Dinuclear copper and zinc complexes of a hexaazamacrocycle containing *p*-xylyl spacers and bridging anions: theoretical and spectroscopic studies†

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The hexaazamacrocycle 7,22-dimethyl-3,7,11,18,22,26-hexaazatricyclo[26.2.2.2^{13,16}]tetratriaconta-1(30),13,15,-28,31,33-hexaene ($Me_2[30]pbz_2N_6$) was synthesized and characterised by single crystal X-ray diffraction. The macrocycle adopts a conformation with the two aromatic rings almost parallel at a distance of *ca.* 4.24 Å, but displaced relative to each other by *ca.* 1.51 Å. The protonation constants of this compound and the stability constants of its complexes with Cu^{2+} and Zn^{2+}, were determined in water–methanol (9 : 1 v/v) at 25 °C with ionic strength 0.10 mol dm^{-3} in KCl. The potentiometric and spectroscopic studies (NMR of zinc, cadmium and lead complexes, and EPR of the copper complexes) indicate the formation of only dinuclear complexes. The association constants of the dinuclear copper complex with anions (thiocyanate, terephthalate and glyphosate) and neutral molecules (1,4-benzenedimethanol, *p*-xylylenediamine and terephthalic acid) were determined at 20 °C in methanol. The structural preferences of this ligand and of its dinuclear copper(II) complex with a variety of bridging ligands were evaluated theoretically by molecular mechanics calculations (MM) and molecular dynamics (MD) using quenching techniques.

Introduction

Hexaazamacrocycles are interesting and versatile receptor molecules being capable to coordinate one or two metal ions and in addition their protonated forms can also encapsulate anionic guests *via* electrostatic interactions or/and hydrogen bonds.[1,2] In particular macrocyles containing '*p*-xylyl' (*p*-CH$_2$-C$_6$H$_4$CH$_2$) spacers have preorganized sites to accommodate two metal centres forming dinuclear species.

This type of macrocyclic compounds can be used as models to understand the reactivity changes caused by the proximity of the two metals, and also to understand the reactivity of metalloenzymes which require two metal centres located at specific distances to accomplish their biological function. Macrocycles having two triamine moieties separated by spacers are especially useful for such studies because the distance between the metals can be tuned by the type and size of the spacers. The properties of these complexes are modified by the introduction of bridging ligands, which cause structural changes in the macrocyclic framework.[3]

In this work we investigate a 30-membered macrocycle containing two dipropylenetriamine units linked by *p*-xylyl spacers ($Me_2[30]pbzN_6$). The propyltriamine moieties confer considerable flexibility to the macrocycle while the aromatic rings of the *p*-xylyl groups impose special rigidity to the framework. Additionally the *p*-xylyl spacers preorganize the macrocyclic cavity of the dinuclear complex to further accommodation of neutral or anionic substrates. In the present work the ability of $Me_2[30]pbzN_6$ to form dinuclear copper(II) complexes bridging neutral or anionic species, such as thiocyanate, 1,4-benzene-dimethanol, *p*-xylylenediamine, terephthalic acid, terephthalate

anion and the pesticide glyphosate anion, was monitored experimentally *via* spectrophotometric methods and EPR spectroscopy. The conformational preferences of the ligand as well as of the copper(II) dinuclear species were evaluated theoretically through molecular dynamics using quenching techniques.

Results and discussion

Synthesis of the macrocycle

The macrocycle, $Me_2[30]pbz_2N_6$, was synthesized through the condensation of *N,N*-bis(3-aminopropyl)methylamine with terephthaldialdehyde at 0 °C, in acetonitrile, followed by the reduction of the obtained Schiff-base with NaBH$_4$ in ethanol at r.t.. The pure compound was obtained in 41% yield. The adopted procedure was derived from a combination of already described methods used for the synthesis of other macro-cycles.[4,5] The presence of the methyl group appended to the central tertiary amine prevents the formation of the aminal ring, which lead to the contracted macrocyclic form, obtained when the imine group of the extended Schiff-base macrocycle is attacked by the nearby secondary amine function.[6,7]

Another approach to synthesize the same macrocycle was described[8] using silver ion as metal template. However, using this procedure we did not obtain good results.

Acid–base behaviour

The acid–base reactions of $Me_2[30]pbz_2N_6$ were studied by potentiometric methods in water and in H$_2$O–methanol (9 : 1, v/v), at 25 °C, at 0.10 M ionic strength (KCl). The proton-ation constants that were determined are collected in Table 1 together with the constants of the related compounds: $[30]pbz_2N_6$,[9] $[26]pbz_2N_6$,[10–12] $Me_6[26]pbz_2N_6$,[13] $[24]mbz_2N_6$,[14–18] and $[28]mbz_2N_6$.[19]

The values obtained in both media differ only slightly and are of the same order of those determined for $[30]pbz_2N_6$.[9]

Table 1 Protonation (log K^H_i) constants of Me$_2$[30]$p$bz$_2$N$_6$,[a] [30]$p$bz$_2$N$_6$, [26]$p$bz$_2$N$_6$, Me$_6$[26]$p$bz$_2$N$_6$, [24]$m$bz$_2$N$_6$ and [28]$m$bz$_2$N$_6$ ($T = 25.0$ °C; $I = 0.10$ mol dm^{-3} in KCl)

Ion	Equilibrium quotient	Me$_2$[30]$p$bz$_2$N$_6$	[30]$p$bz$_2$N$_6$[d]	[26]$p$bz$_2$N$_6$[e,f,g,h]	Me$_6$[26]$p$bz$_2$N$_6$[i]	[24]$m$bz$_2$N$_6$[j,k,l,m,n]	[28]$m$bz$_2$N$_6$[o]
H$^+$	[HL]/[L][H]	10.41(1);[b] 10.35(1)[c]	9.99[d]	9.52;[e] 9.54;[f] 9.48;[g] 9.73[h]	8.93	9.49;[j] 9.51;[k] 9.57;[l] 9.58;[m] 8.73[n]	10.33;[o]
	[H$_2$L]/[HL][H]	9.82(1);[b] 9.54(1)[c]	9.92[d]	8.57;[e] 8.76;[f] 8.88;[g] 9.05[h]	8.22	8.73;[j] 8.77;[k] 8.84;[l] 8.79;[m] 8.06[n]	9.62;[o]
	[H$_3$L]/[H$_2$L][H]	8.82(1);[b] 8.50(2)[c]	8.43[d]	7.96;[e] 8.16;[f] 8.23;[g] 8.33[h]	7.35	8.03;[j] 7.97;[k] 8.08;[l] 8.08;[m] 7.39[n]	8.57;[o]
	[H$_4$L]/[H$_3$L][H]	7.87(2);[b] 7.41(2)[c]	7.68[d]	7.06;[e] 7.26;[f] 7.37;[g] 7.64[h]	6.44	7.29;[j] 7.09;[k] 7.24;[l] 7.34;[m] 6.60[n]	7.79;[o]
	[H$_5$L]/[H$_4$L][H]	6.79(2);[b] 6.43(2)[c]	6.75[d]	3.2;[e] 3.3;[f] 2.92;[g] 3.68[h]	1.5	3.64;[j] 3.79;[k] 3.59;[l] 3.70;[m] 3.46[n]	7.20;[o]
	[H$_6$L]/[H$_5$L][H]	6.27(2);[b] 5.91(3)[c]	6.42[d]	–;[e] 2.5;[f] 3.37;[g] 2.90[h]	–	3.45;[j] 3.27;[k] 3.06;[l] 3.37;[m] 3.14[n]	6.59;[o]
	[H$_6$L]/[L][H]^6	49.97(1);[b] 48.14(1)[c]	49.19[d]	>36.3;[e] 39.52;[f] 40.44;[g] 41.33[h]	32.44	40.63;[j] 40.40;[k] 40.86;[l] 40.86;[m] 37.38[n]	50.10

