# Copper-Catalyzed Intermolecular C−H Amination of (Hetero)arenes via Transient Unsymmetrical λ^3-Iodanes

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S *Supporting Information*

ABSTRACT: A one-pot two-step method for intermolecular C−H amination of electron-rich heteroarenes and arenes has been developed. The approach is based on a room-temperature copper-catalyzed regioselective reaction of the in situ formed unsymmetrical (hetero)aryl-λ^3-iodanes with a wide range of primary and secondary aliphatic amines and anilines.
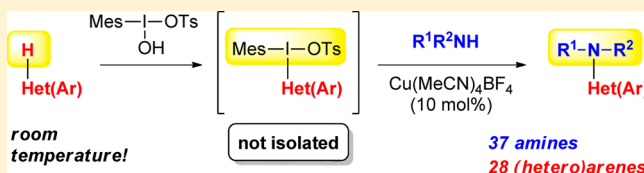
INTRODUCTION

Hypervalent iodine(III) species possessing an iodine−nitrogen bond are efficient reagents in oxidative C−H amination of nonprefunctionalized arenes and heteroarenes.[1] The most widely used are preformed or in situ generated sulfonylimino-λ^3-iodanes, which effect C−H to C−N bond transformations in the presence of transition metal catalyst (eq 1).[2] Phenyl-λ^3-
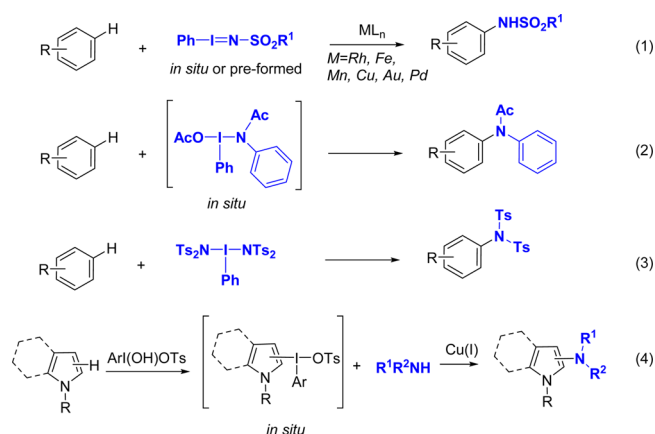
iodane (formed in situ from PhI(OAc)₂ and N-acetanilide) has been proposed as a precursor of acylnitrenium species in a transition metal-free C−H amination of arenes (eq 2).[3−5] Analogous phenyl-λ^3-iodanes possessing an iodine−nitrogen bond have also been suggested as plausible intermediates in an oxidative transfer of the phthalimide moiety to arene rings.[6,7] Recently, a well-defined bis-tosylimido-λ^3-iodane has been introduced by Muñiz for a metal-free oxidative amination of arenes and heteroarenes (eq 3).[8] All of the above-mentioned approaches, however, have a serious limitation: only amides, imides, and sulfonamides can be transferred to arenes or heteroarenes by hypervalent iodine(III) species. Simple amines are not compatible with these C−H amination conditions, as they are oxidized by monoaryl-λ^3-iodane reagents.[9] In contrast, amines are oxidatively stable toward diaryl-λ^3-iodanes, and these hypervalent iodine(III) species have been used for the N-

arylation of amines.[10] Symmetrical diaryl-λ^3-iodanes are preferred for N-arylation because unsymmetrical diaryl-λ^3-iodanes usually form a mixture of N-arylation products.[10d,e]

We envisioned that a versatile method for C−H amination of (hetero)arenes with unprotected amines as the source of nitrogen could be developed, provided that the issue of regioselectivity of amine transfer to the desired aromatic ring of the unsymmetrical diaryl-λ^3-iodanes could be solved. Recently, we reported that a Cu(I) catalyst ensures complete regiocontrol in a reaction of azides with unsymmetrical diaryl-λ^3-iodanes.[11] During this study, it became evident that nucleophiles other than azide could be reacted regioselectively with a variety of unsymmetrical heteroaryl-λ^3-iodanes that are generated as intermediates using suitable ArI(OH)OTs reagent. Herein, we report a mild and versatile Cu(I)-catalyzed method for intermolecular C−H amination of electron-rich heterocycles (pyrroles, pyrrolopyridines, thienopyrroles, pyrrolopyrimidines, and uracil) as well as simple arenes, comprising a one-pot two-step room-temperature reaction between the (hetero)aryl-λ^3-iodanes formed in situ and a wide range of primary and secondary amines (eq 4). The reactivity pattern of the developed C−H amination approach is consistent with that of an electrophilic aromatic substitution (S_EAr) reaction. Because of the operational simplicity, mild reaction conditions, and wide substrate scope, our C−H amination approach provides a convenient way for C−H functionalization of heteroarenes,[12] a topic of high importance in medicinal and pharmaceutical chemistry given the drug-like properties of heteroarenes and abundance of heterocycles in drugs.

RESULTS AND DISCUSSION

At the outset of our investigation, we synthesized the indolyliodonium tosylate **2a** in a pure form from MesI(OH)-OTs[13] and indole **1a**. The structure of **2a** was confirmed by X-ray crystallographic analysis (Figure 1). λ^3-Iodane **2a** is stable in MeCN, DCM, and DMSO solutions at room temperature for
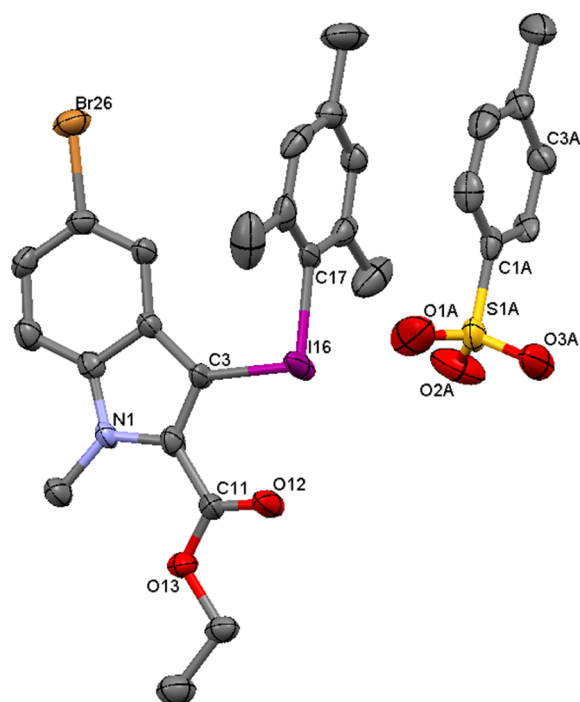
Figure 1. X-ray crystal structure of λ^3-iodane **2a** (ellipsoids at 50% probability) with hydrogen atoms omitted for clarity. Selected bond distances (Å) and angles (deg): I16−C3, 2.086(7); I16−C17, 2.108(8); I16−O12, 2.713(7); I−O1A, 3.088(9); I−O2A, 3.001(8); C3−I16−C17, 98.2(3). See the Supporting Information for details.

at least 72 h, but addition of morpholine and DIPEA to a DCM solution of **2a** brought about its slow transformation to iodoindole **4a** (entry 1, Table 1). The process was facilitated by using DMSO as solvent (entry 2). The conversion of **2a** to **4a** was highly selective, and only traces of indolylamine **3a** were observed. In striking contrast, addition of CuOTf (10 mol %) resulted in complete reversal of selectivity favoring the formation of the desired **3a**. Furthermore, the copper catalyst considerably decreased the reaction time (entry 3 vs entries 1−

