HARNESSING THE CHEMISTRY OF CO_2

DE-FG02-05ER15689

Janis Louie
Department of Chemistry, University of Utah, Salt Lake City, UT 84115

Email: louie@chem.utah.edu; Telephone: (801) 581-7309
DOE/Office of Science Program Office: Basic Energy Sciences, Chemical Sciences
DOE/Office of Science Program Technical Program Manager Contact: Raul Miranda

FINAL PROGRESS REPORT

(9/15/2009 – 11/30/2012)

PERSONNEL

PI: Janis Louie
Post-docs: none
Graduate Students: Puneet Kumar, Timothy Lane, Ryan Stolley

PUBLICATIONS

(1) B. R. Van Ausdall, J. L. Glass,† K. M. Wiggins, † A. M. Arif, J. Louie "A Systematic Investigation of Factors Influencing the Decarboxylation of Imidazolium Carboxylates" *J. Org. Chem.* **2009**, *20*, 7935-7942.
(2) K. Zhang, M. Conda-Sheridan, S. Cooke, J. Louie "N-Heterocyclic Carbene Bound Ni(I)-Complexes and Their Roles in Catalysis" *Organometallics* **2011**, *30*, 2546-2552.
(3) K. Zhang, J. Louie "Rhodium-Catalyzed Decarboxylative Cycloaddition Route to Substituted Anilines" *J. Org. Chem.* **2011**, *76*, 4686-4691.
(4) P. Kumar, D. M. Troast, R. Cella, J. Louie "Ni-Catalyzed Ketene Cycloaddition: A System that Resists the Formation of Decarbonylation Side Products" *J. Am. Chem. Soc.* **2011**, *133*, 7719-7721; *C & E News* May 9, 2011.
(5) B. R. D'Souza, T. K. Lane, J. Louie "Iron Catalyzed Cycloaddition of Cyanoalkynes and Alkynes" *Org. Lett.* **2011**, *13*, 2936-2939.
(6) R. M. Stolley, M. T. Maczka,† J. Louie "Nickel-Catalyzed Cycloaddition of Diynes and Cyanamides" *Eur. J. Org. Chem*. **2011**, *20-21*, 3815-3824; *Invited Contribution to a Special Edition Honoring Women in Chemistry*.
(7) P. Kumar, S. Prescher,† J. Louie "A Serendipitous Discovery of a Nickel-Catalyst for Cycloaddition of Diynes with Unactivated Nitriles" *Angew. Chem. Int. Ed.* **2011**, *50*, 10694-10698*; Synfacts Highlight* 2012, 8(1), 0018 DOI: 10.1055/s-0031-1289949.
(8) P. Kumar, J. Louie "Double the Fun: Nickel-Catalyzed Cycloaddition *via* Two Sequential C-H Activations" *Angew. Chem. Int. Ed.* **2011**, *50*, 10768-10769; *Invited Highlight*.
(9) B. R. Van Ausdall, N. F. Pols,† V. A. Kincaid,† A. M. Aarif, J. Louie "NHC·CO_2-bound $MBPh_4$ Complexes (M = Li, Na) and their Relevance in Transcarboxylation Reactions" *J. Org. Chem.* **2011**, *76*, 8413-8420.
(10) A. Thakur, K. Zhang, J. Louie "Suzuki-Miyaura Coupling if Hetero-aryl Boronic Acids and Vinyl Chlorides" *Chem. Comm.* **2012**, *48,* p203-205.
(11) R. M. Stolley, W. X. Guo,† J. Louie "Palladium-Catalyzed Cross-Coupling of Cyanamides" *Org. Lett.* **2012**, *14*, 322-325; *C & E News* December 19, 2011.

(12) P. Kumar, J. Louie "A Single Step Approach to Highly Substituted Piperidines Via Ni-Catalyzed β-Carbon Elimination" *Org. Lett.* **2012**, *14*, 2026-2029; *Synfacts Highlight* 2012, 8(7), 0715; *Synfacts Highlight* 2012, 8(9), 0949.

(13) P. Kumar, K. Zhang, J. Louie "An Expeditious Route to Eight-Membered Heterocycles by Nickel-Catalyzed Cycloaddition: Low-Temperature C_{sp2}-C_{sp3} Bond Cleavage" *Angew. Chem. Int. Ed.* **2012**, *51*, 8602-8606.

(14) T. K. Lane, B. R. D'Souza, J. Louie "2-Aminopyridines from Iron-Catalyzed Cycloaddition of Diynes and Cyanamides" *J. Org. Chem.* **2012**, *77*, 7555-7563.

(15) R. M. Stolley, H. A. Duong, D. R. Thomas, J. Louie "The Discovery of $[Ni(IPr)RCN]_2$ Species and their Role as Cycloaddition Catalyts for the Formation of Pyridines" *J. Am. Chem. Soc.* **2012**, *134*, 15154-15162.

(16) R. Cella, J. Louie "Transition Metal-NHC catalyzed cyclizations" in *N-Heterocyclic Carbenes in Transition Metal Catalysis and Organocatalysis*; Cazin, C. S. J., ed.; Springer Publishing Co.: New York, **2010**.

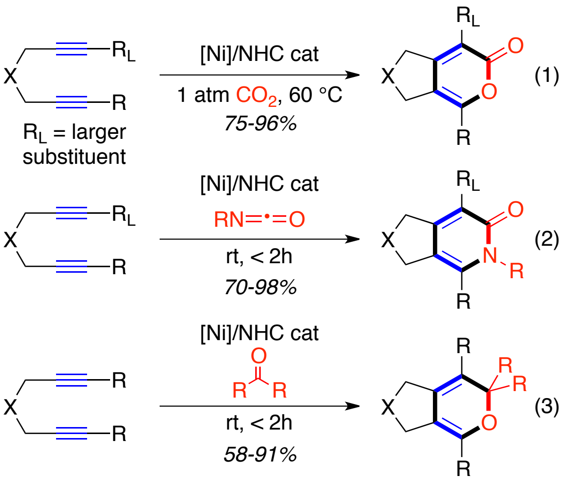
(17) R. M. Stolley, J. Louie "The Organometallic Chemistry of Ni (update)" in *Science of Synthesis*; Plietker, B., ed.; Houben-Weyl: **2012**.

(18) P. Kumar, J. Louie "Nickel-Mediated Cycloaddition (Chapter 2.3 in Chapter 2: [2+2+2] and [2+2+1] Cycloaddition) in *Transition-Metal-Mediated Aromatic Ring Construction*, Tanaka, K., ed.; John Wiley & Sons Ltd.: Chichester, **2012**.

DEVELOPMENT OF A CYCLOADDITION CATALYST[1]

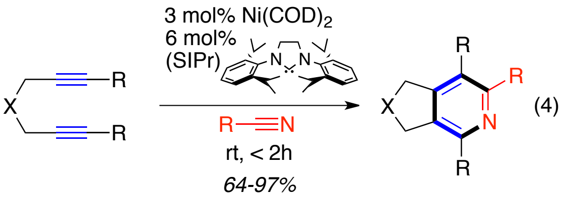
INCREASING THE UTILITY OF THE NI CYCLOADDITION CATALYST[2,3,4]

Our initial efforts focused on *improving* Ni catalyzed cycloaddition chemistry. That is, prior to our work, known Ni cycloaddition catalysts generally afforde/d heterocyclic products (such as pyrones,[5] pyridones,[6] and pyrans[7]) in low to moderate yields and possessed limited substrate scope. We successfully developed a Ni catalyst system based on the use of *N*-heterocyclic carbene (NHC) ligands that not only provided a large array of heterocyclic products (i.e., large substrate scopes) but also provided these products in generally excellent yields (eq 1-3).



