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Article

A Comparative Study of Cationic Copper(I) Reagents Supported by Bipodal Tetramethylguanidinyl-Containing Ligands as Nitrene-Transfer Catalysts

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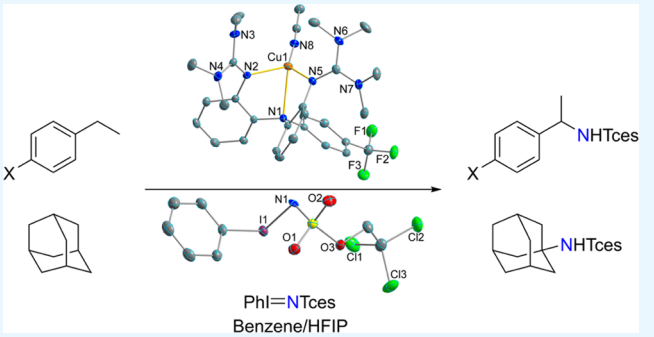
ABSTRACT: The bipodal compounds [(TMG$_2$biphen$^{N\text{-}R}$)Cu^{I}−NCMe](PF$_6$) (R = Me, Ar (4-CF$_3$Ph-)) and [(TMG$_2$biphen$^{N\text{-}Me}$)-Cu^{I}−I] have been synthesized with ligands that feature a diarylmethyl- and triaryl-amine framework and superbasic tetramethylguanidinyl residues (TMG). The cationic Cu(I) sites mediate catalytic nitrene-transfer reactions between the imidoiodinane PhI = NTs (Ts = tosyl) and a panel of styrenes in MeCN, to afford aziridines, demonstrating comparable reactivity profiles. The copper reagents have been further explored to execute C−H amination reactions with a variety of aliphatic and aromatic hydrocarbons and two distinct nitrene sources PhI = NTs and PhI = NTces (Tces = 2,2,2-trichloroethylsulfamate) in benzene/HFIP (10:2 v/v). Good yields have been obtained for sec-benzylic and tert-C−H bonds of various substrates, especially with the more electron-deficient catalyst [(TMG$_2$biphen^{N-Ar})Cu^{I}−NCMe](PF$_6$). In conjunction with earlier studies, the order of reactivity of these bipodal cationic reagents as a function of the metal employed is established as Cu > Fe > Co ≥ Mn. However, as opposed to the base-metal analogues, the bipodal Cu reagents are less reactive than a similar tripodal Cu catalyst. The observed fluorophilicity of the bipodal Cu compounds may provide a deactivation pathway.



INTRODUCTION

Transition-metal-mediated atom/group transfer reactions open avenues toward exploiting ubiquitous C−H and C=C bond feedstock, such as that present in hydrocarbons, to insert new functionalities found extensively in commodity and fine chemicals.[1] Among different atom- (e.g., H, O, S, Halogen)[2−7] or group-transfer processes (e.g., boryl, carbene, nitrene),[8−10] nitrene insertion/addition to C−H/C=C bonds generates aminated and aziridinated products that are encountered in a plethora of natural products possessing antineoplastic and antibiotic properties or in fine chemicals, pharmaceuticals, and agrochemicals.[11,12] In addition, highly strained three-membered aziridines can act as valuable intermediates, since they can undergo stereo- or regio-specific transformations via ring opening, expansion, or rearrangement to afford a vast array of chemicals.[13]

Among three commonly employed synthetic strategies (cyclization of 1,2-amino precursors, addition of C_1 sources to imines, addition of N_1 sources to olefins),[14] the N_1+C_2 methodology is used more frequently than others by means of organocatalytic and metal-dependent reagents, the latter employing middle or late first-row transition-metal elements,[15−20] coinage metals,[21,22] and platinum-group elements.[23−25] Issues of selectivity (chemo, regio, stereo, or enantio) have been addressed by using suitably developed supporting frameworks, such as porphyrinoid, C_2-symmetric chiral salen, and bis(oxazoline) ligands, as well as by virtue of the more recently developed genetically engineered hemeproteins.[26] The nitrene moiety (NR) transferred with the assistance of these reagents to olefinic substrates or C−H bonds is sourced from a variety of nitrene or nitrenoid precursor groups (NR, NR(X)), most commonly by means of iminoiodinanes,[27] organic azides,[28] haloamines,[29] N/O-substituted hydroxyl amines,[30] and N-tosyl carbamates.[31]

In previous work from our laboratory,[32] a Cu(I) cationic reagent supported by an [N_3N] ligand scaffold (Figure 1, left) featuring superbasic tetramethylguanidinyl arms (TMG$_3$trphen, relevant to TMG$_3$tren)[33,34] was explored as a versatile catalyst in various olefinic aziridination and hydrocarbon C−H amination reactions. More recently, the

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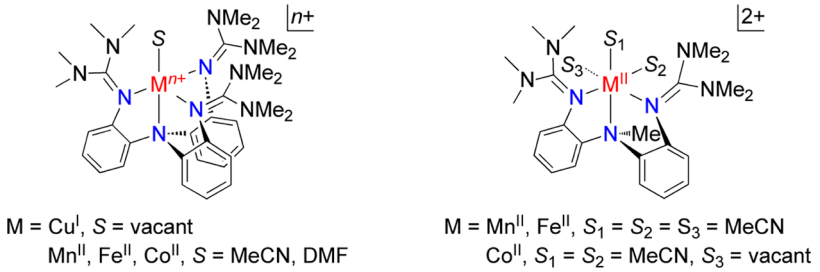


Figure 1. Previously Employed Catalysts in Nitrene-Transfer Chemistry.

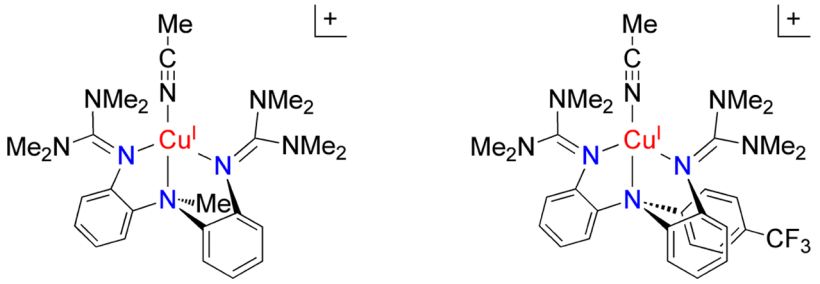
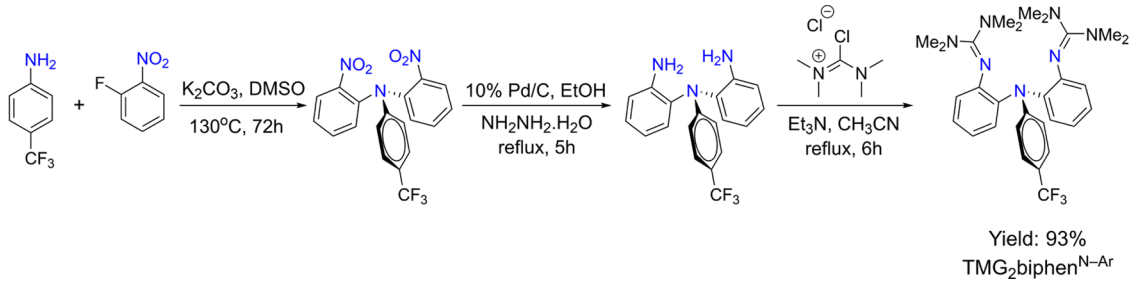


Figure 2. Bipodal [N_2N] Copper(I) Compounds Used in This Study (PF_6^- Counteranion).

