Block Copolymer Nanoparticles | **Hot Paper**

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A Facile Synthesis of Dynamic, Shape-Changing Polymer Particles[**]

*Daniel Klinger, Cynthia X. Wang, Luke A. Connal, Debra J. Audus, Se Gyu Jang, Stephan Kraemer, Kato L. Killops, Glenn H. Fredrickson, Edward J. Kramer, and Craig J. Hawker**

***Abstract:** We herein report a new facile strategy to ellipsoidal block copolymer nanoparticles that exhibit a pH-triggered anistropic swelling profile. In a first step, elongated particles with an axially stacked lamellae structure are selectively prepared by utilizing functional surfactants to control the phase separation of symmetric polystyrene-b-poly(2-vinylpyridine) (PS-b-P2VP) in dispersed droplets. In a second step, the dynamic shape change is realized by cross-linking the P2VP domains, thereby connecting glassy PS discs with pH-sensitive hydrogel actuators.*

The ability of nature to precisely control the shape and functionality of nanoparticles in a range of biological systems has long motivated researchers to strive for similar control in synthetic nanomaterials.[1] This challenge has been partially fulfilled in inorganic systems, where the ability to tailor the shape and size to tune the properties has been extensively studied.[2] In direct contrast, the ability to control the shape and functionality of polymer-based nanoparticles is still in its infancy,[3] with future success being critical for the preparation of bio-inspired materials with applications ranging from drug-delivery systems to artificial camouflage.[1c]

In addressing this need, the development of dynamic, shape-changing polymer particles requires three main structural features to be incorporated into a single system: shape anisotropy, spatial control over the internal morphology, and the introduction of stimuli-responsiveness to the nanoparticles. Unfortunately, current examples address each aspect separately, with multifunctional, dynamic systems not being realized.[3] Anisotropic particles, for example, have been prepared by a multistep procedure which relies on the stretching of spherical particles.[3a,4] Even though such elongated particles show interesting properties[5] only a few examples combine shape anisotropy with either well-defined internal morphologies[6] or stimuli-responsive properties.[7] For example, we have recently reported the use of tailored Au nanoparticles as surface-active agents for the preparation of shape-anisotropic particles with an internally structured morphology.[8] Although the potential of block copolymer self-assembly in colloidal systems is promising,[9] the use of Au nanoparticles represents a significant synthetic limitation and did not lead to a dynamic, stimuli-responsive material. As a result, the facile formation of multifunctional nanoparticles that combine all three of the mentioned features (shape anisotropy, internal morphology, and stimuli-responsiveness) remains a major challenge.

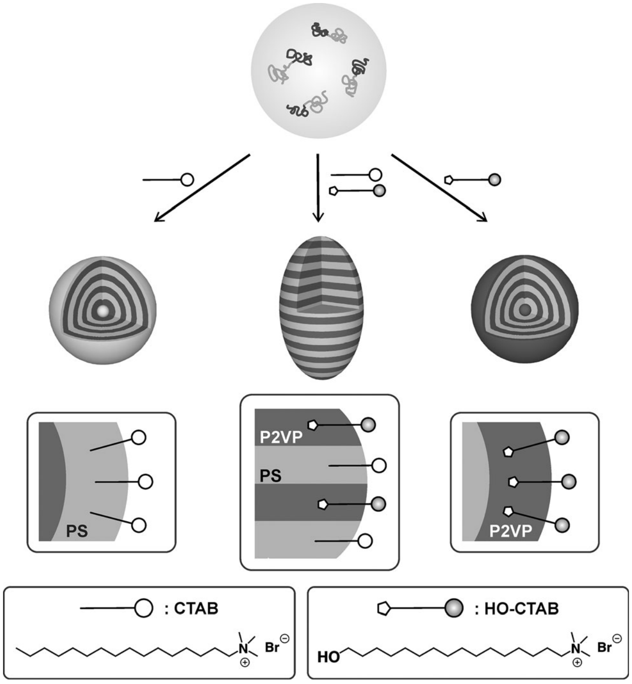

Figure 1. Schematic representation of a mixed surfactant strategy for controlling the self-assembly of PS-*b*-P2VP and the generation of particles with defined shape and internal morphology by solvent evaporation from droplets.

