PROTONATION OF POLYACID ORGANIC BASES. V.*

IONIZATION CONSTANTS OF DIACID CONJUGATED ACIDS OF 4-SUBSTITUTED 1,2-DIAMINOBENZENES AND 6-SUBSTITUTED 2,3-DIMETHYLQUINOXALINES

P.VETEŠNÍK, J.KAVÁLEK and V.BERÁNEK

Department of Organic Chemistry,
Institute of Chemical Technology, Pardubice

Ionization constants of diprotonated forms of fourteen 4-substituted 1,2-diaminobenzenes and twelve 6-substituted 2,3-dimethylquinoxalines have been studied. Partial ionization constants have been calculated from experimental values $pK_a^{BH_2^{2+}}$ by the methods previously suggested. Now a new iterative calculation method has been suggested which optimizes the constants of empirical equations using the equations for both $pK_A^{BH^+}$ and $pK_a^{BH_2^{2+}}$. Tautomeric equilibrium constants have been computed for the system of monoacid conjugated acids from the partial ionization constants. This report confirms both the validity of model conception concerning the action of substituent effects in diacid systems and the posibility of the use of linear free energy relationships for solution of prototropic tautomerism problems.

In the previous reports[1-4] of this series we studied the dissociation of monoprotonated forms of diacid bases of the type of 4-substituted 1,2-diaminobenzenes and 6-substituted 2,3-dimethylquinoxalines. We tried to find relationships between structure, effective ionization constants and partial ionization constants of the individual basicity centres, and to determine approximatively the tautomeric constants for the equilibrium between the both possible monoacid conjugate acids. Diprotonated forms of the 6-substituted 2,3-dimethylquinoxalines described in the Part II (ref.[2]), of this series and diprotonated forms of the 4-substituted 1,2-diaminobenzenes of the Part IV (ref.[3]) are dealt with in this paper. The both series have been extended by the tert-butyl derivatives.

Diprotonated compounds of the type of quinoxaline and 1,2-diaminobenzene can splitt off any of the both protons (giving thus the respective monoacid conjugated acids) in such cases only when the molecular orbital symmetry is not disturbed by substitution. An unsymmetrical position of substituent, however, will change the readi-

---

* Part IV: This Journal **33**, 2902 (1968).

ness of the individual basic centres to splitt off the proton and hence the ratio of the tautomers formed according to the Eq. (1).

$$K_T = \frac{[II]}{[III]} = \frac{K_{ij}}{K_{rs}} = \frac{K'_{ij}}{K'_{rs}} . \qquad (1)$$

In the Part II (ref.[2]) of this series two methods were suggested for calculation of partial ionization constants and tautomeric equilibrium constant of the systems given, *viz.* method A and B. The both methods of calculation are based on the conception that the properties of diacid compounds can be represented as a superposition of properties of the respective monoacid models. According to the method A special substituent constants, σ^{spec}, are calculated using the monoacid models, and therefrom the values of partial ionization constants are computed using the modified Hammett equation. The reaction constants ϱ are modified in such a way that the optimum agreement of the calculated and experimental values of the effective ionization constants is obtained. The method B uses a more general procedure. The reaction constants ϱ and therefrom, as the first approximation, partial and effective ionization constants of diacid compounds are computed using the ionization constants of a series of monoacid models and conventional values of substituent constant. By comparing the calculated and experimental values of the effective ionization constants the values ϱ are modified and then used for computing the partial ionization and tautomeric constants. The both procedures given can be, in principle, applied even on the diprotonated forms of diacid bases.

Another possibility of solution of the whole dissociation process consists in the optimalization of constants of the Hammett-type linear relationships using the equilibrium constants of the first and second ionization (method C). Let us have a finite series of the compounds which dissociate according to a general Scheme 1; their. pK_{eff} and pK'_{eff} values are given with a mean error $\pm s$ and $\pm s'$ respectively Let us further have σ_1 and σ_2 values (*e.g.* σ_m and σ_p). We presume the validity of equations (2) to (5).

$$\log K_{ij} = \log K_H + \varrho_i \sigma_j , \qquad (2)$$

$$\log K_{rs} = \log K_H + \varrho_r \sigma_s , \qquad (3)$$

$$\log K'_{ij} = \log K'_H + \varrho'_i \sigma_j , \qquad (4)$$

$$\log K'_{rs} = \log K'_H + \varrho'_r \sigma_s . \qquad (5)$$

Our task is to find such ϱ_i, ϱ'_i, ϱ_r, ϱ'_r, K_H, and K'_H to obtain the optimum agreement of experimental values K_{eff} and K'_{eff} with the values calculated from the Eq. (6) and (7):

$$1/K_{eff} = 1/K_{ij} + 1/K_{rs} , \qquad (6)$$

$$K'_{eff} = K'_{ij} + K'_{rs} \qquad (7)$$

and, at the same time, the optimum fulfilment of the Eq. (8):

