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Article

Synthesis and Reactivity of $Ni^{II}(Phpy)_2$ (Phpy = 2-Phenylpyridine)†

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This article describes the synthesis and reactivity of $Ni^{II}(Phpy)_2$ (Phpy = 2-phenylpyridine) with a variety of oxidants, including O_2, Br_2, $PhICl_2$, *N*-fluoropyridinium salts, Cu^{II} salts, and *N*-halosuccinimides. High-oxidation-state Ni intermediates were not detected in any of these transformations. In all cases, the major organic product resulted from oxidatively induced C−C bond formation to generate the Phpy−Phpy dimer. Traces (2−16%) of organic products resulting from C−O, C−Br, C−Cl, and C−N bond-forming reductive elimination were also observed.

Introduction

Carbon−heteroatom (C−X) bond-forming reductive elimination at late-transition-metal centers is a topic of great current interest in organometallic chemistry.[1] Such reactions serve as the product release step of many catalytic transformations, including C−H functionalization,[2] allylic substitution,[3] carbonylation,[4] cross-coupling,[1a] and alkene functionalization.[1a,5,6] Fundamental studies of C−X bond-forming processes can provide insights for the design and optimization of new catalytic transformations with improved scope, efficiency, and selectivity.

Our group has been particularly interested in C−X bond formation at high-oxidation-state group 10 metal centers.[7−10] As part of this effort, we recently reported that the monocyclometalated Ni^{II} complex $(Phpy)Ni^{II}(pic)(Br)$ (**1**; Phpy = 2-phenylpyridine, pic = picoline) reacts with Br_2, $CuBr_2$, and $PhICl_2$ to afford halogenated organic products (for an example, see eq 1).[11] These transformations were proposed to proceed via high-oxidation-state Ni^{III} or Ni^{IV} intermediates; however, such species could not be directly detected in this system. As such, we sought to design ligand architectures that could potentially stabilize high-oxidation-state Ni organometallic complexes.[12−14]

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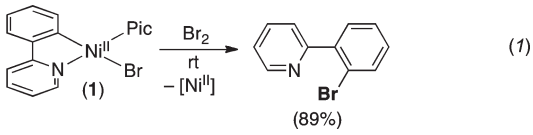
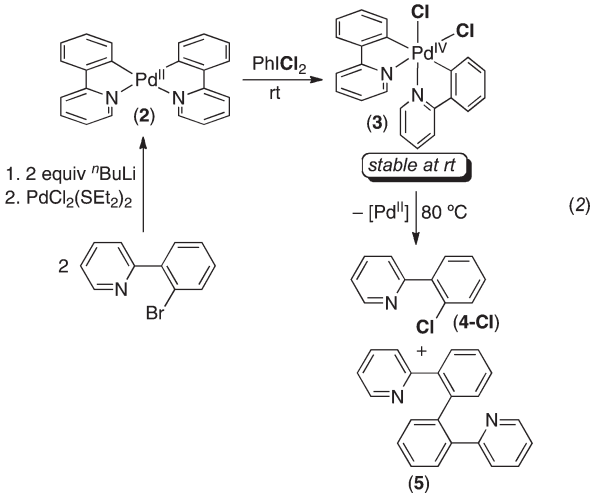


(1)

The bis-cyclometalated Pd^{II} complex $Pd^{II}(Phpy)_2$ (**2**) is known to react with strong oxidants (e.g., $PhICl_2$, *N*-chlorosuccinimide (NCS), $PhI(OAc)_2$, and Br_2) to afford unusually stable octahedral Pd^{IV} products such as **3** (eq 2).[7a,b,d] While these compounds are typically isolable at room temperature, they react at 40−80 °C to afford mixtures of organic products derived from carbon−heteroatom (**4**) and carbon−carbon (**5**) bond-forming reductive elimination. We reasoned that this ligand set might also stabilize Ni^{IV} or Ni^{III} complexes and allow us to directly observe C−heteroatom bond-forming reactions from such high-oxidation-state Ni species. This paper describes the synthesis of $Ni^{II}(Phpy)_2$ (**6**) and its reactivity with diverse oxidants.

