

BASICITY OF SYMMETRICAL 2-SUBSTITUTED 4,6-DIAMINOTRIAZINES

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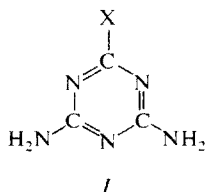
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Dissociation constants of some 2-substituted 4,6-diaminotriazines have been measured potentiometrically. The studied compounds underwent neutralization as triacid bases, their first and second protonation taking place probably at the triazine ring nitrogen atoms.

Acid-base properties of diamino- and triaminotriazines have not yet been studied systematically. These polyacid bases were studied only in a simplified way as monoacid bases using photometrical^{1,2} and potentiometric methods³⁻⁵.

The aim of this work was a potentiometric study of basicity of symmetrical 2-substituted 4,6-diaminotriazines of general formula *I* where X = —CH₃ (*I*), —CH₂C₆H₅ (*II*), —H (*III*), —C₆H₅ (*IV*), —OCH₃ (*V*), furyl (*VI*), —OC₆H₅ (*VII*). Basicity of symmetrical 2,4,6-trimethoxytriazine (*VIII*) was measured, too.

The compounds *I* to *VII* were considered to be pentaacid bases, the compound *VIII* was considered a triacid base. All the nitrogen atoms were considered *a priori* to be basicity centres. The non-simplified equation of titration curve was used for the calculation.



EXPERIMENTAL

Reagents

2,4-Diaminotriazine was prepared by reaction of dicyandiamide with formamide⁶. After sublimation at 220°C and two crystallizations from water the substance melted at 327–331°C (ref.⁶ 323°C). For C₃H₅N₅ (111·1) calculated: 32·40% C, 4·53% H, 63·20% N; found: 31·83% C, 4·50% H, 62·97% N. 2,4-Diamino-6-alkyl(aryl)triazines were prepared by heating of the mixture of dicyandiamide, the respective acid nitrile and piperidine at 190–200°C for 4 to 5 hours⁷. Crystallization from ethanol or water gave the following compounds: 2,4-diamino-6-methyltriazine,

m.p. 265°C (ref.⁷ 263°C); 2,4-diamino-6-phenyltriazine, m.p. 227–228°C (ref.⁷ 222°C); 2,4-diamino-6-benzyltriazine, m.p. 239–241°C (ref.⁷ 232°C); 2,4-diamino-6-furyltriazine, m.p. 251 to 254°C (ref.⁷ 248–250°C). 2,4-Diamino-6-methoxytriazine was prepared by reaction of 2,4-diamino-6-chlorotriazine with sodium methoxide⁸. Three crystallizations from dioxane gave the substance melting at 237–238°C (ref.⁸ 238°C). 2,4-Diamino-6-phenoxytriazine was prepared by reaction of 2,4-diamino-6-chlorotriazine with phenol and sodium hydroxide⁹. After three crystallizations from *n*-butanol the substance melted at 259–262°C (ref.⁹ 255–258°C). 2,4,6-Trimethoxytriazine was prepared by reaction of cyanuric chloride with sodium methoxide⁸. After five crystallizations from water the substance melted at 132–134°C (ref.⁸ 134–136°C).

Purity of the 2-substituted 4,6-diaminotriazines was checked by paper chromatography, using propanol–25% aqueous ammonia (2 : 1) as eluent¹⁰. The spots were made visible by spraying the chromatogram with ethanolic mercury(II) acetate (0.25 g mercury(II) acetate in 100 ml ethanol + 2 drops of acetic acid), drying, spraying with 0.05% diphenylcarbazole solution, and heating at 130°C in a drying oven for 4 to 5 minutes. The compounds studied contained only traces of impurities (Table I).

Measurements of Dissociation Constants

All the measurements were carried out in a stream of pure nitrogen at 25°C in a jacketed beaker connected to an ultrathermostat. The pH measurements were carried out with a PHM-64 apparatus (Radiometer) using a glass G 202 B and a calomel K-401 electrodes. The apparatus was calibrated with the buffers pH 4.01 and 6.98 (Ústav sér a očkovacích látek, Prague). Redistilled water and chemicals of *p.a.* purity grade were used throughout. All the measurements were carried out at constant ionic strength $I = 0.2$ (KCl).

