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Copper-Catalyzed Aerobic Oxidative Functionalization of an Arene C−H Bond: Evidence for an Aryl-Copper(III) Intermediate

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Abstract: Recent studies have highlighted the ability of Cu^{II} to catalyze the aerobic oxidative functionalization of C−H bonds; however, very little is known about the mechanisms of these reactions. Here, we describe the Cu^{II}-catalyzed C−H methoxylation and amidation of a macrocylic arene substrate with O_2 as the stoichiometric oxidant. Kinetic and in situ spectroscopic studies demonstrate the involvement of three different oxidation states of Cu in the catalytic mechanism, including an aryl-Cu^{III} intermediate. These observations establish a novel mechanistic pathway that has implications for numerous other Cu-catalyzed aerobic oxidation reactions.

Introduction

Copper(II) is a versatile reagent for oxidative coupling reactions in organic chemistry, and in many cases Cu^{II} can be used as a catalyst in combination with O_2 as the stoichiometric oxidant.[1] Common substrates for these reactions are electron-rich arenes (e.g., phenols, anilines, indoles), amines, and enolates.[2] Copper(II) is often proposed to serve as a one-electron oxidant, and single-electron transfer from the electron-rich substrate to Cu^{II} is proposed to initiate a sequence of steps that ultimately affords the oxidative coupling product.[3]

Certain Cu-catalyzed oxidative coupling reactions, such as the classic Glaser−Hay homodimerization of alkynes (eq 1),[4] are not readily rationalized on the basis of one-electron-transfer mechanisms. A number of recently reported Cu-catalyzed methods for oxidative functionalization of C−H bonds employ electronically neutral or electron-deficient substrates.[5−7] In 2006, Yu and co-workers reported the chelate-directed oxidative heterofunctionalization of 2-phenylpyridine derivatives (eq 2).[5a] Subsequently, the groups of Buchwald and Nagasawa reported the aerobic oxidative cyclization of anilide derivatives to prepare benzimidazole and benzoxazole derivatives, respectively (eq 3).[6] Such reactions resemble Pd-catalyzed methods for ligand-directed activation and oxidative heterofunctionalization of C−H bonds,[8] although their ability to use O_2 as the oxidant represents an advantage over the use of $PhI(OAc)_2$ and other stoichiometric oxidants that are often required in the Pd-catalyzed reactions.[9]

[†] University of Wisconsin−Madison.
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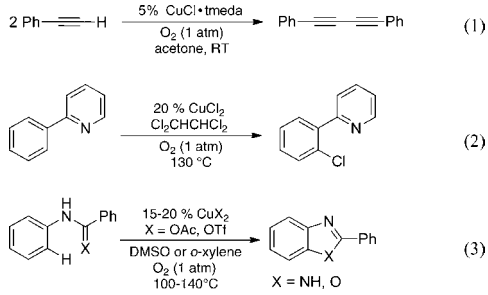
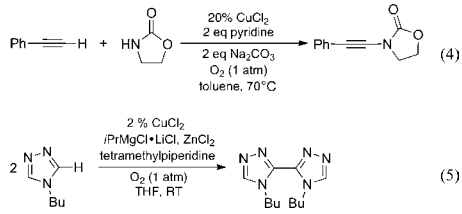


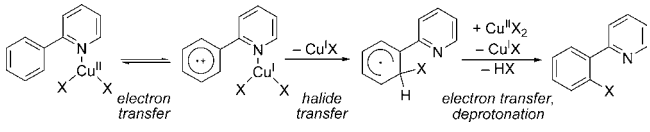
Independently, a series of intermolecular C−H oxidation reactions have been reported that feature (1) the heterofunctionalization of alkynes or electron-deficient (hetero)arenes and (2) homo- and cross-coupling of alkynes or electron-deficient (hetero)arenes.[7] In 2008, we reported the synthesis of ynamides via Cu-catalyzed aerobic oxidative coupling of alkynes and nitrogen nucleophiles, including cyclic amides and carbamates, sulfonamides, and indoles (e.g., eq 4).[7a] Another example is the so-called "aromatic Glaser−Hay" homocoupling reactions of electron-deficient arenes and heterocycles, first reported by Daugulis and co-workers (eq 5).[7c] These C−H oxidation methods resemble Glaser−Hay coupling reactions in that the substrates typically have acidic C−H bonds and do not appear to be susceptible to one-electron oxidation.



