Decarbonylative Cross-Couplings: Nickel Catalyzed Functional Group Interconversion Strategies for the Construction of Complex Organic Molecules

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CONSPECTUS: The utilization of carboxylic acid esters as electrophiles in metal-catalyzed cross-coupling reactions is highly demanded as these protocols employ environmentally friendly and readily available ester derivatives as powerful alternatives to the commonly used organohalides. Key challenges that need to be addressed in these transformations are the stability of ester substrates and their high energy barrier for oxidative addition to low-valent metal species. Along with the recent developments of nickel catalysts that allow for oxidative addition with ease, chemists became interested in applying less reactive electrophiles as coupling counterparts in nickel-catalyzed transformations. Hence, our group and others have independently investigated a series of ester group substitutions and functionalizations enabled by nickel catalysis. Such developed methods are of great interest as they allow for the exchange of ester groups which can be used as directing groups in metal-catalyzed C-H functionalizations prior their replacement.

In this Account, we summarize our recent efforts toward the development of nickel-catalyzed decarbonylative cross-coupling reactions of carboxylic esters. Achievements accomplished by other groups in this area are also included. So far, a number of new transformations have been

successfully developed, including decarbonylative alkylations, cyanations, silylations, borylations, aminations, thioetherifications, stannylations, and hydrogenolysis reactions. The above mentioned methods proceed via a nickel-catalyzed decarbonylative pathway and have shown high reactivity, chemoselectivity as well as unique advantages in terms of substrate availability as they employ esters as coupling partners. In combination with the synthesis of natural products and biologically active molecules, the present ester substitution methods should find many applications in the construction of complex frameworks by late-stage modification and functionalization of ester groups.

Although a deep and detailed mechanistic understanding of these types of reactions has not yet been fully achieved, chemists made already great efforts toward establishing the mechanisms at play. Yamamoto initially explored the stoichiometric nickel-mediated decarbonylation process of esters and proposed a reaction mechanism involving C(acyl)-O bond cleavage and CO extrusion. Moreover, recent DFT studies on the oxidative addition step showed a pronounced ligand effect which results in either C(aryl)-C bond or C(acyl)-O bond cleavage. While more detailed mechanistic investigations need to be undertaken, the successful development of decarbonylative cross-coupling reactions will serve as a solid basis for further studies.

1. INTRODUCTION

Cross-coupling reactions have long been recognized as a powerful tool in synthetic applications ranging from natural product synthesis to drug molecule discovery.¹ Based on the ubiquitous impact of palladium-catalyzed cross-couplings over the past half-century, Heck, Negishi and Suzuki were awarded with the 2010 Nobel Prize in Chemistry. Another group 10 metal in the periodic table is nickel which was not as striking as palladium and was often mistakenly assumed as an inexpensive replacement.² Besides economic considerations nickel has recently become increasingly attractive as chemists recognized its unique characteristics for facile oxidative insertion into carbon-carbon and carbon-heteroatom bonds. This ability enabled the use of electrophiles that are considerably less reactive under palladium catalysis. Owing to this feature the utilization of inert chemical bond-containing electrophiles in nickel catalysis has emerged as a viable and powerful alternative to the classical cross-coupling methods.

Among the existing less reactive electrophiles are esters, a commonly used class of carboxylic acid derivatives which are cheap and abundant in nature. Compared with traditional cross-coupling reactions with aryl halides and sulfonates (Scheme 1a), the utilization of carboxylic acid esters as coupling counterparts in nickel catalysis has received considerable attention not only as it avoids the production of corrosive halide-containing wastes, but since it opens access to the functionalization of a variety of commercially and synthetically available ester-containing molecules. Moreover, the replacement of ester groups is useful in retrosynthetic analysis, as ester groups are considered as suitable directing groups in metal-catalyzed C-H functionalization and could be used as such, prior to the replacement.³⁻⁶ On one hand, the ester group substitution was achieved through nickel-catalyzed cross-coupling via C(aryl)-O bond activation (Scheme 1b).⁷⁻⁹

The range of nucleophiles that can be coupled with aryl esters and even highly inert aryl ethers has been expanded significantly over the past decade. Another attractive option concerns cross-coupling reactions through a nickel-catalyzed decarbonylative pathway, transformations which will be mainly discussed in this Account (Scheme 1c).

