

Nickel NHC-Catalyzed C-N Bond Formation

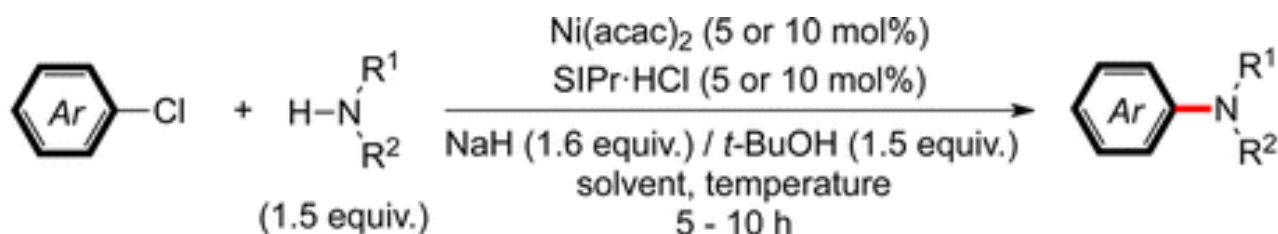
Reporter: Song Feifei
Supervisor: Prof. Yong Huang
2017. 02. 13

Outline

- **Amination of aryl halides**
- Dehydrogenative cross-coupling of aldehydes and amines
- Hydroamination of olefins
- Hydroimination of alkynes
- One-step indoline synthesis from iodoacetanilides and alkenes

Amination of aryl halides

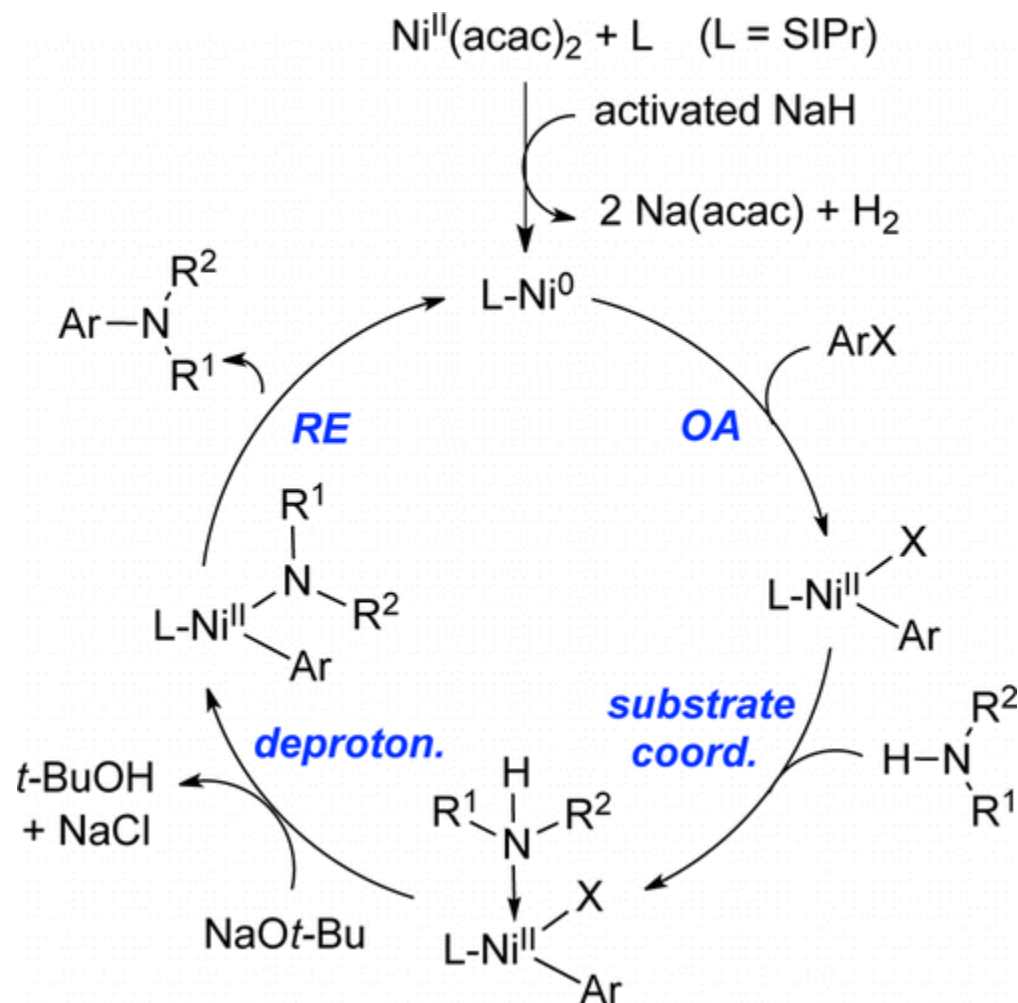
First Ni(NHC)-catalyzed amination of aryl chlorides



Secondary amines: THF, 65 °C, Ni(acac) ₂ (5 mol%), SIPr·HCl (5 mol%)	25 examples 53 - 99%
Anilines: dioxane, 100 °C, Ni(acac) ₂ (5 mol%), SIPr·HCl (10 mol%)	22 examples 47 - 99%
Primary amines: dioxane, 100 °C, Ni(acac) ₂ (10 mol%), SIPr·HCl (10 mol%)	3 examples 37 - 85%

