

Electronic Supplementary Information

A novel and efficient methodology for the construction of quinazolines based on supported copper oxide nanoparticles

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Contents

General information	2
General procedure for the preparation of SCONP-3	3
ICP Atomic Emission, TEM images, XRD and TPR of the catalysts	4
General procedure for the synthesis of quinazolines	7
Further optimizing for the reaction conditions	8
Structures of 3aa-3ra and 3ab-3ak	9
Synthesis of substances	10
Characterization data for the products	14
References	19
Crystallographic data	20
NMR spectra for the products	21

General information

Unless otherwise indicated, all compounds and reagents were purchased from commercial suppliers and used without further purification. XRD data were collected on Rigaku TTR-III. TEM images were measured on JEOL-2010. ICP Atomic Emission was analyzed on Perkin-Elmer Cooperation (USA) Optima 7300 DV. All chemical shifts (δ) are given in ppm. NMR spectra were recorded on Bruker AVANCE 300 NMR spectrometer or Bruker AVANCE III 400 NMR spectrometer. HRMS was recorded on a Micromass UK LTD GCT spectrometer. Melting points were determined on a Beijing Tech Instrument Co., LTD X-6 melting point apparatus and are uncorrected. The data collection for crystallographic analysis were performed on a Oxford Diffraction Gemini S Ultra CCD diffractometer equipped with mirror MoK α ($\lambda = 0.71073 \text{ \AA}$) radiation at room temperature. The structure was solved by direct methods and refined by full-matrix least-squares methods with SHELXL-97 programs.

General procedure for the preparation of SCONP-3

$\text{Cu}(\text{NO}_3)_2 \cdot 3\text{H}_2\text{O}$ (0.966 g, 4 mmol) was dissolved in 50 mL of distilled water in the air and stirred with kaolin (2 g) for 2 hours, then the pH value of the solution was rapidly adjusted to 10 with Na_2CO_3 solution (1 M). The resultant solution was then aged together with mother liquor at room temperature for 12 h. The final product was collected by filtration, washed with deionized water, dried at 60 °C for 24 h, and then calcined at 350 °C for 4 h.

SCONP-1/-2/-4/-5 were synthesized according to the same procedure for **SCONP-3**. (**SCONP-5** was calcined in a flow of N_2)

ICP Atomic Emission, TEM images, XRD and TPR of the catalysts

ICP Atomic Emission

Cu% of fresh SCONP-1 = 8.41%,

Cu% of fresh SCONP-4 = 11.04%,

Cu% of fresh SCONP-2 = 11.83%,

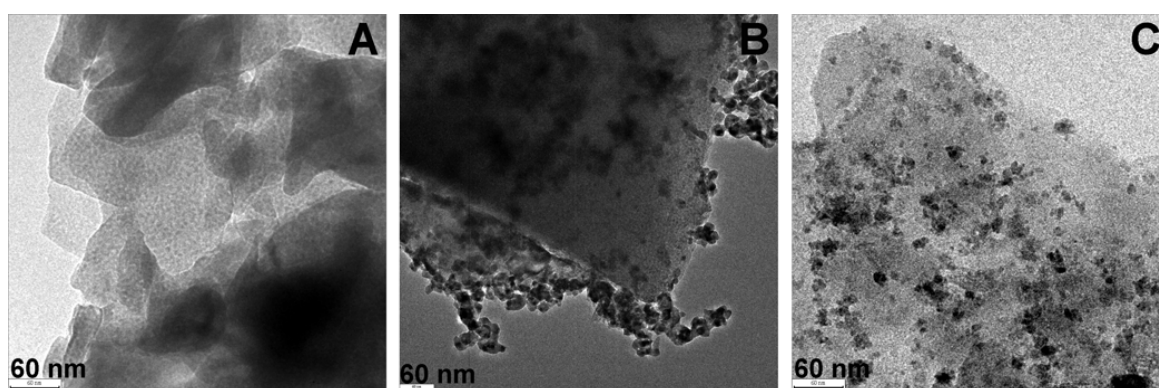
Cu% of fresh SCONP-5 = 5.9%,

Cu% of fresh SCONP-3 = 8.71%,

Cu% of kaolin < 0.01%.

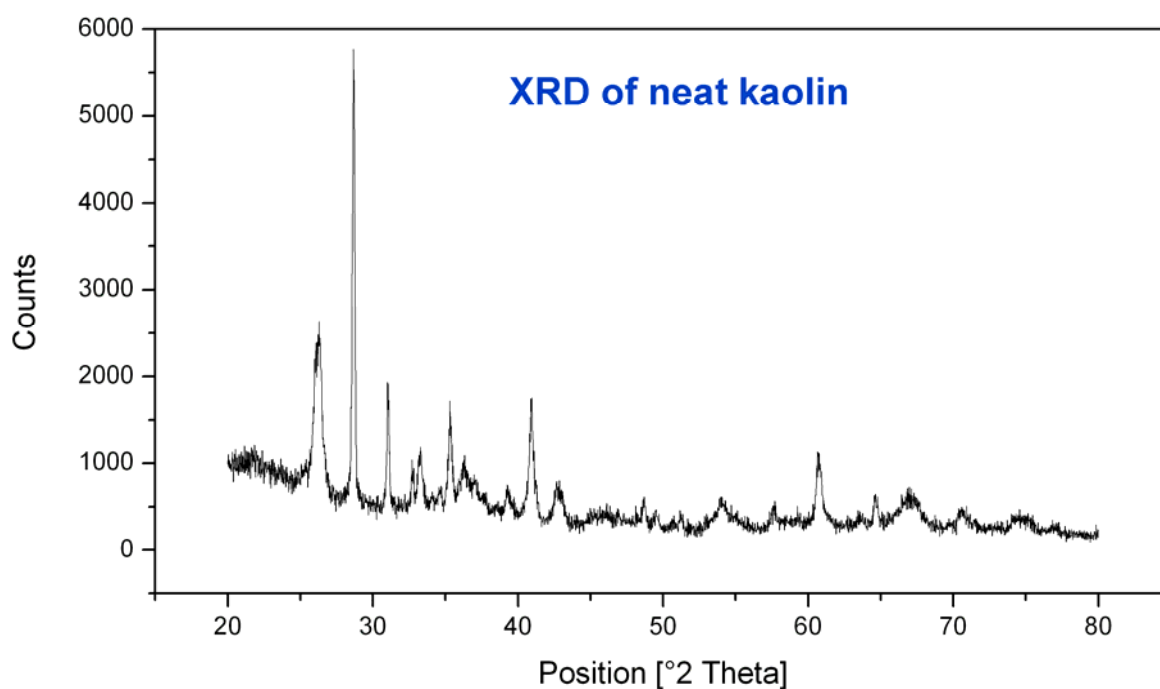
Cu% of SCONP-3 after forth use = 0.15%,

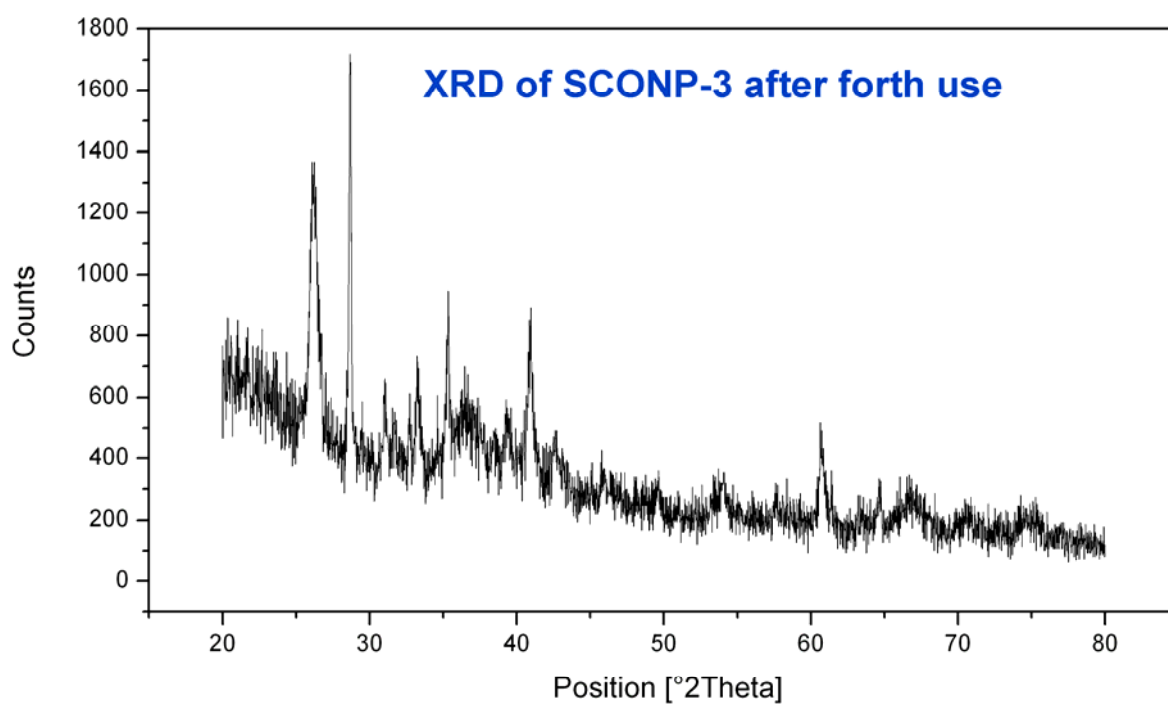
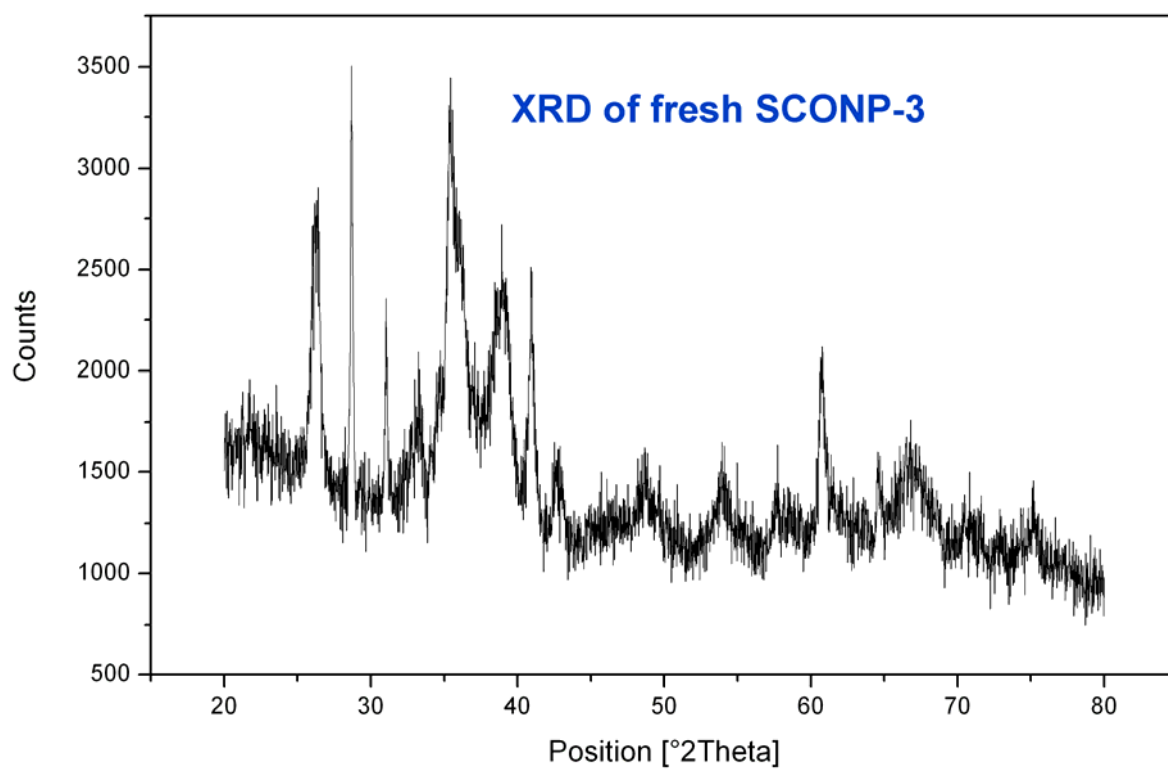
TEM of kaolin, fresh SCONP-3 and SCONP-3 after forth use



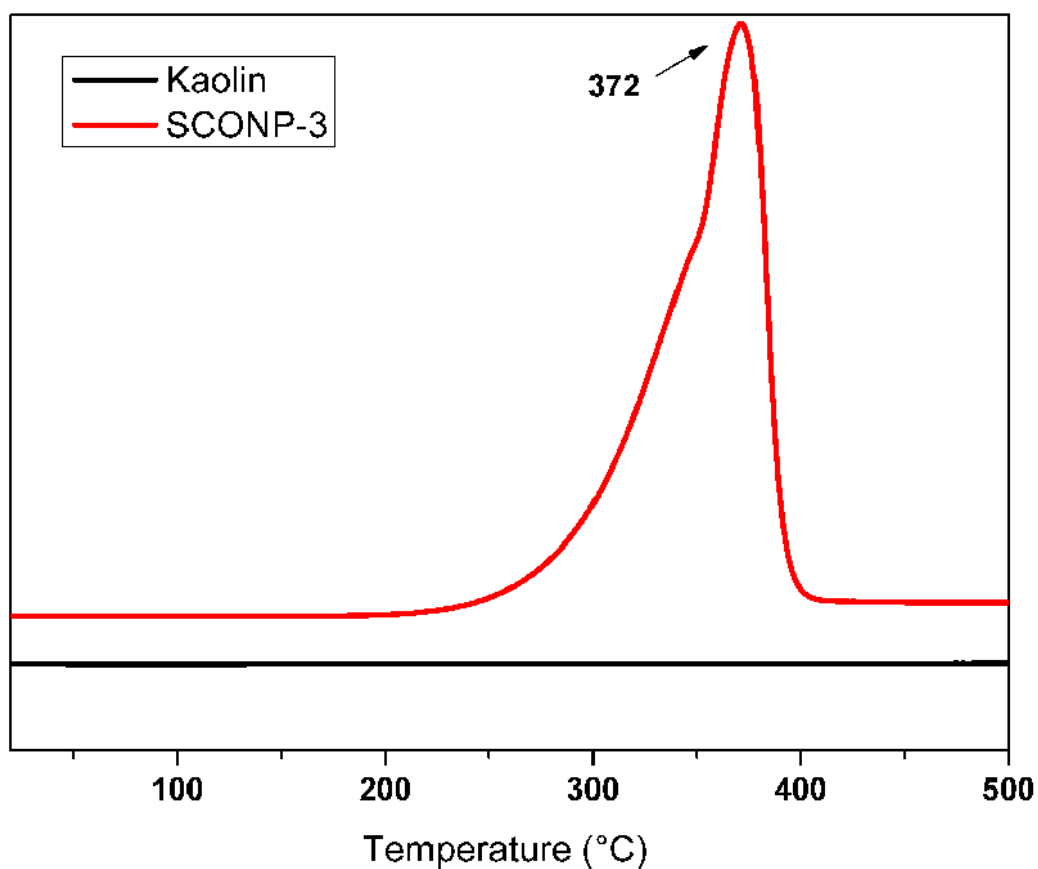
TEM of A: kaolin; B: SCONP-3; C: SCONP-3 after forth use.

XRD of kaolin, fresh SCONP-3 and SCONP-3 after forth use





TPR of SCONP-3 and kaolin



The reduction behaviors of SCONP-3 or kaolin were measured by temperature-programmed reduction (TPR) techniques, including H₂-TPR. 50 mg catalyst was placed in a quartz reactor and heated at a rate of 10 °C/min. In the H₂-TPR, 5% H₂ balanced with Ar was fed at a flow rate of 20 ml/min and the consumption of H₂ was measured by a thermal conductivity detector (TCD).

General procedure for the synthesis of quinazolines

1a (39.4 mg, 0.2 mmol), **2a** (33 μ L, 0.3 mmol), SCONP-3 (5 mg, 3.4 mol %) and TBHP (57 μ L of 70 % aqueous solution, 0.4 mmol) were placed in a tube (10 mL) and sealed with a balloon. After heating at 90 °C for 12 hours, the reaction was worked up and purified by column chromatography over silica gel, affording **3aa** (50.7 mg, 90 % yield).

Further optimizing for the reaction conditions

Table ESI-1 Further optimizing for the reaction conditions ^a

Reaction scheme: 2-aminobenzophenone (**1a**) + benzylamine (**2a**) $\xrightarrow[90\text{ }^{\circ}\text{C, 3 h}]{\text{SCONP-3}}$ 2,3-diphenylquinoxaline (**3aa**)

Entry	SCONP-3 (CuO mol%)	BnNH ₂ (equiv.)	TBHP (equiv.)	Yield (%) ^b
1	6.8	2	2	66
2	6.8	2	- ^c	0
3 ^d	6.8	2	2	14
4 ^e	6.8	2	2	29
5 ^f	6.8	2	2	49
6 ^g	6.8	2	2	17
7 ^h	6.8	2	2	53
8 ⁱ	6.8	2	2	67
9	6.8	1	2	51
10	6.8	1.5	2	76
11	6.8	2.5	2	33
12	6.8	1.5	1	19
13	6.8	1.5	1.5	57
14	6.8	1.5	3	77
15	3.4	1.5	2	76
16	1.7	1.5	2	61
17 ^j	3.4	1.5	2	95

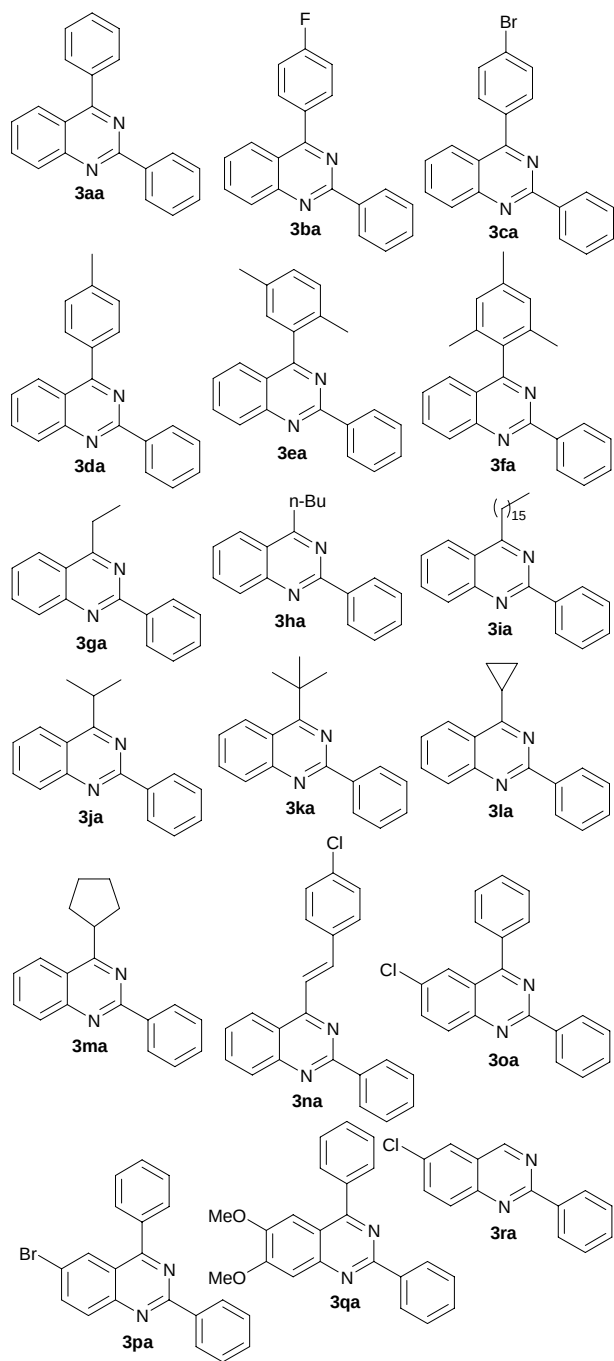
^a Reaction conditions: **1a** (0.2 mmol), **2a**, SCONP-3 and TBHP (70 % aqueous solution) were heated at 90 °C for 3 hours. ^b Determined by GC-MS with internal standard. ^c 2 equivalents of 30 % H₂O₂ solution was used as oxidant. 0.2 mL of solvent was added to the reaction: ^d H₂O; ^e MeCN; ^f Hexane; ^g DMSO. The reaction was carried at ^h 80 °C and ⁱ 100 °C. ^j The reaction time was prolonged to 12 hours.

Description of further optimizing for the reaction conditions (Table ESI-1).

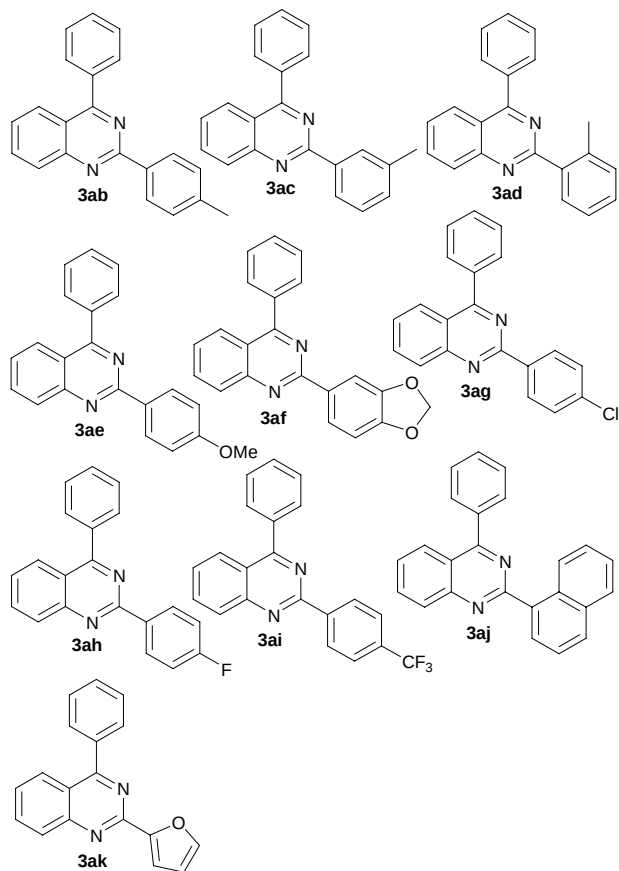
Other oxidants, such as 30 % H₂O₂ solution in water, *m*-CPBA, O₂ and stoichiometric amount of Cu(OAc)₂·2H₂O, were examined in this reaction, but no product was observed (Table ESI-1, entry 2). Different solvents had little influence on this reaction (Table ESI-1, entries 3-6). Subsequently, the reaction temperature and the ratio of benzylic amine and *tert*-butyl hydroperoxide were optimized (Table ESI-1, entries 7-14). 76% yield was obtained at an optimal reaction temperature of 90 °C and 1.5 equivalents of benzylic amine and 2 equivalents of TBHP (Table ESI-1, entry 10). The influence of catalyst loading on the reaction was also investigated. When the catalyst loading was reduced from 6.8 mol % to 3.4 mol %, no decrease of the reaction yield was observed. Further reduce of the catalyst loading from 3.4 mol % to 1.7 mol % resulted in a lower yield (Table ESI-1, entries 15 and 16). The reaction time affected this reaction obviously. When the reaction time was prolonged to 12 h, an excellent reaction yield was obtained (Table ESI-1, entry 17). Thus, the optimum conditions were obtained, that is, 3.4 mol % of SCONP-3 as catalyst, 1.5 equivalents of benzylic amine and 2.0 equivalents of 70 % aqueous *tert*-butyl hydroperoxide reacted at 90 °C for 12 hours.

Structures of 3aa-3ra and 3ab-3ak

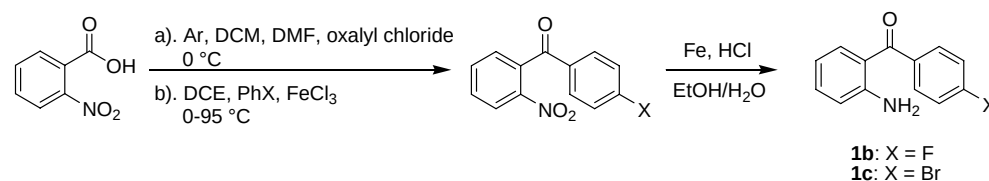
Structures of 3aa-3ra



Structures of 3ab-3ak



Synthesis of substances



Scheme 1. Synthesis of **1b** and **1c**¹

Synthesis of **1b**

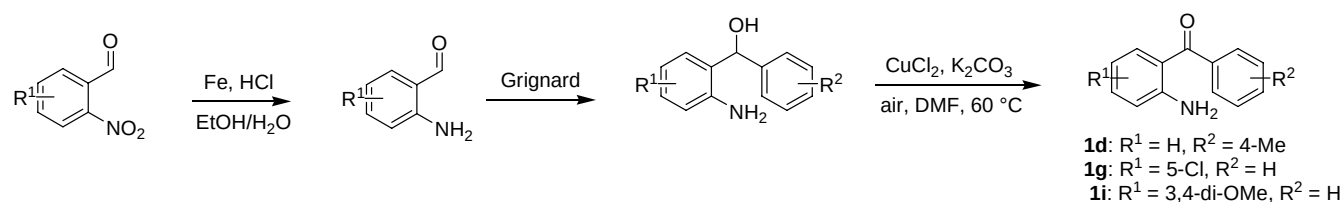
o-nitrobenzoic acid (5.014 g, 29.9 mmol) and anhydrous DMF (0.1 mL) were dissolved in dry DCM (105 mL) under argon. After cooling to 0 °C, oxalyl chloride (5.2 mL, 60 mmol) was added slowly. The mixture was stirred at 0 °C for 30 min, then at ambient temperature until the reaction became clear. Subsequently, the mixture was concentrated to leave the crude acid chloride as a light yellow oil. The oil was directly dissolved in 1,2-dichloroethane (11.6 mL) and fluorobenzene (4.5 mL, 48 mmol) and cooled to 0 °C. Anhydrous iron (III) chloride (5.35 g, 33.0 mmol) was added to the reaction in 3 portions over 30 min, and the reaction was stirred at 0 °C for another 1 h. Then the reaction mixture was poured onto ice-water (60 mL), and heated at 95 °C to remove 1,2-dichloroethane. When the temperature reached 75 °C, isobutanol (20 mL) was added and the hot solution was washed with water (50 mL x 3). After cooling to room temperature, the precipitate was collected and washed with water to give the ((4-fluorophenyl)(2-nitrophenyl)methanone as a light brown solid (6.012g, 82% yield).