[a] Values in parenthesis are standard deviations in the last significant figures. [b] This work in H$_2$O. [c] This work in H$_2$O–methanol (9 : 1, v/v). [d] T, I and the salt are not indicated, ref. 9. [e] $I = 0.10$ mol dm^{-3} (KNO$_3$), ref. 10. [f] $I = 0.10$ mol dm^{-3} (KCl), ref. 10. [g] $I = 0.1$ mol dm^{-3} (KCl), ref. 11. [h] $I = 0.100$ mol dm^{-3} (KCl), ref. 12. [i] $I = 0.15$ mol dm^{-3} (NaCl), ref. 13. [j] $I = 0.100$ mol dm^{-3} (KNO$_3$), ref. 14. [k] $I = 0.10$ mol dm^{-3} (KCl), ref. 15. [l] $I = 0.10$ mol dm^{-3} (NaClO$_4$), ref. 16. [m] $I = 0.1$ mol dm^{-3} (KNO$_3$), ref. 17. [n] $I = 0.100$ mol dm^{-3} (KCl) in 75% ethanol, $T = 35$ °C, ref. 18. [o] $I = 0.100$ mol dm^{-3} (KCl), ref. 19.

The protonation constants corresponding to all basic centres of Me$_2$[30]$p$bz$_2$N$_6$ could be determined successfully by the technique used. This compound has a very high overall basicity, only comparable to that of [28]$m$bz$_2$N$_6$, which also has propyl chains linking the amine centres (see Table 1). This high overall basicity is mainly due to the moderate repulsions between protonated amine centres in contiguous positions, separated by 'propyl' (CH$_2$CH$_2$CH$_2$) chains, compared with the 'ethyl' (CH$_2$CH$_2$) ones of [26]$p$bz$_2$N$_6$, Me$_6$[26]$p$bz$_2$N$_6$ and [24]$m$bz$_2$N$_6$. The first four protonation constants are of similar magnitude for all the compounds listed in Table 1, because they correspond to the protonation of amine centres in alternate positions in the macrocycle, far from each other, and therefore their values are of the order of those of linear amines.[20] Even so it is clear that the macrocycles containing propyl chains have slightly higher values for the first four protonation constants. However, for the fifth and sixth constants, which correspond to the protonation of consecutive amine centres, differences of three or more log units are observed between the compounds having propyl *vs.* ethyl chains. This behaviour can be rationalized in terms of the electrostatic repulsion between positive charged ammonium centres at contiguous positions. Then Me$_2$[30]$p$bz$_2$N$_6$ and [28]$m$bz$_2$N$_6$ have the highest values of the K_5 and K_6 constants. These considerations are supported by NMR titrations carried out for Me$_6$[26]$p$bz$_2$N$_6$.[13]

Crystal structure of Me$_2$[30]$p$bz$_2$N$_6$

The crystal structure of Me$_2$[30]$p$bz$_2$N$_6$·0.5H$_2$O, **1**, is built from an asymmetric unit composed of one discrete molecule and one half solvent water molecule. An ORTEP diagram showing the overall structure of Me$_2$[30]$p$bz$_2$N$_6$ and the atomic notation scheme adopted is presented in Fig. 1.
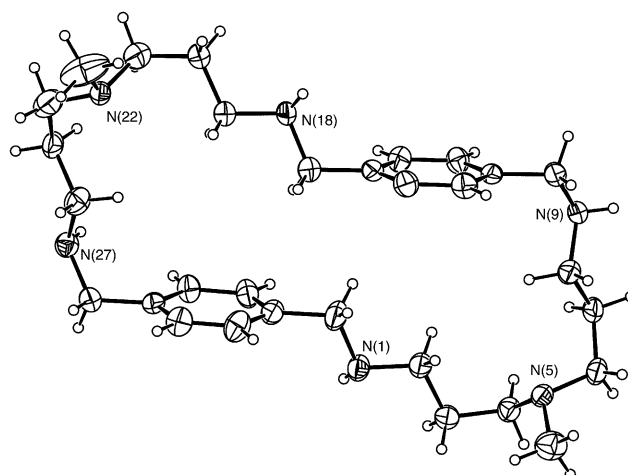
Fig. 1 ORTEP diagram of the compound Me$_2$[30]$p$bz$_2$N$_6$, **1**, with the ellipsoids drawn at 30% probability level showing the labelling scheme adopted.

The macrocycle exhibits a conformation with both phenyl rings almost parallel making a dihedral angle of 5.4° and with centres displaced relative to each other by 1.51 Å. The distance between the aromatic ring planes is 4.24 Å, suggesting that the conformation adopted is stabilised by π–π stacking interactions.

In the Cambridge Data Base[21] only two X-ray structural determinations of dinuclear complexes having related 30-membered hexaazamacrocycles were found: [Cu$_2$([30]p-bz$_2$N$_6$)(CH$_3$CO$_2$)$_2$]$^{2+}$ **2**,[3] and [Ag$_2$(Me$_2$[30]$p$bz$_2$N$_{imine4}$N$_2$)]$^{2+}$ **3** (see Scheme 1).[8] In complex **2** the macrocycle adopts a cleft conformation, in which the aromatic rings are π-stacked with interplanar distances of 3.82 Å. In complex **3** the presence of four imine groups introduced an additional rigidity on the macrocycle and a conformation with a different topology is

R=Me, Me$_2$[30]$p$bz$_2$N$_6$

R=H, [30]$p$bz$_2$N$_6$

Me$_2$[30]$p$bz$_2$N$_2$N$_{imine4}$

R=H, [26]$p$bz$_2$N$_6$

R=Me, Me$_6$[26]$p$bz$_2$N$_6$

[28]$m$bz$_2$N$_6$

[24]$m$bz$_2$N$_6$
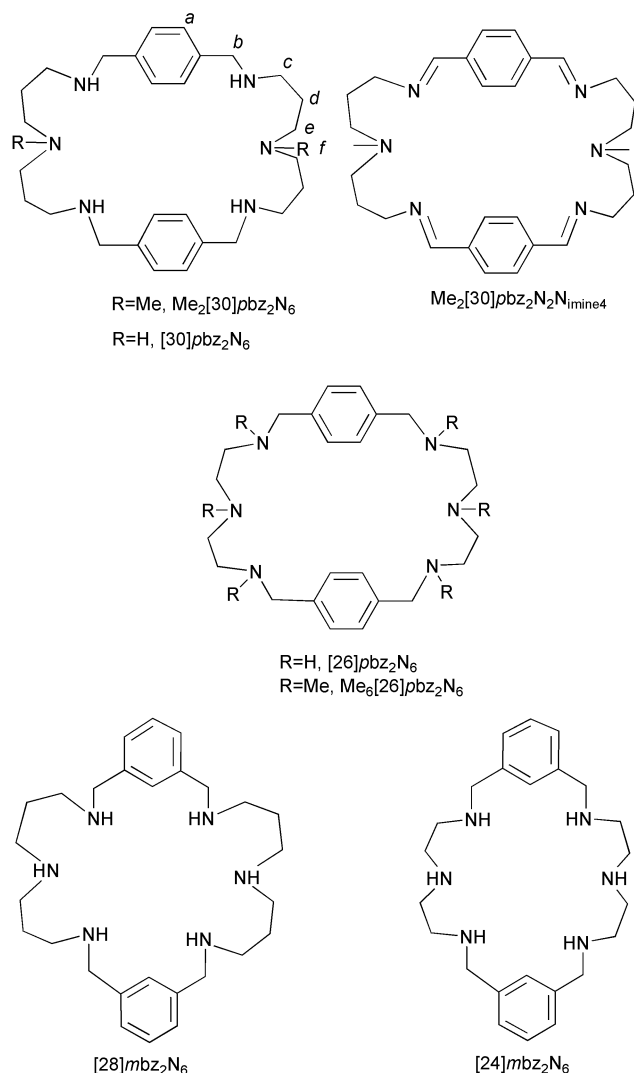
Scheme 1

adopted in which the aromatic rings are almost coplanar. Another structure of a copper complex [Cu$_2$([30]$p$bz$_2$N$_6$)Cl$_4$] **4** is mentioned in the literature,[22] however its structural data are not available.

