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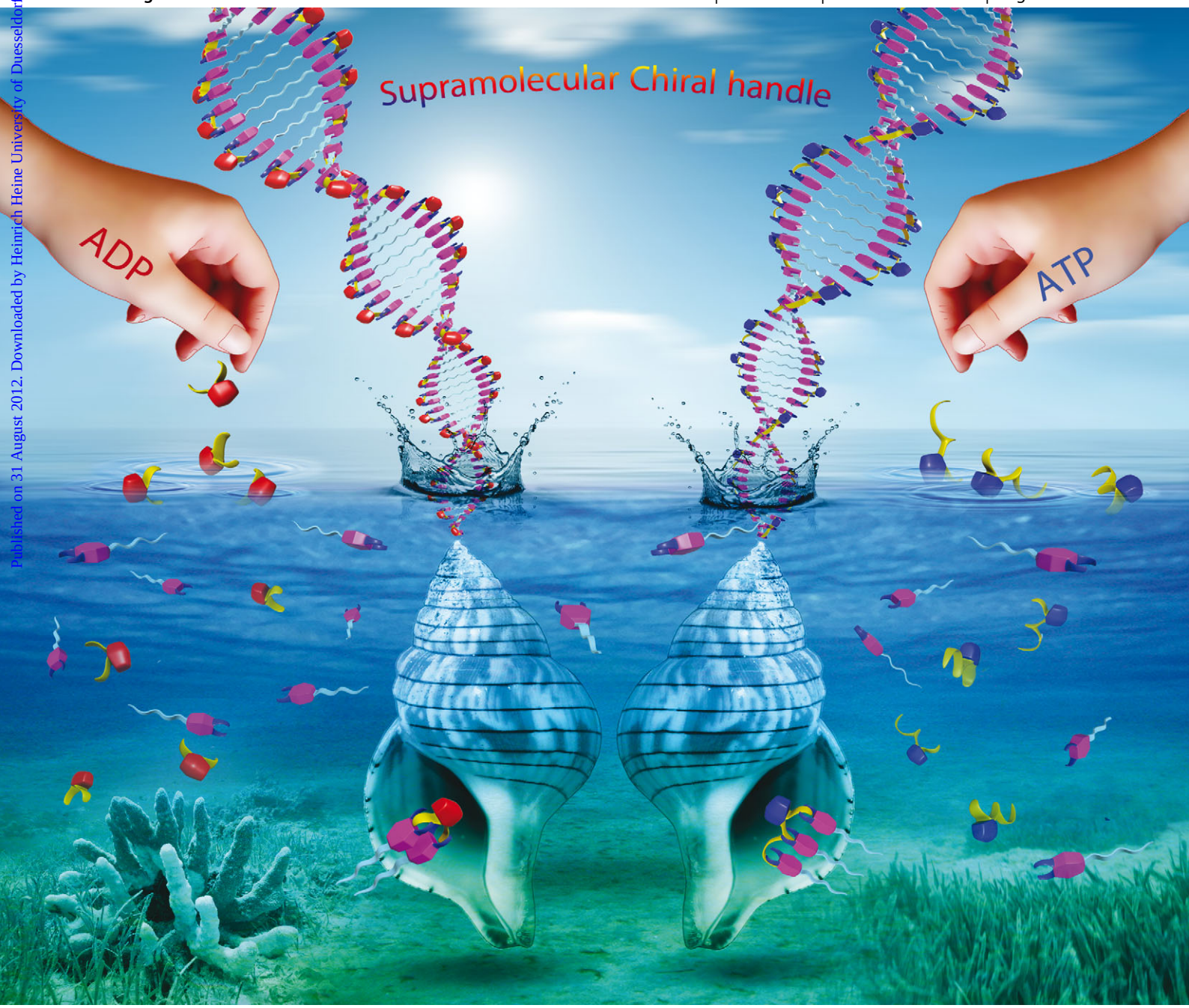

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Subi J. George *et al.*,

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Molecular recognition driven self-assembly and chiral induction in naphthalene diimide amphiphiles†

Mohit Kumar, Narendra Jonnalagadda and Subi J. George*

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Naphthalene diimide amphiphiles functionalized with the dipicolylethylenediamine motif self-assemble with tunable chirality upon molecular recognition with various adenosine phosphates and competitive guest binding leads to the dynamic helix reversal of these assemblies.

