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Formation constants for complexes of 1,4,7,10-tetraazacyclododecane-1,7-diacetic acid and the crystal structure of its nickel(II) complex †

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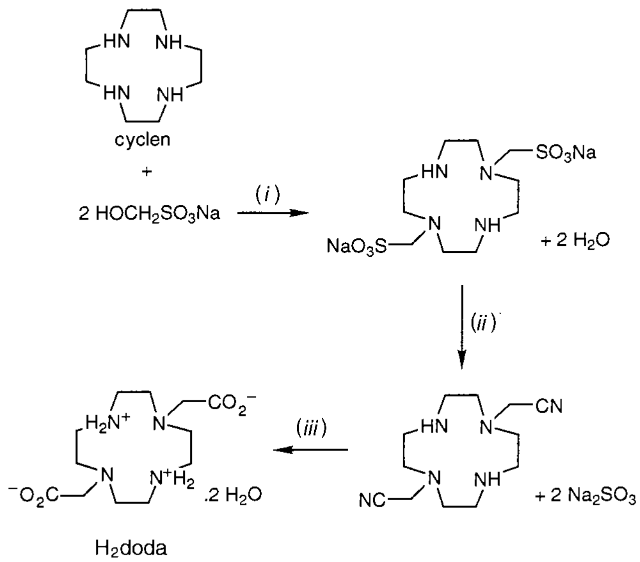
The crystal structure of the nickel(II) complex of 1,4,7,10-tetraazacyclododecane-1,7-diacetic acid (H_2doda) has been determined. The ligand binds in a *cis*-octahedral fashion through the four nitrogen atoms and two carboxylate groups and dimerizes *via* an apparently symmetrical hydrogen bond from the non-bonding oxygen of a carboxylate group to a lone hydrogen ion originating from a perchloric acid molecule of crystallization. Carbon-13 NMR studies of the corresponding zinc(II) complex indicated that it has a similar structure. pK_a Measurements for doda, at 298.2 K in 0.1 mol dm^{-3} NEt_4ClO_4, suggested that the two secondary amines are the first to protonate followed by the two carboxylates and then the two tertiary nitrogen atoms. A marked disparity in the magnitude of the pK_a values for the two carboxylic groups [4.00(1) and 2.36(3)] suggests that internal hydrogen bonding between the two stabilizes one of the protons. Formation constants for some divalent metal complexes (Co, Ni, Cu, Zn, Cd or Pb) of H_2doda have been determined. The results from this work are compared to data for analogous macrocycles having three or four carboxymethyl groups.

A convenient approach to synthesizing the highly stable, neutral metal complexes that are frequently sought for applications in diagnostic and therapeutic medicine has been to use the high stability conferred by a polyaza macrocycle, in conjunction with the metal-ion charge neutralization provided by a group of pendant carboxylates equal in number to the charge on the metal ion.[1–3] Thus, neutral complexes of divalent metal ions with 1,4,8,11-tetraazacyclotetradecane (cyclam) have been formed by appending two carboxymethyl (acetate) groups to two of the nitrogen atoms.[2,3] By selectively appending these carboxymethyl groups on the diagonally related 1,8-nitrogen atoms, advantage can be taken of the fact that when cyclam binds in its most stable *trans*-III configuration one carboxylate will project below the macrocyclic plane and the other above. This allows the complex to assume octahedral stereochemistry without inducing undue ring strain in any of the chelate rings, and in so doing probably maximizes the stability that can be achieved for many metal ions with this particular macrocycle–pendant arm combination. This approach to generating neutral complexes also has the advantage that the lipophilicity of the complex can be further enhanced by alkylation of any secondary amines that are not carboxymethylated.[3]

Synthetic strategies for selectively difunctionalizing the smaller tetraazamacrocycle 1,4,7,10-tetraazacyclododecane (cyclen) have been somewhat limited and thus the possibility of preparing neutral complexes of divalent metal ions, through the attachment of two carboxymethyl groups to two of the nitrogen atoms of the macrocycle, has remained largely unexplored. This is significant as it frequently turns out that complexes originating from cyclen-derived ligands are more stable than their cyclam-derived counterparts, especially when the divalent metal ion is one of large ionic radius.[4,5] Recently, however, van Westrenen and Sherry[6] have demonstrated that selective sulfomethylation at the 1,7 positions of cyclen can be accomplished in quantitative yield, opening a viable pathway to these compounds. Nitrogen atoms at positions 4 and 10 are prevented from reacting by allowing the synthesis to proceed under conditions in which they are protonated, namely in aqueous solution at pH 7. The sulfonate moieties can be replaced by cyano moieties which are then hydrolysed *in situ* giving the amino acid dihydrate in *ca.* 60% isolated yield over the three steps summarized in Scheme 1.



