

## Supplementary Information

### Multifunctional water-soluble molecular capsules based on *p*- phosphonic acid calix[5]arene.

*Adam D. Martin, Ramiz A. Boulos, Lee J. Hubble<sup>1</sup>, Karel J. Hartlieb and Colin L. Raston\**

Centre for Strategic Nano-Fabrication, School of Biomedical, Biomolecular and Chemical  
Sciences, University of Western Australia, 35 Stirling Hwy, Crawley, W.A. 6009, Australia.

colin.raston@uwa.edu.au

<sup>1</sup>Present address: CSIRO Materials Science and Engineering, Lindfield, NSW 2070,  
Australia.

## Full methods

*p*-Phosphonic acid calix[5]arene was prepared according to the literature procedure.<sup>[1]</sup> Carboplatin and D<sub>2</sub>O (99.5 atom %) were purchased from Sigma Aldrich and were used as received. SWCNTs (Elicarb<sup>®</sup>) were purchased from Thomas Swan & Co. and were also used as received.

SWCNTs (1.0 mg) and *p*-phosphonic acid calix[5]arene (2.6 x 10<sup>-2</sup> mmol) were added to MilliQ water (6 mL, >18 MΩ.cm) and the mixture was ultrasonicated for 10 minutes with a sonic lance (4 W RMS power, Sonifier 150, Branson), then a further 30 minutes at 5 W RMS power, affording a black solution. The mixture was divided into 1.5 mL aliquots and centrifuged (5000 rpm, Mini Spin plus, Eppendorf) for 30 minutes. The top three quarters of the supernatant was collected and combined, affording the solubilised product.

All NMR experiments were performed in D<sub>2</sub>O. <sup>1</sup>H and <sup>195</sup>Pt NMR experiments were performed on a Bruker 600 MHz NMR spectrometer, Figure S1. <sup>195</sup>Pt NMR experiments were performed over the course of 60 hours without spinning the solution, and DOSY experiments were carried out on a Bruker 500 MHz spectrometer without spinning the solution.

TEM micrographs were recorded using a 2100 JEOL instrument operating at 120 keV. Sample preparation involved filtration of the supernatant through a 0.2 μm membrane filter with the retentate solid re-dispersed in MilliQ water, from which a drop of solution was placed onto a holey carbon film supported by a copper grid, which was then dried in air. EDX analysis was performed on a JEOL 3000F field emission gun TEM operating at 200 keV, equipped with an Oxford Instruments INCA 200 EDS system, Figure S3. AFM images of the calix[5]arene-coated SWCNT were recorded on a PicoScan system with a PicoScan 3000 PicoSPM II controller utilised in tapping mode using a grade 14 tapping mode cantilever, Figure S2. AFM images of the calix[5]arene fibres were recorded on a PicoScan system with a PicoPlus controller utilised in tapping mode using Nanoworld NCH cantilevers. Samples were either drop cast onto a freshly cleaved mica substrate and excess solution removed using a gentle flow of nitrogen gas, or spin coated for two minutes at 1500 rpm onto a freshly cleaved graphite surface. Raman spectra were recorded using an R-3000CN spectrometer with an excitation wavelength of 785 nm, and laser power < 10 mW, Figure S4.

Dynamic Light Scattering measurements were collected using a Malvern Instruments Zetasizer Nano ZS Series apparatus. Ultrapure milliQ water was used as the solvent and measurements taken under ambient conditions. The same concentration of *p*-phosphonic acid

calix[5]arene (5 mg/mL) was used throughout the measurements, with 10% v/v N,N-dimethylformamide added to obtain Figure S5c.