The mechanisms of Glaser−Hay coupling reactions and the recent Cu-catalyzed oxidative coupling illustrated in eqs 2−5 are poorly understood. In some cases, the mechanisms might resemble the electron-transfer pathways that have been proposed for reactions of electron-rich substrates. For example, Yu and co-workers proposed such a mechanism for the chelate-directed functionalization of 2-phenylpyridine mediated by Cu^{II} (Scheme 1).[5a] Electron-transfer pathways seem implausible, however, for other reactions that utilize alkynes, fluorinated arenes, or electron-deficient heterocycles. Electrophilic C−H activation pathways, such as those established for Pd^{II} and other metals, could be invoked, but direct evidence for the corresponding organocopper intermediates has very little precedent.

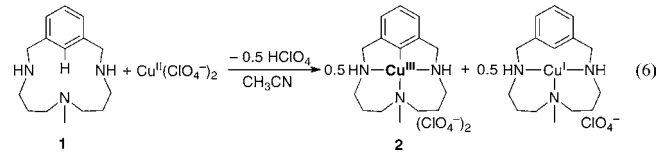
Here, we report the discovery and fundamental investigation of a Cu-catalyzed aerobic oxidative C−H functionalization reaction involving a macrocyclic arene in which we obtain direct spectroscopic evidence for an aryl-copper(III) intermediate under the catalytic reaction conditions. The unusually clear mechanistic picture that unfolds from this study has broad implications for Cu-catalyzed C−H oxidation reactions, particularly those involving substrates not readily susceptible to electron-transfer reactions.

Scheme 1. Electron-Transfer Pathway for Directed C−H Oxidation Mediated by Cu^{II}



Results and Discussion

Aerobic Synthesis of Aryl-Copper(III) Species. Several examples of stoichiometric C−H activation by Cu^{II} have been reported in recent years.[10] One of the earliest examples, reported in 2002,[10b] was observed with the macrocyclic arene **1** (eq 6).



This C−H activation reaction involves a Cu^{II} disproportionation pathway that yields 0.5 equiv of an aryl-Cu^{III} species (**2**) together with 0.5 equiv of a ligated Cu^{I} product. The aryl-Cu^{III} species was characterized by a variety of methods including X-ray crystallography, NMR and UV−visible spectroscopy, and cyclic voltammetry, and assignment of the +3 oxidation state was based on analysis of Cu K-edge X-ray absorption spectra. The present study arose from an effort to optimize the synthesis of the aryl-Cu^{III} complex **2** by performing the reaction in the presence of molecular oxygen. We anticipated that near-quantitative yields of the aryl-Cu^{III} product should be accessible via the mechanism postulated in Scheme 2, which features three key steps: (a) coordination of the macrocyclic substrate to Cu^{II}, (b) activation of the arene C−H bond involving disproportionation of Cu^{II} (a step whose mechanism is the focus of a recent investigation),[10g] and (c) aerobic reoxidation of the ligated Cu^{I} byproduct.

Initial attempts to achieve this goal resulted in little success. The reaction was carried out under the original conditions (ambient temperature, acetonitrile solvent) in the presence of 1 atm of O_2; however, the aryl-Cu^{III} complex **2** was obtained in only 57% yield. In light of the known ability of acetonitrile to stabilize the +1 oxidation state of Cu, we reasoned that use of this solvent might inhibit oxidation of Cu^{I} by O_2 (Scheme 2, step *c*).[11] Use of acetone or DMF as the solvent resulted in substantially better yields (82 and 92%, respectively; Table 1).[12] These observations validated the aerobic oxidation hypothesis depicted in Scheme 2 and provided an improved route to well-defined aryl-Cu^{III} complexes. Wang and co-workers have recently reported a similar strategy for the synthesis of a different macrocyclic aryl-Cu^{III} complex.[10f] The relatively low yield obtained in methanol, even under aerobic conditions, will be the focus of further discussion below.