Scheme 1 (*i*) Water, pH 7; (*ii*) 2NaCN; (*iii*) concentrated HCl, 65 h

In the work reported here we have used this ligand synthesis to prepare 1,4,7,10-tetraazacyclododecane-1,7-diacetic acid (H_2doda) and have made a study of its complexing properties. Its protonation constants, formation constants for a range of divalent metal complexes and the crystal structure of the nickel(II) complex are reported, and compared with the corresponding data for 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (H_4dota), 1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid (H_3dotra) and their complexes. We also investigated the consequences of exposing H_2doda to conditions which favour conversion into the diacid chloride (concentrated HCl or thionyl chloride). With the cyclam analogue this leads to spontaneous internal lactamization to form a tricyclic compound,[2,3] however in the case of H_2doda no corresponding reaction resulted, probably due to the greater steric rigidity of the smaller macrocycle.

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† *Non-SI unit employed:* $\mu_B \approx 9.27 \times 10^{-24}$ J T^{-1}.

Results and Discussion

Macrocycle protonation constants

The stepwise protonation constants for doda were measured by potentiometric titration of H_4doda^{2+} with tetraethylammonium hydroxide using 0.1 mol dm^{-3} tetraethylammonium perchlorate as the background electrolyte. Values for the protonation constants, K_x (x = 1–6), relate to the equilibria shown in equations (1)–(6), where $\log_{10} K_x = pK_{ax}$.

$$doda^{2-} + H^+ \overset{K_1}{\rightleftharpoons} Hdoda^- \quad (1)$$

$$Hdoda^- + H^+ \overset{K_2}{\rightleftharpoons} H_2doda \quad (2)$$

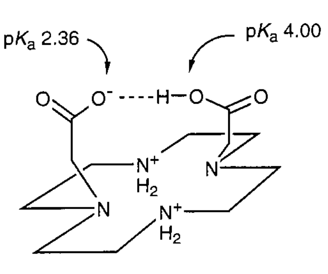
$$H_2doda + H^+ \overset{K_3}{\rightleftharpoons} H_3doda^+ \quad (3)$$

