Covalent self-assembly of a dimeric borazaaromatic macrocycle†

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Bis(10-hydroxy-10,9-boraza-2-phenanthryl) ether is capable of covalent self-assembly upon dehydration in solution to form the corresponding cyclic dimer.

Self-assembly processes,[1] which allow the construction of large, highly ordered molecular or supramolecular arrays, directly and spontaneously, from simple constituents, are an important and developing[2] area of synthetic chemistry. Strict self-assembly[3] processes require that the pathways leading to the desired product must be completely reversible and that the target assembly should be stable at thermodynamic equilibrium. In addition, all of the information necessary to fabricate the target structure must be encoded within the constituent components of the assembly. Traditionally, these requirements have led to assembly pathways that rely upon non-covalent interactions, such as hydrogen bonding or metal–ligand coordination, to achieve the necessary molecular recognition and organisation. This approach, however, has one major disadvantage—the entropic cost of arranging the required constituents is only compensated for by the enthalpic contributions from relatively weak non-covalent interactions and, therefore, a significant number of these interactions are usually required for self-assembly to be successful. This problem can be overcome by exploiting systems in which the pathway leading to the formation of the target assembly makes use of covalent bonds.[4] The higher enthalpic gain as a result of covalent bond formation more than overcomes the entropic cost of organising[5] the components of the assembling structure and, hence, fewer covalent bonds are required to produce a stable assembly.

Here, we describe the use of a bis(borazaaromatic) in the covalent self-assembly of a dimeric macrocycle and the characterisation of this assembly process by ^{1}H NMR spectroscopy, X-ray diffraction and MALDI-TOF mass spectrometry. In order for covalent self-assembly to be successful, we reasoned that the information required to encode the target assembly must be described by the conformational space[4] accessible to the starting monomer. Hence, we identified the competition between the formation of discrete, cyclic structures and the formation of linear polymers from the same bifunctional monomer as an appropriate starting point for these studies. Accordingly, we designed and prepared the bis(borazaphenanthrene) **1** in five steps from Ph_2O. Compound **1** contains two boraza aromatic units connected by a phenyl ether oxygen atom which allows the two borazaphenanthrene rings to pivot with respect to each other. We have demonstrated[6] that hydroxyborazaaromatics can undergo reversible dehydration in solution to the corresponding anhydrides readily under appropriate conditions. Therefore, several dehydration reactions of **1** can be envisaged (Fig. 1). For example, dehydration may occur to afford a series of linear oligomers of varying chain lengths. In addition, ring closure of the linear oligomers could give rise to cyclic oligomers. In the simplest case, this would give rise to the dimeric anhydride **2** which can potentially exist in two isomeric forms—either face-to-face or helical (Fig. 1).

Compound **1** can be converted readily to the dimeric anhydride **2** in acetone solution, at room temperature, through dehydration by the addition of 4 Å molecular sieves. Conversely, **2** can be readily hydrolysed to give **1** in acetone solution by the addition of an excess (> 10 equiv.) of water. In order to assess the progress of the self-assembly process, a sample of **1** was dissolved in acetone and the evolution of the species present in solution, as a function of time, was monitored by MALDI-TOF mass spectrometry [Fig. 2(*a*)]. Initially, the cyclic dimer **2** and acyclic dimer $\mathbf{A}_2$ [Fig. 2(*a*), t = 0.5 h] are observed in solution. As the dehydration progresses, however, higher molecular weight species, such as the acyclic trimer $\mathbf{A}_3$ and tetramer $\mathbf{A}_4$ can be observed [Fig. 2(*a*), t = 7.5 h], in addition to the desired cyclic dimer **2**. After 4 days, the higher molecular weight species have diminished in concentration and after 12 days, the only oligomeric species present in solution is the cyclic dimer **2**. This behaviour can be rationalised in terms of the kinetic scheme shown in Fig. 2(*b*). The first species formed in the oligomerisation process must be the acyclic dimer $\mathbf{A}_2$. Cyclisation of this species to form the cyclic dimer **2** would be expected to be favourable[7] as it is intramolecular. However, if the effective molarity for this cyclisation[8] is not particularly high then the chain extension pathways, leading from $\mathbf{A}_2$ to $\mathbf{A}_3$ and beyond, will be able to compete to some extent with this cyclisation. This behaviour would explain the emergence of higher oligomers at intermediate time periods. Since the pathways leading to the acyclic oligomers $\mathbf{A}_n$ are reversible, all of the material in the reaction manifold will ultimately be recycled back through $\mathbf{A}_2$ and into the cyclic dimer **2**, which is clearly the thermodynamic product of this process. Hence, once the assembly process is complete, the only oligomeric species present in solution is the cyclic dimer **2**.

