Kinetic and Mechanistic Studies on the Complexation of Aquachromium(III) with DL-Tryptophan in Aqueous Acidic Media

Mohammad Shahid,* Iqrar A. Khan, and Kabir-ud-Din
Department of Chemistry, Aligarh Muslim University, Aligarh-202002, India

Aquachromium(III) has been found to form a 1:3 complex with DL-tryptophan. The kinetics of the reaction has been followed over the range pH 2.75—3.75 by visible spectrophotometry. The effect of the total ligand and chromium(III) concentrations, ethanol content, and temperature on the rate of the reaction was determined. The results are best accounted for by the 'Eigen–Tamm' mechanism. A rate law based on the outer-sphere complexation equilibrium preceding the anation has been established. Values for the outer-sphere complex-formation constants were also calculated from the kinetic data. Anations of $[Cr(H_2O)_6]^{3+}$ and $[Cr(H_2O)_5(OH)]^{2+}$ are discussed in terms of associative interchange (I_a) and dissociative interchange (I_d) mechanisms.

Metal ions play a very important role in biological reactions, enzymatic reactions being mostly activated or controlled by metallic cations, which are in combined state with proteins, amino acids, lipids, and related compounds. Thus studies of metal complexes with such ligands are important because they act as a model for complicated proteins.[1]

The first demonstration of a metabolic effect of chromium was reported in 1955.[2] Since then a great deal of evidence for chromium as an essential trace metal has appeared. The biologically active form of chromium is Cr^{III}.

Amino acid complexes of chromium were first characterized in 1910.[3] Chromium(III) chemistry was stimulated by the work of Mertz and co-workers[4] who showed that a low-molecular-weight complex, known as 'Glucose Tolerance Factor', potentiates insulin activity. Interest in this substance has stimulated work on chromium(III) amino acid complexes and reports on various aspects have appeared.[5]

We have undertaken a systematic study of the interaction of Cr^{III} with individual components of the mixture described by Toepfer[5] as well as other amino acids which includes measurements of equilibrium constants, structure determinations, and kinetic studies,[6,7] as not only the composition but other aspects may be helpful in understanding the nature of the glucose tolerance factor.

In the present paper results on the anation kinetics of aquachromium(III) with DL-tryptophan are described with a view to throwing more light on the mechanism of the reactions of aquachromium(III) with amino acids. Many kinetic studies on the Cr^{III} + amino acid system have appeared.[6–10] However, they have concentrated mostly on the complexation kinetics of $[Cr(H_2O)_6]^{3+}$ or $[Cr(H_2O)_5(OH)]^{2+}$; the substitution lability of both these species, though present simultaneously, has rarely been considered. Also, the mechanisms suggested by different authors are not uniform (see Table 5). In the work described herein the acidity range has been chosen such that the participation of both these species can be investigated.

Experimental

Reagents.—DL-Tryptophan (chromatographically homogeneous, SRL, India) was used without further purification. Other chemicals used were of reagent grade. Water was redistilled from alkaline $KMnO_4$ in an all-glass still. Ethanol was distilled twice. The stock solution of $Cr(NO_3)_3 \cdot 9H_2O$ was standardized by passing aliquots through a column of Dowex 50W-X8 (H^+ form) and titrating the effluent with a standard NaOH solution.

Kinetic Procedure.—Solutions of required volumes of DL-tryptophan, HNO_3 or NaOH (for maintaining the desired pH), and KNO_3 (to adjust the ionic strength) were taken in a three-necked flask (100 cm^3) fitted with a double-walled spiral condenser to prevent evaporation. The solution of chromium(III) nitrate was placed in a separate flask. Both solutions were deoxygenated with purified N_2 and kept in a thermostat maintained at the desired temperature (±0.1 °C). To start the reaction, the requisite volume of chromium(III) nitrate solution was added to the reaction vessel, N_2 being bubbled through the solution to ensure thorough mixing and an inert atmosphere. The progress of the reaction was monitored at 545 nm ($\lambda_{max.}$ of the complex formed, Figure 1) using a sampling technique. Pseudo-first-order conditions were maintained in all runs by using a large excess of tryptophan (≥ ten-fold, except in some runs where $[Cr^{III}] > [trp]$). Values of the rate constants, $k_{obs.}$, were obtained from slopes of first-order plots of log $(A_\infty - A_0)/(A_\infty - A_t)$ *versus* time(t) where A denotes measured absorbance and the subscripts have the usual meanings. Such plots were linear for at least two half-lives.

The absorbance measurements were made with a B and L Spectronic 20 spectrophotometer. An ELICO LI-120 digital pH-meter fitted with a CH-41 combination electrode was used for pH measurements.

Results and Discussion

Tryptophan–Chromium(III) Complex.—Upon addition of aquachromium(III) in acidic solution to a solution of tryptophan an increase in absorption in the visible range occurred. The absorption spectra of mixtures containing the reactants in different molar ratios exhibited maxima different from that of a solution of aquachromium(III) (see, for example, Figure 1 for 1:9 molar ratios). The optical density values at the absorption maxima were different for the different reaction mixtures due to the different product concentrations. The spectra consist of a single broad band with a maximum at 545 nm (shoulder at *ca.* 400 nm). Since the variation in wavelength of the maximum absorption for different chromium(III)–amino acid systems is not large (540—560 nm)[6,7] one can infer that in all these cases the bonding between chromium and the amino acids is of a similar nature. As chelation is not favoured when the amino group of an amino acid is protonated,[11] the ligands bind to Cr^{III} only through the carboxylate oxygen. This is in accord with previous findings of Shuttleworth and Sykes[12] who reported

