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Chemoselective Peptide Cyclization and Bicyclization Directly on Unprotected Peptides  

**Synthesis of Cyclic and Bicyclic Peptides**

Significance: Due to their unique properties, cyclic peptides and their synthesis have received considerable attention from medicinal chemists. The authors have developed an ortho-phthalaldehyde-guided chemoselective cyclization of unprotected peptides.

Comment: This cyclization reaction for the synthesis of cyclic and bicyclic peptides is guided successfully by ortho-phthalaldehyde. The target compounds are obtained in high conversion yields with excellent chemoselectivity.

**Selected examples:**

1. AcNH-Lys-Ala-Ala-Ala-Cys-Phe-CONH₂  
   98% conversion yield

2. AcNH-Cys-His-His-Ala-Leu-Thr-His-Ala-Lys-CONH₂  
   >98% conversion yield

3. AcNH-Cys-Lys-Val  
   >98% conversion yield

4. AcNH-Cys-Lys-Leu  
   94% conversion yield

5. AcNH-Cys-Lys-Glu  
   90% conversion yield

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