Fe-FeO_x nanoparticles encapsulated in *N*-doped carbon material: A facile catalyst for selective synthesis of quinazolines from alcohols in water

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1. Experimental

1.1 General

All chemical reagents are obtained from commercial suppliers and used without further purification. All known compounds are identified by appropriate technique such as GC-MS, ^{1}H NMR, ^{13}C NMR, which is matched well with reported data in previously literature.[1-8] Analytical thin-layer chromatography is performed on glass plates precoated with silica gel impregnated with a fluorescent indicator (254 nm), and the plates are visualized by exposure to ultraviolet light. ^{1}H NMR and ^{13}C NMR spectra are recorded on an AVANCE 500 Bruker spectrometer (500 MHz/125 MHz) and a Bruker AFC 400 spectrometer (400 MHz/100 MHz) in $CDCl_3$ and DMSO-d6. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m= multiplet,), coupling constants (Hz) and integration. GC-MS data was recorded on a 5975C Mass Selective Detector, coupled with a 7890A Gas Chromatograph (Agilent Technologies). High resolution mass spectra (HRMS) were acquired on Waters Micromass GCT Premier spectrometer. Inductively coupled plasma optical emission spectrometer (ICP-OES) was analyzed on Varian 720-ES. Scanning electron microscopy (SEM) images were obtained by High Resolution Field Emission FEI quanta 400FEG. Transmission electron microscopy (TEM) images were obtained by FEI Talos F2OOS. X-ray diffraction (XRD) images were obtained by Rigaku Smart lab 9 at 40KV and 150 mA. BET images were obtained by MicroActive for ASAP 2460. The samples were degassed at 150 °C for 12 h before measurement. Raman spectra of images were obtained by horiba evolution with argon ion laser (532 nm) as the excitation light source. X-ray photoelectron spectroscopy (XPS) images were obtained by ESCALAB 250Xi spectrometer (Thermo Scientific, USA).

1.2 Experimental Details

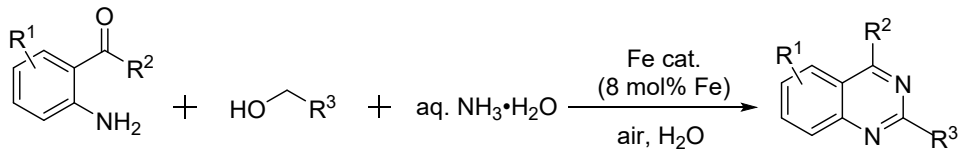
Reagents and chemicals: Heme iron (AR) was purchased from Macklin Co., Ltd. (Shanghai, China). Chitosan (high viscosity, > 400 mPa.s) and melamine (AR) were purchased from Aladdin Co., Ltd. (Shanghai, China). Aqueous ammonia (25-28 wt.%) was purchased from Sinopharm Chemical Reagent Co., Ltd. (Shanghai, China). Benzyl alcohol, *o*-aminoacetophenone and their derivatives were purchased from Macklin Co., Ltd or Aladdin Co., Ltd. All chemicals were used directly without further treatment.

Preparation of Fe-FeO$_x$@NC. First, C_3N_4 was synthesized according to the literature.[39] Then, 1 g of C_3N_4, 100 mg of heme iron and 120 mg of chitosan were mixed and dissolved in 20 mL of ethanol and sonicated for 3 h, followed by vigorous stirring for 24 h at room temperature. The brown cloudy liquid was rotary evaporated to remove the solvent and dried at 60 °C for 12 h. Finally, the powder was placed in a crucible and the powder was heated from room temperature to 800 °C with a heating rate of 5 °C /min under a N_2 flow. After holding for 2 h, it was naturally cooled to room temperature to obtain Fe-FeO$_x$@NC. No further processing required.

Preparation of Fe-FeO$_x$@NC-A. The obtained 200 mg Fe-FeO$_x$@NC and 20 ml 1 mol/L HCl solution were stirred at room temperature for 12 h, and then the mixture was centrifuged and washed with water to neutrality. Subsequently, Fe-FeO$_x$@NC-A was obtained by drying at 60 °C for 12 h. No further processing required.

Preparation of NC. NC was prepared by the method of preparing Fe-FeO$_x$@NC except that the heme iron was not added.

General procedures for the preparation of quinazoline



1 **2** **3** **4**

A mixture of *o*-aminoacetophenone (or its derivatives) **1** 0.25 mmol, alcohols **2** 0.75 mmol and aqueous ammonia **3** 2.00 mmol was added to a 35 mL thick-walled pressure-resistant tube. Then catalyst (20 mg) and H_2O (1 mL) were added followed by heating the mixture at 130 °C and stirring for 24 h. Upon completion, the reaction mixture was diluted with ethyl acetate (4 mL), filtered through a bed of silica gel layered over Celite. The volatiles were removed in *vacuo* to afford the crude product. Further column chromatography on silica gel (EtOAc/petroleum ether) or recrystallization was needed to afford the pure desired products **4**. The reaction instrument used in the reaction is a pressure-resistant tube, which was purchased from Synthware Glass Inc (China). This pressure-resistant tube has an external diameter of 26 mm, a length of 125 mm and a capacity of 35 mL, which can withstand pressure of 6 atm. In addition, the lid of the pressure-resistant tube was tightly

screwed during the reaction. (**Caution: Please check the tube body for any crack to avoid explosions**).

The procedure for recycling catalyst. The recyclability of Fe-FeO_x@NC was investigated under standard reaction conditions with decreased reaction time of 12 h. The catalyst was separated from the solution by centrifugation at the end of each cycle, washed with ethanol and dried under vacuum to remove residual solvent before being used in next reaction cycle.

2. Supplementary figures

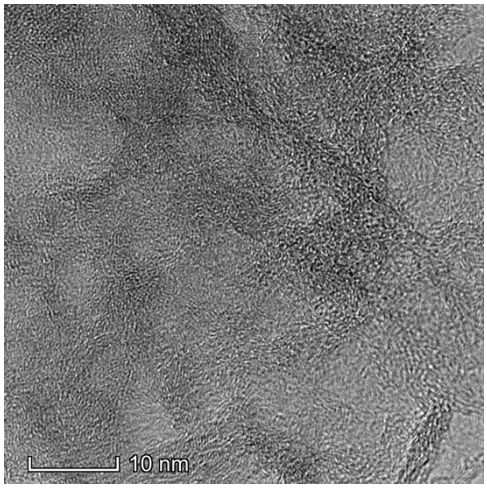


Fig. S1 HR-TEM image of Fe-FeO_x@NC-A.

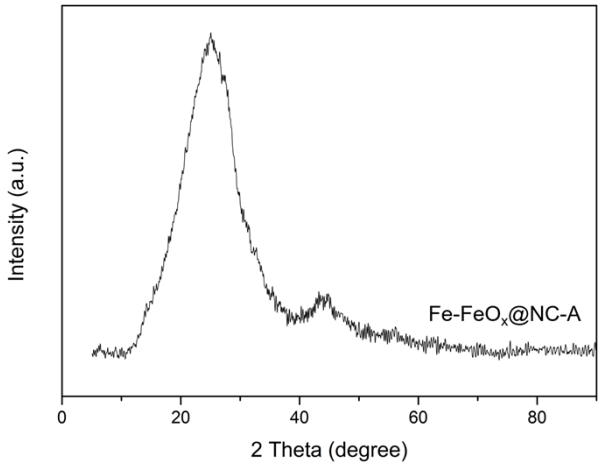


Fig. S2 XRD image of Fe-FeO_x@NC-A.

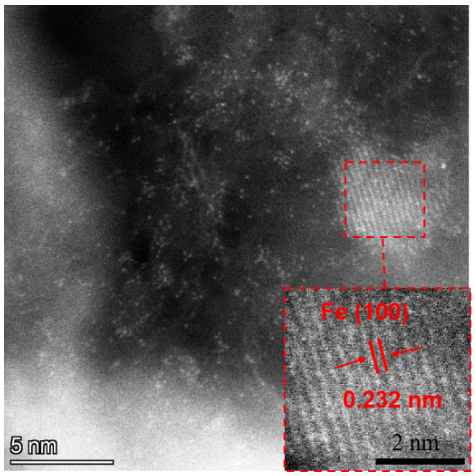


Fig. S3 HAADF-STEM image of Fe-FeO_x@NC.

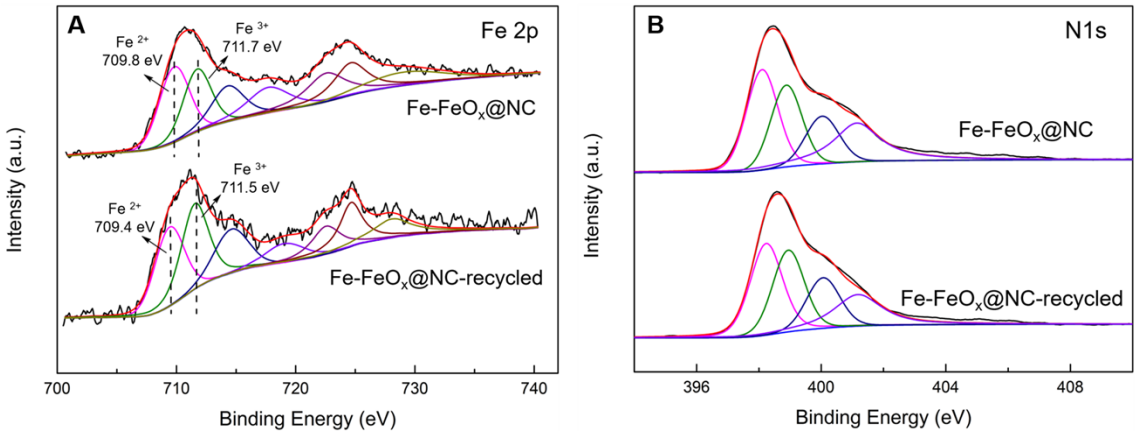


Fig. S4 (A) The Fe 2p and (B) N 1s spectra of the Fe-FeO_x@NC and Fe-FeO_x@NC-recycled.

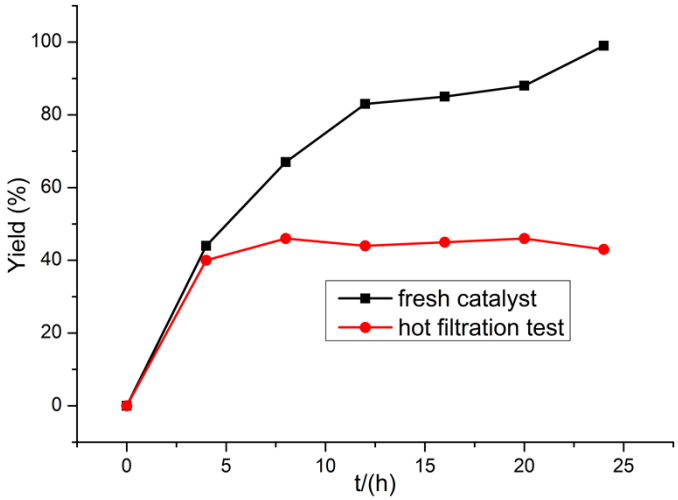


Fig. S5 A hot-filtration test of Fe-FeO_x@NC.

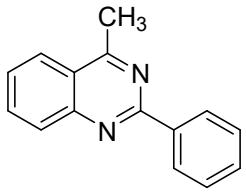
Table S1 ICP-OES analysis

Catalyst	Fe content (%)
Fe-FeO_x@NC	5.4640
Fe-FeO_x@NC-recycled[a]	5.3447

[a] The catalyst is recycled after five runs.

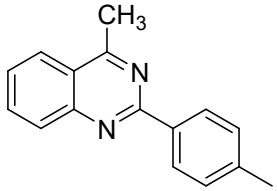
3. Characterization Data of products

4-methyl-2-phenylquinazoline (4a)[1]



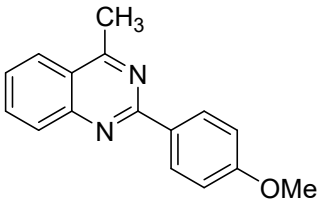
94% yield, white solid. **^{1}H NMR** (500 MHz, DMSO-d6) δ 8.57 - 8.56 (m, 2H), 8.28 (d, *J* = 8.5 Hz, 1H), 8.04 - 7.97 (m, 2H), 7.72 - 7.69 (m, 1H), 7.58 - 7.54 (m, 3H), 2.99 (s, 3H).

4-methyl-2-(p-tolyl) quinazoline (4b)[2]



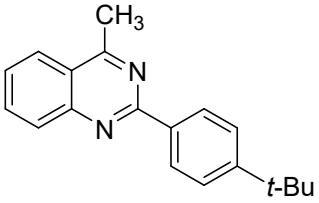
86% yield, white solid. **^{1}H NMR** (500 MHz, DMSO-d6) δ 8.45 (d, *J* = 7.5 Hz, 2H), 8.24 (d, *J* = 8.5 Hz, 1H), 8.00 - 7.94 (m, 2H), 7.67 (t, *J* = 7.5 Hz, 1H), 7.35 (d, *J* = 8.0 Hz, 2H), 2.97 (s, 3H), 2.39 (s, 3H).

2-(4-methoxyphenyl)-4-methylquinazoline (4c)[1]



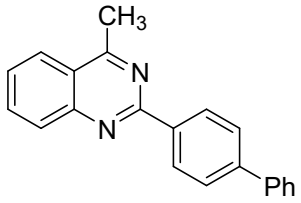
84% yield, white solid. **^{1}H NMR** (500 MHz, DMSO-d6) δ 8.51 (d, *J* = 8.5 Hz, 1H), 8.23 (d, *J* = 8.0 Hz, 1H), 7.98 - 7.93 (m, 2H), 7.66 - 7.63 (m, 1H), 7.09 (d, *J* = 8.5 Hz, 2H), 3.85 (s, 3H), 2.96 (s, 3H).