Scheme 1 Overview of Metal-Catalyzed Cross-Coupling Reactions

Traditional couplings:

Couplings with C(aryl)-O electrophiles:

Decarbonylative couplings of esters:

In 1980, Yamamoto and coworkers reported a stoichiometric nickel-mediated decarbonylation process of aryl carboxylates (Scheme 2).¹⁰ Promoted by a monodentate phosphine nickel complex (e.g. triphenylphosphine), the reaction was proposed to proceed through an oxidative addition mechanism triggered by the nucleophilic attack of the electron-rich nickel complex at the carbonyl group. The following decarbonylation process of carbon monoxide was observed and supported by the isolation and characterization of Ni(CO)L_n complexes. Based on the pioneering work of Yamamoto, carbon-carbon and carbon-heteroatom bond forming reactions proceeding through catalytic decarbonylative cross-coupling of esters and other aryl derivatives with various nucleophiles have been explored.¹¹⁻¹³

Scheme 2 Initial Study of Nickel-Mediated Decarbonylation of Esters by Yamamoto

Although many years of research have passed since the initial discovery, a detailed mechanistic understanding of the decarbonylative cross-coupling processes has not been completely achieved. Combining the mechanistic aspects known to date, two mechanisms can be suggested. In the first mechanism proposed (Scheme 3a), the reaction is triggered by oxidative addition of $\text{Ni}(0)$ species **A** to the C(acyl)-O bond of ester substrates. The resulting acylnickel(II) complex **B** subsequently undergoes a decarbonylation step by extrusion of carbon monoxide, generating the arylnickel(II) species **C**. The transmetalation step is accessed with different nucleophiles and, subsequent reductive elimination releases the corresponding coupling product and regenerates the active $\text{Ni}(0)$ species **A**. This reaction sequence was nicely illustrated by Shi and coworkers who conducted mechanistic experiments through isolation and characterization of crucial nickel intermediates.¹⁴ However, disagreement still exist as some reports suggest that transmetalation may occur prior to the CO extrusion step.¹⁵ Furthermore, a second mechanistic pathway for C(aryl)-C bond cleavage was recently proposed by our group during the investigation of nickel-catalyzed decarbonylative alkylation reaction (see part 2.1 and Scheme 3b).¹⁶ DFT studies on the decisive oxidative addition step showed that low-valent nickel species with the support of a bidentate phosphine ligand [e.g. dcype: 1,2-bis(dicyclohexylphosphino)ethane] favorably insert

into the C(aryl)-C bond, rather than the C(acyl)-O bond. However, more mechanistic studies need to be undertaken to shed light into these intriguing decarbonylative cross-coupling reactions.

Scheme 3 General Proposed Mechanisms for Decarbonylative Cross-Coupling Reactions

In recent years, we and others have independently developed various new transformations applying this decarbonylative concept. Whereas other related synthetic methods including nickel-catalyzed cross-couplings of redox-active esters via single-electron-transfer (SET) pathway appeared,¹⁷⁻²¹ this Account focuses on the recent progress of nickel-catalyzed decarbonylative cross-coupling reactions via a Ni(0)/Ni(II) pathway. The developments in this research area from the discovery of general reaction conditions to the design of new transformations and understanding of reaction mechanisms will serve as a road map for future studies.

