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. Copper has also been extensively used as a catalyst for the synthesis of organic and inorganic compounds, polymers, biomaterials 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. Until now, unambiguous identification of the oxidation states and structures of the catalytic species under realistic conditions was a major obstacle for mechanistic studies. As a result, redox states of +1/2, +1/2 and 0/2, have been proposed for Cu catalyzed reactions, often with limited experimental evidence. 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. 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, 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 benzenesulfonic 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. 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). However, when benzenesulfonic 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. These results provided direct evidence that the sulfinic acid reduces Cu(II) through a single electron redox process.
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$^+$ 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 [CuIBr$_2$].

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 benzenesulfonic acid even at room temperature (Fig. 4B, blue line, edge energy is 8981.6 eV). 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. More importantly, upon addition of benzenesulfonic 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 coordinate saturation of Cu(OAc)$_2$ and the inability for substrate coordination may be the obstacle to Cu(II) reduction by benzenesulfonic acid.

Based on the above results, it appears likely that the sulfonic 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
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smoothly with 2-phenylacrylic acid, affording the corresponding \( \beta \)-keto sulfones \( 3ab-3ah \) in good to excellent yields. Alkyl sulfonic acids, as exemplified by methyl sulfonic acid, also efficiently reacted with \( 1a \) and the product \( 3ai \) was obtained in 61% yield. Besides, the arylocrylic acids, with either electron-rich or electron-poor substituents on the aromatic ring, were all compatible with this transformation, leading to the corresponding decarboxylation products in good yields \( (3ba-3ha) \). Non-terminal arylocrylic acid derivatives, such as \( \alpha \)-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.\(^{12}\) Arylocrylic acids containing chloro, bromo and methyl groups also reacted effectively with \( p \)-toluene-sulfonic acid, offering the expected products \( 3cb-3eh \) in high yields \( (81–88\%) \). Furthermore, \(^{18}O\) labeling experiments indicated that the carbonyl oxygen in the \( \beta \)-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 \( \sigma \) 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 \( \textit{in situ} \), but also provide a useful insight into the mechanism of Cu(II) reduction and further synthetic applications.

Conclusions

In conclusion, X-ray absorption and electron paramagnetic resonance spectroscopies provide direct evidence for the single electron redox process between sulfonic acids and Cu(II), forming Cu(II) 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 arylocrylic 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.

Acknowledgements

This work was supported by the 973 Program [2012CB725302], the National Natural Science Foundation of China [21390400, 21025206, 21272180, and 21302148], the Research Fund for the Doctoral Program of Higher Education of China [20120141130002] and the Ministry of Science and Technology of China [2012QY120060]. The Program of Introducing Talents of Discipline to Universities of China (111 Program) is also appreciated. Use of the Advanced Photon Source was supported by the U. S. Department of Energy, Office of Basic Energy Sciences, under contract no. DE-AC02-06CH11357. MRCAT operations are supported by the Department of Energy and the MRCAT member institutions.

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Fig. 5 LiBr (0.4 mmol) \( \times 3 \) and PhSO\(_2\)H (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\(_2\).

Scheme 1 Unless otherwise specified, all reactions were carried out using \( 1 (0.20 \text{ mmol}) \), \( 2 (0.60 \text{ mmol}) \), and CuBr\(_2\) (0.02 mmol) in DMF (2.0 mL) under air for 2 h at room temperature. Isolated yields shown. *Methanesulfonic acid sodium salt (0.6 mmol) and TsOH (0.6 mmol) were employed.
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13 A tentative pathway for the oxysulfonylation of 2-arylacrylic acids is proposed in Scheme S1†.