Anion recognition properties of new upper-rim bis[rhenium(I) bipyridyl, ruthenium(II) bis(bipyridyl), cobaltocenium]calix[4]arene receptors dictated by lower-rim substituents

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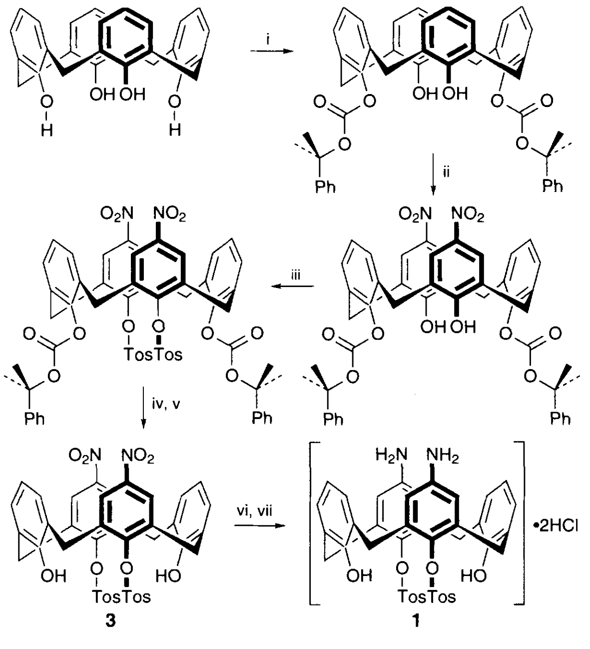
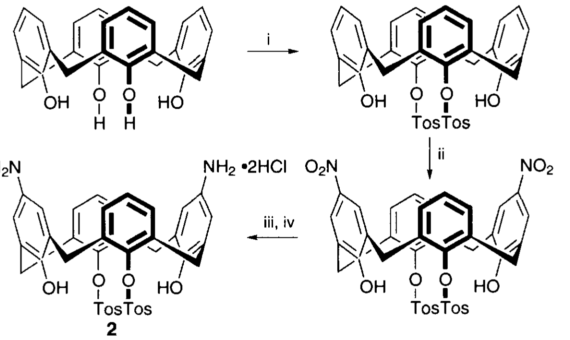
New upper-rim bis[rhenium(I) bipyridyl, ruthenium(II) bis(bipyridyl), cobaltocenium]calix[4]arene receptors exhibit remarkable dihydrogen phosphate selective anion recognition properties dictated by the relative positions of lower-rim tosyl substituents.

The molecular recognition[1] and sensing[2] of anions of biochemical, medical and environmental importance by positively charged or neutral electron-deficient abiotic receptor molecules is an area of intense current research activity. Because of their unique upper- and lower-rim topologies the calixarenes[3] are attractive host molecules on which to construct additional binding sites for target guest species. For example, the calix[4]arene structural framework has been modified and exploited for the recognition of metal cations.[4] In contrast, calixarene anion receptors are still relatively rare.[5] We report here the syntheses of new upper-rim bis[rhenium(I) bipyridyl, ruthenium(II) bis(bipyridyl), cobaltocenium]calix[4]arene receptors whose dihydrogen phosphate selective anion recognition properties over the chloride anion are dramatically dictated by the relative positions of lower-rim tosyl substituents.

The new upper-rim amine-substituted calix[4]arene derivatives containing tosyl groups *para* to the upper-rim amine substituent **1** and the corresponding 1,3-distal isomer **2** were prepared according to Schemes 1 and 2. Condensation reactions



Scheme 1 *Reagents and conditions*: i, $ClCO_2CH_2Ph$, K_2CO_3, MeCN (85–90%); ii, $NaNO_3$, HCl, Ac_2O, $CHCl_2$ (70%); iii, TosCl, NaH, THF (85%); iv, Me_3SiI; v, $Na_2S_2O_3$, H_2O (90–94%); vi, Pd (10%)/C, H_2, THF; vii, HCl–MeOH, $CHCl_2$