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[*] Dr. D. Klinger, C. X. Wang, D. J. Audus, Dr. S. G. Jang, Dr. S. Kraemer, Prof. G. H. Fredrickson, Prof. E. J. Kramer, Prof. C. J. Hawker
Materials Research Laboratory, University of California
Santa Barbara, CA 93106 (USA)
E-mail: hawker@mrl.ucsb.edu

Dr. L. A. Connal
Department of Chemical and Biomolecular Engineering
University of Melbourne, Victoria 3010 (Australia)

Dr. K. L. Killops
U.S. Army Edgewood Chemical Biological Center
Aberdeen Proving Ground, MD 21010 (USA)

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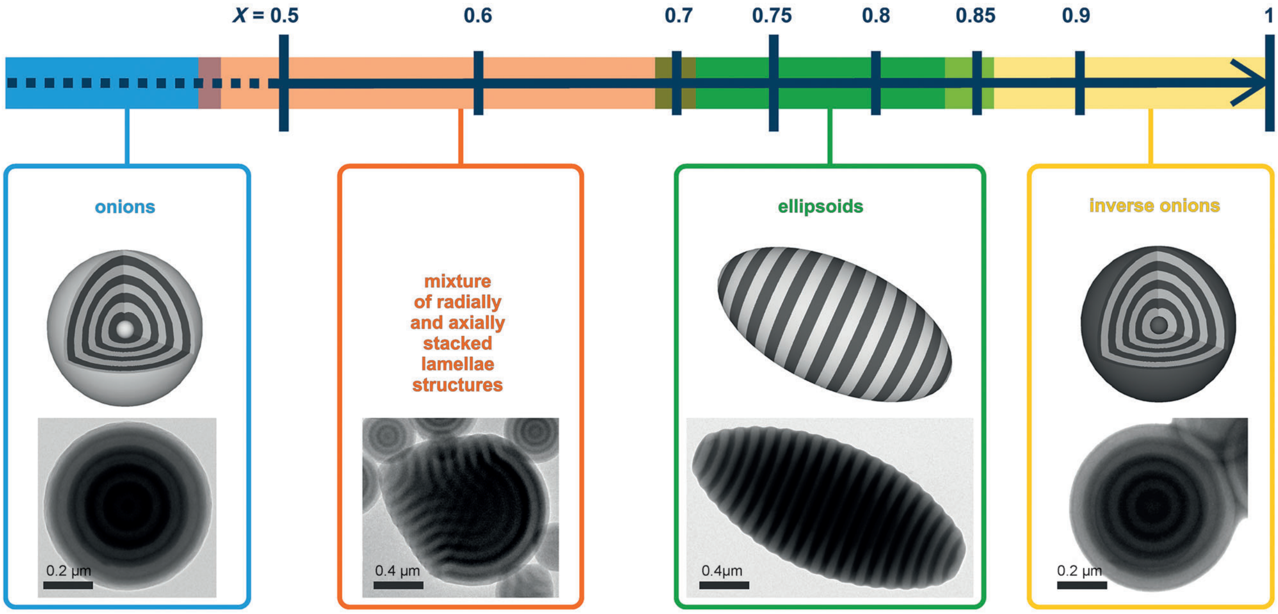

Figure 2. Schematic representation of the influence of the mass fraction (X) of HO-CTAB—in a binary mixture with CTAB—on the shape and internal morphology of particles formed from a PS-*b*-P2VP (MW = 102k–97k Da) diblock copolymer (representative TEM images are provided for each distinct morphological region).

Herein, we report the development of a facile and powerful new strategy for the preparation of functional particles that serves as a broad platform for nanoscale materials. Key to the success of this strategy is the use of functional surfactant mixtures to control the phase separation of the symmetric polystyrene-*b*-poly(2-vinylpyridine) (PS-*b*-P2VP) block copolymers (BCPs) within dispersed nanoparticles. In analogy with the utilization of random copolymers in block copolymer lithography,[10] mixtures of surfactants may allow for the accurate tuning of surface energies, thereby leading to selective switching between the three distinct internal morphologies shown in Figure 1, with the final result being the controlled synthesis of spherical or elongated particles. This approach further allows for secondary chemistry, such as cross-linking of the P2VP domains, to be carried out. These multifunctional particles not only combine an overall shape anisotropy with a well-defined internal morphology but also display a reversible pH-dependent swelling of the P2VP layers. Finally, the axially stacked internal lamellae morphology translates to an anisotropic swelling profile, thus resulting in a pH-triggered dynamic shape change as a result of a preferential stretching/shrinking of the elongated particles along the long axis.

