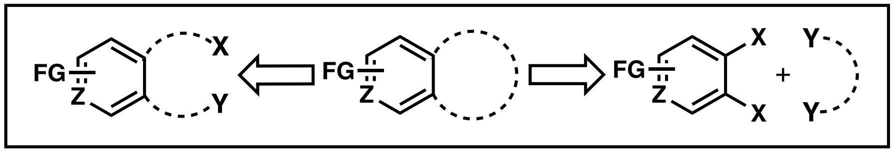
Philipp Neigenfind

Metal Mediated Intramolecular Cross-Couplings To Access Benzannulated Rings

What Are The Common Ways In Literature To Form Benzannulated Rings?



Covered in this GM:

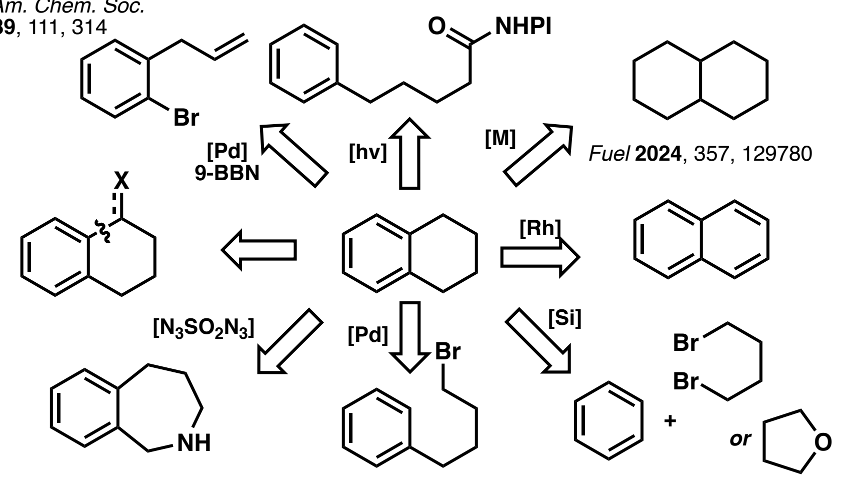
- Focus on Reductive Cross-Coupling
- Major focus on usage of Ni^{II} and Ni^{0} catalysts
- Use of Fe, Cu, Pd, Ru Catalysts
- Applications in Total Synthesis
- Hydroalken-, Acyl- & Arylations
- Exploitation of Minisci reactivity

Retrosynthetic Case Studies:

J. Am. Chem. Soc. **1989**, 111, 314

J. Org. Chem. **2019**, 84, 8360

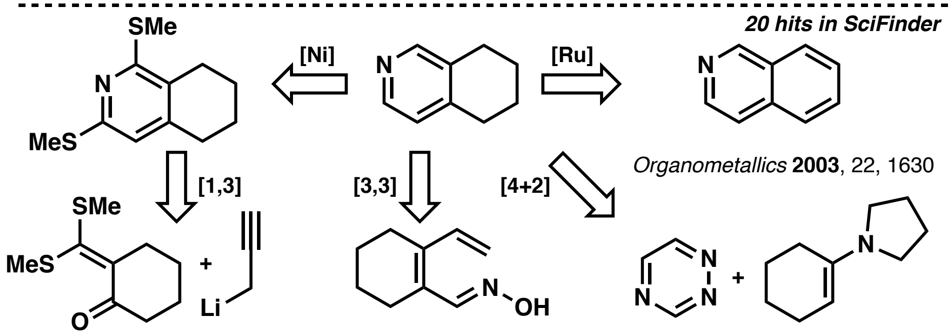
762 hits in SciFinder



Fuel **2024**, 357, 129780

ACIE **2021**, 60, 20678 *J. Am. Chem. Soc.* **2015**, 137, 3731 *ACS Catal.* **2021**, 11, 12186

20 hits in SciFinder



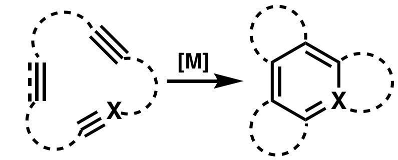
Organometallics **2003**, 22, 1630

Tetrahedron **1990**, 46, 2561 *Tet. Lett.* **1972**, 4, 316 *J. Org. Chem.* **1981**, 46, 2180

Not Covered – Honorable Mentions in Annulation Strategies:

Macrocyclizations - 2020 - Reisberg
Saturated Heterocycles - 2017 - Chu
Hetero and All-Carbon Spirocycles - See 2017 & Cherney 2012
Cycloisomerization in Synthesis - Dam 2008
„Anti-Baldwin“ Cyclizations - 2013 - Wengryniuk

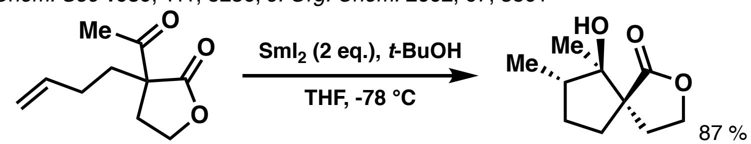
Advances in [2+2+2] Cycloaddition



Chem. Soc. Rev. **2011**, 40, 3430

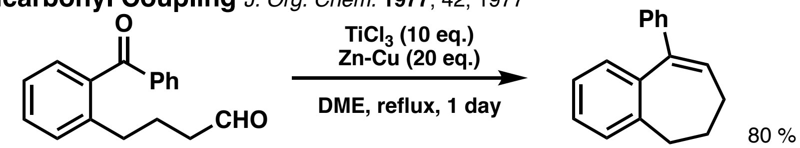
Intramolecular Reductive Coupling Reactions Promoted by SmI_2

J. Am. Chem. Soc **1989**, 111, 8236, *J. Org. Chem.* **2002**, 67, 3861



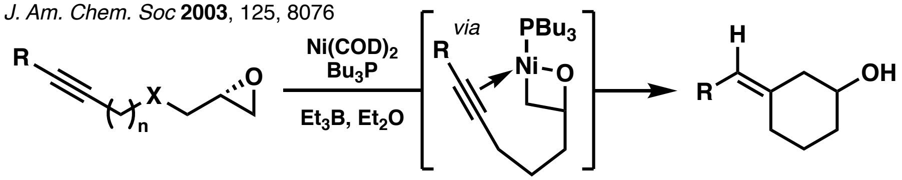
Synthesis of Cycloalkenes by Intramolecular Titanium-Induced Dicarbonyl Coupling

J. Org. Chem. **1977**, 42, 1977

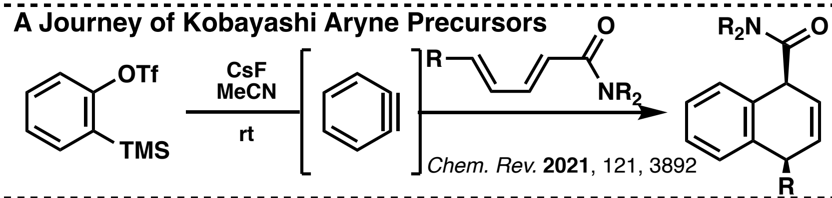


Nickel-catalyzed Reductive Coupling of Alkynes and Epoxides

J. Am. Chem. Soc **2003**, 125, 8076

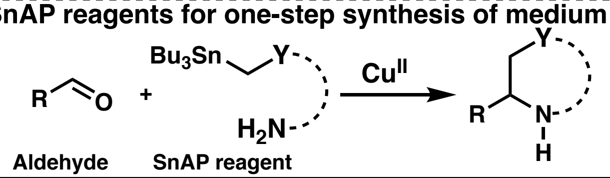


A Journey of Kobayashi Aryne Precursors



Chem. Rev. **2021**, 121, 3892

SnAP reagents for one-step synthesis of medium rings



ACIE **2013**, 52, 1705
Nat. Chem. **2014**, 6, 310
Org. Lett. **2014**, 16, 1236