2. DECARBONYLATIVE CROSS-COUPLING OF ESTERS BY NICKEL CATALYSIS

2.1. Decarbonylative C_{sp2}-C_{sp3} Bond Forming Reactions

Prompted by our initial efforts and achievements in the activation of inert chemical bonds with the aid of nickel catalysis,²²⁻²⁷ our group started to focus on the development of new synthetic protocols based on the decarbonylative coupling strategy. We hence questioned whether a decarbonylative C_{sp2}-C_{sp3} cross-coupling reaction could be accessible under nickel catalysis. To achieve this goal, several difficulties had to be considered: i) the spontaneous decomposition of C(sp³)-organometallics reagents through proto-demetalation or β -hydride elimination, ii) ketone formation in the absence of carbon monoxide extrusion, and iii) air and water sensitivity of the C(sp³)-organometallic reagents.²⁸

In 2017, our group reported the first Ni-catalyzed decarbonylative alkylation reaction of carboxylic ester derivatives with organozinc reagents.²⁹ The use of organozinc reagents in the absence of base was expected to be appropriate, meanwhile addressing the challenges towards destructive β -hydride elimination.³⁰ After a series of attempts, a catalytic system consisting of Ni(cod)₂ and dcype [1,2-Bis(dicyclohexylphosphino) ethane] as supporting ligand was found to be optimal. Thus, a number of carboxylic esters bearing various aryl or heteroaryl substituents could be coupled with different organozinc compounds in good to excellent yields (Scheme 4). Functional groups, such as methoxy, amine, alkenyl, ketone, and amide, are tolerated under the reaction conditions. Moreover, a secondary alkylzinc reagent, such as cyclohexylzinc bromide, is suitable for this decarbonylative alkylation reaction.

Scheme 4 Nickel-Catalyzed Decarbonylative C_{sp2}-C_{sp3} Bond Formation Using Alkylzinc Reagents as Coupling Nucleophiles

Continuing our research into the decarbonylative C_{sp2}-C_{sp3} cross-coupling of esters, we also developed a ligand-controlled decarbonylative alkylation protocol by applying *B*-alkyl-9-BBNs as coupling partners.¹⁶ In this research, *B*-alkyl-9-BBN reagents, which can be generated in situ from the corresponding alkenes via hydroboration,³¹ have shown high efficiency and excellent potential in cross-coupling reactions.

Following the evaluation of different nickel catalysts, ligands, bases, solvents and temperatures, an efficient set of reaction conditions for the coupling of aryl- and heteroaryl-esters with *B*-alkyl-9-BBN reagents was identified. Using 10 mol% Ni(cod)₂ as catalyst, 20 mol% dcype as supporting ligand and caesium fluoride or carbonate as base in toluene at 150 °C, the corresponding alkylated products were obtained in good to excellent yields (Scheme 5).

Scheme 5 Nickel-Catalyzed Decarbonylative C_{sp2}-C_{sp3} Bond Formation Using *B*-alkyl-9-BBNs as Coupling Nucleophiles

Several features of this cross-coupling reaction are noteworthy. Firstly, the use of bidentate dcype ligand was crucial to accomplish this transformation. The exchange of the bidentate ligand with monodentate phosphine ligands or NHC ligands provided low yields or no product. Secondly, the base was necessary for the formation of an active borate complex which provides a strong driving force in the transmetalation step.³² Lastly, this decarbonylative cross-coupling was performed with a wide range of substrates exhibiting functional group tolerance with respect to both esters and alkylboranes. In addition, commercially available triethylborane (BET₃) proved itself an ideal coupling counterpart for this demanding transformation (Scheme 6).

Scheme 6 Nickel-Catalyzed Decarbonylative C_{sp2}-C_{sp3} Bond Formation Using Triethylborane as Coupling Nucleophiles

Driven by the observation that a ketone product was mainly isolated if $Pn\text{-Bu}_3$ ligand (tri-*n*-butylphosphine) was used instead of dcype (Scheme 7), we decided to further explore the ligand effect to the intriguing reaction chemoselectivity. Remarkably, DFT calculations on the decisive oxidative addition step by Ni(0) species highlighted the different energy profiles if either monodentate or bidentate phosphine ligands were applied (Scheme 8).^{16,33} The calculated results revealed that the ketone product can be favorably generated via C(acyl)-O bond activation by nickel complex when mono-dentate phosphine ligands, such as $Pn\text{-Bu}_3$ and PCy_3 , were used. However, when the bi-dentate dcype ligand was used, the nickel complex favored the C(aryl)-C bond cleavage in the oxidative addition step (Scheme 8b), leading to the alkylated product via an irreversible decarbonylative process.

