A Kinetic and Equilibrium Study of the Reaction of Glycine with Chromium(III) in Aqueous Solution †

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The formation of tetra-aquaglycinatochromium(III) from glycine and chromium(III) has been studied at pH = 3.0—3.8, 40—54 °C, and I = 0.4 mol dm^{-3} ($NaClO_4$). The equilibrium constant ($\log_{10} K_1$) is 7.60 at 44.8 °C. The reaction obeys the rate equation $k_{obs.} = k + k'[H^+]^{-1}$ and under all the conditions studied is *zero* order in the concentration of glycine. A mechanism involving extensive outer-sphere complexation of hexa-aquachromium(III) and its conjugate base is proposed. The activation parameters are compared to literature values.

Chromium(III) complexes have been less well studied than the corresponding cobalt(III) systems. One particularly interesting feature of chromium(III) chemistry is that complex-formation reactions from hexa-aquachromium(III) (or its conjugate base) may be studied; redox problems preclude such studies for cobalt(III). Substitution at chromium(III) centres has received attention [1] because of the possibility of A (or I_a) [2] associative mechanisms for the d^3 electronic configuration. The majority of chromium(III) formation reactions follow a rate equation (1),[3] where k_i = interchange rate constant, K_{os} = outer-sphere complexation constant, and L is the ligand.

$$k_{obs.} = k_i K_{os}[L]/(1 + K_{os}[L]) \qquad (1)$$

Such studies are often carried out under sufficiently acidic conditions that the monohydroxy-species of chromium(III) may be ignored. On balance the evidence in the literature seems to favour an associative-interchange mechanism (I_a) *via* a tight ion pair derived from the hexa-aqua-species. However, there are some anomalies; in a series of classic papers Hamm and co-workers [4-6] studied the formation of chromium(III) complexes with dicarboxylic acids and hydroxy acids. Their kinetic results (most notably that the reaction was zero order in ligand concentration) were originally interpreted in terms of a strictly dissociative process. Basolo and Pearson [7] later suggested that a saturated ion-pairing mechanism [for which equation (1) becomes $k_{obs.} = k_i$] provides a more plausible explanation for Hamm's observations. In marked contrast, Banerjea and co-workers found dependence of the reaction rate on ligand concentration for the reactions of malonate [8] and oxalate [9] with hexa-aquachromium(III). The conditions used in the latter studies were considerably more acidic than those used by Hamm. Compilations of rate constants [10] and activation parameters [11,12] for chromium(III) reactions are available but as exemplified above the situation is far from simple.

Chromium(III) chemistry has recently become more topical; Mertz [13] has shown that a low-molecular-weight chromium(III) complex known as the 'Glucose Tolerance Factor' (GTF) potentiates insulin activity. A complex containing nicotinic acid, glycine, glutamic acid, cysteine, and chromium(III) has been isolated from brewers yeast.[14] This substance (of unknown structure) shows remarkable *in vitro* activity, potentiating the action of insulin in glucose oxidation by chromium-deficient rat adipose tissue. Interest in GTF has stimulated work on chromium(III) nicotinic acid complexes including structural studies,[15,16] kinetic work,[17] and measurements of equilibrium constants.[18]

There have been two previous kinetic studies of the reaction between chromium(III) and glycine in aqueous solution.[19,20] In neither of these studies was the pH of the reaction mixture controlled and thus may have varied during the course of the reaction. This is unsatisfactory as protons are liberated during the glycine-complexation reaction. The stability of the chromium(III) glycine complex has been investigated [21] potentiometrically but protic equilibria for chromium(III)-containing species were not considered.

The above studies ignored the participation of the monohydroxy-complex; this seems to be based on the ambient pK_a (4.1).[22] However, at temperatures typically used for kinetic work (40—60 °C) the pK_a value falls to *ca.* 3 (see below). We have studied the reaction of chromium(III) with glycine in the region pH 3.0—3.8 at temperatures 40—54 °C and ionic strength I = 0.4 mol dm^{-3}. In all experiments the pH has been carefully controlled. In the absence of careful pH and ionic strength control, spurious results are obtained.

Results

(1) *Equilibrium Studies.*—Preliminary spectrophotometric studies were undertaken. Solutions of chromium(III) and glycine were equilibrated {pH = 3.25, 44.5 °C, I = 0.4 mol dm^{-3} ($NaClO_4$), [Cr^{III}] = 0.025 mol dm^{-3}} until, as judged by spectrophotometry, no further reaction occurred. The reaction was essentially complete at [glycine] > 0.25 mol dm^{-3}. The final electronic spectrum was characterized by two peaks, $\nu_{max.}$ 18.1 × 10^3 and 24.5 × 10^3 cm^{-1}. The initial solutions showed peaks at 17.1 × 10^3 and 24.1 × 10^3 cm^{-1}. The tris(glycinato) complex is characterized [19] by peaks at 19.2 × 10^3 and 25.6 × 10^3 cm^{-1}. Using Jorgenson's rule of average environment [23a] together with these data and our starting solution values, we would predict peaks at 17.9 × 10^3 and 24.6 × 10^3 cm^{-1} for an NO_5 chromophore which are very close to our observed values.

