

Metal-directed ring-expansion in Schiff-base polypyrrolic macrocycles†

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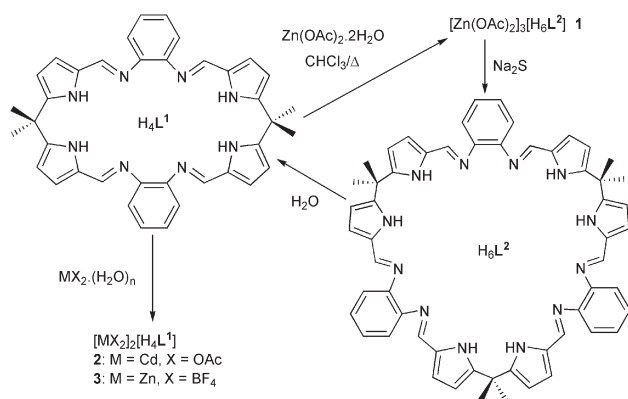
The reaction between a [2 + 2] Schiff-base porphyrin analogue and zinc acetate results in the unusual formation of an enlarged [3 + 3] macrocycle that is stabilised by metal coordination and intramolecular hydrogen-bonding interactions.

Schiff-base, polypyrrolic macrocycles are an important class of compounds that combine the coordinative and physicochemical properties of the pyrrole group with the exceptional design characteristics and synthetic versatility of macrocyclic Schiff-base condensation procedures.^{1,2} These features are particularly apposite to the synthesis and design of ligands that can direct bi- and multinuclear transition metal complex formation in which both the immediate coordination sphere and juxtaposition of metal centres are accurately defined. This approach has been exploited recently in the high yield syntheses of new Schiff-base, polypyrrolic macrocycles (e.g. H_4L^1 , Scheme 1) that contain two N_4 -donor compartments.^{3,4} Significantly, the presence of the rigid, aryl-backbone in this ligand has a profound effect on the molecular topology of subsequent transition metal and actinide complexes, e.g. $[Pd_2(L^1)]$,³ $[Fe_2O(L^1)]$,⁵ and $[UO_2(thf)(H_2L^1)]$,⁶ and promotes the formation of rigid, well-defined bimetallic molecular clefts in which the metal coordination sphere and the $M \cdots M$ separation are constrained in a manner reminiscent to that of cofacial or pacman bisporphyrins.⁷ This contrasts with the more flattened structures observed for binuclear complexes supported by analogues that incorporate flexible, hydrocarbon linkers between

the two N_4 -donor compartments⁸ or bipyrrole head groups,² which are related more to accordion and expanded porphyrins, respectively.⁹

The potential of the binucleating macrocycle H_4L^1 to promote the formation of a wide variety of new, bimetallic compounds that adopt rigid, molecular cleft structures, and the enormous appeal of these complexes in small molecule transformation and catalysis, led us to investigate the complexation chemistry of Zn^{II} ions with H_4L^1 as mono- and binuclear zinc compounds exhibit a rich catalytic and biomimetic chemistry.¹⁰ We report herein that reactions between H_4L^1 and Zn^{II} and Cd^{II} salts result not only in metal complexation, but, in the case of $Zn(OAc)_2$, can also promote macrocycle expansion.

