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Copper-Catalyzed Regioselective C-H Amination of Phenol Derivatives with Assistance of Phenanthroline-Based Bidentate Auxiliary

Kazutaka Takamatsu,[†] *Yoshihiro Hayashi,*[‡] *Susumu Kawauchi,*[‡] *Koji Hirano,**[,†] *and Masahiro Miura**[,†]

[†] Department of Applied Chemistry, Graduate School of Engineering, Osaka University, Suita, Osaka 565-0871, Japan

[‡] Department of Chemical Science and Engineering, School of Materials and Chemical Technology, Tokyo Institute of Technology, 2-12-1 O-okayama, Meguro-ku, Tokyo 152-8552, Japan

ABSTRACT: A copper-catalyzed regioselective direct amination of phenol derivatives with diarylamines via phenanthroline-based bidentate auxiliary directed C-H cleavage has been developed. This reaction proceeds smoothly with only a copper salt and air as a terminal

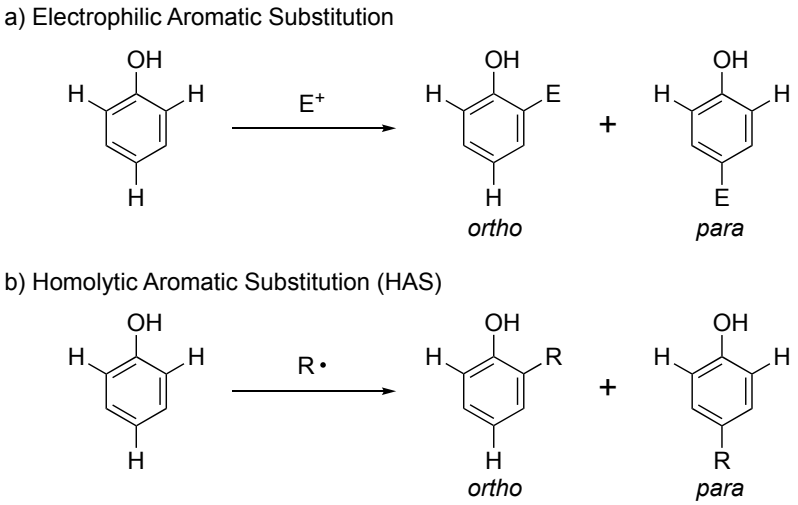
oxidant to produce the corresponding *ortho*-aminophenols in good yields. Moreover, the directing group can be easily attached, detached, and recycled. Additionally, preliminary computational studies of the reaction with DFT have also been performed.

Key words: amination, bidentate auxiliary, copper, C–H functionalization, phenols

INTRODUCTION

Phenol derivatives are important classes of compounds in the food, material, and pharmaceutical fields.[1] Therefore, the efficient strategy to functionalize them are highly desirable. The aromatic electrophilic substitution is one of the most classical and promising methods for the direct transformation of phenols, and it is in common use for the synthesis of various useful compounds (Scheme 1a).[2] Recently, homolytic aromatic substitution (HAS) has also been developed along with rapid advances made in radical chemistry in past thirty years (Scheme 1b).[3] However, the low regioselectivity and narrow substrate scope are often problematic points of these reactions.

Scheme 1. C-H Functionalization of Phenols



On the other hand, the transition-metal-catalyzed, directing-group-assisted C-H functionalization has been attracted much attention as the more atom- and step-economical methods than traditional cross-coupling reactions with organic halides and/or organometallic reagents.[4,5] This strategy overcomes the aforementioned regioselectivity issues in the direct functionalization of phenols, and a variety of

monodentate directing groups including pyridyl/pyrimidyl,[6] ester,[7] carbamate,[8] silyl/silanol,[9] and transient phosphite[10] are developed for the valuable C-H functionalization reactions.[11] However, noble transition metals such as palladium and rhodium are essential in most cases.

Recently, well-designed bidentate directing groups enable otherwise challenging C-H bond functionalization. In particular, since the seminal work by Daugulis, various bidentate auxiliaries have been developed for the regioselective C-H functionalization of carboxylic acids and amines (Figure 1).[12] In contrast, such a bidentate chelation approach has not been reported for the direct functionalization of phenols, to the best of our knowledge. There is only one example of platinum-containing metallacycle formation in a stoichiometric manner (Scheme 2).[13] Herein, we report a new protocol for the base-metal-catalyzed direct functionalization of phenols by using a phenanthroline-based bidentate auxiliary: a copper-catalyzed regioselective C-H amination of phenol derivatives with diarylamines is described (Scheme 3). This reaction proceeds smoothly with only a copper salt and air as a terminal oxidant to produce the corresponding *ortho*-aminophenols. The phenols can also be regarded as triarylamines, which are widely utilized in optoelectronic materials.[14] This reaction is one of limited successful examples of triarylamine synthesis via directed C-H cleavage.[15] Moreover, the directing group can be easily attached, detached, and recycled. Additionally, the original phenol moiety can be readily manipulated to deliver a variety of functionalized triarylamines.

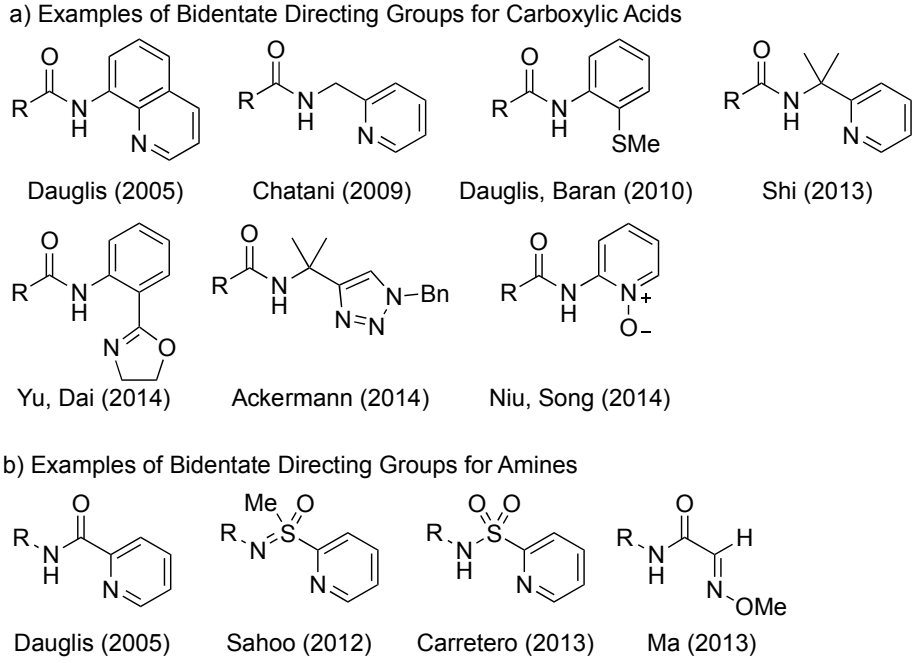
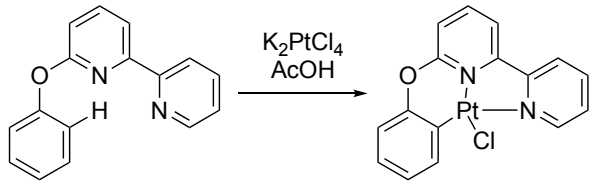
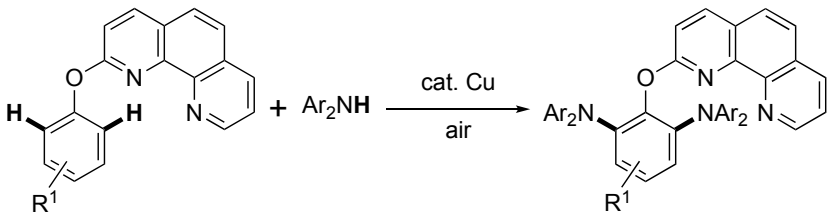


