CHAPTER V

BASE STRENGTH OF HYDROXAMIC ACIDS
BASE STRENGTH OF HYDROXAMIC ACIDS

N-Arylhydroxamic acids behave as weak organic bases in presence of strong mineral acid solutions. Their protonation behaviour has been studied in presence of perchloric acid following the Hammett Acidity Function Method, Bunnett-Olsen Method and Excess Acidity Method. The protonation parameters evaluated are, protonation constants \( pK_{BH^+} \), values of slopes \( m, \phi \) and \( m^* \), and correlation coefficients \( r \), for the protonation reaction.

For the estimation of \( pK_{BH^+} \), distribution ratios of these metal extractants between an inert organic solvent and 1-10M perchloric acid solutions are determined. Percentage of protonated hydroxamic acid as a function of perchloric acid concentration is also estimated.
BASE STRENGTH OF HYDROXAMIC ACIDS

The basicity of organic molecules in strong acid media is the major area of physical-organic chemistry with many practical and theoretical implications. The most common measure of basicity has traditionally been the $pK_{BH+}$ of the conjugate acid of the base. The problem of estimating $pK_{BH+}$ of hydroxamic acids is still a subject of great interest because these reagents are naturally occurring compounds and exhibit several biological and medicinal activities as highlighted in CHAPTER I. The hydroxamic acid functional group, which is responsible for such activities, is the outstanding chemical feature of these molecules.

A substantial number of natural products contain one or more oxidised peptide bonds –CON(OH), which is similar to hydroxamic acid functional group (43). In living cells, protein is converted into peptide, and is digested by gastric juices including mineral acid. Further, literature screening shows that these reagents also serve as PDF (peptide deformylase) inhibitors (93). PDF is a metallo-enzyme which utilizes iron ($Fe^{2+}$) as the catalytic metal for $N$-formyl hydrolysis (196). The metal is co-ordinated to two histidine residues, one cysteine residue, and a molecule of water, which can donate a proton. Thus, understanding of base strength of these reagents is an important factor in research areas such as pharmaceutical drug discovery and development, where knowledge of the $pK_{BH+}$ of a particular functional group is often vital to understand the pharmacokinetic (197) and pharmacodynamic properties of new drug substances, and will help to understand the physiology of the biochemical reactions involving hydroxamic acids.

Review of literature shows a number of methods have been adopted to study the trend of protonation of different compounds including weak bases. Potentiometric methods are included among the most useful for the determination of the protonation constants of a monoprotic acid–base systems. Potentiometric methods are considered to be more precise, but they cannot be applied to systems in which protonation constant is either particularly high or low. Spectrophotometric method has the advantage to being suitable in extreme cases.

The hydroxamic acid functional group is weakly basic in nature, $pK_{BH+}$ being less than zero, hence requires a non-ideal concentrated acid mixture to undergo protonation.
Thus, in the framework of our researches (156-158, 161-162) in the field of protonation studies on weak organic bases, the base strength of ten hydroxamic acids, included in CHAPTER II, are determined following the old classical method of Arnett (198, 199) in perchloric acid solutions. This method can be used when the absorbance of protonated and unprotonated species cannot be determined directly.

EXPERIMENTAL

APPARATUS

As described in earlier CHAPTERS.

A pentium III with 60MB RAM + 30GB HDD computer was used for slope determination and calculations.

CHEMICALS

These have also been described in CHAPTERS II and III.

Analytical grade perchloric acid was used for determining distribution ratios. Perchloric acid was standardised with sodium hydroxide solution, which was standardised against potassium hydrogen phthalate. Phenolphthalein was used as an indicator. Acidic mixtures of different concentrations were prepared by dilution of concentrated acid with glass distilled water.

Carbontetrachloride used was of analytical grade.

MEASUREMENT OF DISTRIBUTION RATIOS, D, AS A FUNCTION OF PERCHLORIC ACID CONCENTRATIONS

For the determination of distribution ratios of these reagents as a function of acid concentrations, a quick technique was adopted to minimise the time of shaking, using mechanical stirrer with teflon leaf (156). It was observed that with sufficient shaking, equilibrium could be achieved within five minutes and provides fairly reproducible results.
A solution of small amount of reagent 20–25 mg in carbon tetrachloride was shaken with perchloric acid solutions of increasing acidity, 1–10M. The volumes of the two phases to be taken were dependent on the magnitude of D. After separation, the phases were analysed following the vanadium (V) method.

All the experiments were done thrice.

ANALYSIS OF PHASES

Hydroxamic acid concentration in the sample solutions, were determined spectrophotometrically using solvent extraction method, as described in CHAPTER III. Although, this method is more time consuming, it gives reproducible and accurate results.

RESULTS AND DISCUSSION

An ability to accurately measure the dissociation constant, $pK_{BH^+}$, for the conjugate acid, BH+, of a weak base B, is essential to understand the reactions that are subject to acid catalysis. In the absence of a reliable value for the dissociation constant, it is impossible to quantitatively analyse the kinetics of reactions that are catalysed by acids. Due to importance of such reactions in organic chemistry and biochemistry, the attempts were made to estimate $pK_{BH^+}$ values of hydroxamic acids in perchloric acid solutions.

Weak organic bases protonated as follows,

$$ B + H^+ \rightleftharpoons BH^+ \quad [1] $$

and the protonation equilibrium or dissociation constant, $pK_{BH^+}$ for the conjugate acid, BH+ of base B, is derived for the reverse of the equation [1]. $pK_{BH^+}$ of organic bases are obtained from an analysis of the variation of some physical properties of the substrate with changing acid concentration. The three properties most commonly used are — (i) the uv–visible spectrum (200–210), (ii) $^1H$ spectrum (211–220) and (iii) $^{13}C$ n.m.r. spectrum (221–223). The change observed with increasing acidity is from spectrum
characteristics of a free base to that of the protonated form. In the present investigation, as the free base and its protonated species do not differ appreciably in their uv properties, hence we apply the solvent extraction technique using visible spectroscopy. Indeed, this method should be capable of yielding more reliable $pK_{BH+}$ values. This chapter describes the protonation behaviour of hydroxamic acids in perchloric acid solutions. Perchloric acid is a monobasic acid and is much more completely dissociated in concentrated solutions renders it an attractive medium for mechanistic studies.

For equation [1], the protonation analysis of hydroxamic acids is done following the three classical procedures –

A. Hammett Acidity Function Method (HAFM).
B. Bunnett–Olsen Method (BOM).
C. Excess Acidity Method (EAM).

The following requirements must be made before $pK_{BH+}$ values can be determined accurately by applying these procedures.

1. **SUITABLE ACIDITY FUNCTION FOR HAFM**

For a weak base, B, which only becomes significantly protonated in strongly acidic media, $pK_{BH+}$ can be defined as the acid dissociation constant of the protonated form BH$^+$ and can be calculated following the equation –

$$pK_{BH^+} = \log I = H_0$$  \[2\]

where, $H_0$ is the Hammett acidity function and $I$ is the ionization ratio, which is the ratio of the concentrations of protonated and unprotonated species.

$$I = \frac{C_{BH^+}}{C_B}$$  \[3\]

where, $C_{BH^+}$ = molar concentration of protonated base.

