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Copper-Mediated Multiple C−H Functionalization of Aromatic *N*-Heterocycles: Bromoamination of Indoles and Pyrroles

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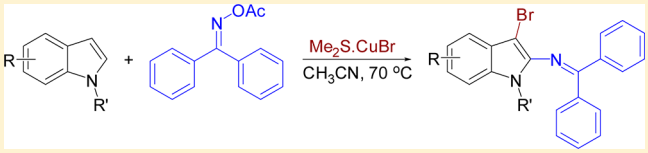
Supporting Information

ABSTRACT: A copper-mediated bromoamination of aromatic *N*-heterocycles has been achieved using oxime esters as the *N*-reagents under mild conditions (ca. 70 °C). The reaction with *N*-alkyl indoles proceeds regioselectively to produce the 2-amino-3-bromo indole derivatives as confirmed by X-ray crystallographic analysis of the bromoaminated product, **3aa-Br**. With *N*-methylpyrrole both the monobromoaminated and dibromoaminated products were produced by this method.



INTRODUCTION

Transition metal promoted aromatic C−H bond functionalization that involves electrophilic metal catalysis to induce C−H bond cleavage has emerged as a promising alternative to classical methods of preparing functionalized arenes.[1] This new methodology of installing functional groups on the aryl skeleton is greener,[2] as it obviates the need for prefunctionalized substrates and, hence, the resulting waste during synthesis, yet presently suffers from several limitations. The more often encountered ones are the need for a directing group, which dictates the regiochemistry of the functionalization,[3] and the use of catalysts derived from expensive second- or third-row late transition metals such as Pd,[4] Pt,[5] Ru,[6] Rh,[7] Ir,[8] and Au.[9] While new reports of C−H functionalization using late metals continue to emerge, growing concerns regarding their toxicity and cost-effectiveness have prompted interest in the use of cheap, benign, and readily available first-row metals such as Fe and Cu.[10] Although copper-promoted reactions are mostly proposed to proceed via a single-electron transfer process[11] or a Cu(II)/Cu(0) pathway,[12] of late the intermediacy of highly electrophilic d^8 Cu(III) intermediates has also been suggested.[13]

The C−H amination reaction, which allows direct access to aromatic/heteroaromatic amines from the corresponding arenes/heteroarenes, is particularly significant owing to the ubiquitous presence of the amine functionality in pharmaceuticals, specialty chemicals, and biologically important molecules.[14] Analogous to other C−H functionalizations, the C−H amination reactions developed to date also rely heavily on the use of precious metal catalysts and prefunctionalized, coordinating substrates.[15] As the C−H amination reaction falls into the broad category of oxidative coupling, successful catalysis requires the use of either a stoichiometric oxidant[16] or more oxidized *N*-reagents such as hydroxylamine derivatives,[17] chloramines,[18] or oxycarbamates.[19] Additionally, C−H amination of azoles and other acidic arenes has been achieved in the presence of a base under transition metal catalysis.[20]

Our continuing interest in the discovery of new, more practical catalyst and *N*-reagent combinations for effecting selective C−H amination reactions[21] led us to consider developing new methods for the amination[22] of indoles, which are widely represented in therapeutic drugs and natural products.[23] We were particularly fascinated by recent reports of C−H arylation of indole[24] and other arenes[25] putatively involving highly electrophilic $(aryl)_2Cu(III)X$ intermediates. Additionally, Liebeskind et al.[26] have reported on the amination of boronic acids and organostannanes presumed to involve an (imino)Cu(III)(OAc)X intermediate, produced by the oxidative addition of *O*-acyl ketoximes to Cu(I)(2-thiophene carboxylate). Also relevant to our objective is the recent report by Li and co-workers of a Cu-catalyzed C-2 selective oxidative amidation of indoles.[27] The potential of oxime acetates as aminating agents has been realized in Hartwig's Pd-catalyzed intramolecular amination of arenes to produce indoles.[28] On the basis of these precedents, we reasoned that with a suitable Cu(I) precursor it would be possible to generate an electrophilic (imino)Cu(III)(OAc)X species, capable of effecting C−H amination of indole (Scheme 1).

