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Copper/oxalohydrazide/ketone catalyzed synthesis of primary arylamines via coupling of aryl halides with aqueous ammonia in water

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ABSTRACT

The coupling reaction of aryl halides with aqueous ammonia was catalyzed by copper/oxalohydrazide/ketone system in water to yield primary arylamines without inert atmosphere. This method was fast and facile. The coupling reaction proceeded at 90 °C for 20–80 min, or at room temperature for a prolonged reaction time. A variety of aryl bromides and iodides were found to be applicable to this three-component catalytic system, which afforded good to excellent isolated yields.

1. Introduction

Aromatic amines are ubiquitous in biological systems, and commonly used for various applications, such as pharmaceutical, agrochemicals, dyestuffs, and conductive and emissive polymers. Among them, primary aromatic amine is probably one of the most important species.[1] Significant effort has been made to prepare primary amine due to its importance. Although ammonia is an abundant and cheap nitrogen source for the industrial production of organic amino compounds,[2] the synthesis of primary aromatic amines by coupling of aryl halides with ammonia has proven to be impractical due to the undesirable side reaction between the reactive aniline product and excessive ammonia, which yields diaryl amine.

The traditional methods to obtain anilines require the usage of ammonia surrogates with palladium or copper catalysts.[3] Recently, the Pd-catalyzed selective amination of aryl halides with ammonia were reported.[4] In addition, Cu-catalyzed coupling of aryl halides with ammonia to afford the desired anilines under mild conditions were reported too.[5] Chang and Zhao reported, respectively, that using CuI as the catalyst, with L-proline as the ligand or without any ligand, the coupling reaction between aryl iodides with NH_4Cl or NH_3 (aq) readily took place even at room temperature. However, these methods did not work well for aryl bromides with electron-donating groups.[6] It is noted that the above-mentioned metal-catalyzed coupling reactions were all performed in organic solvents, which are toxic, expensive, and less environmentally benign.

More recently, it was demonstrated that water can be applied as the solvent for various organic syntheses,[7] of which the copper-catalyzed C–N coupling reactions in aqueous media have attracted much attention.[8] However, there are only a few reports on the copper-catalyzed coupling of aryl halides with aqueous ammonia in water.[9] In addition, those reported approaches are all limited by the somewhat stringent reaction conditions, such as the high temperature and the long reaction time.

Previously, we have demonstrated three-component catalyst CuO/oxalyldihydrazide/hexane-2,5-dione was an effective catalytic system for the amination of aryl halides in water.[10] As an extension, we herein report copper/oxalohydrazide/ketone as an effective catalytic system for coupling of aryl bromides and iodides with aqueous ammonia in water. The current method is attractive due to a few reasons. First, it can be applied for both aryl iodides and bromides. Second, it can tolerate a wide range of functional groups. Moreover, the catalytic system employed is easily accessible and inexpensive. Importantly, aqueous ammonia is used as nitrogen source, which can significantly reduce the cost of the production. Finally, the reaction can proceed at much lower temperature in short time (or even at room temperature for a prolonged reaction time) with no need for the protection of inert atmosphere.

2. Results and discussion

Initially, we screened the reaction parameters with the coupling reaction of 4-bromotoluene and aqueous ammonia as a model

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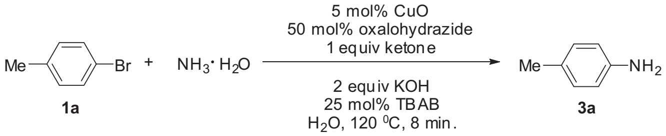
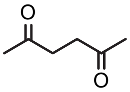
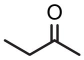
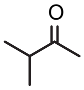
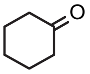
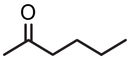
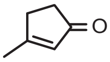
reaction. Consistent with our previous results,[10] we found that when using water as the solvent, the CuO/oxalohydrazide/hexane-2,5-dione catalyzed model reaction generated the target product in 80% GC yield (Table 1, entry 2). We then examined other ketones as additives for the model reaction. As shown in Table 1, hexane-2,5-dione (**L1**) gave the highest conversion and yield. Furthermore, when hexan-2-one (**L5**) was added, the reaction provided good conversion and yield (Table 1, entry 6), only slightly lower than **L1** but much higher than other ketones tested (Table 1, entries 3–5). Almost no product was detected in the absence of ketone (Table 1, entry 1), verifying the importance of ketone additives. It is also interesting to find that 3-methylcyclopent-2-enone (**L6**, entry 7), which could be derivatized from **L1** under the given reaction condition, only shows limited acceleration of the reaction compared to **L1**. Thus, **L1** was chosen as the additive for the following studies.

