Ligand-induced Conformational Switching and Allosteric Effects in Macrocyclic Porphyrin Dimers

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Macrocyclic porphyrin dimers linked by biphenyl or pyromellitimide bridges show major conformational changes on protonation or on binding a single 1,4-diazabicyclo[2.2.2]octane (DABCO) molecule within the cavity; the binding of a second DABCO molecule leads to a further conformational switch.

An understanding of the relationship between conformation and ligand binding is a prerequisite for modelling enzyme behaviour. In the preceding Communication,[1] we reported the synthesis of two porphyrin macrocycles which should be capable of binding both metal ions and organic substrates in close proximity. We describe here some global conformational changes we have been able to induce by binding appropriate substrates.

The ^{1}H n.m.r. and u.v. spectra of the free base compounds (**1**) and (**2**) are consistent with the conformations shown in the

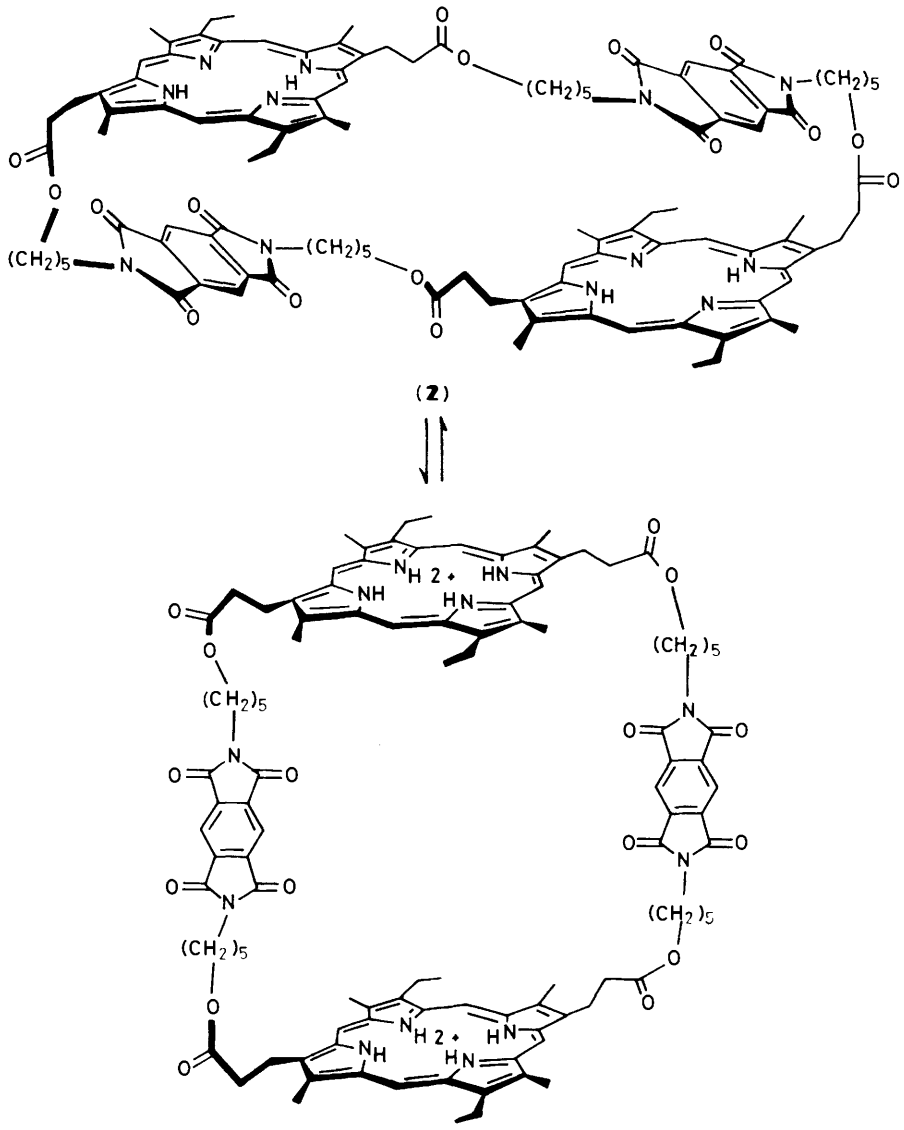

Figure 1. Conformational equilibria associated with protonation of (**2**) [and (**1**)].

preceding paper. However, a major conformational change occurs on addition of trifluoroacetic acid: the ^{1}H n.m.r. spectra show the complete disappearance of the ring current-induced upfield shifts of the biphenyl and pyromellitimide protons.† We interpret these changes as resulting from electrostatic repulsion between the doubly-charged porphyrins in the dimer pair to give maximum separation (Figure 1). The cavity thus formed can be closed by the addition of [$^2H_5$]pyridine. Similar effects have been observed in simpler systems but never accompanied by such a dramatic change in geometry.[2]

The ^{1}H n.m.r. spectrum of the bis-zinc derivative of (**1**) is broadened at room temperature as a result of aggregation or conformational equilibration. On addition of one equivalent of 1,4-diazabicyclo[2.2.2]octane (DABCO), the ^{1}H n.m.r. spectrum at −40 °C shows a signal at δ −5.5. This is attributed to the DABCO methylene signals, shifted upfield by *ca.* 8 p.p.m. by the combined ring currents of both porphyrins. Ring current calculations predict almost exactly this chemical shift for DABCO bound inside the cavity (Figure 2). Furthermore, the biphenyl signals are shifted downfield towards their expected shifts of *ca.* δ 7, while the *meso* signals are shifted upfield by 0.6 p.p.m. as expected from this model: the ring current of one porphyrin now shields the protons of the other porphyrin rather than the biphenyl bridge. When further DABCO is added, a second conformational change is observed. The second molecule of DABCO is bound outside the cavity and the attractive porphyrin–biphenyl interactions force a restoration of the initial dimer conformation and n.m.r. shifts (Figure 2). The DABCO signals are now broadened by rapid on–off exchange.

