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Basicity of Isomeric Ditetrazolylbenzenes and Their *N*-*tert*-Butyl Derivatives

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Abstract—The basicity constants (pK_{BH^+}, $pK_{BH^{2+}}$) of 1,2-, 1,3-, and 1,4-bis(tetrazol-5-yl)benzenes and their *N*-*tert*-butyl derivatives in aqueous sulfuric acid and the dissociation constants (pK_{HB}) of the corresponding H-complexes with *p*-fluorophenol in carbon tetrachloride were determined by UV and IR spectroscopy. Mono- and diprotonation of isomeric ditetrazolylbenzenes is observed in the acidity range (H_0) from –1 to –5 (pK_{BH^+} –2.5 to –3.0; $pK_{BH^{2+}}$ –3.8 to –4.9). Introduction of a *tert*-butyl group into the 2-position of the heteroring almost does not affect the basicity of ditetrazolyl benzenes. Among the examined compounds, 1,2-bis(2-*tert*-butyltetrazol-5-yl)benzene is the strongest proton acceptor with respect to *p*-fluorophenol as standard proton donor, presumably due to formation of a complex with bifurcated (three-center) hydrogen bond.

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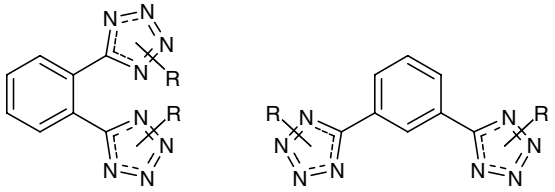
Isomeric ditetrazolylbenzenes are widely used in preparative organic chemistry as starting materials for the synthesis of macrocyclic compounds [1–3], as well as of various oligomers and polymers [4–8]. Despite the fact that ditetrazolylbenzenes have been known over several decades, their acid–base properties have been poorly studied. Kaczmarek et al. [9] were the only to report on the first-step acid dissociation constants K_a^1 of isomeric ditetrazolylbenzenes, which were determined by potentiometric titration in water–organic solvent systems: 1,2-bis(tetrazol-5-yl)benzene, 8.62×10^{-5} (50% ethanol); 1,3-bis(tetrazol-5-yl)benzene, 15.4×10^{-5} (75% DMSO); 1,3-bis(tetrazol-5-yl)-benzene, 12.8×10^{-5} (75% DMSO).

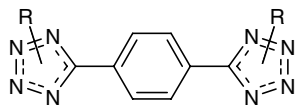
In the present work we used UV spectroscopy to determine the basicity constants pK_{BH^+} and $pK_{BH^{2+}}$ of isomeric ditetrazolylbenzenes **I**–**III** and their *N*-*tert*-butyl derivatives **IV**–**VI** in aqueous sulfuric acid. With the aid of Fourier-transform IR spectroscopy we also determined the dissociation constants pK_{HB} of the H-complexes derived from bis(2-*tert*-butyltetrazol-5-yl)benzenes **IV**–**VI** and *p*-fluorophenol in carbon tetrachloride.

Isomeric ditetrazolylbenzenes, as well as their N-alkyl-substituted analogs, are capable of acting as bases to produce the corresponding mono- and dications upon addition of one or two protons. According to published data, the basicity center in NH- and N-substituted tetrazoles is nitrogen atom in position *4* of the heteroring (Scheme 1) [10–12]. The electronic absorption spectra of isomeric ditetrazolylbenzenes **I**–**VI** strongly differ from each other (Table 1). The presence of a strong long-wave absorption band in the electronic spectrum of 1,4-bis(tetrazol-5-yl)benzene (**III**) and its di-*tert*-butyl derivative **VI** is likely to be related to π–π conjugation between the tetrazole and benzene rings; analogous conjugation in molecules **I**, **II**, **IV**, and **V** is broken for steric reasons. In fact, the results of PM3 semiempirical calculations showed that 1,4-bis(tetra-