We recently communicated the preparation of five-coordinate aryl-Cu^{III}-halide complexes via a Cu^{II}-disproportionation pathway analogous to that observed in the formation of [aryl-Cu^{III}]$(ClO_4)_2$, **2** (eq 7).[13] Whereas complex **2** exhibits a four-coordinate square-planar geometry, the [aryl-Cu^{III}-X]X (X = Cl, Br, I) complexes feature a square-pyramidal geometry with

Scheme 2. Stepwise Mechanism for Aerobic Synthesis of Aryl-Cu^{III} Complex **2**

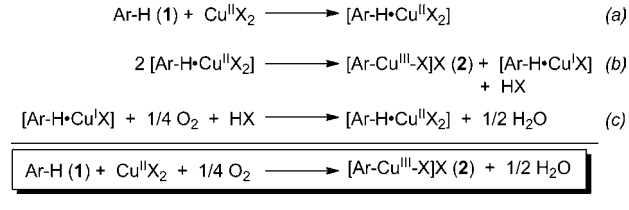
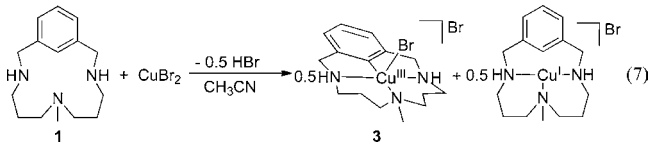


Table 1. Synthesis of [Aryl-Cu^{III}]$(ClO_4)_2$ Complex **2** under Anaerobic and Aerobic Conditions

Entry	Solvent	Yield of **2** under N_2[a]	Yield of **2** under O_2[b]
1	MeCN	49	57
2	Acetone	38	82
3	DMF	53	91
4	Methanol	27[c]	52[d]

[a] Conditions: 16 mM $Cu(ClO_4)_2 \cdot 6H_2O$, 17.6 mM substrate **1**, N_2 atmosphere, dry degassed solvent, 1 mL, ambient temperature. Yield determined by ^{1}H NMR spectroscopy; internal standard = 1,3,5-trimethoxybenzene. [b] Conditions: 75 μmol of $Cu(ClO_4)_2 \cdot 6H_2O$, 75 μmol of **1**, 750 Torr of O_2, 2.5 mL, ambient temperature. Yields determined by ^{1}H NMR spectroscopy; internal standard = 1,3,5-trimethoxybenzene. [c] Product **4** (see below) observed but not quantified due to overlapping resonances. [d] 23% yield of **4** observed.

an axial halide ligand, as revealed by X-ray crystallographic analysis. A second, uncoordinated halide counterion is present in the crystal lattice.[13] We performed a titration of NaBr into an acetonitrile solution of [aryl-Cu^{III}]$(ClO_4)_2$ **2** (Figure 1), and the data indicate that coordination of bromide to copper also occurs in a 1:1 stoichiometry in solution. The electronic absorption data in Figure 1A highlight the appearance of a strong ligand-to-metal charge-transfer band at 550 nm that matches the UV−visible spectrum of **3**.[13]



(7)

The synthesis of [aryl-Cu^{III}-Br]Br complex **3** was tested under aerobic conditions in order to obtain improved yields. Under the original anaerobic conditions, yields of **3** maximized at approximately 50%, in accord with the stoichiometry shown in eq 7. Under an oxygen atmosphere, however, higher yields were obtained (76−82%) when the reaction was carried out in acetonitrile, acetone, DMF, and methanol (Table 2). The improved yield in acetonitrile suggests that bromide can promote aerobic oxidation of Cu^I (contrast with the CH_3CN results above in the synthesis of **2**).

Reactivity of the Aryl-Cu^{III} Complex in Methanol. Reduced yields of aryl-Cu^{III} complexes were typically observed when the reactions were carried out in methanol as the solvent (Tables 1 and 2). Further analysis of these reaction mixtures revealed that another product formed in these reactions, corresponding to methoxylation of the aromatic ring (product **4**). This species could form via in situ reaction of methanol with the aryl-Cu^{III} species to yield the methoxy-substituted arene and Cu^I (eq 8). Support for this mechanistic rationale was obtained by dissolving an independently prepared sample of aryl-Cu^{III} complex **2** in methanol, in which case quantitative formation of the methoxylated arene **4** was observed within 1 h at room temperature. This C−O bond-forming reaction formally corresponds to a bimolecular C−O reductive elimination reaction, analogous to recently reported C−N bond-forming reactions (e.g., eq 9).[14] When the stoichiometric C−O or C−N coupling reactions were carried out in acetonitrile, the Cu^I byproduct, $[Cu(NCMe)_4]ClO_4$, was obtained as a crystalline solid (identity confirmed by X-ray diffraction analysis).

