Cavity effect amplification in the recognition of dicarboxylic acids by initial ditopic H-bond formation followed by kinetic trapping

Peter R. Brotherhood, Richard A.-S. Wu, Peter Turner and Maxwell J. Crossley*

The School of Chemistry, The University of Sydney, NSW 2006, Australia.
Email: m.crossley@chem.usyd.edu.au

Supporting Information

General procedures: Melting points were recorded on a Reichert melting point stage microscope and are uncorrected. Microanalyses were performed by the Campbell Microanalytical Laboratory, The University of Otago, New Zealand. Infrared spectra were recorded in deacidified ethanol free chloroform solutions with a Perkin-Elmer Model 1600 FT-IR spectrophotometer. Electronic absorption spectra were recorded on a Cary 5E UV-vis spectrophotometer at 25 °C.

^{1}H NMR spectra were recorded on a Bruker DPX-400 (400 MHz) spectrometer and signals are quoted in ppm relative to tetramethylsilane ($SiMe_4$, ^{1}H = 0 ppm) or the solvent residue peak (deuterated chloroform ($CDCl_3$); ^{1}H = 7.26 ppm) as the internal standard. The following abbreviations for multiplicity are used: s, singlet; d, doublet; t, triplet; m, multiplet; br s, broad singlet; br t, broad triplet; ABq, AB quartet. All NMR experiments were conducted using a 5 mm ID NMR tube. $CDCl_3$ was dried and deacidified by filtration through a plug of alumina and potassium carbonate, d_6-dimethylsulfoxide (d_6-DMSO) was used as received. For accurate volume measurements of deuterated NMR solutions microlitre syringes were used.

Matrix assisted laser desorption ionisation time of flight (MALDI-TOF) mass spectra were recorded on a VG TofSpec spectrometer in the positive linear mode. No matrix was required. Mass spectra were obtained as an envelope of the isotope peaks of the molecular ion. The mass corresponding to the maximum of the envelope is reported and was compared with the maximum of a simulated spectrum.

Column chromatography was carried out using the gravity feed column technique on Merck aluminium oxide 90 active neutral I, Type 1077 (63-200 mesh). Activity IV alumina refers to the water content (8.1% water added).

Solvents and reagents were purified using standard techniques.[1] All commercial solvents were routinely distilled prior to use. Light petroleum refers to the fraction of b.p. 60-80 °C. Where solvent mixtures are used, the proportions are given by volume.

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Synthesis of dihydroxo[5,5',10,10',15,15',20,20'-octakis(3,5-di-*tert*-butylphenyl)-4"*H*,8"*H* - 1",5" - methano [1",5"] diazocino [2",3"-*b*:6",7"-*b*'] bisporphyrinato] tin(IV), host 2