I, **IV**

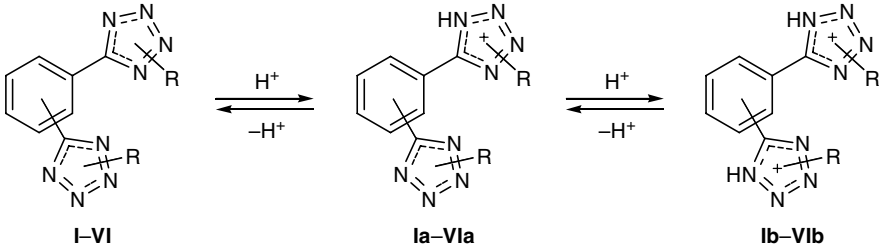
II, **V**



III, **VI**

I–**III**, R = 1-H; **IV**–**VI**, R = 2-*t*-Bu.

Scheme 1.



zol-5-yl)benzene (**III**) in the gas phase is a strongly conjugated planar system and that the dihedral angles between the heteroring and benzene ring planes in 1,2-bis(tetrazol-5-yl)benzene (**I**) approach a value of 50° (Fig. 1).

Compounds **I**–**III** are also characterized by different patterns of variation of the UV spectra upon protonation (Table 1). Protonation of 1,2-ditetrazolylbenzene **I** is accompanied by a considerable red shift of the absorption maxima and insignificant hypochromic effect in the electronic spectrum (Fig. 2), while analogous changes in the spectra of 1,3- and 1,4-isomers **II** and **III** are less appreciable. The character of variations in the UV spectra on protonation of *N*-*tert*-butyl derivatives **IV**–**VI** is analogous to that observed for the corresponding NH-ditetrazolylbenzenes **I**–**III**.

The plots of the molar absorption coefficient ε versus acidity H_0 for mono- and diprotonation of compounds **I**–**VI** have an extended *S*-shape (Fig. 3); this suggests that the examined acidity range covers two ionization processes [13]. Using the procedure described in [13] for the calculation of fairly similar ionization constants of a dibasic acid, we deduced Eq. (1) to calculate the basicity constants of weak dibasic heterocycles **I**–**VI**.

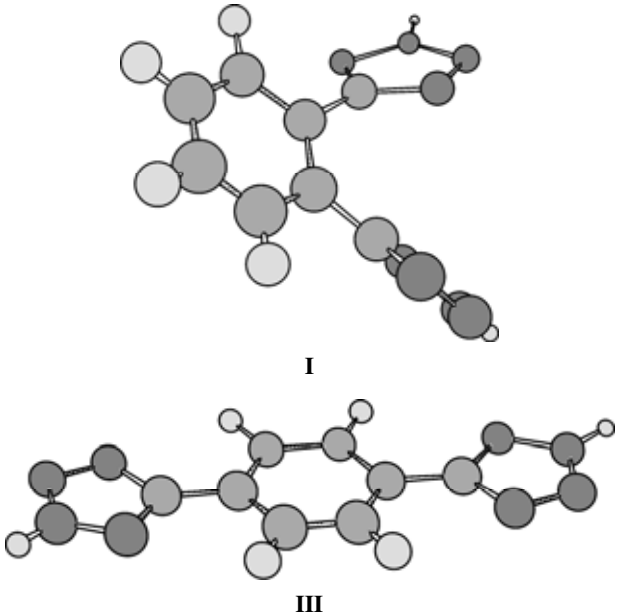


Fig. 1. Structures of the molecules of 1,2- and 1,4-bis(tetrazol-5-yl)benzenes **I** and **III** optimized by the PM3 method.

$$\varepsilon = \frac{\varepsilon_B K_{BH^+} K_{BH^{2+}} + \varepsilon_{BH^+} h_0 K_{BH^{2+}} + \varepsilon_{BH^{2+}} h_0 h_x}{K_{BH^+} K_{BH^{2+}} + h_0 K_{BH^{2+}} + h_0 h_x}. \qquad (1)$$

