Copper-Catalyzed Electrophilic Amination of Arylsilanes with Hydroxylamines

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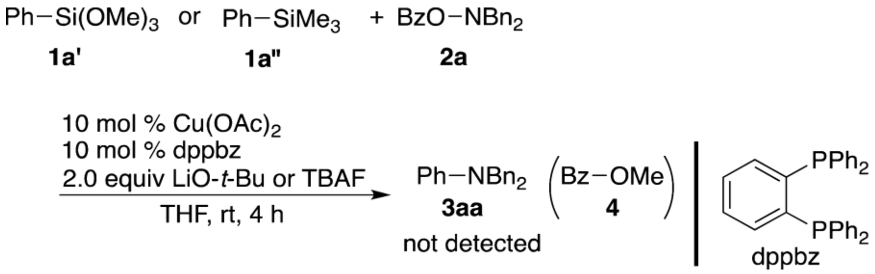
ABSTRACT

A copper-catalyzed electrophilic amination of aryl[(2-hydroxymethyl)phenyl]dimethylsilanes with O-acylated hydroxylamines has been createdto manage the cost of the relating anilines in great yields. The synergist response continues easily under gentle conditions and endures a wide scope of utilitarian gatherings.

INTRODUCTION

Arylamines are special primary themes in numerous organically dynamic mixes, drug targets, and functionalmaterials.1Metal-advanced fragrant CN crosscoupling responses give a ground-breaking and united way to deal with the above amines. Among them, the coppermediated oxidative coupling of arylmetalswith amines (ChanLam-type coupling) positions as quite possibly the most helpfulconventions in manufactured chemistry.2 So far, arylboronic acids also, their subordinates have been mostly utilized as the aryl source. Then again, there are a couple of effective reports of arylsilanes, regardless of their low poisonousness and bounty which are like those of organoboron compounds.3 Then, an umpolung,4 electrophilic amination5 utilizing a reagent of type R2Nþ, for example, chloro-and hydroxylamines has as of late got huge consideration and empowered the successful amination of not just organometallic reagents dependent on Mg,6 Zn,7 Ti,8 Zr,9 and B10 yet additionally(hetero)aromatic CH bonds.11 Our gathering additionally engaged on this sort of change and prevailing in the coppercatalyzed electrophilic aminations of heteroarenes,12ae arylboronates,12f and ketene silyl acetals.12g In the course of this investigation, we imagined that the umpolung technique could be applied to the amination of arylsilanes. Thus, we depict a copper-catalyzed electrophilic amination of aryl- [(2-hydroxymethyl)phenyl]dimethylsilanes with O-acylated hydroxylamines. The copper catalysis endures a different set of useful gatherings and permits different arylsilanes to be embraced proficiently in the amination response for the amalgamation of arylamines.

Scheme 1. Initial Attempts on Copper-Catalyzed Electrophilic Amination of Trimethoxyphenylsilane ($1a^{0}$) or Trimethylphenylsilane ($1a^{00}$) with *O*-Benzoyl-*N,N*-dibenzylhydroxylamine (2a)



Herein, we depict a copper-catalyzed electrophilic amination of aryl- [(2-hydroxymethyl)phenyl]dimethylsilanes with O-acylated hydroxylamines. The copper catalysis endures a different set of utilitarian gatherings and permits different arylsilanes to be received productively in the amination response for the blend of arylamines. Based on our past work with arylboronates,12f we at first endeavored the amination of trimethoxyphenylsilane (1a0) with O-benzoyl-N,N-dibenzylhydroxylamine (2a) within the sight of a Cu(OAc)2/(dppbz = 1,2-bis(diphenylphosphino)benzene) impetus and LiO-t-Bu in THF at room temperature (Scheme 1). Tragically, no ideal aniline 3aa was shaped, and methyl benzoate

