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Cu(I) β-Diketiminates for Alkene Aziridination: Reversible Cu—Arene Binding and Catalytic Nitrene Transfer from PhI═NTs

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β-Diketiminato Cu(I)–lutidine complexes [RMeNN]Cu(2,4-lutidine) (R = Me (**4a**), ^{i}Pr (**4b**)) were prepared in high yield from Tl[RMeNN] and $[CuBr(2,4\text{-lutidine})_2]_2$. Both **4a** and **4b** reversibly dissociate lutidine base in toluene to give [RMeNN]Cu(toluene) solvento complexes. A related base-free dicopper species $\{[Me_2NN]Cu\}_2$ (**6**) bridged via η^2-binding of opposing *N*-aryl rings could be isolated by the addition of Tl[Me_2NN] to CuBr. The lutidine precursors serve as precatalysts for the aziridination of alkenes with PhI═NTs. Styrene, β-methylstyrene, and cyclooctene gave the highest yields (59–96%) with a low olefin to PhI═NTs ratio (3:1) and 5 mol % catalyst loading.

Since Kwart and Kahn's seminal discovery in 1967 that copper promoted the decomposition of benzenesulfonyl azide to give aziridines in the presence of alkenes,[1] copper complexes have held prominence in metal-catalyzed aziridination. A wide variety of chelating *N*-donor ligands with Cu(I) and Cu(II) salts catalyze the aziridination of alkenes with the imidoiodane PhI═NTs,[2−7] the most commonly used nitrene transfer reagent. Variants employing chiral bis(oxazolines)[2] or related chiral diimine ligands[3] can give enantioselectivities as high as 98% ee.[8]

In addition to expanding the range of useful nitrene transfer reagents to allow the incorporation of more diverse N-substituents, a challenge in catalytic aziridination remains the development of systems that do not require a large excess of alkene.[9] In cases where the alkene is valuable or difficult to separate from the aziridine product, the 10−100-fold excess of alkene used with most catalysts becomes impractical. Copper catalysts employing monoanionic ligands such as bis- or tris(pyrazolyl)borates are promising,[4,7] such as the recent report of alkene/PhI═NTs ratios as low as 1:1 in the aziridination of styrene, cyclooctene, and 1-hexene with electron-poor tris(pyrazolyl)borates.[6,7]

We are attracted to monoanionic β-diketiminates in copper-catalyzed aziridination due to the steric and electronic tunability these ancillary ligands afford via modifications to the *N*-aryl and backbone substituents.[10] Our recent isolation of the three-coordinate β-diketiminato Co[11] and Ni[12] complexes [NN]M═NAd has further piqued our interest in Cu(I) β-diketiminates[13−17] for aziridination, as species with M═NR groups have been long proposed as active intermediates in metal-catalyzed aziridination.[2c,3b,f]

Two slightly different β-diketiminate ligands were explored in this investigation. The first is the symmetric β-diketiminate $[Me_2NN]^-$ possessing two 2,6-dimethylphenyl

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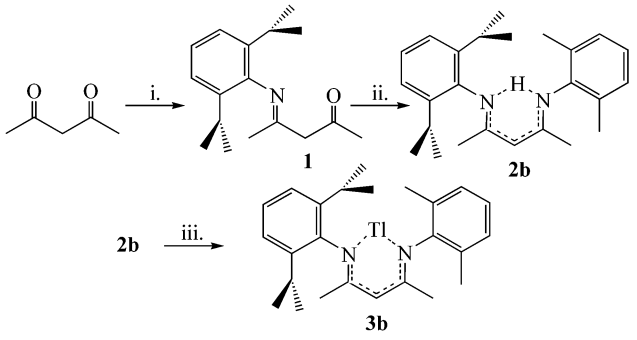
Scheme 1. Synthesis of the Unsymmetric β-Diketiminates **2b** and **3b**[a]



[a] Conditions: (i) 1 equiv of diisoproylaniline, cat. TSA, reflux in toluene 3 h; (ii) 1.5 equiv of dimethylaniline, 1 equiv of TSA, reflux toluene 6 h, Na_2CO_3 workup; (iii) KH in THF, then TlOAc.

