CHAPTER III

PHYSICO-CHEMICAL PROPERTIES OF N-ARYLHYDROXAMIC ACIDS

RESUME

The physico-chemical properties viz. thermogravimetric (TG) and differential thermal analysis (DTA), thermal stability, chemical stability, non-aqueous titration, ionization and hydrolysis constants have been described.

The thermal dissociation of hydroxamic acids are studied by differential thermal analysis (DTA). The DTA curves show exothermic peaks by melting of the compound.

The synthesised hydroxamic acids are titrated visually in non-aqueous media (methanol and dimethylformamide) using thymol blue as indicator against 0.1 N potassium methoxide. Potentiometric titrations were also performed in non-aqueous media with platinum and calomel electrodes. The molecular weights of hydroxamic acids are calculated.

The chemical and thermal stability and thermodynamic ionization constants of the synthesised acids in 50-70% dioxan-water media at 35°C ± 0.1°C have been determined. The hydrolysis constants are also reported.

PHYSICO-CHEMICAL PROPERTIES OF N-ARYLHYDROXAMIC ACIDS

The knowledge of the physico-chemical properties of the hydroxamic acids is essential for understanding their nature, reactivity and analytical applications. The hydroxamic acids are sparingly soluble in aqueous media but readily soluble in organic solvents like benzene, chloroform, dioxan, dimethyl formamide etc. These acids are weak acids. They can be titrated visually in aqueous media but no sharp neutralization point is obtained and gives erroneous results (1,2), hence they can be titrated accurately by non-aqueous titration technique using tetrabutyl ammonium hydroxide or potassium methoxide (3,4).

In the present investigation the thermodynamic proton-ligand stability constants, hereafter termed as thermodynamic ionization constant; pK_a, of N-arylhydroxamic acids are determined by the pH titration method in 70% (v/v) dioxan-water media at 35° ± 0.1°C.

The pH meter cell employed for pK_a determination was of the undernoted typed.

Glass Electrode	HA (0.01M) in dioxan-water mixture	Salt bridge aq saturated KCl	Calomel Electrode aq saturated

The thermodynamic dissociation constant, $K_{a(aq)}$ of hydroxamic acid, HA,

$$HA \rightleftharpoons [H^+] + [A^-]$$

in an aqueous medium is given by equation (1) and (2)

$$K_{a(aq)} = \frac{[H^+]\,[A^-]}{[HA]} \qquad (1)$$

$$pK_{a(aq)} = -\log\,[H^+] + \log\frac{[HA]}{[A^-]} - 2\log y_{\pm} \qquad (2)$$

where $y_{\pm}$ is the mean activity coefficient of the univalent ion $(y_{H^+} = y_{A^-} = y_{\pm})$ at a given temperature and medium; it is assumed that the activity coefficient of the unionized acid y_{HA} is unity.

The Van Uitert and Haas (5-7) relation was used to obtain the hydrogen ion concentration from the value read on the pH meter (B):

$$-\log [H^+] = B + \log U_H^\circ - \log 1/y_\pm \qquad (3)$$

The values of log U_H° were determined experimentally as described by Agrawal (8) and mean activity coefficients were obtained from the data of Harned and Owen (9) and Agrawal (10).

The final equation for calculating ionization constant in dioxan-water medium is obtained by substituting the value of hydrogen ion concentration from equation (3) in equation (2), we get,

$$pK_a = B + \log U_H^\circ + \log \frac{[HA]}{[A^-]} + \log \frac{1}{y_\pm} \qquad (4)$$

The pK_a values, thus determined, are termed as thermodynamic values, for they include correction due to activity coefficients.

EXPERIMENTAL

HYDROXAMIC ACIDS

The synthesis of hydroxamic acids is described in Chapter II. These were recrystallized before use, from benzene and dried in vacuo over P_2O_5.

SOLVENTS

Distilled Water: Pure distilled water redistilled over alkaline potassium permanganate and freed from carbon dioxide was used. It was tested for the absence of carbonate by Kolthoff's method (11).

Dioxan: p-Dioxan was purified by the procedure of Weissberger (12). It was refluxed over pellets of KOH for about 8-10 hrs, distilled and middle fraction of the distillate refluxed over metallic sodium for 5-6 hrs, and fractionally distilled. The middle fraction was used. Its purity was established by freezing point, which varied from 11.65° to 11.80° (uncorrected) against the reported range of 11.65° to 12.0° (13,14).

Methanol: The anhydrous methanol was prepared by the method of Weissberger (12).

Benzene: G.R.,Uvasol, E. Merck was used without purification.

Dimethyl formamide (DMF): Pro Analysis, B.D.H. grade was used without purification.

Acetone: K. Light (England) was used without further purification.

REAGENTS

Tetrabutylammonium hydroxide: 0.1 M solution was prepared in dioxan water medium by the method of Cundiff and Markunas (15).

Potassium methoxide: The potassium methoxide was prepared by reacting potassium metal with methanol and diluting it with benzene so that the benzene-methanol ratio was 10 to 1 (16).

Ferric chloride solution: A 0.05 M solution was prepared by dissolving the requisite amount of ferric chloride in 0.1 N HCl.

Indicator: 0.1% indicator solution of thymol blue was prepared in dimethylformamide or methanol.