Herein we disclose the discovery of an unprecedented copper-mediated C−H *difunctionalization*, namely, haloamination, of the *N*-heterocycles indole and pyrrole, using benzophenone *O*-acetyloxime, a cheap and readily available *N*-reagent.

RESULTS AND DISCUSSION

With the intent of developing a new methodology for synthesizing aminoindoles by C−H amination we chose to

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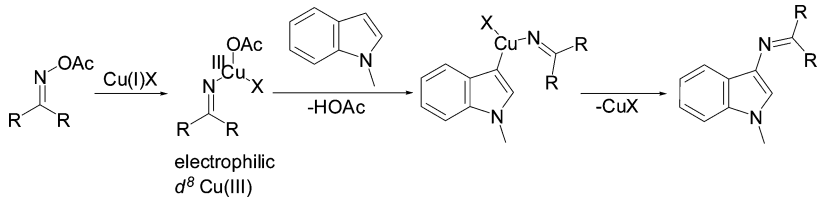
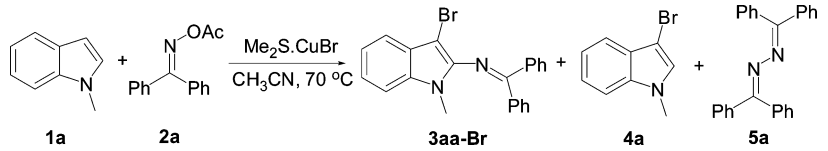
Scheme 1



Scheme 2



focus on Cu(I) catalysts and use oxime esters as the *N*-reagents, which could operate via a Cu(III)-imino intermediate. We began our investigation by attempting the amination of *N*-methylindole (**1a**) with benzophenone *O*-acetyloxime (**2a**) using $\{Cu(I)OTf\}_2$·toluene (20 mol %) as the copper source in CH_3CN at 70 °C. However, to our disappointment we did not observe any conversion of **1a**, while the *N*-reagent was fully consumed; benzophenone azine (**5a**) was identified in the reaction mixture. With various other Cu(I) salts, e.g., $Cu(CH_3CN)_4PF_6$, Cu_2O, and Cu(2-thiophene carboxylate),[29] similar results were obtained. Interestingly, when Me_2S·CuBr (20 mol %) was used as the copper source, we isolated the azine **5a**, *N*-methyl-3-bromoindole **4a** (∼10%), and the yellowish-orange compound **3aa-Br** (Scheme 2). Analysis of **3aa-Br** by ESI-MS suggested that the compound included both a bromo (−Br) and a benzophenone imine (−N=CPh_2) moiety on the indole skeleton (m/z = 389). Surprisingly, the ^{1}H NMR spectrum of **3aa-Br** was devoid of C-2 or C-3 proton resonances of an indole skeleton. The identity and regiochemistry of the bromoaminated indole product, **3aa-Br**, was confirmed as 3-bromo-2-diphenylimino-*N*-methylindole by X-ray crystallography (Figure 1 and Supporting Information). We note that Liu et al. recently reported a related chloroamination of indole by *N*-alkyl chlorosulfonamides with palladium and copper cocatalysts and stoichiometric quantities of Ag_2CO_3.[30]

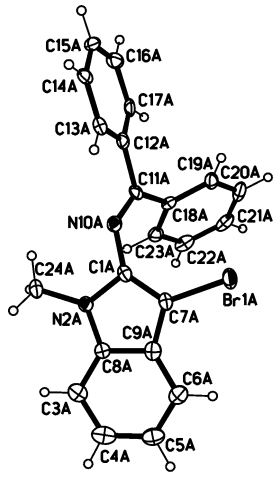


Figure 1. X-ray ORTEP structure of **3aa-Br**.

