ISOXAZOLYLPHENOLS AND THEIR ABSORPTION SPECTRA*

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Simple isoxazole is known to absorb at 211 m μ ,¹ whereas 3-phenyl- and 5-phenylisoxazoles absorb at 240 m μ ² and 260 m μ ³ respectively. Absorption maxima of 3-phenyl- and 5-phenyl-isoxazoles, which are similar to those of the oximes of acetophenone and *trans*-cinnamaldehyde, are due to the chromophores (I) and (II) respectively.



3,5-Diphenylisoxazole, which contains both these chromophores, absorbs at 242 m μ and 268 m μ^4 showing that the two chromophores are acting almost independently, although cross-conjugation is possible.

With a view to studying the effect of substituents on the position of the two bands a number of hydroxy-substituted 3,5-diphenylisoxazoles, commonly called "isoxazolylphenols", have been prepared by the chalcone dibromide method.⁵ The compounds prepared together with the analytical data are included in Table 1. The absorption maxima and $\log \epsilon$ values of these compounds are presented in Table 2, and those of the oximes for comparison in Table 3.

Examination of the data reveals that 3-phenyl-5-(p-hydroxyphenyl)isoxazole has two absorption bands whereas 3-(p-hydroxyphenyl)-5-phenylisoxazole has only one which is quite broad. In the latter case the 242 m μ band, which is displaced by substitution of a hydroxyl group in the *p*-position to longer wavelength, merges with the 268 m μ band and appears as a broad band. In the case of the former, on the other hand, hydroxylic substitution displaces the 268 m μ band to longer wavelengths and the two bands are well separated. This is evident in the 3,5-di(*p*-hydroxyphenyl)-

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- ¹ Pino, P., Speroni, G. and Fuga, V., Gazz. chim. ital., 1954, 84, 759.

² Ley, H., and Wingchen, H., Ber. dt. chem. Ges., 1934, 67, 508.

- ³ Grammaticakis, P., Bull. Soc. chim. Fr., 1948, 979.
- ⁴ Quilico, A., in Weissberger's "Chemistry of Heterocyclic Compounds." (Ed. R. H. Wiley.) Vol. 17, p. 191. (Interscience: New York 1962.)
- ⁵ Goldschmidt, C., Ber. dt. chem. Ges., 1895, 28, 2540.

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No.	Isoxazole		мъ	Recryst.	Nitrogen (%)	
	R	R′	м.г.	Solvent	Found	Calc.
1*	$o\operatorname{-HOC}_6\mathrm{H}_4$	Ph	233°	alcohol		
2	$o\operatorname{-HOC}_6\operatorname{H}_4$	$p\operatorname{-MeOC_6H_4}$	206	benzene	$5 \cdot 7$	$5 \cdot 25$
3	$o\operatorname{-HOC_6H_4}$	$p\operatorname{-HOC}_6\operatorname{H}_4$	267	alcohol	$6 \cdot 0$	5.55
4	$o\operatorname{-HOC}_6\operatorname{H}_4$	o-ClC ₆ H ₄	210	alcohol	$5 \cdot 2$	$5 \cdot 2$
5	$o\operatorname{-HOC}_6\mathrm{H}_4$	$o\cdot \mathrm{HOC}_{6}\mathrm{H}_{4}$	198	alcohol	$5 \cdot 2$	$5 \cdot 55$
6	$p\operatorname{-HOC_6H_4}$	\mathbf{Ph}	186	alcohol	$6 \cdot 2$	$6 \cdot 1$
7	$p\operatorname{-HOC_6H_4}$	$p\operatorname{-MeOC_6H_4}$	198	benzene	$5 \cdot 6$	$5 \cdot 25$
8	$p\operatorname{-HOC}_6\operatorname{H}_4$	$p ext{-}\operatorname{HOC}_6\operatorname{H}_4$	255	alcohol	$5 \cdot 9$	5.55
9*	Ph	$p\operatorname{-HOC_6H_4}$	166	alcohol		

* These compounds have been reported (Shenoi, R. B., Shah, R. C., and Wheeler, T. S., J. chem. Soc., 1940, 247; Värlander, D., Ber. dt. chem. Ges., 1925, 58, 118).

