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Catalytically Relevant Organocopper(III) Complexes Formed through Aryl-Radical-Enabled Oxidative Addition

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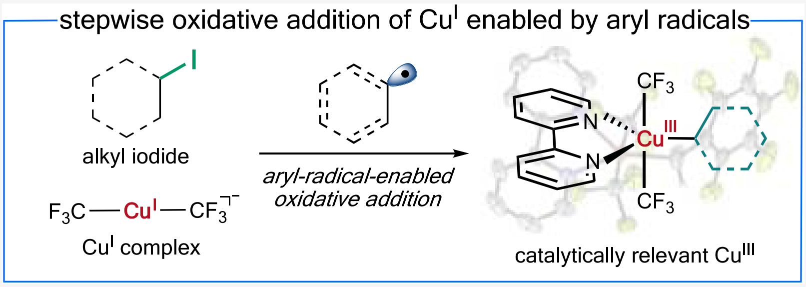

ABSTRACT: Stepwise oxidative addition of copper(I) complexes to form copper(III) species via single electron transfer (SET) events has been widely proposed in copper catalysis. However, direct observation and detailed investigation of these fundamental steps remain elusive owing largely to the typically slow oxidative addition rate of copper(I) complexes and the instability of the copper(III) species. We report herein a novel aryl-radical-enabled stepwise oxidative addition pathway that allows for the formation of well-defined alkyl−Cu^{III} species from Cu^I complexes. The process is enabled by the SET from a Cu^I species to an aryl diazonium salt to form a Cu^{II} species and an aryl radical. Subsequent iodine abstraction from an alkyl iodide by the aryl radical affords an alkyl radical, which then reacts with the Cu^{II} species to form the alkyl−Cu^{III} complex. The structure of resultant [(bpy)-$Cu^{III}(CF_3)_2$(alkyl)] complexes has been characterized by NMR spectroscopy and X-ray crystallography. Competition experiments have revealed that the rate at which different alkyl iodides undergo oxidative addition is consistent with the rate of iodine abstraction by carbon-centered radicals. The Cu^{II} intermediate formed during the SET process has been identified as a four-coordinate complex, $[Cu^{II}(CH_3CN)_2(CF_3)_2]$, through electronic paramagnetic resonance (EPR) studies. The catalytic relevance of the high-valent organo-Cu^{III} has been demonstrated by the C−C bond-forming reductive elimination reactivity. Finally, localized orbital bonding analysis of these formal Cu^{III} complexes indicates inverted ligand fields in $\sigma(Cu-CH_2)$ bonds. These results demonstrate the stepwise oxidative addition in copper catalysis and provide a general strategy to investigate the elusive formal Cu^{III} complexes.

■ INTRODUCTION

Recent developments in copper catalysis have led to numerous Cu-catalyzed cross-coupling reactions of alkyl electrophiles, in which alkyl radicals are formed as key intermediates.[1] A prevalent mechanistic proposition for these transformations starts with a single electron transfer (SET) event, wherein a Cu^I catalyst donates an electron to an alkyl electrophile. This process leads to the formation of a Cu^{II} intermediate and an alkyl radical. Subsequently, this radical recombines with the Cu^{II} species to generate a formal organo-Cu^{III} complex.[2] Reductive elimination of the high-valent Cu^{III} species forms the product and regenerates the Cu^I catalyst (Figure 1a).

Despite the latest advances in the understanding of organo-Cu^{III} species,[3] their involvement in these radical transformations remains largely elusive. In particular, limited experimental evidence exists that supports the formation of organo-Cu^{III} complexes via the stepwise oxidative addition of alkyl electrophiles to Cu^I catalysts. Consequently, such an inner sphere Cu^{III} pathway remains largely hypothetical and is mainly supported by computational chemistry.[4] Indeed, recent calculations by Lan have cast doubts on the participation of Cu^{III} intermediates in coupling reactions.[5] On the other hand, direct group transfer from the Cu^{II} intermediates to alkyl radicals, without the formation of organo-Cu^{III} species, has been proposed as an alternative mechanism and has been supported experimentally. For example, elegant work by Fu

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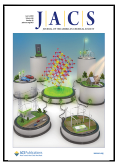

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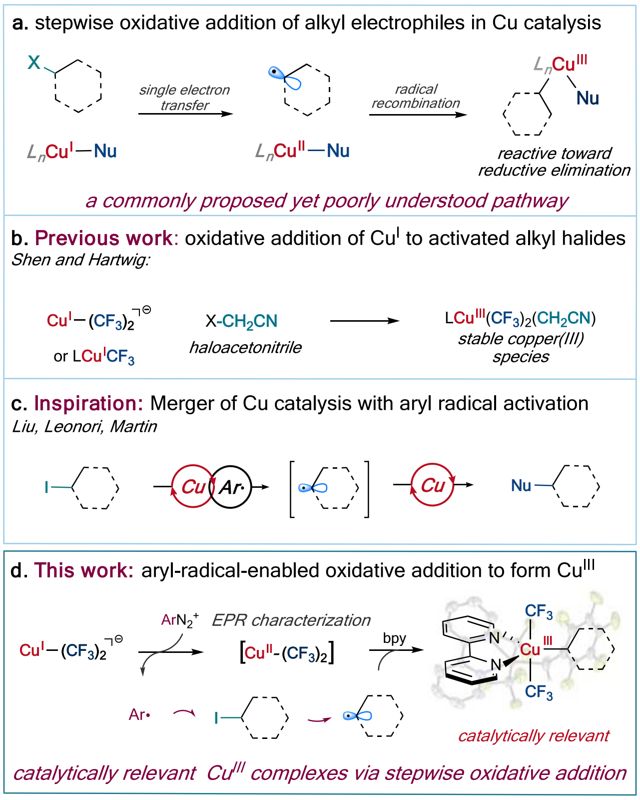


