

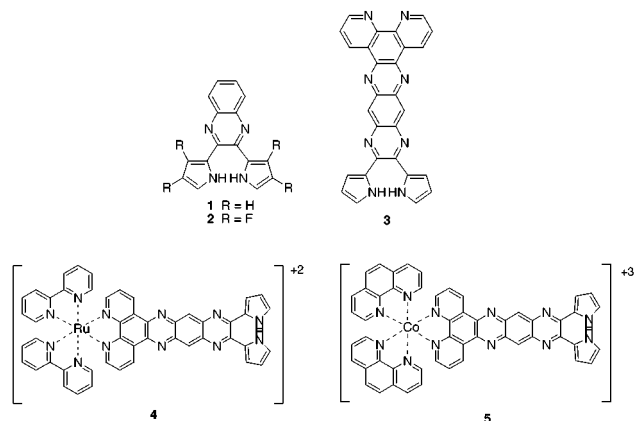
## Phenanthroline Complexes Bearing Fused Dipyrrolylquinoxaline Anion Recognition Sites: Efficient Fluoride Anion Receptors.

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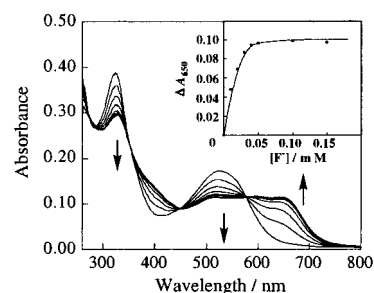
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The development of receptors capable of recognizing neutral and anionic species continues to provide a challenge for supramolecular chemists.<sup>1</sup> For some time now, we have been interested in developing receptors for simple, water-soluble anions such as fluoride, chloride, and phosphate. Such anions play critical roles in a range of biological processes and are implicated in a number of disease states, ranging from fluorosis to cystic fibrosis and are thus considered important targets in terms of receptor design.<sup>2</sup> Prior efforts in our group have focused on the use of pyrrole-based recognition motifs and have led to the recent development of functionalized calixpyrrole (CP) and dipyrrolylquinoxaline (DPQ) receptors.<sup>3–5</sup> The latter systems have the advantage of possessing a built-in chromophore and being readily accessible in two steps from commercially available materials. While the parent DPQ system **1** was found to bind fluoride strongly in dichloromethane-*d*<sub>2</sub> ( $K_a = 18\,200 \pm 1820\text{ M}^{-1}$ ), yet higher affinities are considered desirable for many applications. In an effort to produce a DPQ system that binds fluoride anion more strongly, we have recently introduced a tetrafluorinated DPQ derivative, **2**.<sup>6</sup> In this contribution, we report a new and

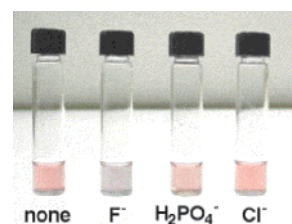


potentially more generalizable strategy that is based on metal coordination. Specifically, we present the synthesis and fluoride anion recognition properties of the fused dipyrrolylquinoxaline phenanthroline derivative, **3**, and its ruthenium(II) and cobalt(III) complexes, **4** and **5**. The latter species, containing as they do electron-withdrawing metal centers, display fluoride anion affinities that are greatly enhanced compared to those of the neutral systems **1** and **3**.<sup>7</sup>

The phenanthroline derivative **3**, which contains a phenanthroline metal coordination site covalently attached to a DPQ-type anion recognition site, was synthesized according to Scheme 1. Briefly, dipyrrolediketone **6** was reacted with 1,2-diamino-4,5-dinitrobenzene<sup>8</sup> in AcOH<sup>5</sup> to give **7**, which was then reduced to the corresponding diamine (**8**). Condensation with 1,10-phenanthroline-5,6-diketone<sup>9</sup> produced ligand **3** in 65%. The target metal complexes

