Proc. Indian Acad. Sci. (Chem. Sci.), Vol. 107, No. 1, February 1995, pp. 11–17.

Mechanism of anation of chromium(III) by L-lysine

KABIR-UD-DIN* and GHULAM JILANI KHAN

Department of Chemistry, Aligarh Muslim University, Aligarh 202002, India

MS received 20 March 1993; revised 2 May 1994

Abstract. The kinetics of L-lysine anation of aquachromium(III) ions have been investigated in the acidity range $5{\cdot}6 \leqslant 10^5[H^+] \leqslant 31{\cdot}6\,\text{mol dm}^{-3}$. The reaction takes place with outer-sphere association between $Cr^{3+}/CrOH^{2+}$ and H_2L^+ ($L = {}^+HGCH({}^+NH_3)(CO_2^-)$, G being the side chain) followed by transformation of the outer- into an inner-sphere complex by slow interchange. The results are discussed in relation to the data of analogous systems and it is concluded that anation of $[Cr(H_2O)_6]^{3+}$ follows an I_a path whereas that of $[Cr(H_2O)_5OH]^{2+}$ follows an I_d path.

Keywords. Kinetics; anation; chromium(III); amino acids; L-lysine.

1. Introduction

Metal ion complex formations are among the prominent interactions in nature (Eichhorn 1973; Sigel 1973; Wood 1975). In an effort to understand the nature of metal ion complexation in biological systems, considerable research has been carried out on model binary and mixed-ligand complexes. The pace of studies on Cr(III) complexes of biologically important ligands has been slow; partly because the metal ion is inert in its reactions and partly because of its late recognition as an essential element (Mertz 1975). Following the demonstration of GTF's (Glucose Tolerance Factor: a low-molecular-weight chromium(III) complex) insulin potentiating activity (Mertz and Schwarz 1959; Mertz *et al* 1974; Mertz 1983), reports on various aspects of Cr(III) complexation with ligands of biological importance (especially amino acids) have appeared (Khan and Kabir-ud-Din 1981; Gerdom and Goff 1982; Gonzalez-Vergara *et al* 1982; McArdle *et al* 1982; Prasad *et al* 1982; Cooper *et al* 1984; Kabir-ud-Din and Khan 1985, 1990, 1992; Khan 1985; Mitra-Mustofy and De 1986; Govindaraju *et al* 1989; Shahid *et al* 1990; Khan *et al* 1991). With the view that not only composition but other aspects may be helpful in understanding the nature of GTF, we present herein our results on the anation kinetics of aquachromium(III) by L-lysine.

2. Experimental

L-Lysine monohydrochloride (chromatographically homogeneous, E. Merck, Darmstadt) and $Cr(NO_3)_3{\cdot}9H_2O$ (AR, ORTANAL, Italy) were used as received. The chromium(III) solution was standarized by ion-exchange method (Banerjea and Dutta Chaudhuri 1968). Other chemicals were guaranteed reagents. Distilled water

*For correspondence

was redistilled (with a little $KMnO_4$ and KOH) in an all-glass still. EtOH was distilled twice.

On addition of an excess of L-lysine to chromic nitrate in acidic solution and heating ($\sim 60°C$), an increase in absorption in the visible range occurred. The adsorption spectra of reactant mixtures in different molar ratios exhibited maxima at 406 and 550 nm. Since variation in λ_{max} for different chromium(III)–amino acid systems is not large (400–410 and 540–560 nm) (Khan and Malik 1963; Khan 1985; Shahid *et al* 1990), one can infer that in all cases the bonding is of similar nature. As chelation is not favoured when the $-NH_2$ group is protonated (Chow and McAuliffe 1975; Ramasami *et al* 1975), the ligands bind to chromium(III) through carboxylate oxygen. This is in conformity with previous findings by Shuttleworth and Sykes (1960) where coordination through carboxylate group is reported at pH < 4.

