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Facile Synthesis of Peptidyl Salicylaldehyde Esters and Its Use in Cyclic Peptide Synthesis
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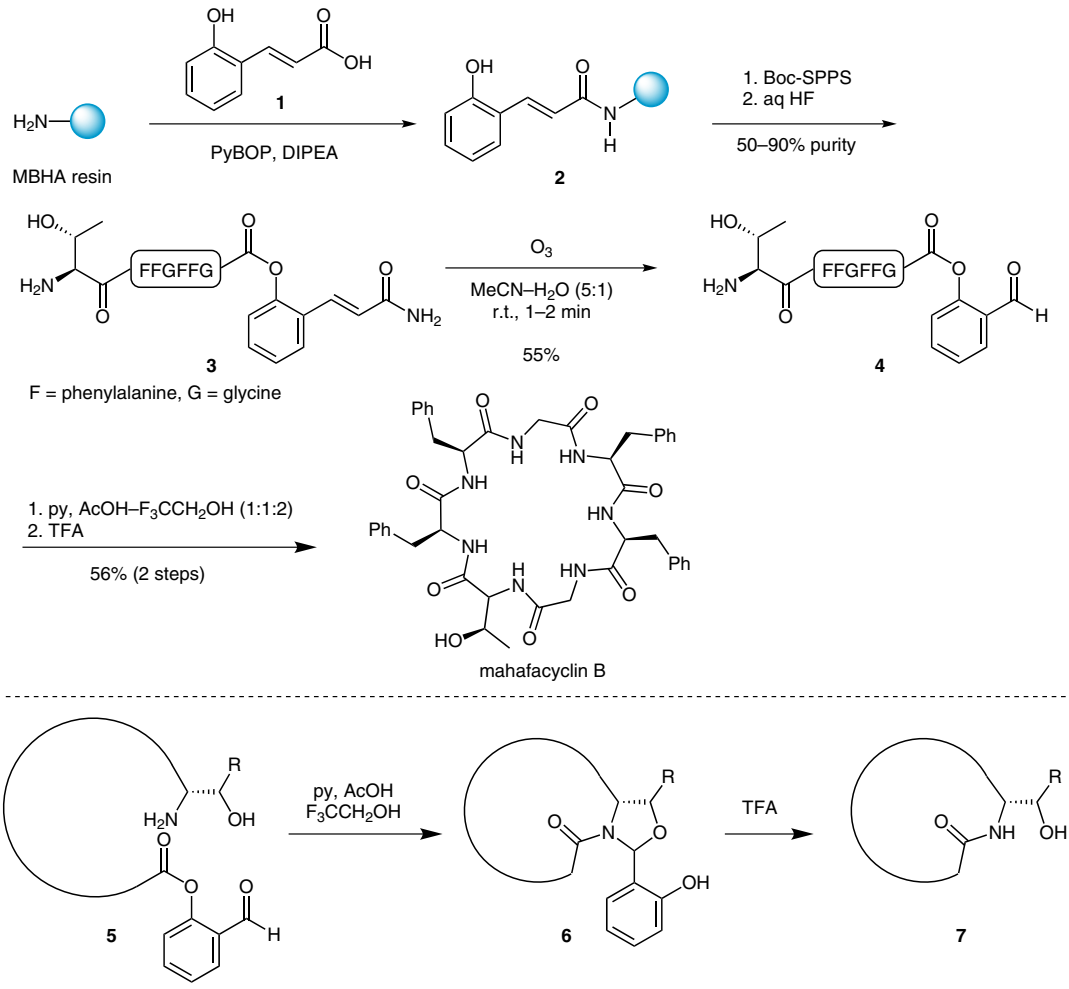
Cyclic Peptide Synthesis Using Peptidyl Salicylaldehyde Esters



Significance: A protocol for the solid-phase synthesis of cyclopeptides was described. Starting from MBHA resin and **1**, peptide **3** was prepared in 50–90% purity utilizing Boc-SPPS. Ozonolysis of **3** afforded a salicylaldehyde ester peptide **4** in 55% yield (other 15 examples: 42–89% yield). The reaction of **4** in the mixture of pyridine, acetic acid and 2,2,2-trifluoroethanol (1:1:2) followed by TFA treatment gave mahafacyclin B in 56% yield over two steps (other 7 examples: 29–65% yield).

Comment: The present cyclization of salicylaldehyde ester peptides bearing a Thr or Ser N-terminal residue (**5**) proceeds via the formation of salicylidene *N*,*O*-acetals **6**. Li's group reported a similar approach on the cyclic peptide synthesis independently (C. T. T. Wong et al. *Angew. Chem. Int. Ed.* **2013**, *52*, 10212).

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Category
Polymer-Supported Synthesis

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