Scheme 7 Ligand-Controlled Ni-Catalyzed Suzuki-Type Cross-Couplings of Esters: C(acyl)-O Bond vs. C(aryl)-C Bond Activation

Scheme 8 DFT-Computed Gibbs Free Energies Profile for the Ligand-Controlled Ni-Catalyzed Oxidative Addition Process by C(acyl)-O Bond and C(aryl)-C Bond Activation.

2.2. Decarbonylative C-CN Bond Forming Reactions

Having shown for the first time that carboxylic esters can be successfully used for the construction of $\text{C}_{\text{sp}2}-\text{C}_{\text{sp}3}$ bonds as a surrogate to organohalides, we went on to explore other types of transformations employing the Ni-catalyzed decarbonylative process. Our attention was drawn to the synthesis of organonitriles, which are important structural motifs in biologically relevant molecules and electronic materials.³⁴ Traditional synthetic methods including the Sandmeyer and Rosenmund von Braun reactions may have drawbacks including limited substrate scope and utilization of halides.^{35,36} In contrast, a targeted C-CN bond formation allowing the use of abundant and readily available ester substrates could indeed be a good alternative. With the aim

of developing the first ester to cyanide functional group interconversion,³⁷ we started our investigation and searched for an appropriate nitrile source. After careful evaluation, zinc cyanide as a cheap and harmless cyanating agent provided a successful decarbonylative introduction of the CN group in the presence of Ni(0)/dcype catalytic system. In this case, the scope was broad and different substituents on the aromatic and heteroaromatic moieties were generally accepted (Scheme 9). Interestingly, a series of alkenyl esters containing various electronic properties as well as a β -substituted alkene derivative also reacted with zinc cyanide to provide alkenyl nitriles in high yields.

Scheme 9 Nickel-Catalyzed Decarbonylative C-CN Bond Formation Using Zinc Cyanide as Coupling Nucleophiles

As illustrated for the decarbonylative cyanation reaction of esters, we also aimed for the realization of a deamidative cyanation protocol. In this case, we were delighted to see that the decarbonylative cyanation of twisted amides³⁸ proceeded smoothly (Scheme 10A) and the results

are similar to the simultaneously developed Pd-catalyzed deamidative cyanation protocol by the Szostak group.³⁹ Furthermore, an intramolecular recombination fragment coupling of acyl cyanides, which efficiently delivered the corresponding organonitriles in good to moderate yields (Scheme 10B), was developed by our group.³⁷ The latter has the advantage that no phenol or imide byproducts are formed; hence, resulting in a cleaner and greener reaction protocol.

Scheme 10 Nickel-Catalyzed Deamidative Cyanation and Intramolecular Cyanation of Acyl Cyanides

2.3. Decarbonylative C-Si Bond Forming Reactions

The role of organosilicon compounds as useful synthetic building blocks has attracted increasing attention from the synthetic community.⁴⁰⁻⁴² Traditional methods for the preparation of aryl- and heteroaryl-silanes involve the addition of organolithium or Grignard reagents to chlorosilanes or cyclosiloxanes,^{43,44} transition-metal-catalyzed silyl substitution of halides,^{45,46} and arene C-H silylation.^{47,48} However drawbacks still existed. To this end, chemists are focusing their attention on exploiting novel routes for the synthesis of organosilicon compounds. Thus, we turned our attention to the development of new decarbonylative protocols for carbon-heteroatom bond formation. In this context, a decarbonylative silylation reaction under combined nickel and

copper catalysis was developed recently by our group (Scheme 11).⁴⁹ After a series of attempts, silylborane compounds were found as efficient silicon nucleophiles owing to their high reactivity and remarkable potential in copper-catalyzed transmetalations.⁵⁰ Even at high temperature, various esters can successfully be coupled with silylborane compounds to give arylsilanes or heteroarylsilanes with excellent functional group tolerance. Heteroaryl esters bearing benzofuran, benzothiophene, indole, quinoline, chromone, furan, pyridine and thiophene motifs, which are often found in bioactive compounds, participated in the reaction, affording the corresponding organosilane products in acceptable yields.

