SYNTHESIS AND SPECTRAL-LUMINESCENCE PROPERTIES OF CARBONYL DERIVATIVES OF 2-(2-THIENYL)-5-ARYLOXAZOLES

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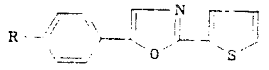
Electrophilic substitution reactions in the 2-(2-thienyl)-5-aryloxazole series and the spectral-luminescence properties of the compounds obtained were investigated

In a continuation of our research [1] to find new effective luminophores we investigated the acylation and formylation of 2-(2-thienyl)-5-aryloxazoles Ia,b, since the introduction of acetyl and formyl groups opens up the possibility for the synthesis of bifluorophore structures with conjugated fragments.



I a,b

I a R=H; b R=CH$_3$

It was found that Ia,b are quite inert and do not undergo these reactions under the conditions that are usually employed. Thus the acylation of Ia with acetic anhydride in the presence of iodine or anhydrone (magnesium perchlorate), as well as acetyl chloride, using stannic chloride or aluminum chloride as the catalyst (in benzene, chlorobenzene, chloroform, dichloroethane, or methylene chloride) does not lead to the formation of even traces of the acetyl derivative. In the case of formylation with DMF or N-methylformanilide in the presence of phosphorus oxychloride we also were unable to isolate any appreciable amounts of the aldehyde. (Monitoring of the formation of a carbonyl derivative was accomplished by means of IR spectroscopy and from the qualitative reaction with 2,4-dinitrophenylhydrazine.)

This low reactivity of Ia,b is associated with the deactivating effect of the oxazole ring, the acceptor properties of which are intensified appreciably in the case of the formation of a complex with the catalyst [2]. The results of calculation of the electron-density distribution in the 2-(2-thienyl)-5-phenyloxazole molecule made taking into account all of the valence electrons by the CNDO/2 method showed that the 2-thienyl radical is the most active for electrophilic substitution; however, the electron density in it is markedly reduced as compared with unsubstituted thiophene (Fig. 1).

We therefore developed a method for the acylation of oxazoles Ia,b under severe conditions. Carying out the reaction in the molten state without a solvent at 100-120°C with a threefold excess of aluminum chloride leads to the formation of acetylderivatives IIa,b in high yields.

The acylation of 2,5-diphenyloxazole was reported in [3]; however, the conditions under which the reaction was carried out (40°C, carbon disulfide) differed from those that we selected. The acetyl group was directed to the para position of the 5-phenyl radical. This means that the oxazole ring deactivates the 2-aryl radical to a greater extent. Replacement of the phenyl radical by a thienyl radical levels out the effect of the azole heteroring, and electrophilic substitution takes place in the 5 position of the thiophene ring.

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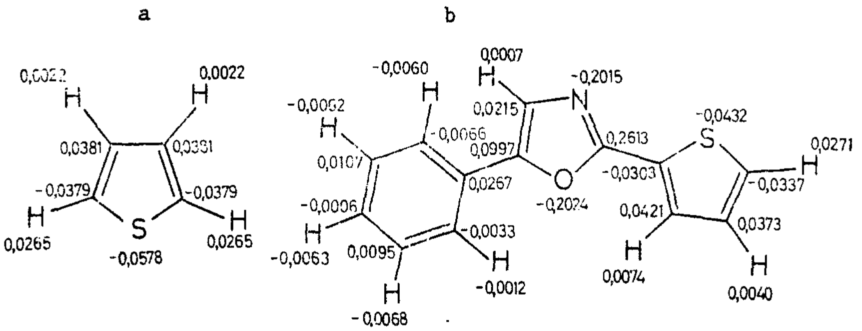


Fig. 1. Diagrams of the electron-density distribution in the thiophene (a) and 2-(2-thienyl)-5-phenyloxazole (b) molecules.

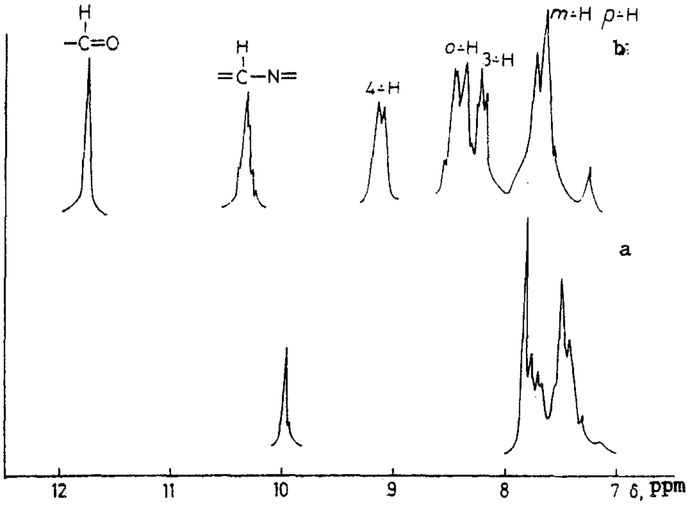
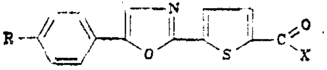


Fig. 2. PMR spectra of 2-(5-formyl-2-thienyl)-5-phenyloxazole (III): a) in deuterochloroform; b) in deuterochloroform with added lanthanide shift reagent Eu(DPM)₃.



