Catalytic C–H Functionalization

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Catalytic C–H Amination with Unactivated Amines through Copper(II) Amides[**]

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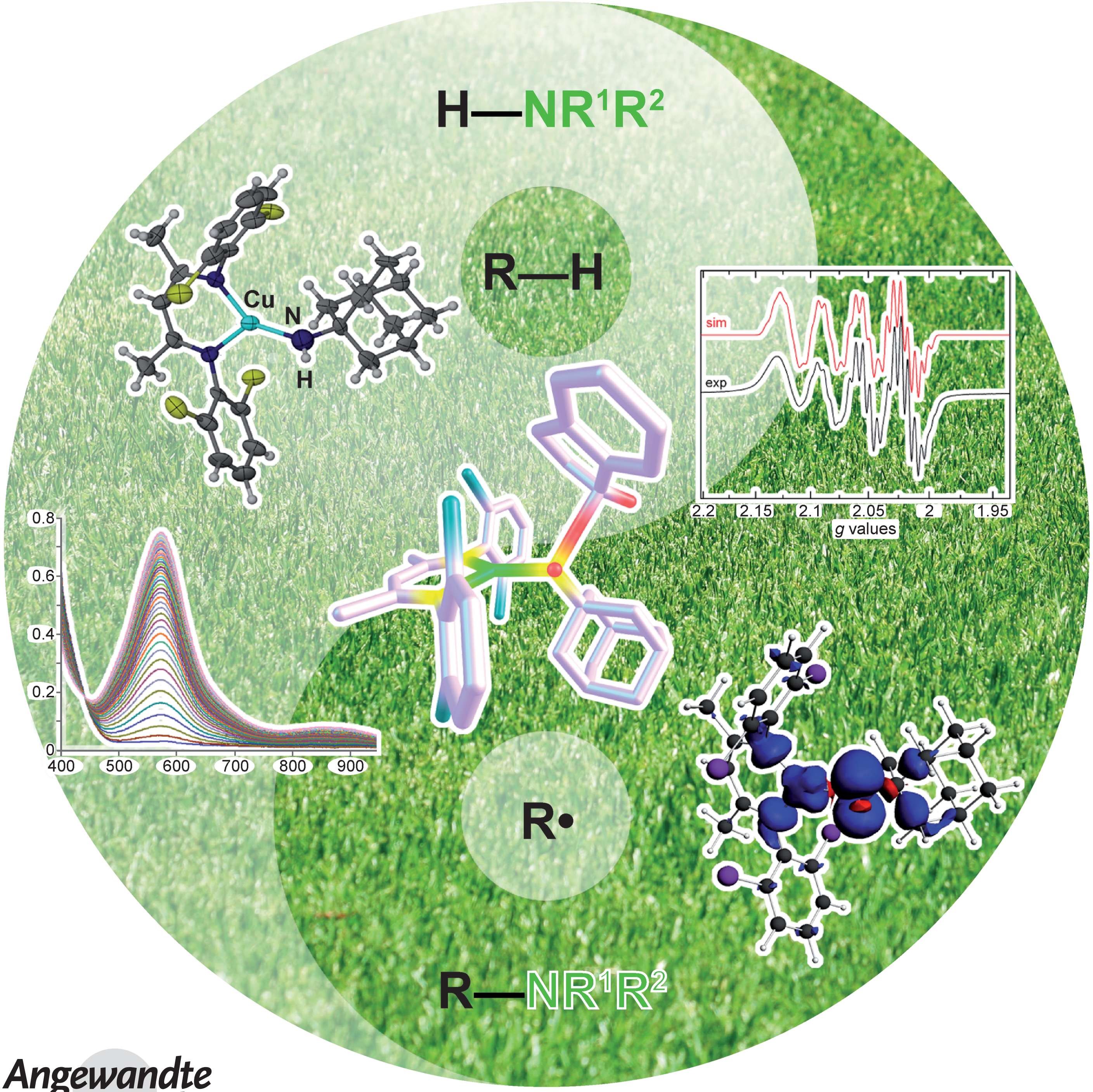

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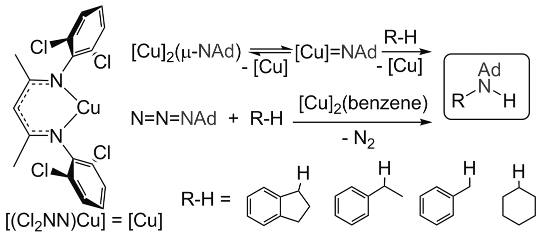
Catalytic C–H amination is an attractive strategy to prepare C–N bonds without the need for a pre-functionalized site.[1–3] This approach offers substantial opportunities to streamline chemical syntheses by decreasing the number of functional-group manipulations such as "hydroxyl to amine".[4] An appealing feature of this and related catalytic C–H functionalization reactions is that protection steps may not be required for these transformations—the relative inertness of the C–H bond insulates it from many traditional functional group modifications.[3,5] The ability to directly effect the C–H to C–N transformation without the need to isolate, purify, and transform oxidized precursors promises reduced cost, energy consumption, and environmental impact.

