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C(sp³)–H Fluorination with a Copper(II)/(III) Redox Couple

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ABSTRACT: Despite the growing interest in the synthesis of fluorinated organic compounds, few reactions are able to incorporate fluoride ion directly into alkyl C–H bonds. Here, we report the $C(sp^3)$ –H fluorination reactivity of a formally copper(III) fluoride complex. The C–H fluorination intermediate, LCuF, along with its chloride and bromide analogs, LCuCl and LCuBr, were prepared directly from halide sources with a chemical oxidant and fully characterized with single-crystal X-ray diffraction, X-ray absorption spectroscopy, UV-Vis spectroscopy, and ¹H nuclear magnetic resonance spectroscopy. Quantum chemical calculations reveal significant halide radical character for all complexes, suggesting their ability to initiate and terminate a $C(sp^3)$ -H halogenation sequence by sequential hydrogen atom abstraction (HAA) and radical capture. The capability of HAA by the formally copper(III) halide complexes was explored with 9,10-dihydroanthracene, revealing that LCuF exhibits rates two orders of magnitude higher than LCuCl and LCuBr. In contrast, all three complexes efficiently capture carbon radicals to afford $C(sp^3)$ –halogen bonds. Mechanistic investigation of radical capture with trityl radical revealed that LCuF proceeds through a concerted mechanism, while LCuCl and LCuBr follow a stepwise electron transfer-halide transfer pathway. The capability of LCuF to perform both hydrogen atom abstraction and radical capture was leveraged to enable fluorination of allylic and benzylic C–H bonds and α -C–H bonds of ethers at room temperature.

INTRODUCTION

Carbon-fluorine bonds are becoming increasingly prevalent in pharmaceuticals and agrochemicals.1 The value of fluorinated compounds in these applications stems from their enhancement of lipophilicity, metabolic stability, and receptor binding affinity.² Given the abundance of C(sp³)-H bonds in organic molecules, the atom-efficient conversion of C(sp³)-H to $C(sp^3)$ -F bonds has been a prominent goal for synthetic methodology development.³⁻⁶ The majority of C(sp³)-H fluorination methods employ a radical approach that depends on electrophilic fluorination reagents, e.g. Selectfluor,⁷⁻¹² and Nfluorosulfonimide (NFSI),¹³⁻¹⁵ to react directly with alkyl radicals to afford C(sp³)-F bonds (Figure 1a).^{16,17} Few C(sp³)-H fluorination protocols employ metal-based, nucleophilic fluorine (F^{-}) sources, i.e. metal fluorides,³ to deliver the C(sp³)-F bond, as most notably demonstrated by Groves and colleagues.^{18,19} Practically, the metal-fluoride-mediated process is advantageous, since it is more suitable for ¹⁸F radiolabeling and controlling the stereochemistry of the C(sp³)-F center.²⁰⁻²² Despite this progress, a remaining challenge is improving the selectivity of alkyl fluorination.¹ As chiral copper complexes are well-known asymmetric catalysts for radical C-H functionalization,²³⁻²⁵ the use of tunable copper fluoride complexes, in principle, would provide the opportunity to further improve the selectivity of C(sp³)-H fluorination. However, the mechanistic step of R• capture at a copper fluoride complex to afford $C(sp^3)$ -F bonds has yet to be established.