ULTRAVIOLET SPECTRAL DATA OF THE ISOXAZOLE DERIVATIVES

Isoxazole R R'		$egin{array}{lll} \lambda_{\max} & \log \epsilon \ (\mathrm{m}\mu) \end{array}$		Isoxazole R R'		λ_{\max} (m μ)	log e
	 Н	211	3.50	0-HOCaH4	 Ph	243	4.69
Ph	H	240	4.00	0 110 00114	1 11	261	4.51
		270	$2 \cdot 60$			305	$4 \cdot 20$
н	\mathbf{Ph}	260	$4 \cdot 20$	$o \cdot HOC_6H_4$	p-HOC ₆ H ₄	243	$4 \cdot 42$
Ph	\mathbf{Ph}	242	$4 \cdot 35$		-	272	4.75
		268	$4 \cdot 40$			305	$4 \cdot 34$
\mathbf{Ph}	$p\operatorname{-HOC}_6\mathrm{H}_4$	242	$4 \cdot 30$	$o-HOC_6H_4$	$o\operatorname{-HOC}_6\mathrm{H}_4$	247	$4 \cdot 16$
		281 - 287	$4 \cdot 40$			260	$4 \cdot 09$
p-HOC ₆ H ₄	\mathbf{Ph}	261 - 271	4.71			310	$4 \cdot 03$
p-HOC ₆ H ₄	p-HOC ₆ H ₄	250	$3 \cdot 91$				
		280	$4 \cdot 22$				

TABLE 3						
ULTRAVIOLET	SPECTRAL	DATA	OF	OXIMES		

Oxime	λ_{\max} (m μ)	$\log \epsilon_{\max}$
Acetophenone oxime ² <i>p</i> -Hydroxyacetophenone oxime	242, 290 259	$4 \cdot 05, 2 \cdot 35$ $4 \cdot 21$
o-Hydroxyacetophenone oxime trans-Cinnamaldoxime ³	$\begin{array}{c} 251,304\\ 290 \end{array}$	$4 \cdot 12, 3 \cdot 75$ $4 \cdot 30$

isoxazole which has a strong absorption at 280 m μ and a shoulder at 250 m μ . This shoulder could not be detected in 3-(p-hydroxyphenyl)-5-phenylisoxazole as the two bands are closer to each other.

It is interesting to note that 3-(o-hydroxyphenyl)-5-phenylisoxazole shows three bands: 243, 261, and 305 m μ . These are characteristic of all the 3-(o-hydroxyphenyl)-5-phenylisoxazoles. The band at 260 m μ , as stated earlier, may be due to chromophore (II) above. The other two bands are similar to those of o-hydroxyacetophenone oxime. The band at 304 m μ which is present in o-hydroxyacetophenone oxime and absent in p-hydroxyacetophenone oxime may be due to chelation between OH and C=N. Due to chelation, the weak 290 m μ band of acetophenone oxime might have undergone a red shift followed by increase in intensity. Similar observations were made in the other chelated systems; for example, the weak 280 m μ (log ϵ 3·1) band of benzaldehyde is shifted to 327 m μ (log ϵ 3·5) in salicylaldehyde. The 310 m μ band of the 3-(o-hydroxyphenyl)-5-phenylisoxazoles may, therefore, be due to chelation.

Further evidence for chelation is obtained from a study of the i.r. spectra of 3-(o-hydroxyphenyl)-5-phenylisoxazole and 3-(p-hydroxyphenyl)-5-phenylisoxazole. The former shows a band in the OH region at 3200 cm⁻¹, the latter at 3600 cm⁻¹, indicating bonded OH in the *o*-hydroxyphenyl compound.

Interaction of a hydroxyl group in general produces a bathochromic shift followed by increase in intensity as is seen in the case of 3-(o-hydroxyphenyl)-5-(p-hydroxyphenyl)isoxazole. But substitution of a hydroxyl group in the ortho position as in the case of 3,5-di(o-hydroxyphenyl)isoxazole does not produce a bathochromic shift and increase in intensity, showing that the hydroxyl in the ortho position has little interaction with chromophore (II).

The physiological activity and the complexing ability of these compounds are under investigation.

Experimental

General Method of Preparation

(i) Chalcone.—The appropriate aldehyde and ketone were mixed in equimolar proportions in alcohol solution and treated with sodium hydroxide (20% aqueous). The mixture was heated on a water-bath at 60° for about 3 hr and the chalcone isolated by acidification. Recrystallization was effected from alcohol.

(ii) *Dibromide.*—The chalcone (0.01 mole) in ether or acetic acid was treated with bromine (0.01 mole) with cooling and stirring. The resulting solid was filtered, washed with a few millilitres of cold ether, and recrystallized from alcohol.

(iii) Isozazole.—The dibromide (0.01 mole) was dissolved by boiling in alcohol and hydroxylamine hydrochloride (0.01 m aqueous solution) was added, followed by potassium hydroxide (30-40%). The mixture was allowed to stand for about 30 min and the isoxazole isolated by acidification. Recrystallization was carried out from alcohol or benzene.

Spectra

Ultraviolet spectra of these compounds were recorded in alcohol on a Hilger-Watts spectrophotometer using 1-cm quartz cells. Infrared spectra were recorded as mulls on a Perkin-Elmer 137 Infracord using sodium chloride optics.

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