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FULL PAPER

Synthesis and coordination chemistry of 1,4,7,10,13-pentakis-(2-hydroxyethyl)-1,4,7,10,13-pentaazacyclopentadecane: a five armed pendant donor macrocycle

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Synthesis of the five armed pendant donor macrocycle 1,4,7,10,13-pentakis(2-hydroxyethyl)-1,4,7,10,13-pentaazacyclopentadecane (phec15) has been achieved by reaction of 1,4,7,10,13-pentaazacyclopentadecane ([15]aneN$_5$) with ethylene oxide in the absence of light and oxygen over an eight day period. The first three pK_a values for phec15 have been determined by potentiometric titration (I = 0.1 mol dm^{-3} NEt$_4$ClO$_4$) to be 8.51 ± 0.01, 7.57 ± 0.01 and 3.74 ± 0.01, respectively, and the final two are < 2.3. The stability constants (log(K/dm^3 mol^{-1}) for [M(phec15)]$^{2+}$ complexes in aqueous solution where M = Co(II), Cu(II), Zn(II), Cd(II) and Pb(II) are 7.45 ± 0.03, 14.69 ± 0.02, 8.47 ± 0.01, 12.57 ± 0.03, and 10.35 ± 0.03, respectively. Gas phase *ab initio* modelling predicts that phec15 adopts the *trans*-I configuration, by virtue of linked hydrogen bonding between the five pendant hydroxyl groups, and that [Ba(phec15)]$^{2+}$ and [Sr(phec15)]$^{2+}$ are ten coordinate with an approximately pentagonal prismatic structure in which the plane of the five oxygen atoms is rotated either clockwise or anticlockwise with respect to the nitrogen atom plane, giving rise to Λ and Δ enantiomers, respectively. Variable temperature ^{13}C{^{1}H} NMR spectra support these structural predictions and in the case of [Ba(phec15)]$^{2+}$ complete lineshape analysis gave the kinetic parameters k = (4.0 ± 0.3) × 10^4 s^{-1}, $\Delta H^{\ddagger}$ = 45.4 ± 2.2 kJ mol^{-1} and $\Delta S^{\ddagger}$ = −4.5 ± 8.5 J K^{-1} mol^{-1} for intramolecular exchange between the Λ and Δ forms. Gas phase *ab initio* modelling and ^{13}C{^{1}H} NMR spectra indicate that [Cd(phec15)]$^{2+}$ is most probably six coordinate with an approximately trigonal prismatic N$_3$O$_3$ donor atom set arising from coordination of non-adjacent nitrogen atoms and their associated pendant hydroxyl groups.

Introduction

Pendant donor polyaza macrocyclic ligands are now utilised in a steadily increasing range of applications. These include enzyme modelling; synthetic ribonuclease investigations; as nucleobase recognition agents, or contrast agents for magnetic resonance imaging; in the formation of luminescent sensors, with either pendant fluorophores or pendant antennae; in tumour directed radioisotope carriers; and as experimental surfactants.[1] The pendant donor polyaza macrocycles used in these applications have so far been derived exclusively from triaza or tetraaza macrocycles, thus limiting the number of pendant arms, which are usually attached through the nitrogen atoms, to a maximum of four. In association with our efforts to build metal ion activated molecular receptors,[2,3] we have become interested in constructing 2-hydroxyethylated pentaaza macrocyclic ligands which could have up to five pendant 2-hydroxyethyl groups. If, under the influence of a ten coordinate metal ion, all five pendant arms of such a ligand were to project in the same direction with respect to a planar array of nitrogen atoms, collectively they would form a receptor cavity with fivefold symmetry when equipped with aromatic appendages. While there is a considerable body of information available concerning the synthesis,[4] and coordination chemistry of 1,4,7,10,13-pentaazacyclopentadecane (hereafter referred to as [15]aneN$_5$),[5–9] which is the simplest pentaaza macrocycle from which nitrogen attached pendant donor derivatives can be formed, there is virtually no information on its pentakis(2-hydroxyethyl) derivative, 1,4,7,10,13-pentakis(2-hydroxyethyl)-1,4,7,10,13-pentaazacyclopentadecane (hereafter referred to as phec15 and shown in Fig. 1); just one brief account of its synthesis and partial purification.[10] It is the purpose of this report to provide a viable synthesis for phec15, to report on its protonation constants and the stability of its coordinative interactions with a series of divalent metal ions, and to describe in detail the structure of its complexes with Ba(II) and Sr(II), where the full decadentate potential of the ligand is realised, and with Cd(II) and Zn(II) where it is not.

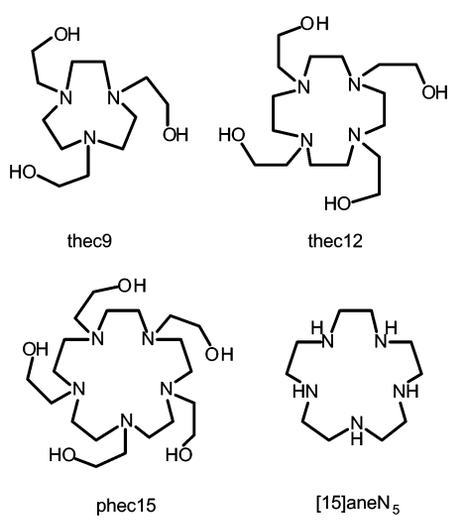

Fig. 1 Ligands discussed in this paper.