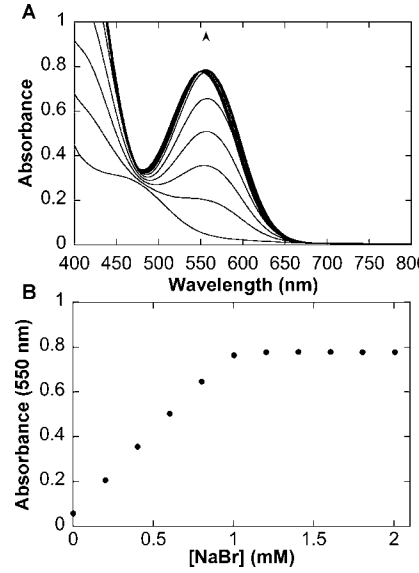


Figure 1. Titration of **2** with sodium bromide to form **3**. (A) Electronic absorption spectrum obtained during titration. (B) Change in absorbance at λ = 550 nm as a function of [NaBr]. Conditions: [**2**] = 1 mM, [NaBr] = 0−2 mM, volume = 3−3.5 mL, acetonitrile solvent.

Table 2. Synthesis of [Aryl-Cu^{III}-Br]Br Complex **3** under Anaerobic and Aerobic Conditions

Entry	Solvent	Yield of **3** under N_2[a]	Yield of **3** under O_2[b]
1	MeCN	52	76
2	Acetone	46	82
3	DMF	41	79
4	Methanol	28[c]	78

[a] Conditions: 16 mM $CuBr_2$, 17.6 mM substrate **1**, N_2 atmosphere, dry degassed solvent, 1 mL, ambient temperature. Yield determined by ^{1}H NMR spectroscopy; internal standard = 1,3,5-trimethoxybenzene. [b] Conditions: 75 μmol of $CuBr_2$, 75 μmol of **1**, 750 Torr of O_2, 2.5 mL, ambient temperature. Yields determined by ^{1}H NMR spectroscopy; internal standard = 1,3,5-trimethoxybenzene. [c] 22% yield of **4** (see below) observed.

Catalytic C−H Functionalization: Representative Examples and Mechanistic Insights. The sequential Cu-mediated reactivity of macrocylic arene **1** in methanol suggested that catalytic oxidative methoxylation of the arene could be achieved with O_2 as the terminal oxidant (eq 10), reactivity that resembles

(9) Examples of Pd-catalyzed C−H oxidation reactions that employ O_2 are also known. Representative examples are presented in the following review articles: (a) Stahl, S. S. *Angew. Chem., Int. Ed.* **2004**, *43*, 3400–3420. (b) Chen, X.; Engle, K. M.; Wang, D. H.; Yu, J. Q. *Angew. Chem., Int. Ed.* **2009**, *48*, 5094–5115. (c) Sun, C.-L.; Li, B.-J.; Shi, Z.-J. *Chem. Commun.* **2010**, *46*, 677–685.

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(11) Zuberbühler, A. D. *Met. Ions Biol. Syst.* **1976**, *5*, 325–368.

(12) See Supporting Information for further details.

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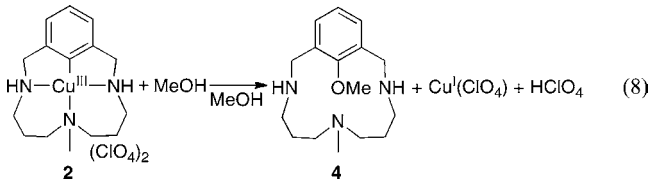
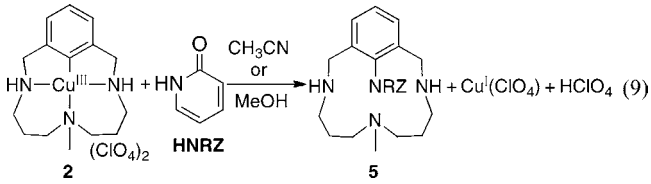
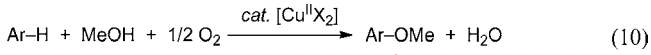
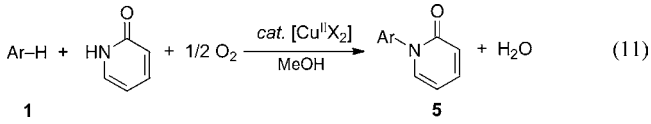




