N–N Bond Formation

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N–N Bond Forming Reductive Elimination via a Mixed-Valent Nickel(II)–Nickel(III) Intermediate

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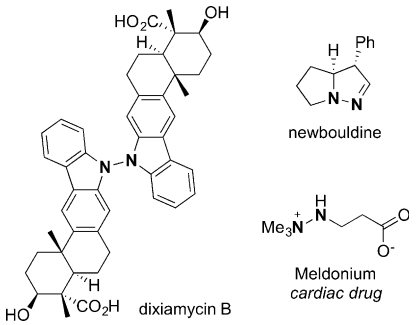
Abstract: *Natural products containing N–N bonds exhibit important biological activity. Current methods for constructing N–N bonds have limited scope. An advanced understanding of the fundamental N–N bond formation/cleavage processes occurring at the transition-metal center would facilitate the development of catalytic reactions. Herein we present an N–N bond-forming reductive elimination, which proceeds via a mixed-valent Ni^{II}–Ni^{III} intermediate with a Ni–Ni bond order of zero. The discrete Ni^{II}–Ni^{III} oxidation states contrast with the cationic dimeric Ni analogue, in which both Ni centers are equivalent with an oxidation state of 2.5. The electronic structures of these mixed-valent complexes have implications for the fundamental understanding of metal–metal bonding interactions.*

Over 200 natural products and pharmaceuticals contain N–N bonds. These linkages are important in their biological activity (Scheme 1).[1] For example, the dimeric, N–N linked dixiamycin B is a more potent antibiotic than its monomeric analogue, xiamycin A.[2] While biosynthetic routes to these natural products are proposed to involve oxidative N–N bond coupling,[3] chemical methods to prepare N–N bonds remain a challenge.[4] The few available methods are substrate specific, including the use of a nucleophilic amine to react with an electrophilic nitro group[5] and an electrochemical oxidation method to couple xiamycin A into dixiamycin B.[6] The current transition-metal-catalyzed reactions for N–N bond-forming oxidative coupling have limited scope and low yield, which have restricted their synthetic utility.[7] The advance of catalytic reactions for N–N coupling would benefit from a fundamental understanding of the bond formation processes occurring at the transition-metal center. While there is precedent for azoarene formation from metal–nitrene/imido intermediates,[8,9] the reductive elimination of metal amino complexes to form N–N single bonds has not been established with well-defined organometallic complexes.



Scheme 1. Selected natural products and commercial drugs with N–N bonds.

The reverse reaction of N–N bond formation, the cleavage of N–N bonds, has been the subject of considerable effort for its applications in amine synthesis[10] and N_2 fixation.[11] Complexes designed for N_2 reduction are primarily based on early and middle transition metals, where the activation of the N–N bond is facilitated by two, cooperative metal centers.[11] In light of the recent recognition that Ni is capable of activating conventionally inert bonds, including ethereal C–O bonds,[12] we reasoned that bimetallic Ni complexes have the potential to activate and form N–N bonds.[13] A handful of binuclear and trinuclear Ni complexes have been reported in the context of fundamentally understanding metal–metal bonding,[14] but their synthetic applications in mediating bond cleavage and formation have seldom been explored. Herein, we present the first nickel-mediated N–N bond forming reductive elimination with a "paddle-wheel" binuclear Ni complex. The reactivity of this Ni complex provides essential insight to facilitate the development of catalytic methods for N–N bond coupling and activation.

