PAPER

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Co(II) and Cd(II) complexation with two dipyridine-containing macrocyclic polyamines in water and dimethyl sulfoxide†

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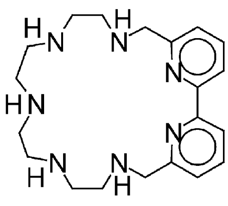
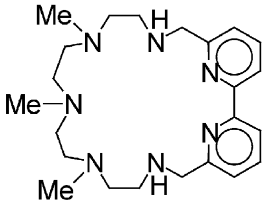
Solvent effects in the formation of Co(II) and Cd(II) complexes with the two macrocyclic ligands 2,5,8,11,14-pentaaza[15]-[15](2,2′)[1,15]-bipyridylophane (L1) and trimethyl-5,8,11-2,5,8,11,14-pentaaza[15]-[15](2,2′)[1,15]-bipyridylophane (L2), both containing dipyridine units, were analysed by determining the thermodynamic parameters (log$K$, ΔH°, $T\Delta S^\circ$) for the complexation reactions in water and dimethyl sulfoxide (DMSO) by means of potentiometric, spectrophotometric and calorimetric techniques. *N*-Methylation leads to different solvation properties of the ligands and to different abilities in stabilizing metal complexes *via* the formation of M–NH···S hydrogen bonds to solvent molecules (S) which enhances the σ-donating properties of the donor atom. In contrast to expectations based on the stronger solvation of Cd(II) and Co(II) in DMSO than in water, complexes with L1 display higher stability in DMSO than in water, indicating that ligand solvation, instead of metal ion solvation, plays a major role in determining the stability of L1 complexes in the two solvents. On the other hand, for ligand L2, in which tertiary amino groups are present, an almost opposite trend of stability is observed. Because L2 is less solvated than L1 in water and tertiary nitrogens are weaker bases in DMSO than in water, the stronger solvation of metal ions in DMSO prevails in determining the stability of L2 complexes. Semi-empirical calculations were also performed to obtain some structural information in the gas phase.

Introduction

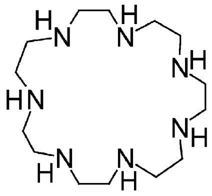
Recently we reported the synthesis of the two macrocyclic polyamines L1 and L2 containing similar pentaamine chains linked to the 6,6′ positions of a dipyridine unit.[1]



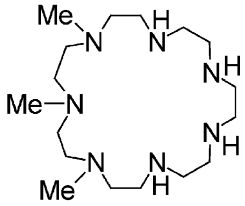
L1



L2



L3



L4

The interest towards this type of ligand, containing both hydrophilic and hydrophobic moieties, arises from their ability to function as metal ion receptors both in aqueous and organic solutions, giving rise to a wide variety of studies and applications based on complexation processes in different solvents, phase transfer, and transport across membranes.[2–14]

Both the presence of a dipyridine unit in the macrocyclic skeleton of the ligands and *N*-methylation affect the coordination properties of L1 and L2. The dipyridine units increase the rigidity of the molecular structures with respect to saturated polyazamacrocycles. As a consequence, L1 and L2 display lower abilities in organizing an optimal arrangement of donor atoms around coordinated metal ions such as Ni(II), Cu(II), Zn(II) and Cd(II),[15–17] which are relatively small, forming less stable complexes in aqueous solution than the analogous saturated heptaazamacrocycles L3 and L4, respectively.[18] On the other hand, L1 and L2 form more stable complexes with the larger and softer Pb(II), whose coordination requires a lower reorganization of the ligands and is favoured by the presence of softer aromatic donor atoms.[17–19]

Regarding *N*-methylation, it is to be noted that the formation of M–NH···OH_2 hydrogen bonds to the solvent by a coordinated nitrogen enhances the σ-donating properties of the donor atom.[20] Therefore, the methylated nitrogens in L2 are weaker σ-donors in water than secondary amine groups, because of their inability to form hydrogen bonds. Moreover, the methyl groups on the donor atoms may cause some steric hindrance of the ligand during complexation, leading to a less efficient metal-to-ligand interaction. Accordingly, L2 forms less stable complexes than L1 in aqueous solution.[17]

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† Electronic supplementary information (ESI) available: ^{1}H spectra and distribution diagrams of the complex systems. See http://www.rsc.org/suppdata/nj/b4/b418221a/

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The possibility of controlling the coordination event *via* the formation of M–NH···S hydrogen bonds with solvent molecules (S) in the second coordination sphere of the metal ion, stimulated our interest to perform a comparative study on the complexation abilities of L1 and L2 in different solvents. To this purpose we have studied the coordination of the small and hard Co(II) ion and of the larger and softer Cd(II) ion with both L1 and L2 in water and in the aprotic solvent dimethyl sulfoxide (DMSO). The results obtained by means of potentiometric, calorimetric and spectroscopic methods are reported here along with some structural and energetic parameters of the complexes, obtained by performing semi-empirical calculations. The choice of these two metal ions was partly dictated by the fact that we used Cd(II) as a competitive cation to determine the stability constants of Co(II) complexes in DMSO (see Experimental).

