

# Unimolecular Janus Micelles by Microenvironment-Induced, Internal Complexation

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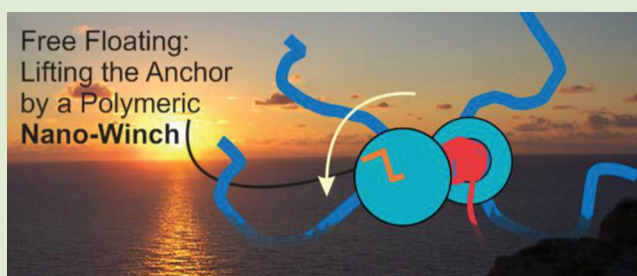
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## S Supporting Information

**ABSTRACT:** A noncentrosymmetric, star-shaped polymeric system is presented, which forms unimolecular micelles upon complexation of poly(propylene oxide) (PPO) with poly(dimethylaminoethyl methacrylate) (PDMAEMA). The influence of macromolecular architecture on the hydrophobicity of PPO and its interaction with PDMAEMA is investigated. Within stars, a complex between PPO and PDMAEMA is formed, lowering the interfacial tension of the hydrophobic domain (PDMAEMA acts as a “microsurfactant” for PPO). This leads to a pronounced drop in aggregation number compared to similar diblock copolymers, as corroborated by a scaling approach.



Architectural effects on polymer properties have been a hot topic in polymer sciences since the rise of living polymerization.<sup>1</sup> For example, polyelectrolyte effects are dependent on branching.<sup>2,3</sup> In contrast, the thermosensitive properties of star polymers are hardly influenced by the star architecture.<sup>4</sup> Reports discussing the architectural influence on the hydrophobicity of a single polymer chain under different topological constraints are rare. Here we go even further by addressing consequences of intramolecular, architectural effects on intermolecular aggregation, which lead to so-called unimolecular micelles.<sup>5,6</sup> Thus, copolymers of poly(propylene oxide) (PPO), poly(dimethylaminoethyl methacrylate) (PDMAEMA), and poly(ethylene oxide) (PEO) are compared. PPO is a thermoresponsive polymer which becomes hydrophobic below room temperature.<sup>4,7</sup> PEO and PDMAEMA are regarded as soluble in the investigated temperature interval (water-insoluble above  $\approx 60$  °C).<sup>4</sup> The miscibility of PPO and PDMAEMA has been found recently, indicating (weak) attraction between this polymer couple in bulk.<sup>8</sup> In contrast to strongly complexing polymers (which favor usually intermolecular micellization),<sup>9,10</sup> reports on PPO/PDMAEMA interaction in aqueous solution are missing. Here, we investigate the solution properties of binary systems (block copolymer PEO<sub>114</sub>-*b*-PPO<sub>69</sub>, PPO<sub>69</sub>-*b*-PDMAEMA<sub>100</sub> indexes assign the number average degree of polymerization per block)<sup>11</sup> and compare their properties with a ternary system, as present in the miktoarm star<sup>12</sup> PEO<sub>114</sub>-(PDMAEMA<sub>90</sub>)<sub>3</sub>-PPO<sub>69</sub> (refer to the Supporting Information and a forthcoming publication).<sup>13–16</sup>

For fluorescence spectroscopy, 4-(dicyanomethylene)-2-methyl-6-(*p*-dimethylaminostyryl)-4H-pyran is used as dye