2-(4-(tert-butyl) phenyl)-4-methylquinazoline (4d)[3]



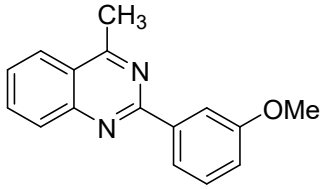
70% yield, white solid. **^{1}H NMR** (400 MHz, DMSO-d6) δ 8.46 (d, *J* = 7.6 Hz, 2H), 8.20 (d, *J* = 8.4 Hz, 1H), 8.00 - 7.91 (m, 2H), 7.65 - 7.62 (m, 1H), 7.52 (d, *J* = 8.0 Hz, 2H), 2.95 (s, 3H), 1.31 (s, 9H).

2-([1,1'-biphenyl]-4-yl)-4-methylquinazoline (4e)[2]



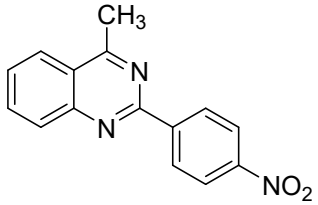
82% yield, white solid. **^{1}H NMR** (500 MHz, DMSO-d6) δ 8.64 (d, *J* = 8.5 Hz, 2H), 8.28 (d, *J* = 8.0 Hz, 1H), 8.04 (d, *J* = 8.0 Hz, 1H), 8.00 - 7.97 (m, 1H), 7.86 (d, *J* = 8.0 Hz, 2H), 7.77 (d, *J* = 8.0 Hz, 2H), 7.72 - 7.69 (m, 1H), 7.52 - 7.49 (m, 2H), 7.43 - 7.40 (m, 1H), 3.00 (s, 3H).

2-(3-methoxyphenyl)-4-methylquinazoline (4f)[4]



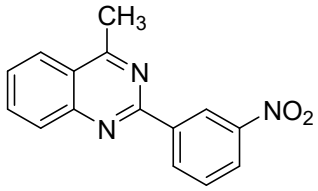
84% yield, white solid. **^{1}H NMR** (400 MHz, DMSO-d6) δ 8.26 - 7.98 (m, 5H), 7.70 (s, 1H), 7.48 (s, 1H), 7.13 (s, 1H), 3.88 (s, 3H), 2.98 (s, 3H).

4-methyl-2-(4-nitrophenyl) quinazoline (4g)[5]



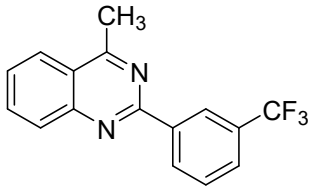
76% yield, white solid. **^{1}H NMR** (500 MHz, DMSO-d6) δ 8.71 (d, *J* = 8.5 Hz, 2H), 8.35 (d, *J* = 8.5 Hz, 2H), 8.28 (d, *J* = 8.5 Hz, 1H), 8.06 - 8.00 (m, 2H), 7.76 - 7.73 (m, 1H), 2.99 (s, 3H).

4-methyl-2-(3-nitrophenyl) quinazoline (4h)[6]



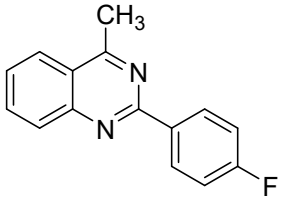
66% yield, white solid. **^{1}H NMR** (400 MHz, DMSO-d6) δ 9.27 (s, 1H), 8.96 (d, *J* =8.0 Hz, 1H), 8.41 - 8.33 (m, 2H), 8.12 - 8.03 (m, 2H), 7.89 - 7.85 (t, *J* =8.0 Hz, 1H), 7.80 - 7.76 (m, 1H), 3.04 (s, 3H).

4-methyl-2-(3-(trifluoromethyl)phenyl) quinazoline (4i)



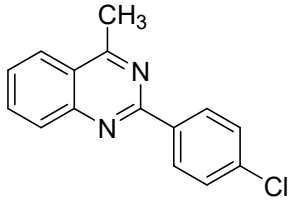
71% yield, white solid. **^{1}H NMR** (400 MHz, DMSO-d6) δ 8.78 - 8.77 (d, *J* = 5.2 Hz, 2H), 8.26 - 8.24 (d, *J* = 8.4 Hz, 1H), 8.04 - 7.96 (m, 2H), 7.90 - 7.88 (d, *J* = 7.6 Hz, 1H), 7.80 - 7.69 (m, 2H), 2.97 (s, 3H). **^{13}C NMR** (125 MHz, DMSO-d6) δ 169.63, 157.57, 149.79, 138.92, 134.88, 132.16, 130.33, 129.94 (q, *J* = 31.6 Hz, 1C), 128.97, 128.32, 127.45 (d, *J* = 3.3 Hz, 1C), 126.24, 124.69 (d, *J* = 270.8 Hz, 1C), 124.55 (d, *J* = 3.9 Hz, 1C), 123.17, 22.25. HRMS (EI) Calcd. For $C_{16}H_{11}F_3N_2$ 288.0874, found 288.0841.

2-(4-fluorophenyl)-4-methylquinazoline (4j)[2]



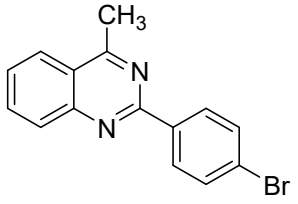
82% yield, white solid. **^{1}H NMR** (400 MHz, DMSO-d6) δ 8.62 - 8.59 (m, 2H), 8.28 (d, *J* = 8.4 Hz, 1H), 8.04 - 7.97 (m, 2H), 7.73 - 7.69 (m, 1H), 7.41 - 7.36 (m, 2H), 3.00 (s, 3H).

2-(4-chlorophenyl)-4-methylquinazoline (4k)[1]



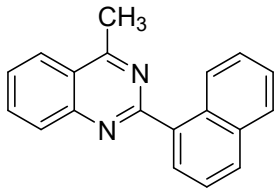
74% yield, white solid. **^{1}H NMR** (500 MHz, DMSO-d6) δ 8.52 (d, *J* = 8.5 Hz, 2H), 8.24 (d, *J* = 8.0 Hz, 1H), 8.00 - 7.95 (m, 2H), 7.70 - 7.67 (m, 1H), 7.58 (d, *J* = 8.5 Hz, 2H), 2.95 (s, 3H).

2-(4-bromophenyl)-4-methylquinazoline (4l)[5]



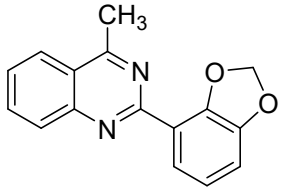
70% yield, light yellow solid. **^{1}H NMR** (400 MHz, DMSO-d6) δ 8.48 (d, *J* =8.4 Hz, 2H), 8.27 (d, *J* =8.4 Hz, 1H), 8.03 - 7.98 (m, 2H), 7.79 - 7.70 (m, 3H), 2.99(s, 3H).

4-methyl-2-(naphthalen-1-yl) quinazoline (4m)[4]



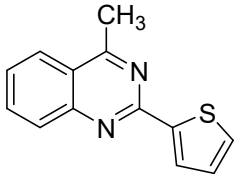
93% yield, white solid. **^{1}H NMR** (500 MHz, DMSO-d6) δ 9.15 (s, 1H), 8.69 (d, *J* = 8.5 Hz, 1H), 8.32 (d, *J* = 8.0 Hz, 1H), 8.17 - 8.15 (m, 1H), 8.10 -8.07 (m, 2H), 8.03 - 7.99 (m, 2H), 7.75 - 7.71 (m, 1H), 7.62 - 7.58 (m, 2H), 3.05 (s, 3H).

2-(benzo[d] [1,3] dioxol-4-yl)-4-methylquinazoline (4n)



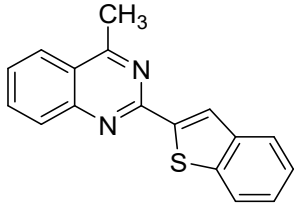
74%yield, yellow solid. **^{1}H NMR** (500 MHz, DMSO-d6) δ 8.23 (d, *J* = 8.5 Hz, 1H), 8.17 (d, *J* = 7.5 Hz, 1H), 8.00 (s, 1H), 7.91 - 7.94 (m, 2H), 7.67 - 7.64 (m, 1H), 7.07 (d, *J* = 8.0 Hz, 1H), 6.13 (s, 2H), 2.95 (s, 3H). **^{13}C NMR** (125 MHz, DMSO-d6) δ 168.94, 158.23, 149.91, 148.94, 147.23, 134.65, 128.83, 128.01, 126.16, 122.96, 122.55, 121.68, 121.48, 110.37, 101.58, 22.22. HRMS (EI) Calcd. For $C_{16}H_{12}N_2O_2$ 264.0899, found 264.0868.

4-methyl-2-(thiophen-2-yl) quinazoline (4o)[4]



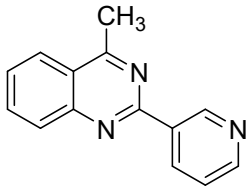
84% yield, white solid. **^{1}H NMR** (500 MHz, DMSO-d6) δ 8.22 (d, *J* = 8.5 Hz, 1H), 8.05 (d, *J* = 3.5 Hz, 1H), 7.96 - 7.91 (m, 2H), 7.77 (d, *J* = 5.0 Hz, 1H), 7.66 - 7.63 (m, 1H), 7.24 - 7.22 (m, 1H), 2.93 (s, 3H).

2-(benzo[b]thiophen-2-yl)-4-methylquinazoline (4p)



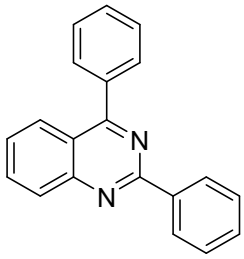
82% yield, light yellow solid. **^{1}H NMR** (500 MHz, DMSO-d6) δ 8.41 (s, 1H), 8.26 (d, *J* = 8.5 Hz, 1H), 8.02 - 7.98 (m, 4H), 7.71 - 7.68 (m, 1H), 7.45 - 7.40 (m, 2H), 2.97 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 168.38, 157.12, 150.12, 144.19, 141.94, 140.39, 133.78, 128.94, 127.03, 125.91, 125.57, 125.08, 124.80, 124.53, 123.02, 122.68, 21.90. HRMS (EI) Calcd. For $C_{17}H_{12}N_2S$ 276.0721, found 276.0690.

4-methyl-2-(pyridin-3-yl) quinazoline (4q)[3]



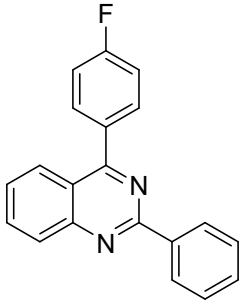
62% yield, white solid. **^{1}H NMR** (400 MHz, DMSO-d6) δ 9.67 (d, *J* = 1.2 Hz, 1H), 8.81 - 8.70 (m, 1H), 8.75 - 8.73 (m, 1H), 8.30 (d, *J* = 8.0 Hz, 1H), 8.06 - 8.00 (m, 2H), 7.76 - 7.72 (m, 1H), 7.61- 7.58 (m, 1H), 3.00 (s, 3H).

2,4-diphenylquinazoline (4r)[1]



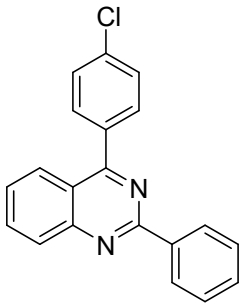
90% yield, white solid. **^{1}H NMR** (400 MHz, DMSO-d6) δ 8.64 - 8.62 (m, 2H), 8.18 - 8.04 (m, 3H), 7.92 - 7.90 (m, 2H), 7.74 - 7.68 (m, 4H), 7.61 - 7.58 (m, 3H).

4-(4-fluorophenyl)-2-phenylquinazoline (4s)[7]



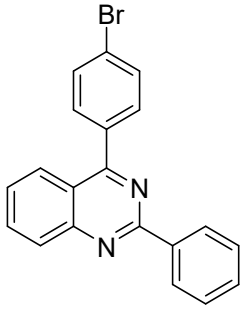
93% yield, white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.75 (d, *J* =6.8 Hz, 2H), 8.21 (d, *J* =8.4 Hz, 1H), 8.13 (d, *J* =8.0 Hz, 1H), 7.97 - 7.91 (m, 3H), 7.61 - 7.56 (m, 4H), 7.37 - 7.31 (m, 2H).

4-(4-chlorophenyl)-2-phenylquinazoline (4t)[7]



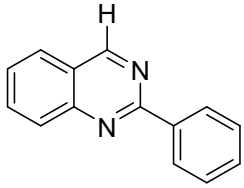
82% yield, white solid. **^{1}H NMR** (400 MHz, DMSO-d6) δ 8.62 - 8.60 (m, 2H), 8.16 (d, *J* =8.4 Hz, 1H), 8.10 - 8.04 (m, 2H), 7.94 (d, *J* =8.0 Hz, 2H), 7.75 - 7.70 (m, 3H), 7.61 - 7.58 (m, 3H).

4-(4-bromophenyl)-2-phenylquinazoline (4u)[7]



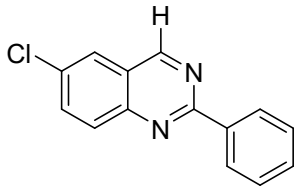
95% yield, white solid. **^{1}H NMR** (400 MHz, DMSO-d6) δ 8.62 - 8.60 (m, 2H), 8.16 (d, *J* =8.4 Hz, 1H), 8.11 - 8.04 (m, 2H), 7.88 (s, 4H), 7.75 - 7.70 (m, 1H), 7.59 - 7.58 (m, 3H).

