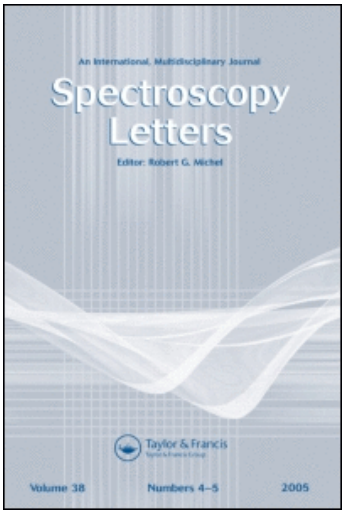

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Spectroscopy of Benzodiazepine-2,4-Dione in Solution

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Spectroscopy of Benzodiazepine-2,4-Dione in Solution

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Abstract: The absorption and emission spectra of benzodiazepine-2,4-dione in solution were measured at room temperature. Assignments of the electronic transitions involved are suggested on the basis of absorption, emission spectra, solvent effects, and fluorescence lifetimes. The shift of the absorption band with increasing solvent polarity is mainly due to dipolar and hydrogen bond interactions between solute and solvent molecules. Furthermore, quantum yields and fluorescence lifetimes have been evaluated in each solvent. Analysis of the results suggests that the hydrogen bond and the dipolar interactions play an equivalent role in stabilization of the first singlet excited state. An energy diagram explaining the different radiative and nonradiative processes has been suggested.

Keywords: Absorption, benzodiazepine-2,4-dione, fluorescence, hydrogen bond, solvent effects

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INTRODUCTION

The benzodiazepine-2,4-dione molecule is composed of a phenyl ring condensed with a seven-membered heterocycle (Fig. 1) and presents a mirror symmetry. Its crystal structure solved at 298 K[1] shows that the molecule is not planar. Benzodiazepine derivatives have been studied because of their biological activity as carcinostatic compounds.[2–5] The study of the behavior of these compounds in solution via experimental photophysics requires a good knowledge of their spectroscopic properties. Our interest in the benzodiazepine-2,4-dione molecule arises from our earlier observations on other heterocyclic molecules.[6–8] However, to our knowledge, no interesting spectroscopy results for this molecule have been reported in the literature. Thus, we discuss in this paper some molecular properties by analyzing the absorption and emission spectra of this molecule at room temperature under the medium effect.

MATERIALS AND METHODS

Benzodiazepine-2,4-dione was synthesized by one of the authors of the current work, and the synthesis and purification methods have been described elsewhere.[9] Electronic absorption and fluorescence spectra in various solvents have been recorded at room temperature. All the solvents used were commercial and of spectroscopy grade. Experimental technique and apparatus for measurements are described elsewhere.[6]

RESULTS AND DISCUSSION

Electronic Absorption Spectra

The absorption spectra of benzodiazepine-2,4-dione in various solvents at room temperature are displayed in Figs. 2(a) and (b). The spectral behavior of the molecule in aprotic solvents (Fig. 2a) and in butanol or dipropylether

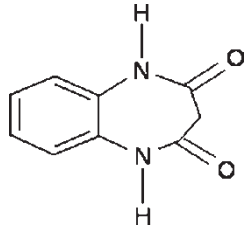

Figure 1. Chemical diagram of benzodiazepine-2,4-dione.

