

Evidence for a Ni^I Active Species in the Catalytic Cross-Coupling of Alkyl Electrophiles

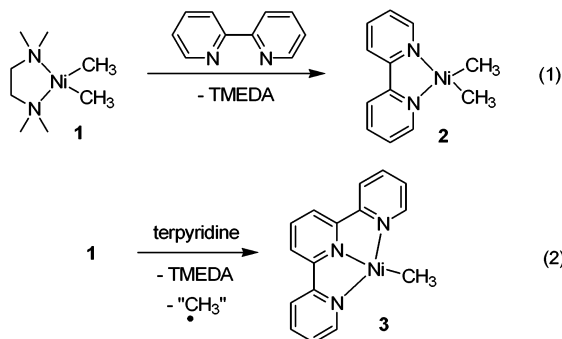
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The cross-coupling reaction between an organometallic reagent and an organic halide is one of the most versatile methods for forming a new carbon–carbon bond. The majority of catalytic cross-couplings involve some type of a C(sp²)-functionalized partner, and there are much fewer reports on methods to couple two C(sp³) partners to form a new alkyl–alkyl bond. However, in recent years, advances in nickel and palladium chemistry have made possible the catalytic cross-coupling of simple alkyl electrophiles with simple alkyl nucleophiles, even using substrates that possess normally reactive β -hydrogens.^{1–10} To expand the scope of these current catalysts to include more sophisticated transformations with alkyl electrophiles, more fundamental information is needed concerning the nature of the catalytically active species so that rational modifications to the catalysts can be made to suit a particular need.

We have been actively trying to develop synthetic methods to prepare nickel dialkyl complexes in order to determine what factors favor reductive elimination of saturated alkanes over the competing β -hydride elimination pathways. While working with polypyridine-based ligands, an interesting organometallic transformation was uncovered that sheds new light on the mechanism of a certain class of alkyl cross-coupling reactions. Reaction of bipyridine with (TMEDA)Ni(CH₃)₂ (**1**, TMEDA = *N,N,N',N'*-tetramethylethylenediamine) is well-known to provide the nickel dimethyl complex **2** (eq 1).¹¹ It was found, however, that reaction of **1** with terpyridine did not provide the related dimethyl complex, but instead led to the high-yield formation of the monomethyl complex **3** (eq 2). This paramagnetic metal complex is a rare example of an isolable Ni^I organometallic species that is stable at room temperature. Magnetic susceptibility ($\mu_{\text{eff}} = 1.64 \mu_{\text{B}}$ in THF) determination by the Evans NMR method^{12,13} confirms a product having one unpaired *d*-electron. It was also found that **3** exhibits two quasi-reversible waves in the cyclic voltammogram at -1.47 and -0.92 V vs Ag/Ag⁺ in THF solution.



Complex **3** was found to crystallize as extremely small violet plates that only weakly diffracted X-rays and afforded an ill-refined data set (see Supporting Information). A connectivity structure could be obtained, however, and a structural diagram of **3** is shown in Figure 1. Of particular note is the “head-to-head” packing¹⁴ between

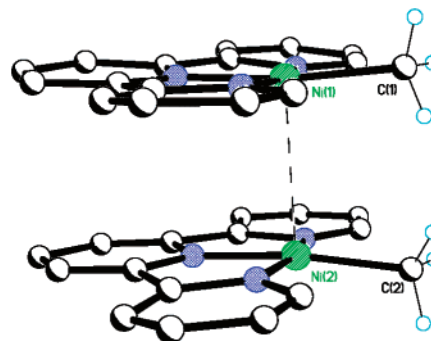


Figure 1. Ball and stick diagram of stacked **3**. Hydrogen atoms on the tpy ligand are omitted for clarity.

the two nickel complexes and the ligand-induced flattening of the Ni(I) centers.¹⁵ The nickel–carbon bond lengths averaged to 1.95–(13) Å, and a short nickel–nickel contact of 3.18(12) Å was also observed.

Presumably the formation of **3** arises from a Ni–C bond homolysis reaction^{16,17} resulting from distortion of a Ni^{II} dialkyl species from square planarity. In the context of alkane cross-coupling reactions, the failure of the dimethyl nickel complex to eliminate a full equivalent of ethane upon addition of terpyridine ligand suggests that Ni^{II} dialkyl intermediates may not be viable in the catalytic cross-coupling of saturated alkyl electrophiles using similar ligands. To probe this possibility, a number of reactions were performed using alkyl halides as electrophilic substrates in both stoichiometric and catalytic cross-coupling reactions.

Reaction of complex **3** with 1 equiv of cyclohexyl iodide at room temperature for 24 h in C₆D₆ solution indeed showed that transfer of the metal-bound methyl group to alkyl halides could occur (eq 3). The reaction was monitored by NMR spectroscopy (referenced to an internal standard), and the yield of methylcyclohexane produced was found to be 79%. Analysis of the volatiles by ¹H NMR spectroscopy also confirmed that the major product of the reaction was methylcyclohexane, with no significant amount of olefinic products resulting from β -hydride elimination reactions. The inorganic product of the reaction was characterized by elemental analysis, which was consistent with the mono-iodo Ni^I complex **4a**. The stoichiometric reaction described in eq 3 is thus further evidence against a Ni⁰/Ni^{II} redox cycle, as no disproportionation products were produced during alkyl transfer.

