Chemistry of Heterocyclic Compounds, Vol. 33, No. 7, 1997

SOLVATOFLUOROCHROMIC PROPERTIES OF SULFONYL FLUORIDE DERIVATIVES OF 5-ARYL(HETEROARYL)-2-PHENYL-1,3,4-OXADIAZOLE, PROMISING FLUORESCENT PROBES

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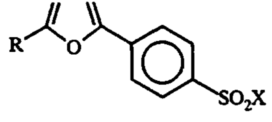
The spectral characteristics of seven 5-aryl(heteroaryl)-2-phenyl-1,3,4-oxadiazole derivatives, containing an expressed electron-accepting grouping such as sulfonyl fluoride or sulfonyldifluoromethane in the para position of the phenyl substituent, have been investigated in solvents of various polarity. The insignificant effect of the $n\pi^*$ *levels of the* SO_2X *grouping on the fluorescence properties of the compounds studied was established, as a result of which they are highly effective organic luminophors in the near ultraviolet and violet spectral ranges. The presence was shown of a significant solvatochromic effect exerted particularly clearly in derivatives with electron-donating groups in the 5-aryl substituent. As a result of this, the compounds indicated may be recommended for use as fluorescent probes in medicine and biology. Adiabatic flattening in the excited state of the sterically hindered methoxy derivative and the formation of a TICT state are considered, leading to quenching of the fluorescence of dimethylamino derivatives in media of high polarity.*

The spectral and luminescence properties of arylsulfonyl derivatives have received the steady attention of physical chemists for a fairly long time. Investigations have covered the electron-accepting properties of substituents of the SO_2X type [1] and their effect on absorption spectra and fluorescence [2, 3]. The primary photophysical processes in molecules of heterocyclic compounds containing the grouping mentioned have been subjected to theoretical and experimental investigation [4]. Also considered was the ratio of inductive and mesomeric effects of substituents of the sulfonyl nucleus [5]. From the point of view of spectral luminescence characteristics, the latter have an appreciable advantage over the most effective electron-accepting substituent, the nitro group. This is deduced from the fact that in the majority of cases the introduction of an SO_2X group does not lead to significant fluorescence quenching although it does not cause such a significant change in the position of spectral bands as does the introduction of a nitro group.

The present paper continues the study of the effect of the sulfonyl group on the spectral characteristics of aromatic derivatives of azoles. The derivatives considered were 2,5-diphenyl-1,3,4-oxadiazole (I, PPD) and its 5-aryl(heteroaryl) analogs containing a sulfonyl fluoride (IIa-f) or sulfonyldifluoromethane (III) group in the para position of the 2-phenyl substituent.



IIa-f, III

IIa–f X = F; a R = C_6H_5; b R = 2- furyl ; c R = C_6H_4—C_6H_5-*p*; d R = C_6H_4—CH_3-*m*;
e R = C_6H_4—OCH_3-*o*; f R = $C_6H_4N(CH_3)_2$-*p*; III X = CHF_2; R = $C_6H_4N(CH_3)_2$-*p*

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TABLE 1. Data of Absorption and Fluorescence Spectra and Photophysical Parameters for Compounds (I), (IIa-f), and (III) for Solutions in Dioxan (D) and Acetonitrile (A)

Compound	Solvent	Spectral characteristics †							
		ν_a (ε_a)	ν_f	$\Delta\nu_{ST}$	φ_f	τ_f	k_f^a	k_f	k_d
I	D	35980 (23500)	28760	7220	0,70	1,18	$7{,}04 \cdot 10^8$	$5{,}92 \cdot 10^8$	$2{,}55 \cdot 10^8$
	A	35880	29020	5520	0,93	1,36	—	$6{,}86 \cdot 10^8$	$5{,}24 \cdot 10^7$
IIa	D	33900 (23100)	26560	7340	0,78	1,26	$5{,}97 \cdot 10^8$	$6{,}23 \cdot 10^8$	1,73 · 108
	A	34120	24980	9140	0,84	1,61	—	$5{,}20 \cdot 10^8$	$9{,}99 \cdot 10^7$
IIb	D	32280 (20600)	24220	8060	0,63	1,69	$3{,}95 \cdot 10^8$	$3{,}71 \cdot 10^8$	$2{,}19 \cdot 10^8$
	A	32660	21560	11100	~1	3,18	—	$(3{,}15 \cdot 10^8)$	—
IIc	D	31800 (32900)	24860	6940	0,79	1,27	$6{,}23 \cdot 10^8$	$6{,}25 \cdot 10^8$	$1{,}62 \cdot 10^8$
	A	32040	20820	11220	~1	3,08	—	$(3{,}24 \cdot 10^8)$	—
IId	D	33680 (24700)	26180	7500	0,78	1,35	$4{,}87 \cdot 10^8$	$5{,}77 \cdot 10^8$	$1{,}66 \cdot 10^8$
	A	34000	24480	9520	~1	1,82	—	$(5{,}49 \cdot 10^8)$	—
IIe	D	32340 (11900)	24260	8080	0,79	2,28	$1{,}75 \cdot 10^8$	$3{,}46 \cdot 10^8$	$9{,}24 \cdot 10^7$
	A	31280	20080	8260	~1	3,38	—	$(2{,}96 \cdot 10^8)$	—
IIf	D	27460 (23500)	18540	8920	0,63	5,21	$3{,}14 \cdot 10^8$	1,21 · 108	$7{,}09 \cdot 10^7$
	A	27500	—	—	~0	—	—	—	—
III	D	27500 (23100)	19080	8420	0,68	4,98	$3{,}23 \cdot 10^8$	$1{,}36 \cdot 10^8$	$6{,}42 \cdot 10^7$
	A	27220	—	—	~0	—	—	—	—