$$H_3doda^+ + H^+ \overset{K_4}{\rightleftharpoons} H_4doda^{2+} \quad (4)$$

$$H_4doda^{2+} + H^+ \overset{K_5}{\rightleftharpoons} H_5doda^{3+} \quad (5)$$

$$H_5doda^{3+} + H^+ \overset{K_6}{\rightleftharpoons} H_6doda^{4+} \quad (6)$$

Previous work has shown that polyaminocarboxylates have the ability to bind sodium and, to a lesser extent, potassium ions, resulting in a reduction of the perceived protonation constants when either of these ions is present during the potentiometric titration.[7] It is for this reason that tetraethylammonium was used as the background cation in this work. For K_1 to K_4 the logarithms of the protonation constants were found to be 11.45(2), 9.54(3), 4.00(1) and 2.36(3). The log K values for the final two protonations were not measured and are presumably below 2.3 since the species H_5doda^{3+} and H_6doda^{4+} were not detected within the pH range of the potentiometric titration (2.3–11.2). These values are shown in Table 1 where they are compared to the corresponding values for dota, dotra and cyclen which have been measured by the same method, at the same ionic strength and in a non-co-ordinating electrolyte. Comparison of these sets of protonation constants shows that there is a progressive trend towards higher basicity at the first protonation site as the number of carboxylate groups increases. This is understandable, as increasing the number of carboxylates increases the overall charge on the macrocyclic anion undergoing protonation. With doda and dotra the question arises as to whether the first protonation occurs on a secondary or a tertiary nitrogen. The crystal structure of H_2dotra has been determined previously[8] and shows, as has been postulated on numerous previous occasions, that it is a *trans*-related pair of nitrogen atoms that accepts the first two protons. Of the two possible *trans* pairs it is the secondary–tertiary rather than the tertiary–tertiary pair that protonate, probably indicating that even though the higher than normal basicity of the molecule arises from the carboxylate groups that are attached to the tertiary nitrogen atoms, it is still the secondary amine that is the more basic. Originally it has been suggested that in dota the high basicity originated from an intrapendant-arm hydrogen-bond stabilization of a proton that had added to a tertiary nitrogen,[12] however the crystal structure of H_2dotra shows no evidence for this and it now seems more likely that the high basicity is simply a function of overall charge and that, where the situation arises, the normal sequence of basicity observed in macrocyclic amines (with secondary amines being more basic than tertiary amines) is preserved. Thus, we suggest here that the first protonation on $doda^{2-}$ occurs at one of the secondary amines, and, since the second protonation will almost certainly occur *trans* to the first, the second protonation will also occur at a secondary nitrogen. This is supported by log K_2 for doda being higher than the value for either dotra or dota, where it can only be ascribed to protonation at a tertiary nitrogen. It is not clear to us, however, why log K_2 for doda should be lower than that for cyclen where the proton would be adding to a cation rather than an anion. The value of log K_3 for doda must correspond to protonation of the first of the carboxylate groups and is similar to the corresponding dota and dotra values. It is interesting that in doda, dotra and dota the first carboxylate site (first and second in dota) is markedly more basic than is normally the case for α-amino acids, where this protonation is typically characterized by a log K value of between about 2.0 and 2.5 (2.35 for glycine[16]), or for a single carboxymethyl group pendant to a tetraazamacrocycle, where a log K of 3.01 has been measured.[17] A possible explanation may be that the first protonated carboxylate group in these polycarboxymethyl macrocyclic molecules undergoes stabilization through intramolecular hydrogen bonding to the *trans*-related carboxylate, as shown in Scheme 2. Alternative hydrogen-bonding interactions involving one of the amine moieties do not account for the fact that the second carboxylate in doda does not show a similar high basicity, but instead has a more normal log K of 2.36, similar to log K_5 and log K_6 of dota which probably also describe protonation of the two carboxylates initially involved in the stabilization of their *trans*-carboxylic partners. The speciation of doda at different pH is shown in Fig. 1.



Scheme 2 Proposed stabilization of a carboxylate proton in macrocycles having more than one pendant acetate, which may account for the pairwise disparity in the pK_a values for the carboxylic groups. The pK_a values shown are those for doda

Metal complex formation constants

Glass-electrode potentiometric titration of H_4doda^{2+} with NEt_4OH in the presence of an M^{2+} (M = Co, Ni, Cu, Zn, Cd or Pb) cation revealed the existence of two complex species, $[M(Hdoda)]^+$ and [M(doda)], for all M. These results indicate that doda can co-ordinate, giving complexes of significant stability, either as a penta- or as a hexa-dentate ligand, although there is no way of being certain, from these data, whether it is an amine or a carboxylate that is protonated in pentadentate $Hdoda^-$. This observation parallels findings with dota where $[M(dota)]^{2-}$, $[M(Hdota)]^-$ and $[M(H_2dota)]$ complexes were observed for all of the metal ions used in this study (except Pb^{2+}, where only the first two species were observed) indicating that complete ligand deprotonation is not essential for stable complex formation.[9] In contrast to dota,[9,18] no 2:1 metal:ligand species were observed, which is consistent with the lower number of donor atoms available in doda. The formation constants for the observed species are given in Table 2, together with data for the cyclen and dota complexes for comparison. The values of the formation constants tend to be intermediate between those measured for cyclen and dota and no particular metal-ion selectivity is seen within the group of metal ions studied here. The cadmium(II) complex shows the greatest stability enhancement ($10^{3.9}$) compared to the corresponding cyclen complex, which is consistent with the observation made by Hancock and co-workers[22] that metal ions with an ionic radius of about 1 Å derive the greatest stability enhancement from attaching pendant acetates to cyclen.

Table 1 Protonation constants[a] at 298.2 K for doda, determined in this study, together with literature values for dota, dotra and cyclen

Ligand	$\log_{10} K_1$	$\log_{10} K_2$	$\log_{10} K_3$	$\log_{10} K_4$	$\log_{10} K_5$	$\log_{10} K_6$
doda[b]	11.45(2)	9.54(3)	4.00(1)	2.36(3)	<2.3	<2.3
dotra[c]	11.59	9.24	4.43	3.48		
dota[c]	11.73	9.40	4.50	4.19		
dota[d]	11.08	9.23	4.24	4.18	1.88	1.71
cyclen[e]	11.32	9.72	<2.3	<2.3		
cyclen[f]	11.04	9.86	<2	<2		

