

## Mesoscopic helical architectures

**Citation for published version (APA):**

Vela, S., Berrocal, J. A., Atienza, C., Meijer, E. W., & Martín, N. (2017). Mesoscopic helical architectures: Via self-assembly of porphyrin-based discotic systems. *Chemical Communications, ChemComm*, 53(29), 4084-4087. <https://doi.org/10.1039/c7cc01670k>

**DOI:**

[10.1039/c7cc01670k](https://doi.org/10.1039/c7cc01670k)

**Document status and date:**

Published: 14/04/2017

**Document Version:**

Accepted manuscript including changes made at the peer-review stage

**Please check the document version of this publication:**

- A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher's website.
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## Mesoscopic helical architectures by self-assembly of porphyrin-based discotic systems †

Received 00th January 20xx,

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Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

**Mesoscopic super-helices with a preferred helicity have been serendipitously formed from the self-assembly of electroactive extended core discotic molecules. The investigation at diluted concentrations reveals intramolecular hydrogen-bonding and  $\pi$ - $\pi$  stacking interactions as driving force of the chiral self-assembly at different lengthscales.**

The expression of supramolecular chirality at different lengthscales is a topic of great interest in a number of research fields,<sup>1-6</sup> such as chiral recognition, asymmetric synthesis and helical crystallization of biomolecules.<sup>2, 7-9</sup> Besides exquisite chemical applications, mesoscopic chiral structures probably hide their most attractive potential in the field of organic materials for chiral induced spin selectivity (CISS),<sup>10-12</sup> where chirality is exploited to select electronic spins.

Mesoscopic objects with a defined chirality are frequent in biological systems,<sup>13</sup> with peptide amyloids and cellulose probably representing the most famous examples. For instance, Seebach *et al* have recently shown  $\mu\text{m}$ -sized helical amyloid fibrils serendipitously obtained from the self-assembly of dodecapeptides.<sup>14</sup> Supramolecular systems in which the chiral information embedded in the chemical structure of the supramolecular monomer is expressed at the mesoscopic level have also been reported.<sup>15</sup> Elemans *et al* have shown that  $C_3$ -symmetrical 1,3,5-benzenetricarboxamide (BTA) cores functionalized with porphyrins (porphyrin trimers) self-assemble via intermolecular hydrogen-bonding and  $\pi$ - $\pi$  stacking interactions into mesoscopic fibers applicable for surface patterning at macroscopic length scales.<sup>16-19</sup>  $C_3$ -symmetrical BTA systems substituted with *N*-monoacylated

3,3'-diamino-2,2'-bipyridine (Bipy) units (BTA-Bipy discotics) have proven to be promising structural moieties for both direct and indirect observation of supramolecular chirality at the mesoscale thanks to their extended  $\pi$ - $\pi$  stacking surface.<sup>20-22</sup> Amabilino *et al* reported a remarkable example of a BTA-Bipy system covalently functionalized with electroactive chiral tetrathiafulvalene (TTFs) units at the periphery which self-assembles into helical fibers with a preferred helicity and twists over several length scales.<sup>23</sup> Despite the increasing number of supramolecular systems characterized by the expression of supramolecular chirality at the mesoscale, a rationale that allows establishing a correlation between the design of the supramolecular monomer and the morphology at different length scales is still missing. With that in mind, even a simple report of a structure that assembles into chiral mesoscopic aggregates is of paramount importance to advance the field.

In this communication we disclose the synthesis (Scheme S1, ESI†) and self-assembly behavior of achiral **1a** and chiral **1b**;  $C_3$ -symmetrical BTA-Bipy cores substituted with three porphyrin units (Fig 1A). We hypothesized that the simple combination of the design of the porphyrin trimers and BTA-Bipy discotics would result in the formation of triple helical bundles more extended than the ones previously reported.<sup>12-15</sup> While studying the morphology of the aggregates formed by **1b** in heptane, we serendipitously observed  $\mu\text{m}$ -sized helical structures characterized by a well-defined handedness with Scanning Electron Microscopy (SEM) (Fig 1B). The approximate length of the super-helix was 150  $\mu\text{m}$ , with a helical pitch of circa 20  $\mu\text{m}$  and a width of 10  $\mu\text{m}$  (Fig S1, ESI†). These structures closely resemble the one reported by Seebach. Admittedly, the super-helix was found in a pretty heterogeneous sample characterized by a number of other undefined assemblies (Figure S1, ESI†).

