The Thermodynamic Proton–Ligand Stability Constants of Some *p*-Substituted *N*-*m*-Chlorophenylbenzohydroxamic Acids in Dioxane–Water

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The thermodynamic proton–ligand stability constants of *p*-substituted *N*-*m*-chlorophenylbenzohydroxamic acids in aqueous dioxane media are determined at 25 and 35 °C. The thermodynamic parameters are calculated. The pK_a varies linearly with the mol fraction of dioxane. The constants were correlated with the Hammett equation and rate of alkaline hydrolysis. The effect of substitution on the ionization and rate constant is discussed.

In recent years many hydroxamic acids have been synthesized and their ionization constants determined.[1–3] The ionization constants in particular are essential for metal–ligand stability constants and provide knowledge of the selectivity and sensitivity of relevant analytical reactions. With this view, in the present investigation the thermodynamic proton–ligand stability constants of *p*-substituted *N*-*m*-chlorophenylbenzohydroxamic acids have been determined in dioxane–water media at 25 and 35 °C by the pH titration method using glass and saturated calomel electrodes. The details of the method and calculations *etc.* are essentially the same as described by Agrawal.[3]

Experimental

Chemicals.—All the chemicals used were of AnalaR and G.R. grades (B.D.H. and E. Merck, respectively) unless otherwise specified. Dioxane was purified by the method of Weissberger.[4] Carbonate-free KOH was prepared by the electrolytic method of Vogel.[5] A 2% $FeCl_3$ solution was prepared in 0.01M-hydrochloric acid. The hydroxamic acids were synthesized by a method described elsewhere.[6,7] They were recrystallized before use from benzene–light petroleum and dried in vacuum over P_2O_5. Their purity was checked by m.p., i.r., and u.v. spectra.

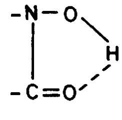
Apparatus.—A Radiometer pH meter model pHM 84 equipped with a combined glass and calomel electrode was used for the pH measurements. A Carl Zeiss Jena VSU 2P spectrophotometer was used for kinetic measurements.

Determination of Ionization Constants.—The titration procedure for determining ionization constants was essentially that given by Agrawal.[8] In a titration vessel (thermostatted at 25 and 35 ± 0.1 °C) 0.01M-hydroxamic acid in 47.5 cm^3 of the solvent of desired composition was titrated, without addition of inert salt (ionic strength not adjusted), with 0.5 cm^3 increments of 0.1M-KOH, after being deaerated by passage of nitrogen (presaturated with solvent) for 15 min, the highest steady B value (pH meter reading) being noted for each increment.

Determination of Rate Constants.—Into a thermostatted (25 °C) cylindrical flask (50 cm^3), 10 cm^3 of each solution of 0.01M-hydroxamic acid in dioxane and 0.10M-potassium hydroxide were added. Aliquot portions (1 cm^3) of this mixture were withdrawn at regular 30 min intervals and then complexed with $FeCl_3$ solution (2 cm^3; 2% v/v). The complex was then diluted to 25 cm^3 with distilled water and dioxane to attain finally 1:1 dioxane–water.

Results and Discussion

The thermodynamic proton–ligand stability constants of *p*-substituted *N*-*m*-chlorophenylbenzohydroxamic acids are given in Table 1. These acids are very weak but stronger than phenols, and their acidity has been attributed essentially to the OH group. The decrease in the acid character may be due to intramolecular hydrogen bonding (I) which has been proved by i.r. spectroscopic studies.[9–11]



(I)

When the pK_a of *p*-substituted *N*-*m*-chlorophenylbenzohydroxamic acids are plotted against $1/D$, distinct curvature is observed.[8] It seems evident that ion electrostatic factors exert a considerable influence on the dissociation of hydroxamic acids.

Agrawal *et al.* observed that the pK_a of hydroxamic acids increases with the increase in mol fraction of dioxane (n_2).[8,12–17] This is because a solvent of low dielectric constant increases the electrostatic forces between the ions and thereby facilitates the formation of molecular species. The pK_a values of hydroxamic acids studied here are plotted against the mol fraction of dioxane, and a linear relationship is observed (Figure 1). The experimental values of pK_a for almost all hydroxamic acids indicate a maximum deviation of 0.05 or *ca.* 0.5% in pK_a from linearity. Linear equations between pK_a and n_2 and respective correlation coefficients r, given in Table 2, have been calculated by the method of least squares. Interpolation of pK_a by these equations is more convenient than by the graphs, while the accuracy is almost of the same order.

The pK_a at lower mol fraction of dioxane ($n_2 < 0.083$) could not be determined as the acids are insoluble.

