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COMMUNICATION

Pertosylated Pillar[5]Arene: Self-Template Assisted Synthesis and Supramolecular Polymer Formation

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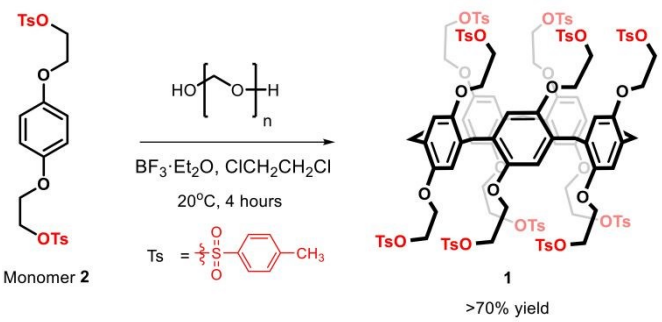
A facile synthesis of decatosylate pillar[5]arene 1 is reported in excellent yield (>70%). The high yield is attributed to a self-template effect of the pendant tosylate arms. The X-ray crystal structure shows the formation of a linear supramolecular polymer, stabilised by intermolecular pillar[5]arene-tosylate inclusion complexes. These polymeric arrays persist in solution and form rod-like microfibril nanostructures evidenced by SEM.

Supramolecular polymers are defined as arrays of monomeric units that link together via non-covalent interactions such as hydrogen bonding, sigma hole and donor-acceptor interactions.[1] The dynamic, tunable and diverse nature of such interactions make supramolecular polymers prime candidates in the development of smart and stimuli-responsive materials for nanotechnological applications. Therefore, exploration of supramolecular host molecules that manipulate multiple and cooperative interactions with new host-guest recognition systems is of great interest to promote the development of the discipline.[1c]

Since Cram, Lehn, and Pedersen set the milestones in supramolecular host-guest chemistry, macrocyclic motifs have served as workhorses in the area of molecular assembly, primarily due to their accessibility, and their established complementarity for a wide variety of guest molecules.[2] In 2008, Ogoshi and co-workers reported their seminal work on the synthesis of a series of novel macrocycles, coined pillararenes, the multifaceted exterior surface of which bears resemblance to their namesake.[3] Structurally, these macrocycles are cyclic oligomers (n = 5-15) of dialkylated hydroquinone monomers covalently linked by methylene spacer units at the 2,5-positions, forming a highly symmetric and rigid cavity. Considering the cavity size and its constituent electron-rich aromatic units, it is unsurprising that pillar[5]arenes are capable of forming inclusion complexes with electron deficient guests, binding a range of linear aliphatic and some simple aromatic molecules.[4] However, compared to other macrocyclic hosts such as calixarenes and crown ethers,[5] pillararenes have a remarkable affinity towards neutral guest species.[6] Moreover, the derivatisation of the rim of pillararenes provides an opportunity to fine-tune their recognition environments.[3d] These advantages highlight the potential of pillararenes as an effective and highly tunable motif for self-assembly in the construction of supramolecular polymers. Indeed, Huang and co-workers demonstrated that a monooctyl functionalised pillar[5]arene can self-assemble into a linear supramolecular network in chloroform solution,[7] whilst changing the side chain to a terminal bromododecyl group switches the assembly mode to form a daisy-chain dimeric species.[8] The interpenetrated complexes formed between pillar[5]arenes and other neutral aliphatic molecules have also been employed in the preparation of supramolecular polymers.[9] In this context, reports of templation by a neutral aromatic moiety has been restricted to imidazole and triazole derivatives.[9a]



Scheme 1. Synthesis of pertosylated pillar[5]arene **1.**

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Although the unique properties that multivalency confers on supramolecular complexes have been known for several years, applications of highly functionalised pillararene derivatives are rare.[10] Indeed, the overwhelming majority of pillar[5]arene-based receptors, polymers or functional materials have employed mono- or bis-functionalised derivatives.[10] The reason is that the synthesis of fully functionalised pillar[5]arene scaffolds remains challenging, requiring numerous synthetic steps or suffering from low yields of macrocyclisation.[3d] In this work, we prepared a pertosylated pillar[5]arene **1** in high yield (>70%) as a useful precursor to prepare a wide range of pillar[5]arene derivatives via post-synthetic modifications. Importantly, we demonstrate that the tosylate side chain in monomer **2** aids cyclisation by self-templation in the absence of a templating solvent. A suite of techniques including; ^{1}H-^{1}H DOSY NMR spectroscopy, dynamic light scattering, viscosity measurement and X-ray crystallography, confirm the formation of a linear supramolecular polymer, **1** in solution and the solid state, induced by the template effect of the pendant tosylate group.

