Polyazacyclophanes. 2,6,9,13-Tetraaza[14]paracyclophane as a Cationic and Anionic Receptor

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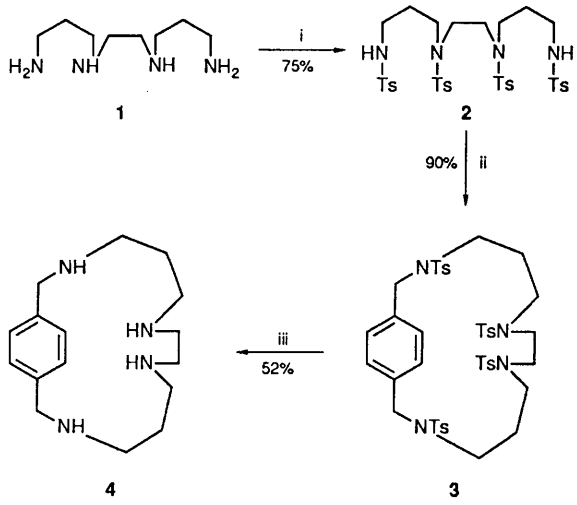
The synthesis and characterization of the new azacyclophane, 2,6,9,13-tetraaza[14]paracyclophane, is described. The acid–base behaviour and the metal and anion coordination capabilities of this compound have been studied by potentiometry at 298.15 K in 0.15 mol dm^{-3} $NaClO_4$, as well as by ^1H and ^{13}C NMR spectroscopy. The protonation patterns show stabilization effects produced by the presence of the aromatic ring. The aromatic spacer prevents simultaneous involvement of all four nitrogens in the coordination to the metal ions Cu^{2+} and Zn^{2+}. Stable mono-hydroxylated species have been detected for both metal ions. The triprotonated species is the main one over a wide pH range around neutrality making this ligand a good coordinating agent for such anionic species as ATP^{4-} and $P_2O_7^{4-}$. Formation of complexed anionic species with degrees of protonation varying from three to six has been detected.

Much effort in molecular recognition has been devoted to the design of receptors having specific structural features so as to achieve selective binding of target molecules and specific catalytic effects.[1] In connection with our work on polyazamacrocyclic receptors,[2] we were interested in the study of macrocyclic compounds having *p*-phenylene subunits as an integral part of the macrocycle. Different cyclophanes having several *p*-phenylene subunits have been synthesized,[3,4,5] but simple macrocycles containing one 1,4-benzo subunit have been only scarcely studied.[5,6] Polyaza[*n*]paracyclophanes are interesting as these receptors should possess a polarizable aromatic surface besides the nitrogen donor atoms and both could converge, from opposite directions, to the guest.[7] In this respect, 2,6,9,13-tetraaza[14]paracyclophane (**4**) presents some notable features. The number of nitrogens and the size of the macrocycle should permit coordination to different metal ions, but, at the same time, the presence of the 1,4-benzo moiety could induce some coordination patterns of interest, especially in order to obtain catalytic effects. On the other hand, the presence of propylenic units would permit an appreciable protonation degree in aqueous solution and accordingly the activity of **4** as an anion receptor.

In the present paper we report on the synthesis of 2,6,9,13-tetraaza[14]paracyclophane and on its properties as an anionic and cationic receptor.

Results and Discussion

One of the most general routes to obtain polyazamacrocycles is that reported by Richman and Atkins.[8] The method involves the reaction of the sodium salt of a tosylamide with a tosylated diol or a dihalogenoalkane in DMF, and does not require high dilution conditions. *In situ* deprotonation of the tosylamide with Cs_2CO_3 or K_2CO_3 in DMF has also been used.[9,10] When preparation of tosylated 2,6,9,13-tetraaza[14]paracyclophane by reaction of tosylamide **1** with, α-α′-dibromo-*p*-xylene in DMF in the presence of K_2CO_3 was attempted, a 10% yield was obtained. This result is comparable to the 7–10% yield described for the preparation of related 1,4-benzo crown ethers.[6] Similarly, a 26% yield has been reported for the base-catalysed synthesis of 2,6,10-tris(trifluoroacetyl)-2,6,10-triaza-[11](2,6)naphthalenophane from tris(trifluoroacetyl)-1,7-diamino-4-azaheptane and 2,6-bis(bromomethyl)naphthalene.[5] As could be expected, better yields have been described for the preparation of two triaza 1,2-benzo macrocycles.[10]



Scheme 1 *Reagents and conditions:* i, TsCl, NaOH; H_2O/THF; ii, α,α′-dibromo-*p*-xylene, K_2CO_3; CH_3CN; iii, HBr/AcOH 33%, PhOH

Yields for the cyclization step, however, were increased to 90% when the reaction was carried out in refluxing CH_3CN with K_2CO_3 as the base (Scheme 1). Detosylation of **3** was difficult to accomplish efficiently. After treatment with $LiAlH_4$ in THF for 24 h, a method which has been shown to successfully effect detosylation of some cupped azacyclophanes,[11a] the starting material (**3**) was recovered unchanged. The use of sodium amalgam in a buffered medium,[10] yielded only a 29% yield of pure amine **4**. Finally, the best results were obtained with HBr/HOAc/PhOH,[11b] and a 52% yield of pure compound **4** could be obtained after chromatographic purification.

