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Copper catalyzed N-arylation between aryl halides and nitriles in water: an efficient tandem synthesis of benzanilides

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ABSTRACT

A series of benzanilide compounds were synthesized through copper-catalyzed tandem reactions. With the assistance of ionic liquid as phase transfer catalyst, aryl halides, and nitriles underwent a hydrolysis/coupling pathway to form benzanilides in water. Advantages of this reaction include the use of water as the environmental friendly solvent, short reaction time, and the tolerance of various functional groups. A proposed mechanism based on control experiments is also presented.

1. Introduction

Benzanilides are very valuable compounds with verity various bioactivities, such as anti-inflammatory,[1a–c] anti-tumor,[1d–f] and potassium channel activation.[1g–i] Many previous synthetic works of benzanilides were based on the copper catalyzed direct C–N bond formation between benzamides and aryl halides.[2] However, these reactions often use expensive polar solvents, such as DMF, DMSO or toxic dioxane, which limited its application in large scale. Although progresses that using water as the solvent in such reaction have been made,[3] these works often give the products in low yield, which may due to the poor solubility of the substrates or intolerance of the catalysts.

On the other hand, as the precursor of amides, nitriles could be used as the substrate for the synthesis of N-substituted amide, as in classic Ritter reaction.[4] However, one limitation of Ritter reaction is that it can't be apply to the N-arylation between aryl halides and nitriles. Recently, a few researchers have reported the copper assisted hydrolysis of nitriles into the corresponding amides in water.[5] As mentioned before, copper is also able to catalyze the cross coupling between amides and aryl halides. So a combination of the two copper catalyzed reactions could be an efficient way of preparing *N*-aryl amides. In this context, Zhou[5f] and Hsieh,[6] respectively, devised a copper catalyzed domino reaction to form an intramolecular amide bond by using 2-bromobenzylnitrile derivatives. And in May 2013, Xiang et al.[7] reported an excellent work on copper catalyzed sequential hydrolysis/coupling reaction between simple nitriles and aryl iodides. However, in Xiang's work, he uses excessive nitriles as the reactant and solvent, which made the method not economical. Herein, our group developed a copper catalyzed tandem amination of aryl iodides with benzonitriles in water, near-stoichiometric amount of the substrates were used and afforded the products in good to excellent yields. In addition, using cheaper aryl bromides instead of aryl iodides could also give acceptable yields. According to this hydrolysis/coupling method, a verity of benzanilides (and *N*-vinyl amide) had been synthesized directly from benzonitriles in an efficient way.

2. Results and discussion

In our initial work, we chose benzonitrile and iodobenzene as model substrates to investigate the reaction condition. As showed in Table 1, we firstly considered the solvents and solubility. The reaction underwent successfully in water and product **3a** was obtained in a yield of 45% (entry 1, Table 1). To our surprise, changing the solvent to toluene, DMSO, DMF or dioxane afforded poor yields even under a prolonged procedure (entries 2–6, Table 1). The result indicated using water as the solvent had special superiorities for this reaction, such as increasing the solubility of the bases or the hydrolysis rate of benzonitrile. Enlightened by previous works,[3e,8] we then tried to introduce phase transfer catalysts, such as ionic liquids to improve the reaction in aqueous system. After a screen of

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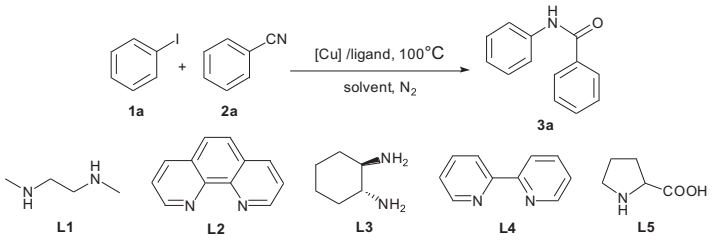
Table 1
N-Arylation of aryl iodobenzene **1a** with benzonitrile **2a** under different conditions[a]



Entry	Catalyst	Ligand	Base	Solvent	Additive[c]	Yield [%]
1	CuI	L1	NaOH (1 equiv)/Cs_2CO_3 (2 equiv)	H_2O	None	45
2	CuI	L1	NaOH (1 equiv)/Cs_2CO_3 (2 equiv)	Toluene[b]	None	5
3	CuI	L1	NaOH (1 equiv)/Cs_2CO_3 (2 equiv)	DMSO[b]	None	30
4	CuI	L1	NaOH (1 equiv)/Cs_2CO_3 (2 equiv)	DMF[b]	None	24
6	CuI	L1	NaOH (1 equiv)/Cs_2CO_3 (2 equiv)	Dioxane[b]	None	17
7	CuI	L1	NaOH (1 equiv)/Cs_2CO_3 (2 equiv)	H_2O	[bmim][Br^-]	71
8	CuI	L1	NaOH (1 equiv)/Cs_2CO_3 (2 equiv)	H_2O	[bmim][BF4$^-$]	57
9	CuI	L1	NaOH (1 equiv)/Cs_2CO_3 (2 equiv)	H_2O	TBAI	49
10	CuI	L1	NaOH (1 equiv)/Cs_2CO_3 (2 equiv)	H_2O	[bmim][PF_6^-]	91
11	CuI	L1	K_2CO_3 (2 equiv)	H_2O	[bmim][PF_6^-]	Trace
12	CuI	L1	KOH (1 equiv)/Cs_2CO_3 (2 equiv)	H_2O	[bmim][PF_6^-]	61
13	CuI	L1	EtONa (1 equiv)/Cs_2CO_3 (2 equiv)	H_2O	[bmim][PF_6^-]	81
14	CuI	L1	NaOH (1 equiv)/Na_2CO_3 (2 equiv)	H_2O	[bmim][PF_6^-]	51
15	CuI	L1	NaOH (1 equiv)/K_3PO_4 (2 equiv)	H_2O	[bmim][PF_6^-]	41
16	CuI	L1	NaOH (1 equiv)/K_2CO_3 (2 equiv)	H_2O	[bmim][PF_6^-]	92
17	Cu_2O[d]	L1	NaOH (1 equiv)/K_2CO_3 (2 equiv)	H_2O	[bmim][PF_6^-]	71
18	Cu	L1	NaOH (1 equiv)/K_2CO_3 (2 equiv)	H_2O	[bmim][PF_6^-]	63
19	CuI	None	NaOH (1 equiv)/K_2CO_3 (2 equiv)	H_2O	[bmim][PF_6^-]	Trace
20	CuI	L2	NaOH (1 equiv)/K_2CO_3 (2 equiv)	H_2O	[bmim][PF_6^-]	51
21	CuI	L3	NaOH (1 equiv)/K_2CO_3 (2 equiv)	H_2O	[bmim][PF_6^-]	49
22	CuI	L4	NaOH (1 equiv)/K_2CO_3 (2 equiv)	H_2O	[bmim][PF_6^-]	19
23	CuI	L5	NaOH (1 equiv)/K_2CO_3 (2 equiv)	H_2O	[bmim][PF_6^-]	Trace

[a] **1a** (1.0 mmol), **2a** (1.5 mmol), catalyst (10 mol %), ligand (10 mol %), 3 h, under N_2. The yields were of isolated products.
[b] 9 mmol H_2O was added to 2 ml solvent, 8 h.
[c] 5% mol additive was added.
[d] 0.05 mmol Cu_2O was added.

