

Palladium-Catalyzed Enantioselective Intermolecular Carboetherification of Dihydrofurans

Gustavo M. Borrajo-Calleja, Vincent Bizet, Clément Mazet*

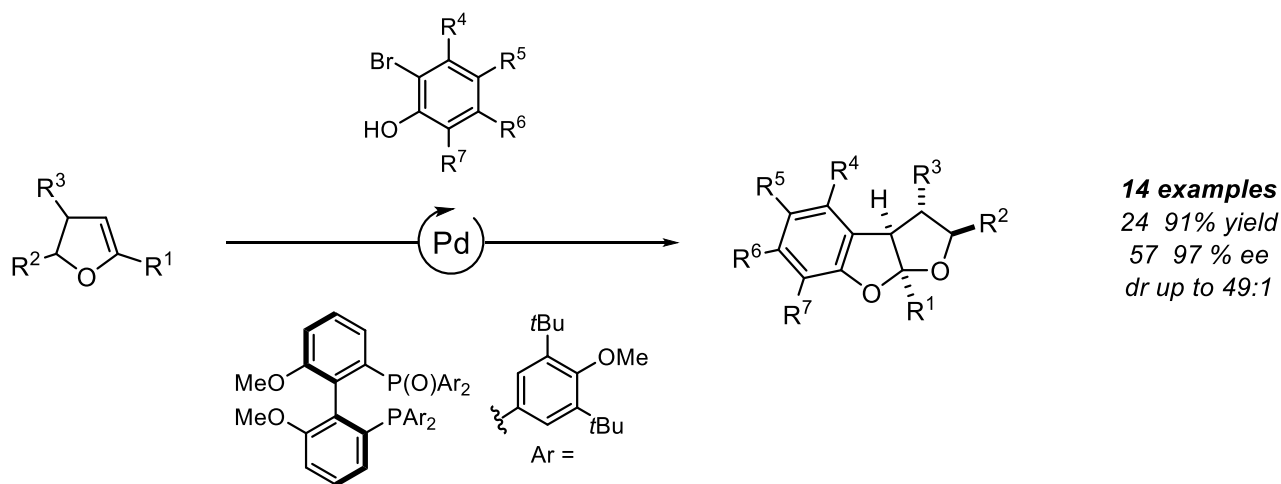
Department of Organic Chemistry, University of Geneva

Quai Ernest Ansermet 30, 1211 Geneva 4, Switzerland

Email: Clement.Mazet@unige.ch

In recent years, efforts have been focused on the development of new methodologies for carbon-heteroatom bond formation,^[1] owing to the ubiquity of aryl C-N and C-O bonds in agrochemicals, pharmaceuticals and natural products. Among these methodologies, the Pd-catalyzed carboetherification of alkenes has emerged as a powerful strategy. Despite remarkable advances in the field, most reported examples proceed via intramolecular reactions and their enantioselective variants are still scarce.^[2,3]

Herein we describe a novel intermolecular carboetherification that gives direct access to fused tetrahydrofurobenzofurans; a scaffold that can be found in numerous biologically active compounds and which is typically accessible via long and unpractical synthetic routes.^[4] Under optimized conditions and using readily available starting materials, the final cross-coupling products are systematically obtained in high yield, enantio- and diastereoselectivity.^[5] A key feature of our methodology is the *in situ* formation of a chiral bisphosphine mono-oxide (BPMP).



[1] J. F. Hartwig, *Nature*, **2008**, 455, 314

[2] a) M. A. Rossi, J. P. Wolfe, *J. Am. Chem. Soc.* **2004**, 126, 1620; b) M. B. Hay, J. P. Wolfe, *J. Am. Chem. Soc.* **2005**, 127, 16468

[3] B. A. Hopkins, Z. J. Garlets, J. P. Wolfe, *Angew. Chem. Int. Ed.* **2015**, 54, 13390

[4] a) B. M. Trost, F. D. Toste, *J. Am. Chem. Soc.* **2003**, 125, 3090; b) Gang Zhou, E. J. Corey, *J. Am. Chem. Soc.* **2005**, 127, 11958

[5] G. M. Borrajo-Calleja, V. Bizet, C. Mazet, *J. Am. Chem. Soc.* **2016**, 138, 4014