

Clickable Janus Particles

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S Supporting Information

ABSTRACT: Janus particles are colloidal analogues of molecular amphiphiles that can self-assemble to form diverse suprastructures, exhibit motility under appropriate catalytic reactions, and strongly adsorb to fluid–fluid interfaces to stabilize multiphasic fluid mixtures. The chemistry of Janus particles is the fundamental parameter that controls their behavior and utility as colloid surfactants in bulk solution and at fluid interfaces. To enable their widespread utilization, scalable methods that allow for the synthesis of Janus particles with diverse chemical compositions and shapes are highly desirable. Here, we develop clickable Janus particles that can be modified through thiol–yne click reactions with commercially available thiols. Janus particles are modified to be amphiphilic by introducing either carboxyl, hydroxyl, or amine moieties. We also demonstrate that regulating the extent of the modification can be used to control the particle morphology, and thus the type of emulsion stabilized, as well as to fabricate composite Janus particles through sequential click reactions. Modifying Janus particles through thiol–yne click chemistry provides a fast-reacting, scalable synthesis method for the fabrication of diverse Janus particles.

Janus particles are colloid surfactants that have two distinct sides with contrasting functionality. Tailoring the chemistry to specific fluid phases enables amphiphilic Janus particles to attach to fluid–fluid interfaces more strongly than chemically homogeneous particles and therefore create extremely stable emulsions.¹ Moreover, the incorporation of stimuli-responsive moieties can also be used to induce changes in the particle morphology enabling phase inversion emulsification² or triggering release of encapsulated materials.³ Janus particles can also undergo self-assembly to form suprastructures^{4–10} and exhibit self-propelled motion when functionalized with catalysts.^{11–13}

Janus particles are typically synthesized using either surface functionalization of homogeneous particles or via phase separation methods.^{14–17} Surface functionalization techniques produce limited quantities of Janus particles because the particles are required to be stabilized in monolayers to perform spatially selective chemical or physical modification.^{18–20} Methods based on phase separation mechanisms allow for the fabrication of Janus particles in bulk solutions; however, the final particle composition and morphology is highly dependent on the interaction energies between precursors, requiring unique synthesis conditions.^{21–25} In order for Janus particles to be viable solid surfactants on a large scale, it is necessary to develop

fabrication methods that are scalable as well as modular to enable the chemical composition to be tailored to specific applications.

Recent advances in click chemistry have opened new avenues for the synthesis of functional particles²⁶ and capsules.²⁷ Click reactions are characterized as making stable carbon–heteroatom–carbon bonds under simple conditions that use readily available reactants, are insensitive to oxygen and water, produce minimal or benign byproducts, and enable product purification by non-chromatographic methods.²⁸ These advantageous reaction conditions have made click chemistry a powerful tool for bioconjugation, drug delivery, and polymer synthesis.²⁹ Click chemistry has been used for the fabrication of Janus particles using a cyclic templating strategy that employed an interfacial azide–alkyne click reaction.³⁰ More recently, click chemistry was used in a bulk synthesis method of polystyrene–poly(vinylbenzene chloride) Janus particles which could undergo a subsequent thiol–chloride click reaction with glucotohiose to render the particles bio-functional for the binding of a lectin protein.³¹ These initial works require reactions times on the order of several days and have been applied to a limited number of precursors due to the presence of multiple reaction steps in the cyclic templating strategy and the rare use of thiol–chloride reactions in literature. Click chemistry remains an untapped resource to develop scalable synthesis methods for Janus particles with diverse chemical compositions.

Inspired by the use of thiol–yne click chemistry to produce polymers with high yield in short reaction times (on the order of minutes),³² we develop clickable polystyrene–poly(propargyl acrylate) (PS-PA) Janus particles that can be subsequently modified via thiol–yne click reactions. Seeded emulsion polymerization^{33,34} is used for the bulk synthesis of the clickable PS-PA Janus particles. The PA monomer is chosen because it contains a click-active acetylene pendant group that can participate in thiol–yne click reactions, enabling the Janus particles to be modified with commercially available thiols. We also show that the extent of modification can be controlled by reaction time and particle concentration. Unlike the prior reports that use click chemistry for Janus particle synthesis, our approach also allows for sequential click modifications to form composite Janus particles in which the chemical composition of the surface and interior can be independently controlled.

