Synthesis, Characterization and Basicity Properties of Two New Oxa-Aza Macrobicyclic Receptors. Crystal Structure of a 'Water Cryptate'

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The synthesis and characterization of the two new oxa-aza macrobicycles 16,21-dimethyl-4,7,10-trioxa-1,13,16,21-tetraazabicyclo[11.5.5]tricosane (**C1**) and 19,24-dimethyl-4,7,10,13-tetraoxa-1,16,19,24-tetraazabicyclo[14.5.5]hexacosane (**C2**) have been reported. Their proton transfer behaviour has been studied in aqueous solution by potentiometry (298.1 ± 0.1 K, I = 0.15 mol dm^{-3}), microcalorimetry and ^{1}H and ^{13}C NMR spectroscopy. Both of them behave as diprotic bases. **C1** and **C2** behave as strong bases in the first protonation step and as moderate bases in the second one. Their basicity is due to a main enthalpic contribution. NMR experiments indicate that the nitrogen atoms involved in the protonation steps are the methylated ones. The crystal structure of $[H_2$**C2**$\cdot H_2O][ClO_4]_2$ [space group $P2_1$, a = 10.450(2), b = 11.391(2), c = 12.666(3) Å, β = 100.21(2)°, V = 1483.8(5) Å^3, Z = 2, R = 0.059 and R_w = 0.052] gives confidence to NMR results, confirming that in the $[H_2$**C2**$\cdot H_2O]^{2+}$ cation the protons are localized on the methylated nitrogen atoms. Furthermore, a water molecule is enclosed into the macrocyclic cavity, interacting *via* hydrogen bonds with both protonated nitrogens and three oxygens of the macrocyclic framework and originating a 'water cryptate'.

In the last few years a variety of oxa-aza macropolycyclic compounds has been examined in search for synthetic host molecules.[1]

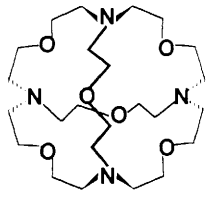
Initially, much effort was devoted to the design and the synthesis of receptors able to coordinate metal ions into their macrocyclic cavity,[2] with the aim of studying their behaviour as selective complexing agents and ionophores. More recently, oxa-aza macropolycyclic molecules able to bind different kinds of substrates, such as ammonium salts,[3-5] neutral molecules[6] and anionic species,[7] have been studied to elaborate their use as selective recognizers, molecular carriers and catalysts.

The topological complementarity between the binding sites of receptor and substrate is one of the fundamental principles for the successful design of strongly binding host molecules.[8] For example, the spherical macropolycyclic ligand **I**, characterized by a tetrahedral recognition site, can selectively coordinate the ammonium cation inside its tridimensional cavity.[4,5] It has also been proposed the formation of a 'water cryptate', in which a water molecule is enclosed into the cavity of the diprotonated macrocycle **I**$\cdot 2H^+$, held by a tetrahedral array of hydrogen bonds.[4] The hexaprotonated species of the macrobicycle **II** can encapsulate the N_3^- unit, which shows a shape and size complementary to the cavity of the receptor. Anion cryptates with F^-, Cl^- and Br^- have been also reported; the non-complementarity between these spherical anions and the ellipsoidal cavity of **II**$\cdot 6H^+$ leads to a lower stability of their complexes with respect to that of N_3^- complex.[9]

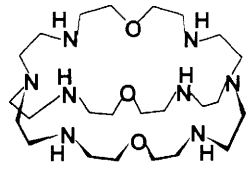
As a matter of fact, the coordination of anionic guests can be achieved by using, as receptors, polyprotonated species of aza or oxa-aza macrocycles, which can interact *via* coulombic forces and hydrogen bonds with the anionic substrate. As a consequence, the basicity properties of such receptors are strictly correlated with their binding features.

