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Benjamin Isare, Mathieu Linares, Roberto Lazzaroni, Laurent Bouteiller. Engineering the Cavity of Self-Assembled Dynamic Nanotubes. *Journal of Physical Chemistry B*, 2009, 113 (11), pp.3360–3364. 10.1021/jp810236z . hal-01696720

HAL Id: hal-01696720

<https://hal.science/hal-01696720>

Submitted on 29 Aug 2020

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Engineering the Cavity of Self-Assembled Dynamic Nanotubes

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ABSTRACT By analogy with hydrogen bonded molecular capsules, self-assembled nanotubes are of interest because they can temporarily isolate guest molecules from the solution. We show here that the stability of a particular bis-urea based dynamic self-assembled nanotube is related to the possibility for solvent molecules to fit inside the tubular cavity. The diameter of the cavity can be finely tuned by introducing a modified monomer in controlled amount.

KEYWORDS supramolecular chemistry, host-guest systems, self-assembly, supramolecular polymer

Introduction

Self-assembled containers create space where guest molecules are temporarily isolated from the solution. They offer a unique approach to study space filling rules or solvation effects. In this respect,

hydrogen bonded molecular capsules are of particular interest, because of their thermodynamic stability and fast dynamics.¹ For instance, they have been used to probe the conformation of flexible guests,² to reveal new forms of isomerism, to generate an asymmetric microenvironment, to stabilize reactive molecules, or for catalysis.¹ However, up to now these studies have been limited to more or less globular hosts, which are able to encapsulate usually one or at most a few guest molecules.³ It would be desirable to extend these studies to tubular hosts, which could combine a large internal capacity (due to the huge length of the tubes), and the selectivity of the encapsulation (if the cross-section of the tube is close to the molecular dimension of the guest). Such systems could be useful for guest protection, controlled release, or models for transmembrane channels.⁴ Moreover, an understanding of guest encapsulation within such self-assembled dynamic nanotubes would bridge the gap between single molecule encapsulation in self-assembled capsules and adsorption into porous organic matrices (organic zeolites).⁵ Hydrogen bonded, self-assembled dynamic nanotubes are well known in the literature,⁶ and some of these systems can potentially be used to study guest encapsulation; however such studies are very rare.⁷

We have recently shown that bis-urea **1** (Figure 1a) self-assembles in non polar solvents to form individual dynamic nanotubes.⁸ These nanotubes can be micrometers long,⁹ and are in dynamic exchange with the monomer and with simple hydrogen bonded filaments.^{8a} However, these nanotubes can only form if the solvent molecules are small enough to be accommodated within the tubes.^{8b} A recent molecular simulation study has made it possible to propose a molecular model (Figure 1b), which is in agreement with FTIR, SANS, flow birefringence and dielectric spectroscopy data.^{8c} Based on this model, it is now possible to rationally design new building blocks in order to tune the nanotube structure and properties. In particular, the aim of this manuscript is to show that it is possible to tune the cross-section of the cavity, and thus the interaction with encapsulated solvent molecules.

Experimental Section

Solvents were used as received. Solutions were prepared under stirring at least 1 day prior to use. Heating at 50°C accelerated the dissolution process, but did not affect the measurements.

Synthesis. The synthesis of **1** was described previously.¹⁰ Bis-urea **2**: 2-ethylhexylisocyanate (5 g, 32 mmol) in dry CH₂Cl₂ (10 mL) was added dropwise to a two necked flask containing a CH₂Cl₂ solution (15 mL) of 1,3,5-trimethyl-2,4-diaminobenzene (2.2 g, 14 mmol) and triethylamine (0.5 mL). The reaction mixture was stirred at room temperature overnight under nitrogen. The precipitate was filtered

and washed with CH_2Cl_2 . Purification was performed by recrystallisation from THF/ethyl acetate to yield the expected compound (5.76 g, 85%). m.p. 204°C ; ^1H NMR (500 MHz, DMSO-d_6 , 70°C , TMS): $\delta = 7.05$ (s, 2H, NH), 6.87 (s, 1H, CH), 5.52 (br t, 2H, NH), 3.04 (t, 4H, $^3J(\text{H,H}) = 11.5$ Hz, N- CH_2), 2.34 (s, 6H, CH_3), 2.05 (s, 3H, CH_3), 1.29 (m, 18H, CH/ CH_2), 0.88 ppm (m, 12H, CH_3); ^{13}C -NMR (75 MHz, DMSO-d_6 , 70°C , TMS) $\delta = 157.2$ (C=O), 135.1/135.0/134.2/129.1 (Ar), 43.4 (N- CH_2), 39.2 (CH), 31.5/29.4/24.8/23.2 (CH_2), 18.5/14.2 (CH_3 -Ar), 14.5/11.6 ppm (CH_3); MS: m/z (%): 483.37 (100) [$\text{M}+\text{Na}^+$]; elemental analysis calcd (%) for $\text{C}_{27}\text{H}_{48}\text{N}_4\text{O}_2$: C 70.39, H 10.50, N 12.16; found: C 70.17, H 10.47, N 12.02.

