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Equilibrium and Kinetics of Complexes of Aquachromium(III) with Nicotinate Ion[1]

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Species of the type $Cr(OH_2)_{6-n}(nic)_n^{(3-n)+}$ (nic = nicotinate anion) where n = 1-3 have been synthesized, isolated, and characterized. The complexes were prepared in aqueous solutions containing hexaaquachromium(III) ion and nicotinate ion in the pH range 3-5. These kinetically inert species are judged to be coordinated through one of the carboxylate oxygens on the nicotinate ligand. The complex ions were characterized in solution by their ion-exchange properties and visible spectra. The equilibrium constant for the formation of the species in which n = 1 was determined at room temperature. The acid dissociation constant for the loss of a proton from a water molecule coordinated to the n = 1 species was also calculated; it appears that the pentaaqua(nicotinato)chromium(III) ion is more acidic than the hexaaquachromium(III) ion. The neutral (n = 3) compound was characterized by infrared, thermogravimetric, and mass spectrometry. A dimer with composition $Cr_2(OH)(nic)(OH_2)_8^{4+}$ was isolated and characterized in solution; the chromium atoms are proposed to be bridged by hydroxide ion and the two oxygen atoms of the carboxylate ion. The rate of aquation of each of these species at 25 and/or 60 °C in perchloric acid-perchlorate solutions was studied, and rate constants were determined. At 25 °C the half-time for the aquation of the n = 1 species was about 35 days; at 60 °C, the half-times for aquation of the various species are in the range 1 h to 3 days.

Introduction

Interest in complex ions of chromium(III) and the anion of nicotinic acid (3-carboxypyridine) has been stimulated by suggestions that these species are present in glucose tolerance factor (GTF) obtained from brewer's yeast.[2] The situation is far from clear, however, as recent work has shown GTF-like activity in chromium-free fractions.[3] The chemistry of this system of a kinetically inert metal ion, chromium(III), and a ligand with two potential binding sites, an O-bonding carboxylate group and an N-bonding pyridine group, is of interest independent of any role the species may play as models for binding in GTF. The coordination of nicotinic acid and its derivatives to chromium(III) (and other ions) has been recently reported,[4-12] but there are no studies concerning the kinetics and equilibria of nicotinic acid-chromium(III) species. The present study deals with the species formed in mildly acidic aqueous solution ($[H^+] = 10^{-3}$-10^{-5} mol L^{-1}) and the aquation of these species in more acidic solution ($[H^+]$ = 0.05-3.0 mol L^{-1}). The relative inertness of these species allows their separation from one another by ion-exchange procedures that have proved useful in the study of other systems of inert chromium(III) complexes (e.g., species of chromium(III) with anionic thiocyanate ion[13] or with neutral dimethylsulfoxide[14]). The disadvantages of inertness in the preparative procedures has been circumvented by using carbon dioxide as a catalyst.[15] Catalysis is due to formation of a low concentration of (hydrogencarbonato)chromium(III) having a lability of coordinated water not displayed by aquachromium(III) ion. Like structures of the chromium(III)-nicotinate species recently characterized in the solid state by X-ray crystallography,[6] the species studied in the present work are judged to be O-bonded complexes.

Experimental Section

Analysis. Analysis for chromium was done by either of two procedures. Accurate analysis involved conversion of the chromium species to chromate ion by alkaline hydrogen peroxide followed by measurement of light absorption at 371.9 nm ($a(CrO_4^{2-}) = 4.82 \times 10^3$ L mol^{-1} cm^{-1}).[16] For complete elution profiles involving analysis of many fractions, atomic absorption (λ = 357.9 nm) was used. Appropriate calibration using solutions of known concentration, with or without added nicotinic acid, allowed analysis with an uncertainty not exceeding 5%. The acid dissociation of protonated nicotinic acid (H_2nic^+) is governed by $K_1 = 9.8 \times 10^{-3}$ mol L^{-1} and $K_2 = 1.9 \times 10^{-5}$ mol L^{-1}. In each of its stages of protonation, nicotinic acid has an absorption maximum at 260-262 nm. The molar absorptivity at this wavelength depends upon pH: at pH 0.26 the cationic species is predominant and $a = 5.81 \times 10^3$ L mol^{-1} cm^{-1}, at pH 3.65 the zwitterion species is predominant and $a = 5.45 \times 10^3$ L mol^{-1} cm^{-1}, and at pH 5.77 the anionic species is ~90% of the total and $a = 3.71 \times 10^3$ L mol^{-1} cm^{-1}. Analysis for free ligand was made in acidic solutions of measured pH.

