2-ARYL-4H-3,1-BENZOXAZIN-4-ONES

ALCOHOLYSIS

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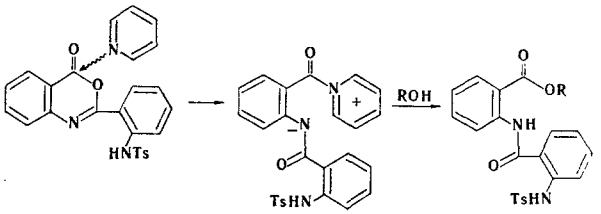
The reaction of 2-(2-tosylaminophenyl)-4H-3,1-benzoxazine-4-one with alcohols in pyridine gives tosylanthraniloylanthranilic acid esters. The synthesized compounds luminesce in the crystalline state and in solutions at room temperature. The anomalously high Stokesian shift characteristic for this series of compounds is due to intramolecular hydrogen bonding with the participation of the tosylamino group. Interaction of polar solvents and irradiation with UV light lead to cleavage of the hydrogen bond, and as a consequence, to a decrease in the Stokesian shift.

The literature contains many indications of unsuccessful attempts to alcoholize the most reactive representatives of the 4H-3,1-benzoxazine-4-one class – its 2-methyl derivatives [1, 2]. We were able to realize the alcoholysis of 2-(2-tosylaminophenyl)-4H-3,1-benzoxazine-4-one in pyridine [3] to give high yields of tosylanthraniloylanthranilic acid esters. The reaction proceeds readily with normal aliphatic alcohols and also with aliphatic–aromatic alcohols. However, the rate of alcoholysis decreases as the length of the alkyl chain of the alcohol increases. Thus 91% alcoholysis occurs when 2-(2-tosylaminophenyl)-4H-3,1-benzoxazin-4-one is refluxed in pyridine–butanol for 2 h, as compared with 76.7% alcoholysis in the case of decanol; in order to achieve complete reaction with methanol, it was necessary to reflux the mixture for 36 h. Alcohols with iso structures and phenol do not react with 2-(2-tosylaminophenyl)-4H-3,1-benzoxazine-4-one.

It might be assumed that the catalytic effect of pyridine consists in the formation of an extremely active intermediate, which also reacts with the alcohol:



2-Phenyl-4H-3,1-benzoxazin-4-one does not react with alcohols even in the presence of pyridine. The higher reactivity of the o-tosylamino-substituted compound becomes understandable if one compares the magnitude of the half-wave potentials for polarographic reduction of 2-phenyl- and 2-(2-tosylaminophenyl)-4H-3,1-benzoxazin-4-ones. In the former compound it is −1.7 V, as compared with −1.52 V in the latter [4]. The high electrophilicity of the tosylamino-substituted compound is also responsible for the ease of its reaction with pyridine and subsequent alcoholysis.

At first glance, the fact presented in [5] that 2-phenyl-4H-3,1-benzoxazin-4-one reacts readily with phenol in the absence of pyridine seems to contradict the explanation proposed above. The apparent "contradiction" is actually due to the fact that the reaction proceeds completely differently in the absence of pyridine. First of all, the benzoxazinone is protonated by phenol. As a result, the electrophilicity of the

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TABLE 1. Tosylanthraniloylanthranilic Acid Esters

Compound	R	mp, °C	Crystallization solvent	Empirical formula	Found, %			Calc., %			Yield, %
					C	H	N	C	H	N	
I	CH_3	164	AcOH	$C_{22}H_{20}N_2O_5S$	62,2	4,7	6,8	62,3	4,7	6,6	94
II	C_2H_5	134	AcOH	$C_{23}H_{22}N_2O_5S$	62,8	5,0	6,4	63,0	5,1	6,4	82
III	C_3H_7	133	PhH	$C_{24}H_{24}N_2O_5S$	63,7	5,5	6,4	63,7	5,3	6,2	88
IV	C_4H_9	113	PhH	$C_{25}H_{26}N_2O_5S$	64,4	5,7	6,2	64,4	5,6	6,0	88
V	C_8H_{17}	100	PhH	$C_{29}H_{34}N_2O_5S$	66,5	6,6	5,3	66,6	6,6	5,3	84
VI	C_9H_{19}	91	PhH	$C_{30}H_{36}N_2O_5S$	67,2	6,8	5,4	67,1	6,8	5,2	74
VII	$C_{10}H_{21}$	99	PhH	$C_{31}H_{38}N_2O_5S$	67,7	7,2	5,0	67,6	7,0	5,1	87
VIII	$C_{16}H_{33}$	87	PhH	$C_{37}H_{50}N_2O_5S$	69,4	7,8	4,8	69,4	8,1	4,5	90
IX	$CH_2C_6H_5$	162	PhH	$C_{28}H_{24}N_2O_5S$	67,3	4,8	5,4	67,2	4,8	5,6	53
X	$CH_2CH_2C_6H_5$	142	PhH	$C_{29}H_{26}N_2O_5S$	67,7	5,1	5,6	67,7	5,1	5,4	89

