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Synthesis of Quinazolines from 2-aminobenzylamines with Benzylamines and *N*-substituted Benzylamines under Transition Metal - Free Conditions

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General Information

All chemicals and solvents were purchased with high purities and used without further purification. The progress of the reaction was monitored by gas chromatography (GC) with a flame ionization detector (FID) with a capillary column (30 m × 0.25 mm × 0.25 µm) and thin layer chromatography (using silica gel 60 F-254 plates). The products were visualized with a 254 nm UV lamp. GC-MS (Rtx- 17, 30 m × 25 mm ID, film thickness (df = 0.25 µm) (column flow 2 mL min^{-1}, 80 °C to 240 °C at 10 °C min^{-1} rise) was used for the mass analysis of the products. Products were purified by column chromatography on 100-200 mesh silica gel. The ^{1}H NMR spectras were recorded on 400 MHz and 500 MHz spectrometer using tetramethylsilane (TMS) as an internal standard. The ^{13}C NMR spectras were recorded on 100 MHz and 125 MHz and Chemical shifts were reported in parts per million (δ) relative to tetramethylsilane (TMS) as an internal standard. Coupling constant (J) values were reported in hertz (Hz). Splitting patterns of proton are described as s (singlet), d (doublet), dd (doublet of doublet), t (triplet) and m (multiplet) in 1H and 13C NMR spectroscopic analysis. The products were confirmed by GCMS, ^{1}H and ^{13}C NMR spectroscopy analysis.

Representative procedure for the synthesis of quinazolines

To an oven dried round bottom flask, 2-aminobenzylamine (**1a**, 0.5 mmol), benzylamine (**2a**, 2.0 mmol), and I_2 (10 mol%) were added under O_2 balloon. Then the reaction mixture was stirred at 80 ^{o}C for 5 h. Progress of the reaction was monitored by TLC and GC. After the completion of the reaction, the reaction mixture was diluted with ethyl acetate (8 - 10 mL), followed by addition of 1-2 pinch of charcoal to remove any colored impurities, filtered and concentrated on the rotary evaporator. The obtained crude product was purified using column chromatography over silica gel using pet ether/ethyl acetate as eluent.

^{1}H NMR and ^{13}C NMR analytical data of compounds (3)

2-(p-tolyl)quinazoline (3b)[1,2]

Petroleum ether/EtOAc = 95:5; Pale yellow solid; m.p. 104−106 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.40 (s, 1H), 8.50 (d, *J* = 8. Hz, 2H), 8.06 (d, *J* = 8.0 Hz, 1H), 7.87 (t, *J* = 8.0 Hz, 2H), 7.59 (t, *J* = 8 Hz, 1H), 7.33 (t, *J* = 8 Hz, 2H), 2.4 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 160.42, 150.8, 140.8, 135.3, 134.03, 129.4, 128.52, 128.49, 127.10, 127.02, 123.49, 21.50; GCMS (EI, 70 eV): m/z (%): 220 (100), 219 (40, M^+), 193 (19), 192 (18), 109 (13), 89 (7), 76 (8).

2-(4-methoxyphenyl)quinazoline (3c)[1,2]

Petroleum ether/EtOAc = 92:8; White solid; m.p. 93-95 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.40 (s, 1H), 8.56 (d, *J* = 8.0 Hz, 2H), 8.02 (d, *J* = 8.0 Hz, 1H), 7.86 (t, *J* = 8.0 Hz, 2H), 7.55 (t, *J* = 8 Hz, 1H), 7.03 (d, *J* = 8.0 Hz, 2H), 3.88 (d, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.79, 160.8, 160.4, 150.8, 134.0, 130.7, 130.2, 128.4, 127.1, 126.8, 123.3, 114.0, 55.4; GCMS (EI, 70 eV): m/z (%): 236 (19), 235 (100, M^+), 220 (36), 192 (35), 191 (34), 106 (13), 95 (16), 77 (7).

