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Light-controlled self-assembly of a dithienylethene bolaamphiphile in water†

Cassidy Creemer, ‡[a] Haydar Kilic, ‡[b,c] Kwang Soo Lee, [a]
Nurullah Saracoglu *[b] and Jon R. Parquette *[a]

The self-assembly of bolaamphiphiles comprised of a central photochromic dithienylethene (DTE) chromophore was investigated in aqueous media. Irradiation at 254 nm induced a conversion from the open to closed states of the DTE chromophores. Whereas, in water, irradiation produced a photostationary state of 20 : 80 (open/closed), in methanol the ratio improved to 10 : 90 (open/closed). The open → closed transition was accompanied by the formation of 1D nanofibers during incubation in darkness.

Many biomolecular systems achieve and modulate their functional characteristics *via* noncovalent self-assembly.[1] Self-assembly provides a convenient, albeit often empirical strategy, to fabricate materials in the nanoscale regime.[2] Strategies to create nanostructured materials by controlled self-assembly offer a diverse array of applications in optoelectronics,[3–5] biomaterials,[6–9] drug delivery,[10] and molecular machines,[11,12] *inter alia*.[13,14] The potential for these materials to display adaptivity, self-healing, and other forms of "intelligent" behavior would be enhanced by the capability to transition between multiple states.[15] Molecules that dynamically modulate their structural features *via* external triggers offer a strategy to create such smart materials.[16,17] "Molecular switches",[18–20] that switch between multiple configurational states upon irradiation[21] have potential to induce changes in local monomer packing as a mechanism to modulate long-range nanostructural order. Although photoswitches have been exploited to modulate supramolecular structure and morphology in organic media, the control of self-assembly in water with light has been less studied.[15,22–25]

A potential strategy to control the nanoscale organization of a self-assembled material would be incorporation of a photoresponsive chromophore within the building blocks that comprise the nanostructure. Dithienylethene (DTE) photoswitches[26–28] have been employed to control the morphology of modified surfaces,[29–31] polymers,[32] organogels,[33] nanofibers,[34] and liquid crystals.[35] Herein, we report the light-controlled self-assembly of photoresponsive DTE-bolaamphiphiles in aqueous media. We have recently demonstrated that lysine-1,4,5,8-naphthalenetetracarboxylic acid diimide (Lys-NDI) amphiphiles and bolaamphiphiles undergo efficient self-assembly into 1D-nanostructures in water.[4,36,37] In these systems, self-assembly was driven by the intermolecular π–π stacking of the NDI group in addition to amphiphilic phase separation. Therefore, based on these systems, photoresponsive monomers **1** and **2** were designed by replacing the NDI chromophores with a light-responsive, DTE chromophore,[36] which serves as the hydrophobic, aromatic component (Fig. 1). Flanking Fmoc-protecting groups were added to provide additional π–π stacking capabilities. The ten-

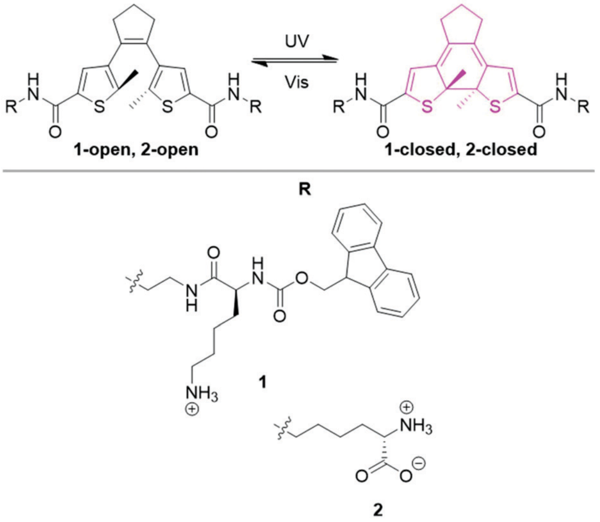

Fig. 1 Photoisomerization of DTE photochromic unit and structures of DTE bolaamphiphiles 1 and 2.

