Polymer-Helix Assemblies

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Nano-to-Macroscale Poly(methyl methacrylate) Stereocomplex Assemblies[**]

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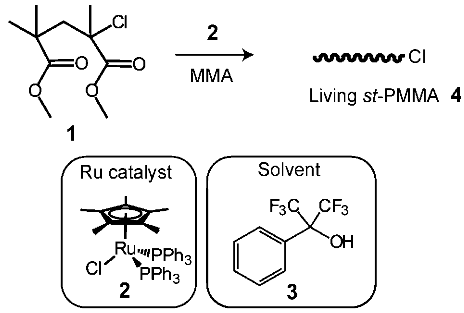
Nature has a specific and predefined approach to the assembly of natural macromolecules that render functionality, uniqueness, and form to all living matter. An elegant example is the helix, which is the native form of DNA[1] and some protein sequences.[2] Some synthetic polymers have also been found to adopt single-strand helical conformations; poly(isocyanates), poly(triphenylmethyl methacrylates), and poly(acetylenes) are well-known examples.[3] Perhaps the most interesting synthetic helix is the poly(methyl methacrylate) (PMMA) stereocomplex, which is a triple-stranded helical supramolecule.[4–6] Multiple-strand artificial helices are rare, which is understandable if one considers that no specific interactions, such as π–π stacking or hydrogen bonding, are used to induce helix formation.

There are limited examples of the use of PMMA stereocomplexes (SCs) as an assembly mode for ultrathin films,[7,8] inclusion complexes,[9] nanoparticles, and nanonetworks,[10] as well as fibers[11] and dialysis membranes.[12] Nevertheless, PMMA SCs display interesting characteristics, such as stereospecific polymerization-templating capabilities[8] and helix-sense stereocomplexation,[9] as well as molecular-weight[13] and peptide-motif recognition.[14] These are remarkable characteristics if one considers that PMMA is a common commodity polymer. In the abovementioned examples, PMMA samples with high stereoregularity are used. This material is typically synthesized by living anionic polymerization; stereospecific PMMA synthesized from controlled/living radical polymerization has not been used previously in stereocomplexation studies. In this study, we utilized a novel syndiotactic (*st*-)PMMA star polymer synthesized by stereospecific living radical polymerization (SLRP)[15] and investigated its stereocomplexation behavior with linear isotactic (*it*-)PMMA. The macromolecular assembly of various nano-to-macroscale structures from a single pair of complementary polymers through helix formation has not been reported previously.

It has been demonstrated previously that *st*-PMMA does not require a high level (> 90%) of syndiotacticity for stereocomplexation to occur, whereas the tacticity of the *it*-PMMA species is more crucial.[6] Therefore, the core cross-linked star (CCS) polymers were synthesized by SLRP, which can provide *st*-PMMA with triad syndiotacticity (*rr*) values of up to 80%.[16] The CCS polymer was synthesized by the two-step arms-first method.[17] First, MMA was polymerized by using the initiator **1** in the presence of the Ru catalyst **2** and tri-*n*-butylamine; the bulky cumyl fluoroalcohol **3** was used as the solvent (Scheme 1). The living nature of the polymerization was observed (see Figure S1 in the Supporting Information), as well as high conversions (> 95%) without the loss of catalyst activity or the living nature of the polymer. The formation of the highly syndiotactic *st*-PMMA **4** was confirmed by ^{13}C NMR spectroscopic analysis (see Figure S1 in the Supporting Information; *mm*/*mr*/*rr* 1:22:78).



Scheme 1. Simultaneous control of molecular weight and tacticity by ruthenium-catalyzed stereospecific living radical polymerization (SLRP).

Secondly, the alkyl chloride chain ends of *st*-PMMA **4** were linked together with ethylene glycol dimethacrylate (EGDMA) in the presence of the Ru catalyst **6** and tri-*n*-butylamine to yield the stereospecific CCS polymer **5**