numerous recent Cu-catalyzed methods for aerobic oxidative functionalization of C−H bonds. The catalytic methoxylation reaction was tested at ambient temperature in methanol with 10 mol % of $Cu(ClO_4)_2 \cdot 6H_2O$ or $CuBr_2$ as the catalyst under 1 atm of O_2, and the macrocylic arene **1** underwent conversion to product **4** in 72% and 81% yield, respectively, with the two Cu^{II} sources. As a proof-of-principle experiment, the catalytic conditions were also tested in the presence of pyridone to determine whether catalytic C−N bond formation could be achieved. Arene **1** was combined with 5 equiv of pyridone in methanol with 10 mol % $Cu(ClO_4)_2 \cdot 6H_2O$ or $CuBr_2$, and a 77% and 84% yield of the C−N coupling product, **5**, was observed by ^{1}H NMR spectroscopy (eq 11).





These reactions have limited synthetic utility; however, they offer unparalleled opportunities to gain insights into fundamental mechanistic issues associated with Cu-catalyzed aerobic oxidative functionalization of C−H bonds. The progress of the methoxylation reaction is readily monitored by gas-uptake kinetic methods (Figure 2), and the methoxylation of arene **1** catalyzed by $Cu^{II}(ClO_4)_2$ was analyzed by initial-rate methods. The kinetic data reveal a first-order dependence of the rate on [**1**] and $[Cu(ClO_4)_2]$ and a zero-order dependence on pO_2 (Figure 3). These results reveal that the rate of the catalytic reaction is controlled by reaction steps(s) involving the arene macrocycle and Cu catalyst, while the catalytic steps involving O_2 are comparatively fast.

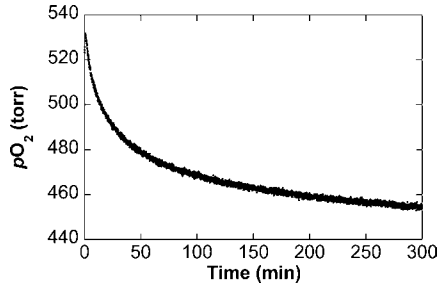


Figure 2. Representative gas-uptake time course for the aerobic copper-catalyzed methoxylation of **1**. Conditions: [**1**] = 50 mM; $[Cu(ClO_4)_2]$ = 2.5 mM; pO_2 = 550 Torr, 5 mL reaction volume.

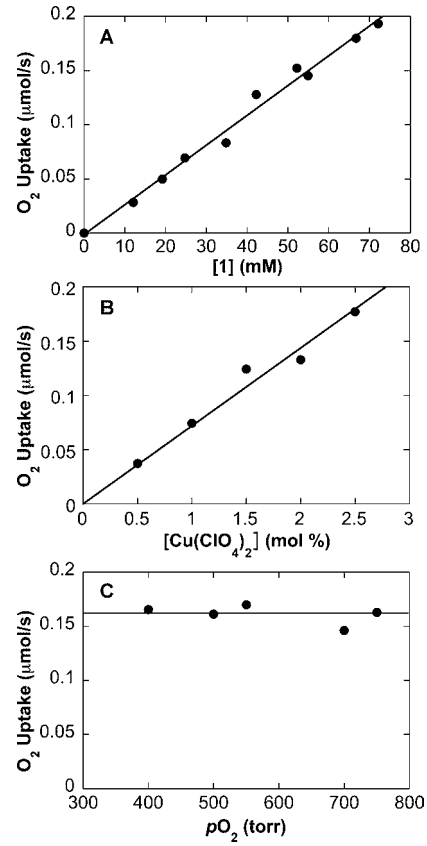


Figure 3. Kinetic dependencies obtained for the $Cu(ClO_4)_2$-catalyzed methoxylation under O_2. (A) Dependence on [**1**]. (B) Dependence on $[Cu(ClO_4)_2]$. (C) Dependence on pO_2. Standard conditions: [**1**] = 50 mM; $[Cu(ClO_4)_2]$ = 2.5 mM; pO_2 = 550 Torr, 5 mL reaction volume.

