

# The synthesis and properties of surfactant aza macrocycles†

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Surfactant derivatives of [9]aneN<sub>3</sub> and [12]aneN<sub>3</sub> are prepared; micelles are formed at low concentrations in water while at higher concentrations lyotropic hexagonal, cubic and lamellar phases are characterised.

The study of surfactant materials is very well established,<sup>1</sup> the materials being used on a vast scale worldwide and in a number of settings such as soaps, detergents and emulsifiers. Surfactants are also important in a number of other areas, for example in cell membranes<sup>2</sup> and in the preparation of mesoporous silicates.<sup>3</sup> Similarly, the study of macrocyclic materials is also a mature area of investigation, especially in the development of sensors for selective cation and anion binding, host–guest chemistry and in supramolecular chemistry.<sup>4</sup>

We have become interested in the synthesis and properties of liquid-crystalline macrocycles with a view to establishing and understanding their structure/property relationships and to combine the substrate binding ability of macrocycles with their known properties as liquid crystals.<sup>5</sup> Previously, Neve has studied difunctionalised derivatives of [18]aneN<sub>2</sub>S<sub>4</sub> which were treated with AgOTf and AgPF<sub>6</sub> to give the corresponding Ag<sup>I</sup> complexes.<sup>6</sup> In the anhydrous state, these complexes showed a viscous, birefringent mesophase which was investigated by X-ray scattering which implied an undulating, bilayer mesophase in which the metal-containing cations describe a ‘U’-shaped motif. The same materials were also found to show lyotropic mesomorphism in acetonitrile at concentrations between 15 and 35 wt% complex, giving a lamellar ripple phase (*i.e.* again, a modulated phase). Later, Fallis<sup>7</sup> reported a related system in which [9]aneN<sub>3</sub> was functionalised with a long-chain secondary alcohol and then complexed to Ni(II) and Cu(II) centres. In this case, the neutral macrocycle was poorly soluble in water and surfactant properties were reported only for the cationic complexes. As part of our own work in this area,<sup>5</sup> we have begun to investigate surfactant derivatives of simple, uncomplexed aza macrocycles and report herein the synthesis of new surfactants derived from [9]aneN<sub>3</sub> and [12]aneN<sub>3</sub>.

A general model for a surfactant consists of a polar head group bound to a non-polar chain and so initially we confined ourselves to systems bearing one alkyl chain. We argued that the simplest way of accessing such systems was *via* orthoamide protection of the triazamacrocycles (Fig. 1). These are obtained after a multistep synthesis for the [9]aneN<sub>3</sub> derivative<sup>8</sup> (1) or after a one-step synthesis for the [12]aneN<sub>3</sub> derivative (2).<sup>9</sup> Once obtained, these orthoamides can be reacted with, for example, a haloalkane which opens up the orthoamide to give a cationic, *N*-alkylated macrocycle with two nitrogens still protected by a bridgehead carbon.<sup>10</sup> Our initial attempts focused on functionalisation using a C<sub>12</sub> chain which ought to be sufficiently long to give rise to surfactant behaviour. However, following reaction of 1-bromododecane with the orthoamide of [12]aneN<sub>3</sub> in acetonitrile, we were unable to recover a pure, alkylated macrocycle. This is most likely due to quaternisation

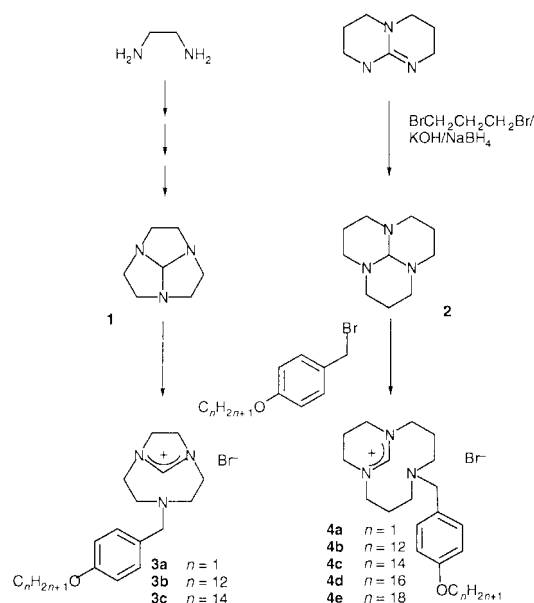


Fig. 1 Synthesis of the surfactant derivatives of [9]aneN<sub>3</sub> and [12]aneN<sub>3</sub>.

at nitrogen followed by Hoffmann elimination to give ring-opened products.