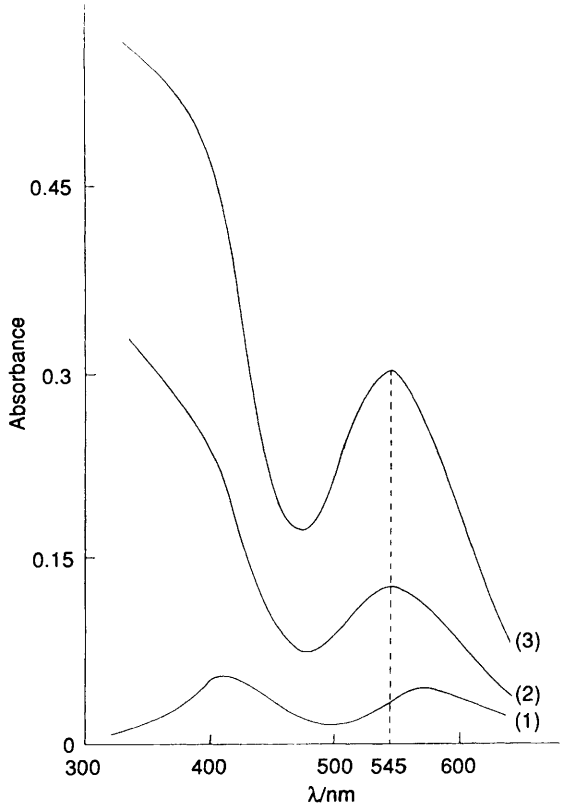


Figure 1. Absorption spectra of chromium(III) and its amino acid complex: (1) $[Cr(NO_3)_3]_T$ = 0.002 mol dm^{-3}; (2) $[Cr(NO_3)_3]_T$ = 0.002, $[trp]_T$ = 0.018 mol dm^{-3} (1:9 molar ratio); and (3) $[Cr(NO_3)_3]_T$ = 0.004, $[trp]_T$ = 0.036 mol dm^{-3} (1:9 molar ratio)

Table 1. Effect of chromium concentration and ethanol content on $k_{obs.}$ at $10^4[H^+]$ = 20.4 mol dm^{-3}, I = 1.0 mol dm^{-3}, and 50 °C

$10^3[Cr^{III}]_T$/mol dm^{-3}	% (v/v) Ethanol	$10^4k_{obs.}/s^{-1}$ $[trp]_T$ = 0.02 mol dm^{-3}
1.0	0	0.39
2.0		0.39
	10	1.11
	15	1.78
	20	2.32
	25	2.76
		$[trp]_T$ = 0.002 mol dm^{-3}
10.0	0	0.37
20.0		0.35
30.0		0.36
40.0		0.34

complex formation with co-ordination of the carboxylate group taking place at pH < 4 and co-ordination of the amino group only at pH > 7. This monodentate carboxylate co-ordination mode is well known for other metal ions, *e.g.* Co^{III} (ref. 13) and Pt^{II}.[14]

The composition of the complex formed, as determined by Job's method, was found to be 1:3 (metal:ligand).

Dependence of Reaction Rate on Chromium(III) Concentration.—In the first set of kinetic experiments the concentration of Cr^{III} was varied at fixed amino acid concentration (0.02 mol dm^{-3}). The ionic strength, pH, and temperature were kept constant. The pseudo-first-order plots were linear giving $k_{obs.}$ = 0.39 × 10^{-4} s^{-1} (Table 1). The linearity shows that the reaction

Table 2. Kinetic data on the anation of Cr^{III} with DL-tryptophan at $10^3[Cr^{III}]_T$ = 2.0 mol dm^{-3} and I = 1.0 mol dm^{-3}

$10^4[H^+]$/ mol dm^{-3}	$10^2[trp]_T$/ mol dm^{-3}	$10^4k_{obs.}/s^{-1}$ 40	45	50	55 °C
20.4	2.0	0.24	0.25	0.39	0.53
	3.0	0.35	0.37	0.53	0.75
	4.0	0.43	0.45	0.69	1.00
	5.0	0.49	0.55	0.79	1.19
	6.0	0.58	0.62	0.85	1.37
11.5	2.0	0.30	0.30	0.45	0.67
	3.0	0.43	0.41	0.64	0.99
	4.0	0.53	0.51	0.76	1.28
	5.0	0.60	0.63	0.92	1.43
	6.0	0.65	0.68	1.00	1.64
6.5	2.0	0.38	0.36	0.57	0.93
	3.0	0.50	0.47	0.78	1.25
	4.0	0.62	0.63	0.94	1.66
	5.0	0.69	0.70	1.11	1.75
	6.0	0.75	0.78	1.16	2.08
3.6	2.0	0.43	0.44	0.68	1.33
	3.0	0.55	0.58	0.93	1.82
	4.0	0.69	0.71	1.12	2.27
	5.0	0.76	0.85	1.23	2.32
	6.0	0.83	0.89	1.33	2.86
2.0	2.0	0.51	0.53	0.88	1.96
	3.0	0.68	0.70	1.16	2.56
	4.0	0.81	0.96	1.49	3.45
	5.0	1.04	1.09	1.78	4.35
	6.0	1.06	1.25	1.92	4.76

is first order in $[Cr^{III}]_T$ (T = total). The independence of $k_{obs.}$ at 50 °C under the conditions $[trp]_T$ = 0.002 mol dm^{-3}, $[H^+]$ = 20.4 × 10^{-4} mol dm^{-3}, and I = 1.0 mol dm^{-3} over a range of $[Cr^{III}]_T$ (Table 1) is in agreement with a first-order dependence on $[Cr^{III}]_T$. The rate law is therefore as in equation (1).

