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Complex supramolecular fiber formed by coordination-induced self-assembly of benzene-1,3,5-tricarboxamide (BTA)

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GRAPHICAL ABSTRACT

Based on a new designed tris-ligand L3 (BTA-DPA3), complex supramolecular fibers are prepared through a coordination-induced self-assembly. Upon mixing metal ion and L3 ligand, the coordination constructs an assembled subunit which further stack into supramolecular fibers based on the strong H-bonding of BTA core. Varying metal ions hardly disturbs the fiber formation and structure, while enables introducing different functionalities from the metal ions. The study demonstrates a novel strategy for constructing supramolecular materials with hierarchical structures and functionalities.

Hypothesis:

In the quest for large but well-controlled supramolecular structures, the discotic benzene-1,3,5-tricarboxamide (BTA) has received quite some attention, because it can form hydrogen-bonded stacks that can be regarded as supramolecular polymers of which the single BTA molecule is the monomer. In this report, we consider a more complex BTA-based supramolecular polymer, namely one that is built up from supramolecular 'monomers'.

Experiments:

We design a tris-ligand L3 consisting of a BTA core carrying three dipicolinic acid (DPA) groups. L3 itself is too small to form polymers, but in the presence of appropriate metal ions, each L3 can form three coordination bonds and so form (L3)n clusters that are large enough to stack successfully: at an appropriate metal dose, long and stable filaments with a cross-sectional diameter of 12 nm appear. We monitor the growth process by UV–vis spectroscopy and light scattering, and use small angle X-ray scattering (SAXS), TEM as well as molecular simulation to confirm the filamentous structure of the fibers and determine their dimensions.

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ABSTRACT

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1. Introduction

If there is a path from non-living chemical objects to advanced biological matter, it is characterized by increasing complexity [1]. Therefore, chemistry in recent years is exploring the behavior and potential functions of complex molecular systems [2–4]. In this context, thread-like molecular assemblies have been considered: they can be regarded as ‘supramolecular polymers’ held together by non-covalent interactions [5]. Hydrogen bonds are most suitable for this purpose. Prominent examples are the chains formed by molecules with two ureopyrimidine (upy) end groups [6], by bisureas with pendant hydrophobic groups [7–8], by small peptides in solvents of low polarity [9–10], by peptides with an alkyl ‘tail’ [11–12], or by folded polypeptides [13–14]. Also, coordination bonds can do the job, e.g., the combination of a bis-ligand with appropriate metal ions in water [15–17]. In most cases, the chains evolve - in polymer terms - by ‘step growth’, but when conformation changes come into play, polymerization can also occur by ‘chain growth’ [18–20], and even ‘living’ supramolecular polymerization has been seen [21–23].

In all cases above, the ‘monomer’, i.e., the building block from which the supramolecular polymer is constructed, is itself a coherent molecule. This is the simplest choice, but in the spirit of enhancing complexity we now require that the ‘monomer’ is itself a supramolecular structure [24–25]. If it is, the supramolecular polymer becomes a hierarchical assembly, with different bonding types along radial and axial coordinates, and properties that are dynamically controlled by multiple equilibria [26–27]. The purpose of the present study is to explore this possibility, by finding an example of such a hierarchical supramolecular polymer and characterize it.

An interesting class to consider here is that of the derivatives of benzoic-1,3,5-tricarboxamide (BTA) [28]. Some of these molecules can form filaments of molecular stacks stabilized by hydrogen bonds [29–32]. In particular, we look for a BTA derivative that can form larger units through coordination bonds. Not only does this realize a higher level of complexity, but it also allows to easily introduce and vary metal-derived functionalities.

Findings: The formation and structure of the fiber are very similar for various transition metal ions, which enables introducing different functionalities, e.g., magnetic relativity, by proper choice of the metal ions. Hence, we obtain a doubly supramolecular polymer, connected axially by hydrogen bonds, and radially by coordination bonds. Not only does this realize a higher level of complexity, but it also allows to easily introduce and vary metal-derived functionalities. © 2021 Elsevier Inc. All rights reserved.

