Control of Polymer Solution Structure via Intra- and Intermolecular Aromatic Stacking

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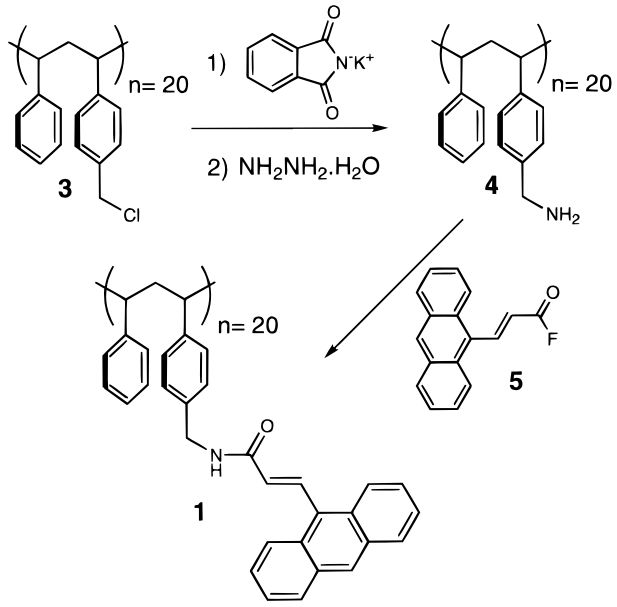
ABSTRACT: Anthracene-functionalized polymer **1** folds into a compact globular structure in nonpolar media. This folding arises from intramolecular aromatic−aromatic interactions of the anthracene side chains. Polymer **1** binds strongly to picric acid (**2**), through donor−acceptor electrostatic interactions between the electron-rich anthracene side chains and the electron-deficient picric acid guests. This binding stabilizes the thermally labile folded conformation of polymer **1**, dramatically altering the temperature dependence of polymer unfolding.

Control of the three-dimensional structure of conformationally flexible macromolecules is of fundamental importance to the fields of biology and material science. In biological chemistry, conformationally defined architecture is critical to proper functioning of proteins[1] and polynucleic acid[2] systems. In materials science,[3] the ability to create specific polymer architectures provides a powerful tool for controlling both the structure and function of molecular materials and devices.[4]

Noncovalent interactions between aromatic groups are responsible for a wide array of phenomena in fields of chemistry and biology.[5] These stacking interactions play a key role in recognition events of proteins[6] and contribute stabilization to structures of biopolymeric systems.[7] Application of these interactions to synthetic polymers allows the creation of higher order architecture required for devices and materials,[8] as well as the dynamic properties required for efficient utilization of these attributes.[9]

To explore the application of this methodology to the creation of dynamically self-assembled materials, we have synthesized anthracene-functionalized polystyrene **1** (Scheme 1).[10] Polymer **1** adopts a folded globular architecture driven by intramolecular aromatic−aromatic interactions. Additionally, polymer **1** strongly binds electron-deficient aromatic guests that are complementary to the electron-rich anthracene moieties found in the core of the folded polymer. This binding reinforces the core of the polymer, imparting greater thermal stability to the folded structure.

Scheme 1



Results and Discussion

The desired homogeneous dispersion of functionality in anthracene-functionalized polymer **1** was obtained via functionalization of **3**, a 1:1 copolymer of styrene and chloromethylstyrene.[11] Reaction of polymer **3** with potassium phthalimide followed by hydrazine monohydrate provided the amine-functionalized polymer **4**. Coupling of 9-anthracenepropenoic acid fluoride **5**[12] with amine-functionalized polymer **4** then provided quantitative conversion to polymer **1** (Scheme 1).

Preliminary molecular dynamics calculations[13] of a model of polymer **1** predict a highly folded structure (Figure 1a), with multiple anthracene−anthracene and anthracene−phenyl interactions (Scheme 2). Further molecular dynamics studies predict that picric acid (**2**) efficiently intercalates[14] *between* the anthracenes in the interior of polymer **1**, with concomitant swelling of the polymer globule (Figure 1b). This predicted intercalation is driven by the increased electrostatic attraction between electron-deficient picric acid molecules and electron-rich anthracene side chains relative to the weaker anthracene-anthracene interactions.