Dynamic helical polymers and supramolecular one-dimensional (1-D) assemblies with tunable handedness, by the specific molecular recognition of chiral guests, have attracted immense attention as model systems to understand the concepts of chiral amplification.[1,2] Moreover, the molecular recognition properties along with the dynamic nature of these helical systems would be very attractive for the design of stimuli responsive and chirotechnological materials. Although, supramolecular helical stacks constructed from the assembly of chiral monomers have been well investigated,[2] the molecular recognition driven 1-D assembly of achiral monomers and the resultant induction of chirality from the guests to the achiral/racemic assemblies is seldom reported. In this respect, chiral induction,[3] (preferential) chiral solvation[4] and chiral memory,[5] well known concepts in their macromolecular counterparts, have been recently demonstrated in 1-D supramolecular systems using the principles of host–guest chemistry. However, gaining detailed mechanistic insights and the design of guest responsive, dynamic helical 1-D assemblies remains challenging.

Herein we communicate the adenosine phosphates induced one-dimensional (1-D) self-assembly and the resultant supramolecular chirality of naphthalenediimide (NDI) amphiphiles *i.e.* **NDPA-Amph** and **NDPA-Bola**. Detailed spectroscopic probing provided mechanistic insights into the dynamic molecular recognition, chiral induction process and stability of the assemblies. The binding of multivalent chiral phosphates resulted in high chiral order, as evident from the unprecedented excitonic, bisignated circular dichroism signals, in the resulting NDI assemblies.[6] Although self-assembly of NDI derivatives has been extensively studied,[6] this is the first report of their guest induced chiral self-assembly. We further present the dynamic reversal of the helical handedness of NDI stacks through competitive guest binding.

Supramolecular Chemistry Laboratory, New Chemistry Unit, Jawaharlal Nehru Centre for Advanced Scientific Research (JNCASR), Bangalore, India 560064. E-mail: george@jncasr.ac.in; Fax: +91 80 22082760; Tel: +91 80 22082964

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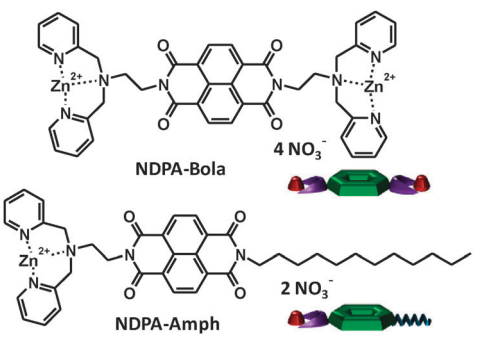
The molecular recognition driven 1-D helical self-assembly of chromophores often employed non-directional electrostatic interactions for guest binding.[7] However, we envisioned that chromophore functionalization with specific guest binding groups would give a better control over the resulting self-assembly.[8] On the other hand, use of biologically benign guest molecules, such as adenosine phosphates, would not only facilitate an efficient self-assembly through additional hydrophobic and π–π interactions between the base units, but would also act as a chiral handle for imparting chirality to the resulting assemblies. Extensive studies on molecular phosphate sensors suggest that the dipicolylethylenediamine–zinc complex (DPA–Zn) motif can specifically bind to various adenosine phosphates with high association constants.[9] Hence we have designed NDI amphiphiles substituted with DPA–Zn motifs (Scheme 1), in order to promote guest induced self-assembly and chiral induction through specific binding interactions. **NDPA-Bola** was synthesized following the literature procedure[9] whereas **NDPA-Amph** was synthesized by a statistical reaction of 1,4,5,8-naphthalenetetracarboxylic dianhydride with dodecylamine and *N*,*N*-bis(2-pyridylmethyl)ethane-1,2-diamine followed by zinc metallation.[10]

The absorption studies of **NDPA-Bola** (5×10^{-5} M, 10 mM aq. HEPES buffer) showed characteristic features of molecularly dissolved NDI chromophores such as sharp absorption bands (λ_{max} = 381 and 361 nm). However, titration of **NDPA-Bola** with increasing molar ratios of ADP (0–2 equivalents), resulted in broadening of absorption spectra, along with reversal of relative intensity of vibronic bands at 361 nm and 381 nm and decrease in fluorescence intensity characteristic of NDI chromophoric self-assembly (Fig. 1a).[10] Corresponding Circular



Scheme 1 Molecular structures of **NDPA-Bola** and **NDPA-Amph**.