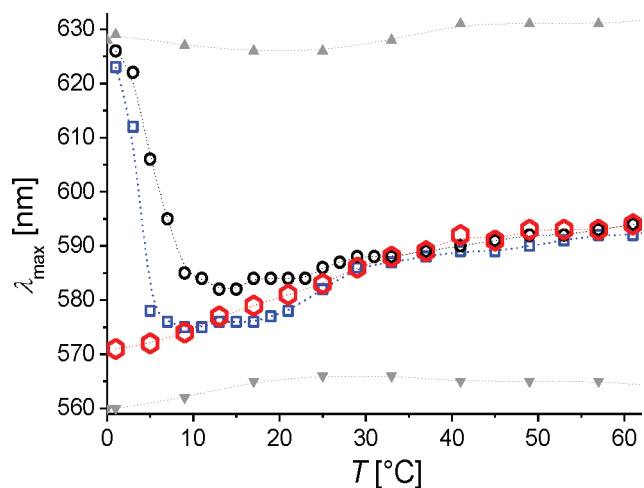
(abbreviated as 4HP or DCM). The wavelength at the maximum of the emission spectrum  $\lambda_{\max}$  correlates with the polarity, detecting the presence of hydrophobic domains (high  $\lambda_{\max}$  indicates a polar environment).<sup>17,18</sup> Mostly, a temperature-dependent appearance of hydrophobic domains is seen, which is not necessarily connected to an intermolecular micellization. Figure 1 shows the response of the 4HP probe, which is solubilized in different equimolar polymer solutions. As expected for the PPO-based diblock copolymers, the fluorescent probes sense a hydrophilic environment at low temperatures (PPO soluble). From 5 °C upward, the 4HP probe shows a sharp drop in the  $\lambda_{\max}$ -value (PPO hydrophobic). At higher temperatures, the indicator of polarity moves again toward the hydrophilic side due to a changing equilibrium distribution of the dye (see the Supporting Information). Both diblocks behave quite similarly, though PPO-*b*-PDMAEMA seems to be slightly more hydrophobic than PEO-*b*-PPO. Compared to similar polymers in literature, the butyl-terminated PPO precursor explains partly the lower onset temperature for the hydrophobization of PPO-*b*-PDMAEMA.<sup>19,20</sup>

In contrast to the block copolymers, solutions of the ternary miktoarm star behave quite differently. 4HP seems to be embedded in a nonpolar environment even at low temperatures, though PPO in the diblock copolymers is well-hydrated at the same conditions. This clear evidence of hydrophobic compartmentalization at low temperatures is not induced by

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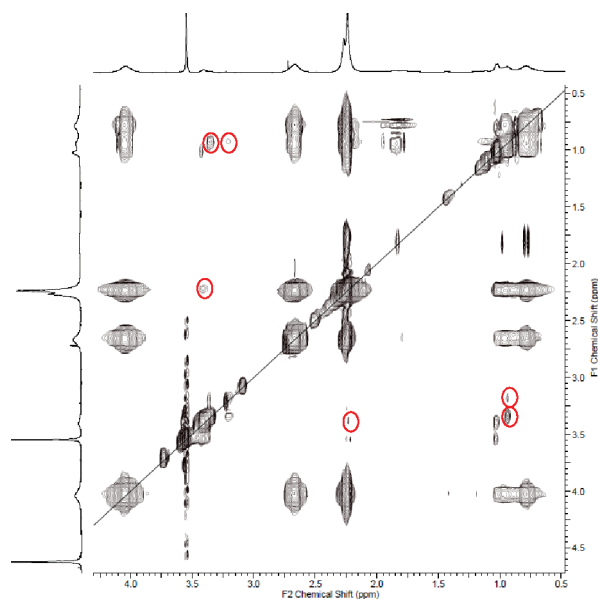
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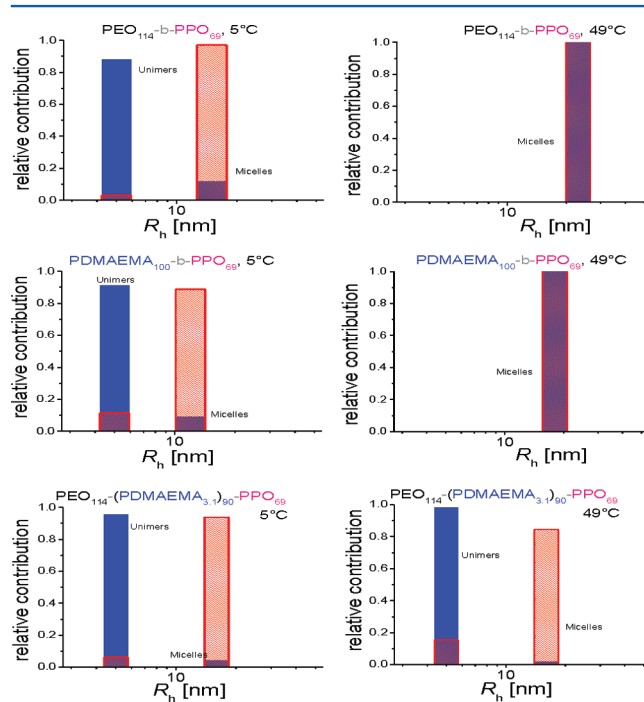
**Figure 1.** 4HP fluorescence spectroscopy of different polymer solutions in pH 8 buffer (+ 0.1 M NaCl); emission maximum  $\lambda_{\max}$  of 4HP as a probe ( $10^{-6}$  M;  $\lambda_{\text{exit}} = 470$  nm,  $\lambda_{\text{em}} = 480\text{--}750$  nm); assignment: 1.0 g/L PEO<sub>114</sub>-(PDMAEMA<sub>90</sub>)<sub>3.1</sub>-PPO<sub>69</sub> (red, open hexagons), 0.4 g/L PPO<sub>69</sub>-b-PDMAEMA<sub>100</sub> (blue, open squares), 0.16 g/L PEO<sub>114</sub>-b-PPO<sub>69</sub> (black, open circles) and for comparison pure PPO<sub>69</sub> (without solvent; downward directed gray triangles) and pure solvent (without polymer; upward directed gray triangles; for all: heating 20 K/h; lines are a guide to the eye).