I. CYCLOADDITION OF DIYNES AND NITRILES[8]

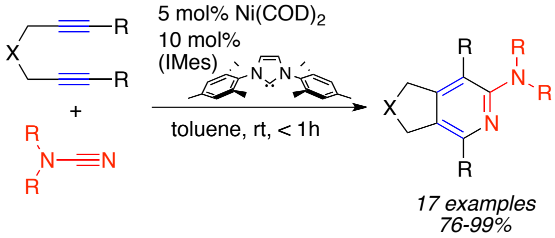
As we anticipated, this chemistry served as a launching pad for the development of a *general* annulation system and allowed us to expand the repertoire of unsaturated hydrocarbons (alkenes and alkynes) and X=C-containing substrates amenable to cycloaddition chemistry. Our first success was in applying the NHC/Ni catalyst system to the cycloaddition of diynes and nitriles to afford pyridines (eq 4). The success of this reaction is intriguing for a number of reasons: 1) Ni



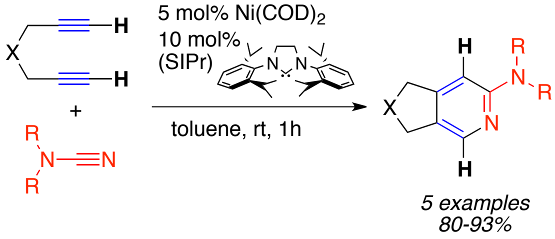
complexes readily undergo oxidative addition of R-CN bonds;[9] 2) Ni complexes are known to cause homodimerization of nitriles;[10] 3) Ni complexes catalyze the carbocyanation of alkynes;[11] and 4) the oxidative coupling of an alkyne and a nitrile is *sluggish* at best for Ni[10] (although the resultant nickelacycle can be prepared through the stoichiometric transmetallation between an azazirconacyclopentenone and $Ni(PPh_3)_2Cl_2$).[12] Despite these potential obstacles, the Ni/NHC catalyst efficiently converts a variety of nitriles and diynes into pyridines in generally high yields. It is likely the high nucleophilic character of our Ni/NHC system allows for the facile oxidative coupling of the alkyne and the nitrile which thereby leads to efficient cycloaddition.

II. CYCLOADDITION OF DIYNES AND CYANAMIDES[13]

Although studies of cycloadditions of alkynes and nitriles are expansive, independent studies of analogous cyanamides are sparse, despite the utility of 2-aminopyridines (i.e., organometallic ligands,[14] chromophores,[15] and intermediates in biologically active molecules[16]). Given the efficacy of our Ni/NHC catalyst, we evaluated cyanamides as a potential substrate in cycloaddition chemistry. Interestingly, 2-aminopyridine product was detected for most ligands evaluated, which is markedly different than Ni-catalyzed cycloadditions of simple nitriles where only select NHC ligands (i.e., no phosphines) afforded appreciable amounts of pyridine products. The highest yields were obtained when IMes (or SIPr, IMes = 1,3-bis(1,3,5-trimethyl)-imidazol-2-ylidene, SIPr = 1,3-bis-(2,6-diisopropylphenyl)-4,5-dihydroimidazol-2-ylidene) was employed as the ligand. The effectiveness of the $Ni(COD)_2$/IMes catalyst is particularly surprising as this catalyst system typically produces significant amounts of a diyne dimerization side product. Using $Ni(COD)_2$/IMes as the catalyst system, a variety of diynes and cyanamides were converted their respective 2-aminopyridine products (eq 5) in excellent yields.



(5)

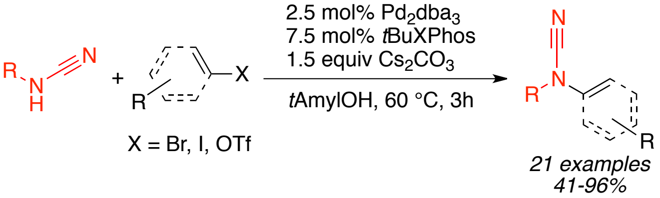


(6)

Terminal diynes, a challenging substrate for the parent Ni-catalyzed nitrile cycloaddition, were also evaluated as potential substrates (eq 6). Initially, the $Ni(COD)_2$/IMes-catalyzed reaction between terminal diynes and cyanamides only yielded trace amounts of desired product in an otherwise unidentifiable reaction mixture. However, when SIPr is substituted for IMes, the reaction is effective and generates aminopyridines in excellent yields, although slightly extended reaction times (i.e., 1 h) are required for the $Ni(COD)_2$/SIPr-catalyzed reactions.

III. PALLADIUM-CATALYZED ARYLATION OF CYANAMIDES[17]

Given our interest in utilizing cyanamides as substrates in cycloaddition chemistry, we required rapid access to a variety of cyanamides. Common methods for the preparation of cyanamides include simple substitution of cyanogen bromide or more exotic cyanating agents.[18] However the reduced nucleophilicity of aryl or diaryl amines (particularly with electron withdrawing groups) can lead to poor

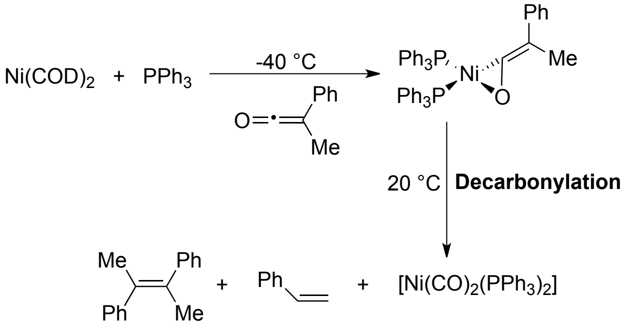


(7)

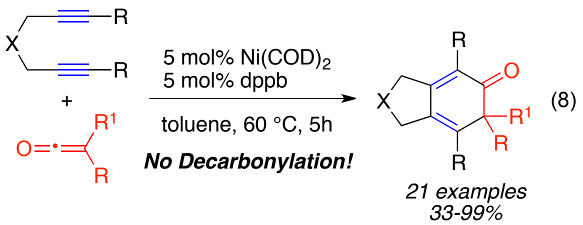
yields. A common alternative, the Von Braun reaction,[19] while effective, requires extraneous formation of a trisubstituted amine thereby potentially leading to moderate to low yields. As an alternative, we believed cross-coupling between an aryl halide (or vinyl halide) and a monosubstituted cyanamide could serve as a direct approach to the desired aryl cyanamide compounds. Yet, despite the incredible progress made in metal-catalyzed cross-coupling methodologies,[20] cyanamides had never been evaluated in a cross-coupling study. We successfully developed a Pd-catalyzed cross-coupling reaction between aryl and vinyl halides (and pseudo-halides such as triflates) that affords cyanamides under mild conditions in moderate to excellent yields (eq 7).

IV. CYCLOADDITION OF DIYNES AND KETENES[21]

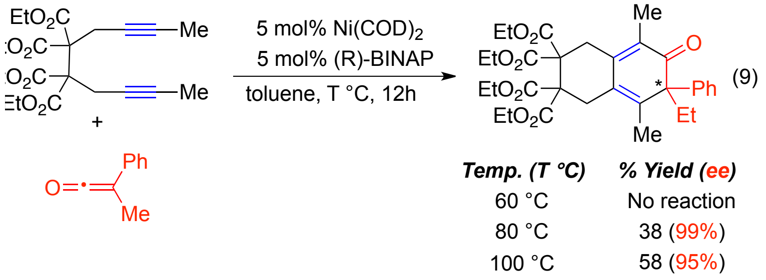
Almost every possible unsaturated starting material (alkynes, alkenes, dienes, CO_2, nitriles, isocyanates, carbonyls etc.) has been employed as a substrate in transition metal catalyzed cycloadditions.[1,22] Despite the rich history of cycloaddition chemistry, ketene substrates were notoriously absent.[23] An insufficient reactivity between potential transition metal catalysts and ketenes is not the problem. Ketenes easily form η^2-complexes with various metals (Ni, Pd, Pt, Co, Rh, Ir etc.).[24] The inability of these η^2-complexes to undergo further reactions with other unsaturated coupling partners lies in their propensity to decarbonylate and form stable, unreactive M-CO complexes (Scheme 1).[25] In addition, ketenes often undergo homo-dimerization under thermal conditions.[26] Given these pitfalls, we were surprised and delighted to discover that Ni-phosphine catalysts mediate the cycloaddition of ketenes and diynes to afford cyclohexadienones, a structure prevalent in a variety of natural products,[27] in good yields (eq 8).