Scheme 2 *Reagents and conditions*: i, TosCl, NaH, THF (95%); ii, HNO_3, AcOH, CH_2Cl_2 (75%); iii, Pd (10%)/C, H_2, MeOH, THF; iv, HCl–MeOH, CH_2Cl_2 (85%)

Table 1 Stability constant data for receptors L^1–L^6 in $(CD_3)_2SO$

Receptor	K/dm^3 mol^{-1} [a] $H_2PO_4^-$	Cl^-
L^1	4400	80
L^2	1700	200
L^3	2550	—[b]
L^4	1220	600
L^5	3100	—[b]
L^6	2500	400

[a] Errors estimated to be ≤ 10%. [b] Very weak binding, a stability constant value could not be calculated in this solvent.

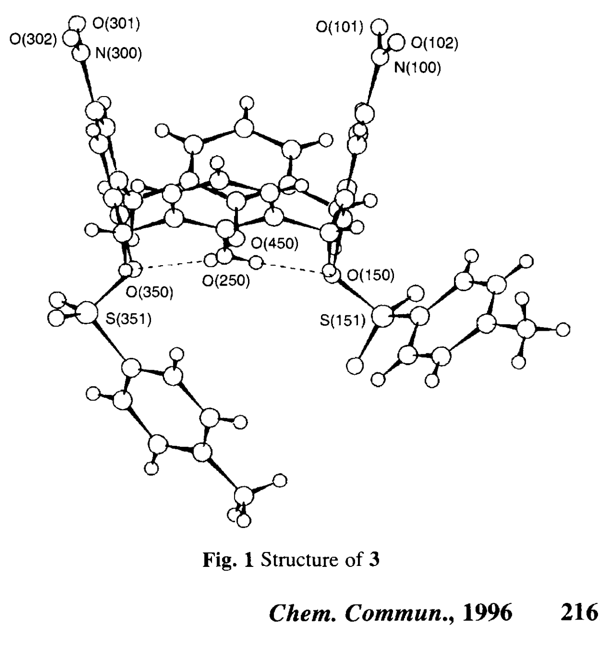
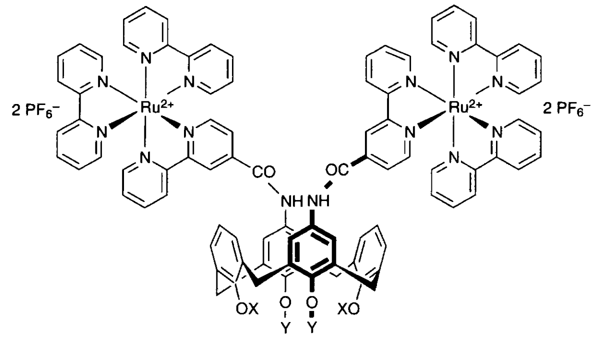
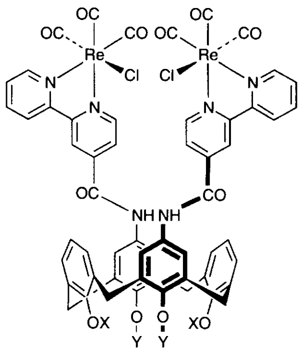