However, we were more successful using 4-alkoxybenzyl bromides which reacted smoothly with the orthoamide derivatives of [9]aneN<sub>3</sub> and [12]aneN<sub>3</sub> to give the desired products (3 and 4) which were isolated in near quantitative yields (Fig. 1).<sup>11</sup> For the methoxy derivative of [12]aneN<sub>3</sub> (4a) we were able to obtain single crystals, and the molecular structure resulting from the X-ray diffraction study<sup>‡</sup> is shown in Fig. 2. The structure confirms the substitution at the macrocyclic core with the bridgehead still in place, forming a 6-membered ring within the macrocycle in an envelope conformation, with the two N–C bonds [N(2)–C(4) and N(3)–C(4)] being virtually identical in length [1.308(3) and 1.312(3) Å respectively]. The conformation of the flexible [12]aneN<sub>3</sub> ring is distorted considerably by the formation of the bridgehead, shown by a comparison of the torsion angles in the bridge ring [C(3)–N(2)–C(5)–C(6) and C(6)–C(7)–N(3)–C(8) = 172.0(2) and 174.9(3)° respectively] with those in the conformationally more flexible region of the macrocycle [C(9)–C(10)–N(1)–C(1) and C(2)–C(1)–N(1)–C(10) = 152.0(2) and 143.5(2)° respectively]. An additional indicator of the strain induced in the macrocycle by the formation of a 6-membered ring is the observed shortening of the non-bonded N⋯N distance about the bridge [N(1)–N(2), N(1)–N(3) and N(2)–N(3) = 3.11(3), 3.10(3) and 2.33(4)° respectively]. Further, the structure reveals that the bromide counter anion is reasonably close to the head group, the average N–Br distance being 4.3(3) Å.

Thus far, we have synthesised three derivatives of [9]aneN<sub>3</sub>, 3a–c, and five derivatives of [12]aneN<sub>3</sub>, 4a–e (Fig. 1) and evaluation of their critical micelle concentration in water was undertaken using an automated tensiometer. The trend in cmc

† Electronic supplementary information (ESI) available: Fig. S1. See <http://www.rsc.org/suppdata/cc/b0/b003368p/>

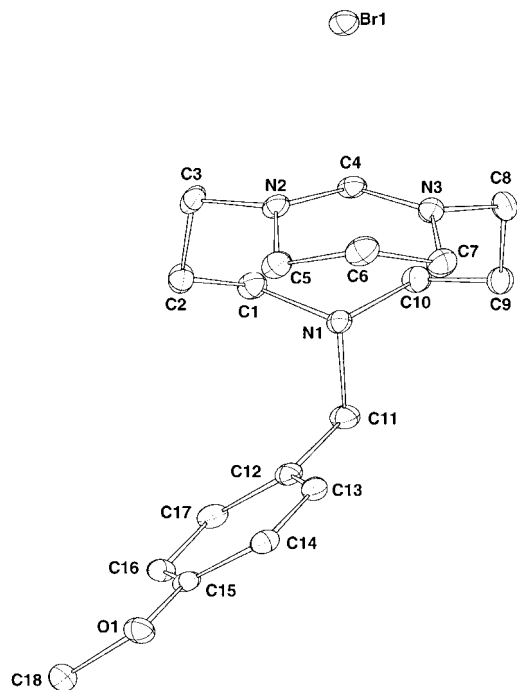


Fig. 2 Molecular structure of compound 4a.