$$d[complex]/dt = -d[Cr^{III}]_T/dt = k_{obs.}[Cr^{III}]_T \quad (1)$$

In order to confirm that the step of 1:1 complex formation is rate-limiting, some experiments were performed in which the 1:1 complex was the only product, *i.e.* under pseudo-first-order conditions where $[Cr^{III}]_T > [amino\ acid]_T$. The rate constants were identical with those obtained under the condition $[amino\ acid]_T > [Cr^{III}]_T$ (Table 1). Thus, the formation of higher complexes must be more rapid than the rate-limiting formation of the 1:1 complex.

Dependence of Reaction Rate on the Hydrogen-ion Concentration.—The reaction was studied as a function of pH between 2.75 and 3.75 at $[Cr^{III}]_T$ = 0.002 mol dm^{-3} and at various fixed $[trp]_T$. Table 2 contains the pertinent data at several constant temperatures. It is evident that the rate constant increases with increasing pH.

To explain the pH dependence of the reaction rate it is necessary to consider the equilibrium (2) for which we can write

$$[Cr(H_2O)_6]^{3+} \rightleftharpoons [Cr(H_2O)_5(OH)]^{2+} + H^+ \quad (pK_h = 4.1, \text{ambient}^{15}) \quad (2)$$

expression (3). At lower pH the substrate exists mainly as

$$4.1 = pH + \log \frac{[Cr(H_2O)_6{}^{3+}]}{[Cr(H_2O)_5(OH)^{2+}]} \quad (3)$$

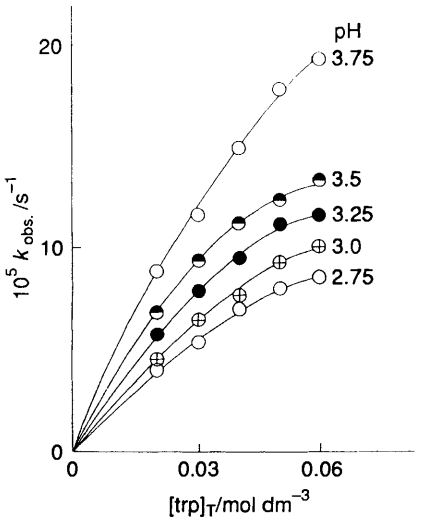


Figure 2. Dependence of pseudo-first-order rate constants, $k_{obs.}$, on the concentration of tryptophan for the anation of aquachromium(III) by DL-tryptophan at different pH and $10^3[Cr^{III}]_T$ = 2.0 mol dm^{-3}, I = 1.0 mol dm^{-3} and 50 °C

$[Cr(H_2O)_6]^{3+}$ and as the pH increases the percentage of pentaaquahydroxochromium(III) species increases which, in turn, increases the reaction rate. The presence of OH^- ligand in hydroxoaqua species in several cases, if not in general, causes increased labilities (due to its π-bonding ability) and therefore increased rates are found with, for example, Al^{III},[16] Ga^{III},[17] Mn^{III},[18] Fe^{III},[19] or Cr^{III}.[7,9,10,20] In the case of Cr^{III}, the OH^- ligand increases by about three orders of magnitude the rate of water exchange of the unhydrolyzed metal and gives a dissociative character to the metal centre.[21]

On the other hand, the ligand also participates in acid–base equilibria (4) and (5) where H_2A^+ represents the cationic

$$H_2A^+ \overset{K_{a1}}{\rightleftharpoons} HA + H^+ \quad (4)$$

$$HA \overset{K_{a2}}{\rightleftharpoons} A^- + H^+ \quad (5)$$

$RCH(NH_3^+)(CO_2H)$, HA the zwitterionic $RCH(NH_3^+)(CO_2^-)$, and A^- the anionic $RCH(NH_2)(CO_2^-)$ forms of the amino acid.

From the K_a values (4.17×10^{-3} and 4.07×10^{-10} mol dm^{-3}) one can ascertain that, under our experimental conditions of pH 2.75—3.75, the monopositive and zwitterionic species exist in significant concentrations. The former species carries a net positive charge which is unfavourable for formation of outer-sphere complexes (the most widely accepted first step of anation reactions). The zwitterionic species can undergo outer-sphere complexation with multivalent cations.

Dependence of Reaction Rate on Tryptophan Concentration.—The effect of varying the entering ligand concentration on the reaction rate was studied at various fixed $[H^+]$. The concentration of ligand was varied in the range 0.02—0.06 mol dm^{-3} at a fixed $[Cr^{III}]_T$ = 0.002 mol dm^{-3} and I = 1.0 mol dm^{-3}. The results are presented in Table 2. Representative plots of the dependence of $k_{obs.}$ on $[tryp]_T$ are illustrated in Figure 2. Similar plots were obtained for the remaining data in Table 2. It is observed that as $[trp]_T$ increases, $k_{obs.}$ increases but non-linearly. A marked curvature is observed in all the cases indicating outer-sphere complexation between the reactive species.[22]

