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Communication

Rational design and synthesis of covalent organic polymers with hollow structure and excellent antibacterial efficacy

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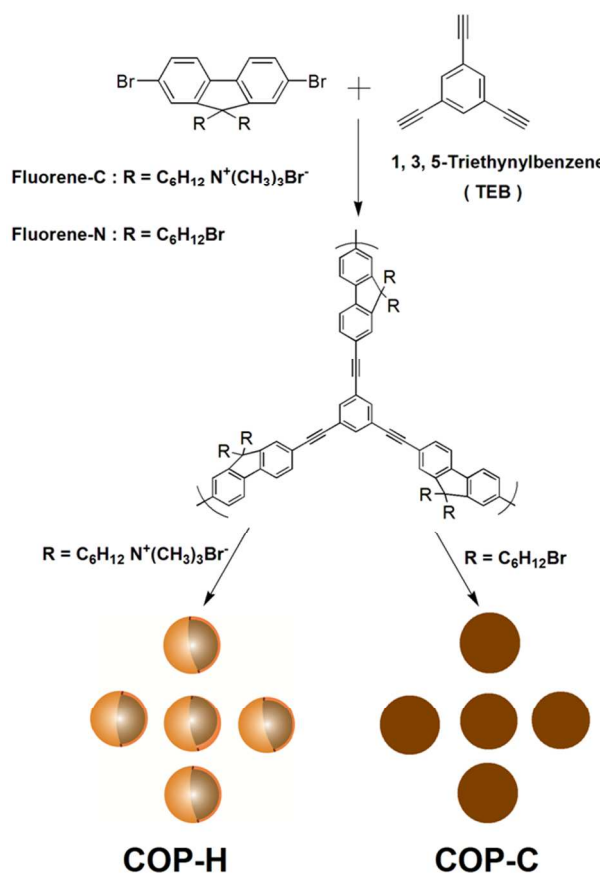
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A covalent organic polymer with hollow structure (COP-H) has been synthesized via Sonigashira coupling from the precursors containing positive charge. The formation of COP-H was confirmed by FTIR, Solid State NMR, SEM and TEM. COP-H showed excellent anti-microbial activity because of the cationic charge on the surface of COP-H.

Covalent Organic polymers (COPs) have drawn a great attention not only for their porosity and large surface area, easy to be designed and functionalized, but also for their strong covalent bonds and high stability compared to metal-organic frameworks (MOFs) counterparts, which made COPs appealing in catalysis, gas storage and separation, chemical sensors, light emitting materials and bioscience.¹ And recently, some progresses have been made in studying the micro-morphology of the hollow structures, they can viewed as capsules or carriers for drug delivery or worked as nanoreactors, and hollow spheres also showed better efficiencies in catalytic performance than nonhollow ones.² In general, the porous polymers with hollow structures were prepared by layer-by-layer method or templated synthesis, such as SiO₂, TiO₂ and some polymers like polystyrene, poly(lactic-co-glycolic acid) and so on.³ For example, Li and his co-workers reported the hollow micro-porous organic capsule templated by SiO₂,⁴ Kim *et al.* also prepared the hollow micro-porous organic network with Sonogashira coupling reaction using SiO₂ as template.⁵ There are also some reports on different templates like ZnO, Poly(methyl methacrylate) (PMMA) and even MOFs.⁶ However, the removal of the templates is quite essential in these systems. The waste of templates and removal agents or energy makes this method not a universal and green chemistry fashion. So it is highly desired to develop a simple method without the aid of any templates and postmodification techniques for making COPs with hollow structure.

Very recently, Zhao *et al.* reported the single-step preparation of 2D polymers and their evolution into hollow sphere which was driven by the reduction of the surface energy.⁷ However, the unstable connection of borate especially in aqueous solution limited the application of this hollow polymeric sphere. Inspired by formation of polymeric vesicles through self-assembling of amphiphic copolymers in aqueous solution,⁸ we hypothesized that the organic polymers with hollow structure could be prepared via similar rational design. Herein, we choose fluorene decorated with positive charge (Fluorene-C) and 1, 3, 5-triethynylbenzene

(TEB) as building blocks to synthesize COP with hollow structure (COP-H) in the absence of templates. And we took out



Scheme 1 Preparation of COP-H and COP-C.

the non-charged fluorene (Fluorene-N) with TEB to synthesize COP with non-specific morphology as control experiment. The anti-microbial activity of COP-H was studied towards gram negative bacteria.

