Use of Ring-Expanded Diamino- and Diamidocarbene Ligands in Copper Catalyzed Azide–Alkyne "Click" Reactions

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S *Supporting Information*

ABSTRACT: The two-coordinate ring-expanded N-heterocyclic carbene copper(I) complexes $[Cu(RE\text{-}NHC)_2]^+$ (RE-NHC = 6-Mes, 7-o-Tol, 7-Mes) have been prepared and shown to be effective catalysts under neat conditions for the 1,3-dipolar cycloaddition of alkynes and azides. In contrast, the cationic diamidocarbene analogue $[Cu(6\text{-}MesDAC)_2]^+$ and the neutral species $[(6\text{-}MesDAC)CuCl]_2$ and $[(6\text{-}MesDAC)_2(CuCl)_3]$ show good activity when the catalysis is performed on water.

INTRODUCTION

The first copper N-heterocyclic carbene mediated catalytic transformation was only reported a little over a decade ago,[1] but in the intervening time, Cu-NHCs have proven to be powerful tools for a range of catalytic reactions, including hydrosilylation, conjugate addition, and carboxylation.[2] The copper-catalyzed 1,3-dipolar Huisgen cycloaddition reaction of alkynes and azides has also attracted considerable interest,[3] principally because it represents perhaps the best known example of a "click reaction".[4] Such processes display a number of characteristic properties: they can be easily carried out neat or in a sustainable solvent such as water, can be performed without the need for air-sensitive techniques, and afford high yields of the desired products with good stereospecificity.

Two general classes of Cu-NHC complexes are used for catalyzing this reaction: neutral Cu(NHC)(halide) and cationic $[Cu(NHC)_2]^+$ systems.[3a,c] In both cases, the presence of very strongly donating, five-membered-ring carbenes affords complexes that display the highest levels of catalytic activity. In the case of $[Cu(NHC)_2]^+$ species, this has been rationalized by the need for one of the two NHC ligands to fulfill a secondary function, acting as a base to deprotonate the alkyne. This facilitates the formation of the alkynyl complex Cu(NHC)(C≡CR), which is a generally accepted intermediate on the catalytic pathway.[3i,5]

With the dual roles of the carbene for both stabilizing low-coordinate Cu(I) species and deprotonating the alkyne in mind, we have investigated the activity of a series of new cationic copper complexes (Scheme 1) containing NHCs with more than five ring atoms. These so-called ring-expanded carbenes (RE-NHCs) exhibit properties considerably different from those of their five-membered-ring counterparts. First, they feature much wider NCN angles,[6] which can aid in the stabilization of low-coordinate metal species.[7] Moreover, they are also known to be far more basic.[8] In an effort to try to differentiate the influence of stabilization vs basicity, we have also looked at the catalytic

behavior of similarly sterically demanding, yet less electron-donating, diamidocarbene (DAC) species.[9]

The use of RE-NHCs and DACs in metal-catalyzed processes is still very much in an embryonic state,[10,11] particularly in comparison to the ubiquitous five-membered-ring systems.[2e,12] We report herein that Cu–RE-NHC species with seven-membered rings show improved reactivity over six-membered ring derivatives and that, in the case of both cationic and neutral Cu-DAC complexes, the presence of the diamidocarbene enhances catalysis performed on water.

RESULTS AND DISCUSSION

Synthesis and Characterization of $[Cu(RE\text{-}NHC)_2]^+$. The cationic bis-RE-NHC complexes $[Cu(6\text{-}Mes)_2]^+$ (**1**), $[Cu(7\text{-}o\text{-}Tol)_2]^+$ (**2**) and $[Cu(7\text{-}Mes)_2]^+$ (**3**) were readily prepared as the $[BF_4]^-$ salts upon addition of 2−3 equiv of carbene (prepared in situ in the case of 7-o-Tol due to base-induced side reactions)[6c] to $[Cu(MeCN)_4][BF_4]$ at room temperature. Complex **1** was reported previously from the reaction of $[6\text{-}MesH]Br/KO^tBu$ with CuCl, although this afforded the cation with a mixed $[CuBrCl]^-$ anion.[13] The three complexes were isolated as air-stable solids in yields of 79, 48, and 17% (increased to 25% by performing a 14 h reaction at 50 °C), respectively, the steadily decreasing yield presumably reflecting the difficulty in coordinating two increasingly bulky carbenes onto the copper center.[14]

The complexes were characterized by a combination of X-ray crystallography and NMR spectroscopy. The X-ray structures (Figure 1) exhibited the expected linear C_{NHC}–Cu–C_{NHC} geometries for the mesityl-substituted complexes **1** and **3** (angles of 178.93(12) and 179.12(9)°, respectively) but a noticeably
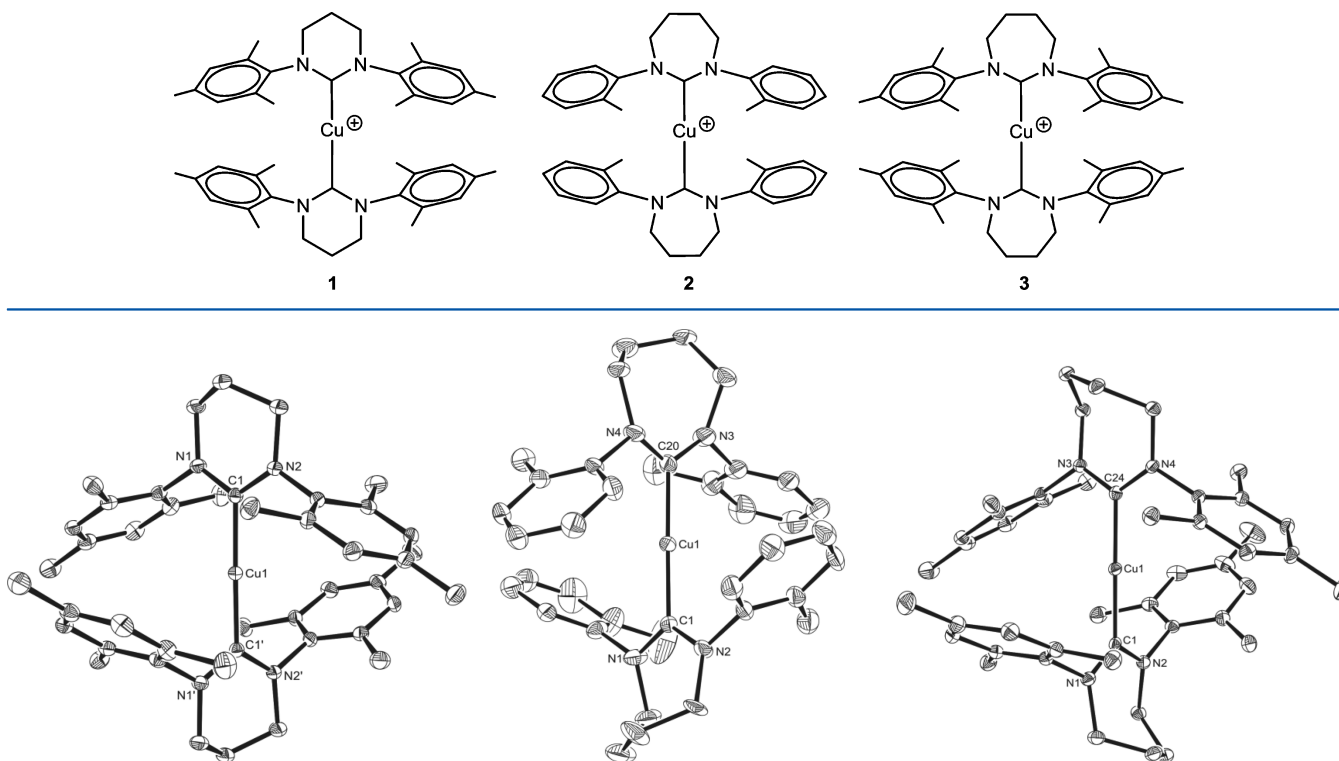
Scheme 1. Ring-Expanded [Cu(NHC)₂]⁺ Complexes