Results and discussion

Co(II) coordination in H_2O

The complex species formed by L1 and L2 with Co(II) in aqueous solution and the corresponding stability constants determined by means of potentiometric (pH-metric) titrations are listed in Table 1 (distribution diagrams of the complex systems are reported within the ESI, Figs. S1–S2†).

As far as the stoichiometry and the stability of the complexes are concerned, three aspects deserve to be evidenced: (i) L1 is able to form both mono- and binuclear metal complexes, while L2 forms exclusively mononuclear complexes; (ii) $[CoL1]^{2+}$ is more stable than $[CoL2]^{2+}$; (iii) $[CoL2]^{2+}$ displays a greater propensity to form protonated species, being able to bind up to three H^+ ions forming the $[CoH_3L2]^{5+}$ species, with respect to $[CoL1]^{2+}$ which binds at most two protons to form $[CoH_2L1]^{4+}$.

Also in the present case, the main effects brought about by nitrogen methylation, namely the lower σ-donating properties of the methylated nitrogen atoms in aqueous solutions[20] and the increased ligand rigidity,[17] can be invoked to account for such differences in the coordination properties of L1 and L2 towards Co(II). Indeed, the methylated ligand L2 gives rise to a weaker interaction with Co(II) and produces a lower neutralization of charge on the metal ion, leading to a less stable mononuclear complex and preventing the simultaneous complexation of two metal cations which strongly repel each other. As a matter of fact, the unmethylated ligand L1 binds two Co(II) cations, forming $[Co_2L1(OH)]^{3+}$, only in the presence of one OH^- anion which reduces significantly the electrostatic repulsion between the two metal centres, stabilizing the complex. On average, the Co(II)–N bonds are weaker in $[CoL2]^{2+}$ than in $[CoL1]^{2+}$, and consequently protonation of the amine groups is much easier for the former complex. Therefore, $[CoL2]^{2+}$ is less stable than $[CoL1]^{2+}$ but interacts more strongly with H^+ ions and binds a greater number of H^+ ions than $[CoL1]^{2+}$ (Table 1).

Table 1 Stability constants of the complexes formed by L1 and L2 with Co(II) in aqueous solution (0.10 mol dm^{-3} NMe_4Cl at 298.1 K)

Reaction[a]	Log*K*
$Co + L1 \rightleftharpoons CoL1$	13.23(4)[b]
$CoL1 + H \rightleftharpoons CoHL1$	6.62(2)
$CoHL1 + H \rightleftharpoons CoH_2L1$	4.86(3)
$CoL1 + OH \rightleftharpoons CoL1(OH)$	4.45(8)
$2Co + L1 + OH \rightleftharpoons Co_2L1(OH)$	22.12(1)
$Co + L2 \rightleftharpoons CoL2$	11.45(3)
$CoL2 + H \rightleftharpoons CoHL2$	7.03(3)
$CoHL2 + H \rightleftharpoons CoH_2L2$	5.96(3)
$CoH_2L2 + H \rightleftharpoons CoH_3L2$	3.22(4)
$CoL2 + OH \rightleftharpoons CoL2(OH)$	5.91(7)

[a] Charges omitted. [b] Values in parentheses are standard deviations on the last significant figure.

In previous studies dealing with the coordination of L1 and L2 to other metal ions, we showed that the UV absorption spectra of the free ligands, characterized by a sharp band at 288 nm (ε = 11700 mol^{-1} dm^3 cm^{-1} for L1 and 12200 mol^{-1} dm^3 cm^{-1} for L2), undergo important changes upon complexation with the appearance of a new red-shifted band.[15–17] This new band, which is diagnostic for coordination of dipyridine nitrogen atoms to metal ions, was also observed upon complexation of Co(II) by L1 (302 nm, ε = 11000 mol^{-1} dm^3 cm^{-1}) and L2 (304 nm, ε = 11900 mol^{-1} dm^3 cm^{-1}) to form $[CoL1]^{2+}$ and $[CoL2]^{2+}$, respectively. Furthermore the band is almost independent of pH in the pH region in which the different complex species are present, revealing that the dipyridine unit remains coordinated to Co(II) in all complexes. Hence, protonation of the complexes takes place on aliphatic amine groups.

