

# Article



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J. Am. Chem. Soc., Just Accepted Manuscript • DOI: 10.1021/jacs.9b08484 • Publication Date (Web): 11 Sep 2019 Downloaded from pubs.acs.org on September 11, 2019

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# Assembling Pentatopic Terpyridine Ligand with Three Types of Coordination Moieties into Giant Supramolecular Hexagonal Prism: Synthesis, Self-Assembly, Characterization, and Antimicrobial Study

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KEYWORDS pyrylium salts, pyridinium salts, self-assembly, terpyridine, antimicrobial activity

**ABSTRACT:** Three dimensional (3D) supramolecules with giant cavities are attractive due to their wide range of applications. Herein, we used pentatopic terpyridine ligands with three types of coordination moieties to assemble two giant supramolecular hexagonal prisms with molecular weight up to 42,608 and 43,569 Da, respectively. Within the prisms, two double-rimmed Kandinsky Circles serve as the base surfaces as well as the templates for assisting the precise self-sorting during the self-assembly. Additionally, hierarchical self-assembly of these supramolecular prisms into tubular-like nanostructures has been discovered and fully studied by scanning tunneling microscopy (STM) and small angle X-ray scattering (SAXS). Finally, these supramolecular prisms show good antimicrobial activities against Gram-positive pathogen methicillin-resistant *Staphylococcus aureus* (MRSA) and *Bacillus subtilus* (*B. subtilus*).

#### Introduction

Self-assembly as an "order-out-of-chaos" strategy is widely utilized by nature to efficiently assemble biological structures with sophisticated functionalities.<sup>1</sup> In supramolecular chemistry field, coordination-driven selfassembly plays an important role in constructing a wide variety of metallo-supramolecules in a well-controlled manner.<sup>2</sup> Particularly. three dimensional (3D) supramolecules<sup>3</sup> with cavities are very attractive due to their applications in catalysis,<sup>4</sup> stabilization of (air/water)sensitive molecules,<sup>5</sup> drug delivery,<sup>6</sup> and artificial transmembrane channels.7 Among these 3D structures, supramolecular prisms have been assembled mainly through the following four strategies: (i) two-component self-assembly with multitopic subunits at the lateral/base faces hinged by ditopic motifs as the vertices or pillars; 8,9 (ii) multi-component self-assembly with lateral face motifs,

base building blocks, and metal vertices;<sup>5b, 5c, 10, 11</sup> (iii) multicomponent self-assembly with the assistance of template molecules;<sup>12</sup> (iv) subcomponent self-assembly with linear ligands as the edges of both base and lateral face.<sup>7a, 13</sup> However, most of the ligands were designed with high symmetry to afford all the metal binding sites with the same chemical environment. It remains a challenge to introduce different coordination environments into the same ligand to further enhance the complexity of prisms.

In supramolecular chemistry, pyridinium salts have been extensively utilized as building blocks to assemble cages with good solubility in water and tunable host-guest interactions on the basis of their multiple positive charges.<sup>14</sup> Consequently, a wide range of 3D structures, e.g., triangular prism,<sup>15</sup> molecular dice,<sup>16</sup> bowl sharp cage,<sup>17</sup> and octahedron,<sup>18</sup> have been constructed with pyridinium moieties. In most of these cases, pyridinium groups were introduced into the backbone via pendent linkers. Without

sufficient rigidity and directionality, the so-formed pyridinium ligands, however, were unable to assemble large 3D supramolecules with higher complexity through directional bonding approach.<sup>2b</sup> Pyrylium salt-aryl primary amine condensation is an alternative synthetic approach to introduce pyridinium group into supramolecular architectures with rigid backbone.<sup>19</sup> Benefiting from the efficient condensation reaction as well as the modularized synthetic strategy, a series of giant 2D Kandinsky Circles (KCs) with concentric hexagon rings was obtained in our previous study, in which pyridinium groups were acting as bridges connecting different rims.<sup>20</sup> In addition, these 2D KCs showed potent antimicrobial activity against Grampositive pathogen methicillin-resistant Staphylococcus aureus (MRSA) through forming transmembrane channels.20a

