Letter

# Effect of the inclusion of sodium cations on the binding properties of a switchable diporphyrin receptor<sup>†</sup>

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The nestling of Na<sup>+</sup> within the oligooxaethylene frame of the switchable diporphyrin receptor 1Zn results in an allosteric effect on the binding of ditopic amines, and remarkably influences the ligand-induced chiroptic properties of the assembly upon inclusion of chiral ditopic guests.

Diporphyrin and oligoporphyrin systems are regarded as excellent tools for the molecular recognition of organic guest molecules.<sup>1</sup> In particular, chiral diporphyrin systems have been successfully employed in the enantiomeric discrimination of amino acid derivatives.<sup>2</sup> Moreover, diporphyrin tweezers constitute interesting devices for the determination of the absolute configuration of amines, amino acids and derivatives.<sup>3</sup>

We recently reported<sup>4</sup> that simple oligooxaethylenespacered diporphyrin arrays undergo a conformational change toward a cofacial geometry upon coordination of alkali metal ions within the ether framework of the receptor. We surmised that this geometrical variation would result in a change of the binding properties of a related zinc derivative toward the inclusion of bifunctional guests (G). In this paper we wish to report on the effect of the inclusion of Na<sup>+ 5</sup> on the binding features of the above mentioned diporphyrin receptor toward some bidentate amines, i.e. trans-1,2-diaminocyclohexane (1,2-DACy, racemic mixture), and 4,4'-bipyridyl (bpy). The results obtained evidence the presence of an allosteric effect exerted by the complexed metal ion, which promotes the attainment of a more rigid structure  $(1Zn \cdot Na@G, Scheme 1)$ . These studies have been extended to the chiral (+)- and (-)-1, 2-DACy stereoisomers evidencing an interesting effect on the ligand-induced chiroptic properties of the resulting supramolecular assemblies.

Diporphyrin derivative 1Zn, and its monotopic counterpart 2Zn, have been synthesised by following a previously published procedure.<sup>5,6</sup> The derivative 1Zn has been found to be a good receptor for several ditopic amines.<sup>7</sup> We focused our attention on bpy and 1,2-DACy owing to their different structural and coordination properties.<sup>8</sup> The formation of the host–guest inclusion complexes was carried out in CH<sub>3</sub>CN–CHCl<sub>3</sub> (90 : 10, v/v). The formation of 1Zn · Na@G adducts was conveniently monitored by following the typical red-shift of the Q visible bands of the porphyrin macrocycles.<sup>‡</sup>

points to a 1:1 binding isotherm<sup>9</sup> to give the corresponding values of the association constants. The binding studies have been carried out with **2Zn** for comparison. The results are reported in Table 1. As expected, receptor **1Zn** binds to the considered ligands more strongly than its monotopic **2Zn** counterpart. On inspection of Table 1 the overwhelming effect of the donor ability of the ligands<sup>10</sup> on the strength of the binding is evident, the relative K values being  $7.3 \times 10^4$  and  $2.6 \times 10^5$  M<sup>-1</sup> for bpy and 1,2-DACy respectively. The corresponding values of effective molarity (EM)<sup>11a</sup> are  $2 \times 10^{-2}$ 



Scheme 1 Schematic structure of the  $1Zn \cdot Na@G$  supramolecular ternary complex. Phenyl rings have been emitted for clarity.

**Table 1** Binding constant values (*K*) for the interaction of amine guests with porphyrin receptors, in  $CH_3CN-CHCl_3$  (90 : 10, v/v) at  $T = 25 \,^{\circ}C$ 

Entry	Receptor	Guest	$K/M^{-1}$ (EM <sup>a</sup> /M)
1	1Zn	bpy	$7.3 \times 10^4 (2.0 \times 10^{-2})$
2		$bpy^b$	$1.1 \times 10^4 (3.0 \times 10^{-3})$
3		bpy <sup>c</sup>	$7.3 \times 10^4 (2.0 \times 10^{-2})$
4		1,2-DACy	$2.6 \times 10^5 (3.0 \times 10^{-4})$
5		1,2-DACy <sup>b</sup>	$4.5 \times 10^5 (5.0 \times 10^{-4})$
6	2Zn	bpy <sup>d</sup>	$9.0 \times 10^{2}$
7		1,2-DACy <sup>d</sup>	$1.5 \times 10^{4}$

<sup>*a*</sup> Effective molarity values are reported in parentheses. <sup>*b*</sup> In the presence of NaClO<sub>4</sub> 0.05 M. <sup>*c*</sup> In the presence of Bu<sub>4</sub>NClO<sub>4</sub> 0.05 M. <sup>*d*</sup> The values of K obtained in the presence of NaClO<sub>4</sub> 0.05 M were identical within experimental error.

