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Selective electrochemical recognition of sulfate over phosphate and phosphate over sulfate using polyaza ferrocene macrocyclic receptors in aqueous solution

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Potentiometric and electrochemical studies have been carried out with a family of ferrocene redox-functionalised polyamines (L^1–L^5) and have been directed towards the discrimination, using electrochemical techniques, between the two oxoanions phosphate and sulfate and the electrochemical sensing of ATP. Potentiometric titrations were carried out in THF–water (70 : 30 v/v, 0.1 mol dm^{-3} tetrabutylammonium perchlorate, 25 °C) for L^1, L^2, L^3, L^5 and in water (0.1 mol dm^{-3} potassium nitrate, 25 °C) for L^4. Potentiometric data indicate that all receptors studied form stable complexes with sulfate, phosphate and ATP. Distribution for the ternary diagram system sulfate–phosphate–L^2 shows pH dependent selectivity patterns; $[L^2H_jSO_4]^{j-2}$ species exist at greater than 90% in the pH range 3–4, whereas the corresponding phosphate complexes are the main species in the neutral and basic pH range. The electrochemical studies are in agreement with the speciation results. Sulfate produces in all cyclic receptors maximum cathodic shifts of the redox potential of the ferrocenyl groups around pH 3–4, whereas maximum cathodic shifts for phosphate were found between pH 7 and 8. This behaviour is not observed for the open-chain tetraamine L^5. Selective quantitative electrochemical recognition of sulfate and phosphate in the presence of competing anions in aqueous solution has been achieved using the redox-active polyaza ferrocene macrocyclic L^2, L^3 and L^4 receptors. Additionally ATP is able to cathodically shift the oxidation potential of the ferrocenyl groups of L^2 and L^3 receptors by up to 100 mV. The electrochemical response of L^3 against ADP and AMP is also reported.

Introduction

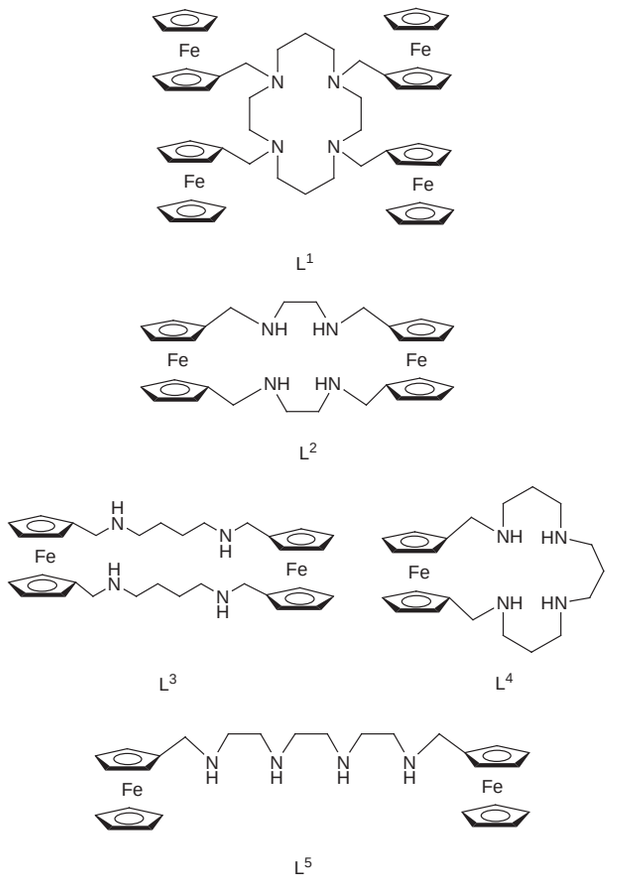
Taking into account the importance of oxoanions in environmental and biological processes, the development of new oxoanion-sensing receptors is of considerable interest in fields such as environmental chemistry. In fact most of the sensors which have been developed for phosphate, sulfate, *etc*. do not fulfil requirements such as sufficient selectivity. With the aim of developing new chemical sensor technology, considerable interest is currently being shown in the synthesis of new receptors containing redox-active groups and binding sites for the electrochemical recognition of cationic, anionic and neutral substrates.[1] This class of receptors has proved effective in transforming host–guest interactions into measurable perturbations of the redox potential of the ligand. Examples of water soluble redox responsive receptors designed to electrochemically sense concentrations of guests in the aqueous environment are rare.[2,3] This is specially so in anion-sensing where most of the studies have been carried out in non-aqueous solvents and very little is known about the potential use of ferrocene functionalised receptors as anion-sensing molecules in water. Polyamines are well known to bind anions in aqueous solution at certain pH values *via* favourable protonated ammonium–anion electrostatic and hydrogen bonding interactions.[4] By means of incorporating the redox-active ferrocene moiety into polyamine ligand frameworks we report the study of the potential sensing behaviour against sulfate, phosphate and ATP anions of a family of ferrocene-functionalised polyamines (L^1–L^5) in water and THF–water mixtures.

Experimental

The synthesis of receptors L^1, L^2, L^3, L^4 and L^5 have been published elsewhere.[5–7]

Physical measurements

Electrochemical data were obtained with a programmable function generator Tacussel IMT-1, 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 THF–water (70 : 30 v/v, 0.1 mol dm^{-3} tetrabutylammonium perchlorate, 25 °C) for L^1, L^2, L^3, L^5 and in water (0.1 mol dm^{-3} potassium nitrate, 25 °C) for L^4, using a reaction vessel water-thermostatted at 25.0 ± 0.1 °C 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. The electrode was calibrated by titration of well-known amounts of HCl with CO_2-free KOH solution and determining the equivalence point by Gran's method[8] which gives the standard potential $E'°$ and the ionic product of water ($K'_w = [H^+][OH^-]$). The computer program SUPERQUAD[9] was used to calculate the protonation and stability constants. The titration curves for each system (*ca*. 250 experimental points corresponding to at least three titration



curves, pH = −log[H], range investigated 2.5–10, concentration of the ligand and anions was *ca.* 1.2×10^{-3} mol dm^{-3}) were treated either as a single set or as separate entities without significant variations in the values of the stability constants.