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Beyond 2D concentric hexagons, we herein designed and assembled hexagonal prisms based on pyrylium salts and pyridinium salts chemistry. We prepared two pentatopic 2,2':6',2''-terpyridine (TPY) ligands, in which the metal-TPY coordinations are settled in three different environments (Scheme 1, TPY<sup>a~c</sup>). After assembly, giant and discrete 3D structures, i.e., supramolecular hexagonal prisms, were constructed with two Kandinsky Circles as the bases and the tail-anchored <TPY-Cd-TPY> linkages as the lateral edges, respectively. The obtained hexagonal prisms have high tendency to further hierarchically assemble into 1D nanostructures by base-to-base stacking in solution. In addition, these hexagonal prisms display antimicrobial activity against Gram-positive bacteria, including MRSA and *Bacillus subtilus* (*B. subtilus*).



**Scheme 1. Synthesis of ligands L1 and L2.** (i) BF<sub>3</sub>•Et<sub>2</sub>O, 100 °C, 2 hours; (ii) Pd(PPh<sub>3</sub>)<sub>4</sub>, NaHCO<sub>3</sub>, H<sub>2</sub>O, toluene, *tert*-butanol, 80 °C, 6 hours; (iii) HBF<sub>4</sub> (35% aqueous solution), MeOH, CHCl<sub>3</sub>, 12 hours; (iv) 4 Å molecular sieve, DMSO, 120 °C, 24 hours.

#### **Results and Discussion**

**Synthesis of the ligands and self-assembly of the complexes.** In order to incorporate 2D **KCs** into 3D hexagonal prisms, additional TPY group is necessary to serve as the lateral edges, which act a distinct structural role compared to the base edges. As such, 1,3-substituted phenyl group was introduced to the ligand as a spacer, providing

the anchored TPY a freely rotating axle as well as the rigid backbone with a proper intrinsic angle for adapting a vertical conformation to the hexagonal base surface during the self-assembly. Accordingly, a new pentatopic TPY ligand, **L1**, was designed as shown in **Scheme 1**, and efficiently synthesized by utilizing the pyrylium-pyridinium salts chemistry.<sup>20</sup> During the synthesis, the key precursor diketone **5** was prepared via a 3-fold Suzuki coupling reaction based on the tribromo-pyrylium salt **3**. Note that the reaction time (6 hours) was one of the most crucial parameters to achieve a good yield (65%), owing to the instability of **5** under basic condition. Another ligand, **L2**, with a longer alkyl chain was prepared via the similar procedure.

With the ligands in hand, another crucial requirement of forming desired prism is precisely narcissistic self-sorting of the three distinct types of TPY groups to form <TPY<sup>a</sup>-Cd(II)-TPY<sup>a</sup>>, <TPY<sup>b</sup>-Cd(II)-TPY<sup>b</sup>>, and <TPY<sup>c</sup>-Cd(II)-TPY<sup>c</sup>> coordination sites during the self-assembly. Without fully excluding the possibilities of undesired coordination, polymeric complex instead of discrete structure could be formed during the assembly. To address the above concerns, self-assembly of the pentatopic ligands with Cd(II) ion was carried owing to its higher reversibility.<sup>20a</sup> The self-assembly was performed in DMSO (10 mg/mL of **L1** or **L2**) at 80 °C for 12 hours with the stoichiometric ratio of ligand/metal = 2/5 (Figure 1a).



**Figure 1**. (a) Self-assembly of hexagonal prisms **HP1** and **HP2**; (b) side view and (c) top view of the representative energy-minimized structures from molecular modeling of **HP1/2**; alkyl chains were omitted for clarity

**Characterization of Supramolecules.** Electrospray ionization-mass spectrometry (ESI-MS) was first utilized to characterize the obtained complexes (the anions were exchanged to  $PF_6^-$ ), as shown in Figure 2. Figure 2a (**HP1**) shows one dominant set of peaks with continuous charge states ranging from 16+ to 32+, due to successive loss of the counterions,  $PF_6^-$ . A very similar spectrum of **HP2** is observed (Figure 2c) with slight shifts of the peaks towards higher m/z region. After deconvolution, the average molar