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<sup>&</sup>lt;sup>†</sup> Electronic supplementary information (ESI) available: full experimental details, NMR labelling scheme for the porphyrin derivatives and UV-visible spectra of 12n@G in the presence of added NaClO<sub>4</sub>. See http://www.rsc.org/suppdata/nj/b1/b102904p/

and  $3 \times 10^{-4}$  M. The EM value estimated in the case of the binding of bpy lies fairly well within the calculated range for a strainless ring closure reaction,<sup>11b,c</sup> whereas the corresponding value for the interaction of 1,2-DACy is about two orders of magnitude lower than that expected. This may indicate that the formation of the latter pseudo-cyclic assembly, owing to the shorter N-N distance of the guest, occurs with some degree of ring strain.<sup>12</sup> The complexation studies were also performed in the presence of added Na<sup>+</sup>,¶ which is known to promote a conformational change of the resulting supramolecular complex toward a pseudo-cyclic structure  $(1Zn \cdot Na)$ <sup>4,5,13</sup> This affects the binding of a given guest by virtue of the tuned preorganisation of the receptor. This is indeed the case for the inclusion of 1,2-DACy, which features a two-fold increase of the binding constant K in the presence of the added cation.<sup>14</sup> Conversely, in the case of the inclusion of the "longer" guest, i.e. bpy, a negative allosteric effect is found. A decrease in K by nearly one order of magnitude is in fact observed, and this can be interpreted in terms of a less favourable interaction of bpy within the less flexible cavity of the host. || The magnitude of these effects is in line with other reports which have recently appeared in the literature,<sup>15</sup> in which the inclusion of some alkali metal ions results in a positive effect on the binding of halides to some ditopic receptors. The allosteric effect is also nicely evident in the CD experiments relative to the binding of chiral diamine guests such as (1R,2R)-(-)-1,2-diaminocyclohexane, and (1S,2S)-(+)-1,2diaminocyclohexane  $[(\pm)G^*]$  stereoisomers. The binding results in the formation of extrinsically chiral supramolecular host-guest complexes  $[1Zn(a)(\pm)G^*]$  as evidenced by the exciton-coupled CD of the interacting porphyrin chromophores.<sup>16</sup> The chiroptic properties of the resulting assemblies are modulated by the absolute configuration of the guest. The inclusion of the (-) isomer, for example, results in a negative bisignate CD spectrum, whereas in the case of the (+) enantiomer a mirrored positive spectrum is observed. Remarkably, the presence of Na<sup>+</sup> results in an increased CD amplitude of the spectra (Fig. 1), as witnessed by the relative  $\Delta \varepsilon$  values for the complex with (-)G\* of -415 and -620 L mol<sup>-1</sup> cm<sup>-1</sup> for 1Zn and  $1Zn \cdot Na$ , respectively, at 436 nm.<sup>17</sup> This finding confirms the hypothesis of the formation of a tighter supramolecular structure, which features a higher degree of ellipticity.<sup>18</sup> Finally, the inclusion of Na<sup>+</sup>, resulting in a more rigid system, promotes an appreciably increased stability of the supramolecular complex toward the presence of an excess (up to 100 equivalents) of the title diamine.\*\*

The cation-induced conformational change of a flexible diporphyrin host results in an allosteric effect toward the binding of ditopic amine ligands, which is dependent on the structural properties of the guests. The interaction with chiral



diamines results in the formation of a supramolecular chiral complex, which features increased ellipticity and stability in the presence of Na<sup>+</sup>. This would have promising application in the construction of receptors and sensors for substrates with biological activity. Further studies on the effect of the inclusion of different metal ions toward the binding of a larger class of ditopic guests are currently under investigation in our laboratories.

