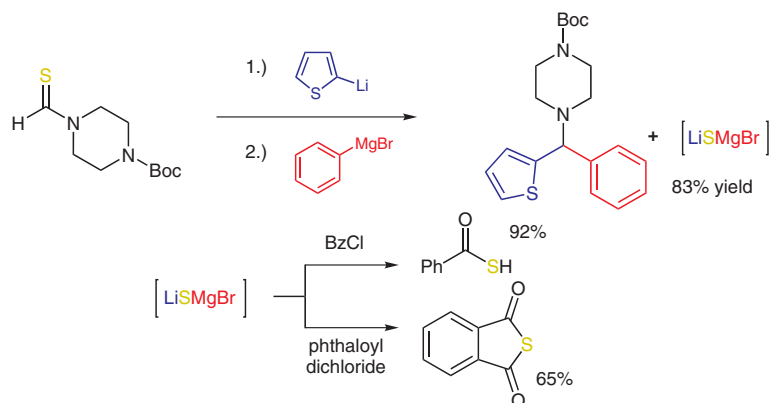
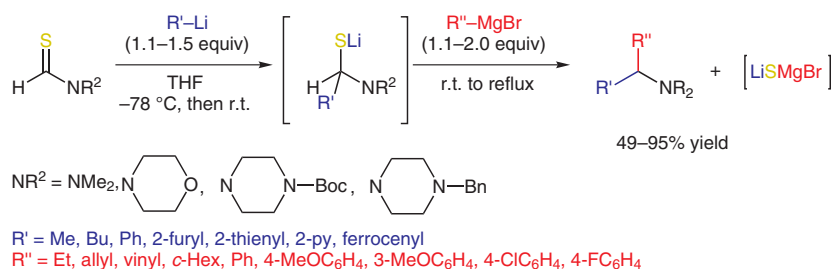


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Three-Component Coupling Reactions of Thioformamides with Organolithium and Grignard Reagents Leading to Formation of Tertiary Amines and a Thiolating Agent

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Three-Component Coupling Reactions of Thioformamides with Organolithium and Grignard Reagents



Significance: The use of *N,N*-dialkylthioformamides for the generation of tertiary amines via a novel three-component coupling reaction with organolithium and Grignard reagents is demonstrated. Thus, a variety of valuable tertiary amines, including the biologically significant diarylmethylpiperazines, were synthesized. It is noteworthy that the order of addition of the organolithium and Grignard reagents is vital to the success of the reaction. Remarkably, an excess of the organolithium reagent, which is first added to the *N,N*-dialkylthioformamide, does not interfere with the outcome of the reaction. In addition to the formation of tertiary amines a new thiolating agent, supposedly LiSMgBr, is formed during the coupling reaction.

Comment: This three-component coupling reaction represents a new practical method for the synthesis of tertiary amines, as the combination of versatile organolithium and Grignard reagents allows for a large diversity of possible products. This method is also potentially relevant for medicinal chemistry, since racemic key intermediates of biologically active compounds, such as cetilidine, a H1-receptor agonist and rivastigmine, a drug administered for the treatment of Alzheimer's disease, can be easily accessed by it. The synthetic scope of the in situ generated thiolating agent has yet to be determined.

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SYNFACTS
of the month