Excited by the discovery of the bromoaminated product **3aa-Br**, we reasoned that since its formation requires a stoichiometric amount of bromide, we could potentially render the reaction catalytic by supplying bromide from an external source. Toward this end we conducted reactions that included equivalent amounts of bromide salts, including NaBr, LiBr, KBr, and Bu_4NBr. However, no significant improvement in the yield of **3aa-Br** resulted. Interestingly, we observed that **1a** was fully consumed during these reactions, and we could trace its fate to 3-bromo-*N*-methylindole, **4a**. Recent reports[31] on Cu(II)-catalyzed 3-bromination of indole led us to reason that we could be generating Cu(II) in our reaction, which impedes the desired bromoamination reaction.[32]

Being unable to achieve catalytic turnover in the bromoamination reaction, we focused on optimizing the stoichiometric reaction. Accordingly, the stoichiometric reaction was improved with a batchwise addition of a 2:1 ratio of *N*-reagent/[CuX] to obtain a 58% yield of **3aa-Br** along with 42% of **4a**.[33] Several attempts were made to improve the selectivity of the reaction in favor of bromoamination. A screening of reaction solvents showed that the indole conversion and the bromoaminoindole/bromoindole selectivity decreased in the order acetonitrile > THF > toluene > t-BuOH ≫ DMSO. Inorganic base additives such as Cs_2CO_3 and KOAc, which were found to be crucial for the related palladium−copper-catalyzed chloroamination reaction,[30] completely suppressed the bromoamination reaction (Table 2). Similarly, the inclusion of various *N*-donor ligands, including bipyridine and electron-poor pyridine ligands (entries 4−6), provided lower conversions and yields of **3aa-Br**.

From our knowledge that **4a** is produced only by $CuBr_2$, we reasoned that if we could sequester the Cu(II) generated during the reaction or reduce it in situ to Cu(I), we might be able to promote the formation of **3aa-Br**. In this respect, we explored the effect of established Cu(II) complexing agents and reducing agents in the bromoamination reaction. Among the additives screened, sodium citrate showed comparable yields, but others resulted in lowered selectivity (Table 1, entries 7−10). Similarly, of the reductants studied, Cu powder and $NaHSO_3$ furnished comparable yields but no significant improvement.

To determine the effect of varying the *N*-reagent on the bromoamination/bromination selectivity and the reaction scope with respect to the *N*-reagent, we employed several electronically modified oxime esters (Table 2). Most of the modifications to the compounds resulted in reduced yields and selectivity. The only *N*-reagents that produced appreciable quantities of the bromoaminated product were the benzophe-

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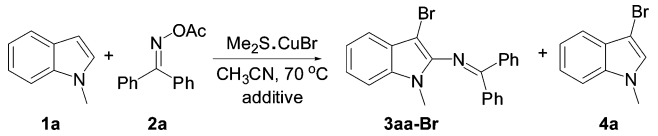
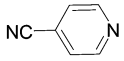
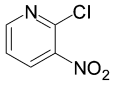
Table 1. Additive Effects on the Bromoamination of *N*-Methylindole (1a)[a]



1a 2a 3aa-Br 4a

entry	additive (2 equiv.)	bromoaminated indole **3aa-Br** (%)	brominated indole **4a** (%)	**1a** conversion (%)
1	none	58	42	100
2	Cs_2CO_3	0	0	0
3	KOAc	0	0	0
4	bipyridine	0	trace	<1
5		9	14	23
6		13	18	31
7	sodium citrate	44	32	76
8	Na_4EDTA	11	17	28
9	tartaric acid	13	71	84
10	2-picolinic acid	29	45	74
11	$NaHSO_3$	53	47	100
12	$PhNHNH_2$	-	15	15
13	Cu powder	56	44	100
14	$K_2C_2O_4$	28	27	55
15[b]	CuI/NaI	18	55	73
16	$Na_2S_2O_5$	-	100	100
17	ascorbic acid	trace	-	<10

[a]Reaction conditions: *N*-methylindole (0.013 mmol), oxime ester (0.026 mmol), and MeS·CuBr (0.013 mmol) in 2 mL of CH_3CN, 70 °C, 16 h. Conversions and selectivity determined by ^1H NMR spectroscopy. [b]Produced iodoaminated product **3aa-I**.

none *O*-benzoyloxime (**2c**) and the 4,4′-dimethoxybenzophenone *O*-acetyloxime (**2e**). No bromoamination product was observed using the dinitrobenzophenone *O*-acetyloxime (**2f**), while the fluoren-9-one oxime (**2g**), which is electronically similar to **2a**, produced only trace amounts (ca. 5%) of the corresponding bromoaminated product.

