

## Systems chemistry of aminoacyl phosphates: Spontaneous and selective peptide oligomerisation in water driven by phase changes.

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**Abstract:** Formation of peptide bonds in biology is initiated by nucleotide triphosphates, where reactive intermediates and complex biological machinery give rise to the construction of polypeptides. Outside of biology, unravelling the pathways and mechanisms that allow spontaneous and selective peptide elongation in aqueous abiotic systems remain challenging. Herein, by following the systems chemistry of aminoacyl phosphates, we demonstrated the autonomous and length-selective peptide oligomerisation in water in the time scale of minutes. We observed spontaneous phase changes, where short oligomers are prevalent in solution, while in the aggregated phase, longer oligomers are populated and self-protected based on their self-assembly propensity. The pathway and the chemical information in the structure of the activated monomers dictate the lifetime of reactive intermediates and the degree of oligomerisation. Thus, oligomers up to dodecamers were observed, where tetramers and pentamers formed in high yield and self-selected from different monomers, capable of assembling into highly ordered architectures. We expanded our approach into multicomponent systems, where by sequential addition of various phosphate monomers continuous synthesis has been achieved, where the distribution in the different phases is dominated by heterooligomers. These findings suggest that the systems chemistry of amino acyl phosphates can activate a selection mechanism for oligoamide formation, by merging aqueous synthesis and self-assembly.