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High Temperature Metalation of Functionalized Aromatics and Heteroaromatics using $(tmp)_2Zn{\cdot}2MgCl_2{\cdot}2LiCl$ and Microwave Irradiation

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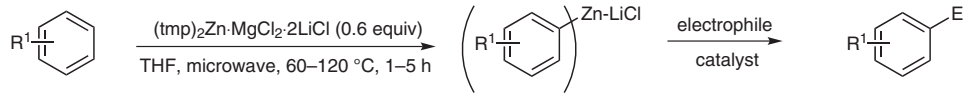
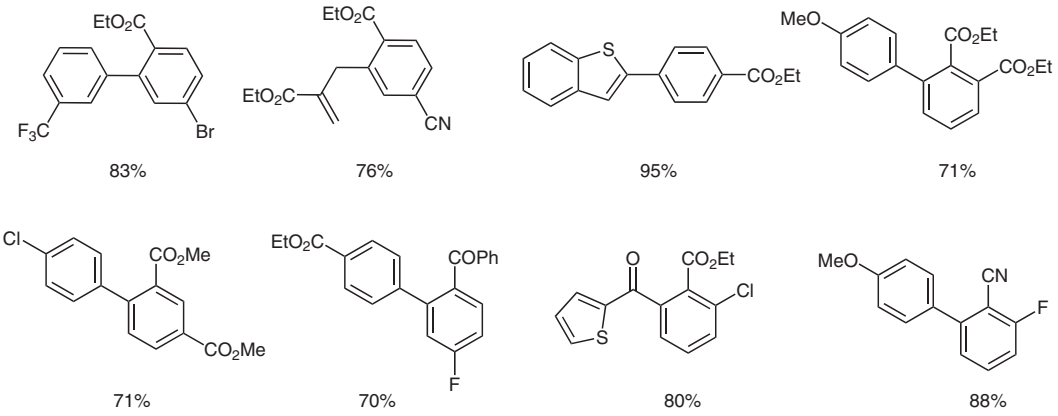
Microwave-Enhanced Zincation of Arenes and Heteroarenes



R^1 = CO_2Et, $CONEt_2$, CN, COPh, etc. E = Ar (cross-coupling), allyl, acyl chloride, etc., Pd(0) or Cu(I) catalysis

Examples (overall 17 reactions):



Significance: Direct metalation of polysubstituted arenes is a highly attractive method of their further functionalization, allowing straightforward routes toward complex industrially important molecules. The compatibility with functional groups makes the use of zincation preferable over the conventional lithiation or magnesiation reactions, offering an outstanding range of functional group compatibility. This method allows simple functionalization of relatively inactive substrates, which were formerly problematic for direct metalation.

Comment: The use of this reagent for the zincation of electron-poor heterocycles has been reported earlier (S. H. Wunderlich, P. Knochel *Angew. Chem. Int. Ed.* **2007**, *46*, 7685). At room temperature, the metalation of simple benzoate esters is too slow (>100 h for completion), but the use of microwave irradiation enhances the reaction to a practical rate.

Review: For a review on microwave-assisted synthesis, see: C. O. Kappe *Angew. Chem. Int. Ed.* **2004**, *43*, 6250-6284.

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