Letter

Boronic Acid Linear Homopolymers as Effective Emulsifiers and Gelators

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S *Supporting Information*

ABSTRACT: We report emulsion studies using poly(vinylphenyl boronic acid) (PVPBA) linear homopolymer as an effective emulsifier and gelator. Two stabilizing regimes were identified depending on the pH of PVPBA aqueous solutions, i.e., emulsions stabilized by the hompolymer nanoparticles (Pickering emulsions) at pH < pK_a and emulsions stabilized by the homopolymer unimers at pH > pK_a. In both cases, gelled emulsions were obtained from medium to high internal phase volume fractions with the unimers exhibiting more effective emulsification and gelling properties. Hydrogen bonding between the boronic acid units is proposed to account for the high strength of the emulsions. The emulsions were shown to be pH- and sugar-responsive. Finally, the stable emulsions were used as templates to directly prepare PVPBA macroporous materials and to fabricate multilayered capsules. This remarkable observation that a simple homopolymer can serve as an effective emulsifier and gelator may dramatically extend the scope of potential emulsifiers and inspire further research in the design of new types of efficient emulsifying agents.

KEYWORDS: *emulsions, gels, H bonding, interfaces, polymers*
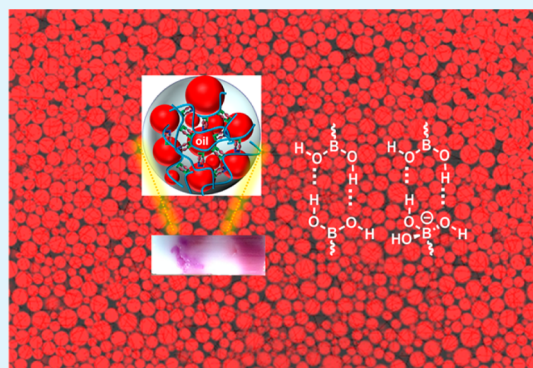
INTRODUCTION

Emulsions, comprising at least two immiscible phases with an internal phase dispersed into a continuous phase, have been widely used in food, cosmetics, pharmaceuticals, and chemical processing. There has been much recent interest in formulating multifunctional and complex emulsions for advanced applications in biocatalysis,[1] encapsulation and delivery,[2,3] responsive assembly,[4] and templated synthesis.[5] Hybrid soft materials known as organohydrogels consisting of oil and hydrogel subdomains are emerging as novel scaffolds that combine the distinct properties of hydrophilic materials with hydrophobic liquids.[6,7] Although cross-linking or polymerization of emulsions stabilized by molecular surfactants was used to form organohydrogels,[6,8] most organohydrogels were based on high internal phase emulsions (HIPEs) with an internal phase volume ≥0.74.[9−11] A wide variety of emulsifiers have been used to stabilize emulsions, including molecular surfactants,[12] inorganic particles,[13] amphiphilic block copolymers,[14] polymer particles,[15] bacteria,[16] carbon-based nanomaterials, and proteins,[17] among others. However, it is incredibly rare for linear homopolymers[18] without an obvious surfactant-like structure to form stable and gelled emulsions.

Boronic acid polymers have promising applications in drug delivery, dynamic-covalent materials, and sensing due to their ability to form reversible boronate esters with diols.[19,20] Rescent developments in controlled polymerization of boronic

acid polymers have made possible the control of molecular weight, dispersity, and end groups.[21,22] For example, glucose-responsive assemblies from well-defined block copolymers containing a boronic acid polymer block have been studied at physiological pH.[23] Despite their diverse applications, boronic acid polymers are not known to function as emulsifiers. In this work, we report our exciting new finding that poly(4-vinylphenylboronic acid) (PVPBA) acts as an effective emulsifier to form gelled emulsions over a broad range of conditions.

