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Identification and Characterization of Monoanionic Tripodal Tetradentate Ligand Complexes of Copper(I) and Copper(II) Involved in Halogen Atom Transfer Reactions

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Copper(I) complexes with polydentate amine ligands play important roles as models for metalloproteins[1] and as catalysts for organic transformations[2,3] and polymerizations.[4,5] A principal mode of reactivity of these complexes is the promotion of halogen atom transfer from an organic halide to yield a free radical that can undergo further addition, coupling, or disproportionation reactions. Selectivity for addition processes frequently is achieved via the persistent radical effect, in which initial radical coupling serves to build up a concentration of copper(II) complex such that the rate at which the radicals are deactivated in a reverse atom transfer step becomes faster than the rate at which the radicals can couple or disproportionate.[6,7] Atom transfer radical polymerization (ATRP) is an example of a polymerization process that functions via such copper(I/II) atom transfer chemistry.[4,5]

The solution structures and fundamental reactivities of the copper centers that promote atom transfer are just beginning to be understood, so direct structure−activity relationships have not been elucidated for these catalyst systems. Deeper insight into the structure, solution dynamics, and chemistry of the copper centers involved in halogen atom transfer would allow for rational design of catalysts for selective transformations. Such studies demand a catalyst system in which the structures and properties of both the copper(I) and copper(II) centers are known. Because the copper(I) ion has a d^{10} electronic configuration, its complexes are labile, and their solution structures can be complex, varying with changes in solvent, temperature, and ligand concentration.

We proposed that a monoanionic, tripodal tetradentate ligand design for copper(I) ions would have structural stabilization properties, such as the chelate effect and ligand−metal electrostatic attraction, that would lead to simplified solution structures.[8,9] Since then, advances have been made toward developing ligand systems that permit the identification and characterization (in solution and the solid state) of the copper(I) and copper(II) complexes involved in halogen atom transfer reactions.[10,11] Here, we report the synthesis and characterization of copper(I) and copper(II) complexes of bis-(2-(2-pyridyl)-ethyl)-(2-(*N*-*p*-toluenesulfonamido)-ethyl)amine (PETAEA) and evidence that these complexes are the primary copper complexes involved in the atom transfer catalytic cycle.

The ligand, PETAEA, was designed to be tetradentate, monoanionic with a soft donor that has a relatively low pK_a, and contain π-accepting pyridyl rings that would help stabilize the +1 oxidation state of copper. PETAEA was synthesized via the Michael addition of mono-*N*-(*tert*-butoxycarbonyl)-ethylenediamine to 2 equiv of 2-vinylpyridine. Removal of the *tert*-butoxycarbonyl protecting group followed by reaction of the primary amine with *p*-toluenesulfonyl chloride produced PETAEA in good yield. Treatment of PETAEA with sodium hydride followed by addition of CuCl yielded complex **1**, which was obtained as red-orange crystals after separation from a colorless precipitate. Elemental analysis confirmed the empirical formula, Cu(PETAEA), and ^{1}H NMR and ^{13}C {^{1}H} NMR spectra confirmed the presence of the deprotonated ligand in the complex. Crystals of complex **1** suitable for X-ray crystallography were grown from saturated solutions of CH_3CN, and the molecular structure of the complex is shown in Figure 1.