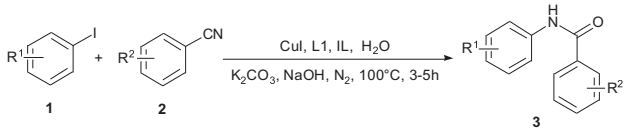
TBAI and some commercial available ionic liquids (entries 7–10, Table 1), we found a catalytic amount of [bmim][PF_6^-] could increase the yield to 91% while formed only trace of benzamide as byproduct. On the other hand, bases seemed to have a great effect on this reaction. Strong base was indispensable (entry 11, Table 1), and the replacement of NaOH by KOH or EtONa decreased the yield of 3a (entries 12, 13, Table 1). The change of Cs_2CO_3 into Na_2CO_3 or K_3PO_4 also gave a decreased yield (entries 14, 15, Table 1). But using K_2CO_3 as the weak base showed a comparable yield with Cs_2CO_3 in 92% (entry 16, Table 1). Other copper sources, such as Cu_2O or copper powder also provided **3a** in moderate to good yield in this condition (entries 17, 18, Table 1). Investigation of ligands effect (entries 19–23, Table 1) showed that **L1** was the most suitable ligand for this reaction. Additionally, it must be mentioned that this reaction must underwent in N_2 atmosphere, or benzamide will be yield as the only product, no sign of N-arylation product. Finally, after an optimization of the reaction conditions, we obtained **3a** in an excellent yield (92%), and the reaction time (3 h) is obvious shorter than the normal amination of aryl iodides with amides, which usually require 12–24 h.

With the optimized reaction condition in hand, the scope of the copper-catalyzed reaction was investigated (Table 2). Firstly, aryl iodides were used as substrates to react with benzonitrile (**3a**–**l**). As showed in Table 2, most of the aryl iodides that bearing electron-donating or electron-withdrawing groups (**3a**–**g**) showed no obvious difference in yield. However, aryl iodides that with amino group or nitro group showed lower yields from 46% (**3h**) to 50% (**3i**). And it was worthy noting that steric hindrance also had great influence on this reaction. For *ortho*-substituted aryl iodides, such as *o*-Chloroiodobenzene and 1-Iodonaphthalene, the corresponding products could only be obtained in 44% (**3j**) and 42% (**3k**). But by using 10 mol % Cu_2O as the catalyst and extending the reaction time (5 h), the yield of the *ortho*-products could be increased to 82% (**3j**) and 63% (**3k**). Other aryl iodide, such as 2-iodo-thiophene that contained a heterocycle, also gave the desired product (**3l**) in moderate yield.

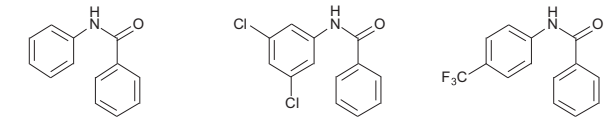
On the other hand, the reactivities of substituted benzonitriles were investigated by reacting with iodobenzene (**3m**–**s**). It was found that benzonitriles with electron-donating or electron-withdrawing groups could afford corresponding products in moderate to excellent yield. However, the reactivity of 4-bromo benzonitrile was obviously lower (21%). It could be explained by its easy sublimation and the oxidative addition of the C–Br bond by the active copper source-CuI. Using the less reactive catalyst CuCl could improve the yield to 41%. Besides, the steric hindrance of the substituted benzonitrile greatly affected such reactions, for instance, from the substrate 2-methyl-benzonitrile can only yield the product (**3s**) in 25%, and the 2-chloro-benzonitrile even gave no desired product. Additionally, aliphatic nitriles, such as acetonitrile or pentanenitrile gave only trace amount of N-arylation products. However, the use of phenylacetonitrile could afford the corresponding product (**3o**) in good yield under this condition.

The good results of aryl iodides encouraged us to extend the substrate scope to aryl bromides, which are more attractive for their lower cost. Firstly, the aforementioned protocol was used in the coupling between aryl bromides and benzonitrile. However, due to the low reactivity of aryl bromides, such attempt was failed even underwent higher temperature (120 °C) and prolonged procedure (24 h). After another screening of the condition, we found cheap Cu_2O[3e,9] were more efficient for such reaction, and

Table 2
Copper catalyzed N-arylation between aryl iodides **1** and benzonitriles **2**[a,b]

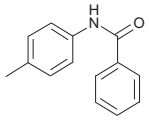


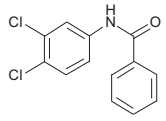
1 2 3

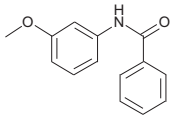

3a: 92%

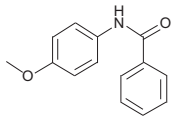
3b: 86%

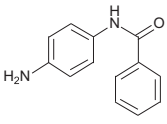
3c: 94%

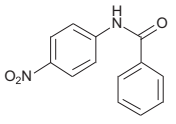

3d: 84%

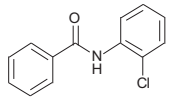

3e: 82%

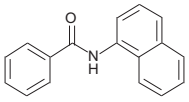

3f: 90%

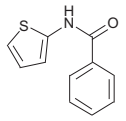

3g: 89%

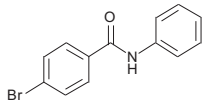

3h: 46%

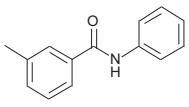

3i: 50%

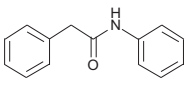

3j: 82%[C]

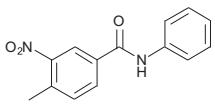

3k: 63%[C]

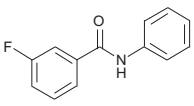

3l: 54%

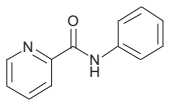

3m: 41%[d]

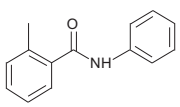

3n: 87%[e]


3o: 79%[e]


3p: 85%[e]


3q: 90%[e]


3r: 49%[e]

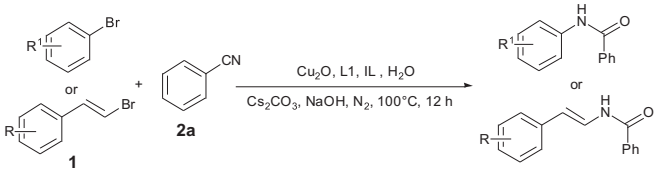

3s: 25%[e]

[a] Reaction condition: Aryl iodides (1.0 mmol), nitriles (1.5 mmol), CuI (10 mol%), L1 (10 mol%) and IL (5 mol%) were heated in 2 mL water under N_2 at 100°C in a sealed tube for 3-5 h.[b] Isolated yield. [C] Using Cu_2O (10 mol%) as catalyst. [d] Using CuCl (10 mol%) as catalyst. [e] Aryl iodides (1.0 mmol), nitriles (2.0 mmol).

