Co-operative stabilisation of a 15-component nanostructure

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2-Amino-4-(4-*tert*-butylphenylamino)-6-{4-[(4-pyridyl)ethynyl]phenylamino}-1,3,5-triazine was synthesised and mixed with dibutylbarbituric acid in $CDCl_3$ to study rosette formation. The formation of a double decker rosette aggregate was studied by complexation of the pyridyl groups to a zinc containing porphyrin dimer.

Keywords: rosette, porphyrin dimer, melamine, hydrogen bond

Molecular self-assembly involves the selective formation of discreet aggregates under equilibrium conditions using noncovalent bonds.[1] Assembly with noncovalent bonds is ubiquitious in biological systems leading to nanostructures such as membranes, proteins, ribosomes, DNA and RNA.[2] The evolution of life has depended upon noncovalent synthesis and the catalytic activity of some of the resulting aggregates. The design of artificial systems that mimic these processes is of interest to help understand the forces involved and represents a 'bottom up' approach to nanotechnology. In particular, the crystal structure of the cyanuric acid: melamine (CA.M) lattice[3] has provided a source of inspiration for the design of hydrogen bonded networks involving a multiple number of components.[4-10] The basic aggregate known as a rosette consists of six components and is held together by 18 hydrogen bonds. X-ray crystal structures formed between barbituric acid **1** or **2** and melamine **3** are both known.[11,12] The X-ray crystal structure of a double rosette aggregate is also known.[13] Unlike the CA.M lattice the rosettes are not planar and are considerably perturbed. It was of interest to us to see if two rosette motifs could be stabilised by noncovalent stacking rather than by using a covalently assembled backbone of melamine or cyanuric acid derivatives. Recently, a paper describing a similar objective appeared.[14]

This paper describes the cooperative stabilisation of a novel supramolecular rosette dimer formed by the stacking of two rosettes with a zinc containing porphyrin dimer.[15] This has two Zn atom binding sites that we studied previously to stabilise a hydrogen bonded porphyrin zip by binding to two 4(3*H*)-pyrimidones (Fig. 1).[16] Our group has studied complexes which require a combination of both pyridyl–Zn

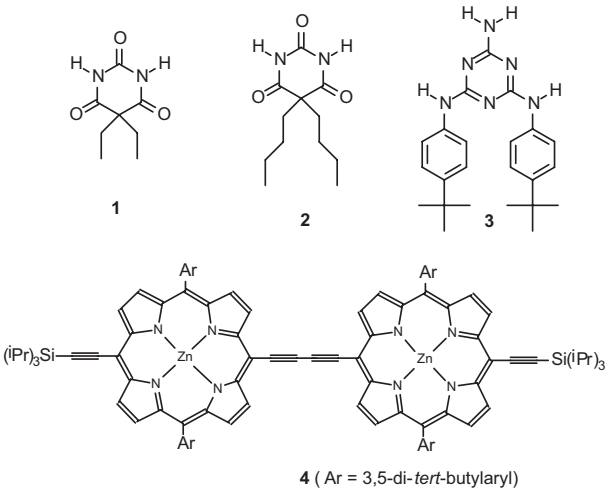
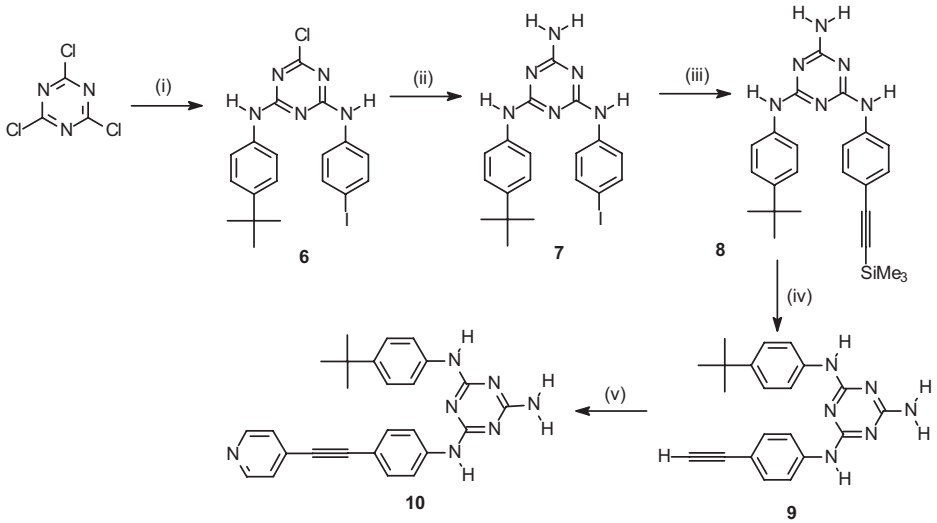