Here, ε_B, ε_{BH+}, and ε_{BH2+} are molar absorption coefficients of the free base B, monocation BH^+, and dication BH_2^{2+}, respectively; h_0 ($H_0 = -\log h_0$) and h_x ($H_x = -\log h_x$) are the acidity factors substituted into Eq. (1) assuming that the monoprotonation is determined by the acidity function H_0, and diprotonation, by H_x ($H_x = H_0$ or H_+). Equation (1) was then linearized and solved by the least-squares procedure. To avoid effect of solvation on the basicity constants, in all cases pK_{BH+} and pK_{BH2+} were assumed to be equal to the ratio of the free term and the slope in Yates–McClelland equations (2) and (3), respectively [14]:

$$\log I = -m_1 H_0 + pK'_{BH+};\ pK_{BH+} = pK'_{BH+}/m_1; \qquad (2)$$

$$\log I = -m_2 H_x + pK'_{BH2+};\ pK_{BH2+} = pK'_{BH2+}/m_2. \qquad (3)$$

Here, I is the ionization ratio: $I = [BH^+]/[B] = (\varepsilon - \varepsilon_B)/(\varepsilon_{BH+} - \varepsilon)$ for monoprotonation, $I = [BH^{2+}]/[BH^+] = (\varepsilon - \varepsilon_{BH+})/(\varepsilon_{BH2+} - \varepsilon)$ for diprotonation, and m_1 and m_2 are solvation coefficients in the linear dependences of $\log I$ upon acidity of the medium (H_0, H_+).

The data in Table 2 indicate that ditetrazolylbenzenes **I**–**III** and their *N*-*tert*-butyl derivatives **IV**–**VI** are weak bases. The basicity constants pK_{BH+} of **I**–**IV** vary over a fairly narrow range. The most basic among the examined compounds is 1,4-bis(tetrazol-5-yl)benzene (**III**). Most probably, the reason is effective π–π conjugation in the planar *para* isomer structure, which favors delocalization of the positive charge; the corresponding *meta* and *ortho* isomers lack such conjuga-

Table 1. UV spectra of isomeric ditetrazolylbenzenes **I–III** and their *N*-*tert*-butyl derivatives **IV–VI** in aqueous sulfuric acid

Compound no.	Base			Dication		
	H_2SO_4, wt % (H_0)	λ^B_{max}, nm	ε^B_{max}, l mol^{-1} cm^{-1}	H_2SO_4, wt % (H_0)	λ^B_{max}, nm	ε^B_{max}, l mol^{-1} cm^{-1}
I	13.77 (–0.71)	207, 237–239	29400, 10400	73.23 (–6.43)	218, 251–252	22000, 9200
II	10.00 (–0.43)	229	32900	72.88 (–6.37)	233	31300
III	24.87 (–1.44)	262	21000	81.47 (–7.76)	265–266	19500
IV	13.77 (–0.71)	205	34700	72.88 (–6.37)	207, 247–248	28600, 11000
V	32.85 (–2.03)	–[a]	–[a]	75.35 (–6.77)	229	34500
VI	37.98 (–2.41)	–[a]	–[a]	73.23 (–6.43)	267	29000

[a] The spectrum was not recorded because of the poor solubility.

Table 2. Basicity constants[a] of ditetrazolylbenzenes **I–VI** in aqueous sulfuric acid and dissociation constants[b] of their H-complexes with *p*-fluorophenol

Compound no.	Acidity function H_0			Acidity function H_0			Acidity function H_+			pK_{HB}
	pK_{BH+}	pK'_{BH+}	m_1	pK_{BH2+}	pK'_{BH2+}	m_2	pK_{BH2+}	pK'_{BH2+}	m_2	
I	–2.63±0.08	–2.69	1.02	–4.66±0.05	–4.65	1.0	–4.66±0.05	–4.94	1.06	–[c]
II	–2.94±0.03	–3.06	1.04	–4.83±0.01	–4.78	0.99	–4.70±0.01	–4.97	1.06	–[c]
III	–2.54±0.02	–2.56	1.01	–4.15±0.01	–3.61	0.87	–3.85±0.01	–3.90	1.01	–[c]
IV	–2.63±0.04	–2.75	1.04	–4.61±0.03	–4.83	1.05	–4.60±0.03	–5.11	1.11	1.79±0.03
V	–[c]	–[c]	–[c]	–4.80±0.28	–5.20	1.08	–4.64±0.53	–5.62	1.21	1.43±0.02
VI	–[c]	–[c]	–[c]	–4.07±0.04	–4.52	1.11	–3.81±0.02	–4.45	1.17	1.47±0.02