$C_B$ = molar concentration of unprotonated base.
2. **MEASUREMENT OF IONIZATION RATIO, I**

For the measurement of I, the first requirement for all the methods is that, measurements are made under conditions, where significant amount of the free base and protonated form are present, simultaneously in solution. In the present investigation, protonation equilibria by UV method cannot be studied because of insufficient differences between the spectra of the substrate and its conjugate acid. Tillet had also faced this difficulty (154). At the same time, hydroxamic acids investigated here are very weak bases, in such systems, conditions may not exist under which it is both fully protonated and stable. Thus, the protonation equilibria are determined, following the solvent extraction technique (156), using visible spectroscopy. This method can be used, when the absorbance of B and BH⁺ cannot be determined directly. For such systems, the most widely quoted reference source for pKₐ BH⁺ has been 1963 review by Arnett (198). According to him, the weak bases are protonated into their conjugate acids in presence of strong acidic solution, and the distribution ratio, D, of a base between organic solvent and aqueous acidic solutions is a function of the respective concentrations. Thus, the ionization ratio can be measured by the equation, that describes the variation of distribution ratio, D, with changing acidity, as in the following equation –

\[ I = \frac{K_0 - D}{D} \]  

[4]

**DISTRIBUTION CONSTANT, K₀**

K₀ is thermodynamic distribution constant of hydroxamic acid between the organic layer and aqueous acids in the region where appreciable protonation is occurring, and is estimated by least square method. The organic solvent chosen for this kind of study is carbontetrachloride, it was found to be most suitable for physico-chemical studies, because of its favourable physical properties, such as non-polar inert solvent, adequate difference in density from water, low dielectric constant and vapour pressure, zero dipole moment and very low mutual solubility with water (224).

**DISTRIBUTION RATIO, D**

D is the distribution ratio of hydroxamic acids between carbontetrachloride and perchloric acid solutions of different molarity.
For the equation [1]

\[ D = \frac{[B]_{\text{org}}}{[B]_{\text{aq}} + [BH^+]} \]  \hspace{1cm} [5]

In strong acidic solutions –

\[ D = \frac{[B]_{\text{org}}}{[B]_{\text{aq}} + [BH^+]_{\text{aq}}} \]  \hspace{1cm} [6]

Applying the law of mass action in the reverse equation.

\[ K_{BH^+} = \frac{a_{H^+} + a_B}{a_{BH^+}} \]  \hspace{1cm} [7]

or

\[ K_{BH^+} = a_{H^+} \frac{f_B}{f_{BH^+}} \cdot \frac{[B]}{[BH^+]} \]  \hspace{1cm} [8]

since

\[ h_0 = a_{H^+} \cdot f_{H^+}/H_{H^+} \]  \hspace{1cm} [9]

\[ K_{BH^+} = h_0 \frac{[B]}{[BH^+]} \]  \hspace{1cm} [10]


\[ D = \frac{[B]_{\text{org}}}{[B]_{\text{aq}} + \frac{h_0[B]_{\text{aq}}}{K_{BH^+}}} \]  \hspace{1cm} [11]

or

\[ D = \frac{[B]_{\text{org}}}{1 + \frac{h_0}{[B]_{\text{aq}} \cdot K_{BH^+}}} \]  \hspace{1cm} [12]
as

\[ K_d = \frac{[B]_{aq}}{[B]_{eq}} \]  \hspace{1cm} [13]

Therefore,

\[ D = \frac{K_d}{1 + \frac{h_0}{K_{BH^+}}} \]  \hspace{1cm} [14] \]

\[ K_d = D + \frac{Dh_0}{K_{BH^+}} \]  \hspace{1cm} [15] \]

\[ \frac{K_d - D}{D} = \frac{h_0}{K_{BH^+}} \]  \hspace{1cm} [16] \]

\[ pK_{BH^+} - H_0 = \log \frac{K_d - D}{D} \]  \hspace{1cm} [17] \]

or

\[ pK_{BH^+} = H_0 + \log \frac{K_d - D}{D} \]  \hspace{1cm} [18] \]

and \( \frac{K_d - D}{D} \) = I, the ionization ratio.

The values of \( K_d \) and \( D \) are presented in Table 1. Figures 11-20 are the plots of \( D \) vs perchloric acid molarity. As the acid concentration increases, the values of distribution ratio decreases. This suggests that protonated hydroxamic acids are hydrophilic in nature.

The solvent extraction method described in CHAPTER III is used to determine the total concentration of both the molecular and protonated species. It is an ideal method for the study of sparingly soluble substances or those substances, whose constants are particularly low or high. Solvent extraction method has the advantage that the occurrence of the side reactions does not necessarily invalidate the measurement.
# TABLE 1.
DISTRIBUTION RATIOS OF HYDROXAMIC ACIDS BETWEEN ORGANIC SOLVENT AND AQUEOUS PERCHLORIC ACID SOLUTIONS AT 25°C

<table>
<thead>
<tr>
<th>S.No.</th>
<th>HYDROXAMIC ACID</th>
<th>$K_n$</th>
<th>PERCHLORIC ACID, M</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>1.</td>
<td>N-Phenyl-2-methylbenzo-</td>
<td>6.13</td>
<td>17.10</td>
</tr>
<tr>
<td>2.</td>
<td>N-Phenyl-4-ethoxybenzo-</td>
<td>63.30</td>
<td>152.16</td>
</tr>
<tr>
<td>3.</td>
<td>N-o-Tolyl-2-methylbenzo-</td>
<td>22.42</td>
<td>51.48</td>
</tr>
<tr>
<td>4.</td>
<td>N-o-Tolyl-4-ethoxybenzo-</td>
<td>49.14</td>
<td>115.53</td>
</tr>
<tr>
<td>5.</td>
<td>N-o-Tolylphenoxyacet-</td>
<td>4.51</td>
<td>9.46</td>
</tr>
<tr>
<td>6.</td>
<td>N-o-Tolyl-4-Chlorobenzo-</td>
<td>84.05</td>
<td>179.71</td>
</tr>
<tr>
<td>7.</td>
<td>N-m-Tolylbenzo-</td>
<td>11.24</td>
<td>26.40</td>
</tr>
<tr>
<td>8.</td>
<td>N-p-Tolyl-2-methylbenzo-</td>
<td>35.46</td>
<td>107.60</td>
</tr>
<tr>
<td>9.</td>
<td>N-p-Tolyl-4-ethoxybenzo-</td>
<td>60.18</td>
<td>162.00</td>
</tr>
<tr>
<td>10.</td>
<td>N-p-Tolylphenoxyacet-</td>
<td>8.36</td>
<td>18.32</td>
</tr>
</tbody>
</table>
MEASUREMENT OF BASE STRENGTH

A. **BY HAFM**

Hammett Acidity Function Method (225), is the first traditional method, suitably modified by using acidity function appropriate to the class of bases under consideration. The acidity function \( H_0 \) was originally proposed by Hammett and Deyrup (225) to describe the ionization behaviour of weak organic bases in concentrated acid solutions. It is generally applicable to uncharged bases, ionizing by simple proton addition as in equation [1].

\[ \text{pK}_{\text{BH}^+} \text{ values are then obtained from the relationship} = \]

\[ \text{pK}_{\text{BH}^+} = H + \log \left( \frac{C_{\text{BH}^+}}{C_B} \right) \]  

where, \( H \) is the acidity function appropriate to the base under consideration.