$$K_T = \frac{K_{ij}}{K_{rs}} = \frac{K'_{ij}}{K'_{rs}} = K'_T . \qquad (8)$$

A perfect agreement between the calculated and experimental values cannot be expected. The minimum value of the sum of weighted absolute values of deviations of experimental and calculated pK_{eff} and pK'_{eff} as well as pK_T and pK'_T (it would be possible to use also the minimum values of the sum of deviation squares) was chosen as a criterion of the "optimum" selection of eligible constants. The values fulfilling the condition (9) were thus considered to be optimum. The values K_T are not devoid
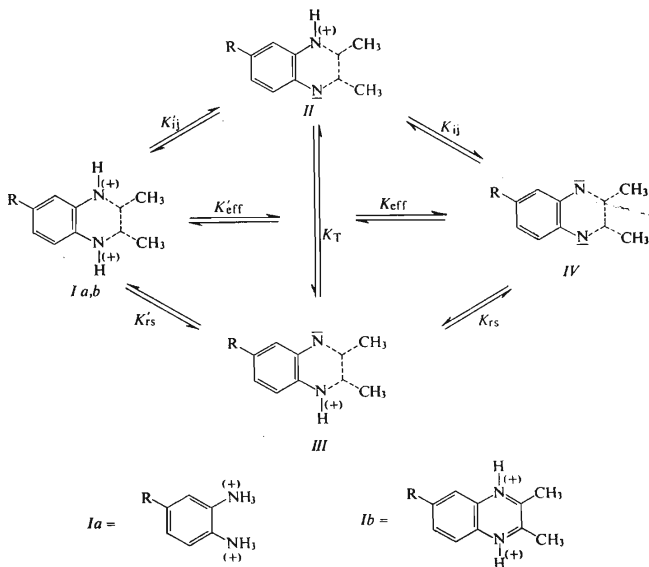
SCHEME 1

of errors, but their accuracy is not known. Therefore, for the purpose of calculation, the weight of this error was left as eligible (the value 0·01 was used for the practical calculation).

$$\sum\left[\left|\frac{(pK'_{eff})_c - (pK'_{eff})_e}{s'_{pK_{eff}}}\right| + \left|\frac{(pK_{eff})_c - (pK_{eff})_e}{s_{pK_{eff}}}\right|\right] + \frac{1}{s_{K_T}}\sum|pK'_T - pK_T| = \min. \quad (9)$$

From the mathematical point of view the problem consists in finding such a set of constants that the derived values calculated from them will minimalize a certain known expression. The solution was obtained on a most simple iterative way. Initial set of constants values and initial iteration circle were chosen. The value of the sum was calculated for the initial set of constants values, and in further iteration the individual constants were changed by the value of iteration circle in such a way that value of the sum decreased. After finding the minimum sum in the range of one iteration circle, *i.e.* finding such constants values that increasing or decreasing of any of them led to a sum increase, the value of iteration circle was diminished and the whole process repeated. The calculation was interrupted at the moment when the iteration circle reached a lower value than the required accuracy in the determination of constants. To speed up the convergency of the method, a better initial point was calculated in the moment of the diminishing of the iteration circle. The procedure can be represented using an example of one of the variables. At the moment of finding the local minimum within the given iteration circle the value of a function (the sum which is being minimalized) is known at this minimum and at two neighbouring points. The point in which the parabola crossing the abovementioned three known functional values reaches the minimum is then chosen as initial point for the further iteration circle. This procedure presumes that the real course of the function in the vicinity of the minimum is approximated by a parabola sufficiently well.

The aim of this work is to estimate the influence of substituents on the dissociation of the individual reaction centres of the diacid conjugated acids formed by addition of two protons to the respective bases by application of the methods *A* and *B* and with the use of the method *C* for the whole protonated system.

EXPERIMENTAL

4-tert-Butyl-1,2-diaminobenzene

A mixture of 30 g conc. sulphuric acid and 15 g nitric acid (*d* 1·4) was added to a solution of 19·2 g (0·1 mol) 4-acetylamino-tert-butylbenzene[5,6] in 50 ml conc. sulphuric acid at 0°C with stirring. The solution was stirred for another 1 hour and poured onto 0·5 kg crushed ice. The precipitated product was collected by suction, washed with water and dried. The obtained mixture of 3- and 2-nitro derivatives was hydrolyzed[7] and the hydrolysis product was isolated, dried, and chromatographically separated on an alumina column (Brockmann II; ∅ 5 cm, length 40 cm) using benzene with 5% ethyl acetate as eluent. After evaporation of fractions 5·11 g 2-nitro-4-amino-tert-butylbenzene and 11·60 g 3-nitro-4-amino-tert-butylbenzene, m.p. 105 to 106°C (Koffler) (30·6% and 39·8% respectively, calculated on 4-acetylamino-tert-butylbenzene) were obtained. R_F values of the 2- and 3-nitro derivatives were 0·5 and 0·2 or on an alumina thin layer using the abovementioned eluent.

