Nitric Oxide

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A Three-Coordinate Copper(II) Amide from Reductive Cleavage of a Nitrosamine**

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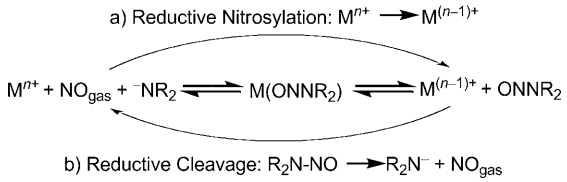
Nitrosamines $R_2N{-}NO$ are endogenous species present at submicromolar concentrations in mammalian plasma[1,2] and tissues.[2] They are similar in physiological abundance and perhaps function as well[2] to *S*-nitrosothiols RS–NO, which have received a great deal of attention in signaling pathways.[3] For instance, each elicits responses such as vasorelaxation.[4] Nitrosamines may serve as sources of NO^+ as in reversible transnitrosation reactions with thiols to give *S*-nitrosothiols.[5] In addition, they may serve as donors of the free radical NO,[6] but possess markedly higher $R_2N{-}NO$ homolytic dissociation energies (e.g. $Ph_2N{-}NO$ 87.7 kcal mol^{-1})[7] than RSNO compounds (RS–NO 20–32 kcal mol^{-1}).[8] Despite their natural occurrence, nitrosamines may be carcinogenic, especially *N*-alkyl derivatives with α-C–H atoms.[9] Nitrosamines are found in common pollutants such as tobacco smoke, motivating approaches for their passivation which involve the use of Cu-exchanged zeolites to trap and decompose nitrosamines to NO_x.[10]

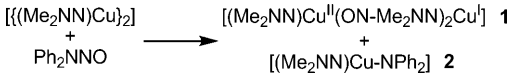
Nitrosamine formation can take place within a metal's coordination sphere through reductive nitrosylation:[11] reduction of an oxidizing metal center by NO with concomitant nitrosylation of an amine or anionic amide equivalent by NO^+ (Scheme 1 a).[12] For instance, a small-molecule NO sensor developed by Ford et al. based on a $[Cu^{II}(dac)]$ macrocycle (dac = 1,8-bis(9-anthracylmethyl)cyclam) reacts with NO to form a new N–NO bond with concomitant reduction to Cu^I which removes fluorescence quenching present in the Cu^{II}-coordinated cyclam.[13] Reductive nitrosylation to generate O–NO bonds also occurs at copper centers in the enzymes cytochrome *c* oxidase and laccase.[14]



Scheme 1. Equilibrium of reductive nitrosylation (metal reduced) and reductive cleavage ($R_2N{-}NO$ bond reduced).

Depending on the nature of the metal center, the reverse process, $R_2N{-}NO$ reductive cleavage, may be favored (Scheme 1 b). We recently reported that an electron-rich nickel(I) β-diketiminate complex $[(Me_3NN)Ni(2,4\text{-lutidine})]$ (Me_3NN = 2,4-bis(2,4,6-trimethylphenylimido)pentyl) cleaves the E–NO bond of *O*-, *S*-, and *N*-organonitroso species to give the nickel nitrosyl $[(Me_3NN)Ni{-}NO]$ along with dimeric nickel(II) alkoxide or thiolate complexes $[\{(Me_3NN)Ni\}_2(\mu\text{-}E)_2]$ or the mononuclear nickel(II) amide $[(Me_3NN)Ni{-}NPh_2]$.[15] Herein we report the reactivity of diphenylnitrosamine (Ph_2NNO) with the related copper(I) β-diketiminate $[\{(Me_2NN)Cu\}_2]$ (Me_2NN = 2,4-bis(2,6-dimethylphenylimido)pentyl).[16]

Addition of 2.0 equivalents Ph_2NNO[15,17] to 1.3 equivalents $[\{(Me_2NN)Cu\}_2]$ at −35 °C in diethyl ether results in a color change from light yellow to dark brown (Scheme 2).



Scheme 2. Reaction of $[\{(Me_2NN)Cu\}_2]$ with Ph_2NNO.

Formation of a copper mirror indicates that this reaction follows a complex course; crystallization attempts from diethyl ether reveal both dark brown and green crystals.