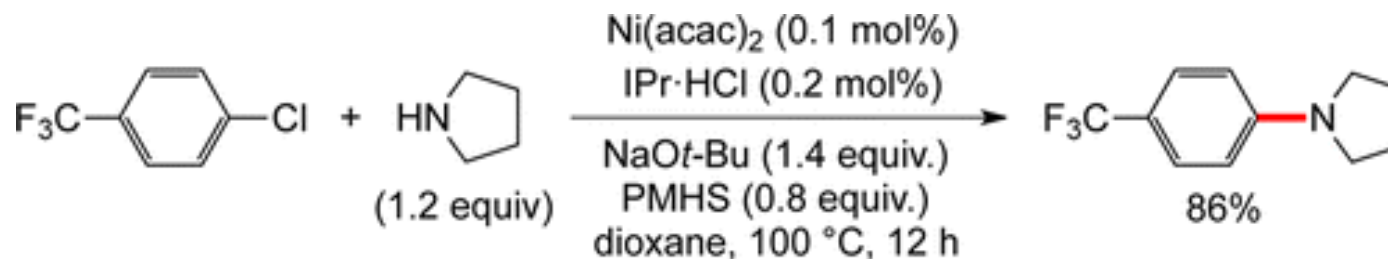
Amination of aryl halides

Proposed mechanism for the amination of aryl chlorides



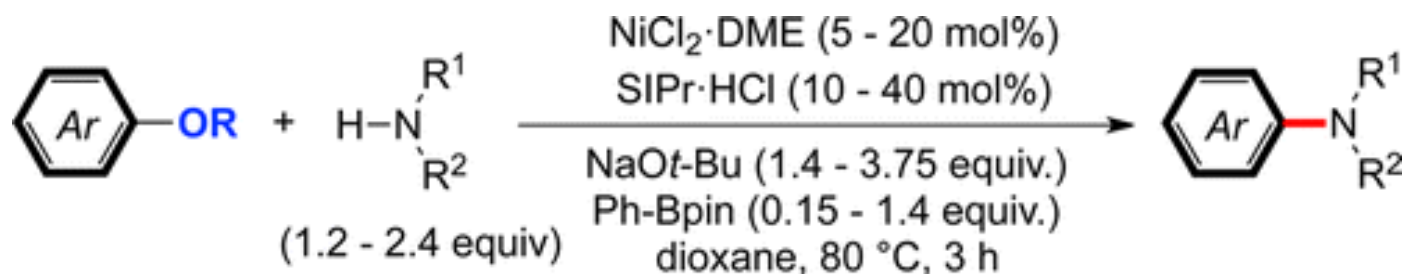
Amination of aryl halides

PMHS as a reducing agent



PHMS: Polymethylhydroxysilane

Ph-Bpin as a reducing agent

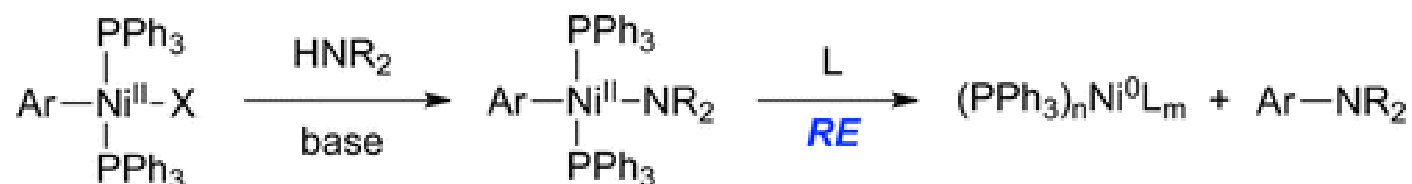


OR = OS(O)₂NMe₂ 22 examples
53 - 98%

OR = OC(O)NEt₂ 22 examples
40 - 91%

Amination of aryl halides

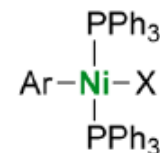
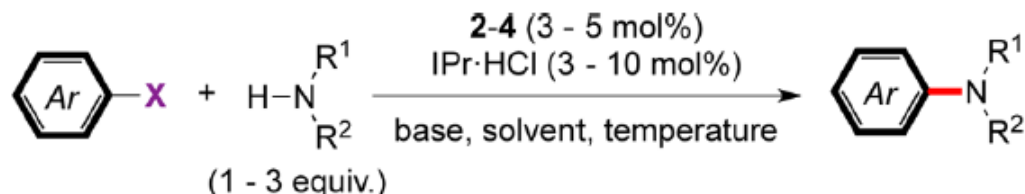
Possible pathway for activating aryl Nickel(II) halide complexes



Without the aid of a reducing agent: by attack of a nucleophile and then reductive elimination to generate in situ an active Ni(0) species.

Amination of aryl halides

Amination of aryl chlorides, tosylates, and phosphates



X = Cl and cyclic secondary amines:

2 (3 mol%), IPr·HCl (3 mol%), NaOt-Bu (1.3 equiv.), THF (65 °C) or dioxane (80 °C), 1 - 3 h
4 (5 mol%), IPr·HCl (5 mol%), KOt-Bu (4.0 equiv.), toluene (RT), 24 h

9 examples
72 - 99% [ref. 34]
19 examples
50 - 99% [ref. 36]

X = Cl and anilines:

3 (5 mol%), IPr·HCl (10 mol%), NaOt-Bu (1.3 equiv.) dioxane (100-120 °C), 3 - 6 h

10 examples
66 - 99% [ref. 34]

X = OTs and cyclic secondary amines:

4 (5 mol%), IPr·HCl (5 mol%), NaOt-Bu (1.6 equiv.) dioxane (110 °C), 15 min

14 examples
24 - 96% [ref. 37]

X = OTs and anilines:

4 (5 mol%), IPr·HCl (10 mol%), NaOt-Bu (1.6 equiv.) dioxane (110 °C), 30 min

19 examples
37 - 95% [ref. 37]

X = OP(O)(OAr)₂ and cyclic secondary amines, aliphatic primary amines and anilines

4 (5 mol%), IPr·HCl (10 mol%), NaH (2.0 equiv.) dioxane (110 °C), 30 min - 1 h

28 examples
21 - 95% [ref. 38]

2: Ar = Ph, X = Br

3: Ar = 1-(*p*-acetylnaphtyl), X = Cl

4: Ar = 1-naphtyl, X = Cl

Yang, L.-M. *et al. J. Org. Chem.* **2007**, *72*, 6324-6327.

