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Amplification of a cyclic mixed-metalloporphyrin tetramer from a dynamic combinatorial library through orthogonal metal coordination†

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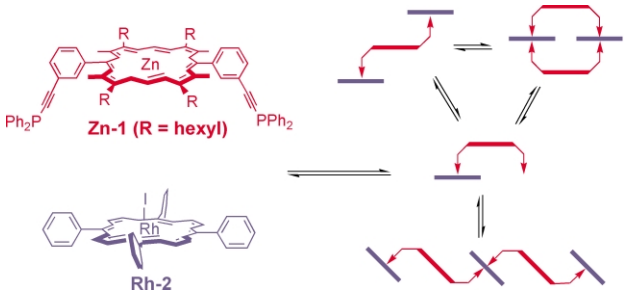
A cyclic porphyrin tetramer, consisting of two bis-phosphine substituted zinc(II) porphyrin units and two Rh(III)TPP units, is selected and amplified virtually quantitatively from a dynamic combinatorial library using 4,4′-bipy as a scaffold and using orthogonal binding modes.

The selective amplification of host–guest complexes from dynamic combinatorial libraries (DCLs) is a relatively young but fast growing field of research.[1] DCLs created from kinetically labile metal complexes have attracted considerable interest, and a variety of thermodynamically stabilised complexes have been obtained by offering suitable guests to the system.[2] All examples up to date describe the use of organic (bio)molecules or metal ions as shape determining guests. No report exists, however, where the reversible binding, which leads to the formation of the DCL, and the recognition binding, which results in the amplification process, are coordination sites of different specificity, *e.g.* according to Pearson's HSAB-principle. Previously, we have reported the use of orthogonal metal–ligand binding to form heterometallic porphyrin assemblies.[3,4] Here we describe what we believe is the first example of selection and virtually quantitative amplification of a thermodynamically stabilised, heterometallic, tetraporphyrinic construct from a DCL, stabilised by orthogonal metal–ligand coordination.

When the bis-diphenylphosphine substituted porphyrin **Zn-1**[5] (Scheme 1) was mixed with a stoichiometric amount of **Rh-2**[4] in $CDCl_3$, a mixture of coordination compounds was formed, as is obvious from the complex ^{1}H NMR and ^{31}P{^{1}H} NMR spectra (Fig. 1a). In the proton NMR spectrum, the resonances of the *meso*-protons of **Zn-1** (δ_H 10.15 ppm) and of the β-pyrrole protons of **Rh-2** (δ_H 8.90 ppm) showed several singlets each. This indicates that a number of different species are present. The resonances of the phenylphosphine protons were shifted upfield (characteristic for binding of the phosphine to **Rh-2**),[5] and significantly broadened. These signals (δ_H ~6.9 ppm, ~6.5 ppm and ~4.2 ppm) were also split into two sets of broad signals. The ^{31}P{^{1}H} NMR spectrum showed the presence of three different phosphorus species, resonating at δ_P −9.5 ppm (d, $^1J_{Rh-P}$ = 114 Hz), at −9.7 ppm (d, $^1J_{Rh-P}$ = 87 Hz), and at –32 ppm, corresponding to the mono-phosphine **Rh-2** complex, bis-phosphine **Rh-2** complex, and free phosphine, respectively.‡ At 2.5 mM concentration, the solution consisted of 10% free phosphine, 46% of the **Rh-2** having one phosphine ligand, and 44% of the rhodium porphyrins being coordinated by two phosphine ligands. Since the rhodium–phosphine bonding is kinetically labile,‡ also shown by a broadening of the phenylphosphine proton resonances, and a variety of complexes of different stoichiometries and geometries are present, the features of this mixture are consistent with a dynamic combinatorial system which is slowly interconverting on the NMR time scale. The mixture can be assumed to contain *cis*/*trans* linear, and probably cyclic species of variable length and ring size, as suggested in Scheme 1.



Scheme 1

† Electronic supplementary information (ESI) available: Fig. S1–3: ^{1}H NMR, ^{1}H–^{1}H COSY and ^{1}H–^{1}H NOESY spectra of (4,4′-bipy)⊂[(**Zn-1**)$_2$/(**Rh-2**)$_2$] at 300 K. See http://www.rsc.org/suppdata/cc/b1/b111019p/

