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Thermodynamic Proton–Ligand Stability Constants of Hydroxamic Acids and Applicability of Hammett Equation

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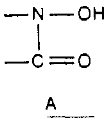
The thermodynamic proton–ligand stability constants, pK_a, of *N*-*p*-chlorophenyl-(m-substituted)benzohydroxamic acids have been determined in dioxane–water media [50–70% (v/v)] at 25 ± 0.1 °C by pH-metry. The proton–ligand stability constants varied linearly with the mole fraction of dioxane. Numerical equations expressing this linear relationship have been obtained by the method of least squares. The order of pK_a of the acids with a succession of the substituents is $CH_3 > H > OCH_3 > F > I > Cl > Br > NO_2$. The effect of the substitution on the ionization of the acid is discussed. The pK_a have also been correlated with the Hammett equation.

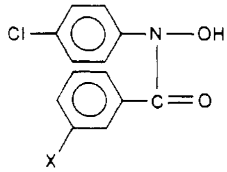
Introduction

Hydroxamic acids with the functional grouping (A) are versatile reagents in organic and inorganic analysis, in pharmaceuticals, in food additives, and in nuclear food processing.



A

They form very stable complexes with transition metals (*1–3*, *4*) and hence serve as useful analytical reagents (*5–9*). Several reports on pK_a values of hydroxamic acids are available in the literature (*10*, *11*); however, no data are available with *N*-*p*-chlorophenyl-(m-substituted)benzohydroxamic acids (B). In the present investigation the pK_a of these acids have been determined in 50–70% (v/v) dioxane–water media at 25 ± 0.1 °C.



B

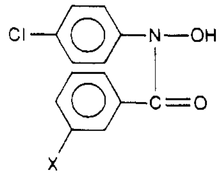
($X = H, OCH_3, CH_3, F, Cl, Br, I, NO_2$)

Experimental Section

Chemicals and Reagents. All the chemicals used were of G.R. and AnalaR grades, of E. Merck and B.D.H., respectively, unless otherwise stated.

Pure distilled water, redistilled over alkaline potassium permanganate and free of carbon dioxide, was used. It was tested for the absence of carbonate by Kolthoff's method (*12*). Dioxane was purified by the procedure of Weissberger (*13*). Carbonate-free potassium hydroxide was prepared according to the method described by Vogel (*14*) and diluted to 0.1 M with the desired composition of dioxane.

Table I. Thermodynamic Ionization Constants of *N*-*p*-Chlorophenyl-(*m*-substituted)benzohydroxamic Acids in Dioxane–Water Media at 25 ± 0.1 °C



		pK_a		
compd. no.	substituent X	$n_2{}^a = 0.174$ $D^b = 33.0$	$n_2 = 0.240$ $D = 25.77$	$n_2 = 0.330$ $D = 17.54$
I	H	10.77	11.47	12.43
II	CH_3	10.88	11.54	12.45
III	OCH_3	10.66	11.36	12.32
IV	F	10.39	11.12	12.11
V	Cl	10.33	11.07	12.08
VI	Br	10.30	11.04	12.06
VII	I	10.36	11.10	12.10
VIII	NO_2	9.90	10.65	11.69

[a] Mole fraction of dioxane. [b] Dielectric constant.

Hydroxamic acids. These acids were prepared by the modified procedure of Agrawal and Tandon (*15*). They were recrystallized from the mixtures of benzene and petroleum ether before use.

Apparatus. A Radiometer pH meter PHM 84 equipped with combined electrode was used for pH-metric titrations.

Procedure. Into a 75-mL three-necked titration vessel having an inlet for nitrogen, the weighed amount of hydroxamic acid (corresponding to 0.01 M in a final volume of 50 mL), freshly distilled dioxane and water of desired composition were added to yield the final composition of dioxane–water media (50–70% dioxane–water). The titration vessel was thermostated at 25 ± 0.1 °C. Nitrogen, presaturated with the volume percentage dioxane–water media under study was bubbled through the solution. The electrode was placed in the cell. This solution was titrated against 0.1 M KOH, also prepared in the required volume percent dioxane–water media, taken in a buret (least count 0.02 mL), adding the same in small aliquots (0.5 mL), and the pH was recorded.

Results and Discussion

The pK_a of the *N*-*p*-chlorophenyl-(m-substituted)benzohydroxamic acids in 50–70% (v/v) dioxane–water media at 25 ± 0.1 °C are given in Table I. The average pK_a generally falls within a spread of ±0.02 but not beyond ±0.03 in any case. The empirical equations for different mole fractions of dioxane are given in Table II. The pK_a values show that these hydroxamic acids are very weak acids.

