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FLUORESCENCE OF 3,5-DIETHOXYCARBONYL-1,4-DIHYDROPYRIDINE DERIVATIVES AND THEIR ANIONS

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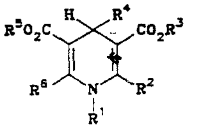
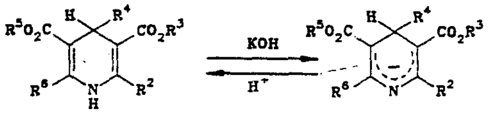
The fluorescence spectra of a group of 3,5-diethoxycarbonyl-1,4-dihydropyridine (1,4-DHP) derivatives were investigated. The introduction of electron-acceptor N-substituents and 2,6-methyl groups decreases Q markedly. The fluorescence spectra of 1,4-DHP anions are shifted bathofluorically, and the Q values are higher than for the corresponding 1,4-DHP. The fluorescence spectra have large Stokesian shifts, which are decreased for 1,4-DHP anions. A good correlation exists between the λ_{max} values of the fluorescence bands of 1,4-DHP anions and the Hammett σ_p^+ constants of the 4-R-aryl substituents.

The literature contains a wealth of information on the electronic absorption spectra of 1,4-dihydropyridines (1,4-DHP) [1, 2] and only a small amount of qualitative data on the fluorescence spectra [3, 4]. The quantitative determination of the fluorescence characteristics of 1,4-DHP derivatives in organic solvents and biological probes is of interest, and systematic studies of the fluorescence spectra of a number of 1,4-DHP derivatives were therefore made.



I-XXIII



II, III, XVI, XVIII-XXIII

IIa, IIIa, XVIa, XVIIIa-XXIIIa

I—III, XI, XII, XV, XVI, XVIII—XXIII $R^1 = H$, IV, V, XIII, XIV, XVII $R^1 = CH_3$, VI $R^1 = iso\text{-}C_3H_7$, VII $R^1 = CH_2COOC_2H_5$, VIII $R^1 = CH_2COOH$, IX $R^1 = COOC_2H_5$, X $R^1 = SO_2CH_3$; I—XIV $R^2 = H$, XV—XXIII $R^2 = CH_3$; I—X, XV—XXIII $R^3 = R^5 = C_2H_5$, XI, XIII $R^3 = R^5 = H$, XII, XIV $R^3 = H$, $R^5 = C_2H_5$; I, XV $R^4 = H$, II, IV, VI—XIV, XVI, XVII $R^4 = C_6H_5$, III, V, XVIII $R^4 = 4\text{-}CH_3OC_6H_4$, XIX $R^4 = 3$-pyridyl, XX $R^4 = 4\text{-}ClC_6H_4$, XXI $R^4 = 4\text{-}HOC_6H_4$, XXII $R^4 = 4\text{-}CH_3C_6H_4$, XXIII $R^4 = 4\text{-}NO_2C_6H_4$

The spectral parameters of 1,4-DHP derivatives (I-XXIII) and their anionic forms (IIa, IIIa, XVIa, XVIIIa-XXIIIa), which are formed in the deprotonation of the nitrogen atom of the DHP ring ($R^1 = H$), are presented in Tables 1 and 2.

3,5-Diethoxycarbonyl-1,4-DHP (I) in ethanol solution has blue luminescence (λ_{max} 461 nm) with relative quantum yield Q = 0.59. The introduction of a 4-phenyl (II) or 4-(4'-methoxyphenyl) (III) substituent shifts the fluorescence spectrum hypsofluorically by 21-23 nm. N-Alkyl substitution (IV, VI) has little effect on the fluorescence spectra ($\Delta\lambda$ = 4 nm), in contrast to the excitation spectra, in which a bathochromic shift of 13 nm is observed when the nitrogen atom of the 1,4-DHP ring is methylated (II and IV). This can be explained in part by the asymmetry of the fluorescence band. Thus a poorly expressed vibrational

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TABLE 1. Fluorescence Spectra of 3,5-Diethoxycarbonyl-1,4-DHP Derivatives

