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How Far Can We Push Polymer Architectures?

Patrick J. M. Stals,[†,#] Yuanchao Li,[‡,#] Joanna Burdyńska,[§,#] Renaud Nicolaÿ,[†,⊥] Alper Nese,[§] Anja R. A. Palmans,[†] E. W. Meijer,[†,*] Krzysztof Matyjaszewski,[§,*] and Sergei S. Sheiko[‡,*]

[†]Institute for Complex Molecular Systems and Laboratory of Macromolecular and Organic Chemistry, Eindhoven University of Technology, 5600 MB Eindhoven, The Netherlands

[‡]Department of Chemistry, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina 27599-3290, United States

[§]Department of Chemistry, Center for Macromolecular Engineering, Carnegie Mellon University, Pittsburgh, Pennsylvania 15213, United States

[⊥]Matière Molle et Chimie (ESPCI-CNRS, UMR 7167), ESPCI ParisTech, 75005 Paris, France

Supporting Information

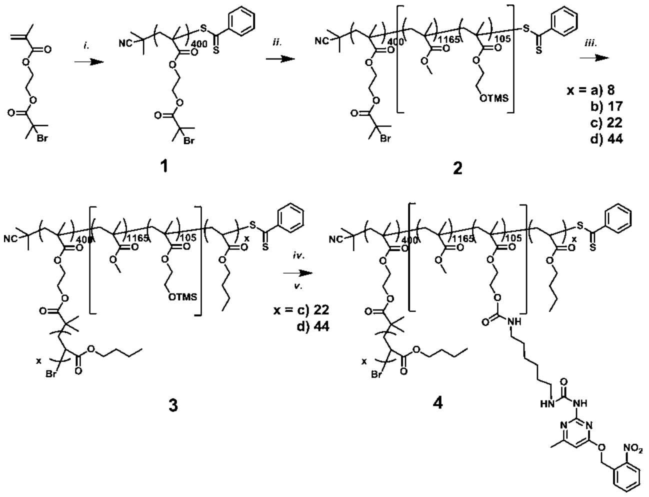
ABSTRACT: We here report the synthesis and characterization of a complex polymeric architecture based on a block copolymer with a cylindrical brush block and a single-chain polymeric nanoparticle block folded due to strong intramolecular hydrogen-bonds. The self-assembly of these constructs on mica surfaces was studied with atomic force microscopy, corroborating the distinct presence of block copolymer architectures.

Historically, polymeric architectures have been limited to relatively simple structures like block copolymers, grafted polymers, and polymer networks.[1] In recent decades, progress in synthetic methodologies, in conjunction with the use of conformational constraints, has led to better control over the size and shape of polymer architectures, as highlighted by the development of complex architectures such as dendrimers[2] and cylindrical brush polymers.[3] In addition, supramolecular interactions are effective in controlling polymer conformations, as demonstrated by the folding of individual polymer chains into well-defined, discrete nanoparticles.[4] Hybrids of several polymeric architectures have also been explored, leading to, for example, super-amphiphiles and protein–polymer conjugates.[5] Atomic force microscopy (AFM) measurements have enabled high-resolution imaging of the structures adopted by these polymer architectures on surfaces.[6] In our search for the synthetic limits of controlling polymer architectures, we started a joint project to include both a cylindrical brush polymer and a single-chain polymeric nanoparticle within one polymer that undergo intramolecular association (collapse) upon deprotection of quadruple hydrogen-bonds. Cylindrical brushes represent a new class of polymeric materials that feature self-assembly on mesoscales,[7] ultra-soft elastomers,[8] intramolecular mechanochemistry,[9] lubrication of cartilage,[10] and mucus clearance in lung airways.[11] Single-chain polymeric nanoparticles have recently attracted considerable research interest as they allow for compartmentalized systems, which show interesting applications in catalysis and sensing.[12]

Here we report on the synthesis and characterization of a block copolymer based on a bottlebrush block and a H-bonding-assisted, folded linear block. As a H-bonding moiety, we choose the ureido-pyrimidinone (UPy) group,[13] which is well-known for its ability to form strong, reversible, quadruple H-bonds, making it an ideal candidate for use in a wide range of self-assembly-based applications.[14]