Analysis for the coordinated ligand of (nicotinato)chromium(III) species eluted from an ion-exchange column was performed spectrophotometrically. Analysis for free ligand could be made after aquation of the complex at pH ≤2, or analysis for coordinated ligand could be made on the intact complex. Nicotinate complexes of chromium(III) absorb in the same region as does free ligand. On the basis of the experiment to be described, the molar absorptivity of coordinated nicotinate is approximately the same as that for free anionic ligand. The light absorption by hexaaquachromium(III) at 260-262 nm is low (a = 9.9 L mol^{-1} cm^{-1}). A chromium(III)-nicotinate species more easily eluted than hexaaquachromium(III) ion was found to have a molar absorptivity at 261 nm of $(3.9 \pm 0.1) \times 10^3$ L mol^{-1} cm^{-1}. Upon aquation at pH ≤2, the light absorption at 261 nm increased to that corresponding to a value of $a = (5.2 \pm 0.1) \times 10^3$ L mol^{-1} cm^{-1}. This indicates that light absorption at 261 nm by coordinated ligand in this 1:1 complex corresponds to a molar absorptivity approximately that for the anionic ligand. Light absorption at this wavelength is, therefore, a convenient method for counting the ligands associated with chromium(III) if the solution contains no excess free ligand; this approach has been used by others.[10,17] The purified species, judged on the basis of elutability to be bis(nicotinato)chromium(III), has a molar absorptivity (per mole of chromium(III)) of $(7.0 \pm 0.8) \times 10^3$ L mol^{-1} cm^{-1}, a value 1.8 ± 0.2 times the value for the 1:1 complex.

Ion-Exchange Procedures. Preliminary experiments disclosed a high affinity of free ligand for Dowex-50 cation-exchange resin in the pH range from 1 to 3. There was no such affinity of free ligand for Sephadex CP-25, and this ion exchanger was used in all experiments. The ion exchanger was equilibrated with a solution of pH ~2 having $[Na^+]/[H^+]$

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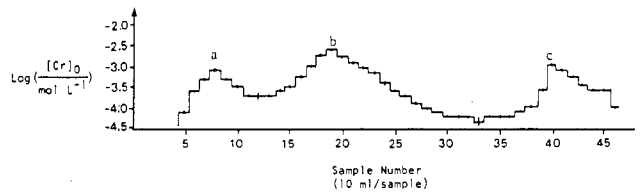

Figure 1. Elution profile showing separation of (a) bis(nicotinato)-tetraaquochromium(III) ion, (b) (nicotinato)pentaaquochromium(III) ion, and (c) hexaaquochromium(III) ion (ion-exchange column, 32 × 3 cm; composition of reaction mixture $[Cr]_{total} = 1.26 \times 10^{-4}$ mol L^{-1}, $[ligand]_{total} = 0.100$ mol L^{-1}, pH 4.8).

= 99 (0.99 M $NaClO_4$, 0.01 M $HClO_4$) prior to use. Reaction mixtures were treated with perchloric acid to lower the pH to ~2 immediately before the chromium species in such mixtures were loaded onto the ion exchanger. This generally was done on a short column that then was rinsed with dilute perchloric acid (10^{-2}–10^{-3} mol L^{-1}) to remove free ligand before the loaded ion exchanger was transferred to the top of a longer column for elution. That this rinsing did not elute chromium(III) species was shown by checking the rinse with alkaline peroxide.

The progress of an elution experiment can be observed visually as the colored species move down the column. In most experiments, quantitative measurements were made on successive 5- or 10-mL portions of eluent, but larger portions, each containing a single elution peak, were collected in some experiments. Eluent portions were diluted appropriately with 0.01 M $HClO_4$, and their light absorption at ~260 nm was measured. This was followed by atomic absorption analysis for chromium.

Preparation and Identification of (Nicotinato)chromium(III) Species

Solutions prepared from a stock solution of chromium(III) perchlorate and perchloric acid, solid nicotinic acid, and sodium hydroxide solution (added to bring the solution to the desired pH (3.0–5.0)) had the green color characteristic of aquachromium(III) species at that pH. This color persists for many hours at room temperature, but addition of carbon dioxide, a catalyst, rapidly (a few minutes) causes a change to blue, the color of some nicotinate–chromium(III) species. Bubbling of carbon dioxide at room temperature was continued during the reaction period, which varied from ~30 min, a time sufficient for equilibrium, to many hours. The pH was monitored during and/or following the reaction period; generally it decreased slightly because formation of chromium(III) nicotinate species involves deprotonation of nicotinic acid. The acidity of the reaction mixtures was sufficiently high to make CO_2 the predominant form of carbon(IV). After the reaction period the bubbling of CO_2 was stopped, and the pH was lowered to ≤2. The solutions then were aerated with nitrogen gas. Loading of the chromium(III) species onto the ion exchanger followed as already described.