There are a growing number of C–H amination catalysts that allow for sp^3-C–N bond formation compatible with multistep syntheses of complex molecules.[1,3,5,6] While typically based on expensive metals like Rh[7] and Ru,[8] catalysts employing base metals such as Fe,[9] Co,[10] and Cu[11,12] have been successfully demonstrated. Existing C–H amination methods typically employ nitrogen sources bearing powerful electron-withdrawing groups such as H_2NSO_2R or $H_2NC(O)OR$ along with oxidants such as $PhI(OAc)_2$ capable of generating sulfonylnitrene ($N\text{-}SO_2R$) or carbamoylnitrene (N-C(O)OR) intermediates in the presence of a transition metal catalyst; in some cases simple organic amides $H_2NC(O)R$ may be employed.[12] Complementary approaches inlcude Pd-based allylic C–H amination with HNTs(COOMe) (Ts = tosyl)[13] or Cu-based benzylic and allylic amination with $HNMe(SO_2Ph)$.[14] In most circumstances use of these methods in complex molecule synthesis requires N-based deprotection of the activating group followed by refunctionalization, thus detracting from the atom-economic promise of C–H amination. A recent report of *N*-alkylcarbazole formation by Pd-catalyzed intramolecular C–H amination of biphenylamines is a notable exception.[15]

We recently described the isolation of the β-diketiminato dicopper nitrene $[\{(Cl_2NN)Cu\}_2(\mu\text{-}NAd)]$ from reaction of $[\{(Cl_2NN)Cu\}_2(benzene)]$ with the organoazide N_3Ad (Scheme 1; Ad = 1-adamantyl).[16] This species reacts readily with hydrocarbons to formally insert the nitrene moiety NAd into sp^3-hybridized C–H bonds under both stoichiometric and catalytic conditions. We were eager to examine the related copper(II) amide [(Cl$_2$NN)Cu-NHAd] as a potential intermediate formed by H-atom abstraction (HAA) of a C–H bond by a terminal copper–nitrene intermediate [(Cl$_2$NN)Cu=NR].[16,17] For instance, the β-diketiminato nickel nitrene [(Me$_3$NN)Ni=NAd] reacts with 1,4-cyclohexadiene by HAA to give [(Me$_3$NN)Ni-NHAd].[18]



Scheme 1. Nitrene-based stoichiometric and catalytic C–H amination.

Herein we describe synthetic studies that target a copper(II) amide intermediate in C–H amination[19,20] which reveal a bifunctional role for [(Cl$_2$NN)Cu-NHAd] in stoichiometric C–H functionalization and result in a new system for catalytic intermolecular C–H amination with simple, unactivated alkylamines.[21] Since N-based activating groups are not required, the method promises broader amine substrate scope than found in known C–H amination systems.

Addition of Li(Cl$_2$NN) to anhydrous $CuCl_2$ gives the dinuclear β-diketiminato copper(II) chloride $[\{(Cl_2NN)Cu\}_2(\mu\text{-}Cl)_2]$ (**1**) in 79 % yield as green crystals.[22] Reaction of **1** with LiNHAd in Et_2O at −35 °C immediately produces a deep purple solution from which the corresponding copper(II) amide [(Cl$_2$NN)Cu-NHAd] (**2**) may be isolated as thermally sensitive purple crystals from pentane in 50–70 % yield (Scheme 2).

The X-ray structure of **2** exhibits a three-coordinate copper center with a short Cu–N$_{amido}$ bond of 1.839(9) Å (Scheme 2 and Figure S33 in the Supporting Information). The Cu–N$_{amido}$ bond is similar to that in the recently reported β-diketiminato copper(II) amide [(Me$_2$NN)Cu-NPh$_2$] (1.841(6) Å)[19] and shorter than in the three-coordinate κ^2-[{Ph$_2$B(CH$_2$P*t*Bu)$_2$}Cu-N(*p*-tolyl)$_2$] (Cu–N 1.906(2) Å)[23] which was described as a copper(I)–aminyl radical complex.[24] The X-ray structure of **2** is distinct from that of the simple amine adduct [(Cl$_2$NN)Cu(NH$_2$Ad)] (Cu–N$_{amine}$ 1.970(2) Å; Cu-N-C 117.69(11)°; Figure S34).