Aiming to obtain further information on proton transfer behaviour and binding ability of oxa-aza macrobicycles, we have synthesized the two new receptors: 16,21-dimethyl-4,7,10-trioxa-1,13,16,21-tetraazabicyclo[11.5.5]tricosane (**C1**) and 19,24-dimethyl-4,7,10,13-tetraoxa-1,16,19,24-tetraazabicyclo-[14.5.5]hexacosane (**C2**)

In this paper we report their synthesis and basicity properties.



I



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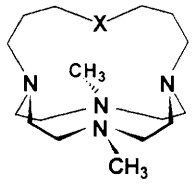
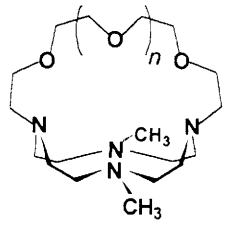


III, X = N-Me
IV, X = O



C1, n = 1
C2, n = 2

The formation of a 'water cryptate' by the diprotonated species of **C2** is also analysed.

Results and Discussion

Protonation.—The protonation equilibria of the macrocycles **C1** and **C2** have been studied in 0.15 mol dm^{-3} Me_4NClO_4 solution at 298.1 ± 0.1 K by potentiometric pH ($-\log[H^+]$) measurements and microcalorimetry. Under the experimental conditions employed, both macrocycles behave at most as diprotic bases. The thermodynamic parameters for their protonation reactions are reported in Table 1. Both of them show similar proton transfer features, exhibiting a high basicity in the first protonation step, and a moderate basicity in the

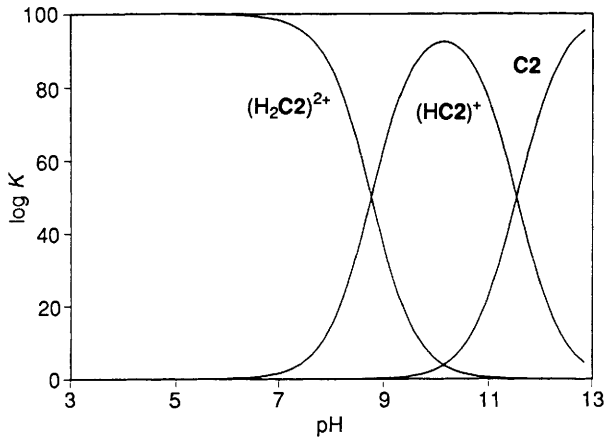


Fig. 1 Distribution diagram of the species formed as a function of pH in the system H^+/**C2** in NMe_4ClO_4 (0.15 mol dm^{-3}) at 298.1 K. [**C2**] = 1.10^{-3} mol dm^{-3}.

Table 1 Protonation constants and thermodynamic parameters (kJ mol^{-1}) for the protonation of **C1** and **C2** in aqueous solution (298.1 ± 0.1 K, NMe_4ClO_4 0.15 mol dm^{-3})

Reaction	log *K*	$-\Delta G°$	$-\Delta H°$	$T\Delta S°$
C1 + H^+ = $[HC1]^+$	11.24(8)[a]	64.1(5)	50.5(4)	13.6(9)
$[HC1]^+$ + H^+ = $[H_2C1]^{2+}$	8.39(8)	47.9(5)	48.1(4)	−0.2(9)
C2 + H^+ = $[HC2]^+$	11.52(7)	65.7(4)	50.9(4)	14.8(8)
$[HC2]^+$ + H^+ = $[H_2C2]^{2+}$	8.76(7)	50.0(4)	55.2(4)	−5.2(8)

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

second step, while the third protonation process is undetectable in the pH range studied (2.5–11). By using these equilibrium data the distributions of the species of **C1** and **C2** formed as a function of pH were calculated and the results, in the case of **C2**, are reported in Fig. 1.