The ^1H NMR spectra of **3** and **4** show a clear shielding effect of the aromatic ring on the central protons of the chain, as

Table 1 Protonation constants of the ligands **4** and **6**

Reaction	4[a]	6[b]
L + H = HL[c]	9.933(4)[d]	10.04
L + 2H = H_2L	19.022(3)	
L + 3H = H_3L	26.456(5)	
L + 4H = H_4L	30.07(1)	
HL + H = H_2L	9.09	9.69
H_2L + H = H_3L	7.43	6.80
H_3L + H = H_4L	3.61	3.54

[a] From this work; values obtained in 0.15 mol dm^{-3} $NaClO_4$ at 298.15 K. [b] Taken from ref. 12. [c] Charges have been omitted for clarity. [d] Values in parentheses are standard deviations in the last significant figure.

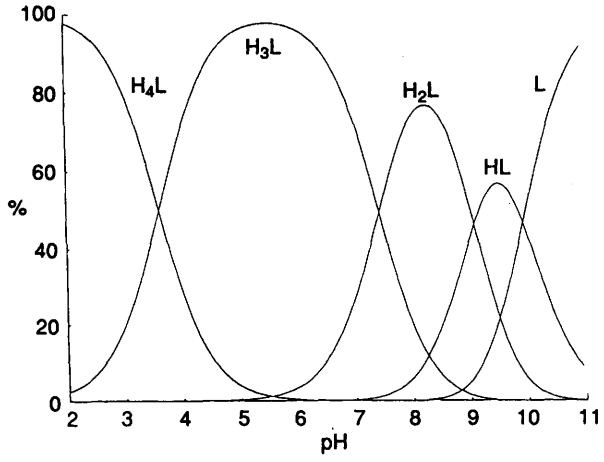
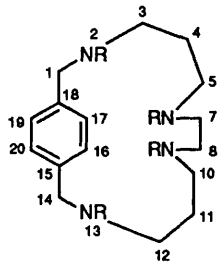
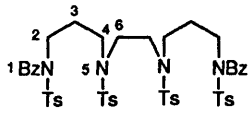


Fig. 1 Distribution diagram of the species in equilibrium for the system H^+–**4**. Charges have been omitted for clarity.

expected for a paracyclophane structure. Thus, for **4**, the singlet corresponding to the protons of the ethylenic moiety appears at 2.31 ppm (H-7,8) and the propylenic protons are observed at 2.37, 2.21 and 1.32 ppm. The effect is even more clear in the tosylated macrocycle **3** when compared with the open-chain analogue **5**. The singlet of the ethylenic protons in **3** (H-7,8) appears 0.3 ppm upfield relative to the singlet of **5** (H-6).



3; R = Ts
4; R = H



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Protonation Patterns.—In Table 1 the basicity constants of **4**, determined potentiometrically at 298.15 K in 0.15 mol dm^{-3} $NaClO_4$, are presented together with those of the related macrocycle 1,4,8,12-tetrazacyclohexadecane (**6**).[12]

Fig. 1 shows the distribution diagram for the species existing in equilibria as a function of pH. **4** Behaves as a relatively strong base in its first two protonation steps and as a very weak base in the last one, the situation for the third protonation step being intermediate. The most noticeable feature in Fig. 1, is that the

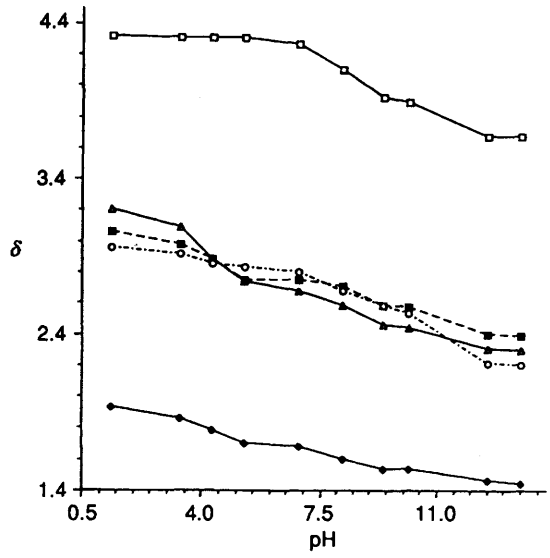


Fig. 2 Plot of the ^1H NMR chemical shifts of the ligand **4** *vs.* pH. □, H-1,14; ■, H-5,10; △, H-7,8; ○, H-3,12; ◆, H-4,11.