The reaction between the [2 + 2] macrocycle H_4L^1 and $Zn(OAc)_2 \cdot 2H_2O$ in 1:1 molar ratio in boiling $CHCl_3/\Delta$ results in the formation of the new Zn^{II} complex, $[Zn(OAc)_2]_3[H_6L^2]$, **1** in moderate, but consistent yield (44%, Scheme 1).† This formulation was confirmed by elemental analysis, while the formation of the new, Schiff-base pyrrolic macrocycle H_6L^2 was inferred from ESMS data; while no molecular ion for **1** was observed in the ESMS spectrum, the peak at m/z 907 can be assigned to the metal-free product, H_6L^2 . The solution 1H NMR spectrum of **1** is consistent with local D_{3h} symmetry, and displays resonances characteristic of imine-H (δ 8.17 ppm) and hydrogen-bonded pyrrolic N-H (δ 11.8 ppm). To unambiguously confirm the nature of this macrocyclic product, the solid state structure was determined by X-ray crystallography (Fig. 1),‡ from which it is clear that the [2 + 2] macrocycle H_4L^1 has indeed been expanded to the new [3 + 3] macrocycle H_6L^2 on reaction with $Zn(OAc)_2$. The six iminopyrrole units are linked alternatively to three rigid *o*-aryl spacers and three sp^3 -hybridised *meso*-CMe₂ groups, thus precluding the full conjugation of the molecule and forming a 39-membered organic macrocycle. Each Zn^{II} ion is bound to two imine nitrogen centres and to two acetate groups; Zn1 and Zn2 are in a tetrahedral geometry as the acetate ligands are monodentate, while for Zn3 the combination of mono- and bidentate acetate coordination results in a distorted trigonal bipyramidal geometry. The macrocycle itself is not planar as the flexibility at the dipyrromethane *meso*-carbons promotes an overall wedge-shape in which three acetate groups are *endo*- to the cleft (acetates O3, O5, O11), with the remainder *exo*. The wedge topology appears to be stabilised by intra- and intermolecular hydrogen-bonding interactions between the oxygen atoms of the acetate groups and the acidic protons of both the pyrrolic groups and chloroform solvent of crystallisation. Hydrogen-bonding to both *endo*- and *exo*-acetate groups occurs [*exo*: N12-O1 2.9380(2), N3-O2 2.9859(2), N8-O9 2.8434(2), N11-O10 3.0564(2); *endo*: N3-O3 3.0937(2), N4-O5 2.8923(2), N7-O6 2.8083(2)], coupled with close interactions between chloroform solvent molecules and acetate oxygen



Scheme 1 Ring expansion, contraction and complexation reactions of the pyrrolic Schiff-base macrocycles L^1 and L^2 .

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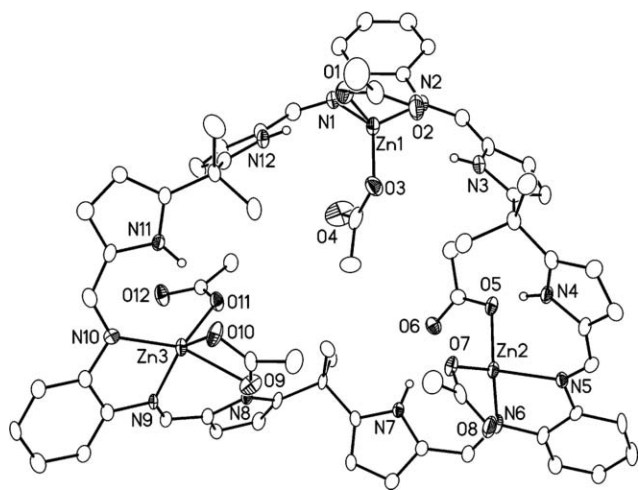


Fig. 1 Solid state structure of $[\text{Zn}(\text{OAc})_2]_3[\text{H}_6\text{L}^2]$, **1** (30% thermal ellipsoids; for clarity, solvent of crystallisation and all hydrogens except those on the pyrrolic nitrogens are omitted). Selected bond lengths (\AA) and angles ($^\circ$): Zn1–O1 1.993(7), Zn1–O3 1.897(7), Zn2–O5 1.969(7), Zn2–O7 1.909(6), Zn1–N1 2.028(8), Zn1–N2 2.022(7), Zn2–N5 2.036(7), Zn2–N6 2.012(8), Zn3–O9 2.303(7), Zn3–O10 2.084(6), Zn3–O11 1.938(6), Zn3–N9 2.030(7), Zn3–N10 2.064(7), O1–Zn1–O2 97.0(3), N1–Zn1–N2 83.1(3), O5–Zn2–O7 96.6(3), N5–Zn2–N6 84.3(3), O10–Zn3–O11 94.2(3), N9–Zn3–N10 82.6(3), N=C(imine) 1.285(11) to 1.307(12).

atoms O1, O4 and O6 (not pictured). The strength and number of these hydrogen-bonding interactions may well be implicated in the formation and unusual stability of this $[3 + 3]$ macrocyclic complex.

