Electronic Supplementary Information

Metal-free oxidative synthesis of Benzo-N-heterocycles by Dehydrogenative Coupling of Aromatic Diamines and Alcohols

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I. General considerations

All reagents and solvents were obtained from commercial suppliers and used without further purification. All HPLC measurements were performed on Agilent 1260 Infinity LC equipment using an EC-C18 column(4μm,4.6*150mm). The structure of the product was further identified by using GC-MS .^{1}H and ^{13}C NMR spectra of all compounds were measured on a Bruker DRX 400 spectrometer at 298k and referenced to the residual proton signals of the $CDCl_3$. The flow microreactor consists of three parts: gas distribution system, liquid conveying device and reaction tube. The gas distribution system adopts the gas mass flow controller (ACU20FD-L) integrated digital control system produced by Beijing measurement Control Co., Ltd. The liquid was mixed with the gas by a syringe pump, which is manufactured by Lead Fluid Technology Co., Ltd (model# TYD01-02). The reaction tube is a PFA tubing (10 m, i.d.: 1.6 mm).

II. Experimental

a) General procedure for batch reaction.

A 25 ml batch bubbling reactor was charged with substrate amine (20 mmol), alcohols (20.5 mmol), NHPI (10 mol%) and benzyl benzoate (10 mL). Then, the reaction mixture was stirred at 100 ℃ for 10 h, and pure oxygen (99.9%) was introduced into the reactor at a certain flow rate. The reaction was monitored by HPLC. After completion of the reaction, the resulting solution was cooled to room temperature, and neutralized with saturated $NaHCO_3$ solution. The product was extracted with EtOAc, dried over anhydrous Na_2SO_4 and concentrated in vacuo. Finally, the crude products were purified by column chromatography using hexane/ethyl acetate as eluent to afford the corresponding pure products.

b) General procedure for flow reaction.

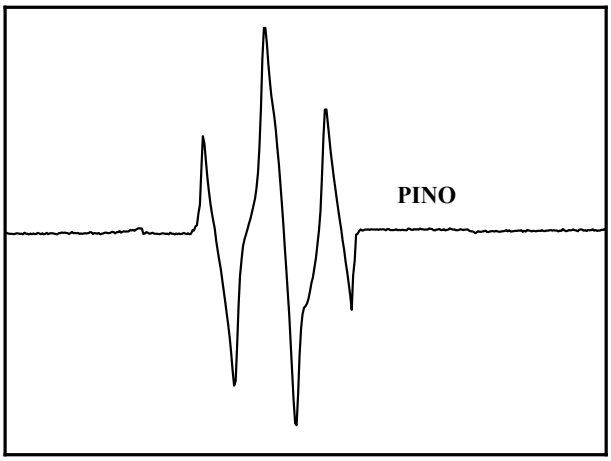
The same reactant solution was configured in accordance with the batch reaction procedure. Then, the solution in the flask was introduced into the microreactor setup with a plunger pump. The pump and the mass-flow controller were operated at a volume ratio of liquid/oxygen of 1:2. The total residence time was 30 min. The backpressure

regulator was adjusted to 0.5 MPa, and was placed in a water bath of 60℃.

c) General procedure for control experiments.

First, benzyl alcohol(20mmol), NHPI (10 mol %) and 10mL benzyl benzoate was heated at 100℃ for 8 h under an oxygen. Next, the reaction of benzaldehyde(20mmol) and o-phenylenediamine(20mmol) under the same conditions in a nitrogen atmosphere was conducted for 5h, which was detected by GC–MS. Then, oxygen was introduced, and the reaction was carried out for 5h. This process calculated the yield by HPLC.

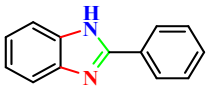
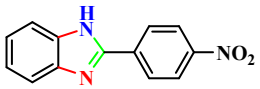
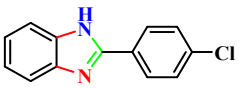
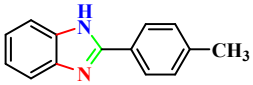
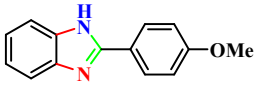
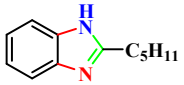
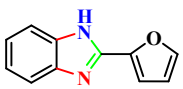
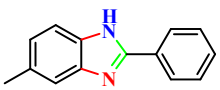
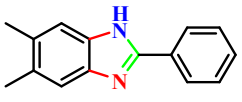
III. EPR experiment for NHPI in solvent

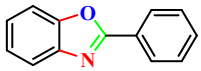
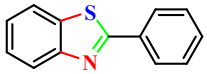
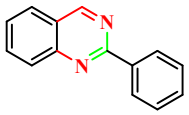
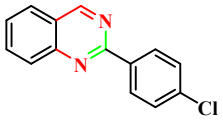
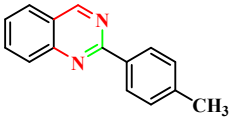
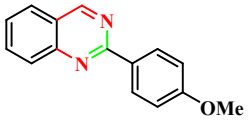
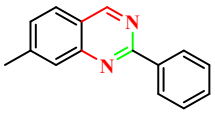


G=2.0,A_N=0.42mT

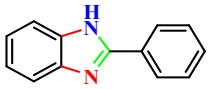
Figure S1. EPR spectrum of phthalimide-*N*-oxyl (PINO)obtained by exposing a mixture of 2mmolNHPI and 10mL benzyl benzoate under an oxygen atmosphere at 100℃ for 2h.

IV. GC-MS data of the Benzo-*N*-heterocycles products

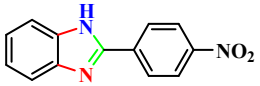
 t_r= 9.6min; m/z=194.0	 t_r= 12.3min; m/z=239.2	 t_r= 11.4min; m/z=228.2
 t_r= 10.2min; m/z=208.0	 t_r=11.0 min; m/z=224.1	 t_r= 8.9min; m/z=188.0
 t_r= 8.8min; m/z=184.1	 t_r=10.2min; m/z=208.0	 t_r= 10.8min; m/z=222.0

 t_r= 9.6min; m/z=195.0	 t_r= 10.3min; m/z=211.1	
 t_r=10.5 min; m/z=206.1	 t_r= 12.8min; m/z=240.1	 t_r= 11.4min; m/z=220.0
 t_r=12.5 min; m/z=236.1	 t_r= 11.5min; m/z=220.0	

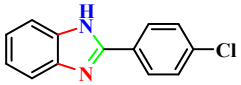
V. ^{1}H and ^{13}C NMR data of the Benzo-*N*-heterocycles products



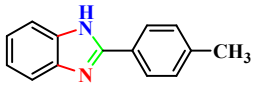
2-phenyl-1H-benzimidazole(3a) [1]**:** 3.3523g; 86.4% isolated yield. **^{1}H NMR** (DMSO-d_6, 400 MHz): δ = 12.89 (s, 1H), 8.24 -8.15 (m, 2H), 7.70 -7.43 (m, 5H), 7.24-7.17 (m, 2H). **^{13}C NMR** (DMSO-d_6, 400 MHz): δ = 151.76, 144.28, 135.47, 130.64, 130.40, 129.49, 126.96, 123.10, 122.23,119.35, 111.87.



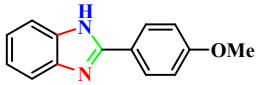
2-(4-nitrophenyl)-1H-benzimidazole(3b) [2]**:** 4.2194g; 88.2% isolated yield. **^{1}H NMR** (DMSO-d_6, 400 MHz): δ = 12.98 (s, 1H), 8.20-8.18 (m, 2H), 7.79 -7.42 (m, 4H), 7.25-7.18 (m, 2H). **^{13}C NMR** (DMSO-d_6, 400 MHz): δ = 153.76, 149.04, 143.14, 141.94, 135.65,129.18,129.12,124.04,118.47,116.90,115.84.



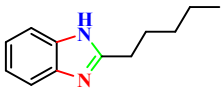
2-(4-chlorophenyl)-1H-benzimidazole(3c) [3]**:** 3.9478g; 86.5% isolated yield. **^{1}H NMR** (DMSO-d_6, 400 MHz): δ = 12.95 (s, 1H), 8.17-8.14 (m, 2H), 7.70-7.49 (m, 4H), 7.22-7.10 (m, 2H). **^{13}C NMR** (DMSO-d_6, 400 MHz): δ =150.68, 144.26, 135.54, 135.02, 129.59, 128.66, 123.30, 122.37, 119.49, 111.95.



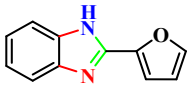
2-(4-methylphenyl)-1H-benzimidazole(3d) [2]**:** 3.4419g; 82.7% isolated yield. **^{1}H NMR** (DMSO-d_6, 400 MHz): δ =12.83 (s, 1H), 8.09-8.07 (m, 2H), 7.64-7.52 (m, 2H), 7.37-7.35 (m, 2H), 7.20-7.18 (m, 2H), 2.38 (s, 3H). **^{13}C NMR** (DMSO-d_6, 400 MHz): δ =151.35, 143.79, 139.51, 134.92, 129.47, 127.43, 126.36, 122.28, 121.52, 118.67, 111.15, 40.12, 39.91, 39.70, 39.49, 39.28, 39.08, 38.87.



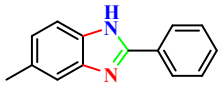
2-(4-methoxyphenyl)-1H-benzimidazole(3e) [4]**:** 3.635g; 81.1% isolated yield. **^{1}H NMR** (DMSO-d_6, 400 MHz): δ = 12.73 (s,1H), 8.11-8.08 (m, 2H), 7.65-7.39 (m, 2H), 7.13-7.06 (m, 4H), 3.79 (s, 3H). **^{13}C NMR** (DMSO-d_6, 400 MHz): δ = 161.12, 151.58, 144.32, 135.37, 131.04, 128.54, 127.93, 123.20,122.26, 118.92, 114.88, 55.83.



2-pentyl-1H-benzimidazole(3f) [5]**:** 3.1961g; 85.0% isolated yield. **^{1}H NMR** (DMSO-d_6, 400 MHz): δ = 12.14 (s, 1H), 7.45 (m,2H), 7.09 (m,2H), 1.82-1.70 (m, 2H), 1.38-1.26 (m, 4H), 0.87 (m, 3H).**^{13}C NMR** (DMSO-d_6, 400 MHz): δ = 151.76, 144.28, 135.47, 130.64, 130.40, 129.49, 126.96, 123.10, 122.23,119.35, 111.87.

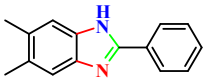


2-(furan-2-yl)-1H-benzimidazole(3g) [6]**:** 2.4625g; 66.8% isolated yield. **^{1}H NMR** (DMSO-d_6, 400 MHz): δ = 12.89 (s,1H), 7.89 (s, 1H), 7.59 (m, 1H), 7.45 (m, 1H), 7.16-7.15 (m, 3H), 6.69-6.67 (m, 1H). **^{13}C NMR** DMSO-d_6, 400 MHz): δ = 146.10, 145.14, 144.17, 134.76, 123.16, 122.33, 119.29, 112.85, 111.87, 111.00.

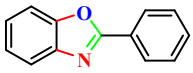


2-phenyl-1H-benzimidazole(3h) [7]**:** 3.5526g; 85.4% isolated yield. **^{1}H NMR** (DMSO-d_6, 400 MHz): δ = 12.72 (s,1H), 8.13-8.11 (m, 2H), 7.51-7.41 (m, 4H), 7.38-7.27 (m, 1H), 7.01-6.69 (m, 1H), 2.39(s, 3H). **^{13}C NMR** (DMSO-d_6, 400 MHz): δ =

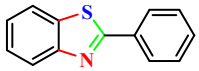
151.25, 142.46, 135.78, 132.40, 130.82, 130.17,129.44, 126.82, 124.51, 123.79, 118.97, 111.57, 21.89.



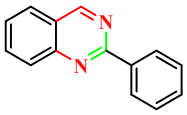
5,6-dimethyl-2-phenyl-1H-benzimidazole(3i) [8]**:** 3.6941g; 83.2% isolated yield. **^{1}H NMR** (DMSO-d_6, 400 MHz): δ = 12.60 (s, 1H), 8.10 (d, J = 7.2 Hz, 2H), 7.48 (t, J = 7.7 Hz, 2H), 7.41 (t, J = 7.1 Hz, 2H), 7.28-7.25 (m,1H), 2.28 (s, 3H), 2.27 (s, 3H).. **^{13}C NMR** (DMSO-d_6, 400 MHz): δ = 150.85, 143.03, 134.05,131.69, 130.97, 130.44, 129.98, 129.38, 126.72, 119.45, 111.85, 20.56.



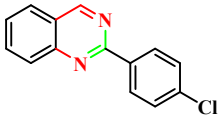
2-phenyl-1H-benzimidazole(3j) [9]**:** 3.3735g; 88.5% isolated yield. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 8.32 -8.22 (m, 2H), 7.83- 7.75 (m, 1H), 7.60 -7.50 (m, 4H), 7.38-7.33 (m, 2H). **^{13}C NMR** ($CDCl_3$, 400 MHz): δ = 150.91, 142.26, 131.66, 129.05, 127.77, 127.32, 125.25, 124.72, 120.16, 110.73, 77.48.



2-phenylbenzothiazole(3k) [10]**:** 3.3691g; 79.8% isolated yield. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 8.15 -8.05 (m, 3H), 7.92-7.7.52, 7.52 -7.47 (m, 4H), 7.42-7.36 (m, 1H). **^{13}C NMR** ($CDCl_3$, 400 MHz): δ = 168.21, 154.31, 135.22, 133.79, 131.11, 129.17, 127.71, 126.46, 125.33, 123.39, 121.76.