While copper(II) chloride and bromide are well-documented C(sp³)-H halogenating reagents,²⁶⁻²⁸ copper(II) fluoride is not amenable to analogous fluorination reactivity, likely due to the highly ionic nature of the Cu^{II}-F bond (Figure 1b). Further underscoring this concept, Lectka and co-workers reported the C(sp³)-H fluorination of unactivated alkanes employing a copper(I) source and Selectfluor.7 Mechanistic studies revealed that the copper(I) complex serves to initiate the reaction through the formation of an inert copper(II) fluoride while Selectfluor mediates the key $C(sp^3)$ -F bond forming step.²⁹ Thus, we questioned whether a more covalent Cu-F bond might enable $C(sp^3)$ -H fluorination at the copper center. Specifically, we envisioned the case of a formally [Cu^{III}-F]²⁺ complex. Oxidation of a copper(II) fluoride to copper(III) would increase the copper effective nuclear charge and lower the Cu d orbital energy to allow for increased fluorine contribution to the lowest unoccupied molecular orbital (LUMO) of the [Cu^{III}- F^{2+} motif (Figure 1b). Consistent with this hypothesis, recent X-ray absorption spectroscopy studies on formally copper(III) complexes showed that a majority of LUMOs are located on the ligand instead of the metal, resulting in an inverted ligand field.^{30,31} The increased hole character on the ligand has been invoked to explain the C(sp³)-H amination reactivity of Cu nitrene complexes.^{32,33} Thus, we propose that the introduction of fluorine hole character will allow a [Cu^{III}-F]²⁺ complex to perform both hydrogen atom abstraction (HAA) and radical capture (RC) to furnish the $C(sp^3)$ -F bond (Figure 1c). Herein, we report the synthesis of formally copper(III) fluoride, chloride, and bromide complexes and detailed mechanistic investigation of their C(sp³)-H halogenation reactivity. While all

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Direct C(sp³)-H fluorination via copper(III) fluoride

Figure 1. (a) Radical $C(sp^3)$ -H fluorination by metal- and organic-mediated approaches. (b) Oxidation of a copper(II) fluoride to formally copper(III) increases the covalency of the Cu-F bond and the hole character on F. (c) Direct $C(sp^3)$ -H fluorination by sequential hydrogen atom abstraction and radical capture with a formally copper(III) fluoride complex.

 $[Cu^{III}-X]^{2+}$ complexes are proficient at radical capture, the $[Cu^{III}-F]^{2+}$ complex is faster at HAA than $[Cu^{III}-CI]^{2+}$ and $[Cu^{III}-Br]^{2+}$ complexes by two orders of magnitude. Leveraging these mechanistic insights, we demonstrate that the copper(III) fluoride is capable of directly fluorinating allylic and benzylic C(sp³)–H bonds as well as α -C–H bonds of ethers at room temperature using F⁻ as the fluorine source.

RESULTS AND DISCUSSION

Synthesis, Characterization, and Electronic Structure of Formally Copper(III) Halides. To examine the ability of the [Cu^{III}-F]²⁺ motif to fluorinate C(sp³)-H bonds, we set out to synthesize a discrete [Cu^{III}-F]²⁺ complex. Additionally, we targeted copper(III) chloride and bromide analogs to provide a detailed understanding of how electronic structure affects reactivity relevant to C(sp³)-H halogenation across the copper(III) halide series. To support the one-electron Cu^{II}/Cu^{III} redox couple central to our hypothesis, we selected the biscarboxamidopyridine ligand (L = [N-N'-bis(2,6diisopropylphenyl)-2,6-pyridinedicarboxamido]²⁻) based on the work by Tolman and co-workers.³⁴ Reaction of LCu^{II}(MeCN) with tetrabutylammonium halide ([TBA]X) salts in tetrahydrofuran afforded the corresponding anionic copper(II) halide complexes [TBA] $LCu^{II}X$ (X = F, Cl, Br) in

88%, 83%, and 84% yield, respectively (Scheme 1). All [TBA]LCu^{II}X complexes were characterized by X-ray crystallography and electron paramagnetic resonance (see Supplementary Information), confirming copper $S = \frac{1}{2}$ centers. Samples of [TBA]LCu^{II}F were unsuitable for single crystal X-ray diffraction, therefore, the bis(triphenylphosphine)iminium (PPN) salt, [PPN]LCu^{II}F, was prepared to obtain structural