It is instructive to compare the stability constants of the Co(II) complexes of L1 (Table 1) with those previously reported for the analogous species of the heptaazamacrocycle L3,[21] containing an ethylenediamine group instead of a dipyridine one. L3 forms a $[CoL3]^{2+}$ complex in which six nitrogen atoms of the ligand are involved in coordination to the metal ion. The stability constant determined for this species ($\log K = 14.69$)[21] is about 1.5 log*K* units higher than that obtained for $[CoL1]^{2+}$ ($\log K = 13.23$; Table 1). Since dipyridine (dipy) and ethylenediamine (en) ligands display almost the same ability in coordinating Co(II) ($\log\beta_1 = 5.8$ for $[Codipy]^{2+}$, $\log\beta_1 = 5.5$ for $[Coen]^{2+}$),[22] the lower stability of $[CoL1]^{2+}$ with respect to $[CoL3]^{2+}$ can be reasonably ascribed to the greater rigidity of the ligand containing the dipyridine group, which prevents an optimal interaction of donor atoms with Co(II). Indeed, it was observed that in the crystal structures of $[ZnL1]^{2+}$ the metal ion is bound to the dipyridine nitrogens while the two benzylic amine groups are not coordinated,[16] giving rise to a couple of very large chelate rings which are known to give a modest contribution to complex stability. Similarly, in the crystal structures of $[CuL1]^{2+}$ and $[NiL1]^{2+}$ one benzylic nitrogen is not coordinated while the other one binds the metal ion at long distance.[15] Similar coordination features are expected to characterize the Co(II) complex. As a matter of fact the equilibrium constant for the binding of one proton to $[CoHL1]^{3+}$ is significantly high ($\log K = 4.86$, Table 1), when compared with the protonation of the uncomplexed $[H_3L1]^{3+}$ species of the ligand ($\log K = 4.16$)[16] bearing the same positive charge as $[CoHL1]^{3+}$, suggesting that even the second protonation of $[CoL1]^{2+}$ takes place on an amine nitrogen not participating in the coordination to Co(II). Consequently, in $[CoL1]^{2+}$ only five nitrogens are bound to the metal ion and facile formation of the hydroxo complex $[CoL1(OH)]^+$ (Table 1) occurs in alkaline solution *via* deprotonation of the water molecules occupying the sixth coordination position.

By means of similar reasoning and taking into account the considerable loss of stability observed for $[CoL2]^{2+}$ ($\Delta\log K = 1.78$, Table 1) with respect to $[CoL1]^{2+}$, the ability of $[CoL2]^{2+}$ to bind three protons and the very high values of the first two complex protonation constants ($\log K = 7.03$ and 5.96, respectively, Table 1) we conclude that in $[CoL2]^{2+}$ at least two nitrogen donors of L2 do not participate in the coordination to Co(II), although we cannot exclude the possibility that a third nitrogen donor is not coordinated, or weakly coordinated, to the metal ion.

Structural information

All solution data up to now, collected in this and in previous works, are generally consistent with the involvement of no more than five ligand donors in the formation of metal complexes with L1 and L2 in water, although in the case of Ni(II) and Pb(II) complexes there is evidence supporting greater coordination numbers.[15–17] Crystal structures of three [ML1]$^{2+}$ (M = Zn, Cu, Ni) complexes showed that in the solid state the dipyridine nitrogens are always coordinated while at least one of the two benzylic nitrogens is not coordinated. In particular, in [ZnL1]$^{2+}$ both benzylic nitrogens are not coordinated,[16] in [CuL1]$^{2+}$ one is not coordinated while the second one binds the metal ion at long distance, and in [NiL1]$^{2+}$ only one is coordinated.[15] On the other hand, in the crystal structure of [PbL2]$^{2+}$ all seven nitrogen atoms of the ligands are bound to the metal ion even if one of the coordinative bonds is significantly longer than the other ones.[17] Hence, a greater number of ligand donor atoms are involved in metal ion coordination in the solid state than in aqueous solution. Both packing effects, in the solid state, and competitive interaction of metal ions with solvent molecules, in solution, can be responsible for such difference. For this reason such crystal structures are only partially representative of complex structures in solution, although they furnish a helpful support for understanding the coordination features in solution. Unfortunately, in the case of Co(II) and Cd(II) complexes with L1 and L2 a similar support from crystal structures has not been available since crystals of appropriate quality for X-ray analysis were not obtained.

In order to obtain some information about the maximum number of donor atoms that ligands are able to involve in metal ion coordination in the absence of any other interaction than coordinative bonds, we performed semi-empirical calculations on free ligands and their Cd(II) complexes in the gas-phase, where M–N interactions can be better evidenced. Only Cd(II) systems have been analysed, mainly because calculated structural parameters can be conveniently compared with some X-ray data on similar compounds.[17]

The optimised structures are reported in Fig. 1, while some geometrical parameters are listed in Table 2. In the calculated structure of the [CdL1]$^{2+}$ complex only five nitrogen atoms of L1, including the dipyridine nitrogens, are involved in metal ion coordination. In particular, one of the benzylic nitrogens (N7, Fig. 1c) does not participate in the coordination to Cd(II) while the other one (N3) binds the metal at a rather long distance (Table 2). In the case of the [CdL2]$^{2+}$ complex, the calculated structure (Fig. 1d) shows that four nitrogen atoms of the ligand, namely the two heteroaromatic donors with one benzylic nitrogen and the adjacent amine group, are coordinated to the metal ion, while a fifth one, the benzylic N7 atom, gives a very weak interaction, at very long distance, with Cd(II) (Table 2). Both ligands assume in the complexes a conformation similar to those observed in the previous crystal structures,[15–17] with the polyamine chains connected to the dipyridine moiety pointing towards opposite sides of the mean plane passing through the aromatic groups.

