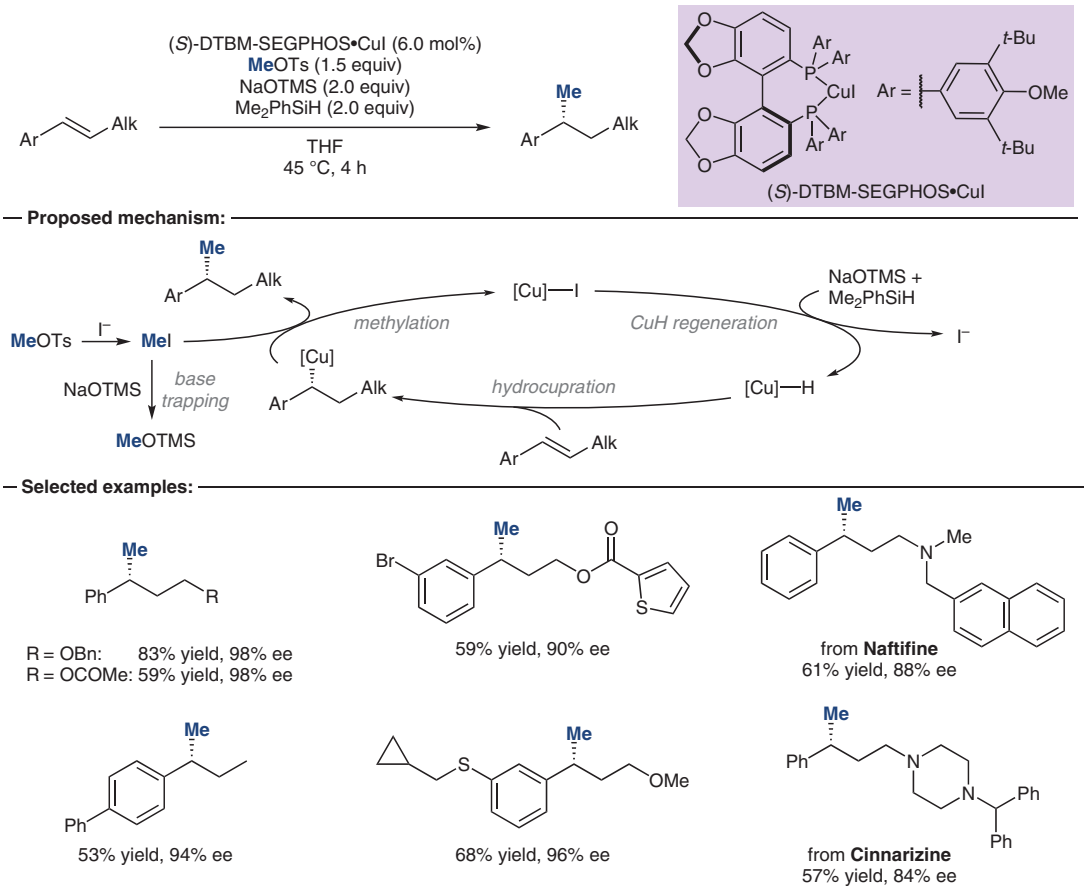
Y. DONG, K. SHIN, B. K. MAI, P. LIU*, S. L. BUCHWALD* (UNIVERSITY OF PITTSBURGH AND MASSACHUSETTS INSTITUTE OF TECHNOLOGY, CAMBRIDGE, USA)

Copper Hydride-Catalyzed Enantioselective Olefin Hydromethylation
J. Am. Chem. Soc. **2022**, *144*, 16303–16309, DOI: 10.1021/jacs.2c07489.

Introducing the Magic Methyl: Enantioselective Hydromethylation of Olefins under Copper Hydride Catalysis



Significance: Liu, Buchwald and co-workers have disclosed a copper hydride catalyzed direct enantioselective hydromethylation of styrene derivatives. The mild reaction protocol tolerates various functional groups, heterocycles and pharmaceutically relevant frameworks. The installation of a methyl group can have profound effects in drug discovery, also known as the 'magic methyl effect'.

Comment: Mechanistic studies including DFT calculations support the shown mechanism. The presence of catalytic amounts of iodide ions is crucial for the asymmetric hydromethylation, transforming the methyl tosylate into the active methylating agent, that is methyl iodide.

SYNFACTS Contributors: Martin Oestreich, Hendrik F. T. Klare, Daniel Brösamlen
Synfacts 2022, 18(12), 1313 Published online: 17.11.2022
DOI: 10.1055/s-0042-1753122; **Reg-No.:** M12222SF

Category
Metals in Synthesis

Key words
copper catalysis
hydromethylation
methyl group
olefins

Synfact of the Month