LITERATURE CITED

1. K. Monah, K. Bharamaramba, and R. V. Venkataraman, Chem. Ind., 125 (1978).
2. G. Henbach, L. Emmel, and A. Waltersdorfer, Ger. Offen 2725148; Chem. Abstr., 90, 196956 (1979).
3. S. Iwai, M. Hatano, I. Ischikawa, and T. Kawano, Japan Kokai Tokkyo Koho 78135981; Chem. Abstr., 90, 152195 (1979).
4. W. Manchot and R. Noll, 343, 1 (1905).
5. G. I. Chipens, R. P. Bokaldere, and V. Ya. Grinshtein, Khim. Geterotsikl. Soedin., No. 1, 110 (1966).
6. C. F. Kröger, K. Mietchen, H. Frank, M. Siemer, and S. Pilz, Chem. Ber., 102, 755 (1969).
7. G. I. Chipens and R. P. Bokaldere, Khim. Geterotsikl. Soedin., No. 2, 159 (1969).
8. T. P. Kofman, I. V. Vasil'eva, and M. S. Pevzner, Khim. Geterotsikl. Soedin., No. 10, 1407 (1977).
9. T. P. Kofman, M. S. Pevzner, L. N. Zhukova, T. A. Kravchenko, and G. M. Frolova, Zh. Org. Khim., 16, 420 (1980).
10. L. I. Bagal, M. S. Pevzner, and V. Ya. Samarenko, Khim. Geterotsikl. Soedin., No. 2, 269 (1970).
11. M. S. Pevzner, T. P. Kofman, E. N. Kibasova, L. F. Sushchenko, and T. L. Uspenskaya, Khim. Geterotsikl. Soedin., No. 2, 257 (1980).
12. T. P. Kofman, T. L. Uspenskaya, N. Yu. Medvedeva, and M. S. Pevzner, Khim. Geterotsikl. Soedin., No. 7, 991 (1976).
13. T. P. Kofman, N. Yu. Medvedeva, T. L. Uspenskaya, and M. S. Pevzner, Khim. Geterotsikl. Soedin., No. 9, 1271 (1977).
14. A. M. Ostapkovich, T. P. Kofman, L. V. Lisitsyna, and M. S. Pevzner, Izv. Vyssh. Uchebn. Zaved., Khim. Khim. Tekhnol., 22, 402 (1979).
15. T. P. Kofman, G. A. Zykova, V. I. Manuilova, T. N. Timofeeva, and M. S. Pevzner. Khim. Geterotsikl. Soedin., No. 7, 997 (1974).
16. A. A. Stotskii and N. N. Tkacheva, Zh. Org. Khim., 10, 2232 (1974).

TETRAZOLES.

9.* ACID–BASE PROPERTIES OF 5-SUBSTITUTED TETRAZOLES

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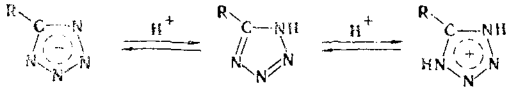
UDC 547.796.1:541.121

The basicities of series of 5-R-tetrazoles in aqueous solutions of sulfuric acid were studied by UV and PMR spectroscopy. The pK_{BH^+} values of these compound correlate with the σ_p substituent constants. The transmission factor of the p-phenylene ring ($\pi' = 0.23$) was calculated from the ratio of the reaction constants for protonation of substituted 5-phenyltetrazoles and 5-R-tetrazoles. A linear dependence between the pK_a values and the pK_{BH^+} values of 5-substituted tetrazoles was established.

It is known that tetrazoles and 5-substituted tetrazoles are heterocyclic N–H acids with moderate strength. When these compounds are dissolved in mineral acids, they behave like weak organic bases [2].



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*See [1] for Communication 8.

Lensovet Leningrad Technological Institute, Leningrad 198013. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 559-562, April, 1981. Original article submitted May 21, 1980.

0009-3122/81/1704-0412$07.50

Although tetrazole and 5-substituted tetrazoles theoretically can exist in the form of 1-H- and 2-H-tautomers, it has been shown in many cases that the 1-H form is preferred. Thus the acidities of tetrazoles are actually estimated from the pK_a values of the 1-H-tautomers.

The protonation of tetrazoles in aqueous solutions of sulfuric and perchloric acids is described by the H_0 acidity function. Since the distribution of the electron density over the tetrazole ring has its maximum value on the 1 and 4 nitrogen atoms [3], the addition of a proton may lead to the formation of two tautomers. This possibility cannot be excluded during a study of the protonation of these compounds. Nevertheless, the available significant amount of experimental data on the basicities of tetrazoles with various structures [2] makes it possible to assume that the protonation center is the ring 3 atom. Below we present new data on the effect of the nature of the substituents attached to the ring carbon atom on the acidities and basicities of tetrazoles and we also discuss the interrelationship between the acidities and the basicities of these compounds.

