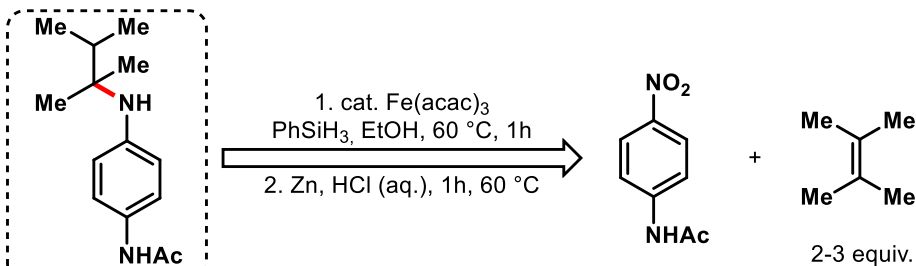
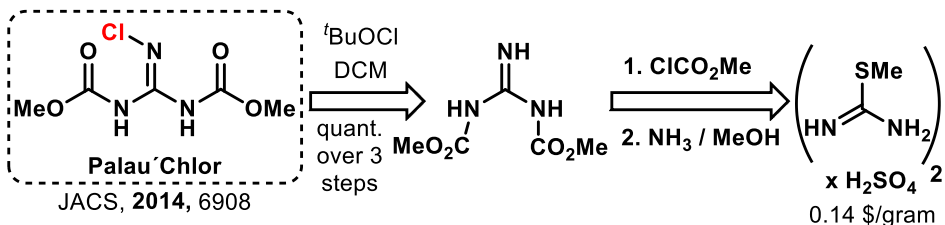


Phil Baran (Scripps)

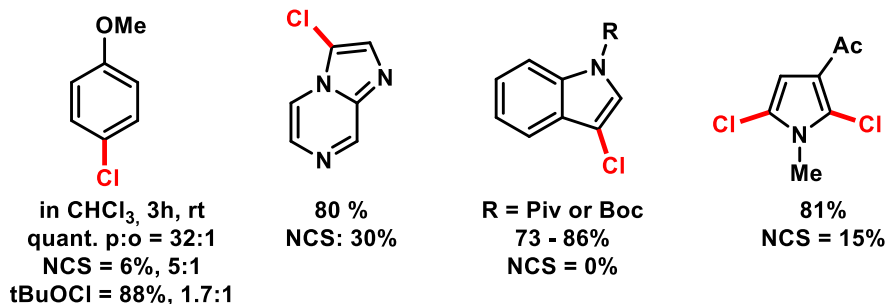
Science, **2015** (348), 886: Synthesis of hindered amines



Mechanism suggestion: Transfer of an H-radical from H-FeL_n onto the olefin generates a tertiary radical. Concurrently H-FeL_n reduces ArNO₂ to ArN=O (nitrosoarene), which combines with the radical to form N- or O-alkylated products. The N-O alkylated sideproduct is reduced to the product in the second reaction step. **Limitations:** free alcohols/ thiols, 2-NO₂-pyridines, substituted styrenes

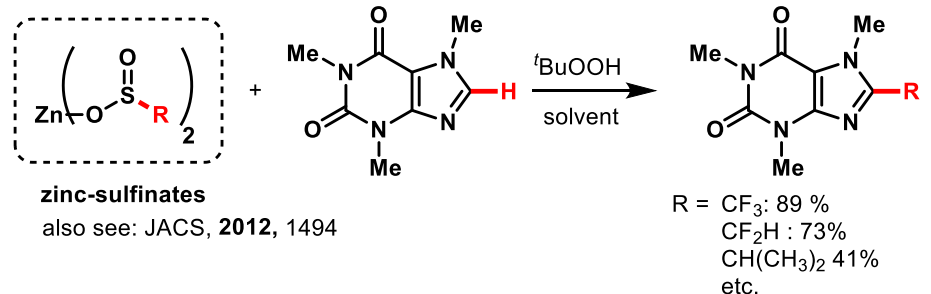


aka CBMG is a bench stable solid that closes the gap between rather weak (NCS) and strong (Cl₂, SO₂Cl₂) chlorinating reagents