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masses of **HP1** and **HP2** are 42,608 and 43,569 Da, respectively, matching well with their expected chemical compositions  $[(C_{164}H_{139}N_{16}O_4)_{12}Cd_{30}(PF_6)_{72}]$  (**HP1**) and  $[(C_{170}H_{151}N_{16}O_4)_{12}Cd_{30}(PF_6)_{72}]$  (**HP2**), ruling out the possibilities of forming other undesired complexes. These two supramolecules are among the largest metallosupramolecules ever reported.<sup>21</sup> Traveling wave ion mobility-mass spectrum (TWIM-MS)<sup>20a, 22</sup> of **HP1** (Figure 2b) displays a series of bands with narrowly distributed drifting time at each charge state, indicating no other isomers or conformers exist. **HP2** also displays similar TWIM-MS spectrum shown in Figure 2d.





NMR spectroscopy was further employed to identify the structural information of the complexes by comparing with their corresponding ligands. Figure 3 displays the <sup>1</sup>H-NMR spectra of HP1 and L1. L1 exhibits three different sets of TPY protons with integration ratio as 1/2/2 (Figure 3a), corresponding to the TPY groups in the tail (TPY<sup>a</sup>), the outer rim (TPY<sup>b</sup>), and the inner rim (TPY<sup>c</sup>) of the ligand, respectively. After coordination, characteristic up-field shifts of all TPY- $H^{6,6''}$  signals are observed with  $\Delta \delta = 0.8 - 1.0$ ppm (Figure 3b), which is attributed to the electron shielding effect of the <TPY-Cd(II)-TPY> coordination environments.<sup>23</sup> Also, much broader spectrum is displayed after coordination, due to the lower tumbling motion of the protons in the large complex.<sup>21</sup> Notably, four sets of distinct TPY-H<sup>3',5'</sup> signals clearly display in the spectrum of **HP1** instead of three sets in the case of L1. The additional set of signals is caused by the splitting of TPY- $H^{a3',5'}$  after the formation of the <TPY-Cd(II)-TPY> lateral edges. One possible reason for the splitting is probably ascribed to the steric hindrance of the lateral faces, which blocks the free rotation of the TPY group and further slows down the tumbling motion of TPY-H<sup>a3',5'</sup>. As a result, much broader TPY-H<sup>a3',5'</sup> signals are observed, compared with TPY-H<sup>b,c3',5'</sup> signals. <sup>1</sup>H-NMR spectrum of HP2 shows exactly the same set of signals in the aromatic region (Figure S41).



9.2 9.0 8.8 8.6 8.4 8.2 8.0 7.8 7.6 7.4 7.2 4.4 4.2 4.0 Chemical Shift (ppm)

**Figure 3.** <sup>1</sup>H NMR spectra (600 MHz, 300 K) of (a) **L1** in  $CDCl_3$ , \* represents the solvent residue of  $CHCl_3$  and (b) **HP1** in  $d_6$ -DMSO.

A 2D diffusion-ordered NMR spectroscopy (2D-DOSY) analysis of **HP1** in  $d_6$ -DMSO reveals a single band at logD  $\approx$  -10.5 (Figure S47); **HP2** also displays one dominant signal band with the same logD value (Figure S48). After conducting calculation by using the modified Stocks-Einstein equation based on the column model (detailed calculating procedure is summarized in the Supporting Information),<sup>24</sup> the experimental diameter of the base is

found to be 7.0 nm, and the height of prism is 2.5 nm. Such sizes are comparable to the predicted results (8.0 nm in base diameter, and 2.7 nm in height) from the molecular modeling of these hexagonal prisms (Figure 1b-c). The other NMR spectroscopic results are summarized in Figures. S1-28, 35-46, including 2D COSY, 2D NOESY, <sup>13</sup>C NMR spectra (see SI).

