Supporting Information

Merging Ullmann-type Cyclization and Ring-Expansion：Facile Assembly of Pyrimidine-Fused Quinazolinones by Copper Catalysis

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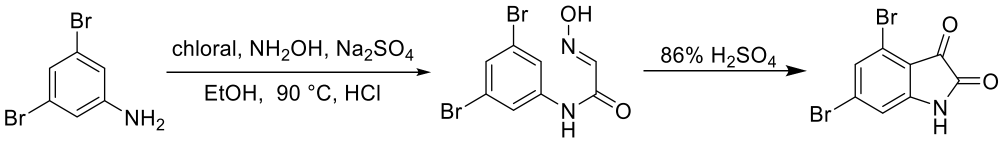
1. General information

Unless otherwise noted, all reagents and solvents were commercially available and used without further purification. We were thankful for the complimentary oxalamide ligands (**L4** and **L5**) of the Ma's group from the Shanghai Institute of Organic Chemistry (SIOC, CAS). TLC analysis was performed using pre-coated glass plates. Column chromatography was performed using silica gel (200-300 mesh). ^{1}H NMR spectra were recorded on a Varian Mercury 300 MHz, 400 MHz or 600 MHz spectrometer. Chemical shifts are reported in ppm, relative to the internal standard of tetramethylsilane (TMS). HRMS were obtained on an Apex-Ultra MS equipped with an electrospray source. The X-ray crystal-structure determinations of **3aa** and **7'** were obtained on a Bruker-AXS D8 Quest diffractometer.

2. General procedure for the synthesis of substrates 1 (Taking 1d as an example):

1c, **1d**, **1e**, **1f, 1g** were prepared according to the literature procedure[1] (Taking **1d** as an example):

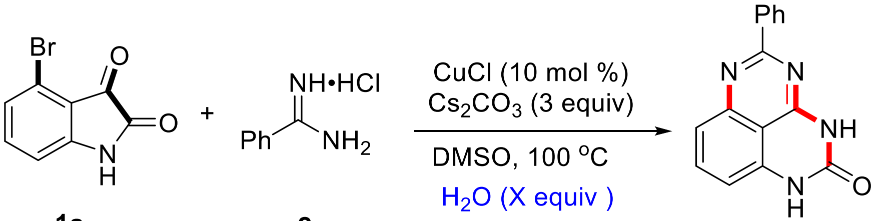


Step 1: A rounded flask was charged with 3,5-dibromoaniline (3.67 g, 14 mmol), and 15 mL water. Then while stirring, concentrated hydrochloric acid (15 mL) was dropwise added under ice-bath in it. Prepared a beaker to heat 60 mL water at the same time, and dissolved anhydrous Na_2SO_4 (4.402 g, 31 mmol) and chloral hydrate (2.5 g, 15.4 mmol) at 90 °C. Poured the hot solution into the rounded flask who was still under ice-bath, then white insoluble matter can be seen. Subsequently the resulting mixture was stirred at 90 °C under oil bath with a mixed solution [dissolving hydroxylamine hydrochloride (3.5 g, 45 mmol) by 15 mL water and 20 mL ethanol] added in. After disappearance of the reactant in the aqueous phase (monitored by TLC) and appearance of the red oil at the bottom of the flask, extracted with EtOAc three times (3 × 50 mL). The extract was washed with 30% NaCl solution (v/v), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was a dark red solid.

Step 2: Under the condition of ice bath and magnetic stirring, concentrated H_2SO_4 (10 mL) was dripped into dry powder preform in rounded flask. Then the flask was placed to oil bath under 90 °C. After one hour for reaction, the flask was taken out and cooled to room temperature, and then poured the solution into 200 mL ice water to quench the reaction. Suction filtration with Brinell funnel, dissolving the filter cake with EtOAc, and combining EtOAc used for extracting filtrate (3 × 100 mL). The extract was washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel using PE/EA (2:1) to yield the desired product **3d** as a dark red solid.

3. Optimization of the reaction conditions

Table S1. Screening the amount of H_2O[a]

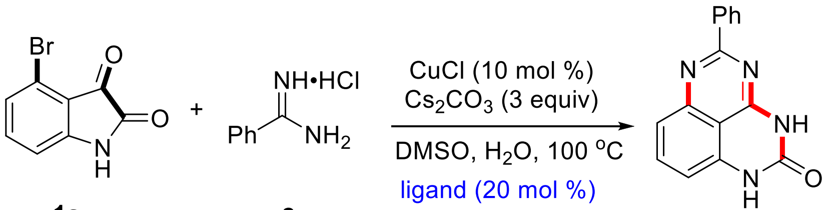


1a **2a** **3aa**

entry	H_2O (equiv)	yield(%)[b]
1	0	76
2	1	78
3	2	80
4	3	82
5	5	77

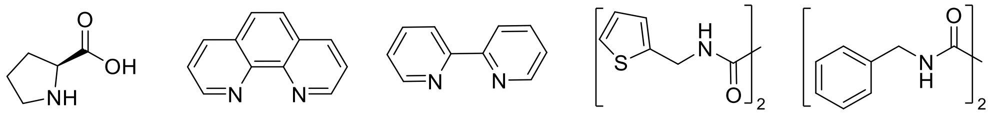
[a]Reaction conditions: **1a** (0.3 mmol, 1.0 equiv), **2a** (0.75 mmol, 2.5 equiv), catalyst (0.03 mmol, 10 mol %), H_2O (X equiv) and Cs_2CO_3 (0.9 mmol, 3.0 equiv) in DMSO (3.0 mL) at 100 °C for 12 h. [b]Isolated yields

Table S2. Screening of the ligands [a]



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

entry	ligand	yield(%)[b]
1	L1	76
2	L2	72
3	L3	69
4	L4	70
5	L5	73



L1 L2 L3 L4 L5

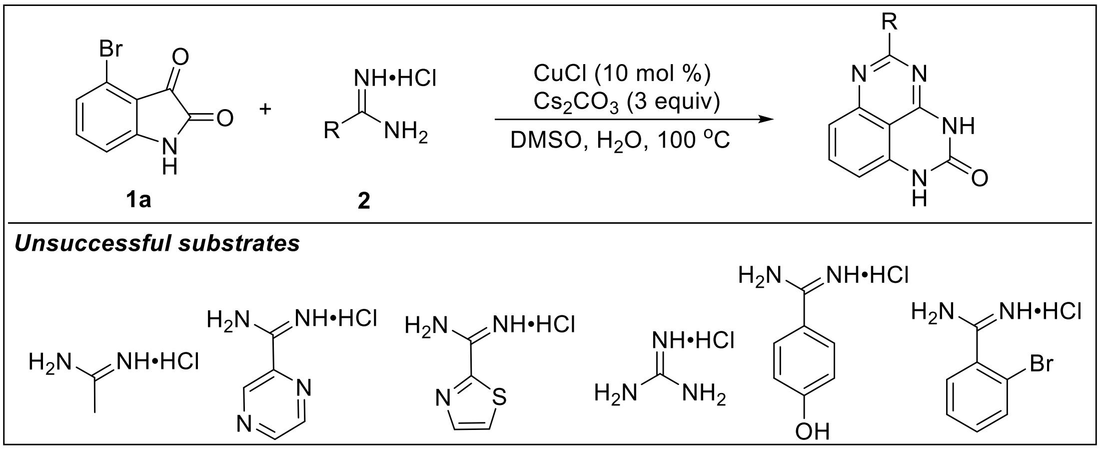
[a]Reaction conditions: **1a** (0.3 mmol, 1.0 equiv), **2a** (0.75 mmol, 2.5 equiv), catalyst (0.03 mmol, 10 mol %), ligand (0.06 mmol, 20 mol %), Cs_2CO_3 (0.9 mmol, 3.0 equiv) and H_2O (0.9 mmol, 3.0 equiv) in DMSO (3.0 mL) at 100 °C for 12 h. [b]Isolated yields.

4. General procedure for preparation of 3 (3aa as an example)

A sealed tube was charged with 4-bromoisatin **1a** (68 mg, 0.3 mmol), benzamidine hydrochloride **2a** (117 mg, 0.75 mmol), CuCl (3 mg, 0.03 mmol), Cs_2CO_3 (293 mg, 0.9 mmol), and H_2O (16 mg, 0.9 mmol) in DMSO (3 mL) was stirred at 100 °C in a sealed vessel, after disappearance of the reactant (monitored by TLC), then added 50 mL water to the mixture, extracted with EtOAc three times (3 × 50 mL). The extract was washed with 30% NaCl solution (V/V), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (Petroleum ether / ethyl acetate = 2:1) to yield the desired product **3aa** as a white solid (64 mg, 82% yield).

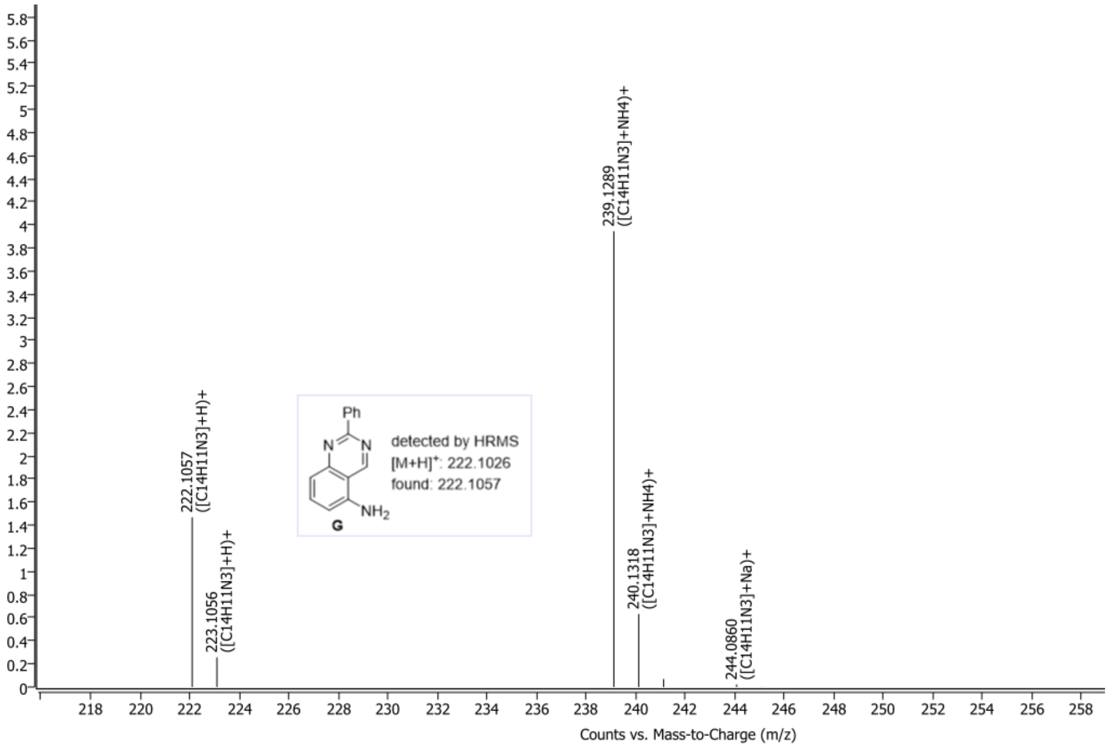
5. Unsuccessful Substrates

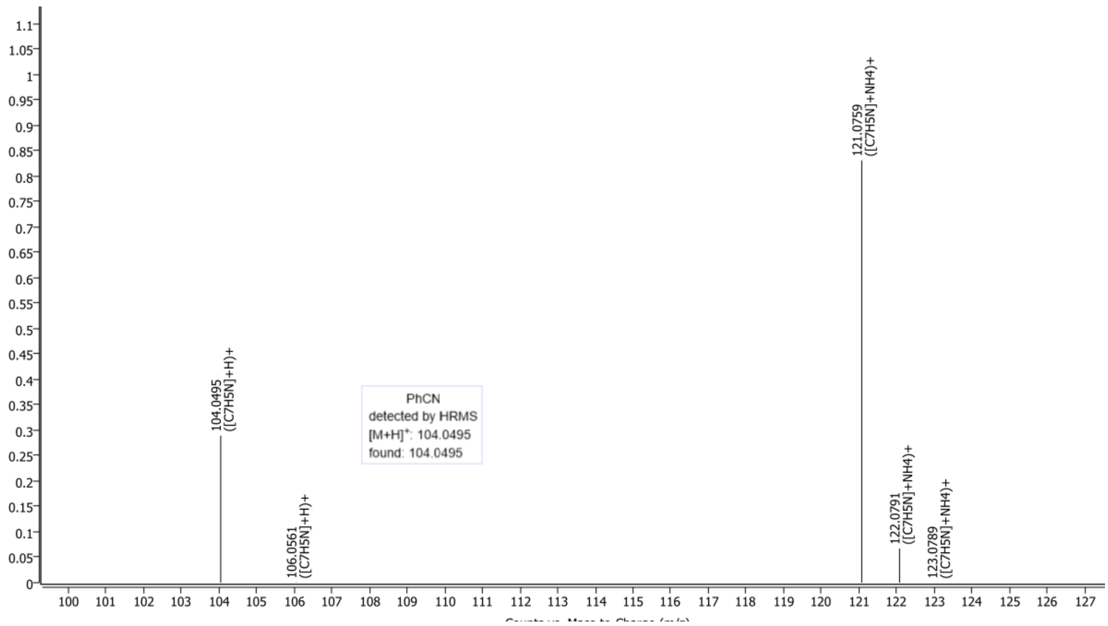
Unfortunately, it was found that amidine hydrochlorides such as acetamidine hydrochloride, pyrazine-2-carboximidamide hydrochloride, 1,3-thiazole-2-carboximidamide hydrochloride, guanidine hydrochloride, 4-hydroxybenzamidine hydrochloride and 2-bromobenzamidine hydrochloride were ineffective in current reaction system.

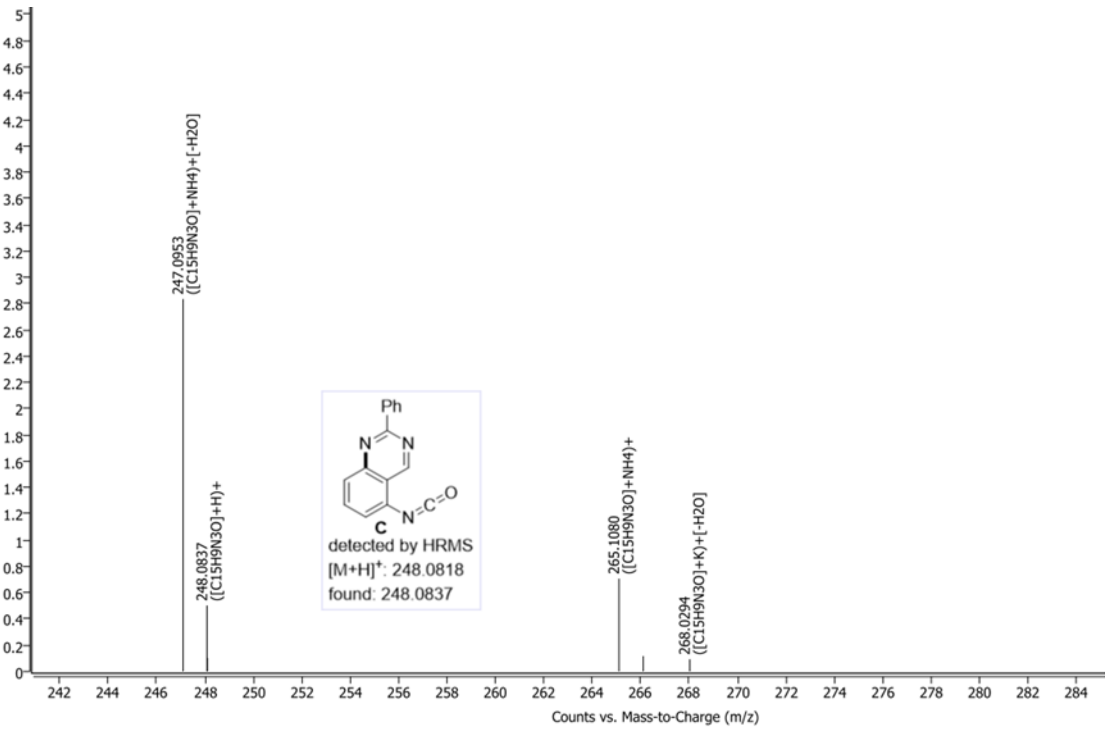


6. Studying the reaction mechanism

A mixture of 4-bromoisatin **1a** (0.3 mmol), benzamidine hydrochloride **2a** (0.75 mmol), CuCl (10 mol %), Cs_2CO_3 (0.9 mmol), and H_2O (0.9 mmol) in DMSO (3 mL) was stirred at 100 °C in a sealed vessel for 5 h. The by-product 2-phenylquinazolin-5-amine (**G**), PhCN and intermediate 5-isocyanato-2 phenylquinazoline (**C**) was detected by HRMS. 2-phenylquinazolin-5-amine (**G**); HRMS (ESI): m/z calcd for $C_{14}H_{12}N_3^+$ $(M+H)^+$: 222.1026; found 222.1057. PhCN; HRMS (ESI): m/z calcd for $C_7H_6N^+$ $(M+H)^+$: 104.0495; found 104.0495. 5-isocyanato-2-phenylquinazoline (**C**); HRMS (ESI): m/z calcd for $C_{15}H_{10}N_3O^+$ $(M+H)^+$: 248.0818; found 248.0837.




104.0495
([C7H5N]+H)+
106.0561
([C7H5N]+H)+
PhCN
detected by HRMS
[M+H]+: 104.0495
found: 104.0495
121.0759
([C7H5N]+NH4)+
122.0791
([C7H5N]+NH4)+
123.0789
([C7H5N]+NH4)+


247.0953
([C15H9N3O]+NH4)+[-H2O]
248.0837
([C15H9N3O]+H)+
Ph
N
N
N=C=O
C
detected by HRMS
[M+H]+: 248.0818
found: 248.0837
265.1080
([C15H9N3O]+NH4)+
268.0294
([C15H9N3O]+K)+[-H2O]
Counts vs. Mass-to-Charge (m/z)

7. X-ray crystal data of compound 3aa

The purified compound **3aa** is dissolved in a mixed solvent of THF and petroleum ether, and placed in a dark cabinet to slowly evaporate. After two days, colourless particles crystals ware obtained. Single Crystal X-ray diffraction data were collected using a Bruker-AXS D8 Quest diffractometer (Mo Kα, λ = 0.71073 Å).

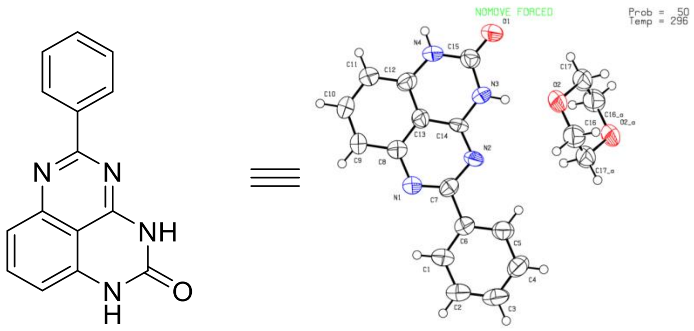


Figure S1 X-ray crystal structure of **3aa** (CCDC: 2206220).

Table S3. Crystal data and structure refinement for **3aa**

CCDC Number	2206220	
Identification code	**3aa**	
Empirical formula	$C_{17}H_{14}N_4O_2$	
Formula weight	306.32	
Temperature	296(2) K	
Crystal system	Triclinic	
Space group	P –1	
Unit cell dimensions	a = 6.992 Å	α = 68.00°.
	b = 9.641 Å	β = 84.19°.
	c = 12.262 Å	γ = 74.40°.
Volume	738.2 Å^3	
Z	2	
ρ_{calc}g/cm^3	1.378	
μ/mm^{-1}	0.094	
F(000)	320.0	
Theta range for data collection	2.386 to 24.997	
Reflections collected	2599	
Independent reflections	2599 [R_{int} = 0, R_{sigma} = 0.1608]	
Data / restraints / parameters	2599/0/208	
Goodness-of-fit on F^2	1.107	
Final R indices [I>2sigma(I)]	R_1 = 0.1212, wR_2 = 0.2298	
R indices (all data)	R_1 = 0.2595, wR_2 = 0.2923	
Largest diff. peak and hole	0.19/-0.282 e Å^{-3}	

8. X-ray crystal data of compound 7’

The purified compound **7’** is dissolved in a mixed solvent of dichloromethane and petroleum ether, and placed in a dark cabinet to slowly evaporate. After two days, colourless particles crystals ware obtained. Single Crystal X-ray diffraction data were collected using a Bruker-AXS D8 Quest diffractometer (Mo Kα, λ = 0.71073 Å).

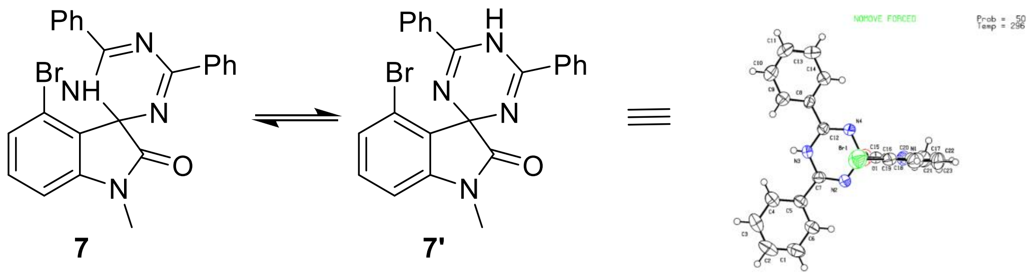


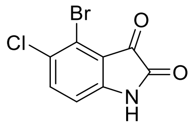
Figure S2 X-ray crystal structure of **7’** (CCDC: 2206166).

Table S4. Crystal data and structure refinement for **7’**

CCDC Number	2206166	
Identification code	**7’**	
Empirical formula	$C_{23}H_{17}BrN_4O$	
Formula weight	445.32	
Temperature	296.15 K	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 9.402(5) Å	α = 75.414(10)°.
	b = 10.072(5) Å	β = 70.202(10)°.
	c = 12.350(7) Å	γ = 65.089(10)°.
Volume	989.8(9) $Å^3$	
Z	2	
ρ_{calc}g/cm^3	1.494	
μ/mm^{-1}	2.099	
F(000)	452.0	
Theta range for data collection	5.268 to 50.388°.	
Reflections collected	28123	
Independent reflections	3547[R_{int} = 0.1341, R_{sigma} = 0.1081]	
Data / restraints / parameters	3547/0/267	
Goodness-of-fit on F^2	1.026	
Final R indices [I>2sigma(I)]	R_1 = 0.0652, wR_2 = 0.1034	
R indices (all data)	R_1 = 0.1701, wR_2 = 0.1378	
Largest diff. peak and hole	0.28/-0.41 e $Å^{-3}$	

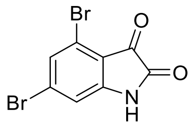
9. Spectral data of compound 1c−1g, 3aa−3an, 3ba−3gf, 5 and 7.

4-bromo-5-chloroindoline-2,3-dione (1c):



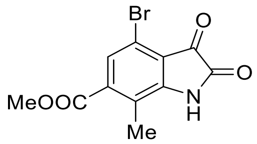
Yield 64% (2320 mg); dark red solid; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.22 (s, 1H), 7.72 (d, J = 8.0 Hz, 1H), 6.89 (d, J = 8.0 Hz, 1H); ^{13}C NMR (150 MHz, DMSO-d_6): δ = 181.01, 158.39, 150.86, 137.81, 127.59, 119.44, 118.11, 112.62. HRMS (ESI): m/z calcd for $C_8H_3BrClNO_2Na^+$ $(M+Na)^+$: 281.8928; found 281.8944.

4,6-dibromoindoline-2,3-dione (1d):



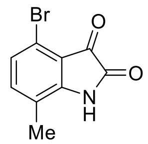
Yield 70% (2969 mg); dark red solid; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.27 (s, 1H), 7.49 (s, 1H), 7.04 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6): δ = 180.76, 158.70, 153.05, 131.54, 128.69, 120.30, 115.94, 114.27. HRMS (ESI): m/z calcd for $C_8H_3Br_2NO_2Na^+$ $(M+Na)^+$: 325.8423; found 325.8405.

methyl 4-bromo-7-methyl-2,3-dioxoindoline-6-carboxylate (1e):



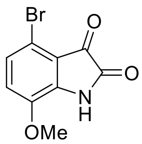
Yield 67% (2786 mg); dark red solid; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.33 (s, 1H), 7.46 (s, 1H), 3.85 (s, 3H), 2.21 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 181.93, 165.62, 159.04, 151.84, 138.70, 127.02, 120.81, 117.89, 115.79, 52.76, 13.14. HRMS (ESI): m/z calcd for $C_{11}H_8BrNO_4Na^+$ $(M+Na)^+$: 319.9529; found 319.9532.

4-bromo-7-methylindoline-2,3-dione (1f):



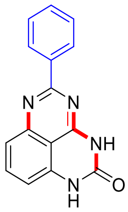
Yield 76% (3501 mg); dark red solid; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.20 (s, 1H), 7.29 (d, J = 8.0 Hz, 1H), 7.11 (d, J = 8.0 Hz, 1H), 2.13 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 182.06, 159.11, 151.05, 139.93, 126.38, 120.84, 116.37, 115.87, 15.14. HRMS (ESI): m/z calcd for $C_9H_6BrNO_2Na^+$ $(M+Na)^+$: 261.9474; found 261.9478.