2-phenylquinazoline (4v)[8]



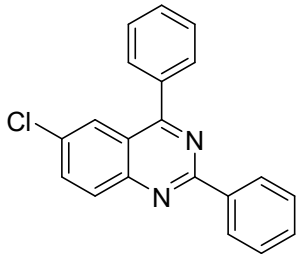
99% yield, yellow solid. **^{1}H NMR** (400 MHz, DMSO-d6) δ 9.70 (s, 1H), 8.59 - 8.57 (m, 2H), 8.18 - 8.10 (m, 3H), 7.75 - 7.72 (m, 1H), 7.57 (d, *J* =3.6 Hz, 3H).

6-chloro-2-phenylquinazoline (4w)[8]



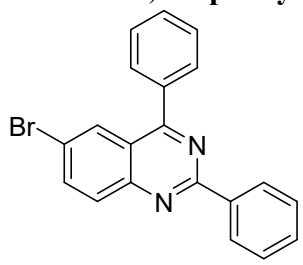
74% yield, white solid. **^{1}H NMR** (400 MHz, DMSO-d6) δ 9.68 (s, 1H), 8.56 (d, *J* =3.2 Hz, 2H), 8.30 (s, 1H), 8.09 - 8.02 (m, 2H), 7.59 (d, *J* =2.8 Hz, 3H).

6-chloro-2,4-diphenylquinazoline (4x)[1]



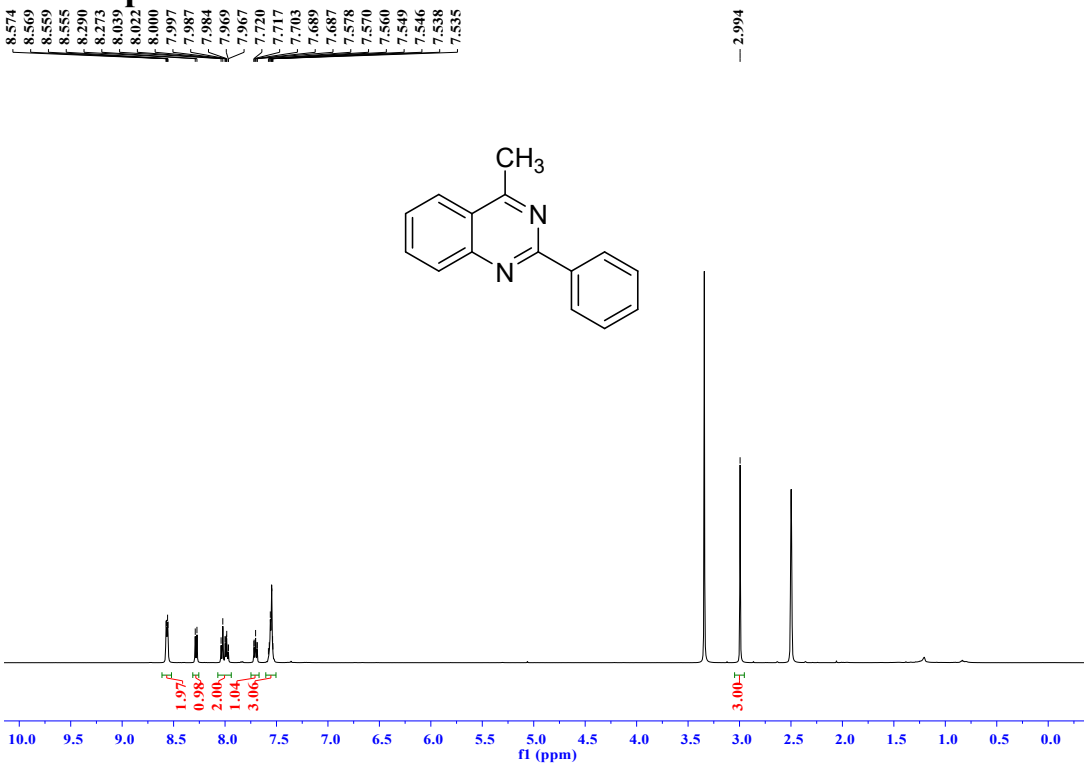
83% yield, white solid. **^{1}H NMR** (500 MHz, DMSO-d6) δ 8.60 - 8.58 (m, 2H), 8.17 (d, *J* =9.0 Hz, 1H), 8.07 - 8.05 (m, 1H), 8.01 (d, *J* =1.5 Hz, 1H), 7.91 - 7.90 (m, 2H), 7.69 - 7.68 (m, 3H), 7.59 - 7.58 (m, 3H).

6-bromo-2,4-diphenylquinazoline (4y)[1]

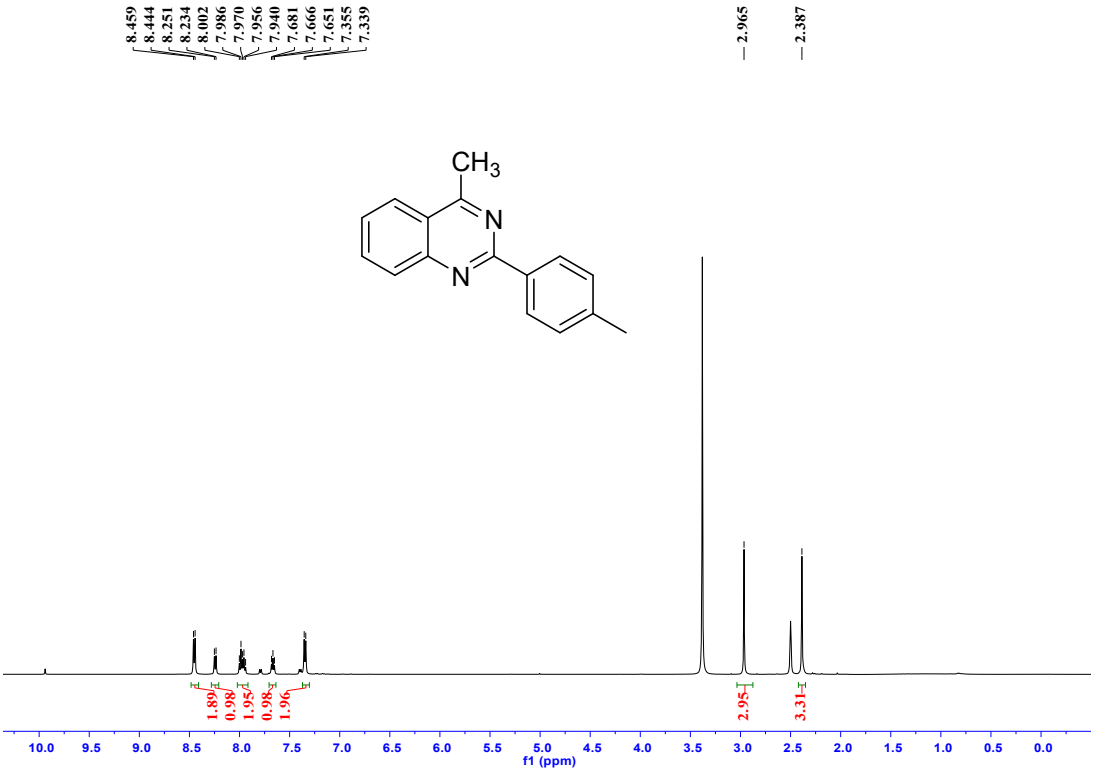


67% yield, yellow solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.71 (d, *J* =7.6 Hz, 2H), 8.30 (s, 1H), 8.06 (d, *J* =9.2 Hz, 1H), 7.98 (d, *J* =9.2 Hz, 1H), 7.90 (d, *J* =5.2 Hz, 2H), 7.67 - 7.65 (m, 3H), 7.56 (d, *J* =5.6 Hz, 3H).