2-(4-chlorophenyl)quinazolines (3e)[1,2]

Petroleum ether/EtOAc = 92:8; White solid; m.p. 130-132 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.43 (s, 1H), 8.55 (d, *J* = 8.0 Hz, 2H), 8.06 (d, *J* = 8.0 Hz, 1H), 7.92-7.88 (m, 2H), 7.61 (t, *J* = 8 Hz, 1H), 7.48 (d, *J* = 8.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.51, 160.01, 150.6, 136.8, 136.5, 134.2, 129.8, 128.8, 128.6, 127.45, 127.13, 123.6; GCMS (EI, 70 eV): m/z (%): 242 (33), 240 (100, M^+), 213 (31), 178 (31), 76 (22), 50 (14).

2-(3-chlorophenyl)quinazoline (3f)[1,2]

Petroleum ether/EtOAc = 92:8; Yellow solid; m.p. 150-152 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.46 (s, 1H), 8.62 (s, 1H), 8.52 – 8.46 (m, 1H), 8.08 (d, *J* = 8.0 Hz, 1H), 7.93 (d, *J* = 8.0 Hz, 2H), 7.65-7.60 (m, 1H), 7.47 (t, *J* = 8, Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 159.7, 150.6, 139.8, 134.3, 133.8, 130.5, 129.8, 128.65, 128.64, 127.63, 127.1, 126.88, 126.77, 126.60, 126.0, 123.7; GCMS (EI, 70 eV): m/z (%): 242 (36), 240.05 (100, M^+), 213 (29), 178 (31), 102 (23), 76 (28), 50 (22), 44 (20).

2-(3-nitrophenyl)quinazoline (3j)[2]

Petroleum ether/EtOAc = 80:20; Yellow solid; m.p. 100-102 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.49 (s, 2H), 8.96 (d, *J* = 8 Hz, 1H), 8.34 (d, *J* = 8.0 Hz, 1H), 8.12 (d, *J* = 8.0 Hz, 1H), 7.96 (t, *J* = 8.0 Hz, 2H), 7.69 (t, *J* = 8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 158.6, 150.6, 148.8, 139.8, 134.56, 134.19, 129.5, 128.73, 128.07, 127.2, 125.0, 123.9, 123.6; GCMS (EI, 70 eV): m/z (%): 251(61, M^+), 205.15 (100), 193.15 (20), 151 (24), 77.05 (29).

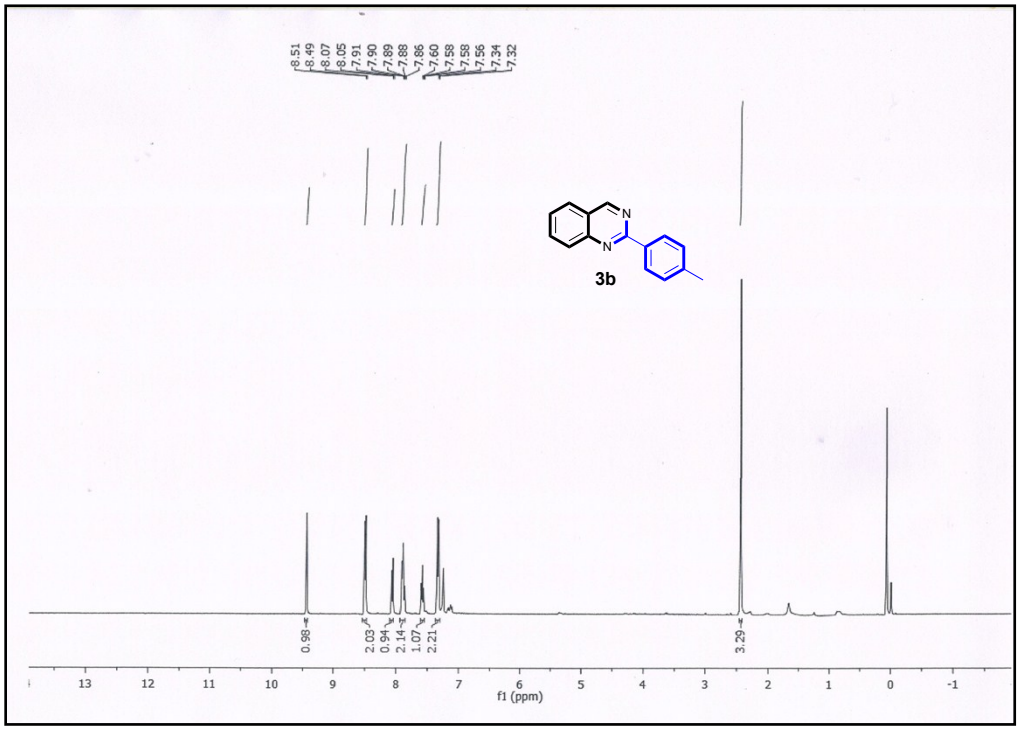
2-(pyridin-3-yl)quinazoline (3k)[1]