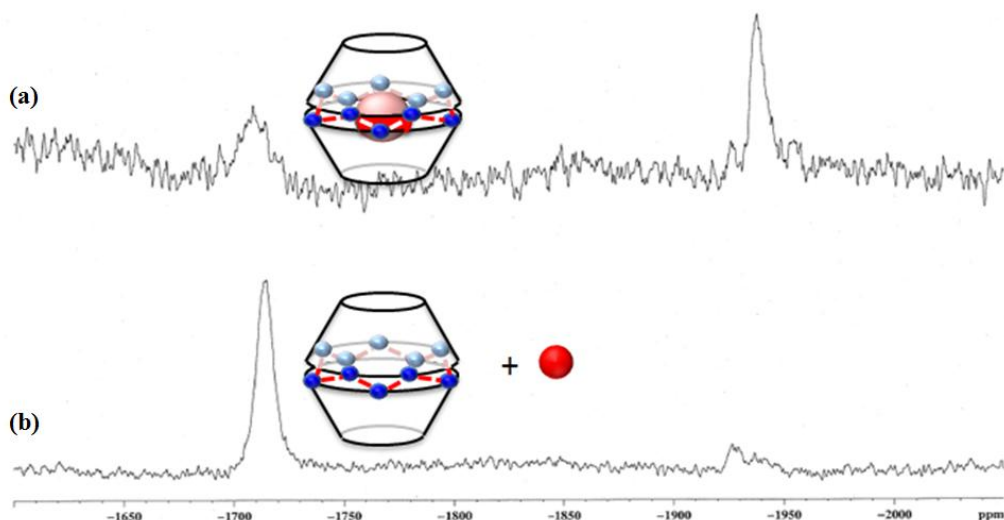
Materials Studio V4.1.0.0 was used for the molecular modelling. The Amorphous Cell module was used to construct a periodic cell with two calix[5]arenemolecules, a carboplatin molecule and 100 water molecules with the target density of the final configurations set to 1 g/mL, Figure S6a. For energy minimisations, the Forcite module was used, employing the smart minimiser with ultra-fine quality and the atom-based summation methods, and the Universal Force Field. The convergence criterion of the average energy derivative was less than  $2 \times 10^{-5}$  kcal/mol. To reduce the likelihood of being in a local minimum, a dynamic simulation at an elevated temperature was undertaken. The NVT ensemble was used at 298 K with a time step of 0.5 fs as appropriate for a system in water. The total number of steps used for the simulation was 1,000,000 giving a total simulation time of 500.0 ps. The dynamics trajectory was then optimized and the final structure from the dynamics run (total energy -  $10.3 \times 10^3$  kcal/mol) was used as the initial structure in the annealing process. The Forcite module was used to anneal the system with ultra-fine quality. A total of 100 annealing cycles were used with 273 K as the initial temperature and 500 K as the mid-cycle temperature. The heating ramps per cycle were set to 5 and 100 dynamics steps. The lowest energy structure from each cycle was saved to an annealing trajectory file giving a total of 100 frames, Figure S6b.

To model the self-assembly of calix[5]arenes around a SWCNT, the capsules were stabilized without carboplatin. When water and carboplatin were removed and the structure minimised, the resultant capsule, Figure S6c, had an accessible volume (at a solvent radius of 1.4 Å) of  $3301 \text{ Å}^3$ . However, when carboplatin was removed and the structure minimised prior to water removal and minimisation for a second time, the resulting capsule, Figure S6d, had a volume of  $3552 \text{ Å}^3$ . The modelling process leading to the capsule in Figure S6d is more representative of the TEM experimental conditions as the capsules in water were first added to the SWCNT followed by evaporation of the water. Twelve such capsules were then assembled in various geometries around a 1.0 nm SWCNT and the structures minimised. Other arrangements of the molecular capsules that were explored included association with the SWCNTs through the equatorial seam of the molecular capsules, and through the aromatic rings of the calix[5]arene, however they were less energetically favourable.

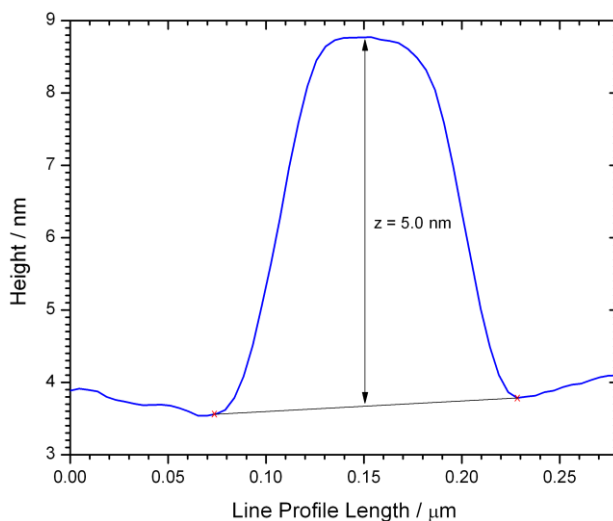
Modelling the assembly of the calix[5]arenes into fibres involved minimisation *in vacuo* of eleven molecules. Both the staggered and eclipsed conformations of the calix[5]arenes were explored.