Fig. 1 Supramolecular building blocks.

atom and hydrogen bonding.[17] Others have studied higher oligomers with DABCO or bipyridyl which require only Zn-N atom binding.[18] Zinc is the atom of choice because it is diamagnetic and does not interfere wirh NMR measurements. Rosette formation was studied between the pyridyl substituted melamine **10** and dibutylbarbituric acid **2**. An acetylene spacer was added into structure **10** to ensure free binding to the porphyrin dimer **4** without any steric hindrance. Melamine **10** was prepared acording to Scheme 1. Trichlorotriazine **5** was treated consecutively with 4-*tert*-butylaniline and



Scheme 1 *Reagents and conditions:* (i) 4-tert-butylaniline and DIEA, then 4-iodoaniline/THF 74% (ii) NH3 (38%)/THF/100 0C 46% (iii) Me3SiC2H/(PPh3)2PdCl2/CuI/Et3N 79% (iv) NaOH/H2O/THF 98% (v) 4-BromopyridineHCl/(PPh3)2PdCl2/CuI/Et3N/∅ 17%

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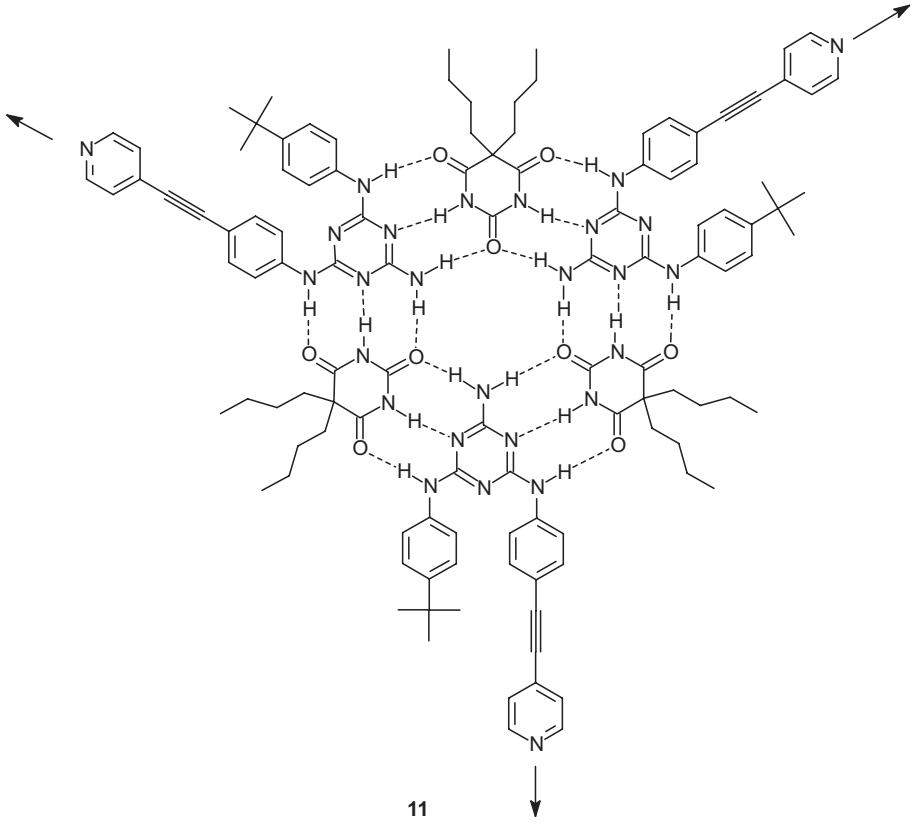

