

LIGAND EFFECTS IN NICKEL CATALYSIS

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INTRODUCTION

The use of transition-metal catalyzed processes in carbon bond formation is arguably the most influential advancement in organic chemistry over the last few decades. While palladium is utilized most often, ever increasing attention has focused on nickel in multi-component reactions, cross-couplings, cycloisomerizations, reductive couplings, and other processes.¹ Particularly, nickel complexes have demonstrated untapped potential in sp^3 couplings with secondary halides and in reductive couplings of alkynes.^{2,3} Moreover, the ligand environment greatly dictates nickel's unique reactivity profile. This seminar will discuss these fundamental ligand effects focusing on their application in nickel catalysis.

ELECTRONIC EFFECTS

The electronics of the nickel ligand greatly alters its reactivity. The main classes encountered are phosphines, *N*-heterocyclic carbenes (NHCs), and π -accepting ligands (Figure 1). The electron-rich ligands make nickel more nucleophilic, such that they can participate in stereoselective reductive couplings between an electrophilic aldehyde and an alkyne to make a substituted allylic alcohol derivative.

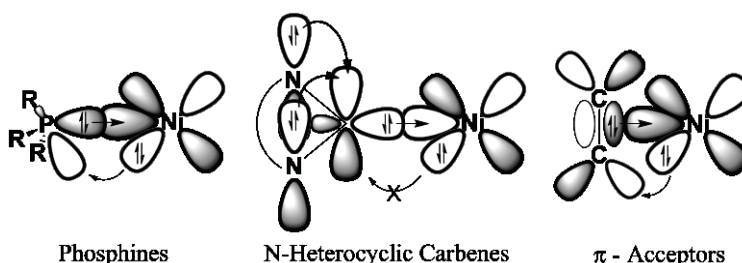


Figure 1. Nickel-ligand complexes.

Furthermore, the use of electron-poor, π -accepting ligands such as pyridine bisoxazoline are used to efficiently cross-couple secondary alkyl halides. Vicic, Fu, and others have shown that these couplings are stereoconvergent with a C_2 symmetric ligand, going through a radical mechanism.^{4,5}

STERIC EFFECTS

Sterically bulky ligands around a nickel center can change its geometry, coordination, selectivity, and reactivity. The use of bulky and chiral alkyl phosphines provide enantioselective reductive couplings.⁶ Furthermore, the advantageous steric characteristics of NHCs have been used in regioselective ynal reductive couplings. Montgomery and coworkers demonstrated that the regioselectivity of a reductive coupling can be reversed to a large degree by switching from an electron-rich, non-sterically demanding mesityl NHC (IMes) ligand to a sterically demanding *iso*-propyl NHC.⁷ He went on to use this methodology in a late stage macrocyclization of an antibiotic (Figure 2).⁸

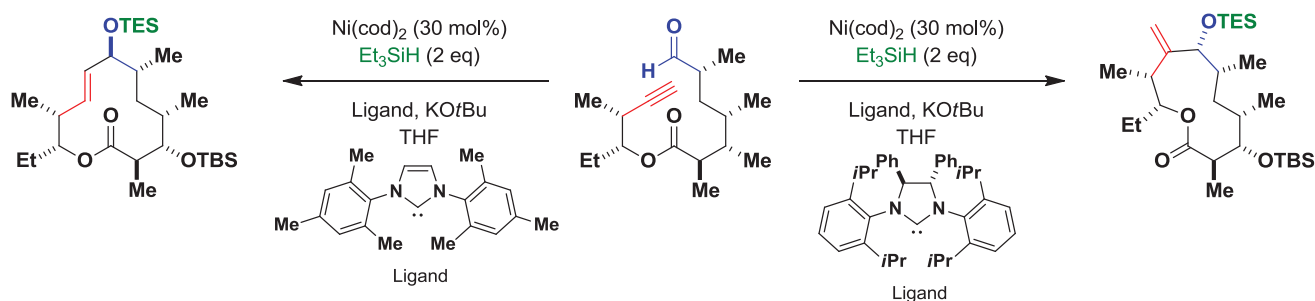


Figure 2. Regioselective macrocyclizations based on sterics of ligand.⁸

CHELATION EFFECTS

Chelating ligands have demonstrated unparalleled efficacy in sp^3 cross-couplings. Secondary alkyl halides containing β -hydrogens present a challenge in cross-couplings for several reasons. Breakthrough studies by Fu with chelating PyBox ligands has enabled the development of new methodologies in the coupling of activated and unactivated secondary alkyl electrophiles.⁵ The tricoordinate ligands make nickel less prone to β -hydride elimination. Additionally, large bite angles increase the rates of reductive elimination. These effects have been used to produce a wide array of sp^3 cross-couplings with activated and unactivated alkyl halides and pseudohalides.

CONCLUSION

The use of nickel-ligand complexes has enabled the development of novel reactivity in the form of sp^3 couplings of activated and unactivated secondary halides and in reductive couplings. Furthermore, the ligand environment greatly affects nickel's reactivity. The predictability and compatibility of nickel is manageable, but a small change drastically alters reactivity. Despite these difficulties, considerable attention focuses on understanding the reactivity of nickel complexes and controlling its innate yet diverse reactivity. Further understanding of the effect of nickel's coordination sphere on its reactivity will facilitate the popularization of nickel in organometallic catalysis. Similarly to palladium, the further understanding of nickel's reactivity will add it to every chemist's arsenal of catalysts to solve problems which seemed unobtainable by previous means.

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