

EXCIPLEX FORMATION IN 2-PROPANOL SOLUTIONS OF IMIDAZO[4,5-*f*]QUINOLINES

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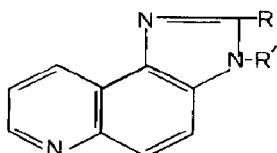
Summary

The association of the excited state derived from four imidazo[4,5-*f*]-quinolines with 2-propanol in cyclohexane has been studied. The unusual bathochromic shift and bandwidth of the fluorescence spectra of these heterocyclic compounds in 2-propanol-cyclohexane solutions compared with those obtained in cyclohexane solutions have been attributed to the association of the excited state imidazoquinolines with the 2-propanol molecules. Hydrogen bonding between the imidazole $>N-H$ moiety of the excited state imidazoquinolines and the 2-propanol is shown to be responsible for the association.

1. Introduction

The fluorescence properties of the *N*-heterocyclic compounds have been extensively studied over the years. The excited state two-proton tautomerism in 7-azaindole and its doubly hydrogen-bonded dimer, as a model for the study of excited state electronic interactions of deoxyribonucleic acid base pairs, has stimulated more interest in an attempt to provide a detailed molecular mechanism for the elucidation of UV-induced mutations in biological systems [1 - 4]. Waluk *et al.* [5] observed that the excited state double proton transfer in the 1-azacarbazole dimer is controlled by the viscosity rather than the temperature. Noda *et al.* [6] studied the proton transfer tautomerism in the excited state of indazole in acetic acid. Making use of the technique of Walker *et al.* [7], Collins [8] has demonstrated the exciplex formation between 7-azaindole and hydroxylic solvent molecules. Recently Nishimura and coworkers [9] isolated a potent mutagen, 2-amino-3-methyl-3*H*-imidazo[4,5-*f*]quinoline, from the neutral fraction of broiled sardines and reported its mutagenicity to be three to four orders of magnitude greater than the previously known quinoline derivatives. Many workers have synthesized imidazoquinolines but most of their investigations have been confined either to the measurement of acidity constants or to electronic spectral studies. As these compounds appear to be potential

mutagens, the excited state associative interactions between the compounds given below and 2-propanol are discussed in this paper. The compounds studied are as follows:



- 1, R \equiv H, R' \equiv H
 2, R \equiv CH₃, R' \equiv H
 3, R \equiv Ph, R' \equiv H

- 4, R \equiv CH₂Ph, R' \equiv H
 5, R \equiv Ph, R' \equiv CH₂Ph

2. Experimental details

The electronic absorption spectra were recorded using a UV-240 Shimadzu UV-visible spectrophotometer. Fluorescence spectra were obtained employing an Aminco-Bowman spectrofluorometer (J₄-8960 model with a J₁₀-222A microphotometer). The fluorescence standard used was quinine sulphate dihydrate (Loba Chemie). Compounds 1 - 4 were prepared by the following methods. Quinoline-5,6-diamine (0.01 mol) and the corresponding aliphatic acid (0.01 mol) were refluxed in 20 ml of 4 N HCl for about 4 h. The reaction mixture was cooled, neutralized with ammonia and extracted with chloroform. The dried compounds were recrystallized in methanol. Compound 5 was prepared by mixing quinoline-5,6-diamine and benzaldehyde in 1:1 molar ratio proportions in 10 ml of acetic acid and left aside for 4 h. The reaction mixture was poured into 100 ml of water, neutralized with ammonia and extracted with chloroform. The extract contained two compounds, 2 and 5; these were separated by chromatography using a benzene-(ethyl acetate) (2:1) solvent mixture. The melting points and IR spectra of all the compounds were confirmed with the reported data [10]. Cyclohexane and 2-propanol were purified by standard procedures [11]. Aerated stock solutions were freshly prepared on the day of measurements and the temperature was kept constant.