2, Table 1). Both Cu(I) and Cu(II) salts could be utilized; however, the Cu(I) species ensured faster reaction (entry 3 vs 4). Faster formation of **3a** helped to improve the **3a**:**4a** ratio by diminishing an impact of the competing noncatalyzed background formation of **4a** (entry 2). The determined initial rates of the noncatalyzed background reaction of **2a** with morpholine in DMSO (initial rate coefficient $k_{obs} = 1.98 \times 10^{-7}$ mmol mL^{-1} s^{-1}, DMSO-d_6, 25 °C) evidence that the background reaction delivers ca. 10% of **4a** within 90 min. By this time, the Cu(I)-catalyzed conversion of **2a** to **3a** is almost quantitative, so the faster is **3a** formation, the higher is **3a**:**4a** selectivity. Screening of various Cu(I) sources helped to identify the relatively stable Cu(MeCN)$_4$BF$_4$ as the most efficient catalyst (entry 5). λ^3-Iodane **2a′** containing a Ph ligand instead of the mesityl group could also be used at the expense of slightly diminished selectivity (entry 6). However, Pd(II), Ni(II), and Sc(III) salts were inefficient as catalysts (entries 7−9, Table 1).[14]

Indolylamine **3a** could also be synthesized in a sequential one-pot approach without isolation of the iodonium salt **2a**. Accordingly, Cu(MeCN)$_4$BF$_4$, morpholine, and EtN(i-Pr)$_2$ were added to the reaction mixture after the corresponding λ^3-iodane **2a** had been formed.[15] The one-pot sequential C−H amination approach afforded lower yields of **3a** as compared to the two-step synthesis (74% vs 85%), but avoided the isolation and handling of potentially unstable intermediate λ^3-iodanes. This advantage compensates for the decreased yields.

Various amines were subsequently examined in the Cu(I)-catalyzed two-step one-pot C−H amination of indole **1a** (Table 2). A wide variety of aliphatic secondary amines (entries 1−11), aliphatic primary amines (entries 12−26), primary and secondary aromatic amines (entries 27−35), as well as a heteroarylamine (entry 36) and ammonia (entry 37) could be employed. Importantly, the reaction conditions are compatible with alkene and alkyne moieties in the amine (entries 10, 22, 23).[16] N-Boc (entry 17), N-acetyl (entry 5), and S-trityl (entry 20) protecting groups, acetals (entry 21), ketals (entry 2), as well as various functional groups such as esters (entry 30), nitriles (entries 9,15), nitro (entry 31), and halides (entries 24, 25, 28) are all tolerated. Sterically hindered amines (entries 14,

Table 1. Reaction of λ^3-Iodane 2a with Morpholine
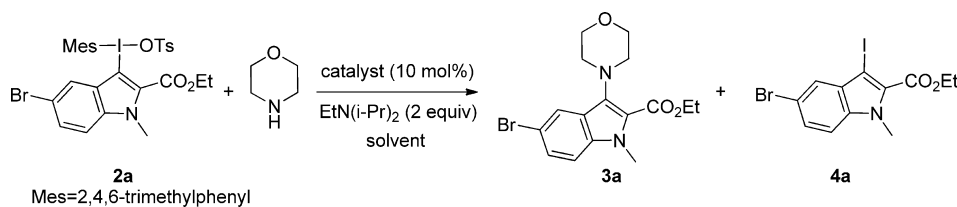
entry	catalyst (10 mol %)	solvent, time	conversion %[a,b]	3a:4a ratio, (yield %)[b,c]
1	none	CH$_2$Cl$_2$, 24 h	15	1:99 (8)
2	none	DMSO, 24 h	81	1:99 (67)
3	CuOTf·PhH	CH$_2$Cl$_2$−DMSO 4:1, 1.5 h	60	97:3 (46)
4	Cu(OTf)$_2$	CH$_2$Cl$_2$−DMSO 4:1, 1.5 h	22	93:7 (14)
5	Cu(MeCN)$_4$BF$_4$	CH$_2$Cl$_2$−DMSO 4:1, 1 h	92	97:3 (85)[d]
6[e]	Cu(MeCN)$_4$BF$_4$	CH$_2$Cl$_2$-DMSO 4:1, 1.5 h	93	89:11 (76)
7	Pd(OCOCF$_3$)$_2$	CH$_2$Cl$_2$−DMSO 4:1, 1.5 h	5	1:99 (3)
8	Ni(OTf)$_2$	CH$_2$Cl$_2$−DMSO 4:1, 1.5 h	5	1:99 (5)
9	Sc(OTf)$_3$	CH$_2$Cl$_2$−DMSO 4:1, 1.5 h	7	1:99 (5)

[a]Conditions: λ^3-iodane **2a** (1.0 equiv), morpholine (1.2 equiv), solvent (10 mL/1 mmol of **2a**), room temperature. [b]Determined by LC−MS assay. [c]Yield of the major product. [d]Isolated yield of >95% pure indole **3a**. [e]λ^3-Iodane **2a′** possessing Ph ligand instead of a mesityl group (Mes = Ph) was used.

Table 2. Sequential One-Pot Synthesis of Indolylamines 3a−3ak[a]

Mes=2,4,6-trimethylphenyl

entry	R^{1}R^{2}NH	Yield (%)	entry	R^{1}R^{2}NH	Yield (%)	entry	R^{1}R^{2}NH	Yield (%)
1		**3a**, 74	14		**3n**, 76	26		**3z**, 79
2		**3b**, 66	15		**3o**, 63	27		**3aa**, 73
3		**3c**, 75	16		**3p**, 67	28		**3ab**, 74
4		**3d**, 71	17		**3q**, 73	29		**3ac**, 54
5		**3e**, 76	18		**3r**, 40	30		**3ad**, 69
6		**3f**, 76	19		**3s**, 75	31		**3ae**, 67
7		**3g**, 70	20		**3t**, 73	32		**3af**, 62
8		**3h**, 35[b]	21		**3u**, 80	33		**3ag**, 79
9		**3i**, 65	22		**3v**, 80	34		**3ah**, 76
10		**3j**, 67	23		**3w**, 71	35		**3ai**, 77
11		**3k**, 65	24		**3x**, 83	36		**3aj**, 65
12		**3l**, 71	25		**3y**, 77	37		**3ak**, 71[c]
13		**3m**, 70						

[a]Conditions: Indole **1a** (1.0 equiv), MesI(OH)OTs (1.1 equiv), CF$_3$COOH (1.2 equiv), CH$_2$Cl$_2$ (4 mL/1 mmol of **1a**), room temperature, 15 min; then amine (1.2 equiv), EtN(*i*-Pr)$_2$ (2.0 equiv), Cu(MeCN)$_4$BF$_4$ (0.1 equiv), 1:1 CH$_2$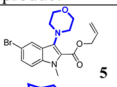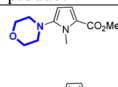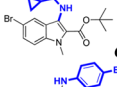Cl$_2$: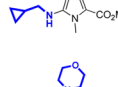DMSO (4 mL/1 mmol of **1a**), room temperature, 2 h. [b]Reaction time for the formation of **3h** from λ^3-iodane: 18 h. [c]3 equiv of EtN(*i*-Pr)$_2$ was used.
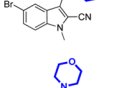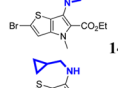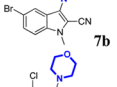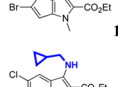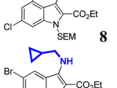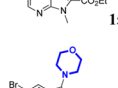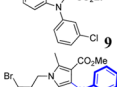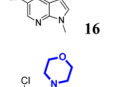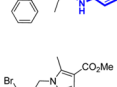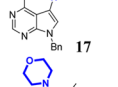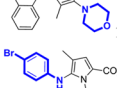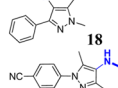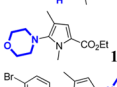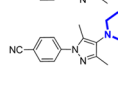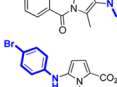
33, 34) are also suitable as substrates.[17] Amines react chemoselectively in the presence of unprotected alcohol (entry 16), amide (entry 6), and sulfonamide moieties (entry 32), and monoamination with piperazine is also possible (entry 7). It should be noted that moderate yields were obtained for bi- and tridentate amines potentially capable of chelating the Cu(I) catalyst (entries 8, 18).

