CHAPTER III

THERMODYNAMIC PROTON-LIGAND STABILITY CONSTANTS
OF HETEROCYCLIC HYDROXAMIC ACIDS
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SUMMARY

The thermodynamic proton-ligand stability constants of heterocyclic hydroxamic acids have been determined in different mole fractions of dioxan (0.174-0.330) at 25 and 35±0.1°C. Empirical correlations to the pH meter readings in mixed aqueous media have been applied. The $pK_a$ varies linearly with mole fraction of dioxan. Numerical equations expressing this linear relationship have been obtained using the method of least square and relevant correlation coefficients have been calculated. The thermodynamic functions $\Delta G^\circ$, $\Delta H^\circ$ and $\Delta S^\circ$ are calculated. The effect of medium, temperature and substitution on ionization constants of hydroxamic acids is discussed.
INTRODUCTION

In recent years several heterocyclic hydroxamic acids have been synthesised and their ionisation constants have been determined. (18-22). The choice of the reagent for the analytical purposes depends on their physico-chemical properties in particular ionization constants are essential for metal-ligand stability constants and give better knowledge of the selectivity and sensitivity of relevant analytical reactions. With this view in the present investigation the thermodynamic proton-ligand stability constants of heterocyclic hydroxamic acids (I) have been determined in dioxan-water media at 25 and 35±0.1°C.

\[ X' - N \equiv OH \]
\[ X - C = 0 \]

(I)

where \( X = \text{Furan, Thiophene, } X' = \text{Phenyl, Chlorophenyl and Tolyl} \),

Since the heterocyclic hydroxamic acids are not soluble in water the mixed aqueous media has been used.

The \( pK_a \) were determined by the pH titration method using glass and saturated calomel electrode. The details of the method and calculations etc. are essentially the same
as described by Agrawal (1). Choice of dioxan-water mixture for this study has been deliberated for several reasons.

1,4 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 and metal-ligand ionic equilibria, are accurately known and easily available (1,4).

Many determinations could not be made due to the poor solubility of the hydroxamic acids in lower percentage of the dioxan.

To evaluate the free energy, enthalpy and entropy changes involved in the ionization process, the $pK_a$ of hydroxamic acids have been determined at 25 and 35°C.

It is essential to calibrate the glass electrode being used for mixed aqueous solvent, so that pH meter readings are valid for the system. Such calibration also affords a simple method for evaluation of thermodynamic data directly from the measurement. The calibration of the glass electrode has been established (1,5-7) to measure the hydrogen ion concentration $[H^+]$ from the pH meter reading (referred to as B when obtained from aqueous-mixed solutions) in dioxan-water media by the relation:
\[- \log [H^+] = B + \log U_H \tag{i}\]

where

\[\log U_H = \log U_H^0 + \log y_\pm \tag{ii}\]

or

\[- \log [H^+] = B + \log U_H^0 + \log y_\pm \tag{iii}\]

Here \(y_\pm\) is the mean activity coefficient of HCl for the solvent composition, temperature and ionic strength for which \(\log U_H\) has been determined, \(\log U_H^0\) is the correction factor at zero ionic strength which depends on the composition and temperature of the solvent media. The values of \(\log U_H^0\) which were determined by Agrawal (7) are given in Table 1.
<table>
<thead>
<tr>
<th>Dioxan % (v/v)</th>
<th>Mole fraction of Dioxan ($n_2$)</th>
<th>log $U_H^0$</th>
<th>25°C</th>
<th>35°C</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>0.174</td>
<td>0.20</td>
<td>0.24</td>
<td></td>
</tr>
<tr>
<td>60</td>
<td>0.240</td>
<td>0.40</td>
<td>0.42</td>
<td></td>
</tr>
<tr>
<td>70</td>
<td>0.330</td>
<td>0.80</td>
<td>0.83</td>
<td></td>
</tr>
</tbody>
</table>

1 Agrawal, Y.K., Talanta, 20, 1354 (1973)
Calculation of Thermodynamic Proton-Ligand Stability Constants

The thermodynamic dissociation constants \( K_{a}^{\text{aq}} \) of hydroxamic acid, HA,

\[
\text{HA} \rightleftharpoons H^+ + A^- 
\]

in an aqueous medium is given by equations (iv) and (v).