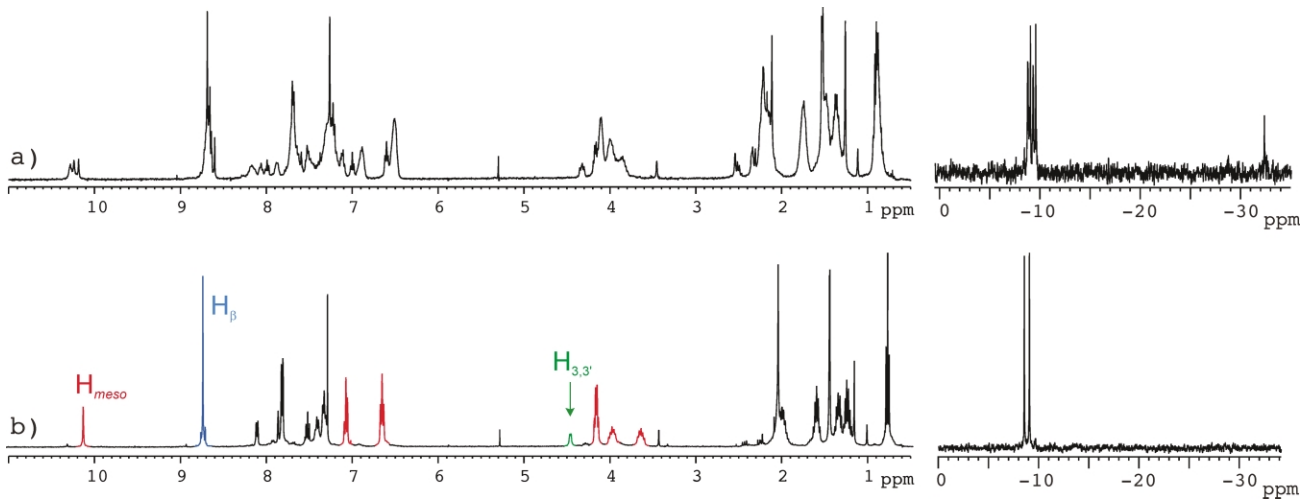


Fig. 1 (a) ^{1}H NMR (left) and ^{31}P{^{1}H} NMR (right) spectra of the DCL produced from the building blocks **Zn-1** and **Rh-2**. (b) ^{1}H NMR (left) and ^{31}P{^{1}H} NMR (right) spectra after addition of 0.5 equiv. 4,4′-bipy to the DCL; colour code is according to Fig. 2. Spectra are recorded in $CDCl_3$ at 400 MHz.

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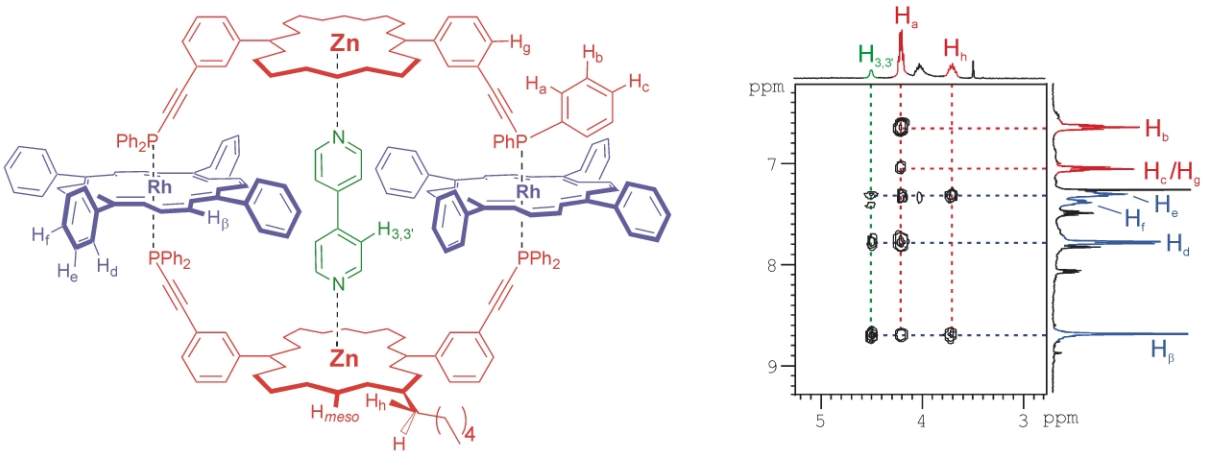

Fig. 2 Structure of the amplified host–guest complex, and partial ^{1}H–^{1}H NOESY spectrum displaying the relevant through-space connectivities.

