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BASICITY OF 2-PHENYL-5-R-1,3,4-OXADIAZOLES

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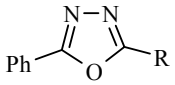
We have studied the basicity of 2-phenyl-5-R-1,3,4-oxadiazoles (R = H, Me, CH_2Ph, t-Bu, CH_2Cl, CCl_3, CF_3) in aqueous sulfuric acid solutions. These compounds are weak organic bases (pK_{BH}^+ is -1.8 to -5.2). The values of pK_{BH}^+ determined on the H_0 and X acidity function scales agree well with each other. The substituent at the 5 position has a substantial effect on the basicity of the 1,3,4-oxadiazole ring.

Keywords: 1,3,4-oxadiazoles, weak bases, basicity, UV spectroscopy, acidity function, electronic substituent constants.

Compounds of the 1,3,4-oxadiazole series are widely used in various areas of modern technology [1]. Considering the unique luminescent spectral properties of aryl-substituted 1,3,4-oxadiazoles and their ability to form stable molecular and coordination complexes with various substrates, these compounds may be considered as promising components of new materials for advanced technologies, including as components for active media of lasers [2]. The basicity of 1,3,4-oxadiazoles, reflecting their ability to act as electron density donors, has been insufficiently studied. We previously determined the basicity constants for a series of 2-aryl-5-phenyl-1,3,4-oxadiazoles, and also quantitatively established the effect of the electronic properties of the benzene ring substituents on the pK_{BH}^+ of these heterocycles [3]. For 2,5-diphenyl-1,3,4-oxadiazole, we determined the basicity constants in the S_0 and S_1 states, and we also studied the effect of the acidity of the medium on its luminescent spectral properties [4].

In this paper, we use the spectrophotometric method to determine the basicity constants of a series of 2-phenyl-5-R-1,3,4-oxadiazoles containing different types of substituents at the 5 position of the heterocycle (**1**-**7**), plus 2,2'-diphenyl-5,5'-di-1,3,4-oxadiazole (**8**).



1–**8**

1 R = H; **2** R = Me; **3** R = CH_2Ph; **4** R = *t*-Bu; **5** R = CH_2Cl; **6** R = CCl_3; **7** R = CF_3; **8** R = 2-phenyl-1,3,4-oxadiazol-5-yl

The pK_{BH}^+ values for these compounds were calculated by the Yates–McClelland and Cox–Yates methods, using the acidity functions H_0 and X respectively. We consider the dependences of the basicity constants on the substituent constants.

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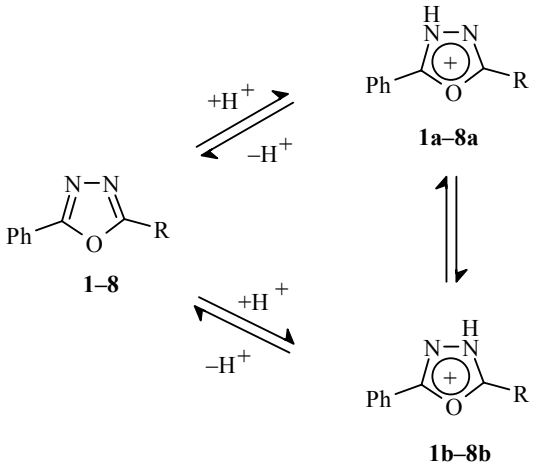
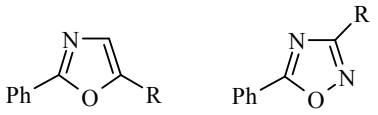
The basic centers of the compounds in this series are pyridine nitrogen atoms, while at the same time protonation at the oxygen atom is unlikely [5]. Thus upon ionization of 2-phenyl-5-R-1,3,4-oxadiazoles **1-8**, containing nonequivalent substituents at the 2 and 5 positions, two different tautomeric forms of the conjugate acid **1a-8a** and **1b-8b** can form.