Complexation between polymer **1** and picric acid (**2**) was established experimentally via fluorescence titration in $CHCl_3$. Addition of guest **2** strongly quenched the fluorescence of the anthracene side chains of polymer **1** (Figure 2). Multiple binding modes and stoichiometries are apparent from the titration curve for the polymer **1**−guest **2** complex, preventing establishment of a binding constant. The binding curve in Figure 2, however, gradually leveled off with increasing molar equivalencies of guest **2**, a diagnostic feature of recognition processes.[15]

Additionally, we have performed variable temperature fluorescence experiments on solutions of polymer **1** and the polymer **1**·**2** complex in chloroform. Increasing temperatures resulted in greater quenching for both

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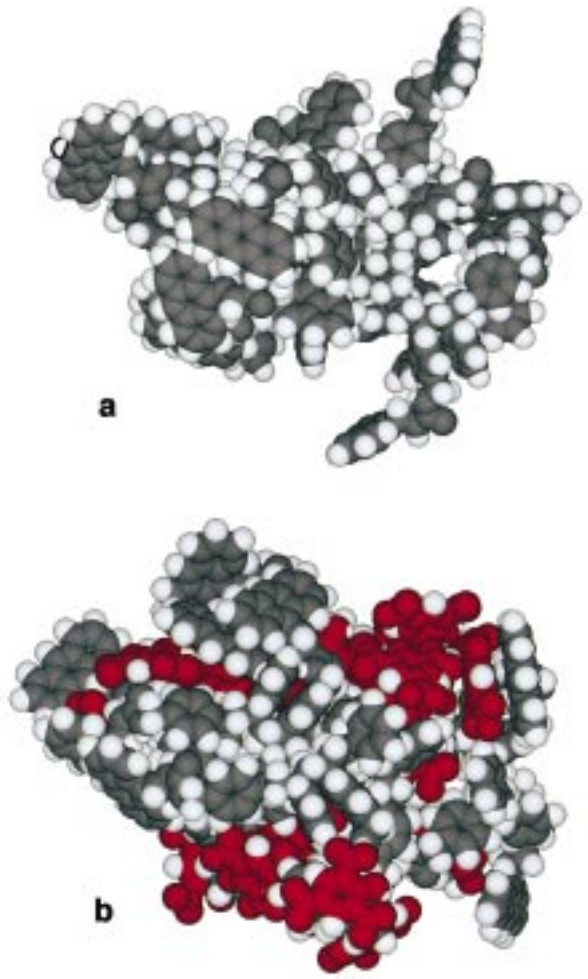
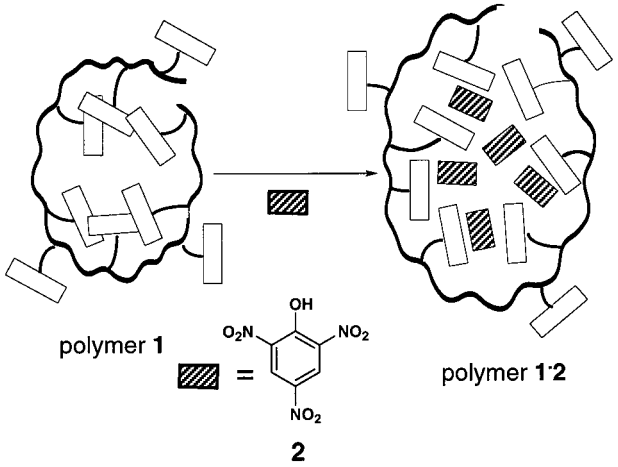


Figure 1. Compact globular structure predicted (Amber force field) for atactic polystyrene (40 monomer units total) with anthracene amide substitution at every other styrene: (a) Sampled structure of polymer from a final 20 ps dynamics simulation (300 K, $CHCl_3$); (b) Sampled structure of a complex between polymer and 20 molecules of picric acid (**2**), shown in red.

Scheme 2. Schematic Diagram of Polymer 1−Picric Acid (2) Host−Guest Complexation



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polymer **1** and polymer **1·2**; however, the increase in quenching was more dramatic for polymer **1** alone (Figure 3). This can be attributed to enhanced thermostability of the polymer **1·2** structure due to complexation.