Figure 1. Molecular structures of the cations in (left to right) $[Cu(6-Mes)_2]^+$ (**1**), $[Cu(7-o-Tol)_2]^+$ (**2**), and $[Cu(7-Mes)_2]^+$ (**3**). Ellipsoids are shown at the 20% level for **2** and 30% level for both **1** and **3**. In **1**, atoms with primed labels arise via the $1 − x, y, {}^3/_2 − z$ symmetry operation. All hydrogen atoms are removed for clarity. Selected bond lengths (Å) and angles (deg): for **1**, Cu(1)−C(1) 1.9266(19), C(1)−Cu(1)−C(1′) 178.93(12), N(1)−C(1)−N(2) 117.29(17); for **2**, Cu(1)−C(1) 1.910(5), Cu(1)−C(20) 1.905(5), C(1)−Cu(1)−C(20) 173.3(2), N(1)−C(1)−N(2) 118.3(4), N(3)−C(20)−N(4) 117.7(5); for **3**, Cu(1)−C(1) 1.9540(19), Cu(1)−C(24) 1.9436(19), C(1)−Cu(1)−C(24) 179.12(9), N(1)−C(1)−N(2) 118.48(17), N(3)−C(24)−N(4) 118.47(17).

more acute angle in **2** (173.3(2)°). The Cu−C$_{NHC}$ distances elongate from **1** (1.9266(19) Å) to **3** (1.9540(19)/1.9436(19) Å), presumably as a consequence of the increased repulsion of the N-aryl groups; in accord with this, in all cases the distances were longer than those reported in either $[Cu(IMes)_2][BF_4]$ (1.884(2) Å) or $[Cu(SIMes)_2][BF_4]$ (1.896(4) Å).[15,16] For **2**, the Cu−C$_{NHC}$ distances were 1.905(5) and 1.910(5) Å, shorter than those in **3**.

While the ligand conformations about the metal center can be quantified by the angle between two least-squares planes, each containing the carbene carbon and the two NHC nitrogens from the ligands present (69.7, 89.7, and 88.2° for **1**−**3**, respectively), this is not especially revealing in itself. Overall, the steric demand of the ligand substituents appears to afford the greatest impact on possible access to the metal center. This variation is illustrated in Figure 2, which shows the access windows in each case. It is clear that, in **2**, entrance to the metal is more easily facilitated due to reduced steric congestion. Of course, this may have no bearing on solution behavior or catalytic activity (vide infra), where either ligand flexibility or ligand dissociation may be relevant.

In solution, the previously noted shift to higher frequency of the ^{13}C carbene resonance with increasing ring size was evident in going from **1** (δ 199.3) to **3** (δ 208.6).[17] In the case of **2**, the room-temperature ^{13}C{^{1}H} spectrum was broad, and no carbenic signals could be observed. This broadening appears to be a consequence of rotamers being present in solution, most likely resulting from different orientations of the tolyl Me substituents; some of these are shown in Scheme 2. Thus, the ^{1}H

NMR spectrum at 298 K showed four, broad overlapping methyl signals, which resolved to five much sharper, but still overlapping, signals at 224 K. At this temperature, the ^{13}C{^{1}H} NMR spectrum contained eight methyl signals; one major carbene resonance was now apparent at δ 207.2, along with a smaller signal (ca. 1/6 intensity) at δ 206.6 (see the Supporting Information).

Catalysis with RE-NHC and DAC Copper Complexes. The catalytic activity of the RE-NHC complexes **1**−**3** was compared using a test cycloaddition reaction of benzyl azide and PhC≡CH at room temperature with 2 mol % of the copper complex. All three complexes gave quantitative conversions to the triazole under neat conditions over 3 h (Table 1). Lowering the catalyst loading (0.5 mol %) and shortening the reaction time to 45 min allowed the relative activities of the complexes to be established, the 7-o-Tol species **2** emerging as by far the most active system with 98% conversion to the triazole.[18] At 0.1 mol %, this complex afforded a conversion of 58% in 45 min.

When the reactions were run on 0.5 mL of water, both of the 7-NHC species **2** and **3** were again more active than the 6-Mes complex **1**, although the relative ordering of **2** and **3** was now reversed. **2** showed no activity at all in CHCl$_3$; however, quantitative conversion was found in MeCN, albeit very slowly, over a period of 3 days.

