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Terpyridine-Based Cruciform–Zn^{2+} Complexes as Anion-Responsive Fluorophores

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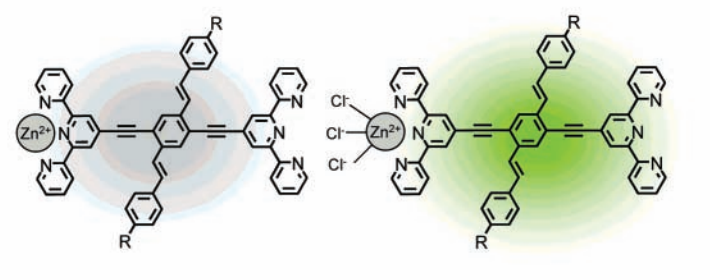
ABSTRACT



The synthesis of a terpyridine-appended, zinc-complexed cruciform, 3–Zn^{2+}, and the anion-reactive modulation of its emissive properties in acetone–water mixtures are reported.

The detection, identification, and quantification of organic and inorganic anions is important in biology, medicine, environmental science, and food science.[1−5] While several concepts are successfully employed, our goal was to explore the construction of self-assembled probes capable of differentiating simple inorganic anions. We reasoned that fluorophore−metal cation complexes should be easily accessible and tuneable leading to turn-on, dosimeter-type, anion-responsive systems. The operating principle would involve mixing the suitably appended fluorophore with a metal cation (zinc in this specific case) and then exposing the fluorophore−metal ion complex to different anions. Depending upon the affinity of the anions for zinc, either decomplexation or formation of an "ate"-type complex, incorporating the fluorophore, could result.[6] The only important prerequisite for this type of dosimeter to work is a change in fluorescence upon the addition of the zinc salt

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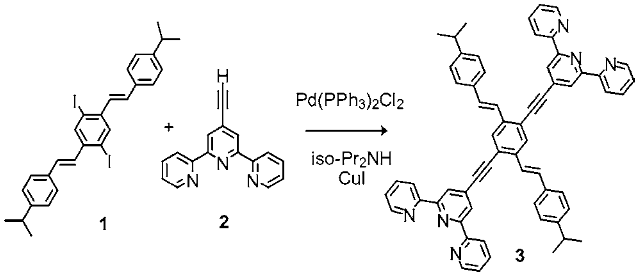
and a second change in fluorescence upon uptake of the anions by the zinc−fluorophore complex.

Cruciform chromophores and fluorophores (XF) encompass a family of different molecular architectures.[7−11] The most common cruciform motif is that of a 1,2,4,5-substituted benzene ring, in which the peripheral unsaturated substituents represent the arms of the cross. These 1,2,4,5-substituted benzene-derived XFs display distinct metal cation and acid-induced changes in their fluorescent behavior, including two-stage ratiometric responses. The issue with the hitherto investigated XFs is that their responsive elements, dialkylanilines and pyridines, only allow the study of fluorescence responses toward metal cations in relatively unpolar solvents such as dichloromethane or THF. In more polar and hydrogen-bonding solvents, metal coordination of such XFs is weak, and the associated spectral responses are invisible unless a highly concentrated solution of metal salt is used. It was therefore of interest to construct XFs that are metal sensitive in more polar solvents. The terpyridine unit is an excellent general metal cation binder, particularly if an octahedral or square-planar coordination geometry can be attained. We therefore envisioned the XF **3** as an excellent target compound.

Scheme 1. Synthesis of the Terpyridine XF **3**



Starting from the literature known distyrylbenzene **1**, reaction with ethynylterpyridine[12] **2** using 6 mol % $(Ph_3P)_2PdCl_2$, in diisopropylamine with CuI as co-catalyst,[13] provided XF **3** in 52% yield after aqueous workup. Chromatography, resulting in heavy losses, furnished spectroscopically pure **3** after subsequent crystallization from chloroform/hexanes in 23% yield (silica gel; dichloromethane:triethylamine gradient, 1:0 to 9:1 v/v ratio).

