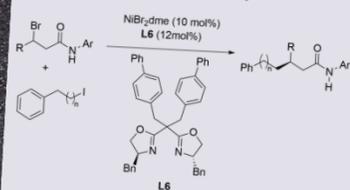


Homogeneous Catalysis Papers of the Month

July 2023

New Methodology

Enantioselective nickel catalysis

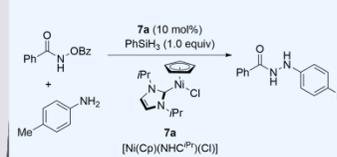


Challenge: Ni-catalyzed alkyl cross-coupling generally requires pregenerating an organometallic reagent.

Solution: Ni(Br₂dme)-catalyzed reductive alkyl-alkyl cross-coupling uses only alkyl electrophiles and produces enantioselective Csp³-Csp³ bonds with a range of functional groups.

Zhao and Shu, *Science Advances* **2023**, doi: 10.1126/sciadv.adg9898

Nickel-catalyzed hydrazide synthesis

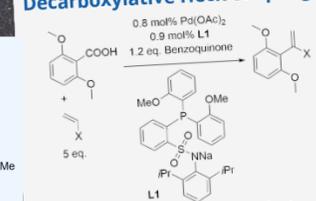


Challenge: Synthesis of N-N compounds generally requires a series of protection/deprotection steps and derivatization.

Solution: An air-stable Ni(II) half-sandwich precatalyst allows coupling of a broad range of aryl and aliphatic amines to give hydrazides with 81% yield.

Barbor et al., *J. Am. Chem. Soc.* **2023**, doi: 10.1021/jacs.3c04834

Decarboxylative Heck coupling

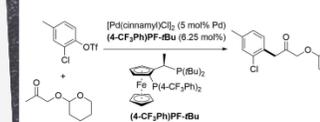


Challenge: Few decarboxylative Heck-type methods are available to form branched olefin products.

Solution: Pd(OAc)₂ and a bulky phosphine-sulfonamido ligand produced 1,1-disubstituted olefins with high selectivity, and a less bulky ligand produced inverse regioselectivity.

Jenthra et al., *ACS Catal.* **2023**, doi: 10.1021/acscatal.3c02224

Pd-catalyzed arylation

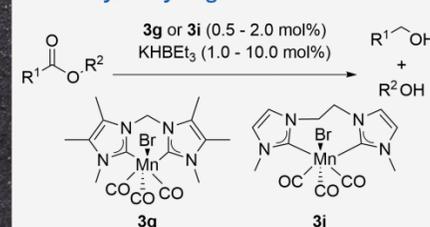


Challenge: Selective mono- α -arylation can be impeded by unwanted Aldol or Claisen reactions and can require strong oxidizing conditions or thiol reagents.

Solution: [Pd(cinnamyl)Cl]₂ and the JosiPhos ligands PhPF-tBu or (4-CF₃Ph)PF-tBu provide terminal-selective mono- α -arylation of O-protected hydroxyacetone under more mild conditions.

MaMillan et al., *Adv. Synth. Catal.* **2023**, doi: 10.1002/adsc.202300566

Mn-catalyzed hydrogenation



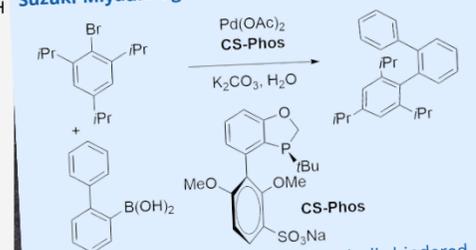
Challenge: Traditional ester reduction often requires either stoichiometric amounts of metal hydrides or harsh reaction conditions with H₂ gas.

Solution: A series of bidentate bis(NHC) Mn complexes allow efficient hydrogenation of carboxylic acid esters at low temperatures and low catalyst loadings.

Both et al., *Angew. Chem. Int. Ed.* **2023**, doi: 10.1002/anie.202307987

New Catalysts

Suzuki-Miyaura ligands

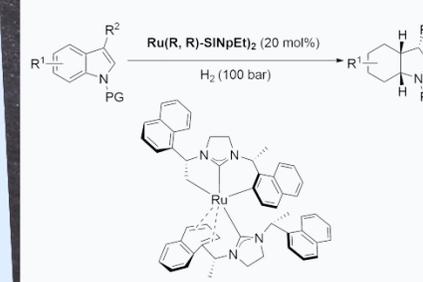


Challenge: C-C cross-couplings of sterically hindered substrates in aqueous media are limited.

Solution: Benzooxophosphole-based water-soluble ligands CS-Phos and Mono-CSPhos facilitate hindered C-C couplings with a catalyst load of 0.1 mol% Pd(OAc)₂.

Shada et al., *Org. Lett.* **2023**, DOI: 10.1021/acs.orglett.3c01663

Ru-catalyzed hydrogenation

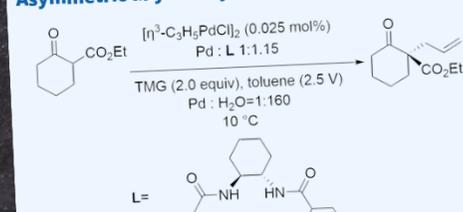


Challenge: Asymmetric hydrogenation of arenes has been difficult due to the lack of enantioselective catalysts.

Solution: A Ru-NHC-catalyzed asymmetric hydrogenation of indoles and benzofurans resulted in good yields and enantioselectivities.

Zhang et al., *J. Am. Chem. Soc.* **2023**, doi: 10.1021/jacs.3c04983

Asymmetric allylic alkylation (AAA)



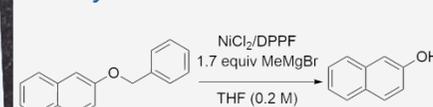
Challenge: Pd-catalyzed AAA has rarely been used on a large scale in the pharma industry.

Solution: The catalyst (η^3 -C₃H₅PdCl)₂ at 0.025% was used to synthesize a key pharmaceutical raw material on a metric ton scale.

Zhang et al., *Org. Process Res. Dev.* **2023**, doi: 10.1021/acs.oprd.3c00160

Process Development

Ni-catalyzed continuous reaction

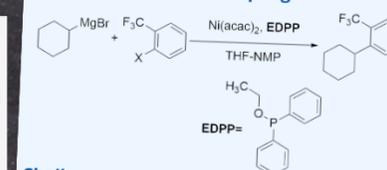


Challenge: Continuous-flow hydrogenolysis has problems such as H₂ gas handling.

Solution: Ni-catalyzed Kumada coupling under superheated conditions deprotected benzyl ethers without H₂ gas, and with an average assay yield of 97%.

Griesbach et al., *Org. Process Res. Dev.* **2023**, doi: 10.1021/acs.oprd.3c00125

Ni-catalyzed Kumada coupling



Challenge: A key intermediate of siponimod was the result of a long, inefficient, and costly process.

Solution: A Kumada-Corriu coupling catalyzed by Ni(acac)₂ was used to produce the intermediate with a shorter process, an inexpensive starting material, and a yield increase of 32.5%.

Lin et al., *Org. Process Res. Dev.* **2023**, doi: 10.1021/acs.oprd.3c00170

SINOCOMPOUND
Accelerate to the next phase