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Aggregation of Rod−Coil Block Copolymers Containing Rigid Polyampholyte Blocks in Aqueous Solution

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The electrostatic interaction (neutralization) between a pair of oppositely charged blocks can act as the driving force for the formation of polyion complex (PIC) micelles and vesicles which combine properties of polyelectrolytes and block copolymer aggregates.[1−5] It has been suggested that these PIC aggregates could be used as controlled drug delivery systems and carriers of DNA for gene therapy.[6] PICs are also employed to enhance the stability of polymeric aggregates.[7,8] Since the driving force of the PIC formation is electrostatic attraction, the reported PIC aggregates are salt-sensitive and they fall apart as the salt concentration reaches a critical value.[2,3] Chemical cross-linking can be employed to stabilize PIC aggregates.[3,9] Another possible way to enhance the stability is to increase the rigidity of the polyelectrolyte backbones since attractive interactions are possible between stiff polyelectrolytes.[10−12]

Recently, we reported the synthesis of rigid pH responsive polyampholytes via alternating copolymerization of *N*,*N*,*N*′,*N*′-tetraalkyl-4,4′-diaminostilbenes (TDAS) with maleic anhydride and the subsequent hydrolysis of the anhydride groups.[13] In this contribution, we report the synthesis of novel rod−coil block copolymers containing the polyampholyte based on *N*,*N*,*N*′,*N*′-tetraethyl-4,4′-diaminostilbene and a poly(methoxy-capped oligo-(ethylene glycol)methacrylate) (OEGMA) block (Figure 1a,b) for the investigation of the aggregation process driven by electrostatic interactions between the rigid polyampholyte blocks. The rod−coil block copolymers were synthesized by reversible addition−fragmentation chain transfer (RAFT) polymerization. The poly-OEGMA segment was synthesized first and used as the macro-RAFT agent for the polymerization of the second alternating TDAS maleic anhydride (TDASMA) block. Well-defined OEGMA-*b*-TDASMA diblock copolymers were obtained (Table 1, see also the Supporting Information). To the best of our knowledge, this is the first study of the solution properties of rigid polyampholyte based rod−coil block copolymers. We report here that rigid polyampholytes exhibit intriguing differences from flexible ones.[14]

The rod−coil block copolymers were dissolved in dilute HCl solution (pH 3) and aged for 2 h for the complete hydrolysis of the anhydride groups. To locate the isoelectric point (IEP), the ζ-potential of the polymeric aggregates was monitored as a function of pH (Figure 1c). A simple acid−base equilibrium calculation[15] shows that theoretical IEP is 5.9 at which point 80% of the amine and carboxylate acid groups are charged. The experimental IEP of the polyampholyte was found to be around 5.7, very close to the theoretical value.

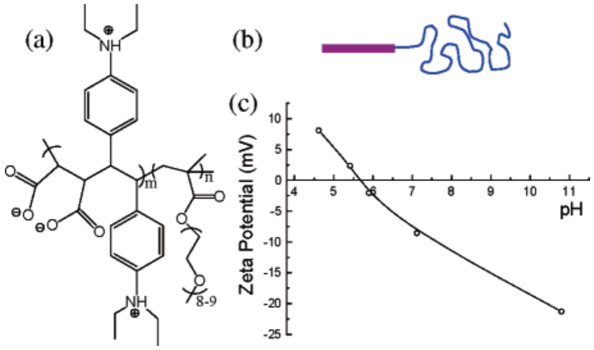

Figure 1. (a) Structure of the block copolymers; (b) rod−coil type structure; (c) ζ-potential of the PIC aggregates at different pH values.

Table 1. Compositions, Molecular Weights, and Molecular-Weight Distributions of Segments and Block Copolymers

entry	structure	M_n	M_w/M_n
1	$OEGMA_{26}$	7860	1.09
2	$OEGMA_{105}$	31600	1.15
3	$OEGMA_{26}$-*b*-$TDASMA_{31}$	20800	1.23
4	$OEGMA_{105}$-*b*-$TDASMA_{38}$	47600	1.14

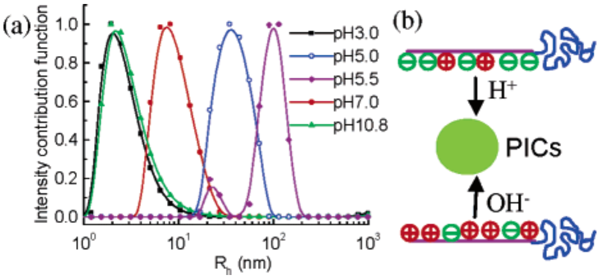

Figure 2. (a) R_h distributions of PICs formed by $OEGMA_{26}$-*b*-$TDASMA_{31}$ at different pH without the addition of salt; (b) a schematic of pH responsive aggregation of rod−coil block copolymers.