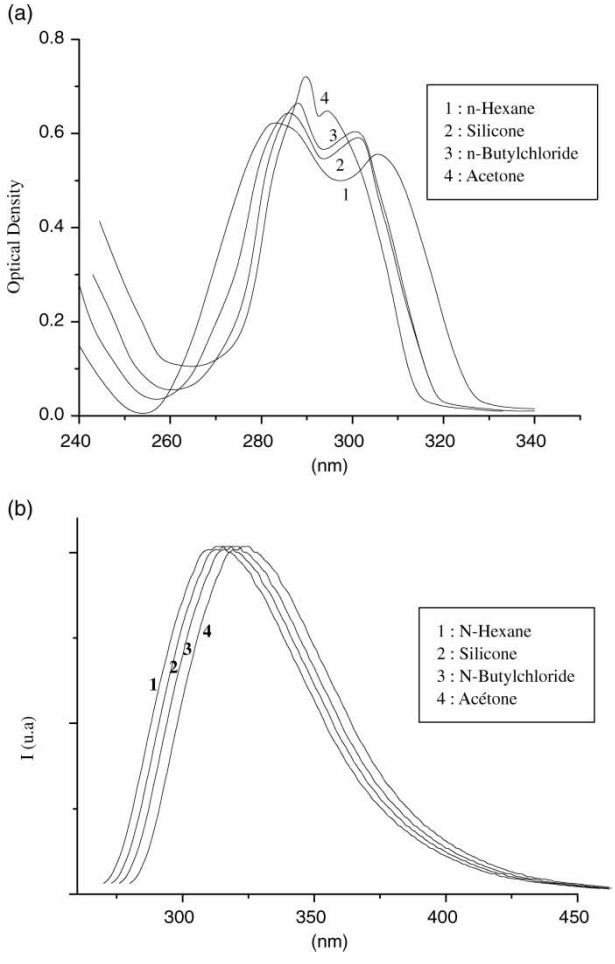

Figure 2. Absorption spectra of the benzodiazepine-2,4-dione at room temperature in various solvents: $C = 10^{-4}$ M. (a) Solvent polarity effect; (b) hydrogen bond effect.

(Fig. 2b) are different. In *n*-hexane, *n*-butylchloride, and acetone, the intense $\pi-\pi^*$ absorption band is localized around 283 nm and has a shoulder around 306 nm. The low-intensity shoulder is attributed to the singlet $n-\pi^*$ transition band absorption. This transition appears often in the molecules containing nonbonding (n) electrons and is almost always lower in energy than singlet $\pi-\pi^*$ transitions

Increasing solvent polarity shifts the $n-\pi^*$ transition to higher energy, broadens out the band, and also shifts the high-intensity $\pi-\pi^*$ absorption to lower energy. However, in butanol and dipropylether, the spectral behavior (Fig. 2b) shows only one large band with high intensity and a maximum at almost 288 nm. A weak redshift is detected when the polarity increases.

The absence of the low-intensity shoulder in these protic solvents indicates that the absorption spectra are characteristic of the complexed molecule by hydrogen bonding interactions in the ground state. The free electrons of the heteroatom can induce hydrogen bonding complex with the solvent molecules. The ($n\pi^*$) electronic level has not been placed in a prominent position. This permits us to suppose that the energetic levels of ($\pi\pi^*$) and ($n\pi^*$) electronic transitions are very close, which provokes the overlapping of their absorption bands and the appearance of one broad band, also observed in the case of benzimidazolone[6] and other aromatic cetones.[10–12]

Fluorescence Spectra

In order to know the benzodiazepine-2,4-dione reaction behavior in the excited state, we have analyzed the fluorescence spectra at room temperature in different solvents. Figure 3 shows the fluorescence spectra of the molecule in polar and nonpolar solvents at room temperature. In *n*-hexane, the spectrum presents a wide band located between 290 nm and 450 nm having a maximum at 313 nm. These characteristics vary with the solvent polarity.

Indeed, the increase of solvent polarity provokes significant redshifts (Fig. 3a) evaluated to $-303\ cm^{-1}$, $-601\ cm^{-1}$, $-989\ cm^{-1}$, and $-1367\ cm^{-1}$ on going from *n*-hexane to silicon, *n*-butylchloride, acetone, and acetonitrile, respectively (see Table 1). This variation of energy under the polarity effect, may be explained by the dipolar interactions stabilizing the excited state S_1. From this result, we can conclude that the excited state of benzodiazepine-2,4-dione is of $\pi\pi^*$ nature having a charge transfer character. On the other hand, in the medium susceptible to form a hydrogen bond (Fig. 3b), the molecule fluorescence spectrum presents a different behavior with respect to the polarity effect considered in aprotic solvents.