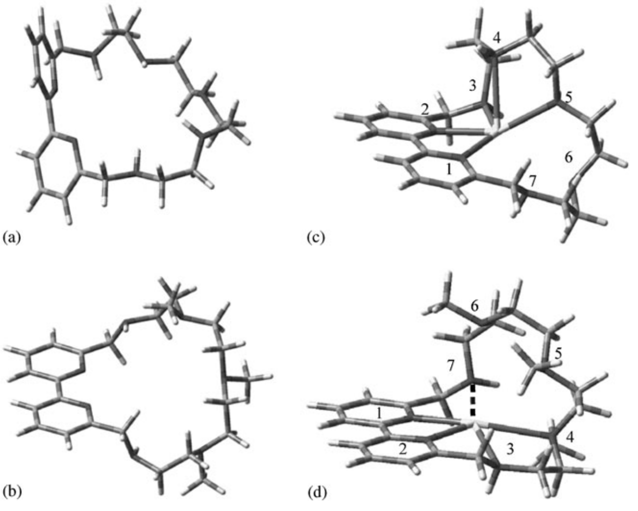


Fig. 1 Optimised structures of: (a) L1; (b) L2; (c) [CdL1]$^{2+}$ and (d) [CdL2]$^{2+}$.

Table 2 Calculated structural data for [CdL]$^{2+}$ (L = L1, L2)

	Calculated lengths (Å)	
Bond	[CdL1]$^{2+}$	[CdL2]$^{2+}$
Cd–N1	2.404	2.363
Cd–N2	2.370	2.368
Cd–N3	2.710	2.523
Cd–N4	2.542	2.629
Cd–N5	2.529	3.784
Cd–N6	3.898	3.892
Cd–N7	4.045	2.958

Hence, such semi-empirical calculations indicate that, even in the absence of any other interaction than coordinative bonds, these ligands are not able to involve all their donor atoms in the binding of relatively small metal cations, in agreement with the general trend observed both in solution and in the solid state. The heteroaromatic donor atoms are always involved in the coordination, while the contiguous benzylic nitrogens are not able to bind simultaneously and completely the metal ion, probably due to the rigidity of the linkage connecting them.

Cd(II) and Co(II) coordination in DMSO

Cd(II) and Co(II) coordination by L1 and L2 in the aprotic solvent DMSO was studied by means of potentiometric, calorimetric and UV-Vis measurements. The thermodynamic parameters for the complexation reactions are listed in Table 3, together with those determined in water for the analogous species of Co(II) (Table 1) and Cd(II) (ref. 17). As can be seen, the HYPERQUAD[23] computer treatment of the potentiometric data revealed that the ligands form only mononuclear [ML]$^{2+}$ complexes [M = Cd(II), Co(II); L = L1, L2] in DMSO. Accordingly, calorimetric titrations performed by adding increasing amounts of ligand solution to a metal ion solution, showed that the heat evolution due to the complexation reaction is over when the ligand-to-metal concentration ratio $R_c = 1$ ($R_c = C_L/C_M$), as shown in Fig. 2, where the total molar enthalpy changes Δh_v, *vs.* R_c are reported for Cd(II) and Co(II) with both L1 and L2.

In order to discuss these results, it is of primary importance to get some information on which nitrogen atoms of the ligands are coordinated to the metal ions.

As shown before for Co(II) complexation in water, the UV-Vis spectra of the complexes are diagnostic for indicating the involvement of dipyridine in metal binding. DMSO solutions of the [ML]$^{2+}$ complexes show that red-shifted absorption bands appear at 310 nm for [ML1]$^{2+}$ and 306 nm for [ML2]$^{2+}$ ($\varepsilon_{CdL1} = 13580$ mol^{-1} dm^3 cm^{-1}; $\varepsilon_{CoL1} = 13020$ mol^{-1} dm^3 cm^{-1}; $\varepsilon_{CdL2} = 12800$ mol^{-1} dm^3 cm^{-1}; $\varepsilon_{CoL2} = 13052$ mol^{-1} dm^3 cm^{-1}), with respect to absorption bands of the free ligands centred, respectively, at 295 and 292 nm ($\varepsilon_{L1} = 12900$ mol^{-1} dm^3 cm^{-1}; $\varepsilon_{L2} = 12400$ mol^{-1} dm^3 cm^{-1}), pointing out that also in DMSO the dipyridine nitrogens participate in the complexation of the metal ions. In addition, FT-IR spectral evidence that the band at 1573 cm^{-1}, assigned to the aromatic C=C and C=N bond stretches of the free ligands, splits into two peaks centred at 1588 cm^{-1} in the complexes (Fig. 3a), confirms the binding of dipyridine. Nevertheless, other nitrogen atoms are involved in complex formation, as the thermodynamic stabilities of the [ML]$^{2+}$ complexes with these macrocyclic polyamines are noticeably higher than that of dipyridine complexes in DMSO ([Cd(dipy)]$^{2+}$: $\log\beta_1 = 1.56$, $\Delta H^\circ_1 = -15.3$ kJ mol^{-1}, $T\Delta S^\circ_1 = -6.4$ kJ mol^{-1}; [Co(dipy)]$^{2+}$:

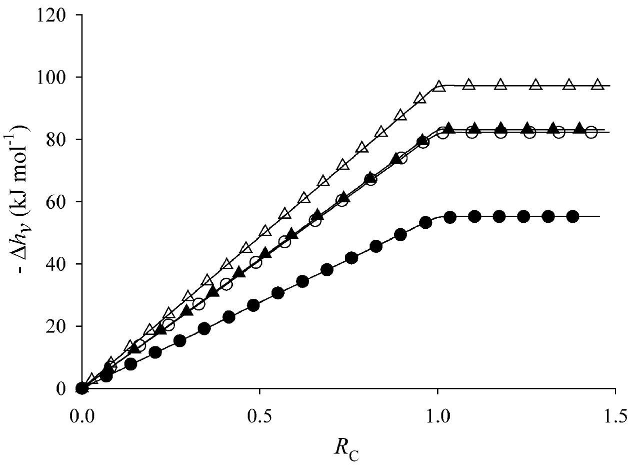
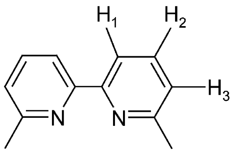


Fig. 2 The total molar enthalpy changes, Δh_v, as a function of $R_c = C_L/C_M$ for Cd(II)/L (open symbols) and Co(II)/L (filled symbols) systems in DMSO: (△) $C_{Cd^{2+}} = 2.91$, (▲) $C_{Co^{2+}} = 2.14$ mmol dm^{-3}, L = L1; (○) $C_{Cd^{2+}} = 1.72$, (●) $C_{Co^{2+}} = 2.02$ mmol dm^{-3}, L = L2. The solid lines were calculated by using log*K* and $\Delta H°$ values from Table 1.

$\log\beta_1 = 3.86$, $\Delta H°_1 = -29$ kJ mol^{-1}, $T\Delta S°_1 = -7$ kJ mol^{-1})[24a] and higher than that reported for the complexes with the tetradentate 1,4,7,10-tetraazadecane (trien),[24b] the amine with the highest number of nitrogen atoms so far investigated in DMSO.

The interaction of amine ligands with metal ions can be followed in DMSO also by observing the bathochromic shift of the N–H stretching modes of secondary nitrogens occurring when metal ions are added to ligand solutions.[25] In Fig. 3b it is evident that the peak at 3308 cm^{-1} (N–H groups of free L2) is shifted upon complexation to 3256 cm^{-1}, accounting for the interaction of NH groups with the metal ions, but a component at 3308 cm^{-1} is still present after coordination. Taking into account the high stability constant (log$K = 12.13$, Table 3) of the [CdL2]$^{2+}$ complex at the concentration used to record the spectrum (0.040 mol dm^{-3}), we can exclude the presence of free ligand in solution. Hence, the 3308 cm^{-1} absorption demonstrates that one NH group is not involved, or is only weakly involved, in the coordination to the metal ion. As a matter of fact, a previous study dealing with the formation of Cd(II) complexes with acyclic polyamines showed that, when all secondary amine groups are coordinated to the metal ion, the absorbance ascribed to the NH groups of the free amine disappears completely.[24c] All [ML]$^{2+}$ (M = Cd, Co; L = L1, L2) complexes studied here display analogous FT-IR spectral features, revealing that in all these complexes the ligand rigidity, determined by the dipyridine moiety, prevents the full coordination of both benzylic amine groups.

In order to obtain additional information on the structure of these complexes, we performed ^{1}H NMR spectroscopic measurements on solutions containing, respectively, [CdL1]$^{2+}$ and [CdL2]$^{2+}$ in DMSO-d_6 (Figs. S3 and S4 in ESI†). Unfortunately, the spectra were not amenable to analysis due to a marked fluxionality that occurs over a large temperature range, preventing a confident assignment of all signals. Only the signals of the three aromatic protons (H1, H2, H3) in the complexes were unambiguously identified: the system consists of two doublets of doublets for H1 and H3 protons and one triplet due to identical values of the *J*(H2-H1) and *J*(H2-H3) coupling constants.



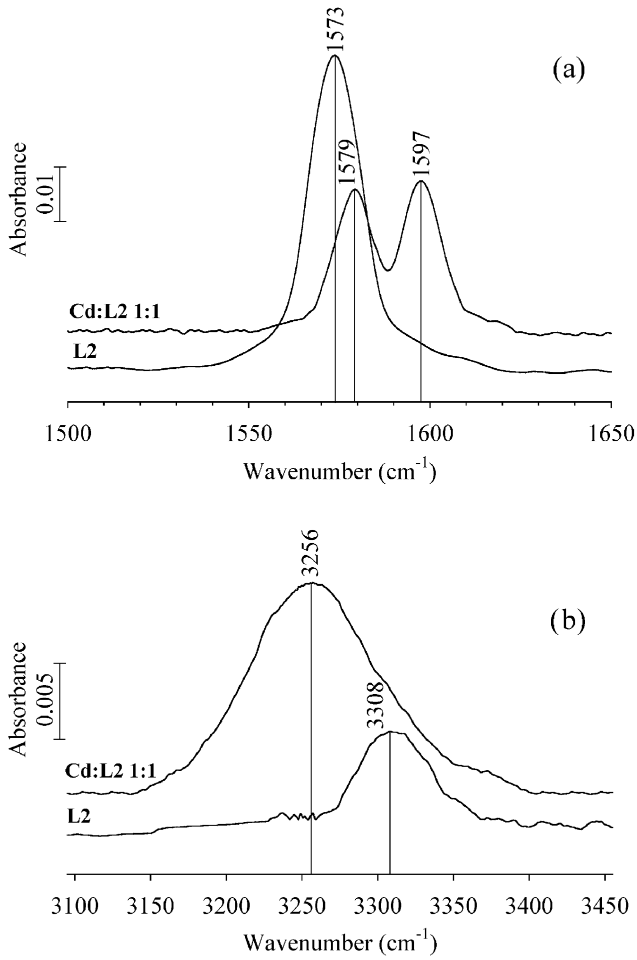


Fig. 3 FT-IR spectra of free L2 and 1 : 1 Cd : L2 DMSO solutions: (a) aromatic and (b) N–H stretching regions.

