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Coexisting Hydrophobic Compartments through Self-Sorting in Rod-like Micelles of Bisurea Bolaamphiphiles

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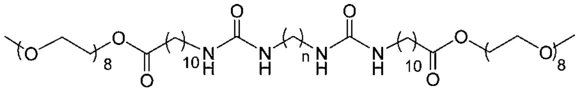
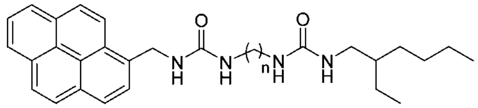
The creation of multiple, coexisting hydrophobic compartments in water is an important step toward systems that emulate the structural complexity of biological cells. Discrete hydrophobic compartments can keep mutually incompatible reagents or catalysts apart and are, therefore, essential in developing complex chemical systems. When amphiphilic polymers are employed to create multiple compartments, use can be made of the incompatibility between chemically different segments.[1] However, when small molecule amphiphiles are used, phase separation is limited to combinations of highly incompatible molecules such as hydrocarbons and fluorocarbons.[2] In small molecule systems, a more versatile process is molecular self-sorting. Self-sorting entails the ability to differentiate between self and nonself and distinguishes itself from microphase separation by the specificity and directionality of the recognition process.[3] Specificity can be based on any of a number of supramolecular interactions,[4] including metal−ligand interaction, hydrogen bonding, and ion−dipole interactions. In aqueous systems, self-sorting via specific supramolecular interactions offers an attractive alternative to microphase separation for creation of separate, coexisting aggregates. For instance, self-sorting via hydrogen bonding has been used in the orthogonal formation of self-assembled fibers and micelles or vesicles.[5,6] However, the formation of multiple hydrophobic compartments by means of self-sorting has not been reported. Here, we demonstrate that self-sorting among mixtures of bisurea bolaamphiphiles (U*n*U) results in rod-like micelles that form multiple hydrophobic environments. In hydrogen bond mediated self-assembly, the urea group is one of the most reliable motifs, which has been used in self-sorting of small molecules and in self-assembly of gels,[7] surfaces,[8] sol−gel materials,[9] and thermoplastic elastomers.[10,11] Bisurea motifs in the hard block of the elastomers were shown to allow selective incorporation of matching bisurea guest molecules[10] and to allow the self-sorting of dissimilar hard segments in a mixed polymer matrix.[11] Self-sorting in these mixed matrices was studied by making use of the fluorescent probes Py-U*n*U and DMA-U*n*U, which display exciplex emission when they are in molecular contact. Recently, we have shown that the bisurea based bolaamphiphile U7U self-assembles in water to form rod-like micelles.[12] The bisurea motif in U7U was shown to specifically bind probe molecules with an identical hydrogen bonding unit and to lead to unfolding of the bisurea probe molecule, which is present in a folded conformation in the absence of U7U. We now use the highly selective incorporation of Py-U*n*U and DMA-U*n*U probes in bisurea bolaamphiphiles to show that the micelles dynamically coexist in solution, each micelle specifically binding to its correspondingly functionalized guests.

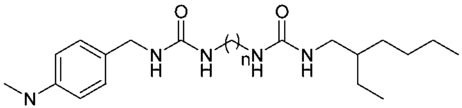
Oligoethyleneglycol-bisurea bolaamphiphiles U3U, U4U, U6U, U7U formed stable micelles upon dissolution in water (up to ∼3% w/v), whereas U12U was insoluble and was not studied further. Critical micellar concentrations (cmc's) of the amphiphiles were determined from the ratio I_1/I_3 of the vibronic bands of pyrene. With increasing spacer chain length, the cmc's decrease from 3.22×10^{-5} M to 9.1×10^{-6} M, 5.6×10^{-6} M, and 3.6×10^{-6} M for U3U, U4U, U6U, and U7U respectively.



U*n*U, *n* = 3, 4, 6, 7, 12 (**1a-1e**)



Py-U*n*U, *n* = 3, 4, 6, 7 (**2a-2d**)



DMA-U*n*U, *n* = 3, 4, 6, 7 (**3a-3d**)

Cryo-TEM images of 1 wt % micellar solutions of the three stable amphiphiles showed rod-like structures ($d_{\text{core}} \approx 8$ nm), although the detailed behavior of the rods depended on the spacer length. U4U formed rods in a compact arrangement (Figure 1a) whereas the solution of U7U showed a random arrangement of rods (Figure 1b).

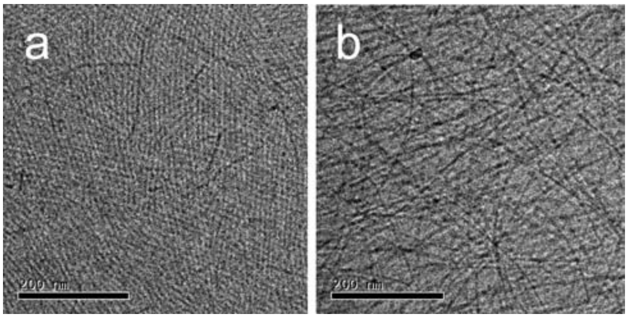


Figure 1. Cryo TEM images of 1 wt % micellar solutions of (a) U4U and (b) U7U.