Copper amide **2** is reactive towards benzylic C–H bonds at room temperature (Scheme 2). Reaction of 2 equivalents of **2** with ethylbenzene or indane (100 equiv in heptane) at room temperature for 24 h results in formation of PhCH-

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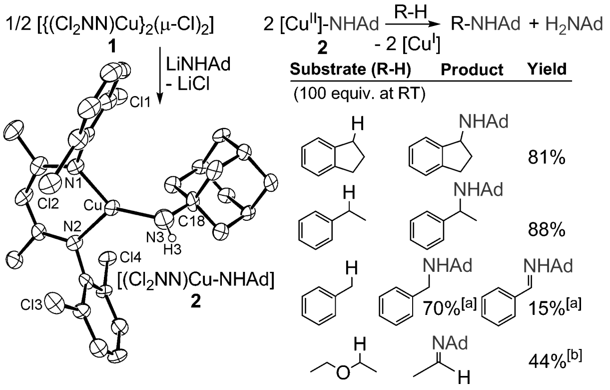
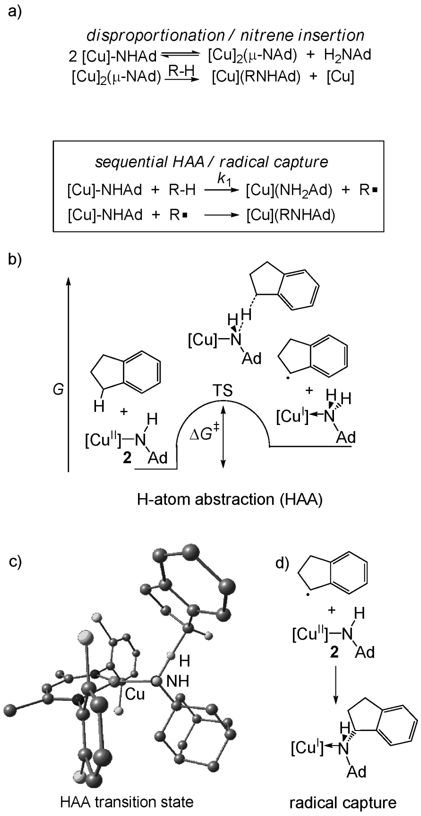


Scheme 2. Synthesis, structure, and reactivity of **2**.[a] 500 equiv substrate at 60 °C.[b] 1000 equiv substrate at RT.



Scheme 3. Mechanistic steps considered by experiment and theory in the stoichiometric C–H amination of indane by **2**. a) Two mechanisms considered. b) Pathway for HAA. c) Structure of rate-determining HAA transition state by theory. d) Combination of indanyl radical with **2**.

(NHAd)Me or (1-indanyl)NHAd in 87 % and 81 % yield, respectively, along with 1 equivalent of H_2NAd. The stronger primary benzylic C–H bond of toluene requires heating at 60 °C to provide the corresponding amine $PhCH_2NHAd$ along with imine PhCH=NAd, its subsequent oxidation product. The solvent diethyl ether is also aminated at room temperature to ultimately provide the imine AdN=CHMe in 41 % yield upon loss of EtOH from EtOCH(NHAd)Me.

Based on the stoichiometry of this C–H amination reaction, we considered two mechanistic pathways (Scheme 3 a). First, the copper nitrene $[\{(Cl_2NN)Cu\}_2(\mu\text{-}NAd)]$, known to participate in C–H amination,[16] could be formed by disproportionation of 2 equivalents of **2**. Alternatively, the copper amide **2** could effect C–H amination in a stepwise fashion. The first molecule of **2** abstracts an H-atom from the substrate R–H to give copper(I)–amine adduct $[(Cl_2NN)Cu(NH_2Ad)]$ and an organic radical R$^{\bullet}$. In a rapid subsequent step, another equivalent of **2** captures the radical R$^{\bullet}$ to form the product amine RNHAd coordinated to copper.

Kinetic analysis following the loss of **2** at 25 °C by UV/Vis spectroscopy (λ_{max}(heptane) = 572 nm (2350 $M^{-1}cm^{-1}$)) with excess ethylbenzene or indane (500–2000 equiv) in heptane indicates that the rate law follows: rate = k_1[**2**][RH]. Thus, kinetic data support a HAA/radical capture pathway since disproportionation would require a second-order dependence on the reacting **2**. Eyring analysis of indane amination (1000 equiv in heptane) over the temperature range 20–50 °C gives activation parameters $\Delta H^{\ddagger} = 11.4(4)$ kcal mol^{-1} and $\Delta S^{\ddagger} = -38.7(14)$ e.u. with $\Delta G^{\ddagger} = 22.9(8)$ kcal mol^{-1} at 298 K. These activation parameters are similar to those in the tosyl-amidation of ethylbenzene by the nitrene species $[(porph)Ru(=NTs)_2]$ ($\Delta H^{\ddagger} = 8.9(2)$ kcal mol^{-1} and $\Delta S^{\ddagger} = -39.8(20)$ e.u.) thought to proceed by initial HAA followed by radical capture.[25] We observe a large primary kinetic isotope effect ($k_H/k_D = 70(9)$) at room temperature in the amination of ethylbenzene, which suggests a tunneling pathway.[26]