Results and discussion

Potentiometric anion binding studies

Phosphate and sulfate complexation. Speciation studies have been carried out in THF–water (70:30 v/v, 0.1 mol dm^{-3} tetrabutylammonium perchlorate, 25 °C) for L^1, L^2, L^3 and L^5 and in water (0.1 mol dm^{-3} potassium nitrate, 25 °C) for L^4. Tables 1 and 2 report the stability constants found for the L–H^+–A systems (L = L^1, L^2, L^3, L^4, A = sulfate, phosphate). It is well known that macrocyclic polyamines in solution form protonated species which can interact with anions *via* electrostatic forces and hydrogen bonds.[10] With receptors L^1–L^4 an additional favourable electrostatic interaction with the anionic guest will result from the oxidised ferrocenium moieties in electrochemical experiments (see below). Table 1 gives the stoichiometry of the species formed and the stability constants with phosphate. There is interaction between the receptors and the phosphate anion in a wide pH range (*ca.* 1–10). Despite the use of different solvents (THF–water and water) the stoichiometries found in solution for the phosphate complexes formed are quite similar. In all cases 1:1 complexes were found. Fig. 1 shows the distribution diagram of the species for the L^2–H^+–phosphate system. Taking into account the complexity of the studied system the evaluation of the existing species in solution throughout the pH range studied is rather difficult.[11]

Table 1 Logarithms of the stability constants for the interaction of L^1, L^2, L^3, L^4 or L^5 with phosphate in THF–water (70:30 v/v, 25 °C, 0.1 mol dm^{-3} tetrabutylammonium perchlorate) for L^1, L^2, L^3, L^5 and water (25 °C, 0.1 mol dm^{-3} potassium nitrate) for L^4 [a]

Reaction	L^1	L^2	L^3	L^4	L^5
$L + 2H + PO_4 \longleftrightarrow H_2LPO_4$ [b]				25.66(1) [c]	24.88(2)
$L + 3H + PO_4 \longleftrightarrow H_3LPO_4$		31.03(5)		36.27(1)	33.49(1)
$L + 4H + PO_4 \longleftrightarrow H_4LPO_4$	41.63(2)	37.72(4)	40.51(3)	45.13(1)	41.18(1)
$L + 5H + PO_4 \longleftrightarrow H_5LPO_4$	48.23(2)	43.96(6)	48.58(1)	52.60(1)	46.94(1)
$L + 6H + PO_4 \longleftrightarrow H_6LPO_4$	50.28(3)	49.49(3)	53.12(2)	59.51(1)	50.07(3)
$H_2L + PO_4 \longleftrightarrow H_2LPO_4$				5.54	8.74
$H_3L + PO_4 \longleftrightarrow H_3LPO_4$		9.21		8.14	11.82
$H_4L + PO_4 \longleftrightarrow H_4LPO_4$	15.55	11.01	12.65	10.36	16.23
$H_4L + HPO_4 \longleftrightarrow H_5LPO_4$	10.11	5.21	8.85	5.8	10.14
$H_4L + H_2PO_4 \longleftrightarrow H_6LPO_4$	4.65	2.68	5.08	5.68	4.90

[a] Basicity constants for L^1 ref. 13, L^2 ref. 6. L^3 in THF–water (70:30 v/v, 25 °C, 0.1 mol dm^{-3} tetrabutylammonium perchlorate): $\log\beta_1 = 9.00(1)$, $\log\beta_2 = 16.89(1)$, $\log\beta_3 = 24.00(1)$, $\log\beta_4 = 27.86(1)$. L^5 in THF–water (70:30 v/v, 25 °C, 0.1 mol dm^{-3} tetrabutylammonium perchlorate): $\log\beta_1 = 8.83(1)$, $\log\beta_2 = 16.14(1)$, $\log\beta_3 = 21.67(1)$, $\log\beta_4 = 24.95(1)$, phosphate in THF–water (70:30 v/v, 25 °C, 0.1 mol dm^{-3} tetrabutylammonium perchlorate): $\log\beta_1 = 11.85(1)$, $\log\beta_2 = 20.22(1)$, $\log\beta_3 = 24.41(1)$. L^4 in water (25 °C, 0.1 mol dm^{-3} potassium nitrate): $\log\beta_1 = 10.67(1)$, $\log\beta_2 = 20.12(1)$, $\log\beta_3 = 28.13(2)$, $\log\beta_4 = 34.77(3)$. [b] Charges have been omitted for clarity. [c] Values in parentheses are the standard deviations in the last significant digit.

Table 2 Logarithms of the stability constants for the interaction of L^1, L^2, L^4 or L^5 with sulfate in THF–water (70:30 v/v, 25 °C, 0.1 mol dm^{-3} tetrabutylammonium perchlorate) for L^1, L^2, L^5 and water (25 °C, 0.1 mol dm^{-3} potassium nitrate) for L^4 [a]

Reaction	L^1	L^2	L^4	L^5
$L + H + SO_4 \longleftrightarrow HLSO_4$ [b]				12.05(3) [c]
$L + 2H + SO_4 \longleftrightarrow H_2LSO_4$				20.05(2)
$L + 3H + SO_4 \longleftrightarrow H_3LSO_4$				26.64(1)
$L + 4H + SO_4 \longleftrightarrow H_4LSO_4$	30.98(5)	29.80(2)	37.01(1)	31.89(1)
$L + 5H + SO_4 \longleftrightarrow H_5LSO_4$	35.02(5)	35.16(4)	40.83(1)	35.09(2)
$HL + SO_4 \longleftrightarrow HLSO_4$				3.22
$H_2L + SO_4 \longleftrightarrow H_2LSO_4$				3.91
$H_3L + SO_4 \longleftrightarrow H_3LSO_4$				4.97
$H_4L + SO_4 \longleftrightarrow H_4LSO_4$	4.9	3.09	2.24	6.94
$H_4L + HSO_4 \longleftrightarrow H_5LSO_4$	5.77	5.28	3.52	6.86

[a] Basicity constants for sulfate in THF–water (70:30 v/v, 25 °C, 0.1 mol dm^{-3} tetrabutylammonium perchlorate): $\log\beta_1 = 3.28(1)$. [b] Charges have been omitted for clarity. [c] Values in parentheses are the standard deviations in the last significant digit.

