2252 *J. Chem. Eng. Data* **2010,** *55,* 2252–2256

Study of the Interaction between Chromium(III) and Hydroxamic Acids

Mehmet Suat Aksoy*

Department of Chemistry, Faculty of Arts and Science, Uludağ University, 16059-Bursa, Turkey

---

The complexes of the chromium(III) ion formed by acetohydroxamic acid (Aha, HL) and benzohydroxamic acid (Bha, HL) were investigated by means of potentiometry and spectroscopy, at (25.0 ± 0.1) °C and an ionic strength of 0.1 M KNO_3 and 0.1 M KCl, respectively. Over the acidic pH range, the coordination of the Cr(III) ion to acetohydroxamic acid and benzohydroxamic acid occurs in a 1:1 mole ratio, and the CrL^{2+} type complex is formed. At near neutral pH, the $CrL(OH)^+$ type hydroxo complex is formed. The acid dissociation constants of the ligands and the formation constants of the chromium(III) complexes were determined in 0.1 M KNO_3 ionic medium by potentiometric titration using the BEST computer program. In terms of the ligands, the stability of the complexes ranks in an order such as acetohydroxamic acid > benzohydroxamic acid. The stabilities of hydroxamic acid complexes for V(IV), Cr(III), and Fe(III) ions that have similar ionic radii increase in the order CrL < VOL < FeL.

Introduction

Chromium(III) is one of the most stable, general, and biologically important oxidation states of chromium with a d^3 configuration. The radius of Cr(III) is 0.76 Å for coordination number 6, and it acts as a hard acid in aqueous solution.[1,2] There is no evidence for any toxic effects of Cr(III), which is an essential trace element in mammals (required daily intake (50 to 200) μg), and it was shown that Cr(III) is required for proper carbohydrate and lipid metabolism in mammals.[1,3−6]

Hydroxamic acids (RC(=O)N(OH)R′) are naturally occurring compounds of great biological importance. Hydroxamic acids form stable, five-membered [O,O] chelates with many metal ions. On the basis of this interaction, numerous microorganisms developed hydroxamate type metal sequestering siderophores for the uptake, storage, and transport of metal ions with biological relevance.[7−9]

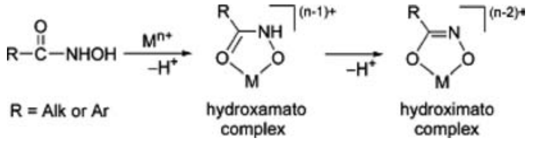
Metal binding to hydroxamic acids (1:1) usually occurs in a bidentate fashion (Scheme 1) with the formation of singly or doubly deprotonated (hydroxamato or hydroximato) ligands.[10] Complexes of hydroxamic acids and derivatives with many transition metals have been reported in the literature,[7−21] but information about the interactions of chromium(III) and hydroxamic acids is restricted.

We continue our studies on the complex equilibria between Cr(III) with acetohydroxamic acid (Aha) and benzohydroxamic acid (Bha). The structural formulas of the studied ligands are shown in Figure 1. Currently, our main aim is to investigate the binding abilities of Aha and Bha to Cr(III) and to determine the formation constants of their complexes.

In previous studies, we demonstrated the coordination of Cr(III) to salicylic acid and its derivatives and to hydroxynaphthoic acids, and we also described the stabilities of various complex species of Cr(III).[22−26]

The stoichiometric protonation constants of these two ligands and the stoichiometric stability constants of Cr(III)−hydroxamic acid complexes were calculated.

Scheme 1. Common Modes of Binding of Hydroxamic Acids to Transition Metal Ions (M^{n+})



Experimental Section

Chemicals and Solutions. Aha (Fluka) and Bha (Merck) were of analytical reagent grade; the other chemicals were from Merck and were used as received. The purities of the ligands were further checked by the Gran method.[27] The stock solution of Cr(III) was prepared for potentiometric measurement by dissolving the proper amounts of $Cr(NO_3)_3 \cdot 9H_2O$ (98 %, Merck) in a small excess of 0.1 M HNO_3 (100 % purity, $d = 1.52$) to prevent hydrolysis as described previously.[22] The concentration of free acid in the Cr(III) solution was systematically checked by potentiometric titrations before each series of experiments. Sodium hydroxide solution (0.1 M) was prepared as a carbonate-free solution by dissolving in doubly distilled water and was standardized against potassium hydrogen phthalate. The stock solution of chromium(III) nitrate was standardized complexometrically by EDTA titration using a suitable indicator.[28] The supporting electrolyte was 0.1 M KNO_3 in potentiometric studies. For spectroscopic measurements, $CrCl_3 \cdot 6H_2O$ was dissolved in 0.1 M HCl, and the ionic strength was adjusted to

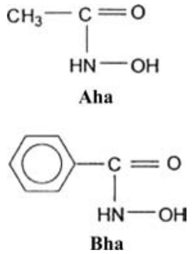


Figure 1. Structural formulas of the ligands studied.

