CHAPTER – III

A. GENERALITIES—ABOUT THE AMINO ACIDS USED

B. DISCUSSION
A. GENERALITIES—ABOUT THE AMINO ACIDS USED

Before the results of the present work are discussed, the nature of amino acids in aqueous solutions, in general, and species of those used in investigations, in particular, has to be considered.

No other class of compounds is involved in such a variety of functions, all essential to life, as proteins (polymers), whose monomers are α-amino acids. All proteins are constructed from the same basic set of 20 amino acids (Table 3.1), covalently linked in characteristic sequences. Each of these amino acids has a distinctive side chain which lends it chemical individuality.

When proteins are boiled with strong acid or base, their amino acid blocks are released from the covalent linkages that join them into chains. The free amino acids so formed are relatively small molecules, and their structures are all known.

In every amino acid molecule, one carbon holds an amino group, a carboxyl group, another group (G) called a side chain, and a hydrogen. Since the amino function is alpha to the carboxyl group, these are called α-amino acids (except proline
<table>
<thead>
<tr>
<th>Name</th>
<th>Three-letter symbol</th>
<th>( pK_{(25^\circ C)} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alanine</td>
<td>Ala</td>
<td>2.35; 9.69</td>
</tr>
<tr>
<td>Arginine</td>
<td>Arg</td>
<td>2.17; 9.04 (( \alpha )-amino); 12.8 (guanidino)</td>
</tr>
<tr>
<td>Asparagine</td>
<td>Asn</td>
<td>2.02; 8.8</td>
</tr>
<tr>
<td>Aspartic acid</td>
<td>Asp</td>
<td>2.09 (( \alpha )-carboxyl); 3.86 (( \beta )-carboxyl); 9.82</td>
</tr>
<tr>
<td>Cysteine</td>
<td>Cys</td>
<td>1.71; 8.33 (sulfhydryl) 10.78 (( \alpha )-amino)</td>
</tr>
<tr>
<td>Glutamine</td>
<td>Gln</td>
<td>2.17; 9.13</td>
</tr>
<tr>
<td>Glutamic acid</td>
<td>Glu</td>
<td>2.19 (( \alpha )-carboxyl); 4.25 (( \gamma )-carboxyl); 9.67</td>
</tr>
<tr>
<td>Glycine</td>
<td>Gly</td>
<td>2.34; 9.6</td>
</tr>
<tr>
<td>Histidine</td>
<td>His</td>
<td>1.82; 6.0 (imidazole); 9.17</td>
</tr>
<tr>
<td>iso-Leucine</td>
<td>Ile</td>
<td>2.36; 9.68</td>
</tr>
<tr>
<td>Leucine</td>
<td>Leu</td>
<td>2.36; 9.60</td>
</tr>
<tr>
<td>Lysine</td>
<td>Lys</td>
<td>2.18; 8.95 (( \alpha )-amino); 10.53 (( \varepsilon )-amino)</td>
</tr>
<tr>
<td>Methionine</td>
<td>Met</td>
<td>2.28; 9.21</td>
</tr>
<tr>
<td>Phenylalanine</td>
<td>Phe</td>
<td>1.83; 9.13</td>
</tr>
<tr>
<td>Proline</td>
<td>Pro</td>
<td>1.99; 10.60</td>
</tr>
<tr>
<td>Serine</td>
<td>Ser</td>
<td>2.21; 9.15</td>
</tr>
<tr>
<td>Threonine</td>
<td>Thr</td>
<td>2.63; 10.43</td>
</tr>
</tbody>
</table>

Table 3.1 contd.
<table>
<thead>
<tr>
<th>Name</th>
<th>Three-letter symbol</th>
<th>pK&lt;sub&gt;25°C&lt;/sub&gt; (25°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tryptophan</td>
<td>Trp</td>
<td>2.38; 9.39</td>
</tr>
<tr>
<td>Tyrosine</td>
<td>Tyr</td>
<td>2.20; 9.11 (α-amino); 10.07  (phenolic hydroxyl)</td>
</tr>
<tr>
<td>Valine</td>
<td>Val</td>
<td>2.32; 9.62</td>
</tr>
</tbody>
</table>

\[a\] As recommended by the Joint Commission on Biochemical Nomenclature of IUPAC IUB.

which is an α-imino acid).

In neutral solution the general structure of all the amino acids having one amino group and one carboxyl group is written as $\text{H}_2\text{N}-\text{CH}(\text{G})-\text{COO}^-$. In order to indicate the presence of electrically charged groups rather than employing the conventional formula of the isomeric, uncharged molecule, $\text{H}_2\text{N}-\text{CH}(\text{G})-\text{COOH}$. The indicated structure emphasizes the ionic character of the groups in molecules at neutral pH. The structure contains simultaneously a cationic ammonium group and an anionic carboxyl ion; it is a dipole of very high electric moment, about eight times as great as that of a water molecule. (Amino acids containing more than one carbon atom separating the ammonium and the carboxylate groups give still higher electric moments). Because of the presence of ionic groups these dipolar ions (called zwitterions) dissolve much more readily in highly polar solvents like water than in slightly polar or non-polar solvents of high dielectric constant.

As the amino group can accept a proton and the carboxyl group can donate one, the exact molecular ionic condition of an amino acid in water varies with the pH; being largely in form I in acid (at pH 1 or lower) and form III in alkali (pH 11 or higher) and a mixture of I, II and III between pH 1 and 11. The proportions depend on the exact pH and on the specific amino acid.
On immersing electrodes in an aqueous solution of an amino acid, molecules that happen to be in form I migrate to the cathode, those in the form III to the anode, and those in the dipolar form, II, do not migrate at all. Molecules in form II are isoelectric; the number of (+) charges equals the number of (-) charges and the molecule is electrically neutral. At a particular pH, the system will behave as if all ions were isoelectric and no migration in an electric field would occur. The value of pH at which no net migration occurs is called the isoelectric point of the amino acid and is symbolized by pi. In a solution at its pi value, any amino acid molecule in form I that starts to move to the cathode soon flips a proton to something else and becomes form II (and therefore stops moving) or becomes form III (and reverses its direction). At the pi value, the rates of proton exchange are exactly adjusted to ensure that each unit that is not II spends an equal amount of time as I and as III with the result that no net migration to either electrode can occur.
The isoelectric point is defined as the point at which an amphoteric electrolyte when subjected in solution to a source of direct current will move toward neither anode nor cathode. Under these conditions of zero mobility it may be assumed that the concentration of cations in solution is equal to the concentration of anions:

\[ [\text{H}_2\text{N-CH(G)-COOH}^+] = [\text{H}_2\text{N-CH(G)-COO}^-] \]

Using the defining values of \( K_1 \) and \( K_2 \) one obtains

\[ K_1K_2 = \frac{[\text{H}^+]^2[\text{H}_2\text{N-CH(G)-COO}^-]}{[\text{H}_2\text{N-CH(G)-COOH}]} \]

which gives that \([\text{H}^+] \) at the isoelectric point = \( \sqrt{K_1K_2} \) or, in other words, where \( pI \) is taken as the \( pH \) at the isoelectric point,

\[ pI = \frac{pK_1 + pK_2}{2} \] (2)

Equation (2) is applicable to the isoelectric point of a dipolar ion with two ionizing groups, generally one amino and one carboxyl group. For amphoteric electrolytes with more than two ionizing groups, the isoelectric picture is more complicated, yet reduces to a relatively simplified and valid approximation. The equation for the isoelectric point of a multivalent ampholyte in terms of all its dissociation
constants is

\[ I^2 = \frac{k_{n}k_{n+1}}{1 + \frac{2k_{n}^2}{1} + \frac{3k_{n+1}^2}{I^2} + \ldots} \]

wherein the values of \( K \) refer to the acidic constants, numbered in order of decreasing magnitude, the subscript \( n \) being equal to the maximum positive charge of any of the ampholyte ion.

