Synthesis and anion coordination chemistry of new calix[4]arene pyridinium receptors

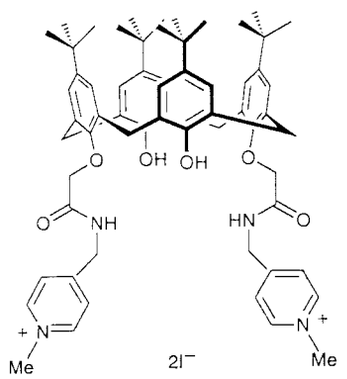
Paul D. Beer,*[a] Michael G. B. Drew[b] and Kate Gradwell[a]

[a] *Department of Chemistry, Inorganic Chemistry Laboratory, University of Oxford, South Parks Road, Oxford, UK OX1 3QR*
[b] *Department of Chemistry, University of Reading, Whiteknights, PO Box 224, Reading, UK RG6 2AD*

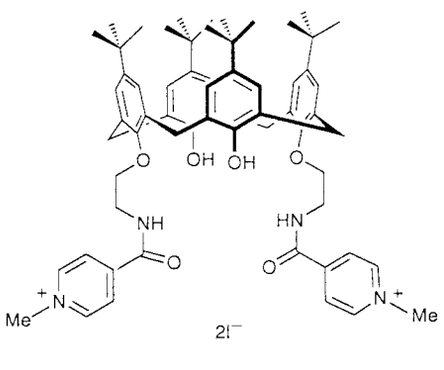
Received (in Cambridge, UK) 8th October 1999, Accepted 3rd December 1999

New lower rim substituted calix[4]arene bis-pyridinium receptors L^1, L^2 and a novel lower rim bridged calix[4]arene pyridinium receptor L^3 have been prepared and shown to bind a variety of anionic guest species. Proton NMR titration studies in deuteriated DMSO solutions reveal L^1 and L^2 to complex $H_2PO_4^-$, Cl^-, Br^-, HSO_4^- anions with $L:2X^-$ stoichiometry with L^1 exhibiting a selectivity preference for $H_2PO_4^-$. L^3 forms 1 : 1 stoichiometric complexes with Cl^- and Br^- of similar stability. Cyclic voltammetric investigations have demonstrated L^1 to electrochemically recognise $H_2PO_4^-$ and Cl^- anions.

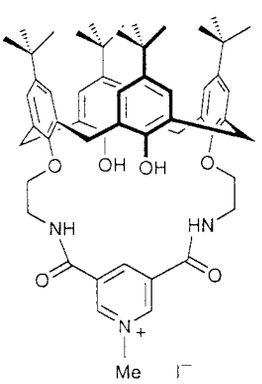
Nature utilises negatively charged species for numerous fundamental roles in biochemically important pathways and polyanions for the storage and transmission of genetic information.[1] Indeed it has been noted that anions participate in 70% of all enzymatic reactions. Also their effects as environmental pollutants have only recently been realised.[2] This has inspired chemists in recent years to synthesise receptors for anion recognition based on acyclic and macrocyclic positively charged or electron deficient molecular systems.[3,4] As part of a research programme aimed at the construction of innovative spectral and electrochemical sensory reagents for anions[5] we have recently demonstrated that simple acyclic quaternary polybipyridinium and polypyridinium receptors can bind and electrochemically sense halide anions.[6] The calixarenes[7] are attractive host molecules on which to construct additional recognition sites for anions[8] and examples of both lower[9] and upper rim[10] functionalised calix[4]arene anion receptors have appeared in the literature. By appending the calix[4]arene lower rim with redox-active positively charged pyridinium moieties we report here the synthesis and anion coordination investigations of new calix[4]arene bis-pyridinium receptors (L^1, L^2) and a novel 1,3-lower rim calix[4]arene pyridinium bridged analogue (L^3).



L^1



L^2



L^3

DOI: 10.1039/a908106b

Experimental

Instrumentation

Nuclear magnetic resonance spectra were obtained on a Bruker AM300 instrument using the solvent deuterium signal as internal reference, fast atom bombardment (FAB) mass spectra at the EPSRC mass spectrometry service, University College, Swansea. Electrochemical measurements were carried out using an E. G. and G. Princeton Applied Research 362 scanning potentiostat. Elemental analyses were performed at the Inorganic Chemistry Laboratory, University of Oxford.

Solvent and reagent pretreatment

Where necessary, solvents were purified prior to use and stored under nitrogen. Acetonitrile was predried over class 4A molecular sieves (4–8 mesh) and then distilled from calcium hydride. Unless stated to the contrary, commercial grade chemicals were used without further purification. 1,3-Bis(chlorocarbonylmethyl)-*p*-*tert*-butylcalix[4]arene (**1**)[11] and 1,3-bis(aminoethyl)-*p*-*tert*-butylcalix[4]arene (**4**)[9b] were prepared according to literature procedures.

Syntheses

5,11,17,23-Tetra-*tert*-butyl-25,27-bis[(4-pyridylmethyl)aminocarbonylmethoxy]-26,28-dihydroxycalix[4]arene (3). A solution of 1,3-bis(chlorocarbonylmethyl)-*p*-*tert*-butylcalix[4]arene (**1**)[11] (1.13 g, 1.41 mmol) dissolved in dry CH_2Cl_2 (50 mL) was added slowly dropwise to a stirred solution of 4-(aminomethyl)-pyridine (**2**) (0.31 g, 2.82 mmol) and triethylamine (0.29 g, 2.82 mmol) in dry CH_2Cl_2 (30 mL). The reaction was allowed to run to completion at room temperature (overnight), after which time the organic solution was washed (3 × 50 mL H_2O) and dried ($MgSO_4$). The solvent was removed *in vacuo* to leave the crude product, which was purified by column chromatography [silica 60 mesh 230–400; eluent—85% ethyl acetate : 15% ethanol; $R_f = 0.50$ (silica TLC plate)] and recrystallisation (CH_2Cl_2–hexane) to give the white crystalline product. Yield = 0.60 g (45%). ^{1}H NMR ($CDCl_3$) δ: 0.99 (s, 18H, *tert*-butyl-CH_3); 1.28 (s, 18H, *tert*-butyl-CH_3); 3.35 (d, ^2J = 13.5 Hz, 4H, ArCH_2Ar$_{eq}$); 4.04 (d, ^2J = 13.5 Hz, 4H, ArCH_2Ar$_{ax}$); 4.52 (s, 4H, –OCH_2–); 4.65 (d, ^3J = 5.1 Hz, 4H, –CONHCH_2py); 6.83 (s, 4H, Ar*H*); 7.03 (s, 4H, Ar*H*); 7.09 (m, 2H, py*H*); 7.30 (d, ^3J = 7.5 Hz, 2H, py*H*); 7.57 (t, ^3J = 7.5 Hz, 2H, py*H*); 8.35 (d, ^3J = 4.2 Hz, 2H, py*H*); 9.14 (t, ^3J = 5.1 Hz, 2H, –CON*H*–). ^{13}C NMR ($CDCl_3$) δ: 30.90 (*tert*-butyl-*C*H$_3$); 31.65 (*tert*-butyl-*C*H$_3$); 31.91 (Ar*C*H$_2$Ar); 33.88 (*tert*-butyl-*C*-CH$_3$); 33.98 (*tert*-butyl-*C*-CH$_3$); 45.30 (–CONH*C*H$_2$py); 74.72 (–O*C*H$_2$CONH–); 122.30 (py*C*H); 125.38, 126.05 (Ar*C*H's); 127.19, 132.04 (Ar*C*'s); 136.46 (py*C*H); 142.68, 148.11 (Ar*C*'s); 149.07 (py*C*H); 149.66 (Ar*C*); 156.85 (py*C*); 168.40 (–*C*ONH–). FAB MS *m*/*z*: 946 [M + H]$^+$; 968 [M + Na]$^+$. IR (KBr disc) ν_{max} (cm^{-1}): 3600–3200 (broad O–H, N–H stretch); 1683, 1528 (secondary amide, C=O stretch and bend). Elemental analysis of $C_{60}H_{72}O_6N_4$: Requires: 75.12% C, 7.93% H, 5.65% N; Found: 75.33% C, 7.84% H, 5.97% N.