Figure 1. Probing the stepwise oxidative addition step in Cu catalysis. (a) Stepwise oxidative addition is a commonly proposed pathway in Cu catalysis (b) previous work by Shen and Hartwig on the formation of stable organo-Cu^{III} species via the oxidative addition of Cu^I complexes. (c) Aryl-radical-enabled iodine abstraction has emerged as a powerful synthetic platform. (d) This work: aryl-radical-enabled oxidative addition of Cu^I to alkyl iodide to form catalytically relevant Cu^{III} species.

and Peters has shown that in a photoinduced Cu-catalyzed enantioselective amination reaction, the formation of the C−N bond does not involve Cu^{III} species.[6]

The main obstacle in investigating the stepwise oxidative addition of Cu^I is the high reactivity of Cu^{III} complexes and the sluggish rate of oxidative addition exhibited by Cu^I catalysts. Consequently, this reaction typically occurs under conditions where Cu^{III} complexes are too unstable to be observed. One strategy to address this challenge involves enhancing the stability of the generated Cu^{III} species, although such complexes might lack catalytically relevant reactivity. To this end, pioneering work by Shen and Hartwig has recently demonstrated that Cu^I species can undergo oxidative addition with reactive α-haloacetonitrile to form stable and well-characterized nitrilemethyl-Cu^{III} species (Figure 1b).[7] Despite this elegant work, the formation of well-defined yet catalytically relevant Cu^{III} species via the stepwise oxidative addition of alkyl electrophiles to Cu^I complexes remains largely elusive.

■ RESULTS AND DISCUSSION

Hypothesis: Aryl-Radical-Enabled Oxidative Addition. We reason that an alternative strategy for delving into this elemental step is to accelerate the rate of oxidative addition of Cu^I complexes under conditions where Cu^{III} complexes could maintain stability (e.g., at subambient temperatures). Pioneering work by MacMillan has demonstrated that oxidative addition on Cu^I could be expedited by integrating silyl-radical-enabled halogen abstraction.[8] Leonori has also shown that α-aminoalkyl radicals could promote Cu-catalyzed cross-coupling of alkyl iodides.[9] More recently, our group[10] along with the Leonori and the Martin groups[11] have developed an aryl-radical-mediated iodine abstraction route to enable Cu-catalyzed cross-coupling of unactivated alkyl iodides (Figure 1c). In our aryl-radical-enabled transformations, we postulated that the prompt SET between diazonium salts and Cu^I complexes, coupled with the swift iodine abstraction rate by aryl radicals, which occurs at a bimolecular rate constant of 10^9 M^{-1} s^{-1},[12] facilitates the generation of reactive alkyl−Cu^{III} intermediates from the Cu^I catalysts.

We recently explored the potential of this aryl-radical-enabled strategy to go beyond its synthetic utility. Specifically, we propose herein its use as a method to enable rapid generation and isolation of Cu^{III} complexes at low temperatures, thus offering a direct and general way to investigate the stepwise oxidative addition step in Cu catalysis. Here, we present the successful application of this strategy in facilitating the oxidative addition of alkyl iodides to Cu^I complexes, leading to the formation of well-defined and catalytically relevant alkyl−Cu^{III} species (Figure 1d). The structure of the high-valent Cu^{III} complex has been characterized by NMR and X-ray crystallography. Mechanistic studies, including electronic paramagnetic resonance (EPR) spectroscopy and density functional theory (DFT) calculations, are consistent with the involvement of Cu^{II} species in the aryl-radical-enabled stepwise oxidative addition. Moreover, the Cu^{III} species formed through this process exhibited the catalytically relevant $C(sp^3)-CF_3$ bond-forming reductive elimination reactivity.

Formation of Cu^{III} Complexes via Aryl-Radical-Enabled Oxidative Addition. Given the known ability of the trifluoromethyl (CF_3) groups to stabilize formal Cu^{III} species,[13] we commenced our study by investigating the reactions of an anionic Cu^I species, $PPh_4^+[Cu^I(CF_3)_2]^-$ (**1**),[14] with alkyl iodides by ^{19}F NMR spectroscopy (Figure 2). At subambient temperatures (−25 °C), no reactions occurred between compound **1** and benzyl iodide **2**, consistent with the slow oxidative addition rate of Cu^I species, especially at low temperatures. Interestingly, the addition of a diazonium salt, $MesN_2OTs$ (**3**) (2 equiv), into the solution of compounds **1** and **2** at −25 °C led to the immediate disappearance of the ^{19}F NMR signal for $[Cu^I(CF_3)_2]^-$ (singlet at −31 ppm) and the appearance of a new diamagnetic species **4** resonating at −41 ppm (Figures 2a and S1). Gas chromatography/mass spectrometry (GC/MS) and ^1H NMR analysis of the reaction mixture confirmed the formation of mesityl iodide (Mes−I) in 86% yield, consistent with the formation of aryl radicals, which abstracted iodine atoms from the benzyl iodide.