(4) was rather recognized as a result, the methoxy gathering of which clearly came from 1a0 13 The utilization of tetrabutylammonium fluoride (TBAF) as a base likewise gave a comparative outcome, while trimethylphenylsilane (1a00) instead of 1a0 demonstrated no change such an arylsilane is fit for specific aryl bunch move through easy arrangement of an intramolecularly pentacoordinated arylsilicate, in spite of its high dependability related with a tetraorganosilane structure. Moreover, 1a is promptly arranged and now industrially accessible from a few providers. To our joy, 3aa was gotten in 12% yield under similar synergist conditions as those for Plan 1 (passage 1). With the starter yet fascinating brings about hand, we screened copper salts (passages 24), and CuI indicated higher synergist movement (section 2). Among different phosphine ligands tried, some Buchwald biarylphosphines16 improved the yield of 3aa (sections 59), with 2-(di-tert-butylphosphino)biphenyl (JohnPhos) ending up being ideal (section 5). Ensuing examination of the dissolvable framework (section 1012) uncovered that 1,4-dioxane moreover expanded the response effectiveness (passage 10).

At last, we could confine 3aa in 77% yield in the presence of 5 mol% of CuI and 10 mol% of JohnPhos (section 13). On the other hand, different bases, for example, K3PO4, Cs2CO3, and NaO-t-Bu didn't outfit 3aa by any stretch of the imagination (information not appeared). Strikingly, the current amination could be done on a 5-overlay bigger scope, demonstrating the great reproducibility and Thus, we turned our attention to [(2-hydroxymethyl)-phenyl]dimethylphenylsilane (1a, Table 1), which was originally developed by Nakao and Hiyama,14,15 because

CuI/DavePhos	THF	47

5[c] 6[c] 7[c] 8[c] 9[c]

10[c]	CuI/JohnPhos	1,4-dioxane	81
11[c]	CuI/JohnPhos	CPME	69
12[c]	CuI/JohnPhos	DME	43
13[d]	CuI/JohnPhos	1,4-dioxane	90 (77)
14[d,e]	CuI/JohnPhos	1,4-dioxane	(71)

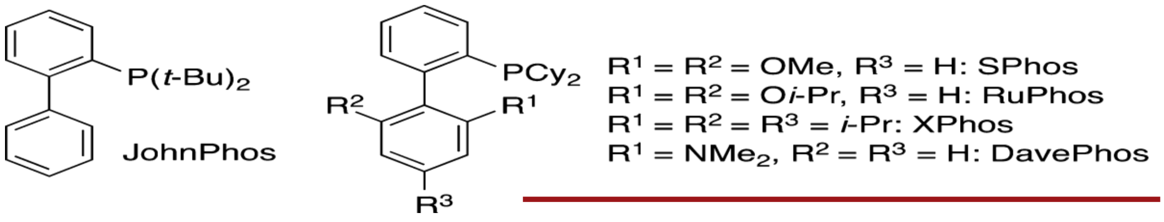
unwavering quality of the copper catalysis (section 14). Also, in this case, the resultant oxasilacyclopentane was recuperated in 65% yield (98% virtue by GC examination) by Kugelrohr refining, which can be reused for the beginning 1a. 17

We next played out the electrophilic aminationofdifferentaryl[(2hydroxymethyl)phenyl]dimethylsilanes1 with 2a under conditions utilized for section 13 in Table 1

Table 1. Optimization Studies for Copper-Catalyzed Electrophilic Amination of [(2-Hydroxymethyl)-phenyl]dimethylphenylsilane (1a) with *O*-Benzoyl-*N*, *N*-dibenzylhydroxylamine (2a)[a]

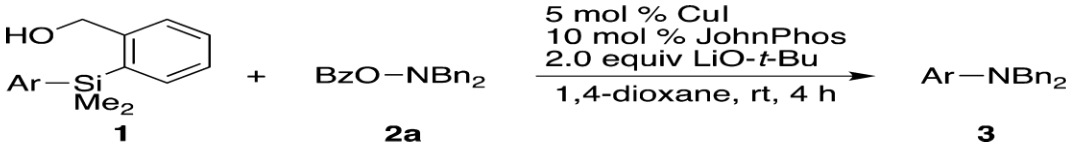
CuI/JohnPhos	THF	68
CuI/SPhos	THF	37
CuI/RuPhos	THF	50
CuI/XPhos	THF	32