2. Materials and methods

2.1. Materials

Triethylamine TEA, 1,3,5-Benzentetrahydroxybenzoic acid chloride TMC, ethyl acetate EtOAc, potassium hydroxide KOH, ethanol EtOH, tetrahydrofuran THF, ferric chloride hexahydrate FeCl3·6H2O, manganese dinitrate Mn(NO3)2·4H2O, and nickel(II) nitrate hexahydrate Ni(NO3)2·6H2O were purchased from Sigma Aldrich, and used as such. Diethyl 4-Aminopyridine-2,6-dicarboxylate was purchased from Accela and used without further purification.

2.4-pyridinedicarboxylic acid was purchased from Sigma Aldrich. Then, we dissolved it in 1 M KOH solution to get DPA (2,4-pyridinedicarboxylic acid potassium salt), then the crude solution was dripped into EtOH for excess KOH removal, finally, after filtration, the white DPA could be collected and used for ITC measurement.

The detailed synthesis procedure of L3 is shown in Supporting Information.

2.2. Preparation of supramolecular fiber

General procedure for preparation of complex supramolecular fiber: typically, for a 1 mL sample, THF (500 µL) and H2O (380 µL) were first mixed, then an aqueous stock solution (1 mM) of the L3 (100 µL) was added under shaking, finally an aqueous stock solution (5 mM) of metal ions (Fe3+, 20 µL) was added under shaking (on a shaker). The final concentration of L3...
is 0.1 mM. The volume ratio of THF and H2O was kept at v/v = 50/50. All stock solutions of ligand and metal ions were separately prepared in DI water.

2.3. Characterization

1H NMR and 13C NMR spectra were recorded on a BRUKER AVANCE 500 spectrometer operating at 500 MHz. UV–vis spectra for all the samples were recorded on a SHIMADZU 1800 spectrophotometer. For the L3 samples with [Fe] > 0.12 mM, we removed the precipitate before UV–vis test. Mass spectra was performed on a matrix-assisted laser desorption/ionization time of flight mass spectrometry. Isothermal titration calorimetry (ITC) measurement was carried out at 23.5 °C using a MicroCal VP-ITC. Fourier Transform Infrared Spectroscopy (FTIR) spectroscopy was performed with Bruker Alpha II spectrometer using the ATR method at room temperature.

2.3.1. Transmission electron microscopy (TEM) and field emission scanning electron microscope (FE-SEM)

TEM was performed on a JEM-1400 electron microscope operating at 100 kV. 230-mesh copper grids were coated with formvar support film, followed by subsequent coating with carbon. 15 μL of the sample solution was placed on the resulting grids. Excess solution was removed by filter paper, and samples were allowed to dry in ambient air at room temperature before TEM observation. FE-SEM was performed on a Nova NanoSEM 450. The precipitate was placed on the test platform for SEM observation.

2.3.2. Cryogenic transmission electronic microscopy (Cryo-TEM)

A few microliters of sample was placed on a bare copper TEM grid (Plano, 600 mesh), and the excess liquid was removed with filter paper. This sample was cryo-fixed by rapidly immersing into liquid ethane cooled to –170 to –180 °C in a cryo-box (Carl Zeiss NTS GmbH). The specimen was inserted into a cryo-transfer holder (CT3500, Gatan, Munich, Germany) and transferred to a Zeiss EM922 EFTEM (Zeiss NTS GmbH, Oberkochen, Germany). Examinations were carried out at temperatures around –180 °C. The TEM was operated at an acceleration voltage of 200 kV. Zero-loss filtered images were taken under reduced dose conditions (500–2000 e/nm2). All images were recorded digitally by a bottom-mounted CCD camera system (UltraScan 1000, Gatan) and processed with a digital imaging processing system (Digital Micrograph 3.9 for GMS 1.4, Gatan).