Figure 1. Examples of bidentate directing groups for C-H functionalization of carboxylic acids and amines

Scheme 2. Bidentate Directing Group Assisted Pt-Containing Metallacycle Formation with Phenol Derivatives



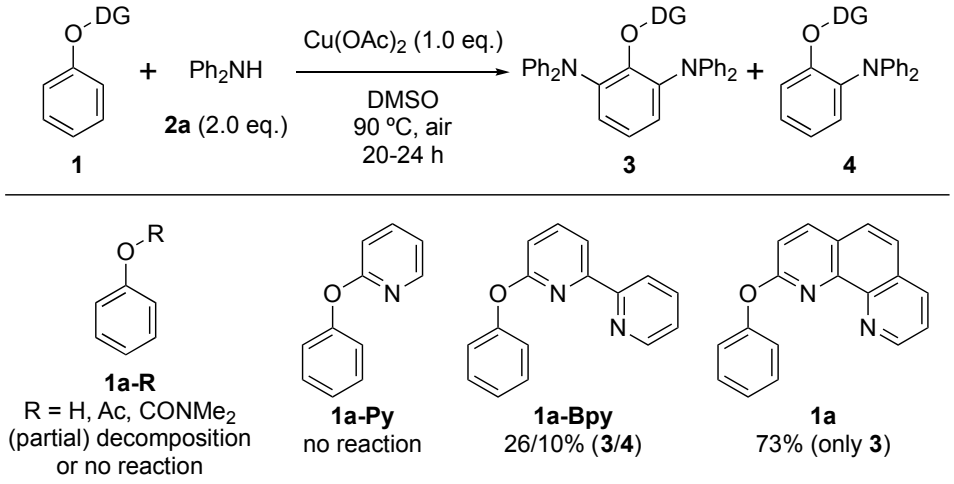
Scheme 3. Copper-Catalyzed C-H Amination of Phenol Derivatives with Diarylamines by Using a Phenanthroline-type Bidentate Directing Group



RESULTS and DISCUSSION

Our group[16] and others[17] have focused on inexpensive, less toxic, and abundant copper salts, and developed copper-mediated unique C-H functionalization reactions. In particular, nitrogen-based bidentate directing groups allow such a base metal to be adopted in place of noble transition metals and sometimes promote otherwise challenging C-H transformations. We envisioned that suitable N,N-bidentate directing groups should be effective not only for carboxylic acids and amines but also for phenols. We thus selected the C-H amination of phenols with diarylamines as the model reaction and tested this hypothesis (Scheme 4). With $Cu(OAc)_2$ (1.0 eq.) under air in DMSO at 90 ºC, the reaction of simple phenol (**1a-H**), phenyl acetate (**1a-Ac**), phenyl dimethylcarbamate **1a-CONMe$_2$**, or phenoxypyridine (**1a-Py**) with diphenylamine (**2a**) did not produce any aminated products. In contrast, a phenol derivative that bears the bipyridyl group (**1a-Bpy**) reacted with **2a** to form mono- and di-aminated products in 10 and 26% yields, respectively. Moreover, the reaction efficiency was greatly enhanced with the phenanthrolyl group (**1a**) to produce the targeted di-aminated product **3aa** in 73% yield with high chemoselectivity.

Scheme 4. Effects of Directing Groups on Oxygen in Copper-Mediated C-H Amination of Phenols 1 with Diphenylamine (2a)



The structure of **3aa** was unambiguously confirmed by NMR, HRMS, and X-ray analysis.[18] The starting **1a** can be easily synthesized from phenol and 2-chloro-1,10-phenanthroline (**5**), which is commercially available but can also be readily prepared on a deca-gram scale from inexpensive phenanthroline monohydrate in two steps (Scheme 5).[19] Thus, we identified **1a** to be the promising substrate and performed additional optimization studies to increase the product yield and turnover of copper (Table 1). We first examined the amount of copper catalyst (entries 1-3). The yield remained even with 50 mol % $Cu(OAc)_2$ (entry 2), but the reaction was not completed with 20 mol % catalyst loading, and mono-aminated **4aa** was formed as the major product (entry 3). We also tried the selective mono-amination by decreasing amounts of diphenylamine (**2a**), but the di-aminated product **3aa** was always competitively formed (entries 4 and 5). Neither increasing and decreasing the reaction temperature improved the product yield (entries 6 and 7). The addition of acid or base decreased the yield (entries 8-11). Attempts to apply other oxidants under N_2 also remained unsuccessful (entries 12-14). We next surveyed various copper catalysts, with $Cu(OPiv)_2$ proving to be optimal (entries 15-18). Finally, we were pleased to find that the C-H amination reaction proceeded smoothly in the presence of 30 mol % $Cu(OPiv)_2$ in DMSO at 90 ºC for 23 hours to produce **3aa** in 83% yield (entry 19): the 30 mol % catalyst loading was essential for the full consumption of starting **1a** under current conditions Notably, the yield was significantly diminished under N_2 even with a stoichiometric amount of $Cu(OPiv)_2$

(entry 20), thus indicating an important role of molecular oxygen in this reaction. The control experiment without $Cu(OPiv)_2$ confirmed the necessity of the copper salt in this reaction (entry 21).

Scheme 5. Synthesis of Directing Group 5 and Substrate 1a

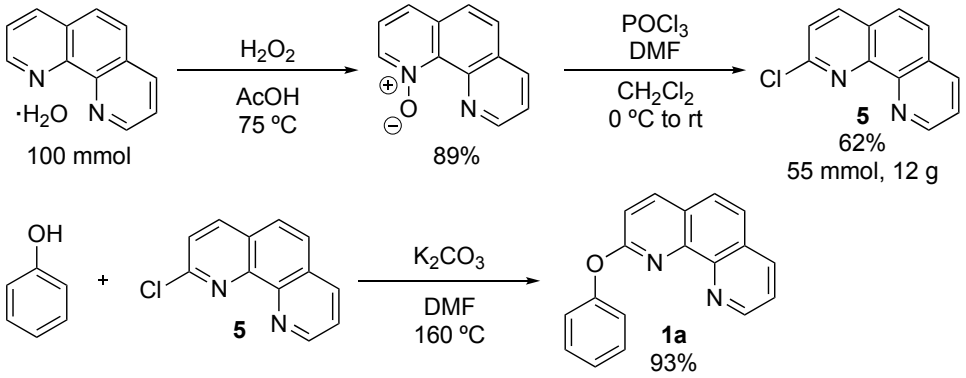
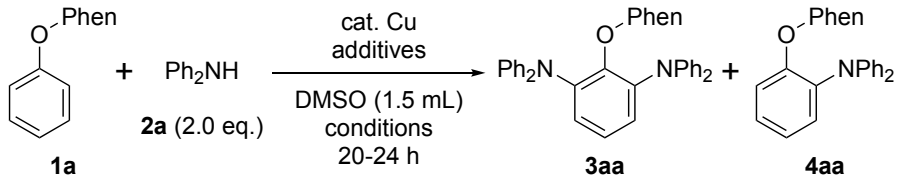


Table 1. Optimization Studies for Diamination of 1a with 2a[a]



entry	cat. Cu (mol %)	additives (mmol)	conditions	yield (%)[b] 3aa/4aa
1	$Cu(OAc)_2$ (100)	-	90 ºC, air	73/n.d.