Molecular simulations. Molecular mechanics and dynamics (MD) simulations were performed with the TINKER package¹¹ and the MM3 force-field,¹² which has been recently reparameterized¹³ to take into account the weak non-bonding interactions such as π - π stacking, and hydrogen bonds. We use periodic boundary conditions to perform calculations on an infinite tube, with a unit cell containing 48 molecules. For each system, we perform molecular dynamics simulations in the canonical ensemble (constant volume, temperature (300K) and number of molecules), with an equilibration time of 100ps. Then during the next 50 ps, we extract several snapshots along the MD trajectory and optimize the geometry, which provides information about the total energy of the full system. The structures were visualized with the VMD program.¹⁴ The cavity was visualized and its volume was measured with the program Swiss-PDBViewer.¹⁵ The influence of solvent was tested by placing 10 toluene molecules within the previously optimized nanotube portion of either **1** or **2** (48 bis-urea molecules, with periodic boundary conditions). Molecular dynamics simulations were performed in the canonical ensemble (constant volume, temperature (300K) and number of molecules), during 900ps.

IR spectroscopy. Infrared spectra were recorded on a Nicolet Avatar 320 spectrometer in KBr cells of 0.1cm path length.

DSC. Thermograms were measured using a N-DSC III instrument from CSC.⁹ The reference cell was filled with pure solvent and the sample cell (0.3mL) with the bis-urea solution. The capillary cells were not capped, and a constant pressure of $6 \cdot 10^5\text{Pa}$ was applied. A baseline scan (solvent in both reference and sample cells) was systematically performed in identical conditions and subtracted from the sample

scan. Transition temperature (T^{**}) was measured as the average of heating and cooling scans, at a scan rate of $1^{\circ}\text{C}/\text{min}$.

SANS. Measurements were made at the LLB (Saclay, France) on the Paxy instrument, at three distance-wavelength combinations to cover the $3.5 \cdot 10^{-3}$ to 0.35 \AA^{-1} q -range, where the scattering vector q is defined as usual, assuming elastic scattering, as $q=(4\pi/\lambda)\sin(\theta/2)$, where θ is the angle between incident and scattered beam. Data were corrected for the empty cell signal and the solute and solvent incoherent background. A light water standard was used to normalize the scattered intensities to cm^{-1} units.