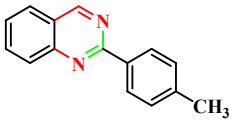


2-phenylquinazoline (4a) [11]**:** 3.4006g; 82.5% isolated yield. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 9.48 (s, 1H), 8.63-8.60 (m, 2H), 8.11-8.09 (m, 1H), 7.95-7.89(m, 2H), 7.64-7.60 (m, 1H), 7.57-7.49 (m, 3H); **^{13}C NMR** ($CDCl_3$, 400 MHz): δ =161.1, 160.5,150.8, 138.0, 134.1, 130.6, 128.6, 128.6, 128.6, 127.2, 127.1, 123.6.

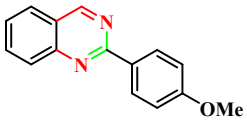


2-(4-chlorophenyl)quinazoline(4b) [11]**:** 3.8512g; 80.2% isolated yield. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 9.47 (s, 1H), 8.60-8.57 (m, 2H), 8.10 (d, J = 8.0 Hz, 1H), 7.96-7.91 (m, 2H), 7.66-7.62 (m, 1H), 7.53-7.49 (m, 2H). **^{13}C NMR** ($CDCl_3$, 400 MHz): δ

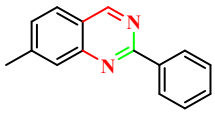
= 160.5, 160.0, 150.6, 136.8, 136.4, 134.3, 129.8, 128.8, 128.5, 127.4, 127.1, 123.5.



2-p-tolylquinazoline(4c) [12]: 3.5112g; 79.8% isolated yield. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 9.45 (s, 1H), 8.52-8.50 (m, 2H), 8.07 (d, J = 8.0 Hz, 1H),7.92-7.87 (m, 2H), 7.61-7.57 (m, 1H), 7.34 (d, J = 8.0 Hz, 2H), 2.45 (s, 3H). **^{13}C NMR** ($CDCl_3$, 400 MHz): δ = 161.1, 160.4, 150.7, 140.8, 135.3, 134.0, 129.4, 128.5, 127.1, 127.0, 123.4, 21.5.



2-(4-methoxyphenyl)quinazoline(4d) [12]: 3.8720g; 82.0% isolated yield. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 9.44 (s, 1H), 8.59 (d, J = 8.0 Hz, 2H), 8.07 (d, J = 8.0 Hz,1H), 7.92-7.87 (m, 2H), 7.61-7.57 (m, 1H), 7.07-7.04 (m, 2H), 3.91 (s, 3H). **^{13}C NMR** ($CDCl_3$, 400 MHz): δ = 161.8, 160.8, 160.4, 150.7, 134.0, 130.6, 130.2, 128.3, 127.1, 126.8, 123.3, 113.9,55.4.



5-methyl-2-phenylquinazoline (4e) [13]: 3.4540g;78.5% isolated yield. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 9.39 (s, 1H), 8.61-8.59 (m, 2H), 7.87 (s, 1H), 7.81 (d, J = 8.0Hz, 1H), 7.55-7.50 (m, 3H), 7.43 d, J = 8.0 Hz, 1H), 2.60 (s, 3H). **^{13}C NMR** ($CDCl_3$, 400 MHz): δ = 161.1, 159.9, 151.1, 145.2, 138.2, 130.5, 129.6, 128.6, 128.5, 127.6, 126.8, 121.9, 22.4.

VI. Copies of ^{1}H and ^{13}C NMR spectra of products

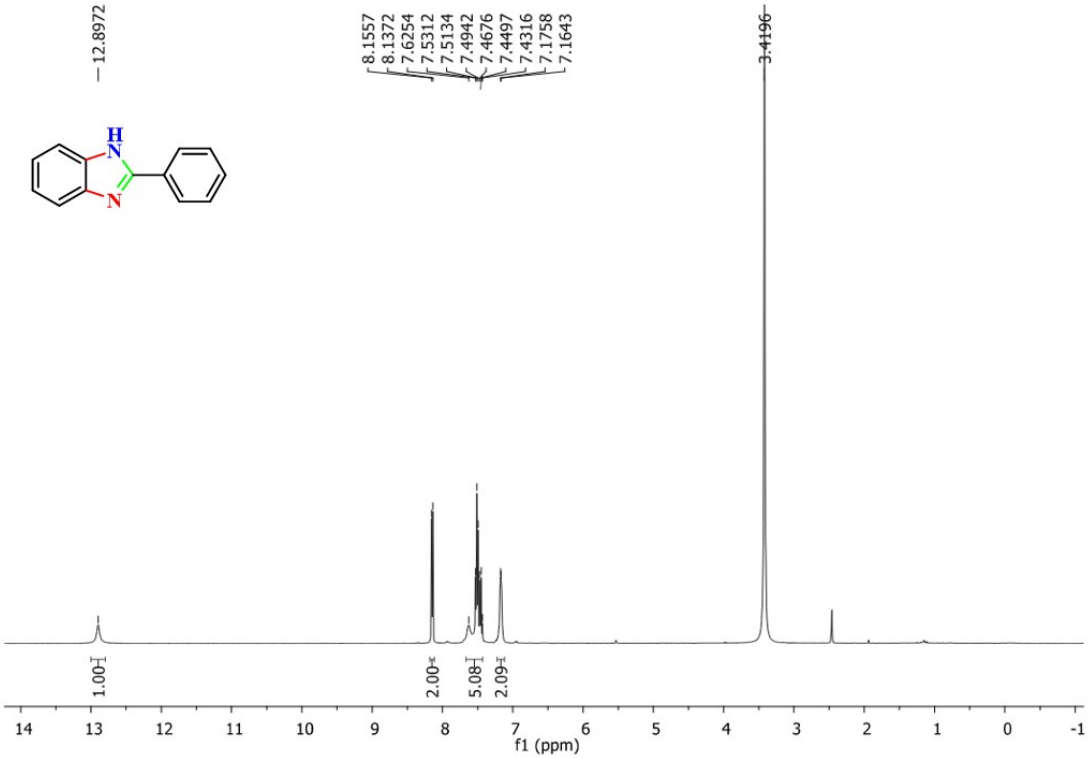


Figure S2. ^{1}H NMR of 2-phenyl-1H-benzimidazole in DMSO-d_6.

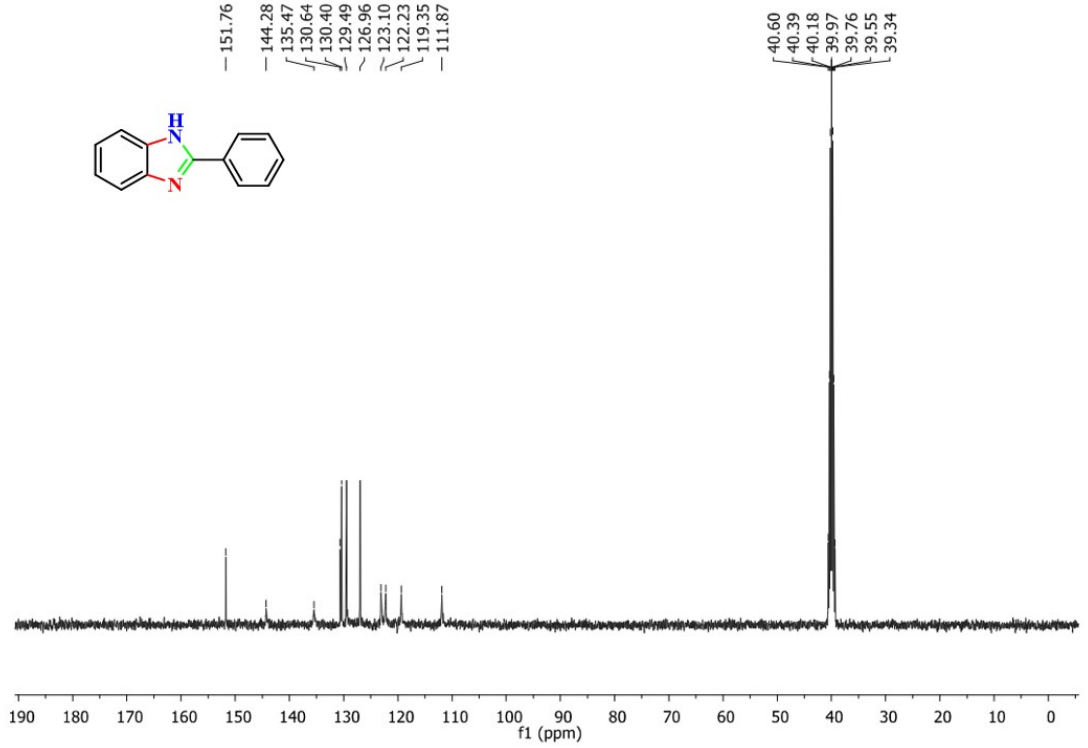


Figure S3. ^{13}C NMR of 2-phenyl-1H-benzimidazole in DMSO-d_6.

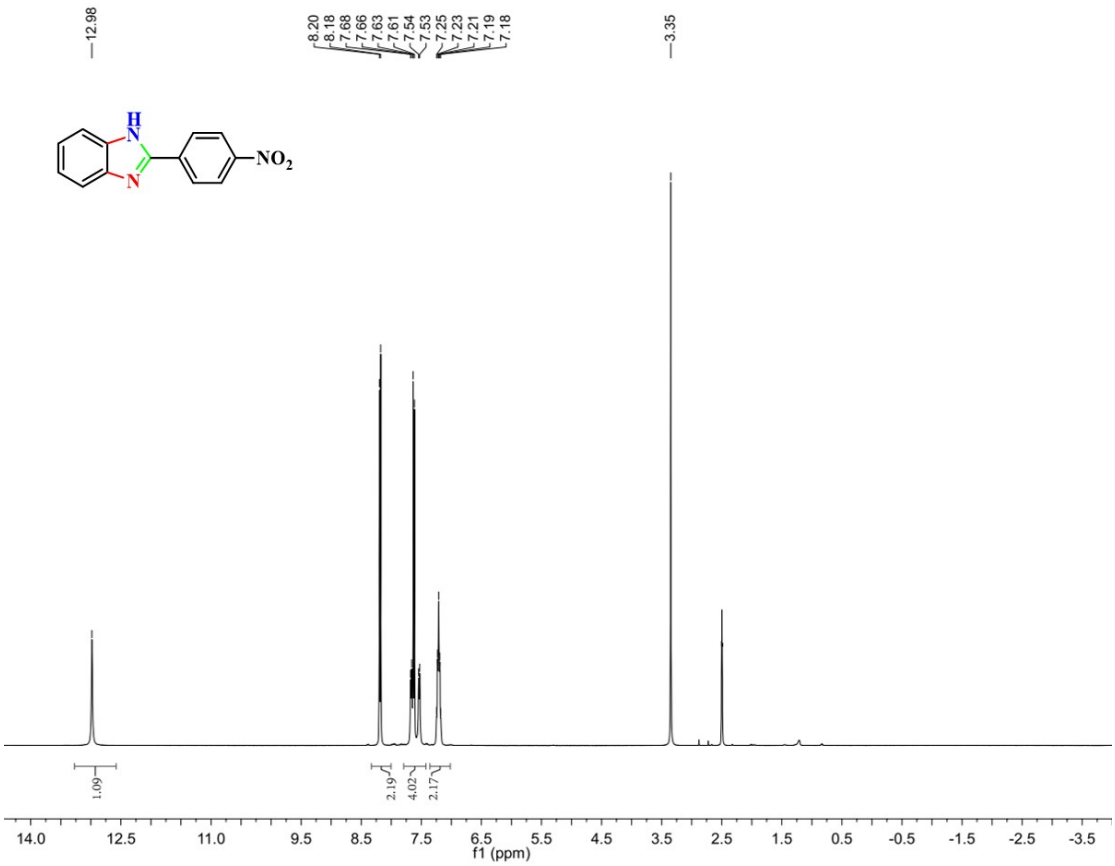


Figure S4. ^{1}H NMR of 2-(4-nitrophenyl)-1H-benzimidazole in DMSO-d_6.

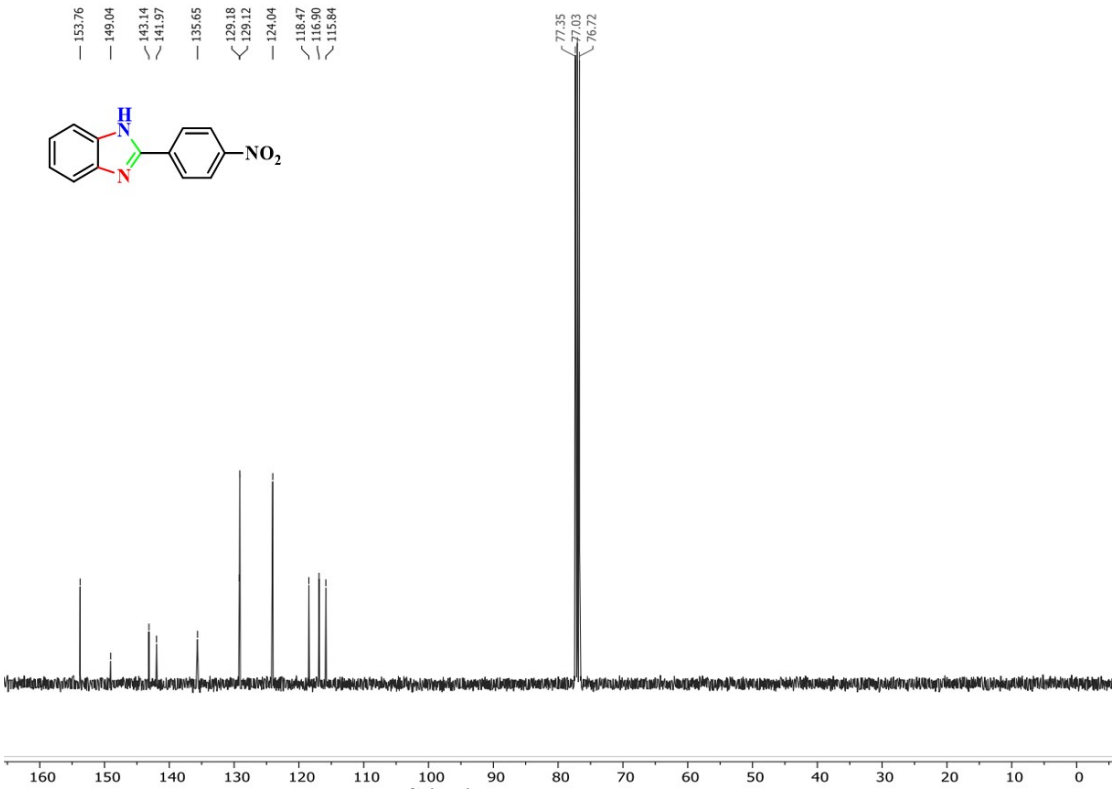


Figure S5. ^{13}C NMR of 2-(4-nitrophenyl)-1H-benzimidazole in DMSO-d_6.

