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.