Uncommon hexagonal microtubule based gel from a simple trimesic amide†

Naien Shi,[a,b] Gui Yin,[a] Hongbian Li,[a] Min Han[a] and Zheng Xu*[a]

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A small molecule of *N*,*N*′,*N*″-tris(3-methylpyridyl)-trimesic amide was assembled into a novel hexagonal microtube through intermolecular hydrogen bonds, and simultaneously formed a gel system in H_2O–THF mixed solvent. Tuning gelator concentration or the preparation method can effectively control the size of the hexagonal tubes.

Introduction

The need to improve miniaturization and device performance in information technology greatly stimulates the research interests in the self-assembly of organic functional materials, because of its tailorability, multifunctionality and low cost.[1] Micro- and nanotubes can perform diverse functions and have various applications in chemistry, biochemistry, and materials science.[2] However, in comparison with the extensively studied carbon nanotubes and inorganic nanotubes, such as metal and oxide ones, nanotubes of small molecular organic compounds have relatively few reports.[3] Self-assembled organic microtubules (1–100 μm) in solution are even rarer,[2,4] although these low-molecular-weight compounds offer great variety and flexibility in molecular design with potential benefits for the fundamental theory of non-covalent self-assembly.

Herein, we report a simple C_3-symmetric compound of *N*,*N*′,*N*″-tris(3-methylpyridyl)-trimesic amide (TMPTA, Scheme 1) which can assemble into hexagonal microtubes and simultaneously form a gel system in diluted THF–H_2O solution at a concentration of ~1.0–2.0 wt%.

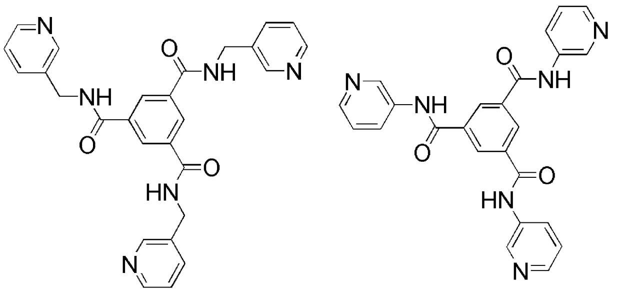
Results and discussions

Synthesis and morphology characterization

TMPTA was synthesized by amidation of trimesic chloride with 3-aminomethyl pyridine in the presence of pyridine as the catalyst (Experimental section in ESI†). It is insoluble in water, but can dissolve in tetrahydrofuran (THF), ethanol (EtOH) or methanol (MeOH). When TMPTA was dissolved in H_2O–THF (5 : 1, v/v), H_2O–EtOH (4 : 1), or H_2O–MeOH (4 : 1) mixed solvents by heating in a screwed tube, and allowed to stand to cool in a refrigerator (10 °C), it self-assembled into hexagonal microtubes. Even after the solvent was dried in vacuum, the structure of the tube was kept stable. Fig. 1 shows the corresponding microtubes formed in H_2O–THF (5 : 1, v/v) mixture at a concentration of 1.36 wt%. From these figures, we can clearly see that TMPTA self-assembled into long microtubes with various sizes of 1–6 μm in diameter and hundreds of micrometres in length (Fig. 1a). The corresponding high magnification image clearly shows the open ends with a hexagonal cross-section (Fig. 1b). Furthermore, the dark edges and relatively bright center in the optical microscopy image further evidenced that they are of tubular structures (Fig. 1c). Similarly, hexagonal microtubes also existed in the H_2O–EtOH mixed solvent (Fig. S1†).

Rheology measurement

During the formation of the microtubes, the solvent turned into a gel like state. The microtubes would not be separated from the solvent under shaken or shear operations. Moreover, the solvent in the inverted hexagonal-microtube-based system would not flow down on the force of gravity (Fig. S2†). That is, the microtubes give a remarkable gelled rheology property to the solvent. Some kinds of low-molecular-weight compounds can self-assemble into fibrous aggregates in the solvent through non-covalent interactions (c < 5.0 wt%). During the aggregation, the fibrous aggregates entangle into a meshlike matrix that holds the solvent by interfacial tension and supramolecular interactions, which results in a supramolecular gel.[5,6] Supramolecular gels have been attracting much interest because of their potential applications in biology



Scheme 1 The chemical structure of TMPTA (left) and TPTA (right).