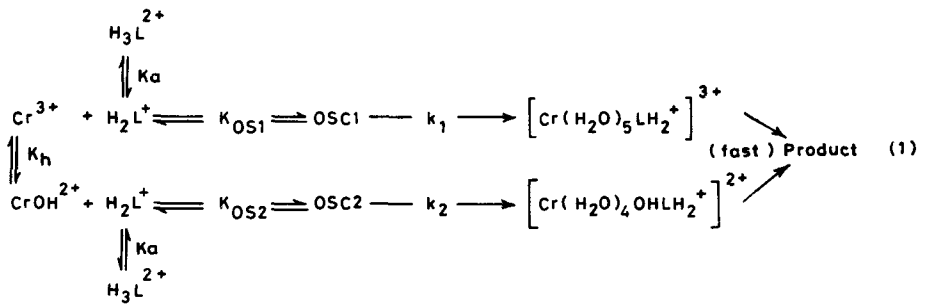
A 1:2 stochiometry of the complex was ascertained by Job's method which is in accord with the literature (Khan and Malik 1963).

Solutions of the required final pH for kinetic measurements were made by mixing deoxygenated and thermally equilibrated solutions of L-lysine and chromic nitrate that contained calculated amounts of HNO_3 or NaOH and KNO_3. After mixing, bubbling of N_2 was continued to maintain an inert atmosphere inside the reaction flask. The kinetics was followed by sampling technique by measuring absorbances at 550 nm (the wavelength of maximum difference between product and substrate absorbances). The pseudo-first-order conditions were maintained with $[\text{lysine}]_T \geqslant 10\,[\text{Cr(III)}]_T$. Preliminary values of the pseudo-first-order rate constants, k_{obs}, were obtained from the slopes of $\log(A_\infty - A_0)/(A_\infty - A_t)$ vs. t plots, but the best k_{obs} values were obtained by linear least-squares regression analysis of the data from a computer-based program (executed on a VAX 11/780 computer).

The instruments used were Bausch and Lomb Spectronic 20 spectrophotometer and ELICO LI-120 digital pH-meter and CH-41 combination electrode.

3. Results and discussion

Values of the k_{obs} obtained as a function of $[\text{lysine}]_T$, acidity, temperature and % EtOH are given in table 1. Plots of k_{obs} vs. $[\text{lysine}]_T$ were hyperbolic at each acidity. This observed saturation of k_{obs} at high ligand concentration is consistent with scheme 1 (Ramasami and Sykes 1976; Joubert and van Eldik 1976) for which the rate expression



Scheme 1. The reaction paths of anation of chromium(III) by L-lysine (OSC = outer-sphere complex).

Table 1. k_{obs} for the anation of aquachromium(III) by L-lysine at $\mu = 1{\cdot}0\,mol\,dm^{-3}$ (KNO_3) and $10^3[Cr(III)]_T = 4{\cdot}0\,mol\,dm^{-3}$.

Temp. (°C)	$10^4[H^+]$ (mol dm^{-3})	$10^5 k_{obs}$(s^{-1}) 10[Lys]$_T$(mol dm^{-3}) 0·4	0·6	0·8	1·0	1·2	1·4	1·6	$10^4 k_1$ (s^{-1})	$10^3 k_2$ (s^{-1})
35	3·16	2·2	3·2	4·0	4·5	4·9	5·5	5·9	1·3	0·19
	1·78	3·9	4·9	6·0	6·8	7·4	7·9	8·3		
	1·00	4·8	6·0	7·3	8·4	9·0	9·5	10·0		
	0·56	5·9	7·6	9·2	10·0	10·7	11·3	11·8		
40	3·16	2·9	4·3	5·2	6·1	7·0	7·5	8·0	2·0	0·27
	1·78	4·7	6·2	7·5	8·7	10·6	10·6	11·0		
	1·00	6·3	8·1	9·5	10·8	12·0	12·9	13·5		
	0·56	8·0	10·0	11·5	12·9	14·0	15·0	15·8		
45	3·16	5·1	6·7	8·3	9·8	11·1	12·0	12·5	2·4	0·29
	1·78	7·3	9·4	11·2	12·5	13·6	14·5	15·1		
	1·00	9·5	12·0	14·1	15·5	16·7	17·6	18·0		
	0·56	11·7	14·8	16·9	18·5	19·6	20·4	21·0		
50	3·16	9·4	13·0	16·4	17·7	20·6	23·4	25·5	5·3	0·71
	1·78	11·3	14·7	18·5	21·3	23·8	25·3	26·5		
	1·00	12·0	16·3	20·3	23·0	25·3	26·5	29·0		
	0·56	12·9	18·0	22·0	24·8	26·9	31·1	32·2		
$\bar{K}_{OS1}$(dm^3 mol^{-1}) = 8·2					$\Delta H^{\#}$(kJ mol^{-1})				61	57
$\bar{K}_{OS2}$(dm^3 mol^{-1}) = 4·7					$\Delta S^{\#}$(JK^{-1} mol^{-1})				−115	−127

