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Open-chain polyazaalkane ferrocene-functionalised receptors for the electrochemical recognition of anionic guests and metal ions in aqueous solution

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New open-chain polyazaalkane N-terminal ferrocene-functionalised receptors, L^1, L^2 and L^3, have been synthesized and characterised and their potential use as selective anion and cation sensing receptors in aqueous solution investigated. Solution studies by potentiometric methods have been carried out in the presence of H^+ and Cu^{2+} in water (25 °C, 0.1 mol dm^{-3} KNO_3). The results have been compared with those of the analogous non-functionalised receptors triethylenetetramine (L^4), tetramethylenepentamine (L^5) and *N*,*N*′′′′-dimethylpentaethylene-hexamine (L^6). Compounds L^1–L^3 form both mono- and di-nuclear complexes with Cu^{2+}. The electrochemical responses as a function of the pH in the presence of the Ni^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+} or Pb^{2+} cations in water and the ATP, phosphate, sulfate and nitrate anions in thf–water (7 : 3 v/v, 25 °C, 0.1 mol dm^{-3} $[Bu^n_4N][ClO_4]$) for L^1, L^2, L^3 and for 1,4,7,10,13,16-hexaferrocenyl-1,4,7,10,13,16-hexaazacyclooctadecane (L^7) in 1,4-dioxane–water (7 : 3 v/v, 25 °C, 0.1 mol dm^{-3} KNO_3) have also been determined. The studies have been directed to determine the pH ranges of selectivity in the electrochemical recognition of cations and anionic guests, pointing out the ability of molecules L^1–L^3 and L^7 to act as selective anion-sensing or cation-sensing receptors. The anion ATP can be selectively detected using the L^2 receptor in the presence of the competing anions phosphate and nitrate.

Introduction

A number of works have been devoted towards the development of new sensing receptors by designing ligands which are able selectively to modify an easily measurable physical property after co-ordination with the target species. An approach to practical sensors, which could selectively recognise the presence of substrates, is the attachment of redox-active groups near co-ordination sites.[1] Two properties are common to those new molecules; their electroactive character and their binding ability. It has been reported that co-ordination shifts the redox potential of the redox groups in these functionalised receptors, and this effect has been used electrochemically to recognise alkali and alkaline-earth cations,[2,3] anions,[4–6] neutral species[7–9] and transition metal ions[10–18] using different redox centres which can be reduced or oxidised. However it is perhaps surprising that the studies have mainly been carried out in non-aqueous solvents. In fact, quantitative or qualitative determination of substrates using these receptors would in the last instance be performed in water. Although the development of amperometric sensing devices would require the use of water insoluble receptors, the study of prototypes in aqueous solutions will allow us to set the basis of the receptor–substrate interaction and to rationalise the relationship between the architecture of the receptor, the nature of the substrate and the electroactive group response.

It is known that receptors can bind anionic guests with various physical interactions,[19] and several types of artificial receptors have been reported to be capable of electrochemically recognising anions.[4–6] With few exceptions, these redox receptors electrochemically sense anionic guest species in organic polar solvents. These include anion receptors containing amide groups linked to positively charged cobaltocenium, ruthenium(II) bipyridyl groups, ferrocenyl moieties, *etc*.[4–6] To our knowledge, apart from a few recent examples,[11,12,18] anion co-ordination studies with electroactive receptors in aqueous solutions are very scarce and have been performed at a fixed pH and attention has not been paid to the role played by proton concentration.

This paper will report on the synthesis of open-chain ferrocene-functionalised polyamines and we shall study their potential as selective anion and cation sensing receptors in aqueous solutions. These receptors can interact with cations *via* the well known co-ordination ability of the amine groups. On the other hand ferrocene-functionalised polyamines can bind anions in three different manners: (i) by electrostatic interaction *via* positively charged protonated amino groups; (ii) by hydrogen bonding and (iii) by electrostatic interaction *via* oxidised ferrocenium cation. The first two modes of interaction can be tuned by the pH. Amine groups can act as both hydrogen-bond donors and acceptors and a change of the binding properties can be achieved by protonation or deprotonation of the amine/ammonium groups. The study is mainly focused on the use of the receptors as anion and cation redox sensors in aqueous solutions.

Experimental

Solvents and reagents

Triethylenetetramine (L^4), tetraethylenepentamine (L^5), pentaethylenehexamine and ferrocenecarbaldehyde were reagent quality used without further purification. Tetrahydrofuran (thf) used was freshly distilled from sodium–benzophenone, and water was distilled from potassium permanganate. Carbonate-free potassium hydroxide and hydrochloric acid solutions were used in the potentiometric and electrochemical experiments. Potassium nitrate (0.1 mol dm^{-3}) was used as supporting electrolyte in water.