### Experimental

#### Syntheses

**Zinc**[**5**-(**4**-hydroxy-3-methoxyphenyl)-10,15,20-triphenylporphyrinato], **2Zn.** <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 9.0–8.9 (m, 8H, β-H), 8.2 (br s, 6H, *o*-C<sub>6</sub>H<sub>5</sub>), 7.7 (br s, 6H, *m*-C<sub>6</sub>H<sub>5</sub>), 7.3–7.2 (m, 6H, C<sub>6</sub>H<sub>5</sub> + aromatics), 3.97 (s, 3H, OCH<sub>3</sub>). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 150.5 (C-α), 150.2 (C-α), 142.9 (C-1″), 134.5 (C-2″, C-6″), 132.0 (C-β), 127.9 (C-4″), 127.5 (C-3″, C-5″), 126.6 (C-β), 121.1 (C*meso*), 117.5 (C-5′), 112.6 (C-2′), 56.2 (CH<sub>3</sub>O). UV-vis (CHCl<sub>3</sub>),  $\lambda_{max}$ /nm (log  $\varepsilon$ ): (Soret, 5.8), 490 (4.1), 552 (3.9). FAB-MS (NBA), *m*/*z*: 723 [M]<sup>+</sup>.

**1,11-Bis**[zinc(2-methoxy-4-(10,15,20-triphenylporphyrinato)phenoxy]-3,6,9-trioxaundecane, 1Zn. <sup>1</sup>H-NMR (CDCl<sub>3</sub>): δ 9.0–8.8 (m, 8H, β-H), 8.18 (br s, 6H, aromatics), 7.7–7.6 (m, 12H, aromatics), 7.65 (d, J = 8.4 Hz, 1H, aromatics), 4.33 (br t, J = 4.8 Hz, 2H, OCH<sub>2</sub>CH<sub>2</sub>O), 3.96 (br t, J = 4.8 Hz, 2H, OCH<sub>2</sub>CH<sub>2</sub>O), 3.89 (s, 3H, CH<sub>3</sub>O), 3.7 (m, 4H, OCH<sub>2</sub>CH<sub>2</sub>O). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): δ 150.3 (C-α), 150.1 (C-α), 150.0 (C-α), 147.9 (C-3'), 147.3 (C-4'), 143.0 (C-1''), 136.1 (C-1'), 134.4 (C-2''), 131.8 (C-β), 127.3 (C-3''), 126.4 (C-β), 122.1 (C-6'), 120.8 (Cmeso), 120.7 (C-meso), 118.7 (C-5'), 111.5 (C-2'), 70.9 (CH<sub>2</sub>CH<sub>2</sub>O), 70.7 (CH<sub>2</sub>CH<sub>2</sub>O), 69.8 (CH<sub>2</sub>CH<sub>2</sub>O), 68.6 (CH<sub>2</sub>CH<sub>2</sub>O), 56.0 (OCH<sub>3</sub>). UV-vis (CHCl<sub>3</sub>),  $\lambda_{max}$ /nm (log ε): 423 (6.1, Soret), 551 (4.3), 594 (4.1). FAB-MS (NBA), *m*/*z*: 1604 [M]<sup>+</sup>.

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#### Notes and references

‡ Evidence for a 1:1 **1Zn**@G complex formation was given by the presence of several well-defined isosbestic points and by a continuous variation plot (Job plot) which shows a sharp inflection point at  $\chi(G) = 0.5$ .

§ The EM calculation has been made on the assumption that the cyclic complexes with bpy and 1,2-DACy posses 19 and 20 rotors (*i.e.* freely rotating single bonds), respectively.