We have assigned complex **4** as a neutral benzyl−Cu^{III}−$(CF_3)_2$ given that a similar species has been synthesized in our prior study via the selective removal of a CF_3 group from a tetra-coordinate and anionic Cu^{III} species.[15] In good agreement with the previous work, compound **4** formed via oxidative addition decomposed rapidly, via a reductive elimination pathway, even at low temperatures (Figure S1). It is noteworthy that this aryl-radical-enabled stepwise oxidative addition occurred much faster (within 1 min) than the oxidative addition of the same species with α-haloacetonitrile reported by Shen and Hartwig (~1 h).[7] This aligns with our hypothesis that the oxidative addition on Cu^I

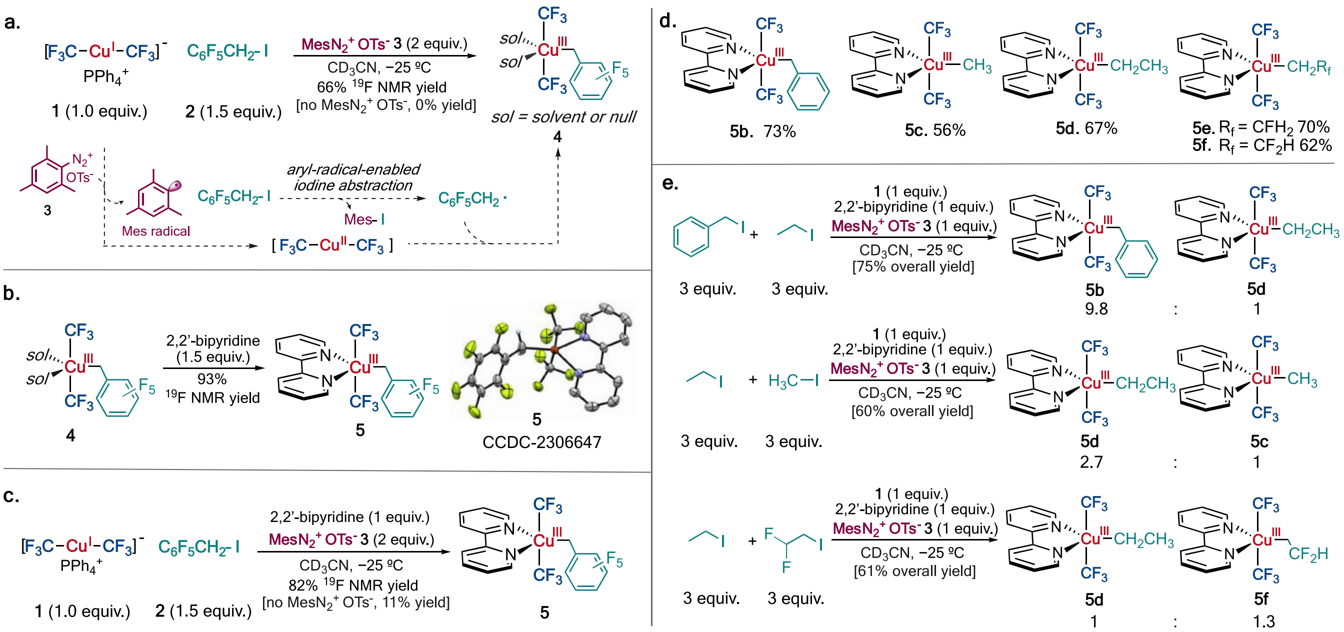


Figure 2. Aryl-radical-enabled formal oxidative addition of a Cu^{I} compound to form well-defined Cu^{III} complexes. (a) Formation of a neutral alkyl–Cu^{III} species **4** via aryl-radical-enabled oxidative addition; (b) the addition of the bpy ligand converts compound **4** to a well-defined five-coordinate alkyl–Cu^{III} compound **5**; (c) direct formation of compound **5** via aryl-radical-enabled oxidative addition; (d) formation of different benzyl– and alkyl–Cu^{III} compounds via aryl-radical-enabled oxidative addition under conditions shown in **2c**. (e) competition experiments between benzyl/alkyl iodides in oxidative addition reactions. Yield determined by ^{19}F NMR of the crude reaction mixture.

could be accelerated by the aryl-radical-enabled iodine abstraction of $C(sp^3)$–I bonds.

