Electronic Supplementary Material (ESI) for RSC Advances.

Electro-oxidative Cyclization: Access to Quinazolinones via $K_2S_2O_8$ without Transition Metal Catalyst and Base

Yongzhi Hu,[a†] Huiqing Hou,[a†] Ling Yu,[b] Sunying Zhou,[a] Xianghua Wu,[c] Weiming Sun,*[a] Fang Ke [a]*

a. Institute of Materia Medica, School of Pharmacy, Fujian Provincial Key Laboratory of Natural Medicine Pharmacology, Fujian Medical University, Fuzhou 350122, China Tel.: +86-0591-22862016; fax: +86-0591-22862016; E-mail: kefang@mail.fjmu.edu.cn.

b. College of Chemistry and Chemical Engineering, Xingtai University, Xingtai 054001, China.

c. School of Chemistry and Chemical Engineering, Yunnan Normal University, Kunming 650092, China.

† These authors contributed equally to this work.

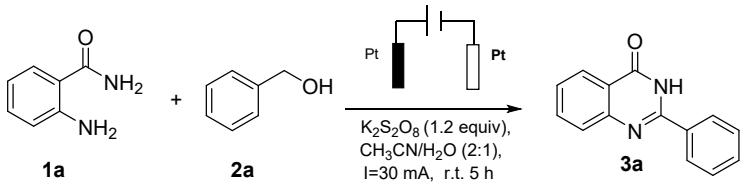
Supporting information

1. General information

All reagents were purchased from commercial sources and used without further purification. All solvents were dried in a standard manner. Reactions were monitored by TLC on silica gel plates. Column chromatography was performed over silica gel (200-300 mesh) and a petroleum ether/ethyl. Shanghai chenhua CHI600E electrochemical workstation was used in the standard configuration as delivered, including proprietary software. All products were characterized by NMR. ^{1}H NMR spectra were recorded at 500and 400 MHz and ^{13}C NMR spectra were recorded at 126 and 101 MHz (Bruker DPX) with DMSO-d_6 as solvent. Chemical shifts are reported in ppm using TMS as internal standard. NMR by the services provided at the Shandong Liaocheng University. HPLC were recorded on an SHIMDZU LC-20A instrument with a HP5-MS 30 m x 0.25 mm capillary apolar columns. A549, HCT-116 and VX-2 cells were all obtained from the Cell Bank of the Chinese Academy of Sciences.

2. General procedure for the catalytic reactions

An undivided cell equipped was charged with 2-aminobenzamide (0.5 mmol) and benzyl alcohol (0.6 mmol), $K_2S_2O_8$ (0.6 mmol) in a mixture of 3 mL CH_3CN/H_2O (v/v=2:1) solvent. The mixture was stirred at room temperature for 5 h in the 30 mA circuit. The reaction mixture was extracted with ethyl acetate (3×15 mL). The combined organic layer was washed with brine (10 mL), dried over $MgSO_4$. The concentrated residue was purified by column chromatography on a silica gel to afford the pure product **3a**.

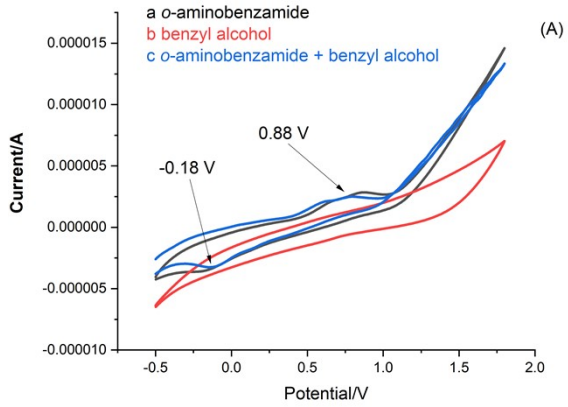


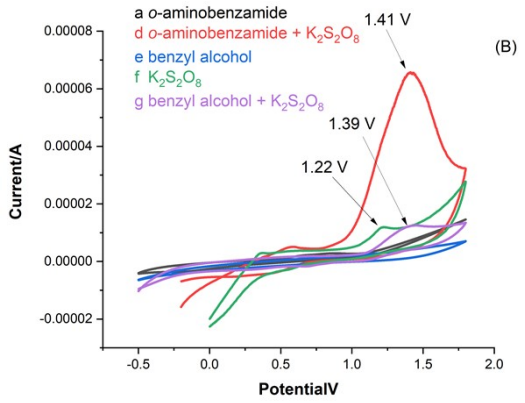
3. General procedure for the gram scale experiment

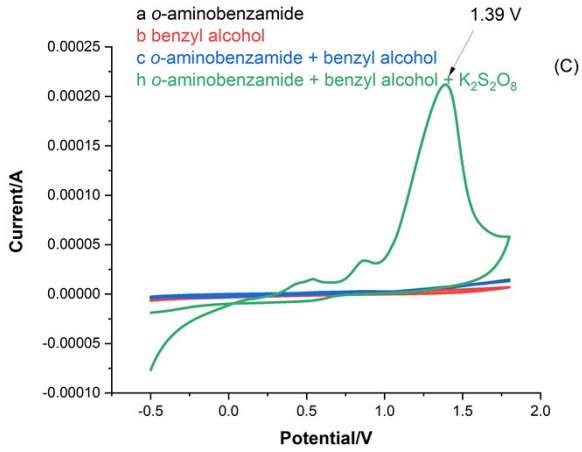
In an 50 mL undivided cell equipped with 2-aminobenzamide (8.0 mmol), benzaldehyde (9.6 mmol), $K_2S_2O_8$ (9.6 mmol) in a mixture of 20 mL CH_3CN/H_2O (v/v=2:1) solvent. The mixture was stirred at room temperature for 15 h in the 30 mA circuit. After the reaction was completed the solution of the crude product was concentrated in vacuo, and the residue was purified by column chromatography on a silica gel (petroleum ether/ethyl acetate=5/1) to afford the target product as a white solid.

4. Cyclic voltammetry experiment

Cyclic voltammograms were measured using Shanghai chenhua CHI600E electrochemical workstation with electrochemical analysis software, using a conventional three-electrode cell. The working electrode was a glassy carbon working electrode, the counter and reference electrodes consisted of a Pt wire and a SCE, respectively. The glassy carbon working electrode was polished with a polishing cloth before each measurement. The concentration of all tested compounds was 1 mmol L^{-1}. The scan rate was 0.1 V/s.





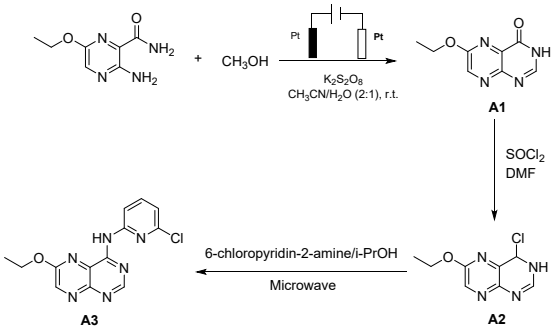


5. Computational methods

All calculations were performed by using the combination of Becke's hybrid 3-parameter exchange functional[1] and Lee-Yang-Parr's correlation functional[2] known as B3LYP method in conjunction with the Grimme's dispersion contribution correction[3] implemented in Gaussian 16 program package. Herein, all the geometries were optimized at SMD-B3LYP-D3(BJ)/6-311+G(d, p) level. The solvation model based on electron density (SMD)[4] was used throughout to simulate the mixed solvent CH_3CN/H_2O (2:1, v:v). The frequency calculations were computed to identify the nature of stationary points (minima and transition structures possess zero and one imaginary

frequency, respectively) at the same computational level. Then, the Gibbs free energy (G) calculation was carried out at temperature 298 K and pressure 1 atm. All the abovementioned calculations were performed using the Gaussian 16 software[5]. Dimensional plots of molecular configurations were generated with the GaussView program[6].

6. Synthesis of N-(6-chloropyridin-2-yl)-6-ethoxypteridin-4-amine (A3).



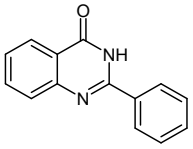
(1) The reaction of 3-amino-6-ethoxypyrazine-2-carboxamide (2 mmol) with methanol (2.4 mmol) was carried out for 7 hours under the irradiation of 30mA circuit with $K_2S_2O_8$ (2.4 mmol), and 5 mL CH_3CN/H_2O (v/v=2:1) as solvent, the yield of 6-ethoxypteridin-4(3H)-one was 87% .

(2) In a 100 mL three-necked flask, 6-ethoxypteridin-4(3H)-one (2 mmol) , 4 mL thionyl dichloride, and 3 drops of anhydrous DMF were added. S Vacuum distillation removes dichlorothionyl and is then dried in vacuum for 30 minutes before being cooled to a yellow solid. then reaction mixture was added $NaHCO_3$ to adjust pH value to 7, and stirred for 10 minutes, filtered, and dried in a vacuum to obtain 4-chloro-6-ethoxypteridine pale yellow powder. The yield was 91%.

(3) 4-chloro-6-ethoxypteridine (2 mmol), aromatic amine (2 mmol) and isopropanol were added into 50 mL single-port round-bottom flask and stirred evenly for several minutes, a drying tube of anhydrous calcium chloride was connected to the upper end of the spherical condensing tube, and the optimal reaction conditions for dichloromethane dissolution were optimized by adjusting the microwave power and reaction time. After the reaction was followed by thin layer chromatography (TLC), it was cooled to 25 ℃ and then extracted with 50 mL water and ethyl acetate (30 mL×3) to concentrate the organic phase of the pale yellow crude. The crude product is separated by silica gel column Chromatography (ethyl acetate/petroleum ether =1/5) and the final product is obtained.

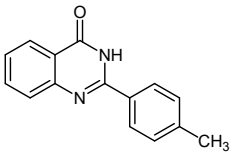
Characterization data

2-phenylquinazolin-4(3H)-one (3a)[7]



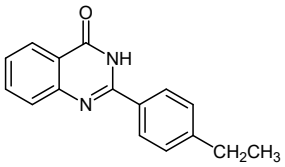
^{1}H NMR (500 MHz, DMSO-d_6) δ 12.52 (s, 1H), 8.18-8.09 (m, 3H), 7.79 (t, J = 7.3 Hz, 1H), 7.70 (d, J = 8.0 Hz, 1H), 7.51 (tq, J = 14.6, 7.5 Hz, 4H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 162.3, 152.3, 148.6, 134.6, 132.7, 131.4, 128.6, 127.7, 127.4, 126.5, 125.8, 120.9. **MS** [EI, m/z]: 222 [M^+].

2-(p-tolyl)quinazolin-4(3H)-one (3b)[7]



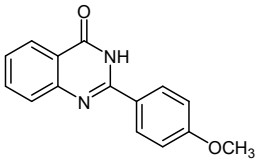
^{1}H NMR (500 MHz, DMSO-d_6) δ 12.43 (s, 1H), 8.09 (dd, J = 7.9, 1.2 Hz, 1H), 8.04 (d, J = 8.3 Hz, 2H), 7.77 (td, J = 7.8, 7.2, 1.5 Hz, 1H), 7.67 (d, J = 7.7 Hz, 1H), 7.48-7.43 (m, 1H), 7.30 (d, J = 8.1 Hz, 2H), 2.34 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 161.8, 151.8, 148.4, 141.0, 134.2, 129.4, 128.8, 127.3, 127.0, 126.0, 125.4, 120.4, 20.6. MS [EI, m/z]: 236 [M^+].

2-(4-ethylphenyl)quinazolin-4(3H)-one (3c)[8]



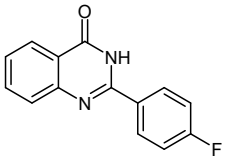
^{1}H NMR (500 MHz, DMSO-d_6) δ 12.45 (s, 1H), 8.13-8.06 (m, 3H), 7.80 (ddd, J = 8.5, 7.2, 1.6 Hz, 1H), 7.69 (d, J = 7.7 Hz, 1H), 7.48 (ddd, J = 8.1, 7.0, 1.1 Hz, 1H), 7.36 (d, J = 8.3 Hz, 2H), 2.66 (q, J = 7.6 Hz, 2H), 1.19 (t, J = 7.6 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 162.2, 152.1, 148.7, 147.5, 134.5, 130.0, 127.9, 127.7, 127.3, 126.3, 125.7, 120.8, 27.9, 15.2. MS [EI, m/z]: 250 [M^+].

2-(4-methoxyphenyl)quinazolin-4(3H)-one (3d)[7]



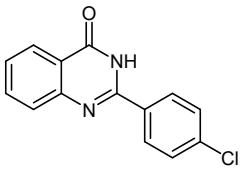
^{1}H NMR (500 MHz, DMSO-d_6) δ 12.38 (s, 1H), 8.17- 8.11 (m, 2H), 8.10-8.05 (m, 1H), 7.79-7.74 (m, 1H), 7.65 (d, J = 8.1 Hz, 1H), 7.47-7.41 (m, 1H), 7.07-7.00 (m, 2H), 3.80 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 162.3, 161.9, 151.9, 148.9, 134.6, 129.4, 127.3, 126.2, 125.8, 124.8, 120.7, 114.0, 55.5. MS [EI, m/z]: 252 [M^+].

2-(4-fluorophenyl)quinazolin-4(3H)-one (3e)[7]



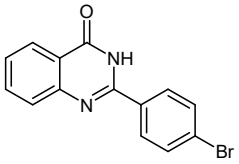
^{1}H NMR (400 MHz, DMSO-d_6) δ 12.55 (s, 1H), 8.29-8.24 (m, 2H), 8.16 (dd, J = 7.9, 1.6 Hz, 1H), 7.85 (ddd, J = 8.5, 7.0, 1.6 Hz, 1H), 7.74 (dd, J = 8.2, 1.4 Hz, 1H), 7.53 (ddd, J = 8.1, 7.1, 1.4 Hz, 1H), 7.43 -7.37 (m, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 165.8, 163.3, 162.8, 152.0, 149.1, 135.1, 130.9, 130.8, 129.8, 129.8, 127.9, 127.1, 126.3, 121.4, 116.2, 116.0. MS [EI, m/z]: 240 [M^+].

2-(4-chlorophenyl)quinazolin-4(3H)-one (3f)[7]



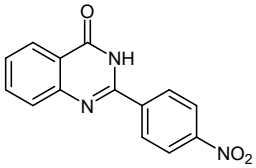
^{1}H NMR (400 MHz, DMSO-d_6) δ 12.99 (s, 1H), 8.84 (d, J = 2.7 Hz, 1H), 8.56 (dd, J = 8.9, 2.7 Hz, 1H), 8.23 (d, J = 7.6 Hz, 2H), 7.92 (d, J = 9.0 Hz, 1H), 7.63 (dt, J = 26.7, 7.3 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 156.2, 145.2, 132.8, 132.5, 129.5, 129.2, 129.0, 128.7, 124.6, 122.5, 115.9. MS [EI, m/z]: 256 [M^+].

2-(4-bromophenyl)quinazolin-4(3H)-one (3g)[7]



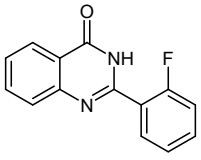
^{1}H NMR (400 MHz, DMSO-d_6) δ 12.71 (s, 1H), 8.23 (d, J = 2.4 Hz, 1H), 8.19-8.16 (m, 2H), 7.98 (dd, J = 8.7, 2.4 Hz, 1H), 7.70 (d, J = 8.6 Hz, 1H), 7.61-7.53 (m, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 161.6, 153.4, 148.2, 137.9, 133.0, 132.1, 130.4, 129.1, 129.1, 128.5, 128.3, 128.2, 123.1, 119.4. MS [EI, m/z]: 300 [M^+].

2-(4-nitrophenyl)quinazolin-4(3H)-one (3h)[9]



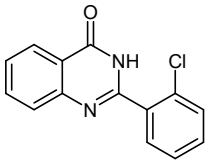
^{1}H NMR (400 MHz, DMSO-d_6) δ 12.52 (s, 1H), 8.24 (dd, J = 8.1, 1.6 Hz, 2H), 8.00 (d, J = 7.0 Hz, 1H), 7.70 (d, J = 7.4 Hz, 1H), 7.64-7.51 (m, 3H), 7.40 (t, J = 7.6 Hz, 1H).^{13}C NMR (101 MHz, DMSO-d_6) δ 163.0, 151.5, 147.6, 136.1, 135.4, 133.4, 131.8, 129.1, 128.2, 126.5, 124.0, 121.4. MS [EI, m/z]: 267 [M^+].

2-(2-fluorophenyl)quinazolin-4(3H)-one (3i)[10]



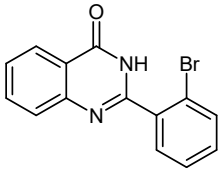
^{1}H NMR (500 MHz, DMSO-d_6) δ 12.60 (s, 1H), 8.18 (dd, J = 7.9, 1.2 Hz, 1H), 7.86 (td, J = 7.8, 7.3, 1.5 Hz, 1H), 7.79 (td, J = 7.5, 1.7 Hz, 1H), 7.74 (d, J = 8.0 Hz, 1H), 7.63 (ddd, J = 15.5, 5.3, 1.7 Hz, 1H), 7.59-7.55 (m, 1H), 7.43-7.36 (m, 2H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 162.0, 161.0, 159.0, 150.4, 149.1, 135.1, 133.4, 133.3, 131.5, 128.0, 127.5, 126.3, 125.1, 125.1, 122.8, 122.7, 121.6, 116.7, 116.6. MS [EI, m/z]: 240 [M^+].

2-(2-chlorophenyl)quinazolin-4(3H)-one (3j)[11]



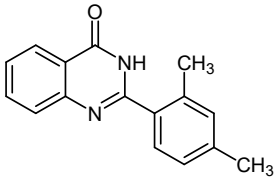
^{1}H NMR (500 MHz, DMSO-d_6) δ 12.66 (s, 1H), 8.19 (dd, J = 7.9, 1.6 Hz, 1H), 7.87 (ddd, J = 8.5, 7.2, 1.6 Hz, 1H), 7.72 (d, J = 8.0 Hz, 1H), 7.68 (dd, J = 7.5, 1.6 Hz, 1H), 7.64-7.61 (m, 1H), 7.61-7.56 (m, 2H), 7.51 (td, J = 7.4, 1.2 Hz, 1H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 161.9, 152.7, 149.0, 135.1, 134.3, 132.1, 131.9, 131.3, 130.1, 127.9, 127.7, 127.6, 126.3, 121.7. MS [EI, m/z]: 256 [M^+].

2-(2-bromophenyl)quinazolin-4(3H)-one (3k)[11]



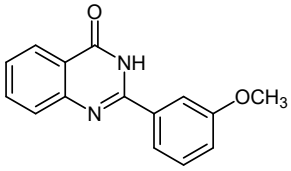
^{1}H NMR (400 MHz, DMSO-d_6) δ 12.62 (s, 1H), 8.19 (dd, J = 7.9, 1.6 Hz, 1H), 7.89-7.83 (m, 1H), 7.78 (dd, J = 7.8, 1.4 Hz, 1H), 7.72 (d, J = 6.9 Hz, 1H), 7.65 (dd, J = 7.5, 1.9 Hz, 1H), 7.61-7.46 (m, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 161.9, 153.8, 149.0, 136.3, 135.1, 133.1, 132.1, 131.9, 131.3, 128.1, 127.95, 127.5, 126.3, 121.7, 121.4. MS [EI, m/z]: 300 [M^+].

2-(2,4-dimethylphenyl)quinazolin-4(3H)-one (3l)[10]



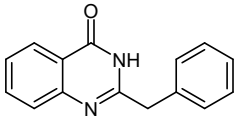
^{1}H NMR (500 MHz, DMSO-d_6) δ 12.41 (s, 1H), 8.16 (d, J = 6.7 Hz, 1H), 7.86-7.81 (m, 1H), 7.68 (d, J = 8.1 Hz, 1H), 7.54 (t, J = 7.5 Hz, 1H), 7.41 (d, J = 7.7 Hz, 1H), 7.21-7.11 (m, 2H), 2.36 (d, J = 9.8 Hz, 6H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 162.3, 154.9, 149.2, 140.0, 136.5, 134.9, 131.9, 131.7, 129.6, 127.8, 127.0, 126.7, 126.2, 121.3, 111.8, 21.3, 20.1. MS [EI, m/z]: 250 [M^+].

2-(3-methoxyphenyl)quinazolin-4(3H)-one (3m)[11]



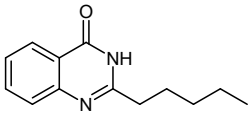
^{1}H NMR (400 MHz, DMSO-d_6) δ 12.52 (s, 1H), 8.17 (dd, J = 7.9, 1.1 Hz, 1H), 7.87-7.79 (m, 2H), 7.76 (dd, J = 4.6, 2.9 Hz, 2H), 7.53 (ddd, J = 8.1, 7.1, 1.3 Hz, 1H), 7.47 (t, J = 7.9 Hz, 1H), 7.16 (ddd, J = 8.3, 2.6, 1.0 Hz, 1H), 3.88 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 162.7, 159.9, 152.5, 149.2, 135.1, 134.5, 130.2, 128.0, 127.1, 126.3, 121.5, 120.6, 118.1, 113.0, 55.9. MS [EI, m/z]: 252 [M^+].

2-benzylquinazolin-4(3H)-one (3n)[9]



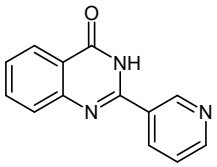
^{1}H NMR (500 MHz, DMSO-d_6) δ 12.44 (s, 1H), 8.08 (dd, J = 7.9, 1.2 Hz, 1H), 7.78 (ddd, J = 8.6, 7.2, 1.6 Hz, 1H), 7.61 (d, J = 7.8 Hz, 1H), 7.50-7.45 (m, 1H), 7.39 (d, J = 7.1 Hz, 2H), 7.33 (t, J = 7.5 Hz, 2H), 7.25 (t, J = 7.3 Hz, 1H), 3.94 (s, 2H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 162.4, 156.5, 137.0, 134.9, 129.3, 129.2, 129.0, 127.3, 127.3, 126.7, 126.2, 121.2, 41.2. MS [EI, m/z]: 236[M$^+$].

2-pentylquinazolin-4(3H)-one (3o)[12]



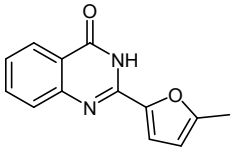
^{1}H NMR (400 MHz, DMSO-d_6) δ 12.14 (s, 1H), 8.08 (dd, J = 7.9, 1.6 Hz, 1H), 7.77 (ddd, J = 8.5, 7.0, 1.6 Hz, 1H), 7.59 (d, J = 7.0 Hz, 1H), 7.45 (ddd, J = 8.3, 7.1, 1.4 Hz, 1H), 2.62-2.57 (m, 2H), 1.73 (p, J = 7.3 Hz, 2H), 1.35-1.28 (m, 5H), 0.89-0.85 (m, 3H).^{13}C NMR (101 MHz, DMSO-d_6) δ 162.3, 158.0, 149.4, 134.7, 127.2, 126.3, 126.1, 121.2, 34.9, 31.2, 26.9, 22.3, 14.3. MS [EI, m/z]: 216 [M$^+$].

2-(pyridin-3-yl)quinazolin-4(3H)-one (3p)[8]



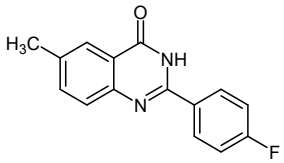
^{1}H NMR (400 MHz, DMSO-d_6) δ 12.70 (s, 1H), 9.30 (dd, J = 7.7, 2.3 Hz, 1H), 8.76 (dd, J = 4.8, 1.7 Hz, 1H), 8.49 (tt, J = 8.0, 2.0 Hz, 1H), 8.18 (dd, J = 7.9, 1.7 Hz, 1H), 7.86 (ddd, J = 8.5, 7.0, 1.6 Hz, 1H), 7.77 (dd, J = 8.3, 1.4 Hz, 1H), 7.61-7.52 (m, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 162.61, 152.27, 151.25, 149.22, 148.95, 135.83, 135.13, 129.21, 127.98, 127.39, 126.35, 123.98, 121.61. MS [EI, m/z]: 223 [M$^+$].