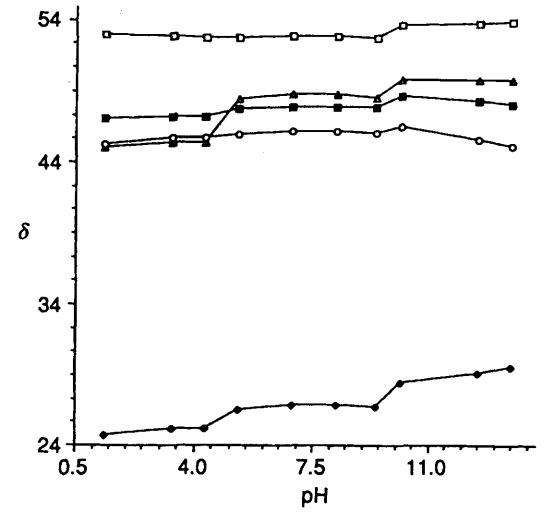


Fig. 3 Plot of the ^{13}C NMR chemical shifts for the aliphatic carbon atoms of the ligand **4** *vs.* pH. □, C-1,14; ■, C-5,10; △, C-7,8; ○, C-3,12; ◆, C-4,11.

triprotonated species is predominant in solution throughout a wide pH range around neutrality. Accordingly, this compound can be a potential receptor for anionic species in aqueous solution. The similar basicity of the first two protonation steps indicates that these protons are attached to the macrocycle in binding sites which are sufficiently separated not to influence each other electrostatically. Therefore, the nitrogens of the ethylenic chains must be discarded as simultaneous receptors of these two first protons and, at least one of the benzyl nitrogens should bear protonation at this stage. In order to understand fully the protonation pattern, an analysis of the variation of ^1H and ^{13}C NMR spectra with pH was carried out for compound **4** and the results are shown in Figs. 2–4.

At pH 5.3 the species H_3L is present in a percentage higher than 90% and so changes accompanying the addition of the fourth proton are easy to understand. For pH values below 5.3, the methylenic protons connected with the ethylenic nitrogens (H-7,8 and H-5,10) shift to lower field by 0.46 and 0.31 ppm respectively, while the methylenic protons connected to the benzylic nitrogens (H-1,14 and H-3,12) remain almost unaffected. The same situation is found in the ^{13}C NMR spectra as carbon atoms isolated from the ethylenic nitrogens do not

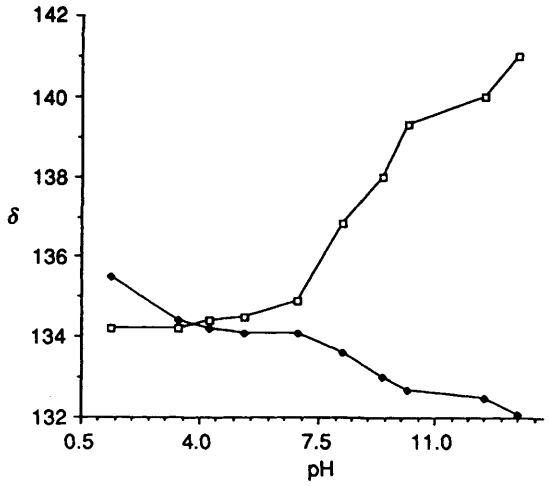
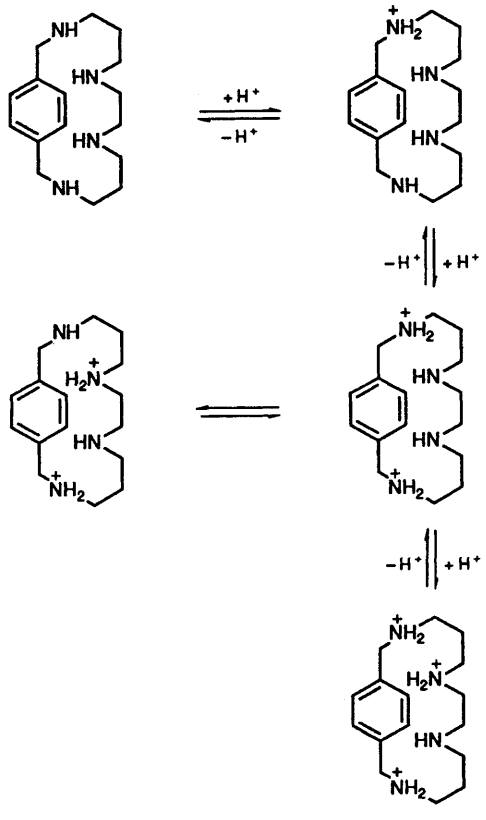


Fig. 4 Plot of the ^{13}C NMR chemical shifts for the aromatic carbon atoms of the ligand **4** *vs.* pH. □, C-15,18; ◆, C-16,17,19,20.