Table 1
Amination of 4-bromotoluene using different ketones as additive[a]

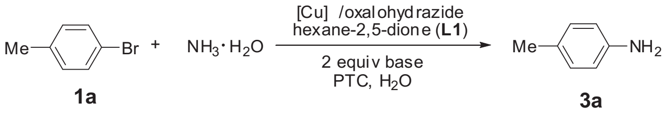


Entry	Ligands		Conversion [b](%)	Yield [b](%)
1	—		2	1
2		**L1**	100	80
3		**L2**	9	9
4		**L3**	3	3
5		**L4**	7	6
6		**L5**	92	72
7		**L6**	14	10

[a] Reaction conditions: 4-bromotoluene (1.0 mmol), commercial 28% aqueous NH_3 (6.0 mmol), CuO (0.05 mmol), oxalohydrazide (0.5 mmol), ketone (1 mmol), KOH (2 mmol), H_2O (1 mL), 120 °C, 8 min.
[b] Calculated by GC/MS.

To further optimize the reaction conditions, copper sources, bases, reaction time and temperature, phase-transfer catalysts, and the proportions among the starting materials, copper sources, ligand, and additives were screened using the same model substrate and additives (oxalohydrazide and hexane-2,5-dione). As shown in Table 2, all copper sources were effective in accelerating the reactions (Table 2, entries 5–8), except for copper powder (Table 2, entry 9). In particular, CuO provided the best catalytic effect. The tested quaternary ammonium salts used as phase-transfer catalyst show similar catalytic efficiency. Among them, TBAB provided the best catalytic effect (Table 2, entry 13). In term of bases tested, K_2CO_3 can yield both the high conversion and selectivity simultaneously (Table 2, entries 1–3), in comparison to KOH and K_3PO_4.

Table 2
Amination of 4-bromotoluene: optimization of the other catalytic conditions[a]



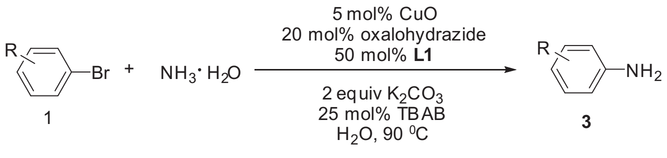
Entry	[Cu]	Base	2/1	Oxalohydrazide/**L1** (mol %)	T (°C)	Time (min.)	Conversion/ Yield [b](%)
1	CuO	KOH	4	50/100	120	8	100/80
2	CuO	K_2CO_3	4	50/100	120	8	91/85
3	CuO	K_3PO_4	4	50/100	120	8	71/66
4	CuO	K_2CO_3	4	50/100	120	10	97/91
5	CuO	K_2CO_3	6	50/100	120	10	99/96
6	$CuSO_4$	K_2CO_3	6	50/100	120	10	80/78
7	CuI	K_2CO_3	6	50/100	120	10	88/79
8	Cu_2O	K_2CO_3	6	50/100	120	10	98/86
9	Cu	K_2CO_3	6	50/100	120	10	15/14
10	CuO	K_2CO_3	6	50/100	90	80	100/92
11	CuO	K_2CO_3	6	20/100	90	80	98/95
12	CuO	K_2CO_3	6	10/100	90	80	96/91
13	CuO	K_2CO_3	6	20/50	90	80	99/94, 96/88[c] 97/89[d] 97/91[e] 91/84[f]
14	CuO	K_2CO_3	6	20/25	90	80	90/76

