Carbon–Nitrogen Bond Formation by Reductive Elimination from Nickel(II) Amido Alkyl Complexes

Kwangmo Koo and Gregory L. Hillhouse*

Searle Chemistry Laboratory, Department of Chemistry, The University of Chicago, Chicago, Illinois 60637

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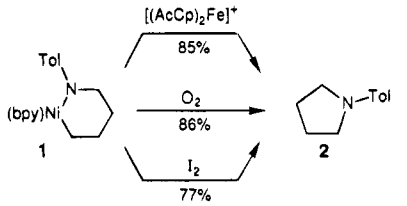
*Summary: Reaction of the azametallacyclohexane complex [(bpy)Ni{N(Tol)(CH$_2$)$_4$}] (**1**) with diacetylferrocenium tetrafluoroborate, O$_2$, or I$_2$ induces N–C reductive elimination, giving high yields of N-p-tolylpyrrolidine (**2**) upon chromatographic workup. Reaction of [(bpy)Ni(CH$_2$CMe$_2$-o-C$_6$H$_4$)] (**3**) with N$_3$Ph gives the azametallacycle [(bpy)Ni(NPh-o-C$_6$H$_4$CMe$_2$CH$_2$)] (**4**), which reacts with CO to give the lactam PhNC(O)CH$_2$CMe$_2$-o-C$_6$H$_4$ (**5**) and with HCl to give 2-tert-butyl-N-phenylaniline. Oxidation of **4** with [(AcCp)$_2$Fe$^+$], I$_2$, or O$_2$ results in N–C reductive elimination and affords high yields of the indoline PhN(CH$_2$CMe$_2$-o-C$_6$H$_4$) (**6**). The azametallacycle **4** is also thermally unstable with respect to C,N-reductive elimination to give **6**. Significantly lower yields of products resulting from N–C reductive elimination are realized when acyclic alkylnickel amides are oxidized. Thus, N,N-dimethyl-p-toluidine (**8**) is produced by the reaction of [(AcCp)$_2$Fe$^+$], I$_2$, or O$_2$ with [(bpy)Ni{N(Tol)(Me)}(Me)] (**7**), [(bpy)Ni{N(Ph)(Et)}(Et)] (**9**) reacts with I$_2$ to afford both N,N-diethylaniline (**10**) and N-ethylaniline (**11**) competitively, and [(bpy)Ni{N(Tol)(i-Bu)}(i-Bu)] (**12**) reacts with I$_2$ to give, primarily, N-isobutyl-p-toluidine (**14**), with smaller amounts of N,N-diisobutyl-p-toluidine (**13**).*

Introduction

Reductive-elimination reactions are ubiquitous across the transition-metal block and are among the most synthetically useful reactions in the organometallic chemist's arsenal. While reductive eliminations that form H–H, C–H, and C–C bonds are common,[1] similar reactions that form C–X bonds (where X is a heteroatom) are rare.[2,3] Nonetheless, reductive eliminations that form C–N bonds are strongly *implicated* in reactions such as Pd-catalyzed hetero cross-coupling reactions that form aryl amines[4] and the synthesis of organic amides and lactams from [(bpy)Ni(R)(NR$_2$)] and CO,[5] and two examples of C,N-reductive eliminations from well-characterized molecules have been reported.[6,7]

Scheme 1



Herein we report on a general class of reductive-elimination reactions, from discrete nickel complexes possessing alkyl and amido ligands, that form new carbon–nitrogen bonds in product amines and indolines.

Results and Discussion

We recently reported that reaction of aryl azides with [(bpy)Ni(R)$_2$] (bpy ≡ 2,2′-bipyridine) derivatives provides a synthetic route to Ni(II) complexes containing arylamido ligands.[5] The azametallacycle [(bpy)Ni{N(Tol)(CH$_2$)$_4$}] (**1**) is an isolable, thermally stable compound that undergoes thermal decomposition in benzene solution at ~130 °C. Remarkably, as shown in Scheme 1, reaction of solutions of **1** with either O$_2$ or I$_2$ at ambient temperature affords high yields of *N-p*-tolylpyrrolidine (**2**) upon chromatographic workup. Moreover, the one-electron oxidant 1,1′-diacetylferrocenium tetrafluoroborate also cleanly converts **1** to **2**, consistent with the notion that oxidation of Ni(II) to Ni(III) induces or facilitates C,N-reductive elimination. The ultimate fate of the Ni in these reactions has not been established, although free bipyridine is observed. Oxidatively induced reductive-elimination reactions that result in C–C bond formation are well established in organometallic chemistry, and several relevant nickel examples have been studied. For example, O$_2$ induces reductive elimination of cyclobutane from [(bpy)Ni(CH$_2$)$_4$][8] and chemical or electrochemical oxidation of Ni(II) to Ni(III) in [(bpy)Ni(R)$_2$] (R = alkyl, aryl) gives R–R-coupled products in high yields.[9]