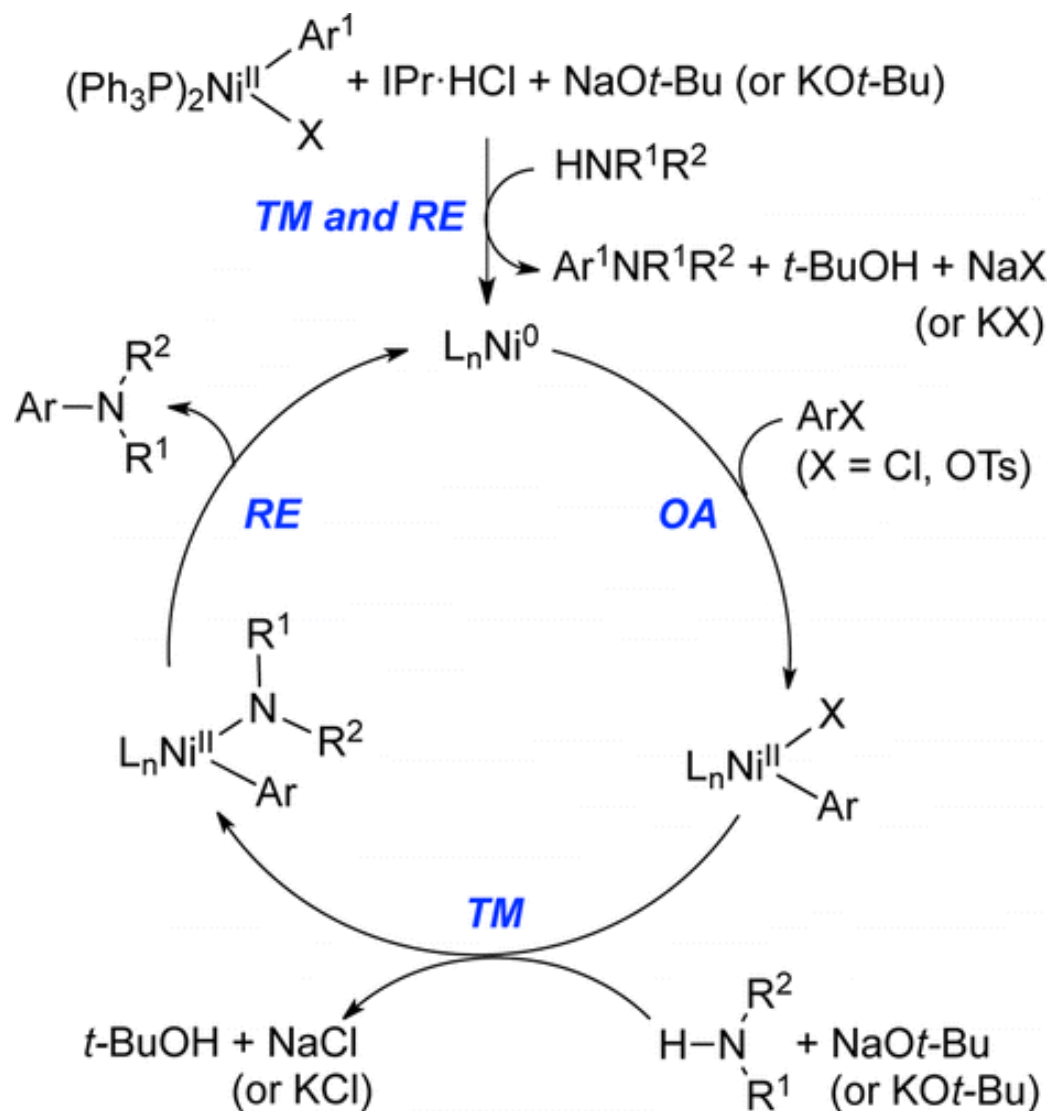
Yang, L.-M. *et al. J. Organomet. Chem.* **2011**, *696*, 2482-2484.

Yang, L.-M. *et al. J. Org. Chem.* **2008**, *73*, 1624-1627.

Yang, L.-M. *et al. Org. Lett.* **2011**, *13*, 3750-3753.

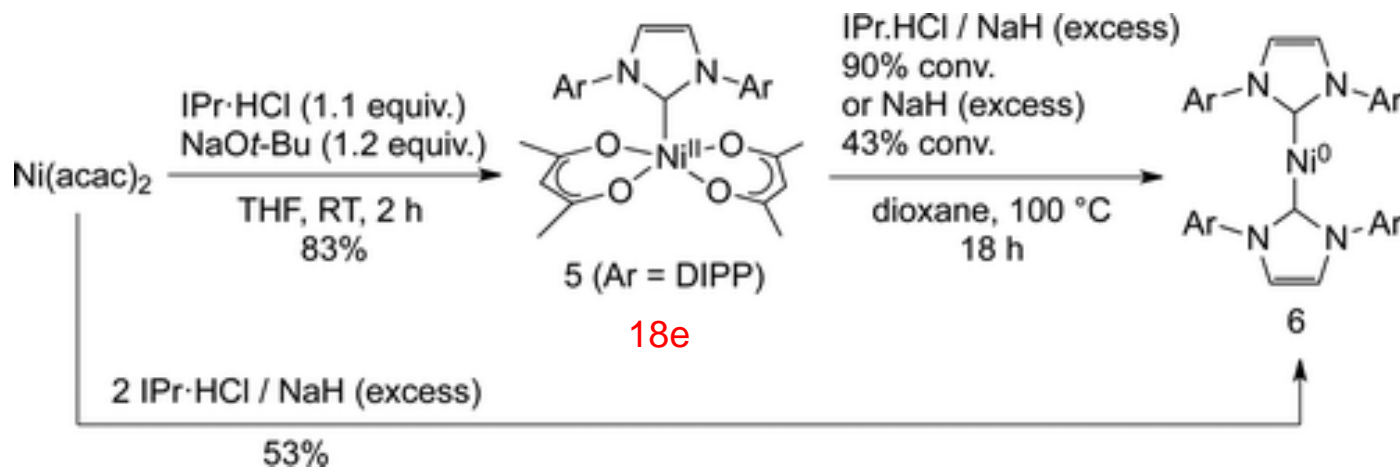
Amination of aryl halides

Proposed mechanism

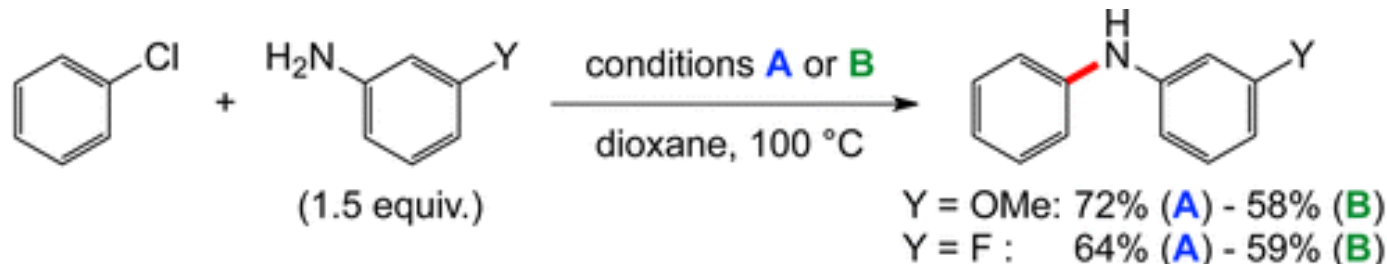


Amination of aryl halides

Synthesis of Ni(IPr)(acac)₂ (5) and Ni(IPr)₂ (6) from Ni(acac)₂



Catalytic amination of chlorobenzene under Matsubara's (A) and Fort's (B) conditions