A solution containing appreciable amounts of species with one and two nicotinate ligands per chromium(III) had the composition $[Cr(III)] = 1.26 \times 10^{-4}$ mol L^{-1}, [Hnic] + [nic$^-$] = 0.100 mol L^{-1}, and pH 4.8. A portion of this solution containing 0.504 mmol of chromium was placed atop a 3 cm × 32 cm column; elution with 0.99 M $NaClO_4$–0.010 M $HClO_4$ yielded three well-defined bands containing bis(nicotinato)tetraaquachromium(III) ion, (nicotinato)pentaaquachromium(III) ion, and hexaaquachromium(III) ion. Highly charged polymeric species were not eluted by this procedure but were removed from the resin with alkaline peroxide. The maximum concentrations of chromium(III) in the bands were as follows: at ~80 mL, 7.5×10^{-4} mol L^{-1}; at ~190 mL, 2.1×10^{-3} mol L^{-1}; at ~410 mL, 9.4×10^{-4} mol L^{-1}. Minima in the elution profile at ~120 and ~340 mL had concentrations of chromium(III) equal to 1.9×10^{-4} and 5.5×10^{-5} mol L^{-1}, respectively. The elution profile is shown in Figure 1. The molar absorptivity at ~261 nm in the four 10-mL portions of eluent containing the first peak was $(7.35 \pm 0.05) \times 10^3$ L mol^{-1} cm^{-1} and in the six 10-mL portions of eluent containing the second peak was $(3.9 \pm 0.1) \times 10^3$ L mol^{-1} cm^{-1}. Eluent portions containing the third peak were essentially transparent at ~260 nm. These light absorption data for the 260-nm spectral region identify these species as containing two, one, and zero nicotinate ligands per chromium(III), respectively. The ease of elution indicates charges

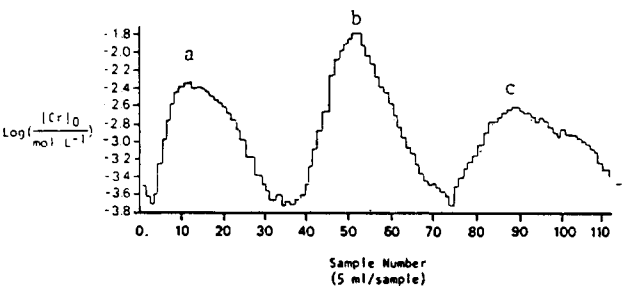

Figure 2. Typical elution profile of chromium(III)–nicotinate complexes (ion-exchange column, 25 × 3 cm; composition of reaction mixture $[Cr]_{total} = 0.150$ mol L^{-1}, $[ligand]_{total} = 0.108$ mol L^{-1}, pH 3.4): (a) (nicotinato)pentaaquochromium(III) ion; (b) hexaaquochromium(III) ion; (c) (nicotinato)chromium(III) dimer.

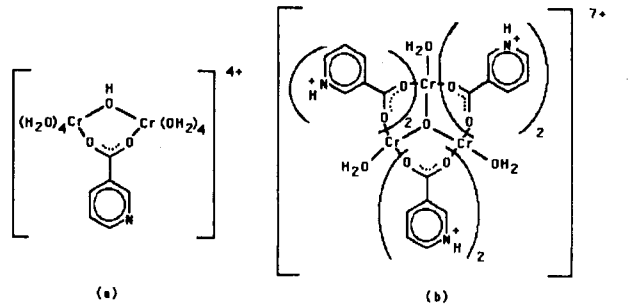

Figure 3. Sketches of (a) the proposed structure of the dimer characterized in solution in this work and (b) the trimer $Na[Cr_3O(nicH)_6(OH_2)_3][ClO_4]_8$ characterized in the solid by Gonzalez-Yergara et al.[6]

on the nicotinate complexes of 1+ and 2+, thereby indicating that these species are monomeric in chromium(III) and that the complexes involve the anionic ligand and are not protonated at the pH of the eluting agent (~2).[18]

A solution containing nicotinic acid and a much higher concentration of chromium(III), $[Cr(III)] = 0.150$ mol L^{-1}, [Hnic] + [nic$^-$] = 0.108 mol L^{-1}, and pH 3.4, equilibrated as was the previously described solution, shows three peaks in the elution profile that was developed with the same eluting agent (0.99 M $NaClO_4$–0.01 M $HClO_4$). This profile is shown in Figure 2. The first and second of these peaks contain the previously identified 1:1 chromium(III)–nicotinate species and hexaaquachromium(III) ion, respectively. The least easily eluted species had an elution volume ~1.6 times that for hexaaquachromium(III) ion. This species has a molar absorptivity, per mole of chromium at 261 nm, of $\sim 2.5 \times 10^3$ L mol^{-1} cm^{-1} (~0.7 times that of the coordinated anionic ligand in the mono and bis species and ~0.5 of that for free ligand). This value coupled with the low elution rate for this species leads to its identification as a species with two chromium(III) ions per nicotinate ion having a charge ≥3+. Relatively pure complex was obtained by the same ion-exchange techniques already outlined.

