

Literature Report

Catalytic Ester and Amide to Amine Interconversion: Nickel-Catalyzed Decarbonylative Amination of Esters and Amides by C-O and C-C Bond Activation

Reporter: Ji Zhou

Checker: Hong-Qiang Shen

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Yue, H.; Guo, L.; Liao, H.-H.; Cai, Y.; Zhu, C.; Rueping, M.
Angew. Chem. Int. Ed. **2017**, *56*, 4282-4285.

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CV of Rueping Magnus

Position: Professor in RWTH Aachen University

Education:

1996-1999 Diploma in Chemistry at Technical University of Berlin, Germany, diploma thesis at Swiss Federal Institute of Technology, Switzerland.

1999-2002 Ph. D. in Chemistry, Swiss Federal Institute of Technology, Switzerland. Mentor: Prof. Dr. D. Seebach.

2002-2004 Postdoctoral Research Fellow, Harvard University, Department of Chemistry & Chemical Biology. Mentor: Prof. Dr. D. A. Evans.

2004-2009 C3-Professor of Organic Chemistry at Goethe University Frankfurt.

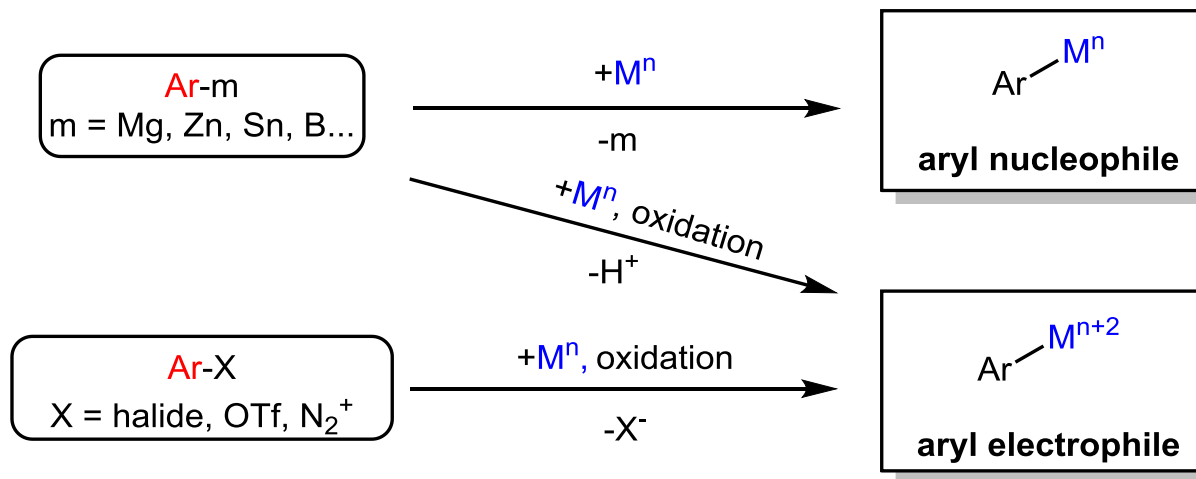
2009- Chair and Full Professorship at RWTH Aachen.



Research

Enantioselective organocatalysis, metal- and biocatalysis, new reaction methodology and technology, new materials as well as photochemistry and flow chemistry.

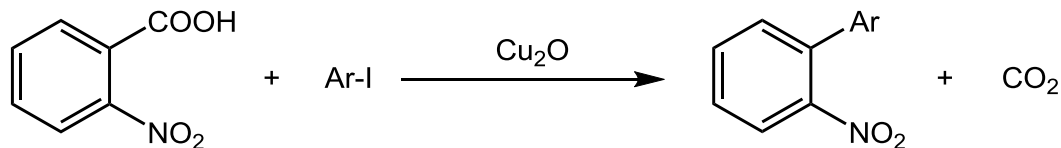
Traditional pathways to aryl-metal species



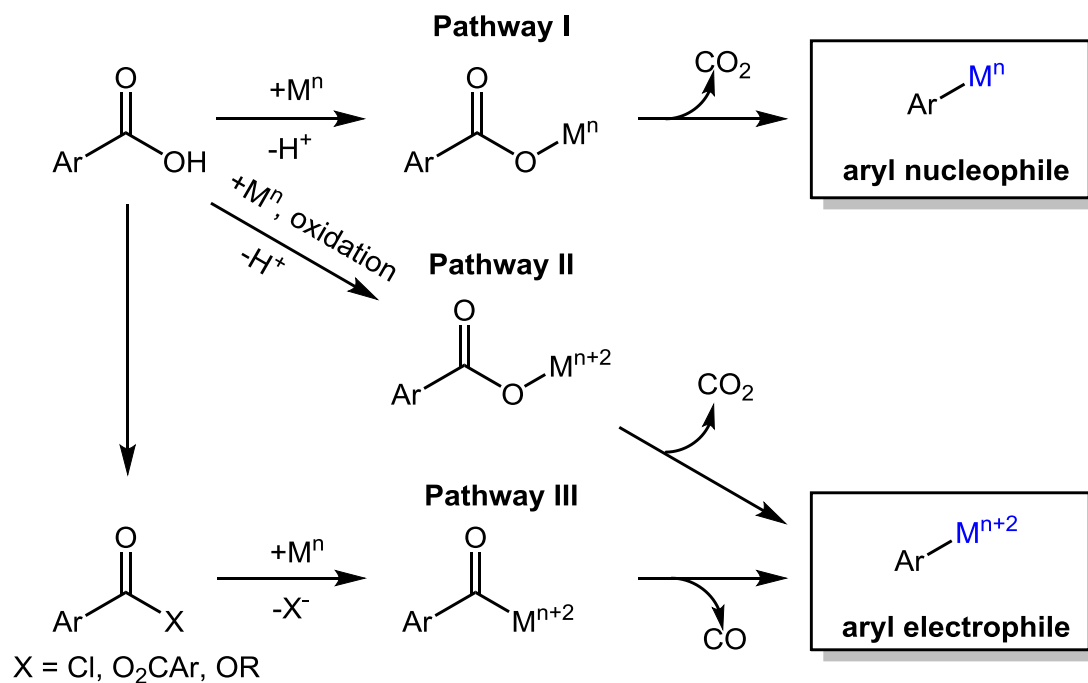
Aryl nucleophile: usually an organometallic reagent, then transfers its carbon residue to the metal centre *via* a transmetallation step.

Aryl electrophile: usually an organohalide or -pseudohalide, oxidatively adds to a metal catalyst with a low oxidation state with formation of an organometallic intermediate in a higher oxidation state.

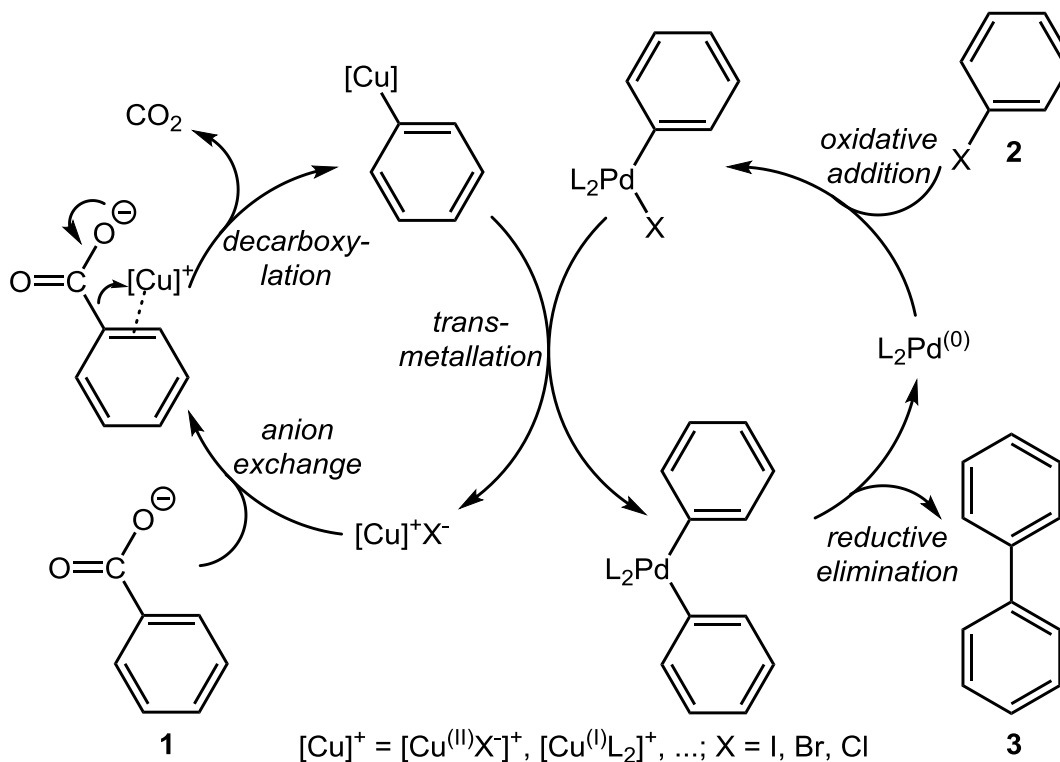
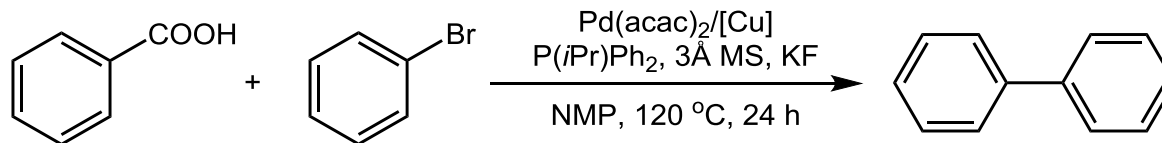
Decarboxylative/decarbonylative couplings