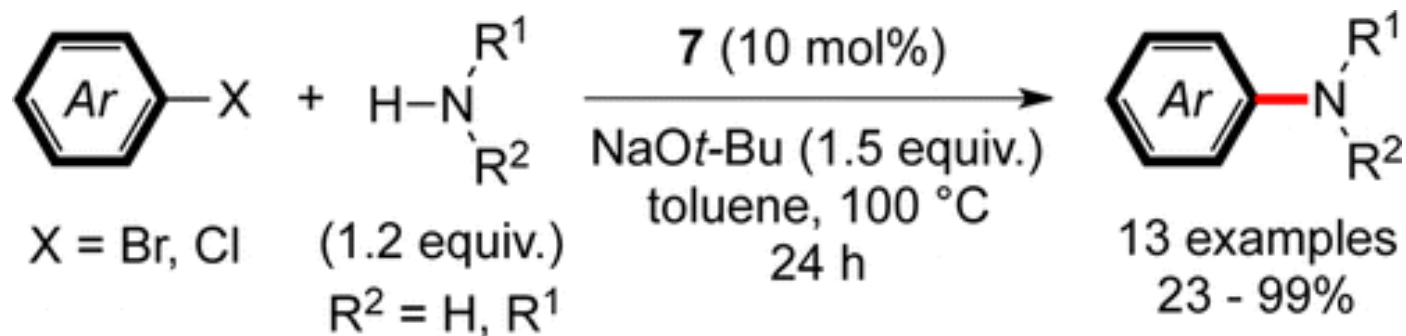


A: 6 (10 mol%), NaOt-Bu (1.8 equiv.)

B: Ni(acac)₂ (10 mol%), SIPr·HCl (20 mol%), NaH (1.6 equiv.), *t*-BuOH (1.5 equiv.)

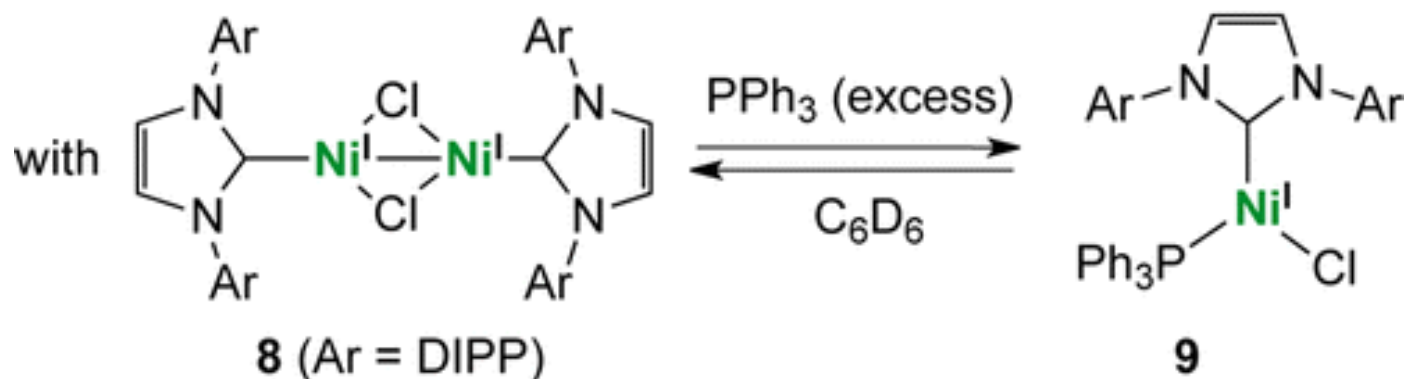
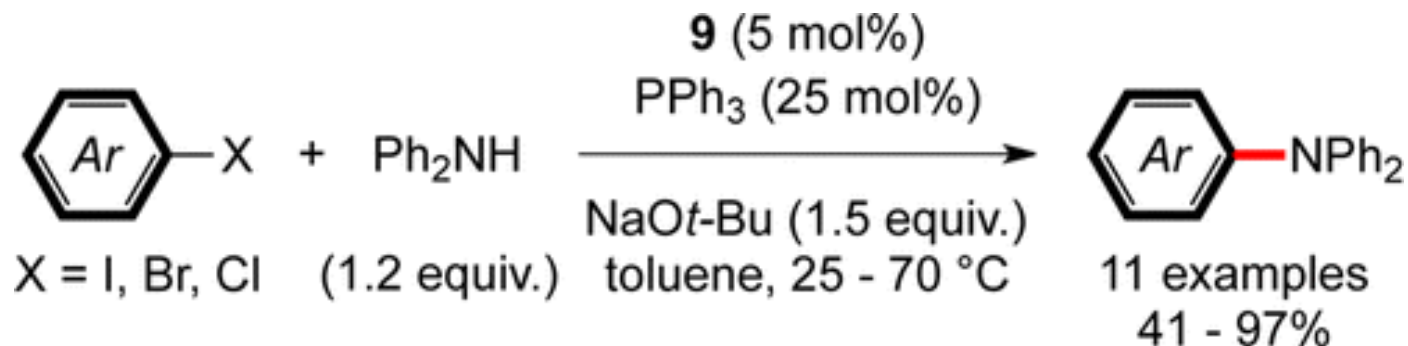
Amination of aryl halides

Amination of aryl halides catalyzed by the mixed PPh₃/IPr Nickel(II) complex **7**