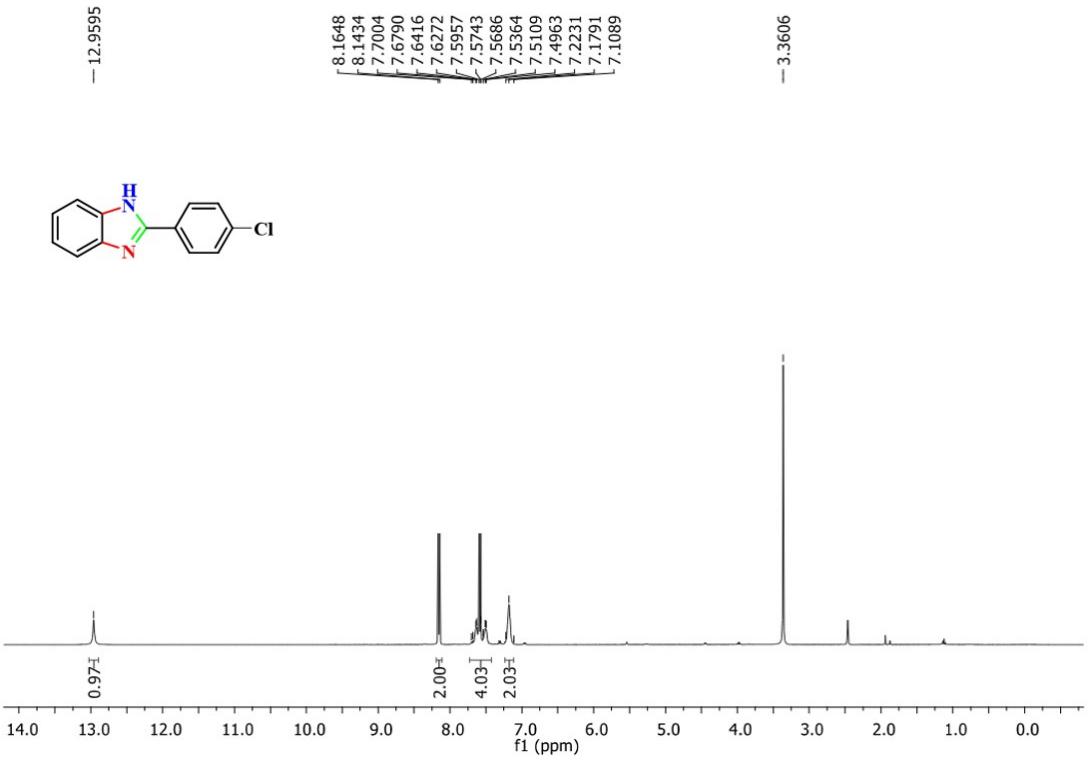


Figure S6. ^{1}H NMR of 2-(4-chlorophenyl)-1H-benzimidazole in DMSO-d_6.

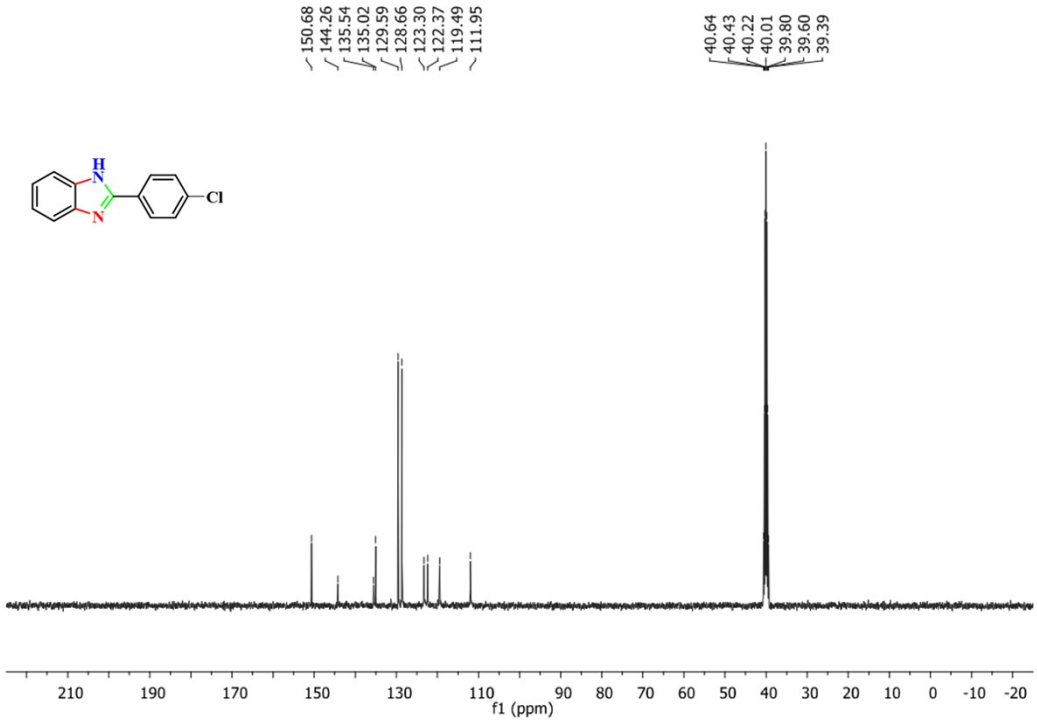


Figure S7. ^{13}C NMR of 2-(4-chlorophenyl)-1H-benzimidazole in DMSO-d_6.

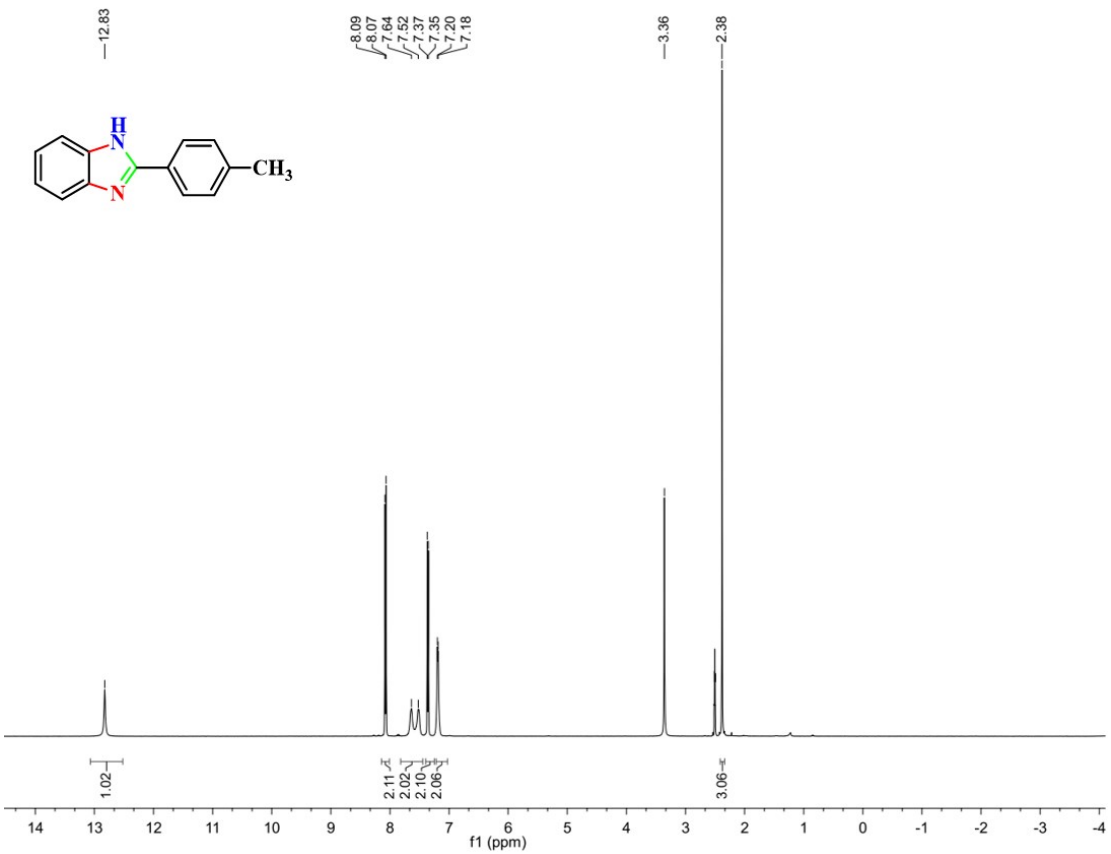


Figure S8. ^{1}H NMR of 2-(4-methylphenyl)-1H-benzimidazole in DMSO-d_6.

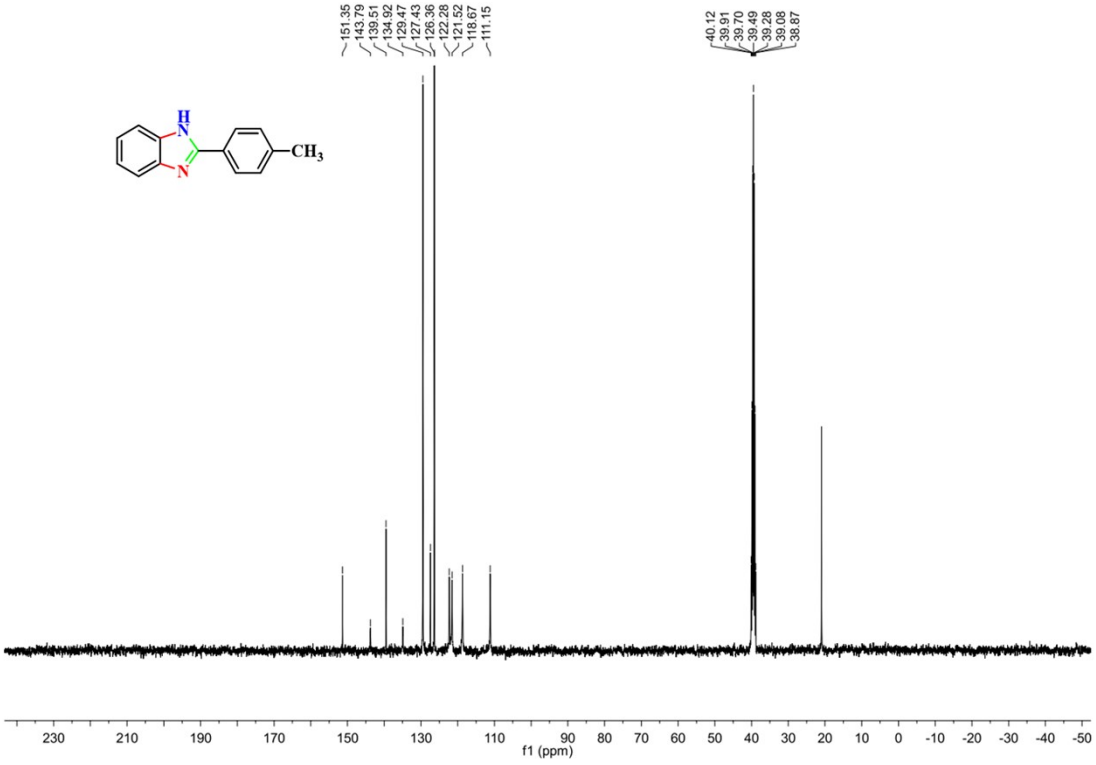


Figure S9. ^{13}C NMR of 2-(4-methylphenyl)-1H-benzimidazole in DMSO-d_6.