Inasmuch as for all known cases, \( k_{n-1} \gg 2I \) and \( I \gg 2k_{n+2} \), the terms involving \( I \) on the right-hand side of equation (3) are small as compared with 1; as a good approximation equation (3) can be written as

\[ I^2 = k_{n}k_{n+1} \]

or \( pI = \frac{pK_{n} + pK_{n+1}}{2} \) \( (4) \)

The structural formulas of amino acids used in the present study are given in the Table 3.2 along with their \( pK \) and \( pI \) (isoelectric point) values. These can be grouped in four main families:

1. **Amino Acids with Nonpolar Side-Chains**

The first set of amino acids in the Table 3.1 have essentially nonpolar, hydrophobic side-chains.
TABLE 3.2: Structural Formulas, pK and pI values of Amino Acids (\( \text{H}_3\text{N-CH-C-O}^- \)) Used in Present Studies (shown with their amino and carboxyl groups ionized, as they would occur at pH 7.0).

<table>
<thead>
<tr>
<th>G (Side Chain)</th>
<th>Formula</th>
<th>Name</th>
<th>Three-letter symbol</th>
<th>pK&lt;sub&gt;b&lt;/sub&gt; (25°C)</th>
<th>pI&lt;sub&gt;b&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Side chain is nonpolar</td>
<td>-CHCH&lt;sub&gt;2&lt;/sub&gt;CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>Isoleucine Ile</td>
<td>2.36; 9.68</td>
<td>6.02</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>CH&lt;sub&gt;2&lt;/sub&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>gN-CH-COO&lt;sup&gt;-&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Proline Pro</td>
<td></td>
<td>1.99; 10.60</td>
<td>6.10</td>
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<td></td>
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<tr>
<td>II. Side chain has a hydroxyl group</td>
<td>-CHCH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>Threonine Thr</td>
<td>2.63; 10.45</td>
<td>6.53</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CH&lt;sub&gt;2&lt;/sub&gt;OH</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>HO-CH</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>CH&lt;sub&gt;3&lt;/sub&gt;N-CH-COO&lt;sup&gt;-&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>III. Side chain has a basic amide group</td>
<td>-CH&lt;sub&gt;2&lt;/sub&gt;CO.NH&lt;sub&gt;2&lt;/sub&gt;</td>
<td>CONH&lt;sub&gt;2&lt;/sub&gt;</td>
<td>Asparagine Asn</td>
<td>2.02; 3.8</td>
<td>5.41</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CH&lt;sub&gt;2&lt;/sub&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

Table 3.2 contd.
### IV. Side chain has a basic amino group

<table>
<thead>
<tr>
<th>G (Side chain)</th>
<th>Formula</th>
<th>Name</th>
<th>Three-letter symbol</th>
<th>pK&lt;sub&gt;b&lt;/sub&gt;&lt;sup&gt;(25°C)&lt;/sup&gt;</th>
<th>pI&lt;sub&gt;b&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-CH&lt;sub&gt;2&lt;/sub&gt;CH&lt;sub&gt;2&lt;/sub&gt;CH&lt;sub&gt;2&lt;/sub&gt;NH&lt;sub&gt;2&lt;/sub&gt; + (CH&lt;sub&gt;2&lt;/sub&gt;)&lt;sub&gt;4&lt;/sub&gt;-NH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>Lysine Lys</td>
<td>2.18; 8.95</td>
<td>(a-amino); 10.53 (ε-amino)</td>
<td>9.74</td>
</tr>
<tr>
<td></td>
<td>-CH&lt;sub&gt;2&lt;/sub&gt;CH&lt;sub&gt;2&lt;/sub&gt;CH&lt;sub&gt;2&lt;/sub&gt;-G-NH&lt;sub&gt;2&lt;/sub&gt; + (CH&lt;sub&gt;2&lt;/sub&gt;)&lt;sub&gt;3&lt;/sub&gt;-N-C-NH&lt;sub&gt;2&lt;/sub&gt;</td>
<td>Arginine Arg</td>
<td>2.17; 9.04</td>
<td>(a-amino); 12.48 (guanidino)</td>
<td>10.76</td>
</tr>
</tbody>
</table>

![Chemical structures](image)

**Histidine His**

1.82; 6.0

(imidazole); 7.58

9.17

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<sup>a</sup> As recommended by the Joint Commission on Biochemical Nomenclature of IUPAC 1963.

(2) **Amino Acids with Hydroxyl Containing Side-Chains**

In the second set of amino acids in Table 3.1 the side-chain carries a hydroxyl group. In the cellular environment the side-chain is neither basic nor acidic, but is polar and hydrophobic.

(3) **Amino Acids with Amide Side-Chains**

Asparagine has an amide as side-chain group which is a good polar, hydrophilic group.

(4) **Amino Acids with Basic Side-Chains**

A lysine molecule has an extra amino group that makes its side-chain basic, hydrophilic and a hydrogen-bond donor or acceptor. The side-chain in arginine has the guanidine group $\text{NH}^+\text{C}=-\text{NH}_2$. One of the most powerful proton-accepting groups found in organism, it exists almost exclusively in its protonated form, $\text{NH}^+\text{C}=-\text{NH}_2$, in a medium of even slightly basic pH. Lysine and histidine side-chains are likewise usually in protonated forms.

For the most part the amino acids may be considered as substituted fatty acids. The effect of all α-substituted groups is to increase the acid strength of the carboxyl group; the most
powerful in increasing the carboxyl acidity is the charged
\( \text{NH}_3^+ \) group (e.g., pK of CH\( _3 \)COOH is 4.76 whereas that of
\( \text{NH}_3^+\text{CH}_2\text{COOH} \) is 2.34). In compounds such as lysine, arginine
and histidine, which contain two positively charged groups,
the effect on the carboxyl group dissociation is even greater,
and, consequently lower than 2.34 values are obtained.

The charged \( \text{COO}^- \) group has a relatively small effect on
the dissociation of \( \text{NH}_3^+ \) as can be seen from the pK\( _3 \) values of
di- and tricarboxylic amino acids (e.g., the pK\( _3 \) of aspartic
acid is 9.82). On the other hand, very considerable effect
which a charged \( \text{NH}_3^+ \) group has on the acid strength of an \( \text{NH}_3^+ \)
group is noted in the pK\( _2 \) value of 8.95 for lysine. For the
same reason, the pK for the imidazole group in histidine is
more acidic than in imidazole itself (7.08); when removed
from the influence of the \( \text{NH}_3^+ \) group as in carnosine or
anserine, the imidazole pK approaches more nearly a value of
7. When the guanidino group in arginine is titrated, the
amino group is already uncharged and its effect on the pK of
the guanidino group should be relatively small.

**Calculation of Concentrations of Species Present at a Given pH**

Amounts of various amino acid species (as fractions of
total amino acid) were calculated using the following equations.
Equations (5)—(7) are applicable for the amino acids with two
ionizing groups (divalent) and equations (8)—(11) for those
which have an additional basic amino group in their side-chains
and thus have three pK values (trivalent).

\[
\begin{align*}
\alpha_1 &= \frac{[H_2L^+]}{\sum_{n=0}^{2} H_nL(n-1)^+} = \frac{[H^+]^2}{[H^+]^2 + K_1[H^+] + K_1K_2} \\
\alpha_2 &= \frac{[HL]}{\sum_{n=0}^{2} H_nL(n-1)^+} = \frac{K_1[H^+]}{[H^+]^2 + K_1[H^+] + K_1K_2} \\
\alpha_3 &= \frac{[L^-]}{\sum_{n=0}^{2} H_nL(n-1)^+} = \frac{K_1K_2}{[H^+]^2 + K_1[H^+] + K_1K_2} \\
\alpha_4 &= \frac{[H_2L^{2+}]}{\sum_{n=0}^{3} H_nL(n-1)^+} = \frac{[H^+]^3}{[H^+]^3 + K_1[H^+]^2 + K_1K_2[H^+] + K_1K_2K_3} \\
\alpha_5 &= \frac{[H_2L^+]}{\sum_{n=0}^{3} H_nL(n-1)^+} = \frac{K_1[H^+]}{[H^+]^3 + K_1[H^+]^2 + K_1K_2[H^+] + K_1K_2K_3} \\
\alpha_6 &= \frac{[HL]}{\sum_{n=0}^{3} H_nL(n-1)^+} = \frac{K_1K_2[H^+]}{[H^+]^3 + K_1[H^+]^2 + K_1K_2[H^+] + K_1K_2K_3} \\
\alpha_7 &= \frac{[L^-]}{\sum_{n=0}^{3} H_nL(n-1)^+} = \frac{K_1K_2K_3}{[H^+]^3 + K_1[H^+]^2 + K_1K_2[H^+] + K_1K_2K_3}
\end{align*}
\]
Distribution diagrams showing fractions of each form at different pHs are shown in Figs. 3.1 to 3.7.