The shift of the equilibrium in one direction or the other will be determined by the nature of the substituent R. Obviously in the case of electron-acceptor substituents, forms **1a-8a** will be preferably formed upon protonation.

When 2-phenyl-5-R-1,3,4-oxadiazoles **1-8**, containing both a donor and an acceptor substituent, are protonated, in the electronic spectra we observe a bathochromic shift of the absorption band maxima (Table 1, Fig. 1). Similar spectral changes were noted previously in protonation of 2-phenyl-1,3-oxazoles and 5-phenyl-1,2,4-oxadiazoles, where the basic center is a nitrogen atom next to a phenyl substituent [6, 7].



This fact may be evidence that for all phenyl-1,3,4-oxadiazoles **1-8**, protonation occurs at the nitrogen atom in the position adjacent to the phenyl substituent, having a rather strong electron-donor effect. Thus we may hypothesize that forms **1a-8a** will be the most stable tautomeric forms.

For compounds **1-7**, the molar absorption coefficient (at the analytical wavelengths) *vs*. acidity of the medium curves have the typical sigmoidal shape of protolytic equilibria (Fig. 2). We calculated the pK_{BH^+} values for oxadiazoles **1-7** by means of two alternative methods: the Yates–McClelland method, using the acidity function H_0 (1); and the "excess acidity" (Cox–Yates) method, using the acidity function X (2) [8]. As the parameter for the basicity constant, we took the ratio of the independent term (pK'_{BH^+}) to the slope (m or m^*) in the linear dependences (1), (2) [9]. The results of the calculations using the above-indicated equations are given in Table 2.

$$\lg I = -m \cdot H_0 + pK'_{BH^+}, \quad pK_{BH^+} = pK'_{BH^+} / m, \tag{1}$$

$$\lg I - \lg [H^+]' = m^* \cdot X + pK'_{BH^+}, \quad pK_{BH^+} = pK'_{BH^+} / m^*, \tag{2}$$

where I is the ionization ratio ($I = [BH^+]/[B]$).

TABLE 1. Spectral Characteristics of Bases and Related Acids of Phenyl-1,3,4-oxadiazole **1-8**

Compound	Base			Conjugate acid		
	λ_{max}, nm	ε, l/(mol·cm)	% wt. H_2SO_4 (H_0)	λ_{max}, nm	ε, l/(mol·cm)	% wt. H_2SO_4 (H_0)
1	245	9920	25.7 (-1.5)	262	10 900	67.3 (-5.5)
2	250	17900	8.7 (-0.3)	259	16 600	56.9 (-4.1)
3	252	17400	15.8 (-0.8)	263	17 300	56.9 (-4.1)
4	250	18500	8.7 (-0.3)	261	17 600	56.9 (-4.1)
5	253	14550	20.2 (-1.1)	270	16 330	64.7 (-5.1)
6	234	11300	41.0 (-2.6)	256	10 400	79.15 (-7.3)
7	251	13000	41.0 (-2.6)	276	14 900	77.1 (-7.2)
8	301	35780	Ethanol	311	30 900	67.3 (-5.5)

TABLE 2. Parameters of Eqs. (1) and (2) for 2-Phenyl-5-R-1,3,4-oxadiazoles **1-8** in Aqueous Sulfuric Acid Solutions

Compound	λ_{anal}, nm	Equation (1)*				Equation (2)*			
		pK'_{BH^+}	m	$r(n)$	pK_{BH^+}	pK'_{BH^+}	m*	$r(n)$	pK_{BH^+}
1	235	-2.97	0.90	0.97 (9)	-3.31±0.04	-2.82	0.88	0.99 (9)	-3.20±0.02
2	235	-1.88	0.97	0.98 (9)	-1.93±0.03	-1.55	0.81	0.99 (8)	-1.92±0.07
3	240	-2.51	1.07	0.99 (9)	-2.35±0.02	-2.50	1.16	0.98 (9)	-2.15±0.02
4	240	-1.66	0.85	0.97 (9)	-1.94±0.02	-1.56	0.77	0.98 (7)	-2.03±0.02
5	265	-3.00	0.97	0.99 (7)	-3.09±0.01	-3.38	1.28	0.98 (7)	-2.64±0.03
6	230	-5.46	0.92	0.99 (10)	-5.91±0.03	-4.98	0.89	0.99 (8)	-5.57±0.02
7	270	-3.58	0.65	0.97 (10)	-5.48±0.04	-3.65	0.66	0.99 (7)	-5.49±0.02
8	—	—	—	—	≈ -4.5*[2]	—	—	—	—