Access to the free ligand H_6L^2 was attempted through a variety of routes. While protonation of **1** by a variety of acids (HX : $\text{X}^- = \text{OTs}^-, \text{O}_2\text{CCF}_3^-, \text{OAc}^-$) did result in displacement of zinc acetate, only the protonated $[2 + 2]$ species $\text{H}_4\text{L}^1 \cdot 4\text{HX}$ were isolated. However, the reaction between **1** and Na_2S resulted in the clean formation of H_6L^2 as a yellow powder that was readily separated by extraction from ZnS and NaOAc by-products.[†] The formulation of H_6L^2 was confirmed by elemental analysis, and promptly-recorded ^1H NMR data revealed a characteristic imine resonance ($\delta = 8.17$ ppm); the $[3 + 3]$ nature of the macrocycle was corroborated by ESMS, which showed a molecular ion at m/z 907 attributable to H_6L^2 . While H_6L^2 is stable against contraction in the solid state, rapid (*ca.* 10 min) and complete conversion into H_4L^1 is observed in solution; this may, in part, be a consequence of the precipitation of highly insoluble H_4L^1 from common organic solvents, but likely reflects underlying thermodynamic instability of H_6L^2 . Attempts to reduce H_6L^2 to a more stable, amine analogue using borohydride were unsuccessful, and yielded H_4L^1 only.

Some insight into the structures and relative stabilities of H_4L^1 and H_6L^2 was gained from MMFF conformational calculations that showed that while both macrocycles adopt global minimum conformations of similar energy (H_4L^1 : 540; H_6L^2 : 549 kJ mol^{-1}),[†] the calculated structure of H_6L^2 adopts a more twisted conformation that, as a consequence, may result in its lack of stability with respect to contraction. In a similar manner, giant porphyrinoids have been shown to adopt, twisted, figure-of-eight conformations in the solid state,¹¹ and have a tendency to react at the “twist” to form spirocycles or even to cleave into two separate porphyrinic products.¹² Furthermore, $[4 + 4]$ to $[2 + 2]$ macrocycle contraction

has been observed during transmetallation reactions of a large, $\text{Pb}_2[4 + 4]$ Schiff-base macrocyclic complex that incorporates pyridazine head units;¹³ in this case, it is evident that coordination to the large Pb^{II} ions stabilises the twisted configuration of the $[4 + 4]$ macrocycle.

Examination of the mother liquors from both ring expansion (*i.e.* from the synthesis of **1**) and ring contraction reactions by ESMS and ^1H NMR spectroscopy shows that the formylimino-fragment $o\text{-H}_2\text{N}(\text{C}_6\text{H}_4)\text{N}=\text{CH}(\text{C}_4\text{H}_2\text{NH})\text{CMe}_2(\text{C}_4\text{H}_2\text{NH})\text{CHO}$, **L**, is present in high concentration (ESMS: m/z 321).[†] This suggests that Zn^{II} ions template the reaction between two $[2 + 2]$ macrocycles with the concurrent expulsion of **L**, and that a concerted $3 \times [2 + 2]$ to $2 \times [3 + 3]$ transformation does not occur.¹⁴ Fragmentation of H_4L^1 into constituent diamine and dialdehyde precursors followed by reformation into macrocyclic products is also unlikely, as the direct $\text{Zn}(\text{OAc})_2$ -template synthesis of H_6L^2 from *o*-phenylenediamine and the diformyldipyrromethane synthon was unsuccessful and yielded an as yet unidentified material.