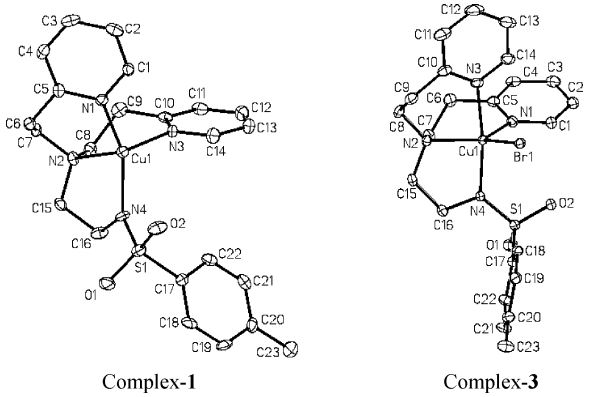


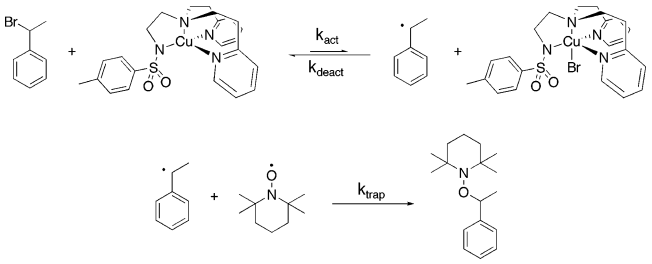
Figure 1. X-ray structure of Cu(I)(PETAEA), complex **1** (left), and X-ray structure of Cu(II)Br(PETAEA), complex **3** (right).

Key features of the structure of complex **1** include a distortion of the coordination sphere away from tetrahedral geometry, as the copper center sits closest to the tetrahedron face comprised of the three pendant donor nitrogen atoms. This distortion can be attributed to the fact that the ethylene bridges from the central nitrogen to the pendant donor groups are not sufficiently long to allow for an ideal 109.5° bite angle (the average was 92°). The Cu−N bond lengths are within the range normally found for copper(I) complexes. The lack of a halide or other counterion indicated that the sulfonamide group was deprotonated. Variable-temperature ^{1}H NMR spectra recorded up to 90 °C in the presence and absence of weakly coordinating functional groups (i.e., ethyl acetate and pyridine) normally found in ATRP monomers did not show either changes in spectral line widths or significant shifts in the positions of the signals. While these results were negative, they suggested that the dynamic solution structure of complex **1** under the conditions studied does not involve ligand exchange, ligand dissociation, or monomer coordination processes.

Evaluation of complex **1** as an atom transfer catalyst was accomplished via ATRPs of styrene and methyl methacrylate (MMA). Both polymerizations were conducted using 200:1:1 molar ratios of monomer:initiator (1-phenylethyl bromide (1-PEBr) for styrene and ethyl 2-bromo-2-methylpropionate for MMA):complex **1**, 60% solvent by volume, and temperatures of 110 °C for styrene and 80 °C for MMA. The polymerization times to reach yields of 72% (styrene) and 77% (MMA) were comparable to those reported for CuBr/2dNbipy-catalyzed ATRPs (480 min for styrene and 60 min for MMA).[12,13] The final molecular weights were 2.37×10^4 for styrene and 2.79×10^4 for MMA, while the molecular weight

10.1021/ja045003g CCC: $27.50

Scheme 1



distributions were narrow (1.14 and 1.09, respectively). However, the experimental molecular weights were 50−60% higher than expected (1.50×10^4 for styrene and 1.56×10^4 for MMA), possibly indicating inefficient initiation. Nevertheless, the data did show that complex **1** was an excellent first generation catalyst for ATRP.

Because complex **1** showed good activity for ATRP and its solid state and solution structures appeared to be similar, its atom transfer equilibrium chemistry was investigated further. When 2 equiv of 1-PEBr were added to complex **1** in the presence of 1.1 equiv of 2,2,6,6-tetramethylpiperidinyl-1-oxy (TEMPO) (Scheme 1), the orange solution turned emerald green.

The formation of the TEMPO adduct of the 1-phenylethyl radical was confirmed by the presence of its molecular ion signal in the ESI-MS spectrum of the product solution. The UV−vis absorption for complex **1** at 370 nm ($\epsilon = 2711\ M^{-1}\ cm^{-1}$) disappeared, and new absorptions appeared at 400 ($\epsilon = 463\ M^{-1}\ cm^{-1}$), 498 ($\epsilon = 102\ M^{-1}\ cm^{-1}$), and 652 ($\epsilon = 110\ M^{-1}\ cm^{-1}$) nm. A clear isosbestic point was observed in overlay plots of the UV−vis spectra taken at varying degrees of conversion, indicating that no intermediate was involved in the conversion of complex **1** into a new copper(II) complex, complex **2**. This result was also consistent with literature conclusions that the mechanism of Cu(I) ATRP does not involve organometallic intermediates or outer-sphere electron transfer.[5]