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[a] Department of Chemistry and Biochemistry, The Ohio State University, 100 W. 18th Ave, Columbus, Ohio 43210, USA. E-mail: parquett@chemistry.ohio-state.edu

[b] Department of Chemistry, Faculty of Sciences, Atatürk University, Erzurum, Turkey 25240. E-mail: nsarac@atauni.edu.tr

[c] Oltu Vocational Training School, Atatürk University, Erzurum, Turkey 25400

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‡ Both authors contributed equally to this work.

dency of bolaamphiphiles to form 1D rods or tubes over spherical structures has been shown to increase for monomers having rigid internal segments, which results in a more ordered packing of the hydrophobic core.[38,39] Thus, we reasoned that the cyclization/cycloreversion reaction between the open- and closed-ring isomers of DTE upon irradiation would alter both the conformational flexibility and/or the π-stacking capability of the monomer, thereby modulating the rigidity of the interior segments, and the resulting structure, of the assemblies.

Two DTE-lysine bolaamphiphiles displaying positively charged (**1**) or zwitterionic headgroups (**2**) were prepared by amidation of 4,4′-(cyclopent-1-ene-1,2-diyl)bis(5-methylthiophene-2-carboxylic acid)(DTE-CO_2H)[40] as described in the ESI (Scheme S1†). Bolaamphiphile **1**, displaying ammonium head groups was prepared by bisamidation of DTE-CO_2H with *tert*-butyl(2-aminoethyl)carbamate followed by acidic removal of the *t*-Boc groups, amide coupling with Fmoc-Lys(Boc)-OH and final deprotection. Similarly, bolaamphiphile **2**, containing a zwitterionic headgroup and flanking Fmoc groups, was obtained by coupling two equivalents of *N*α-Fmoc-L-Lys-OMe with DTE-CO_2H and subsequent deprotection.

Monomers **1** and **2** contain a central DTE photochromic unit capable of undergoing a reversible cyclization/cycloreversion reaction between open- and closed-ring isomers upon UV irradiation.[41] The photochromic behavior of **1** was studied by UV-Vis spectroscopy in water, THF, MeOH, $CDCl_3$, and DMF (Fig. S1†). The open form of **1** exhibited an absorption band with a λ_{max} at ~260–270 nm. Irradiation of the colorless open form of **1** (10 mM) at 254 nm produced a photo-stationary state (PSS) after 40–60 minutes, resulting in the formation of a deep violet-colored solution with absorption bands at 352 and 526 nm, and a concomitant decrease in the 266 nm band.[28] The amount of the closed-form of the DTE chromophore, as determined by HPLC and ^1H-NMR (Fig. S4 and S5†), produced at the PSS was highly dependent on solvent. For example, the amount of closed-form of **1** present at the PSS was 90% in methanol; 80% in H_2O, 63% in THF, and 6% in DMF. The solvent dependence of the isomerization yield at the PSS has been reported by other groups.[42,43]

The self-assembly characteristics of **1** and **2** were explored by transmission electron microscopy (TEM) and atomic force microscopy (AFM) in both the open state and at the PSS following irradiation with 254 nm light. We initially explored the photoisomerization and assembly of **2**. Although irradiation of **2-open** with 254 nm light produced 48% of the closed form (**2-closed**) at the PSS in water (Fig. S2†), both the open and closed states of **2** remained monomeric under the self-assembly conditions (10 mM, 24 h). Reasoning that the central DTE chromophore was not providing a sufficient driving force, *via* π–π interactions, for assembly in water, bolaamphiphile **1** was designed with two appended, terminal Fmoc groups to enhance the potential for intermolecular π–π interactions.

Accordingly, imaging a sample of **1-open**, prepared by diluting a colorless 10 mM solution to 1.0 mM, revealed minimal, nonspecific aggregation with a few liposomal aggregates (Fig. 2A). Irradiation with 254 nm light for ~60 min in water produced a violet solution due to the formation of the closed-form of the DTE. As the solution was kept in darkness, TEM and AFM images of the solution at the PSS revealed a transition in morphology over the course of 24–48 h from the non-specific aggregates to uniform 1D nanofibers with diameters of ~14 nm and heights of ~4.8 nm (Fig. 2B–D). Immediately following irradiation, a slow transition to amorphous ribbons was observed by TEM that converted to nanofibers after 24–48 h.