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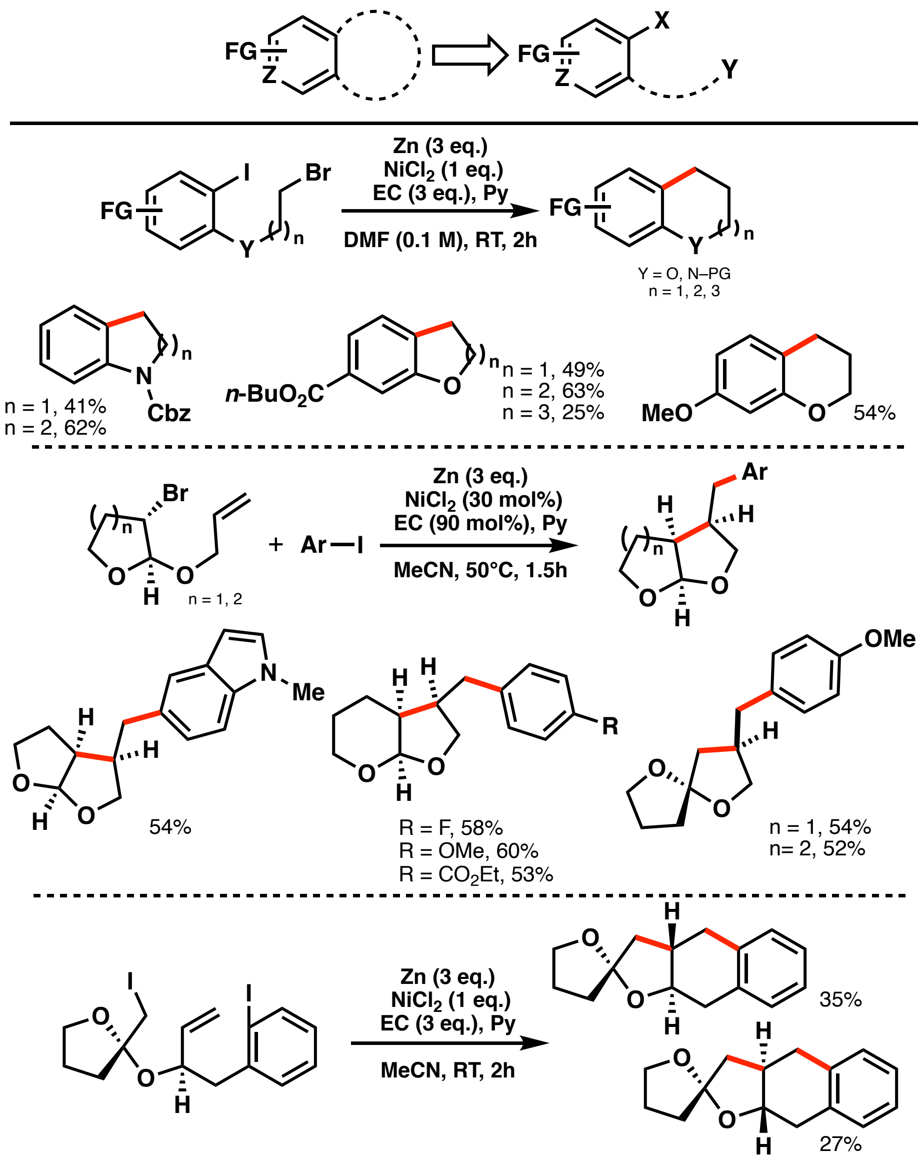
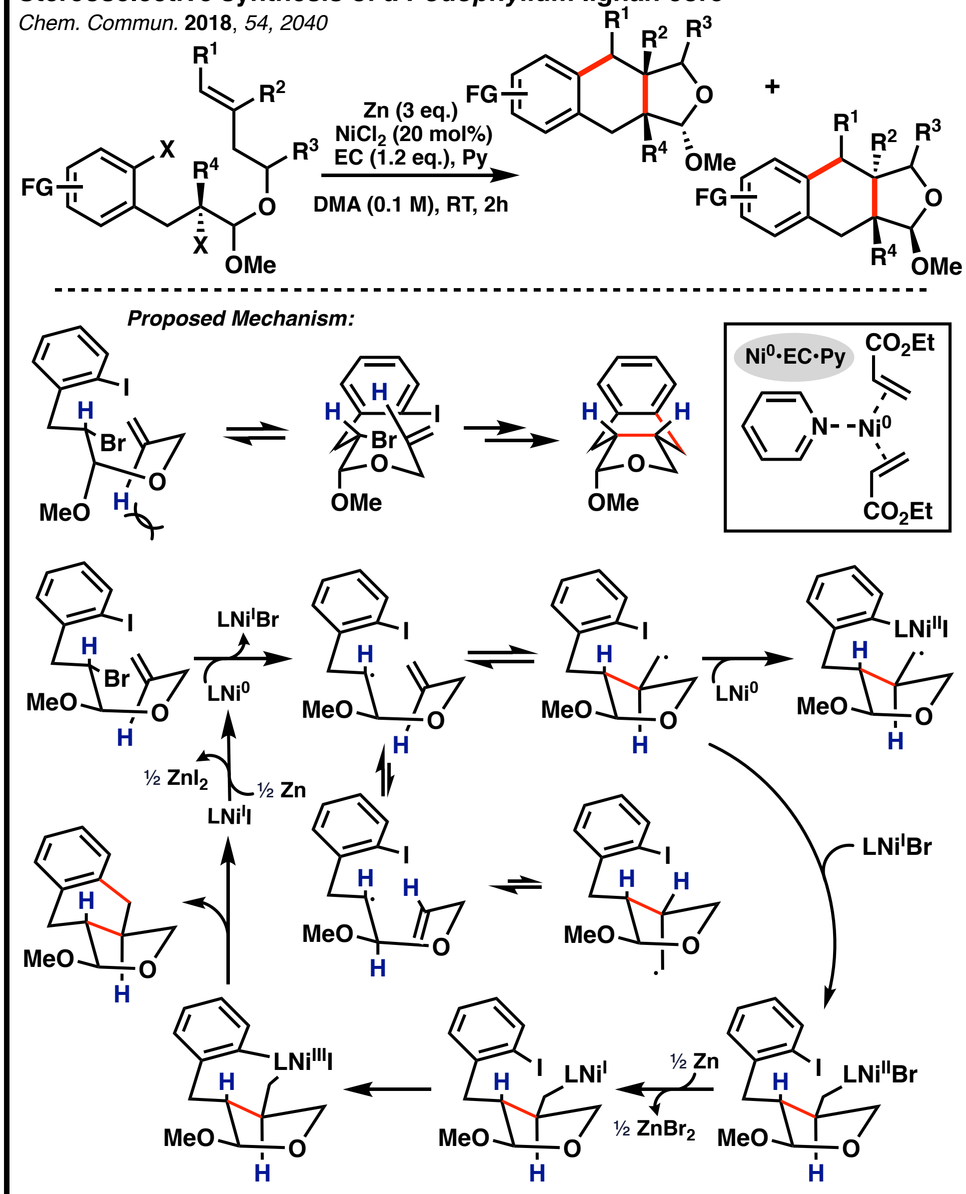
Nickel mediated Intramolecular reductive C–C coupling

Chem. Eur. J. **2012**, *18*, 6039, *J. Organomet. Chem.* **1989**, *375*, 259, *Tett. Let.* **1989**, 30, 689