A guanidine derivative, triazabicyclodecene (TBD), can bridge late transition metals and stabilize complexes at multiple oxidation states.[15] In particular, a $Pd_2(TBD)_4$ complex proved to be active in catalyzing oxidation reactions.[16] Previous attempts to prepare the "paddle-wheel" complex $Ni_2(TBD)_4$ (**1**) resulted in cluster formation or low yield.[17] We initiated our research by optimizing the synthesis of **1**. $Ni(acac)_2$ (acac = acetoacetate) reacted with the TBD ligand in the presence of *n*-BuLi to afford **1** in 75% yield (Scheme 2). The Ni–Ni distance was determined to be 2.3787(4) Å by single crystal X-ray diffraction (Figure S1). The cyclic voltammetry of **1** exhibited one reversible oxidation/reduction wave at $E_{1/2} = 0.024$ V (vs. Fc/Fc^+, $Fc = [(\eta\text{-}C_5H_5)_2Fe]$; Figure S10 in the Supporting Information). Multiple oxidation waves at higher potentials appeared to be irreversible even at reduced temperature and in different solvents, revealing that further oxidation of the complex gave unstable products. The treatment of **1** with MeI led to a trinuclear Ni-TBD cluster $Ni_3(TBD)_4I_2$ **2** (Figure S2) and methylated TBD in high yield.[18]

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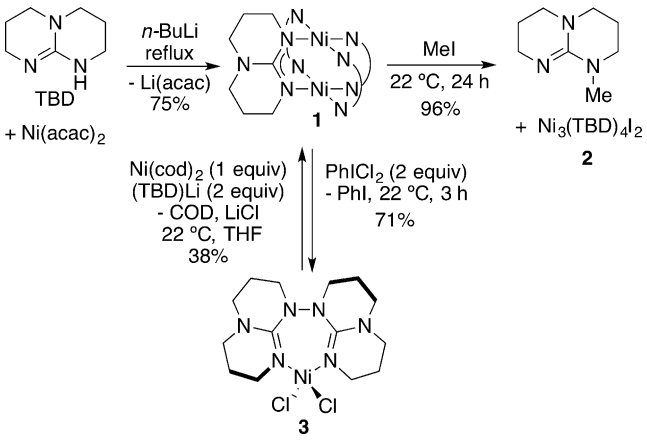


Scheme 2. Synthesis and oxidation of Ni-TBD complexes.

Oxidation of **1** with $PhICl_2$ afforded a dark blue crystal **3** in 71% yield, with the concomitant formation of minor Ni clusters, as an insoluble light blue powder (Scheme 2). Complex **3** exhibited a paramagnetic ^{1}H NMR spectrum.[19] The benzene solution magnetic moment, determined by Evans method, was $3.76 \pm 0.07\ \mu_B$, consistent with a high-spin Ni complex. The magnetic moment remains constant over a temperature range of −50 to 50 °C (Figure S11). X-ray crystallography established a tetrahedral Ni center, ligated with a bis-imine ligand featuring an N−N bond to link two TBD moieties (Figure 1). The N−N bond length is 1.393(2) Å,

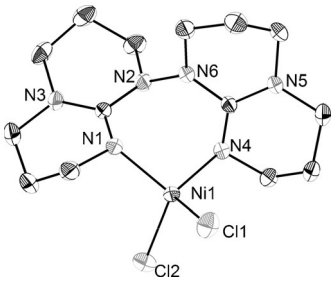
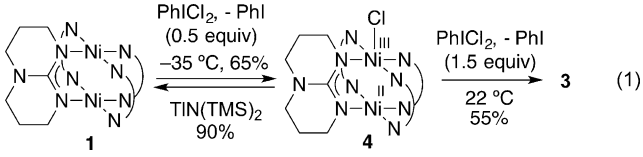


Figure 1. Molecular structure of **3**, thermal ellipsoids set at 50% probability. Hydrogen atoms are omitted for clarity.

slightly shorter than that of tetramethylhydrazine (1.401(4) Å).[20] The bite-angle of the bis-imine ligand is 102.72(7)°, comparable to homoxantphos.[21] Control experiments involving the oxidation of TBD-H and (TBD)Li with $PhICl_2$ furnished no N–N coupling product, suggesting that Ni is essential for mediating the coupling. Our attempts to extract the diimine ligand from **3** led to its decomposition. Addition of an equivalent of $Ni(cod)_2$ to **3** in the presence of (TBD)Li resulted in the oxidative addition of Ni^0 into the N−N bond and formation of **1** at room temperature (Scheme 2).[22]

