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Supramolecular Block Copolymers

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The Link that Lasts: A New Frontier in Supramolecular Block Copolymer Design

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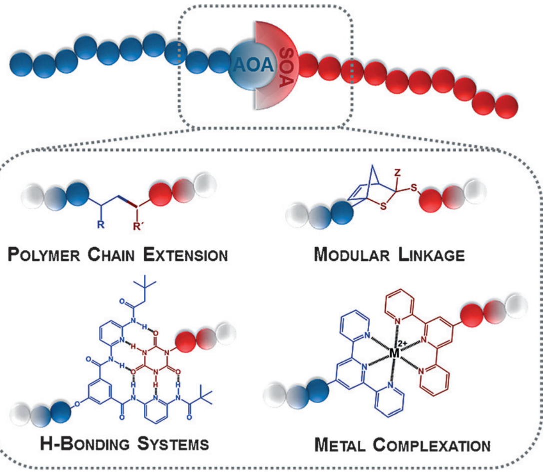
The design of (amphipilic) block copolymers is one of the oldest and most researched themes in polymer chemistry and substantial progress has been made over the last 20 years.[1] Block copolymers can be prepared through living polymerization methods, such as anionic polymerization,[2] or methods that show characteristics of living polymerization systems, such as reversible-deactivation radical polymerization.[3] In these cases, the two segments are joined through a carbon–carbon single bond and they can thus not be cleaved. However, these methods enable the generation of relatively high molecular weights (in the 100000 Dalton range), especially when using anionic polymerization. Functional block copolymers can be utilized for a wide range of applications, including templates, membranes, solar cells, drug delivery, and micelles to name just a few.[4]

However, more interesting from the perspective of nanoengineering are amphiphilic block copolymers where the two segments are joined via a weaker linkage since they offer the opportunity for disassembly in response to an external trigger such as temperature or a change of pH.[5] These linkage points include covalent ones (for example Diels–Alder or hydrolysable units, as well as photocleavable moieties) and supramolecular systems, for example those based on hydrogen-bonding motifs, metal complexes, or host–guest systems.[6] Covalent linkages are typically stronger and require harsher conditions to be opened (e.g. high temperatures or acidic conditions), while supramolecular bonding systems open readily and lead to comparatively unstable block copolymers (Scheme 1). Supramolecular amphiphilic block copolymers are typically not able to withstand sheer forces and exist in an equilibrium between the opened and ligated states in many solvents. These properties strongly limit their uses, for example, in solid-state phase separation for the design of nanostructured films.[7]



Scheme 1. Approaches to block copolymer structures via sequential living polymerization (top left), modular design with reversible linkages, for example, Diels–Alder-Adducts (top right), and weak supramolecular connections, such as H-bonding systems (bottom left) and metal complexation (bottom right).

A recent study by Bernard, Drockenmuller and coworkers[8] introduces a remarkable and highly stable new supramolecular bonding system inspired by a hydrogen-bonding donor–acceptor couple pioneered by Gong and coworkers,[9] which operates by using an asymmetric oligoamide (AOA) and symmetric oligoamide (SOA) binding motif. These motifs enable very strong binding between polymer segments, thereby allowing applications not seen before with existing H-bonding block copolymer systems, as well as the possibility to switch off the bonding system through a well-defined change to the solvent system (see Scheme 2). In order to exploit these motifs for amphiphilic block copolymer design, Bernard, Drockenmuller and co-workers synthesized controlling agents (so-called reversible addition fragmentation chain transfer (RAFT) agents) that enable the positioning of the SOA and AOA units at the chain termini with an additional spacer unit. The long alkyl spacer provides good solubility of the controlling agents in organic solvents and decreases steric interactions between the controlling agent functionalities (i.e., thiocarbonylthio groups) and the associ-

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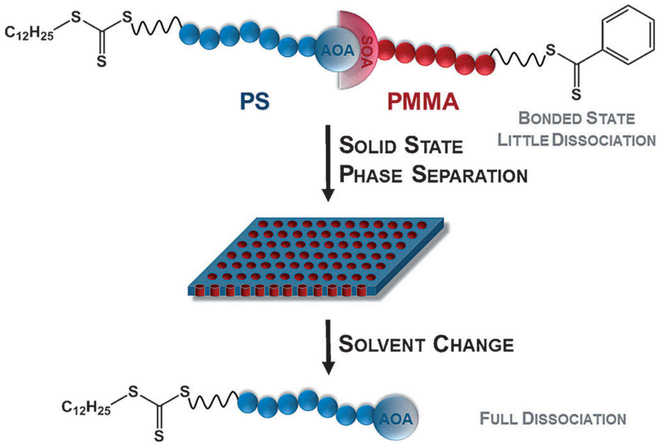