Fig. 2 Rosette formed from dibutylbarbituric acid **2** and melamine **10**.

4-iodoaniline. The ethnyl group was added by palladium catalysed coupling with trimethylsilyl acetylene followed by deprotection with dilute alkali in THF to give compound **9**. The ethynyl spacer was functionalised by palladium catalysed coupling to 4-bromopyridine hydrochloride to give pyridyl substituted melamine **10**. ^{1}H and ^{13}C NMR showed that two *tert*-butyl groups were present indicating the occurrence of rotamers. Rotamers were not observed for any of the preceding precursors. The NH group conjugated to the pyridyl ring may enhance the electron deficiency of the triazine ring allowing the other two NH groups to conjugate more strongly. This could lead to rotamers. Similar rotamers have been observed in 2-chloro-4,6-bis(pyrazolylamino)-1,3,5-triazines.[19]

A 1:1 mixture of melamine **10** and dibutylbarbituric acid **2** were dissolved in $CDCl_3$ with heating to give a clear yellow solution. No D_6DMSO was required which is normally required to dissolve up the melamine. This is indicative of rosette formation (Fig. 2). The imide protons of the barbituric acid moved from 9.0 ppm to 13.7 ppm and the NH protons of the melamine moved from 7.3 ppm to 9.4 ppm and from 4.9 ppm to 7.1 ppm. These chemical shifts are all characteristic of rosette formation. Two possible rosettes may form. It was not possible to detect the isomers. The porphyrin dimer **4** was then added in excess to the solution of the rosette in $CDCl_3$ in a 3:2 ratio to allow complexation of all the Zn and nitrogen atom sites. The chemical shifts of the α and β pyridine hydrogen atoms at 8.55 and 7.42 ppm moved to 2.9 and 5.8 ppm respectively (Fig. 3). The observed shielding is consistent with previous studies on the association of polymeric porphyrins with bipyridyl.[20] After taking the above spectra the solution was gradually diluted. No change in chemical shift of the above protons was observed until the spectrum could not be observed at all. This indicates the stability of a complex. Next a solution of the rosette **11** in $CDCl_3$ was titrated with aliquots of 0.2 equivalents of the zinc porphyrin dimer until the correct stoichiometric ratio of 2:3 (rosette to porphyrin) was achieved (Fig. 4). The movement of the β pyridyl hydrogen atom is plotted as a graph in Fig. 5. The linear change in chemical shift is as expected. Noteworthy is the broadening of the melamine NH protons at 9.6 ppm until they almost disappear and that the stoichiometry of the complex is three porphyrin dimers to two rosettes. Further titration did not change the chemical shift of the β pyridyl hydrogen atom. The melamine is already bound into a rosette so this change is evidence that two rosettes may be close enough to interact with each other. Figure 6 shows a drawing of the proposed supramolecular aggregate **12**. Two rosettes are stacked by three porphyrin dimers. This structure fits the observed NMR data. It contains 15 components held together by 36 hydrogen bonds and 6 coordinative bonds. Rotation of the rosettes in opposite directions would allow them to screw closer together removing cavity space and optimising the Van der Waals distance between them. The dimeric rosettes studied in great detail by Reinhoudte's group packed anti-parallel to each other[13] suggesting that the dimeric rosette proposed here will also have anti-parallel rings. Rosette isomers are unlikely to be present in the dimeric complex because lower symmetry would lower the stability. Since they would interconvert in solution if present they could equilibrate into the more symmetrical C_3 isomer. Further characterisation was sought by mass spectra. In electrospray or CI mode only the individual components were detected. Attempts at crystallisation produced only amorphous material.