The observed formation of **3** and the reverse reaction established the first N−N bond reductive elimination and oxidative addition supported by Ni, which prompted us to characterize the mechanism of the N–N bond formation further. The conversion of **1** into **3** was instant, which complicated our attempted kinetic study. Instead, we focused our research on isolating and characterizing the intermediates. The oxidation of **1** with 0.5 equivalents of $PhICl_2$ at −35 °C proceeded rapidly to afford a dark purple complex in 65% yield [Eq. (1)], which was determined to be Ni_2-



(1)

$(TBD)_4Cl$ (**4**) by single-crystal X-ray crystallography (Figure 2). Warming **4** to 22 °C led to its decomposition, but no N–N coupled product **3** was obtained. Addition of 1.5 equivalents of $PhICl_2$ to **4** immediately generated **3** in 55% yield. Any high-valent Ni species formed prior to **3** were

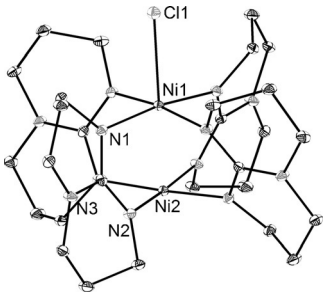


Figure 2. Molecular structure of **4**, thermal ellipsoids set at 50% probability. Hydrogen atoms are omitted for clarity.

not identifiable. This observation is consistent with the lack of reversible waves in the CV of **1** after the first-electron-oxidation. Our attempts to substitute the chloride of **4** with metal alkyls and amides did not generate any stable mixed-valent alkyl or amide complexes. For example, $TlN(TMS)_2$ reduced **4** to **1** in high yield. Halide-abstracting reagents, such as $AgPF_6$, $AgBF_4$, and $TlPF_6$ led to immediate decomposition of **4** into insoluble materials.

Extensive interest in metal–metal bonding of mixed-valent complexes[23] motivated us to characterize the electronic structure of **4**. Single-crystal X-ray diffraction determined that Ni1 has a square-pyramidal geometry, whereas Ni2 is square-planar (Figure 2). The intramolecular Ni–Ni distance is 2.3709(8). The crystal structure of **4** shows chain-like packing via a strong intermolecular Ni···Cl interaction (intermolecular Ni2···Cl′ = 3.1440(10) Å; Figure S3). The ^{1}H NMR resonances remain constant as a function of the concentration of **4** (Figure S4), suggesting the lack of intermolecular aggregation in solution.[24] The paramagnetic ^{1}H NMR resonances exhibit a linear dependence on T^{-1} in accordance with Curie's law (Figures 3 and Figures S5,S6). The EPR spectrum of **4** displays a pseudo-axial signal, corresponding to an $S = 1/2$ Ni species (Figure 4). The super-hyperfine coupling along the perpendicular axis is attributed to the delocalization of the unpaired electron onto the Cl ($I = 3/2$) and the second Ni ($I = 3/2$) atoms.

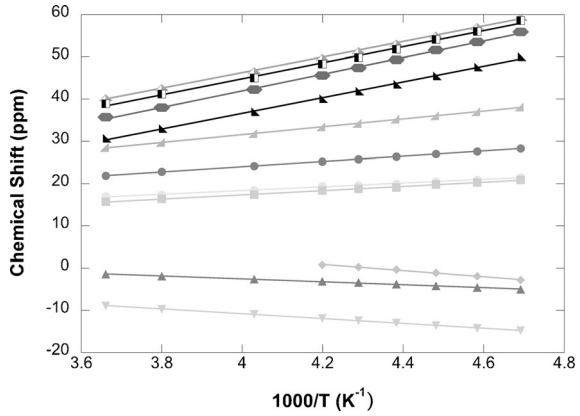


Figure 3. Curie behavior of the ^{1}H NMR chemical shifts of **4** collected in CD_2Cl_2 at 500 MHz and temperatures from −60 °C to 0 °C. For a color version, see the Supporting Information, Figure S6. Each trace corresponds to a different NMR resonance.