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In order to obtain more shape and size information, atomic force microscopy (AFM) and transmission electron microscopy (TEM) were applied to image individual hexagonal prism. AFM images were first collected on fresh mica surface by drop casting diluted DMF solution (3.5  $\times$  $10^{-6}$  mol/L) of **HP1** for a short time (1 min) and then washing and drying, to avoid aggregation. Particles with ring like structures were clearly observed under AFM with uniform diameters (Figure 4a-b, Figure S49) by utilizing ultra-sharp cantilever tip  $(1 \sim 2 \text{ nm})$  to reduce the broadening effect. Detailed analysis of the size and shape of one selected particle (Figure 4c) reveals a hexagonal ring with an outer rim diameter at *ca.* 9 nm and an inner rim diameter as 4.7 nm, comparable to modeling size (Figure 1b-c). The average height of these particles is around 2.5 nm, corresponding to the height of one prism molecule. In addition, individual dots with uniform diameters were also observed under TEM, as shown in Figure 4d. The zoomedin TEM image (Figure 4d inset) shows a ring-like structure, which can also be assigned to the base of HP1 with a comparable size (ca. 8 nm in diameter).



**Figure 4**. AFM images of (a) individual **HP1** on mica surface (b) a selected single **HP1** molecule and its 3D image (right bottom inset), (c) cross-section of the molecule shown in (b); (d) TEM images of individual **HP1**, zoomed-in image in inset.

**Investigation of the hierarchical self-assembly behavior.** In our previous report, we found that **KC**s were able to hierarchically self-assemble into tubular-like nanostructures through the face-to-face packing.<sup>20a</sup> With the similar **KCs** structure acting as the bases, we speculated **HP1** could similarly pack into nanostructures through base-to-base packing, which might provide us additional structural information of the prism. Gels were obtained by slow diffusion of ethyl acetate (the poor solvent) into the DMSO solution of **HP1**, then investigated by TEM (Figures

S50). Worm-like nanostructures with uniform diameters at *ca.* 8 nm were observed, and most of them further interacted with each other to form bigger aggregation without well-defined pattern.

In order to obtain more detailed information of the nanostructures, scanning tunneling microscopy (STM) was utilized to image the samples on highly oriented pyrolytic graphite (HOPG) surface. Acetonitrile instead of ethyl acetate was used as the aggregation solvent, due to its better solubility of the supramolecules, in order to get welldispersed nanostructures on surface (detailed sample preparation procedure was summarized in SI). Tubular-like nanostructure was observed as shown in Figure 5a with a uniform diameter around 8 nm, corresponding to the diameter of the KC base surface. Breakages on the nanowire were clearly observed owing to the spacing between prisms. The periodic distribution of the bright areas and the gaps observed on the nanowires suggest the base-to-base packing of the prisms in the 1D nanostructure. The measured thickness of each repeating sub-structure in the nanostructure (marked distance in Figure 5b) was around 2.5 nm, which was well consistent with the predicted height of each supramolecular prism (Figure 1b). And more STM images of the nanostructures were included in Figures. S51.



**Figure 5.** (a) STM images of tubular-like nanostructure on a HOPG surface, (b) cross-section of the line marked on the nanostructure shown in (a). (c) The hollow cylinder model of the aggregated tubular-like nanostructure is hierarchically self-assembled by hexagonal prism unimer. (d) 1-D SAXS of **HP1** in acetonitrile solution  $(2.5 \times 10^{-4} \text{ mol/L})$ . " $\Box$ " represents the experimental data. The solid black line represents the best fit result.

One dimensional small angle X-ray scattering (1D-SAXS) was further used to study the aggregation of **HP1** in acetonitrile solution ( $2.5 \times 10^{-4}$  mol/L), and the results are summarized in Figure 5d. As expected, a  $q^{-1}$  decay was observed stemming from the low-q region beyond the probing range (Figure 5d, region I), suggesting the existence of long cylindrical objects with the average length over 1000 Å, consistent with the nanostructures observed in STM images. Apparently, the **HP1** aggregates in acetonitrile with the base-to-base configuration prior to the incubation process on HOPG surface for STM imaging. Apart from the tubular-like structure, scattering signals corresponding to individual **HP1** unimer were also observed at higher q