The bis-zinc derivative of (**2**) has a sharp ^{1}H n.m.r. spectrum as a result of internal co-ordination of the pyromellitimide carbonyl groups to the zinc ions. Addition of up to one equivalent of DABCO causes a global conformational change similar to that observed for (**1**), the ligand binding within the cavity; in this case, binding can be studied at room

† In contrast, the corresponding monomeric capped species show a significant increase in the upfield shifts on protonation. We believe that this is caused by a small, but real, increase in the ring current associated with protonated porphyrins.

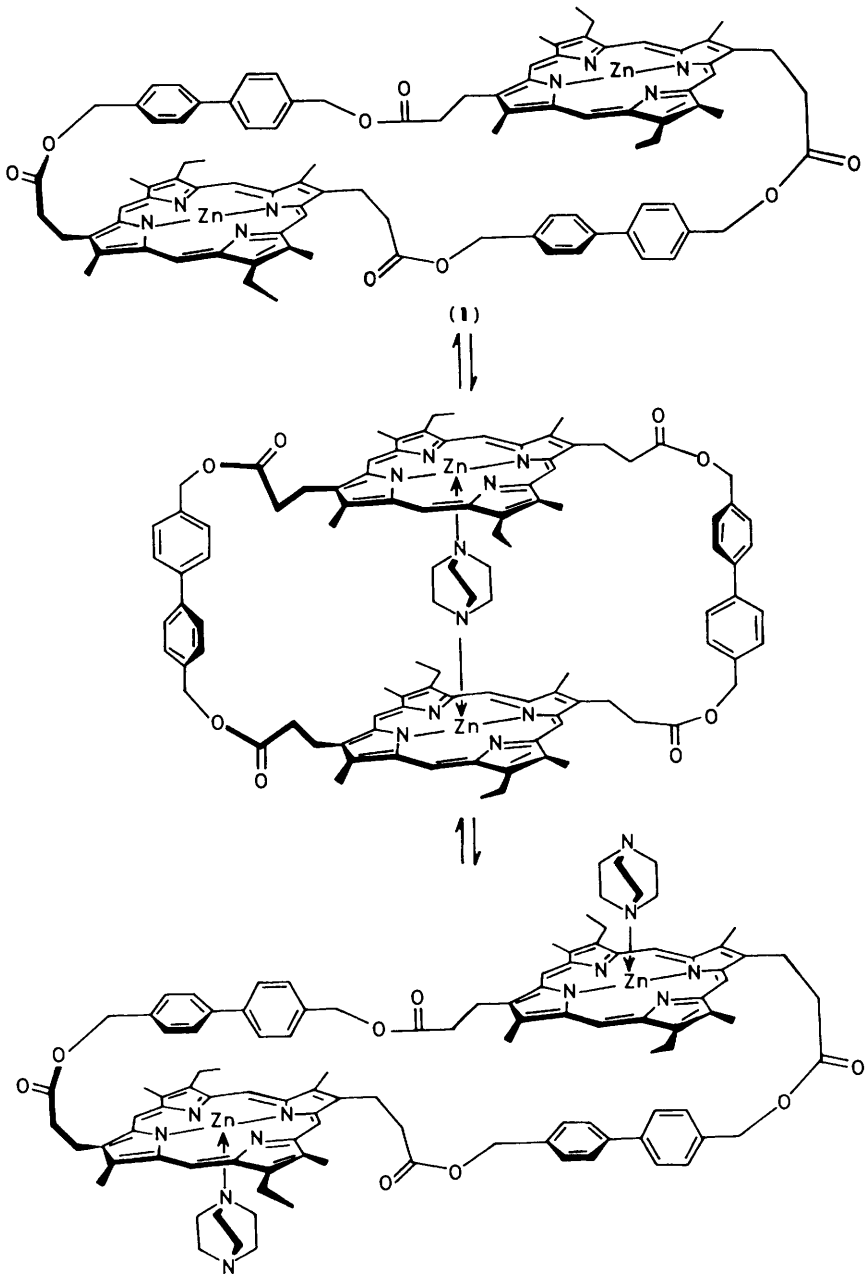

Figure 2. Conformational equilibria associated with DABCO binding to Zn_2 (**1**) [and Zn_2 (**2**)].

temperature. On addition of an excess of DABCO the cavity collapses as above.

These molecules show both allosteric and co-operative behaviour. Binding of one DABCO molecule in a dimer forces a global conformational change, the energy of two Zn–N binding interactions overcoming two attractive donor–acceptor interactions. It is important to note that co-ordination of monofunctional ligands such as pyridine, produces no dramatic conformational changes: only the second nitrogen of the DABCO is effective. Addition of excess DABCO allows satisfaction of both co-ordination chemistry and π–π attractions at a small entropic cost, so the cavity snaps closed again.

These dimers possess a novel 'induced-fit' active site whose conformation is known both in the absence and presence of bound ligand. Further aspects of molecular recognition and switching by these compounds will be reported elsewhere.

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References

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