2.3.3. Light scattering

Light scattering (LS) measurements were performed with an ALV light scattering apparatus, equipped with a 21 mW He-Ne laser operating at a wavelength of 632.8 nm. Measurements were done at a detection angle of 90° unless stated otherwise. All measurements were performed at room temperature. For angular-dependent LS, ten correlation functions g2(t) were recorded at 6 angles θ, from 30 to 130° in increments of 20°, to evaluate the angular dependence of the diffusion coefficient D. It is known that asymmetric particles always give rise to a dependence of D (=Γ/q2) on q2, but for spherical particles, the D values should be independent of the scattering vector, because of the undetectable rotational motion [42]. q is the scattering vector:

\[ q = \frac{4\pi n}{\lambda} \sin \frac{\theta}{2} \]  

(1)

Here, n is the refractive index of the solvent, and λ is the wavelength of incident light.

2.3.4. Isothermal titration calorimetry (ITC) measurement

General procedure: a solution of DPA (15 mM) was titrated to the Fe3+ solution (1 mM), both in THF/H2O (v/v = 50/50) with 20 mM MES buffer (pH = 6) at 23.5 °C. The first titration point of each ITC measurement was omitted.

2.3.5. Small angle X-ray scattering measurement

2.3.5.1. Sample preparation. The samples were prepared at a DPA concentration of 0.3 mM in mixtures of THF/H2O (v/v = 50/50) and allowed to equilibrate 2 h prior to measurements.

2.3.5.2. SAXS measurement. All experiments were performed on a SAXSLAB GANESHA 300 XL system equipped with a GeniX-Cu ultra-low divergence micro focus sealed-tube source producing X-ray photons (λ = 1.54 Å). The scattering intensity was measured as a function of momentum transfer vector, q, defined as:

\[ q = \frac{4\pi}{\lambda} \sin \frac{\theta}{2} \]  

(2)

where 2θ is the scattering angle. The 2D scattering data were recorded on a Pilatus 300 K detector. Small-angle X-ray scattering (SAXS) profiles were measured using 2.0 mm quartz capillaries (Hilgenrein), mounted with custom-built capillary holders. A known sample-to-detector distance of 713 mm gave an accessible q-range of 0.007 < q < 0.44 Å−1. The scattering profile of the background (THF aqueous solution containing Fe ions) and quartz capillary were subtracted to produce a final SAXS profile. For the mixed solvent (THF/H2O, v/v = 50/50) the scattering length density was calculated as the average of that of water and THF [43], corrected for contraction using literature data [44], which gives \( \rho_{\text{solvent}} = 9.0 \times 10^{10} \, \text{cm}^{-2} \).

The SAXS pattern was fitted to a model for rigid cylinders with a uniform scattering length density (ρcyl) and cross-sectional radius r, introducing a Schultz distribution to account for polydispersity. Fitting the scattering data with the model provided a value for \( \rho_{\text{cyl}} = 1.09 \times 10^{11} \, \text{cm}^{-2} \). By fixing the volume fraction (φ = 0.000 0714) and the scattering length density of solvent (ρsolvent = 9.03 × 10^{10} \, \text{cm}^{-2} ) in the model, we found a mean cross-sectional radius of 0.6 nm, and a Schultz root-mean-square deviation of at least 0.9 nm. The radius dispersity could not be determined accurately beyond a lower bound of 0.15 due to the high background. Fitting parameters are collected in Table S1. To account for fiber–fiber interactions, we included a contribution using a generalized Guinier/power law for high-aspect ratio and large object using the term derived from reference [45]. All fitting parameters for the new fit are collected in Table S2.