Figure 2a shows the fluorescence response of the XF **3** after exposure toward different metal cations as their triflates in a mixture of acetone/water (9:1, v/v). We selected an acetone−water mixture because it allows the dissolution of the XF as well as that of the various metal salts and anion-based analytes without problems. We opted for the triflates to exclude anion effects (vide infra). Alkali metal cations and Tl^+ do not change the fluorescence of the XF and do not seem to coordinate at all under these conditions. However, when **3** is exposed to Ag^+, Mn^{2+}, Cu^{2+}, Mg^{2+}, Er^{3+}, or Sn^{2+} we observe that the fluorescence of the XF **3** is efficiently quenched.

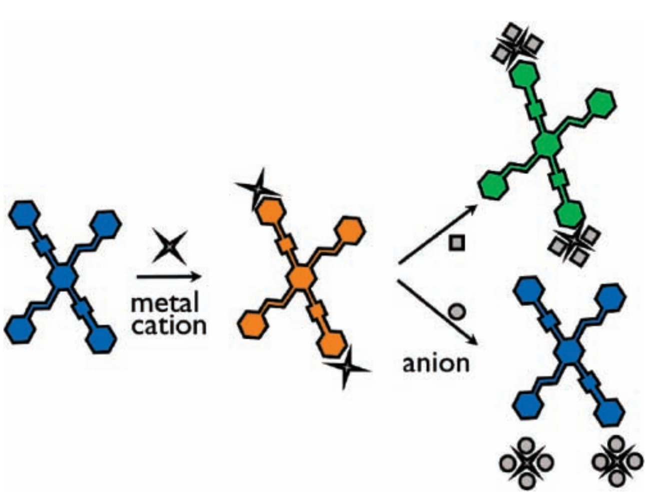


Figure 1. Generalized working principle of a cruciform−metal-ion-based anion probe.

Upon addition of Ca^{2+}, Cd^{2+}, Hg^{2+}, and In^{3+}, we find that the fluorescence changes to green or brown, while the addition of zinc triflate gives an orange-emissive solution. The fluorescent responses of these latter metals were unexpected as the emission of terpyridine-substituted fluorophores is, according to literature reports, quenched by addition of metal cations such as zinc.[14,15] To investigate this surprising behavior further we explored different ratios of Zn^{2+}/XF **3**. Figure 2b shows the results. At a concentration of 1.0×10^{-5} mol L^{-1} of XF **3** we observe at a 1:1 stoichiometric ratio of Zn^{2+}/**3** an emission change from blue to orange.

Upon addition of more zinc triflate the emission color changes from orange to a dull brown. To obtain the correct binding stoichiometries, we performed ITC (isothermal

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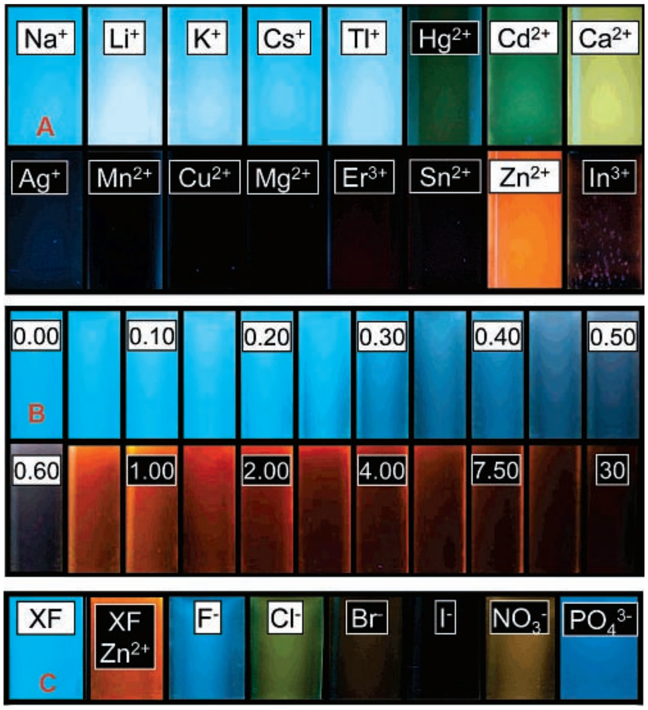

