Dynamic synthesis of a macrocycle containing a porphyrin and an electron donor†

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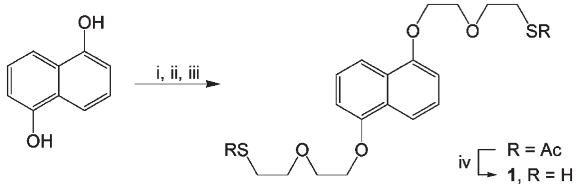
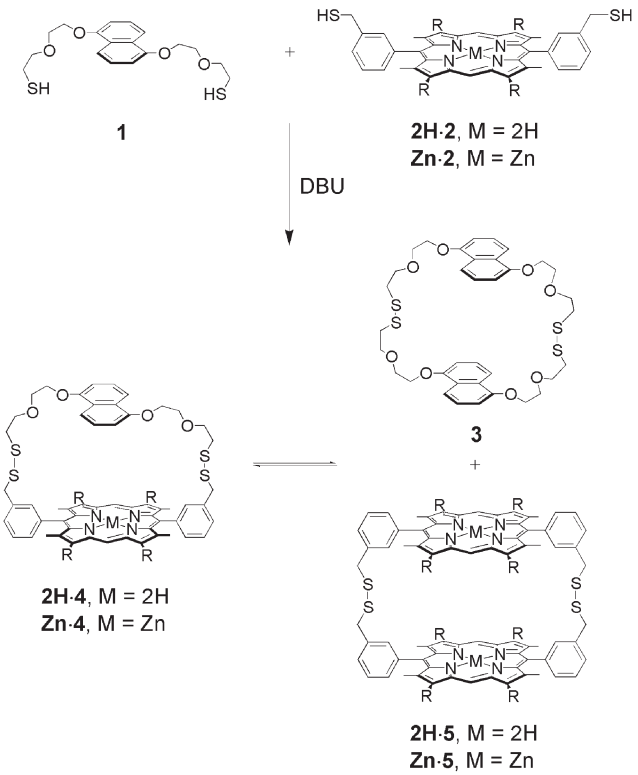
New macrocycles incorporating a porphyrin and a π electron-rich aromatic were prepared from a dynamic disulfide library. The outcome could be influenced by use of templates.

Supramolecular assemblies have been used in biomimetic photodynamic systems that seek to replicate both rapid electron transfer processes and efficient charge-separation.[1,2] These are fundamental characteristics of photosynthetic model systems and artificial photosynthesis devices. While there have been many examples of covalently-linked donor–acceptor systems,[3–5] access to such structures is often limited by intricate synthesis. Thus, non-covalently linked donor–acceptor complexes have been investigated as a way to overcome such obstacles.[6–8]

We have systematically developed super-structured interlocked porphyrins using conventional chemical approaches and explored their binding properties.[6,9] We now report the efficient synthesis of a new porphyrin-containing macrocycle assembled by reversible thiol–disulfide exchange.[10,11] The new building block **1** was synthesised in four steps according to Scheme 1; porphyrins **2H·2** and **Zn·2** were obtained *via* a previously established route.[12] Libraries were set up using 5 mM solutions of building blocks **1** and **Zn·2** in $CHCl_3$, and 0.2 eq. DBU. Thermodynamic equilibrium was reached in 5 days, as observed by HPLC. A minimum of three cyclic products were expected: dimer **3**, mixed dimer **Zn·4** and bis-porphyrin dimer **Zn·5** (Scheme 2). No products due solely to naphthyl species were found, although traces of higher oligomers were observed, in addition to **Zn·4** and **Zn·5**. Fractions of the two main components **Zn·4** and **Zn·5** were isolated and MALDI-TOF analysis showed parent ions at m/z = 1374.6 for **Zn·4** and at m/z = 2016.9 for **Zn·5**. By HPLC, the ratio of the two products was 4:1 heterodimer **Zn·4** to homodimer **Zn·5**.[13] This non-statistical distribution suggests a stabilising interaction that preferentially favours the formation of macrocycle **Zn·4**. The same experiment using the free base porphyrin monomer **2H·2** showed that the heterodimer is again the favoured product and that larger oligomers are somewhat more accessible (Table 1).



Scheme 1 i) 2-(2′-Chloroethoxy)ethanol, K_2CO_3, MeCN, 82 °C, 98%; ii) *p*-toluenesulfonyl chloride (TsCl) 2.2 eq., NEt_3 3 eq., 10% dimethylaminopyridine (DMAP), CH_2Cl_2, 25 °C, 98%; iii) KSAc, MeCN, 82 °C, 33%; iv, NH_2NH_2·OAc, CH_2Cl_2, 95%.



