Evidence of two-state reactivity in alkane hydroxylation by Lewis-acid bound copper–nitrene complexes†

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The behavior of the Lewis-acid adducts of two copper–nitrene [Cu(NR)]+ complexes in nitrene-transfer and H-atom abstraction reactions have been demonstrated to depend on the nature of the nitrene substituents. Two-state reactivity, in which a singlet ground state and a nearby triplet excited-state both contribute, provides a useful model for interpreting reactivity trends of the two compounds.

Copper-nitrene intermediates have attracted much interest in organometallic chemistry because they are implicated as key intermediates in the copper catalyzed alkane hydroxylation and alkene epoxidation reactions.1–9 To engineer further improved catalysts, there is a substantial impetus to characterize fully the active species of existing catalysts, including the relevant higher oxidation states, intermediates and transition states so as to establish the mechanism(s) by which they affect C–N bond formation reactions. However, despite considerable interest, no copper–nitrene intermediates have been isolated to allow for clear mechanistic studies.9,10 In the absence of isolated examples of the proposed active intermediate, the mechanisms of copper–nitrene mediated aziridination and amination reactions have been elucidated by high-level quantum chemical calculations.1–3,7–8 In these calculations two alternative, limiting, electronic valence-bond structures have been characterized, namely, (closed-shell singlet) [CuIII(NR)]+ or (open-shell triplet or singlet) [CuII(NR*)]+ structures. While concerted aziridination reactions have been proposed to be favored on the closed-shell [CuIII(NR)]+ singlet surface, amination reactions were suggested to proceed via a stepwise H-atom abstraction/radical rebound (HAT/RR) pathway on the [CuII(NR*)]+ triplet surface.1 Moreover, in cases where the singlet and triplet states were very close in energy, a mechanistic picture involving both the singlet and triplet pathways for the aziridination7 and amination1 reactions has also been proposed.

What is required to test the theoretically predicted reactivity patterns is more direct experimental evidence that systematically shows the effect of singlet/triplet splitting energy on the reactivity of a copper–nitrene species. Very recently, our group reported the spectroscopic characterization of a Lewis-acid adduct of a cationic copper-tosyl nitrene [CuII(NTs*)Sc(OTf)3]+ species (1; Ts = tosyl; Scheme 1), the electronic structure of which could be best described in terms of a Cu(n) ion antiferromagnetically coupled to a nitrene radical thereby stabilizing an open-shell singlet ground state.11 Reactivity studies revealed that this species aminates sp3 C–H bonds in substrates such as toluene and even cyclohexane in modest yields (21–35%). In this communication we now report the Lewis-acid stabilization of a related copper–nitrene species [CuIII(NMes*)-Sc(OTf)3]+ (2; Mes = mesityl; Scheme 1), where the electron withdrawing heteroatom Ts nitrene substituent of 1 is replaced by the electron donating Mes group in 2. A comparative reactivity study between 1 and 2 shows that a two-state reactivity (TSR) model12,13 applies for the two compounds, in which a singlet ground state and a nearby triplet excited-state both contribute to the reactivity.

Scheme 1 DFT optimized structures of 1 and 2 in their ground singlet states. Triflates bound to scandium and the hydrogen atoms are not shown for clarity.

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Complex 2 is synthesized following the same procedure we reported previously for 1; the only difference is that we have now used an organic azide as a nitrene source in contrast to imidinoamine for the synthesis of 1. Thus the reaction of the previously synthesized [Cu(L1)][BF4] complex (L1 = 3,3′-iminobis(N,N-dimethylpropylamine)) in CH2Cl2 with one equivalent of mesityl azide at -90 °C in presence of 1.5 equivalent of scandium triflate for two hours generates the purple complex 2 with absorption maxima λmax(εmax) centered at 560 nm (2000 L mol⁻¹ cm⁻¹) and 670 nm (1227 L mol⁻¹ cm⁻¹) (Fig. 1). Total consumption of the azide in the reaction was confirmed by the disappearance of the v(N3) stretch at 2123 cm⁻¹ in the IR spectrum of the resultant solution of 2 (Fig. S1, ESI†). Notably, the UV-Vis spectral changes associated with the formation of 2 are similar to that previously observed during the formation of 1; the corresponding bands for 1 are at 530 nm (3500 L mol⁻¹ cm⁻¹) and 750 nm (580 L mol⁻¹ cm⁻¹), respectively (Fig. 1). 1H-NMR resonances of 2 are spread over a chemical shift range of 0 to +10 ppm, thereby, demonstrating a chemical shift range of 0 to +10 ppm, thereby, demonstrating a contrast to the previous report of a distorted square pyramidal (SP) geometry in 1, which may indicate the formation of Cu(I). Second order rate constants (k2; Table 1) for 2 were determined from the dependence of the first-order rate constants on substrate concentrations and then compared with the reported values for 1. A contrasting reactivity pattern is apparent (Table 1), in which complex 2 is a better NT oxidant, while complex 1 is a better HAT agent.

