Porphyrin Analogues of Tröger's Base: Large Chiral Cavities with a Bimetallic Binding Site

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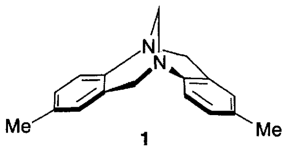
2-Amino-5,10,15,20-tetraarylporphyrins react with formaldehyde to give good yields of the corresponding octaaryl derivatives of the Tröger's base analogue in which two porphyrins are covalently linked by a diazocine bridge; the X-ray crystal structure of the bis(tetraphenylporphyrinato)dipalladium(II) derivative **6** reveals a concave chiral cavity with two metal ion binding sites suitable for ditopic interactions with guest molecules.

Tröger first reported the condensation of *p*-toluidine and formaldehyde in 1887.[1] The product (2,8-dimethyl-5,11-methano-5,6,11,12-tetrahydrodibenzo[*b*,*f*][1,5]diazocine) **1**, now known as Tröger's base, is chiral and was first resolved into its enantiomers more than 50 years later.[2] In recent studies of synthetic enzyme and artificial receptor systems[3] many other derivatives of Tröger's base have been synthesised by the condensation of other substituted anilines with formaldehyde. We now report the first preparation of a Tröger's base system incorporating macrocyclic rings. Thus, condensation of 2-amino-5,10,15,20-tetraarylporphyrins with formaldehyde affords octaaryl bisporphyrins in which the porphyrins are covalently linked through a diazocine bridge. These compounds should be particularly useful for investigation of electronic coupling in porphyrin systems and they also possess a well-defined chiral cavity with the potential for interesting molecular recognition properties.



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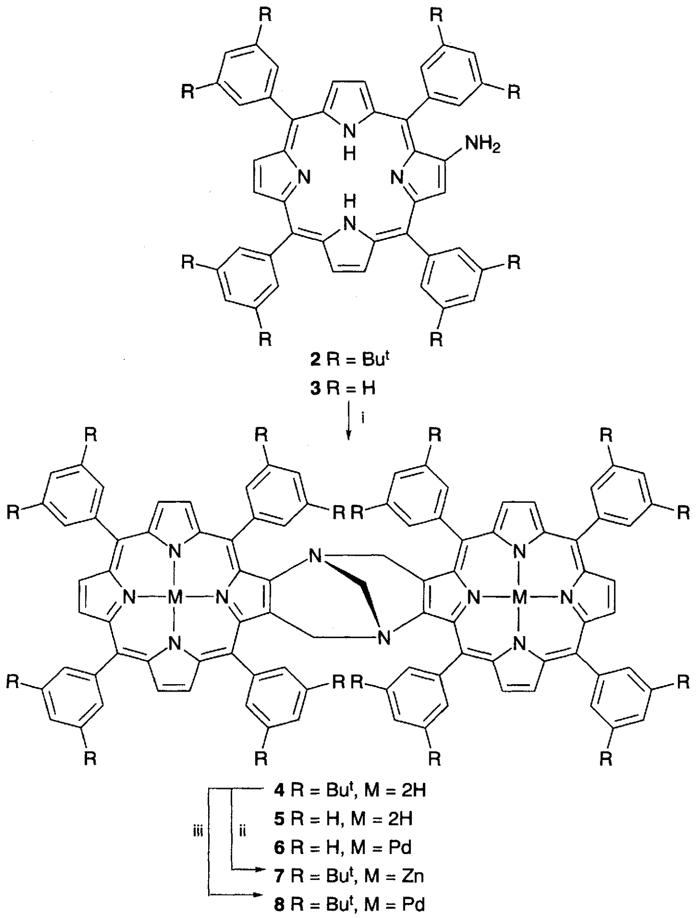
The porphyrin Tröger's base analogue **4** was prepared in 70% yield by the acid-catalysed reaction of 2-amino-5,10,15,20-tetrakis(3,5-di-*tert*-butylphenyl)porphyrin[4] **2** and formaldehyde (Scheme 1).[†] Compound **4** is highly soluble in organic solvents and easily purified by column chromatography. Similar treatment of 2-amino-5,10,15,20-tetraphenylporphyrin[4] **3** with formaldehyde gave the octaphenyl analogue **5** in 73% yield (Scheme 1).