Scheme 1. Typical reactivity between Ni(0) and ketenes



The asymmetric formation of quaternary stereocenters remains a formidable challenge to organic chemists.[28] With this in mind, we also investigated the development of an asymmetric version of the cycloaddition reaction. Initial investigations employing (R)-BINAP as a ligand gave dismal results. That is, no reaction was observed when standard reaction conditions (5 mol% catalyst, 0.1M diyne, 60 °C, and toluene) were employed. However, carbocyclic product was generated when the temperature was elevated to 80 °C. Although a relatively low yield (38%) was obtained, excellent enantioselectivity (99%) was observed (eq 9). A higher yield without a substantial decrease in *ee* was obtained when the reaction temperature was increased to 100 °C.

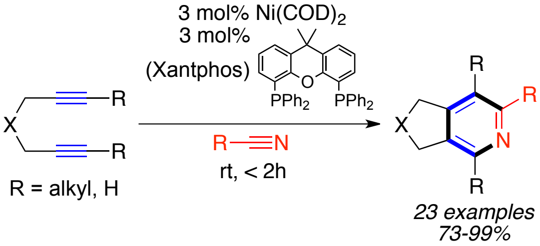


Temp. (T °C)	*% Yield (ee)*
60 °C	No reaction
80 °C	38 (99%)
100 °C	58 (95%)

V. CYCLOADDITION OF NITRILES: A NEW

NI/XANTPHOS CATALYST SYSTEM[29]

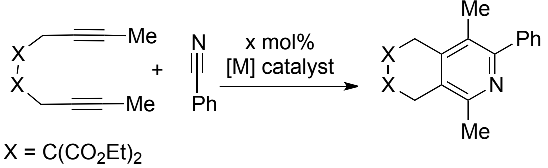
As a corollary to our discovery of a ketene cycloaddition catalyst system, we began investigating the cycloaddition of ketenimines. Upon evaluating conditions to promote this type of cycloaddition (specifically employing methyl 2-methyl-3-(phenylimino)acrylate as the keteinimine substrate), we found a pyridine product rather than the expected carbocycle was obtained in moderate yield when Xantphos was used as the ligand. Surprised by this result, particularly in light of previous difficulties associated with pyridine formation using Ni/PR$_3$ catalysts (*vide supra*), we evaluated a variety of monodentate and bidentate phosphines as potential ligands in the Ni-catalyzed cycloaddition of diynes and the simple, unactivated nitriles. As expected, little to no pyridine product was observed despite good conversion of the diyne. However, a dramatic increase in pyridine formation occurred when Xantphos (β= 111°), a bidentate phosphine ligand with a large bite angle, was evaluated. Further optimization led to a system that provided pyridine in excellent yields under mild reaction conditions (eq 10). Thus, in contrast to our previous hypothesis, sterics may play an equally or more important role in promoting both the challenging oxidative coupling and reductive elimination of C-N bond.



(10)

The efficacy of the Ni/Xantphos cycloaddition catalyst system was compared to other, state-of-the-art transition metal catalysts based on Co, Ru, Rh, and Ni (eq 11, Table 1).[8,30] In all cases, our Ni/Xantphos catalyst system out-performed other cycloaddition catalysts. Although excellent yield and conversion were observed at 60 °C when using Tanaka's Rh catalyst, the reaction afforded the pyridine in lower yield at RT (Table 1, entries 2-3 vs. entry 6). Similarly, higher yields of pyridine were observed with the Ni/Xantphos catalyst when compared to our initial Ni/SIPr catalyst. Thus, lower catalyst loadings, milder reaction conditions, and equimolar substrate stoichiometry make Ni-Xantphos a more efficient catalyst for coupling of diynes and unactivated nitriles.

Table 1. Comparison of Metal Catalysts for Cycloaddition of Diynes and Nitriles



(11)

Entry	[M] Catalyst x mol%	equiv. of Nitrile	Temp	Time	Conv[a]	Yield[a,b]
1	5 mol% [Co][c]	20	RT	24h	86%	70%
2	3 mol% [Rh][d]	1.5	60 °C	3h	>99%	>99%
3	3 mol% [Rh][e]	1.5	RT	3h	32%	15%
4	10 mol% [Ru][f]	1.5	60 °C	24h	6%[g]	-
5	3 mol% [Ni/SIPr][h]	1.5	RT	3h	>99%	80%
6	**3 mol% [Ni/Xant][i]**	**1.5**	**RT**	**3h**	**>99%**	**>99% (98%)**

[a]Analysed by GC using naphthalene as an internal standard. [b]Isolated yield in parenthesis. [c]5 mol% CoCl$_2$, 6 mol% DPPE, xs Zn, diyne (1 equiv., 1 M), nitrile (20 equiv), NMP, RT. [d]3 mol% [Rh(COD)]BF$_4$, 3 mol% Segphos, diyne (1equiv., 0.1 M), nitrile (1.5 equiv.), DCE, 60 °C. [e]Same conditions as in [d], but the reaction was run @ RT. [f]10 mol% Cp*Ru(COD)Cl, diyne (1 equiv., 0.1 M), nitrile (1.5 equiv.), DCE, 60 °C, 24 h. [g]Analysed by NMR. [h]3 mol% Ni(COD)$_2$, 3 mol% SIPr, diyne (1 equiv., 0.1 M), nitrile (1.5 equiv.), THF, RT. [i]3 mol% Ni(COD)$_2$, 3 mol% Xantphos, diyne (1 equiv., 0.1 M), nitrile (1.5 equiv.), toluene, RT.

UNDERSTANDING THE MECHANISM OF NI-CATALYZED CYCLOADDITION

I. REACTIONS WITH WELL-DEFINED NICKEL COMPOUNDS: C-O BOND-FORMING REDUCTIVE ELIMINATION[31]

Little is known about both Ni-imidazolylidene mediated C-C and C-Y (Y = heteroatom) bond-forming reductive elimination. Nevertheless, the formation of heterocycles and carbocycles hinges on the ability to form C-C and C-Y bonds through reductive elimination. As such, we have begun a program revolved around the understanding of this fundamental process. Intimately tied to this research is the side β-H elimination reaction, which can impede product formation in some cases.

Our initial synthetic plan to access the well-defined Ni imidazolylidene species required to evaluate such reactions lead to some intriguing discoveries. Although oxidative addition of aryl halides to Ni(0) complexes has been demonstrated numerous times, the corresponding oxidative addition to Ni(0)-NHC complexes has only been shown in a single experiment.[32] Nevertheless, we presumed oxidative addition should be straightforward and should afford $(NHC)_2Ni(Ar)(X)$ complexes in a rapid fashion. With those complexes in hand, we would then substitute the halide (X) for either an alkyl or a heteroatom-containing ligand and subsequently monitor the rates of reductive elimination as a function of NHC ligand. Surprisingly however, $(NHC)_2Ni(Ar)(X)$ complexes were not obtained. Instead, we found that regardless of ArX, a nickel(I) species, $(NHC)_2Ni(X)$, were formed. Although the reaction of nickel phosphines and aryl halides had been shown to provide Ni(I) complexes,[33] such reactions typically provided low amounts of Ni(I). In addition, no structural information could be obtained when phosphines were employed as ligands.

Given of the importance of aryl halide oxidative addition, not only in our research but in the vast field of coupling chemistry, we examined the reaction of $Ni^0(NHC)_n$ and aryl halides. Our studies suggest that $(NHC)_2Ni(Ar)(X)$ forms first and then readily converts to $(NHC)_2NiX$ complexes. We can confirm the formation of the $(NHC)_2NiX$ complexes by synthesizing them directly via the disproportionation between $(NHC)_2NiX_2$ and $(NHC)_2Ni$. We have crystallized a series of $(IMes)_2Ni(X)$ (X = I, Br, or Cl, Figure 1). Our EPR measurements on these complexes further substantiate the formation of Ni(I) species. In addition to X-ray analysis, ^{1}HNMR and EPR studies further supported the formation of paramagnetic Ni(I) species.