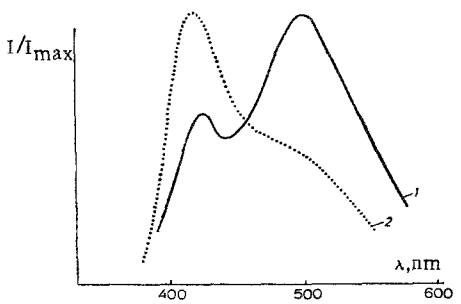


Fig. 1. Dependence of the luminescence spectrum of an alcohol solution of tosylanthraniloylanthranilic acid ester on the wavelength of the exciting light at 293° K: 1) λ_{ex} 313 nm; 2) λ_{ex} 365 nm.

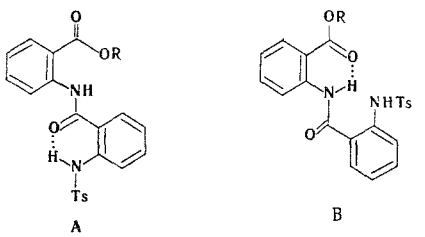
molecule increases sharply, and this also promotes attack on it by phenol. This sort of protonation is possible only in the case of 2-phenyl-4H-3,1-benzoxazin-4-one. The presence of an intramolecular hydrogen bond in the tosylamino derivative makes it impossible to protonate it with phenol. It is precisely for this reason that 2-phenyl-4H-3,1-benzoxazin-4-one reacts with phenol in the absence of pyridine, while its o-tosylamino derivative does not.

Electronic Spectra

The tosylanthraniloylanthranilic acid esters absorb in a shorter-wave region than benzoxazinones. It is interesting that the character of the spectra and the position of the maxima are practically independent of the length of the alkyl chain of the alcohol residue. This indicates that the ester grouping does not enter into the composition of the chromophores responsible for the absorption at 267 and 319 nm.

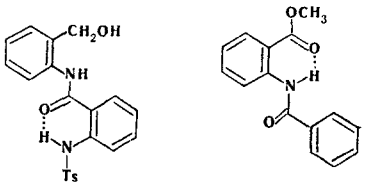
As in the case of benzoxazinones, a capacity for fluorescence is characteristic for tosylanthraniloylanthranilic acid esters. However, in contrast to the former, they fluoresce intensely not only in the crystalline state but also in solution at room temperature. Like the absorption spectrum, the fluorescence spectrum is independent of the length of the alkyl chain of the alcohol residue. One's attention is directed to the anomalously high Stokesian shift, which, in analogy with benzoxazinones [6], can be explained by strengthening of the intramolecular hydrogen bond in the excited state.

The formation of two types of intramolecular hydrogen bonds is possible in the tosylanthraniloylanthranilic acid ester molecule: those with the participation of the tosylamino group and the amide carbonyl group (form A) or those with the participation of the amide hydrogen and the ester carbonyl group (from B).



It seemed of interest to ascertain which of these forms is actually realized and how the fluorescence properties depend on this. If the tosylanthraniloylanthranilic acid esters did exist in form B, the fluorescence properties and, above all, the fluorescence intensity should have been dependent on the length of the alkyl chain, as in the case of 2-hydroxy-4-methyl-5-chloroalkanophenones [7]. However, this is not actually observed. For comparison, we synthesized model compounds in which only form A or only form B can be realized. (See scheme on the following page.)

It was found that 2-(N-tosylanthraniloylamino)benzyl alcohol, like tosylanthraniloylanthranilic acid esters, has an anomalously high Stokesian shift and fluoresces in the green region of the spectrum. 2-(2-



Tosylaminophenyl)benzoxazole and the overwhelming majority of compounds in which the tosylamino group participates in the formation of an intramolecular hydrogen bond have the same properties. At the same time, methyl benzoylanthranilate, which does not contain a tosylamino group, differs substantially from them with respect to its fluorescence properties.