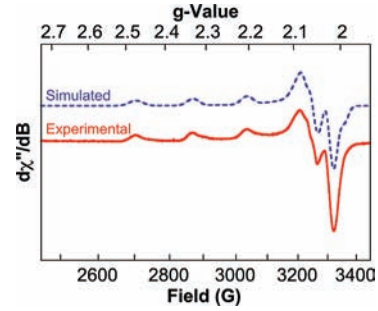


Figure 4. Experimental (red, solid) and simulated (blue, dashed) EPR spectra. The experimental spectrum was obtained from an aliquot of the methoxylation reaction catalyzed by $CuBr_2$ 128 min after initiation of the reaction. Conditions: [**1**] = 10 mM, $[CuBr_2]$ = 1 mM, 7.5 mL MeOH, pO_2 = 730 Torr, 25 °C.

Several mechanistic steps could account for the kinetic data in Figure 3, and these ambiguities prompted us to investigate the reaction by spectroscopic methods. Attempts to monitor the reaction by ^{1}H NMR spectroscopy were complicated by significant line broadening from one or more paramagnetic species present in solution. EPR spectroscopic analysis revealed the presence of a nearly axial signal (g_x = 2.07, g_y = 2.03, g_z = 2.27, and A_z = 504 MHz) consistent with that expected for a Cu^{II} species (Figure 4). Quantitation of this signal revealed that this species accounts for approximately 30−40% of the total [Cu] during the first 40 min of the reaction and then gradually increases throughout the rest of the time course.[15]

The most significant mechanistic insight into the catalytic reaction was obtained by using UV−visible spectroscopy. In

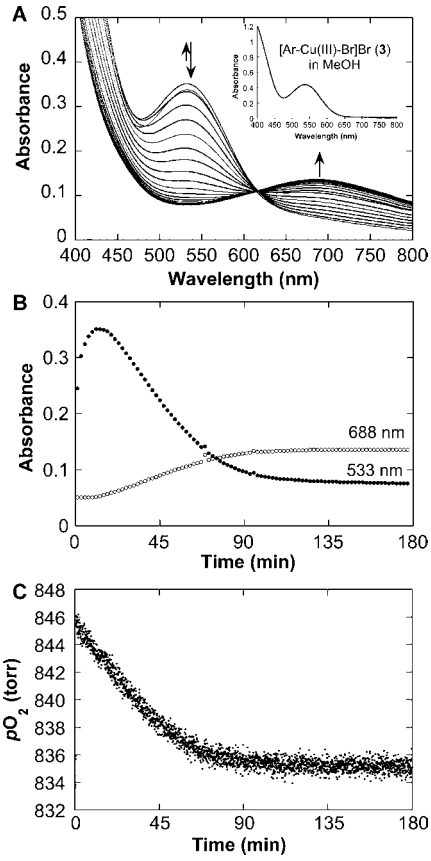
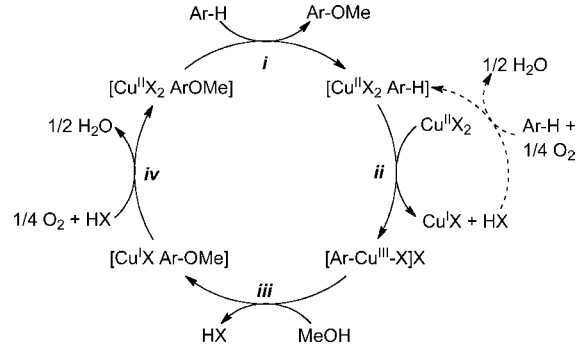


Figure 5. Simultaneous UV−visible spectroscopic and gas-uptake data acquired during the aerobic oxidative methoxylation of arene **1** catalyzed by 10 mol % $CuBr_2$ (cf. eq 10). Conditions: [**1**] = 10 mM, [$CuBr_2$] = 1 mM, pO_2 = 846 Torr, 3 mL of MeOH. (A) Progression of UV−visible spectra acquired during the catalytic reaction. Inset: Spectrum of an independently prepared sample of [aryl-Cu^{III}-Br]Br, **3**. (B) Time course of the absorbance values at 533 and 688 nm (● and ○, respectively) corresponding to the spectra shown in Figure 5A. (C) Gas-uptake data acquired during the catalytic reaction.