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†ν_a, ν_f, $\Delta\nu_{ST}$ are the positions of the long wave maximum in the absorption spectrum, the maximum of the emission spectrum, and the Stokes shift of the fluorescence (cm^{-1}), ε_a is the intensity of the long wave absorption band in dioxan (liter·mole^{-1}·cm^{-1}), φ_f and τ_f are the quantum yield and the lifetime of the fluorescence (nsec), k_f^a and k_f are the rate constants for flourescence emission (sec^{-1}) estimated from the absorption spectra and the quantum yield or lifetime of the fluorescence respectively, and k_d is the overall rate constant for the processes of nonemissive dissipation of the electronic excitation energy (sec^{-1}).

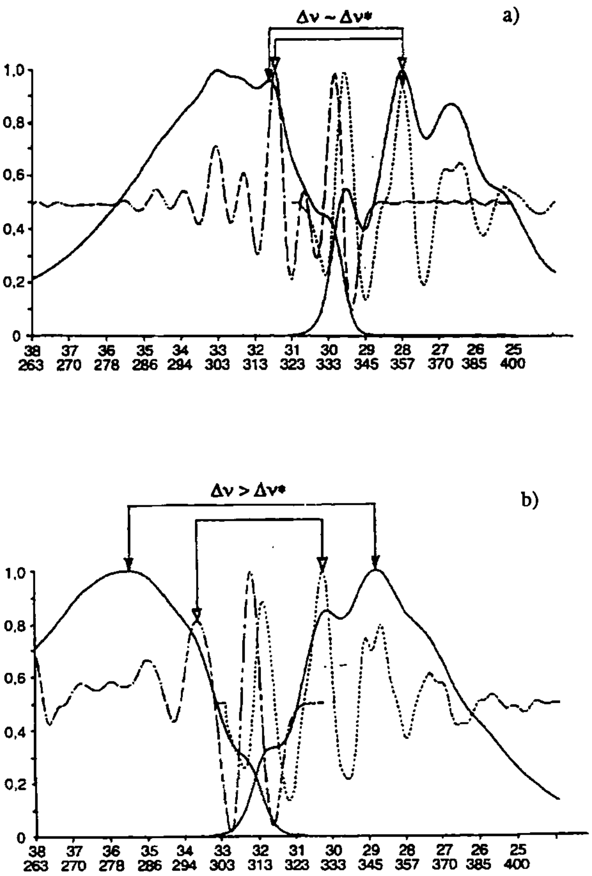

Fig. 1. Absorption and fluorescence spectra and their second derivatives given with sign reversed for a) 2,5-diphenyloxazole-1,3,4 (PPO) in octane and b) 2,5-diphenyloxadiazole (PPD) in dioxan ($\Delta\nu^*$ is the Stokes shift determined in the traditional way, $\Delta\nu^*$ is the Stokes shift calculated as the difference in positions of the same vibrational sublevels in the second derivative spectra).

Several factors were of interest to us. Primarily the conjugated system of the 2,5-diphenyl-1,3,4-oxadiazole (I) molecule is symmetrical, unlike that of its oxazole analogue. Therefore, intramolecular donor–acceptor interactions may be traced in a neater form for oxadiazole derivatives undistorted by the effect of the electronic asymmetry occurring in the oxazole series [6]. On the other hand the fluorescence characteristics of compounds containing a sulfonyl fluoride grouping must depend significantly on the polarity of its surroundings. Consequently they are potential fluorescent probes in biology and medicine. The fairly high reactivity of the sulfonyl fluoride grouping enables these compounds to be used as fluorescent markers. Oxadiazole derivatives usually fluoresce in a shorter wave region than their oxazole analogs [7], consequently the synthesis of similar compounds may lead to efficient short wave luminophors. This problem has also remained urgent for several years.