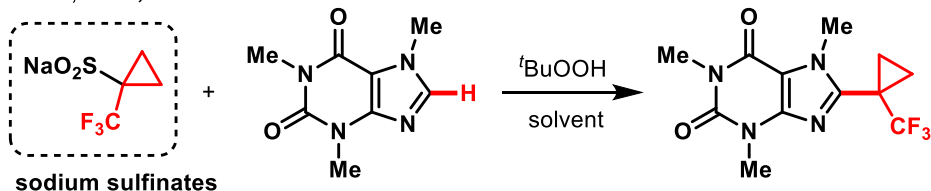


Zinc or sodium sulfonates serve as precursors for radical CH functionalization

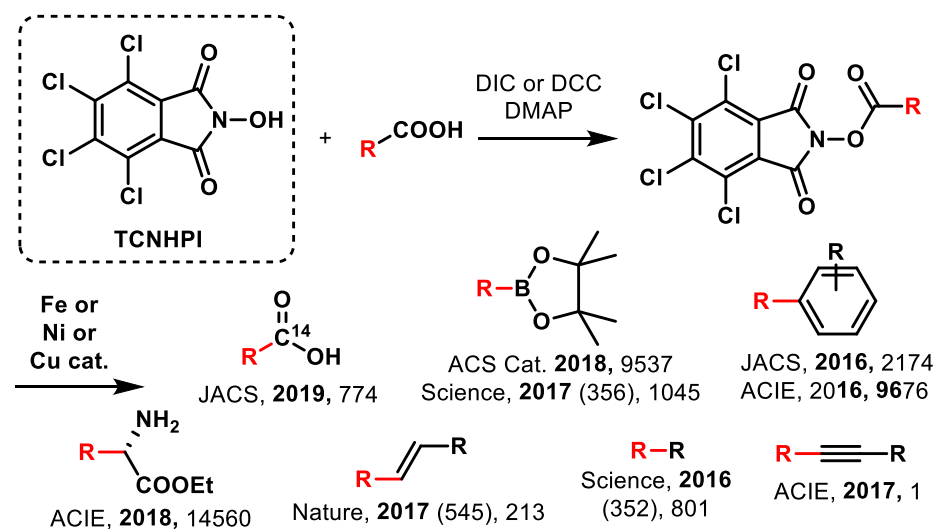
Nature, **2012** (492), 95



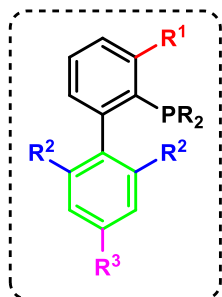
ACIE, **2014**, 9851



Carboxylic acids serve as precursors for radical cross-couplings

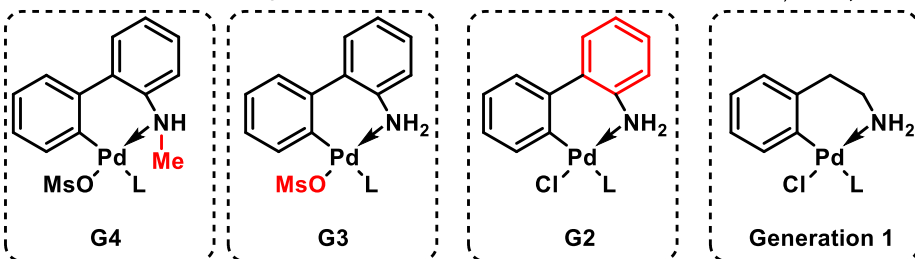


Stephen Buchwald (MIT)



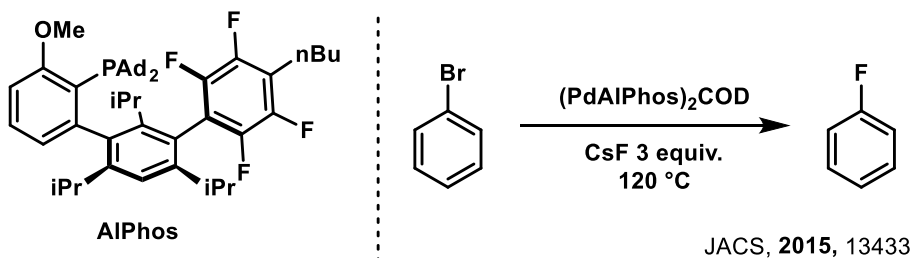
General structure of **Buchwald Ligands**:
Aryl = Prevents oxidation of P by O₂ and accelerates reductive elimination
 R = Electron rich groups facilitate oxidative addition
R¹ = Substitution promotes reductive elimination
R² = Increases stability by preventing cyclopalladation and encourages formation of Pd(0)
R³ = is usually not a hydrogen, but only for ease of synthesis

Buchwald Precatalysts: air stable precursors, which eliminate active Pd(0)-ligand species under basic reaction conditions. Highly successful in Buchwald-Hartwig and Suzuki cross couplings. JOC, 2014, 4161



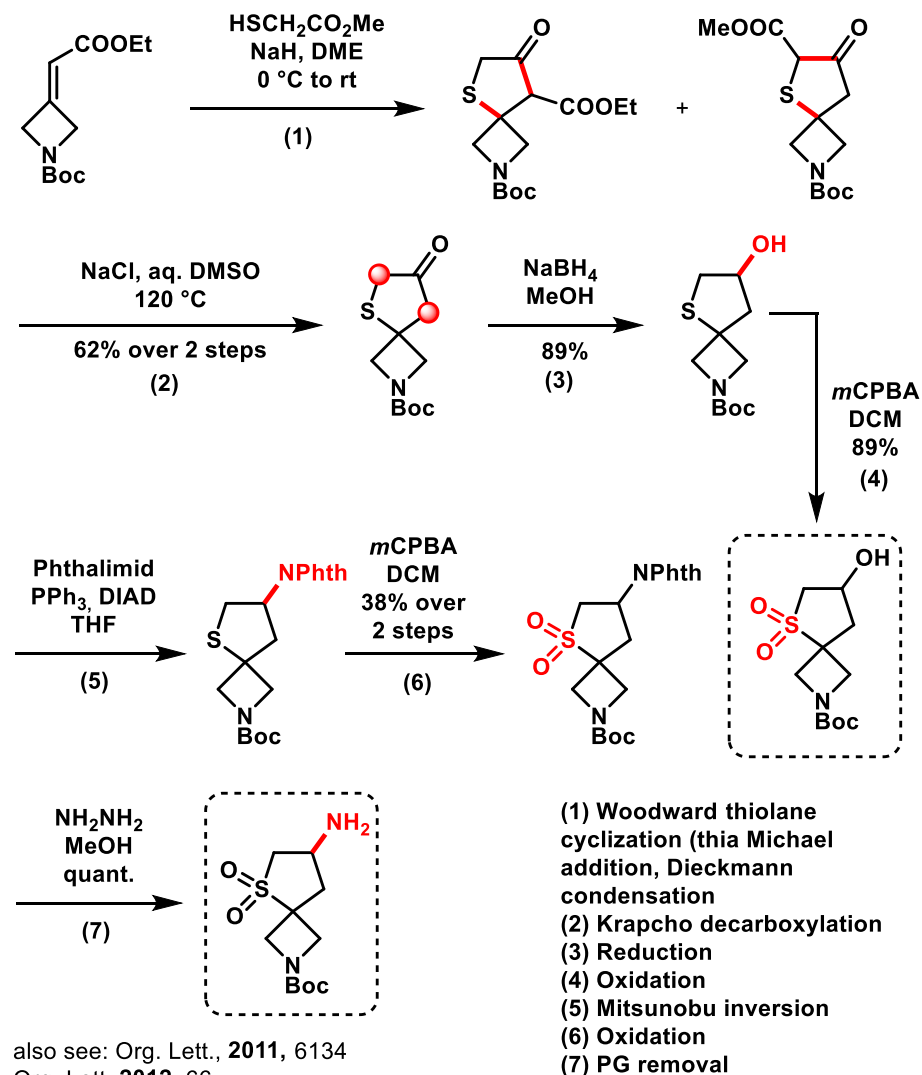
Problems solved over the generations: synthesis of precatalysts, scope of the applications, quantitative generation of active Pd(0)-ligand, great stability in solution, large variety of ligands, health issues of byproduct, substrate consumption by sideproduct