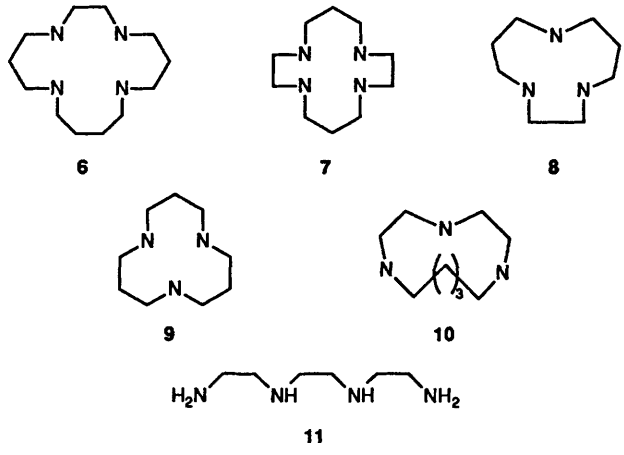
appreciably change in this pH range, but clear highfield shifts are observed for C-7,8, C-5,10 and C-4,11, the β-shifts being higher than the α-shifts, as has been generally described for protonation of amino groups.[13] At pH higher than 10, the first protonation step can be studied, as at pH values of *ca.* 10 only the free ligand and the monoprotonated species are present. All the methylenic protons shift to lower fields but the extent of this shift is larger for methylene groups α to the benzylic nitrogens. Similar trends are observed in the ^{13}C NMR spectra; in this case the remarkably large highfield shift of the quaternary aromatic carbons β to the benzylic nitrogens should be noted. In the pH range 5.0–9.0 where the second and third protonation occurs (Fig. 1), downfield shifts are observed for all the methylenic protons while the carbon signals, except the aromatic ones, remain essentially unchanged. All these data suggest the protonation pattern depicted in Scheme 2.



Scheme 2

The first proton would attach preferentially to the benzylic nitrogens, while the second one would share one benzylic position and the adjacent ethylenic nitrogen. The third proton should fix the first two protons on the benzylic nitrogens so that the fourth protonation step almost exclusively affects the remaining ethylenic nitrogen. Accordingly, the benzylic nitrogens of **4** seem to display a slightly higher basicity than the ethylenic ones. π-Ammonium interactions could be invoked to explain such an effect.[7] This could also account for the differences in basicities found between **4** and **6**. Thus, the first protonation constant for both ligands is very similar which indicates that the stabilizing effect of the π-cloud in **4** would be balanced by the steric hindrance to solvation produced by the aromatic ring.[14] On the other hand, the higher value of the second protonation constant of **6** may also be explained in terms of solvation effects as this proton is shared between both kinds of nitrogens and the stabilization by the π-cloud should be lower. As the third protonation step fixes two protons on the benzylic positions, the third constant of **4** is slightly higher than the corresponding one in **6**.

Interaction with Cations.—In Table 2 the stability constants for the interaction of macrocycle **4** with Cu^{2+} and Zn^{2+} are presented. All these constants, as well as the former protonation constants, have been determined potentiometrically at 298.15 K in 0.15 mol dm^{-3} $NaClO_4$. By means of comparison, the stability constants of some related ligands (**8**–**10**) have also been included in Table 2.[15–18]



Analysis of the EMF data with the computer program SUPERQUAD[19] shows the formation of complexes having 1 : 1 metal : ligand stoichiometry. Distribution diagrams, calculated for 1×10^{-3} mol dm^{-3} concentration in all the reagents, are shown in Fig. 5. The values of the stability constants for the formation of the ML species, M + L = ML, are significantly lower (log K = 13.01 and 6.82 for Cu^{2+} and Zn^{2+}) than those found for other macrocyclic receptors with four nitrogen atoms such as cyclam (**7**) (log K = 26 and 15 for Cu^{2+} and Zn^{2+}).[15] The constants are even lower than those for the non-cyclic receptor **11** (log K = 20.4 and 12.1, respectively).[16] These results are not surprising on account of the structure of **4**. The presence of the rigid aromatic spacer should clearly hinder the simultaneous binding of the cation to all four nitrogen donors. As a matter of fact, the above mentioned log K values for **4** compare much better with those reported for receptors displaying only three nitrogen atoms (see Table 2).[17,18] In the case of Zn^{2+}, the values are lower than those for any other ligand in Table 2 reflecting an inefficient coordination of the metal centre.

