (m, 3H), 7.53 – 7.48 (m, 4H), 7.47 – 7.41 (m, 2H). **^{13}C NMR (101 MHz, CDCl$_3$):** δ 167.8, 155.4, 142.6, 140.2, 138.6, 134.8, 133.6, 131.5, 131.2, 129.8, 129.1, 128.94, 128.87, 128.3, 128.1, 127.5, 126.0, 125.00. **IR (neat / cm^{-1}):** 3435, 1634, 1465, 1290, 846, 770.

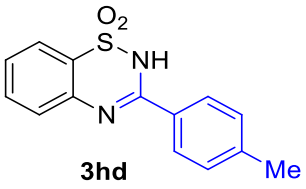
3-phenyl-2*H*-benzo[e][1,2,4]thiadiazine 1,1-dioxide (3ha) [10]



3ha

Analytical TLC on silica gel, 8:2 hexane/ethylacetate R_f = 0.35; Yield of R^3= H, 74% (19 mg, 0.074 mmol) and R^3= CH_3, 69% (18 mg, 0.069 mmol). **^{1}H NMR (500 MHz, DMSO-d$_6$)** δ 8.01 (d, *J* = 7.9 Hz, 2H), 7.85 (d, *J* = 7.9 Hz, 1H), 7.75 – 7.67 (m, 2H), 7.63-7.59 (m, 3H), 7.51 (t, *J* = 7.6 Hz, 1H). **^{13}C NMR (126 MHz, DMSO-d$_6$)** δ 155.4, 135.7, 133.8, 133.4, 132.0, 129.4, 128.7, 128.6, 127.4, 123.7, 121.6, 118.8. **IR (neat / cm^{-1}):** 3412, 1651, 1459, 1160, 1025, 827, 765.

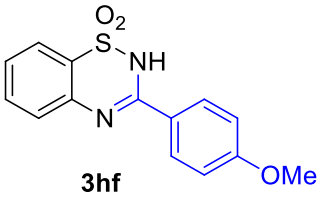
3-(*p*-tolyl)-*2H*-benzo[e][1,2,4]thiadiazine 1,1-dioxide (3hd) [10]



3hd

Analytical TLC on silica gel, 8:2 hexane/ethylacetate R_f = 0.20; Yield 73% (20 mg, 0.073 mmol). **^{1}H NMR (500 MHz, DMSO- d$_6$)**: δ 7.92 (d, *J* = 8.3 Hz, 2H), 7.83 (d, *J* = 7.9 Hz, 1H), 7.71 (t, *J* = 8.5 Hz, 1H), 7.61 (d, *J* = 8.2 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.41 (d, *J* = 8.1 Hz, 2H), 2.39 (s, 3H). **^{13}C NMR (101 MHz, DMSO-D6):** δ 155.8, 144.5, 136.3, 134.2, 130.3, 129.6, 129.1, 127.8, 124.2, 122.2, 119.3, 22.0. **IR (neat / cm^{-1}):** 3410, 1644, 1469, 1025, 828, 766.

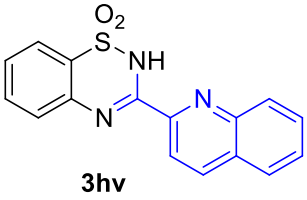
3-(4-methoxyphenyl)-*2H*-benzo[*e*][1,2,4]thiadiazine 1,1-dioxide (3hf) [10]



3hf

Analytical TLC on silica gel, 8:2 hexane/ethylacetate R_f = 0.15; Yield 75% (21 mg, 0.075 mmol). **^{1}H NMR (400 MHz, DMSO-d$_6$)**: δ 8.01 (d, *J* = 8.9 Hz, 2H), 7.82 (d, *J* = 7.8 Hz, 1H), 7.70 (t, *J* = 7.7 Hz, 1H), 7.60 (d, *J* = 8.2 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 1H), 7.13 (d, *J* = 8.9 Hz, 2H), 3.84 (s, 3H). **^{13}C NMR (101 MHz, DMSO-D6):** δ 163.9, 155.3, 136.2, 134.1, 131.1, 130.7, 127.5, 124.1, 122.1, 119.1, 115.2, 56.5. **IR (neat / cm^{-1}):** 3412, 1641, 1465, 1160, 1035, 825, 765.

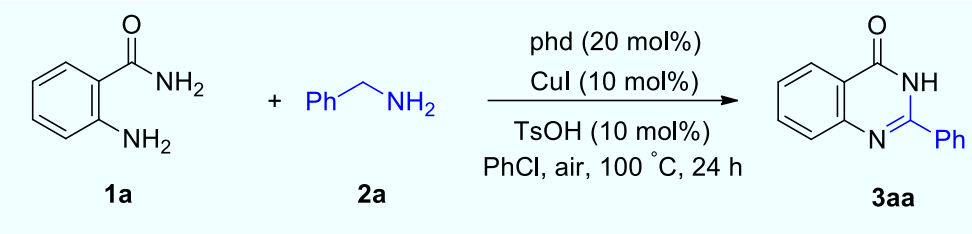
3-(quinolin-2-yl)-*2H*-benzo[*e*][1,2,4]thiadiazine 1,1-dioxide (3hv) [11]



3hv

Analytical TLC on silica gel, 8:2 hexane/ethylacetate R_f = 0.30; Yield 68% (21 mg, 0.068 mmol). **^{1}H NMR (400 MHz, DMSO- d$_6$)**: δ 8.65 (d, *J* = 8.6 Hz, 1H), 8.32 (d, *J* = 8.6 Hz, 2H), 8.12 (d, *J* = 8.1 Hz, 1H), 7.93 (dd, *J* = 17.3, 8.2 Hz, 3H), 7.77 (t, *J* = 7.0 Hz, 2H), 7.55 (t, *J* = 7.6 Hz, 1H). **^{13}C NMR (101 MHz, DMSO-D6):** δ 152.6, 148.4, 147.1, 139.5, 135.6, 134.4, 132.0, 130.3, 130.0, 129.1, 128.1, 124.3, 122.2, 119.9, 119.7. **IR (neat / cm^{-1}):** 3412, 1655, 1359, 1160, 1025, 830, 745.

5. Gram scale experiment:

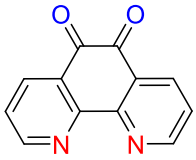


In a 50 mL round bottom flask, 2-aminobenzylamide **1a** (681 mg, 5 mmol, 1 equiv), phd (210 mg, 0.20 mmol, 20 mol%), CuI (190 mg, 0.10 mmol, 10 mol%), TsOH (170 mg, 0.10 mmol, 10 mol%) in chlorobenzene (25 mL) were stirred at room temperature in open air. Then benzylamine **2a** (803.6 mg, 7.5 mmol, 1.5 equiv) was added and the mixture was placed in a preheated oil bath at 100 °C for 24 h. After completion of the reaction, mixture was quenched with 100 mL water and extracted with dichloromethane (3 x 50 mL). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated. The residue was purified by column chromatography over silica gel (100-200 mesh) with hexane/ethyl acetate as eluent to obtain compound **3aa** (1.0 g, 90% yield).

6. Synthesis and characterization of phd and its copper complex

6.1 Synthesis of 1,10-phenanthroline-5,6-dione (phd) [12]

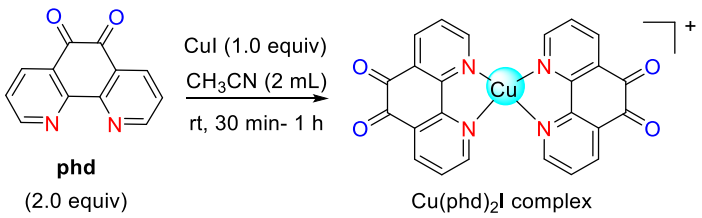
1,10-Phenanthroline-5,6-dione (phd), was prepared according to the previously reported procedure.[12a] 1,10-phenanthroline (0.40 g, 2.2 mmol) and KBr (0.41 g, 3.44 mmol) were combined in a round bottom flak and an ice-cooled mixture of H_2SO_4 and HNO_3 (2:1) was slowly added to the solids. The mixture was heated to reflux for 4 h, and then pour onto 50 mL ice cooled water. The yellow aqueous solution was carefully neutralized with NaOH (pH = 6 – 7), then extracted into DCM, dried over Na_2SO_4, and concentrated to give nearly quantitative 1,10-phenanthroline-5,6-dione. The yellow solid was recrystallized from methanol to give pale yellow compound.



Analytical TLC on silica gel, 8:2 hexane/ethylacetate R_f = 0.50; Yield 93% (430 mg, 2.04 mmol).**^{1}H NMR (400 MHz, $CDCl_3$):** δ 9.12-9.10 (m, 2H), 8.51-8.49 (m, 2H), 7.60-7.57 (m, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)**: δ 178.7, 156.5, 152.9, 137.4, 128.1, 125.7. **IR (neat / cm^{-1}):** 1687, 1560, 1416, 1294, 736.

6.2 Preparation of $[Cu(phd)_2]^{+/+2}$ complex [12c]

Synthesis of $[Cu(phd)_2]I$:

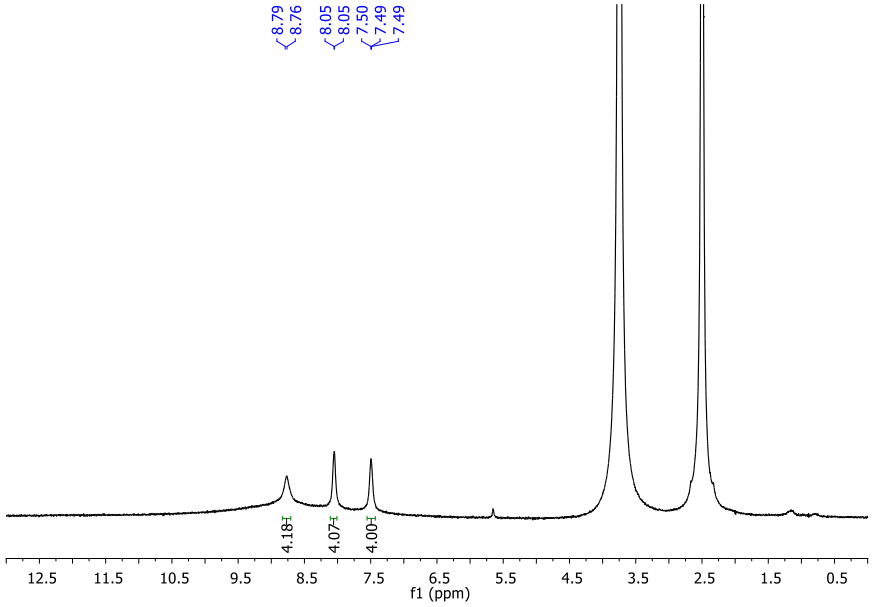


In an oven-dried 15 mL Schlenk tube, CuI (38.0 mg, 0.2 mmol, 1.0 equiv), phd (84.0 mg, 0.4 mmol, 2.0 equiv) were stirred in dry acetonitrile (2 mL) under argon at room temperature. The

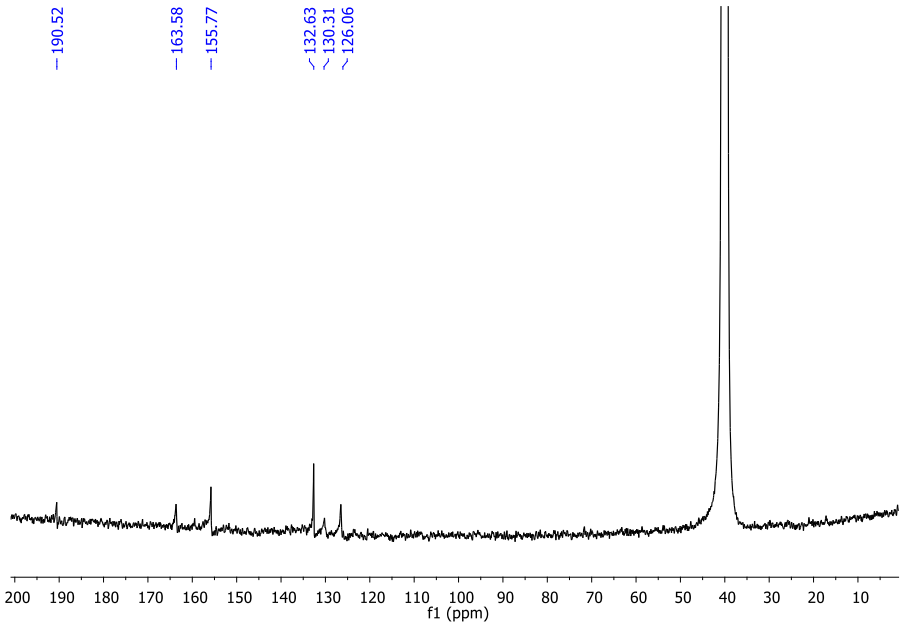
solution turned brown yellow to dark brown in 30 min to 1 h. It indicates that $[Cu(phd)_2]I$ complex was formed. It was then filtered and washed with ether twice. Finally, dark brown precipitate was obtained. The complex was dried in vacuo for 24 h and stored in a desiccator.

Analytical data: Yield 85% (80 mg, 0.17 mmol). **^{1}H NMR (400 MHz, DMSO-d$_6$):** δ 8.78 (d, *J* = 11.0 Hz, 4H), 8.05 (d, *J* = 1.3 Hz, 4H), 7.49 (t, *J* = 3.5 Hz, 4H). **^{13}C NMR (101 MHz, DMSO-d$_6$):** δ 190.5, 163.6, 155.8, 132.6, 130.3, 126.1. **IR (neat / cm^{-1}):** 1699, 1563, 1406, 839, 563. HRMS(ESI$^+$) calcd for $C_{24}H_{12}{}^{63}CuN_4O_4$ $[M]^+$ 483.0149; found 483.0158 and calcd for $C_{24}H_{12}{}^{65}CuN_4O_4$ $[M]^+$ 485.0131; found 483.0149.

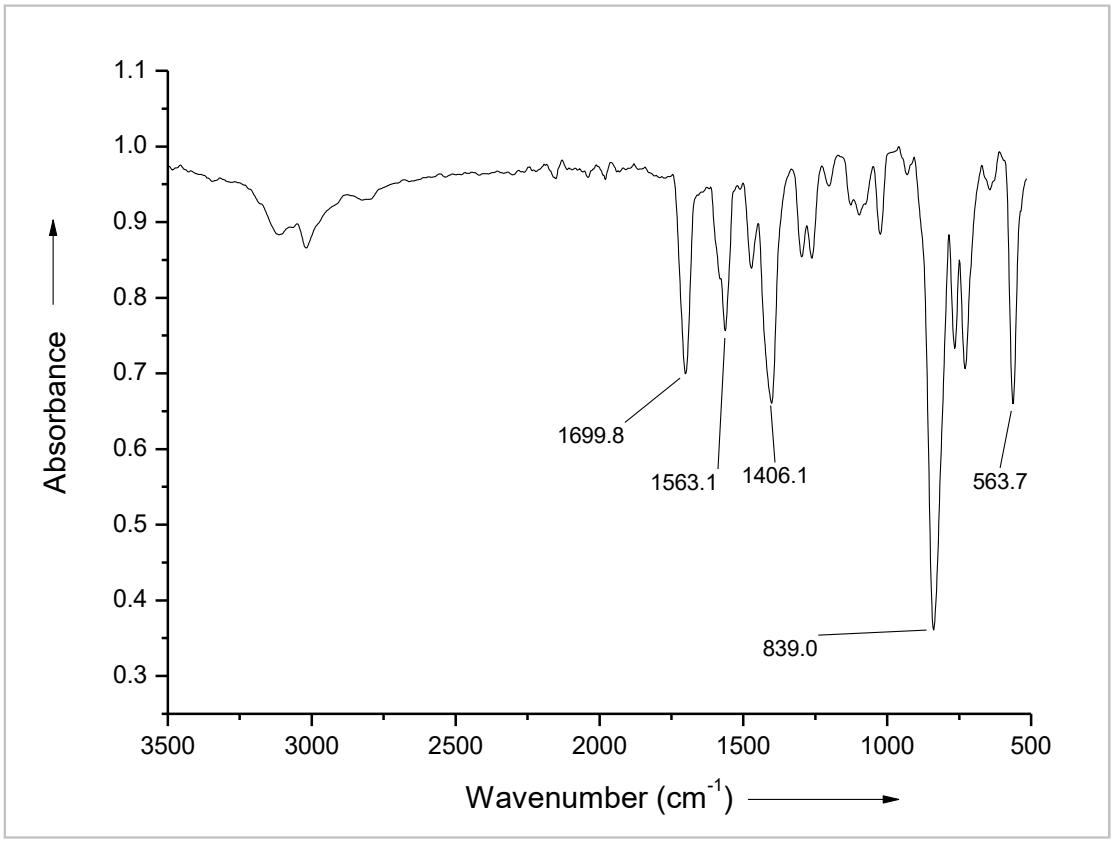
^{1}H NMR (400 MHz, DMSO-D6) spectrum of Cu(phd)$_2$I complex



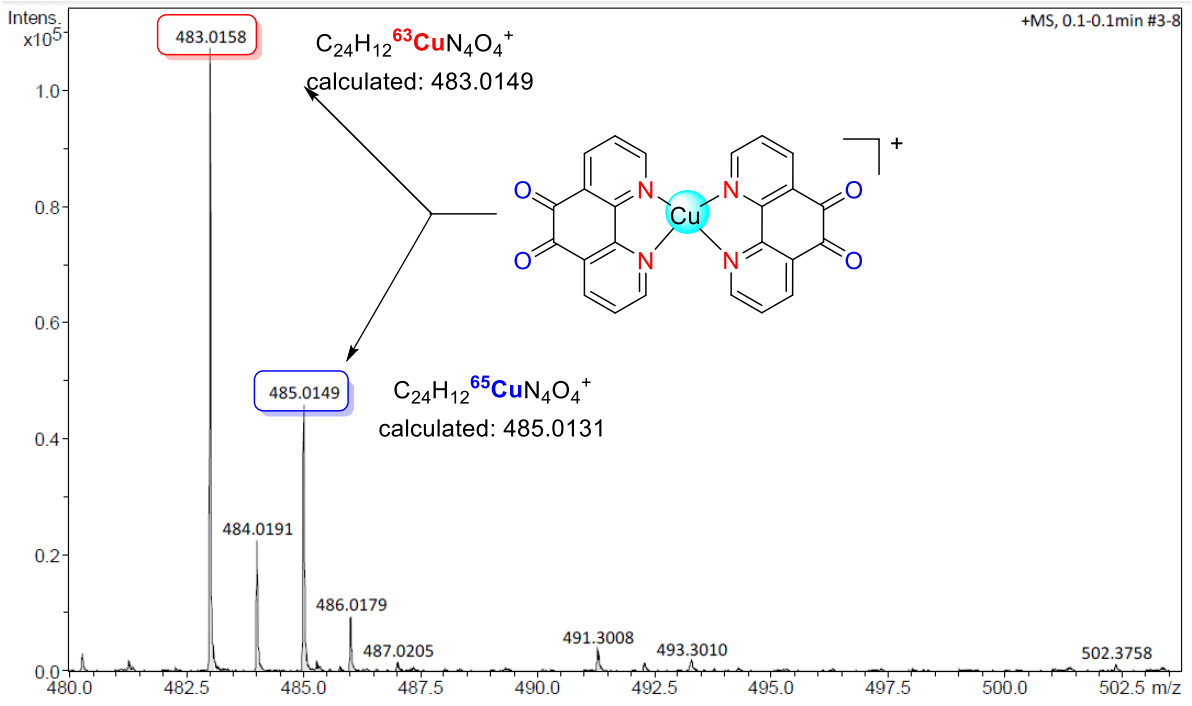
^{13}C NMR (101 MHz, DMSO-D6) Cu(phd)$_2$I complex



IR spectrum of $Cu(phd)_2I$ complex:

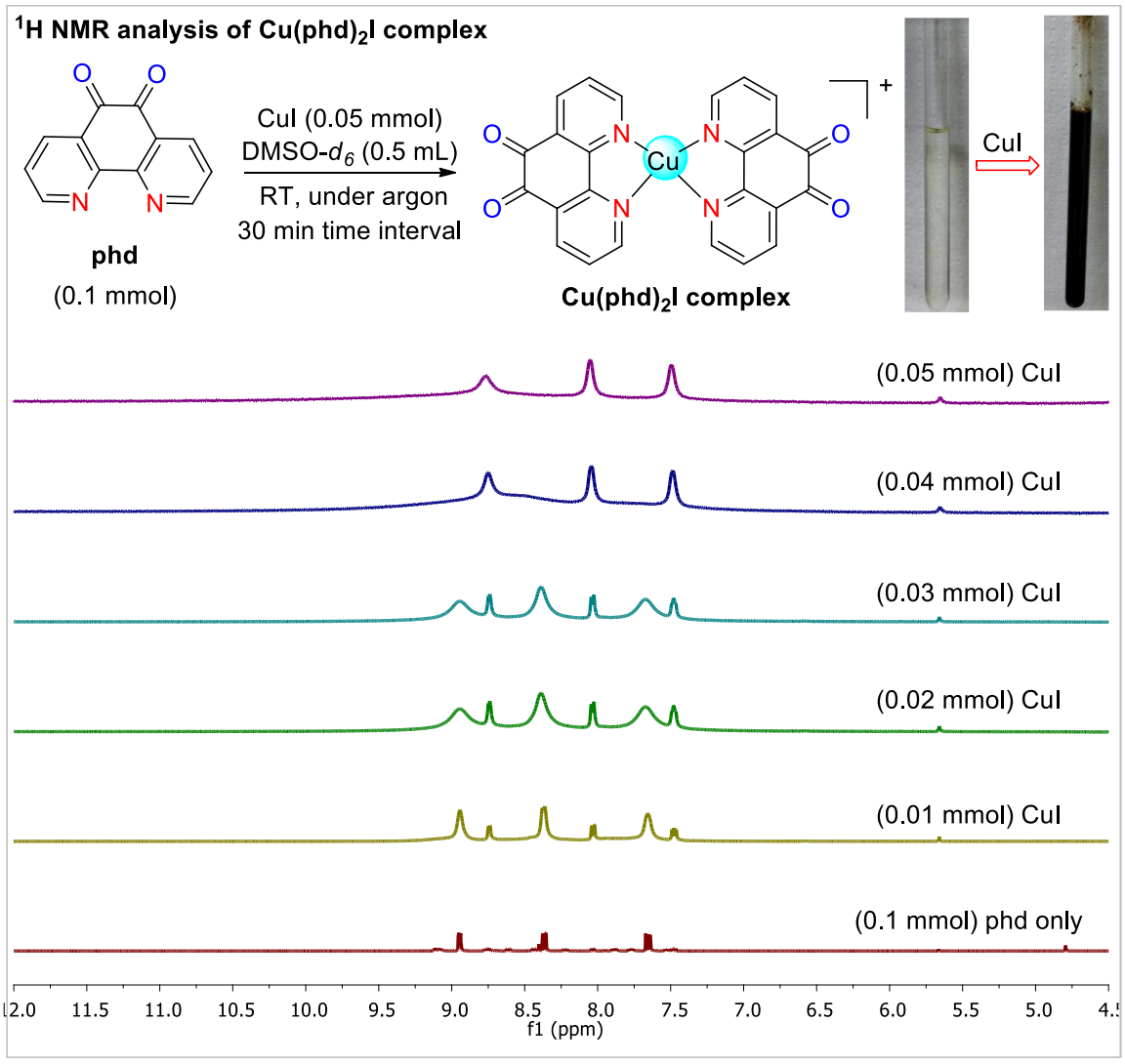


HRMS (ESI^+) spectrum of $Cu(phd)_2I$ complex:



6.3 ^{1}H NMR titration study:

Experimental procedure: In an oven-dried NMR tube, phd (21.0 mg, 0.1 mmol, 2.0 equiv) was taken in 0.5 mL DMSO-d_6 in an argon filled glove box. Then, CuI (1.9 mg, 0.01 mmol) was added at room temperature. After 30 min the reaction mixture was analyzed by using ^{1}H NMR analysis. Every, 30 min time intervals CuI were added sequentially (up to 0.05 mmol) and analyzed by using ^{1}H NMR.



6.4 Synthetic of [Cu(phd)$_2$](PF$_6$)$_2$ .2H$_2$O: A solution of $CuCl_2$ .2H_2O (26.9 mg, 0.2 mmol, 1.0 equiv), phen-dione (phd) (84.1 mg, 0.4 mmol, 2.0 equiv) was mixed with in (2.0 mL) ethanol solvent. Upon mixing, the solution turned green, indicative of complex formation. After the mixture was allowed to stir for 30 min, the complex was precipitated (green solid) by the addition of saturated aqueous NH_4PF_6 (20.8 mg, 0.2 mmol, 1.0 equiv). The complex was collected, washed with water, and dried with ether. Because this material, as well as the other complexes, adsorbed very strongly on alumina and silica gel, recrystallization from acetonitrile/ ether was used for purification. The complex was dried in vacuo for 24 h and stored in a desiccator.

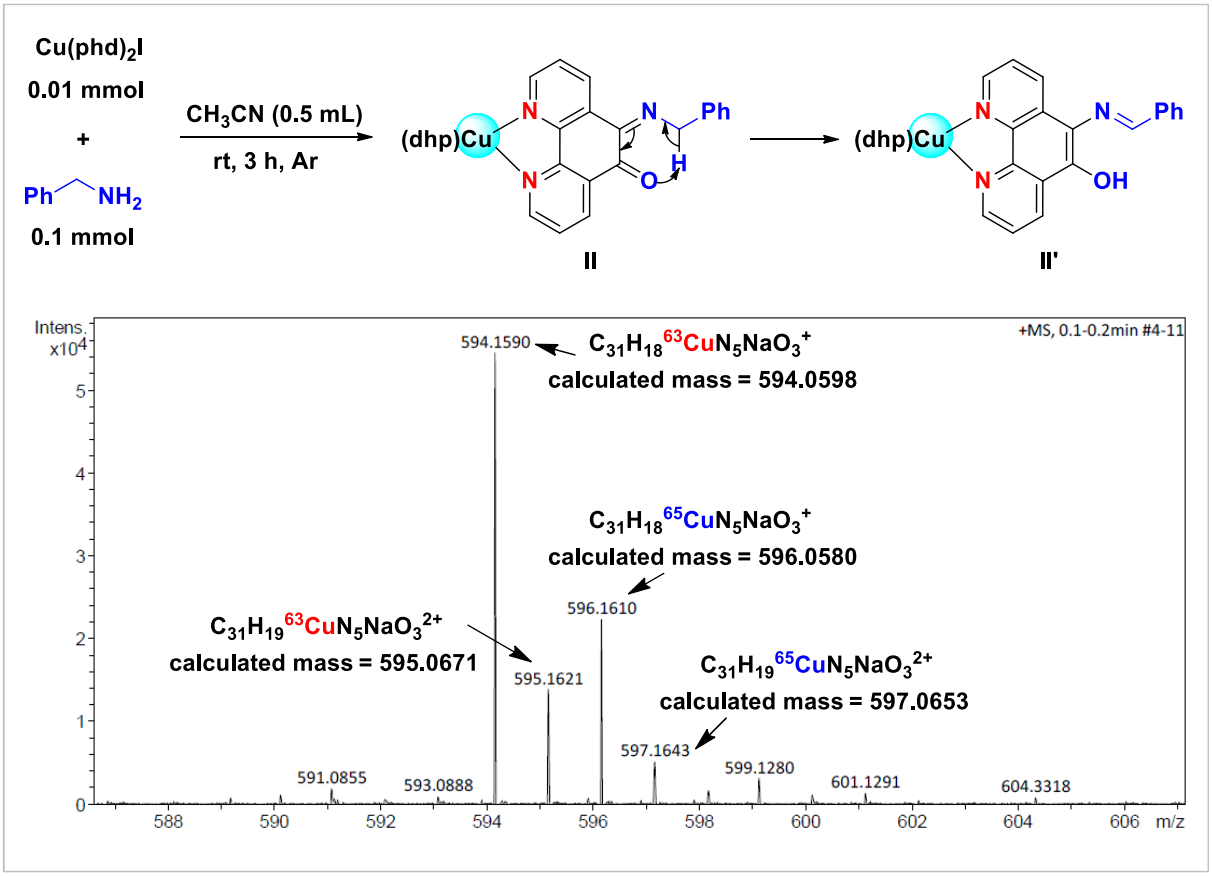
6.5 [Cu(phd)$_2$](BF$_4$)$_2$: A solution of $CuCl_2$ .2H_2O (26.9 mg, 0.2 mmol, 1.0 equiv), phen-dione (phd) (84.1 mg, 0.4 mmol, 2.0 equiv) was mixed with in (2.0 mL) ethanol solvent. Upon mixing, the solution turned green, indicative of complex formation. After the mixture was

allowed to stir for 30 min, the complex was precipitated (blue solid) by the addition of saturated aqueous NH_4BF_4 (32.6 mg, 0.2 mmol, 1.0 equiv). The complex was collected, washed with water, and dried with ether. Because this material, as well as the other complexes, adsorbed very strongly on alumina and silica gel, recrystallization from acetonitrile/ ether was used for purification. The complex was dried in vacuo for 24 h and stored in a desiccator.

7. Mechanistic studies.

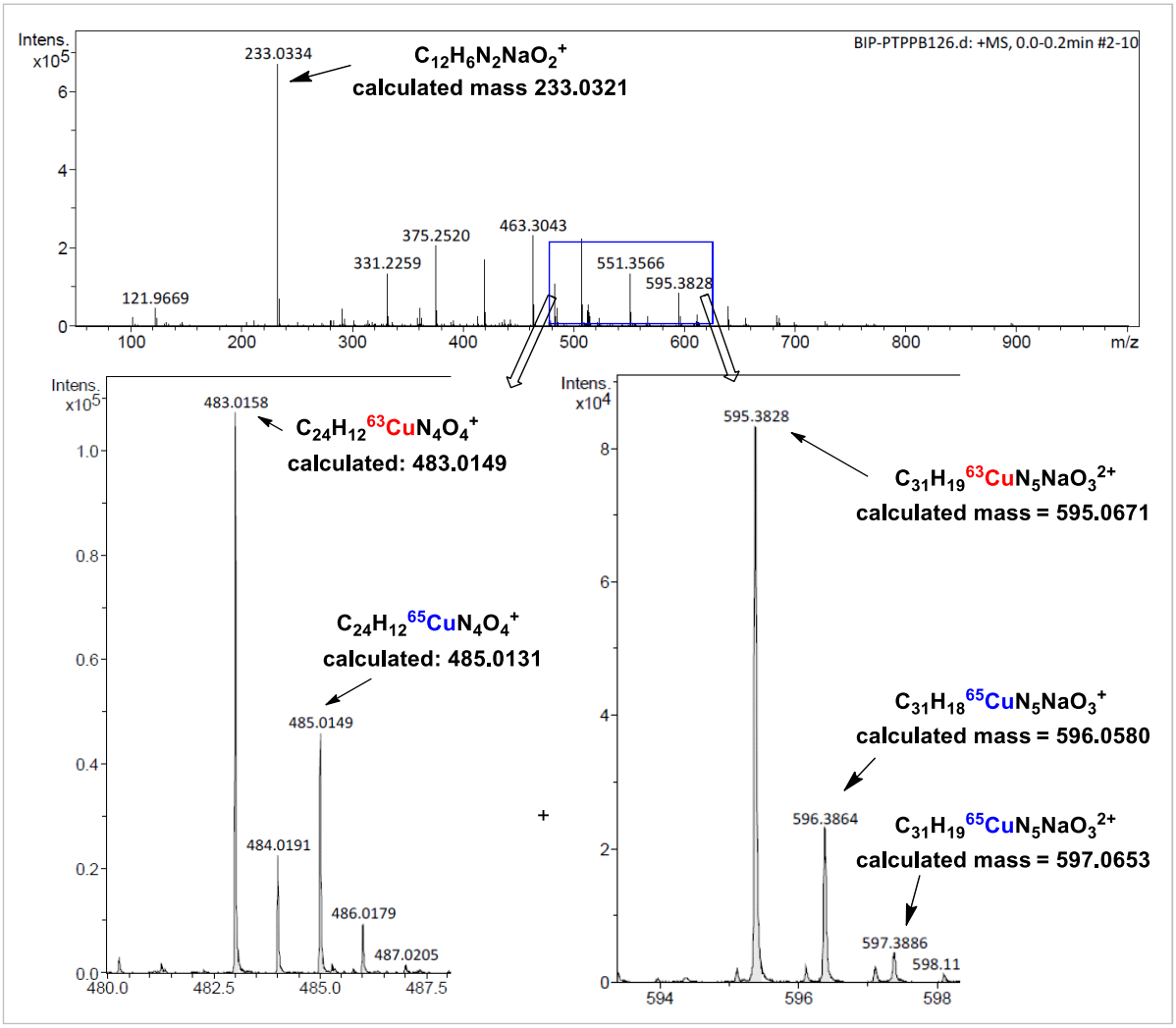
7.1 Detection of the intermediate II/II' via the reaction of $Cu(phd)_2I$ with benzyl amine.

Experimental procedure: In an oven-dried 15 mL Schlenk tube, benzylamine (11.0 mg, 0.1 mmol, 1.0 equiv) and $Cu(phd)_2I$ (4.8 mg, 0.01 mmol, 0.1equiv) were stirred in 0.5 mL of dry acetonitrile. After 3 h at room temperature; crude reaction mixture was analyzed by HRMS (ESI^+). We have observed the mass m/z = 594.0598, 595.1621, 596.0580 and 597.1643, which to the natural isotopic copper complexes of the formula $[C_{31}H_{18}{}^{63}CuN_5NaO_3]^+$, $[C_{31}H_{19}{}^{63}CuN_5NaO_3]^{2+}$, $[C_{31}H_{18}{}^{65}CuN_5NaO_3]^+$, and $[C_{31}H_{19}{}^{65}CuN_5NaO_3]^{2+}$, respectively for the isomeric intermediate **II** or **II'**.

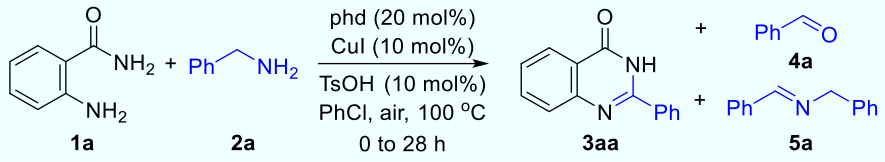


7.2 Detection of the intermediates under catalytic condition:

Experimental procedure: In an oven-dried 5 mL round bottom flask, 2-amino benzamide **1a** (13.6 mg,0.1 mmol, 1.0 equiv), benzylamine **2a** (16.0 mg, 0.15 mmol, 1.5 equiv), phd (20 mol%), CuI (10 mol%), TsOH (10 mol%) were stirred in chlorobenzene (0.5 mL) at 100 ºC under air. After 4 h, the crude reaction mixture was monitor in HRMS (ESI$^+$). We have observed the mass m/z = 233.0344 corresponds to $C_{12}H_6N_2NaO_2^+$ [phd + Na]$^+$, m/z = 483.0158, and 483.0149 corresponds to $C_{24}H_{12}{}^{63}CuN_4O_4$ [Cu(phd)$_2$]$^+$ and $C_{24}H_{12}{}^{65}CuN_4O_4$ [Cu(phd)$_2$]$^+$, respectively, and m/z = 595.3828, 596.3864 and 597.3886, which to the natural isotopic copper complexes of the formula $[C_{31}H_{19}{}^{63}CuN_5NaO_3]^{2+}$, $[C_{31}H_{18}{}^{65}CuN_5NaO_3]^+$, and $[C_{31}H_{19}{}^{65}CuN_5NaO_3]^{2+}$, respectively for the isomeric intermediate **II** or **II'**.



7.3 Kinetic monitoring of the reaction via gas chromatography:



Experimental procedure: In an oven-dried 5 mL round bottom flask, 2-amino benzamide **1a** (13.6 mg,0.1 mmol, 1.0 equiv), benzylamine **2a** (16.0 mg, 0.15 mmol, 1.5 equiv), phd (20 mol%), CuI (10 mol%), TsOH (10 mol%) and *n*-decane (0.1 mmol) were stirred in chlorobenzene (0.5 mL) at 100 ºC under air. The reaction was monitored by taking an aliquot of the reaction mixture and analyzing the distribution of the products *via* gas chromatography at specified time interval.

The same analysis was repeated in the absence of CuI.