N-aryl substituents. We recently reported the Cu(I)−alkene adduct [Me_2NN]Cu(η^2-ethylene) of this ligand which was found to cleave dioxygen[13] as well as react with N_2CPh_2 to give the structurally characterized dicopper carbene {[Me_2NN]-Cu}$_2$(μ-CPh_2) that is reactive toward alkene cyclopropanation.[18] The second ligand we used derives from the new β-diketimine H[^{i}PrMeNN] (**2b**) prepared in a two-step process (Scheme 1). Condensation of 1 equiv of 2,6-diisopropylaniline with 2,4-pentanedione under acid catalysis afforded the corresponding iminoketone **1** as an oil. Further condensation of crude **1** with 1.5 equiv of 2,6-dimethylaniline and 1.0 equiv of toluenesulfonic acid allowed the isolation of H[^{i}PrMeNN] (**2b**) in 61% overall yield after basic workup. A thallium(I) derivative was prepared by deprotonation in THF by KH followed by reaction with TlOAc to give Tl[^{i}PrMeNN] (**3b**) in 77% yield.[13]

Although scouting reactions indicated that [Me_2NN]Cu-(ethylene) catalyzes the aziridination of styrene with PhI═NTs, a Cu catalyst precursor lacking any olefin was desired to eliminate contamination of the alkene substrate. Addition of Tl[RMeNN] (R = Me (**3a**), ^{i}Pr (**3b**)) to 0.5 equiv of {CuBr-(2,4-lutidine)$_2$}$_2$[19] (prepared by addition of anhydrous copper(I) bromide to excess 2,4-lutidine with heating) in toluene results in the immediate precipitation of TlBr and isolation of [RMeNN]Cu(2,4-lutidine) (R= Me (**4a**); ^{i}Pr (**4b**)) as yellow crystals from pentane in 87% and 85% yields, respectively (eq 1).

$$\underset{\substack{\text{R = Me (3a)}\\ \text{R = }^i\text{Pr (3b)}}}{\text{Tl[RMeNN]}} + 0.5\ [\text{CuBr(2,4-lut)}_2]_2 \xrightarrow[\substack{-\text{ TlBr}\\ -\text{ 2,4-lut}}]{\text{toluene}} \underset{\substack{\text{R = Me (4a)}\\ \text{R = }^i\text{Pr (4b)}}}{\text{[RMeNN]Cu(2,4-lut)}} \quad (1)$$

The X-ray crystal structures of **4a** and **4b** revealed three-coordinate copper centers in which the 2,4-lutidine ligand is sandwiched between two β-diketiminato *N*-aryl groups (Figure 1). The most striking feature in these structures is the considerable "bending" of the lutidine toward one *N*-aryl ring such that the N1−Cu−N3 angle (145.80(6)° [**4a**] and 146.44(18)° [**4b**]) is considerably more obtuse that the N2−Cu−N3 angle (114.93(6)° [**4a**] and 115.85(17)° [**4b**]). This is also reflected in the Cu−N1 bond (1.912(2) Å [**4a**] and 1.923(4) Å [**4b**]) and Cu−N2 bond (1.987(2) Å [**4a**] and 1.985(4) Å [**4b**]) distances that indicate unsymmetric chelation of the β-diketiminate ancillary ligand. These parameters stand in contrast to the symmetrically chelated [^{i}Pr$_2$NN]Cu(py) possessing two *o*-^{i}Pr substituted *N*-aryl rings which exhibits a coplanar orientation of the pyridine ring with the β-diketiminate backbone.[15d] In both **4a** and **4b**, the lutidine ring is twisted away from the plane of the β-diketiminato chelate, and the "bent" trigonal geometry likely results from repulsions between the lutidine *o*-Me group and one *N*-aryl ring. In agreement, DFT calculations on a simplified system indicate a soft potential for bending of a pyridine ligand in the absence of steric effects.

The ^{1}H NMR spectrum of **4a** at −80 °C in toluene-d_8 reveals only one Ar−Me resonance at δ 2.425 ppm, indicating that rotation about the Cu−lutidine bond and/or lutidine dissociation/reassociation is still fast on the NMR time scale at this temperature. As the temperature is increased, the lutidine *o*-H resonance in **4a** shifts from δ 7.407 ppm at −80 °C to δ 7.589 ppm at 70 °C. Since this signal appears at δ 8.319 ppm for free lutidine in toluene-d_8, this suggests that an increasing equilibrium amount of free lutidine is formed with increasing temperature. Similar behavior is observed in VT ^{1}H NMR spectra of **4b**; the lutidine *o*-H resonance moves downfield from δ 7.159 ppm at −60 °C to δ 7.384 ppm at 80 °C.