## References

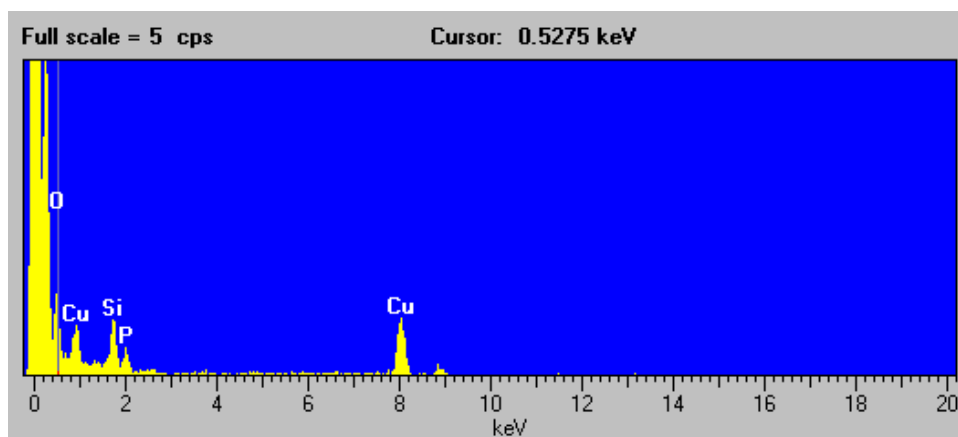
1. T. E. Clark, M. Makha, A. N. Sobolev, D. Su, H. Rohrs, M. L. Gross, J. L. Atwood, C. L. Raston, *New J. Chem.* **2008**, *32*, 1478.



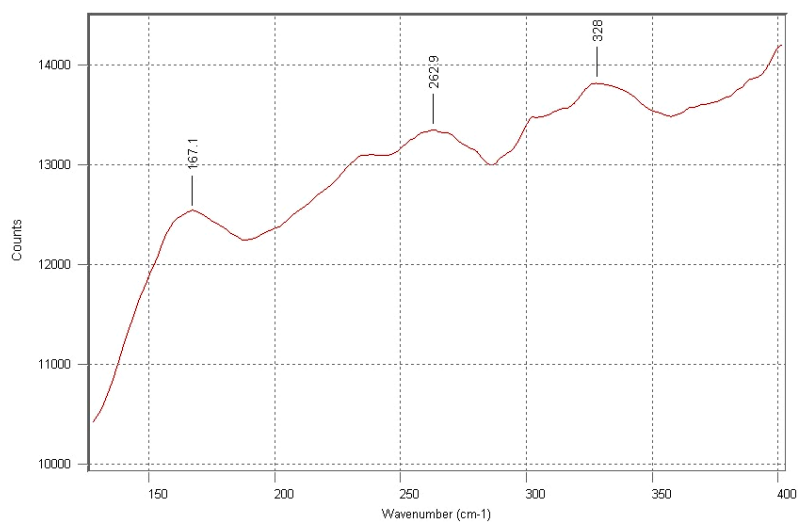
**Figure S1.** | NMR characterisation, **a.**  $^{195}\text{Pt}$  NMR in  $\text{D}_2\text{O}$  of carboplatin and two mol equivalents of *p*-phosphonic acid calix[5]arene after shearing, resulting in 85% encapsulation of the carboplatin. **b.** Solution in **a.** with stirring only, resulting in approximately 15% encapsulation.



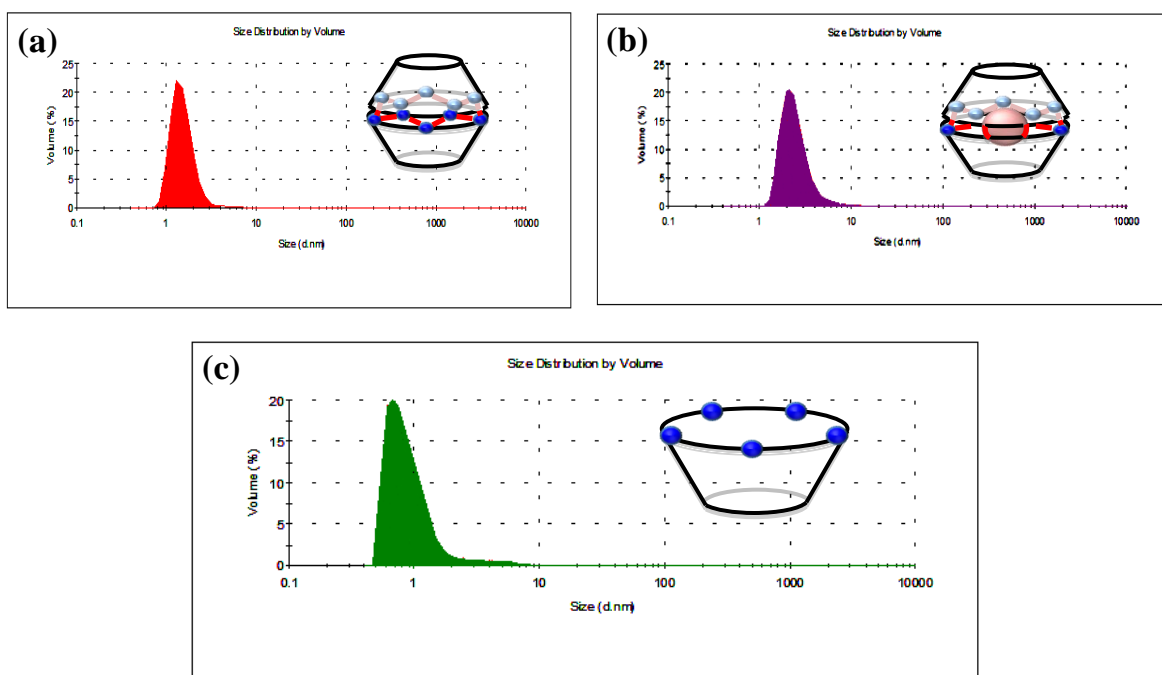
**Figure S2.** | Height profile analysis from AFM data, obtained from an individual SWCNT decorated with *p*-phosphonic acid calix[5]arene on mica.