\[
K_{a}^{\text{aq}} = \frac{[H^+][A^-]}{[\text{HA}]} \cdot \frac{Y_{H^+} Y_{A^-}}{Y_{\text{HA}}} \quad \text{(iv)}
\]

\[
pK_{a}^{\text{aq}} = - \log[H^+] + \log \frac{[\text{HA}]}{[A^-]} - 2 \log y_{\pm} \quad \text{(v)}
\]

where \( y_{\pm} \) is the mean activity coefficient of a 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 \( Y_{\text{HA}} \) is unity.

By substituting the value of \( [H^+] \) concentration from equation (iii) in equation (v) we get the final equation for calculating ionization constant in mixed solvent medium.

\[
pK_{a} = B + \log U_{H} + \log \frac{[\text{HA}]}{[A^-]} + \log \frac{1}{Y_{\pm}} \quad \text{(vi)}
\]

The \( pK_{a} \) values determined are termed as thermodynamic values because they include correction due to activity coefficient. The equation (vi) can be written as

\[
pK_{a} = B + \Delta
\]
where \( \Delta = \log U_H^o + \log \frac{[HA]}{[A^-]} + \log \frac{1}{y_\pm} \)  

The values of \( \Delta \) calculated by Agrawal (1) are summarised in Tables 2-3.

The initial concentration of all acids being titrated should be same and they can be titrated in ten equal steps each corresponding to the neutralization of one-tenth equivalent to acid. So that at a particular step of all titrations, both \([HA]/[A^-]\) and \([A^-]\) will be constant.

If the hydrolysis of the salt is taken into consideration, it can be readily shown (8) that for aqueous medium equation (v) changes to

\[
pK_a(aq) = -\log [H^+] + \log \frac{[HA]}{[A^-]} + \log \frac{[OH^-]}{[OH^+]} + 2\log \frac{1}{y_\pm} \tag{viii}
\]

for mixed aqueous media. Substituting equation (iii) in equation (viii) we get

\[
pK_a = B + \log U_H^o + \log \frac{[HA]}{[A^-]} + \log \frac{[OH^-]}{[OH^+]} + \log \frac{1}{y_\pm} \tag{ix}
\]
### TABLE 2

Values of $\Delta^*$ at 25°C.

\[ \Delta = \log U_H^* + \log \frac{[HA]}{[A^-]} + \log \frac{1}{y_\pm} \]

<table>
<thead>
<tr>
<th>Dioxan, volume per cent</th>
<th>50</th>
<th>60</th>
<th>70</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dioxan, Mole fraction (n2)</td>
<td>0.174</td>
<td>0.240</td>
<td>0.330</td>
</tr>
<tr>
<td>[HA]</td>
<td>0.009</td>
<td>0.008</td>
<td>0.007</td>
</tr>
<tr>
<td>[A^-]</td>
<td>0.001</td>
<td>0.002</td>
<td>0.003</td>
</tr>
<tr>
<td>Values of $\Delta$</td>
<td>1.19</td>
<td>0.87</td>
<td>0.67</td>
</tr>
<tr>
<td></td>
<td>1.43</td>
<td>1.13</td>
<td>0.92</td>
</tr>
<tr>
<td></td>
<td>1.87</td>
<td>1.61</td>
<td>1.43</td>
</tr>
</tbody>
</table>

TABLE 3

Values of $\Delta^*$ at 35°C.

$$\Delta = \log \mathcal{U}_H^0 + \log \frac{[HA]}{[A^-]} + \log \frac{1}{y_\pm}$$