The shift from *n*-hexane to butanol and dipropylether is estimated at $-989\ cm^{-1}$ and $-648\ cm^{-1}$, respectively (Table 1). As indicated in Fig. 3, the fluorescence in butanol does not depend only on the polarity effect as butanol is less polar than the *n*-butylchloride. In this case, other types of interactions may be considered.

In dipropylether, benzodiazepine-2,4-dione is subjected to the same polarity effects as in silicon because these two solvents have the same dipole moment except that the first one is able to form hydrogen bonds with the molecule in solution. Consequently, these specific interactions are responsible for the energy gap observed between the molecule fluorescence spectra in these two media. The hydrogen bond thus formed in the excited state can be only of the NH...O type. Moreover, the resemblance between the benzodiazepine-2,4-dione fluorescence spectrum in the dipropylether and butanol enables us to exclude the existence of a complex by hydrogen bond of the OH...N type.

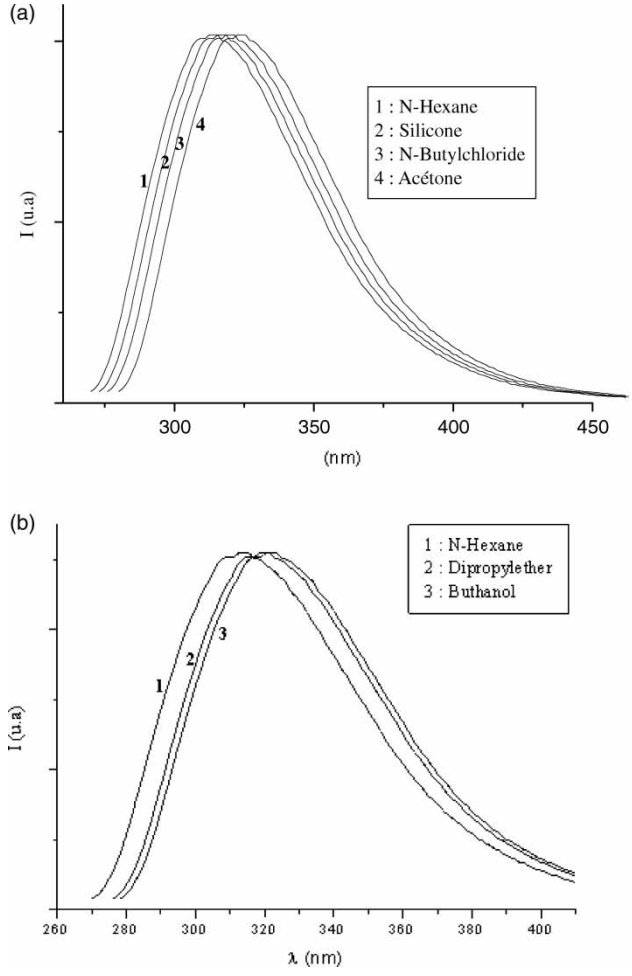

Figure 3. Normalized fluorescence spectra of the benzodiazepine-2,4-dione at room temperature: $C = 10^{-4}$ M, $\lambda_{exc} = 286$ nm. (a) Solvent polarity effect; (b) hydrogen bond effect.

When the energy displacements $\Delta\nu_f$ are caused by simultaneous effects that may be identified as the solvent polarity and the hydrogen bonding, this shift can then be written as: $\Delta\nu_f = {}_{n\text{-hexane}} - \nu_{solvents} = \Delta\nu_p + \Delta\dot{\nu}_{HB}$, where $\Delta\nu_p$ and $\Delta\nu_{HB}$ represent the energies due to the polarity and the hydrogen bonding effects.

In order to evaluate the relative contribution of the specific interaction by hydrogen bond formed between benzodiazepine-2,4-dione and butanol in the excited state, we have plotted in Fig. 4 the benzodiazepine-2,4-dione fluorescence displacement compared with *n*-hexane as a function of solvents dipolar moment.