Other cross couplings are also supported by Buchwald ligands, e.g. highly challenging reductive eliminations from Ar-Pd-F species:

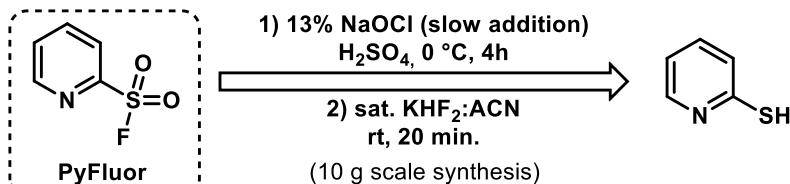


Erick Carreira (ETH Zürich)

Spirocyclic compounds can act as bioisosters due to their unique 3-dimensional structure. In collaboration with Spirochem a wide portfolio of [3.3] and [4.4] spirocycles with various substitutions are offered. Org. Lett., 2013, 4766

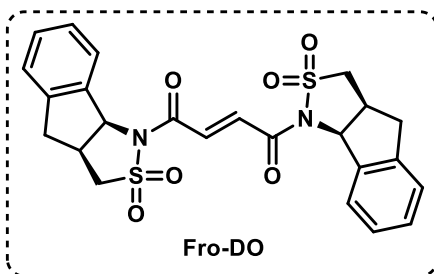
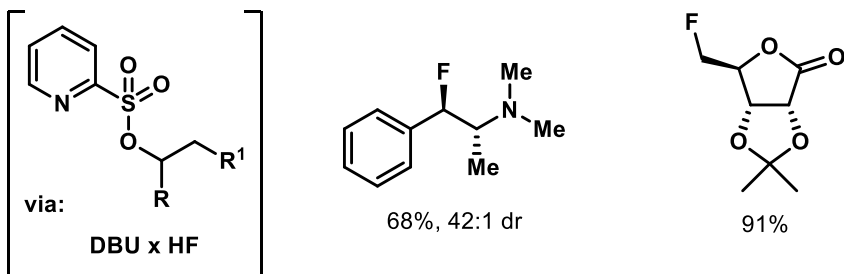


Abigail Doyle (Princeton)



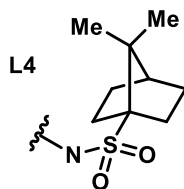
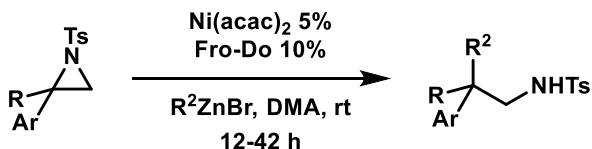
JACS, 2015, 9571

Conversion of 1° and 2° alcohols to fluorides. Air and moisture stable low melting solid. Application in radiolabeling possible.



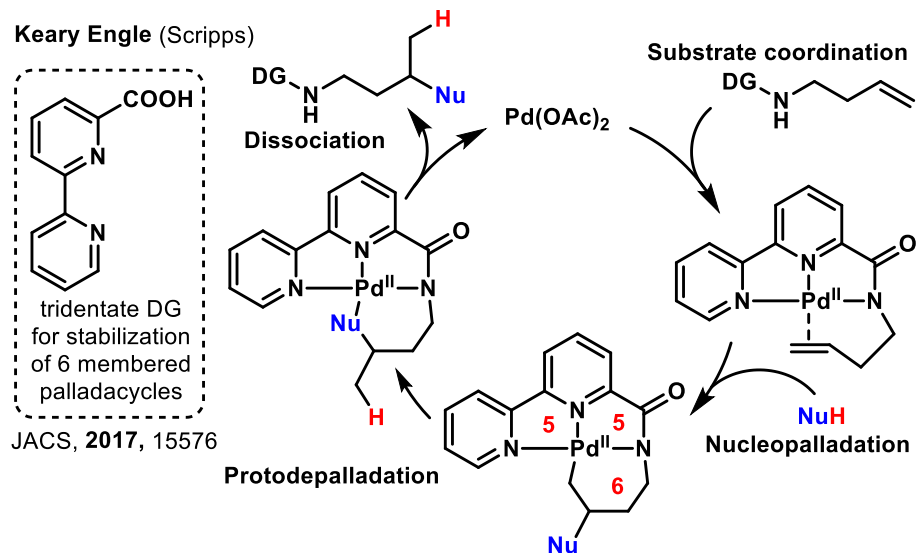
Electron deficient olefin ligand that promotes reductive elimination and therefore prevents β -hydride elimination in challenging cross couplings. In this case: construction of quaternary carbon centers.