¶ From the binding constant value for the interaction of Na<sup>+</sup> with the porphyrin receptor ( $K_{ass} = 500 \text{ M}^{-1}$ , see ref. 4) it can be estimated that the predominant species is the complexed form (**1Zn** · Na) at the chosen cation concentration (0.05 M).

|| The fact that, in a separate experiment, the addition of an excess (up to 0.05 M) of  $Bu_4NClO_4$  does not influence the strength of the binding of 1,2-DACy to 1Zn, safely rules out the occurrence of effects due to the increased ionic strength of the medium. Moreover, the invariance of the *K* values for the binding of bpy to the reference 2Zn receptor in the presence of Na<sup>+</sup> (see entry 6, Table 1) excludes the possibility that the reduced degree of binding observed would be a mere consequence of a Lewis acid-base interaction of the ligand with the sodium cation.

\*\* Related structures, in fact, are known to be unstable, in the presence of an excess of added ligands, toward the conversion into linear oligomers [see, for example, ref. 3(*a*)].



- (a) H. Ogoshi, T. Mizutani, T. Hayashi and Y. Kuroda, Porphyrins and Metalloporphyrins as receptor models in Molecular Recognition, in The Porphyrin Handbook, ed. K. M. Kadish, K. M. Smith and R. Guilard, Academic Press, London, 2000, vol. 6, ch. 46. p. 279; (b) W. Verboom and D. N. Reinhoudt, Simultaneous Binding of Cation and Neutral Molecules, in Comprehensive Supramolecular Chemistry, ed. J. L. Atwood, J. E. Davies, D. D. MacNicol and F. Vögtle, Elsevier Science Publications, Oxford, 1996, vol. 2, ch. 16, p. 495.
- 2 (a) M. J. Crossley, L. G. Mackay and A. C. Try, J. Chem. Soc., Chem. Commun., 1995, 1925; (b) for a recent overview on the chiral recognition of porphyrin derivatives see: H. Ogoshi and T. Mizutani, Acc. Chem. Res., 1998, 31, 81; (c) for a report on the memory effect on chiral recognition of porphyrins see: Y. Mizuno, T. Aida and K. Yamaguchi, J. Am. Chem. Soc., 2000, 122, 5278.
- (a) X. Huang, B. Borhan, B. H. Rickman, K. Nakanishi and N. Berova, Chem. Eur. J., 2000, 6, 216; (b) X. Huang, B. H. Rickman, B. Borhan, N. Berova and K. Nakanishi, J. Am. Chem. Soc., 1998, 120, 6185; (c) H. Jiang, X. Huang, K. Nakanishi and N. Berova, Tetrahedron Lett., 1999, 40, 7645; (d) H. Tamiaki, N. Matsumoto and H. Tsukube, Tetrahedron Lett., 1997, 38, 4239; (e) for boronic acid diporphyrin tweezers in the recognition of sugar derivatives see: M. Takeuchi, T. Imada and S. Shinkai, J. Am. Chem. Soc., 1996, 118, 10658.
- 4 D. Monti, M. Venanzi, G. Mancini, F. Marotti, L. La Monica and T. Boschi, *Eur. J. Org. Chem.*, 1999, 1901.
- 5 Systematic studies on the complexation-induced conformational changes of 1Zn indicate that Na<sup>+</sup> is the ion that induces the most pronounced conformational variation: L. La Monica, D. Monti, G. Mancini, M. Montalti, L. Prodi, N. Zaccheroni, G. D'Arcangelo and R. Paolesse, New J. Chem., 2001, 25, 597.
- P. Bhyrappa and V. Krishnan, *Inorg. Chem.*, 1991, 30, 239.
  Extensive studies on the binding properties of the receptor 1Zn and other related diporphyrin structures toward a series of dinitrogen ligands will be reported elsewhere.
- 8 The distances between the nitrogen interaction sites of the diamines, calculated by AM1 semiempirical molecular orbital method, are 7.15 and 2.92 Å for bpy and 1,2-DACy, respectively: M. J. S. Dewar, E. G. Zoebisch, E. F. Healy and J. J. P. Stewart, J. Am. Chem. Soc., 1985, 107, 3902.
- 9 K. A. Connors, Binding Constants. The Measurement of Molecular Complex Stability, John Wiley & Sons, New York, 1987.
- 10 pKa values for bpy and 1,2-DACy are 4.82 and 9.9, respectively, in water. Although corresponding data in acetonitrile are not available in the literature, good estimates would be that of pyridine (12.3) and ethylenediamine (18.5 and 13.0) which have been reported for that solvent: K. Izutsu, Acid-Base Dissociation Constants in Dipolar Aprotic Solvents, UPAC Chemical Data Series no. 32, Blackwell Scientific Publications, Oxford, 1990.
- 11 (a) The EM values have been calculated on the basis of the equation  $\text{EM} = K/4K_{\text{inter}}^2$ ; where K is relative to the interaction of the