X-ray characterization of the brown crystals revealed the dinuclear $[(Me_2NN)Cu^{II}(ON{-}Me_2NN)_2Cu^{I}]$ (**1**; Figure 1) isolated in 16% yield based on total moles of Cu. This species has two copper ions in vastly different coordination environments. Cu1 is linear (N1-Cu1-N3 176.6(2)°), a geometry observed in copper coordination complexes in the +1 oxidation state (d^{10}). The coordination environment of Cu2 is square planar completed by two O donors resulting from the nitrosation of the former β-diketiminato backbone C–H groups in the two modified β-diketiminate ligands coordinated to the linear Cu1 center in **1**. Both the square planar

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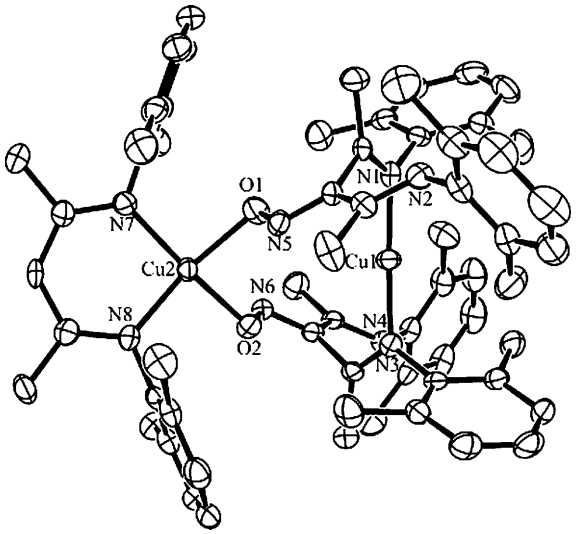

Figure 1. X-ray structure of $[(Me_2NN)Cu^{II}(ON{-}Me_2NN)_2Cu^{I}]$ (**1**).

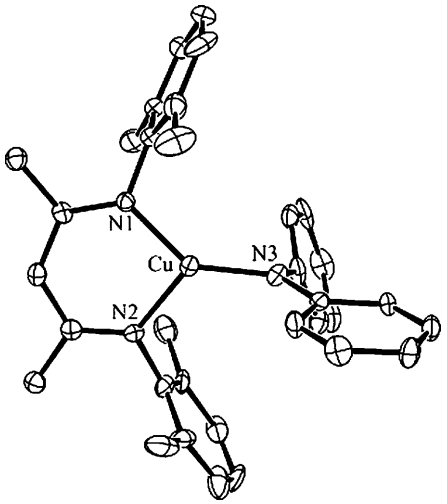

Figure 2. X-ray structure of $[(Me_2NN)Cu{-}NPh_2]$ (**2**).

configuration at Cu2 as well as the axial EPR spectrum of **1** in frozen toluene glass ($g_{\|} = 2.20(1)$, $g_{\perp} = 2.05(1)$ with $A_{\|}(Cu) = 563(10)$, $A_{\perp}(Cu) = 70(10)$ MHz) are consistent with assignment of a Cu^{II} center in **1** (see the Supporting Information, Figures S12 and S13).

Pentane recrystallization of the green product isolated from the reaction of Ph_2NNO with $[\{(Me_2NN)Cu\}_2]$ uncovered the three-coordinate copper(II) amide $[(Me_2NN)Cu{-}NPh_2]$ (**2**) in 31% yield. Identified by a preliminary single-crystal X-ray diffraction study, a higher-quality X-ray structure of **2** was obtained through its independent synthesis. Reaction of $[\{(Me_2NN)Cu\}_2]$ with 1 equivalent I_2 in diethyl ether gives $[(Me_2NN)CuI]$ (**3**) in 37% yield. Curiously, this iodo complex crystallizes as dinuclear $[\{(Me_2NN)Cu\}_2(\mu\text{-}I)_2]$ from pentane and mononuclear, three-coordinate $[(Me_2NN)CuI]$ from diethyl ether as demonstrated by X-ray structures (Figures S7 and S8). Reaction of **3** with $LiNPh_2$ in THF delivers copper amide **2** as green crystals in 81% yield from pentane (Scheme 3).

$$[\{(Me_2NN)Cu\}_2] + I_2 \xrightarrow{Et_2O} \underset{\mathbf{3}}{2\,[(Me_2NN)Cu\text{-}I]}$$

$$\underset{\mathbf{3}}{[(Me_2NN)Cu\text{-}I]} + LiNPh_2 \xrightarrow[-LiI]{THF} \underset{\mathbf{2}}{[(Me_2NN)Cu\text{-}NPh_2]}$$

Scheme 3. Independent synthesis of $[(Me_2NN)Cu{-}NPh_2]$ (**2**).

