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Enhanced Reactivity of Copper Catalysts for Olefin Aziridination by Manipulation of Ligand Denticity

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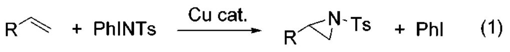
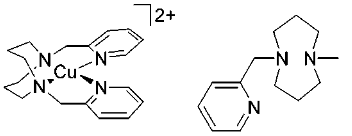
The ability to modulate the reactivity of a transition metal catalyst by altering the supporting ligand's molecular architecture is one of the most attractive features of homogeneous catalytic systems. Contemporary ligand designs are often directed toward improving selectivity in metal-mediated organic reactions; however, optimizing the productivity (yield) and rate of a catalytic process are equally important goals.[1] We have initiated a systematic investigation of ancillary ligand effects on the copper-mediated aziridination of olefins by the iminoiodinane PhINTs (eq 1), a reaction that is applicable to the synthesis of a wide variety of synthetically versatile aziridines from inexpensive alkene feedstocks,[2] with the goal of identifying key ligand structural and electronic properties for optimum copper catalyst performance.[3]



(1)

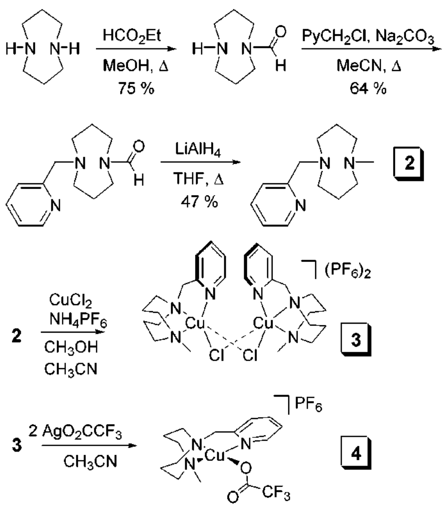
Recently, we described the ability of the copper(II) complex **1** (Chart 1), supported by the tetradentate ligand 1,5-bis(2-pyridylmethyl)-1,5-diazacyclooctane, to mediate the aziridination of olefins.[3b] We concluded that the modest reactivity and slow reaction rates observed for this complex may be rooted in an unfavorable structural reorganization, i.e., dissociation of an equatorial pyridine donor, prior to the complex's entry into the proposed olefin aziridination catalytic cycle.[2f,i,k] Herein we present evidence in support of this hypothesis, obtained by examination of a copper complex supported by 1-(2-pyridylmethyl)-5-methyl-1,5-diazacyclooctane, **2**, a new tridentate ligand that is related to the tetradentate ligand in **1** by elimination of a single pyridyl donor.[4] Our results indicate that a simple change in ligand denticity, from tetradentate to tridentate, can have a significant positive impact on the ability of a copper complex to mediate the aziridination of olefins.

Chart 1



1 **2**

Scheme 1



Tridentate **2** was prepared in three steps from 1,5-diazacyclooctane by formylation with ethyl formate, followed by alkylation with picolyl chloride and subsequent reduction of the *N*-formyl group with $LiAlH_4$ (Scheme 1).[5] Reaction of **2** with $CuCl_2$ and NH_4PF_6 afforded blue-green crystals of the bis(μ-chloro)dicopper(II) complex **3**. Chloride abstraction from **3** with AgO_2CCF_3 followed by recrystallization provided violet crystals of the mononuclear trifluoroacetate complex **4**. Complexes **3** and **4** were subjected to comprehensive structural and spectroscopic analysis.[5]

Crystallographic analysis of **3** reveals an approximately C_2-symmetric bis(μ-chloro)dicopper(II) complex (Figure 1).[6] The chloride donors link the two square-pyramidal copper centers

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(1) For recent reviews, see: (a) *Comprensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Berlin, 1999; Vols. 1−3. (b) *Applied Homogeneous Catalysis with Organometallic Compounds*; Cornils, B., Herrmann, W. A., Eds.; Wiley-VCH: Weinheim, 1999. (c) *Advances in Catalytic Processes*; Doyle, M. P., Ed.; JAI: Greenwich, 1997; Vol. 2. (d) Noyori, R. *Asymmetric Catalysis in Organic Synthesis*; Wiley: New York, 1994.