Figure 2. (a) Exposure of **3** toward different metal cations as their triflate salts. (b) Exposure of **3** toward increasing numbers of equivalents of zinc triflate. (c) Exposure of the **3**−zinc complex toward saturated solutions of different anions in a 9:1 acetone/water mixture. All pictures were taken under blacklight irradiation (366 nm) in a 9:1 acetone−water mixture at concentrations of XF (9 mg L^{-1}; 0.010 mM) and $Zn(OTf)_2$ (0.010 mM); a 1:1 stoichiometry with respect to **3**:Zn^{2+} results. Parts b and c were photographed with a fast shutter speed to prevent overexposure of the solutions containing the highly fluorescent **3**. Due to the shutter speed being held constant for parts b and c, the solutions of **3**−Zn^{2+} appear somewhat darker in than under actual visual inspection, whereas part a is closer to their actual appearance.

titration calorimetry). According to the ITC data, a 2:1 complex and a 1:1 (**3**/Zn^{2+}) complex are consecutively traversed (Figure 3). The 1:2 complex apparently is not produced, even upon addition of a large excess of zinc triflate. According to ITC the ΔH of the first complexation step is −6.38 kcal/mol while that of the second step is −10.5 kcal/mol. The analysis of the ITC data by using different binding models did not give reasonable results for K_{assoc} (see SI). Literature reports of structurally related compounds have shown similar difficulties but estimates for K_{assoc} of 10^6 to $>10^8$ are reported.[14,15] The high binding constant allows facile access to the stable complex **3**−Zn^{2+} even in polar solvents. Zinc ions have a high binding affinity for fluoride and phosphate with dissociation constants of 3.04×10^{-2} and 5×10^{-36}.[16,17] As a consequence, we investigated the reaction of the complex **3**−Zn^{2+} toward different anions.

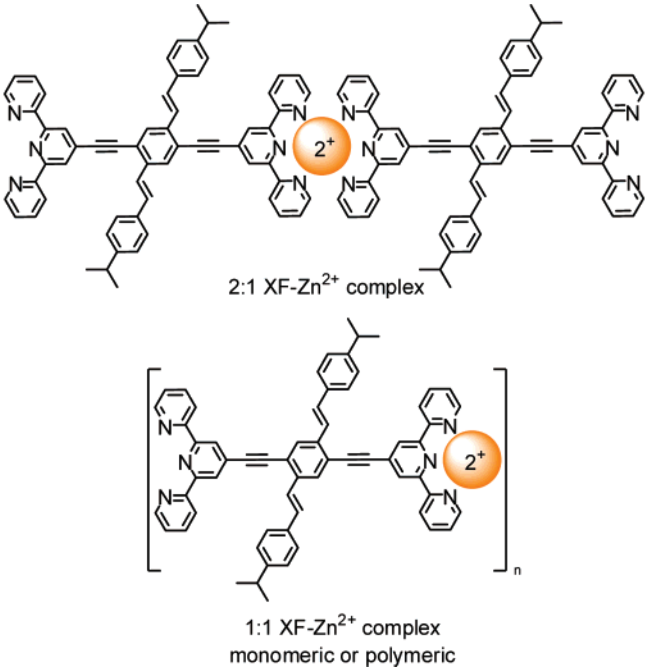

Figure 3. Possible stoichiometries of zinc−cruciform complexes.

Figure 2c and Figure 4 show the results. Addition of fluoride leads to immediate decomplexation and the fluorescence of the starting XF **3** is restored. Upon addition of NaH_2PO_4 a similar shift is visible; however, the recovered fluorescence is 20% less than that of the starting XF **3**. Iodide and bromide shift and/or quench the fluorescence of the XF−Zn^{2+} complex, respectively, while chloride leads to a slight blue shift but not to decomplexation of the XF. Nitrate, a weakly binding anion, has only a minute effect on the fluorescence of the complex. In light of these findings we conclude that phosphate as well as fluoride both remove the zinc stoichiometrically from the XF−Zn^{2+} complex and therefore restore the original fluorescence of the XF **3**.

