Supporting Information

Direct amination of azoles using $CuCl_2$ complexes of amines under mild conditions

Juan Xu, Jiarong Li, Zhen Wei, Qi Zhang, Daxin Shi*

School of Chemical Engineering and Environment,

Beijing Institute of Technology, Beijing 100081, China

E-mail: shidaxin@bit.edu.cn

Table of Contents

1. General Information

Unless otherwise noted, all reagents were purchased from commercial suppliers and used without purification. All reactions were conducted in round bottom flask. All azoles were used as received. Water was distilled prior to use. All $CuCl_2$ and amines, HCl were used as received. Melting points were recorded on an uncorrected Melting Point instrument. ^1H NMR and ^{13}C NMR spectra were recorded on a 400 MHz spectrometer using $CDCl_3$ or d^6-DMSO as solvent and tetrmethylsilane (TMS) as an internal standard. Chemical shifts (δ) were reported as part per million (ppm) in δ scale downfield from TMS. Coupling constants (J) were reported in Hertz (Hz). Mass spectra (MS) were obtained on a mass spectrometer (ESI-MS). The known products were characterized by ESI-MS and a part of them by ^1H NMR and ^{13}C NMR spectra. All amination products described in this manuscript are known compounds.

2. Experimental Section

2.1 General procedures for $CuCl_2$ complexes of amines

To a solution of amines (10 mmol) in EtOH (10 mL) was added HCl (10 mmol) and $CuCl_2$ (5 mmol). The reaction mixture was refluxed for 1 hour. Cooled to room temperature and filtered to get the crystal.

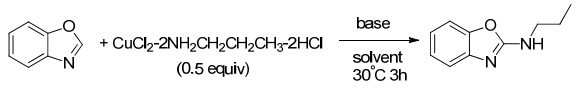
Selected data for $CuCl_2$ complexes of amines: $CuCl_2$ complexes of 4-nitroaniline, crystal data and structure refinement: Empirical formula $C_{12}H_{14}Cl_4CuN_4O_4$; Formula weight 483.61; Anal. calcd for $C_{12}H_{14}N_4Cl_4CuO_4$: C 29.80, H 2.92, N 11.58; found C 29.63, H 2.88, N 11.32.

2.2 General procedures for amination of boronic acids with CuCl2 complexes of amines as nitrogen source

To a solution of azoles (0.1 mmol) in CH_3CN (2 mL) was added $CuCl_2$ complexes of amines (0.06 mmol) and K_2CO_3 (1.2 mmol). The reaction mixture was stirred and concentrated in vacuo. The residue was purified by silica gel chromatography to provide the desired product.

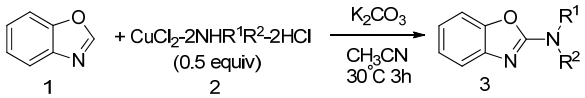
3. Optimazation studies and reaction results

Tabel S1. Optimization Studies of Benzoxazole with $CuCl_2$ Complex of *n*-propylamine



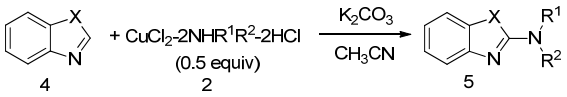
Entry	Base	Solvent	Yield/%
1	K_2CO_3	CH_3CN	89
2	Na_2CO_3	CH_3CN	82
3	$NaHCO_3$	CH_3CN	80
4	Et_3N	CH_3CN	74
5	pyridine	CH_3CN	72
6	no	CH_3CN	0
7	K_2CO_3	CH_2Cl_2	70
8	K_2CO_3	1,4-dioxane	65
9	K_2CO_3	MeOH	71