Variation of hexaaquachromium(III) and its conjugate base, Cr(H₂O)₅OH²⁺, with pH are also shown in Fig. 3.8.
Fig. 3.1: pH profile of iso-Leucine species in aqueous solution at 25°C.
Fig. 3.2: pH profile of Arginine species in aqueous solution at 25°C.
Fig. 3.3: pH profile of Proline species in aqueous solution at 25°C
Fig 3.4: pH profile of Threonine species in aqueous solution at 25°C
Fig. 3.5: pH profile of Asparagine species in aqueous solution at 25°C.
Fig. 3.6: pH profile of Lysine species in aqueous solution at 25°C.
Fig 3.7: pH profile of Histidine species in aqueous solution at 25°C
Fig. 3.8: Distribution curves of Cr(H$_2$O)$_6^{3+}$ and its conjugate base in aqueous solution. — indicates the pH range of kinetic studies made with the particular amino acid.
B. DISCUSSION

From the various pKₐ values (Table 3.2) and the distribution plots (Fig. 3.1-3.7), one can ascertain of the amino acid species present under the experimental conditions. Table 3.3 shows a summary of the dominant species that exist under the conditions used in the present investigations. As regards the metal species, both Cr(H₂O)₆³⁺ and Cr(H₂O)₅OH²⁺ exist in appreciable concentrations (see Fig. 3.8).

Though the pKₐ values depend on temperature, ionic strength, dielectric constant, etc., the effect is not large to alter the general picture shown in Figs. 3.1-3.8.

Solutions of the investigated ligands give upon addition of Cr(III) nitrate in acidic solution an increase of absorption in the visible range. The absorption spectra of mixtures containing chromium(III) and amino acids in different molar ratios exhibited maxima different from a solution of Cr(III) nitrate (see, for example, Figs. 2.1-2.7 for 1:9 molar ratios). However, optical density values at the absorption maxima were different in different reaction mixtures owing to the fact that the product concentrations were different in each case.
TABLE 3.3: Species of Amino Acids that Predominate in the Investigated pH Range.

<table>
<thead>
<tr>
<th>Amino Acid</th>
<th>Predominant Species</th>
</tr>
</thead>
<tbody>
<tr>
<td>iso-Leucine</td>
<td>CH₃ &lt;br&gt;CH₂ &lt;br&gt;CH-CH₃ &lt;br&gt;H₂N-CH-COOH &lt;br&gt;(H₂L⁺) &lt;br&gt;CH₃ &lt;br&gt;CH₂ &lt;br&gt;CH-CH₃ &lt;br&gt;H₂N-CH-COO⁻ &lt;br&gt;(HL)</td>
</tr>
<tr>
<td>Proline</td>
<td>( + ) &lt;br&gt;COOH &lt;br&gt;N &lt;br&gt;H₂ &lt;br&gt;(H₂L⁺) &lt;br&gt;( + ) &lt;br&gt;COO⁻ &lt;br&gt;N &lt;br&gt;H₂ &lt;br&gt;(HL)</td>
</tr>
<tr>
<td>Threonine</td>
<td>CH₃ &lt;br&gt;HO-CH &lt;br&gt;H₂N-CH-COOH &lt;br&gt;(H₂L⁺) &lt;br&gt;CH₃ &lt;br&gt;HO-CH &lt;br&gt;H₂N-CH-COO⁻ &lt;br&gt;(HL)</td>
</tr>
<tr>
<td>Amino Acid</td>
<td>Predominant Species</td>
</tr>
<tr>
<td>------------</td>
<td>---------------------</td>
</tr>
</tbody>
</table>
| Asparagine | \[
\begin{align*}
\text{CONH}_2 \\
\text{CH}_2 \\
\text{H}_3\text{N-CH-COOH} \\
\text{(H}_2\text{L}^+) \\
\end{align*}
\right] 
\text{CONH}_2 \\
\text{CH}_2 \\
\text{H}_3\text{N-CH-COO}^- \\
\text{(HL)}
\] |
| Lysine     | \[
\begin{align*}
\text{(CH}_2\text{)}_4\text{NH}_3 \\
\text{H}_3\text{N-CH-COOH} \\
\text{(H}_3\text{L}^{2+}) \\
\end{align*}
\right] 
\text{(CH}_2\text{)}_4\text{NH}_3 \\
\text{H}_3\text{N-CH-COO}^- \\
\text{(H}_2\text{L}^+)
\] |
| Arginine   | \[
\begin{align*}
\text{H}^+ \\
\text{NH}_2 \\
\text{(CH}_2\text{)}_3\text{N-C-NH}_2 \\
\text{H}_3\text{N-CH-COOH} \\
\text{(H}_3\text{L}^{2+}) \\
\end{align*}
\right] 
\text{H}^+ \\
\text{NH}_2 \\
\text{(CH}_2\text{)}_3\text{N-C-NH}_2 \\
\text{H}_3\text{N-CH-COO}^- \\
\text{(H}_2\text{L}^+)
\] |

Table 3.3 contd.
<table>
<thead>
<tr>
<th>Amino Acid</th>
<th>Predominant Species</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histidine</td>
<td><img src="image.png" alt="Histidine Structure" /> $\overset{+}{\text{HC}}\overset{\text{NH}}{\text{C}}\overset{\text{N}}{\text{H}}\overset{\text{CH}}{\text{CH}}\overset{\text{CH}_2}{\text{H}_3\text{N}^-\text{CH-COO}^-}$</td>
</tr>
</tbody>
</table>
From the observation that the variation in wavelength of maximum absorption for different systems is not much (it is between 530 to 570 nm) one can infer that in all these cases the bonding between chromium and amino acids is of similar nature. As chelation is not a favoured process when the amine group of an amino acid is protonated\(^1,2\), chromium(III) and amino acids are bound through the carboxyl group.

The structure of the complexes with different chromium(III):amino acid ratios, recorded in Table 2.8, can be represented as:

**For ratio 1:2**

![Diagram for ratio 1:2](image)

**For ratio 1:1**

(only in case of proline)

![Diagram for ratio 1:1](image)
The rate of complex formation between aqua-chromium(III) and different amino acids was studied under a variety of conditions. In the first set of experiments the concentration of chromium(III) (hereafter referred to as \( \text{Cr(III)}_T \)) was varied at fixed concentrations of amino acids. The ionic strength and pH were also kept constant. The pseudo-first order rate constant, \( k_{\text{obs}} \), was found to increase with increasing concentration of \( \text{Cr(III)}_T \) and the reaction rate is first order with respect to \([\text{Cr(III)}_T]\), i.e.,

\[
\frac{d}{dt} [\text{complex}] = -\frac{d}{dt} [\text{Cr(III)}_T] = k_{\text{obs}} [\text{Cr(III)}_T] \tag{12}
\]

The rates of reactions were also affected by pH variation and a decrease was observed with decreasing pH. For all conditions investigated the reactions showed similar functionality in \([H^+]\). To explain this effect it is necessary to consider the following acid-base equilibrium:

\[
\text{Cr(H}_2\text{O)}_6^{3+} \rightleftharpoons \frac{K_a'}{K_a} \text{Cr(H}_2\text{O)}_6^{2+} + \text{H}^+ \tag{13}
\]