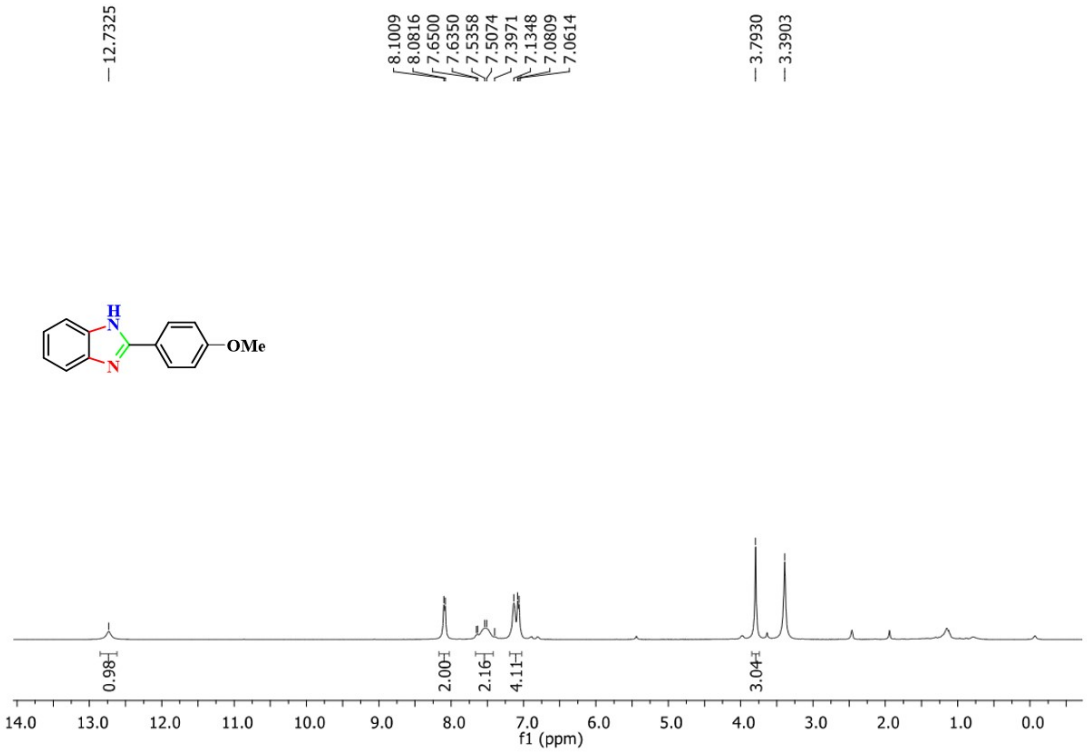


Figure S10. ^{1}H NMR of 2-(4-methoxyphenyl)-1H-benzimidazole in DMSO-d_6.

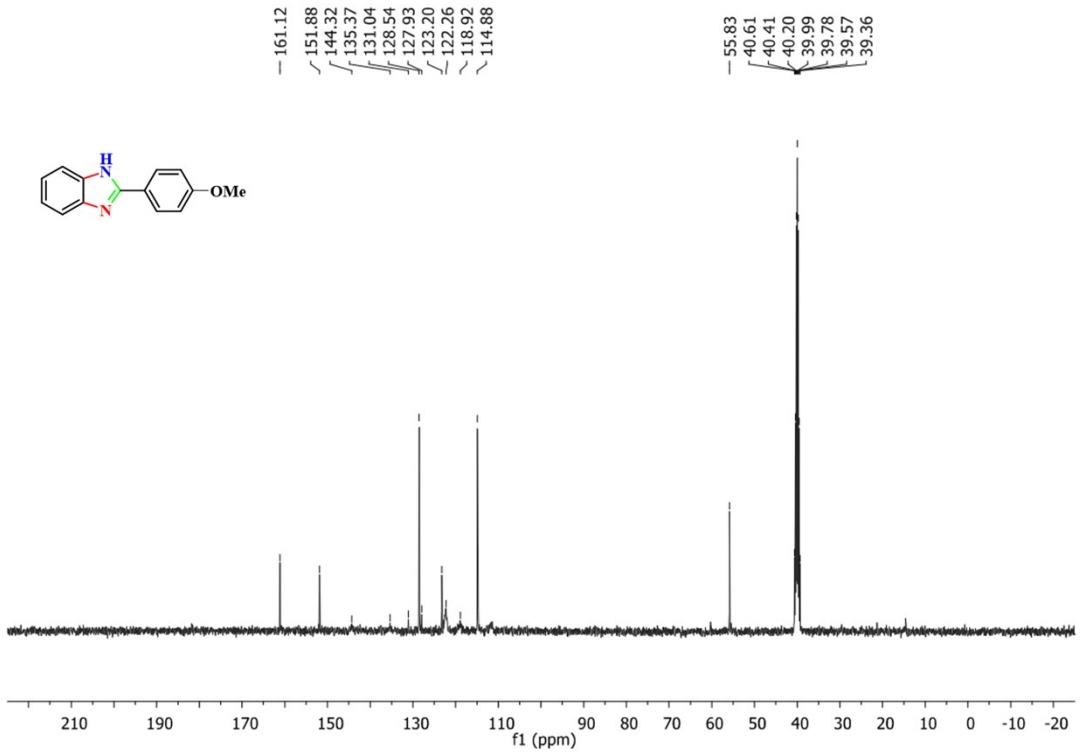


Figure S11. ^{13}C NMR of 2-(4-methoxyphenyl)-1H-benzimidazole in DMSO-d_6.

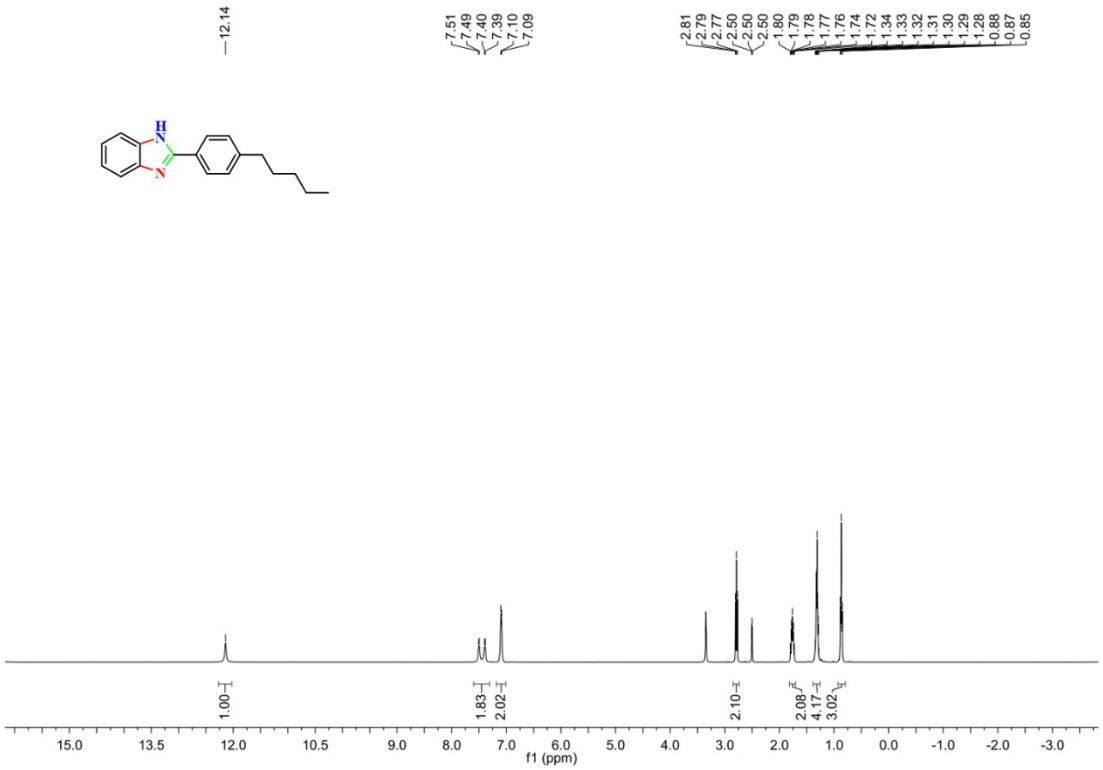


Figure S12. ^{1}H NMR of 2-pentyl-1H-benzimidazole in DMSO-d_6.

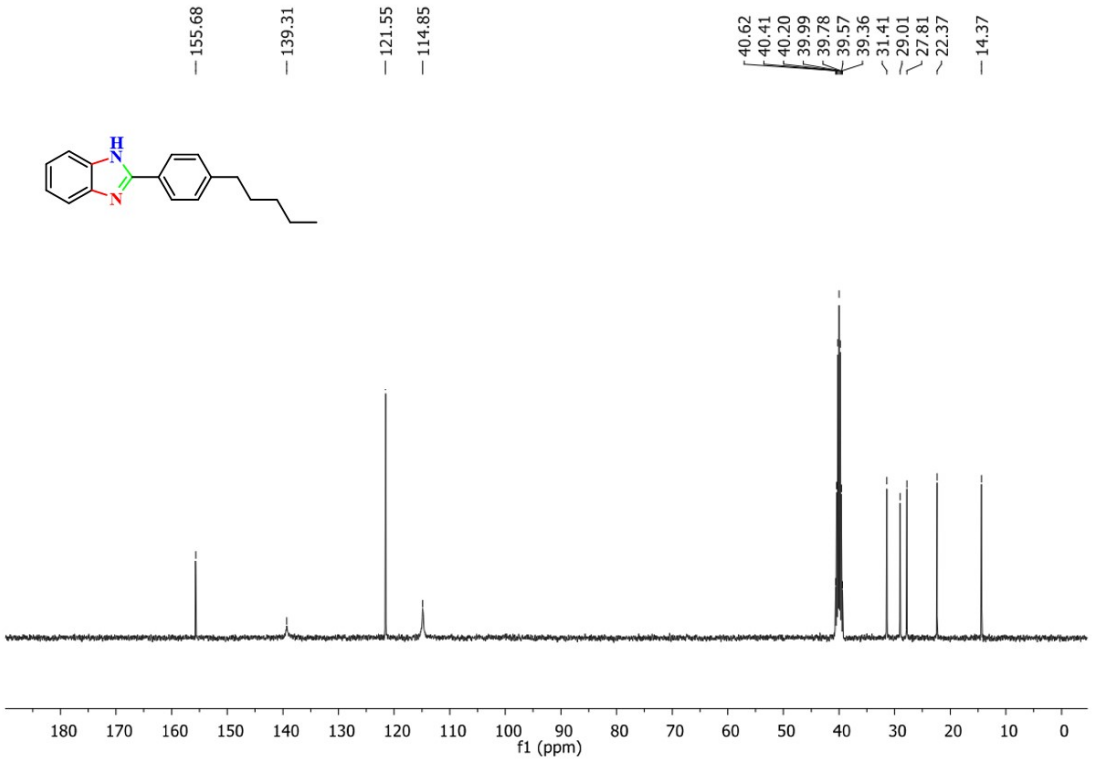


Figure S13. ^{13}C NMR of 2-pentyl-1H-benzimidazole in DMSO-d_6.

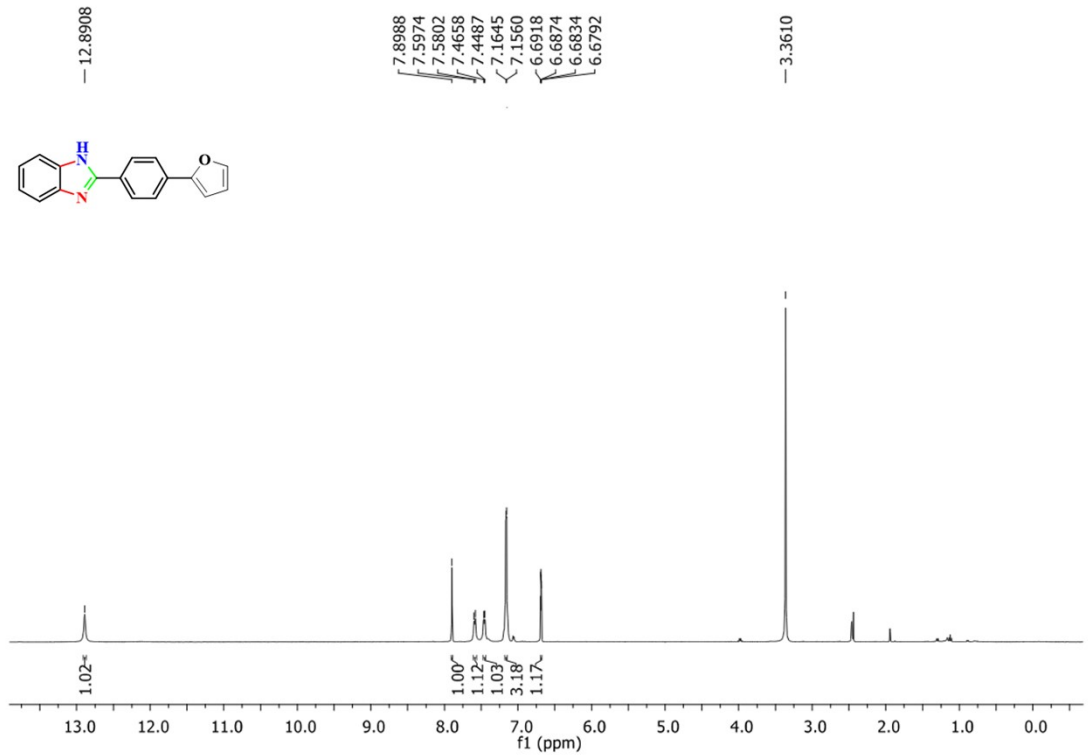


Figure S14. ^{1}H NMR of 2-(furan-2-yl)-1H-benzimidazole in DMSO-d_6.