Tabel S2. Reaction Scopes of the Direct amination of Benzoxazole



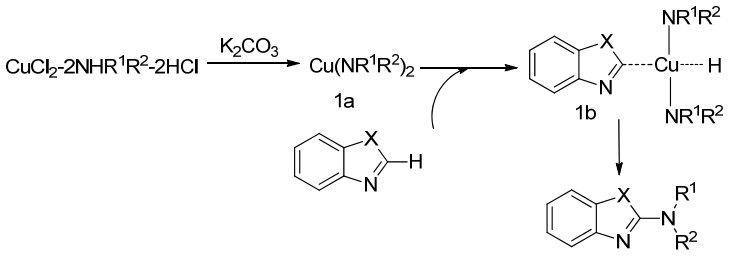
Entry	R^1	R^2	Product	Yield/%
1	$CH_2CH_2CH_3$	H	**3a**	89
2	CH_3	CH_3	**3b**	92
3	$NH_2CH_2CH_2$	H	**3c**	79
4	$(CH_2)_4$		**3d**	90
5	$(CH_2)_2O(CH_2)_2$		**3e**	91
6	$(CH_2)_2N(CH_3)(CH_2)_2$		**3f**	82
7	Ph	H	**3g**	76
8	4-NO_2Ph	H	**3h**	72
9	4-CH_3Ph	H	**3i**	81

Tabel S3. Reaction Scopes of the Direct Amination of Benzothiazole and 1-methylbenzimidazole



Entry	X	R^1	R^2	Product	Yield/%
1	S	$CH_2CH_2CH_3$	H	**5a**	83
2		CH_3	CH_3	**5b**	78
3		$(CH_2)_4$		**5c**	81
4		$(CH_2)_5$		**5d**	79
5		$(CH_2)_2O(CH_2)_2$		**5e**	80
6		$(CH_2)_2N(CH_3)(CH_2)_2$		**5f**	75
7		4-CH_3Ph	H	**5g**	69
8	NCH_3	CH_2CH_3	CH_2CH_3	**5h**	66
9		$(CH_2)_5$		**5i**	68
10		$(CH_2)_2O(CH_2)_2$		**5j**	62
11		4-NO_2Ph	H	**5k**	60

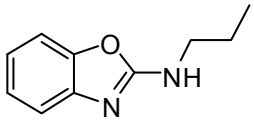
Benzothiazole: 30 °C for 5 h; 1-methylbenzimida zole: 50 °C for 6 h.



Scheme 1 A Proposed Mechanism for the Direct Amination of Azoles

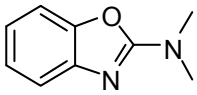
4. Spectra Data for the Products

N-propylbenzo[d]oxazol-2-amine (3a).



MS (ESI): calc. for [$C_{10}H_{12}N_2O$] (M+H) 177.2, measured 177.2.

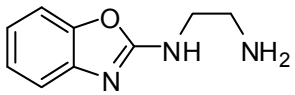
N,N-dimethylbenzo[d]oxazol-2-amine(3b)



^{1}H NMR (400 MHz, $CDCl_3$): δ =7.33-7.31 (m, 1H), 7.24-7.21 (m, 1H), 7.12-7.10 (m, 1H), 6.99-6.96 (m, 1H), 3.17 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.1, 149.1, 143.6, 123.8, 120.2, 116.1, 108.6, 77.4, 77.0, 76.7, 37.3.

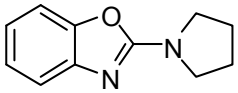
MS (ESI): calc. for [$C_9H_{10}N_2O$] (M+H) 163.2, measured 163.2.

N1-(benzo[d]oxazol-2-yl)ethane-1,2-diamine(3c)



MS (ESI): calc. for [$C_9H_{11}N_3O$] (M+H) 178.1, measured 178.1.

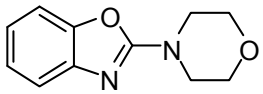
2-(pyrrolidin-1-yl)benzo[d]oxazole(3d)



^{1}H NMR (400 MHz, $CDCl_3$): δ =7.26-7.24 (m, 1H), 7.16-7.12 (m, 1H), 7.00-6.98 (m, 1H), 6.98-6.96 (m, 1H), 3.67-3.63 (m, 4H), 2.05-2.02 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.0, 149.0, 143.7, 123.8, 120.0, 115.9, 108.6, 77.3, 77.0, 76.7, 47.4, 25.6.

