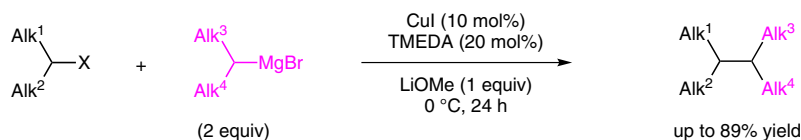


C.-T. YANG, Z.-Q. ZHANG, J. LIANG, J.-H. LIU, X.-Y. LU, H.-H. CHEN, L. LIU* (TSINGHUA UNIVERSITY, BEIJING AND UNIVERSITY OF SCIENCE AND TECHNOLOGY OF CHINA, HEFEI, P. R. OF CHINA)

Copper-Catalyzed Cross-Coupling of Nonactivated Secondary Alkyl Halides and Tosylates with Secondary Alkyl Grignard Reagents

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Cu-Catalyzed Coupling of Secondary Alkyl Electrophiles and Alkyl Grignards



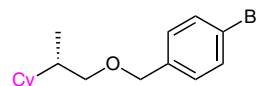
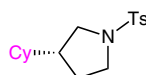
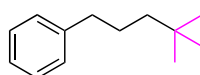
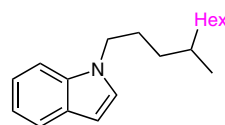
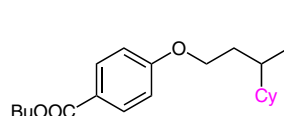
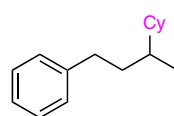
X = OTs, Cl, Br, I

Alk¹ = various substituted alkyl groups

Alk² = linear and branched aliphatic chains

Alk^{3/4} = cyclic and linear aliphatics

Selected examples:



Significance: A novel method for the cross-coupling of nonactivated secondary alkyl halides and pseudo halides with secondary Grignard reagents with a copper catalyst is described. The addition of TMEDA and LiOMe was found to be crucial for the success of the reaction. A broad range of functional groups including esters, amides and aryl halides, is tolerated under the reaction conditions.

Comment: Interestingly, the reaction proceeds according to a classical S_N2 mechanism with inversion of configuration. Therefore, easily accessible chiral secondary alcohols can be converted into chiral tosylates and alkylated with a copper-catalyst with either primary or secondary alkyl Grignard reagents to furnish the products in high enantiomeric excess.

SYNFACTS Contributors: Paul Knochel, Andreas K. Steib
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Category

Metal-Mediated
Synthesis

Key words

copper

inversion

Grignard reagents

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of the month