Supramolecular Polymerization

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Programmable Supramolecular Polymerizations

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Supramolecular polymers represent a unique class of materials whose particular functions are derived from the dynamic noncovalent interactions by which their monomeric units are held together.[1a,b] Current applications of these materials can be found in the area of organic electronics and as biomaterials for drug delivery and tissue engineering. Until a few years ago, the development of novel supramolecular polymers tailored for specific functions mainly relied upon an Edisonian approach, thus yielding a large library of molecules which self-assemble into a wide variety of supramolecular architectures. Although the molecular structures of the monomers were rationally designed to induce anisotropic noncovalent interactions, many of the mechanistic details on the growth mechanisms of supramolecular polymers were unknown at that point. This lack of insight has led to a great discrepancy between the large number of molecules which have been shown to aggregate into one-dimensional structures and the limited ability to program molecular self-assembly pathways to result in supramolecular structures with predefined molecular organization and length distribution.

By recognizing the analogy between supramolecular polymerization of organic molecules and aberrant aggregation of proteins into amyloidal fibers,[2] a number of recent thermodynamic and kinetic studies[1b,3] have shed light on the complex interplay between the molecular information encoded into synthetic monomers and the mechanism by which the corresponding aggregates grow in size. Thermodynamic studies show that monomer addition to the growing aggregates often follows either an isodesmic or nucleation/elongation mechanism. In the isodesmic mechanism, the Gibbs free energy of monomer association is independent of the length of the aggregate and all oligomers and polymers are lower in energy compared to the monomer.[1b,2a] Nucleation/elongation is a cooperative mechanism where growth of large aggregates in the elongation phase is more favorable than the formation of oligomers in the nucleation phase. At low concentration, the nucleus and pre-nucleus oligomers have a higher Gibbs free energy than the monomer, thus providing a significant energetic barrier for self-assembly resulting in characteristic lag phases in supramolecular polymerization kinetics. Kinetic studies[3c] have indeed revealed such lag phases but also showed the presence of competing off-pathway aggregates which are able to exert influence on self-assembly dynamics by buffering the available free monomer.[3c,d] These off-pathway aggregates represent supramolecular architectures in which the monomer assumes a different conformation or orientation compared to on-pathway aggregates. Correlating the formation of these off-pathway assemblies to the molecular information encoded into the monomers is a crucial next step towards programmable supramolecular polymerizations. Next to the role of off-pathway aggregates, the role of cosolvents and fragmentation events have also been discussed.[3d]

The increased mechanistic understanding of supramolecular polymerizations has now culminated in the development of two novel strategies[4,5] which are able to tightly control one-dimensional self-assembly processes, thus resulting in the formation of unprecedented supramolecular polymer architectures. Showing the universality of the two approaches, Würthner et al.[4] and Miyajima and Aida et al.[5] have both based their methodology on the rational design of additional noncovalent interactions which selectively stabilize monomeric species. These interactions introduce an additional layer of kinetic control over the molecular self-assembly pathways and ensures highly controlled aggregate growth (Figure 1). This versatile approach is an extension of previous work by Sugiyasu and Takeuchi et al., wherein living supramolecular polymerization of porphyrin dyes is rationally designed by seed-induced growth in combination with competing isodesmic off-pathway aggregation.[6] The competing off-pathway J-aggregates function as a kinetic trap by sequestering free monomers from solution, thereby preventing nucleation of thermodynamically stable H-aggregates. Addition of H-aggregate seeds, short oligomers prepared in a separate procedure, readily converts the off-pathway assemblies into thermodynamically stable H-aggregates. The seed molecules thus act as an initiator, analogous to conventional polymerizations, and result in a living supramolecular polymerization characterized by assemblies of controlled length and narrow polydispersity.

Showing the generality of this approach, Würthner and co-workers now report the seeded supramolecular polymerization of a perylene bis(imide) organogelator showing similar characteristics but with an important twist. In contrast to the previous work on the π-conjugated porphyrin dyes, off-pathway assemblies are absent in this system. Instead, kinetic control is achieved by a pre-equilibrium in which the monomer is partitioned in an aggregation-competent and aggregation-incompetent conformation as a result of intra-

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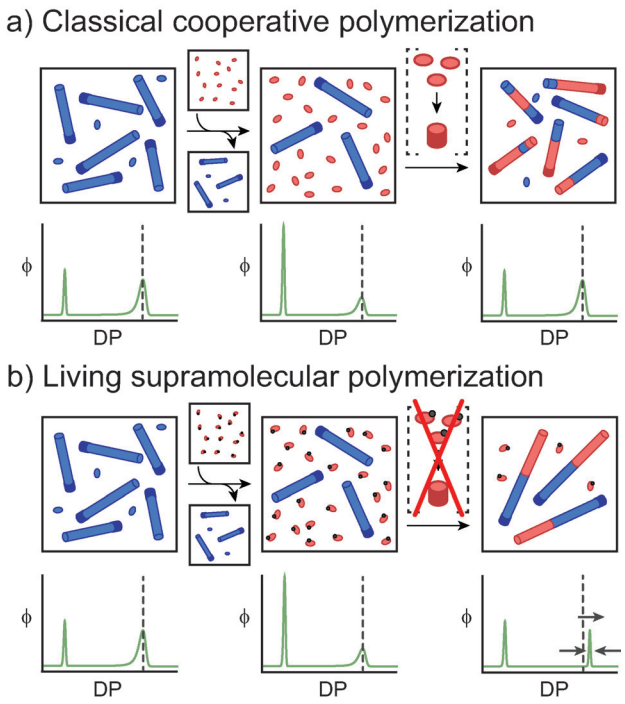

