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Boron-Catalyzed N-Alkylation of Amines Using Carboxylic Acids
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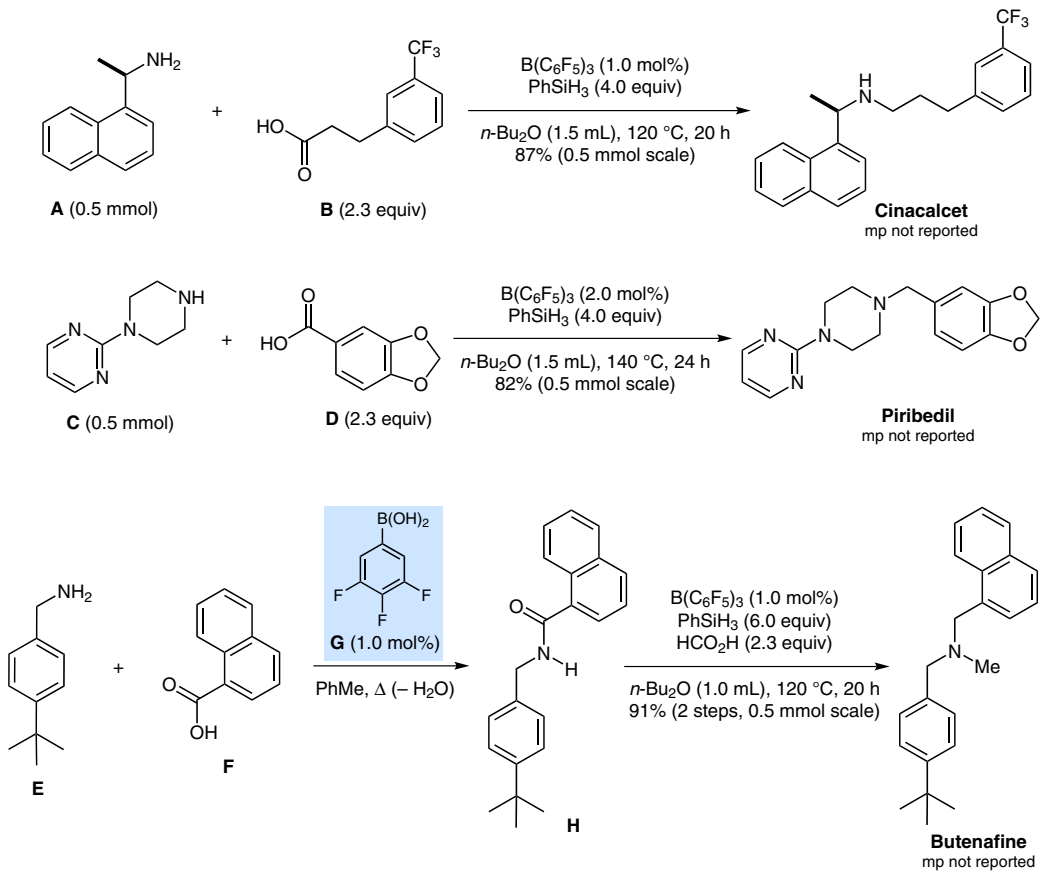

Significance: The boron-based catalyst $B(C_6F_5)_3$, which can form a frustrated Lewis pair (FLP), catalyzes the N-alkylation of amines using carboxylic acids in the presence of a silane reducing agent. The boron catalyst enables reductive carbon–nitrogen bond formation in preference to the reduction of the carboxylic acid. Only 1.0 mol% of the boron catalyst is required. Twenty-four examples of the N-methylation of various primary and secondary amines using formic acid and eighteen examples of the N-alkylation of aniline with various carboxylic acids illustrate the scope of the reaction.

Comment: The utility of the N-alkylation reaction is illustrated by the small-scale synthesis of three pharmaceutical agents. Cinacalcet (Sensipar®, Mimpara®) is a calcimimetic that is useful for the treatment of secondary hyperparathyroidism in patients with chronic kidney disease and hypercalcaemia in patients with parathyroid carcinoma. Piribedil (Pronoran®) is a D_2 and D_3 receptor agonist that is used to treat Parkinson's disease. Butenafine (Mentax®) is a squalene epoxidase inhibitor that blocks the synthesis of ergosterol. It is used as a topical antifungal agent.

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