Synthesis of L^1, L^2 and L^3

Ferrocenecarbaldehyde (500 mg, 2.33 mmol) and triethylene-

tetramine, tetraethylenepentamine or pentaethylenehexamine (1.16 mmol) were heated to reflux in ethanol for 3 h. The solutions were evaporated to dryness and dissolved in freshly distilled thf (60 mL). Hydrogenation was carried out with $LiAlH_4$ (352 mg, 9.28 mmol) at reflux under argon for 1 h. After careful addition of small amounts of water the resulting solutions were filtered and evaporated to dryness. Basic water and dichloromethane were added and the organic phases dried with anhydrous sodium sulfate. The yellow solutions were chromatographed on alumina using first dichloromethane and then dichloromethane–methanol (96:4) as eluent. Addition of hexane gave a yellow oil. Yields: L^1 (430, 68), L^2 (476, 70), L^3 (475 mg, 65%).

1,12-Diferrocenyl-2,5,8,11-tetraazadodecane (L^1) (Found: C, 62.20; H, 7.12; N, 10.31. $C_{14}H_{19}FeN_2$ requires C, 62.04; H, 7.02; N, 10.34%): NMR ($CDCl_3$) ^{1}H, δ 4.17 (s, 4 H, C_5H_4), 4.12 (s, 10 H, C_5H_5), 4.10 (s, 4 H, C_5H_4), 3.49 (s, 4 H, CH_2), 2.72 (br, 6 H, CH_2), 2.70 (br, 6 H, CH_2) and 1.76 (br, 4 H, NH); FAB MS *m*/*z* 542 (M^+).

1,15-Diferrocenyl-2,5,8,11,14-pentaazapentadecane (L^2) (Found: C, 61.65; H, 7.45; N, 11.95. $C_{30}H_{43}Fe_2N_5$ requires C, 61.58; H, 7.36; N, 11.97%): NMR ($CDCl_3$) ^{1}H, δ 4.18 (s, 4 H, C_5H_4), 4.13 (s, 10 H, C_5H_5), 4.10 (s, 4 H, C_5H_4), 3.50 (s, 4 H, CH_2), 2.72 (br, 8 H, CH_2), 2.71 (br, 8 H, CH_2) and 1.75 (br, 5 H, NH); FAB MS *m*/*z* 585 (M^+).

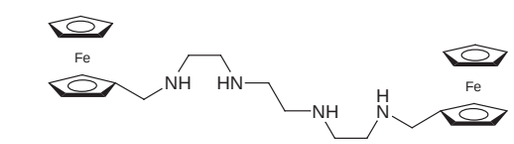
1,18-Diferrocenyl-2,5,8,11,14,17-hexaazaoctadecane (L^3) (Found: C, 61.27; H, 7.70; N, 13.45. $C_{16}H_{24}FeN_3$ requires C, 61.18; H, 7.65; N, 13.38%): NMR ($CDCl_3$) ^{1}H, δ 4.18 (s, 4 H, C_5H_4), 4.12 (s, 10 H, C_5H_5), 4.11 (s, 4 H, C_5H_4), 3.49 (s, 4 H, CH_2), 2.72 (br, 10 H, CH_2), 2.47 (br, 10 H, CH_2) and 1.74 (br, 6 H, NH); FAB MS *m*/*z* 628 (M^+).

Physical measurements

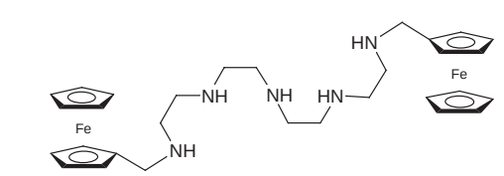
The NMR spectra were measured on a Varian Gemini spectrometer operating at 300 K. Chemical shifts for ^{1}H spectra are referenced to $SiMe_4$. Electrochemical data were obtained with a Tacussel IMT-1 programmable function generator, connected to a Tacussel PJT 120-1 potentiostat. The working electrode was graphite with a saturated calomel reference electrode separated from the test solution by a salt bridge containing the solvent/supporting electrolyte. The auxiliary electrode was platinum wire. Potentiometric titrations were carried out in water using a water-thermostatted (25.0 ± 0.1 °C) reaction vessel under nitrogen. The titrant was added by a Crison microburette 2031. The potentiometric measurements were made using a Crison 2002 pH-meter and a combined glass electrode. The titration system was automatically controlled by a PC computer using a program that monitors the emf values and the volume of titrant added. The electrode was calibrated as a hydrogen concentration probe by titration of well known amounts of HCl with CO_2-free KOH solution and determining the equivalence point by Gran's method[20] which gives the standard potential E'° and the ionic product of water ($K'_w = [H^+][OH^-]$). The concentrations of the Ni^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+} and Pb^{2+} solutions were determined using standard methods. The computer program SUPERQUAD[21] was used to calculate the protonation and stability constants. The titration curves for each system (*ca*. 200 experimental points corresponding to at least three titration curves, pH = −log[H] range investigated 2.5–10, ligand concentration *ca*. 1.2×10^{-3} mol dm^{-3} metal 2.5×10^{-3} to 0.5×10^{-3} mol dm^{-3} according to the formation of mono- and di-nuclear species) were treated either as a single set or as separate entities without significant variations in the values of the stability constants. Finally the sets of data were merged and treated simultaneously to give the stability constants.