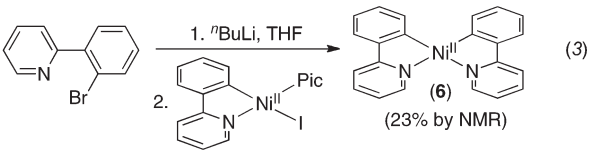


(2)

Results and Discussion

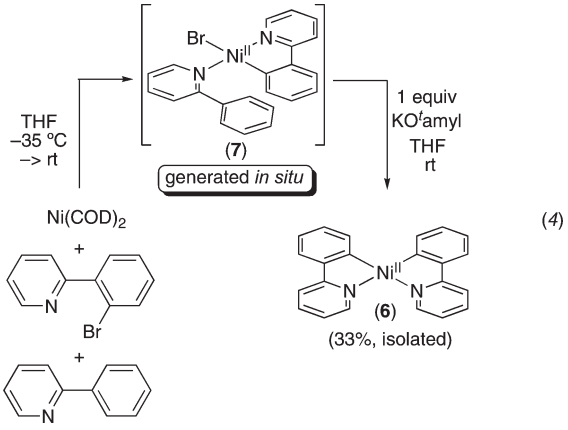
Our initial studies focused on developing an efficient synthesis of $Ni^{II}(Phpy)_2$ (**6**). The analogous Pd^{II} complex **1** is prepared by reaction of $PdCl_2(SEt_2)_2$ with 2 equiv of ortholithiated 2-phenylpyridine (Li-Phpy) (eq 2). On the basis of this precedent, we first examined the reaction between Ni^{II} dihalide precursors (including $NiBr_2(PPh_3)_2$, $NiCl_2(DME)_2$, and $NiCl_2$) and 2 equiv of Li-Phpy at −78 °C in Et_2O or THF.[15] Unfortunately, in all cases, intractable mixtures of Ni^0 and paramagnetic inorganic products were obtained, suggesting that reduction of the Ni^{II} starting material by the Li reagent predominates over the desired transmetalation in these systems.[16]

We hypothesized that this competing reduction could be limited by the use of a more electron rich Ni starting material. As such, the reaction of Li-Phpy with the monocyclometalated Ni^{II} complex $(Phpy)Ni^{II}(Pic)(I)$ was next explored (eq 3). Gratifyingly, ^1H NMR spectroscopic analysis of the crude reaction mixture showed a 23% yield of the desired product **6**. However, separation of this material from other byproducts proved challenging, and **6** could not be reliably isolated in pure form from this reaction.



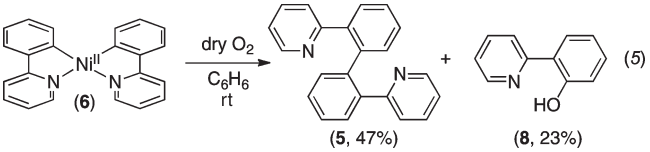
(3)

A recent report by Wolczanski demonstrated the formation of **6** via ortho deprotonation of coordinated 2-phenylpyridine ligands in $[(Phpy)Ni^{II}(Phpy\text{-}H)_2]^+$ and $(Phpy)Ni^{II}(Br)(Phpy\text{-}H)$ (**7**).[17] On the basis of this precedent, we next targeted a one-pot synthesis of **6** via the formation and in situ deprotonation of $(Phpy)Ni^{II}(Br)(Phpy\text{-}H)$ (**7**). Gratifyingly, treatment of $Ni(COD)_2$ with Phpy-Br in the presence of 1 equiv of 2-phenylpyridine followed by the addition of potassium *tert*-amylate resulted in formation of the desired product (eq 4). Recrystallization from benzene/pentanes provided clean samples of **6** in modest yield (33% over two steps), but in a highly reproducible fashion.