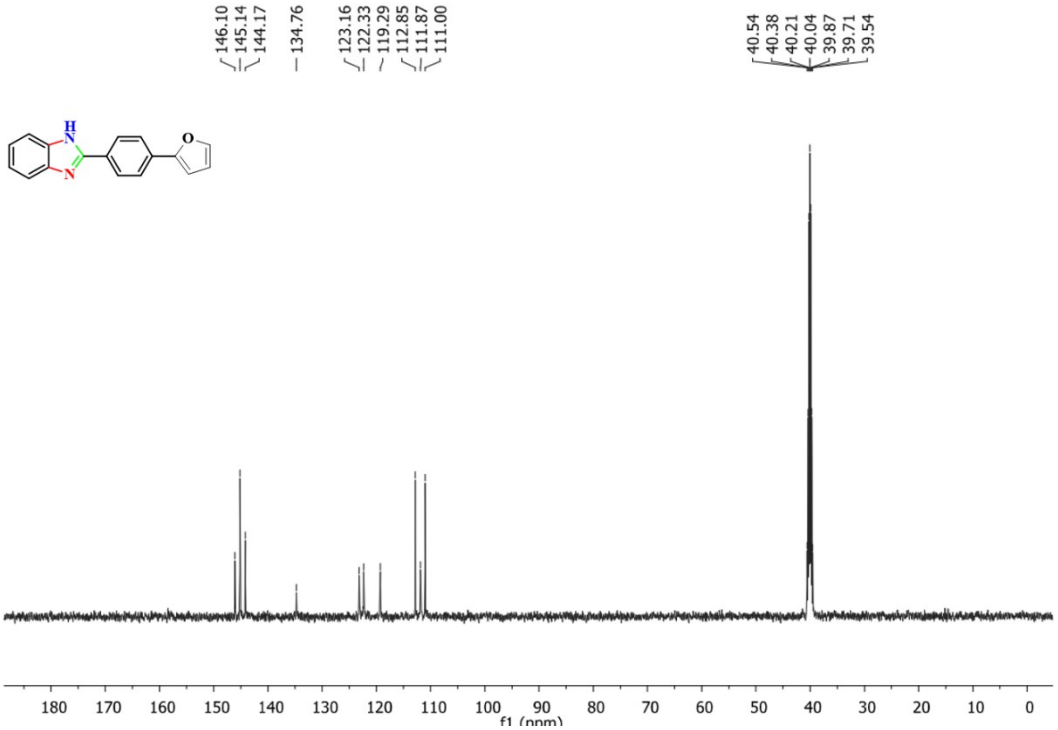


Figure S15. ^{13}C NMR of 2-(furan-2-yl)-1H-benzimidazole in DMSO-d_6.

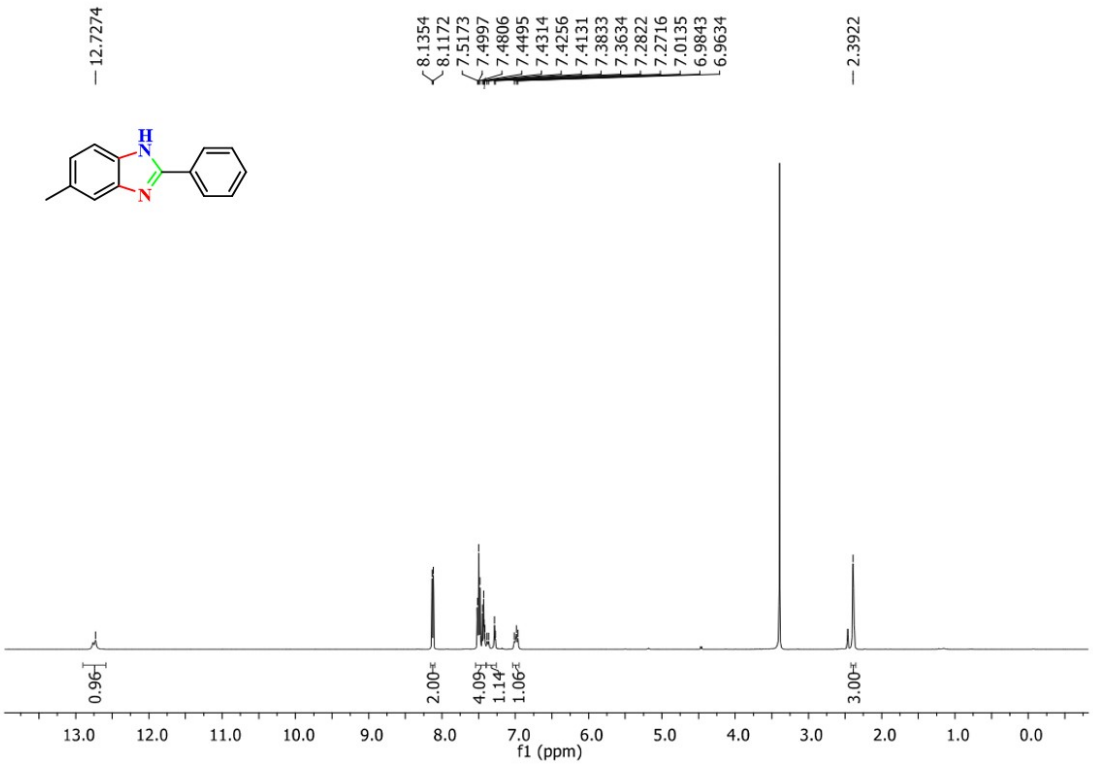


Figure S16. ^{1}H NMR of 2-phenyl-1H-benzimidazole in DMSO.

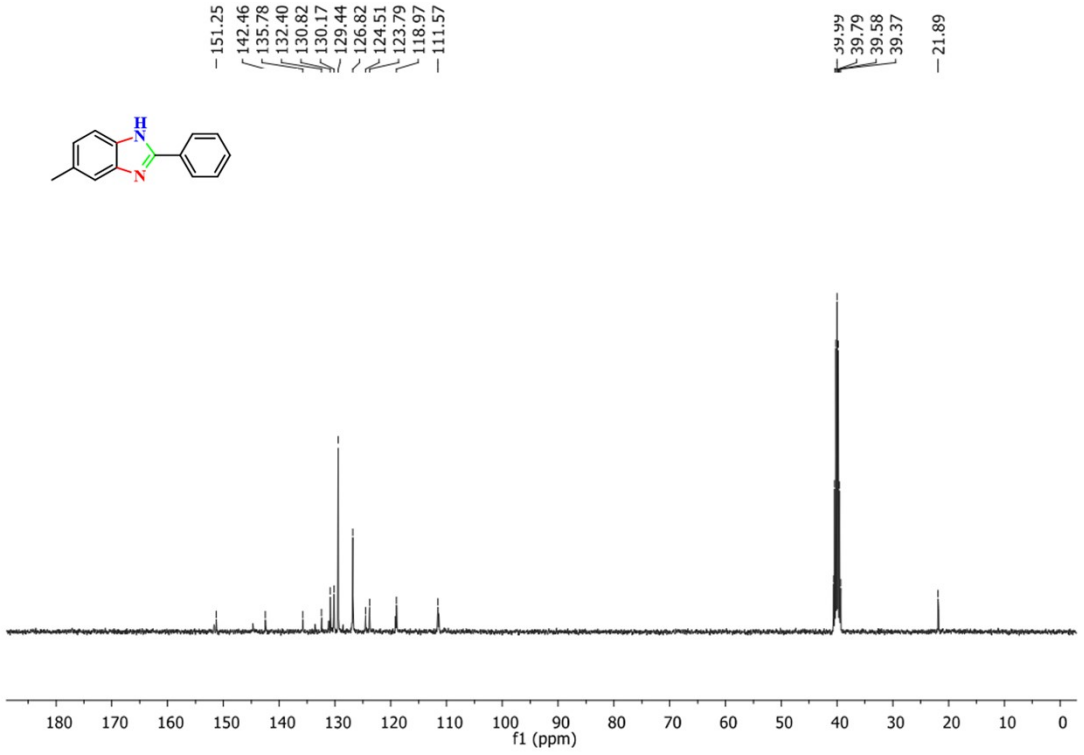


Figure S17. ^{13}C NMR of 2-phenyl-1H-benzimidazole in DMS

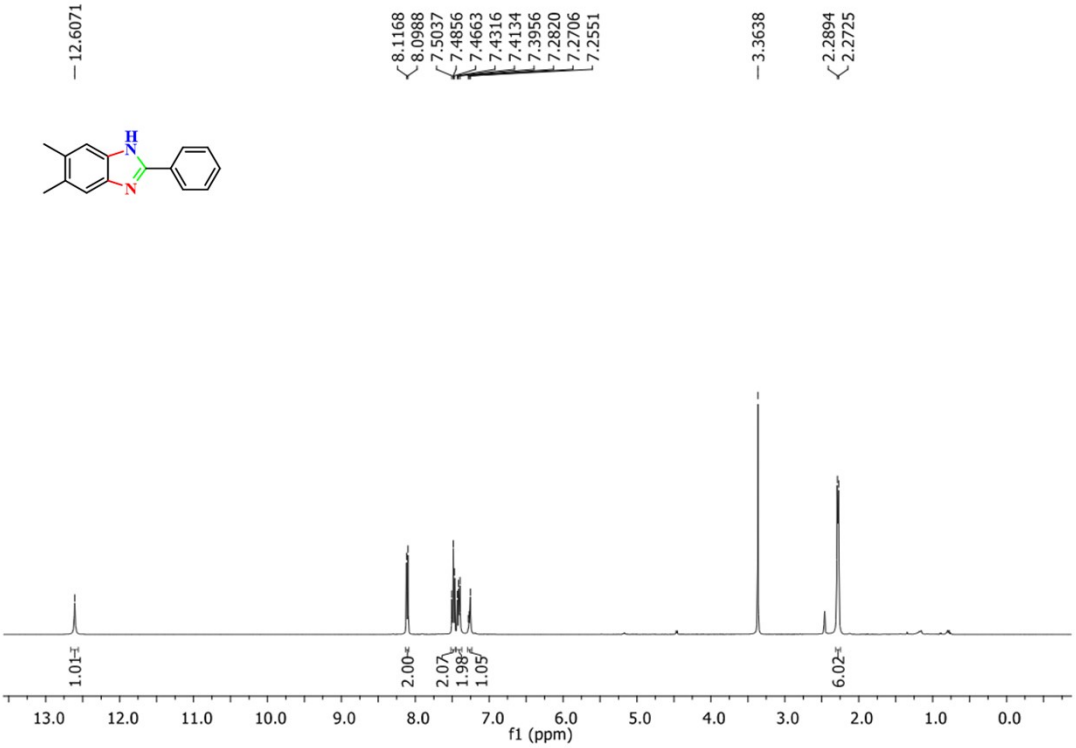


Figure S18. ^{1}H NMR of 5,6-dimethyl-2-phenyl-1H-benzimidazole in DMSO-d_6.

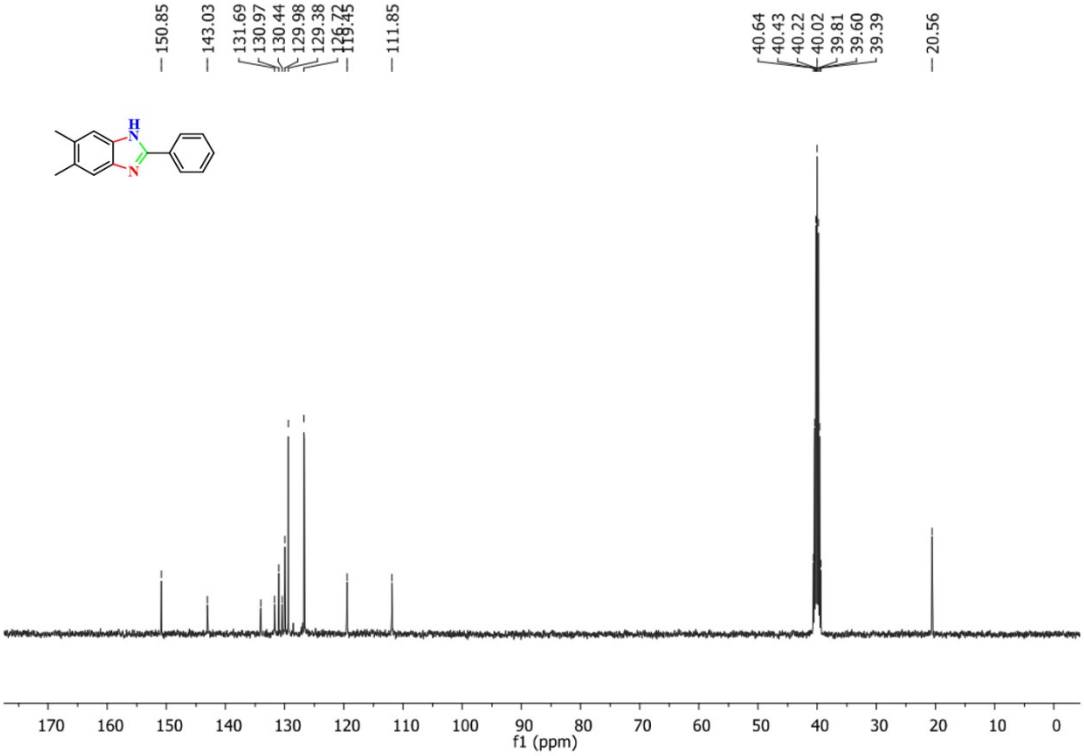


Figure S19. ^{13}C NMR of 5,6-dimethyl-2-phenyl-1H-benzimidazole in DMSO-d_6.