Following earlier reports of Ogoshi and later observations by Neirengarten and Huang,[11] our initial attempt to cyclise the ditosylate monomer **2** with paraformaldehyde was conducted with $BF_3{\cdot}Et_2O$ in 1,2-dichloroethane (DCE) affording pertosylated pillar[5]arene **1** in a 70% yield (Scheme 1). Importantly, TLC, NMR, and ESI-MS analysis of the crude mixture confirmed the formation of the pillar[5]arene product, **1**, with only trace amounts of hexameric and larger homologues. This is in stark contrast to previous reports of low yielding macrocyclisation reactions with 1,4-dialkoxybenzenes, wherein it was suggested that steric hinderance between substituents suppresses cyclisation.[4b, 11b] Reaction conditions catalysed by $FeCl_3$ gave **1** in only 6-9% yield (ESI, Table S1), while Brønsted acids such as TFA, *p*-toluenesulfonic acid (pTSA) failed to give **1** (ESI, Table S1). Replacing DCE with dichloromethane (DCM), a non-templating solvent, in the cyclisation of the ditosylate, gave the pillararene **1** in an isolated 20% yield, while the analogous reaction with 1,4-diethoxybenzene and 1,4-dimethoxybenzene gave black polymeric products with no pillararenes detected (ESI). These results suggest an active role of the pendant tosylate groups of the ditosylate monomer, acting to template the macrocyclisation and favour the formation **1** over polymeric side products.

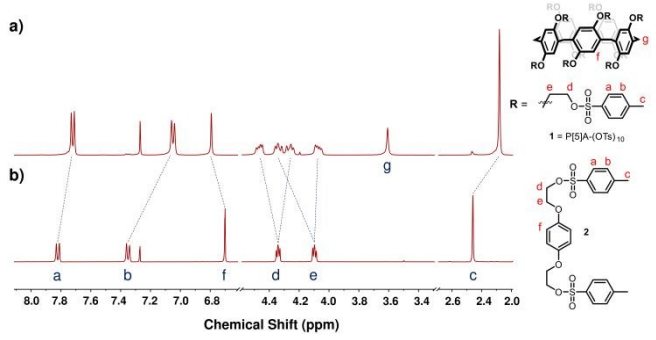

Figure 1. ^{1}H-NMR spectra (400 MHz, 25°C) of (a) pertosylated pillar[5]arene **1** and (b) ditosylate monomer **2** in $CDCl_3$.

The ^{1}H-NMR spectrum of **1** in $CDCl_3$ at room temperature showed well defined resonances corresponding to all protons in the structure. Proton signals of the tosylate group ($\mathbf{H_a}$, $\mathbf{H_b}$, and $\mathbf{H_c}$) in **1** showed upfield shifts compared to those of monomer **2**, while aromatic protons ($\mathbf{H_f}$) showed a singlet peak with downfield perturbation (Figure 1). The introduction of the bulky tosylate substituents inhibits rotation of the hydroquinone unit which reduces the conformational flexibility of **1**.[4a, 11b, 12] The ethylene protons ($\mathbf{H_d}$ and $\mathbf{H_e}$) exhibit a complex splitting pattern in line with previously observed diastereotopic splitting from the planar chirality of highly functionalised pillar[5]arenes.[11b, 13] Moreover, ESI-MS analysis of the product revealed a peak confirming formation of the pertosylated pillar[5]arene **1**. The signal at *m/z* = 2614.5271 corresponds to [**1**+Na]$^{+}$. The FTIR spectrum of **1** showed signals at 1358 and 1176 cm^{-1}, corresponding to S=O stretching, and at 927 cm^{-1} consistent with S-O stretching (ESI, Table S2).