3. Results and discussion

Fluorescence emission in the imidazo[4,5-*f*]quinolines can be traced to the ¹L_b transition [12]. The relationship between the room temperature absorption and the fluorescence spectra of compound 1 in cyclohexane-2-propanol solvents is shown in Fig. 1. The fluorescence maximum of compound 1 in cyclohexane is at 354 nm, while in 2-propanol it is at 393 nm. The red shift of the 352 nm fluorescence band of compound 2 with added 2-propanol is shown in Table 1. It is clear from Fig. 1 and Table 1 that, as

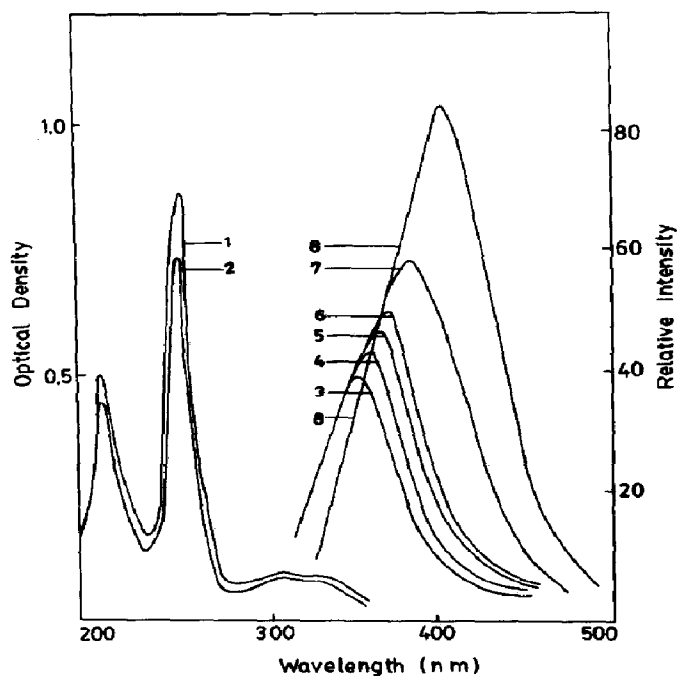


Fig. 1. Absorption and fluorescence spectra of compound 1. Curves 1 and 2 correspond to the absorption spectra in cyclohexane and 2-PrOH; curves 3 - 8 correspond to the cyclohexane-2-PrOH mixtures in which the 2-PrOH is 0 M, 0.015 M, 0.035 M, 0.082 M, 0.120 M and 100% respectively.

TABLE 1

Red shift of 352 nm fluorescence band of 2-methylimidazo[4,5-*f*]quinoline in cyclohexane with the added isopropanol (concentration of the compound fixed at 1.00×10^{-5} M)

Sample	Concentration of isopropanol (M)	λ_f (nm)
1	—	352
2	0.013	360
3	0.026	365
4	0.041	373
5	0.049	376
6	0.065	383
7	0.13	388
8	0.26	389
9	0.52	390
10	0.72	390
11	1.02	390
12	3.72	392
13	5.20	393
14	7.51	395
15	10.44	398
16	100%	401

TABLE 2

Fluorescence spectral data of imidazo[4,5-*f*]quinolines

Compound	Cyclohexane		λ_f (nm) for isopropanol	Exciplex	
	λ_f (nm)	FWHM (cm^{-1})		λ (nm)	FWHM (cm^{-1})
1	354	5312	393	374	5635
2	352	5705	401	387	6057
3	358	4874	398	390	5167
4	364	4123	404	378	4572
5	364	3814	400	—	—

the percentage of 2-propanol in the cyclohexane increases, the fluorescence maximum undergoes a considerable red shift. A remarkable bathochromic shift at 2-propanol concentrations so low as to have a negligible effect on the dielectric constant of the solvent is observed for compounds 1 - 4, whereas for compound 5 the red shift due to the 2-propanol added to the cyclohexane solutions can be attributed to the increased dielectric constant of the medium. All the compounds except 5 have a greater fluorescence intensity in the 2-propanol solvent than in the cyclohexane solvent.