The spectral characteristics of the 1,3,4-oxadiazole derivatives (IIa-f) and (III) in dioxan and acetonitrile are given in Table 1. The use of this pair of solvents enables conclusions to be drawn on the influence of the polarity of the medium on the fluorescence properties of the compounds. As is seen from the data, the majority of the derivatives considered are characterized by fairly high fluorescence quantum yields, approaching unity in a solvent of high polarity. The fluorescence of the compounds of the series studied covers a range from the near ultraviolet to the green region of the spectrum. As might have been expected for compounds with a significant intramolecular donor–acceptor interaction, the introduction of donor substituents and the successive increase in electron-donating properties of the latter (such as in the series $CH_3 < OCH_3 < N(CH_3)_2$) leads to a significant long wave displacement of the absorption and emission spectra.

Comparison of the sizes of the rate constants of the primary photophysical processes, viz. fluorescence (k_f) and nonemissive dissipation of the excitation energy (k_d), for compounds (I) and (IIa) indicates the absence of any marked quenching of the fluorescence by the effect of $n\pi^*$ levels introduced into the system of singlet and triplet terms of the (I) molec-

TABLE 2. Certain Characteristics of Compounds (IIa-f) and (III)

Compound	Empirical formula	Found, % / Calculated, %			mp, °C
		N	S	F	
IIa	$C_{14}H_9FN_2O_3S$	$\frac{9,3}{9,2}$	$\frac{10,8}{10,5}$	$\frac{6,1}{6,2}$	204...206
IIb	$C_{20}H_{13}FN_2O_3S$	$\frac{7,2}{7,4}$	$\frac{8,6}{8,4}$	$\frac{5,3}{5,0}$	223...226
IIc	$C_{12}H_7FN_2O_4S$	$\frac{9,4}{9,5}$	$\frac{11,1}{10,9}$	$\frac{6,6}{6,5}$	197,5...198,5
IId	$C_{15}H_{11}FN_2O_4S$	$\frac{8,3}{8,4}$	$\frac{9,9}{9,6}$	$\frac{5,9}{5,7}$	162...163
IIe	$C_{15}H_{11}FN_2O_3S$	$\frac{8,9}{8,8}$	$\frac{10,5}{10,1}$	$\frac{5,8}{6,0}$	204...204,5
IIf	$C_{16}H_{14}FN_3O_3S$	$\frac{12,0}{12,1}$	$\frac{9,4}{9,2}$	$\frac{5,3}{5,5}$	225...226
III	$C_{17}H_{15}F_2N_3O_3S$	$\frac{10,9}{11,1}$	$\frac{8,8}{8,5}$	$\frac{10,1}{10,0}$	213...215

ule by the SO_2F substituent. Consequently, the energy of the triplet level of $n\pi^*$ type of the sulfonyl fluoride group lies significantly above 34000 cm^{-1} which is the energy of the lower excited singlet state of diphenyloxadiazole (this conclusion is confirmed by the data of [4]) and proved to have no effect on the fluorescence properties of compound (IIa), nor on the properties of its derivatives (IIb-f) containing donor substituents. A similar conclusion may also be drawn for compound (III) containing a sulfonyldifluoromethyl group.

The Stokes shifts of the fluorescence of all the compounds investigated were fairly large and were ~7000-8000 cm^{-1} for solutions in dioxan. A similar value was also characteristic of the unsubstituted molecule (I). This seems fairly strange on comparison with the derivatives of 2,5-diphenyloxazole (PPO) which are close in structure and are characterized by values of $\Delta\nu_{st}$ not exceeding 4000-5000 cm^{-1}. The 2,5-diphenyl-1,3,4-oxadiazole molecule has a more planar structure than 2,5-diphenyloxazole due to the absence of a hydrogen atom at the 4 position of the oxadiazole ring which creates a certain steric hindrance in the PPO molecule. However, in fact, the increase in the Stokes fluorescence shift on going from PPO to PPD is only apparent. In the more planar and consequently more rigid PPD molecule, a redistribution occurs of the intensity of the separate vibrational components in the absorption and fluorescence spectra. If in the PPO molecule the Stokes shift is regarded as a difference of energy of 0-2 transitions, then in the PPD molecule the Stokes shift, determined in the usual way as the difference in energy of the maxima of the long wave absorption band and the fluorescence band, corresponds to a difference of energy of 0-3 transitions and consequently includes in addition the difference of energy of neighboring sublevels of the ground and excited states. This phenomenon is illustrated fairly graphically in Fig. 1 in which the absorption and emission spectra of compound (I) in dioxan are given and also their second derivatives where the vibrational structure is traced more clearly.