Both $-\Delta G°$ and $-\Delta H°$ values for the first step are unusually high for compounds having only tertiary amino groups.[10] Indeed, there is a significant increase in proton affinity for the first protonation step of tertiary nitrogens with respect to the monocycle 1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane ($\Delta G° = -55.18$ kJ mol^{-1}).[10] This can be explained by taking into account the fact that the basicity properties of these compounds are strongly influenced by the molecular topology.[11] Considering the enthalpy contribution to the stepwise protonation of **C1** and **C2**, both the protonation steps are characterized by very favourable enthalpic terms (see Table 1). These features indicate that the added hydrogen ions interact very strongly with the nitrogen atoms to form the mono- and diprotonated species. This suggests that the protons are bound inside the macrocyclic cavity, stabilized by a hydrogen bond network, as already found for other macrobicyclic ligands characterized by the same tetraaza subunit (see, for example, **III** and **IV**).[12,13] In the case of **C2** the enthalpy change for the second step is even larger than that for the first one. The unfavourable entropic contribution observed for the second protonation of **C2** compensates the increase of the enthalpic one and the process does not affect the free energy change.

For both **C1** and **C2**, the entropic term is somewhat favourable for the first protonation step, and negligible or weakly unfavourable in the second one. The increasing positive charge gathered on the ligand with successive protonation produces a strong organization of solvent molecules beyond the protonated receptors leading to an evident decrease in translational entropy.

It is of interest that **C1** and **C2** show a much lower entropic contribution and a more favourable enthalpic term in the second protonation step with respect to the cage-like macrobicycle 5,12,17-trimethyl-1,5,9,12,17-pentaazabicyclo[7.5.5]-nonadecane (**III** X = NMe).* This ligand is characterized by a small tridimensional cavity in which two protons can be lodged.[13b] Such different behaviour between **III** and the present oxa-aza receptors could be ascribed to a strong solvation of the diprotonated species inside the larger cavity of **C1** and **C2**. The crystal structure of the $[H_2C2{\cdot}H_2O]^{2+}$ ion (see Fig. 3) gives confidence to this hypothesis, showing a water molecule embedded into the macrocyclic cavity, and interacting with the bonding sites of the receptor, *i.e.*, the N–H^+ groups and three oxygen atoms. In other words, the formation of a hydrogen bond network, involving the protonated amino groups, the ethereal oxygens, and a guest water molecule could justify the high value found for the enthalpic change and the lower entropic term in the second protonation step, with respect to the cage compound **III**.

Both ligands do not experience further protonation, at least under the experimental conditions employed. This behaviour is probably due to electrostatic repulsion between the positive charges located within the small tetraaza subunit of the macrocycle.

In order to explain the high values of the two first protonation constants of the receptor **I** as well as the much lower value of the third one,[14] Lehn suggested the inclusion of a water molecule into the cavity of the diprotonated macrocycle, with the formation of a 'water cryptate'.[4] An ideal tetrahedral array of hydrogen interactions between the guest and the nitrogens of the macropolycycle would explain the high thermodynamic stability of the diprotonated species $[H_2I]^{2+}$.

In our case the molecular topology presented by **C2** leads to a different coordination environment of the water molecule with respect to that proposed for the $[H_2I{\cdot}H_2O]^{2+}$, as shown by the crystal structure of the $[H_2C2{\cdot}H_2O]^{2+}$ cation. However, both thermodynamic and structural data suggest that also the present receptors can bind a water molecule inside their macrobicyclic cavity, giving rise to such 'water cryptates'.

NMR Analysis.—In order to shed further light on the protonation mechanism of such polyamines, ^1H and ^{13}C NMR spectra in aqueous solution at various pH values have been recorded. The ^{13}C spectrum of **C2** at pH 12.8, where the unprotonated amine predominates in solution (see Fig. 1), exhibits seven peaks, at 71.3, 70.9 (C-6, C-7 and C-8), 69.8 (C-5), 56.5 (C-4), 56.2 (C-2), 50.0 (C-1) and 42.8 (C-3) ppm, with relative intensity approximately 2:1:1:1:2:2:1. The ^1H spectrum shows a singlet at 2.54 ppm (attributed to the hydrogens of the methyl group, C-3), and two complex signal patterns at 2.63–2.84 ppm and 3.63–3.74 ppm (the hydrogen atoms of the carbons in α-position with respect to the oxygens).