4-bromo-7-methoxyindoline-2,3-dione (1g):



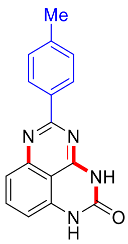
Yield 49% (1749 mg); dark red solid; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.24 (s, 1H), 7.21 (d, J = 8.8 Hz, 1H), 7.14 (d, J = 8.8 Hz, 1H), 3.85 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 181.86, 158.54, 144.17, 142.02, 126.50, 121.64, 116.13, 109.19, 56.34. HRMS (ESI): m/z calcd for $C_9H_7BrNO_3^+$ $(M+H)^+$: 255.9604; found 255.9604.

5-phenyl-1*H*-pyrimido[4,5,6-de]quinazolin-2(3*H*)-one (3aa):



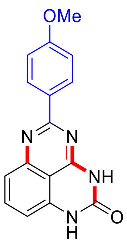
Yield 82 % (64 mg); white solid; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.59 (s, 1H), 11.10 (s, 1H), 8.46-8.37 (m, 2H), 7.73 (t, J = 8.0 Hz, 1H), 7.54–7.46 (m, 3H), 7.27 (d, J = 8.4 Hz, 1H), 6.82 (d, J = 7.6 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 161.59, 158.50, 150.07, 149.78, 138.10, 137.75, 135.80, 130.61, 128.36, 128.01, 117.00, 106.47, 103.93. HRMS (ESI): m/z calcd for $C_{15}H_{11}N_4O^+$ $(M+H)^+$: 263.0927; found 263.0930.

5-(p-tolyl)-1*H*-pyrimido[4,5,6-de]quinazolin-2(3*H*)-one (3ab):



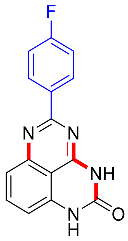
Yield 73% (60 mg); white solid; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 11.53 (s, 1H), 11.06 (s, 1H), 8.30 (d, J = 7.8 Hz, 2H), 7.72 (t, J = 8.1 Hz, 1H), 7.29 (d, J = 7.8 Hz, 2H), 7.24 (d, J = 8.1 Hz, 1H), 6.80 (d, J = 7.8 Hz, 1H), 2.37 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 161.69, 158.43, 150.11, 149.86, 140.46, 138.07, 135.82, 135.07, 129.03, 128.05, 116.98, 106.34, 103.86, 21.06. HRMS (ESI): m/z calcd for $C_{16}H_{13}N_4O^+$ $(M+H)^+$: 277.1084; found 277.1088.

5-(4-methoxyphenyl)-1*H*-pyrimido[4,5,6-de]quinazolin-2(3*H*)-one (3ac):



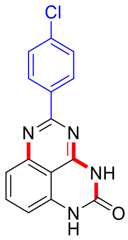
Yield 72% (63 mg); white solid; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.49 (s, 1H), 11.03 (s, 1H), 8.36 (d, J = 8.8 Hz, 2H), 7.69 (t, J = 8.0 Hz, 1H), 7.22 (d, J = 8.4 Hz, 1H), 7.03 (d, J = 8.8 Hz, 2H), 6.77 (d, J = 7.6 Hz, 1H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 161.40, 158.25, 150.06, 149.89, 138.02, 135.66, 130.20, 129.66, 116.79, 113.66, 106.00, 103.59, 55.25. HRMS (ESI): m/z calcd for $C_{16}H_{13}N_4O_2^+$ $(M+H)^+$: 293.1033; found 293.1038.

5-(4-fluorophenyl)-1*H*-pyrimido[4,5,6-de]quinazolin-2(3*H*)-one (3ad):



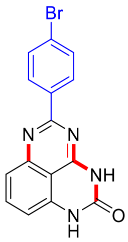
Yield 64% (54 mg); white solid; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.59 (s, 1H), 11.09 (s, 1H), 8.45 (dd, J = 8.0, 6.0 Hz, 2H), 7.74 (t, J = 8.0 Hz, 1H), 7.33 (t, J = 8.8 Hz, 2H), 7.26 (d, J = 8.4 Hz, 1H), 6.82 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 163.81 (d, J = 246.2 Hz), 160.61, 158.48, 149.93, 149.66, 138.07, 135.83, 134.18 (d, J = 2.8 Hz), 130.30 (d, J = 8.8 Hz), 116.89, 115.23 (d, J = 21.5 Hz), 106.56, 103.75. HRMS (ESI): m/z calcd for $C_{15}H_{10}FN_4O^+$ $(M+H)^+$: 281.0833; found 281.0844.

5-(4-chlorophenyl)-1*H*-pyrimido[4,5,6-de]quinazolin-2(3*H*)-one (3ae):



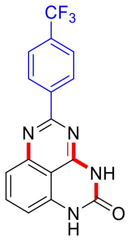
Yield 65% (58 mg); white solid; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.53 (s, 1H), 11.12 (s, 1H), 8.39 (d, J = 8.4 Hz, 2H), 7.73 (t, J = 8.0 Hz, 1H), 7.55 (d, J = 8.8 Hz, 2H), 7.26 (d, J = 8.4 Hz, 1H), 6.82 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 160.50, 158.50, 149.92, 149.57, 138.05, 136.54, 135.80, 135.40, 129.61, 128.36, 116.92, 106.60, 103.85. HRMS (ESI): m/z calcd for $C_{15}H_{10}ClN_4O^+$ $(M+H)^+$: 297.0538; found 297.0541.

5-(4-bromophenyl)-1*H*-pyrimido[4,5,6-de]quinazolin-2(3*H*)-one (3af):



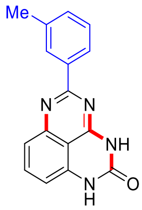
Yield 57% (58 mg); white solid; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.60 (s, 1H), 11.09 (s, 1H), 8.33 (d, J = 8.4 Hz, 2H), 7.82-7.63 (m, 3H), 7.27 (d, J = 8.4 Hz, 1H), 6.83 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 160.62, 158.55, 149.90, 149.58, 138.09, 136.92, 135.89, 131.37, 129.89, 124.38, 116.94, 106.65, 103.90. HRMS (ESI): m/z calcd for $C_{15}H_{10}BrN_4O^+$ $(M+H)^+$: 341.0032; found 341.0035.

5-(4-(trifluoromethyl)phenyl)-1*H*-pyrimido[4,5,6-de]quinazolin-2(3*H*)-one (3ag):



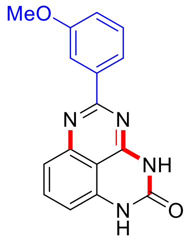
Yield 75% (74 mg); white solid; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.64 (s, 1H), 11.11 (s, 1H), 8.56 (d, J = 8.0 Hz, 2H), 7.85 (d, J = 8.4 Hz, 2H), 7.74 (t, J = 8.0 Hz, 1H), 7.28 (d, J = 8.4 Hz, 1H), 6.84 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 160.13, 158.67, 149.86, 149.48, 141.49, 138.11, 135.91, 130.36 (q, J = 30.0 Hz), 128.51, 125.57 (q, J = 270.7 Hz), 125.24 (q, J = 3.6 Hz), 117.05, 106.95, 104.04. HRMS (ESI): m/z calcd for $C_{16}H_{10}F_3N_4O^+$ $(M+H)^+$: 331.0801; found 331.0805.

5-(m-tolyl)-1*H*-pyrimido[4,5,6-de]quinazolin-2(3*H*)-one (3ah):



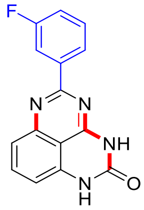
Yield 74% (61 mg); white solid; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.55 (s, 1H), 11.08 (s, 1H), 8.24 (s, 1H), 8.20 (d, J = 7.6 Hz, 1H), 7.72 (t, J = 8.0 Hz, 1H), 7.38 (t, J = 7.6 Hz, 1H), 7.31 (d, J = 7.2 Hz, 1H), 7.27 (d, J = 8.4 Hz, 1H), 6.81 (d, J = 7.6 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 161.66, 158.43, 149.99, 149.76, 138.06, 137.69, 137.40, 135.76, 131.22, 128.48, 128.23, 125.26, 116.93, 106.38, 103.86, 21.10. HRMS (ESI): m/z calcd for $C_{16}H_{13}N_4O^+$ $(M+H)^+$: 277.1084; found 277.1086.

5-(3-(trifluoromethyl)phenyl)-1*H*-pyrimido[4,5,6-de]quinazolin-2(3*H*)-one (3ai):



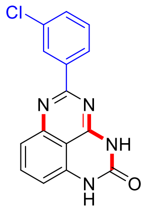
Yield 70% (61 mg); white solid; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.53 (s, 1H), 11.05 (s, 1H), 8.01 (d, J = 7.6 Hz, 1H), 7.97 (s, 1H), 7.73 (t, J = 8.0 Hz, 1H), 7.42 (t, J = 8.0 Hz, 1H), 7.28 (d, J = 8.4 Hz, 1H), 7.08 (dd, J = 8.0, 2.4 Hz, 1H), 6.82 (d, J = 7.6 Hz, 1H), 3.84 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 161.34, 159.38, 158.47, 150.01, 149.70, 139.25, 138.09, 135.83, 129.43, 120.48, 117.02, 116.36, 113.09, 106.50, 103.96, 55.19. HRMS (ESI): m/z calcd for $C_{16}H_{13}N_4O_2^+$ $(M+H)^+$: 293.1033; found 293.1033.

5-(3-fluorophenyl)-1*H*-pyrimido[4,5,6-de]quinazolin-2(3*H*)-one (3aj):



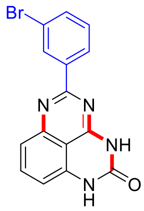
Yield 61% (51 mg); white solid; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 11.62 (s, 1H), 11.12 (s, 1H), 8.23 (d, J = 7.8 Hz, 1H), 8.08 (d, J = 9.9 Hz, 1H), 7.73 (t, J = 8.1 Hz, 1H), 7.54 (dd, J = 14.1, 7.8 Hz, 1H), 7.34 (t, J = 8.4 Hz, 1H), 7.27 (d, J = 8.4 Hz, 1H), 6.82 (d, J = 7.5 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 162.35 (d, J = 240.8 Hz), 160.26 (d, J = 3.8 Hz), 158.60, 149.95, 149.54, 140.37 (d, J = 8.3 Hz), 138.12, 135.93, 130.40 (d, J = 8.3 Hz), 123.94 (d, J = 2.3 Hz), 117.37 (d, J = 21.0 Hz), 117.03, 114.25 (d, J = 23.3 Hz), 106.79, 104.04. HRMS (ESI): m/z calcd for $C_{15}H_{10}FN_4O^+$ (M+H)$^+$: 281.0833; found 281.0833.

5-(3-chlorophenyl)-1*H*-pyrimido[4,5,6-de]quinazolin-2(3*H*)-one (3ak):



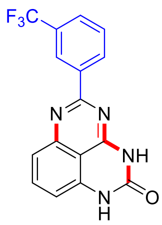
Yield 64% (57 mg); white solid; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.59 (s, 1H), 11.10 (s, 1H), 8.37 (s, 1H), 8.33 (d, J =7.2 Hz, 1H), 7.73 (t, J = 8.0 Hz, 1H), 7.57–7.49 (m, 2H), 7.27 (d, J = 8.4 Hz, 1H), 6.82 (d, J = 8.0 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 160.06, 158.59, 149.90, 149.51, 139.83, 138.10, 135.91, 133.28, 130.30, 127.50, 126.40, 117.02, 106.81, 104.02. HRMS (ESI): m/z calcd for $C_{15}H_{10}ClN_4O^+$ (M+H)$^+$: 297.0538; found 297.0537.

5-(3-bromophenyl)-1*H*-pyrimido[4,5,6-de]quinazolin-2(3*H*)-one (3al):



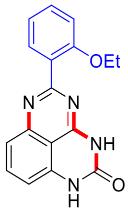
Yield 56% (57 mg); white solid; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 11.60 (s, 1H), 11.11 (s, 1H), 8.53 (s, 1H), 8.37 (d, J = 8.1 Hz, 1H), 7.77–7.67 (m, 2H), 7.47 (t, J = 8.1 Hz, 1H), 7.27 (d, J = 8.4 Hz, 1H), 6.83 (d, J = 7.8 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 160.01, 158.61, 149.91, 149.52, 140.03, 138.12, 135.97, 133.19, 130.63, 130.48, 126.80, 121.83, 117.05, 106.86, 104.03. HRMS (ESI): m/z calcd for $C_{15}H_{10}BrN_4O^+$ (M+H)$^+$: 341.0032; found 341.0032.

5-(3-(trifluoromethyl)phenyl)-1*H*-pyrimido[4,5,6-de]quinazolin-2(3*H*)-one (3am):



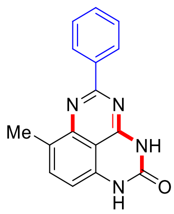
Yield 72% (71 mg); white solid;[1]H NMR (400 MHz, DMSO-d_6): δ = 11.62 (s, 1H), 11.11 (s, 1H), 8.70-8.59 (m, 2H), 7.84 (d, J = 7.6 Hz, 1H), 7.72 (t, J = 7.6 Hz, 2H), 7.27 (d, J = 8.0 Hz, 1H), 6.82 (d, J = 7.6 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 159.94, 158.73, 149.85, 149.49, 138.70, 138.14, 136.00, 131.64, 129.66, 129.24 (q, J = 31.5 Hz), 127.00 (q, J = 3.8 Hz), 124.25 (q, J = 271.0 Hz), 124.16 (q, J = 3.8 Hz), 117.05, 106.93, 104.07. HRMS (ESI): m/z calcd for $C_{16}H_{10}F_3N_4O^+$ $(M+H)^+$: 331.0801; found 331. 0806.

5-(2-ethoxyphenyl)-1*H*-pyrimido[4,5,6-de]quinazolin-2(3*H*)-one (3an):



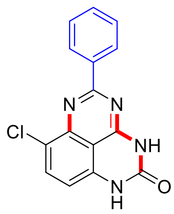
Yield 59% (54 mg); white solid; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.50 (s, 1H), 11.04 (s, 1H), 7.72 (t, J = 8.0 Hz, 1H), 7.48 (dd, J = 7.6, 1.2 Hz, 1H), 7.42–7.36 (m, 1H), 7.21 (d, J = 8.4 Hz, 1H), 7.09 (d, J = 8.0 Hz, 1H), 7.01 (t, J = 7.6 Hz, 1H), 6.83 (d, J = 7.6 Hz, 1H), 4.04 (q, J = 6.8 Hz, 2H), 1.23 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 163.70, 157.84, 156.37, 150.03, 149.62, 138.02, 135.54, 130.41, 130.07, 129.96, 120.03, 116.73, 113.64, 106.37, 103.39, 64.15, 14.60. HRMS (ESI): m/z calcd for $C_{17}H_{15}N_4O_2^+$ $(M+H)^+$: 307.1190; found 307.1195.

7-methyl-5-phenyl-1*H*-pyrimido[4,5,6-de]quinazolin-2(3*H*)-one (3ba):



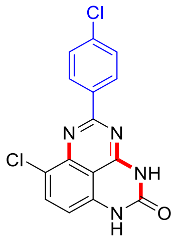
Yield 83% (69 mg); white solid; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.47 (s, 1H), 10.94 (s, 1H), 8.45 (dd, J = 6.8, 3.2 Hz, 2H), 7.58 (d, J = 8.0 Hz, 1H), 7.53–7.47 (m, 3H), 6.72 (d, J = 7.6 Hz, 1H), 2.51 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 160.77, 158.58, 150.11, 147.90, 137.99, 135.76, 135.42, 130.48, 128.30, 128.00, 124.86, 105.89, 103.69, 15.70. HRMS (ESI): m/z calcd for $C_{16}H_{13}N_4O^+$ $(M+H)^+$: 277.1084; found 277.1089.

7-chloro-5-phenyl-1*H*-pyrimido[4,5,6-de]quinazolin-2(3*H*)-one (3ca):



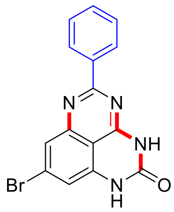
Yield 71% (63 mg); white solid; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.79 (s, 1H), 11.22 (s, 1H), 8.49-8.41 (m, 2H), 7.86 (d, J = 8.4 Hz, 1H), 7.56-7.51 (m, 3H), 6.79 (d, J = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 162.23, 158.73, 149.80, 145.78, 137.37, 137.34, 135.35, 131.00, 128.44, 128.18, 119.30, 106.88, 105.05. HRMS (ESI): m/z calcd for $C_{15}H_{10}ClN_4O^+$ $(M+H)^+$: 297.0538; found 297.0541.

7-chloro-5-(4-chlorophenyl)-1*H*-pyrimido[4,5,6-de]quinazolin-2(3*H*)-one (3ce):



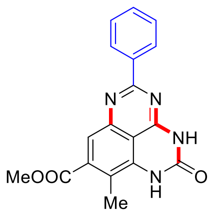
Yield 62% (61 mg); white solid; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.83 (s, 1H), 11.24 (s, 1H), 8.44 (d, J = 8.8 Hz, 2H), 7.88 (d, J = 8.4 Hz, 1H), 7.61 (d, J = 8.8 Hz, 2H), 6.81 (d, J = 8.4 Hz, 1H); ^{13}C NMR (150 MHz, DMSO-d_6): δ = 161.17, 158.80, 149.72, 145.63, 137.36, 136.19, 135.87, 135.46, 129.81, 128.59, 119.25, 107.10, 105.07. HRMS (ESI): m/z calcd for $C_{15}H_9Cl_2N_4O^+$ (M+H)$^+$: 331.0148; found 331.0148.

8-bromo-5-phenyl-1*H*-pyrimido[4,5,6-de]quinazolin-2(3*H*)-one (3da):



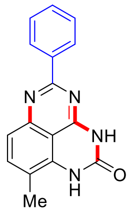
Yield 54% (55 mg); white solid; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.77 (s, 1H), 11.23 (s, 1H), 8.39 (d, J = 4.8 Hz, 2H), 7.56-7.45 (m, 3H), 7.42 (s, 1H), 6.89 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 162.59, 158.36, 150.66, 149.72, 139.49, 137.35, 130.92, 129.07, 128.39, 128.10, 119.06, 109.03, 102.96. HRMS (ESI): m/z calcd for $C_{15}H_{10}BrN_4O^+$ (M+H)$^+$: 341.0032; found 341.0035.

methyl 9-methyl-2-oxo-5-phenyl-2,3-dihydro-1*H*-pyrimido[4,5,6-de]quinazoline-8-carboxylate (3ea):



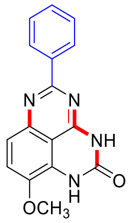
Yield 60% (60 mg); white solid; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.76 (s, 1H), 10.54 (s, 1H), 8.39 (dd, J = 6.8, 3.2 Hz, 2H), 7.53 (s, 1H), 7.52–7.47 (m, 3H), 3.88 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6): δ = 167.56, 161.39, 157.88, 150.37, 147.24, 138.58, 137.41, 136.52, 130.68, 128.36, 127.93, 117.93, 114.05, 104.96, 52.57, 13.44. HRMS (ESI): m/z calcd for $C_{18}H_{15}N_4O_3^+$ (M+H)$^+$: 335.1139; found 335.1144.

9-methyl-5-phenyl-1*H*-pyrimido[4,5,6-de]quinazolin-2(3*H*)-one (3fa):



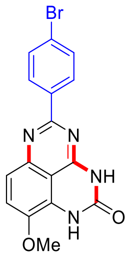
Yield 62% (51 mg); white solid; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.56 (s, 1H), 10.44 (s, 1H), 8.44–8.37 (m, 2H), 7.61 (d, J = 8.4 Hz, 1H), 7.53–7.46 (m, 3H), 7.24 (d, J = 8.4 Hz, 1H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 160.61, 157.98, 150.47, 148.10, 138.05, 137.76, 135.07, 130.44, 128.33, 127.86, 117.13, 115.58, 103.82, 16.35. HRMS (ESI): m/z calcd for $C_{16}H_{13}N_4O^+$ $(M+H)^+$: 277.1084; found 277.1083.

9-methoxy-5-phenyl-1*H*-pyrimido[4,5,6-de]quinazolin-2(3*H*)-one (3ga):



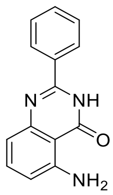
Yield 58% (51 mg); white solid; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 11.48 (s, 1H), 10.55 (s, 1H), 8.38 (dd, J = 6.6, 3.0 Hz, 2H), 7.66 (d, J = 9.0 Hz, 1H), 7.52–7.44 (m, 3H), 7.33 (d, J = 9.0 Hz, 1H), 3.90 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 159.63, 158.26, 150.07, 143.42, 139.81, 137.88, 130.24, 128.30, 127.73, 125.20, 121.45, 117.32, 104.27, 56.87. HRMS (ESI): m/z calcd for $C_{16}H_{13}N_4O_2^+$ $(M+H)^+$: 293.1033; found 293.1039.

5-(4-bromophenyl)-9-methoxy-1*H*-pyrimido[4,5,6-de]quinazolin-2(3*H*)-one (3gf):



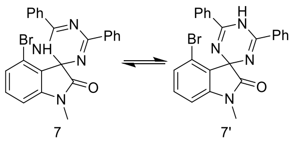
Yield 52% (58 mg); white solid; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.49 (s, 1H), 10.54 (s, 1H), 8.30 (d, J = 8.4 Hz, 2H), 7.69 (t, J = 8.4 Hz, 3H), 7.33 (d, J = 8.8 Hz, 1H), 3.90 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6): δ = 159.63, 158.26, 150.07, 143.42, 139.81, 137.88, 130.24, 128.30, 127.73, 125.20, 121.45, 117.32, 104.27, 56.87. HRMS (ESI): m/z calcd for $C_{16}H_{12}BrN_4O_2^+$ $(M+H)^+$: 371.0138; found 371.0136.

5-amino-2-phenylquinazolin-4(3*H*)-one (5):



Yield 52% (37 mg); white solid; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.09 (s, 1H), 8.14 (d, *J* = 7.2 Hz, 2H), 7.65-7.47 (m, 3H), 7.39 (t, *J* = 8.0 Hz, 1H), 7.17 (s, 2H), 6.75 (d, *J* = 7.6 Hz, 1H), 6.60 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 164.95, 151.26, 150.91, 150.22, 134.96, 132.66, 131.19, 128.54, 127.55, 112.72, 110.79, 104.57. HRMS (ESI): m/z calcd for $C_{14}H_{12}N_3O^+$ $(M+H)^+$: 238.0975; found 238.0990.