5,11,17,23-Tetra-*tert*-butyl-25,27-bis[2-(4-pyridylcarbonylamino)ethoxy]-26,28-dihydroxycalix[4]arene (6). 4-(Chlorocarbonyl)pyridine (**5**) (0.38 g, 2.72 mmol) was dissolved in dry CH_2Cl_2 (60 mL) and this was added slowly dropwise to a stirred solution of 1,3-bis(aminoethyl)-*p*-*tert*-butylcalix[4]arene (**4**) (1.00 g, 1.36 mmol) and triethylamine (0.26 g, 2.72 mmol) also in dry CH_2Cl_2 (100 mL). The reaction mixture was stirred for 16 h under N_2 at room temperature. After this time the solution was washed (2 × 75 mL H_2O) and the organic layer was dried ($MgSO_4$) and the solvent removed under reduced pressure. Purification was carried out by column chromatography (silica 60 mesh 230–400; eluent—95% CH_2Cl_2 : 5% MeOH; second fraction collected $R_f = 0.72$) to give a white crystalline solid after evaporation. Yield = 0.82 g (64%). ^{1}H NMR ($CDCl_3$) δ: 1.08 (s, 18H, *tert*-butyl-CH_3); 1.25 (s, 18H, *tert*-butyl-CH_3); 3.42 (d, ^2J = 13.0 Hz, 4H, ArCH_2Ar$_{eq}$); 3.48 (s, CH_3OH); 3.52 (dt, ^3J = 4.5 Hz, 4H, –CH_2NH–); 4.01 (t, ^3J = 4.5 Hz, 4H, –CH_2O–); 4.11 (d, ^2J = 13.0 Hz, 4H, ArCH_2Ar$_{ax}$); 6.98 (s, 4H, Ar*H*); 7.07 (s, 4H, Ar*H*); 7.77 (d, ^3J = 6.0 Hz, 4H, py*H*); 8.22 (s, 2H, –O*H*); 8.50 (t, 2H, –CON*H*–); 8.58 (d, ^3J = 6.0 Hz, 4H, py*H*). ^{13}C NMR ($CDCl_3$) δ: 31.07, 31.65 (*tert*-butyl-*C*H$_3$'s); 32.08 (Ar*C*H$_2$Ar); 33.95, 34.19 (*tert*-butyl-*C*-CH$_3$'s); 39.84 (–*C*H$_2$NH–); 74.57 (–O*C*H$_2$–); 121.63 (py*C*H); 125.77, 126.10 (Ar*C*H's); 127.44, 132.61, 141.61, 143.16, 148.25 (Ar*C*'s); 149.18 (py*C*); 150.33 (py*C*H); 165.94 (–*C*ONH–). FAB MS *m*/*z*: 945 [M + H]$^+$; 967 [M + Na]$^+$. IR (KBr disc) ν_{max} (cm^{-1}): 3600–3200 (O–H, N–H stretches); 1672 (secondary amide C=O stretch); 1600 (secondary amide –CONH– bend). Elemental analysis for $C_{60}H_{72}N_6O_6\cdot CH_3OH$: Requires: 74.97% C, 7.84% H, 5.73% N; Found: 74.92% C, 7.81% H, 5.85% N.

5,11,17,23-Tetra-*tert*-butyl-25,27-{pyridine-3,5-diylbis[2-(carbonylamino)ethoxy]}-26,28-dihydroxycalix[4]arene (8). A solution of **4** (0.50 g, 0.68 mmol), triethylamine (0.2 g, 1.95 mmol) in dry CH_2Cl_2 (100 mL) was added dropwise to a solution of 3,5-bis(chlorocarbonyl)pyridine (**7**) (0.17 g, 0.82 mmol) in CH_2Cl_2 (100 mL). The reaction mixture was left to stir at room temperature for 16 h. The CH_2Cl_2 solution was washed (1 × 80 mL dil. HCl, 2 × 80 mL H_2O), dried ($MgSO_4$) and the solvent removed *in vacuo*. Purification was carried out by column chromatography (silica 230–400; eluent—90% ethyl acetate : 10% ethanol) and yielded both the desired product as well as the [2 + 2] dimer. Yield of [1 + 1] product (**8**) = 0.11 g (19%), dimer (**9**) 0.2 g (17%).

(**8**) ^{1}H NMR ($CDCl_3$) δ: 0.86 (s, 18H, *tert*-butyl-CH_3); 1.32 (s, 18H, *tert*-butyl-CH_3); 3.38 (d, ^2J = 13.5 Hz, 4H, ArCH_2Ar$_{eq}$); 3.96 (m, 4H, –CH_2NH–); 4.17–4.26 (overlapping d and m, 8H, ArCH_2Ar$_{ax}$ and –CH_2O–); 6.19 (s, 2H, –O*H*); 6.68 (s, 4H, Ar*H*); 7.10 (s, 4H, Ar*H*); 7.98 (t, 2H, –CON*H*–); 8.76 (t, ^4J = 2.0 Hz, 1H, *p*-py*H*); 9.32 (d, ^4J = 2.0 Hz, *o*-py*H*). FAB MS *m*/*z*: 867 [M + H]$^+$; 889 [M + Na]$^+$. Elemental analysis for $C_{55}H_{67}O_6N_3$: Requires: 72.67% C, 7.52% H, 4.58% N; Found: 72.24% C, 7.40% H, 4.44% N.

(**9**) ^{1}H NMR ($CDCl_3$) δ: 0.94 (s, 18H, *tert*-butyl-CH_3); 1.29 (s, 18H, *tert*-butyl-CH_3); 2.11 (*H*$_2$O); 3.34 (d, ^2J = 13.2 Hz, 4H, ArCH_2Ar$_{eq}$); 3.59 (br, 4H, –OCH_2–); 4.08 (m, 4H, –CH_2NH–); 4.18 (d, ^2J = 13.2 Hz, 4H, ArCH_2Ar$_{ax}$); 6.77 (s, 4H, Ar*H*); 7.03 (s, 4H, Ar*H*); 7.09 (s, 2H, –O*H*); 8.42 (t, 2H, –CON*H*–); 8.91 (t, ^4J = 1.8 Hz, *p*-py*H*); 9.21 (d, ^4J = 1.8 Hz, 2H, *o*-py*H*). ^{13}C NMR ($CDCl_3$) δ: 30.87 (*tert*-butyl-*C*H$_3$); 31.46 (Ar*C*H$_2$Ar); 31.65 (*tert*-butyl-*C*H$_3$); 33.86, 33.92 (*tert*-butyl-*C*-CH$_3$'s); 39.86 (–*C*H$_2$NH–); 73.54 (–*C*H$_2$O–); 125.42, 125.76 (Ar*C*H's); 128.11, 128.86, 131.52 (Ar*C*'s); 132.45 (py*C*H); 142.99, 147.52, 149.54, 149.96 (Ar*C*'s/py*C*); 152.08 (py*C*H); 165.16 (–NH*C*O–). ^{13}C NMR DEPT ($CDCl_3$) δ: 30.87 (CH_3); 31.46 (CH_2); 31.65 (CH_3); 39.86, 73.54 (CH_2's); 125.42, 125.76, 132.45, 152.08 (CH's). FAB MS *m*/*z*: 1732 [M]$^+$; 1733 [M + H]$^+$; 1755 [M + Na]$^+$. Elemental analysis for $C_{110}H_{134}O_{12}N_6\cdot CH_2Cl_2\cdot H_2O$: Requires: 72.67% C, 7.52% H, 4.58% N; Found: 72.56% C, 7.59% H, 4.58% N.