Scheme 1. Synthesis of the Bipodal Ligand $TMG_2biphen^{N-Ar}$ (Ar = 4-CF_3Ph-)



TMG_3trphen ligand and its bipodal analogue $TMG_2biphen^{N-Me}$ (Figure 1, right) were employed to generate a family of cationic reagents featuring divalent base metals M(II) (M = Mn, Fe, Co).[35] Among these M(II) reagents, the bipodal catalysts are significantly more productive than tripodal congeners in nitrene-transfer chemistry, with an order of reactivity of Fe > Co ≥ Mn, applicable to both bipodal and tripodal reagents. The relevant reactivity involves aziridination of olefinic substrates as well as construction of five-membered *N*-heterocycles (imidazolines,[36] pyrrolidines,[37] oxazolidines[38]) from olefins and an additional unsaturated co-substrate (dipolarophile: MeCN, olefin, ketone). However, by comparison to the tripodal $[(TMG_3trphen)Cu^I]^+$ reagent noted above, all of these M(II) reagents are by far inferior as catalysts in C−H amination reactions and more modestly yielding in C═C aziridination reactions.

Incidentally, when the equatorial TMG residues of the [N_3N] ligand scaffold are replaced by N-amido residues featuring alkyl, aryl, or acyl substituents, the resulting library of *anionic* tripodal M(II) reagents (M = Mn, Fe, Co)[39,40] is only effective in selective aziridinations of aromatic olefins, presumably due to the diminished electrophilicity of the active metal nitrene moiety.

In the present publication, we explore the missing link in the family of bipodal cationic reagents, i.e., Cu(I) catalysts, which could potentially be most reactive in nitrene-transfer chemistry vis-à-vis alkanes and alkenes, if the trend noted above holds. For this purpose, novel Cu(I) complexes with the aforementioned $TMG_2biphen^{N-Me}$ bipodal ligand (featuring a terminal N−Me moiety) (Figure 2, left) and a new bipodal congener ($TMG_2biphen^{N-Ar}$) (Figure 2, right) are explored. The latter possesses an N−aryl moiety (Ar = 4-CF_3Ph-), in an attempt to evaluate the effect of an electron-deficient and oxidatively robust terminal group in lieu of the oxidatively vulnerable N−Me alternative. Our investigation of C−H aminations and C═C aziridinations with these new catalysts establishes that although the bipodal Cu(I) reagents are superior to the divalent base-metal bipodal congeners (Cu > Fe > Co ≥ Mn), they are curiously inferior to the tripodal Cu(I) analogue, $[(TMG_3trphen)Cu^I]^+$.

RESULTS AND DISCUSSION

Synthesis of Ligands and Compounds. The synthesis of the bipodal ligand $TMG_2biphen^{N-Me}$ has been previously described.[37] The new bipodal ligand ($TMG_2biphen^{N-Ar}$) ($[(Me_2N)_2C{=}N\text{-}(2\text{-}C_6H_4)]_2N\text{-}(4\text{-}(trifluoromethyl)phenyl)$) is synthesized in a similar three-step manner (Scheme 1, ORTEP diagram shown in Figure S1), starting with the synthesis of N-(4-(trifluoromethyl)phenyl)-(2,2′-dinitro)-diphenylamine (ORTEP diagram, Figure S2) via a nucleophilic substitution reaction between 4-(trifluoromethyl)aniline and 1-fluoro-2-nitrobenzene in the presence of K_2CO_3 (base) in DMSO. The nitro compound is then reduced to the

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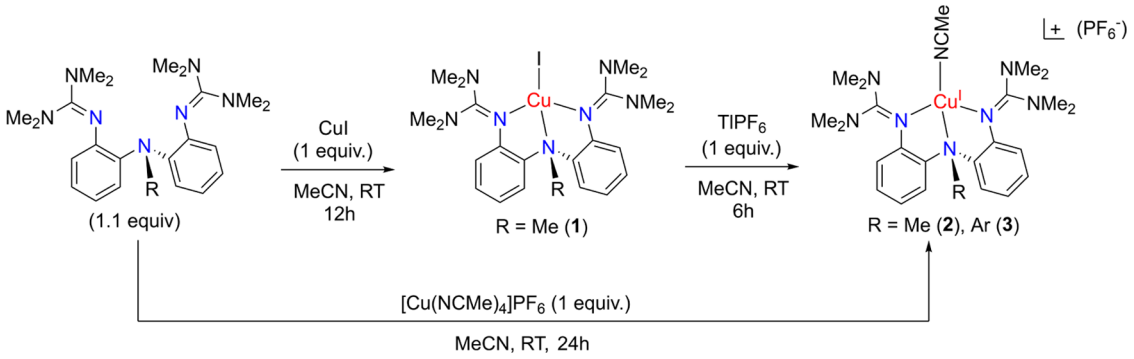
Scheme 2. Synthetic Routes for Bipodal Cu(I) Compounds 1−3



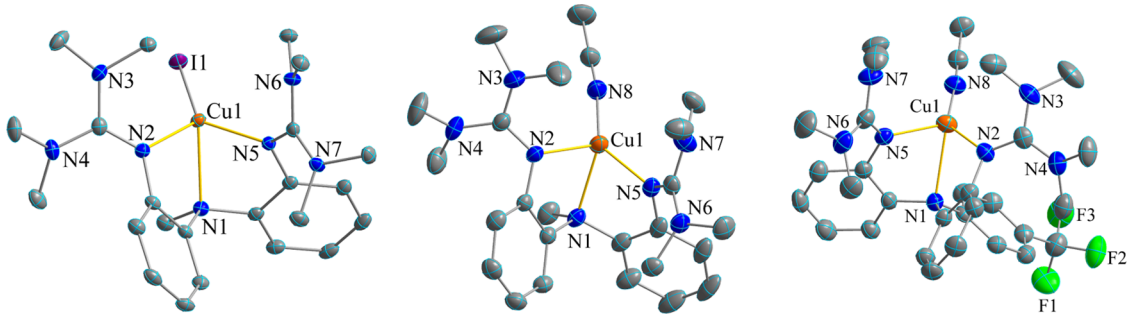
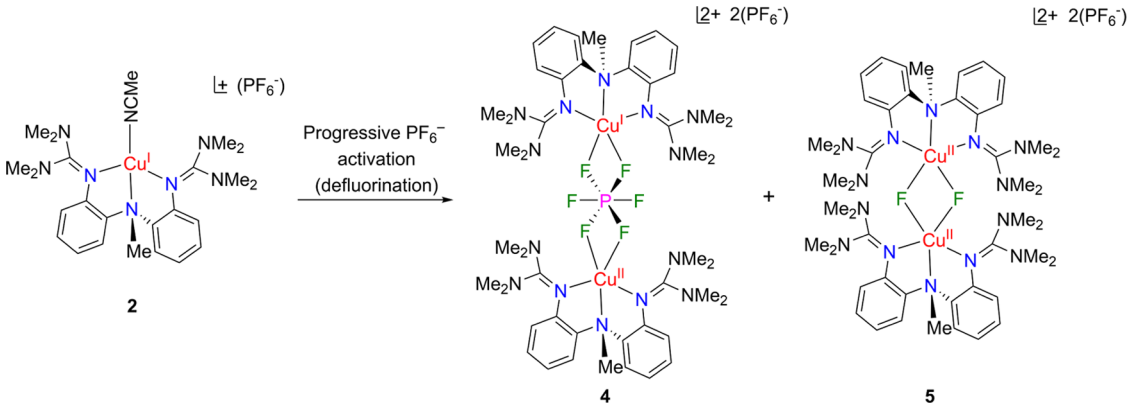