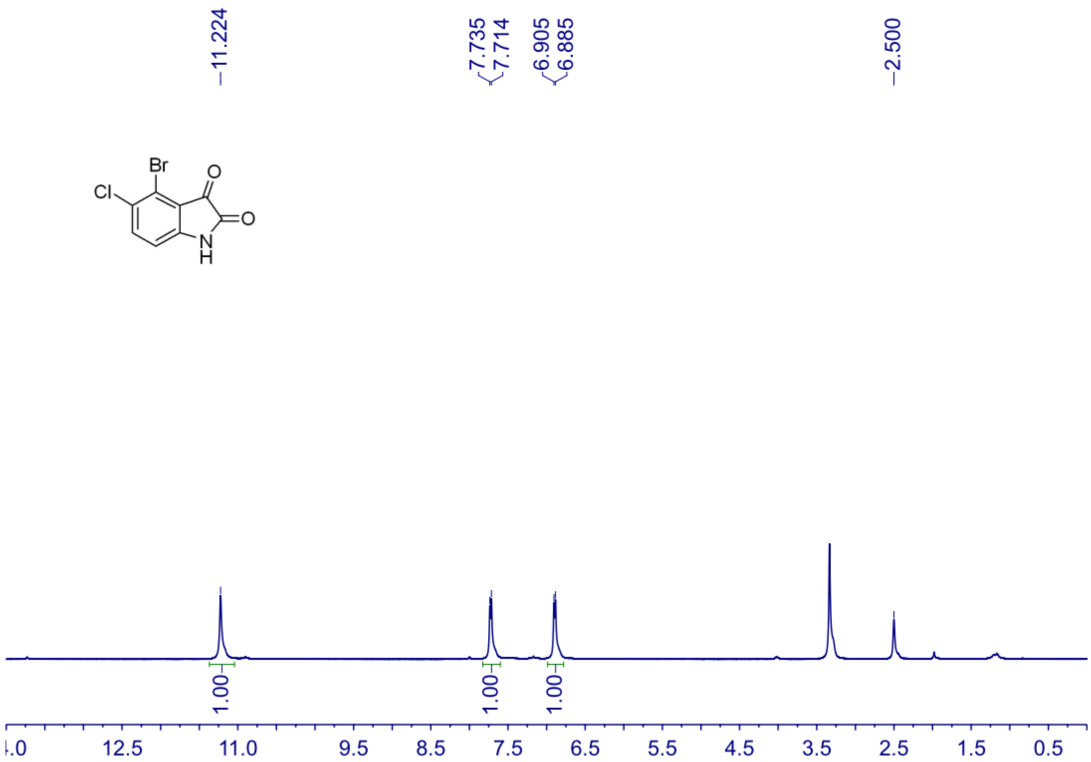
4-bromo-1-methyl-4',6'-diphenyl-1'*H*-spiro[indoline-3,2'-[1,3,5]triazin]-2-one and 4-bromo-1-methyl-4',6'-diphenyl-5'*H*-spiro[indoline-3,2'-[1,3,5]triazin]-2-one (7 and 7'):

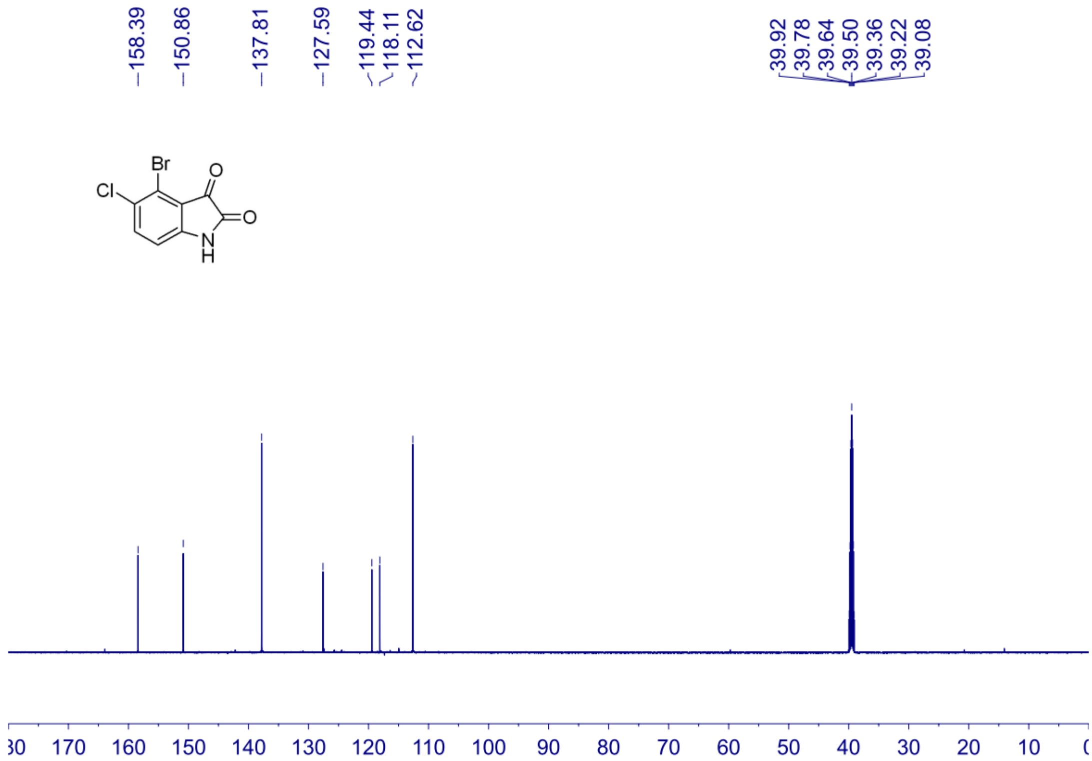


Yield 78% (104 mg)(major:minor ≈1:0.82); white solid; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.45 (s, 1H, major), 9.13 (s, 1H, minor), 8.18 (d, *J* = 7.2 Hz, 2H, minor), 8.09 (d, *J* = 7.2 Hz, 2H, minor), 7.92–7.84 (m, 4H, major), 7.67–7.23 (m, 16H, major+minor), 7.16 (d, *J* = 7.6 Hz, 1H, minor), 7.11 (d, *J* = 7.6 Hz, 1H, major), 3.22 (s, 3H, minor), 3.19 (s, 3H, major); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 174.52, 174.04, 160.13, 159.75, 153.23, 144.60, 144.34, 137.13, 133.18, 132.84, 132.54, 132.29, 131.95, 131.18, 130.50, 128.61, 128.22, 127.90, 127.63, 127.18, 127.04, 126.57, 126.31, 119.89, 119.51, 108.52, 108.31, 79.60, 75.75, 26.44, 26.19. HRMS (ESI): m/z calcd for $C_{23}H_{18}BrN_4O^+$ $(M+H)^+$: 445.0659; found 445.0647.

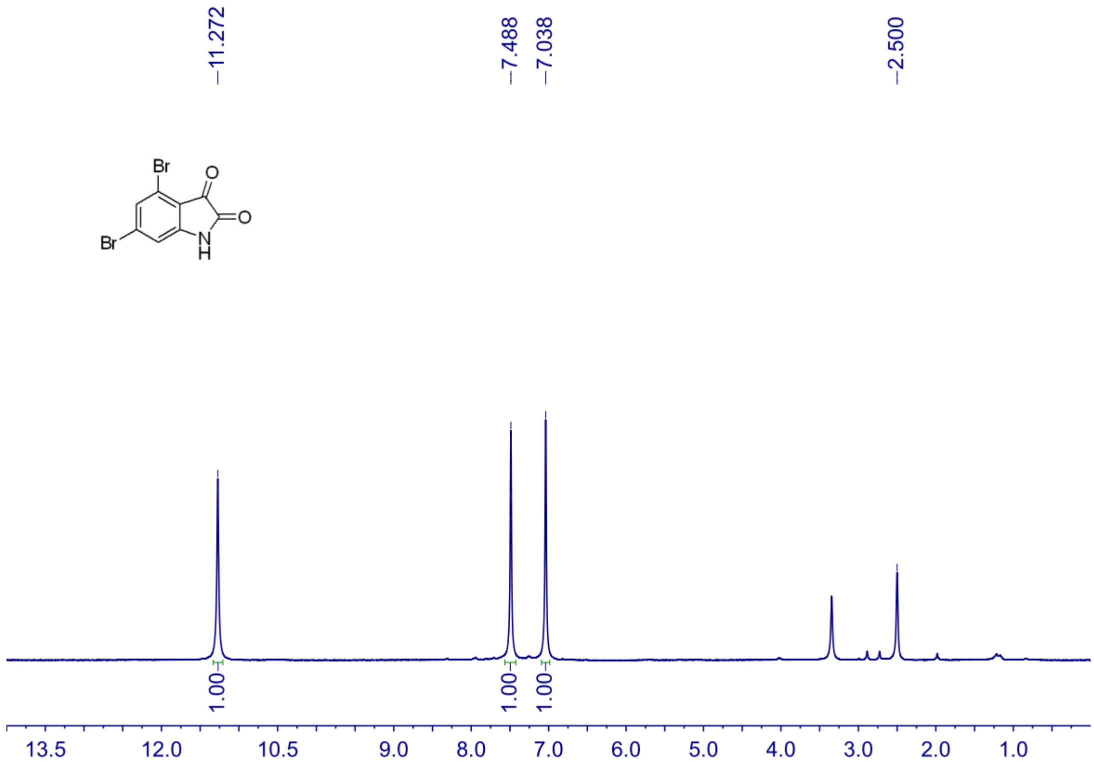
10. NMR Spectra of products 1c−1g, 3aa−3an, 3ba−3gf, 5 and 7.

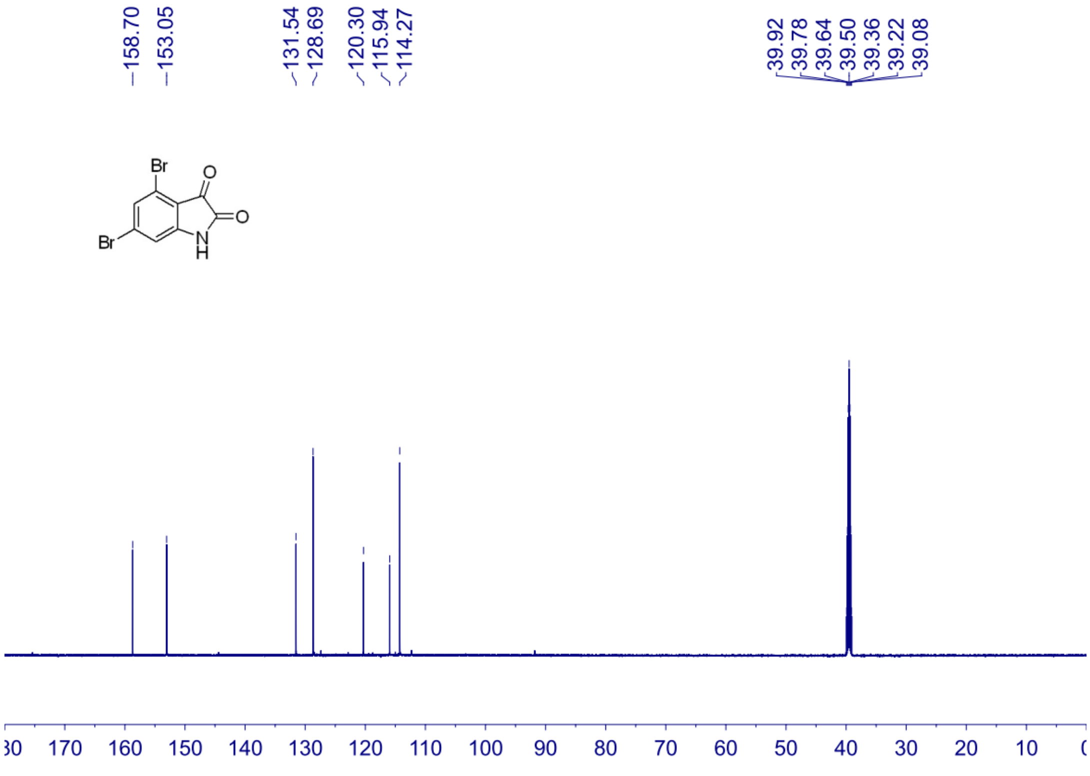
^{1}H NMR (400 MHz, DMSO-d_6) and ^{13}C NMR (150 MHz, DMSO-d_6) spectra of product 1c



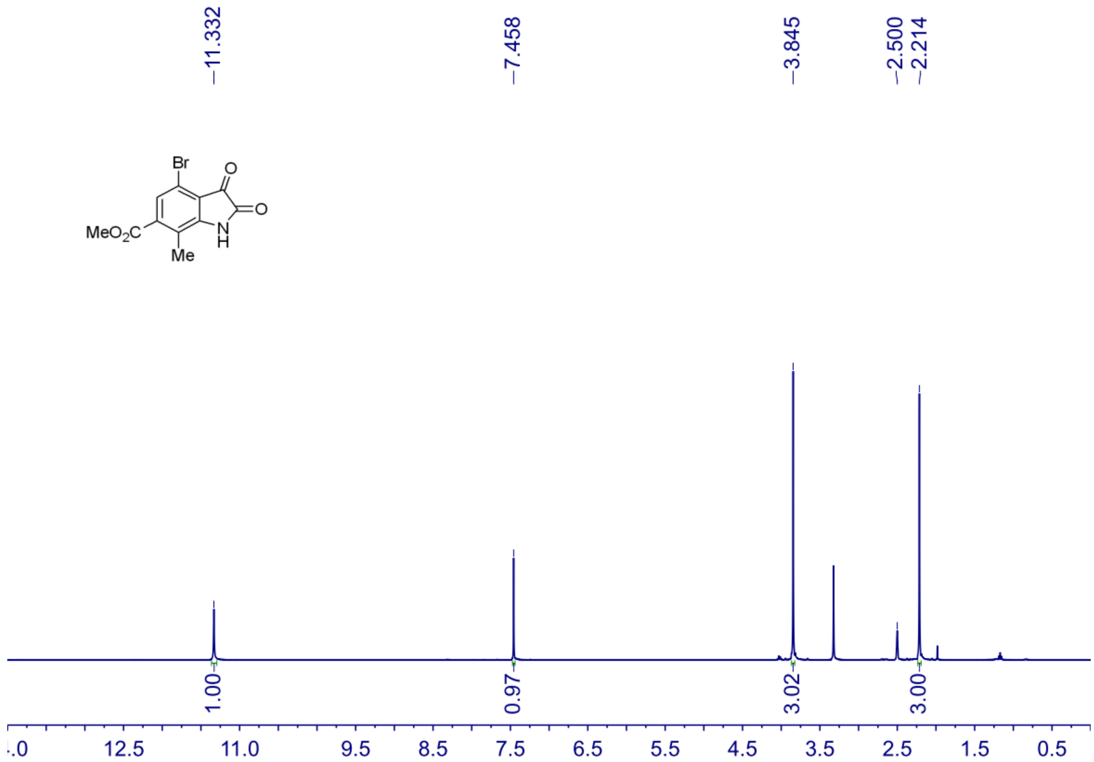


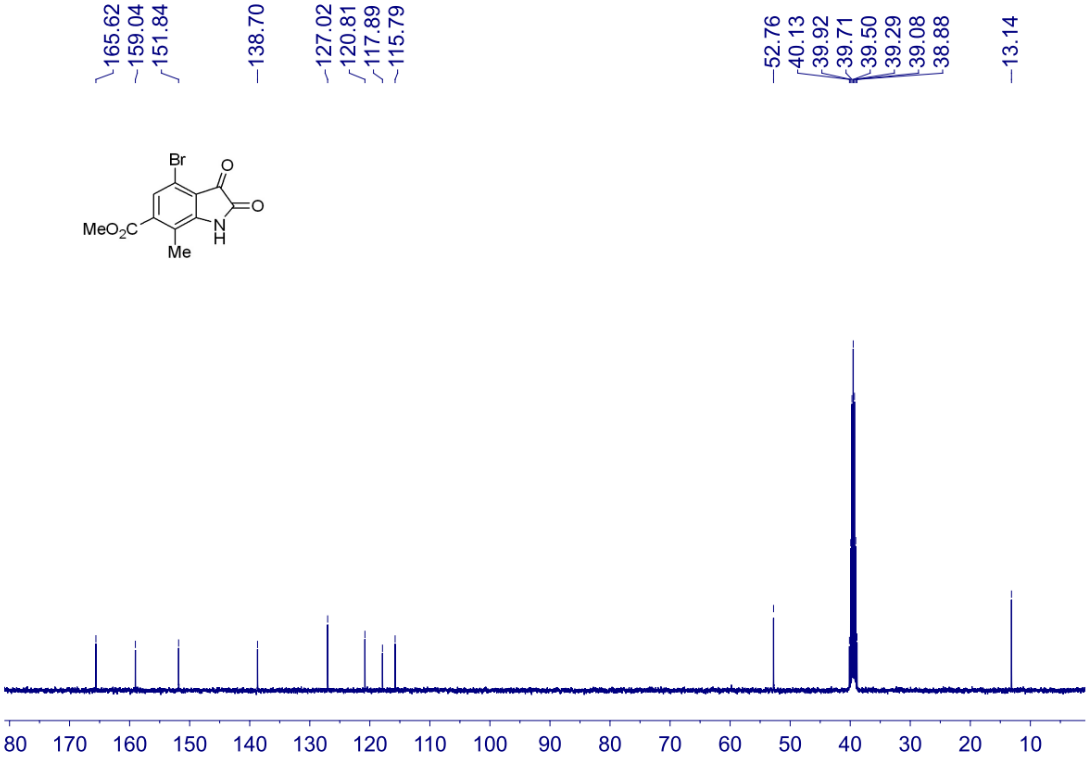
[1] H NMR (400 MHz, DMSO-d_6) and [13]C NMR (150 MHz, DMSO-d_6) spectra of product 1d



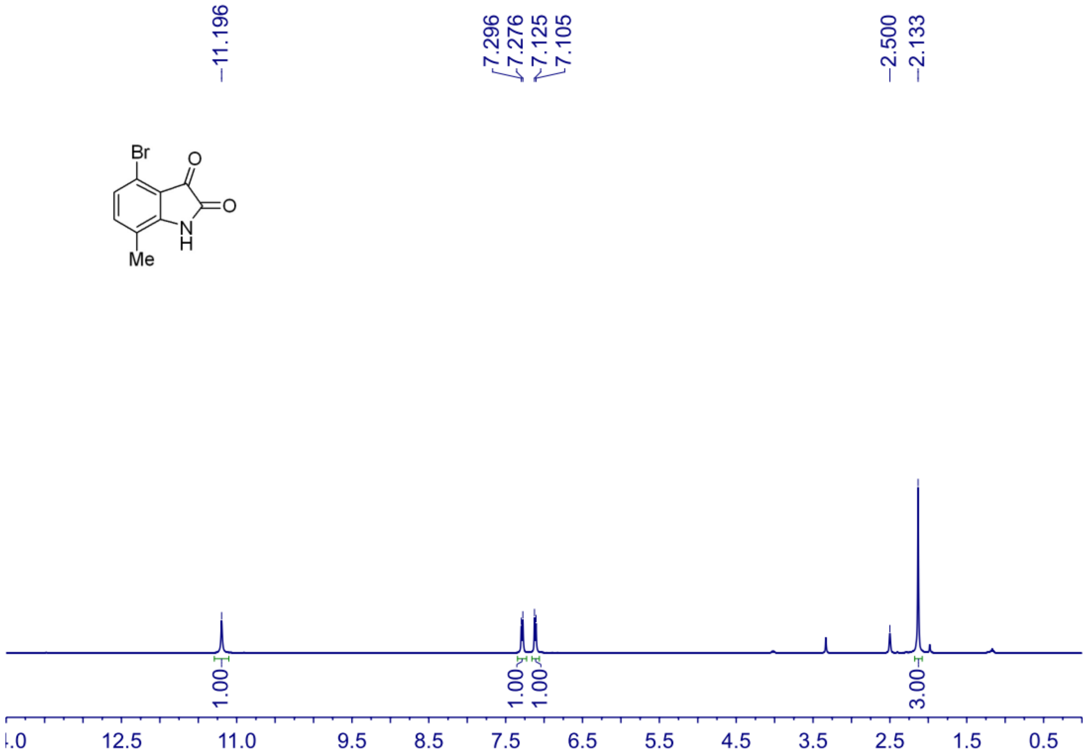


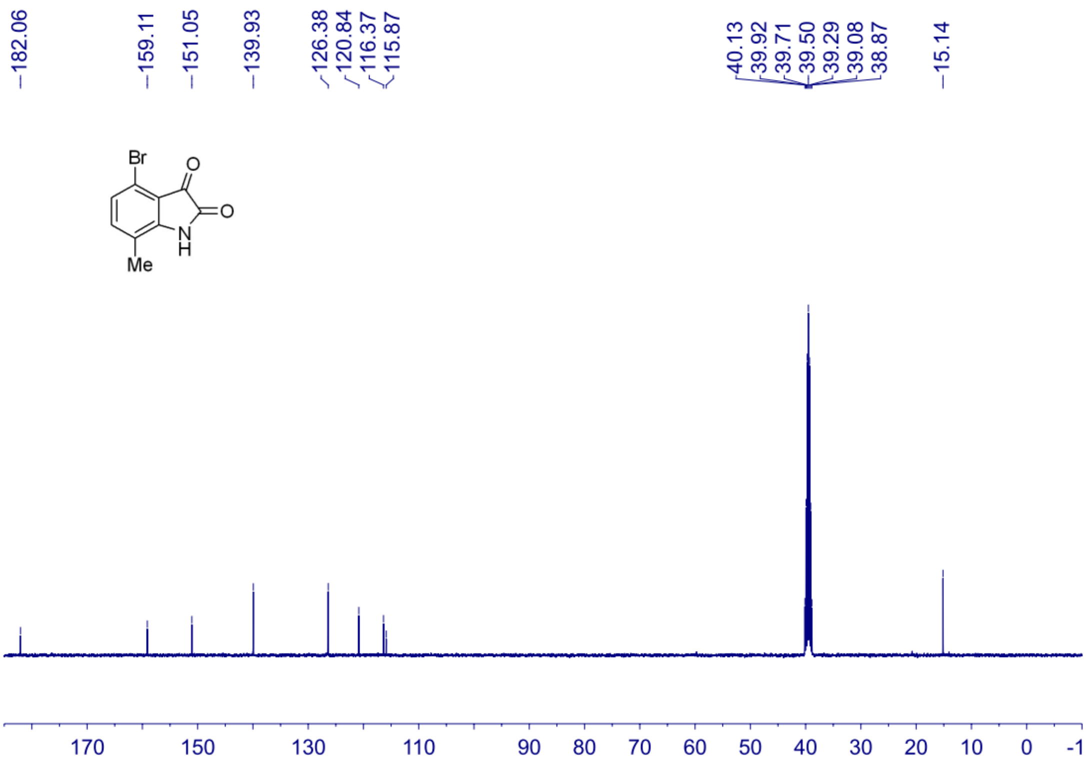
[1] H NMR (400 MHz, DMSO-d_6) and [13]C NMR (100 MHz, DMSO-d_6) spectra of product 1e



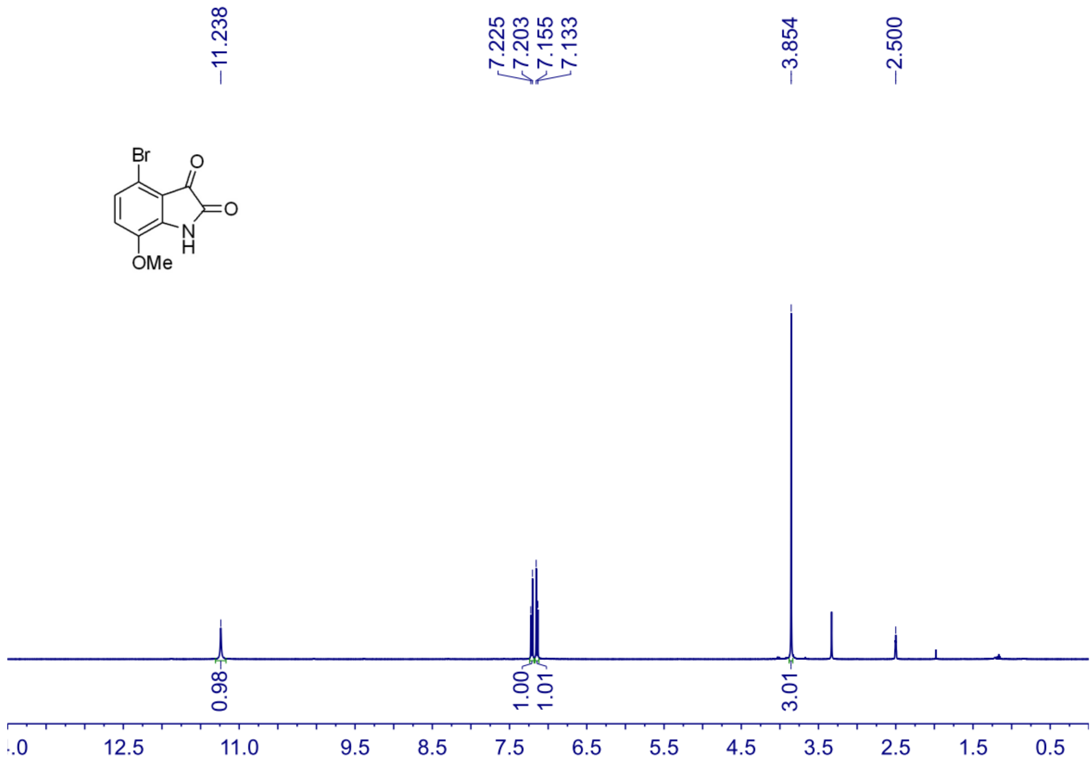


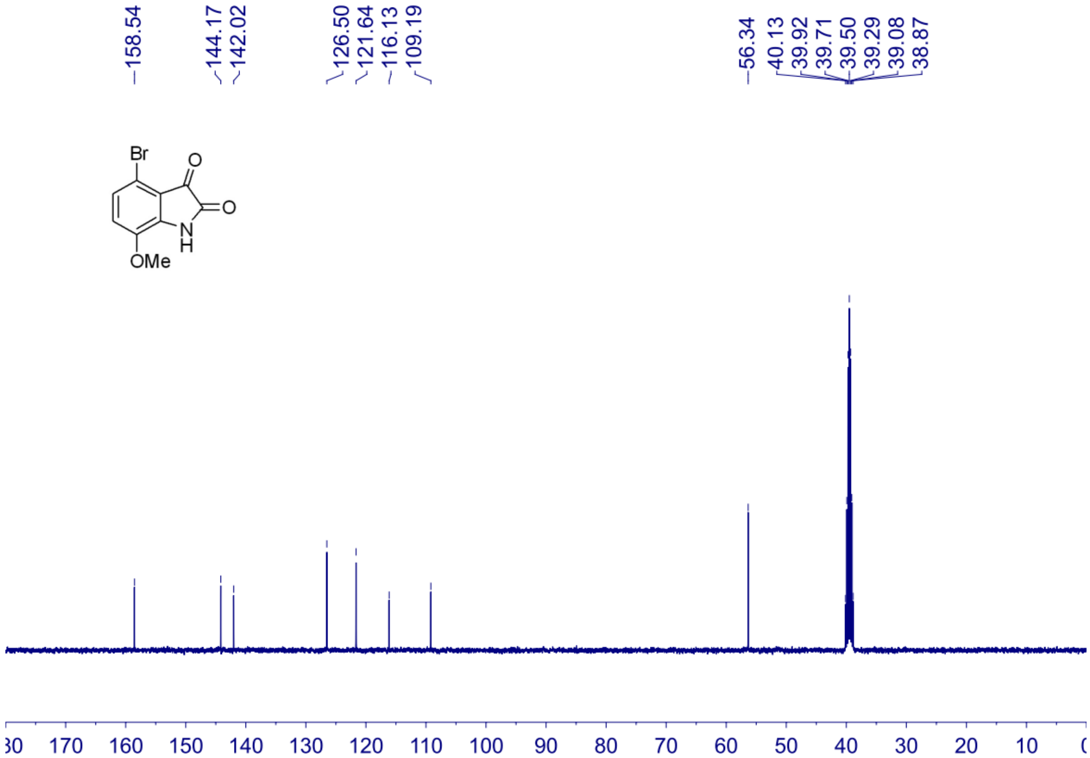
[1] H NMR (400 MHz, DMSO-d_6) and [13]C NMR (100 MHz, DMSO-d_6) spectra of product 1f