As the pH of the reaction medium decreases the ratio of \([\text{Cr(H}_2\text{O)}_6^{2+}] : [\text{Cr(H}_2\text{O)}_6^{3+}] \) decreases which, in turn, decreases the reaction rate. The presence of \( \text{OH}^- \) ligand causes increased labilities and therefore increased rates are found as in the case, for example, of \( \text{Al(III)}^3, \text{Ga(III)}^4, \text{Mn(III)}^5, \text{Cr(III)}^{6-8}, \) or \( \text{Fe(III)}^9 \).
Ligand species also participate in acid-base equilibria and the reaction rates are controlled by equilibrium positions. Under the experimental conditions used, the major ligand species are $H_2L^+$ and $HL$ (in case of iso-leucine, proline, threonine and asparagine—category I ligands and $H_3L^{2+}$ and $H_2L^+$ (in case of lysine, arginine and histidine—category II ligands). On the basis of unfavourable charge factor, reactions between aqua-Cr(III) species and $H_2L^+$ (of category I ligands) or $H_3L^{2+}$ (of category II ligands) are assumed to be insignificant. Both the $HL$ and $H_2L^+$ (of category II ligands) have negative charge on the carboxylate part and can take part in reactions with cations. Since charges far from the reaction centre have been found to have no influence on the reaction rate of complex formation \(^\text{10-13}\), the extra positive charge on the protonated N atom of category II ligands can be ignored and the true nature of active species is $H_2L$ and not $H_2L^+$. In the general scheme, however, they have been indicated as $H_2L^+$ for purpose of clarity (as it is to be shown in equilibrium with $H_3L^{2+}$).

On account of above discussion, the different possible reaction paths that should be taken into consideration are:
Typical plots of $k_{\text{obs}}$ versus total ligand concentration, $[\text{amino acid}]_T$, are illustrated in Figs. 3.9-3.12 for the data at constant temperatures for iso-leucine. Similar plots were obtained for the remaining data in Tables 2.11-2.24. It can be seen that as $[\text{amino acid}]_T$ increases, $k_{\text{obs}}$ increases but not nearly in direct proportions. The deviations from linearity are more pronounced at lower acidity range. In fact, it appears that $k_{\text{obs}}$ is approaching a limiting value as $[\text{amino acid}]_T$ continues to increase. Such behaviour is attri-
Fig. 3.9: Dependence of pseudo-first-order rate constants, $k_{obs}$ ($\mu = 10 \text{ mol dm}^{-3}$) on $[\text{iso-Leucine}]_T$ at different pHs.
Fig. 3.10: Dependence of pseudo-first-order rate constants, $k_{obs}$ ($\mu = 1.0 \text{ mol dm}^{-3}$) on [iso-Leucine]$_T$ at different pHs.

$t = 35^\circ C$

$10^5 k_{obs} \text{(s}^{-1})$

[iso-Leucine]$_T$ (mol dm$^{-3}$)

$pH$

- 3.0
- 2.8
- 2.6
- 2.4

[Image of graph with data points and lines indicating the pH dependence of $k_{obs}$ on [iso-Leucine]$_T$.]
Fig 3: Dependence of pseudo-first-order rate constant $k_{obs}$ ($\mu=10$ mol dm$^{-3}$) on $\text{L}-\text{iso-leucine} \, J_T$ (mol dm$^{-3}$) at different pHs
Fig. 3.12: Dependence of pseudo-first-order rate constants, $k_{obs}$ ($\mu=1.0$ mol dm$^{-3}$) on [iso-Leucine]$_T$ at different pHs.
butable to outer-sphere association between \( \text{Cr(H}_2\text{O)}^3_6/\text{Cr(H}_2\text{O)}_5^+\text{OH}^{2+} \) and the incoming ligand species\textsuperscript{14,15}.

The mechanism consistent with the experimental data is given by following sequence of reactions (for category I ligands where HL i.e., \( \text{H}_3\text{N} - \text{C}^\text{G} - \text{COO}^- \) is the reactive species):

\[
\begin{align*}
\text{H}_2\text{L}^+ & \quad \overset{K_a}{\longrightarrow} \quad \text{HL} + \text{H}^+ \\
\text{Cr(H}_2\text{O)}^3_6 & \quad \overset{K_a}{\longrightarrow} \quad \text{Cr(H}_2\text{O)}_5^+\text{OH}^{2+} + \text{H}^+ \\
\text{Cr(H}_2\text{O)}^3_6 + \text{HL} & \quad \overset{K_{\text{OS}}}{\underset{K_{\text{OS}}'}\longleftrightarrow} \quad \text{Cr(H}_2\text{O)}_5^+\text{.LH} \\
\text{Cr(H}_2\text{O)}_5^+\text{OH}^{2+} + \text{HL} & \quad \overset{K_{\text{OS}}}{\underset{K_{\text{OS}}'}\longleftrightarrow} \quad \text{Cr(H}_2\text{O)}_5^+\text{OH}^{2+}\text{.LH} \\
\text{Cr(H}_2\text{O)}_5^+\text{.LH} & \quad \overset{k_{\text{an}}}{\longrightarrow} \quad [\text{Cr(H}_2\text{O)}_5\text{.LH}]^3+ + \text{H}_2\text{O} \\
\text{Cr(H}_2\text{O)}_5^+\text{OH}^{2+}\text{.LH} & \quad \overset{k_{\text{an}}'}{\longrightarrow} \quad [\text{Cr(H}_2\text{O)}_5\text{.OH.LH}]^{2+} + \text{H}_2\text{O} \\
\text{Cr(H}_2\text{O)}_5^+\text{.LH} & \quad \overset{\text{fast\ ligand}}{\longrightarrow} \quad \text{Product} \\
\text{Cr(H}_2\text{O)}_5^+\text{.OH}^{2+}\text{.LH} & \quad \overset{\text{fast\ ligand}}{\longrightarrow} \quad \text{Product}
\end{align*}
\]

(for category II ligands where \( \text{H}_2\text{L}^+ \) is the reactive species)

\[
\begin{align*}
\text{H}_2\text{L}^2+ & \quad \overset{K_a}{\longrightarrow} \quad \text{H}_2\text{L}^+ + \text{H}^+ \\
\text{Cr(H}_2\text{O)}^3_6 & \quad \overset{K_a'}{\longrightarrow} \quad \text{Cr(H}_2\text{O)}_5^+\text{OH}^{2+} + \text{H}^+ \\
\text{Cr(H}_2\text{O)}^3_6 + \text{H}_2\text{L}^+ & \quad \overset{K_{\text{OS}}}{\underset{K_{\text{OS}}'}\longleftrightarrow} \quad \text{Cr(H}_2\text{O)}_5^+\text{.LH}_2^+
\end{align*}
\]
\[
\begin{align*}
\text{Cr(H}_2\text{O)}_5\text{OH}^{2+} + \text{H}_2\text{L}^+ & \xrightleftharpoons[K_\text{OS}]{\kappa}\text{Cr(H}_2\text{O)}_5\text{OH}^{2+}.\text{LH}_2^+ \quad (18b) \\
\text{Cr(H}_2\text{O)}_6^3+\cdot\text{LH}_2^+ & \xrightarrow[k_\text{an}]{\kappa}\text{[Cr(H}_2\text{O)}_5\text{LH}_2^+]^{3+} \quad (19b) \\
\text{Cr(H}_2\text{O)}_5\text{OH}^{2+}\cdot\text{LH}_2^+ & \xrightarrow[k_\text{an}]{\kappa}\text{[Cr(H}_2\text{O)}_4\text{OHLH}_2^+]^{2+} \quad (20b) \\
\text{[Cr(H}_2\text{O)}_5\text{LH}_2^+]^{3+} & \xrightarrow[\text{fast ligand}]{\text{ligand}} \text{Product} \quad (21b) \\
\text{[Cr(H}_2\text{O)}_4\text{OHLH}_2^+]^{2+} & \xrightarrow[\text{fast ligand}]{\text{ligand}} \text{Product} \quad (22b)
\end{align*}
\]

In fact the same kind of reaction must be operative for all the amino acids; therefore, for category II ligands also the interaction with the metal centre is assumed through the \(\alpha\)-carboxylic structure.