The fact that 2-aminoporphyrins can be used in place of simpler 2-aminoarenes in this condensation has two noteworthy aspects. First, the reaction outcome is further confirmation that 2-aminoporphyrins behave in many ways as a higher homologue of an aniline as we have previously shown.[5] Second, there are seven possible β-pyrrolic sites for acylation of a 2-amino-



Scheme 1 *Reagents and conditions*: i, CH_2O in H_2O (36.5–38% *w*/*w*)–HCl (10 mol dm^{-3})–THF and EtOH, 60–90 °C, 8 h; ii, excess $Zn(OAc)_2 \cdot 2H_2O$–MeOH–CH_2Cl_2 (91% yield); iii, $PdCl_2$ (4 equiv.)–DMF, reflux, 20 min

porphyrin, yet reaction has been directed to the position adjacent to the amino substituent.

While the reaction proceeds most efficiently on the free-base 2-aminoporphyrins, corresponding metallo-2-aminoporphyrins can also be used. Thus, condensation of the palladium(II) chelate of 2-amino-5,10,15,20-tetraphenylporphyrin and formaldehyde gave the bis(tetraphenylporphyrinato)dipalladium(II) derivative **6** in 29% yield. A better method for obtaining metallo derivatives involved metallation of the preformed porphyrin Tröger's base system. Thus, the chelation of zinc by **4** proceeds readily under standard conditions to afford either mono- or di-zinc(II) **7** derivatives, depending upon the number of equivalents of metal salt employed. Treatment of **4** with $PdCl_2$ gave the dipalladium(II) derivative **8** in 92% yield. Dicobalt(II), dinickel(II) and dicopper(II) derivatives of **4** have also been prepared and fully characterised.

The X-ray crystal structure of **6** has been obtained and confirms the C_2 axis of symmetry possessed by the molecule and shows a large, well-defined, chiral cavity (Fig. 1).‡ The unit cell contains two crystallographically independent bisporphyrins with Pd–Pd distances of 8.38 and 8.99 Å, respectively. The lengths and angles of the bridgehead portion of the molecule are mostly similar to those of Tröger's base itself,[6] but the angles between the pyrrole rings connected to the diazocine bridge of **6** are 81.0 and 89.7°, respectively, which is somewhat smaller than other Tröger's base analogues (92–104°).[3a] The porphyrin rings are folded toward one another. Thus, the angles between the least-squares planes through the porphyrins in the two forms of the bisporphyrin are 59.2 and 64.6°, respectively. This buckling of the macrocycles is evidently caused to minimise the interactions of phenyl groups across the diazocine bridge. We may assume a comparable distance for the separation of chelated metals in the 3,5-di-*tert*-butyl analogue **8** in light of the similarity of UV spectra§ and similarity of the chemical shifts of the bridgehead and porphyrin β-pyrrolic protons in the ^1H NMR spectra. These resonances should be very sensitive to changes in shape as they all experience distance-dependent ring-current shifts from the 'remote' porphyrin of the system.

Dimeric porphyrins of many topologies have been investigated as enzyme models[7] and as mimics of the macrocyclic interactions in the Photosynthetic Reaction Centre.[8] The binding properties of such synthetic receptors have also been studied in detail,[9] as hosts with multiple binding sites are capable of molecular recognition and the potential catalysis of reactions within their cavities.