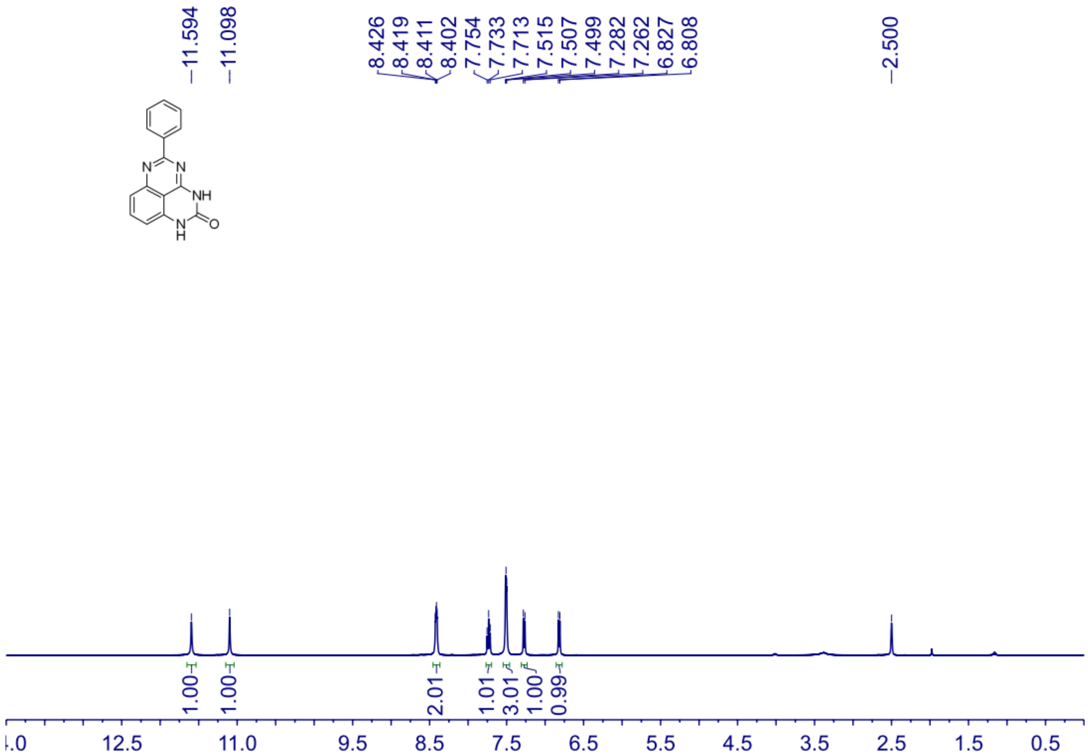


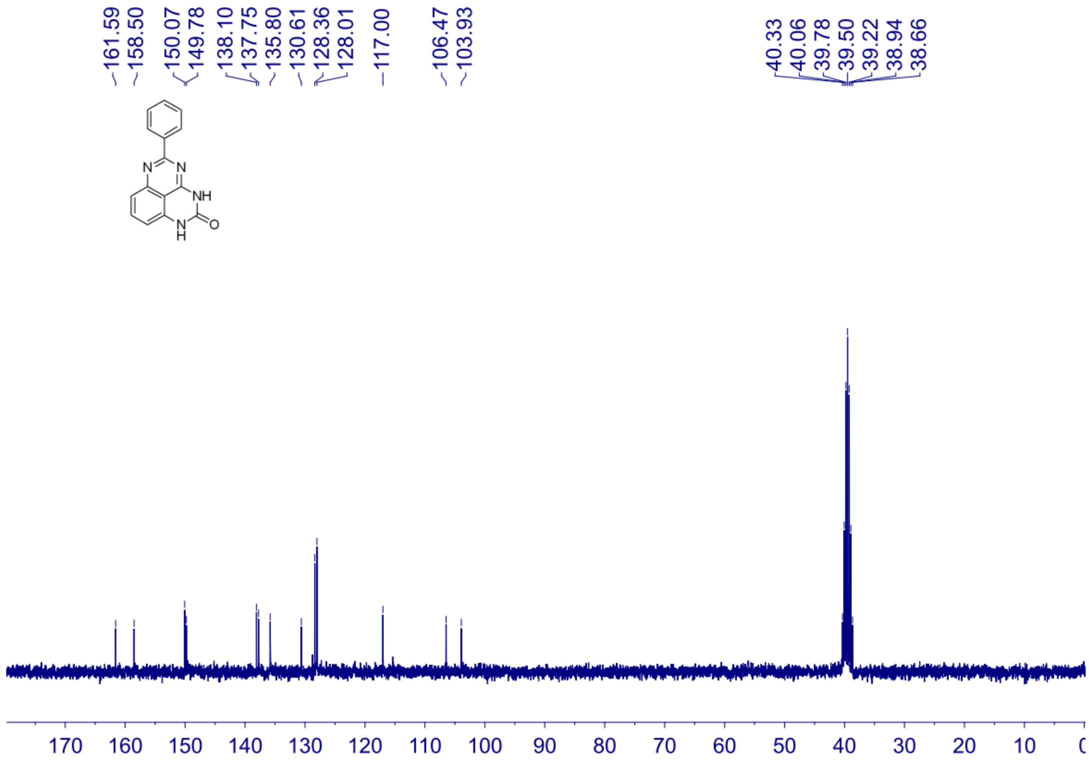
[1] H NMR (400 MHz, DMSO-d_6) and [13]C NMR (100 MHz, DMSO-d_6) spectra of product 1g



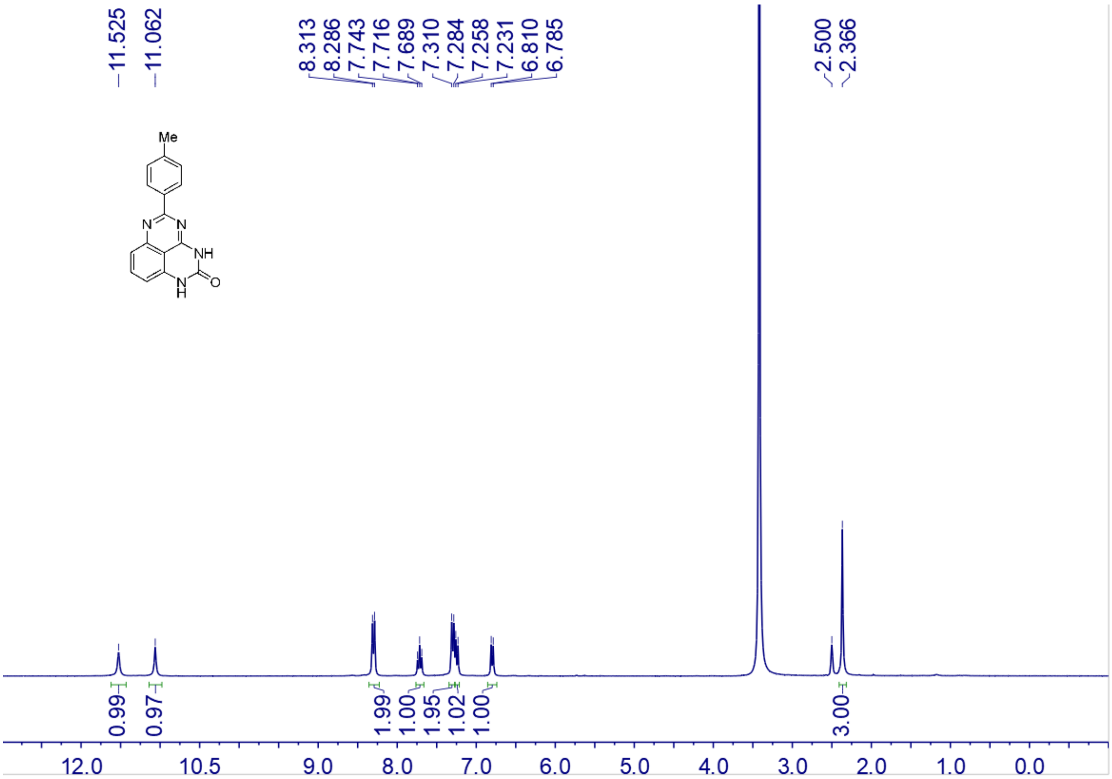


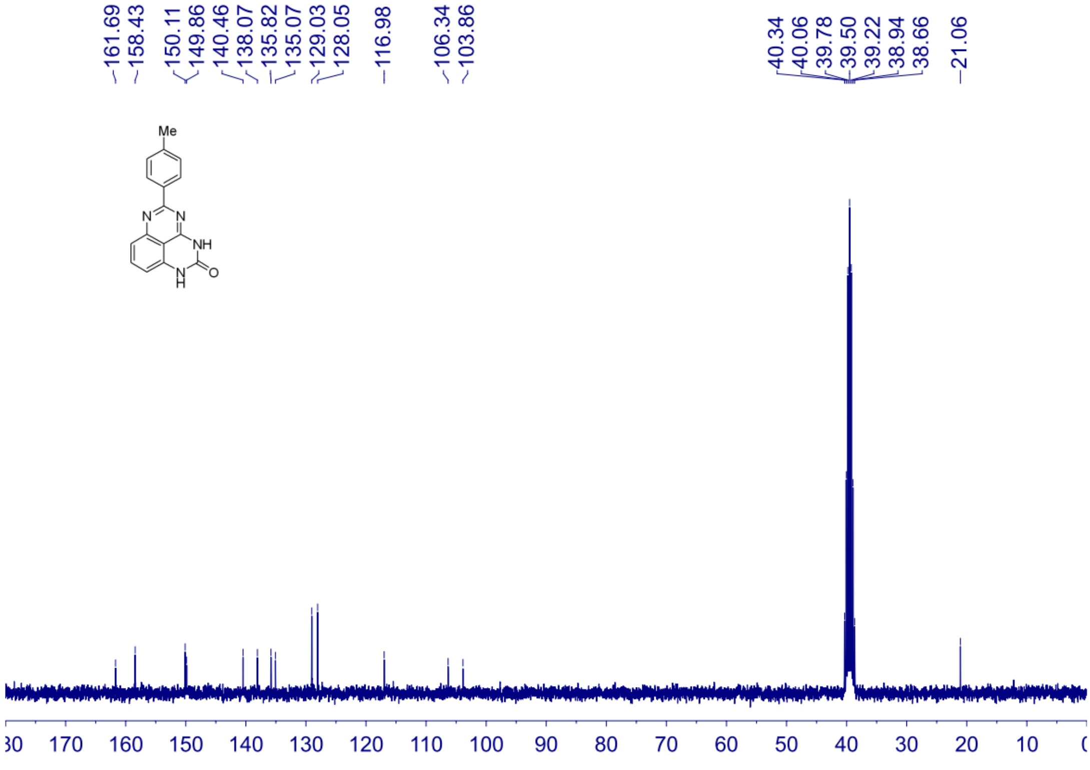
^{1}H NMR (400 MHz, DMSO-d_6) and ^{13}C NMR (75 MHz, DMSO-d_6) spectra of product 3aa



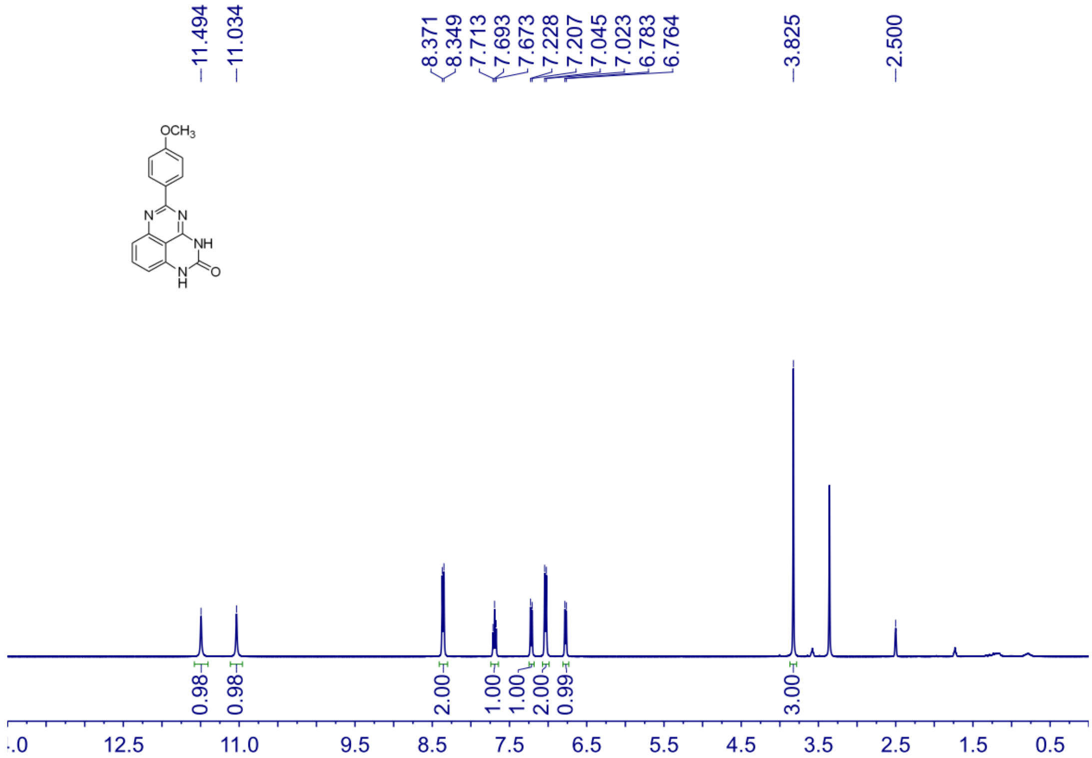


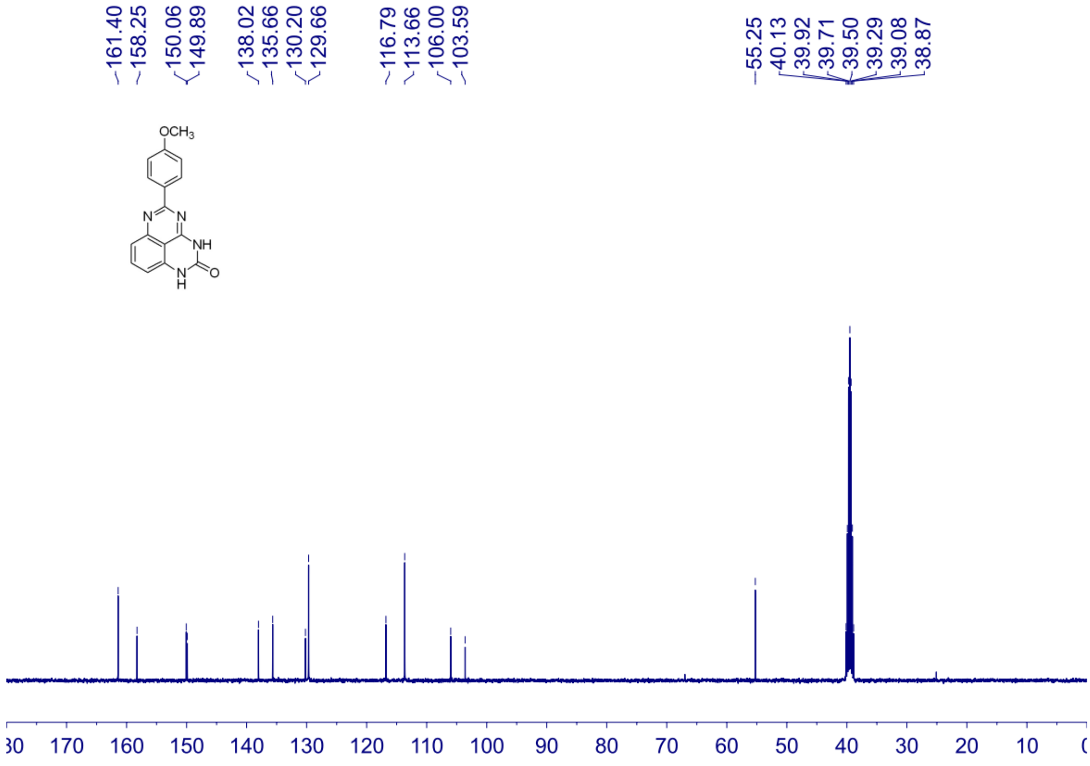
[1] H NMR (300 MHz, DMSO-d_6) and [13]C NMR (75 MHz, DMSO-d_6) spectra of product 3ab



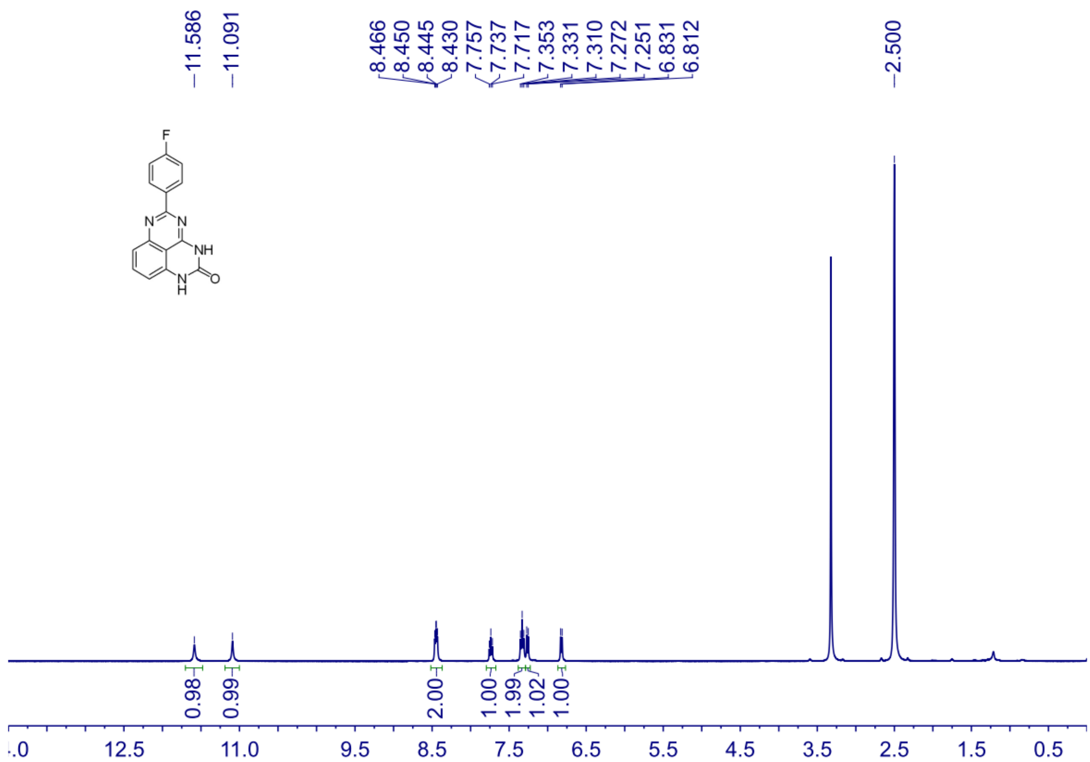


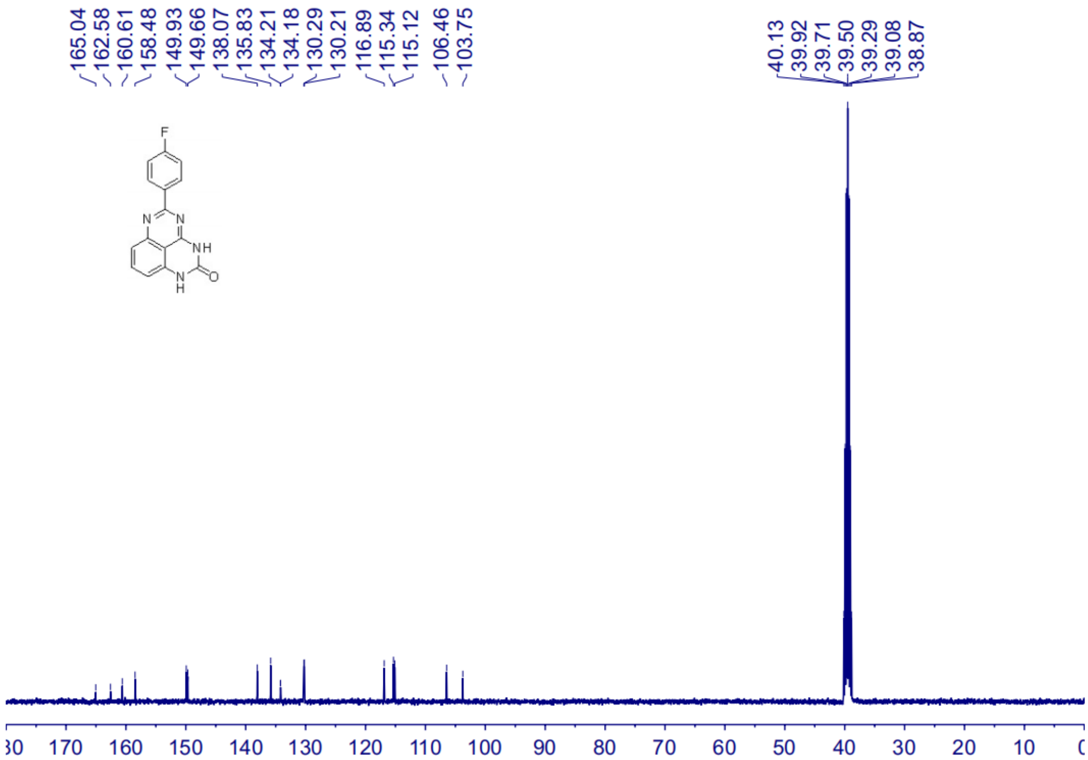
[1] H NMR (400 MHz, DMSO-d_6) and [13]C NMR (100 MHz, DMSO-d_6) spectra of product 3ac