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(Figure 1 a). This globular, covalently bound star polymer contains multiple arms, which are capable of stereocomplexation. The EGDMA-conversion profile as well as molecular-weight and polydispersity evolution with respect to reaction time are shown in Figure 1 b,c. The highly living nature of **4** was demonstrated by its near-quantitative conversion into the CCS polymer **5**. GPC–MALLS RI analysis revealed that the yield of **5** was greater than 95 % ($M_n = 218$ kDa, $M_w/M_n = 1.56$, arm number: 30; Figure 1 d). Therefore, further purification of the CCS polymer **5** was not required. The synthetic efficiency of the formation of the CCS polymer **5** is a significant improvement on the previously described synthesis of stereospecific star polymers by an anionic-polymerization strategy.[18] The complementary, highly isotactic linear PMMA **7** was obtained by living anionic polymerization ($M_n = 10.4$ kDa, $M_w/M_n = 1.13$, *mm*/*mr*/*rr* 93:3:4; see Figure S2 in the Supporting Information).[19] The *it*-PMMA **7** was prepared by anionic rather than living radical polymerization, because no synthetic route to highly isotactic (*mm* > 90 %) polymers on the basis of the latter method has yet been developed.

The *st*-PMMA CCS polymer **5** and linear *it*-PMMA **7** are soluble individually in acetonitrile/water (9:1), and stereocomplexation occurs between the complementary PMMA species when combined (see Figure S3.1 in the Supporting Information). Therefore, the assembly of different SC morphologies could be induced by mixing **5** and **7** in different ratios in ACN/H_2O (9:1)[10] at room temperature (Figure 2). Discrete SC CCS polymers **8** were obtained when the *st*-PMMA CCS polymer **5** was mixed with a large excess of linear *it*-PMMA **7**. When the conventional ratio for stereocomplexation (*it*/*st*(arms) 1:2) was used at low polymer concentrations ($< 2\ \text{mg mL}^{-1}$), larger SC assemblies were obtained; as the *it*-PMMA inner helix is longer than the *st*-PMMA outer helix, it could link multiple *st*-PMMA CCS polymers together to form SC CCS clusters **9**. At high polymer concentrations ($100\ \text{mg mL}^{-1}$), the mixing of **5** and **7** (*it*/*st*(arms) 1:2) led to the formation of a SC macrogel **10**.

The SC morphologies were formed by mixing the solutions of **5** and **7** in ACN/H_2O at room temperature for 50 h. Typically, turbid solutions formed after several hours, and the settling of particles occurred, which indicated poor solvation and aggregation of the PMMA SCs under these conditions (see Figure S3.1 in the Supporting Information). Aggregate formation was reversed by dilution to below the critical aggregation concentration to give stable SC morphologies **8** and **9** (see Figure S3.2 in the Supporting Information), as confirmed by the dilution of samples for dynamic light scattering (DLS) until stable particle-size distributions were observed. Aggregation can be excluded as a driving force for the formation of these stable SC morphologies, since differential scanning calorimetry (DSC) of the mixing products of **5** and **7** confirmed that they were PMMA stereocomplexes, as indicated by a characteristic melting point at 148 °C (see Figure S4 in the Supporting Information).[10] The dilute solutions of **8** and **9** were then cast onto grids for analysis by transmission electron microscopy (TEM). Size data from number-average DLS and TEM analysis are shown in Figure 3. (see Figures S5 and S6 of the Supporting Information for the intensity-, number-, and volume-average DLS traces for **5**, **8**, and **9**, as well as additional TEM images and size-distribution histograms (sample set > 50).)

The *st*-PMMA CCS polymer **5** has a hydrodynamic diameter (D_h) of 15 nm; TEM analysis gave a mean solid-state diameter (D_s) of 23 nm with a standard deviation (σ) of 1.8 nm. The narrow distribution of sizes results from the