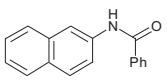
increasing the loading of catalyst (20%) could afford products in moderate to good yields. The yields were slightly affected by the electronic effects. Aryl bromides bearing electron-donating groups (such as aromatic, amino, or methoxyl group) gave higher yield (**3t**, **3A**, **3B**). Additionally, the steric hindrance showed little effect, the *ortho*-substituted aryl bromides, such as 2-bromofluorobenzene (**3v**) or 2-bromotoluene (**3z**) showed no decrease in reactivity, and 2-bromotoluene (**3z**) even gave higher yield than its *meta*- or *para*-substituted analogs. To our delight, β-bromostyrene compounds also gave the corresponding product in fair yields under this condition (**3C**–**E**), This *N*-Vinyl Amide structure is very common in natural products and bioactive compounds[10] (Table 3).

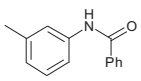
The reaction mechanism was also investigated by several control experiments. The data (see Supplementary data) suggested the copper catalyst was both involved in the hydrolysis of benzonitrile and the coupling of C–N bond. And a possible pathway (Scheme 1) was proposed in Scheme 1. Firstly, the benzonitrile **1** was coordinated with copper and formed the complex A, which then be

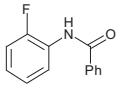
Table 3
Copper catalyzed N-arylation between aryl bromides **1** (or beta-bromostyrenes) and benzonitrile **2a**[a,b]

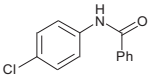


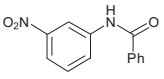
1 2a

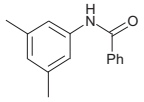

3t: 79%

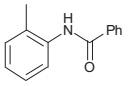

3u: 68%

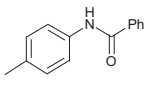

3v: 64%

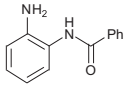

3w: 66%

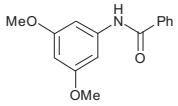

3x: 69%

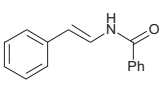

3y: 69%

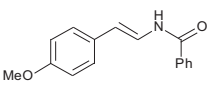

3z: 73%

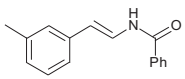

3d: 65%


3A: 80%[C]

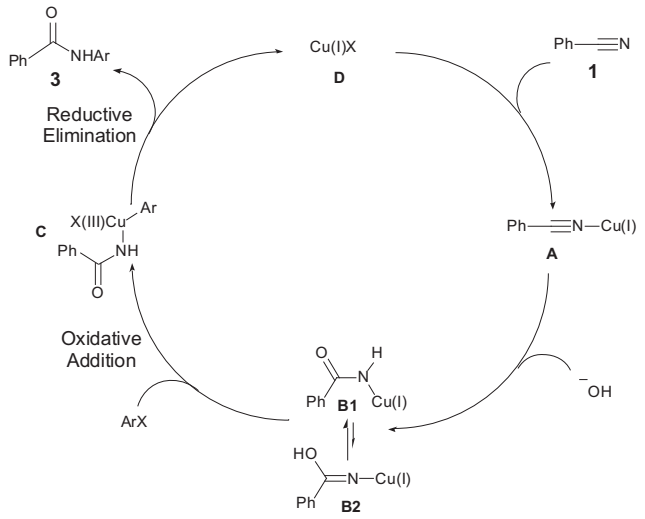

3B: 76%


3C: 58%


3D: 60%


3E: 70%

[a] Aryl bromides (1.0 mmol), nitriles (1.5 mmol), Cu_2O (20 mol%), L1 (20 mol%) and IL (5 mol%) were heated in 2 mL water under N_2 at 100°C in a sealed tube for 12h. [b] Isolated yield. [C] Reacted for 16h.



Scheme 1. Proposed mechanism.

hydrolyzed by NaOH and formed benzamide **B1** after a tautomeric process from **B2**. **B1** could react with aryl halides and gave the oxidative addition product **C**. After the reductive elimination of **C**, the final product **3** was obtained and released the copper catalyst in another catalytic cycle.

3. Conclusions

In summary, an efficient copper catalyzed tandem reaction for the synthesis of benzanilide in water was developed. Ionic liquid was used as a phase transfer catalyst and this method could be applied in the N-arylation between benzonitriles and aryl halides (or alkenyl bromides). This protocol could be used as a green way in the synthesis of benzanilides for several reasons: (1) use of non-toxic, cheap and non-flammable solvent-water; (2) relative short reaction time; (3) using commercial available and easy prepared benzonitrile compounds as the substrates. Accordingly, this reaction is expected to have great potential to be used in industrial application.

4. Experimental

4.1. General

All chemicals were obtained from commercial suppliers and used without further purification. The melting points were determined using XT-4 apparatus and were not corrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker AVANCE DMX-500 spectrometry at 500 MHz and 125 MHz, respectively. Mass spectra were performed on a Bruker Esquire 3000 plus mass spectrometer equipped with ESI interface and ion trap analyzer. HRMS were obtained on a Bruker 7-tesla FT-ICR MS equipped with an electrospray source.

4.2. General procedure 1 for the N-arylation between aryl iodides and benzonitrile (3a–l)

To a screw-capped vial (50 ml) were added aryl iodides **1** (1.0 mmol), benzonitrile **2a** (155 mg, 1.5 mmol), K_2CO_3 (276 mg, 2.0 mmol), NaOH (40 mg, 1.0 mmol), CuI (19 mg, 0.1 mmol), DMEDA (9 mg, 0.1 mmol), and [bmim][PF_6^-] (14 mg, 0.05 mmol) in water (2 ml). The vial was flushed with nitrogen then sealed with the cap, and allowed to stir at 100 °C for the specific reaction time. The reaction mixture was extracted with EtOAc (3×15 ml). The combined organic extracts were dried over Na_2SO_4 for 12 h and evaporated under vacuum. The crude products were purified in a silica gel column for further purification, using PE/EtOAc (5:1) as the eluent.

*4.2.1. N-Phenylbenzamide (**3a**).* Followed the general procedure 1, product was obtained in 3 h as white solid (182 mg, yield 92%) mp: 165–166 °C; IR (KBr, cm^{-1}): 3344, 3052, 1655, 1599, 1531, 1438, 1322, 1260, 750, 715, 690, 650; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.87 (d, ^3J=7.6 Hz, 2H), 7.83 (s, 1H), 7.64 (d, ^3J=7.6 Hz, 2H), 7.57–7.54 (t, 1H), 7.50–7.47 (t, ^3J=7.5 Hz, 2H), 7.39–7.36 (t, 2H), 7.17–7.14 (t, ^3J=7.50 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.7, 137.9, 135.0, 131.8, 129.1, 127.0, 124.6, 120.1; MS (ESI, *m*/*z*) [M−H]$^-$: 196.1; HRMS (ESI, *m*/*z*) (M+H)$^+$: calcd for $C_{13}H_{11}NO$: 198.0913, found: 198.0919.

