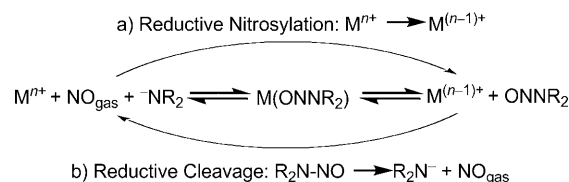


A Three-Coordinate Copper(II) Amide from Reductive Cleavage of a Nitrosamine**

Marie M. Melzer, Susanne Mossin, Xuliang Dai, Ashley M. Bartell, Pooja Kapoor, Karsten Meyer, and Timothy H. Warren*

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 vaso-relaxation.^[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 1a).^[12] For instance, a small-molecule NO sensor developed by Ford et al. based on a $[Cu^{II}(\text{dac})]$ 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 nitro-

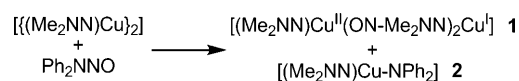


Scheme 1. Equilibrium of reductive nitrosylation (metal reduced) and reductive cleavage (R_2N-NO bond reduced).

sylation to generate O–NO bonds also occurs at copper centers in the enzymes cytochrome *c* oxidase and laccase.^[14]

Depending on the nature of the metal center, the reverse process, R_2N-NO reductive cleavage, may be favored (Scheme 1b). 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 $\{[(Me_3NN)Ni]_2(\mu-E)_2\}$ 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. Cu^I 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 -diketiminate backbone C–H groups in the two modified β -diketiminate ligands coordinated to the linear Cu^I center in **1**. Both the square planar

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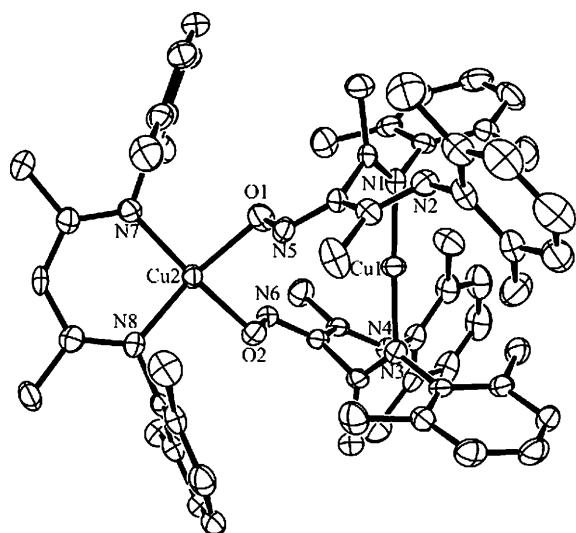
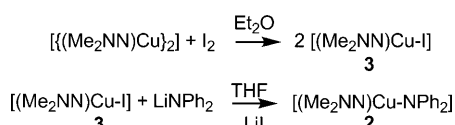


Figure 1. X-ray structure of $[(\text{Me}_2\text{NN})\text{Cu}^{\text{II}}(\text{ON}-\text{Me}_2\text{NN})_2\text{Cu}^{\text{I}}]$ (**1**).

configuration at Cu2 as well as the axial EPR spectrum of **1** in frozen toluene glass ($g_{\parallel} = 2.20(1)$, $g_{\perp} = 2.05(1)$ with $A_{\parallel}(\text{Cu}) = 563(10)$, $A_{\perp}(\text{Cu}) = 70(10)$ 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 $[(\text{Me}_2\text{NN})\text{Cu}]_2$ uncovered the three-coordinate copper(II) amide $[(\text{Me}_2\text{NN})\text{Cu-NPh}_2]$ (**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 $[(\text{Me}_2\text{NN})\text{Cu}]_2$ with 1 equivalent I_2 in diethyl ether gives $[(\text{Me}_2\text{NN})\text{CuI}]$ (**3**) in 37 % yield. Curiously, this iodo complex crystallizes as dinuclear $[(\text{Me}_2\text{NN})\text{Cu}]_2(\mu\text{-I})_2$ from pentane and mononuclear, three-coordinate $[(\text{Me}_2\text{NN})\text{CuI}]$ 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).