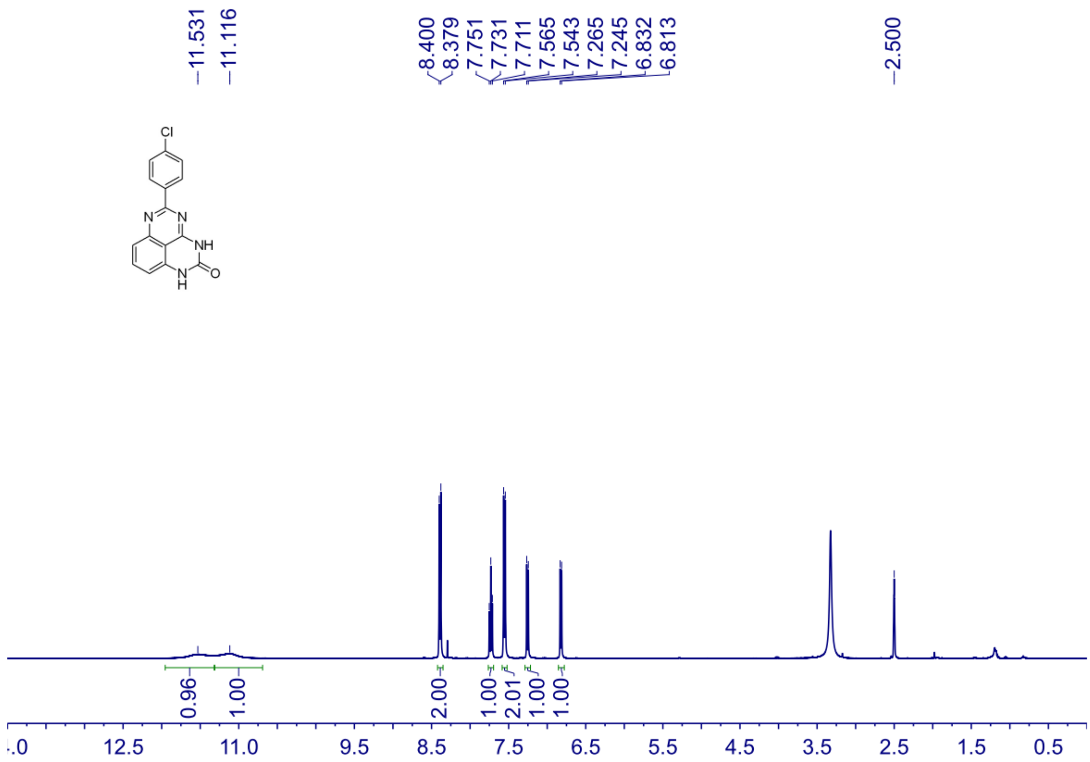


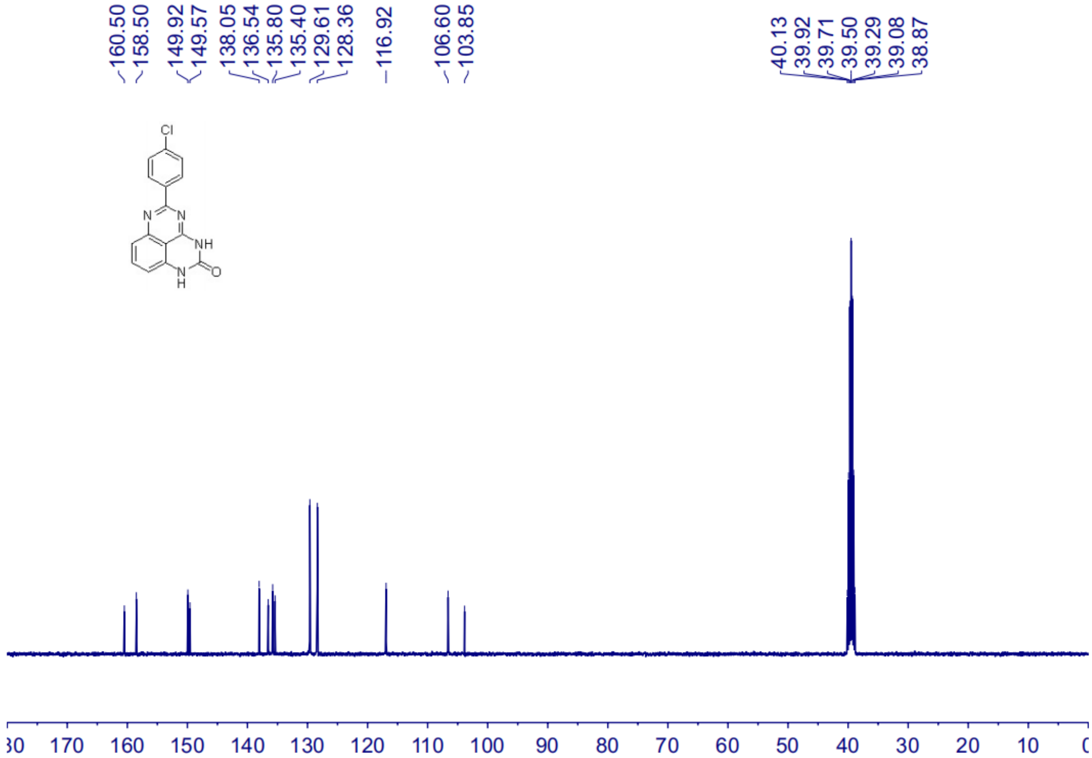
[1] H NMR (400 MHz, DMSO-d_6) and [13]C NMR (100 MHz, DMSO-d_6) spectra of product 3ad



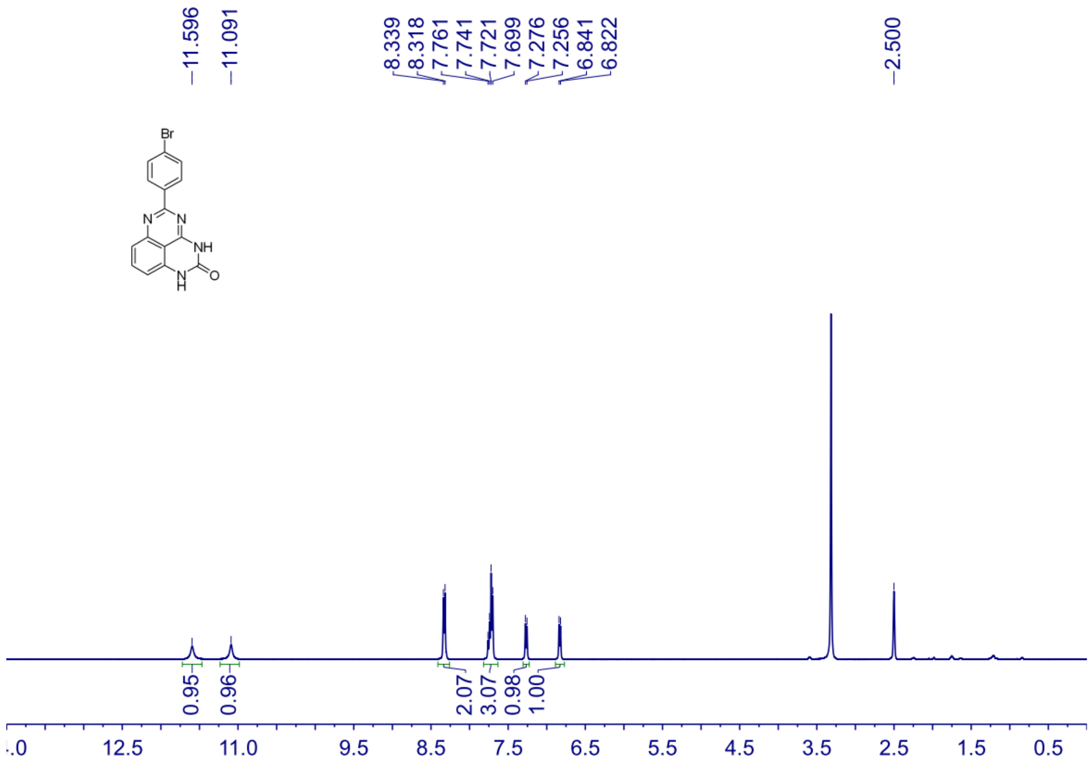


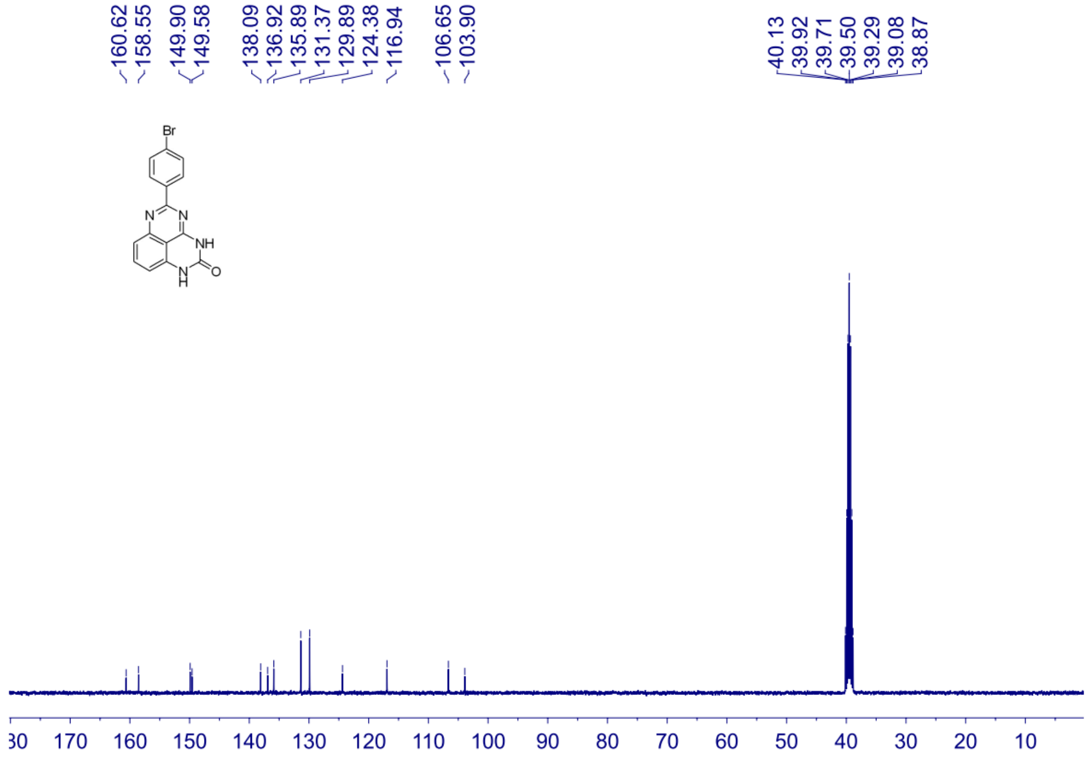
[1] H NMR (400 MHz, DMSO-d_6) and [13]C NMR (100 MHz, DMSO-d_6) spectra of product 3ae



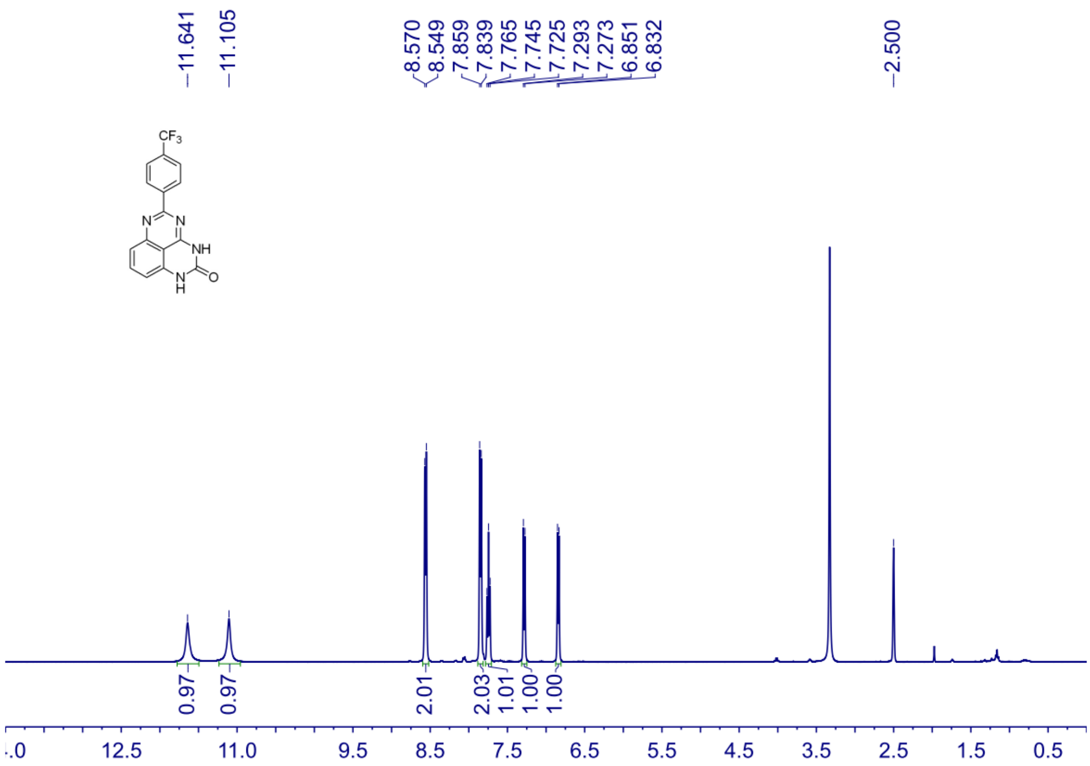


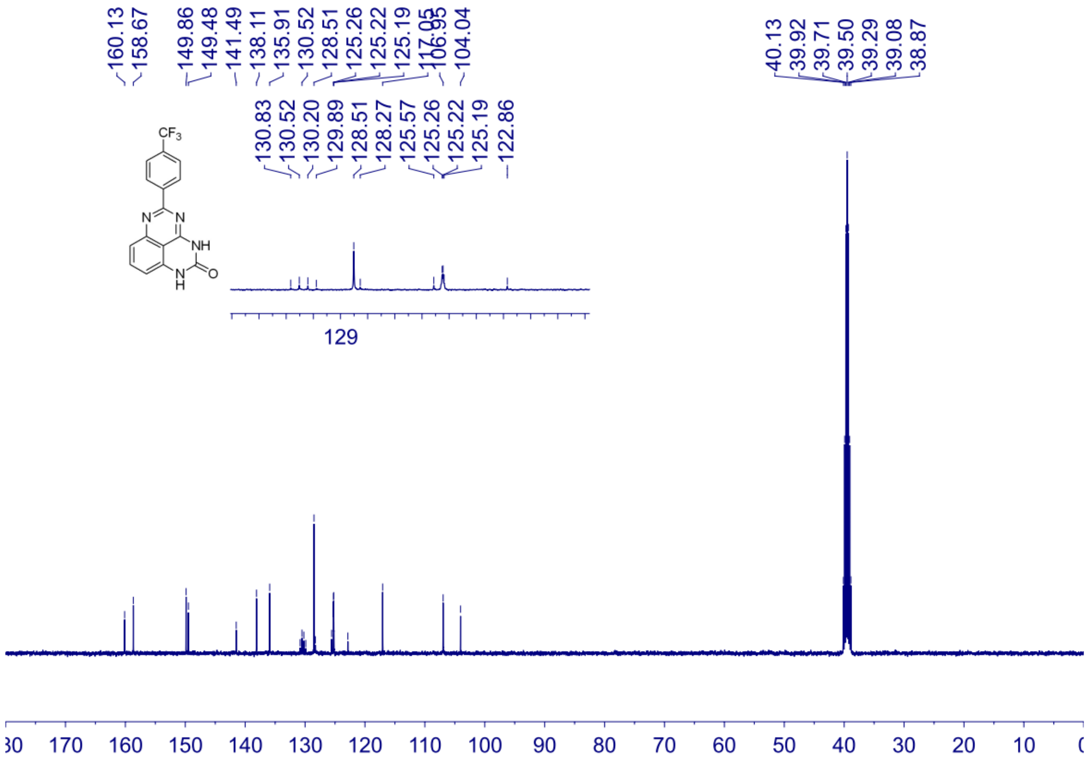
^{1}H NMR (400 MHz, DMSO-d_6) and ^{13}C NMR (100 MHz, DMSO-d_6) spectra of product 3af



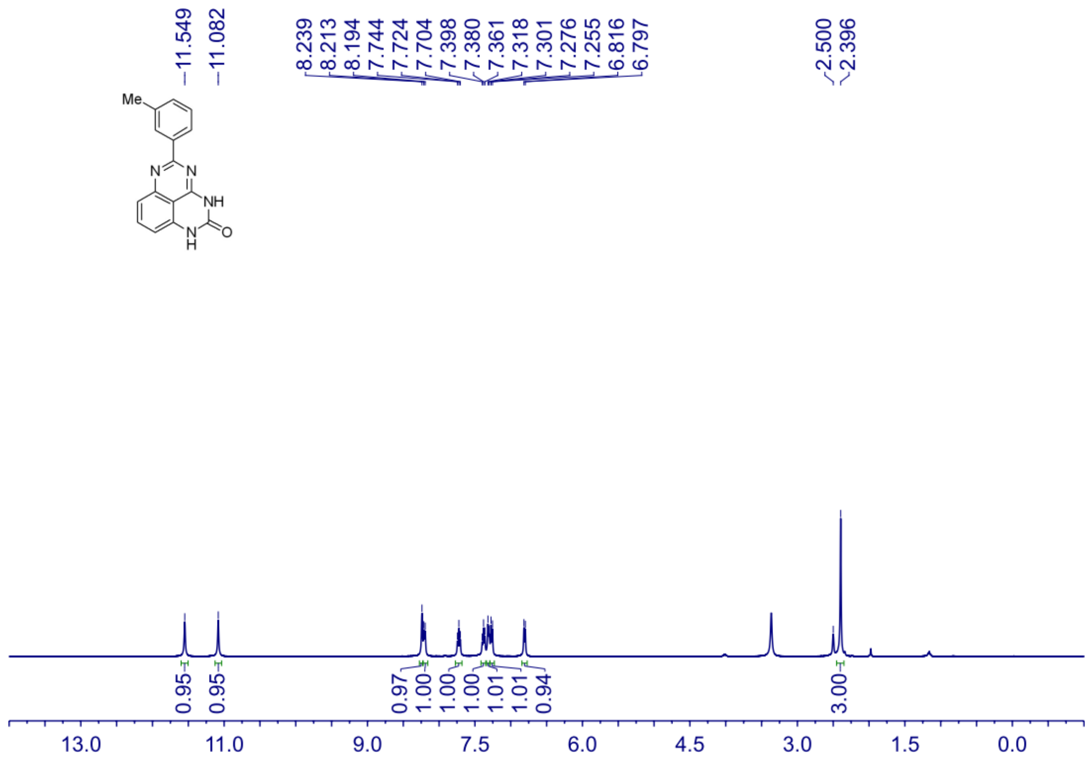


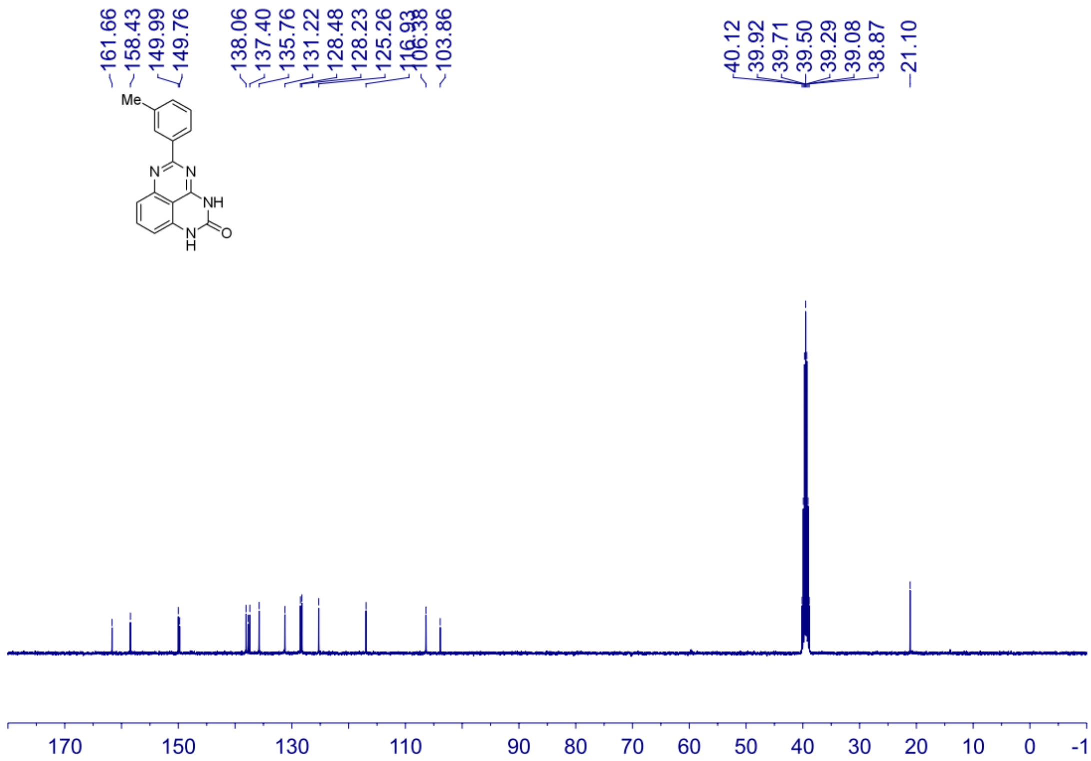
[1] H NMR (400 MHz, DMSO-d_6) and [13]C NMR (100 MHz, DMSO-d_6) spectra of product 3ag



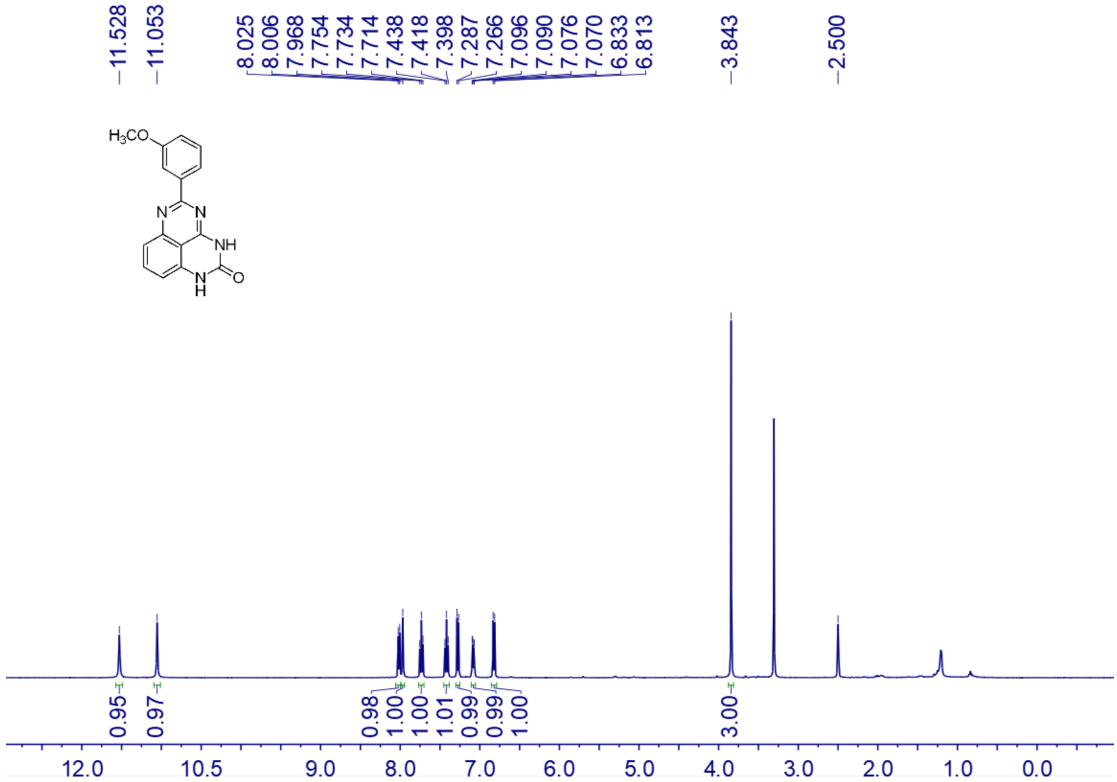


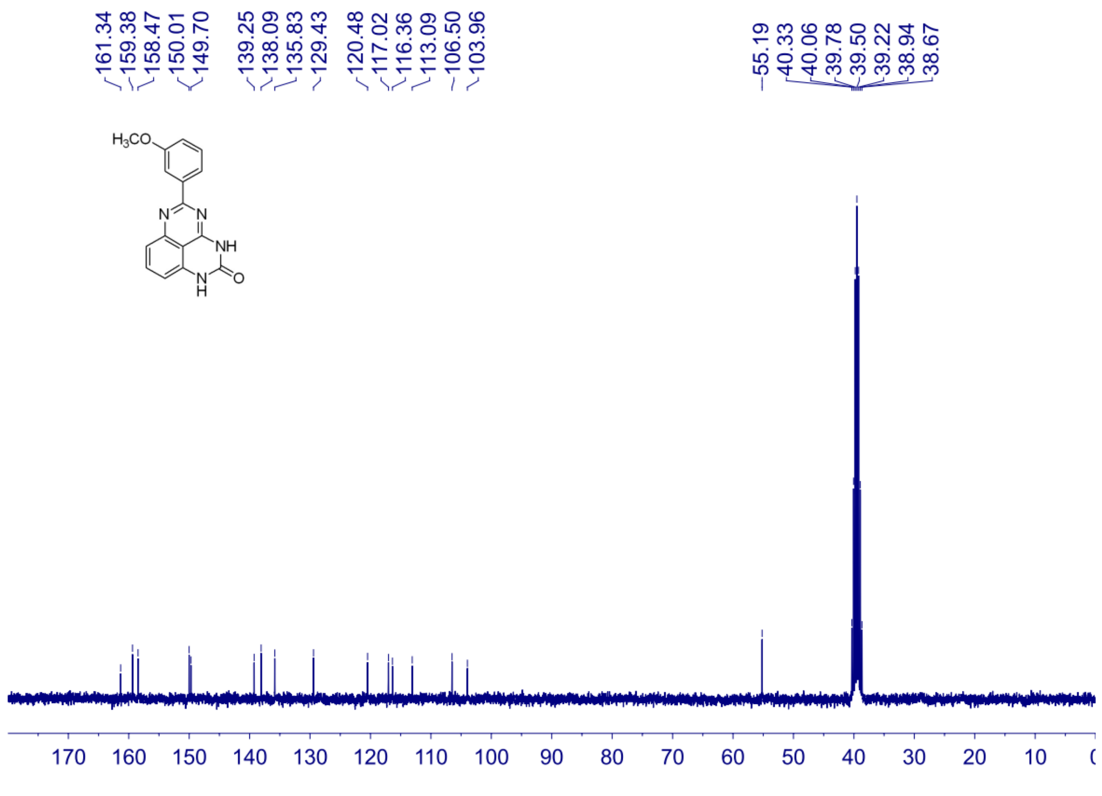
[1] H NMR (400 MHz, DMSO-d_6) and [13]C NMR (100 MHz, DMSO-d_6) spectra of product 3ah