Results and discussion

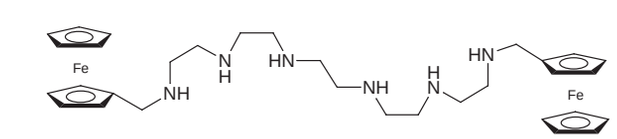
The reaction of triethylenetetramine, tetraethylenepentamine and pentaethylenehexamine with ferrocenecarbaldehyde yields the corresponding Schiff-base derivatives which were hydrogenated without further purification with $LiAlH_4$ in thf to produce the electroactive open-chain polyaza receptors 1,12-diferrocenyl-2,5,8,11-tetraazadodecane (L^1), 1,15-diferrocenyl-2,5,8,11,14-pentaazapentadecane (L^2) and 1,18-diferrocenyl-2,5,8,11,14,17-hexaazaoctadecane (L^3), respectively. The ^{1}H, mass spectrum (FAB) and analytical data are consistent with the proposed formulation. Free L^1, L^2 and L^3 receptors were obtained as oils. They were stable for some weeks but decompose after 2–3 months. They dissolve slowly in water. Water solutions, for both potentiometric and electrochemical studies on L^1, L^2 and L^3, were prepared by boiling the oil in distilled water for several hours to obtain saturated solutions. The concentrations of the solutions were determined by iron analysis following standard atomic absorption methods. Aqueous solutions of L^1, L^2 and L^3 were stable for 2–3 d after which a brown unidentified solid was observed.



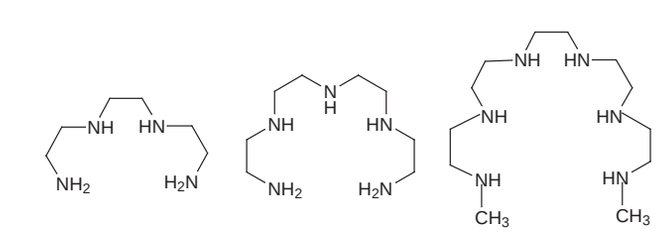
L^1



L^2



L^3



L^4 L^5 L^6

Protonation behaviour

The protonation behaviour of L^1, L^2 and L^3 was studied by potentiometric titrations with KOH of previously acidified solutions in water (0.1 mol dm^{-3} KNO_3) at 25 °C. Table 1 lists the basicity constants. The compounds L^1, L^2 and L^3 contain four, five and six protonation sites due to the presence of secondary nitrogens and they behave as tetra-, penta- and hexa-protic bases, respectively, in water. The first protonation constants of the three receptors are quite close as expected due to the similarity between them. The basicity is only slightly reduced in the second protonation step. However the third protonation constant of L^1 is more acidic than those of L^2 and L^3. That behaviour can be explained assuming that for L^1, L^2 and L^3 the first two protonations take place on two of the nitrogens nearest the ferrocenyl groups. The third proton in L^1 should

Table 1 Stepwise protonation constants (log K) of L^1, L^2 and L^3 determined in water at 298.1 K in 0.1 mol dm^{-3} KNO_3

	L^1		L^2		L^3	
Reaction	log K	Δlog K	log K	Δlog K	log K	Δlog K
$L + H \rightleftharpoons HL$ [a]	9.70(1) [b]		9.79(1)		9.66(1)	
$HL + H \rightleftharpoons H_2L$	8.90(1)	0.80	9.08(1)	0.71	9.00(1)	0.66
$H_2L + H \rightleftharpoons H_3L$	6.24(1)	2.66	7.66(1)	1.42	7.57(1)	1.43
$H_3L + H \rightleftharpoons H_4L$	2.59(2)	3.65	4.99(2)	2.67	5.94(2)	1.63
$H_4L + H \rightleftharpoons H_5L$			2.85(2)	2.14	4.47(2)	1.47
$H_5L + H \rightleftharpoons H_6L$					1.96(4)	2.51

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

occur near one of the already protonated nitrogens, whereas the third protonation in L^2 and L^3 can take place between unprotonated nitrogens. The difference between the third and the fourth protonation constants for L^1 is 3.65 logarithm units, whereas Δlog K is 2.67 for L^2 and 1.63 for L^3. That is in agreement with the fact that the fourth protonation in L^1 and L^2 attacks one central ethylenic nitrogen separated from two adjacent ammonium groups by two ethylenic chains whereas for L^3 the fourth proton should be placed next to only one ammonium group.

