RSC Advances

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Cite this: DOI: 10.1039/c0xx00000x

www.rsc.org/xxxxxx

ARTICLE TYPE

A General Route for Synthesis of *N*-Aryl Phenoxazines via Copper(I)-Catalyzed *N*-, *N*-, and *O*-Arylations of 2-Aminophenols

Nan Liu,[a] Bo Wang,[a] Wenwen Chen,[a] Chulong Liu,[a] Xinyan Wang,*[a] and Yuefei Hu*[a]

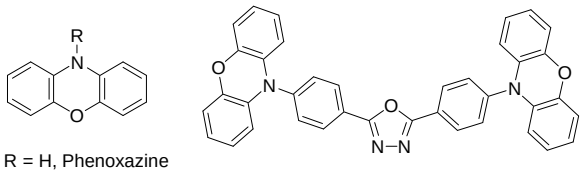
Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX

DOI: 10.1039/b000000x

A novel copper(I)-catalyzed tandem reaction of *N*- and *O*-arylations of 2-[*N*-(2-chlorophenyl)amino]-phenols was developed, by which a series of structurally novel *N*-aryl phenoxazines were synthesized efficiently. This success owes much to the discovery of highly efficient homogeneous copper(I)-catalyzed intramolecular *O*-arylation of chlorobenzenes under ligand-free-like conditions. Since 2-[*N*-(2-chloro-phenyl)amino]phenols were prepared also by copper(I)-catalyzed *N*-arylation of 2-aminophenols, thus a general route for efficient synthesis of *N*-aryl phenoxazines was established via copper(I)-catalyzed *N*-, *N*-, and *O*-arylations of 2-aminophenols in two steps.

Introduction

The structural unit of phenoxazine (**1**) has been well recognized as an electron-donor in numerous organic compounds used in the developments of dye-sensitized solar cells, laser dyes, fluorescent stains and OLEDs. When its *N*-atom bears an electron-accepting group, a donor-acceptor structure is formed to serve as a dipolar push–pull fluorophore or chromophore. Usually, the aryl groups are employed for such purpose and therefore *N*-aryl phenoxazine (**2**) has been gaining increasing importance.[1,2] As shown in Figure 1, an OLED using 2PXZ-OXD as a green emitter was reported recently to exhibit the highest EQE among TADF-based OLEDs to date.[1a]



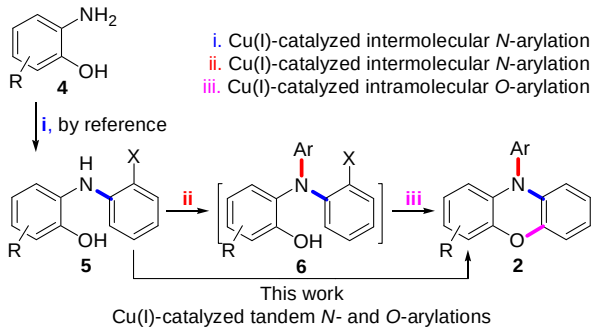
1. R = H, Phenoxazine
2. R = Ar, *N*-Aryl phenoxazine

2PXZ-OXD

Figure 1. Structures of phenoxazine and *N*-aryl phenoxazines.

Investigation showed that the construction of the skeleton of phenoxazine (**1**) at laboratory-scale remains a challenging task to date.[3] Only a few protocols were reported for the synthesis of *N*-aryl phenoxazines (**2**) in literature, such as Pd-,[1] Cu-,[2,4] or base-catalyzed[5] *N*-arylations, as well as the photocyclizations of azides.[6] Despite the rapid development of Cu(I)-catalyzed *N*- and *O*-arylations in the past decade,[7] none of them dealt specifically with the synthesis of *N*-aryl phenoxazines (**2**). As a result, although there are three $C_{(Ar)}$–N bonds and two $C_{(Ar)}$–O bonds in the molecule of **2**, only the $C_{(Ar)}$–N bond on C10 is usually constructed by Cu(I)-catalyzed *N*-arylation[2] between phenoxazine (**1**) and halobenzenes (**3**). Even worse, the most often used procedure for this *N*-arylation was established as early as in 1957, in which the toxic nitrobenzene was used as a solvent for producing high temperature.[4] Thus, it is necessary to develop a mild method for an efficient preparation of **2** to easily achieve the molecular diversity.

As shown in Scheme 1, we report herein a novel Cu(I)-catalyzed tandem reaction for *N*- and *O*-arylations of 2-[*N*-(2-halophenyl)amino]phenols (**5**), by which a series of the derivatives of **2** were prepared efficiently in one-flask. Since the precursor **5** was prepared also by Cu(I)-catalyzed *N*-arylation of 2-aminophenols (**4**), this work in fact presents a general route for efficient synthesis of **2** by Cu(I)-catalyzed *N*-, *N*-, and *O*-arylations of 2-aminophenols (**4**) in two steps.

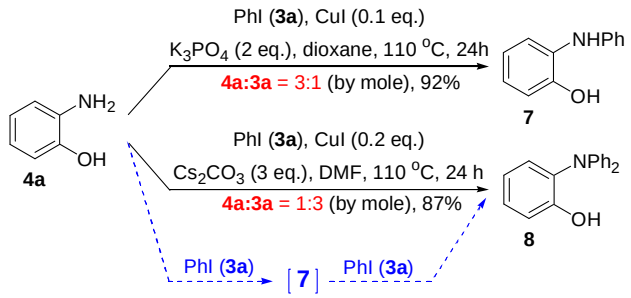


Scheme 1. A general route for efficient synthesis of **2**.