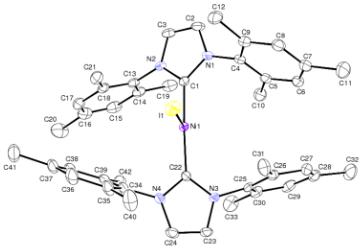
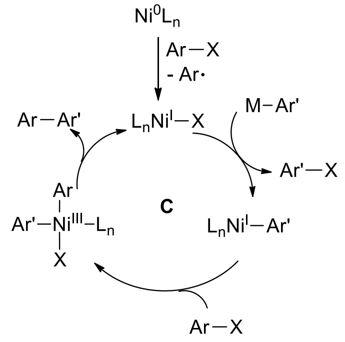


Figure 1. ORTEP diagram of the molecular structure of $Ni(IMes)_2(I)$.

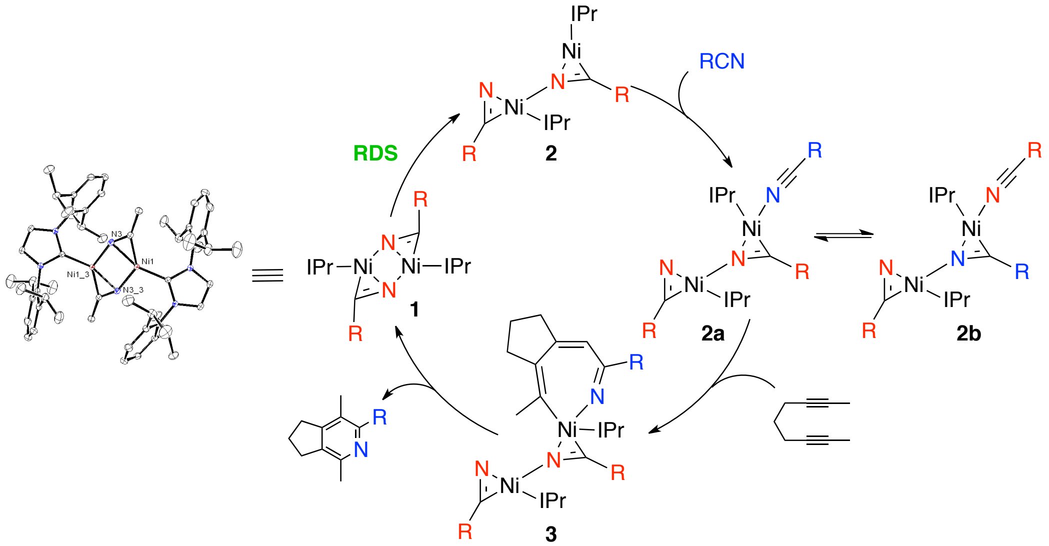
$Ni(IMes)_2$ is an efficient catalyst for the Kumada couplings of aryl halides and Grignard reagents.[34] Although conventional wisdom suggests these couplings mirror analogous Pd-catalyzed couplings, we have performed a series of experiments revolving around cross-coupling reactions catalyzed by $(IMes)_2Ni^IX$ and our results advocate a different mechanism may be operative (Scheme 2). In this mechanism, any Ni(0) present is rapidly converted to Ni(I) via a pseudo oxidative addition with the aryl halide. The Ni(I) complex undergoes transmettallation with the Grignard reagent to form a $Ni^I(IMes)_nAr$ species capable of reacting with the aryl halide. After oxidative addition of the aryl halide to form $Ni^{III}(IMes)_n(X)(Ar)(Ar')$ occurs, reductive elimination of the Ar-Ar' product regenerates a $Ni^I(IMes)_nX$ catalyst.



Scheme 2. Proposed mechanism of Ni(NHC)-catalyzed Kumada Couplings (L = IMes)

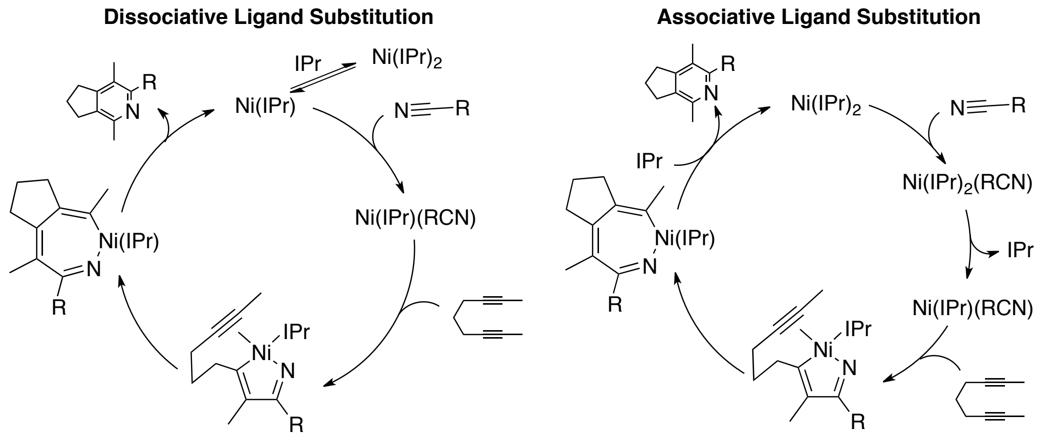
II. EVALUATION OF NITRILE CYCLOADDITION[35]

We embarked on a detailed kinetic analysis of the cycloaddition of diynes and nitriles. Our investigations resulted in the discovery of another viable Ni cycloaddition catalyst system. Specifically, we isolated an interesting eta-2 bound nitrile complex and found that this dimer also catalyzes the cycloaddition of diynes and nitriles. The mechanism of the Ni dimer-catalyzed cycloaddition is quite intriguing for numerous reasons (Scheme 3). Firstly, the sterically crowded nitrile dimers do not dissociate to monomeric nickel compounds (bound by one nitrile and one NHC ligand) nor does an NHC ligand dissociate. Secondly, the 'opening' of the dimer (i.e., from **1** to **2**) is the rate determining step according to our kinetic analysis. That is, our kinetic analysis revealed reactions were zero order in added ligand, nitrile, *and* diyne. The reactions were first order in nitrile dimer **1** *only*. Thirdly, pyridine formation required additional nitrile, despite nitriles already being bound to the metal. Furthermore, what is most non-intuitive, through detailed crossover experiments, we have determined that it is the incoming nitrile – rather than the initial, bound nitrile – that gets incorporated into the pyridine product! Thus, the second Ni center, and its ligands, may act as a large ligand for the first, catalytically operable Ni center. This reasoning may explain the effectiveness of the large Xantphos ligand in nitrile cycloaddition chemistry (*vide supra*). Alternatively, both Ni centers may act in concert (not drawn) as a bimetallic catalyst.



Scheme 3. Proposed Mechanism for Nitrile Dimer-Catalyzed Cycloaddition

Although catalytically competent, dimer **1** cycloaddition is kinetically slower than reactions catalyzed by our original Ni(IPr)$_2$ system. Subsequent to this discovery, we also evaluated the kinetics of the Ni(IPr)$_2$ catalyzed cycloaddition of diynes and nitriles. Again, the mechanism of cycloaddition was not straightforward. As expected, cycloadditions showed a first order dependence on Ni(IPr)$_2$. However, reactions run with excess nitrile showed a zero order dependence for IPr, nitrile, as well as diyne. What is even more perplexing is that although reactions display a zero order dependence in nitrile concentration, the *identity* of the nitrile does influence the rate of the reaction. For example, reactions run with benzonitrile are significantly faster than those run with acetonitrile. Furthermore, reactions run with isopropyl nitrile display a first order dependence in nitrile concentration. It is possible that we are in the range of saturation kinetics with respect to nitrile concentration. Unfortunately, reactions run with excess diyne, rather than excess nitrile, undergo rapid and irreversible diyne oligomerization rather than pyridine formation.