2-(5-methylfuran-2-yl)quinazolin-4(3H)-one (3q)[13]



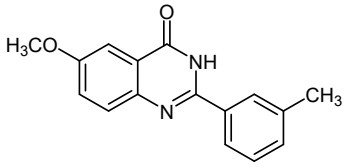
^{1}H NMR (400 MHz, DMSO-d_6) δ 12.37 (s, 1H), 8.11 (dd, J = 7.9, 1.4 Hz, 1H), 7.80 (ddd, J = 8.5, 7.1, 1.6 Hz, 1H), 7.71-7.67 (m, 1H), 7.56 (d, J = 3.4 Hz, 1H), 7.50-7.45 (m, 1H), 6.38 (dd, J = 3.4, 1.1 Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 162.1, 156.6, 149.3, 144.9, 144.4, 135.1, 127.6, 126.7, 126.4, 121.5, 116.3, 109.4, 14.0. MS [EI, m/z]: 226 [M$^+$].

2-(4-fluorophenyl)-6-methylquinazolin-4(3H)-one (3r)[14]



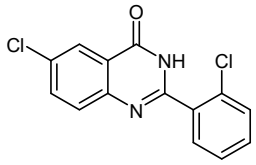
^{1}H NMR (500 MHz, DMSO-d_6) δ 12.52 (s, 1H), 8.28-8.20 (m, 2H), 7.98-7.93 (m, 1H), 7.70-7.62 (m, 2H), 7.44-7.36 (m, 2H), 2.47 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 162.6, 151.0, 147.1, 136.9, 136.4, 130.7, 130.7, 129.8, 127.8, 125.7, 121.1, 116.2, 116.0, 21.3. MS [EI, m/z]: 254 [M^+].

6-methoxy-2-(m-tolyl)quinazolin-4(3H)-one (3s)[15]



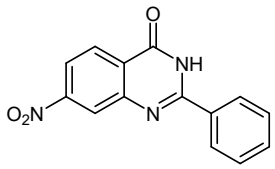
^{1}H NMR (500 MHz, DMSO-d_6) δ 7.88 (d, J = 25.7 Hz, 1H), 7.77 (d, J = 8.4 Hz, 1H), 7.57 (s, 1H), 7.51 (d, J = 8.7 Hz, 1H), 7.26 (t, J = 8.9 Hz, 1H), 7.00-6.89 (m, 2H), 3.77 (s, 3H), 2.50 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 169.21, 168.27, 158.75, 141.54, 140.46, 134.05, 131.89, 129.20, 127.95, 116.98, 114.49, 109.28, 56.04, 21.40. MS [EI, m/z]: 266 [M^+].

6-chloro-2-(2-chlorophenyl)quinazolin-4(3H)-one (3t)[16]



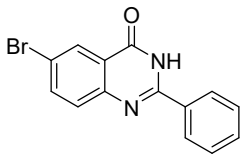
^{1}H NMR (400 MHz, DMSO-d_6) δ 12.84 (s, 1H), 8.12 (d, J = 2.4 Hz, 1H), 7.90 (dd, J = 8.7, 2.6 Hz, 1H), 7.76 (d, J = 8.8 Hz, 1H), 7.68 (dd, J = 7.4, 1.8 Hz, 1H), 7.65 – 7.56 (m, 2H), 7.51 (td, J = 7.4, 1.5 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 161.0, 153.2, 147.8, 135.2, 134.0, 132.3, 131.9, 131.8, 131.4, 130.2, 130.1, 127.7, 125.4, 123.0. MS [EI, m/z]: 290 [M^+].

7-nitro-2-phenylquinazolin-4(3H)-one (3u)[17]



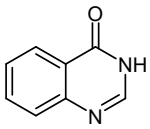
^{1}H NMR (400 MHz, DMSO-d_6) δ 12.92 (s, 1H), 8.45 (d, J = 2.2 Hz, 1H), 8.38 (d, J = 8.7 Hz, 1H), 8.26 -8.21 (m, 3H), 7.66-7.57 (m, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 151.8, 132.6, 132.5, 130.1, 129.2, 128.7, 128.5, 125.8, 125.7, 120.5. MS [EI, m/z]: 267 [M^+].

6-bromo-2-phenylquinazolin-4(3H)-one (3v)[17]



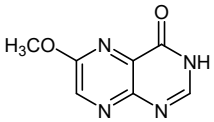
^{1}H NMR (400 MHz, *DMSO-d6*) δ 12.72 (s, 1H), 8.24 (d, *J* = 2.4 Hz, 1H), 8.18 (dd, *J* = 6.8, 1.7 Hz, 2H), 7.99 (dd, *J* = 8.7, 2.4 Hz, 1H), 7.70 (d, *J* = 8.6 Hz, 1H), 7.57 (q, *J* = 6.9 Hz, 3H). **^{13}C NMR** (101 MHz, *DMSO-d6*) δ 161.63, 153.43, 148.24, 137.91, 132.95, 132.10, 130.38, 129.12, 129.08, 128.47, 128.33, 128.24, 123.10, 119.41. MS [EI, m/z]: 300 [M^+].

quinazolin-4(3H)-one (3w)[18]



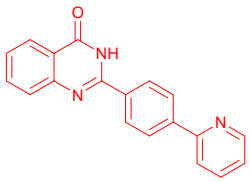
^{1}H NMR (400 MHz, DMSO-d_6) δ 12.22 (s, 1H), 8.16-8.07 (m, 2H), 7.82 (ddd, *J* = 8.5, 7.1, 1.6 Hz, 1H), 7.68 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.56-7.50 (m, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 161.2, 149.3, 145.8, 134.8, 127.7, 127.2, 126.3, 123.1. MS [EI, m/z]: 146 [M^+].

6-methoxypteridin-4(3H)-one (3x)[19]



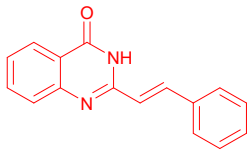
^{1}H NMR (500 MHz, DMSO-d_6) δ 12.78 (s, 1H), 8.69 (s, 1H), 8.23 (s, 1H), 4.01 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 160.61, 158.40, 151.30, 146.59, 143.54, 130.39, 54.76. MS [EI, m/z]: 178 [M^+].

2-(4-(pyridin-2-yl)phenyl)quinazolin-4(3H)-one (3y)[21]



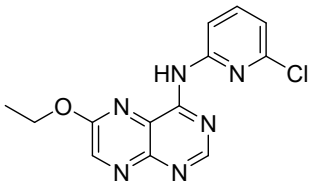
^{1}H NMR (400 MHz, D_2SO_4) δ 8.65 – 8.57 (m, 2H), 8.37 (d, *J* = 6.5 Hz, 1H), 8.27 – 8.06 (m, 6H), 8.04 – 7.96 (m, 1H), 7.95 – 7.84 (m, 2H). ^{13}C NMR (101 MHz, D_2SO_4) δ 156.41, 149.77, 143.49, 143.02, 135.96, 134.71, 131.22, 131.09, 126.53, 124.43, 123.64, 122.28, 121.51, 121.10, 120.74, 114.44, 110.98. MS [EI, m/z]: 299 [M^+].

2-styrylquinazolin-4(3H)-one (3z)[22]



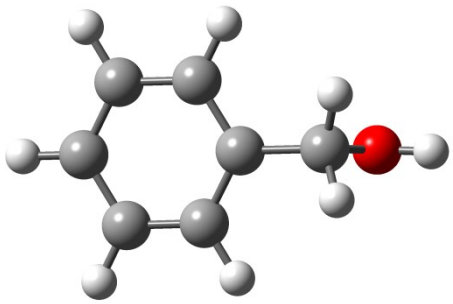
^{1}H NMR (400 MHz, DMSO-d_6) δ 12.32 (s, 1H), 8.06 (d, *J* = 1.8 Hz, 1H), 7.92 (d, *J* = 16.1 Hz, 1H), 7.76 (t, *J* = 8.5 Hz, 1H), 7.63 (t, *J* = 7.5 Hz, 3H), 7.41 (td, *J* = 13.6, 12.8, 7.2 Hz, 4H), 6.97 (d, *J* = 16.2 Hz, 1H).^{13}C NMR (101 MHz, DMSO-*d6*) δ 162.20, 151.86, 149.47, 138.72, 135.46, 134.98, 130.24, 129.54, 128.10, 127.61, 126.70, 126.33, 121.58, 121.54. MS [EI, m/z]: 248 [M^+].

N-(6-chloropyridin-2-yl)-6-ethoxypteridin-4-amine[20]



^{1}H NMR (400 MHz, DMSO-d_6) δ 9.81 (s, 1H), 8.87 (s, 1H), 8.82 (s, 1H), 8.55 (d, J = 8.9 Hz, 1H), 7.97 (t, J = 8.0 Hz, 1H), 7.28 (dd, J = 7.8, 0.8 Hz, 1H), 4.67 (q, J = 7.1 Hz, 2H), 1.46 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 157.5, 156.8, 154.9, 151.7, 150.2, 148.6, 147.1, 142.2, 122.0, 119.7, 113.7, 64.2, 14.5. MS [EI, m/z]: 302 [M^+].

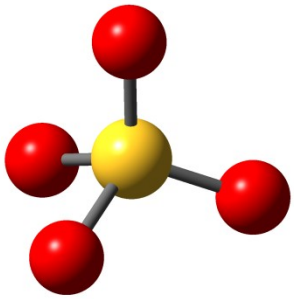
Optimized Structures and Cartesian Coordinates



2a / C_7H_7OH

Gibbs Free Energies= -346.819302 a.u

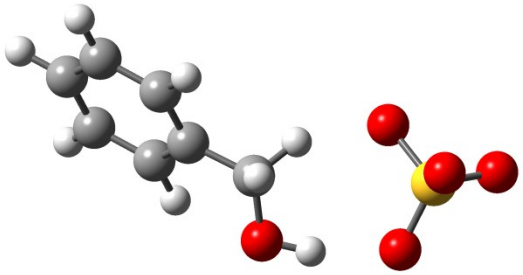
C	1.60309300	1.20503200	-0.10580900
C	0.23130000	1.19355000	0.14057200
C	-0.45568100	-0.01631300	0.28995100
C	0.25641600	-1.21535200	0.19175100
C	1.62973200	-1.20847500	-0.05362600
C	2.30533200	0.00250800	-0.20377600
H	2.12498200	2.14928000	-0.21588100
H	-0.31188100	2.12941500	0.22287300
H	-0.26824800	-2.15787100	0.31011200
H	2.17063400	-2.14557600	-0.12623000
H	3.37313800	0.01029300	-0.39237800
C	-1.94170900	-0.02462900	0.52217200
H	-2.23883800	-0.95576000	1.01608000
H	-2.22703100	0.81521700	1.16527500
O	-2.60470700	0.08951200	-0.75406200
H	-3.55490400	0.13314300	-0.58717700



$SO_4^{-\bullet}$

Gibbs Free Energies= -699.27586 a.u

S	0.07859400	-0.00000400	-0.00002800
O	0.88087500	1.23703600	-0.00040800
O	0.88083400	-1.23705900	-0.00035100
O	-0.96008900	-0.00001500	-1.13446700
O	-0.95880700	0.00004600	1.13528200

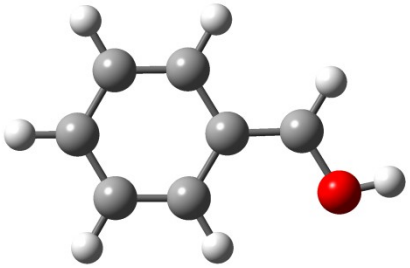


TS1

Gibbs Free Energies= -1046.086454 a.u

C	-3.95873600	-1.32004300	-0.02927200
C	-2.63456100	-1.22007300	-0.44745700
C	-1.93313100	-0.01376500	-0.31266700
C	-2.58261300	1.09078600	0.25143000
C	-3.90923800	0.99164200	0.66631800
C	-4.60127300	-0.21318900	0.52981100
H	-4.49156600	-2.25752100	-0.14377700
H	-2.13836200	-2.07925100	-0.88747200
H	-2.04460500	2.02483700	0.35481500
H	-4.40429500	1.85490600	1.09747000
H	-5.63362000	-0.28862300	0.85265300
C	-0.49655200	0.05512500	-0.73258000
H	0.13051500	-0.35607000	0.10194100

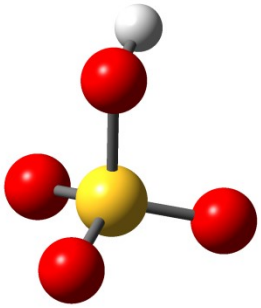
H	-0.30925300	-0.61934200	-1.58067600
O	-0.08714200	1.37026000	-1.01222200
H	0.89181400	1.39044900	-0.95435000
S	2.93333100	-0.14125500	0.14628700
O	3.20496600	-1.23695700	-0.80332600
O	2.58414100	1.14068900	-0.53625700
O	4.01976800	0.04173600	1.16898200
O	1.74860400	-0.51975300	1.09098500



A / C_7H_6OH•

Gibbs Free Energies= -346.192204 a.u

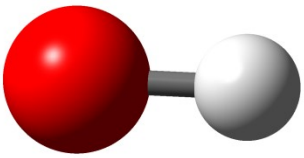
C	1.34646900	-1.34460700	-0.00000100
C	-0.01578200	-1.08485200	-0.00000300
C	-0.49558500	0.25626900	0.00000100
C	0.46603100	1.30811900	0.00000300
C	1.82113100	1.02823300	0.00000400
C	2.27799000	-0.29867200	0.00000300
H	1.69222000	-2.37295900	-0.00000400
H	-0.72573200	-1.90246100	-0.00000600
H	0.12128600	2.33684900	0.00000300
H	2.53588500	1.84423700	0.00000600
H	3.34052000	-0.51187800	0.00000500
C	-1.86537300	0.56631700	0.00000400
H	-2.23331200	1.58501100	-0.00000200
O	-2.78331000	-0.43767300	-0.00001300
H	-3.67367300	-0.06224800	0.00003700



HSO_4^-

Gibbs Free Energies= -699.935737 a.u

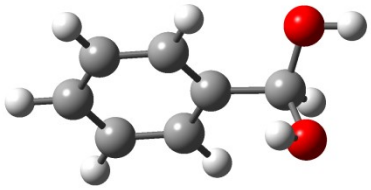
S	-0.14332800	-0.01489000	-0.00116100
O	-0.38411900	-0.76984800	1.24805800
O	-0.35213300	-0.81479000	-1.22819400
O	1.50416500	0.34066200	0.01227700
O	-0.73001500	1.33605100	-0.03215300
H	1.99006300	-0.49836400	0.01866900



•OH

Gibbs Free Energies= -75.77756 a.u

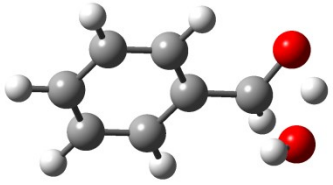
O	0.00000000	0.00000000	0.10889700
H	0.00000000	0.00000000	-0.87117500



C / $C_7H_6(OH)_2$

Gibbs Free Energies= -422.074948 a.u

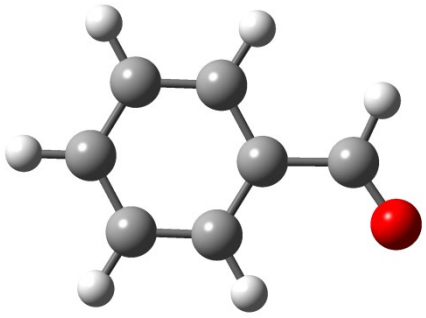
C	-1.77280200	1.27032100	0.25003200
C	-0.39144700	1.12800200	0.12220000
C	0.16195900	-0.12483900	-0.15680400
C	-0.68017400	-1.22906000	-0.31150400
C	-2.06082100	-1.08677300	-0.18308600
C	-2.61002400	0.16455200	0.09898700
H	-2.19563900	2.24573600	0.46351300
H	0.25648000	1.98920100	0.22936100
H	-0.25243400	-2.20123600	-0.53379500
H	-2.70620300	-1.94894500	-0.30806300
H	-3.68395500	0.27790800	0.19594300
C	1.65947300	-0.32573100	-0.23381900
H	1.89648400	-1.17104000	-0.88472200
O	2.21247900	-0.68952900	1.02608400
H	1.91528500	-0.04165100	1.68153700
O	2.25347000	0.86032900	-0.72283400
H	3.20540700	0.70479300	-0.78580400



TS2

Gibbs Free Energies= -422.017024 a.u

C	-1.78924000	1.28457400	0.21774500
C	-0.42241200	1.13977900	0.00274200
C	0.11319600	-0.12917100	-0.24661000
C	-0.72645400	-1.24871200	-0.28378800
C	-2.09369000	-1.10092500	-0.06826200
C	-2.62455400	0.16540000	0.18376900
H	-2.20643200	2.26680900	0.40782000
H	0.23719900	1.99875000	0.01708400
H	-0.30401000	-2.22760700	-0.48464600
H	-2.74489300	-1.96666800	-0.09975800
H	-3.68979400	0.28132300	0.34900000
C	1.56435200	-0.30170300	-0.48736100
H	1.83699800	-1.26978500	-0.91670000
O	2.42511400	-0.50843600	1.07549800
H	1.86640900	-0.21961400	1.81524600
O	2.33610900	0.73943900	-0.74562900
H	2.78754600	0.43331500	0.36359000

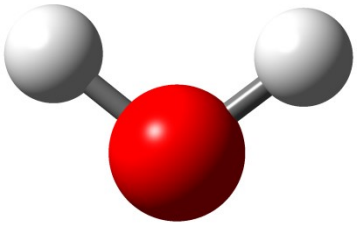


D / C_6H_5CHO

Gibbs Free Energies= -345.633162 a.u

C	-1.33893800	-1.32505100	-0.00001100
C	0.03305600	-1.11080300	-0.00001200
C	0.53514900	0.19896200	-0.00001000
C	-0.34743400	1.28636900	-0.00000500
C	-1.72295100	1.06913500	-0.00001200
C	-2.21674100	-0.23541200	-0.00001400
H	-1.73147000	-2.33529700	-0.00001000
H	0.72533100	-1.94433700	-0.00001200
H	0.05046100	2.29577300	0.00000000
H	-2.40714700	1.90956700	-0.00001200
H	-3.28720100	-0.40734700	-0.00001900
C	1.98591100	0.46336600	-0.00002800

H	2.25750700	1.53629200	0.00011900
O	2.85302600	-0.39175600	0.00006100



H_2O

Gibbs Free Energies= -76.464274 a.u

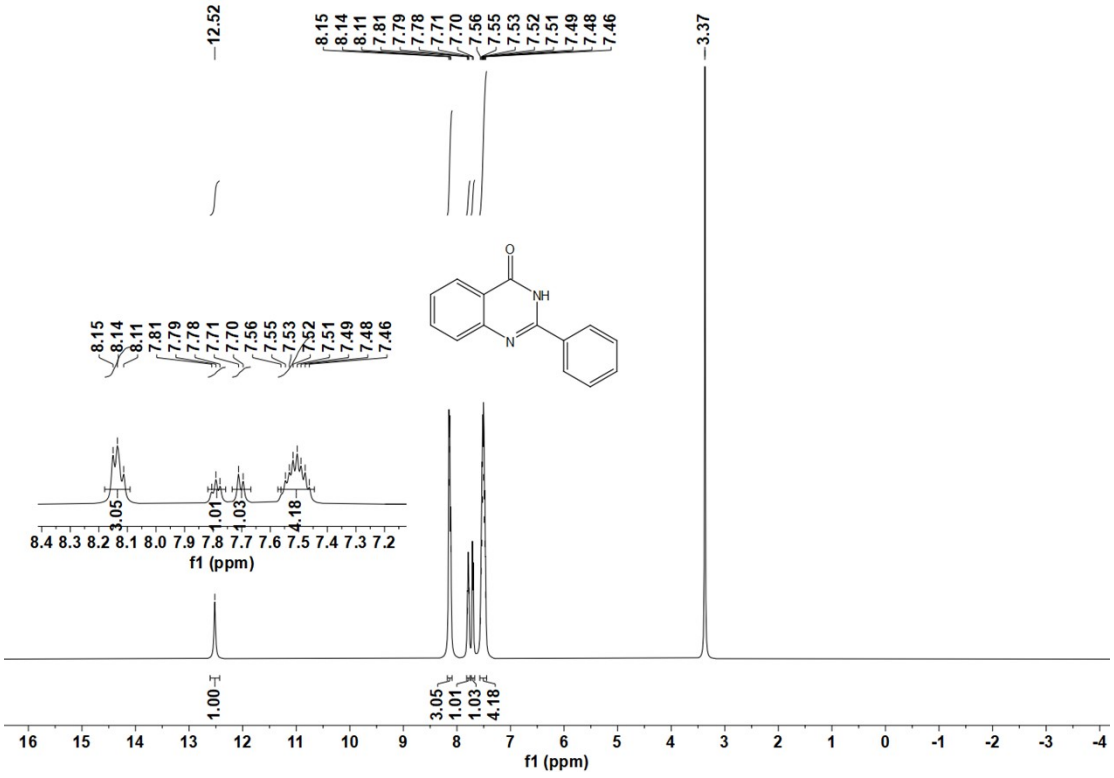
O	0.00000000	0.00000000	0.11821900
H	0.00000000	0.76340800	-0.47287800
H	0.00000000	-0.76340800	-0.47287800