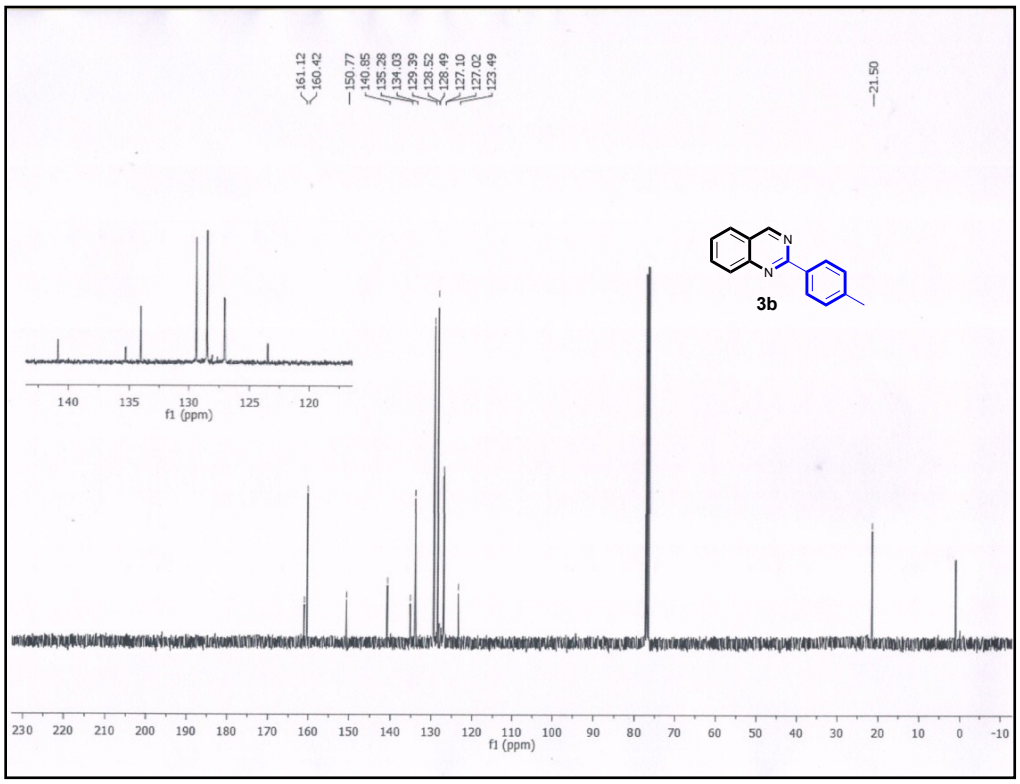
Petroleum ether/EtOAc = 85:15; Pale yellow solid; m.p. 130-132 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.74 (s, 1H), 9.37 (s, 1H), 8.78 (d, *J* = 8 Hz, 1H), 8.67 (s, 1H), 8.01 (d, *J* = 8.0 Hz, 1H), 7.84 (t, *J* = 8.0 Hz, 2H), 7.56 (t, *J* = 8.0 Hz, 1H), 7.40 -7.36 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 159.0, 151.0, 150.5, 150.1, 135.7, 134.3, 133.5, 128.5, 127.7, 127.1, 123.7, 123.4. GCMS (EI, 70 eV): m/z (%): 221 (100), 220 (47, M^+), 194 (18), 179 (7),78 (3).

References:

1. B. Han, X. L. Yang, C. Wang, Y. W. Bai, T. C. Pan, X. Chen, W. J. Yu, *Org. Chem.*, 2012, **77**, 1136.
2. C. C. Malakar, A. Baskakova, J. Conrad, U. Beifuss, *Chem. Eur. J.,* 2012, **29**, 8882.