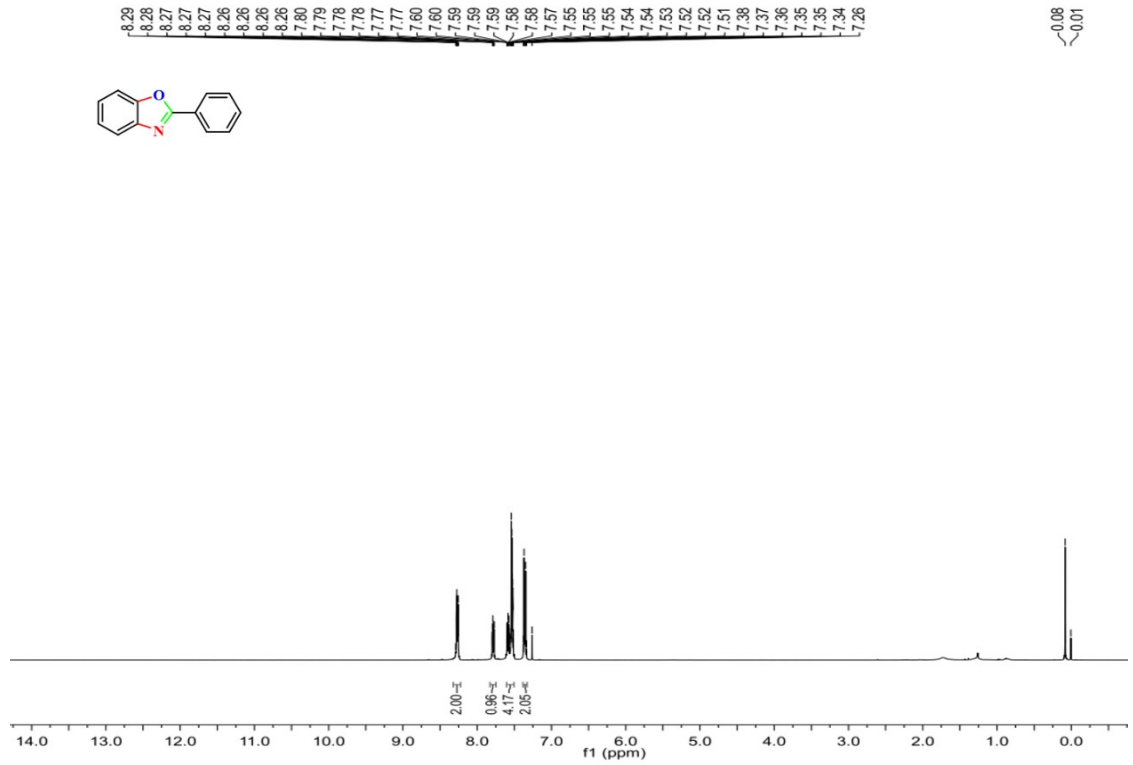


Figure S20. ^{1}H NMR of 2-phenylbenzoxazole in $CDCl_3$.

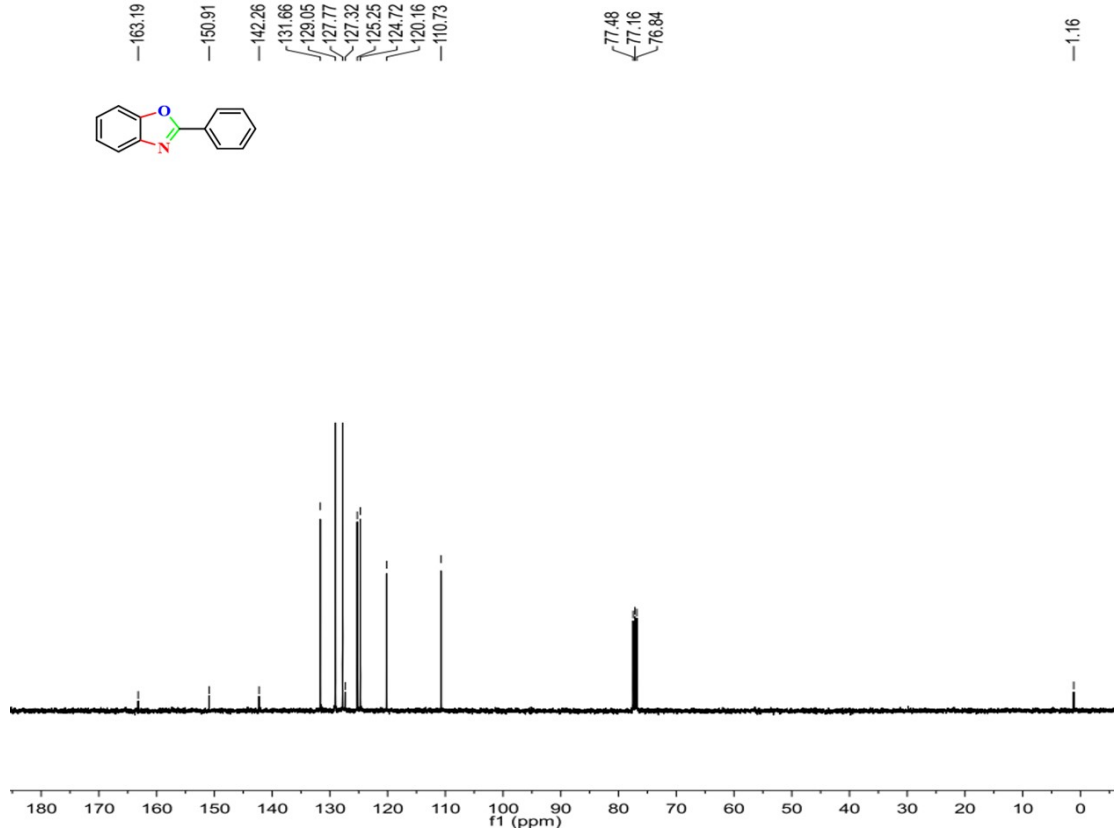


Figure S21. ^{13}C NMR of 2-phenylbenzoxazole in $CDCl_3$.

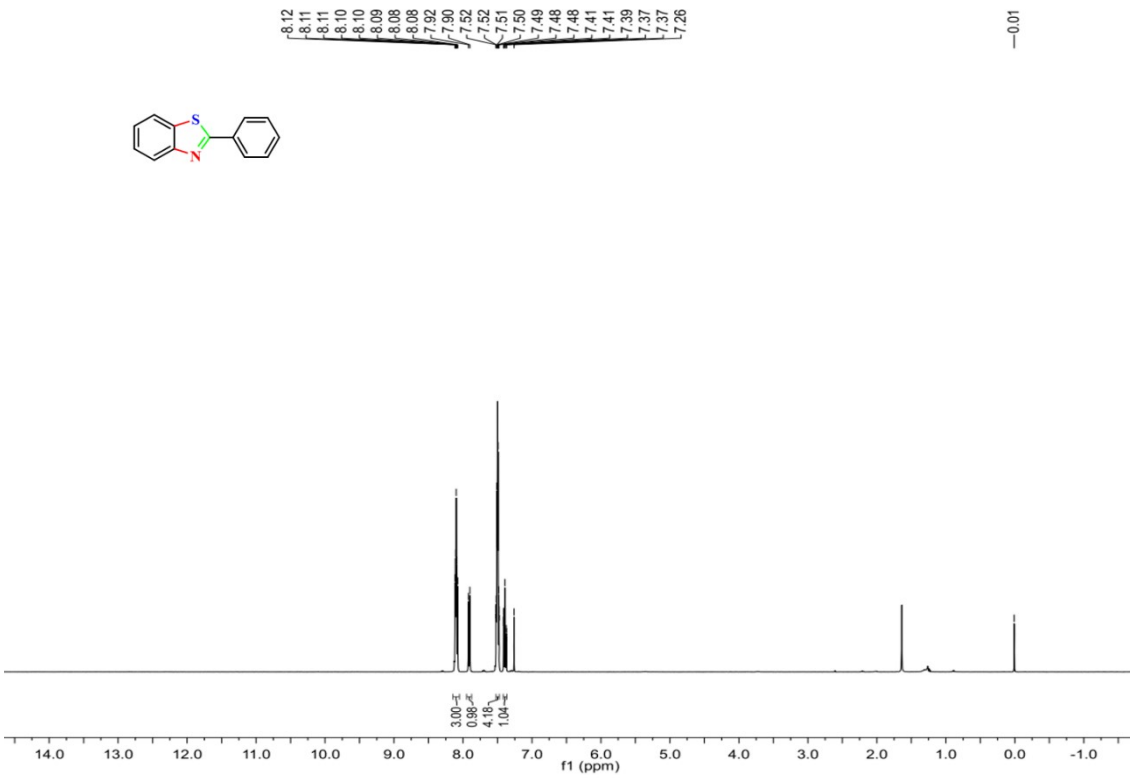


Figure S22. ^{1}H NMR of 2-phenylbenzothiazole in $CDCl_3$.

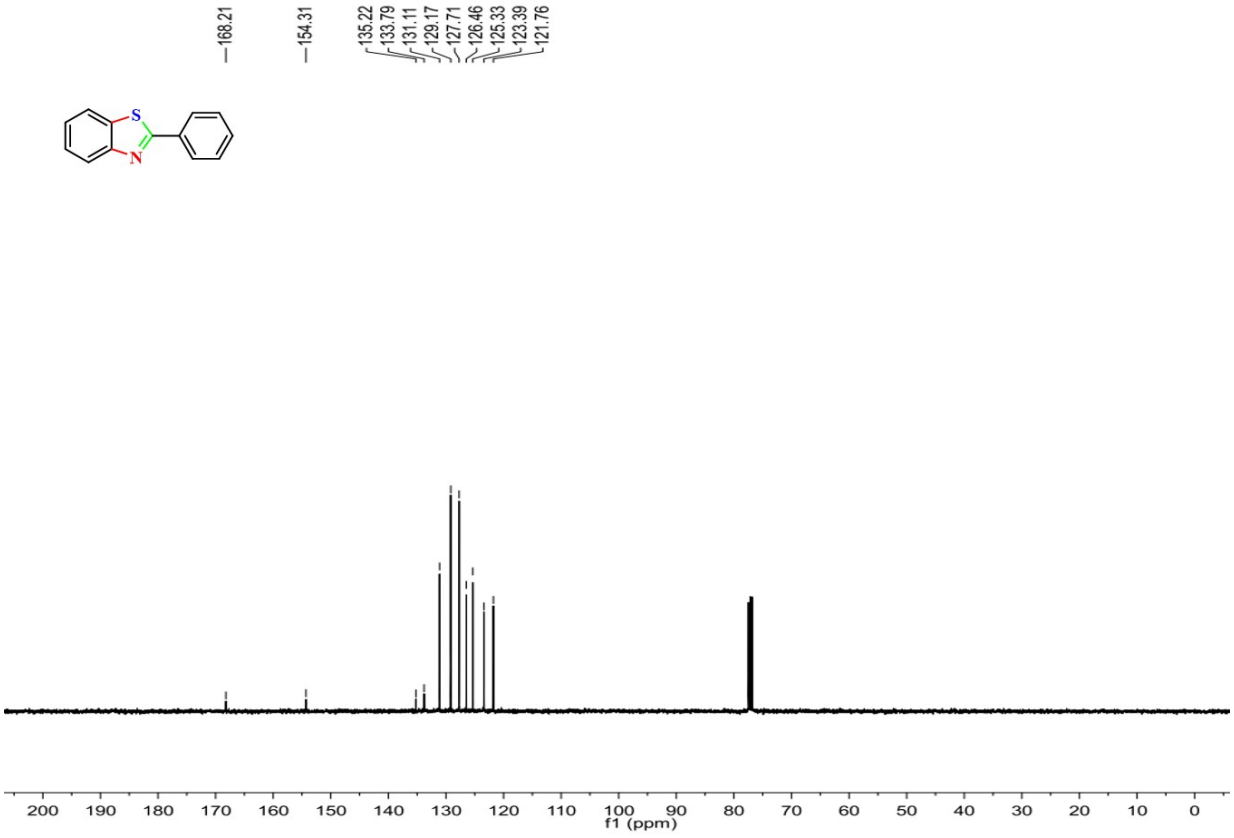


Figure S23. ^{13}C NMR of 2-phenylbenzothiazole in $CDCl_3$.

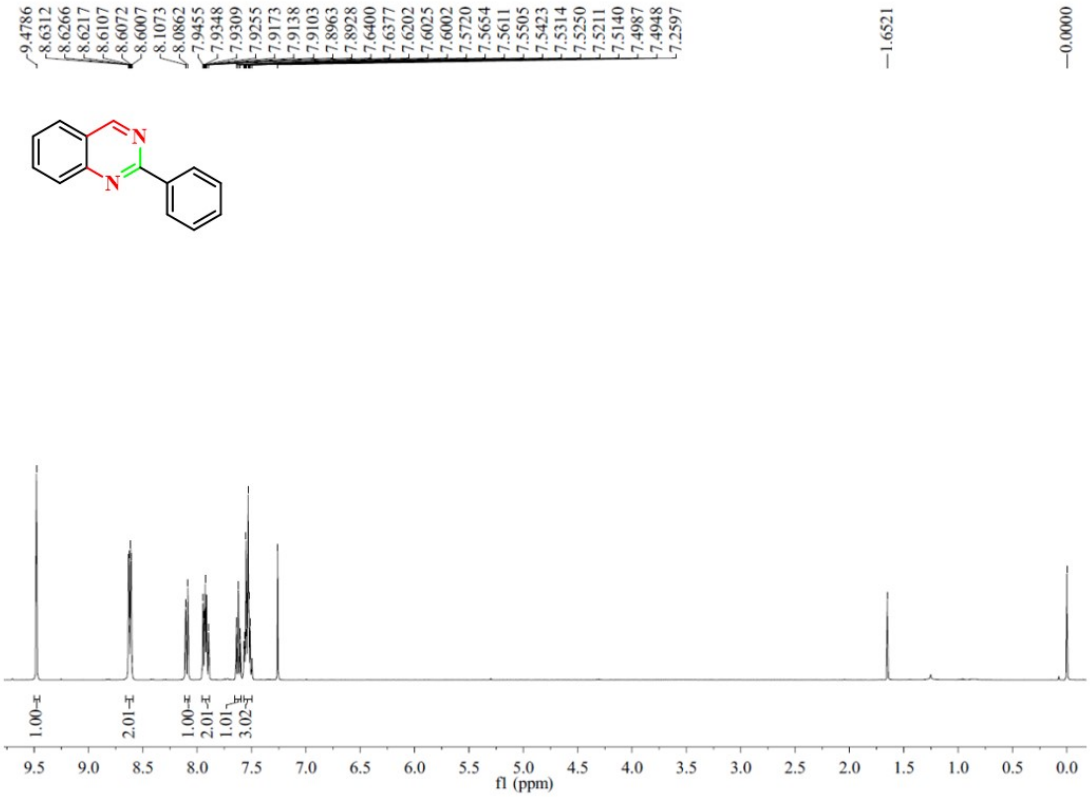


Figure S24. ^{1}H NMR of 2-phenylquinazoline in $CDCl_3$.

