Chelation Effects in the Binding of Bidentate Ligands by a Face-to-Face Zinc Porphyrin

Ian P. Danks, I. O. Sutherland, and Chee Hong Yap
*Department of Chemistry, University of Liverpool, P.O. Box 147, Liverpool L69 3BX*

The face-to-face zinc porphyrin (2) is a selective host for 4,4'-bipyridyl as compared with the diamines $H_2N(CH_2)_nNH_2$. This selectivity arises from a much higher chelation factor (14M) for the bipyridyl guest as compared with the very low factors ($\ll$ M) for the diamines. These results are discussed in terms of host and guest structures and compared with other host–guest systems.

It is well known that the total free energy of binding of two ligands A and B (ΔG_A and ΔG_B) to a protein, or a synthetic receptor, containing two appropriate binding sites may be significantly less than the free energy of binding (ΔG_{A-B}) of a ligand in which A and B are covalently connected, providing that the connection is consistent with the geometrical relationship between the two binding sites.[1] It was of interest to examine a synthetic host–guest system which might show this property (chelation effect) and since the molecular geometry of the complex formed between pyridine and zinc tetrapyridyl porphyrin (1) has been established by crystallography[2] (Zn ··· N distance 2.14 Å) and other amine-zinc porphyrin complexes have been shown to have a similar geometry in solution[3] the amine-zinc porphyrin system was selected for this study.

Accordingly, the face-to-face zinc diaryl porphyrin (2) was synthesised by a conventional procedure (see Experimental section) and complexation of mono- and di-amines studied. The host (2) formed a well defined complex with 4,4'-bipyridyl in CD_2Cl_2 which showed significant upfield shifts ($\Delta\delta$) of the guest signals (2- and 2'-H $\Delta\delta$ − 7.18 ppm and 3- and 3'-H $\Delta\delta$ − 2.49 ppm) in the ^1H NMR spectrum. In the presence of an excess of guest distinct signals were observed for free and complexed guest below 0 °C. This data is consistent with the formation of the expected inclusion complex (3). The absorption spectrum of the zinc porphyrin (2) (λ_{max} 407 nm) is at a similar wavelength to that of an analogous zinc diarylporphyrin (λ_{max} 409 nm)

indicating little interaction between the two chromophores (*cf.* ref. 4) and simple molecular mechanics calculations for the zinc-free face-to-face porphyrin, using the MM2 force field in MACROMODEL,[5] showed that the porphyrin ··· porphyrin separation [see d in (3)] might range from 10.8 to 12.7 Å without introducing significant strain energy. Thus (2) is an ideal host for 4,4'-bipyridyl [N ··· N separation 7.2 Å] which would required a zinc ··· zinc distance of *ca.* 11.6 Å in the complex (3).

Association constants for complexation of 4,4'-bipyridyl and a series of diamines $H_2N(CH_2)_nNH_2$ by host (2) in dichloromethane are recorded in the Table. The magnitude of the chelation effect (in terms of the chelation factor $K_{A-B}/K_A \cdot K_B$) may be obtained by comparison with association constants for the complexation of pyridine and butylamine. For the diamines the chelation factor is significantly less than M (0.01 to 0.12M) but for bipyridyl it is of the same order (15M) as those reported recently[6] for the two binding components of fluorescein [see broken line in (4)] and a range of anti-fluorescyl antibodies (5–70M). This is still significantly less than the theoretical maximum[1] (up to 10^8M). The results of a similar study[7] using a zinc gable porphyrin (5) showed chelation factors $\leqslant$ 1M for the bidentate ligands, *N,N'*-di-imidazolylmethane and 4,4'-dipyridylmethane, whereas face-to-face porphyrins with two long and flexible bridges[8] appear to show much lower factors for guest bidentate ligands.