Next, the scope of substrates for the C−H amination was surveyed employing morpholine, cyclopropylmethylamine, and 4-bromoaniline as representative amines (Table 3). All heterocycles that react with MesI(OH)OTs and form iodonium salts that survive in solution are suitable as substrates, including 2-substituted indoles (entries 1−6),[18] pyrroles (7−14), thieno-[3,2-*b*]pyrrole (entries 15, 16), pyrrolo[2,3-*b*]pyridines (entries 17, 18), pyrrolo[2,3-*d*]pyrimidine (entry 19), pyrazoles (entries 20−22), and *N,N*-dimethyluracil (entry 23). The formation of the intermediate iodonium salts was found to be sensitive to the electronic properties of heterocycle.[19] Thus, relatively electron-rich *N*-alkyl pyrroles (entries 7−10, 12−14) and pyrrolo[2,3-*b*]pyridine (entry 18) reacted rapidly and produced the intermediate iodonium salts within 5 min. In contrast, introduction of an electron-withdrawing *N*-acyl moiety in pyrrole (entry 11) increased the reaction time to 30 min. The formation of iodonium salts from less electron-rich heterocycles such as indoles (entries 1−6), pyrrolo[2,3-*b*]pyridine (entry 17), pyrrolo[2,3-*d*]pyrimidine (entry 19), pyrazoles (entries 20−22), and *N,N*-dimethyluracil (entry 23) was considerably slower. However, the reaction of these substrates with

MesI(OH)OTs could be facilitated by addition of CF$_3$COOH (1.2 equiv). This did not work always, and pyrroles possessing several electron-withdrawing substituents such as *N*-tosyl-1*H*-pyrrole-2-carboxylic acid ethyl ester did not give substantial conversion to the corresponding iodonium salt under our standard conditions with added CF$_3$COOH. Furthermore, potential substrates such as *N*-methylbenzimidazole, benzo[*b*]-thiophene, and ethyl thiophene-2-carboxylate were also unreactive. Apparently, the latter heterocycles are insufficiently electron-rich to produce iodonium salts in the reaction with MesI(OH)OTs. On the other hand, we were especially pleased to find that electron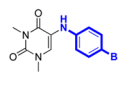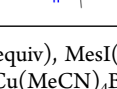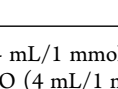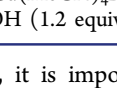-rich carbocyclic arenes undergo C−H amination as exemplified in Table 4. Surprisingly, even the simple substrates such as tetraline (entry 1) and *N*-Boc-*N*-methylaniline (entry 2) could be employed in the C−H amination reaction. The formation of the intermediate diaryl-λ^3-iodane from tetraline (entry 1) required prolonged time (18 h) apparently because of insufficiently electron-rich nature of tetraline. The presence of electron-releasing alkoxy groups facilitates considerably the formation of intermediate diaryl-λ^3-iodane (entries 3−5 vs entry 1). Further improvement of C−H amination yields was achieved for arenes containing two electron-releasing substituents (entries 6−9, Table 4). In general, the more electron-rich is (hetero)arene, the shorter are the times required to produce the intermediate diaryl-λ^3-iodane. However, transient λ^3-iodanes formed from electron-rich (hetero)arenes usually are unstable and are prone to undesired decomposition if the addition of Cu catalyst and/or

Table 3. C−H Amination of Heterocycles

Het-H → [Mes—I—OTs / Het] → Het—N(R1)(R2) **5-20**

Conditions: MesI(OH)OTs, CH₂Cl₂, rt, time (Table 3); then R¹R²NH, Cu(MeCN)₄BF₄ (10 mol%), EtN(i-Pr)₂, 4:1 CH₂Cl₂:DMSO, rt, 2 h

entry	product[a]	time	yield (%)	entry	product[a]	time	yield (%)
1	5	30 min[b]	69	13	13b	5 min	71
2	6	30 min[b]	79	14	13c	5 min	65
3	7a	18 h[b]	84	15	14b	2 h	57
4	7b	18 h[b]	77	16	14c	2 h	62
5	8	18 h[b]	50	17	15	1 h[b]	78
6	9	18 h[b]	72	18	16	5 min[c]	62
7	10a	5 min	70	19	17	3 h[b]	60
8	10b	5 min	62	20	18	5 h[b]	52
9	11a	5 min	60	21	19a	24 h[b]	60
10	11b	5 min	62	22	19b	24 h[b]	62
11	12	30 min	63	23	20	18 h[b]	65
12	13a	5 min	91				

[a]Conditions: Heteroarene (1.0 equiv), MesI(OH)OTs (1.1 equiv), CH₂Cl₂ (4 mL/1 mmol of the starting heteroarene), 15 min; then amine (1.2 equiv), EtN(i-Pr)₂ (2.0 equiv), Cu(MeCN)₄BF₄ (0.1 equiv), 2:1 CH₂Cl₂:DMSO (4 mL/1 mmol of the starting heteroarene), room temperature, 2 h. [b]In the presence of CF₃COOH (1.2 equiv). [c]λ^3-Iodane was formed at −20 °C.

amine is delayed. Therefore, it is important to establish the optimum conversion time of the starting (hetero)arene into λ^3-iodane.

The regioselectivity of the C−H amination is controlled at the stage of the formation of the intermediate iodonium salts. Although the regioselectivity is a result of the combined directing effects of substituents in heterocycles and arenes, in general, it is consistent with that of electrophilic aromatic substitution (S_EAr) reactions. Thus, λ^3-iodanes are formed at the β-position of indoles (entries 1−6, Table 3) and fused pyrroles (entries 15−19), at the α-position of pyrroles[20a] (entries 9, 10, 12−14), and at position 5 of uracil[20b] (entry 23), while 2,5-disubstituted pyrroles (entries 7, 8, 11) produce iodonium salts at the β-position. In the case of simple arenes, intermediate λ^3-iodanes are selectively formed in the para-position to the strongest electron-releasing substituent in the molecule, for example, alkyl moiety (entry 1, Table 4), N-Boc-N-methylamino group (entry 2), alkoxy (entry 4), and MeO groups (entries 3, 5−8).[21] Interestingly, C−H amination proceeds in para-position to the MeO group also in N-protected methoxyanilines (entries 9−11), substrates that

possess two different electron-releasing substituents. The observed regioselectivity of C−H amination in meta-anisidines (entries 10, 11) might also be attributed to stabilization of intermediate λ^3-iodane by the adjacent N-Boc moiety. However, we regard such stabilization unlikely because N-Boc-N-methylaniline underwent C−H amination in the para-position, and not next to the aniline nitrogen (entry 2, Table 4). Notably, all of the other C−H amination products (Tables 3 and 4) were likewise obtained as pure regioisomers, and the formation of minor isomers was not observed within ¹H NMR detection limits.