50 ml of about 10^{-3} M solution of the base neutralized with five (three in the case of 2,4,6-trimethoxytriazine) equivalents of hydrochloric acid was titrated with 0.02M-NaOH (prepared from carbonate-free sodium hydroxide). The titration curve was plotted in a graph and evaluated with the use of a Hewlett-Packard 9100 A calculator.

Derivation of Titration Curve Equation

Concept of a *n*-acid base $B(OH)_n$ was used, the constants K_1, K_2, \dots, K_n denoting the dissociation of the first, the second *etc.* hydroxyl. From the basic conditions, *i.e.* expression of dissociation constants, the constant of autoprotolysis of water, concentration condition, and condition of electroneutrality we derived the equation (*I*) of the titration curve of a *n*-acid base hydrochloride with standard sodium hydroxide solution. The equation involves the volume change

TABLE I
Paper Chromatography of 2-Substituted 4,6-Diaminotriazines

Compound	I ^a	II ^a	III ^a	IV ^a	V	VI	VII
R_F	0.70	0.90	0.57	0.90	0.80	0.80	0.92
Colour	blue	violet	blue	violet	violet	violet	violet

^a Trace of blue impurity, R_F 0.32.

due to dilution. In all the cases we considered only the concentrations

$$v = V(Hc_0Z - K_w + H^2 - Hnc_0)/(K_w - H^2 - Hc_{Na}), \quad (1)$$

where the symbols v , V , K_w , n , c_0 , c_{Na} , H , and Z stand for the added volume of titration reagent (NaOH), the total volume at the beginning, ionic product of water ($K_w = 1.007 \cdot 10^{-14}$ at 25°C), number of the basic centres in the base, concentration of the base hydrochloride at the beginning of titration, concentration of the titration reagent, concentration of H^+ ions, and the fraction involving the influence of dissociation constants on the titration curve, respectively. The quantity Z is given by Eqs (2) and (3) for a triacid and a pentaacid bases, respectively.

$$Z = (HK_w^2K_1 + 2H^2K_wK_1K_2 + 3H^3K_1K_2K_3) / (K_w^3 + HK_w^2K_1 + H^2K_wK_1K_2 + H^3K_1K_2K_3), \quad (2)$$

$$Z = \frac{HK_w^4K_1 + 2H^2K_w^3 \prod_{j=1}^2 K_j + 3H^3K_w^2 \prod_{j=1}^3 K_j + 4H^4K_w \prod_{j=1}^4 K_j + 5H^5 \prod_{j=1}^5 K_j}{K_w^5 + HK_w^4K_1 + H^2K_w^3 \prod_{j=1}^2 K_j + H^3K_w^2 \prod_{j=1}^3 K_j + H^4K_w \prod_{j=1}^4 K_j + H^5 \prod_{j=1}^5 K_j}. \quad (3)$$

Evaluation of Titration Curves

For the evaluation of titration curves we used the Hewlett-Packard calculator model 9100A connected with external memory 9101A and a recorder 9125A. The computer calculated automatically the volume of titration reagent according to Eq. (1) for the given pH, and it constructed directly in the recorder the theoretical calculated titration curve. The calculation was carried out by the steps of 0.01 pH unit from the given starting pH to the final pH for the given dissociation constants and given concentrations c_0 and c_{Na} . The given dissociation constants were varied until the theoretical calculated titration curve crossed the experimental points.