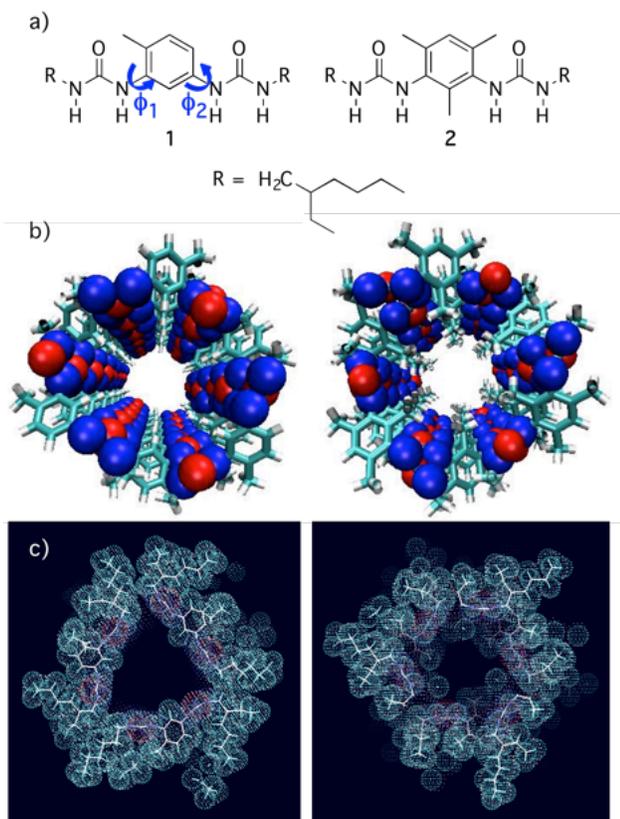


Figure 1. Structure of the monomers (a), optimized tubular geometry determined by molecular mechanics and dynamics (b), and van der Waals surface of the cross-section of the nanotubes (c). The calculations were initiated from the monomer conformation with antiparallel ureido groups.^{8c} The ethylhexyl side chains were included in the calculations, but replaced by methyl groups in (b), for clarity.

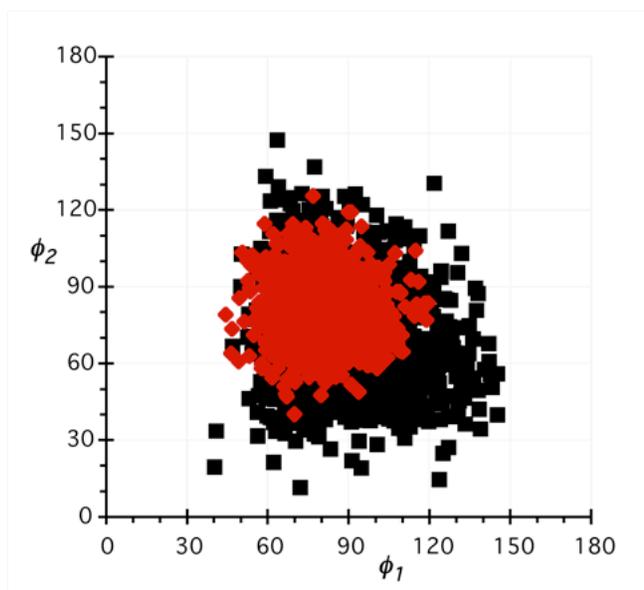


Figure 2. Values of the dihedral angles between the aromatic and the urea groups (see Figure 1a), along a molecular dynamics simulation for the bis-urea **1** nanotube (black) or the bis-urea **2** nanotube (red).

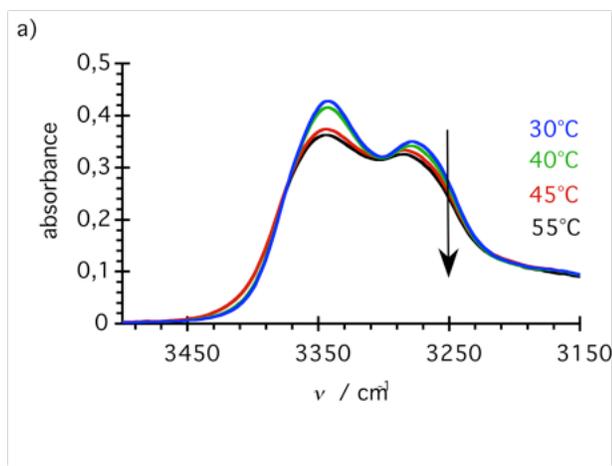
Results and Discussion

The molecular model for bis-urea **1** nanotube (Figure 1) shows that the aromatic proton placed between the 2 urea groups is pointing into the cavity. This suggests that it may be possible to modify the cavity of the nanotubes by replacing this hydrogen atom by a different moiety. The commercial availability of 1,3,5-trimethyl-2,4-diaminobenzene provided a convenient route to a bis-urea with a methyl group in 3-position. Indeed, bis-urea **2** was obtained in a single step in 85% yield (see Experimental Section).

Molecular simulation of both nanotubes was performed with periodic boundary conditions to avoid finite size effects, and in the absence of solvent molecules. The calculated stabilization energy of a monomer in the nanotube is -35.1 kcal/mol for **1** and -43.2 kcal/mol for **2**. These energies mean that the nanotube is reinforced by the presence of the two additional methyl groups. To understand the reason for this stabilization, the values of the dihedral angles between the aromatic and the urea groups were plotted along a molecular dynamics simulation of the nanotubes (Figure 2). This figure shows that for both nanotubes, the dihedral angles fluctuate around a value of about 80 to 90° , which means that the urea groups lie in a plane roughly perpendicular to the aromatic group. Moreover, the conformational behaviour of the free monomers was also probed (see Figures S1 and S2). These potential energy