The transition state (TS) in the reaction of **2** with indane was computed using hybrid ONIOM(BP86/6-311+G(d):UFF) methods (Scheme 3 b–d). Notably, the calculated activation parameters are similar to those experimentally obtained and result from a TS with a nearly linear $C_{indane}\cdots H\cdots N_{amide}$ linkage: $\Delta H^{\ddagger} = 11.3$ kcal mol^{-1}, $\Delta S^{\ddagger} = -46.8$ e.u. with $\Delta G^{\ddagger} = 25.2$ kcal mol^{-1} (Scheme 3 b,c). The TS may be viewed as late with a significant degree of N–H bond formation (N–H 1.284; C–H 1.417 Å). HAA to form $[(Cl_2NN)Cu(NH_2Ad)]$ and the indanyl radical is energetically uphill: $\Delta H = 15.1$ kcal mol^{-1}, $\Delta S = +5.2$ e.u., $\Delta G = +13.6$ kcal mol^{-1}. Addition of the indanyl radical to **2**, however, is considerably downhill to give [(Cl$_2$NN)Cu{NH(indanyl)Ad}]: $\Delta G = -17.2$ kcal mol^{-1}, $\Delta H = -35.1$ kcal mol^{-1}, $\Delta S = -60.0$ e.u. (Scheme 3 d).

To better understand the N-centered HAA and radical capture reactivity of **2** we examined its electronic structure using a combination of EPR spectroscopy and DFT calculations. Simulation of the X-band EPR spectra of **2** (Figure 1 a and b) reveals a nearly axial environment at the Cu center with $g_1 = 2.133(5)$, $g_2 = 2.036(5)$, and $g_3 = 2.031(5)$. These g values, along with the hyperfine coupling constant $A_1(Cu) = 365(10)$ MHz, are consistent with a three-coordinate copper(II) center.[19,27] The superhyperfine interactions are best simulated using a 2N (β-diketiminate), 1N (amide), 1H (amide N–H) model in which there is considerable anisotropy in the Cu–N(amido) interaction (Figures S28 and S29). Consistent with the highly directional nature of the 2-center/3-electron Cu–N$_{amide}$ π interaction,[19] which places significant unpaired electron density at the N$_{amide}$ atom (0.49 e$^-$) (Figures 1 c,d, and S23–S25), calculations indicate

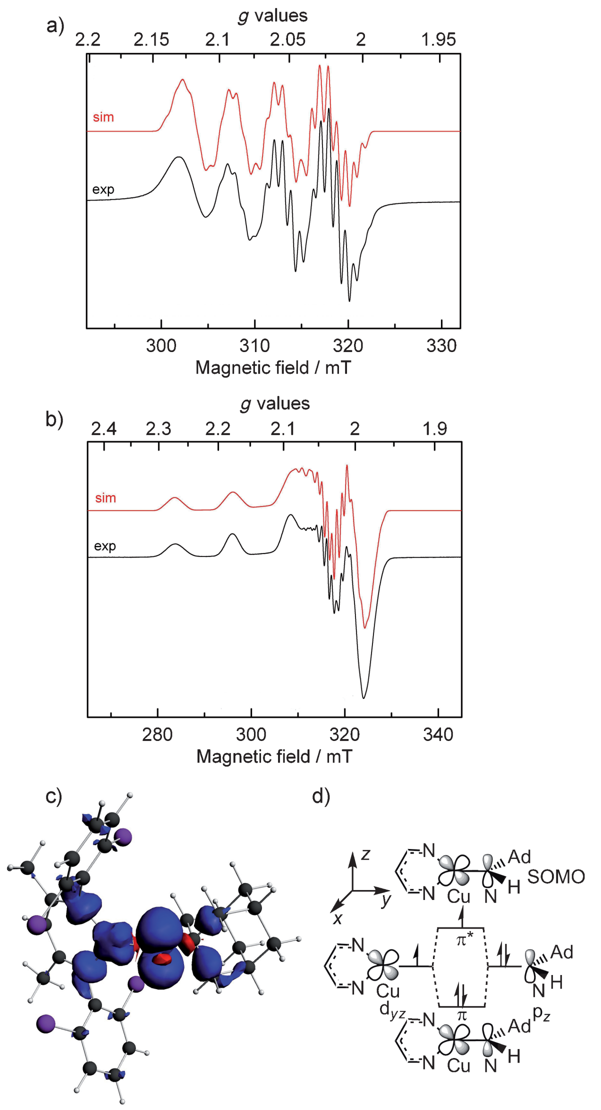
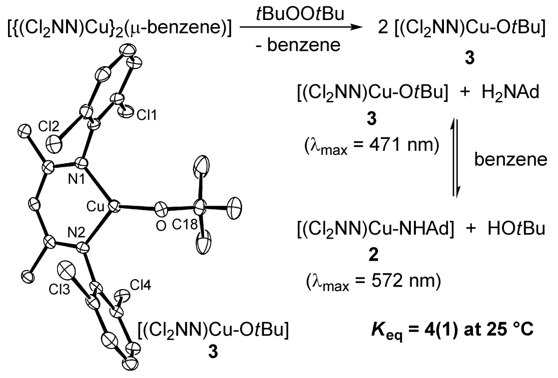