JACS, 2015, 5638



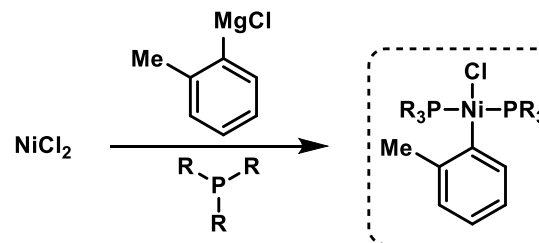
The on the right shown derivate L4 of Fro-DO was able to achieve a promising 27% ee on this transformation. It was the first example of a stereodivergent cross coupling with a tertiary electrophile.

Keary Engle (Scripps)



The ligand design supports 6 membered palladacycles in a rigid transition state, which prevents β -hydride elimination and directs the nucleophile.

Timothy Jamison (MIT)



Air stable

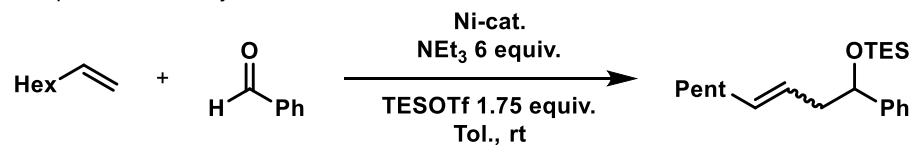
Rapid access

Mono- & bidentate phosphines

Generates active Ni(0)-Phosphine after treating with reductant

Organometallics, 2014, 2012

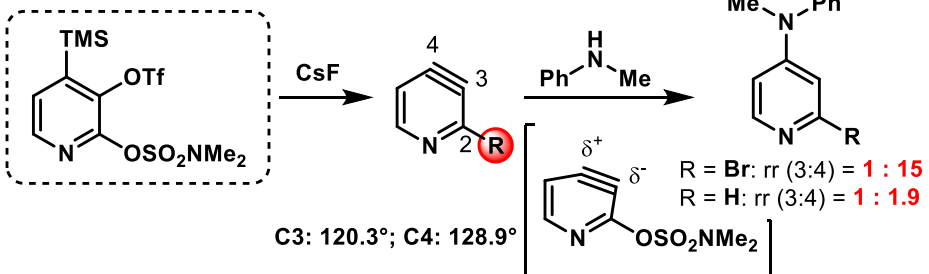
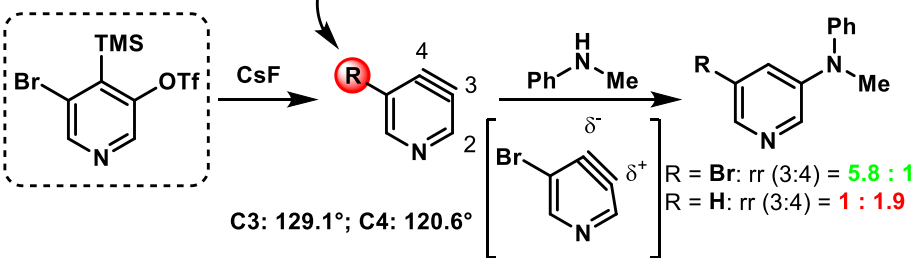
Example of a Carbonyl-Ene reaction:



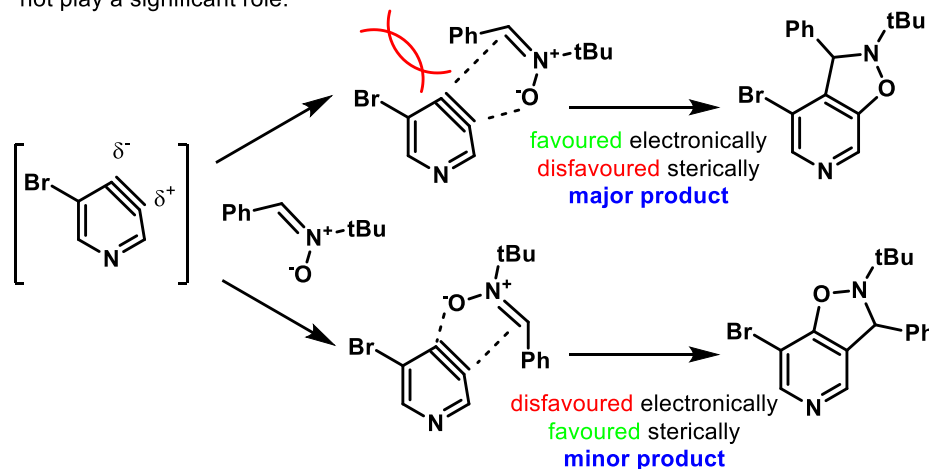
with Ni(COD)₂ and phosphine: 78%

Neil Garg (UCLA)

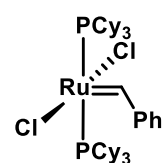
"directing group"

Nat. Chem. **2013** (5), 54
also see: JACS, **2010**, 17933

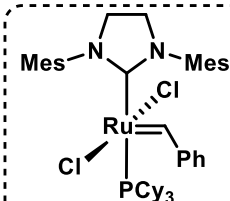
The regioselectivity is controlled by useful substituents on position 5 or 2 that serve as handles for further functionalization. The angles at C2 and C3 are distorted to greater or smaller angles with support of the respecting substituents. Nucleophiles will preferentially attack on the carbon which has the bigger angle. Steric effects do not play a significant role.