The major initial challenge was the development of a method to control the phase separation of block copolymer building blocks in emulsion droplets. Traditionally, the use of a single surfactant or no surfactant at all leads to an "onion-like" radial morphology.[11,3d] This is due to preferential wetting of one block by the surfactant layer surrounding the dispersed particle. Such behavior is in analogy with the selective wetting and associated self-assembly of BCPs in thin films. For thin films, the introduction of a neutral layer, typically a random copolymer, between the BCP and substrate and/or air can induce a perpendicular orientation of lamellae and cylinders.[12] Our new approach to controlling the interaction between block copolymers and the surrounding medium is based on the concept of a neutral layer derived from a mixture of two surfactants. In this design, each surfactant would be preferential for one specific domain. Consequently, intermediate ratios of the two surfactants would lead to nonpreferential interactions, in effect a neutral interface. In initial experiments with PS-*b*-P2VP and 100 % cetyltrimethylammonium bromide (CTAB) as the surfactant, the expected radial morphology was observed with polystyrene as the outermost layer as a consequence of hydrophobic interactions (Figure 2, and see Figure S-1a in the Supporting Information). The ability of the 2VP groups to serve as hydrogen-bond acceptors was exploited when designing a surfactant that would exhibit a preferential interaction with the P2VP phase.[13] A hydroxy group was, therefore, incorporated at the ω-position of CTAB to give HO-CTAB (Figure 1).[14] Significantly, the use of HO-CTAB resulted in the anticipated reverse behavior, and nanoparticles with P2VP as the outermost layer of an "inverse onion" morphology (Figure 2, and see Figure S-1b in the Supporting Information) were obtained. This ability to switch the layer sequence by switching surfactants suggests that a neutral layer will be obtained by adjusting the composition of the surfactant mixture. In analogy to the perpendicular orientation of lamellae in thin films, this neutral wetting behavior will permit particles with the desired internal stacked lamellae structure to be obtained.

To test this hypothesis, a series of PS-*b*-P2VP (MW = 102k–97k Da) particles was prepared using mixtures with various compositions of the two surfactants, whereby X is the mass fraction of HO-CTAB in relation to the total surfactant concentration (see the Supporting Information for the experimental data). The TEM images in Figure 2 demonstrate that tuning the mass fraction of surfactants is a facile technique to control both the self-assembly process and the particle shape. Radial structures with a PS layer clearly at the surface are obtained at high CTAB concentrations ($X \leq 0.50$). Significantly, as the mass fraction of HO-CTAB is increased above a 1:1 ratio ($X \approx 0.50$), a distinct morphology and shape change is observed to give spherical and nonspherical particles with a mixture of radially and axially stacked lamellae morphologies. A distinct transition is then observed at HO-CTAB concentrations X between 0.70 and 0.80, where only the desired stacked lamellae morphology and ellipsoidal particle shape are observed. This confirms the validity of this mixed surfactant approach and the existence of a specific range of HO-CTAB/CTAB ratios for which the interfacial energies between the surfactants layer and the domains of the BCP are balanced. For the mid-point of the neutral range, $X = 0.75$, the interfacial balance results in all the particles assuming an ellipsoidal shape, with axially stacked lamellae persistent throughout the entire particle (Figure 3). The simplicity and scalable nature of this strategy represents a modular synthetic technique for the preparation of nanostructured polymer ellipsoids.