The suggested mechanism is identical with that proposed by Eigen and coworkers\textsuperscript{16,17} for anation reactions of labile aqua complexes. Such a mechanism involving (i) free ions \(\xrightarrow{\text{ion-pair}}\) and (ii) ion-pair \(\xrightarrow{\text{inner sphere complex}}\) seems applicable to all the examples given above with a difference that the contribution of the reverse reaction of step (ii) is very very small (in fact, zero, as the plots of \(k_{\text{obs}}\) against [amino acid]\textsuperscript{T} have zero intercepts). According to the proposed mechanism, the rate of water exchange at the inner coordination sphere of the metal is slow and rate determining.

The overall rate law for the sequence of reactions (15)-(22) can be given by the expression:
\[
\frac{d}{dt} \text{[complex]} = k_{an}[\text{Cr(H}_2\text{O)}^3_6] + k'_{an}[\text{Cr(H}_2\text{O)}^5\text{OH}^2+.\text{LH}] 
\]

(23)

The mass balance equation for chromium(III) is

\[
[\text{Cr(III)}_T] = [\text{Cr(H}_2\text{O)}^3_6] + [\text{Cr(H}_2\text{O)}^5\text{OH}^2+] + [\text{Cr(H}_2\text{O)}^3_6] + [\text{Cr(H}_2\text{O)}^5\text{OH}^2+.\text{LH}] 
\]

(24)

Substituting \(K'_a, K'_0S\) and \(K'O_S\) into equation (23) we obtain

\[
\frac{d}{dt} \text{[complex]} = k_{an}K'_0S[\text{Cr(H}_2\text{O)}^3_6] + \{k'_{an}K'K'O_S[\text{Cr(H}_2\text{O)}^3_6][\text{HL}]/[H^+] \}
\]

(25)

Similarly, from equation (24),

\[
[\text{Cr(H}_2\text{O)}^3_6] = \frac{[\text{Cr(III)}_T][H^+]}{[H^+] + K'_a + K_0S[H^+][\text{HL}] + K'_K'O_S[\text{HL}]} 
\]

(26)

Substitution of \([\text{Cr(H}_2\text{O)}^3_6] \) into equation (25) gives expression (27)

\[
\frac{d}{dt} \text{[complex]} = \{k_{an}K'_0S + k'_{an}K'K'O_S/[H^+] \}[\text{Cr(III)}_T][\text{HL}][H^+] 
\]

\[
[H^+] + K'_a + (K_0S[H^+] + K'_K'O_S)[\text{HL}] 
\]

(27)

Eliminating \([\text{HL}]\) by \([\text{amino acid}])_T\), we obtain

\[
\frac{d}{dt} \text{[complex]} = \frac{k_{an}K_0S[H^+] + k'_{an}K'K'O_S[Cr(III)]_T[\text{amino acid}]}{[H^+] + [H^+]K'_a + K'_0S[Cr(III)]_T[\text{amino acid}]} 
\]

(28)
Comparison of equation (28) with equation (12) gives equation (29)

\[
k_{\text{obs}} = \frac{\{k_{\text{an}}aK_{\text{OS}}[H^+] + k_{\text{an}}aK'K'K'\text{OS}\}[\text{amino acid}]_T}{[H^+]^2 + [H^+]K_a + [H^+]K' + K_{\text{an}}K' + [K_{\text{an}}K_{\text{OS}}[H^+] + K_{\text{an}}K'K'\text{OS}] [\text{amino acid}]_T}
\]  

(29)

Rearrangement of equation (29) yields

\[
\frac{1}{k_{\text{obs}}} = \frac{K_{\text{an}}K_{\text{OS}}[H^+] + K_{\text{an}}K'K'\text{OS}}{K_{\text{an}}K_{\text{OS}}[H^+] + K'K'K'\text{OS}}
\]  

\[
+ \frac{[H^+]^2 + [H^+]K_a + [H^+]K' + K_{\text{an}}K_a}{K_{\text{an}}K_{\text{OS}}[H^+] + K_{\text{an}}K'K'\text{OS}} \cdot \frac{1}{[\text{amino acid}]_T}
\]  

(30)

The above mechanism is confirmed by plotting $1/k_{\text{obs}}$ vs. $1/[\text{amino acid}]_T$ at different $[H^+]$. The plots (Figs.3.13-3.40) are found to be linear for a given $[H^+]$. The intercepts of these plots are dependent on $[H^+]$, as envisaged by equation (30), but only upto $[H^+] < 2 \times 10^{-4}$ moldm$^{-3}$. Above this hydrogen ion concentration the straight lines converge and have a constant intercept (see Figs. 3.29-3.40). Thus, above this hydrogen ion concentration the intercepts become independent of $[H^+]$. At the low pH range, as $K'_{a} \approx 10^{-4}$ moldm$^{-3}$ and $K_{\text{OS}} > K'$, $K_{\text{an}}K'K'$ and $k_{\text{an}}aK'K'\text{OS}$ can be neglected in comparison with $K_{a}K_{\text{OS}}[H^+]$ and $k_{\text{an}}aK_{\text{OS}}[H^+]$, respectively, and also $K'_{a}[H^+]$ and $K_{a}K'$ as compared to $[H^+]^2 + [H^+]K_a$. Then, equation (30) simplifies to equation (31)
Fig. 3.13: Linear dependence of \( k_{\text{obs}}^{-1} \) on iso-leucine \( J_T^{-1} \) (mol\(^{-1}\)dm\(^3\)) at t = 30°C.

- pH = 2.4: \( \Delta \) (Triangle)
- pH = 2.6: \( \Delta \) (Triangle)
- pH = 2.8: \( \bigcirc \) (Circle)
- pH = 3.0: \( \bullet \) (Solid Circle)

\( 10^{-5} k_{\text{obs}}^{-1} \) (s) vs. iso-leucine \( J_T^{-1} \) (mol\(^{-1}\)dm\(^3\))
$10^{-5}k_{\text{obs}}(s)$

$$t = 35^\circ C$$

Fig 3.14: Linear dependence of $k_{\text{obs}}^{-1}$ on [iso-Leucine]$_T^{-1}$ (mol$^{-1}$dm$^3$)

Fig 3.14: Linear dependence of $k_{\text{obs}}^{-1}$ on [iso-Leucine]$_T^{-1}$
Fig. 3.15: Linear dependence of $k_{obs}$ on $[\text{Iso-Leucine}]_T$.

$t = 40^\circ C$

$pH$

$\Delta 2.4$

$\Delta 2.5$

$\Delta 3.6$

$\bullet 5.0$
Fig. 3.16: Linear dependence of $k_{obs}$ on $[\text{iso-Leucine}]^{-1}$.
Fig. 3.17: Linear dependence of $k_{obs}^{-1}$ on $\left[\text{Arginine}\right]_{T}^{-1}$

$t = 45^\circ C$

$pH$

$\triangle 2.50$

$\triangle 2.75$

$3.00$

$3.25$
$t = 50^\circ C$

Fig 3.13: Linear dependence of $k_{obs}$ on $\Xi_1$ 

$10^{-5} k_{obs}^{-1}(s)$

$\Xi_1$ (mole $\cdot$ dm$^{-3}$)
Fig. 3.19: Linear dependence of $k_{\text{obs}}^{-1}$ on $\text{[Arginine]}_T$.
Fig 3: Linear dependence of $k_{obs}^{-1}$ on $[\text{Arginine}]_T^{-1}$.
Fig. 3-21: Linear dependence of $k_{obs}$ on $[\text{Proline}]^{-1}$.
Fig 3.22: Linear dependence of $k_{\text{obs}}$ on $[\text{Proline}]^{-1}$ (moles$^{-1}$ cm$^3$).

$t = 50^\circ\text{C}$
Fig. 3.23: Linear dependence of $k_{obs}$ on $\text{Proline}^{-1}$.
Fig. 3.24: Linear dependence of $k_{obs}^{-1}$ on $[\text{Proline}]^{-1}$.
Fig 3.25. Linear dependence of $k_{obs}$ on $[\text{Threonine}]^{-1}$.
Fig. 326: Linear dependence of $k_{obs}^{-1}$ on $\left[\text{Threonine}\right]^{-1}$.

$t = 45^\circ C$
Fig 3.27. Linear dependence of $k_{obs}^{-1}$ on $[\text{Threonine}]^{-1}$.