It is observed that the pK_a of the hydroxamic acids increase linearly with the increase in dioxane content (mole fraction of

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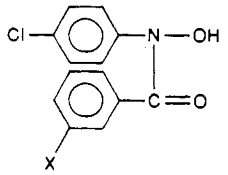
Table II. Empirical Correlation between pK_a and Mole Fraction of Dioxane for *N*-*p*-Chlorophenyl-(*m*-substituted)benzohydroxamic Acid at 25 ± 0.1 °C



compd no.	substituent X	pK_a = mn_2 + C least squares m	c	r	graphically m	c
I	H	10.64	8.92	1.00	10.66	8.95
II	CH_3	10.07	9.13	1.00	10.00	9.15
III	OCH_3	10.64	8.81	1.00	10.72	8.80
IV	F	11.08	8.47	1.00	11.11	8.45
V	Cl	11.22	8.38	1.00	11.20	8.40
VI	Br	11.34	8.33	1.00	11.36	8.35
VII	I	11.15	8.42	1.00	11.11	8.40
VIII	NO_2	12.08	7.80	1.00	12.00	7.85

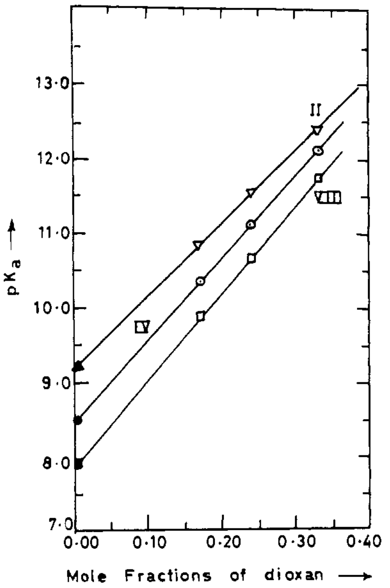


Figure 1. Variation of pK_a with mole fraction of dioxane: –Δ– (II), *N*-*p*-chlorophenyl-*m*-methylbenzohydroxamic acid; –⊙– (IV), *N*-*p*-chlorophenyl-*m*-fluorobenzohydroxamic acid; and –□– (VIII), *N*-*p*-chlorophenyl-*m*-nitrobenzohydroxamic acid. ▲, ●, and ■ are points for pK_a's at zero dioxane.

dioxane, Figure 1), which is due to the decrease in the dielectric constant of bulk solvent. As the dielectric constant decreases, the ionic dissociation of the proton from its oxygen decreases to a greater extent than the ion–dipole interaction between the proton and the solvent molecule.

When the pK_a of hydroxamic acids were plotted against 1/D (Figure 2), where D is the dielectric constant of the medium, it was observed that the plots possess a distinct curvature. This suggests nonelectrical forces which could include geometrical factors, hydrogen bonding, and solvent–solute interaction influencing the dissociation process.

Hammett Correlation. Hammett (*16*) and Jaffe (*17*) correlated the effect of substitution on the reactivity of benzene derivatives. Agrawal et al. (*3*, *18*, *19*) have made an attempt to correlate the pK_a of substituted benzohydroxamic acid with benzoic acid and obtained a good agreement between the two sets of values. In the present investigation a correlation is established between the pK_a values of *N*-*p*-chlorophenyl-(m-substituted)benzohydroxamic acids with Hammett equation

$$\log K/K_0 = \rho\sigma$$

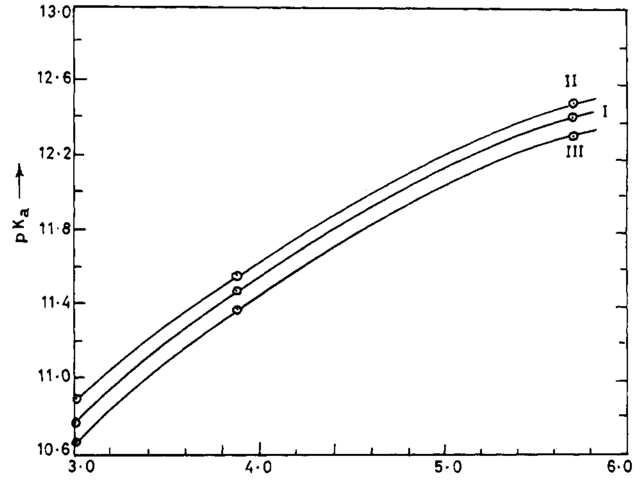


Figure 2. Plot of pK_a's of *N*-*p*-chlorophenyl-(m-substituted)benzohydroxamic acids against 100/*D* at 25 °C.