The C−H amination conditions are compatible with the presence of O-allyl (entry 1, Table 3), O-tert-butyl (entry 2, Table 3), O-alkyl ester moieties (entries 5−10, 12−17, Table 3), as well as amides (entries 7, 8, Table 4) and tert-butyl carbamates (entries 2, 10, 11, Table 4). The successful C−H amination of substrates containing secondary amide (entry 7, Table 4) and carbamate (entry 10, Table 4) moieties is noteworthy, because structurally related N-acetanilides react with PhI(OAc)₂ and generate highly reactive acylnitrenium species.[3b,d] Bromine and chlorine substituents in the substrate

Table 4. C−H Amination of Arenes

entry	product[a]	time	yield (%)
1	**21**	18 h[b]	41
2	**22**	30 min[b]	30[c]
3	**23**	30 min[b]	52
4	**24**	30 min	49
5	**25**	30 min[b]	56
6	**26**	30 min[b]	61
7	**27**	30 min[b]	71
8	**28**	30 min[b]	74
9	**29**	18 h[b]	60
10	**30**	30 min	40
11	**31**	60 min	50

[a]Conditions: Arene (1.0 equiv), MesI(OH)OTs (1.1 equiv), CH_2Cl_2 (4 mL/1 mmol of the starting arene), 15 min; then amine (1.2 equiv), EtN(i-Pr)$_2$ (2.0 equiv), Cu(MeCN)$_4$BF$_4$ (0.1 equiv), 2:1 CH_2Cl_2:DMSO (4 mL/1 mmol of the starting arene), room temperature, 2 h. [b]In the presence of CF$_3$COOH (1.2 equiv). [c]At 70% conversion.

as well as N-benzoyl, N-benzyl, N-tosyl, and N-SEM protecting groups are also tolerated (Tables 3 and 4).

Mechanistic Studies. Although both Cu(I) and Cu(II) salts can be employed as catalysts in the C−H amination reaction, the considerably faster formation of **3a** in the presence of Cu(I) species as compared to Cu(II) (entry 3 vs entry 4, Table 1) suggests that Cu(I) salts are the catalytically active species. The slow formation of **3a** in the Cu(II)-catalyzed reaction (entry 4, Table 1) could be ascribed to an in situ reduction of Cu(II) to active Cu(I) catalyst by amine.[22,23] To verify the catalytic efficiency of Cu(I) species, the Cu(OTf)$_2$-catalyzed C−H amination of **2a** was performed in the presence of 2 equiv of neocuproin, a highly specific chelating agent for Cu(I) ions. Neocuproin (2,9-dimethyl-1,10-phenanthroline) is a bidentate ligand that forms a stable bright orange-colored complex of formula Cu^I(neocuproin)$_2$,[24] thus acting as an inhibitor of Cu(I)-catalyzed reactions.[25] Complete inhibition of

the Cu(OTf)$_2$-catalyzed formation of **3a** in the presence of neocuproin was observed, evidencing that the catalytically active species are indeed Cu(I) salts.

A radical inhibition test was performed to exclude the possibility of C−H amination of **2a** via a radical chain pathway. Accordingly, the addition of radical scavengers such as 2,6-di-$tert$-butyl-4-methylphenol (BHT)[26] and TEMPO[27] (both in 10-fold excess with respect to Cu(I)) did not affect the rate of Cu(MeCN)$_4$BF$_4$-catalyzed conversion of **2a** to **3a** in CH_2Cl_2−DMSO = 4:1. These data strongly argue against the involvement of a radical chain process. Notably, the addition of radical scavengers considerably decelerated the background noncatalyzed reaction of λ^3-iodane **2a** with morpholine to produce **4a** (Table 1, entry 2). Thus, only 27% of **4a** was formed in the presence of TEMPO after 24 h at room temperature (at 31% conversion of **2a**), and 15% of **4a** (at 24% conversion) was observed after 12 h at room temperature with added BHT (both radical scavengers were added in equimolar amounts to the starting **2a**). Presumably, the noncatalyzed reaction of λ^3-iodane **2a** with morpholine proceeds through a radical chain pathway.

Kinetic studies were also carried out to establish the kinetic order of Cu(I)-catalyzed C−H amination of **2a** in each reaction component. Morpholine was employed both as a nucleophile and as a base, and (CuOTf)$_2$·PhH was used as a catalyst. The reactions were monitored by NMR spectroscopy, and the method of initial rates was used to determine rate coefficients. The Cu(I)-catalyzed conversion of **2a** to **3a** in DMSO-d_6 at 25 °C was found to be first-order in (CuOTf)$_2$·PhH (see Supporting Information, Figure S2), first-order in morpholine (see Supporting Information, Figure S3), and zeroth-order in λ^3-iodane **2a** (see Supporting Information, Figure S4). These data indicate that the Cu(I) catalyst and morpholine are both involved in the rate-limiting step of the catalytic cycle, whereas the subsequent reactions of λ^3-iodane **2a** are fast. It is likely that (CuOTf)$_2$·PhH and morpholine form a complex **I**, which exists in equilibrium with the bis-amine complex **II**. Assuming that **II** is a resting state of the catalyst,[28] dissociation of morpholine under equilibrium conditions would produce a catalytically active complex **I** (Scheme 1).

Several plausible pathways for Cu(MeCN)$_4$BF$_4$-catalyzed C−H amination of **2a** are consistent with the data above (Scheme 1). In pathway A, Cu(I)−amine complex **I** coordinates with the electron-rich indole moiety in the λ^3-iodane **2a**, forming a η^2-complex **III**. Subsequent substitution of tosylate by amine in the intermediate **III** and reductive elimination from the highly unstable λ^3-iodane **IV**[29] would lead to aminoheterocycle **3a**. The formation of η^2-coordinated species such as **III** and **IV** has been proposed in the transition state for the oxidative addition of aryl halides to Cu(I) complexes.[28a,30] π-Interaction between the Cu(I)−amine complex **I** and indole **2a** should increase electrophilicity of the heterocycle $ipso$-carbon in the putative intermediates **III** and **IV**, thus facilitating C−N bond forming reductive elimination from λ^3-iodane **IV**. However, other Lewis acids such as Pd(OCOCF$_3$)$_2$, Ni(OTf)$_2$, and Sc(OTf)$_3$ did not catalyze the formation of **3a** (Table 1, entries 7−9), so the involvement of η^2-coordination between Cu(I) species and the indole moiety in intermediates **III** or **IV** can be questioned.

In an alternative possibility, pathway B involves direct oxidative addition of the λ^3-iodane **2a** to Cu(I)−amine complex **I** to form the Cu(III) intermediate **V**.[31] For unsymmetrical diaryl-λ^3-iodanes, regioselectivity of the oxidative addition to Cu(I) species can be controlled by the use of a mesityl group as