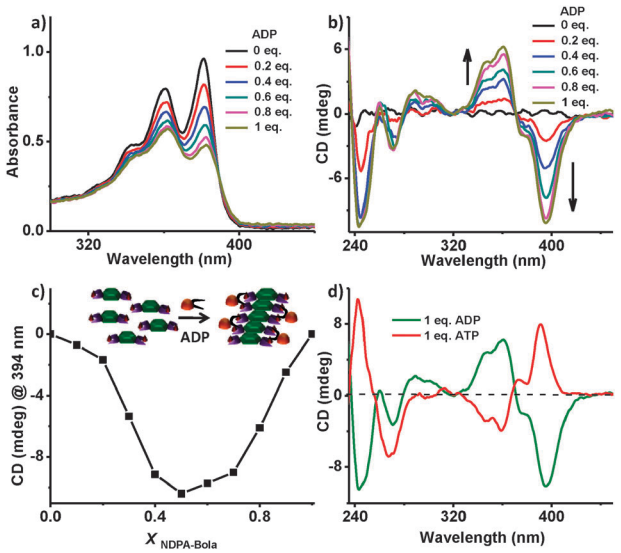


Fig. 1 Changes in (a) absorption, (b) CD and (c) Job plot of **NDPA-Bola** upon titration with ADP. (d) Mirror image CD spectra of **NDPA-Bola** with 1 equiv. of ADP and ATP ($c = 5 \times 10^{-5}$ M, 10 mM aq. HEPES buffer).

Dichroism (CD) spectra showed the gradual evolution of strong Cotton effects, through an isodichroic point at the zero-crossing (370 nm), indicating that ADP binding induces a preferred helical handedness to the resulting assemblies of achiral NDIs (Fig. 1b). Binding of ADP resulted in negative bisignated CD spectrum, with negative and positive maxima at 395 and 360 nm respectively, characteristic of excitonically coupled chromophores. The titration curve obtained by monitoring the CD intensity at 395 nm showed saturation at 1 equivalent of ADP, suggesting a 1 : 1 stoichiometry in the co-assembly.[10] This is further evident from the Job plot, where the CD intensity probed at 395 nm showed maxima at 0.5 mole fraction of NDI (Fig. 1c). This suggests that the divalent ADP molecules bind to two DPA–Zn moieties of adjacent NDIs in the assembly, thereby clipping the chromophores together, in line with the literature (inset, Fig. 1c).[9] This system presents one among the best excitonically coupled NDI chromophoric assemblies known in the literature,[6] as they often showed weak bisignated CD signals either due to their low self-association or lack of aromatic interactions in the self-assembly.

While **NDPA-Bola** showed similar assembly behaviour on titration with monovalent AMP,[10] binding of ATP induces opposite handedness to NDI assemblies as evident from the positive bisignated CD signal, with positive and negative maxima at 390 and 359 nm, respectively (Fig. 1d).[10] The mirror image Cotton effects of **NDPA-Bola** assemblies obtained with the ADP and ATP clearly suggests the induction of chirality with opposite handedness. Furthermore, slow cooling of the various NDI/phosphate co-assemblies from 95 °C to 15 °C, did not show any significant change in the intensity of the CD signal, indicating that room temperature binding of the chiral guest to NDI indeed leads to the most stable assemblies.[10]

In order to understand the role of guest-induced chiral assembly, we further studied the effect of phosphate binding on **NDPA-Amph** derivatives, in its monomeric as well as in the assembled states. The amphiphilic nature of the **NDPA-Amph** derivatives ensures that they can be self-assembled in a THF–water mixture, even in the absence of guest binding. Solvent dependent absorption studies ($c = 7 \times 10^{-5}$ M) showed that upto 70% aq. HEPES buffer in THF, it exists in the monomeric state. However in 90% aq. HEPES buffer, the molecule is self-assembled as evident from the broadening of absorption bands with reversal of the relative intensity ratio of the absorption maxima at 359 and 379 nm.[10] **NDPA-Amph** at these two states, *i.e.* monomeric and aggregated, showed very different behaviour on binding to phosphates. Monomeric **NDPA-Amph** (70% aq. HEPES/THF), self-assembles in a similar way as that of **NDPA-Bola** with various phosphates.[10,11] For example co-assembly with ADP resulted in a negative bisignated CD signal with positive and negative maxima at 357 and 391 nm, respectively.[10] Similarly, helicity induction was observed on binding to AMP and ATP giving negative and positive bisignated CD signals, respectively.[10] Remarkably, when ADP was added to the pre-assembled NDI amphiphiles (90% aq. HEPES/THF), chiral induction was not observed, neither at room temperature nor upon cooling the mixture from higher temperatures.[10] As the amphiphilic chromophoric assemblies are known to be less dynamic,[12] it is evident that at higher amounts of water, the pre-assembled **NDPA-Amph** molecules are not dynamic enough to reorganize into helical stacks upon guest binding.[10] Hence it can be concluded that, in the present system, guest induced molecular organization is crucial for the induction of supramolecular chirality. Remarkably, temperature dependent absorption and CD measurements of the NDI/phosphate co-assemblies have shown that, heating even upto 95 °C does not completely destroy chiral organization indicating the high stability of the stacks and guest binding.[10]