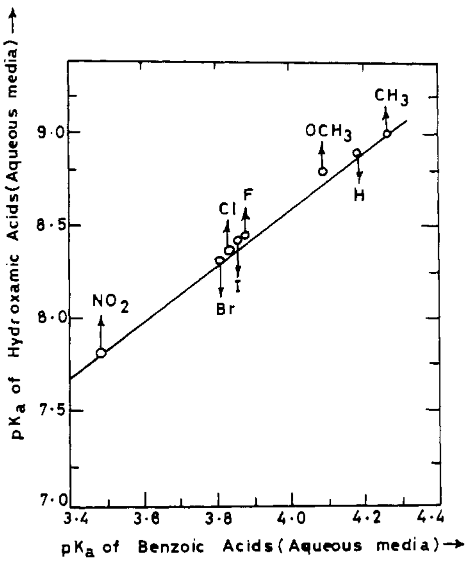
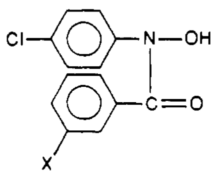


Figure 3. Plot of pK_a's of *N*-*p*-chlorophenyl-(m-substituted)benzohydroxamic acids against pK_a's of benzoic acid at 25 °C.

Table III. Hammett pK_a of the *N*-*p*-Chlorophenyl-(*m*-substituted)benzohydroxamic Acids in Aqueous Media at 25 °C



compd no.	substituent X	pK_a[a]	pK_a[b]	σ	pK_a[c] (ρ = 1.6)	pK_a (benzoic acid)[d]
I	H	8.95	8.92	0.0	8.92	4.18
II	CH_3	9.15	8.13	-0.07	9.03	4.27
III	OCH_3	8.80	8.81	0.12	8.73	4.09
IV	F	8.45	8.47	0.34	8.38	3.87
V	Cl	8.40	8.38	0.37	8.33	3.83
VI	Br	8.35	8.33	0.39	8.30	3.81
VII	I	8.40	8.42	0.35	8.36	3.85
VIII	NO_2	7.85	7.80	0.71	7.78	3.49

[a] pK_a in aqueous media, extrapolated values (graphically). [b] pK_a in aqueous media, by least squares. [c] pK_a obtained from Hammett function (log K − log K_0 = $\rho\sigma$). [d] Benzoic acid with the same substituents.

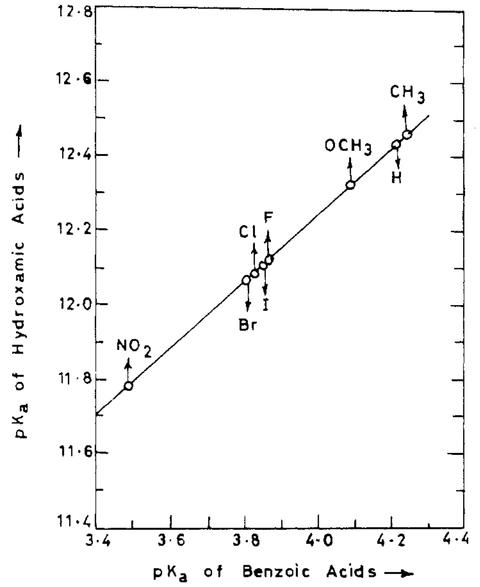


Figure 4. Plot of pK_a of *N*-*p*-chlorophenyl-(m-substituted)benzohydroxamic acids against pK_a of benzoic acids in 70% (v/v) dioxane-water media at 25 °C.

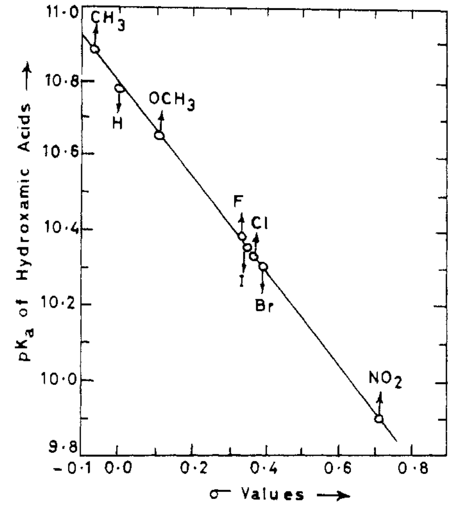


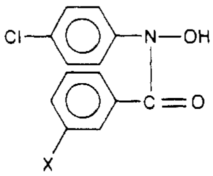
Figure 5. Hammett's σ plots at 25 °C.

where ρ is the reaction constant and σ is the substituent constant; K and K_0 are the pK_a of substituted hydroxamic acids and unsubstituted hydroxamic acids, respectively.