In contrast to the RE-NHC complexes **1**−**3**, the tetrafluoroborate salt of the DAC complex $[Cu(6-MesDAC)_2]^+$ (**4**; Scheme 3)[19] was inactive under neat conditions (as well as in both MeCN and CHCl$_3$). However, changing to on-water
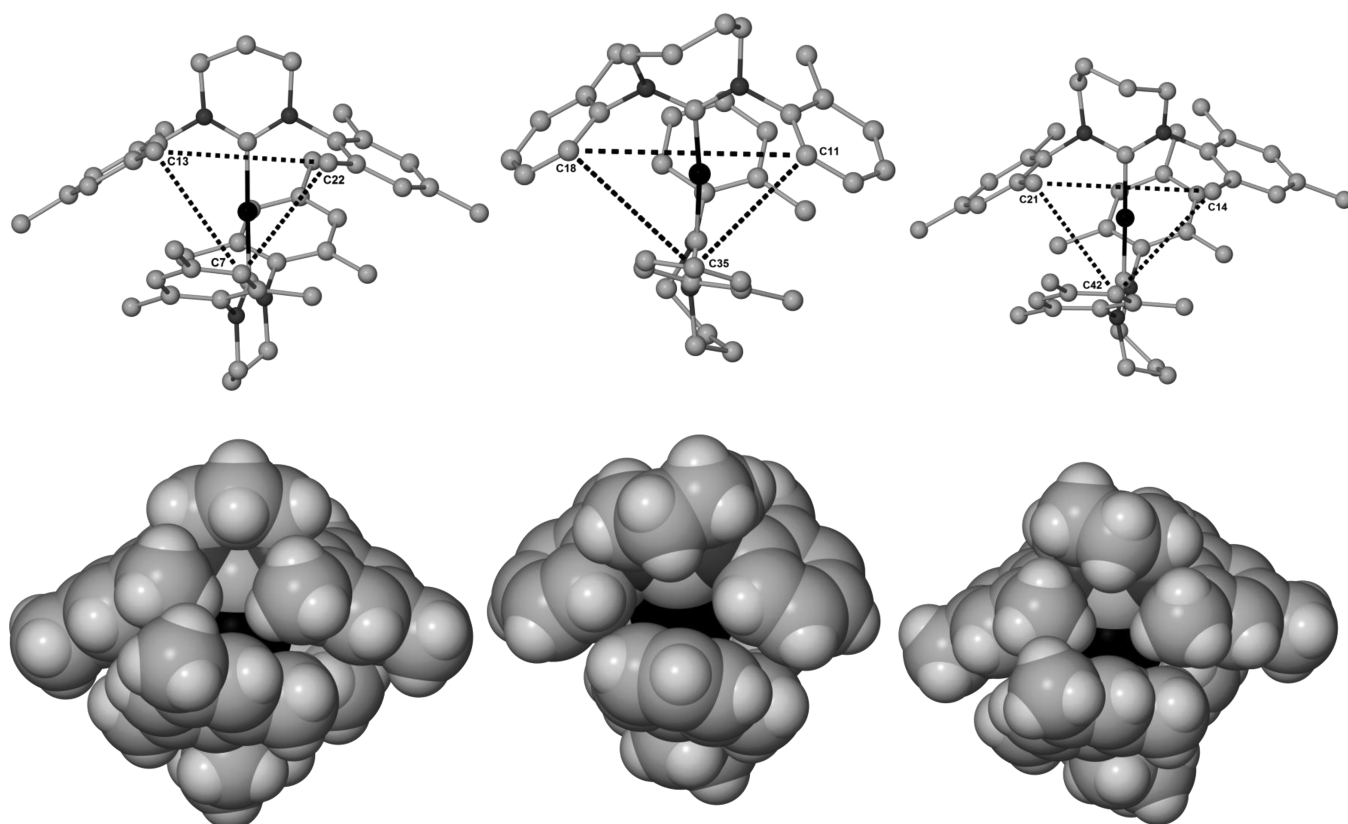
Figure 2. (top) Ball and stick representations to illustrate access to the metal centers in **1** (left), **2** (middle), and **3** (right). Hydrogen atoms are omitted for clarity. Distances in Å: for **1**, C7−C13 4.18, C7−C22 3.95, C13−C22 4.66; for **2**, C11−C18 5.87, C11−C35 4.23, C18−C35 4.85; for **3**, C14−C21 5.16, C14−C42 4.14, C21−C42 4.09. (bottom) Comparative space filling views, with hydrogens included.
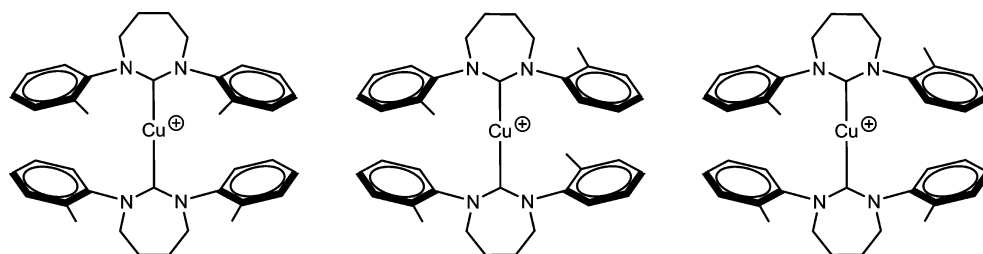
Scheme 2. Examples of Rotameric Forms of 2 in Solution


Table 1. Catalyst Screening[a]

complex	conversion (%)	
	neat	on water
1	98 (18)	58
2	100 (98)	76
3	>99 (59)	>99
4	<1	95 (8)
5	2	100 (13)
6	5	100 (30)

[a]Conditions: azide (0.50 mmol), alkyne (0.51 mmol), Cu precursor (2 mol %), 180 min. Conditions for results in parentheses: azide (0.50 mmol), alkyne (0.51 mmol), Cu precursor (0.5 mol %), 45 min. Conversions were determined by ^{1}H NMR spectroscopy: average of three runs.

conditions afforded 95% conversion over 3 h at 2 mol % loading (Table 1).[20] This accelerating effect from the use of water led us to investigate the activity of recently reported neutral Cu-DAC complexes, the dimer **5** and trimer **6** (Scheme 3).[19] In both cases, conversions of <5% were found neat, whereas quantitative conversions to product were observed on water. We are unaware of any other cases of Cu-NHC catalysts for this reaction in which the influence of water is so apparent.

In light of their effectiveness under quite different conditions, the activity of **2** and **6** toward a range of alkynes with benzyl and hexyl azide was tested under neat and on-water conditions, respectively, at 0.5 mol % loading and 45 min reaction time (Scheme 4). Although conversions were largely found to be poor in most cases under these conditions, two results stand out: the particular effectiveness of **2** toward PhC≡CH and either azide and the extremely high reactivity of **6** for $Me_2NCH_2C≡CH$.[21] The catalytic conditions were chosen to allow relative performances to be discriminated, and no attempts were made to optimize conversions by running reactions for a longer time.