Experimental support to the tri-coordinating characteristics of **4** comes from the important MHL species formed for both

Table 2 Logarithms of the stability constants for the interaction of **4** with Cu^{2+} and Zn^{2+} in 0.15 mol dm^{-3} $NaClO_4$ at 298.15 K and relevant data for related triazacycloalkanes

	4[a]		**8**[b]		**9**[b]		**10**[c]
Reaction	Cu^{2+}	Zn^{2+}	Cu^{2+}	Zn^{2+}	Cu^{2+}	Zn^{2+}	Zn^{2+}
M + L + H = MHL[d]	20.823(5)[e]	14.57(2)					
M + L = ML	13.02(1)	6.83(1)	12.63	8.75	14.44	10.41	7.01
M + L + H_2O = ML(OH) + H	3.92(1)	−1.85(2)					
M + HL = MHL	10.89	4.64					
ML + H = MHL	7.80	7.74					
ML + OH = ML(OH)	4.63	5.06					
ML + H_2O = ML(OH) + H	−9.10	−8.67	−8.1	−7.44		−8.13	

[a] From this work. [b] From ref. 17. [c] From ref. 18. [d] Charges have been omitted for clarity. [e] Values in parentheses are standard deviations in the last significant figure.

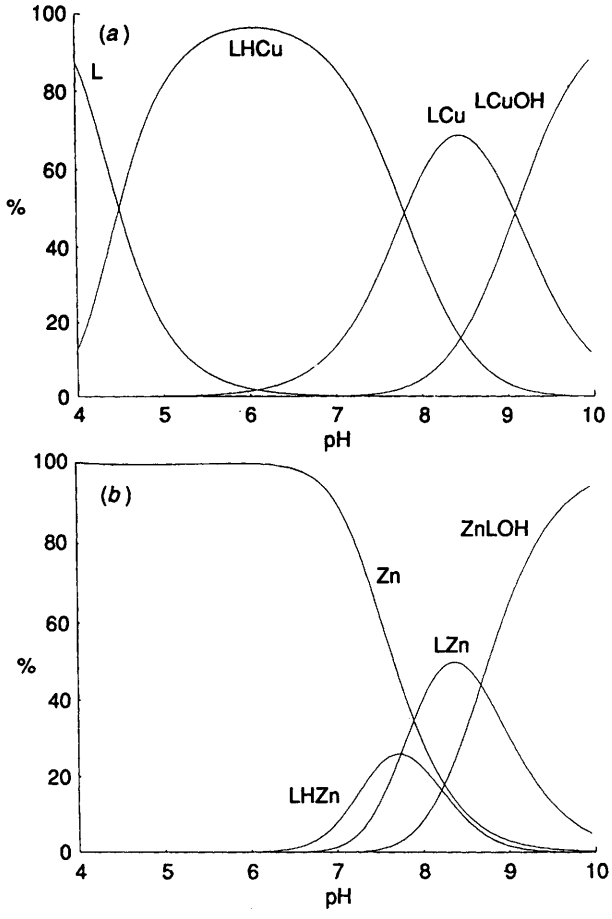


Fig. 5 Distribution diagrams of the species in equilibria for the system M^{2+}–**4**. Charges have been omitted for clarity. [M] = [**4**] = 10^{-3} mol dm^{-3}. (*a*) M = Cu. (*b*) M = Zn.

metal ions (see Fig. 5). The values for the protonation of ML to give MHL are similar and very high (log K = 7.8 for Cu^{2+} and 7.75 for Zn^{2+}) and close to the value of the third protonation constant for the free ligand (log K_3 = 7.43). This is in agreement with protonation taking place on a non-coordinated nitrogen atom which explains that protonation constants obtained for both doubly charged cations, H_2L and ML, are similar. The large constant for the addition of the HL species to both metal ions gives further support to this point.

Molecular modelling also supports the tri-dentate characteristics of **4**. Models obtained after conformational minimization for complexes in which all four nitrogens of the macrocycle are involved in the binding of the metal ion show the existence of very important destabilizing contributions of bond stretching,

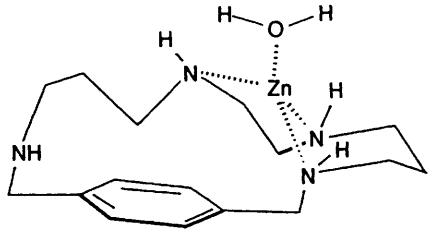


Fig. 6 Possible model for tricoordinate interaction between **4** and Zn^{2+}

angle bending and non-bonded and torsional energy terms.[20] Simultaneous binding of all four nitrogens to the metal centre would require the adoption of a very unfavourable conformation of the receptor. However, binding of the metal to only three nitrogens of the azacyclophane **4** (and probably to the oxygen of a water molecule) seems to release most of those unfavourable terms, and suggest that the best model for ML complexes should be the one shown in Fig. 6 for the case of Zn^{2+}. According to this model, one of the benzylic nitrogens would remain non-coordinated.