*4.2.2. N-(3,5-Dichlorophenyl)benzamide (**3b**).* Followed the general procedure 1, product was obtained in 3 h as white solid (228 mg, yield 86%), mp: 149–150 °C; IR (KBr, cm^{-1}): 3295, 3255, 3185, 3121, 1667, 1594, 1551, 1443, 1405, 1368, 1020, 845, 803, 762; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.85 (s, 2H), 7.83 (s, 1H), 7.63 (s, 2H), 7.59–7.56 (t, ^3J=7.4 Hz, 1H), 7.51–7.48 (t, ^3J=7.5 Hz, 2H), 7.14 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.7, 139.7, 135.3, 134.1, 132.4, 128.9, 127.0, 124.5, 118.3; MS (ESI, *m*/*z*) [M+H]$^+$: 265.8, HRMS (ESI, *m*/*z*) (M−H)$^-$: calcd for $C_{13}H_9Cl_2NO$: 263.9911, found: 263.9900.

*4.2.3. N-(4-(Trifluoromethyl)phenyl)benzamide (**3c**).* Followed the general procedure 1, product was obtained in 3 h as white solid (249 mg, yield 94%), mp: 209–210 °C; IR (KBr, cm^{-1}): 3331, 1655, 1599, 1528, 1407, 1339, 1115, 1070, 835, 717, 690; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.91 (s, 1H), 7.89–7.87 (d, ^3J=8.0 Hz, 2H), 7.79–7.78 (d, ^3J=8.0 Hz, 2H), 7.65–7.63 (d, ^3J=8.2 Hz, 2H), 7.60–7.58 (m, 1H), 7.53–7.50 (t, ^3J=8.2 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.7, 140.9, 140.9, 134.4, 132.3, 128.9, 127.0, 126.45, 126.43, 126.39, 126.36, 119.6; MS (ESI, *m*/*z*) [M−H]$^-$: 263.9; HRMS (ESI, *m*/*z*) (M−H)$^-$: calcd for $C_{14}H_9F_3NO$: 264.0631, found 264.0630.

*4.2.4. N-(p-Tolyl)benzamide (**3d**).* Followed the general procedure 1, product was obtained in 3 h as white solid (177 mg, yield 84%), mp: 159–160 °C; IR (KBr, cm^{-1}): 3309, 1646, 1596, 1578, 1510, 1317, 1265, 813, 694; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.87–7.86 (d, ^3J=7.9 Hz, 2H), 7.74 (s, 1H), 7.56–7.54 (m, 5H), 7.18–7.17 (d, ^3J=7.9 Hz, 1H), 2.34 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.6, 135.3, 135.1, 134.2, 131.7, 129.6, 128.8, 126.9, 120.2, 20.9; MS (ESI, *m*/*z*) [M−H]$^-$: 10.2; HRMS (ESI, *m*/*z*) (M−H)$^-$: calcd for C14H_{12}NO: 263.9911, found 263.9906.

*4.2.5. N-(3,4-Dichlorophenyl)benzamide (**3e**).* Followed the general procedure 1, product was obtained in 3 h as white solid (217 mg, yield 82%), mp: 148–149 °C; IR (KBr, cm^{-1}): 3303, 1649, 1579, 1510, 1378, 1304, 1123, 1026, 860, 819, 688; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.96 (s, 1H), 7.88 (m, 1H), 7.84–7.82 (m, 2H), 7.57–7.54 (t, ^3J=7.4, 1H), 7.48–7.45 (t, ^3J=7.4, 3H), 7.40–7.38 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.8, 137.3, 134.2, 132.9, 132.3, 130.5, 128.9, 127.8, 127.0, 121.9, 119.4; MS (ESI, *m*/*z*) [M+H]$^+$: 266.0; HRMS (ESI, *m*/*z*) (M−H)$^-$: calcd for $C_{13}H_8Cl_2NO$: 263.9977, found 263.9975.

*4.2.6. N-(3-Methoxyphenyl)benzamide (**3f**).* Followed the general procedure 1, product was obtained in 3 h as white solid (204 mg, 90%), mp: 103–105 °C; IR (KBr, cm^{-1}): 3304, 1650, 1601, 1530, 1489, 1412, 1316, 1266, 1176, 1266, 1037, 844, 792, 688; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.92 (s, 1H), 7.88 (d, ^3J=7.8 Hz, 2H), 7.56–7.53 (m, 1H), 7.49–7.45 (m, 3H), 7.27–7.24 (m, 1H), 7.12–7.10 (d, ^3J=7.8 Hz, 2H), 6.74–6.70 (m, 1H), 3.85 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.8, 160.2, 139.1, 134.9, 131.8, 129.7, 128.8, 127.0, 112.2, 110.5, 105.8, 55.3;

MS (ESI, *m*/*z*) $[M+H]^+$: 228.2; HRMS (ESI, *m*/*z*) $(M-H)^-$: calcd for $C_{14}H_{12}NO_2$: 226.0863, found 226.0858.

*4.2.7. N-(4-Methoxyphenyl)benzamide (**3g**).* Followed the general procedure 1, product was obtained in 3 h as white solid (202 mg, yield 89%), mp: 154–155 °C; IR (KBr, cm^{-1}): 3330, 1647, 1514, 1413, 1269, 1249, 1032, 825; ^1H NMR (500 MHz, $CDCl_3$): δ 7.86–7.85 (d, ^3J=7.5 Hz, 2H), 7.75 (s, 1H), 7.53–7.47 (m, 5H), 6.91–6.90 (d, ^3J=7.5 Hz, 2H), 3.82 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.6, 156.6, 135.0, 131.7, 130.9, 128.7, 126.9, 122.0, 114.2, 55.5; MS (ESI, *m*/*z*) $[M+H]^+$: 228.3; HRMS (ESI, *m*/*z*) $(M-H)^-$: calcd for $C_{14}H_{12}NO_2$: 226.0863, found 226.0870.

*4.2.8. N-(4-Amino-phenyl)-benzamide (**3h**).* Followed the general procedure 1, product was obtained in 5 h as brown solid (98 mg, yield 46%), mp126–127 °C; IR (KBr, cm^{-1}): 3330, 1649, 1517, 1424, 1323, 1250, 824; ^1H NMR (500 MHz, $CDCl_3$): δ 7.85–7.84 (d, ^3J=7.55, 2H), 7.67 (s, 1H), 7.54–7.51 (m, 1H), 7.48–7.45 (t, ^3J=7.50, 2H), 7.40–7.39 (d, ^3J=8.25, 1H), 6.70–6.69 (d, ^3J=8.45, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.8, 156.6, 134.6, 132.2, 129.7, 129.3, 129.0, 127.1, 121.5; MS (ESI, *m*/*z*) $[M+H]^+$: 213.1; MS (ESI, *m*/*z*) $(M-H)^-$: calcd for $C_{13}H_{11}N_2O$: 211.0866, found 211.0863.