2.4. Molecular simulation

The hypothetical structure of Fe-L3 is a cluster of L3 molecules connected by coordination bonds. Both L3 itself and several metal-bonded cluster were studied by Density Functional Theory (DFT), using the Gaussian 09 program package [46]. The structures were fully optimized using B3LYP-D3 functions in combination with the def2-SVP basis and the SMD continuum solvent model [47–51]. We constructed various complex subunits with different Fe/DPA ratios p (p = 1/6, p = 1/4, p = 3/10, corresponding to complexes (L3)₂, (L3)₄ and (L3)₁₀, respectively, and these were equilibrated by DFT. The complex (L3)₂ was first optimized by the Gaussian 09 program. The complexes (L3)₄ and (L3)₁₀ were optimized with GPN-XTB, followed by re-optimization using the Gaussian 09 program. The diameter was measured as that of the smallest circle in which the entire structure could be fitted. The results are shown below and in Fig. S13.
2.5. MRI testing and $T_1$ relaxation time

The MRI tests and $T_1$ relaxation time measurements were carried out on a 0.47 T NMR20-Analyst NMR Analyzing and Imaging system (Niumag Corporation, Shanghai, China).

3. Results and discussion

3.1. Preparation and characterization of supramolecular fiber

As shown in Scheme 1, the tris-ligand $L_3$ carries three amide groups which take care of the inter-BTA H-bonding, and three dipicolinic acid groups (DPA) for chelating with metal ions. The detailed synthesis and evidence confirming the structure of the new ligand can be found in SI (Fig. S1-6). Various metal ions ($M^{n+} = Mn^{2+}, Zn^{2+}, Ni^{2+}, Fe^{3+}$) are selected for forming $Me(DPA)_2$ coordination complexes.

In the following, we first select Fe$^{3+}$ as the metal ion, because the coordination compound $Fe(DPA)_2$ produces a typical UV–vis absorption at 390 nm, which allows us to confirm that metal–ligand chelation occurs [52–53], as can be seen in Fig. 1A. Light scattering is then used to investigate the formation of the larger assemblies. By varying the metal concentration, we tune the metal/DPA (e.g., Fe/DPA) ratio $f$. The polar solvent is a mixture of THF and H$_2$O ($v/v = 50/50$). For convenience, we express the $L_3$ concentrations of 0.3 mM for all the samples. In Fig. 1B we show that for $f = 1/3$, the static scattered intensity is large, indicating the occurrence of assembly. Dynamic light scattering shows a clear angular dependence, implying non-spherical objects (Fig. 1C). Finally, TEM (Fig. 1D) and cryo-TEM (Fig. 1E) confirm that filaments are formed.

3.2. Investigation on metal/ligand ratio and the growth process of fiber

We now investigate the effects of the [Fe]/[DPA] ratio ($f$) on the formation of subunits and fibers. Different amounts of Fe$^{3+}$ (0.03 ~ 0.17 mM) are added into the solution of $L_3$ at a fixed concentration (0.3 mM DPA), giving a range for $f$ of 0.1 ~ 0.57. As shown in Fig. 2A, the UV–vis absorption at 390 nm first increases with increasing Fe$^{3+}$, reaching a maximum around 0.1 mM, corresponding to $f = 1/3$. In parallel, the light scattering intensity also displays a maximum at $f = 1/3$ (Fig. 2B). By TEM we find that samples with a Fe/DPA ratio well below 1/3 yield short fibrillary aggregates (Fig. S7). Upon further increasing [Fe$^{3+}$], both the UV–vis absorption and light scattering intensity drop, and a precipitate is seen to develop (Fig. 2A and Fig. S8). Apparently, too much metal compromises the stability of the fiber dispersion and assemblies are depleted from the solution.