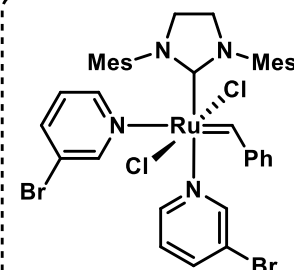
Robert Grubbs (Caltech)

**Generation 1**

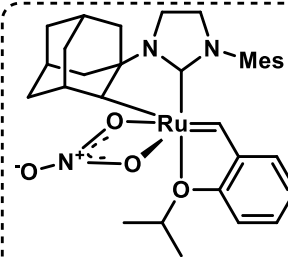
Effective in ring opening metathesis polymerization (ROMP), cross metathesis (CM), ring closing metathesis (RCM) of terminal olefins

**Gen 2**

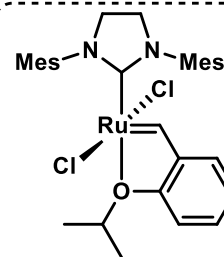
Able to produce trisubstituted olefins and has broader group tolerance

**Gen 3**

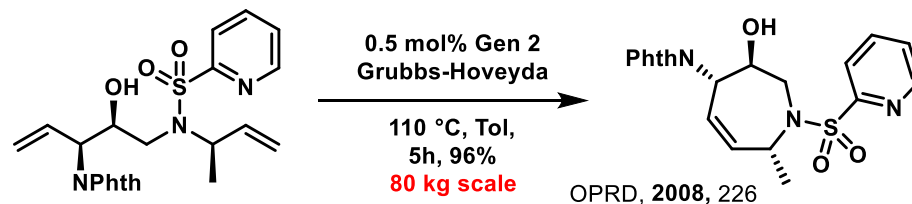
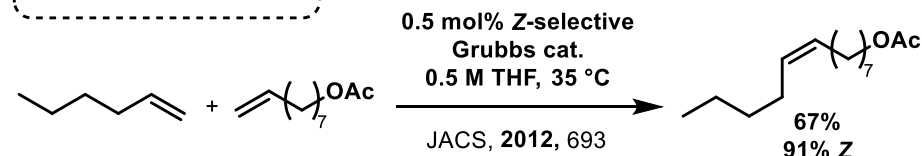
Very labile Py ligands result in fast initiation (even at 0 °C)
Capable of metathesis with acrylonitrile

**Z-selective**

For *cis* selective ROMP and Z-selective CM

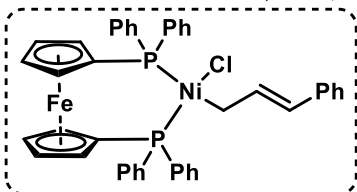
**Gen 2
Grubbs-Hoveyda**

Phosphine free version of G2. Initiates at lower T and is effective for electron deficient (e.g. fluoro substituted) olefins



John Hartwig (UC Berkeley)

ACIE, 2012, 12837

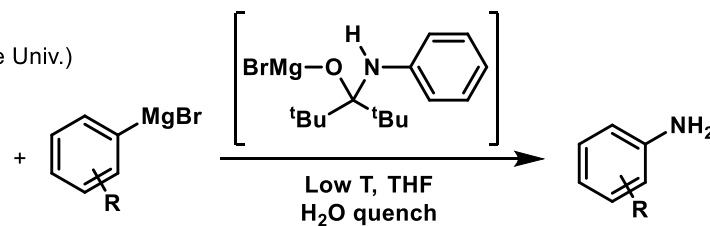
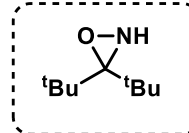


Air and moisture stable Nickel precatalyst especially for Heteroaryl Suzuki couplings

Generates Nidppf upon treatment with reductant (e.g. RB(OH)_2) and base

Readily prepared from Ni(COD)_2 , dppe and cinnamyl chloride

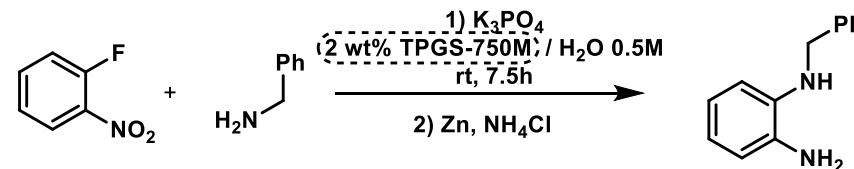
Lázlo Kürti (Rice Univ.)



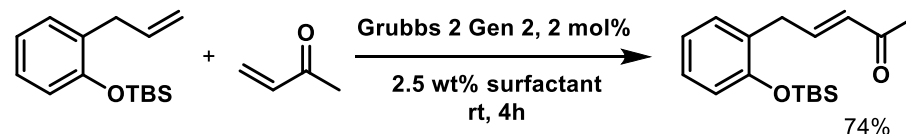
Nat. Chem. 2017 (9), 681

Bruce Lipshutz (UC Santa Barbara)

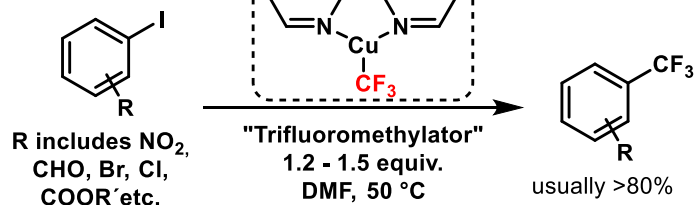
Org. Lett. 2015, 4734



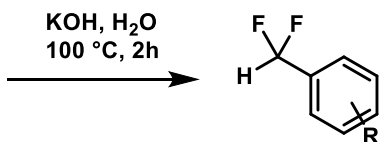
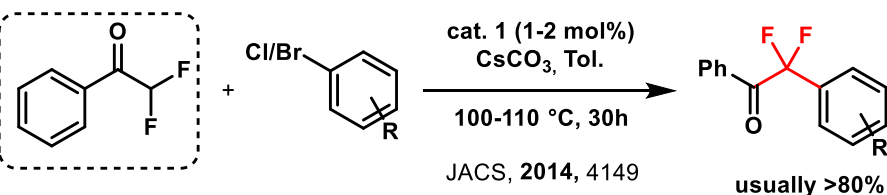
$\text{S}_{\text{N}}\text{Ar}$ reaction in water with support of nonionic surfactants which build "microreactors" (micells). Metal catalysed reactions have also been reported: JOC, 2011, 4379