In the present investigation the pK_a values have been determined with a precision of ±0.02—0.04 and hence the error in ΔG° is estimated to be between ±0.13 and 0.21 kJ mol^{-1}. The temperature coefficient method used here for the computation of ΔH° is subject to large error because (i) the enthalpy change involved in acid ionization is small, and (ii) the pK_a values at a series of temperatures are not determined, which otherwise would have enabled the adoption of the more precise graphical method[18] for its evaluation. It is apparent (Table 1) that an error of 0.01 in pK_a causes an error of 1.76 kJ mol^{-1} in ΔH° while the magnitude of error in pK_a depends upon cancellation or addition of errors of individual sets of pK_a determined at two temperatures. In view of this inherent weakness of the method,

Table 1. Thermodynamic proton–ligand stability constants, pK_a, ΔS°, and ΔH° values of *p*-substituted *N*-*m*-chlorophenylbenzohydroxamic acids in dioxane–water media at 25 and 35 °C

			Mol fraction of dioxane, n_2					
			n_2 0.083		n_2 0.174		n_2 0.240	
Compound	*p*-Substituent		25 °C	35 °C	25 °C	35 °C	25 °C	35 °C
(1)	C_2H_5O	pK_a	10.15	10.00	11.04	10.90	11.70	11.54
		$-\Delta S^\circ$	105.81	105.85	128.82	128.78	129.66	129.62
		ΔH°	26.36		24.68		28.03	
(2)	CH_3O	pK_a	9.98	9.80	10.90	10.72	11.56	11.38
		$-\Delta S^\circ$	84.89	84.81	87.69	102.46	105.18	106.73
		ΔH°	31.79		31.79		31.79	
(3)	CH_3	pK_a	9.78	9.64	10.70	10.54	11.36	11.17
		$-\Delta S^\circ$	104.68	104.64	110.41	110.45	105.35	105.47
		ΔH°	24.68		26.36		33.47	
(4)	H	pK_a	9.60	9.46	10.51	10.36	11.16	11.00
		$-\Delta S^\circ$	101.17	101.25	112.67	112.63	119.28	119.28
		ΔH°	24.68		26.36		28.03	
(5)	F	pK_a	9.44	9.26	10.38	10.19	11.04	10.86
		$-\Delta S^\circ$	74.47	74.51	86.56	86.56	105.22	105.18
		ΔH°	31.79		33.47		31.79	
(6)	Cl	pK_a	9.26	9.07	10.20	10.00	10.86	10.70
		$-\Delta S^\circ$	65.27	65.14	77.32	77.36	113.51	113.47
		ΔH°	33.47		35.14		28.03	
(7)	Br	pK_a	9.30	9.14	10.24	10.12	10.90	10.71
		$-\Delta S^\circ$	83.59	83.59	125.14	125.26	96.52	96.60
		ΔH°	28.03		20.92		33.47	
(8)	NO_2	pK_a	9.12	8.93	10.04	9.83	10.71	10.50
		$-\Delta S^\circ$	62.42	62.55	68.32	68.40	81.25	81.17
		ΔH°	33.47		36.82		36.82	

* ΔS° Is in J mol^{-1} K^{-1} and $-\Delta H^\circ$ in kJ mol^{-1}.

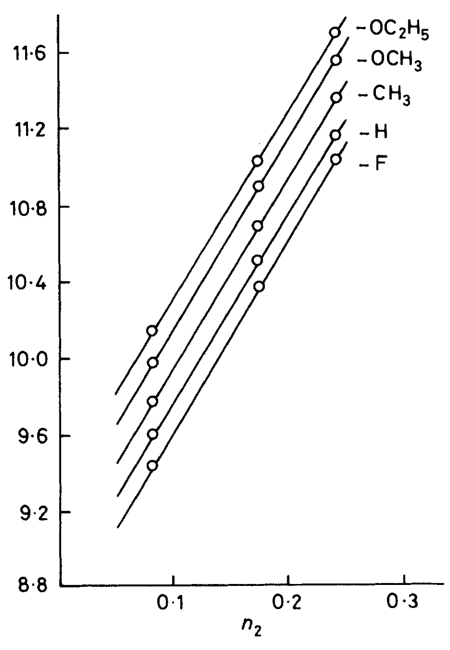


Figure 1. Variation of pK_a with mol fraction of dioxane n_2, at 25 °C

no definite trends in the magnitudes of the values of ΔH° with change of media could be observed. This is illustrated by the data given in Table 1.

In any case, the positive value of ΔH° found in all solvent media and for all hydroxamic acids has a real significance; it implies that the ionization process at 25 °C is endothermic.