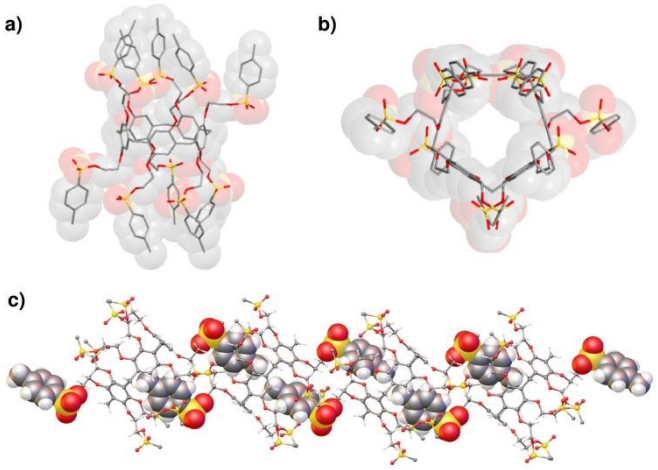

Figure 2. View of **1** showing the macrocycle a) side-on, b) from above, c) the supramolecular chain in **1** with the tosylate groups drawn as spacefill models and the remaining tosylates trimmed to the *ipso* carbon in the interests of clarity.

Crystals of **1** were grown from a THF-MeOH solution with X-ray crystallography revealing that they belong to the monoclinic space group *C*2/*c* (see ESI for details). The asymmetric unit contains half of the macrocyle with one of the tosylate side chains slightly disordered (Figures 2a and 2b). However, the most obvious structural feature is that one of the tosylate arms inserts into the cavity of a neighbouring pillararene forming a self-assembled 1D supramolecular chain (Figure 2c). This arrangement is supported by moderately strong C-H···O interactions between an aromatic C-H and sulfonyl O atom (C39-H39···O16: 2.364 Å, Figure S12).

The evidence of the self-insertion from the crystal structure, led us to explore the supramolecular polymerization behaviour of **1** in solution. The ^{1}H-NMR spectra of **1** in $CDCl_3$ at room temperature were recorded upon increasing concentration of **1**, a significant downfield shift of all protons, except $\mathbf{H_c}$ which showed an upfield shift, was observed. All signals of **1** became broad at high concentrations (Figure 3). These results suggest a concentration dependent behaviour of **1** in solution. Similar

temperature dependent spectral changes were also observed, although much less pronounced (ESI, Figure S7)

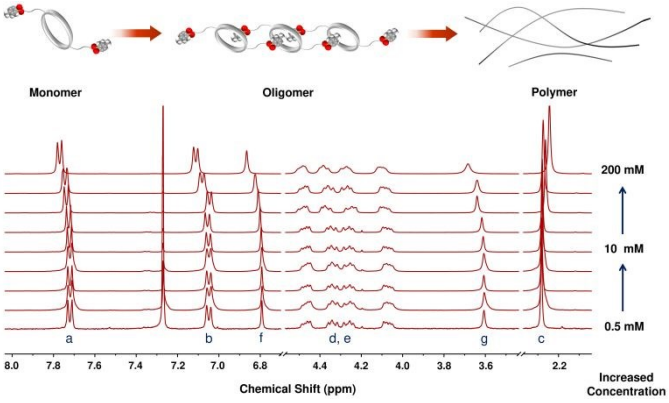

Figure 3. ^{1}H-NMR spectra (400 MHz, 25°C) of pertosylated pillar[5]arene **1** in $CDCl_3$ at different concentrations.