[a] K_1, K_2, *etc.* refer to the equations $L^{x-} + H^+ \rightleftharpoons HL^{(x-1)-}$, $HL^{(x-1)-} + H^+ \rightleftharpoons H_2L^{(x-2)-}$, *etc.* where $x = 2$, 3, 4 and 0 for doda, dotra, dota and cyclen, respectively. [b] $I = 0.1$ mol dm^{-3} NEt_4ClO_4. [c] From ref. 8, $I = 0.1$ mol dm^{-3} NMe_4Cl, earlier determinations for dota may be found in refs. 7 and 9–12. [d] From ref. 12, $I = 1$ mol dm^{-3} NaCl, corrected for sodium complexation. [e] From ref. 5, $I = 0.1$ mol dm^{-3} $NaNO_3$. [f] From ref. 13, $I = 0.1$ mol dm^{-3} $NaClO_4$; earlier values may be found in refs. 14 and 15.

Table 2 Formation constants at 298.2 K for doda,[a] dota[b] and cyclen complexes of some divalent metal ions

		$\log_{10} \beta$					
Overall reaction	Ligand	Co^{2+}	Ni^{2+}	Cu^{2+}	Zn^{2+}	Cd^{2+}	Pb^{2+}
$M + L + 2H^+ \rightleftharpoons M(H_2L)^{2+}$	doda	*c*	*c*	*c*	*c*	*c*	*c*
	dota	27.73	28.26	29.80	28.79	28.73	*c*
$M + L + H^+ \rightleftharpoons M(HL)^+$	doda	21.9(1)	>19.3[d]	24.1(1)	22.2(1)	21.7(1)	21.9(1)
	dota	24.35	23.54	26.03	25.28	25.70	26.55
$M + L \rightleftharpoons ML$	cyclen	13.8[e]	16.4[f]	23.3[g]	16.2[h]	14.3[h]	15.9[h]
	doda	16.9(1)	>13.3[d]	21.1(2)	18.2(1)	18.2(1)	18.3(1)
	dota	20.27	20.03	22.25	21.10	21.31	22.69
Derived reactions							
$M + H_2L^{2+} \rightleftharpoons M(H_2L)^{2+}$	doda	*c*	*c*	*c*	*c*	*c*	*c*
	dota	5.88	6.41	7.95	6.94	6.88	*c*
$M + HL^+ \rightleftharpoons M(HL)^+$	doda	10.5(1)	>7.9[d]	12.7(1)	10.8(1)	10.3(1)	10.5(1)
	dota	12.26	11.45	13.94	13.19	13.61	14.46

[a] This work, $I = 0.1$ mol dm^{-3} NEt_4ClO_4. A value of 13.8 was obtained for the apparent pK_w under these conditions. [b] From ref. 9, $I = 0.1$ mol dm^{-3} NMe_4NO_3; earlier values may be found in refs. 7 and 10. [c] Reaction not observed. [d] Only the lower limit is given owing to very slow and hence doubtful equilibration during the titration. [e] From ref. 19. [f] From ref. 20. [g] From ref. 21. [h] From ref. 14.