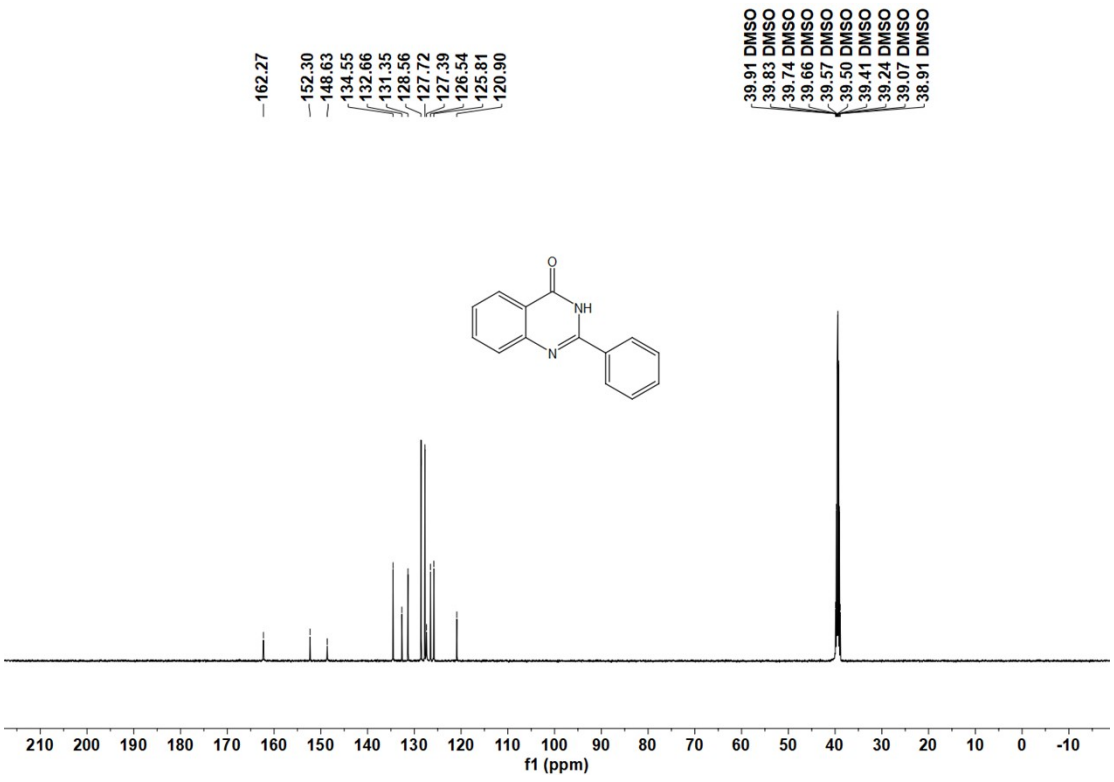
References

1. A. D. Becke, *J. Chem. Phys*. 1993, **98**, 5648-5652.
2. C. Lee, W. Yang and R. G. Parr, *Phys. Rev. B*. 1988, **37**, 785-789.
3. S. Grimme, S. Ehrlich, L. Goerigk, *J. Comput. Chem.* **2011**, *32*, 1456-1465.
4. A. V. Marenich, C. J. Cramer, D. G. Truhlar, *J. Phys. Chem. B* **2009**, *113*, 6378-6396.
5. M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, G. Z. J. Bloino, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, T. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, D. J. Fox, Gaussian 16, Revision A.03, Gaussian, Inc., Wallingford, CT **2016**.
6. R. D. Dennington II., T. A. Keith, J. M. Millam, GaussView, Version 6, Semichem Inc., Shawnee Mission, KS **2016**.
7. J. K. Laha, K. V. Patel, K. S. Satyanarayana Tummalapalli, N. Dayal. *Chem. Commun*. **2016**, *52*, 10245-10248.
8. M. Abdullaha, S. Mohammed, M. Ali, A. Kumar, R. A. Vishwakarma, S. B. Bharate. *J. Org. Chem*. **2019**, *84*, 5129-5140.
9. Y. K. Hu, L. Chen, B. D. Li. *RSC Adv*. **2016**, *6*, 65196-65204.
10. S. Maiti, J. Kim, J.-H. Park, D. Nam, J. B. Lee, Y.-J. Kim, J.-M. Kee, J. K. Seo, K. Myung, J.-U. Rohde, W. Choe, O.-H, Kwon, S. Y. Hong. *J. Org. Chem*. **2019**, *84*, 6737-6751.
11. S. Das, S. Sinha, D. Samanta, R. Mondal, G. Chakraborty, P. Brandaõ, N. D. Paul. *J. Org. Chem*. **2019**, *84*, 10160-10171.
12. X. H. Tian, L. N. Song, E.T. Li, Q. Wang, W. Q. Yu, J. B. Chang. *RSC Adv*. **2015**, *5*, 62194-62201.
13. G. Latha, N. Devarajan and P. Suresh, *ChemistrySelect* **2020**, *5*, 10041-10047.
14. Z. Li, J. Dong, X. Chen, Q. Li, Y. Zhou and S.-F. Yin, *J. Org. Chem.* **2015**, *80*, 9392-9400.
15. D. B. Khadka, G. H. Tran, S. Shin, H. T. M. Nguyen, H. T. Cao, C. Zhao, Y. F. Jin, H. T. M. Van, M. V. Chau, Y. Kwon, T. N. Le, W.-J. Cho. *Eur. J. Med. Chem*., **2015**, *103*, 69-79.
16. S. M. Patel, H. Chada, S. Biswal, S. Sharma and D. S. Sharada, *Synthesis* **2019**, *51*, 3160-3170.
17. R. S. Rohokale, R. G. Kalshetti and C. V. Ramana, *J. Org. Chem.* **2019**, *84*, 2951-2961.
18. S. A. Samim, B. C. Roy, S. Nayak and S. Kundu, *J. Org. Chem.* **2020**, *85*, 11359-11367.
19. C. Duan, J, Jia, R. Zhu and J. Wang, *J. Heterocyclic Chem.* **2012**, *49*, 865-872.
20. J. Lin, P. P. Wang, Z. M. Zhang, G. Z. Xue, D. J. Zha, J. Wang, X. Z. Xu and Z. L. Li, *Synth. Commun.*, **2020**, *50*, 823-830.
21. L. Sancineto, N. Iraci, S. Massari, V. Attanasio, G. Corazza, M. L. Barreca, S. Sabatini, G. Manfroni, N. R. Avanzi, V. Cecchetti, C. Pannecouque, A. Marcello, O. Tabarrini, *ChemMedChem*, **2013**, *8*, 1941-1953.
22. Z. Zhang, M. Wang, C. Zhang Z. Zhang, J. Lu and F. Wang, *Chem. Commun*., **2015**, *51*, 9205-9207.

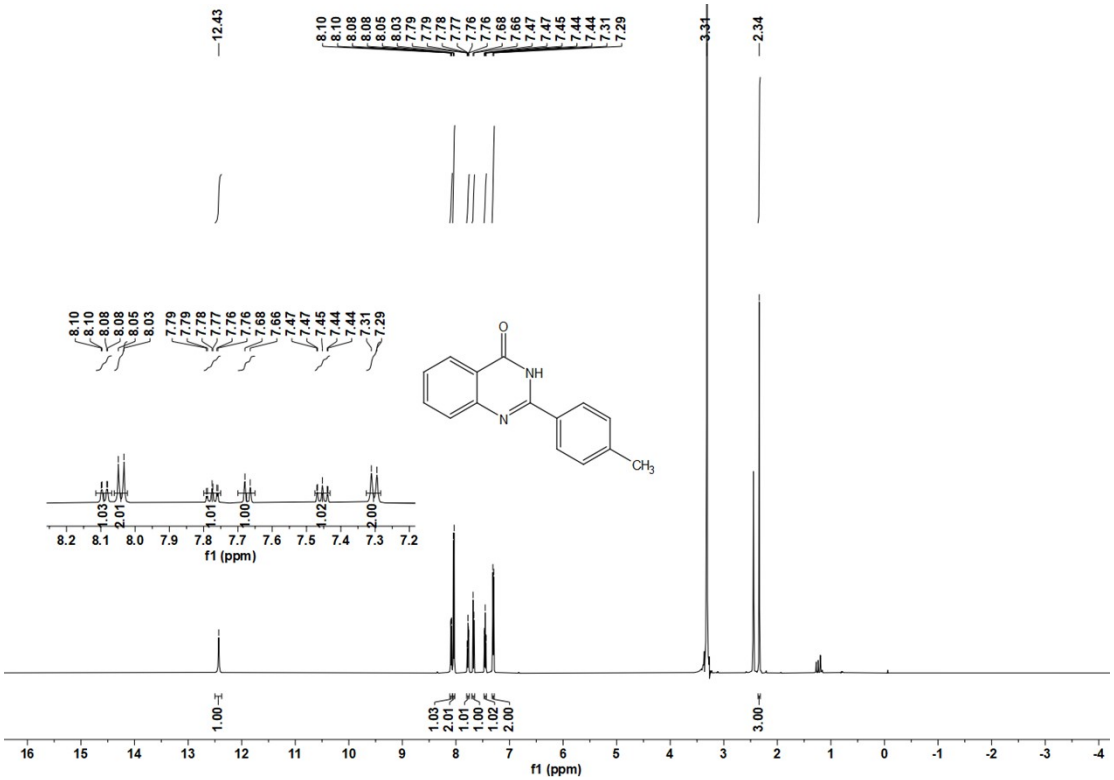
^{1}H NMR and ^{13}C NMR spectra for the products

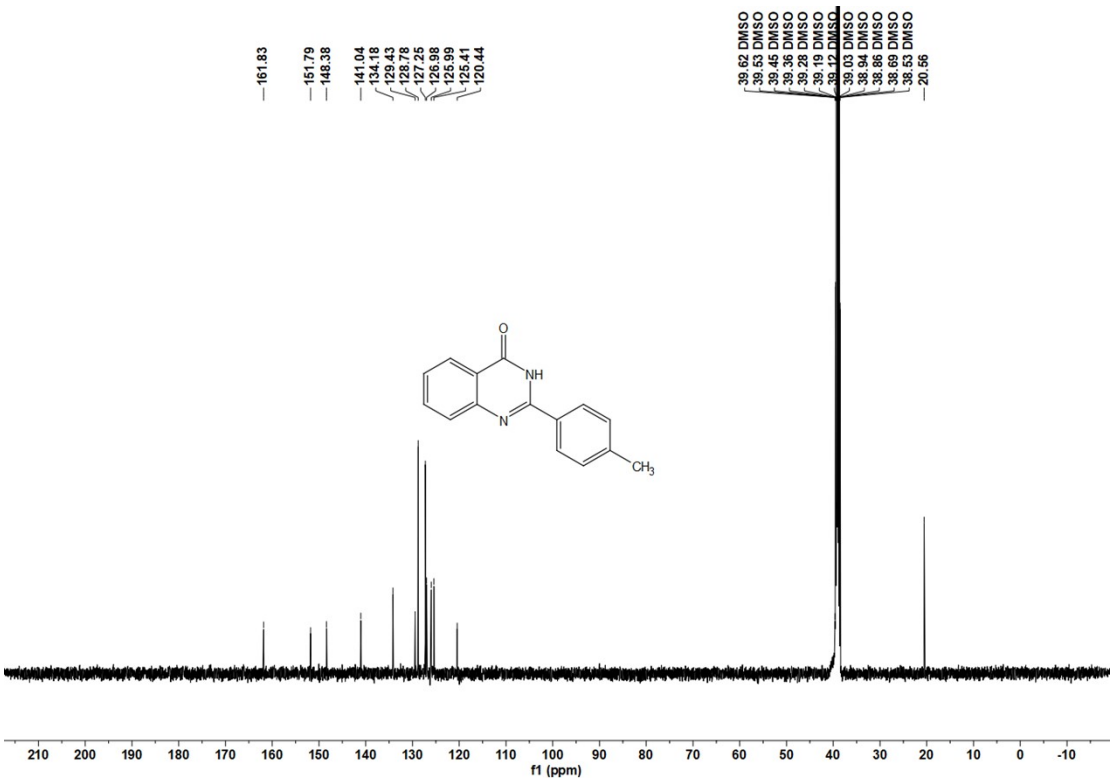
2-phenylquinazolin-4(3H)-one (3a)



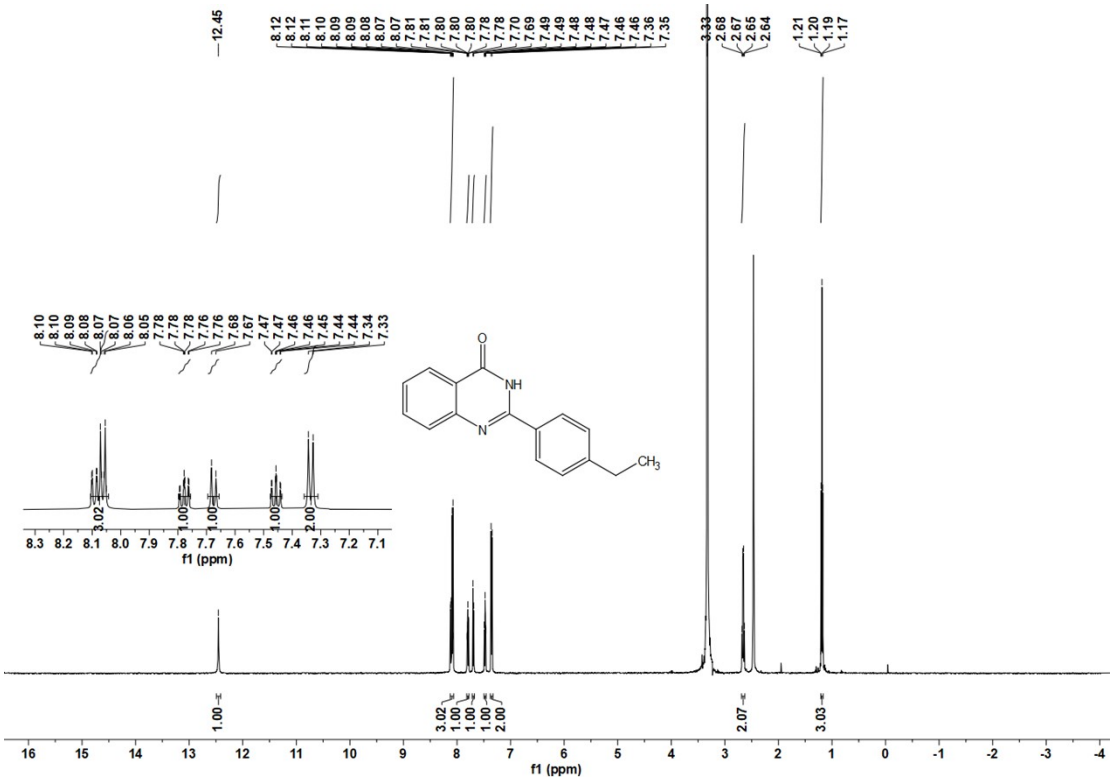


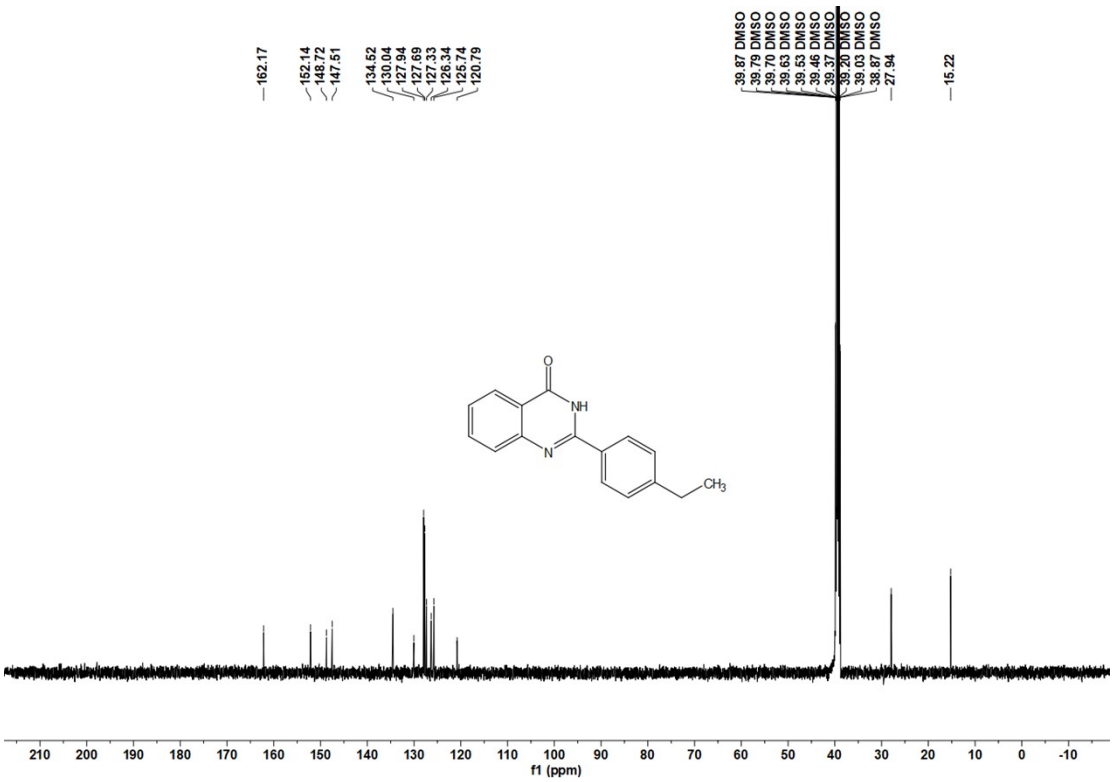
2-(p-tolyl)quinazolin-4(3H)-one (3b)



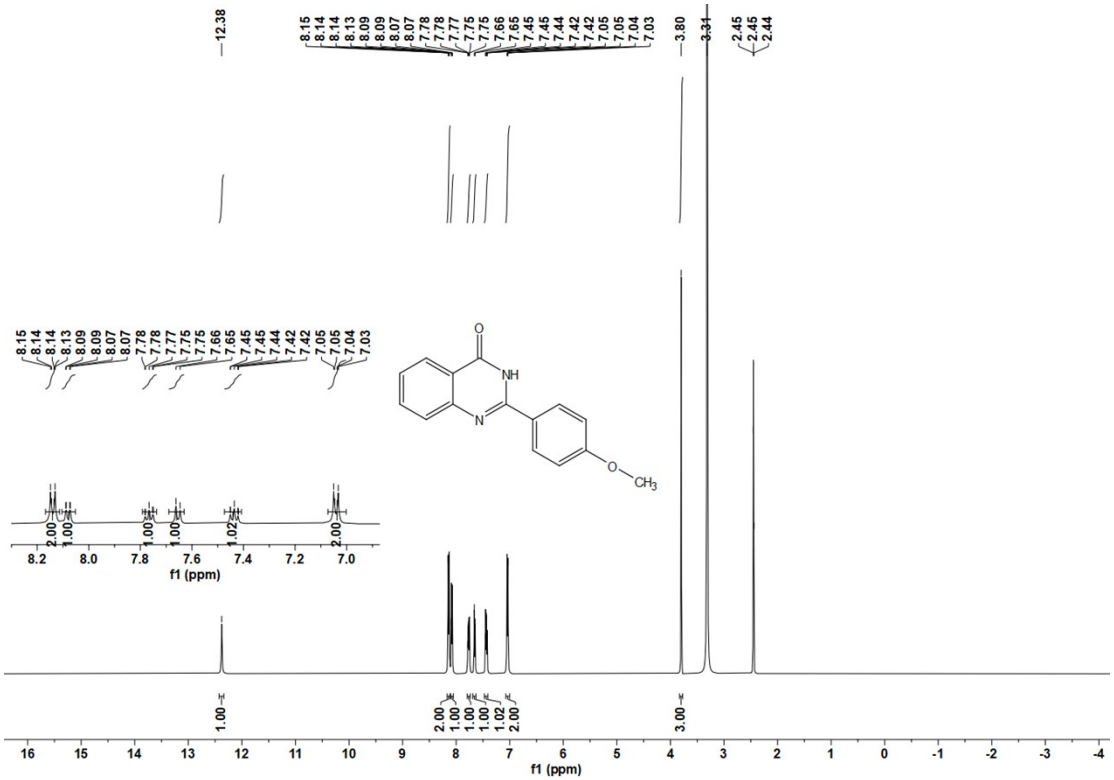


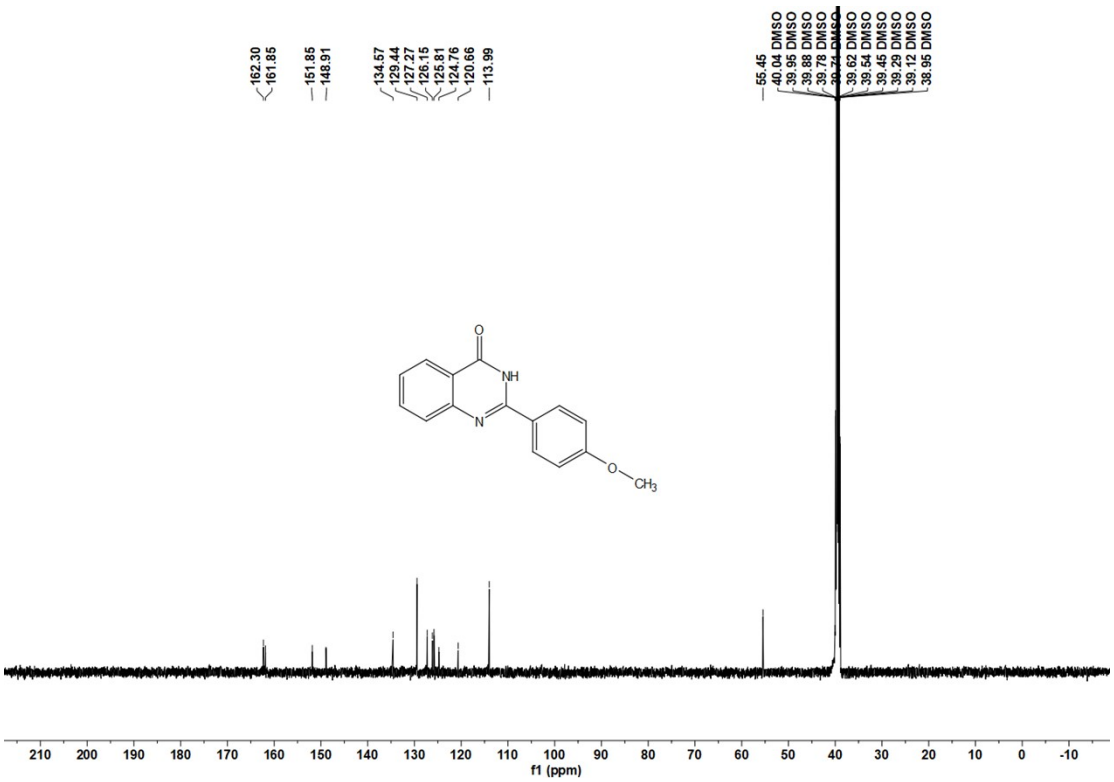
2-(4-ethylphenyl)quinazolin-4(3H)-one (3c)