3-Nitro-4-amino-tert-butyl-benzene was hydrogenated on a Raney-Urushibara nickel catalyst in ethanol at room temperature and atmospheric pressure. After filtration of the catalyst and evaporation of solvent, 4-tert-butyl-1,2-diaminobenzene was obtained quantitatively. It was resublimed at 0·2 Torr. m.p. 46—46·5°C. For $C_{10}H_{16}N_2$ (164·26) calculated: 73·12% C, 9·82% H, 17·06% N; found: 73·24% C, 9·66% H, 17·17% N.

6-tert-Butyl-2,3-dimethylquinoxaline

A mixture of 3·30 g (0·02 mol) 4-tert-butyl-1,2-diaminobenzene, 1·90 g (0·022 mol) biacetyl and 50 ml 96% ethanol were heated to boiling for 4 hours. The solvent was evaporated and the dry residue was resublimed at 1 Torr.; 2·65 g (84·4%) needles m.p. 56—59°C was obtained. Further three times repeated sublimation gave a product melting 59—59·5°C. For $C_{14}H_{18}N_2$ (214·3) calculated: 78·47% C, 8·46% H, 13·07% N; found: 78·39% C, 8·68% H, 13·16% N.

The Methods and Apparatus Used

The ionization constants were determined by the spectrophotometric method in aqueous sulphuric acid solutions at $25 \pm 0.1°C$. Informative spectral measurements were carried out on an Unicam SP 800 B apparatus, and the precise extinction measurements were on a Zeiss VSU-1 apparatus. The sulphuric acid concentration was determined by a potentiometric titration using an auto-titrator of the firm Orion Budapest. The acidity function H_+ described in the Part III (ref.[4]) of this series was used for calculations.

TABLE I

Ionization Constants $pK_a^{BH_2^{2+}}$ of Diacid Conjugated Acids of 4-Substituted 1,2-Diaminobenzenes and 6-Substituted 2,3-Dimethylquinoxalines in Water at 25°C

R	4-R-1,2-Diaminobenzenes	6-R-2,3-Dimethyl-quinoxalines
OCH_3	$0·76 \pm 0·03$	$-3·47 \pm 0·04$
OC_2H_5	$0·71 \pm 0·05$	$-3·76 \pm 0·05$
$(CH_3)_3C$	$1·16 \pm 0·02$	$-3·37 \pm 0·03$
CH_3	$0·98 \pm 0·01$	$-3·45 \pm 0·07$
H	$0·67 \pm 0·03$	$-3·84 \pm 0·07$
F	$-0·17 \pm 0·08$	$-4·16 \pm 0·06$
Cl	$-0·27 \pm 0·03$	$-4·21 \pm 0·05$
Br	$-0·27 \pm 0·05$	$-4·38 \pm 0·04$
I	$-0·30 \pm 0·03$	$-4·18 \pm 0·06$
COOH	$-1·26 \pm 0·05$	$-4·30 \pm 0·06$
$COCH_3$	$-1·58 \pm 0·03$	$-4·30 \pm 0·06$
SO_3H	$-1·26 \pm 0·05$	—
CN	$-2·07 \pm 0·05$	$-4·92 \pm 0·05$
NO_2	$-2·75 \pm 0·05$	$-5·02 \pm 0·03$

Themodynamic ionization constants of monoprotonated forms of the both compounds not previously studied were determined at $25 \pm 0.1°C$: $pK_a^{BH^+}$ was found to be 4.87 ± 0.01 and 2.36 ± 0.02 for 4-tert-butyl-1,2-diaminobenzene and 6-tert-butyl-2,3-dimethylquinoxaline respectively. The values of the ionization constants of diprotonated forms of the compounds studied are summarized in Table I.

The calculations of equilibrium systems for application of the method C were carried out on a computer National Eliot 803 B.

RESULTS AND DISCUSSION

A model of 4-substituted 1,2-diaminobenzenes can be obtained by a superposition of 4- and 3-substituted aniline molecules. The special substitution constants were calculated by applying the method A for $\varrho = 1$, and used in Eq. (4) and (5). The K_H constant was obtained form the Eq. (7) applied on the unsubstituted compounds for which $K'_{ij} = K'_{rs}$ (log $K_H = -0.98$). From the partial ionization constants K'_m and K'_p obtained (the former concerns the proton dissociation from m-amonium group with respect to the substituent, and the latter that from p-amonium group) the effective ionization constants were computed using Eq. (7). Fig. 1 where the calculated and experimental values of effective ionization constants are compared