Although the high reactivity of compound **4** prevented its isolation in pure form from the reaction mixture, we postulated that the addition of exogenous bidentate ligands could help stabilize the 18-electron complex.[3h] Consistent with this hypothesis, the addition of 2,2′-bipyridine (bpy, 1.5 equiv) into the reaction mixture led to the formation of a new species **5** that resonated at −43 ppm in ^{19}F NMR spectroscopy (Figure S2). The newly formed complex **5** was found to be stable at low temperatures (−25 °C), and X-ray quality crystals of **5** were obtained by vapor diffusion of pentane into a DCM solution at −35 °C (Figure 2b). The crystal structure of **5** (CCDC−2306647) confirmed that this complex was a five-coordinate neutral Cu^{III} species bound with a pentafluorobenzyl group and two CF_3 groups. In the solid state, compound **5** exhibited a distorted trigonal bipyramidal geometry at the Cu^{III} center, with two CF_3 groups trans to each other and the benzyl group trans to the bpy ligand. The $CH_2C_6F_5$ group shows disorder and was refined with a two-component model (major component occupancy is 78%, shown in Figure 2b, see Supporting Information for details). Interestingly, the copper center in $(bpy)Cu^{III}(CH_2CN)(CF_3)_2$, reported by Shen and Hartwig, is closer to a square pyramidal configuration.[7] The isolation and characterization of compound **5** provided strong support for the assignment of complex **4** as a neutral benzyl–Cu^{III}–$(CF_3)_2$ species with weakly bound solvent molecules.

We next explored whether compound **5** could be formed via the aryl-radical-enabled oxidative addition when the bpy ligand was present. The addition of the bpy ligand (1.5 equiv) to a solution of **1** in CD_3CN did not lead to a significant change in the ^{19}F NMR signal (Figure S3). This finding suggests that the bpy ligand might not strongly bind to the Cu^{I} center. The tendency to form anionic and homoleptic Cu^{I} complexes was observed in other Cu-catalyzed systems under conditions of low ligand concentration.[16] Intriguingly, adding diazonium salt **3** into a mixture of **1**, benzyl iodide **2**, and bpy ligand at −25 °C resulted in the rapid generation of compound **5** in 82% yield (Figures 2c and S4). Additionally, Mes–I was formed in 94% yield, consistent with the aryl-radical-enabled iodine abstraction. Notably, in the absence of diazonium salt **3**, only a small amount of **5** was formed (11% yield) under otherwise identical conditions (Figure S4), likely through a less efficient S_N2-type oxidative addition pathway.

We have further investigated this aryl-radical-enabled oxidative addition pathway with other benzyl and alkyl iodides in the presence of the bpy ligand. Nonsubstituted benzyl iodide could also engage in this pathway to afford complex **5b** in good yield. Moreover, unactivated alkyl iodides, including methyl iodide, ethyl iodide, and their fluorinated derivatives, could oxidatively add to complex **1** via the aryl radical-enabled pathway (**5c** − **5f**). It is worth mentioning that compound **5c** has been previously synthesized by Shen from a Cu^{III} precursor.[3h]

Notably, in all these cases, the oxidative addition reactions occurred swiftly (<5 min) at low temperatures (<−25 °C), and only trace Cu^{III} products were detected when the reactions were conducted in the absence of diazonium salt **3** (Figure S5). No significant difference was observed between the reactions conducted in the dark compared to those in ambient light, ruling out the involvement of photoinduced pathways.[18] Furthermore, despite the known reactions between diazonium salts and $[Cu^{I}–CF_3]$ species to form CF_3 arenes,[19] only small amounts of CF_3 mesitylene (<5%) were observed in these oxidative addition reactions, owing partially to the fast iodine abstraction and the steric hindrance of the Mes radical. Finally, although unstable at ambient temperatures, these formal Cu^{III} complexes could be isolated at low temperatures (<−40 °C)

