A New Class of Fluorescent pH Indicators based on Photo-induced Electron Transfer

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Aminomethyl-anthracene derivatives (**1**) and (**2**) form a series of fluorescent pH indicators with spectral properties independent of substituents and pH except for the fluorescent quantum yield, which shows that their pK_a^* values are identical to the corresponding pK_a values.

Photo-induced electron transfer has become established as an important principle in photochemistry.[1] Now we show that this principle can be profitably applied to solve several problems concerning fluorescent pH indicators. The majority of these are phenols, anilines, or heterocyclic derivatives where the acid–base site is an integral part of the chromophore.[2]

The results in Table 1 show that, with the appropriate statistical corrections, the relation $pK_a^* = pK_a$ is obeyed for (**1**) and (**2**).[†] We also find that all the cases possess virtually identical spectral parameters which are also independent of pH (except for Φ_F). These favourable features are achieved because, in contrast to the conventional fluorescent pH indicators, (**1**) and (**2**) have spatially separated chromophores and acid–base sites as well as negligible charge separation in the hydrocarbon chromophores upon excitation. The methylene group spacer ensures the substituent independence (and therefore the pH independence) of the absorption and emission spectra. However the methylene group does not prevent the electron donor amine group from efficiently quenching the fluorescence of the anthracene (electron acceptor) moiety by electron transfer[3] in polar aqueous media. Photo-induced electron transfer can occur over a distance of 10 Å.[4] Exciplex emissions are neither observed nor expected. When the amine group is protonated, of course, no such quenching is possible,[5] thus rationalizing the fluorescence pH indicator action.

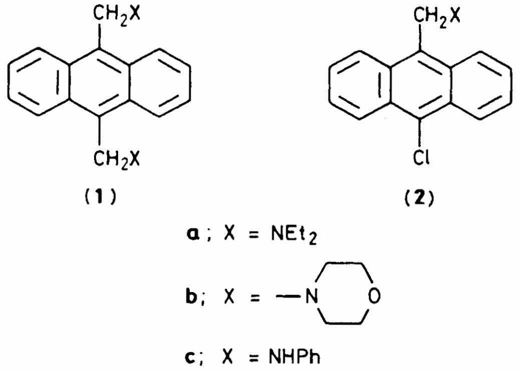
Compounds (**1**) and (**2**) are free from the following

[†] Compounds (**1a**) and (**1b**) were prepared as described by A. H. Beckett and J. Walker, *Tetrahedron*, 1963, **19**, 545, and compound (**1c**) as described by E. Gudrinice and G. Vanags, *Zh. Obshch. Khim.*, 1956, **26**, 3123 (*Chem. Abs.*, 1957, **51**, 8054i). Compounds (**2a—c**) were prepared from 9-chloromethyl-10-chloroanthracene (A. D. Mosnaim and D. C. Nonhebel, *Tetrahedron*, 1969, **25**, 5047) by reaction with the appropriate amine as for compounds (**1**). The spectral data were as expected.

Table 1.[a]

	pK_{a1}^*	pK_{a2}		pK_a^*	pK_a
(1a)	7.6	7.9	**(2a)**	7.9	7.7
(1b)	5.6	6.2	**(2b)**	5.9	5.8
(1c)	1.8[b]	2.5	**(2c)**	2.4[b]	—

[a] pK_a^*, and pK_a apply to the monoamines (**2**) whereas for the diamines (**1**), pK_{a1}^*, pK_{a2}^*, pK_{a1}, and pK_{a2} are applicable of which only pK_{a1}^* and pK_{a2} are measurable. These are statistically related [assuming reasonably that the environment of the acid–base site is identical in (**1**) and (**2**)]: $pK_{a1} = pK_a - 0.3$, $pK_{a2} = pK_a + 0.3$. 10^{-5} M Solutions of (**1**) and (**2**) in water–methanol (8 : 2) at 30 °C, $\mu = 0.1$ M. All the absorption and emission (when observable) properties are typical of anthracene systems and are independent of pH within experimental error over the pH range 1—11, except for the fluorescence quantum yield (Φ_F). Excited state acidity (±0.1) measured from fluorescence intensity (I_F)–pH profiles. The experimental points fitted the expected relation (*e.g.* B. Eistert and W. Reiss, *Chem. Ber.*, 1954, **87**, 108): $\log\{[I_F(\text{max. limit})/I_F] - 1\} = \text{pH} - pK_a^*$. $\lambda_{\text{exc.}}$ = (0,1) band maximum, 377 ± 2 nm; $\lambda_{\text{em.}}$ = (0,1) band maximum, 428 ± 2 nm in all cases, though other wavelengths also give equivalent results. Ground state acidity (±0.2) measured from solubility (*S*)–pH profiles (*e.g.* K. G. Stone and L. Friedman, *J. Am. Chem. Soc.*, 1947, **69**, 209) using the relation: $\log\{[S/S(\text{min. limit})] - 1\} = pK_a - \text{pH}$. [b] Experimental I_f values are lower than the predicted values at pH <1.