Several structures can be proposed for a binuclear species containing a single nicotinate anion. In order to place an upper limit on the charge of the species, well-characterized chromium(III) dimers having charges 4+ and 5+ ($Cr_2(OH)_2(OH_2)_8^{4+}$ and $Cr_2(OH)(OH_2)_{10}^{5+}$) were prepared.[19] When the elution characteristics of these dimers are compared to the polymeric nicotinate species under the same column conditions, the possibility of a charge >4+ for the complex is eliminated. A species expected to have elution properties consistent with those of the observed complex is (μ-hydroxo)(μ-nicotinato)bis(tetraaquachromium(III)), in which nicotinate bridges through the two oxygens of the carboxylate group. This dimer would have charge 4+ and be related structurally to the trinuclear complex $[Cr_3O(nicH)_6(OH_2)_3]^{7+}$,

(18) Cooper et al.[10] report the protonation of the ligand at $[H^+] \approx 2$ mol L^{-1}. The acid dissociation constant for the coordinated ligand, however, has not been determined.

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Table I. Wavelengths and Molar Absorptivities for Hexaaquachromium(III) and Chromium(III)–Nicotinate Species in Aqueous Solution

species	λ/nm	a/L mol^{-1} cm^{-1}
$Cr(OH_2)_6^{3+}$ [a]	570	13.6
	405	15.8
	269	5.4
$Cr(OH_2)_5nic^{2+}$ [a]	566	24.8
	407	24.2
$Cr(OH_2)_4(nic)_2^{+}$ [a]	570	38.8
	406	34.5
$Cr(OH_2)_3(nic)_3$ [b]	555	42.4
	407	37.1
$Cr(OH_2)_4(OH)nic^{+}$ [b]	570	31.5
	410	30.3
trans-H[Cr(mal)$_2$(nic-N)$_2$]·1.5H$_2$O [c]	536	33.8
	382	34.0

[a] Species for which values were measured. [b] Species for which values were calculated or extrapolated. [c] Reference 12.

characterized in the solid state by a crystal structure of the compound $Na[Cr_3O(nicH)_6(OH_2)_3][ClO_4]_8$·Hnic·6$H_2O$ reported by Gonzalez-Vergara et al.[6] A drawing showing the similarity between the proposed structure of the dimer characterized in solution and the observed structure of the trinuclear complex is shown in Figure 3.

A solution with the composition [Cr(III)] = 0.0028 mol L^{-1}, [Hnic] + [nic$^-$] = 0.10 mol L^{-1}, and pH 4.5 through which carbon dioxide was bubbled became purple and developed a pale purple precipitate after 10 h. The solid was suction filtered, washed with dilute perchloric acid (0.010 mol L^{-1}) and water, and then dried in a vacuum desiccator overnight. A 30% yield based on chromium was obtained by using these preparative procedures. This material was analyzed for chromium by dissolving weighed portions in base followed by peroxide oxidation of chromium to chromate ion, the concentration of which was determined spectrophotometrically. The material was analyzed for nicotinate ion by treating a weighed portion with 6.4 M $HClO_4$ at 60 °C. After several hours, the solid dissolved completely, and the solution was blue. On the basis of kinetic data to be presented, this solution contains 1:1 complex not yet aquated, plus protonated nicotinic acid that was freed from the complex in the partial aquation. Light absorption of this solution showed that the ratio of total nicotinate ion (bound plus unbound) to chromium(III) was (2.9 ± 0.2):1.

Spectra of Chromium(III)–Nicotinate Species

Visible spectra of the aqueous chromium(III) nicotinate species were determined. Positions of absorption maxima and the corresponding molar absorptivities are given in Table I. The spectrum of $Cr(OH_2)_5nic^{2+}$ was measured at pH ~2.0; the elutability of the cationic species suggests the net charge shown above, which indicates nicotinate anion and coordinated water make up the coordination shell of chromium. The nicotinate ligand is judged to be oxygen bonded in all of these species on the basis of elutability. It is unlikely that the carboxylate in a nitrogen-bonded complex would remain deprotonated at the pH of the eluting agent (2.0). This observation indicates that the ligand is bonded through the oxygen of the carboxylate.