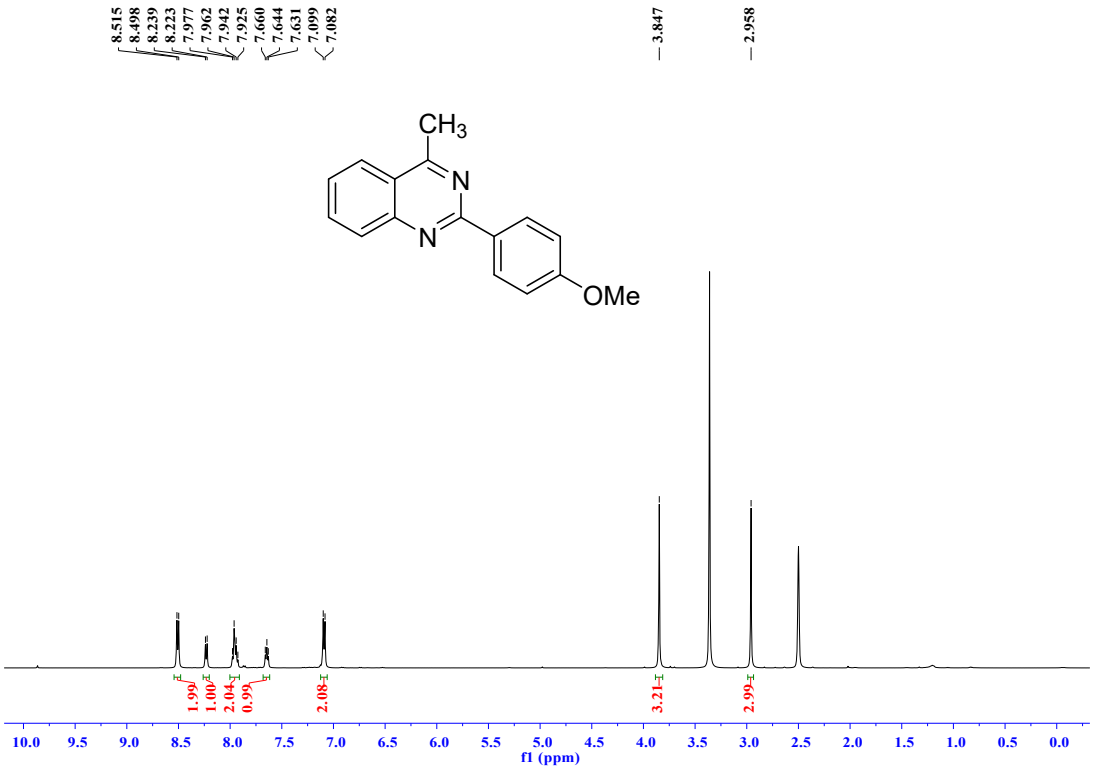
4. NMR Spectra of All Products



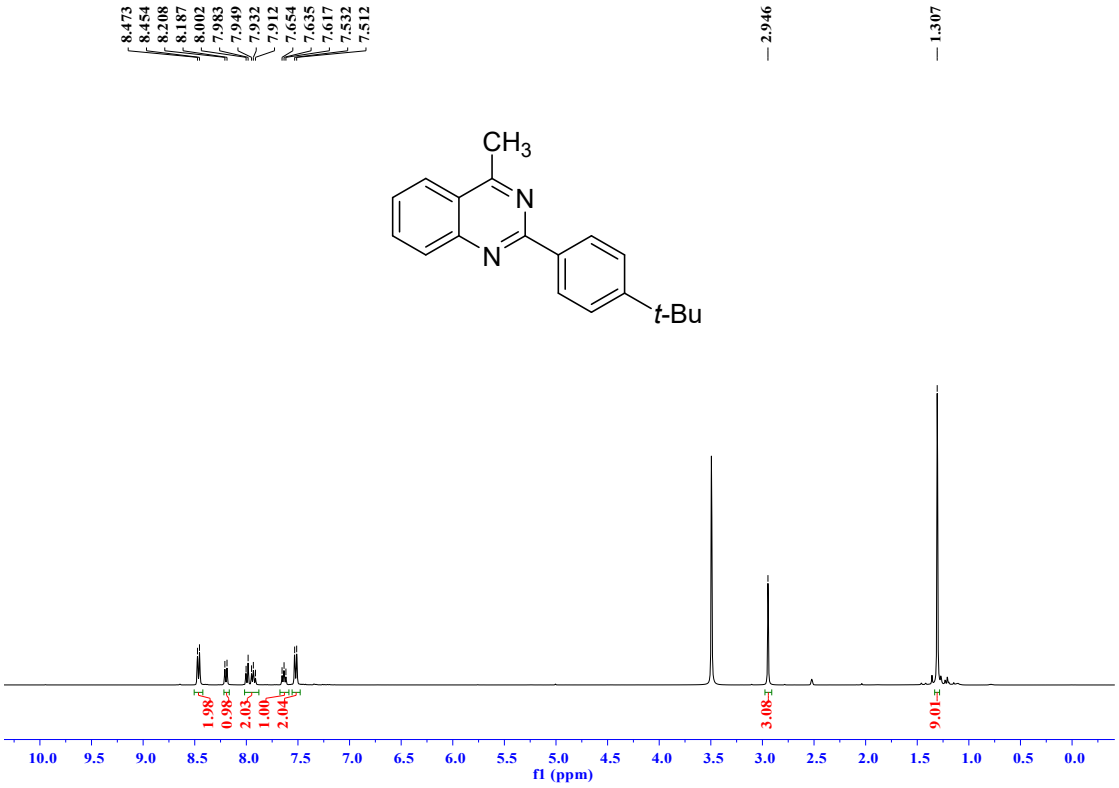
^{1}H of **4a**



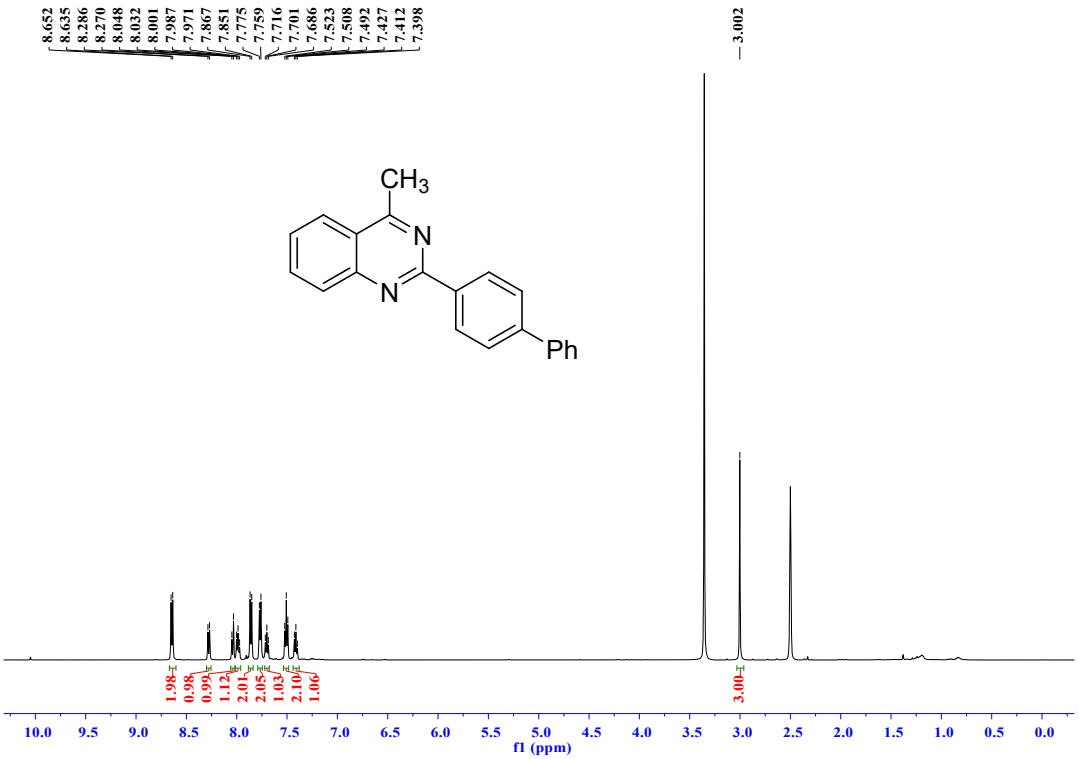
^{1}H of **4b**



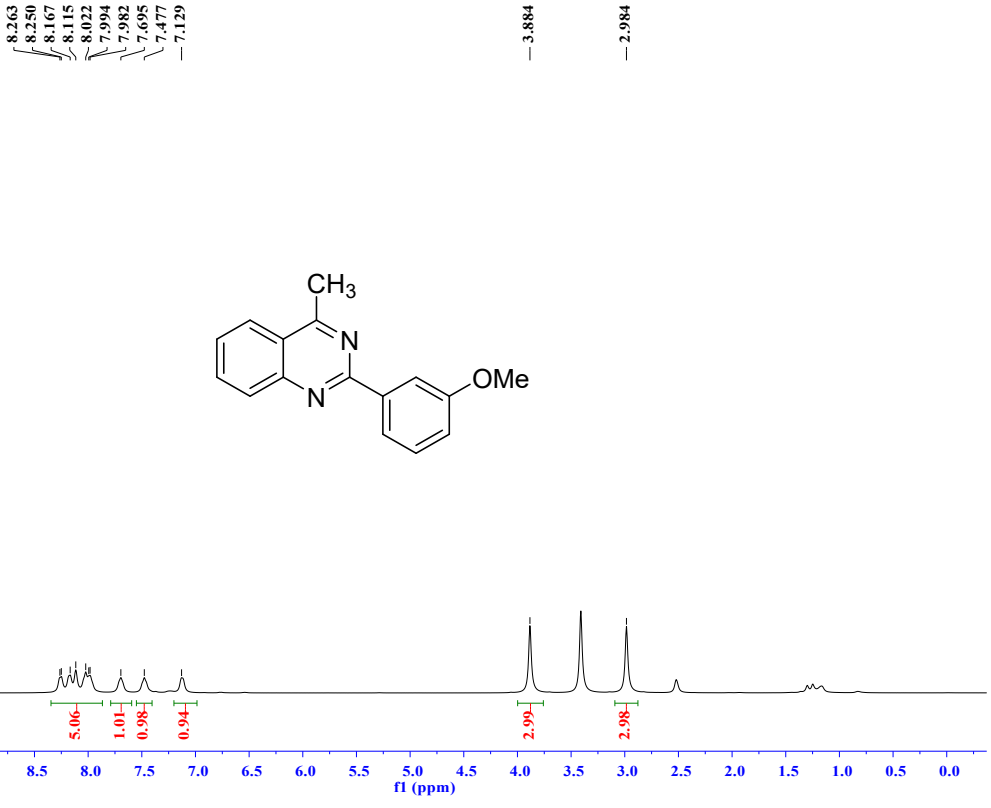
^{1}H of **4c**



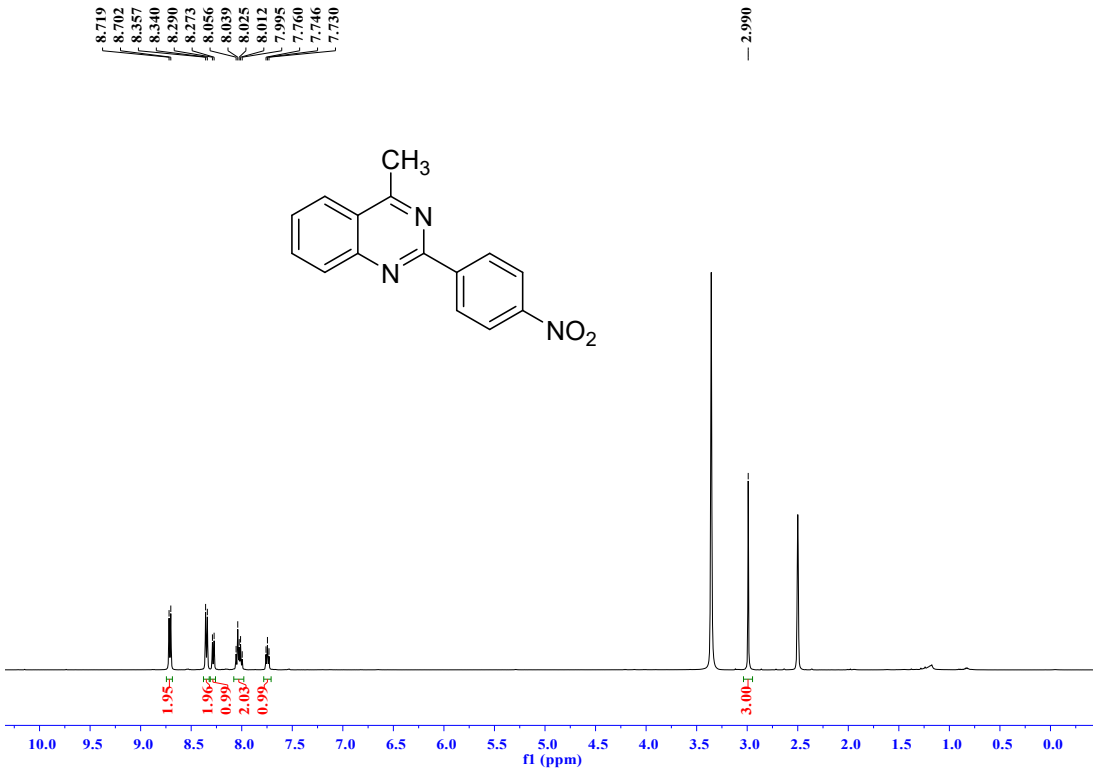
^{1}H of **4d**



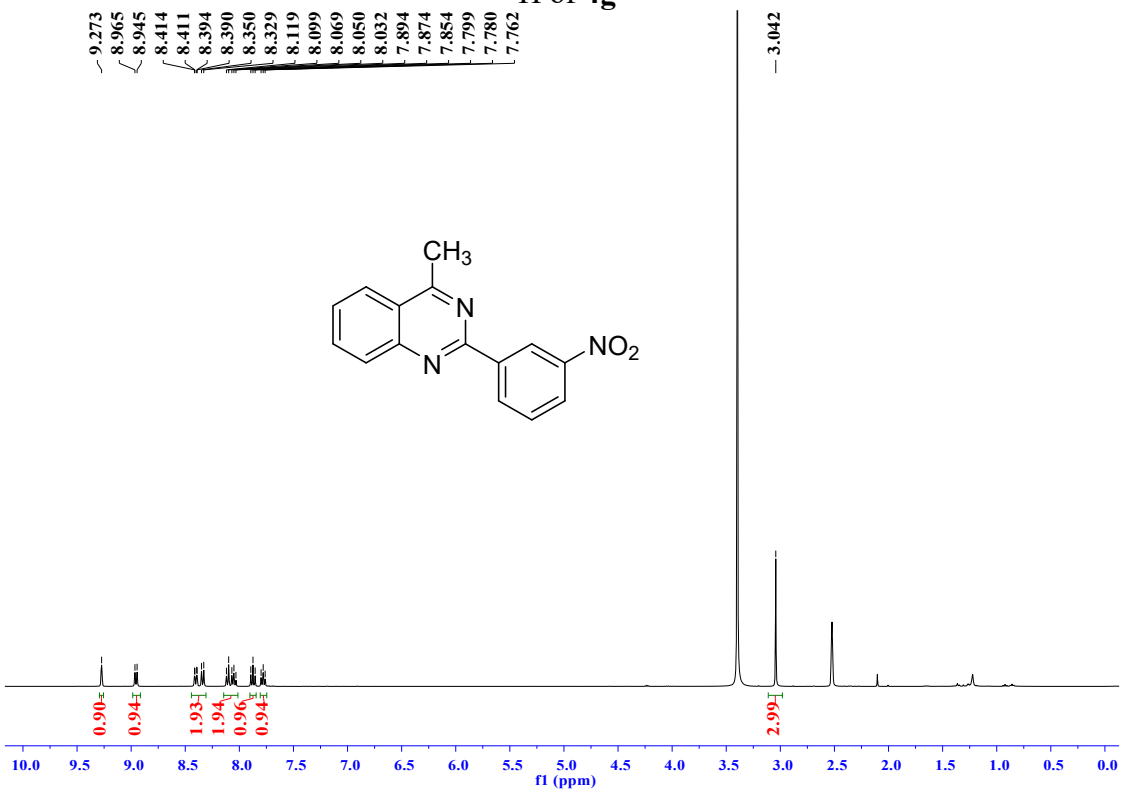