Figure 3. ORTEP Diagrams of [(TMG$_2$biphen^{N-Me})Cu^I–I] (**1**), [(TMG$_2$biphen^{N-Me})Cu^I–NCMe](PF$_6$) (**2**) and [(TMG$_2$biphen^{N-Ar})Cu^I–NCMe](PF$_6$) (**3**) (cations only) drawn with 40% thermal ellipsoids. Selective interatomic distances (Å) and angles (deg) for **1**: Cu(1)–N(1) = 2.302(2), Cu(1)–N(2) = 2.076(2), Cu(1)–N(5) = 2.069(2), Cu(1)–I(1) = 2.4978(4), N(1)–Cu(1)–N(2) = 78.14(8), N(1)–Cu(1)–N(5) = 77.31(8), N(2)–Cu(I)–N(5) = 104.88(9), N(1)–Cu(1)–I(1) = 115.26(6), N(2)–Cu(1)–I(1) = 124.10(6), N(5)–Cu(1)–I(1) = 130.70(6). For **2**: Cu(1)–N(1) = 2.289(2), Cu(1)–N(2) = 2.069(2), Cu(1)–N(5) = 2.035(2), Cu(1)–N(8) = 1.902(3), N(1)–Cu(1)–N(2) = 78.78(9), N(1)–Cu(1)–N(5) = 77.85(9), N(1)–Cu(1)–N(8) = 120.48(11), N(2)–Cu(1)–N(5) = 112.2(9), N(2)–Cu(1)–N(8) = 111.53(10), and N(5)–Cu(1)–N(8) = 135.20(10). For **3**: Cu(1)–N(1) = 2.474(3), Cu(1)–N(2) = 2.004(3), Cu(1)–N(5) = 2.085(3), Cu(1)–N(8) = 1.897(3), N(1)–Cu(1)–N(2) = 76.71(11), N(1)–Cu(1)–N(5) = 74.42(10), N(1)–Cu(1)–N(8) = 120.44(12), N(2)–Cu(1)–N(5) = 104.65(12), N(2)–Cu(1)–N(8) = 135.23(13), and N(5)–Cu(1)–N(8) = 119.47(12).

Scheme 3. Formation of 4 and 5 from "Aged" Samples of 2



corresponding N-(4-(trifluoromethyl)phenyl)-(2,2′-diamino)-diphenylamine (ORTEP diagram, Figure S3) with the assistance of hydrazine over 10% Pd/C in ethanol. The bipodal ligand TMG$_2$biphen^{N-Ar} can then be obtained in excellent yields by coupling the diamine with chlorotetramethylformamidinium chloride (prepared by chlorination of tetramethylurea with oxalyl chloride) in the presence of triethylamine in acetonitrile.

The bipodal copper(I) reagents can be obtained via two different synthetic procedures (Scheme 2). The iodide precursor [(TMG$_2$biphen^{N-Me})Cu^I–I] (**1**) was first synthesized from the reaction of ligand TMG$_2$biphen^{N-Me} and anhydrous copper(I) iodide in acetonitrile, followed by removal of the iodide with the assistance of TlPF$_6$ in MeCN to afford [(TMG$_2$biphen^{N-Me})Cu^I–NCMe](PF$_6$) (**2**). The compound can be recrystallized from MeCN/Ether as colorless crystals under strict anaerobic conditions. A similar procedure has been previously followed in the synthesis of [(TMG$_2$biphen^{N-Me})M^{II}–(NCMe)$_x$](PF$_6$)$_2$ (M = Mn (x = 3), Fe (x = 3), Co (x = 2)).[37] Alternatively, compounds [(TMG$_2$biphen^{N-Me})Cu^I–NCMe](PF$_6$) (**2**) and [(TMG$_2$biphen^{N-Ar})Cu^I–NCMe](PF$_6$) (**3**) can be obtained

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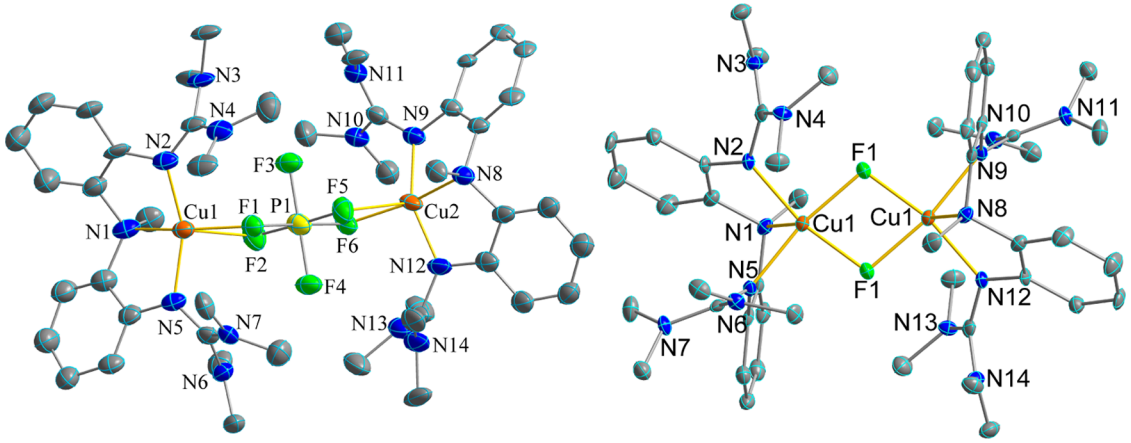