For a weak base, \( B \), which only becomes significantly protonated in strong acidic media, \( \text{pK}_{\text{BH}^+} \) for equation [1] can be defined as the acid dissociation constant of the protonated base \( BH^+ \) and for equation [1] –

\[ K_{\text{BH}^+} = \frac{a_B a_{\text{H}^+}}{a_{\text{BH}^+}} = \left( \frac{C_B}{C_{\text{BH}^+}} \right) C_{\text{H}^+} \left( \frac{f_B f_{\text{H}^+}}{f_{\text{BH}^+}} \right) \]

where,  
\( a = \) Activity  
\( C = \) Molarity  
\( f = \) Molar activity

On taking logarithm, the equation becomes –

\[ \text{pK}_{\text{BH}^+} = \log \left( \frac{C_{\text{BH}^+}}{C_B} \right) - \log C_{\text{H}^+} - \log \left( \frac{f_B f_{\text{H}^+}}{f_{\text{BH}^+}} \right) \]
This equation is thermodynamically exact. The ratio \( f_{f_i}^f / f_{f_i}^H \) is symbolised as \( h \). \( h \) serves as a unique definition of the acidity of the medium, and:

\[
H_0 = -\log h \quad [22]
\]

In water equation [21] reduces to:

\[
pK_{BH^+} = \log I + \text{pH} \quad [23]
\]

If this equation is extended into non-ideal, strongly acidic media, the activity coefficient term in equation [20], must be taken into consideration. This was first attempted by Hammett and Deyrup (225). They postulated that, there exists an Acidity Function, \( H_0 \), defined so as to be an extension of pH scale.

\[
pK_{BH^+} = \log I - \log C_{H^+} - \log \left( \frac{f_{f_i}^f}{f_{f_i}^H} \right) \quad [24]
\]

\[
pK_{BH^+} - \log I = -\log C_{H^+} - \log \left( \frac{f_{f_i}^f}{f_{f_i}^H} \right) = H_0 \quad [25]
\]

\[
pK_{BH^+} = H_0 + \log I \quad [26]
\]

Here \( H_0 \) represent the quantitative measure of acidity of solutions. \( H_0 \) values from literature are presented in Table 2.

The \( pK_{BH^+} \) values calculated following the equation [26], along with the values of slope, \( m \), and correlation coefficients, \( r \), are presented in Table 3. The slopes are the plots of \( \log I \) against \( H_0 \) as presented in Figures 1A to 10A.

Hydroxamic acids are structurally related to amides, thus amide acidity function, \( H_A \), may describe the protonation behaviour of these metal extractants following the HAFM method. Thus, it is of interest to analyse the ionization data in terms of \( H_A \). For equation [26], it \( H_0 \) is replaced by \( H_A \), then the plots of \( \log I \) vs \( H_A \) are close to unity as observed in Figures 1B to 10B. The \( pK_{BH^+} \) values calculated on the basis of \( H_A \) are presented in Table 4 along with the values of slopes and \( r \).
TABLE 2.
VALUES $H_0$, $H_A$ AND $X$ AS A FUNCTION OF PERCHLORIC ACID CONCENTRATION

<table>
<thead>
<tr>
<th>S.No.</th>
<th>ACIDITY, M</th>
<th>$-H_0$</th>
<th>$-H_A$</th>
<th>$X$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>1</td>
<td>0.02</td>
<td>0.04</td>
<td>0.120</td>
</tr>
<tr>
<td>2.</td>
<td>2</td>
<td>0.49</td>
<td>0.50</td>
<td>0.280</td>
</tr>
<tr>
<td>3.</td>
<td>3</td>
<td>0.87</td>
<td>0.86</td>
<td>0.490</td>
</tr>
<tr>
<td>4.</td>
<td>4</td>
<td>1.23</td>
<td>1.20</td>
<td>0.725</td>
</tr>
<tr>
<td>5.</td>
<td>5</td>
<td>1.62</td>
<td>1.51</td>
<td>1.145</td>
</tr>
<tr>
<td>6.</td>
<td>6</td>
<td>2.07</td>
<td>1.83</td>
<td>1.585</td>
</tr>
<tr>
<td>7.</td>
<td>7</td>
<td>2.60</td>
<td>2.15</td>
<td>2.100</td>
</tr>
<tr>
<td>8.</td>
<td>8</td>
<td>3.29</td>
<td>2.60</td>
<td>2.730</td>
</tr>
<tr>
<td>9.</td>
<td>9</td>
<td>4.17</td>
<td>3.09</td>
<td>3.470</td>
</tr>
<tr>
<td>10.</td>
<td>10</td>
<td>5.28</td>
<td>3.56</td>
<td>4.365</td>
</tr>
</tbody>
</table>
### TABLE 3.
**PROTONATION PARAMETERS OF HYDROXAMIC ACIDS IN PERCHLORIC ACID BY HAFM (H\textsubscript{g})**

<table>
<thead>
<tr>
<th>S.No.</th>
<th>HYDROXAMIC ACID</th>
<th>pK\textsubscript{un}</th>
<th>m</th>
<th>r</th>
<th>σ</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>N-Phenyl-2-methylbenzo-</td>
<td>-2.35</td>
<td>0.55</td>
<td>0.97</td>
<td>0.22</td>
</tr>
<tr>
<td>2.</td>
<td>N-Phenyl-4-ethoxybenzo-</td>
<td>-2.57</td>
<td>0.54</td>
<td>0.98</td>
<td>0.16</td>
</tr>
<tr>
<td>3.</td>
<td>N-o-Tolyl-2-methylbenzo-</td>
<td>-2.56</td>
<td>0.56</td>
<td>0.97</td>
<td>0.26</td>
</tr>
<tr>
<td>4.</td>
<td>N-o-Tolyl-4-ethoxybenzo-</td>
<td>-2.69</td>
<td>0.46</td>
<td>0.97</td>
<td>0.16</td>
</tr>
<tr>
<td>5.</td>
<td>N-o-Tolylphenoxyaceto-</td>
<td>-2.68</td>
<td>0.50</td>
<td>0.99</td>
<td>0.10</td>
</tr>
<tr>
<td>6.</td>
<td>N-o-Tolyl-4-Chlorobenzo-</td>
<td>-2.63</td>
<td>0.54</td>
<td>0.99</td>
<td>0.14</td>
</tr>
<tr>
<td>7.</td>
<td>N-m-Tolylbenzo-</td>
<td>-2.55</td>
<td>0.58</td>
<td>0.98</td>
<td>0.20</td>
</tr>
<tr>
<td>8.</td>
<td>N-p-Tolyl-2-methylbenzo-</td>
<td>-2.29</td>
<td>0.55</td>
<td>0.98</td>
<td>0.19</td>
</tr>
<tr>
<td>9.</td>
<td>N-p-Tolyl-4-ethoxybenzo-</td>
<td>-2.41</td>
<td>0.54</td>
<td>0.99</td>
<td>0.13</td>
</tr>
<tr>
<td>10.</td>
<td>N-p-Tolylphenoxyaceto-</td>
<td>-3.01</td>
<td>0.45</td>
<td>0.99</td>
<td>0.07</td>
</tr>
</tbody>
</table>
SLOPES FOR PLOT OF LOG I VS $-H_0$ FOR HAFM (HClO$_4$)