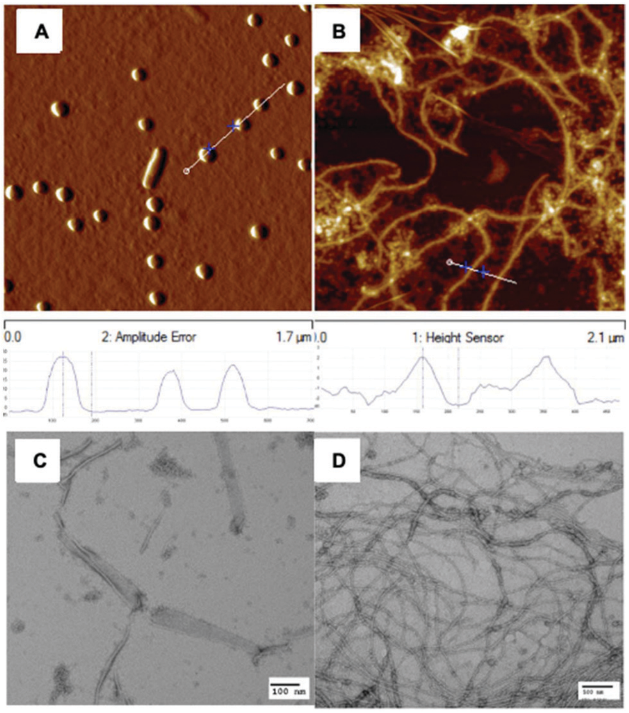

Fig. 2 Tapping-mode AFM images of **1** (A) in the open state and, (B) 24 h after irradiation in water with 254 nm light. (C) TEM images of **1** after exposure to 254 nm light and subsequent aging for 0 h and (D) 24 h. Samples were prepared by dissolving **1** in water (10 mM), prior to diluting to 500 µM (TEM) and evaporating onto a carbon-coated copper grid with uranyl acetate as a negative stain (TEM) or diluting to 100 µM and evaporating onto freshly cleaved mica (AFM).

To induce maximal isomerization, **1** was irradiated in methanol at 10 mM, resulting in a 90% conversion to the closed state, then the solvent was evaporated and replaced with water. Imaging of this sample after 24 h revealed only short, non-uniform twisted fibers, in contrast to the initially formed nanofibers produced by direct irradiation in water (Fig. 3A and S6†).

We hypothesized that the self-assembly of **1-closed** could be accelerated by ultrasonication. Ultrasonication accelerates the self-assembly process by producing mechanical forces that facilitate the reorganization of initial aggregates into elongated structures with optimal intermolecular interactions.[44–46] Accordingly, sonication of an aqueous solution of **1-closed** (10 mM, 20% amplitude, 1 min, pulsed 10 s on, 5 s off), formed by irradiation in methanol, induced a rapid transition from the initial aggregates to short nanofibers within 10 min

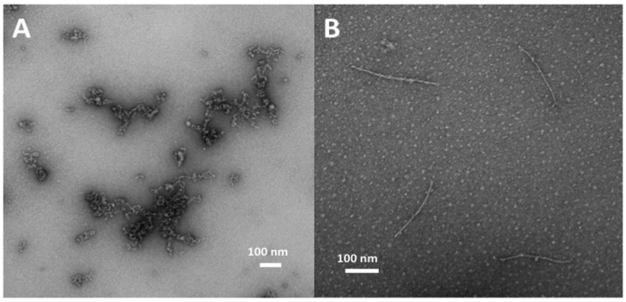

Fig. 3 TEM images of **1-closed** after 254 nm irradiation in methanol, evaporation, and redissolution in water (10 mM): (A) without sonication after 24 h and (B) 10 min after sonication (20% amp., 5 min, pulsed 10 s on, 5 s off). TEM images were recorded after diluting in water (1 mM) and evaporating onto a carbon-coated copper grid with 2% aq. uranyl acetate as a negative stain.

(Fig. 3A, B and 4A, C) and, after 24 h, into uniformly elongated, helical nanofibers with diameters of ∼13 nm and AFM heights of 4.0–4.5 nm (Fig. 4B, D and S7†). It is noteworthy that sonication of the open state of **1** did not induce self-assembly after 24 h (Fig. S6†).