Two drops of concentrated HCl were added to the solution of ((4-fluorophenyl)(2-nitrophenyl)methanone (999 mg, 4.0 mmol) in EtOH (12 mL) and water (3 mL) with iron powder (291 mg, 5.2 mmol). The reaction was heated to reflux. After 1 h, the reduction completed as detected by TLC. And the reaction was filtrated through a pad of silicon, washed with EtOAc. The filtrate was extracted with EtOAc for three times, washed with brine and dried over Na₂SO₄. The organic phase was concentrated in vacuum, and purified by chromatographic column of gel, giving (2-aminophenyl)(4-fluorophenyl)methanone as a light yellow solid (805 mg, 94% yield).

Synthesis of **1c**

This reaction was performed according to the procedure for (2-nitrophenyl)(4-fluorophenyl)methanone with *o*-nitrobenzoic acid (10.045 g, 60.1 mmol). 5.546 g of (2-nitrophenyl)(4-bromophenyl)methanone (30% yield) was obtained as a dark brown solid.

(2-aminophenyl)(4-bromophenyl)methanone was synthesized according to the procedure for (2-aminophenyl)(4-fluorophenyl)methanone in 90% yield.



Scheme 2. Synthesis of **1d**, **1g** and **1i**²

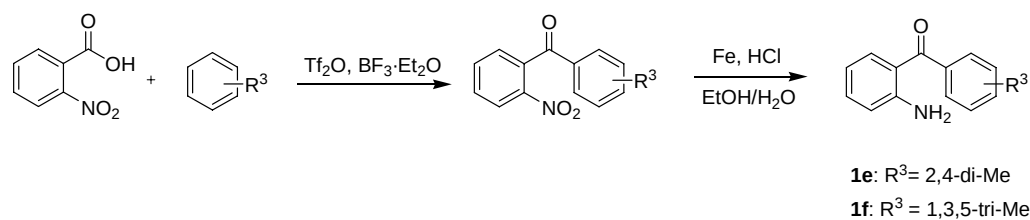
Synthesis of **1d**

1.046 g of 2-aminobenzaldehyde was synthesized according to the procedure for (2-aminophenyl)(4-fluorophenyl)methanone with 2-nitrobenzaldehyde (3.021g, 20 mmol) in 43% yield.

Subsequently, p-tolylmagnesium bromide (51.6 mL, 1 M in THF, 51.6 mmol) was added to the solution of 2-aminobenzaldehyde (1.046 g, 8.6 mmol) in dry Et₂O (20 mL) dropwise. The reaction was quenched with saturated NH₄Cl aqueous solution after the completion of the reaction as detected by TCL, and extracted with Et₂O for three times. The organic phase was washed with water and brine, and dried over Na₂SO₄. Then the organic phase was concentrated in vacuum, and purified by chromatographic column of gel, giving (2-aminophenyl)(p-tolyl)methanol as a light yellow solid (1.063 g, 58% yield).

(2-aminophenyl)(p-tolyl)methanol (426 mg, 2 mmol) was dissolved in DMF (15 mL) with CuCl₂·H₂O (34.1 mg, 0.2 mmol) and K₂CO₃ (552 mg, 4 mmol), the mixture was then stirred at 60 °C in air for 24 h. Then the reaction mixture was diluted with water, extracted with EtOAc for three times, washed with water for three times and brine once, and dried over Na₂SO₄. The organic phase was concentrated in vacuum, and purified by chromatographic column of gel, giving (2-aminophenyl)(p-tolyl)methanone (**1d**) as a light yellow solid (262 mg, 62% yield).

1g and **1i** were synthesized according to the procedure for (2-aminophenyl)(p-tolyl)methanone (**1d**).



Scheme 3. Synthesis of **1e** and **1f**³

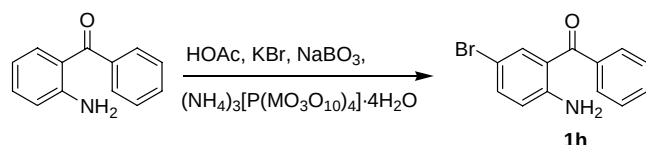
Synthesis of **1e**

2-Nitrobenzoic acid (1.997 g, 12 mmol) and trifluoroacetic anhydride (4 g, 19 mmol) were stirred to homogeneous. After cooling in ice bath, boron trifluoride-ether (1.701 g, 12 mmol) was added to the solution dropwise. The deep red solution was dropped to mesitylene (2.255g, 18.75 mmol) in ice bath, and stirred for another 2 h. Then the reaction mixture was poured onto ice and extracted with chloroform. The extract was washed with aqueous sodium hydroxide (40%), dried over Na₂SO₄, and concentrated to

give a greyish-white solid. After recrystallization from EtOH, mesityl(2-nitrophenyl)methanone was obtained as white needles (1.102 g, 34% yield).

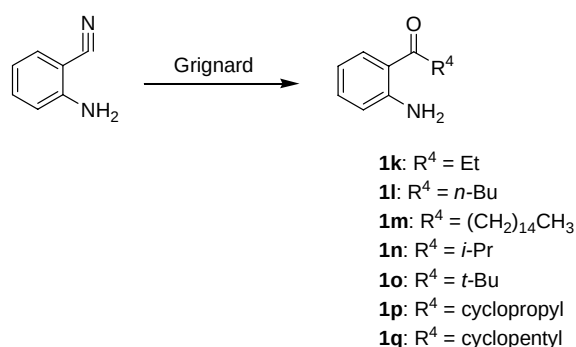
Mesityl(2-nitrophenyl)methanone was reduced according to the procedure for (2-aminophenyl)(4-fluorophenyl)methanone (**1b**), giving (2-aminophenyl)(mesityl)methanone in 83% yield.

1f was synthesized according to the procedure for (2-aminophenyl)(mesityl)methanone (**1e**).



Scheme 4. Synthesis of **1h**⁴

2-Aminobenzophenone (600 mg, 3.04 mmol) was suspended in acetic acid (6 mL). Potassium bromide (399 mg, 33.4 mmol), sodium perborate tetrahydrate (562 mg, 36.6 mmol), and ammonium molybdate tetrahydrate (30 mg) were added and stirring continued for 3 h at 0 °C. The resulting thick yellow precipitate was diluted with ice water (6 mL), filtered off, washed with ice water, dried at HV/50 °C and purified by chromatographic column with gel, giving (2-amino-5-bromophenyl)(phenyl)methanone (**1h**) (739 mg, 88% yield) as a yellow solid.



Scheme 5. Synthesis of **1k-1q**¹

Synthesis of **1k**

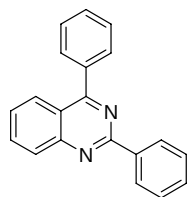
Ethylmagnesium bromide (15 mL, 1 M in THF, 15 mmol) was added to a solution of 2-aminobenzonitrile (590 mg, 5 mmol) in THF (10 mL) at 0 °C over 30 min. Then the reaction was allowed to warm to ambient temperature and allowed to stir at this temperature for 6 h. The reaction was quenched by slow addition of 10% HCl and made basic by the addition of NaOH at 0 °C. The organic layer was separated and the remaining aqueous layer was extracted with Et₂O for three times. The

combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated. The crude product was purified by chromatographic column with gel, giving 1-(2-aminophenyl)propan-1-one (**1k**) (361 mg, 48% yield) as a yellow solid.

1l-1q were synthesized according to the procedure for 1-(2-aminophenyl)propan-1-one (**1k**).

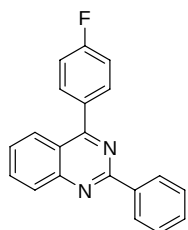
Characterization data for the products

2,4-diphenylquinazoline (3aa) ⁵



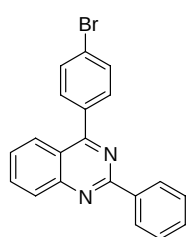
m.p. 117-119 °C (from CDCl₃). ¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.70 (m, 2 H), 8.17-8.10 (m, 2 H), 7.90-7.84 (m, 3 H), 7.60-7.47 (m, 7 H). ¹³C NMR (75 MHz, CDCl₃) δ (ppm) 168.3, 160.3, 152.1, 138.3, 137.8, 133.6, 130.6, 130.3, 130.0, 129.3, 128.8, 127.0, 121.8. HRMS calc. C₂₀H₁₄N₂: 282.1157, found: 282.1154.

4-(4-fluorophenyl)-2-phenylquinazoline (3ba)



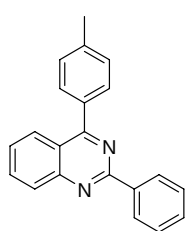
m.p. 144-146 °C (from CDCl₃). ¹H NMR (400 MHz, CDCl₃) δ (ppm) 8.69-8.66 (m, 2 H), 8.15 (d, *J* = 8.8 Hz, 1 H), 8.09-8.07 (m, 1 H), 7.92-7.86 (m, 3 H), 7.57-7.48 (m, 4 H), 7.32-7.25 (m, 2 H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 167.2, 165.3, 162.8, 160.3, 152.2, 138.2, 133.93, 133.90, 133.7, 132.4, 132.3, 130.7, 129.4, 128.8, 128.7, 127.2, 126.8, 121.6, 115.9, 115.7. HRMS calc. C₂₀H₁₃FN₂: 300.1063, found: 300.1060.

4-(4-bromophenyl)-2-phenylquinazoline (3ca) ⁵



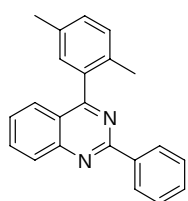
m.p. 154-156 °C (from CDCl₃). ¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.69-8.66 (m, 2 H), 8.16 (d, *J* = 8.4 Hz, 1 H), 8.06 (d, *J* = 8.4 Hz, 1 H), 7.92-7.86 (m, 1 H), 7.79-7.72 (m, 4 H), 7.58-7.49 (m, 4 H). ¹³C NMR (75 MHz, CDCl₃) δ (ppm) 167.2, 160.3, 152.2, 138.1, 136.7, 133.8, 131.90, 131.86, 130.7, 129.4, 128.8, 128.7, 127.3, 126.6, 124.7, 121.5. HRMS calc. C₂₀H₁₃BrN₂: 360.0262, found: 360.0261.

2-phenyl-4-p-tolylquinazoline (3da) ⁵



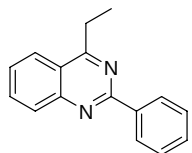
m.p. 128-130 °C (from CDCl₃). ¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.71-8.68 (m, 2 H), 8.13 (d, *J* = 8.7 Hz, 2 H), 7.87-7.77 (m, 3 H), 7.55-7.48 (m, 4 H), 7.382 (d, *J* = 7.8 Hz, 2 H), 2.48 (m, 3 H). ¹³C NMR (75 MHz, CDCl₃) δ (ppm) 168.4, 160.3, 152.1, 140.3, 138.4, 135.0, 133.5, 130.5, 130.3, 129.4, 129.3, 128.8, 128.6, 127.2, 127.0, 121.8, 21.6. HRMS calc. C₂₁H₁₆N₂: 296.1313, found: 296.1311.

4-(2,5-dimethylphenyl)-2-phenylquinazoline (3ea)



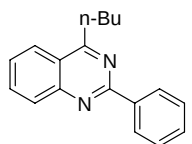
m.p. 114-116 °C (from CDCl₃). ¹H NMR (400 MHz, CDCl₃) δ (ppm) 8.67-8.65 (m, 2 H), 8.15 (d, *J* = 8.4 Hz, 1 H), 7.89-7.85 (m, 1 H), 7.70-7.68 (m, 1 H), 7.54-7.46 (m, 4 H), 7.30-7.22 (m, 3 H), 2.40 (s, 3 H), 2.16 (s, 3 H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 170.2, 160.5, 151.6, 138.4, 137.0, 135.3, 133.8, 133.4, 130.7, 130.6, 130.2, 130.1, 129.1, 128.9, 128.6, 127.3, 127.1, 122.8, 21.1, 19.6. HRMS calc. C₂₂H₁₈N₂: 310.1470, found: 310.1468.

4-ethyl-2-phenylquinazoline (3ga) ⁶



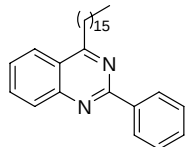
m.p. 44-46 °C (from CDCl₃). ¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.67-8.64 (m, 2 H), 8.13-8.07 (m, 2 H), 7.87-7.82 (m, 1 H), 7.60-7.49 (m, 4 H), 3.38 (dd, *J* = 7.5 Hz, 2 H), 1.54 (t, *J* = 7.5 Hz, 3 H). ¹³C NMR (75 MHz, CDCl₃) δ (ppm) 172.2, 160.2, 150.7, 138.6, 133.4, 130.5, 129.5, 128.7, 128.6, 126.9, 124.6, 122.4, 27.8, 12.5. HRMS calc. C₁₆H₁₄N₂: 234.1157, found: 234.1154.

4-butyl-2-phenylquinazoline (3ha)



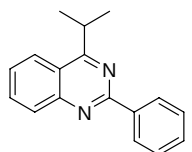
m.p. 45-47 °C (from CDCl₃). ¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.66-8.62 (m, 2 H), 8.12-8.06 (m, 2 H), 7.87-7.81 (m, 1 H), 7.59-7.48 (m, 4 H), 3.33 (t, *J* = 7.8 Hz, 2 H), 2.02-1.92 (m, 2 H), 1.64-1.48 (m, 2 H), 1.02 (t, *J* = 7.5 Hz, 3 H). ¹³C NMR (75 MHz, CDCl₃) δ (ppm) 171.6, 160.2, 150.8, 138.6, 133.3, 130.4, 129.5, 128.7, 128.6, 126.8, 124.7, 122.6, 34.4, 30.8, 22.9, 14.1. HRMS calc. C₁₈H₁₈N₂: 262.1470, found: 262.1470.

4-ethyl-2-phenylquinazoline (3ia)



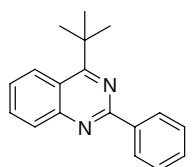
m.p. 66-68 °C (from CDCl₃). ¹H NMR (400 MHz, CDCl₃) δ (ppm) 8.65-8.63 (m, 2 H), 8.12-8.06 (m, 2 H), 7.86- 7.81 (m, 1 H), 7.58-7.46 (m, 4 H), 3.32 (t, *J* = 8.0 Hz, 2 H), 2.02-1.94 (m, 2 H), 1.54-1.47 (m, 2 H), 1.42-1.37 (m, 2 H), 1.25-1.20 (m, 22 H), 0.88 (t, *J* = 8.8 Hz, 3 H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 171.6, 160.2, 150.9, 138.6, 133.3, 130.4, 129.5, 128.7, 128.6, 126.8, 124.7, 122.7, 34.7, 32.1, 29.83, 29.81, 29.73, 29.66, 29.5, 28.7, 22.8, 14.2. HRMS calc. C₃₀H₄₂N₂: 430.3348, found: 430.3344.

4-isopropyl-2-phenylquinazoline (3ja) ⁷



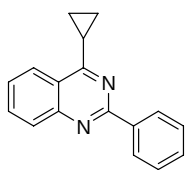
m.p. 64-66 °C (from CDCl₃). ¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.70-8.67 (m, 2 H), 8.17-8.07 (m, 2 H), 7.86- 7.81 (m, 1 H), 7.59-7.49 (m, 4 H), 4.00-3.91 (m, 1 H), 1.52 (s, 3 H), 1.50 (s, 3 H). ¹³C NMR (75 MHz, CDCl₃) δ (ppm) 175.6, 160.2, 151.1, 138.7, 133.2, 130.4, 129.7, 128.7, 128.6, 126.7, 124.2, 121.8, 31.3, 21.9. HRMS calc. C₁₇H₁₆N₂: 248.1313, found: 248.1310.

4-tert-butyl-2-phenylquinazoline (3ka)



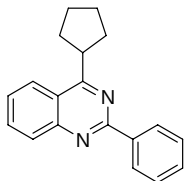
m.p. 70-72 °C (from CDCl₃). ¹H NMR (400 MHz, CDCl₃) δ (ppm) 8.69-8.67 (m, 2 H), 8.45-8.43 (m, 1 H), 8.13-8.10 (m, 1 H), 7.82-7.78 (m, 1 H), 7.55-7.50 (m, 4 H), 1.72 (s, 9 H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 176.5, 159.0, 152.2, 138.7, 132.4, 130.52, 130.48, 128.7, 128.6, 126.6, 125.7, 121.7, 40.7, 30.8. HRMS calc. C₁₈H₁₈N₂: 262.1470, found: 262.1469.

4-cyclopropyl-2-phenylquinazoline (3la)



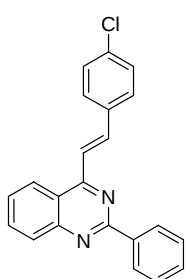
m.p. 103-105 °C (from CDCl₃). ¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.61-8.57 (m, 2 H), 8.27 (d, *J* = 8.4 Hz, 1 H), 8.05 (d, *J* = 8.7 Hz, 1 H), 7.85-7.80 (m, 1 H), 7.58-7.46 (m, 4 H), 2.83-2.74 (m, 1 H), 1.56-1.52 (m, 2 H), 1.27-1.21 (m, 2 H). ¹³C NMR (75 MHz, CDCl₃) δ (ppm) 172.1, 159.9, 150.4, 138.6, 133.2, 130.3, 129.3, 128.53, 128.47, 126.6, 124.4, 123.0, 13.0, 12.2. HRMS calc. C₁₇H₁₄N₂: 246.1157, found: 246.1152.

4-cyclopentyl-2-phenylquinazoline (3ma)



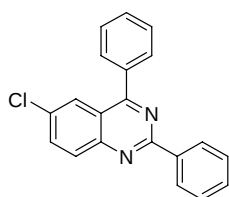
m.p. 79-81 °C (from CDCl₃). ¹H NMR (400 MHz, CDCl₃) δ (ppm) 8.68-8.65 (m, 2 H), 8.18-8.15 (m, 1 H), 8.072 (d, *J* = 8.0 Hz, 1 H), 7.85-7.81 (m, 1 H), 7.57-7.46 (m, 4 H), 4.08-4.04 (m, 1 H), 2.28-2.13 (m, 4 H), 2.02-1.92 (m, 2 H), 1.86-1.76 (m, 2 H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 174.5, 160.0, 151.0, 138.8, 133.1, 130.4, 129.5, 128.7, 128.6, 126.6, 124.7, 122.6, 42.7, 32.7, 26.4. HRMS calc. C₁₉H₁₈N₂: 274.1470, found: 274.1471.

(E)-4-(4-chlorostyryl)-2-phenylquinazoline (3na)



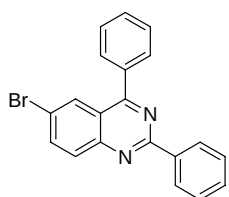
m.p. 123-125 °C (from CDCl₃). ¹H NMR (400 MHz, CDCl₃) δ (ppm) 8.72-8.69 (m, 2 H), 8.39 (d, *J* = 15.2 Hz, 1 H), 8.27 (d, *J* = 8.0 Hz, 1 H), 8.09 (d, *J* = 8.4 Hz, 1 H), 7.94-7.90 (m, 1 H), 7.89-7.85 (m, 1 H), 7.71-7.67 (m, 2 H), 7.62-7.50 (m, 4 H), 7.44-7.41 (m, 2 H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 161.7, 160.3, 152.2, 138.6, 138.1, 135.6, 134.8, 133.7, 130.6, 129.6, 129.3, 128.73, 128.69, 127.1, 123.9, 121.8, 121.6. HRMS calc. C₂₂H₁₅ClN₂: 342.0924, found: 342.0921.

6-chloro-2,4-diphenylquinazoline (3oa)⁷



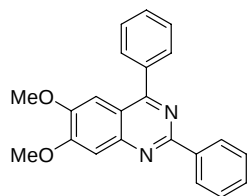
m.p. 190-192 °C (from CDCl₃). ¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.69-8.66 (m, 2 H), 8.11-8.08 (m, 2 H), 7.88-7.79 (m, 3 H), 7.62-7.60 (m, 3 H), 7.56-7.51 (m, 3 H). ¹³C NMR (75 MHz, CDCl₃) δ (ppm) 167.6, 160.6, 150.6, 137.9, 137.2, 134.6, 132.7, 131.0, 130.9, 130.3, 130.2, 128.8, 128.7, 125.9, 122.3. HRMS calc. C₂₀H₁₃ClN₂: 316.0767, found: 316.0762.

6-bromo-2,4-diphenylquinazoline (3pa)



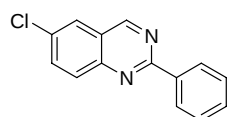
m.p. 209-211 °C (from CDCl₃). ¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.68-8.65 (m, 2 H), 8.26-8.25 (m, 1 H), 8.03-8.00 (m, 1 H), 7.95-7.92 (m, 1 H), 7.87-7.84 (m, 2 H), 7.62-7.60 (m, 3 H), 7.54-7.50 (m, 3 H). ¹³C NMR (75 MHz, CDCl₃) δ (ppm) 167.5, 160.6, 150.8, 137.9, 137.1, 131.1, 130.9, 130.3, 130.2, 129.2, 128.8, 128.7, 122.8, 120.7. HRMS calc. C₂₀H₁₃BrN₂: 360.0262, found: 360.0258.

6,7-dimethoxy-2,4-diphenylquinazoline (3qa)



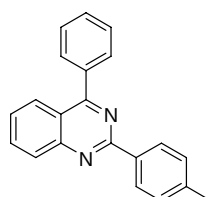
m.p. 178-180 °C (from CDCl₃). ¹H NMR (400 MHz, CDCl₃) δ (ppm) 8.64-8.62 (m, 2 H), 7.90-7.88 (m, 2 H), 7.62-7.57 (m, 3 H), 7.53-7.47 (m, 4 H), 7.36 (s, 1 H), 4.11 (s, 3 H), 3.92 (s, 3 H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 165.3, 159.5, 155.8, 150.1, 150.0, 138.7, 138.4, 130.1, 129.9, 129.7, 128.7, 128.6, 128.4, 117.2, 107.5, 104.3, 56.5, 56.2. HRMS calc. C₂₂H₁₈N₂O₂: 342.1368, found: 342.1364.

6-chloro-2-phenylquinazoline (3ra)⁸



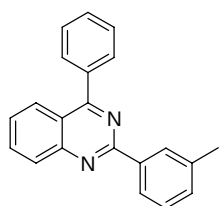
m.p. 157-159 °C (from CDCl₃). ¹H NMR (400 MHz, CDCl₃) δ (ppm) 9.383-9.382 (m, 1 H), 8.61-8.58 (m, 2 H), 8.02 (m, 1 H), 7.894-7.888 (m, 1 H), 7.83-7.80 (m, 1 H), 7.55-7.51 (m, 3 H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 161.4, 159.6, 149.4, 137.7, 135.2, 132.9, 131.0, 130.5, 128.8, 128.7, 125.9, 124.1. HRMS calc. C₁₄H₉ClN₂: 240.0454, found: 240.0452.

4-phenyl-2-p-tolylquinazoline (3ab)⁵



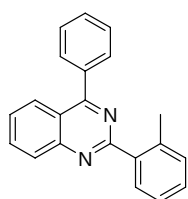
m.p. 166-168 °C (from CDCl₃). ¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.59 (d, *J* = 7.8 Hz, 2 H), 8.14-8.08 (m, 2 H), 7.89-7.82 (m, 3 H), 7.59-7.57 (m, 3 H), 7.53-7.48 (m, 1 H), 7.32 (d, *J* = 8.1 Hz, 2 H), 2.43 (s, 3 H). ¹³C NMR (75 MHz, CDCl₃) δ (ppm) 168.3, 160.4, 152.1, 140.8, 137.9, 135.6, 133.5, 130.3, 129.9, 129.4, 129.2, 128.8, 128.6, 127.1, 126.8, 121.7, 21.6. HRMS calc. C₂₁H₁₆N₂: 296.1313, found: 296.1311.

4-phenyl-2-m-tolylquinazoline (3ac)



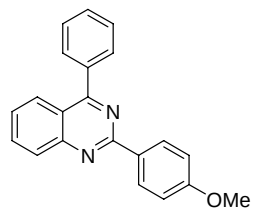
m.p. 115-117 °C (from CDCl₃). ¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.51-8.48 (m, 2 H), 8.17-8.09 (m, 2 H), 7.90-7.84 (m, 3 H), 7.61-7.50 (m, 4 H), 7.44-7.39 (m, 1 H), 7.32-7.30 (m, 1 H), 2.48 (s, 3 H). ¹³C NMR (75 MHz, CDCl₃) δ (ppm) 168.4, 160.5, 152.1, 138.3, 138.2, 137.8, 133.6, 131.4, 130.3, 130.0, 129.3, 129.2, 128.62, 128.56, 127.1, 127.0, 126.1, 121.8, 21.7. HRMS calc. C₂₁H₁₆N₂: 296.1313, found: 296.1309.

