

PROTONATION OF POLYACID ORGANIC BASES. VI.*
 SUBSTITUTION INFLUENCE
 ON IONIZATION PROPERTIES
 OF 5-SUBSTITUTED 1,3-DIAMINOBENZENES

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Thermodynamic ionization constants of unsubstituted and 5-substituted 1,3-diaminobenzenes have been measured in water at 25°C. The first and the second dissociations follow the Hammett equation $\text{p}K_a = K_a^0 + \rho r_m$ the constants of which have been computed. The found value of the reaction constant agree with that found by Biggs and Robinson for 3- and 4-substituted anilines

Few authors only have studied the dissociation properties of 1,3-diaminobenzenes so far. Ionization constants of the parent compound were determined by Willi¹ by means of potentiometric method: $\text{p}K_1$ 5.11 and $\text{p}K_2$ 2.50 at 25°C. Further authors²⁻⁵ determined these constants under different conditions. Of the substituted compounds, only 2,6-dihydroxy and 2-hydroxy derivatives were studied⁶.

The addition of protons to the 1,3-diaminobenzene molecule can proceed in two steps giving mono and diacid conjugated acids respectively (Scheme 1), the mono-protonated forms *II* and *III* of the unsubstituted and 5-substituted derivatives being equivalent because of symmetrical position of substituents with respect to the reaction centres. Tautomeric constant K_T will, therefore, equal unity in this case, and the partial constants of the individual protonation steps will be mutually equal.

The effective and partial ionization constants are then bound by relationships (1) and (2).

$$K_{\text{eff}}^{\text{BH}^+} = \frac{1}{2}K_{5,1}^{\text{BH}^+} = \frac{1}{2}K_{5,3}^{\text{BH}^+}, \quad (1)$$

$$K_{\text{eff}}^{\text{BH}_2^{2+}} = 2K_{5,1}^{\text{BH}_2^{2+}} = 2K_{5,3}^{\text{BH}_2^{2+}}. \quad (2)$$

If we express the values of partial ionization constants by the basic form of the Hammett equation, we can write the relationships (3) and (4).

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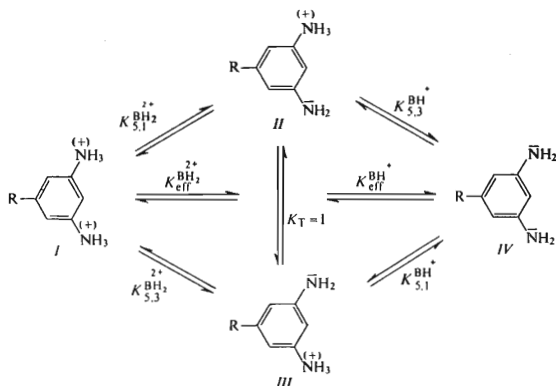
$$\log K_{5,1}^{\text{BH}^+} = \log K_{5,3}^{\text{BH}^+} = \log K_{\text{H}}^{\text{BH}^+} + \rho\sigma^0, \quad (3)$$

$$\log K_{5,1}^{\text{BH}_2^{2+}} = \log K_{5,3}^{\text{BH}_2^{2+}} = \log K_{\text{H}}^{\text{BH}_2^{2+}} + \rho'\sigma_m, \quad (4)$$

where $K_{\text{H}}^{\text{BH}^+} = 2K_0^{\text{BH}^+}$ and $K_{\text{H}}^{\text{BH}_2^{2+}} = \frac{1}{2}K_0^{\text{BH}_2^{2+}}$ (K_0 are the effective ionization constants of the unsubstituted compound). After introducing into the logarithmic forms of equations (1) and (2), we obtain two linear relationships (5) and (6) for values of effective ionization constants of the both conjugated acids.

$$\log K_{\text{eff}}^{\text{BH}^+} = \log K_0^{\text{BH}^+} + \rho\sigma_m, \quad (5)$$

$$\log K_{\text{eff}}^{\text{BH}_2^{2+}} = \log K_0^{\text{BH}_2^{2+}} + \rho'\sigma_m. \quad (6)$$