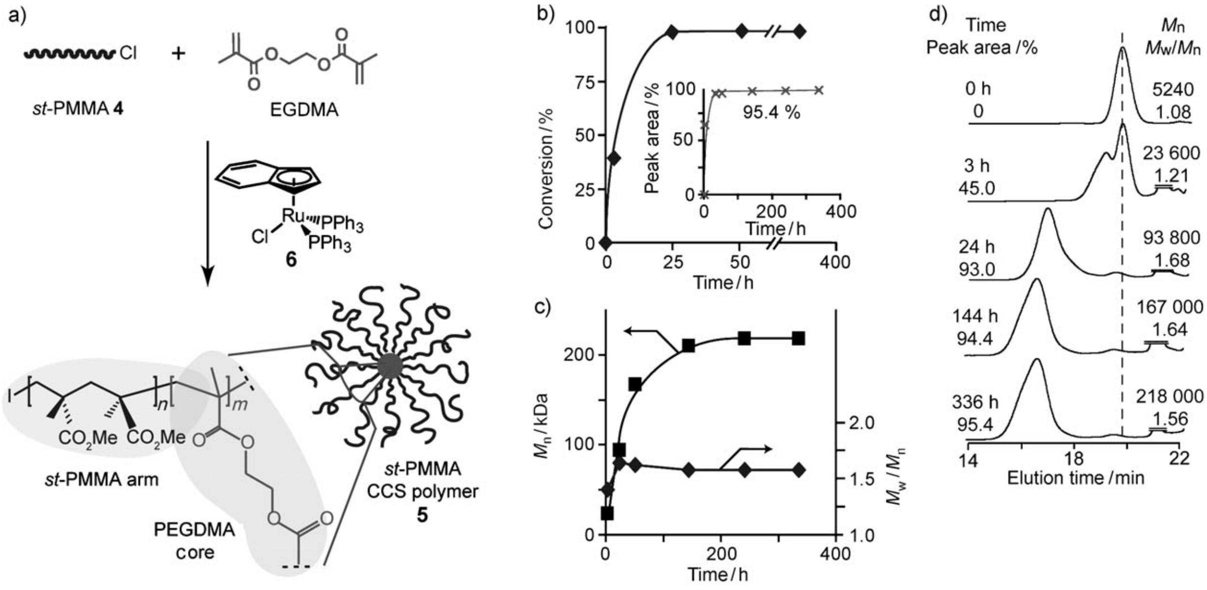

Figure 1. a) Synthesis of the *st*-PMMA CCS polymer **5** at 80 °C in toluene; [EGDMA] = 100 mM, [**4**] = 10 mM, [**6**] = 2 mM, [nBu$_3$N] = 40 mM. b) EGDMA conversion during core cross-linking (measured by ^{1}H NMR spectroscopy). Inset: Yield of the CCS polymer **5**, as determined by integration of the peak area in GPC–MALLS RI traces. c) Evolution of M_n and M_w/M_n for the CCS polymer **5** with respect to reaction time. Arrows indicate the appropriate *y* axis. d) The formation of the CCS polymer **5** was monitored by GPC–MALLS RI analysis of kinetic samples; a high star yield (95 %) was observed after 336 h. GPC = gel permeation chromatography, MALLS = multiangle laser light scattering, RI = refractive index.