In summary a new approach has been reported to form two stacked rosette motif's giving a 15 component nanostructure. The method differs from previous approaches because none of the individual rosette components are covalently bonded. In previous studies to form rosette stacks they always have been. This strategy reported here is flexible and may be adapted for further architectures. These results were reported in preliminary form previously.[21]

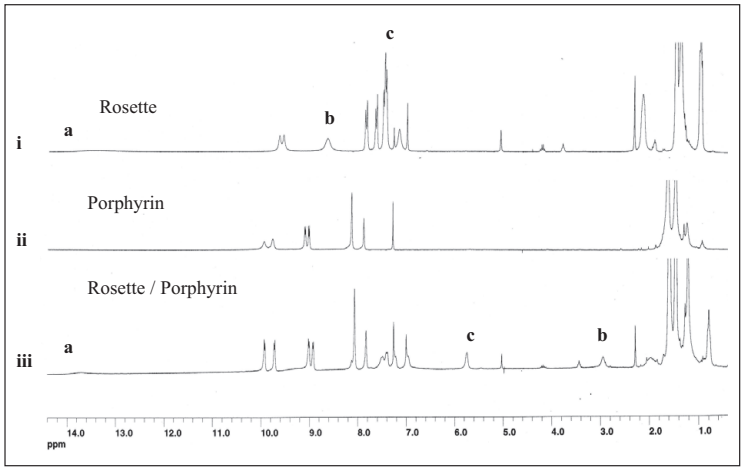

Fig. 3 ^{1}H NMR spectrum of (i) The rosette **11** (ii) Zinc porphyrin dimer **4** (iii) Rosette/porphyrin dimer complex **12** [a = δ_H imide; b = δ_H pyridyl H_α; c = δ_H pyridyl H_β].

Experimental

See previous paper for details of equipment.[22] DIEA is *N,N*-diisopropylethylamine.

2-Chloro-4-(4-tert-butylphenylamino)-6-(4-iodophenylamino)-1,3,5-triazine **6:** A stirred solution of cyanuric chloride **5** (1.24 g, 6.7 mmol) in anhydrous THF (40 ml) was cooled in an ice bath and treated with a solution of 4-*tert*-butylaniline (1.0 g, 6.7 mmol) and DIEA (0.87 g, 6.7 mmol) in THF (10 ml) over 20 min. The cloudy reaction mixture was left to rise to room temperature then heated with an oil bath to 50°C. This was followed by the addition of an equivalent of 4-iodoaniline (1.47 g, 6.7 mmol) and DIEA (0.87 g, 6.7 mmol) in THF (10 ml) to produce a clear yellow solution, after which stirring was continued at 50°C for 1 h. The reaction mixture was diluted with H_2O, extracted with CH_2Cl_2 (3 × 50 ml), dried over anhydrous Na_2SO_4, filtered and concentrated in vacuum to a yellow solid. This was washed several times with ethyl acetate to give the *title compound* (2.38 g, 74%) as a white powder, m.p. 219–220°C (from dichloromethane) ν_{max}(KBr)/cm^{-1} 3258br, 2961 m, 1617 m, 1593 s, 1567 s, 1510 s, 1485 s, 1405 m, 1382 m, 1232 m, 1008 m, 821 m and 796 m; δ_H(250 MHz; DMSO-d_6) 1.2 (9H, s, $C(CH_3)_3$), 7.32 (2H, br d, Ph), 7.36 (2H, br d, Ph), 7.45 (2H, br d, Ph), 7.6 (2H, br d, Ph) and 10.23 (2H, m, 2 × NH); δ_c(62.9 MHz; DMSO-d_6) 31.2, 34.1, 87.1, 121.5, 123.0, 125.2, 137.1, 137.3, 138.4, 163.8, 163.9 and 168.2 (1 resonance is missing); *m/z* (ES$^+$) 480.0455 ([M]$^+$, $C_{19}H_{19}N_5ClI$ requires 480.0446); *m/z* (CI$^+$) 480.1 (M$^+$, 70%), 354.2 (96) and 320.3 (100).