<table>
<thead>
<tr>
<th>Dioxan, volume per cent</th>
<th>50</th>
<th>60</th>
<th>70</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dioxan, Mole fraction ($n_2$)</td>
<td>0.174</td>
<td>0.240</td>
<td>0.330</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>$[HA]$</th>
<th>$[A^-]$</th>
<th>Values of $\Delta$</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.009</td>
<td>0.001</td>
<td>1.25 1.47 1.92</td>
</tr>
<tr>
<td>0.008</td>
<td>0.002</td>
<td>0.93 1.16 1.65</td>
</tr>
<tr>
<td>0.007</td>
<td>0.003</td>
<td>0.71 0.95 1.47</td>
</tr>
<tr>
<td>0.006</td>
<td>0.004</td>
<td>0.53 0.77 1.30</td>
</tr>
<tr>
<td>0.005</td>
<td>0.005</td>
<td>0.36 0.61 1.15</td>
</tr>
<tr>
<td>0.004</td>
<td>0.006</td>
<td>0.20 0.45 0.99</td>
</tr>
<tr>
<td>0.003</td>
<td>0.007</td>
<td>0.02 0.27 0.82</td>
</tr>
<tr>
<td>0.002</td>
<td>0.008</td>
<td>-0.21 0.05 0.61</td>
</tr>
<tr>
<td>0.001</td>
<td>0.009</td>
<td>-0.55 -0.29 0.27</td>
</tr>
</tbody>
</table>

Thermodynamic Functions for Ionic Equilibria

The standard free energy $\Delta G^\circ$ of the ionization reaction, $HA \rightleftharpoons H^+ + A^-$, can be determined from the following equation.

$$\Delta G^\circ = 2.303 \, RT \, pK_a$$

which can be simplified as:

$$\Delta G^\circ (298.2^\circ) = 5.711 \, pK_a \, (K_j) \quad \text{for} \ 25^\circ C \quad (x)$$

$$\Delta G^\circ (308.2^\circ) = 5.904 \, pK_a \, (K_j) \quad \text{for} \ 35^\circ C \quad (xii)$$

The standard enthalpy change $\Delta H^\circ \ (K_j)$ is obtained by integrating the Van't Hoff equation for two temperatures $T_1$ and $T_2$:

$$\log \frac{K_2}{K_1} = \frac{\Delta H^\circ (T_2 - T_1)}{19.146 \, T_1 \, T_2} \quad (xiii)$$

Equation (xiii) is approximate, since $\Delta H^\circ$ varies with temperature. For measurement at 25 and 35°C equation (xiii) can be simplified as

$$\Delta H^\circ \ (K_j) = 176.02 \ \Delta pK_a \quad (xiv)$$

The standard entropy changes, $\Delta S^\circ$ is calculated from the Gibbs-Halmholtz equation.

$$-\Delta S^\circ = \frac{\Delta G^\circ - \Delta H^\circ}{T} \quad (xv)$$
At 25 and 35°C equation (xv) can be written as:

\[-\Delta S^\circ (\text{Kj}) = 14.033 \times 10^{-3} \ (\Delta G^\circ - \Delta H^\circ) \quad \text{for 25°C} \ (\text{xv a})\]

\[-\Delta S^\circ (\text{Kj}) = 13.573 \times 10^{-3} \ (\Delta G^\circ - \Delta H^\circ) \quad \text{for 35°C} \ (\text{xv b})\]
EXPERIMENTAL

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

Heterocyclic hydroxamic acids

These were synthesised by the general method of Agrawal and Tandon (10). The purity of the acids was established by mp, elemental analysis, UV and IR spectra.

Dioxan

p-Dioxan was purified by the method of Weissberger (11). It was refluxed over KOH pellets for 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°-11.80°C against the reported range 11.65°-12.00°C (12,13).

Distilled water

Pure distilled water was redistilled over alkaline potassium permanganate and was tested for absence of carbonate by Kolthoff's method (9).

pH meter

The Elico pH meter, Model LI 120, equipped with combined glass and calomel electrodes was used.
Carbonate free potassium hydroxide:

Carbonate free potassium hydroxide was prepared by electrolysis according to the method described by Vogel (35) and diluted to 0.1 M with the desired solvent media.