The dissimilar results obtained by the structurally similar compounds with 2-propanol and the remarkable bathochromic shift of the fluorescence maximum in compounds 1 - 4 due to 2-propanol concentrations below 0.2 M, at which no considerable change in dielectric constant takes place, reveal that there is a specific interaction between these compounds and 2-propanol [13].

The relationship between the shift in the fluorescence maximum of the imidazoquinolines in cyclohexane with respect to the 2-propanol concentration is shown in Fig. 2. It is seen that, for compounds 1 - 4, the shift in the fluorescence maximum with added 2-propanol gives two straight lines with different slopes, indicating that there are two kinds of fluorescing species present in the cyclohexane-2-propanol mixture. From the work of Collins [8] the spectrum obtained at longer wavelengths with 2-propanol concentrations below 0.2 M is attributed to the emission due to the association of the excited state imidazoquinolines with the 2-propanol molecules. Once the normal heterocyclic compound has been converted into its associative, the spectrum can be shifted towards longer wavelengths as a result of the increased dielectric constant of the medium. This is reflected by the horizontal lines of Fig. 2. The emission maximum for the associated heterocycles (exciplex) for compounds 1 - 4 is obtained from the intersection of the two straight lines (Fig. 2) and the data are presented in Table 2.

Further, evidence for the existence of exciplexes in compounds 1 - 4 comes from the fluorescence band half-width (full width at half-maximum (FWHM)) data. The FWHM values of the normal and exciplex fluorescence bands are reported in Table 2. The values due to the normal species vary