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Table 1 Protonation constants at 298.2 K and $I = 0.1$ mol dm^{-3} (NEt_4ClO_4) for phec15, determined in this study, together with literature values for thec9, thec12 and [15]aneN$_5$

Ligand	log K_1	log K_2	log K_3	log K_4	log K_5
thec9[a]	11.52	3.42	< 3.42	—	—
thec12[b]	9.78	8.01	2.28	< 2.3	—
phec15	8.51 ± 0.01	7.57 ± 0.01	3.74 ± 0.02	< 2.3	< 2.3
[15]aneN$_5$[c]	10.85	9.65	6.00	1.74	1.16

[a] Ref. 12, $I = 0.1$ mol dm^{-3} $NaNO_3$. [b] Ref. 13, $I = 0.1$ mol dm^{-3} $NaNO_3$. [c] Ref. 14, $I = 0.2$ mol dm^{-3} $NaClO_4$.

Table 2 Formation constants at 298.2 K for phec15 and related ligand metal complexes together with pK_a values for the pendant hydroxyl group[a]

Reaction	Ligand	log$_{10}K$					
		Co^{2+}	Cu^{2+}	Zn^{2+}	Cd^{2+}	Pb^{2+}	Ba^{2+}
$M^{2+} + LH^+ \rightleftharpoons MLH^{3+}$	thec12[b]	5.8	3.5	4.0	5.2	3.1	[c]
	phec15	4.63 ± 0.03	[c]	5.10 ± 0.04	7.34 ± 0.04	6.05 ± 0.06	[c]
	15aneN$_5$[d]	[c]	21.7	11.3	11.7	10.2	[e]
$M^{2+} + L \rightleftharpoons ML^{2+}$	thec9[f]	[e]	15.5	12.1	10.6	12.1	[e]
	thec12[b]	6.0	15.2	12.8	14.6	15.3	4.84[g]
	phec15	7.45 ± 0.03	14.69 ± 0.02	8.47 ± 0.01	12.57 ± 0.03	10.35 ± 0.03	< 2[h]
	15aneN$_5$[d]	16.8[i]	28.3	19.1	19.2	17.3	[e]
pK_a							
$ML^{2+} \rightleftharpoons ML_{-H}^{+} + H^+$	thec12[b]	8.5	9.3	8.3	9.7	11.1	[c]
	phec15	9.33 ± 0.06	10.01 ± 0.02	8.95 ± 0.01	9.99 ± 0.03	10.79 ± 0.03	[c]
	15aneN$_5$[d]	[c]	[c]	[c]	[c]	[c]	[e]

[a] This work, unless otherwise noted. $I = 0.1$ mol dm^{-3} NEt_4ClO_4, unless otherwise noted. A value of 13.81 was obtained for pK_w under these conditions. [b] Ref. 13, $I = 0.1$ mol dm^{-3} $NaNO_3$. [c] Reaction not observed. [d] Ref. 16, $I = 0.2$ mol dm^{-3} $NaClO_4$. [e] Reaction not carried out. [f] Ref. 15, $I = 0.1$ mol dm^{-3} $NaNO_3$, $[MLH]^{3+}$ and $[ML_{-H}]^+$ species were not reported for thec9. [g] Ref 17. [h] The same result was also found for Sr^{2+}. [i] Ref. 18, 308.2 K, $I = 0.2$ mol dm^{-3} $NaClO_4$.

Results and discussion

Phec15 synthesis and protonation constants

The synthesis of phec15 reported by Dale *et al.*,[10] was achieved by reaction of [15]aneN$_5$ with ethylene oxide in water over a 30 hour period, however, these conditions apparently gave rise to a product badly contaminated by partially 2-hydroxyethylated compounds that were difficult to remove completely.[10] We have found it possible to produce the pure product in 78% yield from the same reaction if it is carried out at room temperature in ethanol, in the absence of light, over an eight day period. Shorter reaction periods result in partially 2-hydroxyethylated compounds, as noted previously, but not in a useful succession of non-overlapping steps that would permit easy isolation of any of them. A complicating feature of this synthesis, not reported for the triaza or tetraaza analogues (hereafter referred to as thec9 and thec12, respectively), is the tendency that phec15 has to convert from a colourless oil to a more viscous reddish-brown material when exposed to a combination of light and air. This decomposition is exacerbated by heat and is presumably the familiar, though poorly understood, occurrence of tertiary amine autoxidation, known to be promoted by the presence of a hydroxyl group on the carbon atom β to the amine.[11]

The protonation constants for phec15 were measured by potentiometric titration at 298.2 K in aqueous NEt_4ClO_4, at $I = 0.1$ mol dm^{-3}, and are given in Table 1 with the corresponding values for thec9, thec12 and [15]aneN$_5$. Phec15 follows the trend established by thec9 and thec12 of displaying a lower first protonation constant than the preceding, smaller, member of the series. The first proton added to polyaza macrocycles with exclusively tertiary amines is believed to become positioned inside the macrocyclic annulus by multiple hydrogen bonds to the adjacent non-protonated nitrogen atoms.[15] It is understandable, therefore, that while this retention is highly effective within the confines of the small rigid structure of thec9, it is less so as the size, and consequent flexibility, of the polyaza macrocycle increases. Subsequent protonation constants show the usual pattern of decreasing magnitude that reflects steadily increasing electrostatic repulsion between successively protonated sites, however, the initial decrease is less marked in phec15 compared with the smaller ligands owing to the greater spacial separation of the early protonation sites.