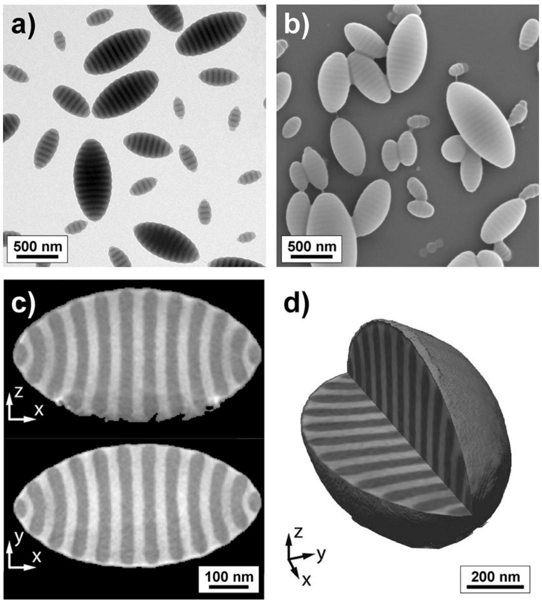

Figure 3. Electron micrographs of the prolate ellipsoids with axially stacked lamellae obtained by the solvent evaporation-driven self-assembly of PS-*b*-P2VP (MW = 102k–97k Da) from $CHCl_3$ droplets emulsified with a mixture of surfactants, X(HO-CTAB) = 0.75: a) TEM, b) SEM, c) TEM slices extracted from the full 3D reconstructed image, and d) reconstructed 3D image from TEM tomography.

Importantly, the aspect ratio of these shape-anisotropic particles is not a fixed parameter, since the elongation is determined by the counterbalance of three different contributions to the free energy. Theoretical calculations (see the Supporting Information) indicate that it is possible to shift this balance and thus tune the particle aspect ratio.[8] To understand the effect of the BCP molecular weight, three different lamellae forming PS-*b*-P2VP diblock copolymers with molecular weights of 102k–97k, 40.5k–41k, and 20k–20k Da were examined. By plotting both the theoretical and experimental aspect ratio (A) versus the long axis (L) of ellipsoidal particles (formed from a HO-CTAB/CTAB ratio of 3:1, that is, $X = 0.75$; see Figure 4b) it is evident that elongation not only increases with block copolymer molecular weight but also with particle size. Regarding the latter, the