$t = 50{}^\circ C$
Fig. 3.28 Linear dependence of $k_{obs}^{-1}$ on Ethreonine $T^{-1}$ (mol$^{-1}$cm$^3$).
Fig. 3.29: Linear dependence of $k_{obs}$ on $\frac{[Asparagine]}{[T]}$.
Fig. 3.30: Linear dependence of $k_{\text{obs}}^{-1}$ on $[\text{Asparagine}]_T^{-1}$.
Fig 3.31: Linear dependence of $k_{obs}^{-1}$ on $[\text{Asparagine}]_T^{-1}$.
Fig 3.32: Linear dependence of $k_{obs}^{-1}$ on $[\text{Asparagine}]_{T}^{-1}$.
Fig 3.33: Linear dependence of $k_{\text{obs}}^{-1}$ on $[\text{Lysine}]_{\text{T}}^{-1}$.
Fig. 3.34: Linear dependence of $k_{\text{obs}}^{-1}$ on $[\text{Lysine}]_T^{-1}$.
Fig 3.35. Linear dependence of $k_{\text{obs}}$ on $\ell_{\text{Lysine}}^{-1}$.
Fig 3.36: Linear dependence of $k_{\text{obs}}^{-1}$ on $[\text{Lysine}]_T^{-1}$.
Fig. 3.37: Linear dependence of $k_{obs}^{-1}$ on $[\text{Histidine}]^{-1}_{T}$.
Fig.3.38: Linear dependence of $k_{obs}$ on $[\text{Histidine}]_{T}^{-1}$.
Fig. 3.39 Linear dependence of $k_{obs}$ on $[\text{Histidine}]_T$.

$t = 45^\circ C$

$\text{pH}$

$3.50$

$3.73$

$4.00$

$4.23$

$10^{-5}k_{obs}(s)$

$[\text{Histidine}]_T^{-1}$ (mol$^{-1}$ dm$^3$)
Fig. 3.40: Linear dependence of $k_{\text{obs}}^{-1}$ on $[\text{Histidine}]_T^{-1}$

$t = 50^\circ \text{C}$

$10^{-5}k_{\text{obs}}^{-1}(s)$

$[\text{Histidine}]_T^{-1} \text{(mol}^{-1}\text{dm}^3)$
\[
\frac{1}{k_{\text{obs}}} = \frac{1}{k_{\text{an}}} + \frac{[H^+] + K_a}{k_{\text{an}} K_a K_{\text{OS}}} \cdot \frac{1}{[\text{amino acid}]_p}
\]  

(31)

The same rate law was derived previously for all the 
\([\text{Cr}L_5\text{OH}_2] + X\) systems \((L = \text{H}_2\text{O} \text{ or } \text{NH}_3\) and \(X = \text{glycine}^{18}, \text{alanine}^{9,19}, \text{serine}^{20}, \text{valine}^{21}\) where the part played by 
the hydrolysed species \([\text{Cr}L_5\text{OH}]^{2+}\) was omitted.

Plots producing straight lines according to equations (31) 
(covering lines in the limited low pH range) and (30) (at 
higher pH values) were used to calculate the values of \(k_{\text{an}'},\)
\(k_{\text{an}}', K_{\text{OS}}\) and \(K_{\text{OS}'}\). These values are given in Tables 3.4-3.10.

Activation parameters for \(k_{\text{an}}\) and \(k_{\text{an}}'\) were obtained from 
plots of \(\log (k_{\text{an}} \text{NH}/RT)\) vs. \(1/T\). The values are recorded in 
Table 3.11.

The \(k_{\text{obs}}\) obtained in alcohol-water mixed solvents show 
an increase with increasing \% of alcohol (v/v). The plots 
of \(\log k_{\text{obs}}\) and \(1/D\) were linear with a positive slope, 
supporting that the reactions under study are of ion-dipole 
type. Obviously, according to Bjerrum's equation^{22}, the values 
of outer-sphere association constants will increase with 
decrease in the dielectric constant of the medium, and, therefore, outer-sphere association is enhanced with a consequent increase in the rate.
TABLE 3.4: Summary of Kinetic Data for the Anation of Cr(III) by L-iso-Leucine in Aqueous-Acidic Medium ($\mu = 1.0$ moldm$^{-3}$).

<table>
<thead>
<tr>
<th>$t$ (°C)</th>
<th>$10^4k_{an}$ (s$^{-1}$)</th>
<th>$K_{OS}$ (dm$^3$mol$^{-1}$)</th>
<th>$10^3k_a$ (dm$^{-3}$mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30</td>
<td>1.0</td>
<td>3.57</td>
<td>4.82</td>
</tr>
<tr>
<td>35</td>
<td>2.0</td>
<td>4.65</td>
<td>4.82</td>
</tr>
<tr>
<td>40</td>
<td>2.5</td>
<td>4.72</td>
<td>4.79</td>
</tr>
<tr>
<td>45</td>
<td>3.3</td>
<td>4.76</td>
<td>4.73</td>
</tr>
</tbody>
</table>

Mean value 4.42

---

*P.K. Smith, A.C. Taylor and E.R.B. Smith, J. Biol. Chem., 122 (1937) 109, values were calculated by Harned and Embree's eq., $pK = pK_{max} + p(t-\theta)^2$ with $pK_{max} = 2.32$, $p = 5 \times 10^{-5}$ and $\theta = 32.40$.\*
<table>
<thead>
<tr>
<th>t (°C)</th>
<th>$10^4k_{an}$ (s$^{-1}$)</th>
<th>$K_{OS}$ (dm$^3$mol$^{-1}$)</th>
<th>$10^3k_a^*$ (dm$^{-3}$mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>-</td>
<td>-</td>
<td>6.76</td>
</tr>
<tr>
<td>45</td>
<td>1.54</td>
<td>8.35</td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>3.33</td>
<td>5.59</td>
<td></td>
</tr>
<tr>
<td>55</td>
<td>5.71</td>
<td>4.46</td>
<td></td>
</tr>
<tr>
<td>60</td>
<td>10.00</td>
<td>4.09</td>
<td></td>
</tr>
</tbody>
</table>

Mean value 5.62

TABLE 3.6: Summary of Kinetic Data for the Anation of Cr(III) by L-Proline in Aqueous-Acidic Medium 
($\mu = 1.0$ moldm$^{-3}$).

<table>
<thead>
<tr>
<th>$t$ ($^\circ$C)</th>
<th>$10^4k_{an}$ (s$^{-1}$)</th>
<th>$K_{OS}$ (dm$^3$mol$^{-1}$)</th>
<th>$10^3k_a$ (dm$^{-3}$mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>45</td>
<td>4.0 10$^4$</td>
<td>7.24</td>
<td>11.13</td>
</tr>
<tr>
<td>50</td>
<td>5.0 10$^4$</td>
<td>6.98</td>
<td>10.96</td>
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<td>55</td>
<td>6.67 10$^4$</td>
<td>6.58</td>
<td>10.73</td>
</tr>
<tr>
<td>60</td>
<td>10.0 10$^4$</td>
<td>5.26</td>
<td>10.45</td>
</tr>
<tr>
<td>Mean value</td>
<td>6.51</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Calculated values from the equation of Harned and Embree; from P.K. Smith, A.T. Gorham and E.R.B. Smith, J. Biol. Chem., 144 (1942) 737 ($pK_{max} = 1.95$, $p = 5 \times 10^{-5}$ and $\Theta = 34.40$).*
TABLE 3.7: Summary of Kinetic Data for the Anation of Cr(III) by DL-Threonine in Aqueous-Acidic Medium

\( (\mu = 1.0 \text{ moldm}^{-3}) \).