(4)

Complex **6** is a brick red solid that shows no signs of decomposition after 1 month at −35 °C in a N_2-filled drybox. This bis-cyclometalated Ni^{II} adduct is also stable in benzene solution for at least 24 h at room temperature under N_2. However, exposure of a benzene solution of **6** to dry O_2 under otherwise identical conditions resulted in a rapid (within 1 min) color change from red to yellow-brown accompanied by the formation of Phpy dimer **5** (47% yield) and the phenol product **8** (23% yield) (eq 5). This result demonstrates that **6** is highly susceptible to oxidatively induced C−C and C−heteroatom bond-forming reactions.



(5)

Treatment of a benzene solution of **6** with Br_2 resulted in a color change from red to dark brown within seconds at room temperature. Even at −78 °C, this reaction was extremely fast, and no high-oxidation-state intermediates were detected by ^1H NMR or EPR spectroscopy.[18] Analysis of the organic products showed the formation of Phpy dimer **5** (70%) along with significant amounts (16%) of the C−Br

(15) Wei, P.; Chan, K. T. K.; Stephan, D. W. *Dalton Trans.* **2003**, 3804.

(16) For example, the use of $Ni^{II}Br_2(PPh_3)_2$ as the Ni^{II} starting material produced $Ni^{I}Br(PPh_3)_3$ as the major inorganic product (characterized by EPR spectroscopy and X-ray crystallography). For a similar observation, see ref 15.

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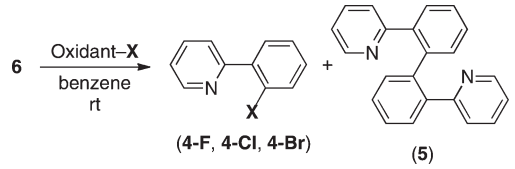
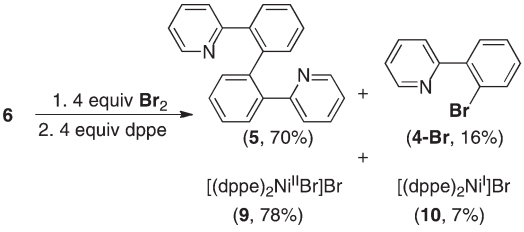
Table 1. Reaction of 6 with Electrophilic Halogenating Reagents



entry	oxidant	yield C−X (**4**),[a] %	yield C−C (**5**),[a] %
1	Br_2	16	70
2	NBS[b]	10	53
3	$CuBr_2$	2	59
4	$PhICl_2$	3	69
5	NCS	nd[c]	68
6	$CuCl_2$	nd[c]	79
7	NFTPT[d]	nd[c]	58

[a] Yields determined by ^{1}H NMR spectroscopy based on an average of two runs. [b] The C−N coupled product **11** was also formed in 7% yield (see Table 2). [c] nd = not detected. [d] *N*-Fluoro-2,4,6-trimethylpyridinium triflate.

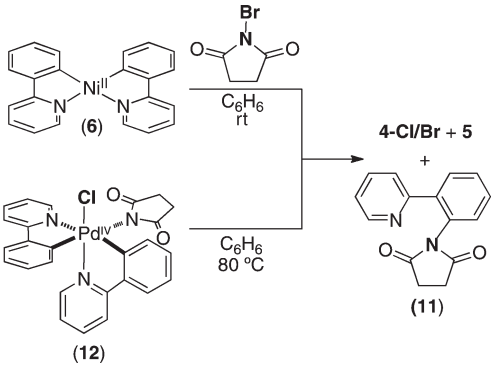
coupled product Phpy-Br (**4-Br**) (eq 6). Attempts to directly characterize the inorganic byproducts were complicated by the low crystallinity and paramagnetic nature of these Ni species. However, the addition of 4 equiv of dppe to the crude reaction mixture resulted in formation of the diamagnetic Ni^{II} species $[(dppe)_2Ni^{II}Br]Br$ (**9**) in 78% yield, as determined by ^{31}P NMR spectroscopy. The paramagnetic Ni^{I} species $[Ni^{I}(dppe)_2]Br$ (**10**) was also formed as a minor side product of this reaction (7% isolated yield of yellow crystals) and was characterized by X-ray crystallography (see the Supporting Information for details). On the basis of these results, we propose that the initial inorganic products of this transformation are a mixture of Ni^{II} and Ni^{I} complexes containing arylpyridines **4-Br** and **5** as L-type ligands.