In order to ascertain if macrocyclic expansion is limited to the use of a $\text{Zn}(\text{OAc})_2$ template, experiments that varied both metal cation and anion were carried out. Surprisingly, the reaction between H_4L^1 and $\text{Cd}(\text{OAc})_2 \cdot 2\text{H}_2\text{O}$ in boiling CHCl_3 did not generate any $[3 + 3]$ macrocyclic product, but instead resulted in the formation of the $[2 + 2]$ macrocyclic product $[\{\text{Cd}(\text{OAc})_2\}_2(\text{L}^1)]$, **2** in good yield.[†] The $[2 + 2]$ macrocyclic nature of **2** was confirmed by ES and FAB MS, which showed ions at m/z 605 (H_4L^1)⁺ and 826 ($\text{Cd}_2[\text{H}_4\text{L}^1]$)⁺ respectively. Analysis of **2** by ^1H NMR spectroscopy showed Cd-coupling to the imine H (J_{CdH} 30.3 Hz), consistent with complexation of the Cd^{II} cations to the imine nitrogens, a coordination mode that is further corroborated by the presence of hydrogen-bonded, pyrrolic NH resonances at 12.2 ppm. The solid state structure of **2** was determined by X-ray crystallography (Fig. 2)[‡] and shows that the metal acetates are bound to the macrocycle H_4L^1 via imine nitrogens N3, N4, N7, and N8 only, while the pyrrolic nitrogens remain protonated. A unique Cd-acetate environment is observed that consists of asymmetric terminal- and, significantly, bridging-bidentate acetate coordination. This complexation mode for acetate groups has only previously been structurally characterised in the binuclear lanthanide complexes $[\{(\mu\text{-CF}_3\text{CO}_2)_2\text{Ln}(\mu\text{-CF}_3\text{O}_2\text{H})\text{AlR}_2(\text{THF})_2\}_2]$ ($\text{Ln} = \text{Nd}, \text{Y}$, $\text{R} = \text{Bu}^i$; $\text{Ln} = \text{Eu}$, $\text{R} = \text{Et}$);¹⁵ presumably, the high coordination numbers accessible for the large, electropositive Cd^{II} and Ln^{III} ions contribute to the occurrence of this interaction. In a similar manner to **1**, close interactions between the pyrrolic nitrogen and acetate oxygen atoms are evident in **2** (2.76–2.83 \AA), and are consistent with the presence of intramolecular hydrogen-bonding.

In a manner similar to $\text{Cd}(\text{OAc})_2$, the reaction between H_4L^1 and $\text{Zn}(\text{BF}_4)_2 \cdot 2\text{H}_2\text{O}$ in boiling CHCl_3 does not result in macrocycle expansion, but instead generates the $[2 + 2]$ macrocyclic complex $[\text{Zn}_2(\text{H}_4\text{L}^1)][\text{BF}_4]_4$, **3** in high yield (85%).[†] As with **2**, examination of the mother liquors by ESMS showed no $[3 + 3]$ macrocyclic products. The ^1H NMR spectrum of **3** clearly shows the presence of pyrrolic NH resonances (δ 10.7 ppm), and ESMS data confirm the formation of a $[2 + 2]$ structure (m/z 605 H_4L^1)⁺. Thus, the combination of highly electropositive zinc(II) cations and coordinating anions that are capable of engaging in hydrogen-bonding interactions are prerequisites for the observed $[2 + 2]$ to