surfaces show that the lowest energy conformer of free bis-urea **1** is obtained when the urea and aromatic groups are coplanar, whereas the lowest energy conformer of free bis-urea **2** is obtained when the urea and aromatic groups are perpendicular. Therefore, the methyl groups in bis-urea **2** force the urea groups to leave the plane of the aromatic spacer and limit the urea mobility, i.e. they preorganize the monomer in a suitable conformation for hydrogen bonding within the nanotube. This is confirmed by the fact that the dihedral angles between the aromatic and the urea groups fluctuate much less (i.e., are better defined) along the molecular dynamics simulation for the bis-urea **2** nanotube than for the bis-urea **1** nanotube (Figure 2).

In order to test this experimentally, solutions of **1** or **2** were prepared in toluene and characterized. At room temperature, FTIR spectroscopy (Figure 3) and viscosimetry (Figure 4) show that both compounds self-assemble by hydrogen bonding to form large objects. However, solutions of **2** are much less viscous than solutions of **1**. The q^{-1} dependence of the SANS intensity (Figure 5) confirms in both cases the formation of long and rigid rods. The dimensions of the scatterers were deduced from a fit according to a model valid for long and rigid isolated fibrillar species with a circular cross-section and a uniform scattering length density profile.^{8a} The fit of the room temperature data yielded values (Table 1) which are characteristic for the formation of nanotubes in the case of **1**,^{8a} but not in the case of **2**. Bis-urea **2** forms simple filaments with a single molecule in the cross-section. Variable temperature experiments (Figure 3) show that the nanotubes formed from bis-urea **1** at 12mM in toluene are stable below 40°C, whereas the nanotubes formed from bis-urea **2** are stable only below -5°C. Thus, the additional methyl groups in **2** actually destabilize the nanotube assembly in toluene.¹⁶



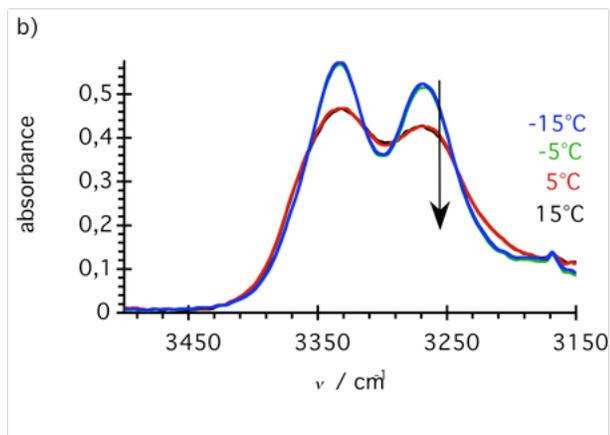


Figure 3. FTIR spectra for solutions of **1** (a) or **2** (b) in toluene at 5g/L (12mM) at several temperatures, showing the absence of free NH band (3440cm^{-1}): only hydrogen bonded NH groups ($3340, 3270\text{cm}^{-1}$) are detected. The spectra also reveal the transition between nanotubes and filaments between 40 and 45°C for **1** and between -5 and $+5^\circ\text{C}$ for **2**.

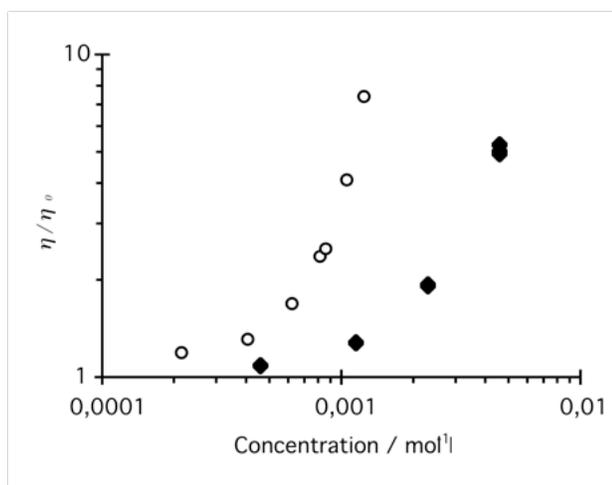


Figure 4. Relative viscosity versus concentration for solutions of **1** (o) or **2** (♦) in toluene, at 25°C .