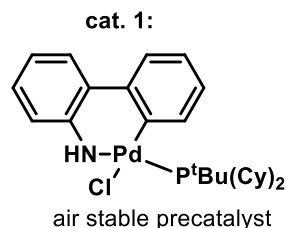
ACIE, 2011, 3793



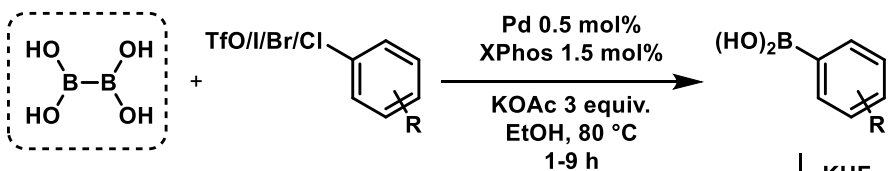
Catalytic version does not work smoothly, but the reagent can be generated *in situ* prior to the addition of aryl iodide. Costs in *in situ* generation are 1\$/mmol. The mechanism is not of radical nature.



The cross coupled difluoroarene presents an excellent platform for further modification. One example is the C-C bond cleavage to yield difluoromethylated arenes.

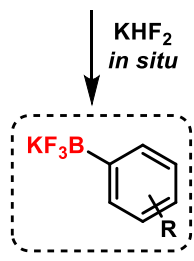


Gary Molander (UPenn)



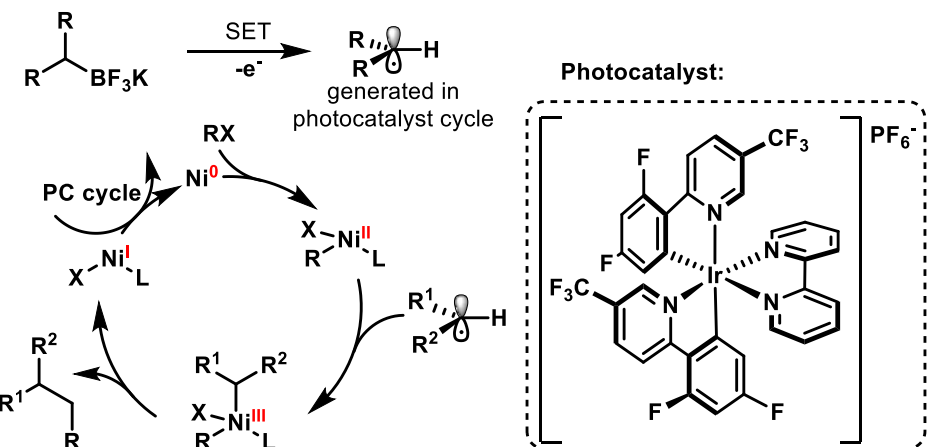
JACS, 2012, 11667

The reactions change their color upon finishing. Reactions with arylchlorides turn yellow and arylbromides turn orange

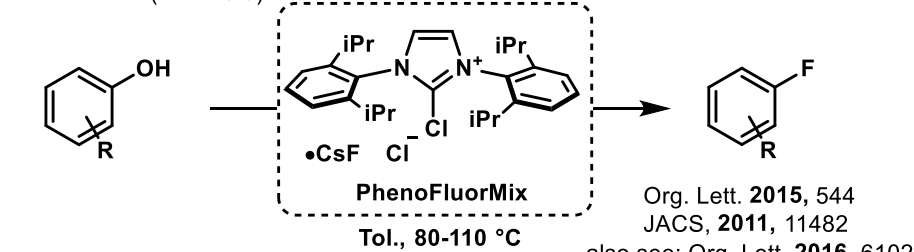


Direct conversion into arylboronic acids instead of Bpin reagents. The pinacol makes up >90 wt% of the Bpin group which shows poor atom economy. Standard methods for preparation of boronates include Miyaura borylation and transmetalation after Hal/M exchange (both resulting in Bpin).

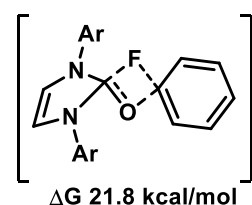
C-sp³ hybridized boron reagents show a sluggish transmetalation and present a challenge. This is due to the standard 2 electron mechanism. In the presented work the problem was addressed by leveraging 1 electron transmetalations by support of dual Ni-(redox)-Ir-(photoredox) catalysis. Science, 2015 (345), 433



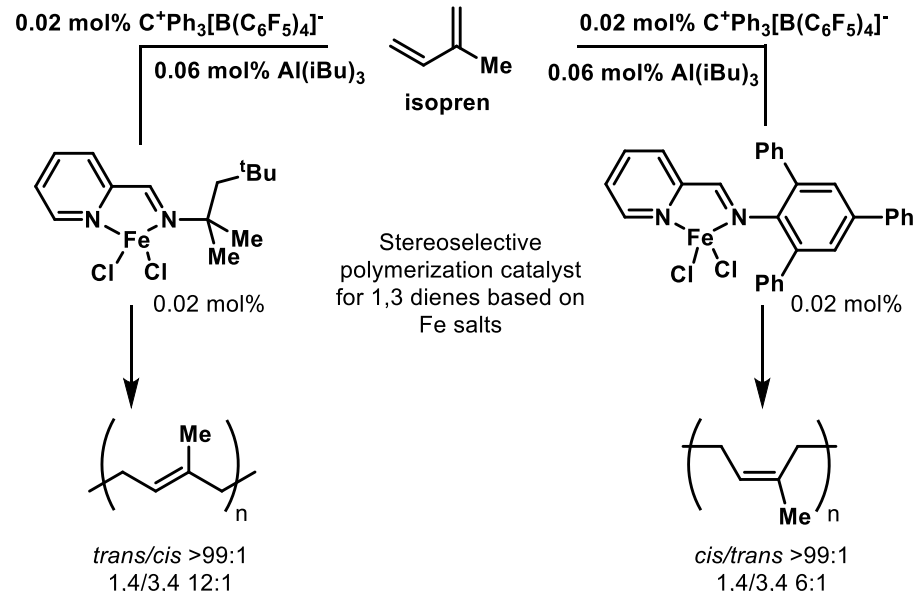
Tobias Ritter (MPI Kofo)