Scheme 3. Range of Cu(6-MesDAC) Complexes Employed in Catalysis
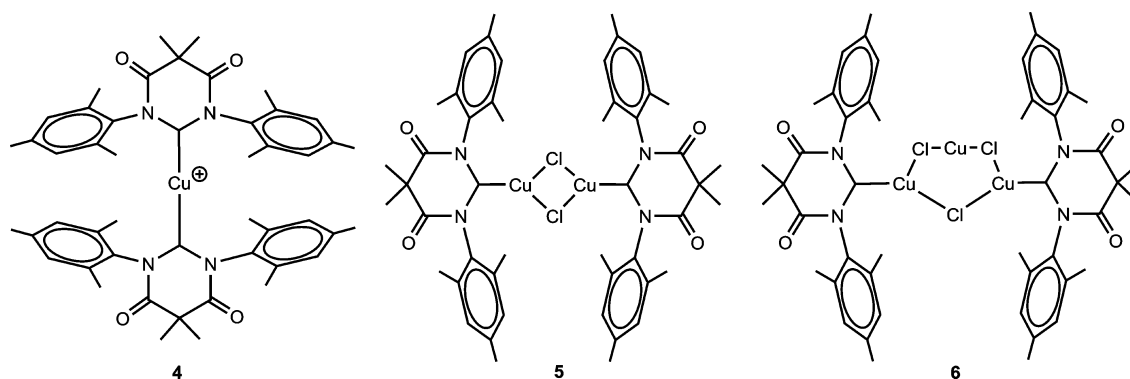
Scheme 4. Substrate Screening (0.50 mmol Azide, 0.51 mmol Alkyne, 0.5 mol % of Cu Precursor, 45 min) with 2 under Neat Conditions (Percent Conversions in Red) and with 6 on 0.5 mL of Water (Percent Conversions in Blue)
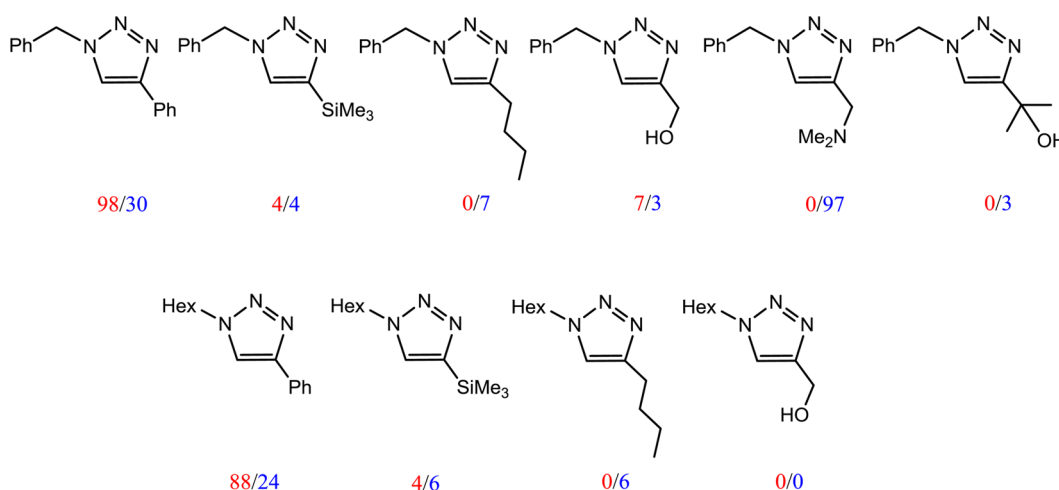
However, better conversions can almost certainly be achieved over longer times; for example, 0.5 mol % of **6** gave a 77% conversion of PhC≡CH and hexyl azide to triazole in 180 min.

SUMMARY AND CONCLUSIONS

We have shown that copper complexes incorporating either ring-expanded N-heterocyclic carbenes or diamidocarbenes are viable catalysts for the "click" reaction of alkynes and benzyl/alkyl azides. Of particular note is the ability of both cationic and neutral complexes containing poorly donating DAC ligands to show enhanced activity when used on water. This raises some interesting questions relating to the mechanisms through which the DAC complexes react. In the case of the cationic species **4**, one carbene is presumed to act as a base toward RC≡CH, although the resultant conjugate acid of 6-MesDAC, which would be formed in such a step, is known to be extremely sensitive to water.[22] In the case of the neutral complexes **5** and **6**, we have established[19] that they most likely stay intact as the dimer and trimer in solution. Given that a dinuclear Cu species is now thought to be catalytically important,[5] could this account for their good performance? A wider point relates to whether the DAC complexes benefit from a stabilizing hydrophilic interaction to the amido carbonyl groups, which might catalysis in the presence of water. Whether metal DAC complexes exhibit useful catalytic properties in other reactions in which water is a desirable or acceptable solvent remains to be established.

EXPERIMENTAL SECTION

All syntheses were carried out using standard Schlenk, high-vacuum, and glovebox techniques using dried and degassed solvents. NMR spectra were recorded at 298 K (unless otherwise stated) on a Bruker Avance 500 or 400 MHz NMR spectrometer and referenced to residual solvent signals for ^{1}H and ^{13}C spectra as follows: CD_2Cl_2 (δ 5.32, 53.8), $CDCl_3$ (δ 7.26, 77.2), and CD_3CN (δ 1.94, 1.3). IR data were recorded on a Nicolet Nexus spectrometer in KBr. Elemental analyses were performed by the Elemental Analysis Service, London Metropolitan University, London, U.K., or Elemental Microanalysis Ltd., Okehampton, Devon, U.K. Literature methods were used to prepare 6-Mes,[6b] 7-Mes,[6b] 6-MesDAC,[9d] [7-o-TolH][BF$_4$],[6c] [(6-MesDAC)(CuCl)]$_2$,[19] and [(6-MesDAC)$_2$(CuCl)$_3$].[19]

[Cu(6-Mes)$_2$][BF$_4$] (1). A benzene solution (15 mL) of 6-Mes (0.180 g, 0.562 mmol) was added to [Cu(MeCN)$_4$][BF$_4$] (0.059 g, 0.187 mmol), and the mixture was stirred for 30 min to afford a colorless precipitate, which was isolated by filtration, washed with benzene (3 × 10 mL) and hexane (2 × 10 mL), and dried under vacuum. Yield: 0.117 g (79%). Single crystals suitable for X-ray diffraction analysis were grown from CH$_2$Cl$_2$/hexane. ^{1}H NMR (CD$_2$Cl$_2$, 500 MHz): δ 6.94 (8H, s, m-ArH), 3.06 (8H, t, $^3J_{HH}$ = 5.8 Hz, NCH$_2$), 2.35 (12H, s, p-ArCH$_3$), 2.04 (4H, m, NCH$_2$CH$_2$), 1.75 (24H, s, o-ArCH$_3$). ^{13}C{^{1}H} NMR (CD$_2$Cl$_2$, 126 MHz): δ 199.3 (s, NCN), 141.9 (s, i-Ar), 138.6 (s, p-Ar), 135.3 (s, o-Ar), 130.2 (s, m-Ar), 44.6 (s, NCH$_2$), 21.2 (s, p-ArCH$_3$), 20.7 (s, NCH$_2$CH$_2$), 18.1 (s, o-ArCH$_3$). Anal. Found (calcd for C$_{44}$H$_{56}$BN$_4$F$_4$Cu): C, 66.65 (66.79); H, 6.99 (7.13); N, 7.17 (7.08).

