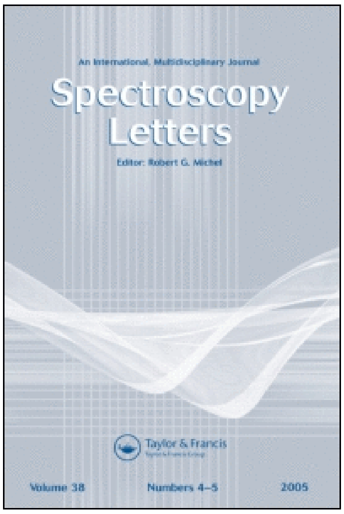

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Electronic Spectral Studies and Determination of the First Excited Singlet-State Dipole Moments of New Benzo[a]phenothiazine Derivatives

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ELECTRONIC SPECTRAL STUDIES AND DETERMINATION OF THE FIRST EXCITED SINGLET-STATE DIPOLE MOMENTS OF NEW BENZO[a]PHENOTHIAZINE DERIVATIVES*

Key words: 12H-benzo[a]phenothiazine, 9-methyl-12H-benzo[a]phenothiazine, 10-methyl-12H-benzo[a]phenothiazine, 11-methyl-12H-benzo[a] phenothiazine, 5-oxo-5H-benzo[a]phenothiazine, 6-hydroxy-5-oxo-5H-benzo[a]phenothiazine, 6-methyl-5-oxo-5H-benzo[a] phenothiazine, Electronic Absorption Spectra, Fluorescence Spectra, Solvent effects, Ground-State Dipole Moments, Excited Singlet-State Dipole Moments.

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ABSTRACT

The room temperature (298 K) electronic absorption, and fluorescence excitation and emission spectra of seven new, pharmacologically-important benzo[a]phenothiazines (12H-benzo[a]phenothiazine (1), 9-methyl-12H-benzo[a] phenothiazine (2), 10-methyl-12H-benzo[a] phenothiazine (3), 11-methyl-12H-benzo[a]phenothiazine (4), 5-oxo-5H-benzo[a]phenothiazine (5), 6-hydroxy-5-oxo-5H-benzo[a]phenothiazine (6) and 6-methyl-5-oxo-5H-benzo[a] phenothiazine (7).) were measured in several solvents of different polarities and hydrogen bonding abilities. In combination with the ground state dipole moments of these benzo[a]phenothiazines, the spectral data were used to determine their first excited singlet-state dipole moments by means of the solvatochromic shift method. These excited singlet-state dipole moments were found to be significantly higher (1.9 to 2.5 Debye units) than their ground-state counterparts.

INTRODUCTION

Phenothiazine derivatives possess a great variety of applications[1-5]. Some of these heterocycles, such as promethazine, chlopromazine, and trifluopromazine are used as psychotropic sedative and antidepressant drugs[1,2]. Also, methylene blue, methylene violet, Azure A and methylene green were investigated for their photochemotherapeutic activity against carcinomas[3]. Besides, their medical and biological interest, phenothiazines are widely utilized as insecticides, dyes, pigments and indicators[4,5].

Recently, a number of benzo[a,b or c]phenothiazine derivatives, were prepared by several ways[6-9], and received a great deal of attention because of their electronic and/or therapeutic properties[10-16]. In fact, some benzophenothiazines, absorbing in the visible (> 500 nm), are strongly colored and generally used as polycyclic dyes[10] or pigments for synthetic polymers[11], and also in optical recording media[12]. Some benzo[a or c]phenothiazine derivatives are potential anthelmintics[13], and possess an antiviral activity, inhibiting the multiplication of encephalomyocarditis, Ranikhet disease, and New Castele disease viruses in tissue cultures[2]. Other benzo[a] phenothiazines and their hydro derivatives were shown to be strong leukotriene inhibitors, useful in the treatment of allergic inflammatory and cardiovascular conditions[14]. The relationship between the antitumor activity of benzo[a]phenothiazines and their π-electron density measured by the Huckel and MNDO orbital methods was investigated by Motohashi et al[16].