Org. Lett. 2015, 544
JACS, 2011, 11482
also see: Org. Lett. 2016, 6102



Although rich arenes are the scope of interest for this method (and the following might seem counterintuitive), the mechanism is believed to proceed through a concerted nucleophilic substitution. Nucleophilic attack and formation of PhenoFluor urea happen concurrently and the amount of negative charge is believed to be predominantly on the incoming Nuc and the urea LG. Acc. Chem. Res. 2017 (50), 2822

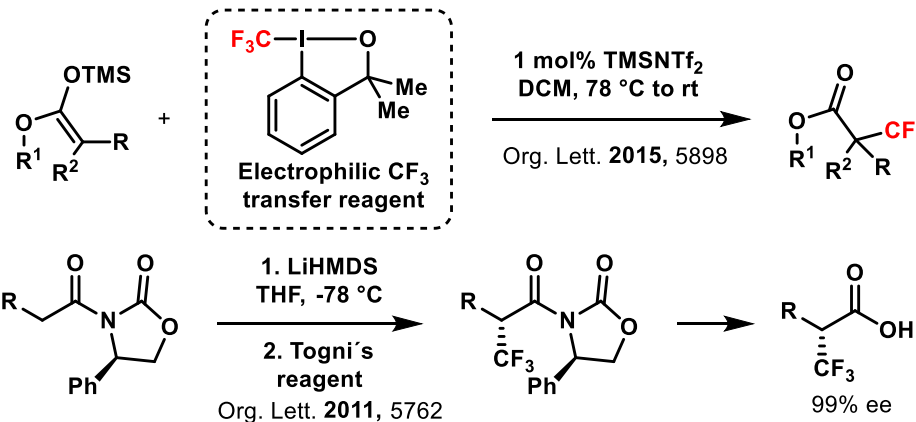


Stereoselective polymerization catalyst for 1,3 dienes based on Fe salts

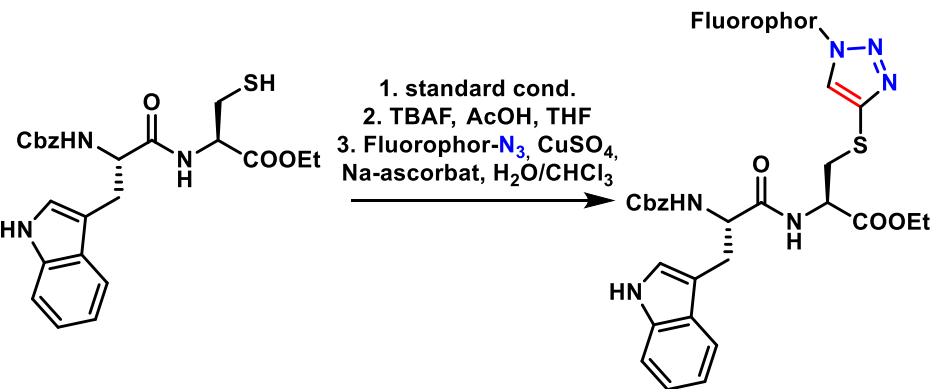
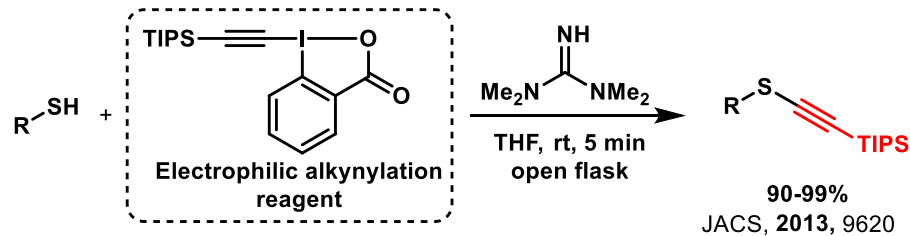
cis/trans >99:1
1,4/3,4 6:1

ACIE, 2012, 11805

Antonio Togni (ETH Zürich)

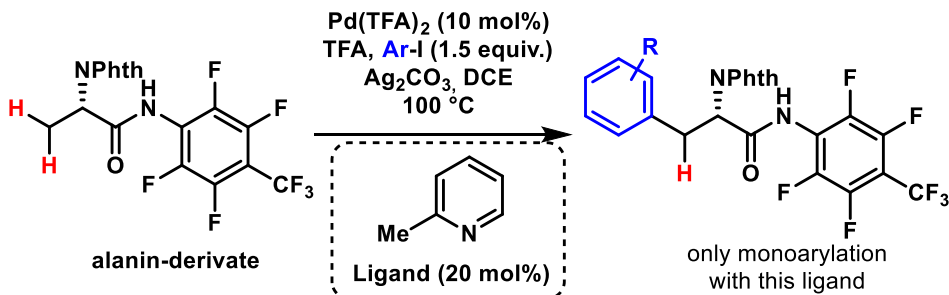


Jérôme Waser (Lausanne)