By using ^1H–^1H homonuclear and ^1H–^{13}C heteronuclear correlation, the ^1H and ^{13}C signals have been fully assigned [see Fig. 2(*a*)]. These features indicate a C_{2v} time averaged symmetry. At pH 10, where the $[HC2]^+$ prevails in solution, the ^1H and ^{13}C NMR signals [Fig. 2(*b*)], even on heating, are much broader, most likely due to the formation of slowly interchanging (on the NMR time scale) conformers. However,

* For 5,12,17-trimethyl-1,5,9,12,17-pentaazabicyclo[7.5.5]nonadecane (**III** X = NMe), $\log K_1 = 11.83$, $\log K_2 = 9.53$, $-\Delta H° = 54.4$ and $T\Delta S° = 13.2$ kJ mol^{-1} in the first protonation step and $-\Delta H° = 42.7$ and $T\Delta S° = 11.7$ kJ mol^{-1} in the second one. Values taken from ref. 12.

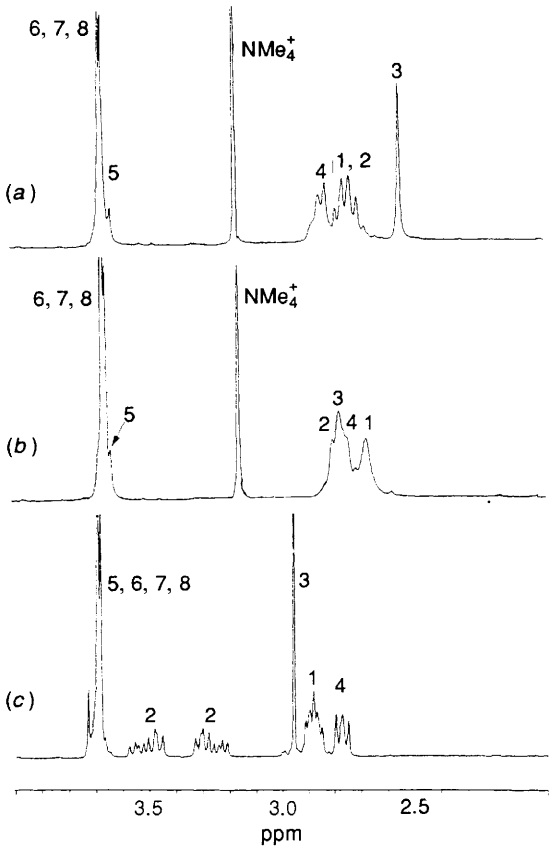
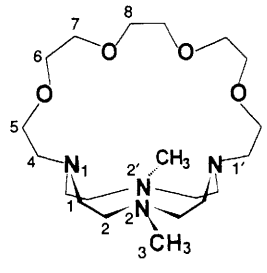


Fig. 2 ^{1}H NMR spectra of **C2** at pH 12.8 (*a*), pH 10 (*b*) and pH 4 (*c*)



in the ^{1}H spectrum, the resonance of the hydrogens of the methyl group shifts downfield suggesting that the first proton binding the macrocycle is mainly localized on the methylated nitrogen atoms. The features of both ^{1}H and ^{13}C NMR spectra of $[H_2\mathbf{C2}]^{2+}$ (pH 4) accord again with a C_{2v} time-averaged symmetry. The ^{1}H spectrum at this pH is reported in Fig. 2(*c*). With respect to the free amine spectrum, the resonances of the hydrogens of the methyl groups and C-2, in α-position to 2-N and 2′-N bear a remarkable downfield shift, while those of C-1 and C-4 do not shift appreciably, indicating the methylated nitrogens as the two protonation sites. The characteristics of the ^{13}C spectrum at this pH value give confidence to this protonation mechanism; in fact, with respect to the ^{13}C spectrum at pH 12.8, the resonance of C-2, in the α-position to the methylated nitrogens, shifts downfield (*ca.* 1.5 ppm) while the signal of C-1, in the β-position with respect to 2-N and 2′-N bears an upfield shift (*ca.* 2.5 ppm), in agreement with the β-shift reported for protonation of polyamines.[15] The other ^{13}C resonances do not shift appreciably.