is given by (2) below.

$$k_{obs} = \{(k_1 K_a K_{OS1}[H^+] + k_2 K_a K_h K_{OS2})[\text{lysine}]_T\}/\{[H^+]^2 + [H^+]K_a - [H^+]K_h + K_a K_h + (K_a K_{OS1}[H^+] + K_a K_h K_{OS2})[\text{lysine}]_T\}. \quad (2)$$

Equation (2) can be written as (3) below with $A = K_a K_{OS1}[H^+] + K_a K_h K_{OS2}$, $B = [H^+]^2 + [H^+]K_a + [H^+]K_h + K_a K_h$, and $C = k_1 K_a K_{OS1}[H^+] + k_2 K_a K_n K_{OS2}$.

$$k_{obs}^{-1} = A/C + B/C[\text{lysine}]_T^{-1}. \quad (3)$$

The mechanism was confirmed by plotting k_{obs}^{-1} vs $[\text{lysine}]_T^{-1}$ at different acidities. In the low *p*H range, the part played by the conjugate base $CrOH^{2+}$ is negligible and (3) simplifies to (4) with $B' = [H^+] + K_{a'}$ and $C' = k_1 K_a K_{OS1}$,

$$k_{obs}^{-1} = 1/k_1 + B'/C'[\text{lysine}]_T^{-1}. \quad (4)$$

As amino acids take part in acid-base equilibria, the exact molecular/ionic condition of an amino acid in water varies with the *p*H. From the known pK_a-values of L-lysine, a speciation plot is drawn and lysine species present under the experimental conditions are ascertained as H_3L^{2+} and H_2L^+. Likewise, both Cr^{3+} and $CrOH^{2+}$ metal species exist in appreciable concentrations.

The scheme involves formation of an outer-sphere complex in pre-equilibrium step followed by the rate-determining interchange of the coordinated aqua ligand by H_2L^+. The H_2L^+ species has a separated negative charge on the carboxylate moiety 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 (Mentasti and Saini 1972; Perlmutter-Hayman and Shinar 1976), the extra positive charge on the protonated N atom (of ε-amino group) can be ignored and the true nature of the active species can be considered as H_2L and not H_2L^+ (in scheme 1, however, it is indicated as H_2L^+ – in equilibrium with H_3L^{2+} – for clarity). Like charges on chromium(III) species and H_3L^{2+} make reactions most unlikely between these species.

Both (3) and (4) envisage linearity in the k_{obs}^{-1} vs [lysine]$^{-1}$ plots: this indeed was the case and accordingly, $[H^+]$-dependent/$[H^+]$-independent intercepts were obtained for the respective high/low *p*H regions.

The graphically evaluated values of k_1, k_2, k_{OS1} and K_{OS2} (according to (3) and (4)) are given in table 1.