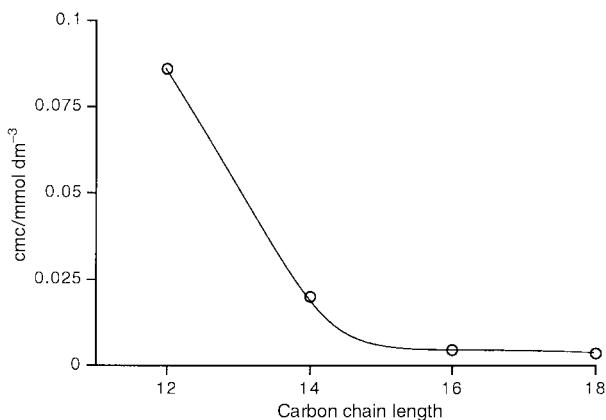


Fig. 3 Plot of cmc vs chain length for compounds 4.

values for the [12]aneN<sub>3</sub> derivatives is shown in Fig. 3 and reveals the expected decrease in cmc with increasing chain length on account of the increasing hydrophobicity of the chain. While it is perhaps surprising that the cmc of the two longest-chain derivatives are very similar, we have repeated these measurements and found them to be reproducible. We did not attempt to measure the cmc of **3a** and **4a** which were synthesised for the purpose of single crystal structural analysis.

Absolute and relative values of the cmc for these materials deserve some comment. In general, the cmc values for simple monocationic surfactants are of the order of 10<sup>-3</sup> mol dm<sup>-3</sup> while those of neutral surfactants are up to two orders of magnitude lower.<sup>12</sup> The reason for this difference is accounted for by the greater driving force required to push together head groups of like charge. However, the cmc is also affected by the hydrophobicity of the headgroup and as, in these examples, this contains not only the macrocyclic ring but a benzyl group, too, then the fact that the cmc values are < 10<sup>-4</sup> mol dm<sup>-3</sup> is not entirely unexpected. For such an argument to hold, we would predict that the cmc values for the [9]aneN<sub>3</sub> derivatives would be higher for the [12]aneN<sub>3</sub> derivatives since the head group in this system is smaller, less hydrophobic and more charge-dense. This prediction appeared to be borne out by initial experiments which indicated that the cmc value of surfactant **3b** was approximately three times higher than that of **4b**. Similar arguments had been advanced by Fallis *et al.* to explain lower-than-expected cmc values in their cationic surfactant com-

plexes.<sup>7</sup> However, subsequently we found that the [9]aneN<sub>3</sub> derivatives were unstable in water and NMR studies in D<sub>2</sub>O implied that between 5–10% decomposed over 24 h. The nature of the decomposition was not clear, but we suspect that the instability of compounds **3** was due to the greater ring strain present when compared to **4**. Thus, we cannot say anything conclusive about the relative cmc values of **3** and **4**.

We have studied the properties of one of the surfactants in more concentrated solution to see whether lyotropic liquid crystal phases can be observed. Using the Lawrence penetration method,<sup>13</sup> we studied **4b** and found that at temperatures of 40 °C a normal hexagonal (H<sub>1</sub>) phase was observed, while at 50 °C, a bicontinuous cubic (V<sub>1</sub>) phase was also observed (Fig. S1a†). At much higher temperatures, a lamellar (L<sub>α</sub>) phase was observed (Fig. S1b†). Thus, we have the possibility of organising and tuning the behaviour of these macrocyclic materials in a predetermined fashion.

The present study has shown that rather simple, functionalised triazamacrocycles can lead to materials which aggregate on a local (micelle) or extended (mesophase) scale. These bridgehead-protected materials will not complex to metal cations and so we are now investigating free-base derivatives with respect to both solution behaviour and to metal complexation chemistry. Details of these studies will be reported in due course.