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region (Figure 5d, region II) with three quasi-Bragg peaks located between 0.15 and 0.5 Å<sup>-1</sup> corresponding to the high order harmonics ( $q^*$ ,  $2q^*$  and  $3q^*$ ), likely originating from the well-defined repeating spacing, D of the hexagonal prisms in the cylindrical aggregate. As a result, the best fitting model contains the contributions from discoidal shells, hollow cylinders and three Gaussian peaks (Figure 5c). As shown in Figure 5d, the best fit agrees well with the experimental data and the fitting parameters are listed in Table S1. And the best fitting prism height, outer rim and inner rim diameters are  $(2.5 \pm 0.2)$ ,  $(6.8 \pm 1.1)$  and  $(4.0 \pm 1.1)$ 0.2) nm, respectively, which are consistent with the molecular modeling results (Figure 1b-c). Moreover, the cylindrical aggregates share the same inner rim and outer rim diameter with those of the unimer, except for an ultralong length. The uniform *D* derived from  $q^*$  as  $D = \frac{2\pi}{q^*} \approx 4.2$ nm is also consistent with the STM result (Figure 5b).



**Figure 6.** (a) ESI-MS and (b) TWIM-MS (m/z vs drift time) of the self-assembly of **L1** with Cd(II) under a milder condition. Both intermediates (A series of signals) and **HP1** (B series of signals) were observed, right inset of (a): theoretical and experimental isotope patterns of A19+.

**Mechanism study of the self-assembly.** After characterization of the desired supramolecular hexagonal prisms, we further studied the self-assembly mechanism of these prism structures. Briefly, the self-assembly of **L1** with Cd(II) (molar ratio: 2/5) was performed under a milder condition (i.e.,2 mg/mL of **L1** in DMSO, 50 °C for 3 hours) in order to determine the intermediate state of the assembling procedure. ESI-MS spectrum (the anions were transferred to PF<sub>6</sub><sup>-</sup>) shows two dominant sets of sharp peaks (Figure 6a), locating at lower *m/z* (700 – 1500 Da) and higher *m/z* (1500 – 2300 Da) regions, respectively. After

deconvolution, the averaged molar mass of the signals at lower m/z region was 20,094 Da, which exactly fits the chemical composition of  $[(L1)_6Cd_{12}(PF_6)_{30}]$ . In addition, the isotope pattern of each charge state (12+ - 22+) agrees well with the corresponding simulated one (Figure 6 inset and Figure S52). Such a chemical composition is assigned to a double-rimmed **KC** with 6 tailed anchored free TPY groups (Scheme 2). It can be viewed as an intermediate prior to the formation of our desired prism structure (HP1). The peaks at higher m/z region are assigned to **HP1** with 18+ to 23+ charge. The coexistence of KC intermediates with HP1 was further confirmed by the TWIM-MS spectrum (Figure 6b) with two sets of signals. The signal bands at the lower m/zregion with relative shorter drifting time are attributed to the intermediates, while the well splitted signal bands at higher m/z region correspond to the hexagonal prism structure with longer drift time. Between  $[(L1)_6Cd_{12}(PF_6)_{30}]$ and HP1, other intermediates such as  $[(L1)_6Cd_{13}(PF_6)_{30}(OH)_2]$ and  $[(L1)_6Cd_{14}(PF_6)_{30}(OH)_4]$ (Scheme 2) were also detected by isotope analysis of mass spectra (Figures S53-S54). Every two of these KCs intermediates together with proper amount of Cd(II) finally formed HP1 via forming the lateral edges as the scaffold of the 3D structure. Such a step-wise assembly mechanism leads to the precise self-sorting of the three types of TPY groups into three distinct coordination environments (Scheme 2). As a result, the **KC** rings plays dual roles during the formation of the supramolecular hexagonal prisms through acting as the structural base surface, and the template to guide the formation of the lateral edges.



Scheme 2. Proposed self-assembly mechanism of L1 coordinating with Cd(II) to form HP1.