In the course of examining the scope of this chemistry, we have studied the reaction of [(bpy)Ni(CH$_2$CMe$_2$-*o*-C$_6$H$_4$)] (**3**)[10] with N$_3$Ph at ambient temperature. As shown in Scheme 2, the reaction proceeds regiospecifically with insertion of the NPh fragment into the Ni–C(aryl) bond of **3** to give **4** and N$_2$. The regiochemistry of the insertion reaction was determined by quenching solutions of **4** with anhydrous HCl, giving 2-*tert*-butyl-*N*-phenylaniline (73% yield) on chromatographic workup. Similarly, reaction of solutions of **4** with carbon

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(1) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987.

(2) For an example of C,S-reductive elimination, see: Barañano, D.; Hartwig, J. F. *J. Am. Chem. Soc.* **1995**, *117*, 2937.

(3) For examples of C,O-reductive eliminations, see: (a) Koo, K.; Hillhouse, G. L.; Rheingold, A. L. *Organometallics* **1995**, *14*, 456. (b) Matsunaga, P. T.; Mavropoulos, J. C.; Hillhouse, G. L. *Polyhedron* **1995**, *14*, 175. (c) Hoberg, H.; Schaefer, D.; Burkhart, G.; Krüger, C.; Romao, M. J. *J. Organomet. Chem.* **1984**, *266*, 203.

(4) (a) Guram, A. S.; Buchwald, S. L. *J. Am. Chem. Soc.* **1994**, *116*, 7901. (b) Paul, F.; Patt, J.; Hartwig, J. F. *J. Am. Chem. Soc.* **1994**, *116*, 7901.

(5) Matsunaga, P. T.; Hess, C. R.; Hillhouse, G. L. *J. Am. Chem. Soc.* **1994**, *116*, 3665.

(6) Berryhill, S. R.; Price, T.; Rosenblum, M. *J. Org. Chem.* **1983**, *48*, 158.

(7) Villanueva, L. A.; Abboud, K. A.; Boncella, J. M. *Organometallics* **1994**, *13*, 3921.

(8) Takahashi, S.; Suzuki, Y.; Sonogashira, K.; Hagihara, N. *J. Chem. Soc., Chem. Commun.* **1976**, *839*.

(9) Tsou, T. T.; Kochi, J. K. *J. Am. Chem. Soc.* **1978**, *100*, 1634.

(10) Cámpora, J.; Gutiérrez, E.; Monge, A.; Palma, P.; Poveda, M. L.; Ruíz, C.; Carmona, E. *Organometallics* **1994**, *13*, 1728.

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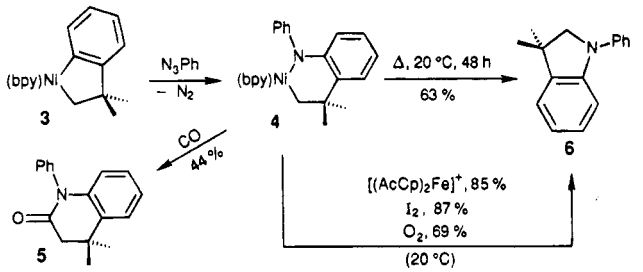
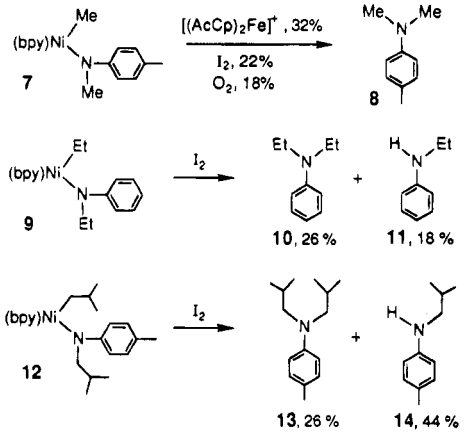
Scheme 2