RESULTS AND DISCUSSION

PVPBA homopolymers were synthesized by direct RAFT polymerization of unprotected VPBA monomer (Scheme S1). PVPBA is a weak polyacid with a pK_a ≈ 9. At pH > pK_a, PVPBA is highly charged and becomes completely soluble in water as unimers. For example, PVPBA with M_n = 11.1 kg/mol and M_w/M_n = 1.14 existed as molecularly dissolved unimers with D_h < 10 nm at pH > 10.0, as determined by dynamic light scattering (DLS) (Figure 1). At pH < pK_a, however, only a small portion of the units in PVPBA are charged, with the majority of the chain remaining in the neutral, hydrophobic
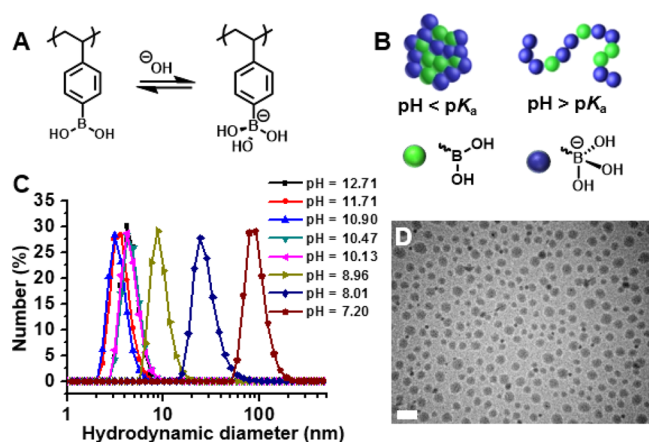
Figure 1. (A) Ionization equilibrium of PVPBA, (B) proposed schematic representation of PVPBA conformation in different pH regimes, (C) DLS results of PVPBA (M_n = 11.1 kg/mol, M_w/M_n = 1.14) as a function of pH at a PVPBA concentration of 0.5%, and (D) TEM micrograph of PVPBA nanoparticles at pH 7.2. Scale bar is 200 nm.

form. Thus, PVPBA homopolymer at intermediate pH resembles an amphiphilic random "copolymer", which can self-assemble into homopolymer nanoparticles, presumably with the neutral hydrophobic units being stabilized by the negatively charged units. The formation of PVPBA homopolymer nanoparticles was confirmed by transmission electron microscopy (TEM) (60 ± 22 nm at pH 7.2). Zeta potential measurement (Supporting Information) showed more negative values for the nanoparticles than for the unimers, due to a higher surface charge density of the more compact nanoparticles than the loose coil conformation of the unimers. Therefore, we reasoned that if PVPBA was used as an emulsifier, two types of emulsions could be generated depending on the pH with emulsions stabilized by water-soluble unimers being formed at pH > pK_a and emulsions

stabilized by homopolymer nanoparticles (Pickering emulsions) being formed at pH < pK_a.

PVPBA emulsification behavior was initially investigated using dodecane as the model oil (Figure 2). At pH 8.0, conditions under which PVPBA is expected to exist as homopolymer nanoparticles, stable oil-in-water (o/w) Pickering emulsions were formed over a broad range of oil fractions (up to 85%). Interestingly, gelation was observed to occur from medium to high internal phase emulsions (50−85%). We previously reported gelled HIPEs stabilized by star polymers.[10] However, formation of gelled emulsions with an internal phase fraction down to 50% using such a low concentration of stabilizer (0.5%) was not possible because of low droplet packing density. Surprisingly, gelled emulsions with oil fractions from 50 to 85% were also observed at pH 10.4, where PVPBA exists as water-soluble unimers. Typically, Pickering emulsions are believed to be more stable than emulsions stabilized by molecular emulsifiers, due to a much higher adsorption energy ($\Delta E \propto r^2$, r is radius) of particulate emulsifiers.[24] HIPEs usually have a higher viscosity and in some cases they form gels in part due to the high packing density of the oil droplets. The fact that PVPBA unimers could generate gelled emulsions with oil fractions down to 50% demonstrates that PVPBA unimers are very effective emulsifiers and gelators. Hydrogen bonding between the hydroxyl groups of phenyl boronic acid is known to occur and has been exploited in capsule design.[25] We attribute the formation of gelled emulsions herein to hydrogen bonding among the PVPBA units (at the interface and in aqueous solution). Gelled emulsions (including gelled HIPEs) of varied oil fractions could be reliably fabricated over pH 7.2−11.7. Higher pH resulted in unstable emulsions due to the subtle change in hydrophilicity of the anionic PVPBA. These gelled emulsions exhibited long-term stabilities; no creaming or phase separation was observed for at least one year. Remarkably, to the best of our knowledge, this is the first time a water-soluble linear homopolymer has been used to stabilize and gel emulsions over such broad oil fractions.
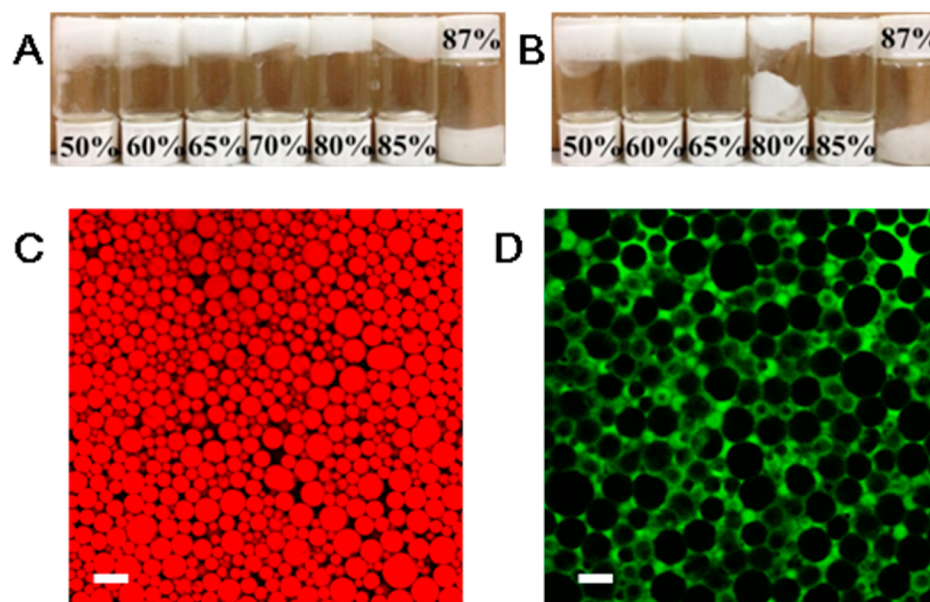