The acid dissociation of hexa-aquachromium(III) was studied spectrophotometrically and pK_a values determined as described by Rossotti.[23b] The results are summarized in Table 1. Clearly the monohydroxy-species will be of significance in kinetic and thermodynamic studies at elevated temperatures.

An equilibrium study of the chromium(III) glycine system was undertaken. Solutions of the amino acid and chromium(III) were equilibrated at a constant pH, and equilibrium absorbance measurements were made (normally at λ = 560 nm). Conditional equilibrium constants were then

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† *Supplementary data available* (No. SUP 23927, 6 pp.): expressions for equilibrium constants, selected rate constants at various pH values and temperatures. See Instructions for Authors, *J. Chem. Soc., Dalton Trans.*, 1984, Issue 1, pp. xvii—xix.

Table 1. Acid dissociation constants for hexa-aquachromium(III)

θ_c/°C	pK_a	ΔH/kJ mol^{-1}
27	4.37 ± 0.02	87.2 [a]
35	4.15 ± 0.02	
40.25	3.78 ± 0.02	
50	3.32 ± 0.02	
0	4.66	40.32 (0—100 °C) [b]
25	4.01	
50	3.47	
46.2	3.37	39.48 (46—96 °C) [c]
63.5	3.069	

[a] This work; [Cr^{III}] = 0.025 and I = 0.4 mol dm^{-3} (NaClO$_4$). [b] N. Bjerrum, *Z. Phys. Chem.* (*Leipzig*), 1907, **59**, 336. [c] C. Postmus and E. L. King, *J. Phys. Chem.*, 1955, **59**, 1208.

Table 2. Equilibrium data [a] for the reaction of chromium(III) with glycine

Constant	Value	A	Method
K_{cond}/mol dm^{-3}	12.3 ± 0.4	0.31 [b]	$A_{obs.}$ *vs.* $(A_{obs.} - A_0)[gly]_T$
	15.8 ± 1.0	0.30 [c]	Hill plot; slope = 1.0 ± 0.05
pK_a	3.58	—	Calculated from data in Table 1
pK_1	2.54		pK_a values for glycine[24] at 45 °C, corrected [d] to I = 0.4 mol dm^{-3}
pK_2	9.51		
log$_{10}K_1$	7.60		$[Cr(glyO^-)(H_2O)_4]/[Cr(H_2O)_6][glyO^-]$

[a] Measurements at 44.8 °C, pH = 3.25, and I = 0.4 mol dm^{-3}. [b] Calculated. [c] Observed. [d] C. W. Davies, *J. Chem. Soc.*, 1938, 2093.

calculated from Hill plots of log $(A_{obs.} - A_o)/(A_\infty - A_{obs.})$ *vs.* log$[gly]_T$ * and plots of $[gly]_T(A_{obs.} - A_o)$ *vs.* $A_{obs.}$. The slopes of the Hill plots were always close to unity, again suggesting that only the 1 : 1 complex was being formed; the intercepts provide an estimate of the conditional equilibrium constant in terms of total glycine and chromium. Typical results are shown in Table 2. In this moderate range of pH (3.0—3.8) we propose that the equilibria described in the Scheme account (see below) for our observations on formal equilibria. From the value of K_{cond} (using the measured values of K_a and the literature values [24] for the pK_a of glycine of 2.31 and 9.28 at 45 °C) corrected to the ionic strength used in this study, we may calculate (see SUP 23927) values of equilibrium constants as in equation (2).

$$K_1 = [Cr(glyO^-)(H_2O)_4]/[Cr(H_2O)_6][glyO^-] \quad (2)$$

The value in Table 2 is in reasonable agreement with the previously published value [21] logK_1 = 8.62 (25 °C, I = 0.1 mol dm^{-3}), which must be an overall value in terms of total chromium as reactant.

(2) *Kinetic Studies.*—The rate of complex formation was studied under a variety of conditions. The reaction was followed at 560 nm. First-order plots of ln $(A_{obs.} - A_\infty)$ *vs.* time were good straight lines over two to three half-lives. Rate constants obtained by the Guggenheim method [25a] were in good agreement with those obtained from first-order plots. All reactions followed a single first-order process which strongly suggests that ring closure is rapid.