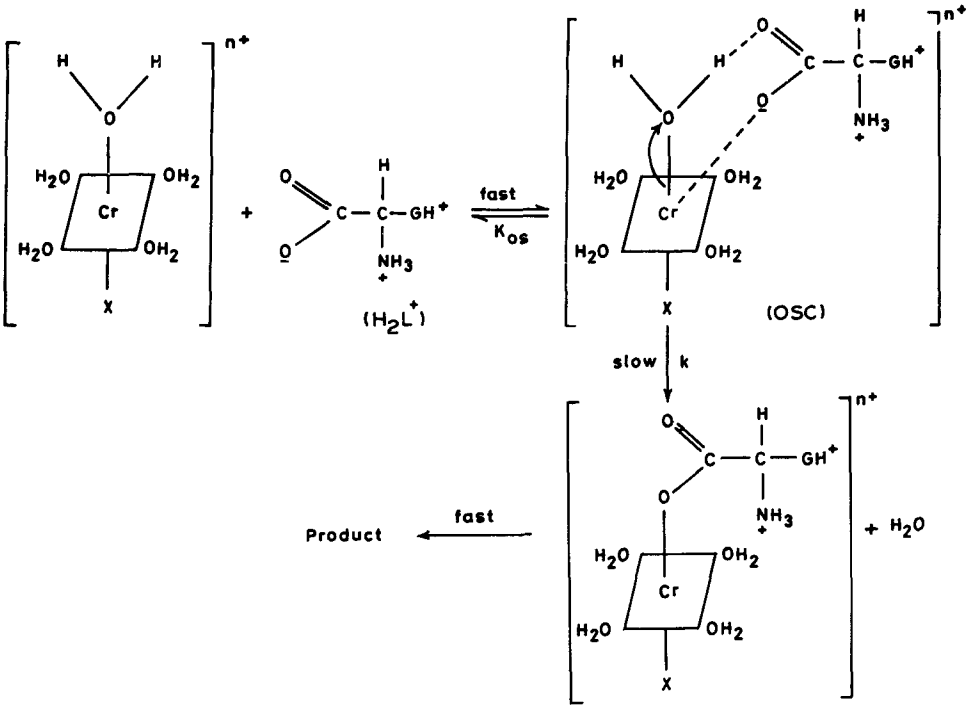
Table 2. First-order rate constants, k_1 and k_2, for the anation of $[Cr(H_2O)_6]^{3+}$/$[Cr(H_2O)_5OH]^{2+}$ by different ligands at $t = 45°C$ and $\mu = 1{\cdot}0$ mol dm^{-3}.

Ligand	$10^4 k_1(s^{-1})$	$10^3 k_2(s^{-1})$	Reference, remarks
H_2O^{18}	$36{\cdot}1 \times 10^{-2}(k_{ex})$	$3{\cdot}26(k'_{ex})$	Xu *et al* (1985), $\mu = 0{\cdot}7$ mol dm^{-3}
ΔH^* (kJ mol^{-1})	108·6	111·0	Thermodynamic parameters for isotopic water-exchange
ΔS^* (JK^{-1} mol^{-1})	+ 11·6	+ 55·6	
DL-α-Alanine	0·8	0·17	Kabir-ud-Din and Khan (1992)
		0·76	Mitra-Mustofy and De (1986), $\mu = 0{\cdot}03$ mol dm^{-3}
L-Hydroxyproline	1·3	0·42	Kabir-ud-Din and Khan (1992)
DL-Tryptophan	1·3	0·27	Shahid *et al* (1990)
L-Arginine	1·5	3·70(55°C)	Kabir-ud-Din and Khan (1992)
DL-Serine	1·9	—	Kabir-ud-Din and Khan (1992)
L-Lysine	2·4	0·29	Present work
DL-H_2asparagine	2·5	—	Khan and Kabir-ud-Din (1986)
L-Phenylalanine	3·2	0·70	Kabir-ud-Din and Khan (1992)
		0·59	Mitra-Mustofy and De (1986), $\mu = 0{\cdot}0075$ mol dm^{-3}
L-*iso*-Leucine	3·3	0·70	Kabir-ud-Din and Khan (1990)
L-Asparagine	5·0	1·25	Kabir-ud-Din and Khan (1985)
DL-H asparagine	5·1	—	Khan and Kabir-ud-Din (1986)
DL-Methionine	5·1	0·99	Khan *et al* (1991),
		2·02	Mitra-Mustofy and De (1986), $\mu = 0{\cdot}00753$ mol dm^{-3}, water/EtOH medium
Sarcosine	5·3	1·23(50°C)	Kabir-ud-Din and Khan (1992)
L-Histidine	5·6	1·54	Khan (1985)
DL-Valine	7·3	—	Khan and Kabir-ud-Din (1984)
Glycine	7·8	—	Khan and Kabir-ud-Din (1981)
Anthranilic acid	15·4	—	Tyagi and Khan (1978), $\mu = 0{\cdot}1$ mol dm^{-3}, 50% EtOH