Scheme 2 Reaction of a two component library. Conditions: 5 mM solutions of building blocks **1** and **2H·2** or **Zn·2** (1:1 ratio) and 0.2 eq. DBU.

Templated libraries were set up using 1 eq. or 5 eq. of hexyl-substituted naphthyldiimide **6** as a guest, and the product distribution was again monitored by HPLC (Table 1). When the libraries were equilibrated in the presence of a five-fold excess of **6**, the homoporphyrin dimers **M·5** (M = 2H or Zn) were preferred, *i.e.* 53% yield when M = Zn and 61% when M = 2H.

The template-containing products are pseudorotaxanes since it is expected that the naphthyl guest inserts between the porphyrin planes (for **M·5**) or the porphyrin plane and the naphthyl cap (for **M·4**) to maximise the stabilising π–π interactions.[6,14] Since we have demonstrated earlier[15] the use of alkali halides as templates for the association of crown ethers with similar naphthyl guests, we

† Electronic supplementary information (ESI) available: experimental section. See http://www.rsc.org/suppdata/cc/b4/b418811j/

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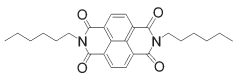
Table 1 Yields of the oligomers in porphyrin–naphthoquinol libraries based on HPLC analysis

Experiment	Conditions	Product M·4	Product M·5	Larger oligomers
1	**Zn·2**	—	87	13
2	**Zn·2** + **6** (1 eq.)	—	96	4
3	**1** + **Zn·2**	81	19	—
4	**1** + **Zn·2** + **6** (1 eq.)	79	21	—
5	**1** + **Zn·2** + **6** (5 eq.)	47	53	—
6	**1** + **Zn·2** + **6** (1 eq.) + LiBr (10 eq.)	77	23	—
7	**1** + **Zn·2** + **6** (1 eq.) + NaBr (10 eq.)	87	13	—
8	**1** + **2H·2**	92	5	3
9	**1** + **2H·2** + **6** (1 eq.)	75	24	1
10	**1** + **2H·2** + **6** (5 eq.)	39	61	—



investigated here the ability of lithium or sodium cations to promote the amplification of the receptor **Zn·4**. While the use of Li^+ did not significantly affect the yield of the heterodimer **Zn·4**, the effect of Na^+ on the equilibrium composition led to an 8% increase of the heterodimer **Zn·4** at the expense of the homodimer **Zn·5** (Table 1). Li^+ is probably too small for the receptor's cavity. Both systems reached equilibrium in 2 days instead of 5 as in the absence of the alkali salt. This is a new mode of templating within porphyrin libraries and an exciting addition to the tools available for supramolecular synthesis.

All results achieved on the analytical scale were reproduced on the preparative scale. In solution, ^{1}H NMR spectra of **Zn·4** and **2H·4** indicated highly symmetrical conformations (240 K–340 K, 500 MHz, $CDCl_3$) with a fast rotation of the naphthyl moiety (on the NMR time-scale). NOE experiments provided evidence that the ethylene glycol chain and the naphthyl ring are strapping across the face of the porphyrin. At temperatures below 230 K ^{1}H NMR spectra indicated 'closed up' conformations of **Zn·4** and **2H·4**. The orientation of naphthoquinol with respect to the porphyrin plane is closer to perpendicular thus maximising the π–π interactions. Significant chemical shifts are given in supplementary materials.†

In each case the X-ray structures‡ of **Zn·4** and **2H·4** confirm that the ethyloxy chains are strapped over the face of the saddled porphyrins (Fig. 1). The conformations observed at low temperature by ^{1}H NMR experiments are maintained in the solid-state. The naphthyl rings are held above the plane of the porphyrin by the glycol straps, aligned along, although slightly offset from, one N–N axis. In this strapped conformation the C–Hs of the naphthyl have a close approach to the electron cloud above the plane of the porphyrin, as indicated by NMR experiments. This geometry allows the maximisation of attractive interactions whilst minimising the electron–electron repulsion. The lower carbons of the naphthyl ring are located at 3.501(1) and 3.511(1) Å (**Zn·4**) and 3.488 and 3.601 Å (**2H·4**) above the best-fit porphyrin planes. This suggests that there is a significant CH–π interaction between the porphyrin aromatic ring and the naphthyl hydrogens giving edge-to-face (T-type) π-stacking geometries.[14,16,17] The naphthyl ring is closer to perpendicular to the mean plane of the porphyrin in **2H·4** than in **Zn·4**, with an angle between the mean plane of the naphthyl ring and the mean porphyrin plane of 80.33(1)° in the former *vs* 64.83(1)° in the latter. In the crystal structures of **M·4** the porphyrins pack in a π-stacked fashion, uncapped sides together, and the naphthyl rings also π-stack with each other. Unlike **Zn·4**, where the porphyrins that π-stack are rotated by 90° with respect to each other, the porphyrins in **2H·4** are not rotated. In each case, the porphyrin planes are offset by *ca.* 3.5 Å in the classical manner.