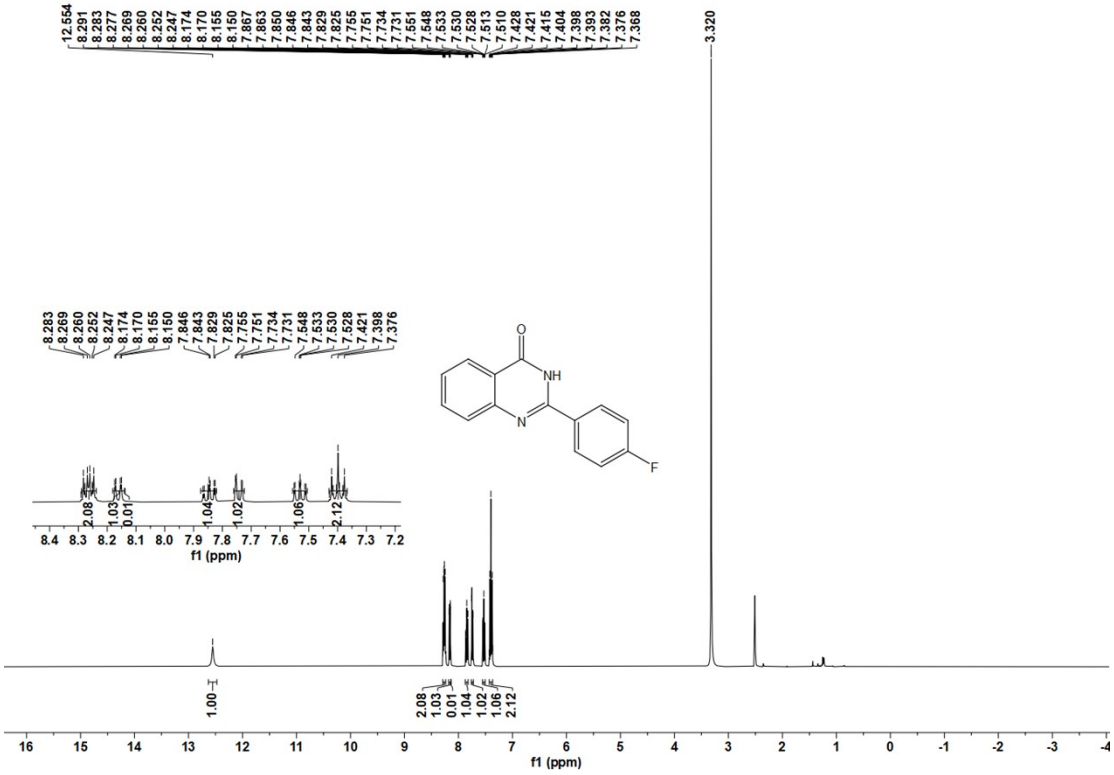


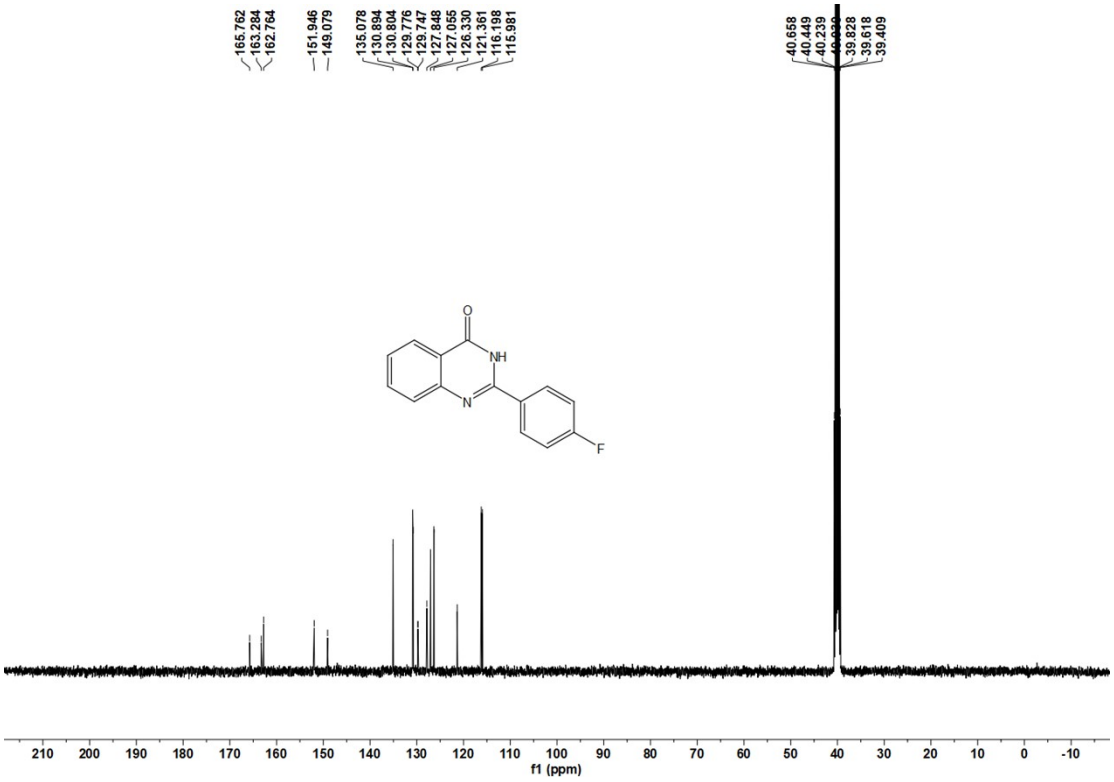
2-(4-methoxyphenyl)quinazolin-4(3H)-one (3d)



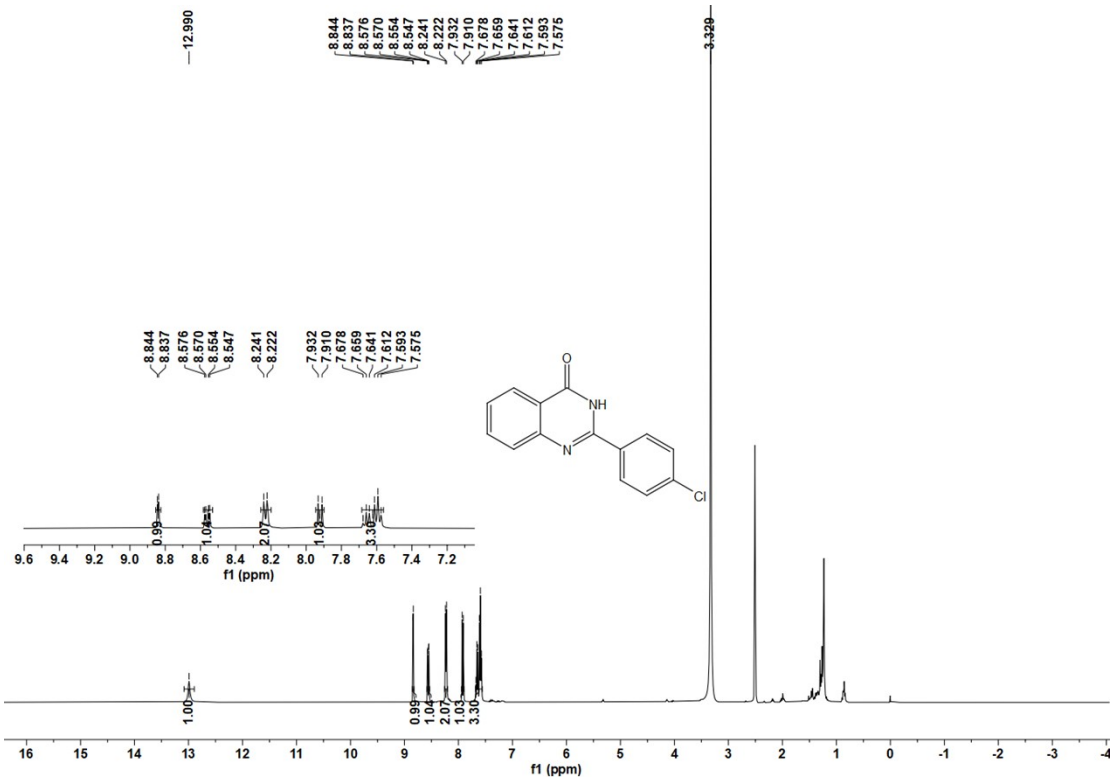


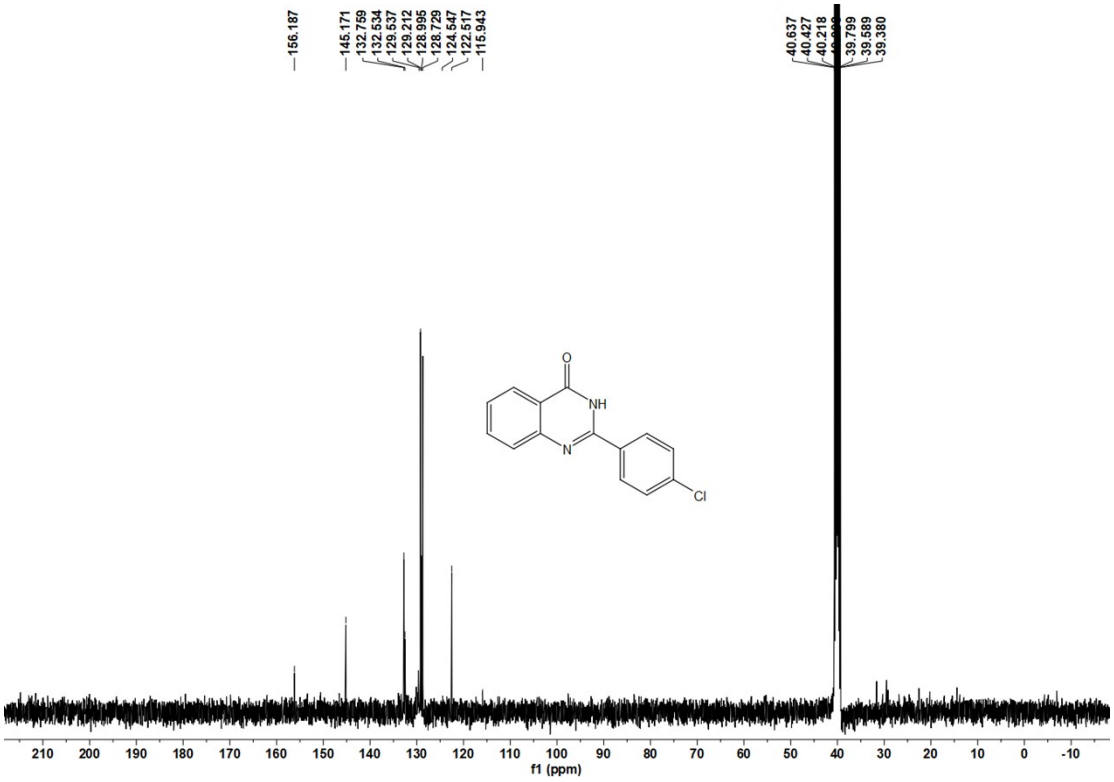
2-(4-fluorophenyl)quinazolin-4(3H)-one (3e)



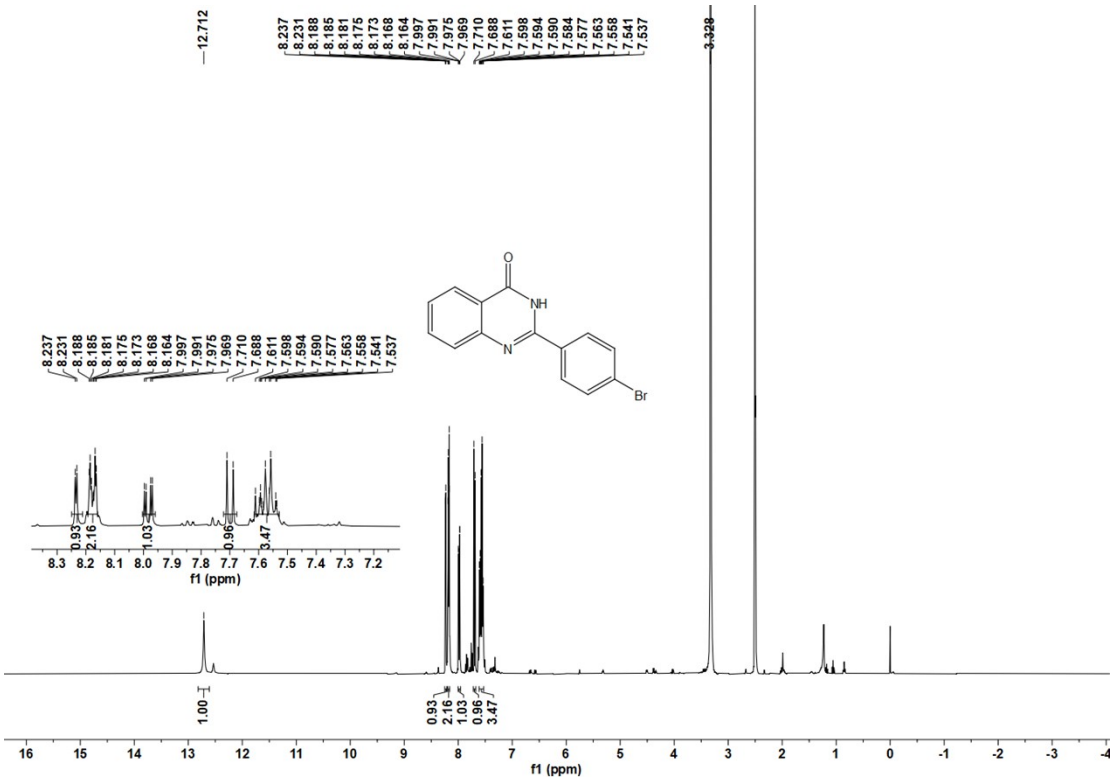


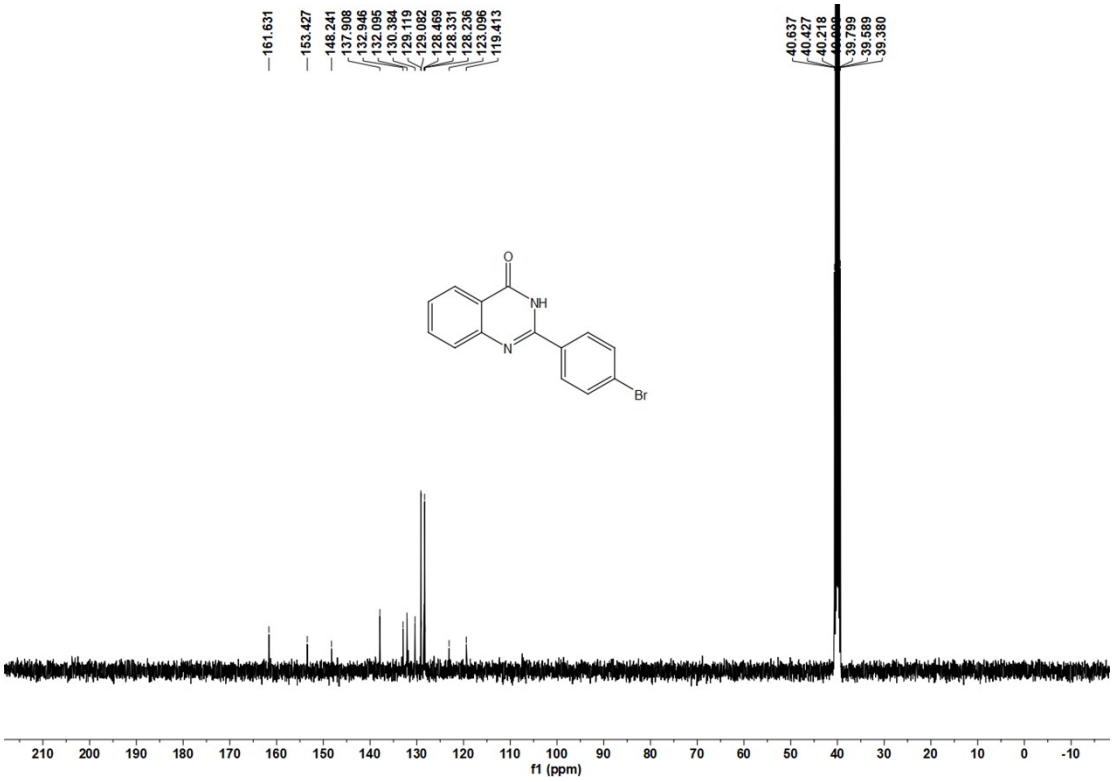
2-(4-chlorophenyl)quinazolin-4(3H)-one (3f)



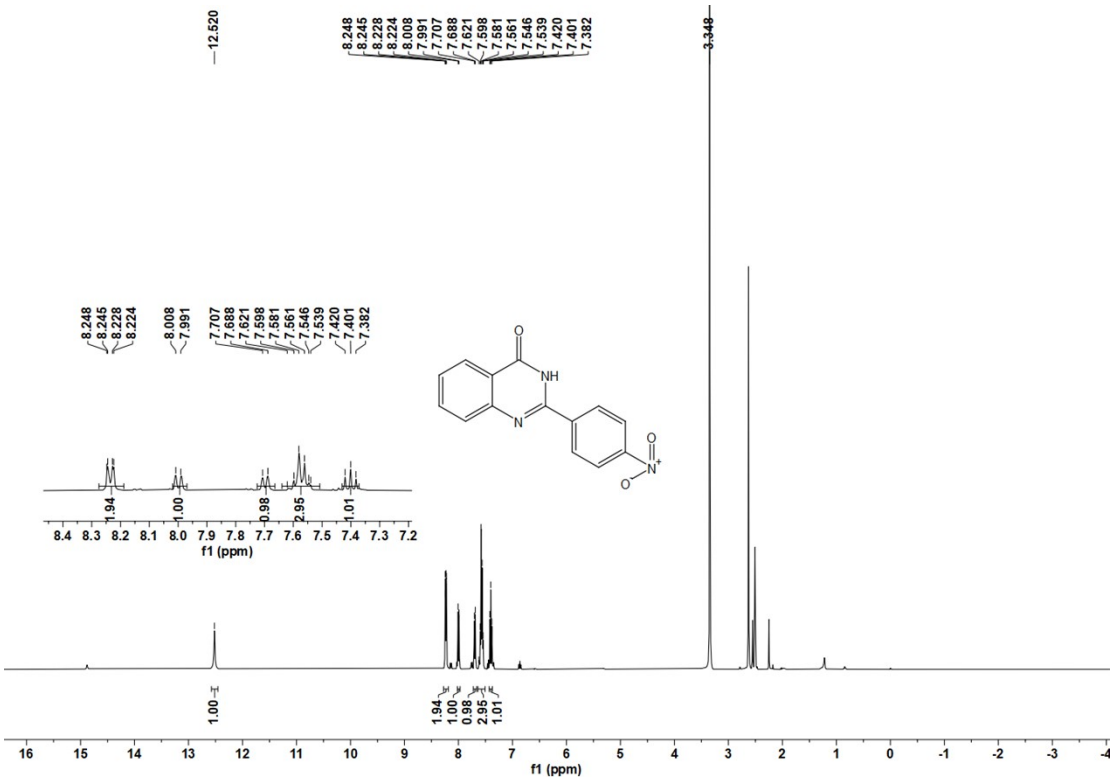


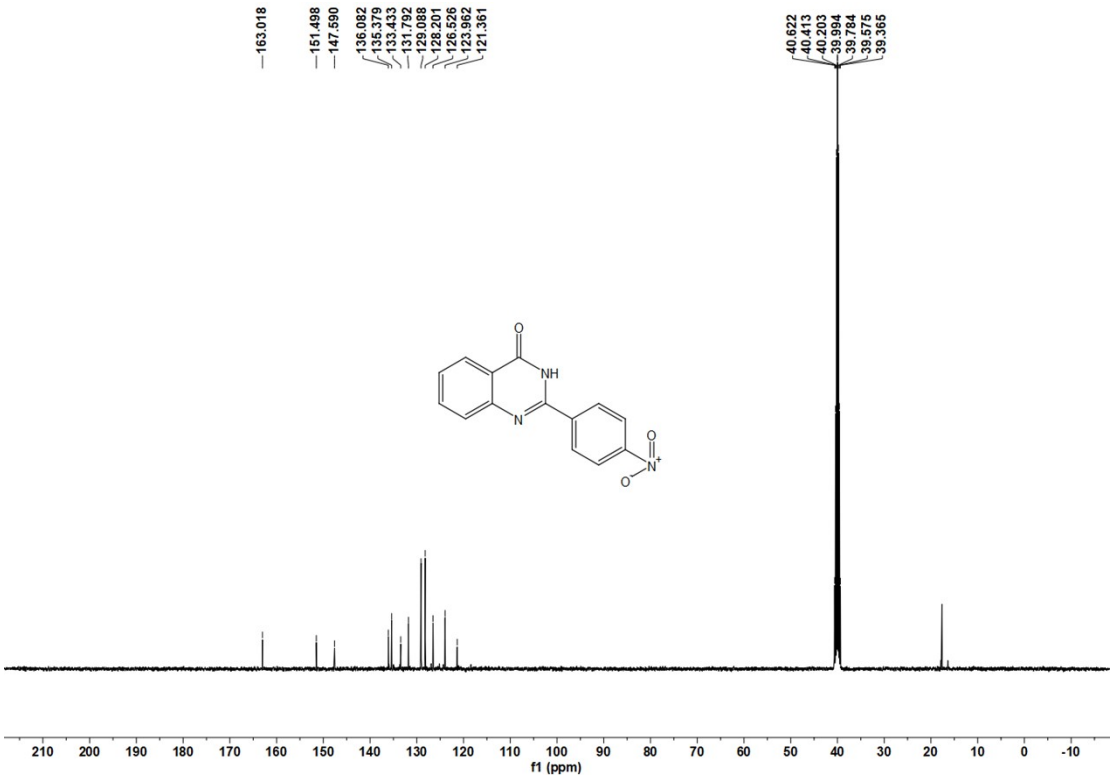
2-(4-bromophenyl)quinazolin-4(3H)-one (3g)



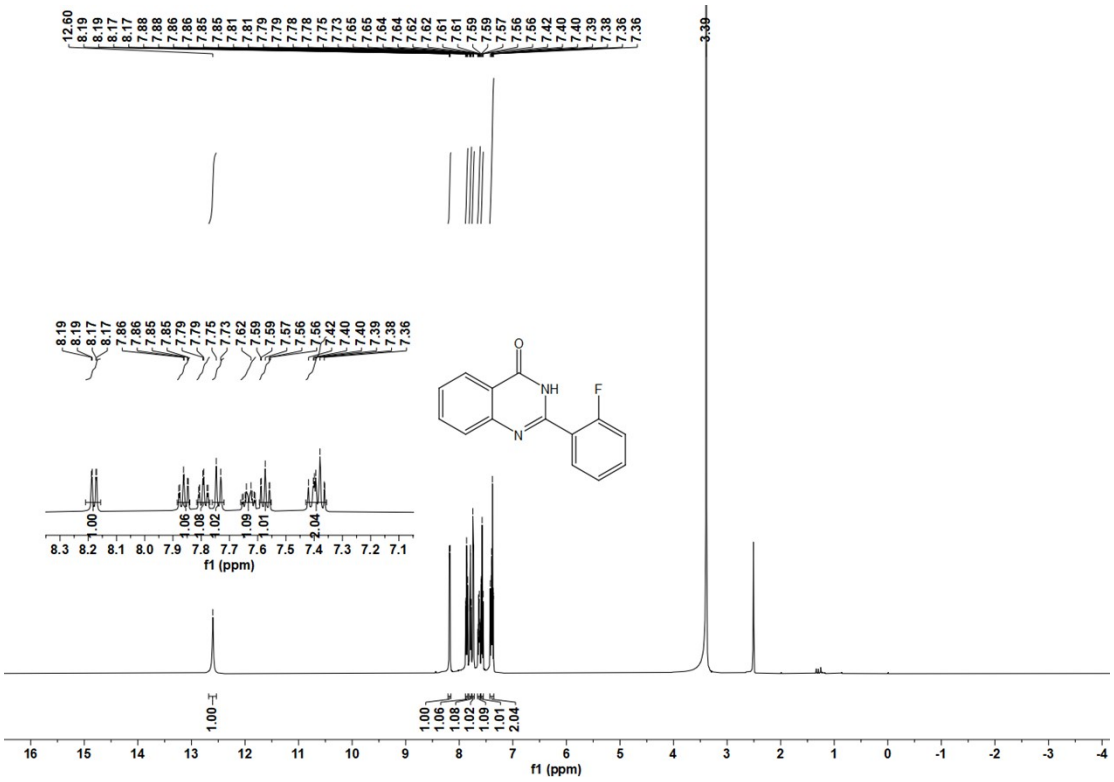


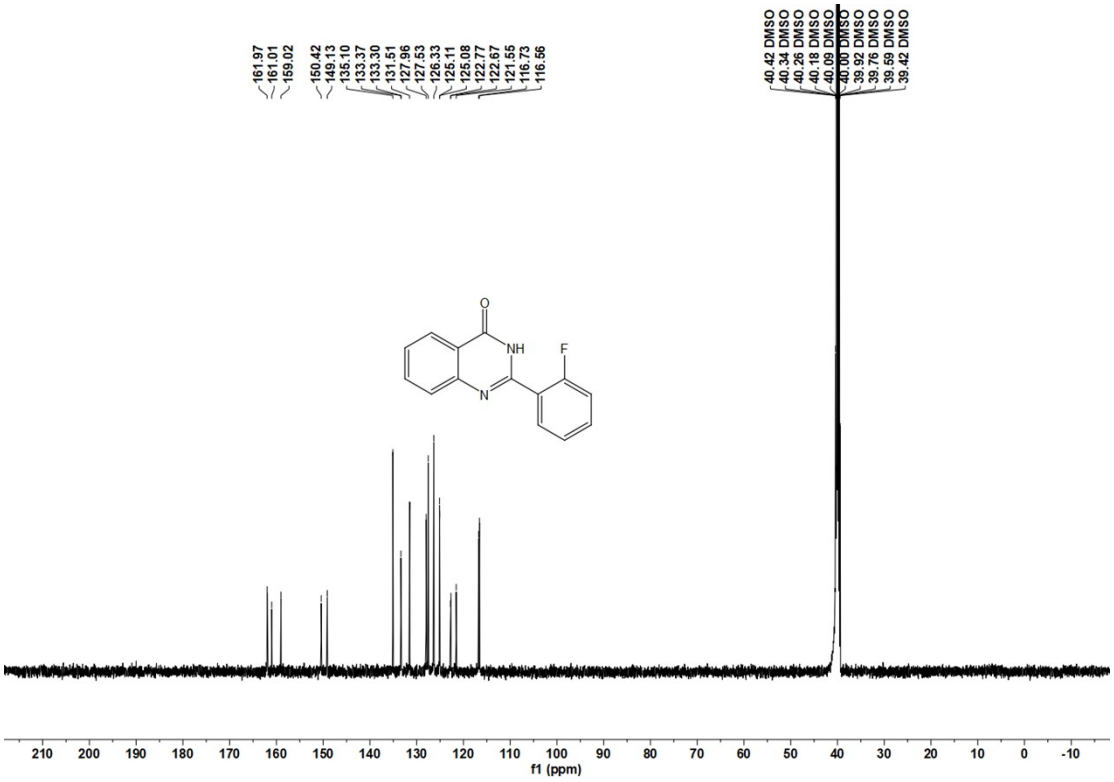
2-(4-nitrophenyl)quinazolin-4(3H)-one (3h)