The sequence of reactions given in Scheme 1 is consistent with

$$[Cr(H_2O)_6]^{3+} \overset{K_h}{\rightleftharpoons} [Cr(H_2O)_5(OH)]^{2+} + H^+ \quad (2)$$

$$H_2A^+ \overset{K_a}{\rightleftharpoons} HA + H^+ \quad (4)$$

$$[Cr(H_2O)_6]^{3+} + HA \overset{K_{o.s.1}}{\rightleftharpoons} o.s.1 \quad (6)$$

$$[Cr(H_2O)_5(OH)]^{2+} + HA \overset{K_{o.s.2}}{\rightleftharpoons} o.s.2 \quad (7)$$

$$o.s.1 \xrightarrow{k_1} [Cr(H_2O)_5(HA)]^{3+} + H_2O \quad (8)$$

$$o.s.2 \xrightarrow{k_2} [Cr(H_2O)_4(OH)(HA)]^{2+} + H_2O \quad (9)$$

$$\left.\begin{array}{l}[Cr(H_2O)_5(HA)]^{3+} \xrightarrow{\text{fast ligand}} \\ [Cr(H_2O)_4(OH)(HA)]^{2+} \xrightarrow{\text{fast ligand}}\end{array}\right\} \text{Product} \quad (10)$$

Scheme 1.

the experimental data where o.s.1 = $\{[Cr(H_2O)_6]^{3+}\cdot HA\}$ and o.s.2 = $\{[Cr(H_2O)_5(OH)]^{2+}\cdot HA\}$. The proposed mechanism is similar to the so-called 'Eigen-Tamm'[23] mechanism given for anation reactions of labile aqua-complexes, the only difference being that the contributions of the reverse reactions in equations (6) and (7) are very small (in fact, zero, as the plots of $k_{obs.}$ against $[tryp]_T$ have zero intercepts). The rate of exchange of the first water molecule in the inner co-ordination sphere of the metal centre is slow and rate determining. As soon as one molecule of the tryptophan zwitterion enters into the inner co-ordination sphere and $[Cr(H_2O)_5(HA)]^{3+}$/$[Cr(H_2O)_4(OH)(HA)]^{2+}$ is formed the electron density on the chromium(III) centre is increased owing to the inductive effect. As a result, the remaining water ligands are labilized very easily and subsequent substitutions are rapid.

The rate law corresponding to Scheme 1 can be expressed as in equation (11). Using the mass balance for Cr^{III}, the usual

$$\text{Rate} = d[\text{complex}]/dt = k_1[o.s.1] + k_2[o.s.2] \quad (11)$$

expressions for K_h, $K_{o.s.1}$, and $K_{o.s.2}$, and assuming rapid establishment of these equilibria, the rate law (12) was obtained which, on comparison with equation (1), gives (13). Equation

$$d[\text{complex}]/dt = \frac{(k_1K_aK_{o.s.1}[H^+] + k_2K_aK_hK_{o.s.2})[Cr^{III}]_T[trp]_T}{[H^+]^2 + [H^+]K_a + [H^+]K_h + K_aK_h + (K_aK_{o.s.1}[H^+] + K_aK_hK_{o.s.2})[trp]_T} \quad (12)$$

$$k_{obs.} = \frac{(k_1K_aK_{o.s.1}[H^+] + k_2K_aK_hK_{o.s.2})[trp]_T}{[H^+]^2 + [H^+]K_a + [H^+]K_h + K_aK_h + (K_aK_{o.s.1}[H^+] + K_aK_hK_{o.s.2})[trp]_T} \quad (13)$$

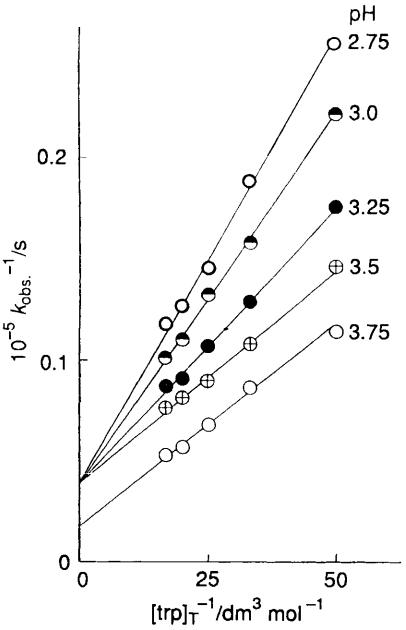


Figure 3. Plots of $1/k_{obs.}$ *versus* $1/[trp]_T$ at 50 °C, $10^3[Cr^{III}]_T$ = 2.0 mol dm^{-3}, and I = 1.0 mol dm^{-3}

Table 3. Anation and outer-sphere complexation constants of Cr^{III} + DL-tryptophan at I = 1.0 mol dm^{-3}