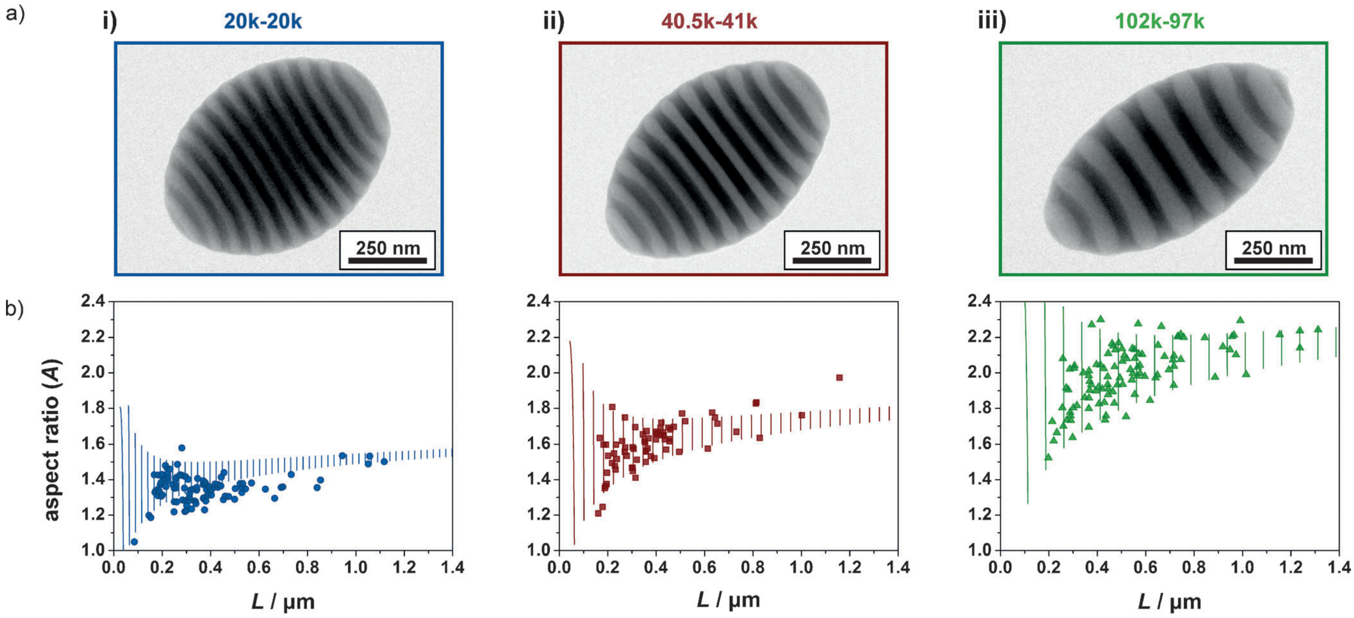

Figure 4. Influence of BCP molecular weight on the shape anisotropy of ellipsoidal PS-*b*-P2VP nanoparticles with axially stacked lamellae obtained for neutral wetting conditions at a 3:1 ratio of HO-CTAB/CTAB ($X = 0.75$): a) TEM images of similar sized ($L \approx 550$ nm) BCP nanoparticles obtained from PS-*b*-P2VP diblock copolymers with molecular weights of i) 20k–20k, ii) 40.5k–41k, and iii) 102k-97k Da; b) plots of experimental (●) and theoretically (——) predicted aspect ratios (L/D) as a function of the long axis (L) for representative populations of the three respective diblock copolymer molecular weights.

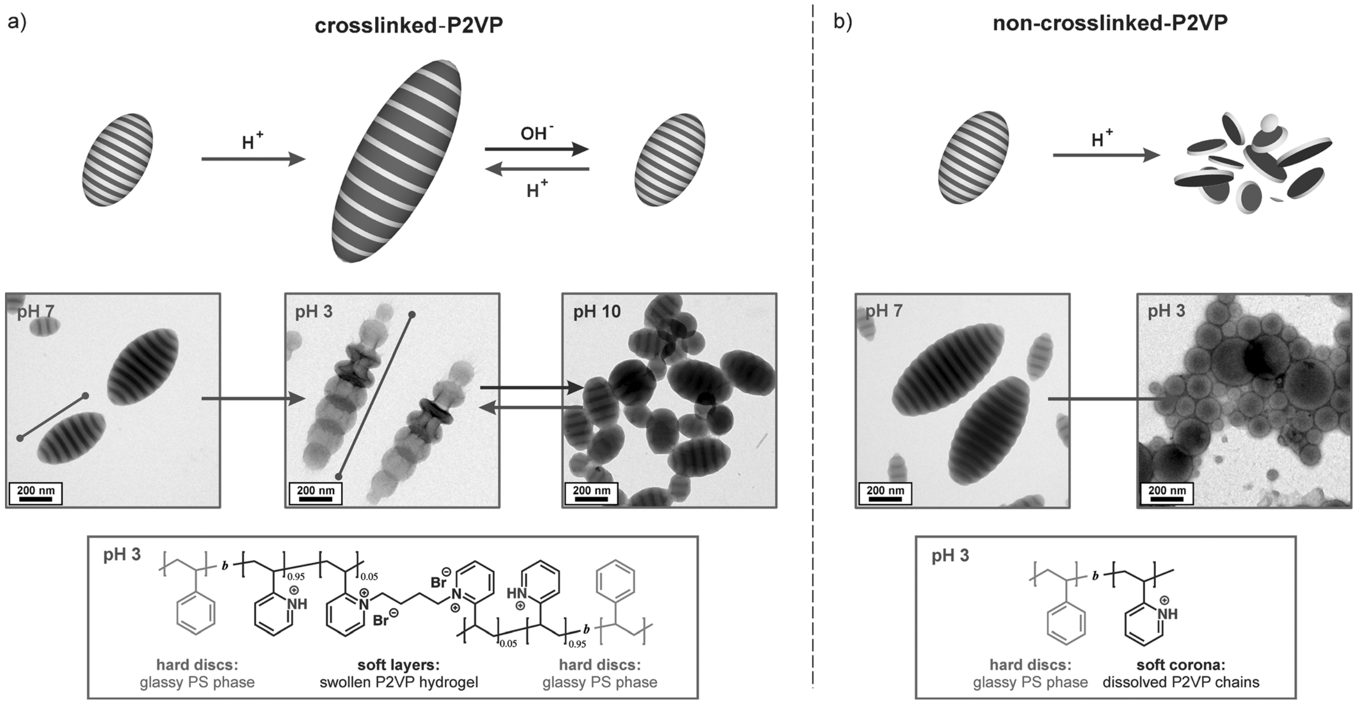

Figure 5. Investigations on the pH-responsive behavior of PS-*b*-P2VP ellipsoidal particles with axially stacked lamellae: a) pH-triggered dynamic shape change for particles with cross-linked (5 mol% 1,4-dibromobutane) P2VP domains as a result of swelling/deswelling of the P2VP-based hydrogel discs. The demonstrated variation of the aspect ratio was fully reversible for at least three cycles; b) discrete nanodiscs were obtained for non-cross-linked systems because of solubilization of the P2VP chains.