Time (h)	[**1a**] mmol	[**2a**] mmol	[**4a**] mmol	[**5a**] mmol	[**3aa**] mmol	[**3aa**] mmol w/o CuI
0	0.1	0.15	0	0	0	0
1	0.098	0	0.004	0.07	0	0
2	0.092	0	0.002	0.072	0	0
3	0.086	0	0.009	0.072	0	0
5	0.072	0	0.011	0.068	0.002	0.0015
7	0.064	0	0.015	0.058	0.004	0.003
9	0.055	0	0.016	0.06	0.01	0.005
11	0.043	0	0.011	0.049	0.021	0.008
14	0.033	0	0.014	0.055	0.037	0.0105
17	0.02	0	0.012	0.045	0.053	0.012
19	0.009	0	0.007	0.042	0.068	0.016
22	0.002	0	0.009	0.03	0.083	0.028
25	0	0	0.007	0.027	0.087	0.042
28	0	0	0.003	0.026	0.088	0.043

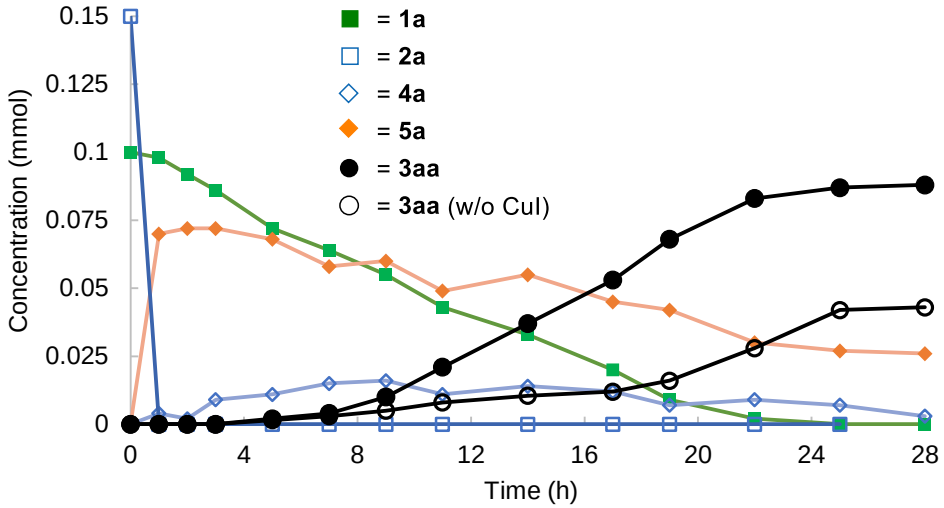
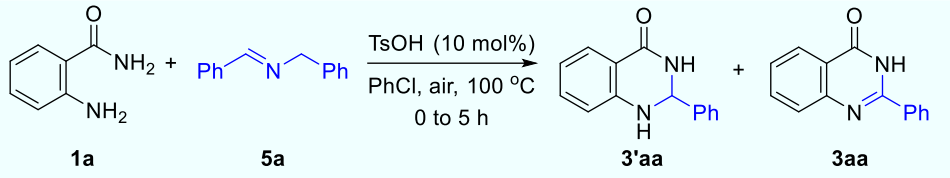


Figure S1. Kinetic monitoring of the bio-mimicking synthesis of **3aa**.

7.4 Monitoring the reaction of 1a with 5a *via* gas chromatography.



Experimental procedure: In an oven-dried 5 mL round bottom flask, 2-amino benzamide **1a** (13.6 mg, 0.1 mmol, 1.0 equiv), *N*-benzylidene-1-phenylmethanamine **5a** (29.2 mg, 0.15 mmol, 1.5 equiv), TsOH (1.7 mg, 0.010 mmol, 10 mol%), H_2O (1.0 equiv) and *n*-decane (0.1 mmol) in chlorobenzene (0.5 mL) was added at room temperature and then the mixture was placed in a preheated oil bath at 100 °C. The reaction was monitored by taking an aliquot of the reaction mixture and analyzing the distribution of the products *via* gas chromatography at specified time interval. Small amount of **3aa** (0-5%) was formed due to areal oxidation of **3'aa**. The same analysis was repeated in the presence of phd (20 mol%) and CuI (10 mol%).

Time (h)	Without CuI/phd		With CuI/phd	
	[**1a**] mmol	[**3aa** + **3'aa**] mmol	[**1a**] mmol	[**3aa** + **3'aa**] mmol
0	0.1	0	0.1	0
1	0.099	0.0027	0.0955	0.0054
2	0.087	0.0139	0.0948	0.00998
3	0.0798	0.0218	0.0926	0.01232
4	0.0794	0.0205	0.09	0.015
5	0.0786	0.0204	0.0857	0.0156

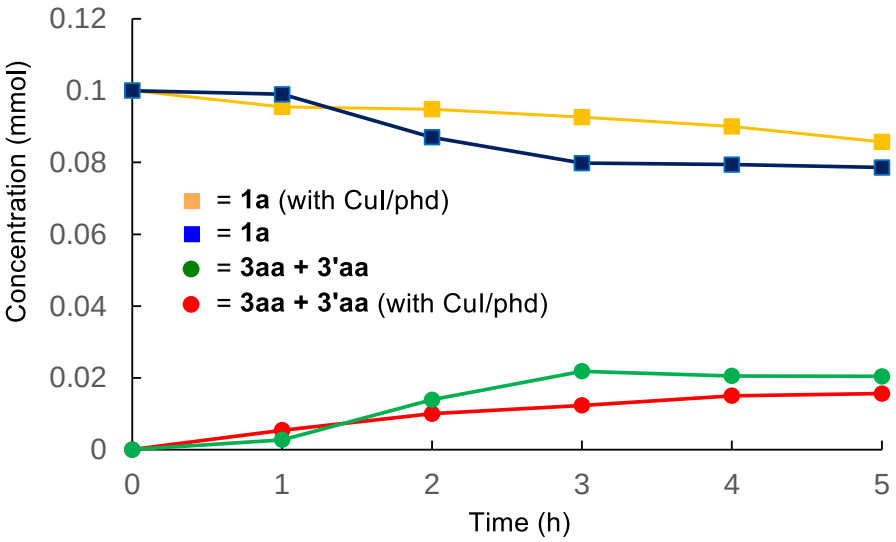
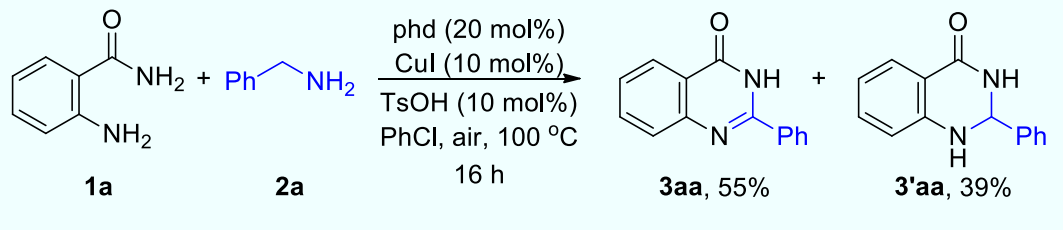


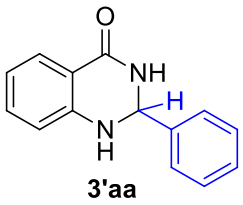
Figure S2. Kinetic monitoring of the bio-mimicking synthesis of **3aa**.

7.5 Isolation of the intermediate 3'aa.



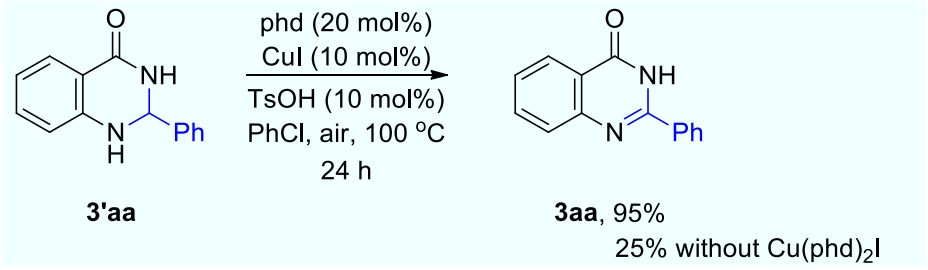
Experimental procedure: In a 5 mL round bottom flask, 2-amino benzyl amide **1a** (13.6 mg, 0.1 mmol, 1.0 equiv), CuI (1.9 mg, 0.010 mmol, 10 mol%), phd (4.2 mg, 0.020 mmol, 20 mol%), TsOH (1.7 mg, 0.010 mmol, 10 mol%), benzylamine **2a** (0.15 mmol, 1.5 equiv) were taken in chlorobenzene (0.5 mL) at room temperature in aerial condition. Then the mixture was placed in a preheated oil bath at 100 °C for 16 h. The mixture was then quenched with 2 mL water and extracted in dichloromethane (3 x 5 mL). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated. The residue was purified by column chromatography over silica gel (100-200 mesh) with hexane/ethyl acetate as eluent to obtain compound **3'aa** (8.8 mg, 39%) along with **3aa** (12.2 mg, 55%**)**.

2-phenyl-2,3-dihydroquinazolin-4(1*H*)-one (3'aa) [2]



Analytical TLC on silica gel, 8:2 hexane/ethylacetate R_f = 0.50; Yield 39% (8.8 mg, 0.039 mmol).**^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.95 (d, *J* = 7.8 Hz, 1H), 7.63 – 7.57 (m, 2H), 7.48 – 7.42 (m, 3H), 7.34 (t, *J* = 7.8 Hz, 1H), 6.91 (t, *J* = 7.6 Hz, 1H), 6.67 (d, *J* = 8.0 Hz, 1H), 5.95 (s, 1H), 5.91 (s, 1H), 4.40 (s, 1H). **^{13}C NMR (126 MHz, $CDCl_3$):**165.1, 147.4, 138.8, 134.2, 130.3, 129.3, 128.9, 127.6, 119.9, 115.8, 114.8, 69.3. **IR (neat / cm^{-1}):** 3436, 3305, 2922, 2850, 1653, 747, 698, 665.

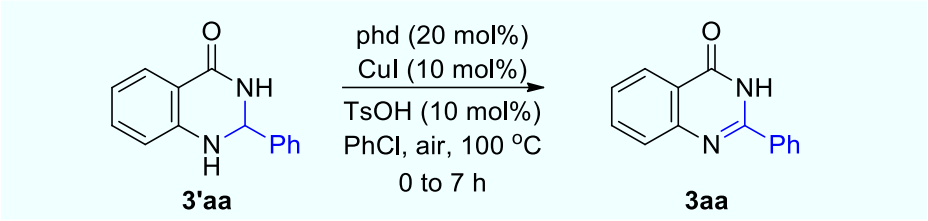
7.6 Oxidation of the intermediate 3'aa to 3aa.



Experimental procedure: In a 5 mL round bottom flask, the intermediate **3'aa** (22.4 mg, 0.1 mmol, 1.0 equiv), CuI (1.9 mg, 0.010 mmol, 10 mol%), phd (4.2 mg, 0.020 mmol, 20 mol%), TsOH (1.7 mg, 0.010 mmol, 10 mol%) were taken in chlorobenzene (0.5 mL) at room temperature in aerial condition. Then the mixture was placed in a preheated oil bath at 100 °C for 24 h. The mixture was then quenched with 2 mL water and extracted in dichloromethane (3 x 5 mL). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated. The residue was purified by column chromatography over silica gel (100-200 mesh) with hexane/ethyl acetate as eluent to obtain **3aa** (21.3 mg, 95%**)**.

On the other hand, in the absence of CuI/phd catalyst system **3aa** was isolated in 5.6 mg, 25% yield.

7.7 **Kinetics of the oxidation of the intermediate 3'aa to 3aa.**



Experimental procedure: In a 5 mL round bottom flask, the intermediate **3'aa** (22.4 mg, 0.1 mmol, 1.0 equiv), CuI (1.9 mg, 0.010 mmol, 10 mol%), phd (4.2 mg, 0.020 mmol, 20 mol%), TsOH (1.7 mg, 0.010 mmol, 10 mol%), and *n*-decane (0.1 mmol) were taken in chlorobenzene (0.5 mL) at room temperature in aerial condition. Then the mixture was placed in a preheated oil bath at 100 °C. The reaction was monitored by taking an aliquot of the reaction mixture and analyzing the distribution of the products via gas chromatography at specified time interval.

The same analysis was repeated in the presence of phd (20 mol%) and CuI (10 mol%).

Time (h)	**3aa** (mmol) in the presence of phd/CuI	**3aa** (mmol) in the absence of phd/CuI
0	0	0
1	0.008	0
2	0.014	0.002
3	0.02	0.003
4	0.026	0.0042
5	0.033	0.006
6	0.0385	0.0071
7	0.044	0.008

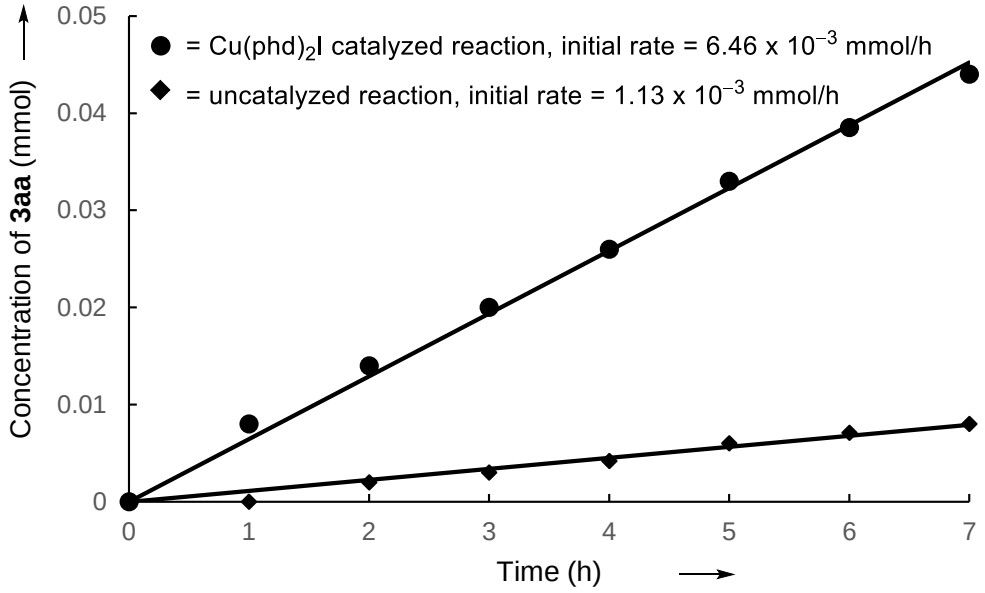
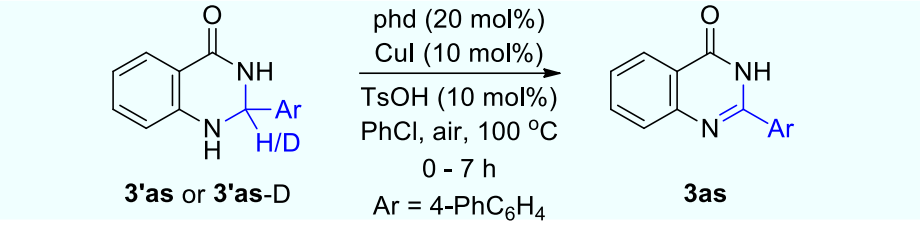


Figure S3. Kinetics of the oxidation of the intermediate **3'aa** to **3aa**.

7.8 Determination of the kinetic isotope effect.



Experimental procedure: In a 5 mL round bottom flask, the intermediate 2-([1,1'-biphenyl]-4-yl)-2,3-dihydroquinazolin-4(1H)-one **3'as** (30.0 mg, 0.1 mmol, 1.0 equiv), CuI (1.9 mg, 0.010 mmol, 10 mol%), phd (4.2 mg, 0.020 mmol, 20 mol%), TsOH (1.7 mg, 0.010 mmol, 10 mol%), and *n*-decane (0.1 mmol) were taken in chlorobenzene (0.5 mL) at room temperature in aerial condition. Then the mixture was placed in a preheated oil bath at 100 °C. The reaction was monitored by taking an aliquot of the reaction mixture and analyzing the products via gas chromatography at specified time interval.

The same analysis was repeated deuterium isotopologue **3'as**-D (30.1 mg, 0.1 mmol).

The KIE = k_H/k_D = 1.73 was determined from the initial rates of such reaction.

Time (h)	**3as** (mmol) from **3'as**	**3as** (mmol) from **3'as**-D
0	0	0
1	0.005	0.0015
2	0.009	0.004
3	0.0125	0.0065
4	0.017	0.009
5	0.0205	0.0115
6	0.024	0.0145
7	0.0278	0.017

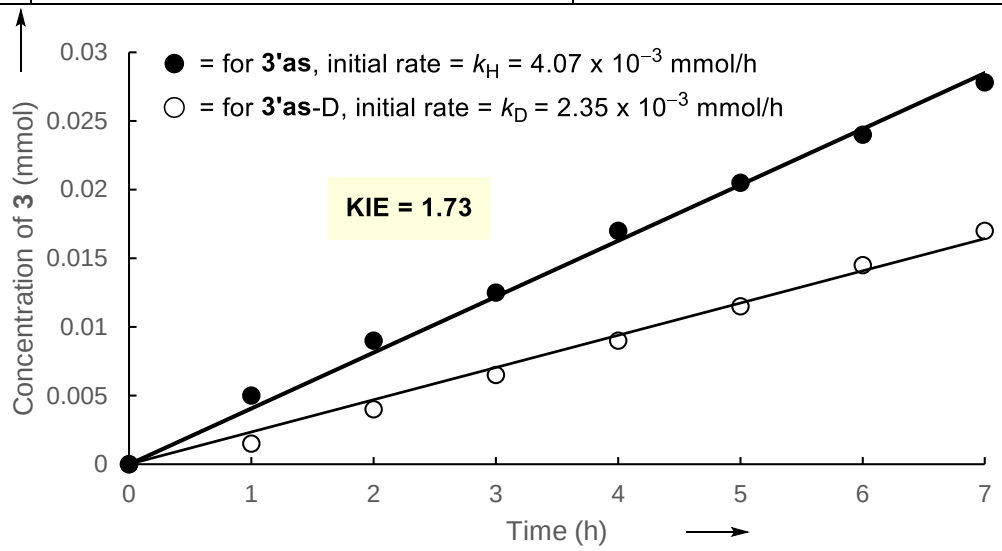
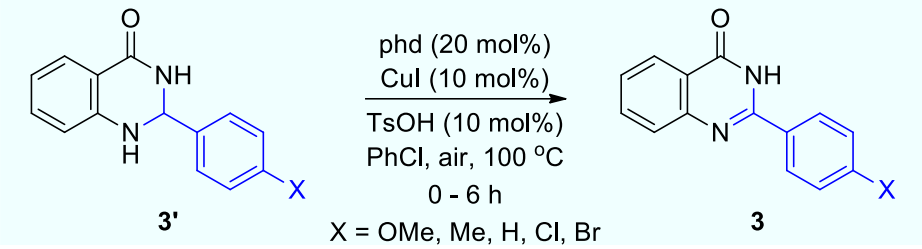


Figure S4. Determination of the kinetic isotope effect.

7.9 Hammett correlation study.



Experimental procedure: In five different 5 mL round bottom flask, **3'af** (X = OMe), **3'ad** (X = Me), **3'aa** (X = H), **3'al** (X = Cl), and **3'am** (X = Br) (0.1 mmol) were taken. Then, CuI (1.9 mg, 0.010 mmol, 10 mol%), phd (4.2 mg, 0.020 mmol, 20 mol%), TsOH (1.7 mg, 0.010 mmol, 10 mol%), *n*-decane (0.1 mmol), and chlorobenzene (0.5 mL) were added at room temperature. The mixture was then placed in a preheated oil bath at 100 °C. The reactions were monitored by taking an aliquot of the reaction mixture and analyzing the products via gas chromatography at specified time interval.

Initial rates were determined. The plot of $\log(k_X/k_H)$ against the Hammett substituent constants σ was found to be linear indicating the applicability of the Hammett linear-free-energy relationship. The slope of such linear plot gave the ρ = -0.16.

Time (h)	**3'af** (mmol) X = OMe	**3'ad** (mmol) X = Me	**3'aa** (mmol) X = H	**3'al** (mmol) X = Cl	**3'am** (mmol) X = Br
0	0	0	0	0	0.007
1	0.009	0.0085	0.008	0.0072	0.0123
2	0.0155	0.015	0.014	0.0128	0.0185
3	0.022	0.021	0.02	0.019	0.024
4	0.029	0.028	0.026	0.025	0.031
5	0.038	0.038	0.033	0.032	0.035
6	0.042	0.04	0.0385	0.036	0.007

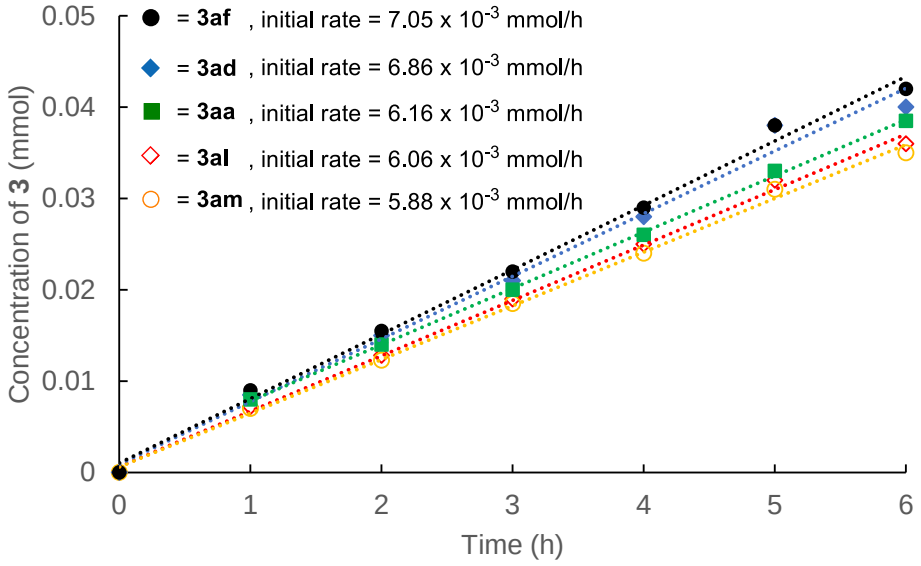


Figure S5. Determination of the initial rates for the oxidation of the intermediate **3'**.

Hammett analysis

	3'af (mmol) X = OMe	**3'ad** (mmol) X = Me	**3'aa** (mmol) X = H	**3'al** (mmol) X = Cl	**3'am** (mmol) X = Br
Initial rates k_X	7.05×10^{-3}	6.86×10^{-3}	6.16×10^{-3}	6.06×10^{-3}	5.88×10^{-3}
σ	–0.27	–0.17	0	0.23	0.23
log (k_X/k_H)					

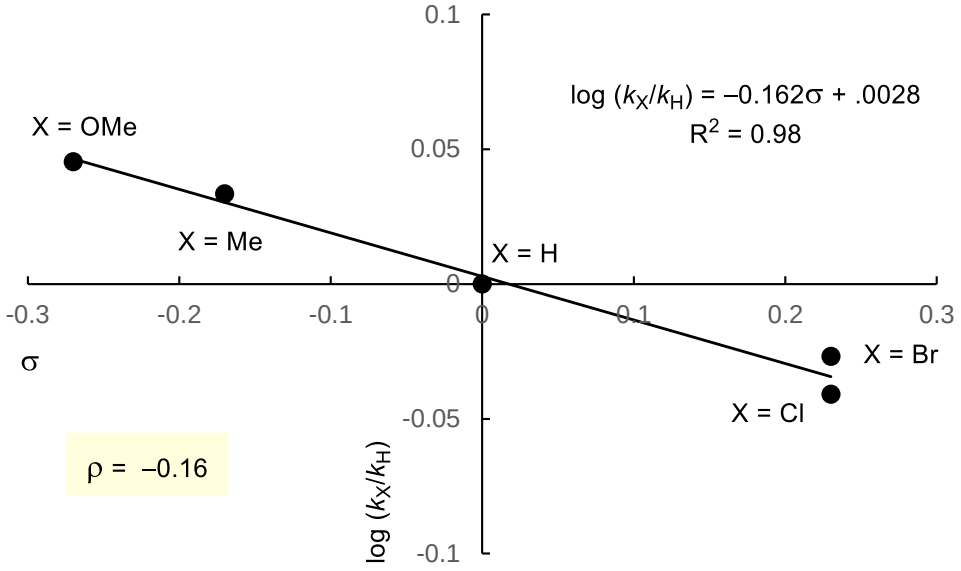


Figure S6. Hammett correlation study.

7.10 Cyclic voltammetry Studies

Experimental procedure: Cyclic Voltammetry of **Cu(phd)$_2^+$**, **3'aa**, and mixture of (**Cu(phd)$_2^+$** complex and **3'aa**) was performed using a CHI760D workstation at a scan rate of 0.1 V/s in acetonitrile with 0.1 M tetrabutylammonium tetrafluoroborate as supporting electrolyte. Polished glassy carbon, platinum wire and Ag/AgCl (0.01 M KCl) were used as the working, counter, and reference electrodes, respectively. To convert the potentials from Ag/AgCl (0.1 M KCl) to SCE, ferrocene was measured under the above conditions into acetonitrile (3 mL), and 0.11 mV were added from the measured values. The **Cu(phd)$_2^+$** and **3'aa** was added into acetonitrile (3 mL) respectively. The solutions stirred 15 mins, and carried the respective experiments. As showed in Figure, the oxidation potential peak of **Cu(phd)$_2^+$** (E = 0.35 V vs SCE in CH_3CN), **3'aa** (E = 1.22 V vs SCE in CH_3CN), and mixture of (**Cu(phd)$_2^+$** complex and **3'aa**)$^+$ was (E = 0.37, and 1.20 V vs SCE in CH_3CN), respectively.

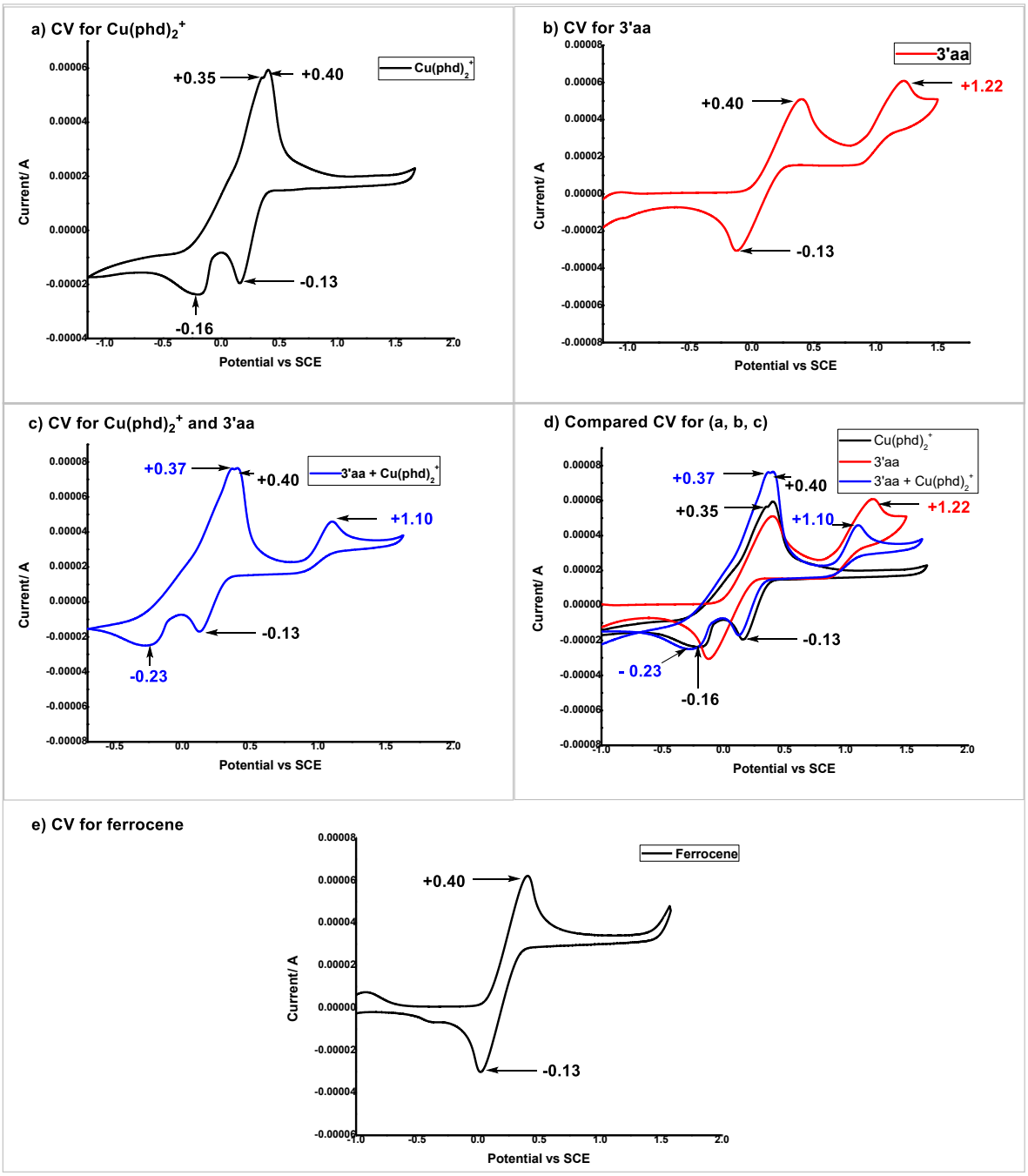


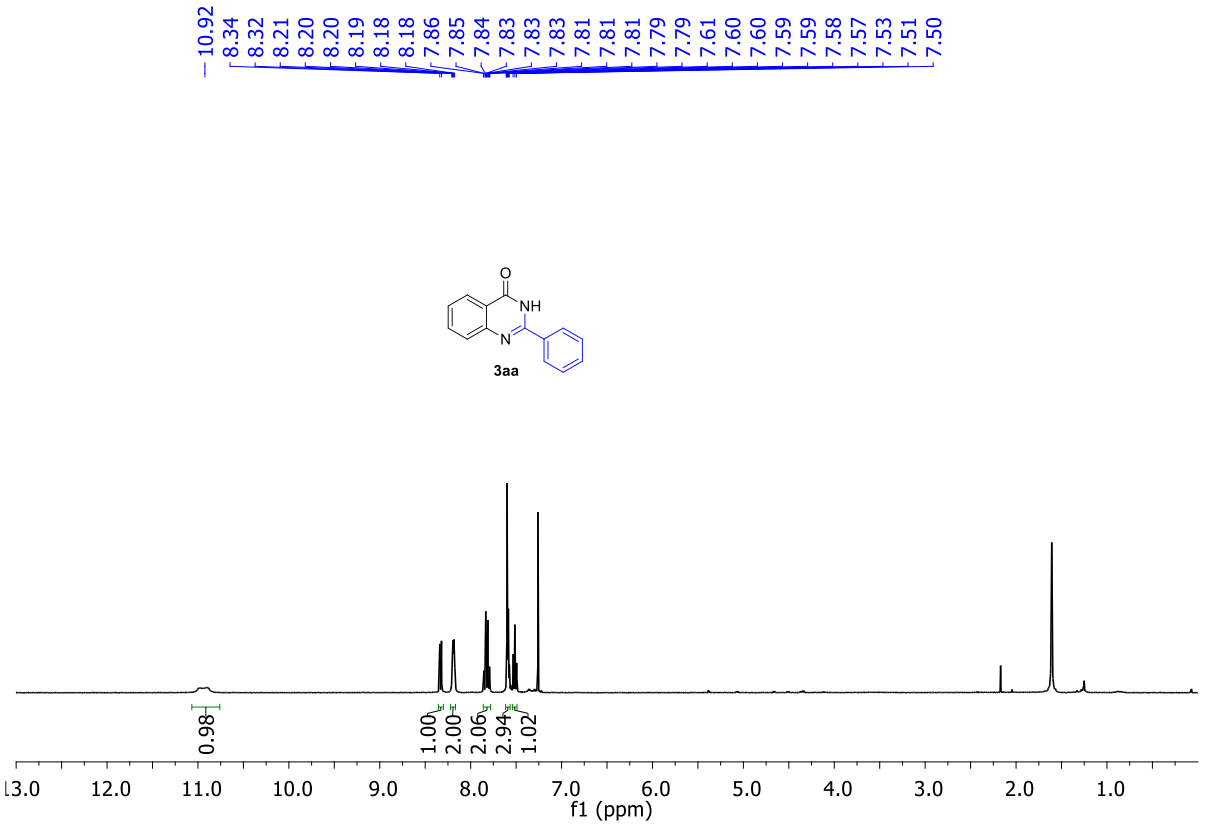
Figure S7. Cyclic voltammograms graph: (a) **Cu(phd)**$_2^+$ complex, (b) **3'aa,** (c) Mixture of (**Cu(phd)**$_2^+$ complex and **3'aa**), and (d) Comparison plot with ferrocene as an internal standard. CV of ferrocene is shown in plot (e).

8. References:

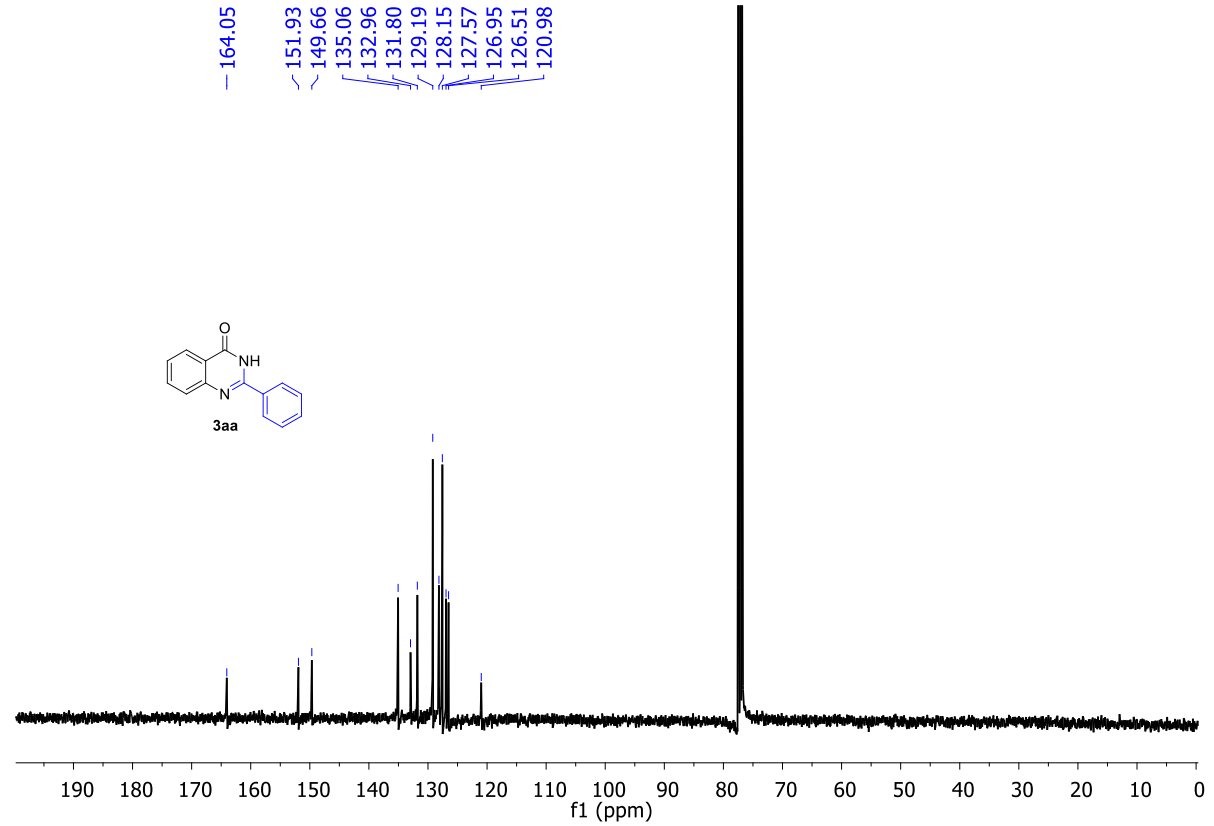
1. (a) M. J. Mphahlele, M. M. Maluleka and T. A. Khoza, *Bull. Chem, Soc. Ethiop,*, 2014, **28**, 81; (b) L. Long, Y. H. Wang, J. X. Zhuo, Z. C. Tu, R. Wu, M. Yan, Q. Liu and G. Lu, *Eur. J. Med. Chem.*, 2018, **157**, 1361-1375; (c) M. J. Mphahlele, H. K. Paumo, L. Rhyman and P. Ramasami, *Molecules*, 2015, **20**, 14656-14683; (d) M. S. Hamasharif, O. E. P. Smith, C. J. Curran and K. Hemming, *ACS Omega*, 2017, **2**, 1222-1231; (e) M. Novanna, S. Kannadasan and P. Shanmugam, *Dyes and Pigments*, 2020, **174**, 108015; (f) H. K. Paumo, M. J. Mphahlele, L. Rhyman and P. Ramasami, *Tetrahedron*, 2016, **72**, 123-133.
2. Y. Hu, L. Chen and B. Li, *RSC Adv.*, 2016, **6**, 65196-65204.
3. S. Das, S. Sinha, D. Samanta, R. Mondal, G. Chakraborty, P. Brandao and N. D. Paul, *J. Org. Chem.*, 2019, **84**, 10160-10171.
4. K. M. Khan, S. M. Saad, N. N. Shaikh, S. Hussain, M. I. Fakhri, S. Perveen, M. Taha and M. I. Choudhary, *Bioorg. Med. Chem.*, 2014, **22**, 3449-3454.
5. M. T. Alam, S. Maiti and P. Mal, *Beilstein J Org Chem*, 2018, **14**, 2396-2403.
6. M. Abdullaha, S. Mohammed, M. Ali, A. Kumar, R. A. Vishwakarma and S. B. Bharate, *J. Org. Chem.*, 2019, **84**, 5129-5140.
7. (a) S. Fu, L. Wang, H. Dong, J. Yu, L. Xu and J. Xiao, *Tetrahedron Lett.*, 2016, **57**, 4533-4536; (b) T. K. Mukhopadhyay, C. L. Rock, M. Hong, D. C. Ashley, T. L. Groy, M.-H. Baik and R. J. Trovitch, *J. Am. Chem. Soc.*, 2017, **139**, 4901-4915.
8. S. Pan and T. Shibata, *ACS Catal.*, 2013, **3**, 704-712.
9. Y. Wu, Y.-Q. Chen, T. Liu, M. D. Eastgate and J.-Q. Yu, *J. Am. Chem. Soc.*, 2016, **138**, 14554-14557.
10. A. S. Karpe, P. A. Sathe, P. Patil, B. N. Patil and A. C. Chaskar, *Tetrahedron Lett.*, 2019, **60**, 1526-1529.
11. K. Gobis, H. Foks, J. Sławin´ski, E. Augustynowicz-Kopec´ and A. Napio´rkowska, *Monatsh Chem.*, 2013, **144**, 1197–1203.
12. (a) T. S. Eckert and T. C. Bruice, *J. Am. Chem. Soc.*, 1983, **105**, 4431-4441; (b) A. E. Wendlandt and S. S. Stahl, *J. Am. Chem. Soc.*, 2014, **136**, 506-512; (c) C. A. Goss and H. D. Abruna, *Inorg. Chem.*, 1985, **24**, 4263-4267.