FIG. 1

Correlation of the Experimental Constants $pK_{eff}^{BH_2^{2+}}$ of 4-Substituted 1,2-Diaminobenzenes with those Calculated in the First Approximation. Method A

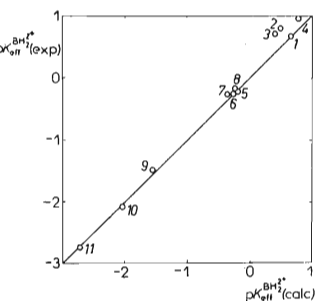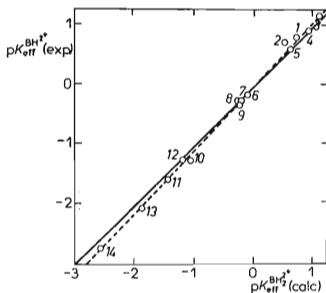*1* H; *2* OCH$_3$; *3* OC$_2$H$_5$; *4* CH$_3$; *5* F; *6* Cl; *7* Br; *8* J; *9* CH$_3$CO; *10* CN; *11* NO$_2$.

FIG. 2

Correlation of the Experimental Constants $pK_{eff}^{BH_2^{2+}}$ of 4-Substituted 1,2-Diaminobenzenes with those Calculated in the First Approximation. Method B

1 OCH$_3$; *2* OC$_2$H$_5$; *3* C(CH$_3$)$_3$; *4* CH$_3$; *5* H; *6* F; *7* Cl; *8* Br; *9* J; *10* COOH; *11* COCH$_3$; *12* SO$_3$H; *13* CN; *14* NO$_2$.

TABLE II

Calculated Values of Partial and Effective Ionization Constants of Diacid Conjugated Acids of 4-Substituted 1,2-Diaminobenzenes

Substituent	$pK_m^{BH_2^{2+}}$	$pK_p^{BH_2^{2+}}$	$pK_{eff}^{BH_2^{2+}}$	Δ^a
	Method A^b			
OCH_3	0·51	1·62	0·48	0·28
OC_2H_5	0·46	1·48	0·42	0·29
$(CH_3)_3C$	1·00	1·26	0·82	0·34
CH_3	1·01	1·36	0·85	0·13
H	0·97	0·97	0·67	0·00
F	−0·13	0·93	−0·17	0·00
Cl	−0·20	0·43	−0·29	0·02
Br	−0·14	0·14	−0·32	0·05
I	0·11	0·06	−0·23	−0·07
$COOH^c$	—	—	—	—
$COCH_3$	−0·16	−1·53	−1·55	−0·03
SO_3H	—	—	—	—
CN	−0·97	−1·98	−2·02	−0·05
NO_2	−1·25	−2·72	−2·74	−0·01
	Method B^d			
OCH_3	0·62	1·76	0·59	0·17
OC_2H_5	0·52	1·71	0·49	0·22
$(CH_3)_3C$	1·33	1·55	1·13	0·03
CH_3	1·26	1·47	1·05	−0·07
H	0·97	0·97	0·67	0·00
F	−0·05	0·79	−0·11	−0·06
Cl	−0·16	0·30	−0·29	0·02
Br	−0·22	0·29	−0·34	0·07
I	−0·10	0·16	−0·29	−0·01
COOH	−0·11	−1·17	−1·21	−0·05
$COCH_3$	0·14	−1·60	−1·61	0·03
SO_3H	−0·28	−1·29	−1·33	0·07
CN	−0·85	−1·97	−2·00	−0·07
NO_2	−1·19	−2·76	−2·77	0·02
	Method C^e			
OCH_3	0·67	1·72	0·64	0·12
OC_2H_5	0·58	1·67	0·55	0·16
$(CH_3)_3C$	1·29	1·53	1·09	0·07
CH_3	1·16	1·45	0·98	0
H	0·98	0·98	0·67	0
F	−0·08	0·80	−0·14	−0·03

Table II

(Continued)

Substituent	$pK_m^{BH_2^{2+}}$	$pK_p^{BH_2^{2+}}$	$pK_{eff}^{BH_2^{2+}}$	Δ^a
Cl	−0·02	0·34	−0·17	−0·10
Br	−0·06	0·33	−0·21	−0·06
I	−0·04	0·21	−0·24	0·06
COOH	−0·03	−1·06	−1·12	−0·14
COCH$_3$	0·16	−1·47	−1·48	−0·10
SO$_3$H	−0·11	−1·17	−1·21	−0·05
CN	−0·82	−1·84	−1·88	−0·09
NO$_2$	−0·91	−2·57	−2·58	−0·17

^{a} $\Delta = pK_{exp} - pK_{calc}$; ^{b} average absolute deviation 0·106; ^{c} no reliable value of pK_a for the model can be found in the literature; ^{d} reaction constants ϱ'_m 3·036, ϱ'_p 2·938; average absolute deviation 0·063; ^{e} reaction constants ϱ'_m 2·791, ϱ'_p 2·655; average absolute deviation = 0·082.