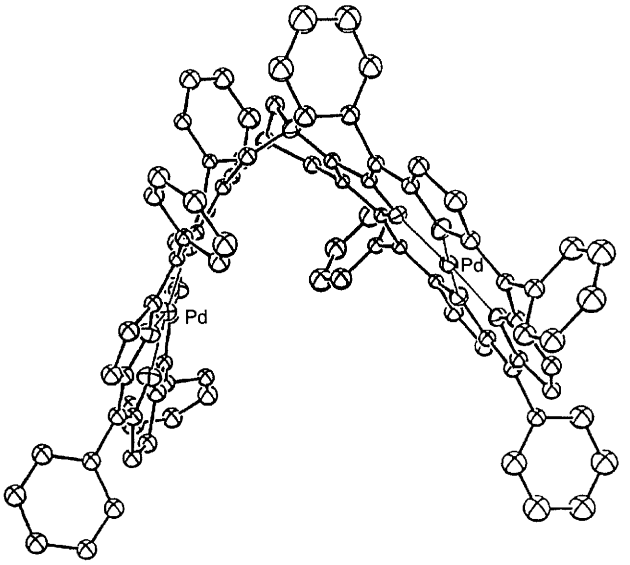


Fig. 1 An ORTEP plot (hydrogen atoms have been omitted for clarity) of one of the two forms of the bis(tetraphenylporphyrinato)dipalladium(II) derivative **6** in the unit cell. In this form the Pd–Pd distance is 8.384 Å.

In order to explore the rigidity of the system, we have initially examined the binding of a series of α,ω-diamines to the dizinc(II) chelate **7**. The dimetallated host **7** should bind diamines in a bidentate fashion in the interior of the cavity as shown in Fig. 2. The strength of the binding observed throughout the homologous series of α,ω-diamines from 1,2-diaminoethane to 1,6-diaminohexane is high enough to result in a slow exchange process on the ^1H NMR timescale, indicating binding affinities for the diamines of at least *ca.* 10^6 dm^3 mol^{-1}. The ligand resonances are shifted upfield as a result of complexation to the hosts to between δ −1.7 and −6.3, which constitutes shifts of between 3 and 8 ppm. The large magnitude of these shifts confirms that these ligands bind within the cavity and experience the ring currents of both macrocycles in the host.[10] The chiral nature of the host is apparent from the large splitting of the diastereotopic protons of the guests when complexed. Small variations (up to 0.3 ppm) were seen in the positions of the resonances of the protons of host **7** in the diamine complexes, suggesting that the dimensions of the cavity can be adjusted slightly to better accommodate the guest species.

The large magnitude of these binding constants precluded the use of ^1H NMR spectroscopy to determine their actual values, but estimates of the binding affinities of the diamines were obtained from spectrophotometric titrations,¶ employing the racemic host **7** at a concentration of 1.5×10^{-6} mol dm^{-3}. These titrations were carried out under an argon atmosphere to avoid decomposition of the very dilute solutions involved;[9b] the values thus determined are given in Table 1. Very strong complexation was observed for all of these diamines as these ligands can presumably bind by adjusting their conformation to give an $NH_2\cdots NH_2$ separation suitable for bidentate binding. In contrast to this, a simple monodentate ligand such as hexylamine has a binding affinity of only 5.1×10^4 dm^3 mol^{-1}.‖ Of the five bidentate ligands, 1,2-diaminoethane displays the greatest affinity; the affinities of the larger ligands are

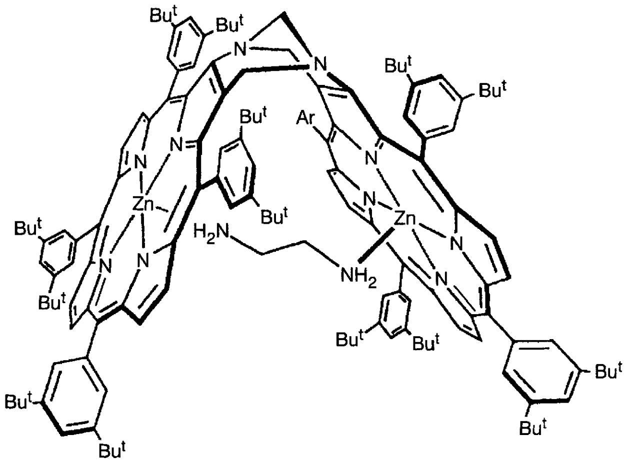


Fig. 2 Representation of 1,2-diaminoethane binding within the cavity of the dizinc(II) bisporphyrin **7**