9. Copies of NMR spectra.

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



^{13}C NMR (101 MHz, $CDCl_3$):



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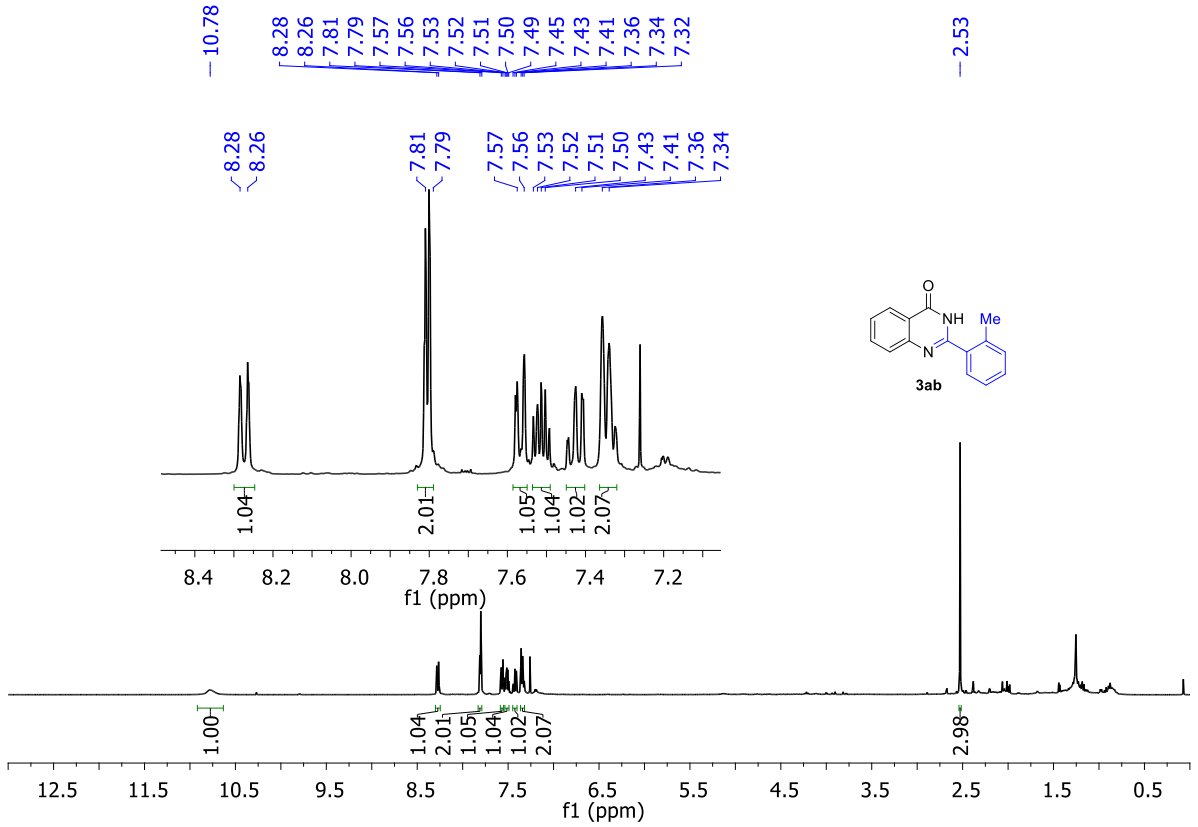

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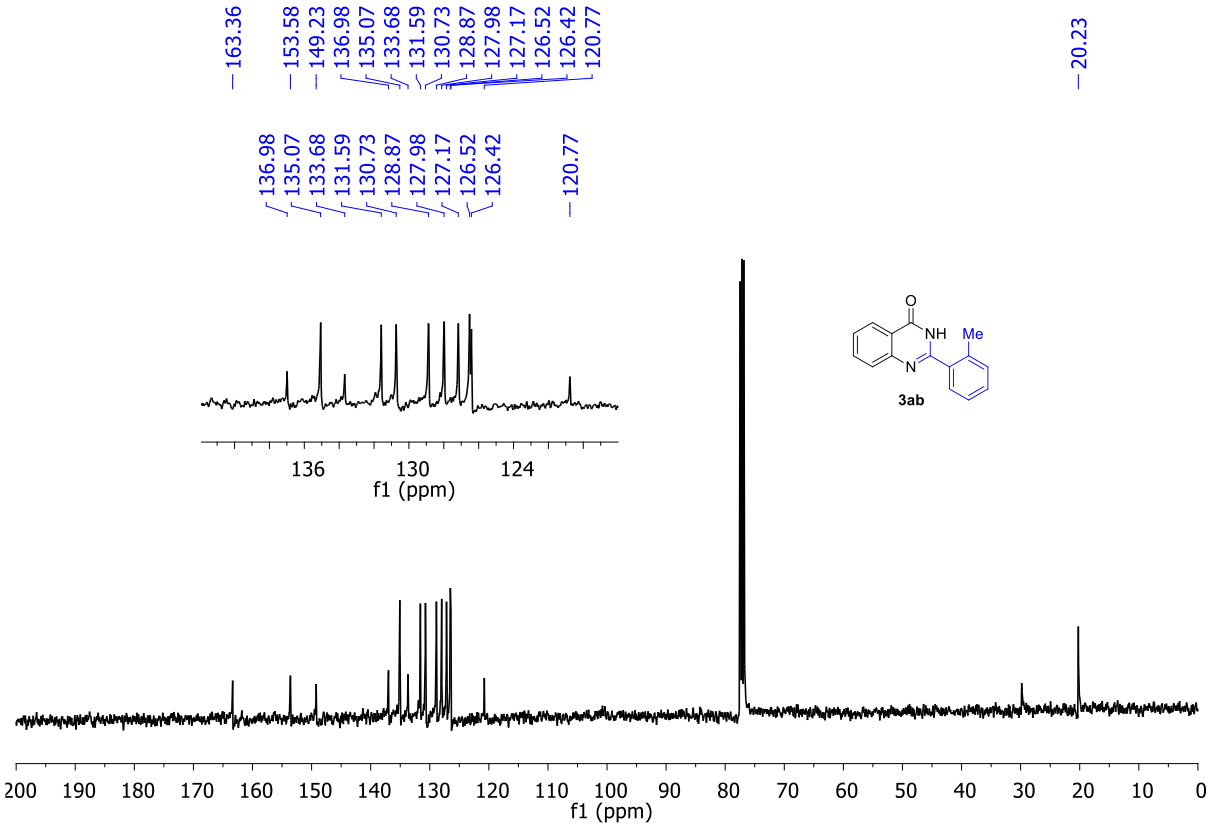

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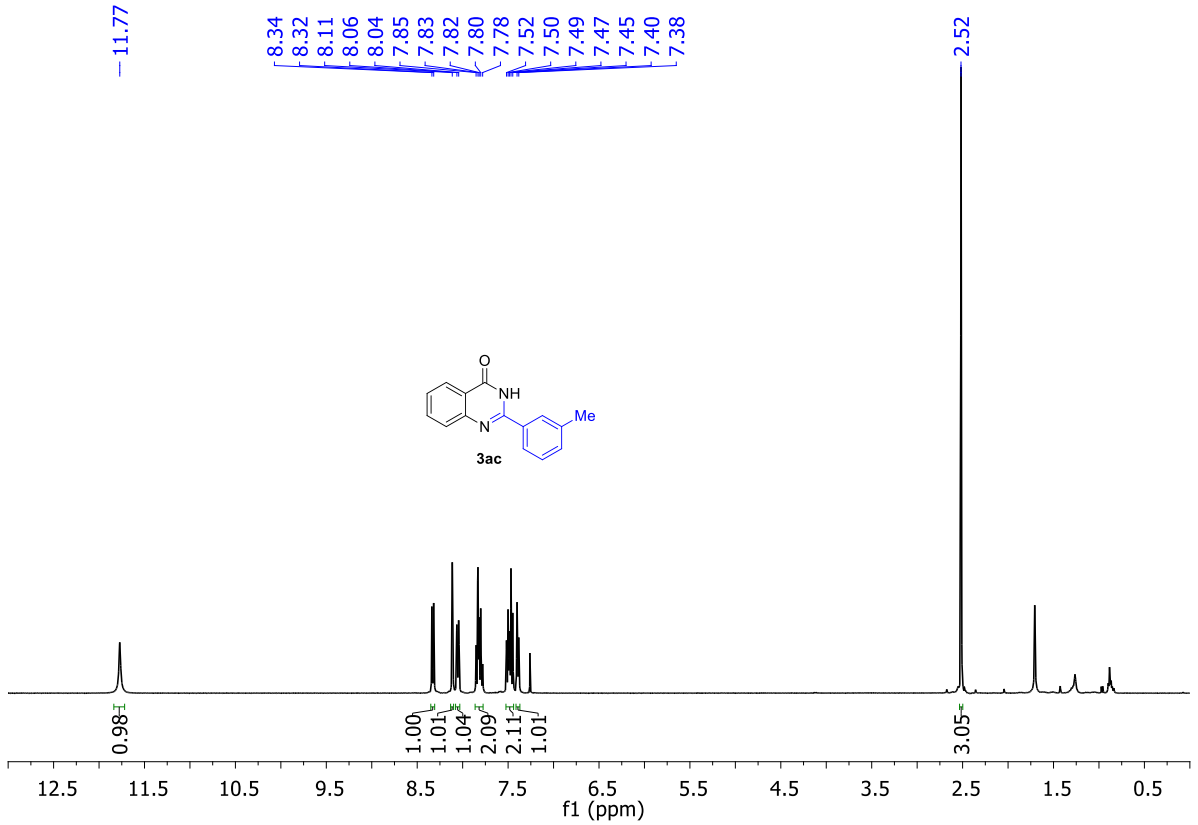

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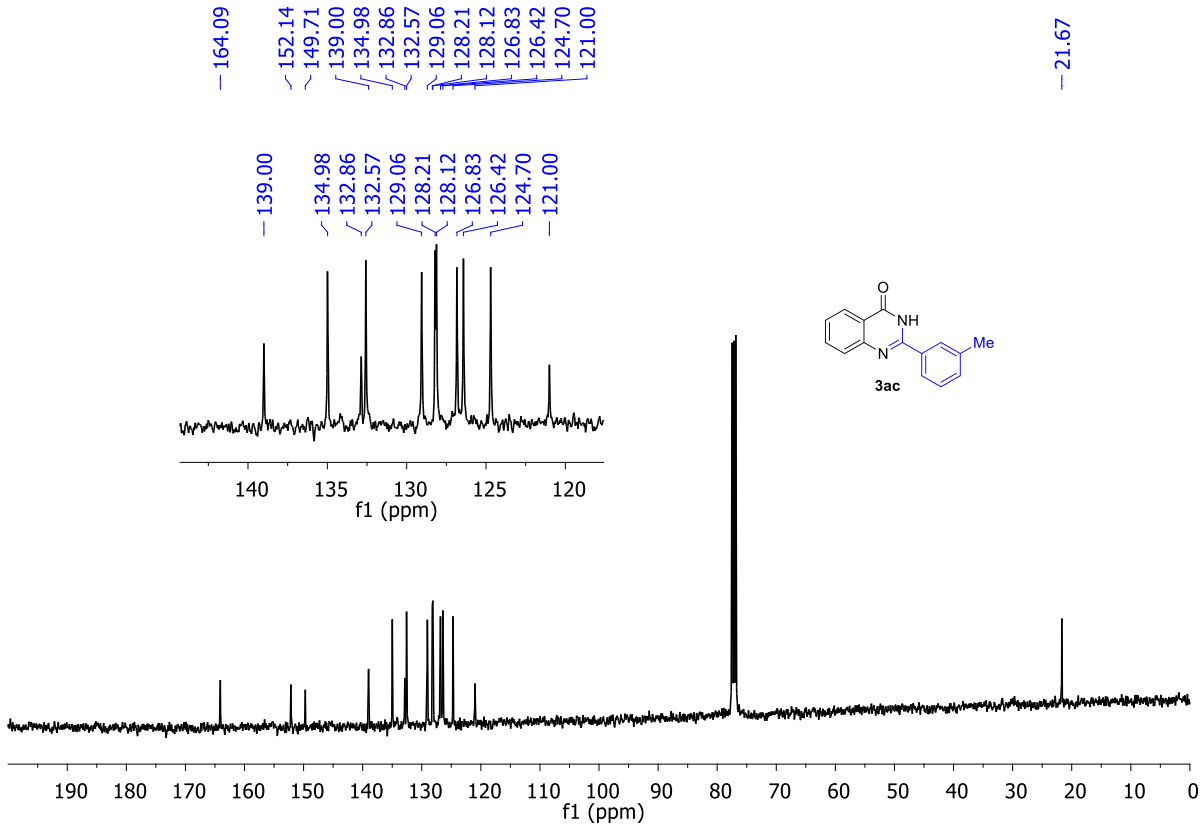

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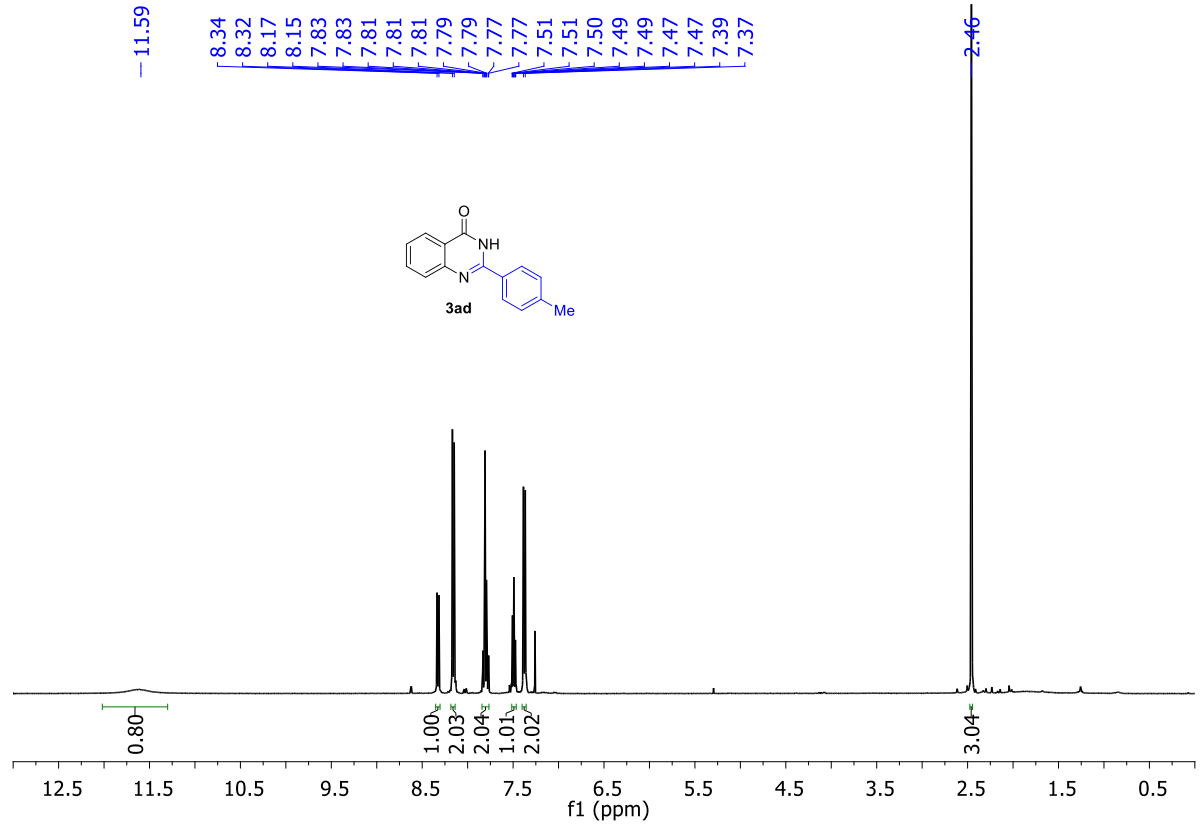
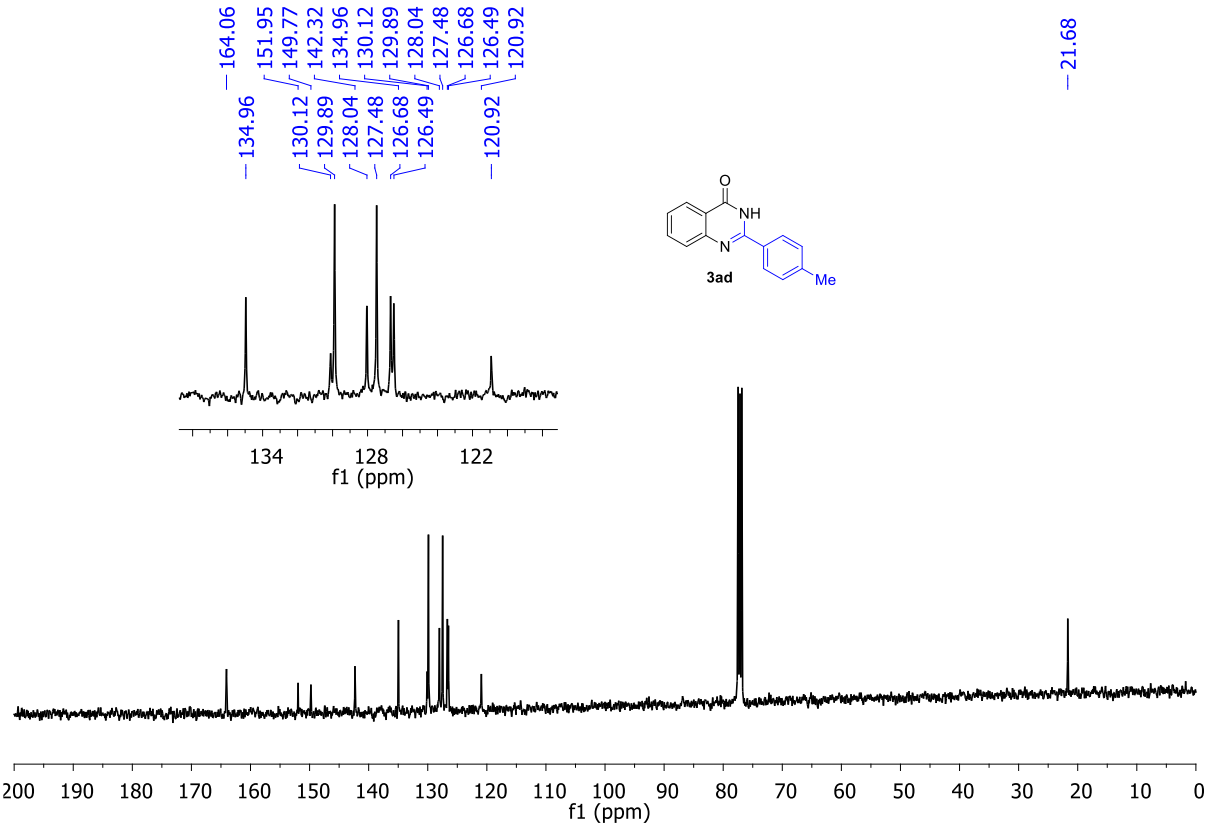
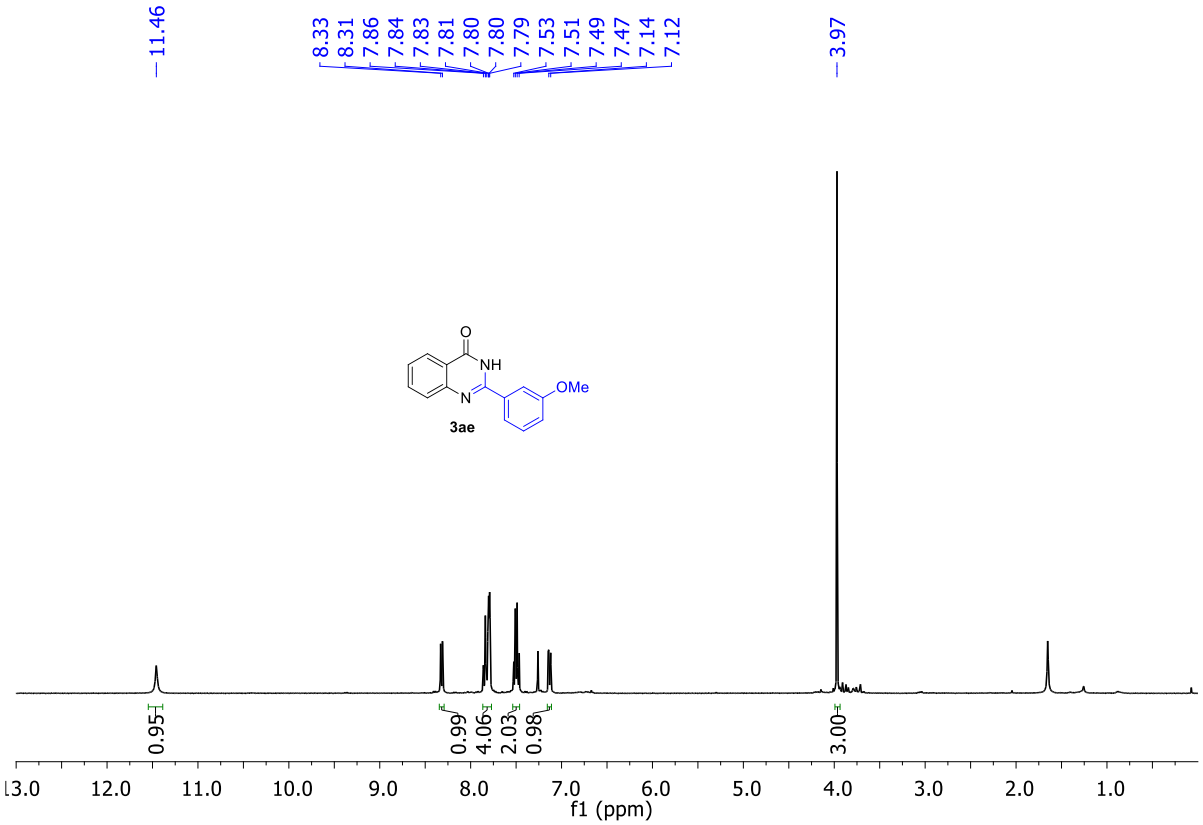


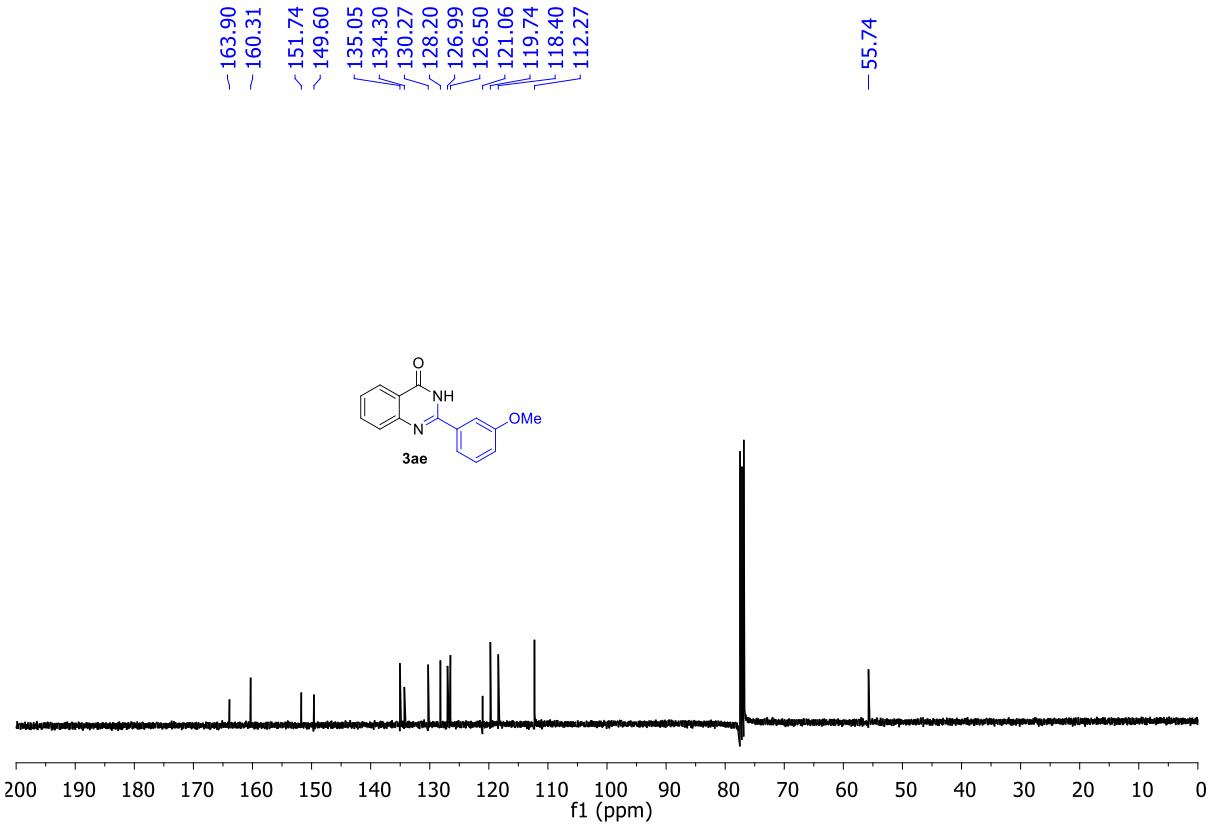
^{13}C NMR (101 MHz, $CDCl_3$):



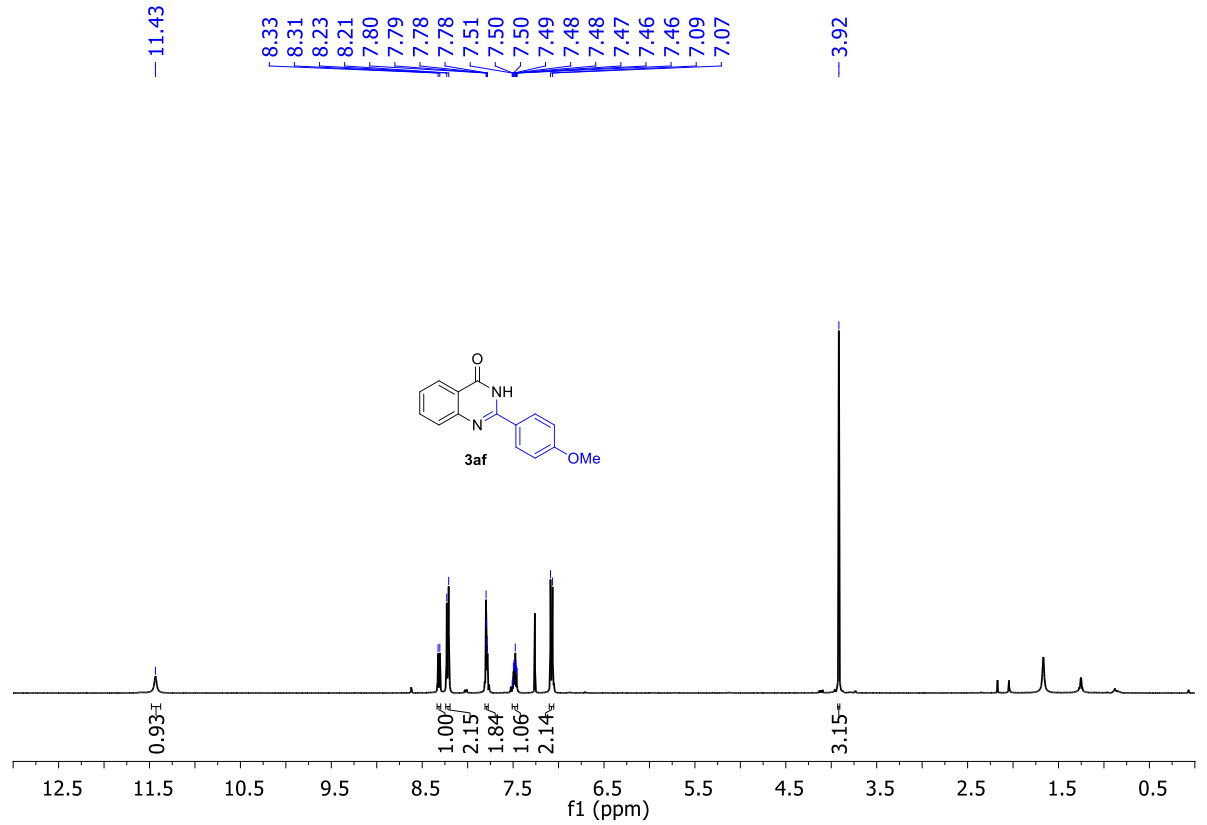
^{1}H NMR (400 MHz, $CDCl_3$):



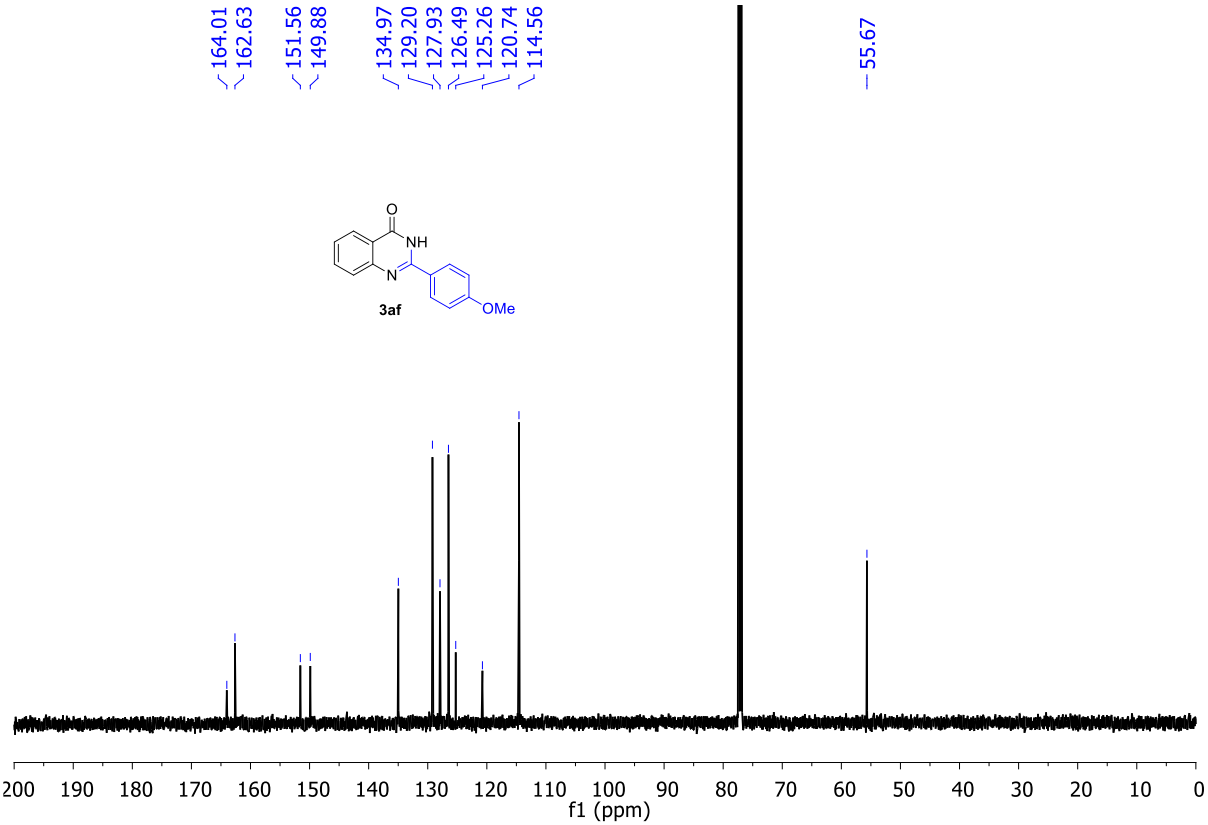
^{13}C NMR (101 MHz, $CDCl_3$):



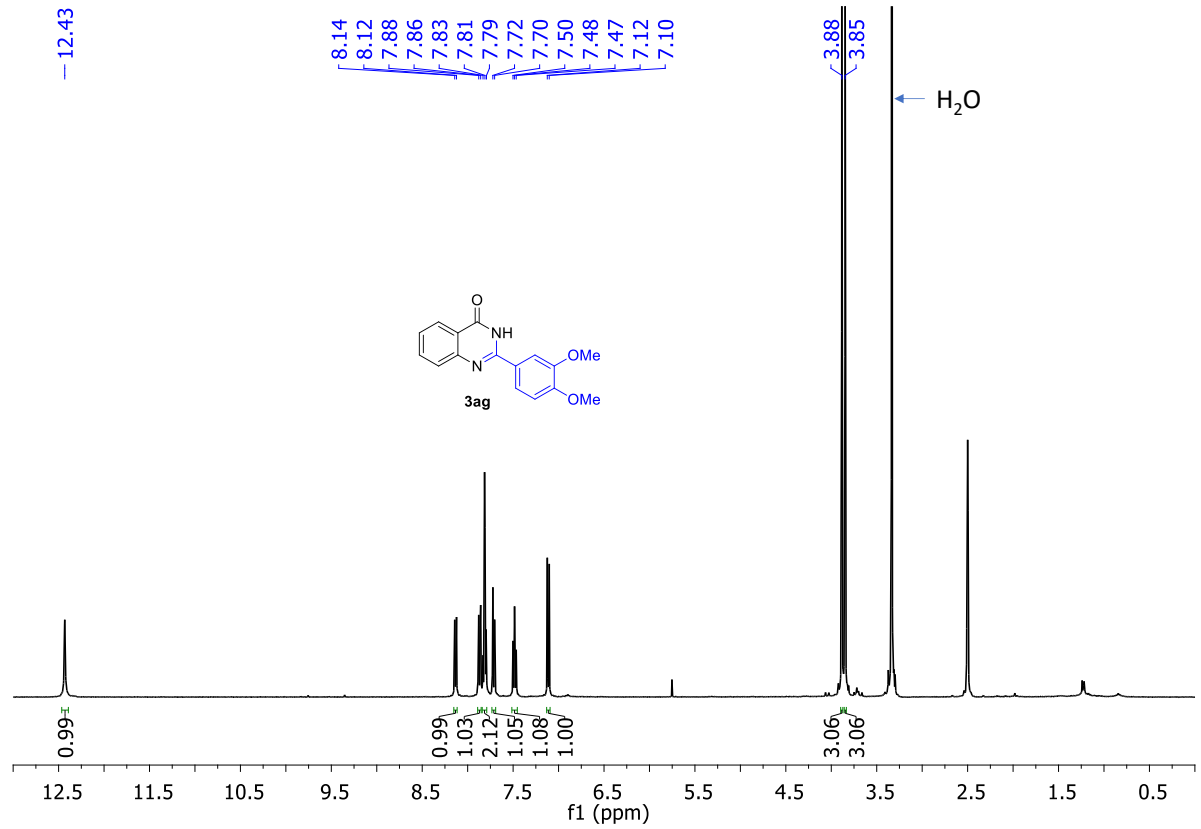
^{1}H NMR (400 MHz, $CDCl_3$):



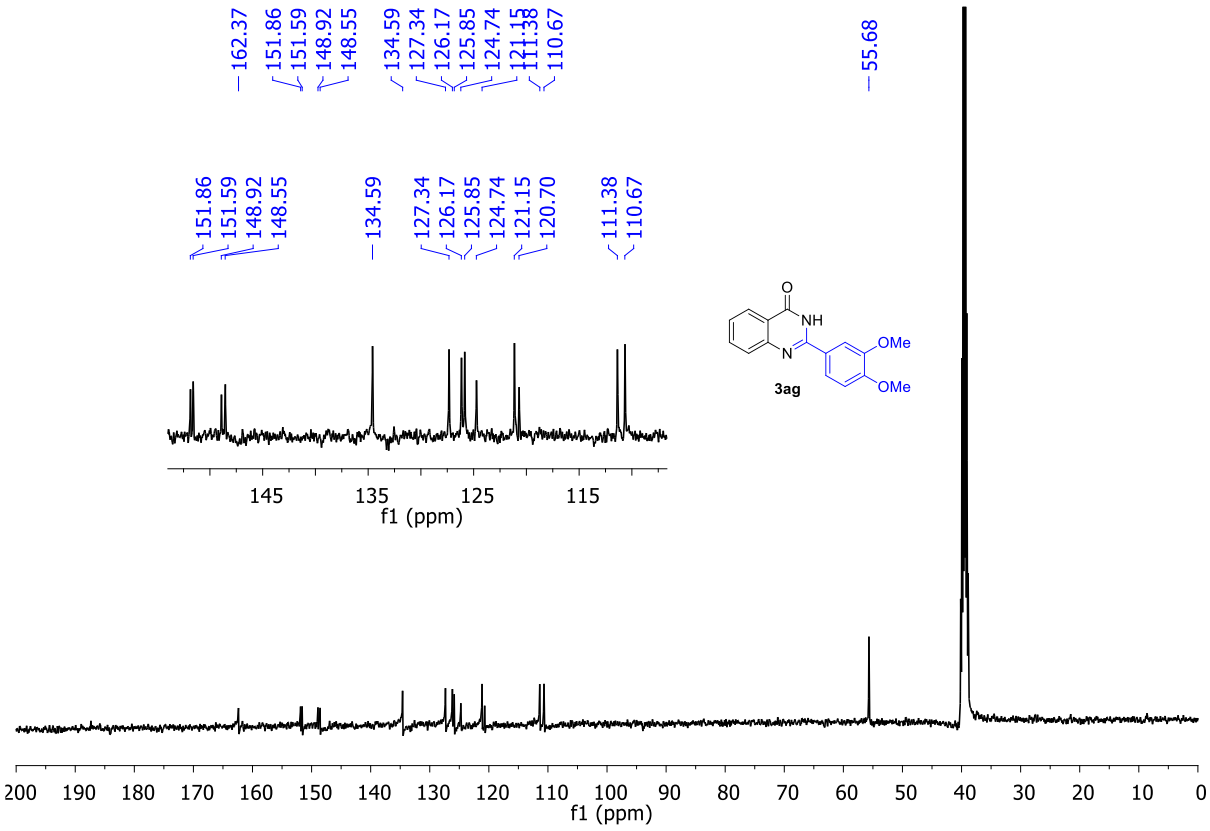
^{13}C NMR (126 MHz, $CDCl_3$):