FIG. 1A N-PHENYL-2-METHYLBENZOHYDROXAMIC ACID

SLOPE = 0.55

FIG. 2A N-PHENYL-4-ETHOXYBENZOHYDROXAMIC ACID

SLOPE = 0.54
SLOPES FOR
PLOT OF LOG I VS -H_o FOR HAFM (HClO_4)

FIG. 3A N-o-TOLYL-2-METHYLBENZOXYDROXAMIC ACID

FIG. 4A N-o-TOLYL-4-ETHOXYBENZOXYDROXAMIC ACID
SLOPES FOR
PLOT OF LOG I VS \(-H_o\) FOR HAFM (HClO₄)

FIG. 5A N-\(\text{o}\)-TOLYPHOXYACETOHYDROXAMIC ACID

FIG. 6A N-\(\text{o}\)-TOLYL-4-CHLOROBENZOHYDROXAMIC ACID
SLOPES FOR
PLOT OF LOG I VS -H_a FOR HAFM (HClO_4)

FIG. 7A N-m-TOLYL-BENZOHYDROXAMIC ACID

FIG. 8A N-p-TOLYL-2-METHYLBENZOHYDROXAMIC ACID
SLOPES FOR
PLOT OF LOG I VS $-H_0$ FOR HAFM ($\text{HClO}_4$)

**Fig. 9A** N-p-TOLYL-4-ETHOXYBENZOHYDROXAMIC ACID

**Fig. 10A** N-p-TOLYLPHENOXYACETOHYDROXAMIC ACID
TABLE 4.
PROTONATION PARAMETERS OF HYDROXAMIC ACIDS
IN PERCHLORIC ACID BY HAFM (APPLYING AMIDE
ACIDITY FUNCTION, $H_A$).

<table>
<thead>
<tr>
<th>S.No.</th>
<th>HYDROXAMIC ACID</th>
<th>$K_a$</th>
<th>$pK_{m+}$</th>
<th>m</th>
<th>r</th>
<th>σ</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>N-Phenyl-2-methylbenzo-</td>
<td>9.94</td>
<td>-1.42</td>
<td>0.87</td>
<td>0.98</td>
<td>0.15</td>
</tr>
<tr>
<td>2.</td>
<td>N-Phenyl-4-ethoxybenzo-</td>
<td>105.95</td>
<td>-1.52</td>
<td>0.90</td>
<td>0.99</td>
<td>0.09</td>
</tr>
<tr>
<td>3.</td>
<td>N-o-Tolyl-2-methylbenzo-</td>
<td>37.47</td>
<td>-1.55</td>
<td>0.98</td>
<td>0.99</td>
<td>0.16</td>
</tr>
<tr>
<td>4.</td>
<td>N-o-Tolyl-4-ethoxybenzo-</td>
<td>69.20</td>
<td>-1.93</td>
<td>1.16</td>
<td>0.88</td>
<td>0.61</td>
</tr>
<tr>
<td>5.</td>
<td>N-o-Tolylphenoxyacet-</td>
<td>6.02</td>
<td>-1.75</td>
<td>0.89</td>
<td>0.98</td>
<td>0.14</td>
</tr>
<tr>
<td>6.</td>
<td>N-o-Tolyl-4-Chlorobenzo-</td>
<td>113.55</td>
<td>-1.80</td>
<td>0.86</td>
<td>0.97</td>
<td>0.15</td>
</tr>
<tr>
<td>7.</td>
<td>N-m-Tolylbenzo-</td>
<td>13.87</td>
<td>-1.74</td>
<td>0.86</td>
<td>0.97</td>
<td>0.19</td>
</tr>
<tr>
<td>8.</td>
<td>N-p-Tolyl-2-methylbenzo-</td>
<td>67.99</td>
<td>-1.21</td>
<td>0.88</td>
<td>0.99</td>
<td>0.11</td>
</tr>
<tr>
<td>9.</td>
<td>N-p-Tolyl-4-ethoxybenzo-</td>
<td>92.21</td>
<td>-1.51</td>
<td>0.85</td>
<td>0.98</td>
<td>0.18</td>
</tr>
<tr>
<td>10.</td>
<td>N-p-Tolylphenoxyacet-</td>
<td>10.68</td>
<td>-2.07</td>
<td>0.83</td>
<td>0.96</td>
<td>0.23</td>
</tr>
</tbody>
</table>
SLOPES FOR
PLOT OF LOG I VS -Hₐ FOR HAFM (HClO₄)

SLOPE = 0.87

FIG. 1B N-PHENYL-2-METHYL BENZOHYDROXAMIC ACID

SLOPE = 0.90

FIG. 2B N-PHENYL-4-ETHOXY BENZOHYDROXAMIC ACID
SLOPES FOR
PLOT OF LOG $I$ VS $-H_A$ FOR HAFM (HClO$_4$)

FIG. 3B N-o-TOLYL-2-METHYLBENZOHYDROXAMIC ACID

FIG. 4B N-o-TOLYL-4-ETHOXYBENZOHYDROXAMIC ACID
SLOPES FOR
PLOT OF LOG I VS $-H_A$ FOR HAFM (HClO$_4$)

FIG. 5B N-o-TOLYLPHENOXYACETOHYDROXAMIC ACID

FIG. 6B N-o-TOLYL-4-CHLOROBENZOHYDROXAMIC ACID
SLOPES FOR
PLOT OF LOG I VS $-H_A$ FOR HAFM (HClO$_4$)

FIG. 7B N-m-TOLYL-BENZOHYDROXAMIC ACID

FIG. 8B N-p-TOLYL-2-METHYLBENZOHYDROXAMIC ACID
SLOPES FOR
PLOT OF LOG I VS $-H_\alpha$ FOR HAFM (HClO$_4$)

FIG. 9B N-p-TOLYL-4-ETHOXYBENZOHYDROXAMIC ACID

FIG. 10B N-p-TOLYLPHENOXYACETOHYDROXAMIC ACID
B. BY BOM

An alternative method of determining the base strength of weak organic bases, in terms of $pK_{BH^+}$, is to use the linear free energy approach of Bunnett and Olsen (226) following the equation,

$$\log I + H_0 = \phi (H_0 + \log C_{H^+}) + pK_{BH^+}$$  \[27\]

provided the plot of the left hand side of equation [27] against $[H_0 + \log C_{H^+}]$ is linear. The slope $\phi$ is a measure of the susceptibility of the equilibrium to changing acid concentration and $(1 - \phi)$ is the slope of free energy relationship. In equation [27], $\phi$ is a constant characteristic of a base and $H_0$ is the original Hammett Acidity Function. The values of $\phi$ obtained by plotting $(H_0 + \log C_{H^+})$ vs $(\log I + H_0)$ are shown in Figures 1C to 10C. The data therefrom are summarized along with $pK_{BH^+}$ values and values of correlation coefficient, $r$, in Table 5.