Stereoselective synthesis of a *Podophyllum* lignan core

Chem. Commun. **2018**, *54, 2040*



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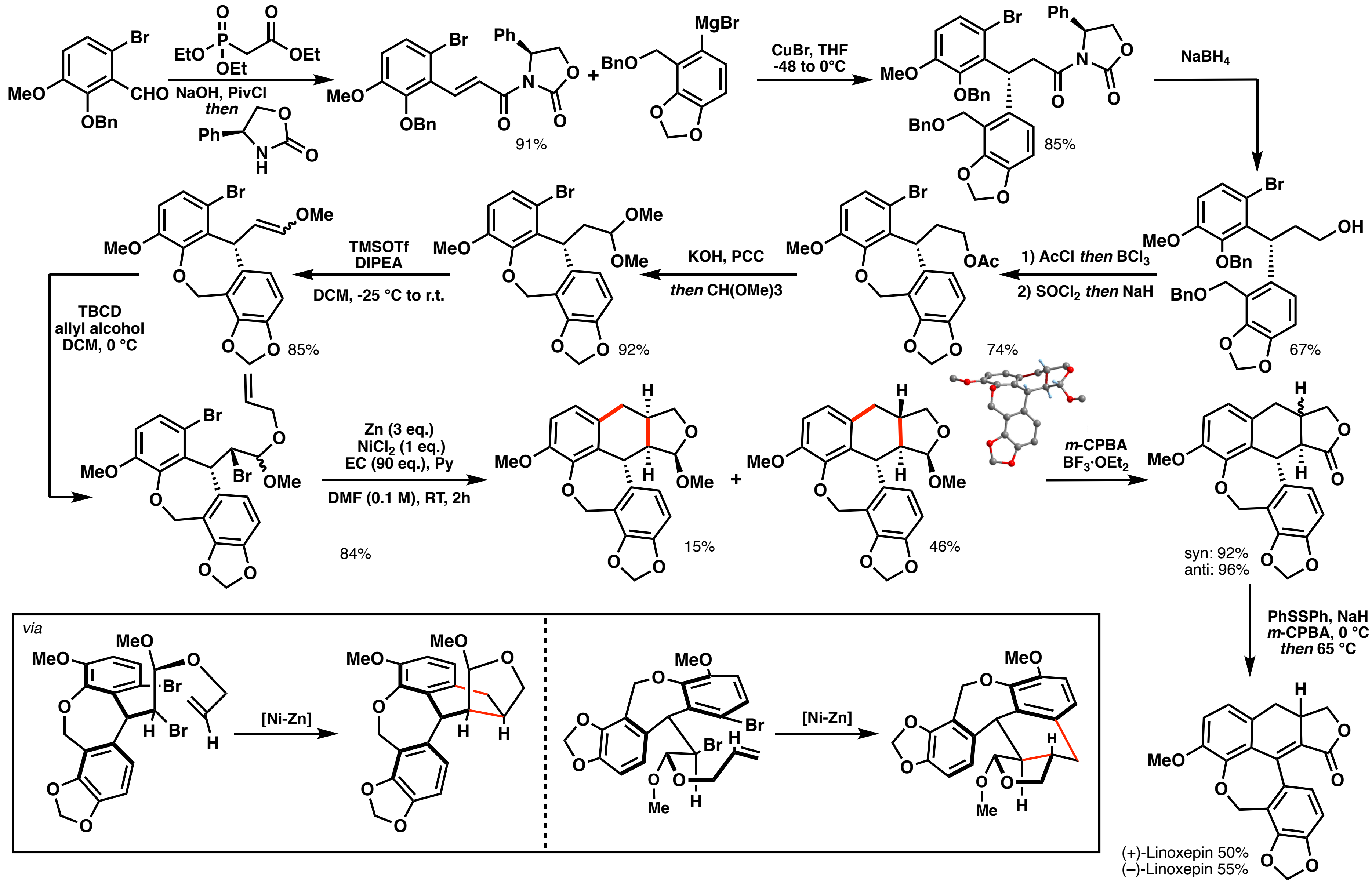
Intramolecular Nickel-Catalyzed Reductive Coupling enables enantiodivergent synthesis of Linoxepin *Chem. Commun.* **2024**, 60, 694



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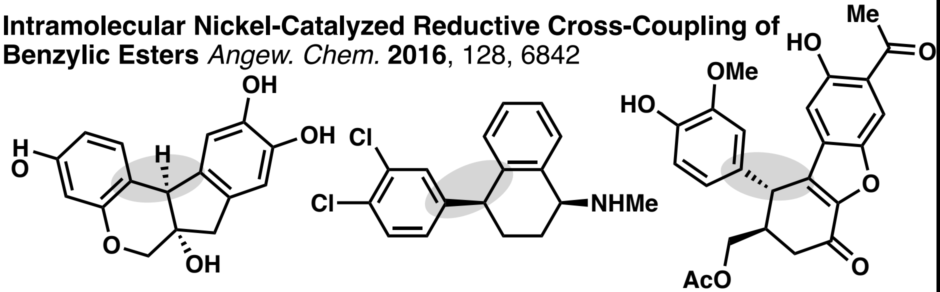
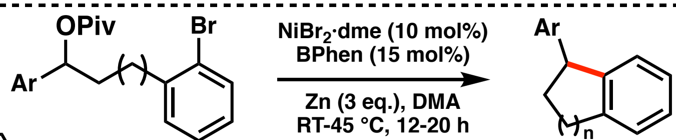
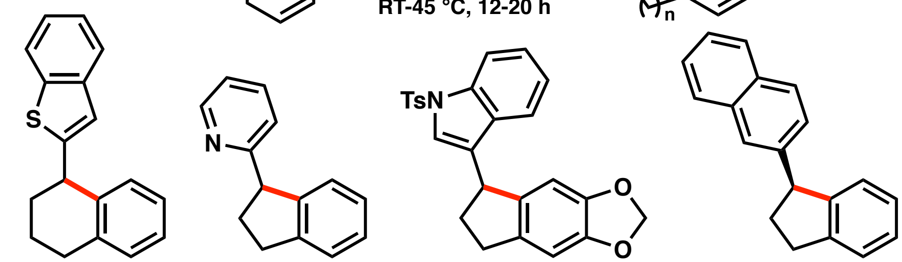
Intramolecular Nickel-Catalyzed Reductive Cross-Coupling of Benzylic Esters *Angew. Chem.* **2016**, 128, 6842



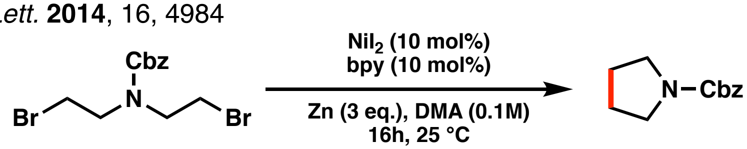
Brazilin | Sertraline (Zoloft™) | Propolisbenzofuran B

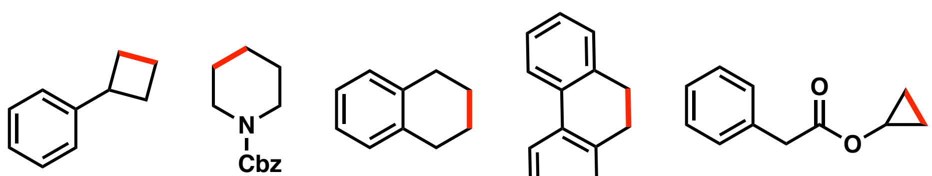




75% | 65% | 44% | 90%, 88% ee from enantiopure SM

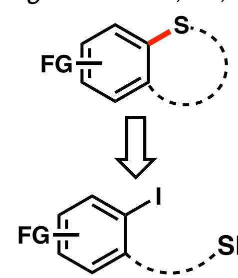
Nickel-Catalyzed Reductive Cyclization of Alkyl Dihalides
Org. Lett. **2014**, 16, 4984