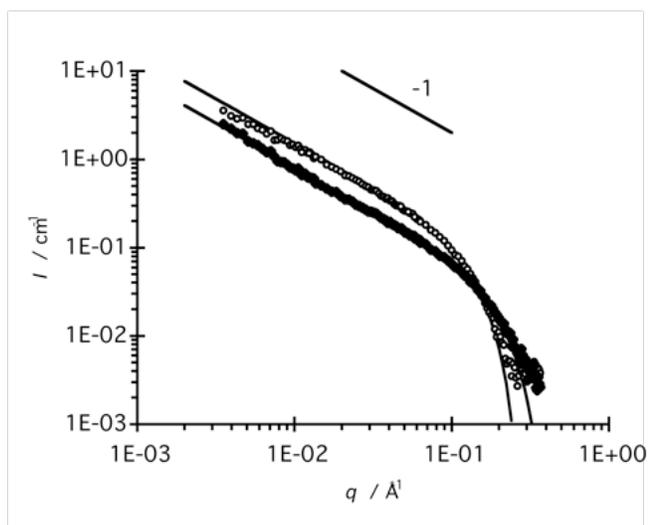


Figure 5. SANS intensity (I) versus scattering vector (q) for solutions of **1** (o) or **2** (◆) in D_8 -toluene at 5g/L (12mM) at 22°C. The plain curves are fits according to a model for long rigid rods with a circular cross-section.^{8a}

This experimental result is apparently in contradiction with the above molecular simulations. However, the previous simulations were performed in the absence of solvent molecules, and it is therefore possible that the calculated increase in stability for bis-urea **2** nanotube in vacuum is more than compensated by an unfavourable packing of - or by the absence of - solvent molecules inside the cavity.¹⁷ Indeed, the size of the cavity is very significantly affected by the monomer structure: a portion of tube of length 10Å has a cavity of volume 710Å³ and 540Å³ for **1** and **2**, respectively. Our interpretation is therefore that toluene molecules can be accommodated in the cavity of the bis-urea **1** nanotubes, while they cannot in the cavity of the bis-urea **2** nanotubes at room temperature. In order to test this interpretation, the following molecular dynamics simulations were performed. Toluene molecules were placed within the previously optimized nanotubes of either **1** or **2**, and a molecular dynamics simulation of the whole system (nanotube and solvent) was performed. Figure 6 shows the state of the assemblies after 900ps of simulation: bis-urea **1** nanotube is perfectly stable in the presence of toluene guests, whereas bis-urea **2** nanotube is ruptured.¹⁸ This result confirms that the addition of a methyl group between the 2 urea groups of the monomer reduces the cavity so much that the nanotube is unstable in the presence of toluene guests.

Table 1. Geometrical radius (r) and linear density (n_l) of the fibrillar scatterers, obtained from $\ln(qI)$ versus q^2 plots of SANS data for bisureas **1** or **2** at 22°C.^{8a}

Bisurea	Solvent	Concentration (mM)	r (Å)	n_l (Å ⁻¹)	Structure
1	D ₅ -toluene	12mM	13.8	0.57	tube ^a
2	D ₅ -toluene	12mM	9.5	0.28	filament ^b
1	CDCl ₃	32mM	9.6	0.23	filament ^b
2	CDCl ₃	32mM	9.3	0.27	filament ^b

^a the tube structure is characterized by a linear density of 0.5 to 0.7.^{8a}

^b the filament structure is characterized by a linear density of 0.2 to 0.3.^{8a}

Consequently, we tried to adjust the size of the cavity to the solvent bulkiness, by considering mixtures of **1** and **2**. Indeed, it was shown previously that bis-ureas with the same associating core form mixed structures (supramolecular copolymers).¹⁹ Figure 7 shows the evolution of the transition temperature below which the nanotubes are stable (T^{**} , measured by high sensitivity DSC).⁹ The mixed nanotubes are considerably more stable than both pure nanotubes: for instance, the 50/50 mixture of **1** and **2** displays a T^{**} of 73°C, which is more than 30°C higher than for either pure bis-urea. We attribute this synergistic effect to the enhanced preorganization of bis-urea **2** (see Figure 2) and to the wider cavity created by bis-urea **1** (see Figure 1). Indeed, addition of bis-urea **2** in the mixture is favourable only if its content is low enough, so that the tubular cavity is large enough to accommodate the solvent molecules.²⁰ In order to probe the generality of this effect, mixtures of bis-ureas **1** and **2** in other solvents (o-xylene, t-butylbenzene and chloroform) were prepared. In all solvents tested, similar bell-shaped curves were obtained. Moreover, in chloroform, this was coupled to a spectacular macroscopic effect. In chloroform both **1** and **2** form fluid solutions at room temperature, because they self-assemble into simple filaments (Table 1). However, a 50/50 mixture of **1** and **2** in chloroform forms a viscoelastic gel (Figure 8), probably because of the formation of nanotubes. Indeed, **1** has been shown to form viscoelastic gels in non-polar solvents, because of the entanglement of the nanotubes.²¹ At any rate, simply mixing the fluid parent solutions at room temperature instantaneously yields a viscoelastic gel.