Figure 4. ORTEP diagrams of $[(TMG_2biphen^{N-Me})_2Cu_2(PF_6)](PF_6)_2$ (**4**) and $[(TMG_2biphen^{N-Me})_2Cu_2(\mu_2\text{-}F)_2](PF_6)_2$ (**5**) species drawn with 40% thermal ellipsoids. Selective interatomic distances (Å) and angles (deg) for **4**: Cu(1)−N(1) = 2.043(12), Cu(1)−N(2) = 1.922(11), Cu(1)−N(5) = 1.942(11), Cu(1)−F(1) = 1.992(8), Cu(2)−N(8) = 2.074(11), Cu(2)−N(9) = 1.948(11), Cu(2)−N(12) = 1.898(10), Cu(2)−F(5) = 2.404(7), Cu(2)−F(6) = 1.984(8), N(2)−Cu(1)−N(1) = 84.8(5), N(5)−Cu(1)−N(1) = 86.9(5), N(2)−Cu(1)−N(5) = 154.8(5), N(2)−Cu(1)−F(1) = 97.2(4), N(5)−Cu(1)−F(1) = 98.6(4), F(1)−Cu(1)−N(1) = 160.3(4), N(9)−Cu(2)−N(8) = 86.3(5), N(12)−Cu(2)−N(8) = 86.1(5), N(12)−Cu(2)−N(9) = 151.3(5), N(9)−Cu(2)−F(5) = 112.5(4), N(12)−Cu(2)−F(5) = 95.8(4), N(8)−Cu(2)−F(5) = 96.2(4), N(9)−Cu(2)−F(6) = 97.3(4), N(12)−Cu(2)−F(6) = 98.9(4), F(6)−Cu(2)−N(8) = 160.6(4), F(6)−Cu(2)−F(5) = 64.7(3). For **5**: Cu(1) − N(1) = 2.395(3), Cu(1) − N(2) = 1.959(3), Cu(1) − N(5) = 1.996(3), Cu(1)−F(1) = 1.947(2), Cu(1)−F(1)#1 = 1.916(2), F(1)#1−Cu(1)−F(1) = 77.31(9), F(1)#1−Cu(1)−N(2) = 167.10 (11), F(1)−Cu(1)−N(2) = 89.81(11), F(1)#1−Cu(1)−N(5) = 92.58(10), F(1)−Cu(1)−N(5) = 168.67(10), N(2)−Cu(1)−N(5) = 100.17(12), F(1)#1−Cu(1)−N(1) = 106.34(10), F(1)−Cu(1)−N(1) = 112.48 (10), N(2)−Cu(1)−N(1) = 79.12(11), and N(5)−Cu(1)−N(1) = 75.02(11).

more conveniently, and in slightly better yields, via the direct reaction of the ligand with $[Cu(NCMe)_4](PF_6)$ in acetonitrile (Figure 3).

Notably, aged solutions of $[(TMG_2biphen^{N-Me})Cu^I\text{–}NCMe](PF_6)$ (**2**), even under anaerobic conditions, show partial decomposition in MeCN/THF, precipitating a small amount of light-brown needles and green-plate crystals (Scheme 3). While no significant samples can be garnered from these solutions for detailed analytical studies, the two phases have been characterized by single-crystal X-ray analysis (Figure 4) to reveal an intriguing dimeric mixed-valent Cu(I)/Cu(II) compound $[(TMG_2biphen^{N-Me})_2Cu_2(PF_6)](PF_6)_2$ (**4**) (light brown) and a dimeric Cu(II) species $[(TMG_2biphen^{N-Me})_2Cu_2(\mu_2\text{-}F)_2](PF_6)_2$ (**5**) (green), featuring progressive PF_6^- activation (defluorination).

Solid-State Structures and Solution Behavior. The three distinct copper(I) compounds $[(TMG_2biphen^{N-Me})\text{-}Cu^I\text{–}I]$ (**1**), $[(TMG_2biphen^{N-Me})Cu^I\text{–}NCMe](PF_6)$ (**2**), and $[(TMG_2biphen^{N-Ar})Cu^I\text{–}NCMe](PF_6)$ (**3**) have been crystallographically characterized by single-crystal X-ray diffraction analysis (Figure 3). All three Cu(I) compounds are four-coordinated by a facially attached $[N_2N]$ ligand and a fourth residue (I or MeCN), demonstrating an overall geometry that according to Houser's τ_4 index (0.75 (**1**), 0.74 (**2**, **3**)) lies between trigonal pyramidal and seesaw.[41] As expected, slightly tighter $Cu\text{–}N_{gua}$ bond distances are revealed for cationic compounds **2** and **3** by comparison to those of neutral compound **1**. The difference of basicity between the diarylmethylamine- (**2**) and triarylamine-supported (**3**) frameworks is reflected in the length of the corresponding Cu(1)–N(1) bond distance (2.289(2) (**2**), 2.474(3) (**3**) Å). The strong donor character of the superbasic TMG residue upon metalation can be evaluated by the degree of charge delocalization over the CN_3 triangle, as depicted by the structural parameter $\rho = 2a/(b + c)$, where a is the C═N bond distance and b and c are the two $C\text{–}NMe_2$ bond distances.[42] Although for the bipodal ligands $TMG_2biphen^{N-Me}$ and $TMG_2biphen^{N-Ar}$ the length of the C═N bond is 94 and 96%, respectively, of the average $C\text{–}NMe_2$ bonds (i.e., ρ = 0.94, 0.96), for the three Cu(I) compounds that are supported by TMG residues, the corresponding bond lengths are essentially equivalent (ρ = 0.97 (**1**–**3**)).

Compound **4** is a dimeric species with a central PF_6^- unit bridging the two Cu sites via fluorine atoms (Figure 4). Each Cu site is coordinated facially by a $[N_2N]$ ligand scaffold and by two PF_6^--derived F atoms, although the two Cu–F bond distances vary considerably (by approximately 0.5 Å), further affecting the corresponding P–F bond distances to a lesser degree. The two Cu sites are related by an approximate pseudoinversion center lying at the central P atom. No significant metrical differences are observed in the coordination sphere of the two Cu centers, suggesting that the oxidation state is rather delocalized. The mean Cu–N bond distance in **4** is shorter than that observed with **2**, in accordance with the higher oxidation state of the former compound. Compound **5** features similar characteristics, but in this case, a rigorous inversion center lies in the middle of the $Cu_2(\mu_2\text{-}F)_2$ parallelogram (Figure 4). The two Cu–F bond distances only differ by 0.031 Å and are shorter than those encountered in **4**, presumably due to the expulsion of the phosphorus core and the higher oxidation state of Cu in **5**. The average Cu–N bond distances are a little longer in **4** rather than **5**, probably in response to the stronger Cu–F bonds in the latter compound, making **5** a bona fide 5-coordinate species. Summaries of crystallographic data are collected in Tables S1 – S3.

^1H NMR data for Cu(I) complexes **1**–**3** in CD_3CN solutions show that all eight methyl groups coalesce to a broad signal at 27 °C, indicating exchange due to rotation around all three N–C bonds. The rotation is progressively restricted with decreasing temperature (Figures S4 and S5),

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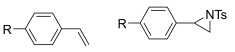
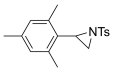
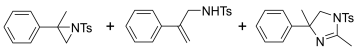
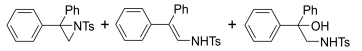
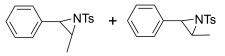
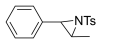
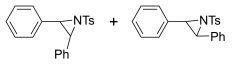
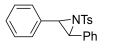
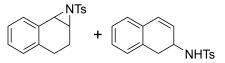
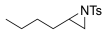
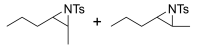
Table 1. Yields of Aziridination and Amination Products Generated in Cu(I)-Mediated Nitrene Transfer to Various Olefins[a]

Entry No.	Substrates	Products	Yield (%) (2)	Yield (%) (3)
1.		R = H	98	93
2.		R = Me	92	94
3.		R = ^{t}Bu	94	95
4.		R = OMe	80	90
5.		R = O^{t}Bu	90	95
6.		R = Cl	97	92
7.		R = F	98	92
8.		R = CF_3	98	91
9.		R = NO_2	88	86
10.			67	65
11.			49, 2, n.d.	50, 4, 6
12.			44, 8, 18	42, 7, 12
13.			54, 31	55, 30
14.			74	73
15.			40, 39	37, 34
16.			71	65
17.			46, 3	42, 5
18.			58	60
19.			29, 28	31, 30
20.			65	61

[a]Catalyst, 0.0125 mmol (5 mol %); PhINTs, 0.25 mmol; olefin, 2.0 mmol; MS 5 Å, 20 mg; MeCN 0.250 g; 30 °C; 2 h.

and eventually, all eight methyl groups resolve to eight distinct peaks ranging from δ 1.2 to 3.5 ppm at −30 °C.