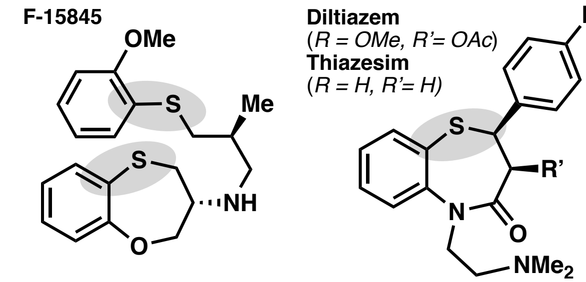


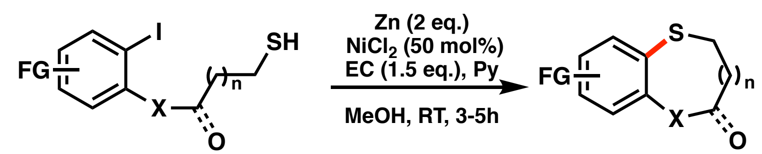


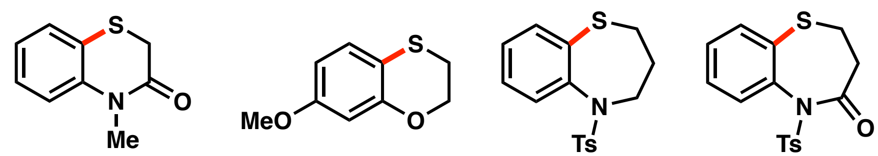
10% | 50% | 30% | 66% | ND

Nickel mediated Intramolecular C–S coupling of Thiols and Thioacetates
Org. Lett. **2013**, *15*, 550

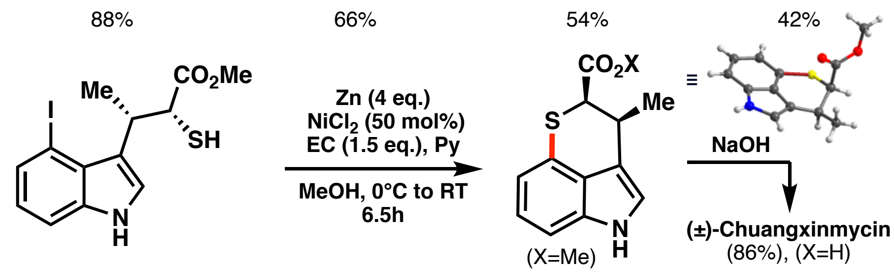




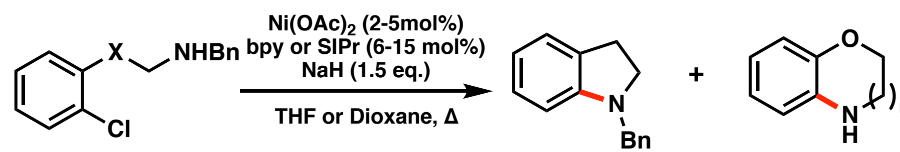




88% | 66% | 54% | 42%



Nickel-Catalyzed Intramoleuclar Amination
Org. Lett. **2003**, 13, 2311



X = CH$_2$, O

n = 1, 98%
n = 2, 96%; n = 3, 81%

n = 1, 51%
n = 2, 49%

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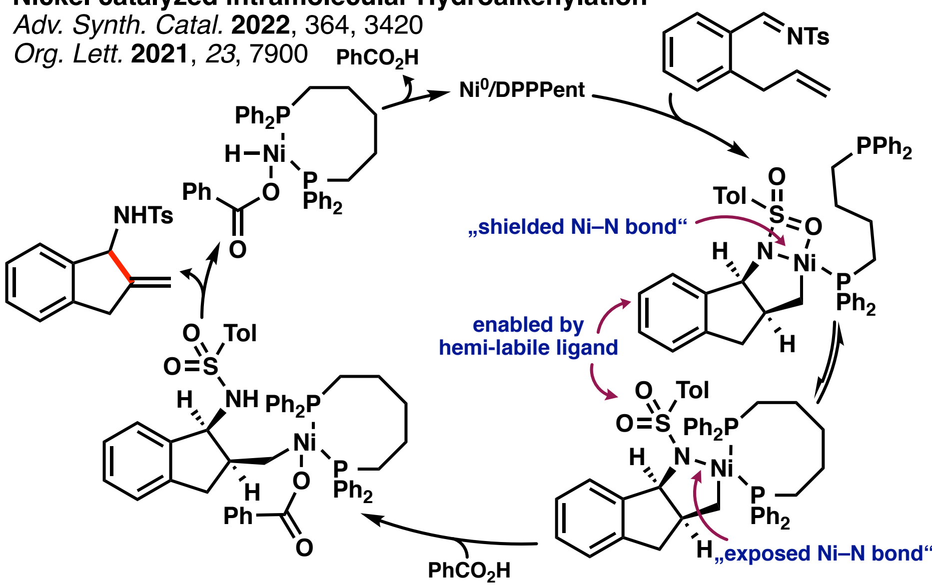
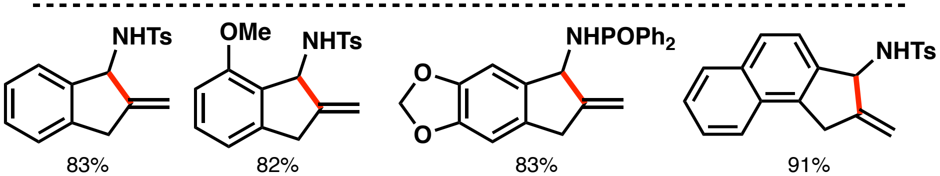
Nickel catalyzed intramolecular Hydroalkenylation

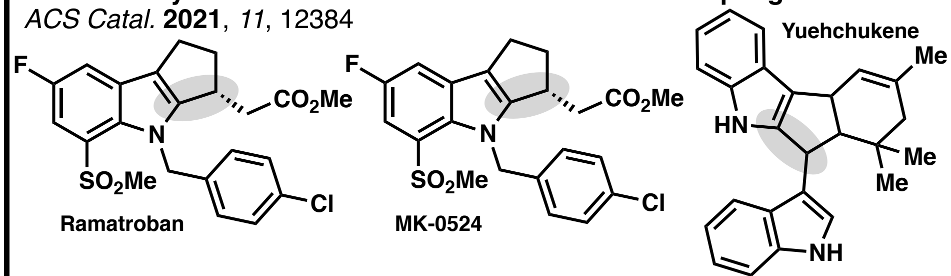
Adv. Synth. Catal. **2022**, 364, 3420
Org. Lett. **2021**, *23*, 7900