5,11,17,23-Tetra-*tert*-butyl-25,27-[pyridine-2,6-diylbis(aminocarbonylmethoxy)]-26,28-dihydroxycalix[4]arene (11). A suspension of (**1**) (0.78 g, 0.97 mmol) in dry CH_2Cl_2 (100 mL) was stirred under N_2. A second solution of 2,6-diaminopyridine (**10**) (0.11 g, 0.97 mmol) and triethylamine (0.20 g, 1.95 mmol) in CH_2Cl_2 (100 mL) was then added slowly dropwise and the reaction mixture was left to stir for 16 h. After this time the crude product was washed (1 × 80 mL dil. HCl, 2 × 80 mL H_2O), dried ($MgSO_4$) and the solvent removed under reduced pressure. Further purification was carried out by column chromatography [silica mesh 230–400; eluent—90% ethyl acetate : 10% ethanol; $R_f = 0.69$ (silica TLC plates)] and recrystallisation

(CH_2Cl_2–hexane) to leave the product as a white crystalline solid. Yield = 0.20 g (24%). ^{1}H NMR ($CDCl_3$) assigned with the aid of ^{1}H–^{1}H 2D correlation (Gradient HSQC, $CDCl_3$) δ: 1.14 (s, 18H, *tert*-butyl-CH_3); 1.21 (s, 18H, *tert*-butyl-CH_3); 3.45 (d, ^2J = 13.5 Hz, 4H, ArCH_2Ar$_{eq}$) correlated to 4.16; 4.16 (br, 4H, ArCH_2Ar$_{ax}$) correlated to 3.45; 4.63 (br, 2H, –OCH_2CO-a); 4.96 (br, 2H, –OCH_2CO-b); 6.67 (br, 1H, *m*-py*H*) correlated to 7.75; 7.02 (s, 4H, Ar*H*); 7.04 (s, 4H, Ar*H*); 7.75 (t, 1H, *p*-py*H*) correlated to 6.67 and 8.06; 8.06 (br, 1H, *m*-py*H*) correlated to 7.75; 8.16 (br s, 1H, –O*H*); 8.22 (br s, 2H, –CON*H*–); 11.35 (br s, 1H, –O*H*). ^{13}C NMR ($CDCl_3$) assigned with the aid of ^{13}C–^{1}H 2D correlation (Gradient HSQC, $CDCl_3$) δ: 29.66 (*tert*-butyl-*C*-CH$_3$); 31.14 (*tert*-butyl-*C*H$_3$) correlated to 1.14 (*tert*-butyl-CH_3); 31.57 (*tert*-butyl-*C*H$_3$) correlated to 1.21 (*tert*-butyl-CH_3); 32.53, 32.96 (Ar*C*H$_2$Ar's) correlated to 3.45, 4.16 (ArCH_2Ar's); 33.79 (–O*C*H$_2$CO–) correlated to 4.63, 4.96 (–OCH_2CO–); 109.32 (py*C*H) correlated to 6.67 (py*H*); 110.05 (py*C*H) correlated to 8.06 (py*H*); 125.55 (Ar*C*H) correlated to 7.02 (Ar*H*); 126.18 (Ar*C*H) correlated to 7.04 (Ar*H*); 126.83, 127.04, 132.06, 132.71 (Ar*C*'s); 140.93 (py*C*H) correlated to 7.75 (py*H*); 142.22, 150.13 (Ar*C*'s); 169.20 (–NH*C*O–). FAB MS *m*/*z*: 839 [M + H]$^+$. IR (KBr disc) ν_{max} (cm^{-1}): 3600–3200 (O–H, N–H stretches); 1707, 1685 (inequivalent secondary amide C=O stretches); 1586, 1546 (inequivalent amide N–H bends). Elemental analysis of $C_{53}H_{63}O_6N_3$: Requires: 75.99% C, 7.53% H, 5.02% N; Found: 76.18% C, 7.63% H, 5.15% N.

5,11,17,23-Tetra-*tert*-butyl-25,27-{pyridine-2,6-diylbis[2-(carbonylamino)ethoxy]}-26,28-dihydroxycalix[4]arene (13). A similar procedure to that used to prepare compound **11** was used to make this new bridged pyridine amide calix[4]arene from the starting materials: **4** (1.80 g, 2.45 mmol) and pyridine-2,6-dicarbonyl chloride (**12**) (0.50 g, 2.45 mmol). The crude material was purified by column chromatography [silica 230–400; eluent—95% CH_2Cl_2 : 5% MeOH; R_f = 0.78 (silica TLC plates)] and recrystallisation (CH_2Cl_2–hexane) to give the product as a white solid. Yield = 0.66 g (31%). ^{1}H NMR ($CDCl_3$) δ: 0.89 (s, 18H, *tert*-butyl-CH_3); 1.30 (s, 18H, *tert*-butyl-CH_3); 3.32 (d, ^2J = 13.0 Hz, 4H, ArCH_2Ar$_{eq}$); 4.07 (m, 4H, –CH_2NH–); 4.18 (overlapping m, 8H, ArCH_2Ar$_{ax}$ and –CH_2O–); 6.73 (s, 4H, Ar*H*); 6.76 (s, 2H, –O*H*); 7.07 (s, 4H, Ar*H*); 7.94 (t, ^3J = 7.5 Hz, 1H, py*H*); 8.32 (d, ^3J = 7.5 Hz, 2H, py*H*); 9.04 (t, 2H, –CON*H*–). ^{13}C NMR ($CDCl_3$) assigned with the aid of ^{1}H–^{13}C 2D correlation (Gradient HSQC, $CDCl_3$) δ: 30.82 (*tert*-butyl-*C*H$_3$); 31.27 (Ar*C*H$_2$Ar); 31.66 (*tert*-butyl-*C*H$_3$); 33.78, 39.37 (*tert*-butyl-*C*-CH$_3$); 53.21 (–*C*H$_2$NH–); 74.23 (–*C*H$_2$Oar–); 124.72 (py*C*H) correlated to 8.32 (py*H*); 124.97 (Ar*C*H) correlated to 7.07 (Ar*H*); 125.54 (Ar*C*H) correlated to 6.73 (Ar*H*); 127.76, 131.84 (Ar*C*'s); 138.83 (py*C*H) correlated to 7.94 (py*H*) and less so to 8.32 (py*H*); 141.93, 147.20, 148.43, 149.31, 150.08 (Ar*C*'s); 163.75 (–NH*C*O–). FAB MS *m*/*z*: 866 [M + H]$^+$; 888 [M + Na]$^+$. IR (KBr disc) ν_{max} (cm^{-1}): 3600–3200 (O–H, N–H stretches); 2960–2870 (CH_2, CH_3 stretches); 1683 (secondary amide C=O stretch); 1536 (secondary amide CONH bend). Elemental analysis of $C_{55}H_{67}O_6N_3$: Requires: 76.26% C, 7.80% H, 4.85% N; Found: 75.92% C, 7.82% H, 4.26% N.