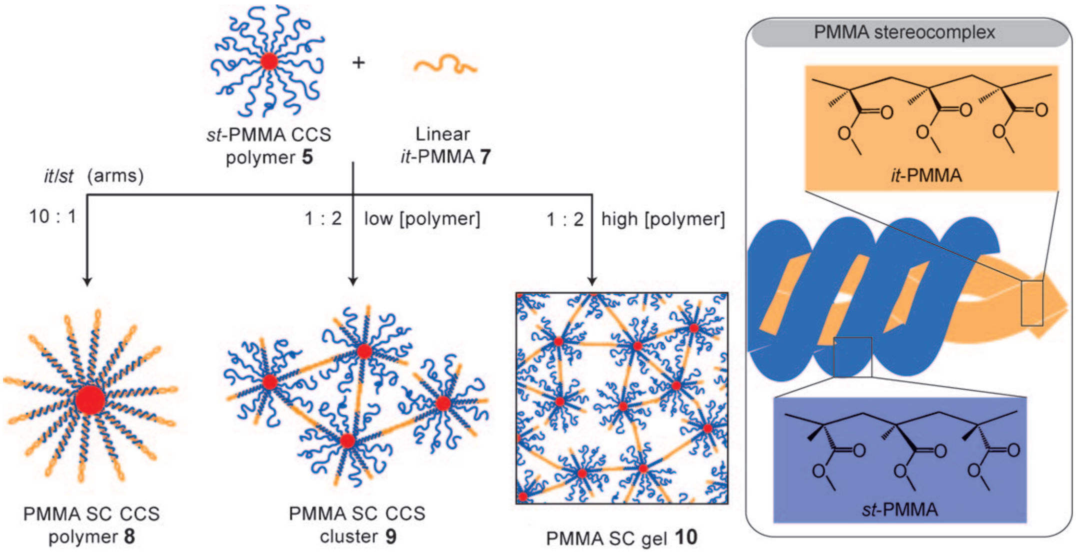

Figure 2. Stereocomplexation of the *st*-PMMA CCS polymer **5** with linear *it*-PMMA **7** at different ratios gave different stereocomplex morphologies. The SC CCS polymer **8** was obtained when excess *it*-PMMA was added (*it*/*st*(arms) 10:1). Alternatively, the conventional stereocomplexing ratio (*it*/*st*(arms) 1:2) afforded either the SC CCS cluster **9** or the SC gel **10** (at polymer concentrations of 2 or 100 mg mL^{-1}, respectively). Right: The PMMA SC adopts a triple-stranded helical structure comprising a double-stranded *it*-PMMA helix within an *st*-PMMA helix.[4]

moderate polydispersity of **5** ($M_w/M_n = 1.56$). The hydrodynamic diameter of the CCS polymer **5** was, however, smaller than its solid-state diameter. It was initially expected that D_s would be similar to D_h for the CCS polymer **5** because of low "molecular softness"[20] (i.e. a low arm degree of polymerization (DP) and high arm numbers). We propose two explanations for this observation. First, DLS analysis can underestimate the hydrodynamic diameter of star polymers as a result of the decreased density of the polymeric arms on their periphery. Second, star polymers with high-DP arms undergo a much greater collapse in size in the dry state ($D_s < D_h$) than star polymers with low-DP arms because of their high molecular softness. The latter do not collapse significantly ($D_s \geq D_h$) because they have low molecular softness.[20] The occurrence of $D_s > D_h$ was similarly observed by Gurr et al.[21] and Wooley and co-workers[22] for atactic PMMA CCS polymers and polyisoprene-*block*-polyacrylic acid shell-cross-linked knedel-like nanostructures, respectively (both star macromolecules had a low arm DP and high arm numbers). Furthermore, Yashima and co-workers observed particle expansion ($D_s > D_h$) for small PMMA–C_{60} micelles and particle shrinkage ($D_s < D_h$) for large PMMA–C_{60} micelles.[10]

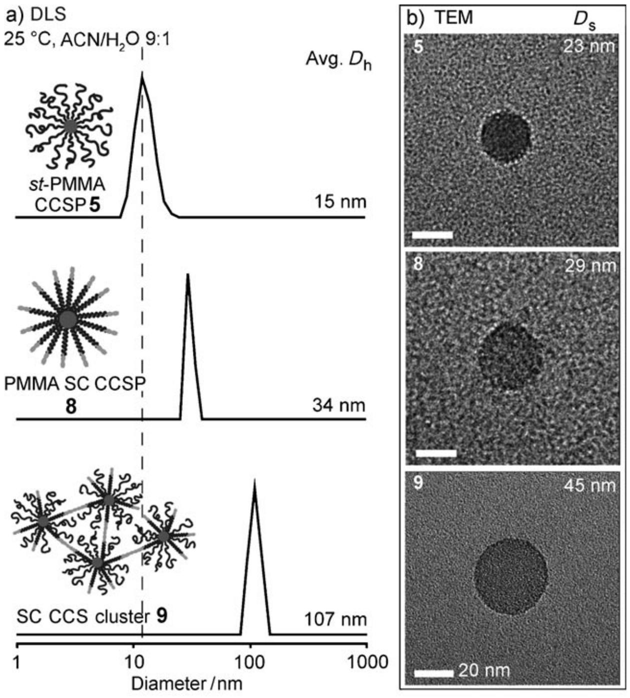

Figure 3. a) Number-average DLS distributions and b) TEM images for the CCS polymer (CCSP) **5** and SC CCS polymers **8** and **9**.

The PMMA SC CCS polymer **8** was observed to have a D_h value of 34 nm and a mean D_s value of 29 nm ($\sigma = 3.9$ nm). The similarity in the sizes of the solvated and solid-state species is not surprising when the rigidity of the PMMA stereocomplex is taken into account.[23] We postulate that **8** has stereocomplexed PMMA arms, although segmental stereocomplexation or stereocomplexation on the star periphery cannot be ruled out without further analysis. However, molecular-sorting experiments[13] with linear *it*- and *st*-PMMA have shown that the complete inclusion of the inner *it*-PMMA helix in the outer *st*-PMMA helix is highly favored, as the PMMA SC is the more thermodynamically stable structure.