In the crystal structure of **1** the molecules of Me$_2$[30]$p$bz$_2$N$_6$ are self-assembled *via* N–H ··· N bonding interactions into a 1-D network, as shown in Fig. S1 (ESI†). The hydrogen bonds comprise the concomitant interaction of four neighbouring Me$_2$[30]$p$bz$_2$N$_6$ molecules which give rise to the formation of eight-membered centrosymmetric rings constructed *via* two independent N–H ··· N bonds with distances of 2.51(2) and 2.42(3) Å and angles of 171(4) and 151(5)°, respectively. The oxygen atom of the lattice of water is also involved in the hydrogen bonding network bridging two adjacent Me$_2$[30]$p$bz$_2$N$_6$ molecules with one independent distance N(1)–H ··· O(100) of 2.51(3) Å and an angle for N(1)–H ··· O(100) of 158(2)°.

Metal complex studies

The stability constants of Me$_2$[30]$p$bz$_2$N$_6$ with Cu^{2+} and Zn^{2+} were also determined and the results are collected in Table 2, together with those of [26]$p$bz$_2$N$_6$,[10–12] Me$_6$[26]$p$bz$_2$N$_6$,[23] and [28]$m$bz$_2$N$_6$ [19] (values only for the Cu^{2+} complexes are available) and [24]$m$bz$_2$N$_6$ [14,16,17,24,25] for comparison. For reasons of solubility, the values were obtained in H$_2$O–methanol (9 : 1 v/v) at 25 °C and 0.10 M ionic strength in KCl.

In spite of studying the formation of complexes in several metal : ligand ratios, only dinuclear complexes (M$_2$L^{2+}, M$_2$HL^{3+} and M$_2$L(OH)$_k^{2−k}$, k = 1–4), L = Me$_2$[30]$p$bz$_2$N$_6$, were

formed, as can be observed in the speciation diagram obtained with the HYSS program[26] shown in Fig. S2 (ESI†) for the case of Cu^{2+} complexes. The maximum percentage of the dinuclear complex occurs at pH 7.8 and after pH 8.5 hydroxo-complexes are the main species. It was impossible to determine the constant corresponding to the formation of Zn$_2$L(OH)$_2^{2+}$ due to precipitation. The Zn$_2$L(OH)$^{3+}$ complex is the dominant species above pH 8.

The comparison with the other hexaazamacrocycles listed in Table 2 shows that the complexes with Me$_2$[30]$p$bz$_2$N$_6$ have lower stability constants, in spite of its high basicity. This is expected because several six-membered chelate rings are formed on complexation compared to the five-membered chelate rings formed by [26]$p$bz$_2$N$_6$, Me$_6$[26]$p$bz$_2$N$_6$ and [24]$m$bz$_2$N$_6$. The position at which the benzene rings are linked to the triamine moieties, *para*- or *meta*-, is also important. The comparison of the Me$_2$[30]$p$bz$_2$N$_6$ *vs.* [28]$m$bz$_2$N$_6$ complexes revealed that the last ligand forms with copper(II) only slightly stable complexes, taken into account the higher basicity of the ligand, but it is able to form also mononuclear complexes. Indeed, the introduction of a rigid spacer increases the tendency of the molecule to form dinuclear complexes by a cooperative process, because the coordination of both ends of the molecule lead to a lower energy conformation.[11] However, Clifford *et al.*[11] have observed in the study of [26]$p$bz$_2$N$_6$ *vs.* [24]$m$bz$_2$N$_6$ that the *p*-xylyl linkages increase the stability of the dinuclear complex relative to that of *m*-xylyl, but substantially destabilise the formation of mononuclear complexes. The discrepancy of values given by different authors do not allow a generalization, but it is possible to say that the differences of stability constants for the complexes of both compounds are small and that the tendency of the *para*-derivatives to stabilise dinuclear complexes seems to be confirmed.

The introduction of N-methyl groups in the macrocyclic backbone lead to lower stability constants, see the values of Me$_6$[26]$p$bz$_2$N$_6$ given in Table 2, and this can be ascribed to the lower overall basicity of the macrocycle rather than to other electronic or structural factors.

Ternary species between the dinuclear copper(II) complex and substrates

The association constants of ternary species formed by the addition of different molecules or anions to the dicopper complex of Me$_2$[30]$p$bz$_2$N$_6$ were determined in methanol at 20 °C, using spectrophotometric measurements. The results are summarized in Table 3. The added molecules (1,4-benzenedimethanol, *p*-xylylenediamine, terephthalic acid) and anions [SCN$^−$, terephthalate and glyphosate or *N*-(phosphonomethyl)-glycine], see Scheme 2, have different sizes, different donor atoms and some of them contain a benzene ring which offers the possibility of forming π–π interactions with the benzene rings of the macrocycle. 1,4-Benzenedimethanol does not form ternary complexes with this dinuclear copper complex.

1,4-benzenedimethanol

p-xylylenediamine

terephtalate

glyphosate
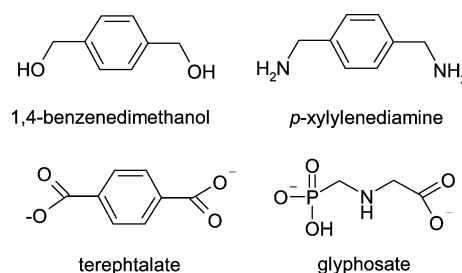
Scheme 2

In the starting complex, [Cu$_2$(Me$_2$[30]$p$bz$_2$N$_6$)Cl$_4$], each metal centre is coordinated to three nitrogen donors of the macrocycle and two chloride anions or water molecules,[22] allowing a

Table 2 Stability constants ($\log \beta_{M_mH_hL_l}$ or $\log K_{M_mH_hL_l}$)[a] of the complexes of Me$_2$[30]$p$bz$_2$N$_6$, [26]$p$bz$_2$N$_6$, [24]$m$bz$_2$N$_6$ and [28]$m$bz$_2$N$_6$ with Cu^{2+} and Zn^{2+} at $T = 25.0$ °C and $I = 0.10$ mol dm^{-3}