More detailed studies on the protonation of polyazaalkanes usually have been carried out by ^1H or ^{13}C-{^1H} NMR techniques.[22] From a different point of view, we have recently found that the decrease of the successive protonation constants can be correlated with an increase of the electrostatic repulsion between the ammonium cations. Taking that into account the overall protonation constants for a given polyamine can be calculated using eqn. (1)[23] where r_{kl} is the distance between

$$\log \beta_i = i \log K_1 - \left(\frac{e^2 N_A}{2.3RT4\pi\varepsilon_o\varepsilon} \sum_{k=1}^{i} \sum_{l=1}^{k-1} \frac{1}{r_{kl}} + B \sum_{k=1}^{i} \sum_{l=1}^{k-1} \frac{1}{r_{kl}^2} \right) \quad (1)$$

ammonium groups, log K_1 is the first protonation constant, and ε the relative permittivity of the medium. The constant expression $e^2N_A/2.3RT4\pi\varepsilon_o\varepsilon = 3.144$ Å^{-1} is related to the Coulombic repulsion between charges, whereas B is an experimental parameter which would account for the variation of the permittivity with the distance ($B = 30.6$ Å^{-2} in water). Distances r_{kl} for the successive protonated species H_iL^{1i+}, H_iL^{2i+} and H_iL^{3i+} have been calculated from a simple molecular analysis using the modelling program PCMODEL.[24]

Eqn. (1) allows one to check different possible protonation paths for a given polyazaalkane. The actual protonation path will be most likely the one showing a better agreement between the theoretically calculated protonation constants using eqn. (1) and the experimental protonation constants obtained from potentiometric data. We have calculated all possible protonation paths for L^1, L^2 and L^3 and selected those showing a better agreement between the basicity constants calculated using eqn. (1) and the experimental ones. Table 2 shows the protonation paths found for L^1, L^2 and L^3 and the good agreement between the theoretically calculated and experimental overall protonation constants.

Table 2 Protonation path for L^1, L^2 and L^3

	Protonation path	log β_i(calc.) [a]	log β_i(exptl.) [b]
L^1	N–N–N–N		
	H H H H	28.13	27.43
	N–N–N–N		
	H H H	24.81	24.84
	N–N–N–N		
	H H	17.87	18.60
L^2	N–N–N–N–N		
	H H H H H	33.79	34.37
	N–N–N–N–N		
	H H H H	31.26	31.52
	N–N–N–N–N		
	H H H	25.71	26.53
	N–N–N–N–N		
	H H	18.41	18.87
L^3	N–N–N–N–N–N		
	H H H H H H	38.09	38.60
	N–N–N–N–N–N		
	H H H H H	35.55	36.64
	N–N–N–N–N–N		
	H H H H	32.57	32.17
	N–N–N–N–N–N		
	H H H	26.37	26.23
	N–N–N–N–N–N		
	H H	18.35	18.66

[a] Calculated from eqn. (1). [b] From potentiometry.

Metal co-ordination

Solution studies directed to the determination of the stability constants for the formation of complexes of L^1, L^2 and L^3 with Cu^{2+} have been carried out in water (0.1 mol dm^{-3} KNO_3) (see Table 3). The L^1, L^2 and L^3 receptors form both mono- and dinuclear complexes with copper. Although it has to be pointed out that precise information about the co-ordination number cannot be deduced from the stability constants when L^1, L^2 and L^3 receptors are compared with the analogous non-functionalised polyamines, the solution studies appear to suggest that L^1 and L^2 form complexes where the total number of nitrogens attached to the metal ion in the 1:1 complex $[CuL]^{2+}$ is less than in the analogous non-functionalised receptors, whereas L^3 appears to act as pentadentate in $[CuL^3]^{2+}$ in the same way as was reported for the L^6 ligand. Table 4 lists the stability constants for the L–H^+–Cu^{2+} systems (L = L^4, L^5 or L^6). Compound L^5 forms the mononuclear $[CuL^5]^{2+}$ complex, which shows two protonation processes. However the logarithms of the first and second protonation steps of $[CuL^5]^{2+}$ {$[CuL^5]^{2+} + H^+ \rightleftharpoons [Cu(HL^5)]^{3+}$ and $[Cu(HL^5)]^{3+} + H^+ \rightleftharpoons [Cu(H_2L^5)]^{4+}$} are lower than the logarithms of the third protonation step ($[H_2L^5]^{2+} + H^+ \rightleftharpoons [H_3L^5]^{3+}$) and the fourth protonation step ($[H_3L^5]^{3+} + H^+ \rightleftharpoons [H_4L^5]^{4+}$) (8.05 and 4.70, respectively)[25] of free L^5 indicating that the protonation process in $[CuL^5]^{2+}$ species appears to involve M–N cleavage in accordance with a pentadentate co-ordination of the amine in $[CuL^5]^{2+}$.[26] The analogous L^2 receptor, however, shows not two but three protonation processes for the $[CuL^2]^{2+}$ species. The logarithm of the constant for the first protonation step {$[CuL^2]^{2+} + H^+ \rightleftharpoons [Cu(HL^2)]^{3+}$} is 8.1 whereas that for the third protonation of L^2 is 7.66 suggesting that the first protonation occurs on a N atom which is not co-ordinated to the metal ion. However the constant for the second stepwise protonation {$[Cu(HL^2)]^{3+} + H^+ \rightleftharpoons [Cu(H_2L^2)]^{4+}$} is lower than the fourth protonation of L^2 suggesting that the second protonation occurs upon N–M cleavage and that the L^2 receptor is acting as tetradentate. The distribution diagram for the L^2–H^+–Cu^{2+} system (L^2:Cu^{2+} 1:2 molar ratio) as a function of pH is depicted in Fig. 1. On the other hand, the first protonation constant for $[CuL^1]^{2+}$ {$[CuL^1]^{2+} + H^+ \rightleftharpoons [Cu(HL^1)]^{3+}$}