APPARATUS

N.P.L. certified graduated apparatus of Gallenkamp, Technico, grade 'A' was used for measurements. The 5-ml microburette graduated to 0.01 ml

pH meter: A Systronics digital pH meter equipped with glass (0-14 pH) and saturated calomel electrodes was used for pH measurements.

The platinum and calomel (saturated with KCl in methanol) electrodes were used for non-aqueous titrations. The pH meter was calibrated in 0.01 unit of pH.

Potentiometer: Cambridge potentiometer equipped with platinum and calomel (saturated with KCl in methanol) electrodes was used for potentiometric titrations.

Thermal analyzer: Simultaneous TG and DTA curves of hydroxamic acids were recorded on a Mettler thermal analyzer fitted with a 12 channel recorder.

TITRATION VESSEL

A titration vessel, capacity of about 75-ml, was specially fabricated for pH titrations. Besides an inlet from the side for nitrogen gas, it had three necks, which accomodated the glass electrode, the calomel electrode and the microburette.

STANDARD BUFFERS

The pH meter was standardized at 35°C with buffer solutions such as 0.05 M potassium hydrogen phthalate (pH, 4.019 at 35°) (17,18), 0.01 M borax (pH, 9.100 at 35°) (17, 18) and National Bureau of standard buffers. Standardization was checked, both before and after each titration by at least two buffers.

PERCHLORIC ACID

E. Merck, G.R. 70% perchloric acid was approximately diluted with glass distilled water to give 0.5 M solution. The solution was finally standardized volumetrically.

NITROGEN

Nitrogen was passed through a series of bubblers containing a saturated alkaline solution of pyrogallol, 2 N sulphuric acid, distilled water and finally the required solvent.

TG AND DTA

The TG and DTA curves of hydroxamic acids in air were recorded on a Mettler thermal analyzer maintaining the following instrumental factors in all the experiments:

TG range - 1 mg full scale sensitivity,
DTA range - 50 V, heating rate - 8°/min,
Gas flow rate - 100 ml min^{-1}, mass of the sample - 10mg.

Alumina was used as a reference material for DTA.

NON-AQUEOUS TITRATIONS

A weighed amount of hydroxamic acid was taken into 50-ml titration vessel. The vessel has C-10 joints for burette and nitrogen gas. Next 20 ml of dimethylformamide or methanol was added and the solution was stirred with a magnetic stirrer. Then 2-3 drops of indicator were added and titrated against 0.1 M potassium methoxide in an atmosphere of nitrogen.

DETERMINATION OF IONIZATION CONSTANTS

The titration procedure was essentially the same as recommended by Agrawal et.al. (10,19-21).

Generally, hydroxamic acid (0.5mM) in dioxan : H_2O (47.5 ml) were placed in a three necked titration vessel, thermostated at 35° ± 0.1°C, carrying the glass and calomel electrodes, microburette (5 x 0.01 ml) and inlet for nitrogen. Nitrogen gas, presaturated with carbonate free water and the desired solvent mixture, was passed through the solution. The solution was titrated with 0.1 M tetrabutylammonium hydroxide which too was also prepared as to contain the required dioxan percentage (50-70%) by adding aliquots (0.5 ml). The highest appropriate drift free pH reading was recorded.

HYDROLYSIS OF N-ARYLHYDROXAMIC ACIDS

In a thermostated (35 ± 0.1°C) 150-ml conical flask having B-24 joint and stopper, transferred 25 ml of 0.01 M solution of hydroxamic acid in acetone and added 25 ml of 0.1 M solution of sodium hydroxide and thoroughly mixed. The aliquots of the reaction mixture were withdrawn periodically starting from the time of mixing and complexed with 1 ml of ferric chloride solution. The complex is then diluted to 10 ml with acetone and water to get a final composition of solvent (acetone : water :: 50 : 50). Measured the absorbance of the pink coloured ferric hydroxamate at the respective maximum absorbance against the $FeCl_3$ blank. Absorbance at infinite time (A_∞) is measuredkeeping the reaction mixture for 48 hrs.

RESULTS AND DISCUSSION

TG AND DTA

The thermal data are given in Table 1. The DTA curves are reproduced in Fig. 1.

The hydroxamic acids were heated upto 700°C in an atmosphere of air. The thermogram shows no change in weight till the melting point of the hydroxamic acids, indicating the absence of water molecules. The weight loss starts after the compounds get melted and continues till it finally tars. The DTA curves show mainly one endothermic and two exothermic peaks. The endotherm corresponds to the melting of the compound, soon after which the decomposition starts shown by exothermic peak. The decomposition is gradual and the end is denoted by an exotherm showing the complete decomposition of the acids which finally tars. The products obtained by the thermal decomposition of these hydroxamic acids were analysed and found to be mainly their carboxylic acids, anilides and finally tars.

THERMAL STABILITY

A 0.5 ml of 0.1 M chloroform solution of hydroxamic acid was transferred into fifteen 25-ml volumetric flasks.