The X-ray crystal structure of **2** (Figure 2) shows a short $Cu{-}N_{amide}$ distance of 1.841(6) Å with $Cu{-}N_{\beta\text{-}dik}$ distances of 1.914(6) and 1.885(6) Å. Both the Cu atom and N_{amido} atoms are planar (sum of angles 359.7(3) and 357.2(5)°, respectively). One of the two *N*-aryl rings is coplanar with the N center, while the other is twisted out of the Cu-N-C plane by ca. 65°. The metal–nitrogen distances in **2** are longer than in the related β-diketiminato nickel(II) amide $[(Me_3NN)Ni{-}NPh_2]$[15] ($Ni{-}N_{amide} = 1.823(1)$; $Ni{-}N_{\beta\text{-}dik} = 1.826(1)$ and 1.833(3) Å).

$[(Me_2NN)Cu{-}NPh_2]$ (**2**) represents a rare example of a crystallographically characterized three-coordinate copper(II) amide. Peters et al. have recently reported the structure of the diphosphinoborate $[\kappa^2\text{-}\{Ph_2B(CH_2PtBu_2)\}Cu{-}N(p\text{-tolyl})_2]$ which exhibits a Cu–N bond distance of 1.906(2) Å.[18] Based on several spectroscopic measurements, this species was best described as a Cu^{I}-coordinated aminyl radical.[19] Employing chelating ligands, X-ray structures of two square planar copper(II) amides with electron-deficient sulfonyl amido substituents[20] as well as distorted tetrahedral phosphine amide species[21] have been reported. In copper(I) chemistry, Gunnoe et al. described the structures of three- and two-coordinate amides such as $[(tBu_2PCH_2CH_2PtBu_2)Cu{-}NHPh]$[22] and the N-heterocyclic carbene based [(IPr)Cu–NHPh] (IPr = 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene).[23]

The electronic spectrum of **2** in diethyl ether exhibits four bands in the visible to near IR at 426 nm ($530\,M^{-1}cm^{-1}$), 532 nm ($280\,M^{-1}cm^{-1}$), 774 nm ($1200\,M^{-1}cm^{-1}$), and 908 nm ($1200\,M^{-1}cm^{-1}$). TD-DFT analysis suggests that the two lowest-energy bands at 774 and 908 nm correspond to $Cu{-}N_{amide}$ σ–π* and π–π* transitions, respectively (Figure S10 and Table S1). As monitored by UV/Vis spectroscopy, toluene solutions of **2** (1.2 mM) have a half-life of approximately 7 h at room temperature, turning colorless after a day. GC/MS studies reveal that Ph_2NH is the primary organic product of decomposition.

Simulation of the X-band EPR spectrum of **2** in frozen toluene glass (Figure 3) indicates a rhombic signal ($g_1 = 2.146(3)$, $g_2 = 2.043(5)$, $g_3 = 2.018(5)$) with $A_1(Cu) = 298(5)$ MHz. The hyperfine coupling to Cu is modest relative to that found in other three-coordinate β-diketiminato copper(II) halide species such as $[(Me_2NN)CuI]$ (**3**) and [LCuCl][24] ($A_1(Cu) = 410(5)$ and 400 MHz, respectively; L = related β-diketiminate ligand with 2,6-$iPr_2C_6H_3$ *N*-aryl groups). Instead, the $A_1(Cu)$ observed in **2** is more similar to that in Tolman's three-coordinate Cu^{II} phenoxide [LCuOAr] (Ar = *p*-$MeOC_6H_4$; $g_1 = 2.22$, $g_2 = 2.07$, $g_3 = 2.02$, $A_1(Cu) = 280$ MHz) in which delocalization of the unpaired

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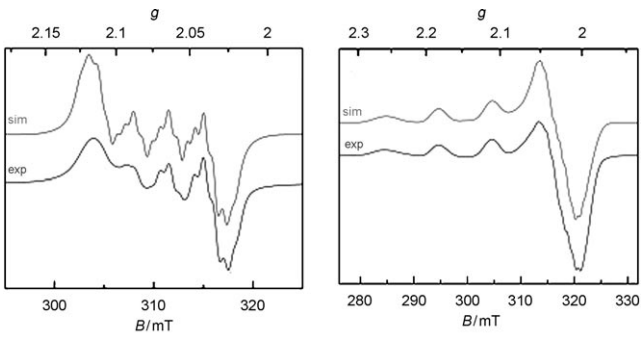


Figure 3. EPR spectra of [(Me$_2$NN)Cu–NPh$_2$] (**2**) at room temperature (left) and 30 K (right) in toluene (liquid solution or frozen glass).

electron onto the phenoxide ring is possible.[25] The EPR spectrum of **2** is distinct from Peters' Cu^{I} aminyl complex [κ^2-{Ph$_2$B(CH$_2$P*t*Bu$_2$)}Cu–N(*p*-tolyl)$_2$] which exhibits g values (2.030, 2.008, 2.008) close to that of the free electron with a significantly depressed A_1(Cu) of 170 MHz.[18]