To demonstrate the versatility of our technique, we generate three different types of Janus particles from a single seed particle using three independent thiol–yne click reactions as illustrated in Figure 1. Linear polystyrene (LPS) particles (~850 nm diameter) are first prepared via dispersion polymerization. These LPS particles are swollen with a monomer mixture of styrene,

Received: June 1, 2016

Published: August 22, 2016

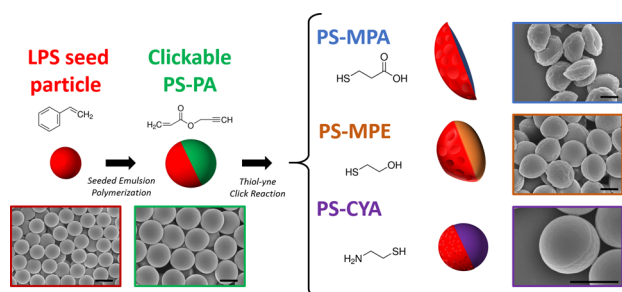


Figure 1. Schematic and corresponding SEM images depicting the synthesis of clickable PS-PA Janus particles and subsequent modification via thiol–yne click reactions. The LPS particles are spherical, while all Janus particles are non-spherical. Scale bars on the SEM images represent 1 μm .

propargyl acrylate, and divinylbenzene, and an emulsion polymerization produces click-active PS-PA Janus particles. Interestingly, these PS-PA seed particles are non-spherical, which suggests that polymerization induced phase separation results in the formation of Janus particles rather than core–shell particles which would have yielded spherical particles (Supporting Information, Figure S1). The thermodynamics of phase separation dictates that systems move from a mixed state to phases that are rich in either component. The copolymerization and cross-linking during polymerization induced phase separation will incorporate both PS and PA into both sides resulting in PS-rich and PA-rich faces of the Janus particles. The PS-PA seed particles are modified through thiol–yne click reactions with three commercially available thiols: 3-mercaptopropionic acid (MPA), 2-mercaptoethanol (MPE), and cysteamine (CYA). The solutions for the click reactions with MPA and MPE comprised of 0.3 mg/mL PS-PA particles dispersed in 10 mL of neat thiol (which is liquid at room temperature) that contains 1 wt% photoinitiator. The CYA thiol is solid at room temperature and therefore is dissolved in 10 mL methanol at 1 M concentration with 1 wt% photoinitiator (by thiol). The click reactions are carried out by stirring and irradiating the solutions with UV light for 30 min. The particles are then washed in DI water by centrifugation. After the thiol–yne click reactions, a distinct boundary is observed between smooth and rough faces of the particles. To identify which side of the modified particles is hydrophobic (PS-rich) and hydrophilic (thiol-rich), particles are allowed to attach to toluene–water interfaces. A solution of 10 wt % polystyrene in toluene is added; the toluene is then allowed to evaporate, thereby trapping the particles in polystyrene films. Scanning electron microscopy (SEM) images show the smooth sides are preferentially oriented into the water phase and thus are hydrophilic (Figure S2). The dimples on the hydrophobic side are present likely due to incomplete phase separation of PS and PA and the differences in the particle morphologies are attributed to different degrees of swelling (Figure S3).