Scheme 1. Plausible Pathways for C−H Amination of Heteroarenes
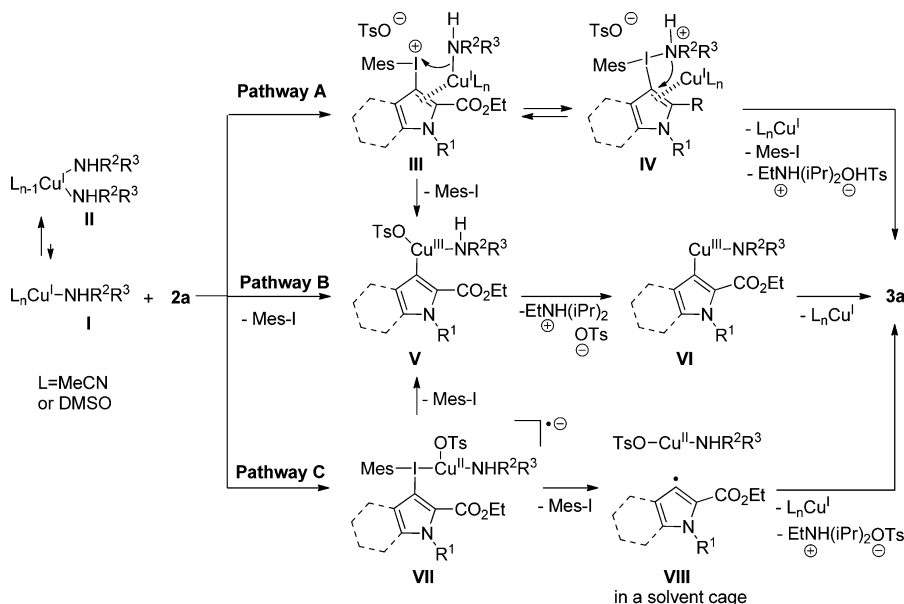
Scheme 2. C−H Amination of λ^3-Iodane 32 Containing a Radical Probe
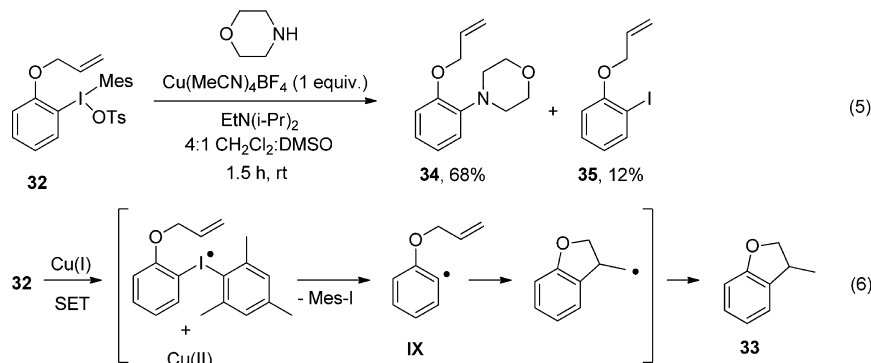
a nontransferable aryl ligand.[31c−f,32] The Cu(III) intermediate **V** undergoes N−H deprotonation of the Cu(III)-coordinated amine with EtN(i-Pr)$_2$.[33] Product-forming reductive elimination from the resulting Cu(III)−amide complex **VI** would afford **3a** and regenerate a catalytically active Cu(I) species.[34] However, the proposed transient Cu(III) complexes **V** or **VI** could not be detected, presumably because they undergo rapid C−N bond forming reductive elimination.[35] This behavior is expected because related, highly reactive Cu(III) species have only been observed in chelation-stabilized complexes based on stabilizing triazamacrocyclic ligands.[36]

As a third option, pathway C involves a Cu(I)/Cu(II) catalytic cycle, which starts with an inner-sphere single-electron transfer (SET) from Cu(I)-complex[22,25b,37] to the λ^3-iodane **2a**, generating an intimate radical anion−Cu(II) complex **VII**.[38] Experimental redox potentials versus SCE were determined by cyclic voltammetry for λ^3-iodane **2a** ($E = -0.76$ V) and for Cu(MeCN)$_4$BF$_4$ ($E = +0.85$ V),[39] and they support the feasibility of SET between Cu(I) catalyst and iodonium salt **2a**. The radical anion−Cu(II) complex **VII** might undergo fragmentation to a radical pair **VIII**, which couples with the amine moiety with a second SET that regenerates the Cu(I) species.[40] To test for the intermediacy of heteroaryl radicals in the Cu(I)-catalyzed C−H amination reaction, diaryl-λ^3-iodane **32** containing an O-allyl moiety as a radical clock probe was

employed as substrate in the reaction with morpholine in the presence of equimolar and catalytic (10 mol %, not shown) amounts of Cu(MeCN)$_4$BF$_4$ (Scheme 2, eq 5). It has been demonstrated that the λ^3-iodane **32**-derived aryl radical **IX** undergoes extremely rapid 5-exo-trig cyclization (rate constant $k = 9.6 \times 10^9$ s^{-1}) to furnish 3-methyl-2,3-dihydrobenzofurane **33** after abstraction of the hydrogen atom from the medium (Scheme 2, eq 6).[41] In our hands, N-substituted morpholine **34** was obtained as the major product, and no detectable amount of the cyclization product **33** was observed (Scheme 2, eq 5).[42] These data provide strong evidence that the Cu(I)-catalyzed C−H amination occurs without involvement of free heteroaryl radicals such as **VIII** (Scheme 1, pathway C). On the other hand, the putative radical anion−Cu(II) complex **VII** may undergo a radical recombination to furnish aryl−Cu(III) species **V**.[43] The subsequent steps would involve the same conversion from **V** to **VI** as in pathway B. Although we regard the latter scenario as the most probable, neither pathway A nor pathway C could be ruled out. Further mechanistic studies are necessary to fully elucidate the mechanism of the newly developed C−H amination approach.

■ **CONCLUSIONS**

In summary, a versatile method for an intermolecular C−H amination of electron-rich heteroarenes and arenes has been

developed. The one-pot sequential two-step procedure comprises the in situ formation of unsymmetrical (hetero)-aryl-λ^3-iodanes followed by their Cu(I)-catalyzed reaction with a wide range of primary and secondary aliphatic amines and anilines. The Cu(I) catalyst ensures the desired selectivity in the reaction between the intermediate unsymmetrical λ^3-iodanes and amines. Initial mechanistic studies point toward a stepwise oxidative addition and involvement of single electron transfer from Cu(I) catalyst to unsymmetrical (hetero)aryl-λ^3-iodanes. The reaction proceeds at room temperature and tolerates a number of functional groups both in the amine and in the (hetero)arene. The regioselectivity of the C−H activation is typical for electrophilic aromatic substitution (S_EAr) reactions. Our C−H amination approach is an alternative and complementary method to transition metal-catalyzed direct intermolecular C_{sp2}−H amination of arenes,[44] which often requires the presence of a metalation-directing group in substrate[45] and employs imides, amides, sulfonamides, as well as organic azides or preactivated amino precursors such as N-chloroamines as sources of nitrogen.[46] In cases where the transition metal-catalyzed amination is not applicable, our method may be especially useful for late-stage amination of pharmaceutically relevant aromatics, and especially hetero-cycles.

■ EXPERIMENTAL SECTION

Ethyl 5-Bromo-1-methyl-3-({[[(4-methylphenyl)sulfonyl]oxy}-(2,4,6-trimethylphenyl)-λ^3-iodanyl)-1H-indole-2-carboxylate (2a). To a solution of MesI(OH)OTs (2.39 g, 5.50 mmol, 1.1 equiv) in CH_2Cl_2 (10 mL) was added TsOH·H_2O (1.05 g, 5.50 mmol, 1.1 equiv), and the resulting suspension was stirred for 5 min at room temperature. Next, a solution of indole **1a** (1.41 g, 5.00 mmol, 1 equiv) in CH_2Cl_2 (10 mL) was added rapidly to the well-stirred suspension. The progress of the reaction was monitored by TLC (disappearance of the starting material spot, R_f = 0.55, 1:5 EtOAc/petroleum ether), and complete conversion of the starting **1a** was observed within 30 min. Solvent was concentrated to ca. 2/3 of the original volume, and Et_2O was added (50 mL). Formed precipitate was filtered, washed with Et_2O (100 mL), and dried in vacuo to afford **2a** as a white powder (3.30 g, 95% yield); analytical TLC on silica gel, 20:80:5 MeOH/CH_2Cl_2/AcOH, R_f = 0.49. Pure material was obtained by crystallization from CH_2Cl_2/diethyl ether: mp 125 °C. dec IR (film, cm^{-1}): 1710 (C=O), 1206 (SO_2). ^1H NMR (400 MHz, DMSO-d_6, ppm): δ 7.79 (1H, d, J = 9.0 Hz), 7.61 (1H, dd, J = 9.0, 1.8 Hz), 7.48−7.43 (3H, m), 7.21−7.16 (2H, m), 7.10 (2H, d, J = 8.0 Hz), 4.45 (2H, q, J = 7.2 Hz), 4.08 (3H, s), 2.58 (6H, s), 2.28 (6H, s), 1.38 (3H, t, J = 7.2 Hz). ^{13}C NMR (100.6 MHz, DMSO-d_6, ppm): δ 159.4, 145.8, 142.9, 141.9, 137.5, 137.2, 131.8, 129.8, 128.1, 128.0, 125.5, 122.7, 121.7, 115.7, 115.1, 81.2, 62.8, 33.8, 26.1, 20.8, 20.4, 13.8. HRMS−ESI (m/z) calcd for $C_{21}H_{22}BrINO_2$ [M − OTs]$^+$ 525.9873, found 525.9861.