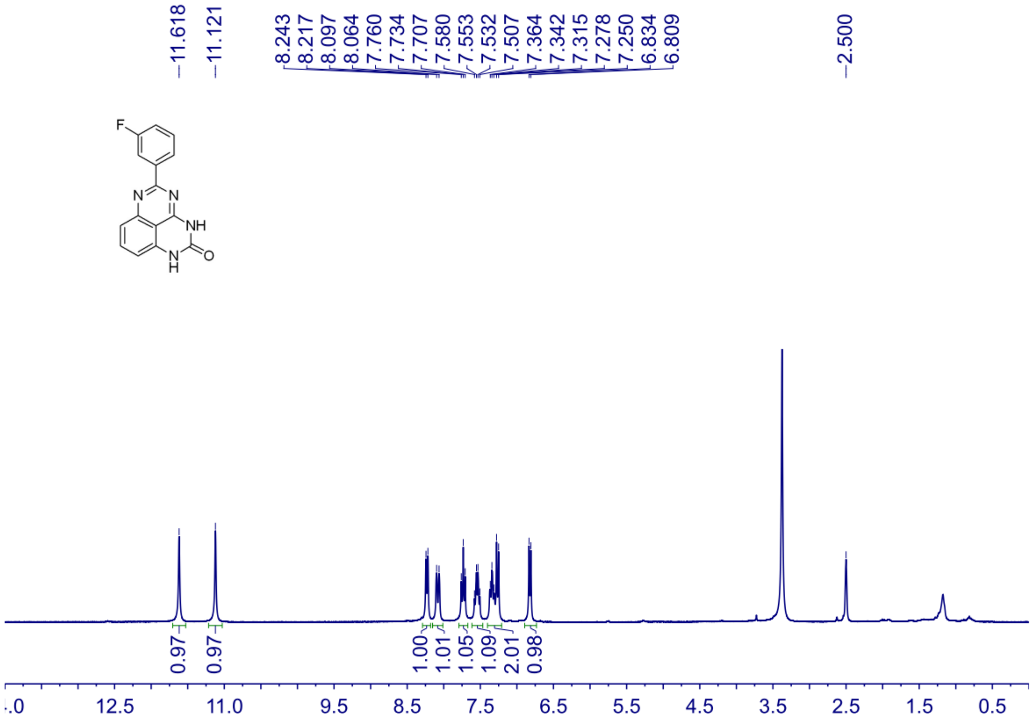


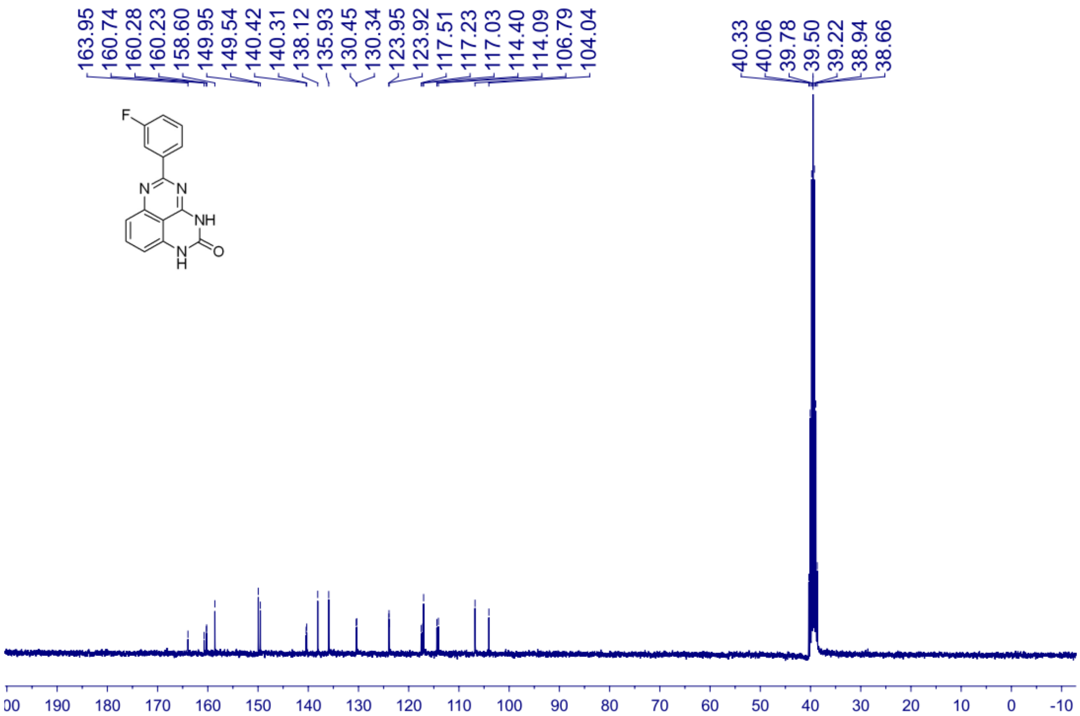
^{1}H NMR (400 MHz, DMSO-d_6) and ^{13}C NMR (75 MHz, DMSO-d_6) spectra of product 3ai



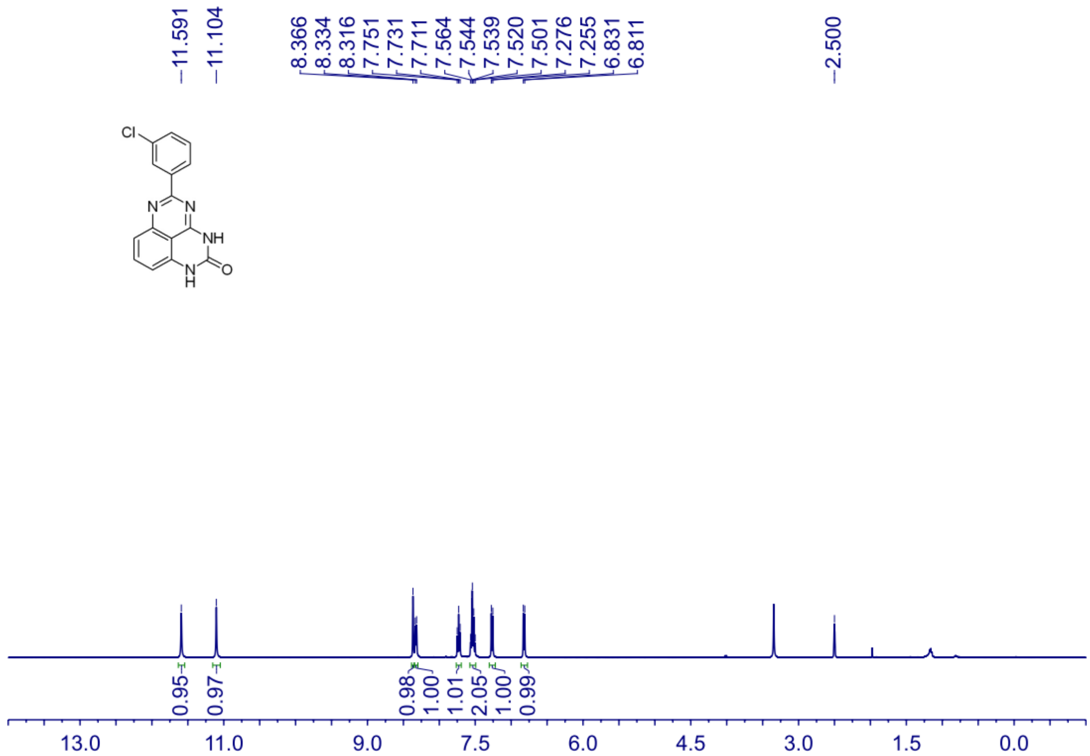


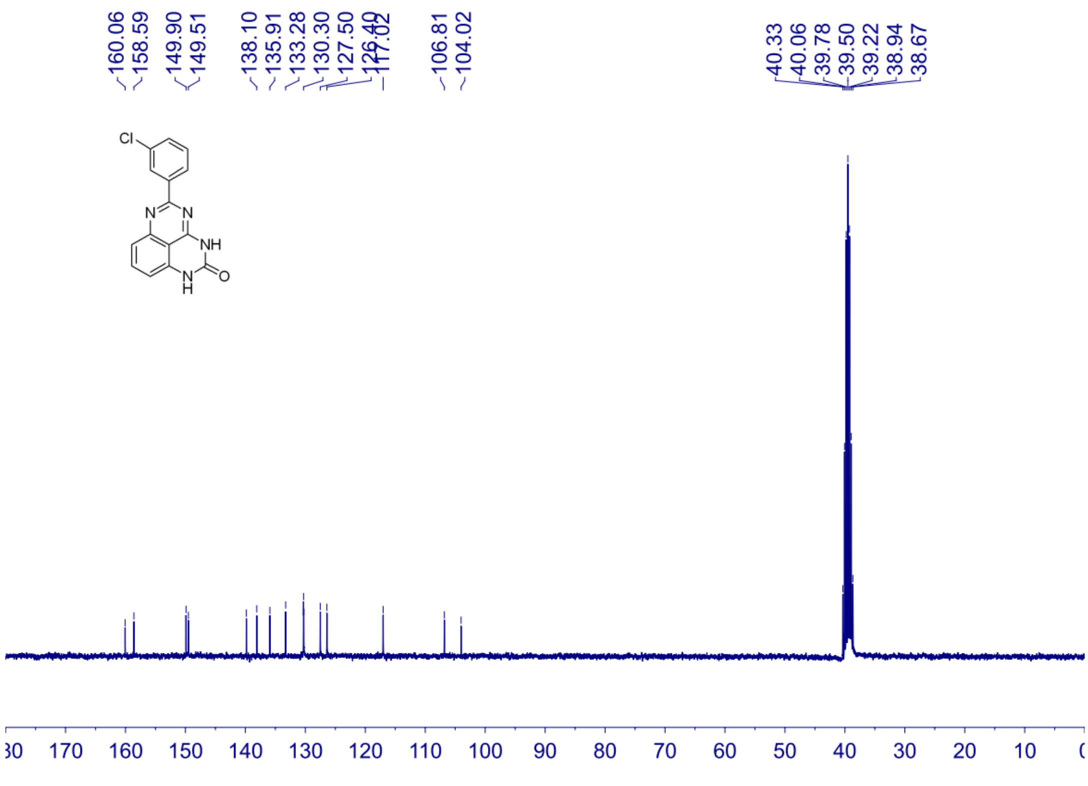
^{1}H NMR (300 MHz, DMSO-d_6) and ^{13}C NMR (75 MHz, DMSO-d_6) spectra of product 3aj



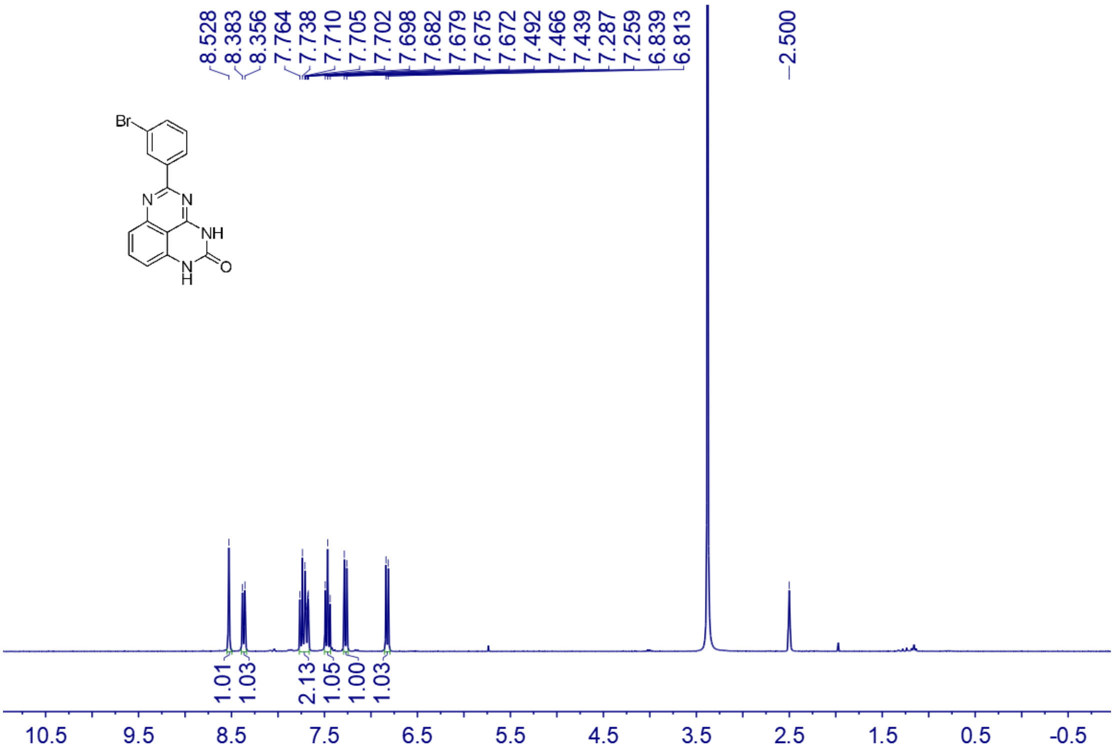


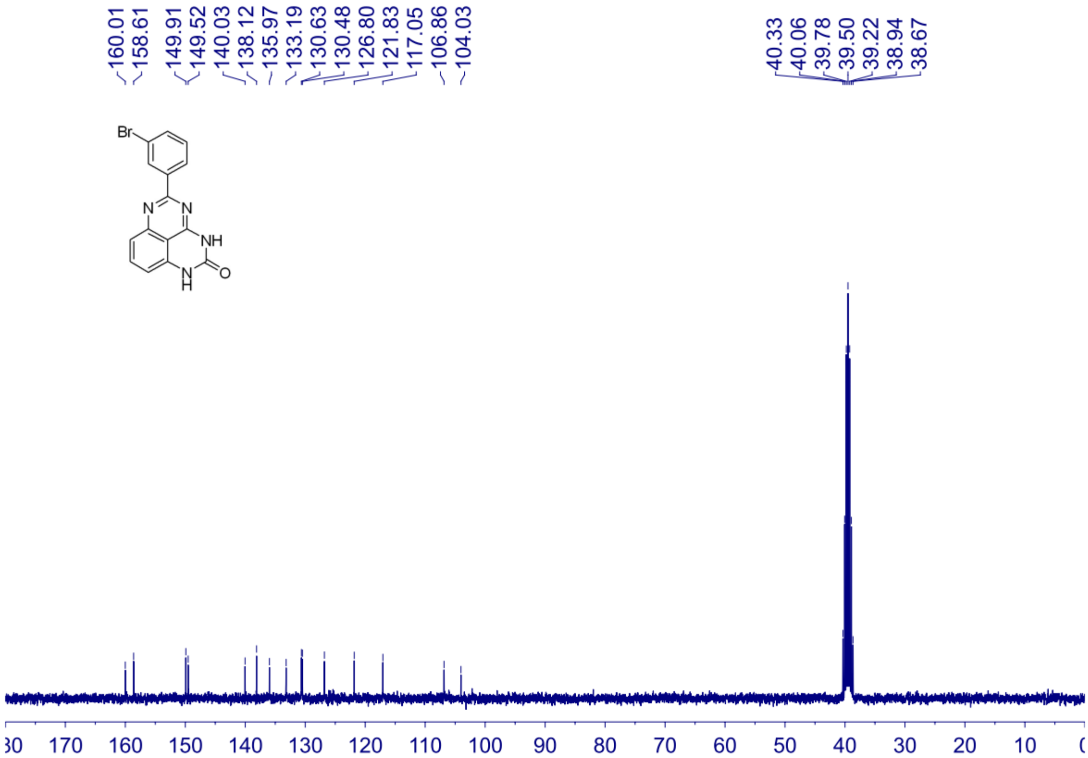
[1] H NMR (400 MHz, DMSO-d_6) and [13]C NMR (75 MHz, DMSO-d_6) spectra of product 3ak



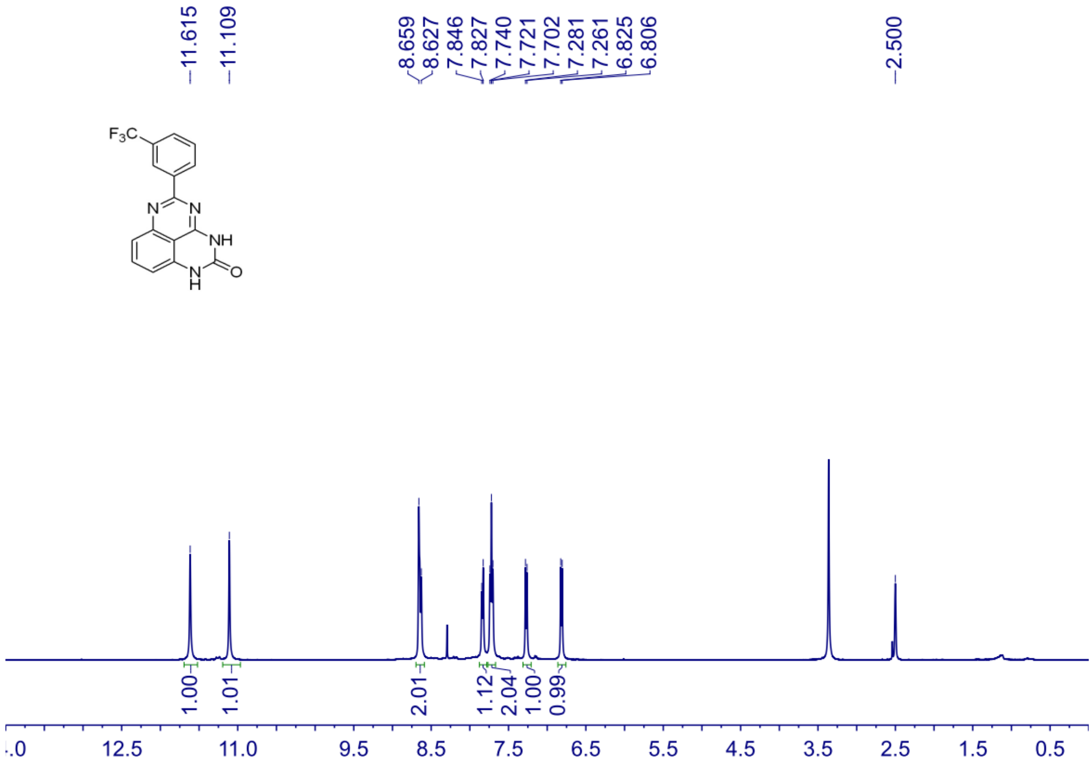


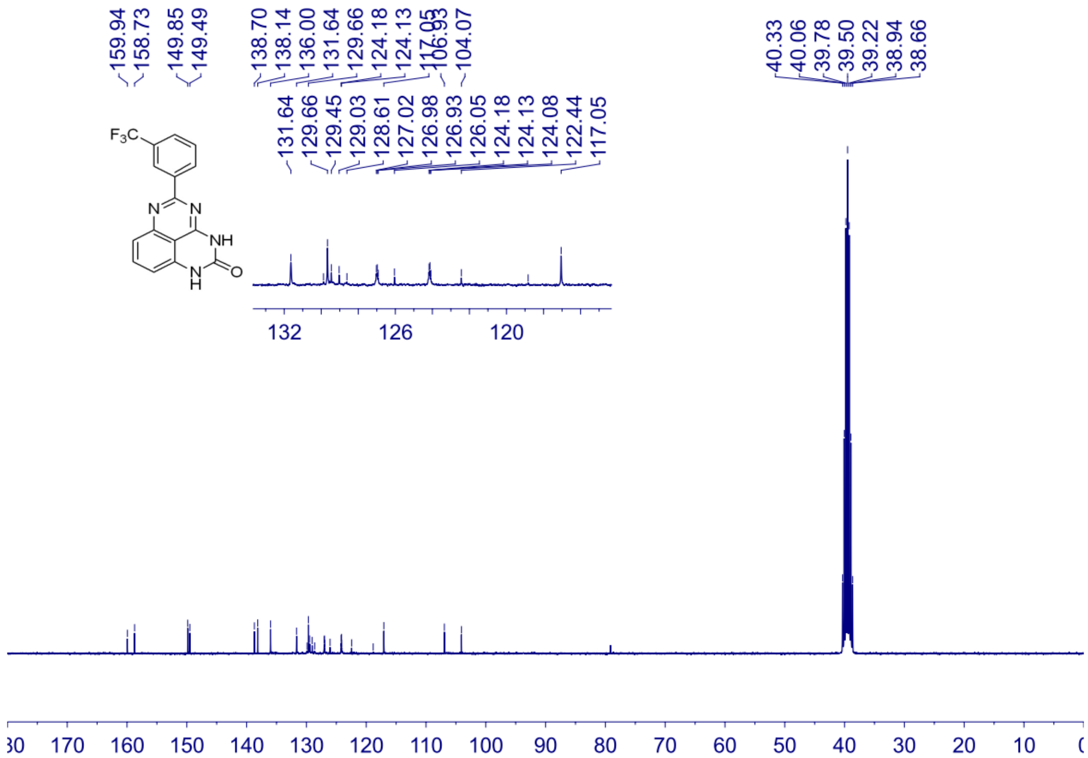
^{1}H NMR (300 MHz, DMSO-d_6) and ^{13}C NMR (75 MHz, DMSO-d_6) spectra of product 3al



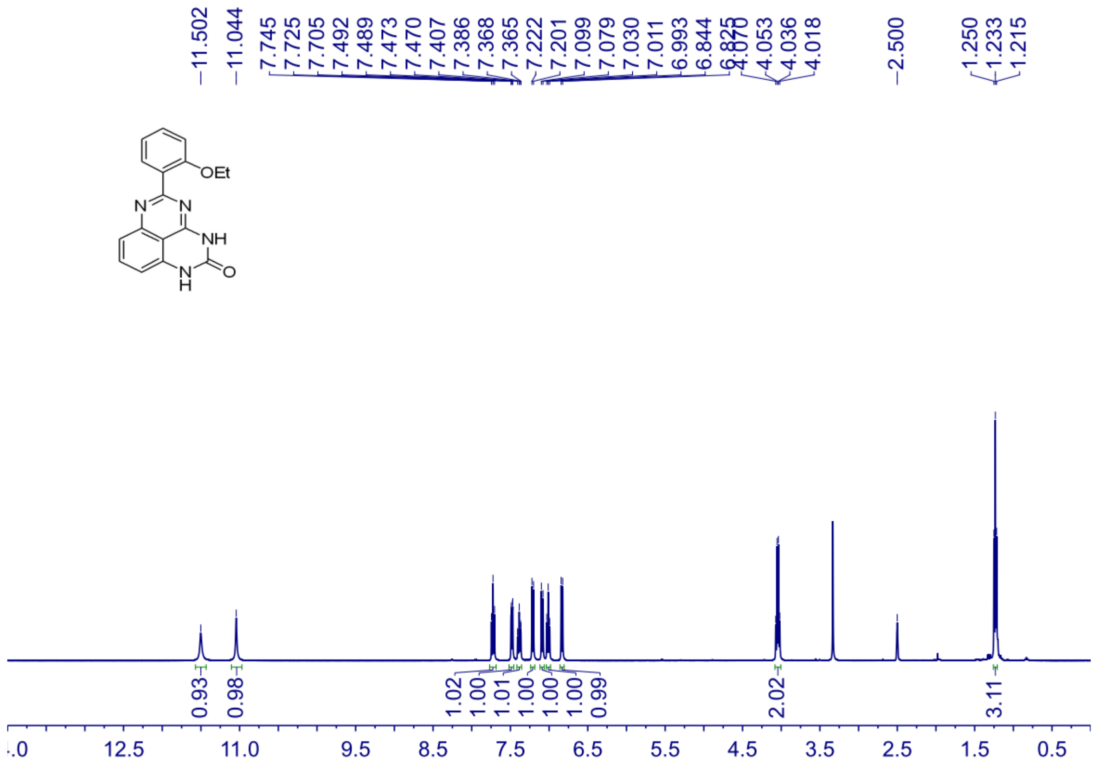


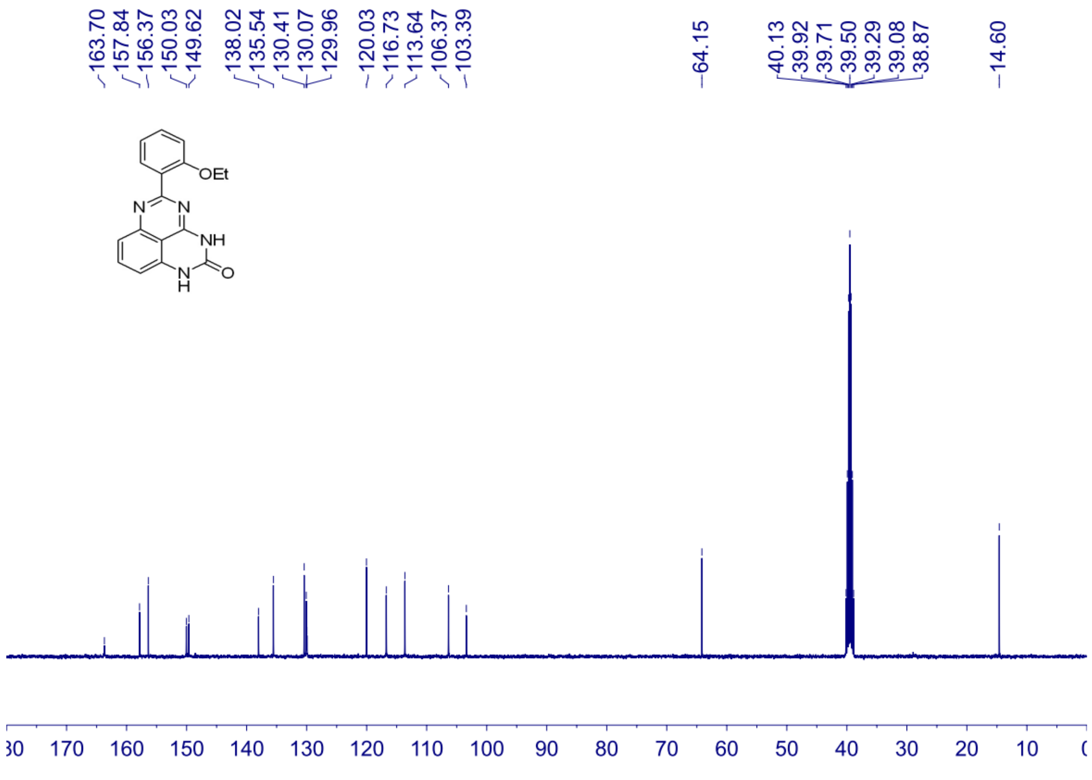
[1] H NMR (400 MHz, DMSO-d_6) and [13]C NMR (75 MHz, DMSO-d_6) spectra of product 3am