Results and Discussion

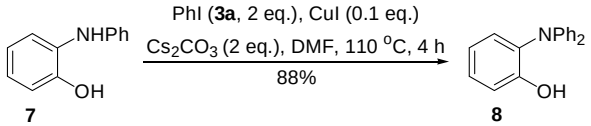
Due to the steric hindrance, Cu(I)-catalyzed *N*-arylation of diarylamine is much more difficult than that of monoarylamine. Thus, the synthesis of triarylamines usually required refluxing the mixture of the reactants, catalyst and/or ligand in high boiling solvent (toluene, NMP or DMF) in the presence of a strong base (KO^tBu, NaO^tBu or $LiNH_2$).[8] However, when 2-aminophenols (**4**) were used as the substrates, their *N*-arylations could proceed with weak bases under ligand-free conditions.[9] As shown in Scheme 2,

by using different ratios of 2-aminophenol (**4a**) and iodobenzene (**3a**), the desired diarylamine **7** or triarylamine **8** was synthesized in high yields. It has been confirmed that the compounds **4a** and **7** not only were reactants, intermediates, or products, but also served as ligands. Therefore, the ligand-free conditions for these *N*-arylations can be considered as ligand-free-like conditions. So far, only the derivatives of **8** bearing two identical aryl groups were prepared by this method.



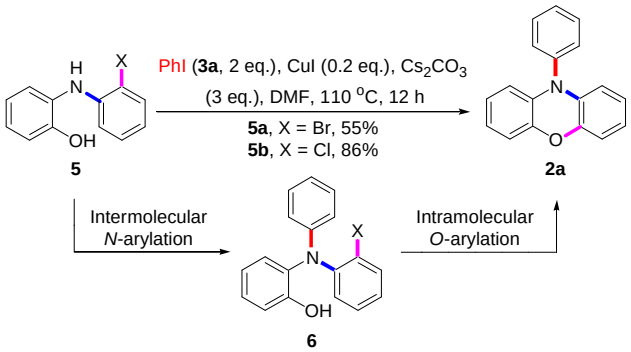
Scheme 2. Ligand-free-like *N*-arylations of **4a**.

When we repeated the procedure for the synthesis of **8** starting from **4a**, we found that the yield of the intermediate **7** remained in less than 3% during the entire process. It was clearly revealed that the conversion of **4a** into **7** was the rate-determining step and the conversion of **7** into **8** was a fast process. As shown in Scheme 3, this hypothesis was proved by using the pre-made **7** as a substrate to give **8** in 88% yield within 4 h.



Scheme 3. A fast conversion of **7** into **8**.

This result also strongly indicated that the unsymmetric triphenylamine 2-[*N*-(2-halophenyl)-*N*-phenylamino]phenol (**6**) may be synthesized easily via Cu(I)-catalyzed *N*-arylation between iodobenzene (**3a**) and 2-[*N*-(2-halophenyl)amino]phenol (**5**). Thus, we may expect that *N*-phenyl phenoxazine (**2a**) is synthesized via Cu(I)-catalyzed intramolecular *O*-arylation of **6**. To our surprise, a novel tandem reaction for *N*- and *O*-arylations of **5** occurred to yield **2a** directly instead of the excepted **6** when the mixture of **3a** and **5** was treated with CuI (Scheme 4). As shown in Figure 2, the structure of **2a** was confirmed by single crystal X-ray diffraction analysis.



Scheme 4. The tandem reaction for *N*- and *O*-arylations of **5**.

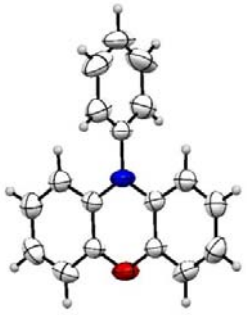
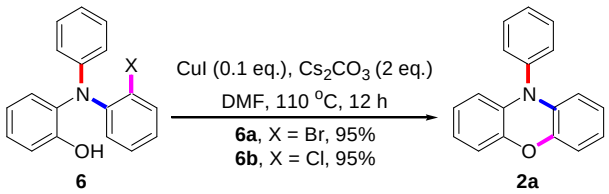


Figure 2. The structure of **2a**.

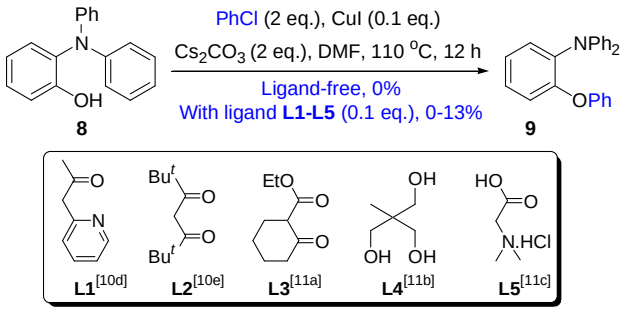
To further understand the results in Scheme 4, the pre-made compounds **6a** and **6b** were tested as starting materials. As shown in Scheme 5, both of them carried out Cu(I)-catalyzed *O*-arylations smoothly to give **2a** in 95% yields. Thus, two conclusions were drawn: first, the compound **6** was the intermediate for the tandem reaction; secondly, the problem that **5a** gave the lower yield of **2a** in the tandem reaction occurred in the conversion of **5a** into **6a**, in which the highly reactive bromide group may carry out an undesired *N*-arylation between two molecules of **5a**, besides the desired *N*-arylation between **5a** and **3a**.



Scheme 5. Cu(I)-catalyzed intramolecular *O*-arylations of **6a** and **6b**.