Scheme 3

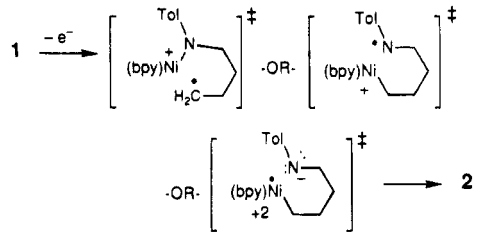


monoxide affords the lactam **5** as colorless crystals in 44% yield. An intriguing observation is that, unlike **1**, the azametallacycle **4** is thermally unstable with respect to C,N-reductive elimination to give the *N*-phenyl indoline **6**. Thus, stirring solutions of **4** for 2 days at ambient temperature affords **6** in 63% isolated yield. From a synthetic perspective, this Ni-based route to an indoline is interesting because it introduces the nitrogen functionality into the bicyclic ring system in the last step, in contrast to other protocols to indolines and indoles that incorporate nitrogen at earlier stages.[11] The most convenient route to the indoline **6**, however, is the treatment of **4** with an oxidizing agent (I_2, O_2, or $[(AcCp)_2Fe]^+$), which rapidly and cleanly effects the reductive elimination (Scheme 2).

Scheme 3 shows three acyclic alkylnickel(II) amido complexes, accessible by the reaction of aryl azides with dialkylnickel(II) derivatives,[5] that we have investigated with regard to C,N-reductive elimination to give trisubstituted arylamines. Oxidation of **7** by 1,1′-diacetylferrocenium gives **8** in 32% isolated yield. Somewhat lower yields of the C,N-coupled product are realized using I_2 or O_2 as the oxidant. In reactions of **7**, no secondary amine (i.e., MeNHTol) was detected, although in reactions of complexes having alkyl ligands with β-H atoms, the yields of secondary amines rival or exceed those of products derived from C,N-elimination. Thus, **9** reacts with I_2 to afford **10** (26%) and **11** (18%) competitively, while **12** reacts with I_2 to give **14** (44%) as the primary product, with smaller amounts of **13** (26%). The azametallacycle **1**, however, does not react to give a

(11) (a) Hegedus, L. S. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1113. (b) Tidwell, J. H.; Senn, D. R.; Buchwald, S. L. *J. Am. Chem. Soc.* **1991**, *113*, 4685. (c) Krolski, M. E.; Renaldo, A. F.; Rudisill, D. E.; Stille, J. K. *J. Org. Chem.* **1988**, *53*, 1170. (d) Kozikowski, A. P. *Heterocycles* **1981**, *16*, 267. (e) Robinson, B. *The Fischer Indole Synthesis*; Wiley-Interscience: New York, 1982. (f) Brown, R. K. *Indoles*: Wiley-Interscience: New York, 1972.

Scheme 4



secondary amine product even though it possesses β-H atoms, perhaps because constraints imposed by the ligand's cyclic structure prevent the β-hydrogens from interacting with Ni. It is also noteworthy that the yields are considerably higher for C,N-reductive elimination from the cyclic derivatives **1** and **4** (75–87%) than for the acyclic examples **7**, **9**, and **12** (26–32%), suggesting that the mechanism of reductive elimination might be a stepwise sequence involving intermediates akin to those shown in Scheme 4. Such an *intramolecular* process for metallacycles such as **1** and **4** could be efficient and give rise to high yields of cyclic amines, but a similar process for acyclic molecules would be an *intermolecular* one in which cage escape results in diminished yields of C,N-coupled products.

Experimental Section

General Considerations. Reactions were carried out using standard high-vacuum and Schlenk techniques and dry, air-free solvents. ^1H and $^{13}C\{^1H\}$ NMR spectra were recorded in C_6D_6 solution using a General Electric Ω-500 spectrometer (^1H at 500 MHz; ^{13}C at 125.8 MHz). Infrared spectra were recorded on a Nicolet 20SXB spectrometer in Nujol mulls with KBr plates. Quantitative GC data were obtained on a Hewlett-Packard 5890 instrument with an integrator. Mass spectra were recorded on a VG Analytical LTD 70-70 EQ double-focusing (EB) mass spectrometer. Spectral data for new compounds are tabulated in Table 1. Elemental analyses were performed by Desert Analytics (Tucson, AZ). Authentic samples of *N*,*N*-dimethyl-*p*-toluidine (**8**), *N*,*N*-diethylaniline (**10**), and *N*-ethylaniline (**11**) were purchased from Aldrich Chemical Co. The following compounds were prepared according to literature procedures: [(bpy)Ni{N(Tol)(CH_2)$_4$}] (**1**),[5] [(bpy)Ni(CH_2CMe_2-*o*-C_6H_4)] (**3**),[10] [(bpy)Ni{N(Tol)(Me)}(Me)] (**7**),[5] [(bpy)Ni{N(Ph)(Et)}(Et)] (**9**),[5] and [(bpy)Ni(*i*-Bu)$_2$].[3b]