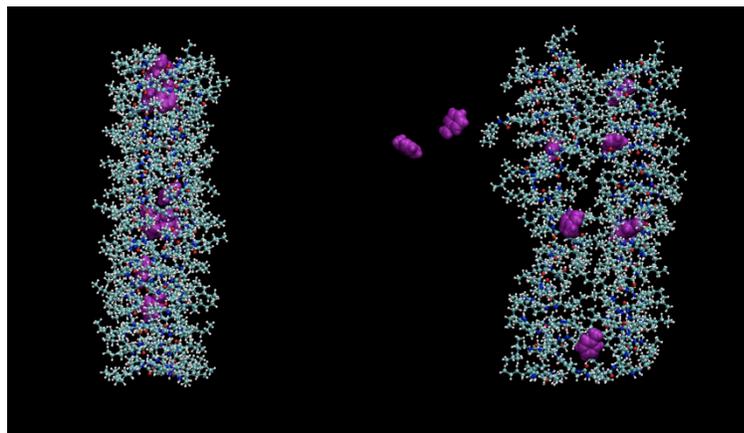


Figure 6. Snapshot at 900ps of a molecular dynamics simulation for nanotubes initially filled with toluene guest molecules.¹⁸ Left: bis-urea **1**: the nanotube is stable with encapsulated toluene guests. Right: bis-urea **2**: hydrogen bonds have been disrupted and toluene guests have escaped.

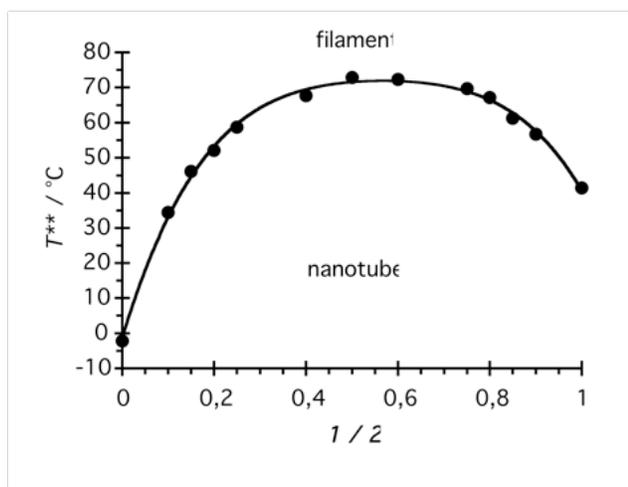


Figure 7. Transition temperature (T^{**}) versus molar ratio for mixed solutions of **1** and **2** in toluene at 10mM, measured by DSC.

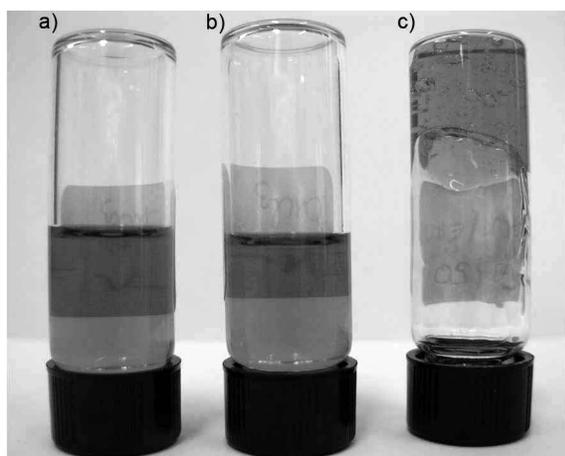


Figure 8. Photograph showing mixed solutions of **1** and **2** in chloroform at 4.3g/L (10mM) and room temperature, for different proportions: 100/0 (a); 0/100 (b); 50/50 (c).