Figure 1. Experimental and theoretical determination of the electronic structure of **2**. a,b) X-band EPR spectra of **2** a) at room temperature in toluene and b) at 51 K in frozen toluene. c) Spin density plot for **2** (blue: net spin *a*; red: net spin *b*; 0.001 isospin value). d) Cu–N_{amide} π interactions in **2**.

that interaction of the unpaired electron with the amido N atom is much more anisotropic (A_1(N) = 7, A_2(N) = 5, A_3(N) = 61 MHz) than with the β-diketiminate N donors (A_{1-3}(N) = 19–28 MHz). TD-DFT calculations suggest that the strong optical band observed at $\lambda = 572$ nm for **2** originates from the Cu–N_{amide} $\pi \rightarrow \pi^*$ transition (Figures 1d and S24).

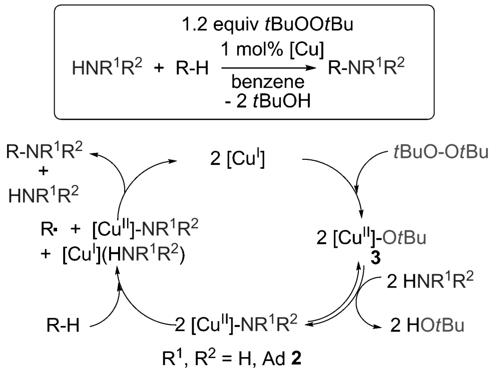
The key copper(II) amide intermediate **2** may be generated under conditions that allow for catalysis. Inspired by the alkoxide–amide exchange that takes place in some variants of the Buchwald–Hartwig amination[28] between [Pd]–O*t*Bu intermediates and amines HNR^1R^2 to form reactive [Pd]–NR^1R^2 species,[29] we were eager to explore an analogous [Cu]–O*t*Bu to [Cu]–NHAd transformation in our system. The reaction of $[\{(Cl_2NN)Cu\}_2(\mu\text{-benzene})]$ with *t*BuOO*t*Bu cleanly provides $[(Cl_2NN)Cu\text{-O}t\text{Bu}]$ (**3**) in greater than 90% spectroscopic yield (λ_{max}(benzene) = 471 nm (2950 $M^{-1}cm^{-1}$)) upon reaction in benzene (Scheme 4). It may also be isolated in 53% yield as thermally sensitive red crystals from pentane. X-ray structure analysis of **3** shows a short Cu–O bond (1.785(2) Å) along with shortened Cu–N distances (1.884(2), 1.889(2) Å) relative to those in **1** or **2** (Scheme 4). Frozen glass EPR spectra of **3** indicate a roughly axial environment ($g_1 = 2.243(5)$, $g_2 = 2.059(5)$, $g_3 = 2.042(5)$) with A_1(Cu) = 353(10) MHz similar to that found in amide **2** (Figure S31).



Scheme 4. Synthesis, structure, and reactivity of **3**.

Dissolution of **3** in ether followed by addition of excess H_2NAd results in instantaneous loss of the UV/Vis band of **3** centered at $\lambda = 471$ nm concomitant with growth of a band at $\lambda = 572$ nm corresponding to the copper(II) amide **2** (Scheme 5). Quantitative analysis in benzene at 25 °C reveals an equilibrium constant $K_{eq} = 4(1)$ favoring amido species **2**. Thus, a rapid acid–base reaction ensues between $[(Cl_2NN)Cu\text{-O}t\text{Bu}]$ (**3**) and H_2NAd to generate $[(Cl_2NN)Cu\text{-NHAd}]$ (**2**).