Table 3 Stability constants (log K) for the formation of Cu^{2+} complexes of L^1, L^2 and L^3 in water at 298.1 K in 0.1 mol dm^{-3} $NaNO_3$

Reaction	L^1	L^2	L^3
$Cu + L + 3H \rightleftharpoons [Cu(H_3L)]$ [a]		32.72(4) [b]	37.68(1)
$Cu + L + 2H \rightleftharpoons [Cu(H_2L)]$	24.92(2)	28.80(2)	33.65(1)
$Cu + L + H \rightleftharpoons [Cu(HL)]$	21.07(1)	24.20(3)	28.17(2)
$Cu + L \rightleftharpoons [CuL]$	14.34(3)	16.10(3)	19.31(2)
$Cu + L + H_2O \rightleftharpoons [CuL(OH)] + H$	4.92(3)		
$2Cu + L \rightleftharpoons [Cu_2L]$	18.78(2)	20.95(5)	24.71(4)
$2Cu + L + 2H_2O \rightleftharpoons [Cu_2L(OH)_2] + 2H$	6.04(2)	7.22(4)	10.46
$2Cu + L + 3H_2O \rightleftharpoons [Cu_2L(OH)_3] + 3H$	−1.53(2)	−1.99(5)	
$Cu + [CuL] \rightleftharpoons [Cu_2L]$	4.4	4.9	5.4
$H + [CuL] \rightleftharpoons [Cu(HL)]$	6.7	8.1	8.9
$H + [Cu(HL)] \rightleftharpoons [Cu(H_2L)]$	3.9	4.6	5.5
$H + [Cu(H_2L)] \rightleftharpoons [Cu(H_3L)]$		3.9	4.0
$[CuL] + H_2O \rightleftharpoons [CuL(OH)] + H$	−9.4		
$[Cu_2L] + 2H_2O \rightleftharpoons [Cu_2L(OH)_2] + 2H$	−12.7	−13.7	−14.2
$[Cu_2L(OH)_2] + H_2O \rightleftharpoons [Cu_2L(OH)_3] + H$	−7.6	−9.2	

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

Table 4 Stability constants (log K) for the formation of Cu^{2+} complexes of L^4, L^5 and L^6

Reaction	L^4	L^5	L^6
$Cu + L \rightleftharpoons [CuL]$*	20.4	22.8	21.6
$H + [CuL] \rightleftharpoons [Cu(HL)]$	3.5	5.2	8.6
$H + [Cu(HL)] \rightleftharpoons [Cu(H_2L)]$		3.8	3.9

* Charges have been omitted for clarity. Data taken from refs. 25, 26.

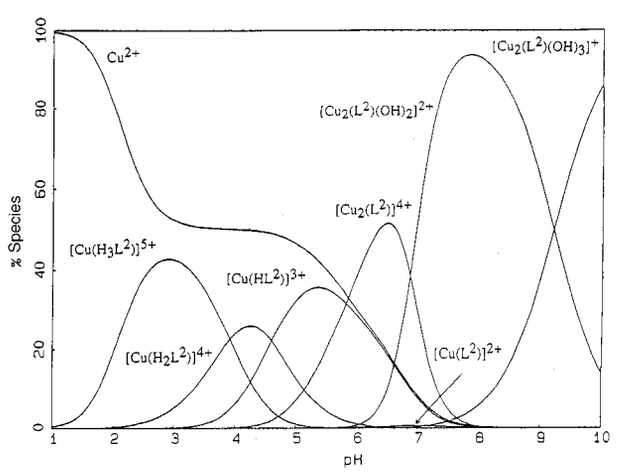


Fig. 1 Distribution diagram for the L^2–H^+–Cu^{2+} system (L^2:Cu^{2+} 1:2 molar ratio) as a function of pH.