Conclusion

In conclusion, we have shown that the stability of the bis-urea based dynamic self-assembled nanotubes is related to the possibility for solvent molecules to fit inside the tubular cavity. The diameter of the cavity can be finely tuned by introducing a modified monomer in controlled amount. This work opens the possibility to study the influence of other functionalities than simple methyl groups pointing into the cavity and raises the question of whether the distribution of the two monomers is statistical or regular. We are currently addressing these issues.

ACKNOWLEDGMENT B. I. acknowledges financial support from the European Science Foundation (ESF) activity entitled 'Experimental Theoretical Design of Stimuli-Responsive Polymeric Materials'. The modelling work in Mons has been supported by the Interuniversity Attraction Pole program of the Belgian Federal Science Policy Office (PAI 6/27) and by FNRS-FRFC. We thank François Boué (LLB, Saclay) for assistance with SANS experiments.

Supporting Information Available: Potential energy surfaces for the free monomers. This information is available free of charge via the Internet at <http://pubs.acs.org>.

REFERENCES

(1) (a) Hof, F.; Craig, S. L.; Nuckolls, C.; Rebek, Jr., J. *Angew. Chem. Int. Ed.* **2002**, *41*, 1489-1508. (b) Palmer, L. C.; Rebek, Jr., J. *Org. Biomol. Chem.* **2004**, *2*, 3051-3059. (c) Rebek, Jr., J. *Angew. Chem. Int. Ed.* **2005**, *44*, 2068-2078. (d) Böhmer, V.; Vysotsky, M. O. *Aust. J. Chem.* **2001**, *54*, 671-677. (e) Schmuck, C. *Angew. Chem. Int. Ed.* **2007**, *46*, 5830-5833.

(2) Schramm, M. P.; Rebek, Jr., J. *Chem. Eur. J.* **2006**, *12*, 5924-5933.

(3) Recent examples of expanded capsules: (a) Kerckhoffs, J. M. C. A.; ten Cate, M. G. J.; Mateos-Timoneda, M. A.; van Leeuwen, F. W. B.; Snellink-Ruel, B.; Spek, A. L.; Kooijman, H.; Crego-Calama, M.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **2005**, *127*, 12687-12708. (b) Ajami, D.; Rebek, Jr., J. *J. Am. Chem. Soc.* **2006**, *128*, 5314-5315. (c) Ajami, D.; Rebek, Jr., J. *Proc. Natl. Acad. Sci. USA* **2007**,

104, 16000-16003. (d) Ajami, D.; Rebek, Jr., J. *Angew. Chem. Int. Ed.* **2007**, *46*, 9283-9286. (e) Huerta, E.; Metselaar, G. A.; Fragoso, A.; Santos, E.; Bo, C.; de Mendosa, J. *Angew. Chem. Int. Ed.* **2007**, *46*, 202-205. (f) Baillargeon, P.; Dory, Y. L. *J. Am. Chem. Soc.* **2008**, *130*, 5640-5641.

(4) (a) Fernandez-Lopez, S.; Kim, H.-S.; Choi, E. C.; Delgado, M.; Granja, J. R.; Khasanov, A.; Kraehenbuehl, K.; Long, G.; Weinberger, D. A.; Wilcoxon, K. M.; Ghadiri, M. R. *Nature* **2001**, *412*, 452-455. (b) Bong, D. T.; Clark, T. D.; Granja, J. R.; Ghadiri, M. R. *Angew. Chem. Int. Ed.* **2001**, *40*, 988-1011. (c) Percec, V.; Dulcey, A. E.; Balagurusamy, V. S. K.; Miura, Y.; Smidrkal, J.; Peterca, M.; Nummelin, S.; Edlund, U.; Hudson, S. D.; Heiney, P. A.; Duan, H.; Magonov, S. N.; Vinogradov, S. A. *Nature* **2004**, *430*, 764-768. (d) Cazacu, A.; Tong, C.; van der Lee, A.; Fyles, T. M.; Barboiu, M. *J. Am. Chem. Soc.* **2006**, *128*, 9541-9548. (e) Davis, J. T.; Spada G. P. *Chem. Soc. Rev.* **2007**, *36*, 296-313.