Scheme 2. Supramolecular amphiphilic block copolymers based on AOA and SOA motifs [polystyrene (PS) and poly(methyl methacrylate) (PMMA), respectively] with high stability in $CHCl_3$. Nanopatterning and subsequent release of the hydrophilic segment takes place in response to a solvent trigger.

ating motifs. They applied these novel RAFT agents to synthesize polystyrene and poly(methyl methacrylate) with AOA and SOA terminal groups, respectively, resulting in macromolecules that exhibit narrow polydispersity and molecular weights of up to 30 kDa.

Subsequently, the polystyrene AOA and poly(methyl methacrylate) SOA terminal groups were linked to give a highly stable block copolymer. Remarkably, these block copolymers were even stable to size-exclusion chromatographic analysis in chloroform, which is typically associated with high sheer forces on the macromolecules. In alternative solvents such as THF, however, no chromatographic trace of the block copolymer could be recorded, but rather traces associated with the separate blocks were observed. This observation already hints at a very strong solvent-dependent switchable interaction of the SOA and AOA chain termini.

Even more remarkably, the amphiphilic supramolecular block copolymer could be fashioned into nano-phase-separated patterns, for example, through a high-temperature annealing step. The hydrophilic block was removed from the nanopattern by a solvent-switchable disconnection of the SOA–AOA link to provide ready access to nanoimprinted surfaces (Scheme 2).

While Bernard, Drockenmuller and co-workers have shown one exciting example for the use of this highly solvent-orthogonal supramolecular block copolymer disassembly system in the field of nanopatterning, many applications are now ready to be explored. These include:

1) The generation of step-growth polymers based on telechelic precision polymers carrying the SOA and AOA motifs or—as a variant—step polymers based on small bifunctional units carrying both units. Such step-growth polymers could subsequently be debonded on demand.
2) The design of (hyper)branched macromolecular structures carrying SOA and AOA motifs for the generation of cross-linked networks (including hydrogels) that can be disassembled on demand by a solvent trigger and could be highly useful, for example, in the field of cell-growth systems.
3) Recodable surfaces covered, for example, with AOA units that can be patterned in a spatially resolved fashion through light-triggered chemistry, which can serve as receptors for SOA functional polymer chains as well as peptides and proteins. The patterned moieties could subsequently be released through solvent switching.
4) Even more challenging, yet not out of the realm of possibility, is the self-assembly in solution to form micellar systems that can be cross-linked in their outer shell via an AOA/SOA association and disassembled in response to a solvent trigger to release cargo from the inner phase of the micelle.

As enticing as these prospective applications might sound, substantial research effort is required to demonstrated that the bonding system is applicable to other combinations of polymer segments (including those of a stimuli-responsive nature) and that the motifs can be incorporated into more complex macromolecular architectures. We see the fine adjustment of the solvent combinations that allow switching between strong bonding and the open configuration, in conjunction with the requirements for the individual polymer solubilities, as a particular challenge. Furthermore, certain applications, such as the construction of reversibly forming hydrogels, require solvent systems that are compatible with cellular material. It is an open question how far the molecular nature of the bonding motifs can be tuned to enable adjustment of the required solvent mixtures for for bonding and debonding. Finally, we submit that the unique SOA/AOA macromolecular H-bonding system is susceptible to strong entropic effects on the bonding equilibrium as a function of the length of the ligated macromolecular building blocks (and possibly their persistence length), as has recently been demonstrated for the Hamilton wedge/cyanuric acid couple.[10] The exploitation of entropic effects may offer a wide range of unique design opportunities for influencing the equilibrium position.

In summary, the highly innovative combination of an extremely strongly binding hydrogen-bonding motif that is coupled in a specific solvent but can be triggered to disassemble in another solvent mixture with precision polymer design based on RAFT technology is one of the finest examples of contemporary soft matter science of this year and we expect that the system will find applications in a wide range of fields, including those noted above.

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