Table 1 Binding constants[a] for bisporphyrin **7**

Ligand	K/dm^3 mol^{-1}
1,2-Diaminoethane	1.9×10^8
1,3-Diaminopropane	1.7×10^8
1,4-Diaminobutane	1.6×10^8
1,5-Diaminopentane	6.1×10^7
1,6-Diaminohexane	3.7×10^7
Hexylamine	5.1×10^4

[a] Measured in toluene at 293 K, errors estimated as ±10%.

presumably reduced through a requirement for the loss of more internal motion on binding and/or the introduction of conformational strain upon binding.

Diamines of this nature can be considered as crude transition state analogues for a bimolecular reaction between two amine substrates within the dimer cavity. The strong binding observed for the diamines suggests that we may be able to exploit these hosts as bimolecular catalysts in a similar manner to that achieved with other polytopic hosts.[11] The resolution of the chiral dizinc(II) bisporphyrin[**] **7** has been achieved and will be reported shortly with our initial enantioselective recognition studies.

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Footnotes

[†] All new compounds have been fully characterised by UV–VIS spectroscopy, FAB MS, ^{1}H NMR and elemental analysis or single crystal X-ray crystallography.

[‡] *Crystal data* for **6**: $C_{182}H_{116}N_{20}Pd_4\cdot 0.5C_5H_{12}$, red crystals grown by diffusion of pentane into a chloroform solution, M_r = 3044.7, triclinic, space group $P\bar{1}$, a = 18.097(3), b = 18.688(4), c = 22.797(5) Å, α = 101.54(2), β = 97.72(2), γ = 103.73(2)°, V = 7314(2) Å^3, Z = 2, D_c = 1.382 g cm^{-3}. Independent reflections were measured and refined on an Enraf-Nonius CAD-4F diffractometer employing graphite monochromatized Mo-Kα radiation (λ = 0.71069 Å). Data reduction and application of Lorentz, polarization and decomposition corrections were carried out using the Enraf-Nonius Structure Determination Package.[12] The structure was solved by direct methods within the SHELXS-86[13] program. This enabled the location of the four palladium atoms and the solution was extended by difference syntheses. Palladium and nitrogen atoms were refined anisotropically, carbon atoms isotropically and hydrogen atoms were included at calculated sites (C–H 0.97 Å) with group isotropic thermal parameters. Blocked-matrix least-squares refinement was carried out using program SHELX-76[14] with R = 0.053 and R_w = 0.053 and plots were drawn with ORTEP.[15] Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Information for Authors, Issue No. 1.

[§] Bis(tetraphenylporphyrinato)dipalladium(II) derivative **6**: λ_{max}/nm (CHCl$_3$) 412 (log ε 5.43), 432sh, (5.22), 490sh (3.79), 530 (4.54), 561 (3.89). Bis[tetrakis(3,5-di-*tert*-butylphenyl)porphyrinato]dipalladium(II) derivative **8**: λ_{max}/nm (CHCl$_3$) 417 (log ε 5.56), 490sh (3.83), 533 (4.67), 563 (3.89).

[¶] Spectrophotometric titrations were carried out in toluene at 20.0 ± 0.2 °C and were analysed using a SIMPLEX least-squares curve-fitting procedure.[16]

[‖] The binding constant quoted in this case for a monodentate amine binding to the dimer is an avarage value of the two stepwise binding constants K_1 and K_2.

[**] Since the submission of this paper, another example of a chiral bisporphyrin has been reported by Sanders *et al.*[17]

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