With respect to the scope of the bromoamination reaction, we found that *N*-benzylindole and other electronically diverse indoles could be bromoaminated as well, e.g., to produce the products **3ba**, **3ca**, and **3da** in moderate yields (Chart 1, yields in parentheses), along with the corresponding bromoindoles. The CuX-promoted reaction can also be extended to effect chloroamination as well as iodoamination, using CuCl and CuI, producing indole derivatives **3aa-Cl** and **3aa-I**, respectively.

We also established the viability of the Cu-promoted bromoamination reaction on a representative pyrrole substrate, *N*-methylpyrrole (**6a**). Operating under typical reaction conditions, (pyrrole:oxime ester:Me_2S·CuBr = 1:2:1, CH_3CN, 70 °C), a mixture of a single bromoaminated pyrrole (**6aa-Br**, 14%) and a single dibromoaminated derivative (**6aa-Br$_2$**, 39%) was produced judging by their NMR and mass spectral features (Scheme 3). Changing the pyrrole:oxime ester:Me_2S·CuBr ratio to 1:1.25:1 allowed us to isolate a 69% yield of **6aa-Br** (6% of **6aa-Br$_2$** was detected by NMR). The presence of two pyrrole proton doublets (J = 6 Hz) at 4.6 and 5.9 ppm for **6aa-Br** is indicative of a 2,3- or a 2,5-substitution pattern. On the basis of NMR correlation studies (gHMBC, C−H 2-3 bond correlation; see Supporting Information) and considering the typical C-2 attack by electrophiles on pyrroles[34] and the proven indole bromoamination regioselectivity, we assign the structure of **6aa-Br** as the 2-bromo-3-amino derivative and, analogously, the dibromoaminated compound as the 2,5-dibromo-3-amino derivative (**6aa-Br$_2$**).

Since the bromoindole **4a** was consistently produced in the copper bromide-mediated indole reactions, we wondered if it is a precursor to the bromoaminated product **3aa-Br**. To further understand the reaction pathway, we monitored the time-dependent production of both **3aa-Br** and **4a** by ^1H NMR analysis. A plot of the NMR-determined conversions for the consumption of **1a** and the evolution of **3aa-Br** and **4a** (Figure 2) suggests that these two products are generated by independent pathways. Further evidence of **4a** not being a precursor to **3aa-Br** was obtained by subjecting **4a** to the bromoamination reaction, which failed to produce any **3aa-Br**. This observation is in contrast to that made by Liu et al.,[30] where the presence of the chlorine atom at the 3-position was seen to improve the amination efficiency.

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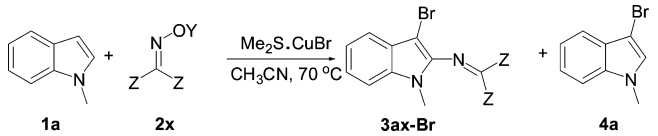
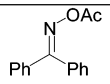
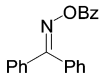
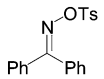
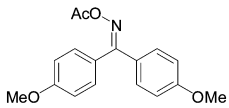
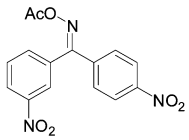
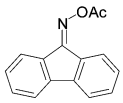
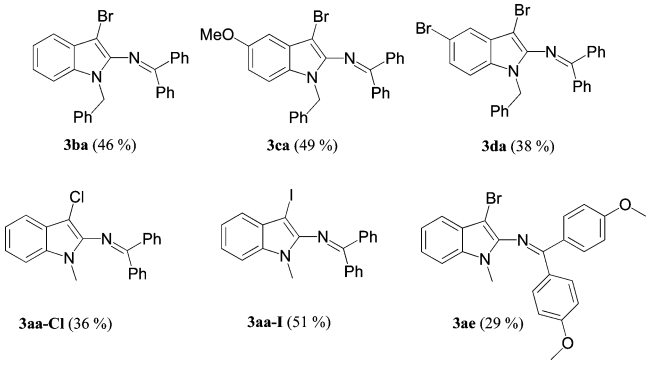
Table 2. Screening of Oxime Esters for Bromoamination of *N*-Methylindole (1a)[a]