These observations may be understood as follows. It is easily verified that when the ratio between bound metal and DPA units in a cluster, as pictured in Scheme 1, is denoted $p$, the average size $n$ of a ($L_3)_n$ cluster satisfies $n = 1/(1-3p)$. E.g., for $p = 0.3$ we should have an average cluster of size 10 (as shown in Scheme 1). Since there is an equilibrium between free and bound metal, $p$ is always slightly lower than the overall mixing ratio $f$, but binding is strong so that $p$ is fairly close to $f$. We determined the binding constants for $Fe(DPA)$ and $Fe(DPA)_2$ by isothermal titration calorimetry (ITC) (See Fig. S9) and find $K_1 = 6.05 \times 10^6$ M$^{-1}$ and $K_2 = 1.53 \times 1 0^5$ M$^{-2}$ for the singly and doubly coordinated complexes, respectively. These numbers imply that in excess of DPA, where Fe (DPA)$_2$ is the dominant species and the relevant binding constant is the product of $K_1$ and $K_2$ (equaling 9.2565 $\times 10^{11}$ M$^{-2}$), the concentration of free Fe$^{3+}$ must be very small indeed [54]. Apparently, the range where fiber formation becomes prominent corresponds to $f \sim 0.3$, i.e., the average cluster size $n$ is of order 10 or more. Note that $n$ is very sensitive to $p$ in this range; in fact, it diverges for $p = 1/3$ (or $f \geq 1/3$), which implies that when more Fe is added we get infinite-sized clusters, leading to precipitation. The range in [Fe]/[DPA] = $f$, where stable fibres appear turns out to be roughly from 0.25 to 0.4 (1/4 ~ 1/2.5); at smaller $f$ only short fragments can be seen, whereas beyond 0.4 precipitation sets in. Hence, there is a certain tolerance to deviations from $f = 1/3$.

One may wonder why the fibers do not aggregate. As is clear from Scheme 1, DPA groups at the periphery of the cluster do not carry a metal ion, so they remain as potassium salt and are likely to be at least partially dissociated (the THF/H$_2$O mixture has a fairly high dielectric constant [55]). As there is no added salt in our system, electrostatic repulsion is capable of keeping the fibers apart. To confirm this, we prepared a sample in the same solvent but with 10 mM NaCl so as to screen the surface charges. Indeed, the TEM image shows that fibers now tend to form bundles (See Fig. S10).

A related question is why the clustered BTAs can stack at all. Apart from the negative charge on their periphery, there is also one residual negative charge at each coordination bond, unless the potassium counterions remain bound. This depends on the solvent; in pure water the counterions are easily dissociated and stacking would indeed be prohibited, but added THF suppresses the dissociation just enough to allow stacking to occur (See Fig. S11).

Some insight into the growth rate of the supramolecular polymers can be obtained from time-dependent experiments. We conducted these again at the Fe/DPA ratio of 1/3. Interestingly, Fig. 2C exhibits different growth kinetics for UV–vis absorption and light scattering intensity, respectively. Both quantities level off after about 2 h, but the UV–vis absorption increases quickly to more than 90% of the final level (likely corresponding to nearly full coordination of all metal ions). This trend suggests that full coordination is achieved within the first 20 min. In contrast, the light scattering intensity (already at 75% at the first data point) lags

Scheme 1. A) Chemical structure of ligand $L_3 = BTA-DPA_3$, and B) its hierarchical self-assembly (artist impression) into a supramolecular fiber with coordination bonds in the radial direction and H-bonds in the axial direction.
behind; it shows a roughly linear increase up to 60 min, followed by a slow growth and a plateau at 120 min (See Fig. S12). In order to investigate the structural development of Fe-L₃, we took TEM images at different time points (0 min, 40 min). As shown in Fig. 2D, the solution already exhibits short (0.5 μm) fibers immediately after mixing, these fibers then grow over time (1 μm at 40 min, see Fig. 2E) and after 120 min finally reach a length of several μm (Fig. 1D, 1E). In view of these findings, we propose that Fe-DPA chelation is fast; many coordination-induced clusters form immediately upon mixing the metal and ligand. The stacking of these units into short filaments also occurs rapidly, but is followed by more time-consuming processes, possibly involving cluster break-ups and rearrangements. We emphasize that, although we distinguish between coordination-bonded L₃s in the radial direction of the fibers, and hydrogen bonding of such clusters in the axial direction, our data do not allow to conclude that the growth is a two-step process of (L₃)n cluster formation followed by stacking. In fact, radial and axial bonds may well develop simultaneously.

