ACID – BASE PROPERTIES OF
3(5)-AZIDO-1,2,4-TRIAZOLES

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The pK_a and pK_{BH^+} values of a series of 3(5)-azido-1,2,4-triazoles are correlated with the σ_I and σ_C constants according to the equation $pK = \rho_I \sigma_I + \rho_C \sigma_C + pK_0$. The high ρ_I values in both cases are due to the closeness of the substituent to the reaction center. The ρ_C / ρ_I ratio attests to different contributions of the inductive and mesomeric effects of a substituent during transmission of its effect from the 5-position to the N_1 and N_4 heteroatoms.

It has been shown [1-3] that the acidities of 1,2,4-triazoles correlate with the Hammett σ_M constants. In order to compile data on the acid–base properties and ascertain the transmission of substituent effects we determined the acidity (pK_a) and basicity (pK_{BH^+}) constants of a number of 3(5)-azido-1,2,4-triazoles.

The first ionization constant of 3-azido-5-carboxy-1,2,4-triazole (VII) is related to the carboxyl group, while the second is related to the ring NH group. This follows from a comparison of the pK_a values of 3-azido-5-carbomethoxy- and 1-methyl-3-azido-5-carboxy-1,2,4-triazoles (VIII and XVII, Table 1). If primary ionization of acid VII were to occur at the imino group, the pK_{a1} value would be considerably larger.

It is known that organic azides decompose rapidly after protonation by mineral acids [4]. However, the azidotriazoles proved to be stable in acidic media and did not change even at 90° in 95% sulfuric acid. This fact attests to the addition of the proton to the ring heteroatom rather than to the azido group.

It might be assumed that the protonation of azidotriazoles (which we studied by UV and PMR spectroscopy) is described by the Brönsted scheme $B + H^+ \underset{K_{BH^+}}{\rightleftarrows} BH^+$, where B is the azidotriazole. Considering the proportionality of the acidity scales [5] ($H_X = mH_0$), the K_{BH^+} value can be found from the equations

$$pK'_{BH^+} = mH_0 + \lg \frac{BH^+}{B}, \tag{1}$$

$$pK_{BH^+} = \frac{pK'_{BH^+}}{m}. \tag{2}$$

In our investigation by PMR spectroscopy we measured the chemical shift of the C−H protons or of the functional group with respect to a standard as a function of the acidity of the medium. The pK_{BH^+} value for II was determined by both methods, and there was good agreement in the results; this makes it possible to compare the results of the determinations of the pK_{BH^+} values of the entire series of investigated compounds (Table 1).

The slopes (m) in formula (1) differ little from unity (Table 1), and all of the investigated azidotriazoles are consequently Hammett bases. Upon examination of the data obtained, one's attention is drawn first of all to the high sensitivity of the pK_a and pK_{BH^+} values to the effect of a substituent. A comparison of the pK_a and pK_{BH^+} values with the polar substituent constants demonstrated the distinct correlation of the pK_a values with the σ_M constants (the σ values were taken from [6-8]):

$$pK_a = -7.99\sigma_M + 9.58 \quad (R = 0.995:\ n = 8:\ S = 0.25).$$

TABLE 1. pK_a^* and pK_{BH^+} Values of 3(5)-Azido-1,2,4-triazoles

Compound	Name	pK_{a_1}	pK_{a_2}	pK_{BH^+}	m	Method	λ_{anal}, nm
I	3-Azido-1,2,4-triazole	9,37	—	−0,24	1,00	PMR	—
II	3-Azido-5-methyl-1,2,4-triazole	10,31	—	+0,25	1,07	PMR	—
				+0,30	0,97	UV	230
III	3-Azido-5-ethyl-1,2,4-triazole	10,47	—	−0,02	1,07	PMR	—
IV	3-Azido-5-phenyl-1,2,4-triazole	9,23	—	−0,36	1,01	UV	262; 280
V	3-Azido-5-(3¹-nitrophenyl)-1,2,4-triazole	7,81	—	−1,00	1,18	UV	262; 280
VI	3-Azido-5-(4¹-nitrophenyl)-1,2,4-triazole	7,56	—	−1,23	1,01	UV	280; 290
VII	3-Azido-5-carboxy-1,2,4-triazole	3,51	9,96	—	—	--	—
VIII	3-Azido-5-carbomethoxy-1,2,4-triazole	6,66	—	−2,82	1,03	PMR	—
IX	3-Azido-5-carbethoxy-1,2,4-triazole	6,65	—	—	—	—	—
X	3-Azido-5-carbopropoxy-1,2,4-triazole	6,85	—	—	—	—	—
XI	3-Azido-5-bromo-1,2,4-triazole	6,52	—	−2,83	1,03	UV	235
XII	3-Azido-5-nitro-1,2,4-triazole	3,85	—	−7,14	0,94	UV	225
XIII	3,5-Diazido-1,2,4-triazole	7,59	—	−1,86	1,01	UV	245
XIV	Bis(3,3¹-diazido-1,2,4-triazol-5-yl	6,87	10,26	−4,53	1,00	UV	250; 255
XV	Bis(3,3¹-diazido-1,2,4-triazol-5-yl)methane	8,20	10,53	—	—	—	—
XVI	1,2-Bis(3,3¹-diazido-1,2,4-triazol-5-yl)ethane	9,16	10,70	—	—	—	—
XVII	1-Methyl-3-azido-5-carboxyl-1,2,4-triazole	3,01	—	—	—	—	—
XVIII	1-Methyl-3-azido-1,2,4-triazole	—	—	−0,54	0,99	PMR	—
XIX	1-Methyl-5-azido-1,2,4-triazole	—	—	−0,70	1,00	PMR	—
XX	3-Azido-4-methyl-1,2,4-triazole	—	—	−0,36	1,16	PMR	—
XXI	1-Methyl-3-azido-5-carbomethoxy-1,2,4-triazole	—	—	−2,93	0,94	PMR	—
XXII	1-Methyl-3-carbomethoxy-5-azido-1 2,4-triazole	—	—	−2,46	0,97	PMR	—
XXIII	1-Methyl-3-nitro-5-azido-1,2,4-triazole	—	—	−6,52	1,06	PMR	—