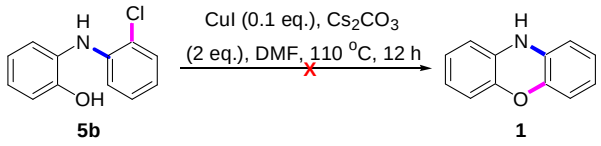
It was well known that Cu(I)-catalyzed *O*-arylation of chlorobenzenes was the most difficult task compared with that of bromo- and iodobenzenes. Only a few successful procedures were reported in literature, such as by using heterogeneous nano-catalysts[10a-c] or large amounts of ligands (0.2-0.8 equiv).[10d-e] To the best of our knowledge, the conversion of **6b** into **2a** is the first example of highly efficient homogeneous Cu(I)-catalyzed *O*-arylation of chlorobenzene under the ligand-free-like conditions. This work is so important because the *O*-arylation by using chloroaromatics as arylating reagents to replace bromo- or iodoaromatics in the synthesis of aryl ethers has been identified to be one of "dream reactions" by the ACS-GCI Pharmaceutical Roundtable in 2005.[11]

Therefore, we were encouraged to study the *O*-arylation of chlorobenzene further. As shown in Scheme 6, no intermolecular *O*-arylation product **9** was obtained at all from the substrate **8** and chlorobenzene under ligand-free-like conditions. Very low yields of **9** were obtained with the ligands **L1-L5** (the most efficient ligands reported in literature).[10d-e,12] In a recent reference, the synthesis of xanthones by using Cu(I)-catalyzed intramolecular *O*-arylation of chlorobenzenes was reported to fail,[13] even though the corresponding bromo- and iodobenzenes worked well. Therefore, we strongly believed that the highly efficient formation of **2a** from **6b** may depend on the structural nature of **6b** rather than the differences between the intermolecular and intramolecular *O*-arylations.



Scheme 6. Cu(I)-catalyzed intermolecular *O*-arylations of **8** and PhCl.

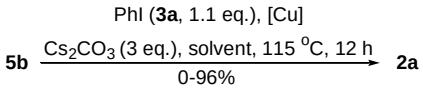
As shown in Scheme 7, when **5b** was treated with CuI in the absence of PhI (**3a**), it was recovered in 93% yield without any intramolecular *O*-arylated product phenoxazine (**1**). Thus, we hypothesized that the Cu(I)-catalyzed *O*-arylations of **5b**, **6b** and **8** may be mainly controlled by the electronic effect rather than by the steric effect. Those phenomena may arise from the fact that **5b**, **6b** and **8** are also redox-active ligands, which may have different abilities to store and release electrons during the catalytic reactions,[14] but how remains unknown.



Scheme 7. Cu(I)-catalyzed intramolecular *O*-arylations of **5b**.

Next, the reaction solvents and copper-resources were screened by using the conversion of **5b** into **2a** as a model reaction. As shown in Table 1, the best result was still obtained when the amounts of PhI (**3a**) and CuI were reduced as low as 1.1 equiv and 0.05 equiv, respectively, in *n*-butylnitrile (entry 3). But, all other solvents gave relatively lower yields of **2a** (entries 6-13). Although CuI, CuCl, and CuCN (entries 3, 14 and 15) gave comparable yields of **2a**, we preferred to choose CuI for its chemical stability and easy performance.

Table 1. Effects of the copper resources on the cycloaddition[a]

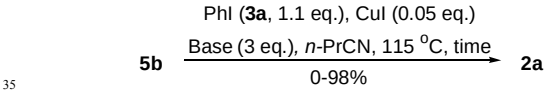


Entry	[Cu]-resource (eq.)	Solvent	**2a** (%)[b]
1	CuI (0.2)	*n*-PrCN	96
2	CuI (0.1)	*n*-PrCN	96
3	CuI (0.05)	*n*-PrCN	96
4	CuI (0.04)	*n*-PrCN	90
5	CuI (0.00)	*n*-PrCN	6
6	CuI (0.05)	DMF	86
7	CuI (0.05)	PhMe	83
8	CuI (0.05)	1,4-dioxane	52
9	CuI (0.05)	$(CH_2OH)_2$	49
10	CuI (0.05)	$(CH_2Cl)_2$	20
11	CuI (0.05)	MeCN	12
12	CuI (0.05)	THF	10
13	CuI (0.05)	MeOH	trace
14	CuCl (0.05)	*n*-PrCN	95
15	CuCN (0.05)	*n*-PrCN	92
16	$Cu(OAc)_2.H_2O$ (0.05)	*n*-PrCN	82
17	Cu_2O (0.05)	*n*-PrCN	75
18	CuBr (0.05)	*n*-PrCN	73
19	$Cu(CO_2)_2.4H_2O$ (0.05)	*n*-PrCN	63
20	$CuF_2.H_2O$ (0.05)	*n*-PrCN	31

[a]The mixture of **5b** (1 mmol), **3a**, [Cu] and Cs_2CO_3 in solvent (2 mL) in a Schlenk tube was heated under N_2. [b]Isolated yields were obtained.

Then, the effects of reaction time and bases were tested. As shown in Table 2, the yield of **2a** was increased by increasing the reaction time (entries 1-3). Both Cs_2CO_3 (entry 1) and K_3PO_4 (entry 4) were suitable bases for this reaction, but all others were inactive (entries 5-8). Finally, the entry 3 was assigned as our standard conditions.

