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).