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(4) Related monofunctionalized diazacyclooctanes have been recently described: Bu, X.-H.; Du, M.; Zhang, L.; Liao, D.-Z.; Tang, J.-T.; Zhang, R.-H.; Shionoya, M. *J. Chem. Soc., Dalton Trans.* **2001**, 593−598.

(5) Synthetic details and characterization data for **2**−**4** are provided as Supporting Information.

(6) Light blue crystals of **3** ($C_{26}H_{42}Cl_2Cu_2F_{12}N_6P_2$) are monoclinic, space group $P2/n$, with $a = 22.017(4)$ Å, $b = 7.356(1)$ Å, $c = 23.263(4)$ Å, $\beta = 114.744(3)°$, $V = 3421(1)$ Å^3, and $Z = 4$ at −100 °C. Refinement on F^2 provided residuals R1 = 0.0521, wR2 = 0.1073, and GOF = 0.980 for 3700 reflections [$I > 2\sigma(I)$] and 451 variables.

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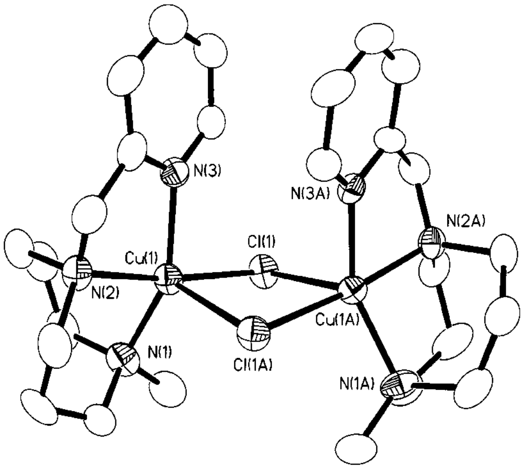

Figure 1. Thermal ellipsoid representation of the cationic portion of the X-ray crystal structure of **3** (50% probability boundaries), with hydrogen atoms omitted for clarity. Selected interatomic distances (Å): Cu1−N1, 2.081(4); Cu1−N2, 2.035(4); Cu1−N3, 2.030(4); Cu1−Cl1, 2.2683(15); Cu1−Cl1A, 2.6308(16); Cu1A−N1A, 2.054(5); Cu1A−N2A, 2.031(4); Cu1A−N3A, 2.023(5); Cu1A−Cl1A, 2.2952(15); Cu1A−Cl1, 2.6485(16).

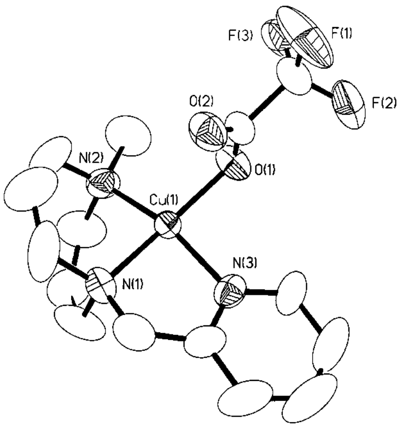

Figure 2. Thermal ellipsoid representation of the cationic portion of the X-ray crystal structure of **4** (50% probability boundaries), with hydrogen atoms omitted for clarity. Selected interatomic distances (Å): Cu1−N1, 1.981(5); Cu1−N2, 2.011(5); Cu1−N3, 1.977(5); Cu1−O1, 1.945(4); Cu1···O2, 2.631(5).

through one basal and one apical coordination site on each metal ion. The highly asymmetric Cu−Cl bonds in the $Cu_2(\mu\text{-}Cl)_2$ core, in conjunction with the presence of two very long (apical) Cu−Cl bonds, indicate that the two halves of the complex are linked together only weakly. The X-ray crystal structure of **4** reveals a mononuclear, distorted square planar copper(II) complex featuring the mer-coordinating ligand **2** and a single, monodentate $CF_3CO_2^-$ ion bound in the remaining equatorial site (Figure 2).[7]

