Efficient Method for Cyclic Peptide Synthesis Mediated by Acylammonium Species

Significance: Cyclic peptides are one of the most useful compounds as drugs. Although these compounds are generally synthesized by head-to-tail cyclization, the use of an excess amount of expensive coupling reagents and long reaction times are problematic. The authors have revealed that the acylammonium species generated from inexpensive tertiary amine and alkylchloroformate is an efficient coupling reagent for this approach.

Comment: Acylammonium species selectively react with C-terminal carboxylate by ionic interaction to give the active anhydride. Subsequently, head-to-tail cyclization occurs smoothly at the C-terminal anhydride with N-terminal amine. This method dramatically improved the efficiency of reactivity compared with traditional pathways to synthesize penta- and tetra-peptides.