* $r(n)$ is the linear regression coefficient (number of points).

*[2] Due to the extremely low solubility of the free base in aqueous sulfuric acid solutions, this value is obtained by extrapolation.

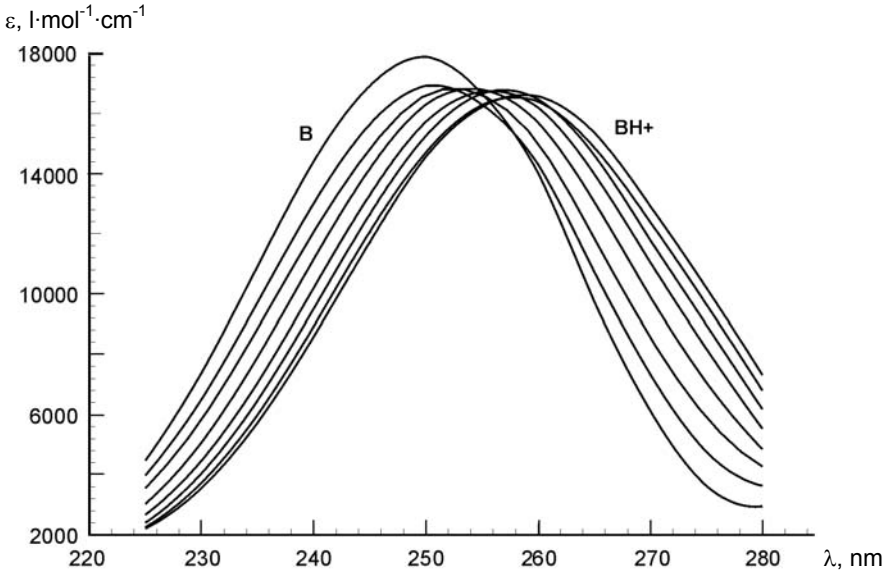


Fig. 1 UV absorption spectra of 2-methyl-5-phenyl-1,3,4-oxadiazole (**2**)
in aqueous sulfuric acid solutions, wt. % (H_0): 8.7 (-0.30); 20.1 (-1.1); 25.7 (-1.50); 30.7 (-1.84); 36.6 (-2.23); 41.0 (-2.59); 46.5 (3.10); 51.8 (-3.58).