These individual steps may be tied together into a novel catalytic cycle for C–H amination (Scheme 5). A mixture of 1 equivalent of H_2NAd, 1 equivalent of *t*BuOO*t*Bu, and 10 equivalents of indane in heptane in the presence of 10 mol% $[\{(Cl_2NN)Cu\}_2(\mu\text{-benzene})]$ gives a 78% yield of (1-indanyl)NHAd after standing at room temperature for 5 days. Increasing the reaction temperature to 90 °C allows for increased yields with decreased catalyst loadings (1 mol%



Scheme 5. Catalytic cycle for C–H amination of unactivated amines HNR^1R^2 by copper(II) amides $[Cu^{II}]$–NR^1R^2.

mononuclear [Cu]) and reaction times (24–72 h). Employing either 10 or 1 equivalents of indane in benzene with 1.2 equivalents of *t*BuOO*t*Bu and 1 mol % [Cu] provides the product amine in 83 % and 46 % yields, respectively. Importantly, in situ UV/Vis analysis demonstrates the presence of copper amide **2** in catalytic C–H amination reaction mixtures (10 equiv indane in benzene; 30, 50 and 75 °C) which builds to a maximum mole fraction of approximately 0.8 relative to the initial amount of [Cu] employed (Figures 2 and S21, S22).

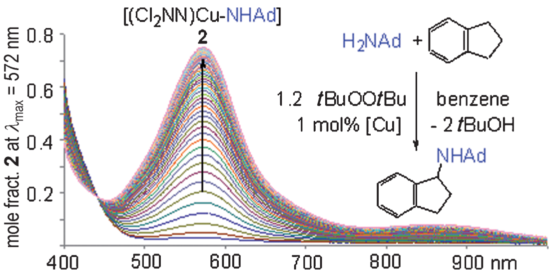
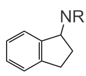
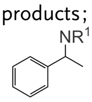
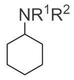
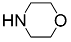


Figure 2. In situ UV/Vis analysis of catalytic amination of indane (10 equiv) with H_2NAd in benzene at 30 °C with 1 mol % [$(Cl_2NN)Cu$] showing growth of [$(Cl_2NN)Cu$-NHAd] (**2**) signal at $\lambda_{max} = 572$ nm (scan interval 5 min, total time 250 min).

Consistent with stoichiometric studies that reveal complete consumption of [$(Cl_2NN)Cu$-O*t*Bu] (**3**) in the presence of excess H_2NAd, alkoxide **3** is not observed in catalytic reactions. Rather, the $\lambda_{max} = 572$ nm band of **2** grows in from the initial copper(I) species present (likely [$(Cl_2NN)Cu(NH_2Ad)$]) with isosbestic behavior.

A brief survey of other unactivated primary (H_2NCy and $H_2NCH_2CH_2Ph$) and secondary (morpholine) alkylamines in this catalytic protocol with indane and ethylbenzene results in the expected secondary or tertiary amines in good to excellent yields (Table 1). The use of morpholine is noteworthy as secondary amines are not amenable to nitrene-based C–H amination protocols. This method also allows for the C–H amination of strong, unactivated sp^3-hybridized C–H bonds with primary amines. Using cyclohexane (C–H bond dissociation energy (BDE) ca. 97 kcal mol^{-1})[30] as a solvent, yields of 91–61 % are obtained. Attempted amination of cyclohexane with morpholine results in oxidation of morpholine to the corresponding heterocyclic imine[31] as the major product.

Table 1: Catalytic C–H amination of unactivated primary and secondary amines.[a]

Amine substrates↓	Amination products; yields [%] 		
H_2NAd	98 (83)	93 (65)	91[c]
H_2NCy	97 (65)	73 (52)	70[c]
$H_2NCH_2CH_2Ph$	74 (59)	81 (49)	61[c]
	79 (40)[b]	53 (40)[b]	2[c,d]

[a] Catalysis conditions employ 0.5 mol % [$\{(Cl_2NN)Cu\}_2$(benzene)] at 90 °C for 24 h in neat substrate; yields in parentheses correspond to 10 equiv substrate in benzene solvent. Secondary amine products isolated as HCl salts, tertiary amine products isolated as pure substances. [b] 72 h, yield by ^1H NMR. [c] 72 h, neat substrate. [d] GC/MS yield.

The synthesis of the copper(II) amide [$(Cl_2NN)Cu$-NHAd] (**2**) and its stoichiometric C–H amination chemistry with benzylic substrates serves as a springboard to a new protocol for *catalytic* C–H amination. [$(Cl_2NN)Cu$-NHAd] (**2**) represents a rare example of a discrete metal–amido complex that engages in H-atom abstraction chemistry with C–H bonds. A recent, related example is κ^2-[$\{Ph_2B(CH_2PtBu)_2\}Cu$-N(*p*-tolyl)$_2$][23] that exhibits HAA chemistry with the weak C–H bond of 9,10-dihydroanthracene (BDE = 76 kcal mol^{-1})[30] and Sn–H bond of Bu_3Sn-H (BDE = 78 kcal mol^{-1}),[30] though this species is best described as a copper(I)–aminyl complex.[24] The copper(II) amide [$(Cl_2NN)Cu$-NHAd] (**2**) reacts with much stronger C–H bonds such as those found in indane and ethylbenzene (BDE = 84–87 kcal mol^{-1}).[30] Perhaps the key to heightened reactivity of **2** is the formation of strong N–H bonds upon HAA. The N–H bond strength in free primary alkylamines H_2NR is 100–102 kcal mol^{-1},[30] though this is certainly lower in copper(I) amine adducts [$(Cl_2NN)Cu(NH_2R)$] estimated by theory (ONIOM(BP86/6-311 + G(d):UFF)) at 68 kcal mol^{-1} for [$(Cl_2NN)Cu(NH_2Ad)$]. Owing to its N-based radical character, the amide moiety in [$(Cl_2NN)Cu$-NHAd] (**2**) exhibits bifunctional reactivity, capable of abstracting H atoms from C–H bonds as well as forming new C–N bonds from carbon-based radicals. The significant amount of unpaired electron density at the N atom contributes to facile C–N bond formation.