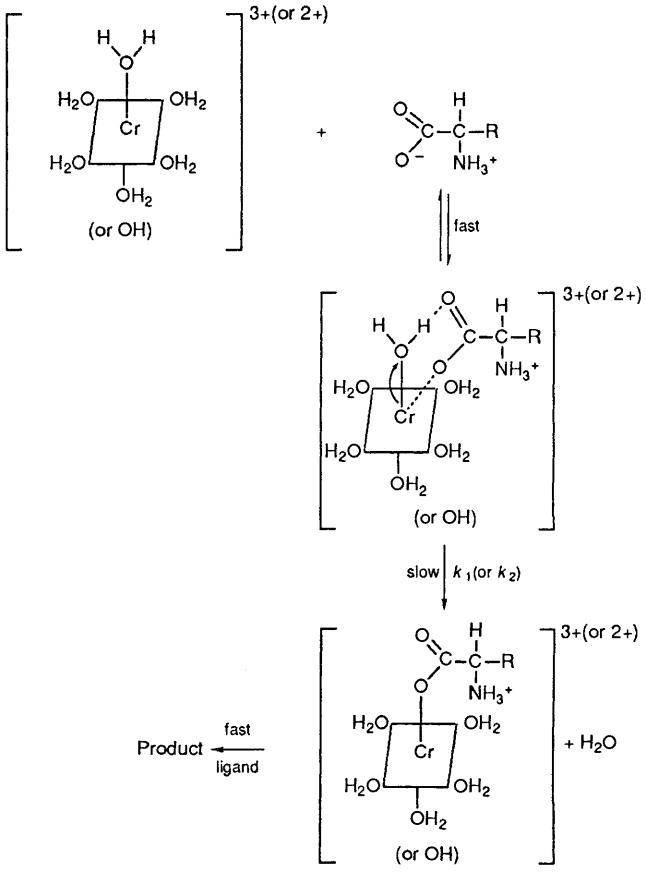
T/°C	10^4k_1/s^{-1}	$K_{o.s.1}$/ dm^3 mol^{-1}	10^3k_2/s^{-1}	$K_{o.s.2}$/ dm^3 mol^{-1}	$10^3K_a^*$/ mol dm^{-3}
25	—	—	—	—	4.17
40	1.17	13.81	0.25	12.20	
45	1.25	10.89	0.27	9.41	
50	1.75	14.24	0.38	12.89	
55	4.00	9.80	1.25	8.30	
		average 12.19		average 10.70	

* H. R. Mahler and E. H. Cordes, 'Biological Chemistry,' 2nd edn., Harper and Row, New York, 1971, p. 43.

(13) can be rewritten as (14) with $Y = k_1K_aK_{o.s.1}[H^+] + k_2K_aK_hK_{o.s.2}$.

Plots of $1/k_{obs.}$ values against $1/[trp]_T$ at each acidity show the expected linear relationship (Figure 3). Equation (14) also indicates that the intercepts of such plots should be dependent on $[H^+]$. The experimental results obtained at higher acidities are not in agreement with this and, at $[H^+] \geqslant 3.6 \times 10^{-4}$ mol dm^{-3}, the straight lines converge to a common intercept, and thus become independent of $[H^+]$ below pH 3.75 (Figure 3). At low pH it is evident, as $K_h \approx 10^{-4}$ mol dm^{-3} and $K_{o.s.1} > K_{o.s.2}$, that $K_aK_hK_{o.s.2}$ and $k_2K_aK_hK_{o.s.2}$ can be neglected in comparison with $K_aK_{o.s.1}[H^+]$ and $k_1K_aK_{o.s.1}[H^+]$, respectively, and also $[H^+]K_h + K_aK_h$ as compared to $[H^+]^2 + [H^+]K_a$. By introducing these approximations equation (14) simplifies to (15). Under these conditions too a linear plot is obtained on plotting $1/k_{obs.}$ against $1/[trp]_T$ at a given $[H^+]$. This is also confirmed by the plots of Figure 3 where the intercepts are independent of $[H^+]$ (upper plots).

Equation (15) may also be derived independently if the interactions with $[Cr(H_2O)_5(OH)]^{2+}$ are neglected in the mechanism. This confirms our previous conclusions[6,7] that



Scheme 2.

$$\frac{1}{k_{obs.}} = \frac{1}{k_1} + \frac{[H^+] + K_a}{k_1K_aK_{o.s.1}} \cdot \frac{1}{[trp]_T} \qquad (15)$$

above $[H^+] \approx 3 \times 10^{-4}$ mol dm^{-3} the only reactive species is $[Cr(H_2O)_6]^{3+}$ and contributions of hydroxy species to the anation kinetics of aquachromium(III) may be neglected.

A convenient way of treating the experimental rate data is to calculate the values of k_1 first. The constant $K_{o.s.1}$ can then easily be determined. These were obtained from plots producing convergent straight lines [according to equation (15)]. With the knowledge of k_1 and $K_{o.s.1}$, k_2 and $K_{o.s.2}$ were determined from plots of $1/k_{obs.}$ against $1/[trp]_T$ obtained at higher pH values. The results are collected in Table 3.

Dependence of Reaction Rate on Ethanol Content.—In order to determine the influence of the dielectric constant of the medium on reaction rate the anation reaction was studied in ethanol–water solvents also. An increase in $k_{obs.}$ was obtained with decrease in the dielectric constant, D, of the medium (Table 1). A plot of log $k_{obs.}$ and $1/D$ was linear with positive slope indicating that the reactions studied are of ion–dipole type. Obviously, according to Bjerrum's equation,[24] the values of the outer-sphere complex-formation constants ($K_{o.s.1}$ and $K_{o.s.2}$) will increase with decrease in the dielectric constant of the medium and, therefore, outer-sphere complexations are enhanced with a consequent increase in the rate.

$$\frac{1}{k_{obs.}} = \frac{K_aK_{o.s.1}[H^+] + K_aK_hK_{o.s.2}}{Y} + \frac{[H^+]^2 + [H^+]K_a + [H^+]K_h + K_aK_h}{Y} \cdot \frac{1}{[trp]_T} \qquad (14)$$

Table 4. Comparison of anation rate constants, k_1, and activation parameters for the complexation of $[Cr(H_2O)_6]^{3+}$ with amino acids[a]