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[a] State Key Laboratory of Coordination Chemistry, National Laboratory of Solid State Microstructures, School of Chemistry and Chemical Engineering, Nanjing University, Nanjing 210093, P. R. China. E-mail: zhengxu@netra.nju.edu.cn; Fax: +86-25-83594502; Tel: +86-25-83593133
[b] Jiangsu Key Laboratory of Organic Electronics & Information Displays and Institute of Advanced Materials, Nanjing University of Posts and Telecommunications, Nanjing 210046, P. R. China

† Electronic supplementary information (ESI) available: Experimental details, SEM image of the tubes obtained in a mixed solvent of H_2O–EtOH, direct observation of the system in H_2O–THF (5 : 1, v/v) mixture, crystal structure of TPTA reported, X-ray diffraction patterns and proposed formation process of the hexagonal microtubes. For ESI see DOI: 10.1039/b804455d

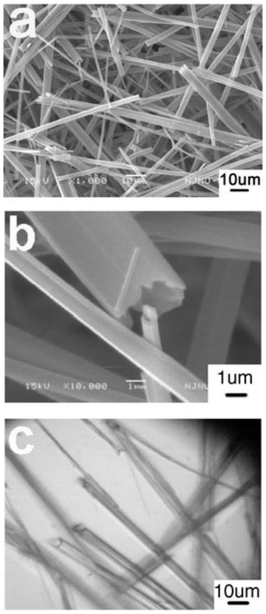

Fig. 1 (a) SEM image of the microtubes obtained in solvent of H_2O–THF = 5 : 1 (v/v, 1.36 wt%), (b) higher magnification of (a), (c) corresponding optical microscopy image (×400).

arising from their special biodegradability.[7] Typically, two criteria of rheology and structural features for supramolecular gel should be included: (i) that it appears solid-like and yet is predominately composed of a liquid at the microscopic scale; (ii) that the material returns to its original form when an applied stress is removed (below a certain limit).[8] The rheology measurement of the system was performed and corresponding viscoelastic stress sweep response was shown in Fig. 2. We can see that the value of the storage modulus G' (the elastic response) exceeds that of G'' (viscous response) by one order of magnitude. The G' value of this system is at the magnitude of 6×10^4 Pa while the G' value of some peptide hydrogels is 50 Pa at a frequency of 1 Hz.[9] The corresponding yield stress (the critical applied stress after which the gel starts to flow[10]) is about 108 Pa. All these indicate the typical features of a gel for this system. Almost all kinds of nanofibers in hydrogels or organogels are less than 500 nm in diameter, and the corresponding minimum gelation concentration (MGC) is less than 1.0 wt%.[5–8] Such a hexagonal microtube based gel system is very rare, and other trimesamide-based gelators were reported to form fibril structures.[11]

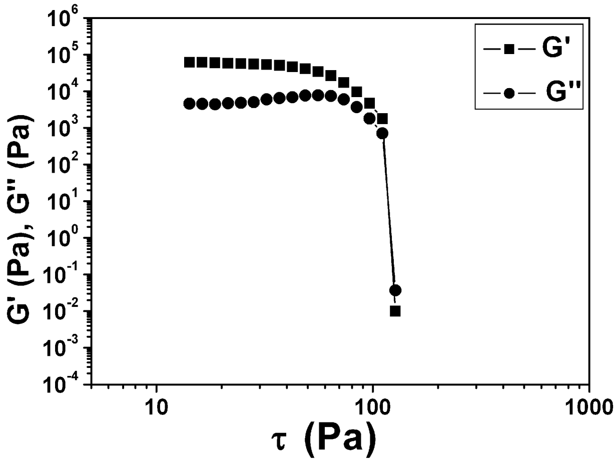

Fig. 2 Plots of storage modulus G' and loss modulus G'' *versus* stress for the system in H_2O–THF (5 : 1, v/v, 1.36 wt%).

