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A New Pyridyloxadiazole Incorporated Acridone Offering Selective Optical Detection of Fluoride

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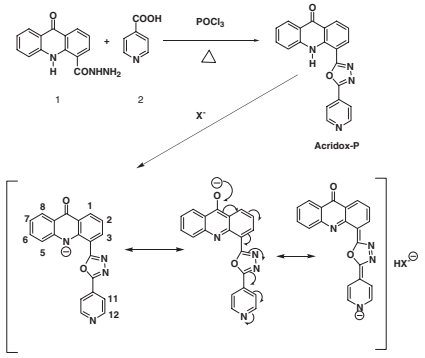
An acridone-based receptor, Acridox-P, offers sensitive and selective detection of F^- by means of color change from yellow to orange and emission switch-on response. Other anions, AcO^-, Cl^-, Br^-, I^-, NO_3^-, SCN^-, and HSO_4^- revealed none or at best weak optical perturbation even at 10-fold higher concentration. The N–H deprotonation is supported by ^{1}H NMR and the detection limit is 1.93×10^{-7} mol L^{-1}.

Anion recognition is important because of their crucial roles in biological, clinical, and environmental sciences.[1] Typically, anion chemosensors carry H-acidic receptors such that the anion interaction modulates the optical properties of the probes, thereby signaling the identity of the interacting anion.[2] Currently, fluoride detection is receiving immense interest in part because of its beneficial role in dental treatment and osteoporosis and in part due to its deleterious effects upon over-exposure, leading to fluorosis, immune system disruption and thyroid disorder.[3] Though many fluoride sensors featuring fluorescence and/or colorimetric response have been described,[4] cross affinities with other anions, particularly AcO^-, moderate sensitivity or fluorescence quenching detract from their practical application. Consequently, it is challenging to design colorimetric as well as fluorescence off–on signaling chemosensors for dual optical targeting of fluoride, while minimizing interferences from potentially competing anions.

Acridone is a photostable fluorophore,[5] but surprisingly it finds limited application in chemosensor development.[6] With a view to enhancing the role of acridone motif in anion sensing, we presently report synthesis and anion binding potential of a new acridone chemosensor, 4-(5-pyridin-4-yl-[1,3,4]oxadiazol-2-yl)-4a,10-dihydro-9a*H*-acridin-9-one, abbreviated as Acridox-P. The purpose to introduce an electron-withdrawing and π-conjugated pyridyloxadiazole was to boost the proton ionizability of its N–H group. As illustrated in Scheme 1, we anticipated that the charged delocalized structures generated upon anion interaction could significantly alter the internal-charge-transfer (CT) character of Acridox-P, thereby inducing highly contrasting optical responses for anion detection.[7] Acridox-P is accessible in a single step by condensing the known acridonecarbohydrazide **1**[8] with isonicotinic acid (**2**) in the presence of $POCl_3$.[9]

The sensitivity of Acridox-P toward various anions as tetrabutylammonium (TBA) salts was evaluated both by absorbance and fluorescence spectral analysis. Acridox-P in DMSO showed an absorption maximum at 413 nm, attributable to π–π^* electronic transition with partial charge-transfer (CT) character. Among different anions examined, drastic absorbance changes were observed only upon exposure to F^-. As shown in Figure 1, the spectrophotometric titration with TBAF ($0–1.7 \times 10^{-3}$ M) revealed the evolution of a red-shifted maximum at 476 nm with concomitant reduction in the original absorbance at 413 nm. The red-shifted maximum is attributable to an enhanced intramolecular CT transition originating from the interaction of F^- with the probe and the well-defined isosbestic points imply an equilibrium process involving the Acridox-P–F^- complexation.



Scheme 1. Synthesis of Acridox-P and its proposed interaction with anions, X^-.

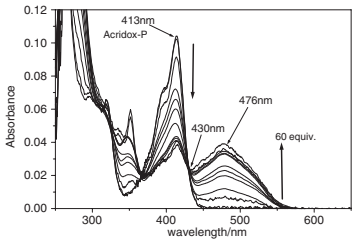


Figure 1. Spectrophotometric titration of Acridox-P (2.83×10^{-5} M) with $0–1.7 \times 10^{-3}$ M TBAF in DMSO.