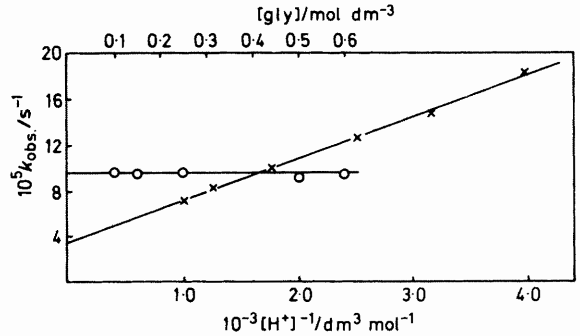

Figure. Dependence of pseudo-first-order rate constant on acid (×) and glycine (O) concentrations. Conditions as in Table 3

Table 3. Typical pseudo-first-order rate constants for the reaction of glycine and chromium(III) [a] at I = 0.4 mol dm^{-3}

[glycine]/mol dm^{-3}	pH	$10^5k_{obs.}/s^{-1}$	
0.25	3.0	7.20	*b*
0.25	3.1	8.30	
0.25	3.25	10.00	
0.25	3.4	12.5	
0.25	3.5	14.60	
0.25	3.6	18.33	
0.10	3.25	9.58	*c*
0.15	3.25	9.50	
0.25	3.25	9.60	
0.50	3.25	9.16	
0.60	3.25	9.33	

[a] The source of chromium(III) was chrome alum. [b] At 44.5 °C and [Cr^{III}] = 0.025 mol dm^{-3}, $k_{obs.} = (3.55 \pm 0.24) \times 10^{-5} + (3.63 \pm 0.01) \times 10^{-8}/[H^+]$. [c] At 44.8 °C and [Cr^{III}] = 5 × 10^{-3} mol dm^{-3}.

The most striking results are that the reaction is zero order in glycine at all available concentrations and obeys the rate equation (3). Typical results are summarized in Table 3 and

$$k_{obs.} = k + k'[H^+]^{-1} \quad (3)$$

plotted in the Figure. As illustrated the rate constant shows little or no dependence on the total concentration of chromium(III) and exactly similar results are obtained using chromium(III) perchlorate as the source of the metal ion. There is no significant variation in the rate constant between chromium(III) concentrations of 5 × 10^{-3} and 2.5 × 10^{-2} mol dm^{-3}.

The acid-independent rate constants obtained from plots of $k_{obs.}$ *vs.* $[H^+]^{-1}$ are summarized in Table 4, together with activation parameters obtained from Eyring plots [25b] of the temperature dependence of these constants.

Discussion

Under the experimental conditions studied, the reaction proceeds (in general) 80—100% toward an equilibrium mixture of product and reactant. The rate however showed no dependence on the percentage reaction in the concentration ranges studied. For all conditions investigated the reaction showed similar functionality in both [H$^+$] and [glycine]. The vast majority of our experiments were performed under conditions such that glycine was largely (>95%) present as the zwitterion. The reaction rate was also independent of the chromium(III) concentration (see Table 3 and the Figure).

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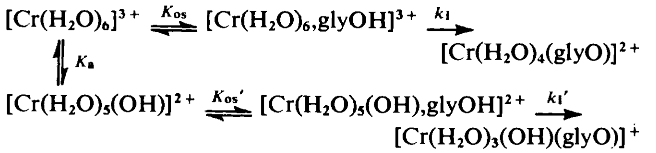
* Throughout this paper glycine concentrations will be represented as follows: total glycine $[gly]_T$; zwitterionic glycine [glyOH]; anionic glycine [glyO$^-$].

Table 4. Acid-independent rate constants and derived activation parameters

θ_c/°C	10^5k/s^{-1}		$10^8k'$/mol dm^{-3} s^{-1}	
40.25	2.29 ± 0.26		1.29 ± 0.08	
44.5	3.55 ± 0.24	$\Delta H^\ddagger$ = 75.7 ± 9.5 kJ mol^{-1},	3.63 ± 0.09	$\Delta H^\ddagger$ = 156 ± 7.5 kJ mol^{-1},
47.0	4.64 ± 0.62	$\Delta S^\ddagger$ = −92 ± 9.6 J K^{-1} mol^{-1}	4.91 ± 0.03	$\Delta S^\ddagger$ = 103 ± 23 J K^{-1} mol^{-1}
54.5	8.52 ± 0.67		19.29 ± 0.55	



Scheme.

In explaining our results we need to consider carefully the possibility that the equilibrium position controls the reaction rate. In general, for a reaction proceeding to equilibrium, the pseudo-first-order rate constant is the sum of forward and backward rate constants.[25c] In our experiments we can vary the equilibrium position both by controlling the pH of the reaction mixture and the glycine concentration. Varying the glycine concentration has been shown not to effect the reaction rate; we conclude that the equilibrium position is not the significant factor controlling the rate of reaction as pH is varied.

