Remarkable Chloride over Dihydrogen Phosphate Anion Selectivity Exhibited by Novel Macrocyclic Bis[Ruthenium(II) Bipyridyl] and Ruthenium(II) Bipyridyl–Metallocene Receptors

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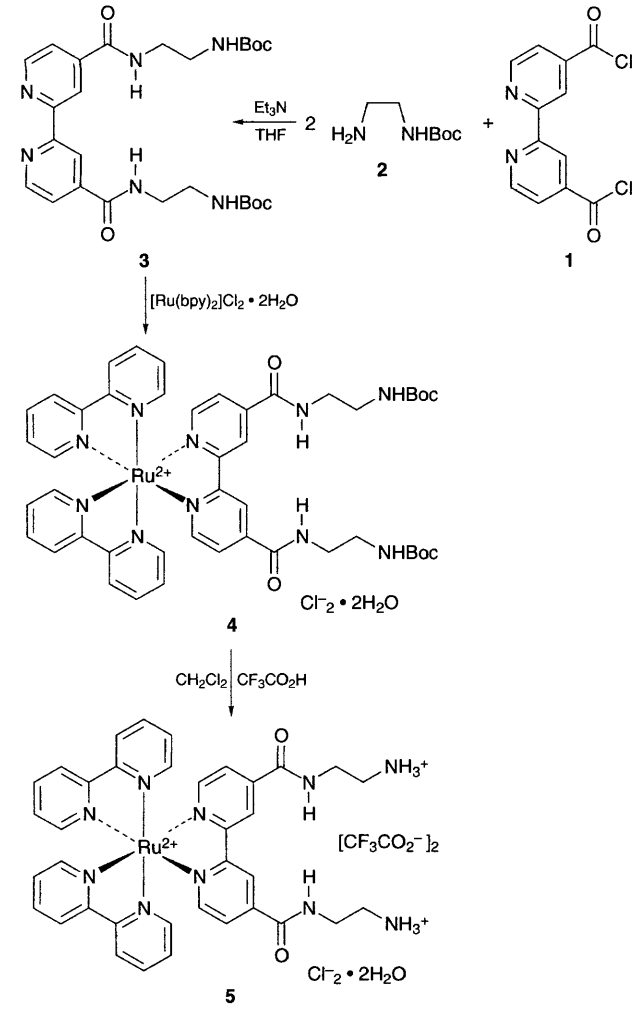
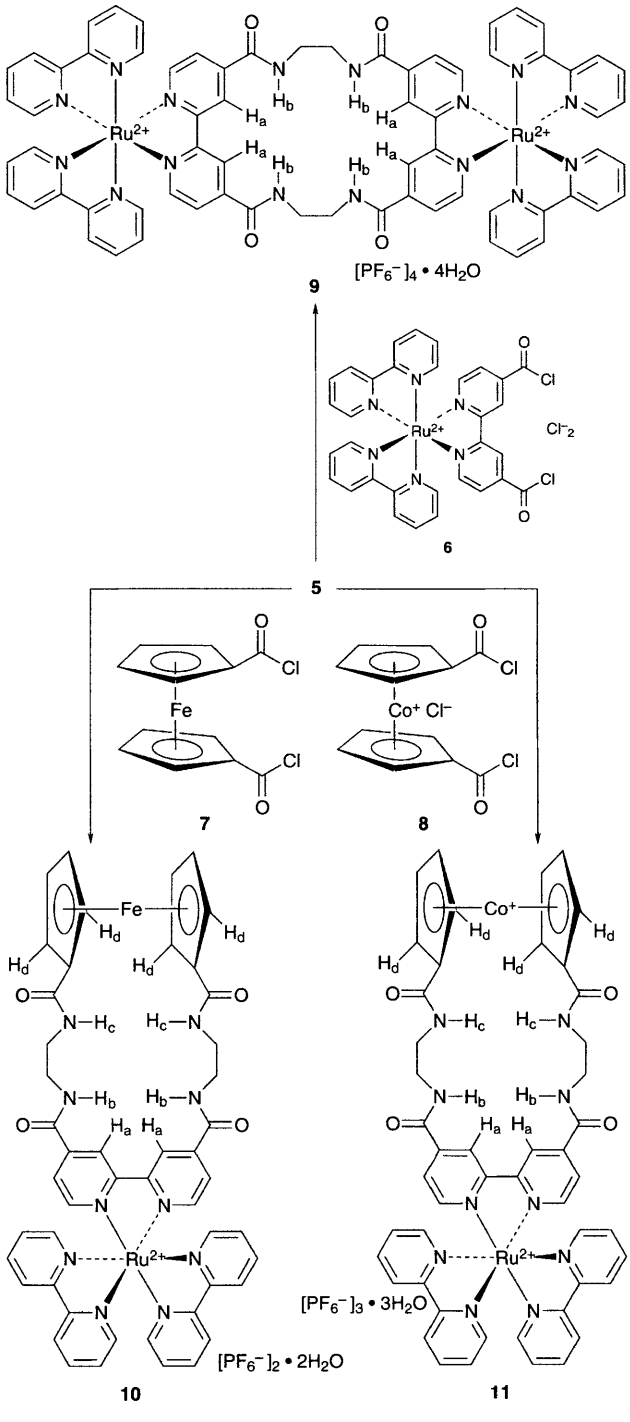
Novel macrocyclic bis[ruthenium(II) bipyridyl] and ruthenium(II) bipyridyl–metallocene receptors are prepared and shown by ^{1}H NMR and fluorescence emission spectroscopy to exhibit remarkable selectivity for the chloride anion in preference to dihydrogen phosphate.