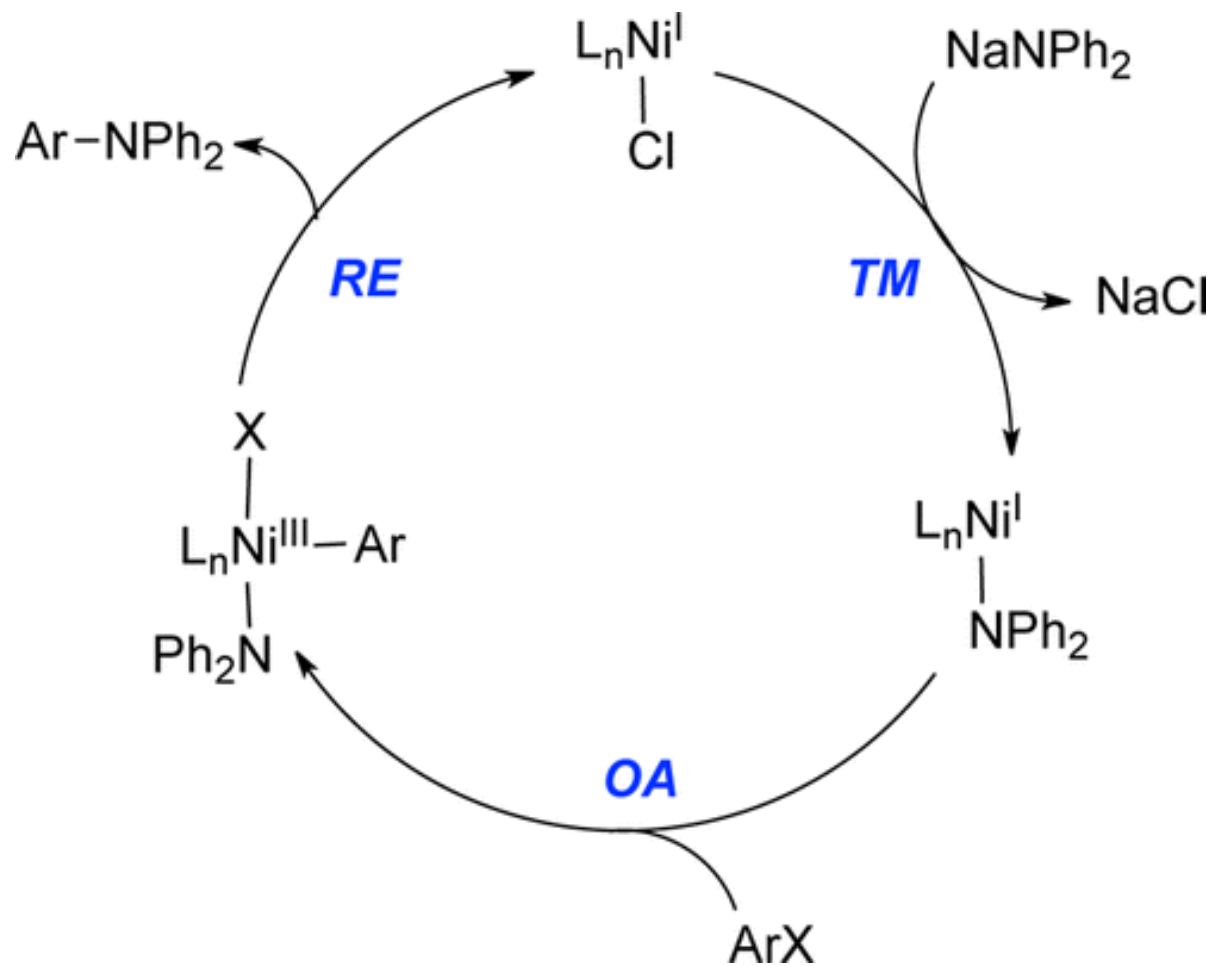
Amination of aryl halides

Diphenylamination of aryl halides catalyzed by the Y-shaped monovalent complex **9**



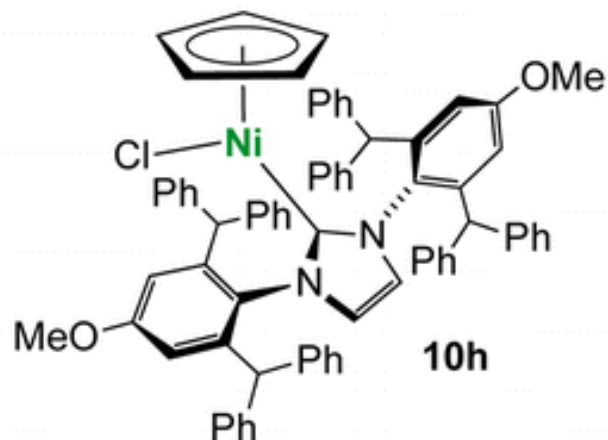
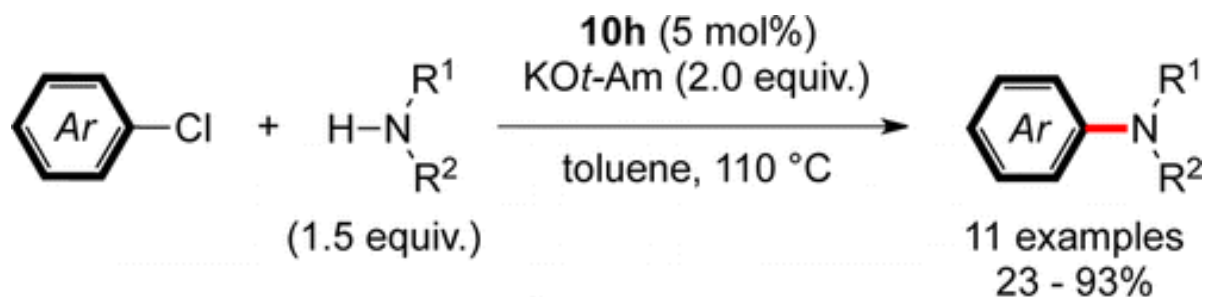
Amination of aryl halides

Proposed Ni(I)/Ni(III) Mechanism by the Nickel(I) Complex 9



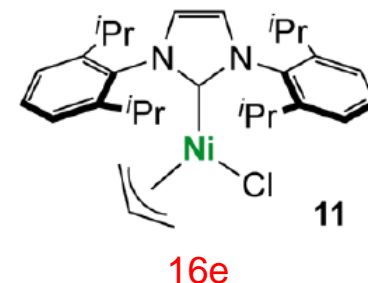
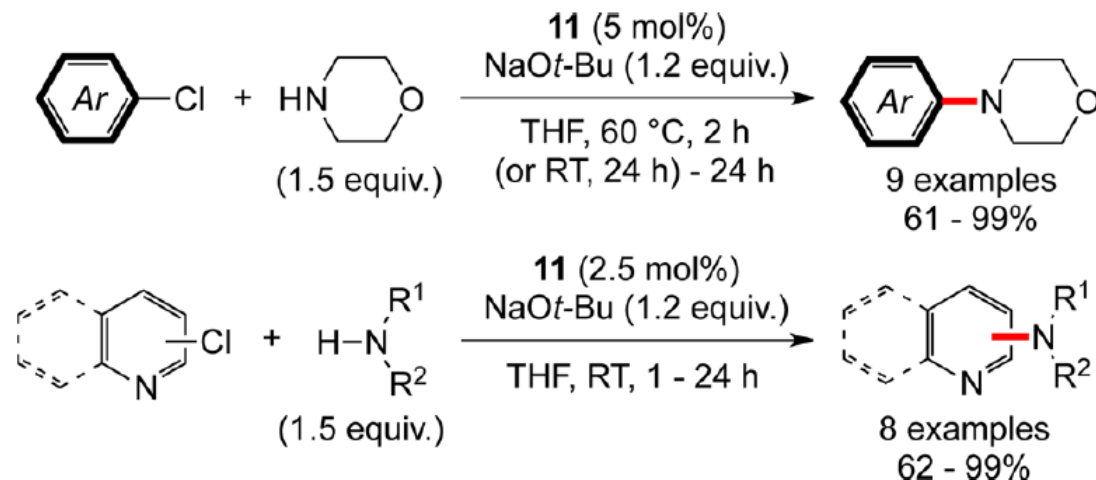
Amination of aryl halides