Figure 1. Schematic representation of supramolecular polymerization for: a) a classical nucleation/elongation mechanism and b) supramolecular living systems. Polymerization starting from existing seeds (left panels; existing polymer in blue) is initiated by addition of a large amount of monomers (middle panels; new molecules in red). In a classical cooperative system (a), the high concentration of monomer leads to new nucleation and subsequent re-equilibration of the system (right panel), as evident from the molecular size distribution (green traces), which is identical to the initial state. In living supramolecular polymerizations (b) monomers are present in a trapped state which kinetically inhibits nucleation, thus allowing only elongation (right panel) and leading to aggregates of high degree of polymerization (DP) with narrow dispersity, particularly after iterative monomer addition.

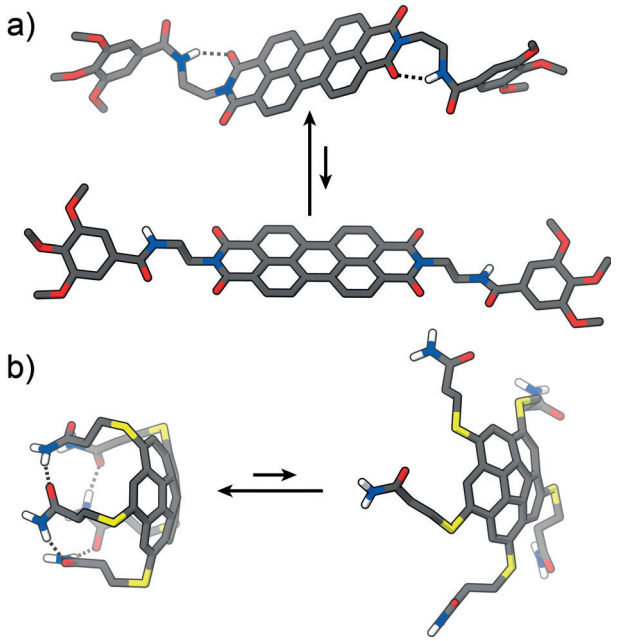

Figure 2. a) Pre-equilibria between aggregation-incompetent and aggregation-competent conformations of the monomer in the perylene bis(imide) system used by Würthner et al. (a). b) The corannulene derivative designed by Miyajima, Aida et al. The aggregation incompetent conformation is created by intramolecular hydrogen bonding (indicated by dotted lines), and the pre-equilibrium strongly favors this conformation, which is a prerequisite to achieving living supramolecular polymerizations. In (a) and (b), atoms are color-coded by element, nonpolar hydrogens have been omitted, and the solubilizing alkyl sidechains have been removed for clarity.

molecular hydrogen bonding (Figure 2a). Because this equilibrium is in favor of the aggregation-incompetent form and the rate of nucleation is highly dependent on the concentration of monomer, the nucleation of perylene bis(imide) aggregates is kinetically retarded and elongation can only take place after addition of seed assemblies. The simplicity of adapting the well-defined intramolecular interactions responsible for the aggregation-incompetent state provides many new avenues for rational engineering of living supramolecular polymerizations.

An elegant chiral example is provided in simultaneous work by Miyajima, and Aida et al., who capitalize on the preorganized amide groups in a corannulene derivative to create a trapped monomer (Figure 2b). With this array of intramolecular hydrogen bonds working in concert, the concentration of available monomer is extremely low and spontaneous nucleation is absent. In this example, cooperative aggregation is induced by addition of an N-methylated initiator molecule which lacks the internal hydrogen bonds and thus cannot aggregate by itself. However, it assists in the unfolding and subsequent self-assembly of the trapped monomer, again yielding well-defined aggregates through a living supramolecular aggregation mechanism. The highly ordered hydrogen-bonded structure of this molecule is also apparent in the aggregated state, as shown by CD and VCD measurements, and reflected in the perfectly homochiral aggregates which are formed when assembling chiral monomers. This homochirality can even be exploited to perform an optical resolution of a racemic mixture of monomers using a chiral initiator molecule, thus demonstrating the utility that a full understanding of all processes occurring in a supramolecular polymerization affords.

These two examples demonstrate that the increasing knowledge on the mechanistic details of supramolecular polymerizations has come to a stage where one-dimensional self-assembly pathways can be rationally engineered based on the chemical information encoded into the monomers. Conceivably, this high level of understanding gives access to a general route towards advanced aggregate architectures which were previously only attainable in very select systems, for example, supramolecular block copolymers.[7,8] These breakthroughs are only possible if supramolecular polymerization mechanisms are studied in depth and generalized at the system level, thus requiring a combination of carefully designed experiments and theoretical modeling. Parallel to the work on equilibrium supramolecular polymerizations, an exciting new direction that has emerged is that of far-from-equilibrium assemblies where aggregate growth is coupled to dissipation of chemical energy.[9,10] Such systems most closely

resemble the aggregation of cytoskeletal polymers such as actin and microtubule, and would, in theory, display functions unachievable by equilibrium supramolecular polymerizations.

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