TABLE 1

THERMAL ANALYSIS OF N-ARYLHYDROXAMIC ACIDS

Compound No	Hydroxamic acid	mp (°C)	TG (wt.loss)		DTA (°C)		
			°C	°C	Endotherm	Exotherms	
						1st	2nd
I	N-p-Cl-phenyl-3,4,5-trimethoxycinnamo-	169	170-400	450-625	170	180	535
II	N-p-Cl-phenyl-p-butoxybenzo-	164	165-410	500-610	165	180	550
III	N-phenyl-p-butoxybenzo-	136	136-425	450-550	136	175	500
IV	N-p-Cl-phenyl-p-Cl-phenoxy-isobutyro-	144	150-325	450-525	145	170	510
V	N-phenyl-p-Cl-phenoxyisobutyro-	125	125-350	475-625	125	170	600

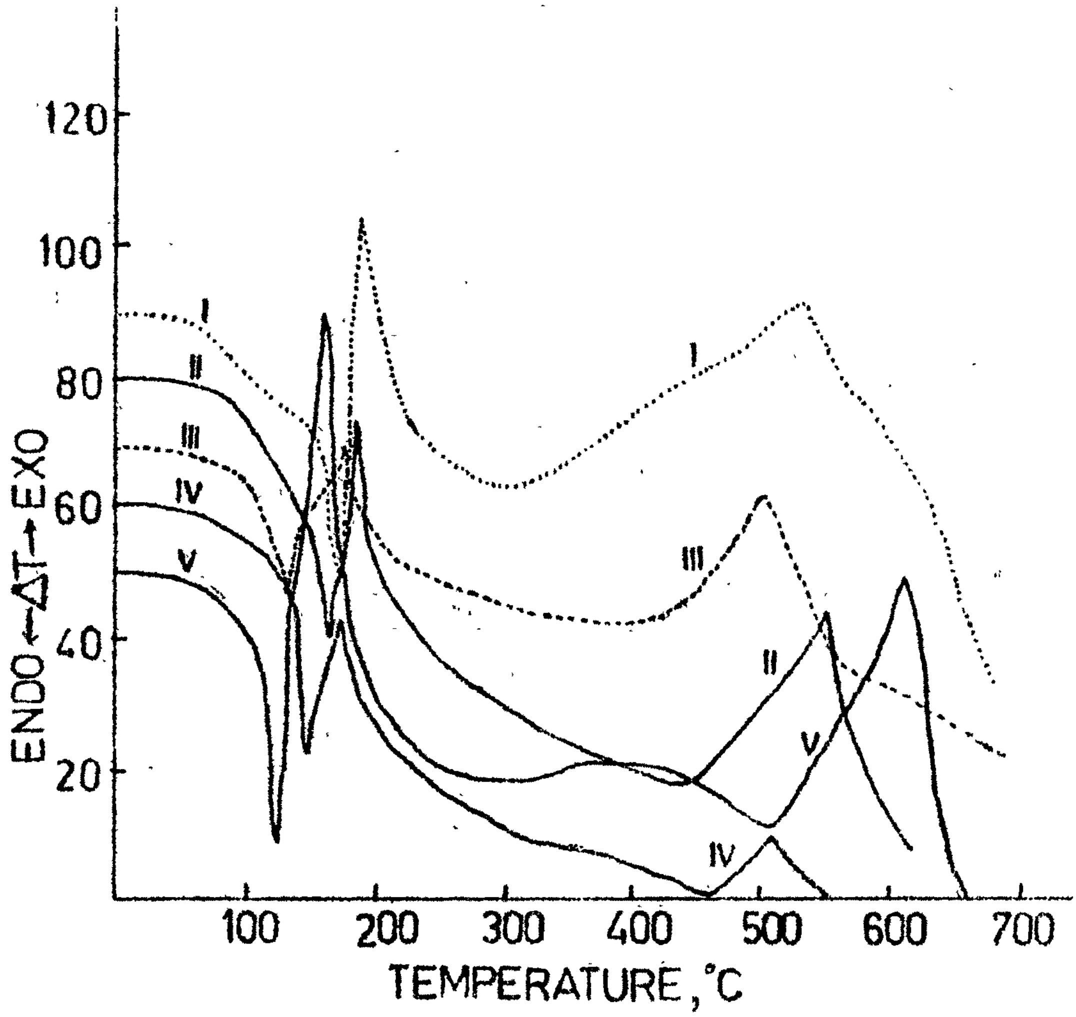


Fig. 1 DTA curves of N-Arylhydroxamic acids

After evaporation of chloroform under vacuum, the flasks were heated in the thermostated oven.

CHEMICAL STABILITY

0.1 M solutions of hydroxamic acid in 6 M $HClO_4$, 6 M HCl or 0.8 M HNO_3 were kept in a thermostatic bath at 50 ± 0.1° and hydroxamic acid was determined colorimeterically at regular intervals. The data are given in Table 2.

Non-Aqueous Titrations

The N-arylhydroxamic acids can be titrated visually as well as potentiometrically in dimethyl formamide with reasonable accuracy (Table 3).

The indicator, thymol blue colour changes from acid to base, yellow-greenishyellow for compound I, yellow-blue for compounds III-V and yellow-bluishgreen for compound II, respectively in dimethyl formamide and methanol. The non-aqueous titrations are also performed in dimethyl formamide and methanol potentiometrically using platinum and calomel (saturated KCl in methanol) electrodes. The data (Table 3) show that potentiometric titration technique is more accurate as compared to visual titrations. Mostly in the potentiometric determination of these acids a sharp end point is obtained. The results thus obtained (Table 3) are in agreement with the theoretical values.

