PEPTIDE SELF ASSEMBLY CONFERENCE 2026
MAINZ. GERMANY
FROM DYNAMIC STRUCTURES TO FUNCTIONAL MATERIALS

Beyond Acyl Adenylates: Tailored Phosphate Esters Drive Pathway-Dependent Peptide Assembly

A. Sharma,[1,2] K. Dai[3], T. Pramod[2,3], R. Thoman[1,4], Y. Thoman[1], C.G. Pappas[2,3*]

[1]FIT – Freiburg Center for Interactive Materials and Bioinspired Technologies, University of Freiburg, Georges-Köhler-Allee 105, 79110, Freiburg, Germany. [2]Institute of Organic Chemistry, University of Freiburg, Albert-Strasse 21, 79104, Freiburg, Germany. [3]DFG Cluster of Excellence Cluster of Excellence livMatS @FIT, University of Freiburg, Germany. [4]Freiburg Materials Research Center (FMF), University of Freiburg, Stefan-Meier-Strasse 21, 79104, Freiburg, Germany.

Phosphate esters and anhydrides are central to life, known for their unique combination of reactivity and stability, powering key biological processes. Acyl and phosphoryl transfer reactions in particular, underpin essential functions in metabolism, signaling and molecular construction. However, outside of biology, coupling of acyl phosphates with selective processes such as acyl and phosphoryl transfer remain challenging. Here, we explore the potential of amino acyl phosphate esters as structural intermediates in abiotic peptide assembly. By systematically varying the phosphate leaving group ethyl, phenyl, naphthyl, or dodecyl, while keeping the amino acid residue constant, we demonstrate how subtle structural differences dictate divergent supramolecular outcomes and guide distinct reaction pathways. Ethyl and phenyl substitution resulted in soluble phosphate esters while naphthyl and dodecyl formed compartments. Each amino acyl phosphate reacts with amino acid nucleophiles to yield an identical covalent product, yet their assemblies differ profoundly. The self-assemblies of the formed dipeptides depend on the followed pathway (Figure 1). This approach also enables selective acyl transfer reactions for peptide coupling tailored to the reactivity profiles of specific phosphate esters in competitive experiments. We also harnessed these amino acyl phosphate esters for phosphoryl transfer reactions using different phosphoryl agents such as adenosine monophosphate, orthophosphoric acid, and pyrophosphoric acid to investigate their influence on peptide oligomerization, owing to variations in reactivity.[1,2]

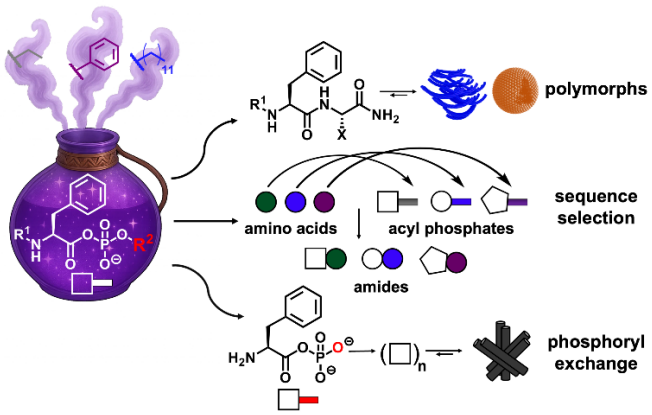

Figure 1. Tailored Phosphate Leaving Groups Direct Pathway-Dependent Self-Assembly.

References:

[1]Sharma, A. et al., *Nat. Commun*. ***16*** (1), 1306 (2025).
[2]Sharma, A. et al., *J. Am. Chem. Soc*. ***148*** (8), 8200-8212 (2026).