



Novel highly selective anion chemosensors based on 2,5-bis(2-hydroxyphenyl)-1,3,4-oxadiazole

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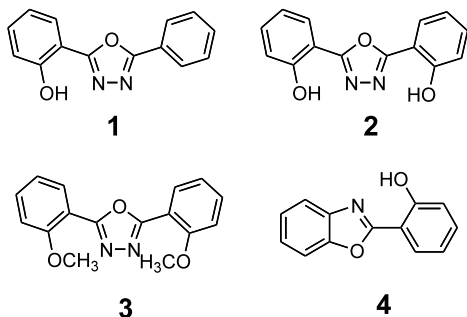
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Abstract—2-(2-Hydroxyphenyl)-5-phenyl-1,3,4-oxadiazole **1** and 2,5-bis(2-hydroxyphenyl)-1,3,4-oxadiazole **2** were used as anion fluorescent and colorimetric chemosensors with high selectivity for H_2PO_4^- and F^- over Cl^- , while **2** can even distinguish H_2PO_4^- from F^- . © 2002 Elsevier Science Ltd. All rights reserved.

The molecular recognition and sensing of anionic analytes is emerging as an area of ever increasing research activity, because of their importance in numerous biological and chemical processes.¹ In recent years, considerable efforts have been devoted to the development of anion fluorescent and colorimetric sensors, which are both highly sensitive at low analyte concentration and convenient to use.² However, simple and easily synthesized electroneutral anion fluorescent and colorimetric sensors remain rare.³ Among these chemosensors for anions, phosphate and fluoride ion sensing are of special interest due to their importance in a number of disease states and environmental pollutants,⁴ but their sensors are rather few,⁵ and there is still a need for good anion sensors with an improved specific response, in particular, in selectivity for H_2PO_4^- and F^- in the presence of Cl^- . Here we report the new electroneutral anion chemosensors (**1** and **2**) for phosphate and fluoride ions with high fluoride/chloride and phosphate/chloride selectivity.



Compounds **1** and **2** were synthesized in good yields according to the procedure described in the literature.⁶ Compound **3**, prepared by the modified method,^{6a} was chosen for the control experiments. In non-polar solvents (such as hexane and toluene), **1** exhibits both a short-wavelength fluorescence (~ 354 nm) and a strong long-wavelength fluorescence (~ 498 nm). In polar solvents (such as acetonitrile and DMF), it emits a strong intermediate wavelength light around 448 nm and weak short-wavelength light (~ 354 nm). The optical behavior of **1** in different solvents is very similar to that of 2-(2-hydroxyphenyl)benzoxazole **4**. Based on the results on **4** reported in the literature,⁷ we can preliminarily attribute the short-wavelength emission band at 354 nm to the excited state of the rotamer form (**II**) of **1**, the long-wavelength emission band at 498 nm to the excited state intramolecular proton transfer (ESIPT) process of the phenol form (**I**), and the intermediate emission around 448 nm to the excited state of a polar tautomeric form (**III**),⁸ which equilibrates with the rotamer form (**II**) ($\lambda_{\text{em}} = 354$ nm) of **1** as shown in Eq. (1). Similar phenomena are observed for **2**, which exhibits two emission bands at 365 and 500 nm in non-polar solvents and two emission bands at 365 and 436 nm in polar solvents, respectively. However, for **3**, only an emission at 360 nm was observed in either non-polar or polar solvents.

The ability of **1** and **2** to coordinate to F^- , Cl^- and H_2PO_4^- (as their tetrabutylammonium salts) in DMF was investigated using UV–vis absorption and fluorescence methods.

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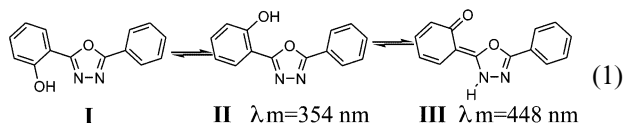
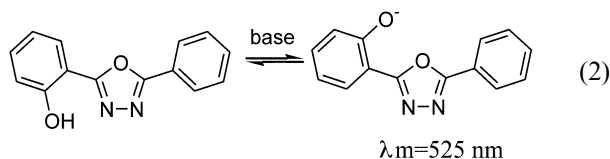