TABLE - 2

Analytical Data on N-Arylhydroxamic Acids

Compd. No.	Vanadium Extraction			Thermal Stability at 80°C hrs	pK_a		
					Dioxane water %		
	Colour	λmax	Molar absorptivity ($l\ mol^{-1}\ cm^{-1}$)		50	60	70
I	BV	570	6.9×10^3	9	ins	ins	12.00
II	V	540	5.0×10^3	10	ins	ins	12.56
III	V	535	4.5×10^3	10	ins	ins	12.92
IV	RV	510	4.3×10^3	10	12.55	12.87	13.30
V	RV	505	4.2×10^3	11	12.90	13.31	13.78

BV = Bluish violet; V = Violet; RV = Reddish violet

ins = insoluble; the pK_a values are accurate to ± 0.03.

TABLE - 3

Non-Aqueous Titration Data of Hydroxamic Acids

Compd. No.	Hydroxamic acid	Molecular weight (calculated)	Visible colour change	Molecular weight found, titration	
				Titration visible	Potentiometric
I	N-p-Chlorophenyl-3,4,5-trimethoxycinnamo-	363.80	Y-GY	263.0	263.2
II	N-p-Chlorophenyl-p-butoxybenzo-	319.80	Y-BG	320	320.1
III	N-Phenyl-p-butoxybenzo-	285.34	Y-B	285	285.0
IV	N-p-Chlorophenyl-p-chlorophenoxyisobutyro-	340.22	Y-B	341	339.8
V	N-Phenyl-p-chlorophenoxyisobutyro-	305.76	Y-B	305	304.7

Y = Yellow; GY = Greenishyellow; BG = Bluishgreen.

TABLE 4

EFFECT OF CARBON DIOXIDE ON APPARENT MOLARITY OF TITRANT

Final solution, in DMF, 0.1 M in tetrabutylammonium hydroxide and 0.025 M in carbonate

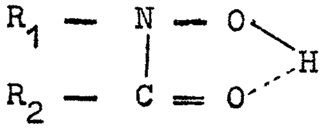
Hydroxamic acid/M.	Apparent molarity	Molarity change
0.01	0.089	0.011
0.02	0.087	0.013
0.05	0.085	0.015
0.25	0.079	0.021
0.50	0.072	0.028

The carbon dioxide decreases the apparent molarity of the titrant (Table 4), indicating the formation of carbonate (22,23). It also became apparent that the change in molarity of the titrant was dependent on the amount of acid titrated and solvent used (23). The error due to the carbon dioxide was eliminated by carrying out the titrations in the atmosphere of nitrogen and ensuring that the titration and solvents are themselves free from carbon dioxide.

IONIZATION CONSTANTS

The knowledge of the proton ligand stability constants (ionization constant) is essential for understanding the nature and their complexing capacity.

Hydroxamic acids are found to be versatile reagents for organic and inorganic analysis (24-28). Though they are weak acids due to the strong intramolecular hydrogen bonding, they are much stronger than phenols. The suppression of acidic character may be attributed to the intramolecular hydrogen bonding in these compounds. Evidence in support of the intramolecularly hydrogen bonded structure has been presented on several occasions



by infrared spectroscopic studies (29-31).

The hydroxamic acids synthesised here are insoluble in water but soluble in most of the organic solvents like chloroform, alcohol, dioxan, acetone, ether, benzene etc. The extend of solubility in the solvents differ from compound to compound. Choice of dioxan-water mixture for the study has been delibrated for several reasons. Dioxan is completely miscible with water and has a neutral character. The boiling range of both the solvents are approximately same. Many of the physical properties of dioxan-water mixtures needed for studying the proton-ligand equilibria are accurately known and are easily available (5-9,14). The thermodynamic significance of operational pH numbers obtained with pH meters in dioxan-water solution is fairly well understood as a result of extensive studies of Van Uitert et.al. (5,6) and others (7,8,10,32-34).

The ionization constants of the synthesised hydroxamic acids were determined in 50-70% dioxan-water mixtures for compounds IV and V. The compound I-III are insoluble in

50 and 60% dioxan-water mixtures and hence the pK_as were determined in 70% dioxan-water media. The experimental observations for only three representative titrations are recorded in Tables 5-7. The values of pK_a of N-arylhydroxamic acids in various dioxan-water media at 35° ± 0.1°C are given in Table 2. The average pK_a generally falls within a spread of ± 0.02 but not beyond ± 0.03 in any case.

In Fig. 2, the pK_a are plotted against mole fraction of dioxan, n_2, a linear relationship is observed. The empirical values of pK_a indicate the maximum deviation from linearity of the order of about 0.5% in pK_a.