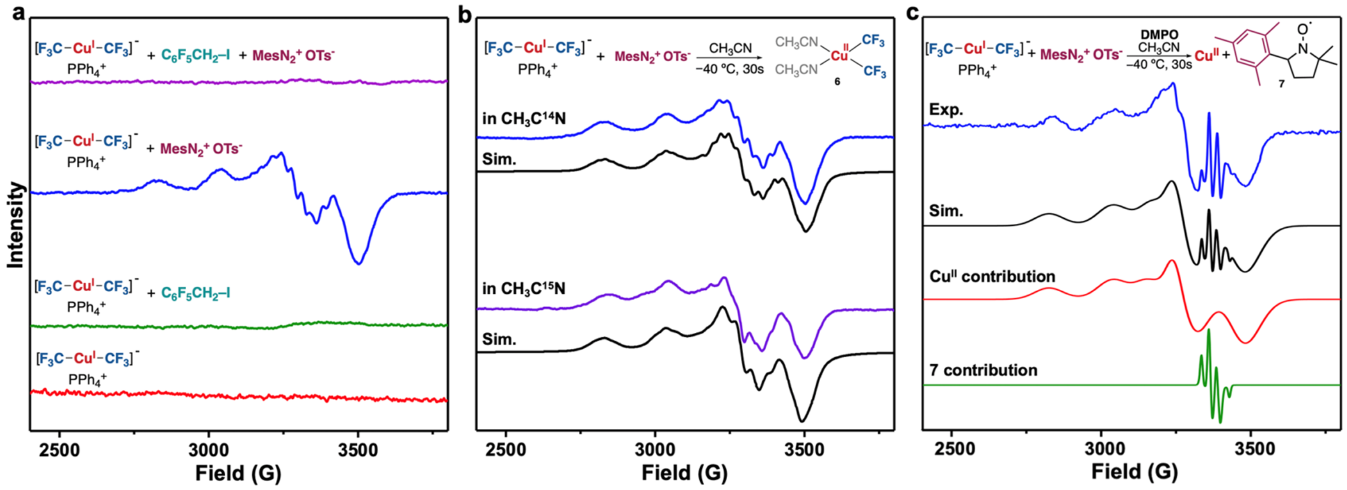


Figure 3. EPR characterization of the Cu^{II} and Mes radical intermediates formed between the Cu^I salt **1** and diazonium salt **3**. EPR spectra were conducted under the following conditions: modulation amplitude of 4 G, microwave power of 10.0 mW, and a microwave frequency of approximately 9.47 GHz. EPR spectra were obtained at 80 K and were simulated using EasySpin.[17] (a) EPR spectra of the Cu^I salt **1** (red) reacting with benzyl iodide **2** (green), or diazonium salt **3** (blue), or a combination of both (purple); (b) EPR spectra of the Cu^{II} intermediate in the SET process with ^{14}N- and ^{15}N-labeled acetonitrile. Simulations indicate that in both cases, two equivalent nitrogen atoms coordinate the Cu^{II} intermediate. Easyspin simulation parameters: $g = 2.162, 2.078, 2.004$; $A_{Cu} = 619.6, 126.0, 109.2$ MHz; $A_{14_N} = 78.6, 97.0, 74.3$ MHz or $A_{15_N} = 110.0, 134.0, 104.0$ MHz to 2 equiv N atoms. (c) EPR spectrum of **1** reacting with **3** in the presence of DMPO (3 equiv). The simulation suggests the formation of a Cu^{II} species and a DMPO-carbon radical adduct **7** coupled to a nitrogen and a hydrogen nucleus. The spectrum was simulated using the following parameters: $g_{Cu} = 2.159, 2.092, 2.014$; $A_{Cu} = 619.6, 126.0, 109.2$ MHz; $g_7 = 2.008, 2.008, 2.003$; $A_N = 18.4, 18.4, 95.9$ MHz; $A_H = 71.8, 42.0, 78.0$ MHz.

by silica gel column chromatography (Figure S7) and have been characterized by ^1H and ^{19}F NMR spectroscopy.

To assess the relative reactivity of different benzyl and alkyl iodides during oxidative addition, we conducted competition experiments using equimolar amounts of two distinct iodides (Figure 2e). Intriguingly, compound **1** showed a pronounced preference for reacting with benzyl iodide over ethyl iodide, forming compound **5b** as the predominant product with only small amounts of **5d** observed. In addition, ethyl iodide reacted faster than methyl iodide in the oxidative addition, whereas fluorine substitutions at the ß position moderately accelerated the oxidative addition rate. This trend in reactivity aligns closely with the established rates of iodine abstraction from alkyl iodides by carbon-centered radicals, which follows the order of benzyl ≫ ethyl > methyl. Additionally, the fluorine substitution is known to accelerate the iodine abstraction via the inductive effect.[20] These results indicate that the iodine abstraction is the rate-determining step in the stepwise oxidative addition process.

EPR Characterization of Reaction Intermediates. To further understand this stepwise oxidative addition pathway, electronic paramagnetic resonance (EPR) spectroscopy was employed to investigate the SET steps between Cu^I complex **1**, benzyl iodide **2**, and the diazonium salt **3**. $PPh_4^+[Cu^I(CF_3)_2]^-$ (**1**) possesses a d^{10} electron configuration without any unpaired electrons, rendering it EPR silent (Figure 3a, red). Addition of 1 equiv benzyl iodide **2** into a solution of the diamagnetic Cu^I salt **1** at −40 °C led to no observable change in the EPR signal (Figure 3a, green). This suggests no direct SET occurs between Cu^I salt **1** and benzyl iodide **2**, consistent with the slow oxidative addition of the Cu^I species to **2** observed in ^{19}F NMR studies.

Based on these observations, we hypothesized that a rapid SET should initially occur between Cu^I salt **1** and diazonium salt **3**.[19,21] This SET process is anticipated to yield a Cu^{II} complex and a Mes radical, both of which can be detected by EPR. Aligning with our hypothesis, adding diazonium salt **3** (2 equiv) into a CH_3CN solution of the diamagnetic Cu^I salt **1** at −40 °C resulted in the rapid formation of a distinct $S = 1/2$ Cu^{II} signal within 30 s (Figure 3a, blue). EPR simulations identified the parameters of this species as $g_x = 2.162$, $g_y = 2.078$, $g_z = 2.004$, and $A_x = 619.6$ MHz, $A_y = 126.0$ MHz $A_z = 109.2$ MHz (Figure S14 and Table S1). Remarkably, the EPR signal for the Cu^{II} species completely vanished when the same reactions were conducted in the presence of 1 equiv of benzyl iodide **3** (Figure 3a, purple). This observation aligned well with the postulation that the aryl radical rapidly abstracted an iodine atom from the benzyl iodide, forming a benzyl radical. This radical then reacted with the Cu^{II} species, resulting in the formation of the diamagnetic Cu^{III} complexes **4**.