just combining PDMAEMA and PPO (as for a diblock), but architectural effects play a role (as discussed later). Thus, a more detailed analysis reveals microscopic differences in the polarity of the hydrophobic domains both for diblock copolymers and miktoarm star. Therefore, thermodynamic data of the fluorescent dye uptake into the hydrophobic environment were extracted by use of a two-site model. Hereby, the thermodynamic data for the dye uptake are very similar for the diblocks (Supporting Information; e.g.,  $\Delta H(\text{PEO-}b\text{-PPO}) = -11.0$  kJ/mol and  $\Delta H(\text{PPO-}b\text{-PDMAEMA}) = -10.2$  kJ/mol). In contrast, the miktoarm star shows a rather different value both at high ( $\Delta H = -1.7$  kJ/mol) and low temperatures ( $\Delta H = -24.2$  kJ/mol). This implies a different chemical environment within the miktoarm stars compared to the PPO environment in the diblocks. A complexation between PPO and PDMAEMA (miscible in bulk)<sup>8</sup> has occurred, which leads to different uptake abilities into a changed microenvironment. These conclusions are well in line with IR and NMR results (see the Supporting Information). For example, <sup>1</sup>H 2D NOESY corroborated the proximity between PPO and PDMAEMA, while PEO/PDMAEMA interactions are hardly present (Figure 2).

So far, we have learned about the special interactions within the star-shaped geometry. We performed light scattering to learn about the morphology of the polymer aggregates and the structural changes. Summarizing a detailed and combined DLS and SLS evaluation (dynamic and static light scattering; Figure 3; Supporting Information),<sup>21,22</sup> both diblocks show a rather similar self-assembly behavior. DLS revealed the presence of fast-diffusing species (unimers) up to 17 °C, whereas the first micellar-like structures appeared already at 5 °C (regarding loose aggregates refer to Supporting Information). Then, the aggregation number and/or the number of the (spherical) micelles rises between 13 and 25 °C, which coincides well with the turbidity onset of pure PPO<sub>69</sub>.<sup>7,23</sup> In contrast, unimers are detected for the miktoarm star solution over a broad



**Figure 2.** <sup>1</sup>H 2D NMR NOESY spectra of the miktoarm star (10 mg/mL) in D<sub>2</sub>O (containing pH 8 buffer and 0.1 M NaCl; marked by red circles: relevant cross peaks showing the interaction between PDMAEMA and PPO).



