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Reactivity of (*NNN*)-pincer nickel(II) aryl complex towards oxidative carbon-heteroatom bond formation

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ABSTRACT

The reactivity of an (*NNN*)-Ni(II) aryl complex towards C–X bond formation upon exposure to a panel of one- and two-electron oxidants is reported. High selectivity for C(sp^2)–N bond formation is observed in all cases, except under conditions when C–C bond formation is accessible. Preliminary mechanistic investigations indicate access to either a Ni(III) or Ni(IV) intermediate dependent on oxidant used and that C–N bond formation is more efficient via Ni(IV) pathway due to geometry of reactive species.

1. Introduction

Over the last decade, the field of high-valent metal catalysis has emerged as a new and powerful tool in organic synthesis. In particular, high oxidation state metal centers can facilitate challenging C–X bond forming reductive eliminations, including carbon-halogen, carbon-oxygen, and carbon-nitrogen bond formation.[1,2] While palladium catalysis has played a central role in this field over the last 20 years, there has been a growing interest in C–X bond forming reactions from high-valent nickel intermediates.[3–8] The development of analogous nickel-catalyzed methods would be particularly attractive as nickel is more economical and sustainable, however significant challenges still remain.[9] Firstly, nickel can undergo facile one- or two-electron redox events allowing access to both Ni(II)/Ni(III) or Ni(II)/Ni(IV) manifolds, hindering reaction development due to limited mechanistic understanding.[5,6] Second, the relatively low stability of high-valent nickel centers makes the design of ligand scaffolds capable of stabilizing these intermediates and facilitating efficient catalyst turnover challenging, particularly at the Ni(IV) oxidation state.[10] Thus, there are continued efforts towards the design, synthesis and characterization of high-valent nickel complexes to probe their reactivity towards C–X bond formation, providing key insights for the development of catalytic manifolds.[11–13]

In this area, seminal work from the Hillhouse group has shown that cyclic Ni(II) complexes possessing alkyl and amido ligands undergo facile C(sp^3)–N reductive elimination upon exposure to one-electron oxidants including O_2, I_2, or $[(AcCp)Fe]^+$, via a Ni(III) intermediate.[14–16] Recent mechanistic investigations from the Sanford group have reported the synthesis and isolation of several stable Ni(II) precursors and the study of their reactivity upon exposure to a range of one- and two-electron oxidants under stoichiometric conditions.[3,5,10,17,18] In 2009 they reported that (phpy)(picoline)Ni(II)Br complex **1** (phpy = 2-phenylpyridine) underwent efficient C–Br bond formation upon treatment with either Br_2 or $CuBr_2$, via a proposed Ni(III) intermediate (Scheme 1A).[3] Subsequently, bis(phpy)Ni(II) species **7**, was found to undergo preferential C–C bond formation to give **4** along with trace C–Br (**3**) and C–N (**6**) products upon oxidation with N-bromosuccinimide (Scheme 1B). Although no high-valent nickel species were characterized, an analogous Pd(IV) species gave a similar product distribution, suggesting the possible intermediacy of a Ni(IV) species.[4,19] In a recent high profile report, Sanford employed [(bpy)$Ni^{II}(CH_2CMe_2\text{-}o\text{-}C_6H_4)$] complex **7** and found that upon oxidation by several $2e^-$ oxidants (**10**–**13**), **7** underwent selective C–C bond

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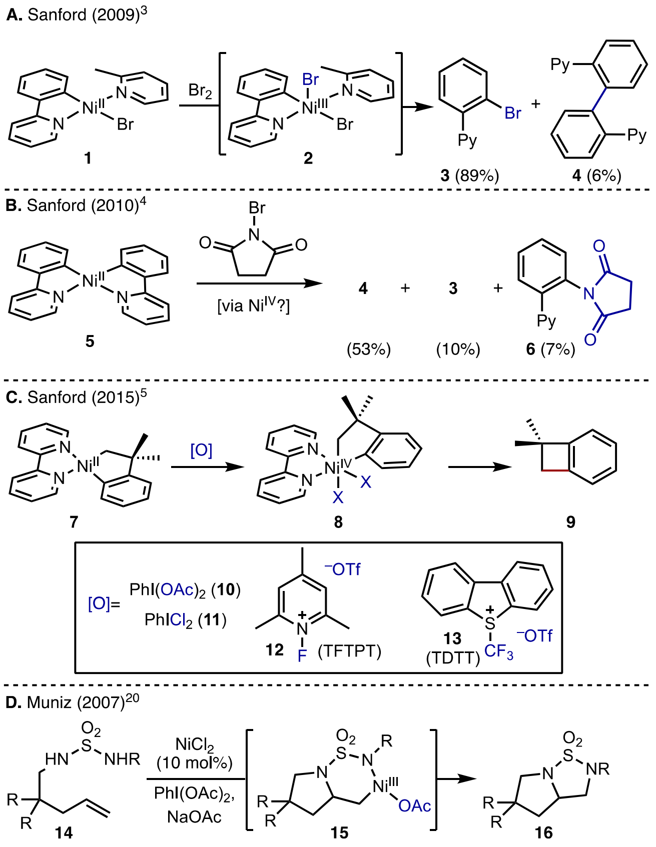
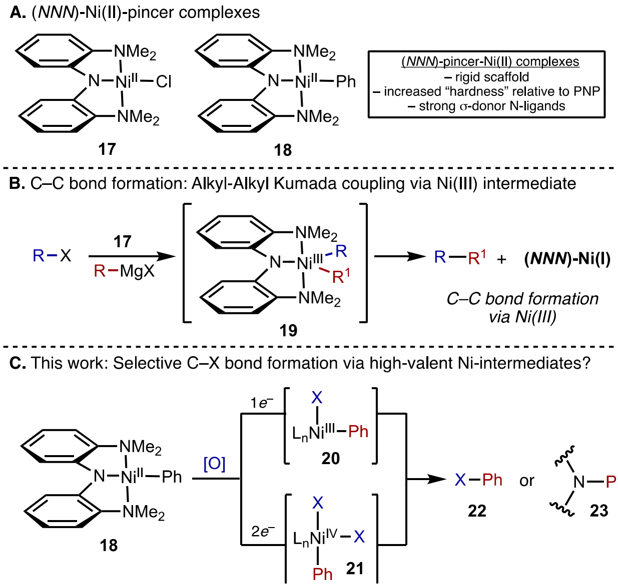