In order to distinguish between I_a and I_d mechanisms a well-accepted procedure is the examination of the span of values of rate constants (Langford and Gray 1965; Swaddle 1974). A narrow spread suggests that the rate of entry of various ligands to the inner coordination sphere is controlled in each complex by largely the same factor (the fission of the metal–solvent bond) and hence the mechanism is dissociatively activated. A larger span is indicative of ligand-assisted anation and therefore the mechanism is associatively activated. First-order rate constants for the anation of aquachromium(III) ions by a series of ligands of similar nature are collected in table 2. The span of k_1 is much larger than of k_2. Accordingly an I_a mechanism can be assigned to the k_1-route and an I_d to the k_2-route.

The mechanistic conclusions outlined above are supported by a second criterion, namely, whether k_i is greater or less than isotopic water-exchange rate constants (Espenson 1969; Swaddle 1974) in the two aquachromium(III) species. The far greater value of k_1 compared to that of k_{ex} is in support of the proposition that the anation of species $[Cr(H_2O)_6]^{3+}$ by L-lysine is ligand-assisted and hence an I_a mechanism. k_2 and k'_{ex}-values are of the same order of magnitude, supporting the I_d assignment for the anation of $[Cr(H_2O)_5OH]^{2+}$ species by L-lysine.

It may be noted that the conjugate base, $CrOH^{2+}$, is more labile than Cr^{3+}. This labilizing effect is explained as follows: As OH^- ligand is electron donating, it facilitates the loss of H_2O ligand by increasing the electron density at the metal centre. Thus, easy rupture of $Cr–OH_2$ bond in hydroxopentaaquachromium(III) takes place which



Scheme 2. The mechanism of anation of chromium(III) by L-lysine (G = $-CH_2CH_2CH_2NH_2$; X = H_2O/OH; n = 3/2).

favours simultaneous rapid insertion of the outer-sphere ligand into the available inner-sphere and its subsequent coordination.

Results of the experiments carried out at different dielectric constants (D) of the medium corroborate the proposed outer-sphere interchange mechanism. The k_{obs} obtained in EtOH/water mixed solvents show an increase with increasing EtOH (8·3, 8·6, 9·6, 11·6, 14·1, 15·9, 20·0 $\times 10^{-5} s^{-1}$ respectively in 0, 5, 10, 15, 20, 25, 30% EtOH, v/v) and produce a linear log k_{obs} vs $1/D$ plot. Obviously, K_{OS}-values will increase with decrease in D of the medium and, therefore, outer-sphere associations are enhanced with a consequent increase in rates.

4. The mechanism

The mechanism of the anation reaction of aquachromium(III) species by L-lysine is shown in scheme 2. The reactions of the aquachromium(III) species are assumed to occur via outer-sphere associations which are stabilized by hydrogen bonding. The carboxylate moiety of the amino acid forms a weak bond in the reaction of hexaaqua species and a weaker bond in the reaction of hydroxopentaaqua species.

Acknowledgements

GJK is grateful to the Management Board of Shibli National College, Azamgarh, for grant of leave and to the University Grants Commission for fellowship.