SCHEME 1

The values ρ and ρ' which are valid for expression of the effective and partial ionization constants can be found by solving the linear regression of the effective ionization constants with the Hammett substitution constants. By subtraction of the equation (5) and (6) we obtain equation (7).

$$\log K_{\text{eff}}^{\text{BH}^+} - \log K_{\text{eff}}^{\text{BH}_2^{2+}} = \log K_0^{\text{BH}^+} - \log K_0^{\text{BH}_2^{2+}} + \sigma_m(\rho - \rho'). \quad (7)$$

Especially interesting term is the last one which expresses the difference in influencing of the reaction centre by a constant substituent, in this concrete case the difference in influencing of the amonium nitrogen by amino nitrogen or the second amonium nitrogen.

The aim of this report is to find the ionization constants of a series of 5-substituted 1,3-diaminobenzenes and to examine the validity of the abovementioned relationships.

EXPERIMENTAL AND RESULTS

Substances Studied

Most of the compounds used are described in literature and their preparation was reproduced (for references see Table I). Commercial sample of 1,3-diaminobenzene hydrochloride was used after three crystallizations from 20% hydrochloric acid. 5-Chloro- and 5-bromo-1,3-diaminobenzene and 3,5-diamino-N,N-diethylbenzenesulfonamide were prepared by the Béchamps reduction of the respective dinitro derivatives⁷⁻¹⁰ using iron powder and diluted hydrochloric

TABLE I

List of the Compounds Studied

R Form	M.p., °C ^a	Calculated/Found			Ref.
		% C	% H	% N	
H	240 ^b	39.80	5.56	15.47	—
HCl		40.07	5.50	15.52	
CH ₃	158—160 ^c	68.82	8.25	22.93	13
Base		68.70	8.15	22.76	
OCH ₃	240 ^b	39.83	5.73	13.27	14
HCl		40.11	5.72	13.50	
OC ₂ H ₅	240 ^b	42.68	6.27	12.44	15
HCl		42.91	6.31	12.76	
F	260 ^b	36.20	4.56	14.07	16
HCl		36.21	4.90	14.23	
Cl	260 ^b	33.44	4.21	13.00	—
HCl		33.76	4.04	13.24	
Br	260 ^b	27.72	3.49	10.78	—
HCl		28.06	3.33	10.90	
CON(C ₂ H ₅) ₂	260 ^b	46.49	6.74	14.79	—
HCl		46.73	6.65	14.90	
COCH ₃	135—136	63.98	6.71	18.65	17
Base		63.65	6.58	18.43	
COOH	242—243	55.26	5.30	18.41	18
Base		54.99	5.19	18.36	
SO ₂ N(C ₂ H ₅) ₂	300 ^b	38.59	4.53	13.50	—
HCl		38.73	4.37	13.69	
COOC ₂ H ₅	85.5—86.5	59.99	6.71	15.55	19
Base		59.84	6.53	15.12	
CN	194—196	63.14	5.30	31.56	—
Base		62.87	5.01	31.32	
NO ₂	141—141.5	47.06	4.61	27.44	20
Base		46.93	4.60	27.36	

^a Melting points were determined with the use of a Koffler apparatus; ^b decomposition; ^c boiling point at 12 Torr.

acid. The products were isolated as hydrochlorides. 3,5-Diaminobenzonitril was obtained by reduction of 3-nitro-5-aminobenzonitril¹¹ according to Béchamps.

The substances isolated as hydrochlorides were purified by repeated crystallizations from 20% hydrochloric acid. In the cases when the respective bases were isolated, the purification was carried out by recrystallization from ethanol. Purity of the compounds was checked by paper chromatography (Whatman No 3, 1-butanol-hydrochloric acid-water 4:1:3, detection by means of the Ehrlich reagent). The substances and their elemental analyses are summarized in Table I.

Determination of Ionization Constants

The ionization constants were determined by spectrophotometric method using the recording spectrophotometer Unicam SP 800 B and universal spectrophotometer Zeiss VSU-1. The measurements were carried out in water solutions at $25 \pm 0.1^\circ\text{C}$. pH Values of buffered solutions of the substances were measured at the same temperature using OP-201 pH-meter (Orion, Budapest) and glass and saturated calomel electrodes. With respect to a relatively high symmetry of the compounds studied, their electronic spectra show only small changes with the proton concentration change, so that the extinction values of monoprotinated forms are inaccessible by direct measurement (Fig. 1). Therefore, a method of Albert and Serjeant¹² for determination of near ionization constants was modified and adopted.