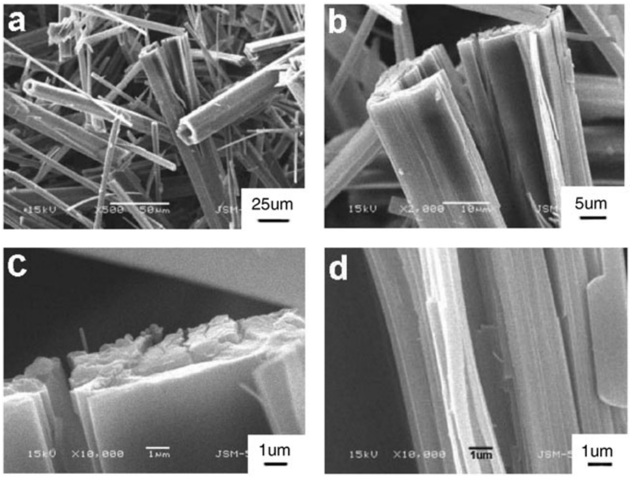

Fig. 3 SEM images of the hexagonal microtubes obtained in the solvent of H_2O–THF = 3 : 1 (v/v) at higher concentration of 2.0 wt% (a) corresponding low magnification image, (b) enlarged view of the broken tube, (c) higher magnification of the cross-section face of the broken tube, (d) higher magnification of the fractured face of the broken tube.

Coarse-texture of the microtubes

Larger tubes were obtained if increasing the concentration of TMPTA. Fig. 3a showed the microstructures obtained from H_2O–THF (3 : 1) mixture at a concentration of 2.0 wt%. The microtubes have larger diameters of 5–30 μm in comparison with that of 1.36 wt% (Fig. 3a and 1). Most of the tubes are hexagonal, and rectangular microtubes occasionally occurred. The special tubular structures generate many more small channels in the tubes, which provide enough compartments and interfacial tension to hold the solvent. Hydrophilic pyridyl groups of TMPTA also fortify the binding of solvent molecules. In the middle of Fig. 3a, there is a broken microtube. The reason for the brake is still not clear, and perhaps the rapid evaporation of solvent trapped inside the tube led to the crack when dried under vacuum. Fig. 3b–d shows the enlarged view of the broken open end, cross-section, and fractured face of the tube, respectively. We can see that the hexagonal tube was composed of many belt-like moieties. It should have been assembled by non-covalent interactions since it is composed of small molecules.

Intermolecular interactions by FT-IR studies

This gel is stable in neutralized conditions and switches to sol by acidifying to pH < 3.0 using HCl (1 N). It switches back to the gel state by neutralizing to pH = 7.0 using NaOH (1 N). This transition is reversible. Since pyridyl groups can be protonated by acid, it is reasonable that protonation of pyridyl groups breaks the hydrogen bonds and therefore damages the microtubular structure, and then the trapped solvent is released out to form a sol. Therefore, pH-responsive properties of the system indicated the role of hydrogen bonding interactions from N–H···Py.