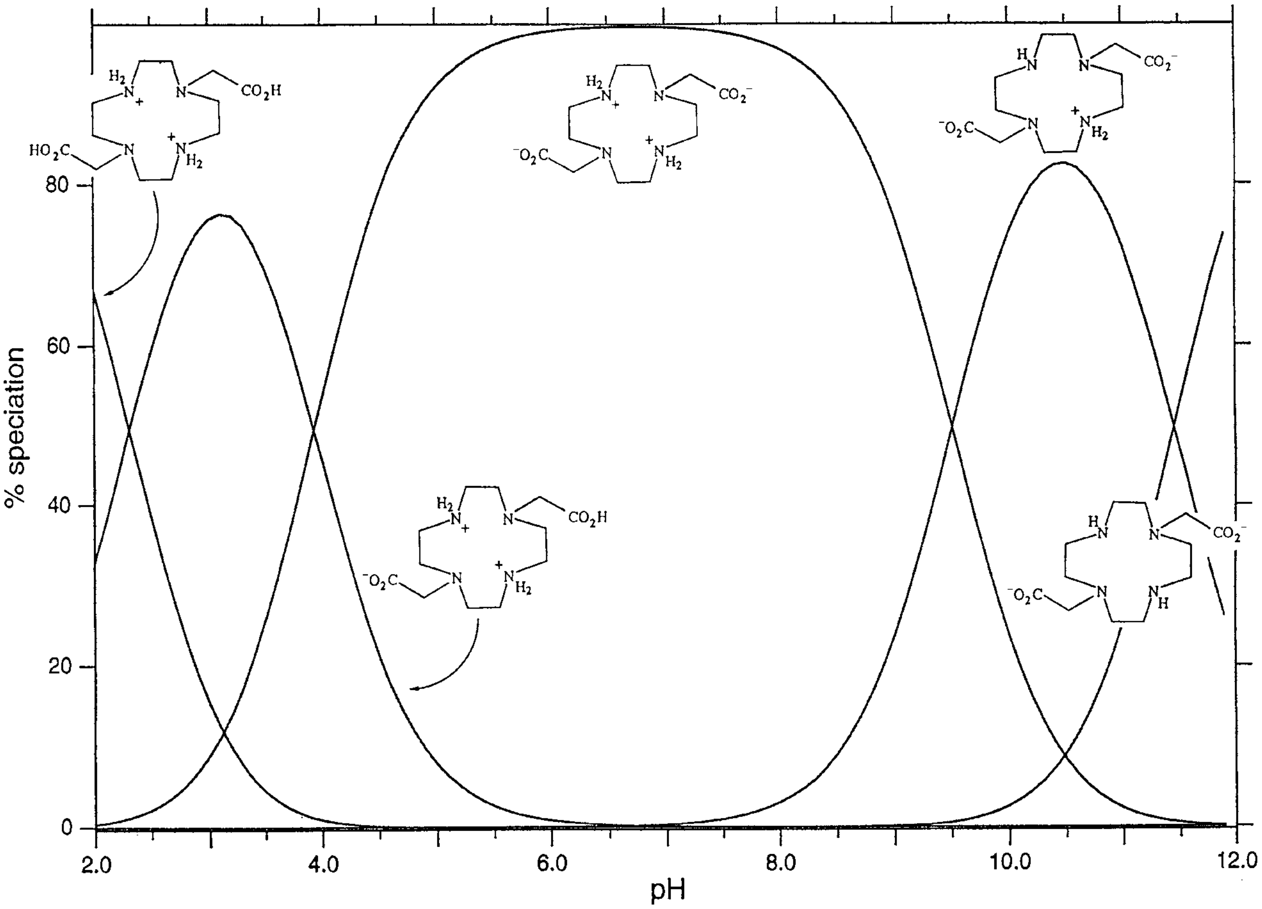


Fig. 1 Speciation diagram for doda produced using data from Table 1

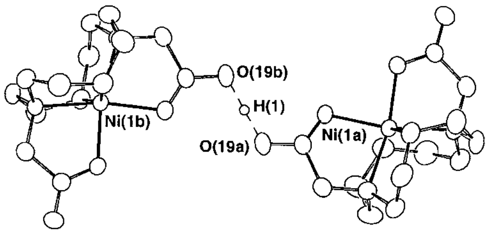


Fig. 2 Structure of the [Ni(doda)] dimer

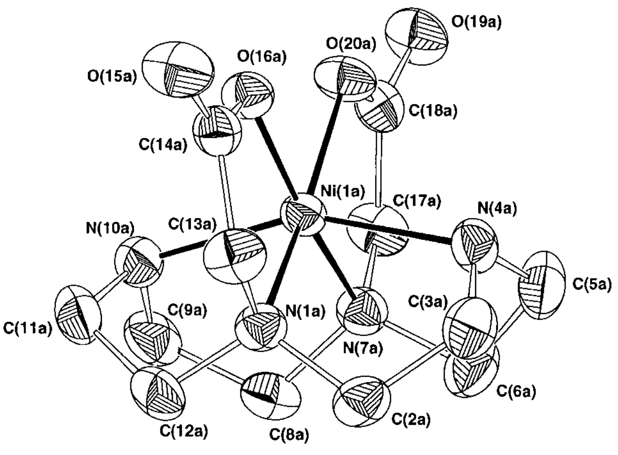


Fig. 3 An ORTEP[23] drawing of one half-unit (**a**) of the [Ni(doda)] dimer showing displacement ellipsoids of the non-hydrogen atoms at the 50% probability level