The same protonation pattern can be deduced for **C1** from the analysis of ^{1}H and ^{13}C NMR spectra.

To corroborate these results and in order to obtain structural information the determination of the crystal structure of the salt $[H_2\mathbf{C2}\cdot H_2O]\cdot[ClO_4]_2$ has been carried out.

Crystal Structure of $[H_2\mathbf{C2}\cdot H_2O]\cdot[ClO_4]_2$.—The structure of the compound consists of discrete $[H_2\mathbf{C2}\cdot H_2O]^{2+}$ cation and ClO_4^- anions. An ORTEP[16] drawing of the cation is shown in Fig. 3. The four nitrogen atoms are almost coplanar, the largest deviation from the mean plane being 0.06 Å for N(4) (PARST[17]). The mean plane described by the four oxygen donors and the two bridge-head nitrogens N(1) and N(3) [max. deviation 0.7 Å for N(1)] is nearly perpendicular to the mean plane above reported, being the dihedral angle 96.15°.

As shown by the values of the torsion angles [N(1)–C(1)–C(2)–N(2), −60.4(7)°; N(2)–C(4)–C(5)–N(3), −57.2(7)°; N(3)–C(6)–C(7)–N(4), −66.1(8)°; N(4)–C(9)–C(10)–N(1), −61.4(8)°; N(1)–C(11)–C(12)–O(1), 53.0(9)°; O(1)–C(13)–C(14)–O(2), 66.9(8)°; O(2)–C(15)–C(16)–O(3), 77.0(8)°; O(3)–C(17)–C(18)–O(4), −62.1(8)°; O(4)–C(19)–C(20)–N(3), −56.3(9)°], the overall conformation of the macrobicycle is consistent with an approximate C_2 symmetry, the hypothetical rotation axis passing through the middle point of the C(15)–C(16) bond and the centre of the plane determined by the nitrogens.

All the nitrogen atoms are in the endo configuration and, as far as the oxygens are concerned, at least one lone pair of O(2), O(3) and O(4) points inside the molecular cavity, while those of O(1) turn outside the cavity.

It is worth noting that the acidic protons are located on the methylated nitrogens N(2) and N(4), confirming the NMR results obtained in aqueous solution. Both protonated nitrogen atoms interact *via* hydrogen bonds with the unprotonated amino groups [H(2)···N(1) 2.63(5) Å, H(2)···N(3) 2.49(5) Å, H(4)···N(1) 2.40(8) Å and H(4)···N(3) 2.48(8) Å] and with a water molecule enclosed into the macrobicyclic cavity [H(2)···O(5) 2.26(4) Å and H(4)···O(5) 2.09(7) Å]. Examples of oxa-aza macrocycles interacting with water molecules have been already reported,[1f,6] most of them regarding monocyclic crown or aza-crown ether compounds as host molecules. In the present case the guest molecule is tightly encapsulated into the tridimensional cavity, forming further hydrogen bonds with the O(2), O(3) and O(4) oxygen atoms, as shown by the orientation of their lone pairs and by the short O···O(5) distances [O(2)···O(5) 3.046(6) Å, O(3)···O(5) 3.087(6) Å and O(4)···O(5) 2.798(7) Å].