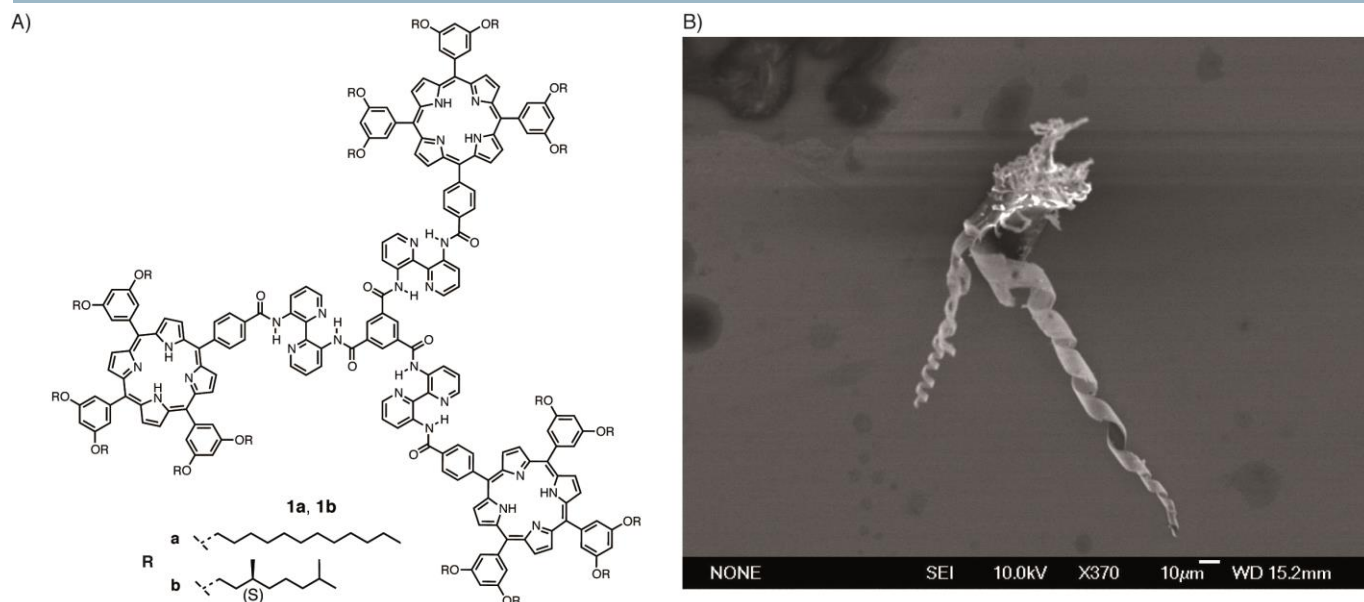
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† Electronic Supplementary Information (ESI) available: experimental details, synthesis and characterization of all new compounds. See DOI: 10.1039/x0xx00000x



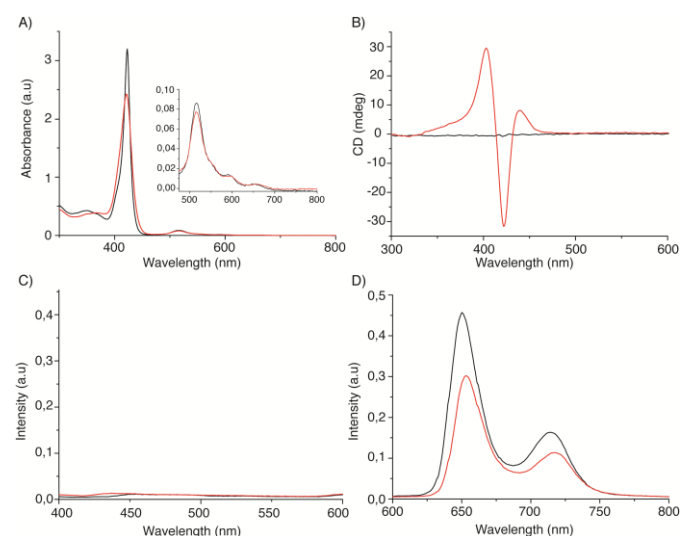
**Fig 1.** A) Molecular structure of achiral and chiral  $C_3$ -symmetrical BTA-porphyrin discotics (**1a** and **1b**, respectively). B) SEM micrograph showing the superhelix obtained from self-assembly of **1b** in heptane (1 mg/mL **1b**; scale bar 10  $\mu$ m).