theoretical model predicts that larger droplets/particles are easier to stretch since the surface energy of the droplets decrease relative to the bulk elastic and interfacial free-energy contributions on increasing the particle size (see the Supporting Information). This strong influence of the droplet volume on elongation is demonstrated by an increase in the aspect ratio with particle size (Figure 4b). Regarding the influence of the BCP molecular weight, the theoretical model predicts that it is easier to stretch particles consisting of BCPs with higher molecular weights since the energetic penalty for chain stretching is higher for shorter polymers. This assumption is strongly supported by the results in Figure 4, where decreasing the overall MW of the symmetrical PS-*b*-P2VP block copolymers decreases the aspect ratio of the colloids. As shown in Figure 4, TEM images of similarly sized particles (ca. 550 nm in length) demonstrate that different aspect ratios are obtained for similar L values, and a direct correlation between the number of layers per particle and molecular weight is obtained.

Having demonstrated the ability to tune the shape and internal morphology, the introduction of stimuli-responsiveness was investigated by taking advantage of the nucleophilicity and basic character of the 2VP units present in the PS-*b*-P2VP block copolymer. To render the ellipsoidal particles pH-responsive while maintaining their integrity, the P2VP chains were cross-linked by the addition of 1,4-dibromobutane (DBB), thereby transforming the P2VP domains into hydrogel materials.[15] Significantly, cross-linking did not change the internal morphology or shape of the particles at neutral pH (Figure 5a). However, lowering the pH value results in the remaining 2VP units being protonated, thus causing the P2VP hydrogel layers to undergo significant swelling. As these hydrogel layers are connected by glassy PS lamellae, the swelling results in a dramatic elongation of the ellipsoids along the long axis L. Particles with 8 lamellae swell from around 550 nm at pH 7 to approximately 1400 nm at pH 3, with TEM analysis showing a unique shape change from ellipsoidal to an "accordion-like", segmented structure (Figure 5a). Since the short axis (D) of the particles remains unaltered, this pH-induced shape change corresponds to a more than 250% increase in the aspect ratio. Of even greater importance is the observation that these dramatic changes are reversible: increasing the pH value from 3 to 10 results in the initial stacked lamellae structure and ellipsoidal shape of the elongated particles being fully restored (Figure 5a). In direct contrast, non-cross-linked materials do not undergo reversible switching or dramatic shape changes. Complete disintegration of the ellipsoid particles into glassy PS nanodiscs with P2VP coronas occurs under acidic conditions ($\text{pH} < 4.5$; Figure 5b). All attempts to reverse this process by increasing the pH value failed, with clusters of nanodiscs remaining. In addition, attempts to exploit the responsive properties of the spherical, radial lamella structures, either before or after cross-linking, did not lead to any changes in shape or morphology. The reversible shape transformation for the ellipsoidal, stacked lamella particles, therefore, represents a unique platform that is enabled by the ability to control the cross-linking, shape, and morphology in a single system.

In summary, we have demonstrated a facile method to control particle shape and morphology through the use of tailored, mixed surfactant systems to tune surface interactions. For PS-*b*-P2VP particles, three disparate morphologies—spherical particles consisting of radial layers with either PS or P2VP as the outer layer and ellipsoidal particles containing axially stacked lamellae—could be reproducibly and exclusively obtained. In addition, control over the aspect ratio and, therefore, the shape anisotropy of these prolate ellipsoids could be realized by adjusting the molecular weight of the block copolymer. In an interesting demonstration of the interplay between chemistry, surface interactions, and nanoscale morphology, cross-linking of the P2VP domains allows the pH-responsiveness of the 2VP moieties to be exploited, thereby leading to shape- and structure-responsive particles. The simplicity and generality of this synthetic strategy allows access to novel, shape-anisotropic and responsive polymer particles, with applications ranging from colloidal self-assembly to photonics and biomedical delivery devices.

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