The molecular recognition of anionic guest species of biochemical, medical and environmental importance is an area of intense current interest.[1] As part of a research programme aimed at designing new optical[2] and/or electrochemical[3] sensory reagents for anions we are currently investigating systems based on acyclic and calix[4]arene heteroleptic ruthenium(II) tris(bipyridyl) receptors containing 4,4′-diamide substituted 2,2′-bipyridines.[4] All of these systems reported to date exhibit pronounced selectivity for the dihydrogen phosphate anion in preference to halide anions. Indeed it is noteworthy that this selectivity trend is also displayed by cobaltocenium[3,5] and uranyl[6] amide based receptors. The chloride anion is crucial for a large number of biological processes:[7] for example, the relatively common hereditary disease cystic fibrosis is known to result from a genetically caused misregulation of chloride anion channels.[8] Thus there is a real need for selective detection as established methods for chloride determination based on titrimetric analysis lack selectivity and are not suitable for biological applications.[9] We report here the synthesis of novel macrocyclic bis[ruthenium(II) bipyridyl] and ruthenium(II)



Scheme 1



Scheme 2

bipyridyl–metallocene receptors that exhibit remarkable chloride over dihydrogen phosphate anion selectivity as shown by ^{1}H NMR and fluorescence emission spectroscopy.

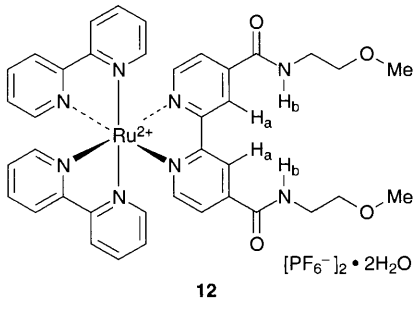
The condensation of 4,4′-bis(chlorocarbonyl)-2,2′-bipyridine **1**[10] with mono-Boc protected ethylenediamine **2** gave **3** in 90% yield. Reaction of **3** with $[Ru(bipy)_2Cl_2]\cdot 2H_2O$ gave the ruthenium(II) complex **4** which on acid deprotection afforded the synthon **5** (Scheme 1). The condensation of **5** with the appropriate ruthenium(II) bipyridyl bis(acid chloride) **6** or 1,1′-bis(chlorocarbonyl)ferrocene **7**[11] or cobaltocenium analogue **8**[12] followed by an excess amount of NH_4PF_6 gave the novel macrocyclic receptors **9**, **10** and **11** in 18, 36 and 13% respective yields† (Scheme 2).