is higher than that of the third protonation of the free receptor L^1. This result contrasts with that found for the parent ligand L^4. The $[CuL^4]^{2+}$ complex shows a first protonation constant lower than the third protonation of the free amine (3.5 and 6.67, respectively).[25] Additionally whereas in $[CuL^1]^{2+}$ two protonation processes took place, only one protonation was found for $[CuL^4]^{2+}$. The data suggest that the number of co-ordinated nitrogens in $[CuL^1]^{2+}$ is less than when L^4 is used. Receptor L^3 with Cu^{2+} shows logarithms of the constants for the first stepwise protonation $\{[CuL^3]^{2+} + H^+ \rightleftharpoons [Cu(HL^3)]^{3+}\}$ higher than that corresponding to the third protonation of the free amine. However although $[Cu(HL^3)]^{3+}$ suffers two additional protonation steps the value of the logarithms of those stepwise protonation processes are lower than the constants of the fourth and fifth protonations of L^3, suggesting that the total number of amine groups attached to the metal ion in $[CuL^3]^{2+}$ is five. A similar behaviour has been reported for L^6 for which a co-ordination number of five has been reported for Cu^{2+}.[27]

The lower co-ordination number of L^1 and L^2 when compared with L^4 and L^5, respectively, appears to be also supported by the values of the stability constants for the formation of $[CuL]^{2+}$ ($L = L^1$ or L^2) species which are lower than those with $L = L^4$ or L^5. The formation of dinuclear species found with L^1 and L^2 for all the bivalent metal ions when compared with the formation of only mononuclear complexes with L^4 and L^5 (Cu^{2+} also forms dinuclear complexes with L^6)[27] could generally reflect again the lower co-ordination number achieved in L^1 and L^2 when compared with L^4 and L^5. We can conclude that the ferrocene-functionalised L^1, L^2 and L^3 receptors display a quite different co-ordination behaviour than that of the non-functionalised L^4, L^5 and L^6 receptors, which is probably due to the presence of bulky ferrocenyl groups.

Electrochemical study

An electrochemical study of the receptors L^1, L^2 and L^3 against H^+ and metal ions has been carried out in water under the same conditions used for the potentiometric measurements. The three receptors L^1, L^2 and L^3 are electroactive molecules whose redox potential is pH-dependent. When the pH is decreased a steady $E_{\frac{1}{2}}$ displacement to more anodic potentials was observed as expected due to the presence of the charged ammonium groups which makes ligand oxidation more difficult. The difference found between the oxidation potential at basic and acidic pH was 126, 148 and 160 mV for L^1, L^2 and L^3, respectively (the oxidation potential at acid pH 0 was obtained from extrapolation of the curves $E_{\frac{1}{2}}$ *vs.* pH because of the instability of the ferrocene groups at pH lower than 1.5–2.5). Based on a Coulombic charge model we have recently been able to deduce eqn. (2) which accounts for the maximum oxidation

$$\Delta E = \frac{1}{jn}\left[\frac{14398}{\varepsilon}\Sigma_j\Sigma_i\frac{1}{r_{ji}} + \left(\frac{2\times10^6}{\varepsilon^2} + 1051\right)\Sigma_j\Sigma_i\frac{1}{r_{ji}^2}\right] \quad (2)$$

potential shift (ΔE, from acidic to basic pH) in ferrocene-functionalised polyamines in their interaction with H^+.[28] In eqn. (2), j is the number of redox-active groups, n the number of electrons in the electrochemical process ($n = 1$ for ferrocene), r_{ji} the distances (in Å) between the redox-active groups (Fe atom) and the ammonium group and ε the macroscopic relative permittivity of the medium (for mixtures of solvents ε is calculated as $\Sigma x_i\varepsilon_i$; x_i = molar fraction of solvent i, ε_i = permittivity of solvent i). From eqn. (2) $\Delta E_{\frac{1}{2}}$ values of 110, 116 and 121 mV for L^1, L^2 and L^3 respectively were predicted; r_{ji} distances for the protonated $[H_4L^1]^{4+}$, $[H_5L^2]^{5+}$ and $[H_6L^3]^{6+}$ species have been obtained by using the modelling program PCMODEL.[24]

The L^1, L^2 and L^3 receptors incorporate redox centres near binding sites. This gives the ability electrochemically to recognise substrates. Owing to the nature of the binding domains, cation and anion recognition studies have been carried out in

Table 5 Values of $\Delta E_{\frac{1}{2}}$ (in mV) for receptors L^1 to L^3 in their interaction with metal ions at five different pH values