Determination of ionization constants:

The method of titration for determining ionization constants, was essentially the same as given by Agrawal (1,2). In a three-necked titration vessel, thermostated at 25 and 35±0.1°C, 0.01 M hydroxamic acid in 47.5 ml of the solvent of desired composition was titrated, without addition of inert salt (ionic strength not adjusted) with 0.5 ml increments of 0.1 M KOH, after being deoxygenated by passing nitrogen (presaturated with solvent) for 15 min. The highest steady B value i.e. pH meter reading, being noted after each increment.
RESULTS AND DISCUSSION

A large number of potentiometric titrations have been performed to determine pK\(_a\) of heterocyclic hydroxamic acids. pK\(_a\) of some of these acids have been reported potentiometrically (36, 37). The data on the thermodynamic ionization constants of heterocyclic hydroxamic acids in various dioxan-water media (50, 60 and 70% v/v) at 25 and 35°C are given in Tables 4-5. The average pK\(_a\) generally falls within a spread of ±0.02 but not beyond ±0.03. The pK\(_a\)'s are plotted against mole fraction of dioxan (n\(_2\)) (Figs. 1-8) and the empirical relations derived are given in Table 6. The pK\(_a\) of hydroxamic acids are plotted against the reciprocal of dielectric constants of the solvent media shown in Figs. 9-12. The values of thermodynamic functions \(\Delta G^o\), \(\Delta H^o\) and \(\Delta S^o\) are summarised in Table 7.

Hydroxamic acids are very weak acids 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 (II) which has been proved by IR spectroscopic studies (14-16).

\[
\begin{array}{c}
\text{-} \quad \text{N} \quad \text{O} \\
\bigg| \\
\text{-} \quad \text{C} \quad \text{= O} \\
\end{array}
\]

(II)
**TABLE 4**

Thermodynamic ionization constants of heterocyclic hydroxamic acids in Dioxan-water media at 25°C.

<table>
<thead>
<tr>
<th>Compd. No.</th>
<th>Hydroxamic acid</th>
<th>( \text{pK}_a )</th>
<th>Mole fraction of dioxan, n2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>0.174</td>
<td>0.240</td>
</tr>
<tr>
<td>I</td>
<td>N-Ph-2-furo-</td>
<td>10.58</td>
<td>11.40</td>
</tr>
<tr>
<td>II</td>
<td>N-p-tolyll-2-furo-</td>
<td>11.10</td>
<td>11.82</td>
</tr>
<tr>
<td>III</td>
<td>N-p-c-ph-2-furo-</td>
<td>11.00</td>
<td>11.72</td>
</tr>
<tr>
<td>IV</td>
<td>N-m-c-ph-2-furo-</td>
<td>10.85</td>
<td>11.60</td>
</tr>
<tr>
<td>V</td>
<td>N-ph-2-theno-</td>
<td>10.61</td>
<td>11.45</td>
</tr>
<tr>
<td>VI</td>
<td>N-p-tolyll-2-theno-</td>
<td>11.15</td>
<td>11.90</td>
</tr>
<tr>
<td>VII</td>
<td>N-p-c-ph-2-theno-</td>
<td>11.05</td>
<td>11.77</td>
</tr>
<tr>
<td>VIII</td>
<td>N-m-c-ph-2-theno-</td>
<td>10.90</td>
<td>11.65</td>
</tr>
</tbody>
</table>
TABLE 5

Thermodynamic ionization constants of heterocyclic hydroxamic acids in Dioxan-water media at 35°C.

<table>
<thead>
<tr>
<th>Compd. Hydroxamic acid No.</th>
<th>$pK_a$</th>
<th>Mole fraction of dioxan, $n_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>0.174</td>
</tr>
<tr>
<td>I N-ph-2-furo-</td>
<td>10.58</td>
<td>11.40</td>
</tr>
<tr>
<td>II N-p-tolyl-2-furo-</td>
<td>11.10</td>
<td>11.82</td>
</tr>
<tr>
<td>III N-p-c-pn-2-furo-</td>
<td>11.00</td>
<td>11.72</td>
</tr>
<tr>
<td>IV N-m-c-ph-2-furo-</td>
<td>10.85</td>
<td>11.60</td>
</tr>
<tr>
<td>V  N-ph-2-theno-</td>
<td>10.61</td>
<td>11.45</td>
</tr>
<tr>
<td>VI N-p-tolyl-2-theno-</td>
<td>11.15</td>
<td>11.90</td>
</tr>
<tr>
<td>VII N-p-c-ph-2-theno-</td>
<td>11.05</td>
<td>11.77</td>
</tr>
<tr>
<td>VIII N-m-c-ph-2-theno-</td>
<td>10.90</td>
<td>11.65</td>
</tr>
</tbody>
</table>
Effect of media

Since the hydroxamic acids have very low solubility in water therefore the equilibrium studies have been carried out in mixed solvents. The mixture of water and dioxan appears to be the most convenient. It may be due to the existence of a linear relationship between the pK\textsubscript{a}s, of hydroxamic acid and reciprocal of dielectric constant and mole fraction of dioxan (1-4).

