Y.-F. ZHANG, B. WANG, Z. CHEN, J.-R. LIU, N.-Y. YANG, J.-M. XIANG, J. LIU, Q.-S. GU, X. HONG*, X.-Y. LIU* (SOUTHERN UNIVERSITY OF SCIENCE AND TECHNOLOGY, SHENZHEN AND ZHEJIANG UNIVERSITY, HANGZHOU, P. R. CHINA)

Asymmetric Amination of Alkyl Radicals with Two Minimally Different Alkyl Substituents
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Dispersion Enables Asymmetric Amination of Near-Symmetric Carbon Radicals

Category

Innovative Drug Discovery and Development

Key words

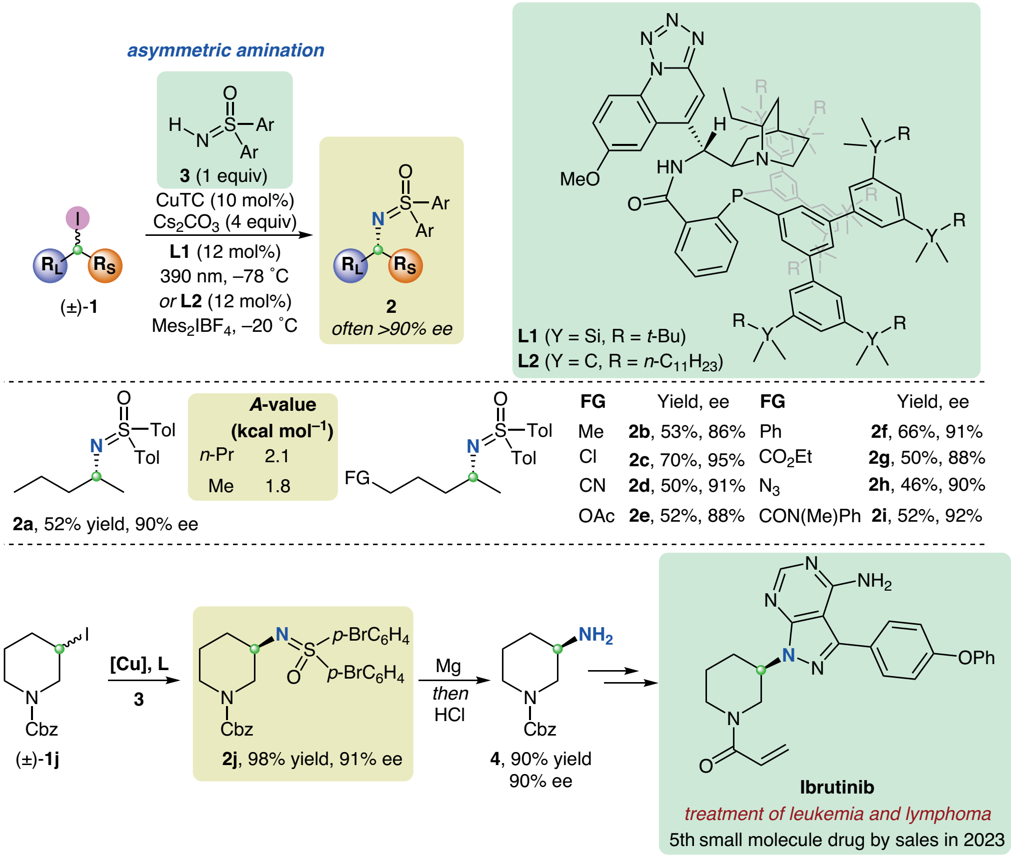
asymmetric amination

radicals

copper catalysis

N,N,P-ligands

sulfoximines



Significance: Nature has mastered the asymmetric synthesis of chiral amines, as evidenced by the widespread presence of amino acids. On the contrary, organic synthesis still struggles with this, often requiring chiral resolution of enantiomers, or multi-step synthesis employing amino acids as building blocks. In this work, Hong, Liu, and co-workers describe a copper-catalyzed asymmetric amination of near-symmetrical secondary alkyl iodides **1** to obtain amines **2** with high enantioselectivity and in good to excellent yields.

Comment: In this reaction, the racemic secondary alkyl iodide **1** generates a radical that is captured by the nitrogen nucleophile (sulfoximine) **3** bound to the copper-ligand manifold (an outer-sphere mechanism). Dispersion interactions between the bulky N,N,P ligand (**L1**/**L2**) and the larger alkyl substituent (R_L) deliver high enantioselectivity. The reaction works well at low temperatures, which results in high enantioselectivity, even when R_S and R_L are very similar substituents (i. e., having similar *A*-values, such as **2a**). The reaction has a broad functional group compatibility (**2b**–**i**).

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