
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 $S_N^2$ 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.

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**Selected examples:**

- **81% yield**
  - $X = OTs$
  - 89% yield
  - $X = Br$
  - 67% yield
  - $X = Br$
  - 99% ee
  - 98% ee
  - $X = OTs$

- **74% yield**
  - $X = Br$

- **64% yield**
  - $X = Br$

- **67% yield**
  - $X = Br$

- **70% yield**
  - $X = OTs$

- **74% yield**
  - $X = OTs$

- **64% yield**
  - $X = OTs$

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**X**

- Alk$_1$ = various substituted alkyl groups
- Alk$_2$ = linear and branched aliphatic chains
- Alk$_3$/4 = cyclic and linear aliphatics

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