The structural characteristics of the targeted block copolymer require a stepwise synthetic approach, combining different polymerization chemistries and post-modification strategies. The synthesis of the final polymers **4**, with a UV-labile protecting group on the UPy unit, is presented in Scheme 1. First, 2-(2-bromoisobutyryloxy)ethyl methacrylate (BIBEM) was polymerized using 2-cyano-2-propyl benzodithioate as a chain-transfer agent (CTA) via reversible addition−fragmentation chain-transfer radical polymerization (RAFT),[15] to afford PBIBEM homopolymer **1**. This pre-polymer, with M_n = 66 900

Scheme 1. Synthesis of Brush-Extended Polymers 4c,d[a]



[a]Reagents and conditions: (i) BIBEM, AIBN, CTA, anisole, 60 °C. (ii) MMA, HEMA-TMS, V-40, anisole, 80 °C. (iii) nBA, CuBr, $CuBr_2$, dNbpy/PMDETA, anisole, 60 °C. (iv) TBAF, THF, rt. (v) Photoprotected UPy-NCO, DBTDL, THF, reflux. For reasons of clarity the dithioester is depicted on the chain-end even though statistically it is more likely to be on the chain-end of one of the grafted side chains.

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and M_w/M_n = 1.34, had an estimated average degree of polymerization (DP) of 400, based on the monomer conversion and assuming initiation efficiencies of 100% and 45% for the RAFT CTA and for the primary radicals generated by the decomposition of AIBN, respectively.

In the second step, the PBIBEM macro-RAFT agent was chain-extended by RAFT copolymerization of methyl methacrylate (MMA) and 2-(trimethylsilyloxy)ethyl methacrylate (HEMA-TMS). The resulting block copolymer, **2**, with an estimated DP = 1270 and a ratio of MMA:HEMA-TMS = 92:8, had M_n = 187 000 and M_w/M_n = 1.31. Next, poly(*n*-butyl acrylate) (P*n*BA) side chains were grafted from the PBIBEM segment via atom-transfer radical polymerization (ATRP).[16] Four brush copolymers (**3a–d**) were obtained, with different DPs of side chains of 8, 17, 22, and 44, respectively. In the last step, the silyl moiety was removed with tetrabutylammonium fluoride (TBAF) to form free alcohol groups, which were further utilized for post-modification with photoprotected UPy isocyanates. Surprisingly, silyl deprotection of brush copolymers **3a,b**, with the shortest side chains, resulted in polymers that were barely soluble, preventing further functionalization. In contrast, deprotected polymers **3c,d** were readily soluble in common solvents such as chloroform and THF. Coupling of polymers **3c,d** with a photoprotected UPy isocyanate[17] yielded the two polymers **4c,d**. Finally, UV irradiation of the precursors **4c,d** (Figure 1) in dilute solutions produced the final products **5c,d**, in which a polymer brush is combined with a folded polymer.

The AFM micrographs in Figure 1 demonstrate the successful implementation of the synthetic strategy, yielding well-defined molecular brushes with a linear-chain tail undergoing a conformational transition. Quantitative and statistically representative analysis of the transition will be discussed with Figures 2 and 3 (*vide infra*).

