

RESEARCH IN THE ISOXAZOLE SERIES

XXXIV.* CONJUGATION IN ARYLISOXAZOLES

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The ionization constants of arylisoxazoles in acetic acid were determined by a spectrophotometric method. The effect of substituents on the conjugation in the arylisoxazole system is discussed.

In order to study the reactivities of arylisoxazoles we obtained diverse representatives with NO_2 , Cl , and CH_3 groups in the benzene ring. As demonstrated in [2], strong transmission of the substituent effects is realized in crystalline arylisoxazoles, and 3,5-diaryliso-azoles constitute unified conjugation systems. We also have observed a phenomenon of this sort in the case of dissolved arylisoxazoles.

To ascertain the effect of aryl substituents in the heterocyclic ring on the electron density on the nitrogen atom we determined the pK_a values of 10 arylisoxazoles (Table 1). The pK_a values of I, III, and V were taken from [3]. Glacial acetic acid was used as the solvent, and sulfuric acid served as the proton donor. In the determination of the ionization constants we used the Hammett H_o acidity function. It is apparent from Table 1 that large deviations from unity for the n criterion are not observed, except for XII and XIII. Consequently, the H_o acidity function is applicable for the determination of the pK_a values of most of the isoxazoles under the conditions that we selected [3], whereas its application for XII and XIII ($n < 0.7$) is problematical.

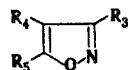
As demonstrated in [2], the mesomeric effect is transmitted along the isoxazole ring more strongly to the C_5 atom than to the C_3 atom. The spectra of I and III in glacial acetic acid served as a confirmation of this. A 9 nm shift of the absorption maximum relative to I and an increase in the extinction coefficient are observed for III. Judging from the spectra in glacial acetic acid of II and IV, the conjugation of the system is intensified when an NO_2 group, which has a $-M$ effect, is introduced. A substantial difference between the 3 and 5 positions is observed when chlorine is introduced into the benzene ring at the C_3 and C_5 atoms (compare VI and IX). This difference once again confirms that conjugation is intensified when a substituent is introduced in the 5 position. The VII and VIII and X and XI pairs are interesting for comparison. Lengthening of the conjugation chain when an NO_2 group is introduced in the para position of the phenyl substituent leads to a bathochromic shift of the absorption maximum as compared with the effect of the same substituent in the meta position: 15 nm for the VII, VIII pair, and 47 nm for the X, XI pair. Thus it may be assumed that the $-M$ effect of the NO_2 group is realized to the greatest extent in XI. The introduction of a bulky mesityl substituent evidently disrupts the unified conjugation chain of the two rings.

As a rule, protonation of phenylisoxazoles I-XIII leads to intensification of the conjugation of the benzene rings with the isoxazolium cations.

The basicities of the compounds with an acceptor substituent in the benzene ring attached to the C_3 atom of the isoxazole ring are always somewhat lower than the basicities of the isomeric 5-arylisoazoles.

*See [1] for communication XXXIII.

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TABLE 1. UV Spectra and pK_a Values of Arylisoxazoles

Com- pound	R ₃	R ₄	R ₅	λ_{max} , nm (lg ε)		pK_a	n
				in CH_3COOH	in a 16.8 M solution of H_2SO_4 in CH_3COOH		
I	C_6H_5	H	H	251 (3.88)	275 (4.17)	-3.19 ± 0.10	1.03
II	$p\text{-O}_2\text{NC}_6\text{H}_4$	H	H	279 (4.13)	281 (4.28)	-4.48 ± 0.09	0.81
III	H	H	C_6H_5	262 (4.27)	290 (4.32)	-2.96 ± 0.05	0.88
IV	H	H	$p\text{-O}_2\text{NC}_6\text{H}_4$	280 (4.05)	282 (4.33)	-4.39 ± 0.10	1.24
V	C_6H_5	H	C_6H_5	268 (4.39)	312 (4.47)	-3.05 ± 0.05	1.03
VI	$p\text{-ClC}_6\text{H}_4$	H	C_6H_5	260 (4.45)	317 (4.51)	-3.26 ± 0.03	1.02
VII	$m\text{-O}_2\text{NC}_6\text{H}_4$	H	C_6H_5	265 (4.40)	315 (4.40)	-4.05 ± 0.05	1.01
						-4.02 ± 0.04	1.03*
VIII	$p\text{-O}_2\text{NC}_6\text{H}_4$	H	C_6H_5	280 (4.50)	320 (4.40)	-3.87 ± 0.10	0.99
IX	C_6H_5	H	$p\text{-ClC}_6\text{H}_4$	274 (4.47)	317 (4.48)	-3.10 ± 0.06	0.81
						-3.15 ± 0.05	0.86*
X	C_6H_5	H	$m\text{-O}_2\text{NC}_6\text{H}_4$	258 (4.41)	300 (4.37)	-3.73 ± 0.05	1.17
						-3.62 ± 0.04	1.07*
XI	C_6H_5	H	$p\text{-O}_2\text{NC}_6\text{H}_4$	305 (4.27)	317 (4.45)	-3.63 ± 0.08	0.88
XII	Mesityl	H	C_6H_5	265 (4.41)	300 (4.41)	-2.89 ± 0.06	0.93
						-2.84 ± 0.01	0.71*
XIII	H	H	Mesityl	253 (3.85)	295 (3.87)	-2.81 ± 0.03	0.67
						-2.86 ± 0.02	0.73*

*The pK_a and n values were obtained by the method in [5], and the remaining values were obtained by the method in [6].

EXPERIMENTAL

The isoxazole derivatives necessary for the study were obtained by described methods, and their physical constants were in agreement with the literature data.

The solvent for the determination of the pK_a values was cp grade glacial acetic acid, which was frozen out twice. The proton donor was 94% analytically-pure-grade (for the Saval test) sulfuric acid, the concentration of which was determined by indicator titration. The H_o acidity functions for the acetic acid solutions were taken from [4].

The UV spectra were recorded with a Perkin-Elmer 402 spectrophotometer with quartz cuvettes with a layer thickness of 1 cm in a thermostatted block at $25 \pm 0.1^\circ\text{C}$. The solutions in the investigated concentrations ($1 \cdot 10^{-4}$ – $2.5 \cdot 10^{-5}$ mole/liter) followed the Lambert-Beer law. The wavelengths at which the maximum on the absorption curve of the protonated (un-protonated) form is found above the minimum on the absorption curve of the other form were used as the analytical wavelengths.

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