<table>
<thead>
<tr>
<th>(t (\degree C))</th>
<th>(10^4k_{an} ) (s(^{-1}))</th>
<th>(K_{0S}) (dm(^3)mol(^{-1}))</th>
<th>(10^3k_a^*) (dm(^{-3})mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>40</td>
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</tr>
<tr>
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<td>2.0</td>
<td>6.52</td>
<td>8.75</td>
</tr>
<tr>
<td>50</td>
<td>3.3</td>
<td>7.62</td>
<td>8.81</td>
</tr>
<tr>
<td>55</td>
<td>8.0</td>
<td>7.58</td>
<td>8.83</td>
</tr>
</tbody>
</table>

Mean value 6.69

\( ^* \) Calculated values from the equation of Harned and Embree; from P.K. Smith, A.T. Gorham and E.R.B. Smith, J. Biol. Chem., 144 (1942) 737 \( (pK_{max} = 2.05, p = 5 \times 10^{-5} \) and \( \Theta = 54.00 \)).
TABLE 3.8: Summary of Kinetic Data for the Anation of Cr(III) by L-Asparagine in Aqueous-Acidic Medium (μ = 1.0 moldm\(^{-3}\)).

<table>
<thead>
<tr>
<th>t (°C)</th>
<th>(10^4k_{an}) (s(^{-1}))</th>
<th>(K_{OS}) (dm(^3)mol(^{-1}))</th>
<th>(10^3k'_{an}) (s(^{-1}))</th>
<th>(K'_{OS}) (dm(^3)mol(^{-1}))</th>
<th>(10^3K_a^x) (dm(^{-3})mol(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>9.55</td>
</tr>
<tr>
<td>40</td>
<td>4.0</td>
<td>4.06</td>
<td>0.49</td>
<td>4.04</td>
<td></td>
</tr>
<tr>
<td>45</td>
<td>5.0</td>
<td>5.0</td>
<td>1.26</td>
<td>4.82</td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>6.66</td>
<td>5.90</td>
<td>3.70</td>
<td>2.07</td>
<td></td>
</tr>
<tr>
<td>55</td>
<td>9.09</td>
<td>6.97</td>
<td>5.75</td>
<td>2.80</td>
<td></td>
</tr>
</tbody>
</table>

Mean value: 5.48

TABLE 3.9: Summary of Kinetic Data for the Anation of Cr(III) by L-Lysine in Aqueous-Acidic Medium (μ = 1.0 mol dm⁻³).

<table>
<thead>
<tr>
<th>t (°C)</th>
<th>10⁴k_an (s⁻¹)</th>
<th>K_Os (dm³ mol⁻¹)</th>
<th>10³k'_an (s⁻¹)</th>
<th>K'_Os (dm³ mol⁻¹)</th>
<th>10³K_a * (dm⁻³ mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>6.61</td>
</tr>
<tr>
<td>35</td>
<td>1.25</td>
<td>11.74</td>
<td>0.19</td>
<td>5.18</td>
<td></td>
</tr>
<tr>
<td>40</td>
<td>2.0</td>
<td>7.78</td>
<td>0.27</td>
<td>1.84</td>
<td></td>
</tr>
<tr>
<td>45</td>
<td>2.38</td>
<td>7.16</td>
<td>0.29</td>
<td>3.67</td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>5.26</td>
<td>6.29</td>
<td>0.71</td>
<td>8.04</td>
<td></td>
</tr>
<tr>
<td>Mean value</td>
<td>8.24</td>
<td>Mean value</td>
<td>4.68</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>t (°C)</th>
<th>$10^4 k_{an}$ (s$^{-1}$)</th>
<th>$K_{OS}$ (dm$^3$mol$^{-1}$)</th>
<th>$10^3 k'_{an}$ (s$^{-1}$)</th>
<th>$K'_{OS}$ (dm$^3$mol$^{-1}$)</th>
<th>$10^3 k_a$ (dm$^{-3}$mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>15.13</td>
</tr>
<tr>
<td>35</td>
<td>1.67</td>
<td>3.47</td>
<td>0.72</td>
<td>2.79</td>
<td></td>
</tr>
<tr>
<td>40</td>
<td>2.5</td>
<td>4.12</td>
<td>0.82</td>
<td>3.23</td>
<td></td>
</tr>
<tr>
<td>45</td>
<td>5.56</td>
<td>4.13</td>
<td>1.54</td>
<td>3.40</td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>6.25</td>
<td>4.41</td>
<td>1.70</td>
<td>4.00</td>
<td></td>
</tr>
</tbody>
</table>

Mean value 4.03 Mean value 3.35

TABLE 3.11: First-order Rate Constants and Activation Parameters$^a$ for the Reaction
\[
\text{Cr(H}_2\text{O)}_6^{3+} + X \rightarrow \text{Cr(H}_2\text{O)}_5X^{2+} + \text{H}_2\text{O}.
\]

<table>
<thead>
<tr>
<th>X</th>
<th>t (°C)</th>
<th>(k_\text{an} (s^{-1}))</th>
<th>(\Delta H^\neq ) (kJmol$^{-1}$)</th>
<th>(\Delta S^\neq ) (JK$^{-1}$mol$^{-1}$)</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>\text{H}<em>2\text{O}</em>{18}</td>
<td>35</td>
<td>4.17x10$^{-6}$ (k_\text{ex} )</td>
<td>110</td>
<td>+ 1</td>
<td>38</td>
</tr>
<tr>
<td>Alanine$^b$</td>
<td>35</td>
<td>0.58x10$^{-4}$</td>
<td>64.89</td>
<td>-107.60</td>
<td>8</td>
</tr>
<tr>
<td>Serine$^b$</td>
<td>35</td>
<td>0.62x10$^{-4}$</td>
<td>78.0</td>
<td>-72.51</td>
<td>20</td>
</tr>
<tr>
<td>Threonine</td>
<td>40</td>
<td>1.0x10$^{-4}$</td>
<td>112.97</td>
<td>-22.05</td>
<td></td>
</tr>
<tr>
<td>Hydroxyproline</td>
<td>40</td>
<td>1.0x10$^{-4}$</td>
<td>72.76</td>
<td>-98.22</td>
<td>39</td>
</tr>
<tr>
<td>Lysine</td>
<td>35</td>
<td>1.25x10$^{-4}$</td>
<td>61.30</td>
<td>-115.10</td>
<td></td>
</tr>
<tr>
<td>Arginine</td>
<td>45</td>
<td>1.54x10$^{-4}$</td>
<td>99.60</td>
<td>-22.98</td>
<td></td>
</tr>
<tr>
<td>Nitrilotriacetic acid$^c$</td>
<td>35</td>
<td>1.67x10$^{-4}$</td>
<td>86.44</td>
<td>-36.82</td>
<td>40</td>
</tr>
<tr>
<td>Histidine</td>
<td>35</td>
<td>1.67x10$^{-4}$</td>
<td>89.99</td>
<td>-58.40</td>
<td></td>
</tr>
<tr>
<td>Phenylalanine</td>
<td>40</td>
<td>1.85x10$^{-4}$</td>
<td>53.61</td>
<td>-141.69</td>
<td>39</td>
</tr>
<tr>
<td>iso-Leucine</td>
<td>35</td>
<td>2.00x10$^{-4}$</td>
<td>65.10</td>
<td>-111.25</td>
<td></td>
</tr>
<tr>
<td>Valine</td>
<td>35</td>
<td>2.35x10$^{-4}$</td>
<td>91.88</td>
<td>-22.89</td>
<td>21</td>
</tr>
</tbody>
</table>

Table 3.11 contd.
<table>
<thead>
<tr>
<th>X</th>
<th>t (°C)</th>
<th>$k_{an}$ (s$^{-1}$)</th>
<th>$\Delta H^\circ$ (kJmol$^{-1}$)</th>
<th>$\Delta S^\circ$ (JK$^{-1}$mol$^{-1}$)</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycine$^b$</td>
<td>35</td>
<td>3.34x10$^{-4}$</td>
<td>58.0</td>
<td>-129.16</td>
<td>18</td>
</tr>
<tr>
<td>Asparagine</td>
<td>40</td>
<td>4.00x10$^{-4}$</td>
<td>46.0</td>
<td>-143.60</td>
<td>Present work</td>
</tr>
<tr>
<td>Proline</td>
<td>45</td>
<td>4.00x10$^{-4}$</td>
<td>54.60</td>
<td>-136.0</td>
<td>Present work</td>
</tr>
<tr>
<td>Anthranilic acid</td>
<td>35</td>
<td>4.66x10$^{-4}$</td>
<td>94.90</td>
<td>-0.58</td>
<td>41</td>
</tr>
<tr>
<td>p-Hydroxybenzoic acid</td>
<td>35</td>
<td>4.90x10$^{-4}$</td>
<td>105.0</td>
<td>+25.0</td>
<td>42</td>
</tr>
<tr>
<td>Acetic acid</td>
<td>35</td>
<td>6.64x10$^{-4}$</td>
<td>103.0</td>
<td>+31.0</td>
<td>43</td>
</tr>
<tr>
<td>Salycilic acid</td>
<td>35</td>
<td>17.82x10$^{-4}$</td>
<td>74.48</td>
<td>-60.49</td>
<td>44</td>
</tr>
</tbody>
</table>

$^a$ All values at $\mu = 1.0$ moldm$^{-3}$, except where otherwise stated.