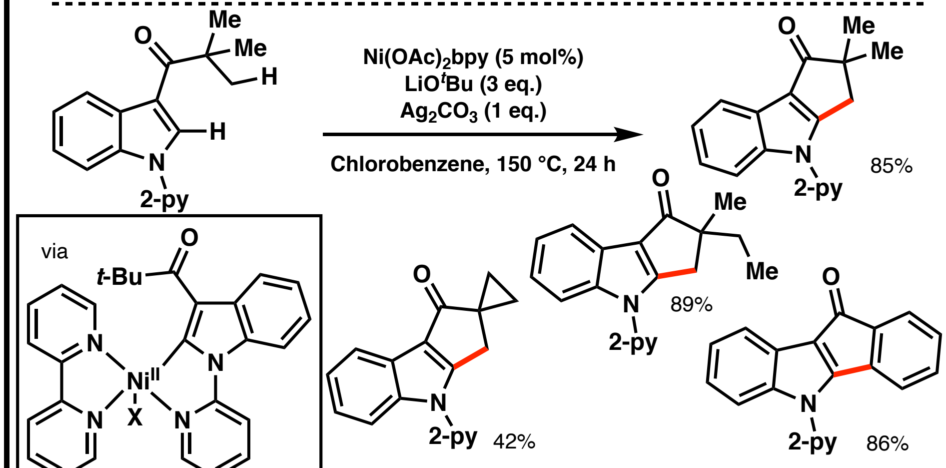




Nickel catalyzed intramolecular C–H/C–H oxidative coupling

ACS Catal. **2021**, *11*, 12384

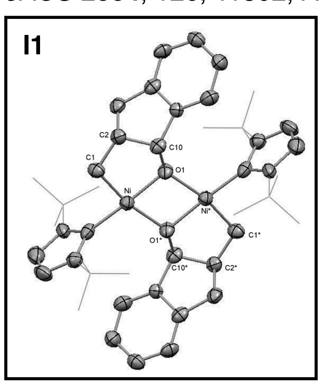


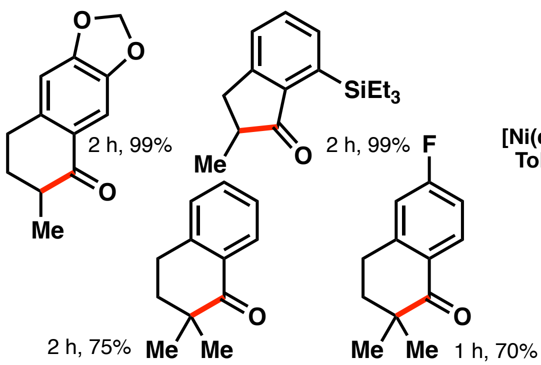


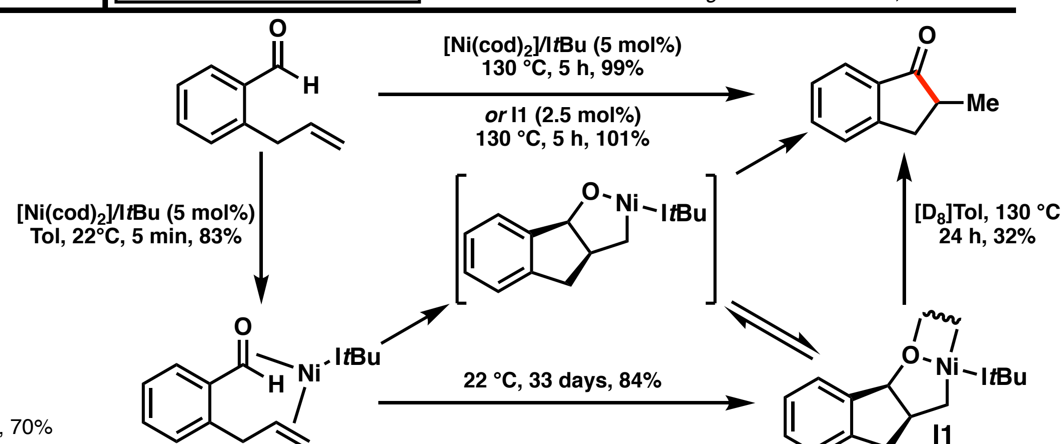
for Palladium Variant see: *Organometalllics* **2008**, 27 4841

Nickel-NHC Catalyzed Intramolecular Hydroacylation

JACS **2004**, 126, 11802, *ACIE* **2012**, 51, 10812







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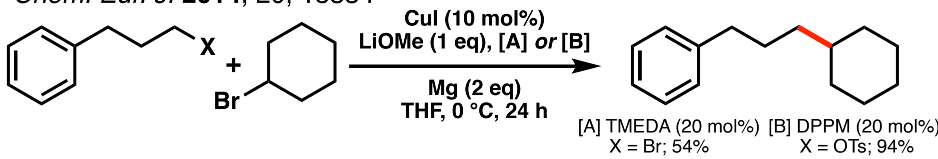
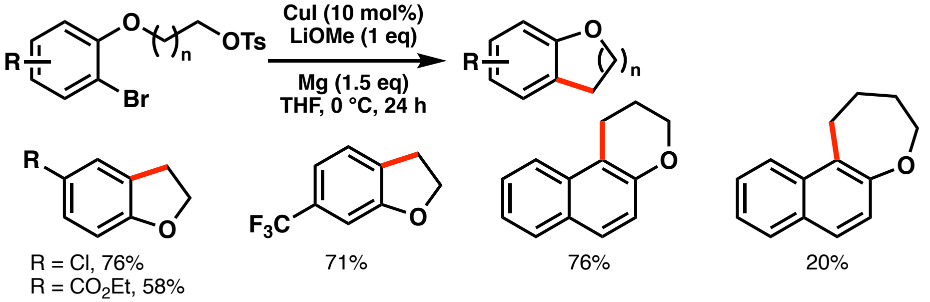
Copper-Catalyzed Inter- and Intramolecular reductive Cross-Coupling

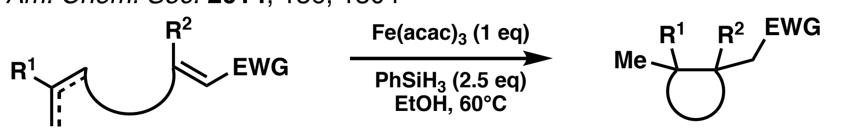
Chem. Eur. J. **2014**, 20, 15334





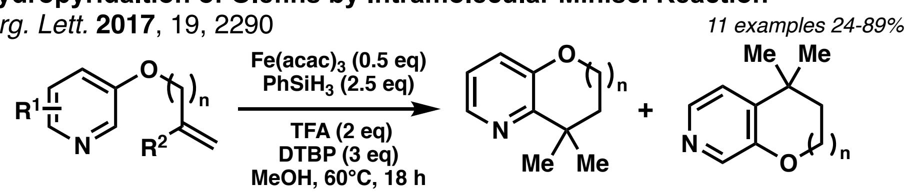
A Practical and Catalytic Reductive Olefin Coupling

J. Am. Chem. Soc. **2014**, 136, 1304



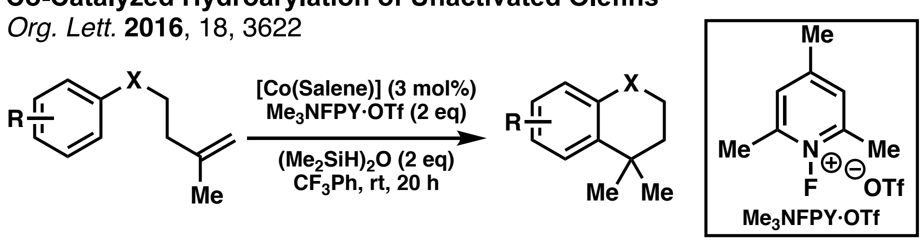
Hydropyridaltion of Olefins by Intramolecular Minisci Reaction

Org. Lett. **2017**, 19, 2290



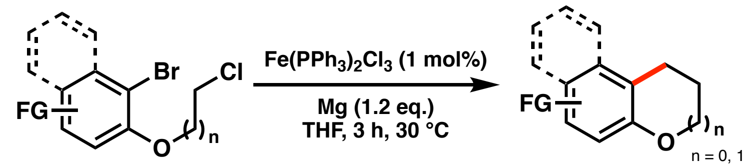
Co-Catalyzed Hydroarylation of Unactivated Olefins

Org. Lett. **2016**, 18, 3622



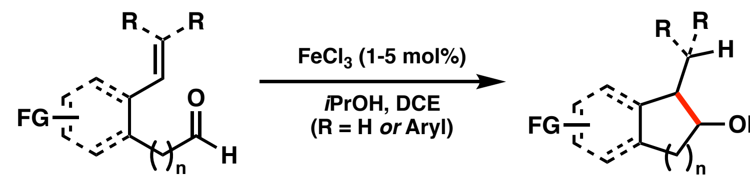
Iron-Catalyzed Inter- and Intramolecular reductive Cross-Coupling