The amorphous solid having 3:1 nic:Cr(III) was characterized by infrared, theremogravimetric, and mass spectral analysis. The infrared stretching frequencies associated with the carboxylate portion of the ligand were observed at 1595 cm^{-1} ($\nu_{C=O}$) and 1360 cm^{-1} (ν_{C-O}). These values are typical for a monodentate carboxylate complex.[20] Water stretches at 820 and 590 cm^{-1} are also observed, indicating that water molecules occupy the remaining coordination sites. These frequencies are higher than those for hexaaquachromium(III) ion (800 and 541 cm^{-1}) possibly due to hydrogen bonding between the ligands and adjacent waters. A blue solid with composition $Cr(OH_2)_3(OH)(nic)_2$ has been reported by Cooper et al.[10] This substance was produced from solutions at higher pH (6.0 vs. 4.5) than those producing the tris(nicotinate) complex. Qualitatively, the infrared spectra of the compound reported by Cooper et al. and the amorphous solid characterized here are very similar. The mass spectrum of the material contained an intense peak at m/e 106. A single charged ion with composition $Cr(OH_2)_3^+$ could be responsible for the observed peak. The evidence that three water molecules are in the first coordination sphere supports the conclusion that the ligand is monodentate. No parent peak was observed; the largest mass peak was at m/e 427 (this corresponds to the composition $(H_2O)_3Cr(OCC_5H_4NH)_3^+$). This mass is greater than that corresponding to the compound prepared by Cooper et al. After a sample of the complex was heated to 500 °C for 3 min under an inert atmosphere, the mass remaining was 22% that of the original mass, consistent with a residue of $Cr(OH)_3$ or Cr_2O_3 with some carbonaceous ash.

Equilibria Involving Chromium(III)–Nicotinate Species

A detailed study of the spectrum of the 1:1 complex as a function of pH in the range 2.77–4.10 revealed small changes that can be attributed to acid dissociation of coordinated water in this species. Five solutions buffered with formic acid–formate ion with I = 1.00 mol L^{-1} (pH 2.77, 3.20, 3.50, 3.80, and 4.10) were measured at 20 wavelengths in the range 630–400 nm. The concentration of formic acid plus formate ion was constant at 0.10 mol L^{-1}. These spectra were analyzed by standard procedures;[21] plots of a vs. $(a - a_{12}) \times 10^{-pH}$ were approximately linear (a = log (I_0/I)/[Cr(III)](cell length) and a_{12} = molar absorptivity of the 1:1 complex of charge 2+). Experimental error and the small spectral changes (10–20%) make the derived acid dissociation constant (the reciprocal of the negative of the slope of these plots) uncertain. The value $K_a = 7 \times 10^{-4}$ mol L^{-1}, judged to have an uncertainty of $\pm 3 \times 10^{-4}$ mol L^{-1}, correlated all of the data. (At this ionic strength, the pK_a of the hexaaquachromium(III) ion is 4.6 ± 0.3.[22]) Thus at the lowest acidity studied, the deprotonation of coordinated water on the 1:1 complex has occurred to an extent of ~90%. The intercept in this plot is the molar absorptivity for the hydroxo species $Cr(OH_2)_4(OH)nic^+$; maxima occur at the same positions as for the conjugate acid, 410 and 570 nm, but values of a are 30.3 and 31.5 L mol^{-1} cm^{-1}, respectively. The spectral characteristics reported by Cooper et al.[10] of $Cr(OH_2)_5nic^{2+}$ based upon measurements at pH 7 must therefore be those of $Cr(OH_2)_4(OH)nic^+$.

The presence of formate ion in the solutions used in this equilibrium study could give rise to the formation of a formate complex. Upon reacidification of the solutions with perchloric acid after the spectra were recorded, the original spectrum characteristic of the mono(nicotinate) complex was observed. Since the nicotinate ion does not appear to have a labilizing effect on chromium(III), it is unlikely that a formate complex thus formed could be rapidly decomposed, regenerating the initial species.

The pK_a of the mono(nicotinato)chromium(III) complex determined from these spectral measurements is surprisingly low, 3.2 ± 0.8. One might expect the coordination of the anion to lower the acid strength of the coordinated water molecules (as in the case of $Cr(OH_2)_5Cl^{2+}$ [23] and $Cr(OH_2)_4O_2CCO_2^+$ [24]). Deutsch and Taube[25] have determined the analogous acid dissociation constant for (acetato)pentaaquachromium(III) ion as a function of temperature. In the acetate system, there is evidence that at lower temperature the acidity of the complex may be greater than the acidity of the hexaaquachromium(III) ion. Additional studies may be required to elucidate the effect of coordinated carboxylate upon the acid strength of the aquachromium(III) moiety.

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Table II. Amounts of Relevant Chromium Species Recovered from Equilibrated Solutions by the Ion-Exchange Procedure

species compn	high-[Cr] reacn[a]/mol	low-[Cr] reacn[b]/mol
ML_2	6.63×10^{-5}	2.74×10^{-5}
ML	2.42×10^{-4}	1.21×10^{-4}
M	5.19×10^{-5}	3.85×10^{-5}

[a] Composition: Cr(III), 0.502 mmol; C^0_{Hnic} = 0.100 mol L^{-1}; volume, 0.201 L; pH 4.80. [b] Composition: Cr(III), 0.502 mmol; C^0_{Hnic} = 0.100 mol L^{-1}, volume, 4.0 L; pH 4.80.