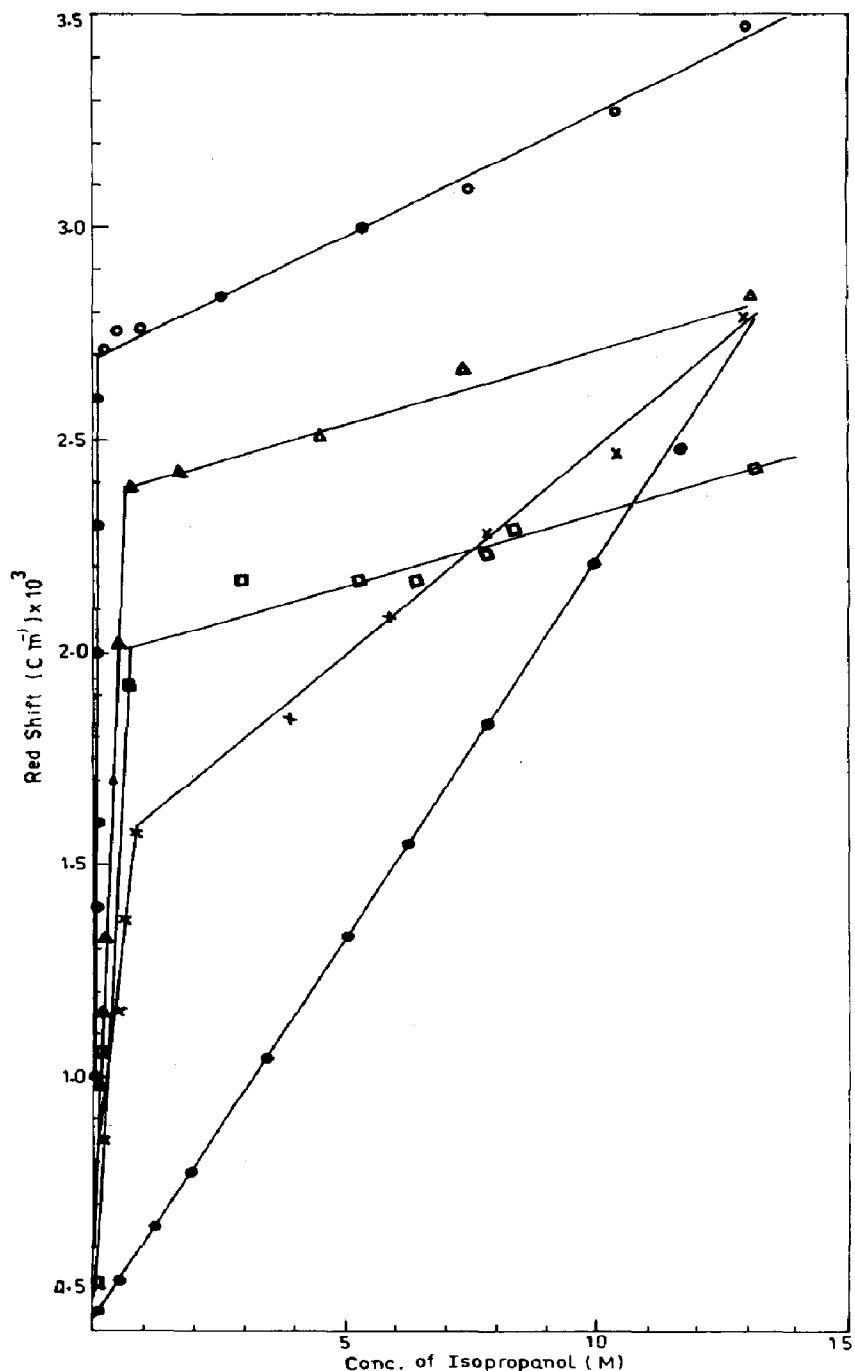


Fig. 2. Typical relationship between the red shift in the fluorescence maximum of imidazoquinolines and 2-PrOH concentration. x, o, □, △ and ● represent compounds 1 - 5.

between 3814 and 5705 cm^{-1} , while those for the exciplex range between 4572 and 6507 cm^{-1} . It has been reported [14] that a 300 cm^{-1} increase over the normal emission exists for the pyrene-ethanol exciplex and that a

700 cm^{-1} increase exists for the pyrene–dimethylaniline (DMA) exciplex [14]. The increase in the FWHM values over the normal FWHM values is greatest for 2-benzylimidazo[4,5-*f*]quinoline (449 cm^{-1}) and is smallest for 2-phenylimidazo[4,5-*f*]quinoline (292 cm^{-1}) which reveals that the red shift of the emission bands below a 2-propanol concentration of 0.2 M is due to the association of the excited state compounds 1 - 4 with one or two 2-propanol molecules.

4. Nature of the interaction

In many cases it has been found that the fluorescence intensity is quenched in polar protic solvents compared with its behaviour in inert non-polar solvents as a result of a radiationless transition [15, 16]. With the exception of compound 5 in which the imidazole hydrogen is replaced by a benzyl group, the compounds displayed an increased fluorescence intensity on the addition of 2-propanol to the cyclohexane solutions. If the increased fluorescence intensity is due to the dipole–dipole interaction with some charge transfer from the lone pair electrons of the oxygen to the vacant π orbital of the excited heterocycle as observed for the *N*-methylindole–alcohol [7] exciplex then the increased intensity should have been observed in all the compounds. Therefore, the above model can be ruled out on the basis that compound 5, which is structurally identical with the rest, has quenched the fluorescence on the addition of 2-propanol. The higher quantum yield of the pyrene–DMA exciplex than the normal fluorescence intensity of pyrene at a low DMA concentration was attributed [14] to an exciplex of excited pyrene and aggregated DMA. A similar reason cannot hold true in the present case because the fluorescence intensity has increased at all the concentrations of 2-propanol for compounds 1 - 4. It is most likely that the electron-deficient nitrogen atom of imidazole in the excited state could act as a proton donor, thereby forming a hydrogen bond with the *n* electrons of the oxygen of 2-propanol. As there is no proton attached to the imidazole nitrogen in compound 5 there is no possibility of a hydrogen bond with 2-propanol.

The abnormal bathochromic shift observed in compounds 1 - 4 below 0.2 M 2-propanol in cyclohexane has been assigned to the excited state hydrogen-bond formation between the imidazole $>\text{N}-\text{H}$ moiety of imidazoquinoline and 2-propanol. After conversion of the normal molecule to the excited state complex the complex further shifted to the red. This corresponds to 2-propanol concentrations greater than 0.2 M.

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