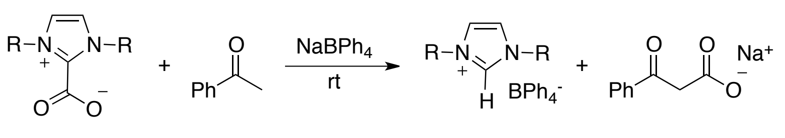


Scheme 4. Kinetic analysis of $Ni(IPr)_2$ catalyzed cycloaddition of diynes and MeCN

Reasonable mechanisms for this reaction are depicted in Scheme 4. Given our kinetic data, we were able to rule out a dissociative ligand substitution mechanism since this mechanism would require the observation of either an inverse first order in ligand or reaction rates that were identical regardless of the identity of the nitrile. Although at first glance, a mechanism involving an associative ligand substitution may not seem to account for all of the kinetic data, a deeper look would reveal that such a mechanism is possible if the rate determining step is dependent on the nitrile. Specifically, if a bulky nitrile such as *i*PrCN is used, the rate determining step is association of the nitrile. Under these circumstances, we would expect to see and do observe first order in $Ni(IPr)_2$ and *i*PrCN as well as zero order in IPr and diyne. However, when a smaller nitrile such as MeCN is employed, binding of the nitrile may be fast and irreversible. As such, the new resting state of the catalyst would be $Ni(IPr)_2(RCN)$ and the rate determining step would be loss of IPr. Our kinetic data fit this scenario. Because formation of the Ni-RCN dimer likely arises from dimerization of Ni(IPr)(RCN), we anticipate that investigation of the mechanism of Ni-RCN dimer formation will corraborate our mechanistic conclusion.

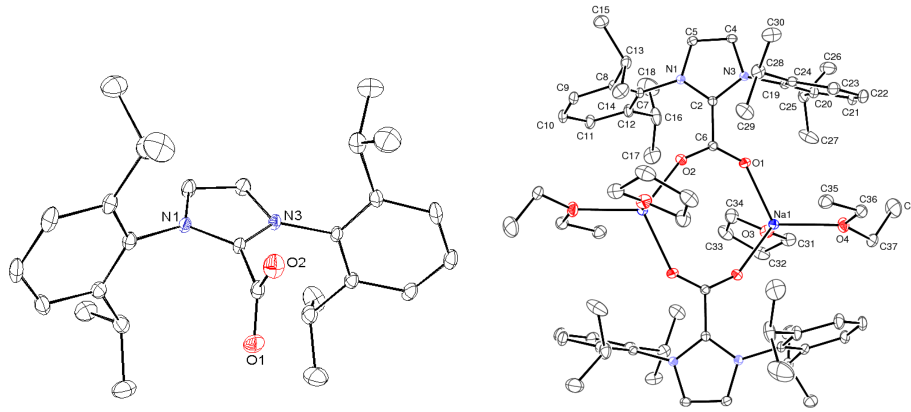
METAL-FREE CO_2 ACTIVATION[36,37]

Through our efforts toward understanding the factors that govern the reactivity of imidazolium carboxylates, we are now uniquely positioned to develop carboxylation reactions[38] that employ these compounds as reactive intermediates. Our discoveries include the size of the substituent has a dramatic effect on the bond strength between the imidazolidene and the carbon of CO_2. In fact, these steric factors will often override any electronic effects that may exist. Importantly, we have also found how subtle changes in the substitution pattern of the imidazolium carboxylate can affect more practical physical properties like solubility.



(12)

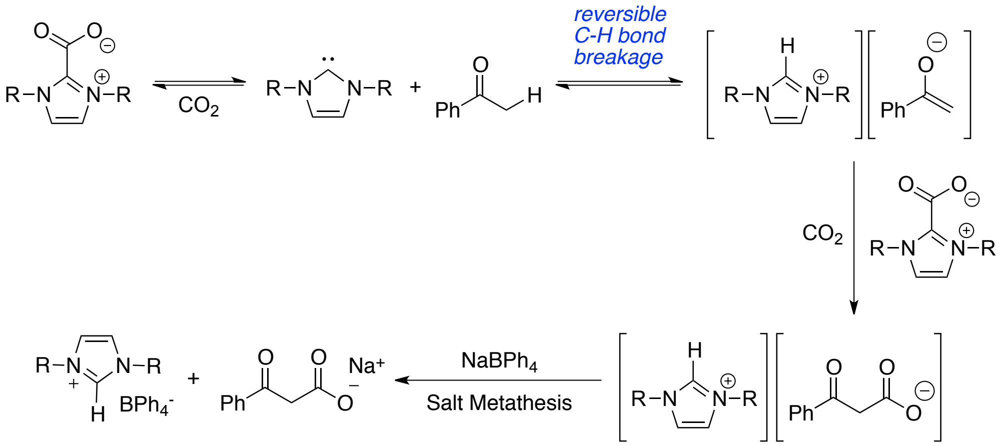
A reaction that we focused our initial efforts is the carboxylation of acetophenone. Although it has been reported that the stoichiometric reaction between $IMeCO_2$ and acetophenone in the presence of NaBPh4 affords a β-keto acid,[39] this reaction appears to be limited to acetophenone as a substrate (eq 12). We believe further advancement (i.e., increased substrate scope, catalytic use of imidazolium salt in an atmosphere of CO_2, etc.) of this process hinges on understanding the mode of reaction for the imidazolylidene carboxylates and embarked on investigating the mechanism of this reaction.



$IPrCO_2$ **$[(IPrCO_2Na)(BPh_4)]_2$**

Figure 2. Carboxylate Pitch, (N(3)-C(2)-C(6)-O(2)):
$IPrCO_2$ = **88°**, **$[(IPrCO_2Na)(BPh_4)]_2$** = **151°**

We successfully isolated an imidazolylidene carboxylate complex of $NaBPh_4$ (**$[(IPrCO_2Na)(BPh_4)]_2$**); this complex carboxylates acetophenone directly. Although **$[(IPrCO_2Na)(BPh_4)]_2$** has similar properties to **$IPrCO_2$** (C-C bond length, C=O stretching frequency, decarboxylation temperature), one striking feature stands out – an increase in the carboxylate torsional angle (Figure 2). We have also successfully prepared other metal bound carboxylates (where metal = Li, Na, K).



Scheme 5. Proposed reaction mechanism for the carboxylation of acetophenone

Despite the isolation of a variety of interesting $NHC{\cdot}CO_2{+}MBPh_4$ complexes, our data suggest that the complexes do not remain aggregated during carboxylation. That is, our kinetic analysis show carboxylation reactions rates that are independent of $NaBPh_4$ concentration. Our evidence also points away from a mechanism that involves a salt-assisted deprotonation of acetophenone (i.e., enhanced acidity of the α-proton through pre-coordination of the Na^+ to either the carbonyl or the arene).[40,41] Thus, the role of $NaBPh_4$ may be to help bring the $NHC{\cdot}CO_2$ into solution such that it is available to react. Indeed, our investigations indicate that the addition of salts to otherwise insoluble $NHC{\cdot}CO_2$ compounds led to homogeneous solutions. Given the propensity of the carboxylated product to undergo spontaneous decarboxylation, the role of the $NaBPh_4$ may also serve to stabilize the product through ion-pairing. A proposed mechanism that is shown in Scheme 5.