^{1}H NMR and ^{13}C NMR spectra of 2-(p-tolyl)quinazolines (3b)





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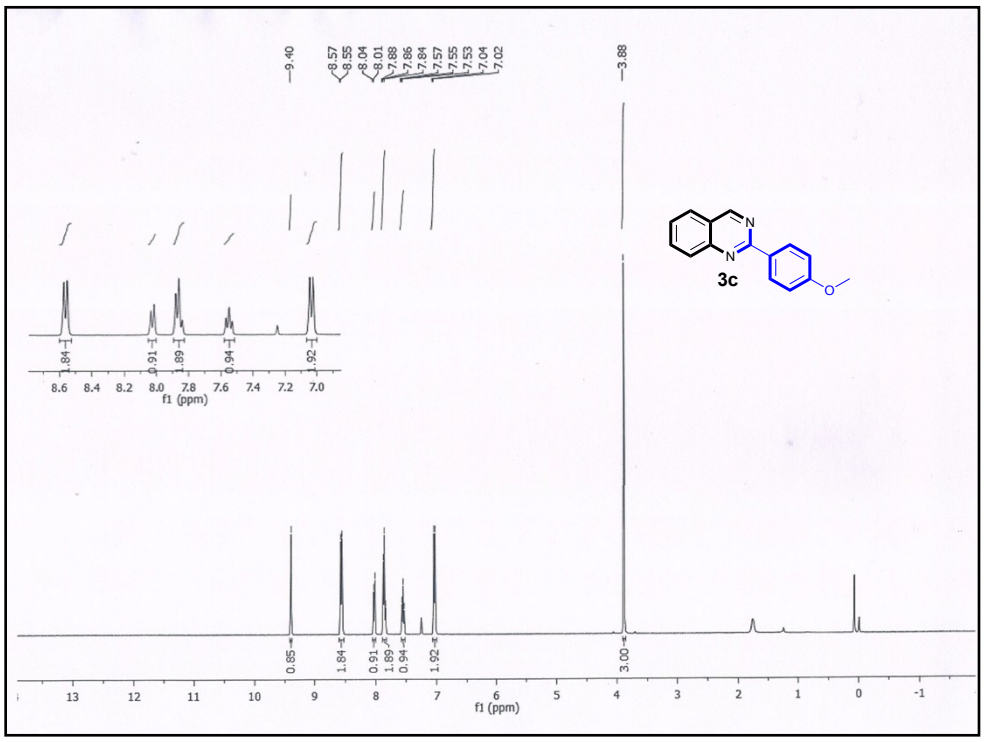