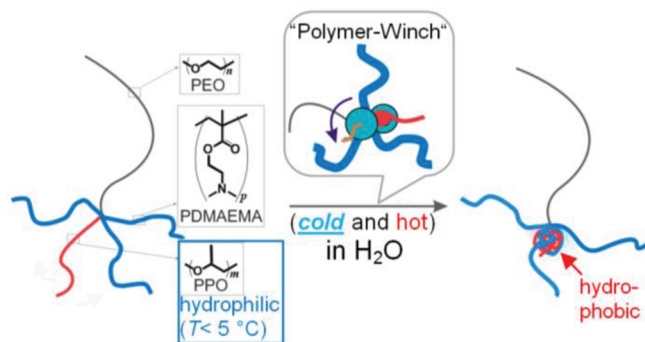
**Figure 3.** Comparison of the micelle's and unimer's scattering intensity (extrapolated to  $q \rightarrow 0$  by use of a combined DLS and SLS approach; red bars) with the mass concentration (by use of the Daoud-Cotton scaling; blue bars); left diagrams are at 5 °C, right-hand side is obtained at 49 °C; top row: PEO<sub>114</sub>-b-PPO<sub>69</sub>, center row: PDMAEMA<sub>100</sub>-b-PPO<sub>69</sub>, bottom row: PEO<sub>114</sub>-(PDMAEMA<sub>90</sub>)<sub>3.1</sub>-PPO<sub>69</sub>.

temperature interval (from 0 °C onward). Simultaneously, the respective scattering intensities hardly change. Using a rough semiquantitative approach, we can estimate the mass concentration of each scattering entity by using the Daoud and Cotton theory for star-shaped objects like star-shaped micelles (Figure 3 and Supporting Information).<sup>24</sup> At low temperature,

the dominant species are the unimers for both diblocks and the star. In contrast, the diblocks have self-assembled predominantly into micelles at an elevated temperature, whereas hardly any aggregation occurs for the miktoarm star. We can conclude that the majority of the stars are present as unimolecular micelles. This statement is corroborated by fluorescence quenching experiments (see the Supporting Information).

The solution behavior of the miktoarm star (Scheme 1) is quite different compared to the behavior of the diblock

**Scheme 1. Internal Complexation Induces Hydrophobicity But Prevents Intermolecular Aggregation (Interfacial Tension Reduction)**



copolymers. Within the investigated temperature region, there is no structural transition, though complexation between PPO and PDMAEMA is detected throughout for the miktoarm star. We think that the local concentration near the core of the star is essential for understanding this behavior. Simple geometrical considerations reveal that the segment density of the center-most shell (within a 0.7 nm radius) approaches even the bulk concentration of PDMAEMA. Thus, close contact of the PDMAEMA units with the PPO units is an inherent feature of the star-shaped system. Locally, this leads to a situation similar to bulk mixtures, where favorable interaction has been found.<sup>8</sup> However, the center-most layer alone does not explain the spectroscopic data (pronounced interaction), since the water accessibility of a hypothetical noncomplexing star is rapidly increasing toward the rim of the molecule (we estimated even water accessibility of the core dipentaerythritol). More likely, this area of close contact triggers further complexation, which is very visible by spectroscopic means.

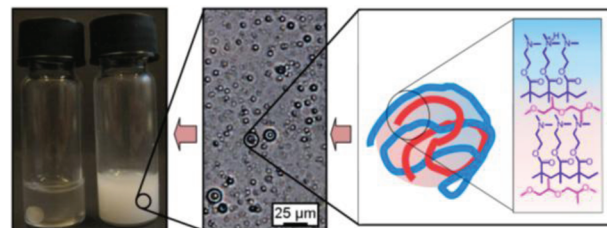
We continue the discussion on the basis of thermodynamic arguments. Regarding the prevalence of unimolecular micelles, kinetic reasons could also lead to a prevention of polymer aggregation (e.g., hydrophilic arms offer an energy barrier for the aggregation). However, the observed structures are believed to be close to equilibrium (Supporting Information). We turn to scaling laws relating the aggregation number  $N_{\text{agg}}$  of miktoarm stars and diblock copolymers (Supporting Information).<sup>25,26</sup> Hereby,  $N_{\text{agg,Diblock}}$  of diblock copolymers with  $m$  segments in the solvophobic block are compared to  $N_{\text{agg,Mikto}}$  of miktoarm stars, which have the same solvophobic block, but  $k$  solvophilic blocks of the same length as the diblock ( $p$  segments each). In addition, we allow complexation of  $l$  solvophilic blocks with PPO (with varying surface tension  $\gamma$  toward solvent). This yields:

