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CuCl-catalyzed aerobic oxidative reaction of primary aromatic amines

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Abstract

The oxidations of primary aromatic amines were investigated. Cuprous chloride-air system can catalyze the oxidation of primary aromatic amines to azo derivatives, anils, and/or quinone anils. The experimental procedure is simple and the products could be easily isolated in high yields.

Keywords: Aromatic amines; Cuprous chloride; Catalytic oxidation; Azo derivatives; Anils

Oxidation of arylamines is an important reaction in the synthesis of many products such as azo, azoxy, anil, and hydroxylamine compounds. Azo derivatives have been utilized as organic dyes,[1] indicators,[2] radical reaction initiators,[3] and therapeutic agents.[4] In addition, azo derivatives have the potential for use in electronic[5] and drug delivery applications.[6] A variety of oxidation methods have been reported for the preparation of these compounds. For example, aromatic amines can be oxidized with oxidants such as peracetic acid,[7] manganese dioxide,[8] lead tetraacetate,[9] $Hg(OAc)_2$,[10] barium manganate,[11] phenyl iodoacetate,[12] sodium hypochlorite,[13] potassium ferricyanide,[14] potassium ferrate,[15] barium ferrate monohydrate,[16] and mercury(II) oxide.[17]

Most of these methods are based on stoichiometric processes. In light of the current interest to develop more efficient and environmentally friendly methods for chemical synthesis,[18] the use of oxygen as the oxidizing agents has clearly the environmental advantages because it is inexpensive, abundant, nontoxic, and convenient. Accordingly, it is highly desirable to develop a transition-metal-catalyzed oxidative reaction of aromatic amines under atmospheric conditions. Only few examples of catalytic oxidation of amines have been reported.[19,20] Herein, we describe a CuCl-catalyzed oxidation of primary aromatic amines to afford azo derivatives, anils, and quinone anils under atmospheric conditions (Scheme 1).

Copper derivatives have been known to mediate the oxidative reaction. In this broad context, copper(II) reagent was mainly used as an oxidant for the oxidative reaction. Recently, we reported that *N*,*N*-dialkylanilines could be oxidized with CuBr in the presence of H_2O_2 in water to give benzidine derivatives in high yields.[21] As part of a general study, we chose CuCl-catalyzed aerobic oxidative reaction of primary aromatic amines. At the beginning, various copper salts such as $CuCl_2$, $Cu(OAc)_2$, CuCl/air, CuBr/air, CuI/air, and $CuCl_2$/air were examined as catalysts in the model reaction of *para*-methoxyaniline **1a** under atmospheric conditions to ascertain the most optimum conditions (Table 1). The Cu(II) salts were inefficient (entries 8 and 9) with the CuCl/air system proving to be superior (entries 1 and 2). Control experiments carried out on *para*-methoxyaniline **1a** showed that, in the absence of CuCl, no oxidation to azo compounds occurred (entry 3). CuBr/air showed lower activity (entries 4 and 5) and CuI/air appeared to be inert in this reaction (entries 6 and 7). In this reaction, several commonly used solvents were tested (Table 1, entries 1 and 10–19). CH_3OH was less

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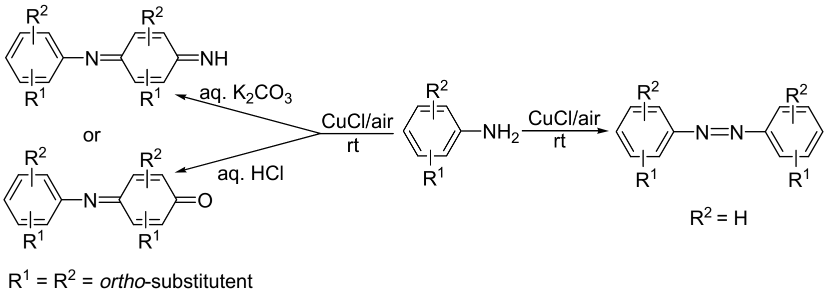
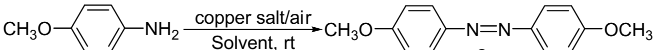


Scheme 1.