IIa,b, III, IV

II a $X=CH_3$, R=H; b $X=CH_3$, $R=CH_3$;
III X=H, R=H; IV X=OH, R=H

Formyl derivative III is formed when Ia is heated with phosphorus oxychloride in DMF (100-105°C, 2 h).

2-(5-Carboxy-2-thienyl)-phenyloxazole (IV) was synthesized to expand the series of 2-(2-thienyl)-5-aryloxazoles with acceptor substituents in the 5 position of the thiophene ring. Carboxy derivative IV was obtained by oxidation of the acetyl group in IIa with sodium hypobromite.

The structures of all of the synthesized compounds were confirmed by the results of elementary analysis and the IR and PMR spectroscopic data. Stretching vibrations of a C=O bond with a frequency of 1645-1650 cm^{-1} and absorption bands of oxazole, thiophene, and benzene rings are observed in the spectra of oxazoles IIa,b, III, and IV measured at 400-4000 cm^{-1} in the solid phase (KBr pellets).

Signals of protons of an aldehyde group and a benzene ring are reliably identified in the PMR spectrum of III; the signal of the oxazole proton is overlapped with the multiplet of the phenyl protons. The two protons of the thiophene ring give a singlet signal; this complicates their assignment. By means of the lanthanide shift reagent EU(DPM)₃ [tris(dipivaloylmethanate)] we were able to obtain a first-order spectrum and accomplish the complete assignment of the signals (Fig. 2). It is apparent from Fig. 2 that the protons of the thiophene ring give two doublets with spin-spin coupling constant (SSCC) 3.5 Hz. This constitutes evidence that the indicated doublets can be related only to the 3-H and 4-H protons; consequently, formylation took place in the 5 position of the thienyl radical.

A signal of an acetyl group (2.50 ppm), a singlet of an oxazole proton (7.38 ppm for IIa and 7.34 ppm for IIb), and a multiplet of protons of the benzene ring are observed in the spectra of IIa,b. Taking into account the similarity in the two-proton singlets of the thiophene ring in the case of IIa,b and formyl derivative III it might be concluded that electrophilic substitution most likely also took place in the 5 position of this heteroring.

The absorption spectra of ethanol solutions of IIa,b, III, and IV consist of two bands: an intense long-wave band of the $\pi\pi^*$ type with a weakly expressed vibrational structure and a less intense short-wave band. In the case of toluene solutions the short-wave band is not visible because of the absorption of the solvent (Table 1).

The introduction of a carbonyl group into the molecules of luminophors Ia,b leads to significant bathochromic and bathofluoric shifts of the spectra; the extinction coefficients remain almost unchanged in this case. This effect cannot be associated only with lengthening of the conjugation chain but is due chiefly to the electron-acceptor effect of the carbonyl group, which leads to an increase in the nonuniformity of the electron-density distribution in the molecules. Compound IV with a weakly acceptor carboxy group is characterized by a smaller shift of the band.

As compared with carbonyl derivatives of 2,5-diphenyloxazole [4] the absorption maxima of thiophene analogs are shifted to the red region of the spectrum. This is evidently associated with both the donor properties of the thiophene ring and with its greater polarizability as compared with the benzene ring [5].

It is known that the introduction of a carbonyl group into the 2,5-diphenyloxazole molecule leads to quenching of the luminescence in hydrocarbon solvents [4]. This is associated with the fact that the triplet $n\pi^*$ level is located close to and somewhat below the singlet $\pi\pi^*$ level, as a result of which the probability of nonemissive deactivation of the energy of electronic excitation is high [6, p. 33]. Replacement of the phenylene fragment by a thiophene ring leads to inversion of the $T^*_{n\pi}$ and $S^*_{\pi\pi}$ states and to a decrease in the constant of intercombination conversion, as a result of which fluorescence, which is intensified appreciably in the crystals, develops in IIa,b and III.