Scheme 11 Nickel-Catalyzed Decarbonylative Silylation Reaction of Esters

It should be noted that a similar nickel-catalyzed decarbonylative silylation reaction has also been developed by Shi and coworkers (Scheme 13).¹⁴

Based on these results, a mechanism for the decarbonylative silylation process was proposed, as illustrated in Scheme 12. The initial step of the catalytic cycle involves oxidative addition to Ni(0) species **A** with the support of monodentate phosphine ligand via C(acyl)-O bond insertion. The resulting acylnickel(II) complex **B** undergoes a transmetalation route to complex **D** facilitated by the in situ generated copper silane complex **C**. Subsequent decarbonylation and reductive elimination releases the targeted aryl silane while regenerating the Ni(0) species.

Scheme 12 Proposed Mechanisms for the Ni-Catalyzed Decarbonylative Silylation Reaction

2.4. Decarbonylative C-B Bond Forming Reactions

As a continuation of our investigations in this research area, we have next explored the decarbonylative borylation reaction of esters by nickel catalysis. Similar to organosilanes, organoboron compounds are generally recognized as valuable building blocks in natural products synthesis as well as important intermediates in the area of medicinal chemistry, material science and molecular self-assembly.⁵¹⁻⁵³ Thus, our group addressed a C-B bond-forming reaction via a decarbonylative process starting from carboxylic esters (Scheme 13).⁵⁴

Scheme 13 Nickel-Catalyzed Decarbonylative Borylation Reaction of Esters

Under the optimized conditions using 10 mol% Ni(cod)_2 and 40 mol% PnBu_3 various borylated products were efficiently generated. Control experiments revealed that the transformation does

not proceed without the nickel catalyst or in the absence of the supporting ligand. The optimized reaction conditions tolerated various aryl esters with electron-donating and electron-withdrawing groups as well as alkenyl and alkyl esters. Furthermore, a large scale experiment was conducted with a reduced amount of nickel catalyst and ligand, which emphasizes the applicability of this method. Based on the above mentioned advantages of this protocol, we provide a new possibility for late-stage modification by the replacement of stable ester groups. The resulting boron functionality can be easily functionalized to other valuable products if required. A similar decarbonylative borylation procedure was reported by Shi and coworkers (Scheme 14).¹⁴

Scheme 14 Nickel-Catalyzed Decarbonylative Borylation Reaction of Esters by Shi

They have developed an efficient Ni/ICyHCl (ICyHCl: 1,3-dicyclohexyl-imidazolium chloride) catalytic system with B₂(nep)₂ [Bis(neopentyl glycolato)diboron] as coupling nucleophile which

is capable of activating the C(acyl)-O bonds of esters for decarbonylative borylation to produce various organoboronates. Importantly, mechanistic experiments on this decarbonylative process were carried out and together with two well-characterized nickel-intermediates (**B** and **C**, Scheme 14) provided evidences for the ligand-promoted C(acyl)-O bond insertion of nickel.