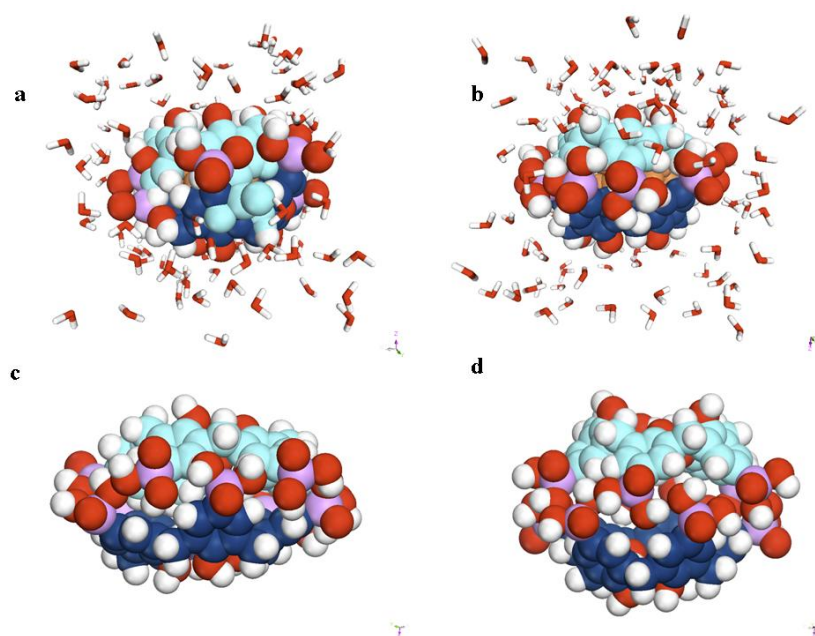
**Figure S3.** | Energy dispersive spectrum of the *p*-phosphonic acid calix[5]arene decorated SWCNT; the Si peaks were observed in multiple samples and arise from impurities present in the synthesis of the calix[5]arene.



**Figure S4.** | Raman spectrum of SWCNTs decorated with *p*-phosphonic acid calix[5]arene showing the radial breathing modes of the carbon nanotubes.



**Figure S5.** | Dynamic light scattering (DLS). **a.** An aqueous solution of *p*-phosphonic acid calix[5]arene in water as a monomodal distribution with a peak at  $1.8 \pm 0.5$  nm, corresponding to a capsule arrangement of the calix[5]arene. **b.** An aqueous solution of *p*-phosphonic acid calix[5]arene and encapsulated carboplatin, showing a monomodal distribution with a peak at  $2.2 \pm 0.5$  nm. **c.** An aqueous solution of *p*-phosphonic acid calix[5]arene after the addition of 10% v/v DMF, showing a peak at  $0.9 \pm 0.3$  nm, which corresponds to the solvation of the calix[5]arene into monomeric units.



**Figure S6.** | Additional molecular simulations. **a.** Initial 'collapsed' system for [carboplatin@ $1_2$ ] in a cell of water molecules. **b.** After minimization of the system in **a.** **c.** Structure minimized in the absence of carboplatin and water. **d.** Structure minimized in the absence of carboplatin in a cell of water. The water was then removed and the structure minimized again.