4-phenyl-2-o-tolylquinazoline (3ad)



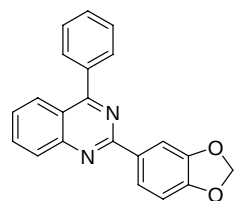
m.p. 72-74 °C (from CDCl₃). ¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.18-8.15 (m, 2 H), 8.00-7.97 (m, 1 H), 7.94-7.84 (m, 3 H), 7.62-7.56 (m, 4 H), 7.37-7.32 (m, 3 H), 2.67 (s, 3 H). ¹³C NMR (75 MHz, CDCl₃) δ (ppm) 168.1, 163.5, 151.8, 138.9, 137.6, 137.5, 133.6, 131.4, 130.9, 130.2, 130.0, 129.3, 129.2, 128.6, 127.4, 127.0, 126.1, 121.1, 21.4. HRMS calc. C₂₁H₁₆N₂: 296.1313, found: 296.1312.

2-(4-methoxyphenyl)-4-phenylquinazoline (3ae) ⁵



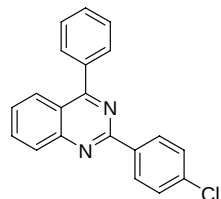
m.p. 158-160 °C (from CDCl₃). ¹H NMR (400 MHz, CDCl₃) δ (ppm) 8.67-8.65 (m, 2 H), 8.12-8.08 (m, 2 H), 7.89-7.85 (m, 3 H), 7.60-7.58 (m, 3 H), 7.52-7.50 (m, 1 H), 7.05-7.05 (m, 2 H), 3.89 (s, 3 H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 168.2, 161.9, 160.1, 152.2, 137.9, 133.5, 131.0, 130.4, 130.3, 129.9, 129.0, 128.6, 127.1, 126.6, 121.5, 114.0, 55.5. HRMS calc. C₂₁H₁₆N₂O: 312.1263, found: 312.1261.

2-(benzo[d][1,3]dioxol-5-yl)-4-phenylquinazoline (3af)



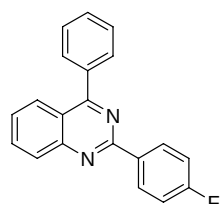
m.p. 148-150 °C (from CDCl₃). ¹H NMR (400 MHz, CDCl₃) δ (ppm) 8.32-8.30 (m, 1 H), 8.194-8.190 (m, 1 H), 8.09 (d, *J* = 6.6 Hz, 2 H), 7.88-7.84 (m, 3 H), 7.53-7.49 (m, 1 H), 6.94 (d, *J* = 6.3 Hz, 1 H), 6.04 (s, 2 H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 168.3, 159.9, 152.2, 150.0, 148.3, 137.9, 133.6, 132.9, 130.3, 129.1, 128.7, 126.8, 123.8, 121.6, 109.0, 108.4, 101.5. HRMS calc. C₂₁H₁₄N₂O₂: 326.1055, found: 326.1050.

2-(4-chlorophenyl)-4-phenylquinazoline (3ag)



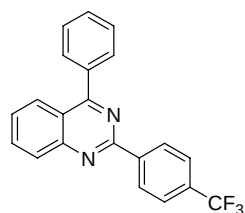
m.p. 190-192 °C (from CDCl₃). ¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.66-8.62 (m, 2 H), 8.14-8.10 (m, 2 H), 7.91-7.85 (m, 3 H), 7.64-7.54 (m, 4 H), 7.52-7.46 (m, 2 H). ¹³C NMR (75 MHz, CDCl₃) δ (ppm) 168.5, 159.3, 152.0, 137.7, 136.8, 133.8, 130.3, 130.1, 129.2, 128.8, 128.7, 127.3, 127.2, 121.8. HRMS calc. C₂₀H₁₃ClN₂: 316.0767, found: 316.0764.

2-(4-fluorophenyl)-4-phenylquinazoline (3ah)



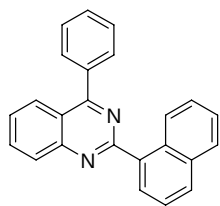
m.p. 153-157 °C (from CDCl₃). ¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.74-8.67 (m, 2 H), 8.15-8.11 (m, 2 H), 7.91-7.86 (m, 3 H), 7.61-7.52 (m, 4 H), 7.26-7.16 (m, 2 H). ¹³C NMR (75 MHz, CDCl₃) δ (ppm) 168.5, 166.4, 163.1, 159.4, 152.1, 137.7, 134.5, 133.7, 130.9, 130.8, 130.3, 129.2, 128.6, 127.1, 121.7, 115.7, 115.4. HRMS calc. C₂₀H₁₃FN₂: 300.1063, found: 300.1059.

4-phenyl-2-(4-(trifluoromethyl)phenyl)quinazoline (3ai)



m.p. 123-126 °C (from CDCl₃). ¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.82 (d, *J* = 8.4 Hz, 2 H), 8.20-8.14 (m, 2 H), 7.95-7.87 (m, 3 H), 7.77 (d, *J* = 8.4 Hz, 2 H), 7.62-7.57 (m, 4 H). ¹³C NMR (75 MHz, CDCl₃) δ (ppm) 168.6, 158.9, 152.0, 141.7, 137.6, 133.9, 132.3, 131.9, 130.3, 130.2, 129.4, 129.0, 128.7, 127.7, 127.2, 126.2, 125.52, 124.47, 122.6, 122.0. HRMS calc. C₂₁H₁₃F₃N₂: 350.1031, found: 350.1029.

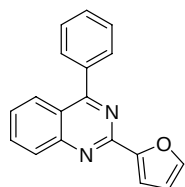
2-(naphthalen-1-yl)-4-phenylquinazoline (3aj) ⁷



m.p. 171-173 °C (from CDCl₃). ¹H NMR (400 MHz, CDCl₃) δ (ppm) 8.81-8.79 (m, 1 H), 8.26-8.19 (m, 3 H), 7.98-7.89 (m, 5 H), 7.65-7.50 (m, 7 H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 168.6, 162.9, 151.9, 137.6, 136.7, 134.4, 133.9, 131.5, 130.4, 130.3, 130.1, 129.8, 129.3, 128.8, 128.6, 127.6, 127.2, 126.9, 126.3, 125.9, 125.5, 121.4.

HRMS calc. C₂₄H₁₆N₂: 332.1313, found: 332.1310.

2-(furan-2-yl)-4-phenylquinazoline (3ak)



m.p. 149-151 °C (from CDCl₃). ¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.17 (d, *J* = 8.7 Hz, 1 H), 8.06 (d, *J* = 8.4 Hz, 1 H), 7.89-7.81 (m, 3 H), 7.694-7.692 (m, 1 H), 7.59-7.49 (m, 5 H), 6.61-6.59 (m, 1 H). ¹³C NMR (75 MHz, CDCl₃) δ (ppm) 169.0, 153.7, 151.7, 145.4, 137.4, 134.0, 131.0, 130.2, 130.1, 129.0, 128.7, 127.3, 127.1, 121.7, 114.3, 112.3.

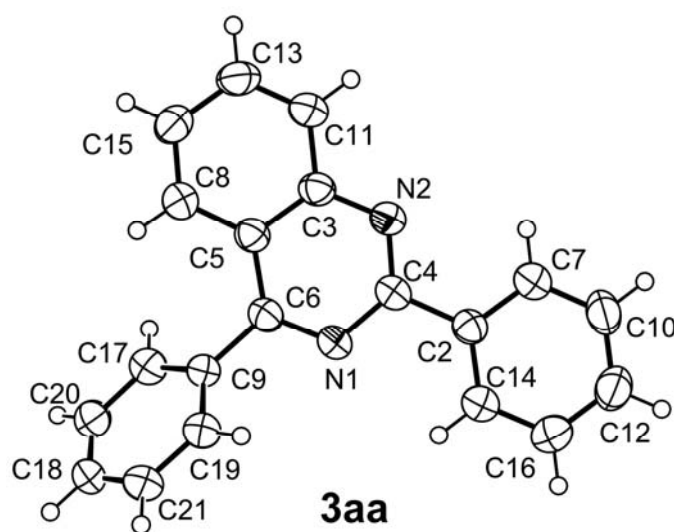
HRMS calc. C₁₈H₁₂N₂O: 272.0950, found: 272.0946.

References:

- 1 C. M. Counciller, C. C. Eichman, B. C. Wray, J. P. Stambuli, *Org. Lett.* **2008**, *10*, 1021.
- 2 C. F. Wan, J. M. Fan, J. T. Zhang, Z. Y. Wang, *Chinese Sci. Bull.* **2009**, in press.
- 3 D. G. Kawkins, O. Meth-Cohn, *J. Chem. Soc., Perkin Trans. I* **1983**, 2077.
- 4 S. Atechian, N. Nock, R. D. Norcross, H. Ratni, A. W. Thomas, J. Verron, R. Masciadri, *Tetrahedron* **2007**, *63*, 2811.
- 5 A. R. Katritzky, B. Yang, J. Jiang, P. J. Steel, *J. Org. Chem.* **2002**, *60*, 246.
- 6 Y. Tamura, M. W. Chun, g. Nishida, S. Kwon, M. Ikeda, *Chem. Pharm. Bull.* **1978**, 2866.
- 7 J. Bergman, A. Brynolf, B. Elman, E. Vuorinen, *Tetrahedron* **1986**, *42*, 3697.
- 8 T. L. Gilchrist, C. J. Moody, C. W. Rees, *J. Chem. Soc., Perkin Trans. I* **1975**, 1964.

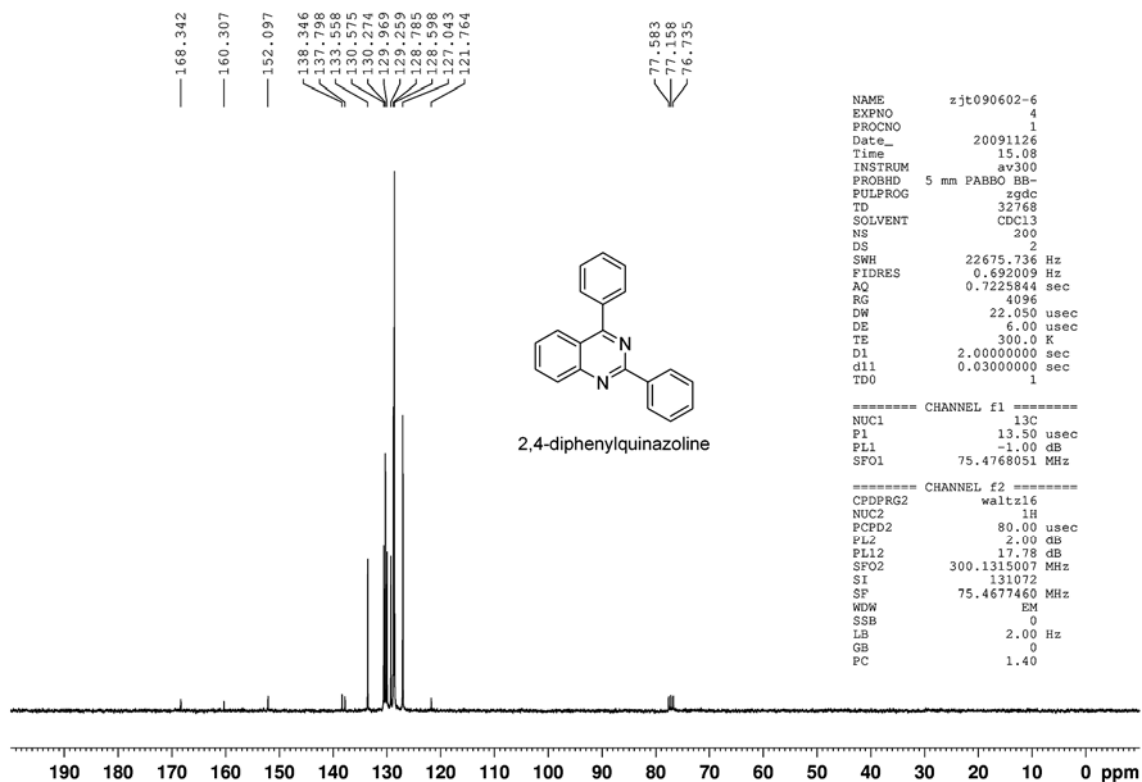
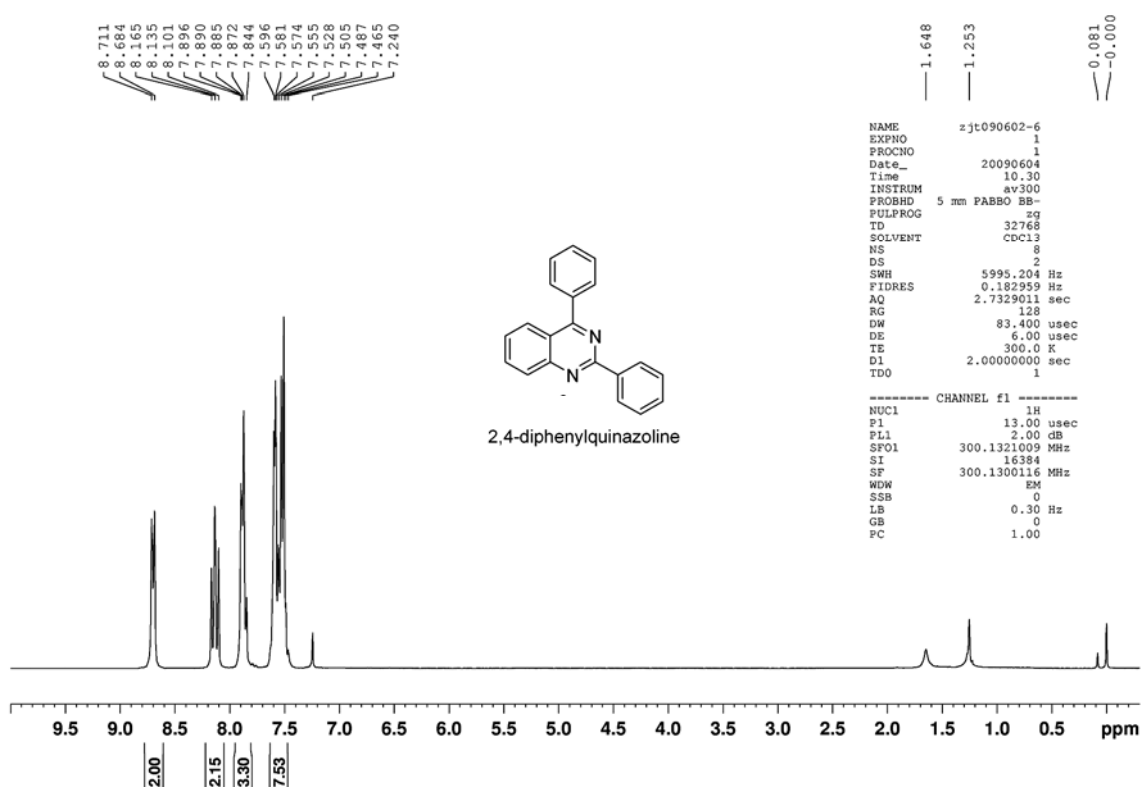
Crystallographic data

The data collection for the above compound were performed on a Oxford Diffraction Gemini S Ultra CCD diffractometer equipped with mirror MoK α ($\lambda = 0.71073$ Å) radiation at room temperature. The structure was solved by direct methods and refined by full-matrix least-squares methods with SHELXL-97 programs. Crystallographic parameters: C₂₀H₁₄N₂, $M = 282.33$, monoclinic, space group P2₁/n, $a = 10.633$, $b = 6.965$, $c = 19.786$ Å, $\beta = 99.74^\circ$, $V = 1444.2$ Å³, $Z = 4$, $D_c = 1.298$ g/cm³, $F(000) = 592$, a total of 2945 reflections, of which 1781 were independent ($R_{int} = 0.0231$). Goodness of fit: 1.039, $R_1[I > 2\sigma(I)] = 0.0376$, $wR_2[I > 2\sigma(I)] = 0.0873$, R_1 (all data) = 0.0645, wR_2 (all data) = 0.0915, residuals ($e \cdot \text{Å}^{-3}$): 0.120, 0.150. CCDC depository number: 757569.

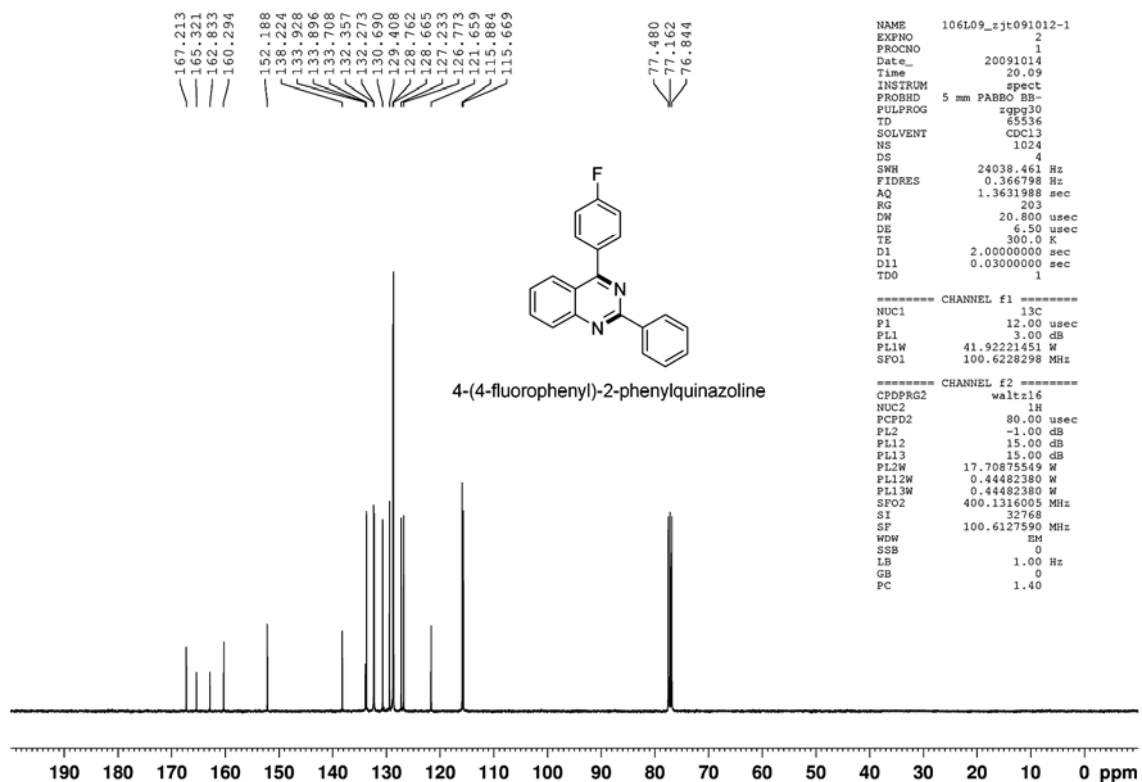
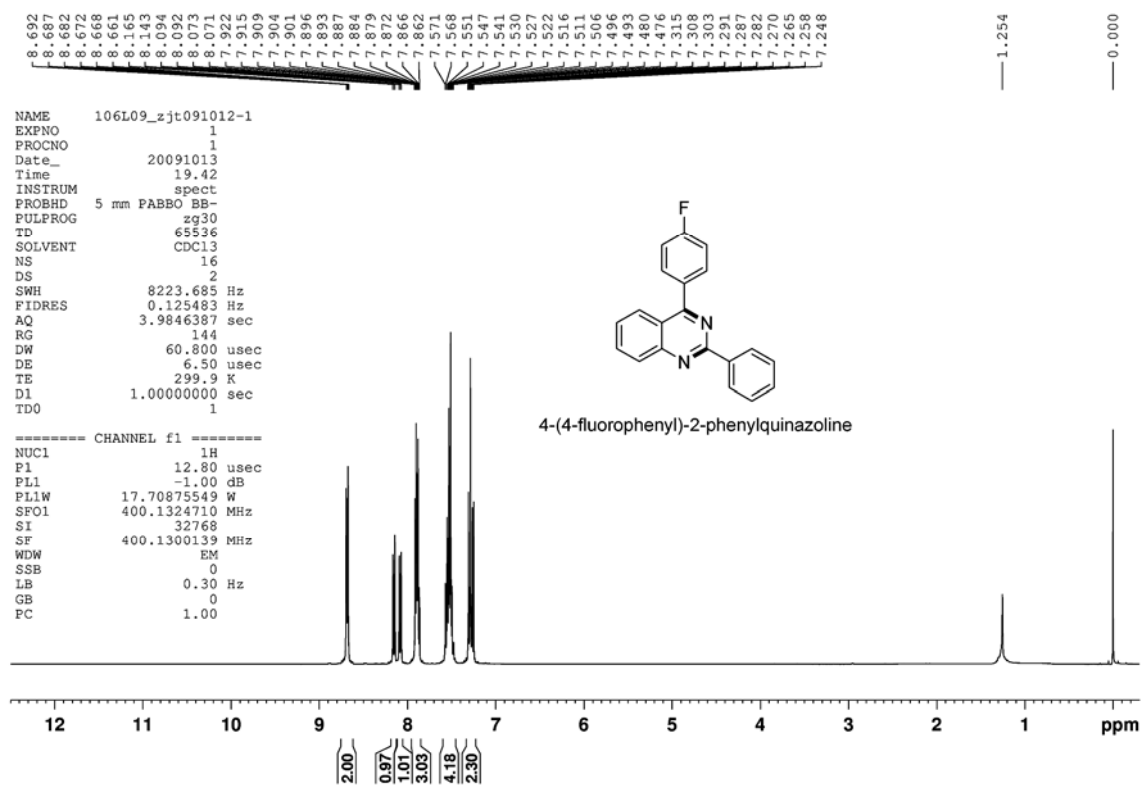


NMR spectra for the products

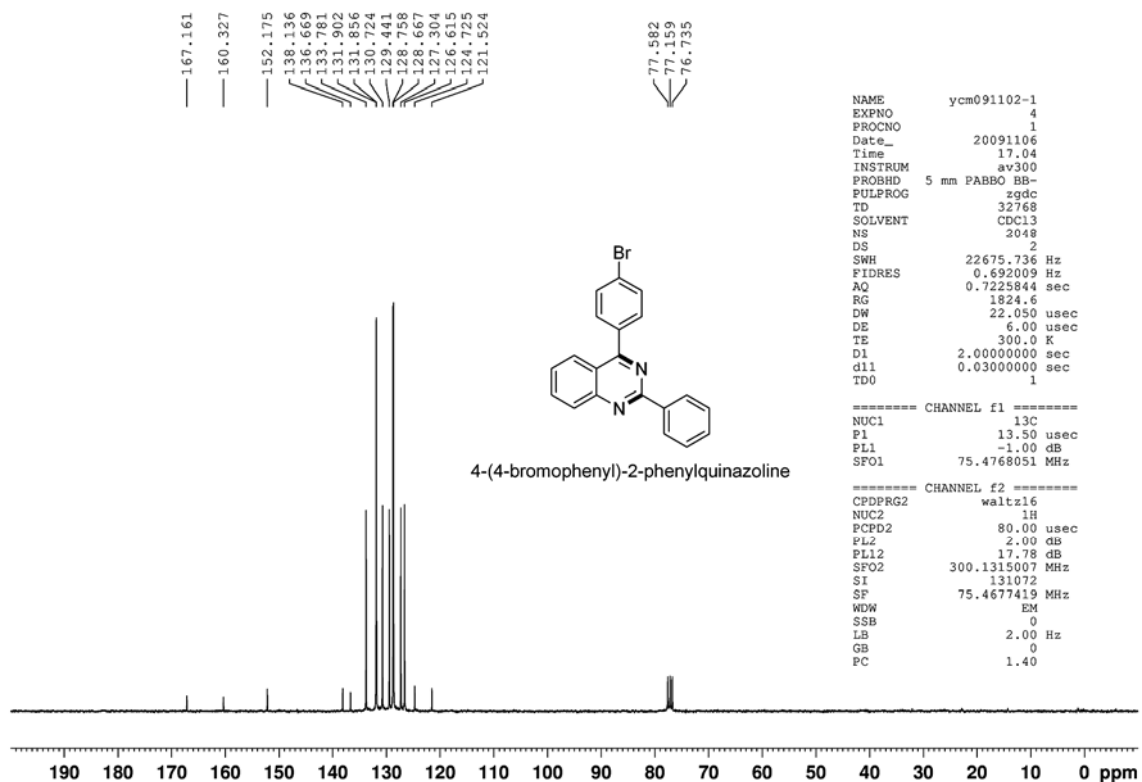
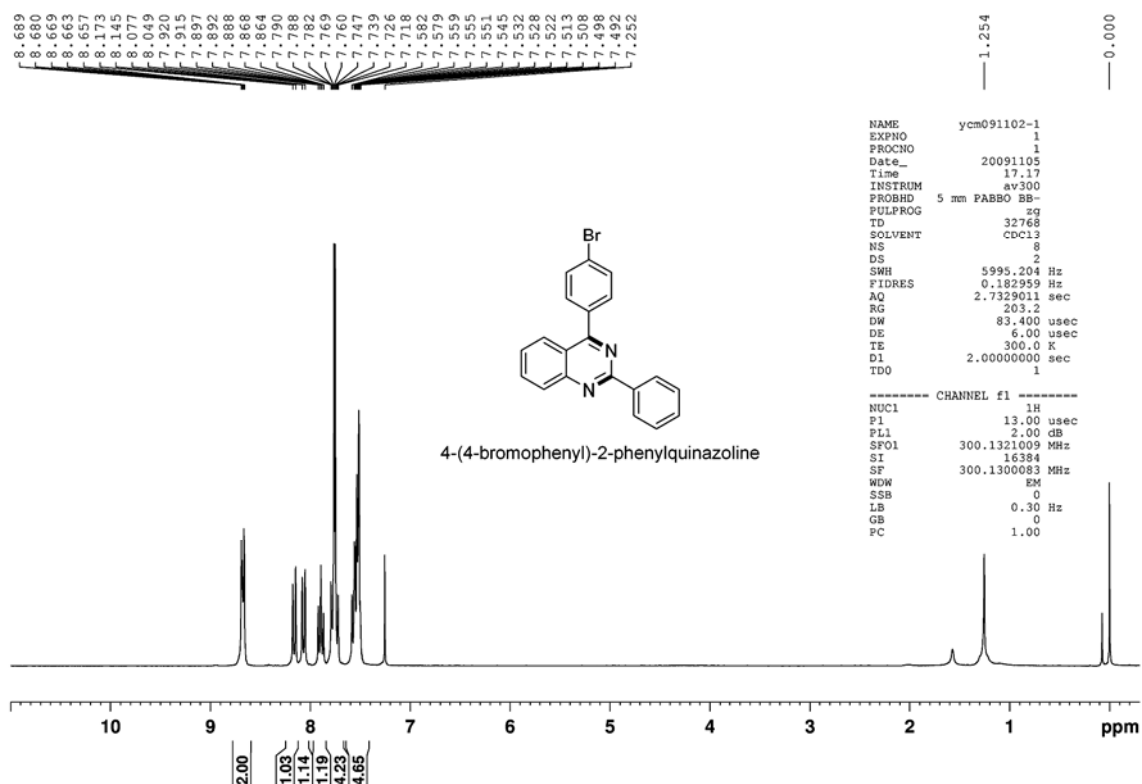
2,4-diphenylquinazoline (3aa)