General Procedure for C−H Amination of Heterocycles and Arenes. To a solution of MesI(OH)OTs (239 mg, 0.55 mmol, 1.1 equiv) in anhydrous CH_2Cl_2 (1 mL) under argon atmosphere was added a solution of heterocycle or arene (0.50 mmol, 1 equiv) in anhydrous CH_2Cl_2 (1 mL). For a less reactive substrate (see Tables 3 and 4), neat TFA (46 µL, 0.60 mmol, 1.2 equiv) was then added slowly (dropwise, within 2−3 min; too fast addition of TFA leads to the formation of side-products). The resulting solution (color range: pale yellow to brown) was stirred at room temperature under argon atmosphere, and the progress of the reaction was monitored by TLC (disappearance of the starting material spot; mobile phase 3:1 light petroleum ether/EtOAc; the intermediate λ^3-iodane does not migrate from the application point). Immediately upon full conversion of the starting heterocycle or arene (see Tables 3 and 4 for appropriate time), the reaction mixture was transferred via cannula to another flask, which contained preweighed solid Cu(MeCN)$_4$BF$_4$ (16 mg, 0.05 mmol, 10

mol %) and a magnetic stirbar, and the source flask was rinsed with CH_2Cl_2 (1 mL). To the resulting well-stirred suspension was immediately added a solution of amine or aniline (0.6 mmol, 1.2 equiv) in anhydrous CH_2Cl_2 (1 mL) (Important: Decomposition of the formed λ^3-iodane begins if the addition of Cu catalyst and/or amine is delayed!). Finally, neat DIPEA (174 µL, 1.00 mmol, 2 equiv) was added, followed by DMSO (1 mL). The resulting solution was stirred at room temperature under argon atmosphere, and the progress of the reaction was monitored by TLC (the intermediate λ^3-iodanes have R_f = 0.4−0.6; mobile phase 20:80:5 MeOH/CH_2Cl_2/AcOH). In most cases, the reaction was completed in 2 h. The solution was poured into 50 mL of water and 20 mL of saturated aqueous ammonia solution, extracted with CH_2Cl_2 (3 × 30 mL), and combined organic extracts were dried over Na_2SO_4, filtered, and concentrated. The residue was purified by column chromatography on silica gel.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information
Experimental procedures, product characterization data, ^1H and ^{13}C NMR spectra, X-ray crystallographic data for λ^3-iodane **2a** (CIF), cyclic voltammograms (CV), and details of the kinetic experiments. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes
The authors declare no competing financial interest.

■ REFERENCES
(1) Recent reviews on chemistry of hypervalent iodine(III): (a) Yusubov, M. S.; Maskaev, A. V.; Zhdankin, V. V. *ARKIVOC* **2011**, *1*, 370. (b) Zhdankin, V. V. *ARKIVOC* **2009**, *1*, 1. (c) Merritt, E. A.; Olofsson, B. *Angew. Chem., Int. Ed.* **2009**, *48*, 9052. (d) Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2008**, *108*, 5299.

(2) (a) Dauban, P.; Dodd, R. H. *Synlett* **2003**, 1571. (b) Zalatan, D.; Bois, J. C−H Activation. In *Topics in Current Chemistry*; Yu, J.-Q., Shi, Z., Eds.; Springer: Berlin/Heidelberg, 2010; Vol. *292*, p 347.

(3) (a) Samanta, R.; Antonchick, A. *Synlett* **2012**, *23*, 809. (b) Antonchick, A. P.; Samanta, R.; Kulikov, K.; Lategahn, J. *Angew. Chem., Int. Ed.* **2011**, *50*, 8605. (c) Samanta, R.; Bauer, J. O.; Strohmann, C.; Antonchick, A. P. *Org. Lett.* **2012**, *14*, 5518. (d) Samanta, R.; Lategahn, J.; Antonchick, A. P. *Chem. Commun.* **2012**, *48*, 3194.

(4) For related intramolecular λ^3-iodane-mediated cyclizations, see: (a) Tellitu, I.; Domínguez, E. *Synlett* **2012**, *23*, 2165. (b) Correa, A.; Tellitu, I.; Domínguez, E.; Moreno, I.; SanMartin, R. *J. Org. Chem.* **2005**, *70*, 2256. (c) Correa, A.; Herrero, M. T.; Tellitu, I.; Domínguez, E.; Moreno, I.; SanMartin, R. *Tetrahedron* **2003**, *59*, 7103. (d) Du, Y.; Liu, R.; Linn, G.; Zhao, K. *Org. Lett.* **2006**, *8*, 5919. (e) Malamidou-Xenikaki, E.; Spyroudis, S.; Tsanakopoulou, M.; Hadjipavlou-Litina, D. *J. Org. Chem.* **2009**, *74*, 7315.

(5) For the use of structurally related sulfonylimino-λ^3-bromanes as a source of nitrenoid species, see: (a) Ochiai, M.; Yamane, S.; Hoque, M. M.; Saito, M.; Miyamoto, K. *Chem. Commun.* **2012**, *48*, 5280.

(b) Ochiai, M.; Miyamoto, K.; Kaneaki, T.; Hayashi, S.; Nakanishi, W. *Science* **2011**, *332*, 448.

(6) (a) Kim, H. J.; Kim, J.; Cho, S. H.; Chang, S. *J. Am. Chem. Soc.* **2011**, *133*, 16382. (b) Kantak, A. A.; Potavathri, S.; Barham, R. A.; Romano, K. M.; DeBoef, B. *J. Am. Chem. Soc.* **2011**, *133*, 19960.

(7) Well-defined λ^3-iodanes ArI(OAc)N(SO$_2$R)$_2$ have been used in C–H amination of acetylenes: Souto, J. A.; Becker, P.; Iglesias, Á.; Muñiz, K. *J. Am. Chem. Soc.* **2012**, *134*, 15505.

(8) Souto, J. A.; Martínez, C.; Velilla, I.; Muñiz, K. *Angew. Chem., Int. Ed.* **2013**, *52*, 1324.

(9) (a) Moriarty, R. M.; Vaid, R. K.; Duncan, M. P.; Ochiai, M.; Inenaga, M.; Nagao, Y. *Tetrahedron Lett.* **1988**, *29*, 6913. (b) Müller, P.; Gilabert, D. M. *Tetrahedron* **1988**, *44*, 7171. (c) Zhu, C.; Sun, C.; Wei, Y. *Synthesis* **2010**, 4235. (d) Desjardins, S.; Jacquemot, G.; Canesi, S. *Synlett* **2012**, 1497.

(10) (a) Beringer, F. M.; Brierley, A.; Drexler, M.; Gindler, E. M.; Lumpkin, C. C. *J. Am. Chem. Soc.* **1953**, *75*, 2708. (b) Rewcastle, G. W.; Denny, W. A. *Synthesis* **1985**, 220. (c) Scherrer, R. A.; Beatty, H. R. *J. Org. Chem.* **1980**, *45*, 2127. (d) Carroll, M. A.; Wood, R. A. *Tetrahedron* **2007**, *63*, 11349. (e) Kang, S.-K.; Lee, S.-H.; Lee, D. *Synlett* **2000**, 1022.