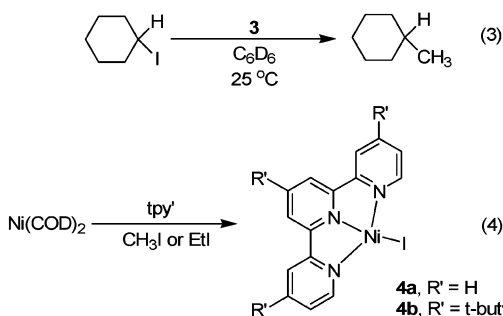
The results described in eq 4 suggest that Ni^{II} alkyl halide complexes derived from the terpyridyl ligand were unstable, similar to the dimethyl counterparts. Reaction of Ni(COD)₂ with 1 equiv of tpy-based ligand and 1 equiv of alkyl iodide did not lead to any stable oxidative addition products, but rather led to isolable Ni^I iodide complexes. The more soluble **4b** has even been structurally characterized (see Supporting Information).

Experiments were also performed to see if a Ni^I alkyl complex such as **3** could be a viable precursor in cross-coupling catalysis.

Table 1. Catalytic Alkyl Cross-Coupling Reactions

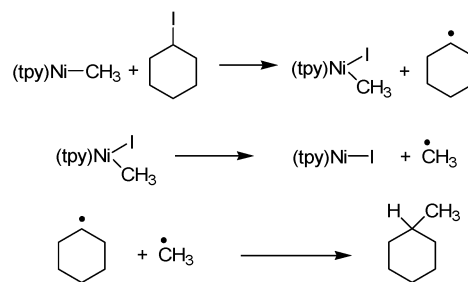
entry	alkyl halide	product	yield (%) ^a
1	hexyl-Br	undecane	15
2	Ph(CH ₂) ₃ Br	Ph(CH ₂) ₇ CH ₃	13
3	Ph(CH ₂) ₃ I	Ph(CH ₂) ₇ CH ₃	60
4	iodocyclohexane	pentylcyclohexane	64
5 ^b	iodocyclohexane	pentylcyclohexane	65

^a Yields based on GC relative to a calibrated internal standard. ^b Catalyst employed was Ni(COD)₂ and tpy (both 5 mol %).



The results of this study are provided in Table 1, and show that, in the presence of a transmetalating agent such as alkylzinc halides, moderate yield formation of cross-coupled alkane could be achieved without any overwhelming formation of β -hydride elimination products. Of note is the greater efficiency of the cross-coupling reaction using alkyl iodides over alkyl bromides. High yields of a product containing a relatively bulky tertiary C(sp³) center could even be achieved using secondary alkyl halides such as iodocyclohexane as the electrophile. Use of the commercially available starting materials Ni(COD)₂ and tpy yielded results (entry 4 vs 5) similar to those seen with **3**. The minor products in the catalysis of alkyl iodides suggest the presence of a radical pathway, as Ph(CH₂)₆Ph and dicyclohexyl were detected for entries 3 and 4, respectively. Additionally, reaction of **3** with the radical clock iodomethylcyclopropane afforded substantial formation of olefinic products as detected by ¹H NMR spectroscopy.

In light of the fact that both the Ni^{III} alkyl halide and dialkyl complexes were found to be unstable with respect to their Ni^I decomposition products, and the fact that **3** can both transfer its methyl group to alkyl halides to form a Ni^I halide complex and to serve as an initiator for catalytic alkyl cross-coupling, we speculate that a radical mechanism of the type shown in Scheme 1 may be operative under catalytic conditions. There are two noteworthy features of the proposed mechanism which we find attractive. First, the 17-electron nickel alkyl complex is thermodynamically capable of reducing alkyl iodides in THF solution. In fact, the reduction potential of **3** is close to that of samarium diiodide, which is a well-known catalyst for alkyl iodide reductions.¹⁸ Second, formation of **4a** after the cross-coupling event allows for the cycle to begin anew in the presence of alkylzinc halide reagents, as transmetalation will provide a new (tpy)NiR complex. A related electron-transfer mechanism has been proposed by Eisenberg and co-workers for

Scheme 1. Possible Mechanism for the Cross-Coupling of Saturated Alkyl Electrophiles Mediated by **3**

the reduction of alkyl halides by odd-electron rhodium complexes.¹⁹ To our knowledge, this is the first time a Ni^I species has been proposed as the *catalytically* active species in the cross-coupling of saturated alkyl groups, and these results build upon the seminal work by Espenson and Kochi, who also observed electron-transfer reactions between organic halides and nickel complexes.^{20,21} The results presented here may also be relevant to the cross-coupling chemistry involving other ligands such as those derived from pybox,⁹ which are also tricoordinating in nature. A survey of new ligands which may be able to support a similar odd-electron redox shuttle and provide higher yields for catalytic cross-coupling of alkanes is currently being undertaken.

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Supporting Information Available: General methods and X-ray data for all relevant compounds (PDF, CIF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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