### 3.3. Small angle X-ray scattering and molecular simulation

The TEM results give us reliable shape information but estimating the fiber cross section from TEM data cannot be done precisely. To further confirm the morphological characteristics of the fibers, we have carried out additional SAXS measurements, because SAXS has the capability to detect characteristic dimensions in the nanometer range. The scattering data for Fe-L₃ is presented in Fig. 3.

As can be seen in Fig. 3A, the Fe-L₃ scattering curve initially decays gradually (indicating scattering objects of high aspect ratio) up to about q = 0.07 Å⁻¹, where the data becomes noisier and the background level is reached. Based on our electron microscopy observations we attempted to fit the data to rigid or flexible
cylindrical models. A flexible cylinder model was almost in full agreement with the scattering data (not shown here); however, the modelling led to unreasonable Kuhn length values, of the same order of magnitude as the cross-sectional radii. Moreover, we did not observe this flexibility on the TEM micrographs, the aggregates where rather stiff. A rigid cylinder model was also in good agreement with the data, but over a finite q range (0.03 Å⁻¹ < q < 0.44 Å⁻¹) and yielded a cylinder cross-sectional diameter of about 12.0 ± 1.8 nm (orange curve, for details, see SI). This latter value matches well with the TEM estimate. At the low q end, the data tend to deviate upwards from the fit and follows a q⁻² dependency. This may indicate a modest degree of fiber–fiber aggregation and need not be surprising, since DPA groups exposed at the surface of the fiber may occasionally coordinate with a few available iron ions, forming fiber–fiber coordination bonds. This q-dependency at low q-values can be also observed in rigid carbon nanotubes dispersions and is usually ascribed to a loose fiber network [56]. Other factors affecting the model discrepancy is that it considers a Fourier power law of q⁻⁴ (corresponding to the mid-q decay). This assumption, however, is only for smooth surfaces and might not apply if the fibers have a rough surface. We attempted to include these contributions by adding a generalized Guinier/Porod law term for high-aspect ratio and large objects into the model. This modification improved the model agreement considerably. Estimating the fiber cross-section is, however, more challenging for this model, due to coupling with the blob scattering contribution in the high-q regime. The values obtained with the more elaborated model are essentially those calculated with the simpler model but yield a higher polydispersity (c.a. 6 nm ± 3 nm). The high polydispersity seems to be consistent with the nature of the

![Fig. 2. A) UV–vis absorption and B) light scattering intensity of Fe-L₃ assemblies upon addition of Fe³⁺ into L₃ solution. C) UV absorption (Abs.) and light scattering intensity (Intensity) of Fe-L₃ sample, at [Fe]/[DPA] = 1/3, as a function of time. TEM image of Fe-L₃ fibers at 0 min (D) and 40 min (E).](image-url)
Finally, neither the length of the fibers nor the fractal mesh size can be determined from the SAXS data, as the lower limit of q does not allow to cover scatterers larger than 50 nm.

In order to further assess the cross-section of the coordination-bonded subunit, we carried out density functional theory (DFT) simulations. We use the Gaussian 09 and XTB program package to explore various possible minimum-energy structures (See Fig. S13). The size of a single L3 ligand is about 2.1 nm. (See Fig. 3B). Since the diameter of the fiber (as determined from TEM images) is around 12 nm this means that the ‘monomer’ subunit is much larger, comprising at least several L3 ligands coordinated with metal ions. By considering a range of cluster sizes (See Fig. 3C), we find a representative cluster; it has threefold symmetry, comprising 10 L3 ligands coordinated with 9 Fe$^{3+}$, and having an in-plane cross-sectional diameter of 11.27 nm, i.e., close to the TEM value. We therefore tentatively assume that this cluster is the most likely building block or supramolecular ‘monomer’. For this cluster, the Fe/DPA ratio is 0.3, i.e., just under the mixing ratio of 1/3, which would mean that about 90% of all available Fe$^{3+}$ is coordinated with two DPA groups, which is consistent with our UV–vis results. One may wonder whether the symmetrical ‘average’ cluster considered here is relevant; other clusters structures are conceivable. It is important to realise, however, that the regular cylinder formed by such a cluster is the structure that maximizes the number of bonds, both axial and radial. Deviations from this structure are therefore energetically highly unfavourable.