(6)

As summarized in Table 1, a variety of other electrophilic brominating, chlorinating, and fluorinating reagents reacted with **6** in a fashion similar to that for Br_2. In all of these cases, C−C bond formation to generate **5** predominated over C−halogen coupling. The brominating reagents Br_2, NBS, and $CuBr_2$ provided the highest (although still modest) yields

Table 2. Comparison of Reaction of 6/NBS to Reductive Elimination from 12



entry	reacn	yield C−X (**4**), %	yield C−N (**11**), %	yield C−C (**5**), %
1[a]	**6**/NBS	10	7	53
2[b]	**12**	13	6	23

[a] Yields determined by ^{1}H NMR spectroscopy based on an average of 2 runs. [b] Data from ref 7b.

of C−halogen coupled Phpy-Br (**4-Br**) (2−16%), along with **5** as the major organic product (entries 1−3).[19]

The reaction of **6** with NBS was particularly notable, because it afforded C−N coupled product **11** (7%) along with **4-Br** (10%) and **5** (53%) (Table 2, entry 1). Interestingly, thermolysis of the palladium(IV) complex $Pd^{IV}(Phpy)_2(Cl)$-(succinimide) (**12**) in benzene was previously reported to afford a similar distribution of C−N, C−X, and C−C products (Table 2, entry 2).[7b] This result suggests the possibility that the Ni reaction may proceed via a similar high-oxidation-state M^{IV} intermediate. However, other pathways for oxidatively induced C−Br/C−N/C−C bond formation at Ni, including the formation of a Ni^{III} species[20] and/or Ni−C bond homolysis/free radical based coupling processes, are also potential routes to these products.

Conclusions

In conclusion, this paper describes the reactivity of Ni^{II}-$(Phpy)_2$ (**6**) with a number of different oxidants. In contrast to analogous Pd systems, no high-oxidation-state Ni intermediates were detected. Additionally, the Ni-bound Phpy ligands appear to be more susceptible to oxidatively induced C−C coupling in comparison to their Pd analogues. These features make it difficult to draw definitive conclusions about the mechanism of C−X bond formation at Ni in these systems. This study clearly indicates that the stabilization/isolation of high-oxidation-state Ni intermediates in carbon−heteroatom bond-forming processes will require supporting ligands that are not susceptible to competing C−C coupling.[13,14] Efforts in this area are underway in our laboratory and will be reported in due course.

Experimental Section

General Procedures. NMR spectra were obtained on Varian Inova 500 (499.90 MHz for ^{1}H; 125.70 MHz for ^{13}C) and Varian Inova 400 instruments (399.96 MHz for ^{1}H; 100.57 MHz for

(18) There were no clearly identifiable peaks in the low-temperature NMR spectra; however, there were several very broad resonances that may be indicative of paramagnetic intermediates. Unfortunately, these proved to be too transient and to be present in concentrations too low to observe by EPR.

(19) Numerous spectroscopic methods (NMR, GC, GCMS) and workup procedures (acidic, basic) have been attempted in an effort to account for the mass balance of the organic ligands in these transformations. The best results are shown in Table 1. We believe that the remaining organic products likely undergo decomposition in the presence of transient coodinatively unsaturated Ni^{I} or Ni^{II} byproducts of these reactions. Similar issues have been observed previously in oxidatively induced reductive elimination reactions at Pd^{IV} and Pd^{III}. For examples, see: (a) Reference 7. (b) Reference 11. (c) Powers, D. C.; Geibel, M. A. L.; Klein, J. E. M. N.; Ritter, T. *J. Am. Chem. Soc.* **2009**, *131*, 17050. (d) Kalyani, D.; Deprez, N. R.; Desai, L. V.; Sanford, M. S. *J. Am. Chem. Soc.* **2005**, *127*, 7330.

(20) For formation of Ni^{III} via reaction of $(PPhMe_2)_2NiBr(C_6Cl_5)$ with NBS, see: Oguro, K.; Wada, M.; Sonoda, N. *J. Organomet. Chem.* **1979**, *165*, C10.