Dihydroxo[5,5',10,10',15,15',20,20'-octakis(3,5-di-*tert*-butylphenyl)-4"*H*,8"*H*-1",5"-methano[1",5"]diazocino[2",3"-*b*:6",7"-*b*']bisporphyrinato]tin(IV)zinc(II)[2] (100 mg, 41.5 μmol) was dissolved in dichloromethane (50 mL), washed with hydrochloric acid (10 M, 3 x 10 mL) and water (4 x 50 mL) and the organic solvent was separated and evaporated. The residue was purified by chromatography over neutral alumina (activity IV, dichloromethane – light petroleum, 1:3) and the major band collected and evaporated. The residue was dissolved in freshly distilled tetrahydrofuran (100 mL) and a solution of anhydrous potassium carbonate (500 mg, 3.62 mmol) in distilled water (25 mL) was added. The mixture was heated at reflux for 12 h, cooled, diluted with freshly distilled diethylether (100 mL), washed with distilled water (3 x 100 mL) and the organic solvent was removed. The residue was dried *in vacuo* for 1 h and recrystallised from freshly distilled dichloromethane and freshly distilled acetonitrile (1:1) to afford *dihydroxo[5,5',10,10',15,15',20,20'-octakis(3,5-di-tert-butylphenyl)-4"H,8"H-1",5"-methano [1",5"] diazocino [2",3"-b:6",7"-b'] bisporphyrinato] tin(IV)* **2** (91.0 mg, 94%) as a purple microcrystalline powder, mp > 300 °C (Found C, 76.7; H, 8.0; N, 5.9. $C_{155}H_{190}N_{10}O_2Sn + CH_2Cl_2$ requires C, 77.1; H 8.0; N 5.8%); υ_{max} ($CHCl_3$)/cm^{-1} 3688, 3346, 3029, 2964, 2865, 2337, 1593, 1476, 1426, 1363; λ_{max} ($CHCl_3$)/nm 318.5 (log ε 3.56), 422.5 (5.52), 531.0 (4.25), 574.0 (4.39), 616.0 (4.13), 664.5(3.56); δ_H(400 MHz; $CDCl_3$; $SiMe_4$) -8.42 (2 H, br s, OH), -3.27 (1 H, br s, NH), -2.97 (1 H, br s, NH), 0.83-1.91 (144 H, m, *t*-butyl H), 3.77 (1 H, d, *J* 17.2, H 4" or H 8"), 3.86 (1 H, d, *J* 17.6, H 4" or H 8"), 4.20 (1 H, d, *J* 17.2, H 4" or H 8"), 4.22 (1 H, d, *J* 17.6, H 4" or H 8"), 4.62 and 4.67 (2 H, ABq, *J* 11.6, H 9"), 6.52 (1 H, t, *J* 1.8, Ar-H), 6.69 (1 H, t, *J* 1.9, Ar-H), 7.34 (1 H, br t, Ar-H), 7.37 (1 H, br t, Ar-H), 7.42 (1 H, br t, Ar-H), 7.44 (1 H, br t, Ar-H), 7.45 (1 H, br t, Ar-H), 7.50 (1 H, t, *J* 2.0, Ar-H), 7.56 (1 H, t, *J* 2.0, Ar-H), 7.58 (1 H, t, *J* 1.9, Ar-H), 7.63 (1 H, t, *J* 1.7, Ar-H), 7.73 (1 H, t, *J* 1.7, Ar-H), 7.75-7.77 (2 H, m, Ar-H and β-pyrrolic), 7.79 (1 H, t, *J* 2.0, Ar-H), 7.80 (1 H, t, *J* 1.9, Ar-H), 7.82 (1 H, t, *J* 1.9, Ar-H), 7.91-7.96 (2 H, m, Ar-H), 7.94 (1 H, d, *J* 4.4, β-pyrrolic) 7.99 (1 H, t, *J* 1.7, Ar-H), 8.10 (1 H, t, *J* 1.9, Ar-H), 8.16 (1 H, t, *J* 1.6, Ar-H), 8.18 (1 H, t, *J* 1.6, Ar-H), 8.39 (1 H, d, *J* 4.8, β-pyrrolic), 8.45-8.49 (2 H, m, Ar-H and β-pyrrolic), 8.35 and 8.50 (2 H, ABq, *J* 4.4, satellites $^4J_{H\text{-}Sn}$ 10.3 and 10.7 β-pyrrolic), 8.76 and 8.84 (2 H, ABq, *J* 5.2, β-pyrrolic), 8.75 and 8.88 (2 H, ABq, *J* 4.8, β-pyrrolic), 9.01 and 9.12 (2 H, ABq, *J* 4.8, satellites $^4J_{H\text{-}Sn}$ 9.8 and 10.2, β-pyrrolic); m/z (MALDI-TOF) 2325.7 [$(M – OH)^+$ requires 2326.9].

Representative procedure for ^{1}H NMR titration binding experiments

In a typical experiment tetrahydroxo[5,5',10,10',15,15',20,20'-octakis(3,5-di-*tert*-butylphenyl)-4"*H*,8"*H*-1"*H*-1",5"- methano [1",5"] diazocino [2",3"-*b*:6",7"-*b*'] bis-porphyrinato]ditin(IV) **1** (3.10 mg, 1.24 μmol) was dissolved in $CDCl_3$ (600 μL), and succinic acid **3** solution in d_6-DMSO-$CDCl_3$ (10:90, 0.100 M) was added by microlitre syringe in successive 0.5 mole equivalent aliquots to a total of 2.0 mole equivalents and subsequently a 1.0 mole equivalent aliquot was added to a total of 3.0 mole equivalents. After each addition ^{1}H NMR spectra were recorded at regular intervals until no further spectral changes indicated binding processes were complete. For titration experiments with acetic acid **4**, stock solutions were prepared in d_6-DMSO-$CDCl_3$ (5:95, 0.100 M).