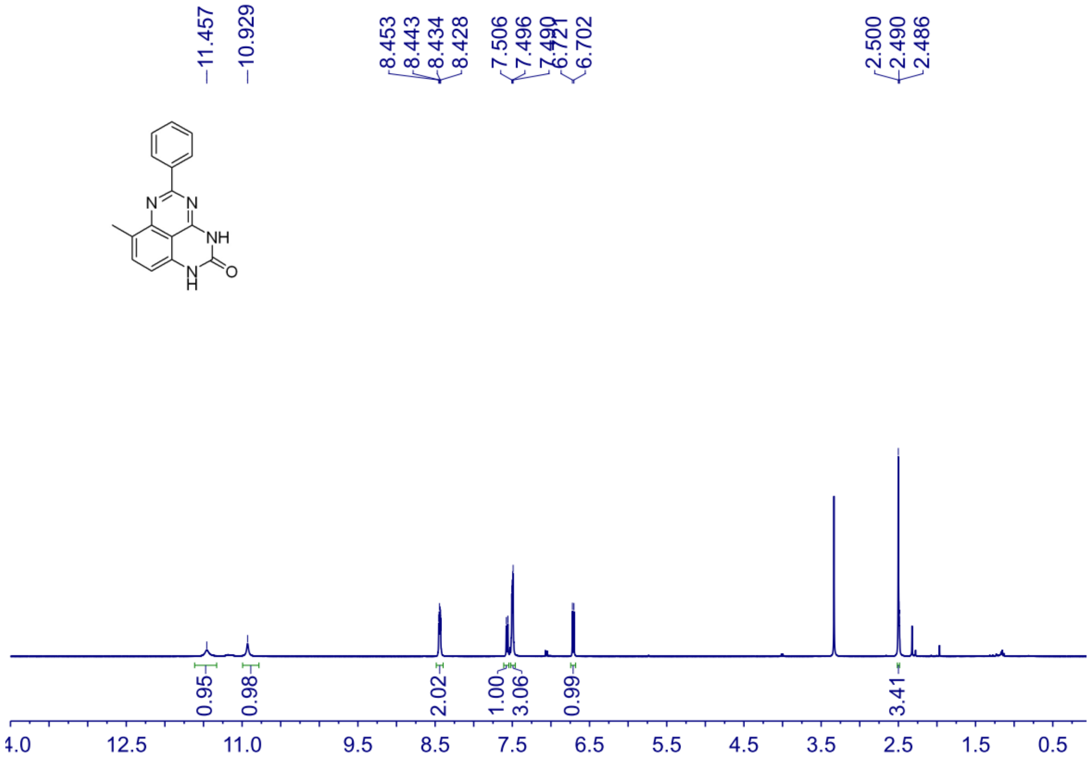


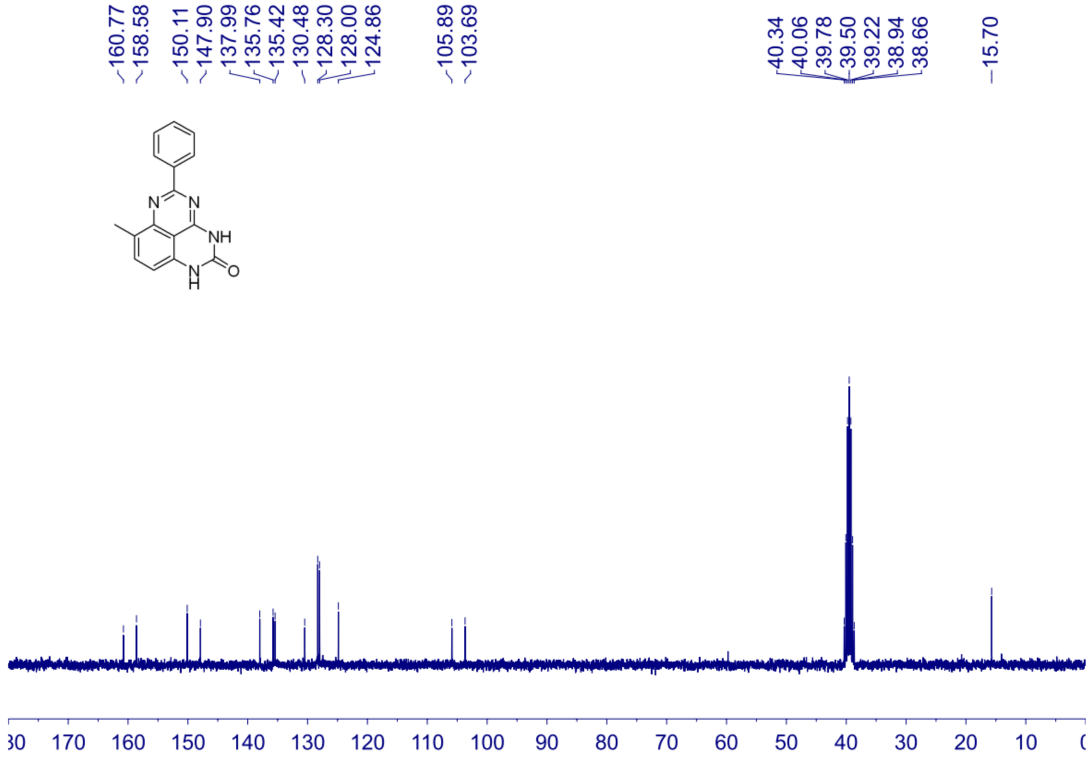
^{1}H NMR (400 MHz, DMSO-d_6) and ^{13}C NMR (100 MHz, DMSO-d_6) spectra of product 3an



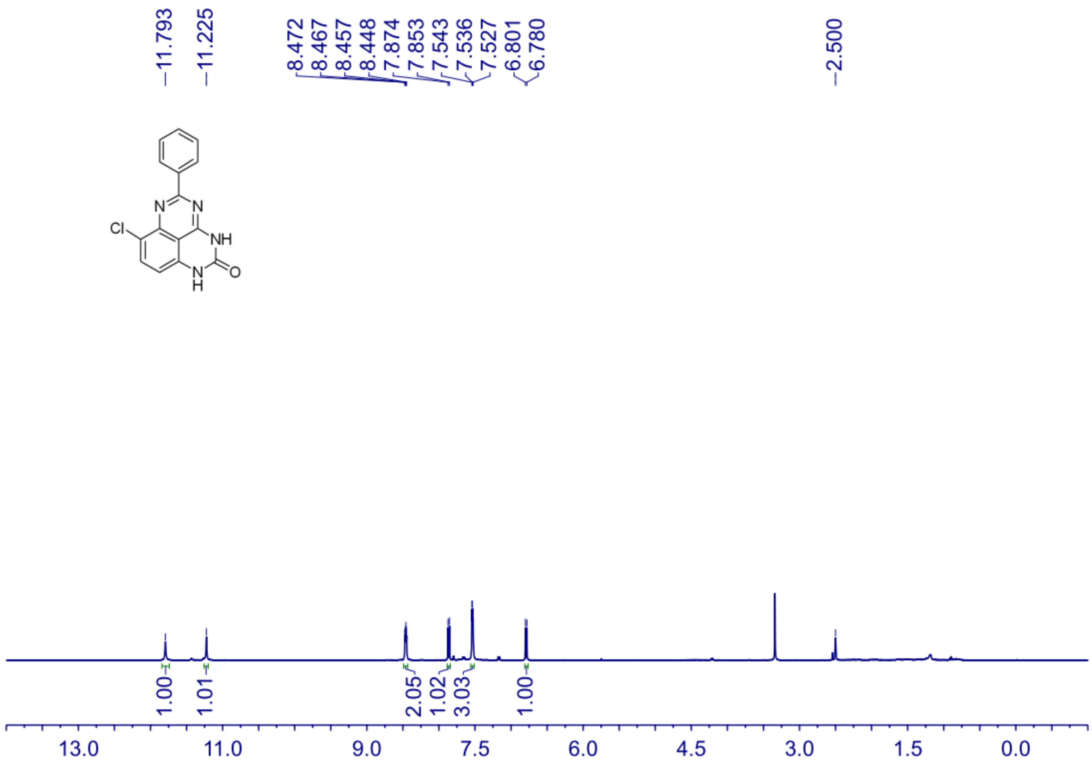


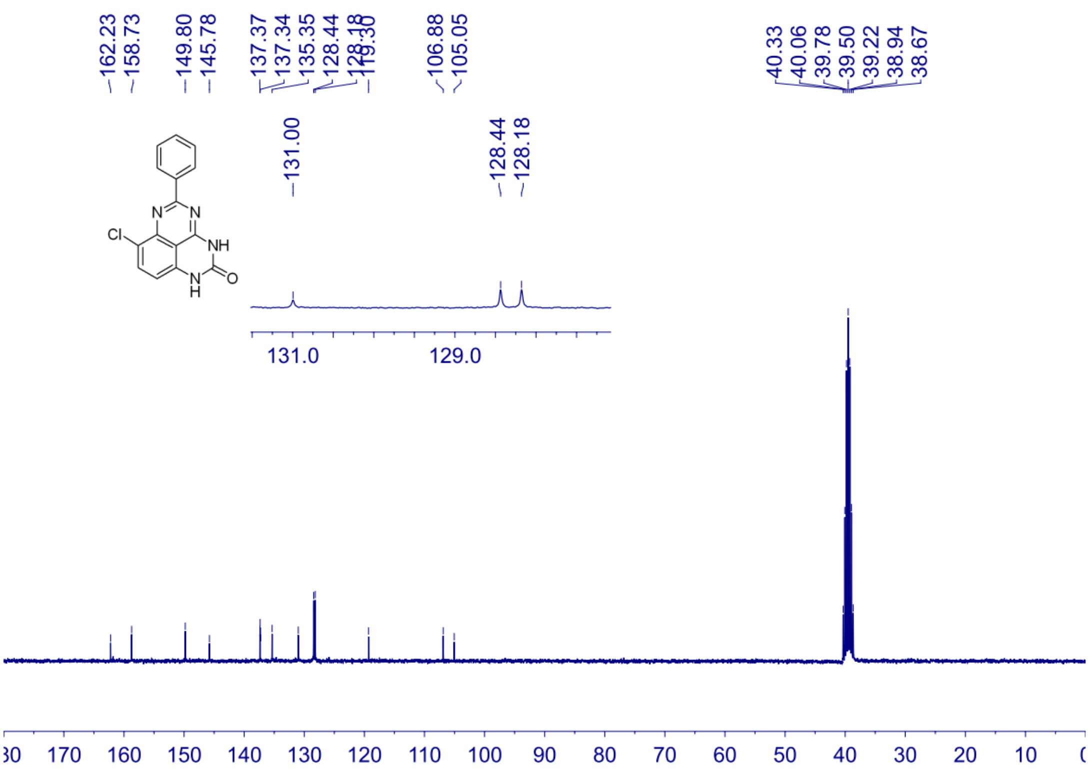
[1] H NMR (400 MHz, DMSO-d_6) and [13]C NMR (75 MHz, DMSO-d_6) spectra of product 3ba



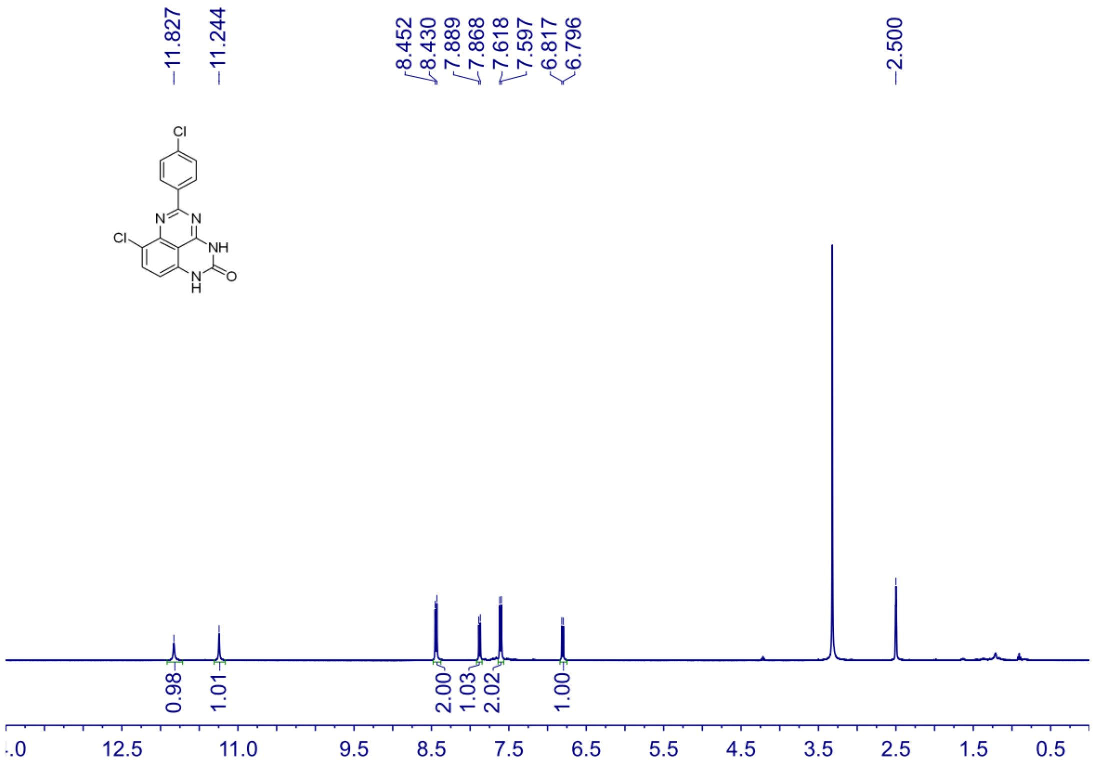


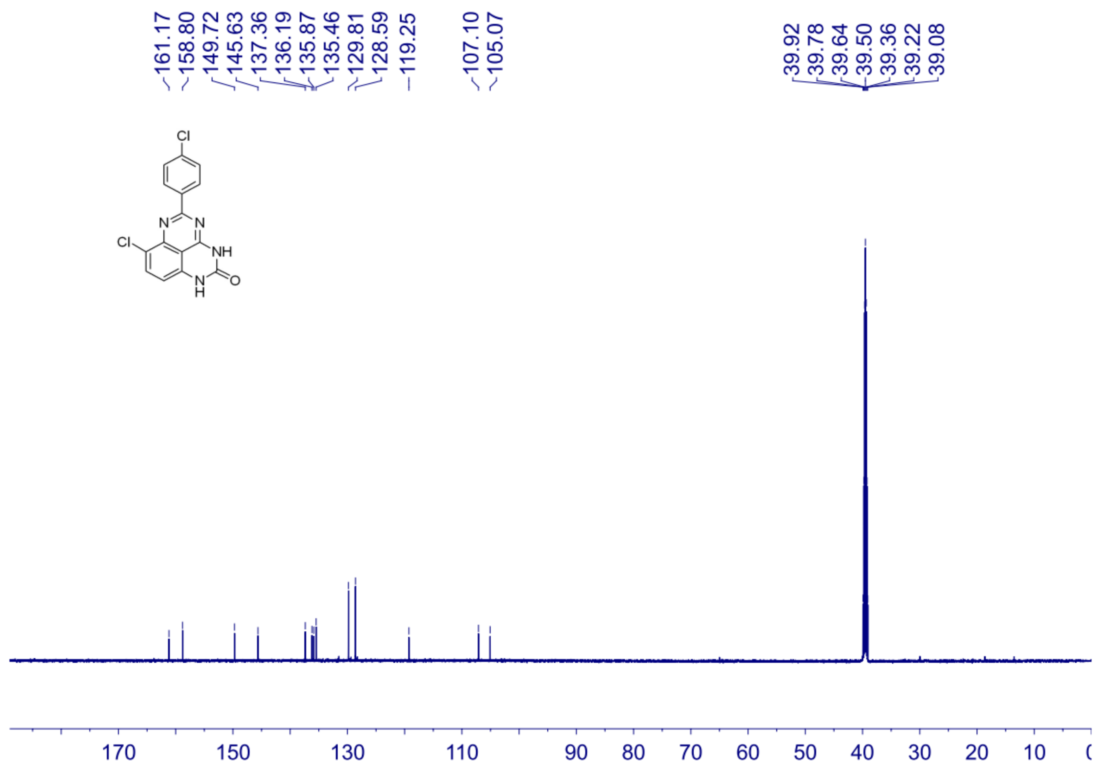
^{1}H NMR (400 MHz, DMSO-d_6) and ^{13}C NMR (75 MHz, DMSO-d_6) spectra of product 3ca



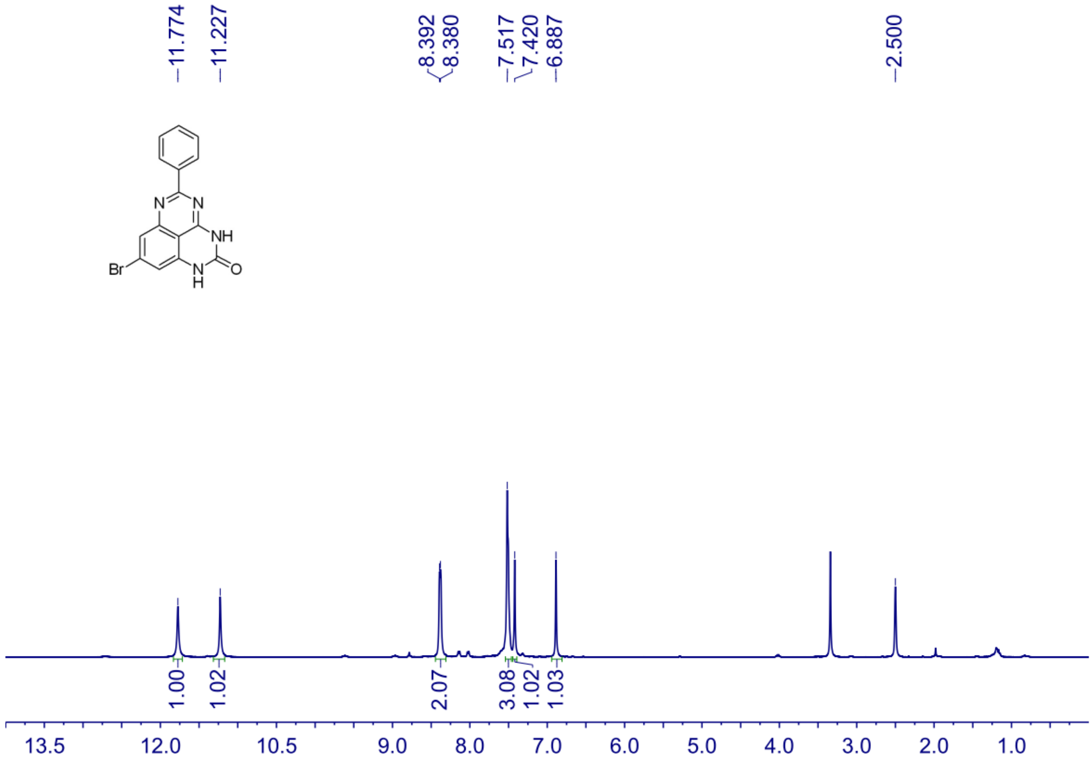


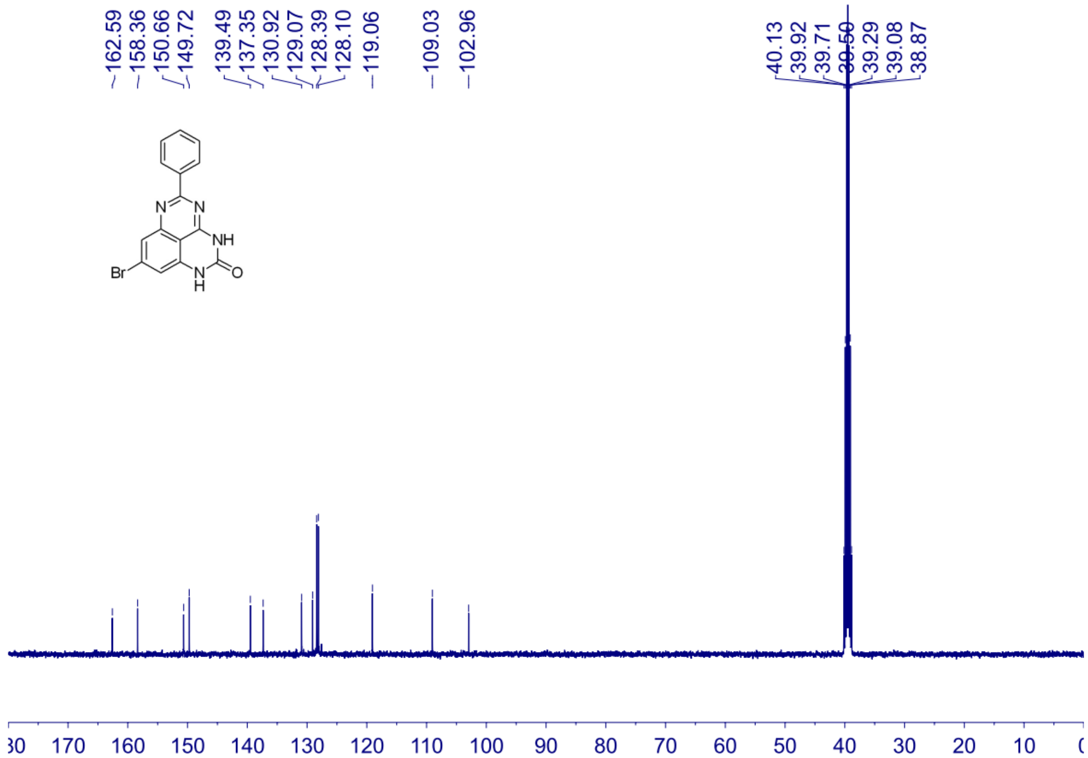
[1] H NMR (400 MHz, DMSO-d_6) and [13]C NMR (150 MHz, DMSO-d_6) spectra of product 3ce