MS (ESI): calc. for [$C_{11}H_{12}N_2O$] (M+H) 189.1, measured 189.1.

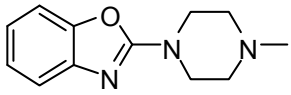
2-morpholinobenzo[d]oxazole(3e)



^{1}H NMR (400 MHz, $CDCl_3$): δ =7.35-7.33 (m, 1H), 7.25-7.22 (m, 1H), 7.16-7.13 (m, 1H), 7.03-6.99 (m, 1H), 3.80-3.77 (m, 4H), 3.67-3.64 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.1, 148.7, 142.6, 124.0, 120.6, 116.4, 108.7, 77.3, 77.0, 76.7, 66.1, 45.7.

MS (ESI): calc. for [$C_{11}H_{12}N_2O_2$] (M+H) 205.1, measured 205.1.

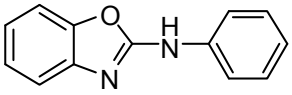
2-(4-methylpiperazin-1-yl)benzo[d]oxazole(3f)



^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.4, 148.8, 142.6, 126.3, 122.4, 116.4, 100.0, 54.8, 48.0, 46.1.

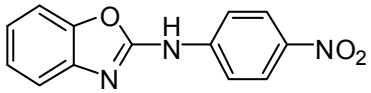
MS (ESI): calc. for [$C_{12}H_{15}N_3O$] (M+H) 218.1, measured 218.1.

N-phenylbenzo[d]oxazol-2-amine(3g)



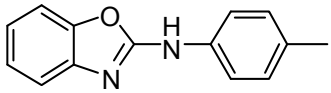
MS (ESI): calc. for [$C_{13}H_{10}N_2O$] (M+H) 211.1, measured 211.1.

N-(4-nitrophenyl)benzo[d]oxazol-2-amine(3h)



MS (ESI): calc. for [$C_{13}H_9N_3O_3$] (M+H) 256.1, measured 256.1.

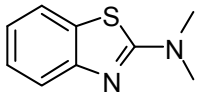
N-p-tolylbenzo[d]oxazol-2-amine(3i)



^{1}H NMR (400 MHz, d^6-DMSO): δ =10.03 (s, 1H), 8.22-8.21 (m, 1H), 7.47-7.45 (m, 2H), 7.12-7.05 (m, 4H), 7.03-6.99 (m, 1H), 2.24 (s, 3H).

MS (ESI): calc. for [$C_{14}H_{12}N_2O$] (M+H) 225.1, measured 225.1.

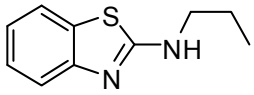
N,N-dimethylbenzo[d]thiazol-2-amine(5a)



^{1}H NMR (400 MHz, $CDCl_3$): δ =7.58-7.53 (m, 2H), 7.28-7.24 (m, 1H), 7.04-7.00 (m, 1H), 3.17 (s, 6H).

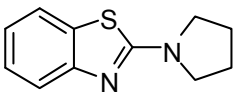
MS (ESI): calc. for [$C_9H_{10}N_2S$] (M+H) 179.1, measured 179.1.

N-propylbenzo[d]thiazol-2-amine(5b)



MS (ESI): calc. for [$C_{10}H_{12}N_2S$] (M+H) 193.1, measured 193.1.

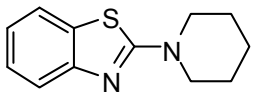
2-(pyrrolidin-1-yl)benzo[d]thiazole(5c)



^{1}H NMR (400 MHz, d^{6}-DMSO): δ =7.39-7.37 (m, 1H), 7.26-7.24 (m, 1H), 7.14-7.10 (m, 1H), 6.99-6.95 (m, 1H), 3.56-3.52 (m, 4H), 1.97-1.91 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.6, 148.6, 143.3, 124.7, 120.0, 115.7, 108.7, 77.3, 77.0, 76.7, 66.1, 47.3, 25.5.