Ion	Species *mhl*	Me$_2$[30]$p$bz$_2$N$_6$[b] $\log \beta_{M_mH_hL_l}$	$\log K_{M_mH_hL_l}$[c]	[26]$p$bz$_2$N$_6$ $\log \beta_{M_mH_hL_l}$	Me$_6$[26]$p$bz$_2$N$_6$ $\log \beta_{M_mH_hL_l}$	[24]$m$bz$_2$N$_6$ $\log \beta_{M_mH_hL_l}$	[28]$m$bz$_2$N$_6$ $\log \beta_{M_mH_hL_l}$
Cu^{2+}	101	–	–	17.50;[d] 18.41;[e] –;[f] 11.30[g]	10.03[h]	13.79; 13.63;[j] –;[k] 13.86[l]	11.46[m]
	111	–	–	24.97;[d] 26.24;[e] –;[f] 25.61[g]	17.96[h]	22.48;[i] 22.03;[j] –;[k] 22.11[l]	20.31[m]
	121	–	–	29.36;[d] 30.41;[e] 29.37;[f] 28.22[g]	24.73[h]	29.80;[i] 29.23;[j] 29.54;[k] 29.75[l]	28.40[m]
	131	–	–	–;[d] –;[e] –;[f] 31.41[g]	–	–;[i] 32.91;[j] –;[k] 33.09[l]	34.67[m]
	1−11	–	–	–	1.34[h]	–;[i] 4.70;[j] –;[k,l]	–
	1−21	–	–	–	−9.78[h]	–;[i] −6.78;[j] –;[k,l]	–
	201	17.12(7)	17.12	24.12;[d] 25.98;[e] 25.24;[f] 22.34[g]	18.35[h]	23.47;[i] 24.49;[j] 24.17;[k] 24.06[l]	19.74[m]
	211	24.54(2)	7.42	–	–	–	–
	2−11	8.85(7)	−8.27	–	10.43[h]	14.52;[i] 16.66;[j] 16.79;[k] 16.58[l]	10.89[m]
	2−21	−0.40(9)	−8.45	–;[d] –;[e] 16.96;[f] 13.62[g]	2.39[h]	6.12;[i] 7.92;[j] 8.21;[k] 7.88[l]	1.28[m]
	2−31	−10.66(9)	−10.26	–;[d] –;[e] 8.13;[f] −4.90[g]	–	–;[i] −3.78;[j] –;[k,k]	–
	2−41	−22.0(1)	−11.34	–	–	–	–
Zn^{2+}	101	–	–	–		7.87;[n] –[o]	
	111	–	–			15.84;[n] 15.64[o]	
	121	–	–			22.77;[n] 22.76[o]	
	131	–	–			27.93;[n] –[o]	
	1−11	–	–			−1.23;[n] –[o]	
	201	11.55(4)	11.55			13.66;[n] 11.08[o]	
	211	–	–			–;[n,o]	
	221	26.93(2)	–			–;[n,o]	
	2−11	3.86(3)	−7.69			6.72;[n] 4.68[o]	
	2−21	–	–			–;[m,n] −3.62[o]	

[a] See Experimental section, calculation of stability constants, for definitions. [b] Values in parenthesis are standard deviations in the last significant figures. [c] In H$_2$O–methanol (9 : 1, v/v) and $I = 0.10$ mol dm^{-3} in KCl. [d] $I = 0.10$ mol dm^{-3} (KNO$_3$), ref. 10. [e] $I = 0.10$ mol dm^{-3} (KCl), ref. 10. [f] $I = 0.1$ mol dm^{-3} (KCl), ref. 11. [g] $I = 0.100$ mol dm^{-3} (KCl), ref. 12. [h] $I = 0.15$ mol dm^{-3} (NaCl), ref. 23. [i] $I = 0.100$ mol dm^{-3} (KNO$_3$), ref. 14. [j] $I = 0.10$ mol dm^{-3} (KCl), ref. 24. [k] $I = 0.10$ mol dm^{-3} (NaClO$_4$), ref. 16. [l] $I = 0.1$ mol dm^{-3} (KNO$_3$), ref. 17. [m] $I = 0.100$ mol dm^{-3} (KCl), ref. 19. [n] $I = 0.100$ mol dm^{-3} (KCl) in 75% ethanol, $T = 35$ °C, ref. 18. [o] $I = 0.10$ mol dm^{-3} (NaClO$_4$), ref. 25.

Table 3 Association constants[a] of ternary complex formation (in log units) in methanol and at 20 °C

Complex M : L : A	SCN⁻	BDM	p-XDA	TP acid	TP²⁻	Glyphosate
2 : 1 : 1	2.12(3)	–	2.48(1)	2.52(4)	3.93(3)	3.07(1)
2 : 1 : 2	–	–	4.79(2)	4.98(5)	–	–

[a] Corresponding to the equilibria $[M_2L] + A \rightleftharpoons [M_2LA]$ and $[M_2L] + 2A \rightleftharpoons [M_2LA_2]$.

further binding of a neutral species or anion bridging the two metal centres. Alternatively, the substrate molecules can also replace the chloride anions or the water molecules in the metal coordination sphere, leading to five- or six-coordinate species. Species containing one and two substrate molecules were found (see Table 3), suggesting that each copper centre has five to six coordination environments; both coordination numbers are consistent with the presence of a bridged ligand. In agreement with this, a new band in the UV-vis spectrum appeared at 375 nm when these substrates are added to a solution of the complex, $[Cu_2(Me_2[30]pbz_2N_6)Cl_4]$, which is generally assigned to a ligand-to-metal charge transfer, providing evidence for the formation of a bridge between the two metal centres.[27,28] The association constants determined for the ternary complexes involving the studied substrates are not markedly different, but the lowest values were found for SCN⁻, and a clear preference is apparent for the terephthalate anion and glyphosate, see Table 3.

NMR spectroscopic data of some complexes in solution

In spite of our best efforts, suitable crystals for X-ray diffraction of complexes with $Me_2[30]pbz_2N_6$ could not be obtained, however the ¹H NMR spectra of some diamagnetic complexes, such as those with Zn^{2+}, Cd^{2+} and Pb^{2+} were acquired in D_2O (Table S1, ESI†) and gave some insight into their structures in solution. The spectral assignments, made by TOCSY and ROESY experiments, correspond to the labelling shown in Scheme 1.

From our results is apparent that only dinuclear complexes are formed. The spectra performed in solutions of 1 : 1 mixtures of metal and ligand showed only slight differences from those of the free ligand at the same pD, as they result from mixtures of the free ligand and the dinuclear species.

The ¹H NMR spectra of all complexes, such as also found for the free ligand, show six resonances, confirming the high symmetry of the dinuclear complexes formed: a singlet for the H_a protons of the benzene ring, one singlet for the H_b protons, two triplets for to the H_c and H_e protons, one quintuplet corresponding to the H_d protons and one singlet for the protons of the methyl H_f. At pD values between 9.4 and 9.8 the protons H_c and H_e form a multiplet due to the approach of both triplets. The exchange of NH for ND in D_2O is complete and the N–H resonances do not appear. All the geminal protons show chemical and magnetic equivalence that can only be explained considering a dynamic process between energetically favourable conformations.

All the complexes present the resonances shifted downfield in comparison with those of the free ligand, at the same pD values. This is clearly observed in the 2 : 1 ratio solutions, because the amount of dinuclear complex is more significant and the percentage of free ligand is very small at the pD used in the experiments. Unfortunately due to solubility reasons the studies with the dinuclear complex of cadmium were limited to pD about 6.5.

EPR spectra of the copper(II) complexes

The X-band EPR spectra of the copper complexes of $Me_2[30]$-pbz_2N_6 were performed in frozen DMSO for 1 : 4, 1 : 2, 1 : 1 and 2 : 1 (M : L) ratios at a large range of temperatures (6–100 K). The typical spectrum of the mononuclear complex, with the

four lines at low field due to the interaction of the unpaired electron spin with the copper nucleus, was never observed, even at 1 : 4 ratio.