Table III. Equilibrium Concentrations of Relevant Chromium Species Used in Equilibrium Constant Calculation

species	high-[Cr] reacn/mol L^{-1}	low-[Cr] reacn/mol L^{-1}
$Cr(OH_2)_6^{3+}$	7.4×10^{-5} [a]	2.7×10^{-6} [a]
nic^-	5.4×10^{-2} [b]	5.4×10^{-2} [b]
$Cr(OH_2)_5nic^{2+}$	2.7×10^{-5} [c]	6.7×10^{-7} [c]
K_f, L mol^{-1}	6.7	4.6

[a] Based on K_{a1}(hexaaquachromium(III)) = 4.0×10^{-5} mol L^{-1}. [b] Based on K_{a2}(nicotinic acid) = 1.9×10^{-5} mol L^{-1}. [c] Based on K_a-($Cr(OH_2)_5nic^{2+}$) = 7×10^{-4} mol L^{-1}.

The formation constant for (nicotinato)pentaaquachromium(III) was determined by separating the various (nicotinato)chromium(III) complexes present in equilibrated reaction mixtures by ion exchange and measuring their concentrations. This technique has been used successfully on similar systems.[13,14] There is complexity in the present system due to the presence of differently protonated forms of the reactants and products at the hydrogen ion concentration of the equilibrated mixtures. Two reaction mixtures with the same amount of chromium(III) (0.502 mmol), the same pH (4.80), and the same ligand concentration, ([Hnic] + [nic^-] = 0.100 mol L^{-1}) were brought to equilibrium in total volumes that varied by a factor of 20 (0.201 and 4.0 L). The ionic strength of the solutions was approximately constant at 0.06 mol L^{-1}. Tables II and III contain the amount of each species recovered from the ion-exchange separations and the calculated equilibrium concentrations of each species, respectively. With a K_a value of hexaaquachromium(III) at this ionic strength of $(4.0 \pm 0.3) \times 10^{-5}$ mol L^{-1},[22] the K_{a2} value of nicotinic acid given earlier, and the K_a of the mono complex determined above, the K_f for the reaction

$$Cr(OH_2)_6^{3+} + nic^- \overset{K_f}{\rightleftharpoons} Cr(OH_2)_5nic^{2+} + H_2O$$

is calculated to be 5.6 ± 1.1 L mol^{-1}. This value is about 1 order of magnitude smaller than that reported for acetate complexation ($K_f \approx 60$ L mol^{-1}).[26]

Kinetic Studies

The aquation reactions of (nicotinato)chromium(III) species occur at measurable rates. (Nicotinato)chromium(III) complexes for study in kinetic experiments were separated from the medium in which they were prepared by ion-exchange procedures. The source of tris(nicotinato)chromium(III) was the amorphous solid in which this is the predominant species.

The rate of aquation of (nicotinato)pentaaquachromium(III) ion in perchloric acid–lithium perchlorate solutions with various concentrations of hydrogen ion at I = 3.00 mol L^{-1} was determined at 25.0 and 60.0 °C. The light absorption at 570.0 nm changes enough with aquation to allow use of this property in following the reaction. Plots of log $(A_t - A_\infty)$ vs. time for experiments at 25.0 °C were linear over the entire course of the reaction studies (≥85%). At the acidities studied, the aquation goes to completion, and the known light absorption of hexaaquachromium(III) ion was used as A_∞, the infinite-time value. Experimentally determined values of the first-order rate constant at 25.0 °C as a function of the concentration of hydrogen ion (given as $[H^+]$/mol L^{-1}, k/s^{-1}) are as follows: 0.0502, 2.28×10^{-7}; 0.102, 2.38×10^{-7}; 0.201, 2.43×10^{-7}, 2.00, 3.12×10^{-7}; 2.46, 3.38×10^{-7}. These data may be fit to the equation

$$k_{apparent} = k_0 + k_1[H^+]$$

with values of $k_0 = 2.3 \times 10^{-7}$ s^{-1} and $k_1 = 4.2 \times 10^{-8}$ L mol^{-1} s^{-1}, respectively. A comparison of k for the acid-independent and acid-dependent pathways of this and similar systems is presented in Table IV. Of the complexes presented, only the nicotinato complex has $k_0/s^{-1} > k_1/L\ mol^{-1}\ s^{-1}$. The carboxylate-bonded nicotinate ligand may be protonated either at the nonbonded carboxylate oxygen or at the aromatic nitrogen. If protonation occurs at the nitrogen, away from the site of coordination, it may not facilitate aquation to the extent observed in the azido,[27] fluoro,[28] and acetato[25] systems.