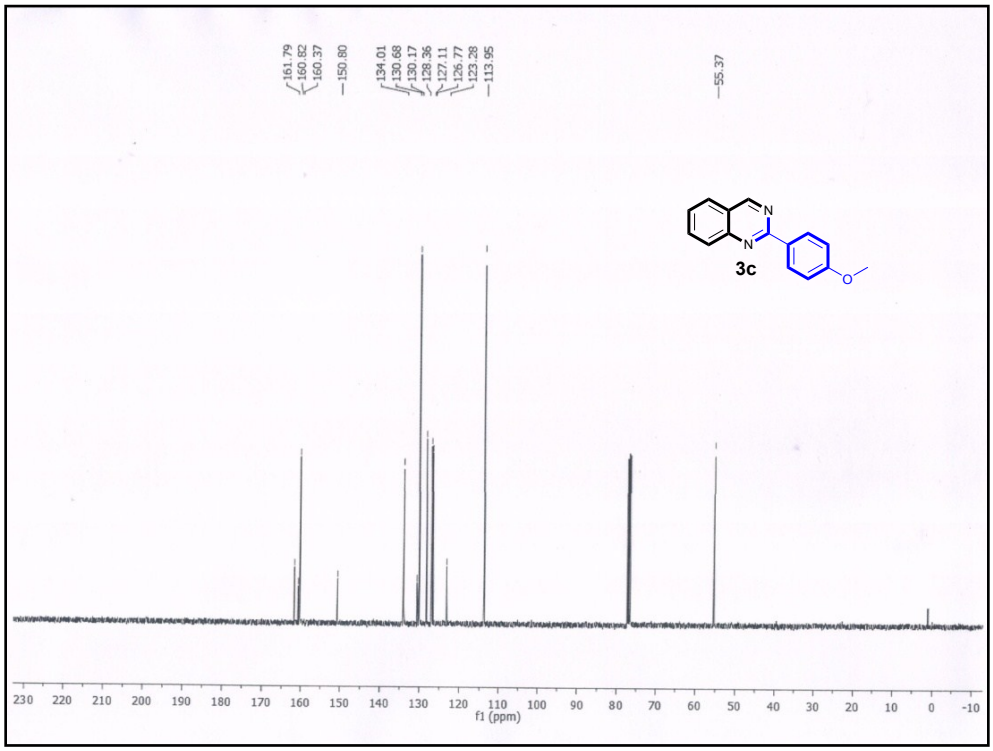

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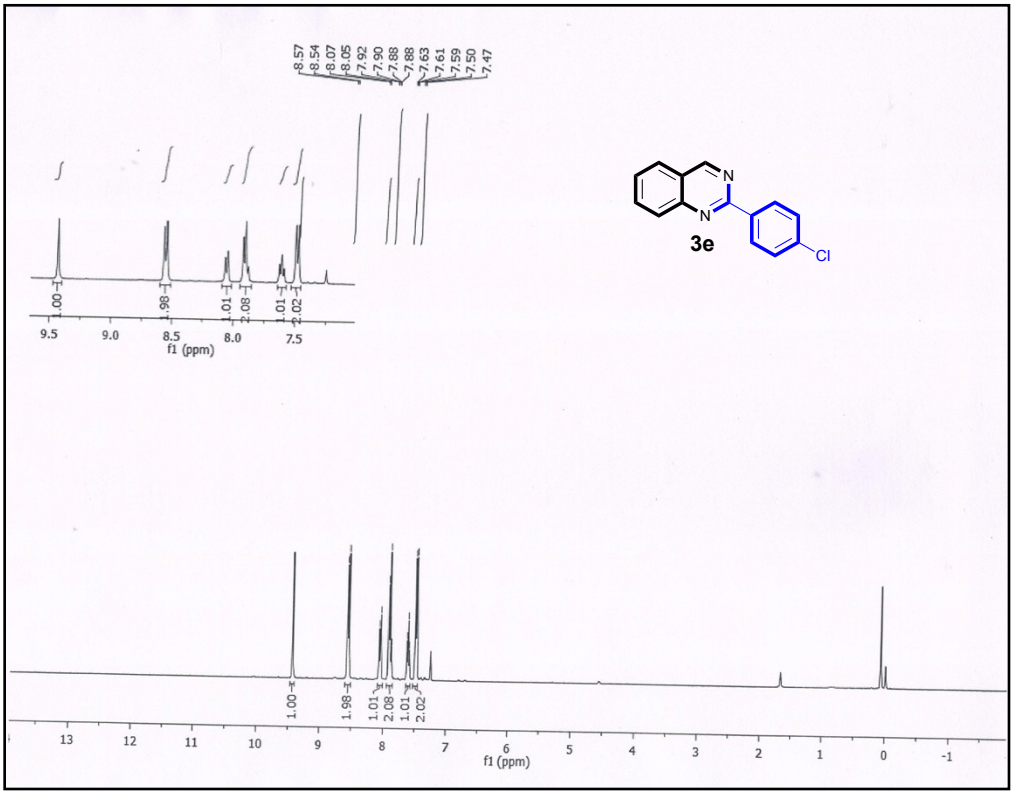