Amination of aryl chlorides catalyzed by complex **10h** bearing the bulky yet flexible IPr^{*OMe} ligand

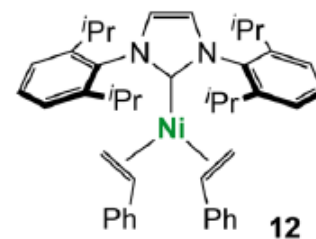
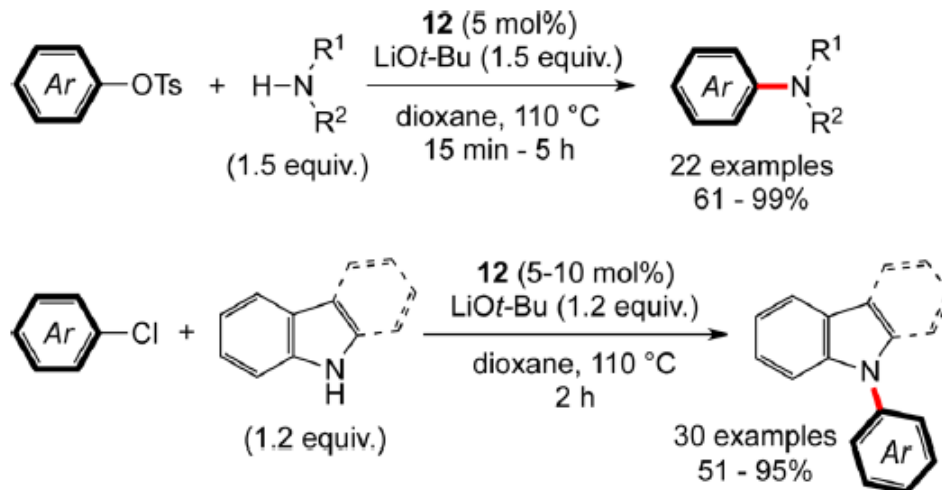


Amination of aryl halides

Amination of aryl and heteroaryl chlorides catalyzed by 11



Coupling of secondary cyclic amines and anilines with aryl tosylates and of indoles and carbazoles with (hetero)aryl chlorides catalyzed by 12



Nicasio, M. C. *et al. Adv. Synth. Catal.* **2010**, 352, 1949-1954.

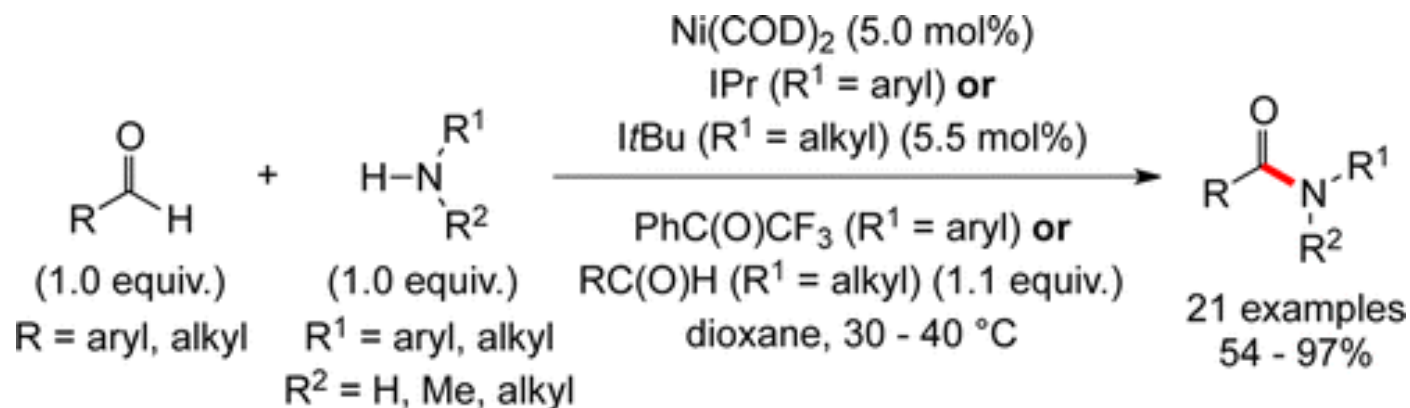
Nicasio, M. C. *et al. Organometallics.* **2012**, 31, 6312-6316.;

Nicasio, M. C. *et al. Adv. Synth. Catal.* **2015**, 357, 907-911.

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Dehydrogenative cross-coupling of aldehydes and amines



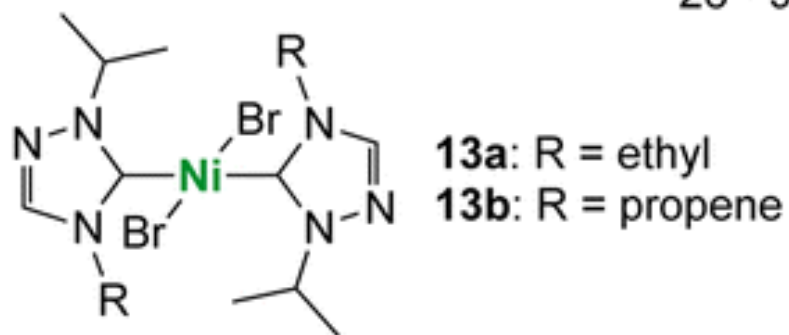
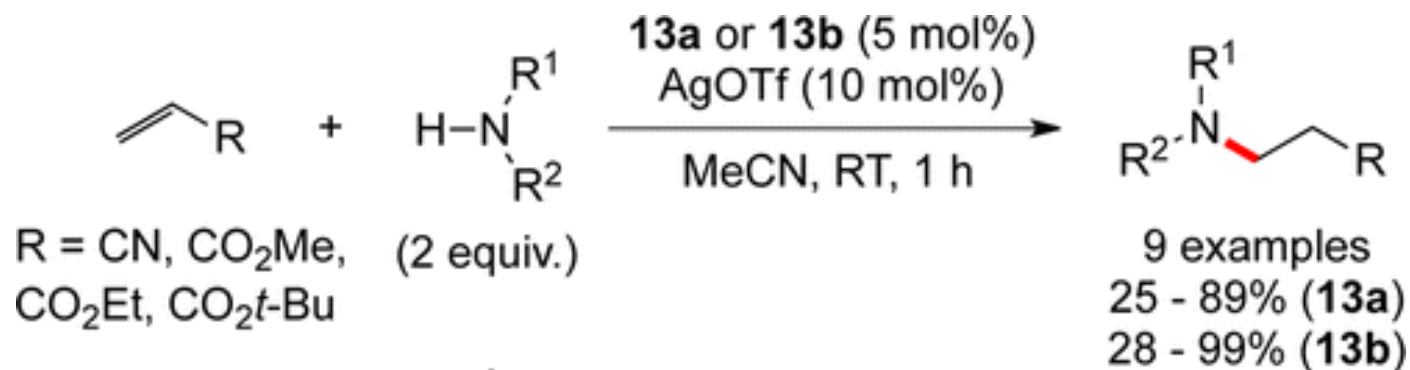
Mechanistic data support a catalytic cycle involving oxidative addition of the aldehyde C–H bond onto an electron-deficient nickel(0) center.