Table 1. The antimicrobial activity and selectivity of the ligands and supramolecules

	HP1	HP2	L1	L2	<b>Cd(NO</b> <sub>3</sub> ) <sub>2</sub>
MRSA ( <i>IC</i> 50, μg/mL)	1	1	3	3	> 25
<i>B. subtilus</i> ( <i>IC</i> 50, μg/mL)	3	2	-	-	3
Hemolysis ( <i>HC</i> 50, µg/mL)	>250	>250	>250	>250	>250
Selectivity HC <sub>50</sub> /IC <sub>50</sub> (MASA)	>250	>250	>80	>80	>10

Selectivity					
$HC_{50}/IC_{50}$	>80	>120	-	-	>80
(B. subtilus)					

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**Antimicrobial activity.** It is expected that these 3D prisms might show antimicrobial activity against Grampositive bacteria for the following reasons: (i) the high density of positive charges on these supramolecules provides high affinity with the negative charged cell envelop of the Gram-positive bacteria;<sup>25</sup> (ii) pyridinium containing agents are widely applied in antimicrobial fields;<sup>26</sup> (iii) the prisms may act as transmembrane channels to disrupt the bacterial membrane.<sup>20a</sup> As a result, the antibacterial activities of **HP1/2** were evaluated with two Gram-positive bacteria, i.e., MRSA and *B. subtilus*, (Table 1).

Both **HP1/2** showed antimicrobial activity on *MRSA* with  $IC_{50}$ s as 1 µg/mL (*ca.* 22 nmol/L), which was lower than the  $IC_{50}$ s of the corresponding ligands (3 µg/mL, 1200 nmol/L) and the control group, Cd(NO<sub>3</sub>)<sub>2</sub>•4H<sub>2</sub>O, ( $IC_{50}$ > 25 µg/mL, 8.1 × 10<sup>5</sup> nmol/L). Compared with the previous reported 2D **KCs**,<sup>20a</sup> **HP1/2** displayed lower antibacterial activity, probably due to their low solubilities and high aggregation tendency proved by TEM/STM/SAXS studies. These features caused the precipitation or aggregation of **HP1/2** in contact with the growth medium before their effective interaction with *MRSA* cells. As a result, supramolecular prisms with better water-solubility are expected to possess enhanced antimicrobial activity.

In addition, to expand the antimicrobial spectrum of this type of supramolecule, *B. subtilus* was used to evaluate the new agents. **HP1/2** showed obvious antimicrobial activity against *B. subtilus*, while **L1/2** did not exhibit any toxicity (Table 1). Note that the weight-based  $IC_{50}$  value of Cd(II) control was comparable to the values of **HP1/2**. However, considering the much lower weight percentage of Cd(II) in **HP1** (8.0%) and **HP2** (7.8%) than in Cd(NO<sub>3</sub>)<sub>2</sub>•4H<sub>2</sub>O (37%), as well as the strong chelation of Cd(II) with the pentatopic TPY ligands in **HP1/2**, the antibacterial potency of the supramolecules should be mainly derived from the ensembles rather than individual component.

The red-blood-cell hemolysis studies of **HP1/2** show negligible hemolytic toxicity ( $HC_{50}$  higher than 250 µg/mL), leading to their good antimicrobial selectivity toward *MRSA* and *B. subtilus*. We speculated that such a good selectivity should be based on the stronger electrostatic interaction of cationic **HP1/2** with the negative charged surfaces of the Gram-positive bacteria,<sup>25</sup> than with the zwitterionic surfaces of the mammalian cells.<sup>27</sup>



Figure 7. 3D deconvolution fluorescence microscopy images of bacteria cells with and without treatment of HP1/HP2 (4  $\mu$ mol/L, DMSO as the control agent). Scale bar: 1  $\mu$ m.

3D deconvolution fluorescence microscopy, combination of optical and computational techniques to maximize the observed resolution and signal from a biological specimen,<sup>28</sup> was further employed to monitor the location of HP1/2 during their inhibiting the growth of MRSA and *B. subtilus*. Benefiting from the strong fluorescence (FL) nature of these two supramolecules (the FL spectra of HP1/2 are recorded in Figure S55-56), no external dye is needed to visualize the cell membrane. As shown in Figure 7, strong fluorescence was observed on the surface of both S. aureus and B. Subtilus after being treated with HP1/2. In addition, in both cases, no free fluorescent material was observed outside of the cells. These results indicate the high selectivity and binding affinity of the antimicrobial materials for the bacteria, which confirm that these supramolecular prisms strongly interact with these Gram-positive bacteria and then inhibit the growth of MASA and B. subtilus.