Overall achiral structures featuring helical inversions were remarkably visualized upon studying the aggregates of achiral **1a** in heptane with SEM (Fig S1, ESI<sup>†</sup>). Intrigued by these results we investigated the self-assembly of **1a** and **1b** in diluted solutions.

Qualitative indications on the self-assembly of **1a/1b** were obtained from  $^1\text{H-NMR}$  spectroscopy in  $\text{CDCl}_3$ . At 4 mM the  $^1\text{H-NMR}$  spectra of **1a/1b** were characterized by broad and unresolved signals which became significantly sharper upon diluting to 0.4 mM (Fig S2, ESI<sup>†</sup>). At this particular concentration all the diagnostic signals of the structure of **1a/1b** were clearly visible in the  $^1\text{H-NMR}$  spectrum, including the protons of the amides between 15–16 ppm range, which unambiguously indicated intramolecular hydrogen bonds with the bipyridine nitrogen atoms.<sup>17</sup> The assignment of the aromatic peaks was performed with two Dimensional-Correlation Spectroscopy (2D-COSY) (Fig S3, ESI<sup>†</sup>). The addition of a small percentage (4%) of  $\text{DMSO-d}_6$  to the 0.4 mM  $\text{CDCl}_3$  solutions of **1a/1b** dramatically affected the sharpness of the spectra, suggesting aggregation induced by the increased polarity. This contrasts starkly with the previously reported porphyrin trimers, for which the addition of a polar, hydrogen-bond competing solvent resulted in the enhancement of the sharpness of the NMR signals.<sup>13</sup> Aggregation of 0.4 mM **1a** or **1b** in  $\text{CDCl}_3$  could also be induced by low temperatures, as witnessed with Temperature Dependent (TD) NMR measurements (Fig S4, ESI<sup>†</sup>).

To gain further insights into the self-assembly process of **1a/1b**, we carried out a number of spectroscopic experiments. Firstly, UV-Vis experiments at diluted concentrations (5  $\mu\text{M}$ ) and different solvents were performed. The UV-Vis spectrum of **1a/1b** in  $\text{CHCl}_3$  showed the intense Soret band at 423 nm with a shoulder at 402 nm, and the four typical, less intense Q bands of free-base porphyrins at 659, 595, 554, and 516 nm (Fig 2a). The same features were detected in toluene ( $\text{PhCH}_3$ ) (Fig S5, ESI<sup>†</sup>). When **1a/1b** were dissolved in heptane, a significant broadening and slight blue shift ( $\sim 3\text{nm}$ ) of the Soret band was observed together with the disappearance of the shoulder at 402 nm (Fig 2). Such spectral variations suggested self-assembly also at these low concentrations and were consistently observed upon replacing heptane with methylcyclohexane (MCH) (Fig S5, ESI<sup>†</sup>). The spectral variations appeared more attenuated compared to the previous porphyrin trimeric systems,<sup>12–15</sup> especially in terms of intensity drop and magnitude of the blue shift of the Soret band.

Next, we investigated the self-assembly of chiral **1b** with CD spectroscopy to assess the chiral amplification at 5  $\mu\text{M}$  (Fig 2b). While the CD spectrum of **1b** in  $\text{CHCl}_3/\text{PhCH}_3$  was silent (Fig 2b and Fig S5, ESI<sup>†</sup>, respectively), the one in heptane showed a trisignated Cotton effect in correspondence of the Soret band with a positive, a negative and a positive Cotton effect at 440, 422, and 403 nm, respectively (Fig 2b). A similar shape of the CD spectrum was measured for **1b** in MCH, although with a lower intensity (Fig S5, ESI<sup>†</sup>).