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Hydroamination of olefins

Hydroamination of activated olefins catalyzed by complexes **13a,b**

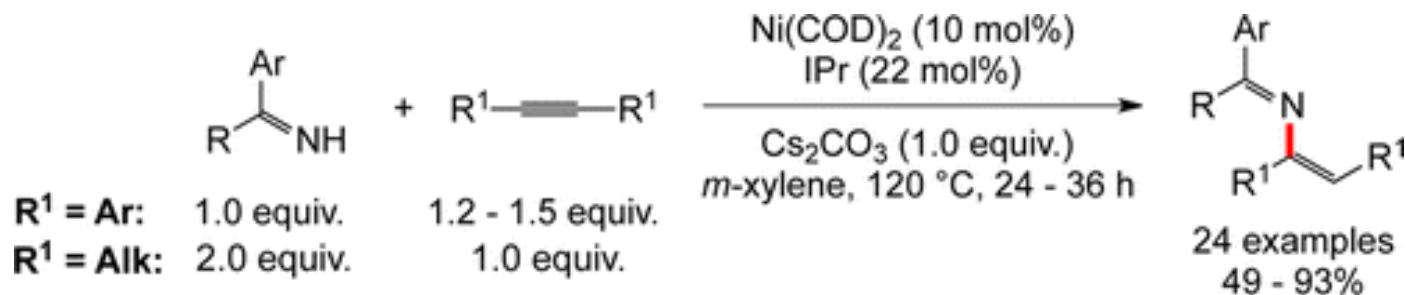


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Hydroimination of alkynes

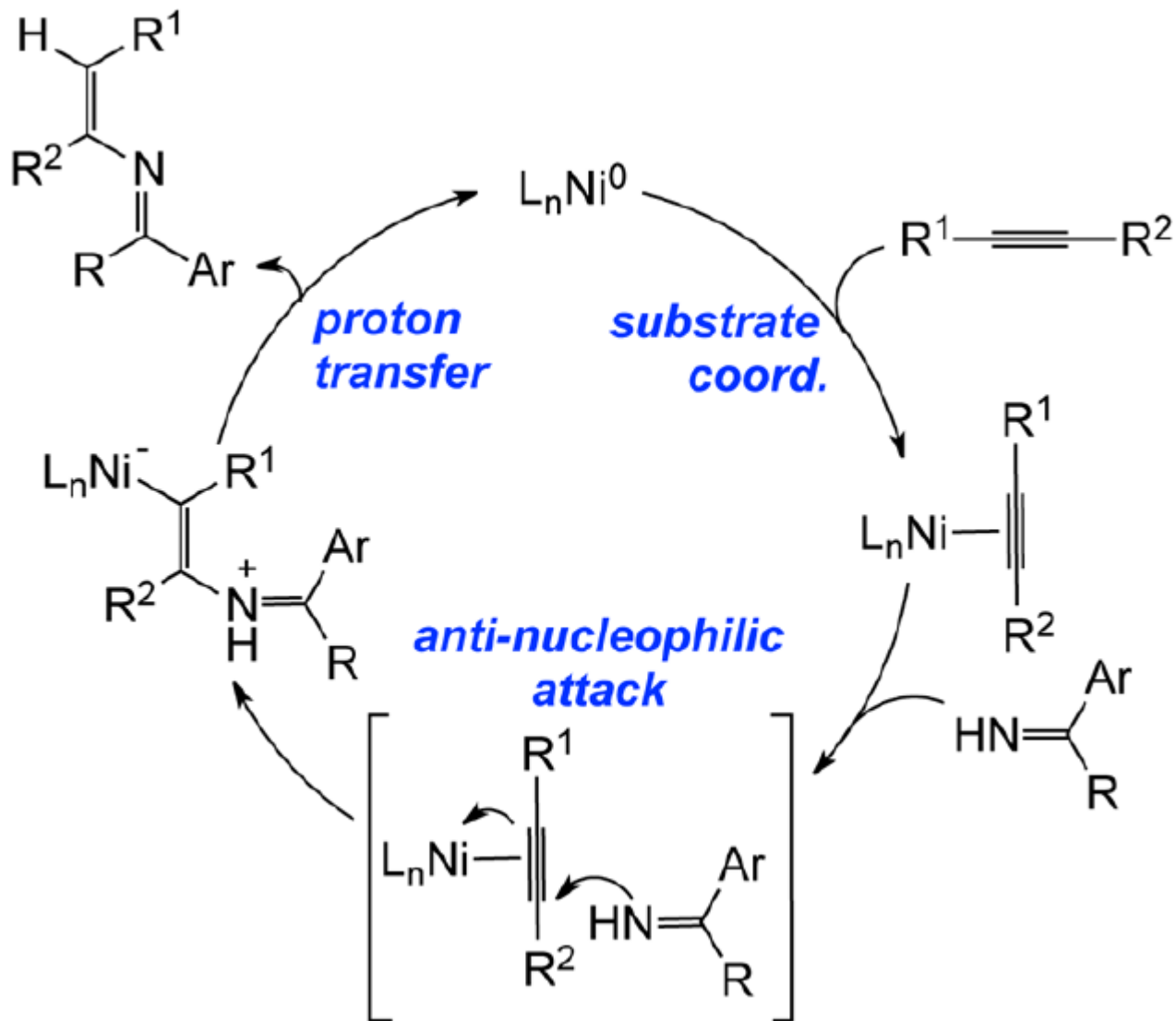
Hydroimination of Alkynes Catalyzed by a Ni(COD)₂/IPr (1/2.2) Combination



The catalytic system was reported to catalyze the formal anti addition of aromatic N-H bond.