The solution structure of **4** was probed by EPR and electrospray mass spectroscopies and by cyclic voltammetry. The nearly axial features of the X-band EPR spectrum of **4** (CH_3CN, 10 K), with $g_{\|}$ (2.24) > $g_{\perp}$ (2.07) > 2.00 and $A_{\|} = 180 \times 10^{-4}$ cm^{-1}, are consistent with a tetragonal Cu(II) environment and a d(x^2-y^2) ground state (Figure S1, Supporting Information).[8] Complex **4** also exhibits the expected mass envelope and isotope pattern in its electrospray mass spectrum (CH_3CN; Figure S2, Supporting Information). These combined experiments indicate that **4** maintains its integrity and its mononuclear structure in CH_3CN solution, consistent with that observed in the solid state. The cyclic voltammogram of **4** (CH_3CN, 0.1 M Bu_4NClO_4) contains a single, quasi-reversible Cu(II)/Cu(I) redox couple with $E_{1/2} = -201$ mV vs Ag/AgCl. This electrochemical behavior compares well with that of **1** ($E_{1/2} = -188$ mV vs Ag/AgCl)[3b] and indicates that removal of an equatorial pyridine substituent does not significantly influence the redox properties of the copper ion in **4**.

Table 1. Aziridination of Styrene Mediated by Copper Complexes[a]

catalyst[b]	styrene equiv[c]	rxn time, h	yield, %
$[Cu(CF_3SO_3)_2]$	5	1	92[d]
$[Tp^{Me2}Cu(C_2H_4)]$	10	2	90[e]
1	20	8	80
4	3.8	1.5	99

[a] Reactions conducted with 0.3−0.5 mmol of PhINTs in 2 mL of CH_3CN. [b] 0.05 equiv vs PhINTs. [c] Equivalents of styrene vs PhINTs. [d] Reference 2e. [e] Reference 2b.

The ability of **4** to mediate the aziridination of olefins by PhINTs was examined using styrene as a model substrate (eq 1, R = Ph) and compared to the ability of **1** to catalyze the same reaction (Table 1). Under optimized conditions, the reaction of styrene with PhINTs in the presence of **4** proceeded rapidly to afford *N*-tosyl-2-phenylaziridine in 99% isolated yield. In contrast, a parallel, optimized reaction mediated by **1** required a far larger excess of styrene and a longer reaction time and afforded the desired aziridine in lower isolated yield. Thus, **4** is a significantly more potent catalyst for the aziridination of styrene than is **1**. We ascribe this enhanced reactivity to the ability of **4** to readily dissociate its single equatorial $CF_3CO_2^-$ ligand, loss of which provides facile entry into the catalytic cycle.[2f,i,k] The parallel pathway in **1** requires dissociation of one of its two equatorial pyridyl donors, an unfavorable process by virtue of the chelate effect.

Herein we have demonstrated that the principles of ligand design may be successfully applied to the elucidation of a key requirement for the generation of active olefin aziridination catalysts, namely, the presence of a tridentate, mer-coordinating ligand bound to the central copper ion, which provides facile access to the copper ion through its remaining equatorial coordination site. This insight may allow for the rational design of new copper catalysts for olefin aziridination and related group-transfer reactions. Studies to this end are underway in this laboratory.

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Supporting Information Available: Synthetic details and characterization data for **2**−**4** (PDF format). X-ray crystallographic information for **3** and **4** (CIF format). This material is available free of charge via the Internet at http://pubs.acs.org.

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(7) Violet crystals of **4** ($C_{15}H_{21}CuF_9N_3O_2P_1$) are triclinic, space group $P\bar{1}$, with $a = 7.306(1)$ Å, $b = 10.276(1)$ Å, $c = 14.324(1)$ Å, $\alpha = 90.84(1)°$, $\beta = 95.74(2)°$, $\gamma = 94.26(1)°$, $V = 1066.8(2)$ Å^3, and $Z = 2$ at 25 °C. Refinement on F^2 provided residuals R1 = 0.0562, wR2 = 0.1411, and GOF = 1.021 for 2413 reflections [$I > 2\sigma(I)$], 345 variables, and 187 geometric restraints on disordered $-CF_3$ and PF_6^- groups.

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