The O(5) oxygen lies on the apex of a distorted square pyramid and is 2.23 Å apart from the basal plane determined by the four nitrogen atoms. Close comparisons can be found in the crystal structure of the diprotonated cage 12,17-dimethyl-5-oxa-1,9,12,17-tetraazabicyclo[7.5.5]nonadecane (IV X = O),[13a] which presents the same twelve-membered tetraaza unit. The overall conformation of $[H_2\mathbf{IV}]^{2+}$ resembles the present one: the two acidic protons are located on the methylated amino-groups, and the ethereal oxygen lies on the apex of a distorted square pyramid, similarly to the water molecule in the $[H_2\mathbf{C2}\cdot H_2O]^{2+}$ cation. Moreover, the N–H···N and N–H···O distances are strictly comparable, the mean values being respectively 2.45 and 2.22 Å in $[H_2\mathbf{IV}]^{2+}$ and 2.50 and 2.17 Å in $[H_2\mathbf{C2}\cdot H_2O]^{2+}$. It is worth noting that the cage **IV** is a strong base in aqueous solution ($\log K_1 > 14$, $\log K_2 = 11.21$).[13a] This suggests that such array of an oxygen and amino groups represents a stable disposition from an energetic point of view and is consistent with the hypothesis above reported to explain the basicity behaviour of these oxa-aza macrobicycles.

Experimental

Synthesis of **C1** *and* **C2**.—The macrocycles **C1** and **C2** were obtained following the synthetic procedure depicted in Scheme 1. 1,7-Dimethyl-1,4,7,10-tetraazacyclododecane (**1**) was syn-

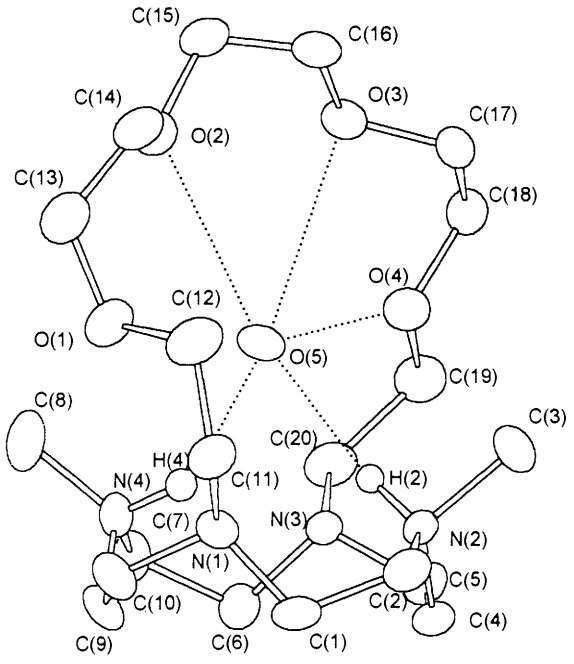
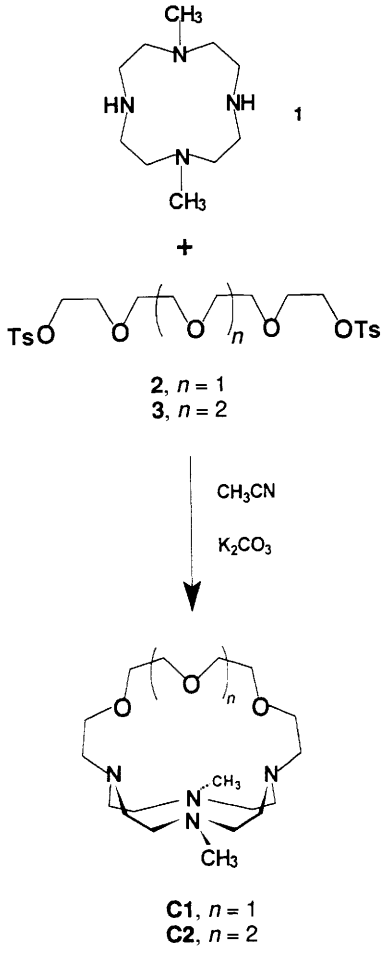


Fig. 3 ORTEP drawing of the $[H_2C2{\cdot}H_2O]^{2+}$ cation



Scheme 1

thesized as reported in ref. 18. Tetraethylene glycol ditoluene-*p*-sulfonate (**2**) and pentaethylene glycol ditoluene-*p*-sulfonate (**3**) were purchased from Aldrich Chemical Co.