Table III

Values of Partial and Effective Ionization Constants of Monoacid Conjugated Acids of 4-Substituted 1,2-Diaminobenzenes

Substituent	$pK_m^{BH^+}$	$pK_p^{BH^+}$	$pK_{eff}^{BH^+}$	Δ^a
		Method C^b		
OCH$_3$	3·94	4·87	4·91	−0·08
OC$_2$H$_5$	3·86	4·82	4·87	−0·05
(CH$_3$)$_3$C	4·46	4·69	4·89	−0·02
CH$_3$	4·34	4·62	4·80	−0·12
H	4·19	4·19	4·49	−0·02
F	3·45	4·04	4·14	0·14
Cl	3·37	3·62	3·81	0·02
Br	3·33	3·61	3·79	−0·10
I	3·42	3·50	3·76	−0·08
COOH	3·41	2·36	3·45	0·04
COCH$_3$	3·52	1·99	3·53	0·03
SO$_3$H	3·29	2·26	3·33	−0·04
CN	2·70	1·65	2·93	0
NO$_2$	2·63	1·00	2·64	−0·03

^{a} $\Delta = pK_{exp} - pK_{calc}$ (for pK_{exp} see Part II of this series); ^{b} the found reaction constants: $\varrho_m = 2·514$, $\varrho_p = 2·205$ and value $pK_a^{BH^+} = 4·191$; average absolute deviation = 0·055.

shows that no corrections of the reaction constant are necessary. The results of calculations are summarized in Table II.

For the calculation according to the method B the series of 3- and 4-substituted anilines were used as models for computing ϱ_m' and ϱ_p' respectively. The values obtained ($\varrho_m' = +2\cdot883; \varrho_p' = +2\cdot791$) were used in the basic equations (4), (5) and (7), and the first approximations of $pK_{calc}^{BH_2^{2+}}$ obtained were correlated with experimental values. From the Fig. 2 it is obvious that the models do not give a quite true picture of the behaviour of the compound series studied, and that the reaction constants need a correcture 1 : 1·053. The Table II shows the calculation results of the partial and effective ionization constants after this correcture. The agreement with the experiment is better than in the method A, and the deviations are comparable with the value of experimental error. A greater deviation is encountered with the compounds carrying positive substituents which obviously suggest a partial protonation of the substituent.

Application of the method C was based on the overall reaction Scheme 1. By an iteration method a system of general equations was solved into which the experimental values $pK^{BH_2^{2+}}$, pK^{BH^+} were introduced as independent variables together with the conventional values of substituent constants σ (ref.[8]). The Tables II and III show

FIG. 3

Correlation of the Experimental Constants $pK_{eff}^{BH_2^{2+}}$ of the 6-Substituted 2,3-Dimethyl-quinoxalines with those Calculated in the First Approximation. Method A
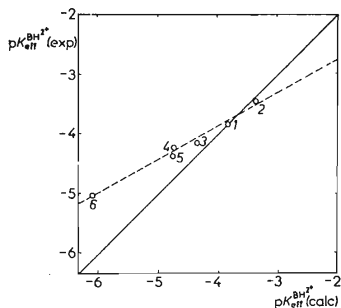
1 H; *2* CH$_3$; *3* F; *4* Cl; *5* Br; *6* NO$_2$.
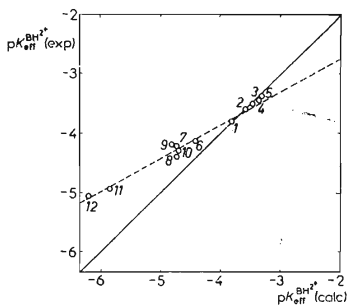
FIG. 4

Correlation of the Experimental Constants $pK_{eff}^{BH_2^{2+}}$ of the 6-Substituted 2,3-Dimethyl-quinoxalines with those Calculated in the First Approximation. Method B

1 H; *2* OC$_2$H$_5$; *3* OCH$_3$; *4* CH$_3$; *5* C(CH$_3$)$_3$; *6* F; *7* Cl; *8* Br; *9* J; *10* COOH; *11* CN; *12* NO$_2$.