Bu (0.50 mmol), 1a (0.25 mmol), 2a (0.30 mmol), solvent (1.5 mL), rt, 4 h, N_2. [b] The yields are determined by GC method. Yield of isolated product is in parentheses. [c] With 0.050 mmol of ligand. [d] With 0.013 mmol of CuI and 0.025 mmol of JohnPhos. [e] On a 1.25 mmol scale.



(Table 2).

Table 2. Copper-Catalyzed Electrophilic Amination of Various Aryl[(2-hydroxymethyl)phenyl]dimethylsilanes 1 with *O*-Benzoyl-*N,N*-dibenzylhydroxylamine (2a)[a]



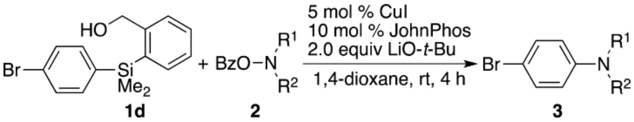
entry	Ar 1	3, yield (%)[b]
1	Ar = 4-MeOC$_6$H$_4$ (1b)	3ba, 73
2	Ar = 4-ClC$_6$H$_4$ (1c)	3ca, 81
3	Ar = 4-BrC$_6$H$_4$ (1d)	3da, 77
4	Ar = 4-EtO$_2$CC$_6$H$_4$ (1e)	3ea, 76
5	Ar = 4-NCC$_6$H$_4$ (1f)	3fa, 88
6	Ar = 2-MeC$_6$H$_4$ (1g)	3ga, 43
7	Ar = 3-ClC$_6$H$_4$ (1h)	3ha, 76
8	Ar = 1-naphthyl (1i)	3ia, 79
9	Ar = 2-thienyl (1j)	3ja,0

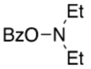
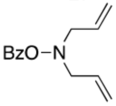
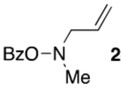
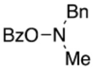
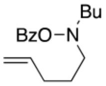
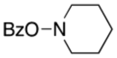
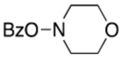
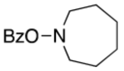
[a] Reaction conditions: CuI (0.013 mmol), JohnPhos (0.025 mmol), LiO-*t*-Bu (0.50 mmol), 1 (0.25 mmol), 2a (0.30 mmol), 1,4-dioxane (1.5 mL), rt, 4 h, N$_2$. [b] Yield of isolated product.

With the Br-substituted arylsilane 1d as the aryl source, the scope of hydroxylamines 2 was evaluated (Table 3). Acyclic amines with *N,N*-diethyl, *N,N*-diallyl, *N*-ally-*N*- methyl, and *N*-benzyl-*N*-methyl substituents underwent the coupling with 1d very smoothly to form the corresponding 4-bromoanilines 3db de in synthetically useful yields (entries 1 4). The resultant N-allyl and N- benzyl moieties can work as a useful synthetic handle for further manipulations.18 These successful examples deserve significant attention because such secondary acyclic alkylamines are an inaccessible substrate class in the conventional Chan Lam-type coupling with arylsilanes.3 The reaction with 2f that contains the pendant olefin gave the usual aminated product 3df exclusively, and any pyrrolidine derivatives were not detected at all (entry 5). Thus, an aminyl radical-promoted pathway is less likely.19 On the other hand, cyclic amines showed somewhat lower efficiency: the reaction of six-membered piperidine 2g and morpholine 2h provided the corresponding anilines 3dg and 3dh in moderate yields, whereas the seven-membered azepane 2i was transformed into 3di in 78% yield.20