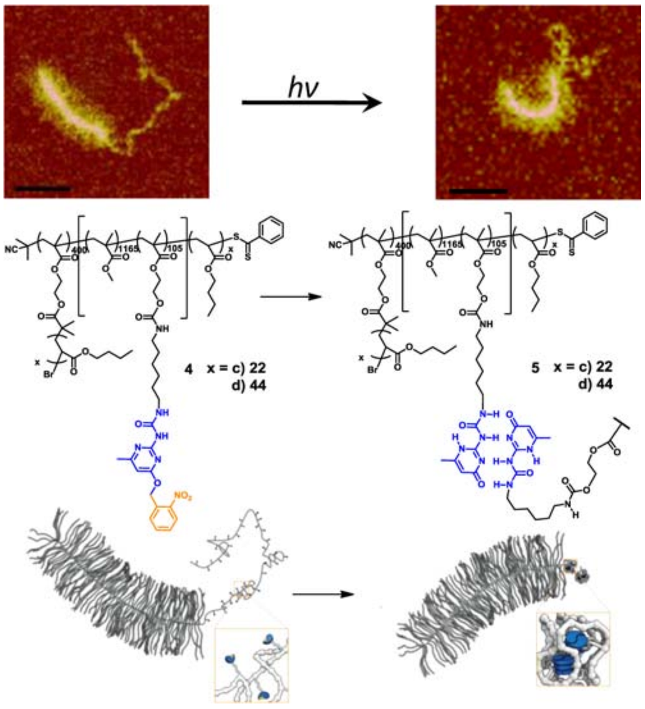

Figure 1. Polymer structures **4c,d** and **5c,d**, including representative AFM height micrographs of **4d** (top left) and **5d** (top right) (scale bar = 50 nm) and schematic representation of the polymer structures on the mica surface (bottom).

Polymers **4c,d** were characterized with a series of analytical tools, including nuclear magnetic resonance (NMR) and size exclusion chromatography (SEC, Figure S1 and S2 in the Supporting Information). ^{1}H NMR spectroscopy demonstrated the incorporation of the protected UPy units. After UV irradiation, the presence of the UPy-UPy dimers was confirmed by the signals at 13.3, 12.0, and 10.3 ppm, typical for the presence of 4[1*H*]-pyrimidinone dimers (Figure S3).[13] The complexity of the synthesized polymers, however, hampers detailed interpretation of the spectroscopic and chromatographic analyses. Although all analytical results are in agreement with the structures assigned as in Scheme 1, it should be noted that the synthesis of polymers **4** and **5** is approaching the limits of today's polymer synthesis and analysis techniques. Hence, deviations in end groups by transfer processes[18] and the presence of small amounts of homo(co)polymers of BIBEM and MMA/HEMA-TMS cannot be excluded, while complete assignment of the NMR spectra of brush polymers is impossible as well. Dynamic light scattering (DLS) experiments as well as SEC, normally very informative for the collapse/folding process, both show no significant differences in the conversions of **4c,d** into **5c,d** after deprotection, since the vast majority of the mass is located in the brush segment (Figure S4).Thus, other techniques are required to evaluate the effect of UPy dimerization on the conformational preferences of the final polymers **5c,d**.

Gratifyingly, AFM studies of polymer **4d** (before deprotection) and polymer **5d** (after deprotection) on mica enabled precise imaging of the transformation from an unfolded to folded brush block copolymer, respectively (Figure 1 and 2). The difference in the side-chain lengths of polymers **4c,d** was clearly visible (Figure 2 and S6), while the lengths of the brush backbones were, as expected, similar (Figure S7). The clear image of the linear block as an individual, randomly coiled polymer chain is ascribed to strong adsorption on mica and anchoring to the brush block. Usually, single linear polymer chains are difficult to image due to their small lateral and vertical dimensions. Figure S9 shows one example of successful molecular imaging of the UPy block only (Figure S8). However, inadequate resolution of the chain contour in coiled conformations did not allow for reliable quantitative analysis.

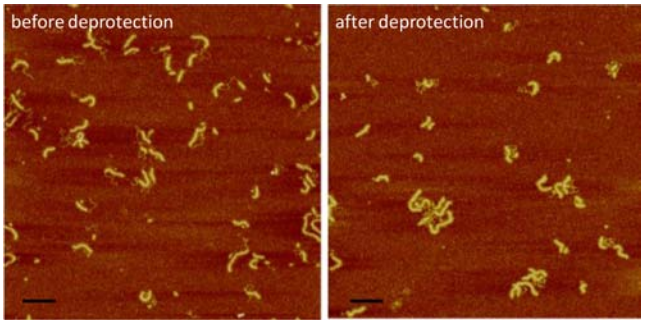

Figure 2. Representative AFM height micrographs of individual macromolecules of polymers **4d** (left) and **5d** (right) adsorbed on a mica substrate (scale bar = 200 nm).