Scheme 1 shows the design and preparation of the COP-H particles. The particles were obtained through Sonogashira coupling reaction between Fluorene-C and TEB, after washed with DMF, water and ethanol for several times, then dried under vacuum at 70°C, details can be seen in Electronic Supporting Information (ESI) for the preparation. To confirm our strategy in designing the COP-H, control experiment with non-charged

Fluorene-N and TEB was carried out at same condition, which formed the covalent organic polymer, denoted as COP-C. The structure of the COP-H and COP-C were verified by fourier transform infrared spectroscopy (FTIR) (Fig. S1, ESI) and solid state nuclear magnetic resonance (NMR) (Fig. 1). In Fig. S1, the peaks centered at 2200 cm^{-1} ascribe to the C-C triple bonds, and the peaks at 2929 cm^{-1} are due to the C-H stretching vibration of the alkyl chain of the fluorene precursors for both the COP-H and COP-C. While the peak centered at 3400 cm^{-1} only appeared in COP-H, which is for the vibration of the positive charged parts. And in Fig. 1a and b for the Solid State NMR ^{13}C Spectrogram, the peak at 92.0 ppm indicate the C-C triple bonds, the peak at 65.7 ppm is attributed to cationic of COP-H which is not shown in COP-C, and other peaks can fit well with the structures of COP materials.^{6c, 9} And these results confirmed the formation of COP-H and COP-C. Thermal gravimetric analysis (TGA) was carried and shown in Fig. S2 (ESI), both COP-H and COP-C are stable over $200\text{ }^{\circ}\text{C}$, and each of the COPs has a weight loss of 100% at nearly $600\text{ }^{\circ}\text{C}$. And fluorescent spectra were recorded to study the emission behaviors of the COPs as synthesized, and the results were shown in Fig. S3. The COPs show different fluorescence spectra for the charged and non-charged alkyl chains. The COP-H has an emission at 525 nm while COP-C shows no fluorescence. This is because the bromide atoms on alkyl chains of the COP-C quenched the fluorescence.

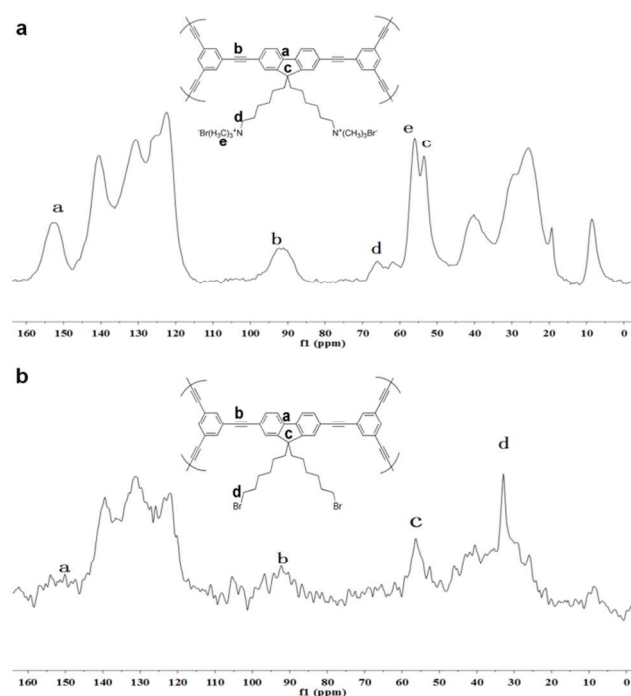


Fig. 1 Solid State NMR ^{13}C Spectrogram of COP-H (a) and COP-C (b).

The morphology of COP-H was examined by transmission electron microscopy (TEM) and scanning electron microscopy (SEM). As shown in Fig. 2a and b, the particles with spherical structure can be seen clearly, hollow structures were found in Fig. 2b). SEM images in Fig. 2c also show the sphere particles, and the hollow structure was further confirmed when the particle was in a broken state (Fig. 2d). And the average size of the particles

was about 120 nm from TEM pictures, which was further confirmed by the result of DLS, as presented in Fig S4 (ESI). The sizes of the particles range from 50 nm to 200 nm , which is due to the growing layers with the reaction going on. Generally speaking, COP materials prepared under such conditions were 2D or 3D non-specific morphology,⁹ which was also supported by control experiment, as presented by SEM in Fig. S5 a and b. The possible mechanism for this hollow structure is that: a 2D material formed during the reaction, while the electrostatic repulsion between the positive charges drove the 2D COP into curling state, and then lead the formation of hollow structure.⁷ And moreover, the positive charged part of the polymer is hydrophilic while the other parts are hydrophobic, with the stirring during reaction, the phase separation drove the planar polymer into hollow sphere, just like the hydrophobic force drives the self-assembly of vesicles and micelles.^{8, 10} The positive charge was verified by Zeta Potential with the value of $+19.15\text{ mv}$. PXRD result was presented in Fig. S6 (ESI) which shows the non-crystallization state of the COP-H, this is reasonable for the formation of covalent bonds which is not dynamic and reversible.