It has been previously shown that the acidities of substituted 5-phenyltetrazoles change only slightly, despite the wide variation in the electronic properties of the substituents [4]. The relatively low value of reaction constant ρ (1.27) constitutes evidence for the weak effect of the substituent attached to the ring carbon atom on the acidities of these compounds in water. A similar principle is observed during a study of the acidities of substituted 5-phenyltetrazoles in aqueous alcohol solutions and in the dimethyl sulfoxide (DMSO)—water system [5].

The reaction constants for the indicated solvents are, respectively, 1.52 and 1.67. At the same time, the dependence of the pK_a values of acidic dissociation in water on the σ_p substituent constants for 5-R-tetrazoles (R = CH_3,* H^*, Br, I, CF_3, and $NO_2{}^*$) has the form

$$pK_a = -(6.65 \pm 0.60)\sigma_n + (4.46 \pm 0.27),$$
$$r = 0.98,\ n = 6,\ s = 0.5.$$

It follows from this that in the acidic dissociation of substituted 5-phenyltetrazoles the phenyl ring isolates to a considerable extent the reaction center from the electronic effect of the substituent. In this case a quantitative measure of the bridging effect of the phenyl ring is transmission factor π' = 0.19 [9], which is calculated from the ratio of the reaction constants for acidic dissociation in water of substituted 5-phenyltetrazoles and 5-R-tetrazoles.

No less interesting information regarding the transmission of the electronic effects of substituents through the phenyl ring can evidently be obtained by a comparison of the basicity constants of substituted 5-phenyltetrazoles and 5-R-tetrazoles. The basicities of substituted 5-phenyltetrazoles depend relatively little on the nature of the substituents in the phenyl ring [10]. Thus the pK_{BH^+} values of 5-(o-methylphenyl)- and 5-(p-nitrophenyl)-tetrazoles are, respectively, −1.96 and −4.19. The reactivity constant ρ = 1.80 obtained from the dependence of the PK_{BH^+} values of substituted 5-phenyltetrazoles on the σ substituent constants also constitutes evidence for the low sensitivity of protonation to the effect of the substituents. Since data on the basicities of 5-substituted tetrazoles that contain "simple" substituents are not available, for comparison with substituted 5-phenyltetrazoles we selected a series of 5-R-tetrazoles, the protonation of which was studied in aqueous solutions of sulfuric acid by UV and PMR spectroscopy (Table 1). The basicity constants of 5-R-tetrazoles were calculated from the expression

$$\log I = -mH_0 + pK'_{BH^+}, \text{ where } I = \frac{[\overset{+}{TH}]}{[T]}. \tag{1}$$

For all of the investigated compounds slopes m in Eq. (1) are close to unity (Table 1). Consequently, it may be assumed that 5-R-tetrazoles are protonated in the same way as Hammett bases and that the thermodynamic pK_{BH^+} values can be obtained by division of the free term of Eq. (1) by slope m. The thermodynamic pK_{BH^+} values of 5-R-tetrazoles correlate with the σ_p substituent constants:

$$pK_{BH^+} = -(7.83 \pm 0.60)\sigma_n - (2.88 \pm 0.50),$$
$$r = 0.99,\ n = 6,\ s = 0.40.$$

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*The pK_a values were obtained by the authors for individual compounds taken from [6-8].

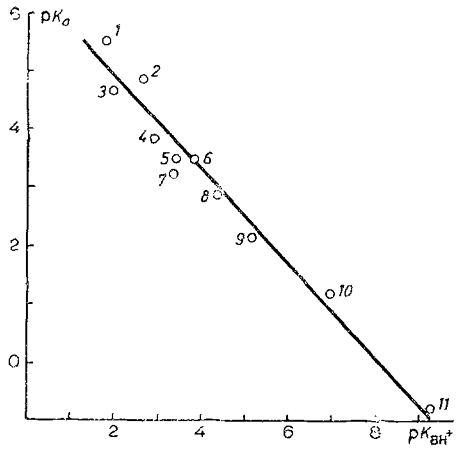

Fig. 1. Dependence of the pK_a and pH_{BH}* values of 5-substituted tetrazoles: 1) 5-methyltetrazole; 2) tetrazole; 3) 5-(p-methoxyphenyl)tetrazole; 4) 5-(m-chlorophenyl)tetrazole; 5) (m-nitrophenyl)tetrazole; 6) 5-(p-nitrophenyl)-tetrazole; 7) 5-(o-nitrophenyl)tetrazole; 8) 5-iodotetrazole; 9) 5-bromotetrazole; 10) 5-trifluoromethyltetrazole; 11) 5-nitrotetrazole.