An increase in the energy of the triplet $n\pi^*$ level and a decrease in the singlet $\pi\pi^*$ level occur on passing from toluene solutions to alcohol solutions. This leads to a significant long-wave shift of the fluorescence maxima (Table 1) and to marked intensification of the luminescence intensity due to an increase in the energy splitting between the $S^*_{\pi\pi}$ and $T^*_{n\pi}$ states [7, p. 178].

The increased Stokesian shifts ($\Delta\nu$) of the investigated compounds provide evidence for substantially different structures of the S_0 and S^*_1 states. In all likelihood, the noncoplanar (in the ground state) molecules become flat upon excitation, i,e., structural relaxation occurs.

It is interesting that the introduction of even the weakly donor methyl group in the 4 position of the phenyl radical (compound IIb) gives rise to a rather strong long-wave shift of the fluorescence band and an increase in its intensity, while the absorption spectrum remains almost unchanged. This principle is not followed for Ia,b; on the contrary, the electronic spectra of 2-(2-thienyl)-5-phenyloxazole (Ia) and its methyl derivative Ib are almost identical and depend only slightly on the solvent [1]. From this it may be concluded that for IIa,b also the methyl group cannot have any substantial effect on either the structure of the excited state or the structure of the solvate shell. In all likelihood, the strong bathofluoric effect and the intensification of the luminescence intensity are due to flattening of the structure of the molecules upon excitation and intensification of the mutual effect of the methyl and carbonyl groups through a unified π-electron system. In adition, the question of the mechanism of this strong effect of the methyl group on the emission spectrum remains open and requires a further detailed examination.

In addition to relaxation processes upon excitation the solvent probably makes a certain contribution to the high values of the Stokesian shifts; a confirmation of this is the increase in $\Delta\nu$ as a result of replacement of toluene by ethanol. For IIa,b and III the indicated

TABLE 1. Physicochemical Characteristics of 2-(2-Thienyl)-5 arylooxazole Derivatives Ia-IV

Compound	Empirical formula	mp, °C	Absorption				Fluorescence						Yield, %
			In ethanol		In toluene		In ethanol			In toluene			
			λ_{max}, nm	$\varepsilon \cdot 10^{-3}$	λ_{max}, nm	$\varepsilon \cdot 10^{-3}$	λ_{max}, nm	η	$\Delta\nu$, cm^{-1}	λ_{max}, nm	η	$\Delta\nu$, cm^{-1}	
Ia	—	—	320	25,2	325	26,9	385	0,47	5280	387	0,32	4930	—
IIa	$C_{15}H_{11}NO_2S$	143,5 ... 145	363 265	24,2 12,2	365	22,8	470	0.53	6270	Weak luminescence			74
IIb	$C_{16}H_{13}NO_2S$	165 ... 167	367 265	26,0 14,4	373	25,7	487	0,69	6710	440	0,10	4080	63
III	$C_{14}H_9NO_2S$	110,5 ... 112,5	365 265	21,3 11,5	370	25,0	485	0,53	6780	Weak luminescence			59
IV	$C_{14}H_9NO_3S$	219 ... 221	335 260	33,9 11,7	355	21,5	427	0,20	6430	425	0,19	4640	80

effect is achieved owing to the strong bathofluoric shift of the fluorescence band vis-á-vis a virtually unchanged absorption spectrum. We link this behavior of the formyl (III) and acetyl (IIa,b) derivatives with the increase in the basicity of the carbonyl grous upon excitation and intensification, as a consequence of this, of the solvation of the luminophore molecules by the polar solvent in the excited state.

In contrast to carbonyl derivatives IIa,b and III, the compound with a carboxy group (IV) is less polar in the excited state than in the ground state. Greater stabilization of the luminophore molecules in the S_0 state and, as a consequence of this, an increase in the Stokesian shift due to a strong hypsochromic shift of the absorption band therefore occur when the toluene solution is replaced by an alcohol solution.

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were recorded with a Specord IR-75 spectrometer. The electronic absorption spectra were recorded with an SF-16 spectrophotometer. The PMR spectra of solutions in $CDCl_3$ were obtained with a Tesla BS-487B spectrometer (80 MHz) with hexamethyldisiloxane (HMDS) as the internal standard. The fluoroescence spectra and the quantum yields were measured with an apparatus consisting of a ZMR-3 monochromator, an FÉU-18 photoelectronic multiplier, and an M-95 microammeter. Photoluminescence was excited with an SVDSh-500 lamp, from the spectrum of which the light with a wavelength of 365 nm was isolated by means of a DMR-4 quartz monochromator. The absolute fluorescence quantum yields were determined by the equal-absorption method [8].

The quantum-chemical calculations were made by means of the CNDO/2 method [9]. The results of elementary analysis of II-IV for N and S were in agreement with the calculated values.