Metal complex speciation and formation constants

Glass electrode potentiometric titration of protonated phec15 with NEt_4OH in the presence of M^{2+} [M = Co(II), Cu(II), Zn(II), Cd(II) and Pb(II)] revealed the presence of three different complex species $[MLH]^{3+}$, $[ML]^{2+}$ and $[ML_{-H}]^+$, (L = phec15) as the pH was increased. Only 1 : 1 metal : ligand complexes were observed even though titrations were performed with metal : ligand ratios of 2 : 1 and 0.5 : 1 as well as 1 : 1. The formation constants for these species are presented in Table 2 with the corresponding data for thec9, thec12 and [15]andN_5.

It is evident from Table 2 that the $[MLH]^{3+}$ species for phec15, in which one of the five nitrogen atoms is protonated, are, with the exception of Co(II), more stable than their thec12 counterparts, where protonation of one of four of the available nitrogen atoms exerts a larger destabilising effect with respect to the corresponding $[ML]^{2+}$ species. The relatively low stability of $[CoLH]^{3+}$ compared to other $[MLH]^{3+}$ [M = Cu(II), Zn(II), Cd(II), Pb(II)] when L is pentaaza has been noted before,[18] and has been attributed to Co(II) having a stronger tendency to utilise all five nitrogen atoms for binding the ligand in a folded, square pyramidal geometry. The $[ML]^{2+}$ species of phec15 tend to be of lower stability than the corresponding thec12 species, again, with the exception of Co(II). This may relate to only partial utilisation of the nitrogen donor set by metal ions other than Co(II). Molecular modelling work with phec15, to be described below, suggests that Cd(II), for example, may coordinate to only three nitrogen and three oxygen atoms, whereas in all known structures of thec12 complexes N_4O_x

(x = 1–4) coordination is utilised.[19] In addition, the generally lower stability of the phec15 $[ML]^{2+}$ complexes, compared to thec12 $[ML]^{2+}$ complexes, is a consequence of the overall lower basicity of phec15, which can be gauged from the sum of the first two protonation constants ($\log K_1 + \log K_2 = 16.09$) compared to the corresponding sum for thec12 (17.79). The lower stability of the phec15 $[ML]^{2+}$ complexes compared to the $[ML]^{2+}$ complexes of [15]aneN$_5$ also correlates with the lower basicity of phec15 where the logarithms of the first three protonation constants total 19.8 compared to 26.5 for [15]aneN$_5$. The $[ML_{-H}]^{+}$ complexes most probably arise from deprotonation of a coordinated pendant hydroxyl group since this has been observed in solid state structures,[20–22] and these species are not observed with [15]aneN$_5$ where the pendant group is absent. Compared to the situation with thec12 the hydroxyl group of phec15 undergoing deprotonation is generally less acidic. This may relate to greater ease of movement of the metal ion into the larger macrocyclic annulus and in consequence to a weakening of the interaction between the metal ion and its coordinating pendant hydroxyl groups. Molecular modelling of the Cd(II) complex of phec15 indicates that the Cd(II) ion lies out of the plane of the coordinating nitrogen atoms by 0.99 Å whereas similar modelling of the Cd(II) complex of a thec12 derivative places the Cd(II) ion 1.36 Å out of the corresponding plane.[2]

Ab initio modelling of structures of phec15 complexes

Because of our interest in constructing metal ion activated molecular receptors,[2,3] we were principally interested in finding metal ions that would cause phec15 to bind with a planar array of nitrogen atoms and all five arms projecting in the same direction; the *trans*-I configuration.[23] Previous work with [15]aneN$_5$ has shown that whether or not a planar array of nitrogen atoms will eventuate in any particular complex is unpredictable. For example, [Cd([15]aneN$_5$)Cl$_2$] is pentagonal bipyramidal with the macrocycle planar and *trans*-dichloro ligands, whereas [Cd([15]aneN$_5$)NO$_3$]NO$_3$ is pseudo-octahedral with the macrocycle folded and one monodentate nitrate ligand.[24] In the case of phec15 it was even less clear just how the N$_5$ donor set would dispose itself around a metal ion, when faced with competition for binding sites from the set of pendant hydroxyl groups. In previous work, gas phase structures that were predicted for these types of complex by *ab initio* molecular orbital calculations have correlated well with solid state structures determined from X-ray diffraction data.[2,25] In view of this, we carried out *ab initio* modelling of free phec15 and of its complexes with metal ions likely to produce ten coordinate complexes to see if *trans*-I complexes were likely to form. The Ba(II) and Sr(II) complexes were modelled first because the oxygen analogue of [15]aneN$_5$, [15]-crown-5, has been shown to produce the complex $[Ba([15]\text{-crown-}5)_2]^{2+}$,[26] which has a pentagonal antiprismatic structure, and [Sr([15]-crown-5)-(H$_2$O)(NO$_3$)$_2$] which is also ten coordinate.[27]