As we have formerly mentioned, the particular structure of **4** is reflected in the much lower stability of its metal complexes with respect to other tetraazamacrocycles. The presence of the aromatic spacer prevents simultaneous involvement of all four nitrogens of **4** in the binding to the metal. However, this low coordination of the metal ions imposed by the topology of the ligand could lead to a very interesting feature, especially when considering the potential catalytic activity of these complexes. In this respect, consideration of the acidity of the coordinated water is important. As can be observed in the distribution diagrams, species MLOH are important for both metals at basic pH values and become the predominant species at pH > 9 for Cu^{2+} or even at slightly lower values for Zn^{2+}. For copper, the pK_a value for deprotonation of water coordinated to the metal centre is calculated to be 9.1, higher, for instance, than the value of *ca.* 8 reported for the complex with [12]aneN_3.[17] The pK_a value of 8.7 for the Zn^{2+} complex of **4** is lower than the value of 9 for deprotonation of water coordinated to uncomplexed Zn^{2+} and can be compared with the values reported for some carbonic anhydrase models.[18,21] However, a more acidic nature has been described for other models containing only three nitrogen donor atoms as is the case of **8** and **9** (pK_a values of 7.3–7.9 and 8.2 respectively).[18] The easy deprotonation of water bound to the metal centre has been considered an essential feature to explain the catalytic activity of carbonic anhydrase and phosphatase models.[18,22] This activity has been generally connected, as well as in the structure of the active sites of these enzymes, with the presence of a Zn^{2+} ion coordinated to only three nitrogen donors and to one water molecule.[18] In the case of receptor **4**, another promising structural feature is

Table 3 Logarithms of the stability constants for the interaction of **4** with ATP^{4-} and $P_2O_7^{4-}$ in 0.15 mol dm^{-3} $NaClO_4$ at 298.15 K

Reaction	A = ATP^{4-}	A = $P_2O_7^{4-}$
A + 3H + L = AH_3L[a]	29.04(1)[a]	29.65(5)
A + 4H + L = AH_4L	36.09(1)	37.37(4)
A + 5H + L = AH_5L	40.78(1)	43.37(7)
A + 6H + L = AH_6L	44.13(1)	47.68(5)
A + H_3L = AH_3L	2.58	3.32
A + H_4L = AH_4L	6.02	7.53
HA + H_3L = AH_4L	3.39	2.90
HA + H_4L = AH_5L	4.47	5.39
H_2A + H_3L = AH_5L	4.08	2.87
H_2A + H_4L = AH_6L	3.81	3.69

[a] Charges have been omitted for clarity. [b] Values in parentheses are standard deviations in the last significant figure.

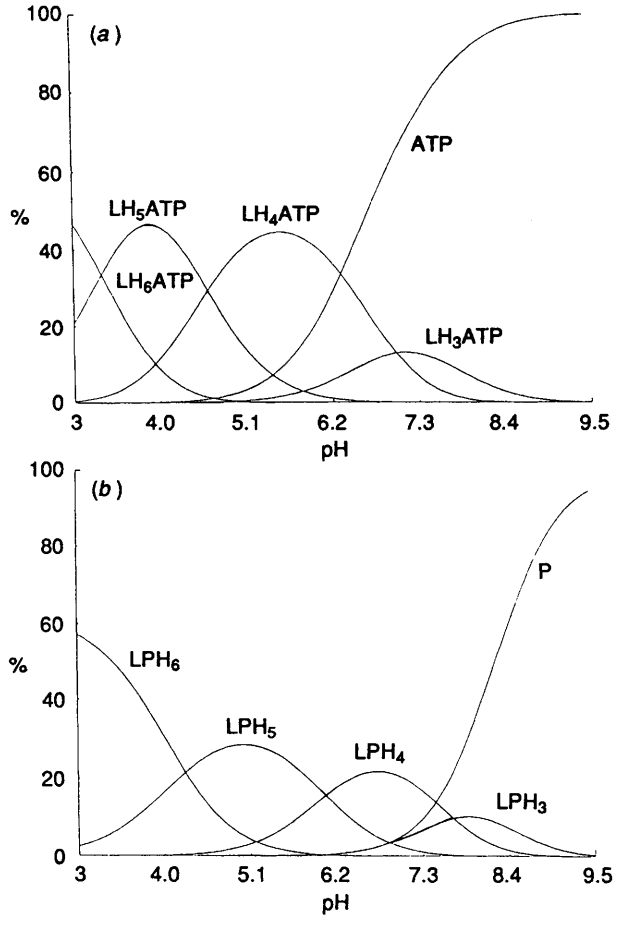


Fig. 7 Distribution diagrams of the species in equilibria for the system A–**4**. Charges have been omitted for clarity. [A] = [**4**] = 10^{-3} mol dm^{-3}. (*a*) A = ATP. (*b*) A = pyrophosphate.

the presence of an additional nitrogen atom not coordinated to the metal centre which could play an important role in the catalytic behaviour of these complexes.