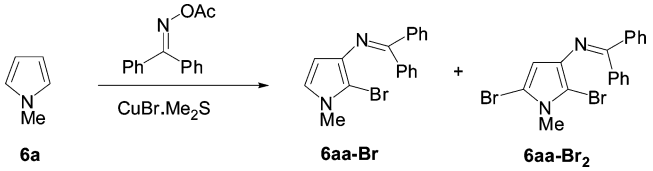
entry	oxime ester	bromoaminated indole **3ax-Br** (%)	brominated indole **4a** (%)	**1a** conversion (%)
1	 **2a**	58	42	100
2	 **2b**	5	54	60
3	 **2c**	31	48	79
4	 **2d**	0	85	85
5	 **2e**	29	36	65
6	 **2f**	0	57	57
7	 **2g**	5	40	45

[a]Reaction conditions: *N*-methylindole (0.013 mmol), oxime ester (0.026 mmol), and Me_2S·CuBr (0.013 mmol) in 2 mL of CH_3CN, 70 °C, 16 h. Conversions and selectivity determined by ^1H NMR spectroscopy.

Chart 1. Scope of the Bromoamination Reaction Mediated by CuX (X = Cl, Br, I)



Scheme 3



Aside from the apparent independence of the processes leading to the brominated and bromaminated products, we have no direct mechanistic evidence on the reaction pathways. The previously cited precedents and the general features of Cu-redox chemistry prompt us to speculate that a Cu(III)-imino species, e.g., $Cu(NCAr_2)X(OAc)$, could be involved in the formation of the haloaminated products, while $Cu(II)X_2$ is responsible for the halogenation.[31] These copper species could be generated as outlined in Scheme 4A. The novel haloamination process could proceed via addition of the electrophilic Cu(III)-imino species to the unsaturated hetero-

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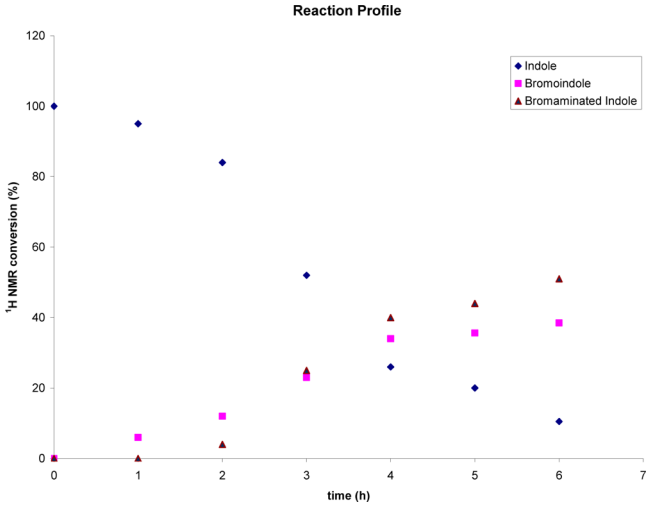


Figure 2. Time-dependent reactant/product evolution during the bromination−bromoamination of *N*-methylindole (**1a**).

cycle (Scheme 4B). A similar addition has been supported computationally[35] in the Cu-promoted amidation of indoles[27] and accounts for the observed regioselectivity in directing the Cu-electrophile to the more nucleophilic C-3 of indole,[34a,36] delivering the nucleophilic imino unit to C-2. Sequential elimination of acetic acid and copper hydride would produce the 3-halo-2-imino products. Alternative pathways such as the initial addition of an iminyl radical ($Ph_2C{=}N^{\bullet}$) to the indole skeleton followed by oxidation with Cu(II) and subsequent electrophilic bromination of the resulting 2-amino indole product[37] can be envisioned, but their distinction must await future investigations of this novel reaction.

In conclusion, we have discovered a novel and regioselective heterodifunctionalization method for the aromatic *N*-heterocycles indole and pyrrole. The bromoimino products will allow easy access to the respective halo-2-aminoindoles via acidic hydrolysis.[38] Furthermore, the halogen functionality could enable further synthetic manipulations through cross-coupling and other substitution reactions.[39]