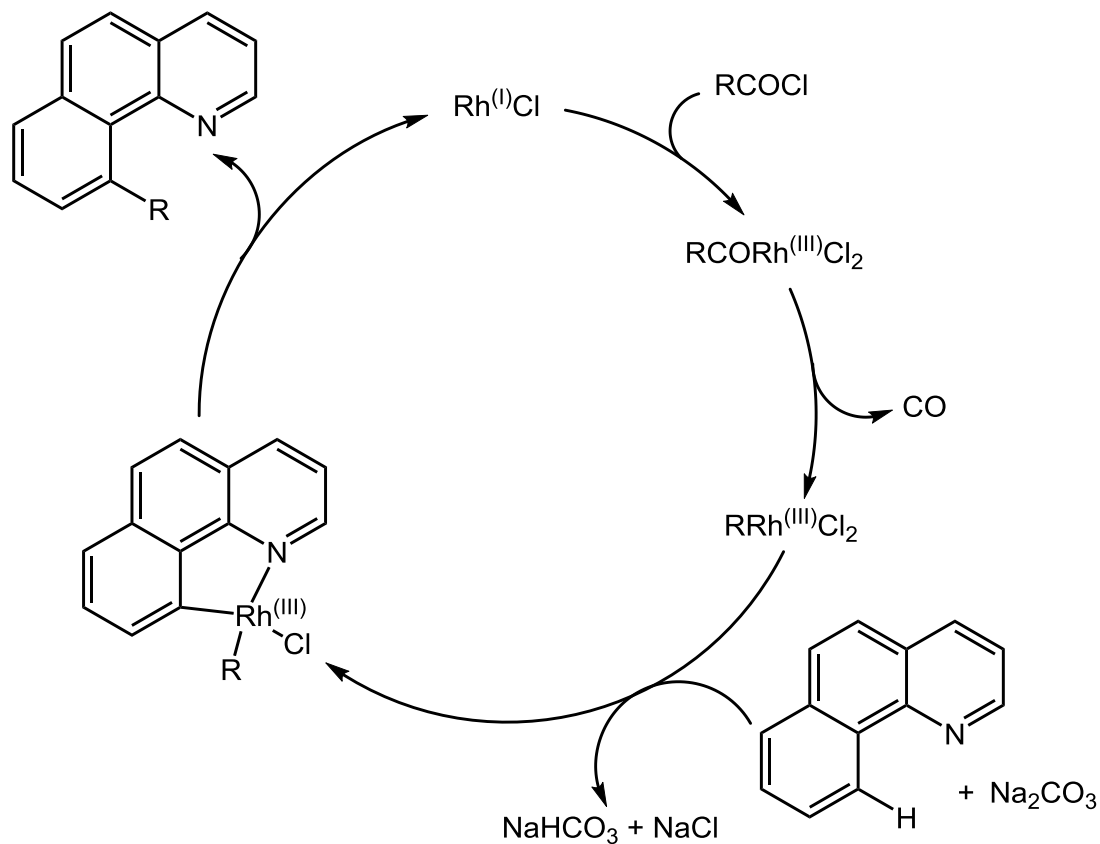
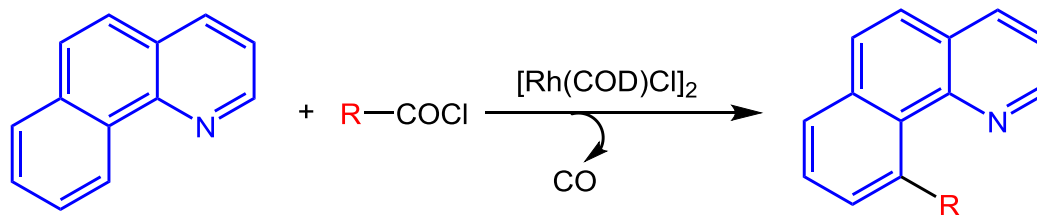
Nilsson, M. *et al. Acta Chem. Scand.* **1966**, *20*, 423.



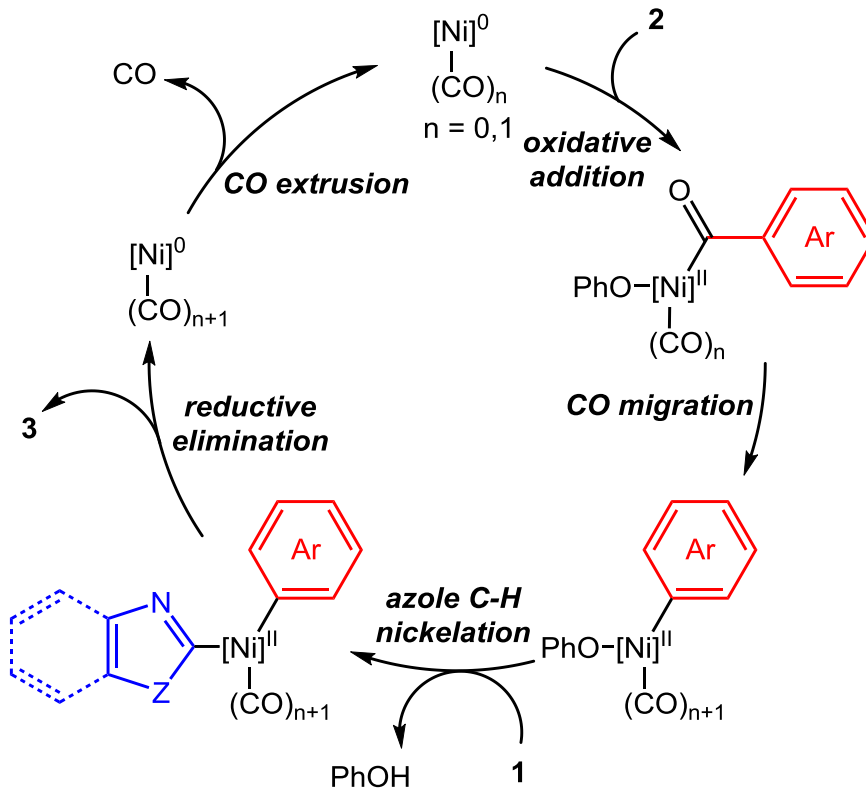
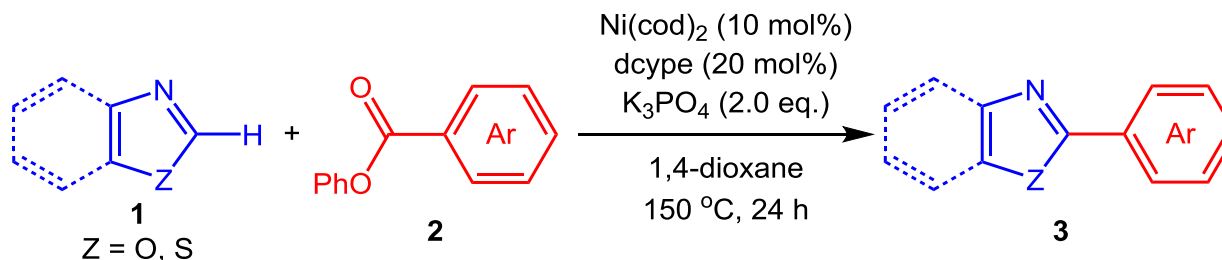
Pd/Cu catalyzed decarboxylative coupling



