G. CAHIEZ,* C. CHABOCHE, C. DUPLAIS, A. MOYEUX (CNRS - UNIVERSITÉ DE PARIS 13, BOBIGNY, FRANCE)

A New Efficient Catalytic System for the Chemoselective Cobalt-Catalyzed Cross-Coupling of Aryl Grignard Reagents with Primary and Secondary Alkyl Bromides Org. Lett. 2009, 11, 277-280.

Efficient Cobalt-Catalyzed Coupling of Aryl Grignard Reagents with Alkyl Bromides

R1 — MgBr + AlkX
$$\frac{\text{Co(acac)}_3 (5 \text{ mol\%}), \text{ TMEDA } (5 \text{ mol\%})}{\text{THF, 0 °C, 40 min}}$$
 up to 98% yield R1 — H, 2-MeO, 4-MeO Alk = primary, secondary, functionalized X = Br, I $\frac{\text{Alk}}{\text{MeO}}$ $\frac{\text{Alk}}{3}$ $\frac{\text{Co(acac)}_3 (5 \text{ mol\%}), \text{TMEDA } (5 \text{ mol\%})}{\text{THF, 0 °C, 40 min}}$ $\frac{\text{Alk}}{\text{R1}}$ up to 98% yield $\frac{\text{Alk}}{3}$ $\frac{\text{Alk}}{3}$ $\frac{\text{Co(acac)}_3 (5 \text{ mol\%}), \text{TMEDA } (5 \text{ mol\%})}{\text{THF, 0 °C, 40 min}}$ $\frac{\text{Alk}}{\text{R1}}$ $\frac{\text{Alk}}{\text{Up to 98\% yield}}$ $\frac{\text{Alk}}{3}$ $\frac{\text{Co(acac)}_3 (5 \text{ mol\%}), \text{TMEDA } (5 \text{ mol\%})}{\text{THF, 0 °C, 40 min}}$ $\frac{\text{Alk}}{3}$ $\frac{\text{Co(acac)}_3 (5 \text{ mol\%}), \text{TMEDA } (5 \text{ mol\%})}{\text{THF, 0 °C, 40 min}}$ $\frac{\text{Alk}}{3}$ $\frac{\text{Co(acac)}_3 (5 \text{ mol\%}), \text{TMEDA } (5 \text{ mol\%})}{\text{THF, 0 °C, 40 min}}$ $\frac{\text{Alk}}{3}$ $\frac{\text{Co(acac)}_3 (5 \text{ mol\%}), \text{TMEDA } (5 \text{ mol\%})}{\text{THF, 0 °C, 40 min}}$ $\frac{\text{Alk}}{3}$ $\frac{\text{Co(acac)}_3 (5 \text{ mol\%}), \text{TMEDA } (5 \text{ mol\%})}{\text{THF, 0 °C, 40 min}}$ $\frac{\text{Alk}}{3}$ $\frac{\text{Co(acac)}_3 (5 \text{ mol\%}), \text{TMEDA } (5 \text{ mol\%})}{\text{THF, 0 °C, 40 min}}$ $\frac{\text{Alk}}{3}$ $\frac{\text{Co(acac)}_3 (5 \text{ mol\%}), \text{TMEDA } (5 \text{ mol\%})}{\text{THF, 0 °C, 40 min}}$ $\frac{\text{Co(acac)}_3 (5 \text{ mol\%}), \text{TMEDA } (5 \text{ mol\%})}{\text{THF, 0 °C, 40 min}}$ $\frac{\text{Co(acac)}_3 (5 \text{ mol\%}), \text{TMEDA } (5 \text{ mol\%})}{\text{THF, 0 °C, 40 min}}$ $\frac{\text{Co(acac)}_3 (5 \text{ mol\%}), \text{TMEDA } (5 \text{ mol\%})}{\text{THF, 0 °C, 40 min}}$ $\frac{\text{Co(acac)}_3 (5 \text{ mol\%}), \text{TMEDA } (5 \text{ mol\%})}{\text{THF, 0 °C, 40 min}}$ $\frac{\text{Co(acac)}_3 (5 \text{ mol\%}), \text{TMEDA } (5 \text{ mol\%})}{\text{THF, 0 °C, 40 min}}$ $\frac{\text{Co(acac)}_3 (5 \text{ mol\%}), \text{TMEDA } (5 \text{ mol\%})}{\text{THF, 0 °C, 40 min}}$ $\frac{\text{Co(acac)}_3 (5 \text{ mol\%}), \text{TMEDA } (5 \text{ mol\%})}{\text{THF, 0 °C, 40 min}}$ $\frac{\text{Co(acac)}_3 (5 \text{ mol\%}), \text{TMEDA } (5 \text{ mol\%})}{\text{THF, 0 °C, 40 min}}$ $\frac{\text{Co(acac)}_3 (5 \text{ mol\%})}{\text{THF, 0 °C, 40 min}}$ $\frac{\text{Co(acac)}_3 (5 \text{ mol\%})}{\text{THF, 0 °C, 40 min}}$ $\frac{\text{THF, 0 °C, 40 min}}{\text{THF, 0 °C, 40 min}}$ $\frac{\text{THF, 0 °C, 40 min}}{\text{THF, 0 °C, 40 min}}$ $\frac{\text{THF, 0 °C, 40 min}}{\text{THF, 0 °C, 40 min}}$ $\frac{\text{THF, 0 °C, 40 min}}{\text{$

Significance: An efficient cobalt-catalyzed crosscoupling reaction of aryl Grignard reagents with primary and secondary alkyl bromides is reported. The reaction proceeds rapidly under very mild conditions and tolerates many functional groups. A readily available cobalt catalyst is used in the process, which is in general more efficient and versatile than the similar iron-catalyzed sp²-sp³ cross-coupling reactions.

Comment: Due to the relatively fast reaction (0 °C, 40 min) functional groups like ester, amide and ketone are well tolerated. Alkyl iodides give similar yields as bromides, while chlorides and tosylates do not react. Hindered mesitylmagnesium bromide gives low yield of the product. Interestingly, the cobalt source is also important in this reaction, and CoCl₂ is less efficient in the presence of TMEDA than Co(acac)₃.

SYNFACTS Contributors: Paul Knochel, Andrei Gavryushin

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