These signals are shifted downfield by about 0.3 ppm, at room temperature, with respect to the corresponding signals of the free ligands found between 7.0 and 8.5 ppm, thus giving additional evidence of the involvement of ligand dipyridine units in metal coordination.

As far as the thermodynamic parameters reported in Table 3 are considered, first of all it is to be noted that complexation of Cd(II) and Co(II) by L1 and L2 in DMSO is promoted by largely favourable, predominant, enthalpic contributions, the entropy terms being slightly unfavourable for Cd(II) and slightly favourable for Co(II). Similar data are typical of reactions involving complex formation by neutral ligands in aprotic solvents.[24–26] The negative entropy terms found for Cd(II) are in line with the fact that the release of solvent molecules from the coordination sphere of the metal ions does not compensate the decrease in internal entropy of the ligand and the loss of translational entropy of the reagents upon complexation. These entropy terms, however, are much less unfavourable than those previously found for acyclic polyamines.[24c,d] L1 and L2 are much more preorganized than acyclic polyamines, thus requiring a lower entropic cost to coordinate the metal ion. In addition, in the hypothesis that, in solution, the ligands wrap around the metal ions as shown by the calculated structures (Fig. 1c and 1d), metal ion desolvation is expected to play a determinant role. As a matter of fact, the more strongly solvated Co(II) ion[24d] gives rise to more favourable entropy terms of complexation than Cd(II).

As previously observed in aqueous solution, also in DMSO L2 forms less stable complexes than L1, mainly due to a much less favourable enthalpic contribution (Table 3). This seems to be in contrast with the fact that, at least in the gas phase, L2 displays a more preorganized structure for complexation

Table 3 Stability constants and thermodynamic functions for the formation of Cd(II) and Co(II) complexes with L1 and L2 in DMSO (NEt_4ClO_4 0.10 mol dm^{-3}, 298.0 K) and in water

Reaction[a]	Log*K*	$-\Delta G°$ (kJ mol^{-1})	$-\Delta H°$ (kJ mol^{-1})	$-T\Delta S°$ (kJ mol^{-1})
DMSO				
Cd + L1 ⇌ CdL1	16.27 (3)[b]	92.9 (2)	97.3 (2)	4.4
Cd + L2 ⇌ CdL2	12.13 (2)	69.2(1)	82.2 (1)	13
Co + L1 ⇌ CoL1	16.06 (1)	91.7 (1)	83 (2)	−8.7
Co + L2 ⇌ CoL2	11.50 (1)	65.6 (1)	55 (1)	−10.6
H_2O				
Cd + L1 ⇌ CdL1[c]	15.69	89.4	28.0	−61.4
Cd + L2 ⇌ CdL2[c]	13.23	75.3	19.6	−55.7
Co + L1 ⇌ CoL2[d]	13.23 (4)			
Co + L2 ⇌ CoL2[d]	11.45 (3)			

[a] Charges omitted. [b] Values in parentheses are standard deviations on the last significant figure. [c] Taken from ref. 17. [d] Taken from Table 1.

(Fig. 1), that is, the structure of the free L2 ligand is more similar to that assumed in the complex than in the case of L1. Hence, according to the energy parameters reported in Table 4, L2 would spend less energy in achieving the right conformation for complexation, with respect to L1. Most likely, the loss of energy in the metal–ligand interaction brought about by *N*-methylation overcompensates the conformational energy saved by L2.

It is to be noted that in DMSO a lower stability (and exothermicity) is associated with the formation of Co(II) complexes of L1 and L2, with respect to the corresponding Cd(II) species, in contrast to the opposite trend previously observed for acyclic primary and secondary polyamines.[24b,d,26] Such different behaviour can be accounted for by considering that the aromatic nitrogens of L1 and L2 are softer than aliphatic ones, hence, the two macrocyclic ligands give rise, with the soft Cd(II) cation, to stronger metal–ligand interactions, of greater covalent character, enhancing the complexation enthalpy with respect to the smaller and harder Co(II). Also the smaller size of Co^{2+} is expected to play a role in determining such behaviour, since smaller metal ions should suffer much more than larger ones with respect to the ligand's inability to bring all donor atoms in contact with them.