5,11,17,23-Tetra-*tert*-butyl-25,27-bis[(*N*-methylpyridinium-4-yl)methylaminocarbonylmethoxy iodide]-26,28-dihydroxycalix-[4]arene L^1. Compound **3** (0.18 g, 0.19 mmol) was refluxed for 20 h in excess methyl iodide (75 mL). The reaction mixture changed from colourless to yellow and was monitored by TLC (85% CH_2Cl_2 : 15% MeOH; silica TLC plates; product sticks to base-line) until the reaction was complete. The methyl iodide was removed by distillation and the last traces under high vacuum to leave a pale yellow solid, which required no further purification. Yield = 0.23 g (100%). ^{1}H NMR ($CDCl_3$) δ: 0.96 (s, 18H, *tert*-butyl-CH_3); 1.30 (s, 18H, *tert*-butyl-CH_3); 2.13 (H_2O); 3.39 (d, ^2J = 13.2 Hz, 4H, ArCH_2Ar$_{eq}$); 4.16 (d, ^2J = 13.2 Hz, 4H, ArCH_2Ar$_{ax}$); 4.63 (s, 6H, –N$^+$–CH_3); 4.69 (s, 4H, –OCH_2CONH–); 5.14 (d, ^3J = 5.5 Hz, 4H, pyCH_2NH–); 6.82 (s, 4H, Ar*H*); 7.09 (s, 4H, Ar*H*); 7.42 (s, 2H, –O*H*); 7.85 (dd, $^3J^1$ = 6.5 Hz, $^4J^2$ = 1.5 Hz, 2H, py*H*); 8.26 (m, 4H, py*H*'s); 8.82 (d, ^3J = 6.5 Hz, py*H*); 9.31 (t, ^3J = 5.5 Hz, 2H, –CON*H*–). ^{13}C NMR ($CDCl_3$) δ: 30.93, 31.68 (*tert*-butyl-*C*H$_3$'s); 31.91 (Ar*C*H$_2$Ar); 33.93, 33.96 (*tert*-butyl-*C*–CH$_3$'s); 41.16 (py*C*H$_2$NH–); 47.96 (–O*C*H$_2$CO–); 74.26 (–N$^+$–*C*H$_3$); 125.47, 125.95, 126.66, 127.55, 129.03, 132.08, 142.72, 145.33, 146.45, 147.96, 149.17, 149.72, 155.20 (Ar*C*/Ar*C*H/py*C*/py*C*H's); 170.02 (–*C*ONH–). FAB MS *m*/*z*: 1102 [M − I$^-$]$^+$; 974 [M − 2I$^-$]$^+$. Elemental analysis for $C_{62}H_{78}N_4O_6I_2\cdot 3H_2O$: Requires: 58.03% C, 6.55% H, 4.37% N; Found: 58.22% C, 6.64% H, 4.33% N.

5,11,17,23-Tetra-*tert*-butyl-25,27-bis[2-(*N*-methylpyridinium-4-yl)carbonylaminoethoxy iodide]-26,28-dihydroxycalix[4]arene L^2. Compound **6** (0.10 g, 0.11 mmol) was refluxed in methyl iodide (20 mL) for 22 h. During this time a precipitate was seen to form, and the solution changed from colourless to orange. The solvent was removed by distillation and the product dried thoroughly under high vacuum to leave a yellow solid. Yield = 0.12 g (92.2%). ^{1}H NMR (d$_6$-DMSO) δ: 1.10 (s, 18H, *tert*-butyl–CH_3); 1.18 (s, 18H, *tert*-butyl–CH_3); 2.16 (s, CH_3I); 3.41 (d overlaid by d$_6$-DMSO peak, ArCH_2Ar$_{eq}$); 3.90 (m, 4H, –CH_2NH–); 4.18 (d and m overlaid, 8H, ArCH_2Ar$_{ax}$ and –CH_2O–); 4.39 (s, 6H, pyN^+–CH_3); 7.13 (s, 4H, Ar*H*); 7.14 (s, 4H, Ar*H*); 8.22 (s, 2H, –O*H*); 8.45 (d, ^3J = 5.9 Hz, 4H, py*H*); 9.18 (d, ^3J = 5.9 Hz, 4H, py*H*); 9.50 (m, 2H, –CON*H*–). ^{13}C NMR (d$_6$-DMSO) δ: 30.84 (*tert*-butyl-*C*H$_3$); 31.13 (Ar*C*H$_2$Ar); 31.35 (*tert*-butyl-*C*H$_3$); 33.60, 33.97 (*tert*-butyl-*C*–CH$_3$'s); 48.17 (–*C*H$_2$NH–); 73.54 (–O*C*H$_2$–); 125.28 (pyN^+–*C*H$_3$); 125.67, 127.53, 132.87, 141.58, 147.19, 147.88, 149.43, 149.72 (py*C*/py*C*H/Ar*C*/Ar*C*H's); 162.60 (–*C*ONH–). FAB MS *m*/*z*: 1102 [M − I$^-$]$^+$; 975 [M − 2I$^-$]$^+$; 960 [M − 2I$^-$ − CH$_3$]$^+$. IR (KBr disc) ν (cm^{-1}): 3600–3200 (O–H, N–H stretches); 3040–2868 (CH_2, CH_3 stretches); 1671 (secondary amide C=O stretch); 1646 (secondary amide CONH bend). Elemental analysis for $C_{62}H_{78}O_6N_4I\cdot 2MeI$: Requires: 55.46% C, 6.11% H, 4.04% N; Found: 56.32% C, 6.08% H, 4.20% N.

5,11,17,23-Tetra-*tert*-butyl-25,27-{*N*-methylpyridinium-3,5-diylbis[2-(carbonylamino)ethoxy] iodide}-26,28-dihydroxycalix-[4]arene L^3. A 50 mL flask was charged with compound **8** (0.02 g, 0.023 mmol) and methyl iodide (15 mL). The mixture was refluxed for 80 h under N_2 during which time the formation of a yellow precipitate was observed and the precipitate was isolated by filtration. Yield = 0.020 g (95%). ^{1}H NMR (d$_6$-DMSO) δ: 1.14 (s, 18H, *tert*-butyl-CH_3); 1.19 (s, 18H, *tert*-butyl-CH_3); 3.48 (d, ^2J = 12.5 Hz, 4H, ArCH_2Ar$_{eq}$); 3.80 (br, 4H, –OCH_2–); 4.10 (m, 4H, –CH_2NH–); 4.17 (s, 3H, pyN^+–CH_3); 4.25 (d, ^2J = 12.5 Hz, 4H, ArCH_2Ar$_{ax}$); 7.19 (s, 8H, Ar*H*); 8.46 (s, 2H, –O*H*); 9.34 (s, 1H, *p*-py*H*); 9.47 (br overlaid s, 4H, –CON*H*– and *m*-py*H*). FAB MS *m*/*z*: 881 [M − I$^-$]$^+$. Elemental analysis for $C_{56}H_{70}O_6N_3I$: Requires: 66.73% C, 6.95% H, 4.17% N; Found: 66.12% C, 6.86% H, 4.32% N.

Crystallography †

Crystal data (Table 1) were collected with MoKα radiation using the MARresearch Image Plate System. Data analysis was carried out with the XDS program.[12] The structure was solved using direct methods with the SHELX86 program.[13] The non-hydrogen atoms were refined with anisotropic thermal parameters. The hydrogen atoms were included in geometric positions and given thermal parameters equivalent to 1.2 times those of the atom to which they were attached. Refinement for **3**

† CCDC reference number 188/213. See http://www.rsc.org/suppdata/p2/a9/a908106b/ for crystallographic files in .cif format.

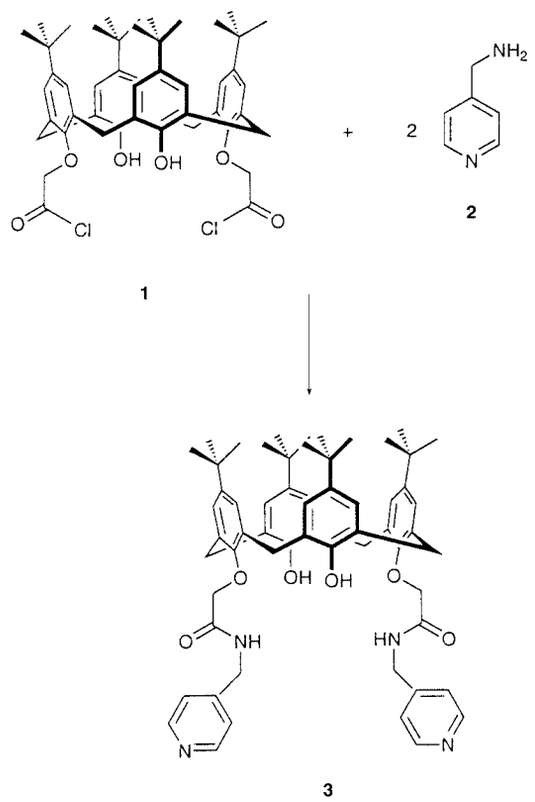
Table 1 Crystal data and structure refinement for **3**, **6**, **11** and **13**

