STYRYL DERIVATIVES OF QUINOLINE N-OXIDE

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A new method has been developed for the synthesis of hitherto unknown styryl derivatives of quinoline N-oxide. Electron spectroscopy has shown the occurrence of intramolecular charge transfer processes in these compounds.

It is known that picolines, containing a methyl group in position 2 or 4 of the aromatic ring, condense with aromatic aldehydes to form styryl derivatives. The presence in the heterocycle of an N-oxide group and particularly of a positively charged nitrogen atom, which possess acceptor properties, enhances the reaction [1].

The interest in the styryl derivatives of quinoline N-oxide is due to several reasons: the absence of relevant literature data, the possibility of investigating intramolecular charge transfer processes (ICTP) in compounds with long conjugation chains, and their potential biological activity (many analogs of the pyridine series possess this activity, for instance [2, 3]).

We have obtained a series of hitherto unknown compounds, containing electron acceptor as well as electron donor groups, by the procedure described for the N-oxides of 2- and 4-picolines (Table 1, method A):



The synthesis described in the literature includes refluxing of the N-oxides with aromatic aldehydes in a 10% solution of potassium methylate in absolute methanol in an atmosphere of nitrogen for 3 h.

It must be pointed out that the reaction of the aromatic aldehydes with the 2-methylquinoline N-oxide (II) at the above conditions proceeds somewhat faster (1.5-2 h) and gives higher yields than in the case of the N-oxides of 2- and 4- methylpyridines [4]. The low yield of the N-oxide Ie (14%) is probably due to the occurrence of side reactions with the participation of benzaldehyde (for instance disproportionation). This approach cannot be used to obtain the N-oxide Ia (X = NO_2 , Y = H), since at the above-mentioned conditions it undergoes further conversions. This is confirmed by the fact that compound Ia, obtained by method B (see Experimental) decomposes when refluxed in 10% methanol.

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Com- pound	x	Y	mp, °C	Yield, %	
				Method A	Method B
Ia	NO ₂	н	231232		67
Ib	OCH3	н	142143	78	62
Ic*	OCH3	ОСН3	112113	88	68
1 d	N(CH ₃) ₂	н	218219	83	68
Iе	н	н	116118	14	60

TABLE 1. Styryl Derivatives of Quinoline N-Oxides

*The composition of compound Ic is given by the formula $C_{19}H_{17}NO_3 H_2O$, as confirmed by elemental analysis and IR spectroscopy (Table 2).

TABLE 2. Infrared and Electron Spectra of 2-Methylquinoline N-Oxides and Styryl Derivatives of Quinoline

Com-	Absorption bands in the	Solvent	Electron spectra, λ_{max} (nm), log ε		
pound	IR spectra, cm ⁻¹		region 1	region 2	
Ia*	1700, 1650, 1600, 1560, 1518, 1345, 1275, 1245, 1200, 1175	Ethanol Chloroform	202, 235, 270 248, 268, 282	315 sh., 330, 390 329, 343, 400	
Ib I	1600, 1560, 1510, 1360, 1290, 1260, 1240, 1200, 1175	Ethanol	202(4,09), 222(4,04), 247(4,14)	311 sh. (4,31), 320(4,34), 377(4,35)	
		Chloroform	242(4,27), 248 sh.	316 sh. 326(4,56), 379(4,41)	
Ic	3400, 1610, 1570, 1510, 1345, 1305, 1280, 1210, 1170	Ethanol	203(4,29), 238(4,18), 262 sh.(4,01)	306(4,14), 322(4,14), 391(4,26)	
Id 1700, 13 1540, 13 1240, 1	1700, 1590, 1570, 1560, 1540, 1520, 1345, 1295,	Ethanol	198(4,47), 228(4,22), 268(4,18)	308 sh., 338(4,06), 420(4,41)	
	1240, 1190, 1170	Chloroform	240 sh. 272(4,30)	309 sh. 346(4,36), 430(4,59)	
<u>I</u> e	1650, 1635, 1560, 1520, 1360, 1280, 1245, 1210, 1130, 1095	Ethanol	202(4,26), 208 sh. 237(4,23), 247 sh.	300(4,54), 308(4,55), 350 sh. (4,35), 360(4,16)	
		Chloroform	243(4,26)	302 sh., 311(4,62), 352 sh. (4,28), 365(4,32)	
II	_	Ethanol	213 sh., 230 sh. 237(4,60)	319(3,79), 328 sh.	
		Chlorofom	_	330(3,83), 341(3,82)	

*log ε of compound Ia could not be determined, due to its low solubility in all available organic solvents.

We have significantly simplified the synthesis of styryl derivatives of quinoline N-oxides (method B) by using KOH as a catalyst (60°C, 0.5-3 h, absolute ethanol) (Table 1). This method can be used only to synthesize the styryl derivatives of the quinoline N-oxides (the less reactive N-oxide of 4-methylpyridine gives condensation products with low yields).