Kinetic experiments at 60 °C were less simple; although plots of ln $(A_t - A_H)$, where A_H is the known light absorption of hexaaquachromium(III) ion, vs. time were nicely linear over 5.0 half-times, at $t \geq 65$ h light absorption started to increase. For this reason the rate constant for aquation of (nicotinato)chromium(III) at 60 °C was determined from observations over ≤3.0 half-times. The values so obtained (given as $[H^+]$/mol L^{-1}, k/s^{-1}) are as follows: 0.501, 1.5×10^{-5} (average of two values at same acidity); 1.72, 1.8×10^{-5}; 2.46, 2.3×10^{-5}. These data are also correlated with the equation used for the 25 °C data ($k_0 = (1.3 \pm 0.1) \times 10^{-5}$ s^{-1} and $k_1 = (4.0 \pm 0.8) \times 10^{-6}$ L mol^{-1} s^{-1}).

As in aquation of the (nicotinato)pentaaquachromium(III) ion, aquation of tris and bis species is accompanied by appreciable change in light absorption at 570 nm. The low rate of aquation of the mono(nicotinato)chromium(III) ion allowed the sequential aquation of tris and bis species to be followed to formation of the mono complex. There was curvature in plots of ln $(A_t - A_{12})$ vs. time, where A_{12} represents the absorbance of the mono(nicotinato) species, but they were approximately linear at longer times. In an experiment at 26.5 °C with $[H^+]$ = 1.0 mol L^{-1}, $[Li^+]$ = 2.0 mol L^{-1}, and $[ClO_4^-]$ = 3.0 mol L^{-1}, 7 data points taken at times between 992 and 4040 min fall nicely on a straight line corresponding to a first-order rate constant of 3.4×10^{-6} s^{-1} (a data point at 4950 min, the last measurement made, falls above the straight line). This straight line was extended to zero time to allow construction of a plot of the logarithm of the absorbance in excess of extrapolated value vs. time. This plot consisting of 17 data points between time 0 and 444 min was approximately linear with a slope corresponding to a first-order rate constant of 1.4×10^{-4} s^{-1}. To refine these values, all of the data (25 points) were fit by a nonlinear least-squares program to the appropriate equation having values of two rate constants and the molar absorptivities of the initial reactant (the tris species) and the intermediate species as adjustable constants. This treatment yielded the rate constants 1.44×10^{-4} and 3.45×10^{-6} s^{-1} and the molar absorptivities a_3 = 42.4 L mol^{-1} cm^{-1} and a_2 = 38.8 L mol^{-1} cm^{-1} (where k_{32} indicates the decomposition from tris to bis, etc.; at this wavelength, a_1 = 24.7 L mol^{-1} cm^{-1}). These data are interpreted in terms of

Table IV. Rate Coefficients of Rate Laws for Aquation of Chromium(III) Complexes Containing Anions of Weak Acids[a]

$$-d[Cr(OH_2)_5L^{2+}]/dt = k_0 + k_1[H^+]$$

L^-	I/mol L^{-1}	k_0/s^{-1}	k_1/L mol^{-1} s^{-1}	(k_0/k_1)/mol L^{-1}	ref
N_3^-	1.0	1.15×10^{-7}	1.53×10^{-6}	7.5×10^{-2}	27
F^-	1.0	6.22×10^{-10}	1.36×10^{-8}	4.6×10^{-2}	28
$CH_3CO_2^-$	4.0	7.4×10^{-7}	9.5×10^{-5}	7.8×10^{-3}	25
$C_5H_4NCO_2^-$	3.0	2.3×10^{-7}	4.2×10^{-8}	5.5	this work

[a] All reaction temperatures were 25 °C except for N_3^-, which was 30 °C.

the sequence (with charges omitted)

$$Cr(OH_2)_3(nic)_3 \xrightarrow{k_{32}} Cr(OH_2)_4(nic)_2 \xrightarrow{k_{21}} Cr(OH_2)_5nic$$

with $k_{32} = 1.44 \times 10^{-4}$ s^{-1} and $k_{21} = 3.45 \times 10^{-6}$ s^{-1}. (An alternate interpretation[29] in which $k_{21} > k_{32}$ does not seem reasonable.) With these values for the two rate constants, the maximum relative concentration of bis species, which occurs at ~440 min, is ~0.91.[30]

The rate of aquation of the dimer $Cr_2(nic)OH^{4+}$ in perchloric acid was determined at 60.0 °C in an experiment with [Cr(III)] = 1.54×10^{-3} mol L^{-1} and [H$^+$] = 0.05 mol L^{-1}. Observations were made at $t = 0$ and from t values from 23 h to 11 days; during this time, the species is aquated completely to hexaaquachromium(III) ion with a decrease in light absorption at 570 nm of ~18%. For comparison a solution of hydrolytic dimer with charge 4+, described by Thompson et al.,[19] was treated similarly. Plots of log $(A_t - A_\infty)$ vs. time for both species were approximately linear over the course of the study (87% completion), suggesting that one of the steps in the aquation mechanism is slower than the others. From these data the empirical rate constants for aquation of the nicotinato dimer and hydrolytic dimer are 2.7×10^{-6} and 6×10^{-5} s^{-1}, respectively.