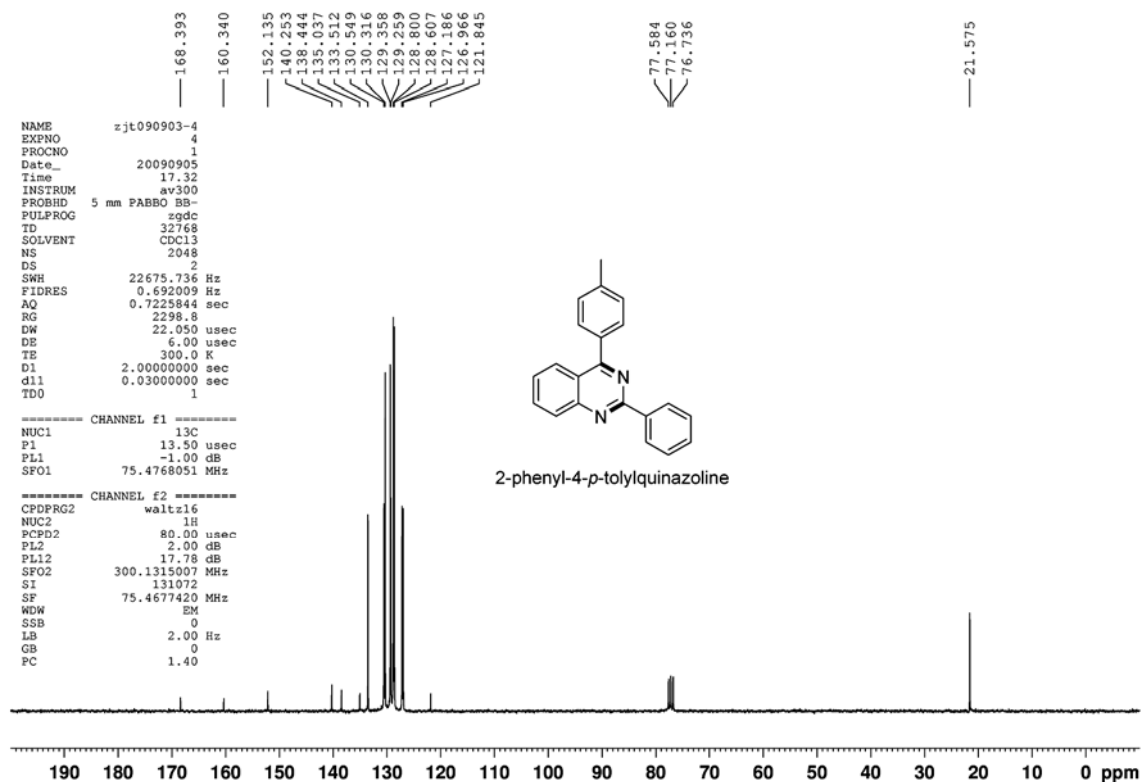
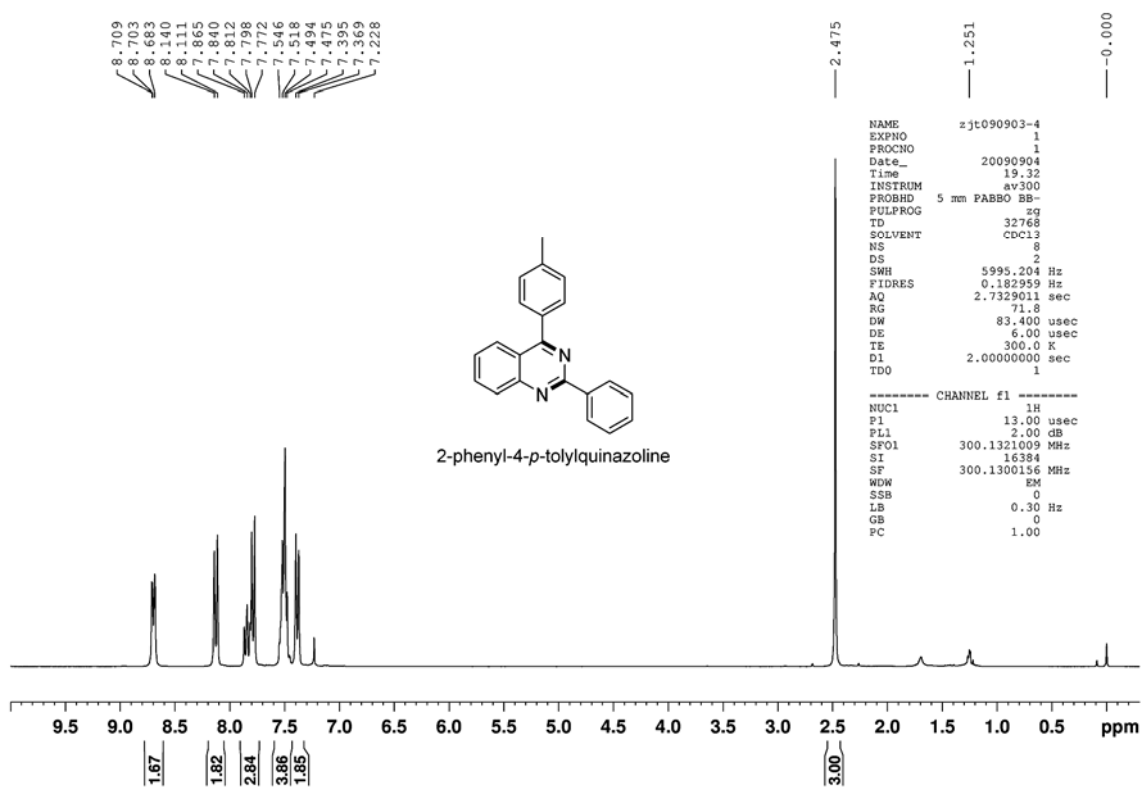
4-(4-fluorophenyl)-2-phenylquinazoline (3ba)



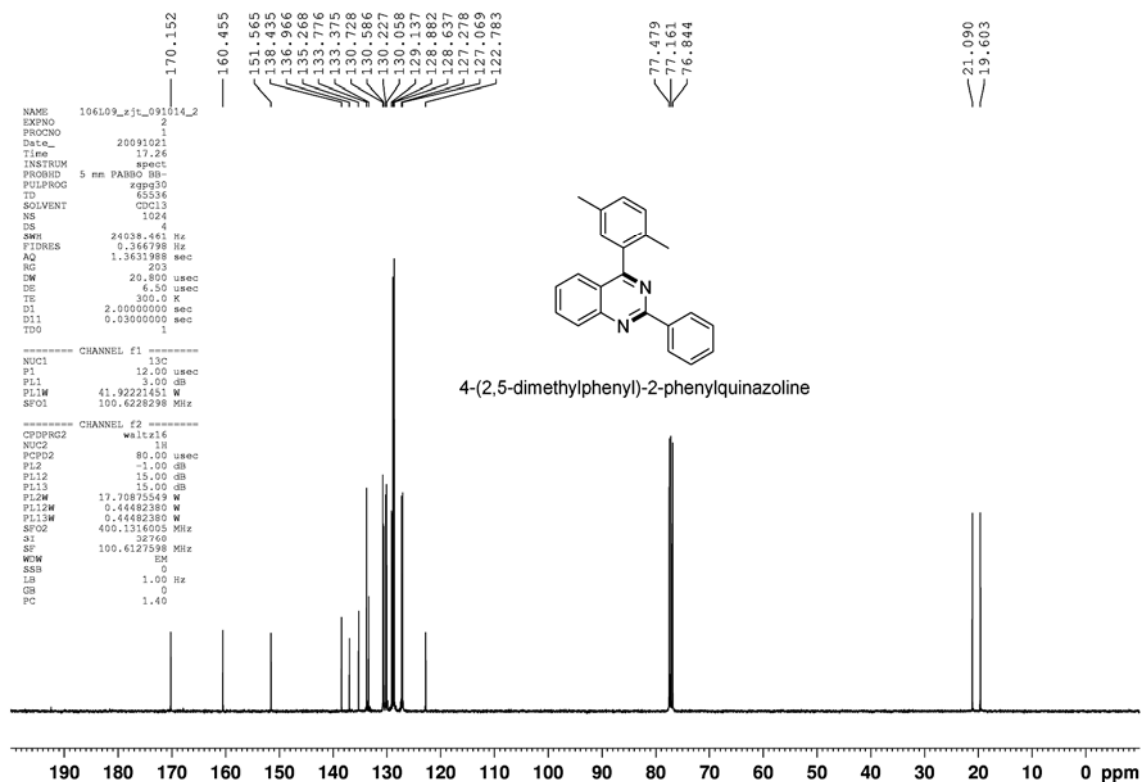
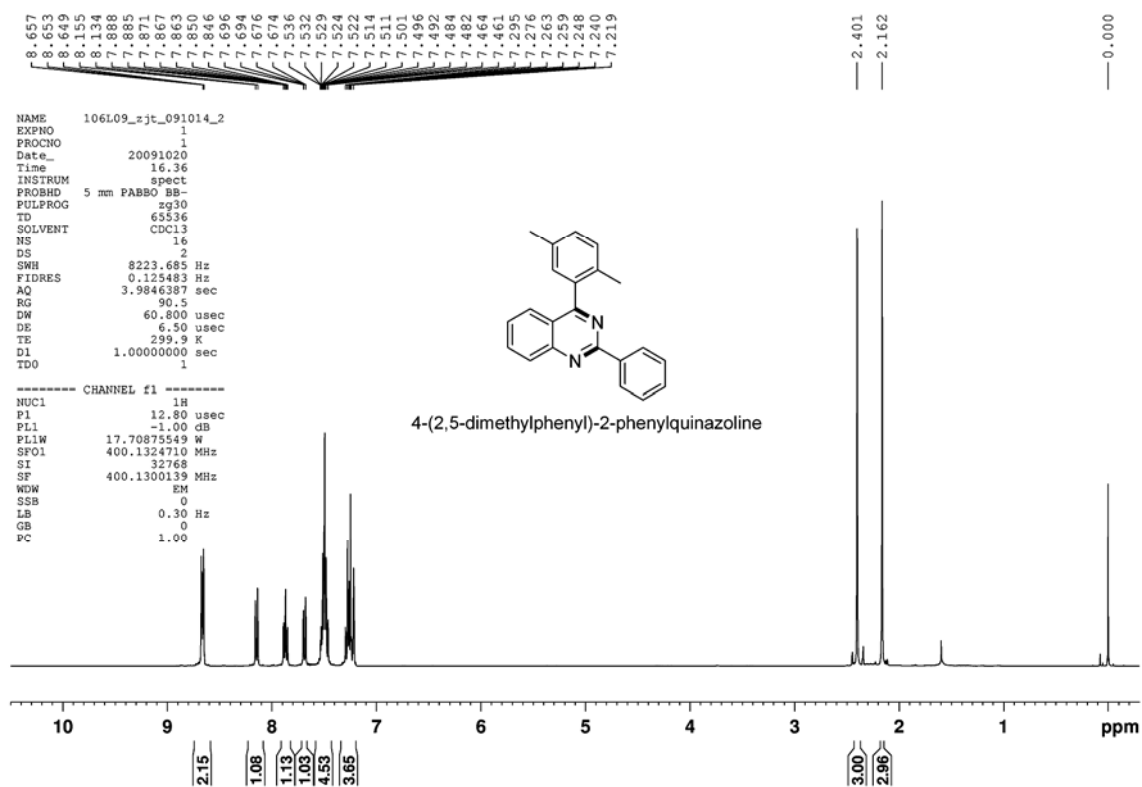
4-(4-bromophenyl)-2-phenylquinazoline (3ca)



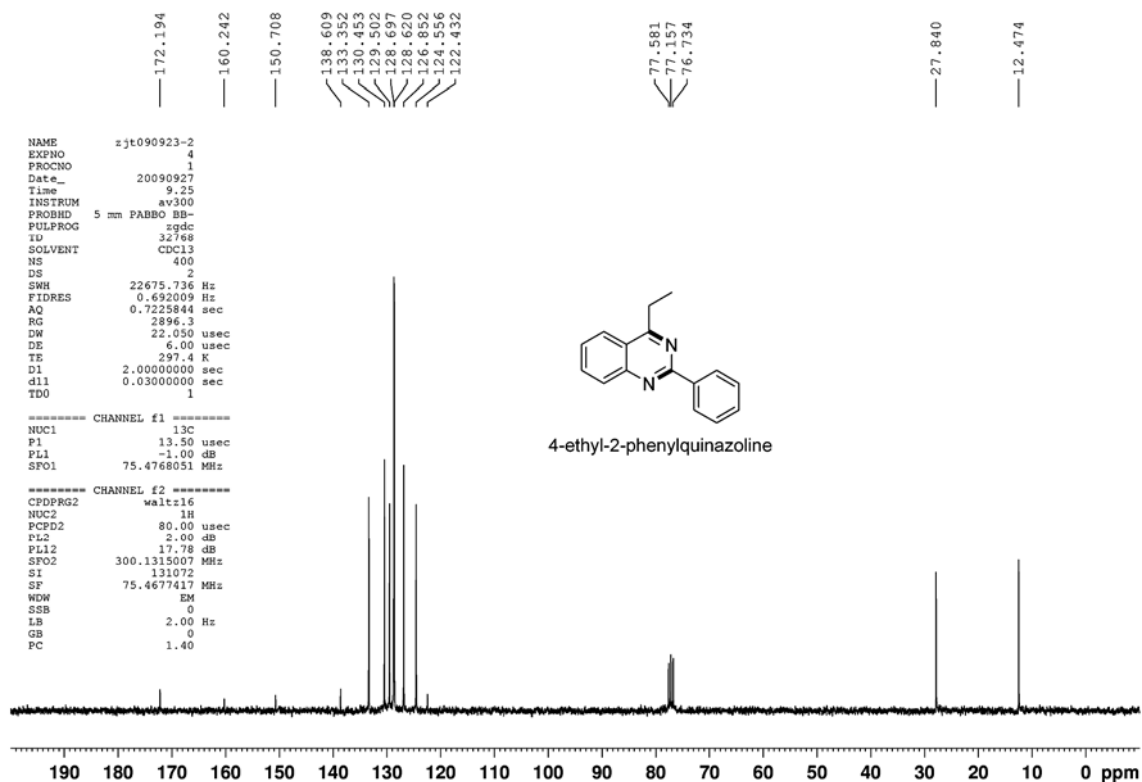
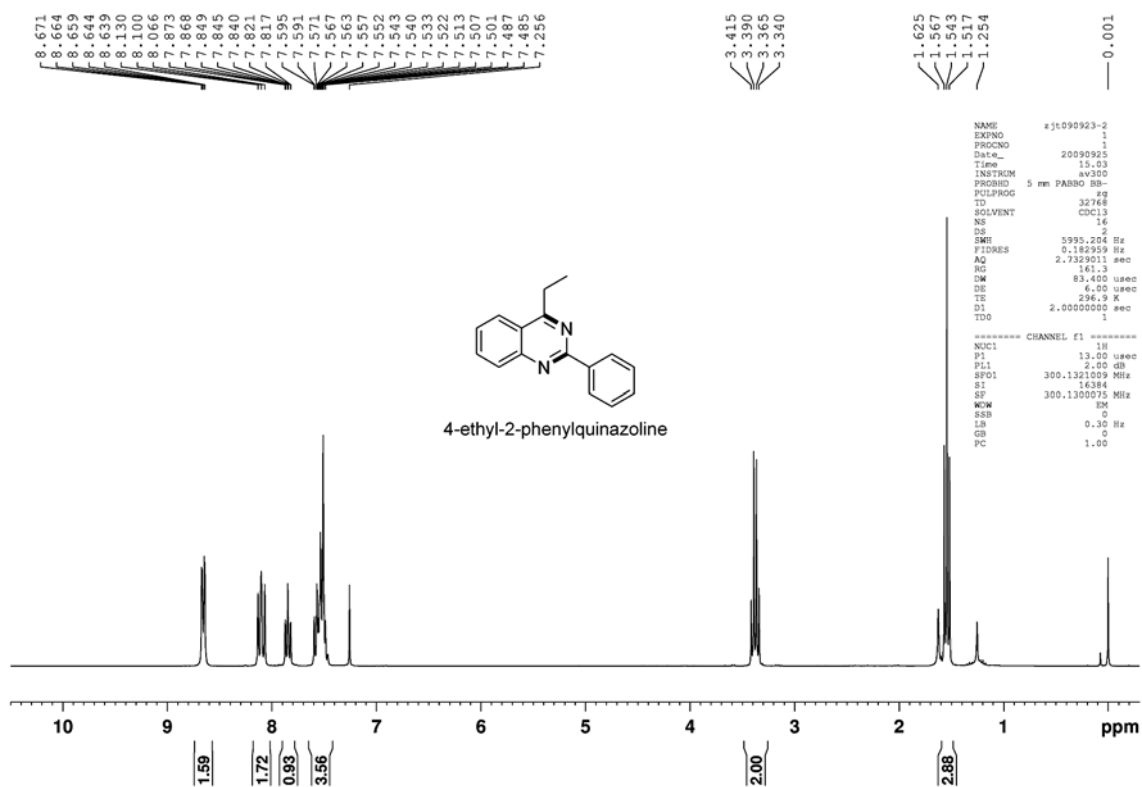
2-phenyl-4-p-tolylquinazoline (3da)



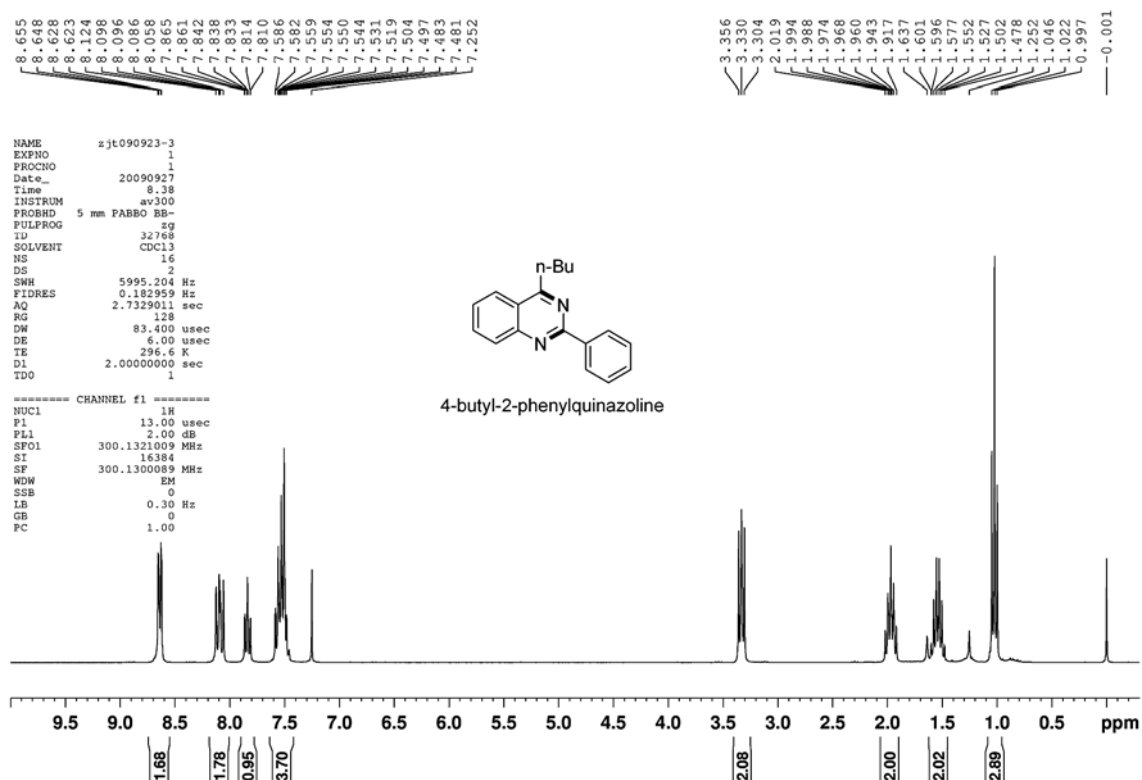
4-(2,5-dimethylphenyl)-2-phenylquinazoline (3ea)



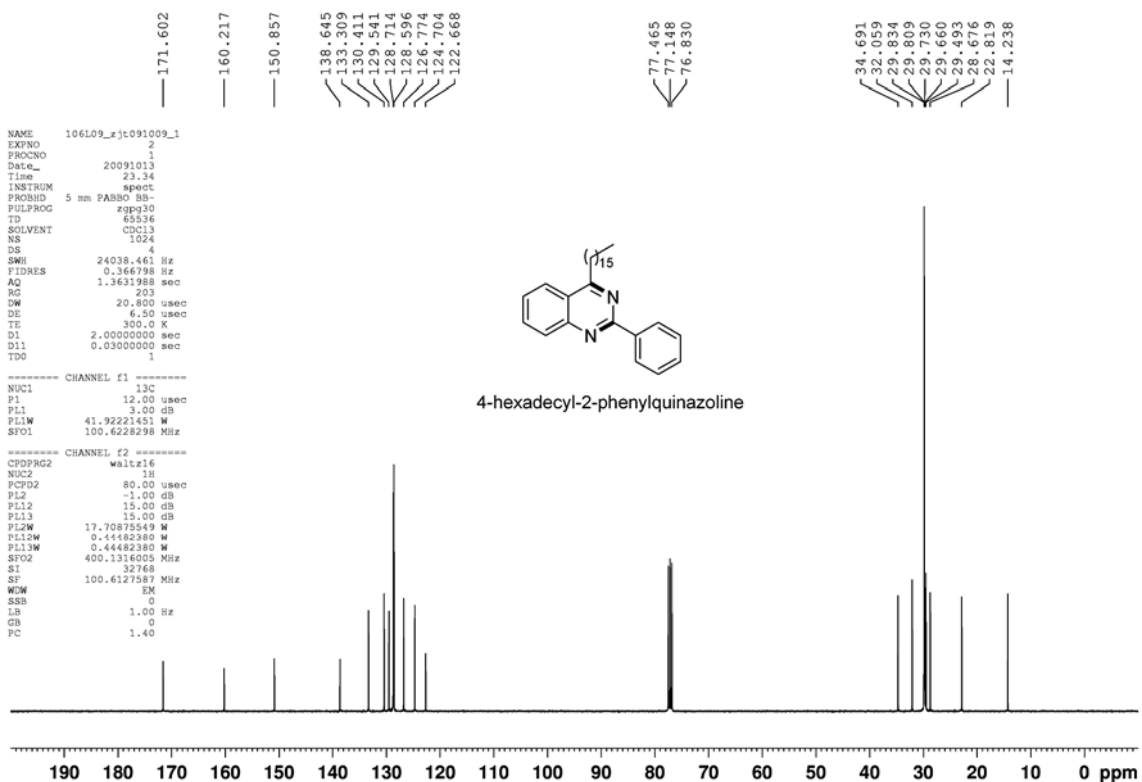
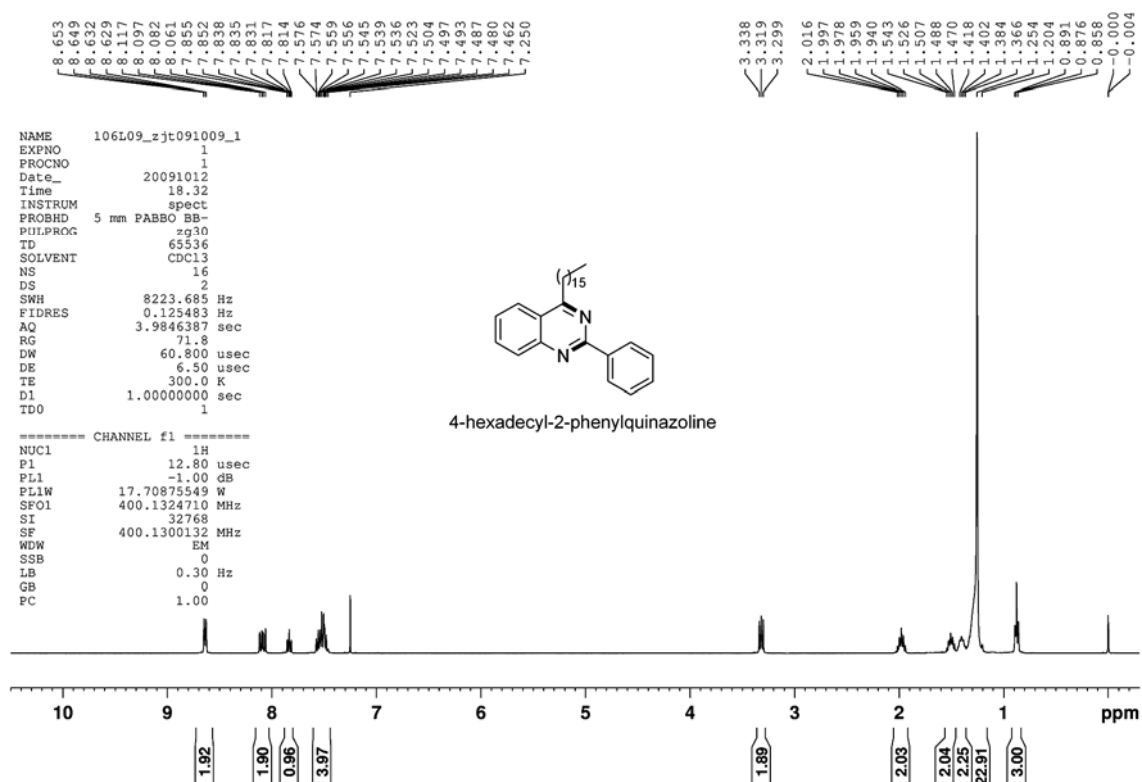
4-ethyl-2-phenylquinazoline (3ga)