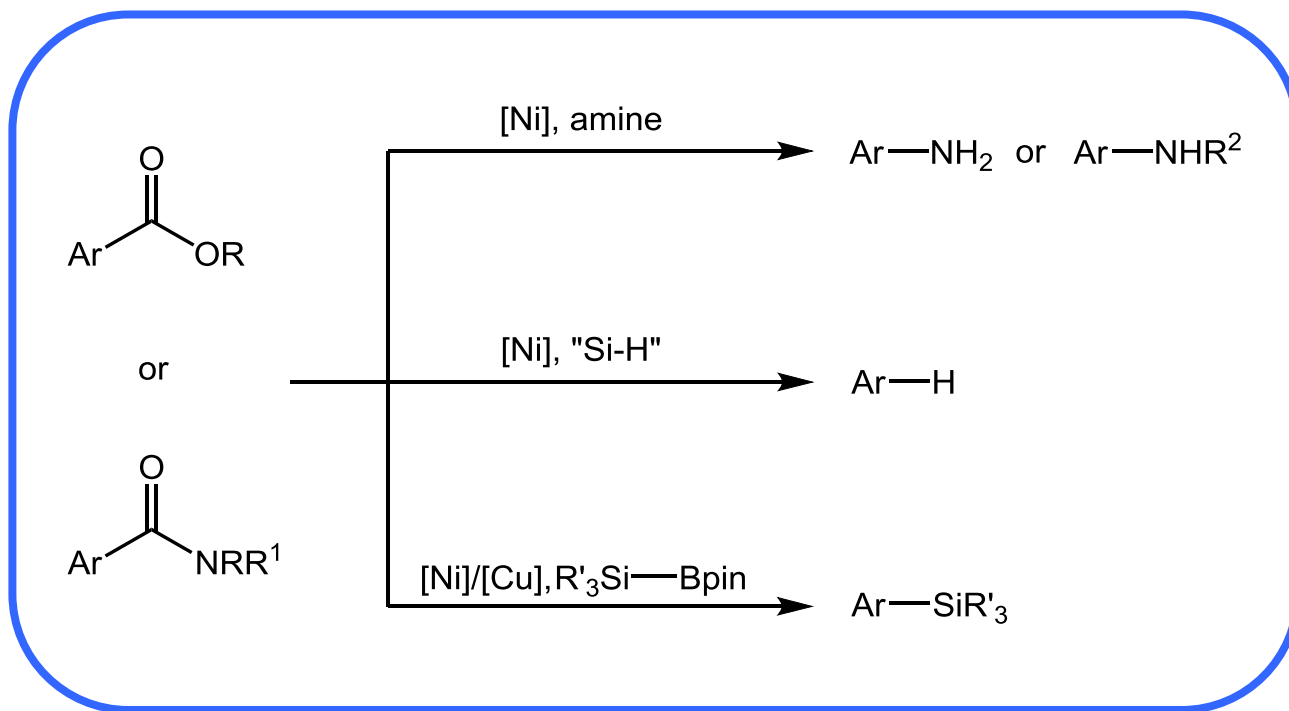
Rh-catalyzed decarbonylative coupling



Ni-catalyzed decarbonylative coupling

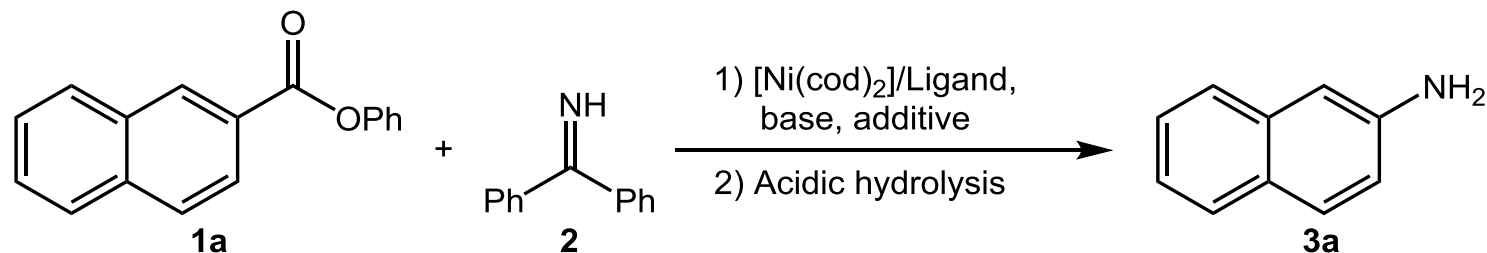


Ni-catalyzed decarbonylative coupling



Rueping, M. *et al. Angew. Chem. Int. Ed.* **2017**, *56*, 4282;
Rueping, M. *et al. Angew. Chem. Int. Ed.* **2017**, *56*, 3972;
Rueping, M. *et al. Angew. Chem. Int. Ed.* **2016**, *55*, 11810.

Ni-catalyzed decarbonylative amination



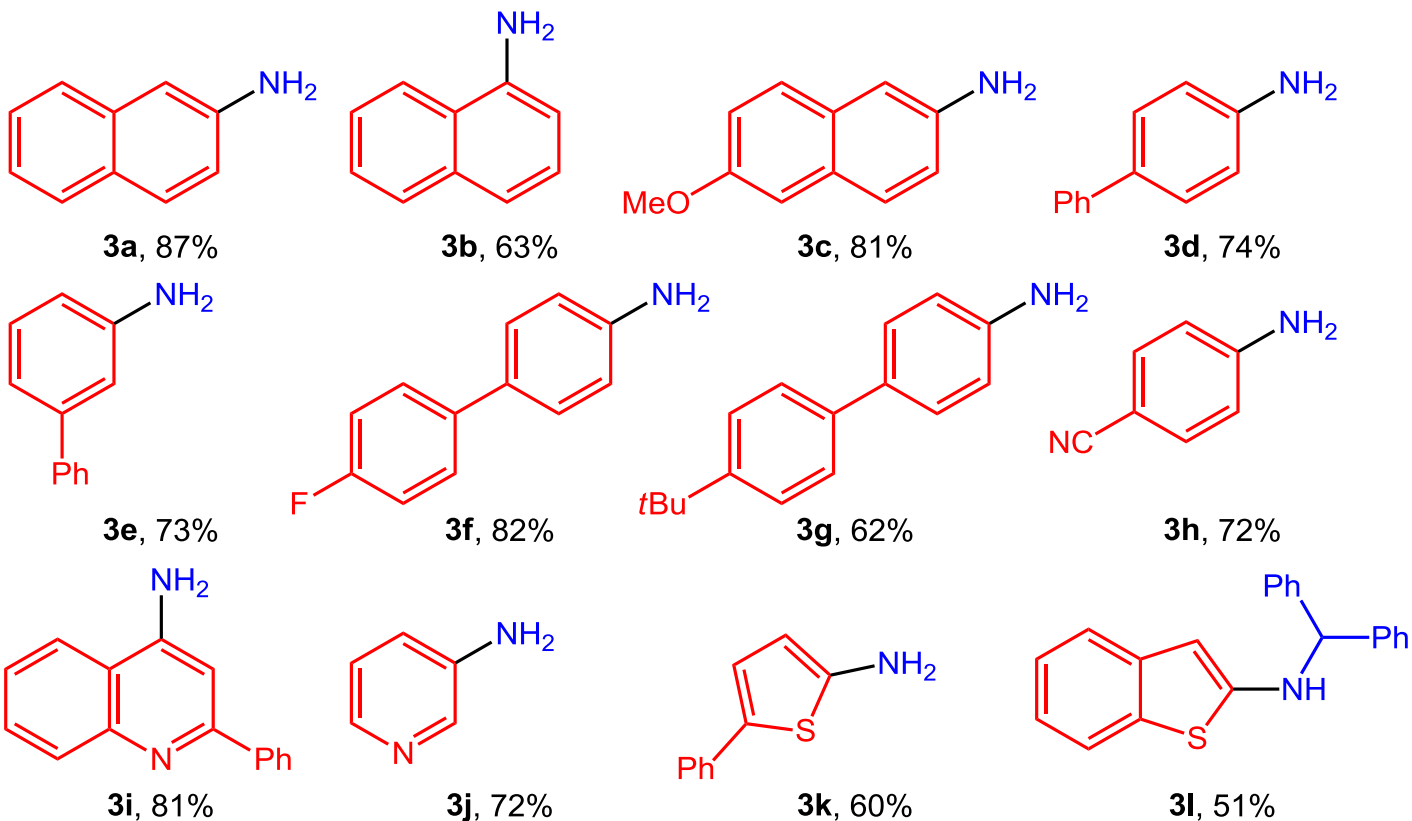
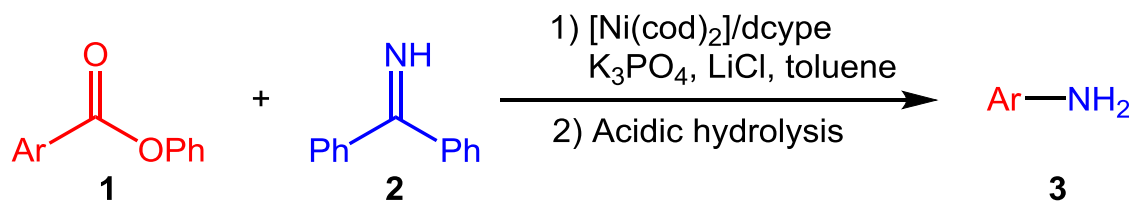
| Entry ^a | Ligand (x mol%) | Base (2.0 eq.) | Additive (2.0 eq.) | Yield (%) ^b |
|--------------------|-----------------------|---------------------------------|--------------------|------------------------|
| 1 | PCy ₃ (20) | Cs ₂ CO ₃ | - | 0 |
| 2 | dcype (10) | Cs ₂ CO ₃ | - | 14 |
| 3 | dcypf (10) | Cs ₂ CO ₃ | - | trace |
| 4 | dcype (20) | Cs ₂ CO ₃ | - | 17 |
| 5 | dcype (20) | Li ₂ CO ₃ | - | 21 |
| 6 | dcype (20) | K ₂ CO ₃ | - | 31 |
| 7 | dcype (20) | Na ₂ CO ₃ | - | 31 |
| 8 | dcype (20) | K ₃ PO ₄ | - | 42 |