(5) (a) Hertzsch, T.; Budde, F.; Weber, E.; Hulliger, J. *Angew. Chem. Int. Ed.* **2002**, *41*, 2282-2284. (b) Nakaoki, T.; Nagano, H.; Yanagida, T. *J. Mol. Struct.* **2004**, *699*, 1-7. (c) Sozzani, P.; Bracco, S.; Comotti, A.; Ferretti, L.; Simonutti, R. *Angew. Chem. Int. Ed.* **2005**, *44*, 1816-1820. (d) Schaffner, A.-P.; Lena, G.; Roussel, S.; Wawrezinieck, A.; Aubry, A.; Briand, J.-P.; Didierjean, C.; Guichard, G. *Chem. Commun.* **2006**, 4069-4071. (e) Roques, N.; Maspoch, D.; Dacu, A.; Wurst, K.; Ruiz-Molina, D.; Rovira, C.; Veciana, J. *Polyhedron* **2007**, *26*, 1934-1948. (f) Cheng, C.-Y.; Bowers, C. R. *J. Am. Chem. Soc.* **2007**, *129*, 13997-14002.

(6) (a) Moralez, J. G.; Raez, J.; Yamazaki, T.; Motkuri, R. K.; Kovalenko, A.; Fenniri, H. *J. Am. Chem. Soc.* **2005**, *127*, 8307-8309. (b) Johnson, R. S.; Yamazaki, T.; Kovalenko, A.; Fenniri, H. *J. Am. Chem. Soc.* **2007**, *129*, 5735-5743. (c) Stoncius, S.; Orentas, E.; Butkus, E.; Ohrström, L.; Wendt, O. F.; Wärnmark, K. *J. Am. Chem. Soc.* **2006**, *128*, 8272-8285. (d) Pantos, G. D.; Pengo, P.; Sanders, J. K. M. *Angew. Chem. Int. Ed.* **2007**, *46*, 194-197.

(7) Pantos, G. D.; Wietor, J.-L.; Sanders, J. K. M. *Angew. Chem. Int. Ed.* **2007**, *46*, 2238-2240.

(8) (a) Bouteiller, L.; Colombani, O.; Lortie, F.; Terech, P. *J. Am. Chem. Soc.* **2005**, *127*, 8893-8898. (b) Pinault, T.; Isare, B.; Bouteiller, L. *Chem. Phys. Chem.* **2006**, *7*, 816-819. (c) Shikata, T.;

- Nishida, T.; Isare, B.; Linares, M.; Lazzaroni, R.; Bouteiller, L. *J. Phys. Chem. B* **2008**, *112*, 8459-8465.
- (9) Bellot, M.; Bouteiller, L. *Langmuir* **2008**, *24*, 14176-14182.
- (10) Lortie, F.; Boileau, S.; Bouteiller, L.; Chassenieux, C.; Demé, B.; Ducouret, G.; Jalabert, M.; Lauprêtre, F.; Terech, P. *Langmuir* **2002**, *18*, 7218-7222.
- (11) <http://dasher.wustl.edu/tinker/>
- (12) Allinger, N. L.; Yuh, Y. H.; Lii, J. H. *J. Am. Chem. Soc.* **1989**, *111*, 8551-8566.
- (13) Ma, B. Y.; Lii, J. H.; Allinger, N. L. *J. Comput. Chem.* **2000**, *21*, 813-825.
- (14) Humphrey, W.; Dalke, A.; Schulten, K. *J. Molec. Graphics* **1996**, *14*, 33-38.
- (15) <http://spdbv.vital-it.ch/>
- (16) Bis-urea **2** did not form nanotubes at room temperature in any solvent tested. In chloroform: **2** forms the same filaments as **1** (Table 1). In dodecane: **2** is not soluble.
- (17) For a related solvation effect in a foldamer cavity, see: Mio, M. J.; Prince, R. B.; Moore, J. S. *J. Am. Chem. Soc.* **2000**, *122*, 6134-6135.
- (18) A video of the whole simulation can be viewed at <http://mail.materianova.be/pub/ehut-ehutmb.mov>
- (19) Isare, B.; Bouteiller, L.; Ducouret, G.; Lequeux, F. *Supramol. Chem.* **2009**, *21*, in press, DOI 10.1080/10610270802105106.
- (20) Up to now, our efforts to find a direct spectroscopic signature of the encapsulated solvent have been unsuccessful, because of the very broad NMR signal for bis-ureas **1** and **2** in non polar solvents.
- (21) For the rheological characterization of solutions of bis-urea **1**: Ducouret, G.; Chassenieux, C.; Martins, S.; Lequeux, F.; Bouteiller, L. *J. Coll. Interface Sci.* **2007**, *310*, 624-629.