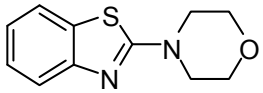
MS (ESI): calc. for [$C_{11}H_{12}N_2S$] (M+H) 205.1, measured 205.1.

2-(piperidin-1-yl)benzo[d]thiazole(5d)



MS (ESI): calc. for [$C_{12}H_{14}N_2S$] (M+H) 219.1, measured 219.1.

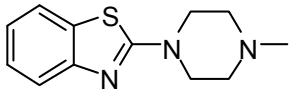
4-(benzo[d]thiazol-2-yl)morpholine(5e)



^{1}H NMR (400 MHz, d^{6}-DMSO): δ =7.42-7.40 (m, 1H), 7.31-7.29 (m, 1H), 7.18-7.14 (m, 1H), 7.05-7.01 (m, 1H), 3.73-3.70 (m, 4H), 3.59-3.57 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.9, 152.4, 130.5, 126.0, 121.6, 120.7, 119.2, 77.3, 77.0, 76.7, 66.2, 48.4.

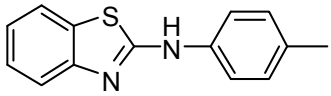
MS (ESI): calc. for [$C_{11}H_{12}N_2OS$] (M+H) 221.1, measured 221.1.

2-(4-methylpiperazin-1-yl)benzo[d]thiazole(5f)



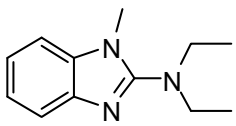
MS (ESI): calc. for [$C_{12}H_{15}N_3S$] (M+H) 234.1, measured 234.1.

N-p-tolylbenzo[d]thiazol-2-amine(5g)



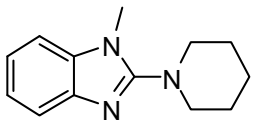
MS (ESI): calc. for [$C_{14}H_{12}N_2S$] (M+H) 241.1, measured 241.1.

N,N-diethyl-1-methyl-1H-benzo[d]imidazol-2-amine(5h)



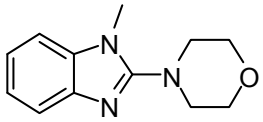
MS (ESI): calc. for [$C_{12}H_{17}N_3$] (M+H) 204.1, measured 204.1.

1-methyl-2-(piperidin-1-yl)-1H-benzo[d]imidazole (5i)



MS (ESI): calc. for [$C_{13}H_{17}N_3$] (M+H) 216.2, measured 216.2.

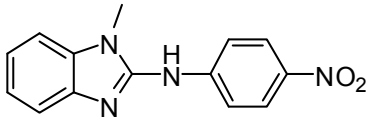
4-(1-methyl-1H-benzo[d]imidazol-2-yl)morpholine (5j)



^{1}H NMR (400 MHz, d^6-DMSO): δ =7.24-7.22 (m, 1H), 7.08-7.05 (m, 1H), 6.97-6.89 (m, 2H), 3.45 (s, 8H), 3.40 (s, 3H).