Ni-catalyzed decarbonylative amination

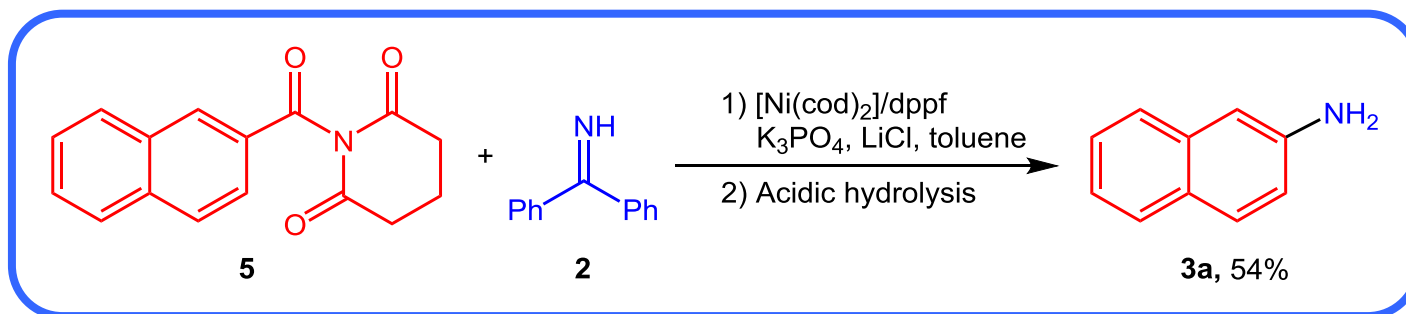
| Entry | Ligand (x mol%) | Base (2.0 eq.) | Additive (2.0 eq.) | Yield (%) |
|-------------------------|--------------------|------------------------------------|-----------------------|--------------|
| 9 ^c | dcype (20) | K ₃ PO ₄ | - | 56 |
| 10 ^c | dcype (20) | K ₃ PO ₄ | LiCl | 63 |
| 11 ^{c,d} | dcype (20) | K ₃ PO ₄ | LiCl | 84 |
| 12^{c-e} | dcype (20) | K₃PO₄ | LiCl | 87 |
| 13 ^{c-e} | - | K ₃ PO ₄ | LiCl | 0 |

dcype=1,2-bis(dicyclohexylphosphino)-ethane, dcypf=1,1'-bis(dicyclohexylphosphino) ferrocene. ^a Reaction conditions: **1a** (0.2 mmol), **2** (0.3 mmol), [Ni(cod)₂] (0.02 mmol), ligand (0.02 mmol or 0.04 mmol), base (0.4 mmol) in toluene (1 mL) at 160 °C, 12 h. ^b Yield of isolated products. ^c **2** (2.0 eq.), K₃PO₄ (3.0 eq.). ^d 48 h. ^e 170 °C.