the $CuBr_2$-catalyzed oxidative methoxylation of **1**, a strong visible absorption band emerges at 533 nm immediately upon mixing the arene and $CuBr_2$ in methanol (Figure 5). This absorption band matches that of an independently prepared sample of the [aryl-Cu^{III}-Br]Br complex in methanol (see inset, Figure 5A). This absorption band reaches a maximum approximately 15 min after the start of the reaction and then decays with concomitant growth of a broad absorption band centered at 688 nm, attributed to Cu^{II} species that accumulate at the end of the reaction (Figure 5B). We estimate that the aryl-Cu^{III} species at t = 15 min accounts for approximately 70% of the total [Cu]. This value is based on the extinction coefficient for the pure [aryl-Cu^{III}-Br]Br complex in methanol (ε_{533nm} = 440 M^{-1} cm^{-1}) and an assumption that Cu^{II} species present at early stages of the reaction (see Figure 4 and discussion above)

Scheme 3. Proposed Catalytic Cycle for Cu-Catalyzed Aerobic Oxidative Methoxylation of Arene **1**



contribute to ≤10% of the absorption at 533 nm.[16] Gas-uptake data, acquired simultaneously with the UV−visible spectroscopic data, reveal that the consumption of O_2 ceases when the absorption band at 533 nm disappears (Figure 5C).

These results provide direct experimental evidence for the formation of an aryl-Cu^{III} intermediate in the Cu-catalyzed methoxylation reaction involving the arene macrocycle **1**. The collective data from kinetic studies and EPR and UV−visible spectroscopic analysis (Figures 3−5) suggest that both the Cu^{II} and aryl-Cu^{III} species are present in solution until the substrate is fully converted, at which point the Cu^{II} species accumulates. This observation suggests that the rates of C−H activation by Cu^{II} and C−O bond formation from aryl-Cu^{III} are closely matched. The kinetic data in Figure 3 can be accommodated if both C−H activation and the C−O bond-forming step exhibit first-order dependences on [Cu] and [**1**] (Figure 3). These fundamental steps are the focus of ongoing investigation, but preliminary data support this hypothesis.[17]

Proposed Mechanism for Cu-Catalyzed Aerobic C−H Functionalization of Arene 1 and Implications for Other Cu-Catalyzed (Oxidative) Coupling Reactions. The kinetic and in situ spectroscopic data described above, taken together with the results of stoichiometric reactions, provide a sound basis for formulation of a catalytic mechanism for this Cu-catalyzed aerobic oxidative coupling reaction (Scheme 3). Complexation of the macrocyclic arene to Cu^{II} (step *i*) is followed by the disproportionative C−H activation reaction that yields the aryl-Cu^{III} intermediate (step *ii*; cf. eq 6). Subsequent reaction of the aryl-Cu^{III} with methanol results in formation of the methoxylated arene and Cu^{I} (step *iii*; cf. eq 7). Rapid reoxidation of Cu^{I} to Cu^{II} by O_2 (step *iv*) completes the catalytic cycle. The final step is essentially the same as the aerobic reoxidation of Cu^{I} in the stoichiometric synthesis of the aryl-Cu^{III} complex (dashed arrows in Scheme 3; see, also, Scheme 2c).

The results presented here represent the first direct evidence for organocopper(III) intermediates in a copper-catalyzed oxidative coupling reaction, and the catalytic mechanism in Scheme 3 provides a compelling alternative to the single-electron-transfer mechanisms commonly proposed for these types of reactions

(15) As shown in Figure 5 below, the balance of the Cu is present as the EPR-silent aryl-Cu^{III} species. Quantitation of EPR active Cu signal maximizes at the end of the reaction at approximately 60% of the total [Cu] added to the reaction mixture. We suspect that all of the Cu is present as Cu^{II} at the end of the reaction but that it is present in various forms. For example, it is reasonable to expect that hydroxide- or methoxide-bridged dimers form as the reaction progresses, which could be EPR silent due to antiferromagnetic coupling between the two Cu^{II} centers.