The zero-order dependence of the rate constant on glycine concentration suggests that a saturated outer-sphere complex may be involved (see Introduction section). However, our efforts to detect such an interaction (spectroscopically) have been unsuccessful. The Scheme successfully accounts for our observations (glycine, water molecules, and protons are omitted).

We assume the reaction of the hexa-aquachromium(III) complex to occur *via* a saturated outer-sphere complex, formed by strong hydrogen bonding and reaction of the hydroxy-complex *via* a more weakly associated outer-sphere complex. The rate of reaction can be expressed as in equation (4). The mass balance for chromium(III) is as in equation (5).

$$\text{Rate} = k_I[Cr(H_2O)_6,glyOH] + k_I'[Cr(H_2O)_5(OH),glyOH] \quad (4)$$

$$[Cr]_T = [Cr(H_2O)_6] + [Cr(H_2O)_5(OH)] + [Cr(H_2O)_6,glyOH] + [Cr(H_2O)_5(OH),glyOH] \quad (5)$$

Substituting K_a and K_{os} into equations (4) and (5) we obtain (6) and (7) respectively. As $K_a \approx [H^+] \approx 10^{-3}$ mol dm^{-3} and $K_{os} \gg K_{os}'$, combining (6) and (7) gives expression (8).

$$\text{Rate} = k_IK_{os}[Cr(H_2O)_6][glyOH] + k_I'K_aK_{os}'[Cr(H_2O)_6][glyOH]/[H^+] \quad (6)$$

$$[Cr(H_2O)_6] = [Cr]_T[H^+]/([H^+] + K_a + K_{os}[glyOH][H^+] + K_aK_{os}'[glyOH]) \quad (7)$$

$$k_{obs.} = k_I + k_I'K_{os}'K_a/K_{os}[H^+] \quad (8)$$

This mechanism is consistent with our observations with $k = k_I$ and $k' = k_I'K_{os}'K_a/K_{os}$. In this analysis k is the unimolecular rate constant for interchange in the glycine-hexa-aquachromium(III) outer-sphere complex. Activation parameters are compared with literature values for reactions of hexa-aquachromium(III) in Table 5. The low activation energy and substantial negative value of $\Delta S^\ddagger$ point to a largely associative character for this reaction. This may be contrasted with the dissociative reaction of $[Cr(NH_3)_5(H_2O)]^{3+}$ with glycine, $\Delta H^\ddagger$ = 106 kJ mol^{-1} and $\Delta S^\ddagger$ = +23.5 J K^{-1} mol^{-1}.[26]

Table 5. Activation parameters for related complexation reactions with chromium(III)

Ligand	$\Delta H^\ddagger$/kJ mol^{-1}	$\Delta S^\ddagger$/J K^{-1} mol^{-1}	Notes
Malonate	102.1	−0.5	[H$^+$] > 0.05 mol dm^{-3}; kK_{IP}[8]
Oxalate	121.3	+59	[H$^+$] > 0.2 mol dm^{-3}; kK_{IP}[9]
Oxalate,malonate, acetate,phthalate	88—97 [a]	—	Zero order in [ligand], pH 3.5—5.5[6]
H_2O exchange	109	+12	*b*
Glycine	75	−92	Zero order in [ligand], pH 3.0—3.6, this work

[a] Activation energy. [b] R. Plane and H. Taube, *J. Phys. Chem.*, 1952, **56**, 33.

As might be expected for chromium(III) reactions, hydroxide has a labilizing effect. The composite nature of k' makes arguments as to the exact nature of this step difficult. The large positive value of $\Delta S^\ddagger$ (even considering ΔS for K_a) suggests a more dissociative nature for the reaction, possibly with a true $\Delta S^\ddagger$ value close to zero. Further discussion of activation parameters is precluded as we have no knowledge of the temperature variation of the relevant outer-sphere association constants.

Experimental

Glycine (BDH, chromatographically homogeneous), chrome alum (BDH, AnalaR), and chromium(III) perchlorate (Strem Chemicals) were used without further purification. All other reagents were of analytical quality. Spectra were recorded using a Perkin-Elmer 253 scanning spectrophotometer and the pH was controlled in equilibrium and kinetic studies with a Radiometer Automatic Titrator 45646 in pH-stat mode.

Kinetic experiments were performed by mixing thermostatted solutions of glycine and chromium(III) and adjusting the pH to approximately the required value with sodium hydroxide. This solution was then introduced into the reaction vessel, thermostatted at the desired temperature. During the course of the reaction the solution was circulated through a flow cell using a peristaltic pump, the spectrophotometer block also being thermostatted at the same temperature.

Equilibrium constants, acid-independent rate constants, and activation parameters were derived from the experimental data by standard least-squares techniques and reported errors are one standard deviation from each mean value. All constants reported are 'Brønsted constants' in terms of the concentrations of all species except the hydrogen ion.

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