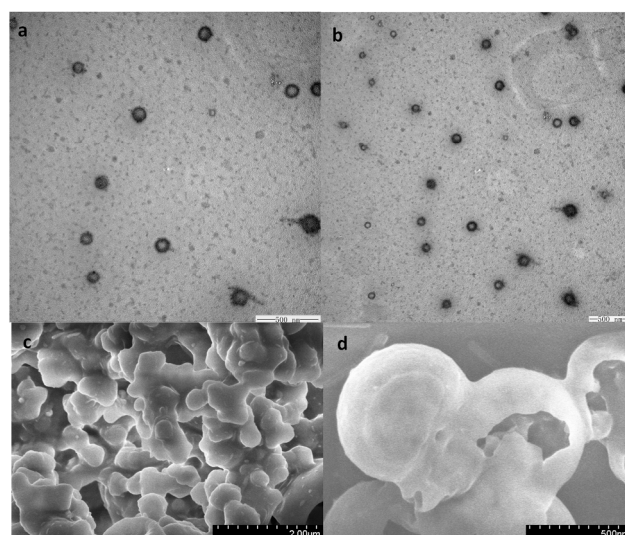


Fig. 2 TEM (a, b) and SEM (c, d) of COP-H. The scale bars are 500 nm for (a and b), $2\text{ }\mu\text{m}$ for (c) and 500 nm for (d).

Many antibacterial materials based on heavy metal ions like Ag^+ and Cu^{2+} are limited to some aspects because of the high toxicity of these metal ions.¹¹ Looking for antibacterial materials without metal is valuable. Recently, Wang *et al.* reported photocatalytic disinfection by graphitic carbon nitride polymers under visible light.¹² And Yang *et al.* reported a metal-free triblock polymer with positive charge with selective lysis of microbial membranes.¹³ To our knowledge, there is no report on the COP as antibacterial material. Herein, the antibacterial properties were studied using COP-H. We hypothesized the particles could work as a nano-scalpel to gash the bacterial, and finally destroys the germs.¹³⁻¹⁴ With this idea in mind, we carried out the antibacterial experiment towards the gram negative bacterial -*Escherichia coli* (*E. coli*). After COP-H with various concentrations were incubated with the *E. coli* for 0 h, 4 h and 16h, optical density (OD) value was tested to evaluate the

efficiency of anti-bacterial, the result was presented in Fig. 3. The result shows that COP-H has inhibited the growth of *E. coli* efficiently compared to the control group with 0 mg/ml COP-H material. And with the increase of COP-H concentration, the inhibiting efficiency increase, due to the total amount of the positive charge increase. The material has a certain antibacterial activity at a quite low concentration. The minimal inhibitory concentration (MIC) is defined as the lowest polymer concentration to inhibit visible bacterial growth,¹⁵ and as reported by Lin *et al.*, the concentration of the demarcation sample whose solution remains clear among the series was determined as the MIC value which was 0.25 mg/ml to our COP-H,¹⁶ which is comparable to the excellent cationic micelle materials.^{14a, 14b} We also took out the control experiment with COP-C for the antibacterial tests. And COP-C showed no antimicrobial activity even at a concentration of 10 mg/ml as seen from the results in Fig. S7.

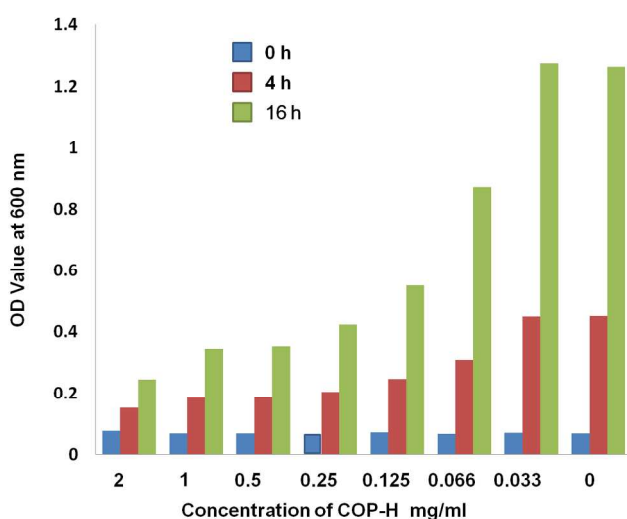


Fig. 3 OD values at 600 nm for the *E. coli* incubated with COP-H.

In summary, we have synthesized a covalent organic polymer (COP-H) with hollow structure through introducing the positive charge on the monomers. The mechanism of forming hollow structure was revealed by using non-charged monomer control experiment. COP-H indicated efficient anti-bacterial properties towards inhibiting the growth of gram negative bacterial. We hope our strategy could provide a new way to synthesize hollow structure materials and highlight the potential application of COP materials.

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Notes and references

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