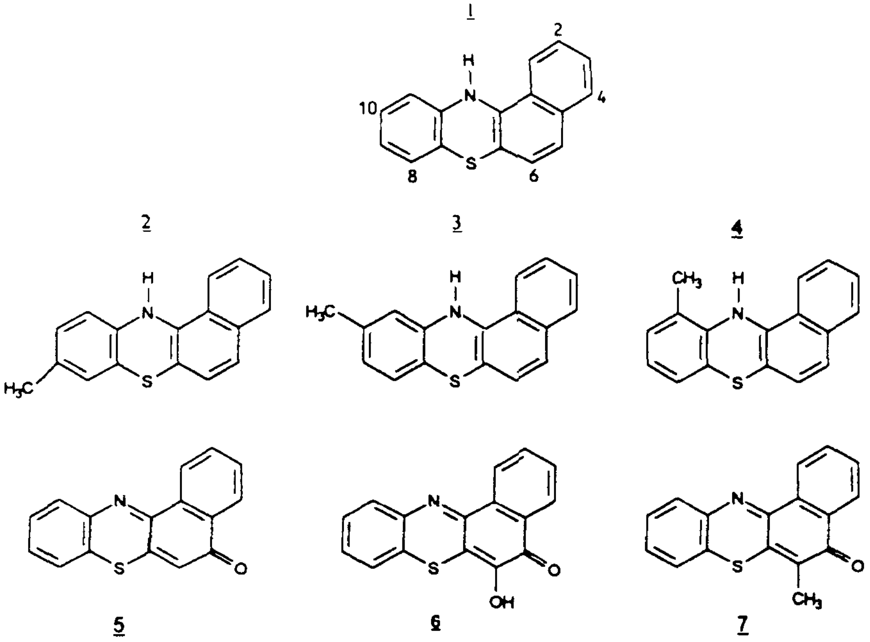
The photophysical and photochemical properties of benzophenothiazines were also studied in several literature reports[10,17-22]. Several benzophenothiazine derivatives were investigated as a group of photosensitizers acting in vitro via an electron transfer mechanism[17-19]. Other works were devoted to tautomerism recognition on the basis of the visible absorption spectral data of quinone imine phenothiazines[10]. Barra et al[20] studied the photochemistry of benzo[c]phenothiazine in polymethacrylate polymers using time-resolved laser techniques. They demonstrated that the luminescence properties of this compound in polymer matrix, are similar to those obtained in solution, and also they found that it exhibited a long-lived triplet-triplet absorption. In our previous works, dealing with the photophysical properties of some phenothiazine and benzophenothiazine derivatives, we found that these aromatic heterocycles are more polar in the excited singlet-state than in the ground-state[21,22].

In this preliminary communication, we will present our results concerning the solvent and substituent effects on the electronic absorption and fluorescence spectra of seven new benzophenothiazine derivatives, and we will report also on their dipole moments in the ground and in the first excited singlet-state.

EXPERIMENTAL

The benzo[a]phenothiazine derivatives (1-7) under study were prepared by Motohashi et al[15,16]. Analytical or spectroscopic grade solvents (dimethylsulfoxide, dimethylformamide, acetonitrile, ethanol, ethyl ether, ethyl acetate, tetrahydrofurane, and cyclohexane) were used to prepare the solutions.

UV-visible absorption and fluorescence spectra were recorded at room temperature (298 K) on a Varian DMS 200 spectrophotometer and a Perkin-Elmer LS-5 spectrofluorimeter, respectively. The ground-state dipole moments were measured in dioxane at 293 K, using a dipole meter DM-01 (Wissenschaftlich-Technische Werkstatten, Weilheim, Germany) equipped with a DFL-2 cell as previously described[21,23-26]. A combination of the PPP method and the σ-bond contribution was used to calculate the theoretical total ground state dipole



Scheme 1 : Structures of the benzo[a]phenothiazine derivatives.

moments, μ_g, as a vector sum of the respective π and σ components[25]. All calculations were carried out on a Hewlett-Packard HP 150 II Touchscreen computer with a 8087 coprocessor. The first excited singlet-state dipole moments of benzo[a]phenothiazines were determined using the solvatochromic method, based on the Bakhshiev and Kawski-Chamma-Viallet formulas[27-29], as discussed in our previous papers[21-26].