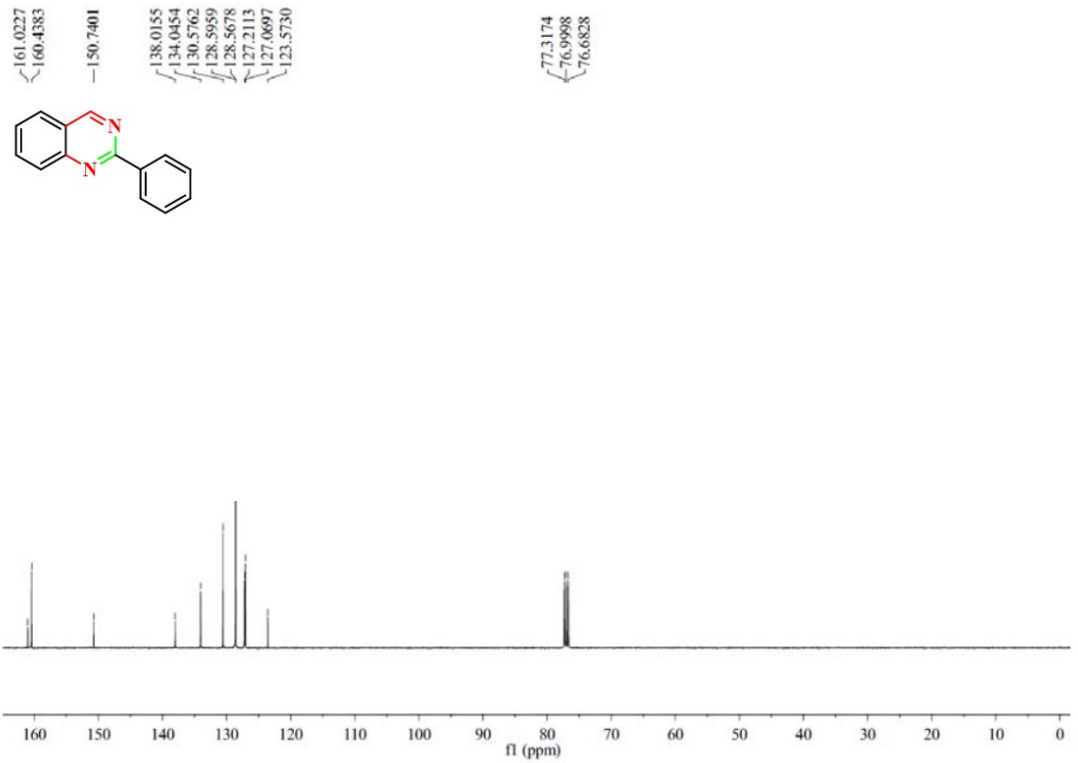


Figure S25. ^{13}C NMR of 2-phenylquinazoline in $CDCl_3$.

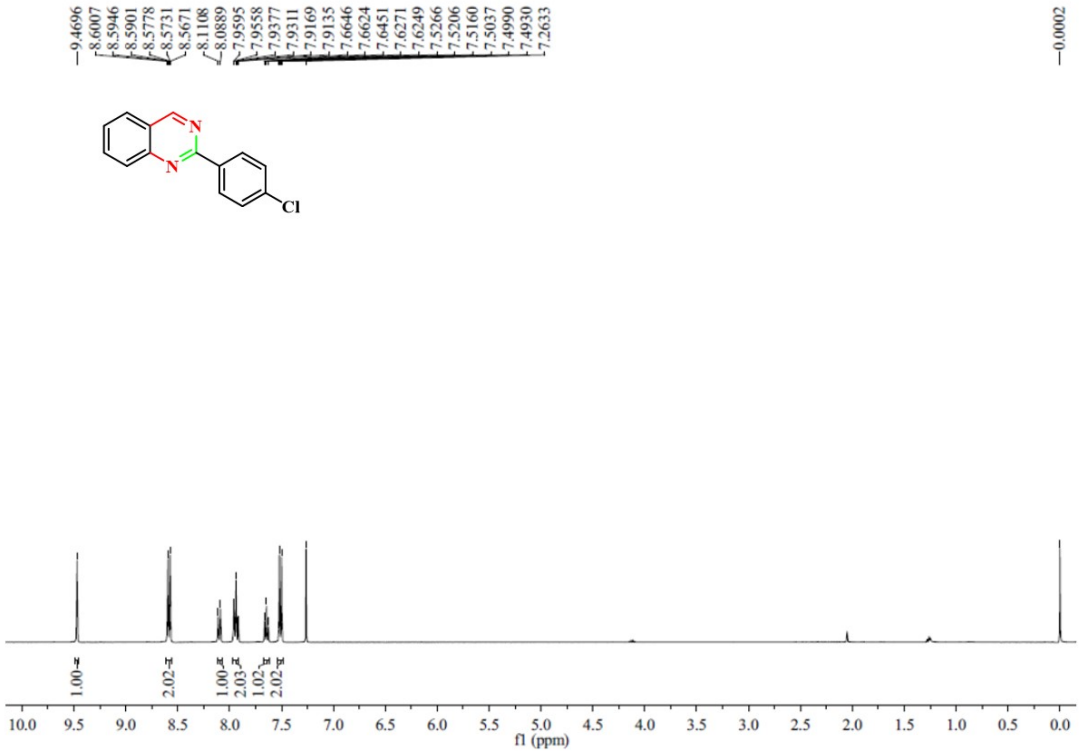


Figure S26. ^{1}H NMR of 2-(4-chlorophenyl)quinazoline in $CDCl_3$.

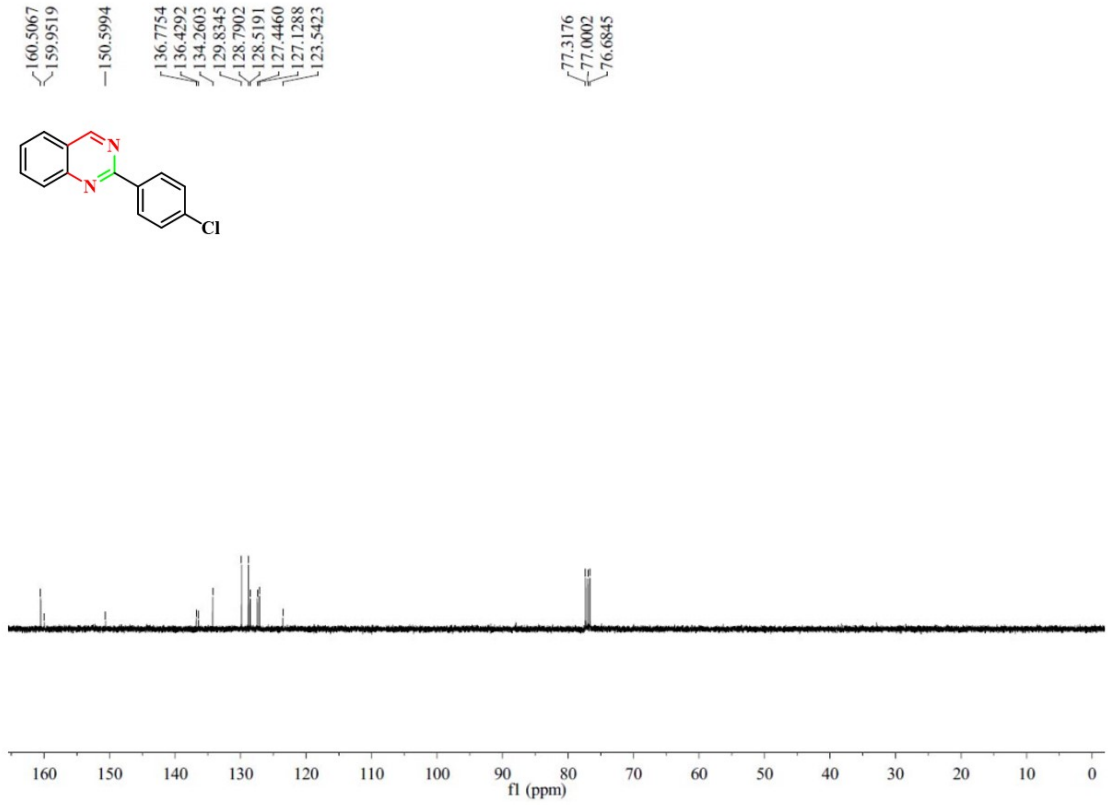


Figure S27. ^{13}C NMR of 2-(4-chlorophenyl)quinazoline in $CDCl_3$.

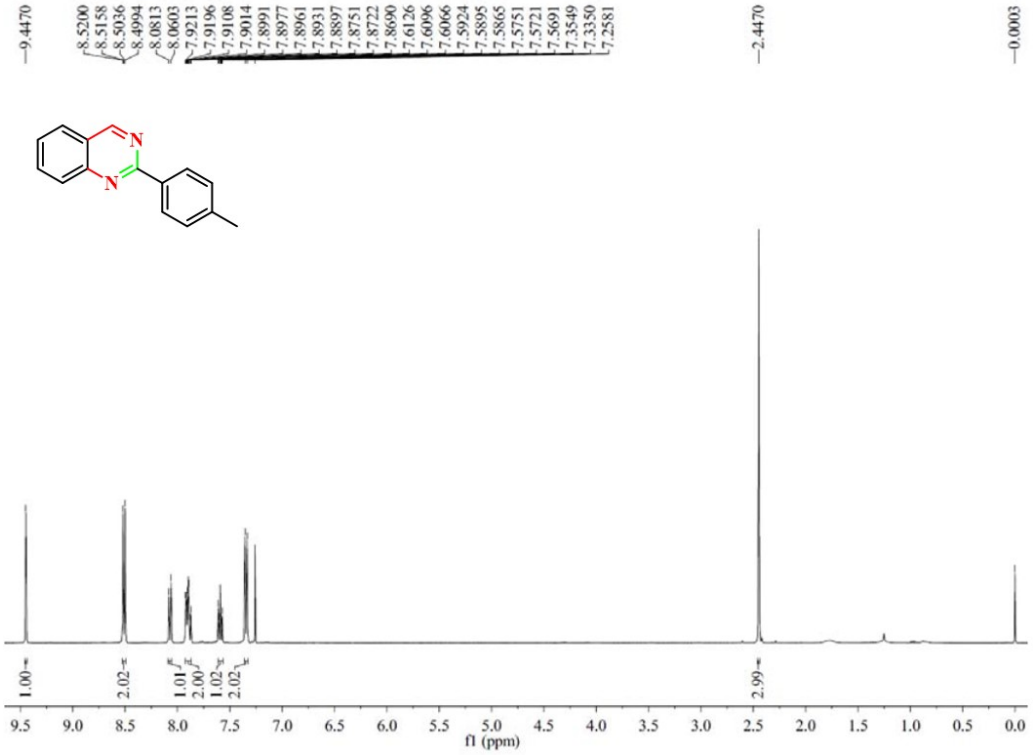


Figure S28. ^{1}H NMR of 2-p-tolylquinazoline in $CDCl_3$.

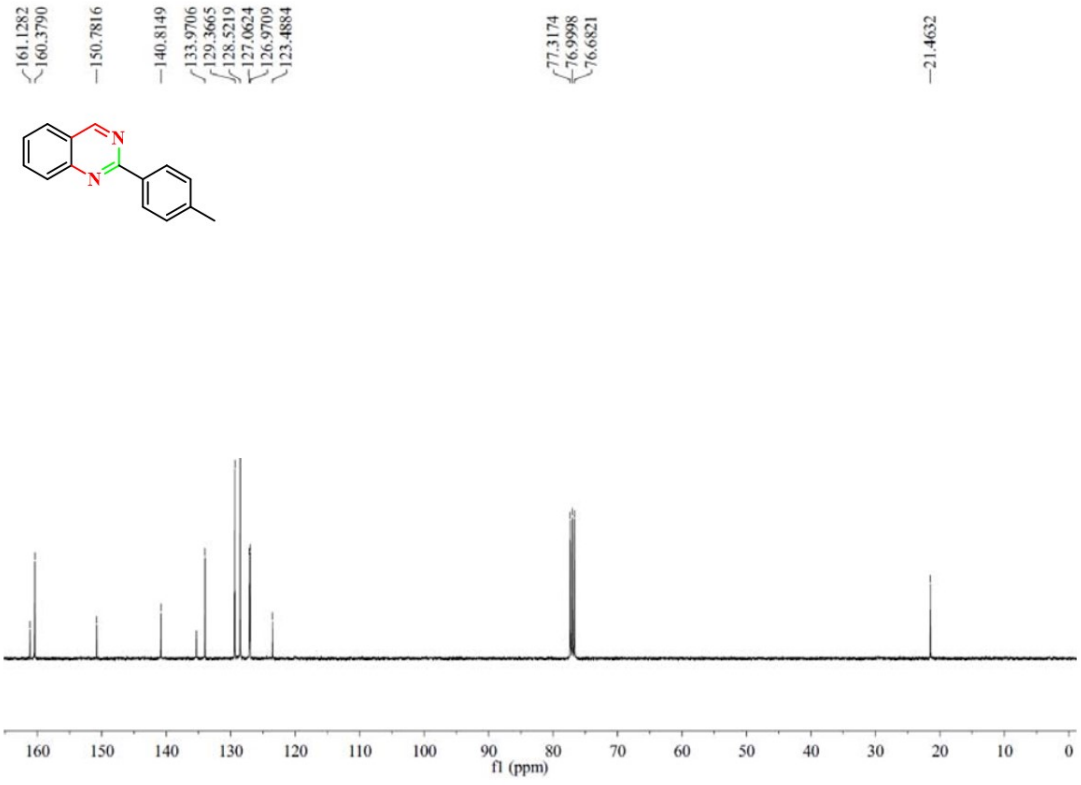


Figure S29. ^{13}C NMR of 2-p-tolylquinazoline in $CDCl_3$.