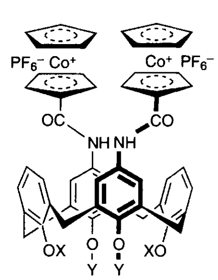
Fig. 1 Structure of **3**



L^1 X=H, Y=Tos
L^2 X=Tos, Y=H



L^3 X=H, Y=Tos
L^4 X=Tos, Y=H



L^5 X=H, Y=Tos
L^6 X=Tos, Y=H

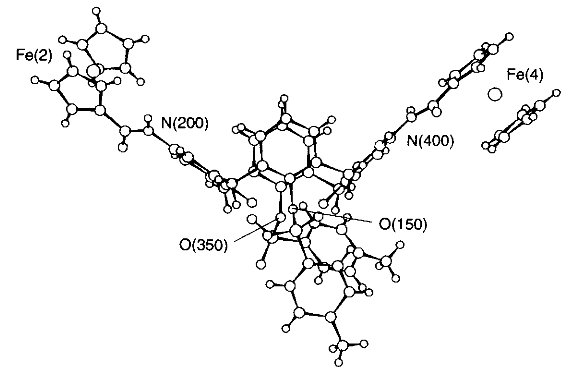


Fig. 2 Structure of **4**

of **1** and **2** with 2 equiv. of 4-chlorocarbonyl 2,2′-bipyridine[6] followed by respective complexation reactions with (bipy)$_2$ RuCl$_2$·2H$_2$O–NH$_4$PF$_6$ and Re(CO)$_5$Cl gave the new receptors L^1–L^4 in good yields. Analogous reactions of **1** and **2** with chlorocarbonyl cobaltocenium chloride[7] and addition of excess NH$_4$PF$_6$ produced L^5, L^6 in 50 and 55% respective yields.

Preliminary anion coordination properties of these new receptors were investigated by ^{1}H NMR anion titration experiments in (CD$_3$)$_2$SO solution with tetrabutylammonium chloride and dihydrogen phosphate salts. In the majority of cases substantial downfield perturbations of the respective receptor's amide and aryl calix[4]arene protons were observed, suggesting anion binding is taking place at the upper-rim vicinity of the receptor. Stability constants were calculated from the resulting titration curves using EQNMR and the values are presented in Table 1. Receptors L^1, L^3, L^5 exhibit remarkable selectivity preferences for H$_2$PO$_4^-$ over Cl$^-$, with the latter two ligands barely able to complex the halide anion in (CD$_3$)$_2$SO at all. In contrast, although L^2, L^4, L^6 also exhibit the same selectivity trend the relative stability constant values for the chloride anion in comparison to L^1, L^3, L^5 have substantially increased by at least two orders of magnitude with L^4, L^6, whereas the H$_2$PO$_4^-$ stability constants have significantly decreased in magnitude. Clearly these results suggest that modifying the positions of the substituents on the calix[4]arene lower rim has a dramatic effect on the anion coordination properties of the upper rim with this class of anion receptor.[8] Molecular modelling calculations (MM2) and CPK models suggest with L^1, L^3, L^5 the lower-rim bulky tosyl groups *para* to the upper-rim amide substituents favours a receptor conformation in which the upper-rim Lewis acidic moieties are rigidly held in close proximity to each other. The X-ray crystal structure of the bis-nitro derivative **3** corroborates this postulation† (Fig. 1), the N(100)–N(300) distance between the nitro groups is 3.805 Å. With the relatively more flexible 1,3-distal isomers, L^2, L^4, L^6, conformations in which the upper-rim Lewis-acidic amide substituents are further apart are predicted by molecular modelling calculations. This is illustrated by the X-ray crystal structure of the bis-ferrocene derivative analogue **4** of L^6 (Fig. 2)† showing the N(200)···N(400) distance of the amide groups to be 11.635 Å. In summary, these preliminary findings suggest that with this class of calix[4]arene anion receptor subtle changes of the size, nature and position of lower-rim substituents will substantially alter the topology of the upper-rim anion recognition site and consequently the receptor's anion coordination properties.

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Footnote

† *Crystal data* for **3**·0.60CH$_2$Cl$_2$, $C_{42.6}H_{35.2}Cl_{1.2}N_2O_{12}S_2$, M = 873.39, a = 12.196(8), b = 14.449(8), c = 23.99(2) Å, β = 104.57(1)°, U = 4091 Å^3, monoclinic, space group $P2_1/n$, Z = 4, 6617 independent reflections were measured and refined on F^2 to R = 0.0784.

For **4**·2.5MeCN, $C_{60}H_{61.5}Fe_2N_{4.5}O_{10}S_2$, M = 1289.5, a = 18.582(17), b = 19.436(18), c = 20.630(20) Å, β = 105.23(1)°, U = 7189 Å^3, monoclinic, space group $P2_1/n$, Z = 4, 9054 independent reflections were measured and refined on F^2 to R = 0.0963.

Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Information for Authors, Issue No. 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 182/199.

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