^{1}H of **4e**



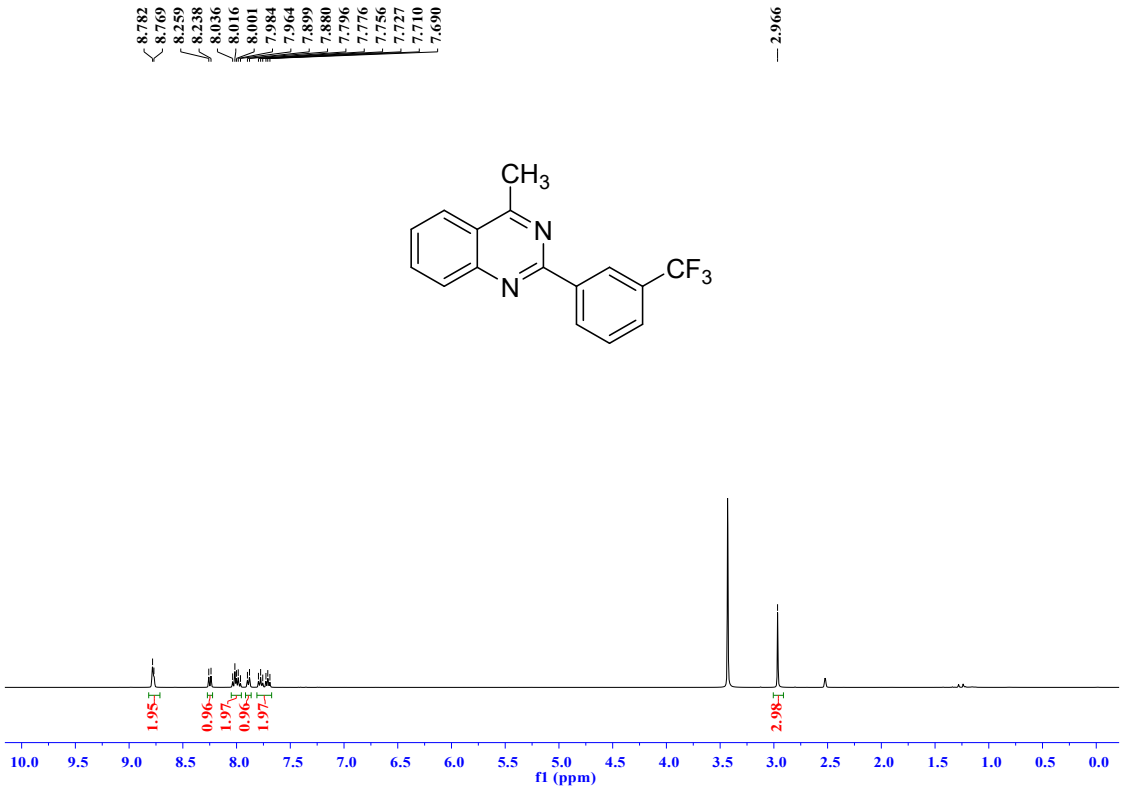
^{1}H of **4f**



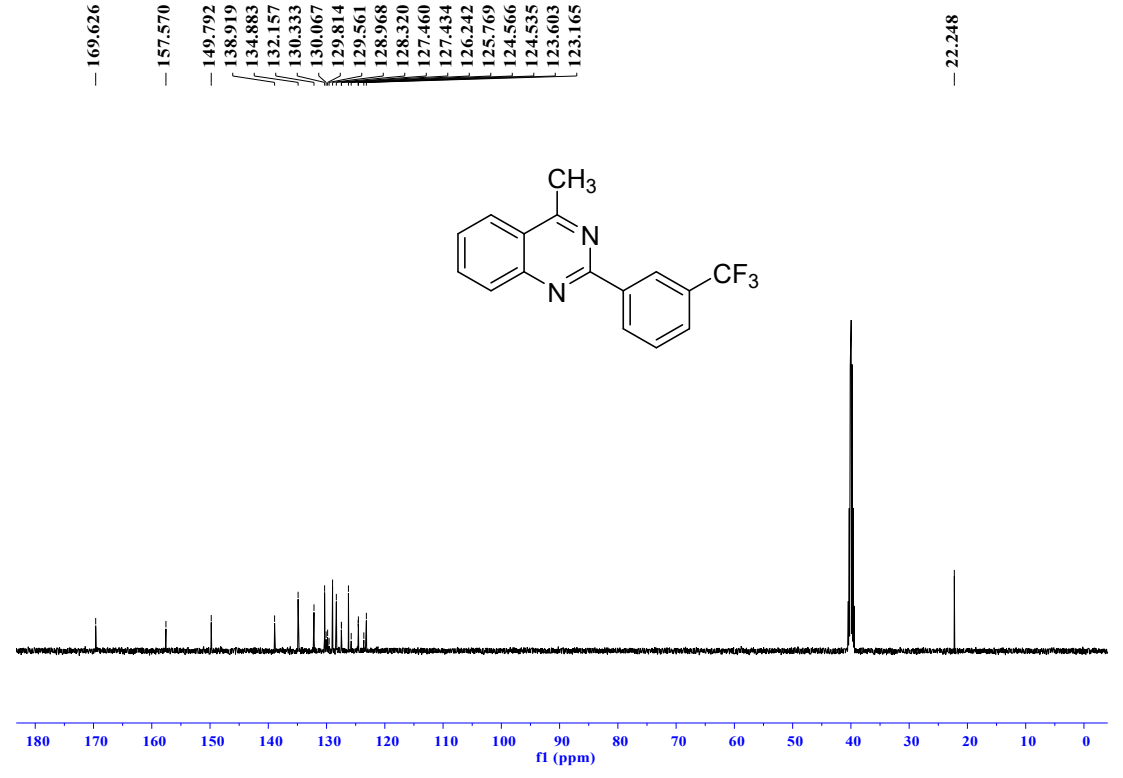
^{1}H of **4g**



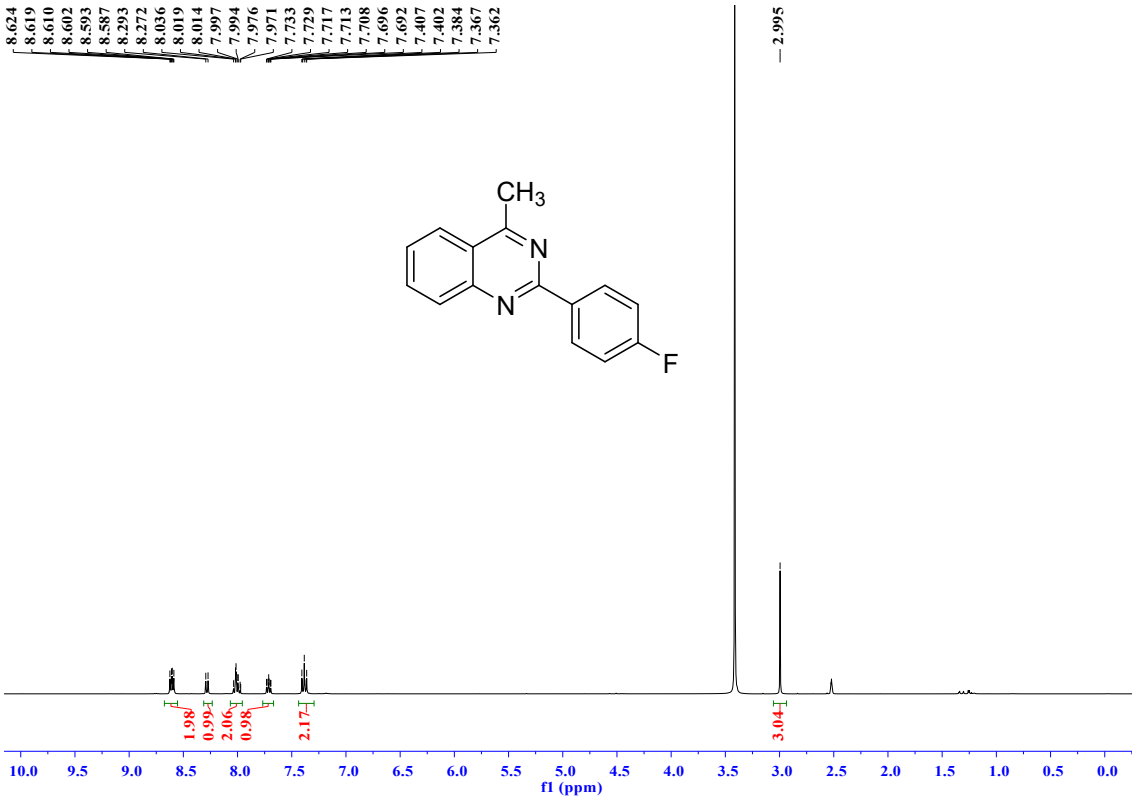
^{1}H of **4h**



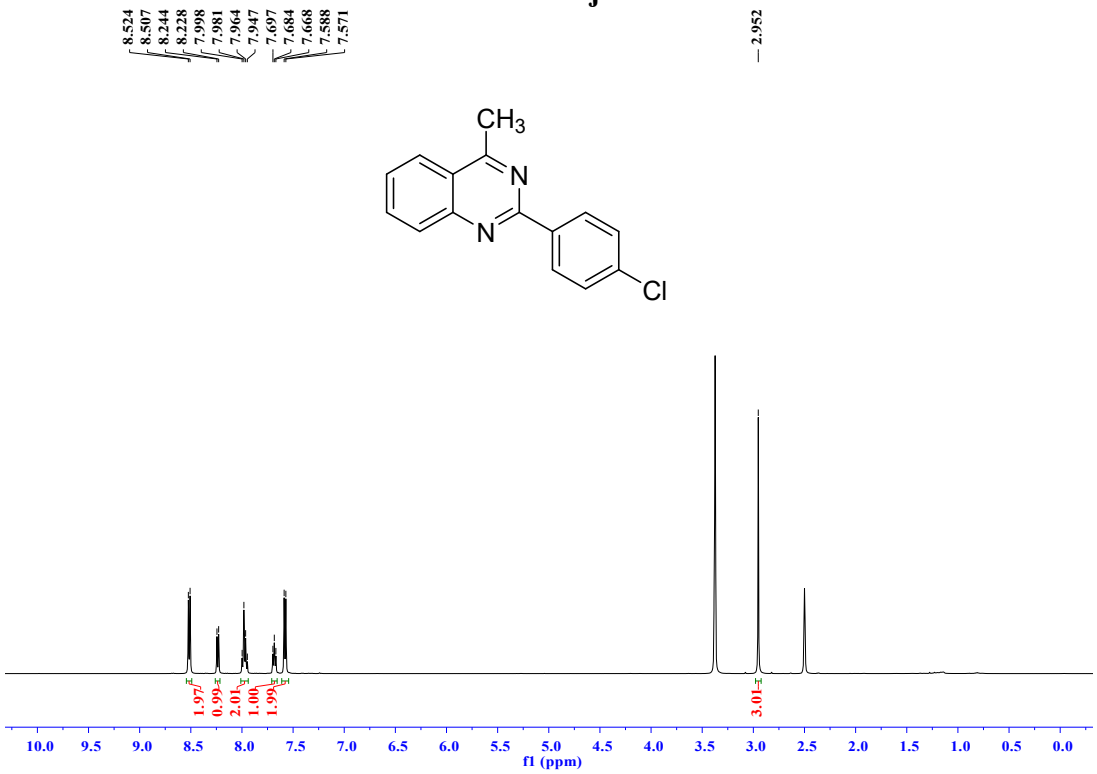
^{1}H of **4i**



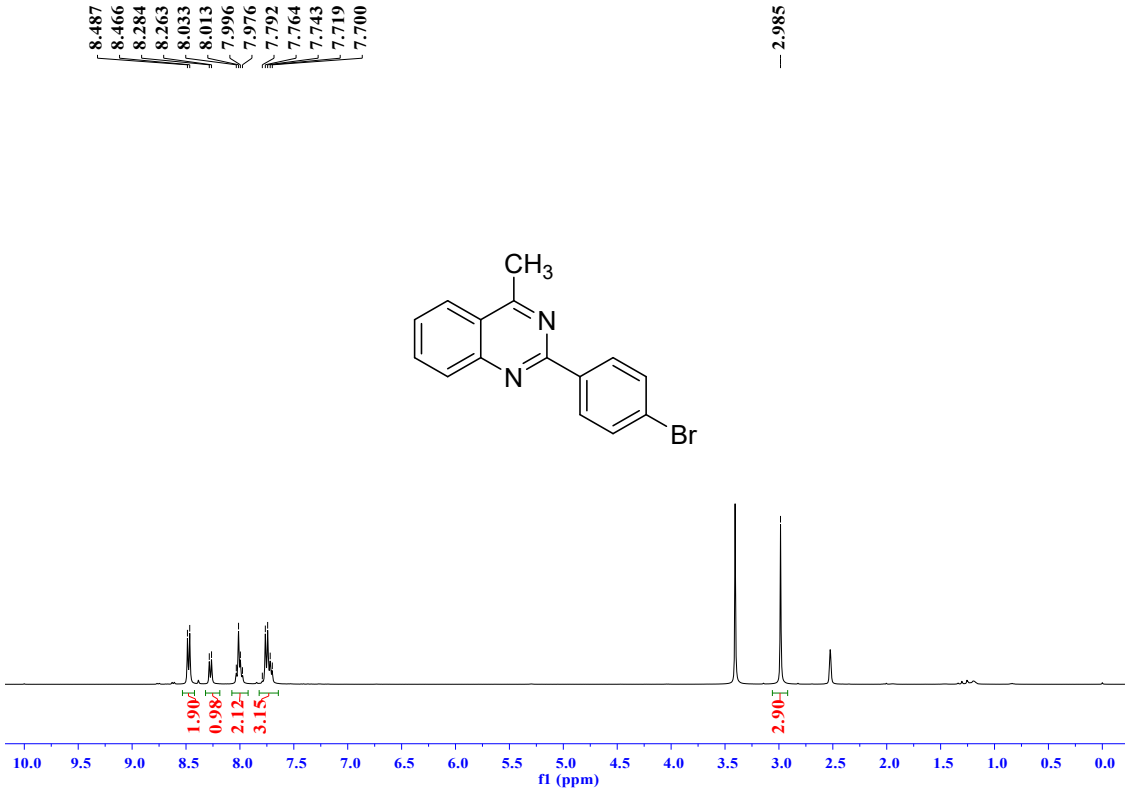
^{13}C of **4i**