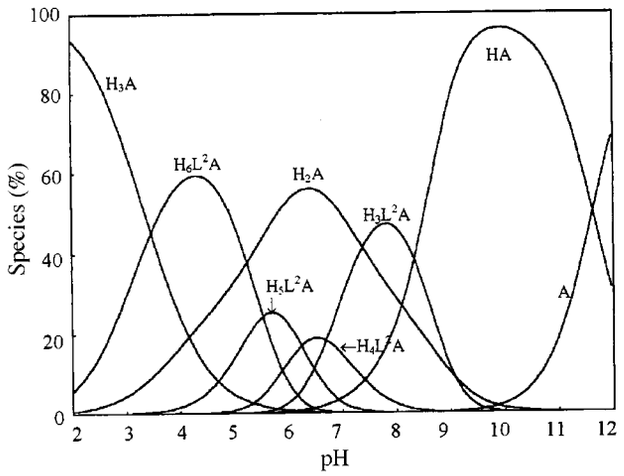


Fig. 1 Distribution diagram of the species for the system L^2–H^+–phosphate.

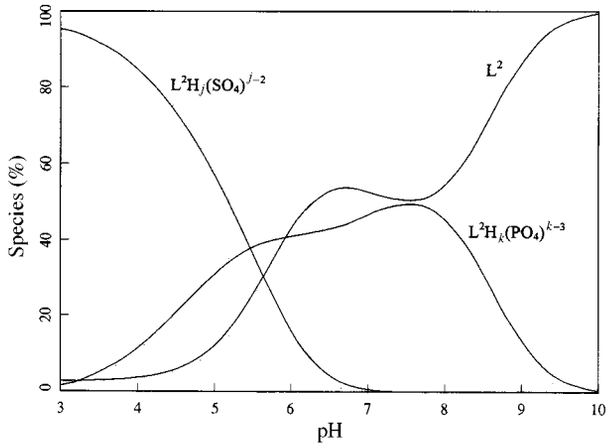


Fig. 3 Distribution diagram for the ternary system sulfate–phosphate–L^2. The sum of percentages of complexed species are plotted *vs.* pH. $[L^2] = [\text{sulfate}] = [\text{phosphate}] = 8 \times 10^{-3}$ mol dm^{-3}.

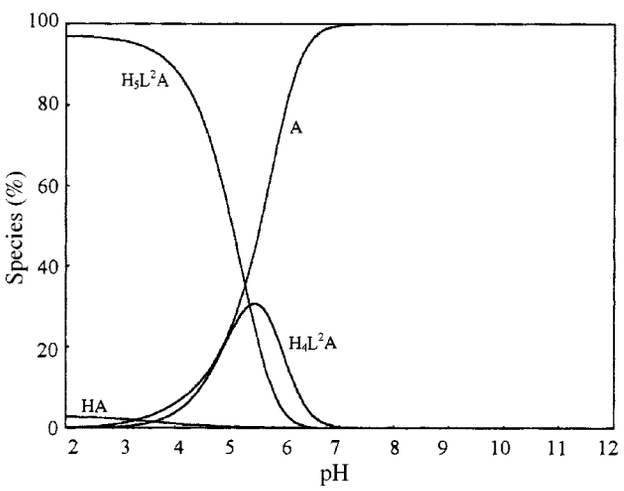


Fig. 2 Distribution diagram of the species for the system L^2–H^+–sulfate.

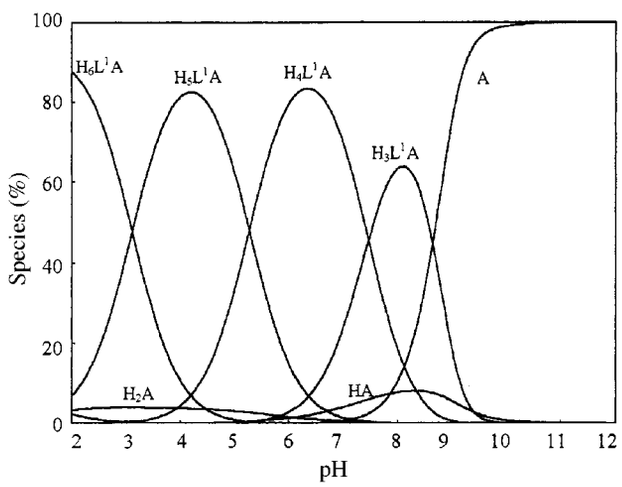


Fig. 4 Distribution diagram of the species for the system L^1–H^+–ATP.

Nevertheless bearing in mind the protonation constants of the receptors and the phosphate we have tentatively assigned the complexes H_4LPO_4 to the interaction of $H_2L^{2+} + H_2PO_4^-$ and H_5LPO_4 to $H_3L^{3+} + H_2PO_4^-$, taking into account that the $H_2PO_4^-$ is in greatest abundance in the pH ranges 4.06–8.08 (in THF–water) and 4.31–8.31 (in water). Assuming these interactions between species, the logarithms of the stability constants for the equilibria $H_2L^{2+} + H_2PO_4^- \rightleftharpoons H_4LPO_4$ and $H_3L^{3+} + H_2PO_4^- \rightleftharpoons H_5LPO_4$ (L = L^1 to L^4) are in the range 1.59–6.28 and 2.04–5.88, respectively. The complex H_6LPO_4 exists at maximum concentration at pH 4–5 and probably involves H_4L^{4+} and $H_2PO_4^-$. The nature of the remaining complexes is less clear.