Compound	Fluorescence spectrum (λ_{max}, nm; Stokesian shift, cm^{-1})											
	Ethanol				Ethylene glycol				Glycerol			
	λ_{max}^{exc}	$\lambda_{max}^{f\ell}$,	Stokesian shift	Q	λ_{max}^{exc}	λ_{max}^{fl}	Stokesian shift	Q	λ_{max}^{exc}	λ_{max}^{fl}	Stokesian shift	Q
I	376	461	4910	0,59	379	472	5200	0,68	381	472	5060	0,69
II	361	440	4970	0,54	364	443	4900	0,64	366	443	4570	0,67
III	360	438	4950	0,38	362	440	4890	0,50	364	443	4900	0,57
IV	374	444	4220	0,43	376	443	4030	0,52	381	446	3830	0,64
V	372	445	4410	0,38	375	444	4150	0,47	380	444	3800	0,60
VI	372	445	4410	0,33	376	445	4130	0,42	379	442	3770	0,57
VII	362	436	4680	0,37	366	440	4590	0,45	368	441	4490	0,55
VIII	366	440	4590	0,44	374	444	4220	0,61	375	444	4150	0,65
IX	310	391	6680	0,05	315	394	6370	0,07	315	400	6750	0,18
X	313	399	6890	0,04	313	404	7200	0,08	313	407	7380	0,12
XI	351	436	5550	0,38	356	441	5410	0,39	361	442	5080	0,53
XII	360	436	4840	0,35	359	440	5130	0,44	363	442	4930	0,54
XIII	368	444	4650	0,28	372	444	4360	0,38	375	446	4250	0,53
XIV	370	445	4560	0,35	373	446	4390	0,41	377	445	4060	0,53
XV	374	463	5140	0,02	375	472	5620	0,06	376	465	5090	0,16
XVI	357	445	5540	0,005	357	447	5640	0,03	359	450	5630	0,09
XVII	353	449	6060	0,001	354	452	6120	0,002	355	459	6380	0,006

TABLE 2. Fluorescence Spectra* of 3,5-Diethoxycarbonyl-1,4-DHP Derivatives (II, III, XVI, XVIII-XXIII) in DMF and of Their Anions (IIa, IIIa, XVIIIa-XXIIIa) in DMF + 1 N KOH

Compound	Fluorescence spectra of 1,4-DHP				Compound	Fluorescence spectra of 1,4-DHP anions				
	λ_{max}^{exc}, nm	$\lambda_{max}^{f\ell}$, nm	A, cm^{-1}	Q		λ_{max}^{exc}, nm	λ_{max}^{fl}, nm	B, cm^{-1}	Q	A − B
II	359	439	5080	0,50	IIa	446	514	2970	0,67	2110
~~III~~	~~357~~	~~437~~	~~5540~~	~~0,50~~	~~IIIa~~	~~441~~	~~509~~	~~3240~~	~~0,71~~	~~2100~~
XVI	352	439	5630	0,005	XVIa	437	519	3620	0,32	2010
XVIII	351	438	5660	0,004	XVIIIa	438	513	3340	0,41	2320
XIX	355	441	5490	0,01	XIXa	445	524	3390	0,58	2100
XX	353	438	5500	0,01	XXa	441	521	3480	0,53	2020
XXI	350	436	5640	0,004	XXIa	438	511	3260	0,18	2380
XXII	352	438	5580	0,01	XXIIa	438	517	3530	0,46	2050
XXIII	Does not fluoresce				XXIIIa	440	527	3750	<0,001	—

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*A are the Stokesian shifts for 1,4-DHP, B are the Stokesian shifts for 1,4-DHP anions, and A − B are the differences in the Stokesian shifts.

structure of the latter is observed at room temperature, and the intensities of the individual bands decrease on the long-wave side. When an electron-acceptor substituent is present in the N-methyl group (VII and VIII), the excitation spectra are shifted hypsochromically as compared with the spectra of IV by 12-14 nm, while the fluorescence spectra have $\Delta\lambda = -4 \ldots -8$ nm. In the case of IX and X, which have electron-acceptor substituents attached to the ring nitrogen atom, the long-wave absorption band is shifted hypsochromically by 50 nm as compared with the absorption band of II [5]. These compounds display weak fluorescence, which is also shifted hypsofluorically as compared with the fluorescence of II. The corrected excitation and fluorescence spectra generally coincide with the long-wave absorption bands given in [5].