TABLE IV

Calculated Values of Partial and Effective Ionization Constants of Diacid Conjugated Acids of 6-Substituted 2,3-Dimethylquinoxalines

Substituent	$pK_{1,6}^{BH_2^{2+}}$	$pK_{4,6}^{BH_2^{2+}}$	$pK_{eff}^{BH_2^{2+}}$	Δ^a
		Method A^b		
CH_3	$-3 \cdot 27$	$-3 \cdot 20$	$-3 \cdot 54$	$-0 \cdot 09$
H	$-3 \cdot 50$	$-3 \cdot 50$	$-3 \cdot 80$	$-0 \cdot 04$
F	$-3 \cdot 78$	$-3 \cdot 78$	$-4 \cdot 08$	$-0 \cdot 08$
Cl	$-3 \cdot 96$	$-4 \cdot 04$	$-4 \cdot 30$	$0 \cdot 09$
Br	$-4 \cdot 01$	$-4 \cdot 03$	$-4 \cdot 32$	$-0 \cdot 06$
NO_2	$-4 \cdot 69$	$-4 \cdot 87$	$-5 \cdot 09$	$0 \cdot 07$
		Method B^c		
CH_3O	$-3 \cdot 35$	$-3 \cdot 21$	$-3 \cdot 59$	$0 \cdot 12$
C_2H_5O	$-3 \cdot 42$	$-3 \cdot 29$	$-3 \cdot 66$	$0 \cdot 10$
CH_3	$-3 \cdot 41$	$-3 \cdot 33$	$-3 \cdot 63$	$0 \cdot 23$
$(CH_3)_3C$	$-3 \cdot 26$	$-3 \cdot 16$	$-3 \cdot 51$	$0 \cdot 14$
H	$-3 \cdot 50$	$-3 \cdot 50$	$-3 \cdot 80$	$-0 \cdot 04$
F	$-3 \cdot 81$	$-3 \cdot 80$	$-4 \cdot 11$	$0 \cdot 05$
Cl	$-3 \cdot 97$	$-4 \cdot 03$	$-4 \cdot 30$	$0 \cdot 09$
Br	$-3 \cdot 99$	$-4 \cdot 04$	$-4 \cdot 32$	$-0 \cdot 06$
I	$-4 \cdot 00$	$-4 \cdot 07$	$-4 \cdot 34$	$0 \cdot 16$
CO_0H	$-3 \cdot 99$	$-4 \cdot 07$	$-4 \cdot 33$	$0 \cdot 03$
CN	$-4 \cdot 51$	$-4 \cdot 71$	$-4 \cdot 92$	0
NO_2	$-4 \cdot 70$	$-4 \cdot 94$	$-5 \cdot 14$	$0 \cdot 12$
		Method C^d		
CH_3O	$-3 \cdot 38$	$-3 \cdot 21$	$-3 \cdot 60$	$0 \cdot 13$
C_2H_5O	$-3 \cdot 42$	$-3 \cdot 25$	$-3 \cdot 64$	$-0 \cdot 12$
CH_3	$-3 \cdot 31$	$-3 \cdot 22$	$-3 \cdot 57$	$0 \cdot 11$
$(CH_3)_3C$	$-3 \cdot 25$	$-3 \cdot 15$	$-3 \cdot 50$	$0 \cdot 13$
H	$-3 \cdot 51$	$-3 \cdot 51$	$-3 \cdot 81$	$-0 \cdot 03$
F	$-3 \cdot 82$	$-3 \cdot 83$	$-4 \cdot 13$	$-0 \cdot 03$
Cl	$-3 \cdot 99$	$-4 \cdot 09$	$-4 \cdot 34$	$0 \cdot 13$
Br	$-4 \cdot 00$	$-4 \cdot 11$	$-4 \cdot 38$	0
I	$-3 \cdot 93$	$-4 \cdot 01$	$-4 \cdot 27$	$0 \cdot 09$
COOH	$-4 \cdot 00$	$-4 \cdot 13$	$-4 \cdot 37$	$0 \cdot 07$
CN	$-4 \cdot 51$	$-4 \cdot 85$	$-5 \cdot 01$	$0 \cdot 09$
NO_2	$-4 \cdot 60$	$-4 \cdot 99$	$-5 \cdot 04$	$0 \cdot 02$

[a] $\Delta = pK_{exp} - pK_{calc}$; [b] reaction constant ϱ' 0·57; $pK_H^{BH_2^{2+}}$ 3·50; average absolute deviation 0·072; [c] reaction constants: ϱ_1' 0·803; ϱ_2' 0·808; ϱ_3' 0·683; ϱ_4' 1·240; $pK_H^{BH_2^{2+}}$ −3·50; average absolute deviation 0·10; [d] reaction constants: ϱ_1' 0·790; ϱ_2' 0·815; ϱ_3' 0·702; ϱ_4' 1·402; $pK_H^{BH_2^{2+}}$ 3·51; average absolute deviation 0·08.

the results of this way of solution. The average absolute deviation is comparable with experimental error, as it was in the case of the method B. The greater deviations encountered with positively substituted compounds also confirm that the supposition of a partial protonation outside the reaction centre is justified, especially so in higher proton concentration ranges where the determination of ionization constants of diacid conjugated acids was carried out.

