Phil Baran (Scripps)
Science, 2015 (348), 866: Synthesis of hindered amines

Mechanism suggestion: Transfer of an H-radical from H-FeL₄ onto the olefin generates a tertiary radical. Concurrently H-FeL₄ reduces ArNO₂ to ArN=O (nitrosamines), 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

Zinc or sodium sulfonates serve as precursors for radical CH functionalization
Nature, 2012 (492), 95

Sodium sulfonates

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

Carboxylic acids serve as precursors for radical cross-couplings

Sigma Aldrich’s Professor Product Portal
Cornella Group Meeting
08.02.2019
Stephen Buchwald (MIT)

General structure of **Buchwald Ligands:**
- Aryl = Prevents oxidation of Pd 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.

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

---

**(1)** Woodward thiolane cyclization (thia Michael addition, Dieckmann condensation)

**(2)** Krapcho decarboxylation

**(3)** Reduction

**(4)** Oxidation

**(5)** Mitsunobu inversion

**(6)** Oxidation

**(7)** PG removal

---

**AlPhos**

**JACS, 2015, 13433**

**Org. Lett., 2011, 6134**

**Org. Lett. 2012, 66**
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.

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.
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 respective substituents. Nucleophiles will preferentially attack on the carbon which has the bigger angle. Steric effects do not play a significant role.
John Hartwig (UC Berkeley)
ACIE, 2012, 12837
Air and moisture stable Nickel precatalyst especially for Heteroaryl Suzuki couplings
Generates Npdppf upon treatment with reductant (e.g. RB(OH)2) and base
Readily prepared from Ni(COD)2, dppf and cinnamyl chloride

Lázlo Kürti (Rice Univ.)
Nat. Chem. 2017 (9), 681
\[
\begin{align*}
\text{BrMg-O} \quad & \quad \text{N-} \quad \text{Bu} \quad \text{Bu} \\
\text{Low T, THF} \quad & \quad \text{H2O quench} \\
\rightarrow \quad & \quad \text{NH2}
\end{align*}
\]

Bruce Lipshutz (UC Santa Barbara)
Org. Lett. 2015, 4734
\[
\begin{align*}
\text{PhNO2} + \text{H2N} & \quad 1) \text{K2PO4} \\
(2\text{ wt% TPGS-750M} / \text{H2O 0.5M}) & \quad 2) \text{Zn, NH4Cl} \\
\rightarrow \quad & \quad \text{NH2} \\
\text{rt}, 7.5h & \quad \text{S_NAr reaction in water with support of nonionic surfactants which build "microreactors" (micells). Metal catalysed reactions have also been reported: JOC, 2011, 4379}
\end{align*}
\]

Catalytic version does not work smoothly, but the reagent can be generated in situ prior to the addition of aryliodide. Costs in in situ generation are $1/\text{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.
The reactions change their color upon finishing. Reactions with arylchlorides turn yellow and arylbromides turn orange.

Direct conversion into aroylboronic 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-sp^3 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
**Sigma Aldrich’s Professor Product Portal**

---

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

\[
\text{SO}_2\text{F}^+ \quad + \quad \text{NH}_2\text{NH}_2\text{N}^+ \quad \rightarrow \quad \text{NH}_{2}\text{NH}_2\text{N}^+\text{SO}_2\text{F}\quad 99% 
\]

---

\[
\text{Ar}-\text{I} + \text{SO}_2\text{F} \quad 2 \text{ mol}\% \text{ Pd(OAc)}_2, 1.2 \text{ equiv. AgTFA} \quad \text{acetone, air, 60 °C} \quad \text{Ar}-\text{SO}_2\text{F} 
\]

---

\[
\text{SO}_2\text{F}_2 \quad \text{gas} \quad 2. \text{MeOTf} \quad \text{OTf}^- \quad \text{Me}-\text{N}^+\text{SO}_2\text{F} \quad \text{Me}-\text{N}^+\text{SO}_2\text{F} \quad \text{Me}-\text{N}^+\text{SO}_2\text{F} 
\]

**ACIE, 2018, 2605**

- Bench stable solid
- Higher reactivity
- Faster reaction times

---

\[
\text{OTf}^- \quad \text{Me}-\text{N}^+\text{SO}_2\text{F} \quad + \quad \text{R}^2\text{NH} \quad \text{ACN} \quad \text{rt, 2h no base} \quad \text{R}^2\text{N}^+\text{SO}_2\text{F} \quad \text{primary & secondary} 
\]

---

\[
\text{OTf}^- \quad \text{Me}-\text{N}^+\text{SO}_2\text{F} \quad + \quad \text{OMeOH} \quad \text{ACN} \quad \text{rt, 2h no base} \quad \text{OMeO}^+\text{SO}_2\text{F} 
\]

**94%**

---

\[
\text{OTf}^- \quad \text{Me}-\text{N}^+\text{SO}_2\text{F} \quad + \quad \text{NH}_2\text{NH}_2\text{N}^+ \quad \text{ACN} \quad \text{rt, 2h no base} \quad \text{N}^+\text{SO}_2\text{F} 
\]

**91%**

double sulfonylation with 2.5 equiv. reagent and Et\text{3}N