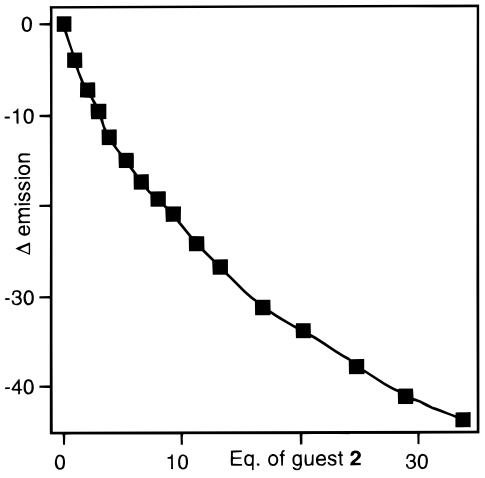

Figure 2. Fluorescence emission changes of polymer **1** upon addition of picric acid (**2**). Excitation: 409 nm. Emission: 480 nm,; reported in arbitrary units. Concentration of polymer **1** = 5×10^{-6} M.

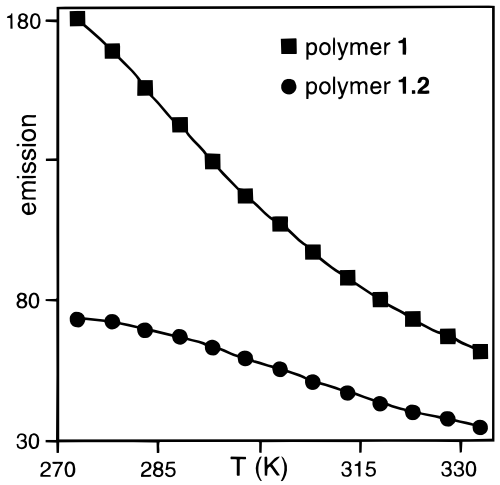

Figure 3. Fluorescence emission changes of polymer **1** and polymer **1·2** with varying temperatures**.** Excitation: 409 nm. Emission: 480 nm; reported in arbitrary units. Concentration of polymer **1** = 5×10^{-6} M, picric acid (**2**) = 8.6×10^{-3} M.

The effect of host−guest interaction on the solution structure of polymer **1** was explored using gel permeation chromatography (GPC).[16] To maintain consistent concentrations of guest **2** during the chromatographic process, varying concentrations of **2** were added to the chloroform eluent. For comparison purposes, polystyrene standards were eluted with each concentration of picric acid (**2**): these reference values were obtained separately for each variable concentration and variable temperature GPC measurement described below. Compared to the reference polystyrenes, retention times of polymer **1** decreased with increasing concentrations of **2** (Figure 4). This indicates swelling of polymer **1** upon incorporation of guest **2** molecules, fully consistent with computational predictions. This steady increase in size of the polymer **1·2** complex reached a constant value at 1×10^{-4} M due to saturation of the binding sites within the polymer.[17]

Variable-temperature GPC experiments were performed to determine the thermal stabilities of the folded polymer **1** and polymer **1**−guest **2** structures. Polymer **1** undergoes a relatively sharp dimensional transition initiating at 300 K (Figure 5). In contrast, the host−guest complex of polymer **1** with guest **2** shows a

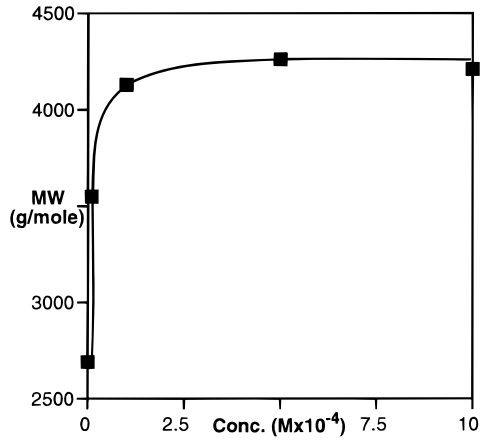

Figure 4. Changes in size of polymer **1** vs concentrations of guest **2**. MW represents M_w of polystyrene standards. Molarities given are the concentrations of picric acid (**2**) in the $CHCl_3$ eluent of both polymer **1** and the M_w standards.