In the case of the exposure of the **3**−Zn^{2+} to other halide ions, i.e., Cl^-, Br^-, and I^-, we see changes in the emission color which we attribute to the formation of ate-type

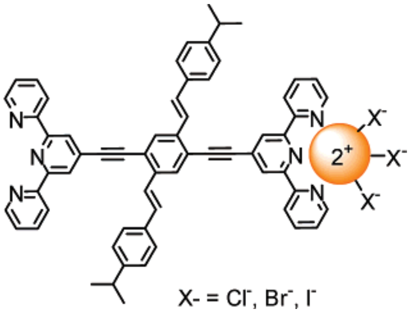

Figure 4. Proposed structure of the Zn−XF complex after addition of halide anions.

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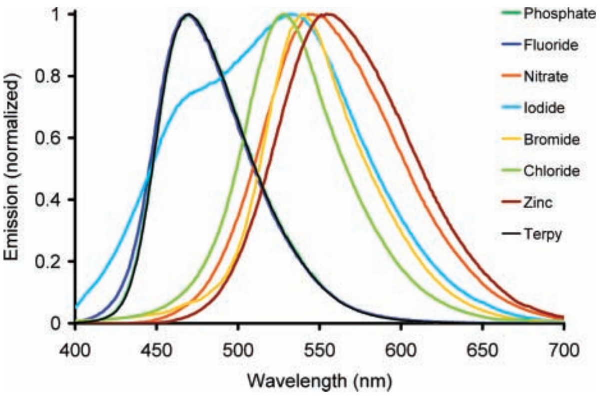

Figure 5. Normalized emission spectra of the XF **3** (Terpy), its zinc complex, and after addition of different anions to the XF **3**$-$Zn^{2+} complex. The **3**$-$Zn(OTf)$_2$ complex was obtained by mixing **3** and Zn(OTf)$_2$ in a 1:1 ratio at a concentration of 0.01 mmol L^{-1}. The number of anions necessary to reach full fluorescence response ranges from 200 equiv for NaF to 2000 equiv for NaI. To obtain a full shift using phosphate ions, the addition of 1000 equiv of NaH$_2$PO$_4$ was necessary. For a non-normalized version of this figure and the concentration of specific anions added see the Supporting Information (Figure SI 5).

complexes arising from a 1:1 XF$-$Zn^{2+} complex. In the case of I$^-$, significant quenching occurs in addition to the blue shift. Literature values for the complex formation constant between iodide and zinc ions in water suggest partial decomplexation, if we compare the bonding strength of the zinc ions to the terpy ligand with that of the iodide ion.[17] The emission spectrum of **3**$-$Zn^{2+} with added I$^-$ does display two local emission maxima, suggesting that both the ate-type complex (λ_{max}= 531 nm) and the decomplexed species (local λ_{max}= 471 nm) are present.

In conclusion, we have prepared the XF **3** containing two terpyridine units. Upon exposure toward metal cations this XF gives emission color changes. In the case of zinc triflate the XF forms 2:1 (**3**/Zn^{2+}) and 1:1 (**3**/Zn^{2+}) complexes, which could be used to detect halide ions. A clear differentiation of fluoride from the other halides was possible, as only fluoride efficiently decomplexes the XF$-$Zn^{2+} complex and restores the original fluorescence of the XF **3**. This simple system allows for the future construction of libraries of self-assembled[18] anion sensors or dosimeters, by combining suitable cruciform fluorophores containing sensory appendages with different metal ions that display differential anion recognition and/or binding.

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Supporting Information Available: Experimental details and characterization of **3** and spectroscopic data and ^{1}H and ^{13}C spectra for **3**. This material is available free of charge via the Internet at http://pubs.acs.org.

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