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N-Heterocyclic Carbene-Catalyzed Enantioselective Mannich Reactions with α-Aryloxyacetaldehydes
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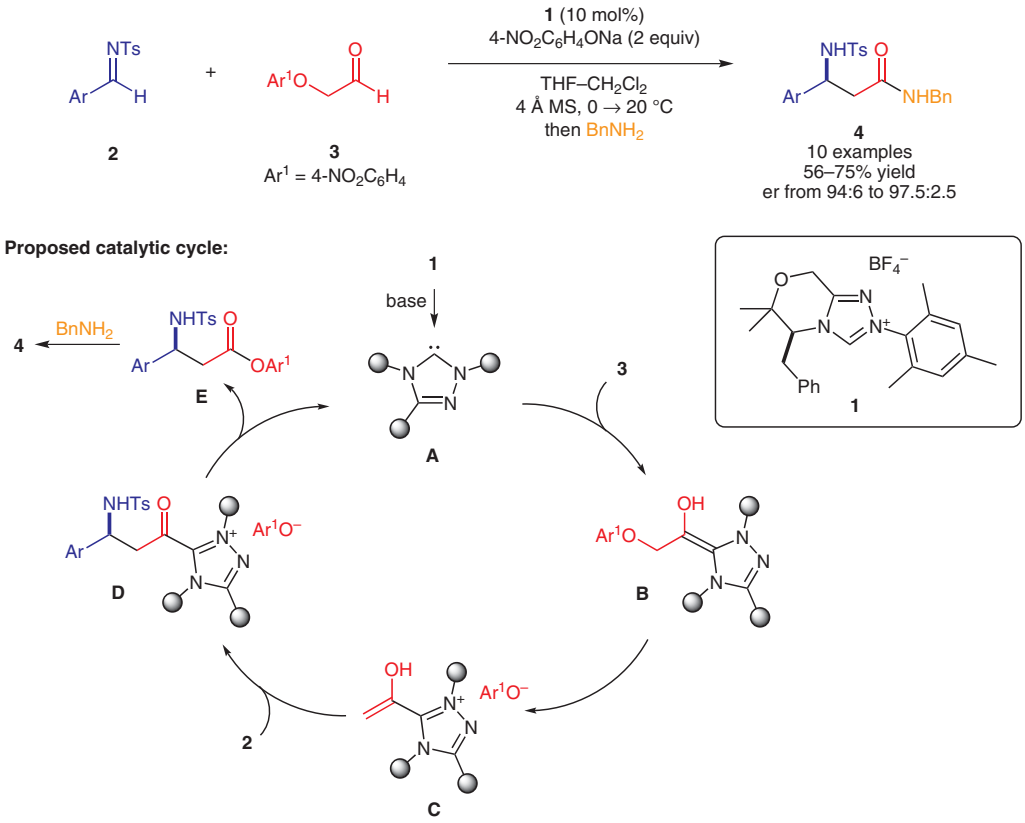
Enantioselective N-Heterocyclic Carbene Catalyzed Mannich Reaction



Significance: An enantioselective addition of α-aryloxyacetaldehyde **3** to aromatic imines **2** was reported to proceed under N-heterocyclic carbene catalysis. Initial products, amino esters **E** were transformed to the corresponding amides by treatment of the reaction mixture with benzylamine. With chiral precatalyst **1**, β-amino amides **4** have been obtained in useful yields and high enantioselectivity. Other in situ transformations of **E** were also demonstrated affording β-amino alcohols, esters, carboxylic acids or peptides in a one-pot reaction.

Comment: The catalytic generation of enolates is of a great importance due to their broad utility in organic synthesis. The Scheidt group previously reported that N-heterocyclic carbenes catalyze the formation of enolates/enols through an elimination process of α-aryloxyaldehydes (*Org. Lett.* **2009**, *11*, 105). Here, they use this strategy to perform a Mannich reaction. Enolate/enol intermediate **C** is trapped by tosylimine to afford β-amino acyl azolium intermediate **D**. Aryloxy anion liberated during enol formation step reacts with **D** to regenerate the catalyst and deliver the product **E** which serves as an activated intermediate for subsequent transformations.

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Key words
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NHC catalysis
enolates
β-amino acids