Org. Biomol. Chem. **2016**, 14, 3314

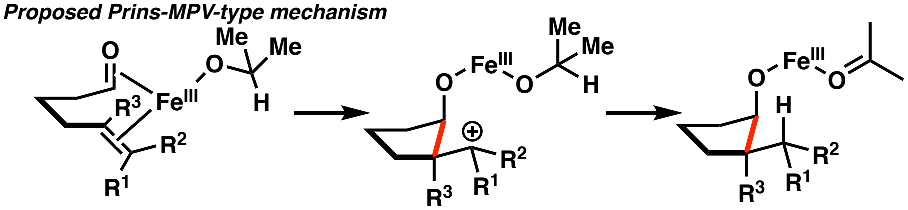


Iron-Catalyzed Intramolecular Reductive Coupling of Arylalkenes

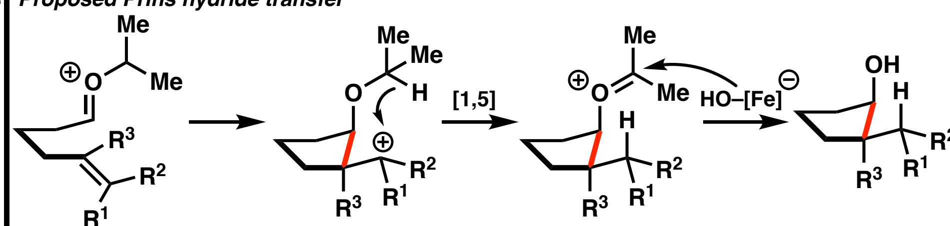
Angew. Chem. **2016**, 128, 6423, *Asian J. Org. Chem.* **2018**, 7, 554

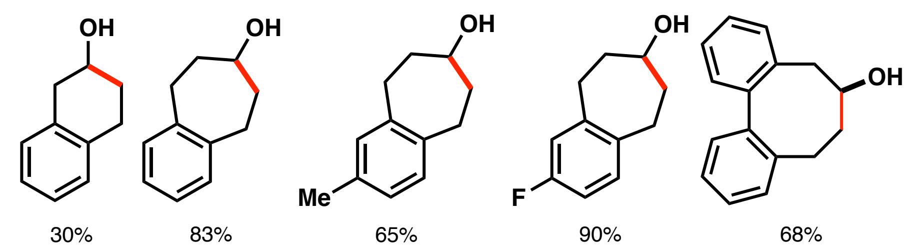


Proposed Prins-MPV-type mechanism



Proposed Prins hydride transfer





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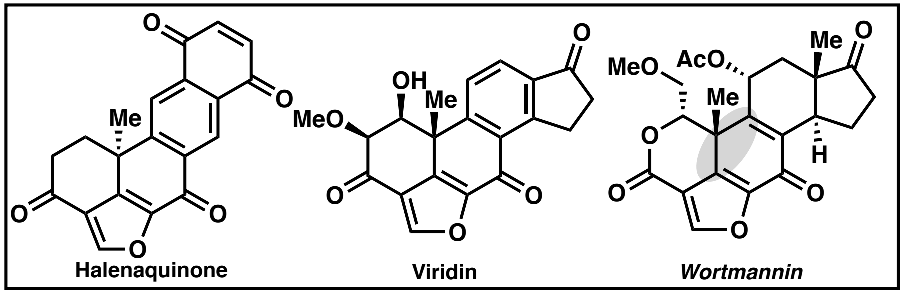
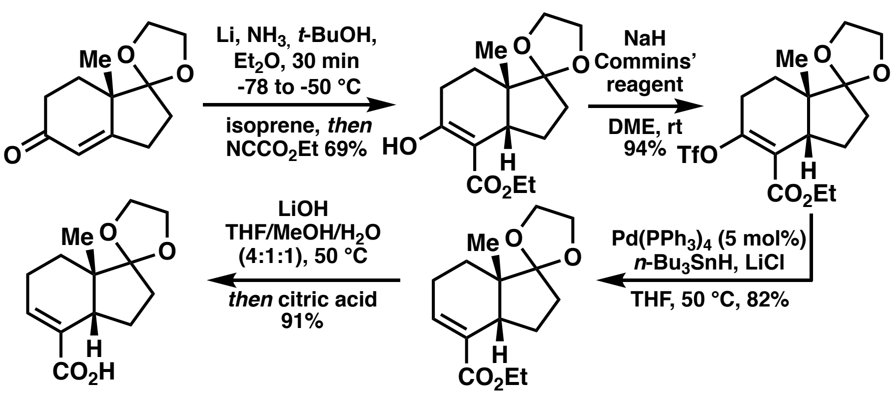
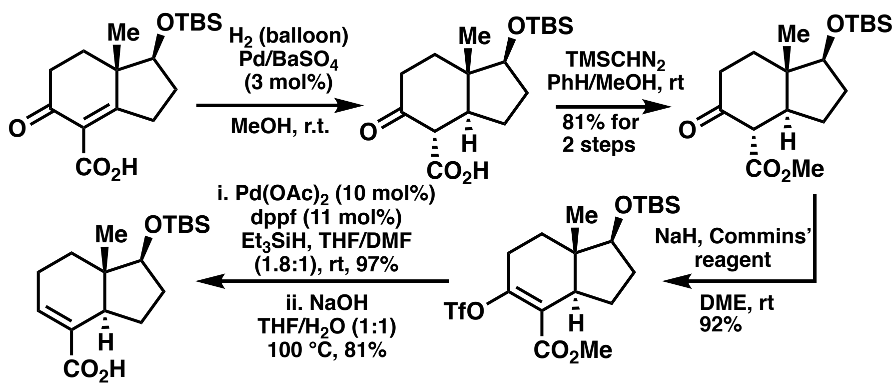
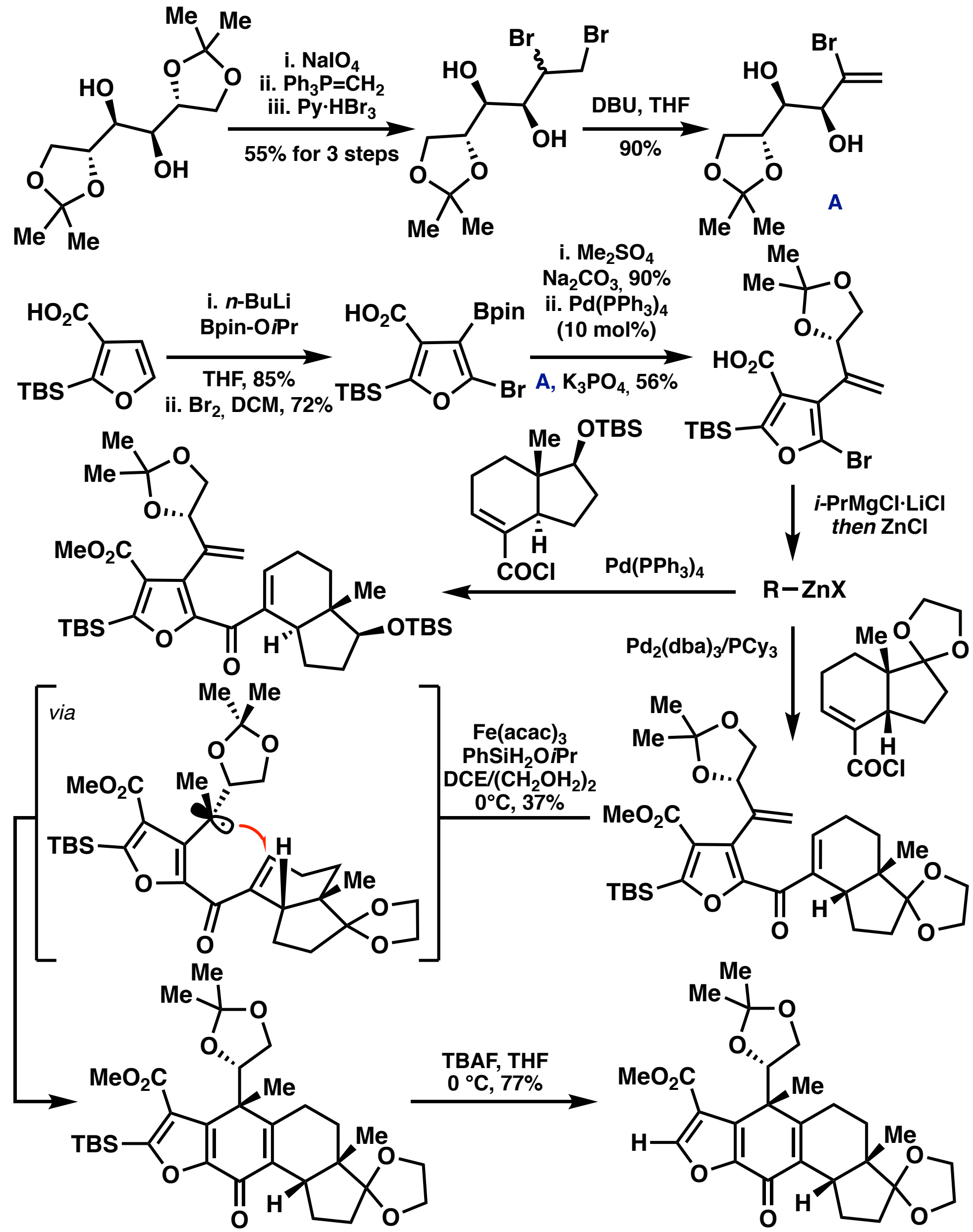
Rapid Access to Tetracyclic Core of Wortmannin via an Intramolecular Olefin Coupling *Org. Lett.* **2020**, 22, 6308