All the spectra exhibit a very broad signal in the $g = 2$ region and no signal at the $g = 4$ region. The broad signal gives rise to the typical hyperfine structure of dinuclear complexes when the 1 : 4 ratio solution was used, see Fig. 2(a). The addition of NaSCN to this solution changes the spectrum and two other broad bands appeared, at 3483 and 3586 G, Fig. 2(b). While the addition of terephthalic acid to the solution containing the dinuclear complex not only changed the upfield region of the spectrum, which now exhibits the expected seven bands, with relative intensity 1 : 2 : 3 : 4 : 3 : 2 : 1 (with an hyperfine split of 121.3×10^{-4} cm⁻¹) of dinuclear copper complexes, but also the expected signal at about 1600 G ($g = 4.299$) was also observed at $T \leq 20.3$ K, increasing in magnitude with decrease of temperature, see Fig. 2(c). Indeed, this EPR spectrum can be interpreted as that of a triplet-state of a coupled dinuclear copper centre with an $S = 1$ state and zero-field splitting, with two types of signals in the $\Delta M_s = 1$ and $\Delta M_s = 2$ regions, see Fig. 2(c).[29]
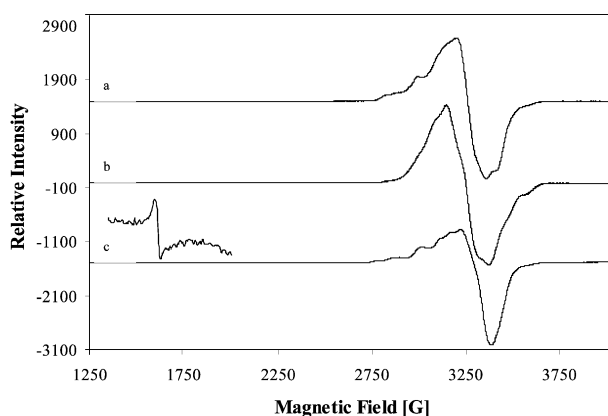
Fig. 2 EPR X-band spectra of (a) the dinuclear copper(II) complex of $Me_2[30]pbz_2N_6$ at 100 K; (b) of the ternary complex with thiocyanate at 20.4 K, and (c) the ternary complex with terephthalic acid at 10.3 K. The signal at low field was obtained also at 10.3 K and is amplified. All the complexes were prepared at 1.0×10^{-2} mol dm⁻³ in DMSO and 1.0 mol dm⁻³ NBu₄NO₃. All the spectra were recorded at a microwave power of 2.4 mW, modulation amplitude of 1.0 mT and at the frequency (ν) 9.643 GHz.

If it is assumed that two unpaired electrons, each located on a Cu^{2+}, are exchanged with an energy larger than the hyperfine coupling energy, each unpaired electron ($S = 1/2$) couples with two copper nuclei ($I_{Cu} = 3/2$) in an equivalent manner, the hyperfine structure consists of seven lines. The hyperfine constant is approximately half the value found in mononuclear copper(II) complexes having the same donor atoms and geometry.

The triplet state ($S = 1$) involving the coupling of two copper(II) ions can be represented by the spin Hamiltonian (1), assuming that the system is axially symmetric:

$$H = g_{\parallel}\beta H_z S_z + g_{\perp}\beta\left(H_x S_x + H_y S_y\right) + D\left[S_z^2 - \frac{1}{3}S(S+1)\right] \quad (1)$$

where D describes the zero-field splitting constant within the triplet state and can be considered to be built up from a dipolar D_{dip} and an exchange, D_{ex} contributions:

$$D = D_{ex} + D_{dip}$$

where

$$D_{ex} = -\frac{1}{8} J \left[\frac{1}{4} \left(g_\| - 2 \right)^2 - \left(g_\perp - 2 \right)^2 \right] \text{ and } D_{dip} = -\frac{(g_\|^2 + \frac{1}{2} g_\perp^2) \beta^2}{r^3}$$

$-J$ is the Heisenberg spin–spin coupling constant and r is the distance between the two copper centres, which appears in the dipole–dipole contribution.[29,30]

The J value was determined by the signal intensity of the EPR spectra at different temperatures by the expression: $I = c\{T[3 + \exp(-J/kT)]\}$, where I is the spectral intensity of the $\Delta M_s = 2$ signal, which is proportional to the paramagnetic susceptibility of the dinuclear system, c being the proportionality constant and k the Boltzmann constant. As the line-width did not depend on the temperature the relative intensity of the triplet spectra is equal to the relative peak height of a given line in the first derivative spectra of the $\Delta M_s = 2$ transition.[31] The determined value was -5.1 cm^{-1} for the dinuclear complex with terephthalic acid.

The $2D$ value was calculated by the difference between the H_{z2} and H_{z1} transitions, respectively,[30–32] giving a value of 0.0208 cm^{-1}. In general, it is difficult to observe all the lines of the two expected septets, however in our case five of the seven lines of each septet are observed in the spectrum, see Fig. 2(c), leading to an accurate value of the zero-field splitting constant. Taking $g_\| = 2.220$ and $g_\perp = 2.080$, obtained directly from the spectrum, a value of 7.7 ± 0.2 Å was determined for the copper–copper distance of the ternary complex.

The fact that in the dinuclear copper complex, before the addition of terephthalic acid, the $\Delta M_s = 2$ signal was not observed can be ascribed as an indication of a large distance between the metal centres.[29,30] This fact suggests that the ternary complex, having a bridged ligand between the two copper centres, adopts a structure to which corresponds a smaller separation between the two metal centres.

Molecular modelling

The crystal structures of complexes **2** and **4**, mentioned above, show that the macrocycle [30]$p$bz$_2$N$_6$ can incorporate two metal centres. In fact, the presence of two p-xylyl spacers in Me$_2$[30]-$p$bz$_2$N$_6$ and in [30]$p$bz$_2$N$_6$ introduces a steric conformational rigidity into the macrocyclic framework creating two pre-organised binding sites for metal ions within the macrocycle. On the other hand, the presence of propyl chains suggests that both macrocycles have enough flexibility to adopt different conformations from that found for the free ligand Me$_2$[30]$p$bz$_2$N$_6$ or [30]$p$bz$_2$N$_6$ in complex **2** (see above). This complex adopts a cleft conformation with the two copper centres separated by a long distance of 8.40 Å, which suggests that small ligands, such as imidazolate, oxalate or fumarate cannot be incorporated in the macrocyclic cavity at least in the cleft topology adopted.[3] On the other hand, our solution studies revealed that anions of different sizes, such as terephthalate, p-xylylenediamine and glyphosate form bridged dinuclear copper complexes with Me$_2$[30]$p$bz$_2$N$_6$. Unfortunately the crystallization of these species in a wide range of experimental conditions did not provide suitable single crystals for X-ray studies. In this context, the conformational preferences of the macrocycles Me$_2$[30]p-bz$_2$N$_6$ and its N–H derivative (we assumed that the presence of the two N-methyl groups is marginal in the structural preferences of this type of ligand) and the ability of their dinuclear copper complexes to incorporate bridging ligands were

evaluated theoretically through MM and MD calculations in gas phase using the Universal Force Field.[33]

The modelling studies were initiated with the conformational analysis of the free ligand Me$_2$[30]$p$bz$_2$N$_6$ following quenched dynamics methods as described in the Experimental section. 2000 conformations were generated and subsequently were minimised by MM. The final structures have energies in the wide range of 65.79 to 100.24 kcal mol^{-1}. In addition between these two limits the energy changes almost continuously indicating that the macrocycle is flexible, in spite of the presence of the two p-xylyl spacers in the Me$_2$[30]$p$bz$_2$N$_6$ macrocycle. This result is expected due to the number of single bonds with corresponding endocyclic torsion angles defining a geometric arrangement between *gauche* and *trans* configurations. In order to characterise the π–π interactions the dihedral and the intermolecular distances between aromatic rings was also evaluated. Thus, in the lowest energy conformation the aromatic rings are almost perpendicular making a dihedral angle of 92.5°. A conformation with aromatic rings in a parallel orientation, but different from that found in the crystal structure appears at 72.74 kcal mol^{-1} with a dihedral angle of 11.1° and a distance between the centroids of two aromatic rings of 10.76 Å. The exact conformation observed in the crystal structure and described above was not observed in the conformational analysis. Presumably in the crystal structure the conformation is stabilised by intermolecular hydrogen bonds.