Mole fraction of Dioxan

It has been observed by Agrawal, that the pK\textsubscript{a} of hydroxamic acids increases with the increase in mole fraction of dioxan (n\textsubscript{2}), (1-3,17-22). This is because a solvent of low dielectric constant increases the electrostatic force between the ions and thereby facilitates the formation of molecular species.

The pK\textsubscript{a} of hydroxamic acids are plotted against the mole fraction of dioxan and a linear relationship is observed (Figs. 1-8). The experimental values of pK\textsubscript{a} for almost all hydroxamic acids show a maximum deviation of 0.05 or about 0.5% in pK\textsubscript{a} from linearity. Linear equations between pK\textsubscript{a} and n\textsubscript{2} and correlation coefficients, \(r\), given in Table 6, have been calculated by method of least square. The pK\textsubscript{a} at lower mole fraction of dioxan (i.e. less than 0.174) could not be determined because the acids were insoluble.
Empirical correlation between pK\textsubscript{a} and mole fraction of Dioxan for heterocyclic hydroxamic acids at 25 and 35°C.

<table>
<thead>
<tr>
<th>Compd. No.</th>
<th>Hydroxamic acid</th>
<th>pK\textsubscript{a} = mn\textsubscript{2} + c</th>
<th>m</th>
<th>c</th>
<th>r</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>N-ph-2-furo</td>
<td></td>
<td>12.56</td>
<td>8.38</td>
<td>1.000</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(12.76)</td>
<td>(8.19)</td>
<td>(1.000)</td>
</tr>
<tr>
<td>II</td>
<td>N-p-tolyl-2-furo-</td>
<td></td>
<td>11.02</td>
<td>9.17</td>
<td>1.000</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(10.88)</td>
<td>(9.03)</td>
<td>(1.000)</td>
</tr>
<tr>
<td>III</td>
<td>N-p-c-ph-2-furo-</td>
<td></td>
<td>10.95</td>
<td>9.09</td>
<td>1.000</td>
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<td></td>
<td></td>
<td></td>
<td>(11.15)</td>
<td>(8.89)</td>
<td>(1.000)</td>
</tr>
<tr>
<td>IV</td>
<td>N-m-c-ph-2-furo-</td>
<td></td>
<td>11.27</td>
<td>8.88</td>
<td>1.000</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>(11.21)</td>
<td>(8.77)</td>
<td>(1.000)</td>
</tr>
<tr>
<td>V</td>
<td>N-ph-2-theno-</td>
<td></td>
<td>12.82</td>
<td>8.37</td>
<td>1.000</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(12.82)</td>
<td>(8.22)</td>
<td>(1.000)</td>
</tr>
<tr>
<td>VI</td>
<td>N-p-tolyl-2-theno-</td>
<td></td>
<td>11.40</td>
<td>9.16</td>
<td>1.000</td>
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<td></td>
<td></td>
<td></td>
<td>(11.34)</td>
<td>(8.99)</td>
<td>(1.000)</td>
</tr>
<tr>
<td>VII</td>
<td>N-p-c-ph-2-theno-</td>
<td></td>
<td>10.95</td>
<td>9.14</td>
<td>1.000</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(11.02)</td>
<td>(8.94)</td>
<td>(1.000)</td>
</tr>
<tr>
<td>VIII</td>
<td>N-m-c-ph-2-theno-</td>
<td></td>
<td>11.47</td>
<td>8.89</td>
<td>1.000</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(11.15)</td>
<td>(8.80)</td>
<td>(1.000)</td>
</tr>
</tbody>
</table>

The values in parentheses are at 35°C.