2-Amino-4-(4-tert-butylphenylamino)-6-(4-iodophenylamino)-1,3,5-triazine **7:** 2-Chloro-4,6-bis(4-*tert*-butylphenylamino)-1,3,5-triazine (0.5 g, 1.26 mmol) in 38% ammonia (5 ml) and tetrahydrofuran (8 ml) was sealed in a pyrex pressure bottle and placed under sand in a container. This was then placed in an oven at 100°C for 3 h. The oven was left to cool overnight after which a white precipitate was filtered and washed with water to give the title compound (0.22 g, 46%) as a white powder, m.p. 237–238°C (from water) ν_{max}(KBr)/cm^{-1} 3402 m, 2958 m, 1610 s, 1564 s, 1498vs, 1398 s, 1235 m and 816 m; δ_H(250 MHz; DMSO-d_6) 1.26 (9H, s, $(CH_3)_3$), 6.58 (2H, s, NH_2), 7.26 (2H, d, *J* = 8.9, Ph), 7.62 (6H, m, Ph), 8.99 (1H, s, NH) and 9.14 (1H, s, NH); δ_C(62.9 MHz; DMSO-d_6) 31.3, 33.9, 84.4, 120.2, 122.1, 124.8, 136.9, 137.4, 140.4, 144.2, 164.4, 164.5 and 166.8; *m/z* (EI) 460.0870 (M$^+$, $C_{19}H_{21}N_6I$ requires 460.0867); *m/z* (EI) 460.2 ([M$^+$, 80%) and 445.2 (100).

2-Amino-4-(4-tert-butylphenylamino)-6-[4-(trimethylsilylethynyl)phenylamino]-1,3,5-triazine **8:** A degassed solution of compound **7** (0.5 g, 1.1 mmol), trimethylsilylacetylene (0.44 g, 4.5 mmol), $(PPh_3)_2PdCl_2$ and copper(I)iodide in catalytic amounts in anhydrous THF (40 ml) under anhydrous conditions were treated with freshly distilled Et_3N (4 ml). The reaction mixture was refluxed for 5 h, then concentrated and redissolved in THF and filtered through a silica plug. The concentrated filtrate was slurried with cold EtOH and refiltered and dried in a vacuum oven to yield the title compound (0.38 g, 79%) as a dark grey powder, m.p. > 250°C (decomp.) (from dichloromethane); λ_{max}(DMSO)/nm 298 (log ε 4.6); ν_{max}(KBr)/cm^{-1} 3406 m, 3320br, 2960 m, 2157 m, 1619 m, 1570 s, 1502 s, 1409 s, 1248 s, 868 s, 840 s, 760w, 644w, 551w, and 541w; δ_H(250 MHz; DMSO-d_6) 0.21 (9H, s, $Si(CH_3)_3$), 1.27 (9H, s, $C(CH_3)_3$), 6.7 (2H, br s, NH_2), 7.30 (4H, m, Ph), 7.60 (2H, br d, Ph), 7.81 (2H, br d, Ph), 9.07 (1H, s, NH) and 9.31 (1H, s, NH); δ_c(62.9 MHz; DMSO-d_6) 0.1, 31.3, 33.9, 92.4, 106.1, 114.6, 120.4, 120.8, 125.1, 132.0, 137.3, 141.2, 144.3, 164.1, 164.2 and 166.53; *m/z* (EI) 430.2295 (M$^+$, $C_{24}H_{30}N_6Si$ requires 430.2296), *m/z* (EI) 430.3 (M$^+$, 100%) and 415.3 (92).