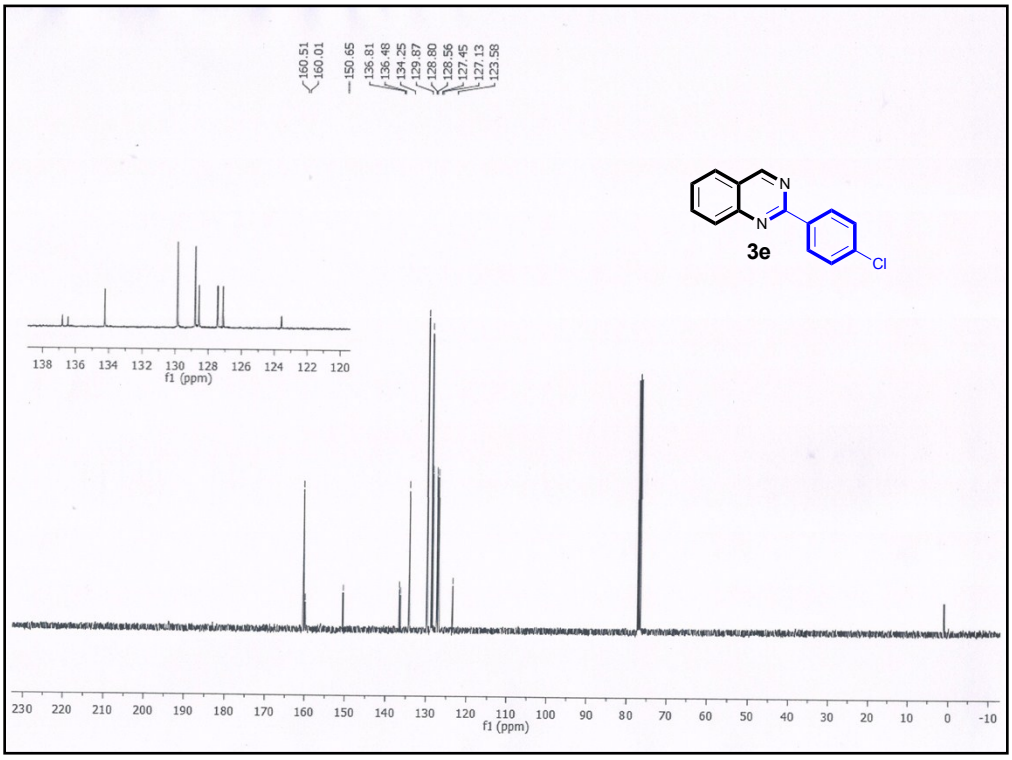

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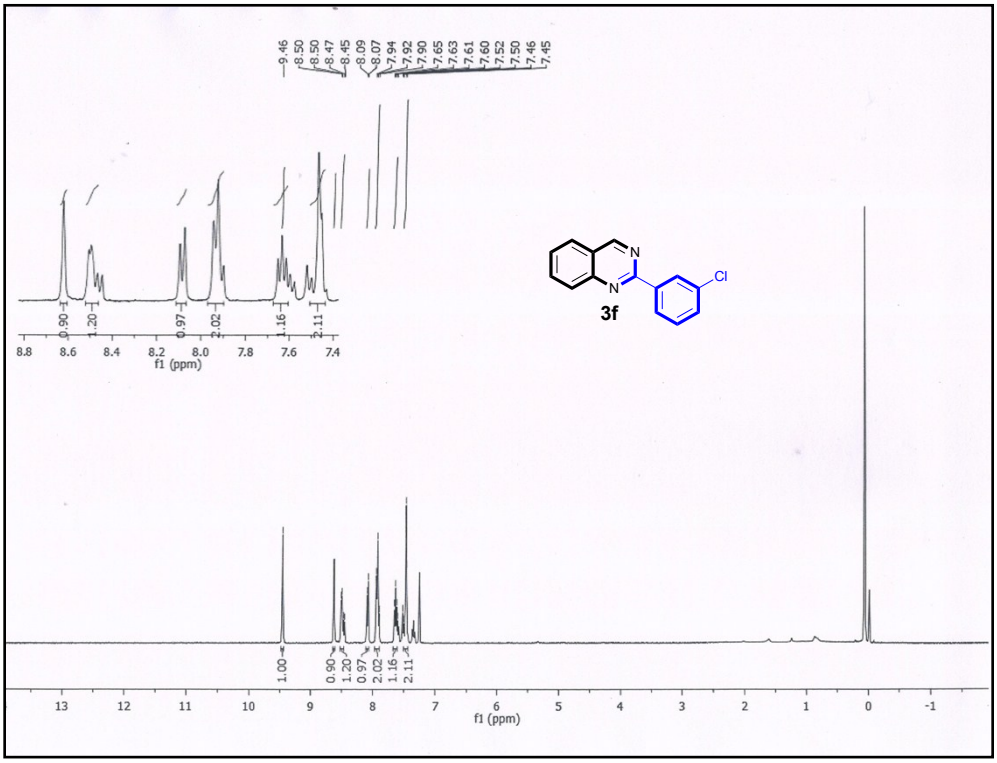