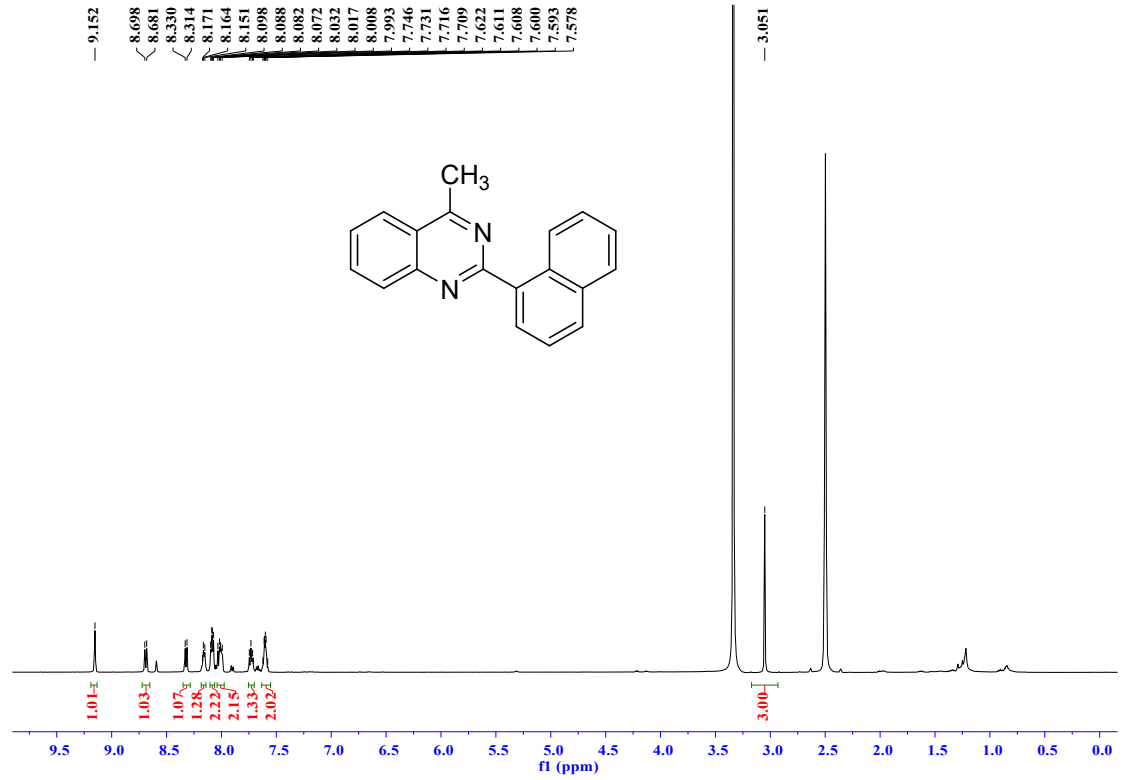
^{1}H of **4j**



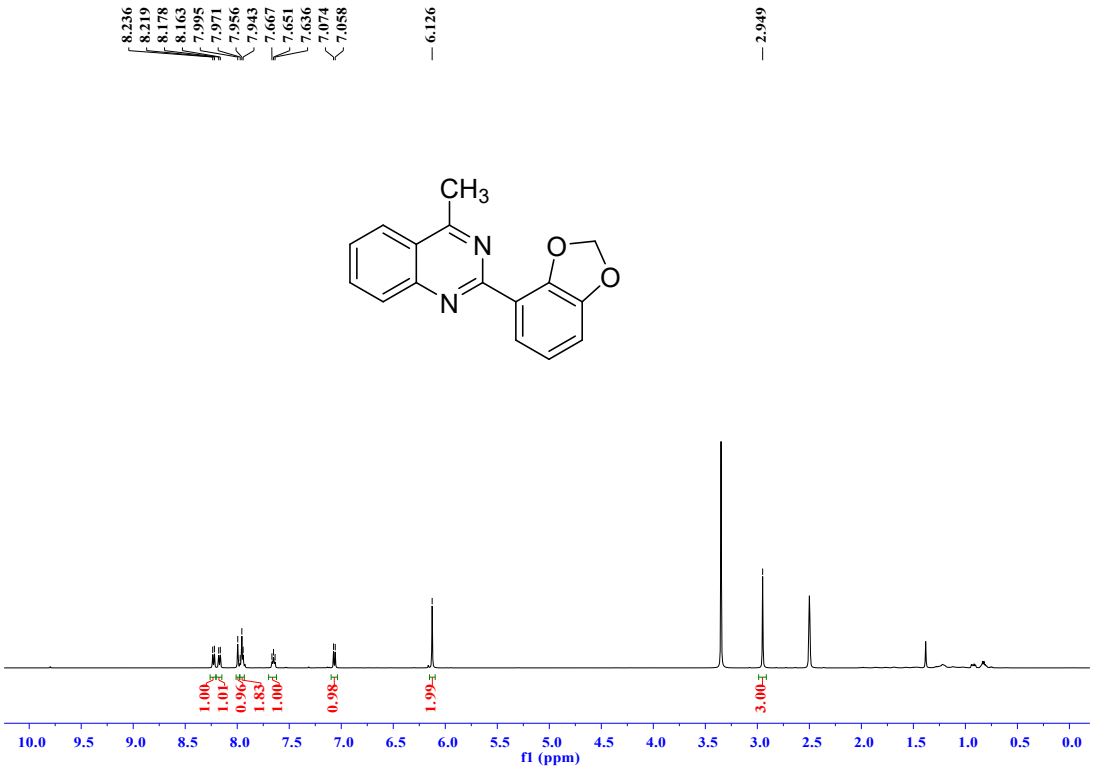
^{1}H of **4k**



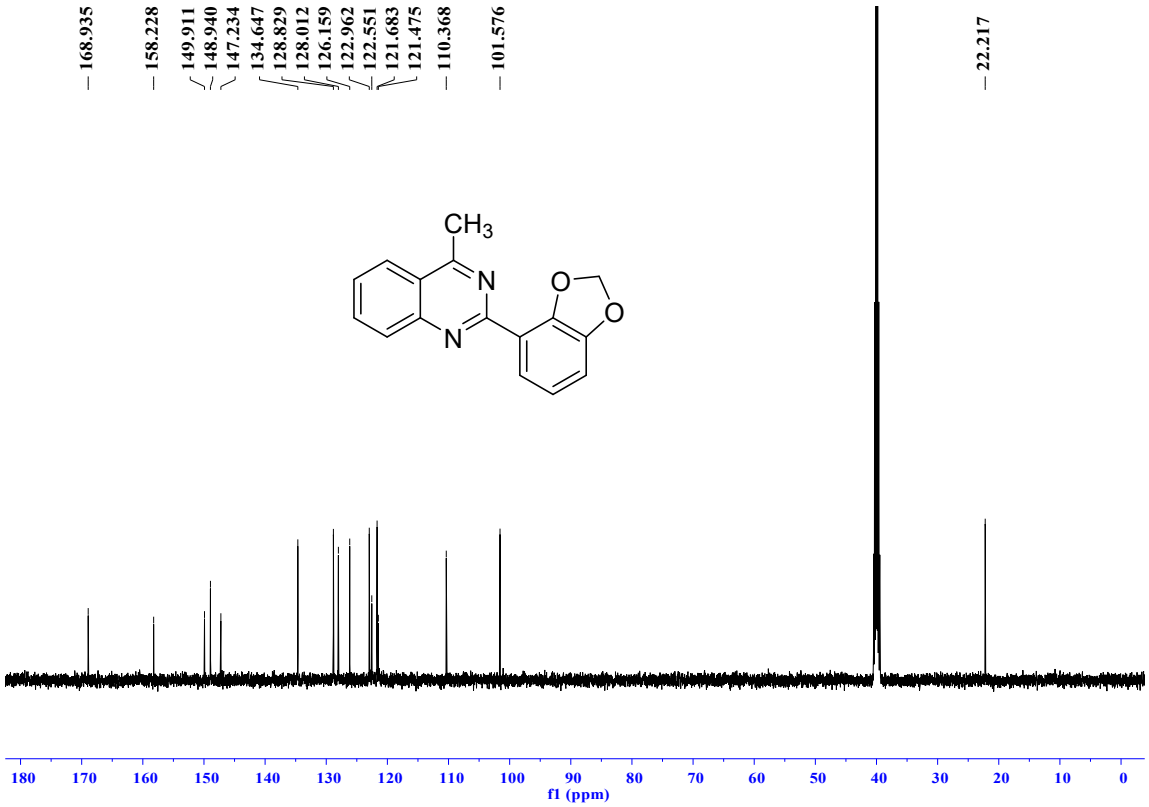
^{1}H of **4l**



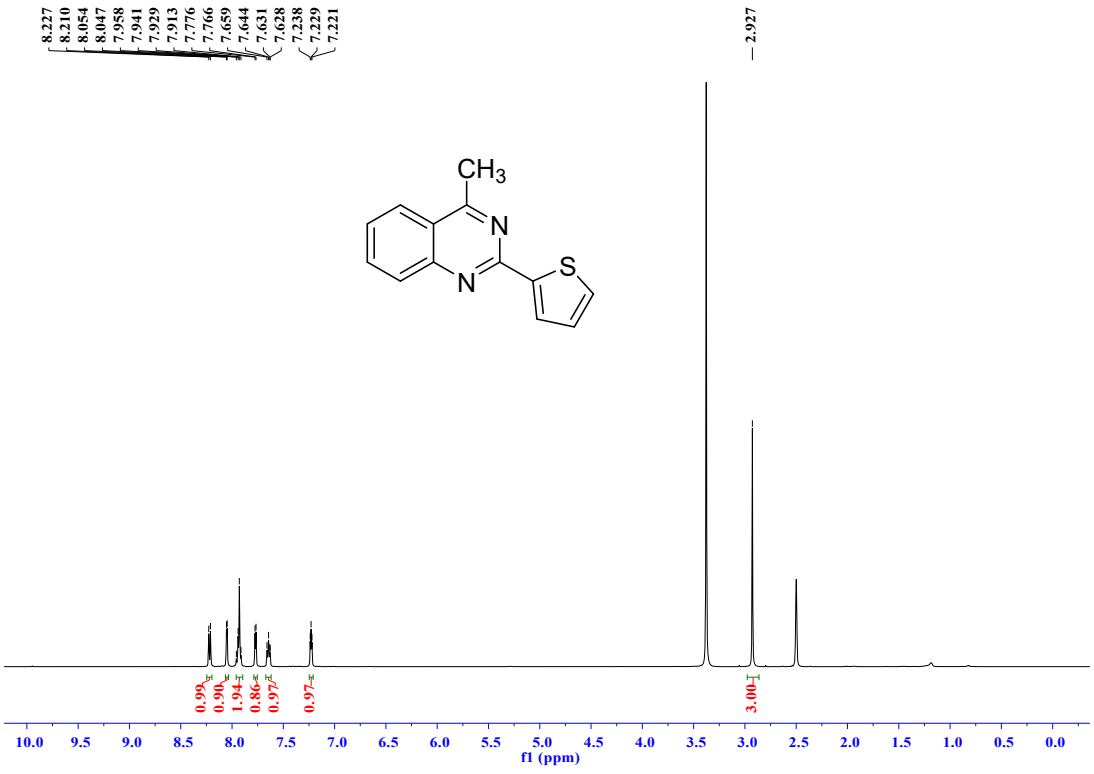
^{1}H of **4m**



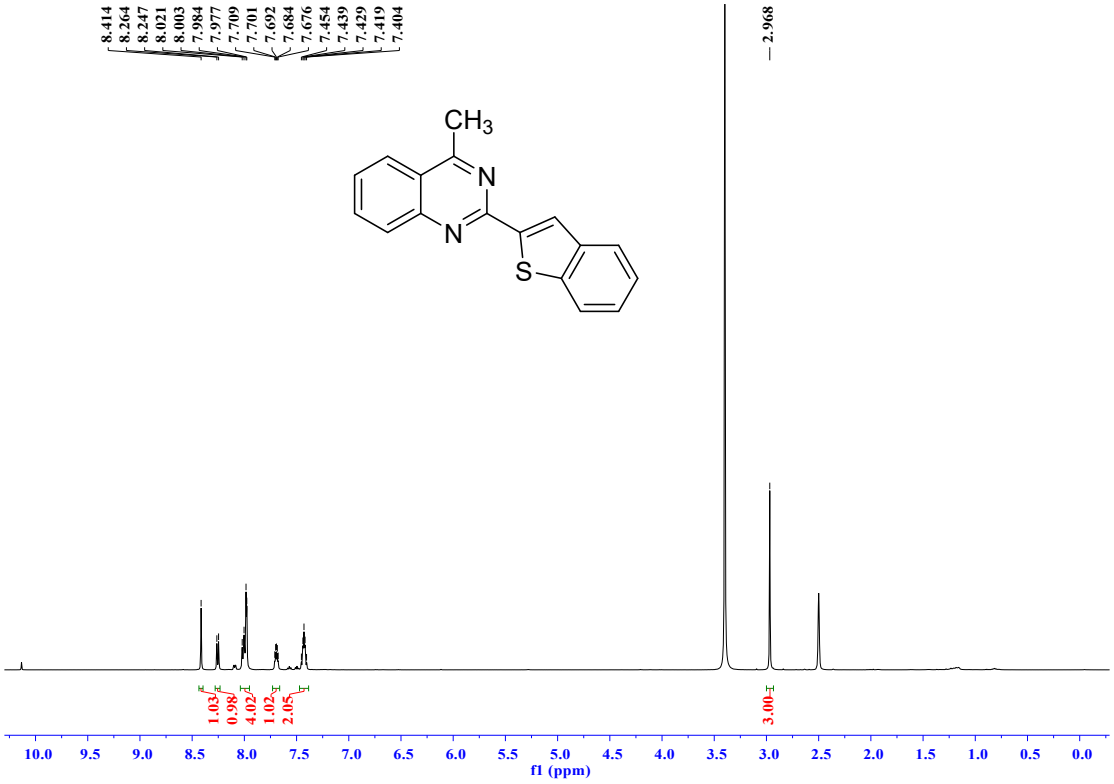
^{1}H of **4n**



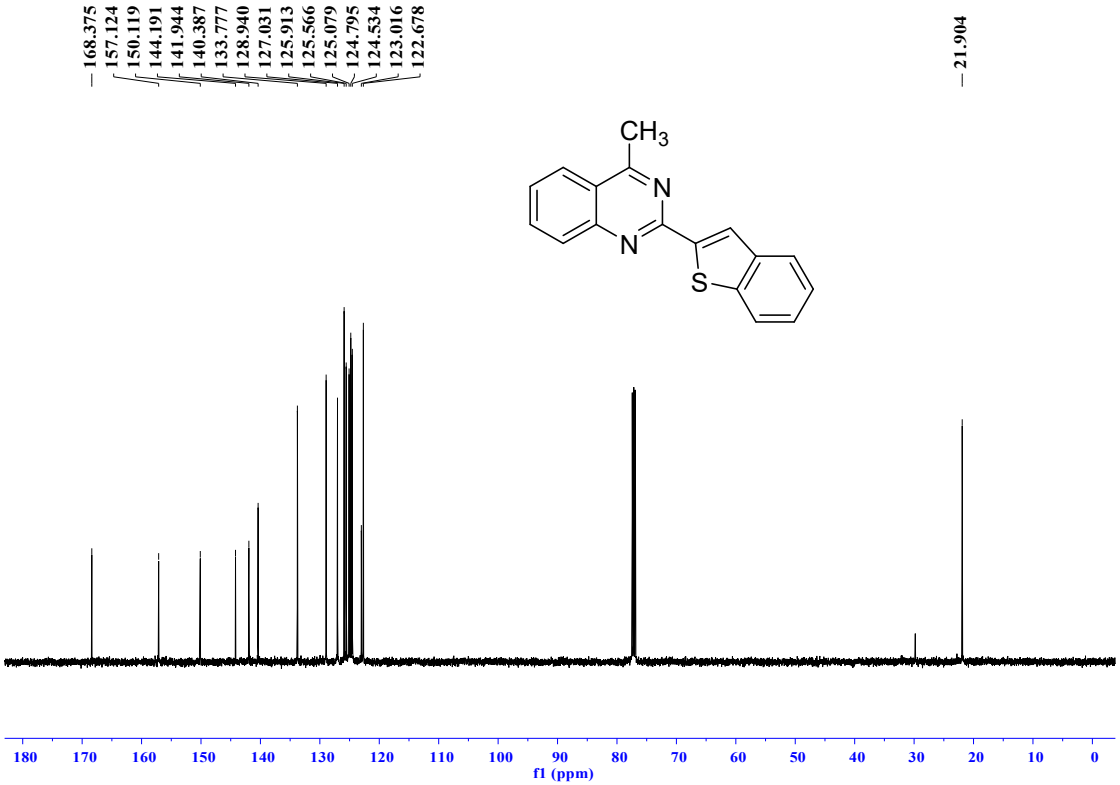
