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SYNFACTS Highlights in Chemical Synthesis

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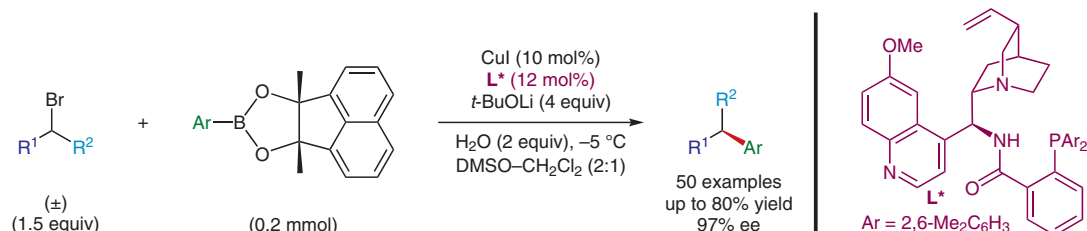
 **Thieme**

S.-P. JIANG, X.-Y. DONG, Q.-S. GU, L. YE, Z.-L. LI*, X.-Y. LIU* (SOUTHERN UNIVERSITY OF SCIENCE AND TECHNOLOGY, SHENZHEN, P. R. OF CHINA)

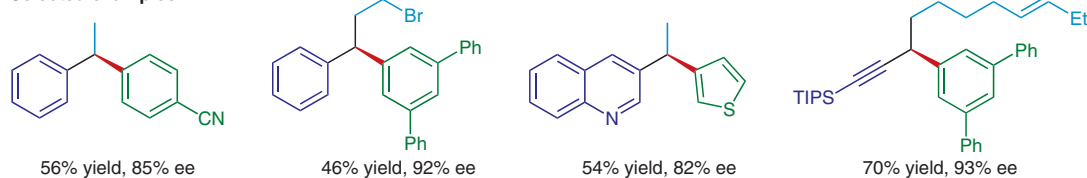
Copper-Catalyzed Enantioconvergent Radical Suzuki–Miyaura C(sp³)–C(sp²) Cross-Coupling

J. Am. Chem. Soc. **2020**, *142*, 19652–19659, DOI: 10.1021/jacs.0c09125.

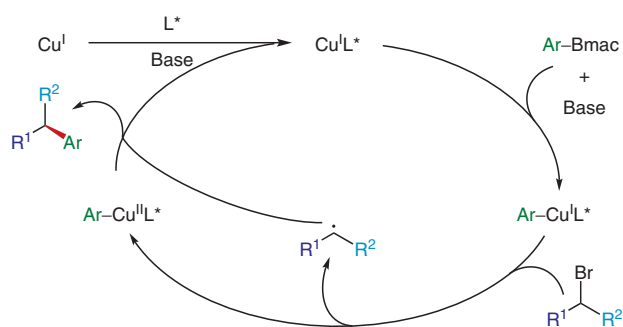
Enantioconvergent Copper-Catalyzed Cross-Coupling of Racemic Alkyl Halides with Boronate Esters



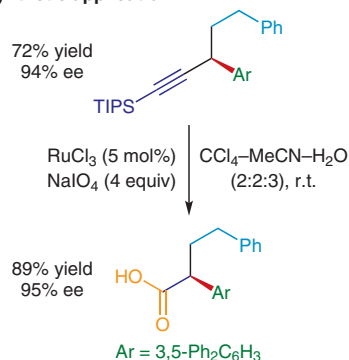
Selected examples:



Proposed mechanism:



Synthetic application:



Significance: The authors report a stereoconvergent Suzuki–Miyaura cross-coupling of racemic benzylic, heterobenzylic and propargyl halides with aryl and heteroaryl B(mac)-derived boronate esters using a low-cost copper catalyst. The chemoselectivity of the reaction is demonstrated by a high functional group tolerance, including the exclusive reaction of a secondary benzylic bromide in the presence of a primary alkyl bromide. A broad array of chemical transformations were performed on the alkyne substrates to show synthetic utility, such as the oxidative cleavage of the alkyne shown, with further esterification and reduction.

Comment: Separate experiments with both a radical clock substrate and a radical trap (TEMPO) were used to support the proposed radical intermediate. Through other mechanistic studies, the possibility of a dynamic kinetic resolution or dynamic kinetic asymmetric transformation were ruled out. In order to readily furnish a prochiral radical intermediate, the cinchona alkaloid-derived N,N,P-ligand was specifically chosen because it increases the reducing ability of the copper catalyst. The scalability of the reaction was demonstrated on a 1 g scale of aryl bromide without reduction of either yield or enantioselectivity.

SYNFACTS Contributors: Mark Lautens, Rachel Ross
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