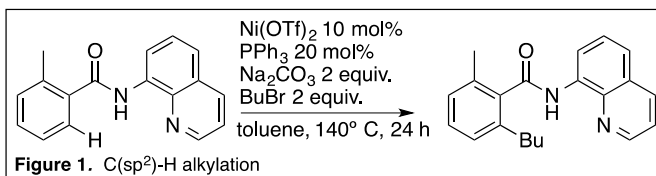


INTRODUCTION

Transition-metal catalyzed cross-coupling reactions are one of the most widely used methods for the construction of C-C and C-X bonds. Although a majority of these transformations utilize palladium catalysts, the past few decades have witnessed a resurgence in the use of nickel complexes for cross-coupling reactions.¹ Nickel, unlike palladium, is an inexpensive, earth-abundant metal, making it an attractive choice for the development of new catalytic methods. In addition, nickel enables transformations that are challenging with palladium catalysts, such as cross-couplings reactions using tertiary alkyl halides or phenol derivatives as electrophiles. However, nickel complexes promote different cross-coupling reactions depending on the oxidation state of the active catalytic species. Indeed, MacMillan and others have shown that accessing high oxidation states of nickel allows access to important C-O bond forming reactions, otherwise inaccessible with traditional nickel(II) catalysis.² Consequently, accessing and utilizing nickel(IV) complexes have the potential to offer a new approach for the design of C-heteroatom bond forming reactions.

TRANSFORMATIONS INVOLVING NICKEL(IV) COMPLEXES

Chatani has reported many nickel-catalyzed reactions, some of which may involve a high oxidation state nickel intermediate. In 2013, these authors developed a nickel-catalyzed, direct C(sp²)-H alkylation utilizing a bidentate directing group (Figure 1).^{3,4} The transformation has a broad substrate scope with respect to the amide and alkyl bromide used. This work has since been extended to include C(sp³)-H alkylations using a similar bidentate directing group. Mechanistic experiments suggest the presence of a nickel(IV) intermediate.



Deuterium-labeling studies as well as product distribution for Ni(OTf)₂ and Ni(cod)₂ were examined to gain an understanding of the differences in mechanism between these two catalysts. The results indicate that a Ni(II) complex is the catalytically active species in the reaction, implicating a Ni(IV) intermediate. From these observations the authors propose the mechanism shown in Figure 2. Although they were able to provide mechanistic evidence for the involvement of a nickel(IV) complex, they were unable to isolate and characterize the intermediate of interest. Only a handful of isolated Ni(IV) complexes have been reported. Klein and coworkers were first to describe the isolation and characterization of organonickel(IV) complexes, shown in Figure 3.⁵ These complexes exhibited little to no catalytic activity and were used as a proof of concept.

The Klein and Chatani work provided a foundation for Sanford's pursuit of isolating and characterizing a Ni(IV) intermediate in a catalytic cycle.⁶ Sanford and coworkers used TDDT, a trifluoromethylating agent frequently used in catalysis, to oxidize a Ni(II) complex to Ni(IV), which was then characterized by NMR in situ (Figure 4a). Changing from a bidentate bipyridine ligand to a tridentate ligand greatly increased stability, and oxidation of this new complex led to a nickel (IV) complex that was stable in acetonitrile for 3 days. The authors were able to characterize this complex by x-ray crystallography, which confirmed the high oxidation state of the nickel center. This complex reacted with Me₄NOAc to create a C(sp³)-O bond (Figure 4b).

RESULTS AND CONCLUSIONS

The mechanistic studies performed in Chatani's group led them to believe that a Ni(IV) intermediate was involved in the catalytic cycle. Sanford was able to isolate and characterize a

reactive intermediate which gave spectroscopic evidence of the existence of a Ni(IV) complex in the reaction. Sanford also carried out some of the first C-C and C-X cross coupling reactions employing this Ni(IV) intermediate. These findings provide a foundation for the development of novel catalytic C-C and C-X coupling reactions employing new Ni(IV) complexes.

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