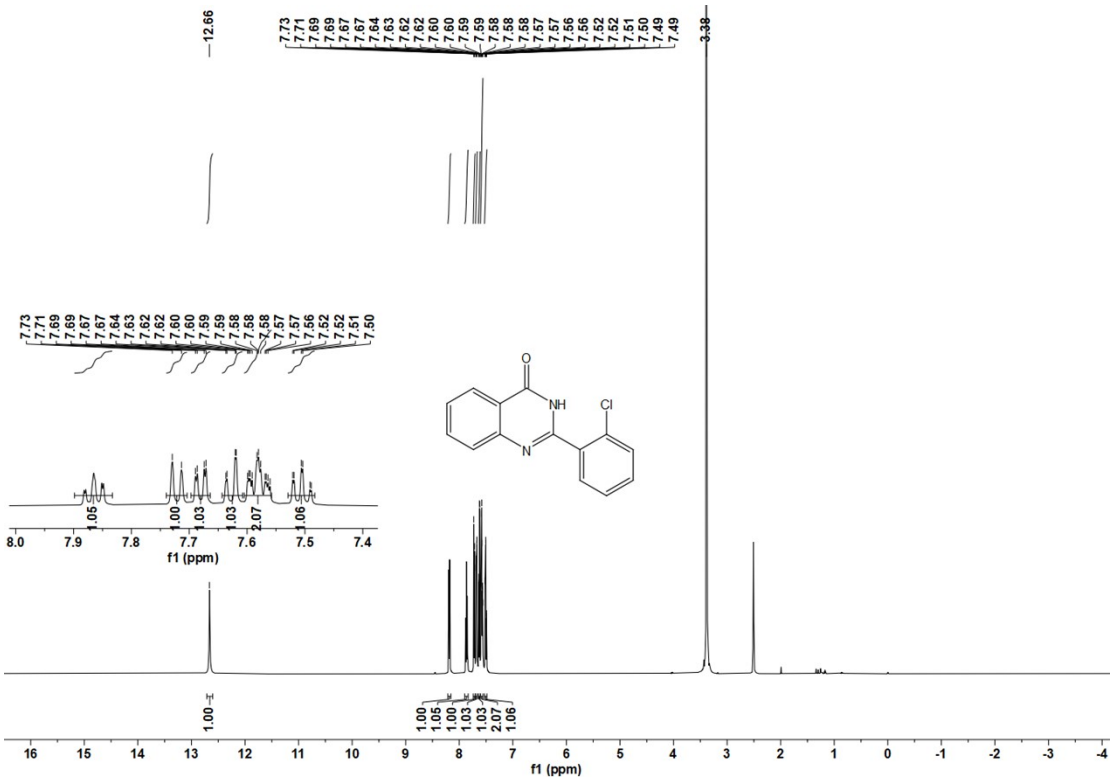


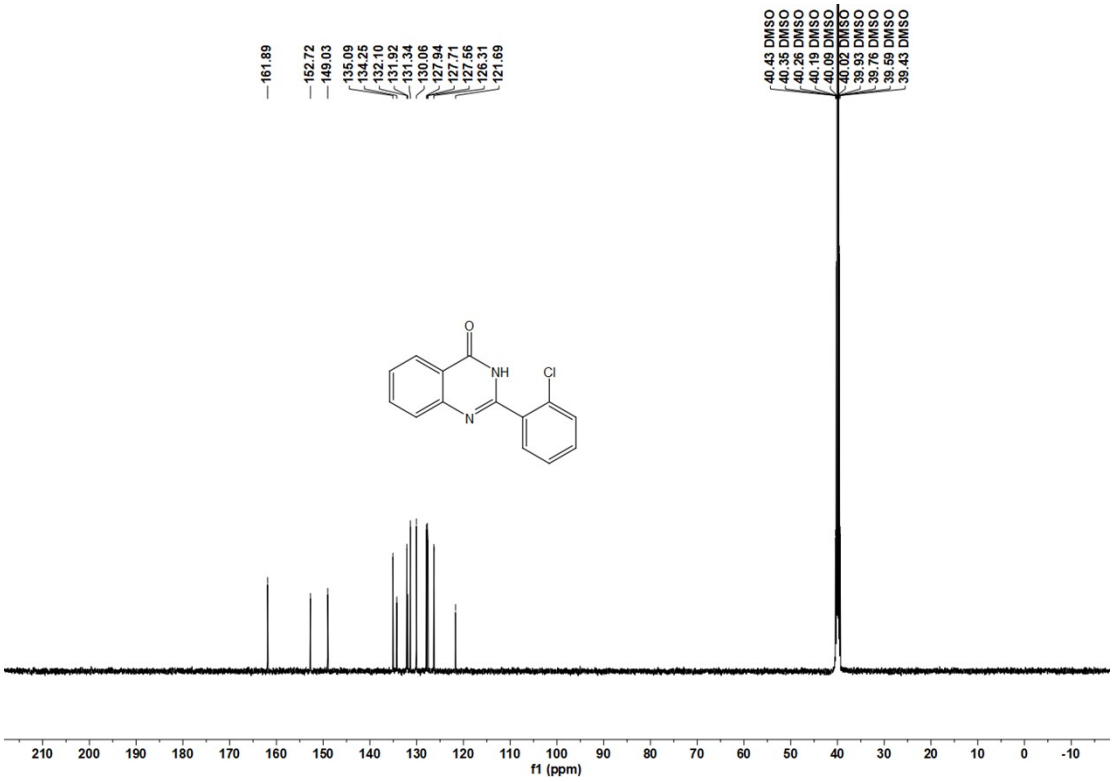
2-(2-fluorophenyl)quinazolin-4(3H)-one (3i)



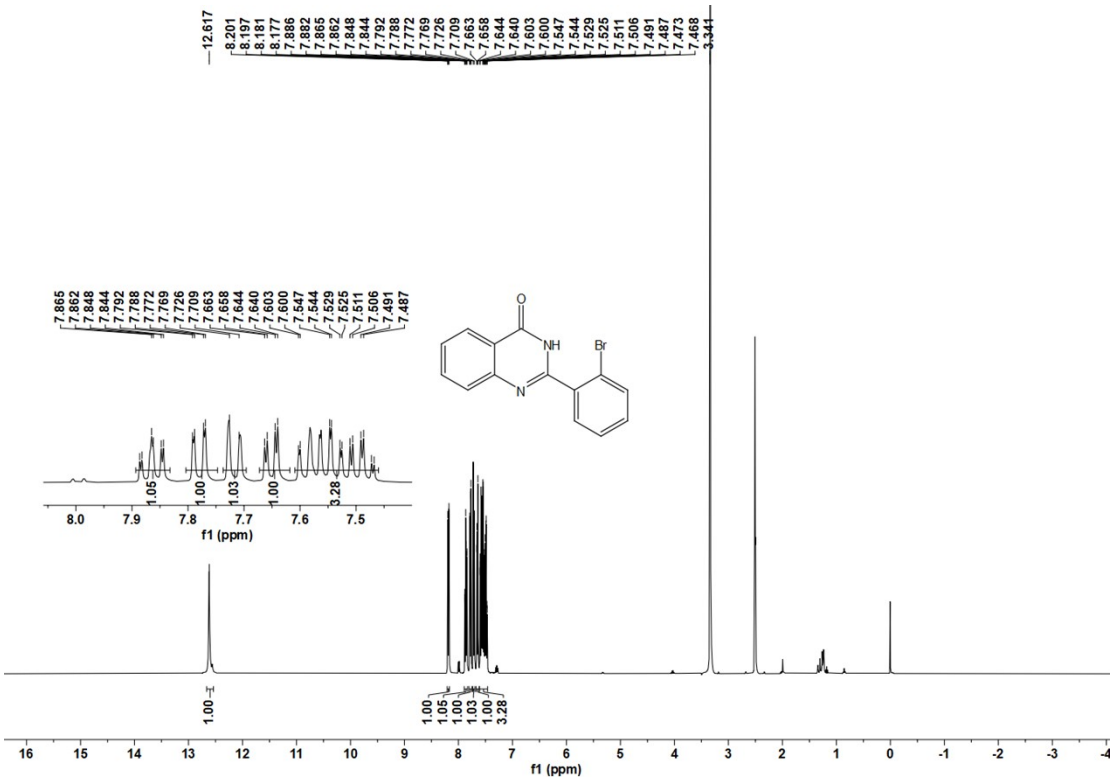


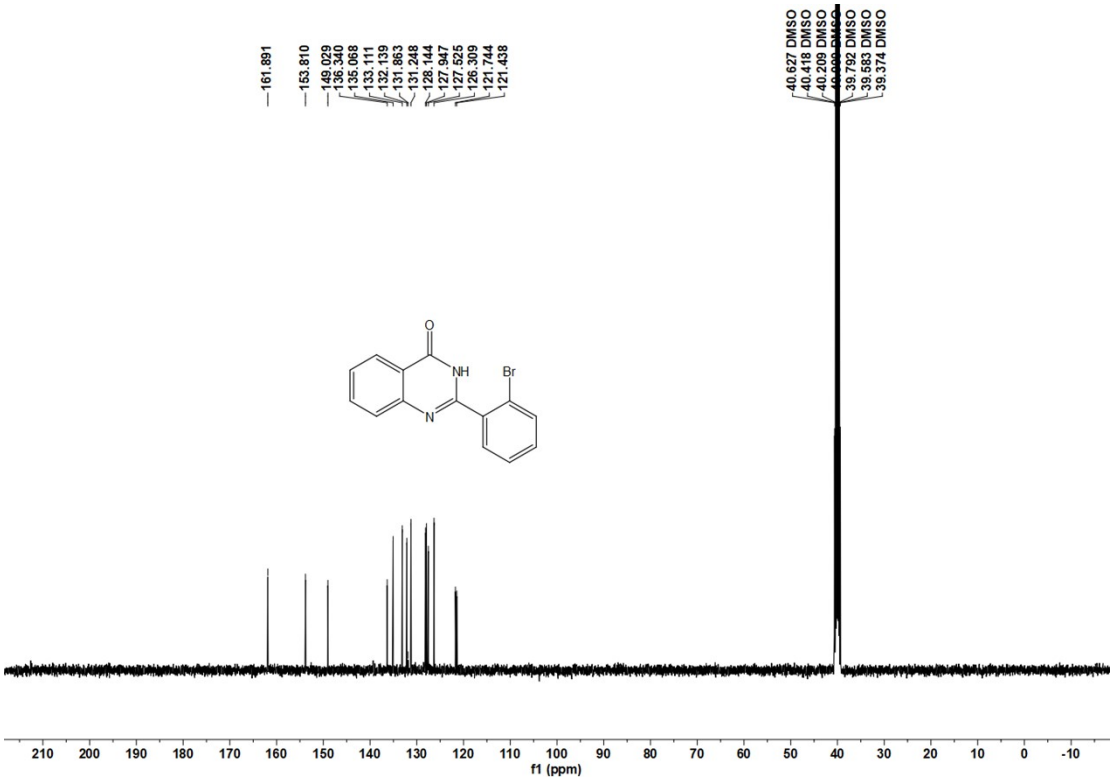
2-(2-chlorophenyl)quinazolin-4(3H)-one (3j)



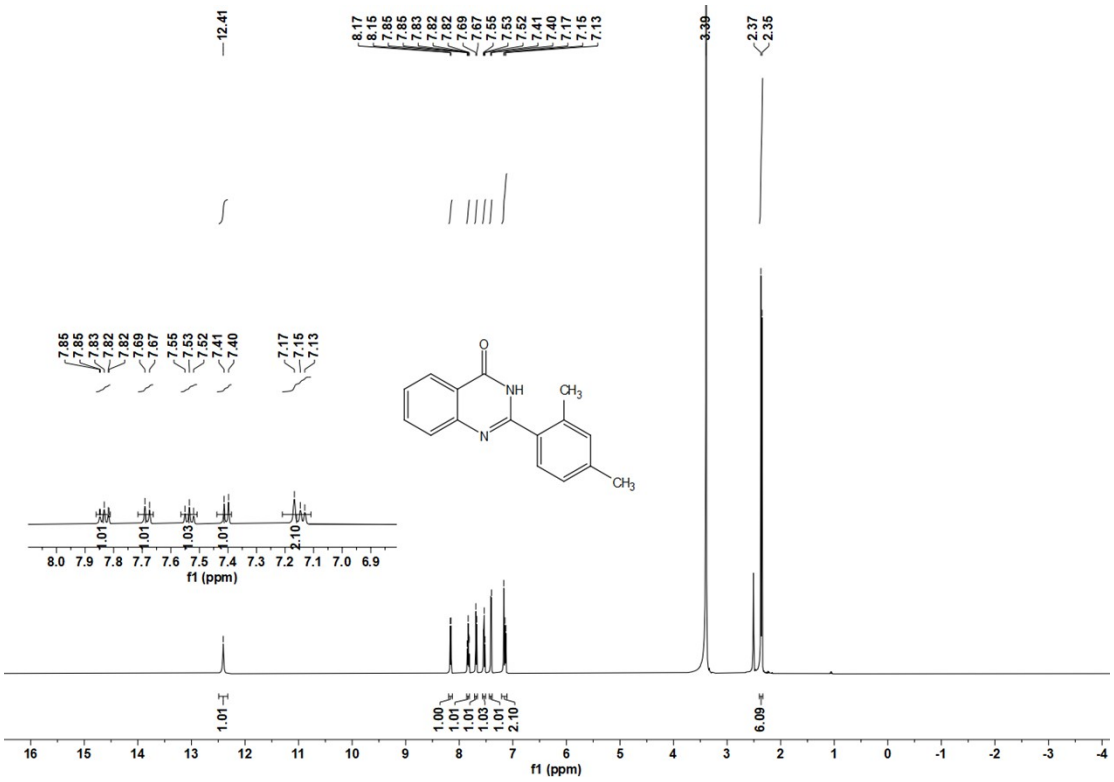


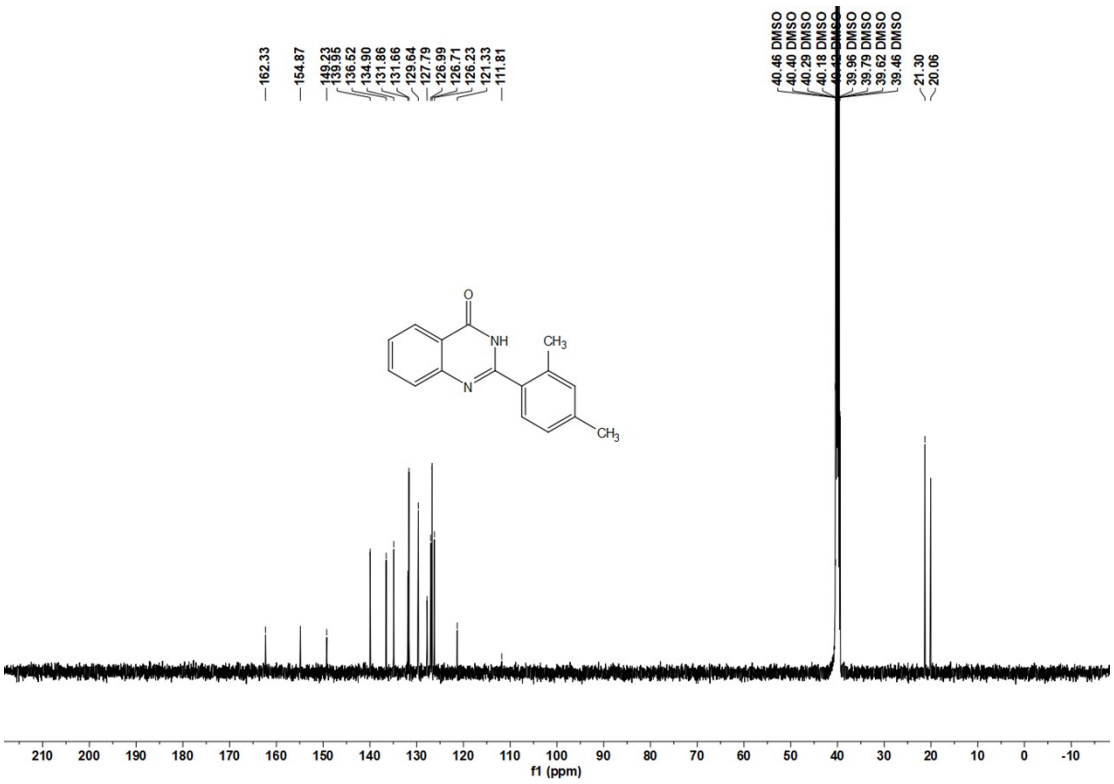
2-(2-bromophenyl)quinazolin-4(3H)-one (3k)



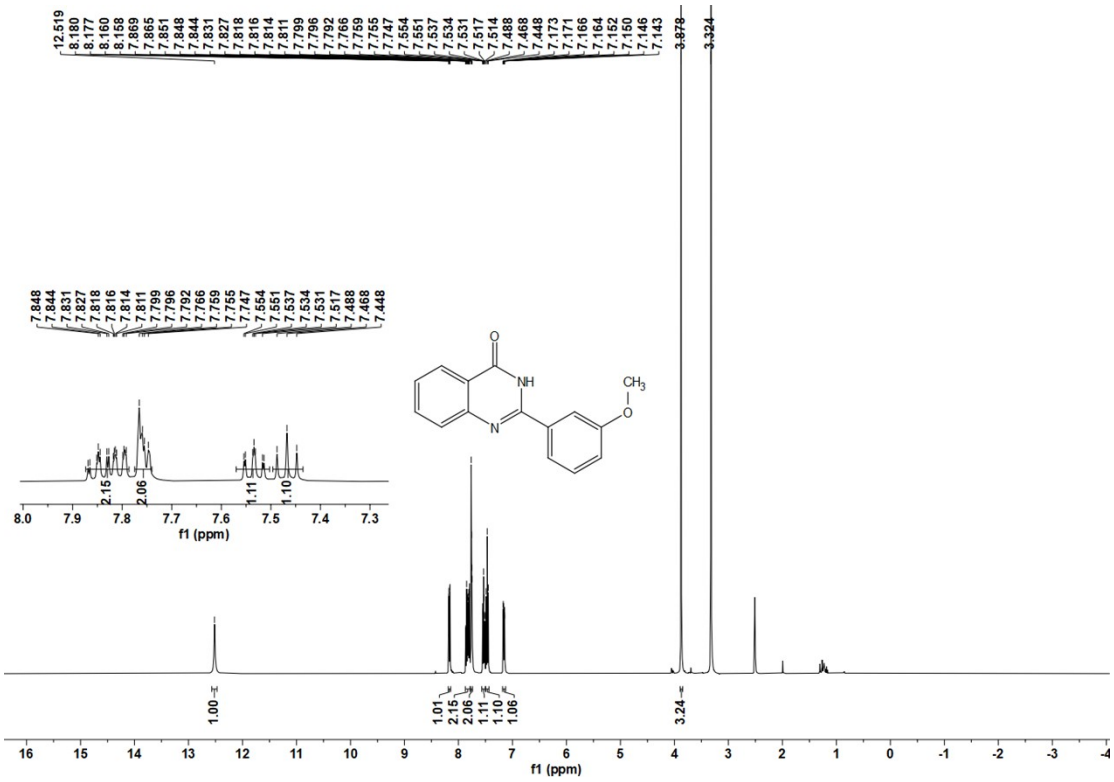


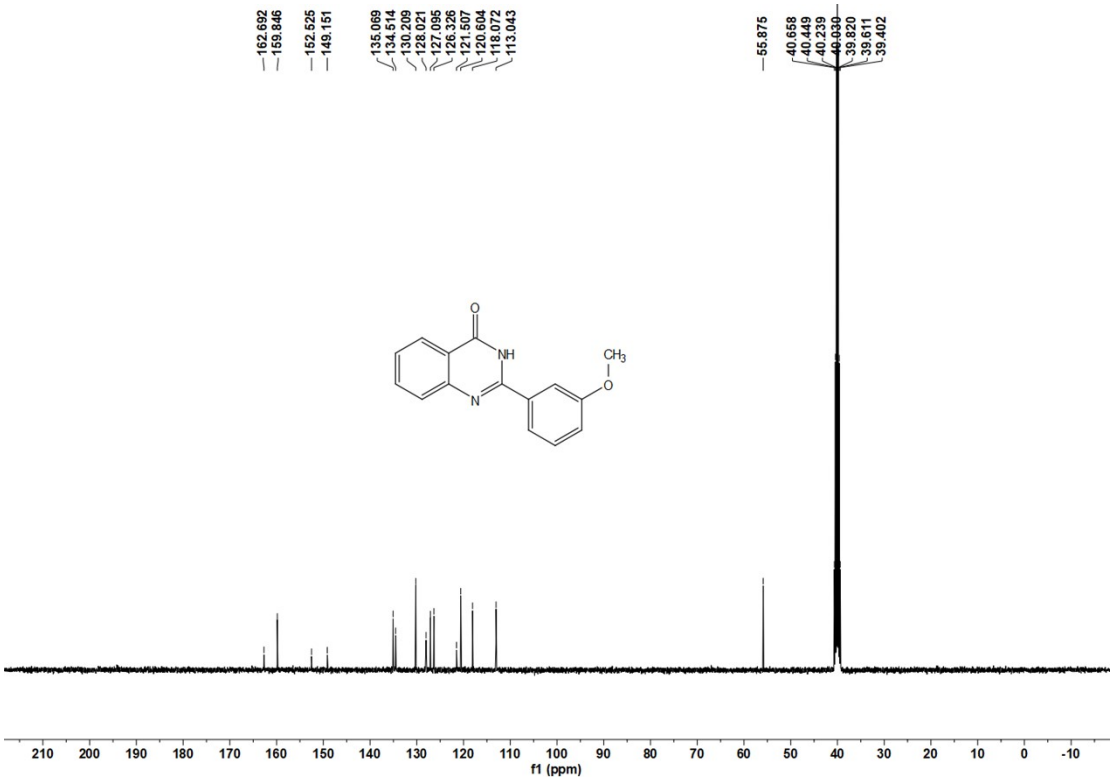
2-(2,4-dimethylphenyl)quinazolin-4(3H)-one (3l)