Ab initio modelling of phec15 was performed using the Gamess-US program[28] at the restricted Hartree–Fock level of theory with the in-built effective core potential-containing basis set of Stevens, Basch, Krauss, Jasien and Cundari (hereafter referred to as the SBKJC basis set). This modelling predicts that the global energy minimized structure for the free ligand in the gas phase is one in which it has C_5 symmetry and is consequently dissymmetric. The five nitrogen atoms of the macrocycle and five oxygen atoms of the pendant hydroxyl groups define the pentagonal faces of a pseudo-pentagonal prism, as shown in Fig. 2. The O$_5$ plane is rotated by an angle ϕ of 4.5° with respect to the N$_5$ plane (for a regular pentagonal prism, having C_{5v} symmetry, $\phi = 0°$) as a consequence of the spiralling of the pendant arms. In Fig. 1, the structure is arbitrarily drawn as the Δ enantiomer, with the spiralling in the anticlockwise sense when viewed from above the O$_5$ plane. As will be shown

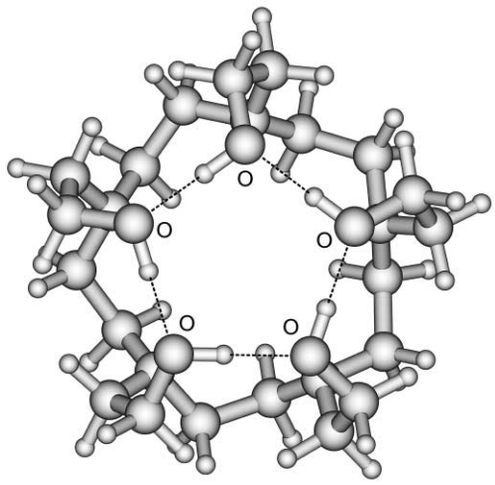


Fig. 2 *Ab initio* modelled global energy minimum structure for phec15 viewed down the C_5 axis with the plane of the five oxygen atoms uppermost. Hydrogen bonds are dotted.

below, rapid interconversion between this and the isoenergetic Λ enantiomer is believed to occur in solution. The low steric energy associated with these particular conformers presumably derives from the stabilising effect of the network of five hydrogen bonds that link the pendant hydroxyl groups together. Details of important predicted bond lengths and angles for the structure are given in Table 3.

Modelling of the Ba(II) and Sr(II) phec15 complexes in the same way predicts that in each case the metal ion will insert into the ligand with minimal disruption to its predicted structure, apart from the loss of the linked hydrogen bonding, and become ten coordinate. Details of important predicted bond lengths and angles are given in Table 3 and a plan view of the predicted Ba(II) structure, also arbitrarily drawn as the Δ enantiomer, is provided in Fig. 3. The only major difference between

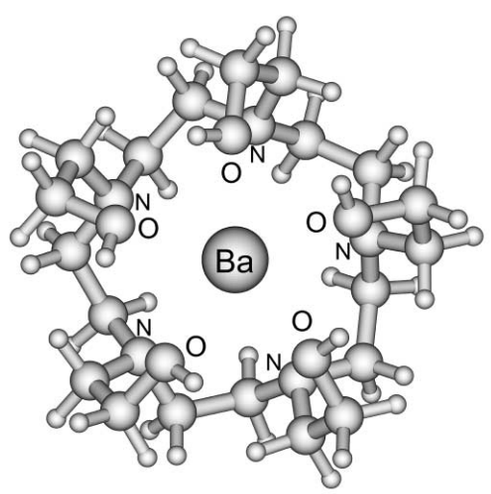


Fig. 3 *Ab initio* modelled global energy minimum structure for $[Ba(phec15)]^{2+}$ viewed down the C_5 axis with the plane of the five oxygen atoms uppermost. For clarity the ten bonds from the five oxygen and five nitrogen atoms to the central Ba(II) ion are not shown.

this and the predicted Sr(II) structure lies in the positioning of the larger Ba(II) ion 0.15 Å further away from the N$_5$ plane, which in turn increases the O–O through space separations by 0.22 Å.

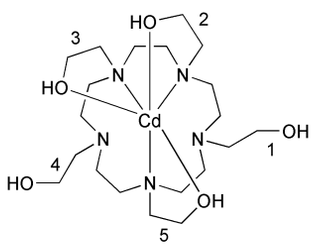
To assess the nature of structures of phec15 complexes likely to be adopted by metal ions of smaller ionic radius and less likely to be ten coordinate, $[Cd(phec15)]^{2+}$ was modelled in the same way. The prediction is that $[Cd(phec15)]^{2+}$ will have a six coordinate structure in which three non-adjacent nitrogen

Table 3 Bond lengths (Å) and angles (°) for either enantiomer of phec15, $[Ba(phec15)]^{2+}$ and $[Sr(phec15)]^{2+}$ derived from *ab initio* calculations using Gamess-US with the SBKJC basis set[a]

	phec15	$[Ba(phec15)]^{2+}$	$[Sr(phec15)]^{2+}$
O–O distance	2.69	2.94	2.72
N–N distance	3.28	3.19	3.15
O plane–N plane distance	2.95	2.88	2.84
M–O distance	—	2.83	2.73
M–N distance	—	3.12	3.02
M–O plane distance	—	1.34	1.45
M–N plane distance	—	1.54	1.39
H ⋯ O distance	1.71	2.50	2.10
O–H ⋯ O angle	178.84	107.15	120.32
Twist angle ϕ	4.5	4.0	1.1

[a] The global minimum energies for phec15, $[Ba(phec15)]^{2+}$ and $[Sr(phec15)]^{2+}$ are −261.964287 H, −261.336379 H and −261.388193 H, respectively, where 1 H = 2622.99 kJ mol^{-1}.