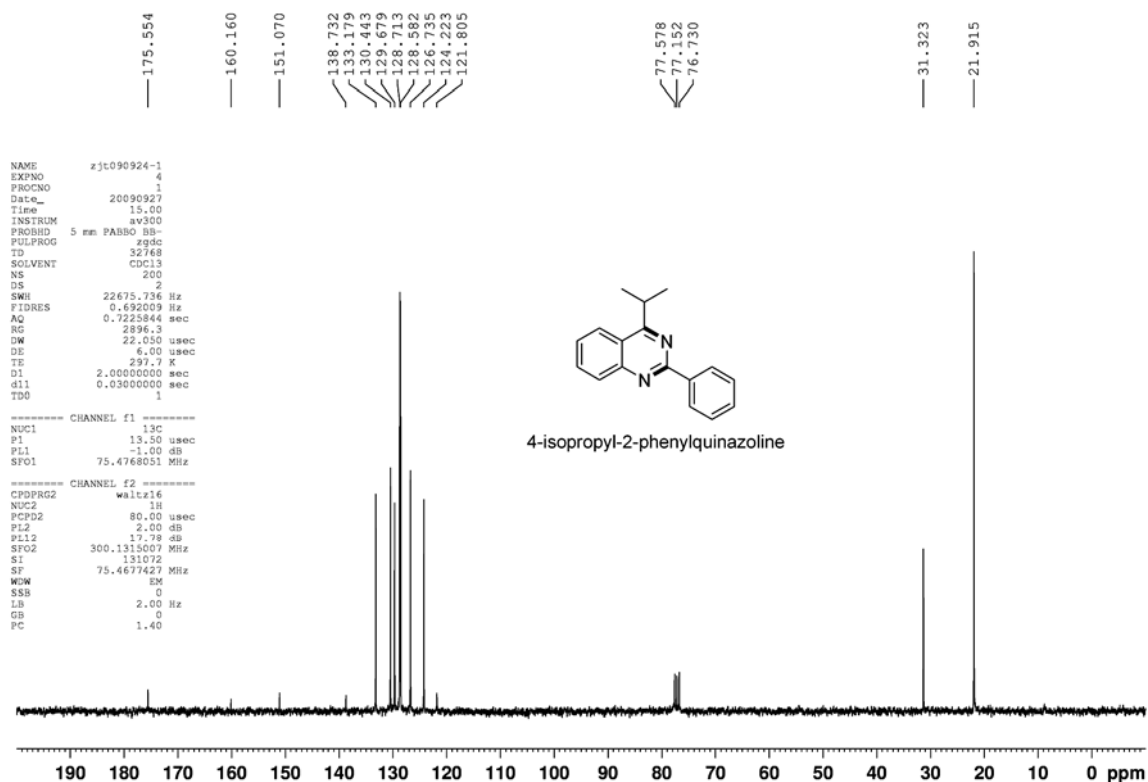
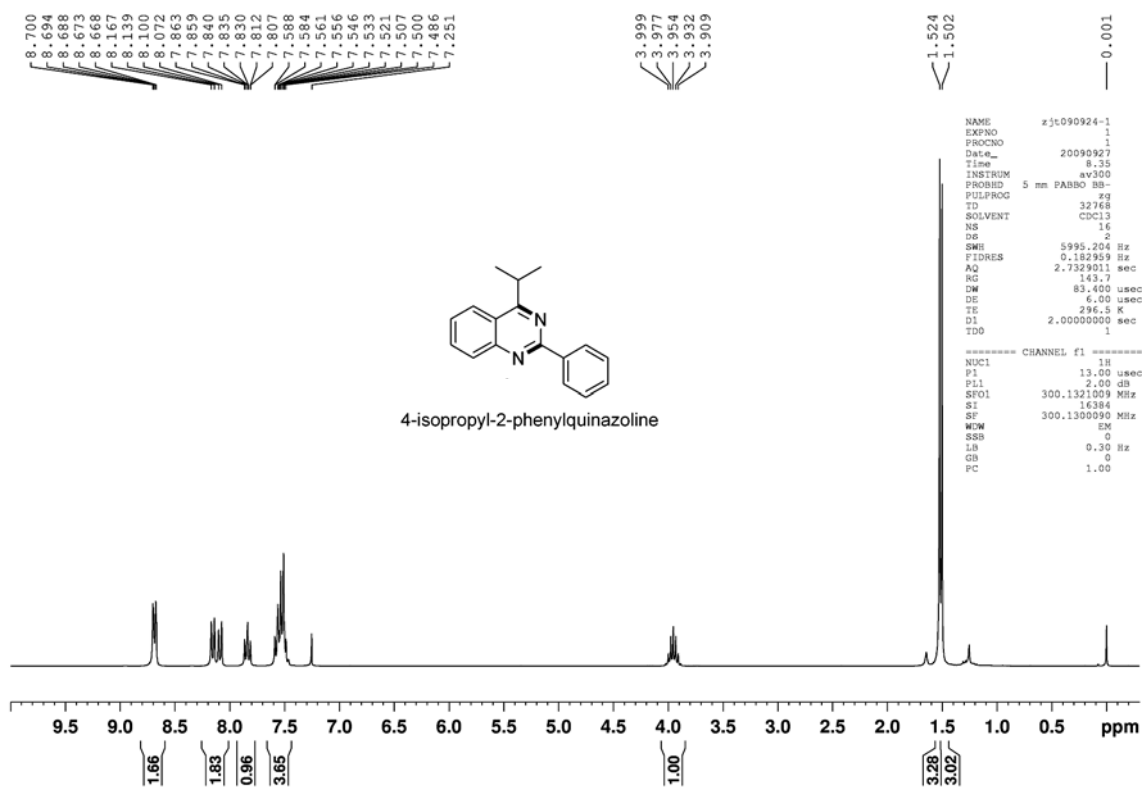
4-butyl-2-phenylquinazoline (3ha)



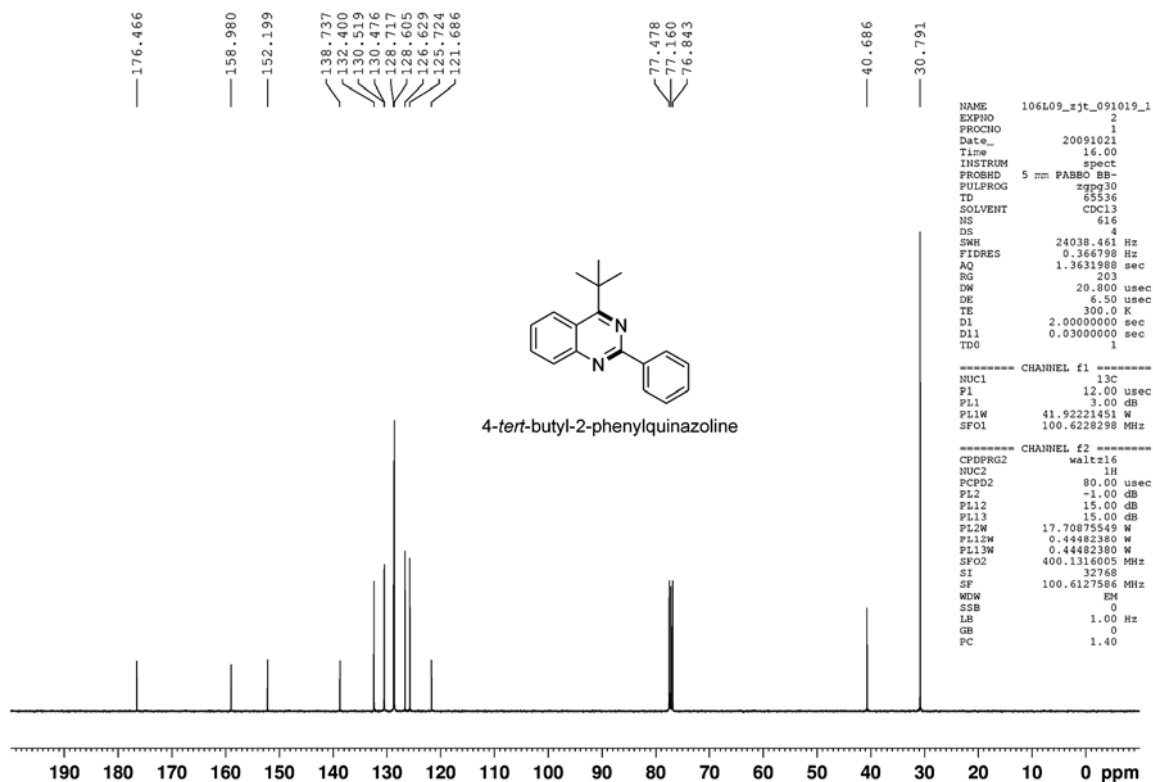
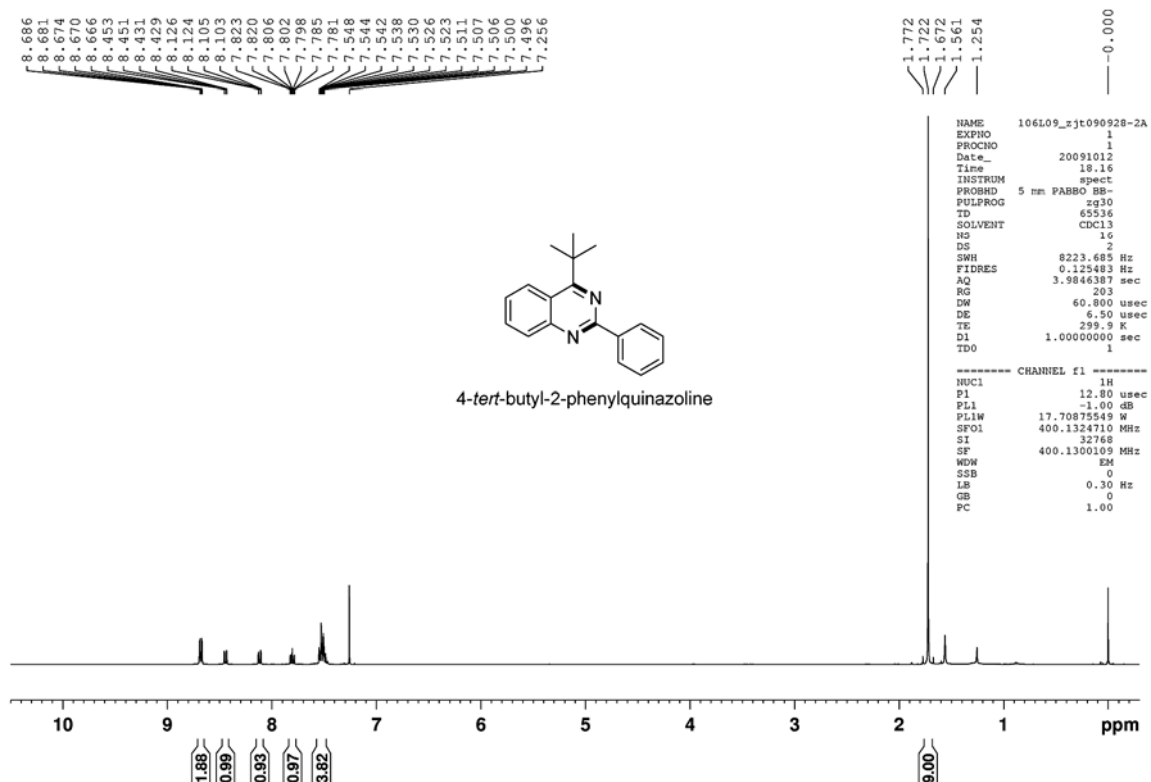
4-hexadecyl-2-phenylquinazoline (3ia)



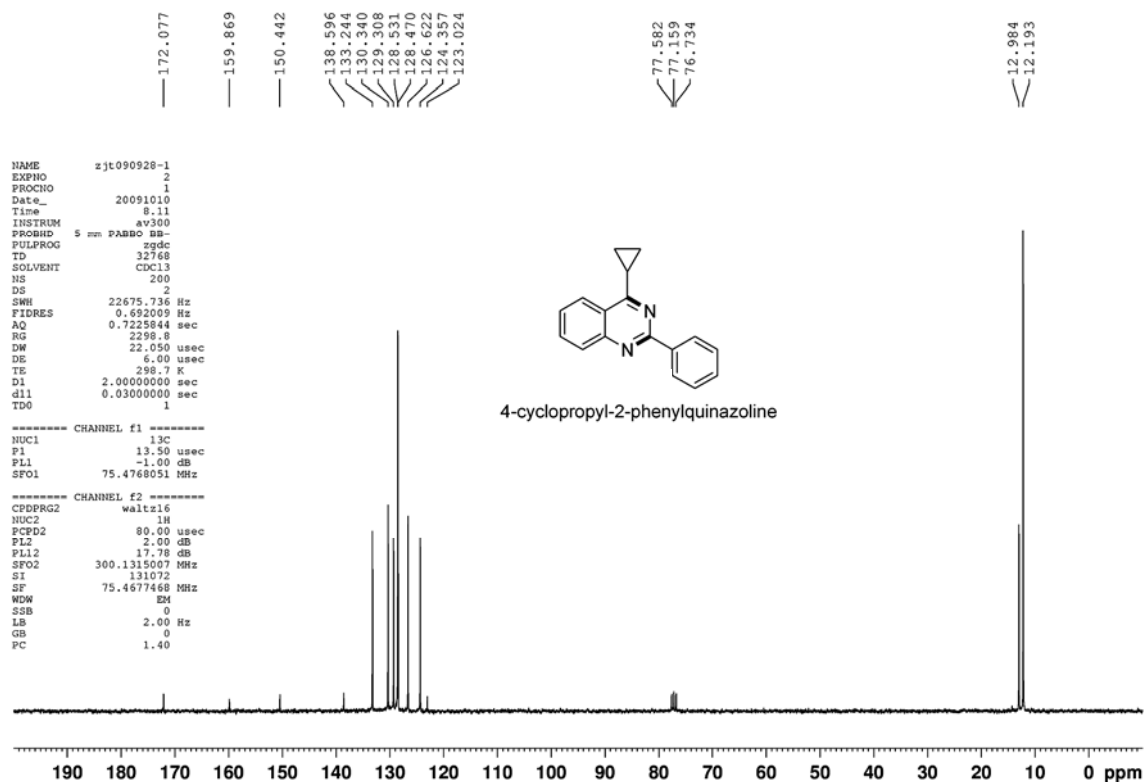
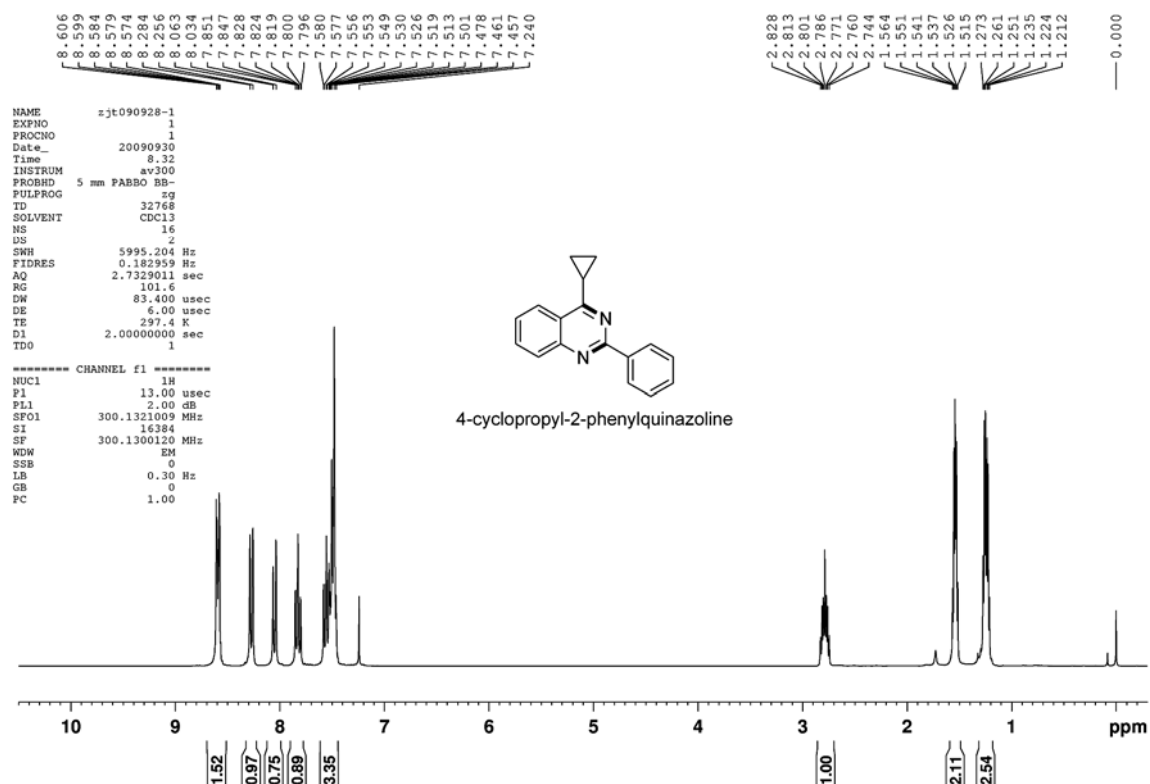
4-isopropyl-2-phenylquinazoline (3ja)



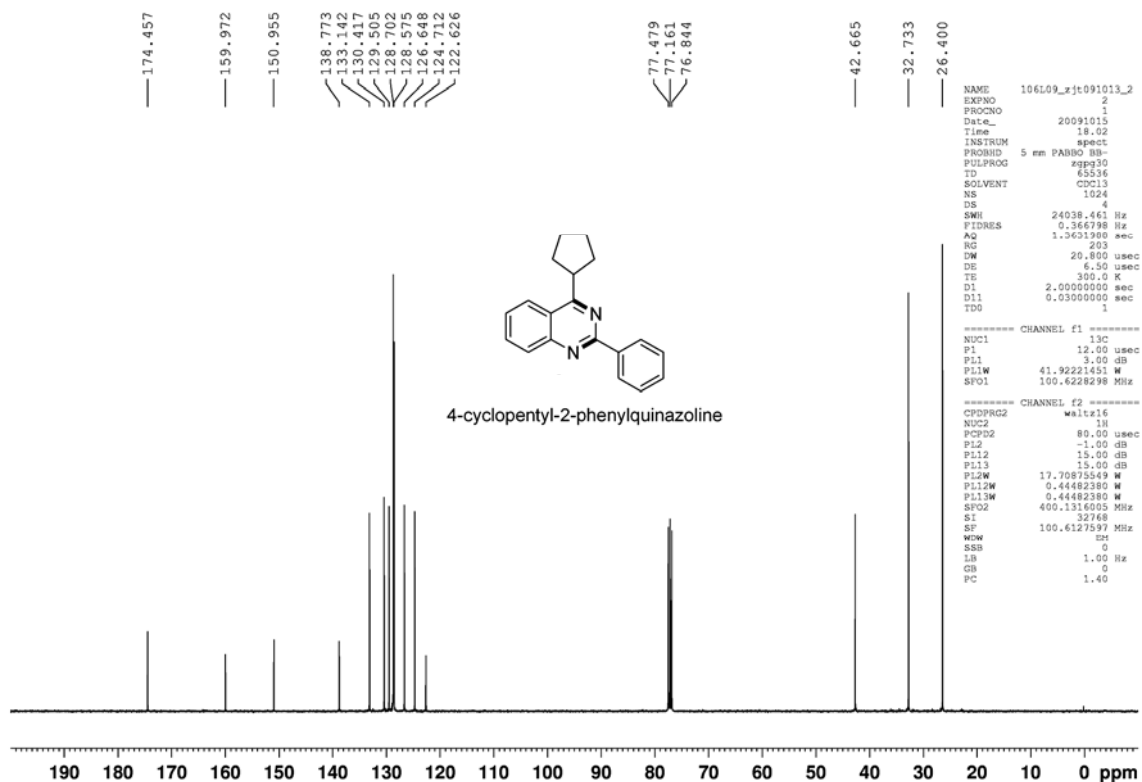
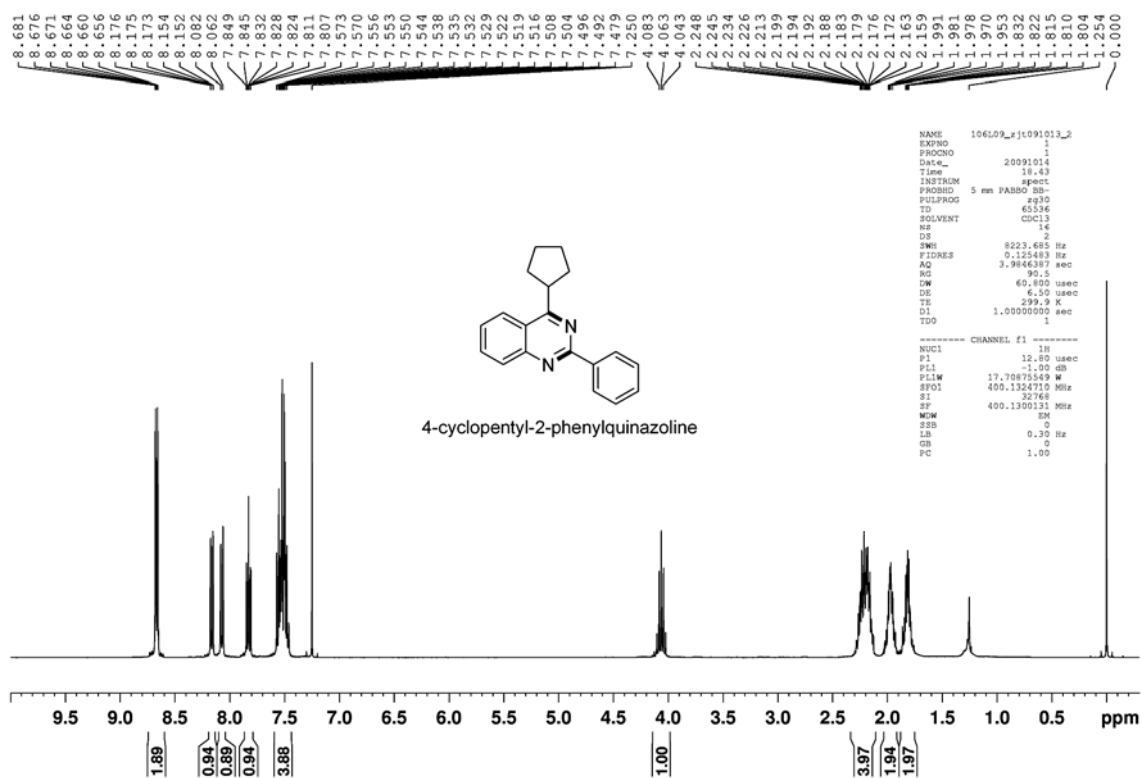
4-tert-butyl-2-phenylquinazoline (3ka)