^{13}C of **4n**



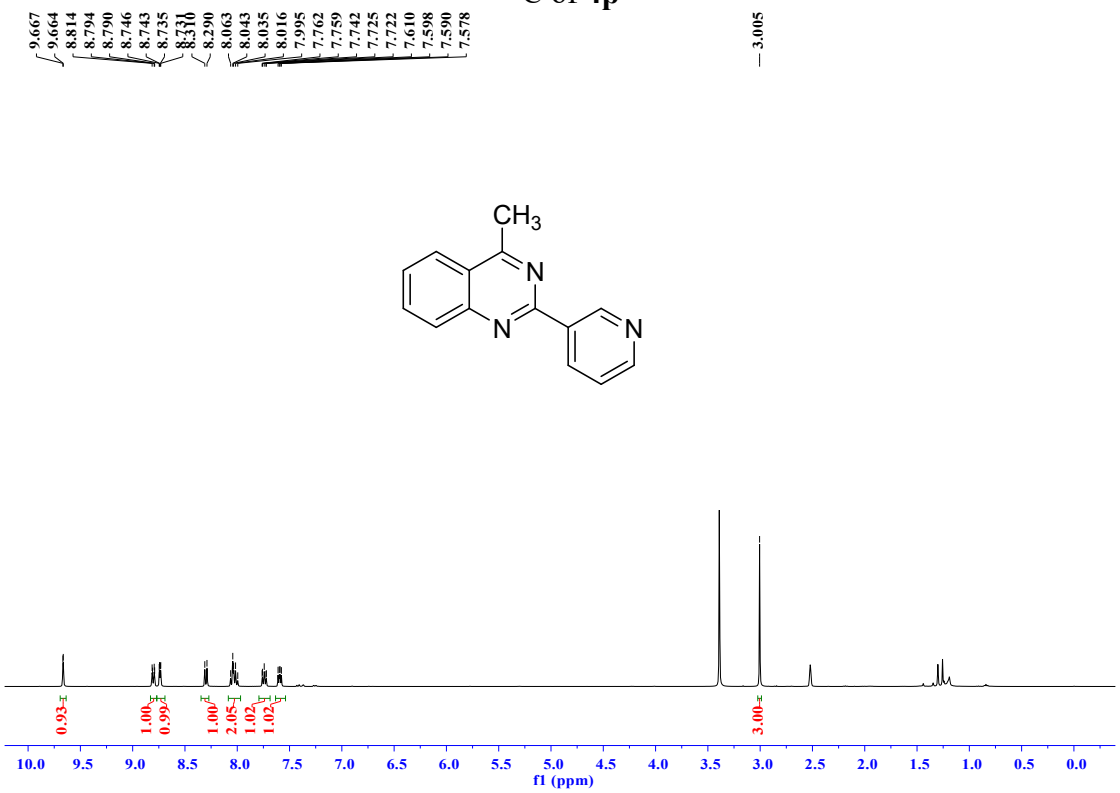
^{1}H of **4o**



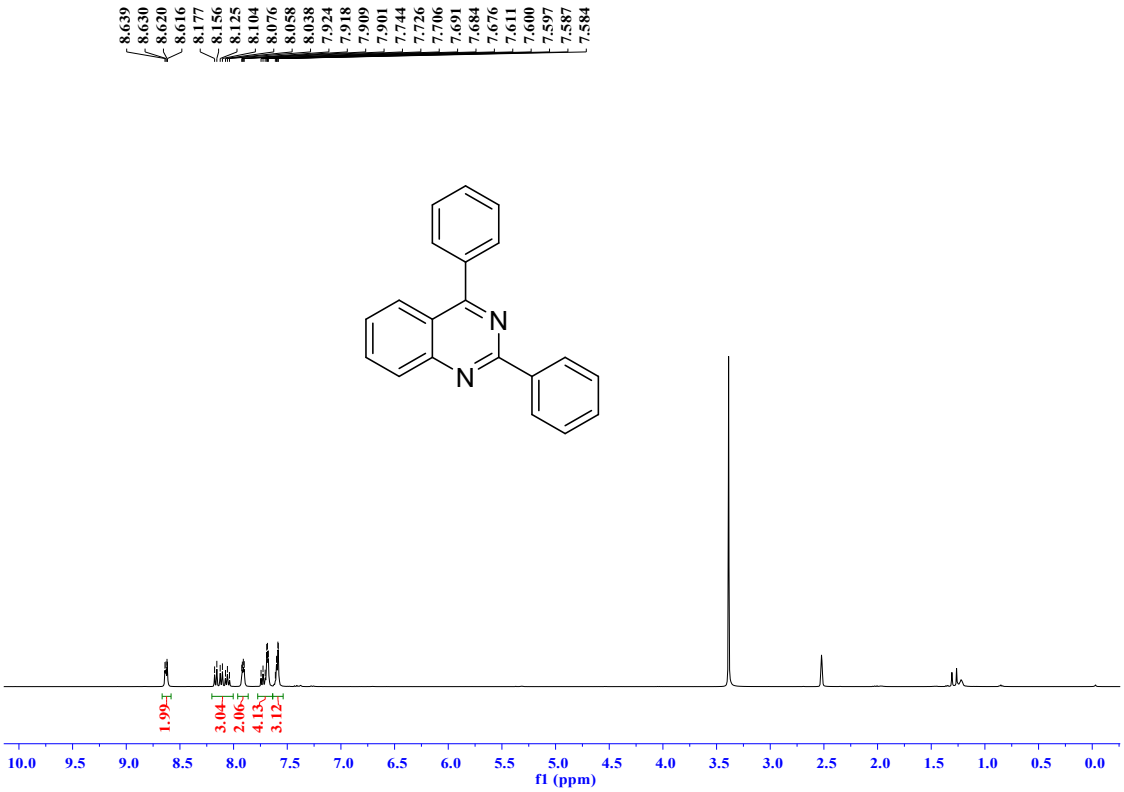
^{1}H of **4p**



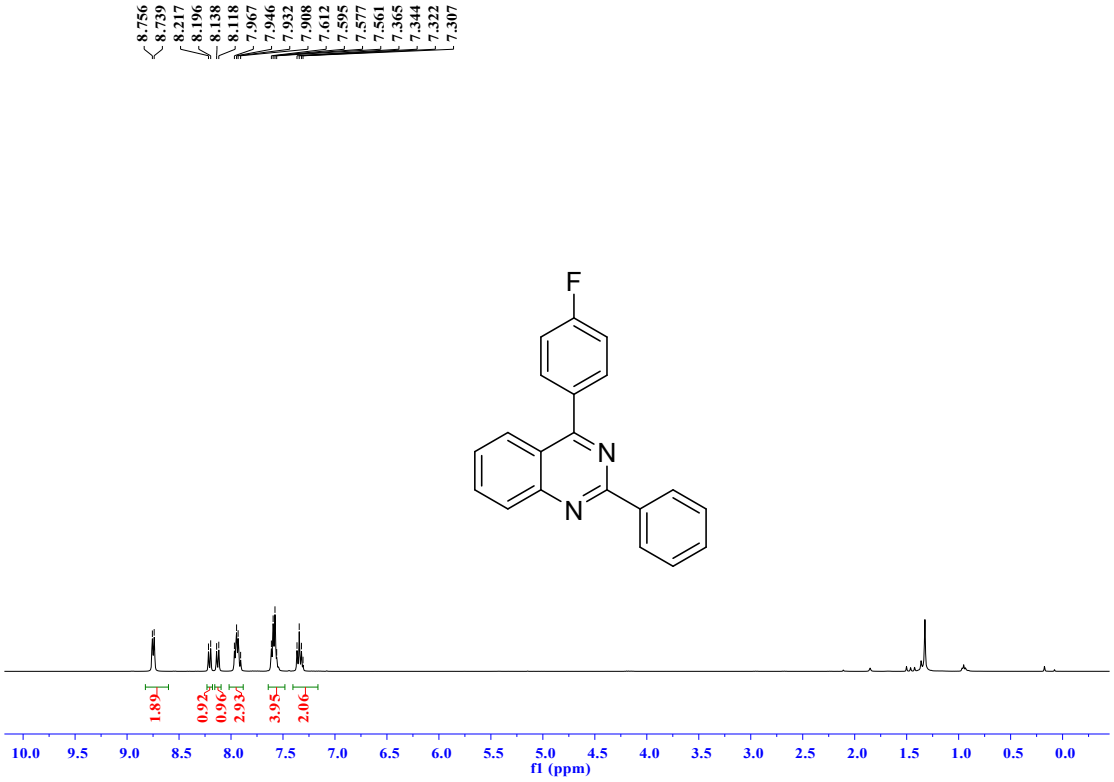
^{13}C of **4p**



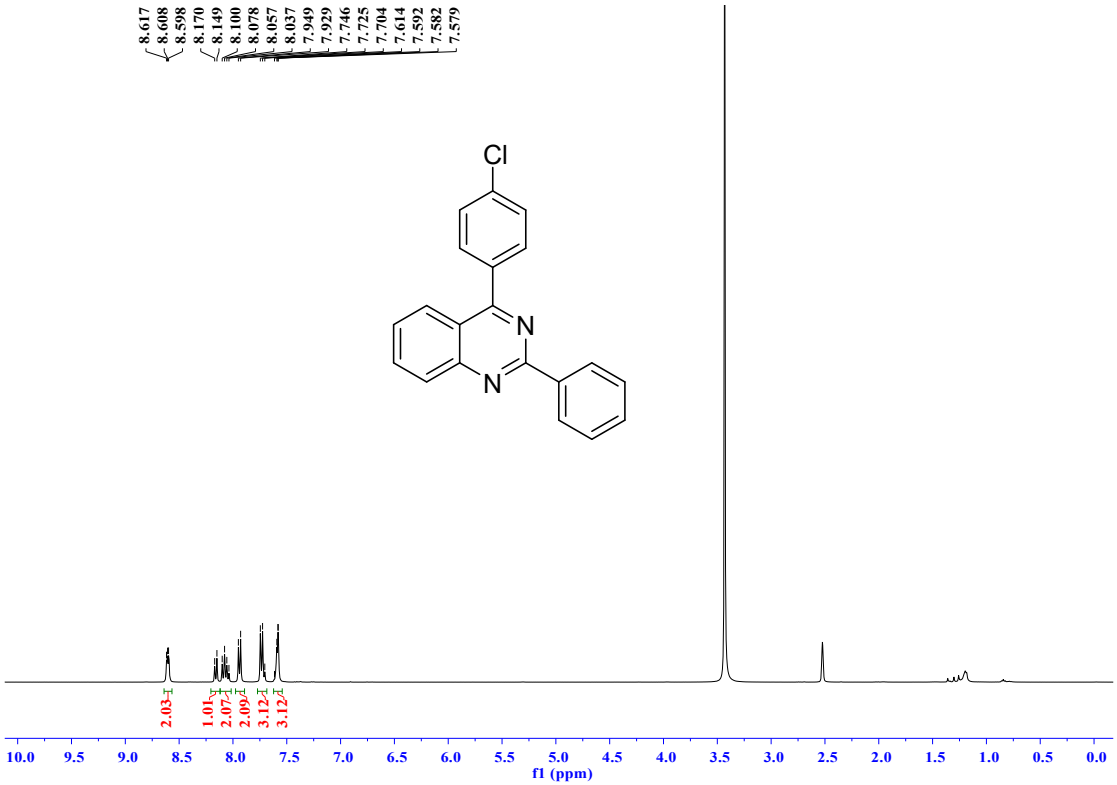
^{1}H of **4q**



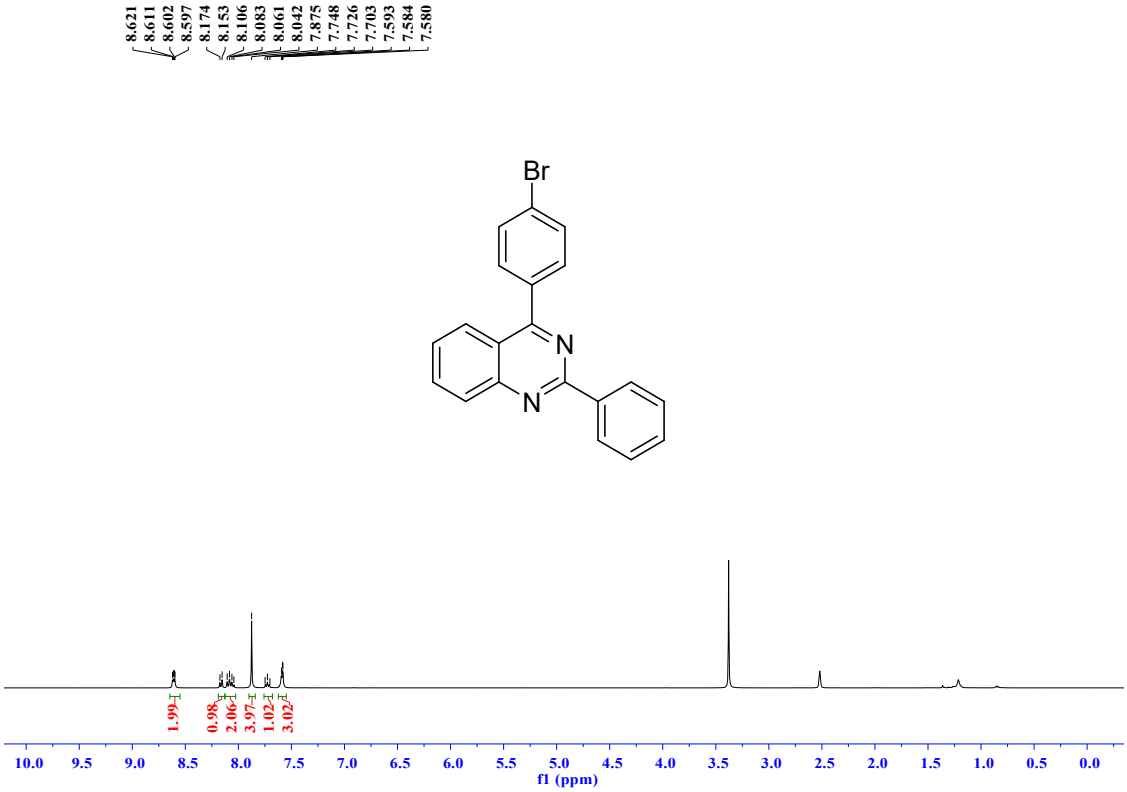
^{1}H of **4r**