Compound	**3**	**6**	**11**	**13**
Empirical formula	$C_{60}H_{80}N_4O_6$	$C_{61}H_{72}N_4O_5$	$C_{57}H_{88}C_{14}N_3O_{11.5}$	$C_{61}H_{40}N_6O_6$
Formula weight	953.28	941.22	1141.10	952.99
Temperature/K	293(2)	293(2)	293(2)	293(2)
Wavelength/Å	0.71073	0.71073	0.71073	0.71073
Crystal system, space group	Monoclinic, *I*2/*c*	Triclinic, $P\bar{1}$	Triclinic, $P\bar{1}$	Orthorhombic, *Pnma*
Units cell dimensions *a*/Å	22.32(2)	10.442(7)	11.197(14)	28.00(2)
b/Å	21.09(2)	13.208(9)	14.68(2)	15.619(14)
c/Å	22.89(2)	23.11(2)	17.61(2)	13.818(14)
α/°	(90)	72.32(1)	90.17(1)	(90)
β/°	94.58(1)	85.09(1)	97.25(1)	(90)
γ/°	(90)	73.50(1)	92.82(1)	(90)
Volume/Å^3	10 744	2912	2868	6042
Z Calculated density/Mg m^{-3}	8, 1.179	2, 1.074	2, 1.321	4, 1.048
Absorption coefficient/mm^{-1}	0.075	0.068	0.269	0.069
Reflections collected/unique	16974/8873	6654	8701	14628/4203
R(int)	0.0529	—	—	0.0470
Data/restraints/parameters	8873/0/645	6654/0/646	8701/0/660	4203/9/368
Final *R* indices [$I > 2\sigma(I)$] *R*1	0.0973	0.0793	0.0561	0.0492
*wR*2	0.1999	0.2218	0.1676	0.1373
R indices (all data) *R*1	0.1851	0.1096	0.0761	0.0816
*wR*2	0.2382	0.2453	0.1745	0.1483

and **6** was straightforward. **11** contained one dichloromethane molecule with full occupancy and two with 50% occupancy, one methanol refined with full occupancy and four water molecules, two of which were refined with full occupancy and two with 50% occupancy. In **13** the calix[4]arene contains a crystallographic mirror plane passing through the axis of the calixarene and bisecting two of the phenyl rings. The two *tert*-butyl groups attached to these rings had two sets of positions which were refined with 50% occupancy. In addition there were three acetonitrile molecules, two of which were situated on crystallographic mirror planes and the third was in a general position but refined with 50% occupancy. The four structures were all refined on F^2 using SHELXL[14] to convergence.

^{1}H NMR titrations

A solution of the receptor (500 μl) was prepared at a concentration typically of the order of 0.01 mol dm^{-3} in deuteriated DMSO. The initial ^{1}H NMR spectrum was recorded and aliquots of anion were added by gas-tight syringe from a solution made such that 1 mole equivalent was added in 20 μl. After each addition and mixing, the spectrum was recorded again and changes in the chemical shift of certain protons were noted. The result of the experiment was a plot of displacement in chemical shift as a function of the amount of added anion, which was subjected to analysis by curve-fitting since the shape is indicative of the stability constant for the complex. The computer program EQNMR[15] was used which requires the concentration of each component and the observed chemical shift (or its displacement) for each data point. Typically these titration experiments were repeated three times with at least 15 data points in each experiment.



Scheme 1

Results and discussion

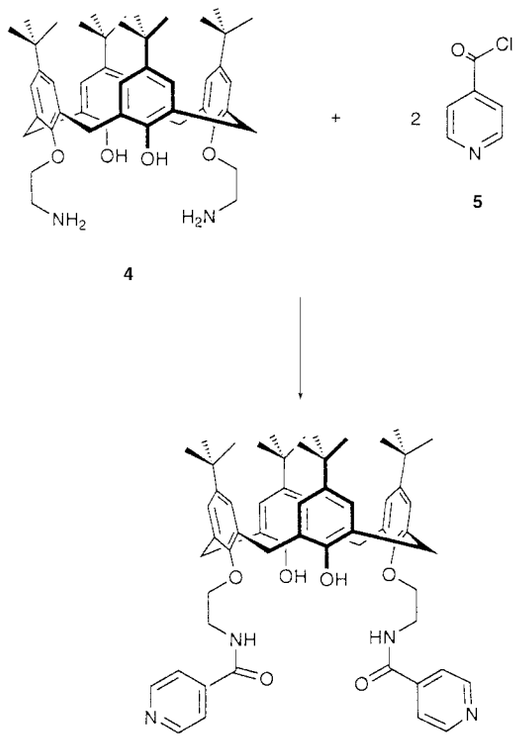
Syntheses of lower rim pyridinium calix[4]arene receptors

Whilst Pappalardo[16] and others[17] have prepared a variety of pyridine appended calixarenes, primarily for metal cation coordination, to the best of our knowledge pyridinium analogues for anion recognition have not been reported.

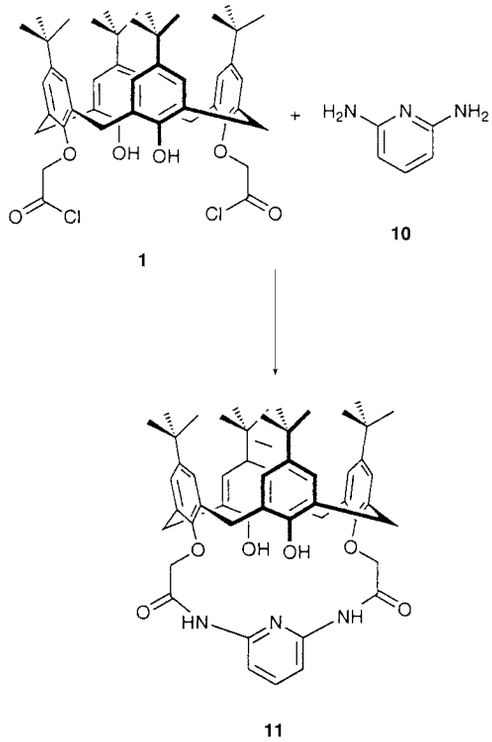
The condensation of 1,3-lower rim substituted bis(chlorocarbonyl) calix[4]arene **1**[11] with two equivalents of 4-(aminomethyl)pyridine (**2**) gave the corresponding bis-pyridine amide calix[4]arene (**3**) in 45% yield (Scheme 1). The reaction of 1,3-lower rim substituted bis(aminoethyl) calix[4]arene (**4**)[9b] with two equivalents of 4-(chlorocarbonyl)pyridine (**5**) afforded the corresponding bis-pyridine amide calix[4]arene (**6**) in 64% yield (Scheme 2). The condensation of 3,5-bis(chlorocarbonyl)pyridine (**7**) and **4** in the presence of trimethylamine gave the desired [1 + 1] product (**8**) in 19% yield and the [2 + 2] dimeric compound (**9**) in 17% yield (Scheme 3). The addition of 2,6-diaminopyridine (**10**) to a dry dichloromethane solution of **1** in the presence of triethylamine produced **11** as a white solid in 24% yield (Scheme 4). In a similar condensation reaction between 2,6-bis(chlorocarbonyl)pyridine (**12**) and **4**, the new lower rim bridged calix[4]arene **13** was isolated in 31% yield (Scheme 5). Quaternisation reactions of **3**, **6** and **8** with methyl iodide produced the calix[4]arene pyridinium receptors L^1, L^2 and L^3 in near quantitative yields. Analogous quaternisation reactions with methyl iodide or dimethyl

sulfate with **11** and **13** were disappointingly unsuccessful, only starting materials were recovered from the reaction mixtures. These findings suggest the pyridyl nitrogen in these receptors is sterically inaccessible to methylation.