Cyclic voltammograms of Cu(I) compounds **2** and **3** in MeCN are quite complex but similar (Figure S6), demonstrating an irreversible anodic event followed by a semireversible wave at higher potentials ($E_{1/2}$ = −0.01 (**2**) and −0.47 (**3**) V, referenced versus the Fc^+/Fc couple).[43] It is not clear at the present time whether these electrochemical changes may encompass defluorination steps as those noted in Scheme 3.

Catalytic Nitrene Transfer to Olefins. Table 1 summarizes the yields of the aziridination of a panel of styrenes (2.0 mmol) by the imidoiodinane PhI = NTs (0.25 mmol) conducted in MeCN in the presence of catalytic amounts of Cu(I) catalysts **2** and **3** (5 mol %) at 30 °C. Molecular sieves are necessary for obtaining good yields.

Entries 1−9 feature a series of electron-diverse, para-substituted styrenes, which undergo facile aziridination with excellent yields, achieving reaction completion under 2 h, even if electron-withdrawing para-substituents are employed (entries 8, 9). Good but more moderate yields are observed in the aziridination of the bulky ortho-substituted 2,4,6-trimethylstyrene (entry 10). This substrate is also electronically hampered due to the orthogonal orientation of the aromatic/olefinic planes.[44] Good yields are further observed in the aziridination of α-substituted styrenes (entries 11 and 12). Small amounts of allylic amination are observed with α-methylstyrene as noted in previous studies.[32,37] Interestingly, minute amounts of a 2,4-substituted 2-imidazoline[45] are observed with the more acidic catalyst **3**, most likely resulting from MeCN insertion upon aziridine ring opening, as discussed in a previous publication from our lab.[37] For α-phenylstyrene (entry 12), the corresponding aziridine remains the main product, but small amounts of enamine (due to aziridine ring-opening and rearrangement)[46] and a hydroamination byproduct (apparently via nucleophilic attack by residual water on an intermediate ring-opened benzylic carbocation) are also observed. The mechanistically instructive β-substituted styrenes (entries 13−16) afford good to high yields of the corresponding aziridines, although poor retention of stereochemistry is observed with the diagnostic cis-β-R-styrenes (cis/trans = 1:0.57 (**2**), 1:0.55 (**3**), R = Me; 1:0.98 (**2**), 1:0.92 (**3**), R = Ph). By way of contrast, previously studied Fe(II) sites supported by $TMG_2biphen^{N-Me}$ provide lower yields but higher retention of stereochemistry (up to 93%) in the aziridination of cis-β-methylstyrene.[37] Entry 17 provides an example in which both aziridination and allylic amination

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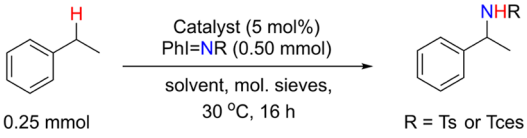
occur, although the aziridinated product dominates the product profile with both copper reagents. Certain electron-rich, alkyl-substituted olefins (entries 18−20) have also been subjected to aziridination. Gratifyingly, they provide good aziridination yields but no further improvement in the retention of stereochemistry (entry 19). Overall, catalysts **2** and **3** do not show any significant variations in product yields or selectivity outcomes.

Catalytic Nitrene Transfer to Alkanes. Initial investigations involving C−H bond aminations, mediated by catalysts **2** and **3**, were carried out by employing the benchmark substrate ethylbenzene and two different nitrene sources (PhINTs, PhINTces[47−52]), in several solvents. Although PhINTs proved to be a good nitrene source for aziridination reactions, it provided rather moderate yields in ethylbenzene amination under various conditions (Table 2).

Table 2. Optimization of Ethylbenzene Amination Using PhINTs and PhINTces[a]



		yield (%) catalyst 2		yield (%) catalyst 3	
entry no	solvent	PhINTs	PhINTces	PhINTs	PhINTces
1.	DCM	20	37	22	38
2.	HFIP	53	**55**	44	**56**
3.	PhCl	35	38	18	32
4.	$PhCF_3$	36	39	25	38
5.	benzene	20	46	10	33
6.	PhCl:HFIP (1:1 v/v)	46	**59**	40	51
7.	PhCl:HFIP (10:2 v/v)	38	49	35	42
8.	benzene:HFIP (10:2 v/v)	35	**53**	30	50

[a]Catalyst, 0.0125 mmol (5 mol %); PhINTs or PhINTces, 0.50 mmol; ethylbenzene, 0.25 mmol; MS 5 Å, 20 mg; solvent 0.250 g; 30 °C; 16 h.

On average, the more electrophilic and significantly more soluble PhINTces (presynthesized)[50] afforded better yields, as shown in Table 2. Interestingly, PhINTces can be crystallized from acetonitrile or acetone to afford XRD-quality crystals (Figure 5), but it is known to be sensitive to light and heat, especially in halogenated solvents.

The most productive reaction stoichiometry was proven to be with an excess of PhI = NR (2 equiv) over substrate and 5 mol % catalyst (**2** or **3**) in a variety of halogenated and nonhalogenated solvents at 30 °C over a period of 16 h. In one instance, TFE (trifluoroethanol) was used as a solvent in the presence of catalyst **2** and PhINTs, and the solvent was found to undergo nitrene insertion preferentially, to form the hemiaminal N-(1-hydroxy-2,2,2-trifluoroethyl)−4-methyl-benzenesulfonamide[53] in 50% yields (Scheme 4). Further trials indicated that HFIP (entry 2) was beneficial with both catalysts, affording ≥50% yields. This can be attributed to the fact that HFIP offers better solubility to the nitrene sources (especially with PhINTces) but may also offer moderate Lewis-acid characteristics in enhancing the electrophilicity of the putative metal nitrene oxidant.[54] It was further found that

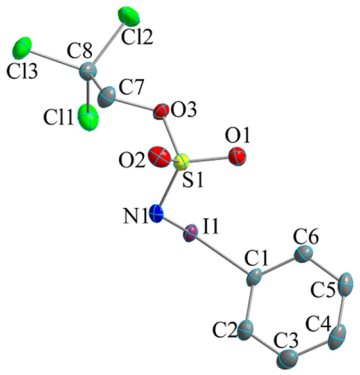
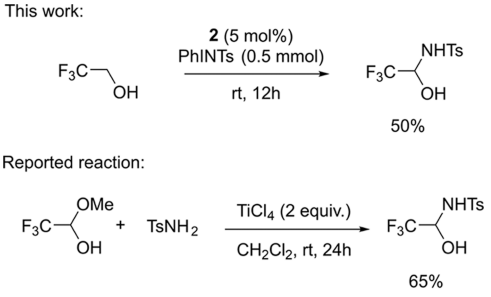