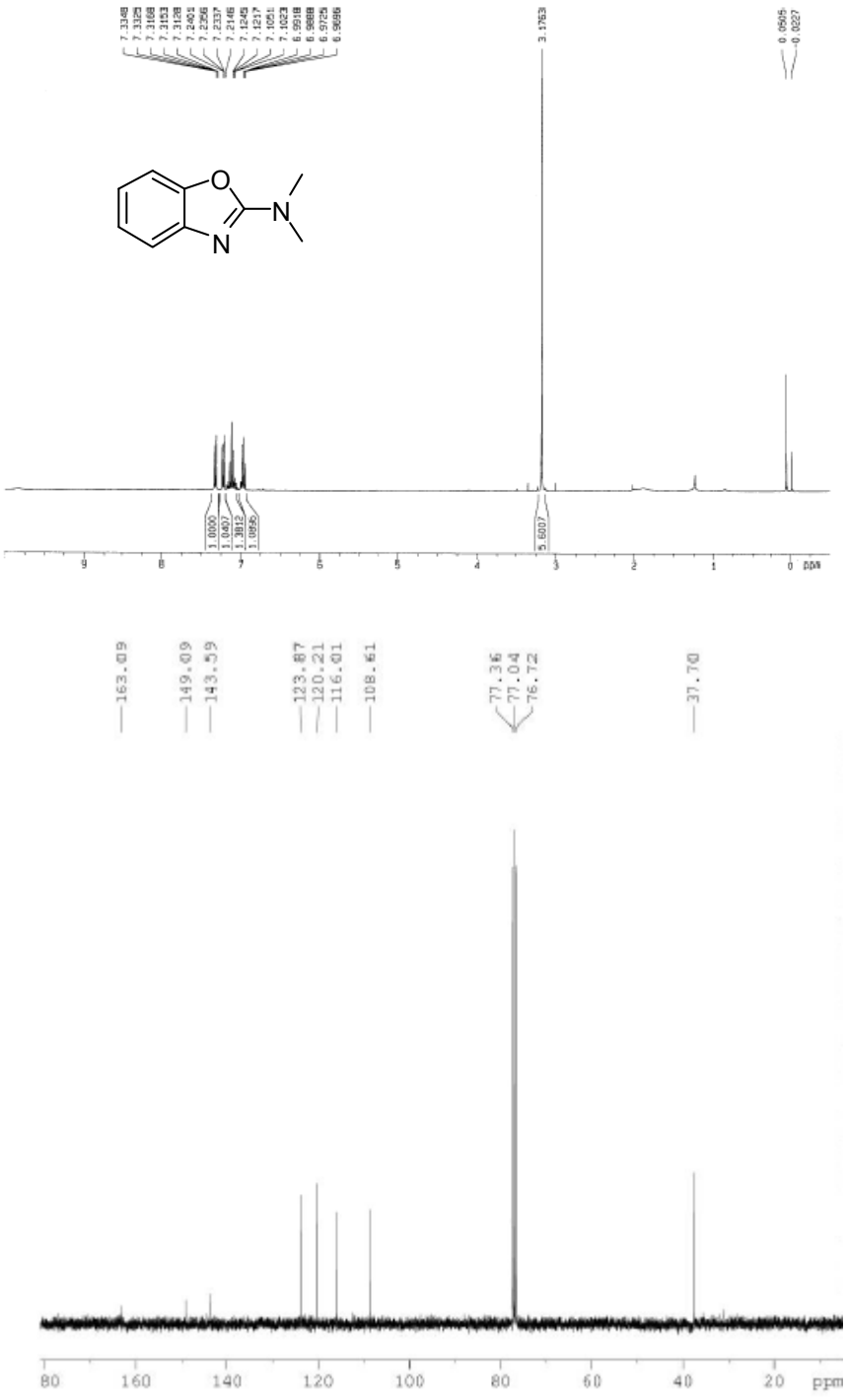
MS (ESI): calc. for [$C_{12}H_{15}N_3O$] (M+H) 218.1, measured 218.1.