### 3.4. Investigation on BTA hydrogen bond

The driving force for the stacking of subunits into a filament is tentatively attributed to the many BTA-BTA hydrogen bonds (maximum 30 for (L3)$_{10}$) that can form between them. A single BTA unit can form 3H-bonds, and in the water-rich solvent (THF/H$_2$O, v/v = 50/50) that we use these three bonds are possibly too weak to drive the stacking, but 30 bonds apparently add up to sufficient strength. In other words, the H-bonding amide groups are essential to get the supramolecular fiber. Unfortunately, it is difficult to directly prove the existence of amide-amide H-bonds by spectroscopy: NMR cannot be used because of severe line broadening and the amide band in IR spectra was perturbed too much by solvent signals. Therefore, in order to confirm the H-bonding hypothesis, we modified the system in two ways. Firstly, we synthesized BL3 (Benzene-DPA$_3$) in which amide groups have been replaced by –CH$_2$–O– (See Fig. 4A). The detailed synthesis has been described elsewhere [52]. We find that in the presence of iron ions ([Fe]/[DPA] = 1/3), BL3 only forms some non-fibrous clusters (See Fig. 4B), even though UV–vis spectra confirm the existence of coordinated Fe-(DPA)$_2$ (Fig. 4A). This implies that without the H-bonding amides, the coordination-based cluster cannot polymerize to fiber, i.e., cannot act as a ‘monomer’. Secondly, we added 1 M urea to the Fe-L3 complexes, which is widely accepted in the literature as a method to destroy (and hence prove the occurrence of) H-bonds [57]. We found that in this case spherical nanoparticles appear instead of fibers (Fig. 4C), which most likely implies that coordination complexes still form, but the interactions between them are no longer directional (as is the case for hydrogen bonds) but isotropic. In other words, H-bonds between L$_3$s do not form in this case. The results of both experiments are consistent with the claim that the L3 ligands, clustered by metal–ligand chelation, stack by intramolecular H-bonding between the BTA cores, and consequently create long supramolecular fibers. Finally, we removed THF from the system after fiber formation, by means of dialysis against pure water. A TEM image (Fig. 4D) reveals that, as expected, the initially long fibers break up into short fibers. Similarly, we directly prepared
fibers in a mixed solvent with lower volume fraction of THF and again obtained short fibers which seem to have a tendency to stick (Figs. S11, S14). In conclusion, in a solvent richer in water some H-bonds are disrupted so that the long fiber structure cannot survive; it is the mixing with THF (which is not a proton donor) which both reduces electrostatic repulsion and enhances H-bonding so that subunit stacking and fiber formation can occur[58].

The role of the metal ions is to form just enough coordination bonds to create clusters of the right size: when the clusters are too small (at \( f \ll 1/3 \)) long fibers do not appear, but when the cluster size diverges (\( f > 1/3 \)) their cross-sectional size diverges, and/or they lose their stability against aggregation and precipitate, because they no longer have the ‘bare’, negatively charged DPA groups on the filament surface. We speculate, however, that stability may be restored when \( f \) exceeds values of order 2/3. Then, clusters of size \( 1/(3p-2) \) might appear, forming fibers which now are stabilized by ‘metal-covered’ DPA units on their surface. Hence, beyond the ‘forbidden’ range \( 1/3 < f < 2/3 \) a new stable range most likely appears; we expect it to ‘mirror’ the low-\( f \) range. Exploration of this range is beyond the scope of the present work.