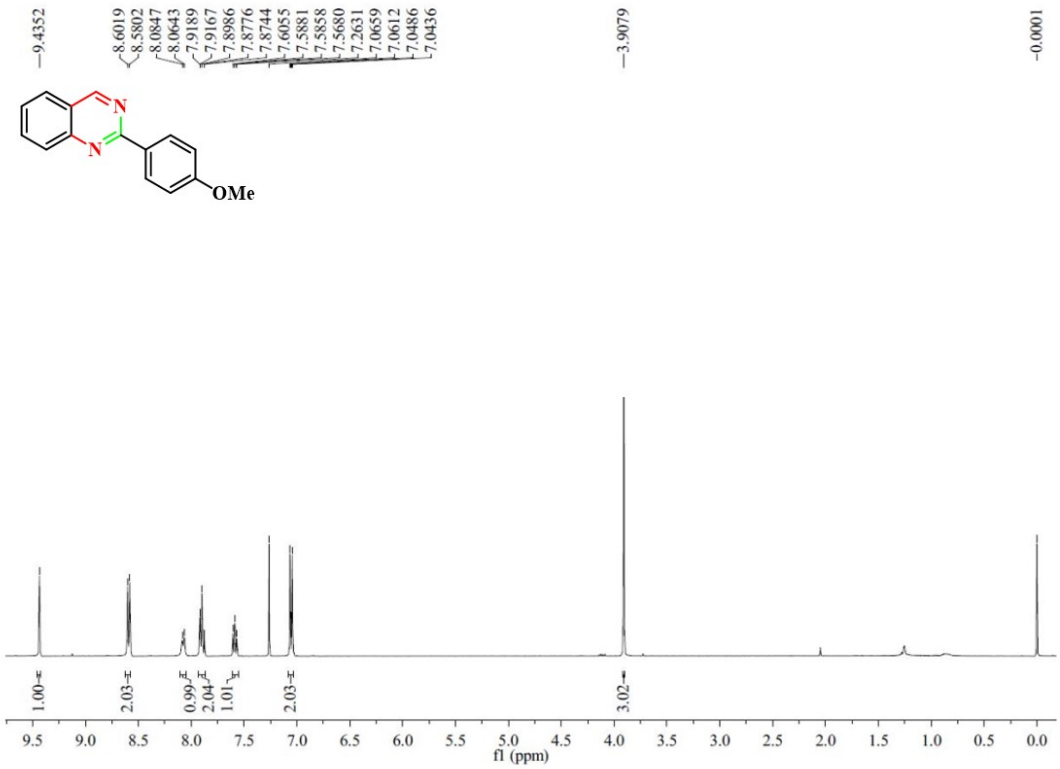


Figure S30. ^{1}**H NMR** of 2-(4-methoxyphenyl)quinazoline in $CDCl_3$.

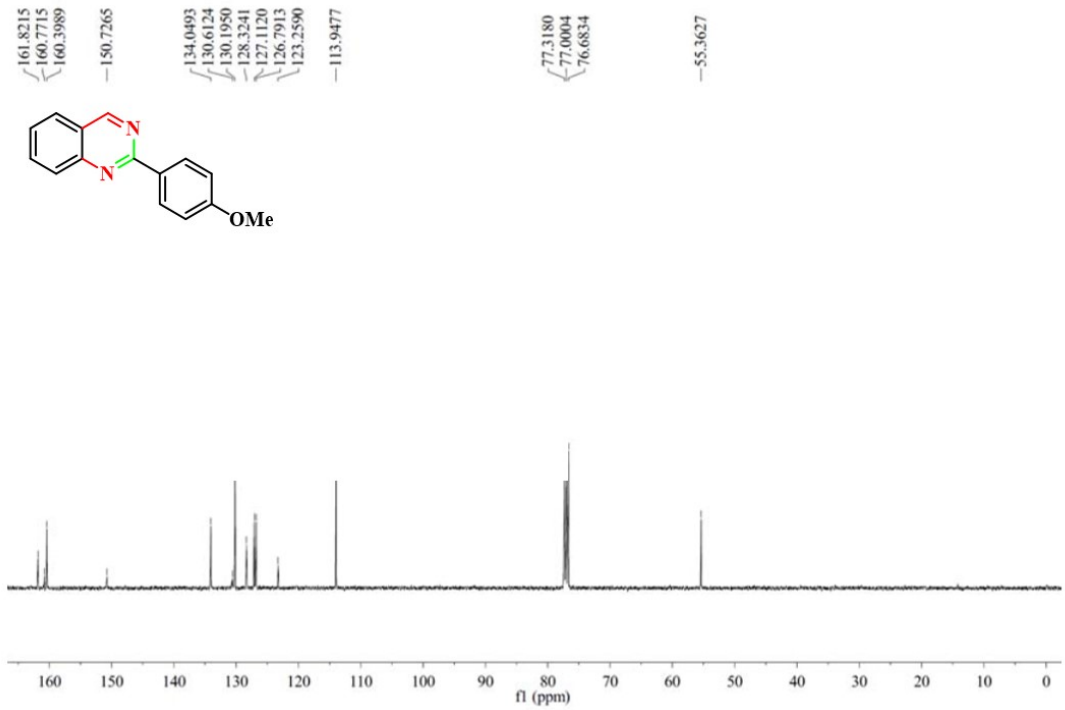


Figure S31. ^{13}**C NMR** of 2-(4-methoxyphenyl)quinazoline in $CDCl_3$.

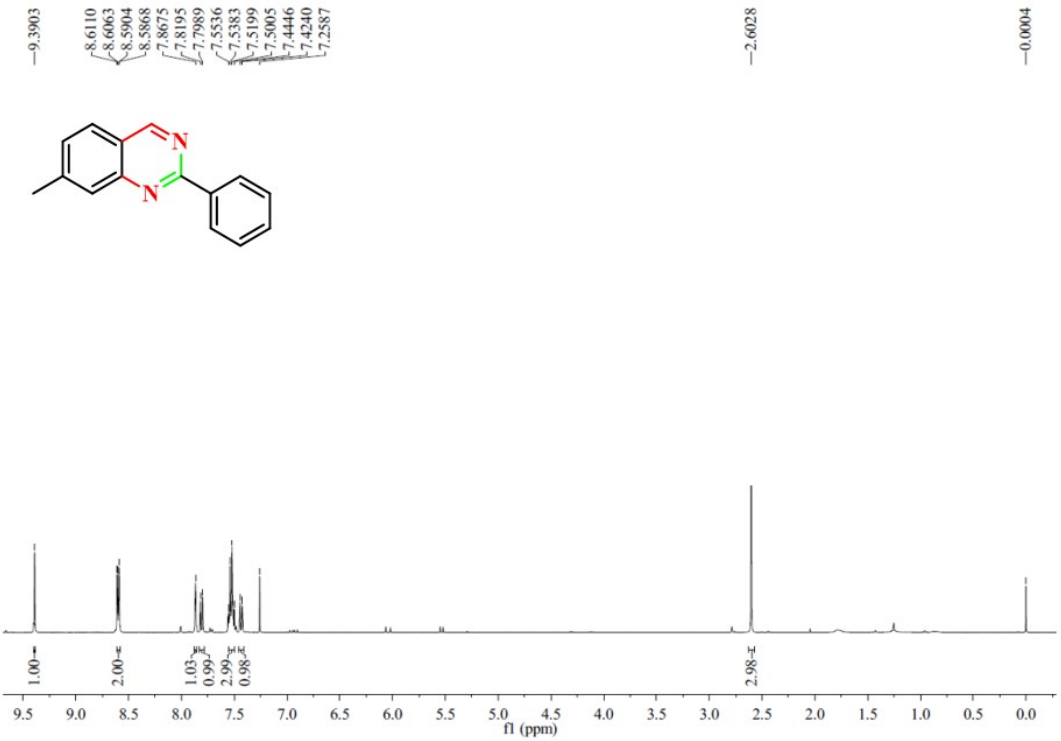


Figure S32. ^{1}H NMR of 2-phenyl-1H-quinazoline in $CDCl_3$.

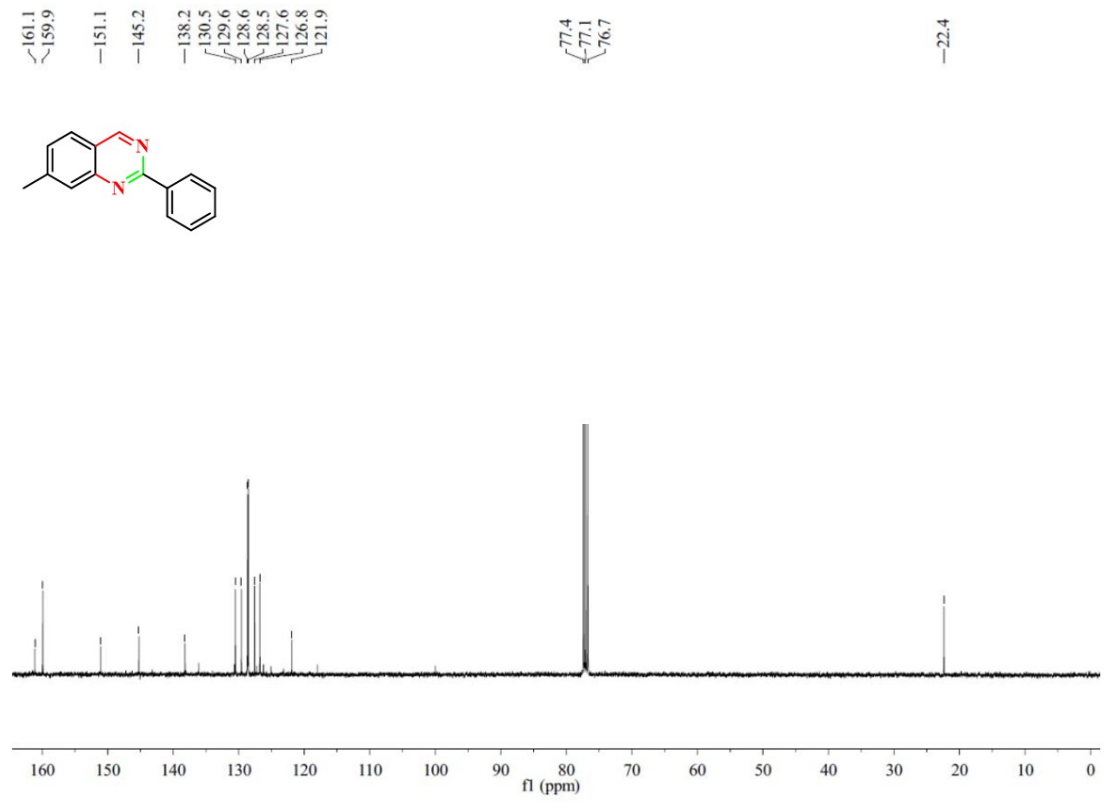


Figure S33. ^{13}C NMR of 2-phenyl-1H-quinazoline in $CDCl_3$.

VII. References

[1] K. Das, A. Mondal and D. Srimani, *J. Org. Chem.*, 2018, **83**, 9553-9560.

[2] O. Ravi, A. Shaikh, A. Upare, K. K. Singarapu, S. R. Bathula, *J. Org. Chem.*, 2017, **82**, 4422.

[3] L. Li, Q. Luo, H. Cui, R. Li, J. Zhang and T. Peng, *ChemCatChem*, 2018, **10**, 1607-1613.

[4] A. Rostami, O. Pourshiani, Y. Navasi, N. Darvishi and S. Saadati, *New J. Chem.*, 2017, **41**, 9033-

9040.

[5] P. Daw, Y. Ben-David and D. Milstein, *ACS Catal.*, 2017, **7**, 7456-7460.

[6] R. Zhang, Y. Qin, L. Zhang and S. Luo, *Org. Lett.*, 2017, **19**, 5629-5632.

[7] R. Ghadari, H. Namazi and M. Aghazadeh, Appl. *Organomet. Chem.*, 2018, **32**, e3965.

[8] C. Bäumler and R. Kempe, *Chem. Eur. J.*, 2018, **24**, 8989-8993.

[9] G. Evindar and R- A. Batey, *J. Org. Chem.*,2006171,5,1802-1808.

[10] B. d. P. Cardoso, J.-M. Bernard-Schaaf, S. Shahane, L. F. Veiros, M. J. Chetcuti and V. Ritleng, *Dalton Trans.*, 2018, 47, 1535-1547.

[11] R. Gujjarappa, S. K. Maity, C. K. Hazra, N. Vodnala, S. Dhiman, A. Kumar, U. Beifuss and C. C.Malakar, Eur. *J. Org. Chem.*, 2018, **2018**, 4628-4638.

[12] D. S. Deshmukh and B. M. Bhanage, *Synlett*, 2018, **29**, 979-985.

[13] Omar, M. A.; Conrad, J.; Beifuss, U. *Tetrahedron.* 2014, **70**, 3061