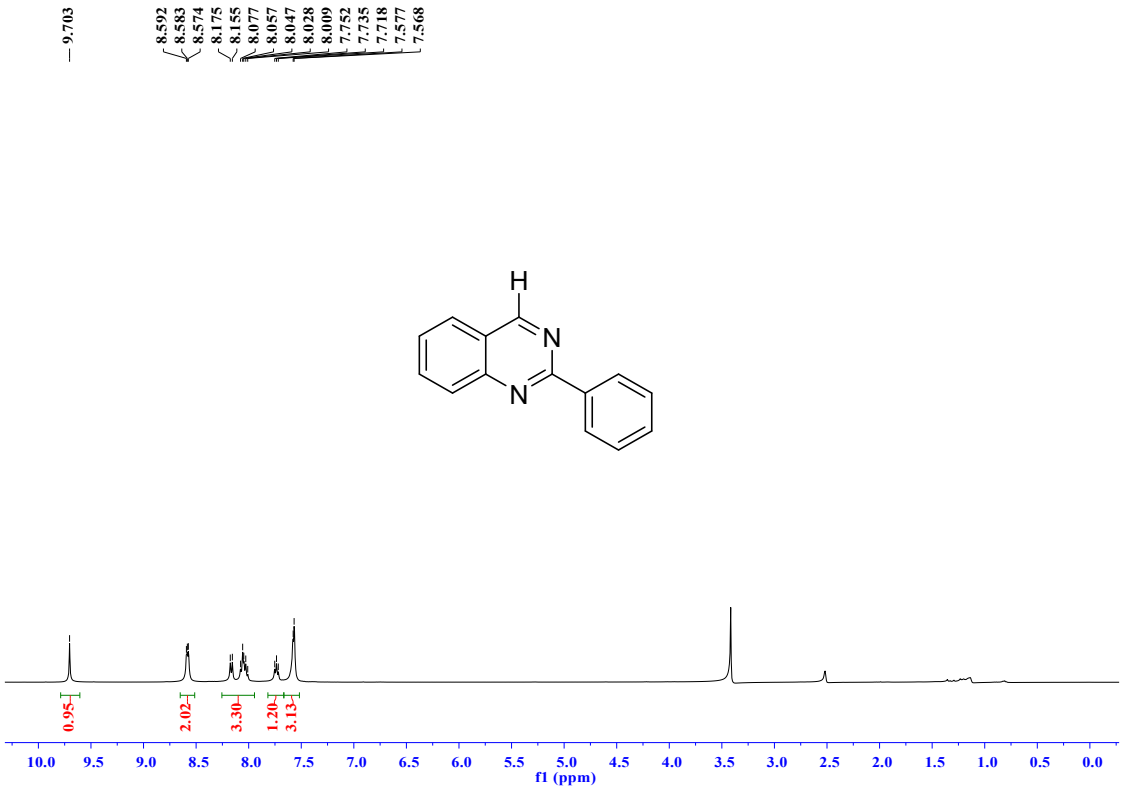
^{1}H of **4s**



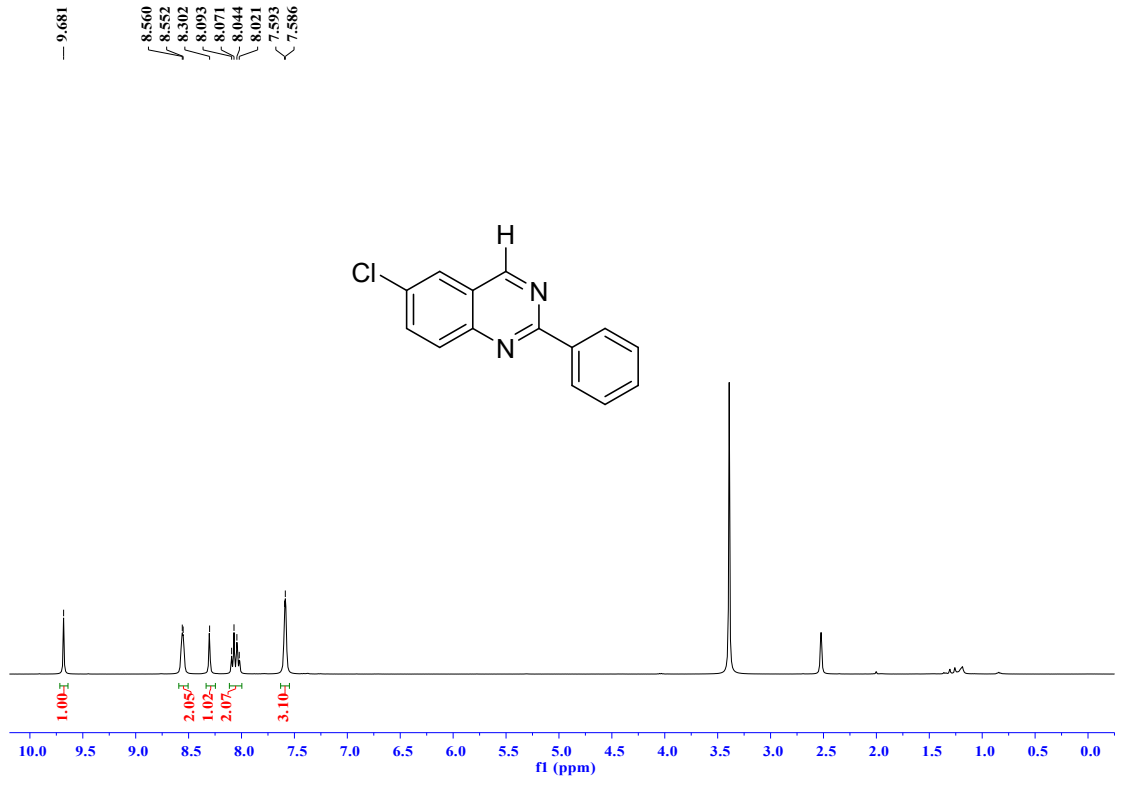
^{1}H of **4t**



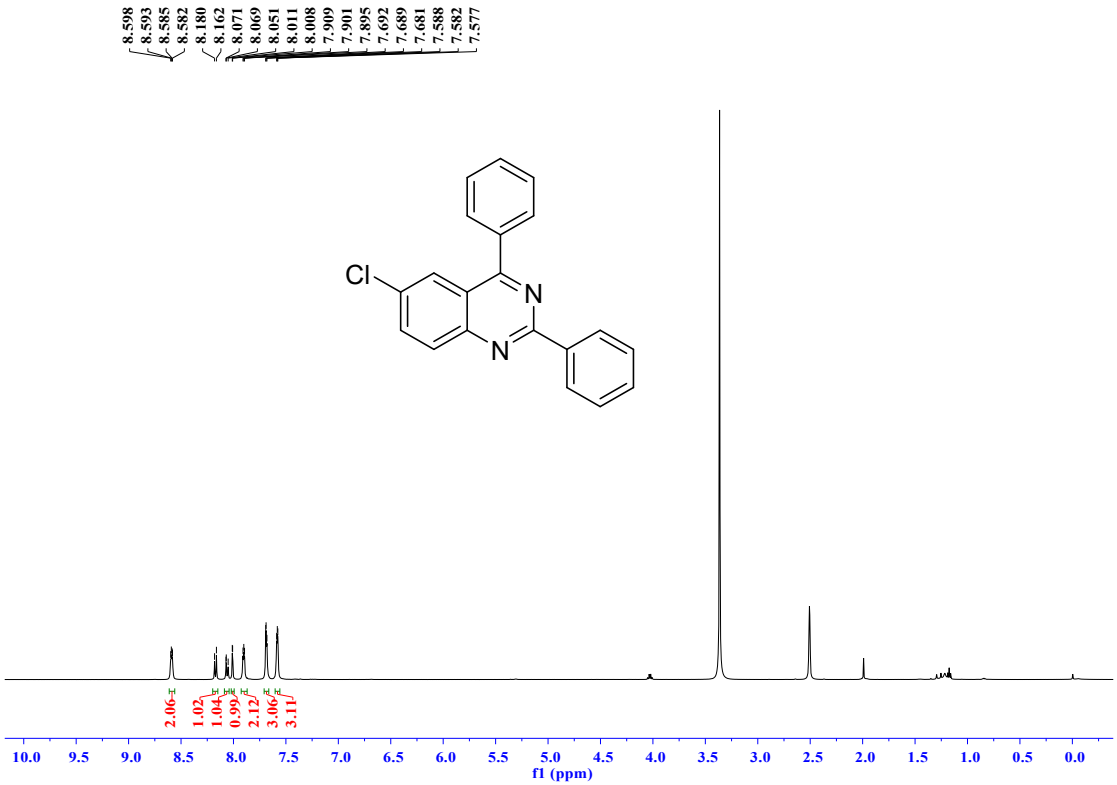
^{1}H of **4u**



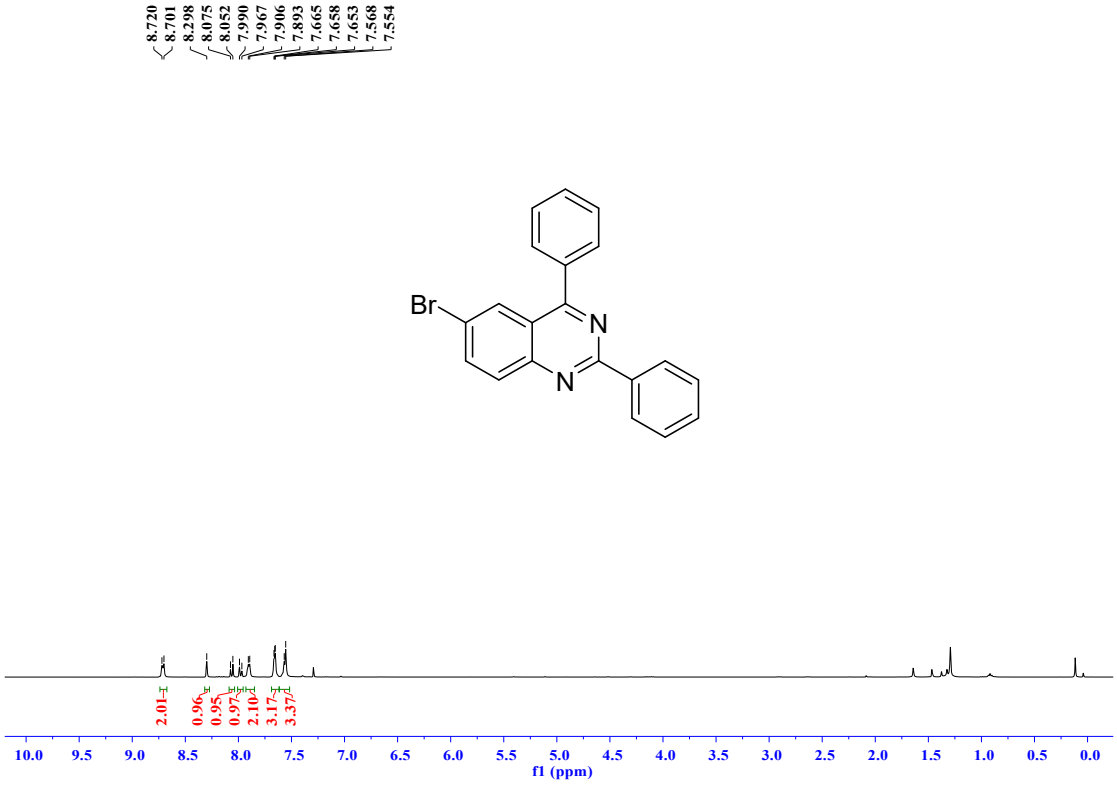
^{1}H of **4v**



^{1}H of **4w**



^{1}H of **4x**



^{1}H of **4y**

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