The stability constants corresponding to the equilibrium of L^1, L^2 and L^4 with sulfate have also been determined by pH-metric titrations. Stability constants are reported in Table 2. For receptors L^1, L^2 and L^4 receptor–sulfate interactions have only been found at pH lower than 7. Tentatively H_4LSO_4 and H_5LSO_4 species are attributed to $H_4L^{4+} + SO_4^{2-}$ and $H_4L^{4+} + HSO_4^-$, respectively. Fig. 2 shows the distribution diagram for the L^2–H^+–sulfate system.

One of our main goals in this study was the development of selective electrochemical sensing receptors able to discriminate between the oxoanions sulfate and phosphate. In order to detect selectivity and determine which are the prevailing species in solution in a mixture of sulfate and phosphate with the receptors L^1, L^2 and L^4, we have calculated the distribution diagram of the ternary sulfate–phosphate–L systems by plotting the overall percentages of the free receptors and the sulfate–L and phosphate–L complexes as a function of the pH.[11] These diagrams show the competition between sulfate and phosphate (equimolecular amounts) to interact with a target receptor. Fig. 3 shows the ternary diagram for the L^2–sulfate–phosphate system. The figure clearly displays the pH dependent selectivity patterns. $[L^2H_jSO_4]^{j-2}$ species exist at greater than 90% in the pH range 3–4, whereas the corresponding phosphate complexes are the main species in the neutral and basic pH range. Similar ternary diagrams are obtained for L^1–sulfate–phosphate systems, with predominant sulfate complexes at acid pH and predominant phosphate complexes at neutral and basic pH. This trend is also observed for L^4 but phosphate predominates in the presence of sulfate in the pH range studied. This data strongly suggests that some receptors are able to selectively complex sulfate or phosphate by pH modulation.

For the sake of comparison the protonation and formation of sulfate and phosphate complexes with the open-chain tetraamine L^5 have also been determined in THF–water 70:30 v/v. Tables 1 and 2 list the stability constants found. Despite the different geometric architecture of L^5 (open-chain against cyclic) the stoichiometries and stability constants of the complexes are in general similar to those found for the cyclic receptors L^1, L^2, L^3 and L^4. Additionally the ternary diagram for L^5–sulfate–phosphate also displays sulfate species as predominant at acid pH and phosphate complexes as the main species at neutral pH.

Table 3 Logarithms of the stability constants for the interaction of L^1, L^2, L^3, L^4 or L^5 with ATP in THF–water (70:30 v/v, 25 °C, 0.1 mol dm^{-3} tetrabutylammonium perchlorate) for L^1, L^2, L^3, L^5 and water (25 °C, 0.1 mol dm^{-3} potassium nitrate) for L^4 [a]

Reaction	L^1	L^2	L^3	L^4	L^5
$L + H + ATP \longleftrightarrow HLATP$ [b]			12.67(7) [c]		
$L + 2H + ATP \longleftrightarrow H_2LATP$			22.29(5)	23.32(9)	21.39(1)
$L + 3H + ATP \longleftrightarrow H_3LATP$	28.99(4)		30.43(6)	31.96(9)	29.34(1)
$L + 4H + ATP \longleftrightarrow H_4LATP$	36.45(5)	33.69(5)	38.59(5)	39.58(8)	35.75(1)
$L + 5H + ATP \longleftrightarrow H_5LATP$	41.72(3)	38.27(4)	45.47(5)	45.99(11)	39.54(1)
$L + 6H + ATP \longleftrightarrow H_6LATP$	44.84(3)	43.67(4)	50.46(7)	50.40(14)	41.07(9)
$L + 7H + ATP \longleftrightarrow H_7LATP$				53.44(16)	
$HL + ATP \longleftrightarrow HLATP$			3.67		
$H_2L + ATP \longleftrightarrow H_2LATP$			5.40	3.20	5.25
$H_3L + ATP \longleftrightarrow H_3LATP$	6.15		6.43	3.83	7.67
$H_4L + ATP \longleftrightarrow H_4LATP$	10.37	6.98	10.73	4.81	10.80
$H_4L + HATP \longleftrightarrow H_5LATP$	7.78	3.70	10.10	4.44	7.08
$H_4L + H_2ATP \longleftrightarrow H_6LATP$	4.82	3.02	11.33	4.84	4.60
$H_4L + H_3ATP \longleftrightarrow H_7LATP$				5.86	

[a] Basicity constants for ATP in THF–water (70:30 v/v, 25 °C, 0.1 mol dm^{-3} tetrabutylammonium perchlorate): $\log\beta_1 = 7.51(1)$, $\log\beta_2 = 11.52(1)$, $\log\beta_3 = 14.07(3)$. Basicity constants for ATP in H_2O (25 °C, 0.1 mol dm^{-3} potassium nitrate): $\log\beta_1 = 6.78(1)$, $\log\beta_2 = 10.79(2)$, $\log\beta_3 = 12.81(5)$. [b] Charges have been omitted for clarity. [c] Values in parentheses are the standard deviations in the last significant digit.

