

## Janus-Shaped Single-Chain Nanoparticles Formed by One-Shot Intrablock Cross-Linking of Linear Block Copolymer

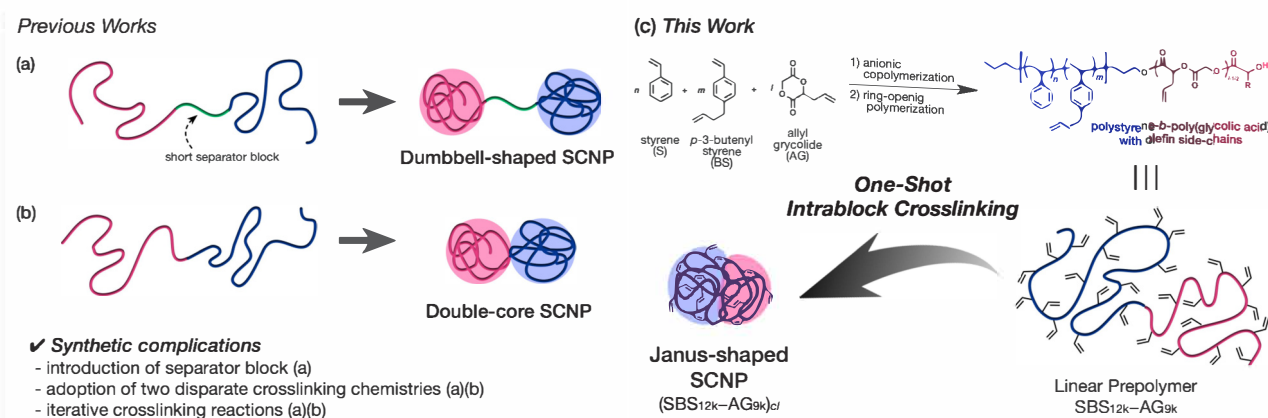
Transforming a single polymer chain into a shape-defined nano-object is an important challenge to mimic the sophisticated biological functions of proteins and nucleic acids in a synthetic polymer system. In this study, we developed an efficient and versatile means to produce single chain nanoparticles (SCNP) with two chemically compartmentalized domains, i.e., Janus-shaped SCNPs, from a single block copolymer chain by one-shot intermolecular cross-linking. Structural analysis by  $^1\text{H}$  nuclear Overhauser effect spectroscopy and small-angle X-ray scattering supported the generation of Janus-shaped SCNPs. Interestingly, the Janus-shaped SCNP showed a much smaller microphase-separated structure compared to the linear block copolymer precursor.

The self-folding of biomacromolecules, such as proteins and nucleic acids, has inspired chemists to mimic their sophisticated biological functions in a synthetic polymer system. Recently, the process of synthesizing single chain nanoparticles (SCNPs) has attracted attention as an artificial polymer folding process. SCNPs are synthesized by intramolecular cross-linking of a linear polymer chain having cross-linkable functional groups along the main chain [1]. The intramolecular cross-linking basically takes place randomly along the polymer chain, resulting in a globular nanoparticle. To mimic natural proteins more closely, it is of particular interest to construct SCNPs having chemically disparate nanodomains. Indeed, the synthesis of such compartmentalized SCNPs is reminiscent of the tertiary structure formation in natural proteins with multiple functional domains. Several types of compartmentalized SCNPs have been reported: for example, dumbbell-shaped and double-core SCNPs. The former consisted of two chemically different intramolecularly cross-linked blocks tethered by a short spacer block while the latter consisted of two directly bonded different cross-linked blocks. Interestingly, a double-core SCNP was found to self-assemble into nanostructured aggregate with ultra-small periodic-

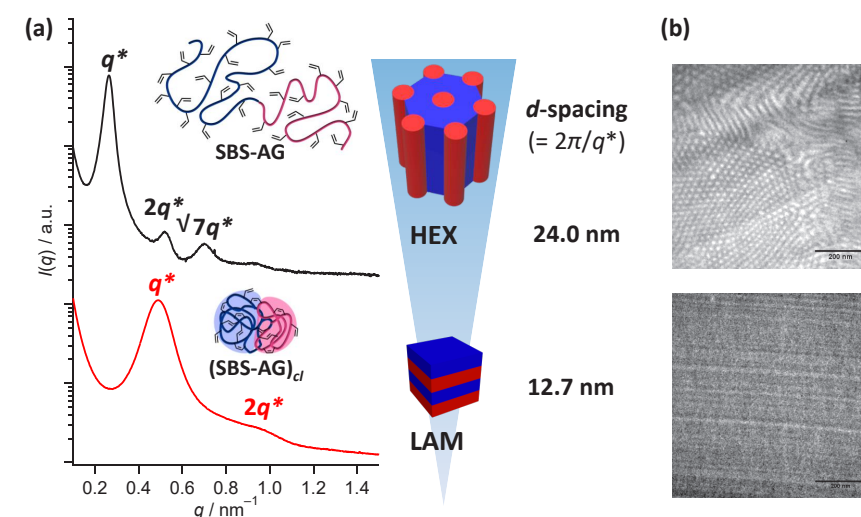
ity in solution [2]. Thus, compartmentalized SCNPs are interesting not only from a fundamental point of view but also from their potential application as a nanomaterial. However, previous syntheses required complicated multistep reactions, hindering the study and utilization of compartmentalized SCNPs.

