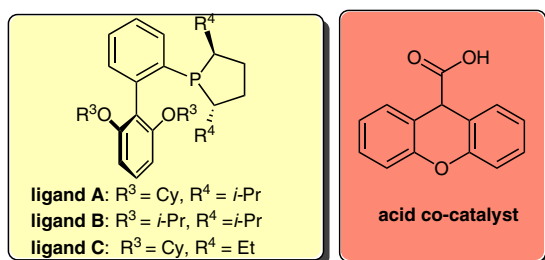
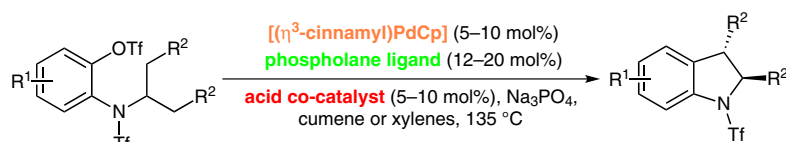


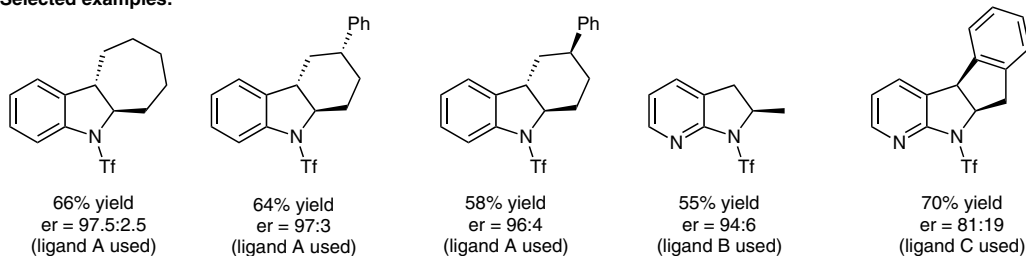
T. SAGET, S. J. LEMOUZY, N. CRAMER* (EPFL, LAUSANNE AND ETH ZÜRICH, SWITZERLAND)

Chiral Monodentate Phosphines and Bulky Carboxylic Acids: Cooperative Effects in Palladium-Catalyzed Enantioselective C(sp³)-H Functionalization
Angew. Chem. Int. Ed. **2012**, *51*, 2238–2242.

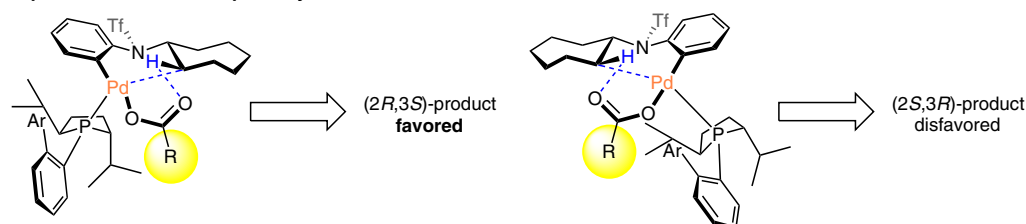
Asymmetric Synthesis of Indolines by Pd-Catalyzed C(sp³)-H Activation



Selected examples:



Proposed stereochemical pathway:



Significance: The development of a new class of phosphine ligands and their application to asymmetric C–H activation is described. The ligand design incorporates several features that distinguish it from other chiral phosphine ligands: the phosphine is electron-rich, monodentate, highly tunable (R³ and R⁴ groups) and bears a C₂-symmetric phospholane rather than P-centered chirality. These ligands display excellent reactivity and selectivity in the synthesis of the important indoline motif.

SYNFACTS Contributors: Hisashi Yamamoto, Patrick Brady
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Comment: Working under the hypothesis that the C–H activation step proceeds by a concerted deprotonation–metallation pathway, the authors screened various ligands and carboxylic acid co-catalysts. The bulky acid shown above was found to be optimal. The authors propose that the phosphine ligand induces a chiral environment through the spatial orientation of the carboxylate ligand. Indeed, chiral acids were also found to influence selectivity.