EPR spectra of this solution of complex **2** showed values of $g(||) = 2.256$, $g(\perp) = 2.032$, and $A(||) = 159$ G, which are consistent with data found for other trigonal bipyramidal complexes of copper(II) with nitrogen-based ligands. Typically, hyperfine coupling to the copper nucleus would result in a four-line signal for $A(||)$, but only three were discerned in the spectrum. This observation may be due to a significant rhombic distortion of coordination geometry that is seen in the X-ray crystal structure of an independently prepared complex (vide infra).[14]

A copper(II) complex of PETAEA was prepared by adding a solution of the deprotonated ligand to a suspension of anhydrous $CuBr_2$ in CH_3CN. The green solution was filtered from the white precipitate and cooled, and green crystals formed, complex **3**. Elemental analysis confirmed the empirical formula of the complex, Cu(PETAEA)Br. Crystals of complex **3** suitable for X-ray crystallography were grown from saturated solutions of CH_3CN, and the molecular structure of the complex is shown in Figure 1. Key features of this structure include a rhombic distortion of the trigonal bipyramidal coordination geometry due to the constraining lengths of the ethylene-bridge arms. The bromide ligand occupies an axial position. The lack of a second bromide or other counterion indicates that the sulfonamide group is deprotonated.

The spectroscopic signatures of complex **3** matched those found for complex **2**: UV−vis signals at 400 ($\epsilon = 931\ M^{-1}\ cm^{-1}$), 498 ($\epsilon = 188\ M^{-1}\ cm^{-1}$), and 652 ($\epsilon = 217\ M^{-1}\ cm^{-1}$) nm and an EPR signal with $g(||) = 2.259$, $g(\perp) = 2.032$, and $A(||) = 159$ G (three-line hyperfine coupling pattern). Furthermore, we were able to grow crystals of complex **2** from the final reaction mixture, and X-ray analysis showed that the unit cell of this compound was identical to that of complex **3**. The match between characterization data for complexes **2** and **3** strongly indicated that the two species were identical.

Identification of all the species formed in Scheme 1 permitted a kinetic study of the process. The conversion of 1-PEBr into 1-phenylethyl TEMPO was monitored using LC-MS and under reaction conditions in which complex **1** was present in a 10-fold excess relative to 1-PEBr. The kinetics could be analyzed using a rate law based on a mechanism consisting of a fast equilibrium step followed by a fast, irreversible trapping step (Scheme 1). A plot of k_{obs} versus the initial concentration of complex **1** yielded a linear fit with a slope from which k_{act} could be extracted ($1.7 \pm 0.2 \times 10^{-2}\ M^{-1}\ s^{-1}$). The reaction was repeated, but the ratio [complex **3**]$_o$/[[TEMPO]$_o$ was varied, and [complex **1**]$_o$ was kept constant and in excess of [1-PEBr]$_o$. A plot of $1/k_{obs}$ versus [complex **3**]$_o$/[[TEMPO]$_o$ yielded a linear fit with a slope from which k_{deact} could be extracted ($3 \pm 3 \times 10^8\ M^{-1}\ s^{-1}$). These kinetic values were of a similar order of magnitude as the CuBr/2dNbipy/1-PEBr system.[15] Along with the characterization data, the kinetic studies supported the conclusion that the mechanism of atom transfer follows the steps outlined in Scheme 1 with no other intermediates.

We note that complexes **1** and **3** represent a unique ATRP catalyst system in which the structures of each species involved in atom transfer is known with a high degree of certainty. Specific structural parameters such as the addition of electron-withdrawing/donating groups at various points of the complex, chelate bite angles, and donor atom types can now be modified systematically so that direct structure−reactivity relationships can be probed.

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Supporting Information Available: Experimental procedures, characterization data, and crystallographic data for complexes **1** and **3** and experimental procedures and data for polymerizations, reactions, and reaction kinetics using complex **1** (PDF, CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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