Bakhshiev's formula[27]:

$$\tilde{\nu}_A - \tilde{\nu}_F = \frac{2(\vec{\mu}_e - \vec{\mu}_g)^2}{hca_0^3} \cdot \left[\frac{D-1}{D+2} - \frac{n^2-1}{n^2+2}\right] \cdot \frac{2n^2+1}{n^2+2} = \frac{2(\vec{\mu}_e - \vec{\mu}_g)^2}{hca_0^3} \cdot F_1 \qquad (1)$$

Kawski-Chamma-Viallet's formula[28,29]:

$$-\frac{\bar{\nu}_A + \bar{\nu}_F}{2} = -\frac{2(\mu_e^2 - \mu_g^2)}{hca_0^3} \cdot \left[\frac{2n^2+1}{2(n^2+2)} \cdot \left(\frac{D-1}{D+2} - \frac{n^2-1}{n^2+2}\right) + \frac{3(n^4-1)}{2(n^2+2)^2}\right] = -\frac{2(\mu_e^2 - \mu_g^2)}{hca_0^3} \cdot F_2 \qquad (2)$$

where $\overline{\nu}_A$ and $\overline{\nu}_F$ are the absorption and emission maxima wavenumbers (in cm^{-1}), respectively; $\vec{\mu}_g$ and $\vec{\mu}_e$ are the permanent dipole moments in the ground and in the first excited singlet-state, respectively; D is the solvent dielectric constant, n is the solvent refractive index; F_1 and F_2 are the solvent functions; a_0 is the Onsager cavity radius. In formula (3), M is the molecular weight of the solute, δ is the density of the solute, and N is the Avogadro's number:

$$a_0 = \left[\frac{3M}{4\pi\delta N}\right]^{\frac{1}{3}} \tag{3}$$

RESULTS AND DISCUSSION

Electronic spectral properties

The fluorescence and UV-visible absorption spectral properties of benzo[a]phenothiazine derivatives in ethanol are summarized in Table 1. The electronic absorption spectra present several strongly-absorbing peaks in the 250-280 nm, 320-380 nm, and, for compounds 5-7, 470-520 nm regions. These various peaks can be attributed respectively to the π,π* ^1B, ^1L_a, and ^1L_b transitions. It is worthwhile to note that the absorption spectra of unsubstituted and methyl substituted benzophenothiazines (compounds 1-4) are similar to those of unsubstituted phenothiazine and promethazine[21]. All oxo-benzophenothiazine derivatives (compounds 5-7) present an additional absorption band in the visible (λ_{max} >460 nm) which is due to the more stabilized quinone-like electronic structure of these heterocycles. When varying the solvent polarity, relatively small absorption maxima shifts were observed, ranging from 2-7 nm for the first bands to 4-22 nm for the second ones.

The fluorescence excitation spectra were close to their absorption counterparts. Compounds (6) and (7) were found not to be fluorescent. Fluorescence emission bands occurring in the 470-525 nm regions correspond to the π,π* transition type. In all solvents under study, the fluorescence emission wavelength of the five remaining benzophenothiazine derivatives, was larger than 440 nm. The fluorescence intensity increased generally with the solvent polarity, denoting a stabilization of the benzophenothiazine excited singlet-state by dipolar interactions, within the solvent cage. Moreover, for most compounds the

TABLE 1

Electronic Absorption and Fluorescence Spectral Properties of Benzo[a]phenothiazine Derivatives in ethanol [a].

