FLUORESCENCE SPECTRA AND CATION-PSEUDOBASE EQUILIBRIA OF SOME BENZOPHENANTHRIDINE ALKALOIDS[1]

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Abstract - The fluorescence spectra of sanguinarine (1), chelerythrine (2), nitidine (3), and N-methylphenanthridinium iodide were studied in different solvents and in dependence upon pH. The equilibrium constants (pK_{R^+}) of pseudobase formation of the investigated compounds were measured.

The benzophenanthridine alkaloids sanguinarine (1), chelerythrine (2), and nitidine (3) belong to intensively studied biologically active substances. There probably exists a relationship between the specificity of their effect and the reactivity of the iminium bond.[2] The quaternary nitrogen heteroaromatic cations are, in dependence upon the concentration of the hydrogen ions, in equilibrium with the hydroxide adducts (pseudobases) (Scheme 1).[3]
The fluorescence spectra of the alkaloids 1-3 and of N-methylphenanthridinium iodide are given in Table 1. In organic solvents and in aqueous 0.01M NaOH, the fluorescence of sanguinarine (1) and chelerythrine (2) is characterized by an intense fluorescence band. In aqueous NaOH, this band is shifted bathochromically contrary to that measured in organic solvents. The fluorescence structure is the form of pseudobases stabilized either by addition of hydroxide ions (in 0.01M NaOH) or by a nonbonded electron pair of the solvent molecule. In water, 0.01M HCl, and in organic solvents saturated with dry hydrogen chloride there appear two fluorescence maxima of small intensity. In these media, the possibility of formation of the adduct by nucleophilic addition to the iminium bond is suppressed. The fluorescence structure is the iminium salt. Figs 1 and 2 show the representation of two fluorescence structures of sanguinarine (1) and nitidine (3) in dependence on the mixture of ethanol and water. The spectrum of sanguinarine (1) in ethanol exhibits the presence of

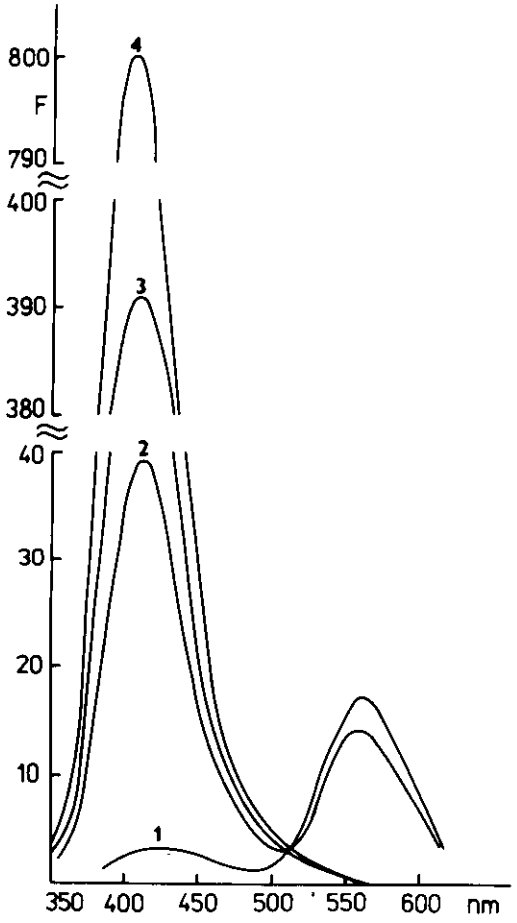


Fig. 1. Fluorescence spectra of sanguinarine (1) in mixture ethanol-water. 1 water 2 0.25 ethanol 3 0.50 ethanol 4 0.96 ethanol

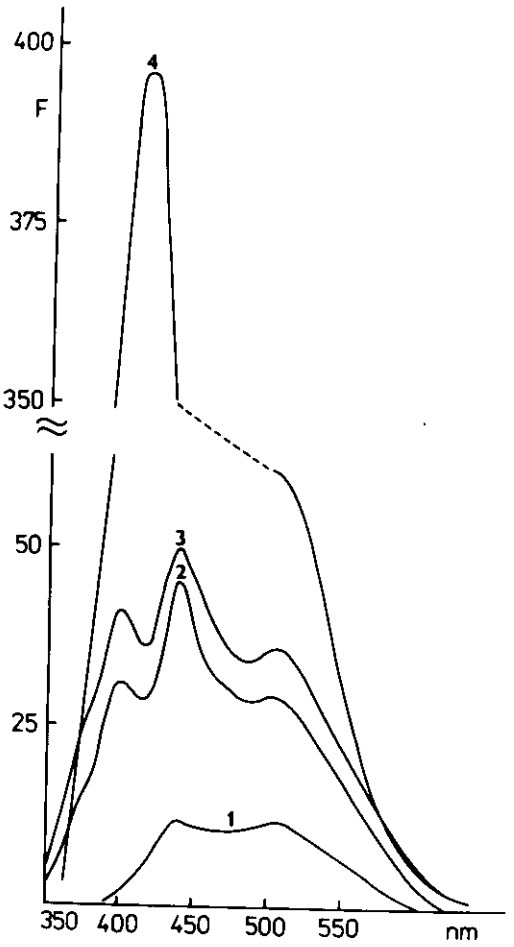
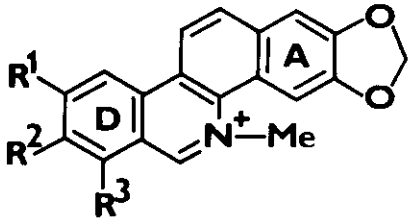
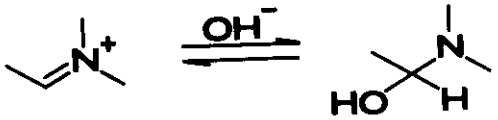