Table 3 Selected bond lengths (Å) and angles (°) for the [Ni(doda)] dimer

	Half-unit **a**	Half-unit **b**
Ni(1)–N(1)	2.113(3)	2.115(3)
Ni(1)–N(4)	2.144(3)	2.132(3)
Ni(1)–N(7)	2.135(3)	2.144(3)
Ni(1)–N(10)	2.137(3)	2.138(3)
Ni(1)–O(16)	2.019(2)	2.031(2)
Ni(1)–O(20)	2.068(2)	2.061(2)
N(4)–Ni(1)–N(10)	155.0(1)	155.8(1)
N(1)–Ni(1)–N(7)	109.3(1)	109.5(1)
O(16)–Ni(1)–O(20)	86.4(1)	86.6(1)

Equilibration of the titration solution following the addition of each aliquot of base was judged to be complete when the rate of change of potential fell below 0.1 mV min^{-1}. This occurred within a period of 5 min for all metal ions studied with doda except nickel(II) and is similar to the rate of equilibrium noted previously for dota.[9]

Structure of the doda complexes

To provide some information about the co-ordination mode of H_2doda in the solid state the nickel(II) complex was isolated and the crystal structure solved. The complex was synthesized by adding an ethanolic solution of hydrated nickel(II) perchlorate to a refluxing aqueous solution of H_2doda·$2H_2O$, in a 1 : 1 molar ratio. The resulting solution precipitated purple crystals on cooling. These were recrystallized, from a slowly evaporating aqueous solution, giving crystals, suitable for X-ray diffraction studies, that analysed as [Ni(doda)]·$0.5HClO_4$·$1.5H_2O$.

The X-ray diffraction data revealed that the complex is dimeric, as shown in Fig. 2, with each half-unit symmetrically hydrogen bonded to the other through the interaction of a non-co-ordinating carboxylate oxygen with a lone hydrogen ion. The hydrogen ion is located on an approximate centre of symmetry within the dimer. The remainder of the asymmetric unit is composed of a perchlorate anion and three water molecules. The water molecule oxygen atoms are separated by distances that indicate possible hydrogen bonding between them [range 2.742(6)–2.880(7) Å] and they appear to be hydrogen bonded to the perchlorate ion. The only possible hydrogen bond to the dimer is from water O(2) to O(15b) [2.815(4) Å]. The individual half-units have approximate C_{2v} symmetry. Each consists of an octahedrally co-ordinated nickel(II) ion about which the macrocycle has folded, along the N(4)–N(10) axis, so that it binds through the four nitrogen atoms and two carboxylate groups, which occupy *cis*-related co-ordination sites, as shown in Fig. 3. The equatorial N–Ni–N angles average 109.4°, while the axial N–Ni–N angles average 155.4°. There are no significant distortions in the Ni–N bond lengths which range from 2.113 to 2.144 Å. A selected listing of bond lengths and angles is provided in Table 3. Both NH groups and both carboxymethyl groups project in the same direction, thus, using the terminology of Bosnich *et al.*,[24] the macrocycle has the *cis*-I configuration. Each half-unit has a similar arrangement of atoms to those in [Ni(H_2dota)] and [Cu(H_2dota)], which have been analysed previously,[25] and in which the two carboxylate groups not present in doda are protonated and directed away from the inner co-ordination sphere of the metal ion. The hydrogen atom, H(1), lies on the line of centres between O(19a) and O(19b) (Fig. 2) at distances of 1.21(4) and 1.24(4) Å from the O atoms, respectively. The apparently symmetrical hydrogen bond O(19a)···H(1)···O(19b), responsible for the dimeric [Ni(doda)] structure, has an O···O separation of 2.448(4) Å which is at the short end of the known spectrum of hydrogen bond lengths. A search of the Cambridge Crystallographic Data Base[26] showed that this pattern of hydrogen bonding between co-ordinated carboxylates is not uncommon, but revealed only ten structures containing an O···O hydrogen-bonded distance (where the two oxygen atoms were specified as the non-metal-co-ordinating carboxylate oxygen atoms of a co-ordinated carboxylate) of less than 2.5 Å.[27]

The zinc(II) complex of H_2doda was prepared and purified in the same way as the nickel(II) complex, described above, but analysed as [Zn(doda)]·$1.5HClO_4$·$2H_2O$, suggesting that this complex also hydrogen bonds in the solid state through hydrogen ion incorporation into the crystal lattice, but in a different manner to that seen with [Ni(doda)]. The ^{13}C NMR spectrum of [Zn(doda)] in D_2O is superficially similar to the spectrum of uncomplexed H_2doda, with a pattern of resonances (detailed in the Experimental section) consistent with C_{2v} symmetry. Thus it appears that the zinc(II) complex is *cis*-octahedral in solution, at least on a time-averaged basis, with doda bound in the same fashion as seen for [Ni(doda)] in the solid state.