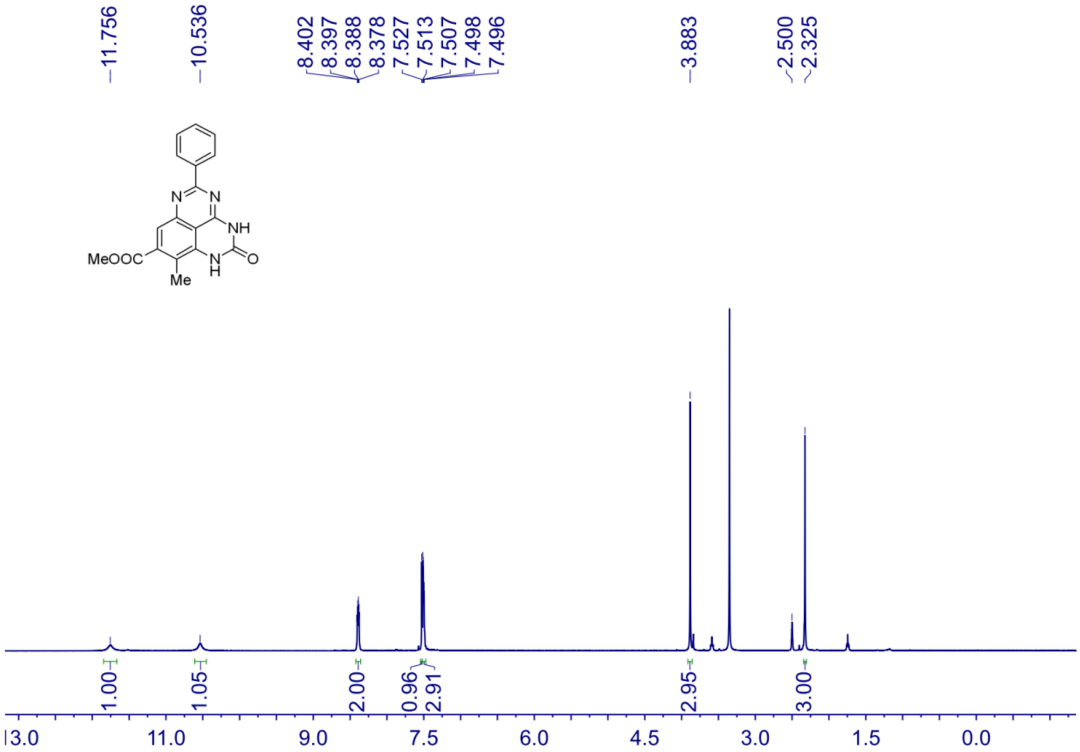


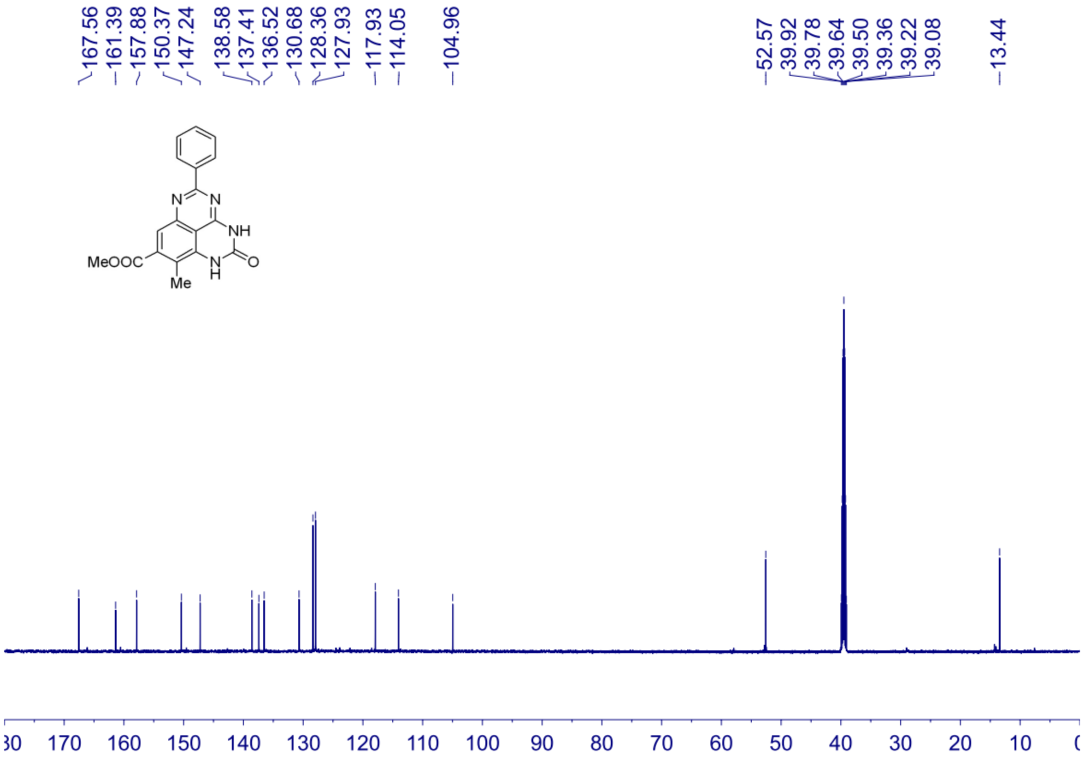
[1] H NMR (400 MHz, DMSO-d_6) and [13]C NMR (100 MHz, DMSO-d_6) spectra of product 3da



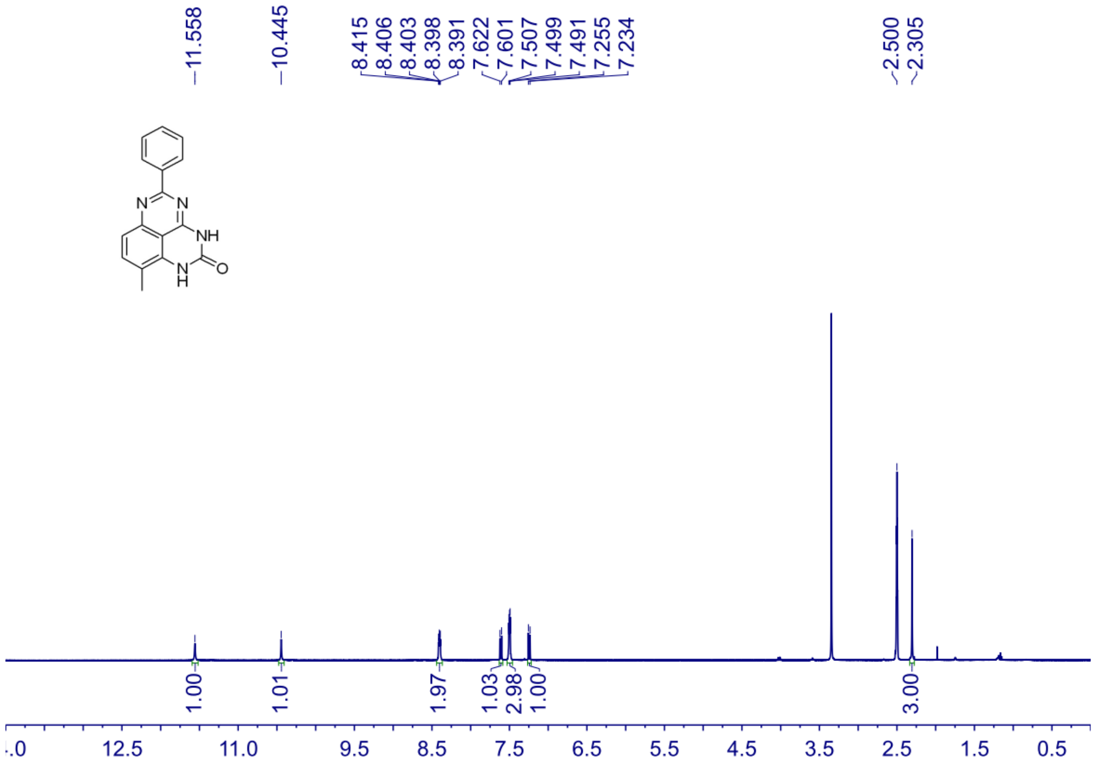


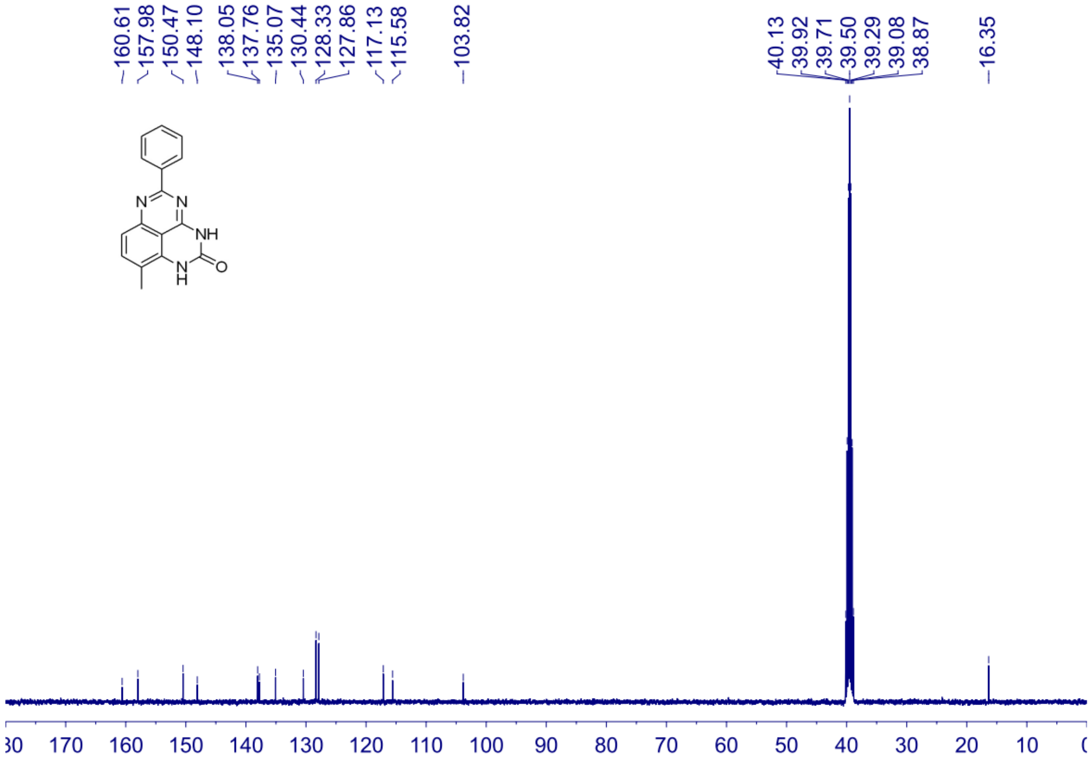
[1] H NMR (400 MHz, DMSO-d_6) and [13]C NMR (150 MHz, DMSO-d_6) spectra of product 3ea



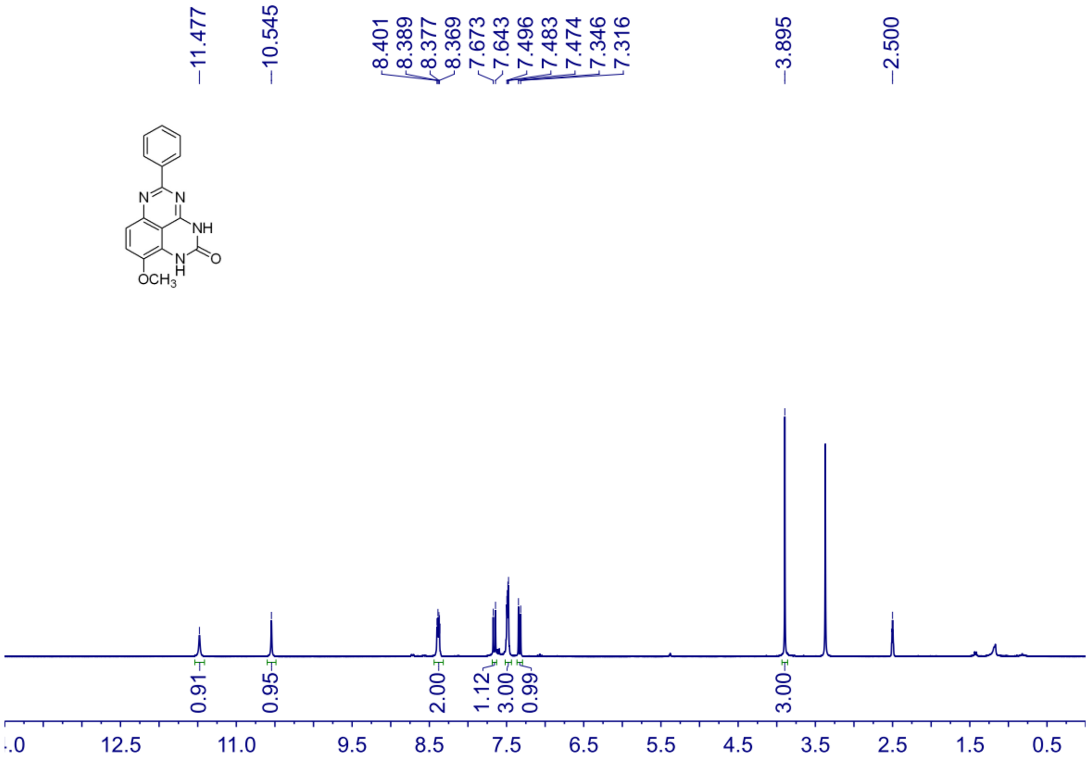


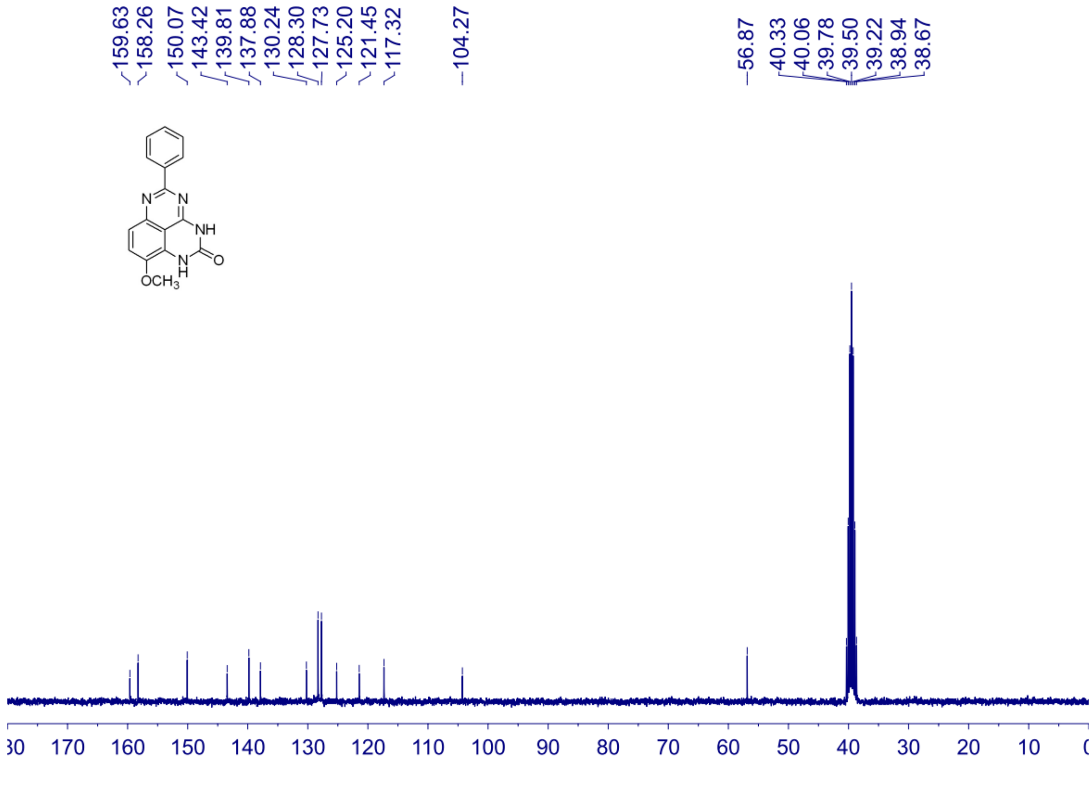
^{1}H NMR (400 MHz, DMSO-d_6) and ^{13}C NMR (100 MHz, DMSO-d_6) spectra of product 3fa



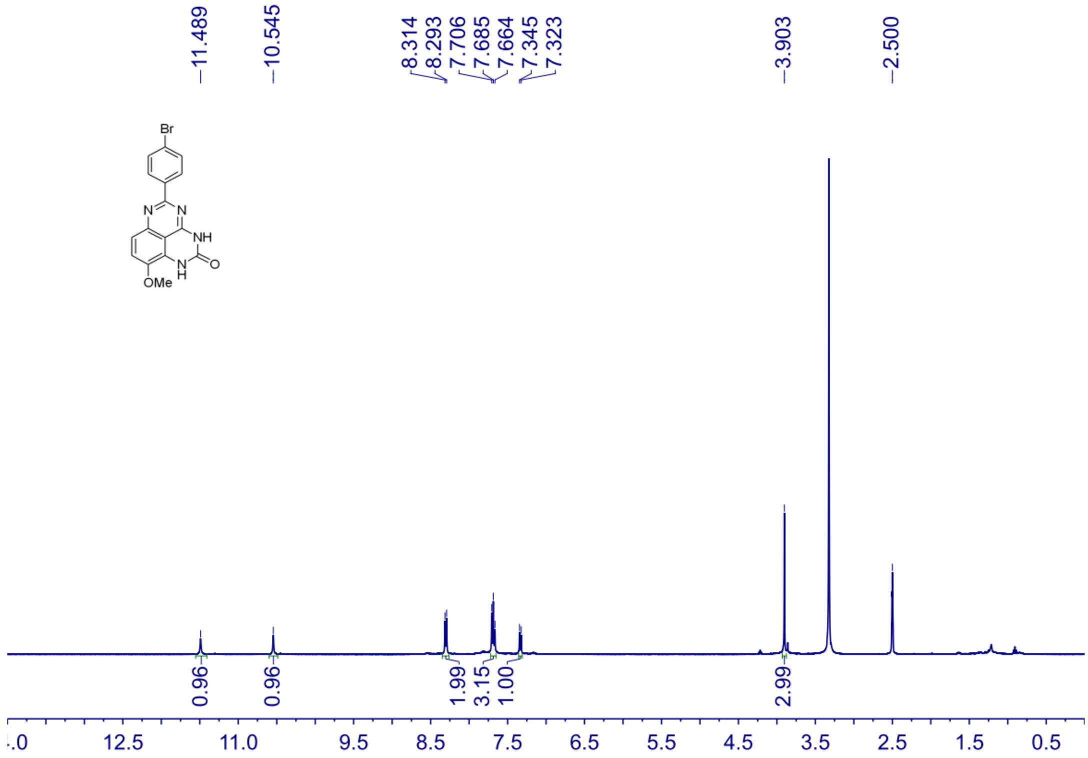


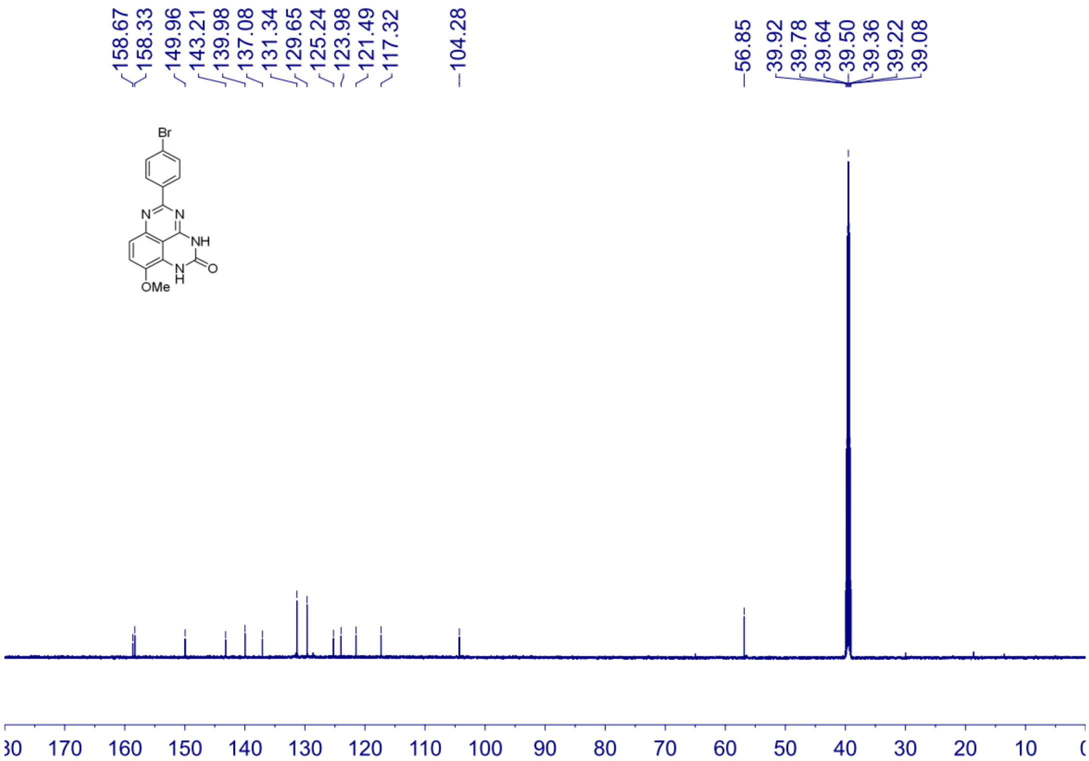
[1] H NMR (300 MHz, DMSO-d_6) and [13]C NMR (75 MHz, DMSO-d_6) spectra of product 3ga



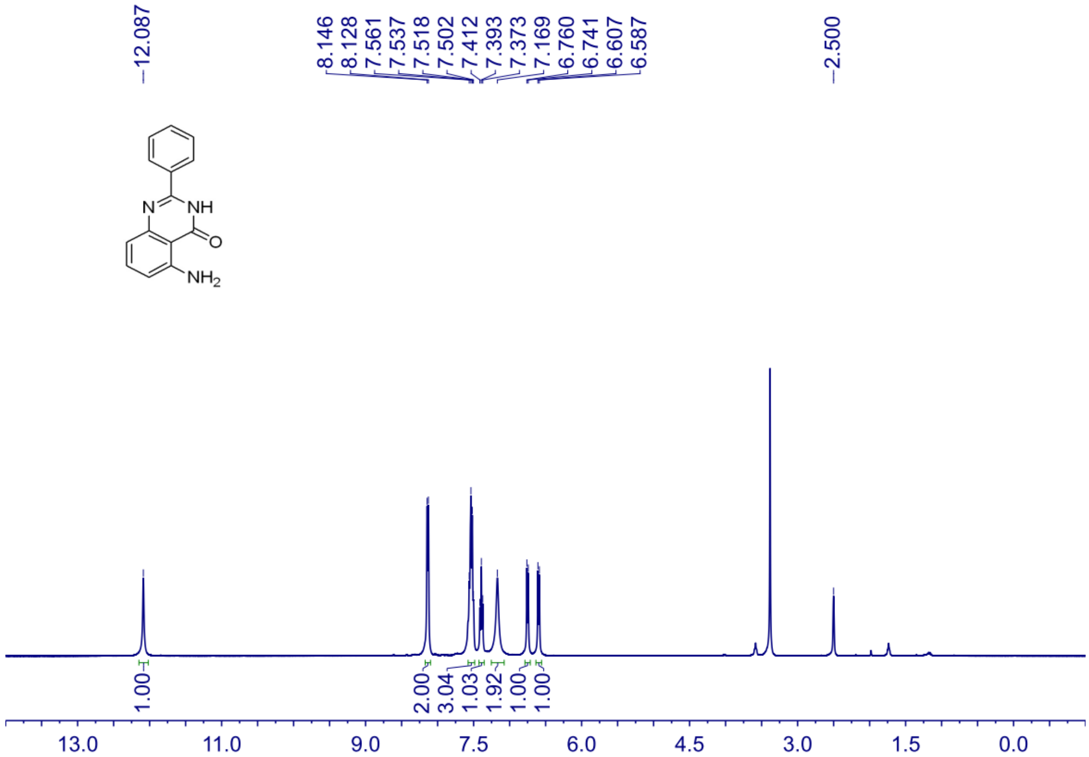


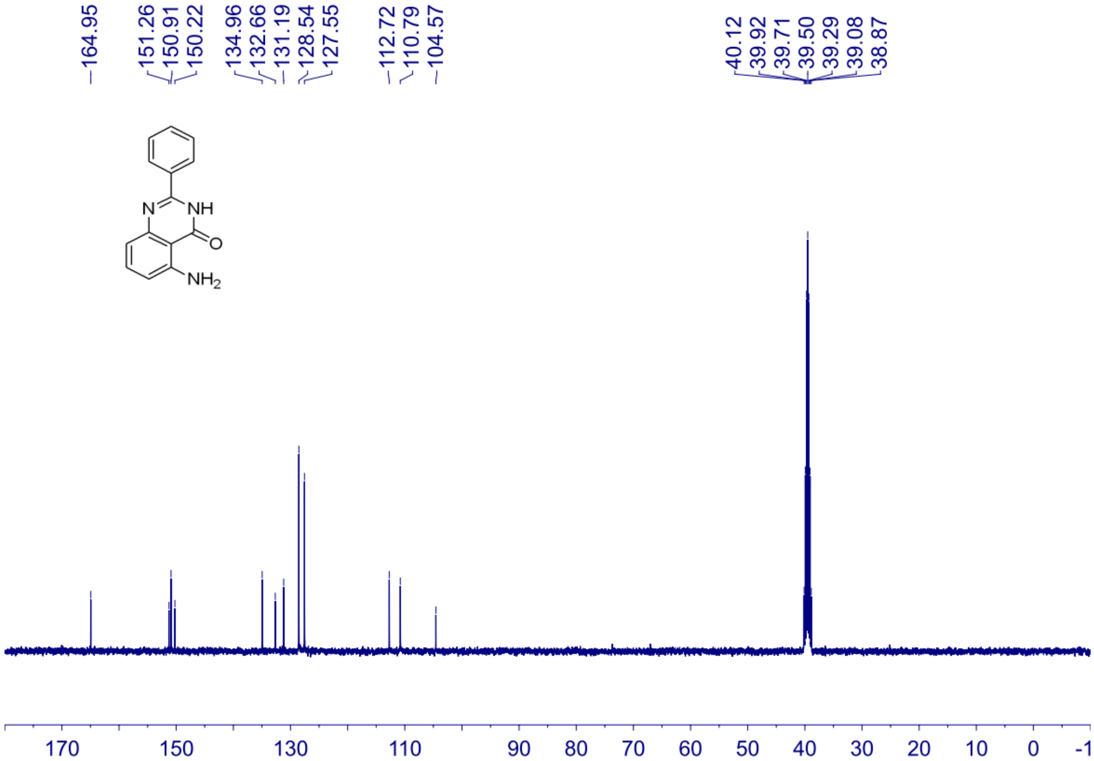
[1] H NMR (400 MHz, DMSO-d_6) and [13]C NMR (150 MHz, DMSO-d_6) spectra of product 3gf





[1] H NMR (400 MHz, DMSO-d_6) and [13]C NMR (100 MHz, DMSO-d_6) spectra of product 5





^{1}H NMR (400 MHz, DMSO-d_6) and ^{13}C NMR (100 MHz, DMSO-d_6) spectra of product 7 and 7'