Furthermore, superhyperfine features of the Cu^{II} species can be discerned in the 3200−3400 G range. Examining these features will yield insights into the coordination characteristics of the Cu^{II} intermediate formed during the SET process. The simulation of the superhyperfine structure indicates the hyperfine coupling of two ^{14}N nuclei to the Cu^{II} center, suggesting the coordination of two acetonitrile solvent molecules (Figure 3b, top). To verify the presence of acetonitrile ligands, the same EPR experiments were performed using ^{15}N-labeled acetonitrile, noting that ^{15}N has an I value of 1/2, which should produce fewer but broader superhyperfine peaks compared to ^{14}N ($I = 1$). Indeed, with ^{15}N-labeled acetonitrile, a noticeable reduction in the splitting pattern was observed in the EPR spectrum (Figure 3b, bottom). This change corresponds to the hyperfine coupling transition from two ^{14}N to two ^{15}N in the isotopically labeled solvent. Additionally, the hyperfine coupling constant showed an increase by a factor of 1.4 in these simulations, reflecting the difference in the gyromagnetic ratios between the two isotopes.[22] These EPR results are consistent with the

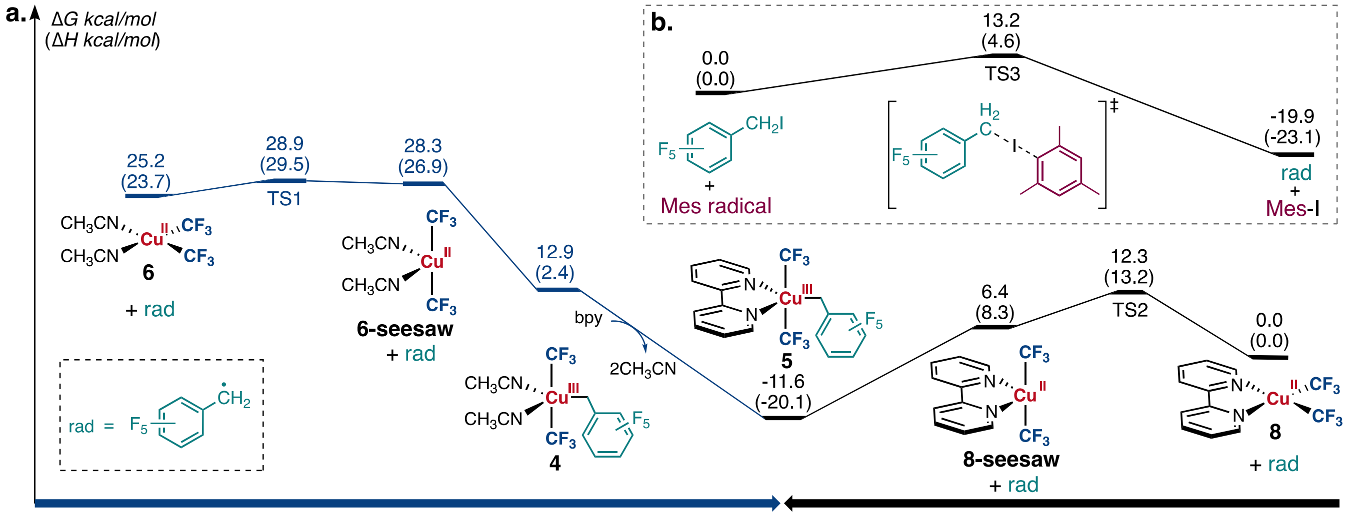
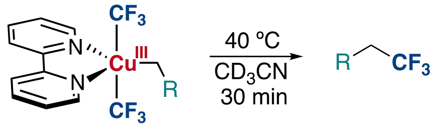


Figure 4. Free energy profiles calculated for (a) the reaction of Cu$^{\text{II}}$ intermediates with the benzylic radical and (b) the iodine abstraction by the mesityl radical from the benzyl iodide **2**. Free energies are in kcal/mol.

Scheme 1. Reductive Elimination of Cu$^{\text{III}}$ Complexes Formed via Oxidative Addition



R = C_6F_5 90%
R = C_6H_6 91%
R = H 99%
R = CH_3 94%
R = CFH_2 45%
R = CF_2H 5%

formation of a four-coordinate complex, [Cu$^{\text{II}}$(CH_3CN)$_2$(CF_3)$_2$] **6**. Notably, the formation of this species has been indicated in our recently reported Cu$^{\text{III}}$−C bond homolysis process.[15]

To further probe the formation of the Mes radical, we conducted the reaction of **1** with diazonium salt **2** in the presence of 5,5-dimethyl-1-pyrroline-*N*-oxide (DMPO), a commonly used radical trapping agent.[23] EPR spectra of the reaction showed a distinct Cu$^{\text{II}}$ signal and sharp organic radical peaks at $g = \sim 2$ (Figure 3c). Further simulations suggested that the radical is coupled to a nitrogen and a hydrogen nucleus, with parameters: g = 2.008, 2.008, 2.003; A_{N} = 18.4, 18.4, 95.9 MHz; A_{H} = 71.8, 42.0, 78.0 MHz (see Figure S15 and Table S2 for simulation details). Such nitrogen and hydrogen couplings are typical for DMPO-carbon radical adducts, in which the nitroxide radical is coupled to an adjacent nitrogen and a β-proton. Additionally, the average A_{N} (44.2 MHz) and A_{H} (63.9 MHz) values from our simulations align closely with the reported isotropic A values for EPR spectra of DMPO radical adducts measured at room temperature.[24] Therefore, we assigned the organic radical as the paramagnetic DMPO-Mes radical adduct **7**. Notably, the absence of superhyperfine patterns in the Cu$^{\text{II}}$ EPR signals may be attributed to the known binding affinity of *N*-oxide compounds and nitroxyl radicals with Cu$^{\text{II}}$ species.[25]