The absence of relaxation processes in the lower singlet excited state in the majority of the compounds investigated in a nonpolar medium, leading to an increase in the Stokes shift of the fluorescence, is indicated by the closeness of the rate constants for fluorescence emission determined from the values of the quantum yield and lifetime ($k_f = \varphi_f\tau_f$) and the size of k_f estimated from absorption spectra (k_f^a). The exception was the o-OCH_3 derivative (IIe) for which $k_f > k_f^a$. A fairly bulky substituent in the ortho position creates steric hindrance in this molecule as a result of which its planarity is disturbed. Correspondingly, the conjugation is weakened between the donor and acceptor centers of the molecule, namely the benzene rings into which the OCH_3 and SO_2F groups were introduced. This hypothesis is supported by the reduction in intensity of the long wave absorption band to almost one half and the analogous reduction in the size of k_f^a accompanying it. In the excited state similar molecules display a tendency to be flattened [8], as a result of which the conjugation between the separate parts of the molecule is reduced. The energy of the fluorescent state is reduced and the Stokes shift is increased by this. The almost twofold increase in k_f compared with k_f^a in our opinion confirms the suggestion of flattening of the (IIe) molecule in the excited state.

On the other hand the opposite tendency was observed for the dimethylamino derivatives (IIf) and (III). There was a reduction of k_f to less than half the value of k_f^a. This may indicate a reduction in the planarity of these molecules in the S_1^* state. It is known that the formation of dipolar TICT states is characteristic of dimethylamino derivatives of organoluminophors, particularly in cases when marked electron-accepting substituents are present [9]. In this the $N(Alk)_2$ grouping is unfolded to an angle of 90° relative to the plane of the molecule. The formation of TICT states is considered to be the main reason for the deterioration of the fluorescence characteristics of dialkylamino derivatives in polar solvents [10]. A similar phenomenon also takes place in our case, the fluorescence of compounds (IIf) and (III) in polar acetonitrile proved to be practically completely extinguished. Thus, the reduction of k_f relative to k_f^a in dioxan may act as an indicator of the possibility of forming TICT states in polar media. It is probable that this relationship is linked with the so-called dioxan effect, by the presence in this solvent of two conformations [11] (a polar boat and a nonpolar chair) the equilibrium between which, particularly in neighboring solvated films, may be shifted in the direction of the more polar form by the action of a dissolved activator substance, increasing the dipole moment significantly in the excited state. As a result, the excited luminophor molecules prove to be solvated effectively by the more polar solvent than the corresponding unexcited molecules. It is probable that this also determines the marked sensitivity of compounds (IIf) and (III) towards flattening in the excited state in dioxan.

For the remaining compounds investigated, the transition from a nonpolar to a polar solvent is accompanied by an increase in emission intensity. As might have been expected for molecules increasing in polarity in the excited state a significant growth in the Stokes shift in acetonitrile compared with dioxan was a characteristic of compounds (IIa-e). This was accompanied by a significant increase in the lifetime and quantum yield of the fluorescence. This corresponds with a fall in the efficiency of the processes of nonemissive dissipation of electronic excitation energy. For compounds (IIb-e) the tendency recorded was displayed so clearly that the deactivation of the lower activated singlet state in acetonitrile was effected practically only by the emission pathway. The quantum yield of fluorescence which is close to 1 indicates this, as does the fact that the size of $1/\tau_f$ for these compounds proved to be close to the size of k_f in dioxan (the size of k_f is in practice an intramolecular characteristic and must not change on going from a nonpolar to a polar solvent). The solvatofluorochromic displacement, assessed as the difference in energies of the emitted fluorescence quanta in dioxan and in acetonitrile, was maximal for compounds (IIc) (4040 cm^{-1}) and (IIe) (4180 cm^{-1}). These compounds therefore possess high fluorescence characteristics and a significant sensitivity towards the polarity of the medium. They may be recommended for use as efficient fluorescent probes.

EXPERIMENTAL

The absorption spectra were measured on Specord M-40 and Hitachi U-3210 spectrophotometers and the fluorescence spectra on a Hitachi F-4010 spectrofluorimeter. Quantum yields of fluorescence were determined relative to quinine bisulfate in 1 N sulfuric acid (φ = 0.546 [12]) with the introduction of a correction to the difference in the refractive index of the standard and test solutions. The fluorescence kinetics were studied with the equipment described in [13] operating in a mode of counting single photons in the nanosecond range. Mathematical processing of the quenching curves was carried out by the least squares method as described in [14, 15].

Synthesis of the fluorosulfonyl derivatives (IIa-f) and (III) was carried out according to a scheme comprising acylation of monoaroyl hydrazines with p-fluorosulfonyl- and p-difluoromethylsulfonylbenzoic acid chlorides and subsequent cyclodehydration of the resulting N,N'-diaroylhydrazines in the presence of $POCl_3$ by the procedures of [7, 16]. Some characteristics of the compounds synthesized are given in Table 2. The purity of the substances investigated was checked by chromatography of their solutions in toluene on aluminum oxide with subsequent recrystallization from benzene.

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