ChemComm
www.rsc.org/chemcomm

Effective recognition of $H_2PO_4^-$ by a new series of dendrimers functionalized with ferrocenyl-urea termini

Beatriz Alonso,[a] Carmen M. Casado,[a] Isabel Cuadrado,*[a] Moisés Morán[a] and Angel E. Kaifer*[b]

[a] *Departamento de Química Inorgánica, Facultad de Ciencias, Universidad Autónoma de Madrid, Cantoblanco, 28049 Madrid, Spain. E-mail: isabel.cuadrado@uam.es; Fax: 34 91-397-4833; Tel: 34 91-397-4834*

[b] *Center for Supramolecular Science and Department of Chemistry, University of Miami, Coral Gables, FL 33124-0431, USA. E-mail: akaifer@miami.edu; Fax: 305 444-1777; Tel: 305 284-3468*

Received (in Cambridge, UK) 11th June 2002, Accepted 3rd July 2002
First published as an Advance Article on the web 15th July 2002

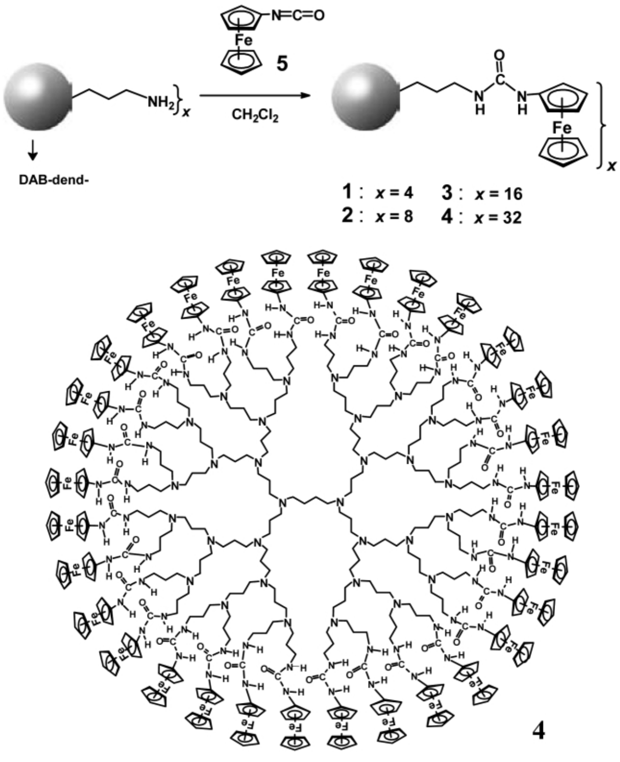
A new series of dendrimers with poly(propylene imine) backbones and 4, 8, 16, or 32 peripheral ferrocenyl-urea groups were prepared and characterized; their voltammetric behavior in DMSO solution was very sensitive to the presence of hydrogenphosphate anions at submillimolar concentration levels.

Anion recognition and sensing has received considerable attention in the last twenty years.[1] In this context, dendrimers offer an interesting molecular framework for the design and construction of anion recognition sites. The extensive work of Astruc and coworkers has made use of ferrocenyl-amide-terminated dendrimers for the electrochemical recognition of anions.[2] This group has recently extended their voltammetric anion sensing work to gold nanoparticles capped with monolayers containing terminal ferrocenyl-amide groups.[3] We have also investigated ferrocenyl-terminated dendrimers as anion receptors.[4] The groups of Vögtle[5] and Meijer[6] have recently reported the functionalization of dendrimers with surface urea residues for molecular recognition. Based on this body of work, we decided to combine in a dendrimer framework the redox activity of ferrocenyl groups with the anion binding ability of urea residues. In this work, we report the synthesis, characterization and preliminary electrochemical data corresponding to the ferrocenyl-urea-terminated DiAminoButane-based poly(propylene imine) dendrimers **1–4** (see Scheme 1). The voltammetric behavior of these new dendrimers in DMSO solution is very sensitive to the presence of low concentrations of hydrogenphosphate anion.

Ferrocenecarboxylic acid was first converted to isocyanatoferrocene (**5**), *via* its acyl azide derivative, using modified literature procedures.[7] Isocyanate **5** was found to be relatively unstable and was stored at temperatures below 5 °C. Reaction of the DAB dendrimers with excess **5** in CH_2Cl_2 produced the desired dendrimers in moderate yields (30–50%). Dendrimers **1–4** were fully characterized by ^1H and ^{13}C NMR spectroscopies and FAB or MALDI-TOF mass spectrometry.† Dendrimers **2–4** gave rise to intense molecular peaks in their MALDI-TOF mass spectra and **1** did so in its FAB mass spectrum, thus providing unequivocal evidence for the completion of the surface functionalization reaction.