The length of the bridge supported by the macrocyclic cavity can be established ascertaining the Cu ··· Cu distances allowed by the macrocycle without steric strain. With this proposal the conformational analysis on the [Cu$_2$(Me$_2$[30]$p$bz$_2$N$_6$)]$^{4+}$ complex was also undertaken (see Experimental section for details), and the results are given in Table S2 (ESI†). When the macrocycle Me$_2$[30]$p$bz$_2$N$_6$ is coordinated the conformations adopted can be described in terms of the relative positions, above (+) or below (−), the N–Me and N–H groups from the plane formed by the six nitrogen donors. This nomenclature is used and the conformations listed in Table S2 are the lowest energy ones. It should be considered that in spite of the binding of all six nitrogen atoms many other conformations with the same stereochemistry but with higher energies and different endocyclic torsion angles were found, which is basically a consequence of the length of the two N-propyl chains. The two aromatic rings oscillate considerably with the dihedral angle between them ranging from 0.2 and 85.2°. The lowest energy conformation has an energy of 709.94 kcal mol^{-1} while the $--+--+$ conformation with the same stereochemistry of complex **2** appears with a higher energy of 741.13 kcal mol^{-1}. The electrostatic term is the largest contributor for the final energy. For example, in the lowest energy conformation this term is 579.96 kcal mol^{-1}.

Furthermore the conformations in which the two terminal nitrogen atoms of both N-propyl linkages adopt a *trans* spatial disposition have higher energies than those that these atoms define a *cis/cis* or a *trans/cis* arrangement. The scatter plot of the steric energy *vs.* Cu ··· Cu distance for all conformations found in the conformational analysis is presented in Fig. 3 and shows that the number of conformations having longer Cu ··· Cu distances, above 8.40 Å, is significantly greater than the number having shorter ones, typically below 8.10 Å, which have in general lower energies. The scatter of points reflects naturally the variations of stereochemistry (including the variations on the angles N–Cu–N) and of endocyclic torsion angles in conformations giving arise to an average Cu ··· Cu distance of 8.82 Å with a larger standard deviation of 0.69 Å. Therefore, the conformational analysis results suggest that the structural unit of [Cu$_2$(Me$_2$[30]$p$bz$_2$N$_6$)]$^{4+}$ can accommodate bridging ligands with different sizes probably in different conformations (as well as the N–H derivative). In addition the assembling of small bridges should result in a considerable increase of energy (see Fig. 3).

Table 4 Average distances (Å) observed in molecular simulations of Cu(II) Me$_2$[30]$p$bzN$_6$ dinuclear species at 300 K

|	Cu · · · Cu	Cu–O$_{carboxylate}$	Cu–O$_{phosphonate}$	Cu–N	Cu–S
[Cu$_2$(Me$_2$[30]$p$bzN$_6$)]$^{4+}$	9.50(11)	–	–	–	–
Thiocyanate	6.40(10)	–	–	2.128(50)	2.294(40)
p-Xylylenediamine	8.35(16)	–	–	2.245(80)	–
Terephthalate	8.13(10)	2.108(57)	–	–	–
Glyphosate	7.48(27)	2.092(53)	2.196(90)	–	–
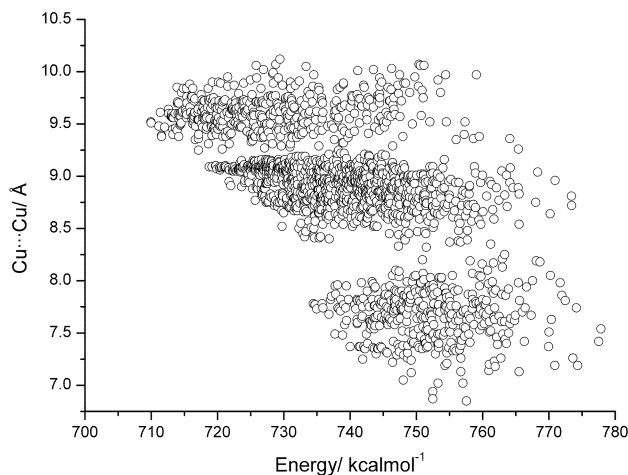
Fig. 3 Scatter plot showing the variation of Cu · · · Cu distances *vs.* steric energy for the dinuclear copper(II) Me$_2$[30]$p$bz$_2$N$_6$ complex.

Subsequently the interaction between the [Cu$_2$(Me$_2$[30]-$p$bz$_2$N$_6$)]$^{4+}$ complex and thiocyanate, terephthalate, glyphosate and p-xylylenediamine was investigated at room temperature by MD simulations during 500 ps. No bonds between the donor atoms of the bridging ligands and the copper centres were considered and therefore the host–guest bonding interactions are purely electrostatic. The remaining experimental details are described below. Snapshots taken from the simulations illustrating the interaction of each one of the bridging ligands with the dinuclear host are shown in Fig. 4. During the entire time of the simulation all substrates remained above the macrocyclic cavity. In addition, with terephthalate, the aromatic ring of this anion stays in a position almost parallel to both aromatic rings of the macrocycle, suggesting face-to-face π–π interactions. In contrast, the aromatic ring of p-xylylenediamine and those of the macrocycle are almost perpendicular during the large periods of simulation indicating that edge-to-face π–π interactions must occur. The average distances between the copper centres and the donor atoms of the substrates and the intramolecular Cu · · · Cu distances are given in Table 4. The distances of the metal-donor atoms and their standard deviations showed unequivocally that all donor atoms are coordinated to the copper centres during the entire period of simulation. Thus with terephthalate the two carboxylate groups remain tilted relatively to the aromatic ring by a tilt angle in the range 74.5–141.6 and 66.0–147.8°, respectively.

With glyphosate the three oxygen atoms from the phosphate group are bonded simultaneously to one copper centre and the two oxygen donors from the carboxylate group coordinated to the second one.

The average Cu–N distance involving the p-xylylenediamine is longer than that found with thiocyanate and reflects basically a charge effect rather than any structural effect. However, all average bond distances quoted for the Cu–N, Cu–S and Cu–O bonds are within the normal values for these bonds.[21]

The values of the Cu · · · Cu distances in these bridging structures show clearly that the separation between both copper atoms are affected by the length of the bridging ligand. In fact, the initial Cu · · · Cu distance in the lowest energy [Cu$_2$(Me$_2$[30]$p$bz$_2$N$_6$)]$^{4+}$ conformation (the starting model) of
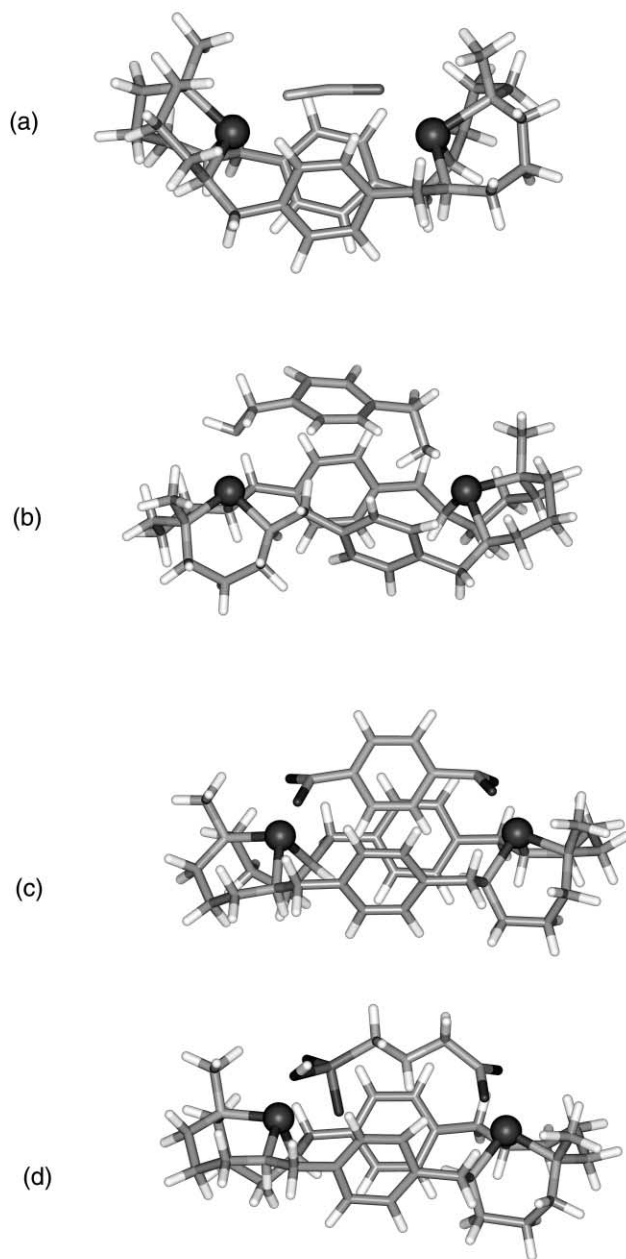
Fig. 4 Snapshots taken at 250 ps of simulation showing the interaction between [Cu(II)$_2$(Me$_2$[30]$p$bz$_2$N$_6$)] and substrates: thiocyanate (a), p-xylylenediamine (b), terephthalate (c) and glyphosate (d).