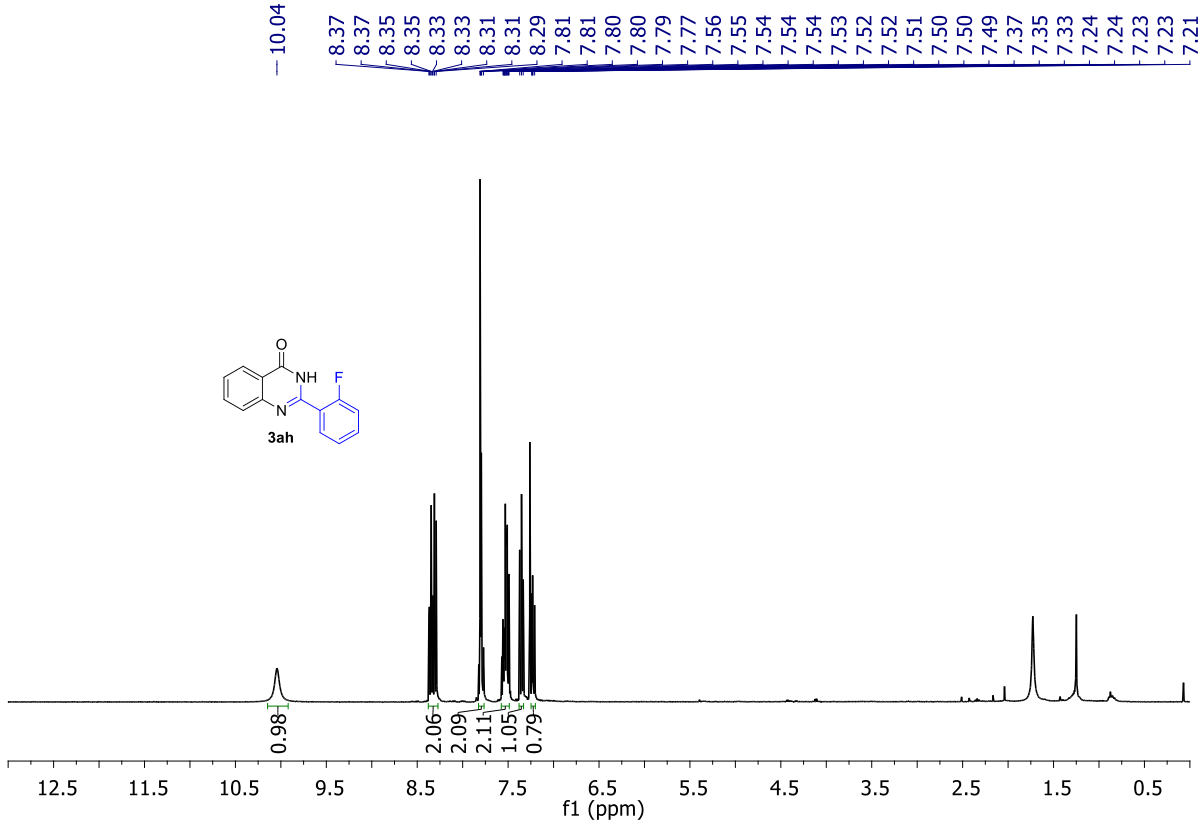
^{1}H NMR (400 MHz, DMSO-D6):



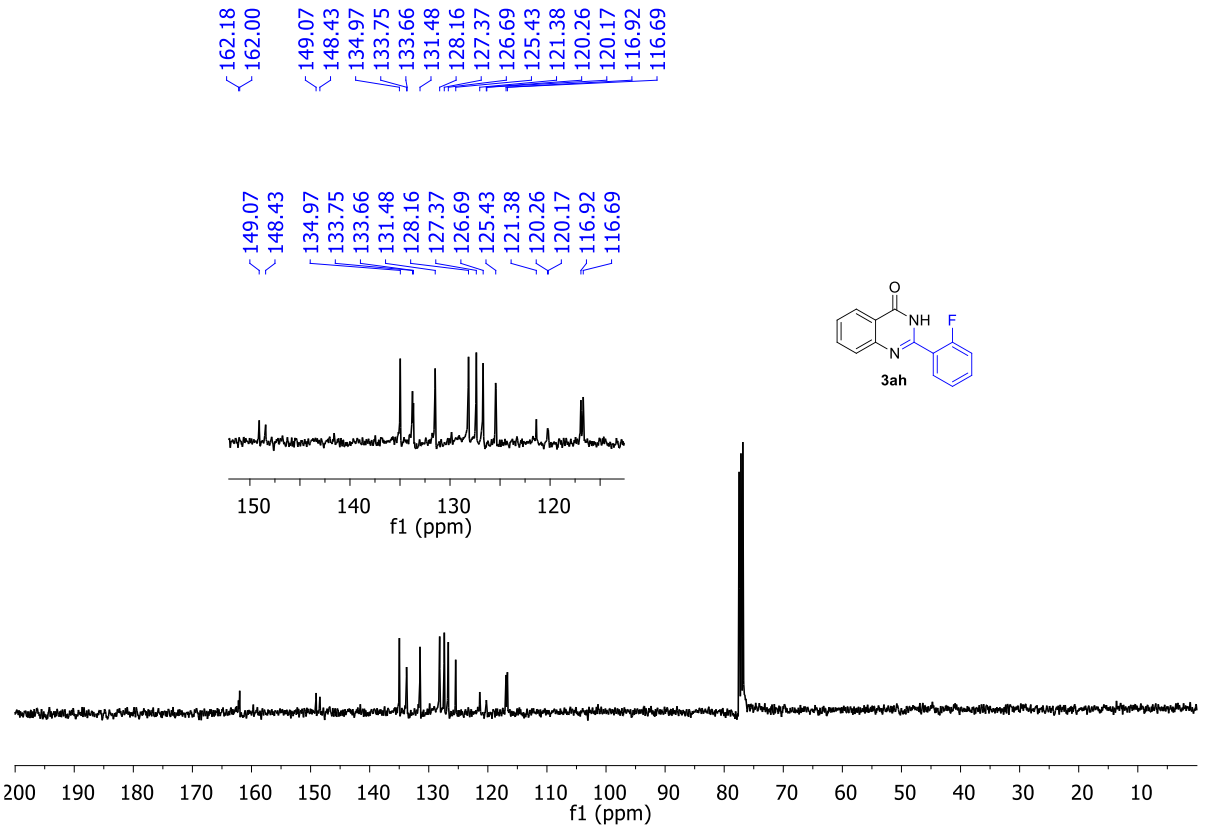
^{13}C NMR (101 MHz, DMSO-D6):



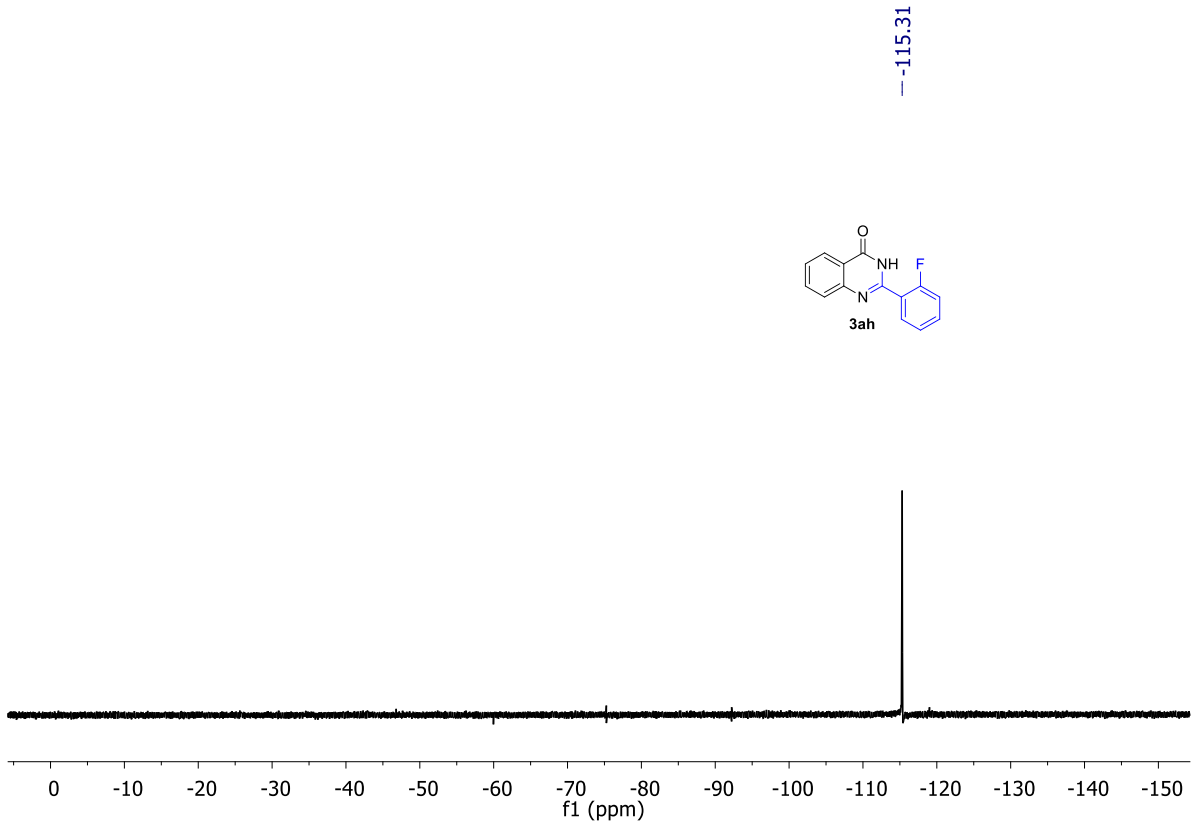
^{1}H NMR (400 MHz, $CDCl_3$):



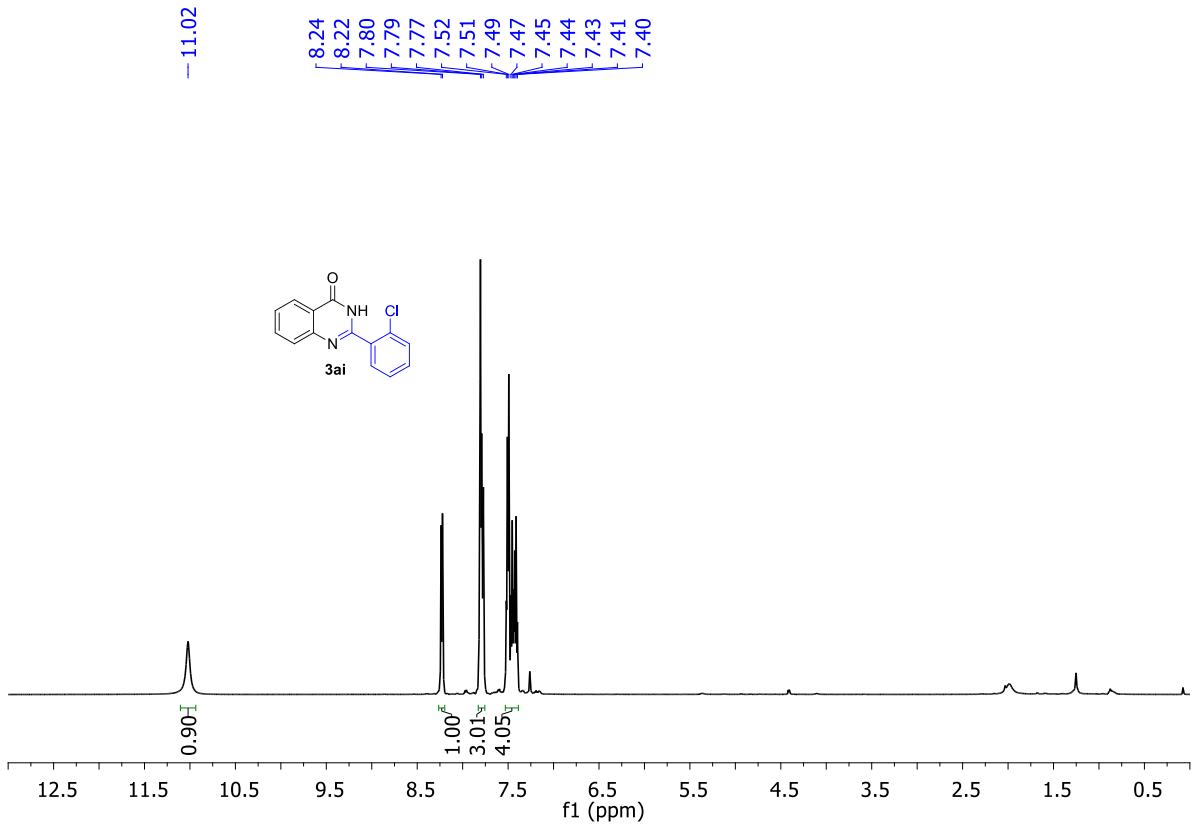
^{13}C NMR (101 MHz, $CDCl_3$):



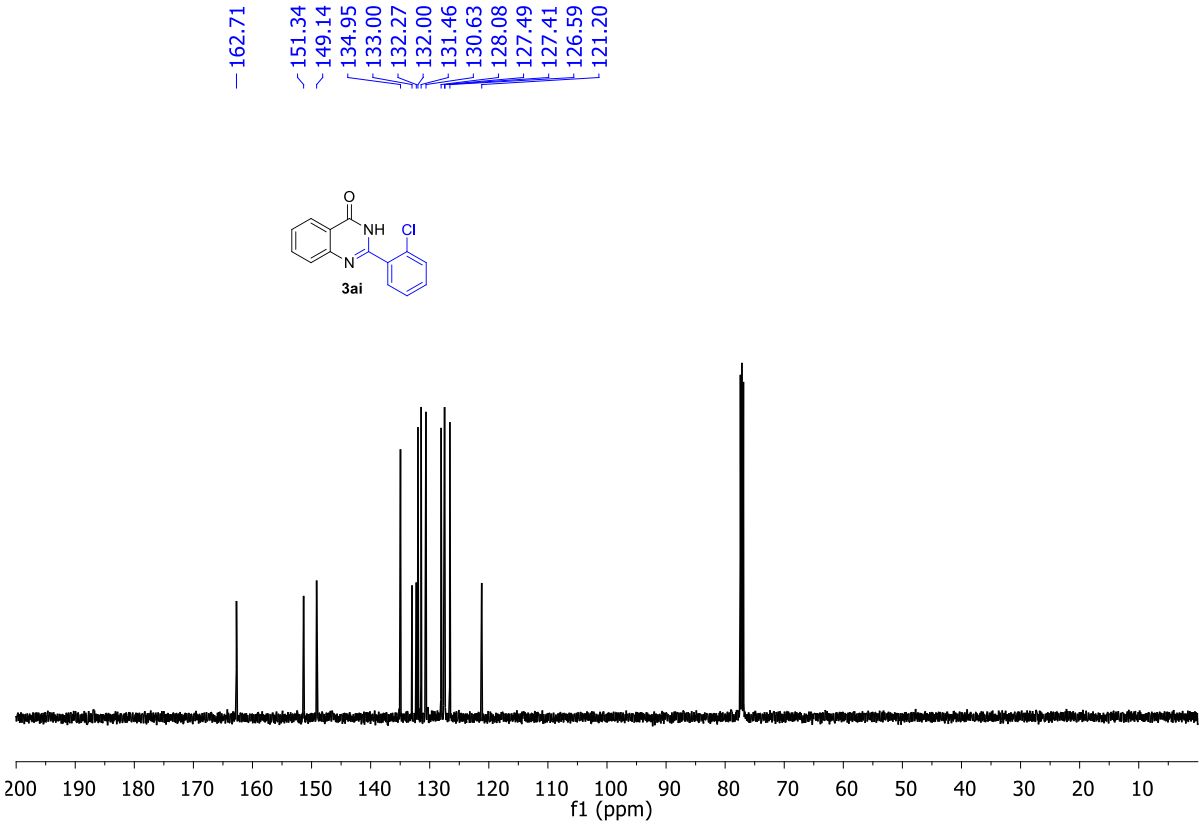
^{19}F NMR (376 MHz, $CDCl_3$):



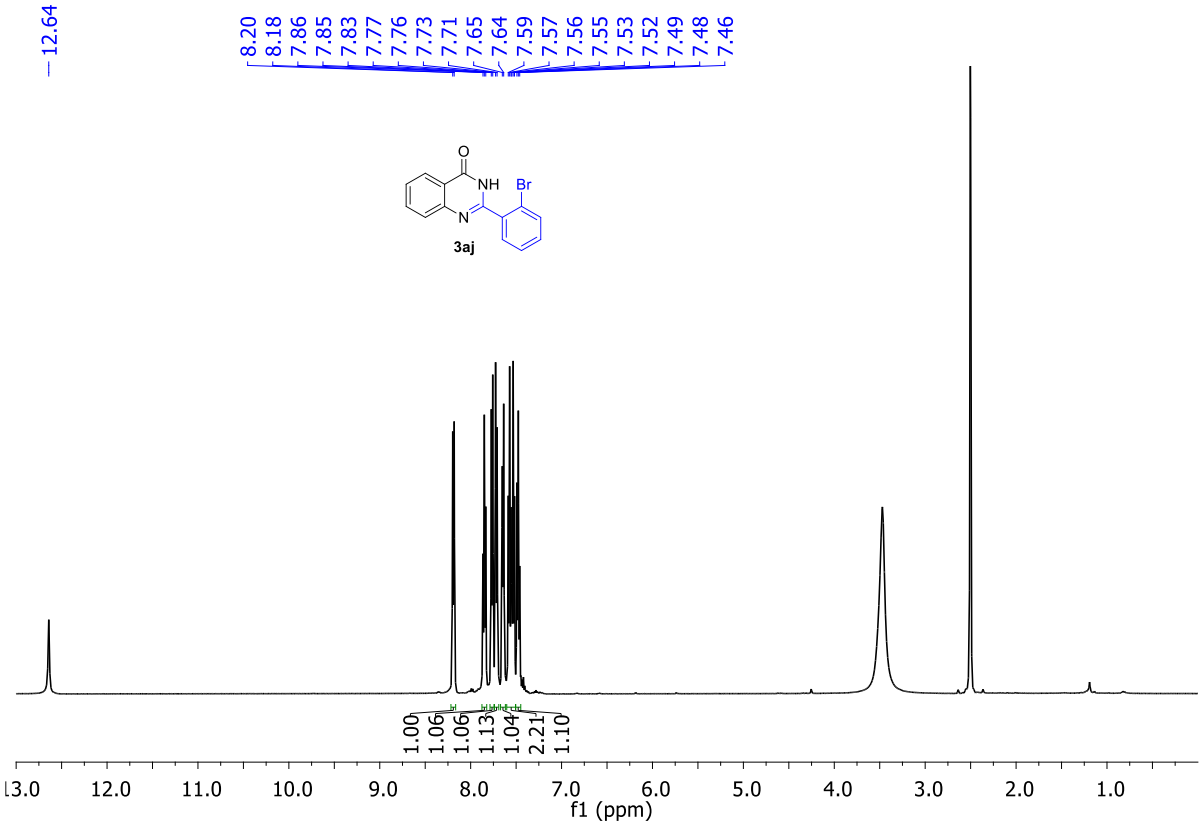
^{1}H NMR (500 MHz, $CDCl_3$):



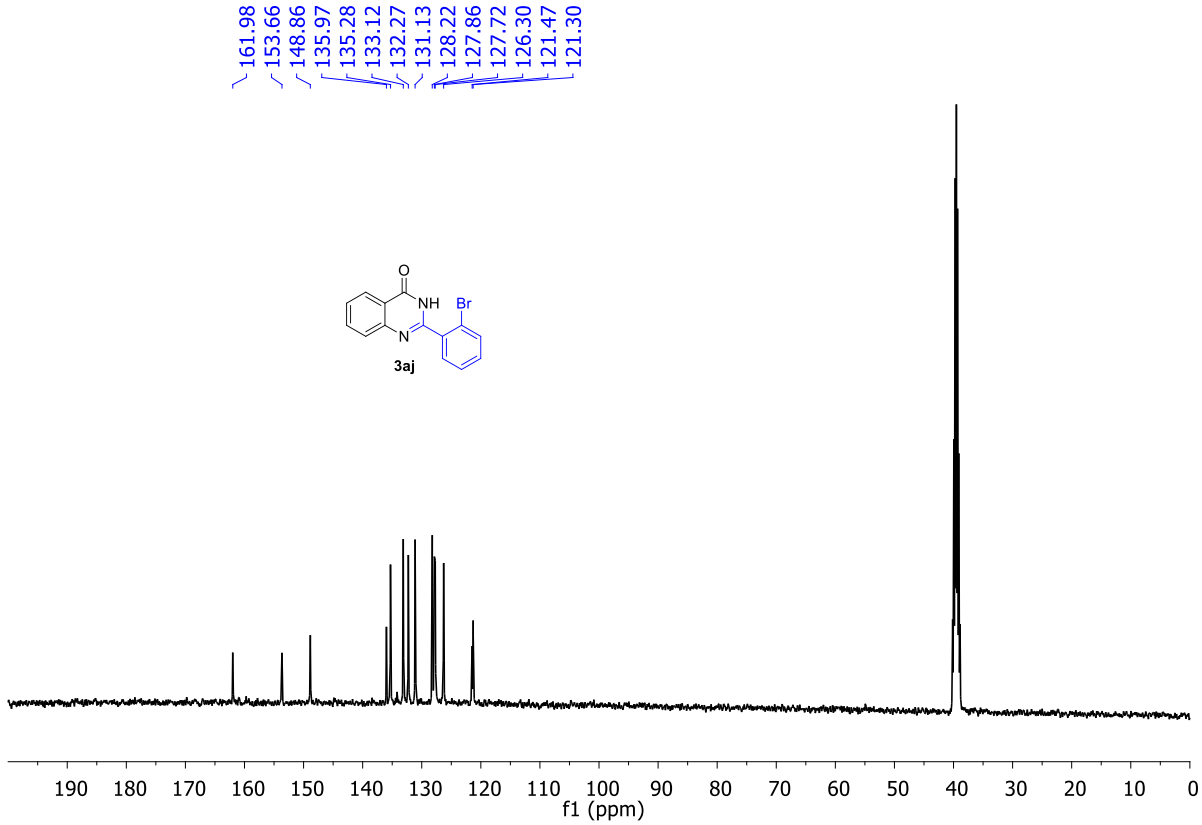
^{13}C NMR (125 MHz, $CDCl_3$)



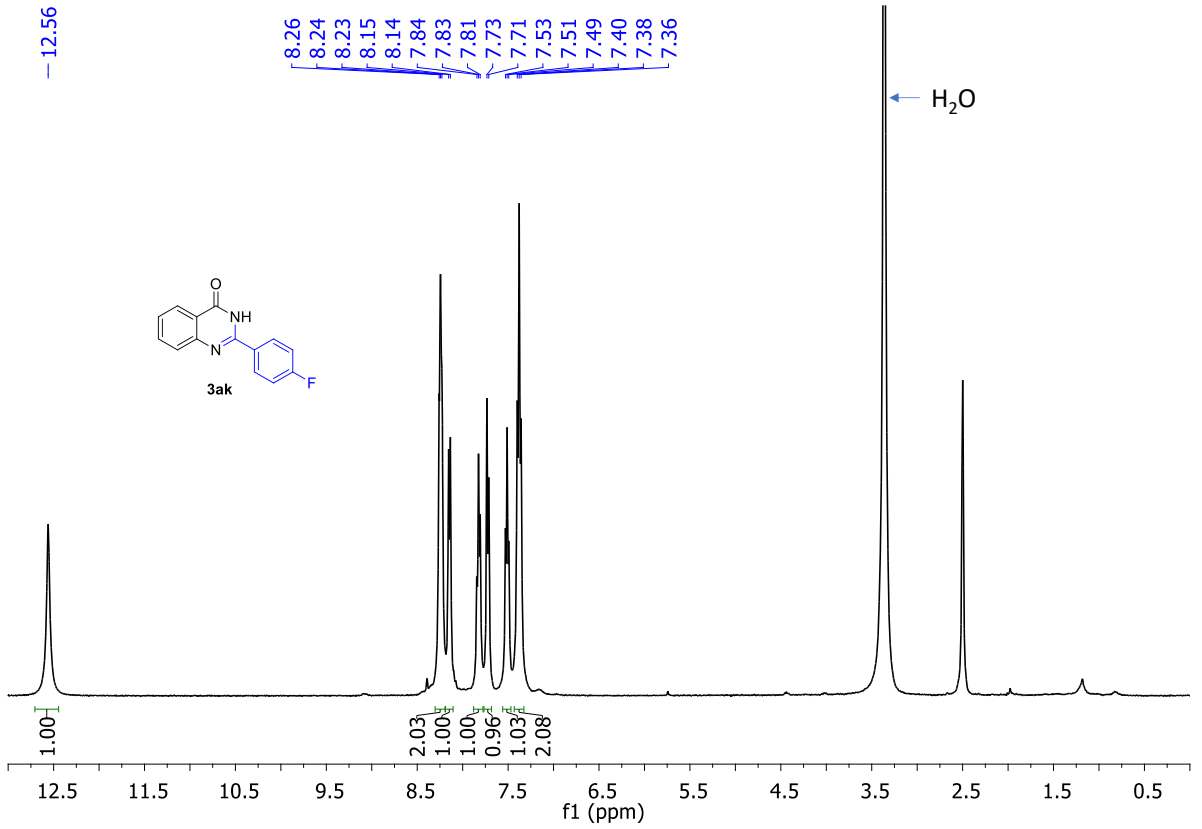
^{1}H NMR (500 MHz, DMSO-D6):



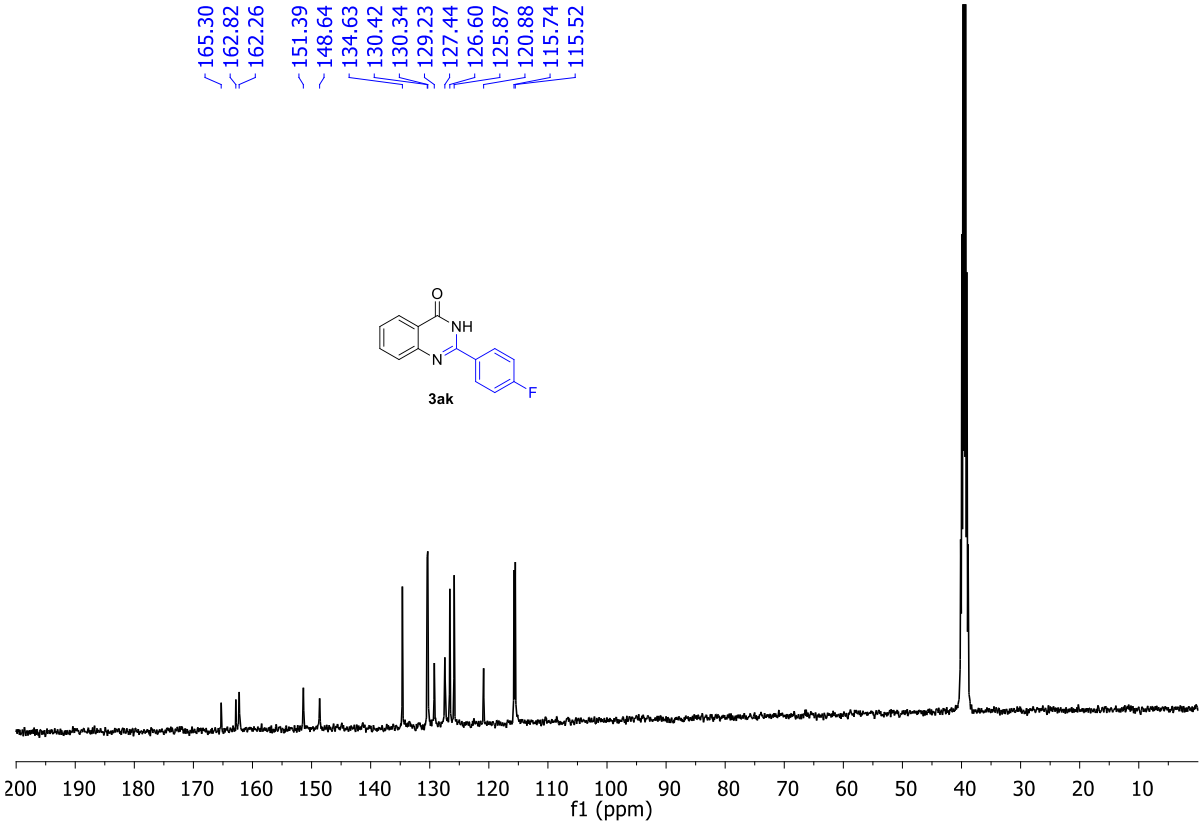
^{13}C NMR (101 MHz, DMSO-D6):



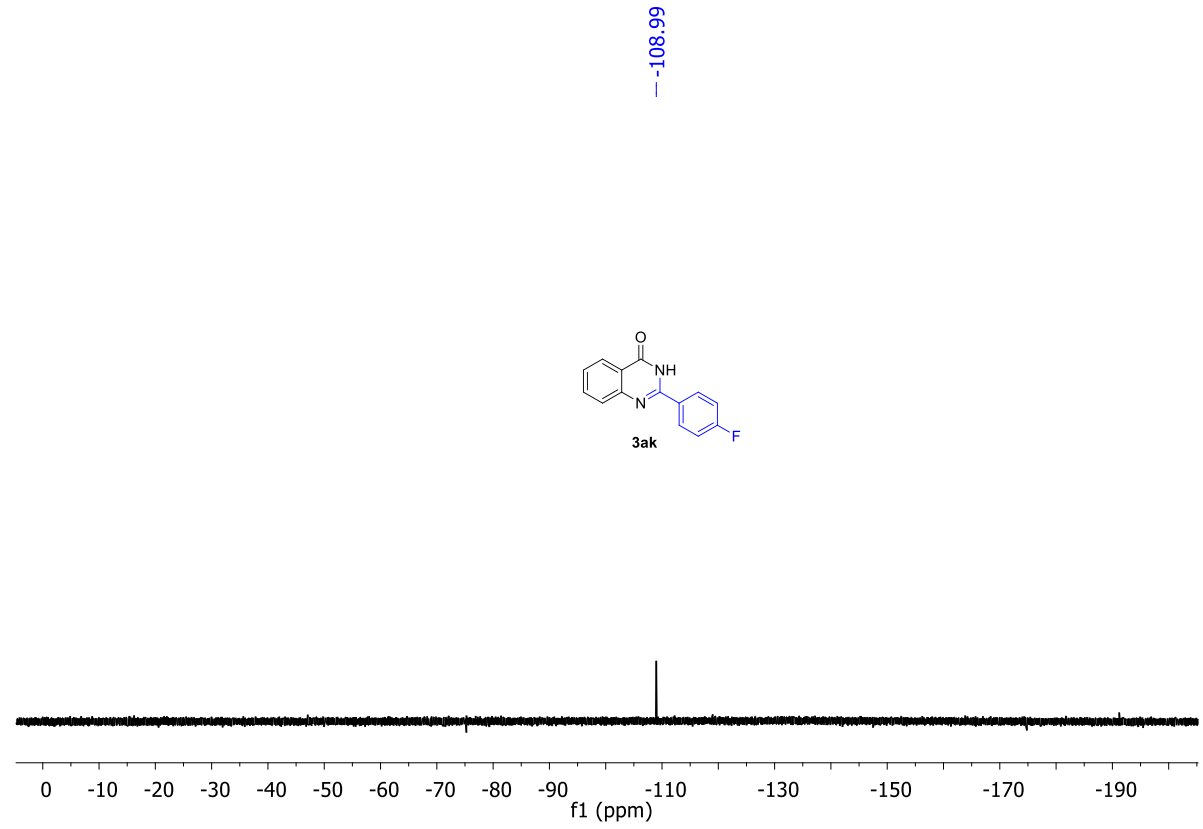
^{1}H NMR (400 MHz, DMSO-D6):



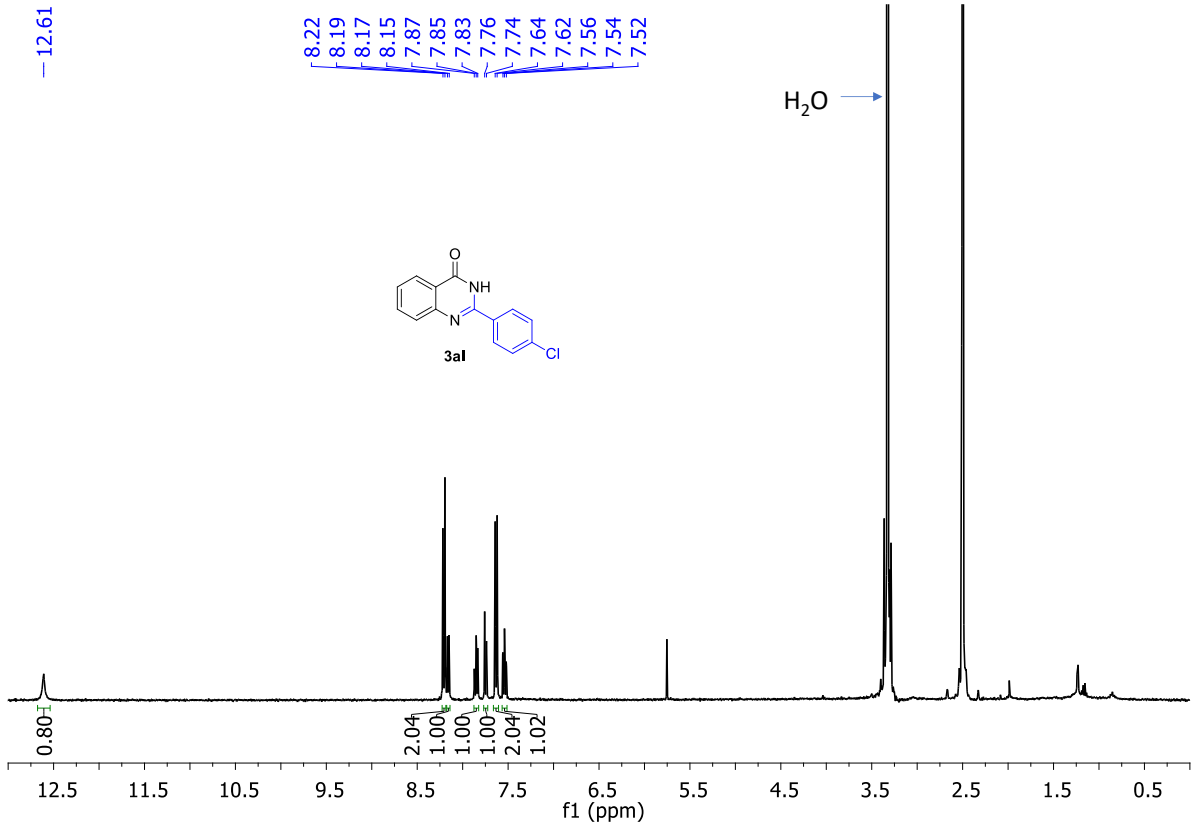
^{13}C NMR (101 MHz, DMSO-D6):



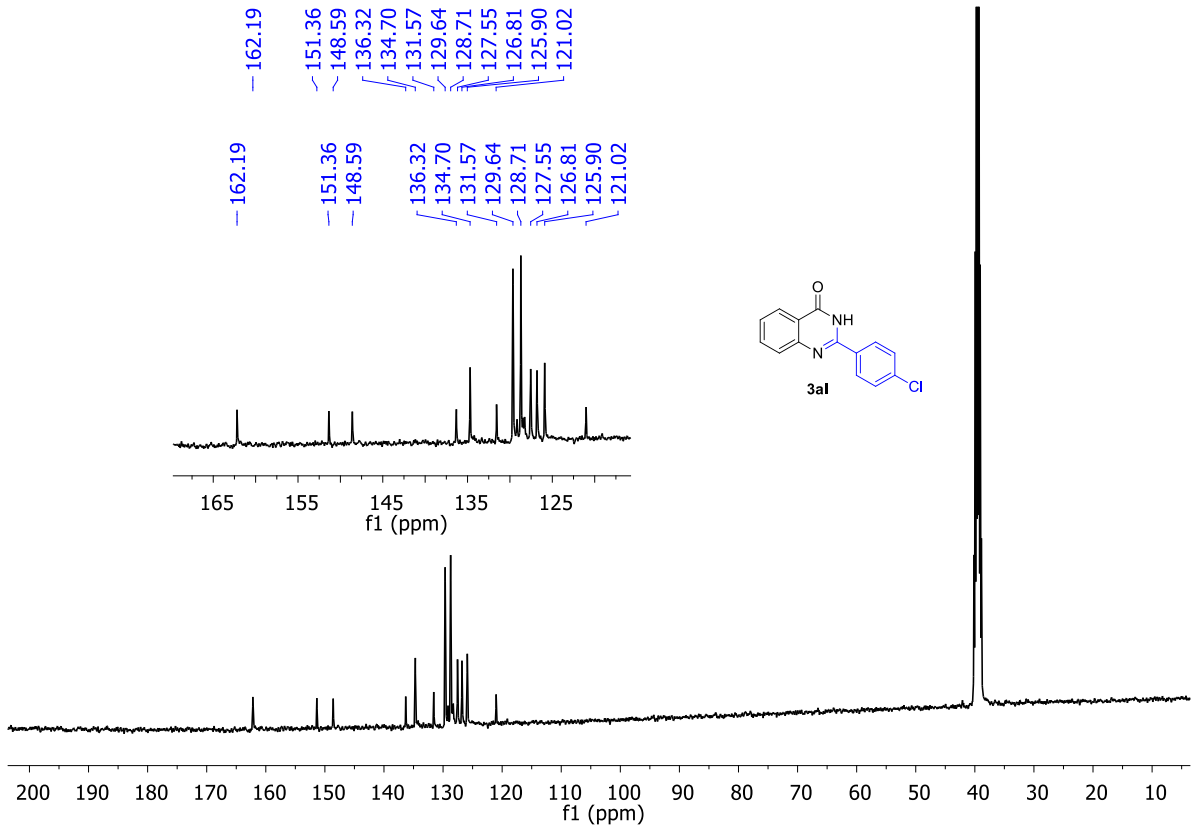
^{19}F NMR (376 MHz, $CDCl_3$):