2	$Cu(OAc)_2$ (50)	-	90 ºC, air	73 (76)/n.d.
3	$Cu(OAc)_2$ (20)	-	90 ºC, air	23/40
4	$Cu(OAc)_2$ (100)	-	90 ºC, air	20/39
5	$Cu(OAc)_2$ (100)	-	90 ºC, O_2 (1 atm, balloon)	21/36
6	$Cu(OAc)_2$ (50)	-	110 ˚C, air	58/n.d.
7	$Cu(OAc)_2$ (50)	-	70 ºC, air	73/n.d.
8	$Cu(OAc)_2$ (50)	AcOH (0.25)	90 ºC, air	46/8
9	$Cu(OAc)_2$ (50)	PivOH (0.25)	90 ºC, air	45/14
10	$Cu(OAc)_2$ (50)	K_2CO_3 (0.25)	90 ºC, air	trace/22
11	$Cu(OAc)_2$ (50)	Cy_2NMe (0.25)	90 ºC, air	66/n.d.
12	$Cu(OAc)_2$ (20)	MnO_2 (1.0)	90 ºC, N_2	7/34
13	$Cu(OAc)_2$ (20)	NMO (1.0)	90 ºC, N_2	n.d./n.d.
14	$Cu(OAc)_2$ (20)	$K_2S_2O_8$ (1.0)	90 ºC, N_2	n.d./n.d.

15	$Cu(OPiv)_2$ (20)	-	90 ºC, air	63/16
16	$Cu(eh)_2$ (20)	-	90 ºC, air	47/23
17	$CuCl_2$ (20)	-	90 ºC, air	n.d./n.d.
18	$Cu(OTf)_2$ (20)	-	90 ºC, air	n.d./n.d.
19	*$Cu(OPiv)_2$ (30)*	*-*	*90 ºC, air*	*79 (83)/n.d.*
20	$Cu(OPiv)_2$ (400)	-	90 ºC, N_2	11/20
21	-	-	90 ºC, air	n.d./n.d.

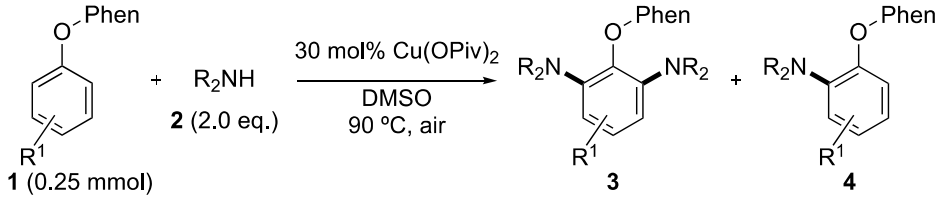
[a] Reaction conditions: **1a** (0.25 mmol), **2a** (0.50 mmol), copper catalyst, additives, DMSO (1.5 mL).

[b] Determined by ^{1}H NMR with dibenzyl ether as internal standard. Isolated yield in parentheses. Phen = 2-(1,10-phenanthrolyl), Piv = *tert*-butylcarbonyl, eh = 2-ethylhexanoate, Tf = trifluoromethanesulfonyl.

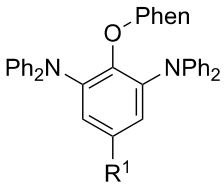
With the optimal conditions in hand, we examined the substrate scope (Scheme 6; 0.25 mmol scale). Phenol derivatives bearing both electron-donating and electron–withdrawing substituents at the *para*-position reacted with diphenylamine (**2a**) to produce di-aminated products in good yield (**3aa**-**3ha**; 70-

92%). Only one exception was CF_3-substituted phenol (**3ia**), in which the reaction efficiency was slightly decreased and the mono-aminated **4ia** was also formed. It is noteworthy that the C-H amination preferably occurred over the Ullmann-type amination to afford **3fa** and **3ga** with the Ar-Br and Ar-I moieties left intact, which can be good synthetic handles for further derivatizations. The reaction of *meta*-Me-substituted substrate and 2-naphthol derivative proceeded at less sterically hindered positions to produce mono-aminated products exclusively (**4ja** and **4la**). The electron-withdrawing and smaller F substituent at the *meta* position also showed the mono-amination selectivity and good regioselectivity in a ratio of 9.2:1, albeit with the moderate reactivity (**4ka** and **4ka'**). The o*rtho*- substituents were also compatible to form the triarylamines in good yields (**4ma** and **4na**). We next performed the C-H amination of **1a** with various amines **2**. Diarylamines with methyl (**3ab**, **3af**, **3ai**, and **3ak**), methoxy (**3ah** and **3aj**), halogen (**3ac**, **3ad**, and **3ag**), and phenyl (**3ae** and **3ag**) groups underwent the reaction to afford the corresponding di-aminated compounds. As a general trend, the electron-rich amine gave a lower yield, probably because of competitive oxidative decomposition (**3ha**). Again, bromo and iodo groups in the diarylamines were tolerated (**3ac**, **3ad**, and **3ag**). The mono- and di-aminated products (**3al**/**4al** and **3am**/**4am**) were also obtained from cyclic amine **2l** and *N*-methylaniline (**2m**) albeit in moderate combined yields. The *N*-benzylaniline (**2n**) also underwent the reaction with efficiency and selectivity to similar to those of *N*-methylaniline (**2m**; **3an** + **4an**). The benzyl group can be deprotected under hydrogenolysis, possibly giving the corresponding secondary NH amine. Moreover, electron-rich carbazoles could be coupled with **1a** to form the corresponding mono- and di-aminated products (**3ap**/**4ap** and **3aq**/**4aq**). Additionally, the C-H amination could be easily conducted on a ten- or four-fold larger scale, thus indicating the good reproducibility and practicality of this process (**3aa**, **3ba**, and **4ja**). On the other hand, attempts to apply primary amines and dialkylamines remained unsuccessful. These amines removed the phenanthroline auxiliary from **1a** by attack at the imine moiety to form the parent phenol (data not shown).

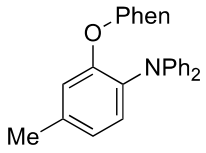
Scheme 6. Copper-Catalyzed C-H Amination of Various Phenol Derivatives 1 with Amines 2.[a]



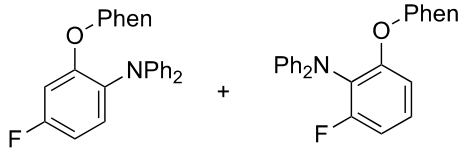
Scope of phenol derivatives **1** with diphenylamine (**2a**)



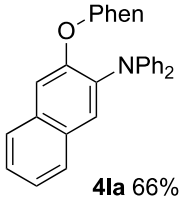
R^1= H: **3aa** 83%, 85%[b,c], 70%[c,d]
R^1= *t*Bu: **3ba** 80%, 81%[b,c]
R^1= OMe: **3ca** 92%
R^1= F: **3da** 77%
R^1= Cl: **3ea** 70%
R^1= Br: **3fa** 70%
R^1= I: **3ga** 77%
R^1= Ph: **3ha** 82%
R^1= CF_3: **3ia** + **4ia** 55% (4.1:1)



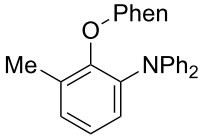
4ja 81%, 71%[b,c]



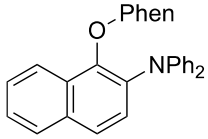
4ka + **4ka'** 35% (9.2:1)[e]