Figure 5. ORTEP diagram of PhINTces drawn with 40% thermal ellipsoids. Selective interatomic distances (Å) and angles [°]: I(1)−N(1) = 2.011(4), I(1)−C(1) = 2.091(5), S(1)−N(1) = 1.578(5), S(1)−O(1) = 1.419(4), S(1)−O(2) = 1.416(4), S(1)−O(3) = 1.618(4), and O(3)−C(7) = 1.422(6), Cl(1)−C(8) = 1.742(6), Cl(2)−C(8) = 1.769(6), Cl(3)−C(8) = 1.772(6), N(1)−I(1)−C(1) = 98.00(19), N(1)−S(1)−O(3) = 107.1(2), and O(1)−S(1)−N(1) = 115.2(2), O(2)−S(1)−N(1) = 107.6(2), O(2)−S(1)−O(1) = 118.8(2), and O(3)−C(7)−C(8) = 107.5(4), Cl(1)−C(8)−Cl(3) = 109.7(3), and Cl(2)−C(8)−Cl(3) = 109.0(3).

Scheme 4. Preferential Nitrene Insertion into 2,2,2-Trifluoroethanol



yields can be improved more economically by employing small amounts of HFIP in solvents such as benzene or chlorobenzene (entries 6−8). Since PhINTces has poor stability in chlorobenzene over a period of 24 h, we chose to explore benzene/HFIP (10:2 v/v) for further experimentation.

Other benzylic substrates indicate that both prim and tert sites (entries 1 and 2, Table 3) are aminated in low yields, presumably due to stronger C−H bonds (toluene, 90 kcal/mol)[55] and steric encumbrance, respectively. Indeed, sec-benzylic sites are preferentially aminated, with yields increasing crudely with decreasing BDE values (diphenylmethane, 82 kcal/mol, entry 3).[56] Slightly better yields are obtained with catalyst **3** for these benzylic substrates, potentially because of the higher electrophilicity anticipated for the metal nitrene oxidant with this catalyst. Tertiary sites of polycyclic alkanes undergo amination in good yields as opposed to any competing secondary sites (entry 4). In general, sec-C−H bonds of cycloalkanes (entries 5 and 6) are low yielding, even if a higher mol % of catalyst is used. Competition between tert/sec/prim−C−H bonds in acyclic hydrocarbons (entry 7) affords only tert-C−H aminations, albeit in low yields. Finally, competition between sec-benzylic and tert-C−H bonds (entry 8) indicates exclusive amination of the benzylic site. Overall, catalyst **3** affords slightly better yields for the entire panel of

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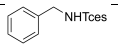
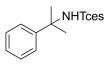
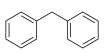
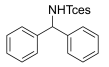
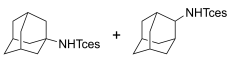
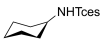
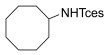
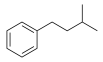
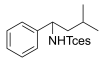
Table 3. Amination (NHTces) of Various Hydrocarbons Mediated by 2 and 3 in Benzene/HFIP (10:2 v/v).[a]

Entry No.	Substrate	Products	2 Yield (%)	3 Yield (%)
1.			11	17
2.			18	25
3.			54	61
4.			50, 6	52, 6
5.			12[b]	15[b]
6.			13[b]	20[b]
7.			7[b]	12[b]
8.			36	40

[a]Reaction conditions: catalyst, 0.0125 mmol (5 mol %); substrate, 0.25 mmol; PhI = NTces, 0.50 mmol; benzene/HFIP (10:2 v/v), 0.15 mL; molecular sieves (5 Å), 20 mg; t = 16 h; T = 30 °C. [b]Catalyst, 0.0187 mmol (7.5 mol %).

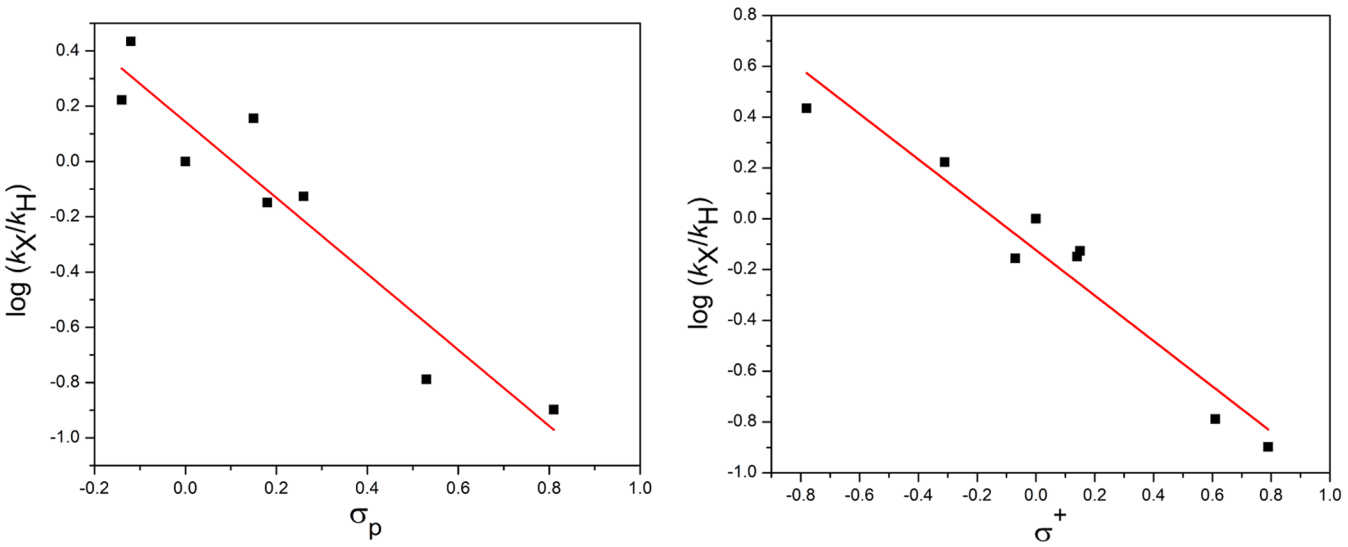


Figure 6. Linear free energy correlation of $\log(k_X/k_H)$ as a function of σ_p (left) and σ^+ (right) for the competitive amination of para-substituted ethylbenzenes versus ethylbenzene catalyzed by $[(TMG_2biphen^{N-Ar})Cu^{I}-NCMe](PF_6)$ (**3**).

substrates shown in Table 3. However, previous studies with Cu(I) sites supported by the analogous tripodal TMG-containing ligand ($[(TMG_3trphen)Cu](PF_6)$) provide significantly higher yields for the amination (PhI = NTs) of all types of C−H bonds examined in this study, best highlighted with the challenging sec-C−H bonds (50% yield for the amination of cyclohexane).[32]