Table 1
Various copper salts for the oxidation of 4-methoxyaniline[a]



1a **2a**

Entry	Salts	Solvent	Amount (equiv)	Time (h)	Yield[b] (%)
1	CuCl	CH_3CN	0.2	10	71
2	CuCl	CH_3CN	0.5	5	74
3	CuCl	CH_3CN	0	10	0
4	CuBr	CH_3CN	0.2	24	11
5	CuBr	CH_3CN	1	24	13
6	CuI	CH_3CN	0.2	48	Trace
7	CuI	CH_3CN	1	48	Trace
8	$CuCl_2$	CH_3CN	1	48	0
9	$Cu(OAc)_2$	CH_3CN	1	48	0
10	CuCl	Toluene	0.2	30	70
11	CuCl	Pyridine	0.2	10	70
12	CuCl	Et_3N	0.2	48	67
13	CuCl	THF	0.2	10	57
14	CuCl	Et_2O	0.2	10	51
15	CuCl	CH_3COCH_3	0.2	10	50
16	CuCl	CH_2Cl_2	0.2	24	53
17	CuCl	DMF	0.2	48	45
18	CuCl	CH_3OH	0.2	30	15
19	CuCl	H_2O	0.2	48	0

[a] Reaction conditions: 4-methoxyaniline (1 mmol), solvent (5 mL).
[b] Isolated yield.

effective (entry 18). H_2O was not effective (entry 19) for this reaction. Tetrahydrofuran (THF), ethoxyethane, propan-2-one, dichloromethane, and *N*,*N*′-dimethylformamide (DMF) were effective to give moderate yields for this reaction (entries 13–17). Acetonitrile, toluene, pyridine, and triethylamine were much more effective to give high yields for this reaction (entry 1 and entries 10–12). Finally we chose the acetonitrile as a solvent and CuCl as a catalyst at room temperature under atmospheric conditions for proceeding the reactions.

Under the optimized conditions, various aromatic amines were transformed to the corresponding azo derivatives. Representative results are listed in Table 2. Using *para*-activated aromatic amines led to excellent yields of the oxidative reaction products (entries 1 and 5). Using *meta*-activated aromatic amine resulted in good yields of the desired product (entries 2 and 6). Using *ortho*-activated aromatic aniline resulted in a moderate yield of the desired product (entry 3). The oxidative reaction of aromatic amines with electron-withdrawing substituted group such as nitryl on the phenyl ring did not proceed (entry 9) and chlorine on the phenyl ring gave low yields under the reaction conditions (entries 7 and 8). This was suspected to be the result of low electron density of phenyl ring. Representative procedure was shown in Ref. 22.

Table 2
Oxidation of aromatic anilines in the CuCl/air system[a]

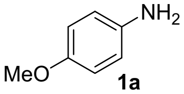
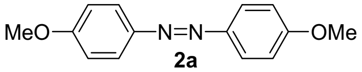
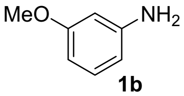
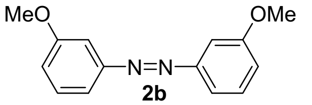
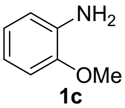
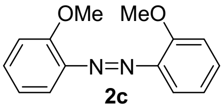
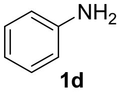
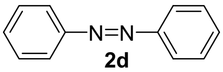
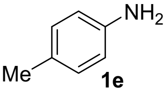
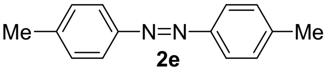
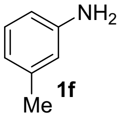
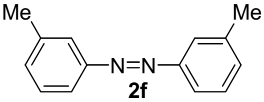
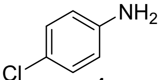
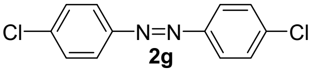
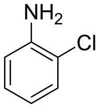
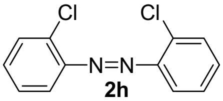
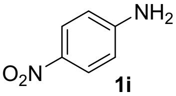
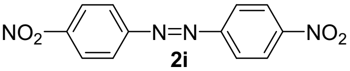
Entry	Substract	Time (h)	Product	Yield[b] (%)
1	 **1a**	10	 **2a**	71
2	 **1b**	48	 **2b**	53
3	 **1c**	10	 **2c**	46

Table 2 (*continued*)

Entry	Substract	Time (h)	Product	Yield[b] (%)
4	 **1d**	48	 **2d**	33
5	 **1e**	10	 **2e**	85
6	 **1f**	48	 **2f**	63
7	 **1g**	96	 **2g**	26
8	 **1h**	96	 **2h**	8
9	 **1i**	96	 **2i**	0

[a] Reaction conditions: aromatic amine (1 mmol), solvent, CH_3CN (5 mL), CuCl (0.2 mmol).