r = Correlation coefficient
FIG. 1 VARIATION OF pKa WITH MOLE FRACTION OF DIOXAN
FIG. 2 VARIATION OF pK_a WITH MOLE FRACTION OF DIOXAN
FIG. 3 VARIATION OF $pK_a$ WITH MOLE FRACTION OF DIOXAN
FIG. 4 VARIATION OF pKₐ WITH FRACTION OF DIOXAN
FIG. 5 VARIATION OF pK WITH MOLE FRACTION OF DIOXAN
FIG. 6 VARIATION OF $pK_a$ WITH MOLE FRACTION OF DIOXAN
FIG. 7 VARIATION OF pKa WITH MOLE FRACTION OF DIOXAN

VII

\[ \text{Mole fraction of dioxan (n_2)} \rightarrow \]

\[ \begin{array}{c}
\text{Cl} \\
\text{N—OH} \\
\text{C=S}
\end{array} \]

FIG. 7 VARIATION OF pKa WITH MOLE FRACTION OF DIOXAN
FIG. 8 VARIATION OF $pK_a$ WITH MOLE FRACTION OF DIOXAN
Effect of Substituent on the $pK_a$

Table 4 results that the hydroxamic acid derived from 2-thenoic acid are having the higher $pK_a$ values than those derived from 2-furoic acid. The relative high strength in the substituted furohydroxamic acid may be due to that the electron attraction nature of the furan oxygen compared to the sulphur of thiophene. The introduction of methyl group usually exhibits weak selection-repulsive character (+I) and fails to reveal any polar influence as shown by the negative dipole moments and hence there is a decrease in acid strength. Thus (Table 4) $\text{CH}_3 > H$; e.g. $pK_a$, compound II $> I$ and similarly VI $> V$. When halogen (Cl) is attached to aromatic nucleus (N-phenyl ring) have -I (inductive) and +T (tautomeri) properties and hence causes increase in acid strength. The electron withdrawing effects are less at para position than in the meta position and hence the order of the acid is as under (Table 4).

$pK_a$; Compound III $> IV$ and similarly VII $> VIII$. 
Dielectric constants

The effect of solvent on the Gibbs energy for the dissociation of a weak acid has sometimes been ascribed to a change in the electrostatic self energy of the ions. Gurney (24) and others (25,26), have pointed out the standard free energy change of proton transfer may be considered in two parts, electrostatic (ΔG°el) and nonelectrostatic (ΔG°non). The simplest expression for electrostatic energy of a mole of univalent ions is that of Born (27).

\[ \Delta G°_{el} = \frac{N e^2}{2} \left( \frac{1}{D_s} - \frac{1}{D_w} \right) \left( \frac{1}{r^+} + \frac{1}{r^-} \right) \]  

(xvi)

Where \( N \) is the Avogadro number, \( e \) is the electronic charge, \( D \) is the dielectric constant of the medium and \( r_s \) the radius of the ion. The dissociation of a weak acid in the mixture of the solvents of a charge type \( HA \rightleftharpoons H^+ + A^- \), the electrostatic forces between the cation and anion are increased and formation of molecular species is facilitated (28). The change in the energy on the transfer from water to 70% dioxan is then

\[ \Delta G°_{el} = \frac{N e^2}{2} \left( \frac{1}{D_s} - \frac{1}{D_w} \right) \left( \frac{1}{r^+} + \frac{1}{r^-} \right) \]

where \( D_s \) is the dielectric constant of dioxan-water per cent and \( D_w \) is that of water. For \( \Delta G°_{el} \) in KJ mol\(^{-1}\) (1 KCal = 4.184 KJ) and ionic radius in Angstroms, equation (xvi) becomes (xvii).
The equation (xvii) derived from simple electrostatic consideration, shows that the free energy of transfer should be positive when the dielectric constant of the solvent $D_S$ is less than that of the water. The free energy and escaping tendency of the ionic species are greater in 'S' than in 'water', and the medium effect is positive.