DFT Calculations on the Formation of the Cu$^{\text{III}}$ Species. As these data were consistent with a stepwise oxidative addition process that involves Cu$^{\text{II}}$ intermediates, a more detailed mechanistic picture of the reaction between the Cu$^{\text{II}}$ species with the alkyl radical to form Cu$^{\text{III}}$ complexes was attained by DFT calculations (Figure 4a and see Supporting Information for computational details). The reactions of two plausible Cu$^{\text{II}}$ intermediates, [(CH_3CN)$_2$Cu$^{\text{II}}$(CF_3)$_2$] **6** and (bpy)Cu$^{\text{II}}$(CF_3)$_2$ **8**, with the benzyl radical were investigated. It is worth mentioning that Grushin has also suggested the formation of **8** as an unstable intermediate in a trifluoromethylation reaction.[26] Although Cu$^{\text{II}}$ complexes were calculated to be most stable in a square planar geometry, both complexes were calculated to transform into less stable seesaw-shaped structures. Notably, a higher activation barrier is required for the reorganization of **8** ($\Delta G^{\ddagger}$ = 12.3 kcal/mol) compared to that of **6** ($\Delta G^{\ddagger}$ = 3.7 kcal/mol). In the seesaw configuration, both Cu$^{\text{II}}$ complexes readily merge with the benzyl radical, leading to the formation of the Cu$^{\text{III}}$ complexes **4** and **5** through barrierless pathways with high thermodynamic driving forces (ΔG = −15.4 and −18.0 kcal/mol, respectively). Moreover, the coordination of the bpy ligand to compound **4** to form compound **5** was also found to be thermodynamically favored (ΔG = −24.5 kcal/mol), consistent with the experimental results. Importantly, the iodine abstraction from benzyl iodide **2** by the Mes radical was calculated to proceed with an activation energy ($\Delta G^{\ddagger}$) of 13.2 kcal/mol (Figure 4b), aligning with our postulation that this could be the rate-determining step in the oxidative process.

Reductive Elimination Reactivity of the Cu$^{\text{III}}$ Species Generated through Oxidative Addition. We next aimed to investigate the catalytic relevance of these formal Cu$^{\text{III}}$ compounds in Cu-catalyzed aliphatic trifluoromethylation reactions. Organo-Cu$^{\text{III}}$ species bearing CF_3 groups have been widely proposed as key intermediates within these transformations.[27] The reductive elimination of high-valent Cu complexes is postulated as the product-forming step. Therefore, we intended to explore whether these Cu complexes, produced through aryl-radical-enabled oxidative addition, could engage in the C−CF_3 bond-forming reductive elimination. In fact, Shen has previously shown that compound **5c** could undergo smooth reductive elimination at 40 °C to form 1,1,1-trifluoroethane in nearly quantitative yield.[3h] Aligning well with Shen's result, the Cu$^{\text{III}}$ complexes derived from benzyl (**5** and **5b**), methyl (**5c**), and ethyl (**5d**) groups,

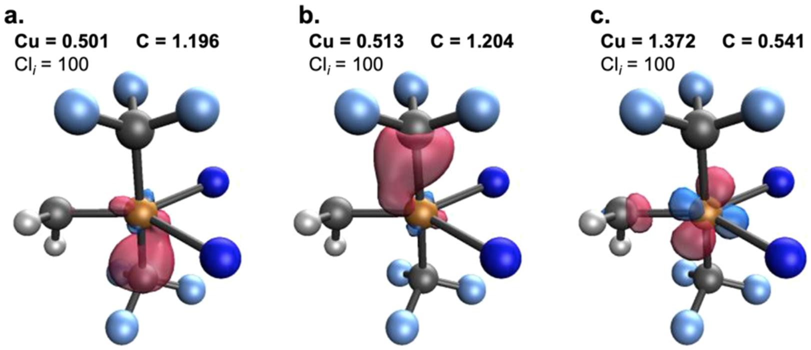


Figure 5. Selected valence Pipek−Mezey localized orbitals for **5** with Löwdin population and clarity index value (CI_i). The isocontour value is 0.3 au. At the B3LYP/Lanl2DZ+6-31G** level of theory. Noncoordinating atoms are omitted for clarity.

reductively eliminated to form the corresponding trifluoromethylation products in good yield (Scheme 1). On the other hand, a slower transformation was observed for complex **5e** (R = CFH_2), whereas compound **5f** (R = CF_2H) was relatively stable at this temperature. The high stability of compound **5f**, which contains an electron-deficient difluoromethyl group, echoes Shen and Hartwig's work on the stabilization of Cu^{III} complexes with a CH_2CN group.[7] Overall, these results represent rare examples of the reductive elimination from organo-Cu^{III} species generated through oxidative addition from Cu^{I} complexes.