Figure 2. Photographs of PVPBA (M_n = 11.1 kg/mol, M_w/M_n = 1.14)-stabilized emulsions at pH 8.0 (A) and 10.4 (B) as a function of dodecane volume fraction in water (0.5% PVPBA). CLSM micrographs of an emulsion (pH 8.9) with the oil phase stained by Nile red (C) and an emulsion (pH 8.9) prepared using fluorescein-labeled PVPBA (0.5% PVPBA) (D). Scale bar is 50 μm.

Interfacial tension measurements indicated both PVPBA nanoparticles and unimers could effectively lower the interfacial tension of dodecane/water from 52.8 to ~44.9 mN m^{-1} for nanoparticles (pH 7.2−8.9) and 32.6−36.6 mN m^{-1} for unimers (pH 10.1−11.7), in the presence of 0.5% PVPBA. It is remarkable that PVPBA unimers reduced the interfacial tension to a larger extent than PVPBA nanoparticles, which partially explains why PVPBA unimers are effective stabilizers at pH > pK_a.

Confocal laser scanning microscopy (CLSM) confirmed that the emulsions were of o/w type with polydisperse spherical oil droplets (stained with Nile red) dispersed within a continuous aqueous phase. Fluorescein-labeled PVPBA (see Supporting Information) was shown to stay in the aqueous phase and adsorb onto the oil−water interface.

The gel nature of the emulsions was further investigated by rheology tests. Figure 3A shows the change of moduli during
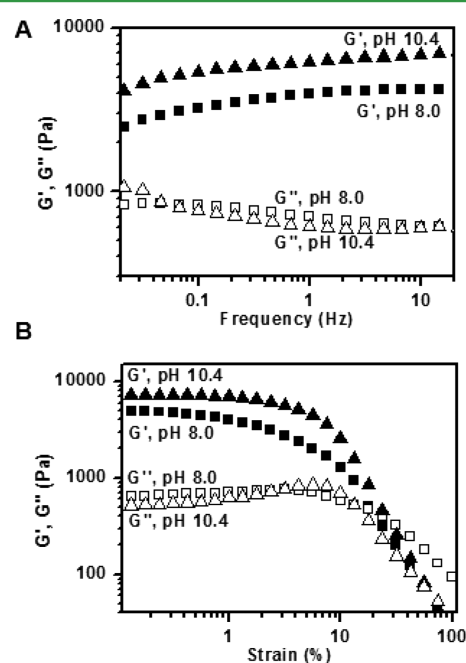