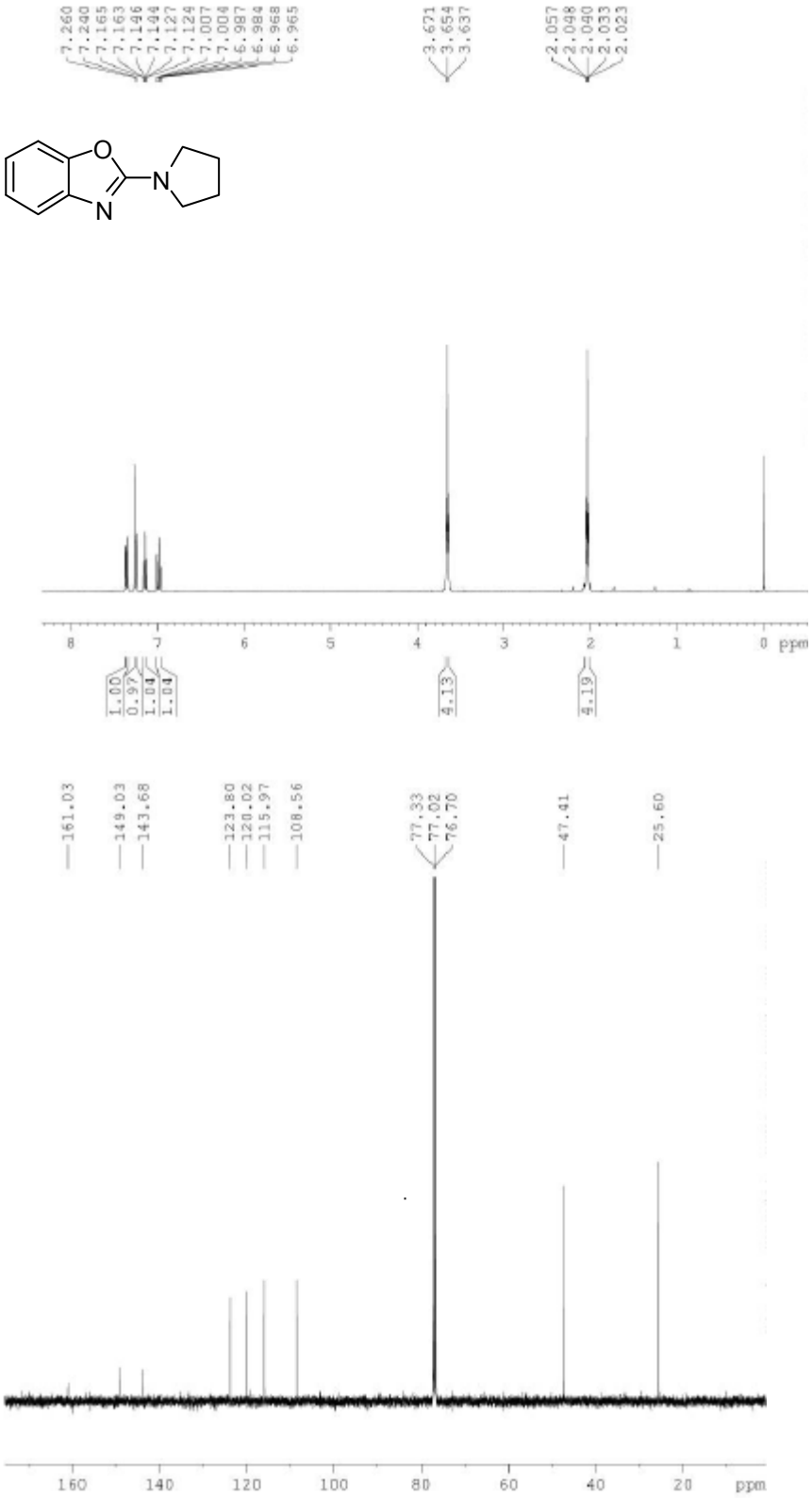
1-methyl-N-(4-nitrophenyl)-1H-benzo[d]imidazol-2-amine (5k)