DFT calculations (Fig. S6–S9 and Tables S1–S5, ESI†) were carried out to understand the effect of the nitrene substituent on the reactivity of the [L1Cu(NR)Sc(OTf)3]⁺ (R = Ts for 1 and Mes for 2) complexes. Broken symmetry (BS) solutions were obtained for both 1 and 2. For 2 the calculated ground state is an open-shell [CuI(NMes*)]⁺ singlet with the excited triplet state lying 14.2 kcal mol⁻¹ higher in energy (Table S1, ESI†). For complex 1 the calculated ground state is also an open-shell singlet [CuI(NTs*)]⁺ singlet; the excited BS triplet state (Table S1, ESI†) was, however, found to be only 2.5 kcal mol⁻¹ higher in energy. The smaller singlet-triplet gap of 1 is consistent with a recent DFT study on Ni-nitrene complexes, which predicted that singlet ground states are favored when aryl/alkyl groups are on the nitrene, while the triplet is favored with electron withdrawing heteroatom groups.

![Absorption spectra of [Cu(L1)][BF4] and [Cu(L1)][BF4] 2 (Fig. 1)](image-url)
The optimized geometry of 2 in the experimentally observed singlet ground state reveals a three-coordinate TP geometry (Scheme 1; Fig. S8 and Table S4, ESf) fully consistent with the Cu K-edge XAS study; the ligand L1 acts as a bidentate ligand with one of the terminal tertiary amine nitrogen atoms remaining outside of the coordination sphere of Cu. For 1 (Scheme 1; Fig. S6 and Table S2, ESf), in contrast, a SP geometry at copper is predicted for the BS singlet state, with a $^{13}$NO binding mode of the tosyl nitrene ligand, consistent with the results of the previous calculations.\(^{8,11,12}\) Notably, the calculated Cu–N distance (Table S1, ESf) in 1 of 1.95 Å is significantly longer than the calculated distance for 2 of 1.84 Å, in their ground singlet states, thereby implying a more covalent Cu–N bond in 2.

Our DFT results provide a basis for interpreting the reactivity properties of 1 and 2 using a two-state reactivity model. In 1, the triplet state with a low activation barrier\(^{4}\) for HAT is low lying and easily accessible, which accounts for the higher HAT reactivity of 1 than 2. The NT reaction, in contrast, is thought to proceed predominantly on the singlet surface;\(^{8}\) the higher reactivity of 2 can then be possibly explained by the greater electrophilicity of the copper–nitrile unit in 2, owing to the larger contribution of the $[\text{Cu}^{2}\text{(NR)}]\) valence-bond resonance form compared to 1.

In summary, we have demonstrated that the behavior of $[\text{L}1\text{Cu(NR)Sc(OTf)}]^{\text{+}}$ (R = Ts for 1 and Mes for 2) complexes in both nitrene-transfer and H-atom abstraction reactions depends on the nature of the nitrene substituent. Interestingly, whereas complex 2 is a better nitrene-transfer reagent than 1, an opposite reactivity trend is apparent for the H-atom abstraction reactions. DFT calculations provide a plausible framework within which to rationalize these reactivity patterns. It is postulated that the observed HAT reactivity reflects the availability of two closely lying spin states for 1 and 2, the so-called TSR hypothesis,\(^{12,13}\) wherein the excited triplet state has a much lower reaction barrier than the ground singlet state. Thus, the tosyl substrate of 1 results in a decrease in the singlet–triplet gap and an increased participation of the triplet state in determining the rate of reaction. Hence, in this study we provide evidence that the TSR theory, well established for iron-oxo complexes,\(^{15,26}\) may also provide a framework for understanding reactivity of copper–nitrenes. This study may therefore be of extreme importance in understanding the reactivity of mononuclear copper monoxygenases,\(^{27–30}\) where copper-oxo intermediates, which are isoelectronic to the presently described copper–nitrile species, have often been implicated as the active species responsible for oxidations.

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### Notes and references

10. A copper bis nitrene complex has been structurally characterized (F. Delfmann, D. M. Andradia, G. Frenking and G. Bertrand, *J. Am. Chem. Soc.*, 2014, 136, 3800–3802), but no reactivity study is reported.
15. Complex 2 is EPR silent. However, when the reaction is performed in the absence of scandium a new species 3 is formed which shows a typical Ce(II) (EPR signal (Fig. S10, ESf)) Although further characterization of 3 is not performed we assign it to the copper(II)–amidate complex $[\text{L}1\text{Cu}^{2}\text{HNMe}_{2}]$ based on our previous study.