Table 4 Bond lengths (Å) for $[Cd(phec15)]^{2+}$ derived from *ab initio* calculations using Gamess-US with the SBKJC basis set.[a] Atom numbering is in accordance with the arm numbering on the following figure:



	$[Cd(phec15)]^{2+}$
O–O distance	O1–O2 = 4.52
	O2–O3 = 2.68
	O3–O4 = 3.81
	O4–O5 = 2.94
	O5–O1 = 2.65
N–N distance	N1–N2 = 3.23
	N2–N3 = 3.10
	N3–N4 = 3.11
	N4–N5 = 3.30
	N5–N1 = 3.12
M–O distance	Cd–O1 = 4.15
	Cd–O2 = 2.39
	Cd–O3 = 2.34
	Cd–O4 = 4.28
	Cd–O5 = 2.30
M–N distance	Cd–N1 = 3.33
	Cd–N2 = 2.56
	Cd–N3 = 2.54
	Cd–N4 = 3.38
	Cd–N5 = 2.60
O plane–N plane distance	2.51
Cd–N_3 plane	0.99
Cd–O_3 plane	1.52

[a] The global minimum energy for $[Cd(phec15)]^{2+}$ is −427.671729 H, where 1 H = 2622.99 kJ mol^{-1}.

atoms define one triangular face of a pseudo-trigonal prism, together with their associated pendant hydroxyl groups, which define the opposite face. The structure is strictly asymmetric, but is close to having a plane of symmetry which passes through the unique N–O chelate ring that is positioned between the non-coordinating nitrogen atoms. The Cd(II) ion is further removed from the nitrogen atom of this chelate ring (2.60 Å) than from either of the other nitrogen atoms to which it coordinates (2.56 and 2.54 Å), each of which is part of an N–N chelate as well as an N–O chelate. Full details are given in Table 4 and Fig. 4.

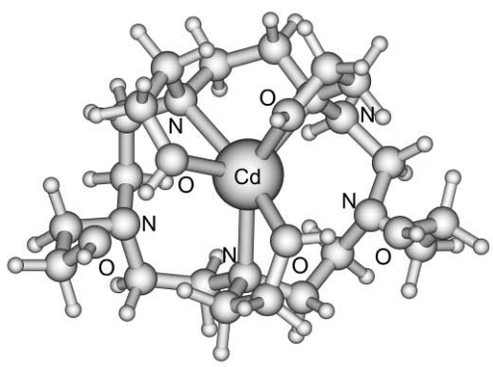


Fig. 4 *Ab initio* modelled global energy minimum structure for $[Cd(phec15)]^{2+}$ viewed from above the plane of the oxygen atoms.

Synthesis and $^{13}C\{^1H\}$ NMR of phec15 complexes

Complexes of phec15 with Ba(II), Sr(II), Cd(II) and Zn(II) were precipitated as their perchlorate salts upon dissolution of the appropriate metal perchlorate in ethanol followed by addition of an ethanolic solution of the ligand.

The $^{13}C\{^1H\}$ NMR spectra of phec15, $[Ba(phec15)](ClO_4)_2$ and $[Sr(phec15)](ClO_4)_2 \cdot 3H_2O$ at 295 K in d_4-MeOH all show a pattern of three resonances in an intensity ratio of 5 : 5 : 10, attributable to the $-CH_2OH$, $-CH_2CH_2OH$ and macrocycle carbon atoms, respectively (partial overlap of the last two resonances occurs with $[Sr(phec15)]^{2+}$). This pattern of ^{13}C NMR resonances is consistent with the molecules having higher symmetry than that predicted by the modelling, for which a pattern of four resonances in a 5 : 5 : 5 : 5 intensity ratio would be expected, but this is unsurprising since apparent symmetry enhancements are well known in molecules of this type where molecular dynamics can cause environmental averaging.[29] To test for this we recorded the $^{13}C\{^1H\}$ NMR spectrum of phec15 and each complex at temperatures down to 205 K. In the case of $[Ba(phec15)]^{2+}$ the ten atom resonance originating from the macrocycle carbon atoms split into two resonances of equal intensity, as shown in Fig. 5, giving a total of four resonances in the intensity ratio consistent with the predicted structure. For $[Sr(phec15)]^{2+}$ the same resonance underwent broadening but did not split, above the freezing point of the solvent, indicating nonetheless that the predicted structure is supported by experimental findings. No resonance broadening was observed in the corresponding spectra of phec15. This could indicate that the predicted gas phase structure is not that which exists in d_4-MeOH solution, where intermolecular hydrogen bonding involving solvent molecules may disrupt the linked intramolecular hydrogen bonding. However, we know from other work with derivatives of thec12 that hydrogen bonded structures predicted for the gas phase on the basis of similar calculations do correlate with NMR observations in d_4-MeOH,[30,31]