Two-dimensional diffusion-ordered ^{1}H-NMR spectroscopic (2D-DOSY) experiments provided further evidence of the macrocyclic repeating unit in **1** self-assembling into high-molecular weight supramolecular polymers in solution (Figure 4a). As the concentration of the macrocycle solution in $CDCl_3$ increased from 0.10 to 100 mM, the measured weight-average diffusion coefficients at 25°C decreased from 4.98×10^{-10} to 2.55×10^{-10} m^2 s^{-1} (Figure 4b), indicating formation of polymeric aggregates at high solution concentration. Dynamic Light Scattering (DLS) results also support host-guest induced formation of a higher molecular weight polymer network at high concentration. At 1.00 mM, the average size of **1** was around 0.7 nm and increased significantly to 221 nm at 20.0 mM (Figure 4c). Concentration-dependent viscosity studies of **1** were conducted in DCM at 298K. Upon increasing concentration, the specific viscosity of the solution also increases, after 65 mM a dramatic increase is observed and the critical polymerization concentration is reached, indicating the formation of large supramolecular networks (ESI, Figure S10). Moreover, the self-assembly behaviour of **1** in chloroform was further investigated by scanning electron microscopy (SEM). A rod-like microfibril structure with a regular diameter of 200-250 µm was drawn from the solution of **1** at 50 mM (Figure 4d), providing direct evidence for the formation of linear supramolecular polymer in solution. Examples of neutral pillararene based microfibres are rare, and to the best of our knowledge, this is the first example of such microstructures formed by a neutral perfunctionalised pillar[5]arene, in contrast to the mono-octyl copillararene reported by Huang and co-workers.[7]

Preliminary host-guest binding studies of **1** were carried out via ^{1}H-NMR spectroscopic titrations with 1,4-dicyanobutane (**dcb**), an electron deficient alkane known to strongly bind to the cavity of pillar[5]arenes. Upon addition of 0.5 equivalent of host **1** to a solution of **dcb** in $CDCl_3$, the ^{1}H-NMR spectrum shows well defined signals corresponding to free and complexed **dcb**, indicating that complexation between **1** and **dcb** is slow on the NMR timescale (Figure S15). The methylene protons ($\mathbf{H_x}$ and $\mathbf{H_y}$) of **dcb** when complexed exhibit a significant upfield shift (δ = -0.03 and -1.54 ppm, respectively) and peak broadening compared to signals of the free guest, **dcb**. This is consistent with these protons being shielded by the macrocyclic cavity due to the pseudorotaxane equilibria. The free guest disappeared after being titrated with 1.2 equivalents of **1** and the association constant (K_a) of this complex was determined by the single-point method, giving a K_a value of 157 $\pm$ 7 M^{-1} (see ESI for details).[14] This is in stark contrast to the binding affinities from other pillar[5]arenes which showed K_a >10^5 M^{-1}.[6b] The attenuated affinity of **1** for linear guest molecules also provides evidence for tosylate inclusion in the pillararene cavity, effectively competing in the formation of the host-guest complex.

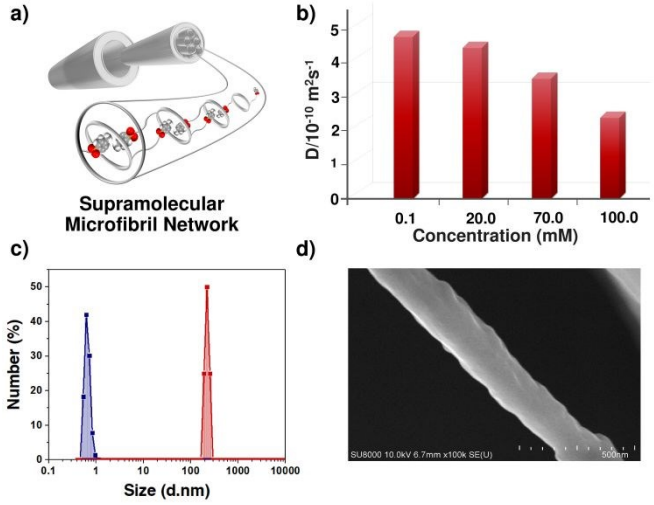

Figure 4. (a) cartoon representation of formation of a microfibril structure of **1**, (b) Diffusion coefficients of **1** in $CDCl_3$ at 25 °C at different concentrations, (c) DLS results for the self-assembly of **1** in DCM solution at 1.00 mM and 20.0 mM, (d) SEM image of gold coated fibre drawn from a solution of **1** in $CHCl_3$ at a concentration of 50mM.