Preparation of 2. To a solution of **1** (0.07 g, 0.18 mmol) in C_6H_6 (10 mL) was added I_2 (0.047 g, 0.18 mmol). The solution was stirred at ambient temperature for 3 h, during which time the color changed from purple to dark yellow. The solution was filtered, the volatiles were removed under vacuum, and the residue was extracted with *n*-hexane (20 mL). The extracts were concentrated and chromatographed on silica gel (eluent *n*-hexane/ethyl acetate, 4:1) to give **2** (0.023 g, 77%) as a yellow oil. Using a procedure analogous to that described above, reaction of **1** with O_2 (1 atm) or $[(AcCp)_2Fe][BF_4]$ yielded **2** in 86% and 85% yields, respectively.

Preparation of 5. A sample of **3** (0.095 g, 0.27 mmol) in 15 mL of benzene was treated with N_3Ph (32 μL, 0.27 mmol) and stirred for 3 h at ambient temperature. The resulting purple solution of **4** was exposed to CO (1 atm) and stirred for an additional 10 min; then the solution was filtered and taken to dryness under vacuum and the residue extracted with hexane. The extracts were concentrated and chromatographed on silica gel using hexane/ethyl acetate (1:1) to give **5** (0.03 g, 44%) as colorless crystals (mp 118–119 °C).

Preparation of 6. (a) Oxidative Route. Using a procedure and workup analogous to that described for **5**, reaction of **3** (0.09 g, 0.25 mmol) with N_3Ph (30 μL, 0.25 mmol) for 3 h

Table 1. Spectroscopic Data for New Compounds

2: ^{1}H NMR δ 7.14 (d, 2 H, aryl), 6.52 (d, 2 H, aryl), 2.98 (t, 4 H, CH_2), 2.32 (s, 3 H, CH_3), 1.54 (t, 4 H, CH_2); $^{13}C\{^1H\}$ NMR δ 146.5, 129.9, 124.4, 122.2, 47.6, 25.4, 20.6; EIMS 160 ($M^+ - 1$)

5: ^{1}H NMR δ 7.2–7.1 (m, 4 H, aryl), 7.06 (d, 1 H, aryl), 7.04 (d, 1 H, aryl), 6.78 (quintet, 2 H, aryl), 6.42 (d, 1 H, aryl), 2.39 (s, 2 H, CH_2), 1.12 (s, 6 H, CH_3); $^{13}C\{^1H\}$ NMR δ 167.9, 141.2, 139.5, 134.6, 129.6, 129.4, 127.7, 127.1, 124.2, 123.1, 118.0, 46.5, 33.4, 27.2; EIMS 251 (M^+); IR ν(CO) 1677 cm^{-1}

6: ^{1}H NMR δ 7.22–7.11 (m, 5 H, aryl), 7.02 (t, 1H, aryl), 6.96 (d, 1H, aryl), 6.95 (t, 1H, aryl), 6.80 (t, 1 H, aryl), 3.30 (s, 2 H, CH_2), 1.14 (s, 6 H, CH_3); 1.14 (s, 6 H, CH_3); $^{13}C\{^1H\}$ NMR δ 145.9, 144.5, 140.4, 129.4, 127.6, 122.4, 121.0, 119.6, 117.9, 108.6, 66.2, 39.7, 27.7; EIMS 223 (M^+)

12: ^{1}H NMR δ 8.91–6.30 (m, 12 H, bpy/aryl), 3.58 (m, 1 H, CH), 3.26 (m, 1 H, NC*H*H), 2.98 (m, 1 H, NC*H*H), 2.38 (s, 3 H, CH_3), 1.90 (m, 1 H, CH), 1.36 (d, 6 H, CH_3), 1.30 (m, 2 H, $NiCH_2$), 1.25–1.20 (m, 6 H, CH_3); $^{13}C\{^1H\}$ NMR δ 158.4, 155.9, 152.2, 151.2, 149.7, 135.8, 134.9, 129.6, 125.3, 125.1, 120.2, 118.9, 118.0, 112.6, 61.2, 31.1, 30.9, 26.8, 24.9, 22.9, 22.7