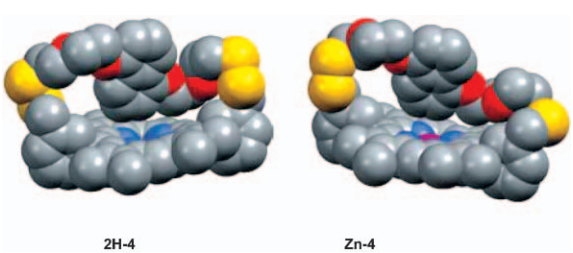


Fig. 1 Molecular structures of the **M·4** receptors (hydrogen atoms and hexyl chains are omitted for clarity).

In summary, we have discovered an extremely efficient dynamic synthesis of a new macrocycle and have shown that the naphthyldiimide template **6** amplifies the best-fit library members (with the most effective π–π host–guest stacking) which unexpectedly, in this case, were the bis-porphyrin receptors **M·5**. The weaker π–π stacking of this guest inside the heterodimer **Zn·4** was strengthened when additional interactions (coordination of Na^+ cations to the glycol chains of the receptor) were introduced.

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Notes and references

‡ Crystals were grown from a $CHCl_3$ solution of receptor layered with MeOH. Data were collected at 180 K on a Nonius KappaCCD with graphite monochromated Mo Kα radiation (λ = 0.71073 Å). The images were processed with the DENZO and SCALEPACK programs.[18] The structures were solved by direct methods using the program SIR92.[19] The refinement (on *F*) and graphical calculations were performed using the CRYSTALS[20] program suite.

Zn·4 (two independent molecules in the asymmetric unit): $C_{160}H_{200}N_8O_8S_8Zn_2$, M = 2750.69, Z = 2, triclinic, space group $P\bar{1}$, a = 17.5480(4) Å, b = 19.9870(5) Å, c = 25.2150(9) Å, α = 95.4860(11)°, β = 99.0310(11)°, γ = 106.4290(13)°, U = 8285.5(4) Å^3, T = 180(2) K, μ = 0.445 mm^{-1}. Of 52898 reflections measured, 21019 were independent (R_{int} = 0.15). Final R = 0.1479 [7822 reflections with $I > 3\sigma(I)$] and wR = 0.1594. Treatment of 0.5 molecules of CH_3CN and 1.5 molecules of H_2O (disordered) per asymmetric unit was performed using the procedure described by Spek *et al.*[21] implemented in PLATON.[22] Thus the structure contains solvent accessible voids of 230.00 A^3. Identification of the crystallising solvents is based upon additional chemical evidence from ^{1}H NMR.

2H·4 (two independent molecules in the asymmetric unit): $C_{160}H_{204}N_8O_8S_8$, M =2623.96, Z = 2, triclinic, space group $P\bar{1}$, a = 15.45070(10) Å, b = 18.8773(2) Å, c = 26.9207(3) Å, α = 90.5208(3)°, β = 99.9292(3)°, γ = 102.8035(4)°, U = 7532.83(12) Å^3, T = 180(2) K, μ = 0.176 mm^{-1}. Of 106913 reflections measured, 26438 were independent

(R_{int} = 0.17). Final R = 0.1055 [12878 reflections with $I > 3\sigma(I)$] and wR = 0.1243. Both **Zn·4** and **2H·4**, yielded extremely weakly diffracting crystals; disorder of *S*-alkyl chains (modelled with refined occupancies and restraints on distances, vibrations and temperature factors) and hexyl chains (modelled with restraints on distances, vibrations and temperature factors) account for the high R factors.

CCDC 256715 and 256716. See http://www.rsc.org/suppdata/cc/b4/b418811j/ for crystallographic data in CIF or other electronic format.

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