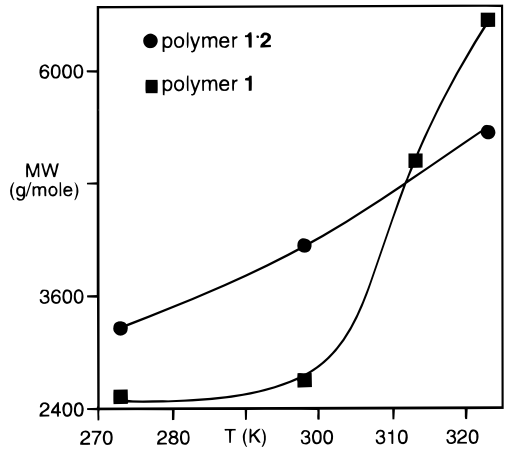

Figure 5. Changes in the relative sizes of polymer **1** and polymer**1·2** with varying temperatures. MW represents M_w of polystyrene standards. Concentration of **2** $= 1 \times 10^{-4}$ M for both polymer **1** and the M_w standards, $CHCl_3$ eluent.

considerably weaker and more linear temperature dependence.

The sharp dimensional transition observed for polymer **1** indicates a highly cooperative unfolding process similar to that seen in protein and nucleic acid folding.[18] This cooperativity arises from the multiple aromatic–aromatic interactions possible for each anthracene in the polymer core; unfolding of a single unit greatly destabilizes the folded conformation (Figure 6a). The stabilization observed upon intercalation of guest **2** between anthracene side chains arises from the much stronger interactions that are possible between the electron-rich anthracenes and the electron-deficient picric acid guests (Figure 6b). As above, the thermal behavior of the polymer **1**–guest **2** complex behavior mirrors that of DNA, where intercalation increases the unfolding temperature and broadens the melting range of the DNA duplex or triplex.[19]

In summary, we have synthesized a polystyrene-based system that self-assembles through aromatic stacking of electron-rich anthracene side chains. This polymer strongly complexes with picric acid, a complementary electron-deficient guest. Complexation between the polymer host and the monomeric guest imparts enhanced thermostability to the globular polymer structure. Applications of this supramolecular control of

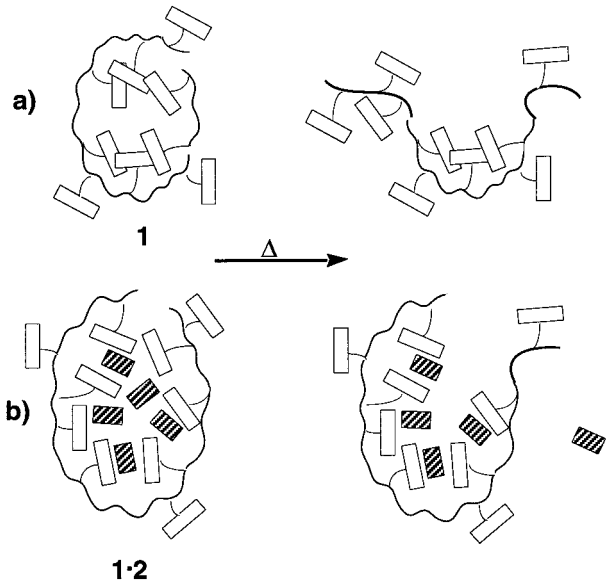

Figure 6. Schematic representation of the thermal unfolding process: (a) polymer **1**; (b) the polymer **1**–picric acid (**2**) complex.

polymer architecture in both fundamental and applied aspects of polymer research are underway and will be reported in due course.

Experimental Section

Materials and General Methods. All chemicals were reagent grade, and were used without further purification. Picric acid (**2**) was obtained as an emulsion in water; it was extracted with CH_2Cl_2 and dried in vacuo.