Table 2. Empirical relation between pK_a and mol fraction of dioxane (n_2)

	pK_a (25 °C) = $mn_2 + C$			pK_a (35 °C) = $mn_2 + C$		
Compd.	*m*	*c*	*r*	*m*	*c*	*r*
(1)	9.86	9.33	0.999	9.82	9.19	1.000
(2)	10.06	9.14	0.999	10.07	8.96	1.000
(3)	10.10	8.94	0.999	9.76	8.83	1.000
(4)	9.94	8.78	0.099	10.00	8.62	0.999
(5)	10.19	8.60	0.999	10.20	8.41	1.000
(6)	10.20	8.42	1.000	10.36	8.21	1.000
(7)	10.19	8.46	0.999	10.05	8.32	0.999
(8)	10.12	8.28	0.999	10.00	8.09	1.000

Further, it is certain that the magnitude of change in ΔH° with change in media is relatively small and is within the range of experimental error. It is because of this that the slopes of the straight lines in the plots of pK_a *versus* n_2 are either the same or nearly the same at the two temperatures for individual hydroxamic acids (Table 2). In other words, the two lines are parallel.

It is observed that there is a general tendency to increase the magnitude of ΔS° with an increase in dioxane content of the solvent medium. If the acid ionizes in two media the free energy change for the transfer reaction from one medium to another is given by $2.303RT$pK_a. With *N*-*m*-chlorophenyl-*p*-methoxybenzohydroxamic acid, ΔG° (n_2 0.083) and ΔG° (0.240) = 56.99 and 66.02 kJ mol^{-1}, respectively, and ΔG° change 10.92 kJ

$$HA_{(diox)} + H^+_{(aq)} + A^-_{(aq)} \rightleftharpoons HA_{(aq)} + H^+_{(diox)} + A^-_{(diox)} \qquad (1)$$

mol^{-1} in the transfer reaction (1) and this is essentially due to a change of 30.29 J K^{-1} mol^{-1} in ΔS°.

Table 3. Thermodynamic pK_a of *p*-substituted *N*-*m*-chlorophenylbenzohydroxamic acids in 30% (v/v) dioxane–water medium at 25 °C and Hammett applicability

Compound	pK_a expt.	σ	pK_a^i Hammett	pK_a^j Least squares	pK_a Benzoic acid
(2)	9.98	−0.268	9.98	9.98	4.47
(3)	9.78	−0.170	9.84	9.79	4.34
(4)	9.60				4.21
(5)	9.44	+0.062	9.51	9.49	4.14
(6)	9.26	+0.227	9.28	9.27	3.99
(7)	9.30	+0.232	9.28	9.29	4.00

$^i\rho = 1.4$, $^j{}_{\mathrm{p}K_a} = 1.50x + 3.28$.

Table 4. Applicability of Hammett equation in dioxane–water media at 25 and 35 °C

Dioxane percentage	n_2	25 °C			35 °C		
		ρ	*m*	*c*	ρ	*m*	*c*
30	0.083	1.40	1.50	3.28	1.40	1.53	3.00
50	0.174	1.26	1.42	4.56	1.26	1.40	4.50
60	0.240	1.26	1.42	5.22	1.26	1.54	4.51

Table 5. First-order rate constants for alkaline hydrolysis of *p*-substituted *N*-*m*-chlorophenylbenzohydroxamic acids in 1:1 (v/v) dioxane–water at 25 °C

Compound	Rate constant *k*/min^{-1}
(1)	2.9×10^{-3}
(2)	3.1×10^{-3}
(3)	3.3×10^{-3}
(4)	5.5×10^{-3}
(5)	5.7×10^{-3}
(6)	8.6×10^{-3}
(7)	8.7×10^{-3}
(8)	10.8×10^{-3}

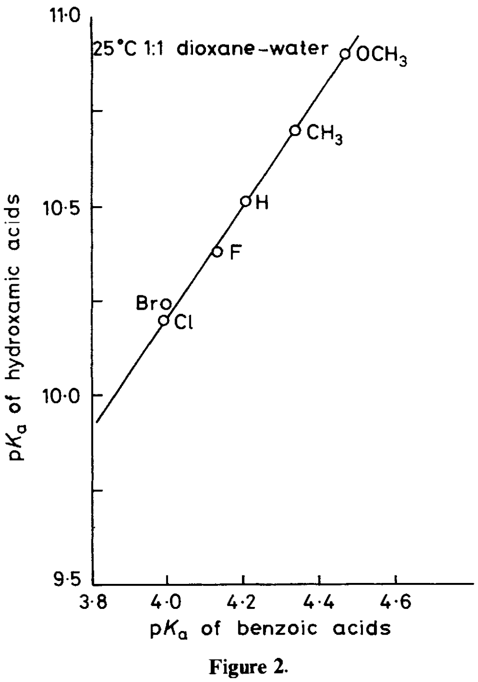


Figure 2.

