Boron-Catalyzed N-Alkylation of Amines Using Carboxylic Acids

**Significance:** The boron-based catalyst \( \text{B(C}_6\text{F}_5\text{)}_3 \), 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 hypercalcemia in patients with parathyroid carcinoma. Piribedil (Pronoran®) is a D2 and D3 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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