POTENTIAL IMPACT IN SCIENCE & TECHNOLOGIES OF INTEREST TO DOE

Pollution prevention and waste management continue to be profound challenges for modern society. One potential solution to this problem is the development and utilization of ideal reactions for the production of valuable commodities. In an ideal synthetic reaction, raw materials are converted to the desired product with complete selectivity and without any waste products. Only heat, light, and/or a catalyst are necessary to facilitate the reaction. For example, annulations of unsaturated hydrocarbons with CO_2 could efficiently provide oxygen-containing heterocycles, an important structural motif found in numerous economically important and biologically relevant systems. As added benefits, CO_2 is relatively non-toxic, non-flammable, and abundant and a wide range of unsaturated hydrocarbons are already used chemical feed stocks on an industrial scale. Although considerable effort has been directed toward the discovery of new and efficient protocols, activation of CO_2 has yet to reach its full potential.

Our research presents several strategies for addressing the challenges of activating CO_2. In addition, our cycloaddition chemistry addresses several fundamental issues pertaining to catalysis as it applies to energy conservation. Our research was highlighted *twice* last year in *Chemical & Engineering News*.

BIBLIOGRAPHY AND REFERENCES

(1) (a) Chopade, P; Louie, J. "[2+2+2] Cycloaddition Reactions Catalyzed by Transition Metal Complexes" *Adv. Synth. Catal.* **2006**, *348*, 2307-2327.
(b) Louie, J. "Transition Metal Catalyzed Reactions of Carbon Dioxide and Other Heterocumulenes" *Curr. Org. Chem.* **2005**, *9*, 605-623.
(2) (a) Louie, J.; Gibby, J. E.; Farnworth, M. F.; Tekavec, T. N. "Efficient Nickel-Catalyzed [2+2+2] Cycloaddition of CO_2 and Diynes" *J. Am. Chem. Soc.* **2002**, *124*, 15188-15189.
(b) Tekavec, T. N.; Arif, A. M.; Louie, J. "Regioselectivity in the Nickel-Catalyzed Cycloaddition of Diynes and CO_2" *Tetrahedron* **2004**, *60*, 7431-7437.
(c) Chopade, P. R.; Louie, J. "[2+2+2] Cycloaddition Reactions Catalyzed by Transition Metal Complexes" *Adv. Synth. Catal.* **2006**, *348*, 2307-2327.
(3) (a) Duong, H. A.; Cross, M. J.; Louie, J. "Nickel-Catalyzed Cycloadditions of Alkynes and Isocyanates" *J. Am. Chem. Soc.* **2004**, *126*, 11438-11439.
(b) Duong, H. A.; Cross, M. J.; Louie, J. "*N*-Heterocyclic Carbenes as Highly Efficient Catalysts for the Cyclotrimerization of Isocyanates" *Org. Lett.* **2004**, *6*, 4679-4681.
(c) Duong, H. A.; Louie, J. "Regioselectivity in Ni/Phosphine Catalyzed Cycloadditions of Alkynes and Isocyanates" *J. Organomet. Chem.* **2005**, *690*, 5098-5104.
(d) Duong, H. A.; Louie, J. "A Nickel-Catalyzed Cycloaddition of Alkynes and Isocyanates that Affords Pyrimidine-diones" *Tetrahedron* **2006**, *62*, 7547-7551.
(e) Zhang, K.; Chopade, P. R.; Louie, J. "Coupling of Vinyl Aziridines and Isocyanates" *Tetrahedron Lett.* **2008**, *49*, 4306-4309.

(f) D’Souza, B. R.; Louie, J. “Nickel Catalyzed Cycloadditive Couplings of Enynes and Isocyanates” *Org. Lett.* **2009**, *11*, 4168-4171.

(4) (a) Tekavec, T. N.; Louie, J. “Nickel-Catalyzed Cycloadditions of Unsaturated Hydrocarbons and Carbonyls Compounds” *Org. Lett.* **2005**, *7*, 4037-4039.

(b) Tekavec, T. N.; Louie, J. “Nickel-Catalyzed Cycloadditions of Unsaturated Hydrocarbons, Aldehydes, and Ketones” *J. Org. Chem.* **2008**, *73*, 2641-2648.

(5) (a) Tsuda, T.; Sumiya, R.; Saegusa, T. “Nickel-Mediated Cycloaddition of Diynes with Carbon Dioxide to Bicyclic α-Pyrones” *Synth. Comm.* **1987**, *17*, 147-154.

(b) Tsuda, T.; Morikawa, S.; Sumiya, R.; Saegusa, T. “Nickel(0)-Catalyzed Cycloaddition of Diynes and Carbon Dioxide to Bicyclic α-Pyrones” *J. Org. Chem.* **1988**, *53*, 3140-3145.

(c) Tsuda, T.; Morikawa, S.; Saegusa, T. “Functionalized Phosphine Ligands in Transition Metal-catalysed Organic Synthesis. Nickel(0)-catalysed Cycloaddition of Terminally Unsubstituted Diynes and Carbon Dioxide to Bicyclic 2-Pyrones” *J. Chem. Soc., Chem. Comm.* **1989**, 9-10.

(d) Tsuda, T.; Hasegawa, N.; Saegusa, T. “Nickel(0)-catalysed Novel Co-oligomerization of Ethoxy(trimethylsilyl)ethyne with Carbon Dioxide to 4,6-Diethoxy-3-[1-ethoxy-2,2-bis(trimethylsilyl)vinyl]-5-(trimethylsilyl)-2-pyrone” *J. Chem. Soc., Chem. Comm.* **1990**, 945-947.

(e) Tsuda, T.; Morikawa, S.; Hasegawa, N.; Saegusa, T. “Nickel(0)-Catalyzed Cycloaddition of Silyl Diynes with Carbon Dioxide to Silyl Bicyclic α-Pyrones” *J. Org. Chem.* **1990**, *55*, 2978-2981.

(f) Tsuda, T.; Maruta, K.; Kitaike, T. “Nickel(0)-Catalyzed Alternating Copolymerization of Carbon Dioxide with Diynes to Poly(2-pyrones)” *J. Am. Chem. Soc.* **1992**, *114*, 1498-1499.

(6) Hoberg, H.; Oster, B. W. “Nickel(0)-katalysierte [2+2+2’]-Cycloaddition von Alkynen mit Isocyanaten zu 2-Oxo-1,2-dihydropyridinen” *Synthesis* **1982**, 324-325.

(7) Tsuda, T.; Kiyoi, T.; Miyane, T.; Saegusa, T. “Nickel(0)-Catalyzed Reaction of Diynes with Aldehydes” *J. Am. Chem. Soc.* **1988**, *110*, 8570-8572.

(8) (a) McCormick, M. M.; Duong, H. A.; Louie, J. “A Nickel-Catalyzed Route to Pyridines” *J. Am. Chem. Soc.* **2005**, *127*, 5030-5031.

(b) Tekavec, T. N.; Zuo, G.; Simon, K.; Louie, J. “An in Situ Approach for Nickel-Catalyzed Cycloaddition” *J. Org. Chem.* **2006**, *71*, 5834-5836.

(9) (a) García, J. J.; Arévalo, A.; Brunkan, N. M.; Jones, W. D. “Cleavage of Carbon-Carbon Bonds in Alkyl Cyanides Using Nickel(0)” *Organometallics* **2004**, *23*, 3997-4002.

(b) Wilting, J.; Müller, C.; Hewat, A. C.; Ellis, D. D.; Tooke, D. M.; Spek, A. L.; Vogt, D. “Nickel-Catalyzed Isomerization of 2-Methyl-3-butenenitrile” *Organometallics* **2005**, *24*, 13-15.

(10) Eisch, J. J.; Ma, X.; Han, K. I.; Gitua, J. N.; Krüger, C. “Mechanistic Comparison of the Nickel(0)-Catalyzed Homo-Oligomerization and Co-Oligomerization of Alkynes and Nitriles“ *Eur. J. Inorg. Chem.* **2001**, *2001*, 77-88.

(11) (a) Nakao, Y.; Oda, S.; Hiyama, T. “Nickel-Catalyzed Arylcyanation of Alkynes” *J. Am. Chem. Soc.* **2004**, *126*, 13904-13095.