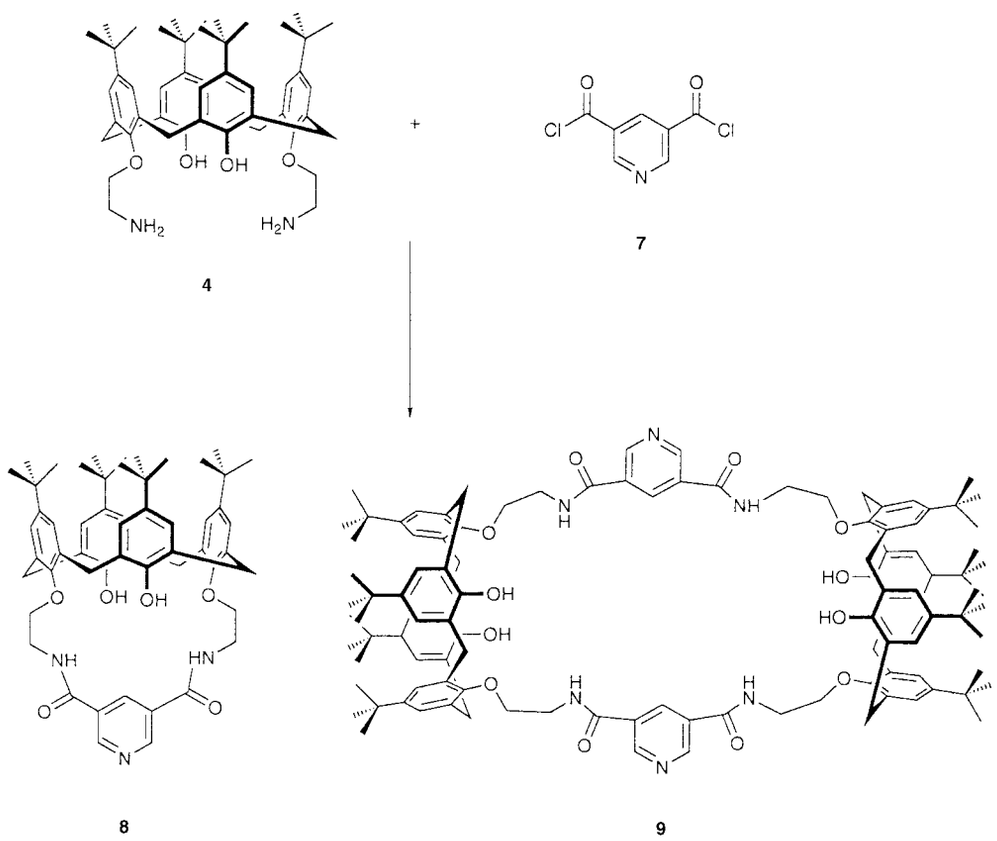
All of these new pyridine and pyridinium functionalised calix[4]arenes were characterised by ^{1}H, ^{13}C NMR, fast atom bombardment mass spectrometry and elemental analyses. (See Experimental section). In all cases the single AB pair of doublets observed for the methylene calix[4]arene protons in the ^{1}H NMR spectra and the ^{13}C NMR chemical shift of



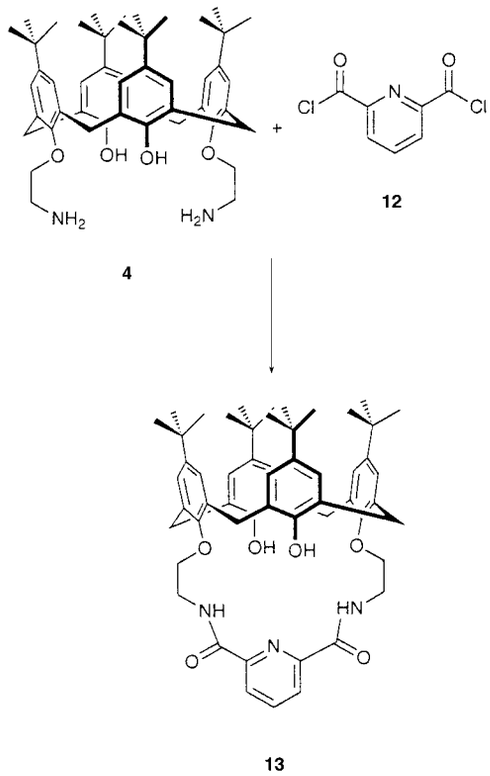
Scheme 2



Scheme 4



Scheme 3



Scheme 5

the methylene calix[4]arene carbons in the 32 ppm region are characteristic of the calix[4]arene moieties being in the cone conformation.[18]

X-Ray structural investigations of 3, 6, 11 and 13

Crystals of **3** and **13** were grown from slow evaporation of dilute dichloromethane–hexane solutions whilst for **6** and **11**, dichloromethane–methanol was the solvent mixture of choice.

The four structures have equivalent numbering schemes such that O(150) and O(350) represent the unsubstituted phenolic hydroxys at the lower rim and O(250) and O(450) are substituted with the particular diamides. In all four structures the calix[4]arene has a distorted cone conformation. The distortion can be seen from the least squares planes calculations in Table 2 which show the angles of intersection between the phenyl rings and the plane of the four methylene carbon atoms. In all four cases the angles subtended by the unsubstituted rings 1 and 3 are between 38.7 and 52.5°, significantly less than the angles subtended by the substituted rings 2 and 4, which range between 64.4 and 87.0°. All four structures show interesting and different patterns of intramolecular hydrogen bonds around the bottom rim of the calix[4]arene involving the oxygen atoms both substituted and unsubstituted and the amide groups and these are listed in Table 3.

The structure of **3** is shown in Fig. 1 together with the atomic numbering scheme. There are two strong hydrogen bonds at the bottom rim between oxygen atoms, *viz* O(150)–H···O(250) and O(350)–H···O(450) at 2.678, 2.760 Å respectively. In addition the two N–H groups form hydrogen bonds with the phenolic–OH groups N(253)···O(350) 3.077, N(453)···O(150) 3.341 Å. There are also 1–4 contacts between these amide groups and adjacent oxygen O(250)···N(253) 2.603, O(450)···N(453) 2.632 Å which could represent weak hydrogen bonds. The torsion angles O(*n*50)–C(*n*51)–C(*n*52)–N(*n*53) are −6.3° (for $n = 2$), −18.6° (for $n = 4$). A similar weak interaction is found between the nitrogen atom of one of the pyridine rings and an amide nitrogen, *viz* N(461)···N(453) 2.731 Å and this could also represent a weak hydrogen bond. In **3** no intermolecular hydrogen bonds are found.

Table 2 Least squares planes. Angles of intersection (°) are given between the four phenyl rings and the plane of the four methylene atoms

	Structure			
	3	**6**	**11**	**13**
Ring 1	48.0	42.7	45.4	38.7
Ring 2	64.4	81.1	71.5	69.5
Ring 3	47.8	39.1	48.0	52.5
Ring 4	72.6	87.0	68.9	69.5

Table 3 Hydrogen bond distances/Å

In **3**		In **11**	
O(150)···O(250)	2.678	O(150)···O(250)	2.673
O(350)···O(450)	2.760	O(250)···N(253)	2.545
N(253)···O(350)	3.077	O(254)···O(7)	2.782
N(453)···O(150)	3.341	N(253)···O(350)	3.030
O(250)···N(253)	2.603	N(253)···Cl(3)$1	3.325
O(450)···N(453)	2.632	O(350)···O(450)	2.673
N(453)···N(461)	2.731	O(350)···O(5)$1	3.155
		N(51)···O(5)$1	3.116
		N(453)···O(7)$2	2.932
In **6**		In **13**	
O(350)···O(250)	2.908	O(150)···O(250)	2.837
O(150)···O(450)	3.270	O(250)···O(350)	2.924
N(253)···O(454)	2.963	N(253)···N(257)	2.622
N(453)···O(254)$1	3.136	N(253)···N(500)	3.219
$1 Symmetry element $1 + x, y, z$.		Symmetry elements $1 $1 − x, 1 − y, 1 − z$; $2 $x − 1, y, z$.	