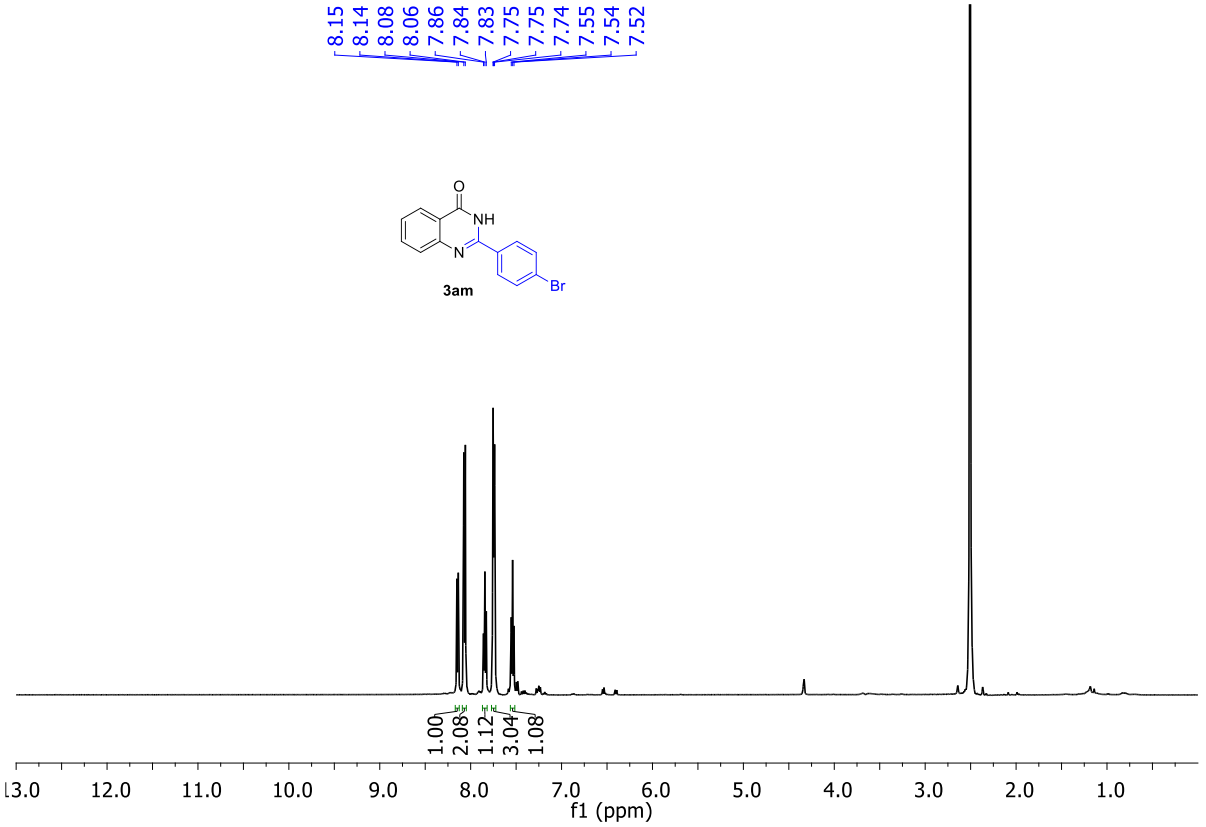
^{1}H NMR (400 MHz, DMSO-D6):



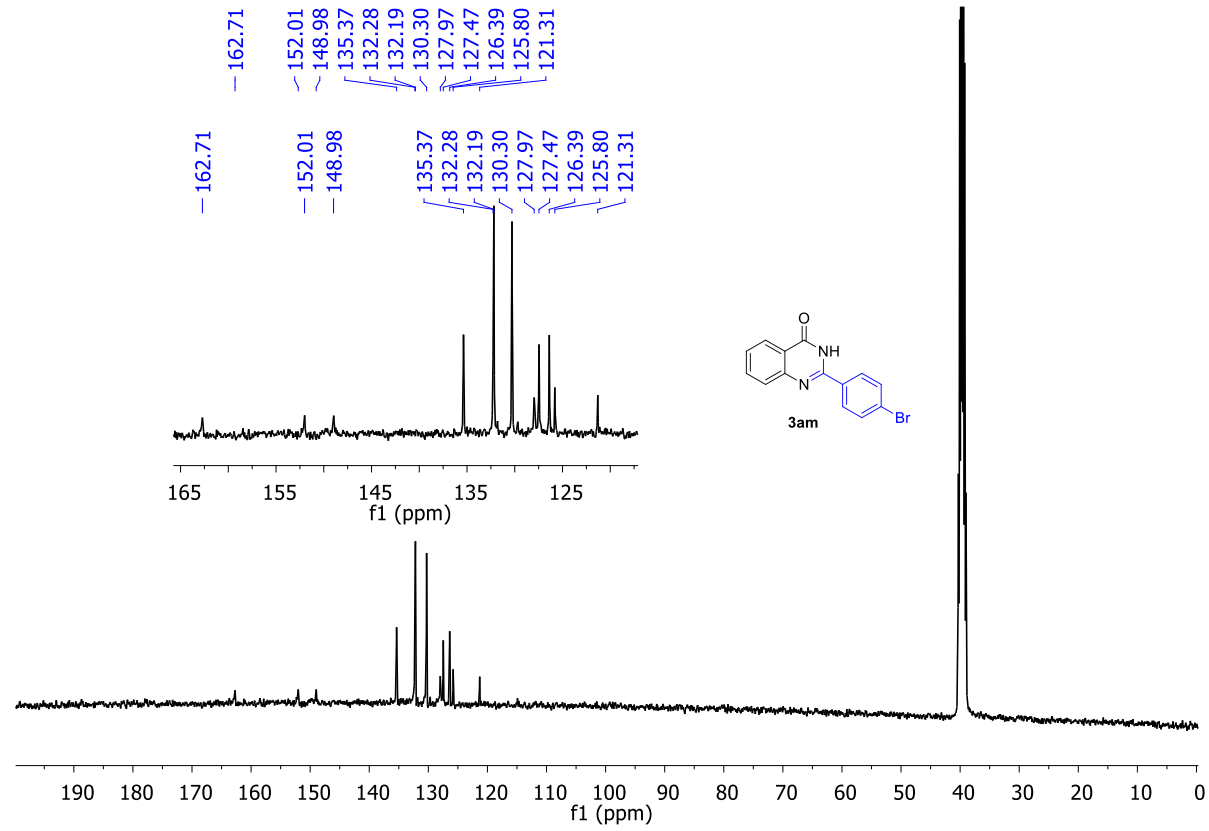
^{13}C NMR (101 MHz, DMSO-D6):



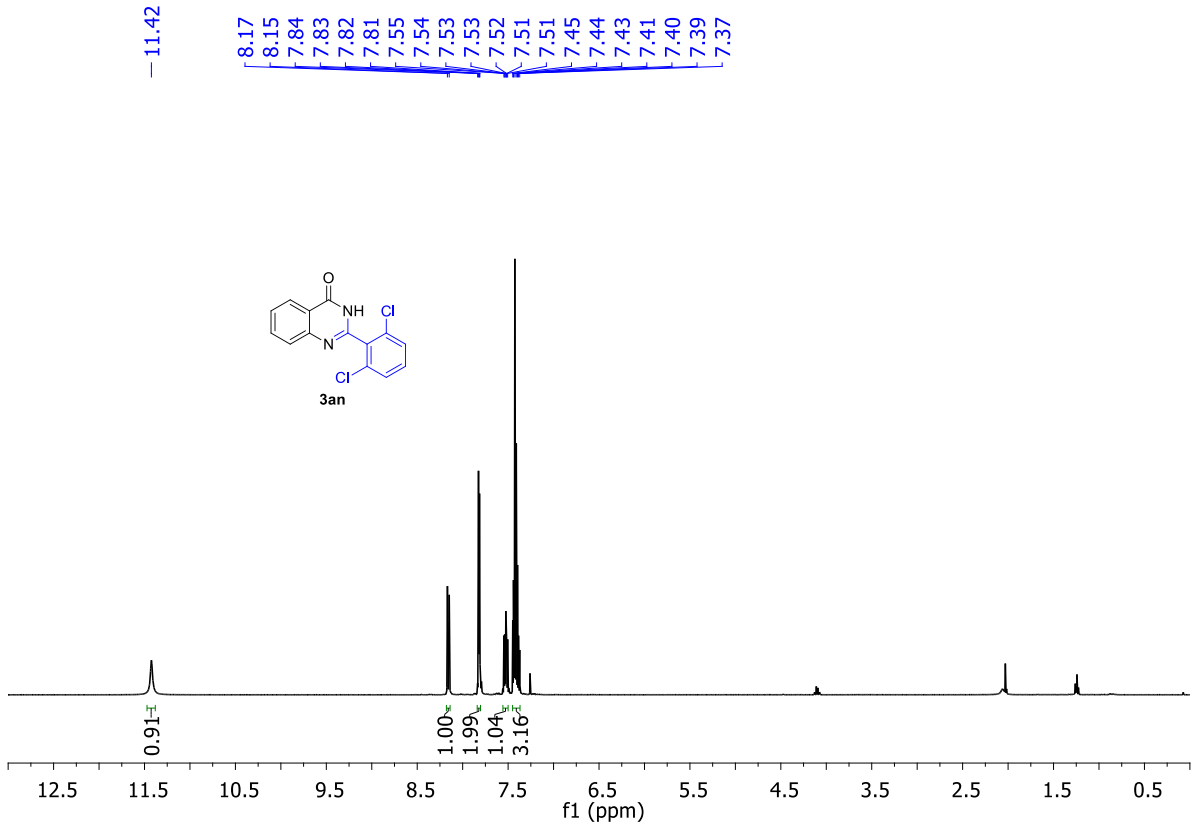
^{1}H NMR (500 MHz, DMSO-D6):



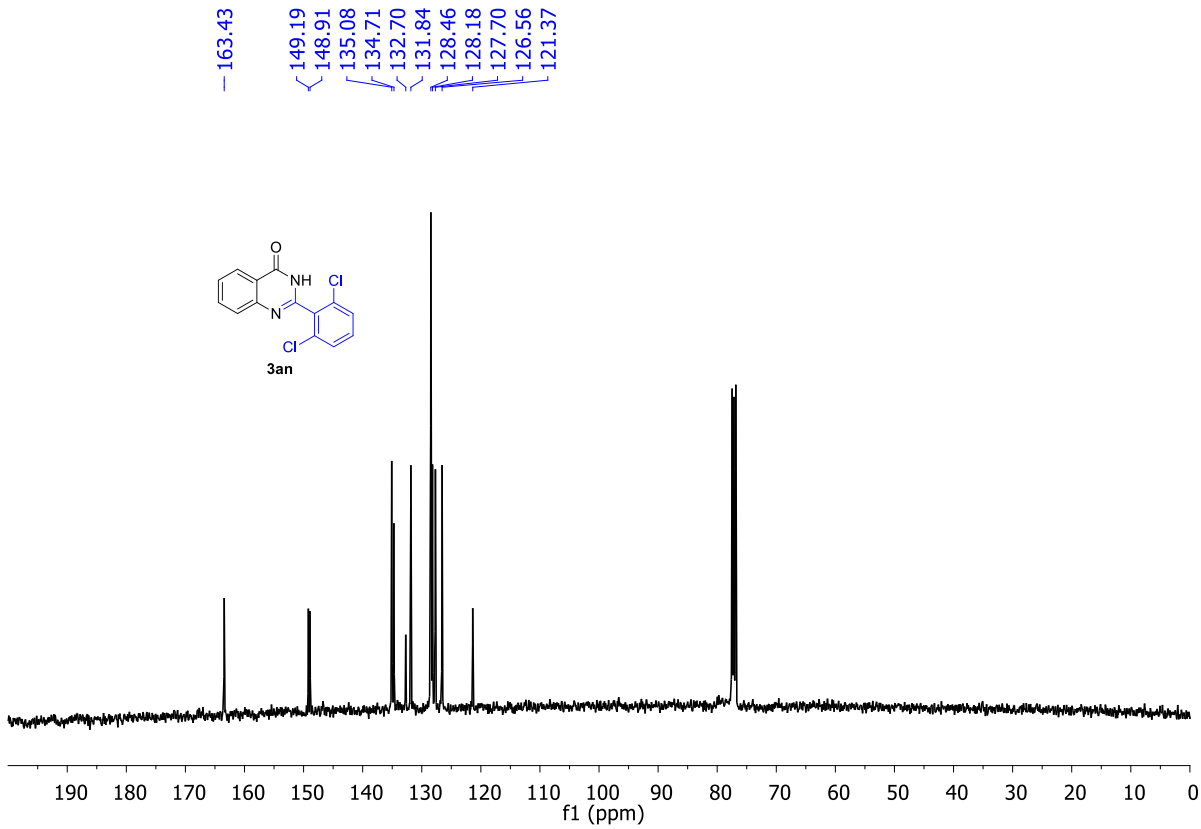
^{13}C NMR (101 MHz, DMSO-D6):



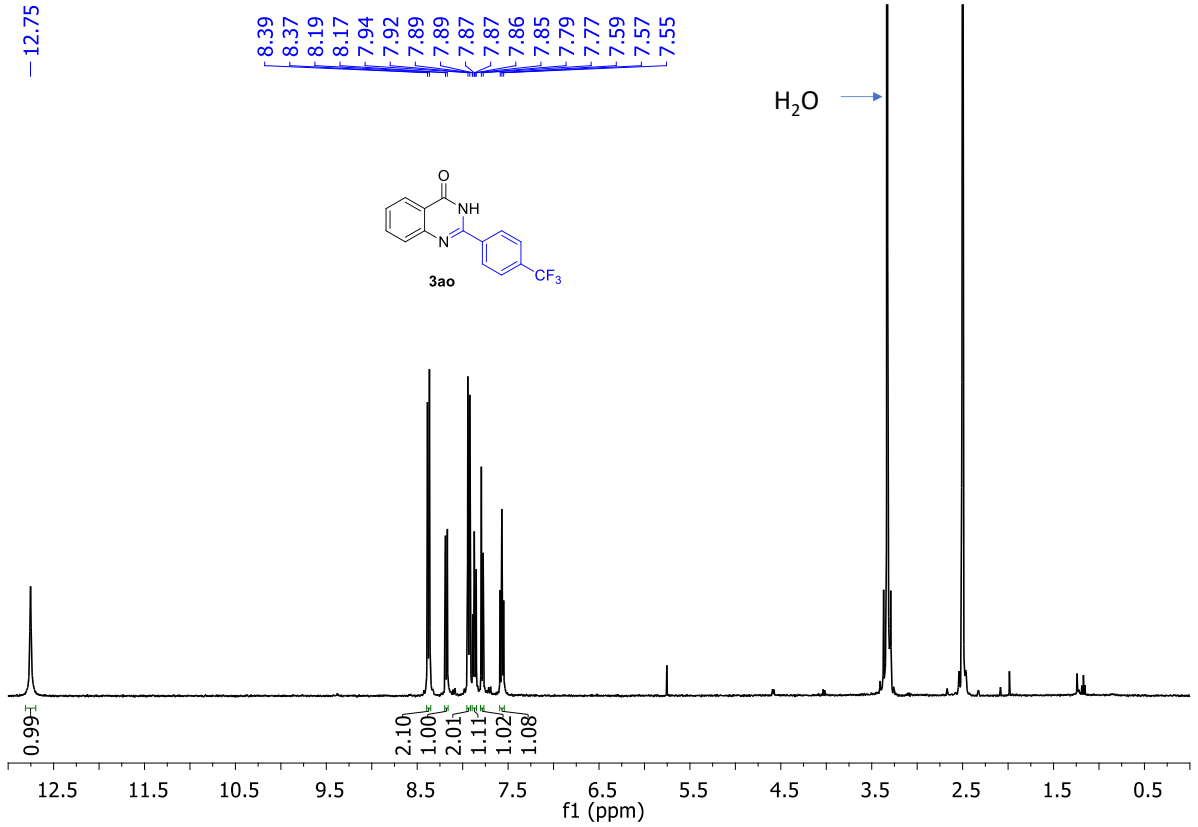
^{1}H NMR (400 MHz, $CDCl_3$):



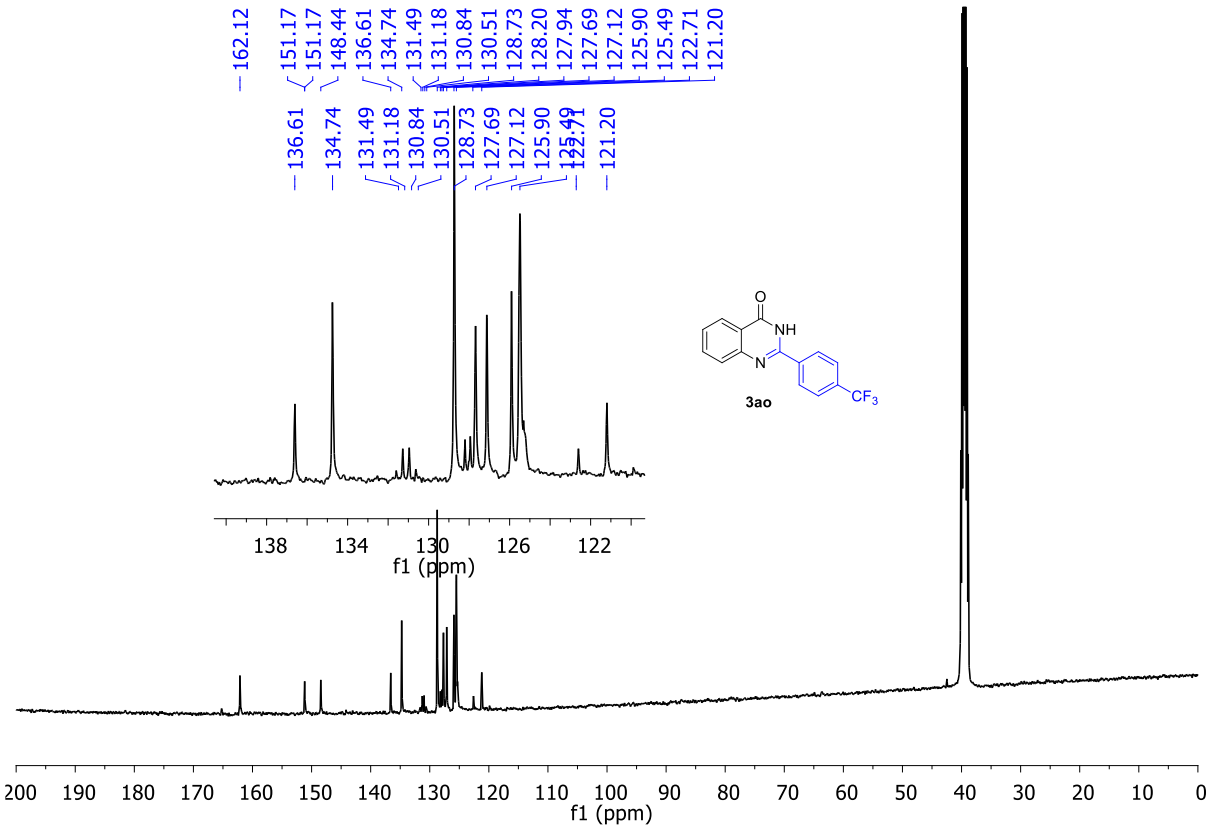
^{13}C NMR (101 MHz, $CDCl_3$):



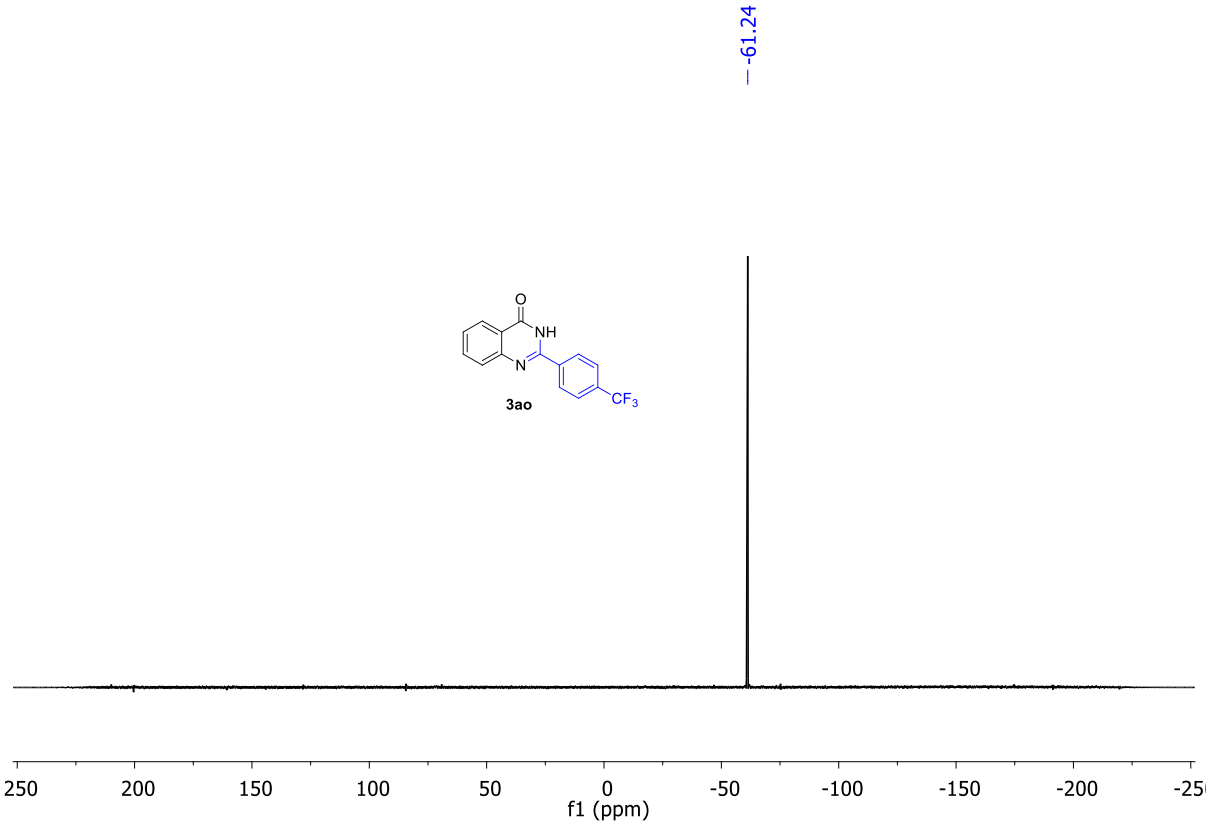
^{1}H NMR (400 MHz, DMSO-D6):



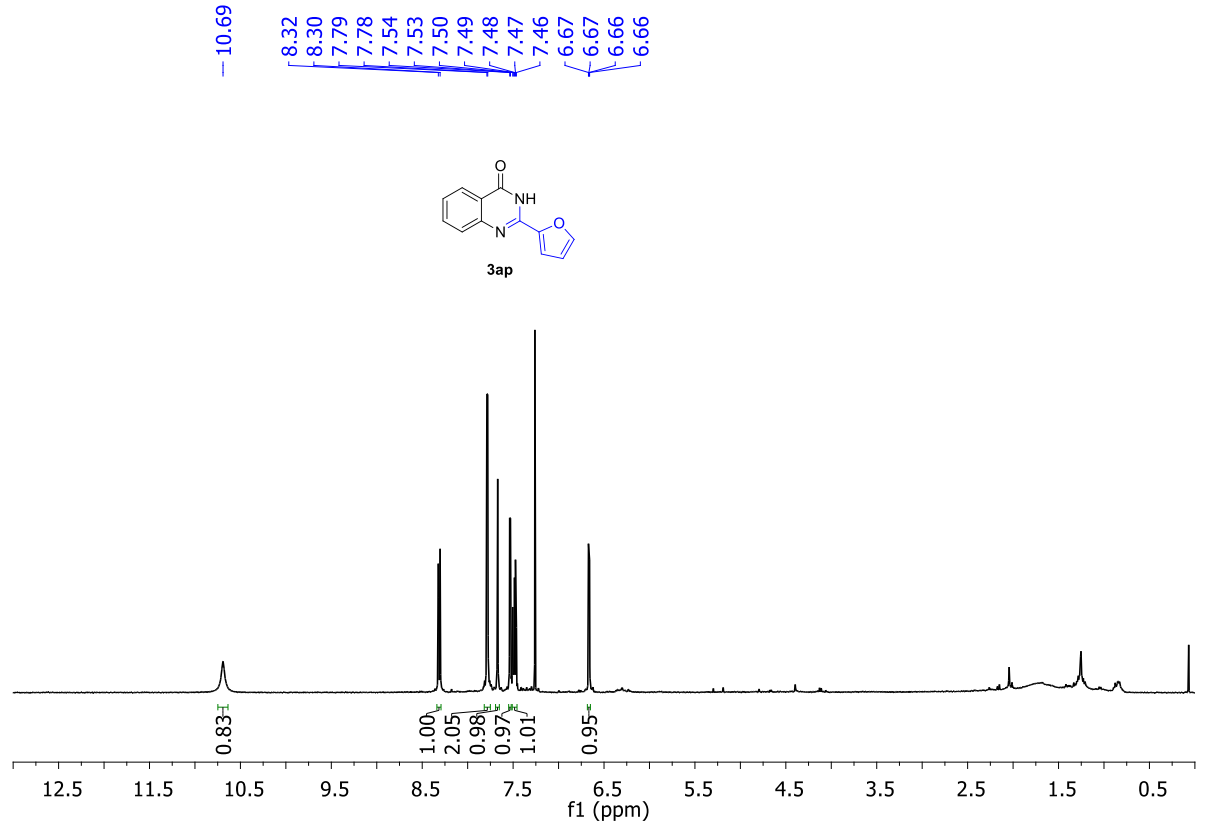
^{13}C NMR (101 MHz, DMSO-D6):



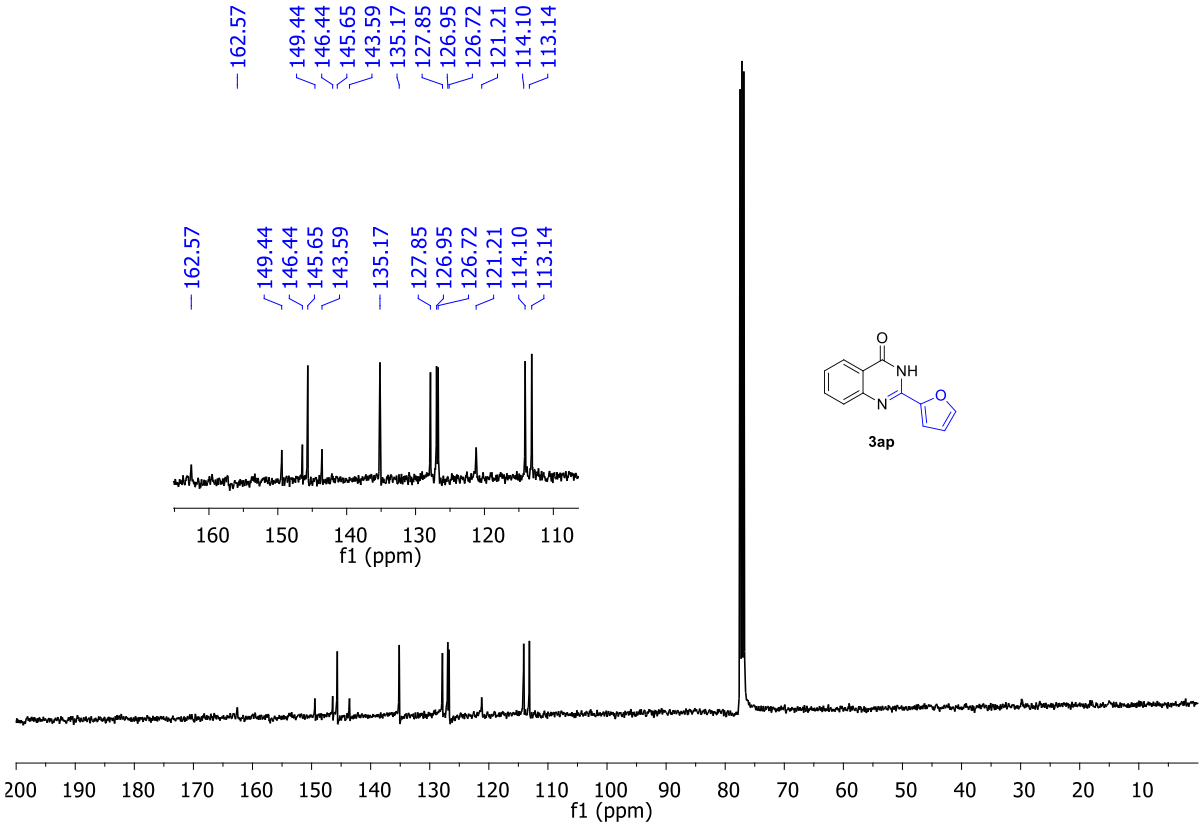
^{19}F NMR (376 MHz, DMSO-D6):



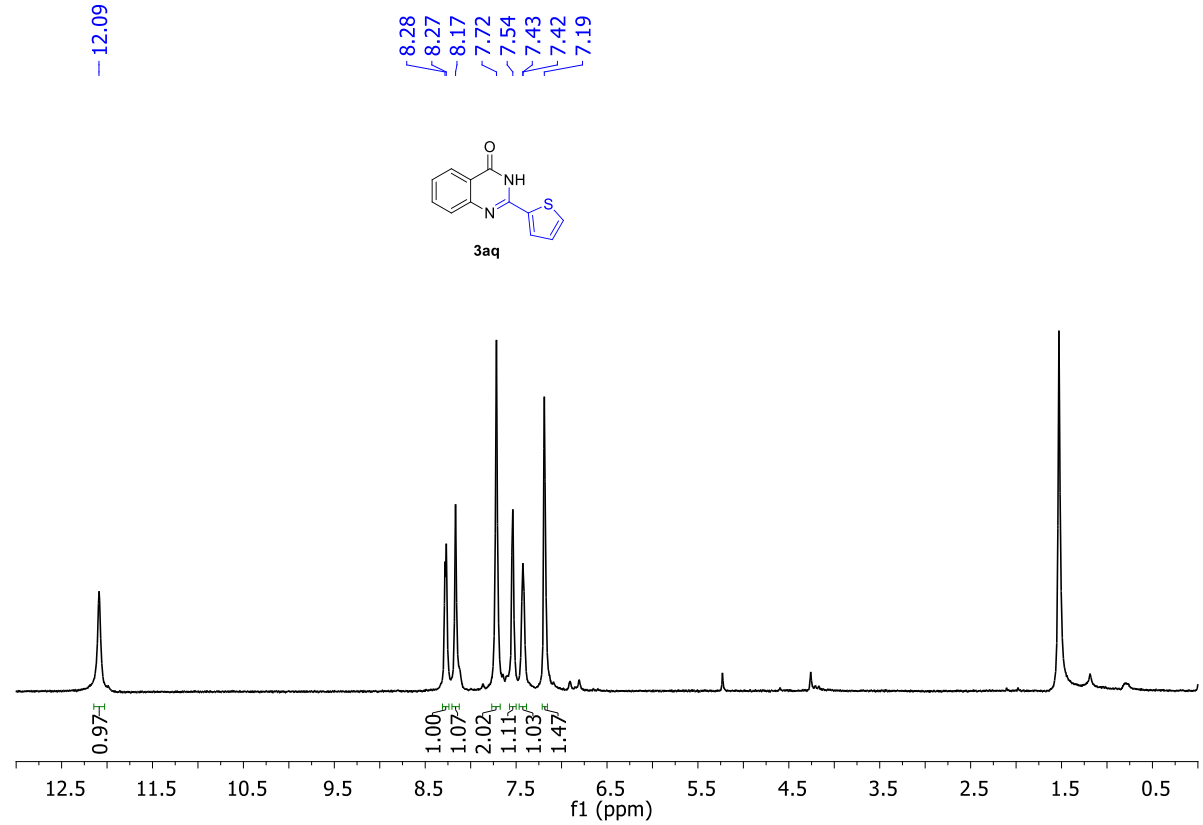
^{1}H NMR (400 MHz, $CDCl_3$):



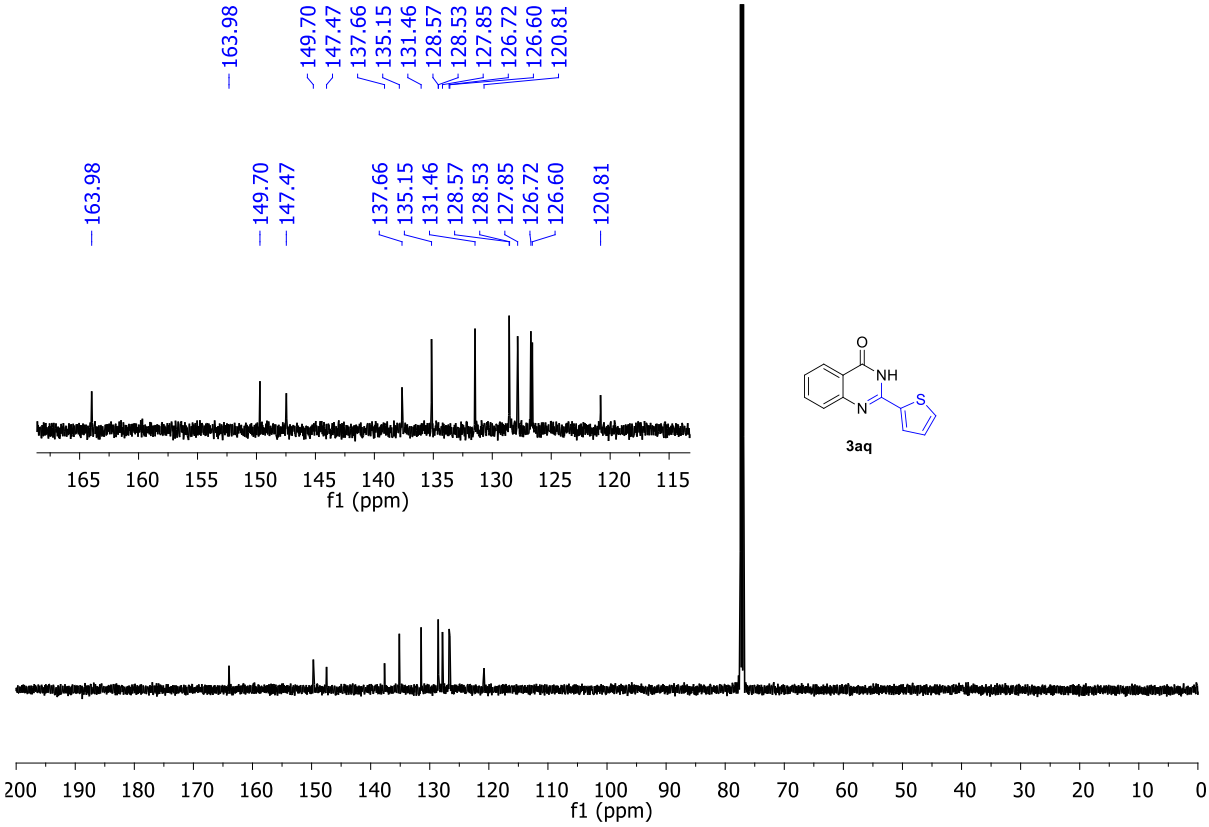
^{13}C NMR (101 MHz, $CDCl_3$):



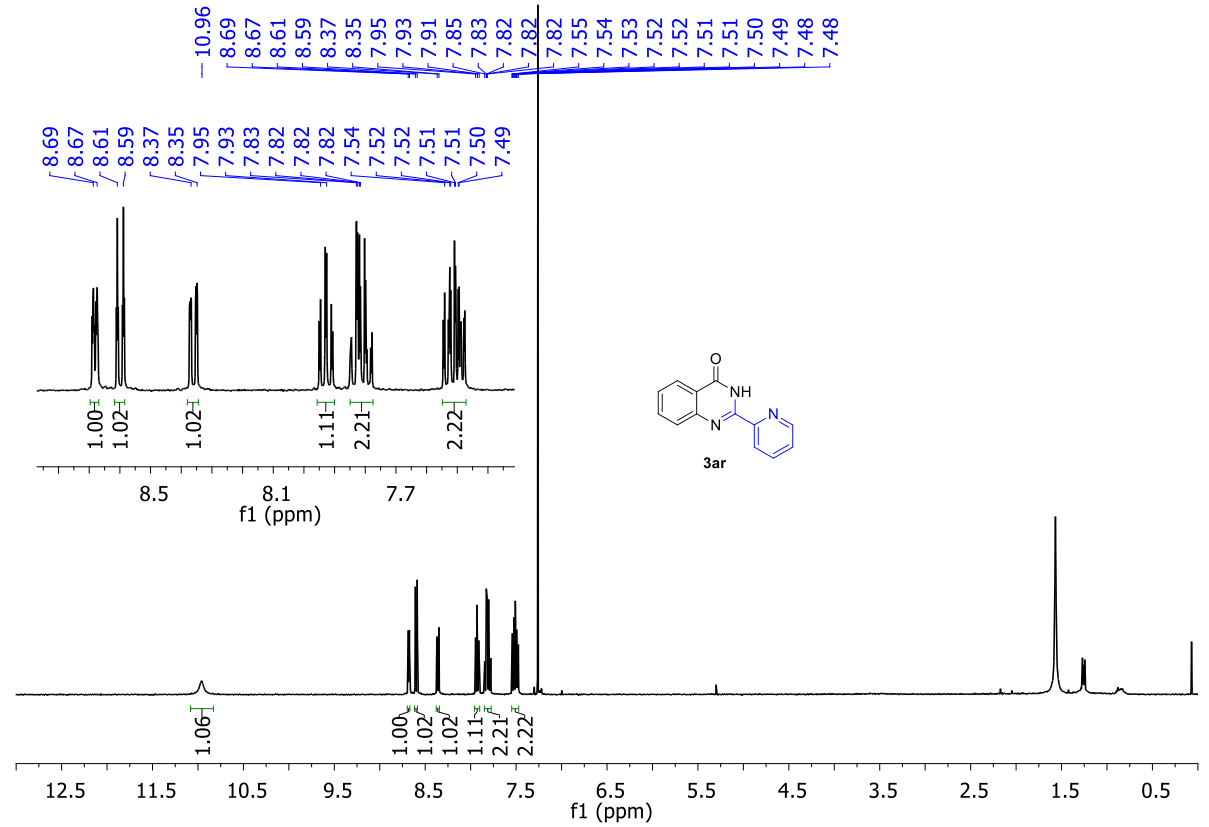
^{1}H NMR (500 MHz, $CDCl_3$):