The electrochemical behavior of dendrimers **1–4** is dominated by the reversible one-electron oxidation of the ferrocenyl groups. In cyclic voltammetric (CV) experiments in DMSO solution—also containing 0.1 M $TBAPF_6$ as supporting electrolyte—a single reversible oxidation wave was observed for each dendrimer. This finding reveals that there is no electronic communication between the multiple ferrocenyl centers in one dendrimer. The observed half-wave potentials ($E_{1/2}$) are all in the range 364 to 400 mV *vs.* Ag/AgCl, and they tend to increase with dendrimer generation, a reflection of the enhanced steric congestion on the surface of the larger dendrimers.

Electrochemical anion sensing experiments were carried out using square wave voltammetry (SWV) because this technique has a lower detection limit than CV. Therefore, experiments at lower concentrations of dendrimers and anions are feasible with SWV. Fig. 1 shows the SWV response of dendrimer **1** (50 μM) in 0.1 M $TBAPF_6$–DMSO. The observed peak potential corresponds to a $E_{1/2}$ value of 364 mV *vs.* Ag/AgCl, identical to



Scheme 1

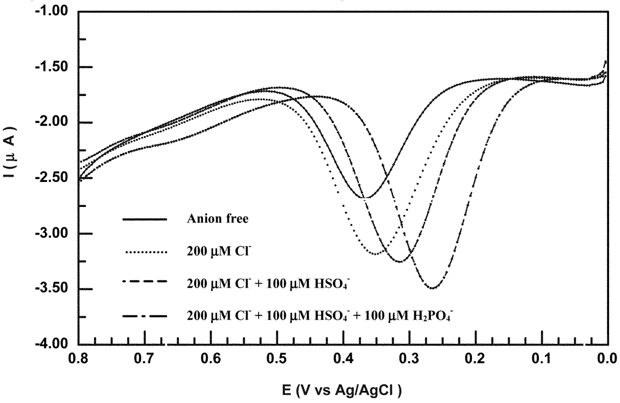


Fig. 1 Square-wave voltammograms of **1** (5×10^{-5} M) recorded in DMSO containing 0.1 M $TBAPF_6$ using a glassy-carbon working electrode, in the presence of various anions X^- added as their TBA^+ salts. Scan rate: 100 mV s^{-1}.

DOI: 10.1039/b205619d

the value observed in CV experiments. Addition of 200 μM Cl^- (as its TBA^+ salt) gives rise to a small shift of the observed $E_{1/2}$ value to 348 mV. When 200 μM of HSO_4^- (as its TBA^+ salt) was added to this solution, the half-wave potential shifts to 310 mV (see Table 1). The largest potential shift (to 248 mV) was observed upon addition of 200 μM $H_2PO_4^-$ (also as its TBA^+ salt). This shift, observed with 200 μM of each of the three anions (Cl^-, HSO_4^- and $H_2PO_4^-$) in the medium, is within a few mV of the potential shift observed with only 200 μM $H_2PO_4^-$ (in the absence of Cl^- and $H_2SO_4^-$). This finding underscores the selectivity of the ferrocenyl-urea dendrimers for the hydrogenphosphate anion.

Table 1 Cathodic perturbations of the ferrocene redox couple observed in the SWV of **1** on addition of various anions as their TBA^+ salts[a]

Equiv. X^- added per ferrocene center	$\Delta E_{1/2}$/mV[b]					
	$H_2PO_4^-$	HSO_4^-	$H_2PO_4^{-c}$	Cl^-	HSO_4^{-d}	$H_2PO_4^{-e}$
0.25	72	24	88	12		
0.50	96	32	108	12	48	104
0.75	108	36	112	16		
1.00	112	40	116	16	54	116

[a] Obtained in DMSO containing 0.1 M $TBAPF_6$. Solutions were 5×10^{-5} M in **1**. [b] $\Delta E_{1/2} = E_{1/2}$ (free) $- E_{1/2}(X^-)$. $E_{1/2}$ (free) = 364 mV. [c] In the presence of 1 equiv. of HSO_4^-. [d] In the presence of 1 equiv. of Cl^-. [e] In the presence of 1 equiv. of Cl^- and 1 equiv. of HSO_4^-.