Table 2. Effects of reaction time and bases[a]



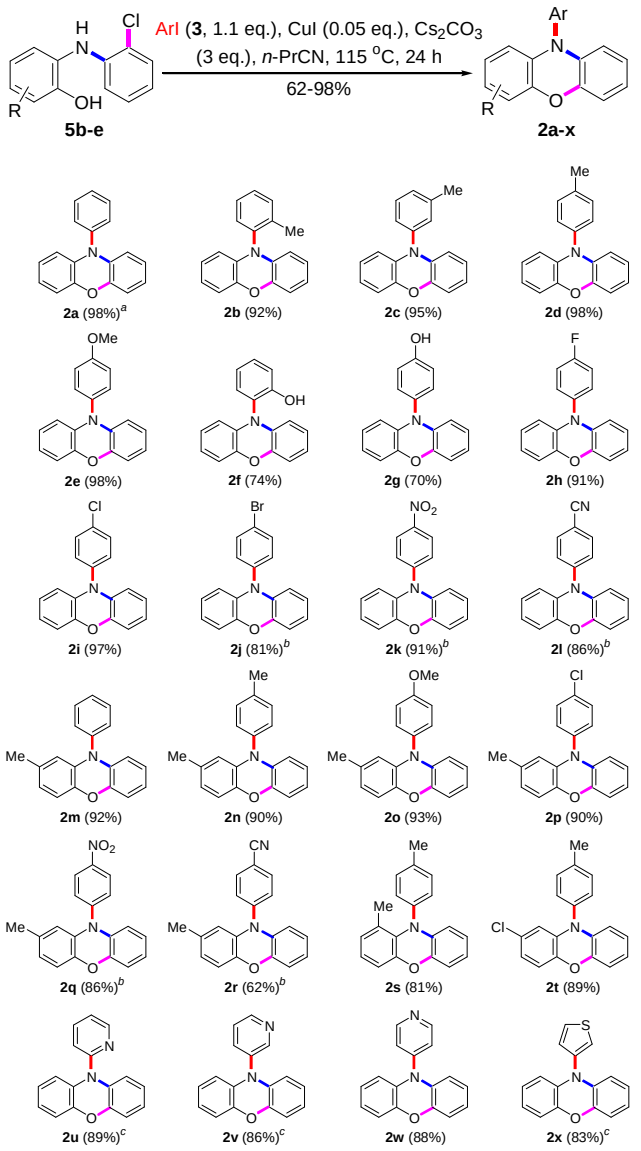
Entry	Time (h)	Base	**2a** (%)[b]
1	6	Cs_2CO_3	67
2	12	Cs_2CO_3	96
3	24	Cs_2CO_3	98
4	12	K_3PO_4	94
5	12	K_2CO_3	45
6	12	Na_2CO_3	0
7	12	NEt_3	0
8	12	pyridine	0

[a]The mixture of **5b** (1 mmol), **3a**, CuI and a base in *n*-PrCN (2 mL) in a Schlenk tube was heated under N_2. [b]Isolated yields were obtained.

To generalize this novel method, the substrate scope was tested. As shown in Scheme 8, all desired products **2a-2x** were obtained in good to excellent yields and some of them (**2a**, **2d**, **2e**, and **2i**) were obtained in almost quantitative yields. However, the iodobenzenes substituted by -Br, $-NO_2$ and -CN could not give the satisfactory yields of products (**2j-2l** and **2q-2r**) under the standard conditions. It may be caused by the fact that 4-bromo-iodobenzene has two reaction sites and both of them could carry out the Cu(I)-catalyzed *N*-arylations. The $-NO_2$ or –CN substituted iodobenzenes may have high reactivity to carry out both Cu(I)-catalyzed *N*- and *O*-arylations simultaneously with the substrates. But, these problems could be solved easily by heating the reaction mixture at 65 °C for the first 6 h to finish the *N*-arylation and then at 115 °C for another 18 h to finish the *O*-arylation. Unfortunately, dissatisfactory yields of **2a** (34%), **2d** (23%), and **2q** (70%) were obtained when bromobenzene, 2-bromo-toluene, and 2-bromo-nitrobenzene were used as the *N*-arylating reagents.

Conclusions

A novel Cu(I)-catalyzed tandem reaction for *N*- and *O*-arylations of 2-[*N*-(2-chlorophenyl)amino]phenols was developed, by which a series of *N*-phenyl phenoxazines were prepared efficiently in "one-pot". This work not only provides a general route for efficient synthesis of *N*-phenyl phenoxazines from the commercially available 2-aminophenols in two steps, but also presents an interesting example to construct the complicated molecules entirely by Cu(I)-catalyzed arylations from the simple starting materials.



[a] Isolated yields were obtained for all products.
[b] The reaction proceeded at 65 °C for 6 h firstly and then at 115 °C for another 18 h.
[c] 0.1 Equiv of CuI was used.

Scheme 8. Substrate Scope of the Tandem Reaction

Experimental

General information

All melting points were determined on a Yanaco melting point apparatus and were uncorrected. IR spectra were recorded as KBr pellets on a Nicolet FT-IR 5DX spectrometer. All spectra of ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) were recorded on a JEOL JNM-ECA 300 spectrometer in $CDCl_3$ (otherwise as indicated). TMS was used as an internal reference and *J* values are given in Hz. HRMS were obtained on a Bruker microTOF-Q II spectrometer. The substituted 2-[*N*-(2-chlorophenyl)amino]-phenols **5b** (R = H), **5c** (R = 4-Me), **5d** (R = 3-Me) and **5e** (R = 4-Cl) were prepared by the reported procedure[9b] (See Supporting Information).

A Typical Procedure for the Preparation of 10-Phenyl-phenoxazine (2a).