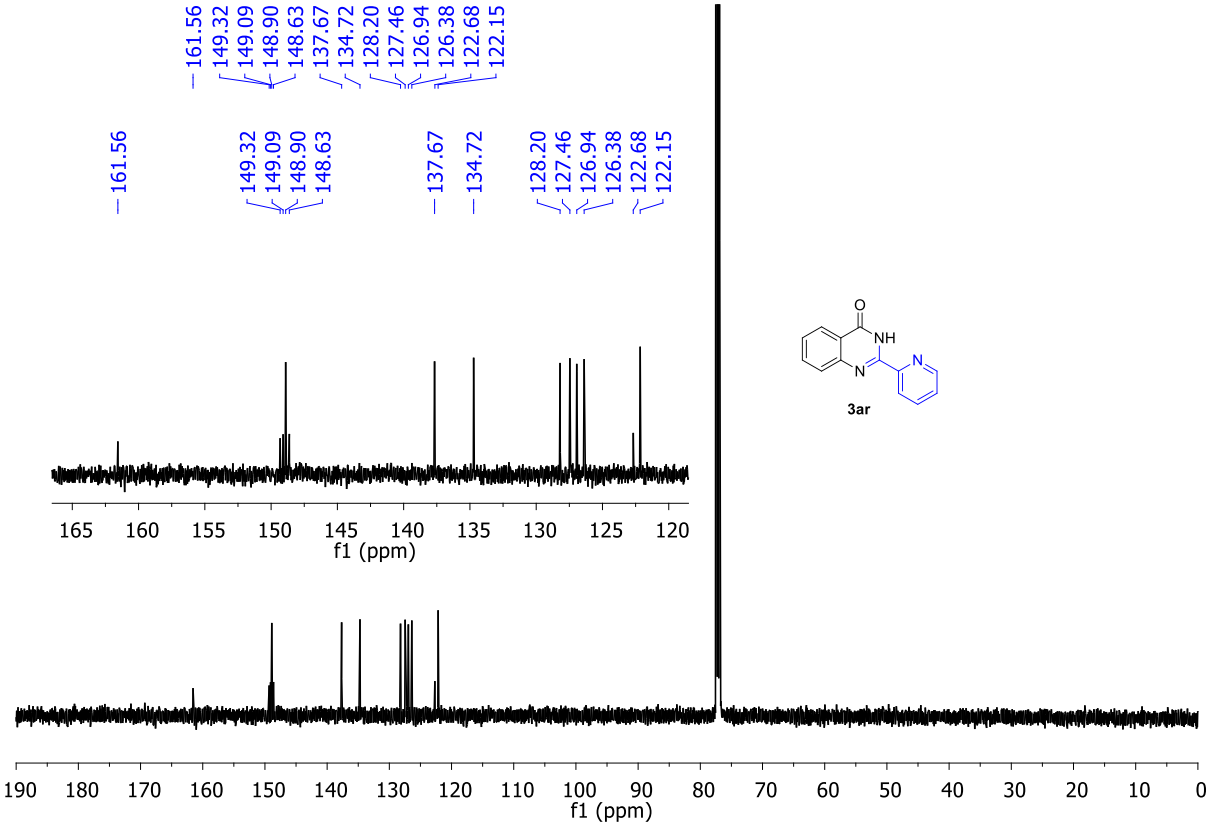
^{13}C NMR (126 MHz, $CDCl_3$):



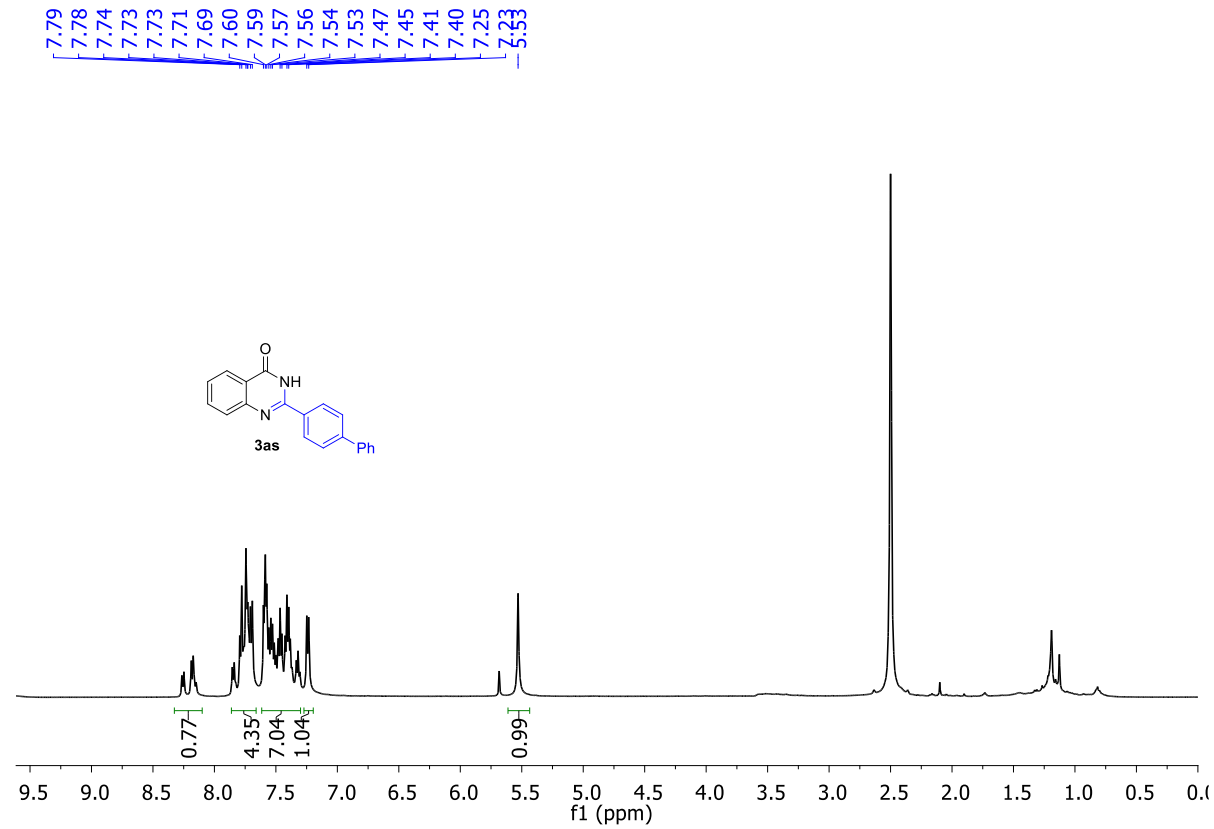
^{1}H NMR (400 MHz, $CDCl_3$):



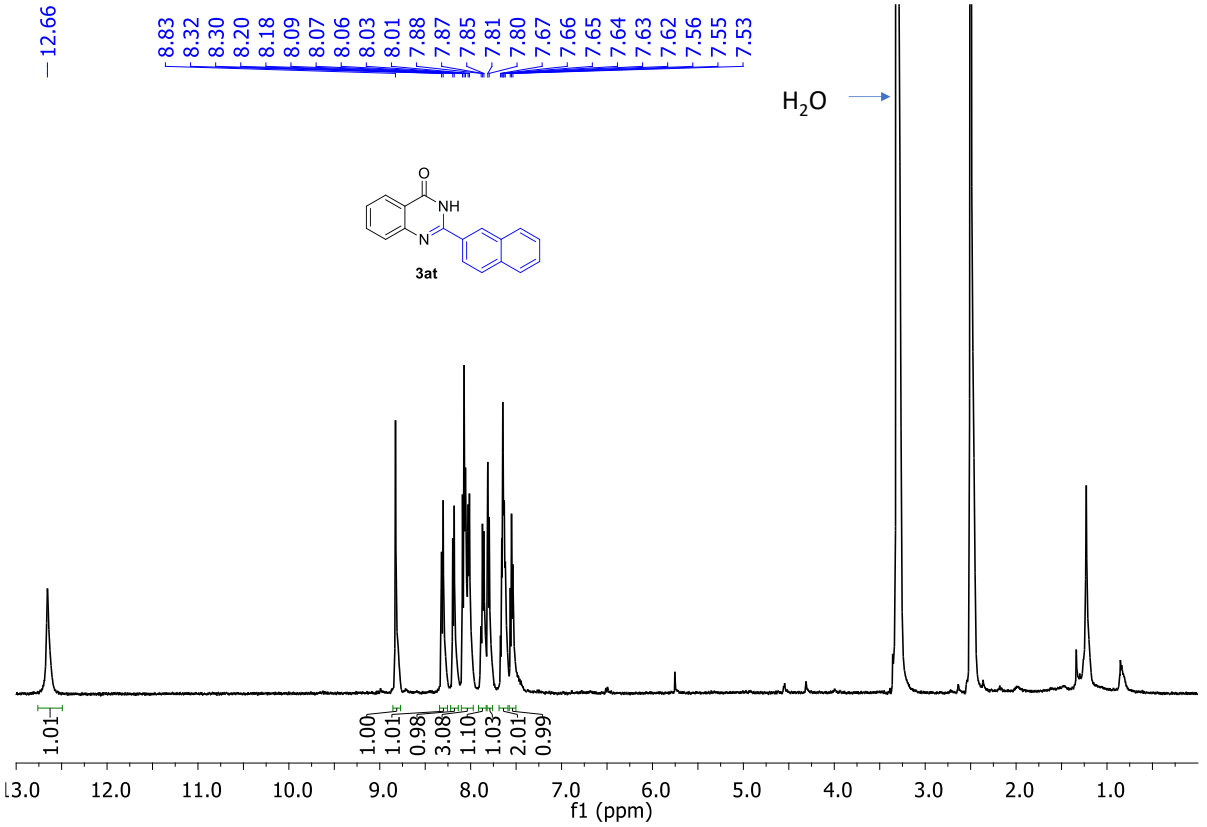
^{13}C NMR (126 MHz, $CDCl_3$):



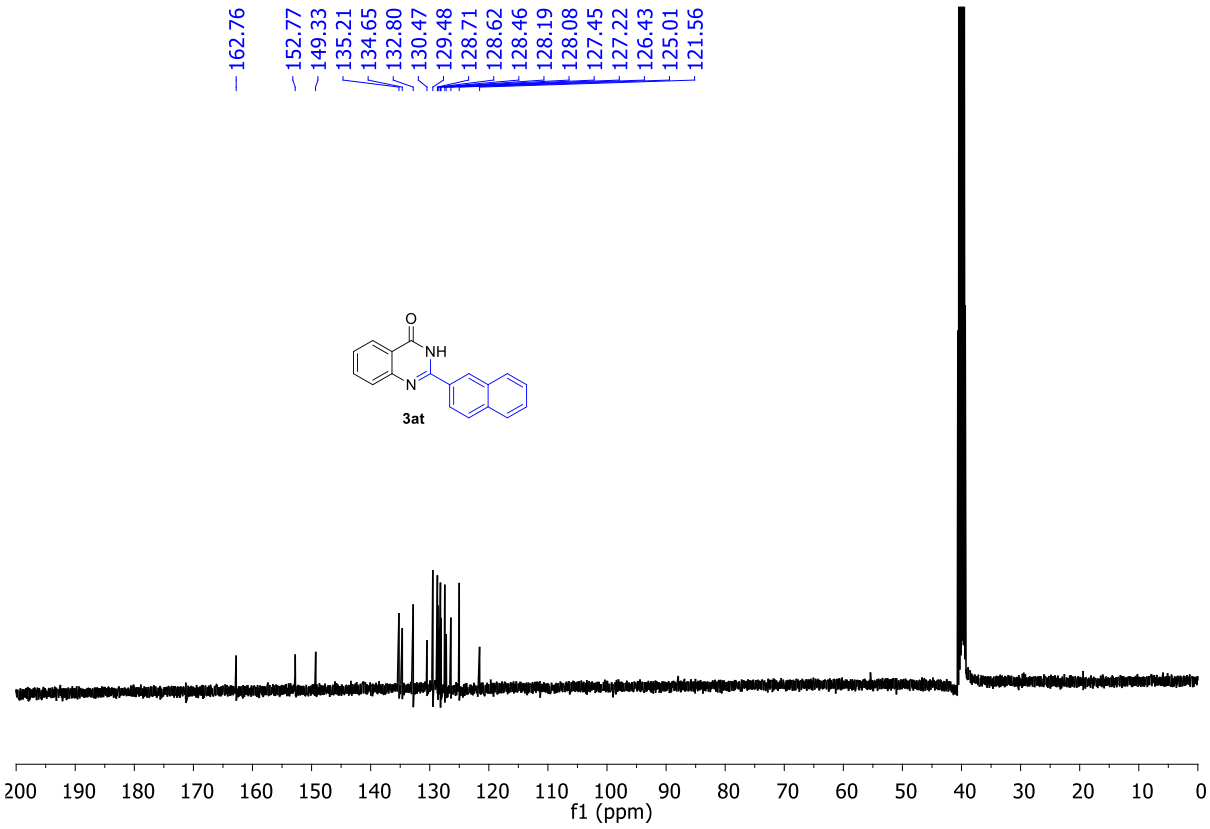
^{1}H NMR (500 MHz, DMSO-D6):



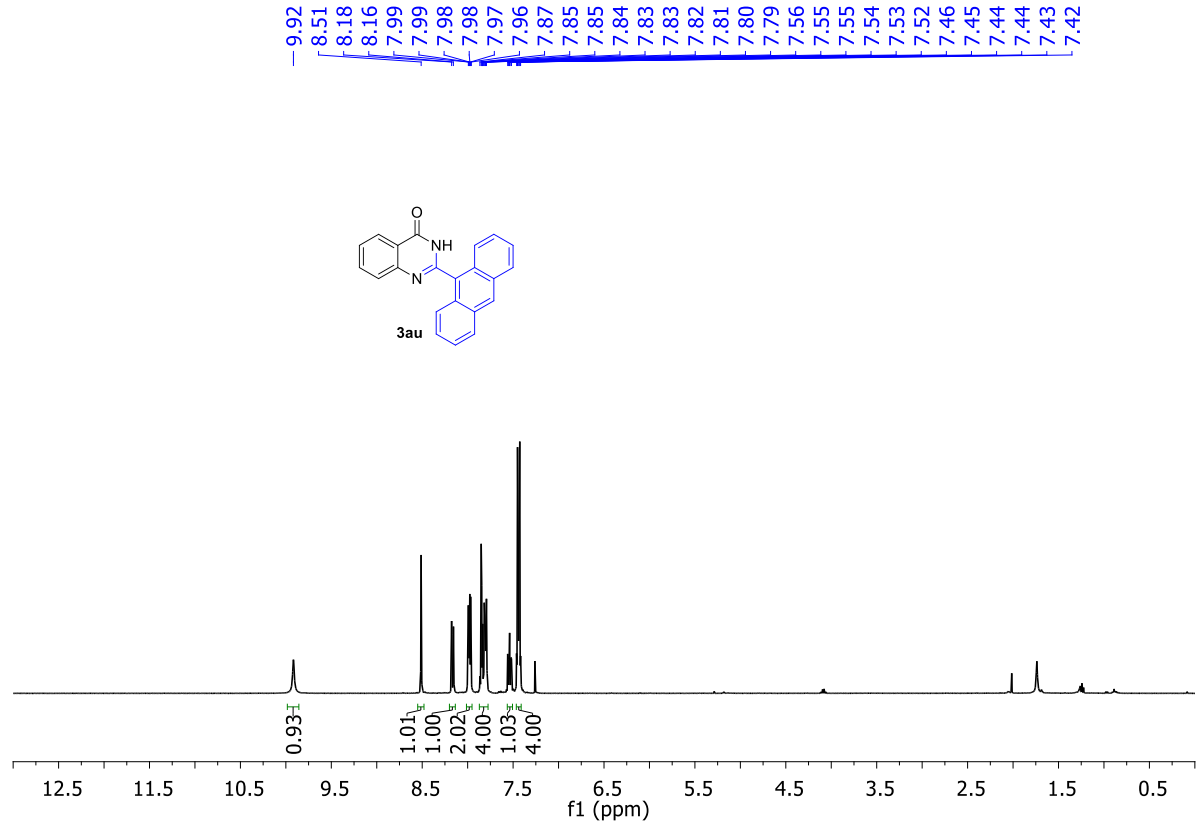
^{1}H NMR (500 MHz, DMSO-D6):



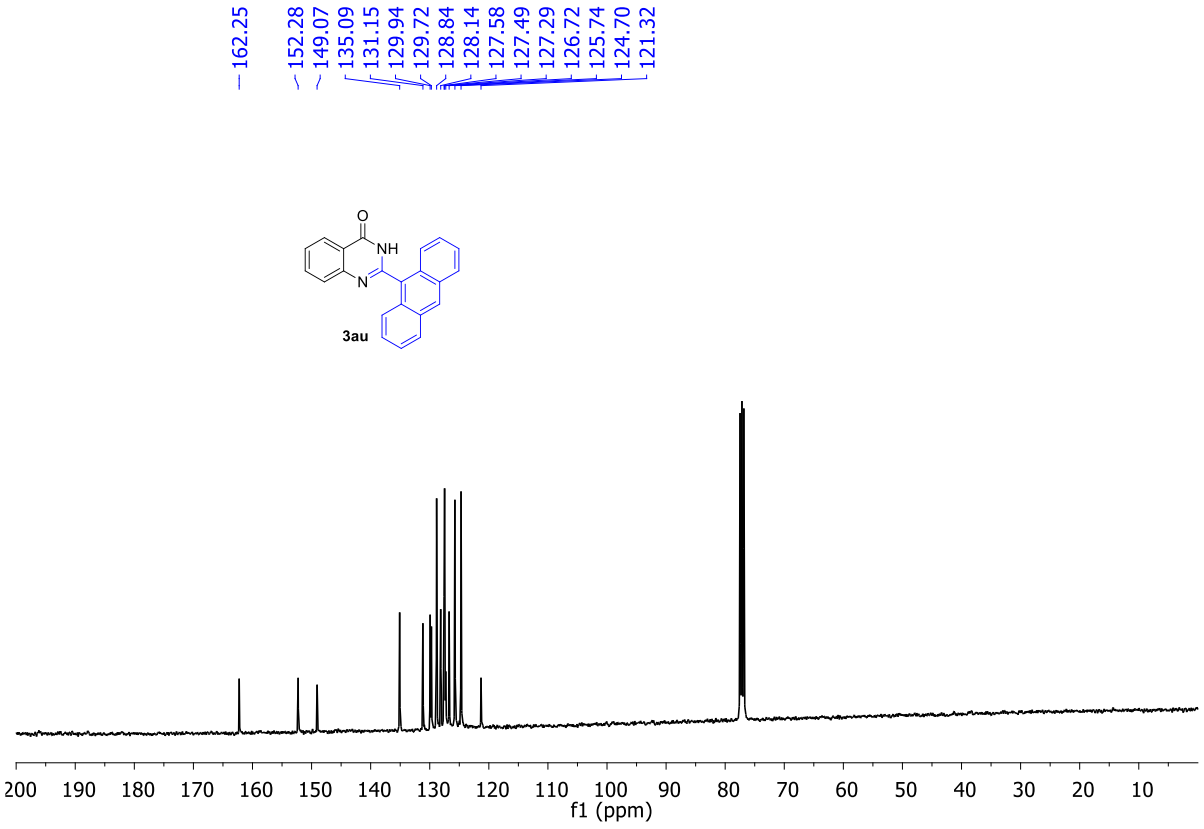
^{13}C NMR (101 MHz, DMSO-D6):



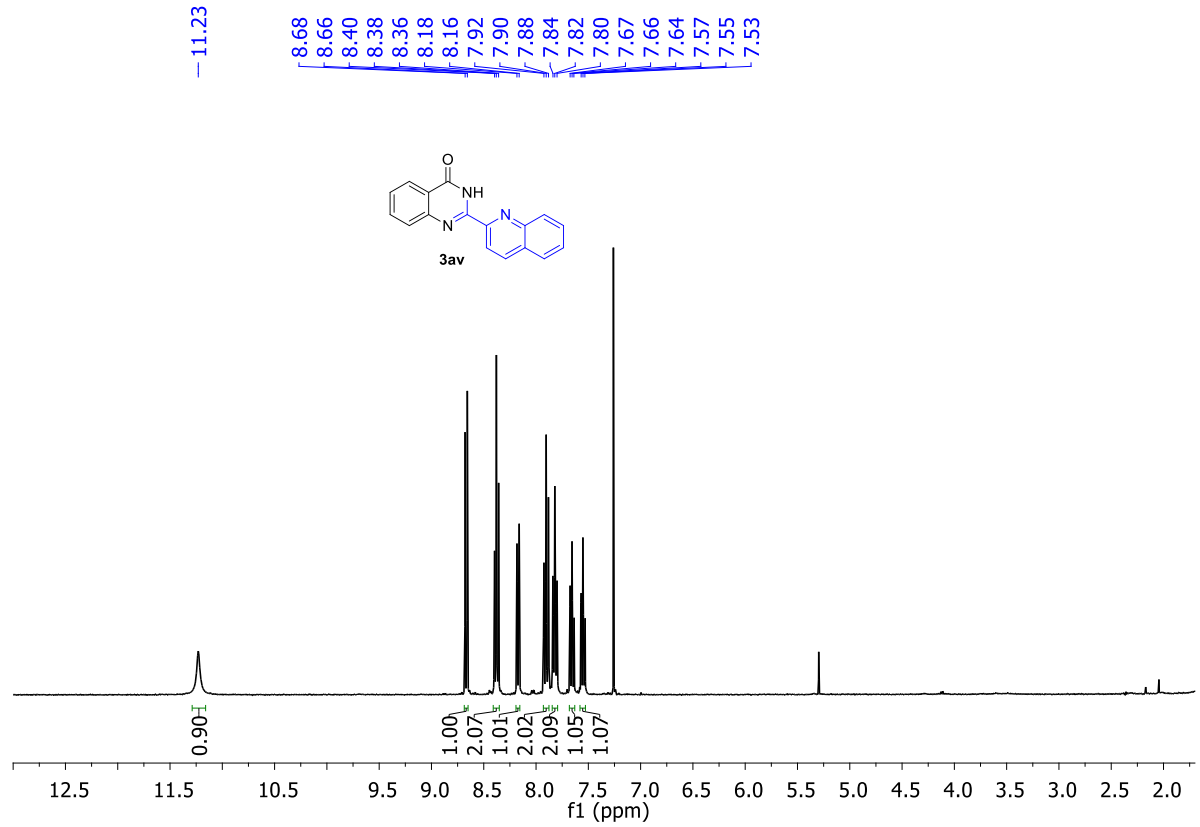
^{1}H NMR (400 MHz, $CDCl_3$):



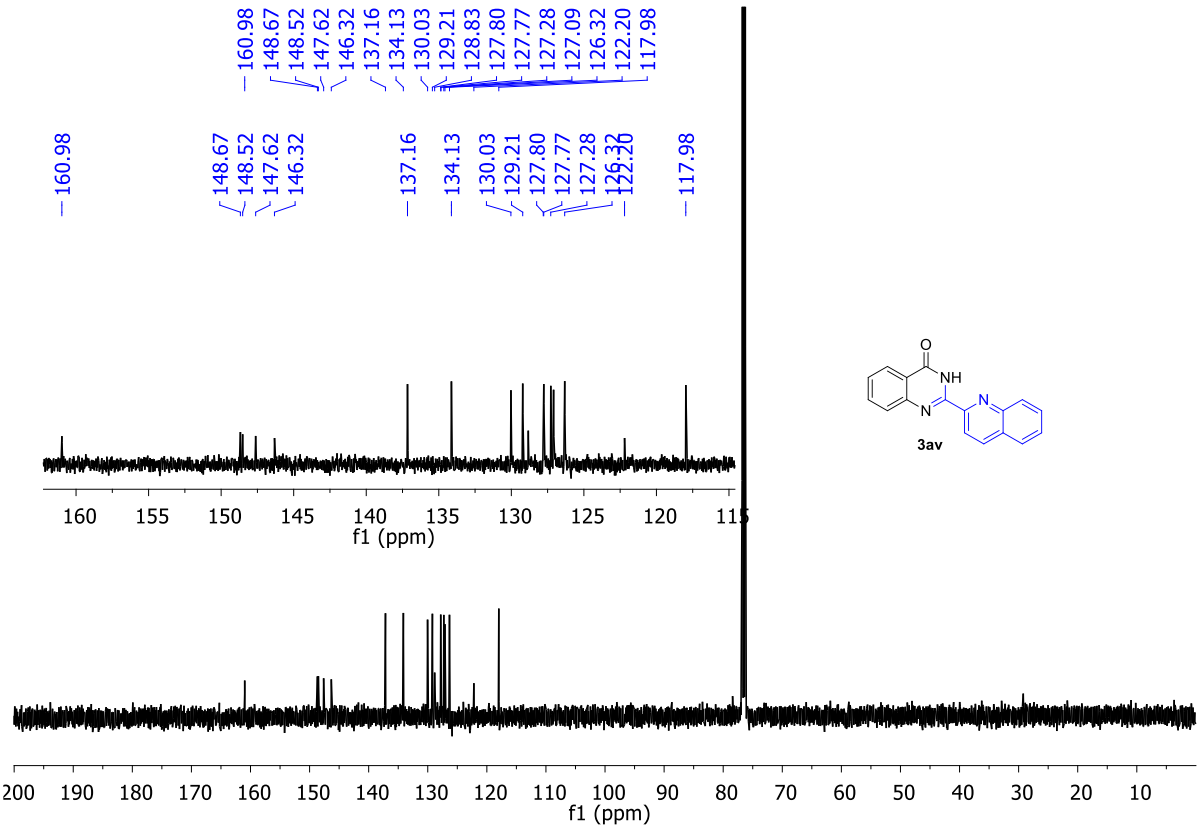
^{13}C NMR (101 MHz, $CDCl_3$):



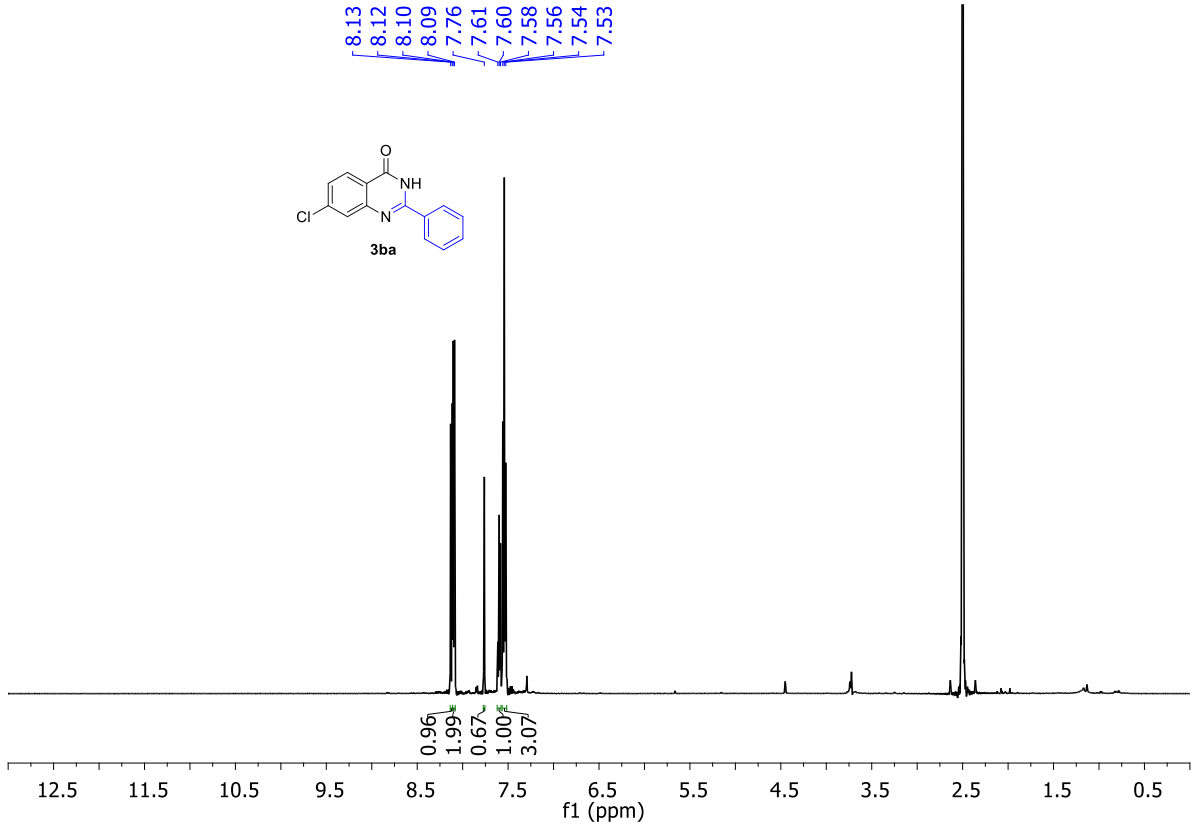
^{1}H NMR (400 MHz, $CDCl_3$):



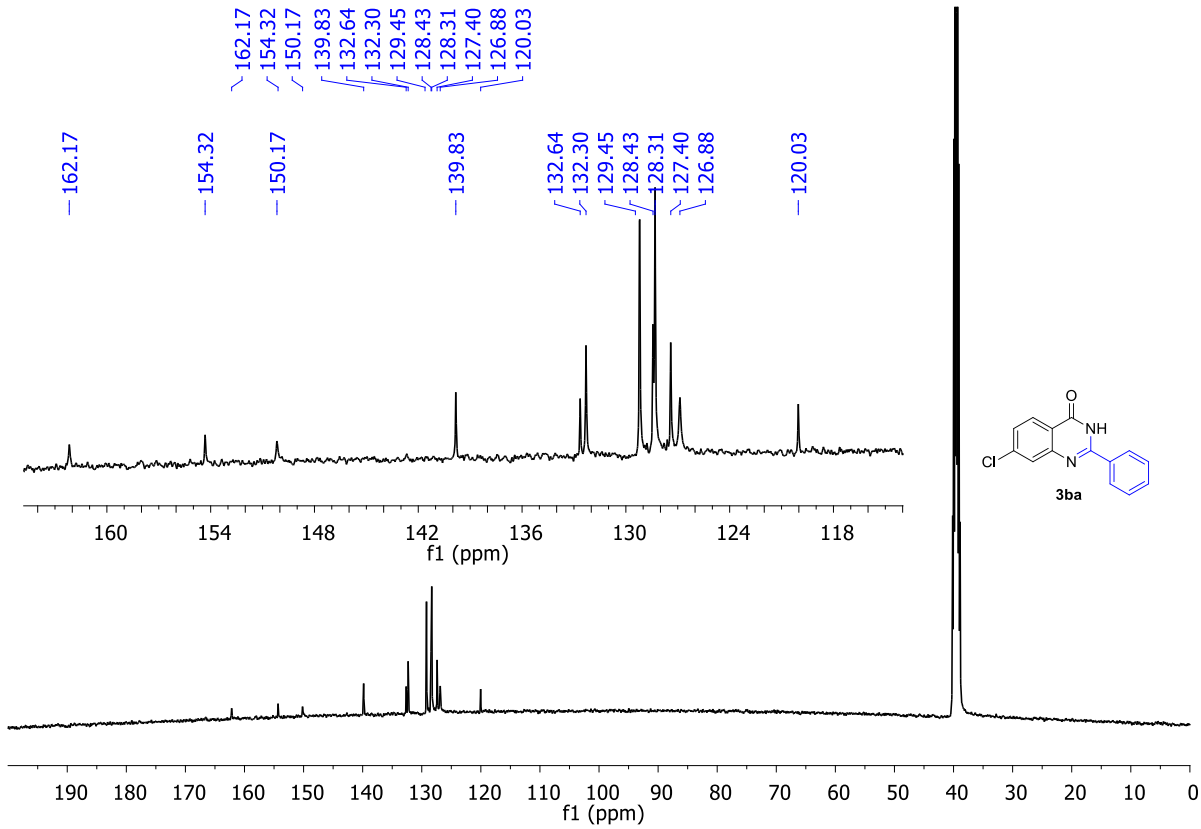
^{13}C NMR (126 MHz, $CDCl_3$):



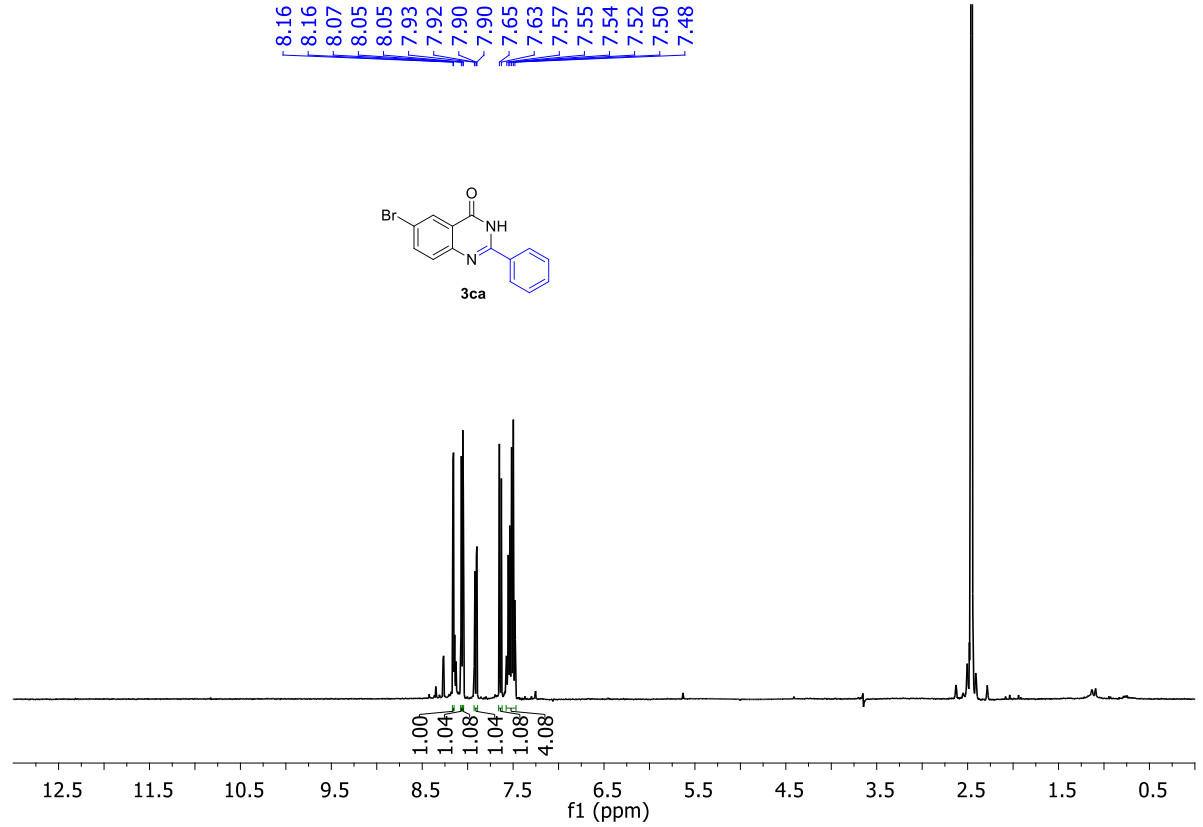
^{1}H NMR (500 MHz, DMSO-D6):