Figure 3. Rheology measurements of HIPEs (80% dodecane, 0.5% PVPBA, M_n = 11.1 kg/mol, M_w/M_n = 1.14): (A) strain sweep at 1.0 Hz, (B) frequency sweep at 1.0% strain.

strain sweeps for two HIPEs at pH 8.0 and 10.4. A linear regime is observed at low strains, where the storage moduli (G') are much higher than the loss moduli (G''), indicating solid-like properties of the gelled HIPEs. The G' value is 7.1 and 5.0 kPa for pH 10.4 and 8.0, respectively. It is noteworthy that these values are more than 1 order of magnitude larger than those reported for microgel-stabilized Pickering emulsions,[26] hydrogen-bond-reinforced HIPE gels,[7] charge-driven assembled HIPE gels, and gelled HIPEs stabilized by star polymers.[10] As the strain increases, G' and G'' crossover at yield points of 19 and 66% strain for the HIPE at pH 8.0 and 10.4, respectively. The significantly larger yield strain of the latter suggests the HIPE at pH 10.4 is much more viscoelastic, pointing to a more effective gelling capability when PVPBA exists as unimers. Frequency sweep measurements (Figure 3A) again confirm the solid-like properties of the HIPEs, as G' is higher than G'' and is almost independent of the frequency in the linear viscoelastic regime.

Further emulsification studies were performed using other oils, including hexane, toluene, and 1-octanol. For the former two oils, when the oil fraction was fixed at 80%, gelled o/w HIPEs were observed at pH > pK_a. These results demonstrate that PVPBA is able to emulsify other oils of low polarity and further demonstrate that PVPBA unimers at pH > pK_a are indeed more effective stabilizers and gelators than PVPBA nanoparticles. For octanol, which has a higher polarity, o/w emulsions were formed up to 70% oil, and inversion of emulsion type to w/o was observed at 80% oil (Figure S4, Supporting Information). Gelation was not observed for octanol, which may be attributed to competition for hydrogen bonding formation with PVPBA by its hydroxyl group.

PVPBA is a pH-responsive polymer and, therefore, we envisioned that an abrupt change in pH may be employed to trigger demulsification on demand.[27] For this, a HIPE (80% dodecane, 0.5% PVPBA) with a total volume of 1.5 mL was first prepared at pH 9.0. Addition of 50 μL of a NaOH solution (1 M) resulted in instant demulsification with complete oil−water separation, the final pH of which was 13.0. This result was consistent with the fact that no emulsion could be formed at pH greater than 12.7. Phenyl boronic acids are known to form reversible boronate esters with diols such as sugars. To test the effect of diols on the emulsion properties, emulsions were prepared in the presence of 0.5 M glucose at different pH values. At pH 8.0 in the presence of glucose, gelled emulsions were formed only with 70−85% dodecane, which was in contrast to the 50−85% oil range for the gelled emulsions prepared without glucose at the same pH. Similarly, 80% oil was required to form a gelled emulsion at pH 10.1 in the presence of glucose, whereas much lower oil fractions down to 50% could form gelled emulsions without glucose. These results can be interpreted from two possible effects induced by glucose. On the one hand, boronate ester formation with glucose lowers the pK_a of boronic acid, which makes the emulsifier more hydrophilic at a given pH. Because emulsifiers must be suitably amphiphilic to be effective, the shift toward hydrophilicity can lower the emulsifying ability of PVPBA in the presence of glucose. On the other hand, the presence of excess glucose can screen the formation of hydrogen bonds between the boronic acid units, which should lower the gelling ability of PVPBA.