Assuming that lutidine is not appreciably dissociated at the low-temperature limit, the equilibrium constant K_{eq} for lutidine dissociation from **4a** and **4b** can be derived from the lutidine *o*-H ^{1}H NMR chemical shift. van't Hoff plots of ln K_{eq} versus $1/T$ over a wide temperature range (ca. −70 to 70 °C) allowed for the determination of ΔH (2.3(3) and 5.6(3) kcal/mol) and ΔS (3(1) and 7(1) cal/mol·K) for the dissociation of lutidine from **4a** and **4b**, respectively (Figures S1 and S2). The low ΔH and ΔS values suggest that a molecule of toluene-d_8 solvent likely coordinates to the Cu-center in the lutidine-free form (eq 2).

$$\underset{\substack{\text{R = Me (4a)}\\ \text{R = }^i\text{Pr (4b)}}}{\text{[RMeNN]Cu(2,4-lut)}} \overset{\text{toluene-}d_8}{\rightleftharpoons} \underset{\substack{\text{R = Me (5a)}\\ \text{R = }^i\text{Pr (5b)}}}{\text{[RMeNN]Cu(toluene)}} + \text{2,4-lut} \quad (2)$$

A related lutidine-free complex {[Me_2NN]Cu}$_2$ (**6**) could be isolated in moderate yield by chemical removal of lutidine from **3a** with BF_3·OEt_2 in pentane, or, more conveniently, via the addition of Tl[Me_2NN] to CuBr in toluene followed by crystallization from pentane in 53% yield. The asymmetric unit in the X-ray structure of **6** (Figure 1) consists of 1.5 molecules of {[Me_2NN]Cu}$_2$ of which one set of bridged [Me_2NN]Cu fragments is related by inversion. (Disorder in 3 of the 6 unique *N*-aryl rings is observed.) Complementary η^2-arene interactions with an opposing *N*-aryl group link each

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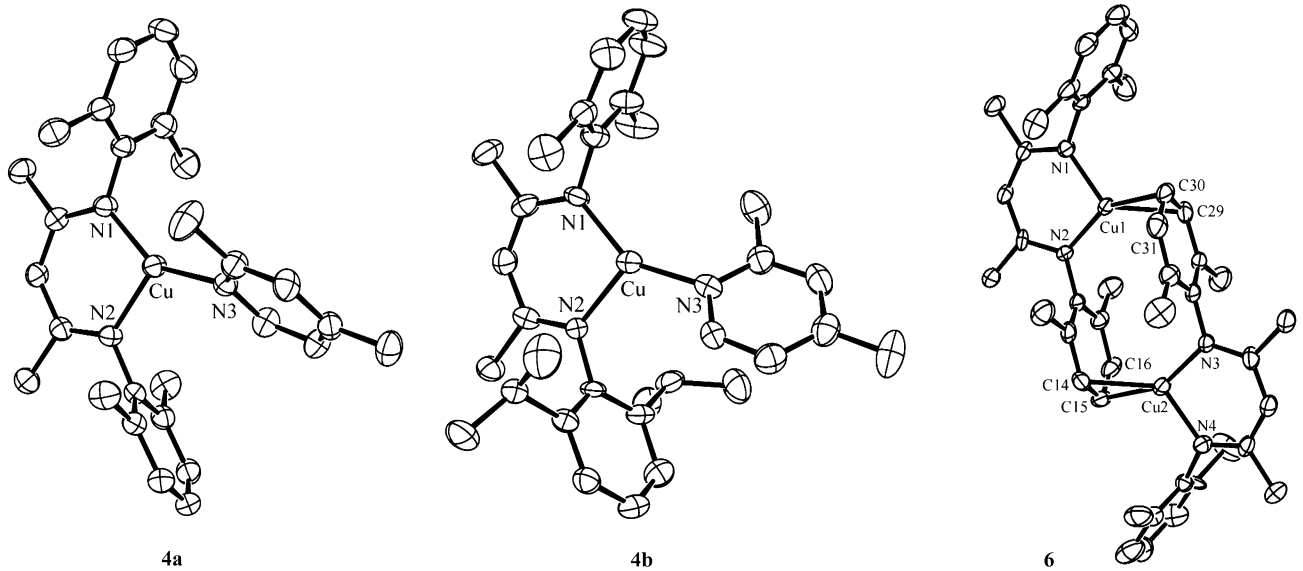

Figure 1. X-ray structures of β-diketiminato Cu(I) complexes **4a**, **4b**, and **6** (only one unique $\{[Me_2NN]Cu\}_2$ dimer is shown).