Hydroamination of alkynes

Proposed mechanism for the hydroamination of alkynes

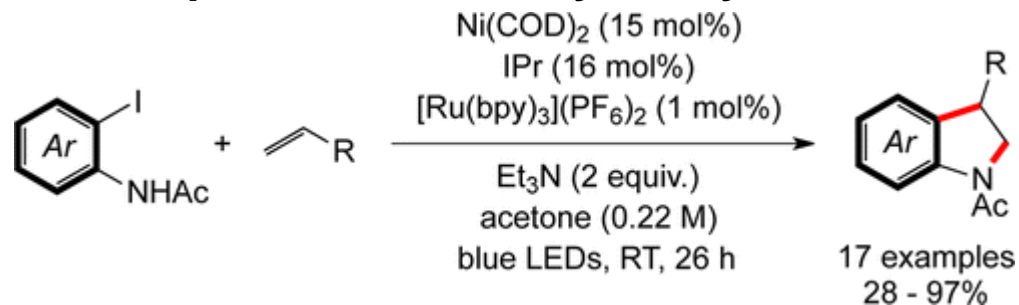


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- **One-step indoline synthesis from iodoacetanilides and alkenes**

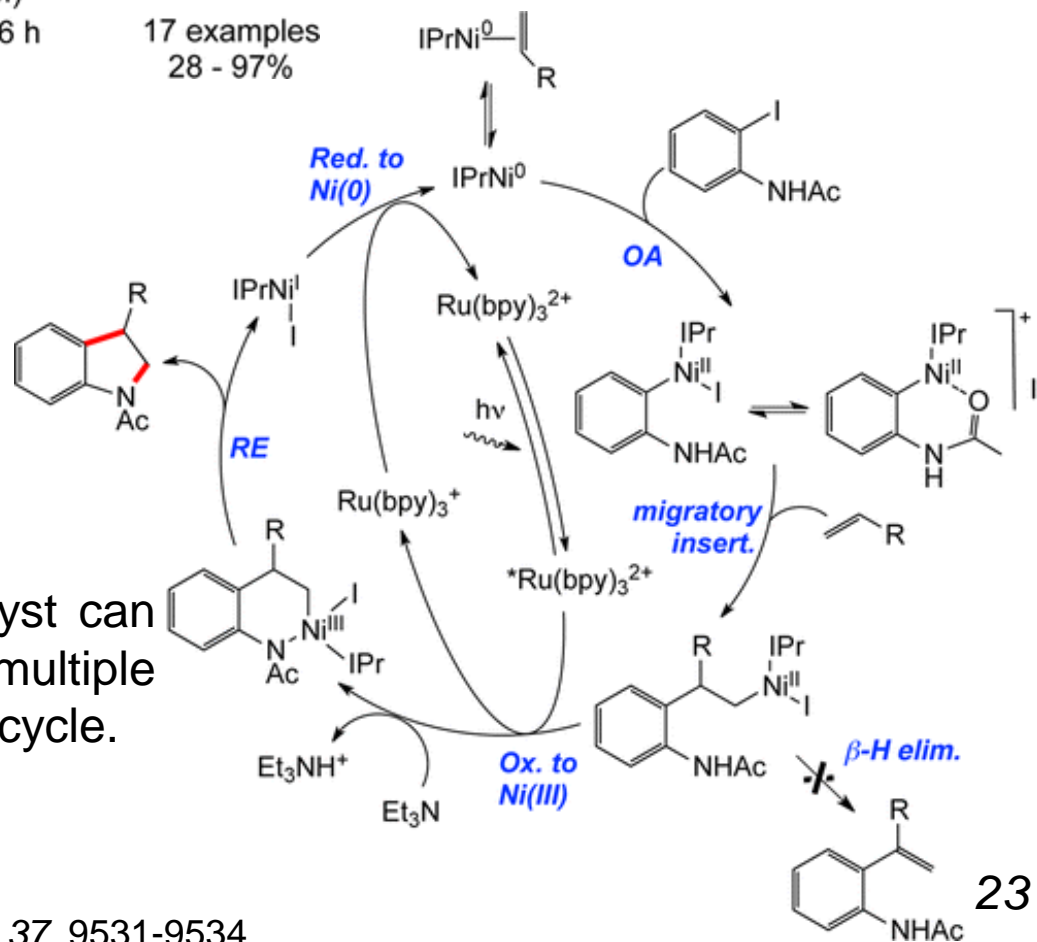
One-step indoline synthesis from iodoacetanilides and alkenes

Nickel/photoredox catalyzed synthesis of indolines



Proposed mechanism

The addition of a photoredox catalyst can allow controlled access to multiple oxidation states in a single catalytic cycle.

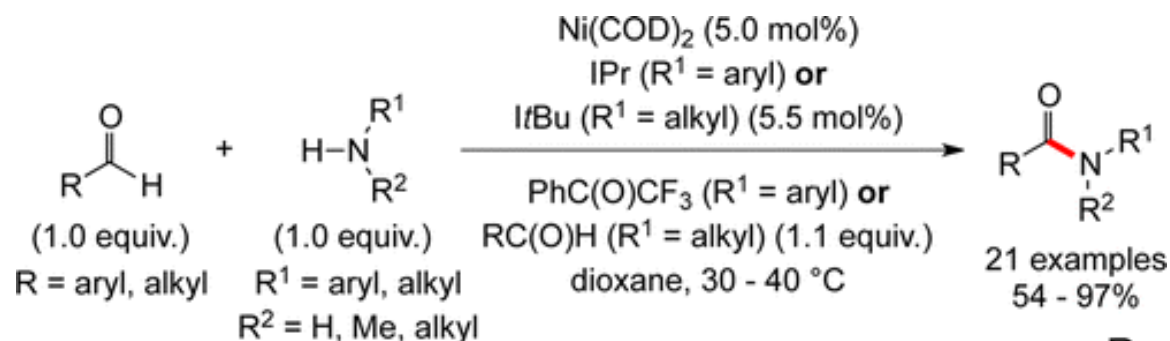




Acknowledgment

Thanks for your attention!

Dehydrogenative cross-coupling of aldehydes and amines



Proposed mechanism