ATP complexation. In Table 3 the stability constants of the cyclic L^1, L^2, L^3 and L^4 and the open-chain L^5 polyamines with ATP are reported. Stability constants found due to the interaction of the protonated forms of the receptors with ATP are generally higher in THF–water 70:30 v/v than those found for L^4 in water. Fig. 4 shows the distribution diagram for the L^1–H^+–ATP system. Receptor L^4 is fully protonated $(H_4L^4)^{4+}$ at pH lower than 6.6. On the other hand the first protonation of free ATP in water is *ca*. 6.7. Therefore the complexes expected to exist in solution involve the interaction of H_jL^{j+} species and ATP^{4-} (H_2L, H_3L and H_4L for species H_2LATP, H_3LATP and H_4LATP species in Table 3). Further protonated species H_5LATP and H_6LATP are probably related to the interaction of H_4L^{4+} with $HATP^{3-}$ and H_2ATP^{2-}, respectively. The value found for the open-chain tetraamine spermine $[H_2N(CH_2)_3NH(CH_2)_4NH(CH_2)_3NH_2]$ in water for its tetraprotonated form with ATP has been reported to be 3.97 which is a value close to that found for $(H_4L^4)^{4+}$ and ATP^{4-}.[12] In THF–water with receptors L^1, L^2 and L^3 the situation is more complex. The first protonation constant of ATP in THF–water is *ca*. 7.51. On the other hand the last protonation constants for L^1, L^2, L^3 and L^5 are *ca*. 3.2–4.8. The difference between the first protonation constant of ATP and fully protonated species L^1, L^2, L^3 and L^5 is now larger than for L^4 in water and therefore several species can coexist in solution and it is more difficult to determine the nature of the complexes taking into account only stability constant values.

Electrochemical anion recognition investigations

One of the most interesting features in receptors L^1 to L^5 is the presence near co-ordination sites of redox-active groups. These can be affected by the presence of closely bound anionic guest species and transform the receptor–substrate interaction into a macroscopic electrochemical response. The shift of the redox potential of the ferrocenyl groups as a function of the pH in the presence and absence of sulfate, phosphate, ATP and nitrate anions was monitored in THF–water (70:30 v/v, 0.1 mol dm^{-3} tetrabutylammonium perchlorate, 25 °C) for L^1, L^2, L^3, L^5 and in water (0.1 mol dm^{-3} potassium nitrate, 25 °C) for L^4. A unique oxidation potential wave was observed for all the receptors throughout the pH range, except for L^4 at neutral pH in which two unresolved waves were observed. Plots of $E_{1/2}$ *vs*. pH show for all receptors that a steady anodic shift of the redox potential occurs when the solution is acidified. The difference found between the oxidation potential at basic pH (pH = 12) and acidic pH (pH = 0) (obtained by extrapolation of the curves $E_{1/2}$ *vs*. pH because of the instability of ferrocenyl groups at pH lower than 2) was 100, 260, 250, 326 and 110 mV, for L^1–L^5 respectively. As a general rule the fewer the number of ferrocenyl centres and the closer the N-donor atoms are to the redox-centres, the larger is $\Delta E_{1/2}$.[13]

Electrochemical response towards sulfate and phosphate. The electrochemical response of sulfate, phosphate and nitrate anions was monitored as a function of pH range. Plots of $E_{1/2}$ *vs*. pH for the systems $L–H^+–A$, ($L = L^1$ to L^5; A = sulfate, phosphate, nitrate) with a ligand-to-anion molar ratio of 1:1 have been determined. Fig. 5 graphically displays the electrochemical anion response found for receptors L^1, L^2, L^3, L^4 and L^5 as a function of the pH [$\Delta E_{1/2}$ defined as $E_{1/2}$ (receptor) − $E_{1/2}$ (anion–receptor)]. Nitrate does not produce any significant redox potential shift at any pH value. Sulfate produces in all receptors maximum cathodic shifts of the redox potential of the ferrocenyl groups around pH 3–5, whereas maximum cathodic shifts for phosphate were found between pH 6 and 8. Maximum selective redox potential shifts ($\Delta E_{1/2}$) of 54 and 50 mV were observed for sulfate and phosphate, using receptors L^2 and L^4 at pH 4 and 7, respectively (see Fig. 5).

If we compare the potentiometric data and the electrochemical response as a function of the pH the results appear to suggest that the contributions to $\Delta E_{1/2}$ of the different species found in solution are not the same. For example from Fig. 1 and Fig. 5 it can be observed that although phosphate interacts with L^2 in the range pH 2 to 9, the maximum electrochemical response was found in the pH range 5–7 suggesting that only the $[H_5L^2PO_4]^{2+}$ and $[H_4L^2PO_4]^+$ species are able to significantly perturb the oxidation potential of the ferrocenyl moiety, whereas the $[H_6L^2PO_4]^{3+}$ and $[H_3L^2PO_4]$ complexes are not capable of doing so. This is also observed for the remaining receptors L^1, L^3 and L^4, for which the maximum phosphate–receptor interaction always coincides with the pH range of existence of the $[H_5LPO_4]^{2+}$ and $[H_4LPO_4]^+$ species. Assuming that $[H_5LPO_4]^{2+}$ and $[H_4LPO_4]^+$ species are associated with the interaction of the $H_2PO_4^-$ anion with H_2L^{2+} and H_3L^{3+} species it can be concluded that receptors L^1 to L^4 are able to selectively detect the presence of the $H_2PO_4^-$ anion. From our point of view this is of importance because the data suggests for the first time, to the best our knowledge, that there is a selective electrochemical speciation in the sense that not all the $H_jPO_4^{j-3}$ species produce the same oxidation potential shift of the ferrocene groups. For all the L^1, L^2, and L^4 receptors sulfate produces oxidation potential shifts at pH values lower than 7, where the species $[H_4L^2SO_4]^{2+}$ and $[H_5L^2SO_4]^{3+}$ exist.