16,21-*Dimethyl*-4,7,10-*trioxa*-1,13,16,21-*tetraazabicyclo*[11.5.5]*tricosane* (**C1**). To a refluxing suspension of **1** (2 g, 0.01 mol) and of K_2CO_3 (5.6 g) in acetonitrile (100 cm^3), was added, over a period of *ca.* 6 h, a solution of **2** (5.02 g, 0.01 mol) in acetonitrile (50 cm^3). The reaction mixture was maintained at reflux for 2 h. After cooling at room temperature, the resulting suspension was filtered and evaporated under reduced pressure to give a yellowish oil, which was dissolved in the minimum quantity of chloroform and chromatographed on neutral alumina (70–230 mesh, activity I), eluting with chloroform. The eluted fractions were collected and evaporated to dryness to obtain a colourless solid (1.7 g; 47%). M.p. 36–39 °C (Found: C, 59.9; H, 10.9; N, 15.5. Calc. for $C_{18}H_{38}N_4O_3$: C, 60.30; H, 10.68; N, 15.62%).

C1·2$HClO_4$·H_2O. The diperchlorate salt was obtained in a quantitative yield by adding 70% $HClO_4$ to an ethanolic solution containing the free amine. The white solid formed was filtered off and recrystallized from water (Found: C, 37.5; H, 7.2; N, 9.7. Calc. for $C_{18}H_{42}N_4O_{12}Cl_2$: C, 37.44; H, 7.33; N, 9.70%).

19,24-*Dimethyl*-4,7,10,13-*tetraoxa*-1,16,19,24-*tetraazabicyclo*[14.5.5]*hexacosane* (**C2**). This compound was synthesized from **1** (2 g, 0.01 mol) and **3** (5.46 g, 0.01 mol) following the procedure reported for **C1** (2.2 g, 54%). M.p. 54–56 °C (Found: C, 59.5; H, 10.7; N, 13.8. Calc. for $C_{20}H_{42}N_4O_4$: C, 59.67; H, 10.52; N, 13.92%).

C2·2$HClO_4$·H_2O. The diperchlorate salt was synthesized in a quantitative yield by adding 70% $HClO_4$ to an ethanolic solution containing the free amine. The white solid which precipitated was filtered off and recrystallized from water (Found: C, 38.7; H, 7.5; N, 9.0. Calc. for $C_{20}H_{46}N_4O_{13}Cl_2$: C, 38.65; H, 7.46; N, 9.01%). Crystals of this compound suitable for X-ray analysis were obtained by slow evaporation of a diluted aqueous solution.

EMF Measurements.—All the potentiometric measurements were carried out in 0.15 mol dm^{-3} NMe_4ClO_4 at 298.1 ± 0.1 K, in the pH range 2.5–11, by using the equipment described above.[19] The reference electrode was an Ag/AgCl electrode in saturated KCl solution. The glass 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 the Gran's method[20] which allows to determine the standard potential $E°$, and the ionic product of water (pK_w = 13.83 ± 0.01). Solutions were prepared from **C1**·2$HClO_4$·H_2O and **C2**·2$HClO_4$·H_2O. At least three measurements (about 100 experimental points each one) were performed for each system. The computer program SUPERQUAD[21] was used to calculate the protonation constants from EMF data. The titration curves for each system were treated either as a single set or as separated entities without significant variations in the values of the stability constants.