$[Me_2NN]Cu$ fragment of **6**. The inequivalent Cu−C(arene) distances at each Cu center (Cu1−C30 2.103(5) Å, Cu1−C29 2.204(5) Å; Cu2−C15 2.069(5) Å, Cu2−C14 2.242(5) Å; Cu3−C57A′ 2.12(2) Å, Cu3−C58A′ 2.26(2) Å) indicate a less-symmetric binding of the arene than observed in Sadighi's electron-poor [NN]Cu(η^2-benzene) possessing 3,5-$(CF_3)_2C_6H_3$ *N*-aryl and CF_3 backbone substituents (Cu−C 2.117(4) and 2.102(4) Å).[16] Dissolution of **6** in benezene-d_6 gives a C_{2v}-symmetric NMR spectrum identical to that of $[Me_2NN]Cu$(toluene)[18] with the absence of resonances due to free toluene.

Scouting runs of styrene aziridination with PhI═NTs catalyzed by 5 mol % **4a** in benzene, dichloromethane, and acetonitrile identified the latter as the best solvent as judged by the short time (ca. 20 min) required for consumption of insoluble PhI═NTs. It should be noted that the solvento species [RMeNN]Cu(NCMe)[15] are likely present in room temperature acetonitrile-d_3 solutions of **4** as the lutidine *o*-H resonance appears at δ 7.94 and 8.04 ppm for **4a** and **4b**, respectively, approaching the expected value for free lutidine in this solvent (δ 8.31 ppm).

In the aziridination of eight different olefins with PhI═NTs using 3 equiv of olefin catalyzed by 5 mol % **4a** in acetonitrile, styrene, *trans*-β-methylstyrene, and cyclooctene gave the highest yields (Table 1). The use of the somewhat larger **4b** marginally increased the yield of *N*-tosyl aziridines derived from these three alkenes. Other substrates surveyed under these conditions with **4a** included the aromatic alkenes α-methylstyrene and *cis*-stilbene which gave poor yields (<10%), and the aliphatic alkenes 1-hexene, *cis*-2-octene, and cyclohexene which gave marginally higher yields (10−30%).

Further decreasing the alkene/PhI═NTs ratio to 1:1 with styrene, *trans*-β-methylstyrene, and cyclooctene still resulted in aziridine formation, albeit in lower yields (47−58%) (Table 1). The decreased yield results in the increased formation of the byproduct amine H_2NTs which forms in near quantitative yield in the absence of added olefin. The

Table 1. Alkene Aziridination with PhI═NTs Catalyzed by **4a** and **4b**[a]

catalyst	alkene	alkene : PhI═NTs	aziridine	yield (%)
4a		3 : 1	Ts N	59
4a	Ph	1 : 1		47
4b		3 : 1		75
4b		1 : 1	Ph	68
4a		3 : 1	Ts N	68
4a		1 : 1		58
4b	Ph	3 : 1		74
4b		1 : 1	Ph	55
4a		3 : 1	Ts N	85
4a		1 : 1		58
4b		3 : 1		96
4b		1 : 1		52

[a] Conditions: 0.1393 mmol of PhI═NTs, 5 mol % **4a** or **4b** in 2 mL of acetonitrile. Yields determined by GC.

effect of catalyst loading on styrene aziridination was also investigated. Decreasing the amount of **4b** to 2.5 and 1.25 mol % (styrene/PhI═NTs = 1) resulted in a decrease in aziridine yield to 61% and 28%, respectively. At the lowest loading, the PhI═NTs reagent was no longer completely consumed, indicating enhanced susceptibility to catalyst decomposition pathways.

In summary, this system allows the use of a low alkene/PhI═NTs ratio to achieve acceptable aziridination yields with styrene, *trans*-β-methylstyrene, and cyclooctene. Furthermore, details involving the solution behavior of this β-diketiminato catalyst system may be important in understanding interactions with alternative, soluble nitrene transfer reagents. Studies with organoazides, which could potentially yield a diverse range of *N*-substituted aziridines, are underway and will be reported in due course.

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Supporting Information Available: Experimental and computational details (PDF) and X-ray crystallographic data (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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