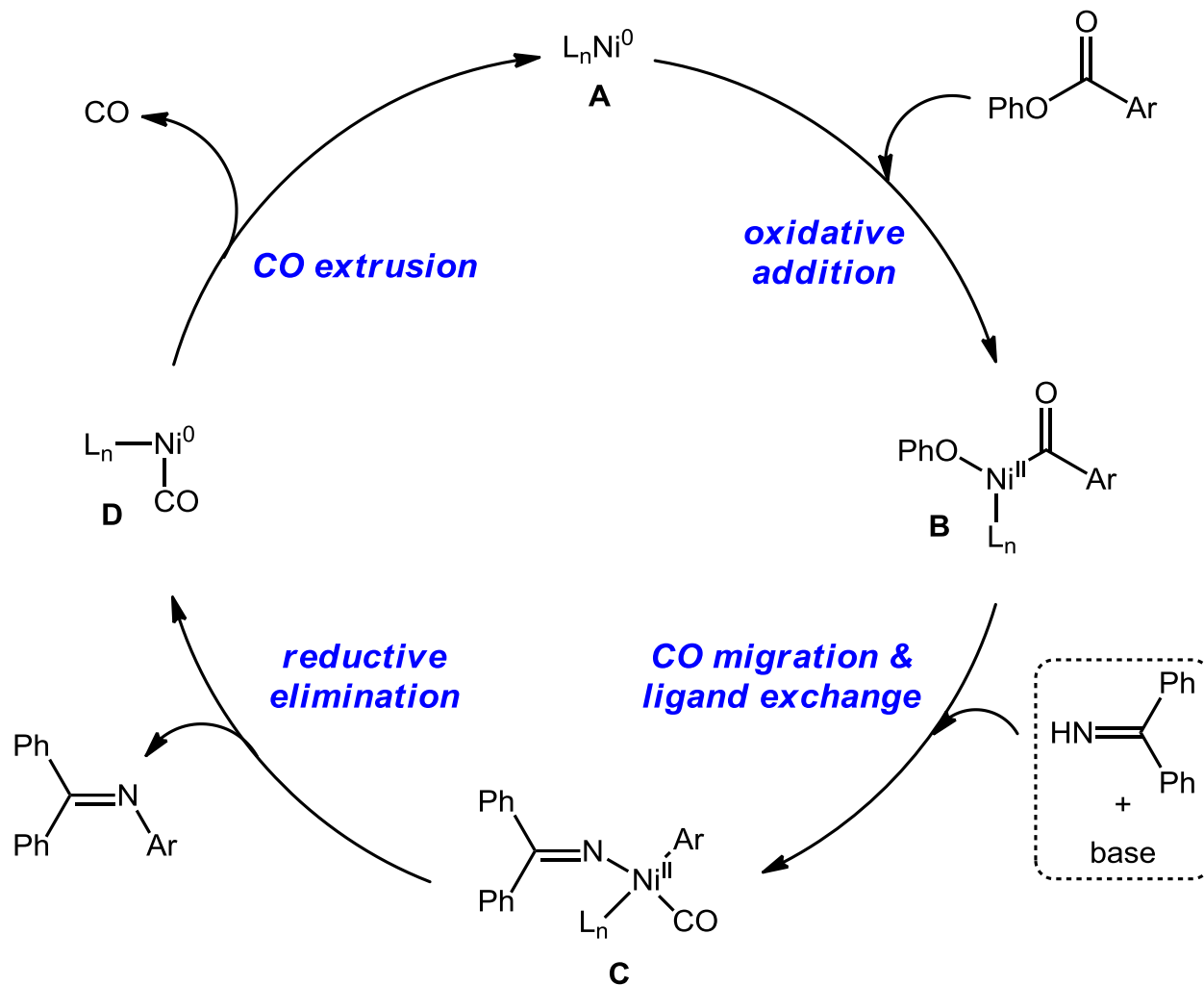
Substrate scope



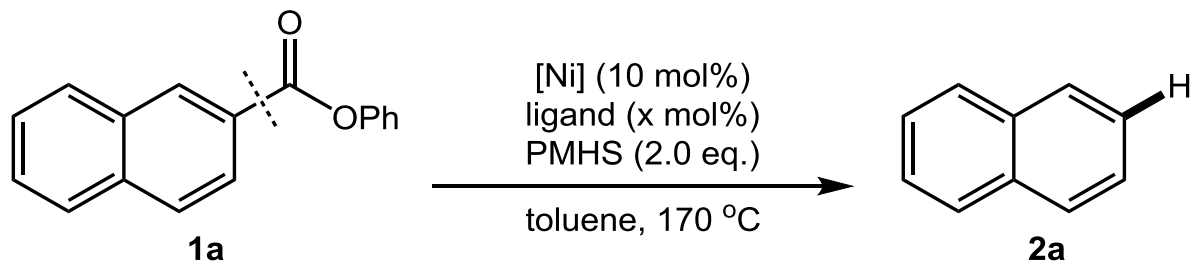
Synthetic application



Proposed mechanism



Ni-catalyzed decarbonylative reductive removal of ester and amide groups



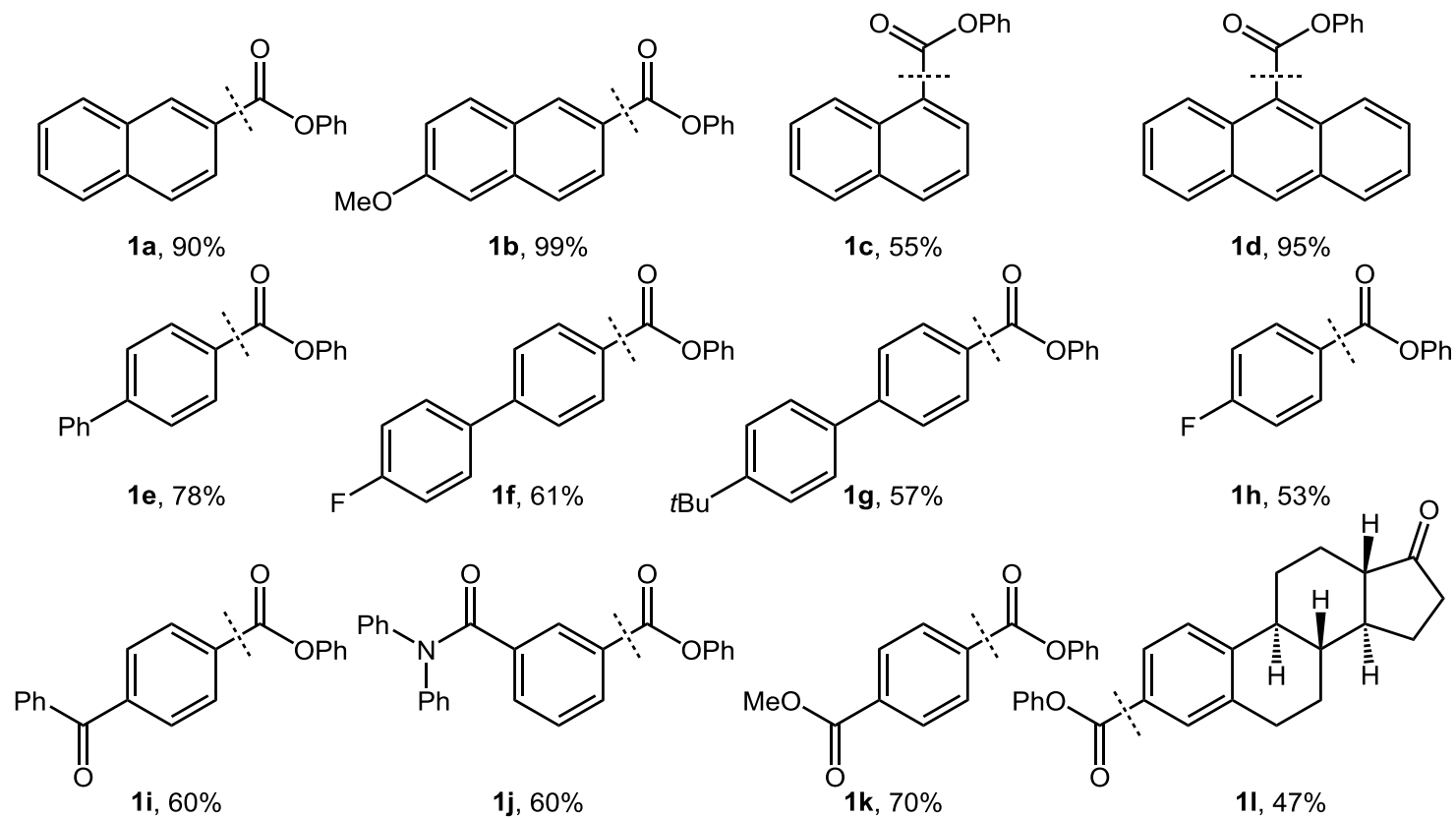
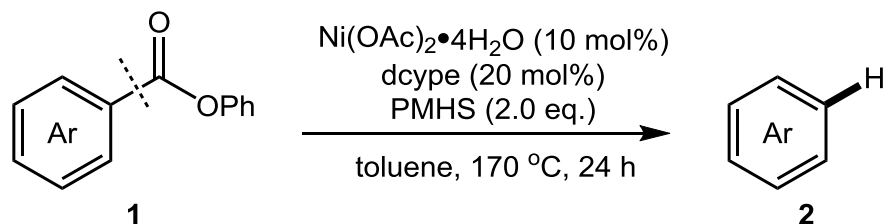
| Entry ^a | [Ni] | Ligand (x mol%) | t (h) | Yield (%) ^b |
|--------------------|--|-------------------------------------|-----------|------------------------|
| 1 | [Ni(cod) ₂] | dcype (20) | 12 | 69 |
| 2 | [Ni(cod) ₂] | PCy ₃ (40) | 12 | trace |
| 3 | [Ni(cod) ₂] | P ⁿ Bu ₃ (40) | 12 | 43 |
| 4 ^c | [Ni(cod) ₂] | dcype (20) | 12 | 57 |
| 5 | [Ni(cod) ₂] | dcype (20) | 24 | 88 |
| 6 | Ni(OAc)₂ • 4H₂O | dcype (20) | 24 | 90 |