13: ^{1}H NMR δ 7.06 (d, 2 H, aryl), 6.68 (d, 2 H, aryl), 2.98 (d, 4 H, CH_2), 2.26 (s, 3 H, CH_3), 2.03 (m, 2 H, CH), 0.82 (d, 12 H, CH_3); $^{13}C\{^1H\}$ NMR δ 154.0, 129.9, 120.4, 113.9, 60.9, 26.6, 20.4;[a] EIMS 219 (M^+)

14: ^{1}H NMR δ 7.13–6.30 (d, 2 H, aryl), 6.68 (d, 2 H, aryl), 3.09 (br, 1 H, NH), 2.67 (d, 2 H, CH_2), 2.24 (s, 3 H, CH_3), 1.60 (m, 1 H, CH), 0.80 (d, 6 H, CH_3); $^{13}C\{^1H\}$ NMR δ 146.9, 129.9, 125.9, 113.2, 52.2, 28.6, 20.6, 20.5; EIMS 163 (M^+)

[a] Two CH_3 resonances are accidentally degenerate (δ 20.4), confirmed by selective decoupling.

followed by addition of I_2 (0.06 g, 0.25 mmol) gave **6** (0.05 g, 87%) as a yellow oil after chromatography. Alternatively, reaction of solutions of **4** with O_2 (1 atm) or $[(AcCp)_2Fe][BF_4]$ yielded **6** in 69% and 85% yields, respectively.

(**b**) **Thermal Route.** Using a procedure and workup analogous to that described for **5**, reaction of **3** (0.10 g, 0.28 mmol) with N_3Ph (34 μL, 0.28 mmol) for 48 h gave **6** (0.04 g, 63%) as a yellow oil after chromatography.

Preparation of 8. To a solution of **7** (0.12 g, 0.33 mmol) in THF (15 mL) was added I_2 (0.083 g, 0.33 mmol). The solution was stirred at ambient temperature for 3 h, during which time the color changed from magenta to orange. Workup as for **5** (eluent *n*-hexane/Et_2O, 5:1) gave **8** (0.012 g, 22%) as a yellow oil. The product was identified by spectral comparison with an authentic sample. Using analogous procedures, reaction of **7** with O_2 (1 atm) or $[(AcCp)_2Fe][BF_4]$ yielded **2** in 18% and 32% yields, respectively.

Preparation of 10 and 11. A solution of **9** (0.16 g, 0.44 mmol) in toluene (20 mL) was treated with I_2 (0.11 g, 0.44 mmol) and stirred at ambient temperature for 2 h. The solution was filtered, the filtrate was reduced to dryness using a rotary evaporator, and the residue was extracted using Et_2O (20 mL), which was concentrated and then chromatographed on silica gel (eluent *n*-hexane/Et_2O, 10:1) to give **10** (0.017 g, 26%) and **11** (0.010 g, 18%), which were identified by spectral comparison with authentic samples.

Preparation of 12. To a solution of (bpy)Ni(*i*-Bu)$_2$ (0.48 g, 1.47 mmol) in THF (25 mL) was added N_3Tol (0.33 mL, 2.94 mmol) via syringe, the solution was stirred for 2 h at ambient temperature and filtered, the filtrate was reduced in volume to 5 mL under vacuum, and then *n*-pentane (20 mL) was added by vacuum transfer. The solution was cooled to −78 °C for 1 h, and the resulting crystalline magenta product was isolated by filtration, washed with cold *n*-pentane (3 × 5 mL), and dried to give **12** (0.51 g, 80%). Anal. Calcd for $C_{25}H_{33}N_3Ni$: C, 69.2; H, 7.66; N, 9.68. Found: C, 69.0; H, 7.68; N, 10.98.

Preparation of 13 and 14. Using a procedure analogous to that used for **10** and **11**, reaction of **12** (0.21 g, 0.48 mmol) with I_2 (0.12 g, 0.48 mmol) yielded **13** (0.027 g, 26%) and **14** (0.035 g, 44%) as yellow oils.

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