For PIC aggregates from oppositely charged PEG-poly(amino acid) block copolymers, the charged segments must have matched chain lengths to diminish the electrostatic repulsion from excess charges.[4] For our block copolymers, we found that the PIC aggregates can still exist when pH deviates from the IEP by about 1 unit ($5 < pH < 7$), where the rigid polyampholyte segments are net positively or negatively charged. The hydrodynamic radii (R_h) of the polymeric aggregates formed from $OEGMA_{26}$-*b*-$TDASMA_{31}$ as a function of pH were monitored by dynamic light scattering (DLS) (Figure 2a). The R_h of the aggregates was pH dependent and reached a maximum around the IEP. At low (pH 3) and high pH (pH 10.8) conditions, the polymer was highly positively or negatively charged and no aggregates were observed. As the pH approached the IEP, the rod−coil block copolymers started to form polymeric aggregates where the polyampholyte blocks form the core surrounded by a polyOEGMA corona (Figure 2b). At pH 5.5, close to the IEP, a bimodal distribution of the PIC aggregates was observed, indicating the incomplete transition of the PIC aggregates which was also observed in other polymer systems.[16] The pH responsive aggregation was also observed for $OEGMA_{105}$-*b*-$TDASMA_{38}$ with a longer OEGMA block (Table 2). The effect of pH change is much weaker when the OEGMA block is larger.

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Table 2. Average R_h (Cumulant Analysis) of the PIC Aggregates Formed from the Block Copolymers under Different Conditions

pH	pH = 7		pH = 5.5	
concentration of NaCl (mol/L)	0.01	0.5	0.01	1.0
OEGMA$_{105}$-*b*-TDASMA$_{38}$ R_h (nm)	12 ± 1	17 ± 1	15 ± 1	21 ± 1
OEGMA$_{26}$-*b*-TDASMA$_{31}$ R_h (nm)	9 ± 1	430 ± 10	80 ± 5	turbid

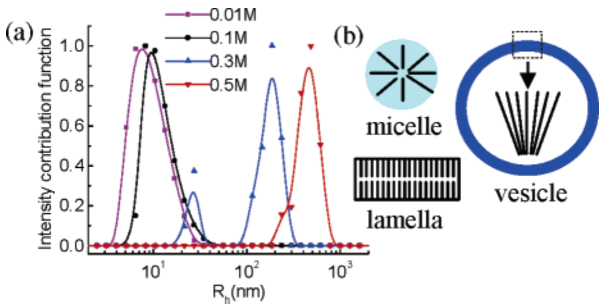

Figure 3. (a) Effect of added NaCl on PICs formed by OEGMA$_{26}$-*b*-TDASMA$_{31}$ at pH 7; (b) a schematic of rigid rods packing for various aggregates.

The aggregation process was also affected by the addition of NaCl. PIC aggregates did not dissociate upon the addition of salt but grew with increasing salt concentration. For OEGMA$_{26}$-*b*-TDASMA$_{31}$ at pH 7, 25 °C, and 0.3 M NaCl, larger aggregates with R_h around 150 nm were observed in addition to the smaller aggregates (Figure 3a). After increasing the salt concentration to 0.5 M, the smaller aggregates were undetectable and the larger aggregates grew to an average R_h around 500 nm. When the salt concentration was increased to 1.0 M, the solution became turbid. For OEGMA$_{105}$-*b*-TDASMA$_{38}$, the effect of added salt is much weaker (Table 2).

The aggregation of the rigid charge-imbalanced polyampholyte segments indicates existence of attractive interchain interactions, significantly different from flexible polyampholytes. For example, charge-imbalanced flexible polyampholytes are soluble through electrostatic repulsions.[15] Like-charge attractions between rod-like polyelectrolytes are relevant to a wide range of colloidal and biomedical processes and have been observed in various systems, such as DNA forming bundles in the presence of divalent counterions.[17] The attractive interactions are suggested to originate from positional counterion correlations, similar to van der Waals interactions: a rigid polyelectrolyte chain with condensed divalent counterions can be treated as a charged rigid polyampholyte (Figure 1 in ref 11), and strong dipole−dipole attractions can overcome repulsions from the net charges on the rods.[10,11] Added univalent salt reduces the effective charge on the rods, while the binding of multivalent ions is unchanged, giving rise to the increase in the net effective attraction.[18]

The same picture is also applicable for our rigid polyampholytes. Negative and positive charges attached to the rigid polyampholyte backbones will impart large dipoles, thereby inducing strong attractions between them.[19] Since the acid−base equilibrium is mainly dependent on the solution pH, the addition of NaCl will not change the surface charge on the polyampholyte blocks but the effective charge will be reduced. As stated above, added NaCl will increase the net effective attraction and therefore promote the aggregation of the rigid polyampholyte blocks (see Supporting Information for the detailed discussion).

Figure 3b shows different ways that rods can pack in aggregates. Denser packing will favor the formation of larger aggregates.[19] For example, vesicles instead of micelles become the predominant aggregates for block copolymers with a rigid block.[20] Adding salt or adjusting pH close to the IEP will diminish the electrostatic repulsions to allow the polyampholyte segments to pack more densely, thereby increasing the size of the PIC aggregates. Interplay between electrostatic interactions and block length can affect the aggregation process. Longer polyOEGMA blocks will occupy more volume and interfere with the packing of polyampholyte blocks. Consequently, OEGMA$_{105}$-*b*-TDASMA$_{38}$ will form smaller aggregates, and the effects of pH and added salt are much weaker compared to OEGMA$_{26}$-*b*-TDASMA$_{31}$.

In summary, novel rod−coil block copolymers containing rigid polyampholyte segments were synthesized and investigated. The chain rigidity has a dramatic effect on the electrostatic interactions between polyelectrolytes. The PIC aggregates formed from these rod−coil block copolymers were found to be responsive to pH changes and added salt. The unique solution properties of the rigid polyampholytes are induced by the like-charge attractions imparted by the rigid chains.

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Supporting Information Available: Synthesis details and summaries of the various characterization studies. This material is available free of charge via the Internet at http://pubs.acs.org.

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