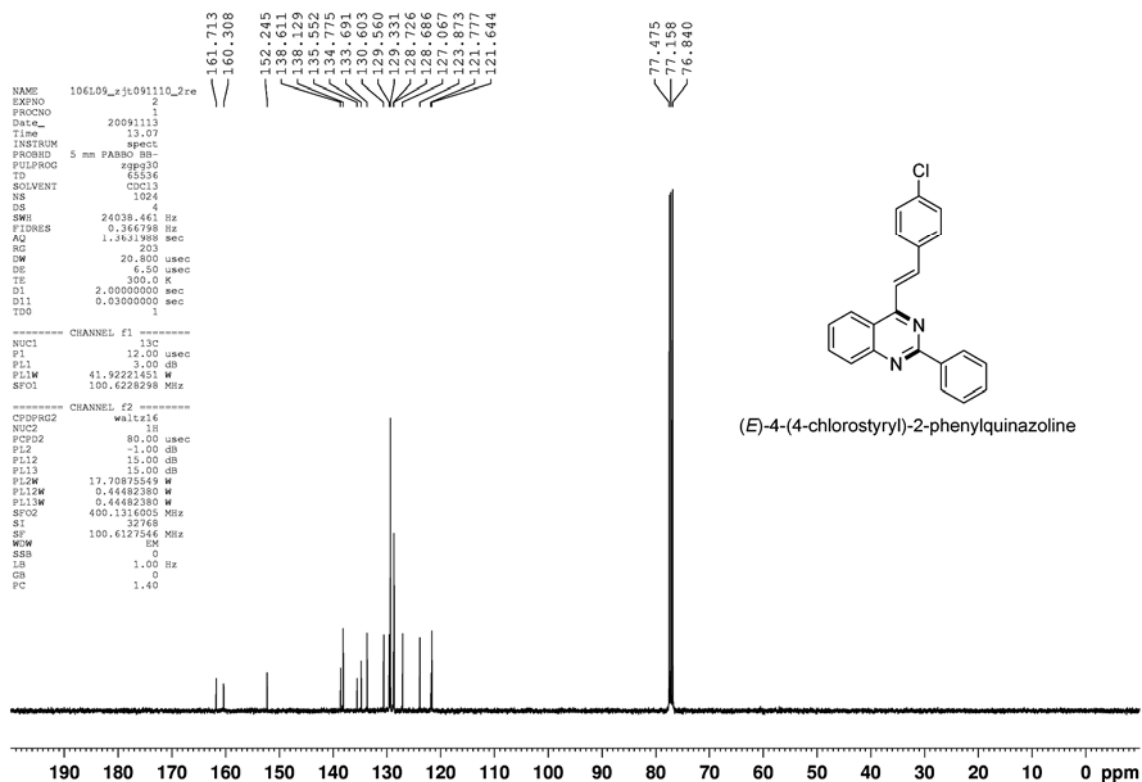
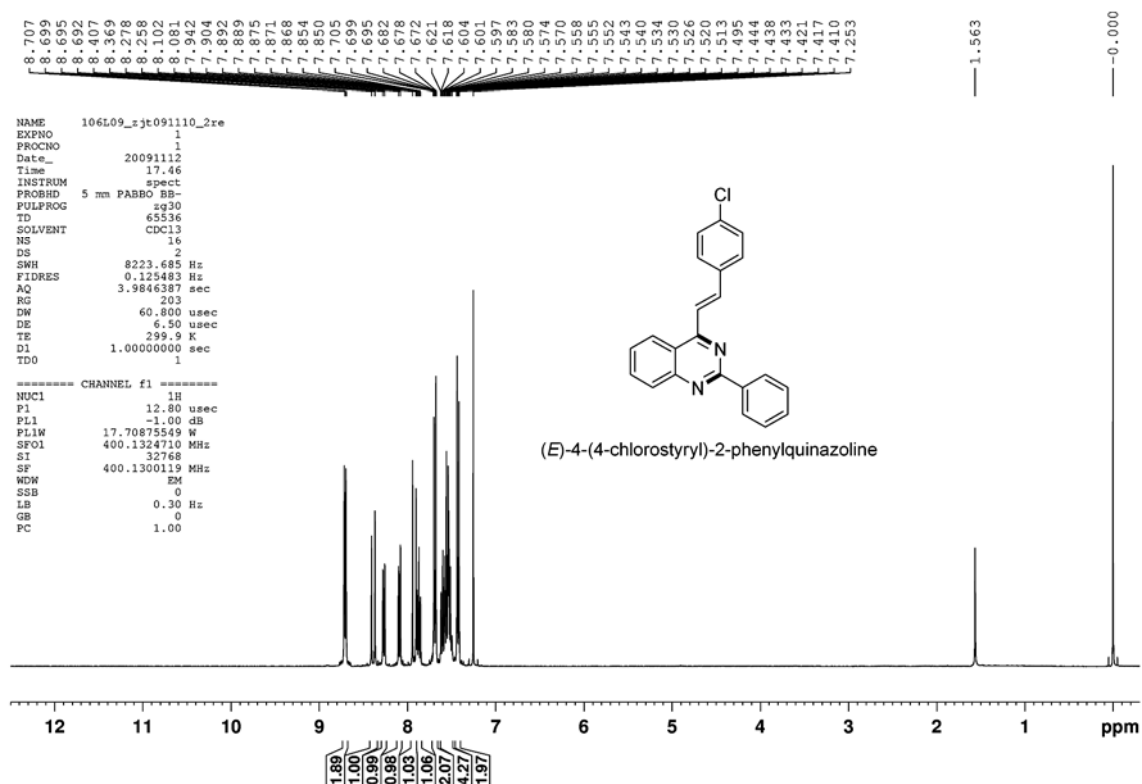
4-cyclopropyl-2-phenylquinazoline (3la)



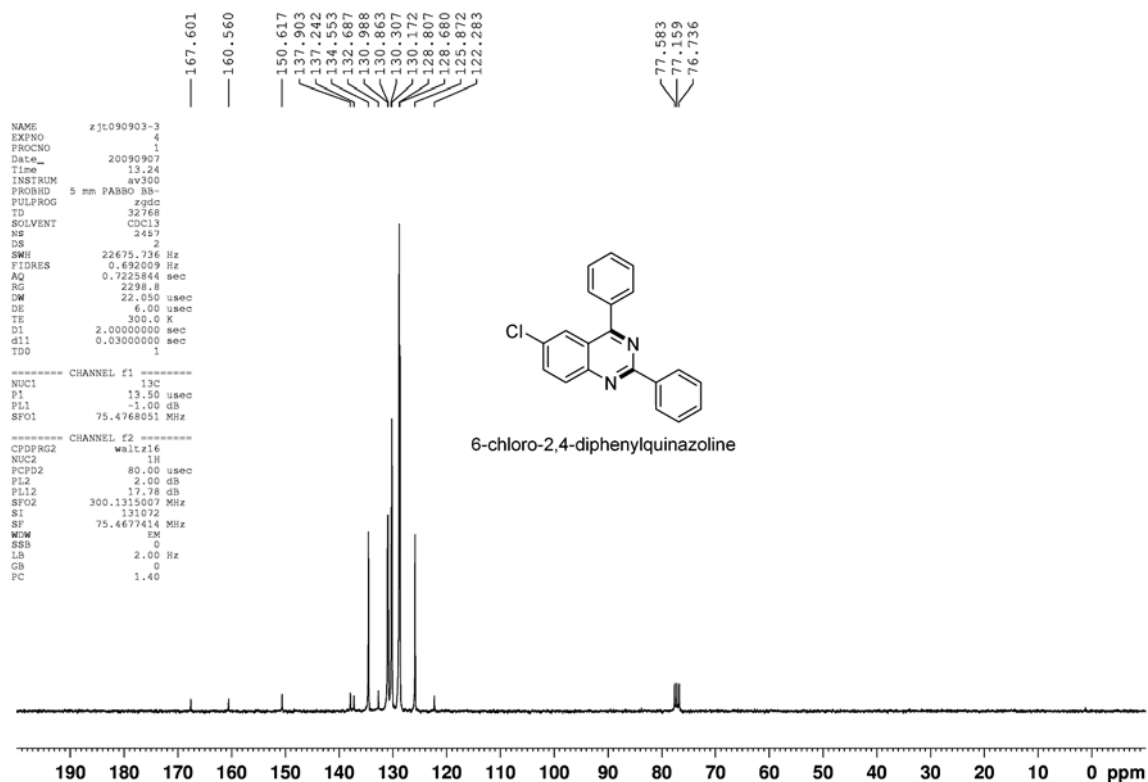
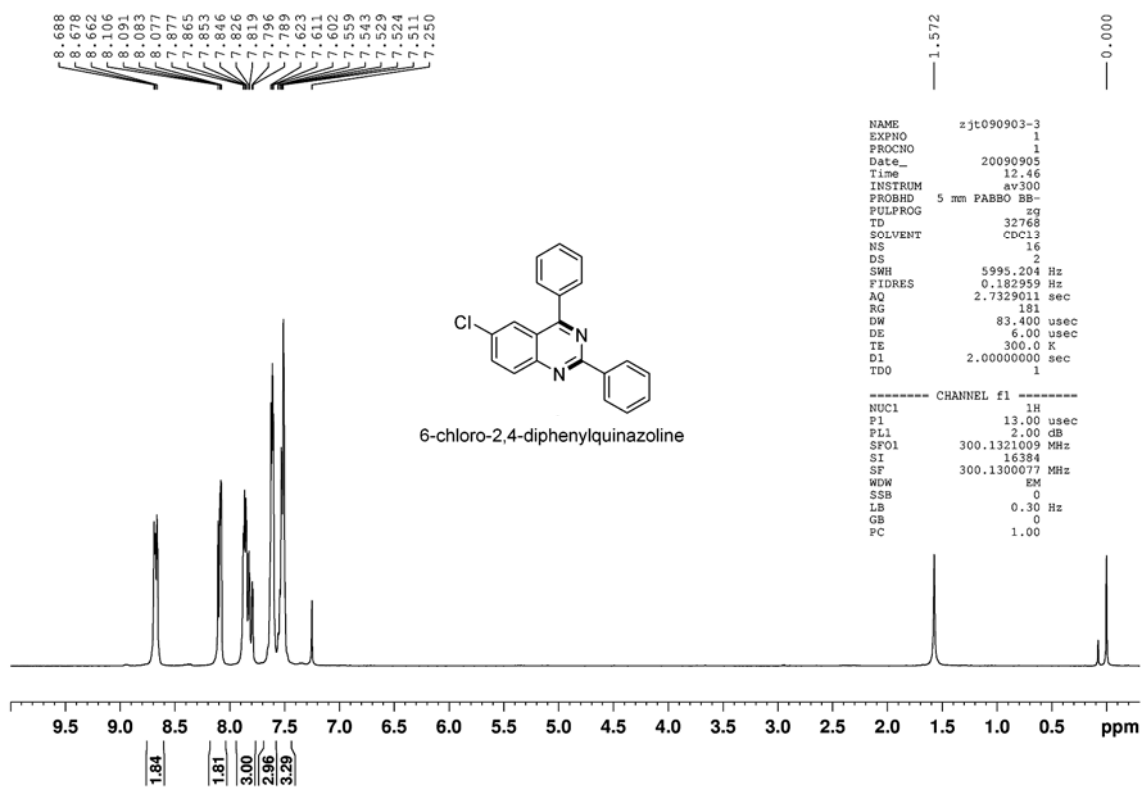
4-cyclopentyl-2-phenylquinazoline (3ma)



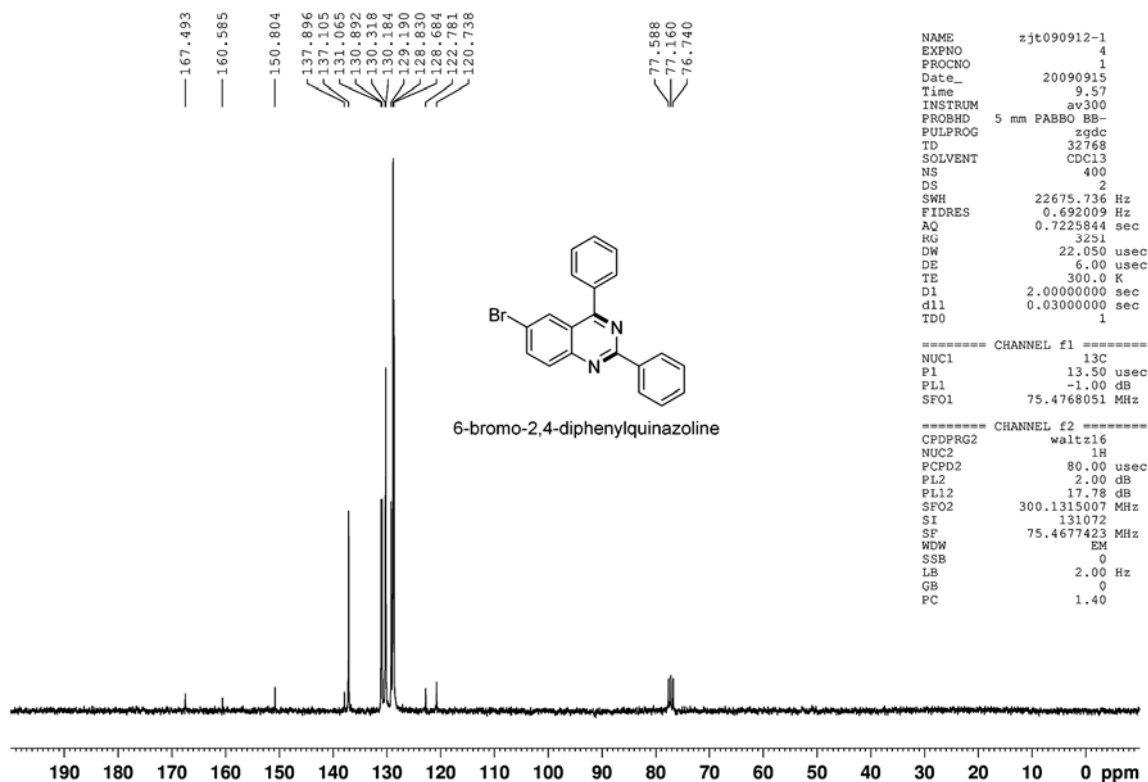
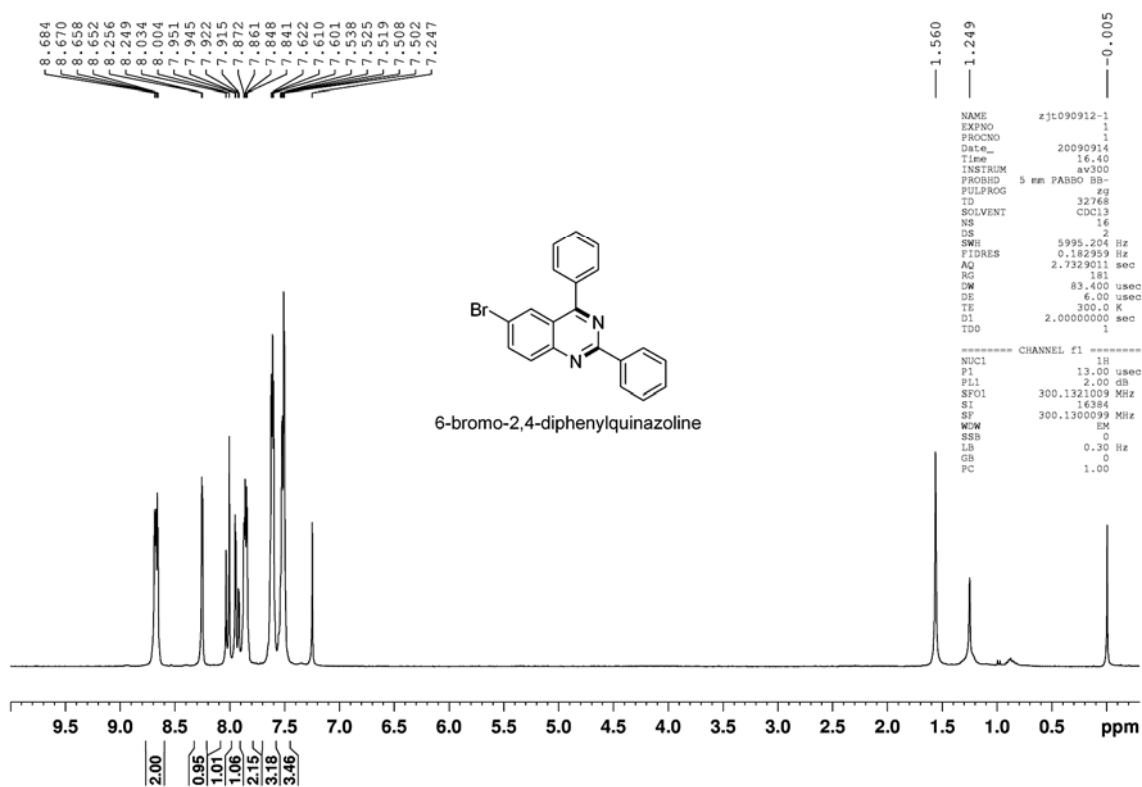
(E)-4-(4-chlorostyryl)-2-phenylquinazoline (3na)



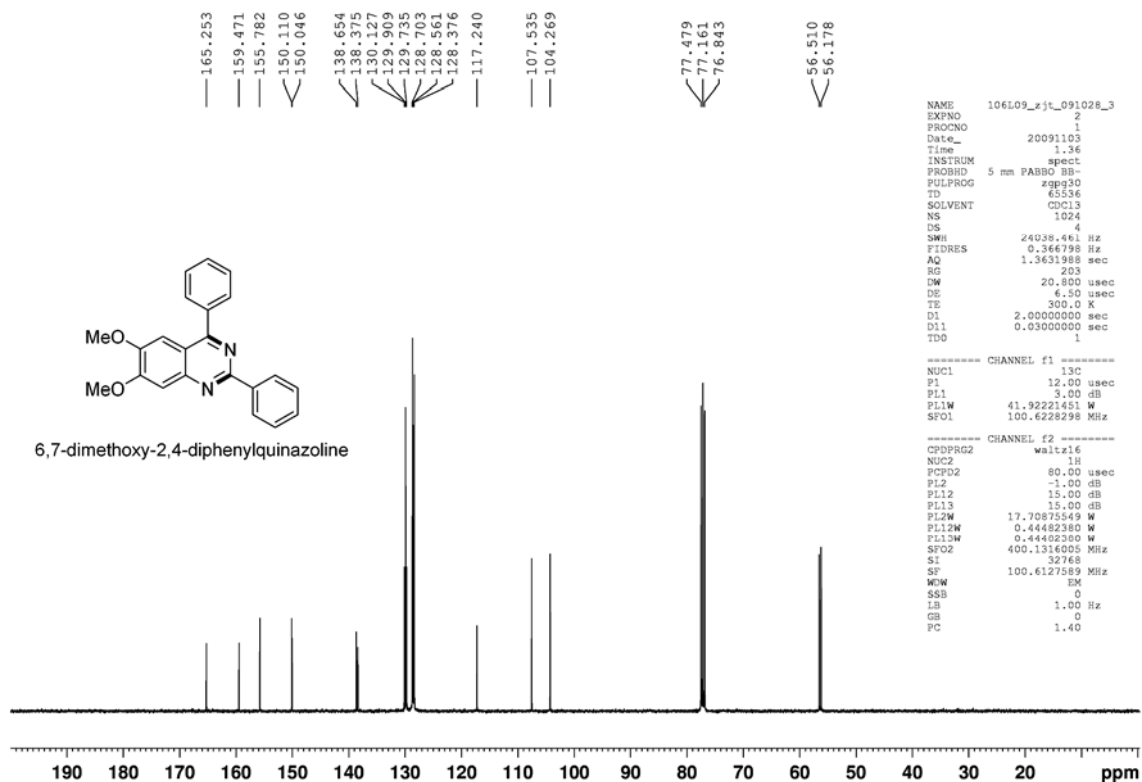
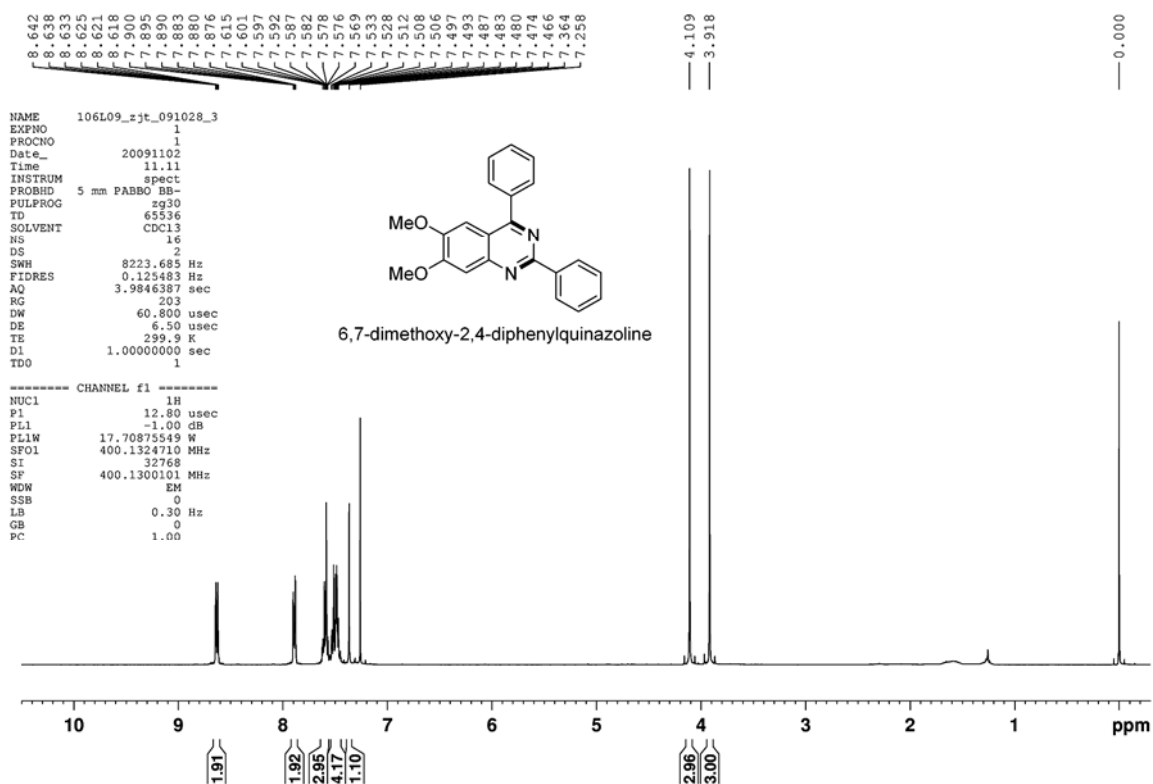
6-chloro-2,4-diphenylquinazoline (30a)



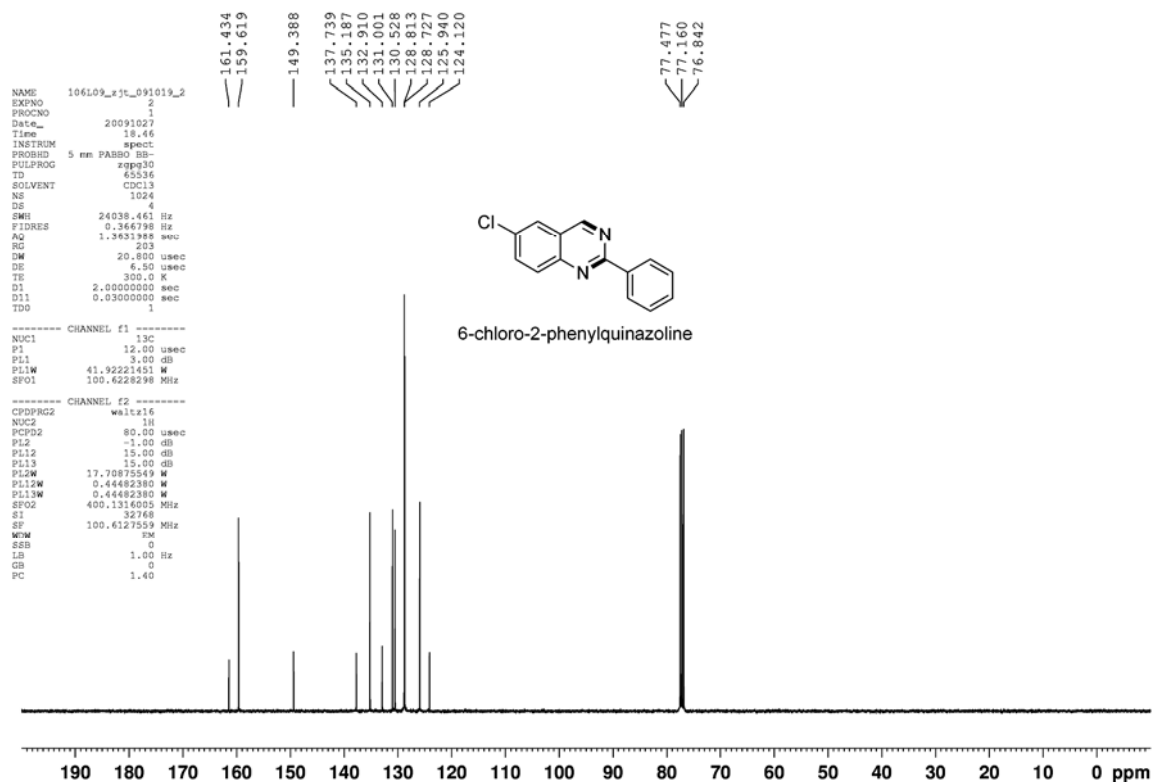
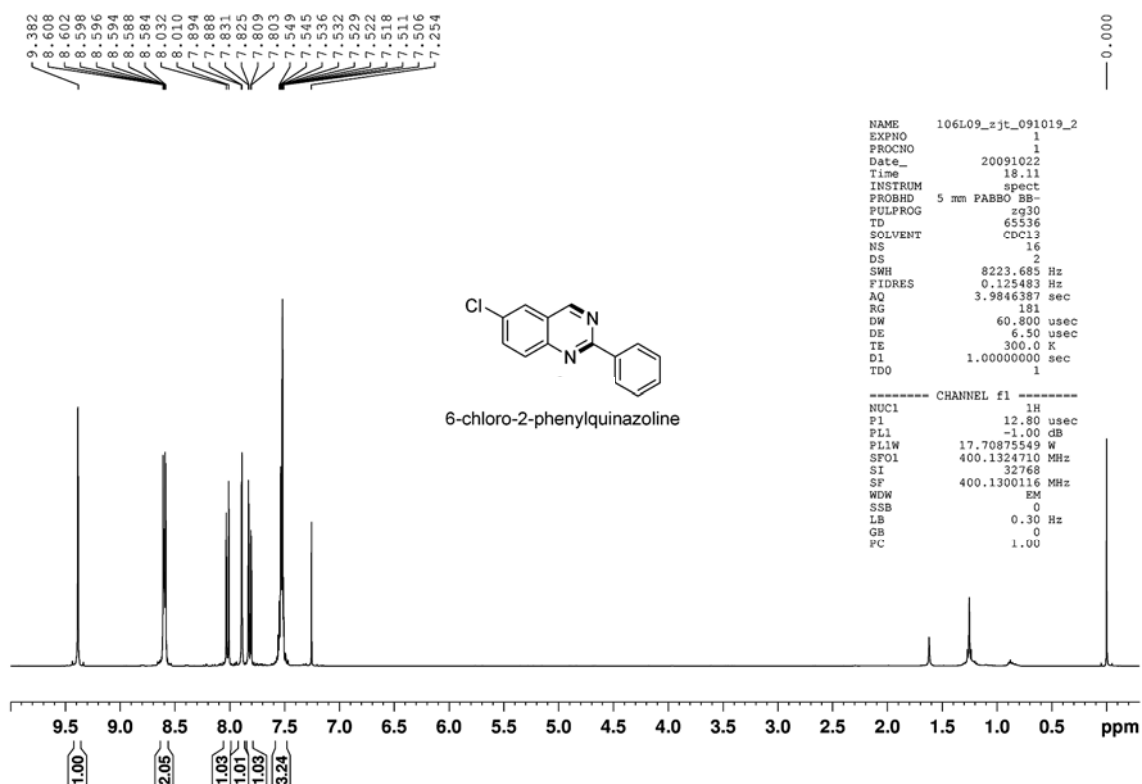
6-bromo-2,4-diphenylquinazoline (3pa)