*4.2.9. N-(4-Nitrophenyl)benzamide (**3i**).* Followed the general procedure 1, product was obtained in 5 h as yellow solid (121 mg, yield 50%) mp: 204–206 °C; IR (KBr, cm^{-1}): 3336, 1657, 1613, 1533, 1506, 1486, 1406, 1345, 1250, 1178, 1111, 848, 749, 720, 694; ^1H NMR (500 MHz, DMSO-d_6): δ 10.81 (s, 1H), 8.27–8.25 (d, ^3J=9.25 Hz, 2H), 8.08–8.06 (d, ^3J=9.20 Hz, 2H), 7.99–7.97 (d, ^3J=7.35, 2H), 7.65–7.62 (t, ^3J=7.30, 1H), 7.57–7.54 (t, ^3J=7.30, 2H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 166.2, 145.4, 142.4, 134.2, 132.1, 128.4, 127.8, 124.7, 119.8; MS (ESI, *m*/*z*) $[M+H]^+$: 241.1; MS (ESI, *m*/*z*) $(M-H)^-$: calcd for $C_{13}H_9N_2O_8$: 241.0608, found 241.0598.

*4.2.10. N-(2-Chlorophenyl)benzamide (**3j**).* Followed the general procedure 1, and using Cu_2O (14 mg, 0.1 mmol) instead of CuI, product was obtained in 5 h as white solid (189 mg, yield 82%), mp: 101–102 °C; IR (KBr, cm^{-1}): 3224, 1652, 1519, 1477, 1427, 1302, 749, 712; ^1H NMR (500 MHz, $CDCl_3$): δ 8.58–8.56 (d, ^3J=8.3 Hz, 1H), 8.45 (s, 1H), 7.93–7.92 (d, ^3J=7.4 Hz, 2H), 7.60–7.57 (t, ^3J=7.4 Hz, 1H), 7.54–7.50 (m, 2H), 7.42–7.40 (d, ^3J=8.0 Hz, 1H), 7.35–7.32 (t, ^3J=8.3 Hz, 1H), 7.10–7.06 (m, ^3J=8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.2, 134.7, 134.6, 132.2, 129.0, 128.9, 127.9, 127.1, 124.7, 123.9, 121.5; MS (ESI, *m*/*z*) $[M+H]^+$: 254.4; HRMS (ESI, *m*/*z*) $(M-H)^-$: calcd for $C_{13}H_9ClNO$: 230.0367, found 230.0357.

*4.2.11. N-(Naphthalen-1-yl)benzamide (**3k**).* Followed the general procedure 1, and using Cu_2O (14 mg, 0.1 mmol) instead of CuI, product was obtained in 5 h as white solid (155 mg, yield 63%), mp: 160–161 °C; IR (KBr, cm^{-1}): 3238, 1648, 1530, 1502, 1342, 1288, 794, 769, 711; ^1H NMR (500 MHz, $CDCl_3$): δ 8.20 (s, 1H), 8.07–8.06 (d, ^3J=6.3, 1H), 8.01–7.99 (d, ^3J=7.2, 2H), 7.92–7.90 (t, ^3J=6.3, 2H), 7.76–7.75 (m, 1H), 7.62–7.59 (t, ^3J=7.2, 1H), 7.53–7.51 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.7, 131.9, 131.2, 132.3, 132.0, 128.9, 127.3, 127.2, 126.4, 126.1, 125.8, 121.1, 120.5; MS (ESI, *m*/*z*) $[M+H]^+$: 248.2; HRMS (ESI, *m*/*z*) $(M-H)^-$: calcd for $C_{17}H_{13}NO$: 246.0913, found 246.0908.

*4.2.12. N-Thiophen-2-yl-benzamide (**3l**).* Followed the general procedure 1, product was obtained in 5 h as white solid (110 mg, yield 54%), mp: 172–174; IR (KBr, cm^{-1}): 3234, 3109, 1630, 1565, 1483, 1348, 1309, 894, 808, 700; ^1H NMR (500 MHz, DMSO-d_6): δ11.53 (s, 1H), 7.99–7.97 (m, 2H), 7.62–7.59 (m, 1H), 7.56–7.53 (m, 2H), 7.00–6.99 (m, 1H), 6.92–6.89 (m, 2H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 163.1, 139.9, 133.1, 131.9, 128.5, 127.6, 124.0, 117.3, 112.1; MS (ESI, *m*/*z*) $[M+Na]^+$: 226.20; HRMS (ESI, *m*/*z*) $(M+H)^+$: calcd for $C_{11}H_9NOS$: 204.0478, found 204.0487.

4.3. General procedure 2: for the N-arylation between iodobenzene and substituted benzonitriles (3m–s)

To a screw-capped vial (50 ml) were added iodobenzene **1a** (1.0 mmol), substituted benzonitrile **2** (2.0 mmol), K_2CO_3 (276 mg, 2.0 mmol), NaOH (40 mg, 1.0 mmol), CuI (19 mg, 0.1 mmol), DMEDA (9 mg, 0.1 mmol), and [bmim][PF_6^-] (14 mg, 0.05 mmol) in water (2 ml). The vial was flushed with nitrogen then sealed with the cap, and allowed to stir at 100 °C for the specific reaction time. The reaction mixture was extracted with EtOAc (3×15 ml). The combined organic extracts were dried over Na_2SO_4 for 12 h and evaporated under vacuum. The crude products were purified in a silica gel column for further purification, using PE/EtOAc (5:1) as the eluent.

*4.3.1. 4-Bromo-N-phenylbenzamide (**3m**).* Followed the general procedure 2, and using CuCl (10 mg, 0.1 mol) instead of CuI, product was obtained in 5 h as white solid (113 mg, yield 41%), mp: 204–206 °C; IR (KBr, cm^{-1}): 3344, 1653, 1530, 1439, 1324, 754, 690, 659; ^1H NMR (500 MHz, CDCl3): δ 7.75–7.73 (m, 3H), 7.63–7.61 (m, 4H), 7.39–7.36 (t, ^3J=7.5, 2H), 7.18–7.16 (m, ^3J=7.5, 1H); ^{13}C NMR (125 MHz, CDCl3): δ 164.7, 137.6, 133.8, 132.0, 129.1, 128.62, 126.6, 124.8, 120.2; MS (ESI, *m*/*z*) $[M+H]^+$: 276.5; HRMS (ESI, *m*/*z*) $(M-H)^-$: calcd for $C_{13}H_9BrNO$: 273.9862, found 273.9858.