Table 1. Physicochemical parameters (lifetimes and fluorescence quantum yields), maximum absorption (ν_a), fluorescence emission (ν_f) bands, and $\Delta\nu = \nu_a - \nu_f$ of benzodiazepine-2,4-dione in each solvent

Solvents	ν_a (cm^{-1})	ν_f (cm^{-1})	$\Delta\nu$ (cm^{-1})	τ_f (ps)	Φ_f
n-Hexane	33200	31948	1252	120	0.08
Dipropylether	34500	31250	2250	—	—
n-Butylchloride	33445	31347	2098	280	0.12
Acetone	33784	30959	2825	140	0.18
Acetonitrile	34129	30581	3548	410	0.30
Propanol	34782	31104	3678	1260	0.36
Butanol	34843	30959	3884	1589	0.46
Ethanol	34843	31152	3691	3130	0.52
Methanol	34782	31104	3678	4000	0.60

Considering a linear variation for the fluorescence displacement as a function of solvents dipolar moment, we found for butanol (dipole moment: 1.66 Debye) a $\Delta\nu_p$ equal to $-555\ cm^{-1}$, whereas the additional energy related to hydrogen bond is approximately $-434\ cm^{-1}$. Comparison of these values indicates that the hydrogen bond and the dipolar interactions play an equivalent role in the stabilization of the first singlet excited state S_1.

Lifetimes τ_f and quantum yields values Φ_f of the molecule in different solvents are collected in Table 1. The fluorescence quantum yield was determined relative to that of PBD ($\Phi = 0.77$).[13] It appears that these two parameters are strongly dependent on the solvent polarity and/or the specific interactions between solute and solvent. Indeed, as shown in Table 1, the respective difference of the lifetimes τ_f and quantum yields Φ_f between two very similar solvents (close permittivity), the acetone (weak donor of hydrogen bond) and methanol (acceptor and donor of hydrogen bond), appears to be very large. The specific interactions play a very important role in the benzodiazepine-2,4-dione photophysics, which can confirm the preceding analysis in stationary spectroscopy, where it is supposed that the molecule changes energy and spectral properties according to the solvents used.

It is well-known that the vibrational coupling between the two $n\pi^*$ and $\pi\pi^*$ excited singlet states would generate a very effective mode of nonradiative relaxation when the levels are close (i.e., in our case, in the polar and hydroxylic medium). On the contrary, in the less polar medium, the difference between the two singlet excited states increases and the effectiveness of the nonradiative relaxation process strongly increases. To explain the 1,5-benzodiazepine-2,4-dione photophysical behavior, it is necessary to consider a mechanism utilizing the two S_1 ($n\pi^*$) and S_2 ($\pi\pi^*$) singlet levels and the two T_1 ($n\pi^*$)

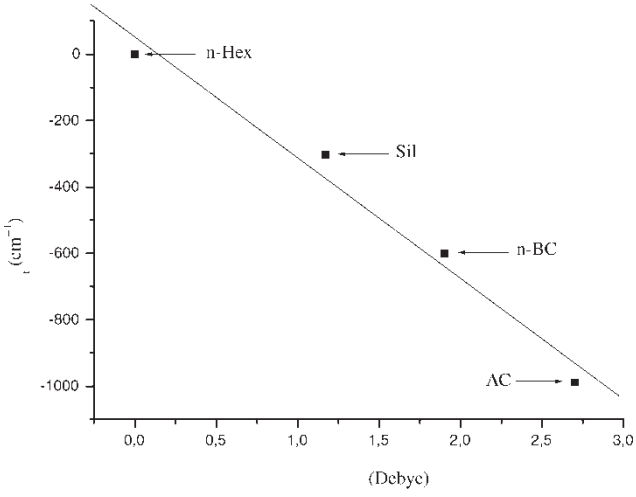

Figure 4. Benzodiazepine-2,4-dione fluorescence band shift compared with *n*-hexane as a function of solvents dipolar moment (correlation factor: R = 98%).

and T_2 ($\pi\pi^*$) triplet levels. Indeed, we managed to propose only one kinetic model based primarily on the three following assumptions:

(i) The intersystem crossing between S_1 and T_2 is a process activated as described by Dalton and Montgomery.[14]

(ii) The energy difference between S_1 and T_1 of the molecule is considered not very large.