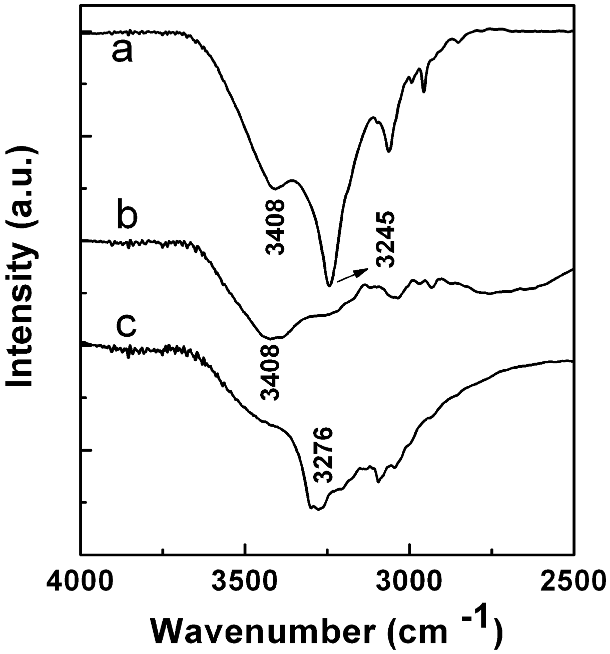

Fig. 4 FT-IR spectra of (a) TMPTA hexagonal microtubes obtained in H_2O–THF = 5 : 1 (v/v), (b) protonated TMPTA, (c) TPTA hexagonal crystals.

FT-IR experiments were also done to characterize the hydrogen bonds. As is known to us all, υ-NH bands of 3200–3300 cm^{-1} are an indicator of a hydrogen bonded N–H group, while the free vibration band of υ-NH ~ 3400 cm^{-1}, which indicates there is absence of hydrogen bonds or specifically here, the hydrogen bonds (N–H···Py) are broken.[12] As seen in the FT-IR spectrum of TMPTA hexagonal microtubes (Fig. 4a), there are both the two bands in υ-NH region centered at 3245 cm^{-1} and 3408 cm^{-1}, respectively. When the gel is acidified and broken by HCl, vibration band for free N–H at ~3400 cm^{-1} greatly increased and simultaneously hydrogen-bonded υ-NH band 3245 cm^{-1} significantly decreased (Fig. 4b). This means 3245 cm^{-1} in FT-IR spectrum of the microtubes mainly comes from hydrogen bonding of N–H···Py. Therefore, FT-IR results confirm that the TMPTA hexagonal tube is stabilized by hydrogen bonds of N–H···Py.

Formation process

However, it is very difficult to get the crystal structure of the microtube because the crystal is too thin to determine by X-ray crystallography. Hexagonal crystals of a similar trimesic amide of 3-aminopyridine, *N*,*N*′,*N*″-tris(3-pyridyl)-trimesic amide (TPTA) has been reported by Meijer *et al.*[13] In their report, the obtained hexagonal crystal of TPTA is affiliated to the space group $P\bar{3}$. The molecules self-assembled to form a 2-D sheet architecture along *x* and *y* direction of the basic unit of six amide molecules stabilized by twelve hydrogen bonds of N–H···Py (Fig. S3†). The 2-D sheet further stacked along its *z*-axis to form a hexagonal crystal. In this structure, all the amide N–H groups are hydrogen bonded to pyridyl groups. This is in accordance with its FT-IR spectrum (Fig. 4c). As seen, only the hydrogen-bonded υ-NH band at 3276 cm^{-1} occurred. Comparing X-ray diffraction patterns of TPTA hexagonal crystals and our TMPTA hexagonal microtubes, we can see that both of their strongest peaks are much stronger than others and located at about 7° (Fig. S4†), which indicates a similar preferred growth direction for them. Based on the above structure, the organization mode of TMPTA may be as follows. Six amide molecules are assembled into a rosette basic unit through six hydrogen bonds of N–H···Py (black line indicated) shown in Fig. 5. Six basic units are further assembled to form a small hexagonal 2-D sheet. Then six assemblies were organized into a C_3-symmetric small hexagonal tube. The small tubes further assembled into belt-like moieties, which is the basic component of the large microtubes. Similar assembly mode has been proposed in the assembled tubes of a cyclic peptide.[14] The belt-like moieties further parallel stacked to form the large hexagonal microtube