An increase in the number of methyl groups in the 3,5-diethoxycarbonyl-1,4-DHP molecule or its 4-phenyl derivative is accompanied by a hypsochromic shift of the excitation spectra from 2 nm to 21 nm (I, II, IV, XV-XVII), while the fluorescence spectra have only a small bathofluroic shift (I → XV, II → XVI → XVII, IV → XVII, but not II → IV).

According to the results of x-ray diffraction analysis [6, 7], the molecules of 1,4-DHP derivatives almost always have a boat configuration and, consequently, little likelihood of emissive transitions. Nevertheless, 3,5-diethoxycarbonyl-1,4-DHP (I) has Q = 0.59, but the Stokesian shift is 4910 cm^{-1}. If, after excitation of the molecule, only vibrational relaxation to a lower vibrational level of the first excited singlet state S^*_1, from which emissive transitions occur, takes place, as in the case of molecules with a rigid structure, the Stokesian losses seldom exceed 3000 cm^{-1}. The relatively high fluorescence quantum yields and large Stokesian losses in the case of 1,4-DHP derivatives (Table 1) can be explained by the fact that in the excited state the 1,4-DHP molecule assumes a more planar configuration, for the stabilization of which part of the excitation energy is used. This is confirmed to a certain extent by comparison of the spectral parameters of I, II, XV, XVI, and XVII. In an investigation of a large number of 3,5-diethoxycarbonyl derivatives of 1,4-DHP it was shown that the steric factors of the 2,6 and γ substituents are chiefly reflected in their absorption spectra [8]. It is apparent from the fluorescence spectra that with an increase in the number of substituents in the molecules (I, II, XVI, XVII) and intensification of the effect of their steric factors Q becomes less than 0.001 (XVII), and the Stokesian shift increases to 6060 cm^{-1}. In the absence of 2,6-methyl groups N-alkyl substitution (IV-VII, XII, XIV) somewhat promotes the establishment of the equilibrium state of the molecule in the excited state and gives rise to a decrease in the Stokesian shift by an average of 400 cm^{-1} as compared with the shift of I. However, the introduction of a strong electron-acceptor substituent at the ring nitrogen atom (IX and X) hinders the establishment of a planar state of the emitting molecule, which leads to an increase in the Stokesian shift.

If motions over the time interval 10^{-8} to 10^{-9} sec occur in the conjugated π system of an organic molecule, this leads to appreciable deactivation of the S^*_1 level by intramolecular conversion [9]. The smallest losses of excitation energy are observed for I. An increase in the number of substituents in the 1,4-DHP molecule probably gives rise to quenching of the fluorescence by intramolecular motions and by the steric factors of the effect of the substituents. This is indicated by the certain increase in Q with an increase in the viscosity of the solvent (Table 1). In the absence of methyl groups in the 2 and 6 positions (I-XIV) Q in glycerol increases on average by 0.2; IX and X, with electron-acceptor N substituents, constitute an exception, since Q increases by a factor of three for them. The presence of 1,2,6-methyl groups in the 1,4-DHP molecule decreases Q markedly because of the steric factors of the substituents. Partial retardation of the rotational-vibrational motions of the substituents occurs in glycerol, and Q increases by a factor of 6-18.