(11) Lubriks, D.; Sokolovs, I.; Suna, E. *J. Am. Chem. Soc.* **2012**, *134*, 15436.

(12) For representative reviews on transition metal-catalyzed C–H functionalization of heteroarenes: (a) Seregin, I. V.; Gevorgyan, V. *Chem. Soc. Rev.* **2007**, *36*, 1173. (b) Chen, X.; Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2009**, *48*, 5094. (c) Gulevich, A. V.; Gevorgyan, V. *Chem. Heterocycl. Compd.* **2012**, *48*, 17. (d) Engle, K. M.; Mei, T.-S.; Wasa, M.; Yu, J.-Q. *Acc. Chem. Res.* **2012**, *45*, 788−802. (e) Gulevich, A. V.; Dudnik, A. S.; Chernyak, N.; Gevorgyan, V. *Chem. Rev.* **2013**, *113*, 3084.

(13) Merritt, E. A.; Carneiro, V. M. T.; Silva, L. F.; Olofsson, B. *J. Org. Chem.* **2010**, *75*, 7416.

(14) Increased conversion of **2a** (ca. 30%) was observed at 60 °C using Pd(OCOCF$_3$)$_2$ as catalyst (compare with entry 7, Table 1). However, only trace amounts (~1–2%) of 3-morpholino-indole **3a** were observed, and the major product was iodoindole **4a** (1:99 ratio of **3a:4a**). Furthermore, none of the products corresponding to C–O bond formation were detected in the reaction mixture. For a complete survey of optimization, see Table S1 (page S58) in the Supporting Information.

(15) We found that the formation of λ^3-iodane **2a** was facilitated by addition of CF$_3$COOH.

(16) Monoaryl-λ^3-iodanes effect diamination of alkenes: (a) Reference 8. (b) Röben, C.; Souto, J. A.; González, Y.; Lishchynskyi, A.; Muñiz, K. *Angew. Chem., Int. Ed.* **2011**, *50*, 9478. (c) Röben, C.; Souto, J. A.; Escudero-Adán, E. C.; Muñiz, K. *Org. Lett.* **2013**, *15*, 1008. (d) Lishchynskyi, A.; Muñiz, K. *Chem.—Eur. J.* **2012**, *18*, 2212.

(17) Sterically highly hindered amines such as diisopropylamine do not react.

(18) 2-Unsubstituted indoles as well as indoles possessing relatively electron-rich substituents such as 2-methyl or 2-phenyl groups form intermediate indolyl-λ^3-iodanes, which could be transformed into the corresponding indolyl-3-amines. However, the latter are unstable and undergo rapid oxidation under the C–H amination conditions. The low stability of indolyl-3-amines toward oxidation is well-known, see, for example: (a) Sundberg, R. J. *The Chemistry of Indoles*; Academic Press: New York, 1970; pp 290−291. (b) Huang-Hsinmin; Mann, F. G. *J. Chem. Soc.* **1949**, 2903. (c) Bruni, P.; Colonna, M.; Greci, L. *Tetrahedron* **1971**, *27*, 5893. Consequently, the presence of stabilizing electron-withdrawing substituents at position 2 of indole is necessary to obtain stable indolyl-3-amines.

(19) Correlation between yields of phenyliodonium salts and Hammett σ constants of substituents has been reported: Dohi, T.; Yamaoka, N.; Kita, Y. *Tetrahedron* **2010**, *66*, 5775.

(20) (a) For the substituent effect on regioselectivity of S$_E$Ar reactions of pyrroles, see: Joule, J. A.; Mills, K. *Heterocyclic Chemistry*, 5th ed.; John Wiley & Sons: Chichester, 2010; pp 289−323.

(b) Karele, B. Ya.; Kalnin, S. V.; Grinberga, I. P.; Neiland, O. Ya. *Chem. Heterocycl. Compd.* **1973**, *9*, 510.

(21) The high *para*-selectivity in the reaction between MeO-substituted arenes and phenyliodonium salts has been demonstrated previously: (a) Kitamura, T.; Matsuyuki, J.; Taniguchi, H. *Synthesis* **1994**, 147. (b) Bielawski, M.; Zhu, M.; Olofsson, B. *Adv. Synth. Catal.* **2007**, *349*, 2610. (c) Reference 19.

(22) Paine, A. J. *J. Am. Chem. Soc.* **1987**, *109*, 1496−1502.

(23) Franc, G.; Jutand, A. *Dalton Trans.* **2010**, *39*, 7873−7875.

(24) Davies, G.; Loose, D. J. *Inorg. Chem.* **1976**, *15*, 694−700.

(25) Structurally related cuproine has been used as a specific inhibitor of Cu(I)-catalyzed reactions: (a) Caserio, M. C.; Glusker, D. L.; Roberts, J. D. *J. Am. Chem. Soc.* **1959**, *81*, 336. (b) Lockhart, T. P. *J. Am. Chem. Soc.* **1983**, *105*, 1940.

(26) Cho, S. H.; Yoon, J.; Chang, S. *J. Am. Chem. Soc.* **2011**, *133*, 5996.

(27) (a) Fier, P. S.; Hartwig, J. F. *J. Am. Chem. Soc.* **2012**, *134*, 10795. (b) Wang, X.; Xu, Y.; Mo, F.; Ji, G.; Qiu, D.; Feng, J.; Ye, Y.; Zhang, S.; Zhang, Y.; Wang, J. *J. Am. Chem. Soc.* **2013**, *135*, 10330.

(28) Multiple amide-ligated Cu(I) complex was shown to be catalytically inactive: (a) Strieter, E. R.; Bhayana, B.; Buchwald, S. L. *J. Am. Chem. Soc.* **2009**, *131*, 78. (b) Strieter, E. R.; Blackmond, D. G.; Buchwald, S. L. *J. Am. Chem. Soc.* **2005**, *127*, 4120.

(29) The presence of two ligands with large trans influences (arene and amine) in the hypervalent bond renders λ^3-iodane **IV** highly unstable: (a) Ochiai, M.; Sueda, T.; Miyamoto, K.; Kiprof, P.; Zhdankin, V. V. *Angew. Chem., Int. Ed.* **2006**, *45*, 8203. (b) Zhdankin, V. V.; Koposov, A. Y.; Su, L.; Boyarskikh, V. V.; Netzel, B. C.; Young, V. G. *Org. Lett.* **2003**, *5*, 1583.

(30) (a) Zhang, S.-L.; Liu, L.; Fu, Y.; Guo, Q.-X. *Organometallics* **2007**, *26*, 4546. (b) Tye, J. W.; Weng, Z.; Johns, A. M.; Incarvito, C. D.; Hartwig, J. F. *J. Am. Chem. Soc.* **2008**, *130*, 9971. (c) Zhang, S.; Ding, Y. *Organometallics* **2011**, *30*, 633. (d) Yu, H.-Z.; Jiang, Y.-Y.; Fu, Y.; Liu, L. *J. Am. Chem. Soc.* **2010**, *132*, 18078. (e) Weingarten, H. *J. Org. Chem.* **1964**, *29*, 3624. (f) Aalten, H. L.; Van Koten, G.; Grove, D. M.; Kuilman, T.; Piekstra, O. G.; Hulshof, L. A.; Sheldon, R. A. *Tetrahedron* **1989**, *45*, 5565.

(31) The oxidative addition of diaryl-λ^3-iodanes to Cu(I) salts has been proposed to result in the formation of aryl−Cu(III) species: (a) Phipps, R. J.; Grimster, N. P.; Gaunt, M. J. *J. Am. Chem. Soc.* **2008**, *130*, 8172. (b) Suero, M. G.; Bayle, E. D.; Collins, B. S. L.; Gaunt, M. J. *J. Am. Chem. Soc.* **2013**, *135*, 5332. (c) Walkinshaw, A. J.; Xu, W.; Suero, M. G.; Gaunt, M. J. *J. Am. Chem. Soc.* **2013**, *135*, 12532. (d) Zhu, S.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2012**, *134*, 10815. (e) Allen, A. E.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2011**, *133*, 4260. (f) Harvey, J. S.; Simonovich, S. P.; Jamison, C. R.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2011**, *133*, 13782.