Scheme 1. Synthesis of anionic copper(II) halides





characterization (Figure S1). The copper(II) halide structures exhibit similar Cu-N distances between L and the copper center (Cu-N_(avg) (Å) = 1.977 for [LCu^{II}F]⁻, 1.987 for [LCu^{II}Cl]⁻, 1.982 for [LCu^{II}Br]⁻). All copper(II) centers adopt a distorted square planar geometry ($\tau_4 = 0.15$ for [LCu^{II}F]⁻), 0.20 for [LCu^{II}Cl]⁻), 0.20 for [LCu^{II}Br]⁻, $\tau_4 = 0$ for square planar, $\tau_4 =$ 1 for tetrahedral)³⁵ with the halide positioned slightly out of the N₃Cu plane. Seeking to access copper(III) halides by oneelectron oxidation, we measured the Cu^{II}/Cu^{III} redox potential in solution. The cyclic voltammograms of [TBA]LCu^{II}X complexes in CH₂Cl₂ exhibit quasi-reversible redox couples at $E_{1/2}$ = 0.465 V for [LCu^{II}F]⁻, 0.525 V for [LCu^{II}Cl]⁻, and 0.525 V for [LCu^{II}Br]⁻ (vs Ag/AgNO₃, Figures S2-S4), respectively. As expected, [TBA]LCu^{II}F features the most cathodic redox potential due to the high electronegativity of fluoride. Interestingly, [TBA]LCu^{II}Br is oxidized at nearly the same potential



Figure 2. (a) Synthesis of formally copper(III) halides by chemical oxidation of the copper(II) halide precursor with $[NAr_3]PF_6$ (Ar = 4-bromophenyl). (b) Overlay of the UV-Vis spectra of LCuF, LCuCl, and LCuBr at -80 °C in CH₂Cl₂ (0.1mM).

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Figure 3. Solid-state structures of LCuF, LCuCl, and LCuBr with thermal ellipsoids shown at 50% level of probability. Cocrystallized solvents and minor components of disorder are omitted for clarity. Selected bond lengths (Å) and angles (°): LCuF Cu-F = 1.755(3); Cu-N₁ = 1.841(4); Cu-N₂ = 1.901(4); N₁-Cu-F = 179.68(17). LCuCl Cu-Cl = 2.1085(8); Cu-N₁ = 1.859(2); Cu-N₂/N₂' = 1.9132(16); N₁-Cu-Cl = 180. LCuBr Cu-Br = 2.2562(4); Cu-N₁ = 1.8623(18); Cu-N₂/N₂' = 1.9159(13); N₁-Cu-Br = 180.

as [TBA]LCu^{II}Cl but features the most reversible redox profile of the series, with a peak-to-peak separation of 160 mV.

Variable temperature UV-Vis spectrophotometry was utilized to study the thermal stability of the copper(III) fluoride complex, LCuF. Based on the CV profiles of [TBA]LCu^{II}X, the aminium radical cation, $[NAr_3]PF_6$ (Ar = 4-bromophenyl; $E_{1/2} = 0.66$ V vs Ag/AgNO₃ in MeCN) was selected as the chemical oxidant to prepare LCuX complexes (Figure 2a). Treatment of [TBA]LCu^{II}F with [NAr₃]PF₆ at -80 °C in CH₂Cl₂ resulted in the rapid formation of a new species with intense absorptions at 520 nm ($\varepsilon = 9100 \text{ M}^{-1} \text{ cm}^{-1}$) and 820 nm ($\varepsilon = 18600 \text{ M}^{-1} \text{ cm}^{-1}$), which were attributed to the LCuF complex (Figure 2b). The UV-Vis spectra of LCuCl and LCuBr, prepared analogously via chemical oxidation, share the two main charge transfer bands (Figure 2b). Both UV-Vis bands red-shift along the series from LCuF to LCuCl to LCuBr in accordance with the donating ability of the halide ligands, indicating that these transitions correspond to ligandto-metal charge transfer (LMCT).³⁶ Time-dependent density functional theory (TD-DFT) calculations at B3LYP/def2-TZVP(-f) level reproduced the two intense features as well as their red-shifting trends (Figure S48). Both absorptions originate from charge transfers from halide/L based orbitals to the LUMO, which features the σ^* interaction of the Cu d_{x2-v2} and the halide/L. The TD-DFT calculations also suggest that decreasing peak intensity from LCuF to LCuCl to LCuBr correlates to the reducing contribution of L to the donor orbital (Table S7-S9). While LCuCl and LCuBr are stable in CH₂Cl₂ at 20 °C, LCuF undergoes slow decay at temperatures above -20 °C. The ¹H nuclear magnetic resonance (NMR) spectra of LCuX in CD₂Cl₂ show sharp resonances within the 0-9 ppm range that account for all ligand protons (Figures S18-S23), consistent with a diamagnetic ground state for LCuX complexes. Additionally, a ¹⁹F NMR signal at -209.4 ppm is observed for LCuF.