Ni-catalyzed decarbonylative reductive removal of ester and amide groups

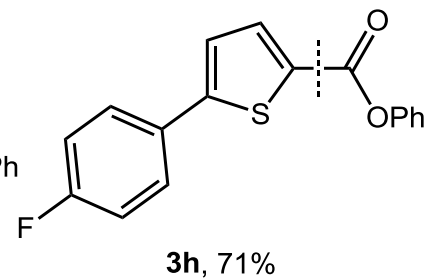
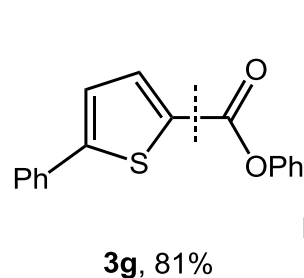
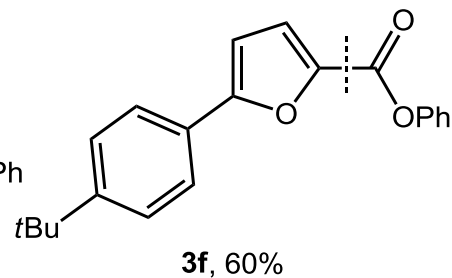
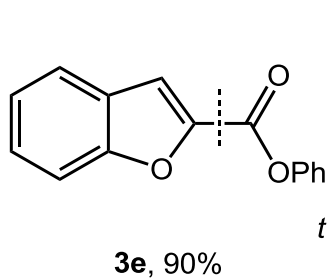
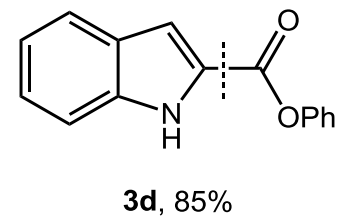
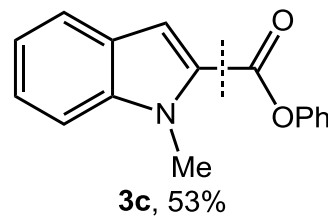
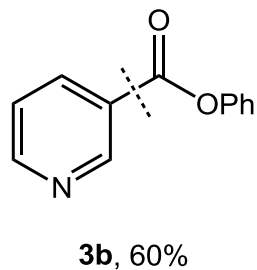
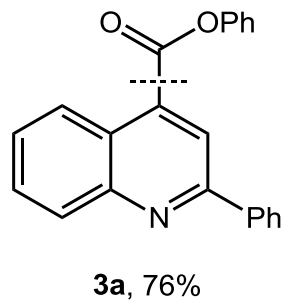
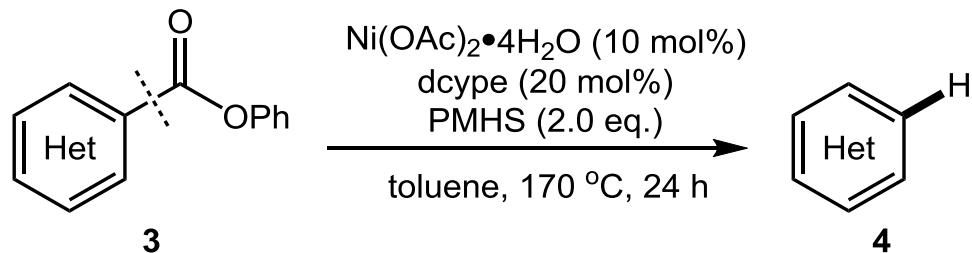
| Entry | [Ni] | Ligand (x mol%) | t (h) | Yield (%) |
|-----------------|--|-----------------|-------|-----------|
| 7 | NiCl ₂ | dcype (20) | 24 | 0 |
| 8 | NiBr ₂ | dcype (20) | 24 | 0 |
| 9 | NiI ₂ | dcype (20) | 24 | 0 |
| 10 | Ni(OAc) ₂ • 4H ₂ O | dcype (10) | 24 | 68 |
| 11 ^d | Ni(OAc) ₂ • 4H ₂ O | dcype (20) | 24 | 51 |
| 12 ^e | Ni(OAc) ₂ • 4H ₂ O | dcype (20) | 24 | 30 |
| 13 | - | dcype (20) | 24 | 0 |

^a Reaction conditions: **1a** (0.2 mmol), PMHS (0.4 mmol), [Ni] (0.02 mmol), ligand (0.04 mmol), toluene (1.0 mL), 170 °C. ^b Yield after purification. ^c KF (2.0 eq.) was added. ^d Dioxane was used as the solvent. ^e The reaction was carried out at 150 °C.

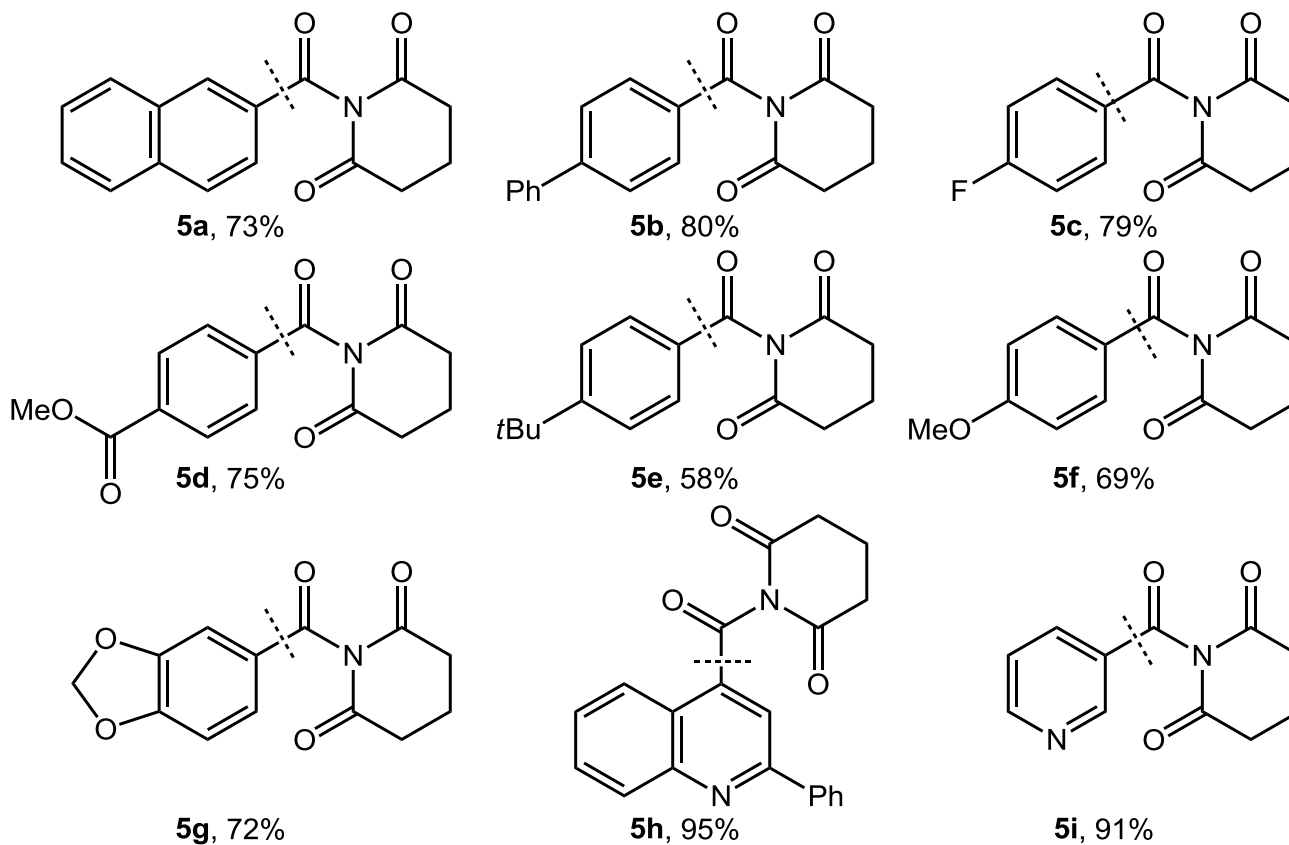
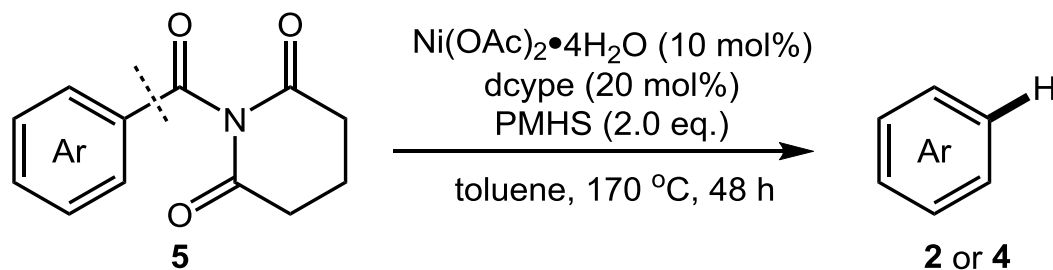
Scope of the reaction of aryl esters