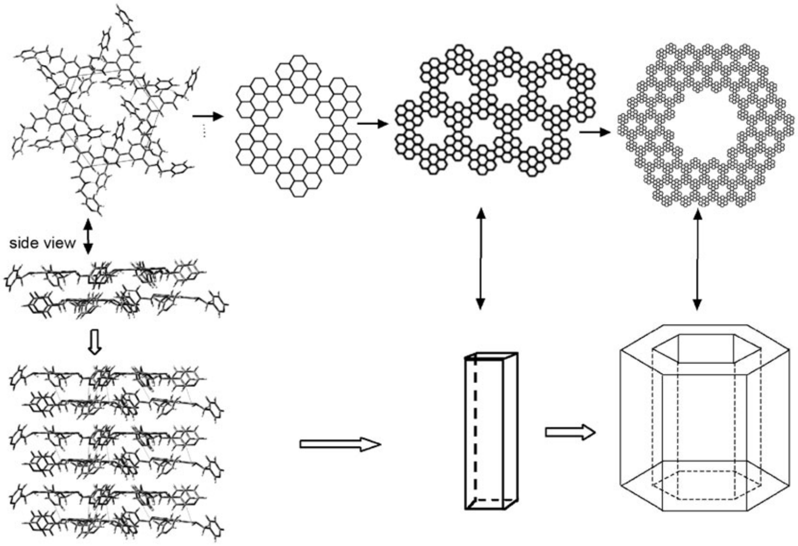

Fig. 5 Proposed formation process of the hexagonal microtubes. This scheme describes the assembly mode of the moieties in the hexagonal microtube, and it doesn't show the definite diameter of the microtube.

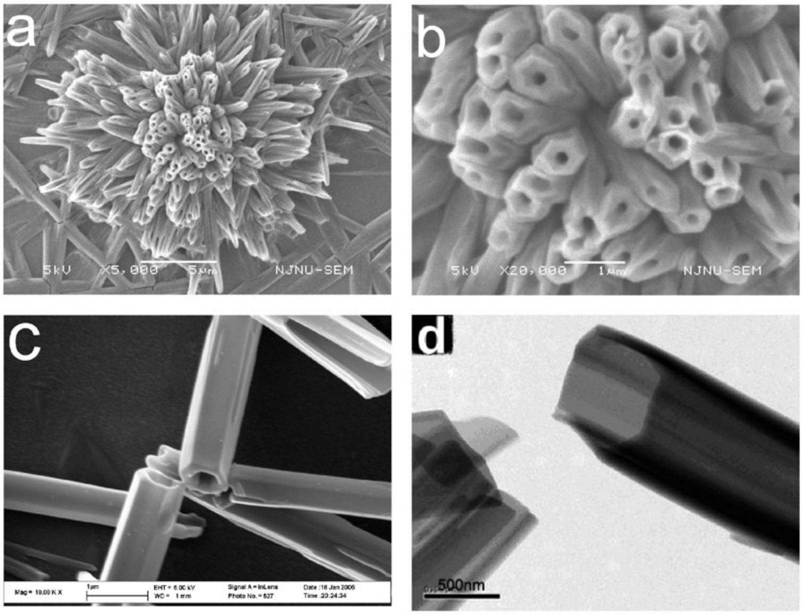

Fig. 6 (a) SEM image of the product from crystallization of a drop of TMPTA THF solution on a glass slide, (b) enlarged view of (a), (c) SEM image of the tubule obtained by the reprecipitation method, (d) corresponding TEM image of the tubule obtained by the reprecipitation method.

under a crystal packing force. In the obtained postulated structure of the TMPTA microtube, only half the N–H groups are hydrogen bonded because the additional methylene group changes the position of the N–H donor and pyridyl nitrogen acceptor. This was also consistent with the FT-IR results, which showed both the hydrogen-bonded υ-NH band (3245 cm^{-1}) and free N–H band ($\sim$3400 cm^{-1}) in its IR spectrum (Fig. 4a), while as mentioned above, there is only the hydrogen-bonded N–H band at 3276 cm^{-1} in FT-IR spectrum of TPTA crystal (Fig. 4c). Additionally, the melting point of TPTA crystal is 276–277 °C, while only 190–192 °C for the TMPTA microtubes although the latter has larger molecular weight. This also confirmed that the intermolecular interactions in TMPTA hexagonal microtubes were much smaller than that in the TPTA hexagonal crystals, which is concordant with the above analysis on hydrogen bonding interactions.