The compounds Ia-e are yellow-orange in color. In their electron spectra in region 2 (Table 2, $\lambda > 300$ nm) a bathochromic shift is observed of the absorption band maxima and a complication of the spectra in comparison with the N-oxide of 2-ethylquinoline (II) in ethanol as well as in chloroform. In the latter instance the red shift is somewhat stronger; this is in agreement with the literature data with respect to its dependence on the solvent polarity [5].

It is known that the N-oxide group can act as electron donor as well as acceptor, depending on the nature of the substituents in direct resonant conjugation with the N-oxide group. We have shown in [6, 7] that in these instances a long-wave shift occurs in the electron spectra of the N-oxides, caused by ICT processes, because polar "quinoid" resonance structures can exist of type III for compound Ia (N-oxide group-electron donor) and type IV for compounds Ib, d (N-oxide group-electron acceptor) with a long conjugation chain:



 $1V X = OMe, NMe_2$

Without any doubt in the case of the N-oxides Ia-d the position and intensity of the absorption band maxima are affected, when compared to the N-oxide of 2-methylquinoline (II), also by the lengthening of the conjugation chain on account of the styryl fragment. However, comparison of the electron spectra of compounds Ia-d, substituted in position 4 of the benzene ring, with the unsubstituted analog Id permits us, in our opinion, to separate this component unambiguously from those, caused by ICT processes on account of direct resonant conjugation of substituents with the group $N \rightarrow O$.

It must be pointed out that for all synthesized styryl derivatives a red shift is observed in the electron spectra of the bands with the longest wavelength in comparison with the corresponding band of compound Ie, combined with an increase in the extinction coefficients. The strengthening of the bathochromic shift in the case of compounds Ib-d evidently correspond to an increase in the electron donor properties of the substituent in the benzene ring.

The IR spectra of the styryl derivatives of quinoline N-oxide Ia-d contain absorption bands in the region 1295-1275 cm^{-1} which are characteristic for the N \rightarrow O group. The strong absorption bands for the Ia N-oxide at 1518 and 1345 cm^{-1} can be assigned to antisymmetrical and symmetrical valence vibrations of the N-O bonds of the nitro group; this is in agreement with data for the majority of aromatic nitro compounds [8] (Table 2).

The results of the present study show that the condensation of the 2-methylquinoline N-oxide with aromatic aldehydes proceeds more easily than with the N-oxides of 2- and 4-picolines. This has led to the development of a simple procedure for its realization. In continuing our studies of the donor – acceptor interaction in the series of aromatic N-oxides we intend to investigate the complex formation of the styryl derivatives of quinoline N-oxides with different types of electron acceptors.

EXPERIMENTAL

The IR spectra of substances in paraffin oil were recorded on an UR-20 spectrometer and the electron spectra on a Specord UV-vis spectrometer in 96% ethanol or in CHCl₃. The chloroform was washed with water, dried with anhydrous K_2CO_3 , and distilled. The progress of the reaction and the purity of the synthesized compounds was controlled by TLC on Silufol UV-254 foils, with chloroform-ethanol (10:1) as the eluent; the spots were revealed in UV light and by exposure to iodine vapors. Elemental analysis data for C, H, N corresponded to the calculated values.

N-Oxide of 2-(4-Dimethylaminostyryl)quinoline (Id). A. A mixture of 0.318 g (2 mmole) of the N-oxide of 2methylquinoline and 0.418 g (2.8 mmole) of dimethylaminobenzaldehyde in 1.5 ml of a 10% solution of potassium methylate in absolute methanol is refluxed for 2.5 h in a nitrogen atmosphere. The alcohol is removed in vacuum, the residue is washed with ether (3 \times 2 ml) and water (3 \times 2 ml), and dried in air. Yield 0.51 g (83%) of compound Id; mp 218-219°C (from aqueous ethanol).

The N-oxides of Ib, c, d are obtained by method A in the same way (Table 1).

N-Oxide of 2-(4-Nitrostyryl)quinoline (Ia). B. A mixture of 0.159 g (1 mmole) of 2-methylquinoline N-oxide and 0.224 g (1.4 mmole) of 4-nitrobenzaldehyde in 1.5 ml 10% KOH solution in absolute ethanol is refluxed for 2 h a 60°C. The alcohol is removed in vacuum, the residue is washed with ether (3 \times 3 ml) and water (3 \times 3 ml), and refluxed 1-2 min in 2 ml acetonitrile; the precipitate is filtered off and dried in air. Yield 0.39 g (67%) of compound Ia; mp 231-232°C.

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The N-oxides of Ib-d are obtained by method B in the same way.

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