In order to demonstrate the potential use of redox-functionalised receptors as practical sensors we have carried out studies on the selective quantitative determination of sulfate

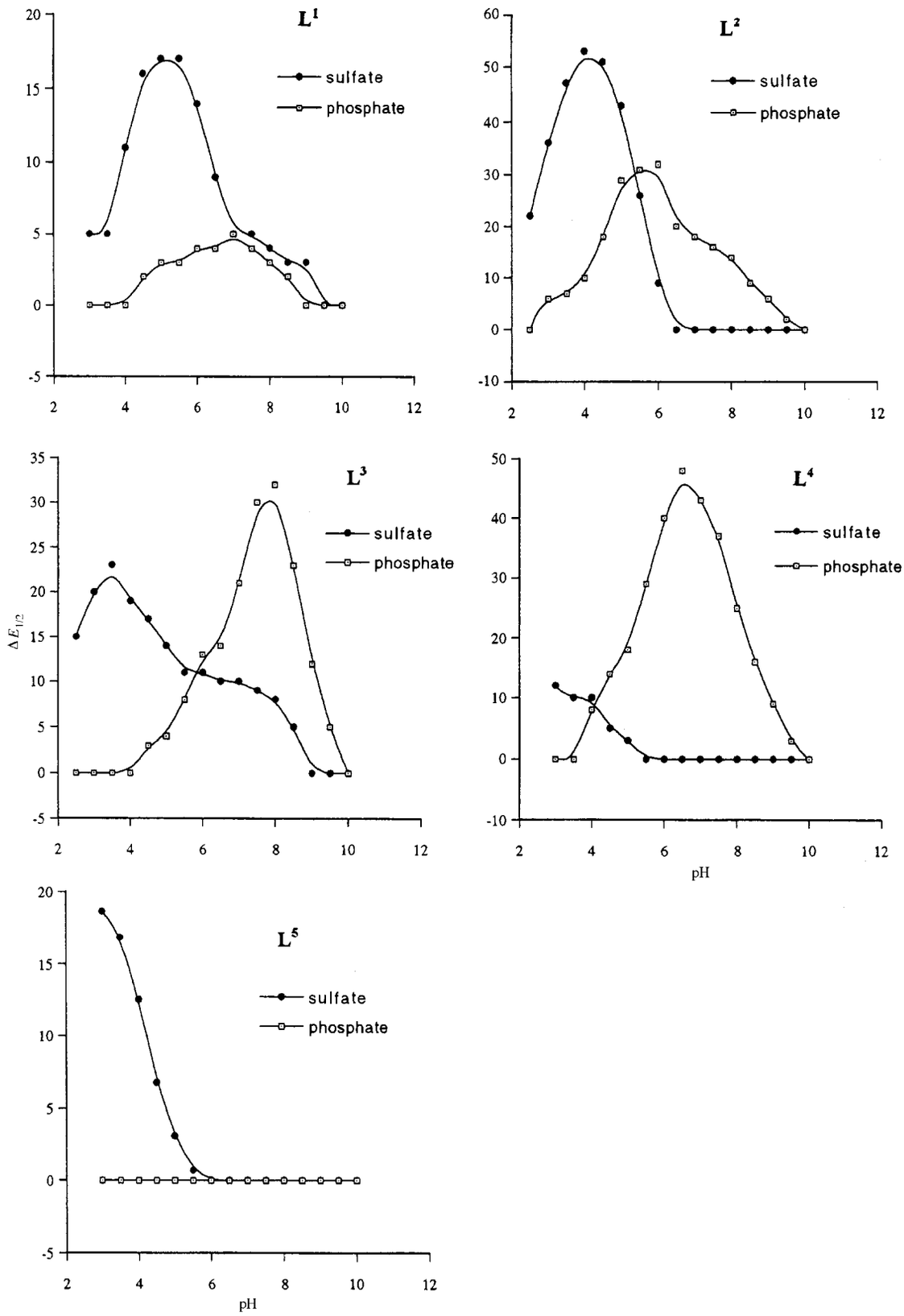


Fig. 5 Redox potential shift ($\Delta E_{1/2}$) for L^1, L^2, L^3, L^4 and L^5 in the presence of phosphate and sulfate as a function of the pH.

and phosphate using receptors L^2, L^3 and L^4. Although the following studies, from a practical point of view, can probably not be applied to a real analytical problem they point out the selective nature of the interaction and reinforce the arguments stated above.

For example Fig. 6 shows $\Delta E_{1/2}$ at pH = 4.0 *versus* sulfate-to-L^2 ratios in the presence and absence of phosphate ($[L^2] = 50 \times 10^{-5}$ mol dm^{-3}; [phosphate] = 52×10^{-5} mol dm^{-3}). Apart from the selectivity exhibited for sulfate in the presence of phosphate, Fig. 6 indicates that 1:1 complexes are formed. This is in agreement with the ternary diagram in Fig. 3 which indicates that in a mixture of sulfate and phosphate at pH 4 the L^2 receptor selectively forms complexes with sulfate. We have also determined $\Delta E_{1/2}$ *vs.* phosphate-to-L ratios for receptor L^3 and L^4 at pH 8 and 7, respectively. The linear range of the curve in Fig. 6 (sulfate anion-to-receptor ratios < 0.9:1) can be used

Table 4 Determination of the concentration of sulfate in the presence of phosphate, nitrate, chloride or acetate with receptor L^2 in THF–water (70 : 30 v/v) at pH 4.0 by using electrochemical methods[a]

[sulfate] × 10^5	[sulfate] × 10^5	[sulfate] × 10^5	[sulfate] × 10^5	[sulfate] × 10^5
14.3(8)[a] [15.2][b]	22.0(7)[c] [15.0][b]	12.8(6)[d] [13.4][b]	11.1(3)[e] [11.1][b]	12.2(8)[f] [11.3][b]
29(1) [29]	31(1) [29]	25(1) [26]	23(1) [21]	23(1) [22]
39(2) [42]	41(1) [42]	33(2) [37]	29(1) [31]	31(2) [32]

[a] Concentration (mol dm^{-3}) determined by electrochemical methods. Values in parentheses are the standard deviations in the last significant digit. [b] Sulfate concentration (mol dm^{-3}). [c] [sulfate] determined in the presence of phosphate, [phosphate] = 52×10^{-5} mol dm^{-3}. [d] [sulfate] determined in the presence of nitrate, [nitrate] = 46×10^{-5} mol dm^{-3}. [e] [sulfate] determined in the presence of chloride, [chloride] = 38×10^{-5} mol dm^{-3}. [f] [sulfate] determined in the presence of acetate, [acetate] = 38×10^{-5} mol dm^{-3}.