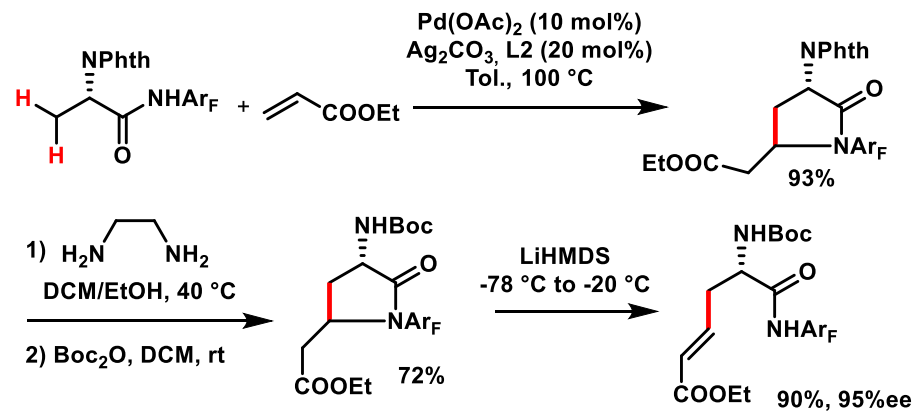
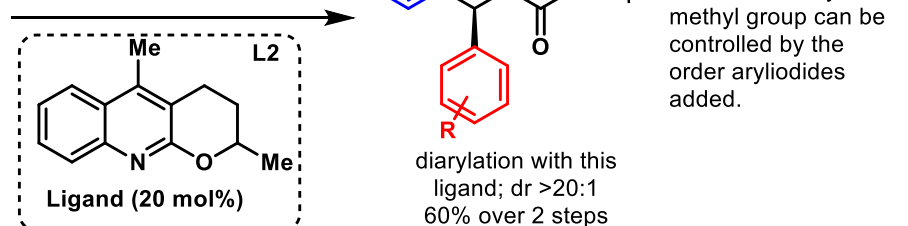


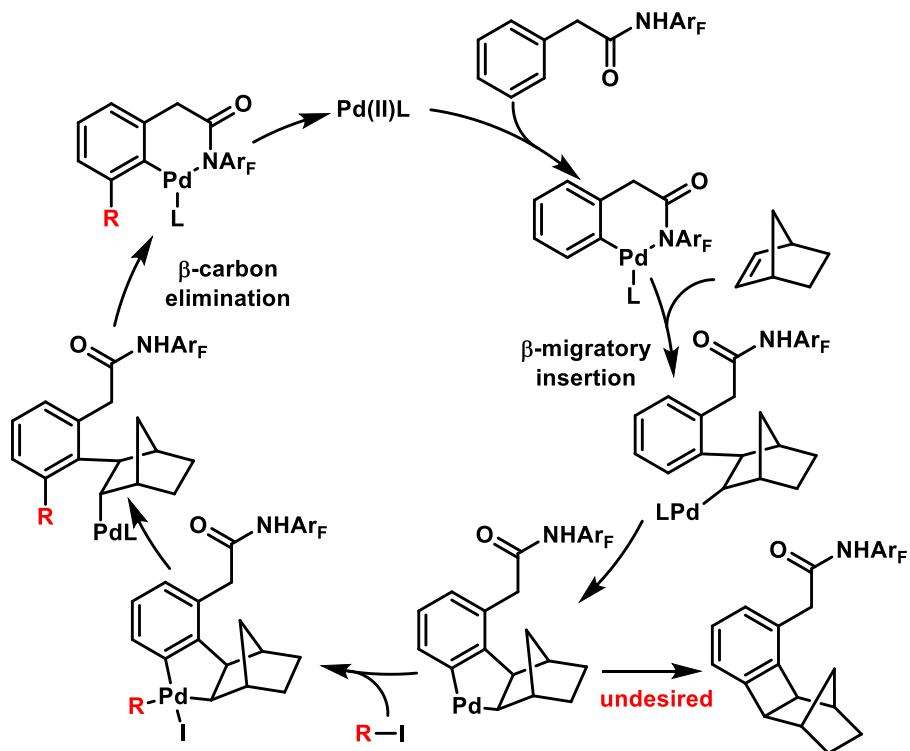
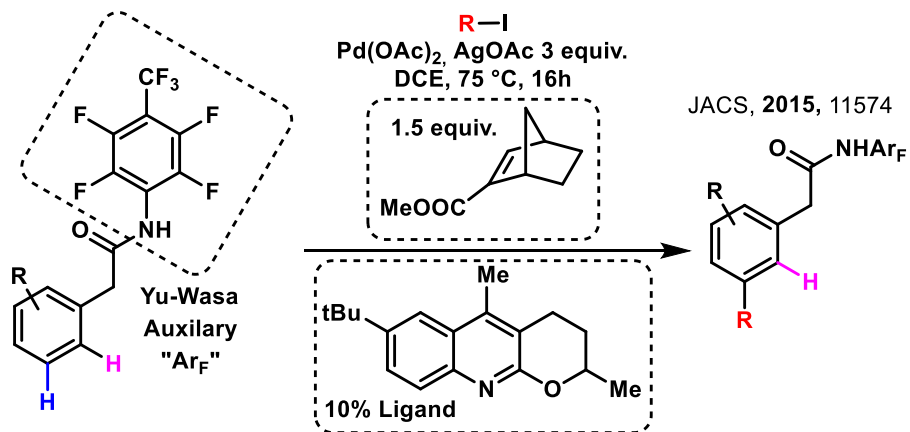
Jin-Quan Yu (Scripps)

Science, 2014 (343), 1216



no isolation, one pot addition of $Ar-I$ (3 equiv.) and ligand; same conditions





Barry Sharpless (Scripps) SuFEx "the next click reaction"