Table 5 Kinetic parameters derived from $^{13}C\{^1H\}$ NMR lineshape analysis for helicity interchange in $[Ba(phec15)]^{2+}$ and related complexes in d_4-MeOH

Complex	k (298.2 K)/s^{-1}	$\Delta H^{\ddagger}$/kJ mol^{-1}	$\Delta S^{\ddagger}$/J K^{-1} mol^{-1}
$[Ba(thec9)]^{2+}$ [a]	6.9×10^4	28.1	−58.1
$[Ba(thec12)]^{2+}$ [b]	4.45×10^2	43.9	−47.0
$[Ba(phec15)]^{2+}$	$(4.0 \pm 0.3) \times 10^4$	45.4 ± 2.2	−4.5 ± 8.5

[a] Ref. 35. [b] Ref. 17.

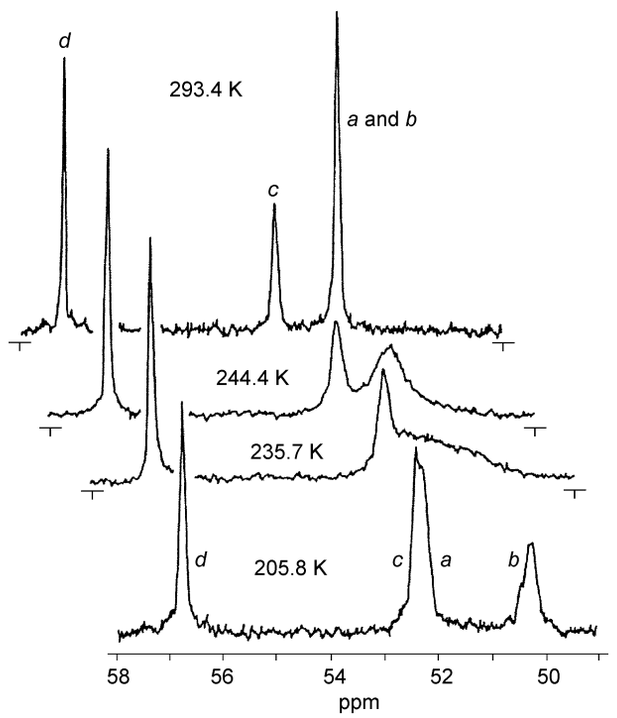


Fig. 5 The temperature variation of the $^{13}C\{^1H\}$ 75.47 MHz NMR spectrum of $[Ba(phec15)](ClO_4)_2$ in d_4-MeOH.

so it seems more probable that the dynamic process responsible for the ^{13}C NMR coalescence in $[Ba(phec15)]^{2+}$ and $[Sr(phec15)]^{2+}$ also operates for phec15, but at a fast rate that results in an environmentally averaged spectrum above 205 K.

The dynamic process implicated above is most likely the helicity interchange process that has previously been observed for complexes of thec9 and thec12.[32,33] This interconverts the Δ and Λ enantiomers of the C_n structure *via* a prismatic (C_{nv}) transition state, where $\phi = 0°$. It is illustrated for $[Ba(phec15)]^{2+}$ in Fig. 6. Complete lineshape analysis of the broadening and

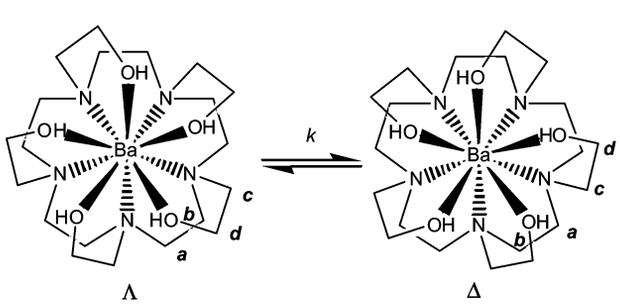


Fig. 6 Interchange between the Λ and Δ enantiomers of $[Ba(phec15)]^{2+}$. For clarity the twist angle ϕ is exaggerated.

coalescence of the macrocycle carbon resonances, a and b (Fig. 5) for $[Ba(phec15)]^{2+}$ gave the kinetic parameters listed in Table 5.[34] In doing this the spectra used were collected at 10 K intervals between 293.4 and 205.8 K and at 5 K intervals around the coalescence temperature. It is interesting to note that when the Ba(II) complexes of the smaller ligands thec9 and thec12 are compared to $[Ba(phec15)]^{2+}$a trend emerges in $\Delta S^{\ddagger}$ which indicates that the ordering of the prismatic transition state decreases as the ring size increases. This decrease becomes significantly more substantial in moving from the tetraaza to the pentaaza ligand than from the triaza to the tetraaza. The trend in $\Delta H^{\ddagger}$ is towards increasing endothermicity as the ring size increases. This is probably related to the increasing number of bond deformations required whilst moving through the transition state, offset to some extent by the increasingly greater flexibility that the larger rings afford.