ligand with the ditopic receptor 1Zn and  $K_{inter}$  is relative to the interaction of the considered ligand with the monotopic 2Zn, corrected for the statistical factor of 2. See for example: G. Ercolani, L. Mandolini, P. Mencarelli and S. Roelens, J. Am. Chem. Soc., 1993, 115, 3901; (b) for general studies on the effect of EM on cyclisation reactions see: C. Galli and L. Mandolini, Eur. J. Org. Chem., 2000, 3117; (c) L. Mandolini, Adv. Phys. Org. Chem., 1986, 22, 1.

- 12 This is different from that observed, for example, in the case of either covalent or self-assembled diporphyrin cages, in which the strength of the binding is driven by the good fit and rigidity of the guest. See for example: (a) I. P. Danks, I. O. Sutherland and C. H. Yap, J. Chem. Soc., Perkin Trans. 1, 1990, 421; (b) I. P. Danks, T. G. Lane, I. O. Sutherland and M. Yap, Tetrahedron, 1992, 48, 7679; (c) H.-J. Schneider and M. Wang, J. Org. Chem., 1994, 59, 7464; (d) Y. Kuroda, A. Kawashima, Y. Hayashi and H. Ogoshi, J. Am. Chem. Soc., 1997, 119, 4929.
- 13 For a recent overview on the host-guest chemistry of acyclic receptors see: G. W. Gokel and O. Murillo, *Podands*, in *Comprehensive Supramolecular Chemistry*, ed. J. L. Atwood, J. E. Davies, D. D. MacNicol and F. Vögtle, Elsevier Science Publications, Oxford, 1996, vol. 1, ch. 1, p. 1.
- 14 The achievement of a tighter conformation in which the two porphyrin platforms are brought to a shorter distance is witnessed by the presence of a blue shift of the 1Zn · Na@G(G = 1, 2-DACy) Soret band, compared to that of the related 1Zn@G (See Fig. S1, supplementary material). A blue shift of the Soret band is characteristic of face-to-face diporphyrin systems. See for example: J. P. Collman, P. S. Wagenknecht and J. E. Hutchinson, Angew. Chem. Int. Ed. Engl., 1994, 33, 1537; J. P. Collman, Inorg. Chem., 1997, 36, 5145.
- 15 (a) P. D. Beer, P. K. Hopkins and J. D. McKinney, Chem. Commun., 1999, 1253; (b) J. E. Redman, P. D. Beer, S. W. Dent and M. G. B. Drew, Chem. Commun., 1998, 231; (c) P. D. Beer and S. W. Dent, Chem. Commun., 1998, 825; (d) P. D. Beer and J. B. Cooper, Chem. Commun., 1998, 129; (e) J. B. Cooper, M. G. B. Drew and P. D. Beer, J. Chem. Soc., Dalton Trans., 2000, 2721.
- 16 G. Snatzke, Circular Dichroism: An Introduction, in Circular Dichroism, Principles and Applications, ed. K. Nakanishi, N. Berova and R. W. Woody, VCH Publishers, New York, 1994.
- 17 It has been reported that the binding of aliphatic  $\alpha, \omega$ -diamines of different length to a binaphthyl-spacered chiral diporphyrin receptor results in a modulation of the CD intensities: T. Ayashi, M. Nonoguchi, T. Aya and H. Ogoshi, *Tetrahedron Lett.*, 1997, **38**, 1603.
- 18 It is known that the interaction of cations with non-cyclic crownether-like podands induces a three dimensional conformation of the inclusion complexes. See for example: G. W. Gokel, Crown Ethers and Cryptands, in Monographs in Supramolecular Chemistry, ed. J. F. Stoddart, The Royal Society of Chemistry, Cambridge, 1991, ch. 4, p. 99.