HIPEs have been used as templates to prepare technologically important macroporous materials (polyHIPEs) via polymerization in the continuous phase. However, most polyHIPEs have limitations due to the requirement of a large amount of surfactant or by their closed-cell structures.[28] The excellent emulsifying and gelling properties of PVPBA prompted us to explore the possibility of producing PVPBA porous materials, whereby PVPBA homopolymer was used as both an emulsifier and a structure-forming material such that no surfactant and no further polymerization step was needed. Taking advantage of the stability of the gelled emulsions, PVPBA porous materials were prepared by simply extruding gelled emulsions into ethanol to remove the oil, followed by vacuum drying. Figure 4 shows scanning electron microscopy (SEM) images of two porous materials made from a gelled emulsion of medium internal phase (65%) and a gelled HIPE (85%). It was encouraging to see that defined porous structures with multiple pore sizes were successfully obtained. As expected, the cells were more densely packed using the HIPE template, reflecting the differing packing density of the oil droplets in the templates. More importantly, most of the cells
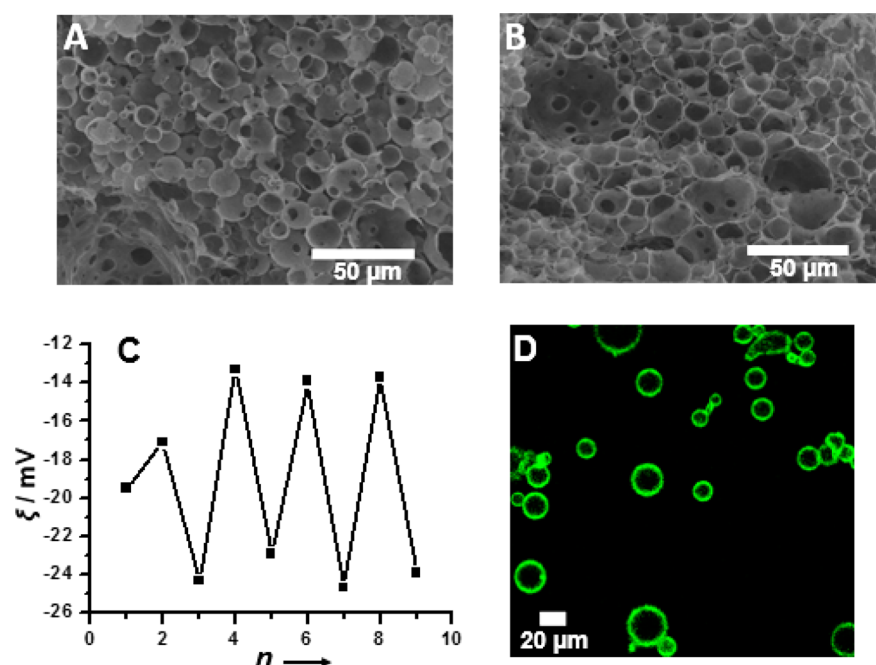
Figure 4. SEM micrographs of PVPBA porous materials prepared using 7% PVPBA (M_n = 16.2 kg/mol, M_w/M_n = 1.21) at pH 11.0 with an internal dodecane fraction of 65% (A) and 80% (B). (C) Zeta potential of multilayered capsules as a function of layer number (n), and (D) CLSM micrograph of 5-layered capsule.

contained one or multiple openings of several micrometers on their walls and interconnected cells, which should impart excellent mass transport in these porous materials.

To further illustrate the potential of PVPBA-stabilized emulsions, we next investigated the possibility of generating multilayered capsules using emulsion droplets as the templates, in which PVPBA served as both an interfacial stabilizer and a building block for multilayers. The multilayered capsules were fabricated using the well-established layer-by-layer technique,[29] capitalizing on the complexation of PVPBA with poly(vinyl alcohol) (PVA).[30] Alternating addition of PVA and PVPBA layers was confirmed by the switch in zeta potentials, that is, PVA addition lowered the zeta potential while PVPBA addition increased the zeta potential (Figure 4C). CLSM confirmed the stability and spherical morphology of the multilayer-coated oil droplets, suggesting the potential to fabricate capsules using PVPBA-stabilized emulsion droplets (Figure 4D).

CONCLUSIONS

In summary, we present a remarkable type of efficient emulsifier based on a boronic acid linear homopolymer, which can stabilize and gel emulsions over a wide range of pH and internal phase fractions. Unexpectedly, the unimers have been shown to be even more effective in emulsification and gelation than the corresponding homopolymer aggregates or nanoparticles. Moreover, the pH- and sugar-responsive nature of these polymers endows additional versatility to the emulsions stabilized by such a simple linear homopolymer. The PVPBA-stabilized emulsions provide unique opportunities to prepare phenylboronic-acid-based porous materials and multi-layered capsules, which may be well-suited for catalysis and sugar-responsive release. We believe our findings may expand the current understanding of emulsifier properties and stimulate future research in the development of simple, yet efficient, emulsifiers for functional soft materials design.

ASSOCIATED CONTENT

S **Supporting Information**

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acsami.5b07456.