The behavior of U4U rod-like micelles was studied further by fluorescence spectroscopy using the pyrene probe Py-U4U and the dimethylaniline probe DMA-U4U. The pyrene probe molecules were shown to be more or less randomly dispersed in the micelles of corresponding U4U amphiphiles, since a band due to excited state pyrene dimers (typical $\lambda_{\max} \approx 480$ nm) was absent when 0.01 equiv (relative to U4U) or less of Py-U4U was added. The dynamics of these micelles was studied by monitoring the intensity of the exciplex band that formed when the DMA-U4U probe was added

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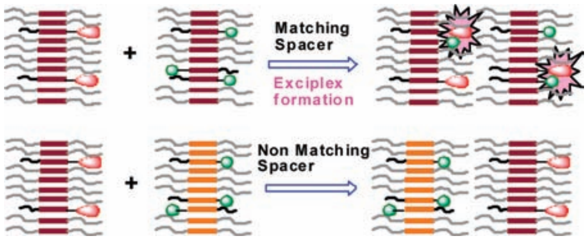
(Scheme 1). Typically, such a band is observed if the pyrene and dimethylaniline chromophores are in molecular contact.[11]

Scheme 1. Cartoon of the Use of Exciplex Fluorescence To Probe Self-Sorting in the Bisurea Rod-Like Micelles



In 4 mM aqueous solutions of U4U containing either 0.01 equiv of Py-U4U or 0.15 equiv of DMA-U4U and 2% of DMSO or DMF used to add the probes,[13] an exciplex band was absent. However, upon mixing these solutions, a band at 520 nm appeared and grew over time with a first-order rate constant of 1.8×10^{-3} s^{-1} (Figure 2a, black line), demonstrating the dynamic nature of the micelles. Interestingly, when the same experiment was performed with a solution in which the DMA-U4U probe was taken up in U6U micelles, the rate constant of exciplex formation was the same, but the final emission intensity was twice as high (Figure 2a, red line), showing that the probes are confined to half the micellar space. However, when nonmatching micelles U4U (containing 0.01 equiv of Py-U4U) and U6U (containing 0.15 equiv of DMA-U6U) were mixed, hardly any exciplex formation was observed (blue line). These observations suggest that U4U and U6U bolaamphiphiles form separate rod-like micelles and that the probes are confined to their matching micelles.

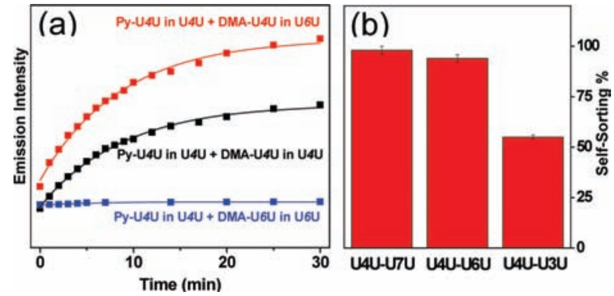


Figure 2. (a) Intensity of the exciplex band at 520 nm as a function of time upon mixing of micellar solutions containing Py-U4U with micellar solutions containing DMA-U4U or DMA-U6U. Data have been fitted with first-order kinetics (see text). (b) Bar diagram indicating extent of self-sorting in binary mixtures of U*n*U micelles.

Formation of separate micelles by self-sorting was corroborated with binary mixtures of amphiphiles and their corresponding probes. For example, on adding DMA-U4U (0.15 equiv relative to total amphiphile) to the binary mixture of U4U and U6U (2 mM each) containing Py-U4U (0.01 equiv), an exciplex band was observed, whereas addition of 0.15 equiv of DMA-U6U to the mixture did not result in exciplex formation (see Supporting Information (SI)). Therefore we conclude that the probes recognize their matching amphiphiles which are self-sorted to form separate micelles. The extent of probe self-sorting was quantified by analyzing the exciplex band intensities in different binary mixtures and is given on a scale of 0% for the exciplex intensity in a fully mixed system of matching probes to 100% when the exciplex band is absent. Figure 2b shows that self-sorting was most pronounced between U4U and U7U or U6U micelles (98 and 94%, respectively), whereas the mixture of U4U and U3U showed moderate self-sorting (55%).

Finally, a mixture of three bisurea amphiphiles U4U−U6U−U7U was used to probe the possibility of creating more than two coexisting micellar compartments in a single solution by self-sorting. For these measurements, one Py-U*n*U probe and two nonmatching DMA-U*n*U probes were added to the ternary mixture of micelles. Py-U4U exhibited the highest self-sorting (97%), while Py-U6U and Py-U7U showed 83% and 73% self-sorting respectively (see SI, Figure S14).

In summary, oligoethyleneglycol-bisurea bolaamphiphiles, differing only in the spacing between urea groups, show remarkably effective self-sorting in aqueous solution, leading to coexisting rod-like micelles with up to 98% demixing of probes in binary solution. The high specificity of the self-sorting even allows the formation of more than two coexisting micellar phases in a single solution. It holds great potential for chiral self-sorting, in keeping apart incompatible catalysts or reagents, and for the suppression of backfolding in supramolecularly cross-linked gels.

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Supporting Information Available: All the experimental procedures, compound characterization data, TEM images, and fluorescence data. This material is available free of charge via the Internet at http://pubs.acs.org.

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