(b) Nakao, Y.; Yada, A.; Ebata, S.; Hiyama, T. "A Dramatic Effect of Lewis-Acid Catalysts on Nickel-Catalyzed Carbocyanation of Alkynes" *J. Am. Chem. Soc.* **2007**, *129*, 2428-2429.

(c) Nakao, Y.; Yukawa, T.; Hirata, Y.; Oda, S.; Satoh, J.; Hiyama, T. "Allylcyanation of Alkynes: Regio- and Stereoselective Access to Functionalized Di- or Trisubstituted Acrylonitriles" *J. Am. Chem. Soc.* **2006**, *128*, 7116-7117.

(12) (a) Takahashi, T.; Tsai, F.-Y.; Kotora, M. "Selective Formation of Substituted Pyridines from Two Different Alkynes and a Nitrile: Novel Coupling Reaction of Azazirconacyclopentadienes with Alkynes" *J. Am. Chem. Soc.* **2000**, *122*, 4994-4995.

(b) Takahashi, T.; Tsai, F. Y.; Li, Y.; Wang, H.; Kondo, Y.; Yamanaka, M.; Nakajima, K.; Kotora, M. "Selective Preparation of Pyridines, Pyridones, and Iminopyridines from Two Different Alkynes via Azazirconacycles" *J. Am. Chem. Soc.* **2002**, *124*, 5059-5067.

(13) Stolley, R. M.; Maczka, M. T.; Louie, J. "Nickel-Catalyzed Cycloaddition of Diynes and Cyanamides" *Eur. J. Org. Chem*. **2012**, *20-21*, 3815-3824.

(14) (a) Horie, H.; Koyama, I.; Kurahashi, T.; Matsubara, S. "Nickel-catalyzed intermolecular codimerization of acrylates and alkynes" *Chem. Commun*. **2011**, *47*, 2658-2660.

(b) Daka, P.; Xu, Z.; Alexa, A.; Wang, H. "Primary amine-metal Lewis acid bifunctional catalysts based on a simple bidentate ligand: direct asymmetric aldol reaction" *Chem. Commun*. **2011**, *47*, 224-226.

(c) Di Nicola, C.; Effendy; Marchetti, F.; Nervi, C.; Pettinari, C.; Robinson, W. T.; Sobolev, A. N.; White, A. H. "Syntheses, structures and spectroscopy of uni- and bidentate nitrogen base complexes of silver(I) trifluoromethanesulfonate" *Dalton Trans*. **2010**, *39*, 908-922.

(d) Yip, J. H. K.; Suwarno; Vittal, J. J. "Syntheses and Electronic Spectroscopy of $[\mathrm{PtL(L')}][\mathrm{ClO_4}]$ Complexes (HL = 6-Phenyl-2,2'-bipyridine; L' = Pyridine, 4-Aminopyridine, 2-Aminopyridine, and 2,6-Diaminopyridine)" *Inorg Chem*. **2000**, *39*, 3537-3543.

(15) (a) Mutai, T.; Cheon, J.-D.; Tsuchiya, G.; Araki, K. "6-Amino-2,2':6',2"-terpyridines as highly fluorescent compounds - effect of the number of pyridine rings on fluorescence properties" *J. Chem. Soc.*, *Perkin Trans. 2* **2002**, 862-865.

(b) Tardioli, S.; Gooijer, C.; van der Zwan, G. "Anomalous Photophysics of H1 Antihistamines in Aqueous Solution" *J. Phys. Chem. B* **2009**, *113*, 6949-6957.

(c) Sathyamoorthi, G.; Soong, M. L.; Ross, T. W.; Boyer, J. H. "Fluorescent tricyclic β-azavinamidine-BF2 complexes" *Heteroatom. Chem*. **1993**, 4, 603.

(16) (a) Tursky, M.; Lorentz-Petersen, L. L. R.; Olsen, L. B.; Madsen, R. "Iridium- and ruthenium-catalysed synthesis of 2,3-disubstituted indoles from anilines and vicinal diols" *Org. Biomol. Chem*. **2010**, *8*, 5576-5582.

(b) Ueno, M.; Nobana, T.; Togo, H. "Novel Oxidative α-Tosyloxylation of Alcohols with Iodosylbenzene and *p*-Toluenesulfonic Acid and Its Synthetic Use for Direct Preparation of Heteroaromatics" *J. Org. Chem*. **2003**, *68*, 6424-6426.

(c) Kamal, A.; Reddy, J. S.; Ramaiah, M. J.; Dastagiri, D.; Bharathi, E. V.; Sagar, M. V. P.; Pushpavalli, S. N. C. V. L.; Ray, P.; Pal-Bhadra, M. "Design, synthesis and biological evaluation of imidazopyridine/pyrimidine-chalcone derivatives as potential anticancer agents" *Med. Chem. Comm*. **2010**, *1*, 355-360.

(d) Nam, T.-G.; Nara, S. J.; Zagol-Ikapitte, I.; Cooper, T.; Valgimigli, L.; Oates, J. A.; Porter, N. A.; Boutaud, O.; Pratt, D. A. “Pyridine and pyrimidine analogs of acetaminophen as inhibitors of lipid peroxidation and cyclooxygenase and lipoxygenase catalysis” *Org. Biomol. Chem.* **2009,** *7*, 5103-5112.

(e) Carlucci, G.; Colanzi, A.; Mazzeo, P.; Quaglia, M. G. “Determination of 2-aminopyridine in piroxicam by derivative UV-spectrophotometry” *Int. J. Pharm.* **1989**, *53*, 257–259.

(f) Acker, R.-D.; Hamprecht, G. “Preparation of 2-aminopyridine derivatives” U.S. Patent 4,395,555, 1981.

(g) Ji, H.; Delker, S. L.; Li, H.; Martásek, P.; Roman, L. J.; Poulos, T. L.; Silverman, R. B. “Exploration of the Active Site of Neuronal Nitric Oxide Synthase by the Design and Synthesis of Pyrrolidinomethyl 2-Aminopyridine Derivatives” *J. Med. Chem.* **2010**, *53*, 7804-7824.

(17) Stolley, R. M.; Guo, W. X.; Louie, J. “Palladium-Catalyzed Cross-Coupling of Cyanamides” *Org. Lett.* **2012**, *20-21*, 3815-3824.

(18) (a) Kim, J.-J.; Kweon, D.-H.; Cho, S.-D.; Kim, H.-K.; Jung, E.-Y.; Lee, S.-G.; Falck, J. R.; Yoon, Y.-J. "2-Cyanopyridazin-3(2H)-ones: effective and chemoselective electrophilic cyanating agents" *Tetrahedron* **2005**, *61*, 5889-5894.

(b) Maezaki, N.; Furusawa, A.; Uchida, S.; Tanaka, T. "3-cyano-2-(N-cyanoimino)thiazolidine (3-cyano-NCT): an efficient electrophilic cyanating agent for activated methylene compounds" *Heterocycles* **2003**, *59*, 161-167.

(c) Wu, Y.-Q., Limburg, D. C.; Wilkinson, D. E.; Hamilton, G. S. "1-Cyanoimidazole as a Mild and Efficient Electrophilic Cyanating Agent" *Org Lett.* **2000**, *2*, 795-797.

(19) (a) Von Braun, I. J.; Heider, K.; Muller, E. "Bromoalkylated aromatic amines. II" *Ber.* **1918**, *51*, 281.

(b) Cressman, H. W. J. "N-Methyl-1-Naphthylcyanamide" *Org. Synth.* **1955**, *3*, 608.

(20) Surry, D. S.; Buchwald, S. L. “Biaryl Phosphane Ligands in Palladium-Catalyzed Amination” *Angew. Chem. Int. Ed.* **2008**, *47*, 6338-6361.

(21) Kumar, P.; Troast, D. M.; Cella, R.; Louie, J. “Ni-Catalyzed Ketene Cycloaddition: A System that Resists the Formation of Decarbonylation Side Products” *J. Am. Chem. Soc.* **2011**, *133*, 7719-7721.