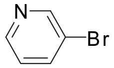
[a] Reaction conditions: 4-bromotoluene (1.0 mmol), commercial 28% aqueous NH_3, [Cu]-catalyst, oxalohydrazide, hexane-2,5-dione (**L1**), base (2 mmol), TBAB (25 mol %), H_2O (1 mL).
[b] Calculated by GC/MS.
[c] TBAC (25 mol %) was used as PTC.
[d] TEBAC (25 mol %) was used as PTC.
[e] TBAB (15 mol %).
[f] CuO (2.5 mol %).

Further investigation of reaction time and temperature revealed that the reaction performed at 90 °C for 80 min had the comparable yield as that performed at 120 °C for 10 min (Table 2, entries 5 and 10). In order to avoid the higher reaction pressure, and for the convenience of the experimentation, the rest of the reactions were performed at 90 °C. A more thorough screening of experimental conditions shows that the yield of the target product did not change significantly even if the ratio of oxalyldihydrazide and **L1** were reduced to 20 mol % and 50 mol %, respectively (Table 2, entry 13). However, when the catalyst concentration was decreased to 2.5 mol % or the concentration of TBAB was reduced to 15 mol %, the yields were decreased (Table 2, entry 13). Based on these results, we chose CuO (5 mol %), oxalohydrazide (20 mol %), **L1** (50 mol %), K_2CO_3 (200 mol %), and TBAB (25 mol %) as the optimized feeding recipe, 90 °C for the reaction temperature, and 80 min of reaction for further investigation.

To demonstrate the scope of the application of this catalytic system, a wide range of functionalized aryl bromides were coupled with aqueous ammonia under the optimized condition. As expected, both aryl bromides with electron-rich or electron-poor *para* or *meso*-substituents and neutral aryl bromide afforded good to excellent yields (Table 3, entries 1–10, 12) when reacted with aqueous ammonia. The electronic effect on the reactivity was limited, except for the aryl bromides with electron-withdrawing groups, which show faster reaction rate (Table 3, entries 9, 10). In comparison, steric hindrance shows a significant influence on the amination of aryl bromides (Table 3, entry 11). The moderate yield was obtained even with prolonged reaction time (120 min) at 120 °C. It is noteworthy that heterocyclic bromides could also be coupled with aqueous ammonia with excellent yield (Table 3, entry 13).

Table 3
Copper/ligand-catalyzed amination of aryl bromides[a]

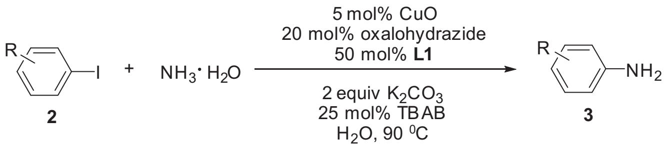


Entry	Aryl bromide	Product	Time (min.)	Yield [b] (%)
1	**1a**: R=4-Me	**3a**	80	79
2	**1b**: R=H	**3b**	80	73
3	**1c**: R=4-Et	**3c**	80	78
4	**1d**: R=4-OMe	**3d**	80	90
5	**1e**: R=4-Ph	**3e**	80	95
6	**1f**: R=4-Cl	**3f**	80	89
7	**1g**: R=4-F	**3g**	80	68
8	**1h**: R=4-CF_3	**3h**	80	73
9	**1i**: R=4-Ac	**3i**	40	90
10	**1j**: R=4-NO_2	**3j**	40	81
11	**1k**: R=2-OMe	**3k**	120	23, 57[c]
12	**1l**: R=3-OMe	**3l**	80	85
13	 N Br **1m**	**3m**	80	90

[a] Reaction conditions: aryl bromide (1 mmol), commercial 28% aqueous NH_3 (6 mmol), CuO (0.05 mmol), oxalohydrazide (0.2 mmol), hexane-2,5-dione (**L1**, 0.5 mmol), K_2CO_3 (2 mmol), H_2O (1 mL), 90 °C.
[b] Isolated yield.
[c] 120 °C.