Scope of the reaction of heteroaryl esters

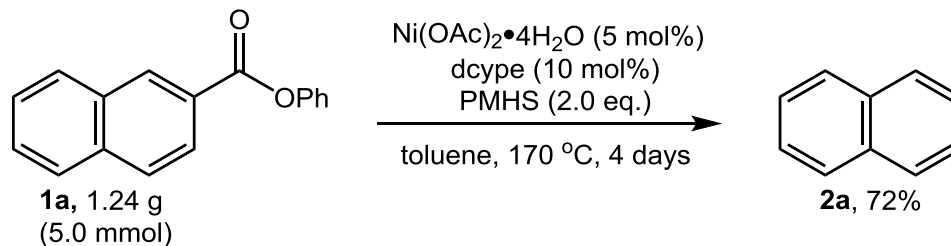


Scope of the reaction of amides

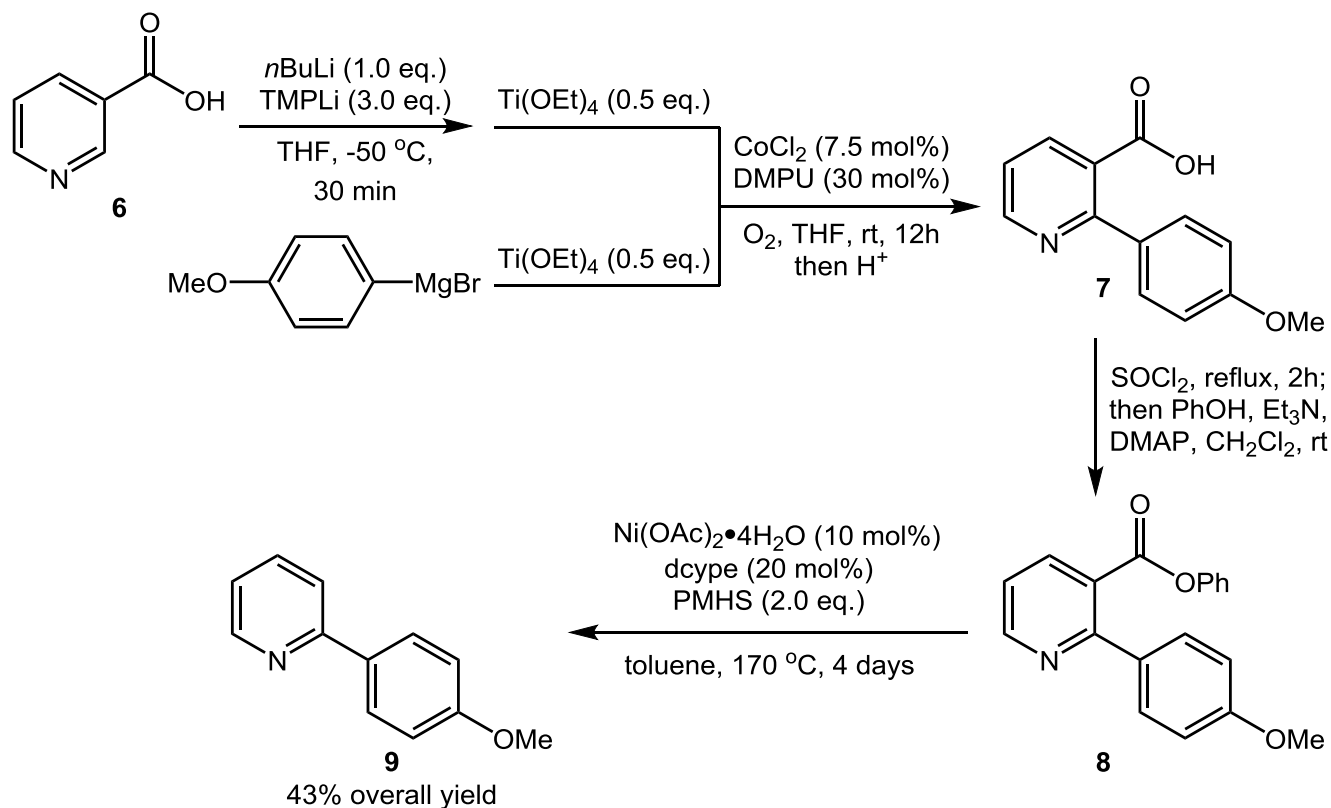


Synthetic application

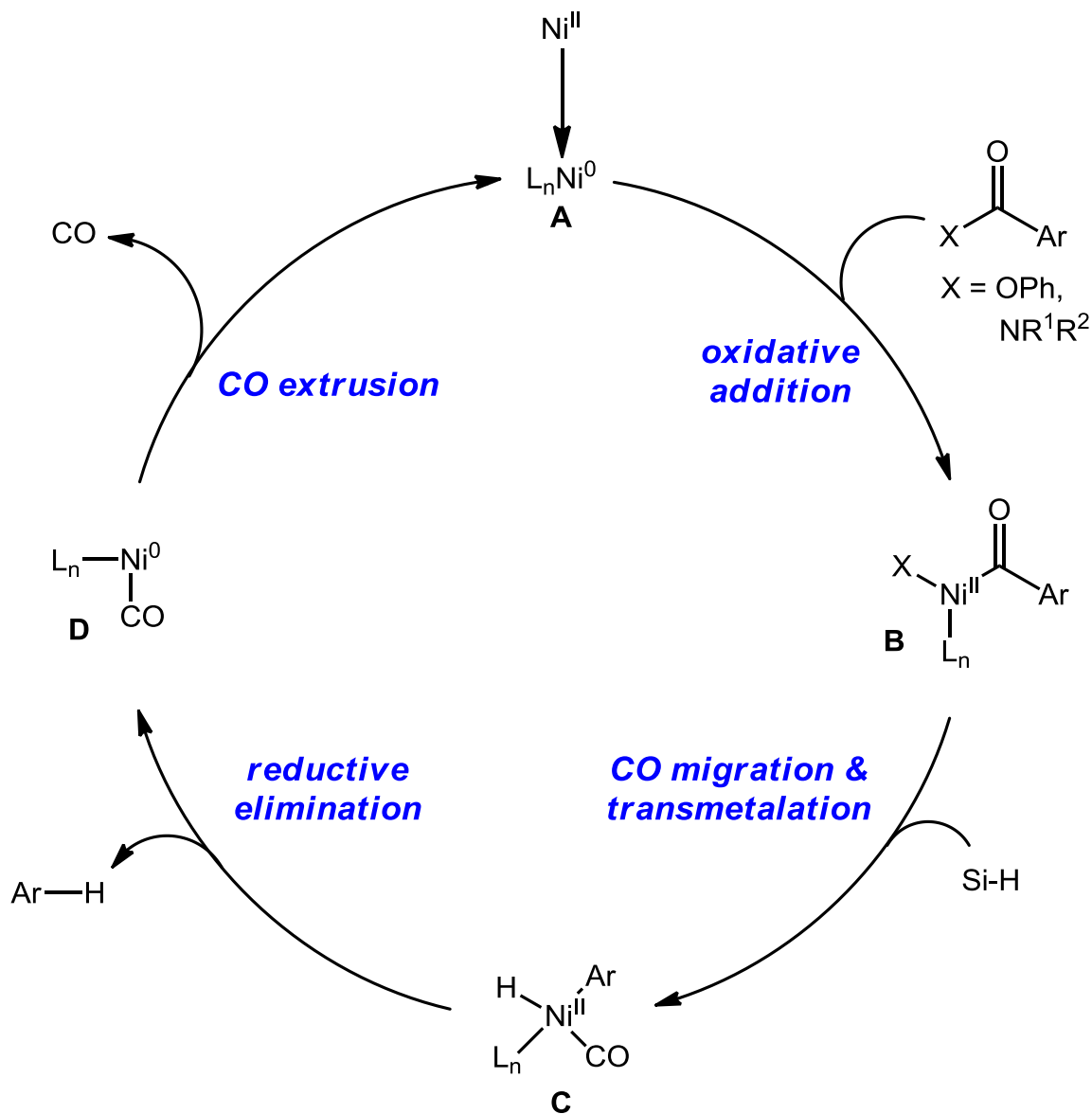
a) Gram-scale reductive defunctionalization