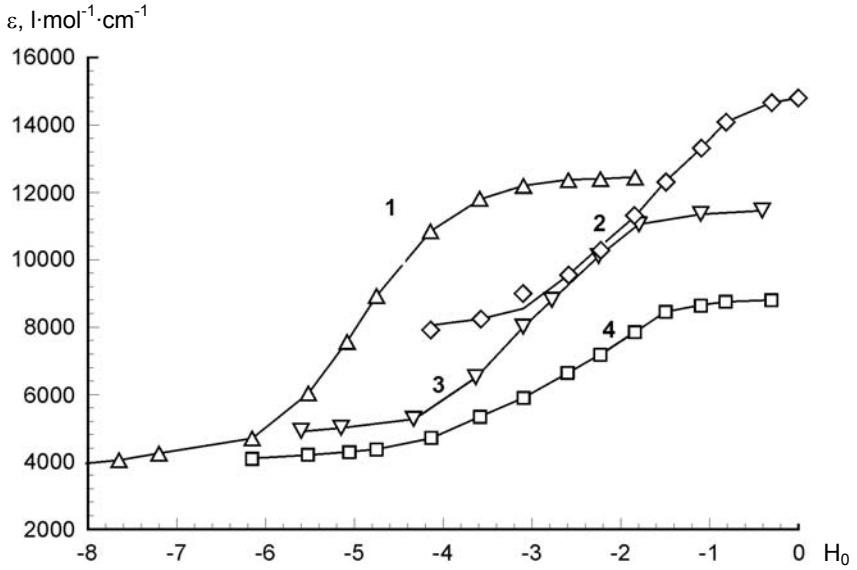


Fig. 2 Molar absorption coefficient *vs*. acidity of the medium for oxadiazoles **1, 4, 5, 7**, R (λ, nm):
1) **7** (270); 2) **4** (240); *3*) **5** (240); *4*) **1** (235).

The investigated derivatives of 1,3,4-oxadiazole are protonated similarly by standard Hammett bases, except for the trifluoromethyl derivative **7**, for which the solvation coefficients (*m*, *m**) in Eqs. (1), (2) are appreciably lower than unity. This effect may be explained by processes involving partial degradation of the protonated form of trifluoromethyloxadiazole **7a** in strongly acid media, which is consistent with literature data: 1,3,4-oxadiazoles containing electron-acceptor substituents exhibit rather high lability [10].

The pK_{BH}^+ values calculated using Eqs. (1) and (2) agree quite well. Discrepancies in these values in the case of chloroalkyloxadiazoles **5, 6** are no greater than 0.5 units, and in all the rest of the cases the discrepancies are no more than 0.2 units. The values of the solvation coefficients *m* and *m** are also close to each other for all the compounds, except for chloromethyloxadiazole **5**.

As we can see from Table 2, compounds **1-8** exhibit the properties of weak bases. The basic properties of 1,3,4-oxadiazoles are appreciably weaker than for 1,2,4-triazoles and 1,3-oxazoles, and are close to the values for tetrazoles and 1,2,4-oxadiazoles [6, 7, 11, 12]. The basicity constants for 1,3,4-oxadiazoles and 1,3-oxazoles, which contain similar substituents on the ring, differ by 2-3 log units [6]. We note that as we go from 2,5-diphenyl-1,3,4-oxadiazole (pK_{BH}^+ -1.83 [2, 3]) to monophenyloxadiazoles **1, 2** (Table 2), the basicity constant is reduced by about 1.5 log units. Thus a phenyl substituent substantially increases the basicity of the 1,3,4-oxadiazole ring, which is consistent with the hypotheses made above based on the spectral data. No effect of the steric factor is observed as we go from methyl-1,3,4-oxadiazole (**2**) to *tert*-butyl-1,3,4-oxadiazole (**4**). The basicity of 5-phenyl-2-trifluoromethyl-1,3,4-oxadiazole (**7**) is somewhat higher than the basicity of 5-phenyl-2-trichloromethyl-1,3,4-oxadiazole (**6**), although based on the electronic constants for the trifluoromethyl and trichloromethyl substituents, we should expect the reverse effect. We may hypothesize that in this case, the trifluoromethyl substituent interacts with the heterocycle according to a hyperconjugation mechanism [13].

The pK_{BH}^+ values for oxadiazoles **1-7**, calculated from Eqs. (1) and (2), correlate satisfactorily with the Hammett σ_p substituent constants (Eqs. (3), (4), respectively, Fig. 3).

$$pK_{BH}^+ \text{(from Eq. 1)} = -(5.38\pm0.54)\sigma_p - (2.92\pm0.16) \quad (3)$$
$$\text{for } r = 0.98;\ s = 0.40,\ n = 7,$$

$$pK_{BH}^+ \text{(from Eq. 2)} = -(5.17\pm0.62)\sigma_p - (2.80\pm0.18) \quad (4)$$
$$\text{for } r = 0.97,\ s = 0.45,\ n = 7$$