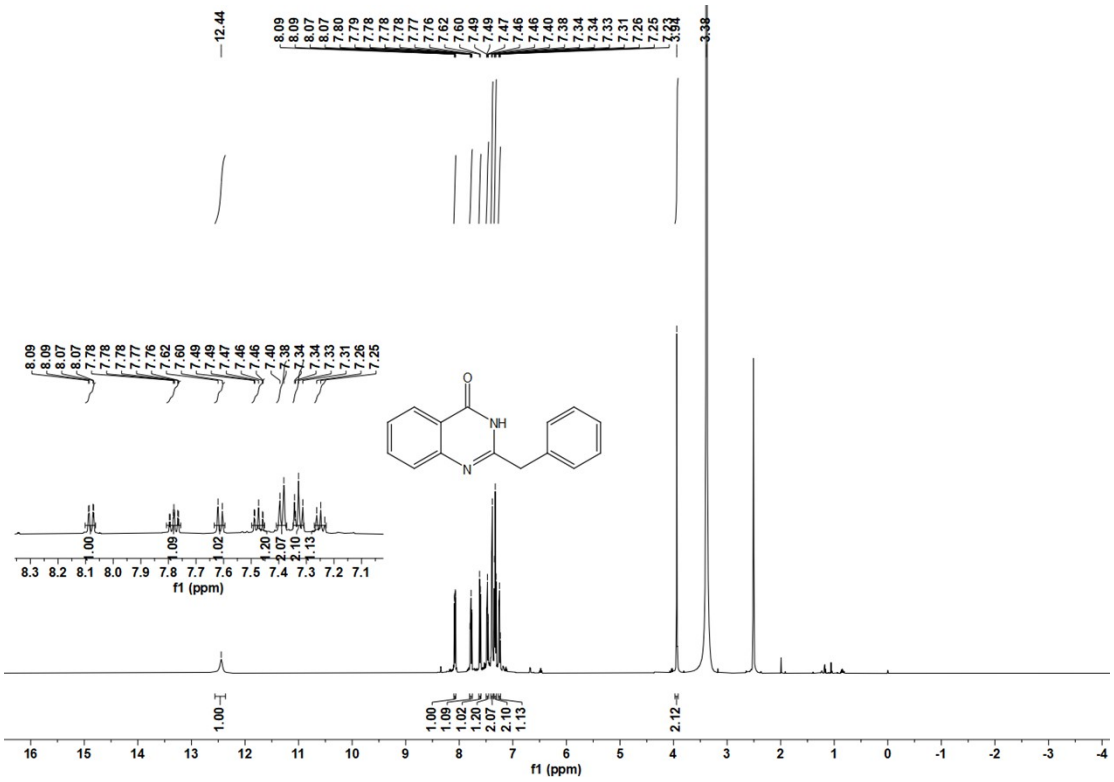


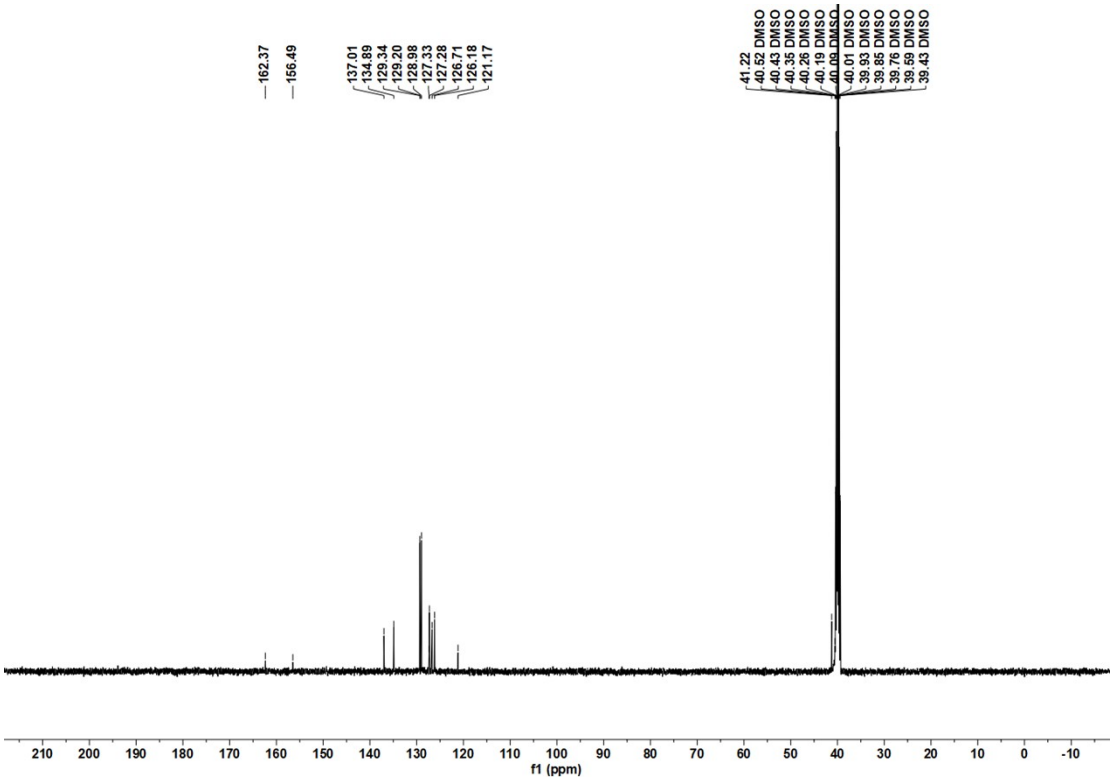
2-(3-methoxyphenyl)quinazolin-4(3H)-one (3m)



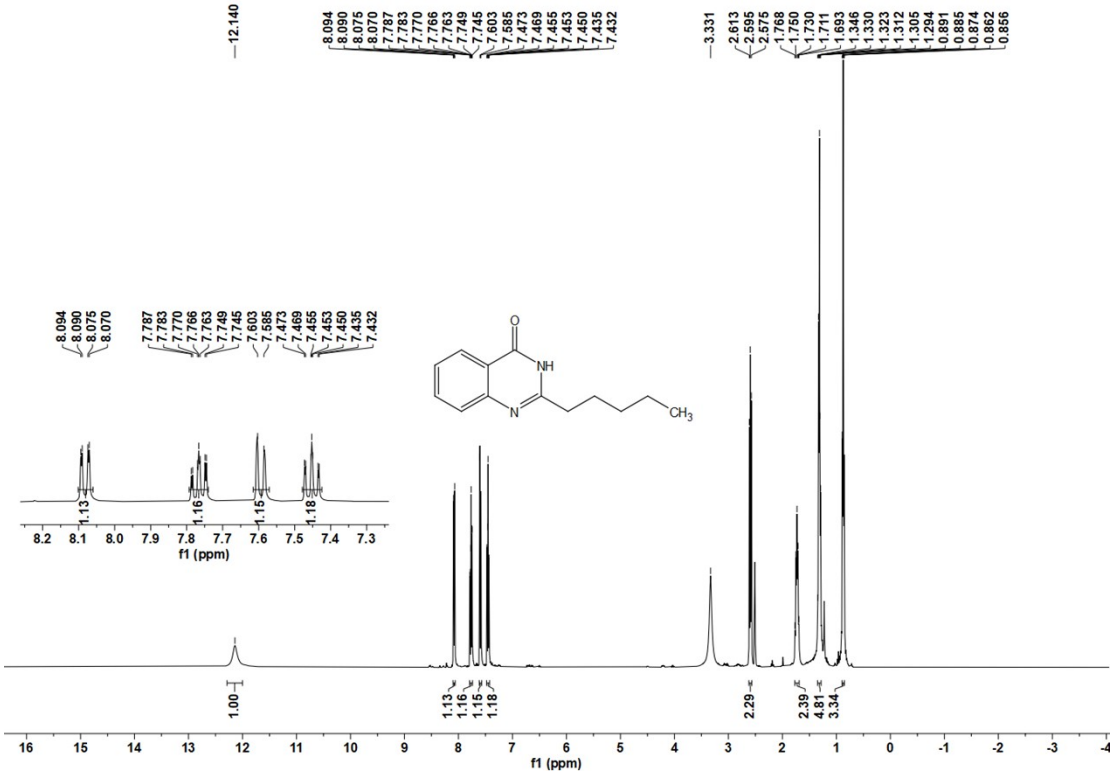


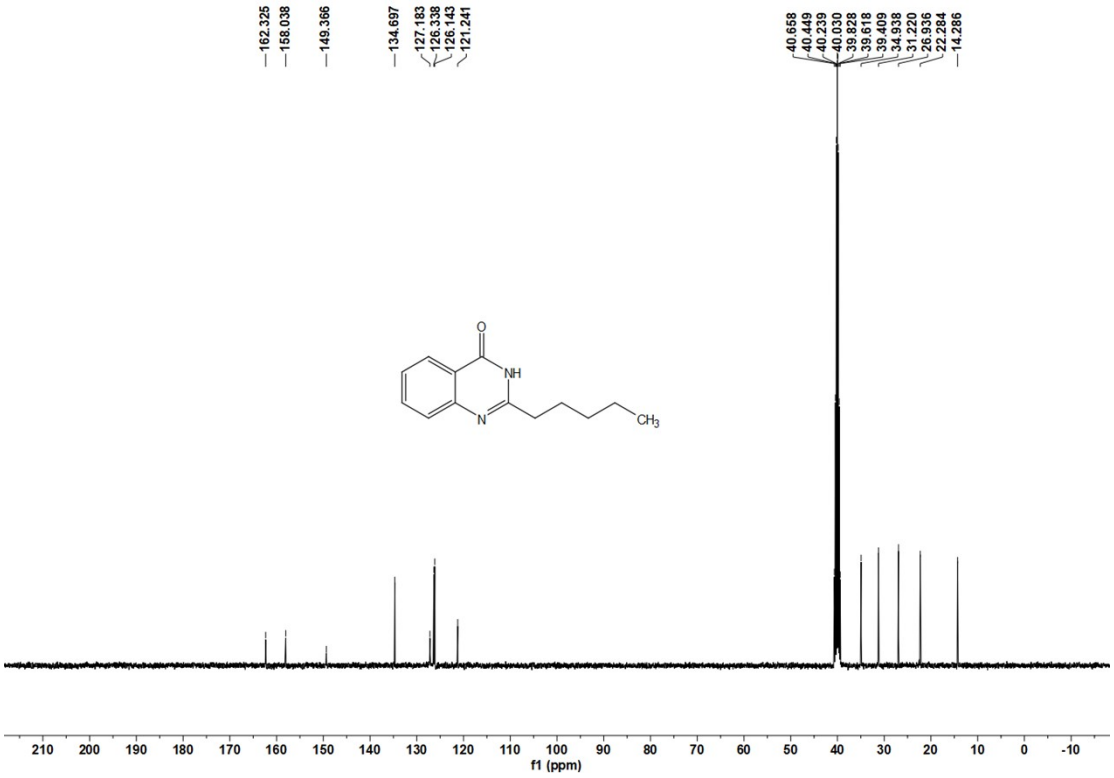
2-benzylquinazolin-4(3H)-one (3n)



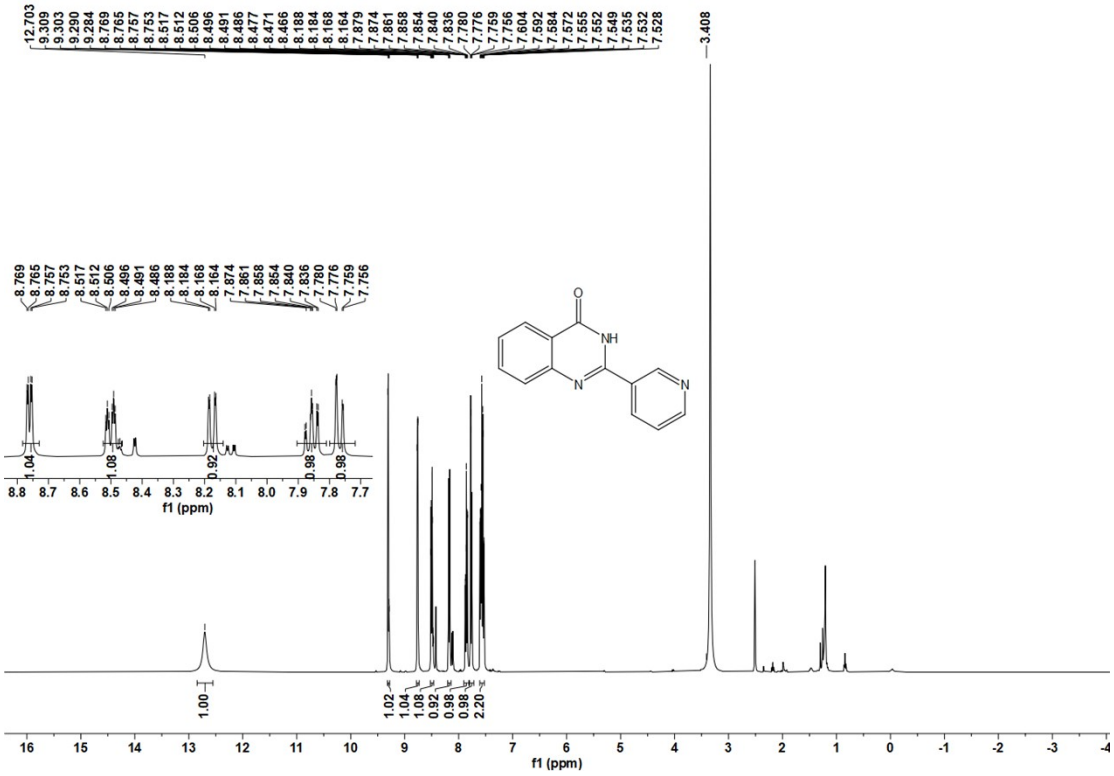


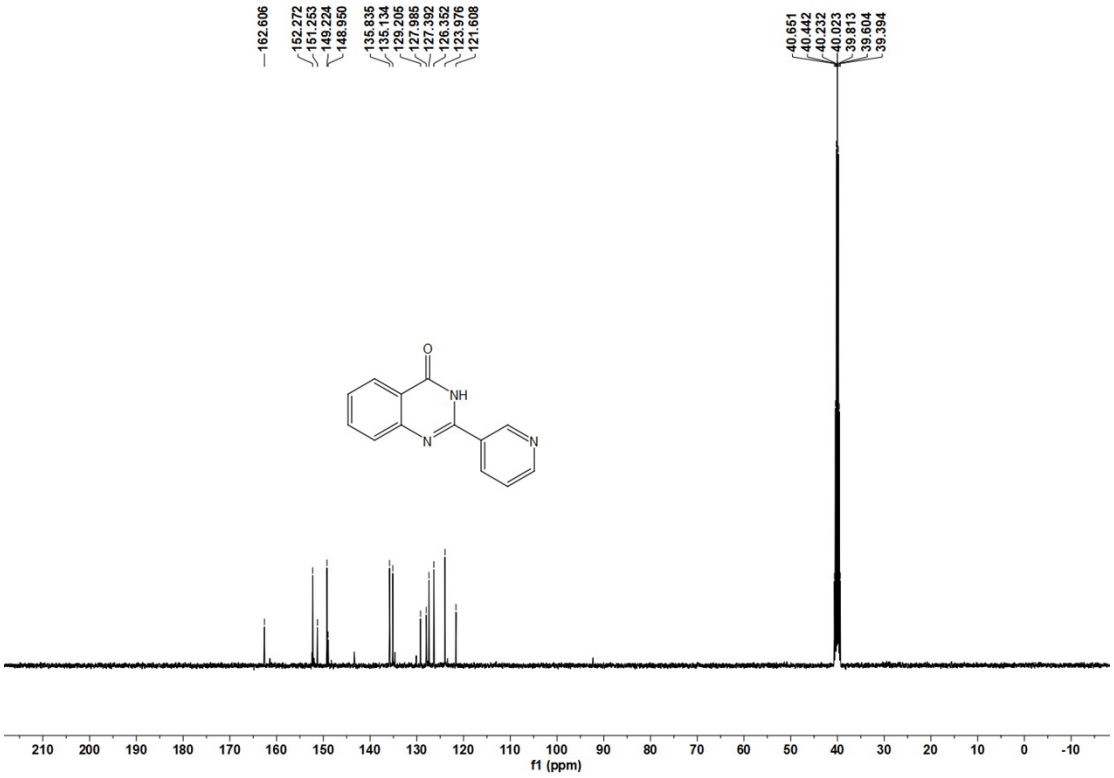
2-pentylquinazolin-4(3H)-one (3o)



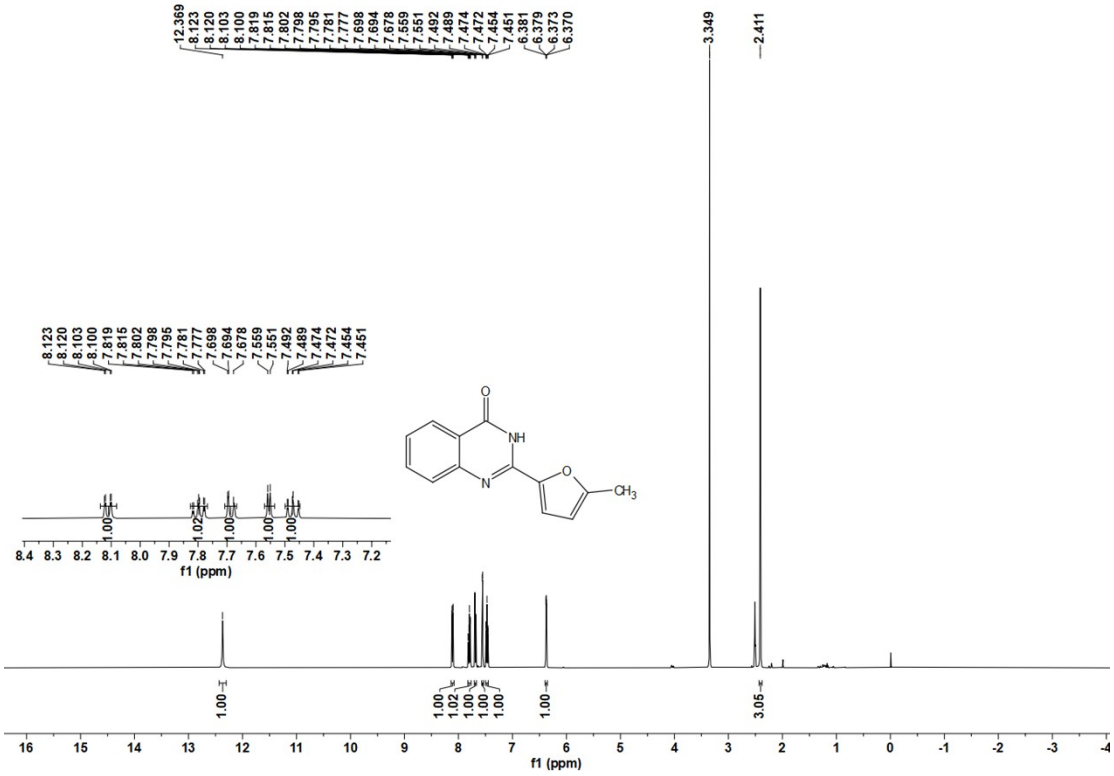


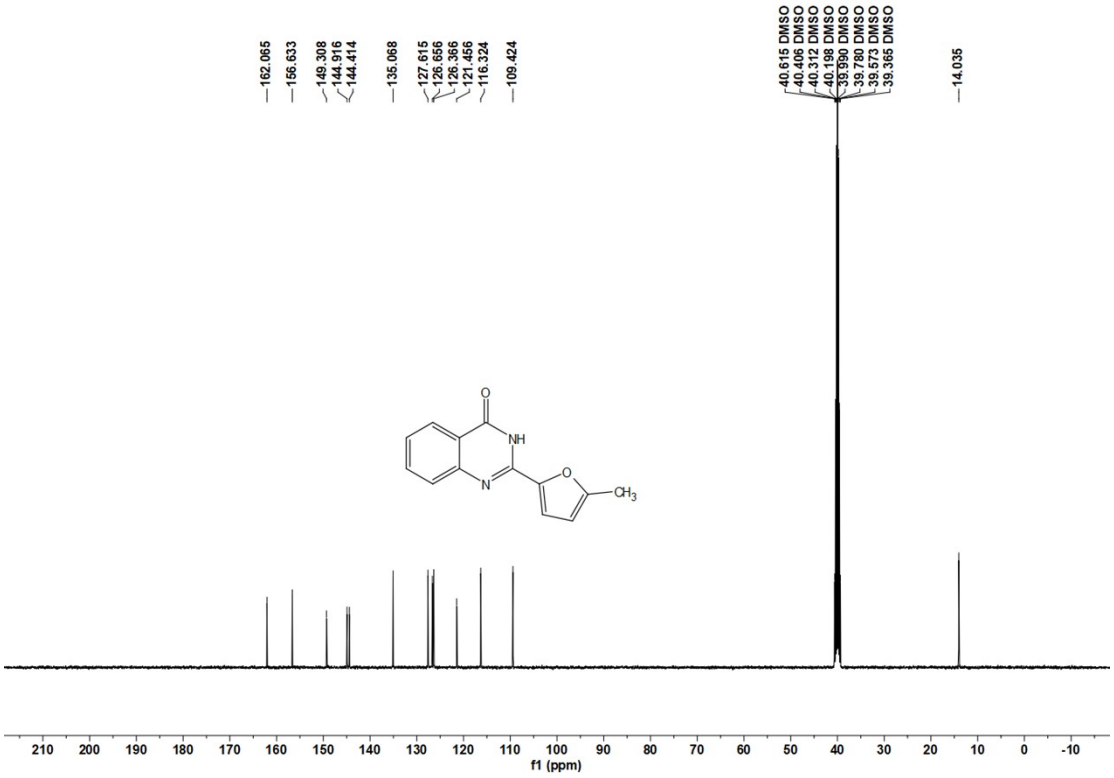
2-(pyridin-3-yl)quinazolin-4(3H)-one (3p)