4la 66%

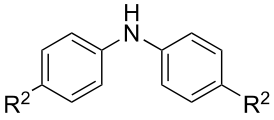


4ma 79%

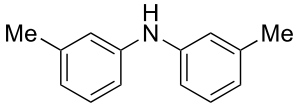


4na 65%

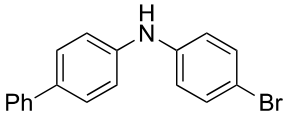
Scope of amines **2** with phenyl phenanthrolyl ether (**1a**)



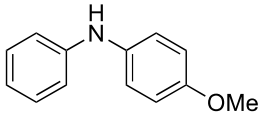
R^2 = Me: **3ab** 84%
R^2 = Br: **3ac** 73%
R^2 = I: **3ad** 64%
R^2 = Ph: **3ae** 69%



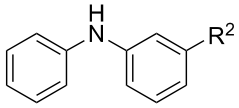
3af 67%



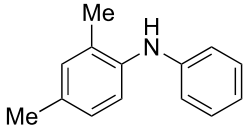
3ag 80%



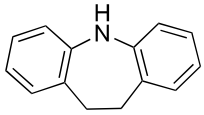
3ah 39%



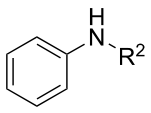
R^2 = Me: **3ai** 69%
R^2 = OMe: **3aj** 70%



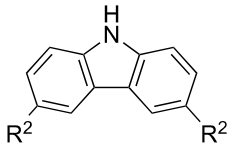
3ak 60%



3al + **4al** 36% (1:1)



R^2 = Me: **3am** + **4am** 43% (1:1)
R^2 = Bn: **3an** + **4an** 40% (1.2:1)

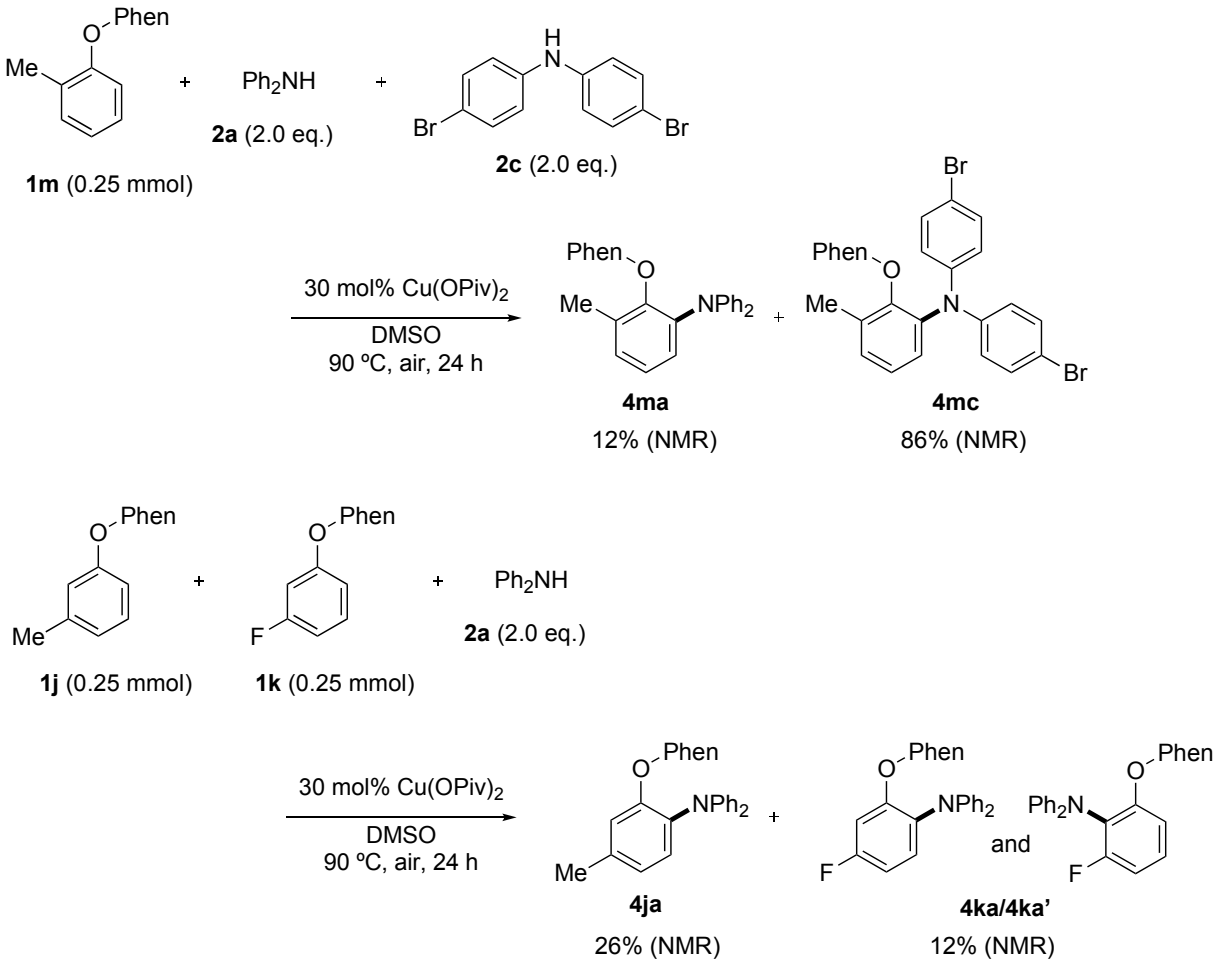


R^2 = H: **4ao** [7%]
R^2 = *t*Bu: **3ap** + **4ap** 53% (1.4:1)[f]
R^2 = OMe: **3aq** + **4aq** [36%] (1:2.6)

[a] Conditions: $Cu(OPiv)_2$ (0.075 mmol), **1** (0.25 mmol), **2** (0.50 mmol), DMSO (5.0 mL), 100 ℃, 20-24 h, air. The combined yield of diaminated product **3** and monoaminated product **4** is shown. The ratio of **3**/**4** is in parentheses. Value in brackets indicates NMR yield. [b] On a 1.0 mmol scale. [c] For two days. [d] On a 2.5 mmol scale. [e] A regioisomeric ratio of **4ka** and **4ka'**. [f] With 0.75 mmol of **2**. Phen = 2-(1,10-phenanthrolyl).

To investigate the reactivity trend, we performed the several competitive experiments (Scheme 7). The substrate **1m** was preferably coupled with the electron-deficient **2c** over the relatively electron-rich **1a**. On the other hand, the more electron-rich phenol derivative **1j** showed higher reactivity than the electron-deficient **1k**.