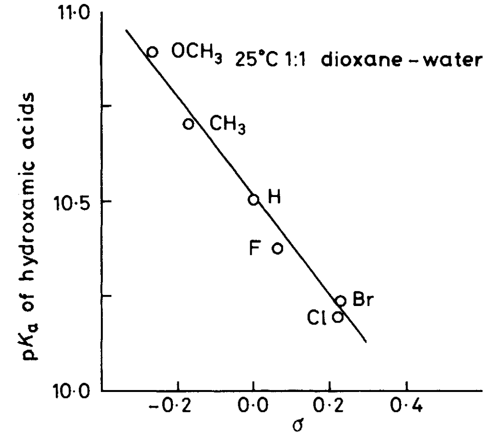
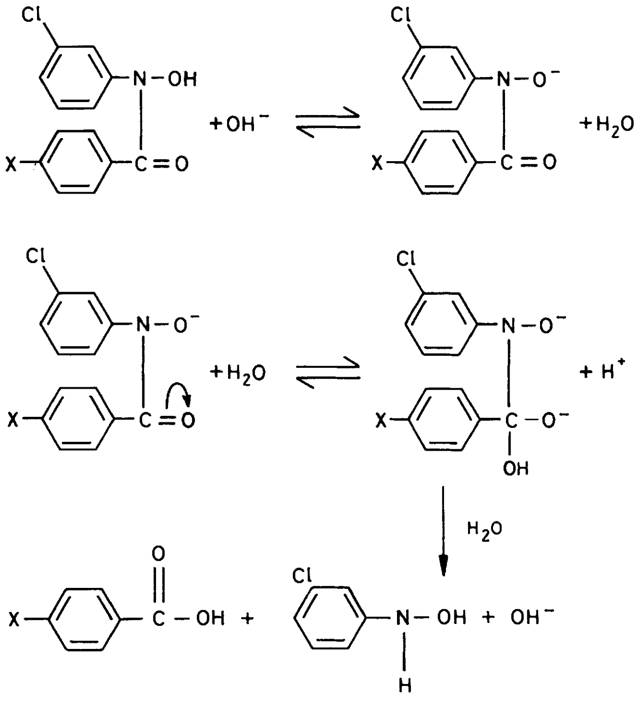


Figure 3.

The effect of substitution on the reactivity of benzene derivatives has been studies by Hammett[19] and Jaffé.[20] Comparative studies on the thermodynamic dissociation constants of *p*-substituted benzohydroxamic acids with the corresponding benzoic acids were found to be in good agreement with experimental pK_a values. In the present investigation an attempt has been made to correlate the *p*-substituted *N*-*m*-chlorophenylbenzohydroxamic acids with the Hammett equation. A straight line is obtained by plotting pK_a of *p*-substituted *N*-*m*-chlorophenylbenzohydroxamic acids against pK_a of benzoic acids (Figure 2). The experimental pK_a and those calculated from the Hammett equation and least-squares method are in good agreement.

The pK_a values in Table 3 indicate that the experimental values (column 2) and those calculated by Hammett equation (column 4) and least squares (column 5) are in good agreement. Similarly a plot of the calculated pK_a of *p*-substituted *N*-*m*-chlorophenylbenzohydroxamic acid in 30, 50, and 60% dioxane–water at 25 and 35 °C against the Hammett σ-function



Scheme.

(Tables 3 and 4) gives a straight line which is in agreement with the experimental pK_a. Further the dependence of the acidity on substitution in benzene molecules was followed by the same reaction constants obtained by two different plots (Figures 2 and 3).

Rate constants for different *p*-substituted hydroxamic acids at 25 °C in 1:1 dioxane–water are given in Table 5. The reaction was found to be pseudo-first-order. The initial concentration of hydroxamic acid in all kinetic runs was 0.01M in 1:1 dioxane–water. It is observed that by changing the substituents in the *para* position, the order of rate constants changes and follows the same order of pK_a: pK_a $C_2H_5O > CH_3O > CH_3 > H > F > Cl \sim Br > NO_2$; *k* $C_2H_5O > CH_3O > CH_3 > H > F > Cl \sim Br > NO_2$.

It has been observed that introduction of electron-attracting groups increases the rate of hydrolysis whereas electron-repelling groups decrease the hydrolysis rate. The mechanism of hydrolysis is shown in the Scheme. The products are substituted benzoic acids and *m*-chlorophenylhydroxylamine which are identified by t.l.c. and i.r. spectra.

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