Ligand	k_1/s^{-1} at 35 °C	$\Delta H^{\ddagger}$/ kJ mol^{-1}	$\Delta S^{\ddagger}$/ J K^{-1} mol^{-1}	Ref.
H_2O^{18}	4.17×10^{-6} (k_{ex})	110.0	+1	*b*
Glycine[c]	3.34×10^{-4}	58.0	−129.2	6
Glycine	6.80×10^{-4}	51.9	−42.7	8
Alanine[c]	0.58×10^{-4}	64.9	−113.6	7
Valine	2.35×10^{-4}	90.4	−21.0	6
Serine[c]	0.62×10^{-4}	78.0	−72.5	6
$Hasp^-$	1.80×10^{-4}	81.0	−54.0	6
H_2asp	1.30×10^{-4}	50.0	−157.0	6
Hydroxyproline	1.00×10^{-4} (40 °C)	72.9	−98.2	7
Phenylalanine	1.85×10^{-4}	53.6	−141.7	7
Sarcosine	3.57×10^{-4} (40 °C)	54.7	−136.6	7
Glutamine	1.81×10^{-4} (40 °C)	52.0	−150.6	Unpublished work[d]
Methionine	2.22×10^{-4}	61.1	−116.3	7
Tryptophan	1.17×10^{-4} (40 °C)	65.6	−112.4	Present work

[a] All mechanisms are I_a except for H_2O. [b] R. A. Plane and H. Taube, *J. Phys. Chem.*, 1952, **56**, 33; D. R. Stranks and T. W. Swaddle, *J. Am. Chem. Soc.*, 1971, **93**, 2783. [c] Extrapolated value. [d] M. Shahid, I. A. Khan, and Kabir-ud-Din.

Table 5. Comparison of anation rate constants, k_2, and activation parameters for the complexation of $[Cr(H_2O)_5(OH)]^{2+}$ and amino acids

Ligand	$10^3 k_2/s^{-1}$ (T/°C)	$\Delta H^{\ddagger}$/ kJ mol^{-1}	$\Delta S^{\ddagger}$/ J K^{-1} mol^{-1}	Mechanism	Ref.
H_2O^{18}	5.00 (50, k_{ex}')	—	—	—	21
Alanine[a]	0.40 (35)	34.0	−201.7	I_a	10
Alanine	0.46 (45)	77.0	−68.0	I_d	7
$Hasp^-$[b]	0.74 (35)	45.4	−144.9	I_a	10
Hydroxyproline	0.21 (40)	63.2	−114.1	I_d	7
Phenylalanine[c]	0.32 (35)	53.9	−135.9	I_a	10
Phenylalanine	0.71 (45)	—	—	I_d	7
Sarcosine	1.23 (50)	—	—	I_d	7
Glutamine	0.46 (40)	43.7	−161.1	I_d	Unpublished work[e]
Methionine[d]	0.80 (35)	59.8	−97.0	I_a	10
Methionine	0.36 (35)	83.4	−48.2	I_d	7
Tryptophan	0.25 (40)	85.0	−44.8	I_d	Present work

[a] I = 0.03 mol dm^{-3}. [b] I = 0.065 mol dm^{-3}. [c] I = 0.0075 mol dm^{-3}. [d] I = 0.0075 mol dm^{-3}, water-ethanol medium. [e] M. Shahid, I. A. Khan, and Kabir-ud-Din.

Dependence of Reaction Rate on Temperature.—The temperature effect on the reaction rate was studied for different ligand and hydrogen-ion concentrations at I = 1.0 mol dm^{-3}. The $k_{obs.}$ values are collected in Table 2 and the k and $K_{o.s.}$ in Table 3. The outer-sphere association constants were assumed to be temperature independent and were taken as constant in the range of temperature investigated.

Activation parameters collected in Tables 4 and 5 (along with some previously studied related systems) were calculated by the least-squares method using Eyring plots of the temperature dependence of k_1 and k_2.

Conclusion and Mechanism.—It is generally accepted[25] that complex-formation reactions of metal ions proceed by a mechanism in which the rate-determining step is the change from an outer-sphere to an inner-sphere complex, preceded by the formation of the outer-sphere complex between the metal ion and ligand. In anation reactions (where water in the co-ordination sphere of the metal ion is replaced by another ligand) the rate constant of the rate-limiting step is unimolecular for the interchange in the outer-sphere complex. It has already been established that the reactions studied are of ion–dipole type.

The reaction mechanism can be illustrated as in Scheme 2. The formation of the activated complex through outer-sphere associations is stabilized by hydrogen bonding. In the activated complex the carboxylate moiety of the amino acid is able to form a weak bond in the reaction of the hexa-aquachromium(III) complex and a weaker bond in the reaction of the corresponding hydroxopenta-aqua-complex. These assumptions are supported by the rate data and their activation parameters.

As pointed out earlier,[11] chelate-ring closure is not a favoured process where the amino group of the amino acid is protonated (as in HA); even if it does occur, it must be rapid and not rate limiting as can be concluded by comparing the observed results with the Cr^{III}–acetic acid system[26] (acetic acid is a monodentate carboxylic ligand where no chelation occurs).