(16) The upper limit of the Abs_{533nm} for Cu^{II} is based on the extinction coefficient for the Cu^{II} species present at the end of the reaction and the fact that EPR spectroscopy suggests that Cu^{II} accounts for 30−40% of the Cu at early stages of the reactions (t < 40 min).

(17) Both C−H activation by Cu^{II} and the reaction of MeOH with aryl-Cu^{III} (eqs 6 and 8, respectively) involve loss of a proton. Preliminary data suggest the first-order dependences of each of these steps on [**1**] reflect the involvement of **1** as a Brønsted base in reactions with precoordinated substrate-Cu species, either a tridentate ArH•Cu^{II} species or a tetradentate Aryl-Cu^{III} species.

(see Introduction). Steps *ii* and *iii* of the mechanism in Scheme 3 involve loss of protons from the respective coupling partners, Ar−H and MeO−H. This feature provides a rationale for the fact that many of the recent Cu-catalyzed oxidative coupling reactions, including those resulting in C−C bond formation, utilize substrates with acidic C−H bonds (alkynes, fluoroarenes, electron-deficient heterocycles).[7] Glaser−Hay coupling reactions (eq 1) trace their origin to the 19th century,[4] yet their mechanism remains poorly understood. To our knowledge, alkynyl-Cu^{III} intermediates have never been proposed for these reactions, but the present results suggest that such a pathway might be viable.[18] An alkynyl-Cu^{III} pathway seems even more conceivable in light of the similarity between the reactions described here and the recently reported Cu-catalyzed methods for amidation and phosphonation of alkynes (cf. eq 4).[7a,b]

The present results also have implications for other types of Cu-catalyzed oxidative coupling reactions. For example, we recently reported a mechanistic study of Cu-catalyzed methods for aerobic oxidative coupling of arylboronic acids and heteroatom nucleophiles ("Chan−Evans−Lam" reactions).[19] Such reactions find considerable use in pharmaceutical and agrochemical discovery efforts.[20] The kinetic data obtained from our mechanistic study support a catalytic mechanism similar to that in Scheme 3, in which arene C−H activation is replaced by a boron-to-copper transmetalation step.

Finally, the catalytic cycle in Scheme 3 highlights the prospect for mechanistic convergence between oxidative and nonoxidative coupling reactions. Ullmann and related Cu-catalyzed cross-coupling reactions of aryl halides are often proposed to proceed via a Cu^{I}/Cu^{III} cycle.[21,22] The disproportionative Cu^{II}-mediated C−H activation step (cf. eq 6) provides access to an aryl-Cu^{III} intermediate directly analogous to that proposed to form via aryl-halide oxidative addition to Cu^{I} in Ullmann-type reactions.[13] Subsequent reductive elimination from the organocopper(III) intermediate can account for product formation in both oxidative and nonoxidative reactions.

In future work, it will be important to begin bridging the gap between experimental model studies of the type described here (see ref 13 for analogous studies relevant to Ullmann-type coupling reactions) and catalytic systems commonly used in organic chemistry. The macrocyclic structure of the arene substrate **1** undoubtedly stabilizes and facilitates detection of the aryl-Cu^{III} species under catalytic conditions. The viability of such intermediates in reactions of substrates that lack strong chelating properties has not yet been demonstrated. In this context, a recent DFT computational study by Houk and Buchwald calls into question the involvement of aryl-Cu^{III} species in Ullmann-type coupling reactions and, instead, supports single-electron-transfer or atom-transfer pathways.[23] Further work is clearly needed to assess mechanistic issues associated with these and related reactions.

Conclusion

The results described above illuminate a series of fundamental steps involved in a Cu-catalyzed aerobic oxidative coupling reaction. The data reveal the participation of three different oxidation states of Cu (+1, +2, and +3), with individual steps including a Cu^{II}-mediated C−H activation, carbon−heteroatom reductive elimination from an organocopper(III) species, and regeneration of the Cu^{II} catalyst via aerobic oxidation of Cu^{I}. Whereas trivalent copper intermediates are virtually never observed (and often not even proposed) in copper-catalyzed oxidative coupling reactions, the present work suggests such species could play an important role in these catalytic reactions.

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Supporting Information Available: Experimental procedures and characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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