The basic equations for determination of the equilibrium constants of individual ionization

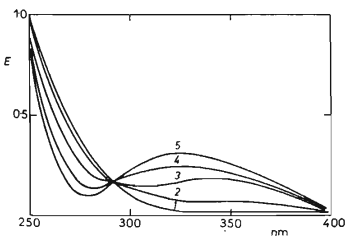


FIG. 1

Electronic Spectra of 5-Nitro-1,3-diaminobenzene

1 2M-HCl; 2 0.1M-HCl; 3 pH = 3.2; 4 pH = 4.3; 5 0.01M-NaOH. Concentration $1.021 \cdot 10^{-4}$ mol/l; 10 mm cell.

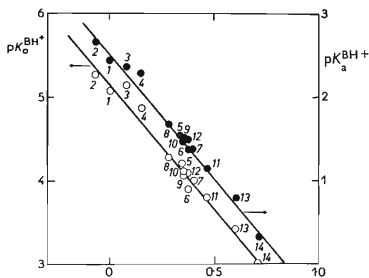


FIG. 2

Correlation of Effective Values of Ionization Constants of 5-R-1,3-diaminobenzenes with the Hammett Substituent Constants

R = 1 H; 2 CH₃; 3 OCH₃; 4 OC₂H₅; 5 F; 6 Cl; 7 Br; 8 CON(C₂H₅)₂; 9 COCH₃; 10 COOH; 11 SO₂N(C₂H₅)₂; 12 CO₂C₂H₅; 13 CN; 14 NO₂.

steps were transformed to (8) and (9).

$$E = E_{\text{BH}^+} + \frac{K_{\text{eff}}^{\text{BH}^+}}{[\text{H}^+]} (E_{\text{B}} - E), \quad (8)$$

$$E' = E_{\text{BH}^+} + \frac{[\text{H}^+]}{K_{\text{eff}}^{\text{BH}_2^{2+}}} (E' - E_{\text{BH}_2^{2+}}). \quad (9)$$

Graphical representation of these relationships in the coordinates (E ; $1/[\text{H}^+] (E_{\text{B}} - E)$) for (8) or (E' ; $[\text{H}^+] (E' - E_{\text{BH}_2^{2+}})$) for Eq. (9) gave the values of the intercept E_{BH^+} (the extinction of the monoprotonated form) which were used in the usual way for ionization constants calculation. The second possibility of the calculation of ionization constants consisted in working up the Eq. (8) and (9) by the least squares method and finding the angular coefficients $K_{\text{eff}}^{\text{BH}^+}$ for Eq. (8) and $1/K_{\text{eff}}^{\text{BH}_2^{2+}}$ for Eq. (9). Photometric measurements were carried out in the range of the main absorption bands at the wavelengths giving the maximum extinction differences in the spectra of the bases and their diprotonated forms. The values of ionization constants were corrected with respect to the influence of ionic strength of the medium using the Debye-Hückel relationship. The results are given in Table II.

DISCUSSION

The found values of ionization constants of mono- and diprotonated forms are linearly dependent on the Hammett substituent constant σ_m (see Fig. 2). The following relationships were found by the least squares method using 12 members of the series (methoxy and ethoxy derivatives were not involved):

$$K_{\text{eff}}^{\text{BH}^+} = 5.099 - 2.848\sigma_m,$$

$$S_{x,y} = \pm 0.051 \quad r = -0.996 \quad s_p = \pm 0.045,$$

$$K_{\text{eff}}^{\text{BH}_2^{2+}} = 2.501 - 2.914\sigma_m,$$

$$S_{x,y} = \pm 0.047 \quad r = -0.997 \quad s_p = \pm 0.041,$$

The angular coefficients of the both relationships are the same (within the experimental error) as it corresponds to the action of a substituent on the dissociation of ammonium group in *meta*-position. In addition to it, their value is practically coincident with that of the reaction constant of dissociation of anilines given by Biggs and Robinson²⁴ (2.889).