The addition of NBu_4Cl to $(CD_3)_2SO$ ^{1}H NMR solutions of **9–11** resulted in substantial perturbations of most notably the respective amide, 3,3′-bipyridyl and cyclopentadienyl receptor protons. In all cases the resulting titration curves suggest a 1 : 1 receptor : chloride anion stoichiometry. The computer program EQNMR[13] was used to determine the stability constants from the ^{1}H NMR titration data and the results are summarised in Table 1 which includes stability constant data for acyclic receptor **12**. Clearly, compared to **12**, the macrocyclic receptors form much stronger chloride anion complexes by up to *ca.* two orders of magnitude. Analogous ^{1}H NMR titration experiments with $NBu_4H_2PO_4$ gave unexpected results. Only very small perturbations of any of the macrocyclic receptor protons ($\Delta\delta \leqslant 0.05$ ppm) were observed even in the presence of five-fold excess amounts of $H_2PO_4^-$. ^{31}P NMR titration experiments also suggested virtually no binding of $H_2PO_4^-$ by the macrocyclic receptors in $(CD_3)_2SO$ solution. This contrasts with acyclic receptor **12** which forms a stronger complex with $H_2PO_4^-$ than with Cl^- (Table 1). This remarkable Cl^- over $H_2PO_4^-$ selectivity preference exhibited by the macrocyclic systems may be attributed to their inherently rigid structures. Molecular modelling calculations (MM2) and CPK models suggest the minimised structure of **9** has all the amide (CO–NH) and 3,3′-bipyridyl protons lying in a coplanar arrangement which creates a host cavity of similar dimensions to the chloride anion (r^- = 1.81 Å)[14] capable of forming eight hydrogen bonds with this spherical anionic guest species. The larger size and tetrahedral shape of $H_2PO_4^-$ is non-complementary to the macrocyclic receptor's host cavity and consequently complex formation with this anion is not favoured.

Table 1 Stability constant data for **9–12** and chloride anion in $(CD_3)_2SO$

Receptor	Proton of receptor monitored[b]	K [a]/dm^3 mol^{-1}
9	H_a	4.05×10^4
	H_b	3.95×10^4
10	H_a	9.00×10^3
	H_b	9.95×10^3
	H_c	1.00×10^4
	H_d	9.88×10^3
11	H_a	1.86×10^4
	H_d	1.23×10^4
12	H_a	2.07×10^2
	H_b	1.52×10^2
12 + $H_2PO_4^-$	H_a	1.57×10^3
	H_b	1.57×10^3

[a] Errors estimated to be ≤10%. [b] EQNMR analysis of titration curve of particular receptor proton.



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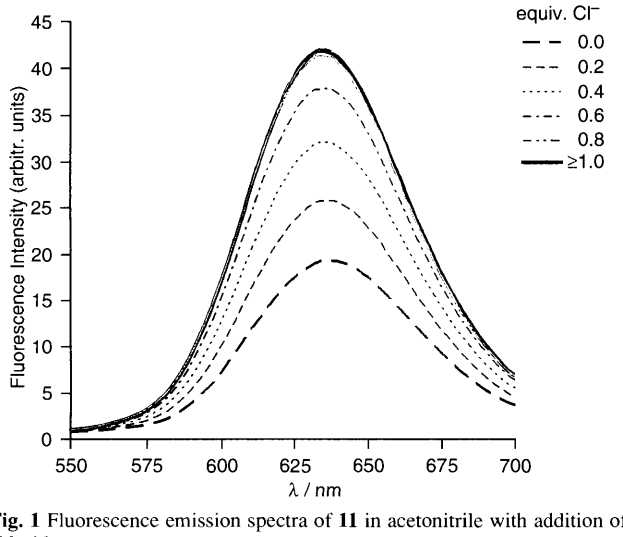

Fig. 1 Fluorescence emission spectra of **11** in acetonitrile with addition of chloride

Preliminary fluorescence emission spectroscopic measurements were also undertaken to probe anion binding. The MLCT emission bands for **10** (λ_{max} = 636 nm) and **11** (λ_{max} = 638 nm) are red shifted compared to $[Ru(bpy)_3]^{2+}$ (λ_{max} = 595 nm) and are relatively quenched by the integrated metallocene moieties. On addition of chloride to acetonitrile solutions of these macrocyclic receptors the fluorescence emission peaks showed substantial blue shifts ($\Delta\lambda_{max}$ = 6 nm) with significant intensity increases‡ (Fig. 1). Interestingly, analogous experiments with $H_2PO_4^-$ had no effect on the respective fluorescence emission spectrum which corroborates with the ^{1}H NMR titration results in demonstrating that **9–11** are first-generation prototype chloride selective sensory reagents.

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Footnotes

† All new compounds were fully characterised by elemental analyses, ^{1}H and ^{13}C NMR and FABMS.

‡ The addition of chloride to acetonitrile solutions of $[Ru(bpy)_3][PF_6]_2$ had no effect on the fluorescence emission spectrum.

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