

Introduction

A challenging target in the non-covalent synthesis of nanostructured functional materials is the formation of uniform features having well-defined properties, e.g. a precise control over the size, spatial resolution and the degree of functionalisation.^{1,2} One approach is based on the use of ‘molecular frustration’³ to control the conformation and size of the self-assemblies. Opposing solvation preferences, attraction versus repulsion and compact ordered packing versus sterically demanding disordered packing are built into the molecular design of the self-assembling components. We have recently developed discotic amphiphiles based on the C_3 -symmetrical benzene-1,3,5-tricarboxamide (BTA) scaffold that self-assembles into helical architectures of preferred handedness.⁴ The peripheral groups of those peptide discotics were chosen to be lanthanide complexes in order to introduce a highly amphiphilic character into the molecular building block design and ultimately target the development of a new class of supramolecular magnetic resonance imaging (MRI) contrast agents via the incorporation of paramagnetic lanthanides (Figure 1). By balancing out attractive forces within the hydrophobic fluorinated core of the molecular building blocks with electrostatic repulsive interactions on the hydrophilic periphery we managed to switch from elongated rod like assemblies (building block 1, picture A) to small and discrete objects (building block 2, picture B).

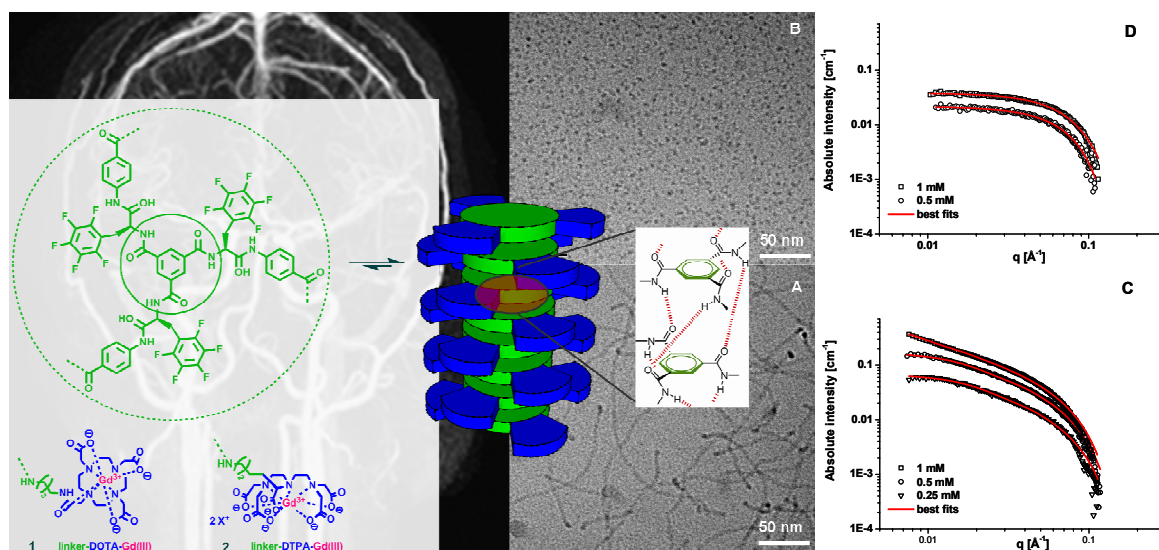


Figure 1: Schematic representation of the self-assembly of discotic amphiphiles 1 and 2.

Ionic strength dependent self-assembly mechanism of the fluorinated Gd(III)-DTPA discotic 2

We have already shown previously that the proposed frustrated growth as described above can be cancelled out via electrostatic screening, by increasing the ionic strength of the buffered medium.⁵ More detailed ‘titration experiments’ have now been carried out. Small Angle X-ray Scattering (SAXS) experiments (Figure 2 A) in collaboration with Dr. Giuseppe Portale (ERSF, Grenoble) clearly show that at 3 M NaCl elongated rod like stacks are formed. The transition from spheres at low ionic strength to rods at very high ionic strength, as indicated by the q^{-1} slope in the small q range, is in line with *cryo*-TEM pictures that have been taken in collaboration with Paul Bomans at the University of Technology in Eindhoven (data not shown). In between 0.4 M NaCl and 1.5 M NaCl the profiles gradually change which could be due to a higher scattering intensity induced by increasing concentrations of NaCl in the buffer. Another more likely explanation is that a small increase in stack length and hence aspect ratio of supramolecular objects can lead to significant changes in the SAXS profiles (Figure 3). Indeed we can safely postulate that this is due to the increasing ionic strength which favours hydrophobic effects in the aqueous self-assembly. Their contribution to an increased association constant would lead to higher degrees of polymerisation. Detailed fitting of the experimental SAXS data (Figure 2 A) will be crucial for the understanding of the sphere to rod transition induced by electrostatic screening of self-assembled stacks based on highly charged discotic 2 and are currently being carried out by Dr. Giuseppe Portale. On a side note we can exclude artefacts originating from the 2 mm glas capillaries contributing to scattering in the small q range after carrying out experiments in a mica cell as well (Figure 2 B). Its flat surface is less likely to lead to any reflections in the small q -range as observed for curved glas capillaries.