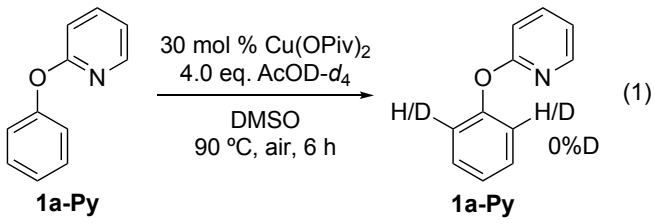
Scheme 7. Competitive Experiments

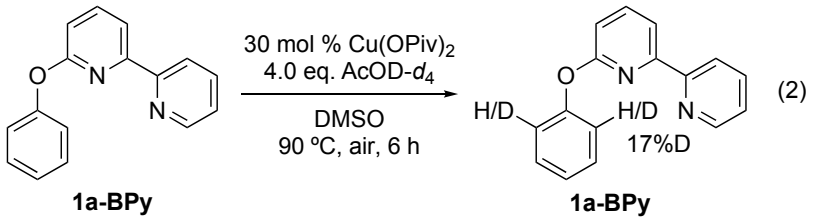


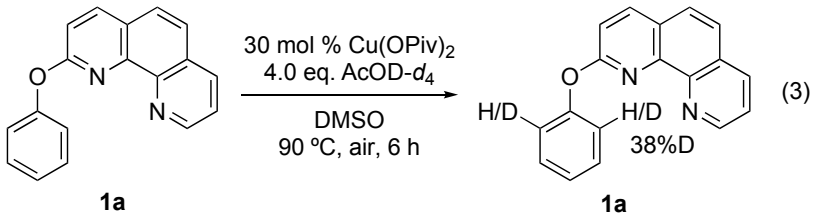
To gain more insight into the mechanism, we first investigated the effect of directing groups in the C-H activation in the absence of the coupling partner, diphenylamine (**2a**). In the presence of $Cu(OPiv)_2$ and AcOD-d_4, the H/D exchange of phenoxypridine (**1a-Py**) was not observed at all (Scheme 8, eq 1). In contrast, deuterium incorporation in the phenol ring with the bipyridyl group (**1a-Py**) and the phenanthrolyl group (**1a**) were detected in 17% and 38%, respectively (eqs 2 and 3). These results apparently indicate positive effects of the bidentate directing group, especially phenanthrolyl group in the C-H activation step. We also carried out kinetic studies with the deuterium-labeled substrate **1a-*d*$_5$**. Even at an early stage of the reaction, the D/H exchange of **1a-*d*$_5$** was not observed (eq 4), thus suggesting that the C-H bond cleavage is irreversible in the presence of diphenylamine coupling partner **2a**. Moreover, KIE value from the parallel reactions with **1a** and **1a-*d*$_5$** was determined to be 1.45, which is relatively small but meaningful (eq 5). On the other hand, Stahl *et al.* recently reported the homo-coupling reaction of diarylamines in the presence of a copper salt under O_2 to produce

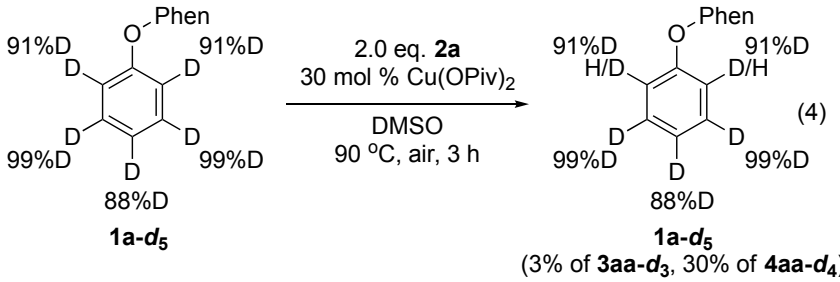
tetraarylhydrazines.[20] The reported conditions are similar to our optimal conditions. Thus, we independently prepared tetraphenylhydrazine (**6a**) and investigated its intermediacy in the C-H amination of **1a**. The reaction with one equivalent of **6a** instead of diphenylamine (**2a**) proceeded smoothly to form the same diaminated product **3aa** in a good yield (eq 6). Moreover, the aminated products **3aa** and **4aa** were obtained even under N_2 atmosphere, albeit with decreased efficiency. However, the reaction of the hydrazine without the copper catalyst produced no product (eq 7). Therefore, the hydrazine generated in situ from the amine may be a truly reactive component in the copper-catalyzed C-H amination, and molecular oxygen plays a role in the hydrazine formation. However, significant amount of tetraphenylhydrazine **6a** rapidly decomposed in DMSO at 90 ºC under air or N_2 to form the parent diphenylamine **2a** in 46% or 42% yield, respectively (eq 8). Thus, the possibility that in eq 6 the reaction with the decomposed **2a** produced **3aa** cannot be excluded. In contrast, the reaction with bicarbazole **6o** did not gave any product in the presence and absence of molecular oxygen, and the hydrazine-type intermediate is thus unlikely involved in the reaction with carbazoles (eq 9).

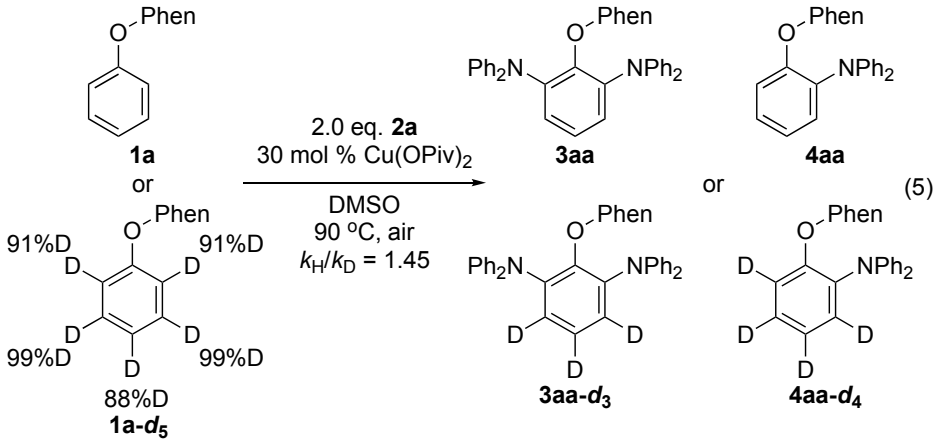
Scheme 8. Mechanistic Studies

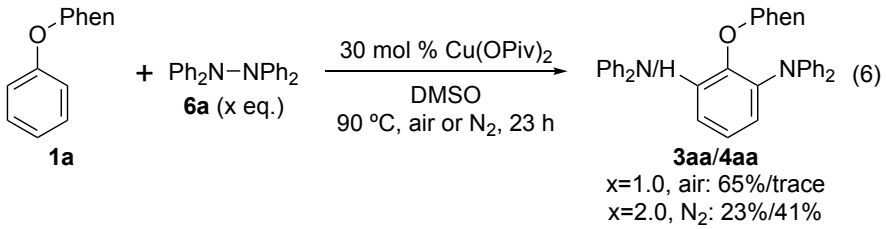

30 mol % Cu(OPiv)2
4.0 eq. AcOD-d4
DMSO
90 ºC, air, 6 h
H/D
H/D
0%D
(1)
1a-Py
1a-Py

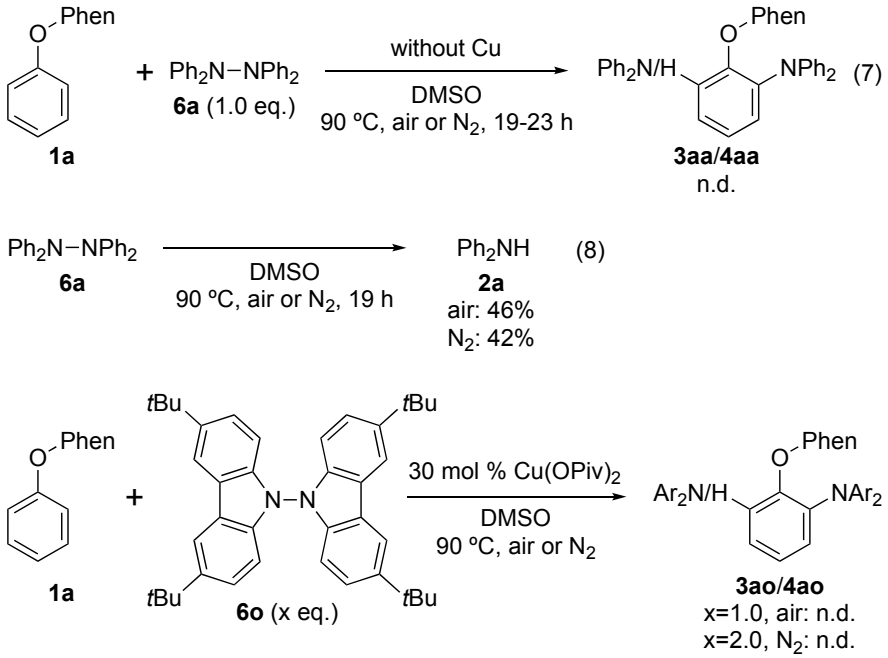

30 mol % Cu(OPiv)2
4.0 eq. AcOD-d4
DMSO
90 ºC, air, 6 h
H/D
H/D
17%D
(2)
1a-BPy
1a-BPy