*4.3.2. 3-Methyl-N-phenylbenzamide (**3n**).* Followed the general procedure 2, product was obtained in 3 h as white solid (184 mg, yield 87%), mp: 127–128 °C; IR (KBr, cm^{-1}): 3276, 3246, 1652, 1596, 1537, 1492, 1437, 1325, 1242, 757, 721, 691; ^1H NMR (500 MHz, $CDCl_3$): δ 7.80 (s, 1H), 7.69 (s, 1H), 7.65–7.63 (m, 3H), 7.39–7.36 (m, 4H), 7.16–7.14 (m, 1H), 2.44 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.9, 138.7, 137.9, 135.0, 132.6, 129.1, 128.6, 127.7, 124.5, 123.9, 120.14, 21.4; MS (ESI, *m*/*z*) $[M+H]^+$: 212.5; HRMS (ESI, *m*/*z*) $(M-H)^-$: calcd for $C_{14}H_{12}NO$: 210.0913, found 210.0909.

*4.3.3. N,2-Diphenylacetamide (**3o**).* Followed the general procedure 2, product was obtained in 3 h as yellow solid (167 mg, yield 79%), mp: 114–115 °C; IR (KBr, cm^{-1}): 3284, 3257, 3195, 3135, 3066, 3022, 1658, 1600, 1550, 1491, 1438, 1355, 1323, 1163, 753, 723, 691; ^1H NMR (500 MHz, $CDCl_3$): δ 7.43–7.40 (m, 4H), 7.36–7.33 (m, 3H), 7.29–7.26 (t, ^3J=7.5, 2H), 7.10–7.07 (t, ^3J=, 7.5, 1H), 7.04 (br, 1H), 3.75 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.1, 137.7, 1346, 129.7, 129.5, 129.1, 127.9, 124.6, 119.9, 45.1; MS (ESI, *m*/*z*) $[M+H]^+$: 212.2; HRMS (ESI, *m*/*z*) $(M-H)^-$: calcd for $C_{14}H_{12}NO$: 210.0913, found 210.0908.

*4.3.4. 4-Methyl-3-nitro-N-phenylbenzamide (**3p**).* Followed the general procedure 2, product was obtained in 3 h as white solid (218 mg, yield 85%), mp: 134–136 °C; IR (KBr, cm^{-1}): 3298, 1647, 1532, 1442, 1336, 758, 696; ^1H NMR (500 MHz, DMSO-d_6): δ 10.45 (s, 1H), 8.56 (d, ^4J=1.8, 1H), 8.22–8.20 (dd, ^3J=8.0, ^4J=1.8, 1H), 7.77–7.75 (d, ^3J=7.7, 2H), 7.69–7.67 (d, ^3J=8.0, 1H), 7.38–7.35 (t, ^3J=7.7, 2H), 7.14–7.11 (m, 1H), 2.59 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 163.1, 148.7, 138.6, 136.2, 133.7, 133.0, 132.1, 128.6, 124.0, 123.5, 120.5, 19.5; MS (ESI, *m*/*z*) $[M+H]^+$: 257.1; HRMS (ESI, *m*/*z*) $(M-H)^-$: calcd for $C_{14}H_{11}N_2O_3$: 255.0764, found 255.0759.

*4.3.5. 3-Fluoro-N-phenylbenzamide (**3q**).* Followed the general procedure 2, product was obtained in 3 h as white solid (194 mg, yield 90%), mp: 147–148 °C; IR (KBr, cm^{-1}): 3346, 3077, 3047, 1655, 1591, 1529, 1441, 1322, 1266, 898, 751, 685, 649; ^1H NMR (500 MHz, $CDCl_3$): δ 7.89 (s, 1H), 7.63–7.61 (m, 3H), 7.58–7.56 (m, 1H), 7.46–7.42 (m, 1H), 7.38–7.35 (t, ^3J=7.6, 2H), 7.26–7.21 (m, 1H), 7.18–7.15 (t, ^3J=7.6, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.48,

163.84, 161.86, 137.60, 137.29, 137.23, 130.51, 130.45, 129.15, 124.89, 122.46, 122.43, 120.35, 118.96, 118.79, 114.64, 114.46; MS (ESI, *m*/*z*) $[M+H]^+$: 216.2; HRMS (ESI, *m*/*z*) $(M-H)^-$: calcd for $C_{13}H_9FNO$: 214.0663, found 214.0659.

*4.3.6. N-Phenylpicolinamide (**3r**).* Followed the general procedure 2, product was obtained in 3 h as white solid (97 mg, yield 49%), mp: 71–72 °C; IR (KBr, cm^{-1}): 3333, 3104, 1670, 1597, 1530, 1440, 1323, 1234, 896, 754, 682; ^1H NMR (500 MHz, $CDCl_3$): δ 10.03 (s, 1H), 8.62–8.61 (m, 1H), 8.31–8.30 (d, ^3J=7.8, 1H), 7.92–7.89 (t, ^3J=7.8, 1H), 7.79–7.78 (m, 2H), 7.48–7.46 (m, 1H), 7.40–7.37 (t, ^3J=7.6, 2H), 7.16–7.13 (t, ^3J=7.6, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.0, 149.8, 147.9, 137.6, 129.1, 126.4, 124.3, 122.4, 119.7; MS (ESI, *m*/*z*) $[M+H]^+$: 198.8; HRMS (ESI, *m*/*z*) $(M-H)^-$: calcd for $C_{12}H_{10}N_2O$: 199.0866, found 199.0867.

*4.3.7. 2-Methyl-N-phenyl-benzamide (**3s**).* Followed the general procedure 2, product was obtained in 5 h as white solid (53 mg, yield 25%), mp: 111–113; IR (KBr, cm^{-1}): 3285, 1652, 1596, 1532, 1491, 1437, 1320, 1259, 754, 697; ^1H NMR (500 MHz, DMSO-d_6): δ 10.29 (s, 1H), 7.75–7.73 (m, 2H), 7.45–7.44 (d, ^3J=7.45, 1H), 7.35–7.28 (m, 5H), 7.10–7.07 (t, ^3J=7.45, 1H), 2.38 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 167.8, 139.2, 137.2, 135.1, 130.4, 129.5, 128.6, 127.1, 125.6, 123.4, 119.5, 19.2; MS (ESI, *m*/*z*) $[M+Na]^+$: 234.2; HRMS (ESI, *m*/*z*) $(M+H)^+$: calcd for $C_{14}H_{13}NO$: 212.1070, found 212.1071.

4.4. General procedure 3: for the N-arylation between aryl bromides (or beta-bromostyrenes) and benzonitrile (3t–E)

To a screw-capped vial (50 ml) were added aryl bromides **1** (1.0 mmol), benzonitrile **2a** (155 mg, 1.5 mmol), Cs_2CO_3 (652 mg, 2.0 mmol), NaOH (40 mg, 1.0 mmol), Cu_2O (28 mg, 0.2 mmol), DMEDA (18 mg, 0.2 mmol) and [bmim][PF_6^-] (14 mg, 0.05 mmol) in water (2 ml). The vial was flushed with nitrogen then sealed with a cap, and allowed to stir at 100 °C for the specific reaction time. The reaction mixture was extracted with EtOAc (3×15 ml). The combined organic extracts were dried over Na_2SO_4 for 12 h and evaporated under vacuum. The crude products were purified in a silica gel column for further purification, using PE/EtOAc (5:1) as the eluent.