The PMMA SC CCS cluster **9** had a D_h value of 107 nm and a mean D_s value of 41 nm ($\sigma = 3.9$ nm). This large difference in size is intriguing, as the PMMA SC was expected to maintain its dimensional integrity, as observed for **8**. We hypothesize that particle shrinkage occurs through collapse of the linear *it*-PMMA segments (which are not in their rigid stereocomplex form as a result of the absence of the outer *st*-PMMA helices). In a previous study, we showed that CCS clusters with linear PMMA segments can undergo large changes in D_h upon alteration of the solvent quality.[24] Alternatively, although it is less likely, the individual PMMA SCs could pack ("bundle") together preferentially in the solid state[25] to cause a forced collapse of the SC CCS cluster.

The stereocomplex formation of PMMA can be disrupted by the solvent or temperature (Figure 4a).[6] The dissolution of PMMA SCs in a good solvent, such as THF, can effectively disassemble the stereocomplex; heating of the SC in the solution used for its stereocomplexation also causes disassembly. When THF was added to the ACN/H_2O solution of the PMMA SC CCS cluster **9**, disassembly was observed almost instantaneously. Partial disassembly was also observed when the ACN/H_2O solution of **9** was heated to 50 °C. Unfortunately, the DLS did not allow for the disassembly to be conducted at temperatures above 50 °C, otherwise it is anticipated that complete disassembly would be observed at such temperatures.

The SC gel **10** was obtained by mixing **5** and **7** at an *it*/*st*(arms) ratio of 1:2 and a concentration of 100 mg mL^{-1}. At this high concentration, a continuous macroscopic network held together exclusively by helical SCs was formed. This mode of gel formation facilitated the temperature-induced assembly and disassembly of **10**. Heating of the SC gel **10** to 90 °C resulted in complete disassembly and the formation of a solution of polymers **5** and **7** (Figure 2b). When this solution was cooled to room temperature, it became cloudy (ca. 30 min), and a macroscopic gel formed (ca. 1 h). The reversibility of this process was demonstrated by the repetition of this cycle without a change in behavior. Although the SC gel **10** was strong enough to support its own weight, physical handling caused breakage, which is unsurprising, as the gel is only held together by van der Waals forces.

Linear PMMA SCs form gels as a result of the physical aggregation and bundling of SC helices, but the gels can be dispersed readily through minor dilution (see Figure S7 in the Supporting Information).[26] The SC gel **10** is unique in that it is held together by the CCS polymer **5**, which serves as a locus for multiple cross-linking. This feature also makes **10** distinct from SC networks formed by PMMA micelles[10] because the cores of the CCS polymer **5** are covalently cross-linked and hence stable against temperature, solvents, and concentration effects. Furthermore, one study suggested that covalently stabilized star SCs are more stable (in the melt) than analogous linear SCs.[27]

Noting this advantage, we investigated the fabrication of PMMA SC microwires **11**. The SC gel **10** was heated to 90 °C to afford a free-flowing solution, which was drawn up into a microliter syringe and allowed to cool to room temperature. After 30 minutes, a viscous white solution was extruded from the syringe onto a glass slide submerged in ACN/H_2O (9:1). The resulting SC microwire **11** (Figure 5a) was kept in

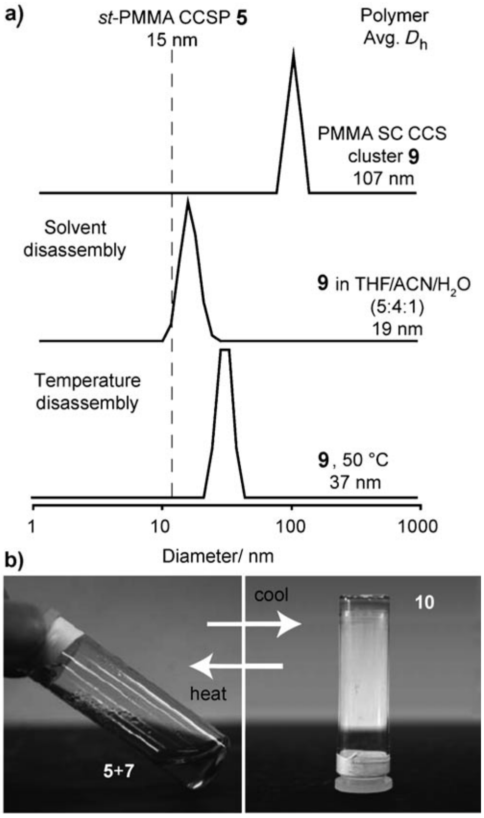

Figure 4. a) Disassembly of the PMMA SC **9** can be induced by the addition of a good solvent (e.g. THF) or by heating. b) Similarly, the PMMA SC gel **10** can be switched between solution and solid states by heating/cooling.