Comparison between complexation reactions in H_2O and DMSO

The stability constants of macrocyclic complexes may change considerably with the medium. In polar solvents where ion pairing of counterions with metal cations and their complexes is negligible, the equilibrium constant for the complexation reaction varies with the solvation energies of reactants (cations and ligands) and products (complexes). In many cases, the free energy changes for ligand and complex solvation cancel each other and the free energy term for cation solvation is largely dominant.[4] The free energy changes for metal ion transfer from water to DMSO, available for Cd(II) ($\Delta G°_{tr} = -60.4$ kJ mol^{-1})[27] and reasonably hypothesized to be negative for Co(II),[26] show that these metal ions are more strongly solvated in DMSO than in water. This is in agreement with the different electron donating abilities of the two solvent molecules, measured by the empirical Gutmann's donor number ($DN = 29.8$ for DMSO, $DN = 18$ for H_2O).[4] Hence, in the hypothesis that the solvation energies of Cd(II) and Co(II) are the dominating solvation terms in our complexation reactions, we should expect a greater complex stability in water than in DMSO.

Table 4 Calculated energies of the optimised L1 and L2 structures, free and frozen at the coordinates found in the Cd complexes

	E (hartree)
L1	
E_{coord}	−146.328
E_{free}	−146.374
ΔE (kJ mol^{-1})	120.9
L2	
E_{coord}	−162.804
E_{free}	−162.837
ΔE (kJ mol^{-1})	86.6

Conversely, the Cd(II) and Co(II) complexes with L1 display higher stability in DMSO than in water, giving a strong indication of the fact that ligand solvation, instead of metal ion solvation, plays a major role in determining the stability of L1 complexes in the two solvents. Indeed, it is known that secondary amines are more solvated in water than in DMSO[28] and, consequently, are stronger bases in DMSO than in water. L1, being more solvated in water, undergoes upon complexation a more expensive desolvation process, in terms of enthalpic contribution, but produces a greater gain in translational entropy. Accordingly, the enthalpic contributions to complexation reactions of L1 are largely more favourable in DMSO, while the entropic ones are more favourable in water (Table 3).

On the other hand, for ligand L2, in which tertiary amino groups are present, an almost opposite trend is observed, given that the $[CdL2]^{2+}$ complex is more stable in water and $[CoL2]^{2+}$ has almost the same stability in the two solvents. Due to the presence of tertiary nitrogens, L2 is less solvated than L1 in water (hydrogen bonds are formed to a lower extent) and this, together with the fact that tertiary nitrogens are weaker bases in DMSO than in water, is the reason why the stronger solvation of metal ions in DMSO prevails in determining the stability of L2 complexes.

In conclusion, the different solvation properties of the ligands, including their aptitude to form hydrogen bonds with the solvents, brought about by *N*-methylation, lead to quite different ligand coordination properties: (1) in the same solvent, L1 form more stable complexes than L2, due to the greater ability of the former ligand to stabilize the complexes *via* the formation of M–NH···S hydrogen bonds with solvent molecules in the second coordination sphere; (2) L1 forms more stable complexes in DMSO than in water, due its greater solvation in the latter solvent, while for L2 an almost opposite trend is observed, L2 being less solvated in water than L1.

Experimental

$Co(DMSO)_6(ClO_4)_2$ and $Cd(DMSO)_6(ClO_4)_2$ employed for all studies in DMSO were prepared as previously described.[26] Tetraethylammonium perchlorate (TEAP) (Aldrich >97%) was recrystallized from methanol and then dried under vacuum at 110 °C. Ligands L1 and L2 were obtained as previously reported.[1] Dimethyl sulfoxide (Aldrich 99%) was purified by distillation according to the described procedures[29] and stored under nitrogen in the presence of molecular sieves. Stock perchlorate solutions of Cd(II) and Co(II) ions were prepared by dissolving in anhydrous degassed DMSO weighed amounts of the adducts and their concentrations were checked by titration with EDTA.[30] Solutions of the ligands were prepared by dissolving weighed amounts in DMSO and standardized by thermometric titration with standard $HClO_4$ solutions. All standard solutions were prepared and stored in an MB Braun 150 glove box under a controlled atmosphere containing less than 1 ppm of water and less than 1 ppm of oxygen. The water content in the solutions, typically 10–20 ppm, was determined by a Metrohm 684 KF Coulometer.

Potentiometric measurements

All pH-metric measurements ($pH = -\log[H^+]$) in aqueous solutions employed for the determination of the stability constants of Co(II) complexes with L1 and L2 were carried out in 0.10 mol dm^{-3} NMe_4Cl at 298.1 ± 0.1 K by means of conventional titration experiments under an inert atmosphere. The combined Ingold 405 S7/120 electrode was calibrated as a hydrogen concentration probe by titrating known amounts of HCl with CO_2-free NaOH solutions and determining the equivalent point by Gran's method[31] which allowed us to determine the standard potential E° and the ionic product of water ($pK_w = 13.83(1)$ at 298.1 ± 0.1 K in 0.1 mol dm^{-3} NMe_4Cl). At least three measurements (each one about 100 data points) were performed for each system in the pH ranges 2.5–10.5. In all experiments the known ligand concentration C_L was about 1×10^{-3} mol dm^{-3} while the known metal ion concentration varied in the range $0.8C_L$–$1.8C_L$. The computer program HYPERQUAD[23] was used to calculate the equilibrium constants from e.m.f. data. Ligand protonation constants employed in calculations were determined in previous works.[16,17]