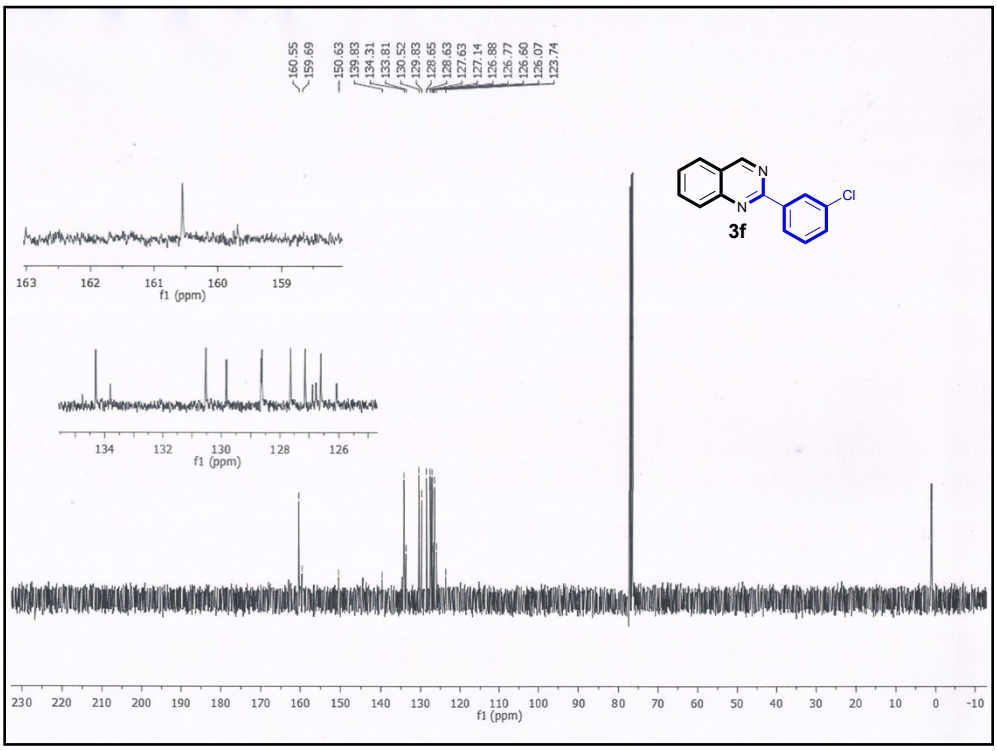

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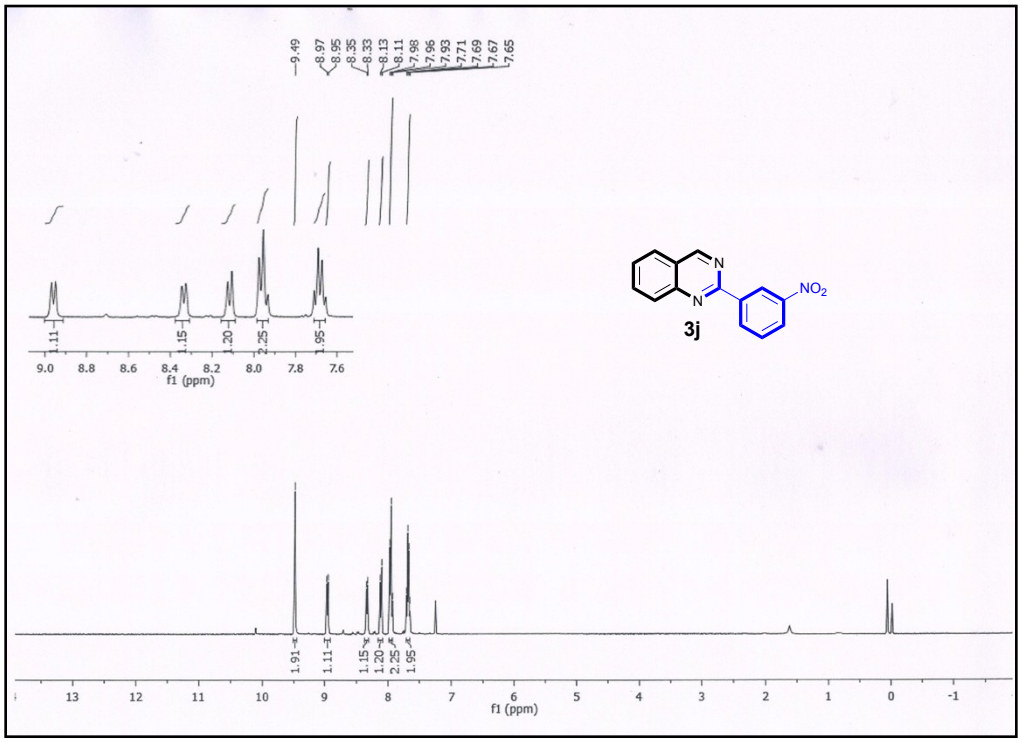