$^b$ Extrapolated values.

$^c$ $\mu = 0.25$ moldm$^{-3}$, water-ethanol medium (30%, v/v).
The ion-dipole mechanism is further corroborated by the observed ionic strength influence on the reaction rate. The values of $k_{obs}$ increase with increase in $\mu$. Although the concentrations employed in studying the effect of $\mu$ on the reaction rate are such that the total ionic strength of the systems is far greater than that permitted by the Debye-Hückel treatment, the results in terms of Bronsted-Bjerrum-Christiansen equation\textsuperscript{23} are consistent with the assumed reactions involving positively charged species and dipoles.

Many workers have studied the anation reactions of hexaaqua- and hydroxopentaaquachromium(III) ions with a variety of ligands—both inorganic and organic. The data were discussed in terms of dissociative interchange ($I_d$)\textsuperscript{24-27} and associative interchange ($I_a$)\textsuperscript{28-30} mechanisms. Later, Swaddle\textsuperscript{31} has reviewed the activation parameters and mechanism of octahedral substitution reactions and has concluded that an $I_a$ mechanism is operative for octahedral cationic complexes of all trivalent metals (except Co(III)) having ionic radii greater than ca. 60 pm (but an $I_d$ mechanism is operative for very largest tripositive ions where charge-to-radius ratio is again small, as for divalent ions, for which the $I_d$ mechanism operates). The field-free ionic radius of Cr$^{3+}$ being 69-69 pm\textsuperscript{32} demands an associative character to anation reactions of Cr(H$_2$O)$_6^{3+}$. 
A well accepted procedure to distinguish between an $I_a$ mechanism from an $I_d$ mechanism for the anation reaction is the examination of the span of values of rate constants for the reaction:

$$\text{ML}_5^3 + X \rightarrow \text{ML}_5^3 X + S, \quad S = \text{solvent}$$

(32)

a wide series of different entering ligands, $X$. For such a purpose, second-order rate constants $k (= k_{\text{an}} K_{\text{OS}})$ have often been used to characterize anation reactions of a number of metal ions; for example, an $I_a$ mechanism has been assigned to simple anation reactions of many Cr(III) complexes, to most of the anation reactions of Rh(NH$_3$)$_5$H$_2$O$^{3+}$, and $I_d$ mechanism to anation reactions of Co(NH$_3$)$_5$H$_2$O$^{3+}$. A more reliable method is that comparisons be made among first-order rate constants ($k_{\text{an}}$), since in this way differences in $K_{\text{OS}}$ be obviated ($K_{\text{OS}}$ values have been found to depend not only on the charge of the entering ligand but also on its nature). A narrow spread of $k_{\text{an}}$ values suggests that the rates of entry of various ligands to the primary coordination sphere is controlled in each complex by largely the same factor (the fission of metal-solvent bond) and hence the mechanism is dissociatively activated. A larger span in $k_{\text{an}}$ is indicative of ligand assisted anation and therefore the mechanism is associatively activated. First-order rate constant data for anation reaction of Cr(III) by a series of ligands of similar nature are collected in Tables 3.11 and 3.12. The span of $k_{\text{an}}$ is
much larger, (0.58-17.82)X10^{-4} (35-45°), than of k'_{an},
(0.19-0.72)X10^{-3} (35-45°). Accordingly, an I_a mechanism
can be assigned to k_{an} route and an I_d to k'_{an} route. We can
also see (Table 3.11) that the values of k_{an} are far greater
than the value of k_{ex} (water exchange in Cr(H_2O)_6^{3+}) which
suggest that the anations of Cr(H_2O)_6^{3+} with the amino acids
used are all ligand assisted and support the associative
interchange (I_a) assignment. The values of k'_{an} and k'_{ex}
(water exchange in Cr(H_2O)_5OH^{2+}) are of the same order of
magnitude supporting the dissociative interchange (I_d) mechanism
for the anation of Cr(H_2O)_5OH^{2+} with the amino acids. It is
found that the conjugate base is more labile by a factor of 10.
The same labilizing effect of the hydroxide has been reported
by many workers, not only for chromium(III)\textsuperscript{6-8} but for other
metal ions also\textsuperscript{3-5,9}. This may be explained on the basis
that coordinated OH\textsuperscript{-} facilitates a dissociative mechanism through
its π-bonding ability.

Activation parameters, compared with literature values
for reactions of Cr(III) in Tables 3.11 and 3.12, also support
the above assignments\textsuperscript{29,31} which are confirmed on the basis of
isokinetic plots (Figs. 3.41 and 3.42).
TABLE 3.12: First-order Rate Constants and Activation Parameters\(^a\) for the Reaction
\[
\text{Cr(H}_2\text{O})_5\text{OH}^{2+} + X \rightarrow \text{Cr(H}_2\text{O})_4\text{OHX}^+ + \text{H}_2\text{O.}
\]

<table>
<thead>
<tr>
<th>X</th>
<th>( t ) (°C)</th>
<th>( k'_{an} ) (s(^{-1}))</th>
<th>( \Delta H^\ddagger ) (kJmol(^{-1}))</th>
<th>( \Delta S^\ddagger ) (JK(^{-1})mol(^{-1}))</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \text{H}_2\text{O} )</td>
<td>50</td>
<td>5.0 \times 10^{-3}(k'_{ex})</td>
<td></td>
<td></td>
<td>31</td>
</tr>
<tr>
<td>Lysine</td>
<td>35</td>
<td>0.19 \times 10^{-3}</td>
<td>57.4</td>
<td>-126.7</td>
<td>Present work</td>
</tr>
<tr>
<td>Hydroxyproline</td>
<td>40</td>
<td>0.21 \times 10^{-3}</td>
<td>63.18</td>
<td>-114.12</td>
<td>39</td>
</tr>
<tr>
<td>Phenylalanine(^b)</td>
<td>35</td>
<td>0.32 \times 10^{-3}</td>
<td>53.94</td>
<td>-135.91</td>
<td>45</td>
</tr>
<tr>
<td></td>
<td>45</td>
<td>0.71 \times 10^{-3}</td>
<td>-</td>
<td>-</td>
<td>39</td>
</tr>
<tr>
<td>Alanine(^c)</td>
<td>35</td>
<td>0.39 \times 10^{-3}</td>
<td>34.04</td>
<td>-201.69</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.46 \times 10^{-3}</td>
<td>77.0</td>
<td>-68.0</td>
<td>8</td>
</tr>
<tr>
<td>Asparagine</td>
<td>40</td>
<td>0.49 \times 10^{-3}</td>
<td>170.4</td>
<td>+212.5</td>
<td>Present work</td>
</tr>
<tr>
<td>Histidine</td>
<td>35</td>
<td>0.72 \times 10^{-3}</td>
<td>42.13</td>
<td>-153.8</td>
<td>Present work</td>
</tr>
</tbody>
</table>

\(a\) All values at \( \mu = 1.0 \text{ moldm}^{-3} \), except where otherwise stated.

\(b\) \( \mu = 0.0075 \text{ moldm}^{-3} \).

\(c\) \( \mu = 0.03 \text{ moldm}^{-3} \).
FIG. 3.42: Isokinetic plot for the anation of 
Cr(H₂O)₅ OH²⁺ by (1) Phenylalanine, 
(2) Hydroxyproline, (3) Alanine (4) Lysine, 
(5) Histidine, and (6) Asparagine.
REFERENCES