The problem of ionization of diacid conjugated acids of 6-substituted 2,3-dimethylquinoxalines was solved with the use of all the three abovementioned methods again. The Jaffé equations for bicyclic systems[9] of model substances of the type of 6- and 7-substituted quinoline derivatives were considered as correlation relationships. Using the method A, the special substituent constants were calculated for $\varrho = 1$. The correlation of calculated and experimental values of effective ionization constants graphically represented in Fig. 3 shows that the models used have not precisely the same properties as the 2,3-dimethylquinoxaline system under investigation. The reaction constant must be changed to 1 : 0·570. The calculations results are summarized in Table IV.

When applying the method B, the first approximations of reaction constants ϱ'_1 to ϱ'_4 were computed by regression analysis for 6- and 7-substituted quinolines. The

TABLE V

Values of Partial and Effective Ionization Constants of Monoacid Conjugated Acids of 6-Substituted 2,3-Dimethylquinoxalines

Substituent	$pK_{1,6}^{BH^+}$	$pK_{4,6}^{BH^+}$	$pK_{eff}^{BH^+}$	Δ^a	
		Method C^b			
CH_3O	2·02	2·23	2·44	0·01	
C_2H_5O	1·95	2·11	2·34	0·14	
CH_3	2·14	2·24	2·49	−0·08	
$(CH_3)_3C$	2·24	2·36	2·60	−0·24	
H	1·82	1·82	2·12	−0·04	
F	1·29	1·31	1·60	−0·12	
Cl	1·02	0·93	1·28	0·01	
Br	0·99	0·90	1·25	−0·03	
J	1·11	1·05	1·38	−0·04	
COOH	0·99	0·88	1·24	−0·19	
CN	0·15	−0·21	0·31	0·10	
NO_2	−0·16	−0·57	−0·02	0·09	

^{a} $\Delta = pK_{exp} - pK_{calc}$; ^{b} the found values of reaction constants: $\varrho_1 = 1·340$; ϱ_2 1·318; ϱ_3 1·142; $\varrho_4 = 2·028$; the average absolute deviation = 0·09.

TABLE VI

Content of the Tautomeric Form *II* in the Equilibrium Mixture of Monoacid Conjugated Acids of 4-Substituted 1,2-Diaminobenzenes

Substituent	Method *A* and *B* %	Method *C* %
OCH_3	9·9 ± 3·3	9·3 ± 1·7
OC_2H_5	10·2 ± 3·7	8·7 ± 1·7
$(CH_3)_3C$	39·1 ± 5·9	36·8 ± 0·4
CH_3	31·9 ± 6·5	34·1 ± 0·3
H	50·0 ± 0·0	50·0 ± 0·0
F	13·4 ± 4·2	15·8 ± 6·6
Cl	25·2 ± 4·9	33·2 ± 3·9
Br	30·7 ± 6·7	31·7 ± 3·8
J	39·4 ± 3·2	40·7 ± 6·7
COOH	89·1 ± 4·3	91·7 ± 0·2
$COCH_3$	94·8 ± 2·9	96·2 ± 1·2
SO_3H	88·1 ± 4·2	91·7 ± 0·4
CN	89·1 ± 3·6	91·6 ± 0·4
NO_2	95·1 ± 2·3	97·8 ± 0·1
Average standard deviation:	±*4·0*%	±*1·9*%

TABLE VII

Content of the Tautomeric Form *II* in the Equilibrium Mixture of Monoacid Conjugated Acids of 6-Substituted 2,3-Dimethylquinoxalines

Substituent	Method *A* and *B* %	Method *C* %
OCH_3	60·2 ± 3·1	60·8 ± 1·8
OC_2H_5	59·6 ± 3·1	60·4 ± 1·8
$(CH_3)_3C$	56·3 ± 0·8	59·4 ± 4·0
CH_3	55·3 ± 1·2	55·5 ± 0·9
H	50·0 ± 0·0	60·0 ± 0·0
F	50·4 ± 0·5	50·5 ± 1·2
Cl	46·4 ± 1·5	44·6 ± 0·5
Br	46·3 ± 0·4	44·7 ± 0·6
J	46·3 ± 0·4	46·2 ± 0·6
COOH	40·7 ± 6·7	43·1 ± 0·3
CN	34·5 ± 5·8	31·2 ± 0·4
NO_2	34·6 ± 5·2	28·1 ± 0·9
Average standard deviation:	±*2·4*%	±*1·1*%

values found $\left(\varrho_1' = +1\cdot417,\ \varrho_2' = +1\cdot408,\ \varrho_3' = +1\cdot199,\ \varrho_4' = +2\cdot176\right)$ gave the first approximation of $pK_{calc}^{BH_2^{2+}}$ which were compared with experiments in Fig. 4. It is obvious that the same phenomenon is encountered here as in the method A (cf. Fig. 3); to obtain an agreement between experimental and calculated values, we had to change the reaction constants $1 : 0\cdot57$. After this correcture calculated values of the partial and effective ionization constants and their deviations from experimental values are summarized in Table IV.