Addition of 0.5 equivalents of 4,4′-bipy per **Zn-1** to the solution resulted in amplification of the cyclic porphyrin tetramer up to virtually 100% (Fig. 1b, Fig. 2). The amplification process could be monitored *in situ* using ^{1}H NMR spectroscopy upon titrating the guest into the host solution.§ Both the proton and the phosphorus NMR spectra showed only one significant species being present. All proton resonances were sharp and well resolved. The characteristic **Zn-1** *meso*-proton signals and **Rh-2** β-pyrrole proton signals showed one singlet each, indicating a high symmetry of the complex formed. At δ_H 4.49 ppm, the resonances of the 3,3′-protons of bipy could be located, which is a typical value for 4,4′-bipy bound to a zinc porphyrin.[6] The signals for the first methylene groups of the **Zn-1** hexyl sidechains appeared at δ_H 4.02 ppm and at δ_H 3.67 ppm; this unusually large splitting indicates highly unsymmetrical α- and β-sides of the porphyrin plane of **Zn-1**. The ^{31}P{^{1}H} NMR spectrum revealed the presence of only fully bound phosphine in the form of the bis-phosphine **Rh-2** complex (d, $^1J_{Rh-P}$ = 87 Hz). Overall, the spectra are consistent with the proposed cyclic (4,4′-bipy)⊂[(**Zn-1**)$_2$/(**Rh-2**)$_2$] host–guest complex as depicted in Fig. 2.

To prove the integrity of the cyclic complex, we performed 2D ^{1}H–^{1}H COSY and NOESY spectroscopy. From the COSY spectrum, all the signals could be unambiguously assigned to the individual units.¶ From the NOESY spectrum (Fig. 2), through-space connectivities were found from 4,4′-bipy to **Rh-2** ($H_{3,3'} \rightarrow H_d$, $H_{3,3'} \rightarrow H_e$, $H_{3,3'} \rightarrow H_f$, $H_{3,3'} \rightarrow H_\beta$), and from **Rh-2** to **Zn-1** ($H_e \rightarrow H_a$, $H_d \rightarrow H_a$, $H_\beta \rightarrow H_a$, $H_e \rightarrow H_h$).

If a competitor for 4,4′-bipy such as Zn(II)TPP is titrated into the system, the scaffold is removed from the complex, and the host starts to collapse. After addition of 6.2 equiv. of ZnTPP per complex (1.5 mM complex solution), 49% of the host–guest complex was still intact, yielding an association constant K_a of 2×10^8 M^{-1} for 4,4′-bipy in the host.‖ In $CHCl_3$, an overall stability constant K_t of $\sim 6 \times 10^{40}$ M^{-1} for the host–guest complex can be estimated.** The Ar–C≡C–P–Rh–P–C≡C–Ar unit seems flexible enough to (a) induce a twisted conformation to accommodate the relatively short scaffold, and (b) allow rotational freedom around the P–Rh bonding, because the C_4-symmetry of the **Rh-2** unit is retained, visible in the equivalence of the **Rh-2** proton resonances (*i.e.* H_β displays a singlet).

In summary, we have demonstrated that the supramolecular building blocks **Zn-1** and **Rh-2** form a dynamic combinatorial system in solution, and the host–guest complex (4,4′-bipy)⊂[(**Zn-1**)$_2$/(**Rh-2**)$_2$] can be amplified virtually quantitatively from the mixture. An analogous result was obtained when using a ruthenium(II) porphyrin instead of **Rh-2**. Even though the building blocks contain a built-in predisposition to form cyclic arrays, this specific tetramer is not accessible by rational synthesis because of the lability of the Rh–P bonding and the *cis*/*trans* isomerism of **Zn-1**.

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Notes and references

‡ The δ_P and $^1J_{Rh-P}$ values for mono- and bis-phosphine **Rh-2** complexes were obtained using the model ligand diphenyl phenylacetylene phosphine (DPAP). We also observed that the iodine in **Rh-2** is readily displaced by DPAP at ambient temperature. DPAP can be transferred from **Rh-2** to a ruthenium(II) porphyrin and *vice versa*, demonstrating the kinetic lability of these coordination complexes; from this, we estimate the affinity of DPAP to **Rh-2** for the first binding to be 2×10^7 M^{-1}.

§ The system was either left to equilibrate at room temperature for several hours, or a short heating-cooling cycle was applied for annealing. In both cases, the outcome of the proton spectrum was identical.

¶ The 2,2′-proton resonances of the bound bipy were found at δ_H 2.11 ppm, and are isochronous with the second methylene groups of the **Zn-1** hexyl sidechains, as well as with the methyl β-pyrrole substituents of **Zn-1**. Therefore, this signal could not be used in nOe assignments due to its strong overlap with other cross peaks.

‖ K_a [(4,4′-bipy)ZnTPP] = 6×10^3 M^{-1} (^{1}H NMR titration).

** To calculate the overall stability constant K_t, the association constants were converted to dimensionless forms using the molar fractions ([$CHCl_3$] = 12.4 M):[7] $K_t^x = (12.4\text{ M})^n \Pi(K_a)_i$; $K_t = K_t^x \cdot (12.4\text{ M})^{-1}$.

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