Single crystals‡ of **2**, suitable for X-ray diffraction, were grown by slow evaporation of a solution of **2** in acetone and hexane. In this structure, each molecule of **2** is present (Fig. 3) as the helical form§ shown schematically in Fig. 1 and the unit cell contains four pairs of enantiomers. The solid state structure contains channels, aligned parallel to the crystallographic c axis, which contain a number of disordered solvent molecules which

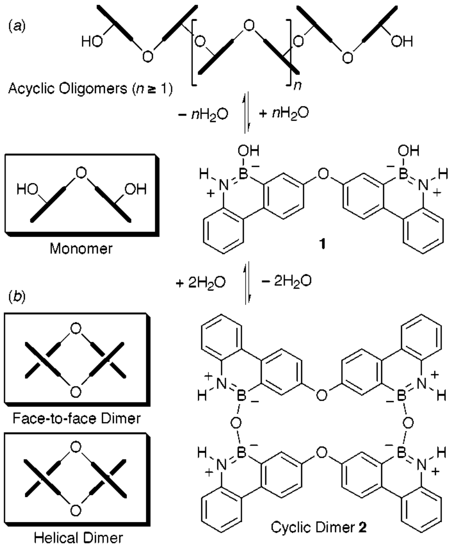

Fig. 1 Compound **1** can be dehydrated to give, for example: (*a*) linear oligomers with a distribution of chain lengths, and (*b*) a discrete cyclic dimer **2** which can adopt either a helical or a face-to-face conformation.

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† These compounds have also been referred to as borazaroaromatic species in earlier papers.

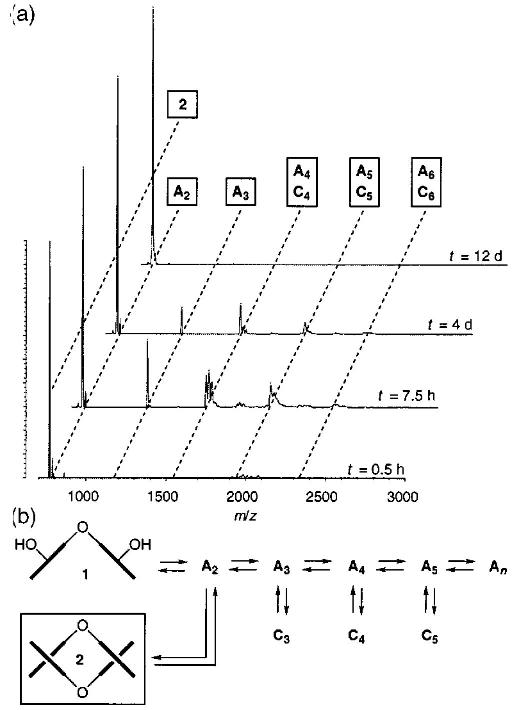

Fig. 2 (*a*) The evolution of the MALDI-TOF mass spectrum of a sample of **1** dissolved in acetone in the presence of 4 Å molecular sieves as a function of time. The elapsed time in this experiment is indicated to the right of each spectrum. (*b*) Proposed kinetic scheme for the equilibration of oligomers of **1**. The acronym $\mathbf{A}_n$ represents acyclic oligomers of **1** containing *n* repeat units and the acronym $\mathbf{C}_n$ represents cyclic oligomers of **1** containing *n* repeat units. Note that, for clarity, all spectra are scaled such that the *m/z* 772 peak, arising from **2**, is the base peak in all spectra. This scaling does not represent the true distribution of species after 0.5 h since the sample contains mostly monomer **1** at this time.

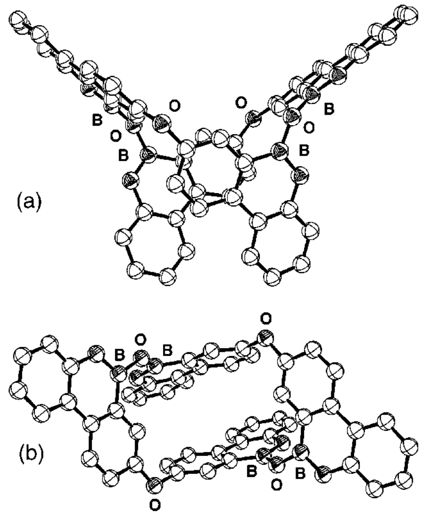

Fig. 3 ORTEP diagrams of the solid state structure of **2** as determined by X-ray diffraction. The molecule is shown in two orientations: (*a*) side view and (*b*) top view. Hydrogen atoms have been omitted for clarity.