Significantly, the key copper amide species **2** that engages in stoichiometric C–H amination may be formed from free amine H_2NAd and [$\{(Cl_2NN)Cu\}_2$(μ-benzene)] through the use of *t*BuOO*t*Bu. The oxidant *t*BuOO*t*Bu cleanly oxidizes the copper(I) catalyst to the three-coordinate [$(Cl_2NN)Cu$-O*t*Bu] (**3**), which engages in acid–base chemistry to generate copper(II) amide intermediates. This ultimately allows for catalytic C–H amination with unactivated amines generating the easily separated *t*BuOH as the sole stoichiometric byproduct. Furthermore, these individual steps illustrate specific roles in which peroxide oxidants may participate in copper-catalyzed C–H functionalization reactions.[14,32]

In contrast to contemporary C–H amination catalyst systems, unactivated primary and secondary alkyl amines may be efficiently utilized in the intermolecular amination of sp^3-hybridized C–H bonds. This method greatly expands the range of amines that may participate in C–H amination and represents a valuable alternative to existing procedures that require N-based electron-withdrawing activating groups. For instance, new *intramolecular* C–H amination variants may be envisioned in which the resulting cyclic amine is devoid of heteroatom activating groups.[1,15,33] Given the especially encouraging *intermolecular* reactivity with primary amines, ammonia (NH_3), the least expensive and most versatile synthetic source of N atoms, becomes a particularly attractive target for direct use in C–H amination reactions.

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[1] a) D. N. Zalatan, J. Du Bois, *Top. Curr. Chem.* **2010**, *292*, 347; b) F. Collet, R. H. Dodd, P. Dauban, *Chem. Commun.* **2009**, 5061.

[2] J. F. Hartwig, *Nature* **2008**, *455*, 314.

[3] H. M. L. Davies, J. R. Manning, *Nature* **2008**, *451*, 417.

[4] D. J. C. Constable, P. J. Dunn, J. D. Hayler, G. R. Humphrey, J. L. J. Leazer, R. J. Linderman, K. Lorenz, J. Manley, B. A. Pearlman, A. Wells, A. Zaks, T. Y. Zhang, *Green Chem.* **2007**, *9*, 411.

[5] K. Godula, D. Sames, *Science* **2006**, *312*, 67.

[6] P. M. Wehn, J. Du Bois, *Angew. Chem.* **2009**, *121*, 3860; *Angew. Chem. Int. Ed.* **2009**, *48*, 3802.

[7] a) K. W. Fiori, J. Du Bois, *J. Am. Chem. Soc.* **2007**, *129*, 562; b) C. Liang, F. Collet, F. Robert-Peillard, P. Müller, R. H. Dodd, P. Dauban, *J. Am. Chem. Soc.* **2008**, *130*, 343; c) K. Huard, H. Lebel, *Chem. Eur. J.* **2008**, *14*, 6222.

[8] a) E. Milczek, N. Boudet, S. Blakey, *Angew. Chem.* **2008**, *120*, 6931; *Angew. Chem. Int. Ed.* **2008**, *47*, 6825; b) S. Fantauzzi, E. Gallo, A. Caselli, F. Ragaini, N. Casati, P. Macchi, S. Cenini, *Chem. Commun.* **2009**, 3952.

[9] Z. Wang, Y. Zhang, H. Fu, Y. Jiang, Y. Zhao, *Org. Lett.* **2008**, *10*, 1863.

[10] a) J. D. Harden, J. V. Ruppel, G.-Y. Gao, X. P. Zhang, *Chem. Commun.* **2007**, 4644; b) H. Lu, V. Subbarayan, J. Tao, X. P. Zhang, *Organometallics* **2010**, *29*, 389.

[11] M. R. Fructos, S. Trofimenko, M. M. Días-Requejo, P. J. Pérez, *J. Am. Chem. Soc.* **2006**, *128*, 11784.