EXPERIMENTAL SECTION

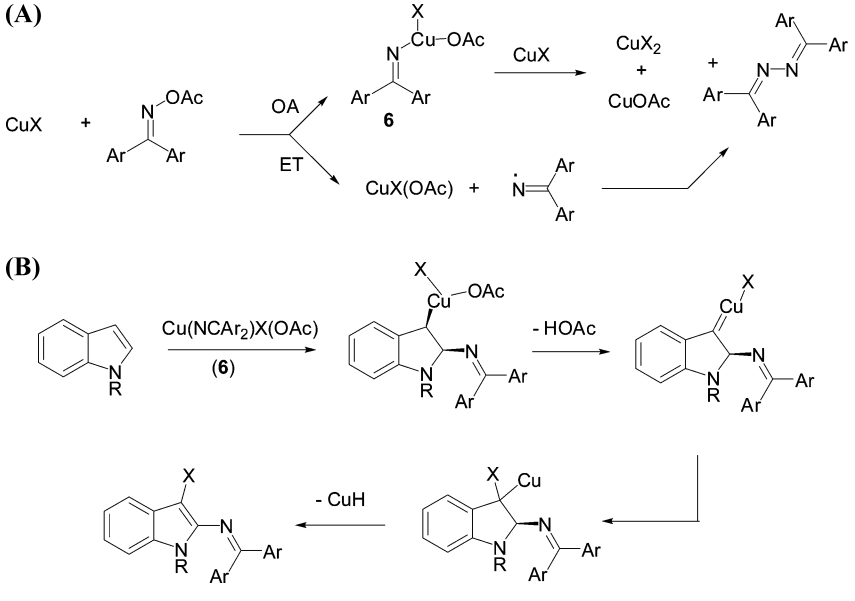
General Procedures. All manipulations were carried out using Schlenk tube techniques under an inert atmosphere. Cu salts, acetonitrile, and indole(s) were purchased from commercial sources. Acetonitrile was freshly distilled over CaH_2 and degassed by repeated freeze−pump−thaw cycles. ^{1}H and $^{13}C\{^1H\}$ NMR spectra were recorded on a 300 MHz NMR spectrometer. 2D NMR data were acquired on a 500 MHz spectrometer. ^{1}H NMR peaks are labeled as singlet (s), doublet (d), triplet (t), and multiplet (m). Mass spectra were acquired in the ESI (+) mode. Benzophenone *O*-acetyloxime (**2a**),[26] acetophenone *O*-acetyloxime (**2b**),[40] benzophenone *O*-benzoyloxime (**2c**),[26] benzophenone *O*-tosyloxime (**2d**),[41] 4,4′-dimethoxybenzophenone *O*-acetyloxime (**2e**),[26] 3,4′-dinitrobenzophenone *O*-acetyloxime (**2f**),[26] fluoren-9-one *O*-acetyloxime (**2g**),[26] *N*-benzylindole (**1b**),[42] *N*-benzyl-5-methoxyindole,[43] and *N*-benzyl-5-bromoindole[43] were synthesized by adapting literature procedures. X-ray quality crystals of **3aa-Br** were grown by slow evaporation from a 1:1 diethyl ether/hexanes solution.

General Procedure for Bromoamination Reactions. To a stirred solution of *N*-methylindole (**1a**) (0.017 g, 0.013 mmol) in dry and degassed solvent (ca. 2 mL) were added the oxime ester (0.026 mmol), $Me_2S{\cdot}CuBr$ (0.013 mmol), and additive (0.026 mmol), and the reaction mixture was stirred at 70 °C for 16 h. The reaction mixture was cooled to room temperature and filtered through a plug of silica using CH_2Cl_2 (ca. 5 mL). The filtrate was concentrated under vacuum, and the residue analyzed by NMR. The crude reaction mixture was purified by silica gel column chromatography to obtain the pure products using 20−40% CH_2Cl_2 in hexane as the elutant. The *N*-alkyl-3-bromoindoles were identified in the reaction mixture by ^{1}H NMR spectroscopy based on literature data.

3aa-Br: orange solid (0.028 g, 55%). ^{1}H NMR ($CDCl_3$, 300 MHz, 25 °C): δ 7.83 (d, $^3J_{HH}$ = 8.7 Hz, 2H), 7.55 (t, $^3J_{HH}$ = 7.5 Hz, 1H), 7.45 (t, $^3J_{HH}$ = 8.4 Hz, 2H), 7.32−7.29 (m, 2H), 7.25−7.21 (m, 5H), 7.14 (t, $^3J_{HH}$ = 6.9 Hz, 1H), 7.08 (t, $^3J_{HH}$ = 7.2 Hz, 1H), 3.69 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz, 25 °C): δ 172.7, 143.1, 137.9, 135.7, 133.8, 130.5, 129.1, 128.7, 128.3, 127.2, 127.0, 126.1, 119.8, 118.9, 117.3, 107.5, 28.7. HRMS (ESI): calcd for $C_{22}H_{18}BrN_2$ $(M + H)^+$ requires m/z = 389.0653, found m/z = 389.0669.