The suspension of 2-[*N*-(2-chlorophenyl)amino]phenol (**5b**, 220 mg, 1 mmol), CuI (9.5 mg, 0.05 mmol) and Cs_2CO_3 (977 mg, 3 mmol) in *n*-PrCN (2 mL) in a Schlenk tube was degassed. Then iodobenzene (**3a**, 224 mg, 1.1 mmol) was added by a syringe. After the resultant mixture was stirred at 115 °C for 24 h under N_2, the solid was filtered off. Then the solvent was evaporated on a rotavapor and the residue was purified by a column chromatography [silica gel, 1% EtOAc in petroleum ether (60–90 °C)] to give 255 mg (98%) of **2a** as white crystals, mp 140–141 °C (lit.[4] 138–139 °C); ^{1}H NMR δ 7.60-7.56 (m, 2H), 7.48-7.44 (m, 1H), 7.33 (d, J = 5.8, 2H), 6.68-6.55 (m, 6H), 5.89 (d, J = 5.8, 2H) ppm; ^{13}C NMR δ 143.9 (2C), 138.9, 134.4, 131.0 (2C), 130.8 (2C), 128.4 (2C), 123.2 (2C), 121.2 (2C), 115.4 (2C), 113.2 (2C) ppm.

The similar procedure was used for the preparation of products **2b-2x**.

*10-(2-Methylphenyl)-phenoxazine (**2b**).* White solid, mp 171–173 °C; IR ν 1633, 1485, 1334, 1269 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 7.56-7.53 (m, 1H), 7.48-7.46 (m, 2H), 7.34-7.31 (m, 1H), 6.75-6.62 (m, 6H), 5.71-5.68 (m, 2H), 2.14 (s, 3H) ppm; ^{13}C NMR (DMSO-d_6) δ 143.9 (2C), 138.9, 136.8, 133.4, 132.2 (2C), 131.0, 128.9 (2C), 128.6 (2C), 123.4 (2C), 121.1, 115.4, 112.6 (2C), 17.6 ppm; HRMS (ESI-TOF) (*m/z*): Calcd for $C_{19}H_{15}NO$, $[M]^+$ 273.1148; found 273.1150.

*10-(3-Methylphenyl)-phenoxazine (**2c**).* White solid, mp 123–125 °C; IR ν 1636, 1485, 1335, 1269 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 7.58-7.52 (m, 1H), 7.35 (d, J = 7.5, 1H), 7.21-7.17 (m, 2H), 6.74-6.63 (m, 6H), 5.86-5.83 (m, 2H), 2.39 (s, 3H) ppm; ^{13}C NMR (DMSO-d_6) δ 143.9 (2C), 141.2, 138.8, 134.4 (2C), 131.1, 130.7, 129.2, 127.6, 123.1 (2C), 121.1 (2C), 115.3 (2C), 113.2 (2C), 21.3 ppm; HRMS (ESI-TOF) (*m/z*): Calcd for $C_{19}H_{15}NO$, $[M]^+$ 273.1148; found 273.1145.

*10-(4-Methylphenyl)-phenoxazine (**2d**).* White solid, mp 124–126 °C; IR ν 2606, 1644, 1484, 1332, 1266 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 7.44 (d, J = 7.9, 2H), 7.24 (d, J = 7.9, 2H), 6.71-6.58 (m, 6H), 5.83-5.80 (m, 2H), 2.39 (s, 3H) ppm; ^{13}C NMR (DMSO-d_6) δ 143.1 (2C), 138.3, 135.6, 134.1 (2C), 131.9 (2C), 130.1 (2C), 123.7 (2C), 121.4 (2C), 115.2 (2C), 113.1 (2C), 20.8 ppm; HRMS (ESI-TOF) (*m/z*): Calcd for $C_{19}H_{15}NO$, $[M]^+$ 273.1148; found 273.1148.

*10-(4-Methoxyphenyl)-phenoxazine (**2e**).* White solid, mp 170–171 °C; IR ν 3062, 1590, 1486, 1335, 1243 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 7.30 (d, J = 8.6, 2H), 7.18 (d, J = 8.9, 2H), 6.72-6.61 (m, 6H), 5.86-5.82 (m, 2H), 3.83 (s, 3H) ppm; ^{13}C NMR (DMSO-d_6) δ 159.0, 143.1 (2C), 134.3 (2C), 131.5 (2C), 130.5, 123.7 (2C), 121.2 (2C), 116.5 (2C), 115.2 (2C), 113.1 (2C), 55.4 ppm; HRMS (ESI-TOF) (*m/z*): Calcd for $C_{19}H_{15}NO_2$, $[M]^+$ 289.1097; found 289.1093.

*10-(2-Hydroxyphenyl)-phenoxazine (**2f**).* White solid, mp 152–153 °C; IR ν 3446, 1590, 1488, 1327, 1272 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 9.79 (s, 1H), 7.33-7.27 (m, 1H), 7.18 (d, J = 7.9, 1H), 7.06 (d, J = 8.3, 1H), 6.99-6.93 (m, 1H), 6.68-6.54 (m, 6H), 5.79-5.74 (m, 2H) ppm; ^{13}C NMR (DMSO-d_6, 125 MHz, 70 °C)

δ155.8, 144.0 (2C), 134.2 (2C), 132.1, 130.6, 124.7, 124.0 (2C), 121.5 (2C), 121.3, 118.5. 115.5 (2C), 113.4 (2C) ppm; HRMS (ESI-TOF) (*m/z*): Calcd for $C_{18}H_{13}NO_2$, $[M]^+$ 275.0941; found 275.0945.

10-(4-Hydroxyphenyl)-phenoxazine ***(2g)***. White solid, mp 181–183 °C; IR ν3459, 1631, 1484, 1332, 1265 cm^{-1}; ^1H NMR (DMSO-d_6) δ9.85 (s, 0.94H), 7.18 (d, J = 8.6, 2H), 7.02 (d, J = 8.6, 2H), 6.73-6.62 (m, 6H), 5.92-5.88 (m, 2H) ppm; ^{13}C NMR (DMSO-d_6, 125 MHz, 70 °C) δ158.0, 143.9 (2C), 135.1 (2C), 131.8 (2C), 129.8, 124.1 (2C), 121.6 (2C), 118.3 (2C), 115.6 (2C), 113.7 (2C) ppm; HRMS (ESI-TOF) (*m/z*): Calcd for $C_{18}H_{13}NO_2$, $[M]^+$ 275.0941; found 275.0940.