The results found thus confirm that the investigated series of 5-substituted 1,3-diaminobenzenes behave during dissociation of mono- and diacid conjugated acids in such a way that the both centres dissociate without any significant mutual influence (the difference $\rho - \rho' = 0.066$) and without any greater reverse influence of the substituents. The small mutual influence of the reaction centres can also be

TABLE II

Thermodynamic Ionization Constants of the 5-Substituted 1,3-Diaminobenzenes in Water at 25°C and Values of the Substitution Constants Used for the Regression Analysis

No	R	$K_{\text{eff}}^{\text{BH}^+}$	$K_{\text{eff}}^{\text{BH}_2^{2+}}$	σ_m^b
1	H	5.09 ± 0.02 ^d	2.47 ± 0.01 ^a	0
2	CH ₃	5.28 ± 0.02	2.67 ± 0.02	-0.07
3	OCH ₃	5.16 ± 0.02	2.40 ± 0.02	0.08
4	OC ₂ H ₅	4.87 ± 0.01	2.31 ± 0.01	0.150 ^c
5	F	4.21 ± 0.01	1.54 ± 0.02	0.34
6	Cl	4.10 ± 0.01	1.39 ± 0.02	0.37
7	Br	4.01 ± 0.02	1.38 ± 0.01	0.39
8	CON(C ₂ H ₅) ₂	4.29 ± 0.02	1.68 ± 0.01	0.280 ^d
9	COCH ₃	4.12 ± 0.01	1.50 ± 0.02	0.35
10	COOH	4.09 ± 0.01	1.47 ± 0.02	0.355 ^c
11	SO ₂ N(C ₂ H ₅) ₂	3.79 ± 0.02	1.16 ± 0.02	0.46 ^d
12	COOC ₂ H ₅	3.91 ± 0.02	1.50 ± 0.02	0.37
13	CN	3.43 ± 0.01	0.79 ± 0.01	0.60
14	NO ₂	3.02 ± 0.02	0.33 ± 0.02	0.71

^a The literature gives 5.11 and 2.50 (ref.¹); ^b see ref.²¹; ^c see ref.²²; ^d values given for amides in ref.²³ were used.

demonstrated by comparing the differences of the first and second ionization constants of the three isomeric diaminobenzenes. Whereas in the case of 1,3-diaminobenzene the difference between $\text{p}K_{\text{a}}^{\text{BH}^+}$ and $\text{p}K_{\text{a}}^{\text{BH}_2^{2+}}$ is 2.62 $\text{p}K_{\text{a}}$ units (5.09 - 2.47; see Table II), the corresponding difference (for unsubstituted compounds only because there is no linear dependence between $\text{p}K_{\text{eff}}$ and substituent constants there) has a value 3.80 (4.47 - 0.67; ref.^{25,26}) for 1,2-diaminobenzene and 3.27 (6.16 - 2.89; ref.²⁷) for 1,4-diaminobenzene. If we admit that the difference 3.27 $\text{p}K_{\text{a}}$ units in the case of 1,4-diaminobenzene is entirely due to the resonance influence of the ammonium group on the amino group protonating in the second step, then the increase to the value 3.80 in the case of 1,2-diaminobenzene represents the resonance influence, the influence of hydrogen bond, and eventually field effect. The difference between 3.27 and 2.62 for 1,4- and 1,3-diaminobenzenes respectively can then be considered to be a difference between the resonance and inductive effect of the ammonium group. The alkoxy derivatives represent an exception to the excellent linear dependence of $\text{p}K_{\text{a}}$ values on substituent constants; of course, their deviation from the regression lines can hardly be ascribed to the influence of the reaction centre on the substituent (resonance participation of the oxygen free electron pairs). More likely, a partial protonation of alkoxy oxygen can be considered which is, of course, contradicted by a smaller increase in $\text{p}K_{\text{a}}^{\text{BH}_2^{2+}}$ value of the ethoxy derivative. The spectral behaviour of the

both abovementioned derivatives does not allow us to formulate any concrete conclusion, and it must even be taken into account that the substituent constants values used are not suitable enough in this case.

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