C. BY EAM

Excess Acidity (227, 228) or X-function or Mc Function (229) are used for the evaluation of base strength of weak bases from ionization ratio measurements in strong acid solutions, by the extrapolation to the aqueous standard state. This extrapolative method was an earlier approach proposed by Marziano and Passerini (230). EAM method has been shown both accurate and general (227, 231-232). Cox assumed that for carbonyl compounds, the situation is more complex, if we use spectrophotometric methods like uv and n.m.r., since the spectra of free base or protonated species or of both are usually subject to substantial medium effects (233-237). In view of this, Cox and his coworkers developed a method for obtaining acidity constants, inspite of possible medium effects, based on the excess medium acidity, $X$, which represents the excess acidity. The term was first used by Perrin (238) as "it is the difference between the observed acidity and that which the system would have, if it were ideal", (227, 228). $X$ scale is derived from indicator ratio data for many bases.
### TABLE 5.
#### PROTONATION PARAMETERS OF HYDROXAMIC ACIDS
#### IN PERCHLORIC ACID BY BOM

<table>
<thead>
<tr>
<th>S.No.</th>
<th>HYDROXAMIC ACID</th>
<th>$pK_{\text{rat}}$</th>
<th>$\phi$</th>
<th>$\tau$</th>
<th>$\sigma$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>N-Phenyl-2-methylbenzo-</td>
<td>-1.32</td>
<td>0.50</td>
<td>0.96</td>
<td>0.20</td>
</tr>
<tr>
<td>2.</td>
<td>N-Phenyl-4-ethoxybenzo-</td>
<td>-1.42</td>
<td>0.50</td>
<td>0.98</td>
<td>0.14</td>
</tr>
<tr>
<td>3.</td>
<td>N-o-Tolyl-2-methylbenzo-</td>
<td>-1.45</td>
<td>0.48</td>
<td>0.95</td>
<td>0.21</td>
</tr>
<tr>
<td>4.</td>
<td>N-o-Tolyl-4-ethoxybenzo-</td>
<td>-1.35</td>
<td>0.58</td>
<td>0.98</td>
<td>0.15</td>
</tr>
<tr>
<td>5.</td>
<td>N-o-Tolylphenoxyacet-</td>
<td>-1.44</td>
<td>0.54</td>
<td>0.99</td>
<td>0.10</td>
</tr>
<tr>
<td>6.</td>
<td>N-o-Tolyl-4-Chlorobenzo-</td>
<td>-1.48</td>
<td>0.50</td>
<td>0.98</td>
<td>0.13</td>
</tr>
<tr>
<td>7.</td>
<td>N-m-Tolylbenzo-</td>
<td>-1.49</td>
<td>0.46</td>
<td>0.97</td>
<td>0.18</td>
</tr>
<tr>
<td>8.</td>
<td>N-p-Tolyl-2-methylbenzo-</td>
<td>-1.17</td>
<td>0.50</td>
<td>0.97</td>
<td>0.17</td>
</tr>
<tr>
<td>9.</td>
<td>N-p-Tolyl-4-ethoxybenzo-</td>
<td>-1.38</td>
<td>0.50</td>
<td>0.99</td>
<td>0.12</td>
</tr>
<tr>
<td>10.</td>
<td>N-p-Tolylphenoxyacet-</td>
<td>-1.65</td>
<td>0.59</td>
<td>0.99</td>
<td>0.08</td>
</tr>
</tbody>
</table>
SLOPES FOR
PLOT OF (LOG 1 + H_1) VS (H_o + LOG C_{in}) FOR BOM (HClO_4)

FIG. 1C  N-PHENYL-2-METHYLBENZOXYDROXAMIC ACID

FIG. 2C  N-PHENYL-4-ETHOXYBENZOXYDROXAMIC ACID
SLOPES FOR
PLOT OF (LOG $I + H_0$) VS ($H_0 + \log C_{n^*}$) FOR BOM (HClO$_4$)

FIG. 3C N-o-TOLYL-2-METHYL BENZOHYDROXAMIC ACID

FIG. 4C N-o-TOLYL-4-ETHOXYBENZOHYDROXAMIC ACID
SLOPES FOR
PLOT OF (LOG I + H₀) VS (H₀ + LOG Cₚ) FOR BOM (HClO₄)

FIG. 5C N-o-TOLYLPHENOXYACETOXYACID

FIG. 6C N-o-TOLYL-4-CHLOROBENZOHYDROXAMIC ACID
SLOPES FOR
PLOT OF (LOG 1 + H_u) VS (H_u + LOG C_H^+ ) FOR BOM (HClO_4 )

FIG. 7C N-m-TOLYL-BENZOHYDROXAMIC ACID

FIG. 8C N-p-TOLYL-2-METHYLBENZOHYDROXAMIC ACID
SLOPES FOR
PLOT OF (LOG 1 + H_p) VS (H_u + LOG C_{n+}) FOR BOM (HClO_4)

FIG. 9C N-p-TOLYL-4-ETHOXYBENZOHYDROXAMIC ACID

FIG. 10C N-p-TOLYLPHENOXYACETOHYDROXAMIC ACID
For a proton transfer to a base, B, as in equation (1), the general thermodynamic equation can be written from the definition of $pK_{BH^+}$,

$$\log \left( \frac{C_{BH^+}}{C_B} \right) - \log C_{H^+} = \log \left( \frac{f_{BH^+}}{f_{BH^+}} \right) + pK_{BH^+}$$

where, $C$ is the molar concentration, $f$ is the molar activity coefficient, and $pK_{BH^+}$ is the acid ionization constant of $BH^+$. The assumption is then made that the activity coefficient term in equation (28) is a linear function of a similar term for standard base, B, slope $m^*$, which is the previously derived $X$-function, gives equation (29).

$$\log \left( \frac{f_{BH^+}}{f_{BH^+}} \right) = m^* \log \left( \frac{f_{BH^+}}{f_{BH^+}} \right) = m^* X$$

For equation [1], it involves proton concentration $C_{H^+}$ and the concept of excess medium acidity rather than classical Hammett type acidity function and is summarised as in equation [30],

$$\log I = pK_{BH^+} + \log C_{H^+} + m^* X$$

Values of $X$ as a function of weight percent composition are available for the aqueous perchloric acid system (228) and are given in Table 2 along with corresponding $H_0$ values. The slope $m^*$ expresses the sensitivity of the substrate to the changing acidity thus, it describes the protonation behaviour of B, relative to the hypothetical standard base $BH^+$, used in defining $X$ values in perchloric acid–water system.

Figures 1D to 10D are the plots of log I vs $X$ for slopes, $m^*$. Table 6 presents the data on $pK_{BH^+}$, $m^*$ and $r$ of hydroxamic acids obtained by EAM method.