Thus, the empirical rate constant for aquation of $Cr_2(nic)OH^{4+}$ is appreciably smaller than that for the production of $Cr(OH_2)_6^{3+}$ either from $Cr(nic)^{2+}$ or from the hydrolytic dimer. For $Cr_2(nic)OH^{4+}$ with the structure already proposed, it is reasonable to assume that breaking of the hydroxo bridge occurs rapidly on the time scale for breaking the nicotinate bridge. (The rate constant for the conversion of hydrolytic dimer to aquachromium(III) ion is approximately 20-fold greater than that for aquation of $Cr_2(nic)OH^{4+}$.) Thus, the spectral changes occurring during the observation period are due to the reactions

$$Cr_2(OH_2)_{10}nic^{5+} + H_2O \xrightarrow{k_1} Cr(OH_2)_6^{3+} + Cr(OH_2)_5nic^{2+}$$

$$Cr(OH_2)_5nic^{2+} + H_3O^+ \xrightarrow{k_2} Cr(OH_2)_6^{3+} + Hnic$$

The independently determined values of k_2 for this temperature can be extrapolated at this acidity; k_2([H$^+$] = 0.050 mol L^{-1}, 60 °C) = 1.3×10^{-5} s^{-1}. If this value is used, the value of k_1 can be derived from the spectral data. In this data treatment, the value of the absorbance due to $Cr(OH_2)_5nic^{2+}$, the reactant in this k_2 step, must be assumed. Rather than use the value determined under different conditions, we assumed various values between the initial value and that due to hexaaquachromium(III). It was found that the value of k_2 was not particularly sensitive to the assumed value for this parameter. The derived value of k_2 changes by ~6% if the assumed value for the light absorption due to $Cr(OH_2)_5nic^{2+}$ is changed by ~5%. (As already mentioned, the total change of light absorption was only ~18%.) For the assumption that light absorption due to equal amounts of $Cr(OH_2)_5nic^{2+}$ and $Cr(OH_2)_6^{3+}$ was midway between that for no aquation ($Cr_2(OH_2)_{10}nic^{5+}$) and 100% aquation ($Cr(OH_2)_6^{3+}$), the derived value of k_1 is 2.8×10^{-6} s^{-1}. (With $k_1 = 2.8 \times 10^{-6}$ s^{-1} and $k_2 = 1.3 \times 10^{-5}$ s^{-1}, one can calculate that during the aquation the maximum relative concentration of $Cr(OH_2)_5nic^{2+}$ is only 7%. Thus, it is reasonable that the value of k_1 derived by considering the sequence of two reactions is very close to that obtained simply as $k = -\Delta[\ln (A - A_\infty)]/\Delta t$.)

Conclusion

It is clear from this work that there are several inert oxygen-bonded (nicotinato)chromium(III) species. The ion-exchange procedures employed in the present study provide the basis for the preparation of solutions of relatively pure species. The role of each of these in glucose tolerance can be tested.

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Biological Analogues. Synthetic Iron(III)-Specific Chelators Based on the Natural Siderophores

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Two synthetic analogues of the the naturally occurring iron(III)-specific siderophores, one with catechol groups and the other with hydroxamic acid groups, have been prepared. Both are sexidentate chelates consisting of three catechol and three hydroxamic acid groups attached to a triamine "platform" via amide linkages. Both ligands are specific for iron(III) and form very stable iron(III) complexes; the stability constant for the iron(III) tris(hydroxamate) complex was determined to be about 28.

Hemochromatosis[1,2] refers to a group of disorders that result from a progressive increase in deposition of iron in the parenchymal and reticuloendothelial cells of the liver, pancreas, heart, and pituitary and that lead, successively, to tissue damage, functional insufficiency of the organs, and eventually death. Idiopathic hemochromatosis is an inherited autosomal recessive trait that manifests itself after the breakdown of the regulatory mechanism for iron absorption. The gene frequency for certain ethnic groups can be high, possibly of the order of 1 in 40 of the population, but the inherent propensity for the disorder appears to be triggered by environmental factors.[3] There are epidemiological associations with alcoholism, and excessive iron intake over a long time, particularly in combination with alcohol (viz. Bantu siderosis).[4] The life expectancy of untreated patients is about 4 years after the disease has become clinically manifest. Idiopathic hemochromatosis is now treated by phlebotomy in combination with chelation therapy.

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