**Fig 2.** Solution phase self-assembly of **1b**. (a) UV-Vis spectra of 5 μM **1b** in CHCl<sub>3</sub> (black) and heptane (red) (298 K, 1 cm optical path). (b) CD spectra of 5 μM **1b** in CHCl<sub>3</sub> (black) and heptane (red) (298 K, 1 cm optical path). (c-d) Fluorescence spectra of 5 μM **1b** in CHCl<sub>3</sub> (black) and heptane (red) ( $\lambda_{\text{exc}}=380$  nm) in BTA-Bipy region (c) and porphyrin region (d).

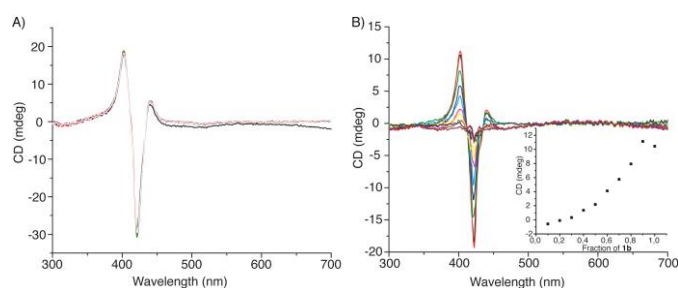
Dynamic Light Scattering (DLS) measurements carried out on solutions of **1a** in both MCH and heptane gave very similar correlation functions, ruling out the size of the aggregates as a potential cause of the weaker CD signal in MCH (Fig S6, ESI<sup>†</sup>). The dependence of the intensity of the CD signal on the shape of the alkane solvents (i.e. linear vs cyclic) has been previously observed in other systems, with always the linear alkane being most effective.<sup>24</sup> Calculations revealed that either the dihedral angle of the amides or subtle differences in the energies of the *P*- and *M*-helices were responsible for such a behavior. The origin of such sensitivity in the present system is not clear, but experimental results clearly suggest a more pronounced chiral bias in the linear alkane.

The experimental evidences reported so far consistently point to a self-assembly process driven by  $\pi$ - $\pi$  stacking interactions, thus triggered by (a)polar solvents due to poor solvation of the extended aromatic cores. Hence, the structural variations introduced by us in the design of the porphyrin trimers significantly affected the self-assembly behavior most likely due to a drastic difference in the shape of the monomers. The presence of the Bipy in our system highly favors the formation of intramolecular hydrogen bonds between the aromatic nitrogen atoms and the N-H of the amides, as observed by <sup>1</sup>H-NMR spectroscopy (Fig S7, ESI<sup>†</sup>). The intramolecular interactions could then force a flat conformation for either the entire molecule or just the Bipy moiety.

Previous reports on BTA-Bipy discotics highlighted a diagnostic green emission (520 nm) when the Bipy is stacked in the aggregate and coplanar to the BTA core.<sup>25</sup> To elucidate the solution-phase shape of our supramolecular monomers we performed fluorescence measurements on **1b** in either CHCl<sub>3</sub> or heptane (Fig 2c-d). Upon excitation of 5 μM **1b** at 380 nm, we measured a luminescence profile consisting of two maxima at 650 and 725 nm, ascribed to the porphyrin units from direct

comparison with **5a** (Fig S8, ESI<sup>†</sup>). The fluorescence intensity of **1a/1b** in heptane was quenched as a consequence of self-assembly (Fig 2c). The typical strong green luminescence of the stacked coplanar bipyridine moiety was not observed even when we used the typical excitation wavelength of the Bipy (380 nm) (Fig 2c).<sup>25</sup> The observed luminescence of **1b** could be the result of two hypotheses: *i*) the Bipy moieties are not stacked strongly enough in the assembly; *ii*) the porphyrins quench the emission of the Bipy as a result of a high proximity-induced energy/electron transfer from the Bipy to the porphyrin. Hence, an additional reference experiment in fluorescence was performed. The addition of model porphyrin **5a** to a previously formed stack of a BTA-Bipy discotic<sup>18</sup> in heptane significantly quenched the green luminescence of the bipyridine (Fig S8, ESI<sup>†</sup>). This is in line with previous reports on fluorescence quenching of Ru-(Bipy)<sub>3</sub> complexes with organic dyes.<sup>26</sup> Interestingly, the quenching of the green fluorescence of the BTA-Bipy discotic was accompanied by a significant quenching of the fluorescence of **5a** that was not observed when the molecule was independently studied in CHCl<sub>3</sub> or heptane. These results suggest an intermolecular energetic/electronic communication between Bipy and porphyrin in solution, enormously favored by connecting the two moieties covalently in **1a/1b**. While the occurrence of a highly efficient intramolecular energy/electron transfer is very likely, no conclusions could be drawn concerning the dihedral angle between the Bipy and BTA core with our available spectroscopic techniques. Such intriguing scientific question may be better addressed with time-consuming theoretical studies that we will reserve for a future investigation.