**SLOPES**

The slopes for the equations, [26], [27] and [30] are the measure of the protonation
### TABLE 6.
PROTONATION PARAMETERS OF HYDROXAMIC ACIDS IN PERCHLORIC ACID BY EAM

<table>
<thead>
<tr>
<th>S.No.</th>
<th>HYDROXAMIC ACID</th>
<th>$pK_{a1}$</th>
<th>$m^*$</th>
<th>$\beta$</th>
<th>$\sigma$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>N-Phenyl-2-methylbenzo-</td>
<td>-1.71</td>
<td>0.62</td>
<td>0.98</td>
<td>0.19</td>
</tr>
<tr>
<td>2</td>
<td>N-Phenyl-4-ethoxybenzo-</td>
<td>-1.85</td>
<td>0.62</td>
<td>0.99</td>
<td>0.13</td>
</tr>
<tr>
<td>3</td>
<td>N-o-Tolyl-2-methylbenzo-</td>
<td>-1.89</td>
<td>0.64</td>
<td>0.98</td>
<td>0.19</td>
</tr>
<tr>
<td>4</td>
<td>N-o-Tolyl-4-ethoxybenzo-</td>
<td>-1.74</td>
<td>0.53</td>
<td>0.98</td>
<td>0.14</td>
</tr>
<tr>
<td>5</td>
<td>N-o-Tolylphenoxyacetato-</td>
<td>-1.84</td>
<td>0.57</td>
<td>0.99</td>
<td>0.12</td>
</tr>
<tr>
<td>6</td>
<td>N-o-Tolyl-4-Chlorobenzo</td>
<td>-1.91</td>
<td>0.61</td>
<td>0.99</td>
<td>0.14</td>
</tr>
<tr>
<td>7</td>
<td>N-m-Tolylbenzo-</td>
<td>-1.94</td>
<td>0.64</td>
<td>0.98</td>
<td>0.19</td>
</tr>
<tr>
<td>8</td>
<td>N-p-Tolyl-2-methylbenzo-</td>
<td>1.56</td>
<td>0.62</td>
<td>0.99</td>
<td>0.15</td>
</tr>
<tr>
<td>9</td>
<td>N-p-Tolyl-4-ethoxybenzo-</td>
<td>-1.75</td>
<td>0.61</td>
<td>0.99</td>
<td>0.11</td>
</tr>
<tr>
<td>10</td>
<td>N-p-Tolylphenoxyacetato-</td>
<td>-2.03</td>
<td>0.51</td>
<td>0.99</td>
<td>0.06</td>
</tr>
</tbody>
</table>
SLOPES FOR
PLOT OF LOG I VS X FOR EAM (HClO₄)

FIG. 1D N-PHENYL-2-METHYL BENZOHYDROXAMIC ACID

FIG. 2D N-PHENYL-4-ETHOXYBENZOHYDROXAMIC ACID
SLOPES FOR
PLOT OF LOG I VS X FOR EAM (HClO₄)

FIG. 3D N-o-TOLYL-2-METHYLBENZOHYDROXAMIC ACID

FIG. 4D N-o-TOLYL-4-ETHOXYBENZOHYDROXAMIC ACID
SLOPES FOR
PLOT OF LOG I VS X FOR EAM (HClO₄)

FIG. 5D N-o-TOLYLPHENOXYACETOHYDROXAMIC ACID

SLOPE = 0.57

FIG. 6D N-o-TOLYL-4-CHLOROBENZOHYDROXAMIC ACID

SLOPE = 0.61
SLOPES FOR
PLOT OF LOG I VS X FOR EAM (HClO₄)

FIG. 7D  N-m-TOLYL-BENZOHYDROXAMIC ACID

FIG. 8D  N-p-TOLYL-2-METHYLBENZOHYDROXAMIC ACID
SLOPES FOR
PLOT OF LOG I VS X FOR EAM (HClO₄)

FIG. 9D N-p-TOLYL-4-ETHOXYBENZOHYDROXAMIC ACID

FIG. 10D N-p-TOLYPHENOXYACETOHYDROXAMIC ACID
behaviour of substrate, hydroxamic acid in equation [1], relative to Hammett base, used for the determination of $H_0$. In other words, slope expresses the sensitivity of the substrate to the changing acidity. The excess acidity slopes like Bunnell-Olsen values are the slopes of LFER plots, and thus have mechanistic values. A substance is a Hammett Base, if the values of slopes are near to unity. For N-arylhydroxamic acids, the slope values are considerably lower than those of around 1.0. These are in the range of 0.45 to 0.58 for HAFM, from 0.46 to 0.59 for BOM and 0.51 to 0.64 for EAM methods. This shows a typical protonation behaviour of carbonyl groups, which have the slope values around 0.6 (227). Values of similar magnitude have been obtained for the structurally related compounds and other carbonyl compounds. For amides, the slope values have been observed in the range 0.51 to 0.57 (226), and for sulfoxide the range is from 0.4 to 0.6 (198). From these data it is inferred that hydroxamic acids do not behave like Hammett Bases. In such cases, the $pK_{BH+}$ values are not thermodynamic quantities, but represent the $pK_{BH+}$ values corresponds numerically to $H_0$ values of the acid, in which the base is half protonated. This statement seems to be correct in case of hydroxamic acids, as observed in Table 7. The derived $pK_{BH+}$ values match exactly to the $H_0$ values, where the 50% protonation of hydroxamic acids takes place.

**PROTONATION BEHAVIOUR OF HYDROXAMIC ACIDS**

Hydroxamic acids are weaker bases than amines and thus are not strong enough to be measurably ionized in dilute acidic solutions. Insufficient protonation at lower acidity hinders the experimental determination of protonation constants at this stage. Thus, the protonation data have been analysed in nonideal strong acid medium, i.e. in 4–10 M perchloric acid solutions. Perchloric acid is a suitable medium for the study of the protonation reaction because, the activity of water in perchloric acid decreases more rapidly with increasing acid concentration than it does in sulphuric acid (239–241). The average $pK_{abh^+}$ values are presented in the Tables 3–6. The $pK_{BH+}$ is a measure of acid strength of the conjugate acid BH\(^+\), of the base B. The stronger is the acid BH\(^+\), the weaker will be the base B. So, the smaller value of $pK_{BH+}$, indicates that hydroxamic acids are weak bases in presence of strong acid media. They are not Hammett bases although they ionize by simple proton addition, but behave like Brønsted bases.

For comparison, and to avoid the necessity of developing a separate scale, the
TABLE 7.
VALUES OF $H_1$ AND $pK_{\text{uH}}$ OF N-ARYLSUBSTITUTED HYDROXAMIC ACIDS AT FIFTY PERCENT PROTONATION.