(1) Ar =

(2) X =

(3)

(4)

(5)
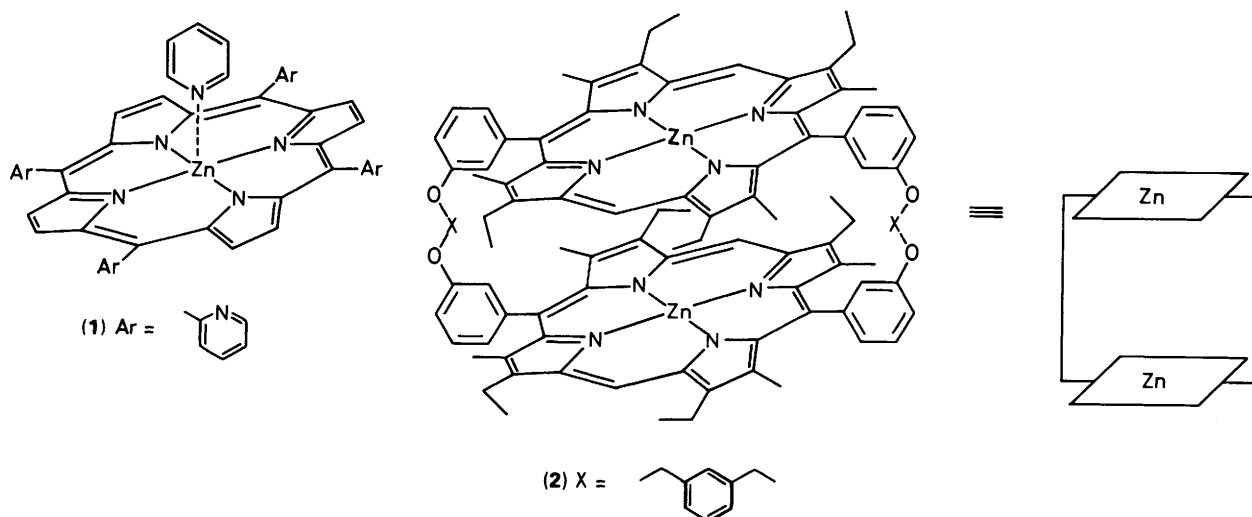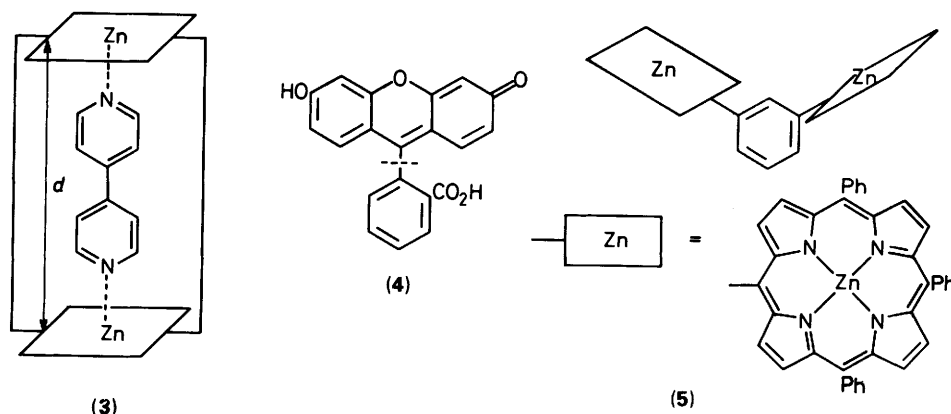
Table. Association constants[a] for complexation of bidentate ligands and analogous monodentate ligands by face-to-face zinc porphyrin (2).

Bidentate guest	K_B/M^{-1}	Monodentate K_M/M^{-1} guest		K_B/K_M^2
4,4'-Bipyridyl	$3 \pm 1 \times 10^7$	Pyridine	$1.4 \pm 0.2 \times 10^3$	15
1,2-Diaminoethane	$6 \pm 2 \times 10^5$			0.024
1,4-Diaminobutane	$6 \pm 2 \times 10^5$			0.024
1,5-Diaminopentane	$1 \pm 0.2 \times 10^6$	Butylamine	$5 \pm 0.5 \times 10^3$	0.04
1,6-Diaminohexane	$3 \pm 1 \times 10^6$			0.12
1,7-Diaminoheptane	$2 \pm 1 \times 10^6$			0.08
1,8-Diamino-octane	$3 \pm 0.5 \times 10^6$			0.01

[a] In CH_2Cl_2 at 25 °C and based upon change in absorbance at 407 and 418 nm on addition of guest to a solution of host (2) ($10^{-6}M$).