Gurney (35) and others (10,36-38) have pointed out that the standard free energy change of proton transfer be considered in two parts - electrostatic (ΔG°_{el}) and non electrostatic (ΔG°_{non}). Born (39) has shown for electrostatic energy as

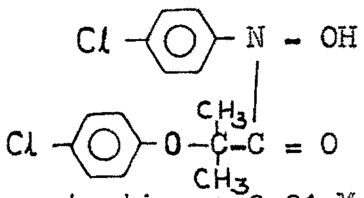
$$\Delta G^\circ_{el} = \frac{Ne^2}{2D}\left(\frac{1}{r_+} + \frac{1}{r_-}\right) \qquad (5)$$

Where r_+ and r_- are the radii of ions and D is the dielectric constant of the solvent. Hence

$$pK_a = \frac{\Delta G^\circ_{non}}{2.303\ RT} + \frac{Ne^2}{2D}\left(\frac{1}{r_+} - \frac{1}{r_-}\right) \qquad (6)$$

TABLE 5

DETERMINATION OF pK_a OF N-p-CHLOROPHENYL-p-CHLOROPHENOXY-ISOBUTYROHYDROXAMIC ACID IN 50% DIOXAN-WATER MEDIA

Structural Formula	Mol.Wt.	Temperature	log U_H°
	340.21	35° ± 0.1°C	0.24

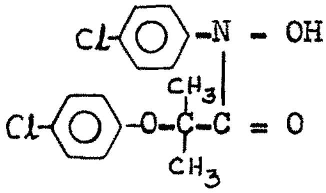
Concentration : 0.01 M at half neutralization. N-p-Chlorophenyl-p-chlorophenoxyisobutyrohydroxamic acid (0.17010 g) was dissolved in 23.75 ml of dioxan + 23.75 ml of water

I	II	III		IV	V	VI	VII
Titrant 0.1000M (TBAH)	B	Stoichiometric concentration [HA]	[A⁻]	$\frac{[HA]}{[A^-]}$	log of column IV	$\log \frac{1}{y_\pm}$	pK_a
0.00	8.62	0.01	-	-	-	-	-
0.50	11.30	0.001	0.009	9/1	0.954	0.055	12.55
1.00	11.63	0.002	0.008	8/2	0.602	0.0825	12.56
1.50	11.85	0.003	0.007	7/3	0.368	0.1024	12.56
2.00	12.02	0.004	0.006	6/4	0.176	0.115	12.55
2.50	12.19	0.005	0.005	5/5	0.000	0.1221	12.55
3.00	12.34	0.006	0.004	4/6	-0.176	0.135	12.54
3.50	12.53	0.007	0.003	3/7	-0.368	0.1457	12.55
4.00	12.76	0.008	0.002	2/8	-0.602	0.155	12.54
4.50	13.11	0.009	0.001	1/9	-0.954	0.16	12.56
5.00	13.51	-	-	-	-	-	-

Results : Average pK_a = 12.55 ± 0.01

TABLE 6

DETERMINATION OF pK_a OF N-p-CHLOROPHENYL-p-CHLOROPHENOXY-ISOBUTYROHYDROXAMIC ACID IN 60% DIOXAN-WATER MEDIA

Structural Formula	Mol.Wt.	Temperature	log U_H°
	340.21	35° ± 0.1°C	0.42

Concentration : 0.01 M at half neutralization. (0.17010 g) was dissolved in 23.75 ml of dioxan + 23.75 ml of water.

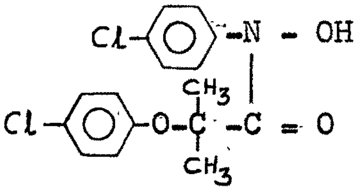
I Titrant 0.1000 M (TBAH)	II B	III $\triangle$	IV pK_a
0.00	9.25	-	-
0.50	11.41	1.46	12.87
1.00	11.72	1.16	12.88
1.50	11.92	0.95	12.87
2.00	12.1	0.77	12.87
2.50	12.26	0.61	12.87
3.00	12.41	0.45	12.86
3.50	12.58	0.27	12.85
4.00	12.83	0.04	12.87
4.50	13.16	-0.29	12.87
5.00	13.58	-	-

Where $= \log \frac{[HA]}{[A^-]} + \log U_H^{\circ} + \log \frac{1}{y_\pm}$

Results : Average $pK_a = 12.87 \pm 0.02$

TABLE 7

DETERMINATION OF pK_a OF N-p-CHLOROPHENYL-p-CHLOROPHENOXY-ISOBUTYROHYDROXAMIC ACID IN 70% DIOXAN-WATER MEDIA

Structural Formula	Mol.Wt.	Temperature	log U_H°
	340.21	35° ± 0.1°C	0.83

Concentration : 0.01 M at half neutralization. (0.17010 g) was dissolved in 23.75 ml of dioxan + 23.75 ml of water.

I Titrant 0.1000 M (TBAH)	II B	III Δ	IV pK_a
0.00	9.80	-	-
0.50	11.36	1.92	13.28
1.00	11.65	1.65	13.30
1.50	11.83	1.46	13.29
2.00	12.01	1.30	13.31
2.50	12.15	1.15	13.30
3.00	12.31	0.99	13.30
3.50	12.49	0.82	13.31
4.00	12.72	0.60	13.32
4.50	13.02	0.27	13.29
5.00	13.42	-	-