Single crystal X-ray diffraction confirmed the formation of $[Cu^{III}-X]^{2+}$ species (Figure 3). The Cu-N and Cu-X bond distances contract by 0.07-0.1 Å upon oxidation from Cu^{II} to the formally Cu^{III} state. All copper(III) complexes exhibit more rigid square planar geometries ($\tau_4 = 0.09$ for LCuF, 0.10 for LCuCl, 0.10 for LCuBr) compared to their copper(II) counterparts. Overall, the structural reorganization upon oxidation is

minimal, consistent with the highly reversible redox couples observed by CV (Figures S2-S4). LCuF is, to the best of our knowledge, the first structurally characterized, discrete copper(III) fluoride complex and features the shortest Cu-F distance (1.755(3) Å) reported in the Cambridge Structural Database. Furthermore, LCuCl and LCuBr feature shorter Cu-Cl (2.1085(8) Å) and Cu-Br (2.2562(4) Å) bonds than previously reported five-coordinate copper(III) halide complexes (CI: 2.2011(18) – 2.468(1) Å; Br: 2.3842(5) – 2.600(1) Å).^{31,36-38}

X-ray absorption spectroscopy (XAS) of the copper K-edge shows a rising edge shift of 1.4 eV upon oxidation of the Cu^{II}-F, Cu^{II}-Cl, and Cu^{II}-Br precursors, consistent with a more oxidized copper center (Figure 4, Figures S37-S38). The edge shift of 1-3 eV is in the range of reported values for oxidation from Cu^{II} to Cu^{III}.^{39,40} Similarly, the pre-edge features are shifted from ca. 8979 eV for the Cu^{II} species to ca. 8981 eV for the Cu^{III} complexes. The edges of both F complexes are also shifted to higher energy than the analogous Cl complexes, consistent with the shorter Cu-F bonds observed crystallographically. Lancaster and coworkers have argued that most formally copper(III) complexes have a LUMO that resides predominantly on the ligands instead of the Cu d_{x2-y2} orbital, suggesting a physical *d*-electron count higher than 8.³¹ Following the experimentally-calibrated computational approach



Figure 4. Copper K-edge X-ray absorption spectra of [TBA]LCu^{II}F (red) and LCuF (black) in CH₂Cl₂ at 10K.

employed by Lancaster, we found that the LUMOs of LCuX

ing the contribution of the inverted ligand field. These interactions can be described with a simplified molecular orbital dia-



Figure 5. (a) Localized HOMO and LUMO from the CASSCF(2 electrons, 2 orbitals) calculation of a truncated model of LCuF in which isopropyl groups are substituted with hydrogens. Orbitals are shown at an isovalue of 0.03. (b) Contributions of electronic configurations to the ground state of LCuX complexes determined by CASSCF calculations.

complexes are 62.5%, 64.8%, and 66.1% ligand-based for LCuF, LCuCl, and LCuBr, respectively (Figure S51), indicative of significant L and halide hole character.