Experimental

General

Carbon-13 NMR spectra were recorded at 75.46 MHz, using a Varian Gemini 300 spectrometer, in D_2O at ambient temperature. Chemical shifts are quoted with respect to internal 1,4-dioxane, for which the resonance position was taken as δ 67.00. Elemental analyses were performed by Chemical and Microanalytical Services Pty Ltd. The compound cyclen was prepared according to the procedure described by Richman and Atkins.[28] Dowex 50W-X8 (H) was supplied by BDH.

Syntheses

1,4,7,10-Tetraazacyclododecane-1,7-diacetic acid dihydrate, H_2doda·$2H_2O$. The crude compound was formed according to the procedure used by van Westrenen and Sherry,[6] summarized in Scheme 1. Final purification of the hydrolysed nitrile was effected in the following way. (At the conclusion of the hydrolysis reaction the product is contaminated with sodium chloride, which arises from the sodium sulfite produced during the formation of the dinitrile. The sodium sulfite is not removed as the combination of stages two and three of the synthesis gives for a better overall yield of the dicarboxylic acid.) The crude hydrolysis product, obtained originally from 3 mmol of cyclen, was dissolved in water (9 cm^3) and the resulting solution divided into three aliquots. Each aliquot was separately applied to a column of Dowex 50W-X8 (particle size 0.39–1.00 mm) cation-exchange resin (bed volume 20 cm^3) in its H^+ form. The column was washed with 0.5 mol dm^{-3} HCl (200 cm^3) to displace sodium cations and then with water (250 cm^3) until the eluent was neutral. Elution of the product was then commenced using 0.5 mol dm^{-3} aqueous ammonia solution. The product began to leave the column following a throughput of 150 cm^3 of ammonia solution, at which stage the pH of the eluent had risen to 10. Collection of the product was complete after the passage of more ammonia solution (175 cm^3) by which stage the pH had risen to 11.5. The fraction containing the product was rotary evaporated to dryness and the residue triturated with ethanol (5 cm^3) giving an off-white powder. This was filtered off, washed with diethyl ether (5 cm^3) and dried *in vacuo*. The combined yield from the three aliquots was 0.56 g, 57% based on cyclen (Found: C, 44.45; H, 8.6; N, 17.05. $C_{12}H_{24}N_4O_4{\cdot}2H_2O$ requires C, 44.45; H, 8.7; N, 17.25%); ^{13}C NMR (D_2O) δ 179.5 (2C), 57.8 (2C), 50.6 (4C) and 43.9 (4C).

$[Ni(doda)]{\cdot}0.5HClO_4{\cdot}1.5H_2O$. CAUTION: perchlorate salts of metal complexes are potentially explosive. Although we have had no incidents with this or the following perchlorate salt suitable precautions should be taken. A solution of $H_2doda{\cdot}2H_2O$ (0.1 g, 0.31 mmol) in water (3 cm^3) was brought to reflux and a solution of hexaaquanickel(II) perchlorate (0.11 g, 0.312 mmol) in ethanol (5 cm^3) was added dropwise over 10 min. Upon cooling the resulting solution to room temperature fine purple crystals precipitated. These were filtered off and recrystallized from water giving the pure product (0.87 g, 68%) (Found: C, 33.85; H, 5.75; N, 12.95. $C_{24}H_{51}ClN_8Ni_2O_{15}$ requires C, 34.15; H, 6.1; N, 13.25%); $\mu_{eff} = 3.1\ \mu_B$.

$[Zn(doda)]{\cdot}1.5HClO_4{\cdot}2H_2O$. This complex was prepared in 71% yield using the same method as described above for the nickel(II) complex (Found: C, 26.8; H, 4.8; N, 10.25. $C_{12}H_{27.5}Cl_{1.5}N_4O_{12}Zn$ requires C, 26.75; H, 5.15; N, 10.4%); ^{13}C NMR (D_2O) δ 179.4 (2C), 57.9 (2C), 53.8 (4C) and 44.7 (4C).