*4.4.1. N-(Naphthalen-2-yl)benzamide (**3t**).* Followed the general procedure 3, product was obtained in 12 h as white solid (195 mg, yield 79%), mp: 159–160 °C; IR (KBr, cm^{-1}): 3269, 3054, 1645, 1551, 1361, 1288, 821, 746, 697; ^1H NMR (500 MHz, $CDCl_3$): δ 8.35 (s, 1H), 7.98 (s, 1H), 7.93–7.91 (m, 2H), 7.82–8.80 (m, 3H), 7.60–7.56 (m, 2H), 7.53–7.46 (m, 3H), 7.44–7.41 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.83, 135.36, 134.99, 133.89, 131.9, 130.81, 128.89, 127.6, 127.0, 126.61, 125.18, 120.04, 117.01; MS (ESI, *m*/*z*) $[M+H]^+$: 247.9; HRMS (ESI, *m*/*z*) $(M-H)^-$: calcd for $C_{17}H_{12}NO$: 246.0913, found 246.0917.

*4.4.2. N-(m-Tolyl)benzamide (**3u**).* Followed the general procedure 3, product was obtained in 12 h as white solid (144 mg, yield 68%), mp: 124–125 °C; IR (KBr, cm^{-1}): 3267, 3059, 1648, 1533, 1303, 1259, 873, 781, 700; ^1H NMR (500 MHz, $CDCl_3$): δ 7.87–7.85 (d, ^3J=8.0 Hz, 2H), 7.75 (s, 1H), 7.56–7.47 (m, 4H), 7.42–7.40 (d, ^3J=8.0, 1H), 7.26–7.24 (m, 1H), 6.98–6.97 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.6, 139.0, 137.8, 135.1, 131.8, 128.9, 128.82, 126.9, 125.4, 120.8, 117.2, 21.5; MS (ESI, *m*/*z*) $[M+H]^+$: 212.3; HRMS (ESI, *m*/*z*) $(M-H)^-$: calcd for $C_{14}H_{12}NO$: 210.0913, found 210.0902.

*4.4.3. N-(2-Fluorophenyl)benzamide (**3v**).* Followed the general procedure 3, product was obtained in 12 h as white solid (138 mg, yield 64%), mp: 102–103 °C; IR (KBr, cm^{-1}): 3315, 1654, 1607, 1532, 1450, 1323, 1260, 1323, 1260, 1193, 1095, 754, 697, 642; ^1H NMR (500 MHz, $CDCl_3$): δ 8.50–8.46 (t, ^3J=8.0, 1H), 8.06 (s, 1H), 7.90–7.88 (d, ^3J=8.0 Hz, 2H), 7.9–7.56 (m, 1H), 7.53–7.50 (m, 2H), 7.21–7.18 (m, 1H), 7.14–7.07 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.4, 153.6, 151.7, 134.5, 132.1, 128.9, 127.0, 126.6, 126.5, 124.7, 124.7, 124.5, 124.4, 121.7, 114.9, 114.7; MS (ESI, *m*/*z*) $[M+H]^+$: 216.2; HRMS (ESI, *m*/*z*) $(M-H)^-$: calcd for $C_{13}H_9FNO$: 214.0663, found 214.0654.

*4.4.4. N-(4-Chlorophenyl)benzamide (**3w**).* Followed the general procedure 3, product was obtained in 12 h as white solid (152 mg, yield 66%), mp: 193–194 °C; IR (KBr, cm^{-1}): 3348, 1655, 1596, 1519, 1396, 1312, 1250, 1092, 824, 716, 647; ^1H NMR (500 MHz, $CDCl_3$): δ 7.86–7.85 (d, ^3J=8.0 Hz, 2H), 7.79 (s, 1H), 7.61–7.58 (m, 2H), 7.56–7.55 (m, 1H), 7.51–7.48 (m, 2H), 7.34–7.33 (d, ^3J=8.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.6, 136.4, 137.6, 132.0, 129.5, 129.1, 128.9, 126.9, 121.3; MS (ESI, *m*/*z*) $[M+H]^+$: 232.1; HRMS (ESI, *m*/*z*) $(M-H)^-$: calcd for $C_{13}H_9ClNO$: 230.0367, found 230.0360.

*4.4.5. N-(3-Nitrophenyl)benzamide (**3x**).* Followed the general procedure 3, product was obtained in 12 h as white solid (167 mg, yield 69%), mp: 152–153 °C; IR (KBr, cm^{-1}): 3360, 3109, 1661, 1591, 1530, 1486, 1418, 1351, 1259, 735, 707; ^1H NMR (500 MHz, DMSO-d_6): δ 10.71 (s, 1H), 8.82–8.81 (m, 1H), 8.21–8.19 (m, 1H), 8.00–7.96 (m, 3H), 7.68–7.56 (m, 4H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 165.8, 147.9, 140.3, 134.2, 132.0, 130.0, 128.5, 127.7, 126.1, 118.1, 114.3; MS (ESI, *m*/*z*) $[M+H]^+$: 243.2; HRMS (ESI, *m*/*z*) $(M-H)^-$: calcd for $C_{13}H_9N_2O_3$: 241.0608, found 241.0597.

*4.4.6. N-(3,5-Dimethylphenyl)benzamide (**3y**).* Followed the general procedure 3, product was obtained in 12 h as white solid (155 mg, yield 69%), mp: 140–141 °C; IR (KBr, cm^{-1}): 3245, 3071, 1653, 1615, 1544, 1448, 1325, 1287, 1255, 844, 708, 685, 618; ^1H NMR (500 MHz, $CDCl_3$): δ 7.86–7.85 (m, 2H), 7.71 (s, 1H), 7.56–7.53 (m, 1H), 7.50–7.47 (m, 2H), 7.28–7.25 (m, 2H), 6.80 (s, 1H), 2.33 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.6, 138.8, 137.7, 135.1, 131.7, 128.8, 126.9, 126.3, 117.9, 21.4; MS (ESI, *m*/*z*) $[M+H]^+$: 226.3; HRMS (ESI, *m*/*z*) $(M-H)^-$: calcd for $C_{15}H_{14}NO$: 224.1070, found 224.1064.