The pK_a in Table III indicate that in aqueous medium the experimental values (extrapolated), values calculated by Hammett equation, and those obtained by least squares are in good agreement.

A plot of pK_a of *N*-*p*-chlorophenyl-(m-substituted)benzohydroxamic acids against the pK_a of respective benzoic acids is linear (Figure 3) in aqueous (extrapolated and dioxane-water media (Figure 4) and is in agreement with experimental values (Table IV). The dependence of the acidity on substitution in benzene nucleus was followed by the same reaction constant obtained by two different plots (Figures 4 and 5).

Table IV. Hammett pK_a of the *N*-*p*-Chlorophenyl-(m-substituted)benzohydroxamic Acids in 70% (v/v) Dioxane-Water Media at 25 °C



compd no.	substituent X	mole fraction of dioxane (n_2)[a] pK_a (exptl)	σ	p$K_a^{e\,b}$ (ρ = 0.92)
I	H	12.43	0.00	12.43
II	CH_3	12.45	-0.07	12.50
III	OCH_3	12.32	+0.12	12.31
IV	F	12.11	+0.34	12.06
V	Cl	12.08	+0.37	12.05
VI	Br	12.06	+0.39	12.03
VII	I	12.10	+0.35	12.07
VIII	NO_2	11.78	+0.71	11.78

[a] n_2 = 0.330. [b] pK_a^e = pK_a obtained from Hammett function (log K = log K_0 = ρσ).

In order to understand the relation between the molecular structure of hydroxamic acids and their pK_a, it is convenient to examine the parent carboxylic acids.

The hydroxamic acids in this investigation have been derived from m-substituted benzoic acids and follow the order of pK_a of the benzoic acids, in all mole fractions of dioxane; thus pK_a of benzoic acids: CH_3 > H > OCH_3 > F > I > Cl > Br > NO_2; pK_a of hydroxamic acids: CH_3 > H > OCH_3 > F > I > Cl > Br > NO_2.

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Literature Cited

(1) Agrawal, Y. K. *Talanta* **1973**, *20*, 1213.
(2) Agrawal, Y. K. *Bull. Soc. Chim. Belg.* **1980**, *87*, 261.
(3) Agrawal, Y. K. *Russ. Chem. Rev.* **1979**, *48*, 948.
(4) Agrawal, Y. K.; Roshania, R. D. *Bull. Soc. Chim. Belg.* **1980**, *87*, 261.
(5) Agrawal, Y. K. *Rev. Anal. Chem.* **1980**, *5*, 3.
(6) Agrawal, Y. K. Technical News Service, Sarabhai M. Chemicals Baroda, 1979 p 11.
(7) Agrawal, Y. K.; Jain, R. K. *Rev. Anal. Chem.* **1982**, *6*, 49.
(8) Agrawal, Y.K.; Mehd, G. D. *Rev. Anal. Chem.* **1982**, *6*, 185.
(9) Agrawal, Y. K.; Patel, S. A. *Rev. Anal. Chem.* **1980**, *4*, 237.
(10) Agrawal, Y. K.; Khare, V. P.; Kapur, A. S. *Rocz. Chem.* **1976**, *50*, 2215.
(11) Menon, S. K.; Agrawal, Y. K. *Russ. Chem. Rev.*, in press.
(12) Kolthoff, I. M.; Sandell, E. B. *Text-Book of Quantitative Inorganic Analysis*; MacMillan: London, 1952; p 517.
(13) Weissberger, A.; Proskauer, E. S.; Riddick, J. A.; Toops, Er. E. E. *Technique of Organic Chemistry*; Interscience: New York, 1955; Vol. VIII, p 126.
(14) Vogel, A. I. *A Textbook of Quantitative Inorganic Analysis*, 3rd ed.; Longmans: London, 1961.
(15) Agrawal, Y. K.; Tandon, S. G. *J. Chem. Eng. Data* **1971**, *16*, 371.
(16) Hammett, L. P. *Chem. Rev.* **1935**, *17*, 125.
(17) Jaffe, H. H. *Chem. Rev.* **1953**, *53*, 191.
(18) Agrawal, Y. K. *Ann. Chim.* **1977**, *2*, 5.
(19) Agrawal, Y. K.; Shukla, J. P. *Z Phys. Chem.* **1979**, *255*, 889.

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