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## Notes and references

‡ *Crystal data for 4a*. Empirical formula: C<sub>18</sub>H<sub>28</sub>BrN<sub>3</sub>O; formula weight: 382.34; crystal system: orthorhombic; space group: *Pbca*; Final *R* indices [*F*<sup>2</sup> > 2σ(*F*<sup>2</sup>): *R*<sub>1</sub> = 0.0410, *wR*<sub>2</sub> = 0.1123; unit cell dimensions: *a* = 13.352(3), *b* = 14.822(3), *c* = 18.105(4) Å; α = β = γ = 90°; *V* = 3583.0(13) Å<sup>3</sup>; 150(2) K; *Z* = 8; μ = 2.303 mm<sup>-1</sup>; reflections collected: 24587; independent reflections: 4107 [*R*<sub>int</sub> = 0.0807]; *R* indices (all data): *R*<sub>1</sub> = 0.0601, *wR*<sub>2</sub> = 0.1283. Absorption corrections applied using SORTAV;<sup>14</sup> solution obtained via direct methods and refined<sup>15</sup> by full-matrix least-squares on *F*<sup>2</sup>, with hydrogens included in idealised positions. CCDC 182/1619. See <http://www.rsc.org/suppdata/cc/b0/b003368p/> for crystallographic files in .cif format.

- R. G. Laughlin, *The Aqueous Phase Behaviour of Surfactants*, Academic Press, London, 1994.
- J. M. Seddon, *Biochim. Biophys. Acta*, 1990, **1031**, 1.
- M. Raimondi and J. M. Seddon, *Liq. Cryst.*, 1999, **26**, 305.
- L. F. Lindoy, *The Chemistry of Macrocyclic Ligand Complexes*, 1989, Cambridge University Press, Cambridge; F. Vögtle, *Supramolecular Chemistry*, 1991, Wiley, Chichester.
- A. J. Blake, B. W. Bruce, I. A. Fallis, S. Parsons and M. Schröder, *J. Chem. Soc., Chem. Commun.*, 1994, 2471; A. J. Blake, D. W. Bruce, I. A. Fallis, S. Parsons, H. Richtzenhain, S. A. Ross and M. Schröder, *Proc. R. Soc. London, A: Math. Phys. Sci.*, 1996, **354**, 395; N. R. Champness, D. W. Bruce and M. Schröder, *New J. Chem.*, 1999, **23**, 671.
- F. Neve, M. Ghedini, G. de Munno and A.-M. Levelut, *Chem. Mater.*, 1995, **7**, 688.
- I. A. Fallis, P. C. Griffiths, D. E. Hibbs, M. B. Hursthouse and A. L. Winnington, *Chem. Commun.*, 1998, 665.
- T. J. Atkins, J. E. Richmann and W. F. Oettle, *Org. Synth.*, 1978, **58**, 86; T. J. Atkins, *J. Am. Chem. Soc.*, 1980, **102**, 6364.
- D. H. Kim, M. Wilson and J. Hesteltnie, *Synth. Commun.*, 1994, **24**, 3109.
- R. W. Alder, R. W. Mowlam, D. J. Vachon and G. R. Weisman, *J. Chem. Soc., Chem. Commun.*, 1992, 507; A. J. Blake, I. A. Fallis, R. O. Gould, S. Parsons, S. A. Ross and M. Schröder, *J. Chem. Soc., Dalton Trans.*, 1996, 4379.
- All new compounds were characterised by elemental analysis and <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy.
- C. Fairhurst, S. Fuller, J. Gray, M. C. Holmes and G. J. T. Tiddy, in *Handbook of Liquid Crystals*, eds. D. Demus, J. Goodby, G. W. Gray, H.-W. Spiess and V. Vill, Wiley-VCH, Weinheim, 1998, vol. 3, ch. VII.
- A. S. C. Lawrence, *Liquid Crystals 2*, ed. G. H. Brown, Gordon and Breach, London, 1969, part 1, p. 1.
- R. H. Blessing, *Acta Crystallogr., Sect. A*, 1995, **51**, 33; R. H. Blessing, *J. Appl. Crystallogr.*, 1997, **30**, 421.
- G. M. Sheldrick, SHELXL-97. Program for refinement of crystal structures. University of Göttingen, 1997.