> Preparation and characterization of PVPBA polymers and emulsions, CLSM and photos of emulsions, interfacial tensions, hydrodynamic diameter and zeta potential, fluorescence spectra of fluorescein-labeled PVPBA, molding emulsions, and SEM images of porous materials (PDF)

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Notes

The authors declare no competing financial interest.

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ABBREVIATIONS

HIPEs, high internal phase emulsions
O/W, oil in water

■ REFERENCES

(1) Chen, Z.; Ji, H.; Zhao, C.; Ju, E.; Ren, J.; Qu, X. Individual Surface-Engineered Microorganisms as Robust Pickering Interfacial Biocatalysts for Resistance-Minimized Phase-Transfer Bioconversion. *Angew. Chem., Int. Ed.* **2015**, *54*, 4904−4908.

(2) Choi, C.-H.; Weitz, D. A.; Lee, C.-S. One Step Formation of Controllable Complex Emulsions: From Functional Particles to Simultaneous Encapsulation of Hydrophilic and Hydrophobic Agents into Desired Position. *Adv. Mater.* **2013**, *25*, 2536−2541.

(3) Wang, W.; Zhang, M.-J.; Xie, R.; Ju, X.-J.; Yang, C.; Mou, C.-L.; Weitz, D. A.; Chu, L.-Y. Hole−Shell Microparticles from Controllably Evolved Double Emulsions. *Angew. Chem., Int. Ed.* **2013**, *52*, 8084−8087.

(4) Weaver, J. V. M; Rannard, S. P.; Cooper, A. I. Polymer-Mediated Hierarchical and Reversible Emulsion Droplet Assembly. *Angew. Chem.* **2009**, *121*, 2165−2168.

(5) Peng, L.; Zhang, J.; Li, J.; Han, B.; Xue, Z.; Yang, G. Macro- and Mesoporous Polymers Synthesized by a CO2-in-Ionic Liquid Emulsion-Templating Route. *Angew. Chem., Int. Ed.* **2013**, *52*, 1792−1795.

(6) Helgeson, M. E.; Moran, S. E.; An, H. Z.; Doyle, P. S. Mesoporous Organohydrogels from Thermogelling Photocrosslinkable Nanoemulsions. *Nat. Mater.* **2012**, *11*, 344−352.

(7) Deng, G.; Ma, Q.; Yu, H.; Zhang, Y.; Yan, Z.; Liu, F.; Liu, C.; Jiang, H.; Chen, Y. Macroscopic Organohydrogel Hybrid from Rapid Adhesion between Dynamic Covalent Hydrogel and Organogel. *ACS Macro Lett.* **2015**, *4*, 467−471.

(8) Zou, S.; Wei, Z.; Hu, Y.; Deng, Y.; Tong, Z.; Wang, C. Macroporous Antibacterial Hydrogels with Tunable Pore Structures Fabricated by Using Pickering High Internal Phase Emulsions as Templates. *Polym. Chem.* **2014**, *5*, 4227−4234.

(9) Sun, G.; Li, Z.; Ngai, T. Inversion of Particle-Stabilized Emulsions to Form High-Internal-Phase Emulsions. *Angew. Chem., Int. Ed.* **2010**, *49*, 2163−2166.

(10) Chen, Q.; Cao, X.; Liu, H.; Zhou, W.; Qin, L.; An, Z. pH-Responsive High Internal Phase Emulsions Stabilized by Core Cross-Linked Star (CCS) Polymers. *Polym. Chem.* **2013**, *4*, 4092−4102.

(11) Chen, Y.; Ballard, N.; Bon, S. A. F. Moldable High Internal Phase Emulsion Hydrogel Objects from Non-Covalently Crosslinked Poly(N-isopropylacrylamide) Nanogel Dispersions. *Chem. Commun.* **2013**, *49*, 1524−1526.

(12) Zhang, H. F.; Cooper, A. I. Synthesis and Applications of Emulsion-Templated Porous Materials. *Soft Matter* **2005**, *1*, 107−113.

(13) Jiang, J.; Zhu, Y.; Cui, Z.; Binks, B. P. Switchable Pickering Emulsions Stabilized by Silica Nanoparticles Hydrophobized In Situ with a Switchable Surfactant. *Angew. Chem., Int. Ed.* **2013**, *52*, 12373−12376.