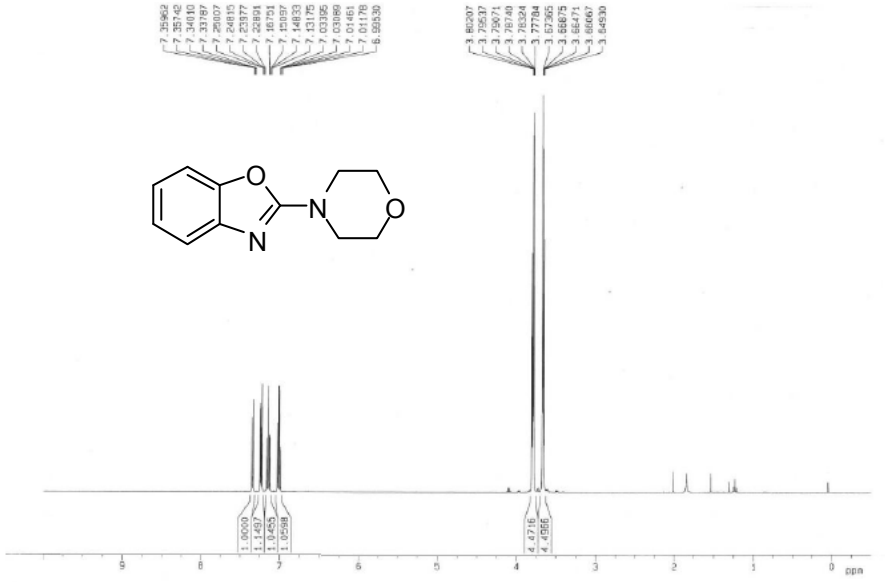


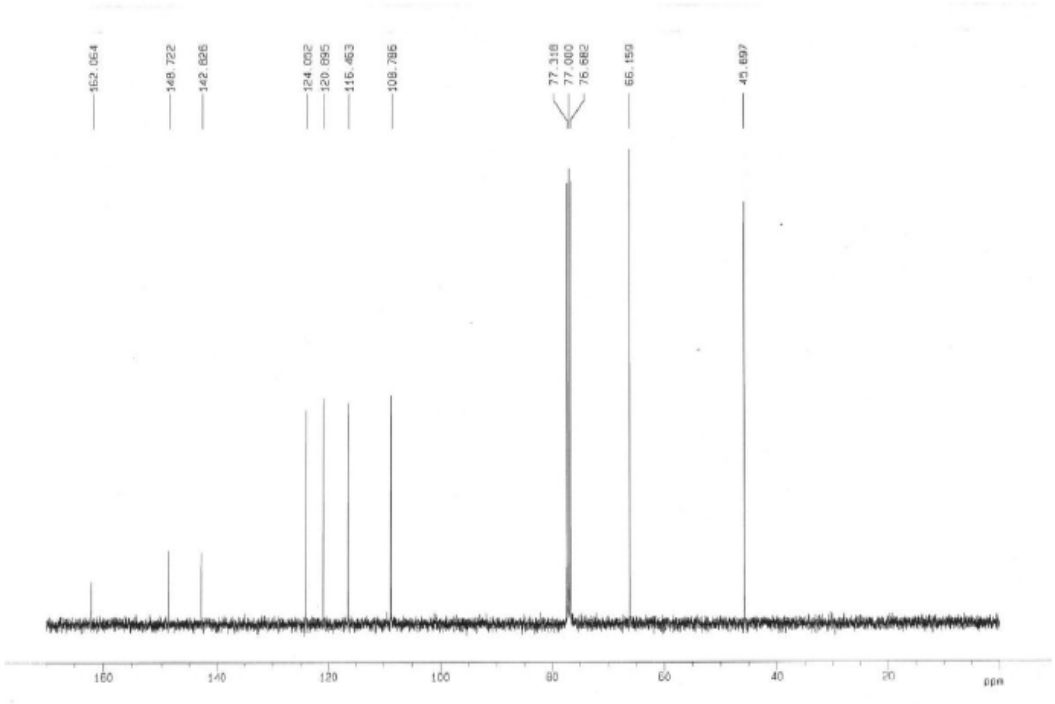
MS (ESI): calc. for [$C_{14}H_{12}N_4O_2$] (M+H) 269.1, measured 269.1.