[Cu(7-o-Tol)$_2$][BF$_4$] (2). A solution of KHMDS (0.538 g, 2.697 mmol) in THF (20 mL) was added to [7-o-TolH][BF$_4$] (0.906 g, 2.473 mmol), and the suspension was stirred for 30 min, yielding a bright green solution and white precipitate. This mixture was transferred by

cannula to $[Cu(MeCN)_4][BF_4]$ (0.390 g, 1.240 mmol), and the suspension was stirred for a further 16 h. The resultant white powder was isolated by filtration and washed with THF (2 × 10 mL). From this powder, the product was extracted into CH_2Cl_2 (3 × 15 mL) and filtered. The volatiles were removed under reduced pressure, and the product was dried in vacuo. Yield: 0.418 g (48%). Single crystals suitable for X-ray diffraction analysis were grown from CH_2Cl_2/hexane. ^1H NMR (CD_2Cl_2, 400 MHz): δ 7.47−6.37 (16H, br, ArH), 3.99−3.31 (8H, br, NCH$_2$), 2.40−1.76 (20H, br, NCH$_2$CH$_2$ + o-ArCH$_3$). ^1H NMR (CD_2Cl_2, 400 MHz, 224 K): δ 7.44−6.31 (16H, m, ArH), 3.91−3.30 (8H, m, NCH$_2$), 2.37−1.69 (20H, m, NCH$_2$CH$_2$ + o-ArCH$_3$). $^{13}C\{^1H\}$ NMR (CD_2Cl_2, 100 MHz, 224 K; C/CH/CH$_2$/CH$_3$ assignments based on $^{13}C\{^1H\}$ PENDANT): δ 207.2 (s, NCN), 206.6 (s, NCN), 147.4, 147.3, 147.1, 147.0, 146.8, 146.6 (all quaternary Ar), 135.0, 134.8, 134.5, 134.4, 134.3 (all quaternary Ar), 131.4, 131.3, 131.1 (all ArH), 128.8, 128.3, 128.2, 128.1, 128.0, 127.7, 127.6, 127.1, 127.0 (all ArH), 53.0, 52.8, 52.7, 52.5 (all NCH$_2$), 25.1, 25.0, 24.7 (all NCH$_2$CH$_2$), 18.9, 18.5, 18.4, 18.3, 18.1, 18.0 (all o-ArCH$_3$). Anal. Found (calcd for $C_{38}H_{44}BN_4F_4Cu$): C, 64.32 (64.54); H, 6.25 (6.27); N, 7.92 (7.92).

[Cu(7-Mes)$_2$][BF$_4$] (3). To a mixture of 7-Mes (0.300 g, 0.897 mmol) and $[Cu(MeCN)_4][BF_4]$ (0.137 g, 0.436 mmol) was added THF (10 mL). The reaction mixture was heated at 50 °C for 14 h, to generate a colorless precipitate. The THF solution was concentrated, and the precipitate was isolated by filtration. It was washed with hexane (3 × 10 mL) and dried in vacuo to afford 0.079 g of **3** (25% yield). Single crystals suitable for X-ray diffraction analysis were grown from CH_2Cl_2/hexane. ^1H NMR (CD_2Cl_2, 500 MHz): δ 6.93 (8H, s, m-ArH), 3.55 (8H, m, NCH$_2$), 2.36 (12H, s, p-ArCH$_3$), 2.00 (8H, m, NCH$_2$CH$_2$), 1.82 (24H, s, o-ArCH$_3$). $^{13}C\{^1H\}$ NMR (CD_2Cl_2, 126 MHz): δ 208.6 (s, NCN), 144.1 (s, i-Ar), 138.3 (s, p-Ar), 135.0 (s, o-Ar), 130.4 (s, m-Ar), 53.6 (s, NCH$_2$), 25.5 (s, NCH$_2$CH$_2$), 21.2 (s, p-ArCH$_3$), 19.0 (s, o-ArCH$_3$). Anal. Found (calcd for $C_{46}H_{60}BN_4F_4Cu$): C, 67.32 (67.43); H, 7.42 (7.38); N, 6.77 (6.84).

[Cu(6-MesDAC)$_2$][BF$_4$] (4). A mixture of 6-MesDAC (0.419 g, 1.113 mmol) and $[Cu(MeCN)_4][BF_4]$ (0.173 g, 0.550 mmol) was stirred in CH_2Cl_2 (20 mL) for 30 min. Volatiles were removed under reduced pressure, yielding a yellow-green solid, which was subsequently washed with THF (2 × 15 mL) and filtered. The resulting green solid was dissolved in the minimum amount of CH_2Cl_2 and precipitated with hexane. The solid was then further washed with hexane (20 mL) and dried under vacuum. Yield: 0.376 g (76%). ^1H NMR (CD_2Cl_2, 500 MHz): δ 7.10 (8H, s, m-ArH), 2.43 (12H, s, p-ArCH$_3$), 1.71 (24H, s, o-ArCH$_3$), 1.61 (12H, s, C(CH$_3$)$_2$). $^{13}C\{^1H\}$ NMR (CD_2Cl_2, 126 MHz): δ 212.7 (s, NCN), 170.8 (s, CO), 141.8 (s, p-Ar), 135.1 (s, o-Ar), 134.6 (s, i-Ar), 130.8 (s, m-Ar), 52.3 (s, C(CH$_3$)$_2$), 24.8 (s, C(CH$_3$)$_2$), 21.3 (s, p-ArCH$_3$), 18.6 (s, o-ArCH$_3$). IR (cm^{-1}): 1768 (ν_{CO}), 1738 (ν_{CO}). Anal. Found (calcd for $C_{48}H_{56}BN_4O_4F_4Cu$): C, 63.80 (63.82); H, 6.24 (6.25); N, 6.13 (6.20).