$$\frac{N_{\text{Agg,Mikto}}}{N_{\text{Agg,Diblock}}} \cong k^{-3/5} \quad (1)$$

$$\frac{N_{\text{Agg,ComplexMikto}}}{N_{\text{Agg,Diblock}}} \cong (k-l)^{-3/5} \cdot \left( \frac{\gamma_{\text{Complex}}}{\gamma_{\text{PPO}}} \right)^{6/5} \cdot \left( \frac{m+lp}{m} \right)^{4/5} \quad (2)$$

$N_{\text{agg}}$  decreases only by a factor of 2 when changing the architecture from diblock to miktoarm star ( $k \approx 4$ ). Disregarding changes in  $\gamma$ , complexation leaves  $N_{\text{agg}}$  almost unchanged (reasonable assumptions:  $m = 69$ ,  $p = 90$ ,  $l = 0.76$ ; a 1:1 complex is formed). Thus, the star-shaped geometry alone cannot explain the drastic reduction of aggregation number in our case (spherical micelles for diblocks but unimers for miktoarm star; Supporting Information). However, the interfacial tension between core domain and bulk solvent is changed for the complex ( $\gamma_{\text{Complex}} \neq \gamma_{\text{PPO}}$ ). It is very reasonable to assume that the outer sphere of the complex consists predominantly of PDMAEMA, which is more hydrophilic than PPO. Thus, the intrinsically soluble PDMAEMA acts as a “microsurfactant” between the interface of hydrophobic complex and bulk water. At the same time, the  $\gamma_{\text{Complex}}$  is considerable lowered. We tried to quantify the reduction in  $\gamma$  between PPO and water and complex and water, respectively. It turned out to be a challenging task (e.g., the complex is highly viscous, but it dissolves in water colloiddally). Therefore, we can make only a qualitative, tentative argument at the moment. Since the complex is easily dispersible in water (Scheme 2),

**Scheme 2. PDMAEMA Acting as a Complexant and as a “Microsurfactant” (Right Hand Side), Leading to a Colloidal Stabilization of PPO in the Aqueous Phase (Images; Left Vial: 5 wt % PPO in Water; Right Vial: Additional 5 wt % Linear PDMAEMA; Optical Micrograph of the Same Dispersion; All Images Taken at Room Temperature)**



$\gamma_{\text{Complex}}$  is very much reduced compared to  $\gamma_{\text{PPO}}$ . In any case, PDMAEMA offers an effective stabilization of PPO in aqueous phase, for example, allowing the dispersion of 5 wt % PPO in water far above the cloud point of PPO. A more detailed analysis of these effects is on the way.

In conclusion, we have demonstrated that the hydrophobicity of a polymer chain can be influenced by the macromolecular architecture. Simultaneously, the local microenvironment can have strong influence on the properties of polymer chains in aqueous solution. This is especially true for systems where small attractive interactions occur between two different homopolymers. Here, higher segment densities of PDMAEMA around one PPO chain are required to induce a complexation between PPO and PDMAEMA in water. Simultaneously, the PPO segments are retracted by complexation with PDMAEMA, lowering the interfacial tension of the hydrophobic domain. Finally, this leads to a pronounced drop in aggregation number, ending up at the limit of  $N_{\text{agg}} = 1$ . Thus, the non-centrosymmetric architecture is copied into Janus-type,

unimolecular micelles.<sup>27,28</sup> Figuratively, the star acts as a polymeric “nano-winch”. It “hauls” PPO aboard and prevents intermolecular “anchoring” by shielding the winch with a PDMAEMA cover.

## ■ ASSOCIATED CONTENT

### ● Supporting Information

Detailed experimental data, molecular characteristics of polymers, derivation of the scaling laws, and application of Daoud and Cotton scaling law. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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### Notes

The authors declare no competing financial interest.

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