According to the method C, the whole system based on the Scheme 1 was solved by computer as in the case of 4-substituted 1,2-diaminobenzenes. The Hammett constants σ_m and σ_p and the experimental ionization constants of mono- and diacid conjugated acids were used as independent variables. The Jaffé three-parameter equation was used as the basic relathionship for describing the partial ionization constants, so that the task of the computer consisted in finding such eight constants ϱ_1 to ϱ_4 and ϱ_1' to ϱ_4' and such $pK_H^{BH^+}$ and $pK_H^{BH_2^{2+}}$ values that the leading relationships were fulfilled with the minimum error. Deviations of calculated and experimental values of effective ionization constants and deviations of the tautomeric equilibrium constans computed from the side of either monoacid or diacid conjugated acids were thus minimalized. The Tables IV and V show that the deviations of experimental and calculated values of the effective ionization constants are comparable to the experimental errors. Reaction constants also agree well with the values obtained by the model procedure B.

In the equilibrium systems of monoacid conjugated acids of 4-substituted 1,2-diaminobenzenes and 6-substituted 2,3-dimethylquinoxalines the values of tautomeric constant K_T is given by the ratio of the respective partial ionization constants. From the equation (1) the expressions (10) and (11) can be calculated for contents of individual monoacid tautomeric acids:

$$II = 100/(1 + K_T)\ \% ,\qquad (10)$$

$$III = 100K_T/(1 + K_T)\ \% . \qquad (11)$$

Here, II represents the tautomeric form having the proton on the m-nitrogen with respect to the substituent whereas III stands for the p-nitrogen protonated tautomer.

As the abovementioned calculations fulfil the basic condition of agreement between calculated and found values of the effective ionization constants to such an extent, as it could be expected on the basis of the calculation methods used, it is possible to determine the composition of the tautomeric mixtures. The calculations were carried out in the both series of compounds separately from the partial ionization constants of the monoacid and diacid conjugated acids, and then the average values and deviations were determined. The method C afforded the results directly. The composition of the tautomeric mixtures is shown in Tables VI and VII.

The results show that the quinoxalines are generally less sensitive towards the substituent effects ($\varrho'_1 = +0.790$, $\varrho'_2 = +0.185$, $\varrho'_3 = +0.702$, $\varrho'_4 = +1.402$) whereas 1,2-phenylenediamines do not substantially differ from anilines in their sensitivity towards substitution ($\varrho'_m = +3.036$, $\varrho'_p = +2.938$). A closer examination, however, shows that the quinoxaline series behave substantially differently from 1,2-phenylenediamines as far as the addition and splitting off of the proton are concerned. The values of the reaction constants show that in the case of 1,2-phenylenediamines the substituent effect is transferred to the basicity centre in the *para*-position more easily than in the *meta*-position. In the case of 2,3-dimethylquinoxalines, however, the connection of the basic centres by an ethylenic bridge causes an inversion of the sensibilities. The 4-nitrogen becomes more sensitive to the effect of substituent which stands *meta* to it. The reason is in that the nitrogens are involved in an alternating system of the heterocyclic chain. The abovementioned phenomena influence in turn the relative proportion of tautomeric forms of monoacid conjugated acids. The Tables VI and VII show that the change from electron-donor to electron-acceptor substituents causes an increase in the content of the 4-substituted 1,2-diaminobenzenes protonated on the basicity centre in *meta*-position to the substituent whereas in the case of 6-substituted 2,3-dimethylquinoxalines the content of the respective form decreases.

The relative success of all the three procedures and especially the agreement between the model methods of solution and the purely mathematical procedure shows above all a close connection between the monoacid models and polyacid aromatic bases. The Hammett constants valid for model substances can be used, after a simple modification, for more complex tautomeric systems. The correlation methods suggested can obviously be used more widely and allow to determine the content of tautomers in mixtures of the polyacid based protonated in various ways, thus extending the range of applicability of linear free energy relationships.

REFERENCES

1. Vetešník P.: This Journal 33, 556 (1968).
2. Vetešník P., Kaválek J., Beránek V., Exner O.: This Journal 33, 566 (1968).
3. Vetešník P., Bielavský J., Kaválek J., Večeřa M.: This Journal 33, 2902 (1968).
4. Vetešník P., Bielavský J., Večeřa M.: This Journal 33, 1687 (1968).
5. Craig D.: J. Am. Chem. Soc. 57, 196 (1935).
6. Senkowski M.: Ber. 23, 2412 (1890).
7. Gelzer C.: Ber. 20, 3253 (1887).
8. Exner O.: Chem. listy 53, 1302 (1959).
9. Jaffé H. H.: J. Am. Chem. Soc. 76, 4261 (1954).