Multireference calculations with the complete active space self-consistent field (CASSCF)⁴¹ method lend further insight into the electronic structure of the $[Cu^{III}-X]^{2+}$ unit as a function of halide identity. Some of us^{42} and others⁴³ have shown that CASSCF computations can provide valuable insights into the electronic structure of highly covalent metal-ligand interactions. An active space of 2e, 2o (2 electrons, 2 orbitals) comprised of σ bonding and antibonding interactions between the Cu d_{x2-y2} and L/halides orbitals (Figure S49) was found to be optimal for this system (see Supplementary Information). State-specific CASSCF calculations reveal that singlet LCuX complexes exhibit increasing multireference character and Cu-X covalency (Table S11) from LCuF to LCuCl to LCuBr with increasing σ^* population: 0.155 e⁻ (LCuF), 0.172 e⁻ (LCuCl), and 0.189 e⁻ (LCuBr). To assist a valence bond-like interpretation of the CASSCF wave function, the CASSCF(2,2) orbitals were localized with an intrinsic atomic orbitals (IAO) localization method. Subsequent recalculation of the CAS wavefunction permitted delineation of the LCuX CAS wavefunction as a combination of various resonance structures: Cu^{III}-X⁻, Cu^{II}-X•, and Cu^I-X⁺.⁴⁴ In the cases of LCuCl and LCuBr, the localized HOMO is ligand-centered while the LUMO is copper-centered (Figure 5a). However, the ligand field of LCuF is inverted, evidenced by the copper-centered HOMO and ligand-centered LUMO.^{30,31} Despite these differences, the leading electronic configuration of all complexes is copper(II) bound to a ligand-centered radical, denoted Cu^{II}-X• (Figure 5b). Interestingly, while the second leading configuration of LCuCl and LCuBr is Cu^{III}-X⁻, that of LCuF is Cu^I-X⁺, reflectgram (Figure 5c). In the case of LCuF, the high effective nuclear charge of formally copper(III) lowers the copper orbital energy below the SALC of F and L. Taken together, the XAS data and CASSCF calculations support that the oxidation of $[LCu^{II}X]^-$ to LCuX is well distributed over copper and ligands.

Hydrogen Atom Abstraction and Radical Capture Reactivity of [Cu^{III}-X]²⁺. The presence of fluorine radical character in LCuF motivated us to explore C(sp³)-H fluorination reactivity by the proposed HAA/RC mechanism. Furthermore, work by Mcdonald illustrated that previous biscarboxamidopyridine nickel chloride complexes is capable of performing HAA.45 To first understand how electronic structures govern HAA reactivity across the copper(III) halide series, we investigated the reaction of LCuX complexes with the hydrogen atom donor, 9,10-dihydroanthracene (DHA). Addition of 100 equivalents of DHA to LCuX complexes at -30 °C leads to their consumption with formation of anthracene as revealed by UV-Vis spectroscopy (Figure S12). To confirm that the LCu^{II} core remains intact after HAA, the reaction of LCuF with DHA was repeated in a scintillation vial. Following workup in acetonitrile, the brown-colored LCu^{II}(MeCN) complex was isolated in 84% spectroscopic yield (Figure S13). The second-order rate constant (k) of HAA was obtained by monitoring the decay of LMCT bands of LCuX (820 nm for LCuF, 920 nm for LCuCl, 980 nm for LCuBr, respectively) under pseudo-first-order conditions (see Supplementary Information). The rate of HAA from DHA for LCuF is k = $0.668 \text{ M}^{-1} \text{ s}^{-1}$, which is greater than 200 times higher than both LCuCl and LCuBr (Figure 6). The rapid rate of HAT by LCuF is intriguing considering LCuF is a weaker oxidant than LCuCl and LCuBr. Since LCuF is expected to be more basic

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Figure 6. Kinetic traces of the reaction between copper(III) halides and 9,10-dihydroanthracene (100 eq, -30 °C).

than LCuCl and LCuBr, the higher HAA reactivity of LCuF can be attributed to the underlying correlation between HAA and basicity of the complex, which was first demonstrated by Tolman's highly basic LCuOH complexes.³⁴