Whether the interchange mechanism of $[Cr(H_2O)_6]^{3+}$/$[Cr(H_2O)_5(OH)]^{2+}$ is I_a or I_d remains undecided. The following three criteria have been utilized in assigning I_d (as opposed to I_a) mechanisms to substitution reactions of $[Co(NH_3)_5(H_2O)]^{3+}$. (*a*) No appreciable change in k on changing the nature of the entering ligand; thus, the span of k values is only about half an order of magnitude for substitution reactions of $[Co(NH_3)_5(H_2O)]^{3+}$ (ref. 27). Earlier,[28] second-order rate constants $k_f(=kK_{o.s.})$ were used to characterize anation reactions of metal ions but this has been shown to be invalid as $K_{o.s.}$ values depend not only on the charge of the entering ligand but also on its nature. (*b*) The value of k is never greater than k_{ex} for solvent water.[21] (*c*) The volume of activation, $\Delta V^{\ddagger}$ (regarded as possessing definite mechanistic discriminating ability being positive for I_d and negative for I_a

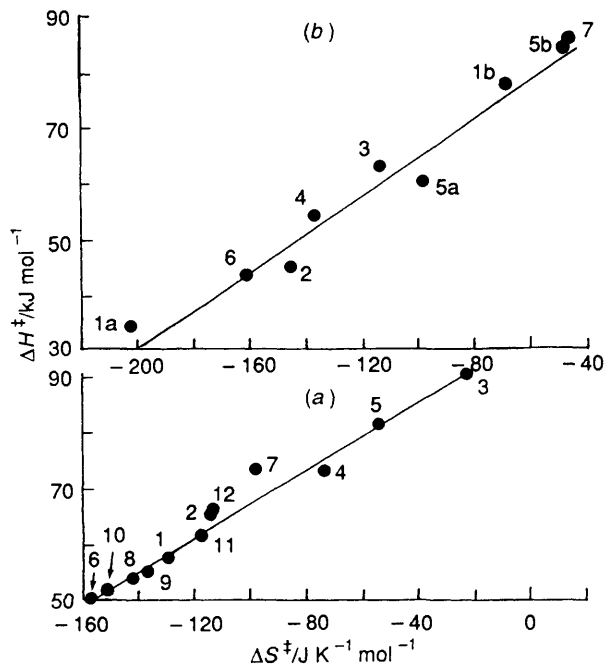


Figure 4. Isokinetic plots of $\Delta H^{\ddagger}$ *versus* $\Delta S^{\ddagger}$ for the anation of $[Cr(H_2O)_6]^{3+}$(*a*) and $[Cr(H_2O)_5(OH)]^{2+}$(*b*) by some amino acids: (*a*) glycine (1), alanine (2), valine (3), serine (4), $Hasp^-$ (5), H_2asp (6), hydroxyproline (7), phenylalanine (8), sarcosine (9), glutamine (10), methionine (11), tryptophan (12), (*b*) alanine ($1a^{10a}$, $1b^{7a}$), $Hasp^-$ (2), hydroxyproline (3), phenylalanine (4), methionine ($5a^{10d}$, $5b^{7e}$), glutamine (6), and tryptophan (7). Slopes: 308 (*a*) and 334 K (*b*)

mechanisms) for water exchange has a positive value for $[Co(NH_3)_5(H_2O)]^{3+}$ [29]

Applying these criteria to substitution reactions of $[Cr(H_2O)_6]^{3+}$/$[Cr(H_2O)_5(OH)]^{2+}$ with amino acids we have: (*a*) spans of k_1 and k_2 of (0.58—6.80) × 10^{-4}(35—40) and (0.21—1.23) × 10^{-3} s^{-1} (35—50 °C), respectively; (*b*) for all the systems investigated k_1 is always greater than k_{ex} {water exchange of $[Cr(H_2O)_6]^{3+}$} whereas k_2 is comparable with k_{ex}' {water exchange of $[Cr(H_2O)_5(OH)]^{2+}$} (Tables 4 and 5), in accord with expectation (due to the labilization effect of hydroxide); and (*c*) $\Delta V^{\ddagger}$ for water exchange of $[Cr(H_2O)_6]^{3+}$ has a negative value (≈ -9.3 cm^3 mol^{-1}).[21]

Thus, on all counts the favoured mechanism is an associative interchange (I_a) for the anation of $[Cr(H_2O)_6]^3$ and a dissociative interchange (I_d) for the reaction of $[Cr(H_2O)_5(OH)]^{2+}$.

Activation parameters, compared with literature values for anation reactions of Cr^{III}, given in Tables 4 and 5 also support the above assignments [21,28] which are confirmed on the basis of isokinetic plots (Figure 4).

Acknowledgements

We thank the Chairman, Department of Chemistry, Aligarh Muslim University, for providing research facilities.