<table>
<thead>
<tr>
<th>Dioxan %</th>
<th>Mole fraction of dioxan ($n_2$)</th>
<th>Dielectric constant ($D_S$)</th>
<th>$\Delta G^\circ$ KJ mol$^{-1}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>0.023</td>
<td>68.5</td>
<td>0.75</td>
</tr>
<tr>
<td>20</td>
<td>0.050</td>
<td>60.5</td>
<td>1.51</td>
</tr>
<tr>
<td>30</td>
<td>0.083</td>
<td>51.8</td>
<td>2.59</td>
</tr>
<tr>
<td>40</td>
<td>0.123</td>
<td>42.5</td>
<td>4.31</td>
</tr>
<tr>
<td>50</td>
<td>0.174</td>
<td>33.0</td>
<td>6.99</td>
</tr>
<tr>
<td>60</td>
<td>0.240</td>
<td>25.7</td>
<td>10.37</td>
</tr>
<tr>
<td>70</td>
<td>0.330</td>
<td>17.5</td>
<td>17.65</td>
</tr>
</tbody>
</table>

Where transfer free energy for hydrochloric acid (mole fraction scale) are calculated by equation (xvii), $r_+$ and $r_-$ were taken to 2.8 and 4.6 Å, respectively (29,30), on presumption that each ion surrounded by a primary solvation layer of water molecules.
Bates, Robinson and others (25,31) have shown that non-electrostatic residuals $\Delta G^o$ (non) calculated from Gibbs energy of dissociation $\Delta G^o_{\text{diss}}$ for a series of weak acids by

\[ \Delta G^o_{\text{diss}} = \Delta G^o_{\text{el}} + \Delta G^o_{\text{non}} \] (xviii)

substituting the value of $\Delta G^o_{\text{el}}$ from equation (xvi) in equation (xviii)

\[ \Delta G^o_{\text{diss}} = \Delta G^o_{\text{non}} + \frac{N e^2}{2} \left( \frac{1}{D_S} - \frac{1}{D_W} \right) \left( \frac{1}{r_+} + \frac{1}{r_-} \right) \] (xix)

Further on substitution of $G^o_{\text{diss}} = 2.303 \text{ RT pK}_a$, equation (xix) becomes

\[ \text{pK}_a = \frac{\Delta G^o_{\text{non}}}{2.303 \text{RT}} + \frac{N e^2}{4.606 \text{RT}} \left( \frac{1}{D_S} - \frac{1}{D_W} \right) \left( \frac{1}{r_+} + \frac{1}{r_-} \right) \] (xx)

assuming $\Delta G^o_{\text{non}}$ to be independent of the solvent. It is conventional to plot pK$_a$ against 1/D assuming $\Delta G^o_{\text{non}}$ to be independent of the solvent. In several cases nearly linear relations have been reported (32-34), especially for water rich media, but so has non-linearity (32).

When the pK$_a$ of heterocyclic hydroxamic acids are plotted against 1/D it gives a distinct curvature, Figs.9-12, and evidently the non-electrostatic factors have a considerable influence on the dissociation of hydroxamic acids.

Moreover the plot of change in free energy from mixed aqueous media to aqueous media (extrapolated pK$_a$), it's
FIG. 9 VARIATION OF $pK_a$ WITH THE DIELECTRIC CONSTANT OF THE MEDIUM.
FIG. 10 VARIATION OF $pK_a$ WITH THE DIELECTRIC CONSTANT OF THE MEDIUM.

25 °C

$pK_a$

$14.0$

$13.0$

$12.0$

$11.0$

$10.0$

$9.0$

$3.0$ $4.0$ $5.0$ $6.0$

$100/D$
FIG. II VARIATION OF $pK_a$ WITH THE DIELECTRIC CONSTANT OF THE MEDIUM.
FIG. 12 VARIATION OF pKa WITH THE DIELECTRIC CONSTANT OF THE MEDIUM.

35 °C
values versus dioxan per cent where \( \delta = \Delta G^0_S - \Delta G^0_W \).

\( \Delta G^0_W \) and \( \Delta G^0_S \) refer to the standard free energy changes in pure water as solvent and in aqueous or organic mixture as solvent, respectively; shows a distinct curvature. Furthermore, a change in the dielectric constant and the consequent change in the shape and size of the individual ions, hydrogen bonding, and other specific forms of solvent-solute interaction also have an appreciable influence on the dissociation of hydroxamic acids.