3aa-Cl: orange solid (0.016 g, 36%). ^{1}H NMR ($CDCl_3$, 300 MHz, 25 °C): δ 7.86−7.80 (m, 3H), 7.57 (t,, $^3J_{HH}$ = 7.2 Hz, 1H), 7.52−7.45 (m, 3H), 7.33−7.30 (m, 1H), 7.26−7.06 (m, 6H), 3.70 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz, 25 °C): δ 173.5, 142.6, 139.1, 137.1, 134.3, 131.7, 130.3, 129.8, 129.3, 128.4, 128.3, 125.7, 121.1, 119.9,

Scheme 4. Proposed Mechanism for the Bromoamination Reaction



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117.7, 108.7, 29.7. HRMS (ESI): calcd for $C_{22}H_{18}ClN_2$ $(M + H)^+$ requires m/z = 345.1159, found m/z = 345.1159.

3aa-I: red-orange solid (0.029 g, 51%). ^1H NMR ($CDCl_3$, 300 MHz, 25 °C): δ 7.86−7.80 (m, 3H), 7.57 (t,, $^3J_{HH}$ = 7.2 Hz, 1H), 7.52−7.45 (m, 3H), 7.33−7.30 (m, 1H), 7.26−7.06 (m, 6H), 3.70 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz, 25 °C): δ 174.2, 147.8, 139.1, 137.7, 136.7, 136.0, 132.6, 131.8, 130.4, 130.2, 130.0, 129.8, 128.5, 128.4, 128.2, 121.0, 120.2, 108.8, 30.3. HRMS (ESI): calcd for $C_{22}H_{18}IN_2$ $(M + H)^+$ requires m/z = 437.0515, found m/z = 437.0508.

3ae: orange solid (0.017 g, 29%). ^1H NMR ($CDCl_3$, 300 MHz, 25 °C): δ 7.79 (d, $^3J_{HH}$ = 9.3 Hz, 2H), 7.32 (d, $^3J_{HH}$ = 8.7 Hz, 1H), 7.23−7.05 (m, 5H), 6.96 (d, $^3J_{HH}$ = 8.7 Hz, 2H), 6.75 (d, $^3J_{HH}$ = 9.0 Hz, 2H), 3.89 (s, 3H), 3.76 (s, 3H), 3.67 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz, 25 °C): δ 173.0, 162.6, 160.6, 145.0, 134.8, 132.3, 132.1, 131.3, 129.3, 127.4, 120.7, 119.9, 118.2, 113.7, 113.6, 108.6, 55.7, 55.3, 29.9. HRMS (ESI): calcd for $C_{24}H_{22}BrN_2O_2$ $(M + H)^+$ requires m/z = 449.0865, found m/z = 449.0860.

3ba: orange solid (0.027 g, 46%). ^1H NMR ($CDCl_3$, 300 MHz, 25 °C): δ 7.76 (d, $^3J_{HH}$ = 9.0 Hz, 2H), 7.54 (t, $^3J_{HH}$ = 7.5 Hz, 1H), 7.43 (t, $^3J_{HH}$ = 7.5 Hz, 2H), 7.36−7.31(m, 1H), 7.28−7.20 (m, 7H), 7.16 (t, $^3J_{HH}$ = 8.4 Hz, 2H), 7.12−7.08 (m, 2H), 6.96 (d, $^3J_{HH}$ = 9.0 Hz, 2H), 5.36 (s, 2H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz, 25 °C): δ 172.9, 143.8, 139.3, 137.8, 136.8, 134.7, 132.6, 131.6, 130.3, 129.7, 129.6, 128.8, 128.4, 128.3, 128.0, 127.6, 121.4, 120.3, 118.7, 109.4, 47.2. HRMS (ESI): calcd for $C_{28}H_{22}BrN_2$ $(M + H)^+$ requires m/z = 465.0966, found m/z = 465.0958.