30 mol % Cu(OPiv)2
4.0 eq. AcOD-d4
DMSO
90 ºC, air, 6 h
H/D
H/D
38%D
(3)
1a
1a


Phen
91%D
91%D
99%D
99%D
88%D
1a-d5
2.0 eq. 2a
30 mol % Cu(OPiv)2
DMSO
90 ºC, air, 3 h
H/D
D/H
(4)
1a-d5
(3% of 3aa-d3, 30% of 4aa-d4)


Phen
1a
or
91%D
99%D
88%D
1a-d5
2.0 eq. 2a
30 mol % Cu(OPiv)2
DMSO
90 ºC, air
kH/kD = 1.45
Ph2N
NPh2
3aa
4aa
or
3aa-d3
4aa-d4
(5)


Phen
1a
+ Ph2N−NPh2
6a (x eq.)
30 mol % Cu(OPiv)2
DMSO
90 ºC, air or N2, 23 h
Ph2N/H
NPh2
(6)
3aa/4aa
x=1.0, air: 65%/trace
x=2.0, N2: 23%/41%

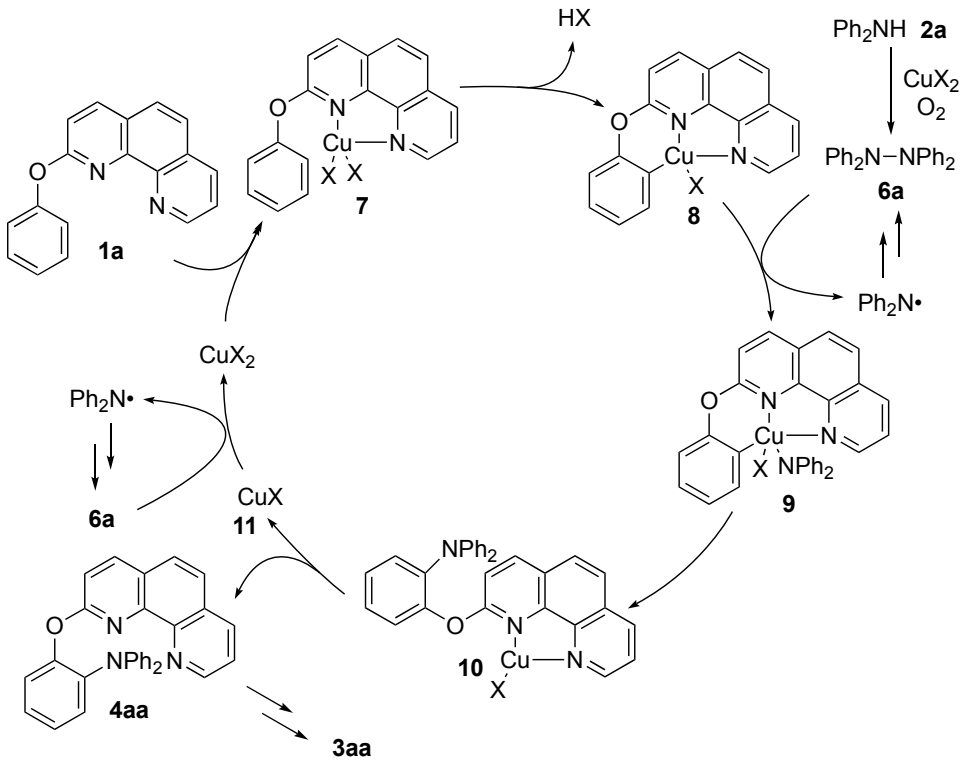


On the basis of the above results and literature information, we propose two reaction mechanisms of **1a** with **2a** as shown in Schemes 9 and 10 (mechanism A and B, respectively). In the mechanism A, tetraphenylhydrazine (**6a**) is formed as the reactive intermediate (Scheme 9). An initial coordination promoted by the N,N-chelation of the phenanthroline moiety in **1a** to copper center generates a chelated complex **7**. Subsequent irreversible C-H bond cleavage forms the six-membered intermediate **8**. This metallacycle is then oxidized to the copper(III) species **9**[21] with the hydrazine **6a**, which is produced by the copper-catalyzed homo-coupling of **2a** in the presence of O_2. The corresponding mono-aminated product **4aa** is obtained by reductive elimination and the following dissociation of the copper salt from complex **10**. The same C-H amination occurs at another *ortho* position to form the observed di-aminated product **3aa**. The resulting copper(I) species **11** is finally oxidized into copper(II) with **6a** to complete the catalytic cycle. The hydrazine **6a** could be regenerated immediately from the amino radical species by the copper catalyst and O_2.

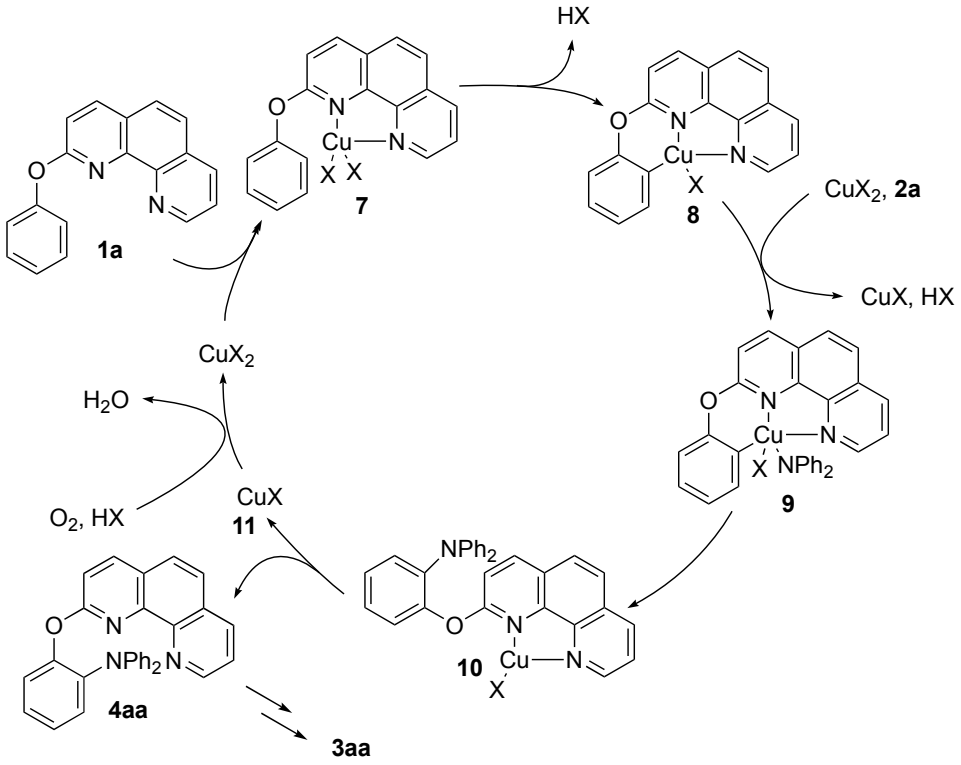
In the mechanism B, diphenylamine (**2a**) directly participates in the amination (Scheme 10). An initial coordination of **1a** to copper center and subsequent C-H bond cleavage produces the metallacycle **8**

through the same mechanism as in mechanism A. This intermediate is then oxidized to the copper(III) species **9** with another copper(II) species. The mono-aminated product **4aa** is obtained by reductive elimination and the following dissociation of the copper salt from complex **10**. The resulting copper(I) species **11** is finally oxidized into copper(II) with molecular oxygen to complete the catalytic cycle. Given the observation in eqs 6 and 7, we cannot provide any conclusive statement on the reaction mechanism of **1a** and **2a**, only with experimental studies. Thus, to confirm which mechanism is likely involved, computational studies with DFT were performed.