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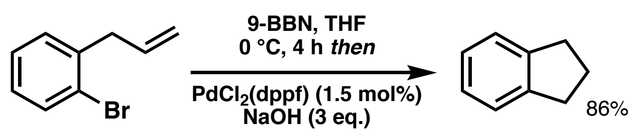
Intramolecular Palladium-Catalyzed:

Stille-Coupling: *J. Chem. Soc.* **1999**, 1235
Heck-Reaction: *Contemp. Org. Synth.* **1996**, 3, 447
C–H Arylation: *J. Am. Chem. Soc.* **2010**, 132, 10706
C–O Bond Formation: *J. Am. Chem. Soc.* **2001**, 123, 12202
C–N Bond Formation: *Tetrahedron* **1996**, 52, 7525

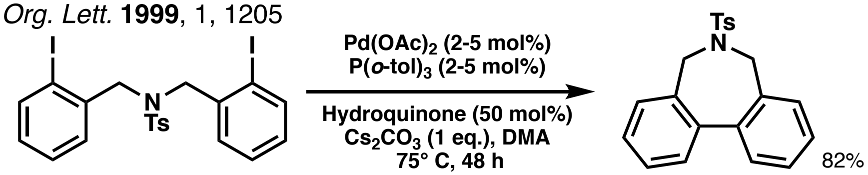
More to read in: *Chem. Rev.* **2006**, 106, 4644

Palladium Catalyzed Intramolecular Cross-Coupling of Alkyl-9-BBN Derivatives *J. Am. Chem. Soc.* **1989**, 111, 314



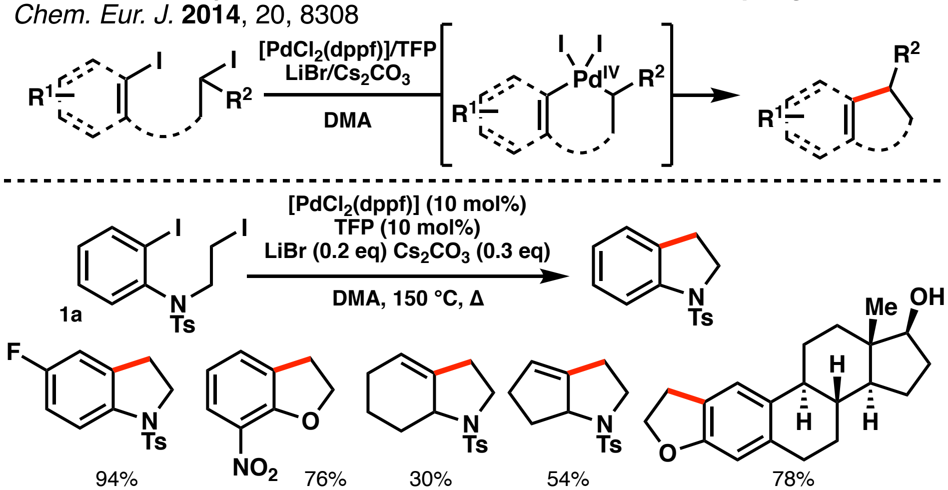
Intramolecular Palladium-Catalyzed Homocoupling of Aryl Halides

Org. Lett. **1999**, 1, 1205



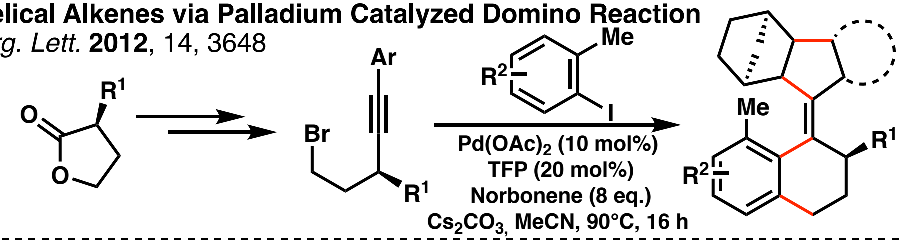
Palladium-Catalyzed Intramolecular Reductive Cross-Coupling