We also explored the dependence of the half-wave potential of each dendrimer on the concentration of $H_2PO_4^-$. Fig. 2 shows the corresponding data for the third-generation dendrimer (**3**). Notice that the apparent $E_{1/2}$ value levels off at 0.5 equiv. of anion, with an equivalent defined as the anion concentration required to equal the total concentration of ferrocenyl groups. Similar results were obtained with the second-generation compound (**2**). This stoichiometry strongly suggests that each $H_2PO_4^-$ anion is bound by two ferrocenyl-urea branches (Fig. 3), in agreement with previously postulated models for the interaction of hydrogenphosphate with bis(urea) derivatives.[8]

The interaction of the first-generation dendrimer (**1**) with $H_2PO_4^-$ is weaker, as reflected by the smaller shift in the $E_{1/2}$ value observed with this system. The fourth-generation dendrimer (**4**) also seems to bind $H_2PO_4^-$ more weakly than **2** and **3**. Therefore, these macromolecules exhibit a measure of the so-called *dendrimer effect*[2a] in going from the first to the second and third generations, but the degree of steric congestion in the fourth generation seems to deteriorate the binding ability towards hydrogenphosphate. In any instance, the results reported here are remarkable because voltammetric sensing of the hydrogenphosphate anion takes place in a relatively polar solvent (DMSO), where hydrogen bonding interactions between the urea functional groups and the anion are usually weakened by competing solvent molecules. Furthermore, our data clearly show anion sensing at relatively low (sub-millimolar) anion and dendrimer concentrations, which also reflects the considerable stability of the anion complexes formed by these dendrimers.

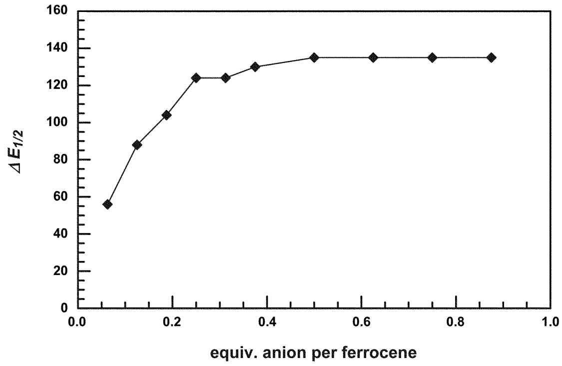


Fig. 2 Potential shift of the ferrocene redox couple *vs.* equivalents of $H_2PO_4^-$ added. Concentration of **3**: 2.5×10^{-5} M, in 0.1 M $TBAPF_6$–DMSO, scan rate 100 mV s^{-1}.

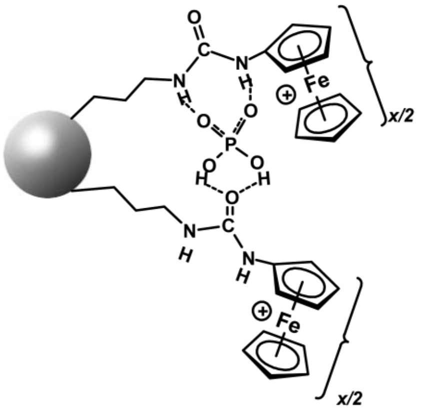


Fig. 3 Schematic representation of the double hydrogen-bonding interaction between two ferrocenium-urea branches and $H_2PO_4^-$.

The authors are grateful to the National Science Foundation (to A. E. K., CHE-9982014), the Spanish Dirección General de Investigación (BQU2001-0210), the Comunidad de Madrid (07M/0066/2000) and the Iberdrola Visiting Professor Program for the generous support of this work.

