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Operando X-ray absorption and EPR evidence for a single electron redox process in copper catalysis†

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An unprecedented single electron redox process in copper catalysis is confirmed using *operando* X-ray absorption and EPR spectroscopies. The oxidation state of the copper species in the interaction between Cu(II) and a sulfinic acid at room temperature, and the accurate characterization of the formed Cu(I) are clearly shown using *operando* X-ray absorption and EPR evidence. Further investigation of anion effects on Cu(II) discloses that bromine ions can dramatically increase the rate of the redox process. Moreover, it is proven that the sulfinic acids are converted into sulfonyl radicals, which can be trapped by 2-arylacrylic acids and various valuable β-keto sulfones are synthesized with good to excellent yields under mild conditions.

Copper is an essential trace element for nearly all aerobic organisms. Multi-copper oxidases (MCOs), for example, are encoded in genomes and play a critical role in the physiology of essentially all aerobes, including metal metabolism and O_2-reduction.[1] Copper has also been extensively used as a catalyst for the synthesis of organic and inorganic compounds,[2] polymers,[3] biomaterials[4] *etc.* Although copper-assisted chemistry has many important applications and is widely researched, the majority of studies are devoted to methodology development, rather than a detailed mechanistic understanding of the catalyst structure, the oxidation states and the effect of ligands on rate and selectivity. The lack of fundamental understanding has limited further developments.

Catalysis is the key technology for organic synthesis, and insight into the nature of the catalytic species has become particularly important in chemical manufacture.[5] Until now, unambiguous identification of the oxidation states and structures of the catalytic species under realistic conditions was a major obstacle for mechanistic studies.[6] As a result, redox states of +1/+3, +1/+2 and 0/+2, have been proposed for Cu catalyzed reactions, often with limited experimental evidence.[2] As is well known, the active metal undergoes oxidation and reduction half reactions in a catalytic cycle. Oxidation of low valent copper, for example, oxidation of copper(I) to copper(II), has been extensively investigated for more than one century, particularly the oxidation of copper(I) by molecular oxygen due to its importance in chemistry and biology.[7] While Cu(I) oxidation has been well studied, the reductive half reaction and factors that influence the Cu(II) reducibility are less well understood and remain rudimentary,[1,8] which has been the main barrier for the development of new catalytic processes. Herein, we communicate a direct observation of the reduction of Cu(II) by a sulfinic acid at room temperature. A single electron transfer from a sulfinic acid to Cu(II) and the formation of Cu(I) are demonstrated using X-ray absorption and electron paramagnetic resonance spectroscopies.

The reaction between benzenesulfinic acid and Cu(II) under an inert atmosphere was initially monitored by electron paramagnetic resonance (EPR). As shown in Fig. 1, upon addition of excess benzenesulfinic acid to a DMF solution of $CuBr_2$, the EPR signal of Cu(II) disappears rapidly at room temperature, suggesting that diamagnetic copper(I) has formed.[9] This interesting phenomenon spurred us to investigate what really happened in the process.

To identify the variation of the valence states of copper in the solution, this reaction was also studied using X-ray absorption near-edge structure (XANES) spectroscopy. Initially, the XANES spectrum of the DMF solution of $CuBr_2$ gave a spectrum with a small pre-edge energy peak at 8977.3 eV, which is typical of Cu(II) compounds (Fig. 2, blue line).[8c,10] However, when benzenesulfinic acid was added at room temperature, a new Cu species with an edge energy of 8981.3 eV was observed (Fig. 2, red line), confirming that Cu(II) was reduced to Cu(I) during the reaction.[8c,10] These results provided direct evidence that the sulfinic acid reduces Cu(II) through a single electron redox process.

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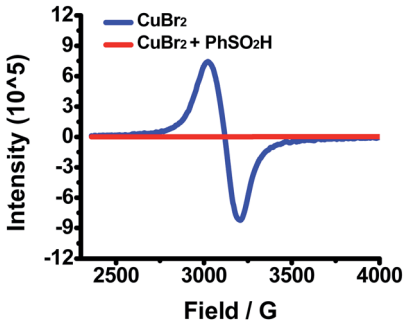


Fig. 1 Blue line: $CuBr_2$ (0.4 mmol) in DMF (4.0 mL) at r.t. under N_2; red line: $CuBr_2$ (0.4 mmol) and benzenesulfinic acid **2a** (0.80 mmol) in DMF (4.0 mL) kept at r.t. for 5 min under N_2.

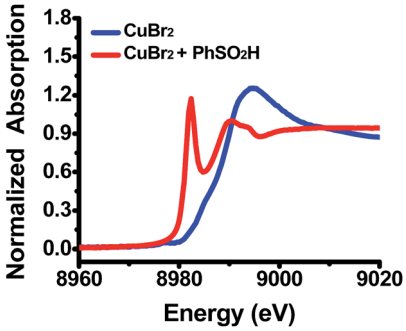


Fig. 2 Blue line: $CuBr_2$ (0.4 mmol) in DMF (4.0 mL) at r.t. under N_2; red line: $CuBr_2$ (0.4 mmol) and benzenesulfinic acid (0.80 mmol) in DMF (4.0 mL) kept at r.t. for 5 min under N_2.