Fourier transform infrared (FTIR) spectroscopy is used to measure the bulk composition and confirm successful modification of the Janus particles (Figure 2). The spectrum of the PS-PA Janus particles contains the characteristic peaks for the benzene ring ($1420\text{--}1620\text{ cm}^{-1}$) of PS as well as the characteristic acrylate carbonyl (1730 cm^{-1}) and click-active acetylene (2130 and 3270 cm^{-1}) of PA.³⁵ The absence of a peak unique to PA around 1600 cm^{-1} indicates that the copolymerization between PS and PA occurred through the acrylate vinyl bond.³⁶ Modification of the PS-PA clickable Janus particles with MPA and MPE is confirmed by detecting the presence of

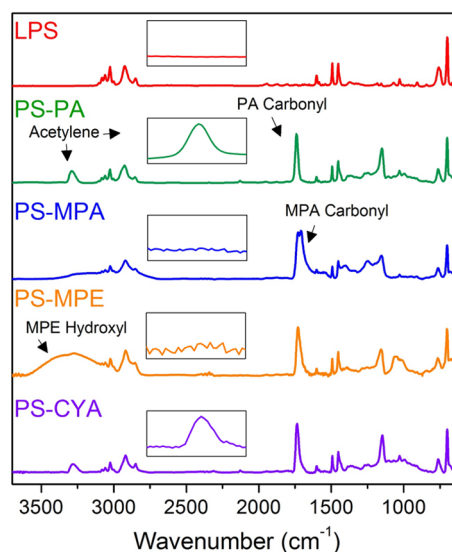


Figure 2. FTIR spectra comparing the LPS seed particle and clickable PS-PA Janus particle to modified PS-MPA, PS-MPE, and PS-CYA Janus particles. The insets are magnifications (20 \times) of $2100\text{--}2160\text{ cm}^{-1}$ to identify the presence of the PA acetylene peak.

the carbonyl stretching (1710 cm^{-1}) for MPA and the hydroxyl stretching ($2700\text{--}3600\text{ cm}^{-1}$) for MPE. The spectra also show that modification is complete by the disappearance of the acetylene peak at 2130 cm^{-1} (insets). For the PS-CYA Janus particles, the spectrum is similar to the PS-PA Janus particles, suggesting that only the surface is functionalized, which is also supported by the minimal morphology change of the particles. The complete modification with MPA and MPE is attributed to performing the click reactions in neat thiol, whereas the surface functionalization with CYA is attributed to the solution conditions necessitated to dissolve the CYA (Figure S4). The incorporation of the amine functionality is confirmed by observing fluorescence for PS-CYA particles labeled with an amine-reactive fluorescent probe (Figure S5). Further confirmation is shown by slight positive shift in the zeta potential from $-43 \pm 1\text{ mV}$ for the precursor PS-PA Janus particles to $-33 \pm 1\text{ mV}$ for the PS-CYA Janus particles (Table S1). Lastly, a final piece of evidence that amine groups are present is the adsorption of negatively charged gold nanoparticles on the surface of PS-CYA Janus particles (Figure S6).

Click chemistry not only allows us to tailor the surface chemistry and surface charge of Janus particles, but also enables us to control the extent of modification (Table S2), which we show influences particle shape and ability to stabilize emulsions. We hypothesize that the modification of the particles occurs via a shrinking-core mechanism in which the surface of the PS-PA particles is functionalized first and then neat MPA diffuses through the functionalized layer to undergo click reaction with the PA in the interior of the particles (Figure 3a). To test this hypothesis, we change the duration of the thiol–yne click reactions simply by varying the UV irradiation time. Completely modified PS-MPA particles are synthesized by 30 min reactions for 0.3 mg/mL PS-PA particles dispersed in neat MPA. Decreasing the reaction time to 0.5 min resulted in particles containing unreacted acetylene bonds. The extent of modification could be further decreased by increasing the PS-PA particle concentration to 3 mg/mL for 30 and 0.5 min reactions, respectively, as shown by continuous increase in the PA acetylene peaks and decrease in the MPA carbonyl peak in the FTIR

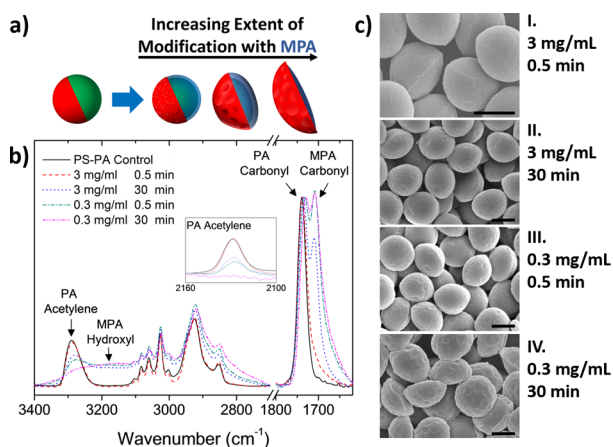


Figure 3. (a) Schematic depicting modification via shrinking-core mechanism. (b) FTIR and (c) SEM images comparing the composition and morphology of PS-MPA particles made at varying reaction times and PS-PA particle concentrations for the thiol–yne click reaction.