In studying the fluorescence properties of the synthesized esters, we noted that the character of the spectrum depends markedly on the solvent. Thus, while only one maximum (λ_{max} 520 nm) is observed in toluene at 77°K, another maximum (λ_{max} 418 nm) appears in alcohol and dimethylformamide (DMF). The ratio of the intensities of the "blue" and "green" fluorescence maxima depends on the wavelength of the exciting light (Fig. 1). This indicates that in this case we are dealing with an equilibrium mixture rather than with an individual compound that has two fluorescence maxima. The assumption of decomposition of the substance as it dissolves in alcohol is excluded, for the tosylanthraniloylanthranilic acid ester is isolated unchanged when the alcohol solution is vacuum evaporated. It must be assumed that we are dealing in this case with an equilibrium mixture of two forms, one of which has green fluorescence, the other of which has blue fluorescence. The "blue" form probably corresponds to the case in which the tosylamino group does not participate in the formation of an intramolecular hydrogen bond. It is precisely this fact that may explain the existence of the "blue" form only in solutions in polar solvents.

Ultraviolet-light irradiation affects the esters in the same way as a polar solvent. In this case, the excitation energy in a portion of the molecules is expended in cleavage of the hydrogen bond, and one observes buildup of the "blue" form. One of the above-mentioned model compounds – 2-(N-tosylanthraniloylamino)benzyl alcohol – behaves in precisely the same way. At the same time, the spectrum of methyl benzoylanthranilate does not change either in the presence of polar solvents or during UV irradiation.

A change in the absorption spectra is observed simultaneously with the change in the fluorescence spectra of tosylanthraniloylanthranilic acid esters. The intensity of the long-wave band falls. Absorption at 350-420 nm appears simultaneously (Fig. 2). The appearance in the absorption spectrum of the ester of a long-wave "tail" as a result of irradiation may be a consequence of cleavage of the intramolecular hydrogen bond and more complete participation of the tosylamino group in conjugation. Thus both the hypsochromic shift of the fluorescence spectrum and the bathochromic shift of the absorption spectrum attest to disruption, during irradiation, of the hydrogen bond in which the tosylamino group participated.

EXPERIMENTAL

The absorption spectra of solutions in alcohol and toluene ($5 \cdot 10^{-4}$–$1 \cdot 10^{-5}$ M) were recorded at room temperature with a cuvette thickness of 1 cm. The fluorescence spectra of the solutions were recorded with

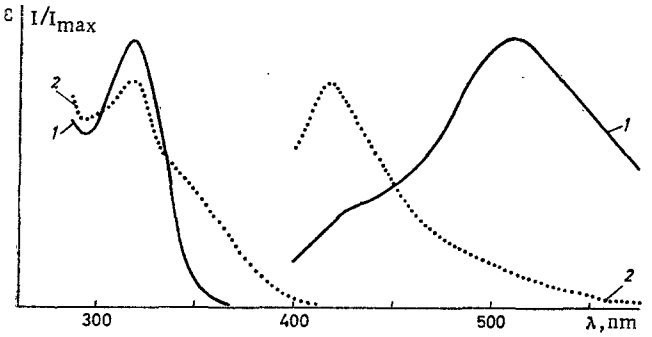


Fig. 2. Reduced absorption and luminescence spectra of an alcohol solution of tosylanthraniloylanthranilic acid ester at 293° K: 1) prior to irradiation with UV light; 2) after irradiation with UV light.

a device assembled from an MDR-3 monochromator with a linear dispersion of 1.3 nm/mm. The spectra were recorded at 77 and 293° K and are presented in this paper with allowance for the quantum sensitivity of the apparatus.

Alcoholysis of 2-(2-Tosylaminophenyl)-4H-3,1-benzoxazin-4-one. A solution of 1 g (2.5 mmole) of benzoxazinone and 0.01 mole of the appropriate alcohol in 5 ml of pyridine was heated for 20 h with gentle refluxing of the reaction mixture, after which 1 ml of water was added to hydrolyze the unchanged benzoxazinone, and the mixture was heated for another hour. It was then cooled to room temperature and poured with stirring into 100 ml of 5% aqueous sodium bicarbonate solution. The precipitated ester was removed by filtration, washed with water, and crystallized from a suitable solvent.

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