10-(4-Fluorophenyl)-phenoxazine ***(2h)***. White solid, mp 118–120 °C; IR ν1631, 1484, 1324, 1266 cm^{-1}; ^1H NMR (DMSO-d_6) δ7.51-7.39 (m, 4H), 6.73-6.59 (m, 6H), 5.83-5.78 (m, 2H) ppm; ^{13}C NMR (DMSO-d_6) δ162.1 (d, J = 246.7), 143.9 (2C), 134.8, 134.3 (2C), 132.7 (d, J = 8.6, 2C), 123.2 (2C), 121.4 (2C), 118.1 (d, J = 22.2, 2C), 115.5 (2C), 113.1 (2C) ppm; HRMS (ESI-TOF) (*m/z*): Calcd for $C_{18}H_{12}FNO$, $[M]^+$ 277.0897; found 277.0894.

10-(4-Chlorophenyl)-phenoxazine ***(2i)***. White solid, mp 178–180 °C; IR ν1628, 1485, 1335, 1274 cm^{-1}; ^1H NMR (DMSO-d_6) δ7.71 (d, J = 8.6, 2H), 7.45 (d, J = 8.6, 2H), 6.74-6.61 (m, 6H), 5.86-5.83 (m, 2H) ppm; ^{13}C NMR (DMSO-d_6) δ143.1 (2C), 137.3, 133.6 (2C), 133.3, 132.6 (2C), 131.5 (2C), 123.8 (2C), 121.7 (2C), 115.4 (2C), 113.2 (2C) ppm; HRMS (ESI-TOF) (*m/z*): Calcd for $C_{18}H_{12}ClNO$, $[M]^+$ 293.0602; found 293.0601.

10-(4-Bromophenyl)-phenoxazine ***(2j)***. White solid, mp 184–185 °C (lit.[4] 200–202 °C); IR ν3031, 1629, 1484, 1332, 1266 cm^{-1}; ^1H NMR (DMSO-d_6) δ7.84 (d, J = 8.3, 2H), 7.54 (d, J = 8.6, 2H), 6.75-6.62 (m, 6H), 5.87-5.84 (m, 2H) ppm; ^{13}C NMR (DMSO-d_6) δ143.1 (2C), 137.7, 134.5 (2C), 133.6 (2C), 133.0 (2C), 123.8 (2C), 121.9, 121.7 (2C), 115.4 (2C), 113.2 (2C) ppm; HRMS (ESI-TOF) (*m/z*): Calcd for $C_{18}H_{12}BrNO$, $[M]^+$ 337.0097; found 337.0093.

10-(4-Nitrophenyl)-phenoxazine ***(2k)***. Red solid, mp 191-193 °C; IR ν1636, 1520, 1487, 1337, 1271 cm^{-1}; ^1H NMR (DMSO-d_6) δ8.47 (d, J = 9.0, 2H), 7.74 (d, J = 8.9, 2H), 6.83-6.69 (m, 6H), 6.02 (d, J = 4.9, 2H) ppm; ^{13}C NMR (DMSO-d_6) δ146.8, 145.0, 143.6 (2C), 132.9 (2C), 131.5 (2C), 126.6 (2C), 123.8 (2C), 122.4 (2C), 115.7 (2C), 114.0 (2C) ppm; HRMS (ESI-TOF) (*m/z*): Calcd for $C_{18}H_{12}N_2O_3$, $[M]^+$ 304.0842; found 304.0845.

10-(4-Cyanophenyl)-phenoxazine ***(2l)***. Yellowish solid, mp 158–159 °C; IR ν2226, 1633, 1596, 1488, 1333, 1273 cm^{-1}; ^1H NMR (DMSO-d_6) δ8.14 (d, J = 8.6, 2H), 7.67 (d, J = 8.2, 2H), 6.79-6.68 (m, 6H), 5.92 (d, J = 7.6, 2H) ppm; ^{13}C NMR (DMSO-d_6) δ143.3 (2C), 143.1, 135.5 (2C), 133.0 (2C), 131.7 (2C), 123.8 (2C), 122.1 (2C), 118.3, 115.6 (2C), 113.5 (2C), 111.4 ppm; HRMS (ESI-TOF) (*m/z*): Calcd for $C_{19}H_{12}N_2O$, $[M]^+$ 284.0944; found 284.0940.

2-Methyl-10-phenyl-10H-phenoxazine ***(2m)***. White solid, mp 92–94 °C; IR ν1628, 1588, 1487, 1329, 1266 cm^{-1}; ^1H NMR (DMSO-d_6) δ7.71-7.39 (m, 5H), 6.71-6.46 (m, 5H), 5.82-5.80 (m, 1H), 5.65 (s, 1H), 1.96 (s, 3H) ppm; ^{13}C NMR (DMSO-d_6) δ144.0, 141.7, 139.0, 134.4, 133.9, 132.6, 131.0 (2C), 130.8 (2C), 128.4, 123.0, 121.3, 121.1, 115.3, 115.0, 113.9, 113.2, 20.8 ppm; HRMS (ESI-TOF) (*m/z*): Calcd for $C_{19}H_{15}NO$, $[M]^+$ 273.1148; found 273.1147.