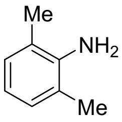
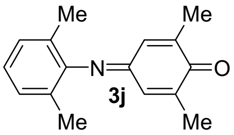
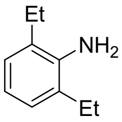
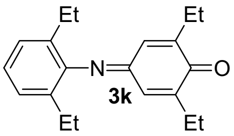
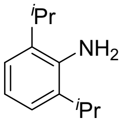
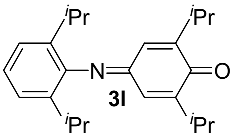
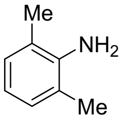
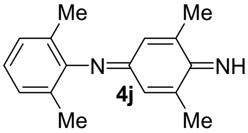
[b] Yields are for isolated aza derivatives.

We next investigated the oxidation of disubstituted benzeneamines in a CuCl/air system.[23] Representative results are listed in Table 3. When disubstituted benzeneamines were treated, quinone anils **3** were exclusively formed in high yield after hydrolysis with acidic solution. No azo derivatives **2** were observed. This may be attributed to the steric hindrance of *ortho*-substituent in benzeneamine. When the reaction mixture was quenched by basic solution, anils **4** were observed. The structure of **4j** was further confirmed by single-crystal X-ray diffraction analysis (Fig. 1).

In connection with the mechanism of this reaction, two key points should be considered: (1) Cu(I)/air was the active species instead of Cu(II) salts. In other words, the copper generated from Cu(I) and air should be a more active species; (2) coordination process of amine to copper species was suspected to be involved. In addition, X-ray photoelectron spectroscopy (XPS) showed the existence of both Cu(II) and Cu(I) in the residues of the reaction mixtures. In combination of the experimental results, accordingly, one possible mechanism is proposed in Scheme 2. Firstly, Cu(I) salt was oxidized by air to give more active Cu(II) precursor **5**, which coordinated with amine leading to complex **6**. Compound **6** underwent one electron transfer process resulting in radical cation **7**, which can be expressed as another resonance structure **8**.[24] Radical **7** dimerized via head-to-head to give hydrazo com-

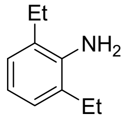
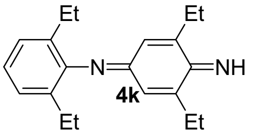
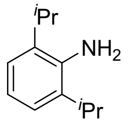
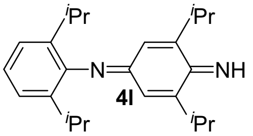
Table 3

Oxidation of disubstituted benzeneamine in the CuCl/air system[a]

Entry	Substract	Product	Yield[b] (%)
1	 **1j**	 **3j**	70
2	 **1k**	 **3k**	70
3	 **1l**	 **3l**	44
4	 **1j**	 **4j**	65

(*continued on next page*)

Table 3 (*continued*)

Entry	Substract	Product	Yield[b] (%)
5	 **1k**		67
6	 **1l**		49

[a] Reaction conditions: disubstituted benzeneamine (1 mmol), solvent (5 mL), CuCl (1 mmol), and products (**3j–l**) were gotten after the reaction mixture was quenched by 3 N HCl; the products (**4j–l**) were gotten after the reaction mixture was quenched by a solution of K_2CO_3.

[b] Isolated yields.