The X-ray crystal structure of **2** (Figure 2) shows a short Cu–N_{amide} distance of 1.841(6) Å with Cu–N_{β-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 [(Me₃NN)Ni–NPh₂]^[15] (Ni–N_{amide} = 1.823(1); Ni–N_{β-dik} = 1.826(1) and 1.833(3) Å).

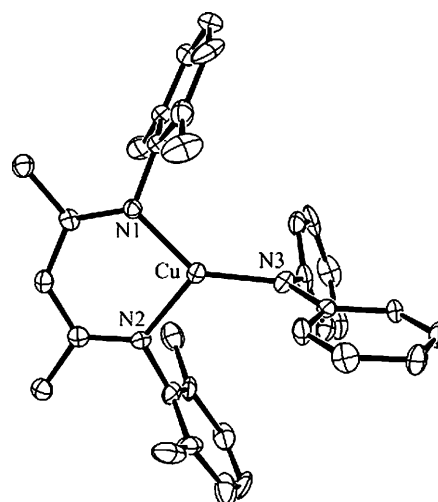


Figure 2. X-ray structure of [(Me₂NN)Cu–NPh₂] (**2**).

[(Me₂NN)Cu–NPh₂] (**2**) represents a rare example of a crystallographically characterized three-coordinate copper(II) amide. Peters et al. have recently reported the structure of the diphosfinoborate [κ²–{Ph₂B–(CH₂PtBu₂)}Cu–N(*p*-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 [(tBu₂PCH₂CH₂PtBu₂)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 ($530\text{ M}^{-1}\text{ cm}^{-1}$), 532 nm ($280\text{ M}^{-1}\text{ cm}^{-1}$), 774 nm ($1200\text{ M}^{-1}\text{ cm}^{-1}$), and 908 nm ($1200\text{ M}^{-1}\text{ cm}^{-1}$). TD-DFT analysis suggests that the two lowest-energy bands at 774 and 908 nm correspond to Cu–N_{amide} $\sigma\text{--}\pi^*$ and $\pi\text{--}\pi^*$ 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 Ph₂NH 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 $A_1(\text{Cu}) = 298(5)$ MHz. The hyperfine coupling to Cu is modest relative to that found in other three-coordinate β -diketiminato copper(II) halide species such as $[(\text{Me}_2\text{NN})\text{CuI}]$ (**3**) and $[\text{LCuCl}]^{[24]}$ ($A_1(\text{Cu}) = 410(5)$ and 400 MHz, respectively; L = related β -diketiminato ligand with 2,6-*i*Pr₂C₆H₃ *N*-aryl groups). Instead, the $A_1(\text{Cu})$ observed in **2** is more similar to that in Tolman's three-coordinate Cu^{II} phenoxide $[\text{LCuOAr}]$ (Ar = *p*-MeOC₆H₄; $g_1 = 2.22$, $g_2 = 2.07$, $g_3 = 2.02$, $A_1(\text{Cu}) = 280$ MHz) in which delocalization of the unpaired

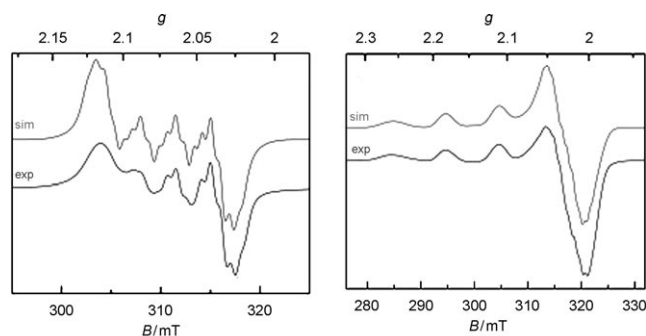


Figure 3. EPR spectra of $[(\text{Me}_2\text{NN})\text{Cu}-\text{NPh}_2]$ (**2**) at room temperature (left) and 30 K (right) in toluene (liquid solution or frozen glass).