N	Absorption maxima[b] λ_{max},nm (Log ε)	Fluorescence maxima[b]	
		λ_{ex} , nm	λ_{em}, nm
1	206(5.21),255(4.85), 276(4.98),(325)(4.2)	243,268,297	499, (516)
2	258(4.43),274(4.49), 335(3.67)	262,275,340	507
3	257(4.43),276(4.57), 338(3.67)	263,277,340	506
4	(260)(4.31),273(4.4)	262,273,(380)	500
5	255(4.22),309(4.02), 369(3.80),476(3.79)	277,346,(377)	517
6	252(4.17),267(4.12), 359(3.88),523(3.74)	-NF[c]-	-
7	253(4.02),307(3.84), 383(3.61),473(3.62)	-NF[c]-	-

a: The concentrations of benzo[a]phenothiazines derivatives were 10^{-5}M for absorption spectra and 10^{-6}M for fluorescence spectra.

b: Underlined wavelengths and values in parentheses correspond, respectively, to the maxima and shoulders.

c: NF= No fluorescence.

fluorescence emission maxima were significantly red shifted (16 to 40 nm) when increasing the solvent polarity.

Solvatochromic correlations

We have plotted the Stokes shift values, ($\overline{\nu}_A$ - $\overline{\nu}_F$) and ($\overline{\nu}_A$ + $\overline{\nu}_F$)/2, against the solvent functions F_1 and F_2 for the different solvents using the Bakhshiev and Kawski-Chamma-Viallet correlations[27-29], respectively The results of the statistical treatment of solvatochromic correlations are summarized in Table 2. The correlation coefficients are larger than 0.91, indicating a good linearity for both types of correlations. It can be seen that, a majority of solvents obey the linear plots, except THF which exhibits generally a deviation to the correlation, probably due to specific solute-solvent interactions (FIG. 1). However, the same solvents do not participate necessarily, to all the correlations. It is

TABLE 2

Statistical Treatement of the Correlations of Solvent Spectral Stokes Shifts of Benzo[a]phenothiazine Derivatives.

Compound N°	Slope (cm^{-1})	Intercept (cm^{-1})	Correlation coefficient	Number of data
Bakhshiev correlations				
1	1544	15488	0.926	6
2	1631	15596	0.931	7
3	1538	15334	0.947	7
4	1574	15589	0.932	7
5	786	19099	0.924	5
6	NF[a]	-	-	-
7	NF[a]	-	-	-
Kawski-Chamma-Viallet correlations				
1	-1608	29129	0.940	7
2	-1807	29620	0.947	7
3	-1744	29680	0.931	7
4	-1080	28901	0.912	6
5	-2376	30630	0.938	5
6	NF[a]	-	-	-
7	NF[a]	-	-	-

a: NF= no fluorescence.

worthwhile to note that the slope absolute values are slightly larger for the Bakhshiev's correlations than the ones obtained for the corresponding Kawski-Chamma-Viallet correlations. The slope values are not very high ($\leq$2000 cm^{-1}), indicating a rather small variation of the dipole moment values between the ground and the excited singlet-state of these benzophenothiazine derivatives.

Experimental and calculated ground state dipole moments

In the majority of the cases, their is a satisfactory agreement between the experimental, and calculated ground-state dipole moment values, with differences going from 0.1 to 2.0 Debye units. However, compound 6 present an experimental