The $^{13}C\{^1H\}$ NMR spectrum displayed by $[Cd(phec15)](ClO_4)_2$ at 295 K in d_4-MeOH shows 11 resonances, which is the pattern consistent with the complex having the predicted structure but with a plane of symmetry passing through the unique N–O chelate ring. Environmental averaging responsible for this apparent symmetry enhancement is readily understandable in terms of molecular movement similar to the helicity interchange discussed above. Attempts to resolve the 11 resonance spectrum into the 20 resonance spectrum expected for the predicted structure in its static form were unsuccessful as only resonance broadening could be observed before the freezing point of the solvent was reached. A similar pattern of $^{13}C\{^1H\}$ NMR behaviour was exhibited by $[Zn(phec15)](ClO_4)_2 \cdot H_2O$.

Experimental

General

$^{13}C\{^1H\}$ and ^1H NMR spectra were recorded at 75.47 and 300.08 MHz, respectively, using a Varian Gemini 300 spectrometer. ^{13}C chemical shifts are quoted with respect to the central resonance of the solvent multiplet for which the resonance position was taken as δ 77.00 for $CDCl_3$, δ 39.60 for d_6-DMSO and δ 47.05 for d_4-MeOH. ^1H NMR chemical shifts in $CDCl_3$ were referenced to the residual $CHCl_3$ resonance taken as δ 7.26. Centrifuging was performed using a Hettich EBA 12 Zentrifugen, all samples were placed in Greiner 50 cm^3 plastic screw top centrifuge tubes. Elemental analyses were performed at the University of Otago, New Zealand. [15]aneN_5 was prepared by a previously published procedure.[4] All solvents were purified before use by established methods.[36] Reactions were carried out under an atmosphere of dry nitrogen.

Syntheses

1,4,7,10,13-Pentakis(2-hydroxyethyl)-1,4,7,10,13-pentaazacyclopentadecane (phec15). Ethylene oxide (1.75 cm^3, 35 mmol) was carefully added to a stirring solution of [15]aneN_5 (1.0 g, 4.65 mmol) in dry ethanol (22 cm^3) at 0 °C. Once added the vessel was sealed under nitrogen, stored in the absence of light and allowed to slowly warm to room temperature. After 8 days the solvent and excess ethylene oxide were evaporated off leaving the crude product as a pale yellow oil. Dichloromethane (100 cm^3) was added to it producing a cloudy suspension due to the presence of an insoluble polymeric residue. The suspension was twice centrifuged at 6000 rpm for 5 min leaving the polymeric residue adhering to the walls of the centrifuge tube. Solvent removal and drying *in vacuo* gave the product as a colourless oil (1.58 g, 78%). ^1H NMR ($CDCl_3$): δ 5.30 (s, OH,

5H) 3.69, (t, $J = 4.8$ Hz, 10H); 2.63, (s, 20H); 2.59, (t, $J = 4.8$ Hz, 10H). ^{13}C NMR ($CDCl_3$): δ 58.59 (5C), 56.03 (5C), 52.55 (10C).

Phec15·5HBr. Hydrobromic acid (48%, 0.37 cm^3, 3.25 mmol) was added dropwise to a stirring solution of phec15 (0.28 g, 0.638 mmol) in dry ethanol (10 cm^3) cooled to 0 °C. The pentahydrobromide salt precipitated out as a fine cream solid and was filtered off under nitrogen, washed with cold ethanol (2 cm^3) and dried *in vacuo*. Yield 279 mg, 52%. ^{13}C NMR (d_6-DMSO): δ 56.02 (5C), 55.11 (5C), 49.00 (10C). (Found: C, 28.8; H, 6.3; N, 8.16. $C_{20}H_{50}Br_5N_5O_5$ requires C, 28.59; H, 6.00; N, 8.34%).

[Ba(phec15)](ClO$_4$)$_2$. Barium(II) perchlorate (0.29 g, 0.86 mmol) was dissolved in dry ethanol (5 cm^3) and the solution was added dropwise to a solution of phec15 (0.25 g, 0.57 mmol) in dry ethanol (15 cm^3) with stirring. The resultant solution was heated to reflux for 2.5 h. On cooling, cream crystals formed which were filtered and washed with ice cold ethanol (5 cm^3). Yield 213 mg, 48%. ^{13}C NMR (d_4-MeOH): δ 57.23 (5C), 53.29 (5C), 52.15 (10C). (Found: C, 31.2; H, 6.1; N, 8.7. $C_{20}H_{45}BaCl_2N_5O_{13}$ requires C, 31.12; H, 5.88; N, 9.07%).

[Sr(phec15)](ClO$_4$)$_2$·3H$_2$O. A solution of strontium(II) perchlorate hexahydrate (220 mg, 0.77 mmol) in dry ethanol (5 cm^3) was added dropwise to a solution of phec15 (334 mg, 0.77 mmol) in dry ethanol (15 cm^3) over several minutes. On addition of the metal perchlorate the solution became cloudy and the resultant suspension was heated to reflux for 3 h. Once cold, the solvent was removed and the resultant cream solid dried *in vacuo*. Yield 480 mg, 87%. ^{13}C NMR (d_4-MeOH): δ 56.77 (5C), 53.39 (very broad, 15C). (Found: C, 30.9; H, 6.2; N, 8.7. $C_{20}H_{51}Cl_2N_5O_{16}Sr$ requires C, 30.95; H, 6.62; N, 9.02%).