Large-scale AFM micrographs demonstrate significant polydispersity of molecular structures including tailed brushes (majority fraction), brushes with indistinguishable tail, and linear chains without a brush section. The lack of tail on some structures can be ascribed to cleavage either during synthesis or post-synthesis due to tension in the brush backbone.[9b,19] Also, a fraction of polymer **1** could not be chain-extended, since it lacked a CTA. The images also show aggregates of brushes that are formed during the adsorption and solvent-drying processes.

The AFM images after deprotection clearly show enhancement in folding of the UPy-containing polymer block. As expected, the length of the brush grafts does not influence the folding behavior of the other block (Figure S6). To verify the conformational transition, we have quantitatively analyzed individual brushes with a clearly visible tail. The difference in the radius of gyration (R_g) of the UPy block before and after deprotection (26 ± 7 vs 20 ± 6 nm respectively for **4d** and **5d**, Figure 3, and 25 ± 6 vs 16 ± 3 nm respectively for **4c** and **5c**, Figure S10) was determined by tracing the linear-chain blocks of over 60 individual molecules to ensure a relative standard deviation of the mean below ~10% at 99.7% confidence, acquiring numbers consistent with DLS and SEC results for polymers of the UPy block only.[17] The effect of changes in the interaction strength between the linear polymer block and mica substrate due to removal of the protecting groups was negligible, since the linear block contains only ~10% UPy groups. Additionally, analysis of the brush section of **4c,d** gave equal contour lengths for both polymers (87 and 85 nm, respectively, Figure S7), which was in excellent agreement with the estimated DP of this block.

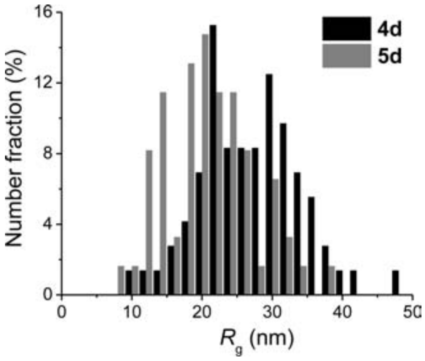

Figure 3. Change in R_g for AFM micrographs shown in Figure 2. Over 60 individual molecules were counted for each histogram.

Due to the unknown topology of intramolecular H-bonding and complex nature of interactions between the substrate and polymer blocks,[20] the development of a theoretical model for quantitative analysis of molecular dimensions would be an ambiguous project. However, we can estimate an upper limit for the linear-block dimension by assuming H-bonds were formed between neighboring UPy groups after deprotection. In this case, H-bonding results in a chain that is approximately 2 times shorter (~$L/2$) and 2 times thicker—i.e., stiffer—with a Kuhn length of ~$2b$, where L and b are the contour length and Kuhn length, respectively, of the linear-chain block before deprotection. Knowing that the scaling factor for real two-dimensional polymer chains is 0.75,[21] we estimate the ratio of the radius of gyration $R_g \approx b^{0.25}L^{0.75}$ before deprotection to that after deprotection to be ~1.4, which is in good agreement with the experimental numbers (26/20 = 1.3 for **4d** and **5d** and 25/16 = 1.6 for **4c** and **5c**).

In conclusion, we introduce a novel synthetic strategy, combining different polymerization techniques and deprotection strategies, to prepare a series of brush–nanoparticle block copolymers. We show the unique architectural features of such block copolymers at different length scales. With this study the frontiers in polymer synthesis, molecular analysis, and three-dimensional architectures of polymers are pushed forward, while at the same time the limitations in this endeavor are made clear.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental methods and synthetic procedures for polymers **1**–**5**, as well as additional characterization of the polymers and additional AFM micrographs. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

e.w.meijer@tue.nl; sergei@email.unc.edu; km3b@andrew.cmu.edu

Author Contributions

#P.J.M.S., Y.L., and J.B. contributed equally.

Notes

The authors declare no competing financial interest.

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