[a] Calculated by Eq. (1); linear regression coefficient $r \geq 0.99$.
[b] Calculated by Eq. (3); CCl_4, 25°C.
[c] The compound was insufficiently soluble to perform spectral measurements.

tion due to steric hindrances. The basicity of the heterocyclic fragment almost does not change in going from NH-tetrazoles **I–III** to their 2-*tert*-butyl-substituted analogs **IV–VI**.

The H-complex formation constants K_h for bis(2-*tert*-butyltetrazol-5-yl)benzenes **IV–VI** and *p*-fluorophenol in carbon tetrachloride [equilibrium (4)] were calculated in terms on the classical concepts using Eq. (5). The dissociation constants (pK_{HB}) of the H-complexes were assumed to be equal to the logarithm of K_h ($pK_{HB} \equiv \log K_h$) [15, 16]. The equilibrium concentrations were calculated from the intensities of the IR absorption band corresponding to stretching vibrations of the free hydroxy group in *p*-fluorophenol.

$$AH + B \underset{}{\overset{K_h}{\rightleftharpoons}} AH\cdots B \qquad (4)$$

$$K_h = \frac{[AH\cdots B]}{[AH][B]} = \frac{AH_0 - [AH]}{[AH](B_0 - AH_0 + [AH])}. \qquad (5)$$

Here, [AH···B] is the equilibrium concentration of the H-complex; AH_0 and B_0 are the initial concentrations of the proton donor and base; and [AH] and [B] are the equilibrium concentrations of the free proton donor and base, respectively. Experiments were carried out in strongly dilute solutions to exclude dimerization of the components of the equilibrium mixture and their interactions with foreign acids or bases.

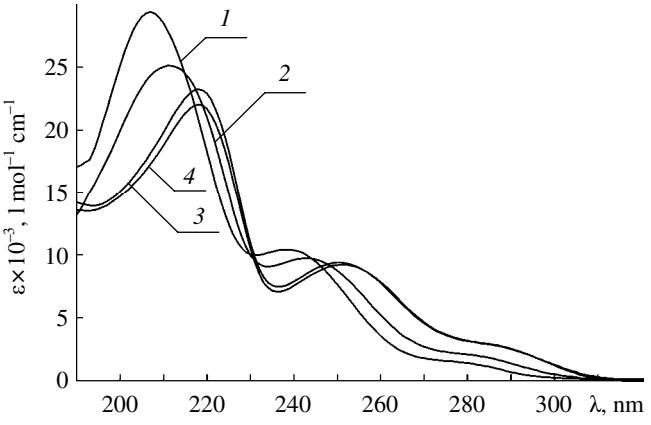


Fig. 2. Electronic absorption spectra of 1,2-bis(tetrazol-5-yl)-benzene (**I**) in aqueous sulfuric acid: (*1*) $H_0 = -0.71$, (*2*) $H_0 = -3.09$, (*3*) $H_0 = -5.52$, (*4*) $H_0 = -6.43$.

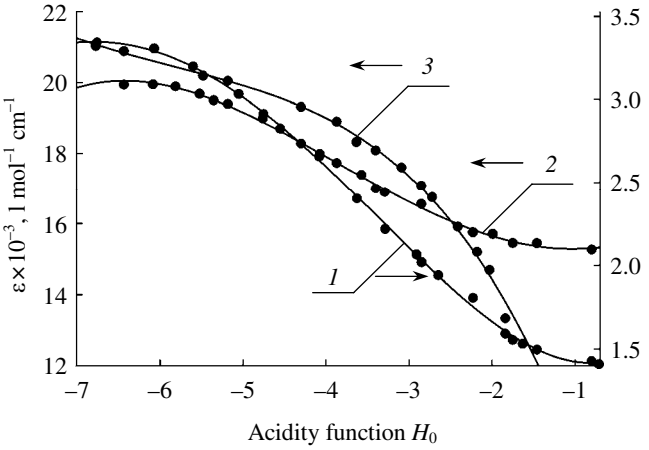
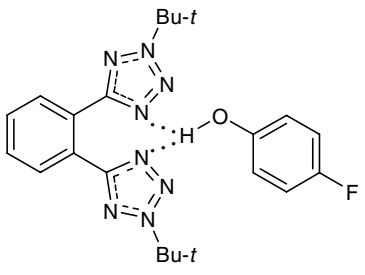