Scheme 1. A. Oxidative C–Br bond formation via proposed Ni(III) intermediate **B.** Preferential oxidative C–C coupling along with trace C–Br and C–N products from bis(phpy)Ni(II) complex. **C.** Selective C–C coupling from Ni(IV) intermediate **D.** First example of catalytic C–N bond formation via proposed Ni(III) intermediate.

formation with no evidence of competitive C–X reductive elimination products.[5] Significantly, use of a more stabilizing tridentate tris(2-pyridyl)methane (tppp) ligand system enabled the isolation and full characterization of key Ni(IV) intermediates for the first time, suggesting the feasibility of this redox manifold for C–X bond formation. Subsequent studies from the Sanford lab have utilized **7**, the (tppp)-ligand system and a closely related trispyrazolylborate scaffold to examine a range of C–X and C–C bond forming processes, providing key mechanistic insights towards the feasibility of catalytic manifolds.[5,10,17,18] Ritter has reported an oxidative radiofluorination method employing stoichiometric Ni(II)–aryl complexes, which upon exposure to a hypervalent iodine oxidant and nucleophilic fluoride, underwent smooth C(sp^2)–F reductive elimination, presumably via a Ni(IV) intermediate.[8] The Muniz group reported the first example of *catalytic* C(sp^3)–N bond formation from a proposed Ni(III) intermediate in an approach to oxidative olefin diamination (Scheme 1D).[20]

In an effort to explore new ligand scaffolds that could enable catalytic, oxidative C–X bond formation via either Ni(III) or Ni(IV), we were drawn to the amido bis(amine) pincer Ni-complexes recently developed by Hu (**17**, **18**, Scheme 2). By replacing the phosphorous atoms of established PNP-pincer ligands with nitrogens, Hu aimed to increase the relative "hardness" in order to better stabilize high-oxidation state metal complexes. To date Hu has successfully utilized *(NNN)*-NiCl complex **17** for a wide variety of nickel-catalyzed C(sp^3) Kumada couplings.[21–31] A detailed mechanistic investigation led to the conclusion that the Kumada coupling proceeds via a Ni(III) intermediate (**19**), accessed via radical oxidation of the Ni(II) center by an aryl iodide after transmetallation (Scheme 2B).[29] However, despite its utility in catalytic C–C bond formation, there have been no reports examining the viability of the (*NNN*)-pincer scaffold to enable analogous C–X bond forming processes via high-valent nickel intermediates. Herein, we report a study of the reactivity of *(NNN)*-NiPh complex **18** upon treatment with a range of both one and two-electron oxidants (Scheme 2C). Our studies have found that **18** will undergo preferential C(sp^2)–N bond formation over competitive carbon-oxygen or carbon-halogen pathways, however carbon-carbon bond formation will predominate upon exposure to an appropriate oxidant. Preliminary mechanistic studies indicate the role of either Ni(II)/Ni(III) or Ni(II)/Ni(IV) redox manifolds depending on the oxidant used and our results indicate that C–N bond formation is more efficient through the proposed Ni(IV) pathway. The findings indicate the viability C–N bond reductive elimination from high-valent nickel complexes, most notably Ni(IV), and reveal the significant role that oxidant selection plays in reaction development, providing valuable insights for further catalytic development.



Scheme 2. A. (*NNN*)-pincer Ni(II) complexes developed by Hu. **B.** Use of **17** for alkyl-alkyl Kumada coupling via Ni(III) intermediate. **C.** This work: examining the reactivity of **18** towards oxidative C–X bond formation.

2. Results and discussion

Our studies focused on the reactivity of (*NNN*)-NiPh complex **18**, which was readily prepared according to the procedure reported by Hu.[32] We hypothesized that, depending on the nature of the oxidant, this could give rise to either a Ni(III) (**20**) or Ni(IV) (**21**) intermediate, stabilized by the strong σ-donor nitrogen-ligands (Scheme 2C). These intermediates could then either undergo reductive C–X bond formation, where X would arise from the oxidant, to give **22**, or reductive C–N bond formation onto the ligand scaffold (**23**). Significantly, complex **18** does not have the ability to undergo a competitive C–C bond reductive elimination, a pathway found to outcompete C–X bond formation in previous studies of high-valent nickel intermediates.[3–5,8,10,17,18]

We began by exposing **18** to a panel of well-established 2e^- electron oxidants, including λ^3-iodanes (tolyl)I(OAc)$_2$, (tolyl)ICl$_2$, and [PhI(Py)$_2$]2OTf, as well as NCS and TDTT (Table 1, entries 1–6).[3–5,8,33,34] In each case we observed exclusive formation of **23** in near quantitative yield, the product of clean C(sp^2)–N bond formation.[35] Surprisingly, no products arising from competitive C–X reductive elimination onto the arene were observed (i.e. **22**) either by GCMS or ^{1}H NMR of the crude reaction mixtures.[36] While