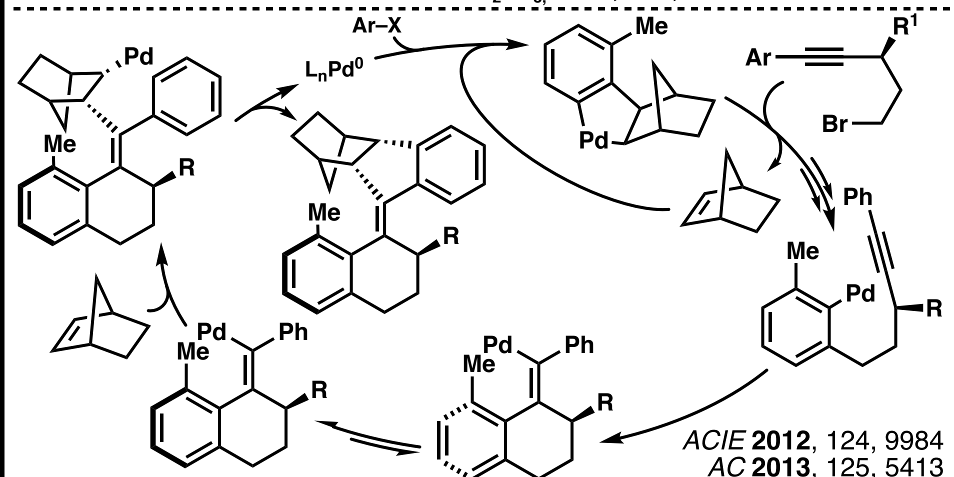
Chem. Eur. J. **2014**, 20, 8308



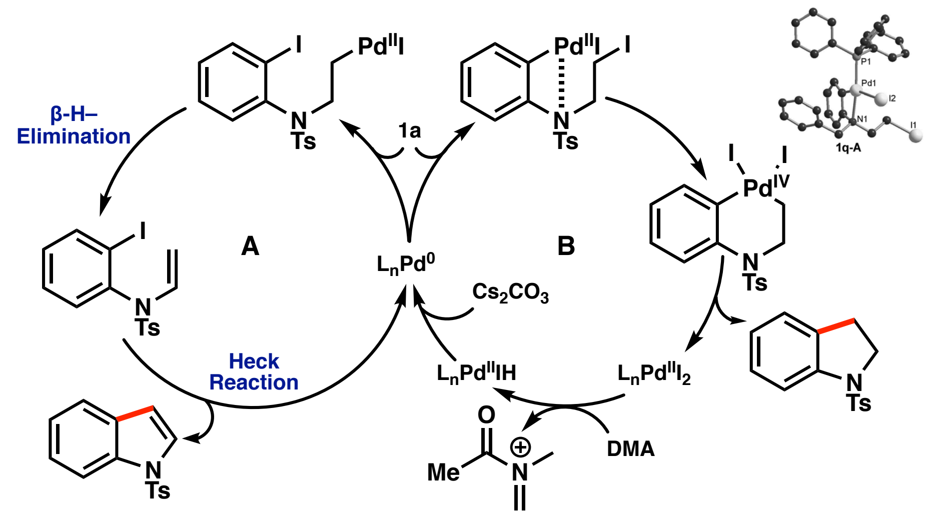
Helical Alkenes via Palladium Catalyzed Domino Reaction

Org. Lett. **2012**, 14, 3648





ACIE **2012**, 124, 9984
AC **2013**, 125, 5413



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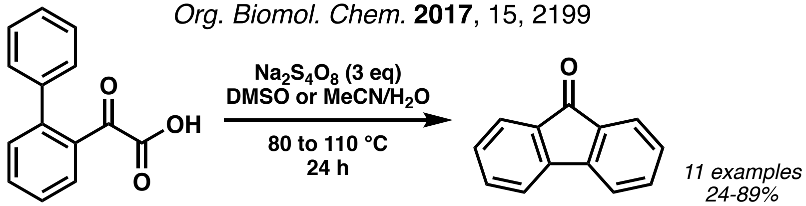
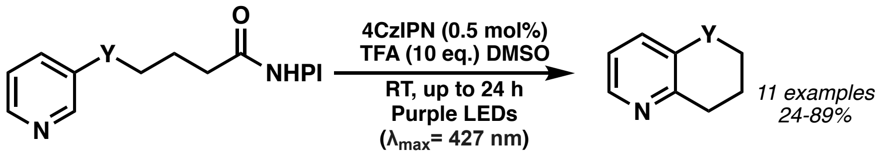
Baran Group Meeting
03/30/24

Intramolecular Minisci Acylation under Silver-Free Neutral Conditions

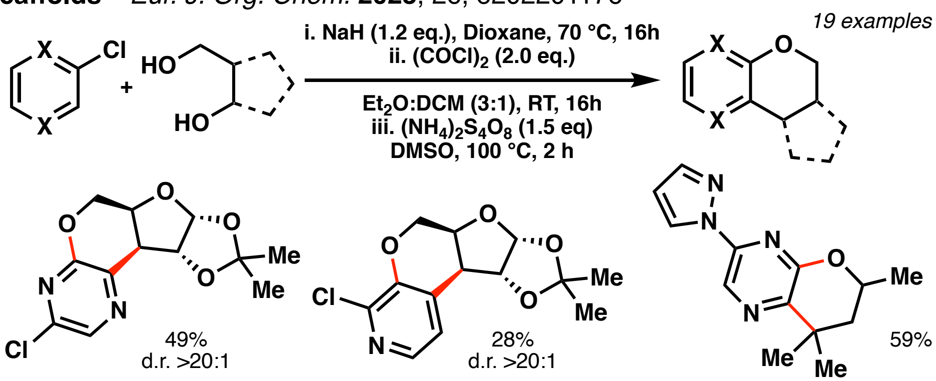
Org. Biomol. Chem. **2017**, 15, 2199



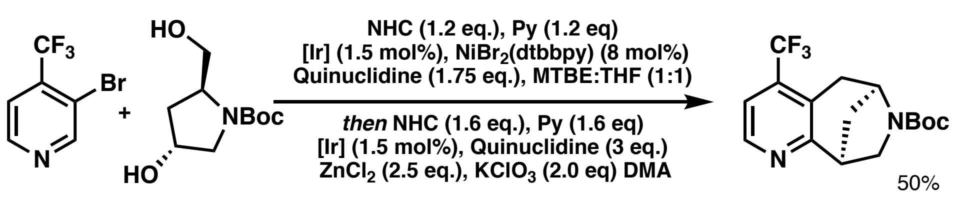
Decarboxylative Intramolecular Arene Alkylation using an Organic Photocatalyst – *J. Org. Chem.* **2019**, 84, 8360



Deoxygenative Intramolecular Minisci Reaction to Access Fused Heterocyclic Scaffolds – *Eur. J. Org. Chem.* **2023**, 26, e202201176

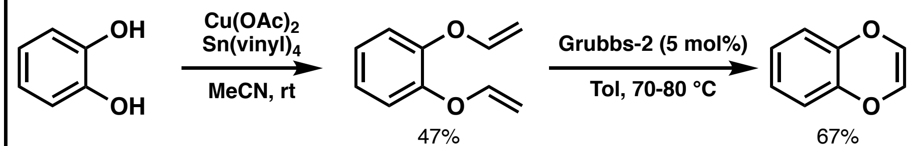


Couple-close construction of polycyclic rings from diradicals – *Nature* 2024



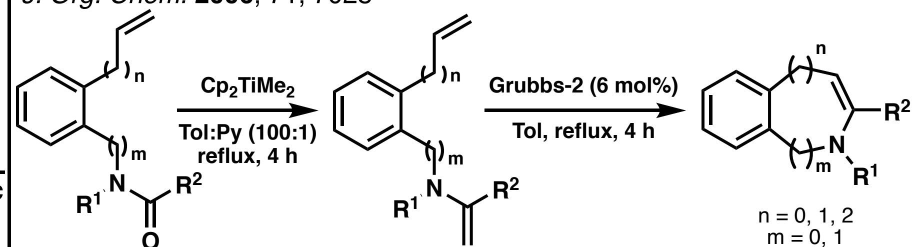
Sequential Isomerization and Ring-Closing Metathesis

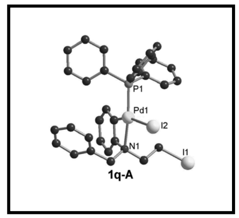
Tet. Lett. **2003**, 44, 6483

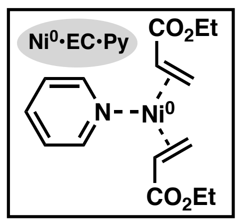


N-Acylamide Methylenation-Enamide Ring-Closing Metathesis

J. Org. Chem. **2006**, 71, 7028







Conclusions - Lessons Learned - Open Questions:

- Wide array of Strategies to form Benzannulated Rings involving various metals
- Most Processes Mediated by Nickel are proposed to involve Ni^0
- Many Methods only mediocrely Strategic due to laborious Starting Material Synthesis
- How to Overcome Simple Radical Reactivity (e.g. Minisci) through directed Cross-Coupling Strategy?
- Utilization of Decarboxylation possible?