2-Methyl-10-(4-methylphenyl)-phenoxazine ***(2n)***. White solid, mp 71–73 °C; IR ν1629, 1585, 1488, 1331, 1266 cm^{-1}; ^1H NMR (DMSO-d_6) δ7.47 (d, J = 7.9, 2H), 7.26 (d, J = 8.6, 2H), 6.72-6.60 (m, 4H), 6.46 (d, J = 7.9, 1H), 5.83-5.80 (m, 1H), 5.66 (s, 1H), 2.42 (s, 3H), 1.96 (s, 3H) ppm; ^{13}C NMR (DMSO-d_6) δ144.0, 141.7, 138.3, 136.2, 134.5, 134.0, 132.6, 131.6 (2C), 130.4, 122.9 (2C), 121.2, 121.0, 115.2, 115.0, 113.9, 113.2, 21.2, 20.8 ppm; HRMS (ESI-TOF) (*m/z*): Calcd for $C_{20}H_{17}NO$, $[M]^+$ 287.1305; found 287.1312.

2-Methyl-10-(4-methoxyphenyl)-phenoxazine ***(2o)***. White solid, mp 102–103 °C; IR ν1604, 1505, 1488, 1331, 1245 cm^{-1}; ^1H NMR (DMSO-d_6) δ7.26 (d, J = 8.6, 2H), 7.15 (d, J = 8.9, 2H), 6.65-6.55 (m, 4H), 6.41 (d, J = 7.9, 1H), 5.80-5.77 (m, 1H), 5.63 (s, 1H), 3.81 (s, 3H), 1.93 (s, 3H) ppm; ^{13}C NMR (DMSO-d_6) δ159.3, 144.1, 141.8, 134.7, 134.3, 132.7, 131.8 (2C), 131.4, 123.0, 121.2, 121.0, 116.2 (2C), 115.2, 115.0, 113.9, 113.2, 55.5, 20.8 ppm; HRMS (ESI-TOF) (*m/z*): Calcd for $C_{20}H_{17}NO_2$, $[M]^+$ 303.1254; found 303.1245.

2-Methyl-10-(4-chlorophenyl)-phenoxazine ***(2p)***. White solid, mp 106–108 °C; IR ν1628, 1488, 1331, 1272 cm^{-1}; ^1H NMR δ7.57 (d, J = 8.6, 2H), 7.28 (d, J = 8.6, 1H), 6.70-6.43 (m, 6H), 5.88 (d, J = 7.9, 1H), 5.70 (s, 1H), 2.02 (s, 3H) ppm; ^{13}C NMR δ144.0, 141.7, 137.6, 134.2, 134.0, 133.6, 132.8, 132.4 (2C), 131.4 (2C), 132.0, 121.7, 121.5, 115.5, 115.2, 113.9, 113.2, 20.8 ppm; HRMS (ESI-TOF) (*m/z*): Calcd for $C_{19}H_{14}ClNO$, $[M]^+$ 307.0758; found 307.0756.

2-Methyl-10-(4-nitrophenyl)-phenoxazine ***(2q)***. Red solid, mp 184–185 °C; IR ν1641, 1514, 1493, 1343, 1328, 1276 cm^{-1}; ^1H NMR (DMSO-d_6) δ8.43 (d, J = 8.9, 2H), 7.69 (d, J = 8.9, 2H), 6.78-6.63 (m. 4H), 6.53 (d, J = 7.9, 1H), 5.97 (d, J = 7.6, 1H), 5.81 (s, 1H) , 1.96 (s, 3H) ppm; ^{13}C NMR (DMSO-d_6) δ146.9, 145.8, 144.4, 142.1, 133.1, 133.0, 132.6, 131.3 (2C), 126.4 (2C), 123.1, 122.7, 122.4, 116.0, 115.7, 114.4, 113.8, 20.8 ppm; HRMS (ESI-TOF) (*m/z*): Calcd for $C_{19}H_{14}N_2O_3$, $[M]^+$ 318.0999; found 318.0998.

2-Methyl-10-(4-Cyanophenyl)-phenoxazine ***(2r)***. Yellowish solid, mp 132–133 °C; IR ν2221, 1637, 1491, 1331, 1268 cm^{-1}; ^1H NMR (DMSO-d_6) δ8.09 (d, J = 8.2, 2H), 7.62 (d, J = 8.2, 2H), 6.73-6.60 (m, 4H), 6.48 (d, J = 7.9, 1H), 5.85 (d, J = 7.2, 1H), 5.69 (s, 1H), 1.94 (s, 3H) ppm; ^{13}C NMR (DMSO-d_6) δ144.2, 143.8, 141.8, 134.9 (2C), 131.2, 132.9, 132.8, 131.8 (2C), 123.1, 122.4, 122.2, 118.1, 115.8, 115.6, 114.1, 113.4, 112.1, 20.8 ppm; HRMS (ESI-TOF) (*m/z*): Calcd for $C_{20}H_{14}N_2O$, $[M]^+$ 298.1101; found 298.1100.

1-Methyl-10-(4-methylphenyl)-phenoxazine ***(2s)***. White solid, mp 82–84 °C; IR ν1649, 1504, 1470, 1314, 1274 cm^{-1}; ^1H NMR

(DMSO-d_6) δ7.26-7.11 (m, 5H), 7.00-6.81 (m, 6H), 2.23 (s, 3H), 1.78 (s, 3H) ppm; ^{13}C NMR (DMSO-d_6) δ151.2, 150.1, 146.8, 135.9, 134.4, 132.9, 132.2, 129.8 (2C), 126.2, 125.3 (2C), 124.5, 124.4, 123.3, 122.4, 116.4, 114.2, 20.8, 18.8 ppm; HRMS (ESI-TOF) (*m/z*): Calcd for $C_{20}H_{17}NO$, $[M]^+$ 287.1305; found 287.1307.

