Synthesis of Alkylated Pyridine Derivatives via S_HAr of N-Methoxypyridinium Salts

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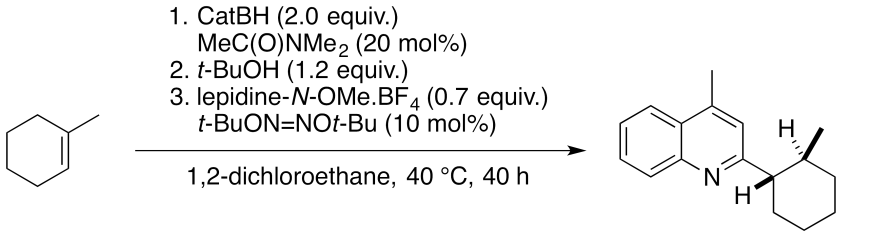
The homolytic aromatic substitution of nitrogen containing heterocycles is a versatile and well-studied class of transformations and is a viable reaction for late-stage functionalization of organic compounds.

The alkylation or acylation of a protonated, electron-poor heteroaromatic base using a nucleophilic carbon-centered radical was extensively studied by Minisci. Due to polar effects, the reaction shows selectivities that would be impossible to obtain under Friedel-Crafts reaction conditions.[1]

However, the reaction suffers from drawbacks such as use of a stoichiometric amount of oxidant, low regioselectivity and polyalkylation. Due to its viability in natural product synthesis and -functionalization, it is of great interest to overcome this reaction's limitations.

Herein, we describe a method that uses non-protic activation of the substrate. Alkylboranes (RBCat[2,3], R_3B) react with N-methoxypyridinium salts in the presence of a radical initiator to afford substituted pyridines. Interestingly, no external oxidizing agent is required to run this reaction. The scope and limitation of this reaction will be discussed.



86% (dr >97:3, trans/cis)

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