(32) (a) Bigot, A.; Williamson, A. E.; Gaunt, M. J. *J. Am. Chem. Soc.* **2011**, *133*, 13778. (b) Phipps, R. J.; Gaunt, M. J. *Science* **2009**, *323*, 1593. (c) Phipps, R. J.; McMurray, L.; Ritter, S.; Duong, H. A.; Gaunt, M. J. *J. Am. Chem. Soc.* **2012**, *134*, 10773.

(33) Neubecker, T. A.; Kirksey, S. T.; Chellappa, K. L.; Margerum, D. W. *Inorg. Chem.* **1979**, *18*, 444.

(34) For C−N bond-forming reductive elimination from well-defined Cu(III)−aryl species, see: (a) Huffman, L. M.; Stahl, S. S. *J. Am. Chem. Soc.* **2008**, *130*, 9196. (b) Casitas, A.; King, A. E.; Parella, T.; Costas, M.; Stahl, S. S.; Ribas, X. *Chem. Sci.* **2010**, *1*, 326. (c) King, A. E.; Huffman, L. M.; Casitas, A.; Costas, M.; Ribas, X.; Stahl, S. S. *J. Am. Chem. Soc.* **2010**, *132*, 12068. (d) Huffman, L. M.; Stahl, S. S. *Dalton Trans.* **2011**, *40*, 8959.

(35) Tran, B. L.; Li, B.; Driess, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2014**, *136*, 2555.

(36) (a) Ribas, X.; Jackson, D. A.; Donnadieu, B.; Mahia, H.; Parella, T.; Xifra, R.; Hedman, B.; Hodgson, K. O.; Llobet, A.; Stack, T. D. P. *Angew. Chem., Int. Ed.* **2002**, *41*, 2991. (b) Yao, B.; Wang, D.-X.; Huang, Z.-T.; Wang, M.-X. *Chem. Commun.* **2009**, 2899. (c) Huffman, L. M.; Casitas, A.; Font, M.; Canta, M.; Costas, M.; Ribas, X.; Stahl, S. S. *Chem.—Eur. J.* **2011**, *17*, 10643. (d) For a recent review of

6927

dx.doi.org/10.1021/ja502174d | *J. Am. Chem. Soc.* 2014, 136, 6920−6928

chemistry of Cu(III) complexes, see: Casitas, A.; Ribas, X. *Chem. Sci.* **2013**, *4*, 2301.

(37) (a) Chen, X.; Hao, X.-S.; Goodhue, C. E.; Yu, J.-Q. *J. Am. Chem. Soc.* **2006**, *128*, 6790. (b) Arai, S.; Hida, M.; Yamagishi, T. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 277. (c) Ochiai, M.; Sumi, K.; Takaoka, Y.; Kunishima, M.; Nagao, Y.; Shiro, M.; Fujita, E. *Tetrahedron* **1988**, *44*, 4095. (d) Suess, A. M.; Ertem, M. Z.; Cramer, C. J.; Stahl, S. S. *J. Am. Chem. Soc.* **2013**, *135*, 9797.

(38) λ^3-Iodanes with Cu species ligated to the hypervalent iodine (III) atom have been proposed: (a) Beringer, F. M.; Bodlaender, P. *J. Org. Chem.* **1969**, *34*, 1981. (b) Reference 25b. (c) Reference 37b.

(39) See the Supporting Information for details.

(40) (a) Sperotto, E.; van Klink, G. P. M.; van Koten, G.; de Vries, J. G. *Dalton Trans.* **2010**, *39*, 10338 and references cited therein. (b) Creutz, S. E.; Lotito, K. J.; Fu, G. C.; Peters, J. C. *Science* **2012**, *338*, 647. (c) Zhu, R.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2013**, *52*, 12655.

(41) Annunziata, A.; Galli, C.; Marinelli, M.; Pau, T. *Eur. J. Org. Chem.* **2001**, 1323.

(42) A mechanistically closely related single electron transfer from Cr(II) to diaryl-λ^3-iodane **32** involves the formation of a transient aryl radical: (a) Reference 38a. (b) Chen, D.-W.; Ochiai, M. *J. Org. Chem.* **1999**, *64*, 6804.

(43) Formation of Cu(III) intermediates by the oxidative addition of iodoarenes to Cu(I) species has recently been suggested as a plausible mechanism of Goldberg-type reactions: (a) Reference 30b. (b) Giri, R.; Hartwig, J. F. *J. Am. Chem. Soc.* **2010**, *132*, 15860.

(44) For recent reviews on C_{sp2}−H amination, see: (a) Armstrong, A.; Collins, J. C. *Angew. Chem., Int. Ed.* **2010**, *49*, 2282. (b) Zhang, M. *Synthesis* **2011**, 3408. (c) Song, W.; Kozhushkov, S. I.; Ackermann, L. *Angew. Chem., Int. Ed.* **2013**, *52*, 6576.

(45) For selected examples, see: (a) Reference 37a. (b) Thu, H.-Y.; Yu, W.-Y.; Che, C.-M. *J. Am. Chem. Soc.* **2006**, *128*, 9048. (c) Ng, K.-H.; Chan, A. S. C.; Yu, W.-Y. *J. Am. Chem. Soc.* **2010**, *132*, 12862. (d) Xiao, B.; Gong, T.-J.; Xu, J.; Liu, Z.-J.; Liu, L. *J. Am. Chem. Soc.* **2011**, *133*, 1466. (e) Yoo, E. J.; Ma, S.; Mei, T.-S.; Chan, K. S. L.; Yu, J.-Q. *J. Am. Chem. Soc.* **2011**, *133*, 7652. (f) Sun, K.; Li, Y.; Xiong, T.; Zhang, J.; Zhang, Q. *J. Am. Chem. Soc.* **2011**, *133*, 1694. (g) John, A.; Nicholas, K. M. *J. Org. Chem.* **2011**, *76*, 4158. (h) Kim, J. Y.; Park, S. H.; Ryu, J.; Cho, S. H.; Kim, S. H.; Chang, S. *J. Am. Chem. Soc.* **2012**, *134*, 9110. (i) Ryu, J.; Shin, K.; Park, S. H.; Kim, J. Y.; Chang, S. *Angew. Chem., Int. Ed.* **2012**, *51*, 9904. (j) Grohmann, C.; Wang, H.; Glorius, F. *Org. Lett.* **2012**, *14*, 656. (k) Ng, K.-H.; Zhou, Z.; Yu, W.-Y. *Org. Lett.* **2012**, *14*, 272. (l) Grohmann, C.; Wang, H.; Glorius, F. *Org. Lett.* **2013**, *15*, 3014. (m) Tran, L. D.; Roane, J.; Daugulis, O. *Angew. Chem., Int. Ed.* **2013**, *52*, 6043. (n) Yu, D.-G.; Suri, M.; Glorius, F. *J. Am. Chem. Soc.* **2013**, *135*, 8802. (o) Thirunavukkarasu, V. S.; Raghuvanshi, K.; Ackermann, L. *Org. Lett.* **2013**, *15*, 3286. (p) Shin, K.; Baek, Y.; Chang, S. *Angew. Chem., Int. Ed.* **2013**, *52*, 8031.

(46) There are few reports on the use of amines as a source of nitrogen in the intermolecular chelation-assisted C_{sp2}−H amination: (a) Reference 45e. (b) Reference 45m.