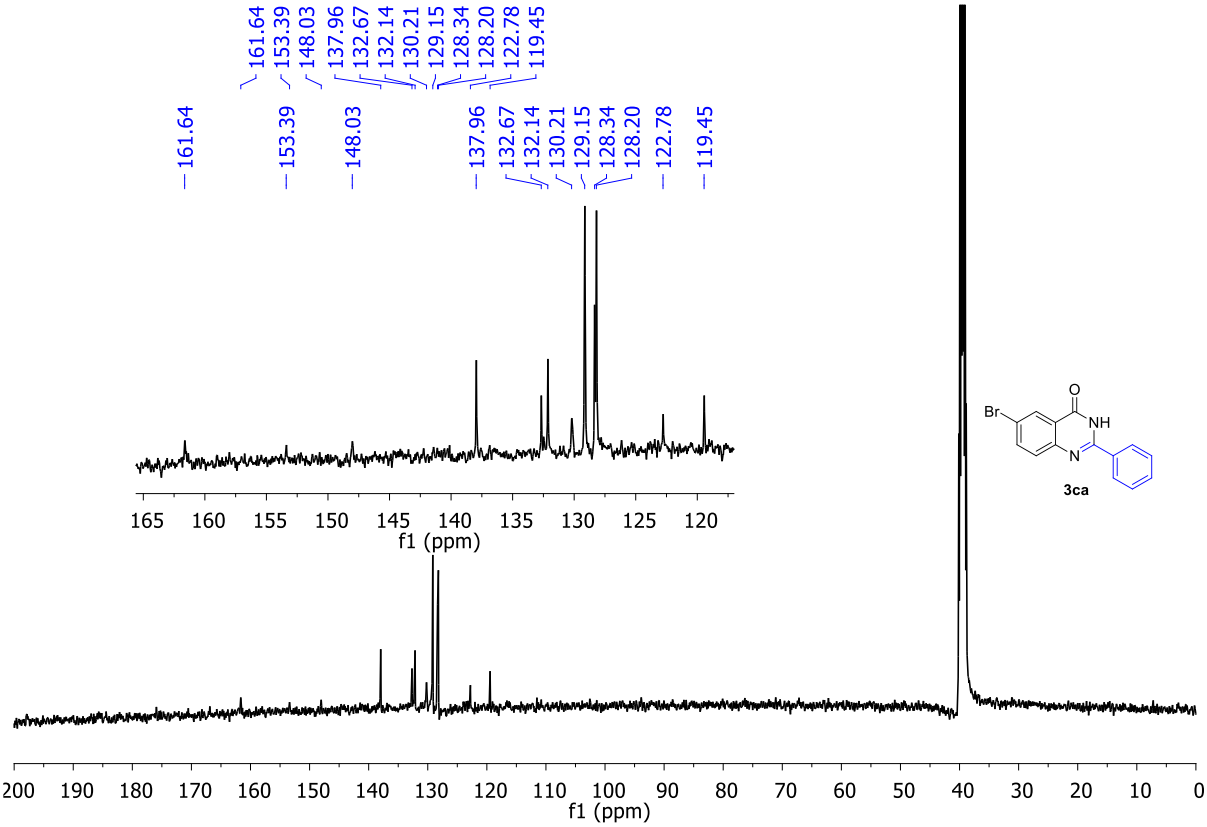
^{13}C NMR (101 MHz, DMSO-D6):



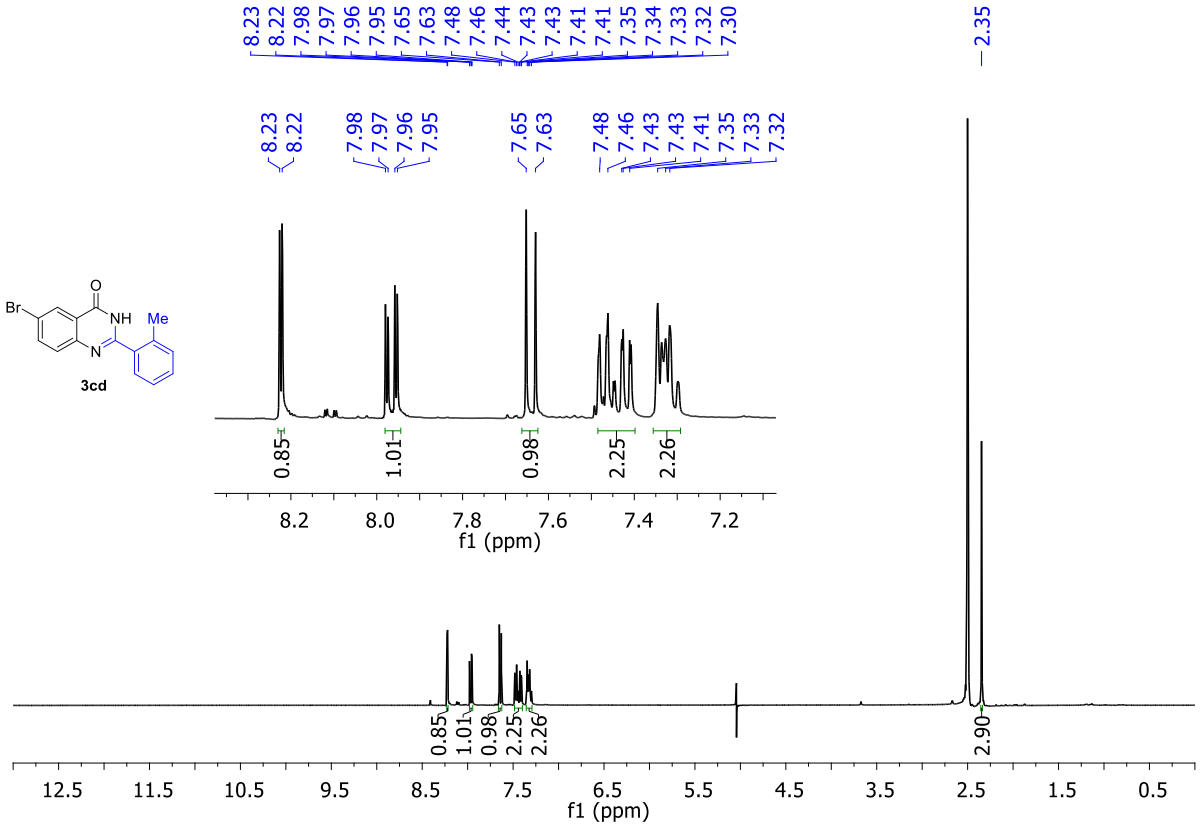
^{1}H NMR (400 MHz, DMSO-D6):



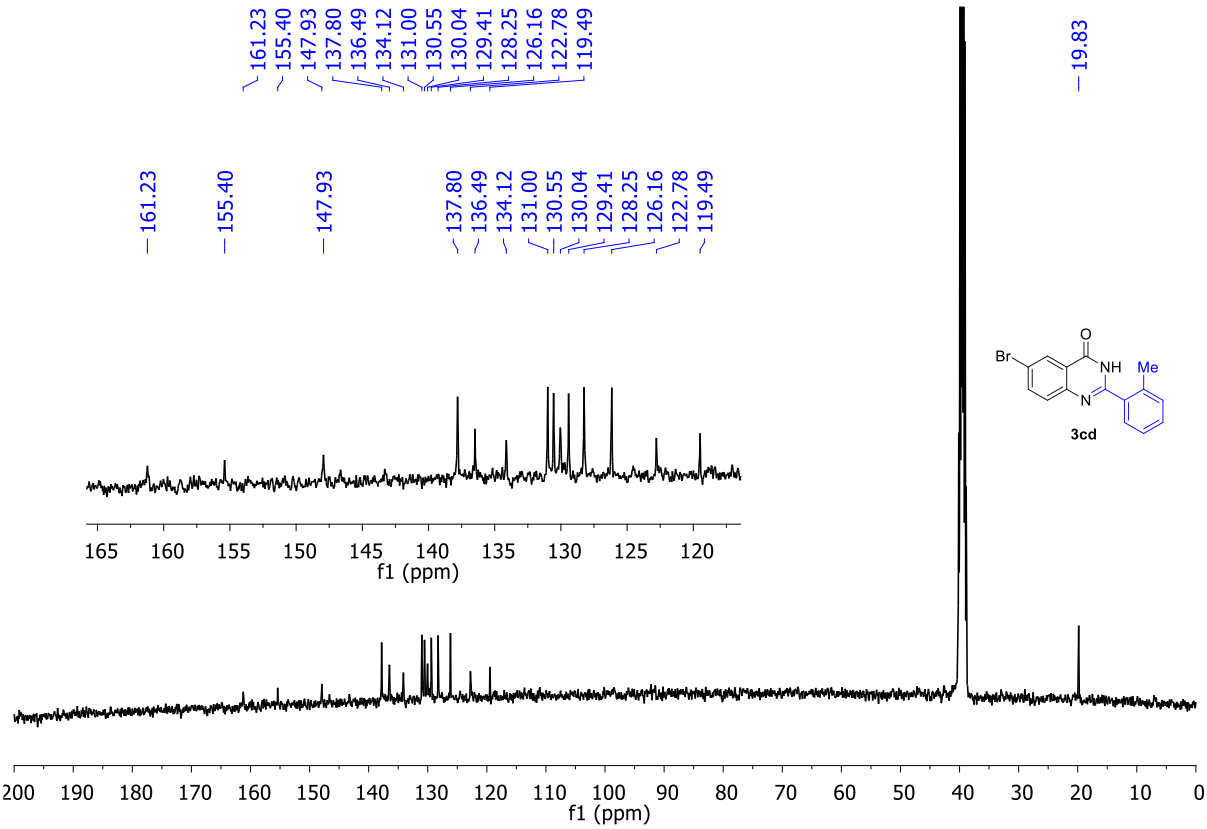
^{13}C NMR (126 MHz, DMSO-D6):



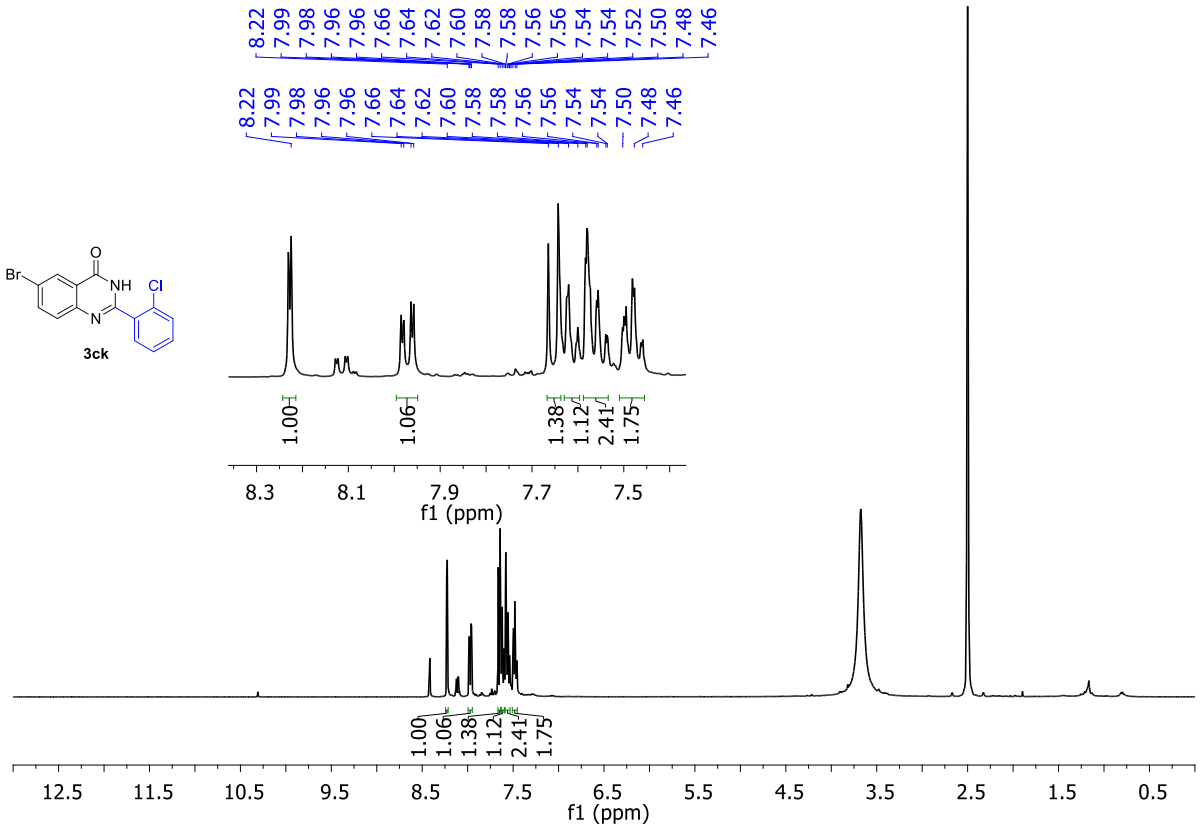
^{1}H NMR (400 MHz, DMSO-D6):



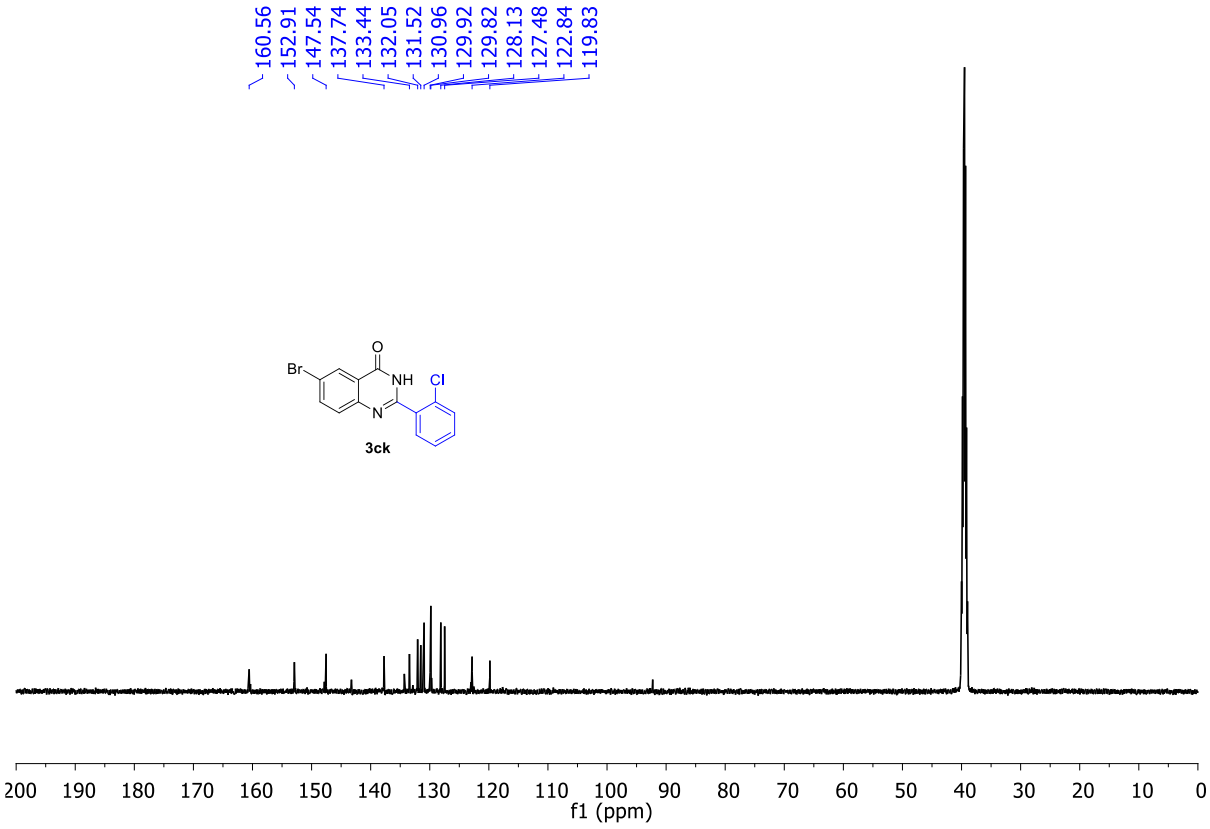
^{13}C NMR (101 MHz, DMSO-D6):



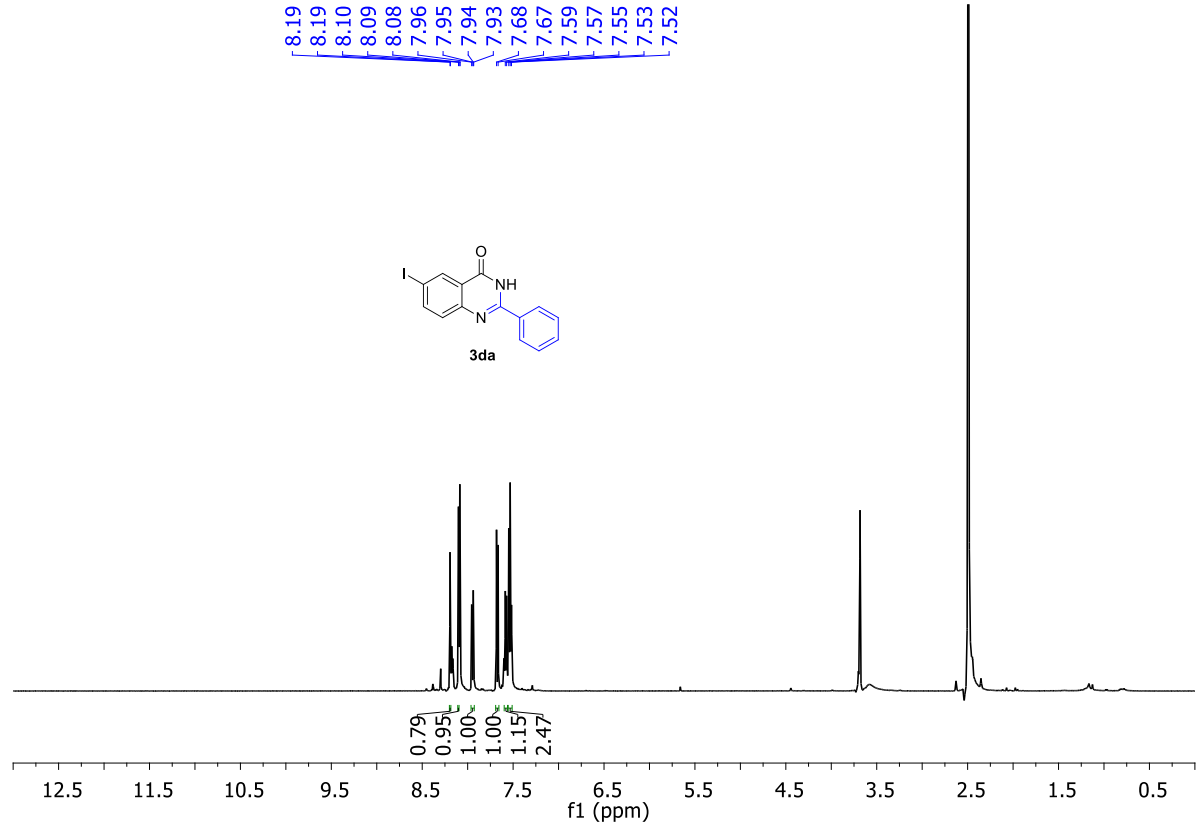
^{1}H NMR (400 MHz, DMSO-D6):



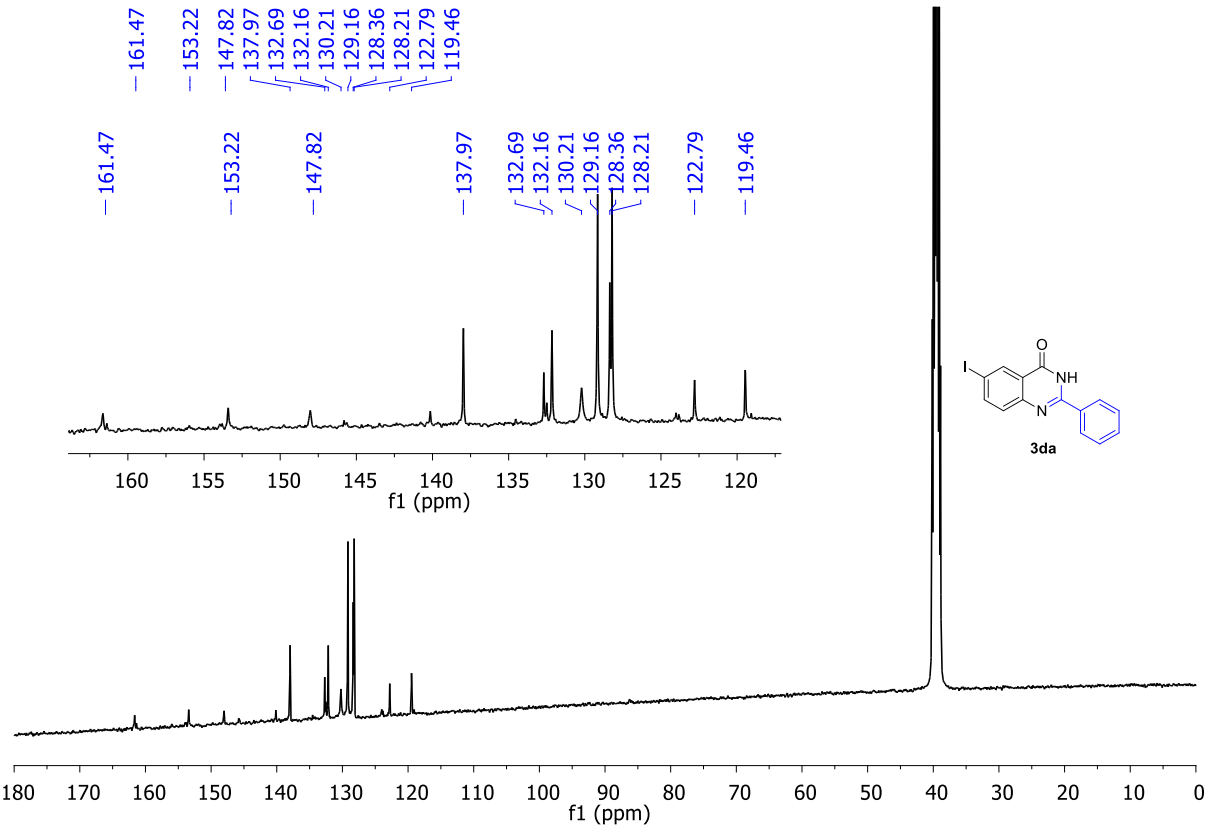
^{13}C NMR (126 MHz, DMSO-D6):



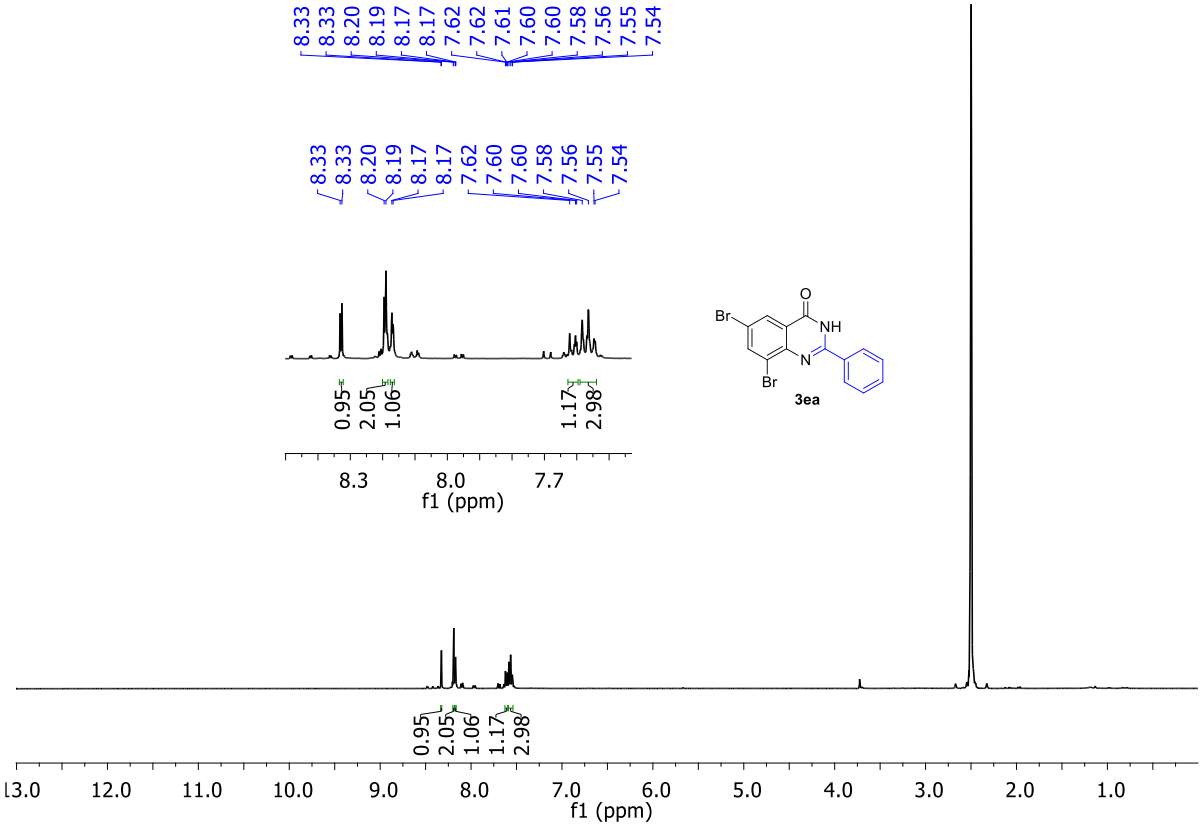
^{1}H NMR (500 MHz, DMSO-D6):



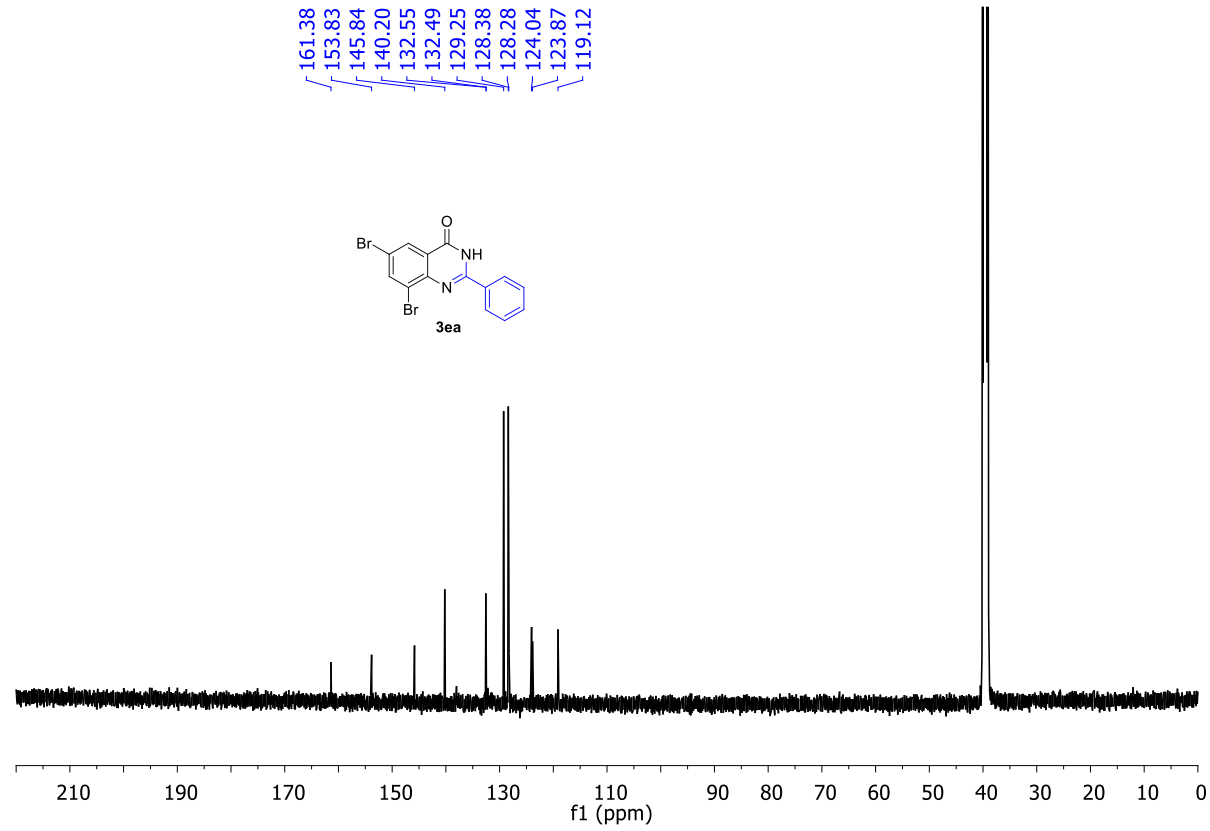
^{13}C NMR (101 MHz, DMSO-D6):



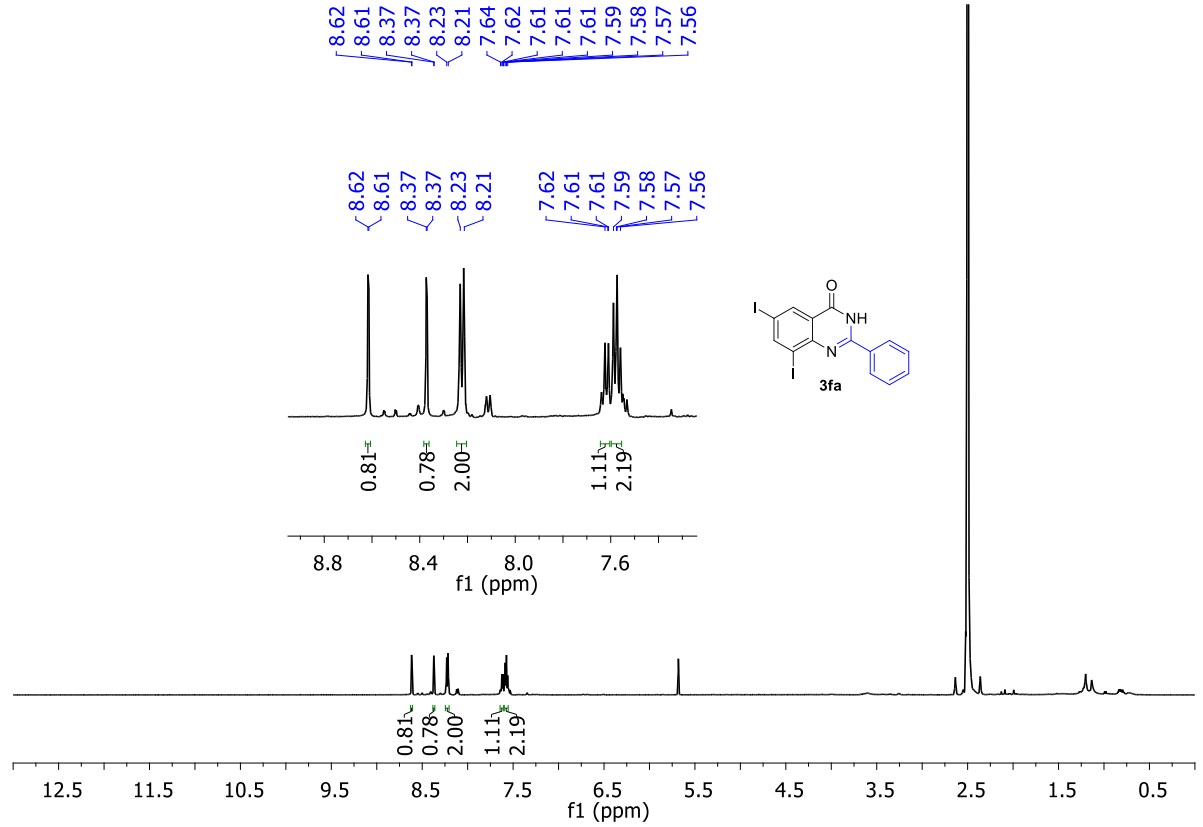
^{1}H NMR (400 MHz, DMSO-D6):



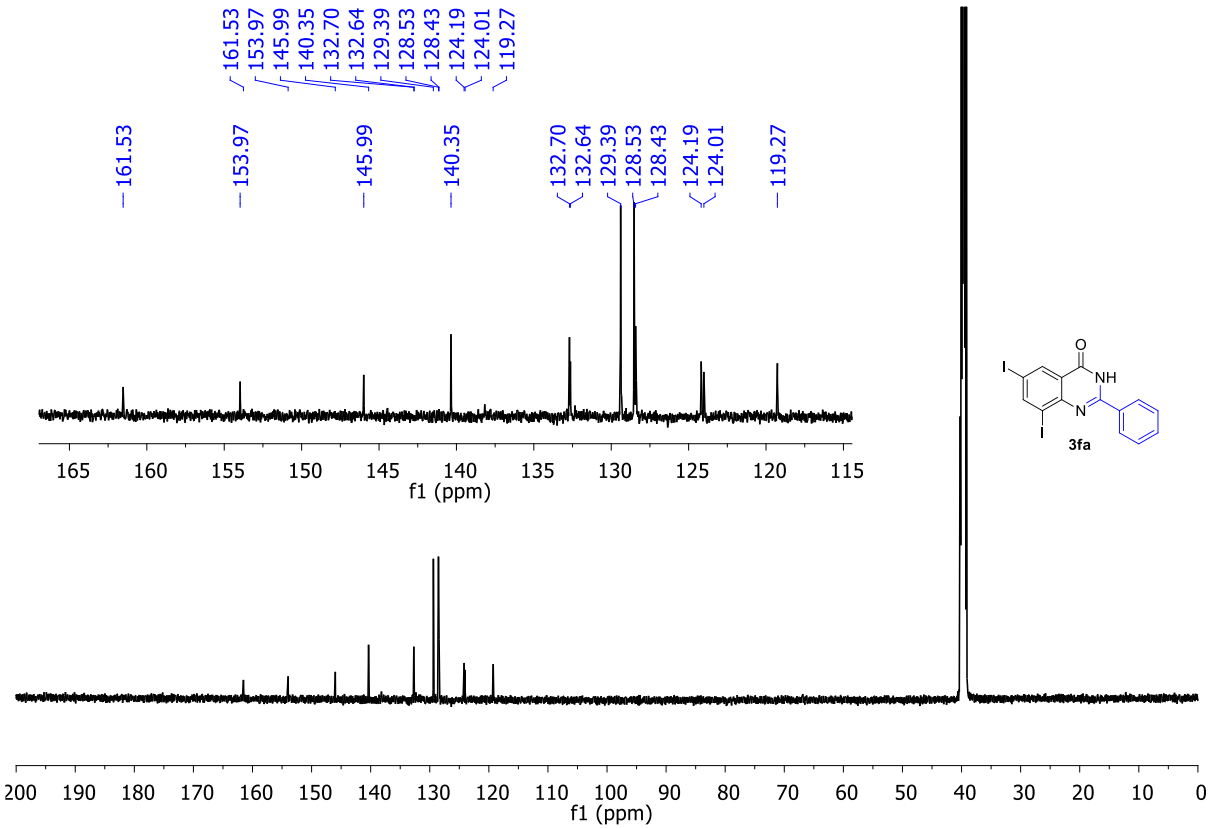
^{13}C NMR (126 MHz, DMSO-D6):



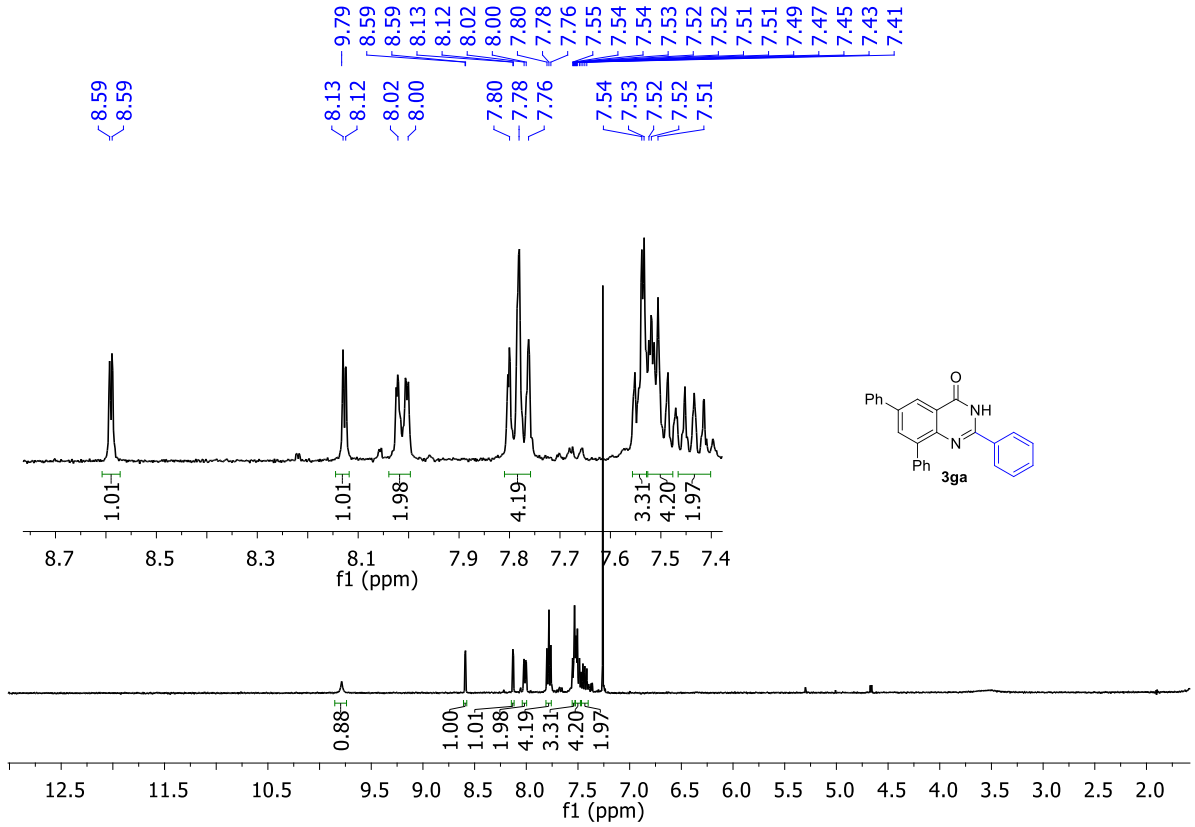
^{1}H NMR (500 MHz, DMSO-D6):