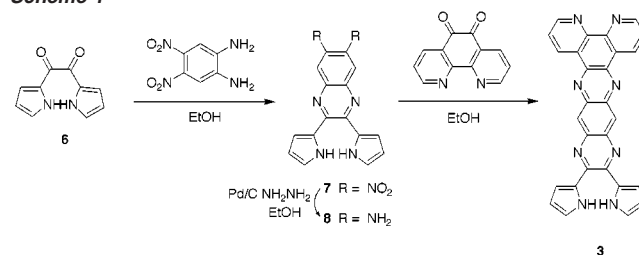


**Figure 1.** UV-vis spectral changes of Co(III) complex **5** upon the addition of fluoride anion;  $[5] = 1.0 \times 10^{-5}\text{ M}$ ,  $[TBAF] = 0-5 \times 10^{-4}\text{ M}$ , DMSO, 25 °C. The inset shows the fit of the experimental data to a 1:1 binding profile.



**Figure 2.** Color changes seen for DMSO solutions of complex **5** upon the addition of anions as TBA salts.

### Scheme 1



**4** and **5** were obtained in ca. 90 and 80% yield, respectively, by reacting **3** with bis-bipyridine ruthenium(II) dichloride monohydrate and bis-phenanthroline cobalt(III) trichloride,<sup>10</sup> as appropriate. Subsequently, treatment of the complexes with NaClO<sub>4</sub> afforded complex **4** and **5** in the form of their perchlorate salts.

The rationale for making **4** and **5** was that they would contain electron-withdrawing moieties that would render the pyrrole N–H protons more acidic, thereby promoting the key anion-to-DPQ interactions, just as in **2**. In the case of complexes **4** and **5**, these electron-withdrawing effects were expected to take place efficiently through the quinoxaline backbone and lead to enhanced anion binding affinities.

As a test of the above hypothesis, the fluoride, chloride, and dihydrogen phosphate anion binding properties of **4** and **5** were studied by UV-vis spectroscopy (Figure 1) in DMSO using the tetra-*n*-butylammonium (TBA) salts of the anions in question. Figure 1 shows the spectroscopic changes observed when Co(III) complex

**Table 1.** Association Constants ( $M^{-1}$ ) of **1–5** with Various Anions in DMSO<sup>a</sup>

	1	2	3	4	5
F <sup>-</sup>	<100 <sup>b</sup>	59000 <sup>c</sup>	440	12000	54000
Cl <sup>-</sup>	ND <sup>d</sup>	ND <sup>d</sup>	ND <sup>d</sup>	10	20
H <sub>2</sub> PO <sub>4</sub> <sup>-</sup>	ND <sup>d</sup>	5000	ND <sup>d</sup>	40	50

<sup>a</sup> Anions used in this assay were in the form of their tetrabutylammonium (TBA) salts. <sup>b</sup> Estimate; clean binding profiles were not observed, presumably as the result of competitions involving solvent. <sup>c</sup> These values have been previously measured in dichloromethane-*d*<sub>2</sub>, wherein values for the binding of F<sup>-</sup> and H<sub>2</sub>PO<sub>4</sub><sup>-</sup> to **2** of 61 000 M<sup>-1</sup> and 17 300 M<sup>-1</sup>, respectively, were observed. <sup>d</sup> ND = not determined.

**Table 2.** Electrochemical Characteristics of Complex **5** in the Presence and Absence of Anions in DMSO<sup>a</sup>

anions	E/mV	$\Delta E/mV^b$
none	160	—
F <sup>-</sup>	<sup>c</sup>	<sup>c</sup>
Cl <sup>-</sup>	320	160
H <sub>2</sub> PO <sub>4</sub> <sup>-</sup>	90	70

<sup>a</sup> Potential measured vs Ag/AgCl (satd KCl) but are tabulated here vs SHE, using a correction factor of 199 mV. <sup>b</sup>  $\Delta E$  refers to change in redox potential observed upon the addition of the anion in question. <sup>c</sup> No Co<sup>III</sup>/Co<sup>II</sup> reduction peak is seen between -500 mV and 500 mV.