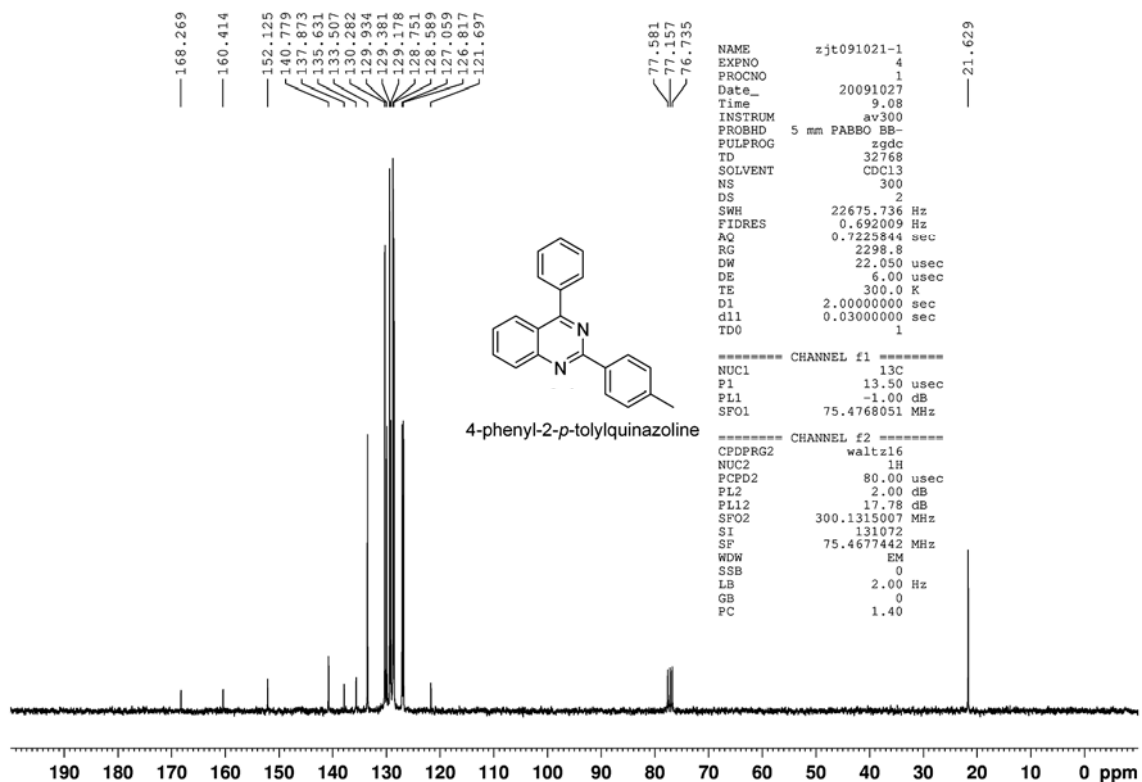
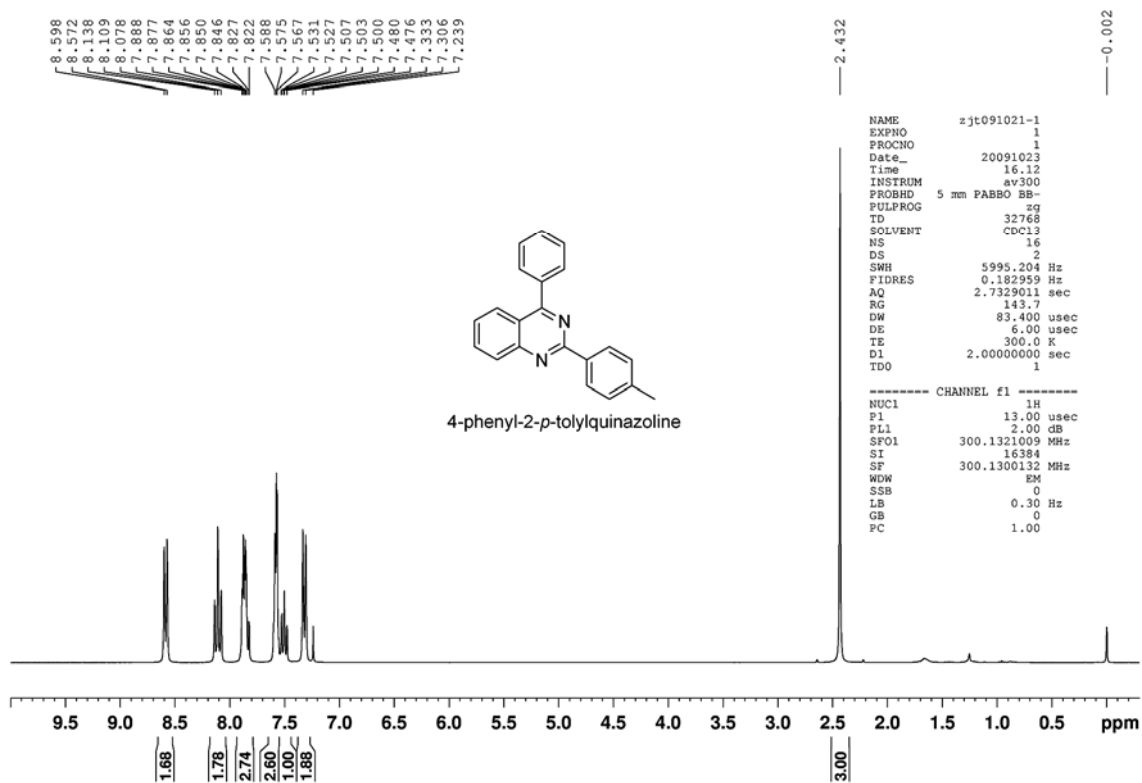
6,7-dimethoxy-2,4-diphenylquinazoline (3qa)



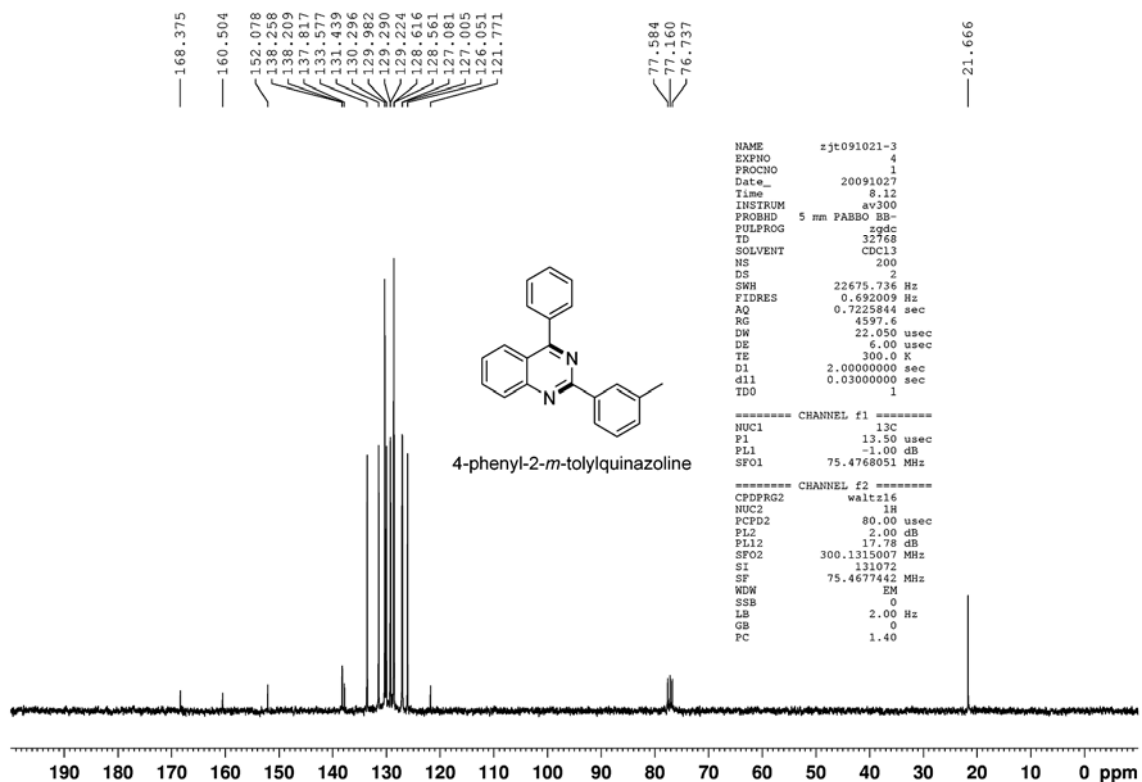
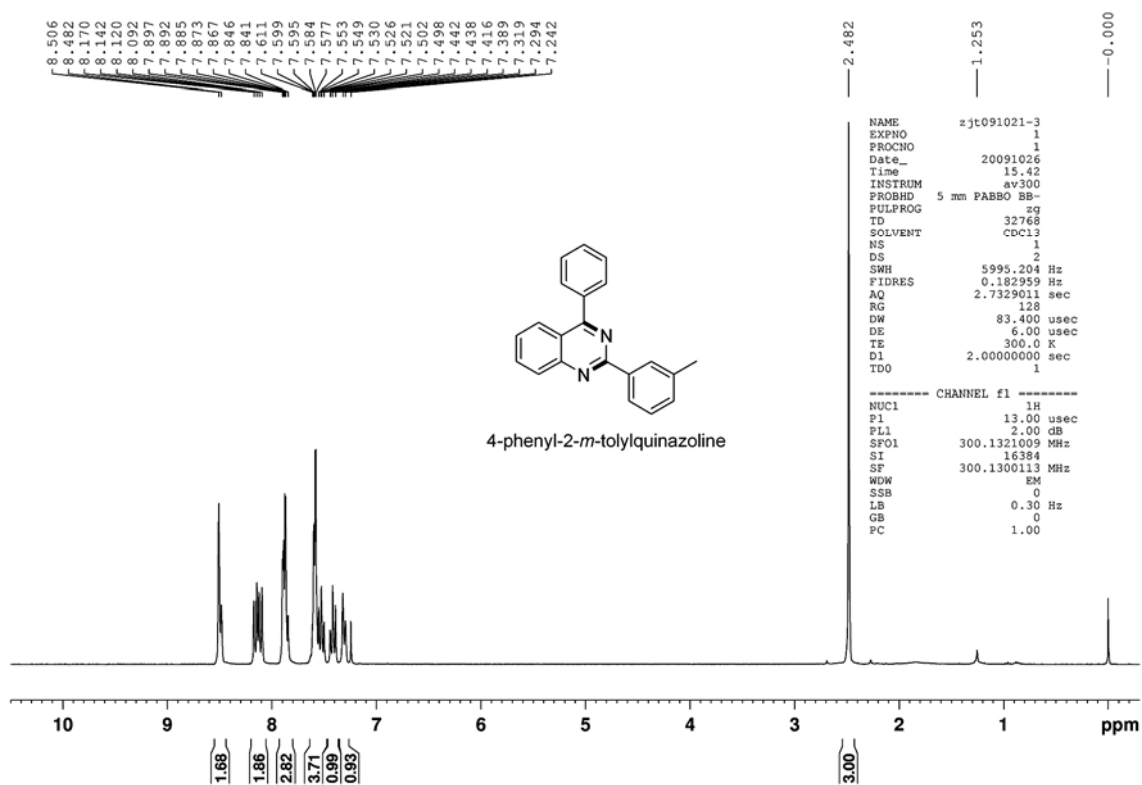
6-chloro-2-phenylquinazoline (3ra)



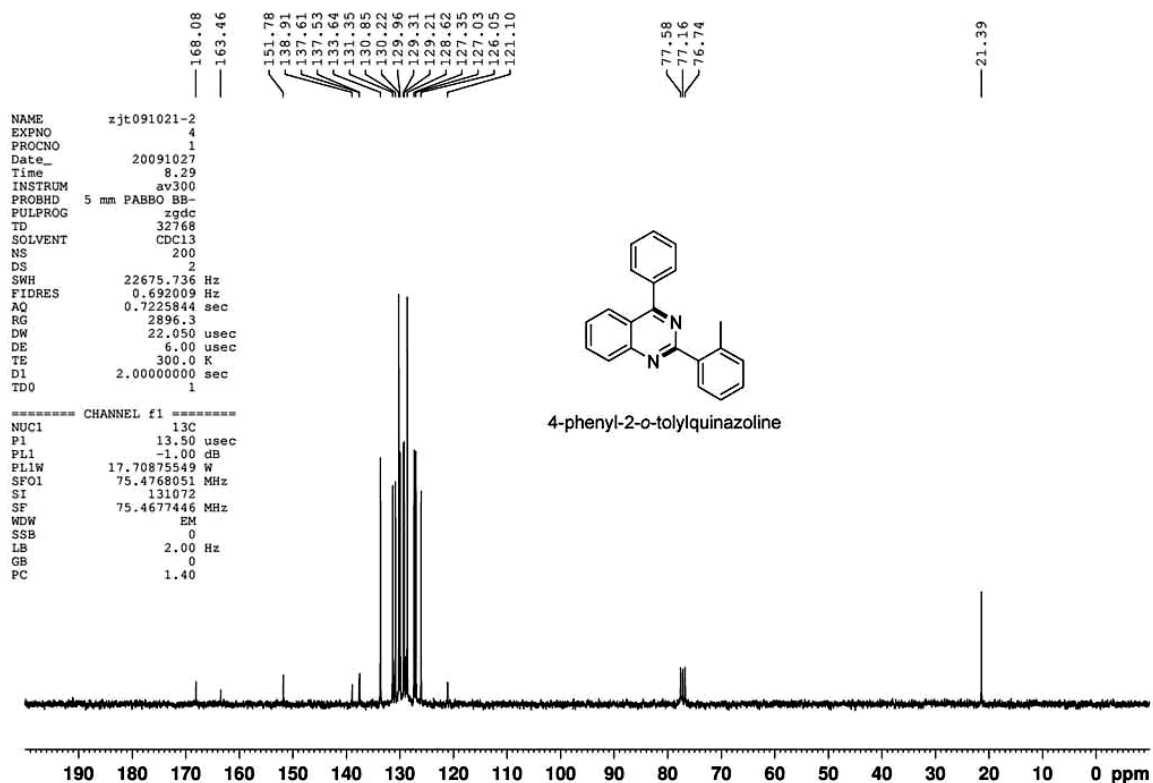
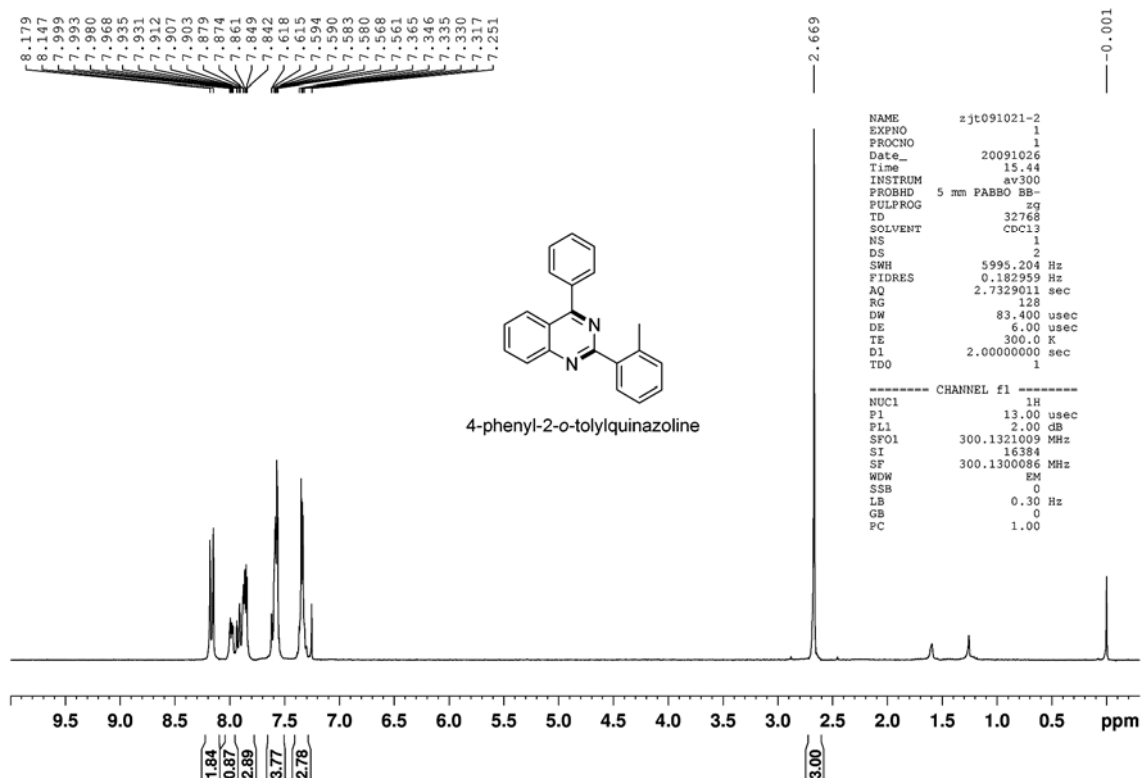
4-phenyl-2-*p*-tolylquinazoline (3ab)



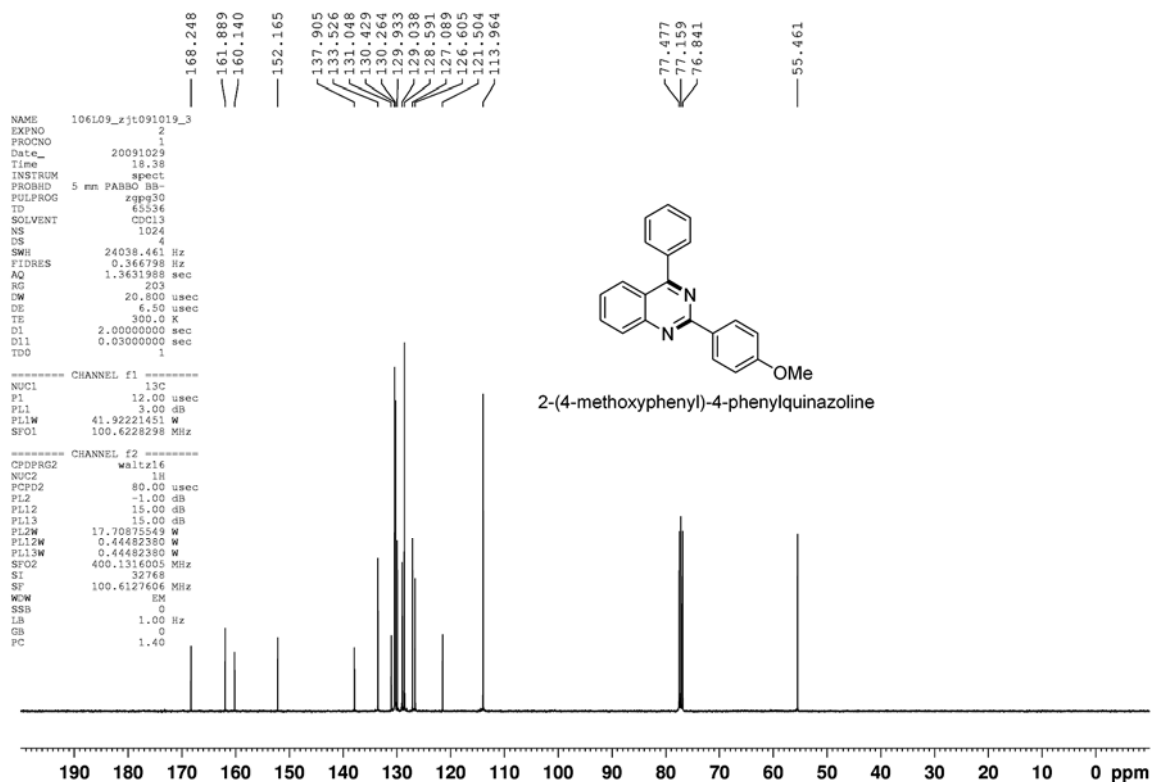
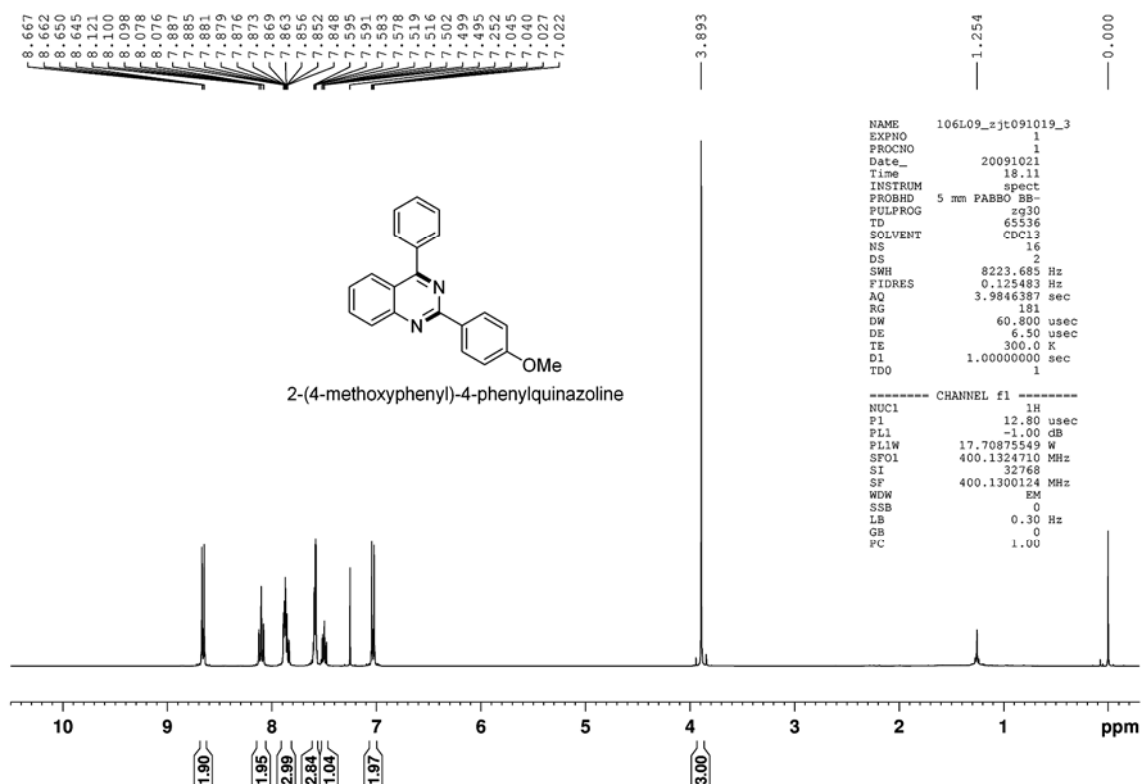
4-phenyl-2-*m*-tolylquinazoline (3ac)



