Multivalent Macromolecules Redirect Nucleation-dependent Fibrillar Assembly into Discrete Nanostructures

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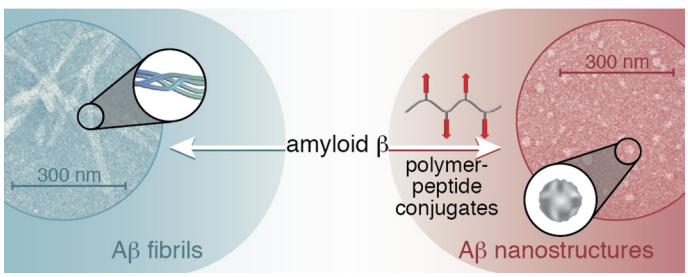
Manipulating the size and shape of non-covalent multivalent assemblies is an ongoing challenge in the field of supramolecular polymers. Following a mechanistic approach, we reasoned that nucleation–elongation kinetics presents unique opportunities for controlled growth since the final outcome is likely to depend on the structure and dynamics of critical-nucleus formation. Taking fibrillar assembly of amyloid β (Aβ) peptide as the model system of nucleation-dependent supramolecular polymerization, here we report multivalent polymer–peptide conjugates (mPPCs) that redirect fibrillar assembly of Aβ to form discrete nanostructures. The mPPCs were rationally designed to target Aβ intermediates formed prior to critical nucleation. Atomic force microscopy and transmission electron microscopy studies show that in the presence of mPPCs, Aβ self-assembles into zero-dimensional discrete nanostructures with lateral dimensions approximately in 5–35 nm, while Aβ alone self-assembles into one-dimensional fibrils in micrometer. Thioflavin T kinetics fluorescence assays demonstrate that mPPCs suppress Aβ fibrillogenesis. The mPPCs may thus represent a prototypical molecular design of multivalent macromolecules able to control the final shape of supramolecular polymers assembled via a nucleation-dependent mechanism.



Rhodium-Catalyzed Amide Bond Formation

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Established approaches for amide bond synthesis rely on stoichiometric generation of an activated carboxylate via the reaction of carboxylic acids and active coupling reagents. These methods, while commonly employed, are expensive and generate significant quantities of waste. As such, the development of a selective transition metal-catalyzed amide synthesis has been an area of significant focus for organometallic chemist. Herein, we report a chemoselective direct amidation of allylic alcohols or aldehydes with an amine, using a Rh(I)/BINAP complex as the catalyst in a benzene/water bi-phasic system and generating ethyl benzene or isopropanol as the only stoichiometric byproducts. Under our conditions, the desired amides are generated in moderate to good yield with both primary and secondary amines.