^{1}H NMR titration binding experiment, host 1 and acetic acid 4

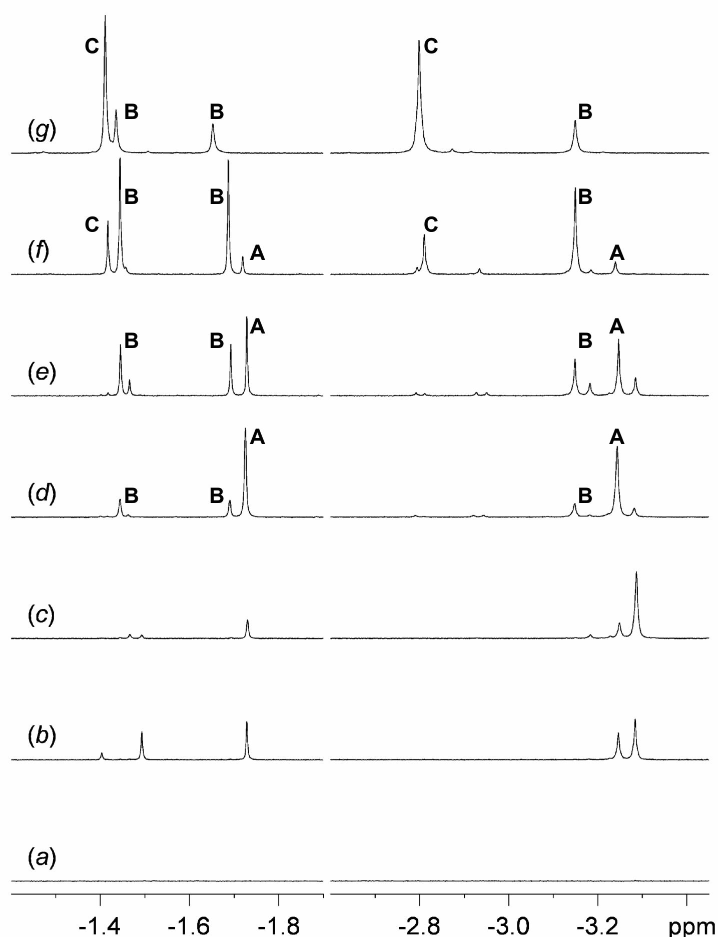

Fig. S1 ^{1}H NMR (400 MHz, $CDCl_3$) spectra showing the titration of acetic acid **4** with host **1**. -1.2 to -1.9 ppm, external acetate ligands, -2.6 to -3.45 ppm, internal acetate ligands. *(a)* Host **1**, *(b)* Host **1** + 1.0 eq **4**, 3 min, *(c)* Host **1** + 1.0 eq **4**, 100 min, *(d)* + 1.0 eq **4**, 2.0 eq total, 15 min, *(e)* 2.0 eq **4** total**,** 4 h, *(f)* + 1.0 eq **4**, 3.0 eq total, 5 h, *(g)* + 3.0 eq **4**, 6.0 eq total, 24 h.

Acetic acid **4** (1 equivalent) binds to host **1** with only a 1.5-fold preference for internal cavity positions at 3 min (Fig. S1b), the time required for quantitative association of succinic acid **3** in the interior of the cavity. Equilibration occurs over 100 min to give a 4.5:1 ratio of acetates bound at the interior (Fig. S1c). Subsequent addition of 1.0 equivalent results first predominantly in the formation of the 2:1 acetate-host complex where one acetate resides in the interior of the cavity and one outside and both tin(IV) porphyrins are in the acetate-hydroxo ligation state (**A** Fig S1d). This 2:1 complex **A** equilibrates over time to generate a mixture of the 2:1 complex **A** and the 3:1 complex where two acetates bind outside (**B**) in a 3:2 ratio (Fig S1e). At 3.0 eq the major complexes formed are the 3:1, **B**, and the 4:1 complex, **C** (Fig S1f). At 6.0 eq the 4:1 complex **C** is the major complex, however, this forms in a 3:2 ratio with the 3:1 complex **B**, indicating the steric hindrance to binding a second acetate ligand in the interior of the cavity. Binding a second acetate in the cavity requires opening of the cavity or displacement of the acetate ligands such that they experience less summation of the shielding effect of the porphyrin ring currents and hence the internal acetate

ligands of the 4:1 complex **C** (-2.79 ppm) resonate 0.36 ppm downfield of the internal acetate ligand of the 3:1 complex **B** (-3.15 ppm). These assignments are consistent with changes in the host resonances during the course of this titration.