Fig. 2. Fluorescence spectra of nitidine (3) in mixture ethanol-water. 1 water 2 0.25 ethanol 3 0.50 ethanol 4 0.96 ethanol



1 R^1 = H, R^2 + R^3 = OCH_2O
2 R^1 = H, R^2 = R^3 = OMe
3 R^1 = R^2 = OMe, R^3 = H



Scheme 1

Table 1. Fluorescence Spectra of Some Benzophenanthridinium Chlorides 1-3 and N-Methylphenanthridinium Iodide in Different Media[6]

Medium	Compounds 1	2	3	N-Methylphenanthridinium iodide
		λ (F)		
Dioxane	411 (1.08)	407 (1.08)	393 (0.57) 438 (0.65)	403 (1.55)
Acetonitrile	408 (6.60)	404 (6.80)	416 (1.34) 450sh	405 (4.90)
Ethanol	407 (8.10)	402 (9.70)	415 (2.10) 450sh	403 (4.70)
Water	418 (0.03) 562 (0.14)	424 (0.02) 552 (0.05)	443 (0.06) 510 (0.06)	406 (5.04)
0.01M HCl	415 (0.13) 564 (0.48)	415 (0.15) 555 (0.18)	440 (0.33) 518 (0.39)	406 (5.10)
0.01M NaOH	413 (8.90)	415 (13.8)	440 (9.80)	409 (6.80)

λ Position of the fluorescence maximum (nm), F relative fluorescence intensity. Concentration of the compounds 2×10^{-5}M, excitation wavelength 324 nm for 1, 320 nm for 2, 325 nm for 3 and 335 nm for N-methylphenanthridinium iodide

Table 2. pK_{R^+} Values of Studied Compounds

Compound	pK_{R^+} (water - ethanol 1:1 (w/w))[a]	pK_{R^+} (water)[b]
Sanguinarine (1)	5.75 ± 0.18	7.92 ± 0.08
Chelerythrine (2)	6.67 ± 0.19	8.77 ± 0.07
Nitidine (3)	9.76 ± 0.15	12.10 ± 0.20

[a] From UV spectral data. [b] From fluorescence data.
For N-methylphenanthridinium iodide the pK_{R^+} value is 10.4 (from ref.[7]).

one fluorescence structure (pseudobase), whereas that of nitidine (3) two fluorescence structures (pseudobase and iminium salt). The hydroxide adduct of nitidine (in 0.01M NaOH) yields only one fluorescence band. In N-methylphenanthridinium iodide, the uncharged form is not present in any of the used solvents. In the excited state there appears only the band of a quaternary cation. Its position is independent of the polarity of the medium (Table 1).

The pK_{R+} values of pseudobase formation for sanguinarine (1), chelerythrine (2) and nitidine (3) are given in Table 2. The equilibrium constants have been measured spectrophotometrically in a mixture of water and ethanol (1:1, w/w) and fluorometrically in water (25°C, ionic strength 0.1).[5] Solvation of the quaternary ion in water leads to a marked decrease in its acidity.

As in the case of berberine and pseudoberberine alkaloids,[3,4] the position of the fluorescence bands of quaternary cations 1-3 and their pK_{R+} values are markedly influenced by the position and the type of the oxygen substituents in ring D.

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5 Equilibrium studies were carried out using techniques and conditions previously described in detail.[1] The fluorescence spectra were measured on a spectrofluorimeter Aminco-Bowman.

6 Sanguinarine (1) and chelerythrine (2) were from the Collection of our Institute, nitidine (3) was obtained from Prof. M. Cushman, Department of Medical Chemistry and Pharmacognosy, Purdue University, Indiana, U.S.A., and N-methylphenanthridinium iodide was prepared by refluxing phenanthridine (Fluka) with methyl iodide in methanol solution.

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Received, 12th February, 1980