9.52 Å was substantially shortened with the inclusion of the substrates following the order 6.40(10) Å for thiocyanate, 7.48(27) Å for glyphosate, 8.13(10) Å for terephthalate and 8.35(16) Å for p-xylylenediamine, which suggest that the macrocycle has enough flexibility to adjust the intramolecular distance between the two copper centres to the stereo-electronic requirements of each one of these bridging ligands. In addition when the copper dinuclear species was submitted to a MD simulation using the same experimental conditions, in the absence of a bridging ligand, Cu · · · Cu distances ranging from

9.09 to 9.94 Å were found, with an average value of 9.50(11) Å. Certainly, other scenarios involving a different approach (including the bridging ligand from the opposite side to the N-methyl groups for instance) of these substrates to the metal complex in this conformation or in others are also possible, but it would be a huge task to evaluate all of them. On the other hand the presence of other ligands in the copper coordination spheres, which are five- or six-coordinated, were not taken into account in our calculations. In spite of these modelling studies being carried out in the gas phase, they suggest that selective binding of the studied substrates to the dinuclear $[Cu_2(Me_2[30]pbz_2N_6)]^{4+}$ complex occurs, giving important structural insights to understand the solution studies.

Conclusions

Our solution studies as well as the modelling studies show that for the macrocycle $Me_2[30]pbz_2N_6$, in spite of the presence of two p-xylyl rigid spacers, the dipropyltriamine linkages confer enough steric flexibility to the macrocycle such that several conformations with similar energies can be adopted. These conformations can be stabilised by π–π interactions between the two aromatic rings ranging from edge-to-face to face-to-face. Additionally the aromatic rings offer two distinct sites to encapsulate two metal centres. Our theoretical studies and EPR spectroscopy indicate unequivocally that a wide range of distances (6.85–10.11 Å) between the two metal centres is possible. However the fitting of the complex to short copper–copper distances results in a considerable increase of the steric energy. When a bridge substrate is inserted into the macrocycle cavity, the Cu $\cdots$ Cu distance changes specifically in order to fit the stereo-electronic requirements of the substrate. Moreover, the comparison of the values of formation constants of the ternary species and the Cu $\cdots$ Cu distances suggests that higher constants correspond to a critical Cu $\cdots$ Cu distance, smaller values of this distance lead to lower formation constants, indicating that the complex loses conformational energy to fold to the right position for the coordination of small substrates. In other words the dinuclear copper complex of the macrocycle $Me_2[30]pbz_2N_6$ has enough flexibility to accommodate bridged ligands with different sizes.

Experimental

The microanalyses were carried out by the ITQB Micro-analytical Service. IR spectra were recorded from KBr pellets on a UNICAM Mattson 7000 spectrometer.

Reagents

Terephthaldialdehyde and N,N-bis(3-aminopropyl)methyl-amine were obtained from Aldrich. Sodium thiocyanate (98.5%), 1,4-benzenedimethanol (99%), p-xylylenediamine (99%), terephthalic acid (98%) and glyphosal (96%) were obtained from Aldrich. All the chemicals were of reagent grade and used as supplied without further purification. The reference used for the ^1H NMR measurements in D_2O was 3-(trimethyl-silyl)propanoic acid-d_4 sodium salt. For ^{13}C NMR spectra dioxane was used as internal reference.

Synthesis and characterization of 7,22-dimethyl-3,7,11,18,22,26-hexaazatricyclo[26.2.2^{13,16}]tetratriaconta-1(30),13,15,28,31,-33-hexaene, Me$_2$[30]$p$bz$_2$N$_6$

N,N-Bis(3-aminopropyl)methylamine (1.85 mmol, 0.3 cm³) was dissolved in CH_3CN (50 cm³) and the mixture left stirring in an ice-bath for a few minutes. To this solution, terephthaldialde-hyde (1.85 mmol, 0.25 g) in 30 cm³ CH_3CN was added during a period of 2 h, and left stirring for 30 min at the same temperature (0 °C). The mixture was stored in a freezer during 5 days, after this time a white precipitate was formed. The solid was

filtered off and was dissolved in ethanol (25 cm³). Then NaBH$_4$ (0.3 g, 7.93 mmol) was added in three portions over a period of 3 h and the solution was left overnight at room temperature. Ethanol was added to the mixture, and then the solvent was removed to dryness. The white precipitate formed was dissolved in water, the pH increased to 11 with NaOH, and an extraction with CH_2Cl_2 (5 × 15 cm³) was carried out. Light petroleum (bp 40–60 °C) was added to the colourless oil obtained after evaporation of the collected organic phases, and the solution stored in a freezer. After a few days, crystals of the desired macrocycle were obtained. Yield: 0.754 mmol (41%); mp 97–99 °C. ^1H NMR (D_2O, ppm): δ 7.32 (8 H, s), 3.67 (8 H, s), 2.50 (8 H, t), 2.35 (8 H, t), 2.18 (6 H, s), 1.59 (8 H, q). ^{13}C NMR (D_2O, ppm): δ 137.27, 128.13, 54.78, 52.74, 46.82, 42.64, 26.64. Found: C, 70.00; H, 9.99; N, 16.34. Calc. for $C_{30}H_{50}N_6 \cdot H_2O$: C, 70.3; H, 10.2; N, 16.4%. IR (KBr pellets, cm^{-1}): 3391.02, 3248.02, 2950.60, 2785.53, 2362.52, 1667.03, 1450.57, 1028.00, 803.30, 736.08, 576.10, 517.81.

Potentiometric measurements

Reagents and solutions. Metal ion solutions were prepared from the chloride salts of the metals, and were standardised as described.[34] Carbonate-free solution of the titrant, KOH, was freshly prepared, maintained in a closed bottle, and discarded when the percentage of carbonate was about 0.5% of the total amount of base (tested by Gran's method).[35,36] All the solutions were prepared in water–methanol (9 : 1, v/v). The methanol was purified by standard methods[37] and the water used was demineralized water obtained using a Millipore/Milli-Q system.

Equipment and working conditions. The equipment used was described before.[38] The glass electrode was pre-treated by soaking it in the water–methanol (9 : 1, v/v) solution over a period of 2 days, in order to prevent erratic responses. The temperature was kept at 25.0 ± 0.1 °C; atmospheric CO_2 was excluded from the cell during the titration by passing purified argon across the top of the solution in the reaction cell. The ionic strength of the solutions was kept at 0.10 mol dm^{-3} KCl.