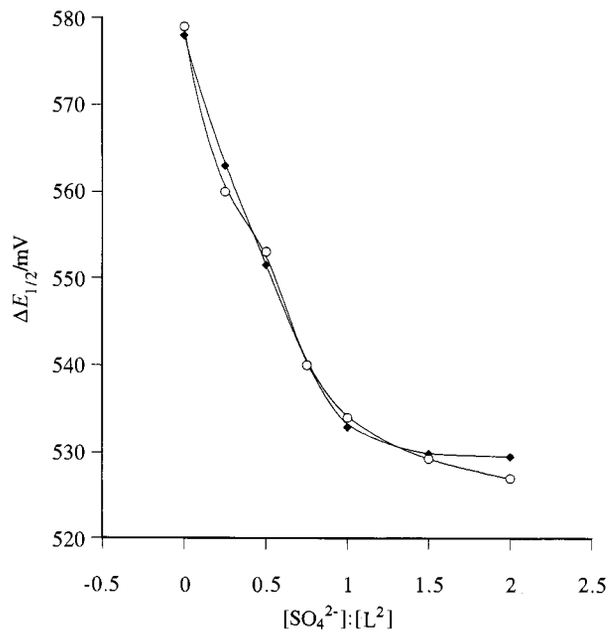


Fig. 6 Redox potential shift ($\Delta E_{1/2}$) of L^2 *vs.* sulfate-to-L^2 ratios in the absence (○) and presence of phosphate (◆).

as a calibration curve for the quantitative determination of sulfate, whereas linear ranges in $\Delta E_{1/2}$ *vs.* phosphate-to-L ratio curves for receptor L^3 and L^4 have been used for the quantitative determination of phosphate. Table 4 shows the selective determination of sulfate in the presence of phosphate, nitrate, chloride, or acetate. The presence of chloride or acetate, which are able to interact with protonated polyamines, does not appear to significantly affect the sulfate determination indicating that sulfate can be selectively determined in the presence of these competing anions. Table 5 gives the results found in the selective quantitative determination of phosphate using receptor L^3 employing electrochemical methods, whereas Table 6 reports the selective determination of phosphate using L^4 in water in the presence of sulfate. Sulfate is not able to perturb the electrochemical response against phosphate at pH 7 in agreement with the tertiary diagram of the L^4–sulfate–phosphate system which shows predominant L^4–phosphate *versus* L^4–sulfate species. Of particular note is the selective quantitative phosphate determination in water even in the presence of other anions such as sulfate and nitrate (often present in water), at the environmentally typical neutral pH.

The importance of the molecular architecture is noteworthy when the comparison is drawn between the electrochemical response found for the cyclic receptors L^1, L^2, L^3 and L^4 and the open-chain tetraamine L^5. The half-wave potential of the open-chain tetraamine L^5 is also pH dependent, but neither the presence of nitrate nor phosphate produce any significant change in the oxidation potential of the ferrocenyl groups in clear contrast with that found for the corresponding cyclic tetraamines L^1 to L^4. On the contrary at acid pH L^5 is able to electrochemically recognise sulfate. Bearing in mind that both cyclic and acyclic tetraamines form stable complexes with

Table 5 Determination of the concentration of phosphate in the presence of sulfate and nitrate with receptor L^3 in THF–water (70 : 30 v/v) at pH 8.0 by using electrochemical methods[a]

$[PO_4^{-3}]$ × 10^5	$[PO_4^{-3}]$ × 10^5	$[PO_4^{-3}]$ × 10^5
14.8(8)[a] [11.8][b]	11(2)[c] [12][b]	14(1)[d] [15][b]
21(1) [23]	21(1) [23]	28(3) [28]
33(2) [33]	33(2) [33]	39(2) [41]

[a] Concentration (mol dm^{-3}) determined by electrochemical methods. Values in parentheses are the standard deviations in the last significant digit. [b] Sulfate concentration (mol dm^{-3}). [c] $[PO_4^{-3}]$ determined in the presence of sulfate, $[SO_4^{-2}] = 42 \times 10^{-5}$ mol dm^{-3}. [d] $[PO_4^{-3}]$ determined in the presence of nitrate, $[NO_3^-] = 50 \times 10^{-5}$ mol dm^{-3}.

Table 6 Determination of the concentration of phosphate in the presence of sulfate with receptor L^4 in water at pH 7.0 by using electrochemical methods[a]

[phosphate] × 10^5	[phosphate] × 10^5
14(2)[a] [14][b]	15(1)[c] [15][b]
27(2) [27]	27(2) [29]
39.1(9) [39.0]	41(2) [42]

[a] Concentration (mol dm^{-3}) determined by electrochemical methods. Values in parentheses are the standard deviations in the last significant digit. [b] Phosphate concentration (mol dm^{-3}). [c] [phosphate] determined in the presence of sulfate, [sulfate] = 52×10^{-5} mol dm^{-3}.

sulfate and phosphate (see above), the different electrochemical response can only be attributed to a different molecular architecture (cyclic *versus* acyclic).

In considering the electrochemically observed behaviour one should be aware of the nature of the interaction process between the ferrocene/ferrocenium groups and the anion. In a first step for a determined pH the anion interacts with the poly-amine/-ammonium cavity *via* electrostatic forces and/or hydrogen bonds. In a second step when the ferrocene groups are oxidised to ferrocenium an additional cation(ferrocenium)–anion interaction would occur. This ferrocenium–anion interaction would probably be the factor having the largest contribution to the oxidation potential shift found using electrochemical techniques. This interaction would be favoured if the ferrocene groups are fixed and are in close proximity to the anion bound within the cavity. By considering the molecular architecture of cyclic and acyclic receptors it seems clear that most of these factors can be better accommodated by receptors L^1, L^2, L^3 and L^4 than by the open-chain molecule L^5 and in general one would expect to obtain a greater degree of selectivity and larger $\Delta E_{1/2}$ shifts in the presence of anions in cyclic rather than in acyclic receptors.

