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Self-Sorting in Rodlike Micelles of Chiral Bisurea Bolaamphiphiles

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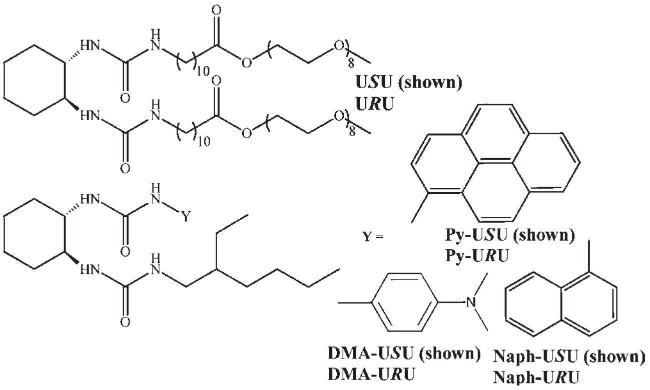
Supporting Information

ABSTRACT: We have demonstrated the formation of segregated enantiomeric dynamic rods in water, from the self-sorting of chiral *trans*-1,2-bisureido cyclohexane-based bolaamphiphiles. Fluorescence probes have been used to investigate the self-sorting through forming exciplex and FRET.

Compartmentalization is a prerequisite for the development of life because it separates mutually incompatible chemical processes. Developing synthetic systems that mimic biological compartmentalization by forming multiple discrete hydrophobic domains is therefore highly relevant.[1] Spontaneous formation of separate domains via self-assembly can be achieved by a process known as molecular self-sorting.[2] Self-sorting has been defined as the ability to differentiate between self and nonself and can be based on many types of supramolecular interactions, among which hydrogen bonding of the urea group is one of the most reliable motifs. The use of two neighboring urea groups adds specificity and strength, and has been used very succcessfully in the self-assembly of gels,[3] on surfaces,[4] in sol−gel materials,[5] and in thermoplastic elastomers.[6] Hydrogen bonding-mediated self-sorting can lead to orthogonally self-assembled fibers, micelles, vesicles,[7] and gels.[8] Recently, we have reported on the formation of discrete hydrophobic compartments in water by self-sorting in mixed solutions of bisurea bolaamphiphiles to form separate populations of rodlike micelles.[9] Herein, we demonstrate self-sorting based on chiral recognition in the *trans*-1,2-bisureido cyclohexane moiety, which has proven value as a building block in self-assembly.[11]

Chiral recognition is a phenomenon that has fascinated chemists ever since Pasteur's original demonstration of the spontaneous resolution of tartrate salts during crystallization. In the context of covalent polymers, formation of homochiral sequences from a racemic mixture of monomeric amino acids by a combination of kinetically determined selection steps has been observed, and its relevance to the origin of biological homochirality has been discussed.[10] We investigate self-sorting in a supramolecular system under thermodynamic equilibrium, for which we designed bolaamphiphiles **U*S*U** and fluorescent probes **Py-U*S*U**, **DMA-U*S*U**, **Naph-U*S*U** and their *R*-stereoisomers.



U*S*U (shown)
U*R*U

Py-U*S*U (shown)
Py-U*R*U

DMA-U*S*U (shown)
DMA-U*R*U

Naph-U*S*U (shown)
Naph-U*R*U

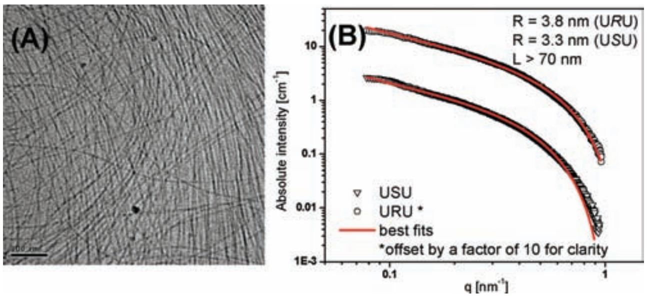


Figure 1. Cryo-TEM images of 1 wt % micellar solution of U*S*U. (B) SAXS data of 1 wt % micellar solution of U*S*U and U*R*U.

Upon dissolution in water **U*S*U** and **U*R*U** formed stable micelles with CMC values $\sim 7 \times 10^{-6}$ M (see SI). Cryo-TEM images of 1 wt % micellar solutions of the two amphiphiles showed micrometer-long rodlike aggregates with a diameter of ~6 nm and a large radius of curvature (Figure 1A, see also SI). On the basis of the literature[11] we propose that the hydrogen bonding motif of *trans*-1,2-bisureido cyclohexane moiety strongly favors anisotropic growth.

Small angle X-ray scattering (SAXS) profiles (Figure 1B) obtained from 1 wt % micellar solutions were fitted with a model for noninteracting cylinders[12] with a monodisperse cylindrical form factor (see SI). Excellent fits were obtained for rod radii of 3.3−3.8 nm, in good agreement with the diameter of the rodlike micelles observed in cryo-TEM.