Furthermore, in order to determine the number and types of ligands on Cu(I), an EXAFS spectrum of the Cu(I) species was next fitted. The k^3-weighted R-space EXAFS spectrum shows that the Cu^I center was coordinated to two Br ligands with an average distance of 2.24 Å (Fig. 3). The Cu(I) species, therefore, was assigned as diBr anion complex $[Cu^IBr_2]^{-1}$.

XANES spectra was also applied to explore the influence of different factors which affect the reduction of Cu(II). It was found that the choice of solvent has only a slight influence, and that the reduction of $CuBr_2$ proceeds in polar solvents, such as DMF, or low-polar solvents including MeCN and THF at room temperature (Fig. 4A). While the solvent has little effect on the reducibility, the type of anion is very important. For example, $Cu(OAc)_2$ shows little reduction at room temperature (Fig. 4B, red line), and reduces only slightly at 80 °C (Fig. 4B, green line). Addition of a stoichiometric amount of LiBr, however, leads to rapid reduction of $Cu(OAc)_2$ with benzenesulfinic acid even at room temperature (Fig. 4B, blue line, edge energy is 8981.6 eV).[8c,10]

The influence of Br^- ions on the reducibility of $Cu(OAc)_2$ was also investigated using EPR spectroscopy. As shown in Fig. 5, $Cu(OAc)_2$ exhibits a very weak EPR signal in DMF, which is consistent with being present as an EPR-silent paddlewheel dimer.[9] However, once LiBr was added to the $Cu(OAc)_2$ solution, a strong EPR signal was observed, which increased in intensity with increasing amounts of LiBr. The addition of LiBr appears to dissociate $Cu(OAc)_2$ into mononuclear Cu(II) species.[9,11] More importantly, upon addition of benzenesulfinic acid to the solution of $Cu(OAc)_2$ and LiBr, the Cu(II) EPR signal disappeared immediately and as shown by the XANES spectrum in Fig. 4B, Cu(I) is formed concurrently. These results suggest that coordinative saturation of $Cu(OAc)_2$ and the inability for substrate coordination may be the obstacle to Cu(II) reduction by benzenesulfinic acid.

Based on the above results, it appears likely that the sulfinic acid serves as the one electron donor for reduction of Cu(II) to Cu(I) with formation of oxidized sulfonyl radicals. If true, it is

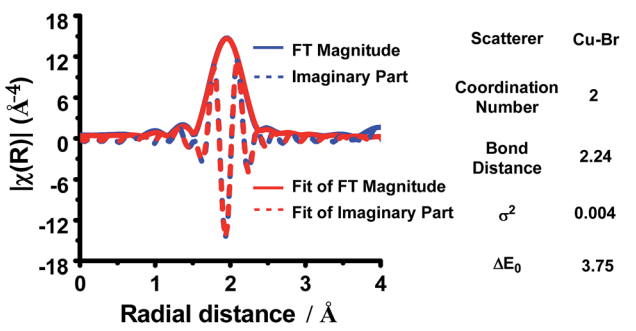


Fig. 3 k^3-Weighted R-space EXAFS spectrum of the solution of the reaction of $CuBr_2$ (0.4 mmol) and benzenesulfinic acid (0.80 mmol) in DMF (k-range: 2.93–13.67 $Å^{-1}$; R-range: 1.40–2.50 Å).

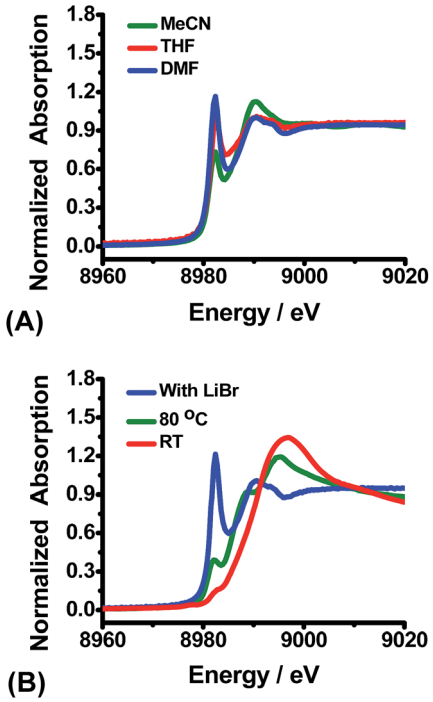


Fig. 4 (A) $CuBr_2$ (0.4 mmol) and benzenesulfinic acid (0.80 mmol) in different solvents (4.0 mL) kept at r.t. for 5 min under N_2; green line: MeCN; red line: THF; blue line: DMF. (B) $Cu(OAc)_2$ (0.4 mmol) and benzenesulfinic acid (0.80 mmol) in DMF (4.0 mL) reacted under different conditions; red line: r.t.; green line: 80 °C (the precipitate of the reaction); blue line: LiBr (1.2 mmol) was added at r.t.