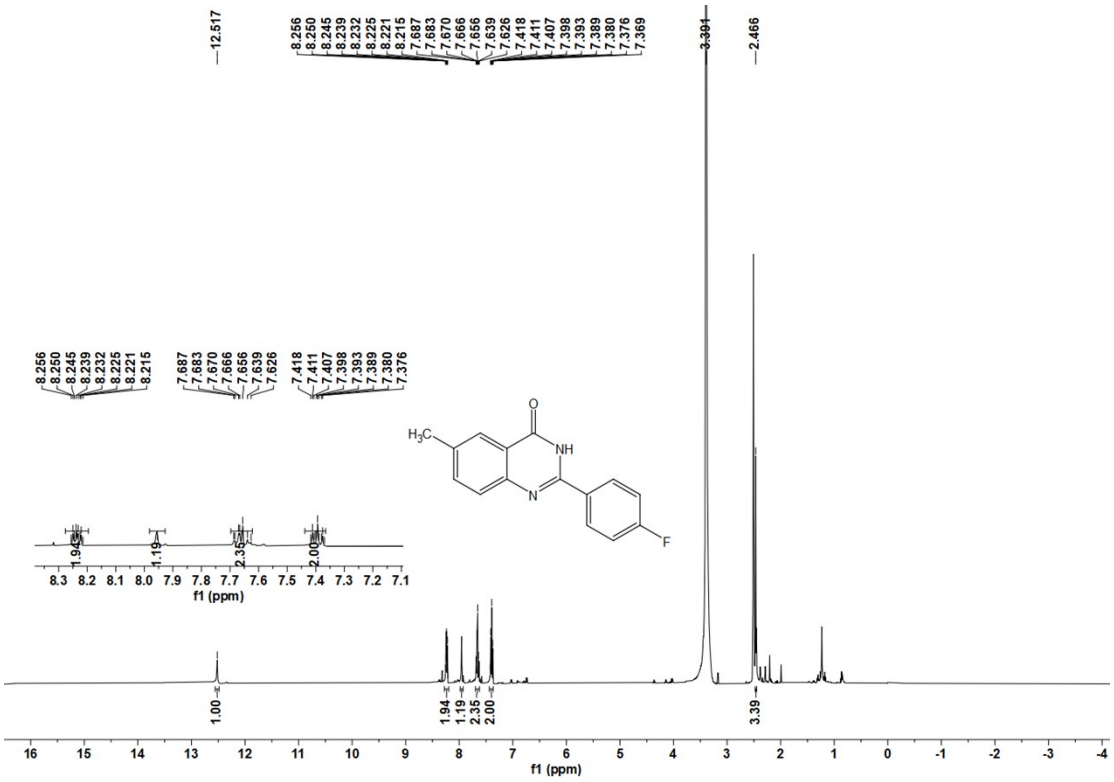


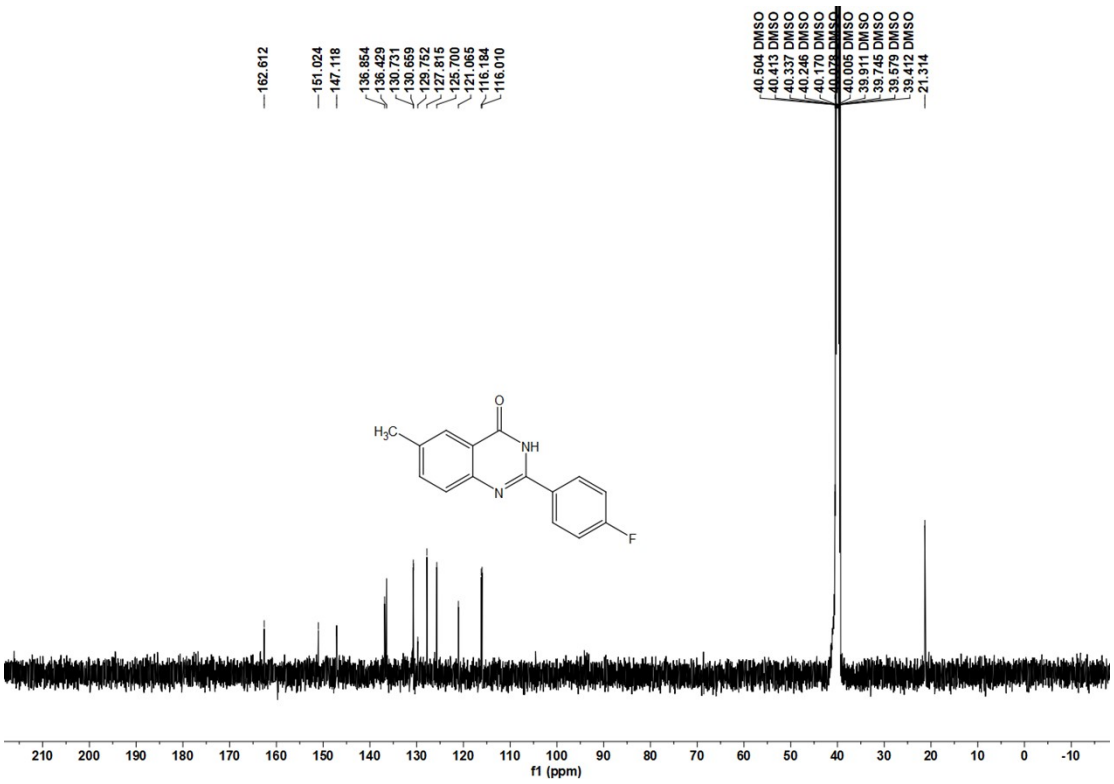
2-(5-methylfuran-2-yl)quinazolin-4(3H)-one (3q)



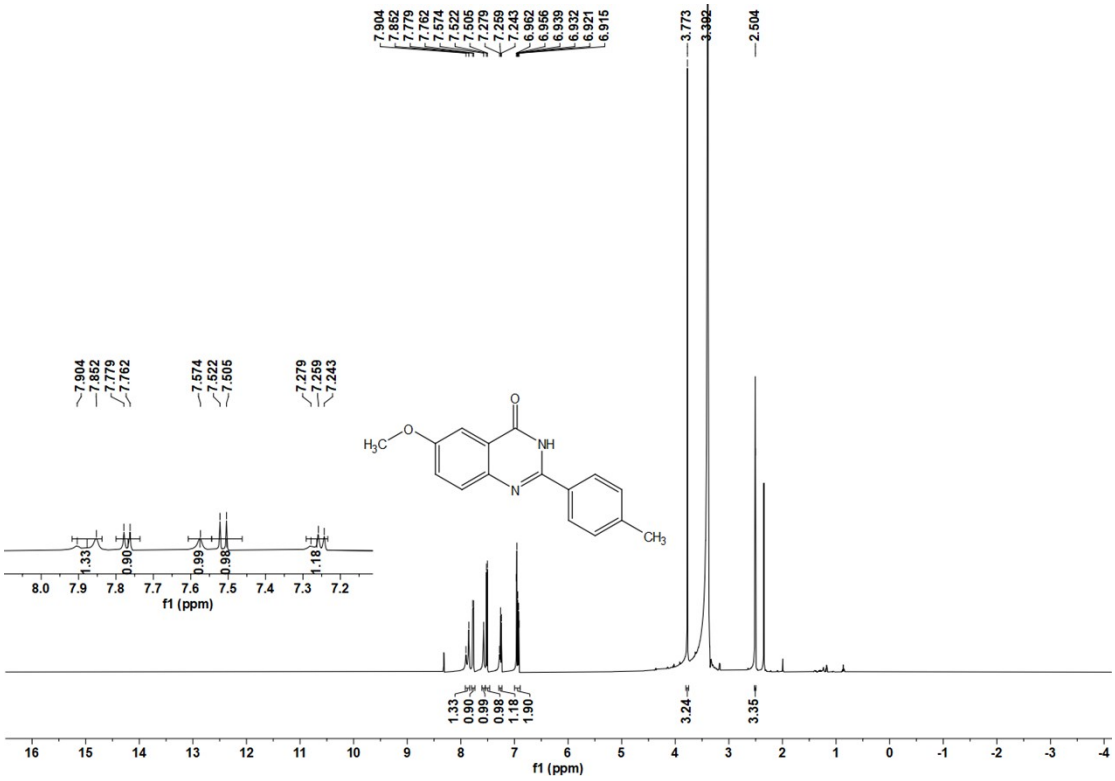


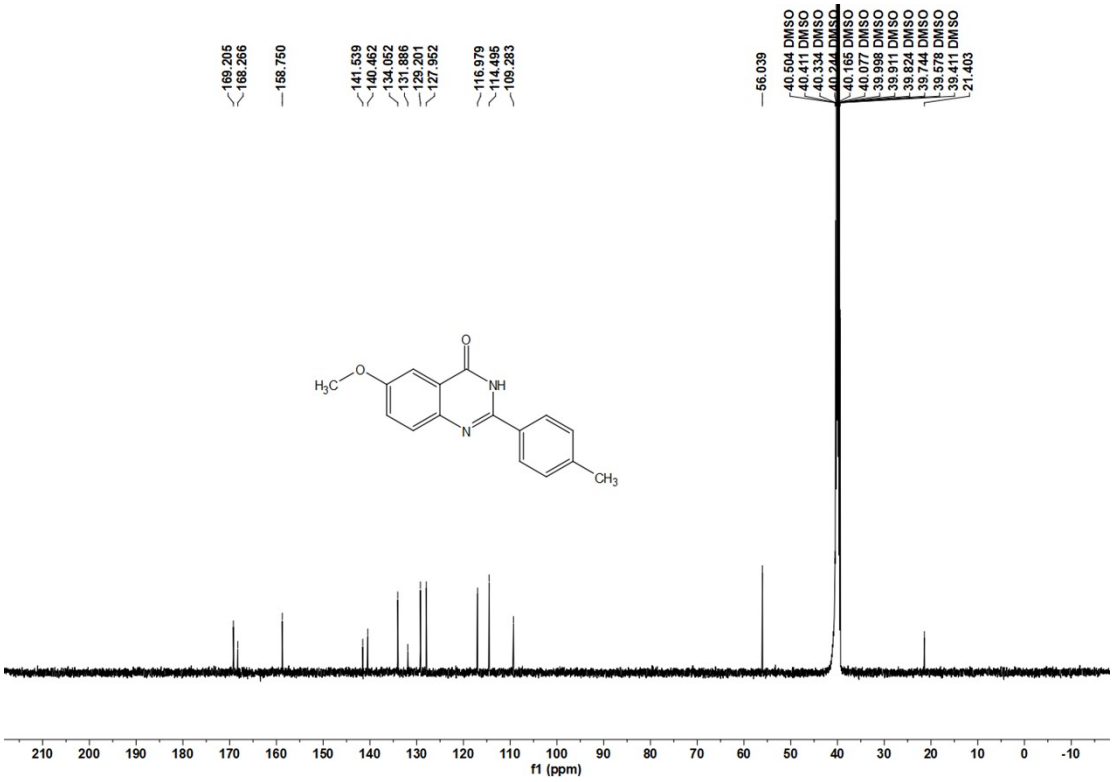
2-(4-fluorophenyl)-6-methylquinazolin-4(3H)-one (3r)



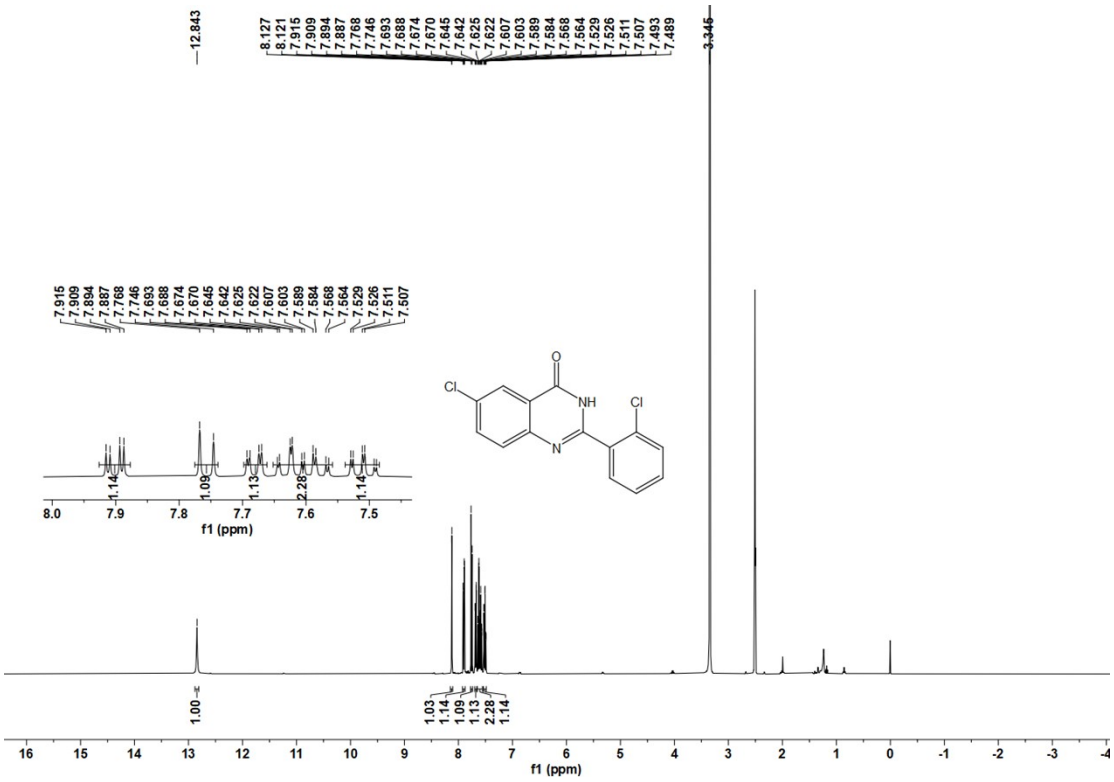


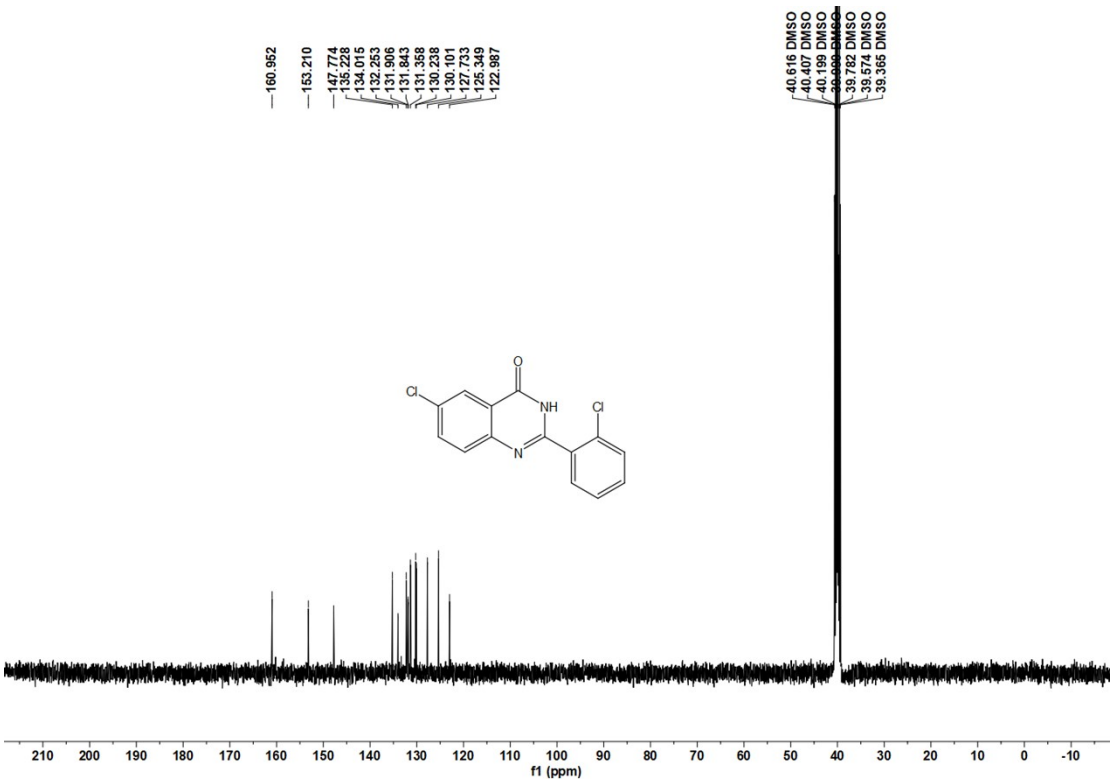
6-methoxy-2-(m-tolyl)quinazolin-4(3H)-one (3s)



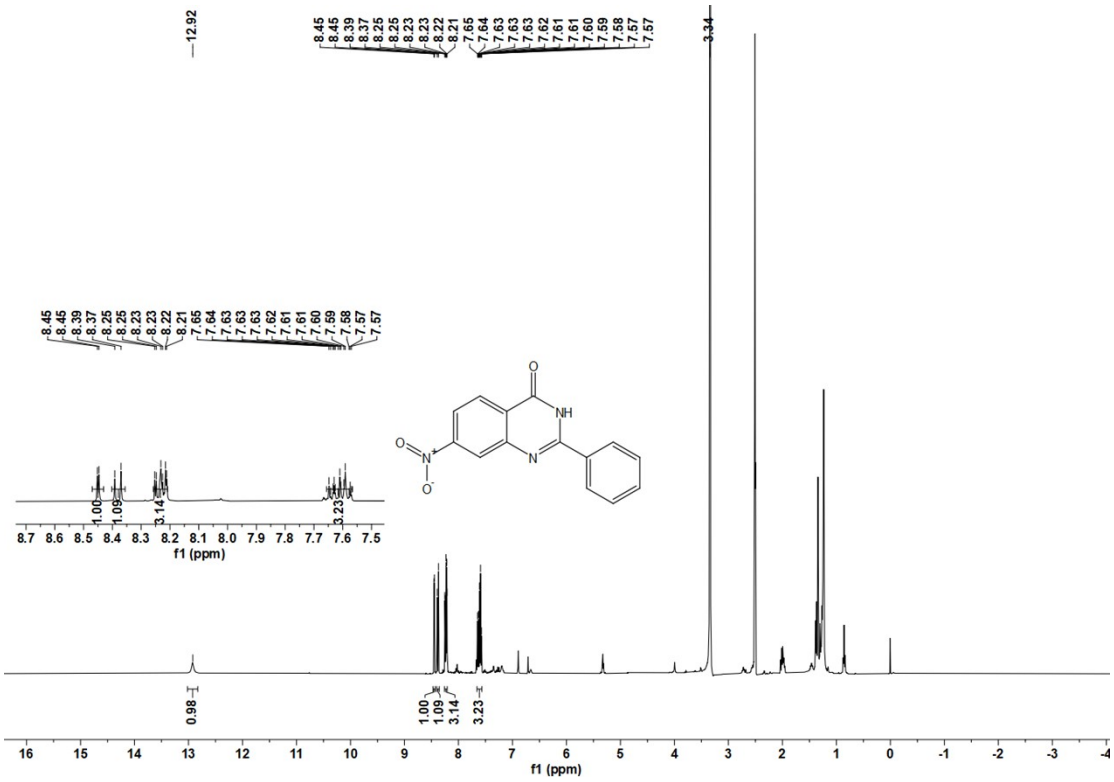


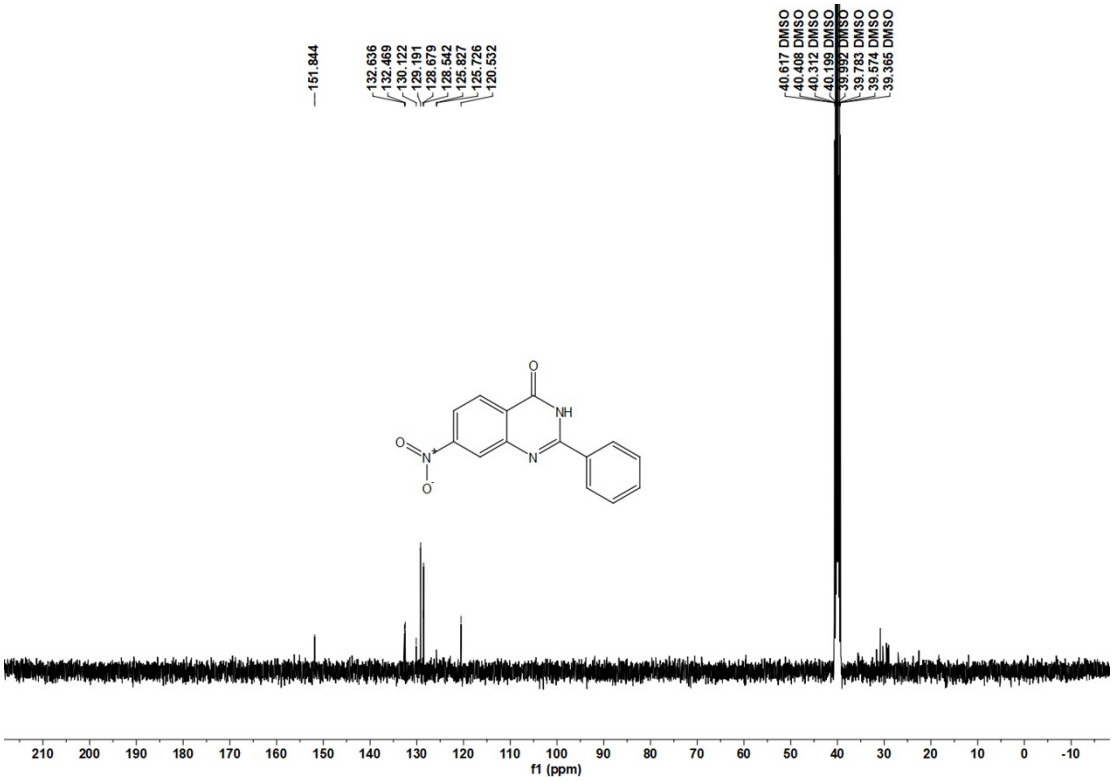
6-chloro-2-(2-chlorophenyl)quinazolin-4(3H)-one (3t)



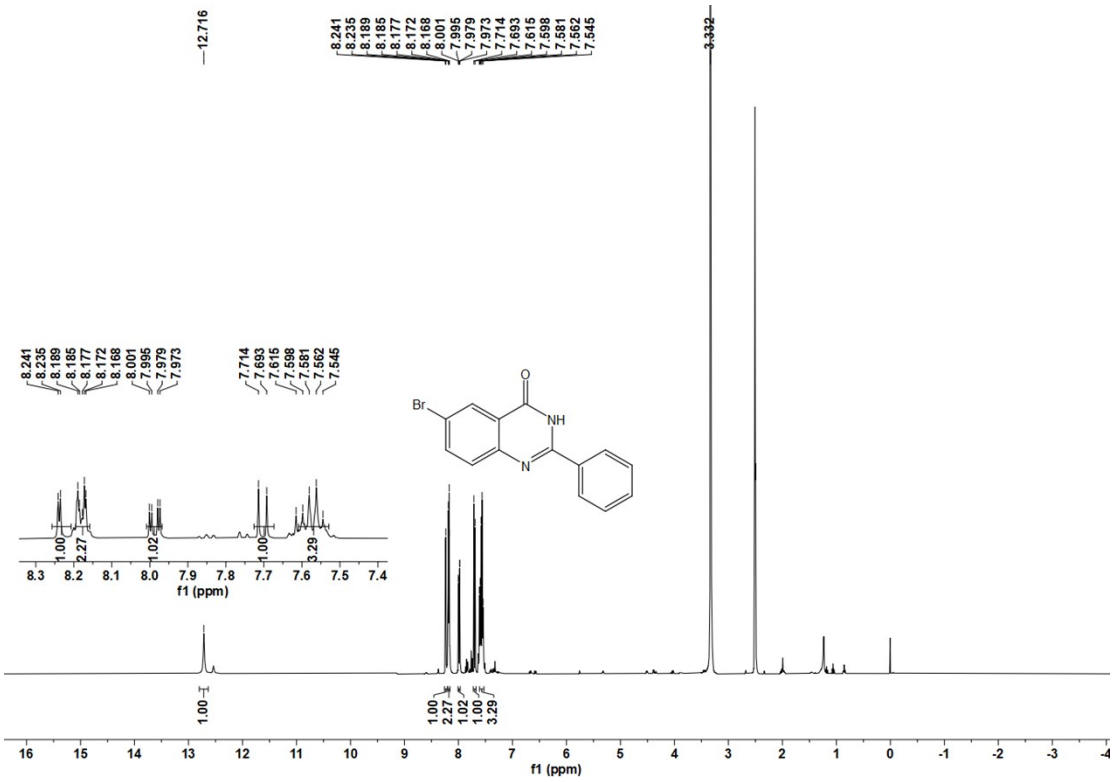


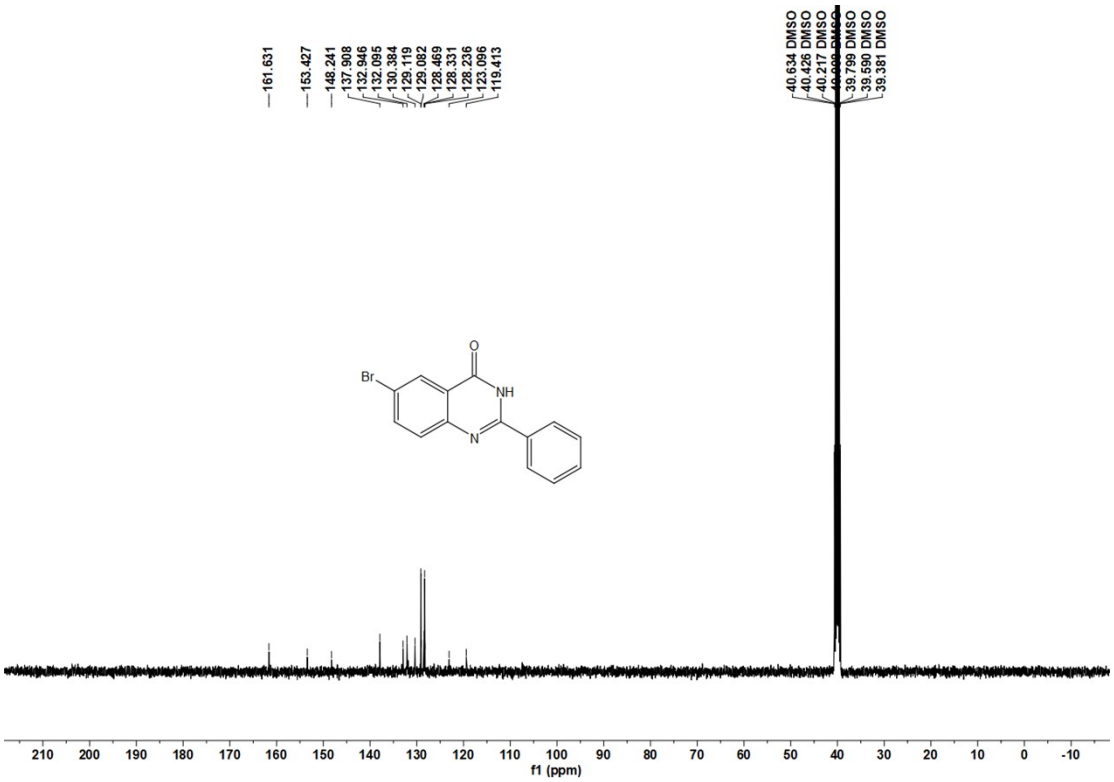
7-nitro-2-phenylquinazolin-4(3H)-one (3u)