Interaction with Anions.—Host **4** is present, over a broad range of pH, as the triprotonated species. In general, more highly charged polyammonium receptors have been used for anion recognition. However, the well defined structural characteristics of **4** led us to the study of this compound as a potential receptor for anions. In Table 3 the stability constants related to the interaction of this polyazacyclophane with ATP and with pyrophosphate are reported.

Distribution diagrams, calculated for 1×10^{-3} mol dm^{-3} concentration in all the reagents, are shown in Fig. 7. From the values of the stability constants several observations can be made. For a 1:1 receptor:substrate ratio, an appreciable interaction results at pH values below *ca.* 9. Both anionic substrates interact with the triprotonated receptor to give species AH_3L (log K = 3.32 and 2.58 for pyrophosphate and ATP respectively). Both anionic substrates form complexes displaying protonation degrees from three to six. The general trend observed in the molecular recognition of anions by polyammonium macrocycles is that the strength of the interaction increases with the charge of the receptor. However, in our case, the maximum charge on the ligand is limited by the low number of nitrogens as well as by the low constant corresponding to the fourth protonation step, and accordingly much higher constants are to be expected for receptors able to display a higher protonation degree. As can be seen in Fig. 1, receptor **4** is only appreciably tetraprotonated at pH values below 4. This suggests that even for the observed complexes AH_4L, which are present in the pH ranges 9–4 (pyrophosphate) and 8–3 (ATP), at least one of the protonations should affect the anion and not the polyazacyclophane. The existence of protonation of the guest anions is more evident for species AH_nL with $n > 4$ as the number of protons is higher than the number of nitrogens in the polyazacyclophane receptor. The existence of such strong interactions with partially protonated anionic substrates represents another interesting and promising feature of **4**. As species AH_6L are detected for both pyrophosphate and ATP, this requires that interaction of the tetra- or tri-protonated ligand with a di- or tri-protonated substrate respectively is very important. Even when we consider this fact, the values obtained for the stepwise stability constants are appreciable (see Table 3). The log K value for the interaction of H_3L with HATP to form the complex AH_4L would be 3.4, a value which is comparable with the values of log K = 3.4–4.5 obtained for the interaction of tetraprotonated polyazacycloalkanes ([3*k*]aneN_k $k > 6$) or TAEC with ATP.[2a,23] The log K value calculated for the interaction of the H_4L with H_2ATP would be 3.82 which again represents a significant value for this kind of interaction. It is noteworthy that no significant anion coordination chemistry has been generally described in aqueous solution for tetraazamacrocycles except for those containing butylenic subunits, partially related to the natural polyamines spermine and spermidine. In this sense, a value of log K = 3.81 has been reported for the tetraazamacrocycle containing four butylenic subunits, for AH_4L species.[24] A value of 3.04 was also given to account for the possible interaction of HATP with triprotonated ligand in AH_4L. The above mentioned topology of the protonated ligand **4** has to be at the origin of this behaviour.

Conclusions

2,6,9,13-Tetrazaza[14]paracyclophane represents an interesting new receptor with a topology that can give rise to very specific interactions. It can form stable complexes with metal ions such as Zn^{2+} or Cu^{2+}, whose most important characteristic seems to be the tricoordinated nature of the ligand. Connected to this structural aspect is likely to be the relatively acidic nature of water coordinated to the Zn^{2+} complex, an effect of great interest in the development of models of active sites of Zn-containing enzymes. Even if the maximum charge available for receptor **4** up to pH values of *ca.* 4 is three, this tetraazamacrocycle has been shown to have a very appropriate topology as receptor for phosphate type anions. Finally, the easy preparation of paracyclophane **4** has to be considered as another appealing property of this compound, as it can permit the development of a new family of related receptors, and their study in the molecular recognition of different species and the catalysis of processes of chemical and biological significance.

Experimental

N,N′,N″,N‴-Tetrakistosylbis(3-aminopropyl)ethylenediamine (**2**). Bis(3-aminopropyl)ethylenediamine (5.2 g, 0.03 mol) and sodium hydroxide (5 g, 0.125 mol) were dissolved in water (50 cm^3). To this stirred solution, *p*-toluenesulfonyl chloride (25 g, 0.13 mol) in THF (100 cm^3) was added dropwise at room temperature. After addition was complete, stirring was maintained for 2 h and then the solvent was vacuum distilled. The residue was washed with water and then suspended in refluxing ethanol for 2 h to give a white solid (18 g, 0.023 mol, 75%), m.p. 144–146 °C. ν_{max}(KBr)/cm^{-1} 3291, 2941, 2855, 1590, 1314, 1147. δ_H($CDCl_3$, 200 MHz) 1.79 (4 H, q), 2.41 (6 H, s), 2.44 (6 H, s), 3.00 (4 H, two doublets), 3.15 (4 H, t), 5.27 (2 H, t), 7.2–7.3 (8 H, m), 7.6–7.7 (8 H, m). δ_C($CDCl_3$, 50.3 MHz) 21.5, 29.1, 48.1, 48.2, 54.7, 127.2, 127.3, 129.1, 129.8, 129.9, 134.9, 135.2, 136.7, 143.5, 143.6.