TABLE 1. Protonation of 5-R-Tetrazoles in Aqueous Solutions of H_2SO_4 at 25°C

R	Method of investigation (λ, nm)	$\log I = -mH_0 + pK'_{BH^+}$					
		m	$-pK'_{BH^+}$	$-pK_{BH^+}$	r	n	s
CH_3	PMR	0,93±0,02	1,60±0,04	1,83	0,99	8	0,03
H	PMR	0,86±0,06	2,28±0,14	2,68	0,96	19	0,13
Br	UV (200)	0,91±0,06	4,72±0,30	5,20	0,99	7	0,12
I	UV (230)	0,88±0,05	3,87±0,20	4,40	0,99	7	0,10
CF_3	UV (210)	0,90±0,02	6,30±0,14	7,00	0,97	8	0,20
NO_2	UV (235)	1,00±0,06	9,28±0,20	9,26	0,99	8	0,13
	UV (240)	0,95±0,05	9,28±0,22		0,99	8	0,09

TABLE 2. Protonation of Substituted Tetrazoles in Aqueous Solutions of H_2SO_4 at 25°C

R	Method of investigation (λ, nm)	$\log I = -mH_0 + pK'_{BH^+}$					
		m	$-pK'_{BH^+}$	$-pK_{BH^+}$	r	n	s
1-Methyl-5-R-tetrazoles							
H	PMR	0,98±0,02	2,94±0,01	3,00	0,99	10	0,04
CH_3	PMR	0,99±0,04	1,66±0,07	1,68	0,99	8	0,08
NO_2	UV (240)	0,95±0,10	8,84±0,60	9,31	0,97	7	0,17
2-Methyl-5-R-tetrazoles							
H	PMR	0,91±0,03	2,96±0,10	3,25	0,99	10	0,06
NO_2	UV (245)	0,99±0,02	8,97±0,19	9,06	0,99	8	0,03

Thus it is apparent that the pK_{BH}^+ value undergoes a change of seven orders of magnitude on passing from 5-methyl- to 5-nitrotetrazole. This circumstance may be associated either with a shift of the protonation center or with the electronic effect of the substituents.

As we have already noted, tetrazoles with different structures, including substituted 5-phenyltetrazoles, undergo protonation at the nitrogen atom in the 4 position of the ring in aqueous solutions of mineral acids. The correlation of the pK_{BH}^+ values of 5-R-tetrazoles with the σ_p substituent constants means that the addition of a proton to the tetrazole ring for all of the members of the reaction series occurs at one and the same reaction center. However, on the basis of this one cannot answer the question as to which of the nitrogen atoms of the ring (1 or 4) is the protonation center. This information can be obtained by a comparison of the basicities of 5-R-tetrazoles and their 1- and 2-methyl-substituted derivatives (Table 2). All of the compounds presented in Table 2 are Hammett bases. It is apparent (Tables 1 and 2) that 5-methyltetrazole is a stronger base than the isomeric 1-methyl- and 2-methyltetrazoles, while 1,5-dimethyltetrazole differs virtually not at all from 5-methyltetrazole. The basicity constants of 5-nitrotetrazole and 1-methyl- and 2-methyl-5-nitrotetrazoles are also very close to one another. A similar principle can be observed by comparing the basicities of 5-phenyltetrazole and 1-methyl- and 2-methyl-5-phenyltetrazoles [11]. It follows from this that the addition of a proton to 5-R-tetrazoles, just as in the case of 5-phenyltetrazoles, takes place at the nitrogen atom in the 4 position of the ring, since otherwise all 1-methyl- and 2-methyl-5-R-tetrazoles should be stronger bases than the corresponding 5-R-substituted compounds.

On the basis of this, the reaction constants for protonation of substituted 5-phenyltetrazoles and 5-R-tetrazoles can be used to calculate the transmission factor. The small transmission factor $\pi' = 0.23$ means that in the protonation, just as in acidic dissociation, of substituted 5-phenyltetrazoles the phenyl ring substantially insulates the reaction center from the electronic effect of the substituent.