Electrochemical response towards ATP. The electrochemical response of receptors L^1, L^2, L^3, L^4 and L^5 towards ATP in THF–water (70 : 30 v/v) has also been monitored as a function of the pH. Fig. 7 shows $\Delta E_{1/2}$ [$\Delta E_{1/2}$ defined as $E_{1/2}$ (receptor) − $E_{1/2}$ (anion–receptor)] for the L–H^+–ATP systems. Although all the receptors L^1, L^2, L^3, L^4 and L^5 have been found to form stable complexes with ATP their electrochemical response is quite different. First it is interesting to point out that

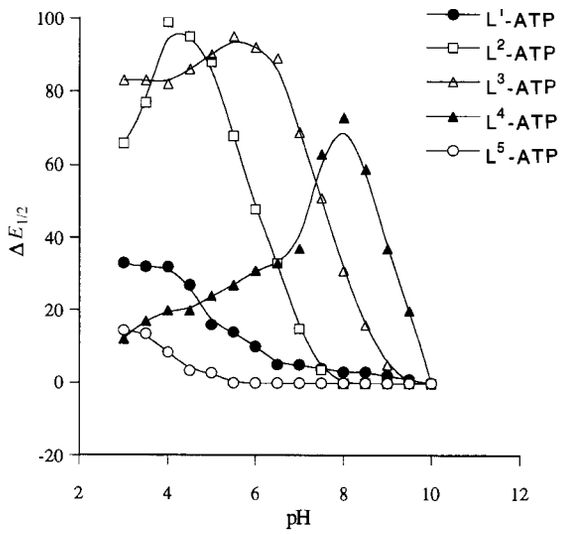


Fig. 7 Redox potential shift ($\Delta E_{1/2}$) for L^1, L^2, L^3, L^4 and L^5 in the presence of ATP.

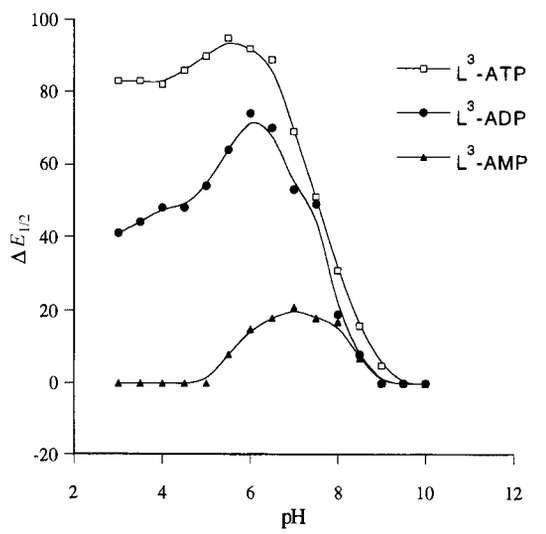


Fig. 8 Redox potential shift ($\Delta E_{1/2}$) for L^3 in the presence of ATP, ADP and AMP anions.

ATP is able to cathodically shift the oxidation potential of the ferrocenyl groups of receptors L^2 and L^3 by up to 100 mV. Thus $\Delta E_{1/2}$ found in aqueous solutions for ATP is quite large and is even larger than some of the $\Delta E_{1/2}$ values found for the interaction of polyazaalkanes with metal ions. In general for the same receptor transition metal ions form more stable complexes than anions, however the large $\Delta E_{1/2}$ found for L^2 and L^3 with ATP suggest that there is no direct relation between stability constants and oxidation potential shift.

The L^5 receptor displays the lowest oxidation potential shift ($\Delta E_{1/2}$ lower than 20 mV) in the presence of ATP. This appears to reinforce the fact that macrocyclic receptors compared to acyclic structures generally exhibit an enhanced electrochemical recognition effect. There is also a contrast between the electrochemical response of receptors L^2, L^3, L^4 and L^1 which could be explained by taking into account the smaller cyclic cavity in L^1 when compared with L^2, L^3 and L^4. Additionally we have also carried out preliminary studies on the electrochemical recognition of ADP and AMP. ATP, ADP and AMP are a series of anions where the charge and the size is steadily reduced from ATP to AMP. Fig. 8 shows $\Delta E_{1/2}$ [$\Delta E_{1/2}$ defined as $E_{1/2}$ (receptor) − $E_{1/2}$ (anion–receptor)] for the L^3–H^+–A (A = ATP, ADP, AMP) systems as a function of the pH. Maximum oxidation potential shift was found about pH 6–7, where the anions are in their deprotonated form ATP^{4+}, ADP^{3+} and AMP^{2+}.

Conclusions

In summary we have shown that redox-active ferrocene polyazamacrocyclic receptors L^1–L^4 can, through an electrochemical response, selectively detect at certain pH values sulfate and phosphate in the presence of competing anions in the aqueous environment. A different electrochemical response has been found for open-chain receptor L^5 pointing out the importance of the molecular architecture in the electrochemical recognition process. Maximum selective redox potential shifts ($\Delta E_{1/2}$) of 54 and 50 mV were observed for sulfate and phosphate, using receptors L^2 and L^4 at pH 4 and 7, respectively. Larger cathodic $\Delta E_{1/2}$ shifts of up to 100 mV have been found for ATP and L^2 and L^3. Both the selectivity and the large redox potential shift found for some anions strongly suggest the potential use of these receptors as transducers in amperometric sensor devices in the near future. Of particular note is the selective quantitative phosphate determination in water in the presence of competing anions at the environmentally common neutral pH.

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