^{13}C; 376.34 MHz for ^{19}F). ^{1}H and ^{13}C NMR chemical shifts are reported in parts per million (ppm) relative to TMS, with the residual solvent peak used as an internal reference. Multiplicities are reported as follows: singlet (s), doublet (d), doublet of doublets (dd), doublet of doublets of doublets (ddd), doublet of triplets (dt), triplet (t), quartet (q), quintet (quin), multiplet (m), and broad resonance (br).

Synthesis of 6. In a glovebox, $Ni(COD)_2$ (0.250 g, 0.91 mmol, 1.00 equiv) was dissolved in THF (5 mL) in a dry 20 mL scintillation vial. In a second 4 mL vial, 2-phenylpyridine (0.143 g, 0.92 mmol, 1.01 equiv) and 2-(2-bromophenyl)pyridine (0.215 g, 0.92 mmol, 1.01 equiv) were also dissolved in THF (2 mL). Both vials were cooled to −35 °C, and then the ligand solution was added to the $Ni(COD)_2$ solution. The resulting yellow-brown mixture was stirred for 10 min at room temperature. A solution of potassium *tert*-amylate (0.117 g, 0.92 mmol, 1.02 equiv) in THF (4 mL) was then added, which resulted in an immediate color change to blood red. The mixture was stirred for an additional 10 min, and then the solvent was removed under vacuum. The resulting red solids were dissolved in dry benzene (15 mL) and filtered through a pad of Celite. Pentanes (100 mL) was added to the red filtrate, and this solution was cooled at −35 °C overnight. The resulting precipitate was collected and dried under vacuum to afford **6** as a brick red solid (112 mg, 33% yield). The ^{1}H and ^{13}C NMR data for **6** matched those reported in the literature.[17]

Reaction of 6 with O_2. In a glovebox, complex **6** (4.8 mg, 0.013 mmol, 1.0 equiv) was dissolved in benzene (1 mL) in a J. Young NMR tube. The sample was removed from the glovebox, degassed via three freeze−pump−thaw cycles, and then filled with 1 atm of dry O_2. The sample was shaken vigorously, which resulted in a color change from deep red to yellow-brown. The resulting mixture was then allowed to stand at room temperature overnight. The solvent was removed under vacuum, and the solid residue was taken up in EtOAc (10 mL). Several drops of HCl were added, and then the organic layer was neutralized with saturated sodium bicarbonate. The EtOAc layer was then extracted with 1.0 M aqueous sodium citrate (2 × 20 mL) and saturated aqueous sodium thiosulfate (1 × 20 mL). The organic layer was collected and concentrated under vacuum, an internal standard (1,3,5-trimethoxybenzene) was added, and the reaction mixture was analyzed by ^{1}H NMR spectroscopy.

Reaction of 6 with Br_2. In a glovebox, complex **6** (9.5 mg, 0.026 mmol, 1.0 equiv) was dissolved in benzene (2 mL) in a 4 mL vial. The vial was equipped with a magnetic stir bar and sealed with a Teflon-lined cap fitted with a rubber septum. The vial was removed from the glovebox, and the oxidant (0.104 mmol, 4.0 equiv) was added via syringe. The reaction mixture was stirred at room temperature overnight. The solvent was then removed under vacuum, the resulting material was taken up in EtOAc (10 mL), and the EtOAc solution was extracted with 1.0 M aqueous sodium citrate (2 × 20 mL) and saturated aqueous sodium thiosulfate (1 × 20 mL). The organic layer was collected and concentrated under vacuum, an internal standard (1,3,5-trimethoxybenzene) was added, and the reaction mixture was analyzed by ^{1}H NMR spectroscopy. The isolation and characterization of inorganic byproducts from this transformation is described in the Supporting Information.

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Supporting Information Available: Text and figures giving experimental details and spectroscopic data for new compounds and a CIF file giving crystallographic data for complex **10**. This material is available free of charge via the Internet at http://pubs.acs.org.