spectra (Figure 3b). It is also observed that the PA carbonyl shifted to lower wavenumber with increasing modification, likely due to increasing resonance.³⁷ In agreement with our proposed mechanism that the particles are formed via a shrinking-core mechanism, we observe that the morphology of the particles transforms from spherical to dome-shaped with increasing modification (Figure 3c). The morphology change is due to higher concentrations of hydrophilic MPA in the interior of the particles resulting in more deformation of the particles upon deswelling when the particles are dried (Figure S7).

One of the most intriguing applications of Janus particles is in the stabilization of multiphasic mixtures, as studies have shown that thermodynamically stable emulsions can be generated using Janus particles.³⁸ Our recent study also has shown that the morphology of emulsions stabilized by Janus particles containing pH-responsive carboxylic acid groups depends strongly on the solution pH.² Moreover, the phase inversion of an emulsion can be induced by changing the solution pH because of changes in the chemistry and shape of such Janus particles. We also observe this pH-responsive emulsion stabilization for completely modified PS-MPA particles; however, partially modified PS-MPA particles (condition III in Table S2) stabilize water-in-oil emulsions at both pH 6 and 12 (Figure 4). All four emulsions solutions are observed to be stable for more than 4 weeks. The surfactant behavior of the Janus particles will depend on the swelling behavior of both sides of the particles; PS-rich side by toluene and MPA-rich side by water. By our proposed shrinking-core mechanism of modification, the partially modified PS-MPA particles would have unreacted PA on the particle interior which results in a lower degree of swelling by water compared to the completely modified particles. Figure 4 demonstrates that we can control the extent of modification to influence the degree of

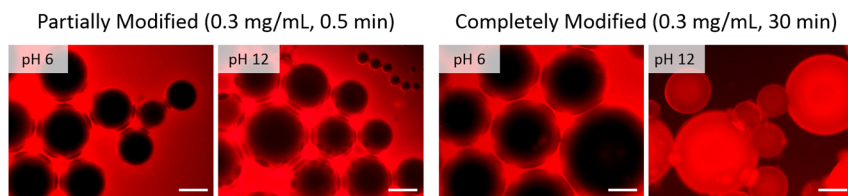


Figure 4. Fluorescence microscopy images of water and toluene emulsions stabilized by PS-MPA particles. The dark regions represent the water phase and the bright regions represent the toluene phase containing 1 wt% Nile Red. Scale bars represent 100 μm.

swelling with water and thus the balance of swelling between the two sides. Furthermore, this shows that regulating the extent of modification allows us to incorporate pH-responsive moieties while still maintaining control over the type of emulsions stabilized.