<table>
<thead>
<tr>
<th>S.No.</th>
<th>HYDROXAMIC ACID</th>
<th>PERCHLORIC ACID</th>
<th>DERIVED $pK_{\text{uH}}$ VALUES</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>ACIDITY, M - $H_0$</td>
<td></td>
</tr>
<tr>
<td>1.</td>
<td>N-Phenyl-2-methylbenzo-</td>
<td>6.55 2.35</td>
<td>-2.35</td>
</tr>
<tr>
<td>2.</td>
<td>N-Phenyl-4-ethoxybenzo-</td>
<td>6.96 2.57</td>
<td>-2.57</td>
</tr>
<tr>
<td>3.</td>
<td>N-o-Tolyl-2-methylbenzo-</td>
<td>6.95 2.56</td>
<td>-2.56</td>
</tr>
<tr>
<td>4.</td>
<td>N-o-Tolyl-4-ethoxybenzo-</td>
<td>7.13 2.69</td>
<td>-2.69</td>
</tr>
<tr>
<td>5.</td>
<td>N-o-Tolylphenoxyaceto-</td>
<td>7.10 2.68</td>
<td>-2.68</td>
</tr>
<tr>
<td>6.</td>
<td>N-o-Tolyl-4-Chlorobenzo-</td>
<td>7.05 2.62</td>
<td>-2.63</td>
</tr>
<tr>
<td>7.</td>
<td>N-m-Tolylbenzo-</td>
<td>6.90 2.55</td>
<td>-2.55</td>
</tr>
<tr>
<td>8.</td>
<td>N-p-Tolyl-2-methylbenzo-</td>
<td>6.06 2.20</td>
<td>-2.20</td>
</tr>
<tr>
<td>9.</td>
<td>N-p-Tolyl-4-ethoxybenzo-</td>
<td>6.69 2.40</td>
<td>-2.41</td>
</tr>
<tr>
<td>10.</td>
<td>N-p-Tolylphenoxyaceto-</td>
<td>7.65 3.00</td>
<td>-3.01</td>
</tr>
</tbody>
</table>
data are analysed in terms of $H_a$ acidity scale. As the hydroxamic acids are structurally related to amides, the analysis is also done by applying amide acidity function, $H_a$. As the Hammett approach was found not to be general, a more general approach was proposed by Bunnell and Olsen and Cox and Yales, in which a single equation and function applied to almost all bases. Thus, the need for individual acidity function is overcome by BOM and EAM methods. BOM method is based on original $H_a$ values. EAM does not involve an acidity function but uses overlapping indicators. BOM and EAM have to be considered as equivalent methods (242). $X$ corresponds approximately to $(-H_a + \log C_W)$. These two are linearly correlated to each other. The slopes and intercept values of these correlations being almost one and zero, respectively. The major difference in BOM and EAM is the use of acidity function in the former, whereas, use of excess acidity function give a physical meaning to slope parameter, $m^*$ in the latter.

An examination of data presented in tables reveals that in perchloric acid, the three different approaches give different $pK_{BH^+}$ values. Bunnell-Olsen $pK_{BH^+}$ are still the most negative ones and the acidity function $pK_{BH^+}$ are least negative values.

Thus, for the weaker bases, like N-aryl substituted hydroxamic acids, HAFM, BOM and EAM methods give different $pK_{BH^+}$ values. Furthermore, it is interesting to notice that $pK_{BH^+}$ values of similar compounds, the weak amides, also furnished different $pK_{BH^+}$ values by HAFM and EAM methods (243). Differences in $pK_{BH^+}$ values have been found for other weak bases also (244).

On comparing HAFM, BOM and EAM, although the practical and theoretical advantage of EAM method should render this method most suitable in less concentrated acid solutions, but in case of weak bases for which more concentrated acid solutions are required, the validity of the results obtained by EAM method is questionable. Sometimes both BOM and HAFM methods are more satisfactory. Even BOM method has been found to be less reliable when used with acidity functions other than $H_a$ (199). In those cases in which disagreement between the three methods is observed, the question arises as to which method gives more accurate estimate of $pK_{BH^+}$. However, it has been observed that particularly in case of weak organic bases HAFM method works better than BOM and EAM methods. At the same time, EAM is capable of providing mechanistic information which the other methods cannot.
A knowledge of base strength of weak organic bases is a useful diagnostic tool to understand a biochemical reaction, structure-reactivity relationship and to study the reaction kinetics. The protonation data will be of value not only to the medicinal chemists and physical chemists concerned with the understanding of structure-reactivity problems but also to the industrial chemist and chemical engineer, who design a higher predictability for acid catalysed system and to the biochemist who is concerned with the proton-transfer properties in enzymatic catalysis.

PERCENTAGE PROTONATION OF N-ARYLHYDROXAMIC ACIDS AS A FUNCTION OF ACID CONCENTRATION

Measurement of percentage protonation of hydroxamic acids as a function of perchloric acid concentrations, were calculated following the equation -

\[
\text{\% Protonated} = \frac{h_0}{h_0 + K_{BH^+}} \times 100
\]  

[31]

Where, \( h_0 = -\log h_c \) and \( \rho K_{BH^+} = -\log K_{BH^+} \)

The data are presented in Table 8. Going from 1 to 10M acid concentrations, the percentage of protonated species increases at different rates in different hydroxamic acids. The extent of protonation with increasing perchloric acid concentration is presented in Figures 11 to 20, and the trend is in accordance with distribution data, which indicates that as the acidity increases, hydroxamic acids become more and more hydrophilic in nature.

SITE OF PROTONATION

The problem of determining the preferred protonation site in hydroxamic acids is still an open question.