The difference in HAA reactivity of LCuF and LCuOH (36x higher) was further probed with an Eyring analysis $(\ln(k/T) \text{ vs } 1/T)$. Although LCuF exhibits a slightly lower activation enthalpy than LCuOH ($\Delta H^{\ddagger}(LCuF) = 3.8(2)$; $\Delta H^{\ddagger}(LCuOH) = 5.4(2)$ kcal mol⁻¹), there is a greater entropic penalty for LCuF ($\Delta S^{\ddagger}(LCuF) = -10(1)$ cal K⁻¹ mol⁻¹; $\Delta S^{\ddagger}(LCuOH) = -7.2(5)$ cal K⁻¹ mol⁻¹; see Supplementary Information). Despite LCuF being ~540 mV more oxidizing than LCuOH, the lower basicity of fluoride results in a lower HAA rate, clearly emphasizing the importance of the proton transfer over electron transfer for the overall rate of HAA from DHA by formally LCu^{III} species. In this context, it is informative to compare the HAA rate constants of LCuX with LCuOH³⁴ and LCu(O₂CR)⁴⁶ complexes. Despite the different solvents used for HAA kinetic study, a positive correlation of log(k) from HAA by LCu^{III} species with the pK_a of the ligand is observed (Figure S15). However, we recognize that basicity is unlikely to be the only contributing factor, especially as the Cu-X covalency also changes as a function of X.^{47,48}

Having established the high rate of HAA by LCuF, we were eager to explore the possibility of radical capture as the terminating step in a $C(sp^3)$ –H fluorination sequence. A common strategy to explore the capture of alkyl radical (R•) is to examine the reaction of metal complexes with carbon-centered radical precursors e.g. azo compounds and acyl peroxides.^{49,50} Heating LCuX complexes in the presence of azobisisobutyronitrile (AIBN) at 80 °C in CD₂Cl₂ results in the formation of 2-haloisobutyronitriles in 45% (LCuF), 60% (LCuCl), and 68% (LCuBr) yield, respectively (Scheme 2). In contrast, treatment of [TBA]LCu^{II}X complexes with AIBN at 80 °C for 2 hours does not furnish halogenated products, consistent with the increased hole character on halides upon oxidation of Cu^{II} to Cu^{III}. The lower yield of halogenated product for LCuF relative to LCuCl and LCuBr is likely due to its higher rate of Scheme 2. Heating azobisisobutyronitrile (AIBN) in the presence of LCuX complexes furnishes C(sp³)–X bonds



self-decomposition at 80 °C (Figure S16). These results show that discrete $[Cu^{\rm III}\text{-}X]^{2+}$ complexes mediate carbon radical capture, which has been previously proposed in copper-catalyzed C(sp³)–H halogenation reactions.^{28}

To gain insights into the mechanism of radical capture by LCuX complexes, we employed trityl radical, generated from the dissociation of Gomberg's dimer.^{51,52} Contrary to the twohundred-fold rate difference for HAA, all LCuX complexes react with trityl radical at similar rates at -80 °C. ¹H NMR analysis of the same reactions at a larger scale confirms the formation of the corresponding Ph₃C-F, Ph₃C-Cl, and Ph₃C-Br products in 86%, 79% and 72% yield, respectively (Figure 7a). Despite the similar efficiency of RC for all three LCuX complexes, there are key mechanistic differences. Careful examination of in situ UV-Vis profiles reveals that trityl radical capture by LCuCl and LCuBr proceeds through the trityl cation intermediate ($\lambda_{max} = 415$ nm), while that by LCuF does not (Figure 7b, Figure S17). This result suggests a stepwise electron transfer-halide transfer (ET-XT) mechanism for LCuCl and LCuBr and a synchronous fluorine atom transfer mechanism for LCuF. These observations are consistent with the lower redox potential and higher nucleophilicity of LCuF compared to LCuCl and LCuBr. There is ambiguity in the literature about the suitability of copper(III) versus copper(II)



Figure 7. (a) Radical capture reactivity study with triphenylmethyl radical at -80 °C reveals the intermediacy of triphenylmethyl cation for LCuCl, but not for LCuF. (b) UV-Vis traces of the reaction between LCuF and LCuCl with 1 equivalent of trityl radical (0.1mM, CH₂Cl₂, -80 °C).

Table 1. Direct C(sp³)–H fluorination by LCuF^a



^aYields determined by ¹⁹F{¹H} NMR analysis with 100 equivalents of substrate. ^bWith 16 equivalents of substrate. ^cCombined yield of branched and linear isomers. ^dAfter 64 hours.

for alkyl radical capture and whether the precise mechanism is concerted or stepwise.^{28,53} Further kinetic studies to quantitate the synchronicity of radical capture by formally copper(III) species are ongoing and will be reported in due course.