The coupling reactions of aryl iodides with aqueous ammonia under the similar reaction conditions were carried out except for the shorter reaction time. Most of the coupling reaction was complete within 60 min with high yields, except for 2-iodoanisole, which was reacted at 120 °C for 100 min due to steric hindrance (Table 4, entry 7). In contrast, 4-iodoanisole afford lower yield because of corresponding bis (4-methoxyphenyl) amine was detected under the same reaction conditions (Table 4, entry 3). However, when using $CuSO_4$, 3-methylbutan-2-one (**L3**), and KOH as catalyst and base, respectively, iodobenzene and the aryl iodides with electron-donating *para*-substituents could afford high yields (Table 4, entries 1–3). It is noteworthy that **L3** shows low efficiency for accelerating amination of 4-bromotoluene (Table 1, entry 4), but was effective for coupling reaction between aryl iodides and aqueous ammonia (Table 4, entry 1–3). Therefore, based on the selectivity of **L1** and **L3**, the amination of 1-bromo-4-iodobenzene was successful with **L3** as additive, providing 4-bromoaniline in moderate yield (Table 4, entry 6) with little detection of 4-iodoaniline. The relatively lower yield was due to the side reactions of dehalogenation and coupling reaction between 4-bromoaniline and 1-bromo-4-iodobenzene.

Table 4
Copper/ligand-catalyzed amination of aryl iodides[a]

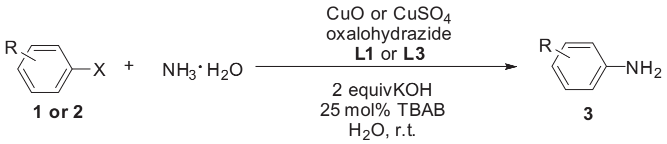


Entry	Aryl iodide	Product	Time (min.)	Yield[b] (%)
1	**2a**: R=4-Me	**3a**	20	84[c]
2	**2b**: R=H	**3b**	20	77[c]
3	**2c**: R=4-OMe	**3d**	60	75
			20	86[c]
4	**2d**: R=4-Ac	**3i**	30	86
5	**2e**: R=4-NO_2	**3j**	20	79
6	**2f**: R=4-Br	**3n**	20	42[c]
7	**2g**: R=2-OMe	**3k**	100	81[d]
8	**2h**: R=3-Cl	**3o**	60	87
9	**2i**: R=3,5-Dimethyl	**3p**	60	80

[a] Reaction conditions: aryl iodide (1 mmol), commercial 28% aqueous NH_3 (6 mmol), CuO (0.05 mmol), oxalohydrazide (0.2 mmol), hexane-2,5-dione (**L1** 0.5 mmol), K_2CO_3 (2 mmol), H_2O (1 mL), 90 °C.
[b] Isolated yield.
[c] $CuSO_4$ (0.05 mmol), oxalohydrazide (0.2 mmol), 3-methyl-2-butanone (**L3**, 1 mmol), KOH (2 mmol).
[d] 120 °C.

Finally, the coupling of 4-iodoanisole with aqueous ammonia was carried out at room temperature. With prolonged reaction time, the reaction proceeded as efficiently as that at high temperature. Based on this observation, a various functionalized aryl iodides and aryl bromides were tested and the results were summarized in Table 5. The result shows that after 24 h, *para*- or *meso*-substituents and neutral aryl iodides reacting with aqueous ammonia at room temperature afforded good to excellent yields (Table 5, entries 1–4, 6, 7). Even for the aryl iodide bearing *ortho*-substituent, the good yield was obtained by extending the reaction to 72 h (Table 5, entry 5). Compared to the aryl iodides, the aryl bromides show lower reactivity; the moderate yields were obtained when the reactions were carried out for 72 h at room temperature with an increase in the loadings of CuO, oxalohydrazide and **L1** to 10 mol %, 50 mol % and 100 mol %, respectively (Table 5, entries 8–14).