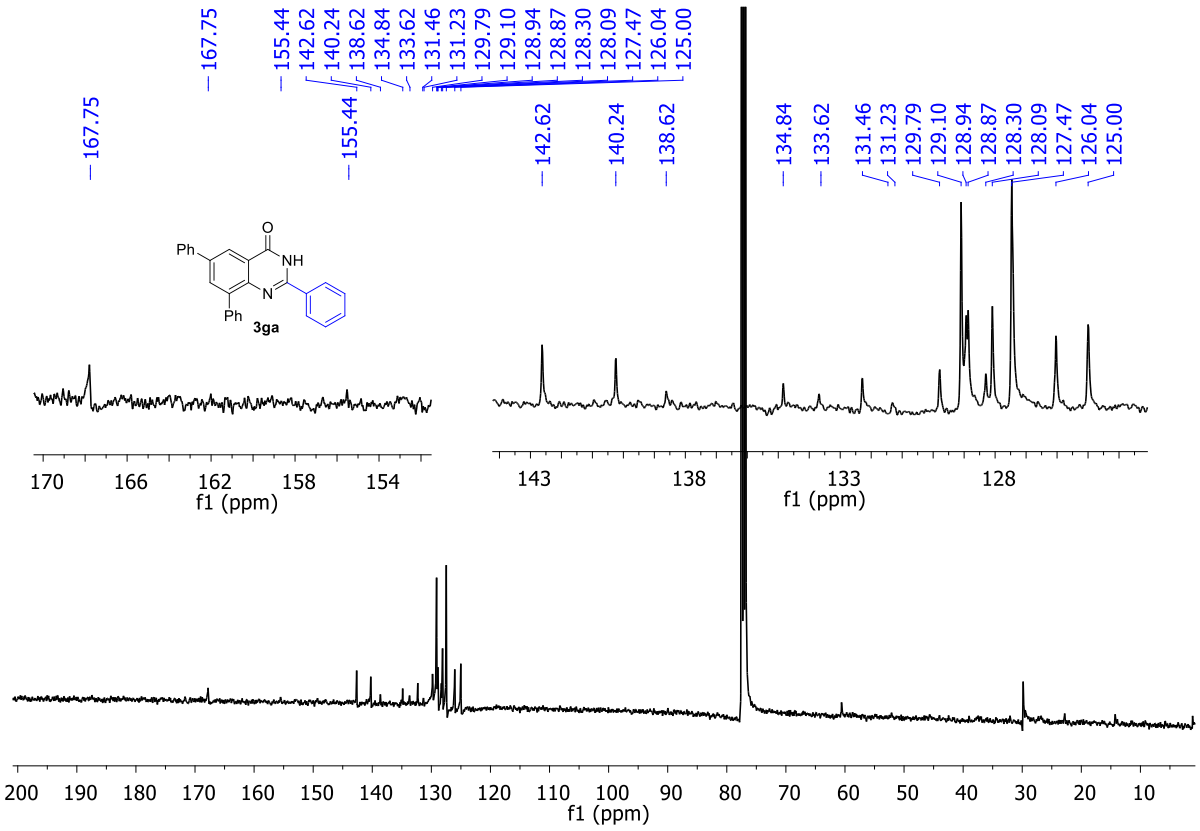
^{13}C NMR (126 MHz, DMSO-D6):



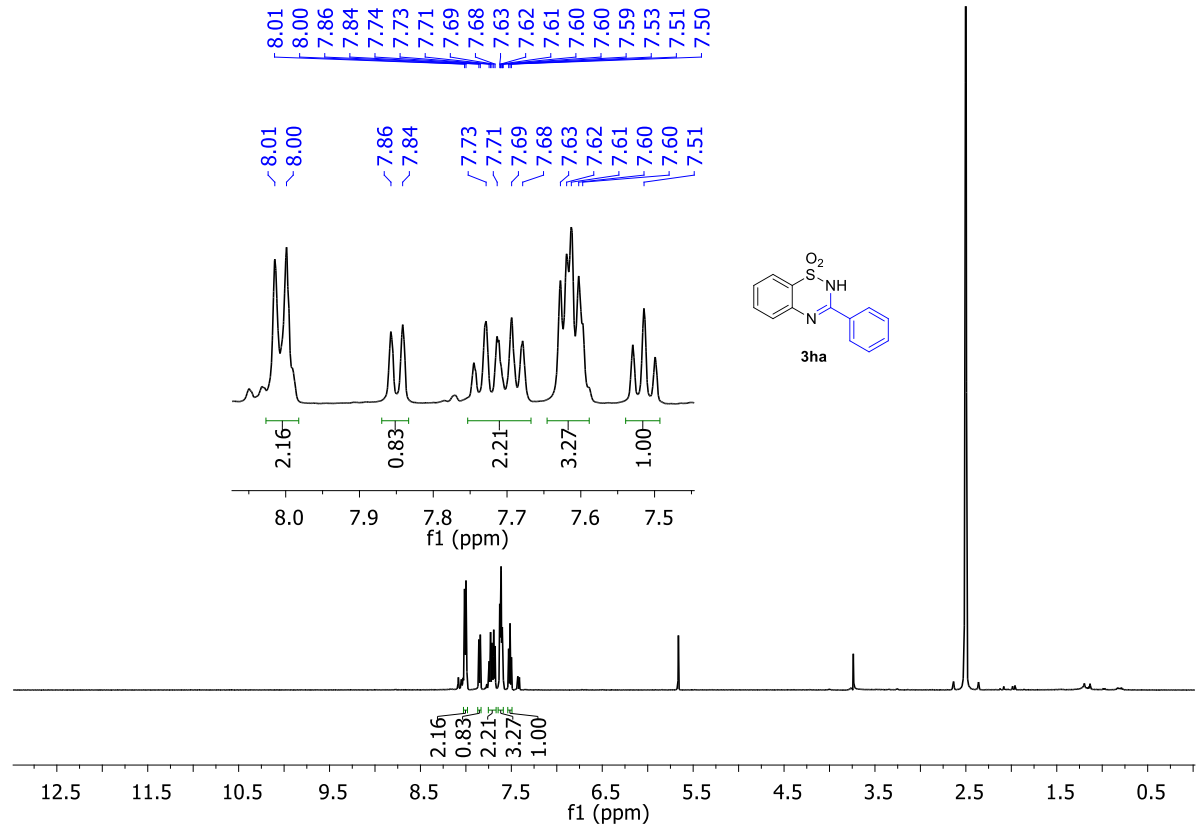
^{1}H NMR (400 MHz, $CDCl_3$):



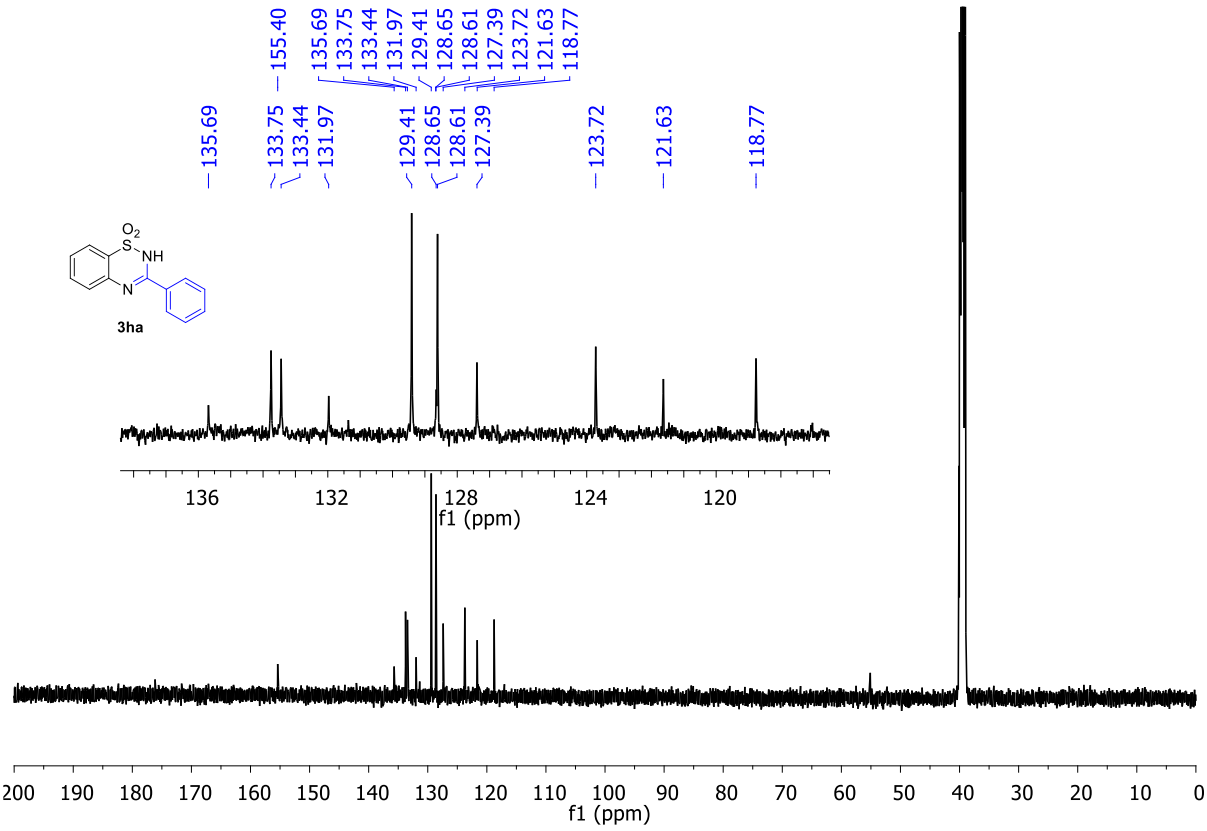
^{13}C NMR (101 MHz, $CDCl_3$):



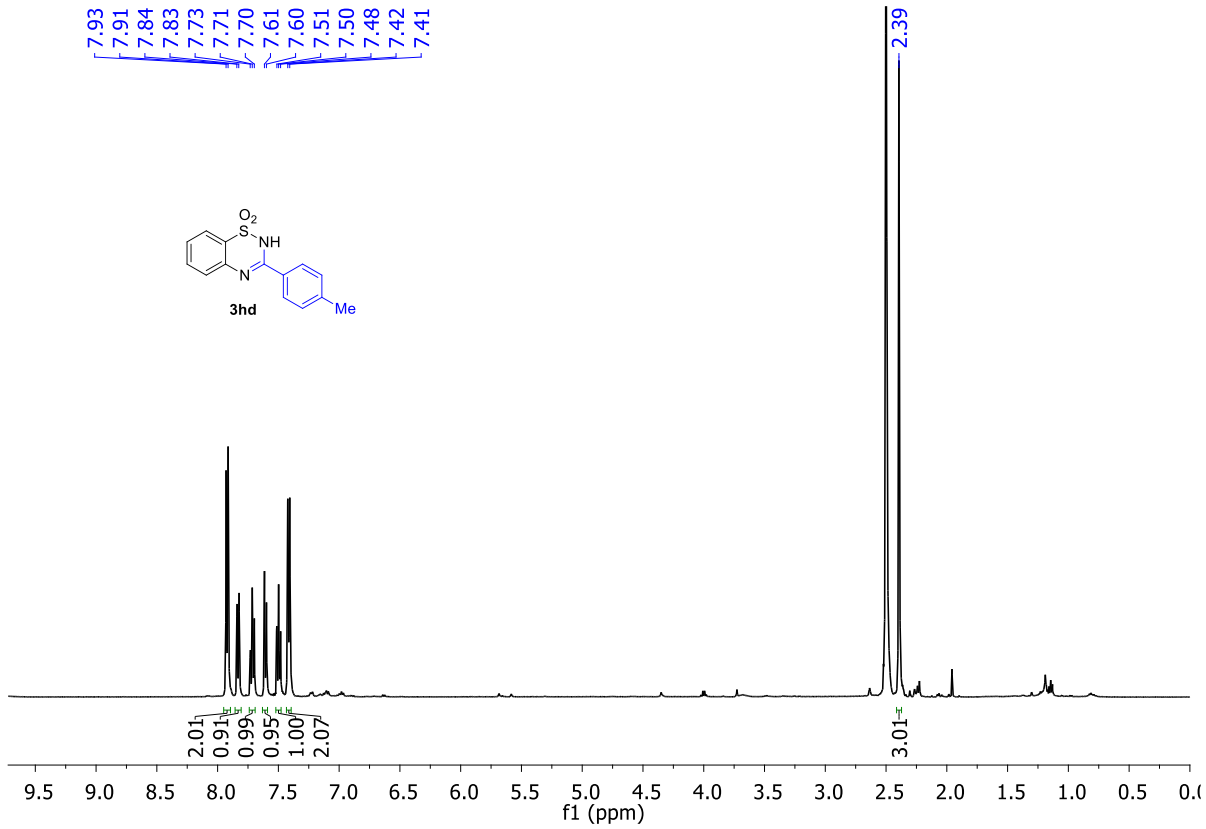
^{1}H NMR (500 MHz, DMSO-D6):



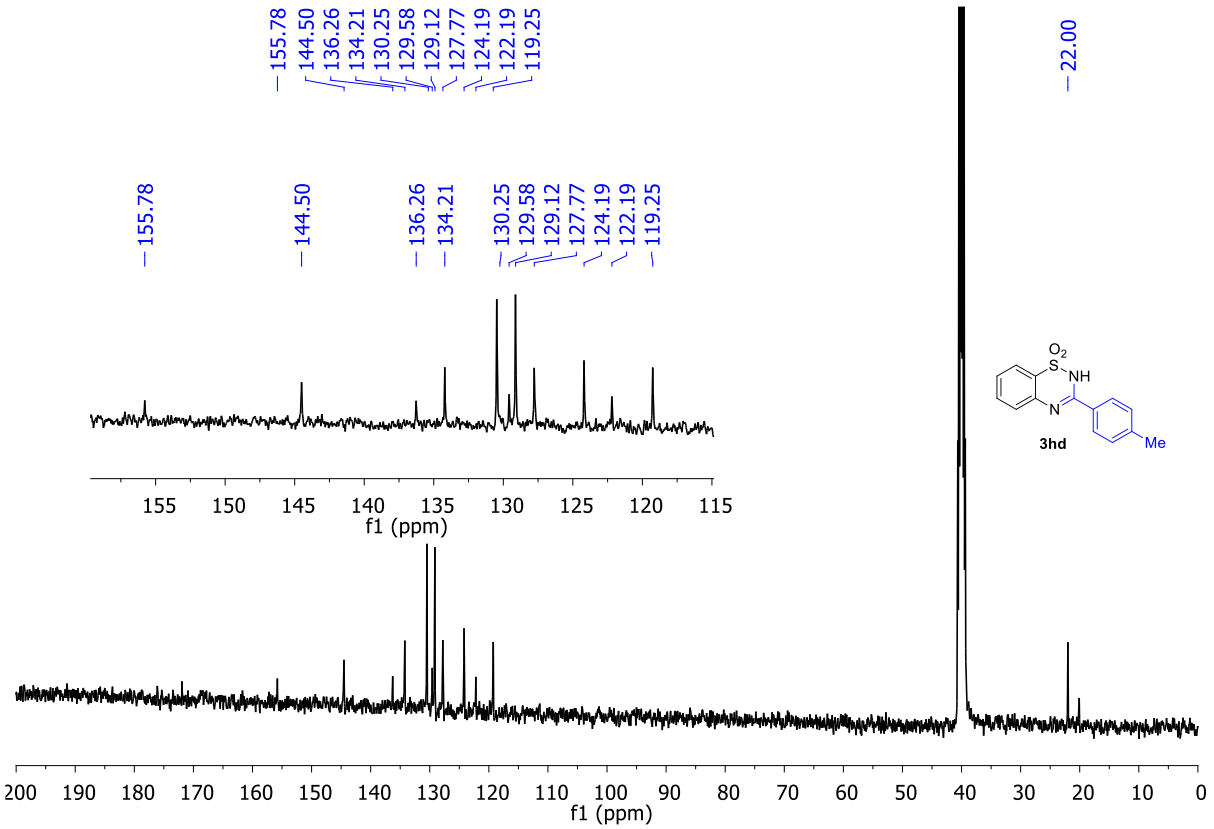
^{13}C NMR (126 MHz, DMSO-D6):



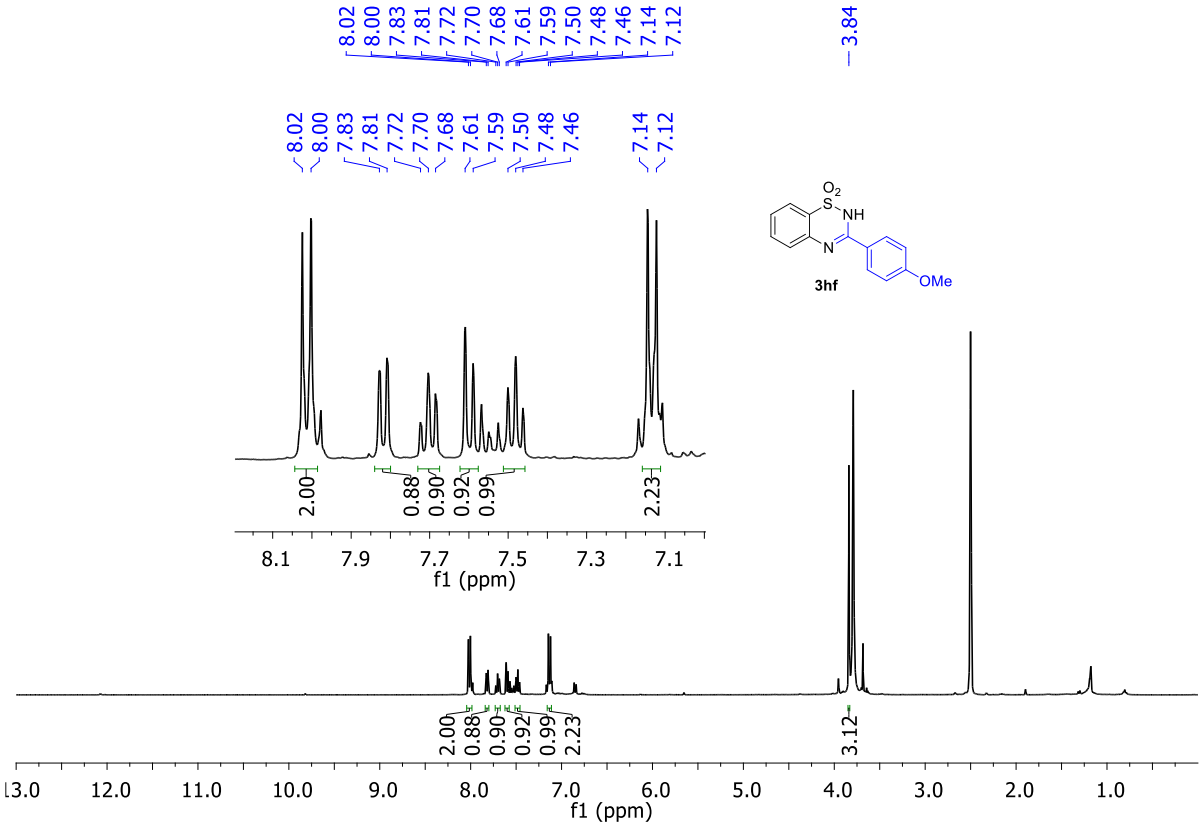
^{1}H NMR (500 MHz, DMSO-D6):



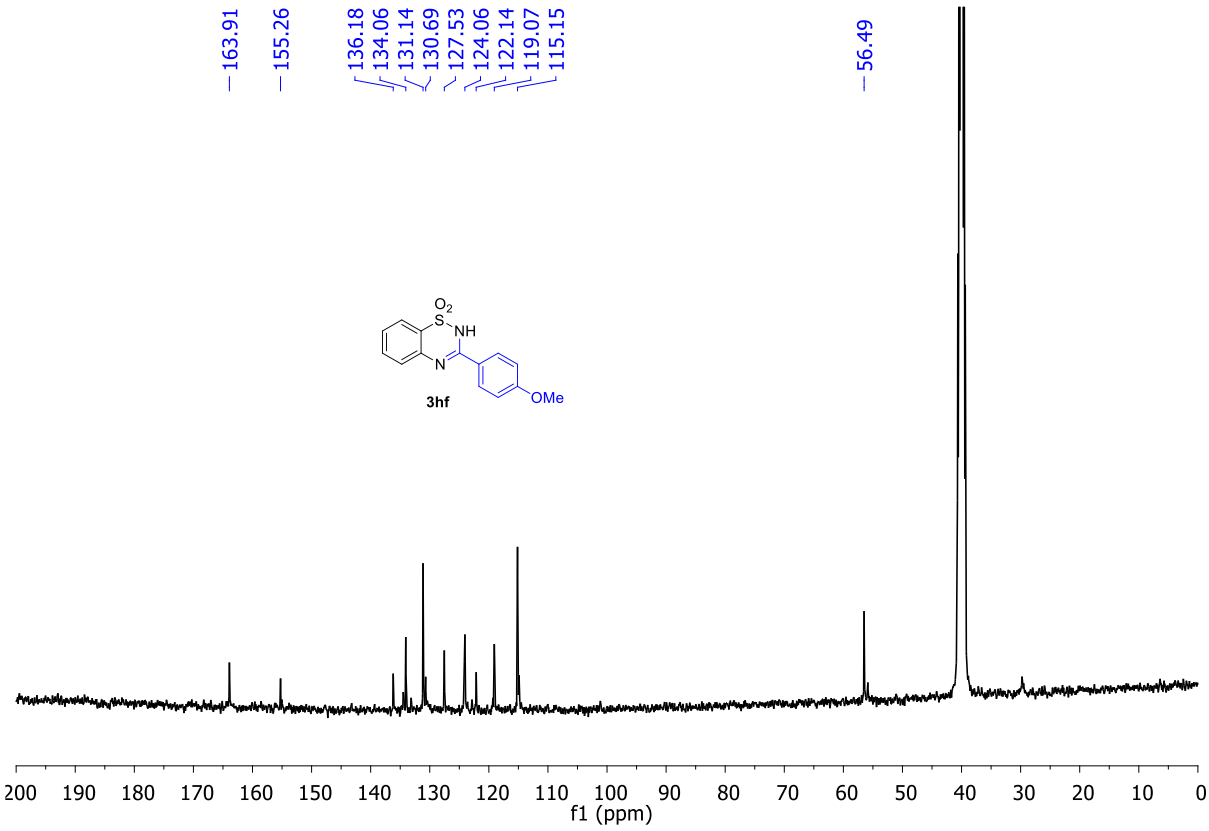
^{13}C NMR (101 MHz, DMSO-D6):



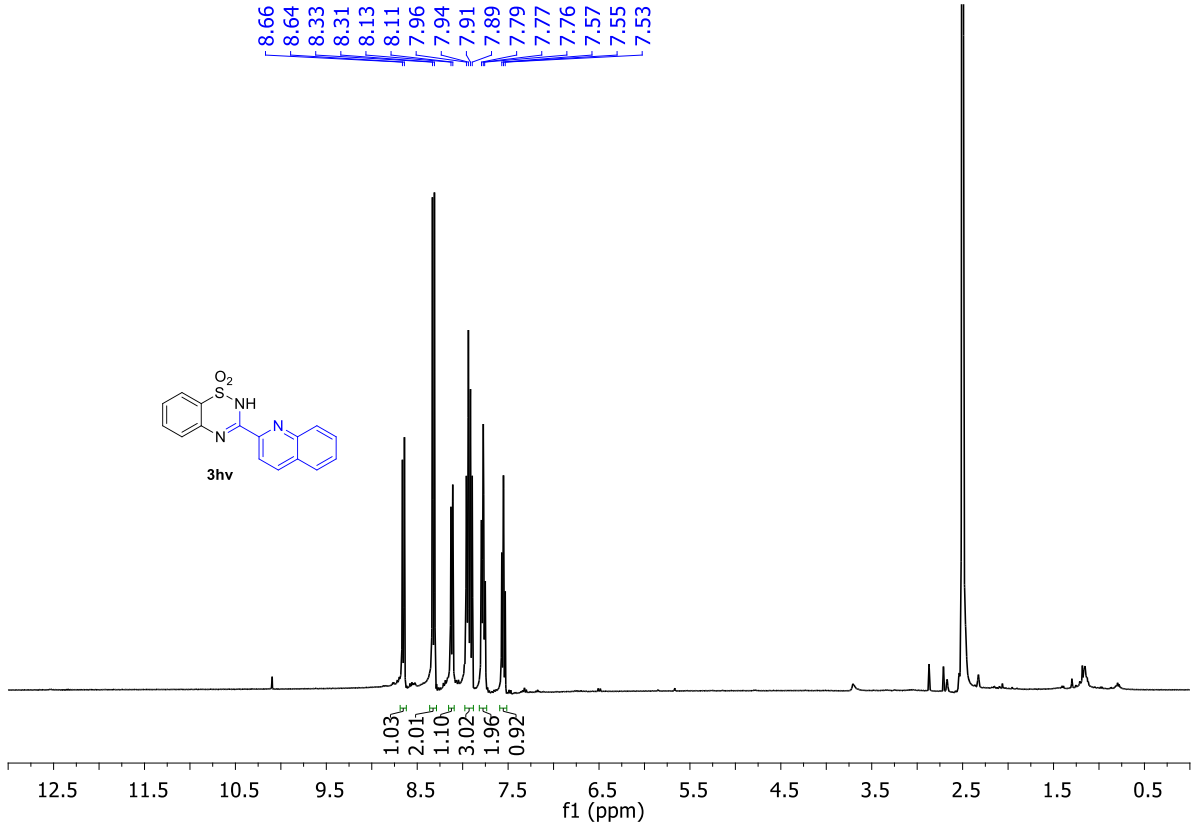
^{1}H NMR (400 MHz, DMSO-D6):



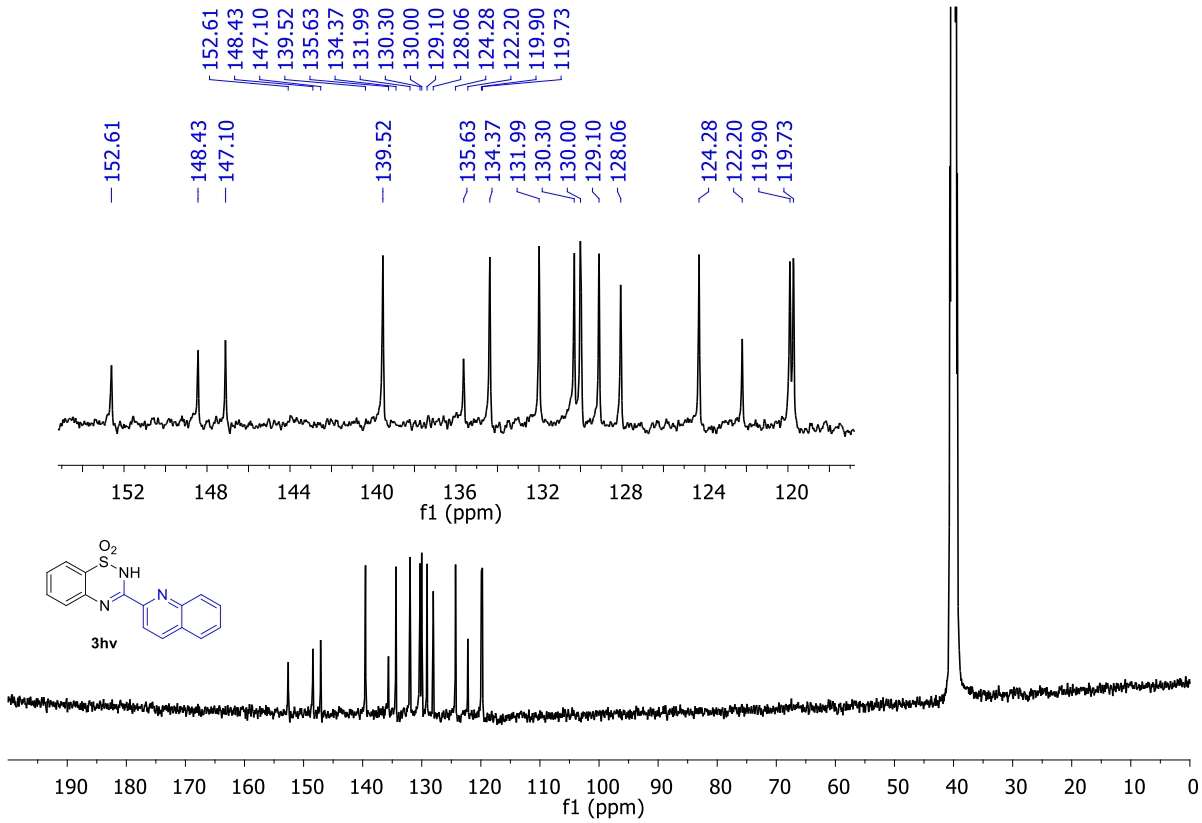
^{13}C NMR (101 MHz, DMSO-D6):



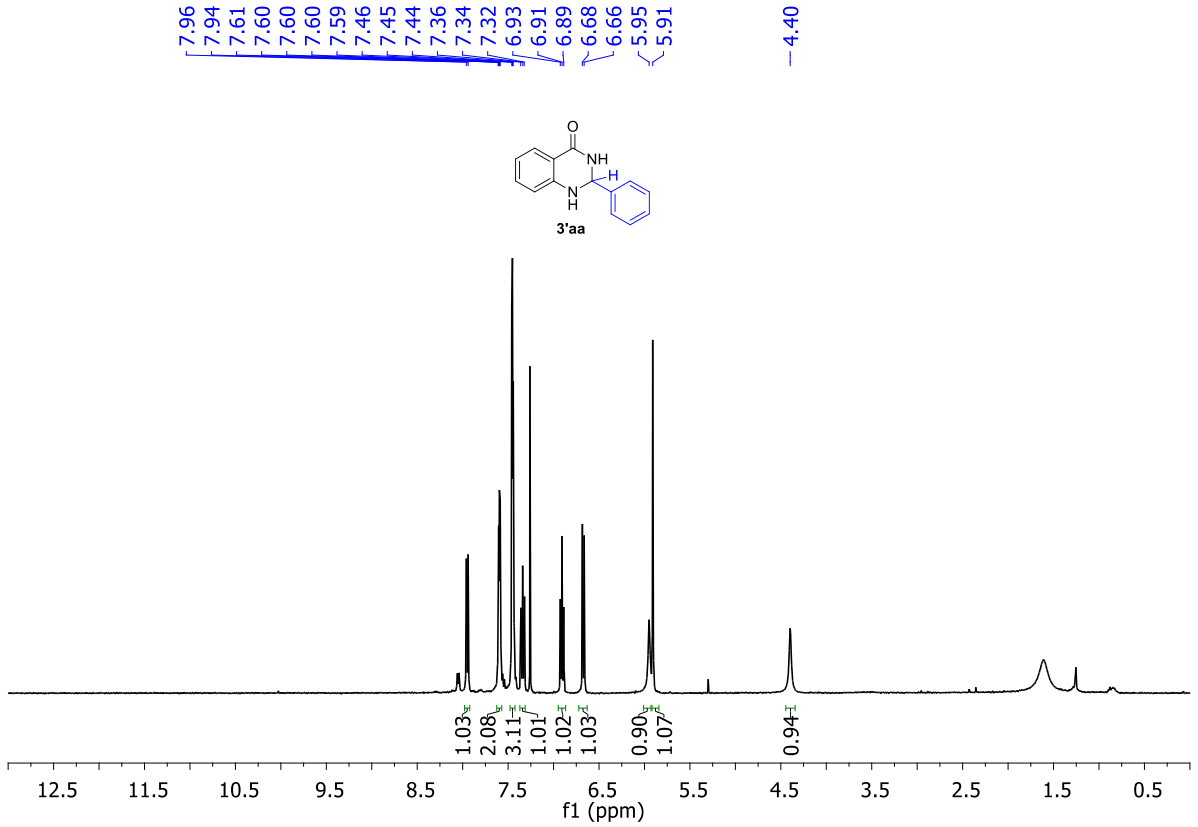
^{1}H NMR (400 MHz, DMSO-D6):



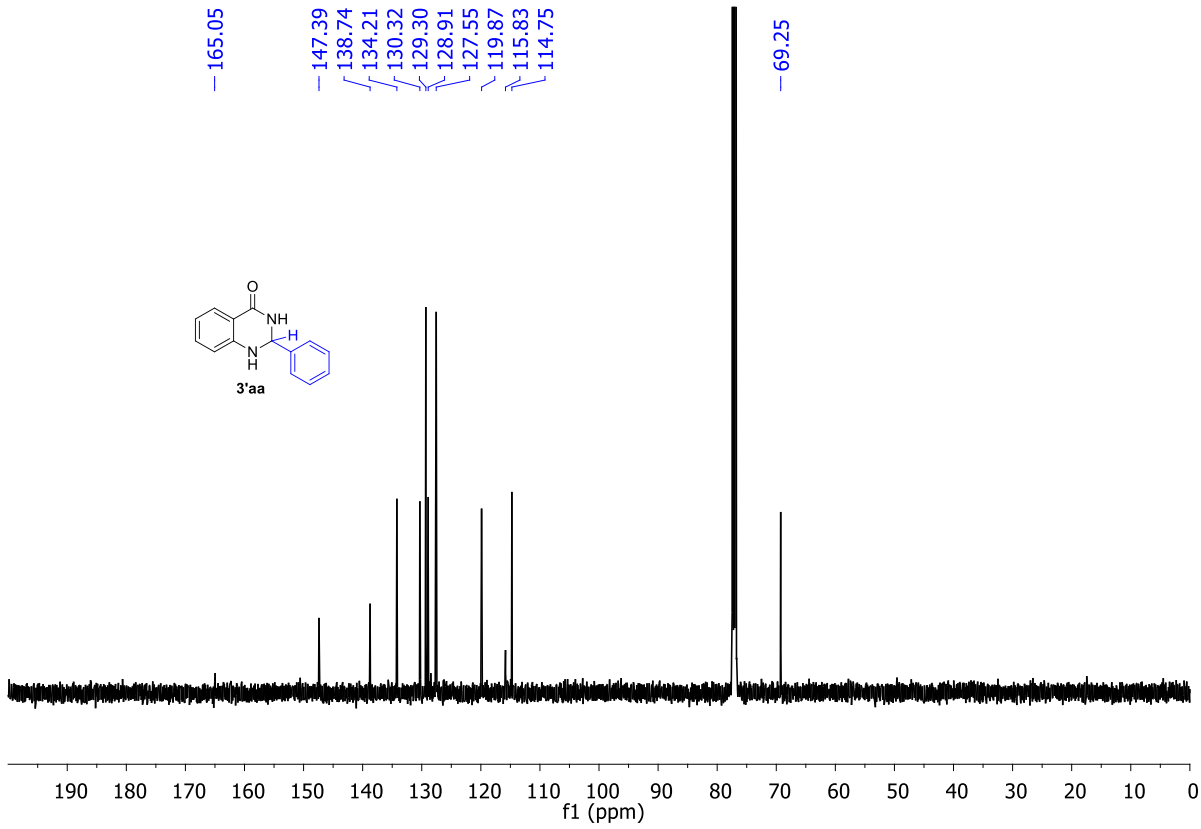
^{13}C NMR (101 MHz, DMSO-D6):



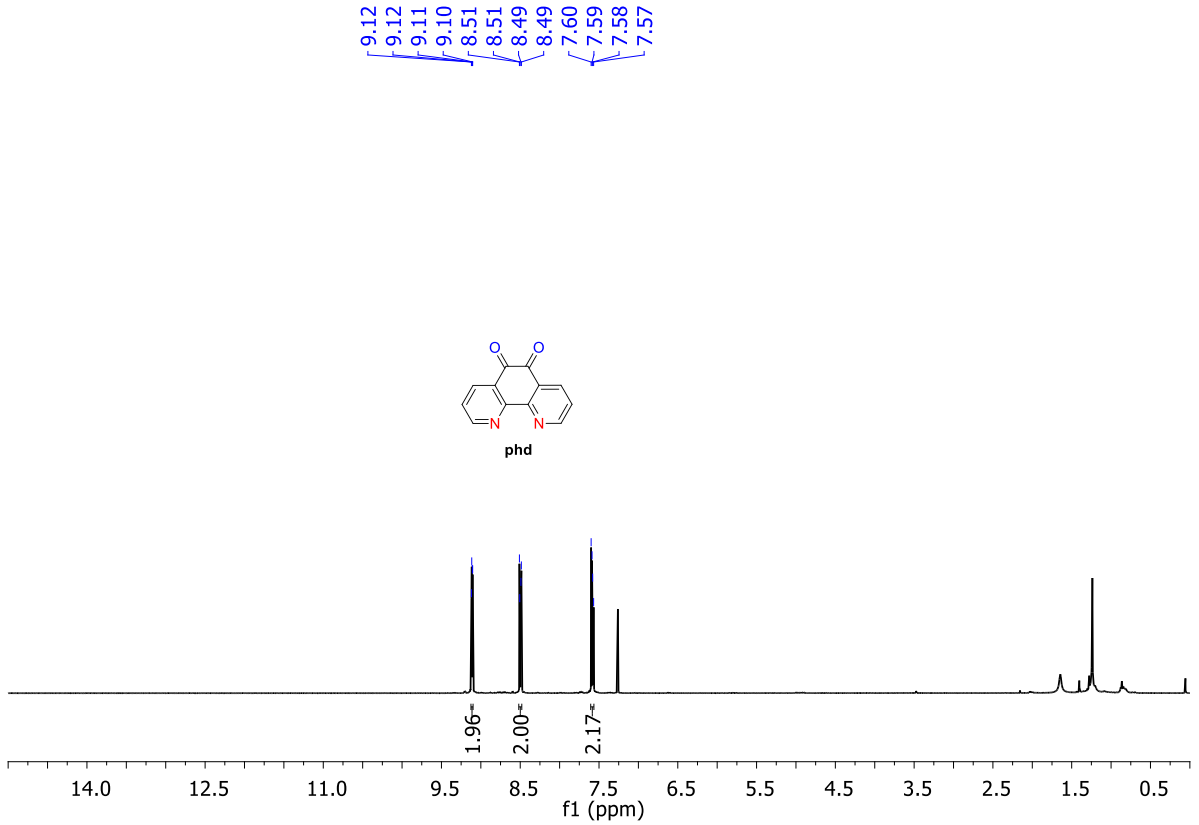
^{1}H NMR (400 MHz, $CDCl_3$):



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



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



^{13}C NMR (101 MHz, $CDCl_3$):