3ca: orange solid (0.031 g, 49%). ^1H NMR ($CDCl_3$, 300 MHz, 25 °C): δ 7.76 (d, $^3J_{HH}$ = 7.2 Hz, 2H), 7.53 (t, $^3J_{HH}$ = 7.8 Hz, 1H), 7.43 (t, $^3J_{HH}$ = 7.5 Hz, 2H), 7.32−7.11 (m, 9H), 6.98 (d, $^3J_{HH}$ = 7.2 Hz, 2H), 6.79 (d, $^4J_{HH}$ = 2.4 Hz, 1H), 6.73 (dd, J_{HH} = 8.1 and 2.4 Hz, 1H), 5.32 (s, 2H), 3.82 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz, 25 °C): δ 172.8, 154.7, 144.2, 139.3, 137.8, 136.8, 132.6, 131.6, 130.3, 129.7, 129.6, 128.8, 128.4, 128.3, 128.0, 127.6, 127.5, 111.3, 110.4, 100.5, 55.9, 47.3. HRMS (ESI): calcd for $C_{29}H_{24}BrN_2O$ $(M + H)^+$ requires m/z = 495.1072, found m/z = 495.1061.

3da: orange solid (0.027 g, 38%). ^1H NMR ($CDCl_3$, 300 MHz, 25 °C): δ 7.77 (d, $^3J_{HH}$ = 7.5 Hz, 2H), 7.55 (t, $^3J_{HH}$ = 7.5 Hz, 1H), 7.46−7.41 (m, 3H), 7.33−7.25 (m, 4H), 7.20−7.18 (m, 4H), 7.12 (t, $^3J_{HH}$ = 8.1 Hz, 2H), 6.95 (d, $^3J_{HH}$ = 6.9 Hz, 2H), 5.33 (s, 2H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz, 25 °C): δ 173.8, 144.9, 139.0, 137.3, 136.6, 133.4, 131.9, 130.4, 129.9, 129.5, 129.2, 128.9, 128.4, 128.1, 127.9, 127.6, 124.1, 121.2, 113.5, 110.9, 47.3. HRMS (ESI): calcd for $C_{28}H_{21}{}^{81}Br^{79}BrN_2$ $(M + H)^+$ requires m/z = 545.0051, found m/z = 545.0035.

6aa-Br: yellow-orange solid (0.030 g, 69%). ^1H NMR ($CDCl_3$, 300 MHz, 25 °C): δ 7.77−7.74 (m, 2H), 7.52−7.49 (m, 3H), 7.38−7.35 (m, 3H), 7.24−7.21 (m, 2H), 5.92 (d, J_{HH} = 4.8 Hz, 1H), 4.65 (d, J_{HH} = 4.2 Hz, 1H), 3.81 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz, 25 °C): δ 158.4, 140.3, 138.9, 129.9, 129.6, 128.8, 128.3, 128.2, 127.6, 110.2, 103.1, 102.1, 31.5. HRMS (ESI): calcd for $C_{18}H_{16}BrN_2$ $(M + H)^+$ requires m/z = 339.0497, found m/z = 339.0490.

6aa-Br$_2$. orange solid (0.019 g, 36%). ^1H NMR ($CDCl_3$, 300 MHz, 25 °C): δ 7.74 (d, $^3J_{HH}$ = 6.9 Hz, 2H), 7.51 (t, $^3J_{HH}$ = 6.9 Hz, 1H), 7.44−7.33 (m, 5H), 7.21 (d, $^3J_{HH}$ = 6.0 Hz, 2H), 5.98 (s, 1H), 3.51 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz, 25 °C): δ 171.4, 139.5, 139.4, 137.3, 131.3, 130.1, 129.8, 129.7, 128.3, 128.2, 111.7, 99.2, 32.6. HRMS (ESI): calcd for $C_{18}H_{15}Br_2N_2$ $(M + H)^+$ requires m/z = 418.9582, found m/z = 418.9576.

■ ASSOCIATED CONTENT

Supporting Information

Spectral data for all new compounds reported and X-ray collection data for **3aa-Br** are available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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