To provide easy access to compartmentalized SCNPs, we have examined the one-shot cross-linking of a linear diblock copolymer having a cross-linkable functionality along the entire polymer backbone [3]. An important hypothesis here is that the spatially closer cross-linkable points preferentially react rather than farther ones. Thus, we conjectured that the one-shot intramolecular cross-linking of block copolymer should result in SCNPs with two chemically compartmentalized spaces, i.e., Janus-shaped SCNP, due to the preferential intrablock cross-linking.

To demonstrate the one-shot cross-linking, we designed and synthesized a polystyrene-*block*-poly(glycolic acid) bearing cross-linkable olefin side chains along both blocks (SBS-AG) (Fig. 1). As we previously reported, the olefin metathesis reaction is a powerful tool for intramolecular cross-linking [4]. According to our established procedure, we performed the one-shot intramolecular olefin metathesis



**Figure 1:** Schematic illustration of the synthesis of (a) dumbbell-shaped and (b) double-core SCNPs. (c) Synthetic pathway of the Janus-shaped SCNP ((SBS-AG)<sub>cl</sub>) via one-shot intrablock cross-linking of linear prepolymer (SBS-AG).



**Figure 2:** (a) Bulk SAXS profiles of SBS-AG (black) and (SBS-AG)<sub>cl</sub> (red). (b) TEM images of SBS-AG (upper) and (SBS-AG)<sub>cl</sub> (lower) (scale bar = 200 nm).

reaction using Grubbs second-generation catalyst. Since the highly diluted condition was applied, the reaction proceeded without intermolecular cross-linking to give an intramolecularly cross-linked product, i.e., (SBS-AG)<sub>cl</sub>. Size exclusion chromatography equipped with light scattering and viscosity detectors revealed no significant change in molecular weight but a large reduction in intrinsic viscosity upon the reaction. Moreover, small-angle X-ray scattering (SAXS) of the diluted solutions confirmed the smaller radius of gyration than that of the linear precursor [Fig. 2(a)]. Kratky plot analysis of the solution SAXS data suggested that the chain conformation transformed from the unfolded random coil state to the folded globule-like state.

We next investigated the localization of each polymer block in the folded macromolecule by  $^1\text{H}$  nuclear Overhauser effect (NOE) spectroscopy, to evaluate the validity of our hypothesis: the two blocks must be compartmentalized in the product obtained by the one-shot intrablock cross-linking.  $^1\text{H}$  NOE analysis of (SBS-AG)<sub>cl</sub> as well as the related model polymers demonstrated that each block was localized at the separated compartments in the macromolecule. This confirms that the cross-linking reaction takes place from spatially closer olefin pairs within each block, and eventually results in the Janus-shaped SCNP. Furthermore, the versatility of the one-shot intrablock cross-linking was demonstrated by application to several different BCPs.

Since the Janus-shaped SCNPs can be regarded as a new type of block copolymer architecture, we expect that they can self-assemble into micelle-like aggregate in selective solvents and microphase-separated structures in the bulk state. Accordingly, we investigated the microphase-separated structures before and after the one-shot cross-linking. The SAXS profiles of SBS-AG

and (SBS-AG)<sub>cl</sub> showed different higher ordered scattering patterns, which can be assigned to hexagonally close-packed cylindrical (HEX) and lamellar (LAM) structures. TEM images also supported the HEX and LAM structures in SBS-AG and (SBS-AG)<sub>cl</sub>, respectively [Fig. 2(b)]. The fact that the Janus-shaped (SBS-AG)<sub>cl</sub> produces an ordered nanostructure is strong evidence of the separated localization of the two blocks in the macromolecule. More interestingly, the Janus-shaped (SBS-AG)<sub>cl</sub> produced a nanostructure with 47% smaller feature size (domain-spacing ( $d$ ) = 12.7 nm) compared to the linear SBS-AG ( $d$  = 24.0 nm), even though the molecular weights of the two polymers are virtually identical. This indicates that ultrafine nanostructures can be produced without deteriorating the molecular-weight-dependent material properties of BCP, which is of great interest for nanopatterning applications.

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### BEAMLINE

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T. Isono (Hokkaido Univ.)