*4.4.7. N-(o-Tolyl)benzamide (**3z**).* Followed the general procedure 3, product was obtained in 12 h as white solid (154 mg, yield 73%), mp: 144–145 °C; IR (KBr, cm^{-1}): 3242, 3055, 1649, 1605, 1525, 1489, 1443, 1307, 908, 751, 712; ^1H NMR (500 MHz, $CDCl_3$): δ 7.98–7.96 (d, ^3J=7.8 Hz, 1H), 7.90–7.88 (d, ^3J=7.8 Hz, 2H), 7.65 (s, 1H), 7.58–7.55 (m, 1H), 7.52–7.49 (m, 2H), 7.29–7.27 (m, 1H), 7.24–7.23 (m, 1H), 7.14–7.11 (m, 1H), 2.35 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.6, 135.7, 135.0, 131.8, 130.5, 129.1, 128.8, 127.0, 126.9, 125.3, 123.0, 17.8; MS (ESI, *m*/*z*) $[M+H]^+$: 212.3; HRMS (ESI, *m*/*z*) $(M-H)^-$: calcd for $C_{14}H_{12}NO$: 210.0910, found 210.0910.

*4.4.8. N-(2-Aminophenyl)benzamide (**3A**).* Followed the general procedure 3, product was obtained in 16 h as white solid (170 mg, yield 80%), mp: 150–152 °C; IR (KBr, cm^{-1}): 3406, 3271, 3058, 1639, 1529, 1448, 1317, 752, 707; ^1H NMR (500 MHz, DMSO-d_6): δ 9.66 (s, 1H), 7.98–7.96 (d, ^3J=7.35, 2H), 7.58–7.55 (t, ^3J=7.3, 1H), 7.51–7.48 (t, ^3J=7.75, 2H), 7.16–7.15 (d, ^3J=7.65, 1H), 6.68–6.94 (m, 1H), 6.78–6.76 (m, 1H), 6.60–6.57 (t, ^3J=7.65, 1H), 4.94 (br, 2H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 165.2, 143.1, 134.5, 131.3, 128.5, 127.7, 126.6, 126.4, 123.2, 116.2, 116.0; MS (ESI, *m*/*z*) $[M+H]^+$: 235.1; HRMS (ESI, *m*/*z*) $(M-H)^-$: calcd for $C_{13}H_{11}N_2O$: 211.0866, found 211.0862.

*4.4.9. N-(3,5-Dimethoxyphenyl)benzamide (**3B**).* Followed the general procedure 3, product was obtained in 12 h as white solid (195 mg, yield 76%), mp: 139–140 °C; IR (KBr, cm^{-1}): 3249, 3070, 3001, 2963, 2837, 1653, 1608, 1533, 1456, 1420, 1351, 1287, 1204, 1158, 928, 710, 640; ^1H NMR (500 MHz, $CDCl_3$): δ 7.85–7.84 (d, ^3J=7.2, 3H), 7.55–7.52 (t, ^3J=7.2, 1H), 7.48–7.45 (m, 2H), 6.90 (d, ^4J=2.1, 2H), 6.28–6.27 (t, ^4J=2.1, 1H), 3.79 (s, 6H); ^{13}C NMR

(125 MHz, $CDCl_3$): δ 165.78, 161.13, 139.73, 131.92, 128.83, 126.99, 98.34, 97.08, 55.44; MS (ESI, *m*/*z*) $[M+H]^+$: 258.3; HRMS (ESI, *m*/*z*) $(M-H)^-$: calcd for $C_{15}H_{14}NO_3$: 256.0968, found 256.0965.

*4.4.10. trans-N-Styrylbenzamide (**3C**).* Followed the general procedure 3, product was obtained in 12 h as white solid (129 mg, yield 58%), mp: 174–175 °C; IR (KBr, cm^{-1}): 3304, 6057, 1639, 1573, 1529, 1484, 1318, 1174, 1071, 953, 925, 751, 695; ^1H NMR (500 MHz, $CDCl_3$): δ 8.10–8.08 (d, ^3J_a=10.0 Hz, 1H), 7.86–7.85 (d, ^3J=7.6 Hz, 2H), 7.76–7.71 (dd, ^3J_a=10.0 Hz, ^3J_b=15.0 Hz), 7.56–7.53 (m, 3H), 7.48–7.45 (t, ^3J=7.6, 2H), 7.35–7.34 (d, ^3J=7.1, 2H), 7.31–7.28 (m, 2H), 7.20–7.18 (t, ^3J=7.1, 1H), 6.29–6.28 (d, ^3J_b=15 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.5, 136.0, 133.4, 132.1, 128.8, 128.7, 127.1, 126.8, 125.67, 123.07, 113.6; MS (ESI, *m*/*z*) $[M+H]^+$: 223.9; HRMS (ESI, *m*/*z*) $(M-H)^-$: calcd for $C_{15}H_{12}NO$: 222.0913, found 222.0922.

*4.4.11. trans-N-[2-(4-Methoxy-phenyl)-vinyl]-benzamide (**3D**).* Followed the general procedure 3, product was obtained in 12 h as white solid (151 mg, yield 60%), mp: 191–192; IR (KBr, cm^{-1}): 3319, 3011, 2951, 2833, 1639, 1604, 1504, 1289, 1240, 1171, 1026, 939, 843, 806, 755, 692; ^1H NMR (500 MHz, DMSO-d_6): δ 10.54–10.52 (m, 1H), 7.96–7.95 (d, ^3J=7.4, 2H), 7.60–7.57 (t, ^3J=7.3, 1H), 7.53–7.50 (t, ^3J=7.2, 2H), 7.51–7.48 (d, ^3J=14.9, 1H), 7.33–7.31 (d, ^3J=8.6, 2H), 6.89–6.87 (d, ^3J=8.6, 2H), 6.43–6.40 (d, ^3J=14.7, 1H), 3.74 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 163.8, 157.9, 133.4, 131.7, 129.0, 128.4, 127.5, 126.4, 122.3, 114.2, 112.8, 55.0. MS (ESI, *m*/*z*) $[M+H]^+$: 254.4; HRMS (ESI, *m*/*z*) $(M+H)^+$: calcd for $C_{16}H_{15}NO_2$: 254.1176, found 254.1174.

*4.4.12. trans-N-(2-m-Tolyl-vinyl)-benzamide (**3E**).* Followed the general procedure 3, product was obtained in 12 h as white solid (166 mg, 70%), mp: 170–171; IR (KBr, cm^{-1}): 3267, 3047, 1630, 1521, 1483, 1315, 1280, 1189, 1157, 967, 928, 790, 701; ^1H NMR (500 MHz, DMSO-d_6): 10.63–10.61 (m, 1H), 7.97–7.96 (d, ^3J=7.3, 2H), 7.66–7.58 (m, 1H), 7.64–7.61 (d, ^3J=14.7, 1H), 7.55–7.52 (t, ^3J=7.75, 2H), 7.22–7.16 (m, 3H), 6.99–6.98 (d, ^3J=6.7, 1H), 6.44–6.41 (d, ^3J=14.7, 1H), 2.30 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 163.9, 137.7, 136.4, 133.3, 131.8, 128.6, 128.4, 127.5, 127.0, 125.7, 123.9, 122.4, 112.9, 20.9; MS (ESI, *m*/*z*) $[M+H]^+$: 238.3; HRMS (ESI, *m*/*z*) $(M+H)^+$: calcd for $C_{16}H_{15}NO$: 238.1226, found 238.1232.

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Supplementary data

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