Fig. 3. Plots of the molar absorption coefficient of (*1*) 1,2-bis-(tetrazol-5-yl)benzene (**I**) (λ = 280 nm), (*2*) 1,3-bis(tetrazol-5-yl)benzene (**II**) (λ = 250 nm), and (*3*) 1,3-bis(2-*tert*-butyltetrazol-5-yl)benzene (**V**) (λ = 250 nm) versus acidity of the medium.

The IR spectra of solutions of **IV**–**VI** and *p*-fluorophenol contained a well-defined absorption band at 3612–3614 cm^{-1}, which belongs to stretching vibrations of the free OH group in *p*-fluorophenol, and a diffuse band with an ill-defined maximum at 3150–3500 cm^{-1} due to vibrations of associated hydroxy group. Raising the concentration of bis-tetrazoles **IV**–**VI** resulted in decrease in the intensity of the first band and simultaneous increase in the intensity of the second band.

The pK_{HB} values of compounds **IV**–**VI**, calculated at several concentrations of **IV**–**VI**, coincided within the experimental error (±0.02–0.03). The results showed (Table 2) that 1,2-bis-(2-*tert*-butyltetrazol-5-yl)benzene (**IV**) is the strongest among the examined isomers proton acceptor with respect to *p*-fluorophenol. The high basicity of the *ortho* isomer may be rationalized in terms of formation of H-complex **A** with bifurcated hydrogen bond: the hydroxy proton in **A** is linked through hydrogen bonds to nitrogen atoms of both heterocyclic fragments. Presumably, the formation of such complex is most favorable for *ortho* isomer **IV**.



A

EXPERIMENTAL

The UV spectra were measured on a Shimadzu UV-2401 PC spectrophotometer. The ^1H and ^{13}C NMR spectra were recorded from solutions in DMSO-d_6 on a Bruker DPX-300 spectrometer at 300 and 75 MHz, respectively, using TMS as internal reference.

The IR spectra of mixtures of *p*-fluorophenol with bis-tetrazoles **IV**–**VI** were recorded in the range from 4000 to 2500 cm^{-1} on a Shimadzu FTIR-8400 spectrometer using 1-cm hermetically capped glass cells maintained at a constant temperature. Commercial *p*-fluorophenol (Aldrich, purity >99%) was additionally purified and dehydrated by vacuum sublimation and was stored over P_2O_5. Carbon tetrachloride was additionally purified and dehydrated by triple distillation over P_2O_5 and was stored over 4-Å molecular sieves. The absence of moisture in the solvent was checked by IR spectroscopy (no stretching vibrations of O–H bonds in water molecules was observed).

The concentration of sulfuric acid in aqueous solutions was determined with an accuracy of ±0.2 wt % by potentiometric titration on a pH-121 potentiometer equipped with ESL-43-07 glass and EVL-1M3 silver chloride electrodes and a temperature-control unit (25°C). The titration was performed using bidistilled water. The H_0 and H_+ values were taken from [17].

Bis-tetrazoles **IV**–**VI** were stored over P_2O_5 under reduced pressure. According to the recommendations given in [16], the concentration of *p*-fluorophenol in working solutions did not exceed 4×10^{-3} M; the concentration of bases **IV**–**VI** was selected in such a way that the fraction of associated *p*-fluorophenol ranged from 20 to 80% of its overall amount. The pK_{HB} values were calculated as average from 3–4 values determined at different concentrations of the base.

Isomeric ditetrazolylbenzenes were synthesized by reactions of the corresponding benzenedicarbonitriles with sodium azide and triethylammonium chloride in toluene according to the procedure described in [18].