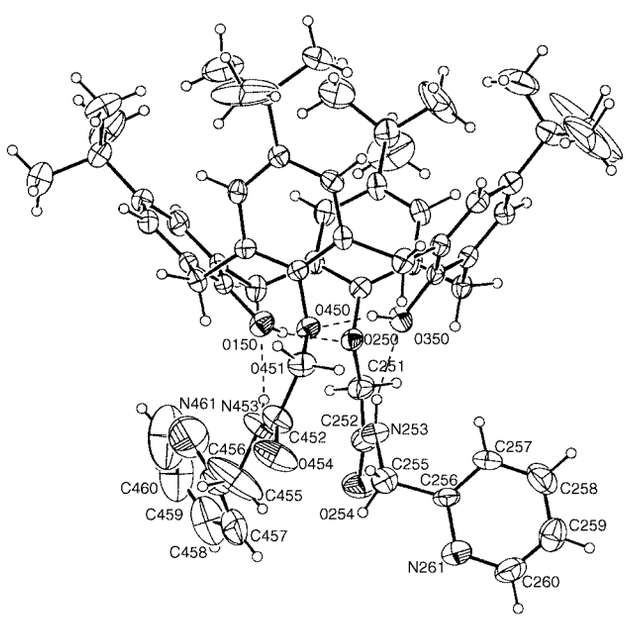


Fig. 1 The structure of **3** with ellipsoids at 30% occupancy. Hydrogen bonds shown as dashed lines.

The structure of **6** is shown in Fig. 2 together with the atomic numbering scheme. There are intramolecular hydrogen bonds between lower rim oxygen atoms, *viz* O(350)–H···O)(250) 2.908, O(150)–H···O(450) 3.270 Å. However in this case only one of the amide nitrogen atoms is involved in an intramolecular hydrogen bond, and this bond N(253)···O(454) 2.963 Å involves the adjacent amide oxygen rather than an oxygen atom at the lower rim as in **3**. The second amide nitrogen is involved in an intermolecular hydrogen bond N(453)···O(254)$1 at 3.136 Å to an adjacent molecule. The 1,4 interactions (*vide supra*) between O(*n*50) and N(*n*53) are much longer than in **3** (2.852, 2.941Å) and are concomit-

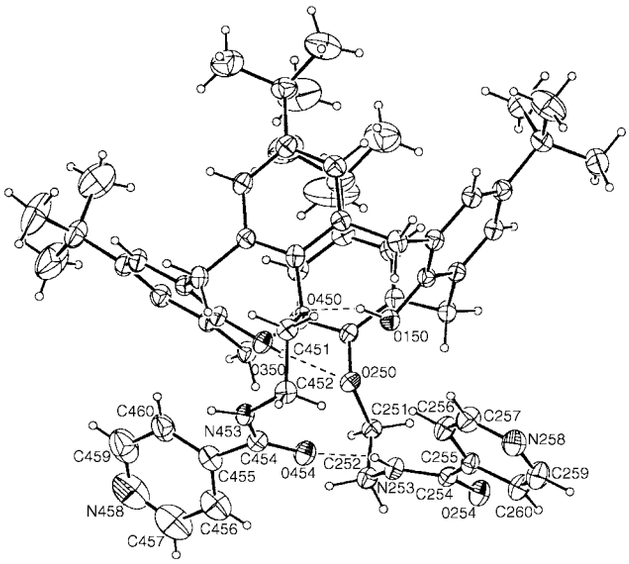


Fig. 2 The structure of **6** with ellipsoids at 30% occupancy. Hydrogen bonds shown as dashed lines.

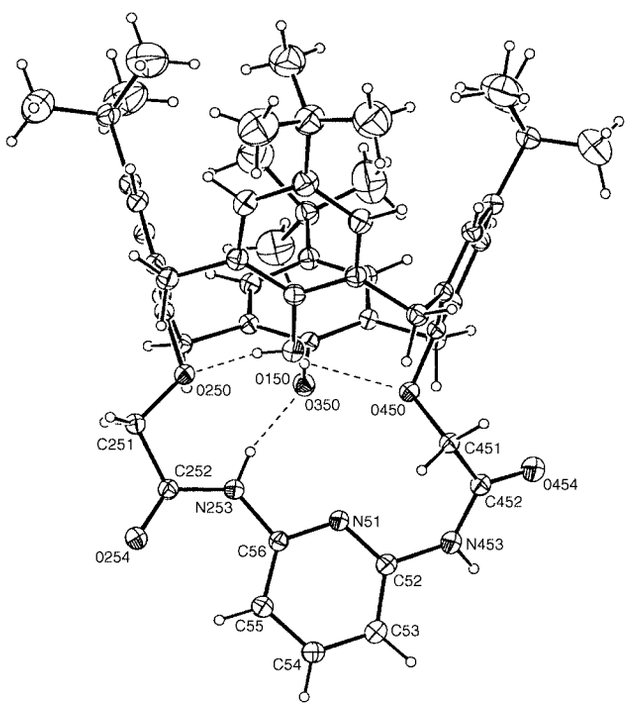


Fig. 3 The structure of **11** with ellipsoids at 30% occupancy. Hydrogen bonds shown as dashed lines.

ant with O(*n*50)–C(*n*51)–C(*n*52)–N(*n*53) torsion angles of 55.5 and −63.2°. There are no other intermolecular hydrogen bonds.

The structure of **11** is shown in Fig. 3. There are two strong hydrogen bonds at the bottom rim between oxygen atoms, *viz* O(150)–H···O(250) and O(350)–H···O(450) at 2.675, 2.673 Å respectively. In addition one N–H group forms hydrogen bonds with the phenolic –OH groups N(253)···O(350) at 3.030 Å. As is apparent from Fig. 3 the other amide nitrogen atom is directed outside the cavity and forms a hydrogen bond to the methanol solvent oxygen atom O(7) at 2.932 Å. The different positions of the two amide nitrogen atoms are clearly indicated by the difference in the two O(*n*50)–C(*n*51)–C(*n*52)–N(*n*53) torsion angles which are −11.6 and −96.7°. It is remarkable that this second amide group has the *cis* conformation with the H(453)–N(453)–C(452)–O(454) torsion angle being 8.5°. There are several other intermolecular hydrogen

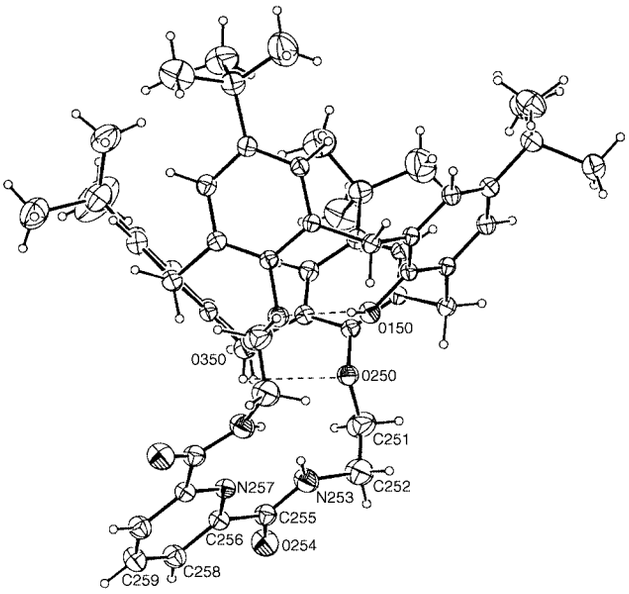


Fig. 4 The structure of **13** with ellipsoids at 30% occupancy. Hydrogen bonds shown as dashed lines.

bonds involving O(254), N(253), O(350), N(51) and N(453) and various solvent molecules and these are listed in Table 3. The dichloromethane molecule with full occupancy sits within the cavity at the top rim of the calix[4]arene.

The structure of **13** is shown in Fig. 4 together with the atomic numbering scheme. The structure has crystallographically imposed mirror symmetry. There are two strong hydrogen bonds at the bottom rim between oxygen atoms, *viz* O(150)–H···O(250) and O(350)–H···O(450) at 2.837, 2.924 Å respectively but surprisingly there are no other strong hydrogen bonds. The amide nitrogen atoms are not directed at the oxygen atoms at the lower rim. It is possible that instead they form cyclic hydrogen bonds to the pyridine nitrogen atom with a N(253)···N(257) distance of 3.219 Å. The two N–H groups also form hydrogen bonds to an acetonitrile solvent molecule N(253)–N(500) at 3.219 Å.