Where $= \log \frac{[HA]}{[A^-]} + \log U_H^\circ + \log \frac{1}{y_\pm}$

Results : Average $pK_a = 13.30 \pm 0.02$

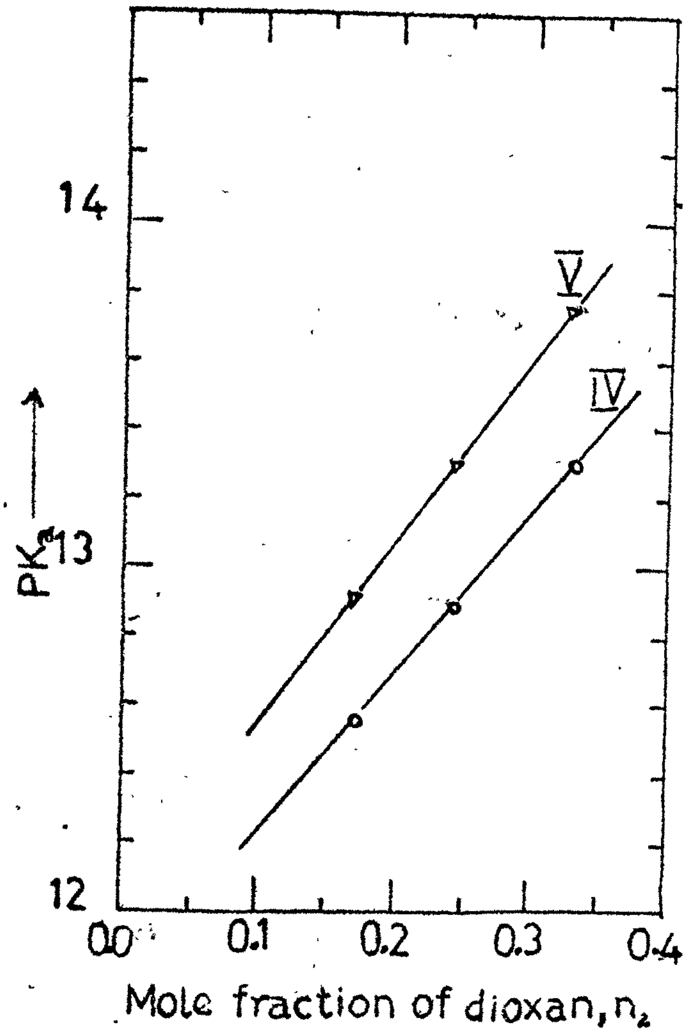
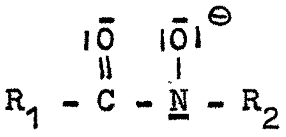
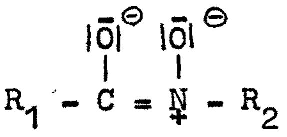


Fig. 2. Variation of pK_a vs mole fraction of dioxan.

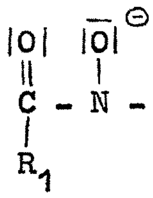
A plot of pK_a against 1/D is curved (Fig. 3). This suggests non electrical forces which could include geometrical factors, hydrogen bonding and solvent solute interactions, influence the dissociation process.

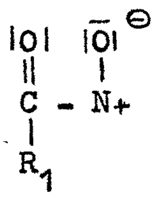
The substitutions have a marked effect in the pK_a values. In examining the effect of R_2 on the pK_a values, it is evident that a substituent which tends to stabilize the anion derived from the hydroxamic acid will be acid strengthening or the pK_a will be decreased. To have an idea of the influence of R_2 on acid strength, the possible resonance forms for the conjugate base anion is essential


(1)


(2)

In the present case, since the group R_2 = phenyl; resonance delocalization of the lone pair on N is easier which enhances the stability of the hydroxamate ion, by the induction of the built up positive charge on N.


(3)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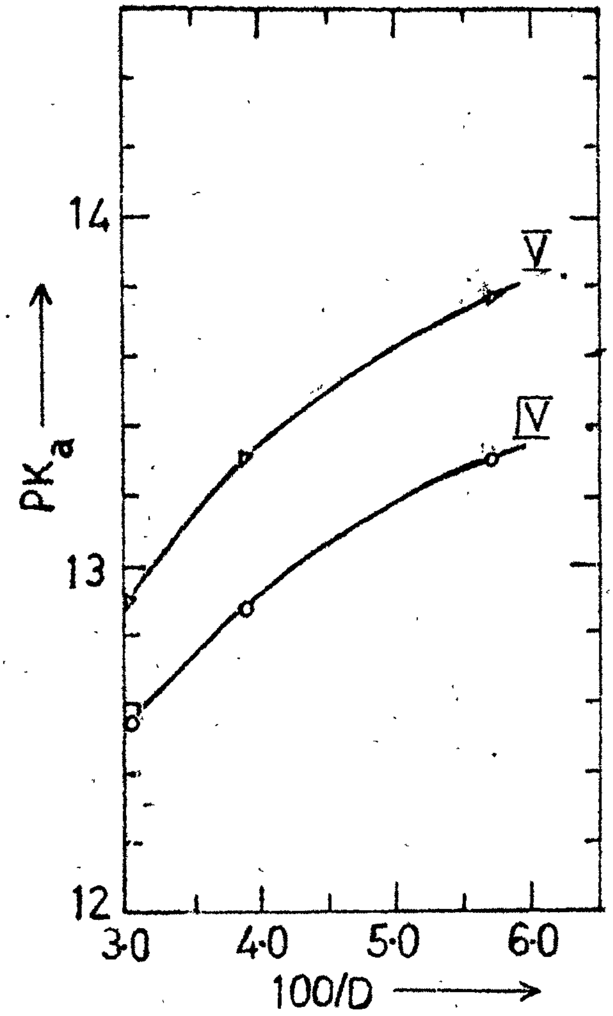

Fig. 3. Plots of pK_a's vs 100/D at 35°C.