Mechanistic Studies: Hammett Plots. Hammett plots (Figure 6 and Table S4) have been constructed by conducting competitive amination reactions with the assistance of a panel of seven para-substituted ethylbenzenes (0.125 mmol) versus ethylbenzene (0.125 mmol) by PhI═NTces (0.50 mmol) mediated by **3** (5 mol %) in benzene/HFIP (10:2 v/v) (Table S4). Liner free energy correlations of $\log(k_X/k_H)$ as a function of σ_p provide marginally acceptable fits (R^2 = 0.88), which can be further improved with σ^+ parameters (R^2 = 0.92). No significant improvement was realized by invoking both polar- and spin-delocalization substituent parameters, confirming the predominance of polar vs spin effects as anticipated for C−H bond cleavage processes. The corresponding ρ^+ value of −0.89 suggests that a significant positive charge develops en route to the transition state at the benzylic position, most likely associated with the frequently turnover-limiting hydrogen-atom abstraction. Slightly more negative ρ^+ values were previously calculated for the amination of toluene by the tripodal $[(TMG_3trphen)Cu^{I}](PF_6)$ catalyst (ρ^+ = −1.16 (NTs), − 0.91 (NNs)),[32] probably reflecting the more modest electrophilic nature of these nitrenes. These sizable negative ρ^+

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values are in general agreement with those reported for stepwise C−H aminations ([$Ru_2(hp)_4Cl$], $\rho^+ = -0.90$; [$Ru_2(esp)_2SbF_6$], $\rho^+ = -1.49$).[23b] In contrast, more modest negative ρ^+ values are encountered in Rh-catalyzed concerted asynchronous benzylic aminations (−0.47,[57] − 0.55,[24a] − 0.66,[58] − 0.73,[48] − 0.90[24d]).

CONCLUSIONS

The following are the most significant findings and insights garnered from this investigation:

(a) Two cationic bipodal Cu (I) compounds [($TMG_2biphen^{N-Me}$)Cu^I−NCMe](PF_6) (**2**) and [($TMG_2biphen^{N-Ar}$)Cu^I−NCMe](PF_6) (**3**) have been synthesized, featuring coordinated ligation composed of an apical diarylmethyl- (**2**) and triaryl-N_{amine} residue (**3**), respectively, and two N_{imine} residues associated with superbasic TMG arms. The general stoichiometry of these reagents has been confirmed by single-crystal X-ray diffraction analysis, revealing in both cases four-coordinate Cu(I) sites with a geometry between trigonal pyramidal and seesaw. ^{1}H NMR data suggests that partial rotation of the TMG moieties is encountered under ambient temperatures, which can be arrested with decreasing temperature.

(b) Aziridination (PhINTs) of a panel of aromatic olefins by either catalyst indicates that para- and α- or β-substituted styrenes afford excellent yields that are only slightly curbed by the presence of olefinic substituents. On the other hand, modest levels of stereochemical retention are observed with cis olefins. The usually less reactive aliphatic olefins also provide good aziridination yields with only modest stereocontrol. In combination with previous work,[35] the order of reactivity of the cationic metal reagents that are supported by the same bipodal ligand $TMG_2biphen^{N-Me}$, is established as Cu > Fe > Co ≥ Mn.

(c) Amination of largely sec-benzylic-C−H bonds and tert-C−H bonds of polycyclic substrates can be achieved in better yields with a more electrophilic and soluble N-donor source (PhINTces), as well as in solvent matrices that contain low amounts of HFIP. As opposed to the previously studied tripodal catalyst [($TMG_3trphen$)-Cu^I](PF_6), the present bipodal catalysts are rather low yielding with cycloalkanes and acyclic hydrocarbon substrates, as well as with prim- and tert-C−H bonds of benzylic sites. The observed reactivity trend is unexpected, as it is the reverse of what has been previously established for the dicationic base-metal congeners (M = Mn, Fe, Co),[35] as well as in similar iron-oxo chemistry with the assistance of TMG_3tren and TMG_2dien ligands.[59] It is conceivable that the observed fluorophilicity of the bipodal Cu reagents may limit their stability.

(d) Mechanistic studies carried out with the more reactive catalyst **3** provide reasonably linear free energy correlations with Hammett's σ^+ parameters, featuring negative ρ^+ coefficients within the range expected for stepwise rate-determining hydrogen-atom abstraction by a putative metal nitrene oxidant, generating an intermediate carboradical (or carbocation). The latter recombines with the incipient Cu−$^{\bullet}$NHR to form the new C−N bond.

Further experimental and computational studies will address more precisely the geometric and electronic nature of the elusive metal nitrene entity in the bipodal Cu reagents vis-à-vis that of the tripodal congeners and establish its mode of operation with typical C−H bonds of substrates. Moreover, the fluorophilicity of the present Cu catalysts will be studied in greater detail.

EXPERIMENTAL SECTION

Safety Warning. *Thallium salts are highly toxic and need to be handled with care.*

Synthesis of Copper Compounds. *[($TMG_2biphen^{N-Me}$)-Cu^I−I] (**1**).* The ligand $TMG_2biphen^{N-Me}$ (0.2047 g, 0.5 mmol) was dissolved in degassed MeCN (15.0 mL), and CuI (0.095 g, 0.5 mmol) was added to this solution. The mixture was stirred overnight to give a pink solution, which was then filtered on an anaerobic frit. Diethyl ether was carefully layered over the MeCN solution, and the solvents were allowed to slowly mix over a period of several days at −35 °C, to afford pale pink to colorless crystalline material suitable for X-ray diffraction analysis. Yield: 0.276 g, 92%. ^{1}H NMR (243 K, CD_3CN, 1.96 ppm): δ 7.55−7.60 (m, 1H), 6.89−7.00 (m, 1H), 6.63−6.49 (m, 1H), 6.30−6.36 (m, 1H), 2.96−3.13 (m, 12H), 2.86 (d, 3H, J = 4.6 Hz), 2.69 (d, 3H, J = 6.5 Hz), 2.62 (d, 3H, J = 5.1 Hz), 2.32 (s, 3H), 1.20 (d, 3H, J = 16.8 Hz). ^{13}C NMR (CD_3CN): δ 158.46, 138.41, 136.71, 128.12, 123.28, 120.67, 119.56, 44.68, 34.35. IR (KBr, cm^{-1}): 3439, 3061, 3012, 2930, 2792, 1626, 1557, 1521, 1488, 1399, 1333, 1265, 1231, 1161, 1035, 859, 745, 691, 520. UV−vis (MeCN): λ_{max} (ε (M^{-1} cm^{-1})) 275 (40120). Elem. Anal. for $C_{23}H_{35}CuIN_7$: C, 46.04; H, 5.88; N, 16.34. Found: C, 45.99; H, 5.81; N, 16.23.

*[($TMG_2biphen^{N-Me}$)Cu^I−MeCN](PF_6) (**2**).* [($TMG_2biphen^{N-Me}$)Cu^I−I] (**1**) (0.300 g, 0.5 mmol) was dissolved in degassed CH_3CN (10.0 mL), to which $TlPF_6$ (0.349 g, 1 mmol) was added. Immediate precipitation of a light-yellow solid was observed, indicating the formation of thallium(I) iodide. The mixture was stirred for 6 h and then filtered on an anaerobic frit. Diethyl ether was carefully layered over the MeCN solution, and the solvents were allowed to slowly mix over a period of several days at −35 °C, to afford colorless crystalline material suitable for X-ray diffraction analysis. Yield: 0.420 g, 75%.