All measurements in DMSO solutions employed for the determination of the stability constants of the Cd(II) complexes with L1 and L2 were carried out in 0.1 mol dm^{-3} NEt_4ClO_4 at 298.0 K by using a thermostated cell maintained at 298.0 ± 0.10 K, and kept under an inert atmosphere in an MB Braun 150 glove box. The concentration of Cd(II) was obtained from the e.m.f. data of a galvanic cell coupled with an Amel 338 pH meter equipped with a Weiss WCD1001 Cd ion selective working electrode and a Metrohm 6.0718.000 reference silver electrode. Aliquots of ligand solutions of known concentrations were added to the cell containing Cd(II) solutions (1.00 mmol $dm^{-3} < C_{Cd^{2+}} < 4.00$ mmol dm^{-3}) of known concentration and the free metal ion concentration was measured after each titrant addition. Equilibrium was reached typically in 2–5 minutes. The Nernstian response of the Cd(II) selective electrode was obtained in the range 10^{-7} mol dm^{-3} < [Cd(II)] < 10^{-2} mol dm^{-3}.

The computer program HYPERQUAD[23] was used to calculate the stability constants.

Calorimetric measurements

A Tronac model 87-558 precision calorimeter was checked by titration of tris(hydroxymethyl)aminomethane (tham) with a standard solution of HCl in water and used to measure the reaction heats. The experimental value of the heat of neutralization of tham was found to be $\Delta H^\circ = -47.58$ kJ mol^{-1}, in good agreement with the accepted value of -47.53 ± 0.13 kJ mol^{-1}.[22] The calorimetric titrations employed to determine the enthalpy changes for the formation of Cd(II) and Co(II) complexes with L1 and L2 in 0.10 mol dm^{-3} NEt_4ClO_4 DMSO solution were performed at 298.10 ± 0.02 K by adding known volumes of ligand solutions (10 mmol $dm^{-3} < C_L < 20$ mmol dm^{-3}) to 20 mL of metal ion [M(II) = Cd(II), Co(II)] solutions (1.50 mmol $dm^{-3} < C_M < 3.0$ mmol dm^{-3}). Corrections for the heat of dilution of titrant were applied by means of separate experiments. The least squares computer program Letagrop Kalle[32] was used to calculate the enthalpy changes.

In the case of Co(II) complexation reactions in aqueous solution, the heat effects observed by means of the calorimetric system above described were very small and affected by large random errors. We also tried to determine these complexation enthalpies by means of a thermal activity monitor (Thermometric AB, model 2277) microcalorimeter, working with samples of higher concentration, but the experiments failed because the apparatus works under aerobic conditions and rapid oxidation of Co(II) complexes occurred.

Spectrophotometric measurements

The stability constants of Co(II) complexes with L1 and L2 were determined in 0.10 mol dm^{-3} NEt_4ClO_4 DMSO solution at 298.0 K, by using Cd(II) as competitor,[33] by means of UV-Vis measurements performed with a Varian Cary 50 spectrophotometer kept inside the MB Braun 150 glove box. Optic fiber probes and a quartz cuvette of 1 cm pathlength (117.100 Bracco cell) were used. The data were recorded over the wavelength range 260–650 nm. Different titrations were carried out at varying Co(II) and Cd(II) concentrations, in order to obtain the best competition between the two metal ions for the same ligand and/or provide evidence of possible formation of mixed or polynuclear species. The absorption maximum for $Co(ClO_4)_2$ in DMSO occurs at 535 nm, with an extinction coefficient $\varepsilon = 11.9$ mol^{-1} dm^{-3} cm^{-1}.

The absorbance data at about 20 different wavelengths in the range 260–600 nm were analysed and the formation constants of the $[CoL]^{2+}$ complexes were determined by using the HYPERQUAD[23] program.

Semi-empirical calculations

The geometry optimisations of the Cd(II) complexes were performed by using the program PC-GAMESS[34] running on a dual processor AthlonMP 2000 machine. Since we were only interested in obtaining information on the maximum number of donor atoms involved by ligands in metal ion binding in the absence of any other interaction than coordinative bonds, we have excluded solvent molecules from calculations, performing the optimisations by means of the semi-empirical PM3 method. The geometries have been optimised in the gas phase without symmetry constraints. Strain energies have been computed by subtracting the energy of the optimised free ligand and the "single point" energy of the ligand at the coordinates in the complex (E_{free} and E_{coord}, respectively, in Table 3).

FT-IR spectroscopy

The FT-IR spectra were recorded by using a Bio-Rad FTS 40 spectrometer (maximum resolution 4 cm^{-1}, 16 scans). Cells with barium fluoride windows (thickness of 25 μm) were used. The cells were filled and closed in a glove box and quickly transferred to the spectrometer. The C_M (M = Cd, Co) and C_L (L = L1, L2) concentrations were both 0.040 mol^{-1} dm^{-3}. Spectra were also collected from solutions containing the ligand alone.

NMR measurements

^1H NMR (and ^{13}C NMR) spectra were recorded at 298 K on a Bruker AC 200F QNP spectrometer. ^1H chemical shifts refer to $SiMe_4$. Measurements were performed on DMSO-d_6 solutions containing the complexes $[CdL1]^{2+}$ and $[CdL2]^{2+}$, and on solutions containing the ligands alone.

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