References

Banerjea D and Dutta Chaudhuri S 1968 *J. Inorg. Nucl. Chem.* **30** 871
Chow S T and McAuliffe C A 1975 *Progress in inorganic chemistry* (ed) S J Lippard (New York: Interscience) vol. 19, p. 51
Cooper J A, Blackwell L F and Buckley P D 1984 *Inorg. Chim. Acta.* **92** 23 and references therein
Eichhorn G L (ed.) 1973 *Inorganic biochemistry* (New York: Elsevier) vols 1, 2
Espenson J H 1969 *Inorg. Chem.* **8** 1554
Gerdom L E and Goff H M 1982 *Inorg. Chem.* **21** 3847
Gonzalez-Vergara E, Hegenauer J, Saltman P, Sabat M and Ibers J A 1982 *Inorg. Chim. Acta.* **66** 115
Govindaraju K, Ramasami T and Ramaswamy D 1989 *J. Inorg. Biochem.* **35** 127, 137
Joubert P R and van Eldik R 1976 *Int. J. Chem. Kinet.* **8** 411
Kabir-ud-Din and Khan G J 1985 *Ann. Chim. (Rome)* **75** 279
Kabir-ud-Din and Khan G J 1990 *Transition Met. Chem.* **15** 39
Kabir-ud-Din and Khan G J 1992 *J. Coord. Chem.* **26** 351, and references therein
Khan A A and Malik W U 1963 *J. Indian Chem. Soc.* **40** 565
Khan G J 1985 Ph D dissertation, Aligarh Muslim University, Aligarh
Khan I A and Kabir-ud-Din 1981 *J. Inorg. Nucl. Chem.* **43** 1082
Khan I A and Kabir-ud-Din 1984 *Indian J. Chem.* **A23** 98
Khan I A and Kabir-ud-Din 1986 *Transition Met. Chem. (Weinheim)* **11** 391
Khan I A, Shahid M and Kabir-ud-Din 1991 *Transition Met. Chem.* **16** 18
Langford C H and Gray H B 1965 *Ligand substitution processes* (New York: W A Benjamin)
McArdle J V, de Laubenfels E, Shorter A L and Ammon H L 1982 *Polyhedron* **1** 471
Mentasti E and Saini G 1972 *Atti Accad. Sci. Torino* **106** 561
Mertz W 1975 *Nutr. Rev.* **33** 129
Mertz W 1983 *Chim. Scr.* **21** 145
Mertz W and Schwarz K 1959 *Am. J. Physiol.* **196** 614
Mertz W, Toepfer E W, Roginski E E and Polansky M M 1974 *Proc. Fed. Am. Soc. Exp. Biol.* **33** 2275

Mitra-Mustofy H G and De G S 1986 *J. Indian Chem. Soc.* **69** 1040, and references therein
Perlmutter-Hayman B and Shinar R 1976 *Inorg. Chem.* **15** 2932
Prasad D R, Ramasami T, Ramaswamy D and Santappa M 1982 *Inorg. Chem.* **21** 850
Ramasami T and Sykes A G 1976 *Inorg. Chem.* **15** 2885
Ramasami T, Wharton R K and Sykes A G 1975 *Inorg. Chem.* **14** 359
Shahid M, Khan I A and Kabir-ud-Din 1990 *J. Chem. Soc., Dalton Trans.* 3007
Shuttleworth S G and Sykes R L 1960 *J. Am. Leather Chem. Assoc.* **55** 154
Sigel H (ed.) 1973 *Metal ions in biological systems* (New York: Dekker) vol. 2
Swaddle T W 1974 *Coord. Chem. Rev.* **14** 217
Tyagi S C and Khan A A 1978 *Indian J. Chem.* **A16** 657
Wood J M 1975 *Naturwissenschaften* **62** 357
Xu F C, Krouse H R and Swaddle T W 1985 *Inorg. Chem.* **24** 267