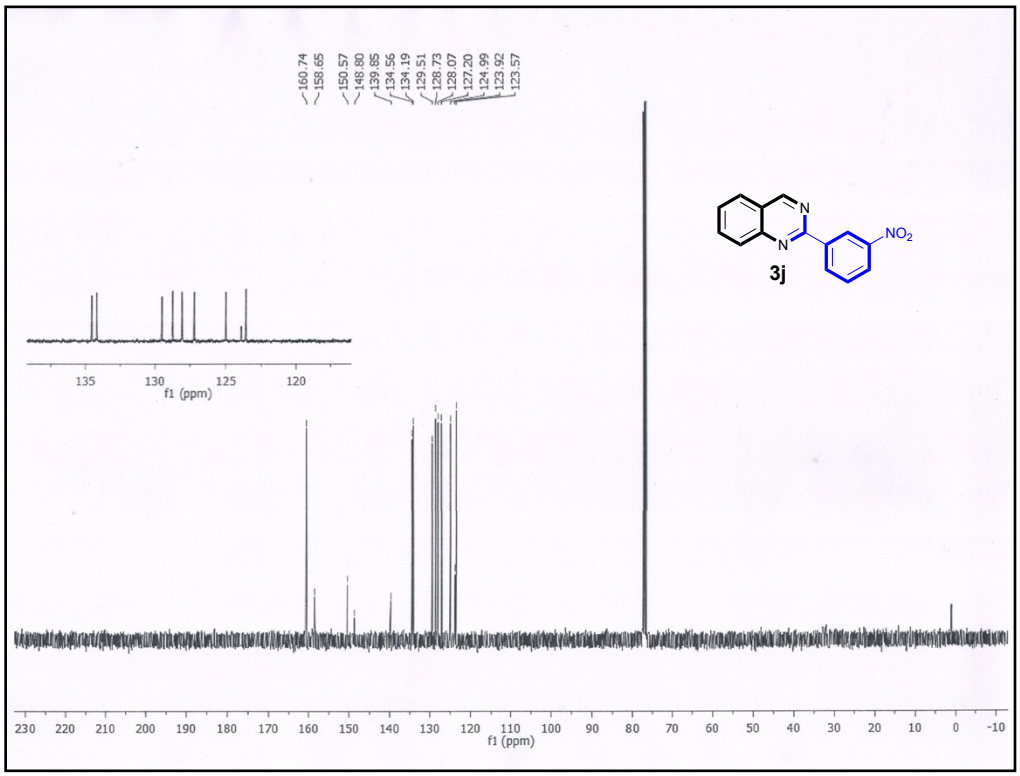

^{1}H NMR and ^{13}C NMR spectra of 2-(pyridin-3-yl)quinazolines (3k)