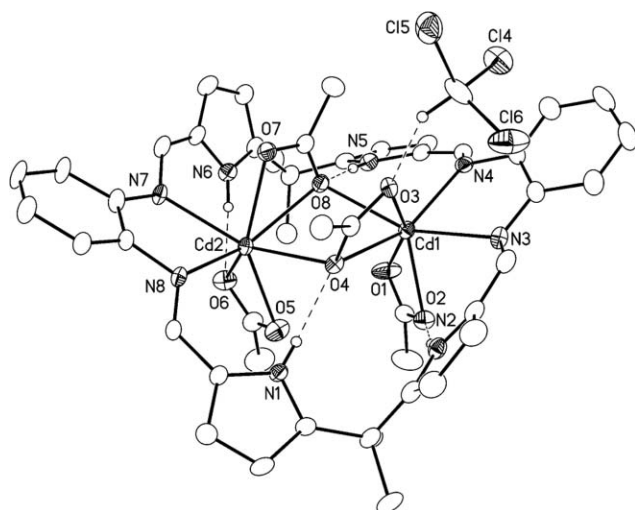


Fig. 2 Solid state structure of $[\text{Cd}(\text{OAc})_2]_2[\text{H}_4\text{L}^1]$, **2** (one molecule from the asymmetric unit pictured, 30% thermal ellipsoids; for clarity, non-hydrogen bonded CHCl_3 and all hydrogens except those on the pyrrolic nitrogens and CHCl_3 are omitted). Selected bond lengths (\AA): Cd1–O1 2.451(5), Cd1–O2 2.283(5), Cd1–O3 2.418(4), Cd1–O4 2.473(4), Cd1–O8 2.391(4), Cd1–N3 2.399(5), Cd1–N4 2.301(5), Cd2–O4 2.434(4), Cd2–O5 2.317(5), Cd2–O6 2.374(5), Cd2–O7 2.357(5), Cd2–O8 2.491(5), Cd2–N7 2.393(5), Cd2–N8 2.294(5), N=C(imine) 1.299(8) to 1.331(8), N1 \cdots O4 2.830(1), N2 \cdots O22.759(1), N5 \cdots O8 2.822(1), N6 \cdots O6 2.793(1), C2S \cdots O3 3.048(1).

[3 + 3] macrocycle expansion. While the use of metal cations to template [2 + 2] Schiff-base macrocyclic condensation reactions from constituent amines and aldehydes/ketones is well known,¹⁴ the formation of [3 + 3] products is rare.¹⁶ Also, whereas templated expansion of a *preformed* [2 + 2] Schiff-base macrocycle to a [4 + 4] analogue has been reported,¹⁷ this is, to our knowledge, the first observation of [2 + 2] to [3 + 3] Schiff-base macrocycle expansion.

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Notes and references

† Crystal data. 1: $\text{C}_{78}\text{H}_{88}\text{Cl}_{15}\text{N}_{12}\text{O}_{13}\text{Zn}_3$, $M = 2129.5$, yellow column, $0.68 \times 0.31 \times 0.25 \text{ mm}^3$, triclinic, space group $P\bar{1}$, $a = 12.124(2)$, $b = 14.423(2)$, $c = 27.710(4) \text{ \AA}$, $\alpha = 87.110(2)$, $\beta = 81.228(2)$, $\gamma = 80.730(2)$, $V = 4724(2)$, $Z = 2$, ρ (calc) = 1.497 mgm^{-3} , $\mu = 1.243 \text{ mm}^{-1}$, $F(000) = 2178$, $T = 150(2) \text{ K}$, Bruker SMART APEX CCD area detector, graphite monochromated $\text{MoK}\alpha$ radiation, $R1 = 0.0788$, $wR1 = 0.1990$,

13539 independent reflections [$2\theta = 46.52^\circ$] and 1094 parameters. **2**: $\text{C}_{49.25}\text{H}_{51.25}\text{Cl}_{9.75}\text{N}_8\text{O}_8\text{Cd}_2$, $M = 1453.7$, yellow block, $0.55 \times 0.27 \times 0.20 \text{ mm}^3$, triclinic, space group $P\bar{1}$, $a = 14.6804(13)$, $b = 20.348(2)$, $c = 25.125(2) \text{ \AA}$, $\alpha = 74.108(1)$, $\beta = 74.961(1)$, $\gamma = 70.241(1)$, $V = 6677(2)$, $Z = 4$, ρ (calc) = 1.446 mgm^{-3} , $\mu = 1.077 \text{ mm}^{-1}$, $F(000) = 2914$, $T = 150(2) \text{ K}$, Bruker SMART1000 CCD area detector, graphite monochromated $\text{MoK}\alpha$ radiation, $R1 = 0.0587$, $wR1 = 0.19690$, 29147 independent reflections [$2\theta = 50.0^\circ$] and 1358 parameters. SQUEEZE was used to account for poorly defined electron density corresponding to approximately 2 molecules of CHCl_3 solvent per asymmetric unit. The structures were solved using direct methods, refined using the SHELXTL software package and expanded using Fourier techniques. All non hydrogen atoms were refined anisotropically except Cl atoms on disordered solvent molecules in **2**. Hydrogen atoms were assigned idealized positions and were included in structure-factor calculations. CCDC 274152 & 274153. See <http://dx.doi.org/10.1039/b507729j> for crystallographic data in CIF or other electronic format.

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