The ability to impart multiple functionalities on one side of Janus particles could potentially provide significant advantages over typical Janus particles. For example, Janus particles that have dual or multiple functionalities on one side could be useful for delivery or catalysis applications where the surface properties would dictate the interaction of particles with the environment, while its interior would provide the necessary functionality or properties. We can fabricate such particles by independently functionalizing the surface and modifying the interior of PS-PA seed particles by performing sequential click reactions in which the first click reaction functionalizes the surface and the second reaction modifies the interior. To demonstrate this, we modify the interior of PS-CYA Janus particles through a second click reaction with MPA to form PS-MPA-CYA composite Janus particles that contain both surface amine groups and pH-responsive shape-changing properties in the interior (Figure S8). The incorporation of MPA into the particles was confirmed by FTIR (Figure S9a). The zeta potential in neutral DI water (-36 ± 1 mV) showed a similar positive shift as the PS-CYA (-33 ± 1 mV) particles compared to the original PS-PA seed Janus particles (-43 ± 1 mV) which confirms that the amine groups remain at the surface of the PS-MPA-CYA particles. SEM images show that the PS-MPA-CYA particles look strikingly similar to PS-PA particles, which is expected, since CYA is only on the surface of the particles as described earlier. Modifying the interior of the particles with MPA integrated shape-changing pH-responsiveness as shown by the increased swelling at high pH, whereas PS-CYA particles exhibit no such transition. The amphoteric nature of the PS-MPA-CYA particles promotes the binding of both cationic and anionic fluorescent dyes demonstrating the ability to load different cargo (Figures 5 and S10). Fluorescence microscopy also indicates that the surface is functionalized with CYA and the interior is modified with MPA. To demonstrate the versatility of this synthesis, we also fabricate PS-MPE-MPA composite Janus particles by reacting partially modified PS-MPA particles (Figure 3) with MPE (Figure S9b–d). Our ability to synthesize functional composite Janus particles through sequential click reactions provides a simple method to optimize the interfacial activity or dictate self-assembly through the surface chemistry while also embedding stimuli-responsive properties or adsorption sites into the interior.

In summary, we have demonstrated the use of click chemistry for the fabrication of three unique amphiphilic Janus particles by modifying a single seed particle with carboxyl, hydroxyl, or amine functional groups. Conventional methods for the bulk synthesis of Janus particles by phase separation are inherently limited in the pairs of precursors that can be incorporated into the particles;

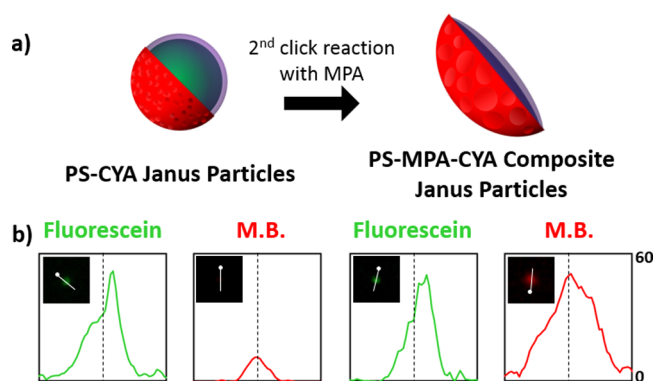


Figure 5. a) Schematic of PS-CYA Janus particles and PS-MPA-CYA composite Janus particles. b) Fluorescence intensity profiles of fluorescein and methylene blue (M.B.). Insets illustrate the line scans ($5 \mu\text{m}$ in length) overlaid on fluorescence images ($10 \times 10 \mu\text{m}^2$). The line scans are centered at the center of the particles identified from the bright field images, and the dots represent the starting position to indicate the direction of the scans.

however our synthesis of clickable PS-PA Janus seed particles widens the palette of moieties that can be incorporated via thiol–yne click reactions. The flexibility of the thiol–yne reaction allows us to vary the particle surface chemistry and surface charge. Moreover, by controlling the extent of modification, we can control the particle morphology and the type of emulsions stabilized by the particles, and also synthesize composite Janus particles through sequential click reactions. The use of thiol–yne click chemistry to modify clickable Janus particles offers a rapid and scalable method to design the chemistry, surface charge, morphology, and self-assembly of Janus particles for potential use as solid surfactants.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: [10.1021/jacs.6b05633](https://doi.org/10.1021/jacs.6b05633).

Experimental details and characterization data, including Figures S1–S10 and Tables S1 and S2 (PDF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We acknowledge funding from the Penn Provost's Fellowship for Academic Diversity, the Africk Family Post-Doctoral Fellowship, and ACS PRF no. 55260-ND10. We thank Dr. Samantha Wilner and Dr. Tobias Baumgart for assistance using Alexa Fluor 488, and Dr. Martin Haase for supplying the gold nanoparticles. We thank the Singh Center for Nanotechnology for use of SEM, and Dr. Cherie R. Kagan for use of FTIR.

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