General Catalytic Procedure. All catalyses were conducted in air, with no purification of reagents. Into a 2 mL sample vial was weighed 0.01 mmol (2.0 mol %) or 0.0025 mmol (0.5 mol %) of copper complex. H_2O (0.50 mL) was added if the reaction was to be conducted on water. Alkyne (0.51 mmol) and then azide (0.50 mmol) were added by microsyringe, and the vial was sealed and secured to an agitator set to 2000 rpm. After the appropriate reaction time (45 or 180 min), the contents of the vial were extracted with CDCl$_3$ (3 × 0.35 mL) and NMR spectra were recorded. Products were assigned by comparison to literature data.[23] Conversions represent the ratio of triazole to unreacted azide, as an average of three separate experiments.

X-ray Crystallography. Single crystals of **1**−**3** were analyzed using a Nonius Kappa CCD diffractometer. Data were collected at 150 K and using Mo Kα radiation throughout. Details of the data collections, solutions, and refinements are given in Table S1 (see the Supporting Information). The structures were solved using SHELXS-97[24] and refined using full-matrix least squares in SHELXL-97.[24]

The asymmetric unit in **1** was seen to comprise half of a cationic copper complex and half of a tetrafluoroborate anion. The copper and boron atoms are coincident with a crystallographic 2-fold rotation axis, which serves to generate the remainder of each moiety. The fluorine atoms in the anion are severely disordered. These were ultimately

modeled as six fractional-occupancy halides after several alternative elaborate models were discarded. The ADPs pertaining to the boron center also suggest some positional disorder, which could not be modeled sensibly. B−F distances in the anion were refined subject to being similar, and ADP restraints were included for the fractional-occupancy fluorine atoms in the final least squares, in order to assist convergence.

The diffraction data for **2** exhibited a sharp falloff in intensity at Bragg angles above 20°. Consequently, the data were truncated to a maximum 2θ value of 50° during the final least-squares refinement. Declining higher-angle intensities reflect, in part, structural disorder which has been modeled. In particular, atoms C2−C5 and C21−C24 exhibit positional disorder in a 65:35 ratio, over two sites. The fluorine atoms in the anion have also been treated as each being evenly split over two sites. This is an approximation, as there is evidence for additional smearing of the electron density in the tetrafluoroborate region of the electron density map. N−C, C−C, B−F, and F···F distances pertaining to fractional-occupancy atoms have been restrained to assist convergence. ADP restraints have also been applied to the disordered atoms in **2**. In addition to one cation and one anion, the asymmetric unit in **3** was seen to contain one molecule of dichloromethane.

Crystallographic data for compounds **1**−**3** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publications CCDC 1000555−1000557. Copies of the data can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K. (fax(+44) 1223 336033, e-mail deposit@ccdc.cam.ac.uk).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Figures giving VT NMR spectra of **2**, CIF files and Table S1 giving crystallographic data for **1**−**3**, and text giving references to the ^1H NMR data of triazoles. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

■ REFERENCES

(1) Fraser, P. K.; Woodward, S. *Tetrahedron Lett.* **2001**, *42*, 2747.

(2) (a) Pérez, P. J.; Díaz-Requejo, M. M. In *N-Heterocyclic Carbenes in Synthesis*; Nolan, S. P., Ed.; Wiley-VCH: Weinheim, Germany, 2006; p 257. (b) Díez-González, S.; Nolan, S. P. *Synlett* **2007**, 2158. (c) Díez-González, S.; Nolan, S. P. *Aldrichim. Acta* **2008**, *41*, 43. (d) Lin, J. C. Y.; Huang, R. T. W.; Lee, C. S.; Bhattacharyya, A.; Hwang, W. S.; Lin, I. J. B. *Chem. Rev.* **2009**, *109*, 3561. (e) Díez-González, S.; Marion, N.; Nolan, S. P. *Chem. Rev.* **2009**, *109*, 3612. (f) Marion, N. In *N-Heterocyclic Carbenes-From Laboratory Curiosities to Efficient Synthetic Tools*; Díez-González, S., Ed.; RSC: Cambridge, U.K., 2011; p 317. (g) Egbert, J. D.; Cazin, C. S. J.; Nolan, S. P. *Catal. Sci. Technol.* **2013**, *3*, 912.

(3) (a) Díez-González, S.; Correa, A.; Cavallo, L.; Nolan, S. P. *Chem. Eur. J.* **2006**, *12*, 7558. (b) Díez-González, S.; Stevens, E. D.; Nolan, S. P. *Chem. Commun.* **2008**, 4747. (c) Díez-González, S.; Nolan, S. P. *Angew. Chem., Int. Ed.* **2008**, *47*, 8881. (d) Teyssot, M.-L.; Chevry, A.; Traïkia, M.; El-Ghozzi, M.; Avignant, D.; Gautier, A. *Chem. Eur. J.* **2009**, *15*, 6322. (e) Teyssot, M.-L.; Nauton, L.; Canet, J.-L.; Cisnetti, F.; Chevry, A.; Gautier, A. *Eur. J. Org. Chem.* **2010**, 3507. (f) Díez-González, S.; Escudero-Adan, E. C.; Benet-Buchholz, J.; Stevens, E. D.; Slawin, A. M. Z.; Nolan, S. P. *Dalton Trans.* **2010**, *39*, 7595. (g) Hohloch, S.; Su, C.-Y.; Sarkar, B. *Eur. J. Inorg. Chem.* **2011**, 3067. (h) Nakamura, T.; Terashima, T.; Ogata, K.; Fukuzawa, S. *Org. Lett.* **2011**, *13*, 620. (i) Lazreg, F.; Slawin, A. M. Z.; Cazin, C. S. J. *Organometallics* **2012**, *31*, 7969.

(j) Hohloch, S.; Scheiffele, D.; Sarkar, B. *Eur. J. Inorg. Chem.* **2013**, 3956. (k) Liu, B.; Chen, C.; Zhang, Y.; Liu, X.; Chen, W. *Organometallics* **2013**, *32*, 5451. (l) Guo, S.; Lim, M. H.; Huynh, H. V. *Organometallics* **2013**, *32*, 7225. (m) Han, X.; Weng, Z.; Young, D. J.; Jin, G.-X.; Hor, T. S. A. *Dalton Trans.* **2014**, *43*, 1305.

(4) (a) Kolb, H. C.; Finn, M. G.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2001**, *40*, 2004. (b) Tornøe, C. W.; Christensen, C.; Meldal, M. *J. Org. Chem.* **2002**, *67*, 3057. (c) Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2002**, *41*, 2596. (d) Bock, V. D.; Hiemstra, H.; van Maarseveen, J. H. *Eur. J. Org. Chem.* **2006**, 51. (e) Meldal, M.; Tornøe, C. W. *Chem. Rev.* **2008**, *108*, 2952. (f) Hein, J. E.; Fokin, V. V. *Chem. Soc. Rev.* **2010**, *39*, 1302. (g) Díez-González, S. *Catal. Sci. Technol.* **2011**, *1*, 166.