^{1}H NMR titration binding experiment, host 2 and succinic acid 3

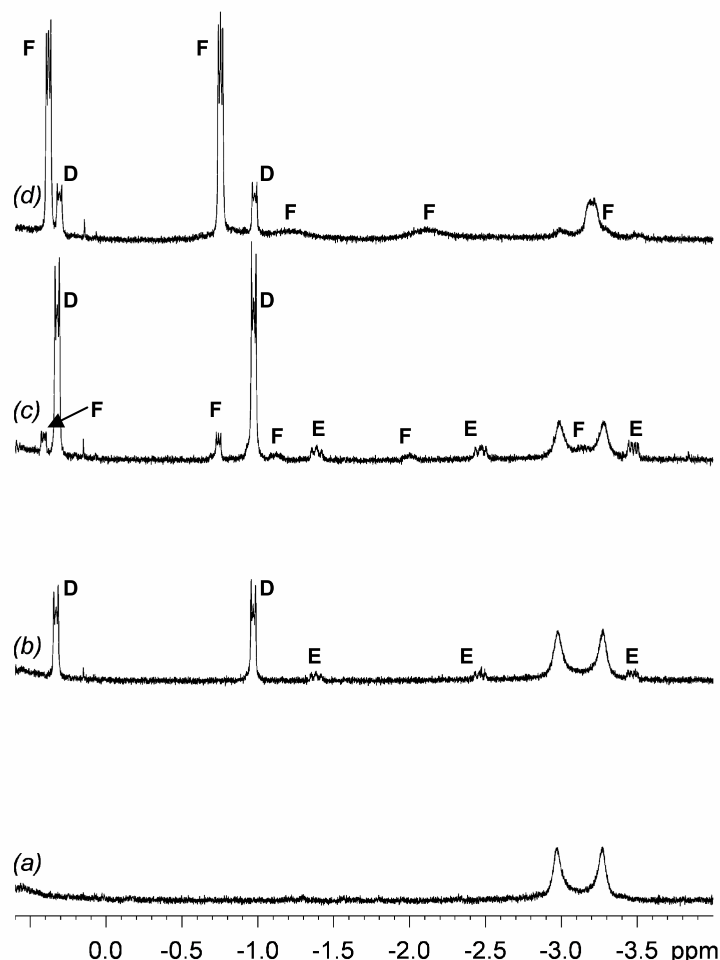

Fig. S2 ^{1}H NMR (400 MHz, $CDCl_3$) spectra showing the titration of succinic acid **3** with host **2**. *(a)* Host **2**, *(b)* Host **2** + 0.4 eq **3**, 17 min, *(c)* + 0.6 eq **3**, 1.0 eq total, 30 min, *(d)* + 1.0 eq **3**, 2.0 eq total, 15 min.

Addition of 0.4 equivalents of succinic acid **3** to host **2** results in binding, with high selectivity, to the exterior site (**D**) (Fig. S1b). Trace ligand exchange is also evident at the interior (**E**) and signals for succinate bound in this position show clear diastereotopicity due to the chirality of the cavity. One signal for succinate bound at the interior is obscured by the inner NH signals at -2.95 ppm and at -3.27 ppm. Subsequent addition of 0.6 eq again results in ligand exchange predominantly at the exterior, however, some formation of the 2:1 complex (**F**) is now clear. Addition of a further 1.0 eq results in formation of the 2:1 complex **F**. Interestingly, the signals for succinate bound at the interior of this complex and the inner NH signals are now broadened compared to these signals for the 1:1 complex **E**. This may be explained by a H-bonding interaction between the free acid group on the interior succinate and the inner periphery of the freebase porphyrin macrocycle that is absent in complex **E** due to conformational changes in the host, such as increasing planarity of the tin(IV)

porphyrin, upon symmetrisation of ligation at the tin(IV) site. Addition of excess acetic acid to host **2** (Fig. S3e) does not affect the inner NH resonance to the same extent.