3.5. Prove the genericity of methodology

One may wonder whether this supramolecular fiber also forms when other metal ions are used. Fig. 5 clearly shows that Zn\(^{2+}\), Ni\(^{2+}\), and Mn\(^{2+}\)-based samples all exhibit analogous fiber structures of similar size. Apparently, the nature of the metal ion (as long as it forms coordination complexes) has a negligible effect on the for-

Fig. 4. A) UV-vis absorption of BL\(_3\) in the absence of Fe\(^{3+}\) ions (black), in the presence of Fe\(^{3+}\) ions at [Fe]/[DPA] = 1/3 (red). The chemical structure of BL\(_3\) (Benzene-DPA\(_3\)) was inserted in the figure. B) Aggregates formed by Fe-BL\(_3\) at [Fe]/[DPA] = 1/3. C) Spherical nanoparticles formed in an Fe-L\(_3\) solution in the presence of 1 M urea. D) Short fibers obtained after dialysis of Fe-L\(_3\) solution against pure water.

Fig. 5. A) TEM image of fibers from Zn-L\(_3\), B) idem Ni-L\(_3\), C) idem Mn-L\(_3\).
mation and structure of these fibers. This opens new possibilities, because the nature of the coordinated metal may be chosen such that specific functionalities can be introduced into the superstructure. For example, the paramagnetic manganese(II) ion carries five unpaired 3d electrons and possesses the ability to effectively enhance positive contrast in magnetic resonance imaging (MRI) [59–60]. As a proof-of-concept, we prepared Mn-L3 fibers and find that the fiber dispersion has a longitudinal relaxivity of about 5.9 mM–1s–1 which is comparable with the relaxivity of other reported Mn-based MR contrast agents [Fig. S15] [61–62]. Indeed, MR images of the fiber solution confirm the considerable enhancement of contrast compared to solvent. With other metals other properties can be introduced, e.g., fluorescent properties (Eu3+, Tb3+), or catalytic properties (Cu2+, ...).

4. Conclusions

From the experiments discussed above we conclude that a discotic molecule that not only forms axial hydrogen bonds, but also radial coordination bonds will self-assemble into cylinders when the number of coordination bonds is controlled by the metal dose.

Common linear assemblies, such as cylindrical (worm-like) micelles, are known to originate from surfactants (amphiphiles) with particular shapes; in those cases, hydrophobic interaction combined with molecular packing controls the micellar shape. A classical example is hexadecyl ammonium bromide (CTAB) in water [63]. In recent work [28–35,37–38], it has been shown that discotic molecules derived from benzene-1,3,5-tricarboxamide (BTA) can also form linear assemblies (sometimes called ‘supramolecular polymers’), but these are stabilized by hydrogen bonds along the assembly axis. Also, stacking of disulfide-based rings has been explored [19,21,21,25]. Our study shows that BTA hydrogen-bonded stacks can be extended to more voluminous cylinders by means of coordination bonds. To achieve this, a BTA derivative is made that carries three dipicolinic acid (DPA) groups. These groups can connect neighboring BTA’s by means of a metal ion, thus forming a reversible coordination bond. We find that this new BTA derivative forms concentric cylinders, the number of which is controlled by the metal/DPA ratio. The cylinders are stabilized by hydrogen bonds in the axial direction, and by the coordination bonds in the radial direction. The choice of transition metal to form the coordination bond is not critical; various choices produce similar structures. The DPA groups on the cylinder surface do not carry a metal ion, which results in a negative surface charge that prevents aggregation of the cylinders.

An interesting aspect of the system is that the radial coordination bonds also enhance the stability of the axial bonds. Without any metal, the DPA-functionalized BTA does not assemble (the hydrogen bonds are too weak in the polar solvent), but at a metal/DPA ratio around 0.3 enough coordination bonds can form to make three concentric cylinders. This enhances the number of axial hydrogen bonds in a cross section by an order of magnitude, which is sufficient to stabilize the cylinder. In summary, we conclude that coordination bonds can play a very constructive role in shaping self-assembled colloids. Extrapolating these findings, it seems that by proper design of a covalent structure which is capable of multiple non-covalent bonding modes, large hierarchical self-assembled structures with a variety of functionalities will come within reach.

CRediT authorship contribution statement


Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

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