2.5 Decarbonylative C-N Bond Forming Reactions

Having shown that decarbonylative cross-couplings are efficient alternatives to the traditional couplings, we went on to study more frequently and widely applied reaction types. Our attention was drawn to the formation of amines. Primary aniline derivatives represent very useful synthetic intermediates in the construction of biologically active molecules and conjugated functional materials.^{55,56} We envisioned that primary anilines could be accessed by a C-N bond forming event, starting from readily available esters. Such a method would constitute an important alternative to the classical reduction of nitrobenzene derivatives and metal-catalyzed Buchwald-Hartwig coupling reactions.^{57,58} As a part of our ongoing studies on ester group replacement, we developed an unprecedented decarbonylative C(sp²)-N bond formation using nickel catalysis (Scheme 15).⁵⁹ Applying commercially available benzophenone imine as a nitrogen source,⁶⁰ a series of aryl and heteroaryl esters underwent decarbonylative amination in the presence of Ni(0)/dcype. Primary anilines were formed after acidic hydrolysis of the imine intermediate. This amination protocol shows high reactivity with broad functional group tolerance, allowing access to a wide range of anilines from readily available esters. Other nitrogen sources, such as morpholine and pyrazole, were also found to be unsuitable for this protocol.

Scheme 15 Nickel-Catalyzed Decarbonylative Amination Reaction of Esters

2.6 Decarbonylative C-S Bond Forming Reactions

As the next stage of our studies, we envisioned that a C-S bond coupling of carboxylic esters with thiols might be achieved in this well-developed decarbonylative manner. Although classic transition-metal-catalyzed couplings of thiols with aryl halides are known, these processes still require expensive and reactive electrophiles as coupling partners.^{61,62} Our group recently reported the first decarbonylative thioetherification reaction of esters using a Ni(II)/dppp system in combination with magnesium as reducing agent.⁶³ Remarkably, such a transformation can be performed in a glove-box-free environment, and it represents a crucial breakthrough to achieve C-S bond formation via inert chemical bond cleavage. The substrate scope was very broad, as a

range of aryl, heteroaryl, and even benzylic esters underwent successfully the decarbonylative C-S bond formation with thiols (Scheme 16).

Scheme 16 Nickel-Catalyzed Decarbonylative Thioetherification Reaction of Esters

Based on our success in the decarbonylative C-S bond forming reaction by ester group substitution, we expected that the reaction conditions can be further applicable to amides as well as thioesters. To test our hypothesis, various aromatic and heteroaromatic amides were first treated with thiols in the presence of NiCl_2 and dppp, giving the corresponding thioethers products in 62-93% yield (Scheme 17A). An intramolecular decarbonylation and thioetherification was also demonstrated by us as well as the Sanford group (Scheme 17B).⁶⁴ Remarkably, the synthesis of benzothiophene could also be achieved from thiochromen via a Ni-catalyzed intramolecular decarbonylative fashion (Scheme 17C).⁶³

Scheme 17 Nickel-Catalyzed Decarbonylative Thioetherification Reaction of Amides and Thioesters

2.7 Decarbonylative C-Sn Bond Forming Reactions

Nickel-catalyzed decarbonylative cross-couplings of esters have been well-developed by our group and others. Unlike the wealth of methods on ester substitution of phenyl esters, the means to promote a decarbonylative reaction of methyl esters still remains rather unexplored due to their highly inert nature. Taking into consideration the benefits of applying commercially available and inexpensive methyl esters in cross-coupling reactions, as well as the great significance of organotin compounds in synthetic chemistry,⁶⁵ we recently decided to explore a novel decarbonylative stannylation reaction of methyl esters by nickel catalysis.⁶⁶ The decarbonylative C-Sn bond forming reaction was developed via a Ni-catalyzed C(acyl)-OMe bond activation using Ni(cod)₂/dppp as catalyst and trimethyl(tributylstannyl)silane as the tin source (Scheme 18A). Notably, a wide range of functional groups such as methyl, fluoro, trifluoromethyl, amide, and methoxy were equally tolerated. Under these conditions, ethyl,

cyclohexyl, and benzyl esters could also be stannylated, albeit with moderate efficiency. These findings constitute a significant step towards the development of cost-efficient stannylation protocols, allowing for the coupling of more challenging methyl ester substrates. Furthermore, a broad range of phenyl esters was tested under Ni(II)/dppp catalytic conditions and, as expected, these reactions proceeded also in good yields (Scheme 18B).

Scheme 18 Nickel-Catalyzed Decarbonylative Stannylation of Methyl Esters and Phenyl Esters.