[Cd(phec15)](ClO$_4$)$_2$. Cadmium(II) perchlorate hexahydrate (895 mg, 2.1 mmol) was dissolved in dry ethanol (10 cm^3) and the solution added dropwise to a solution of phec15 (619 mg, 1.4 mmol) in dry ethanol (10 cm^3). The mixture immediately became cloudy and was refluxed overnight. After cooling half the solvent was removed causing the complex to crystallize as white crystals, which were filtered and washed with ice cold ethanol (5 cm^3). Yield 621 mg, 80%. ^{13}C NMR (d_6-DMSO): δ 58.04 (1C), 56.23 (broad, 4C), 55.71 (2C), 55.32 (2C), 55.10 (2C), 53.63 (2C), 52.18 (2C), 51.52 (2C), 51.48 (1C), 50.80 (2C). (Found: C, 32.1; H, 6.1; N, 9.1. $C_{20}H_{45}CdCl_2N_5O_{13}$ requires C, 32.16; H, 6.07; N, 9.38%).

[Zn(phec15)](ClO$_4$)$_2$·H$_2$O. Zinc(II) perchlorate hexahydrate (188 mg, 0.50 mmol) was dissolved in dry ethanol (5 cm^3) and the solution was added slowly to a stirred solution of phec15 (199.5 mg, 0.46 mmol) in dry ethanol (12 cm^3). A white sticky precipitate formed and the suspension was heated at reflux for 2 h causing complete dissolution. After this time half the solvent was evaporated off. On cooling the solution white crystals of the product formed. These were filtered off, washed with cold ethanol (6 cm^3) and dried *in vacuo*. Yield 107 mg, 33%. ^{13}C NMR (d_6-DMSO): δ 60.02 (1C), 56.32 (broad, 4C), 55.38 (2C), 55.11 (2C), 52.71 (2C), 51.37 (2C), 50.75 (2C), 50.18 (broad, 3C), 48.79 (2C). Found: C, 33.2; H, 6.3; N, 9.4. $C_{20}H_{47}Cl_2N_5O_{14}Zn$ requires C, 33.46; H, 6.60; N, 9.76%).

Potentiometric titrations

The potentiometric titrations were carried out under an inert atmosphere of water-saturated argon in a water jacketed vessel maintained at 25 °C. Data were obtained from 10 cm^3 aliquots of solution containing 0.010 M $HClO_4$, 0.100 M NEt_4ClO_4, and approximately 1.0×10^{-3} M of phec15 titrated with 0.10 M NEt_4OH. A Metrohm E665 Dosimat autoburette equipped with a 5 cm^3 burette was used to deliver the titrant and the potential measured by an Orion Ross Sure Flow 81–72BN combination electrode connected to an Orion SA 720 pH meter. The autoburette and pH meter were interfaced to an IBM compatible personal computer which controlled the addition of titrant using a program written by Drs A. P. Arnold and P. A. Duckworth so that successive additions of titrant caused a decrease of *ca.* 4 mV in the potential reading. The electrode was calibrated by a titration in the absence of ligand and fitting the resulting data from this strong acid strong base titration to the Nernst equation to find correct values for E_o and pK_w. The pK_a and stability constants were determined using the program SUPERQUAD.[37] Stability constant data were gathered from solutions to which 0.1 M metal perchlorate solution was added so as to give a metal-to-ligand ratio in the range 0.5 : 1 to 2 : 1. At least three titrations, with different ratios, were performed for each metal ion.

Variable temperature ^{13}C{^{1}H} NMR and lineshape analysis

^{13}C{^{1}H} NMR spectral data were recorded at 10 K intervals, thermostatted to ±0.3 K, in the temperature range 205–373 K and at 5 K intervals around the coalescence temperature. Lineshape analysis, leading to a determination of the rate constant, k, characterising the rate of intramolecular exchange at each temperature,[34] was conducted using a Digital Venturis 575 computer. The temperature-dependent ^{13}C line widths and chemical shifts employed in the analysis were obtained by extrapolation from low temperatures where no exchange-induced modification occurred.

Ab initio modelling

Ab initio modelling was performed using Gamess-US[28] at the restricted Hartree–Fock level of theory with the in-built effective core potential-containing basis set of Stevens, Basch, Krauss, Jasien and Cundari (the SBKJC basis set).[38–40] All electrons for H, C, N and O were incorporated, but only the valence shell electrons for Ba^{2+}, Sr^{2+} and Cd^{2+}, together with their effective core potentials. To ensure that the predicted structures shown in Figs. 2–4 and described in Tables 3 and 4 best represent the structure having the true global energy minimum, trial structures with pendant arms either all on the same side of the nitrogen atom plane or on differing sides were used as starting points for the minimisation. A range of pendant arm conformations were superimposed on these structures to give a broad selection of starting points. Irrespective of the starting point convergence to the structure shown in Figs. 2–4 and described in Tables 3 and 4 resulted, confirming these as the most likely molecular structures.

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