are lost rapidly when the crystals are removed from the mother liquor. Examination¶ of these desolvated crystals by MALDI-TOF mass spectroscopy demonstrated that the crystals contained only the cyclic dimer **2**. The desolvated crystals were then heated at 150 °C for 3 h. Further analysis by MALDI-TOF mass spectroscopy demonstrated that, in addition to **1** and **2**, significant quantities of higher molecular weight materials were present. Surprisingly, only oligomers containing an even number of monomer units were observed. Whilst the origin of this selectivity and the mechanism of this process are, as yet, not understood, there are, however, suggestions that this behaviour may be intrinsic to monomer **1** and dimer **2**, and is simply an expression of the natural predispositions[4] of these compounds.

Closer examination of the assembly process in solution [Fig. 2(*a*)] reveals that in the case of the trimer ($\mathbf{A}_3/\mathbf{C}_3$) and pentamer ($\mathbf{A}_5/\mathbf{C}_5$), the acyclic species ($\mathbf{A}_3$ and $\mathbf{A}_5$) are strongly favoured. However, in the case of the tetramer ($\mathbf{A}_4/\mathbf{C}_4$) both the cyclic and acyclic species are formed, with $\mathbf{C}_4$ persisting in solution for a much longer period of time than $\mathbf{A}_4$.

In conclusion, we have demonstrated the utility of bis(boraza aromatic)s as building blocks for strict self-assembly mediated by covalent bond formation. The conformational space accessible to compound **1** successfully encodes for the exclusive formation of the cyclic dimer **2** upon dehydration. Logical extensions of this strategy, which allow the synthesis of more complex self-assembled systems, are currently under investigation in our laboratory.

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Notes and references

‡ *Crystal data* for **2**: $C_{48}H_{32}B_4N_4O_4$ M = 942.29, monoclinic, a = 23.120(5), b = 16.007(3), c = 32.068(8) Å, β = 111.177(4)°, U = 11066(4) Å^3, T = 296 K, space group $I2/a$ (no. 15), Z = 8, μ(Mo-Kα) = 0.1 mm^{-1}, 14279 reflections measured, 5765 unique (R_{int} = 0.174). The final R was 0.1013. The relatively poor R factor for this crystal structure is a consequence of the disordered nature of the solvent situated within the channels described in the text. CCDC 182/1431. See http://www.rsc.org/suppdata/cc/1999/2279/ for crystallographic data in .cif format.

§ In solution, **2** can interconvert between the helical and the face-to-face forms readily.

¶ In order to ensure that the mass spectrum obtained was a good representation of the composition of the heated crystal, samples were dissolved in predried acetone (4 Å molecular sieves), spotted immediately on to the MALDI-TOF target upon which a Co powder matrix had been applied and their mass spectrum recorded on a Kratos Kompact MALDI 3 instrument using 50 shots at a linear laser power of 105.

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4 For other elegant examples of covalent self-assembly, see S. J. Rowan, P. A. Brady and J. K. M. Sanders, *Angew. Chem., Int. Ed. Engl.*, 1996, **35**, 2143; P. A. Brady and J. K. M. Sanders, *Chem. Soc. Rev.*, 1997, **26**, 327; S. J. Rowan, D. G. Hamilton, P. A. Brady and J. K. M. Sanders, *J. Am. Chem. Soc.*, 1997, **119**, 2578; S. J. Rowan and J. K. M. Sanders, *J. Org. Chem.*, 1998, **63**, 1536; S. J. Rowan, D. J. Reynolds and J. K. M. Sanders, *J. Org. Chem.*, 1999, **64**, 5804; J. Ipaktschi, R. Hosseinzadeh, P. Schlaf and E. Dreiseidler, *Helv. Chim. Acta*, 1998, **81**, 1821; J. Ipaktschi, R. Hosseinzadeh and P. Schlaf, *Angew. Chem., Int. Ed.*, 1999, **38**, 1658. Sanders uses the term predisposition to describe the encoding of a thermodynamically-favourable oligomeric structure through the conformational properties of the monomer once incorporated into this larger structure. In this language, the conformational space which is open to monomer **1** should predispose, or encode, the formation of a particular oligomer of **1**.
5 An example of this phenomenon, known as nucleation, can be seen in the assembly of oligonucleotides to form double helical structures which is essentially an all-or nothing process once a critical chain length is reached. See D. Pörschke and M. Eigen, *J. Mol. Biol.*, 1971, **62**, 361; M. E. Craig, D. M. Crothers and P. Doty, *J. Mol. Biol.*, 1971, **62**, 383.
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