1,2-Bis(tetrazol-5-yl)benzene (I). mp 227°C. ^1H NMR spectrum, δ, ppm: 7.80–7.90 m (4H, H_{arom}), 16.52 br.s (2H, NH). ^{13}C NMR spectrum, δ_C, ppm: 124.6, 130.8, 131.4 (C_{arom}); 154.8 (C^5). Found, %: C 44.90; H 2.51; N 52.83. $C_8H_6N_8$. Calculated, %: C 44.86; H 2.8; N 52.34.

1,3-Bis(tetrazol-5-yl)benzene (II). mp 260°C. ^1H NMR spectrum, δ, ppm: 7.82–8.77 m (4H, H_{arom}), 16.47 br.s (2H, NH). ^{13}C NMR spectrum, δ_C, ppm: 125.3, 125.6, 129.3, 130.6 (C_{arom}); 155.5 (C^5). Found,

%: C 44.42; H 2.84; N 52.65. $C_8H_6N_8$. Calculated, %: C 44.86; H 2.8; N 52.34.

1,4-Bis(tetrazol-5-yl)benzene (III). mp 300°C. ^{1}H NMR spectrum, δ, ppm: 8.22 m ($4H_{arom}$). ^{13}C NMR spectrum, δ_C, ppm: 126.7, 127.9 (C_{arom}); 155.4 (C^5). Found, %: C 45.14; H 3.27; N 52.86. $C_8H_6N_8$. Calculated, %: C 44.86; H 2.8; N 52.34.

1,2-Bis(2-*tert*-butyltetrazol-5-yl)benzene (IV). 1,2-Bis(tetrazol-5-yl)benzene (**II**), 1.3 g (0.006 mol), was dissolved in 25 ml of 95% H_2SO_4, 0.020 mol of *t*-BuOH was slowly added at 25°C, and the mixture was vigorously stirred for 3 h at 25°C, diluted with water, neutralized with a solution of NaOH, and extracted with CH_2Cl_2 (80 ml). The extract was dried over anhydrous $MgSO_4$ and evaporated, and the residue was recrystallized from aqueous ethanol. Yield 1.53 g (78%), colorless crystals, mp 88.5–90.5°C. ^{1}H NMR spectrum, δ, ppm: 1.62 s (18H, *t*-Bu), 7.71–7.90 m (4H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 127.4, 130.2, 130.3 (C_{arom}); 163.0 (C^5); 28.7 [C(**C**$H_3)_3$]; 63.6 [**C**$(CH_3)_3$]. Found, %: C 59.39; H 7.16; N 34.80. $C_{16}H_{22}N_8$. Calculated, %: C 58.90; H 6.75; N 34.35.

1,3-Bis(2-*tert*-butyltetrazol-5-yl)benzene (V) was synthesized in a similar way. Yield 1.37 g (70%), colorless crystals, mp 114–115.5°C. ^{1}H NMR spectrum, δ, ppm: 1.75 s (18H, *t*-Bu), 7.67–8.70 m (4H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 123.7, 127.7, 127.9, 129.7 (C_{arom}); 162.8 (C^5); 28.6 [C(**C**$H_3)_3$]; 63.8 [**C**$(CH_3)_3$]. Found, %: C 58.96; H 6.92; N 34.48. $C_{16}H_{22}N_8$. Calculated, %: C 58.90; H 6.75; N 34.35.

1,4-Bis(2-*tert*-butyltetrazol-5-yl)benzene (VI) was synthesized in a similar way. Yield 1.25 g (64%), colorless crystals, mp 170–172.5°C. ^{1}H NMR spectrum, δ, ppm: 1.76 s (18H, *t*-Bu), 8.23 m (4H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 127.1, 128.7 (C_{arom}); 163.0 (C^5); 28.8 [C(**C**$H_3)_3$], 64.1 [**C**$(CH_3)_3$]. Found, %: C 59.10; H 6.55; N 34.68. $C_{16}H_{22}N_8$. Calculated, %: C 58.90; H 6.75; N 34.35.

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