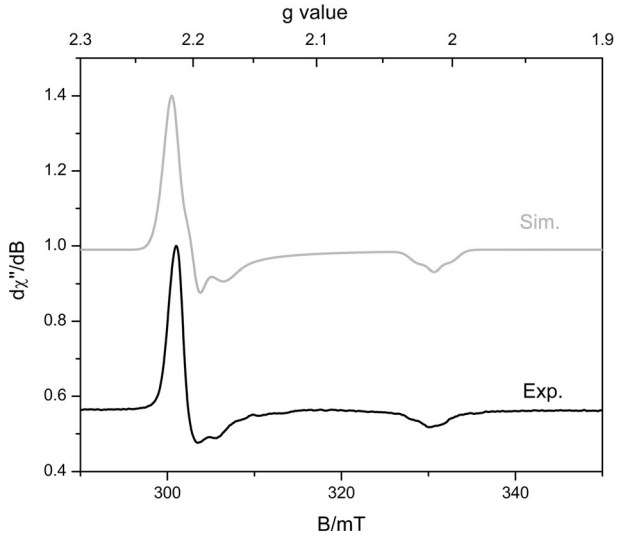


Figure 4. X-band EPR spectrum of **4** recorded in toluene glass at 10 K. Spectroscopic parameters for **4**: $g_x = 2.23$, $g_y = 2.21$, $g_z = 2.03$, $A_{xx} = 0$ MHz, $A_{yy} = 72$ MHz, $A_{zz} = 50$ MHz.

DFT calculations of **4** at the B3LYP level reproduced the X-ray crystal structure and gave a Ni–Ni distance of 2.394 Å.[25] The spin-density plot exhibits a radical primarily located on Ni1 and partially delocalized to Ni2 and the chlorine atom (Figure 5 A). For comparison, we independently prepared the cationic complexes $[(TBD)_4Ni_2]PF_6$ and $[(TBD)_4Ni_2]OTf$ from the oxidation of **1** with $AgPF_6$ and AgOTf, respectively.[14d] The EPR spectra of the cationic complexes display axial signals similar to **4** (Figures S8,S9). The g values of each complex vary slightly with different counter anions. DFT calculations reveal evenly distributed charges on both Ni centers, and the Ni–Ni distance is 2.304 Å (Figure 5 B).[26]

The Ni–Ni distance of **4** (2.3709(8) Å) is similar to that of **1** (2.3787(4) Å). The spin-density plot of **4** suggests a mixed-valent complex with discrete Ni^{II} and Ni^{III} oxidation states and a Ni–Ni bond order of zero.[27] This electronic structure

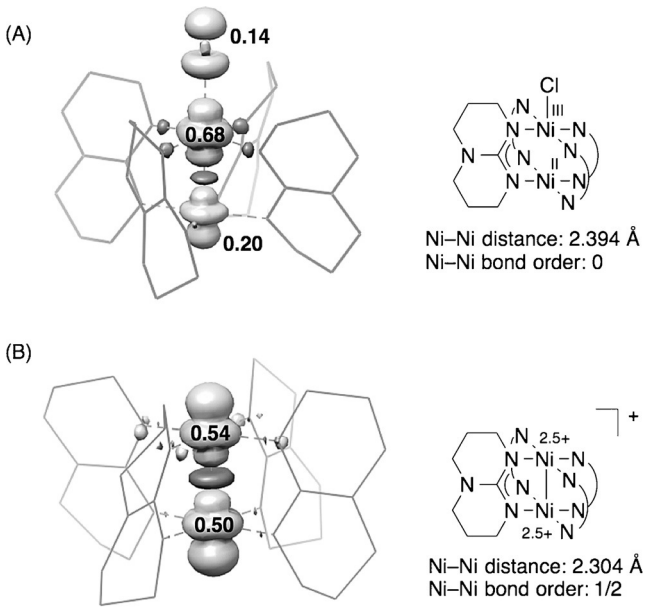
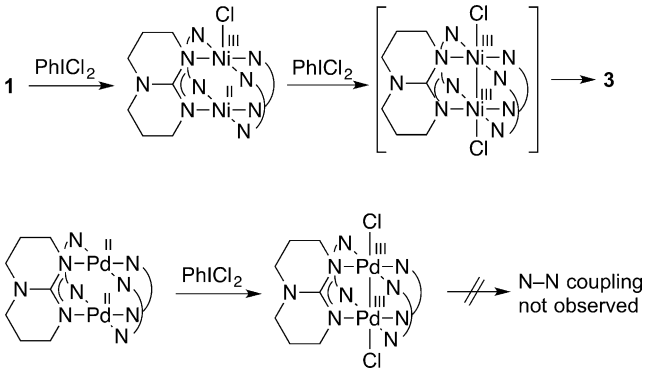