difficulties which are associated with conventional fluorescent pH indicators. (a) The fluorescent intensity–pH profile is a function of the exciting and observation conditions and this usually necessitates excitation at the isosbestic wavelength. (b) Since $pK_a \neq pK_a^*$,[6] pK_a^* cannot be predicted exactly from convenient ground-state measurements.[7] (c) The thermodynamic significance of the experimental apparent pK_a^*[8] (as obtained from fluorescence titrations) can be degraded since the excited state–solvent proton transfer equilibrium may be incomplete within the singlet lifetime.‡

Furthermore, the availability of a series of indicators with identical and pH invariant spectra (except for Φ_F) would also be useful in the design of multielement fibre optic pH sensors[9] with an extended linear dynamic range.

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3 For leading references concerning linked aromatic hydrocarbon–amine systems, see; M. Goldenberg, J. Emert, and H. Morawetz, *J. Am. Chem. Soc.*, 1978, **100**, 7171; J. A. Ibemesi and M. A. El-Bayoumi, *Mol. Photochem.*, 1979, **9**, 243; T. Okada, M. Migita, N. Mataga, Y. Sakata, and S. Misumi, *J. Am. Chem. Soc.*, 1981, **103**, 4715; Y. Wang, M. C. Crawford, and K. B. E. Eisenthal, *ibid.*, 1982, **104**, 5874; A. Sugimoto, R. Sumida, N. Tamai, H. Inoue, and Y. Orsuji, *Bull. Chem. Soc. Jpn.*, 1981, **54**, 3500; S. Tazuke, Y. Iwaya, and R. Hayashi, *Photochem. Photobiol.*, 1982, **35**, 621.

4 A. Weller, *Pure Appl. Chem.*, 1968, **16**, 115; J. S. Lindsey, D. C. Mauzerall, and H. Linschitz, *J. Am. Chem. Soc.*, 1983, **105**, 6528.

5 Some authors have noticed this phenomenon in passing: *e.g.*, Y. C. Wang and H. Morawetz, *J. Am. Chem. Soc.*, 1976, **98**, 3611; B. K. Selinger, *Aust. J. Chem.*, 1977, **30**, 2087; J. A. Ibemesi, M. A. El-Bayoumi, and J. B. Kinsinger, *Chem. Phys. Lett.*, 1978, **53**, 270. Selinger, in particular, used linked hydrocarbon–amine systems as fluorescent pH indicators and assumed $pK_a^* = pK_a$ but did not prove it nor develop its potentialities.

6 J. F. Ireland and P. A. H. Wyatt, *Adv. Phys. Org. Chem.*, 1976, **12**, 131.

7 A. Weller, *Prog. React. Kinet.*, 1961, **1**, 188, gives a thermodynamic relation between pK_a and pK_a^* but its limitations are discussed in ref. 6. See also; R. Schipfer, O. S. Wolfbeis, and A. Knierzinger, *J. Chem. Soc., Perkin Trans. 2*, 1981, 1443.

8 *E.g.*, M. S. Fernandez and P. Fromherz, *J. Phys. Chem.*, 1977, **81**, 1755, probe the thermodynamic properties of micelles. In this case however, the condition $pK_a = pK_a^*$ was achieved by a careful choice of excitation wavelength, and in general this would sacrifice some sensitivity of detection.

9 J. I. Peterson, S. R. Goldstein, and R. V. Fitzgerald, *Anal. Chem.*, 1980, **52**, 864.

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‡ Ref. 6 discusses the difficulty of extracting accurate and thermodynamically significant pK_a^* values from fluorescence titration data.