RESULTS AND DISCUSSION

When determining the dissociation constants of 2-substituted 4,6-diaminotriazines we presumed that there are five basicity centres at five nitrogen atoms in the molecule. From the electrochemical point of view the compounds were considered to be pentaacid bases. Titration curve of retitration of a n -acid base hydrochloride with sodium hydroxide is described by Eq. (1). In this equation the fraction Z plays the decisive part. *E.g.* for a pentaacid base having $pK_{b1} = 10.00$, $pK_{b2} = 11.00$, $pK_{b3} = 12.00$ and $pK_{b4} = pK_{b5} = 13.00$ the value Z is given by Eq. (4).

$$Z = \frac{H \cdot 10^{-66} + H^2 \cdot 2 \cdot 10^{-63} + 3H^3 \cdot 10^{-61} + 4H^4 \cdot 10^{-60} + 5H^5 \cdot 10^{-59}}{10^{-70} + H \cdot 10^{-66} + H^2 \cdot 10^{-63} + H^3 \cdot 10^{-61} + H^4 \cdot 10^{-60} + H^5 \cdot 10^{-59}}. \quad (4)$$

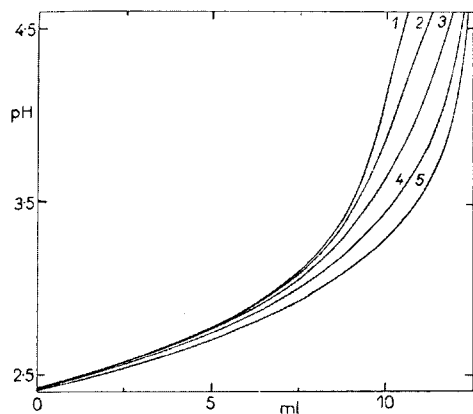


FIG. 1

Theoretically Calculated Titration Curves (ml 0.02M-NaOH) for Determination of pK_{b1} Value

1 pK_{b1} 9.00, 2 pK_{b1} 9.50, 3 pK_{b1} 10.00,
4 pK_{b1} 10.50, 5 pK_{b1} 11.00; pK_{b2} 12.00;
 $pK_{b3} = pK_{b4} = pK_{b5} = 13.00$.

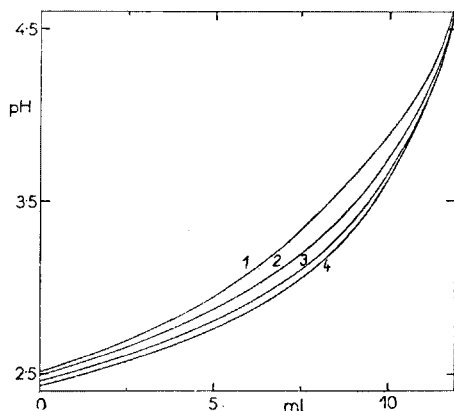


FIG. 2

Theoretically Calculated Titration Curves for pK_{b2} Determination

1 pK_{b2} 10.50, 2 pK_{b2} 11.00, 3 pK_{b2} 11.50, 4 pK_{b2} 12.00; pK_{b1} 10.00; $pK_{b3} = pK_{b4} = pK_{b5} = 13.00$.

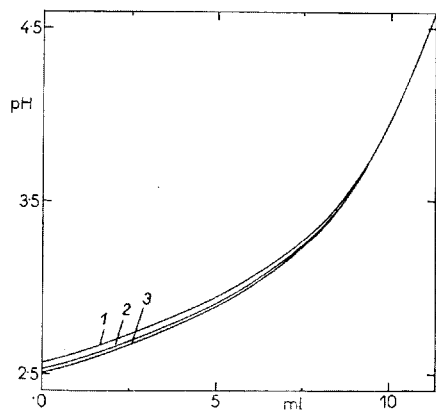


FIG. 3

Theoretically Calculated Titration Curves for pK_{b3} Determination

1 pK_{b3} 11.50, 2 pK_{b3} 12.00, 3 pK_{b3} 12.50; pK_{b1} 9.50; pK_{b2} 11.00; $pK_{b2} = pK_{b4} = 13.00$.

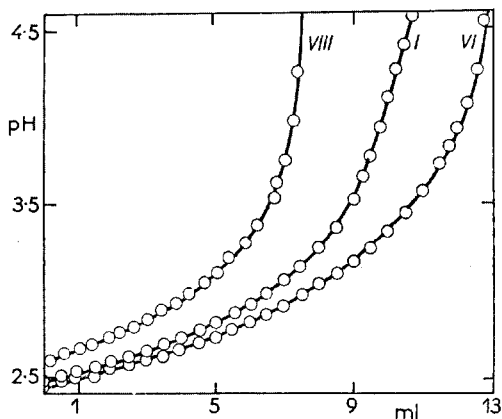


FIG. 4

Titration Curves for some of the Studied Compounds

○ Experimental points, lines theoretically calculated titration curves for the conditions given in Table II.