By the introduction of electronegative group like chlorine in N-phenyl ring, the electron delocalizing capability of the ring will increase, there by increasing the acidic nature of the molecule. This is observed in the pK_a values obtained (compound I-V). This delocalization of the nitrogen electrons can be influenced by the inductive and/or resonance effect of the carbonyl function and R_1 (Table 2).

HYDROLYSIS OF N-ARYLHYDROXAMIC ACIDS

The rate constant (K) for the first order reaction is calculated from the equation (I)

$$K = \frac{2.303}{t} \log \frac{A_o - A_\infty}{A_t - A_\infty} \qquad (7)$$

Where A_o and A_∞ are the absorbances of the reaction mixture at zero and at infinite time respectively. A_t is the absorbance at time 't'.

The rate constants (K) for the alkaline hydrolysis of the hydroxamic acids studied here are given in Table 8. From the experimental results it is inferred that the order of the reaction is of pseudo first order. The plot of $\log \frac{A_o - A_\infty}{A_t - A_\infty}$ against the time 't' showed a linearity in the case of all the hydroxamic acids studied here, which further confirmed the first order reaction.

To assertain the actual route of the reaction, the final products were analysed and found as corresponding arylhydroxylamine and carboxylic acid. It is not confirmed whether the water molecule is attacking the hydroxamic acid molecule or the hydroxamate anion.

The possible mechanism for the hydrolysis of the hydroxamic acid can be as follows:

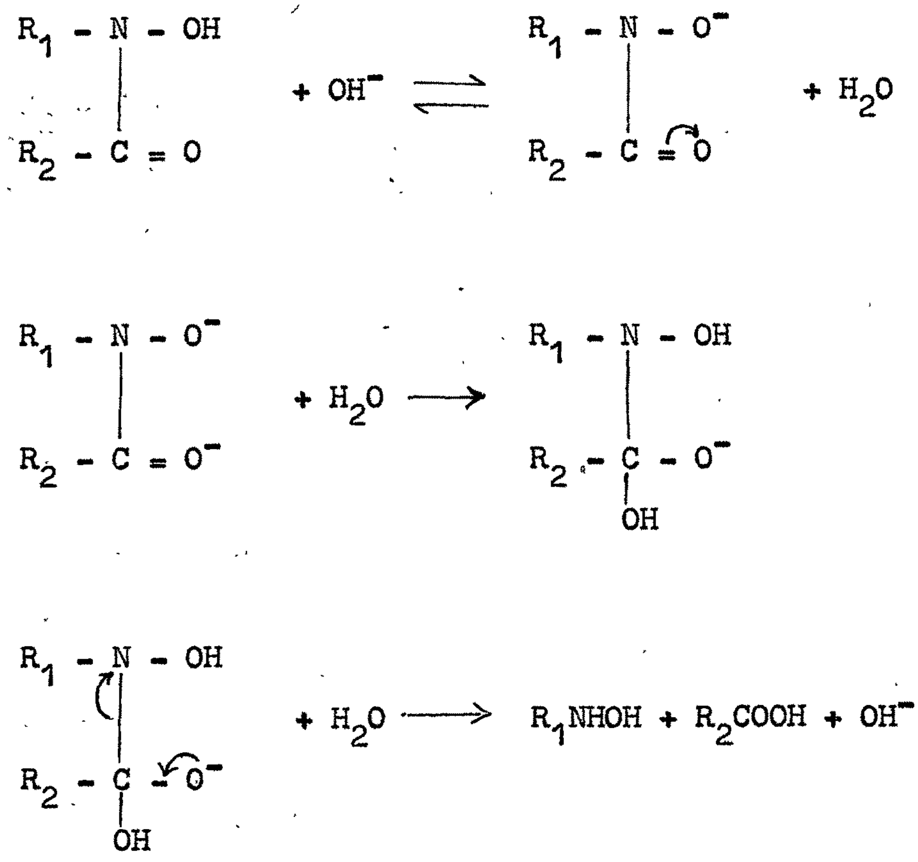

TABLE 8

CHARACTERISTICS OF ALKALINE HYDROLYSIS OF N-ARYLHYDROXAMIC ACIDS IN ACETONE:WATER (70:30)MEDIA

Hydroxamic acid = 0.01 M (in acetone) Temperature = 35 ± 0.1°C

NaOH = 0.1 M (in 40% (v/v) in acetone) Order of reaction = 1st order

$FeCl_3$ = 1 ml (0.2% (w/v)

Compd No	Hydroxamic acid	Absorbance maximum of complex (nm)	Time interval (min)	Aliquot taken (ml)	Rate constant (k/min $\times 10^{-3}$)
I	N-p-chlorophenyl-3,4,5-trimethoxycinnamo-	540	60	1	0.9
II	N-p-chlorophenyl-p-butoxybenzo-	530	15	1	13.5
III	N-phenyl-p-butoxybenzo-	530	30	2	8.3
IV	N-p-chlorophenyl-p-chloro phenoxyisobutyro-	495	2	2	95.5
V	N-phenyl-p-chlorophenoxyisobutyro-	490	5	2	63.4