In addition, the formation of hexagonal tubes doesn't depend on the solvent or method. Dropping a drop of THF solution of TMPTA on a glass slide at room temperature, a cluster of hexagonal tubes was formed after the THF completely evaporated (Fig. 6a). An enlarged SEM image (Fig. 6b) shows that these tubes are $\sim$500 nm in diameter. Additionally, using the reprecipitation method, which is usually utilized to get organic nanoparticles,[15] hexagonal nanotubes can also be obtained (Fig. 6c, 500–800, nm in diameter). Corresponding TEM image clearly shows the outer wall and inner hollow structure of the hexagonal nanotubes (Fig. 6d).

Conclusions

In conclusion, a small molecule of *N*,*N*′,*N*″-tris(3-methylpyridyl)-trimesic amide was assembled into novel hexagonal microtubes through intermolecular hydrogen bonds, and simultaneously formed a gel in water utilizing a small amount of THF, EtOH or MeOH as the co-solvent. It is quite an uncommon hexagonal microtube based gel system compared to others reported. Otherwise, tuning the gelator concentration or preparation method can effectively control the size of the hexagonal tubes. This may greatly benefit the large-scale production of organic functional materials with special microstructures.

Experimental

Synthesis of TMPTA

Trimesic acid (5 g, 23.8 mmol) was put in $SOCl_2$ (10 mL) in the presence of DMF (0.2 mL) and stirred for 1 h at room temperature, then refluxed for 6 h until it all dissolved and reacted. Then the solvent was completely removed. The trimesic chloride was obtained as a solid at room temperature. Then, trimesic chloride (0.92 g, 3.4 mmol) was added in freshly distilled anhydrous THF (20 mL) and 3-aminomethylpyridine (1.44 g, 10.6 mmol) in the presence of pyridine (1.5 mL). The obtained precipitate was washed by water. Finally a white product was obtained. MS m/z (%): 481.3 (M + 1,100). ^{1}H NMR/δ (ppm): 9.36 (brs, 3H, N–H); 8.58 (s, 3H, H-2,4,6); 8.50 (s, 36H, H-2′); 8.46 (d, 3H, H-6′); 7.74 (d, 3H, H-4′); 7.36 (dd, 3H, H-5′); 4.52 (d, 6H , CH_2). EA: anal. calcd. for $C_{27}H_{24}N_6O_3$ C, 67.49; H, 5.03; N, 17.49; found C, 66.98; H, 5.34; N, 17.01.

Preparation of TMPTA hexagonal microtubes

A proper amount of TMPTA was dissolved in a H_2O–THF (5 : 1, v/v), H_2O–EtOH (4 : 1), or H_2O–MeOH (4 : 1) mixed solvent by heating in a screwed tube, and allowed to stand in a refrigerator (10 °C). After cooling the liquid didn't flow down through the tube when the tube was turned upside down, at a TMPTA concentration of 1–2 wt%. The hexagonal tubes were obtained by centrifugation and evaporating the solvent in vacuum.

Preparation of TMPTA tubes by the reprecipitation method

A solution of TMPTA in EtOH (0.08 M, 100 μL) was dropped into 5 mL aqueous solutions under vigorous stirring for one minute. The suspended solid material was dropped on the substrate and sputtered a layer of platinum for SEM characterization.

Characterization

FT-IR spectra were recorded on a Bruker Vector 22 FT-IR spectrophotometer. ESIMS result was obtained on LCQTM electrospray ionization mass spectrometer (Finnigan, American). NMR spectra were collected on AVANCE DAX-500 (Bruker, Sweden) NMR spectrometers. The SEM images were taken on a JEOL JSM-5610LV scanning electron microscope, and JEO-1500VP field emission scanning electron microscope. For the rheology measurement, a German Haake RS-600 rheometer with a cone-plate (C60/1 Ti) was used. The gap distance between the cone and the plate was fixed at 0.052 mm. The hydrogel was placed on the plate of the rheometer. A stress-amplitude sweep experiment was performed at a constant oscillation frequency of 1 Hz at 10 °C. The rheometer had a built-in computer to convert the torque measurements into either G' (storage modulus) or G'' (loss modulus) in oscillatory shear experiments.

Acknowledgements

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