^{1}H NMR titration binding experiment, host 2 and acetic acid 4

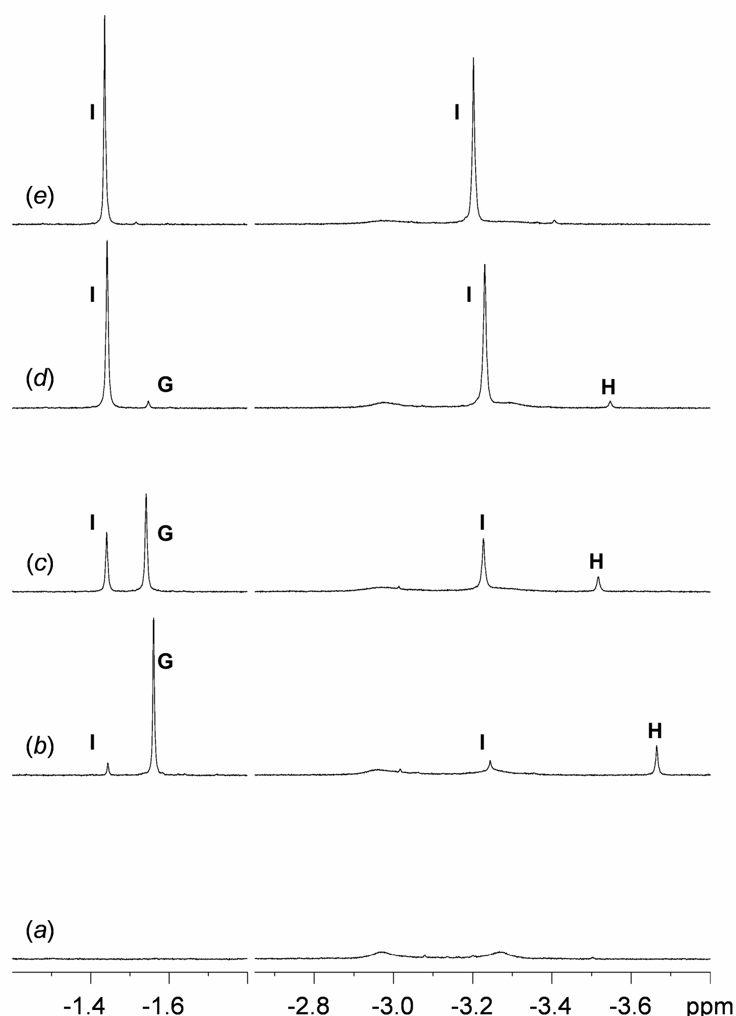

Fig. S3 ^{1}H NMR (400 MHz, $CDCl_3$) spectra showing the titration of acetic acid **4** with host **2**. *(a)* Host **2**, *(b)* Host **2** + 1.0 eq **4**, 23 min, *(c)* + 1.0 eq **4**, 2.0 total, 3 min, *(d)* 2.0 eq **4** total, 140 min, *(e)* + 6.0 eq **4**, 8.0 eq total, 10 min.

Upon addition of 1.0 eq of acetic acid **4** to host **2** the bulk of ligand exchange occurs at the exterior of the cavity (**G**), some exchange occurs at the interior (**H**) and there is trace formation of the 2:1 complex (**I**). Addition of a second equivalent of acetic acid **4** results in formation of the 2:1 complex **I** over 140 min. Addition of acetic acid **4** up to 8.0 equivalents does not have a profound effect on the inner NH signals, such as that seen in the 2:1 succinate **3**-host **2** complex **F** (Fig. S2d) indicating that the broadening seen in this latter complex is due to intramolecular interaction between the inner periphery of the freebase porphyrin and the free acid group of succinic acid **3** bound at the interior.

References

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2. M. J. Crossley, P. Thordarson and R. A.-S. Wu, *J. Chem. Soc., Perkin Trans. 1*, 2001, 2294-2302.