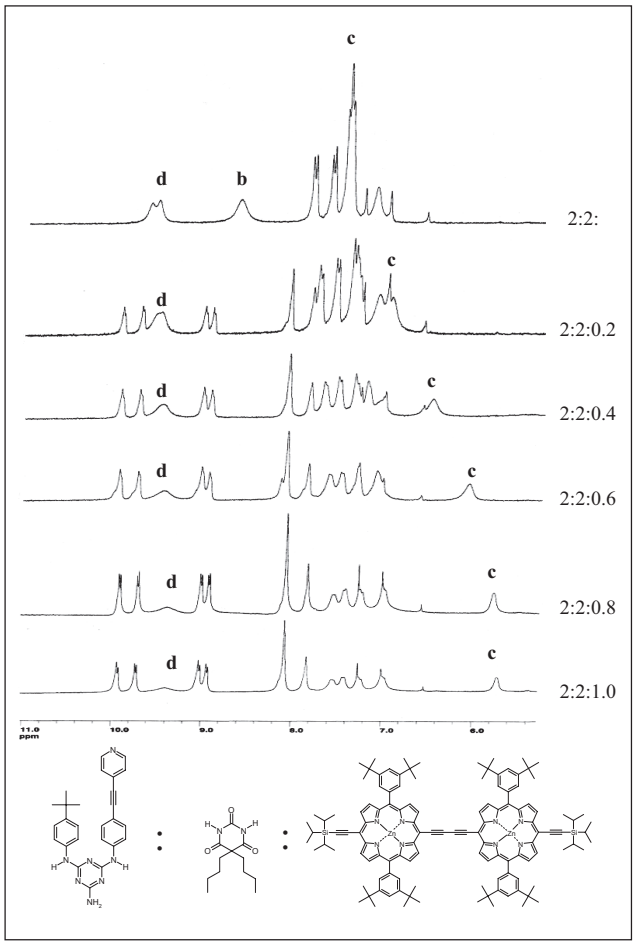

Fig. 4 ^{1}H NMR spectra of a titration of rosette **11** with the zinc porphyrin dimer **4** [b = δ_H pyridyl H_α; c = δ_H pyridyl H_β; d = δ_H melamine NH]. 100% rosette (top) and 2:1 complex (bottom).

2-Amino-4-(4-tert-butylphenylamino)-6-(4-ethynylphenylamino)-1,3,5-triazine **9:** A solution of compound **8** (1.0 g, 2.3 mmol) and NaOH (0.37 g, 9.3 mmol) in H_2O (30 ml) and THF (40 ml) was stirred for 1 h. The THF was removed from the reaction mixture *in vacuo* and the resulting precipitate was collected by filtration, washed

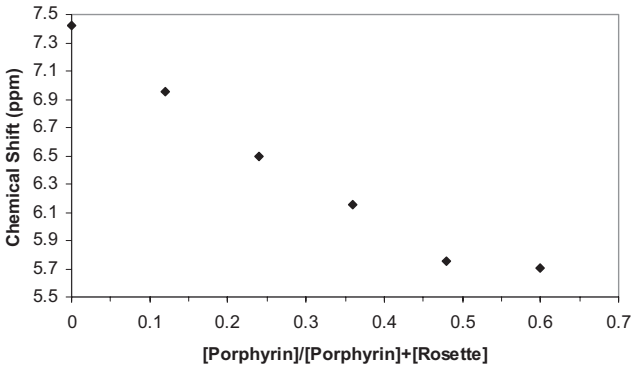

Fig. 5 Plot of the chemical shift of the pyridyl H_β atoms versus the mole fraction of porphyrin.