	L^1					L^2					L^3				
pH	Ni^{2+}	Cu^{2+}	Zn^{2+}	Cd^{2+}	Pb^{2+}	Ni^{2+}	Cu^{2+}	Zn^{2+}	Cd^{2+}	Pb^{2+}	Ni^{2+}	Cu^{2+}	Zn^{2+}	Cd^{2+}	Pb^{2+}
3.0	<5	<5	<5	<5	<5	<5[b]	<5	<5	<5	<5	<5	<5	<5	<5	<5
4.5	<5	<5	<5	<5	<5	<5	−10	<5	<5	<5	−50	−27	<5	<5	<5
6.0	<5	<5	<5	<5	<5	<5	−12	<5	<5	<5	−44	−25	<5	13	<5
7.5	<5	15	<5	<5	<5	<5	8	<5	<5	<5	−8	9	<5	45	<5
9.0	17	30	<5	<5	<5	<5	38	30	<5	<5	<5	14	<5	18	<5

In water, 25 °C, 0.1 mol dm^{-3} KNO_3.

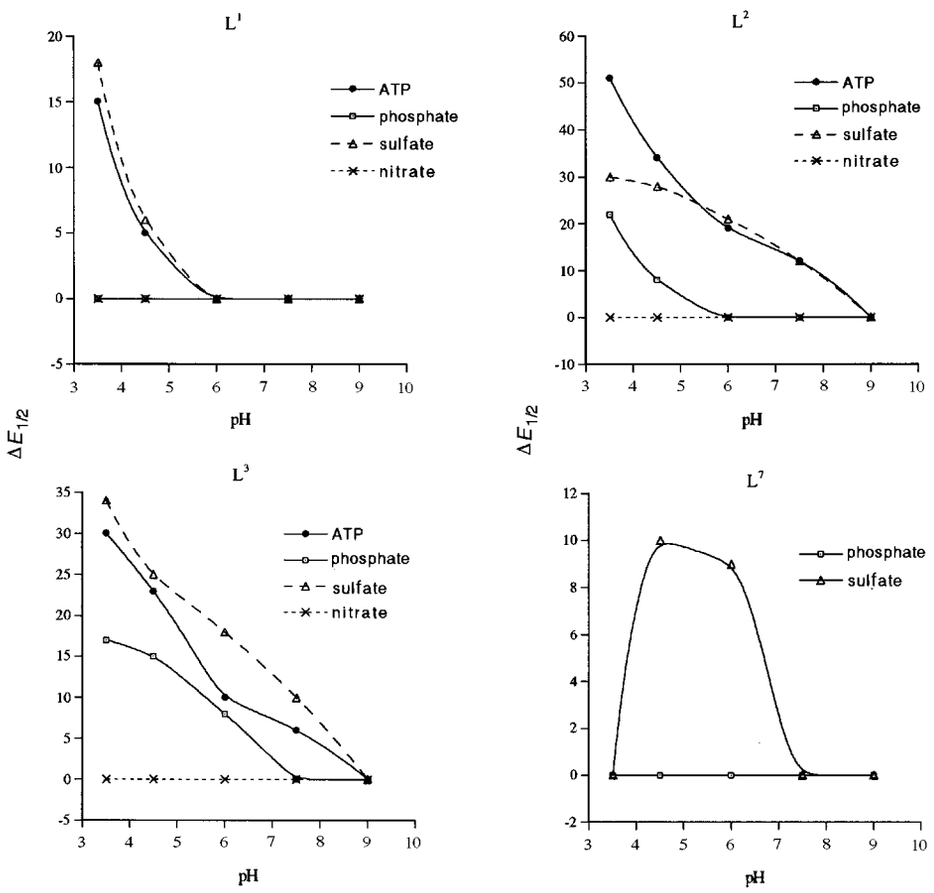


Fig. 2 Plots of $\Delta E_{\frac{1}{2}}$ for the interaction of L^1 to L^3 and L^7 receptors with ATP, phosphate, sulfate and nitrate measured at five different pH values.

aqueous solutions and emphasis has been placed on the potential selective redox recognition. The electrochemical study has been performed in water for cation recognition (25 °C, 0.1 mol dm^{-3} KNO_3), and thf–water (7:3 v/v) for anion recognition (25 °C, 0.1 mol dm^{-3} $[Bu^n_4N][ClO_4]$). We have electrochemically studied the shift of $E_{\frac{1}{2}}$ *versus* pH for the $L–H^+–M^{2+}$ systems (L = L^1, L^2 or L^3; M = Ni^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+} or Pb^{2+}; M^{2+} : L molar ratio = 1:1). The difference found between $E_{\frac{1}{2}}$ for the receptor–metal system and $E_{\frac{1}{2}}$ for the free receptor ($\Delta E_{\frac{1}{2}}$) has been monitored at five different pH values from 3 to 9 and $E_{\frac{1}{2}}$ obtained from rotating disc electrode experiments (scan speed 10 mV s^{-1}, rotation speed 7000 rpm); $\Delta E_{\frac{1}{2}}$ found at different pH values for receptors L^1 to L^3 are shown in Table 5. Some regions of selectivity can be detected. For instance, L^1 shows selectivity for copper and nickel at basic pH values, L^2 is selective for Cu^{2+} and Zn^{2+}, whereas L^3 gives important $E_{\frac{1}{2}}$ shifts in the presence of copper, nickel and cadmium and no variation upon addition of Zn^{2+} and Pb^{2+}.