N,N′,N″,N‴-Tetrakistosyl-2,6,9,13-tetraaza[14]*paracyclophane* (**3**). Tosylated amine **2** (1.2 g, 1.5 mmol) and K_2CO_3 were suspended in refluxing acetonitrile (50 cm). To this mixture a solution of α,α′-dibromo-*p*-xylene (0.39 g, 1.5 mmol) in acetonitrile (50 cm^3) was added dropwise. After addition was complete the suspension was refluxed for 18 h and then filtered. The solution was vacuum evaporated to dryness to yield the product as a white solid which was purified by column chromatography on silica (dichloromethane–ethyl acetate, 97:3, as eluent) (1.2 g, 1.34 mmol, 90%), m.p. 221–223 °C. ν_{max}(KBr)/cm^{-1} 3050, 2941, 2871, 1590, 1438, 1326, 1147. δ_H($CDCl_3$, 200 MHz) 1.47 (4 H, q), 2.43 (6 H, s), 2.46 (6 H, s), 2.74 (4 H, s), 2.96 (4 H, t), 3.08 (4 H, t), 4.14 (4 H, s), 7.3–7.4 (12 H, m), 7.6 (8 H, d), 7.7 (8 H, d). δ_C($CDCl_3$, 50.3 MHz) 21.5, 29.1, 48.1, 48.2, 54.6, 127.2, 127.3, 129.8, 129.9, 134.9, 135.2, 136.7, 143.5, 143.6 (Found: C, 59.3; H, 5.8; N, 6.3. Calc. for $C_{44}H_{52}N_4O_8S_4$: C, 59.1; H, 5.9; N, 6.2%). *m/z* (FAB) 893 ($[M + H]^+$).

2,6,9,13-*Tetraaza*[14]*paracyclophane* (**4**). Tetratosylated macrocycle **3** (1 g, 1 mmol) and phenol (5 g, 50 mmol) were suspended in HBr/HOAc (33%, 30 cm^3). The mixture was stirred at 90 °C for 18 h and then the solution was vacuum evaporated. The residue was suspended in a mixture of dichloromethane (20 cm^3) and water (20 cm^3) and the aqueous layer was washed several times with additional portions of dichloromethane (30 cm^3), basified with sodium hydroxide, and vacuum evaporated. The dry residue was extracted with chloroform (100 cm^3) and the resulting solution vacuum evaporated to give an oily product which was purified by column chromatography over silica gel with MeOH–NH_3–THF as the eluent to afford compound **4** as a waxy solid (161 mg, 52%). ν_{max}(KBr)/cm^{-1} 3272, 2925, 2811, 1441, 1107. δ_H($CDCl_3$, 200 MHz) 1.32 (4 H, q), 2.21 (4 H, t), 2.3 (4 H, s), 2.37 (4 H, t), 3.6 (4 H, s), 7.0 (4 H, s). δ_C($CDCl_3$, 50.3 MHz) 28.8, 43.8, 46.3, 49.0, 52.7, 128.1, 128.7. *m/z* (EI) 276, 104, 71, 58.

For analytical purposes, the tetraperchlorate was prepared by dissolving **4** in EtOH; the solution was cooled in an ice bath and concentrated $HClO_4$ was added. The salt was obtained as a white solid (Found: C, 28.1; H, 4.9; N, 8.2. Calc. for $C_{16}H_{32}N_4O_{16}Cl_4$: C, 28.3; H, 4.8; N, 8.1%).

EMF Measurements.—Potentiometric measurements were performed using the equipment previously described.[25] The reference electrode was Ag/AgCl in saturated KCl solution. The glass electrode (Onion model 91-01) was calibrated as a hydrogen concentration probe by titration of known amounts of HCl with CO_2-free NaOH solutions. The equivalent point was determined by the Gran method,[26] which provides the standard potential of the cell and the ionic product of water [pK_w = 13.73(1) at 298.15 K in 0.15 mol dm^{-3} $NaClO_4$]. The protonation constants of $P_2O_7^{4-}$ and ATP^{4-} were taken from ref. 23. EMF data were monitored by means of the program PASAT.[27] The computer program SUPERQUAD[19] was used to calculate the equilibrium constants. The titration curves for each system were treated either as a single set or separately without finding significant variations in the values of the constants. Furthermore, the sets of data were merged and treated simultaneously to obtain the final stability constants.

NMR Spectroscopy.—^1H and ^{13}C NMR spectra were recorded at 200.0 and 50.3 MHz on a Varian Gemini 200 instrument using either Me_4Si or DSS as the internal reference.

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