Thus it is evident that the effect of substituents on the acidites and basicities of 5-substituted tetrazoles is manifested in the same way and that a linear dependence should consequently exist between the pK_a and pK_{BH^+} values of these compounds. In fact, this sort of correlation does exist (see Fig. 1) and is described by the equation

$$pK_a = (0.78 \pm 0.05)\, pK_{BH^+} + (6.37 \pm 0.25),\ r = 0.98,\ n = 11,\ s = 0.3. \qquad (2)$$

It should be noted that expression (2) encompasses a rather broad range of changes in the pK_a and pK_{BH^+} values, and this makes it possible to make a quantitative evaluation of the acid–base properties of 5-substituted tetrazoles with the most diverse structures.

EXPERIMENTAL

The tetrazole and the disubstituted tetrazoles were obtained by known methods. All of the compounds had characteristics that were in agreement with the literature data [6-8, 12, 13]. Aqueous buffer solutions with ionic strength μ 0.01 were prepared by the method in [14]. The sulfuric acid solutions were obtained by dilution of 96% H_2SO_4 (especially pure-grade) with twice-distilled water, while solutions with higher concentrations were prepared by the addition of oleum (analytical-grade). The concentrations were determined by potentiometric titration with a 0.1 N solution of NaOH with an accuracy of ±0.1%. The acidity constants of tetrazole ($pK_a = 4.86 \pm 0.02$) and 5-methyltetrazole ($pK_a = 5.50 \pm 0.01$) in water were determined by potentiometry in a thermostatted cell (25 ± 0.1°C) with a pH-121 pH meter. The acidity constants of 5-nitrotetrazole ($pK_a = -0.83 \pm 0.03$) were determined spectrophotometrically in aqueous buffer solutions and aqueous solutions of sulfuric acid. During the study of the acidities and basicities of the tetrazoles the UV spectra were recorded with an SF-26 spectrophotometer with a thermostatted block (25 ± 0.1°C); the analytical concentrations of the tetrazoles were $\sim 1 \cdot 10^{-5}$ mole/liter. The PMR spectra were recorded with a Perkin-Elmer R-12 spectrometer; the analytical concentrations of the tetrazoles were $\sim 1 \cdot 10^{-2}$ mole/liter, and the internal standard was tetramethylammonium bromide. The values of the H_0 and H_- acidity functions were taken from [15, 16]. The experimental data were processed by the methods presented in [4, 10].

LITERATURE CITED

1. V. A. Ostrovskii, G. I. Koldobskii, and I. Yu. Shirobokov, Zh. Org. Khim., 17, 146 (1981).
2. G. I. Koldobskii, V. A. Ostrovskii, and B. V. Gidaspov, Khim. Geterotsikl. Soedin., No. 7, 867 (1980).
3. V. A. Ostrovskii, N. S. Panina, G. I. Koldobskii, B. V. Gidaspov, and I. Yu. Shirobokov, Zh. Org. Khim., 15, 844 (1979).
4. V. A. Ostrovskii, G. I. Koldobskii, N. P. Shirokova, I. Yu. Shirobokov, and B. V. Gidaspov, Zh. Org. Khim., 14, 1697 (1978).

5. J. Kaczmarek, H. Smagowski, and Z. Grzonka, J. Chem. Soc., Perkin II, No. 12, 1670 (1979).
6. J. S. Mihina and R. M. Herbst, J. Org. Chem., 15, 1082 (1950).
7. E. Lieber, S. Patinkin, and H. H. Tao, J. Am. Chem. Soc., 73, 1792 (1951).
8. W. P. Norris, J. Org. Chem., 27, 3248 (1962).
9. Yu. A. Zhdanov and V. I. Minkin, Correlation Analysis in Organic Chemistry [in Russian], Rostov-on-Don (1966), p. 56.
10. V. N. Strel'tsova, N. P. Shirokova, G. I. Koldobskii, and B. V. Gidaspov, Zh. Org. Khim., 10, 1081 (1974).
11. A. V. Moskvin, V. A. Ostrovskii, I. Yu. Shirobokov, G. I. Koldobskii, and B. V. Gidaspov, Zh. Org. Khim., 14, 2440 (1978).
12. R. A. Henry and W. G. Finnegan, J. Am. Chem. Soc., 76, 290 (1954).
13. R. A. Henry and W. G. Finnegan, J. Am. Chem. Soc., 76, 923 (1954).
14. D. D. Perrin, Aust. J. Chem., 16, 572 (1963).
15. M. I. Vinnik, Usp. Khim., 35, 1922 (1966).
16. R. H. Boyd, J. Am. Chem. Soc., 83, 4288 (1961).