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

Cu-Catalyzed Coupling of Secondary Alkyl Electrophiles and Alkyl Grignards

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.

Selected examples:

\[
\begin{align*}
\text{Cy} & \quad 81\% \text{ yield} \\
\text{BuOOC} & \quad 74\% \text{ yield} \\
\text{Hex} & \quad 64\% \text{ yield} \\
\text{Cy} & \quad 89\% \text{ yield} \\
\text{Cy} & \quad 70\% \text{ yield} \\
\text{Cy} & \quad 89\% \text{ yield} \\
\end{align*}
\]

\[X = \text{OTs, Cl, Br, I}\]
\[\text{Alk}^1 = \text{various substituted alkyl groups}\]
\[\text{Alk}^2 = \text{linear and branched aliphatic chains}\]
\[\text{Alk}^{3,4} = \text{cyclic and linear aliphatics}\]