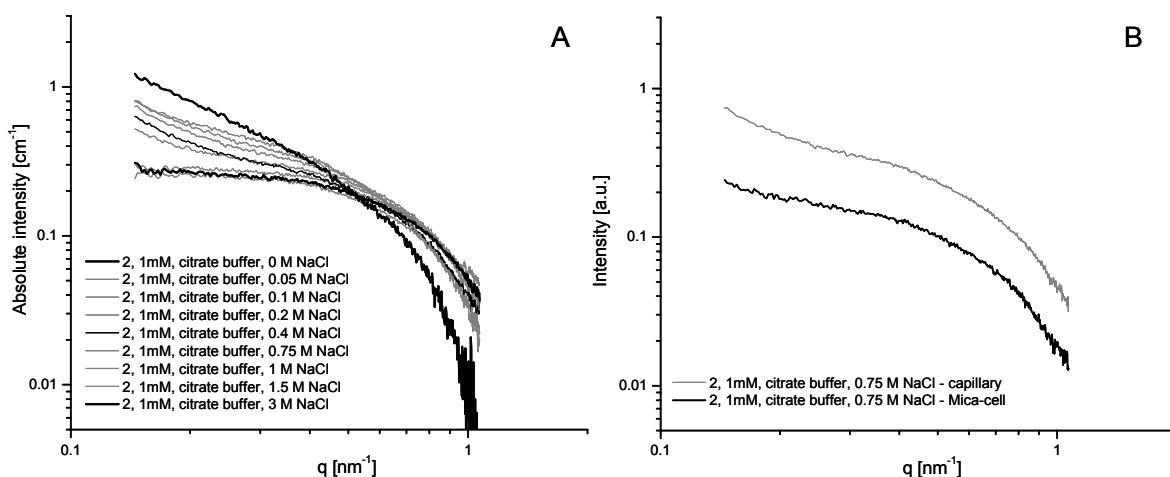


Figure 2: SAXS profiles for discotic **2** in citrate buffer (100 mM, pH 6) at increasing NaCl concentrations.

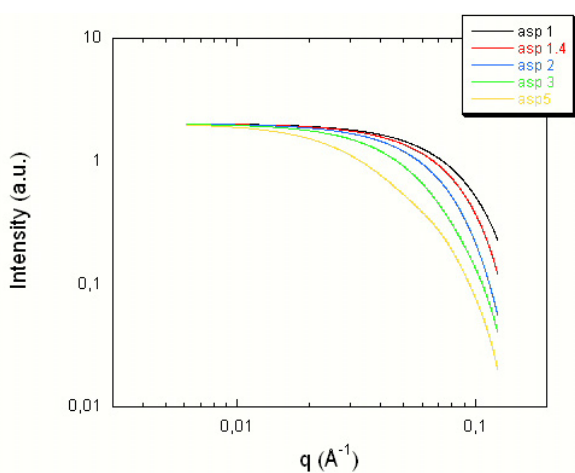


Figure 3: Simulated and normalised SAXS profiles using a cylindrical form factor with increasing aspect ratios (1 to 5).

In combining the above findings with temperature dependent circular dichroism measurements (Figure 4) we are also focussing on extracting thermodynamic parameters regarding association equilibria and effective surface charge densities (in collaboration with Prof. Paul van der Schoot, University of Technology in Eindhoven). We are particularly interested in determining the relationship between stack length and degree of cooperativity that dictates the self-assembly behaviour of highly charged discotic amphiphiles.

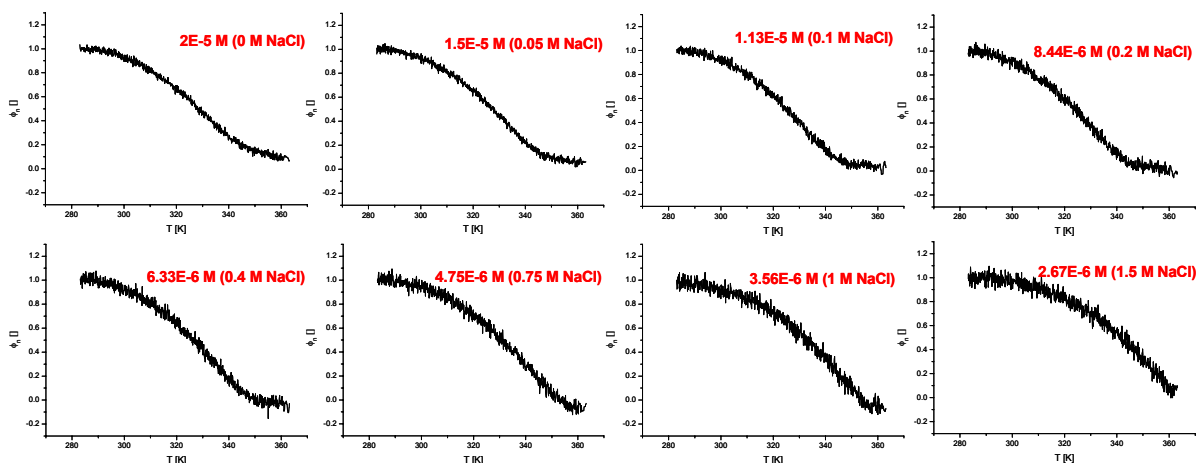


Figure 4: Normalised temperature dependent CD curves of discotic **2** in citrate buffer (100 mM, pH 6) at decreasing monomer concentration and increasing NaCl content.

- 1) L.C. Palmer et al., *Phil. Trans. R. Soc. A* **2007**, 365, 1417.
- 2) L.C. Palmer and S.I. Stupp, *Acc. Chem. Res.* **2008** 41, 1674.
- 3) H. Dong et al., *J. Am. Chem. Soc.* **2007**, 129, 12468.
- 4) K. van den Hout, *PhD Thesis, Eindhoven University of Technology*, **2008**.
- 5) P. Besenius, G. Portale, H.M. Janssen, A.R.A. Palmans, E.W. Meijer, *Proc. Natl. Acad. Sci. U.S.A.* **2010**, 2010-09592, submitted.