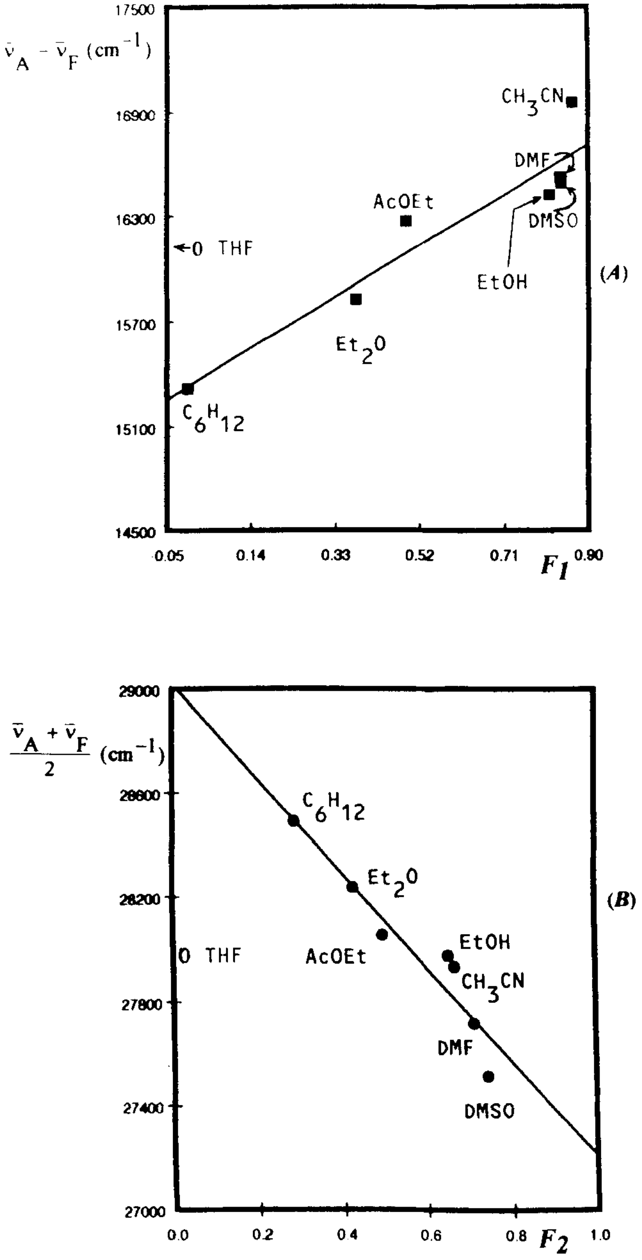


FIG. 1. Bakhshiev (*A*) and Kawski-Chamma-Viallet (*B*) correlation for 10-methyl-benzo[a]phenothiazine (3).
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TABLE 3

Ground and Excited Singlet-State Dipole Moment Values.

Compound N°	μ_g[a] Calcd.	μ_g[a] Exp.	μ_e[b] I	μ_e[b] II
1	2.65	3.69	7.01	5.01
2	2.60	3.47	6.88	5.07
3	2.72	3.91	7.42	5.34
4	2.73	2.87	6.32	4.05
5	4.99	5.53	7.97	6.97
6	1.89	5.39	-	-
7	4.47	2.58	-	-

[a]: Experimental and calculated ground-state dipole moments (in Debye units).

[b]: First excited singlet-state dipole moments (in Debye units): I. Bakhshiev correlations and II. Kawski-Chamma-Viallet correlations.

value significantly higher than the calculated one, and compound 7 shows a reverse behavior (Table 3). It is interesting to note that these values depend on both the nature and position of the substituents. Indeed, dipole moment experimental values vary slightly for unsubstituted, 9- and 10-methyl benzo[a]phenothiazines, whereas, for the 11-methyl derivative a smaller value is found.

This decrease of the dipole moment for the compound 4 may be attributed to the methyl group in 11-position, which would reduce the contribution of dipolar resonance forms, relatively to the other derivatives.

On the other hand, for the 5-oxo substituted benzophenothiazines, the dipole moment values were generally higher than those obtained for unsubstituted or methyl substituted benzophenothiazines, indicating a less symetric electronic distribution and the presence of possible dipolar resonance forms for the compounds 5 and 6. Also, in the case of oxo-derivatives, the ground-state dipole moment values were found to decrease, relative to the unsubstituted derivative, when an hydroxy or a methyl group is present in position 6.

Excited singlet-state dipole moments

The excited singlet-state dipole moment values (determined from the Bakhshiev and Kawski-Chamma-Viallet correlations) are also presented in Table 3.

The dipole moment values of all benzophenothiazines under study are significantly higher in the excited singlet-state than in the ground state. Indeed, the increase of dipole moment in the excited singlet-state range between about 1.9 and 2.5 Debye. This finding indicates that these heterocycles are more polar in their excited singlet-state than in their ground state. The latter property appears to be a general feature for phenothiazine derivatives, in agreement with a similar conclusion reached in our previous papers[21,22].

Work is in progress to evaluate the contribution of the different types of solute-solvent interactions in the excited singlet-state of these benzo[a]phenothiazines. This study and more detailed spectroscopic data will be published in a follow-up paper.

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