(14) Bae, J.; Russell, T. P.; Hayward, R. C. Osmotically Driven Formation of Double Emulsions Stabilized by Amphiphilic Block Copolymers. *Angew. Chem., Int. Ed.* **2014**, *53*, 8240−8245.

(15) Thompson, K. L.; Chambon, P.; Verber, R.; Armes, S. P. Can Polymersomes Form Colloidosomes. *J. Am. Chem. Soc.* **2012**, *134*, 12450−12453.

(16) Shen, X.; Svensson Bonde, J.; Kamra, T.; Bülow, L.; Leo, J. C.; Linke, D.; Ye, L. Bacterial Imprinting at Pickering Emulsion Interfaces. *Angew. Chem., Int. Ed.* **2014**, *53*, 10687−10690.

(17) Li, Z.; Xiao, M.; Wang, J.; Ngai, T. Pure Protein Scaffolds from Pickering High Internal Phase Emulsion Template. *Macromol. Rapid Commun.* **2013**, *34*, 169−174.

(18) Li, Y.; Zou, J.; Das, B. P.; Tsianou, M.; Cheng, C. Well-Defined Amphiphilic Double-Brush Copolymers and Their Performance as Emulsion Surfactants. *Macromolecules* **2012**, *45*, 4623−4629.

(19) Bapat, A. P.; Roy, D.; Ray, J. G.; Savin, D. A.; Sumerlin, B. S. Dynamic-Covalent Macromolecular Stars with Boronic Ester Linkages. *J. Am. Chem. Soc.* **2011**, *133*, 19832−19838.

(20) He, L.; Szopinski, D.; Wu, Y.; Luinstra, G. A.; Theato, P. Toward Self-Healing Hydrogels Using One-Pot Thiol−Ene Click and Borax-Diol Chemistry. *ACS Macro Lett.* **2015**, *4*, 673−678.

(21) Cambre, J. N.; Roy, D.; Gondi, S. R.; Sumerlin, B. S. Facile Strategy to Well-Defined Water-Soluble Boronic Acid (Co)polymers. *J. Am. Chem. Soc.* **2007**, *129*, 10348−10349.

(22) Roy, D.; Cambre, J. N.; Sumerlin, B. S. Sugar-Responsive Block Copolymers by Direct RAFT Polymerization of Unprotected Boronic Acid Monomers. *Chem. Commun.* **2008**, 2477−2479.

(23) Roy, D.; Sumerlin, B. S. Glucose-Sensitivity of Boronic Acid Block Copolymers at Physiological pH. *ACS Macro Lett.* **2012**, *1*, 529−532.

(24) Niu, Z.; He, J.; Russell, T. P.; Wang, Q. Synthesis of Nano/Microstructures at Fluid Interfaces. *Angew. Chem., Int. Ed.* **2010**, *49*, 10052−10066.

(25) Ajami, D.; Dube, H.; Rebek, J. Boronic Acid Hydrogen Bonding in Encapsulation Complexes. *J. Am. Chem. Soc.* **2011**, *133*, 9689−9691.

(26) Li, Z.; Ngai, T. Stimuli-Responsive Gel Emulsions Stabilized by Microgel Particles. *Colloid Polym. Sci.* **2011**, *289*, 489−496.

(27) Tang, J.; Lee, M. F. X.; Zhang, W.; Zhao, B.; Berry, R. M.; Tam, K. C. Dual Responsive Pickering Emulsion Stabilized by Poly[2-(dimethylamino)ethyl methacrylate] Grafted Cellulose Nanocrystals. *Biomacromolecules* **2014**, *15*, 3052−3060.

(28) Silverstein, M. S. PolyHIPEs: Recent Advances in Emulsion-Templated Porous Polymers. *Prog. Polym. Sci.* **2014**, *39*, 199−234.

(29) Johnston, A. P. R.; Cortez, C.; Angelatos, A. S.; Caruso, F. Layer-by-Layer Engineered Capsules and Their Applications. *Curr. Opin. Colloid Interface Sci.* **2006**, *11*, 203−209.

(30) Deng, C. C.; Brooks, W. L. A.; Abboud, K. A.; Sumerlin, B. S. Boronic Acid-Based Hydrogels Undergo Self-Healing at Neutral and Acidic pH. *ACS Macro Lett.* **2015**, *4*, 220−224.