#### Conclusions

In this study, we were able to construct giant metallosupramolecular hexagonal prisms with pentatopic terpyridine ligands, which displayed three different coordination environments during the self-assembly. Such a design fully takes advantage of the rigid scaffold of the pyridinium-aryl group and its facile synthesis. In addition, the detailed study of the self-assembly process reveals that the double-rimmed **KCs** are the key intermediate species to form a hexagonal prism architecture. The assembled supramolecular hexagonal prisms had a strong tendency to form tubular-like nanostructure in solution as evidenced by STM imaging and SAXS study. Furthermore, the pyridinium salt contained supramolecular prisms showed potent antimicrobial activities against two Gram-positive bacteria, possibly due to their high binding affinity on the membrane of these bacteria. Overall, through deep understanding of the design and self-assembly process, this study may shed more lights for designing more sophisticated 3D supramolecular architectures with desired functions.

#### ASSOCIATED CONTENT

**Supporting Information**. Synthetic details, molecular modeling, ligand and complex characterization, including <sup>1</sup>H NMR, <sup>13</sup>C NMR, 2D COSY, 2D NOESY, 2D DOSY, ESI-MS, UV-Vis, emission spectra and additional STM images are included in supporting information. This material is available free of charge via the Internet at http://pubs.acs.org.

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#### Notes

The authors declare no competing financial interest

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# ACKNOWLEDGMENT

We acknowledge the support from NIH (R01GM128037 to X.L.; 5R01AL110098-05 to B.X), and partial support through University of South Florida Nexus Initiative (UNI) Award. The SAXS data were collected with the help of Dr. Lin Yang, at the 16ID-LiX Beamline, National Synchrotron Light Source II, Brookhaven National Laboratory (BNL), NY, USA through a beamtime proposal (BAG-302208). The LiX beamline is part of the Life Science Biomedical Technology Research resource, jointly supported by the National Institutes of Health, National Institute of General Medical Sciences, under Grant P41 GM111244, and by the Department of Energy Office of Biological and Environmental Research under Grant KP1605010, with additional support from NIH Grant S10 OD012331. NSLS-II is a U.S. Department of Energy (DOE) Office of Science User Facility, operated for the DOE Office of Science by Brookhaven National Laboratory under Contract No. DE-SC0012704.

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Scheme 1. Synthesis of ligands L1 and L2. (i) BF<sub>3</sub>•Et<sub>2</sub>O, 100 °C, 2 hours; (ii) Pd(PPh<sub>3</sub>)<sub>4</sub>, NaHCO<sub>3</sub>, H<sub>2</sub>O, toluene, tert-butanol, 80  $^{\rm o}\text{C},$  6 hours; (iii) HBF4 (35% aqueous solution), MeOH, CHCl\_3, 12 hours; (iv) 4 Å molecular sieve, DMSO, 120 °C, 24 hours.

84x64mm (300 x 300 DPI)

8.0 nm



85x73mm (300 x 300 DPI)







Figure 4. AFM images of (a) individual HP1 on mica surface (b) a selected single HP1 molecule and its 3D image (right bottom inset), (c) cross-section of the molecule shown in (b); (d) TEM images of individual HP1, zoomed-in image in inset.

85x68mm (300 x 300 DPI)



Figure 5. (a) STM images of tubular-like nanostructure on a HOPG surface, (b) cross-section of the line marked on the nanostructure shown in (a). (c) The hollow cylinder model of the aggregated tubular-like nanostructure is hierarchically self-assembled by hexagonal prism unimer. (d) 1-D SAXS of HP1 in acetonitrile solution (2.5 × 10<sup>-4</sup> mol/L). "□" represents the experimental data. The solid black line represents the best fit result.

85x57mm (300 x 300 DPI)





Scheme 2. Proposed self-assembly mechanism of L1 coordinating with Cd(II) to form HP1.

85x46mm (300 x 300 DPI)



**Figure 7**. 3D deconvolution fluorescence microscopy images of bacteria cells with and without treatment of **HP1/HP2** (4 μmol/L, DMSO as the control agent). Scale bar: 1 μm.

85x34mm (300 x 300 DPI)



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