The observation of larger chelation effects than those for the host–guest complex (3) evidently requires a more rigid bridge between the two binding sites in addition to a geometrically well defined bidentate ligand. There must, of course, also be an optimum relationship between the two receptor sites of the host and the two binding sites in the guest. A rigid triporphyrin system has recently been reported[9] to show a chelation factor of 26 for one site binding as compared with two site binding, it is interesting to note that in this case both guest and host are highly pre-organised.

Experimental

Synthesis of Host (2).—The corresponding zinc bis(3'-hydroxyphenyl)porphyrin was heated in DMF with caesium carbonate and α,α'-dibromo-m-xylene at 75 °C for several days. The product was purified by flash chromatography on silica and crystallised from $CHCl_3$–EtOH (yield ca. 10%), m.p. > 350 °C; δ(CDCl₃), 10.15 (4 H, s, 4 meso-H), 7.32–7.6 (24 H, m, 24 ArH), 5.11 (8 H, 4 × OCH_2Ar), 3.79 (16 H, q, J 7 Hz, 8 × CH_2CH_3), 2.35 (24 H, s, 8 × CH_3), and 1.56 (24 H, t, 8 × CH_3CH_2) (Found: C, 67.4; H, 5.29; N, 5.89. $C_{104}H_{100}N_8O_4Zn_2 \cdot CHCl_3$ requires C, 67.2; H, 5.42; N, 5.91%). The mass spectrum (FAB source, 3-nitrobenzyl alcohol matrix) in the region m/z 1 653–1 662 shows a pattern of peaks which corresponds to $(M - 1)^+$ plus a small proportion of $(M - 2)^+$.

Determination of Association Constants.—Portions of guest (CH_2Cl_2 solution) were added to a solution of the host (2) ($10^{-6}M$ in CH_2Cl_2) and the absorbance at 407 and 418 nm

measured after each addition. In all cases a good isobestic point was observed except for very high values of [G]. A computational procedure with a range of input values for K was used to find the value of K giving best fit between calculated and observed absorbance. The 'end values' for the absorbance were calculated as 'best values' by this procedure to avoid inaccuracy resulting from systematic errors in experimentally determined 'end values' at high guest concentrations.

References

1 M. I. Page and W. P. Jencks, *Proc. Natl. Acad. Sci. USA*, 1971, **68**, 1678; W. P. Jencks, *ibid.*, 1981, **78**, 4046.
2 D. M. Collins and J. L. Hoard, *J. Am. Chem. Soc.*, 1969, **92**, 3761.
3 R. J. Abraham, G. R. Bedford, D. McNeillie, and B. Wright, *Org. Mag. Res.*, 1980, **14**, 418.
4 A. Osuka and K. Maruyana, *J. Am. Chem. Soc.*, 1988, **110**, 4454.
5 W. Clark Still, Columbia University, 1986 (Version 1.5).
6 N. Janjic, D. Schloeder, and A. Tramontano, *J. Am. Chem. Soc.*, 1989, **111**, 6374.
7 I. Tabushi, S. Kugimiya, M. G. Kinnaird, and T. Sasaki, *J. Am. Chem. Soc.*, 1985, **107**, 4192.
8 C. A. Hunter, M. N. Meah, and J. K. M. Sanders, *J. Chem. Soc., Chem. Commun.*, 1988, 692, 694; H. L. Anderson, C. A. Hunter, and J. K. M. Sanders, *J. Chem. Soc., Chem. Commun.*, 1989, 226.
9 H. L. Anderson and J. K. M. Sanders, *J. Chem. Soc., Chem. Commun.*, to be published. We are grateful to Dr. Sanders for giving us this information prior to publication.