Figure 5. Spin-density plots and Ni–Ni distances obtained from DFT calculations for **4** (A) and $[(TBD)_4Ni_2]^+$ (B). For a color version, see the Supporting Information, Figure S12.

contrasts with $[(TBD)_4Ni_2]^+$ and previously reported "paddle-wheel" Ni_2^{5+} formamidate dimers, whose Ni–Ni distances are considerably shorter relative to Ni_2^{4+}, reflecting a bond order of 1/2.[14d] In these Ni_2^{5+} molecules, the two Ni centers are equivalent, and the oxidation state of each is 2.5 + . The lack of bonding interactions between Ni1 and Ni2 in **4** is attributed to the *trans*-influence of the chloride ligand, which reduces the Ni–Ni interaction. This effect could be enhanced in the solid state by the intermolecular interaction between Ni2 and the Cl from a second molecule of **4**, as evident from the X-ray crystal structure. Similar halide bridging has been reported in a $Rh_2(TBD)_4Br$ complex; the two Rh atoms in the complex are equivalent, reflected by the equal distances between the Br and two Rh centers.[15d]

The data presented above provide insight into the mechanism of N–N bond formation. The fast oxidation of **1** by $PhICl_2$ furnishes the mixed-valent intermediate **4**. Complex **4** does not undergo N–N bond formation. Instead, further oxidation of **4** results in rapid N–N bond-forming reductive elimination, possibly via a high-valent intermediate (Scheme 3). Such an oxidatively induced reductive elimination is reminiscent of a previous C–X bond formation from a dimeric Pd complex, in which a concerted reductive elimination is invoked for the isolated Pd^{III}–Pd^{III} intermediate.[28] However, the analogous high-valent $(TBD)_4Pd_2Cl_2$ complex does not undergo N–N bond coupling.[15a] Our study also shows that the reverse step, oxidative addition of Ni^0 to the N–N bond of **3** to generate **1** is facile. The favorable N–N bond cleavage could result from the strained seven-membered ring of **3**.

In summary, the results described herein establish the first, N–N bond reductive elimination with a "paddle-wheel" $Ni_2(TBD)_4$ complex. The reductive elimination is promoted by oxidants, proceeding through a mixed-valent $Ni_2(TBD)_4Cl$



Scheme 3. Binuclear Ni- and Pd-mediated bond formation reactions via high-valent intermediates.

intermediate. Spectroscopic data, in combination with DFT calculations, reveal that the oxidation states of the two Ni centers are Ni(II) and Ni(III), with a Ni–Ni bond order of zero. This electronic structure contrasts with $[(TBD)_4Ni_2]^+$ and the reported Ni_2^{5+} amidate complexes, where the two Ni centers are equivalent with a metal–metal bond order of 0.5. The elementary reactions presented herein provide the foundation for development of transition-metal-catalyzed N–N bond forming reactions that would find important applications in organic synthesis.

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Keywords: metal–metal bonding · mixed-valent compounds · nickel · N–N bond formation · reductive elimination

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