Figure 1 shows the fluorescence spectra of **1** in the presence of various amounts of H_2PO_4^- in DMF. The addition of H_2PO_4^- leads to strong quenching of the emission at 448 nm, but an enhancement of the emission around 354 nm, indicating that the formation of intermolecular hydrogen bonds between H_2PO_4^- and **1** will shift the equilibrium (Eq. (1)) from the tautomeric form (III) ($\lambda_{\text{em}}=448\text{ nm}$) towards the rotamer form (II) ($\lambda_{\text{em}}=354\text{ nm}$).^{7a} Similar phenomena were observed in the case of F^- . In contrast, the addition of Cl^- leaves its fluorescence spectra almost unchanged. Their association constants (K_a) were determined, as summarized in Table 1. The K_a values for the combination of **1** with H_2PO_4^- , F^- and Cl^- are 7.9×10^5 , 8.6×10^4 and $<1.0 \times 10^3\text{ M}^{-1}$, respectively. These results demonstrate that **1** exhibits excellent selectivity for H_2PO_4^- and F^- relative to Cl^- ($K_a\text{H}_2\text{PO}_4^-/K_a\text{Cl}^- > 790$, $K_a\text{F}^-/K_a\text{Cl}^- > 86$), and can be used for sensing F^- , H_2PO_4^- over Cl^- .



In the presence of an excess of H_2PO_4^- or F^- (0.5 mM), the original absorption band at 376 nm is completely replaced by a new long-wavelength peak around 400 nm (Fig. 2). The maximum intensity of this new absorption peak ($\lambda_{\text{max}}=400\text{ nm}$) is largest for the most basic F^- ion, modest for H_2PO_4^- , and absent for the least basic anion Cl^- . Furthermore, its color in DMF solution changes from colorless to yellow (Table 2). These color changes of **1** in DMF solution can be used for 'naked-eye' detection of F^- and H_2PO_4^- in the

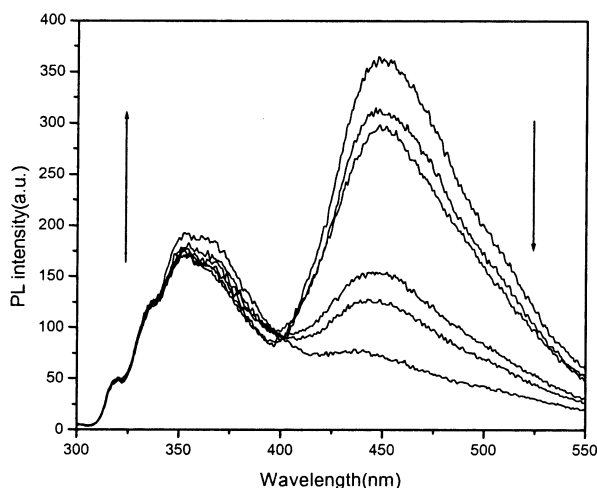


Figure 1. Change in the luminescence spectra of **1** (5 μM) in DMF at 290 K upon addition of H_2PO_4^- , excited at 286 nm.

Table 1. Association constants K_a (M^{-1}) for compounds **1** and **2**^a

	1	2
H_2PO_4^-	7.9×10^5	1.8×10^6
F^-	8.6×10^4	4.1×10^4
Cl^-	$<1.0 \times 10^3$	$<5.0 \times 10^2$

^a All errors are $\pm 15\%$. $[\text{1}]=[\text{2}]=5\text{ }\mu\text{M}$ in DMF at 16°. For **1**, $\lambda_{\text{ex}}=379\text{ nm}$; for **2**, $\lambda_{\text{ex}}=388\text{ nm}$.

presence of Cl^- . Besides, the addition of excess H_2PO_4^- or F^- leads to the appearance of a new weak emission band around 525 nm, which can be used for sensing H_2PO_4^- and F^- . The new long-wavelength absorption ($\lambda_{\text{max}}=400\text{ nm}$) and emission ($\lambda_{\text{em}}=525\text{ nm}$) are the result of a new species generated under basic conditions. A possible explanation is that the new species is the anionic form of **1** in DMF (Eq. (2)),⁹ and these long-wavelength absorptions and emissions are due to the strong intramolecular charge transfer (ICT) effect between the 1,3,4-oxadiazole group, the electron-withdrawing group, and the phenolate anion, the electron-donating group.¹⁰

The anion-binding properties of **2** (5 μM) in DMF are similar to those of **1**, but it exhibits higher selectivity for H_2PO_4^- as shown in Table 1 (for **2** $K_a\text{H}_2\text{PO}_4^-/K_a\text{Cl}^- > 3600$, $K_a\text{H}_2\text{PO}_4^-/K_a\text{F}^- > 43$; while for **1** $K_a\text{H}_2\text{PO}_4^-/K_a\text{Cl}^- > 790$, $K_a\text{H}_2\text{PO}_4^-/K_a\text{F}^- > 9$). It is believed that **2** can form a dimer with H_2PO_4^- through two hydrogen bonds, which is supported by DFT (B3LYP/6-31G*)