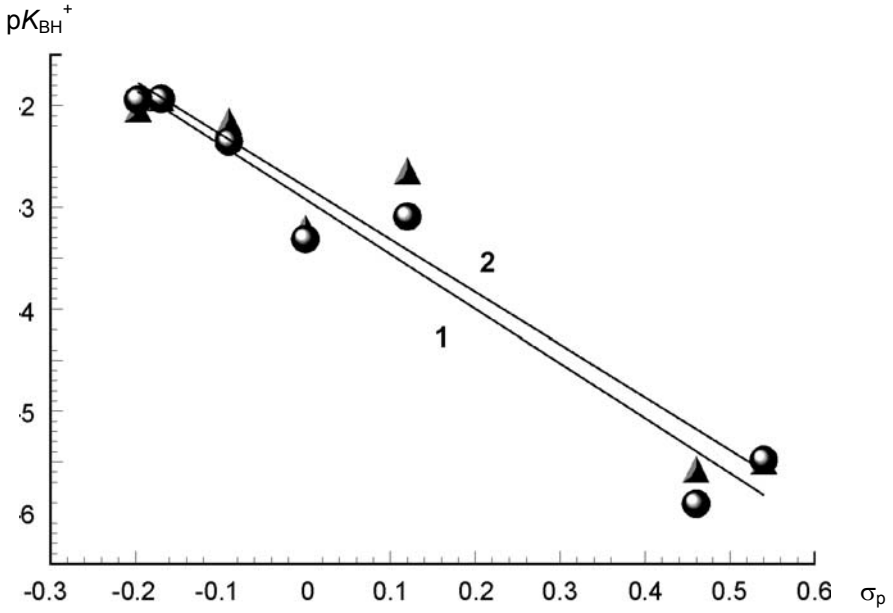


Fig. 3 pK_{BH}^+ values of oxadiazoles **1-7** *vs*. the σp substituent constants:
1) pK_{BH}^+ values calculated from Eq. (1); *2*) pK_{BH}^+ values calculated from Eq.(2).

However, we saw that the best linear correlation is observed when using the electrophilic substituent constants σ_p^+ (Eq. 5). The latter indirectly indicates a significant contribution from direct polar conjugation in the mechanism for transfer of the electronic substituent effect to the basic center [14].

$$pK_{BH}^+ \text{ (from Eq. 1)} = -(3.94\pm0.21)\sigma_p^+ - (3.12\pm0.07) \quad (5)$$
$$\text{for } r = 0.99,\ s = 0.15,\ n = 5$$

Based on the correlations (3), (5) and the pK_{BH}^+ values for bisoxadiazole **8** (Table 2), we calculated the values of the electronic substituent constants for the 2-phenyl-1,3,4-oxadiazol-5-yl group, which were: σ_p 0.30; σ_p^+ 0.36. These values show that the 1,3,4-oxadiazole ring is a rather strong electron acceptor [14].

The values of the slope (ρ) in the correlation equation for pK_{BH}^+ *vs*. σ_p (3) for compounds **1-7**, containing a substituent directly on the 1,3,4-oxadiazole ring, and the slope for the analogous equation for 2-aryl-5-phenyl-1,3,4-oxadiazoles obtained previously in [3], were used to calculate the transmission factor for the phenyl substituent (π'). In the case of aryl-1,3,4-oxadiazoles, $\pi' = 0.2$. We note that according to literature data, π' for an aryl group is usually in the range 0.25-0.30 [14].

EXPERIMENTAL

The UV spectra of compounds **1-8** were recorded on a Shimadzu UV-2401 spectrophotometer. The concentration of the aqueous sulfuric acid solutions was determined by potentiometric titration within ±0.2 wt.%. The acidity function values were taken from [15]; the values of σ_p and σ_p^+ were taken from [14, 16]. The ionization ratios were calculated by the known procedures in [8]. Compounds **1-8** were obtained by previously described procedures from the corresponding 5-substituted tetrazoles and anhydrides or acid chlorides of carboxylic acids, or by cyclization of the corresponding carboxylic acid hydrazides; their properties corresponded to literature data [17-23].

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