Scheme 9. Plausible Reaction Mechanism A (X = OPiv or NPh_2)



Scheme 10. Plausible Reaction Mechanism B (X = OPiv or NPh_2)



The enthalpy profiles of mechanism A and B are shown in Figure 2 and 3. In mechanism A, a chelate complex **A** undergoes the C-H cleavage of *ortho*-position of phenoxy leading to the six-membered intermediate **B** with 17.7 kcal mol^{-1} of activation enthalpy and 15.6 kcal mol^{-1} reaction enthalpy. **B** is oxidized and aminated by the hydrazine forming the copper(III) species **C** and NPh_2 radical. This step was 33.6 kcal mol^{-1} endothermic. If oxidation of **B** by the hydrazine directly leads to **C** and half equivalent of the hydrazine, this step was 14.8 kcal mol^{-1} endothermic process. The reductive elimination of **C** leading to the mono-aminated **D** was nearly barrierless and 53.8 kcal mol^{-1} exothermic reaction.

In mechanism B, the six-membered intermediate **B** was generated by the same C-H cleavage as mechanism A. **B** is oxidized by the copper cluster species of $[Cu(OAc)_2]_2$ to the copper(III) species **E**. This step was 3.4 kcal mol^{-1} endothermic. The amination of **F** to the aminated species **G** was almost barrierless. Although AcOH was removed from **G** to lead **C** for the convenience of calculation, the

continuous reductive elimination can progress from **G**. The reductive elimination was barrierless and highly exothermic reaction. The oxidation and amination steps by $[Cu(OAc)_2]_2$ and $NHPh_2$ (mechanism B) are energetically favored than those by the hydrazine (mechanism A), indicating that mechanism B is likely involved.

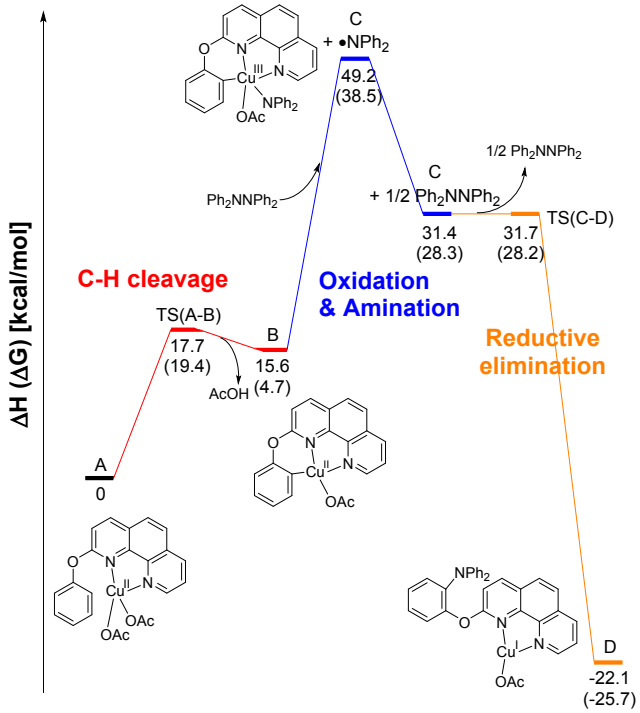


Figure 2. Enthalpy (Gibbs energy) profile of Mechanism A.