References

1 H. Sigel, 'Metal Ions in Biological Systems,' Marcel Dekker, New York, 1973, vol. 2.
2 W. Mertz and K. Schwarz, *Arch. Biochem. Biophys.*, 1955, **58**, 504.
3 L. Tschugaeff and E. Serbin, *Compt. rend.*, 1910, **151**, 1361.
4 W. Mertz, *Science*, 1981, **213**, 1332; W. Mertz, E. W. Toepfer, E. E. Roginski, and M. M. Polansky, *Fed. Proc., Fed. Am. Soc. Exp. Biol.*, 1974, **33**, 2275; W. Mertz, *Physiol. Rev.*, 1969, **49**, 165.
5 E. W. Toepfer, W. Mertz, M. M. Polansky, E. E. Roginski, and W. R. Wolf, *J. Agric. Food Chem.*, 1977, **25**, 162; W. Mertz, *Nutr. Rev.*, 1975, **33**, 129; J. A. Cooper, B. F. Anderson, P. D. Buckley, and L. F. Blackwell, *Inorg. Chim. Acta*, 1984, **91**, 1; E. Gonzalez-Vergara, J. Hegenauer, P. Saltman, M. Sabat, and J. A. Ibers, *ibid.*, 1982, **66**, 115; J. V. McArdle, E. de Laubenfels, A. L. Shorter, and H. L. Ammon, *Polyhedron*, 1982, **1**, 471; D. R. Prasad, T. Ramasami, D. Ramaswamy, and M. Santappa, *Inorg. Chem.*, 1982, **21**, 850; L. E. Gerdom and H. M. Goff, *ibid.*, p. 3847.
6 I. A. Khan and Kabir-ud-Din, *J. Inorg. Nucl. Chem.*, 1981, **43**, 1082; *Indian J. Chem., Sect. A*, 1984, **23**, 98; I. A. Khan, M. Shahid, and Kabir-ud-Din, *ibid.*, 1983, **22**, 382; I. A. Khan and Kabir-ud-Din, *Transition Met. Chem. (Weinheim Ger.)*, 1986, **11**, 391.
7 (*a*) I. A. Khan and Kabir-ud-Din, *Int. J. Chem. Kinet.*, 1985, **17**, 1263; (*b*) Kabir-ud-Din, I. A. Khan, and M. Shahid, *Transition Met. Chem. (Weinheim, Ger.)*, 1987, **12**, 557; (*c*) I. A. Khan, M. Shahid, and Kabir-ud-Din, *ibid.*, p. 393; (*d*) Kabir-ud-Din, M. Shahid, and I. A. Khan, *Z. Phys. Chem. (Leipzig)*, 1990, **271**, 101; (*e*) I. A. Khan, M. Shahid, and Kabir-ud-Din, *Transition Met. Chem.*, in the press.
8 D. Banerjea and S. D. Chaudhuri, *J. Inorg. Nucl. Chem.*, 1968, **30**, 871.
9 M. A. Abdullah, J. Barrett, and P. O'Brien, *J. Chem. Soc., Dalton Trans.*, 1984, 1647.
10 (*a*) B. K. Niogy and G. S. De, *Proc. Ind. Acad. Sci. (Chem. Sci.)*, 1983, **92**, 153; (*b*) B. K. Niogy and G. S. De, *Indian J. Chem., Sect. A*, 1985, **24**, 208; (*c*) B. K. Niogy and G. S. De, *J. Indian Chem. Soc.*, 1984, **61**, 389; (*d*) H. G. Mitra Mustofy and G. S. De, *ibid.*, 1986, **63**, 1040.
11 S. T. Chow and C. A. McAuliffe, *Prog. Inorg. Chem.*, 1975, **19**, 60; T. Ramasami, R. K. Wharton, and A. G. Sykes, *Inorg. Chem.*, 1975, **14**, 359.
12 S. G. Shuttleworth and R. L. Sykes, *J. Am. Leather Chem. Assoc.*, 1960, **55**, 154.
13 J. Fujita, T. Yasui, and Y. Shimura, *Bull. Chem. Soc. Jpn.*, 1965, **38**, 654.
14 T. G. Appleton, J. R. Hall, and S. F. Ralph, *Inorg. Chem.*, 1985, **24**, 673.
15 K. Emorson and W. M. Graven, *J. Inorg. Nucl. Chem.*, 1959, **11**, 309.
16 F. Secco and M. Venturini, *Inorg. Chem.*, 1975, **14**, 1978.
17 B. Perlmutter-Hayman, F. Secco, E. Tapuhi, and M. Venturini, *J. Chem. Soc., Dalton Trans.*, 1980, 1124; A. Campisi and P. A. Tregloan, *Inorg. Chim. Acta*, 1985, **100**, 251.
18 E. Pelizzetti, E. Mentasti, and G. Giraudi, *Inorg. Chim. Acta*, 1975, **15**, L1.
19 E. Mentasti. F. Secco, and M. Venturini, *Inorg. Chem.*, 1982, **21**, 602; S. Funahashi, K. Ishihara, and M. Tanaka, *ibid.*, 1983, **22**, 2070.
20 M. Kimura and J. Shirai, *J. Inorg. Nucl. Chem.*, 1978, **40**, 1085; C. R. Krishnamoorthy and G. M. Harris, *J. Coord. Chem.*, 1980, **10**, 55.
21 T. W. Swaddle, *Coord. Chem. Rev.*, 1974, **14**, 217.
22 P. R. Joubert and R. van Eldik, *Int. J. Chem. Kinet*, 1976, **8**, 411; T. Ramasami and A. G. Sykes, *Inorg. Chem.*, 1976, **11**, 2885.
23 M. Eigen, *Z. Elektrochem.*, 1960, **64**, 115; M. Eigen and K. Tamm, *ibid.*, 1962, **66**, 93, 107.
24 F. Basolo and R. G. Pearson, 'Mechanisms of Inorganic Reactions,' 2nd edn., Wiley, New York, 1958, ch. 6.
25 R. G. Wilkins, 'The Study of Kinetics and Mechanism of Reactions of Transition Metal Complexes,' Allyn and Bacon, Boston, Massachusetts, 1974.
26 S. C. Tyagi and A. Aziz Khan, *J. Inorg. Nucl. Chem.*, 1979, **41**, 1447.
27 J. M. Coronas, R. Vicente, and M. Ferrer, *Inorg. Chim. Acta*, 1981, **49**, 259.
28 D. Thusius, *Inorg. Chem.*, 1971, **10**, 1106; J. H. Espenson, *ibid.*, 1969, **8**, 1554.
29 H. R. Hunt and H. Taube, *J. Am. Chem. Soc.*, 1958, **80**, 2642.

Received 14*th March* 1990; *Paper* 0/01132K