Aggregation Behavior of Block Copolymers Integrating Sugar Binding Motif and Zwitterionic Chains in Aquatic Environments

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Abstract

A novel diblock copolymer consisting of a polyacrylamide with phenylboronic acid (PAEBB) and a poly(carboxybetaine acrylamide) (PCBAAm) was synthesized by radical addition-fragmentation chain transfer (RAFT) polymerization. The diblock copolymer produces particles with hydrodynamic radius of gyration of 56 nm in water through the aggregation of PAEBB chains, while the aggregation behavior depends on pH and glucose concentration. A model compound of PAEBB was synthesized to study the effect of zwitterion on the pK_a of phenylboronic acid.

1. Introduction

Mucosal layers of epithelial cells involve mucin. Since the defects in mucin secretion or the structure are associated with the immune system of the mucosa leading to infections, mucosal modification with macromolecular chains is expected to enhance the biological defense system.[1)] Phenylboronic acid can produce ester with 1,2- and 1,3- diols so that bind specifically to sugars allowing it to binding motifs for a number of important biological molecules including saccharides and glycoproteins.[2)] Meanwhile, zwitterionic polymers exhibit hydrophilicity due to the static charges and dipole in the zwitterions while inhibiting nonspecific protein adsorption due to the charge neutrality[3)].[3)] In this study, we address the aggregation behavior of a novel diblock copolymer composed of a polyacrylamide with phenylboronic acid (PAEBB) and a poly(carboxybetaine acrylamide) (PCBAAm) in aqueous solutions and the pH and glucose concentration responsibility (**Fig.1**).

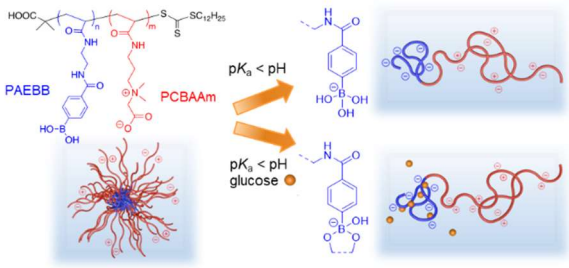
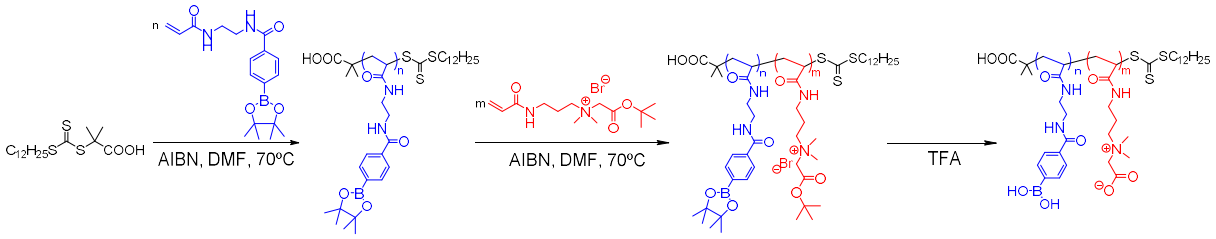


Fig. 1. Schematic representation of pH dependent aggregation of PAEBB-*b*-PCBAAm diblock copolymers in aqueous solutions.

2. Experiment

PAEBB-*b*-PCBAAm diblock copolymers were synthesized by reversible addition-fragmentation chain transfer (RAFT) polymerization of acrylamide with phenylboronic acid pinacol ester (AEBB) and acrylamide with *tert*-butyl carboxybetaine bromide (CBAAm) followed by deprotection with trifluoroacetic acid (TFA) (**Scheme 1**).[3,4,5)] The hydrodynamic radius of gyration (R_h) of the PAEBB-*b*-PCBAAm aggregates formed in the aqueous solutions was determined by dynamic light scattering (DLS).



Scheme 1. Synthesis of PAEBB-*b*-PCBAAm

3. Results and discussion

Degree of polymerization (DP) ratio of the PAEBB-*b*-PCBAAm diblock copolymer was determined by the integration of the signals in the ^{1}H-NMR spectrum to be PAEBB/PCBAAm = 0.12/1. The PAEBB-*b*-PCBAAm formed aggregates with R_h of 68 nm in water at pH of 9.0 while the aggregates dissociated in 100 mM glucose aqueous solution at pH of 9.0 (**Fig. 2, Fig. 3**). The PAEBB-*b*-PCBAAm aggregates dissociated at pH of 10.9 in the absence of glucose, while dissociated at pH of 8.3 in 100 mM glucose aqueous solution. Thus, the phenylboronic acid groups with an electron withdrawing amide carbonyl in the PAEBB-*b*-PCBAAm transformed to boronate anion with p$K_{a,BA}$ of 10.9 in glucose-free pure water, while they form a cyclic boronate ester through binding with a 1,2- or 1,3-diol in the glucose then transformed to boronate ester anion with p$K_{a,BE}$ of 8.3. The p$K_{a,BA}$ is higher than the value reported previously in the PAEBB-*b*-polydimethylacrylamide (p$K_{a,BA}$: 8.2). The p$K_{a,BA}$ rise is probably due to the interaction of boronic acid with carboxybetaine.

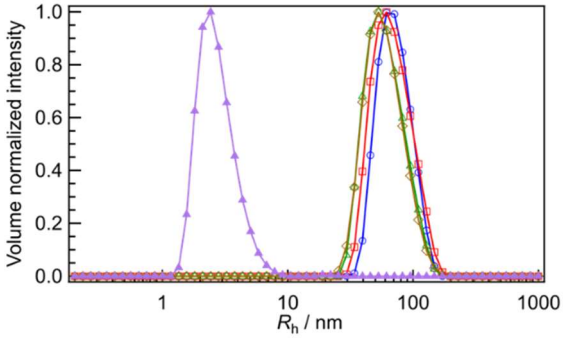


Fig. 2. R_h distributions of PAEBB-*b*-PCBAAm aggregates in pure water [pH = 3.0 (blue), 5.1 (red), 7.1 (green), 9.0 (brown), 12 (purple)] at 25°C.

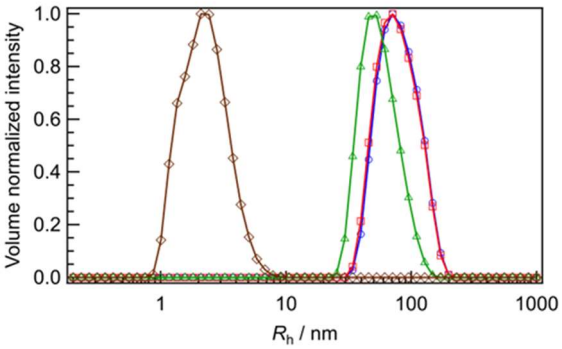


Fig. 3. R_h distributions of PAEBB-*b*-PCBAAm aggregates in 100 mM glucose aq. [pH = 3.0 (blue), 5.0 (red), 7.0 (green), 9.0 (brown)] at 25°C.

4. Conclusions

A diblock copolymer consisting of a sugar-binding polymer with boronic acid groups and a zwitterionic polycarboxybetaine was successfully synthesized by RAFT. In the presence of zwitterions, PAEBB-*b*-PCBAAm aggregates were shown to change their aggregation behavior in a specific pH range above physiological pH. We are going to investigate the effect of zwitterions on the p$K_{a,BA}$ of PAEBB-*b*-PCBAAm using a model compound of PAEBB by means of UV-visible absorption spectroscopy.

Acknowledgments

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