(5) Worrell, B. T.; Malik, J. A.; Folkin, V. V. *Science* **2013**, *340*, 457.

(6) For a recent review of RE-NHCs, see: (a) Li, J.; Shen, W. X.; Li, X. R. *Curr. Org. Chem.* **2012**, *16*, 2879. For representative examples in the primary literature, see: (b) Iglesias, M.; Beetstra, D. J.; Knight, J. C.; Ooi, L. L.; Stasch, A.; Coles, S.; Male, L.; Hursthouse, M. B.; Cavell, K. J.; Dervisi, A.; Fallis, I. A. *Organometallics* **2008**, *27*, 3279. (c) Iglesias, M.; Beetstra, D.; Kariuki, B.; Cavell, K. J.; Dervisi, A.; Fallis, I. A. *Eur. J. Inorg. Chem.* **2009**, 1913. (d) Kolychev, E. L.; Portnyagin, I. A.; Shuntikov, V. V.; Khrustalev, V. N.; Nechaev, M. S. *J. Organomet. Chem.* **2009**, *694*, 2454. (e) Lu, W. Y.; Cavell, K. J.; Wixey, J. S.; Kariuki, B. *Organometallics* **2011**, *30*, 5649.

(7) (a) Tang, C. Y.; Smith, W.; Vidovic, D.; Thompson, A. L.; Chaplin, A. B.; Aldridge, S. *Organometallics* **2009**, *28*, 3059. (b) Davies, C. J. E.; Page, M. J.; Ellul, C. E.; Mahon, M. F.; Whittlesey, M. K. *Chem. Commun.* **2010**, *46*, 5151. (c) Phillips, N.; Rowles, J.; Kelly, M. J.; Riddlestone, I.; Rees, N. H.; Dervisi, A.; Fallis, I. A.; Aldridge, S. *Organometallics* **2012**, *31*, 8075. (d) Poulten, R. C.; Page, M. J.; Algarra, A. G.; Le Roy, J. J.; López, I.; Carter, E.; Llobet, A.; Macgregor, S. A.; Mahon, M. F.; Murphy, D. M.; Murugesu, M.; Whittlesey, M. K. *J. Am. Chem. Soc.* **2013**, *135*, 13640.

(8) Higgins, E. M.; Sherwood, J. A.; Lindsay, A. G.; Armstrong, J.; Massey, R. S.; Alder, R. W.; O'Donoghue, A. C. *Chem. Commun.* **2011**, *47*, 1559.

(9) (a) Hudnall, T. W.; Bielawski, C. W. *J. Am. Chem. Soc.* **2009**, *131*, 16039. (b) César, V.; Lugan, N.; Lavigne, G. *Eur. J. Inorg. Chem.* **2010**, 361. (c) Hudnall, T. W.; Tennyson, A. G.; Bielawski, C. W. *Organometallics* **2010**, *29*, 4569. (d) Hudnall, T. W.; Moerdyk, J. P.; Bielawski, C. W. *Chem. Commun.* **2010**, *46*, 4288. (e) Blake, G. A.; Moerdyk, J. P.; Bielawski, C. W. *Organometallics* **2012**, *31*, 3373. (f) Braun, M.; Frank, W.; Ganter, C. *Organometallics* **2012**, *31*, 1927.

(10) RE-NHCs: (a) Mayr, M.; Wurst, K.; Ongania, K.-H.; Buchmeiser, M. R. *Chem. Eur. J.* **2004**, *10*, 1256. (b) Imlinger, N.; Mayr, M.; Wang, D.; Wurst, K.; Buchmeiser, M. R. *Adv. Synth. Catal.* **2004**, *346*, 1836. (c) Bortenschlager, M.; Mayr, M.; Nuyken, O.; Buchmeiser, M. R. *J. Mol. Catal. A* **2005**, *233*, 67. (d) Imlinger, N.; Wurst, K.; Buchmeiser, M. R. *J. Organomet. Chem.* **2005**, *690*, 4433. (e) Rogers, M. M.; Wendlandt, J. E.; Guzei, I. A.; Stahl, S. S. *Org. Lett.* **2006**, *8*, 2257. (f) Schneider, S. K.; Herrmann, W. A.; Herdtweck, E. *J. Mol. Catal. A* **2006**, *245*, 248. (g) Özdemir, I.; Gürbüz, N.; Gök, Y.; B, Ç. *Heteroat. Chem.* **2008**, *19*, 82. (h) Scarborough, C. C.; Bergant, A.; Sazama, G. T.; Guzei, I. A.; Spencer, L. C.; Stahl, S. S. *Tetrahedron* **2009**, *65*, 5084. (i) Binobaid, A.; Iglesias, M.; Beetstra, D.; Kariuki, B.; Dervisi, A.; Fallis, I.; Cavell, K. J. *Dalton Trans.* **2009**, 7099. (j) Binobaid, A.; Iglesias, M.; Beetstra, D.; Dervisi, A.; Fallis, I.; Cavell, K. J. *Eur. J. Inorg. Chem.* **2010**, 5426. (k) Park, J. K.; Lackey, H. H.; Rexford, M. D.; Kovnir, K.; Shatruk, M.; McQuade, D. T. *Org. Lett.* **2010**, *12*, 5008. (l) Park, J. K.; Lackey, H. H.; Ondrusek, B. A.; McQuade, D. T. *J. Am. Chem. Soc.* **2011**, *133*, 2410. (m) Dunsford, J. J.; Cavell, K. J.; Kariuki, B. *J. Organomet. Chem.* **2011**, *696*, 188. (n) Dunsford, J. J.; Cavell, K. J. *Dalton Trans.* **2011**, *40*, 9131. (o) Spallek, M. J.; Riedel, D.; Rominger, F.; Hashmi, A. S. K.; Trapp, O. *Organometallics* **2012**, *31*, 1127. (p) Newman, P. D.; Cavell, K. J.; Kariuki, B. *Dalton Trans.* **2012**, *41*, 12395. (q) Park, J. K.; McQuade, D. T. *Synthesis* **2012**, *44*, 1485. (r) Dunsford, J. J.; Cavell, K. J.; Kariuki, B. *Organometallics* **2012**, *31*, 4118. (s) Siemeling, U.; Färber, C.; Bruhn, C.; Fürmeier, S.; Schulz, T.; Kurlemann, M.; Tripp, S. *Eur. J. Inorg. Chem.* **2012**, 1413. (t) Dunsford, J. J.; Tromp, D. S.; Cavell, K. J.; Elsevier, C. J.;