Alternatively, the ligand $TMG_2biphen^{N-Me}$ (0.204 g, 0.5 mmol) was dissolved in degassed MeCN (15.0 mL), and [$Cu(NCMe)_4$](PF_6) (0.186 g, 0.5 mmol) was added to this solution. The mixture was stirred overnight to give a pale pink solution, which was then filtered on an anaerobic frit. Diethyl ether was carefully layered over the MeCN solution, and the solvents were allowed to slowly mix over a period of several days at −35 °C, to afford colorless crystalline material suitable for X-ray diffraction analysis. Yield: 0.309 g, 90%. ^{1}H NMR (243 K, CD_3CN, 1.96 ppm): δ 7.58−7.61 (m, 1H), 6.95−7.02 (m, 3H), 6.90 (d, 1H, J = 7.8 Hz), 6.68 (t, 1H, J = 7.0 Hz), 6.49 (d, 1H, J = 7.9 Hz), 6.35 (dd, 1H, J = 1.8, 7.3 Hz), 3.08 (s, 3H), 3.07 (s, 3H), 2.99 (s, 3H), 2.96 (s, 3H), 2.86 (s, 3H), 2.71 (s, 3H), 2.63 (s, 3H), 1.98 (s, 3H), 1.18 (s, 3H). ^{13}C NMR (CD_3CN): δ 164.01, 147.35, 126.42, 121.39, 121.23, 118.05, 117.87, 117.68, 44.85, 39.43. ^{19}F-NMR ($CDCl_3$): −71.99, − 73.87. FT-IR (KBr, cm^{-1}): 3002, 2934, 2891, 1530, 1479, 1423, 1410, 1393, 1343, 1155, 1027, 834, 757, 557, 526,

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498. UV−vis (MeCN): λ_{max} (ε (M^{-1} cm^{-1})) 280 (26583), 220 (46658). Elem. Anal. Calcd for $C_{25}H_{38}CuF_6N_8P$: C, 45.56; H, 5.81; N, 17.00. Found: C, 45.59; H, 5.87; N, 17.05.

*[($TMG_2biphen^{N-Ar}$)Cu^{I}−MeCN](PF_6) (**3**).* The ligand $TMG_2biphen^{N-Ar}$ (0.269 g, 0.5 mmol) was dissolved in degassed MeCN (15.0 mL), and [Cu($NCMe)_4$](PF_6) (0.186 g, 0.5 mmol) was added to this solution. The mixture was stirred overnight to give a pale gray solution, which was then filtered on an anaerobic frit. Diethyl ether was carefully layered over the MeCN solution, and the solvents were allowed to slowly mix over a period of several days at −35 °C, to afford colorless crystalline material suitable for X-ray diffraction analysis. Yield: 0.306 g, 85%. ^{1}H NMR (243 K, CD_3CN, 1.96 ppm): δ 7.51 (d, 1H, J = 8.8 Hz), 7.46 (d, 1H, J = 8.3 Hz), 7.03−7.17 (m, 5H), 6.81−6.91 (m, 2H), 6.57 (d, 2H, J = 8.2 Hz), 6.49 (d, 1H, J = 9.0 Hz), 3.07 (s, 3H), 3.05 (s, 3H), 2.85 (s, 3H), 2.82 (s, 3H), 2.73 (s, 3H), 2.66 (s, 3H), 2.21 (s, 3H), 1.98 (s, 3H), 1.20 (s, 3H). ^{13}C NMR (CD_3CN): δ 164.79, 153.75, 148.65, 127.88, 126.73, 126.29, 126.25, 124.05, 122.76, 122.44, 122.17, 121.93, 117.88, 65.86, 39.77. ^{19}F-NMR ($CDCl_3$): − 62.04, − 72.04,, − 73.91. FT-IR (KBr, cm^{-1}): 2935, 2893, 1613, 1530, 1483, 1422, 1394, 1324, 1279, 1158, 1103, 1064, 1028, 833, 752, 556, 509. UV−vis (MeCN): λ_{max} (ε (M^{-1} cm^{-1})) 294 (28082). Elem. anal. for $C_{31}H_{39}CuF_9N_8P$: C, 47.18; H, 4.98; N, 14.20. Found: C, 47.09; H, 4.93; N, 14.15.

Catalytic and Mechanistic Studies. *General Catalytic Olefin Aziridination Procedure.* All catalytic reactions were carried out under nitrogen atmosphere in an MBraun Drybox (O_2, H_2O < 1 ppm). In a typical experiment, a 20 mL screw-cap vial containing a small magnetic bar was charged in sequence with the catalyst (0.0125 mmol with respect to Cu), N-(*p*-tolylsulfonyl)imido-phenyliodinane (93.3 mg, 0.25 mmol), molecular sieves (5 Å) (20 mg), olefin (2.0 mmol), and acetonitrile (0.250 g) (as stated in Table 1). The reaction mixture was stirred vigorously at 30 °C for 2 h (unless otherwise stated). After completion of the reaction, the products were isolated by column chromatography (silica gel) and quantified by ^{1}H NMR (in $CDCl_3$ or CD_3CN) versus an internal standard (4′-methoxyacetophenone). All aziridines,[32,39,40] any allylic/benzylic amination products[39,40,60] and insertion products[35] (Table 1) are known compounds. They have been identified with the assistance of ^{1}H NMR, by comparison with spectroscopic features reported for authentic samples in the literature.

General Procedure for Amination of Hydrocarbons. All catalytic reactions were carried out under nitrogen atmosphere in an MBraun Drybox (O_2, H_2O < 1 ppm). In a typical experiment, a 20 mL screw-capped vial containing a small magnetic stir-bar was charged with the catalyst (0.0125 or 0.01875 mmol with respect to Cu), N-(p-tolylsulfonyl)imino-phenyliodinane (186.6 mg, 0.50 mmol), or 2,2,2-trichloroethyl(phenyl-λ^3-iodanylidene)sulfamate (215.24 mg, 0.50 mmol), molecular sieves (5 Å) (20 mg), substrate (0.25 mmol), and the specified solvent (0.15 mL), added sequentially. The reaction mixture was stirred vigorously for 16 h. After completion of the reaction, the products were isolated by column chromatography (silica gel) and quantified by ^{1}H NMR (in $CDCl_3$ or CD_3CN) versus an internal standard (4′-methoxyacetophenone). All amination products are known compounds[32] (Tables 2 and 3), and were identified with the assistance of ^{1}H NMR, by comparison to their literature-reported spectroscopic signatures.

General Procedure for Competitive Aminations of p-X-Ethylbenzenes/Ethylbenzene. The same reaction as that described above for the general amination of hydrocarbons was conducted, with the exception that a mixture of ethylbenzene and *p*-X-ethylbenzene (X = MeO, Me, F, I, Br, CF_3, NO_2) was present (0.125 mmol each). The nitrene source employed was PhI = NTces (0.50 mmol). The reaction was allowed to run for 5 h and was then flash chromatographed on silica gel with methylene chloride. The solvent was then evaporated, and the residue was quantitatively evaluated by using ^{1}H NMR analysis ($CDCl_3$).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.4c00909.

Experimental details: additional synthetic protocols, NMR data, X-ray crystallography data, and additional figures and tables as noted in the text (PDF)

Accession Codes

CCDC 2304246−2304254 contain the supplementary crystallographic data for this paper. This data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: + 44 1223 336033.

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Notes

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