Table 5
Amination of aryl halides at room temperature[a]



Entry	Aryl halide	Product	Time (h)	Yield[b] (%)
1	**2a**	**3a**	24	85
2	**2b**	**3b**	24	81
3	**2c**	**3d**	24	91
4	**2d**	**3i**	24	86
5	**2g**	**3k**	24	38
			48	51
			72	73
6	**2h**	**3o**	24	72
7	**2i**	**3p**	24	80
8	**1a**	**3a**	72	55[c]
9	**1d**	**3d**	72	58[c]
10	**1g**	**3g**	72	53[c]
11	**1h**	**3h**	72	43[c]
12	**1i**	**3i**	72	83[c]
13	**1l**	**3l**	72	60[c]
14	**1m**	**3m**	72	57[c]

[a] Reaction conditions: aryl halide (1 mmol), commercial 28% aqueous NH_3 (1 mL), $CuSO_4$ (0.05 mmol), oxalohydrazide (0.2 mmol), 3-methyl-2-butanone (**L3**, 1 mmol), KOH (2 mmol), H_2O (1 mL), r.t.
[b] Isolated yield.
[c] CuO (0.1 mmol), oxalohydrazide (0.5 mmol), hexane-2,5-dione (**L1**, 1.0 mmol).

3. Conclusion

We have established a universal, efficient, low-cost, and environmentally benign method for converting aryl halides into primary arylamines in water with a three-component catalyst system including copper catalytic system, [Cu]/oxalyldihydrazide/ketone. A variety of functionalized aryl iodides and aryl bromides were coupled with aqueous ammonia efficiently under mild conditions, affording good to excellent isolated yields. This method has two main advantages: (1) Fast and flexible. Compared to the methods reported in the existing literature, the coupling reaction described here proceeded at lower temperature (90 °C) with shorter time (20–80 min). The amination of aryl iodides could even be accomplished in water at room temperature within 24 h; the yield was excellent. Even for the aryl bromides, the good isolation could be achieved at room temperature via prolonging the reaction time to 72 h. Thus, the optimized experimental conditions can be adjusted based on the different substrates and synthetic requirements. (2) Low-cost and environmentally friendly. The ammonia was used as nitrogen source and the nontoxic and cheap water was selected as solvent in current study. Moreover, the ingredients of catalytic system are all commercially available and inexpensive. The low reaction temperature producing the lower operational pressure allows the reactions to be performed without special autoclaves. This is a significantly advantage considering both cost and safety for further scaling-up. We believe that the current method can adopted in custom synthesis and applied to industrial-scale production. Further application of this flexible three-component copper catalytic system for Cu-catalyzed organic reactions in water is under investigation.

4. Experimental section

4.1. General

All aryl halides and 28% aqueous ammonia were commercially available and used as received. Flash column chromatography was performed with silica gel (200–300 mesh). Thin-layer chromatography was carried out with Merck silica gel 60 F_{254} plates. All yields reported in the publication represent an average of at least two independent runs. All products were characterized by MS, ^1H NMR, and ^{13}C NMR data with which compared to the previously reported data. NMR spectra were recorded at room temperature on a Mercury-Plus 300 instrument with TMS as an internal reference. ESI-MS was run on a LCMS-2010A. EI-MS was run on a Thermo EI-mass spectrometer. GC/MS was run on a Voyager GC/MS instrument with an electron impact (70 eV) mass selective detector.