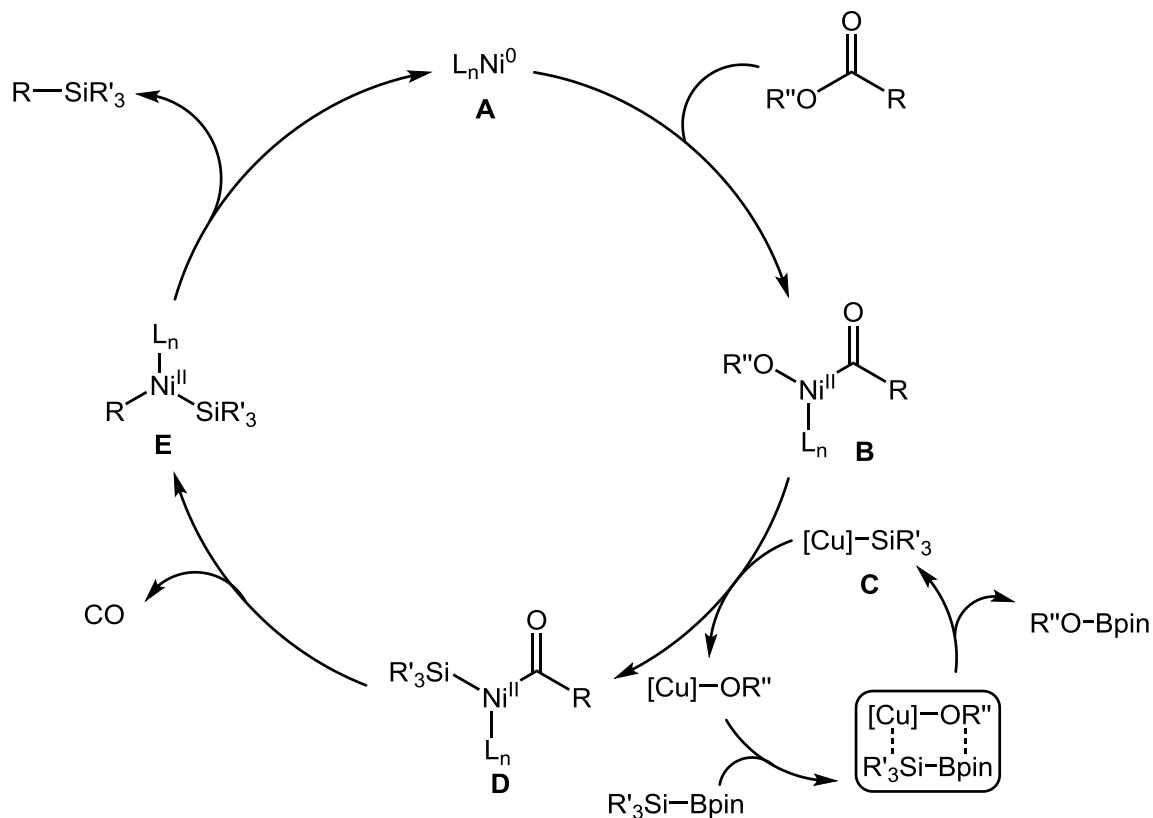
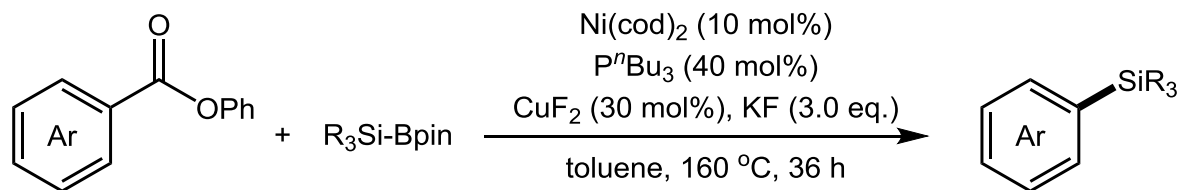
b) Aryl acid group as a removal directing group



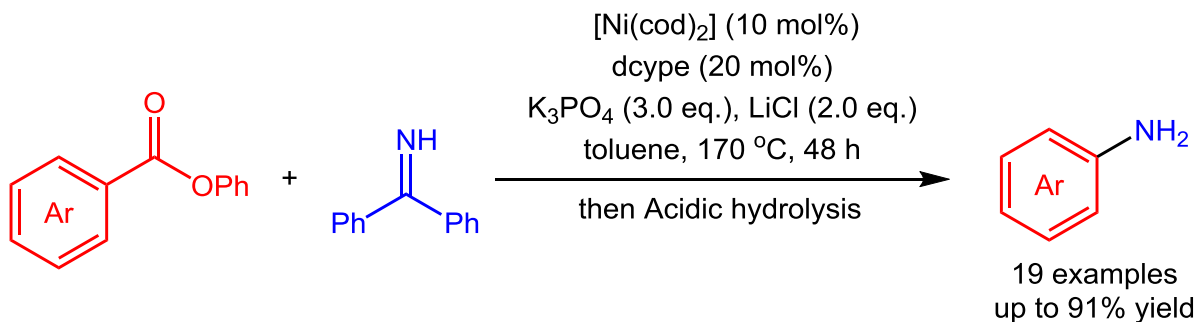
Proposed mechanism



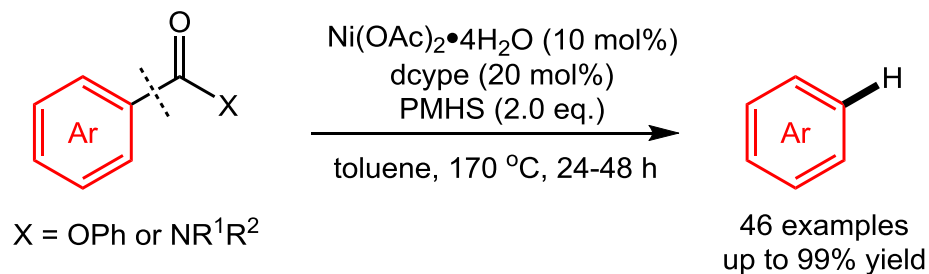
Ni-catalyzed decarbonylative silylation



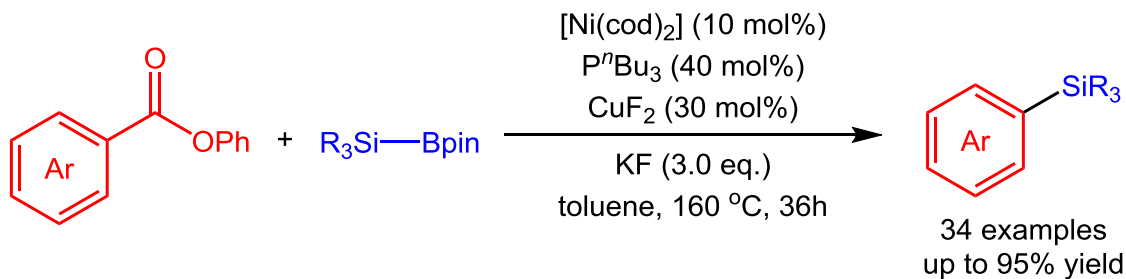
Summary



Rueping, M. *et al. Angew. Chem. Int. Ed.* **2017**, *56*, 4282.



Rueping, M. *et al. Angew. Chem. Int. Ed.* **2017**, *56*, 3972.



Rueping, M. *et al. Angew. Chem. Int. Ed.* **2016**, *55*, 11810.

The first paragraph

Aromatic amines are important synthetic building blocks in chemistry because of their application in the preparation of pharmaceuticals, biologically active molecules, natural products, polymers, as well as functional materials. Accordingly, the development of new methodologies to access these valuable molecules continues to be of great importance in synthetic organic chemistry. Conventionally, the palladium catalyzed Buchwald–Hartwig reaction represents a valuable C(sp²)-N bond-formation method which makes a great contribution to this field. Although palladium is dominating the field, and a considerable number of powerful catalytic systems for the conversion of aryl (pseudo) halides into aromatic amines has been reported, recent efforts are devoted to the disclosure of improved protocols based on nonprecious metal catalysts.

The first paragraph

Particular attention has been drawn to the use of inexpensive and earth-abundant nickel catalysts, along with easily available and versatile C(sp²)-O electrophiles. Despite the advances in this field, it is still highly desirable to further explore different electrophilic coupling partners for metal-catalyzed amination reactions with the aim of developing protocols based on cheaper, more-stable, and readily available substrates. Considerable progress has been achieved in metal-catalyzed decarboxylative and decarbonylative cross-coupling reactions using carboxylic acids and its derivatives.

The last paragraph

In summary, we have developed the first catalytic decarbonylative amination protocol which allows, for the first time, the transfer of a series of readily available aryl and heteroaryl esters, and even amides, to the corresponding amines. In contrast to classical multistep rearrangement procedures, the method relies on the use of either $[\text{Ni}(\text{cod})_2]/\text{dcype}$ catalytic system or the use of a nickel (II) salt to directly provide the desired amines. Considering the substrate scope of this protocol, the method provides a new and efficient route to aryl amines from readily available esters. The protocol shows good chemoselectivity, and functional groups including C-OMe, C-SMe, C-F, and CN moieties, previously used in cross-couplings, remain intact. Since aryl and heteroaryl amines are highly valuable products for many different applications this new ester to amine interconversion will be of value and may become a good alternative to aryl halides amination reactions. Efforts to investigate the mechanism and broaden the scope further are currently ongoing in our laboratories and will be reported in due course.