NMR Spectroscopy.—200.0 MHz ^1H and 50.32 MHz ^{13}C NMR spectra in D_2O solutions at different pH values were recorded at 298 K in a Bruker AC-200 spectrometer. In ^1H NMR spectra peak positions are reported relative to HOD at 4.75 ppm. Dioxane was used as reference standard in ^{13}C NMR spectra (δ 67.4). Small amounts of NMe_4OH were added to a solution of **C1**·2$HClO_4$·H_2O or **C2**·2$HClO_4$·H_2O to adjust the pD. The pH was calculated from the measured pD values using eqn. (1):[22]

$$pH = pD - 0.40 \quad (1)$$

Microcalorimetry.—The enthalpies of protonation of the ligands have been determined in 0.15 mol dm^{-3} NMe_4ClO_4 at 298.15 ± 0.01 K. The automated system as well as the calibration procedure have been fully described elsewhere.[12] The calorimeter stability is within 0.0002 K. In a typical

experiment a NMe_4OH (0.15 mol dm^{-3}, addition volumes of 15 mm^3) solution was added to 1.5 cm^3 of **C1**·$2HClO_4$·H_2O or **C2**·$2HClO_4$·H_2O (5×10^{-3}–0.01 mol dm^{-3}). Corrections for the heat of dilution were applied. Under the reaction conditions and employing the determined equilibrium constants, the concentration of each species present in solution before and after each addition was calculated and the corresponding enthalpies of reaction were determined by means of the KK88 program.[23] At least three measurements were performed. The titration curves for each system were treated either as a single set or as separated entities without significant variations in the values of the enthalpy changes.

Crystal Data.—$C_{20}H_{46}Cl_2N_4O_{13}$, $M = 621.51$. Monoclinic, $a = 10.450(2)$, $b = 11.391(2)$, $c = 12.666(3)$ Å, $\beta = 100.21(2)°$, $V = 1483.8(5)$ Å^3 (by least-squares refinement of diffractometer setting angles of 25 carefully centred reflections, $\lambda = 1.5418$ Å), space group $P2_1$, $Z = 2$, $D_c = 1.39$ g cm^{-3}. Prismatic colourless crystals. Crystal dimensions 0.4 × 0.2 × 0.1 mm, μ(Cu-Kα) = 25.67 cm^{-1}.

Data Collection and Processing.[24]*—Enraf–Nonius CAD4 diffractometer, $\theta/2\theta$ scan mode with θ scan width = 0.6 + 0.15 tan θ, θ scan speed 4.1 deg min^{-1}, graphite monochromatized Cu-Kα radiation; 2687 reflections measured ($2.5 \leq \theta \geq 65°$, $\pm h, k, l$), 2363 unique with $I > 3.0\sigma(I)$. Two standard reflections monitored: no loss of intensity observed. Lorentz and polarization effects correction applied.

Structure Analysis and Refinement.—Direct methods. Absorption correction applied after structure resolution. Full-matrix least-squares refinement with all non-hydrogen atoms anisotropic and methylic and methylenic hydrogens in calculated positions with overall fixed temperature factors ($U = 0.05$ Å^2). Acidic protons H(2) and H(4) localized by ΔF map and isotropically refined. Function minimized: $\Sigma w(|F_o| - |F_c|)^2$, with $w = a/\sigma^2(F)$ where a is an adjustable parameter. Absolute structure determined performing two separate refinements for the two enantiomorphs. 359 Refined parameters. Final R and R_w values are 0.059 and 0.052 for the correct one, whereas for the other are 0.062 and 0.055, respectively. Programs and computer used and sources of atomic scattering factors and anomalous dispersion corrections are given in ref. 24. Details of positional and thermal parameters, atomic coordinates, bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre.†

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* Computer used IBM PS/2 Model 80.

† For details of the deposition scheme see Instructions for Authors, *J. Chem. Soc., Perkin Transactions 2*, 1994, Issue 1.

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