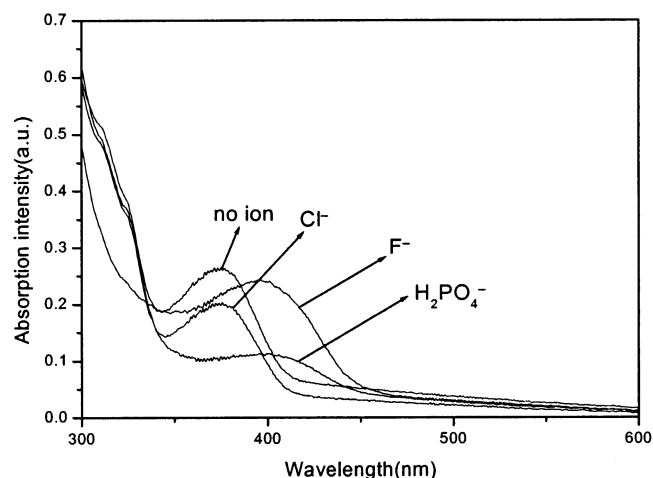


Figure 2. Absorption spectra of **1** (5 μM) in DMF after the addition of 100 equiv. of representative anions.

Table 2. Color changes of **1** and **2** (5 μM) in DMF induced by addition of 100 equiv. of anions

	1	2
No anions	Colorless	Colorless
H_2PO_4^-	Yellow	Yellow
F^-	Yellow	Yellow
Cl^-	Colorless	Colorless

calculations, contained in the GAUSSIAN 98 package.¹¹ The binding properties of **2** and H_2PO_4^- were further investigated by using ^1H NMR titration experiments in $\text{DMSO}-d_6$. Although the ^1H NMR spectrum of **2** shows a signal at 10.34 ppm for the HO proton, the signal becomes broad and undetectable upon the addition of H_2PO_4^- anions. However, the addition of H_2PO_4^- leads to significant upfield shifts (up to 0.2 ppm) for the signals arising from the protons of the phenyl group. The ^1H NMR titration curve of **2** and H_2PO_4^- in $\text{DMSO}-d_6$ implies that they form complexes with a 1:1 stoichiometry.¹² The color change of **2** upon the addition of excess representative anions is similar to **1** (Table 2). Compound **2** can be used as a colorimetric sensor to detect H_2PO_4^- and F^- from Cl^- conveniently. Surprisingly, **2** exhibits different responsive behavior to high concentrations of H_2PO_4^- and F^- (0.1 mM). The addition of excess H_2PO_4^- (over 20 equiv.) produces the new emission band at 525 nm. In contrast, no new band is observed even after the addition of a 100 equiv. excess of F^- (Fig. 3), perhaps because the still rather strong emission at 436 nm in F^- solution covers the emission band around 525 nm completely. This fact demonstrates that **2** can distinguish H_2PO_4^- from F^- .

The control experiments were carried out using **3** instead of **1** and **2**. However even in the presence of 100 equiv. of tetrabutylammonium anions (F^- , Cl^- , H_2PO_4^-), no change was observed in both the absorption and fluorescence spectra of **3** in DMF. This fact illustrates the importance of the effective anion binding.

In conclusion, we have presented novel electroneutral fluorescence sensors **1** and **2** for H_2PO_4^- and F^- sensing. Both **1** and **2** show high phosphate/chloride and fluoride/chloride selectivity and can detect H_2PO_4^- and F^- in the presence of Cl^- by UV-vis absorption and fluorescence methods. Compound **2** can even distinguish H_2PO_4^- from F^- . This molecular system appears to be general for developing more useful anion sensors

for H_2PO_4^- and F^- by appending different chromophores or lumophores. Further work will be reported in the near future.

Acknowledgements

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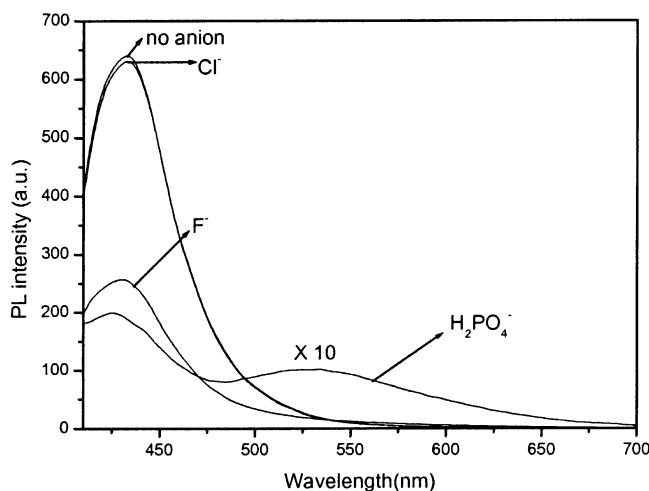


Figure 3. The emission spectra of **2** (5 μM) in DMF (λ_{ex} = 388 nm) after the addition of 100 equiv. of representative anions.

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