Table 3

Copper-Catalyzed Electrophilic Amination of Bromo- substituted Arylsilane 1d with Various *O*-Benzoyl-hydroxyla- mines 2[a]

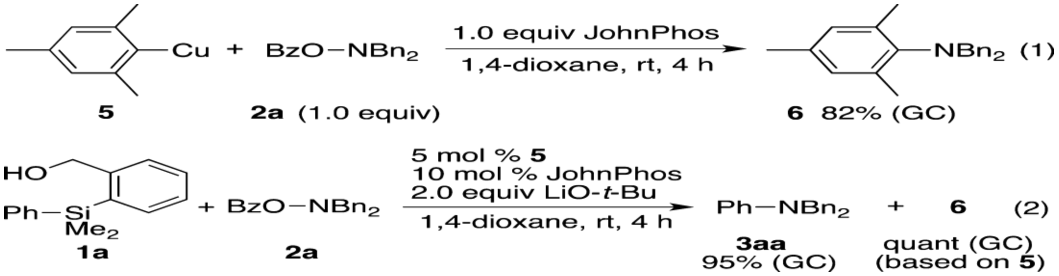


entry	**2**	**3**, yield (%)[b]
1	 **2b**	**3db**, 77
2	 **2c**	**3dc**, 82
3	 **2d**	**3dd**, 60
4	 **2e**	**3de**, 74
5	 **2f**	**3df**, 71
6	 **2g**	**3dg**, 58
7	 **2h**	**3dh**, 40
8	 **2i**	**3di**, 78

[a] Reaction conditions: CuI (0.013 mmol), JohnPhos (0.025 mmol), LiO-*t*-Bu (0.50 mmol), 1d (0.25 mmol), 2 (0.30 mmol), 1,4-dioxane (1.5 mL), rt, 4 h, N_2. [b] Yield of isolated product.

To attain some insight into the mechanism and inter- mediates of the reaction, we prepared the mesitylcopper complex 5[21] and investigated its reactivity (Scheme 2). Upon treatment with a stoichiometric amount of *O*-ben- zoyl-*N*,*N*-dibenzylhydroxylamine (2a) and JohnPhos, the

Scheme 2. Stoichiometric and Catalytic Reactions with Mesi- tylcopper Complex 5



comparing C N coupling item 6 was framed in 82% yield (GC, eq 1). Also, 5 catalyzed the amination of 1a with 2a successfully to outfit 3aa in 95% yield (GC, eq 2), with associative arrangement of 6 (quantitative dependent on 5 utilized). These discoveries propose that a monoarylcopper animal varieties, for example, 5 would be framed in the reactant cycle and answerable for the C N bond shaping step.10e,12c

In any case, given that in our past work12f the mesityl-copper 5 didn't respond with 2a at all within the sight of dppbz, the reactivity profile of the arylcopper toward O-benzoyl-hydroxylamines would be drastically impacted by the auxiliary ligand facilitated to the copper place.

In view of the above contemplations, a conceivable mechan-ism includes (1) base-helped transmetalation22 of a Cu(I) complex with the arylsilane 1, producing a JohnPhos-ligated unbiased monoarylcopper species, and (2) electro- philic amination with the hydroxylamine 2 to shape the noticed aniline 3.6b,10e,12c,12e An option is the invol-vement of a Cu(III) transitional preceding the C N bond formation.23 Further endeavors to explain the definite mechan-ism are progressing.

All in all, we have built up a copper-catalyzed electrophilic amination of aryl[(2-hydroxymethyl)phenyl]-dimethylsilanes with O-acylated hydroxylamines. The umpolung, electrophilic amination methodology permits aryl-silanes to fill in as an effective aryl hotspot for the synthe-sister of aniline subsidiaries. Besides, the high halogen similarity of the cycle can give an easy admittance to bromide-subbed arylamines and supplement the ordinary Pd-based amination science. Further devel-opments of related electrophilic aminations are in progress.

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SUPPORTING INFORMATION AVAILABLE.

Detailed experimen- tal procedures and characterization data of compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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