2-(5-Acetyl-2-thienyl)-5-phenyloxazole (IIa). A mixture of 25.7 g (0.113 mole) of oxazole Ia and 52 g (0.390 mole) of anhydrous aluminum chloride was heated with stirring until the mixture melted (110-120°C), and 9 ml (0.126 mole) of acetyl chloride was added slowly dropwise at this temperature. The reaction mass was maintained for 15 min at 100-110°C, and the hot mixture was transferred to 500 g of ice. The resulting yellow precipitate was washed with water until the wash water was neutral, after which it was removed by filtration and dried. The product was recrystallized from isopropyl alcohol with the addition of activated charcoal to give 43.6 (74%) of IIa. For the spectral measurements the acetyl derivative was purified with a continuous-operation chromatographic column using Silochrome C-120 as the adsorbent and hexane as the eluent. Additional recrystallization from benzene did not lead to a change in the physicochemical properties of the product.

2-(5-Acetyl-2-thienyl)-5-(4-tolyl)oxazole (IIb). This compound was similarly obtained.

2-(5-Formyl-2-thienyl)-5-phenyloxazole (III). A 10-g (0.044 mole) sample of oxazole Ia was dissolved in 40 ml of dry DMF, and 25 ml (0.272 mole) of phosphorus oxychloride was added slowly dropwise with vigorous stirring at a rate such that the temperature did not exceed 25°C. The reaction mass was stirred for 2 h at 20-25°C and heated for 2 h on an oil bath at 100-105°C. The cooled mass was transferred to 500 g of ice with 70 g of sodium acetate such that the reaction medium remained neutral. The resulting precipitate was removed by filtration, recrystallized from ethanol—water (7:1), and purified as in the case of IIa to give 6.63 g (59%) of derivative III.

2-(5-Carboxy-2-thienyl)-5-phenyloxazole (IV). A 7.5-ml (0.15 mole) sample of bromine was added dropwise at 2-5°C to a solution of 20 g (0.5 mole) of sodium hydroxide in 100 ml of water, after which a suspension of 13.5 g (0.05 mole) of oxazole IIa in 100 ml of dioxane was added in small portions at a temperature below 10°C. The reaction mass was stirred for 1 h at 5-10°C and for 2 h at 18-22°C. It was then acidified with a solution of 25 ml of concentrated HCl in 70 ml of water, and the resulting precipitate was removed by filtration and dissolved in 100 ml of 2% NaOH solution. The resulting solution was refluxed with activated charcoal and filtered, and product IV was precipitated with 5% HCl solution to give 10.9 g (80%) of IV, which was recrystallized from acetic acid and chromatographed with a continuous-action column using Silochrome S-120 as the adsorbent and methylene chloride as the eluent.

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SYNTHESIS OF MACROHETEROCYCLIC ANALOGS OF DIBENZOCROWN-COMPOUNDS.

3.* 18-MEMBERED OXATHIAZACROWN-COMPOUNDS

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Condensation of 1,7-bis(2-aminophenyl)-4-thia-1,7-dioxaheptane with dichloroanhydrides of glutaric, diglycolic, thiodiglycolic, and N-tosyliminodiacetic acids under high dilution conditions with subsequent reduction of the macrocyclic diamides by borohydride leads to formation of 18-membered macrocylic diamines which contain a sulfur atom in the 4 position. An analogous series of reactions using 1,7-bis(2-aminophenyl)-4-(carba, oxa, aza)-1,7-dioxaheptanes and the dichloroanhydride of thiodiglycolic acid allows the sulfur atom to be introduced in the 13 position. The structure of the synthesized compounds was confirmed by IR, NMR, and mass spectral data.

Introduction of nitrogen, sulfur, and other heteroatoms into a crown-ether molecule along with oxygen atoms leads to a significant change in the complexing character of such macroheterocycles. The values of the stability constants of the complexes which are prepared from aza-, thia-, or azathiacrown-ethers with alkali or alkaline earth metals decrease significantly by comparison with those for corresponding crown-ethers upon a change in 18-crown-6- or dibenzo-18-crown-6-ethers of a part of the oxygen atoms by sulfur or nitrogen [2]. Relative to ions of transition or heavy metals, the complexing ability of azathiacrown-ethers increases markedly. Thus, exchange of two oxygen atoms by two sulfur atoms in the crown-ether molecule was shown to increase the extraction of Ag(I) from 6 to 92% [3]. An analogous effect was observed for Hg(II) [4], Cu (I), and Pd(III) [5-7].

Replacement of oxygen atoms by sulfur atoms in a series of diazadibenzo-15-crown-5-compounds described earlier by us [8] leads to a significant improvement of Hg(II) and Ag(I) extraction [9, 10].

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*For communication 2, see [1].

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