electron onto the phenoxide ring is possible.^[25] The EPR spectrum of **2** is distinct from Peters' Cu^{I} aminyl complex $[\kappa^2\text{-}\{\text{Ph}_2\text{B}(\text{CH}_2\text{PrBu}_2)\}\text{Cu}-\text{N}(p\text{-tolyl})_2]$ which exhibits g values (2.030, 2.008, 2.008) close to that of the free electron with a significantly depressed $A_1(\text{Cu})$ 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 -diketiminato ligand (d_{yz}) and the filled lone pair of an sp^2 hybridized amido N atom (p_y ; Figure 4). The $d^9 \text{Cu}^{\text{II}}$ center of the β -diketiminato

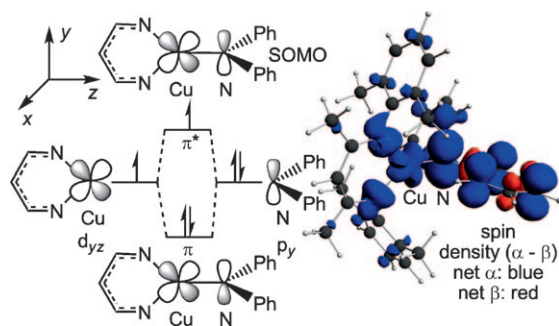


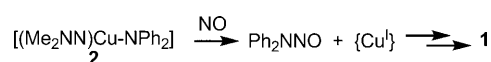
Figure 4. Copper amido two-center/three-electron π -orbital interactions (left) and net spin density plot for **2** (right; isospin value 0.001).

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 $\text{Cu}-\text{N}$ π^* orbital, representing the SOMO of **2**. The DFT spin densities at Cu and N are 0.30 and $0.27e^-$, 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 $0.49e^-$, respectively).^[18] Spectroscopic and theoretical analysis indicates that the Cu amido π interaction in **2** is rather covalent consistent with the modest value of $A_1(\text{Cu})$ 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 $\text{Cu}-\text{S}$ bonds.^[26]

Whereas the superhyperfine interactions involving the β -diketiminato N atoms are predicted to be relatively isotropic

($A(\text{N}) = 22(7)$ MHz), DFT suggests a highly anisotropic interaction with the amido N atom ($A_2(\text{N}) = 37$, $A_{1,3}(\text{N}) = 4(1)$ MHz) leading to a low predicted value of $A_{\text{iso}}(\text{N}) = 15$ MHz. Complete simulation of the experimental spectrum of **2** at room temperature (Figure 3) with $g_{\text{iso}} = 2.071(3)$ and $A_{\text{iso}}(\text{Cu}) = 103(3)$ MHz is best achieved with two different sets of $A_{\text{iso}}(\text{N})$ values of 27(2) MHz (two N atoms) and 14 MHz (one N atom). Confirming that $A_{\text{iso}}(\text{N})$ for the amido N atom is smaller than that of the β -diketiminato N donors, $[(\text{Me}_2\text{NN})\text{Cu}-^{15}\text{NPh}_2]$ leads to very similar EPR spectra with $A_{\text{iso}}(^{15}\text{N})$ 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_2NNO when 1 equivalent NO_{gas} is added to isolated $[(\text{Me}_2\text{NN})\text{Cu}-\text{NPh}_2]$ (Scheme 4), though at this stage



Scheme 4. Reaction of NO_{gas} (1 equiv) with $[(\text{Me}_2\text{NN})\text{Cu}-\text{NPh}_2]$ (**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_2NNO initially formed since it can be consumed by any $\{(\text{Me}_2\text{NN})\text{Cu}^{\text{I}}\}$ species formed in solution to give $[(\text{Me}_2\text{NN})\text{Cu}^{\text{II}}(\text{ON}-\text{Me}_2\text{NN})_2\text{Cu}^{\text{I}}]$ (**1**).

This model system allows for the observation of both the cleavage and formation of the $\text{Ph}_2\text{N}-\text{NO}$ bond at a common copper center. While the β -diketiminato ligand is not an innocent spectator, it provides a framework to allow for the isolation of the novel three-coordinate copper(II) amide $[(\text{Me}_2\text{NN})\text{Cu}-\text{NPh}_2]$. Additionally, the electron-rich β -diketiminato coordination environment enables the reductive cleavage of a nitrosamine $\text{N}-\text{NO}$ 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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