Kariuki, B. *Dalton Trans.* **2013**, *42*, 7318. (u) Hauwert, P.; Dunsford, J. J.; Tromp, D. S.; Weigand, J. J.; Lutz, M.; Cavell, K. J.; Elsevier, C. J. *Organometallics* **2013**, *32*, 131. (v) Kolychev, E. L.; Asachenko, A. F.; Dzhevakov, P. B.; Bush, A. A.; Shuntikov, V. V.; Khrustalev, V. N.; Nechaev, M. S. *Dalton Trans.* **2013**, *42*, 6859. (w) Page, M. J.; Lu, W. Y.; Poulten, R. C.; Carter, E.; Algarra, A. G.; Kariuki, B. M.; Macgregor, S. A.; Mahon, M. F.; Cavell, K. J.; Murphy, D. M.; Whittlesey, M. K. *Chem. Eur. J.* **2013**, *19*, 2158. (x) Morozov, O. S.; Lunchev, A. V.; Bush, A. S.; Tukov, A. A.; Asachenko, A. F.; Khrustalev, V. N.; Zalesskiy, S. S.; Ananikov, V. P.; Nechaev, M. S. *Chem. Eur. J.* **2014**, *20*, 6162.

(11) DACs: (a) Hudnall, T. W.; Tennyson, A. G.; Bielawski, C. W. *Organometallics* **2010**, *29*, 4569. (b) Moerdyk, J. P.; Bielawski, C. W. *Organometallics* **2011**, *30*, 2278. (c) Arumugam, K.; Varghese, B.; Brantley, J. N.; Konda, S. S. M.; Lynch, V. M.; Bielawsi, C. W. *Eur. J. Org. Chem.* **2014**, 493. For studies with anionic amidocarbenes: (d) César, V.; Lugan, N.; Lavigne, G. *Chem. Eur. J.* **2010**, *16*, 11432. (e) César, V.; Barthes, C.; Farré, Y. C.; Cuisiat, S. V.; Vacher, B. Y.; Brousses, R.; Lugan, N.; Lavigne, G. *Dalton Trans.* **2013**, *42*, 7373. (f) César, V.; Castro, L. C. M.; Dombray, T.; Sortais, J.-B.; Darcel, C.; Labat, S.; Miqueu, K.; Sotiropoulos, J.-M.; Brousses, R.; Lugan, N.; Lavigne, G. *Organometallics* **2013**, *32*, 4643.

(12) (a) Bourissou, D.; Guerret, O.; Gabbaï, F. P.; Bertrand, G. *Chem. Rev.* **2000**, *100*, 39. (b) Herrmann, W. A.; Weskamp, T.; Böhm, V. P. W. *Adv. Organomet. Chem.* **2001**, *48*, 1. (c) Herrmann, W. A. *Angew. Chem., Int. Ed.* **2002**, *41*, 1290. (d) *N-Heterocyclic Carbenes in Synthesis*; Nolan, S. P., Ed.; Wiley-VCH: Weinheim, Germany, 2006. (e) *N-Heterocyclic Carbenes in Transition Metal Catalysis*; Glorius, F., Ed.; Springer-Verlag: Heidelberg, Germany, 2007. (f) Kantchev, E. A. B.; O'Brien, C. J.; Organ, M. G. *Angew. Chem., Int. Ed.* **2007**, *46*, 2768. (g) Hahn, F. E.; Jahnke, M. C. *Angew. Chem., Int. Ed.* **2008**, *47*, 3122. (h) Poyatos, M.; Mata, J. A.; Peris, E. *Chem. Rev.* **2009**, *109*, 3677. (i) Dröge, T.; Glorius, F. *Angew. Chem., Int. Ed.* **2010**, *49*, 6940. (j) *N-Heterocyclic Carbenes in Transition Metal Catalysis and Organocatalysis*; Cazin, C. S. J., Ed.; Springer-Verlag: Heidelberg, Germany, 2011. (k) *N-Heterocyclic Carbenes-From Laboratory Curiosities to Efficient Synthetic Tools*; Díez-González, S., Ed.; RSC: Cambridge, U.K., 2011.

(13) Bantu, B.; Wang, D. R.; Wurst, K.; Buchmeiser, M. R. *Tetrahedron* **2005**, *61*, 12145.

(14) The Samb*V*ca program was used to determine %V_{bur} values for each of the carbene ligands in **1**−**4**: **1**, 41.2, 41.2; **2**, 40.8, 41.4; **3**, 41.9, 42.4; **4**, 41.8, 41.6. Poater, A.; Cosenza, B.; Correa, A.; Giudice, S.; Ragone, F.; Scarano, V.; Cavallo, L. *Eur. J. Inorg. Chem.* **2009**, 1759.

(15) Díez-González, S.; Stevens, E. D.; Scott, N. M.; Petersen, J. L.; Nolan, S. P. *Chem. Eur. J.* **2008**, *14*, 158.

(16) The aforementioned widening of the NCN angles in RE-NHC complexes is also apparent in **1** (117.29(17)°), **2** (117.7(5)°, 118.3(4)°) and **3** (118.47(17)°, 118.48(17)°) in comparison to the IMes (104.33(15)°) and SIMes (109.2(4)°) complexes in ref 15.

(17) Tapu, D.; Dixon, D. A.; Roe, C. *Chem. Rev.* **2009**, *109*, 3385.

(18) By way of contrast, Nolan has reported in ref 3c that $[Cu(ICy)_2][PF_6]$ affords 99% conversion to the same triazole (0.5 mol % loading) in 5 min under neat conditions.

(19) Collins, L. R.; Lowe, J. P.; Mahon, M. F.; Poulten, R. C.; Whittlesey, M. K. *Inorg. Chem.* **2014**, *53*, 2699.

(20) This activity compares favorably to the two most active five-membered NHC systems under in-water conditions, $[Cu(ICy)_2][PF_6]$ (99% conversion in 1.5 h) and $[Cu(IAd)_2][BF_4]$ (100% conversion in 3 h). See ref 3c.

(21) At 0.1 mol % loading, 100% conversion was achieved in 45 min.

(22) $[6\text{-MesDACH}]^+$ has been shown to be too electrophilic to occur as the chloride salt, $[6\text{-MesDACH}]Cl$, instead existing as 6-MesDAC(H)Cl.[9b] This reacts instantly with water to form 6-MesDAC(H)OH.[9d]

(23) See the the Supporting Information for references to NMR data of triazoles.

(24) Sheldrick, G. M. *Acta Crystallogr., Sect. A* **1990**, 467−473, A46. Sheldrick, G. M. *SHELXL-97, a computer program for crystal structure refinement*; University of Göttingen, Göttingen, Germany, 1997.