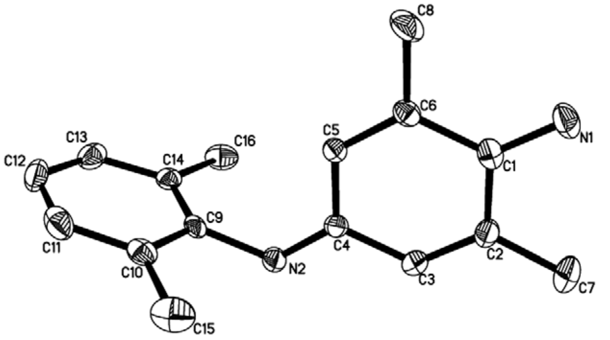
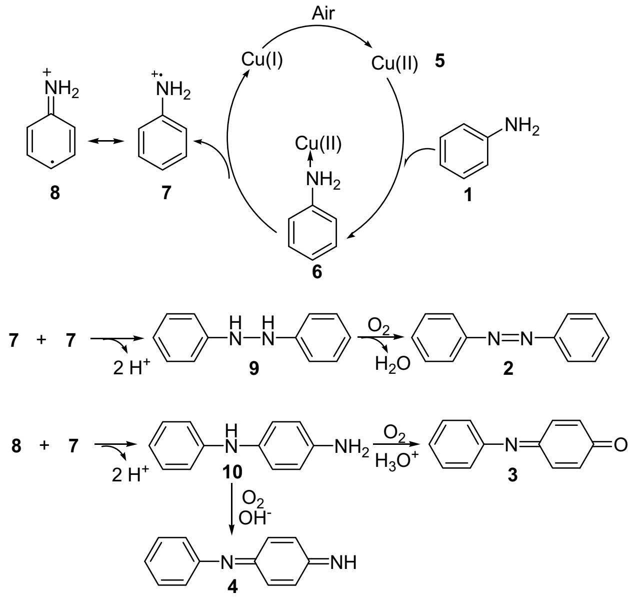


Fig. 1. X-ray structures of **4j** (CCDC 683434).



Scheme 2.

pound **9**, which underwent another oxidation process to form the final product azobenzene **2**. The resonance structure **8** coupled with **7** via tail-to-head to form compound **10**, which underwent oxidation process and hydrolysis to afford quinone anil **3** and anil **4**, respectively.

In summary, we have developed a CuCl-catalyzed oxidative coupling reaction of primary aromatic amines under atmospheric conditions to afford azo derivatives, anils, and quinone anils, respectively. This approach was highly efficient, low cost, and easy handling.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2008.04.089.

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22. A mixture of CuCl (20 mg, 0.20 mmol), CH_3CN (5.0 mL), and aromatic amine (1.0 mmol) under air was stirred at room temperature for 1–48 h. The reaction mixture was quenched with aqueous solution of K_2CO_3, followed by extraction of the organic phase with 3×5 mL portions of diethyl ether. The combined organics were dried over Na_2SO_4, filtered, and concentrated. The residue was isolated by column chromatography on silica gel eluting (petroleum ether/ethyl acetate = 10/1) to provide the azo derivative **2**. ^1H NMR and ^{13}C NMR spectra were recorded on a JEOL 300 NMR spectrometer with tetramethylsilane (TMS) as an internal standard. Mass spectra were obtained using a Bruker Esquire ion trap mass spectrometer in positive ion mode. Elemental analyses were performed on a Flash EA 1112 instrument. The IR spectra were obtained on a Perkin–Elmer FT-IR 2000 spectrophotometer by using the KBr disc in the range of 4000–400 cm^{-1}. Melting points were determined with a digital electrothermal apparatus without calibration. GC–MS spectra were obtained with a Hewlett Packard GC–MS system.
23. A mixture of CuCl (100 mg, 1.0 mmol), CH_3CN (5.0 mL), and disubstituted benzeneamine (1.0 mmol) under air was stirred at room temperature until aromatic amine totally disappeared. The reaction mixture was quenched with 3 M HCl, followed by the extraction of the organic phase with 3×5 mL portions of diethyl ether. The combined organics were dried over $MgSO_4$, filtered, and concentrated. The residue was isolated by column chromatography on silica gel eluting (petroleum ether/ethyl acetate = 10/1) to provide the quinone anil **3**. The reaction mixture was quenched with aqueous solution of K_2CO_3, followed by the extraction of the organic phase with 3×5 mL portions of diethyl ether. The combined organics were dried over Na_2SO_4, filtered, and concentrated. The residue was isolated by column chromatography on neutral Al_2O_3 eluting (petroleum ether/ethyl acetate = 10/1) to provide anil **4**.
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