**Effect of Temperature**

The ionization constant is a function of temperature and generally it has maximum value \( K_a \) (max) or \( pK_a \) (min), near the room temperature. The data given in Tables 4-5 show that the \( pK_a \) of all hydroxamic acids in all the solvent media are lower at 35° than at 25°C. Their temperature of maximum \( K_a \), \( T_{max} \), can be known if \( pK_a \) are determined at several temperatures.

**Thermodynamic Functions**

The data on \( \Delta G^0, \Delta H^0 \) and \( \Delta S^0 \) are given in Table 7. The temperature coefficient method used here for calculation of \( \Delta H^0 \) is subject to a large error because the enthalpy change during acid ionization is small, and \( pK_a \) at a series of temperatures are not determined which, otherwise, would have enabled the adoption of more precise graphical method (23).
<table>
<thead>
<tr>
<th>Compd. No.</th>
<th>( \Delta G^o )</th>
<th>( \Delta H^o )</th>
<th>( -\Delta S^o )</th>
<th>( \Delta G^o )</th>
<th>( \Delta H^o )</th>
<th>( -\Delta S^o )</th>
<th>( \Delta G^o )</th>
<th>( \Delta H^o )</th>
<th>( -\Delta S^o )</th>
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<td>60.42</td>
<td>28.16</td>
<td>0.45</td>
<td>65.10</td>
<td>26.40</td>
<td>0.54</td>
<td>71.56</td>
<td>22.88</td>
<td>0.68</td>
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<td></td>
<td>(61.52)</td>
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<td>(67.50)</td>
<td>(68.78)</td>
<td>(68.25)</td>
<td>(73.20)</td>
<td>(74.51)</td>
<td>(74.21)</td>
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<tr>
<td>II</td>
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<td>0.470</td>
<td>67.50</td>
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<td>0.53</td>
<td>73.16</td>
<td>33.44</td>
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<td>(74.21)</td>
<td>(74.51)</td>
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<td>(0.56)</td>
</tr>
<tr>
<td>III</td>
<td>62.82</td>
<td>28.16</td>
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<td>72.53</td>
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<td>(73.62)</td>
<td>(73.62)</td>
<td>(73.62)</td>
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<tr>
<td>V</td>
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<td>(75.22)</td>
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<td>(74.27)</td>
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<td>(74.27)</td>
<td>(0.60)</td>
</tr>
<tr>
<td>VIII</td>
<td>62.25</td>
<td>26.40</td>
<td>0.50</td>
<td>66.53</td>
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<td>0.49</td>
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<td>(73.68)</td>
<td>(73.68)</td>
<td>(73.68)</td>
<td>(73.68)</td>
<td>(0.52)</td>
</tr>
</tbody>
</table>

\( \Delta G^o, \Delta H^o \) and \( -\Delta S^o \) are in k.J. The values in parentheses are at 35°C.
for its evaluation. It is apparent from equation (xiii) that an error of 0.01 in $pK_a$ causes an error of 1.76 KJ in $\Delta H^o$ while the magnitude of error in $\Delta pK_a$ depends on the cancelation or addition of errors of an individual set of $pK_a$ determined at two temperatures.

Despite the relative large error in the value of $\Delta H^o$ computed by the temperature coefficient method the data are still of great significance for drawing certain valuable conclusions. In any case, the positive value of $\Delta H^o$ which 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 and will be exothermic only above $T_{\text{max}}$. Further it is certain that the magnitude of change in $\Delta H^o$ with change in media is relatively small and is within the range of experimental error. Hence the slopes of straight lines in the plots of $pK_a$ vs. $n_2$ are either same or nearly same at the two temperatures for individual hydroxamic acids (Table 6).

In other words, the two lines are parallel. It has been observed that there is a general tendency of increase in magnitude of $\Delta S^o$ with increase in dioxan 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 $2.303 \, RT \, \Delta pK_a$, e.g. with N-p-chlorophenyl-2-furo-hydroxamic acid, $\Delta G^o (n_2=0.174)$ and $\Delta G^o (n_2=0.330)$ is 62.82 and 72.53 KJ mol$^{-1}$, respectively and $\Delta G^o$ change 9.71 KJ mol$^{-1}$ in the transfer reaction.
REFERENCES