*Determined at 20°C in aqueous 60% ethanol, except for XVII, for which the pK_a in water was determined.

The correlation between the pK_a values and the σ_I and σ_p constants is somewhat poorer. The correlation of the pK_{BH^+} values with the σ_M, σ_I, and σ_p constants proved to be only approximate. This could be a consequence of the different contributions of the inductive and resonance effects of the substituents in the α position with respect to the reaction center [9-11]. In order to make quantitative allowance for the contribution of the inductive and resonance effects, we made a correlation of the pK_a and pK_{BH^+} values with respect to the modified Hammett—Taft equation

$$pK = \rho_I\sigma_I + \rho_C\sigma_C + pK_o, \text{where } \sigma_C = \sigma_{para} - \sigma_I.$$

The correlation equations have the form

$$pK_a = -7.96\sigma_I - 3.88\sigma_C + 9.50 \quad (R=0.997; \ S=0.14; \ n=10),$$
$$pK_{BH^+} = -8.10\sigma_I - 5.37\sigma_C - 0.43 \quad (R=0.980; \ S=0.43; \ n=8).$$

In both cases, $\rho_I > \rho_C$, which indicates the predominant contribution of the inductive effect. The high and close ρ_I values are due to the closeness of the substituent to the reaction center (N_1 for acid dissociation, and N_4 for protonation). The fact serves as a confirmation of protonation of the azidotriazoles at the N_4 heteroatom adjacent to the substituent. The high ρ values are characteristic for a number of azoles and azines during transmission to the reaction center of the effect of a substituent in the α position relative to the heteroatom [9]. It follows from the correlation equations that the effects of a substituent in the 5-position on the N_1 and N_4 reaction centers are of different character because of the different contributions of the inductive and resonance effects. In acid dissociation, $\rho_C/\rho_I = 0.49$, which is in agreement with Charton's conclusions regarding the possibility of the correlation of such systems with the use of the σ_M constants. The ρ_C/ρ_I ratio is larger for protonation (0.67).

Thus, in the case of azidotriazoles the contribution of the resonance effect during transmission of an effect to heteroatom N_4 is greater than during transmission to N_1. This may be a consequence of the non-uniformity of the ring bonds and the higher multiplicity of the N_4–C_5 bond as compared with the N_1–C_5 bond. The results of quantum-chemical calculations of 1,2,4-triazole derivatives [12] make this assumption completely likely.

EXPERIMENTAL

The 3(5)-azido-1,2,4-triazoles were obtained by known methods [13, 14].

Potentiometric titration was carried out with an LPM-60M pH-meter by the standard method; the pK_a values were calculated with allowance for the hydroxide ion concentration [15]. The sulfuric acid solutions were prepared by dilution of ultrapure-grade H_2SO_4 with twice-distilled water, and their concentrations were determined to an accuracy of $\pm 0.1\%$ by potentiometric titration.

The azidotriazole concentrations in sulfuric acid were $\sim 1 \cdot 10^{-5}$ M in the UV method and ~ 2-$5 \cdot 10^{-2}$ M in the PMR method. The UV spectra were recorded with an SF-16 spectrophotometer at 25°. The PMR spectra were recorded with a Perkin-Elmer P-12 spectrometer (60 MHz) at 40° with tetramethylammonium bromide as the internal standard. The H_0 values at 40° were taken from [16]. The H_0 value at the half-protonation point was found by a graphical method from the dependence of the extinction coefficients (ε) or the chemical shifts (δ) on H_0, while the $\varepsilon (\delta)$ values located at ± 1.5 H_0 units from the half-protonation point were taken for the $\varepsilon_B (\delta_B)$ and $\varepsilon_{BH^+} (\delta_{BH^+})$ values [17]. These values were used for the calculation of the ionization ratios:

$$\frac{BH^+}{B} = \frac{\varepsilon_B - \varepsilon}{\varepsilon - \varepsilon_{BH^+}} \text{ (UV)}, \quad \frac{BH^+}{B} = \frac{\delta_B - \delta}{\delta - \delta_{BH^+}} \text{ (PMR)}.$$

The parameters of Eq. (1) were then calculated by the method of least squares in the interval of ± 1 H_0 unit, after which the pK_{BH^+} values were calculated from formula (2). The error in the determination of the pK_a values was ± 0.03 pK unit, while the error in the determination of the pK_{BH^+} values was ± 0.1 pK unit.

The correlation equations were derived by the method of multiple correlation [18].

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