All the members of the equation are significant at pH 2 to 3, whereas at pH 3 to 4 the terms with H^5 can be neglected, and at pH 4 to 5 the terms with H^4 and H^5 can be neglected.

Figs 1 to 3 show the change of the titration curve shape with changing dissociation constant; they give the theoretically calculated curves of retitration of hydrochloride of a pentaacid base for various pK_b values. The values pK_{b1} , pK_{b2} and pK_{b3} were changed within the limits 9.00 to 11.00, 10.5 to 12.0 and 11.5 to 12.5, respectively. The constants pK_{b4} and pK_{b5} have no effect on the shape of the titration curve and, therefore, cannot be determined potentiometrically. In all the cases we used the value 13.00 for these constants. From Figs 1 to 3 it is obvious that the titration curve shape is affected chiefly by the value pK_{b1} , less by pK_{b2} , and slightly by the value pK_{b3} . It is impossible to distinguish the constants pK_{b4} and pK_{b5} with the given accuracy of the potentiometric pH measurements. Thereby the accuracy of determination of the individual constants is given, too.

Fig. 4 gives experimental points and the theoretically calculated titration curves (full line) for some bases. The calculated titration curves cross the experimental points very well, which demonstrates a good agreement of theory and experiment. The values of pK_{b1} , pK_{b2} and pK_{b3} could be determined with accuracy of 0.02, 0.1 and 0.3 pK units, respectively. The results are given in Table II. The pK_b values given in literature are also involved for comparison.

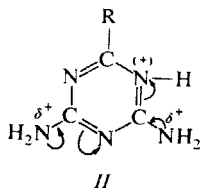
Thus the 2-substituted 4,6-diaminotriazines are triacid bases having the pK_{b1} , pK_{b2} and pK_{b3} values within the limits 9 to 11, 11.6 to 12 and 11.9 to 12.3, respectively. Although it can be presumed that basicity of amino groups in 2-substituted 4,6-diaminotriazines is weakened by the effect of triazine ring nitrogen atoms, the pK_{b1} values are comparable with the pK_b values of substituted anilines. Therefore we presume

TABLE II

Concentration Dissociation Constants of the 2-Substituted 4,6-Diaminotriazines at 25°C at I 0.2

Compound	$c_0 \cdot 10^3$	pK_{b1}	pK_{b2}	pK_{b3}	$pK_b^{ref.}$
<i>I</i>	1.0235	9.19	11.74	12.1	9.35(5)
<i>II</i>	0.9987	9.74	11.70	12.3	—
<i>III</i>	1.0692	9.82	11.64	12.0	9.50(2)
<i>IV</i>	0.9997	10.10	12.00	12.3	10.14(5)
<i>V</i>	1.0016	10.30	11.76	11.9	10.46(5)
<i>VI</i>	1.0842	10.46	11.92	12.1	—
<i>VII</i>	1.0790	10.92	11.82	12.1	11.22(5)
<i>VIII</i>	1.0161	11.70	>12.5	>12.5	—

that the first protonation does not take place at the amino groups but at 1- or 3-nitrogen atom of the triazine ring according to formula II. With respect to the induced positive charge at the amino groups after the first protonation it is probable that also



the second protonation will take place at one of the two remaining ring nitrogen atoms. Craig and Short¹¹ came to analogous conclusion in the case of protonation of 4-aminopyridine and similar compounds, and Brown with coworkers¹² measured the UV spectra of 2-aminopyrimidine and 4-aminopyrimidine cations with the same results. Substitution of amino groups by methoxy groups lowers the basicity of triazine ring nitrogens. In potentiometric titration 2,4,6-trimethoxytriazine appeared to be a monoacid base, being weaker than 2-methoxy-4,6-diaminotriazine by almost 1.5 pK units.

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