Poly(styrene –*p*-(chloromethyl)styrene), PS-*co*-CH_2Cl (3). AIBN (4.00 g, 24.4 mmol) was added to a solution of styrene (24.54 g, 235 mmol) and p-(chloromethyl)styrene (35.73 g, 234 mmol) in chlorobenzene (200 mL). The reaction mixture was heated at 78 °C for 20 h, followed by cooling to room temperature. The reaction mixture was then added to methanol (800 mL); vigorous mixing resulted in precipitation of a white solid (40.95 g, 68%), which was collected by filtration, and washed with methanol. The product was dried in vacuo. GPC: $M_n = 5278$, $M_w = 7729$, PD $= 1.465$.

Poly(styrene–*p*-(aminomethyl)styrene), PS-*co*-CH_2NH_2 (4). A solution of polymer **3** (2.01 g, 0.381 mmol), potassium phthalimide (3.52 g, 19 mmol) and 20 mL DMF was reacted at 100 °C for 8 h under an argon atmosphere. The cooled solution was filtered to remove KCl. The filtrate was concentrated in vacuo and precipitated into methanol. The cream-colored solid product (2.99 g) was collected by filtration and washed with methanol. The ^1H NMR of this product indicates quantitative conversion of the chloromethylstyrene into its phthalimide derivative.

The resulting phthalimide derivative (2.99 g, 0.4 mmol) was mixed with 3 mL of hydrazine monohydrate (1 g/mL) in 25 mL ethanol. The reaction was refluxed for 20 h. During the reaction course a white solid precipitated. The reaction mixture was filtered, and the filtrate was concentrated in vacuo. After precipitation of the filtrate into water, the resulting mixture was kept at 0 °C overnight. The off-white solid product (1.34 g) was collected with filtration and washed with water.

9-Anthracenepropenoic Acid Fluoride (5). A suspension of 9-anthracenepropenoic acid (0.372 g, 1.5 mmol) and pyridine (0.12 mL, 1.5 mmol) in dry CH_2Cl_2 (9 mL) was cooled to 0 °C under an argon atmosphere. To this was added cyanuric fluoride (0.54 mL, 3 mmol), and the contents stirred for 90 min. Crushed ice/water (10 g) was then added, the suspension filtered, and the organic layer separated and washed with water (2 × 25 mL). Concentration in vacuo, followed by

chromatography (SiO_2, Hex/EtOAc) provided 0.11 g (29%) of 9-anthracene propenoic acid fluoride (**5**),[20] as a dark yellow solid.

PS-*co*-CH_2NH−(9-anthracene propenoic acid) (1). 9-Anthracene propenoic acid fluoride (**5**) (0.035 g, 0.14 mmol) was added to a solution of amino-functionalized polymer **4** (0.03 g) in 2 mL of THF. The reaction mixture was stirred for 16 h under an argon atmosphere. The resulting solution was then precipitated into hexane. The bright yellow colored solid product (0.046 g, 82%) was collected by filtration, washed with hexane and dried in vacuo. The ^{1}H NMR of this product indicates a quantitative conversion of the aminomethylstyrene into its amide derivative.

GPC. All comparison, molecular weight values were obtained through use of calibration curves. Gel permeation chromatography was performed on a PLgel mixed-E column (3 μm, 7.5 × 300 mm, Polymer Laboratories Ltd.), using polystyrene as standard, flow rate 1 mL/min, with detection at 254 nm for standards and 400 nm for polymer **1**. Elution was performed with varying concentrations of picric acid (**2**) in spectrometric grade $CHCl_3$.

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Supporting Information Available: Figures showing ^{1}H NMR and IR spectra for polymer **1**, polymer **4,** and 9-anthracenepropenoic acid fluoride (**5**), ^{1}H NMR spectra for polymer **3**, phthalimide functionalized polymer**,** and 9-anthracenepropenoic acid, and GPC for polymer **1** using $CHCl_3$ and 1×10^{-4} M picric acid (**2**) in $CHCl_3$ as eluents, a Stern−Volmer plot for fluorescence quenching of polymer **1** with picric acid (**2**), and a ^{1}H NMR titration curve for picric acid (**2**)−polymer **1**. This material is available free of charge via the Internet at http://pubs.acs.org.

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