Transmission Electron Microscopy (TEM) imaging of **NDPA-Amph** (70% water in THF, 7×10^{-5} M) assemblies with 0.5 equiv. of ADP, stained with uranyl acetate showed the formation of 1-D nanofibers with a uniform diameter of 8 nm (Fig. 2). Based on the energy minimized molecular dimensions of ADP bound **NDPA-Amph** (~4 nm), this indicates that the fibers are formed by the π-stacking and solvophobic interactions of the NDI bilayers with non-interdigitated alkyl chains as the hydrophobic interior (inset, Fig. 2). TEM analysis of **NDPA-Bola/ADP** co-assemblies revealed the formation of fibers with a 4 nm diameter, suggesting that they are constructed from single NDI π-stacked columns with bound adenosine phosphates on both DPA–Zn sites.[10]

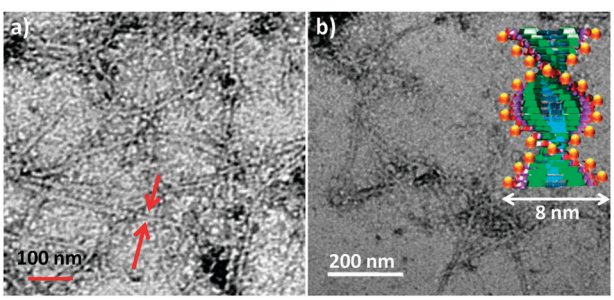


Fig. 2 (a) and (b) TEM images of a 7×10^{-5} M solution of **NDPA-Amph**/0.5 equiv. ADP (70% water in THF). Inset of b shows the schematic of the corresponding helical stack.

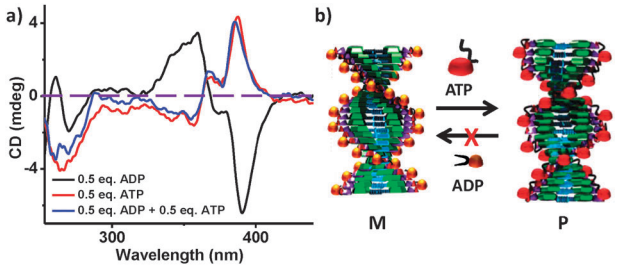


Fig. 3 (a) CD spectra and (b) the schematic of the dynamic helical reversal of **NDPA-Amph**/ADP assembly upon competitive guest binding experiments with ATP ($c = 7 \times 10^{-5}$ M, 70% aq. HEPES buffer in THF).

The formation of self-assembled NDI structures in solution is further confirmed by Dynamic Light Scattering (DLS).[10]

Finally, the induction of opposite chirality in NDI assemblies by different adenosine phosphates motivated us to attempt dynamic helix reversal through competitive binding of multivalent guests. When a solution of **NDPA-Amph** ($c = 7 \times 10^{-5}$ M, 70% aq. HEPES/THF) with 0.5 equiv. ADP was titrated with increasing amounts of ATP, a gradual reversal of helicity was observed without any indication of chiral amplification. Interestingly, addition of 0.5 equiv. ATP to **NDPA-Amph**/ADP assemblies resulted in a positive bisignated CD signal which exactly matches with that of **NDPA-Amph**/ATP stacks alone (Fig. 3). This clearly suggests the competitive replacement of ADP by ATP from the assemblies, as expected and an instantaneous reversal of its helical handedness.[10] We envisage that the dynamic helix reversal proceeds through an intra-stack mechanism, as the other reversal pathway through equilibrium between monomers and the assemblies is unlikely due to the high stability of the assemblies.

In summary, we showed a novel supramolecular design, based on dipicolylethylenediamine functionality, for the adenosine phosphate recognition driven one-dimensional helical assembly of chromophores. Chiroptical probing has provided mechanistic insights into the self-assembly process and showed that guest binding driven molecular reorganization is indeed necessary for helicity induction. We have also shown a novel strategy for the dynamic helical reversal of supramolecular assemblies, based on competitive binding of the guest molecules. Such versatile systems interacting with biologically benign chiral phosphates will be further studied for chiral amplification and memory.

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10 See ESI†.

11 Addition of higher equivalents of phosphates resulted in higher order aggregation, due to cross-linking, resulting in the decrease of CD intensity. See ESI† for details.

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