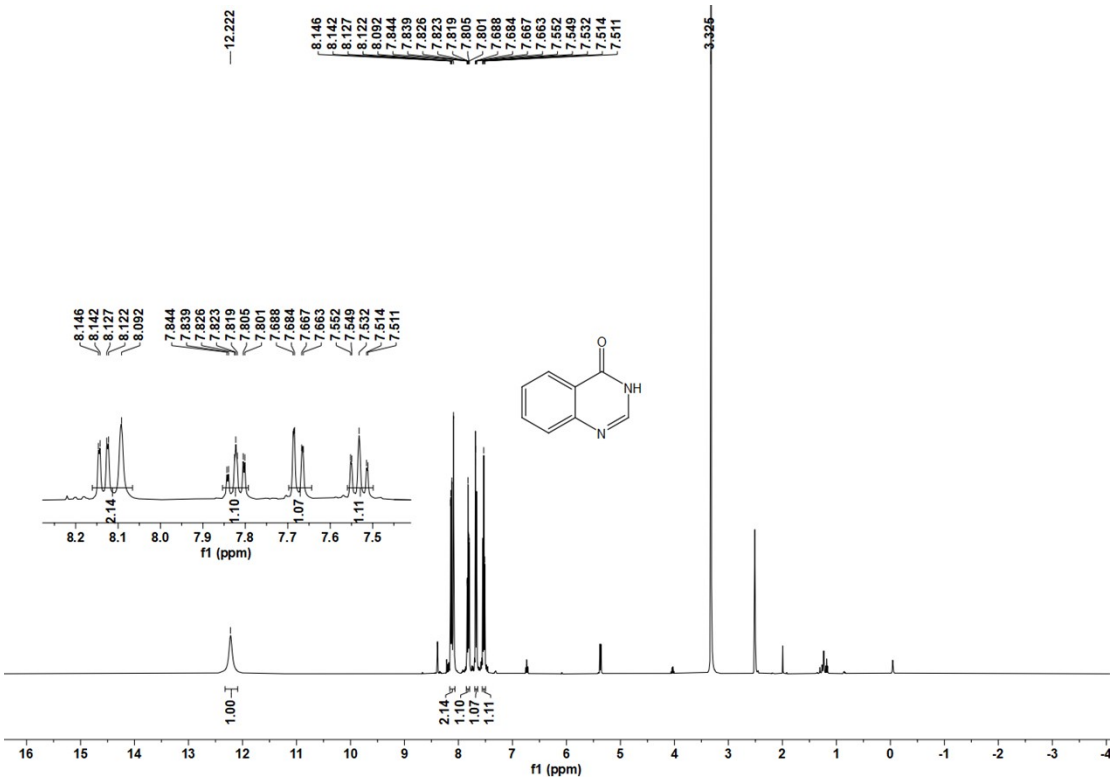


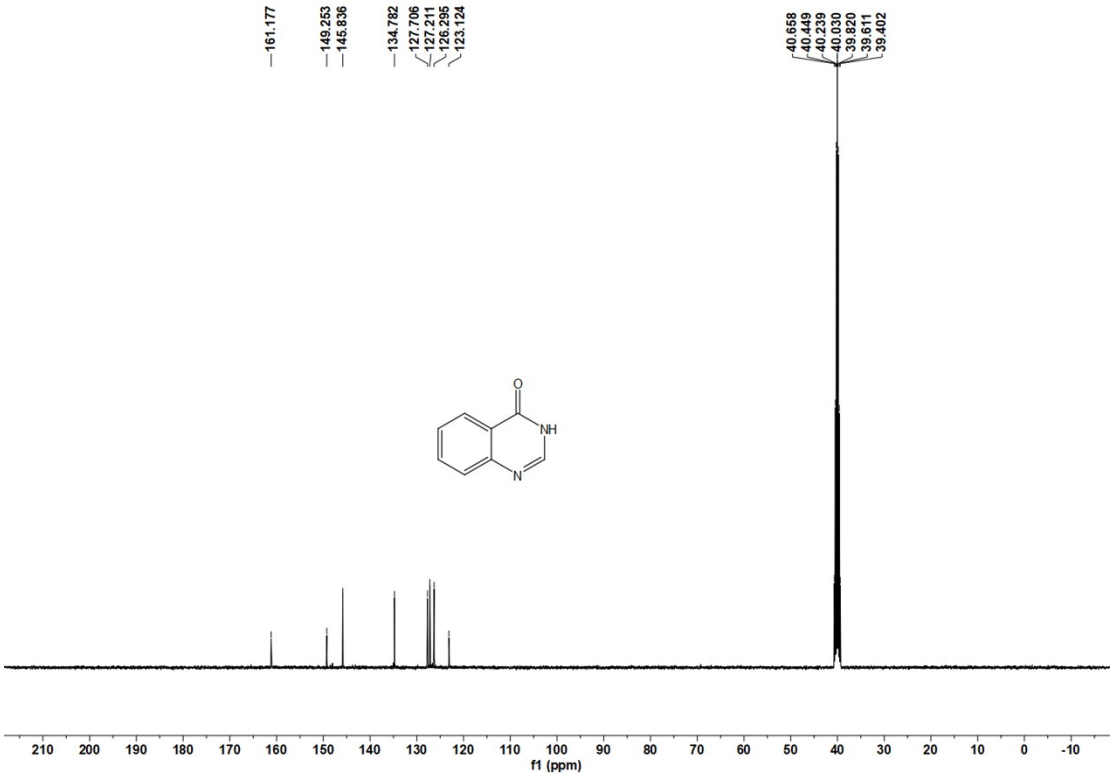
6-bromo-2-phenylquinazolin-4(3H)-one (3v)



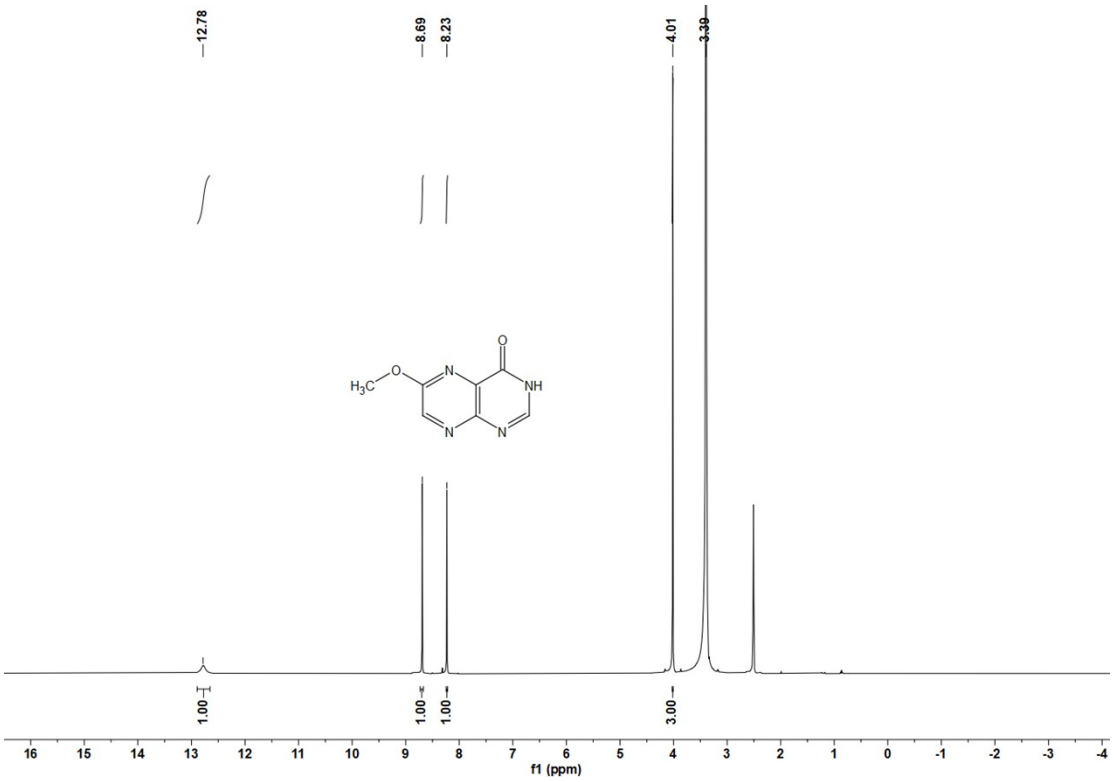


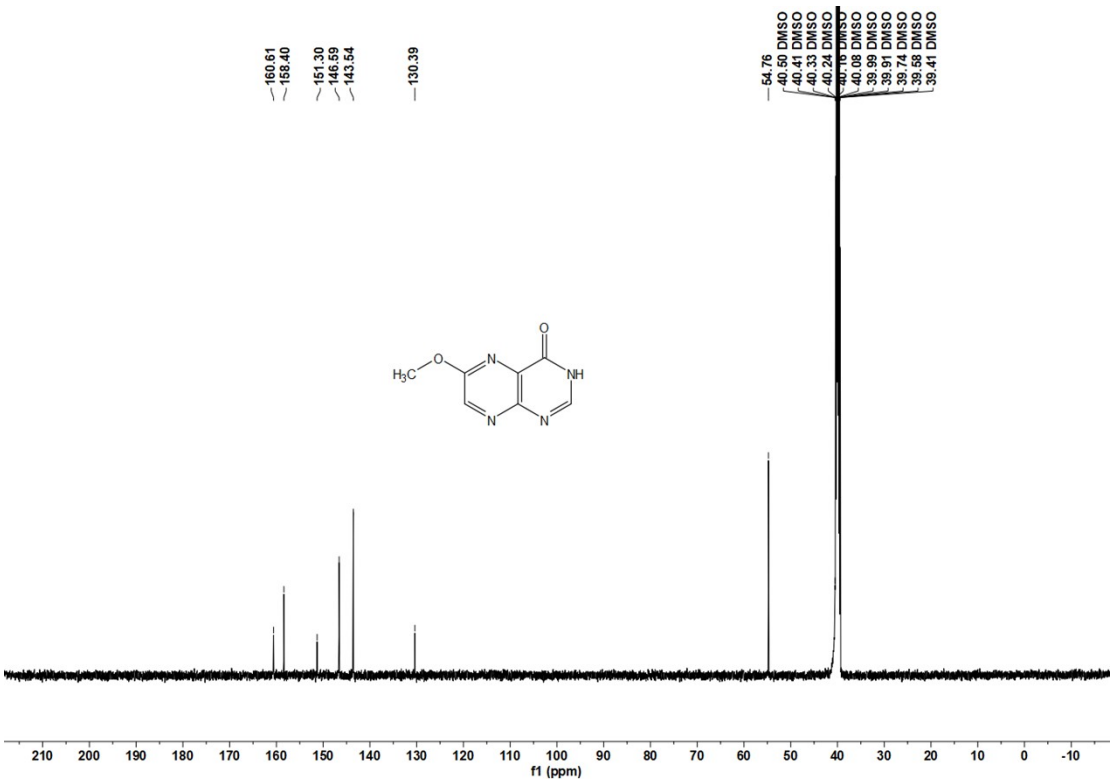
quinazolin-4(3H)-one (3w)



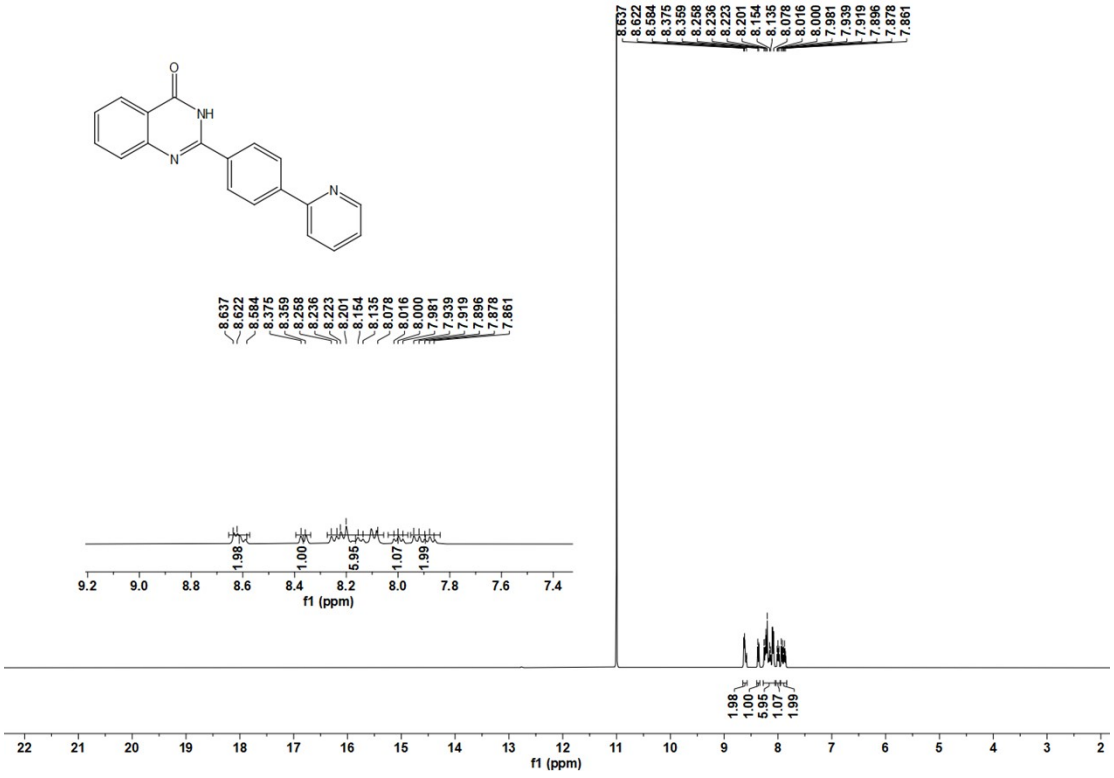


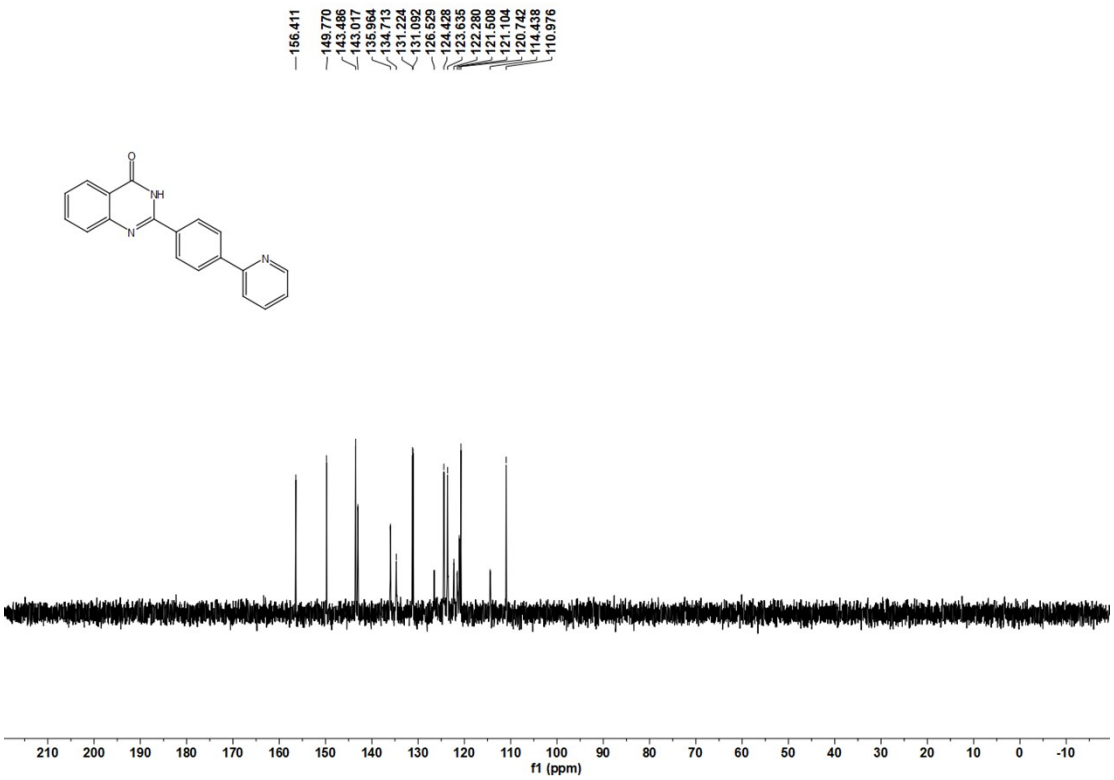
6-methoxypteridin-4(3H)-one (3x)



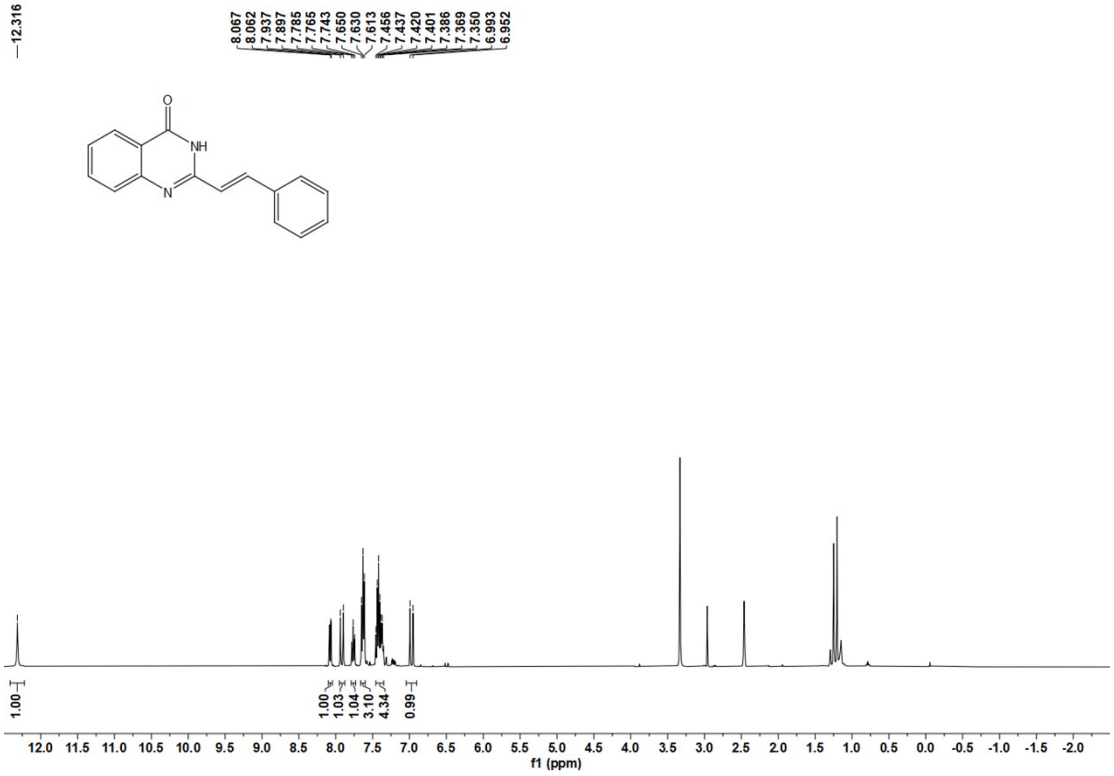


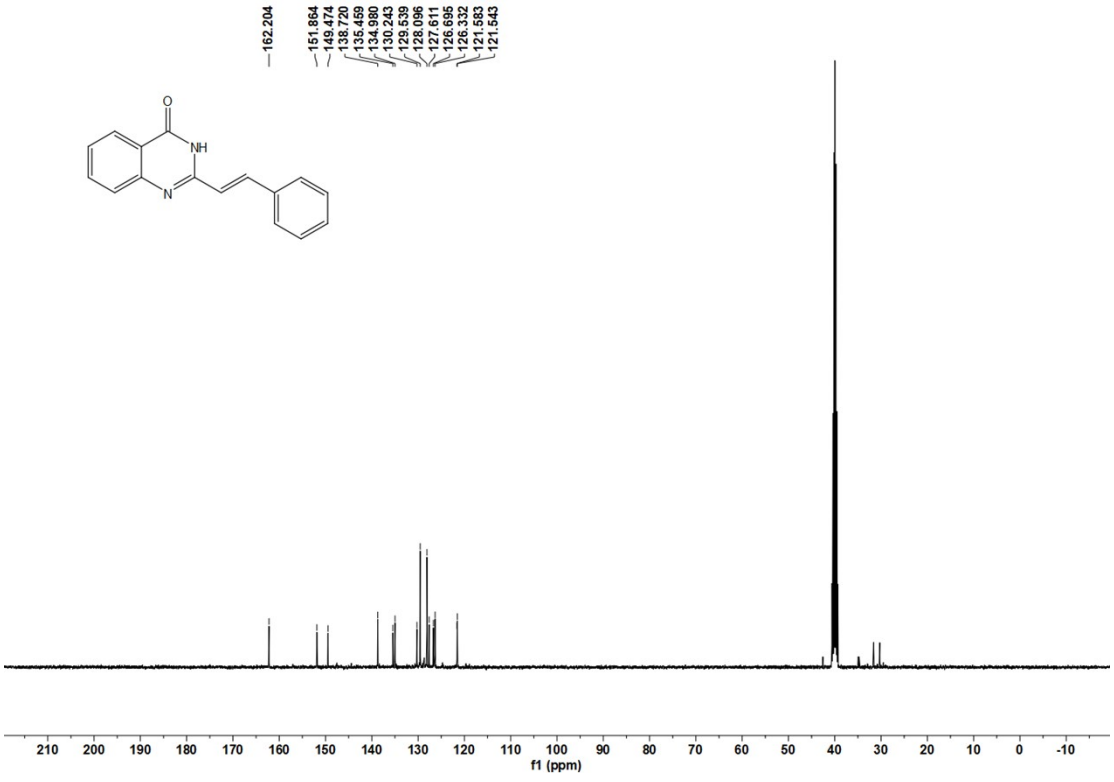
2-(4-(pyridin-2-yl)phenyl)quinazolin-4(3H)-one (3y)





2-styrylquinazolin- 4(3H)-one (3z)





\

N-(6-chloropyridin-2-yl)-6-ethoxypteridin-4-amine