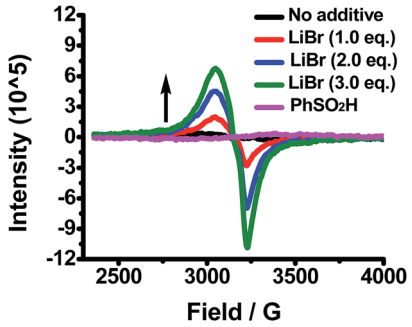
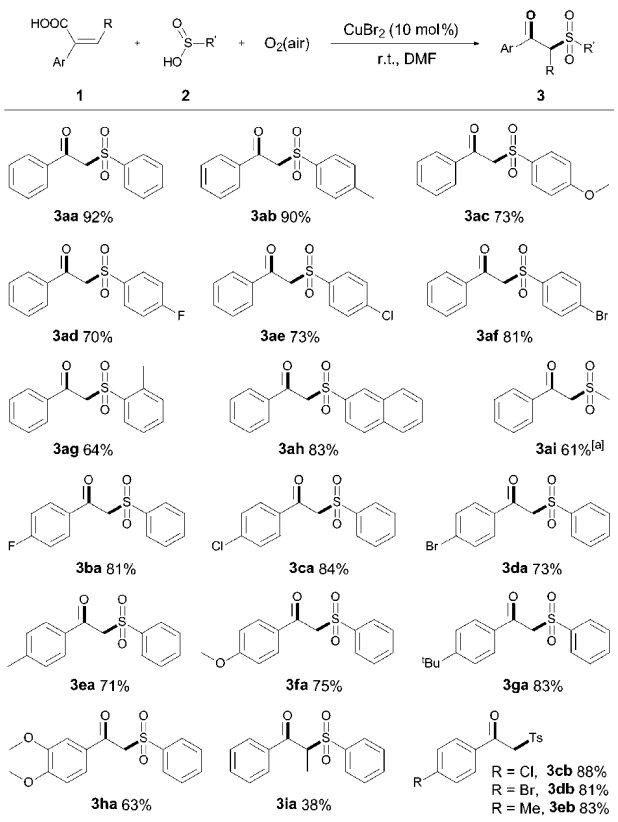


Fig. 5 LiBr (0.4 mmol) × 3 and $PhSO_2H$ (0.80 mmol) were successively added to the DMF (4.0 mL) solution of $Cu(OAc)_2$ (0.4 mmol) at r.t. under N_2.

reasonable to expect that a catalytic redox process could be used for the synthesis of fine chemicals with suitable radical acceptors. When 2-arylacrylic acid was reacted with $CuBr_2$/sulfinic acid, the product β-keto sulfones **3** could be isolated in good to excellent yields at room temperature under air (Scheme 1).

As shown in Scheme 1, a variety of aryl sulfinic acids, bearing either electron-donating groups (R = OMe, Me) or electron-withdrawing groups (R = F, Cl, Br) on the aryl ring, reacted smoothly with 2-phenylarcylic acid, affording the corresponding β-keto sulfones **3ab–3ah** in good to excellent yields. Alkyl sulfinic acids, as exemplified by methyl sulfinic acid, also efficiently reacted with **1a** and the product **3ai** was obtained in 61% yield. Besides, the arylacrylic acids, with either electron-rich or electron-poor substituents on the aromatic ring, were all compatible with this transformation, leading to the corresponding decarboxylative products in good yields (**3ba–3ha**). Non-terminal arylacrylic acid derivatives, such as α-ethylidene benzeneacetic acid, exhibited relatively low reactivity and the product **3ia** was afforded in moderate yield, presumably due to the steric hindrance from the pyramidal structure of the sulfonyl radical.[12] Arylacrylic acids containing chloro, bromo and methyl groups also reacted effectively with *p*-toluenesulfinic acid, offering the expected products **3cb–3eb** in high yields (81–88%). Furthermore, ^{18}O labeling experiments indicated that the carbonyl oxygen in the β-keto sulfones comes from dioxygen (for details, see ESI†). To the best of our knowledge, this is the first example of the combination of S–H bond alkylation, C–C σ bond cleavage, and aerobic oxygenation in a single step.[13] These results not only serve as indirect evidence to support the formation of the sulfonyl radical *in situ*, but also provide a useful insight into the mechanism of Cu(II) reduction and further synthetic applications.



Scheme 1 Unless otherwise specified, all reactions were carried out using **1** (0.20 mmol), **2** (0.60 mmol), and $CuBr_2$ (0.02 mmol) in DMF (2.0 mL) under air for 2 h at room temperature. Isolated yields shown. [a]Methanesulfinic acid sodium salt (0.6 mmol) and TsOH (0.6 mmol) were employed.

Conclusions

In conclusion, X-ray absorption and electron paramagnetic resonance spectroscopies provide direct evidence for the single electron redox process between sulfinic acids and Cu(II), forming Cu(I) and a sulfonyl radical at room temperature. Addition of bromide ions increases the rate of Cu(II) reduction. Based on these observations, catalytic oxysulfonylation of arylacrylic acids under simple and mild conditions was developed for the first time. Ongoing research including further mechanistic details and expanding the substrate scope is currently underway.

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