[12] X. Liu, Y. Zhang, L. Wang, H. Fu, Y. Jiang, Y. Zhao, *J. Org. Chem.* **2008**, *73*, 6207.

[13] a) S. A. Reed, A. R. Mazzotti, M. C. White, *J. Am. Chem. Soc.* **2009**, *131*, 11701; b) G. Liu, G. Yin, L. Wu, *Angew. Chem.* **2008**, *120*, 4811; *Angew. Chem. Int. Ed.* **2008**, *47*, 4733.

[14] G. Pelletier, D. A. Powell, *Org. Lett.* **2006**, *8*, 6031.

[15] J. A. Jordan-Hore, C. C. C. Johansson, M. Gulias, E. M. Beck, M. J. Gaunt, *J. Am. Chem. Soc.* **2008**, *130*, 16184.

[16] Y. M. Badiei, A. Dinescu, X. Dai, R. M. Palomino, F. W. Heinemann, T. R. Cundari, T. H. Warren, *Angew. Chem.* **2008**, *120*, 10109; *Angew. Chem. Int. Ed.* **2008**, *47*, 9961.

[17] S. M. Tekarli, T. G. Williams, T. R. Cundari, *J. Chem. Theory Comput.* **2009**, *5*, 2959.

[18] E. Kogut, H. L. Wiencko, L. Zhang, D. E. Cordeau, T. H. Warren, *J. Am. Chem. Soc.* **2005**, *127*, 11248.

[19] M. M. Melzer, S. Mossin, X. Dai, A. M. Bartell, P. Kapoor, K. Meyer, T. H. Warren, *Angew. Chem.* **2010**, *122*, 916; *Angew. Chem. Int. Ed.* **2010**, *49*, 904.

[20] a) H. Han, S. B. Park, S. K. Kim, S. Chang, *J. Org. Chem.* **2008**, *73*, 2862; b) J. A. Mayoral, R.-R. S. L. Salvatella, *Chem. Eur. J.* **2008**, *14*, 9274; c) K. Smith, C. D. Hupp, K. L. Allen, G. A. Slough, *Organometallics* **2005**, *24*, 1747; d) M. S. Kharasch, A. Fono, *J. Org. Chem.* **1958**, *23*, 325.

[21] T. H. Warren (Georgetown University), PCT Int. Appl. WO 2010028159, **2010**.

[22] Related β-diketiminato copper(II) chlorides $[Cu]_2(\mu\text{-}Cl)_2$ have been prepared previously, see: D. J. E. Spencer, A. M. Reynolds, P. L. Holland, B. A. Jazdzewski, C. Duboc-Toia, L. Le Pape, S. Yokota, Y. Tachi, S. Itoh, W. B. Tolman, *Inorg. Chem.* **2002**, *41*, 6307.

[23] N. P. Mankad, W. E. Antholine, R. K. Szilagyi, J. C. Peters, *J. Am. Chem. Soc.* **2009**, *131*, 3878.

[24] R. G. Hicks, *Angew. Chem.* **2008**, *120*, 7503; *Angew. Chem. Int. Ed.* **2008**, *47*, 7393.

[25] S.-M. Au, J.-S. Huang, W.-Y. Yu, W.-H. Fung, C.-M. Che, *J. Am. Chem. Soc.* **1999**, *121*, 9120.

[26] L. Roecker, T. J. Meyer, *J. Am. Chem. Soc.* **1987**, *109*, 746.

[27] P. L. Holland, W. B. Tolman, *J. Am. Chem. Soc.* **1999**, *121*, 7270.

[28] a) J. P. Wolfe, S. Wagaw, J.-F. Marcoux, S. L. Buchwald, *Acc. Chem. Res.* **1998**, *31*, 805; b) J. F. Hartwig, *Angew. Chem.* **1998**, *110*, 2154; *Angew. Chem. Int. Ed.* **1998**, *37*, 2046.

[29] G. Mann, J. F. Hartwig, *J. Am. Chem. Soc.* **1996**, *118*, 13109.

[30] Y.-R. Luo, *Handbook of Bond Dissociation Energies in Organic Compounds*, CRC, Boca Raton, **2002**.

[31] T. Kauffmann, J. Albrecht, D. Berger, J. Legler, *Angew. Chem.* **1967**, *79*, 620; *Angew. Chem. Int. Ed. Engl.* **1967**, *6*, 633.

[32] a) W.-J. Yoo, C.-J. Li, *J. Am. Chem. Soc.* **2006**, *128*, 13064; b) Q. Shuai, G. Deng, Z. Chua, D. S. Bohle, C.-J. Li, *Adv. Synth. Catal.* **2010**, *352*, 632.

[33] H. M. L. Davies, M. S. Long, *Angew. Chem.* **2005**, *117*, 3584; *Angew. Chem. Int. Ed.* **2005**, *44*, 3518.