Although anion binding recognition has been studied with receptors containing ferrocenyl or cobaltocenium groups, all the previous work has been mainly carried out in non-aqueous solvents. The study here is concerned with selective anion sensing by electrochemical methods in aqueous solutions. We have carried out anion recognition studies with L^1, L^2 and L^3 receptors in thf–water (7:3 v/v) against ATP, phosphate, sulfate and nitrate. The screening strategy involves the ability of these substrates to shift the $E_{\frac{1}{2}}$ of a target receptor. Fig. 2 shows the electrochemical response of receptors L^1 to L^3 in the presence of anionic guests. Ferrocenyl redox potentials are cathodically shifted by anions, and $\Delta E_{\frac{1}{2}}$ is now defined as $E_{\frac{1}{2}}$(receptor) − $E_{\frac{1}{2}}$(receptor–anion).

The biologically important polyanion ATP is electrochemically recognised by the electroactive receptors L^2 and L^3 over a wide range of pH. Compound L^1 shows a poor electrochemical response for this anion (less than 20 mV would probably be insufficient from a practical viewpoint). Of special interest is the electrochemical response of L^2 against ATP, since phosphate and nitrate do not perturb the oxidation potential of these receptors in pH ranges where the ATP response is significant. In order to study whether a selective determination of ATP in the presence of phosphate and nitrate can be carried out, L^2 was chosen as sensing receptor and a quantitative electrochemical determination of ATP in thf–water (7:3 v/v) was performed at a fixed pH of 4.9. The linear range of the curve of $\Delta E_{\frac{1}{2}}$ *versus* ATP-to-L^2 ratios (linear range found for ATP: receptor ratios < 0.9:1) was used as calibration curve for the

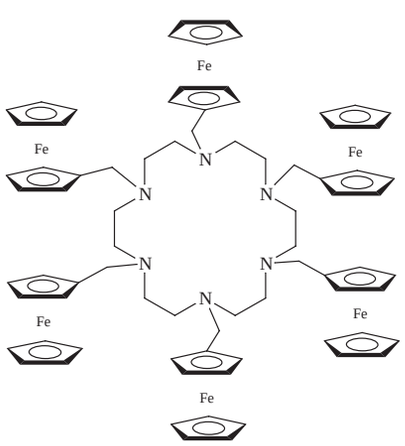
Table 6 Determination of the concentration of ATP in the presence of phosphate and nitrate with L^2 receptor at pH 4.9 by using electrochemical methods[a]

10^4 [ATP]		
a	*b*	*c*
1.38(8) [1.34]	1.61(8) [1.42]	1.50(4) [1.36]
2.62(4) [2.58]	3.0(2) [2.7]	2.71(7) [2.62]
3.64(8) [3.73]	3.7(2) [4.0]	3.71(2) [3.79]

[a] Concentration (mol dm^{-3}) determined by electrochemical methods. Values in brackets are the standard deviations of the last significant digit, those in square brackets are the actual concentrations. [b] Determined in the presence of phosphate, 52×10^{-5} mol dm^{-3}. [c] Determined in the presence of nitrate, 46×10^{-5} mol dm^{-3}.

quantitative determination of ATP. This curve does not basically change in the presence of phosphate or nitrate. In fact the quantitative determination of ATP can be carried out in the presence of these competing anions (see Table 6). Therefore L^2 is acting as an ATP-selective redox sensor in the presence of phosphate or nitrate. The data suggest that a future use of these systems in modified electrodes might lead to new methodologies for the determination of anions as alternative procedures to those currently used.

In order to compare molecules with different molecular architecture, the electrochemical behaviour of L^7 against anionic guests has also been studied. This compound contains six amine groups and gives highly charged species at a neutral and acid pH, however its electrochemical response against anionic species is quite small (see Fig. 2); the origin of the poor electrochemical response is most likely due to the presence of six ferrocenyl bulky groups which make an outer sphere around the ammonium groups which would introduce some constraints to the ammonium–anion interaction. These constraints do not exist for instance in L^3 and a shift of the oxidation potential in the presence of ATP, phosphate and sulfate was found.



L^7

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