Potentiometric titrations

The potentiometric titrations were carried out under an inert atmosphere of water-saturated nitrogen in a water-jacketed vessel maintained at 25 °C. Data were obtained from aliquots (10 cm^3) of solution containing 0.005 mol dm^{-3} $HClO_4$, 0.100 mol dm^{-3} NEt_4ClO_4 and approximately 1.0×10^{-3} mol dm^{-3} macrocycle titrated with 0.10 mol dm^{-3} 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 81-65BN combination electrode connected to an Orion 290A 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 macrocycle and fitting the resulting data from this strong acid–strong base titration by use of the Nernst equation to find correct values for E_0 and pK_w. The pK_a and stability constants were determined using the program SUPERQUAD.[29] Stability constant data were gathered from solutions to which 0.1 mol dm^{-3} 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.

Crystallography

Unit-cell and intensity data for $[Ni(doda)]{\cdot}0.5HClO_4{\cdot}1.5H_2O$ were measured on a Rigaku AFC7/R diffractometer using graphite-monochromated Cu-Kα X-radiation. Parameters associated with unit-cell dimensions, intensity data collection, structure solution and refinement are given in Table 4. Absorption corrections were calculated by Gaussian integration. Computer programs of the XTAL system[30] were used throughout the structure solution and refinement. The structure was solved by direct methods. Non-hydrogen atomic coordinates and anisotropic displacement parameters for all atoms were refined by full-matrix least squares on F^2 minimizing $\Sigma w(|F_o|^2 - |F_c|^2)^2$, where $w = 1/\sigma^2(F_o^2)$. Values of $1/\sigma^2(F_o^2)$ were obtained from counting statistics. Neutral atom scattering factors with anomalous dispersion corrections were used. An extinction correction was refined [$g = 635(67)$].[31] The perchlorate anion showed high thermal motion and disorder. It was modelled by placing two differently oriented rigid groups on the site and refining individual anisotropic displacement parameters for all atoms and a group population parameter. The highest shift/error values at the end of the refinement were associated with the eulerian angles of the rigid groups. With the exception of the hydrogen atoms on the water molecules and the bridging hydrogen atom, hydrogen atoms were placed at calculated positions and although their coordinates and isotropic displacement parameters were not refined the coordinates were readjusted several times during the refinement. The water molecule hydrogen atoms were not included in the calculations. The position of the bridging hydrogen atom was located in a difference map and its positional and isotropic displacement parameters refined.

There is non-crystallographic symmetry present in the structure as revealed by the program BUNYIP.[32] The half-units **a** and **b** are related by an approximate inversion centre at 0.239(4), 0.749(5), 0.2522(4) and the Cl atoms of the perchlorate groups appear to be similarly related about this point and symmetrically equivalent points. The water molecule O atoms, however, are not. The assignment of the crystal system and

Table 4 Crystal data and refinement summary for the [Ni(doda)] dimer

Empirical formula	$(C_{12}H_{22}N_4NiO_4)_2{\cdot}HClO_4{\cdot}3H_2O$
M	844.50
Crystal system	Monoclinic
Space group	$P2_1/c$
a/Å	16.815(8)
b/Å	8.494(1)
c/Å	24.333(2)
β/°	98.81(2)
U/Å^3	3434(2)
λ/Å	1.541 80
Z	4
D_m[a]/g cm^{-3}	1.61(2)
D_c/g cm^{-3}	1.633
F(000)	1776
T/K	293(2)
μ/mm^{-1}	0.278
T_{min}, T_{max}	0.475, 0.896
θ_{max}/°	60
h, k, l ranges	0–18, 0–9, −27 to 26
No. reflections sampled	8646 (ω–2θ scans)
No. reflections measured	5117
No. used in refinement	4904 ($F^2 > 0$)
No. parameters refined	477
R[b]	0.051
$wR(F^2)$	0.113
Goodness of fit	4.18
Final shift/error (maximum, average)	0.041, 0.004
Minimum, maximum Δρ/e Å^{-3}	−0.56, 0.52

[a] By flotation in a mixture of chloroform and dibromoethane. [b] $R = \Sigma(||F_o| - |F_c||)/\Sigma|F_o|$ based on 4904 reflections.

space group was initially made by inspection of precession photographs for Laue symmetry and systematic absences. The program CREDUC[33] did not reveal a unit cell other than the metrically monoclinic one reported here. It is also noted that if there were an exact inversion centre at 0.25, 0.75, 0.25 the cell would be A-centred. Although the reflections with $k + l$ odd are weak their average intensity is substantial and some are quite intense. We conclude that the extra symmetry is indeed non-crystallographic.

Atomic coordinates, thermal parameters, and bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Instructions for Authors, *J. Chem. Soc., Dalton Trans.*, 1997, Issue 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 186/313.

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