Once ascertained the limitations of the spectroscopic techniques in determining the solution-phase shape of supramolecular monomers **1a/1b**, we investigated the stability of the aggregates formed by 5 μM **1b** in the two alkane solvents with TD-CD experiments by monitoring the full spectrum at regular time intervals. Remarkably, no intensity decrease was detected by CD even when the solutions were heated up to 80 °C for 12 hours (Fig 3a; Fig S9, ESI<sup>†</sup>), highlighting the high thermal stability. Such property may be the macroscopic manifestation of either single helices held together by threefold  $\pi$ - $\pi$  stacking interactions of completely flat monomers or an undefined network of monomers in which the dominant driving force is the dimerization/oligomerization of porphyrins. We speculate the network hypothesis to be more reasonable.



**Fig 3.** (a) CD spectra of 5 μM **1b** in heptane (t= 80 °C during 12 h). (b) CD spectra of the "sergeant and soldiers" experiment in which solutions of varying concentrations of **1a** and **1b** in heptane were mixed.

Partial disruption of the supramolecular architectures formed at room temperature was only observed after addition of a significant amount of good solvent (35% CHCl<sub>3</sub> or 1,1,2,2-tetrachloroethylene), as witnessed by the considerable drop in Cotton effect detected (Fig S10, ESI<sup>†</sup>).

Finally, we carried out “Sergeant-and-Soldiers” experiments by mixing **1a** and **1b** to assess whether the high thermodynamic stability of the aggregates of the individual molecules also resulted in a profound kinetic stability. Stock solutions of **1a** and **1b** in *n*-heptane were mixed at different ratios to achieve a final 9 μM total concentration in cuvette. The process was monitored by CD spectroscopy at 422 nm (Fig 3b). No amplification of chirality was observed even after sonication or leaving the solutions to stand for prolonged times. In stark contrast with the previous porphyrin trimers<sup>12-15</sup> the amplification of chirality was even not observed after pre-mixing stock solutions of **1a** and **1b** in good solvents such as CHCl<sub>3</sub> or PhCH<sub>3</sub>, followed by solvent removal and redissolution in heptane (Fig S11, ESI<sup>†</sup>). We concluded that monomer exchange is not thermodynamically favorable and the aggregation in non-solvents is kinetically controlled. Hence, with **1a/b** we are at the edge of solubility and assembly, giving rise to even more complex pathways for self-assembly with the risk to be trapped in stable kinetic states of different morphologies, some of them being unique in shape.

In summary, we reported the synthesis and assembly behavior of (a)chiral porphyrin trimers based on benzenetricarboxamide-bipyridine discotics. The realization of such molecular architectures resulted in the serendipitous discovery of the first μm-sized helical structure not deriving from a peptidic system. The study of the self-assembly at diluted concentrations revealed only π-π stacking as driving force of the process. However, our investigation also depicted a system characterized by kinetic considerations in the formation of aggregates that do not seem to show thermodynamic reversibility. Our work stresses the paramount importance of translating the design of high molar mass supramolecular monomers into solution-phase molecular shapes.

## Acknowledgements

JAB and EWM would like to thank The Netherlands Organization for Scientific Research (NWO TOP-PUNT Grant 10018944) and the Dutch Ministry of Education, Culture and Science (Gravity Program 024.001.035). NM thanks to the Spanish Ministry of Economy and Competitiveness (MINECO) CTQ2014-520456-R, Community of Madrid Government (Photocarbon project. S2013/MIT-2841) and the European Research Council ERC-320441-Chirallcarbon. CA thanks to the Ramón y Cajal granted and SV thanks to Spanish Ministry of Education for FPU granted.

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