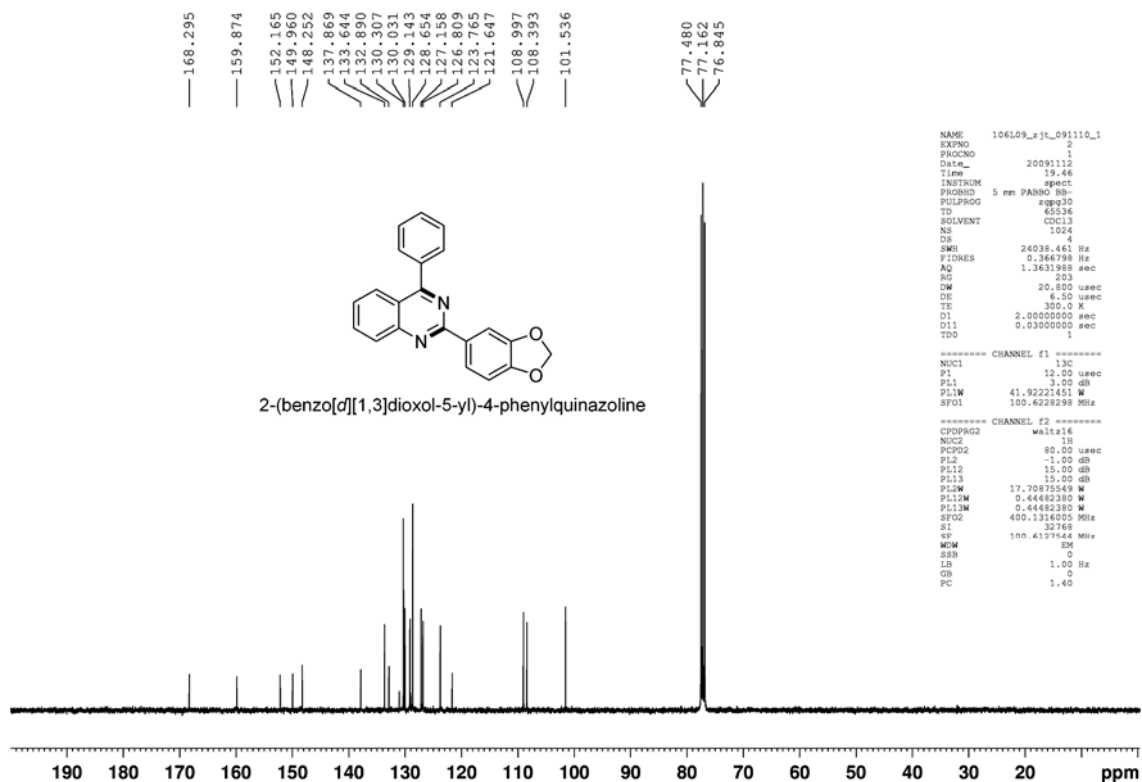
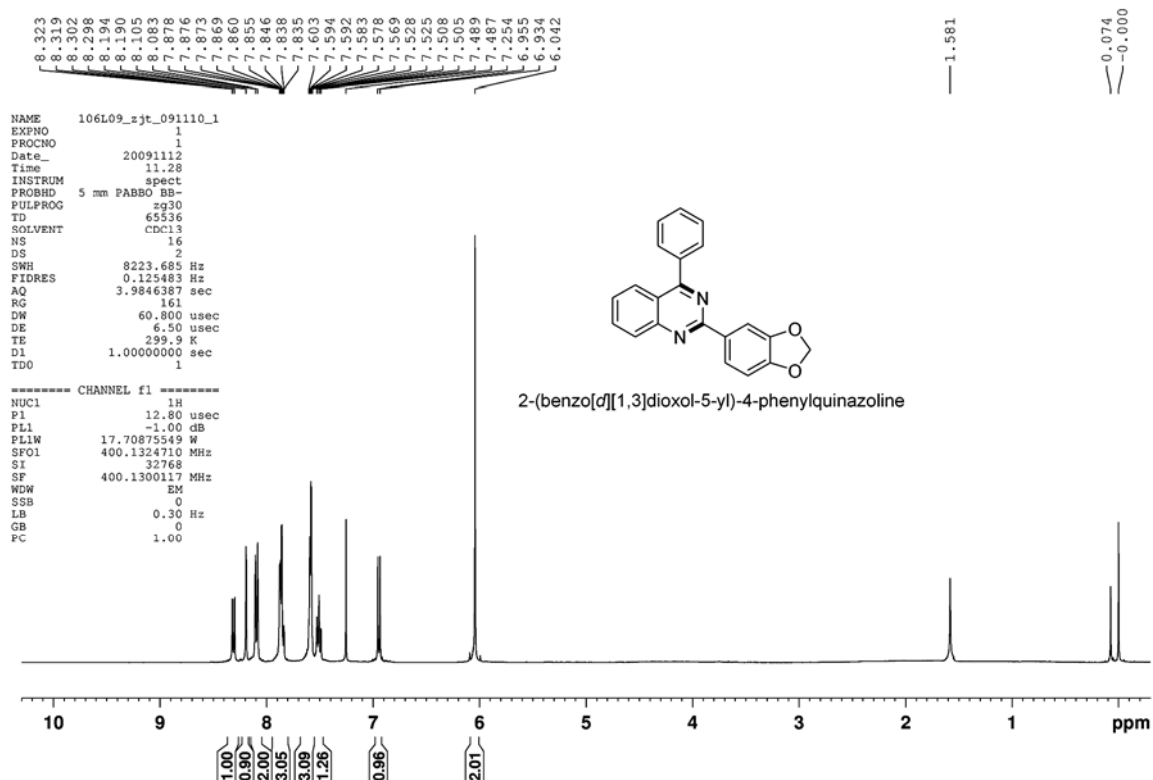
4-phenyl-2-o-tolylquinazoline (3ad)



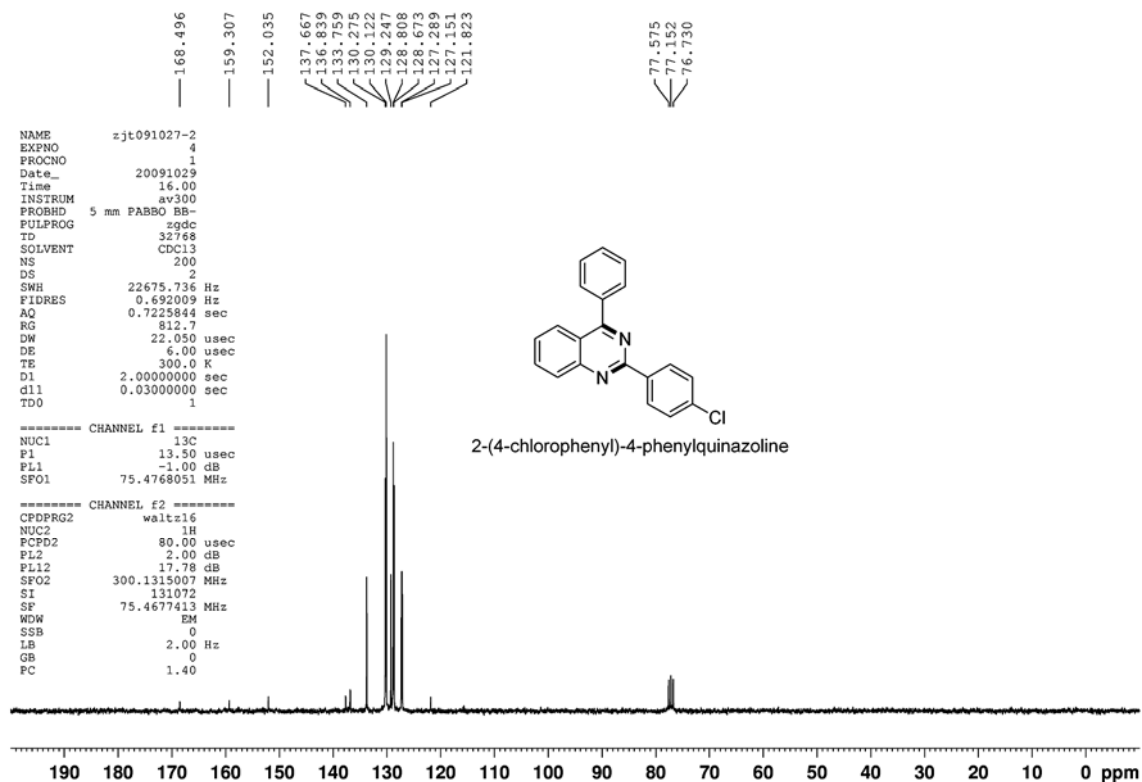
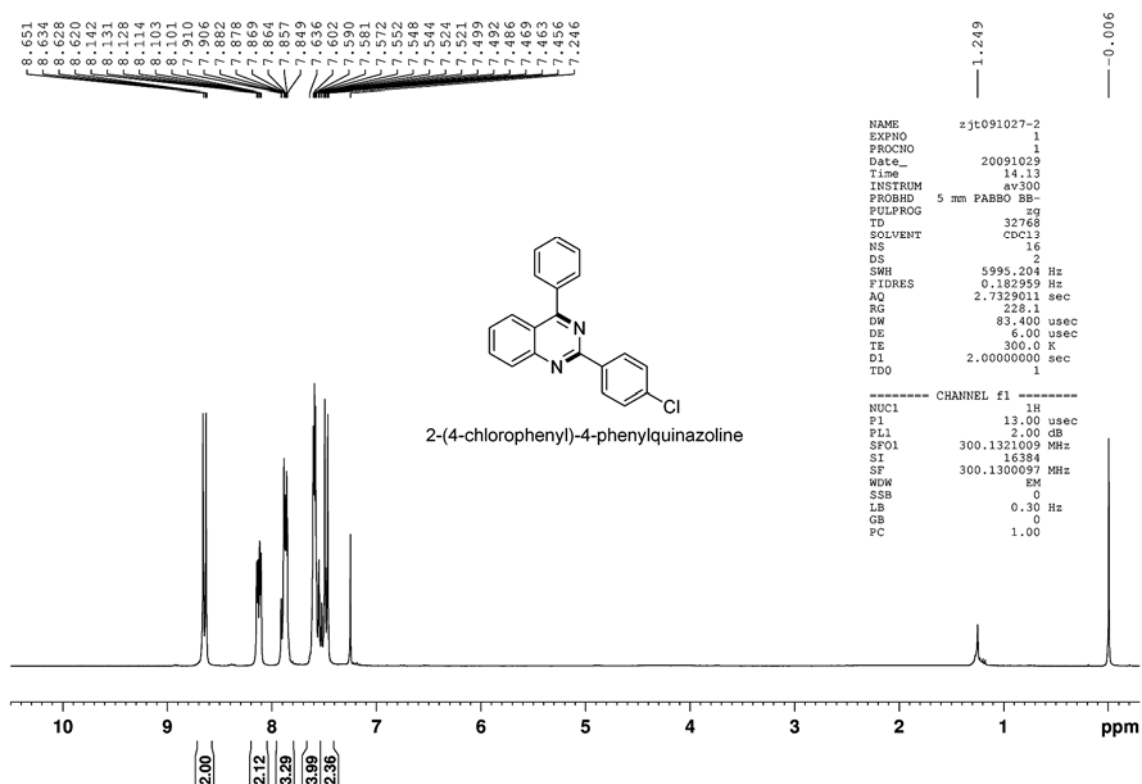
2-(4-methoxyphenyl)-4-phenylquinazoline (3ae)



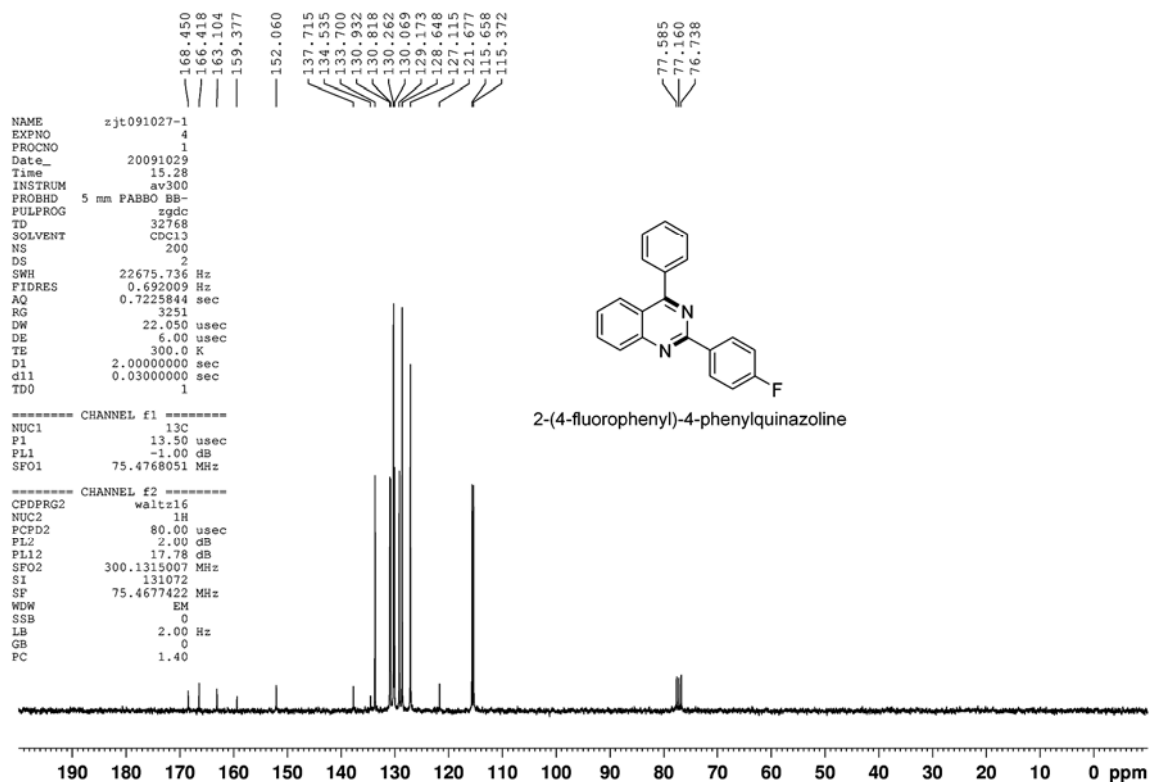
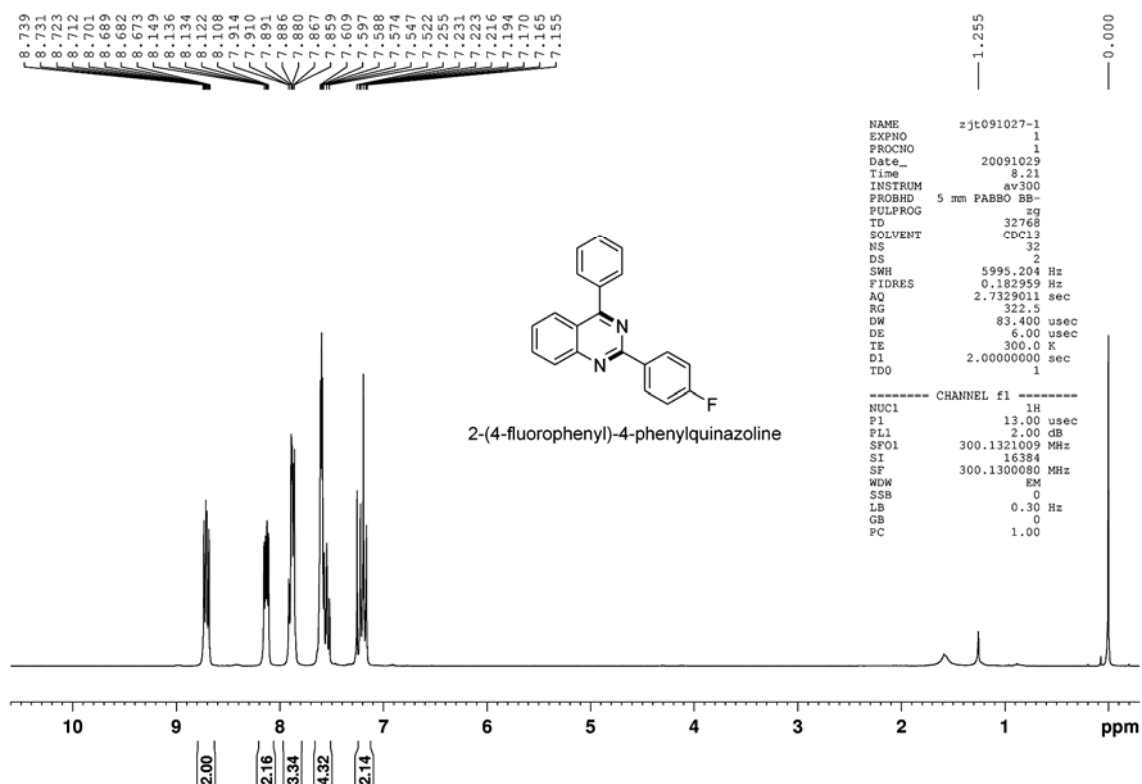
2-(benzo[d][1,3]dioxol-5-yl)-4-phenylquinazoline (3af)



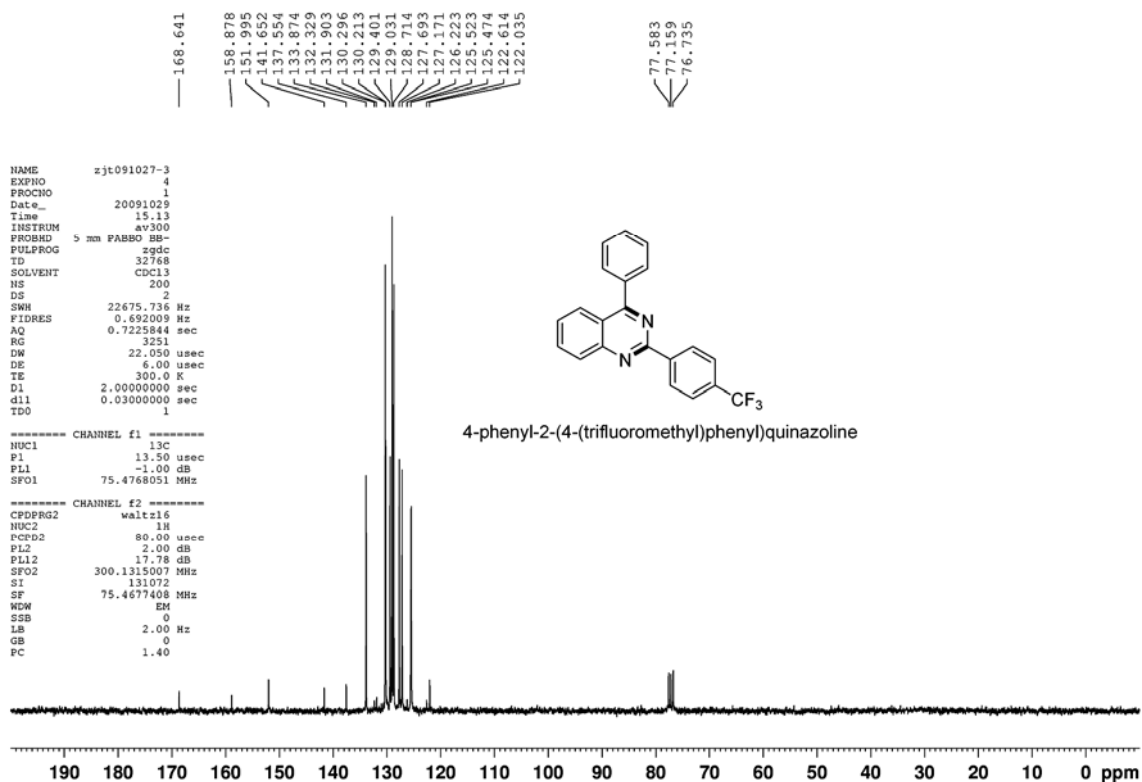
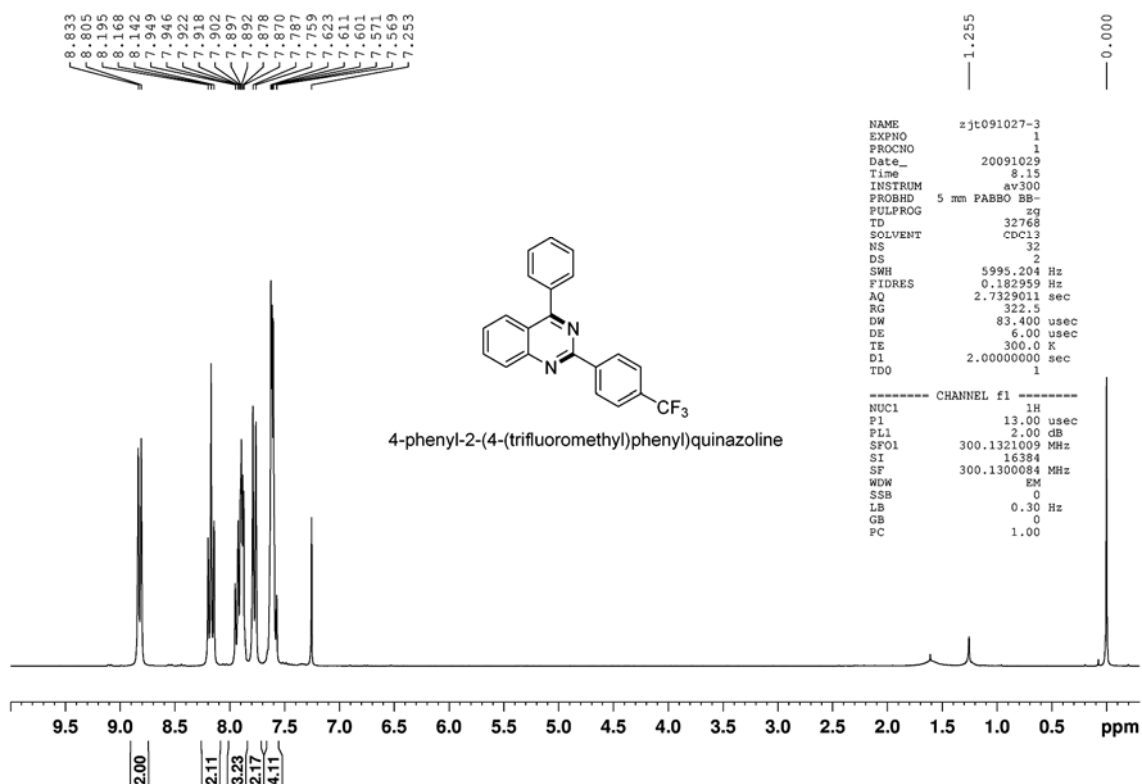
2-(4-chlorophenyl)-4-phenylquinazoline (3ag)



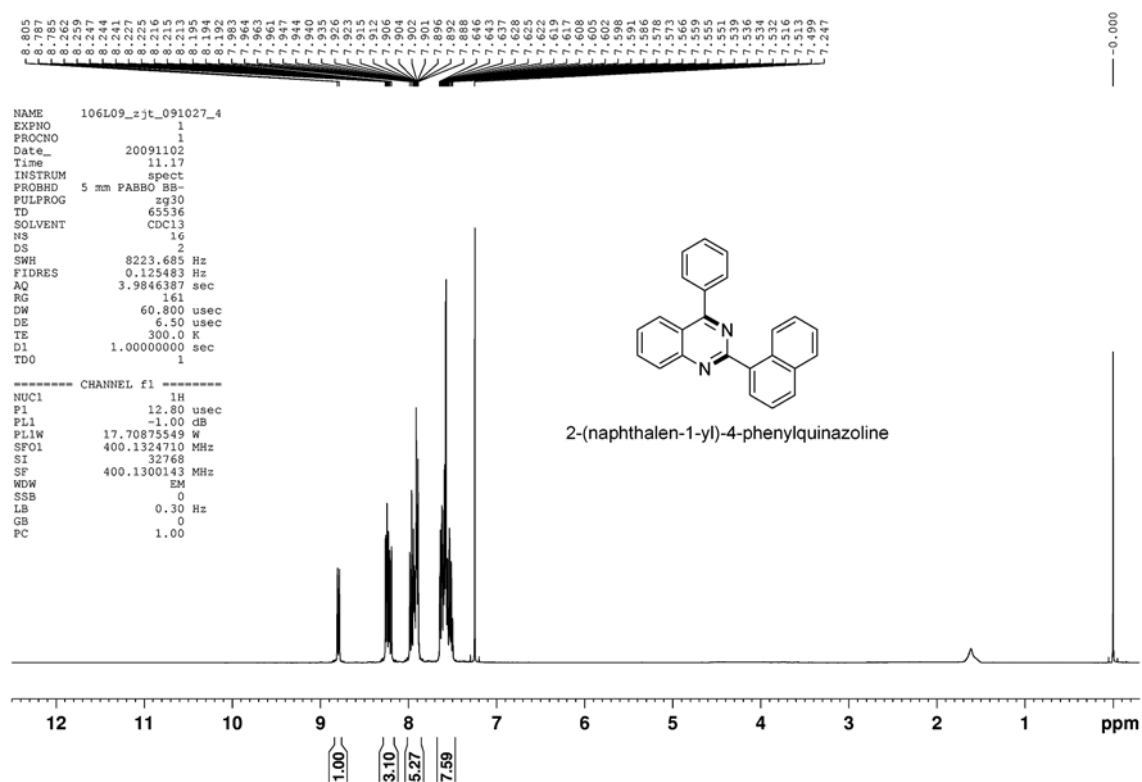
2-(4-fluorophenyl)-4-phenylquinazoline (3ah)



4-phenyl-2-(4-(trifluoromethyl)phenyl)quinazoline (3ai)



2-(naphthalen-1-yl)-4-phenylquinazoline (3aj)



2-(furan-2-yl)-4-phenylquinazoline (3ak)