The fluorescence of 1,4-DHP anions is yet another confirmation of the important role of structural peculiarities of the fluorescing molecule in increasing the luminescence intensity (Table 2). The literature contains data on the absorption spectra of 1,4-DHP anions [10-12], but information regarding their fluorescence spectra is not available. We have shown that the anions of 1,4-DHP derivatives (IIa, IIIa, XVIa, XVIIIa-XXIIIa) fluoresce in the green-yellow region of the spectrum with relatively high quantum yields (0.18-0.71; Table 2). Anions that are resistant to irradiation with exciting light are formed only in the case of γ-substituted 1,4-DHP, and quantitative evaluation of the fluorescence is therefore possible for this group of compounds.

The fluorescence spectra for all of the investigated 1,4-DHP anions are shifted bathofluorically as compared with the corresponding 1,4-DHP. It is known [13] that the λ_{max} values of the long-wave absorption bands of derivatives of 4-(R-aryl)-2,6-dimethyl-3,5-diethoxycarbonyl-1,4-DHP correlate well with the Hammett σ_p^+ substituent constants. The λ_{max} values of the excitation and fluorescence bands of 1,4-DHP and the bands of the excitation spectra of 1,4-DHP anions change within the limits of the error in the determination of the wavelengths, but good correlation between the λ_{max} and σ_p^+ values of the 4-(R-aryl) substituents (correlation coefficient r = 0.99) was observed for the fluorescence spectra of 1,4-DHP anions. The Stokesian shifts of the fluorescence spectra of the anionic forms do not exceed 3650 cm^{-1}; on average this is 2160 cm^{-1} smaller as compared with the corresponding 1,4-DHP. The latter indicates the more planar structure of the anions as compared with the 1,4-DHP in the ground singlet state. Pronounced redistribution of the electron density occurs in the skeleton of the 1,4-DHP molecule after the formation of anions; this leads to a more coplanar state of the anion molecule. As a result, luminescence Q values increase, particularly on passing to the anionic forms of 4-(R-aryl)-2,6-dimethyl-3,5-diethoxycarbonyl-1,4-DHP (XVIa, XVIIIa, XXa-XXIIIa).

The 76-fold (on average) increase in Q for the 1,4-DHP anions (XVIa, XVIIIa-XXIIIa) as compared with the corresponding 1,4-DHP indicates a ponderable decrease in processes involving intercombination conversion, which is one of the principal processes involved in the emissionless deactivation of the lowest S^*_1 state. Following the systemization of the luminescence types of molecules of Nurmukhametov [14] on the basis of the relative orientation of the ππ* and nπ* levels, the 1,4-DHP anions can be compared with compounds for which the S^*_1 and T_0 states are the $S_{\pi\pi^*}$ and $T_{\pi\pi^*}$ states. The energies of the $T_{n\pi^*}$ and $S_{n\pi^*}$ states are greater than the energy of the $S_{\pi\pi^*}$ state, and the probability of the $S^* \rightarrow T$ intercombination conversion is therefore low.

Since the processes involved in deactivation of the excited state of the molecules have complex character and we do not have data on the phosphorescence of 1,4-DHP at our disposal, the assumptions expressed above have descriptive character. However, the numerical results obtained indicate the possibility of the use of the fluorescence spectra of both 1,4-DHP derivatives and 1,4-DHP anions for the quantitative determination of the latter in solutions and biological media.

The 1,4-DHP derivatives I and XV-XVIII were kindly provided by Ya. R. Uldrikis and N. V. Makarova in the form of chromatographically pure samples.

EXPERIMENTAL

The corrected excitation and fluorescence spectra were recorded with a Hitachi-850 spectrometer. The error in the determination of the wavelengths was ±1 nm, and the concentration of the solutions ranged from 10^{-6} to 10^{-5} M. The fluorescence quantum yields of the 1,4-DHP derivatives were determined relative to quinine bisulfate (Q = 0.55); the fluorescence quantum yields of the 1,4-DHP anions were determined relative to an aqueous solution of fluorescein (Q = 0.84 [15]). The 1,4-DHP anions were obtained in dimethylformamide by the addition of 1 N KOH in a volume ratio with the solvent of (1-5):100. The error in the determination of the fluorescence quantum yields was ±0.01; the results were statistically reliable for XVI-XVIII and XXI.

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