(iii) The triplet level T_2 is depopulated very quickly toward T_1, in the same manner that it has been proposed by Cavaleri et al.[15] This assumption also allows complying with the ruling selection of El Sayed.[16]

In the nonpolar medium, the low values of the quantum yield and lifetimes of the molecule fluorescence can be due to an increase in the quantum yield of intersystem crossing, consecutive with the formation of the triplet level T_1; in this case, T_1 can be formed starting from the S_1 ($n\pi^*$) singlet and T_2 ($\pi\pi^*$) triplet level according to the following mechanism:

$$S_1(n\pi^*) \rightarrow T_2(\pi\pi^*) \rightarrow T_1(n\pi^*).$$

An increase in the polarity of the medium destabilizes more S_1 than T_2; then we expect a reduction of the K_{ISC} intersystem crossing rate, consequently increasing quantum yield and the lifetime. In fact, it was shown[17,18] that, for not too high energy variations $S_1 \rightarrow T_2$, the

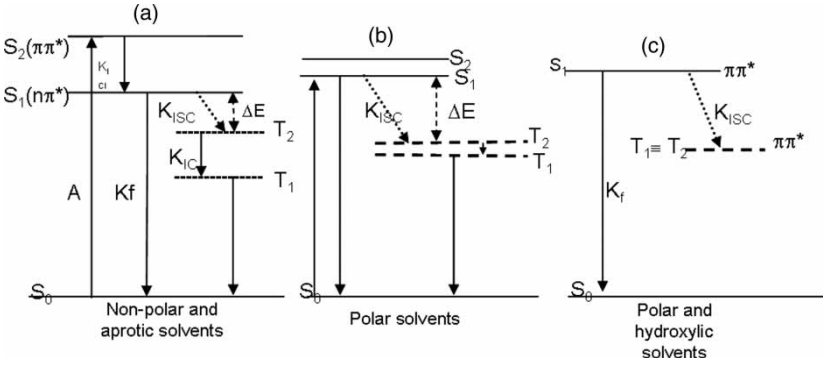

Figure 5. Kinetic diagram showing the benzodiazepine-2,4-dione photophysical behavior with the polarity of solvent where K_f is the fluorescence constant rate, K_{ISC} the intersystem crossing constant rate, and K_{CI} the internal conversion constant rate: (a) in nonpolar solvents; (b) in polar solvents; (c) in polar and hydroxylic solvents.

intersystem crossing rate constant of S_1 toward T_2 increases when the two electronic levels move away. This approach, known as "opposite effect of gap," considers a reduction of the K_{ISC} intersystem crossing rate constant when the solvent polarity increases, in agreement with our experimental results. However, in a very polar medium, the existence of a possible inversion of the first two electronic levels remains valid with the kinetic model that we have proposed (Fig. 5).

CONCLUSIONS

Properties of molecular interactions based on the absorption and the emission spectra of fluorescence of benzodiazepine-2,4-dione have been studied. Assignments of the electronic transitions involved are suggested on the basis of absorption, emission spectra, solvent effects, and fluorescence lifetimes. From this result, we note that the molecule emission state in nonpolar solvents is of $\pi\pi^*$ nature, having a charge transfer character. Moreover, we have considered a possible inversion of the first two electronic levels in the polar medium involving a stabilization of the $\pi\pi^*$ state compared with the $n\pi^*$ state.

On the other hand, in emission, the total energy interaction in butanol is controlled by hydrogen bond and polarity effects, which are equal to $-434\ \text{cm}^{-1}$ and $-555\ \text{cm}^{-1}$, respectively. This means that the hydrogen bond and the dipolar interactions play an equivalent role in stabilization of the first singlet electronic level of the benzodiazepine-2,4-dione molecule. These results have been exploited to envisage an energy diagram involving a principal photophysical process for the benzodiazepine-2,4-dione molecule in different media.

ACKNOWLEDGMENT

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