Anion co-ordination studies

Proton NMR titrations. Proton NMR titration experiments were carried out in deuteriated DMSO with L^1–L^3 and various tetrabutylammonium anion salts. Typically significant downfield shifts of the amide and pyridinium protons by up to $\Delta\delta = 0.72$ ppm with dihydrogen phosphate were observed following the addition of anions. EQNMR [15] analysis of the resulting titration curves (Fig. 5) gave in the case of L^1 and L^2 stability constant values for $2A^-$: 1L solution anion complexes shown in Table 4. It is evident from the titration curves (Fig. 5) and from Table 4 that L^1 exhibits a degree of selectivity for $H_2PO_4^-$ over Cl^-, Br^- and forms a very weak complex with HSO_4^-. This selectivity trend has also been noted for simple tripodal amide-substituted tren based ligands [19] and may be rationalised by considering the relative strengths of anion basicity. Dihydrogen phosphate is the most basic anionic guest species and consequently interacts strongly with the amide protons of the receptor. Interestingly in comparison to L^1, L^2 forms a relatively much weaker complex with chloride and in contrast to L^1 exhibits a significant interaction with HSO_4^-. Disappointingly a stability constant could not be determined for the complexation of the $H_2PO_4^-$ by L^2 because of the unusual titration curve binding isotherm. As Fig. 6 shows upfield proton perturbations were initially observed up to the addition of two equivalents of the anion. Addition of further equivalents resulted in significant downfield proton shifts which suggest the presence of a series of receptor–anion complex equilibria.

Table 4 Anion stability constant data for L^1 and L^2 in $(CD_3)_2SO$

Anion	K^a/dm^6 mol^{-2}	
	L^1	L^2
$H_2PO_4^-$	45225	—
Cl^-	8350	1150
Br^-	170	285
HSO_4^-	<20	160

[a] $2A^-$: 1L stability constant values, determined at 298 K; errors <15%.

Table 5 Anion stability constant data for L^3 in $(CD_3)_2SO$

Anion	K^a/dm^3 mol^{-1}
Cl^-	1015
Br^-	705

[a] Determined at 298 K, monitoring the 4-H-pyridyl proton; errors <10%.

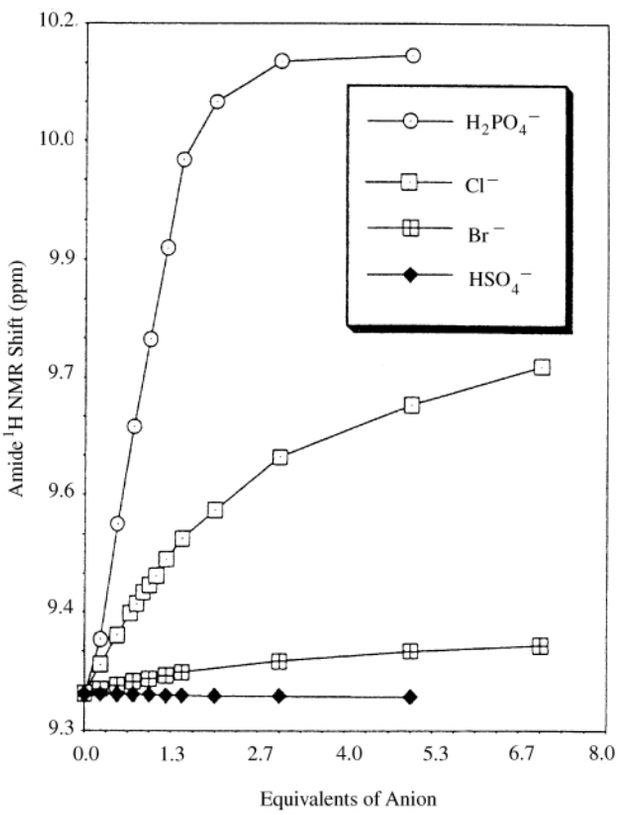


Fig. 5 Proton NMR titration curves for the binding of anions by L^1.

Receptor L^3 forms 1:1 stoichiometric complexes with chloride and bromide anions with stability constant values (Table 5) indicating a preference for the former anion. The addition of $H_2PO_4^-$ to ^{1}H NMR d_6-DMSO solutions of L^3 caused significant perturbations and broadening of the receptor's amide and pyridinium protons, however, it was not possible to plot a titration curve due to overlapping of proton signals.

Electrochemical investigations with L^1. The electrochemical properties of L^1 were investigated by cyclic voltammetry in acetonitrile with NBu_4BF_4 as supporting electrolyte. L^1 displayed a single irreversible two electron reduction wave at −1.30 V (*versus* Ag/$AgNO_3$ reference electrode) corresponding to the independent one electron reduction of each of the pyridinium moieties. The progressive addition of stoichiometric

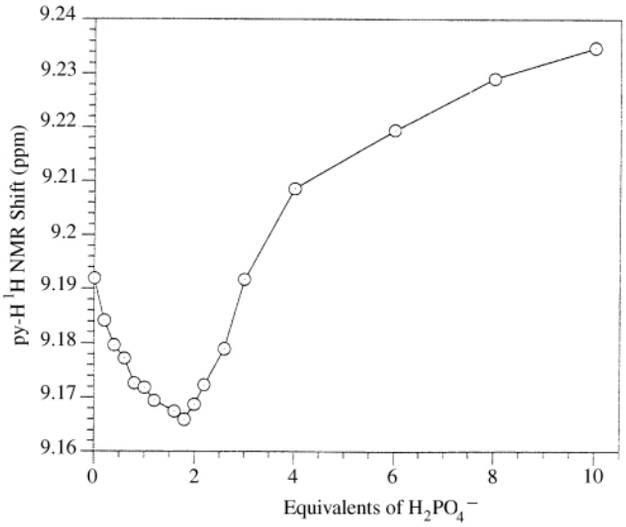


Fig. 6 Proton NMR titration curve for the binding of $H_2PO_4^-$ by L^2.

equivalents of chloride and dihydrogen phosphate anions to electrochemical solutions of L^1 caused the reduction wave to undergo significant cathodic perturbations of up to 50 mV for Cl^- and 160 mV for $H_2PO_4^-$ after ten equivalents of anion had been added. The complexed anion effectively stabilises the overall positive charge of the receptor. The larger magnitude of shift observed with $H_2PO_4^-$ and L^1 suggests a stronger complexation interaction occurs with this anion in comparison with chloride. Similar chloride anion induced cathodic perturbations have been noted with simple acyclic polypyridinium receptors.[6] Disappointingly, solubility problems and a limited supply of compounds thwarted analogous electrochemical investigations being carried out with L^2 and L^3.

Conclusions

New lower rim substituted calix[4]arene bis-pyridinium receptors L^1, L^2 and a novel lower rim bridged calix[4]arene pyridinium receptor L^3 have been synthesised. Proton NMR anion titration studies in deuteriated DMSO have shown L^1 and L^2 to complex anions with $L:2X^-$ stoichiometry. Stability constant determinations suggest L^1 exhibits a selectivity preference for $H_2PO_4^-$ over Cl^- and much weaker complexes are formed with Br^- and HSO_4^-. L^2 also binds Cl^- in preference to Br^- and HSO_4^-. In contrast L^3 forms 1:1 stoichiometric complexes with Cl^- and Br^- of similar thermodynamic stability. Electrochemical investigations reveal L^1 can electrochemically recognise $H_2PO_4^-$ and Cl^- anions *via* significant cathodic perturbations of up to $\Delta\delta = 160$ mV with the former anionic guest species.

Acknowledgements

We thank the EPSRC for a studentship (to K. G.) and for use of the mass spectrometry service at the University of Wales, Swansea. The University of Reading and the EPSRC are gratefully acknowledged for funding towards the crystallographic image plate system.

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Paper a908106b