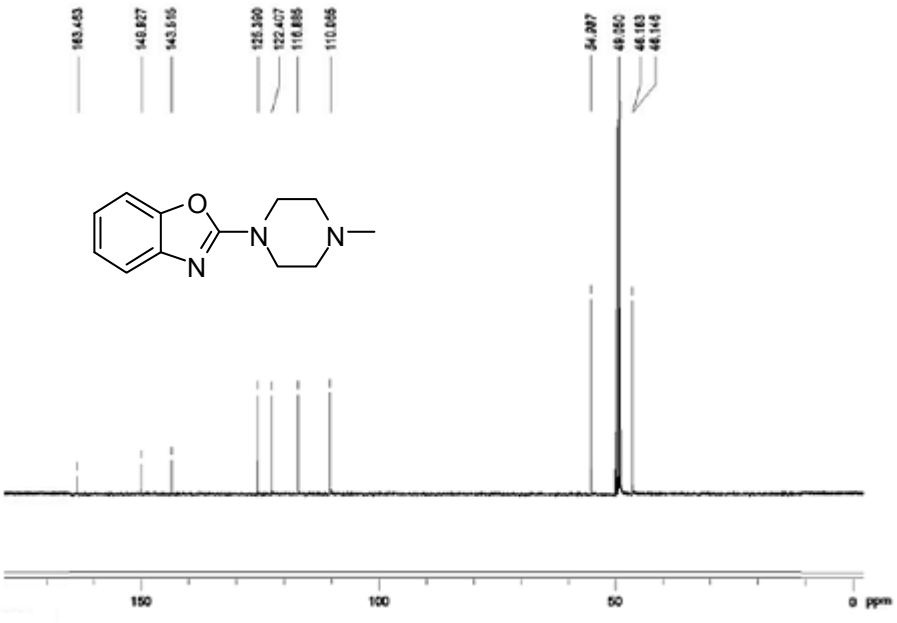
5. 1H NMR and 13C NMR Spectra of products

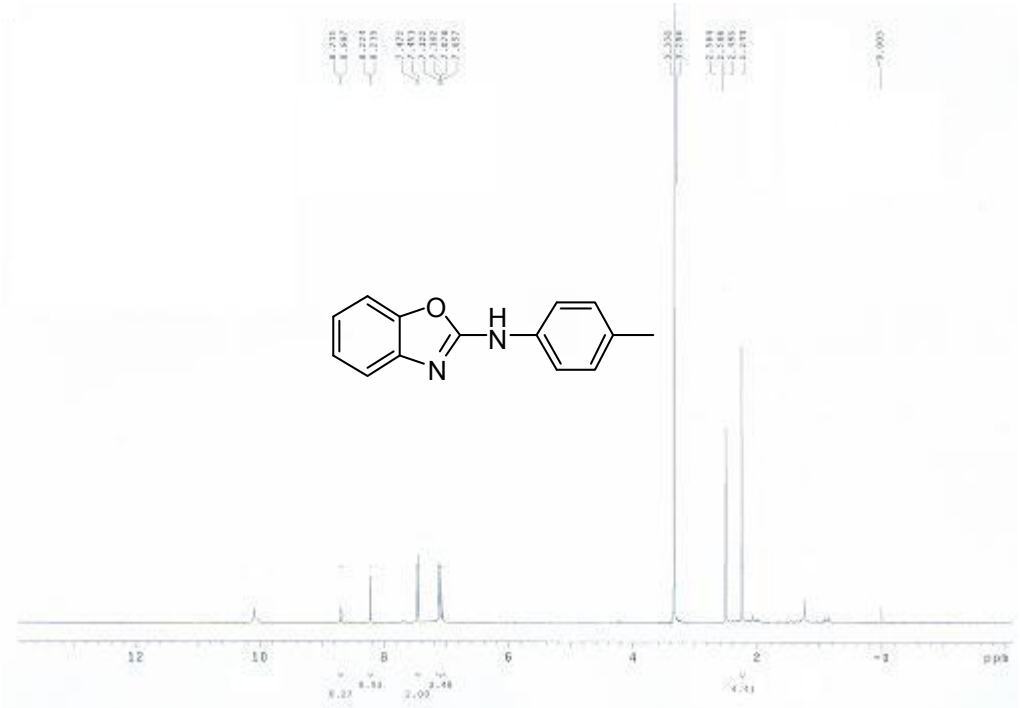









163.453
140.827
143.516
125.300
122.407
110.886
110.056
54.307
49.350
46.183
46.148
O
N
N
N
150
100
50
0 ppm


O
H
N
N
12
10
8
6
4
2
0
ppm