Development of 1,3,2-Dioxaborolan-4-one Catalyst for Dehydrative Condensation toward Peptides Synthesis

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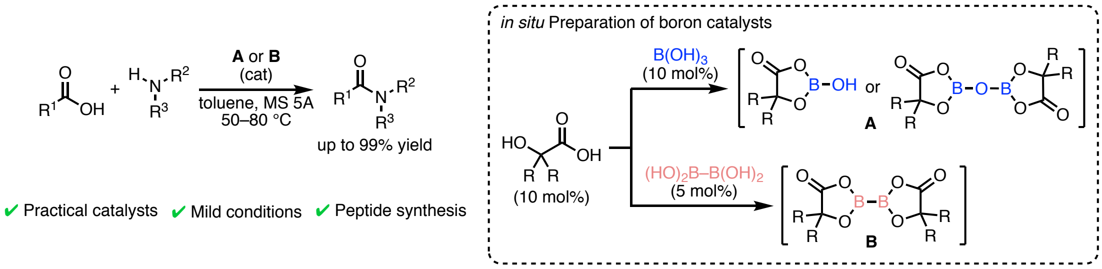
Dehydrative condensation of carboxylic acids with amines is one of the most straightforward methods to synthesize amides including peptides, which are present in various pharmaceuticals. Compared with the traditional methods using coupling reagents, catalytic methods are more environmentally friendly and atom-economic because they generate water as a sole byproduct. Since Yamamoto and Ishihara's pioneering work using boronic acids as catalysts,[1] great progress has been made in developing several highly effective boron catalysts for direct amidation. However, their involvements in peptide synthesis were limited due to high reaction temperature.[2] Recently, some innovative multi-boron catalysts were reported to perform high activities in catalytic peptide coupling, but they still suffer from increasing complexities and cost.[3] Therefore, with a target of practical boron catalysts for mild amide bond formation, our strategy is to enhance the catalytic efficiency of commercially available and simple $B(OH)_3$[4] and $(HO)_2B–B(OH)_2$[5] by using an appropriate additive.

Here, we developed practical dehydrative condensations catalyzed by 1,3,2-dioxaborolan-4-one that could be generated *in situ* from $B(OH)_3$ or $(HO)_2B–B(OH)_2$ with α,α-disubstituted α-hydroxycarboxylic acid as an additive. Under relatively mild conditions, carboxylic acids and amines were condensed to provide the corresponding amides in high yield, which also finds a potential application in direct peptide synthesis.



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