Measurements. The $[H^+]$ of the solutions was determined by the measurement of the electromotive force of the cell, $E = E'^\circ + Q\log[H^+] + E_j$. The term pH is defined as $-\log[H^+]$. E'°, Q, E_j and K'_w were obtained as described previously.[38] The value of K'_w, the ionic product of water in the methanol–water mixture used was $10^{-13.82}$ mol² dm^{-6} in our experimental conditions, in agreement with that determined by Rochester.[39]

The potentiometric equilibrium measurements were made in the absence of metal ions and in the presence of each metal ion for 1 : 1 and 2 : 1 $C_M : C_L$ ratios in a minimum of two replicates. Care was taken to maintain constant the water–methanol ratio in the measured solution.

Calculation of equilibrium constants. The HYPERQUAD program[40] was used to determine the overall protonation constants and stability constants of the various species formed in solution. Differences, in log units, between the values $\beta_{M_n(H,L)}$ [or $\beta_{M_2(H_{-i})_jL}$] and $\beta_{M_n(H_{i-1}L)}$ [or $\beta_{M_2(H_{-1})_{i-1}L}$] provide the step-wise protonation reaction constants, also shown in Table 2. The errors quoted are the standard deviations of the overall stability constants given directly by the program for the input data, which include all the experimental points of all titration curves.

Spectroscopic studies

Solutions of the ligands and respective complexes for the measurements (≈ 0.01 mol dm^{-3}) in D_2O were made up and the pD was adjusted by addition of DCl or CO_2-free KOD with a Orion 420A instrument fitted with a combined Ingold 405M3 microelectrode. The $-\log[D^+]$ was measured directly in the

NMR tube, after the calibration of the microelectrode with buffered aqueous solutions. The final pD was calculated from pD = pH* + 0.40.[41] The value of pH* corresponds to the reading of the pH meter previously calibrated with two standard aqueous buffers at pH 4 and 7.

The electronic spectra of the ternary complexes in methanol were recorded with a UNICAM UV-vis spectrophotometer model UV-4 at 20.00 ± 0.01 °C. The dinuclear copper complex was prepared by the addition of increasing amounts of the metal ion (in the form of chloride salts) to the ligand, and the concentration calculated by the method of continuous variation.[42] To the solution of 9.6×10^{-4} mol dm^{-3} of dinuclear complex (2.5 dm^{-3}) the anion or neutral molecule (1.8×10^{-2}–3.0×10^{-3} mol dm^{-3}) was added in small portions with a micropipette and after stabilisation of the solution the spectrum was recorded. The ternary constants were determined using HYPERQUAD program.[40]

EPR spectroscopy measurements were recorded with a Bruker ESP 380 spectrometer equipped with continuous-flow cryostats for liquid helium or liquid nitrogen, operating at X-band. The spectra of the dinuclear copper(II) complexes, 1.0×10^{-2} mol dm^{-3}, were recorded in the range 100–6.3 K, in DMSO and 1.0 mol dm^{-3} TBAN. The ternary complexes were prepared in the same range of concentrations and recorded in the same conditions.

Molecular modelling

The molecular mechanics and dynamics calculations were carried out using the Universal Force Field[33] within the Cerius^2 package software.[43] All MD simulations were carried out during 500 ps with a step size of 1.0 fs at 300 K. A constant NVT thermostat was used with default parameters. For all simulations, snapshots of the events were saved every 0.25 ps leading to a total of 2000 frames.

The conformational analysis of the free ligand Me$_2$[30]-$p$bz$_2$N$_6$ was carried out following quenched dynamics methods. The structure taken from the crystal was minimised *via* MM to create the starting model. The atomic charges were calculated with the Qeq equilibration method implemented within Cerius^2. The minimised structure was subsequently heated at 3000 K and 2000 conformations were generated at 0.25 ps intervals. Concomitantly, the generated conformations were minimised by molecular mechanics calculations. This procedure was also used on the conformational analysis of [Cu$_2$(Me$_2$[30]$p$bz$_2$N$_6$)]$^{4+}$ complex. The starting model was taken from the crystal structure of the metal complex **2** with the N–H groups of the central nitrogen atom of the N-propyl chains replaced by N–CH$_3$ groups. The two Cu^{2+} ions were given charges of +2 and the charges on the atoms of the macrocycle were calculated independently of the metal centres *via* the Qeq equilibration method assuming a neutral ligand. The structure was subsequently minimised and the charges recalculated, then this process was repeated successively until the steric energy remained constant. The Cu–N bonds were retained in the calculation and the bending terms of angles centred at the copper centre were described using a cosine periodic function which incorporates the possibility of these angles taking more than one ideal value, *e.g.* 90 or 180°. Thus, the geometric arrangement of the nitrogen atoms around the two copper centres can change freely with all N–Cu–N ideal angles taking values of 90 or 180°.

The MD simulations of the host–guest interactions of [Cu$_2$(Me$_2$[30]$p$bz$_2$N$_6$)]$^{4+}$ with bridging ligands were performed at 300 K. The starting models were built with the lowest energy conformation of [Cu$_2$(Me$_2$[30]$p$bz$_2$N$_6$)]$^{4+}$ found in the conformational analysis and the bridging ligands positioned above the macrocyclic cavity and on the same side of the N-methyl groups. The substrates were previously minimised by MM. Their charges were also calculated *via* the Qeq equilibration

method with the total charge adjusted to −1 for thiocyanate, and −2 for terephthalate and glyphosate. No bonds between the donor atoms of the bridging ligands and the copper centres were considered and therefore the host–guest bonding interactions are purely electrostatic.

All simulations runs were carried out for 500 ps using a time step size of 1.0 fs and set of atomic positions were saved every 0.25 ps over all periods of simulation of 500 ps. The equilibration period was 3 ps. A constant NVT thermostat was used with default parameters.

Crystallography for 1

C$_{30}$H$_{51}$N$_6$O$_{0.5}$, M_r = 503.77, monoclinic, space group $P2/c$, a = 15.451(11) b = 9.902(17), c = 20.311(13) Å, β = 102.82(1) U = 3030 Å^3, Z = 4, D_c = 1.104 Mg m^{-3}, μ(Mo-Kα) = 0.067 mm^{-1}.

X-Ray data were collected at room temperature on a MAR research plate system using graphite monochromated Mo-Kα radiation (λ = 0.71073 Å) at Reading University. The crystals were positioned at 70 mm from the image plate. 95 Frames were taken at 2° intervals using an adequate counting time with the diffraction pattern observed. Data analysis was performed with the XDS program.[44] Intensities were not corrected for absorption effects.

7541 Reflections measured were merged in the Laue symmetry 2/m to 4765 unique reflections with a R_{int} of 0.0801. The structure was solved by direct methods and by subsequent difference Fourier syntheses using the SHELX-97 system programs.[45] The hydrogen atoms on the parent carbon and nitrogen atoms were included in calculated positions. The hydrogen atoms of the water molecule were located from difference Fourier maps and refined with geometric restraints on O–H (0.82 Å) and H · · · H distances consistent with a H–O–H angle of 104.5°. Anisotropic thermal parameters were used for all non-hydrogen atoms while the thermal movement of hydrogen atoms was described using isotropic parameters equivalent 1.2 times those of the atom to which were attached. The structure was refined by full-matrix least-squares method against F^2 until convergence to be achieved leading to final indices R_1 = 0.1105 and wR_2 = 0.3112 for 2757 reflections with $I > 2\sigma(I)$ and R_1 = 0.1778 and wR_2 = 0.3512 for all data. The largest peak and hole in the final difference Fourier map were −0.316 and 0.806 e Å^{-3}.

CCDC reference number 212402.

See http://www.rsc.org/suppdata/dt/b3/b306486g/ for crystallographic data in CIF or other electronic format.

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