C-H Fluorination Reactivity. The proficiency of LCuF for both hydrogen atom abstraction and radical capture led us to envision the possibility of direct $C(sp^3)$ -H fluorination by a sequential HAA/RC mechanism. Treatment of LCuF with 100 equivalents of tetrahydrofuran at room temperature for 3 hours resulted in the selective formation of 2-fluorotetrahydrofuran in 69% yield based on the requirement of two LCuF complexes to furnish one fluorinated product. Fluorination of 1,4dioxane and 18-crown-6 with LCuF proceeds selectively to furnish monofluorinated products formed in 45% and 35% yield, respectively (Table 1). Fluorine atom transfer from a metal fluoride to the α -position of ether, to our knowledge, has vet to be demonstrated. Such direct fluorination by LCuF is also amenable to other activated $C(sp^3)$ -H bonds. Treatment of LCuF with allylic and benzylic substrates selectively afforded the corresponding allylic or benzylic fluorinated compounds, albeit in moderate to low yields (8 - 42%, Table 1). The low yield of benzylic substrates suggests that steric hinderance by the four iPr moieties around the [Cu^{III}-F]²⁺ unit might be detrimental to $C(sp^3)$ -H fluorination reactivity. This demonstration of C(sp³)–H fluorination, despite requiring stoichiometric amount of LCuF, suggests that copper fluoride complexes that support the Cu^{II}/Cu^{III} redox couple, in principle, are suitable for fluorination of $C(sp^3)$ -H bonds with an oxidant and F- source.

SUMMARY AND CONCLUSIONS

In summary, we have synthesized a series of formally copper(III) halide complexes, LCuX (X = F, Cl, Br), by the use of halide (X⁻) sources and an oxidant. The electronic structure of these species, as shown by a suite of spectroscopic and computational techniques, features significant halogen radical character, which relates to their ability to perform hydrogen atom abstraction and radical capture. Expanding on these insights, LCuF was employed for the direct fluorination of a variety of alkyl substrates with allylic and benzylic C-H bonds as well as α -C-H bonds of ethers. With the establishment of a radical capture mechanism at a copper(III) fluoride center, the use of tunable copper complexes, in principle, can provide further practicality and generality to C(sp³)-H fluorination, i.e. regioselectivity and stereoselectivity.

Our demonstration of C(sp³)-H fluorination with LCuF adds to the growing list of formally copper(III) intermediates in biological^{54,55} and abiological^{56,57} copper-mediated carbonheteroatom bond-forming reactions. Conceivably, the generality of this Cu^{II}/Cu^{III} C(sp³)-H functionalization paradigm relies on the ability of LCuX to abstract H atoms (depending on pK_a) and capture R• (depending on redox potential, $E_{1/2}$). Therefore, an interesting mechanistic question arises from the inverse correlation of pK_a and $E_{1/2}$ of LCuX – can the LCuX complex be efficient at RC and HAA at the same time? As shown by our study, the efficiency of R• capture remains high even with less oxidizing LCuX, e.g. LCuF. Albeit through two different mechanisms (concerted for LCuF, stepwise ET-XT for LCuCl and LCuBr), the high proficiency of RC at different LCuX raises the possibility of realizing other mechanistically related C(sp³)–H functionalization with [Cu^{III}-X]²⁺ species.

ASSOCIATED CONTENT

The Supporting information is available free of charge on the ACS Publications website at DOI:.

Experimental details, including characterization data, spectra, kinetic data, computational procedures and results.

Crystallographic data for [PPN]LCu^{II}F (1985735) Crystallographic data for [TBA]LCu^{II}Cl (19857356) Crystallographic data for [TBA]LCu^{II}Br (1985737) Crystallographic data for LCuF (1985738) Crystallographic data for LCuCl (1985739) Crystallographic data for LCuBr (1985740)

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AUTHOR CONTRIBUTION

Notes

The authors declare no competing financial interest.

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