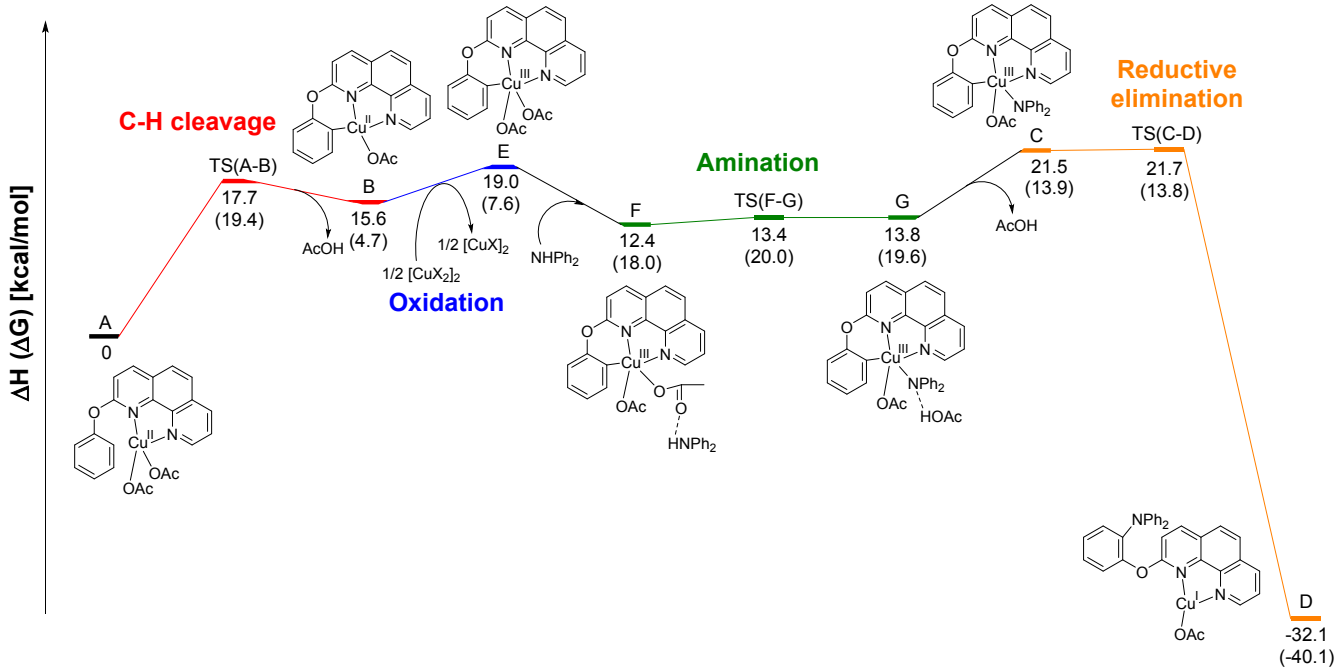
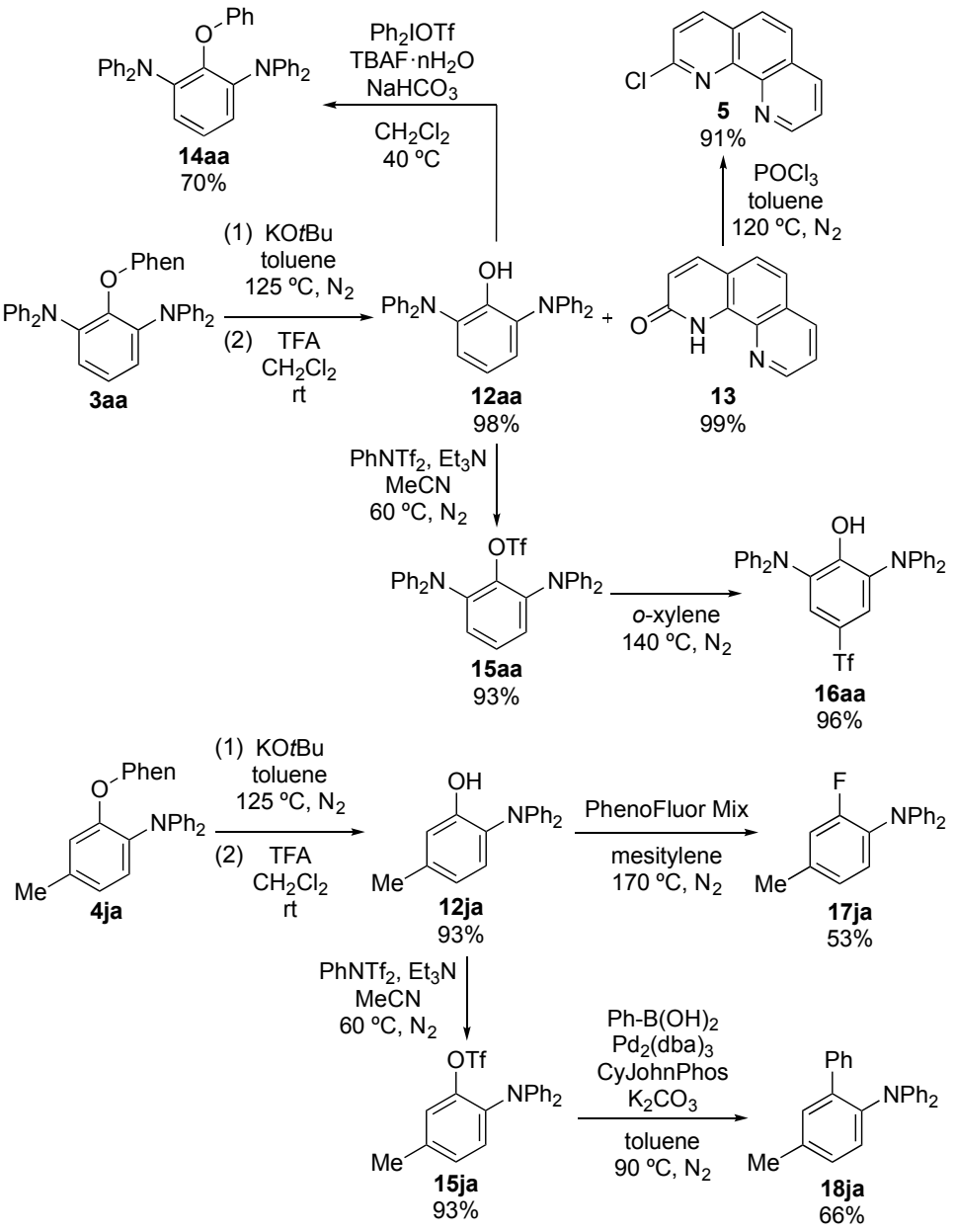


Figure 3. Enthalpy (Gibbs energy) profile of Mechanism B.

Given the results observed in Scheme 7, the more acidic amine is more easily deprotonated, leading to the aminated intermediate corresponding to **G** preferably. The C–H cleavage can involve the acetate-ligand-assisted concerted metalation-deprotonation (CMD)-type pathway, but the electrophilic nature is also important in the product-determining step.[22] However, the role of molecular oxygen still remains unclear even from DFT calculation, and further studies are required for clarification. On the other hand, a mechanism of type B can be operative also in the C-H amination with carbazoles because the reaction of **1a** with bicarbazole **6o** did not occur at all (eq. 9, vide supra).

We finally attempted the derivatization of the aminated products (Scheme 11). The directing group of **3aa** could be easily removed with potassium *tert*-butoxide in toluene at 125 ºC, and both free phenol **12aa** and phenanthrolidone (**13**) were obtained in nearly quantitative yields after treatment of the crude mixture with trifluoroacetic acid (TFA) in CH_2Cl_2. Subsequent dehydrative chlorination of **13** furnished the chlorophenanthrizine **5** in a good overall yield, which can be recycled as the directing group (Scheme 3). The phenol **12aa** was coupled with Ph_2IOTf in the presence of tetrabutylammonium fluoride hydrate ($TBAF{\cdot}nH_2O$) and $NaHCO_3$ to form the *O*-arylated product **14aa** in 70% yield.[23] Moreover, **12aa** reacted with $PhNTf_2$ in acetonitrile at 60 ºC to furnish the triflate **15aa**, and successive thia-Fries rearrangement of **15aa** produced **16aa** in 96% yield. The directing group of mono-aminated product **4ja** could also be removed to produce phenol **12ja** in 93% yield. The deoxyfluorination reaction of **12ja** with PhenoFluor Mix[24] was also possible, and the fluorine-containing triarylamine **17ja** was obtained in an acceptable yield. Finally, the triflate **15ja** prepared from **12ja** underwent the Suzuki-Miyaura coupling with phenylboronic acid to produce **18ja** in 66% yield.

Scheme 11. Derivatization of the Aminated Products



CONCLUSIONS

In conclusion, we have developed a copper-catalyzed direct amination of phenol derivatives with diarylamines via phenanthroline-based, bidentate auxiliary directed C-H cleavage. The reaction proceeds smoothly with only a copper salt and air as a terminal oxidant to produce the

corresponding *ortho*-aminophenols in good yields. Moreover, the directing group can be easily attached, detached, and recycled. Additionally, preliminary computational studies with DFT are also performed. The obtained results will find wide applications in other base-metal-catalyzed C-H functionalization of phenols and even more challenging aliphatic alcohol derivatives.

ASSOCIATED CONTENT

Supporting Information:

The Supporting Information is available free of charge on the ACS Publications website at DOI: xxx.

Procedures and characterization data (PDF)

X-ray crystallographic data for **3aa** (CIF)

AUTHOR INFORMATION

Corresponding Authors

*E-mail: k_hirano@chem.eng.osaka-u.ac.jp.

*E-mail: miura@chem.eng.osaka-u.ac.jp.

ORCID

Koji Hirano: 0000-0001-9752-1985

Masahiro Miura: 0000-0001-8288-6439

Notes

The authors declare no competing financial interest.

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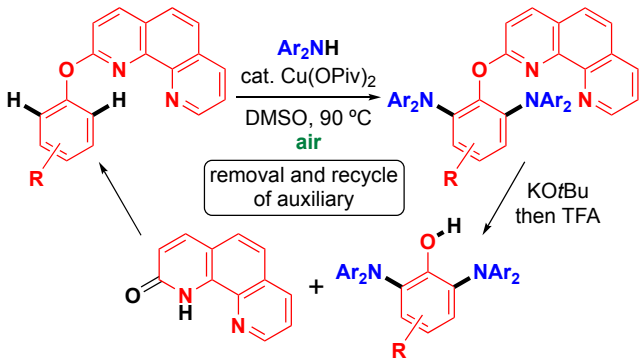
TOC Graphic: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