2-Chloro-10-(4-methylphenyl)-phenoxazine ***(2t).*** White solid, mp 105–107 °C; IR ν2923, 1629, 1485, 1330, 1265 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ7.47 (d, J = 7.9, 2H), 7.29 (d, J = 8.2, 2H), 6.74-6.61 (m, 5H), 5.84-5.81 (m, 1H), 5.70 (d, J = 2.1, 1H), 2.40 (s, 3H) ppm; ^{13}C NMR (DMSO-d_6) δ143.7, 142.6, 138.8, 135.6, 135.4, 133.7, 131.9 (2C), 130.1 (2C), 128.0, 123.4, 121.6, 120.4, 116.0, 115.3, 113.5, 113.2, 21.2 ppm; HRMS (ESI-TOF) (*m/z*): Calcd for $C_{19}H_{14}ClNO$, $[M]^+$ 307.0758; found 307.0762.

10-(2-Pyridyl)-phenoxazine ***(2u).*** White solid, mp 103–104 °C; IR ν3061, 1587, 1489, 1329, 1274, 1043 cm^{-1}; ^{1}H NMR δ8.69-8.67 (m, 1H), 7.88-7.82 (m, 1H), 7.38-7.26 (m, 2H), 6.81-6.68 (m, 6H), 6.43-6.40 (m, 2H) ppm; ^{13}C NMR δ153.7, 150.5, 145.4 (2C), 139.3, 132.8 (2C), 123.2 (2C), 122.6 (2C), 122.2, 122.1, 115.9 (2C), 115.6 (2C) ppm; HRMS (ESI-TOF) (*m/z*): Calcd for $C_{17}H_{12}N_2O$, $[M+H]^+$ 261.1022; found 261.1020.

10-(3-Pyridyl)-phenoxazine ***(2v).*** White solid, mp 147–149 °C; IR ν 3050, 1588, 1485, 1329, 1270, 1021 cm^{-1}; ^{1}H NMR δ8.74 (d, J = 4.1, 1H), 8.64 (s, 1H), 7.76-7.72 (m, 1H), 7.57-7.53 (m, 1H), 6.76-6.58 (m, 6H), 5.87 (d, J = 7.6, 2H) ppm; ^{13}C NMR δ152.8, 149.5, 143.9 (2C), 139.0, 135.7, 133.8 (2C), 125.4, 123.3 (2C), 121.9 (2C), 115.7 (2C), 113.1 (2C) ppm; HRMS (ESI-TOF) (*m/z*): Calcd for $C_{17}H_{12}N_2O$, $[M+H]^+$ 261.1022; found 261.1025.

10-(4-Pyridyl)-phenoxazine ***(2w).*** White solid, mp 118–120 °C; IR ν 3061, 1578, 1489, 1332, 1274 cm^{-1}; ^{1}H NMR δ8.79 (d, J = 4.8, 2H), 7.32 (d, J = 6.2, 2H), 6.81-6.68 (m, 6H), 6.19 (d, J = 7.6, 2H) ppm; ^{13}C NMR δ152.6 (2C), 147.9, 145.1 (2C), 132.5 (2C), 123.5 (2C), 123.3 (2C), 122.8 (2C), 116.1 (2C), 114.8 (2C) ppm; HRMS (ESI-TOF) (*m/z*): Calcd for $C_{17}H_{12}N_2O$, $[M+H]^+$ 261.1022; found 261.1021.

10-(3-Thienyl)-phenoxazine ***(2x).*** White solid, mp 123–125 °C; IR ν 3095, 1531, 1481, 1321, 1268 cm^{-1}; ^{1}H NMR δ7.56-7.54 (m, 1H), 7.35-7.34 (m, 1H), 7.02 (d, J = 4.8, 1H) 6.70-6.60 (m, 6H), 6.07-6.04 (m, 2H) ppm; ^{13}C NMR δ144.0 (2C), 136.8, 134.0 (2C), 127.7, 127.2, 124.7, 123.3 (2C), 121.5 (2C), 115.4 (2C), 113.3 (2C) ppm; HRMS (ESI-TOF) (*m/z*): Calcd for $C_{17}H_{12}N_2O$, $[M]^+$ 265.0561; found 265.0557.

Acknowledgements

This work was supported by the National Natural Scientific Foundation of China (No. 21372142, 21472107 and 21072112).

Notes and references

[a] *Department of Chemistry, Tsinghua University, Beijing 100084, P. R. China. Fax: +86-10-62771149; Tel: +86-10-62795380; E-mail: yfh@mail.tsinghua.edu.cn and wangxinyan@mail.tsinghua.edu.cn.*

† Electronic Supplementary Information (ESI) available: [Characterizations of compounds **5b-e**, ^{1}H and ^{13}C NMR spectra for products **2a-2x** and CIF file for the single crystal X-ray diffraction analysis of **2a**]. See DOI: 10.1039/b000000x/

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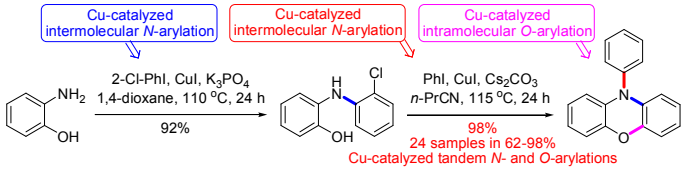
Graphical Abstract

A General Route for Synthesis of *N*-Aryl Phenoxazines via Copper(I)-Catalyzed *N*-, *N*-, and *O*-Arylations of 2-Aminophenols

Nan Liu,[a] Bo Wang,[a] Wenwen Chen,[a] Chulong Liu,[a] Xinyan Wang,*[a] and Yuefei Hu*[a]



A novel copper(I)-catalyzed tandem reaction of *N*- and *O*-arylations was developed and a general route for synthesis of *N*-aryl phenoxazines via copper-catalyzed *N*-, *N*-, and *O*-arylations of 2-aminophenols was established.