Self-sorting behavior of **U*R*U** and **U*S*U** rodlike micelles was studied by fluorescence spectroscopy using the pyrene and dimethylaniline probes which display exciplex emission being in molecular contact with each other. The pyrene probe molecules were shown to be more or less randomly dispersed in the micelles of corresponding amphiphiles, since a band due to excited-state pyrene dimers (typical $\lambda_{max} \approx 480$ nm) was absent when less than 0.5 mol % (relative to **U*R*U** or **U*S*U**) of **Py-U*S*U** was added. When **DMA-U*S*U** was titrated into (final 15 mol % relative to total amphiphile) a binary solution of **U*S*U** and **U*R*U** in water (2 mM each) containing **Py-U*S*U** (0.5 mol %), formation of an exciplex band was observed, whereas addition of

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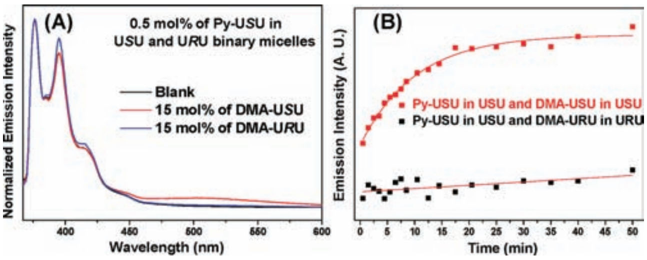

Figure 2. (A) Fluorescence emission spectra of binary micellar solution containing bisurea guest molecules. Black, red, and blue lines indicate Py-U*S*U, Py-U*S*U with 15 mol % of DMA-U*S*U, and Py-U*S*U with 15 mol % of DMA-U*R*U in mixed micelles of U*S*U−U*R*U (2 mM each). The excitation wavelength used was 347 nm, and spectra are normalized to the peak at 377 nm for comparison. (B) Intensity of the exciplex band at 490−510 nm as a function of time upon mixing of micellar solutions containing Py-U*S*U with micellar solutions containing DMA-U*S*U or DMA-U*R*U. Data have been fitted with first-order kinetics (see text).

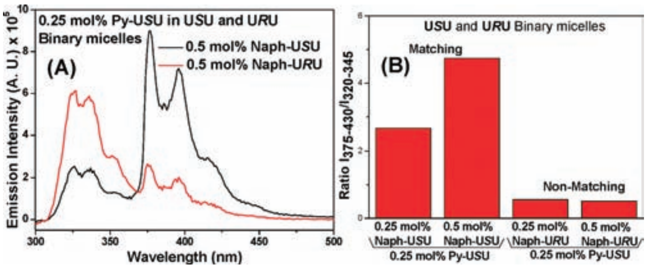

Figure 3. (A) FRET of binary micellar solution containing bisurea guest molecules. Emission spectra of 0.25 mol % of Py-U*S*U and 0.5 mol % of Naph-U*S*U and Naph-U*R*U in mixed micelles of U*S*U−U*R*U. The excitation wavelength used was 290 nm, and spectra are corrected for direct pyrene excitation. (B) Comparison of the ratios of integrated intensities between 375−430 nm and 320−345 nm of the U*S*U−U*R*U binary micelles containing matching and nonmatching naphthalene and pyrene probes molecules.

15 mol % of **DMA-U*R*U** to the mixture did not result in exciplex formation (Figure 2A, see also SI). Therefore, we conclude that the probes recognize their matching amphiphiles which are self-sorted to form separate coexisting 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). A value of 80% of self-sorting between **U*S*U** and **U*R*U** micelles was determined under the conditions described above (see SI).

In 2 mM aqueous solutions of **U*S*U** containing either 0.5 mol % of **Py-U*S*U** or 15 mol % of **DMA-U*S*U** an exciplex band was absent. However, upon mixing these solutions, a broad band at 490−510 nm appeared and grew over time with a first order rate constant of 7.1×10^{-4} s^{-1} (Figure 2B, red squares), demonstrating the dynamic nature of the micelles. However, when nonmatching micelles **U*S*U** (containing 0.5 mol % of **Py-U*S*U**) and **U*R*U** (containing 15 mol % of **DMA-U*R*U**) were mixed, hardly any exciplex formation was observed (black squares). These observations suggest that **U*S*U** and **U*R*U** bolaamphiphiles form separate rodlike micelles and that the probes are confined to their matching micelles.

Although exciplex formation between DMA and pyrene probes strongly supports self-sorting of micelles, the high loading with 15% DMA probes may perturb the system. Therefore, we resorted to the use of fluorescence resonance energy transfer (FRET) between naphthalene probe **Naph-U*S*U** (as donor) and **Py-U*S*U** (as acceptor) {Förster radius (R_o) is 2.86 nm}. Fluorescence emission spectra of binary solutions of **U*S*U** and **U*R*U** containing probes were recorded with an excitation wavelength of 290 nm where the donor naphthalene absorbs. Figure 3A shows that for the matching system (**Py-U*S*U** and **Naph-U*S*U**) the intensity of characteristic pyrene fluorescence in the wavelength region 375−430 nm increases with the increase in amount of **Naph-U*S*U** (see also SI). Increased energy transfer is attributed to the increased fraction of pyrene that is within a few nanometers of naphthalene. In contrast to this, only a minimal increase in intensity of pyrene emission with increasing concentration of naphthalene donor occurs in the nonmatching system of **Py-U*S*U** and **Naph-U*R*U** (Figure 3A, also see SI). Moreover, the absolute intensity of characteristic naphthalene fluorescence in the wavelength region 320−345 nm is higher in the nonmatching system than in the matching system, which is also indicative of considerably lower amount of energy transfer in the nonmatching system. The corresponding FRET ratios ($I_{375-430}/I_{320-345}$) for the matching and nonmatching FRET pairs are shown in Figure 3B.

In summary we have demonstrated the formation of segregated enantiomeric compartments in water, from the self-sorting of chiral *trans*-1,2-bisureido cyclohexane-based bolaamphiphiles. The use of both exciplex and FRET is shown to be a versatile methodology to probe chiral self-sorting. Additionally, being more sensitive, FRET allows a large reduction in loading of the micelles with probe molecules. We are currently investigating the use of FRET probes as an alternative method to quantitatively determine the degree of self-sorting in this and similar systems.

■ ASSOCIATED CONTENT

Ⓢ **Supporting Information.** 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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