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Pd-Catalyzed Kumada–Corriu Cross-Coupling Reactions at Low Temperatures Allow the Use of Knochel-type Grignard Reagents

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# Low-Temperature Cross-Coupling of Functionalized Grignard Reagents

Category

Metal-Mediated Synthesis

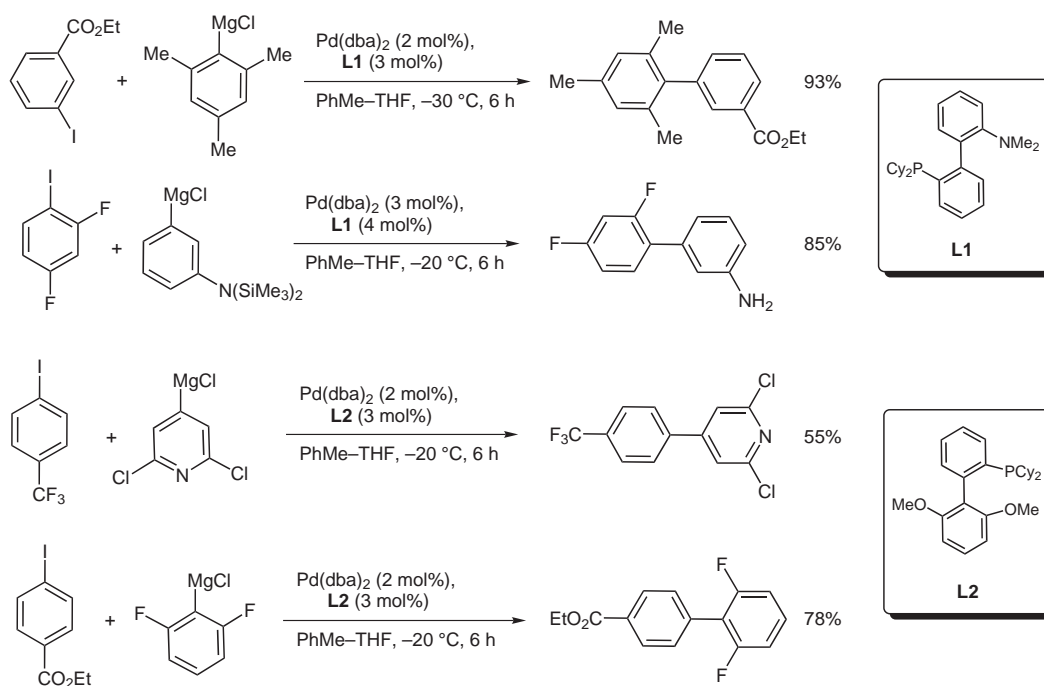
Key words

Kumada–Corriu cross-coupling

palladium catalysis

Grignard reagents

**SYNFACT**  
of the month



**Significance:** The Kumada–Corriu cross-coupling process is very attractive since the required (het)arylmagnesium species, including polyfunctionalized ones, can be readily prepared directly by the halogen–magnesium exchange or a metalation reaction. The group of Buchwald report herein a robust protocol, allowing a very efficient coupling of polyfunctionalized arylmagnesium species at the temperatures, which tolerate a vast majority of functional groups. This method is therefore extremely attractive for the direct synthesis of functionalized biaryls starting from (het)aryl halides.

**Comment:** While the preparation of polyfunctionalized (het)aryl Grignard reagents has become recently a great progress, the low temperatures (around  $-40\text{ }^{\circ}\text{C}$  in some cases) required for their stability limited their direct use in cross-coupling processes. The use of the new generation of biaryl phosphine catalysts, developed in the group of Buchwald, overcomes this problem. Several reactions can be performed even at  $-65\text{ }^{\circ}\text{C}$ , which has never been found for a Pd-catalyzed cross-coupling reaction.

**Review:** For a recent review on the preparation of polyfunctionalized Grignard reagents, see: H. Ila, O. Baron, A. J. Wagner, P. Knochel *Chem. Commun.* **2006**, 583–593.

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