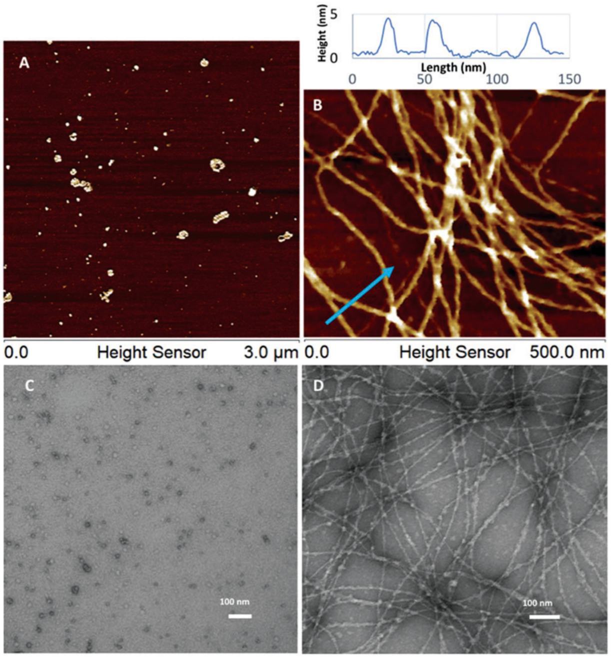

Fig. 4 Tapping-mode AFM (top) and TEM (bottom) images of **1**: (A/C) **1-open** (10 mM) and (B/D) **1-closed**. Samples of **1-closed** were prepared by irradiation with 254 nm light in methanol for ∼40 min (for **1-closed**), evaporation and redissolution in water (10 mM), sonication (20% amp., 5 min, pulsed) and aging for 24 h in darkness. AFM and TEM images were recorded after diluting in water (1 mM) and evaporating onto a carbon-coated copper grid with 2% aq. uranyl acetate as a negative stain (TEM) or onto freshly cleaved mica (AFM).

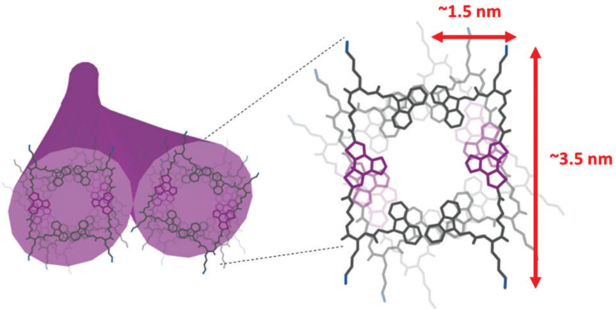

Fig. 5 Notional depiction of amphiphilic assembly of **1-closed** into 1D nanofibers.

The photoisomerization of the DTE ring system leads to conversion from a non-planar, conformationally flexible structure to a rigid, planar ring. However, a comparison of the CD spectra of the open and closed forms of **1** exhibited transitions only in the region 200–350 nm (Fig. S3†). In the spectral region of 520–530 nm, corresponding to the π–π* absorption of the closed DTE chromophore, no Cotton effects were observed. The lack of CD signals in this region suggested that π–π aggregation of the DTE chromophore was not sufficiently promoting self-assembly, consistent with the lack of **2-closed** to assemble. This likely emerged from the steric requirements of the axially-oriented, trans methyl substituents in the DTE chromophore, which also rendered the closed DTE form chiral. Changes in the flexibility of the bolaamphiphile induced by photoisomerization of the DTE unit, likely mediated the observed differences in self-assembly characteristics of the open and closed forms of **1**. A model for the self-assembly process could be envisaged based on the extended length of **1-closed** of ∼3.5 nm, which was similar to the heights of the helical fibers measured by AFM (Fig. 4B). Thus, the fully formed nanofibers likely emerge from the helical twisting of smaller fibrils, with diameters of ∼4 nm, created by the amphiphilic aggregation of **1-closed** (Fig. 5).

In conclusion, the self-assembly of bolaamphiphiles containing a central DTE chromophore was controlled by photochemical interconversion between open and closed states. The open → closed transition induced a change from small, non-specific aggregates to 1D nanofibers in aqueous media.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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