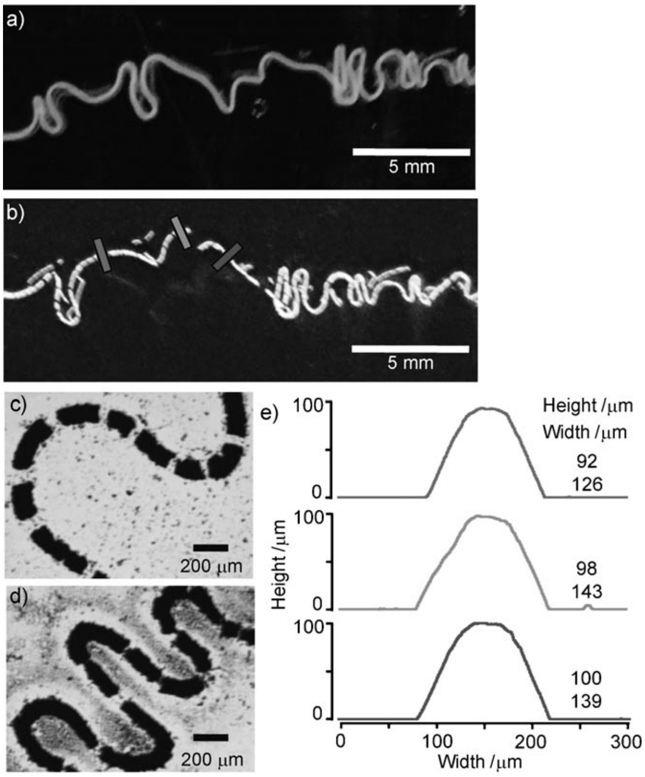

Figure 5. a) The PMMA microwire **11** was extruded as a solution in ACN/H_2O (9:1) from a microliter syringe onto a glass slide. b) The dried microwires broke apart lengthwise as a result of the large shrinkage of the SC network, but nevertheless maintained their shape. c,d) Optical-microscope images (2×) of the microwires. e) Profilometer contours for **11** (locations shown in (b): left-hand position: top; middle position: middle; right-hand position: bottom). The results indicate that the cylindrical shape of the wire persisted after drying.

solution at room temperature for a further 50 hours to facilitate complete stereocomplexation. Microwires of several centimeters in length were obtained by this method. They were observed to be shape-persistent in solution with no visible dissolution (see Figure S8 in the Supporting Information). However, the lengthwise breakage of **11** into shorter segments occurred after the ACN/H_2O solvent mixture had completely evaporated (Figure 5 b). This breakage is caused by the large shrinkage of the stereocomplexed structure as the solvents evaporate; the weak van der Waals forces that bind the PMMA helices cannot maintain the structural integrity of **11**. Such a large decrease in size was also observed for the SC CCS cluster **9** in its dry state relative to its size in solution (Figure 3). Nevertheless, the dried microwires could be observed with an optical microscope, and their diameter was determined to be approximately 100 μm (Figure 5 c,d). Furthermore, the dried microwires were shape-persistent, and their profiles could be measured with a profilometer (Figure 5 e). The profilometer contours for microwire **11** indicated that its width and height were approximately 137 and 97 μm, respectively. The fabrication of PMMA SC microwires clearly demonstrates the utility of *st*-PMMA CCS polymers for the formation of stereocomplex networks that can be tailored and shaped as required. In contrast, linear PMMA SC gels cannot form such a wide assortment of assemblies.

In summary, we have described the near-quantitative synthesis of the *st*-PMMA CCS polymer **5** by SLRP. This polymer and the complementary linear *it*-PMMA **7** were utilized in the assembly, through helix formation, of a fascinating array of SC morphologies that ranged from SC CCS polymers of less than 50 nm in diameter to micron-sized SC microwires and macrogels.

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