Notes and references

† Characterization data for **1**: ^1H NMR (DMSO-d_6): δ 7.55 (s, 4H, $CH_2NHCON\mathit{H}$), 5.97 (t, 4H, $CH_2N\mathit{H}CONH$), 4.41 (t, 8H, $C_5\mathit{H}_4$), 4.07 (s, 20H, Cp), 3.87 (t, 8H, $C_5\mathit{H}_4$), 3.07 (m, 8H, $NHC\mathit{H}_2$), 2.26 (br, 12H, $C\mathit{H}_2NC\mathit{H}_2$), 1.51 (br, 8H, $CH_2C\mathit{H}_2CH_2$), 1.36 (br, 4H, $NCH_2C\mathit{H}_2C\mathit{H}_2CH_2N$). $^{13}C\{^1H\}$ NMR (DMSO-d_6): δ 156.70 ($\mathit{C}O$), 69.40 (Cp), 64.12, 61.00, (C_5H_4), 51.88 and 51.56 ($\mathit{C}H_2N\mathit{C}H_2$), 38.54 (NH-$\mathit{C}H_2$), 27.12 and 25.02 ($CH_2\mathit{C}H_2CH_2$). MS (FAB; *m*/*z*): 1225 (M^+). **2**: ^1H NMR (DMSO-d_6): δ 7.53 (br, 8H, $CH_2NHCON\mathit{H}$), 6.00 (br, 8H, $CH_2N\mathit{H}CONH$), 4.41 (t, 16H, $C_5\mathit{H}_4$), 4.07 (s, 40H, Cp), 3.87 (t, 16H, $C_5\mathit{H}_4$), 3.10 (br, 16H, $NHC\mathit{H}_2$), 2.32 (br, 36H, $C\mathit{H}_2NC\mathit{H}_2$), 1.52 (br, 24H, $CH_2C\mathit{H}_2CH_2$), 1.36 (br, 4H, $NCH_2C\mathit{H}_2C\mathit{H}_2CH_2N$). $^{13}C\{^1H\}$ NMR (DMSO-d_6): δ 156.75 ($\mathit{C}O$), 69.42 (Cp), 64.15, 61.05 (C_5H_4), 52.48, 51.90 ($\mathit{C}H_2N\mathit{C}H_2$), 38.58 (NH-$\mathit{C}H_2$), 28.28 ($CH_2\mathit{C}H_2CH_2$). MS (MALDI-TOF; *m*/*z*): 2590.6 (MH^+). **3**: ^1H NMR (DMSO-d_6): δ 7.56 (br, 16H, $CH_2NHCON\mathit{H}$), 6.07 (br, 16H, $CH_2N\mathit{H}CONH$), 4.41 (br, 32H, $C_5\mathit{H}_4$), 4.07 (s, 80H, Cp), 3.87 (br, 32H, $C_5\mathit{H}_4$), 3.10 (br, 32H, $NHC\mathit{H}_2$), 2.35 (br, 84H, $C\mathit{H}_2NC\mathit{H}_2$), 1.51 (br, 56H, $CH_2C\mathit{H}_2CH_2$), 1.38 (br, 4H, $NCH_2C\mathit{H}_2C\mathit{H}_2CH_2N$). $^{13}C\{^1H\}$ NMR (DMSO-d_6): δ 156.73 ($\mathit{C}O$), 69.43 (Cp), 64.12, 61.05 (C_5H_4), 52.38, 51.80 ($\mathit{C}H_2N\mathit{C}H_2$), 38.78 (NH-$\mathit{C}H_2$), 28.14 ($CH_2\mathit{C}H_2CH_2$). MS (MALDI-TOF; *m*/z): 5319.4 (M^+). **4**: ^1H NMR (DMSO-d_6): δ 7.58 (br, 32H, $CH_2NHCON\mathit{H}$), 6.10 (br, 32H, $CH_2N\mathit{H}CONH$), 4.42 (br, 64H, $C_5\mathit{H}_4$), 4.07 (s, 160H, Cp), 3.87 (br, 64H, $C_5\mathit{H}_4$), 3.10 (br, 64H, $NHC\mathit{H}_2$), 2.33 (br, 180H, $C\mathit{H}_2NC\mathit{H}_2$), 1.54 (br, 64H, $CH_2C\mathit{H}_2CH_2$). $^{13}C\{^1H\}$ NMR (DMSO-d_6): δ 156.75 ($\mathit{C}O$), 69.40 (Cp), 64.13, 61.10 (C_5H_4), 52.36 ($\mathit{C}H_2N\mathit{C}H_2$), 38.76 (NH-$\mathit{C}H_2$), 28.25 ($CH_2\mathit{C}H_2CH_2$). MS (MALDI-TOF; *m*/*z*): 10777 (M^+).

1 For a recent review, see: P. D. Beer and P. A. Gale, *Angew. Chem., Int. Ed.*, 2001, **40**, 486.
2 (*a*) C. Valério, J.-L. Fillaut, J. Ruiz, J. Guittard, J.-C. Blais and D. Astruc, *J. Am. Chem. Soc.*, 1997, **119**, 2588; (*b*) C. Valério, E. Alonso, J. Ruiz, J.-C. Blais and D. Astruc, *Angew. Chem., Int. Ed.*, 1999, **38**, 1747.
3 (*a*) A. Labande and D. Astruc, *Chem. Commun.*, 2000, 1007; (*b*) M.-C. Daniel, J. Ruiz, S. Nlate, J. Palumbo, J.-C. Blais and D. Astruc, *Chem. Commun.*, 2001, 2000; (*c*) A. Labande, J. Ruiz and D. Astruc, *J. Am. Chem. Soc.*, 2002, **124**, 1782.
4 C. M. Casado, I. Cuadrado, B. Alonso, M. Morán and J. Losada, *J. Electroanal. Chem.*, 1999, **463**, 87.
5 H. Stephan, H. Spies, B. Johannsen, L. Klein and F. Vögtle, *Chem. Commun.*, 1999, 1875.
6 U. Boas, A. J. Karlsson, B. F. M. de Waal and E. W. Meijer, *J. Org. Chem.*, 2001, **66**, 2136.
7 (*a*) K. Schlögl and H. Seiler, *Naturwissenschaften*, 1958, **337**, 337; (*b*) F. S. Arimoto and A. C. Haven Jr., *J. Am. Chem. Soc.*, 1955, **77**, 6295.
8 T. R. Kelly and M. H. Kim, *J. Am. Chem. Soc.*, 1994, **116**, 7072.