2.8. Decarbonylative Hydrogenolysis

As a next stage of our studies, we decided to move away from nucleophilic substitution of ester groups and instead investigate whether a decarbonylative hydrogenolysis could be achieved. The removal of ester groups could be useful to retrosynthetic analysis, as ester groups are considered as suitable directing groups in metal-catalyzed C-H functionalizations.³⁻⁶ To the best of our knowledge, the removal of ester groups from aromatic and heteroaromatic rings via a decarbonylative pathway was still unknown,⁶⁷ despite the attractiveness of removing functionalities from organic molecules. Inspired by the recent progress in reductive C(aryl)-O bond cleavage by Martin and Chatani groups,⁶⁸⁻⁷⁰ we started to search for a potential reducing agent and finally found that inexpensive, non-toxic and air-stable polymethylhydrosiloxane (PMHS) functions as an efficient reducing agent in the nickel-catalyzed reductive decarbonylation reaction (Scheme 19).⁷¹ At the same time Lahiri and Maiti developed an elegant deamidative reaction protocol.⁷² In our case Ni(OAc)₄·4H₂O was chosen as catalyst. In addition, we found that the bidentate phosphine ligand dcype was the best performing ligand, and the reaction was performed efficiently in the absence of base. As expected, this decarbonylative hydrogenolysis approach is general and the chemoselectivity profile of this process was illustrated by the fact that functional groups, such as methoxy, boronic ester, alkenyl, fluoride, trifluoromethyl, methyl ester, methylthio, ketone, amine and amide moieties were perfectly tolerated under the reaction conditions. Moreover, a great variety of heteroaryl esters bearing benzofuran, indole, quinoline, furan, pyridine and thiophene motifs could also successfully undergo reaction under the optimized hydrogenolysis conditions.

Scheme 20 Nickel-Catalyzed Decarbonylative Hydrogenolysis of Esters

3. CONCLUSION AND PERSPECTIVE

Owing to the unique reactivity of nickel that allows for oxidative addition with ease, we and others have recently developed a number of exciting new protocols that have not been achieved with precious-metal catalysts before. In this Account we summarized our recent progress in decarbonylative cross-coupling reactions in which inexpensive and abundant carboxylic acid esters are employed as coupling counterparts (Scheme 20).

Scheme 20 Overview of Decarbonylative Cross-Coupling Reactions of Ester

A series of ester group substitutions has been successfully achieved, including decarbonylative alkylation, cyanation, silylation, borylation, amination, thioetherification, stannylation, and hydrogenolysis. Compared with traditional methods using organohalides as coupling electrophiles, these decarbonylative protocols avoid the production of corrosive halide-containing waste. Furthermore, such developed protocols will be of interest as they allow for the replacement of ester groups, which can be used as directing groups in metal-catalyzed C-H functionalizations prior replacement. Driven by the initial discovery of Yamamoto chemists are still seeking to understand the mechanism of decarbonylative cross-coupling reactions. On one hand the mechanism of C(acyl)-O bond insertion by low-valent nickel species with a monodentate phosphine ligand or NHC ligand has been established, and on the other hand, our experimental studies and DFT calculations on oxidative addition step suggest that the Ni(0) species with a bidentate phosphine ligand insert more likely into C(aryl)-C bond. Nevertheless, all these studies primarily focused on the decisive oxidative addition step due to its high energy barrier, and further efforts towards the mechanistic understanding of the individual

transformations from both, theoretical and methodological side are still required. Meanwhile, we hope that further new and synthetically useful transformations with respect to the decarbonylative research concept will be developed as the ester functional group interconversion strategy should be of use in retrosynthesis, late stage functionalization and organic synthesis in general.

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Notes

The authors declare no competing financial interest.

Biographies

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Magnus Rueping studied at the Technical University of Berlin, Trinity College Dublin and ETH Zürich. He obtained his Ph.D. from the ETH in 2002 working with Prof. Dieter Seebach on the synthesis and structural and biological aspects of oligo(hydroxybutanoates) and of β - and γ -

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