with H_2O, and dried in a vacuum oven to yield the title compound (0.82 g, 98%) as a grey powder, m.p. 209–211°C (from methanol) λ_{max}(DMSO)/nm 280 (log ε 4.3); ν_{max}(KBr)/cm^{-1} 3406 m, 3299 m, 3190br, 2962 m, 1620 m, 1571 s, 1500 s, 1410 s, 831 m, 809 m, 801 m, 552 m and 536 m; δ_H(250 MHz; DMSO-d_6) 1.26 (9H, s, C(CH_3)$_3$), 4.05 (1H, s, acetylenic H), 6.70 (2H, br s, NH_2), 7.30 (4H, m, Ph), 7.60 (2H, br d, Ph), 7.80 (2H, br d, Ph), 9.05 (1H, s, NH) and 9.30 (1H, s, NH); δ_c(62.9 MHz; DMSO-d_6) 31.3, 38.5, 79.5, 84.1, 113.9, 119.2, 120.2, 125.1, 132.0, 137.4, 141.3, 144.2, 163.3, 164.5 and 166.8; *m/z* (ES$^+$) 359.1976 ([M$^+$ + H], $C_{21}H_{22}N_6$ requires 359.1979); *m/z* (EI$^+$) 358.2 (M$^+$, 71%) and 342.2 (100).

2-Amino-4-(4-tert-butylphenylamino)-6-{4-[(4-pyridyl)ethynyl] phenylamino}-1,3,5-triazine **10:** A degassed solution of compound **9** (0.5 g, 1.4 mmol), 4-bromopyridine hydrochloride (0.28 g, 1.5 mmol), $(PPh_3)_2PdCl_2$ and copper(I)iodide in catalytic amounts; in freshly distilled Et_3N (40 ml) was refluxed for 1 day under anhydrous conditions. The reaction mixture was then concentrated and dry-loaded onto a column with THF. The column was eluted with dichloromethane then with tetrahydrofuran to give the crude product. Repeated extraction into ethyl acetate and concentration followed by drying in a vacuum oven at 50°C gave the title compound (100 mg, 17%) as a yellow/orange crystalline solid, m.p. 140–144°C (from tetrahydrofuran) λ_{max}(DMSO)/nm 272 (log ε 4.4), 333 (4.1); ν_{max}(KBr)/cm^{-1} 2412 m, 3335 m, 3956 m, 2214 m, 1565 s, 1490vs, 1412 s, 1238 m and 825 m; δ_H(250 MHz; DMSO-d_6) 1.30 (18 d, C(CH_3)$_3$), 6.66 (2H, br s, NH_2), 7.28 (2H, d, J = 8.9, Ph), 7.48 (4H, m, Ph), 7.63 (2H, br d, Ph), 8.6 (2H, br d, Ph), 9.06 (1H, s, NH) and 9.36 (1H, s, NH); δ_c(62.9 MHz; DMSO-d_6) (30.4, 31.3), (33.9, 34.4), 85.8, 94.8, 113.2, 120.2, 120.3, 124.9, 128.1, 132.2, 137.4, 139.2, 142.1, 144.2, 151.5, 164.3, 164.5 and 166.8; *m/z* (ES) 436.2242 ([M]$^+$, $C_{26}H_{26}N_7$ requires 436.2244), *m/z* (EI) 435.3 (M$^+$, 75%) and 420.3 (100).

Mass spectra were obtained by the EPSRC National Mass Spectrometry Service Centre. Funding was from the University of Aberdeen.

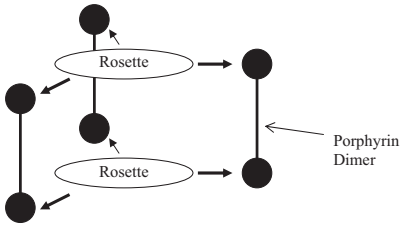

Fig. 6 Artists sketch of the predicted dimeric aggregate formed from rosette **11** and zinc porphyrin dimer **4.**

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