Oxidation State and Inverted Ligand Field. Finally, the oxidation state (OS) of these formal Cu^{III} complexes merits consideration. The inverted ligand field theory, originally proposed by Snyder, argues that a formal Cu^{III} complex, $[Cu(CF_3)_4]^-$, would be more accurately described as Cu^{I}.[28] Recent computational and spectroscopic work by Hoffman[2b] and Lancaster[2a29] has shown that ligand field inversion is common in formal Cu^{III} and Ni^{IV} complexes. On the other hand, a recent study by Cutsail that employed a combination of X-ray absorption and valence core X-ray emission spectroscopies supports a Cu^{III} assignment for $[Cu(CF_3)_4]^-$.[30] Although determining the true OS of these newly synthesized Cu complexes is beyond the scope of current work, we offer below our viewpoint based on our preliminary computational studies and NMR spectroscopy data.

We explored the electronic configuration of compound **5** using the Localized Orbital Bonding Analysis (LOBA), an analysis method developed by Thom[31] and Head-Gordon[32] aimed at calculating the OS of transition metal complexes. LOBA analysis on **5** has shown that the electron pairs from two $\sigma(Cu-CF_3)$ bonds are assigned to the CF_3 groups. (Figure 5a,b). Meanwhile, the electrons from the $\sigma(Cu-CH_2)$ bond are assigned to the Cu center, leading to a formal cationic $CH_2C_6F_5$ moiety (Figure 5c). According to IUPAC's winner-takes-it-all rule on OS assignment,[33] we tentatively assign Cu (+1) OS for complex **5** based on the LOBA analysis. A similar assignment could be made using the LOBA analysis with different density functionals (Figure S20) or employing an alternative analysis method − Oxidation State Localized Orbitals (Figure S21).[34] Notably, the electron assignment is similar to Klein's computational analysis on a formal $Ni^{IV}(CF_3)_2Ph$ complex,[35] reported previously by Sanford,[36] which suggests two anionic CF_3 groups with a cationic phenyl group. In addition, the assignment of the OS is consistent with the recent work by Beier, Ribas, and Motornv, which assigns +1 OS for $(bpy)Cu(CF_3)_3$.[37]

The electron density leaning toward the Cu center in the $\sigma(Cu-CH_2)$ bond could be reflected by the ^1H NMR chemical shifts of the CH_2 groups of these formal Cu^{III} complexes. Methylene protons in $M-CH_2R$ groups typically show chemical shifts at low frequencies,[38] such as 1.43 ppm for a recently reported tetravalent $[Ce^{IV}-CH_2C(CH_3)_3]$ complex.[39] Contrastingly, in complexes **5** and **5b**−**5f**, the CH_2 groups resonate at higher frequencies, e.g., 4.08 and 3.45 ppm for **5** and **5d**, respectively. Notably, the CH_2 protons in our previously reported four-coordinate and anionic complex, $PPh_4[(CF_3)_3Cu(CH_2C_6F_5)]$, resonate at a lower frequency (2.85 ppm).[15] In addition, the CH_2 protons in the related Au^{III} complexes, $[(IPr)Au^{III}(CF_3)_2(CH_2R)]$, reported by Toste, resonate at the range of ~1.5 (R = CH_3) to 2.5 (R = alkenyl) ppm.[40] The unusual downfield shifts of the methylene protons in these neutral, five-coordinate Cu complexes are indicative of the relatively high electronegativity of the Cu center. Despite these observations, further spectroscopic studies, including X-ray absorption spectroscopy, along with higher-level calculations, are necessary to elucidate the detailed electronic configurations of these formal Cu^{III} compounds. These studies are currently ongoing in our laboratories.

■ CONCLUSIONS

In conclusion, we reported herein the conversion of Cu^{I} complexes to well-defined and catalytically relevant alkyl−Cu^{III} species via a stepwise oxidative addition pathway—a step that has been proposed in numerous Cu-catalyzed reactions. This is enabled by the fast SET from a Cu^{I} species to a diazonium salt and the rapid iodine abstraction by aryl radicals from alkyl iodides. The Cu^{II} intermediate generated in the SET process has been characterized as a four-coordinate $[Cu^{II}(CH_3CN)_2(CF_3)_2]$ complex through EPR studies employing isotope labeling. These formal Cu^{III} species generated via the aryl-radical-enabled oxidative addition underwent $C(sp^3)-CF_3$ bond-forming reductive elimination. These results provide strong evidence for the commonly proposed stepwise oxidative addition of Cu^{I} and the formation of a Cu^{III} species in Cu-catalyzed cross-couplings of alkyl electrophiles. More importantly, given the efficiency and generality of the aryl-radical-enabled oxidative addition pathway, we anticipate that the strategy opens a new avenue for the investigation of the oxidative addition step and the putative organo-Cu^{III} species in Cu catalysis. These studies are currently ongoing in our laboratories.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/jacs.4c01668.

> Experimental details; ^{19}F NMR spectra of reaction mixture; competition experiment between different alkyl iodides; DFT calculation details; reductive elimination of organocopper(III) complexes, and EPR simulation details (PDF)
>
> Copies of NMR spectra (PDF)

Accession Codes

CCDC 2306647 contains the supporting crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Center, 12 Union Road, Cambridge CB2 1EZ, U.K.; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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