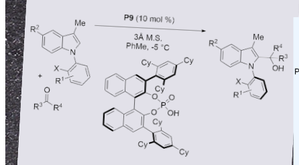
Homogeneous Catalysis Papers of the Month

September 2023

New methodology

Chiral catalysis

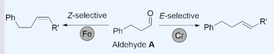


Challenge: Catalytic control of axial chirality is difficult when there is minor variation in substrate structure.

Solution: Dynamic kinetic resolution of arylindoles with ketomalonate was catalyzed by a chiral phosphoric acid, in an effective and atroposelective method for 46 different substrates.

A. Kim et al., *Nature Commun.* **2023**, doi: 10.1038/s41467-023-41299-2

Carbonyl cross-metathesis



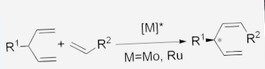
Challenge: Stereoselective carbonyl cross-metathesis is an unsolved challenge.

Solution: Carbonyl cross-metathesis is possible via iron-catalyzed carbene-to-ylide transfer (forming Z-alkenes) or by chromium-catalyzed gem-di-metalation (forming E-alkenes).

L. Zhang et al., *Nature Chem.* **2023**, doi: 10.1038/s41557-023-01333-8

Reviews

Asymmetric olefin metathesis

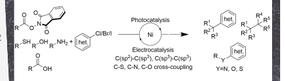


Challenge: Enantioselective metathesis transformations to form Z-alkenes are very important for the synthesis of natural products.

Solution: This overview of Z-enantioselective olefin metathesis covers a broad range of catalysis by Mo, W, and Ru complexes, including Grubb's catalysts and Hoveyda's catalysts.

J. Morvan et al., *Eur. J. Org. Chem.* **2023**, doi: 10.1002/ejoc.202300671

Photo- and electrocatalysis



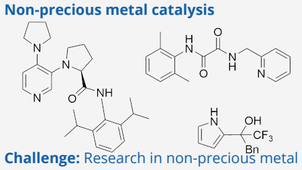
Challenge: Redox cross-coupling mechanisms are a mild and chemoselective alternative to palladium catalysis.

Solution: Photo- and electrochemically mediated Ni-catalyzed cross-couplings allow a wide range of bond formations with broad functional group tolerance.

M. D. Palkowitz et al., *Acc. Chem. Res.* **2023**, doi: doi.org/10.1021/acs.accounts.3c00479

Non-PGM catalysis

Non-precious metal catalysis

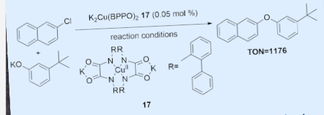


Challenge: Research in non-precious metal catalysis is expanding, providing a number of advances between November 2022 and February 2023.

Solution: This review discusses advances in catalysis of a wide range of reactions, including coupling and functionalization, by iron, manganese, copper, and nickel.

D. Bernhardson et al., *Org. Process Res. Dev.* **2023**, doi: 10.1021/acs.oprd.3c00260

Cu-catalyzed Ullmann coupling

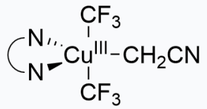


Challenge: Mechanisms of copper catalysis are often difficult to determine.

Solution: A copper-catalyzed cross-coupling with oxalamide ligands shows a different mechanism than was previously considered.

C. P. Delaney al., *Science* **2023**, DOI: 10.1126/science.adi9226

Cu(III) mechanistic studies



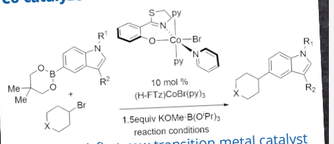
Challenge: Cu-catalyzed cross-couplings are difficult to study due to the instability of the Cu(III) intermediate.

Solution: Oxidative addition of haloacetonitriles was used to form stable Cu(III) complexes, which were used for mechanistic studies that suggest two different addition pathways.

Y. Luo et al., *Science* **2023**, doi: 10.1126/science.adg9232

API synthesis

Co-catalyzed Suzuki coupling

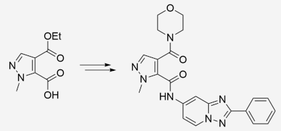


Challenge: A first-row transition metal catalyst was desired for the synthesis of afimetoran.

Solution: Air-stable phenoxythiazoline-cobalt(II) precatalysts were designed and applied to a Suzuki-Miyaura arylation, with catalyst lifetime extended with a base-borate additive.

L. R. Mills et al., *ChemRxiv* **2023**, doi: 10.26434/chemrxiv-2023-7631n

Process optimization



Gemlapodect

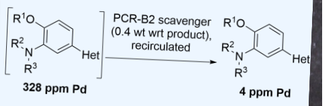
Challenge: The initial route for the drug candidate Gemlapodect had safety issues and a low yield.

Solution: The streamlined synthetic route solved the safety issues with a copper-catalyzed oxidative cyclization, and the yield issues with a palladium-catalyzed amidation.

S. Fantasia et al., *Helv. Chim. Acta,* **2023**, doi: 10.1002./hlca.202300116

Metal removal

Palladium recovery



Challenge: Residual palladium must be removed after catalysis so that it does not negatively impact downstream reactions or contaminate drug product, and so that it might be recycled.

Solution: This review examines palladium recovery through adsorption, extraction/precipitation, and crystallization.

M. Economidou et al., *Org. Process Res. Dev.* **2023**, doi: 10.1021/acs.oprd.3c00210

Selected papers from the catalysis literature published online in September 2023 (including pre-prints)

SINOCOMPOUND
Accelerate to the next phase