To gain further insight into the binding abilities of **1**, crystals of **1@dcb** were grown from THF-MeOH in the presence of **dcb**. The compound crystallises in the triclinic $P\bar{1}$ space group with a pertosylated pillar[5]arene and one **dcb** molecule in the asymmetric unit (Figure 5; see ESI for details). The **dcb** molecule is disordered over three sites and located in the cavity of the pillar[5]arene, held in place by C-H···N interactions (2.55-2.74 Å). The structure is very different from that of **1**, with the tosylate groups now sitting almost directly above the rim of the macrocycle, angled inwards and trapping the **dcb** molecule in the cavity (Figure S14).

In conclusion, we report a rapid and efficient synthesis of pertosylated pillar[5]arene **1** from a readily accessible precursor. Importantly, single crystal X-ray structural analysis of **1** revealed a linear supramolecular network created by intermolecular host-guest inclusion complexes formed between pendant tosylate arms and pillar[5]arene cavities. The results suggest that the *p*-toluenesulfonate group functions as an effective template in the macrocyclisation reaction during the synthesis of **1**. The formation of the supramolecular

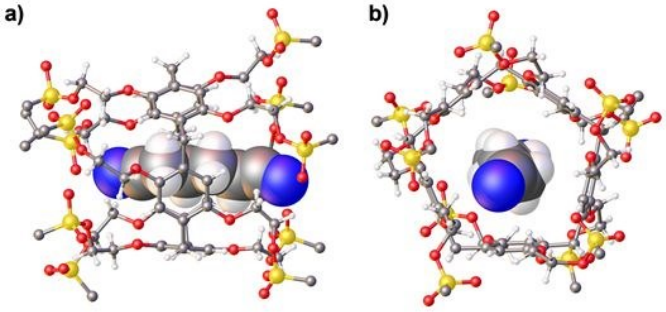

Figure 5. View of the structure of **1@dcb** a) side-on and b) from above with **dcb** drawn as a spacefill model and the tosylates trimmed to the *ipso* carbon for clarity.

polymer was shown to persist in solution by concentration dependent as well as diffusion-ordered ^{1}H-NMR investigations and DLS measurements. Furthermore, consistent with solid-state analysis, SEM studies reveal that the morphology of the self-assembled polymers is linear rod-like microfibril structures. The present work demonstrates not only expeditious access to highly-functionalisable pillar[5]arene scaffolds, but also the supramanostructures formed by *p*-toluenesulfonate group templation.

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Conflicts of interest

There are no conflicts to declare.

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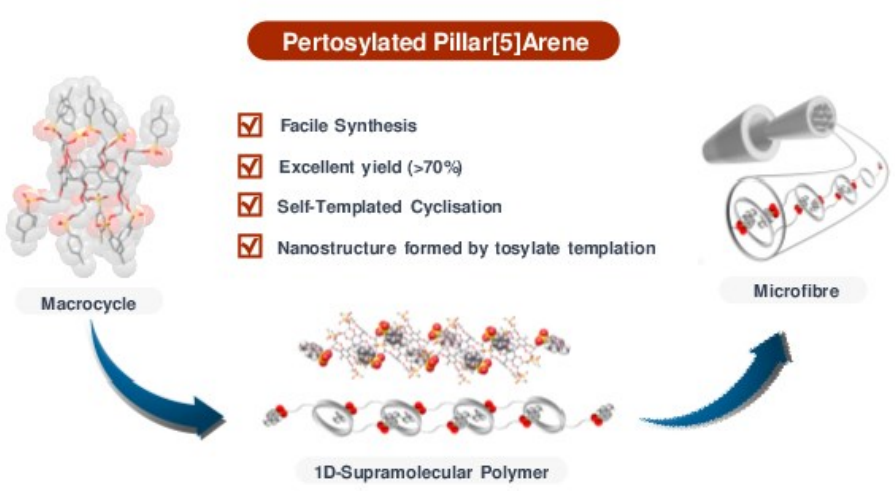

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