In principle, hydroxamic acid presents three basic centres, one on nitrogen and
<table>
<thead>
<tr>
<th>S.No.</th>
<th>HYDROXAMIC ACID</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>N-Phenyl-2-methylbenzo-</td>
<td>0.47</td>
<td>1.36</td>
<td>3.20</td>
<td>7.05</td>
<td>15.70</td>
<td>34.42</td>
<td>64.01</td>
<td>89.70</td>
<td>98.51</td>
<td>99.88</td>
</tr>
<tr>
<td>2</td>
<td>N-Phenyl-1-ethoxybenzo-</td>
<td>0.28</td>
<td>0.82</td>
<td>1.95</td>
<td>4.37</td>
<td>10.09</td>
<td>24.02</td>
<td>51.73</td>
<td>84.00</td>
<td>97.55</td>
<td>99.80</td>
</tr>
<tr>
<td>3</td>
<td>N-o-Tolyl-2-methylbenzo-</td>
<td>0.29</td>
<td>0.84</td>
<td>2.00</td>
<td>4.47</td>
<td>10.30</td>
<td>24.45</td>
<td>52.30</td>
<td>84.30</td>
<td>97.60</td>
<td>99.81</td>
</tr>
<tr>
<td>4</td>
<td>N-o-Tolyl-4-ethoxybenzo-</td>
<td>0.21</td>
<td>0.63</td>
<td>1.49</td>
<td>3.35</td>
<td>7.84</td>
<td>19.35</td>
<td>44.84</td>
<td>79.92</td>
<td>96.79</td>
<td>99.74</td>
</tr>
<tr>
<td>5</td>
<td>N-o-Tolylphenoxacycto-</td>
<td>0.22</td>
<td>0.64</td>
<td>1.52</td>
<td>2.74</td>
<td>8.01</td>
<td>19.71</td>
<td>45.41</td>
<td>80.29</td>
<td>96.87</td>
<td>99.75</td>
</tr>
<tr>
<td>6</td>
<td>N-o-Tolyl-4-Chlorobenzo-</td>
<td>0.30</td>
<td>0.86</td>
<td>2.05</td>
<td>4.57</td>
<td>10.51</td>
<td>24.88</td>
<td>52.88</td>
<td>84.60</td>
<td>97.66</td>
<td>99.81</td>
</tr>
<tr>
<td>7</td>
<td>N-m-Tolylbenzo-</td>
<td>0.30</td>
<td>0.86</td>
<td>2.04</td>
<td>4.57</td>
<td>10.51</td>
<td>24.88</td>
<td>52.88</td>
<td>84.60</td>
<td>97.66</td>
<td>99.81</td>
</tr>
<tr>
<td>8</td>
<td>N-p-Tolyl-2-methylbenzo-</td>
<td>0.66</td>
<td>1.91</td>
<td>4.47</td>
<td>9.68</td>
<td>20.82</td>
<td>42.57</td>
<td>71.52</td>
<td>92.48</td>
<td>98.94</td>
<td>99.92</td>
</tr>
<tr>
<td>9</td>
<td>N-p-Tolyl-4-ethoxybenzo-</td>
<td>0.41</td>
<td>1.19</td>
<td>2.80</td>
<td>6.20</td>
<td>13.95</td>
<td>31.37</td>
<td>60.77</td>
<td>88.35</td>
<td>98.29</td>
<td>99.87</td>
</tr>
<tr>
<td>10</td>
<td>N-p-Tolylphenoxyacetox-</td>
<td>0.10</td>
<td>0.30</td>
<td>0.72</td>
<td>1.63</td>
<td>3.19</td>
<td>10.30</td>
<td>28.01</td>
<td>65.58</td>
<td>93.53</td>
<td>99.46</td>
</tr>
</tbody>
</table>
FIG. 11 DISTRIBUTION RATIOS AND PERCENTAGE PROTONATION OF N-PHENYL-2-METHYL.BENZOHYDROXAMIC ACID AS A FUNCTION OF PERCHLORIC ACID CONCENTRATIONS.
FIG. 12 DISTRIBUTION RATIOS AND PERCENTAGE PROTONATION OF N-PHENYL-4-ETHOXYBENZOHYDROXAMIC ACID AS A FUNCTION OF PERCHLORIC (---) ACID CONCENTRATIONS.
FIG. 13 DISTRIBUTION RATIOS AND PERCENTAGE PROTONATION OF N-\textbeta-TOLYL-2-METHYLBENZOHYDROXAMIC ACID AS A FUNCTION OF PERCHLORIC (---) ACID CONCENTRATIONS.
FIG. 14 DISTRIBUTION RATIOS AND PERCENTAGE PROTONATION OF N-o-TOLYL-4-ETHOXYBENZOHYDROXAMIC ACID AS A FUNCTION OF PERCHLORIC (---) ACID CONCENTRATIONS
FIG. 15 DISTRIBUTION RATIOS AND PERCENTAGE PROTONATION OF N-o-TOLYL PHENOXYACETOHYDROXAMIC ACID AS A FUNCTION OF PERCHLORIC (---) ACID CONCENTRATIONS.
FIG. 16 DISTRIBUTION RATIOS AND PERCENTAGE PROTONATION OF N-6-TOLYL-4-CHLOROBENZOHYDROXAMIC ACID AS A FUNCTION OF PERCHLORIC (---) ACID CONCENTRATIONS.
FIG. 17  DISTRIBUTION RATIOS AND PERCENTAGE PROTONATION OF m-TOLYL BENZOHYDROXAMIC ACID AS A FUNCTION OF PERCHLORIC (→→) ACID CONCENTRATIONS
FIG. 18 DISTRIBUTION RATIOS AND PERCENTAGE PROTONATION OF N-\textit{p}-TOLYL-2-METHYLBENZOHYDROXAMIC ACID AS A FUNCTION OF PERCHLORIC (---) ACID CONCENTRATIONS
FIG. 19 DISTRIBUTION RATIOS AND PERCENTAGE PROTONATION OF N-\(p\)-TOLYL-4-ETHOXYBENZOHYDROXAMIC ACID AS A FUNCTION OF PERCHLORIC (\(\bullet\bullet\bullet\)) ACID CONCENTRATIONS.
FIG. 20 DISTRIBUTION RATIOS AND PERCENTAGE PROTONATION OF N-p-TOLYLPHENOXYACETOHYDROXAMIC ACID AS A FUNCTION OF PERCHLORIC (---) ACID CONCENTRATIONS.
two on oxygen for protonation (one on carbonyl oxygen and other on the oxygen in the −OH group) presented in structures I, II and III.

\[
\begin{align*}
&\text{I} \quad R_1-N^+\text{OH} \quad \text{II} \quad R_1-N^+\text{OH} \quad \text{III} \quad R_1-N^+\text{OH}_2 \\
&\text{R}_2-C=O \quad \text{R}_2-C=O \quad \text{R}_2-C=O
\end{align*}
\]

But only two of them, the carbonyl oxygen and the nitrogen atoms, are actual protonation sites. Some of the workers have attempted to solve this problem (154, 245–249).

Due to similarity in chemical behaviour with amides, it is usually accepted that protonation site is the carbonyl oxygen (249), rather than nitrogen or hydroxyl oxygen, presumably due to its better charge delocalisation available, into the ring and the oxygen. Lobo (245) has examined the n.m.r. spectra of alkylhydroxamic acid and concluded that it is protonated on carbonyl oxygen. Further, the carbonyl oxygen protonation has the characteristics m* values in the range 0.6–0.7 (246) and it is observed in the present system also. On the other hand analysing the infrared absorption peaks of these reagents, it was observed that both \( \nu_\text{o-H} \) and \( \nu_\text{c=0} \) appear at lower wave numbers than expected, and the position of these bands remain unaffected by dilution. It is thus inferred that intramolecular hydrogen bonding exists in the molecule and hence the conjugated acid can be written in the N–protonated form,

\[
\begin{align*}
&\text{IV} \quad R_1-N^+\text{OH} \quad \text{V} \quad R_1-N^+\text{OH} \\
&\text{R}_2-C=O \quad \text{R}_2-C=O
\end{align*}
\]

this will be in equilibrium with an O–protonated form at lower acidity. Besides, the acidity at which the solvent extraction is performed, does not greatly influence the complex formation. This also suggests that protonation may be possible at the
nitrogen site, rather than at the oxygen site. Moreover, chelation occurs through both oxygen atoms –

\[
\begin{align*}
2 \text{R}_1\text{N}-\text{OH} & + \text{V}^{(V)} \text{HCl} \\
\text{R}_2\text{C}=\text{O} & \rightarrow \text{R}_1\text{N}-\text{O}\equiv\text{O}=\text{C}=\text{R}_2 \\
\text{R}_2\text{C}=\text{O} & \rightarrow \text{O}\equiv\text{N}\equiv\text{R}_{\text{Cl}}
\end{align*}
\]

which also indicate the possibility of the N-protonation in hydroxamic acids.

A very little information is available in the literature (199, 245, 247) regarding the site of protonation, concerned with the hydroxamic acids. According to Tillet and Lobo (154, 245) both hydroxamic acids and amides show similar protonation behaviour as they are structurally related compounds, and favoured protonation at carbonyl oxygen, in presence of strong acidic solutions, whereas at lower acidity both O-protonated and N-protonated forms are present. Still, N-protonation is not completely impossible in amides, since tertiary amides show an acid catalysed isomerism, which can occur only by N-protonation. Besides, amides with electron donating substituents exchange by N-protonation (248).

To investigate the site of protonation, further and detail studies are needed, applying a modern technique of n.m.r. spectroscopy.