

Fluorescent PET (Photo-induced Electron Transfer) Sensors for Alkali Metal Ions with Improved Selectivity against Protons and with Predictable Binding Constants

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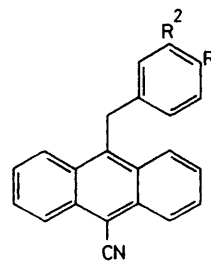
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Alkali metal ions enhance the fluorescence quantum yield of the benzocrown ether derivatives (**1c**) and (**1d**) in methanol by factors of ≤ 15 with no other visible changes in the electronic spectra and with predictable stability constants for the sensor-cation interaction, whereas protons exert a much smaller influence.

The *in situ* monitoring of sodium and potassium ions in biological systems is an exciting prospect which has prompted the development of optical sensors for the alkali metal ions.¹ Several recent reports²⁻⁴ focus on azamacrocyclic derivatives with fluorophores non-adjacent to nitrogen, whose sensor action presumably depends on photo-induced electron transfer. While these sensors are useful in certain contexts, the presence of a basic nitrogen atom leads to an undesirable large enhancement of the fluorescence quantum yield (ϕ_F) by protons.^{2,3,5} We have now overcome this obstacle with the sensors (**1c**) and (**1d**),⁶ which satisfy our previous design logic.^{3,7,8}

Derivatives (**1c**) and (**1d**)[†] display a very simple fluorescent

sensor action (Table 1), with all the observable electronic spectral parameters being independent of analyte nature and



(1)

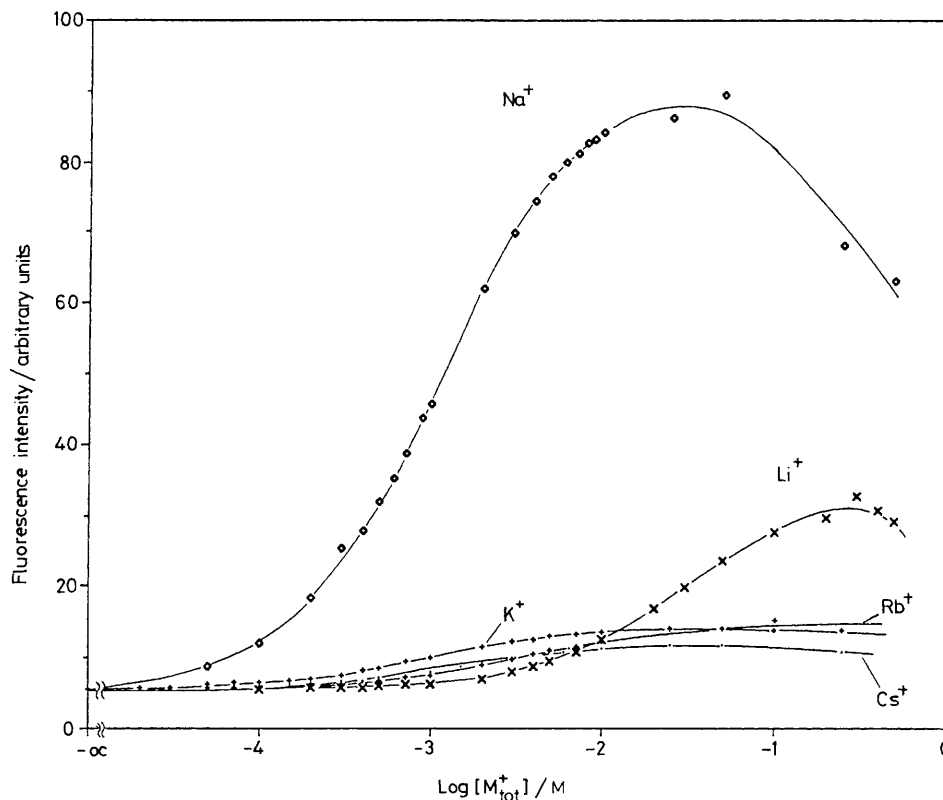
- a; R¹ = OMe, R² = H
- b; R¹ = R² = OMe
- c; R¹ = R² = (OCH₂CH₂)₄O
- d; R¹ = R² = (OCH₂CH₂)₅O

[†] 4-(9-Anthryl methyl)-anisole and -veratrole⁹ were formylated at the 10 position¹⁰ and converted to (**1a**) and (**1b**), respectively, by dehydration of the oximes (*e.g.*, ref. 11). Derivatives (**1c**) and (**1d**) were prepared similarly. All compounds had the expected spectral properties.