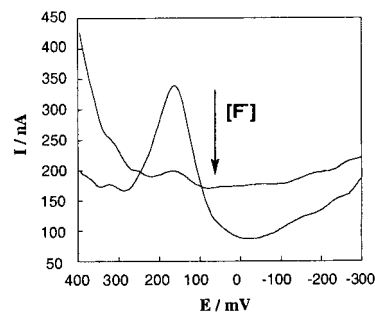
**5** is treated with increasing quantities of TBAF. In this case, the peaks at 323 and 525 nm decreased upon the addition of TBAF, and a new peak at 652 nm appeared (Figure 1), with saturation being observed after the addition of ca. 3 equiv (cf. Supporting Information for corresponding observations). Furthermore, the color of the solution was seen to change from red-pink to pale purple (Figure 2).

From Job-plot analyses, these spectral changes are ascribed to the formation of 1:1 complexes between the metal complex and fluoride anion. Standard curve-fitting procedures were then used to derive binding constants.<sup>11</sup> The resulting values are collected in Table 1, along with those for **1–3**.

Inspection of Table 1 provides support for the proposal that appending cationic charges to a DPQ binding entity can indeed be used to increase anion affinities. For instance, while the free phenanthroline **3** displayed a rather low F<sup>-</sup> affinity, presumably as a result of the additional electron density donated to the DPQ NH anion binding functionality from the nitrogen-rich phenanthroline moiety, the Ru(II) complex **4** displayed a fluoride anion affinity that is higher than DPQ **1** (i.e., ca. 30 times higher than **3**). Moreover, the Co(III) complex **5**, with its incrementally greater charge, displayed an affinity that was even higher.

In an effort to characterize **5** more thoroughly, it was studied by both cyclic voltammetry (CV) and differential pulse voltammetry (DPV) in DMSO (Table 2). It is known that bis-phenanthroline dipyridophenadine Co(III) displays a reversible Co<sup>III</sup>/Co<sup>II</sup> redox wave at approximately 400 mV (vs SHE).<sup>12</sup> In the case of **5**, a clearly reversible redox signal was observed at 160 mV (vs SHE) in the CV in the absence of anions that we likewise assign to a Co<sup>III</sup>/Co<sup>II</sup> reduction wave. A sharp reduction peak was also observed when **5** was studied by DPV. In the DPV studies, the addition of F<sup>-</sup> led to a complete disappearance of the Co<sup>III</sup>/Co<sup>II</sup> reduction signal (or at least its displacement from the observable electrochemical window).

These changes, illustrated in Figure 3, are interpreted in terms of the complexes formed between **5** and fluoride being very strong and, perhaps as a consequence, redox inactive. Consistent with this hypothesis, the addition of a small amount of H<sub>2</sub>O, thought to dissociate the anion-DPQ complex, leads to a restoration of the Co<sup>III</sup>/Co<sup>II</sup> wave. Likewise, the addition of other anions, notably chloride and dihydrogen phosphate, lead to observable shifts in the Co<sup>III</sup>/Co<sup>II</sup> reduction potential, but not to a complete loss of the associated wave (Table 2).

**Figure 3.** Changes in the DPV (vs SHE) spectrum of anion complex **5** observed upon the addition of fluoride. The two curves are those seen in the absence of fluoride and in the presence of 5 equiv. The voltage scale is plotted vs SHE.

The fact that the Co<sup>III</sup>/Co<sup>II</sup> wave may be restored upon the addition of water indicates that the complexation between **5** and F<sup>-</sup> is not irreversible. As such, the results presented here provide a hint that complex **5** and its congeners could prove useful in the fabrication of electrochemical sensors. The present results also provide support for the notion that modifying the electronic features of DPQs through metal complexation might allow for a convenient and general approach to enhancing the anion affinities and, possibly, modulating the selectivities of DPQ-type anion receptors. Further studies of this theme are ongoing in our group.

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**Supporting Information Available:** Experimental procedures, characterization data, and titration results (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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