It is evident from the results shown in the Table 8 that the substitution of R and R_1 in the hydroxamate moiety has a marked effect on the rate of alkaline hydrolysis of the hydroxamic acids. Compound I has shown more stability towards alkalie as shown by a low rate constant which can be due to the presence of conjugated double bonds which require high energy for hydrolysis. While the hydroxamic acids derived from the p-chlorophenoxyisobutyric acid have higher rate constants due to the presence of the tertiary carbon atom, which lower the activation energy of the molecule. The order of the K value is

$$I < III < II < V < IV$$

The electron/withdrawing effect of the chlorine atom has shown an enhancing effect on the rate of the reaction.

REFERENCES

1. Goldenberg, V., Ph.D. Thesis, Polytechnic Institute of Brooklyn, New York (1957).
2. Stamey, T.W. and Christian, R., Talanta, 13, 144 (1966).
3. Agrawal, Y.K., Analyst, 97, 578 (1972).
4. Agrawal, Y.K. and Roshania, R.D., Bull. Soc. Chim. Belg., 89, 175 (1980).
5. Van Uitert, L.G. and Haas, C.G., J. Am. Chem. Soc., 75, 451 (1953).
6. Van Uitert, L.G., Ph.D. Thesis, Pennsylvania State University (1952).
7. Agrawal, Y.K., D.Sc. Thesis, A.P.S. University, Rewa (1979).
8. Agrawal, Y.K., Talanta, 20, 1354 (1973).
9. Harned, H.S. and Owen, B.B., "The Physical Chemistry of Electrolytic Solutions", 3rd ed. Reinhol, New York (1958).
10. Agrawal, Y.K., Russ. Chem. Revs., 48, 947 (1979); cfp. Uspekhi Khim, 48, 1773 (1979).
11. Kolthoff, I.M. and Sandell, E.B., "A Textbook of Quantitative Inorganic Analysis", Macmillan, London

12. Weissberger, A. Proskauer, E.S., Riddick, J.A. and Toops, E.E. Jr., "Techniques of Organic Chemistry," Vol. VII, Interscience, New York (1955).

13. Vogel, A.I., "A Textbook of Organic Practical Chemistry," Longmans (1978).

14. Convey, B.E. "Electrochemical Data," Elsevier Publishers, New York, p. 16 (1952).

15. Cundiff, R.H. and Markunas, P.C. Anal. Chem., 34, 584 (1962).

16. Huber, H., "Titrations in Non-Aqueous Solvents," Academic Press, New York (1967).

17. Robinson, R.A. and Stoke, R.H., "Electrolytic Solutions," Butterworths, London (1961).

18. Perrin, D.D. and Dempsey, B., "Buffers for pH and Metal Ion Control," Chapman and Hall, London (1974).

19. Agrawal, Y.K. and Tandon, S.G., Talanta, 19, 700 (1972).

20. Agrawal, Y.K. and Tandon, S.G., J. Electro and Chem., 43, 158 (1973).

21. Agrawal, Y.K. and Kapoor, H.L., J. Chem. Eng. Data, 22, 159 (1977).

22. Agrawal, Y.K., Analyst, 104, 873 (1979).

23. Kucharsky, J. and Safric, L., "Titrations in Non-Aqueous Solvents," Elsevier, New York (1965), p.117.

24. Agrawal, Y.K., Revs. Anal. Chem., 5, 3 (1980).

25. Agrawal, Y.K. and Patel, S.A., Revs. Anal. Chem., 4, 237 (1980).

26. Agrawal, Y.K. and Jain, R.K., Revs. Anal. Chem., 6, 49 (1982).

27. Agrawal, Y.K. and Roshania, R.D., Bull. Soc. Chim. Belgs., 89, 159 (1980).

28. Agrawal, Y.K. and Mehd, G.D., Revs. Anal. Chem., 6, 185 (1983).

29. Agrawal, Y.K. and Tandon, S.G., J. Indian Chem. Soc., 49, 911 (1972).

30. Agrawal, Y.K. and Khare, V.P., Bull. Soc. Chem. (France), 9-10, 873 (1977).

31. Cohen, W. and Erlanyer, B.E., J. Am. Chem. Soc., 82, 3928 (1960).

32. Agrawal, Y.K., Talanta, 26, 599 (1979); J. Electroanal. Chem., 108, 369 (1980).

33. Housmon, Jr., W.B., Ph.D. Thesis, Purdue University, (1955).

34. Irving, H.M.N.H. and Mahnot, U.S. J.Inorg.Nucl.Chem., 30, 1215 (1968).

35. Gurney, R.W., J. Chem. Phys., 6, 499 (1938).

36. Agrawal, Y.K., Bull.Soc.Chim.Belg., 87, 831 (1978),

37. Agrawal,Y.K. and Tandon,S.G., Talanta, 19, 700 (1972).

38. Agrawal, Y.K. and Sharma, T.P., J. Inorg. Nucl. Chem., 39, 1823 (1977).

39. Born, M., Z. Phys., 1, 45 (1920).