Table 1.^a

Metal ion M ⁺	$\phi_{Fmax}^b (M_{tot,max}^+)^c$		$\log \beta^d$		$\log \beta_{parent}^e$	
	(1c)	(1d)	(1c)	(1d)	B15C5	B18C6
Li	0.007 (3.0×10^{-1})	0.0012 (—)	1.7	— ^f	2.3	—
Na	0.019 (5.0×10^{-2})	0.0017 (2×10^{-3})	3.0	4.35	3.1	4.3
K	0.0038 (1.0×10^{-2})	0.0039 (6×10^{-4})	3.1	5.3	2.9	5.3
Rb	0.0028 (2.5×10^{-2})	0.0024 (1×10^{-3})	2.85	4.6	2.4	4.9
Cs	0.0030 (3.7×10^{-2})	0.0028 (2×10^{-3})	2.55	4.05	2.1	3.9

^a 10^{-6} M Fluors with $\leq 10^{-1}$ M alkali metal acetates in aerated MeOH (acetate salts are soluble in MeOH at the required concentrations). λ_{ex} 368, λ_{em} 449 nm, though many other wavelength combinations within the band envelopes are usable. The solutions were handled in polyethylene and quartz vessels as far as possible to minimize contamination by trace sodium and potassium ions. Derivatives (1a–d) have essentially identical u.v. absorption spectra [λ_{max}/nm , (ϵ_{max} dm³ mol⁻¹ cm⁻¹) 411(9600), 390(11500), 370(8600)], and fluorescence spectral shapes and positions [λ_{max}/nm 449,428]. ^b The ϕ_F values of (1a) and (1b) are 0.59 and 0.0019, respectively, and are independent of all metal ions tested, as are their other electronic spectral parameters. The ϕ_{Fmin} values of (1c) and (1d) are both 0.0012. Values of ϕ_F measured from corrected spectra with respect to the standard 9,10-diphenyl anthracene, whose ϕ_F is taken as 1.00 in deaerated MeOH.¹² H₂SO₄ (10^{-2} M) changes the ϕ_F of (1a–d) by 0, +8, +20 and +20%, respectively. Me₄NOH (10^{-2} M) [with 25% (v/v) water and 5×10^{-3} M 18-crown-6 (alkali cation scavenger)] changes the ϕ_F of (1a–d) by 0, -70, -40 and -12%, respectively. ^c (M_{tot}^+) value at which ϕ_F (or I_F) is a maximum. ^d Calculated according to the logarithmic form of equation (1) from $I_F - (M_{tot}^+)$ profiles (Figure 1) with linear least-squares analysis. Average correlation coefficient = 0.997 (average $n = 11$). I_F values deviate negatively from equation (1) at ion concentrations greater than ($M_{tot,max}^+$) and these are excluded from the correlation. ^e Averaged values, where possible, are taken from ref. 13. ^f The ϕ_{Fmax} value is insufficiently different from ϕ_{Fmin} to apply, equation (1).

Figure 1. Fluorescence intensity $I_F - M_{tot}^+$ profiles for (1c) with various alkali metal acetates.

concentration [and essentially identical to those of (1a) and (1b)] except for the fluorescence intensity (I_F) (Figure 1) which is, however, well described by equation (1). It is notable that the $\log \beta$ values so obtained for the (1c)- or (1d)-alkali cation interaction are essentially predictable from those involving the corresponding parent benzocrown ethers.¹³

$$\frac{(I_F - I_{Fmin})}{(I_{Fmax} - I_F)} = \beta \left[\frac{M_{tot}^+ - L_{tot}}{(I_{Fmax} - I_{Fmin})} \right] \quad (1)$$

When free of alkali cations, (1c) and (1d) have ϕ_F values close to that of the control molecule (1b), but are enhanced

≤15-fold upon interaction with these cations, while (1b) shows no such enhancement. However, these enhanced ϕ_F values are still well below that of the other molecule (1a), and may result from the modest alkali cation-induced increase of the oxidation potential of the relatively well delocalized electron donor 1,2-dioxybenzene moiety.¹⁴

We are now working to improve further the ϕ_F enhancements and selectivities in these and other (logically related) molecules. However, (1c) should be usable as it is for *in situ* (Na⁺) monitoring in certain simple microsystems.‡

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‡ Note added in proof. Two Na⁺ sensors employing azamacrocycles of reduced basicity have recently come to our attention: A. Minta, A. T. Harootunian, J. P. Y. Kao, and R. Y. Tsien, *J. Cell Biol.*, 1987, **105**, 89a; G. A. Smith, T. R. Hesketh, and J. C. Metcalfe, *Biochem. J.*, 1988, **250**, 227.