4.2. General procedure for the coupling of aryl halides with aqueous ammonia in water

Under heating conditions: A 10 mL of vessel was charged with CuO (4 mg, 0.05 mmol)/$CuSO_4$ (13 mg, 0.05 mmol), oxalyldihydrazide (24 mg, 0.2 mmol), hexane-2,5-dione (57 mg, 0.5 mmol) or 3-methylbutan-2-one (86 mg, 1.0 mmol), TBAB (81 mg, 0.25 mmol), aryl halide (1 mmol), commercial 28% aqueous ammonia (6 mmol), K_2CO_3(276 mg, 2 mmol) or KOH(112 mg, 2 mmol), H_2O(1.0 mL). The vessel was sealed with a septum and placed into an oil bath, which was pre-heated to 90 °C. The reaction mixture was stirred for 80 min at this temperature. After cooling to room temperature, the reaction mixture was extracted with ethyl acetate. The combined organic phases were washed with water and brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The residual oil was purified by column chromatography on silica gel (eluting with petroleum ether/ethyl acetate) to afford the desired products.

At room temperature: A 10 mL of vessel was charged with $CuSO_4$ (13 mg, 0.05 mmol, for aryl iodides) or CuO (8 mg, 0.10 mmol, for aryl bromides), oxalyldihydrazide (24 mg, 0.2 mmol or 59 mg, 0.5 mmol), hexane-2,5-dione(57 mg, 0.5 mmol or 114 mg, 1.0 mmol), TBAB (81 mg, 0.25 mmol), aryl halide (1 mmol), commercial 28% aqueous ammonia (1 mL), KOH(112 mg, 2 mmol), H_2O(1.0 mL). The vessel was sealed with a septum and the reaction mixture was stirred at room temperature for 24 h (for aryl iodides) or 72 h (for aryl bromides). Then the reaction mixture was extracted with ethyl acetate. The combined organic phases was washed with water and brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The residue oil was purified by column chromatography on silica gel (eluting with petroleum ether/ethyl acetate) to afford the desired products.

*4.2.1. p-Toluidine (**3a**)*[5c]. White solid; mp: 41–44 °C; ^1H NMR (300 MHz, $CDCl_3$) δ: 6.93 (d, J=8.4 Hz, 2H), 6.58 (d, J=8.3 Hz, 2H), 3.40 (br s, 2H), 2.22 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 144.0, 130.0, 128.0, 115.5, 20.9; ESI-MS: m/z=108 $[M+H]^+$.

*4.2.2. Aniline (**3b**)*[5c]. Pale yellow oil; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.18–7.09(m, 2H), 6.74–6.71(m, 1H), 6.69–6.62(m, 2H), 3.46(br s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 146.9, 129.6, 118.8, 115.5; ESI-MS: m/z=94 $[M+H]^+$.

*4.2.3. 4-Ethyl-aniline (**3c**)*[11]. Pale yellow oil; ^1H NMR (300 MHz, $CDCl_3$) δ: 6.96 (d, J=8.5 Hz, 2H), 6.59 (d, J=8.4 Hz, 2H), 3.37 (br s, 2H), 2.53 (q, J=7.6 Hz, 2H), 1.18 (t, J=7.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 144.2, 134.7, 128.8, 115.6, 28.4, 16.4; ESI-MS: m/z=122 $[M+H]^+$.

*4.2.4. 4-Methoxybenzenamine (**3d**)*[5c]. Dark red solid; mp: 56–58 °C; ^1H NMR (300 MHz, $CDCl_3$) δ: 6.72 (d, J=8.8 Hz, 2H), 6.62 (d, J=8.8 Hz, 2H), 3.72 (s, 3H), 3.24 (br s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 152.9, 140.2, 116.6, 115.0, 56.1; ESI-MS: m/z=124 $[M+H]^+$.

*4.2.5. Biphenyl-4-amine (**3e**)*[5b]. Pale yellow solid; mp: 52–54 °C; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.62–7.50 (m, 2H), 7.47–7.35 (m, 4H), 7.33–7.21 (m, 1H), 6.76 (d, J=8.6 Hz, 2H), 3.73 (br s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 146.1, 141.4, 131.8, 128.9, 128.2, 126.6, 126.5, 115.7; ESI-MS: m/z=170 $[M+H]^+$.