Noteworthily, the UV–vis profile of the probe was essentially unchanged up to 0.5 mM of TBA salts of Cl^-, Br^-, I^-, NO_3^-, SCN^-, and HSO_4^-, while AcO^- induced a weak maximum at 474 nm, but largely retained the 413 nm absorption band due to the free probe.[9] The yellow color of the probe instantly turned to orange in the presence of F^- (1.7×10^{-3} M), thereby allowing its ready visual detection. By contrast, no perceptible color changes occurred upon adding other anions even at 10 times higher concentration than used for F^-.[9]

Excitation of Acridox-P (1 μM) at the isosbestic point 430 nm resulted in a weak emission band at 495 nm with a quantum yield (Φ_F) of 0.068, measured with respect to Coumarin-153 ($\Phi_F = 0.89$).[10] As shown in Figure 2, the emission band was red shifted to 505 nm and its intensity increased progressively with incremental addition of TBAF, with ca. 10-fold emission enhancement (Φ_F rising to 0.173) being observed at the saturating concentration of 4.5×10^{-4} M. The F^--induced emission red shift is consistent with the similar shift also observed in the absorbance. The inset in Figure 2 shows linear response in emission intensity as a function of

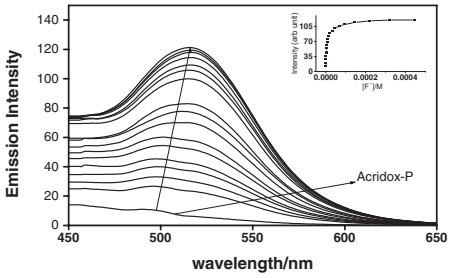


Figure 2. Fluorimetric titration of Acridox-P (10^{-6} M) with 0–4.5 × 10^{-4} M of TBAF in DMSO.

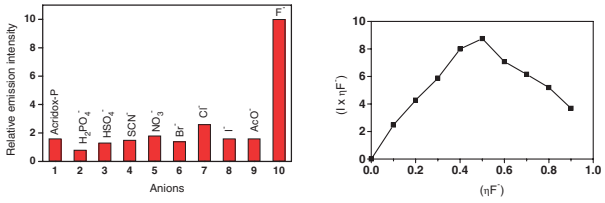


Figure 3. a) Relative emission intensity of Acridox-P with F^- (4.5 × 10^{-4} M) and other anions (4.45 × 10^{-3} M). b) Job's plot of F^- interaction with Acridox-P based on the emission data.

increasing TBAF concentrations. In contrast to F^-, as highlighted in Figure 3, other anions viz. AcO^-, Cl^-, Br^-, I^-, NO_3^-, SCN^-, and HSO_4^- induced none or relatively less pronounced fluorescence responses, amounting to ≤2-fold emission amplification up to 10-fold higher concentrations than F^-. These results demonstrate that in addition to color change, the probe can also effectively discriminate F^- over other anions by means of emission modulations. While the high basicity of F^- would contribute to strong NH–F^- interaction, its small ionic radii would allow relatively unencumbered access to the NH bond hindered by the proximate oxadiazole substituent.[4a,4n]

The 1:1 binding stoichiometry was confirmed from Job's plot (Figure 3b) and the log K derived by nonlinear regression analysis of the fluorimetric data are 5.25 and the detection limit is 1.93 × 10^{-7} mol L^{-1}.[9] For other anions, the optical modulations are insufficient to allow a reliable measure of their log Ks. Noteworthily, many fluoride chemosensors exhibit varying degrees of competitive binding, especially from AcO^- with basicity nearly comparable to that of F^-.[4a] On the other hand, Acridox-P offers highly selective colorimetric as well as fluorescence switch-on responses only with F^-.[11]

In order to evaluate the binding interaction, we carried out the ^{1}H NMR analysis of the probe in the presence of TBAF in DMSO-d_6 (Figure 4). The disappearance of the N–H signal at δ 11.6 confirms the deprotonation by F^-. In addition, many of the protons associated with acridone as well as pyridyl rings also exhibited slight, but detectable upfield shifts as a consequence of the delocalized acridone anion. Clearly, the F^- induced N–H deprotonation leads to observed optical perturbations.

In summary, a newly designed acridone-based chemosensor can signal the presence of F^- by dual naked eye detection and emission amplification, while several other anions including the potentially interfering AcO^- exert none or at best insignificant optical modulation. This feature, coupled with low detection limit of 1.93 × 10^{-7} mol L^{-1} can allow environmental monitoring of fluoride.

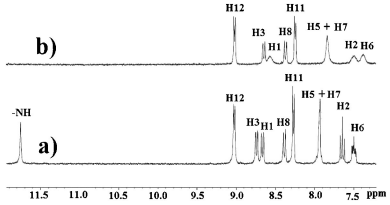


Figure 4. ^{1}H NMR (300 MHz) of a) Acridox-P and b) Acridox-P + TBAF (1:5) in DMSO-d_6.

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9 Supporting Information is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html Supporting Information includes, synthesis and spectral characterization of Acridox-P, UV–visible profile in presence of different anions and detection limit.

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11 Not unexpectedly, the less electron-withdrawing 4-*t*-butylphenyloxadiazole incorporated acridone analog exhibited F^- selective, but less sensitive optical responses than observed with Acridox-P.