Nonetheless, DFT analysis of **2** points to appreciable radical character on the amido N atom as a result of the three-electron/two-center π interaction between the Cu d orbital most destabilized by σ interactions with the β-diketiminate ligand (d$_{yz}$) and the filled lone pair of an sp^2 hybridized amido N atom (p$_y$; Figure 4). The d^9 Cu^{II} center of the β-diketiminato

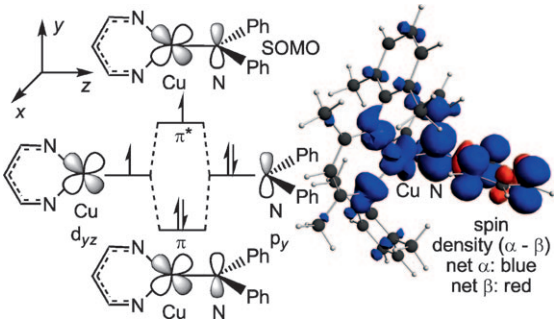
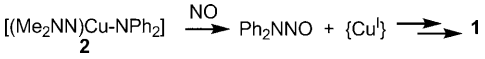


Figure 4. Copper amido two-center/three-electron π-orbital interactions (left) and net spin density plot for **2** (right; isospin value 0.001).

fragment possesses one electron in this d$_{yz}$ orbital, which interacts with the lone pair of the sp^2 hybridized amido N donor to singly populate the Cu–N π* orbital, representing the SOMO of **2**. The DFT spin densities at Cu and N are 0.30 and 0.27 e$^-$, respectively, with significant delocalization of unpaired electron density over the two aryl rings (Figure 4). These values track opposite to those calculated for Peters' conceptually related Cu^{I} aminyl radical complex (Cu and N spin densities 0.13 and 0.49 e$^-$, respectively).[18] Spectroscopic and theoretical analysis indicates that the Cu amido π interaction in **2** is rather covalent consistent with the modest value of A_1(Cu) observed in the EPR spectrum of **2**. This bonding description for **2** is qualitatively similar to that for related copper(II) thiolates which possess considerably covalent Cu–S bonds.[26]

Whereas the superhyperfine interactions involving the β-diketiminato N atoms are predicted to be relatively isotropic (A(N) = 22(7) MHz), DFT suggests a highly anisotropic interaction with the amido N atom (A_2(N) = 37, $A_{1,3}$(N) = 4(1) MHz) leading to a low predicted value of A_{iso}(N) = 15 MHz. Complete simulation of the experimental spectrum of **2** at room temperature (Figure 3) with g_{iso} = 2.071(3) and A_{iso}(Cu) = 103(3) MHz is best achieved with two different sets of A_{iso}(N) values of 27(2) MHz (two N atoms) and 14 MHz (one N atom). Confirming that A_{iso}(N) for the amido N atom is smaller than that of the β-diketiminate N donors, [(Me$_2$NN)Cu–^{15}NPh$_2$] leads to very similar EPR spectra with A_{iso}(^{15}N) simulated as 18(10) MHz (Figures S14 and S15).

The presence of unpaired electron density at the amido N atom in **2** identifies it as a site of potential reactivity with other radical species such as NO. We observe the immediate formation of Ph$_2$NNO when 1 equivalent NO$_{gas}$ is added to isolated [(Me$_2$NN)Cu–NPh$_2$] (Scheme 4), though at this stage



Scheme 4. Reaction of NO$_{gas}$ (1 equiv) with [(Me$_2$NN)Cu-NPh$_2$] (**2**).

we cannot discriminate between the location of initial attack by NO (at Cu or N) in this low-coordinate species. We were unable to quantify the Ph$_2$NNO initially formed since it can be consumed by any {(Me$_2$NN)Cu^{I}} species formed in solution to give [(Me$_2$NN)Cu^{II}(ON–Me$_2$NN)$_2$Cu^{I}] (**1**).

This model system allows for the observation of both the cleavage and formation of the Ph$_2$N–NO bond at a common copper center. While the β-diketiminate ligand is not an innocent spectator, it provides a framework to allow for the isolation of the novel three-coordinate copper(II) amide [(Me$_2$NN)Cu–NPh$_2$]. Additionally, the electron-rich β-diketiminato coordination environment enables the reductive cleavage of a nitrosamine N–NO bond whereas the reverse process has been observed in other copper systems. This may be of particular relevance in the biologically important generation of NO at copper sites[27] from *S*-nitrosothiols RSNO such as *S*-nitrosoglutathione which serve as circulating reservoirs of NO in blood plasma.[3,28]

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