*4.2.6. 4-Chloroaniline (**3f**)*[5f]. Pale yellow solid; mp: 67–69 °C; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.09 (d, J=8.8 Hz, 2H), 6.60 (d, J=8.8 Hz, 2H), 3.68 (br s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 145.2, 129.3, 123.3, 116.5; MS (EI^+): m/z=127 $[M^+]$.

*4.2.7. 4-Fluoroanline (**3g**)*[9a]. Pale yellow oil; ^1H NMR (300 MHz, $CDCl_3$) δ: 6.83 (t, J=8.7 Hz, 2H), 6.64–6.53 (m, 2H), 3.48 (br s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 158.1, 155.0, 142.6, 116.3, 116.0, 115.7; ESI-MS: m/z=112 $[M+H]^+$.

*4.2.8. 4-(Trifluoromethyl)anline (**3h**)*[6a]. Yellow oil; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.35 (d, J=8.2 Hz, 2H), 6.64 (d, J=8.3 Hz, 2H), 3.90 (br s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 149.6, 126.8, 123.3, 120.5, 120.1, 119.7, 114.4; MS (EI^+): m/z=161 $[M^+]$.

*4.2.9. 4-Aminoacetophenone (**3i**)*[5f]. White solid; mp: 103–105 °C; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.76 (d, J=8.7 Hz, 2H), 6.61 (d, J=8.8 Hz, 2H), 4.09 (br s, 2H), 2.47 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 196.7, 151.7, 131.0, 127.7, 113.9, 26.4; ESI-MS: m/z=136 $[M+H]^+$.

*4.2.10. 4-Nitroanline (**3j**)*[5f]. Yellow solid; mp: 146–147 °C; ^1H NMR (300 MHz, DMSO) δ: 7.90 (d, J=9.2 Hz, 2H), 6.67 (s, 2H), 6.56 (d, J=9.2 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 156.3, 136.3, 127.03, 113.03; MS (EI^+): m/z=138 $[M^+]$.

*4.2.11. 2-Methoxybenzenamine (**3k**)*[5f]. Pale red oil; ^1H NMR (300 MHz, $CDCl_3$) δ: 6.78(m, 4H), 3.87(s, 3H), 3.80(br s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 147.5, 136.4, 121.3, 118.7, 115.3, 110.7, 55.8; ESI-MS: m/z=124 $[M+H]^+$.

*4.2.12. 3-Methoxybenzenamine (**3l**)*[5c]. Pale yellow oil; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.02(t, J=8.0 Hz, 1H), 6.26(m, 3H), 3.73(s, 3H), 3.45(br s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 160.9, 147.9, 130.3, 108.2, 104.2, 101.4, 55.4; ESI-MS: m/z=124 $[M+H]^+$.

*4.2.13. Pyridine-3-amine (**3m**)*[5b]. Pale yellow solid; mp: 61–63 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.07–7.96(m, 2H), 7.05–6.93(m, 2H), 3.49(br s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 143.0, 139.7, 137.4, 124.0, 121.7; ESI-MS: m/z=95 $[M+H]^+$.

*4.2.14. 4-Bromoaniline (**3n**)*[5b]. Pale solid; mp: 60–63 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.21 (d, J=8.6 Hz, 2H), 6.53 (d, J=8.6 Hz, 2H), 3.60 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 145.6, 132.2, 116.9, 110.4; MS (EI$^+$): m/z=173 $[M^+]$.

*4.2.15. 3-Chloroaniline (**3o**)*[5c]. Red oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.01(t, J=7.9 Hz, 1H), 6.70–6.62(m, 2H), 6.51–6.48(m, 1H), 3.68(br s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 147.8, 135.0, 130.5, 118.7, 115.1, 113.5; ESI-MS: m/z=128 $[M+H]^+$.

*4.2.16. 3,5-Dimethylaniline (**3p**)*[5c]. Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 6.41(s, 1H), 6.32(s, 2H), 3.37(br s, 2H), 2.22(s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 146.5, 139.2, 120.8, 113.4, 21.7; ESI-MS: m/z=122 $[M+H]^+$.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2011.05.068.

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