(22) (a) Lebœuf, D.; Gandon, V.; Malacria, M. "Transition Metal-Mediated [2+2+2] Cycloadditions" In Handbook of Cyclization Reactions, Ma, S., Ed., Wiley-VCH: Weinheim, 2009, Vol. 1, 367-406.

(b) Lautens, M.; Klute, W.; Tam, W. “Transition Metal-Mediated Cycloaddition Reactions“ *Chem. Rev.* **1996**, *96*, 49-92.

(23) Kondo, T.; Niimi, M.; Yoshida, Y.; Wada, K.; Mitsudo, T.; Kimura, Y.; Toshimitsu, A. “Rhodium-Catalyzed Linear Codimerization and Cycloaddition of Ketenes with Alkynes” *Molecules* **2010**, *15*, 4189-4200.

(24) Geoffroy, G. L.; Bassner, S. L. “Interaction of ketenes with organometallic compounds: ketene, ketenyl, and ketenylidene complexes” *Adv. Organomet. Chem.* **1988**, *28*, 1.

(25) Hofman, P.; Perez-Moya, L. A.; Steigelman, O.; Riede, J. “eta-2-(C,O) Ketene coordination at nickel(0). Synthesis, bonding, and molecular structure of (dtbpm)Ni[eta-

2-(C,O)-Ph2C2O] [dtbpm = bis(di-tert-butylphosphino)methane]“ *Organometallics*, **1992**, *11*, 1167-1176.

(26) Tidwell, T. T. *In: Ketenes*, Wiley-Interscience; New York, 1995.

(27) (a) Kaouadji, M. “Grenoblone, Nouvelle Oxodihydrochalcone des Bourgeons de Platanus acerifolia” *J. Nat. Prod.* **1986**, *49*, 500-503.

(b) Kuo,Y.; Li, S.; Huang, R.; Wu, M.; Huang, H.; Lee, K. “Schizarin B, C, D, and E, Four New Lignans from *Kadsura matsudai* and Their Antihepatitis Activities” *J. Nat. Prod.* **2001**, *64*, 487-490.

(c) Shen, Y.; Cheng, Y.; Liaw, C.; Liou, S.; Khalil, A. “Kadsuphilols A-H, Oxygenated Lignans from *Kadsura philippinensis*” *J. Nat. Prod.* **2007**, *70*, 1139-1145.

(d) Quideau, S.; Pouysegu, L.; Deffieux, D. “Oxidative Dearomatization of Phenols: Why, How and What For?” *Synlett* **2008**, 467-495.

(28) (a) Corey, E. J.; Guzman-Perez, A. “The Catalytic Enantioselective Construction of Molecules with Quaternary Carbon Stereocenters” *Angew. Chem., Int. Ed.* **1998**, *37*, 388-401.

(b) *Challenges and Solutions For Organic Synthesis*; Christoffers, J., Ed.; Wiley-VCH: Weinhein, 2005.

(c) Douglas, C. J.; Overman, L. E. “Catalytic asymmetric synthesis of all-carbon quaternary stereocenters” *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 5363-5367.

(29) Kumar, P.; Prescher, S.; Louie, J. “A Serendipitous Discovery of a Nickel-Catalyst for Cycloaddition of Diynes with Unactivated Nitriles” *Angew. Chem. Int. Ed.* **2011**, *50*, 10694-10698.

(30) (a) For [Co] : Kase, K.; Goswami, A.; Ohtaki, K.; Tanabe, E.; Saino, N.; Okamoto, S. “On-Demand Generation of an Efficient Catalyst for Pyridine Formation from Unactivated Nitriles and α,ω-Diyens Using $CoCl_2$-$6H_2O$, dppe, and Zn” *Org. Lett.* **2007**, *9*, 931–934.

(b) For [Rh] : Tanaka, K.; Suzuki, N.; Nishida, G. “Cationic Rhodium(I)/Modified-BINAP Catalyzed [2+2+2] Cycloaddition of Alkynes with Nitriles” *Eur. J. Org. Chem.* **2006**, *17*, 3917-3922.

(c) For [Ru] : Yamamoto, Y.; Ogawa, R.; Itoh, K. “Significant Chemo- and Regioselectivities in the Ru(II)-Catalyzed [2+2+2] Cycloaddition of 1,6-Diynes with Dicyanides“ *J. Am. Chem. Soc.* **2001**, *123*, 6189–6190.

(31) Zhang, K.; Conda, M. S.; Cooke, S.; Miller, J. S.; Louie, J. “N-Heterocyclic Carbene Bound Ni(I)-Complexes and Their Roles in Catalysis” *Organometallics* **2011**, *30*, 2546-2552.

(32) McGuinness, D. S.; Cavell, K. J.; Skelton, B. W.; White, A. H. “Zerovalent Palladium and Nickel Complexes of Heterocyclic Carbenes: Oxidative Addition of Organic Halides, Carbon-Carbon Coupling Processes, and the Heck Reaction ” *Organometallics* **1999**, *18*, 1596-1605.

(33) (a) Tsou, T. T.; Kochi, J. K. “Mechanism of oxidative addition. Reaction of nickel(0) complexes with aromatic halides ” *J. Am. Chem. Soc*. **1979**, *101*, 6319-6332.

(b) Tsou, T. T.; Kochi, J. K. “ Mechanism of biaryl synthesis with nickel complexes” *J. Am. Chem. Soc*. **1979**, *101*, 7547-7559.

(34) (a) Chen, C.; Yang, L.-M. “Arylation of diarylamines catalyzed by Ni(II)-PPh_3 system” *Org. Lett.* **2005**, *7*, 2209-2211.

(b) Chen, C.; Yang, L.-M. “Ni(II)-(σ-Aryl) Complex: A Facile, Efficient Catalyst for Nickel-Catalyzed Carbon-Nitrogen Coupling Reactions” *J. Org. Chem.* **2007**, *72*, 6324-6327.

(c) Gao, C.-Y.; Yang, L.-M. “Nickel-Catalyzed Amination of Aryl Tosylates” *J. Org. Chem.* **2008**, *73, 1624*.

(35) (a) Thomas, D. R.; Duong, H. A.; Stolley, R. M.; Louie, J. “Synthesis of $[Ni(IPr)RCN]_2$ Dimer Complexes and their Catalytic Activity Toward the Formation of Pyridines” **2011**, *submitted.*

(b) Stolley, R. M.; Duong, H. A.; Louie, J. “Insights on the Mechanism of Nickel Catalyzed Formation of Pyridines via the Cycloaddition of Alkynes and Nitriles” **2011**, *manuscript in preparation.*

(36) Duong, H. A.; Tekavec, T. N.; Arif, A. M.; Louie, J. “Reversible Carboxylations of N-Heterocyclic Carbenes” *Chem. Comm.* **2004**, *1*, 112-113.

(37) (a) Van Ausdall, B. R.; Glass, J. L.; Wiggins, K. M.; Arif, A. M.; Louie, J. “A Systematic Investigation of Factors Influencing the Decarboxylation of Imidazolium Carboxylates” *J. Org. Chem.* **2009**, *20*, 7935-7942.

(b) Van Ausdall, B. R.; Pols, N. F.; Kincaid, V. A.; Aarif, A. M.; Louie, J. “NHC•CO_2-bound $MBPh_4$ Complexes (M=Li, Na) and their Relevance in Transcarboxylation Reactions” *J. Org. Chem.* **2011**, *76*, 8413-8420.

(38) Tudose, A.; Demonceau, A.; Delaude, L. *J. Organometallic Chem.* **2006**, *691*, 5356.

(39) Tommasi, I.; Sorrentino, F. *Tetrahedron Lett.* **2006**, *47*, 6453-6456.

(40) House, H. O.; Chu, C.-Y. *J. Org. Chem.* **1976**, *41*, 3083.

(41) Crist, D. R.; Hsieh, Z. H.; Quicksall, C. O.; Sun, M. K. *J. Org. Chem.* **1984**, *49*, 2478.