---

* Corresponding author. Phone: 0224 2941740. Fax: 0224 4428136. E-mail: msaksoy@uludag.edu.tr.

10.1021/je900780n

Table 1. Equilibrium Constants of Proton Complexes (log K) and Formation Constants (log β) of Cr(III): Aha and Bha Complexes at (25 ± 0.1) °C and 0.1 M KNO_3

row	equilibrium	Aha	Bha
row	proton compexes	log K	log K
1	$L^- + H^+ \rightleftharpoons HL$	9.33 ± 0.01[33] 9.29 ± 0.06[a]	8.10 ± 0.05[33] 8.07 ± 0.06[a]
row	Cr(III) complexes	log β	log β
2	$Cr^{3+} + L^- \rightleftharpoons CrL^{2+}$	7.99 ± 0.04[a]	7.30 ± 0.04[a]
3	$CrL^{2+} + OH^- \rightleftharpoons CrL(OH)^+$	4.68 ± 0.07[a]	5.10 ± 0.07[a]

[a] This work.

0.1 M by KCl. The Cr(III) complexes were formed at (70 to 75) °C, and then the potentiometric titration and spectrophotometric measurements were carried out (1 to 2) h later.

Potentiometric Measurements. Potentiometric measurements were made using an automatic titration apparatus (Schott, Hofheim, Germany) equipped with a water-jacketed vessel and a combined pH electrode. Before each experiment, the potentiometric cell was standardized in acetic acid buffer (Merck) and dilute hydrochloric acid (Merck) for the measurement of hydrogen ion concentration rather than its activity according to Irving et al.[29] In the calibration step of the pH meter, the pH reproducibility is < 0.005 units in the acidic pH region and < 0.015 units in the basic pH region. The autoprotolysis constant, K_w, was determined from dilute HCl solution titrations in 0.1 M KNO_3, and the reproducible values were found to be 13.76. The formation constants of the proton and Cr(III) complexes of Aha and Bha were determined by potentiometric titration of 50 cm^3 samples at (25.0 ± 0.1) °C. The titrations were performed within the limits $3 \leq pH \leq 10$ under a purified nitrogen (99.99 %, Bos, Turkey) atmosphere to prevent oxidation of the ligands. At least (10 ± 1) min passed between each pH reading to reach thermodynamic equilibrium in the acidic solution. However, to prevent the partial oxidations of these ligands, "quasi-equilibrium" titrations were performed in the basic pH region with the waiting time to record the pH readings never being more than 15 min. At least four different potentiometric titrations were performed for each ligand studied: the first one was carried out with the ligand alone, and the others were for the Cr(III)−HL systems in which the Cr(III) concentrations were in the $(2.24 \text{ to } 4.48) \cdot 10^{-3}$ M range and molar ratios of Cr(III) to ligand were 1:1 and 1:2.

Spectroscopic Measurements. The absorption spectra of the ligands alone and the Cr(III)−HL systems in different mole ratios were taken at defined pH values and wavelength ranges on a Shimadzu GDU-20C Spectrophotometer (Kyoto, Japan). To define the stoichiometries of the complex species, Job's method of Continuous Variation[30] was applied. The solutions were allowed to equilibriate overnight under a nitrogen atmosphere at (25.0 ± 0.1) °C.

Data Treatment. The results of potentiometric titrations were evaluated using the computer program BEST, which computes and refines the equilibrium constants of H^+ and Cr(III) complexes of these two ligands and provides the standard deviation of the fit (σ_{fit}) between the observed and calculated pH values obtained by potentiometric titration.[31] The mathematical analysis of the data comprising at least four titrations was performed, and the averages of protonation and formation constants obtained from the BEST program are tabulated in Table 1.

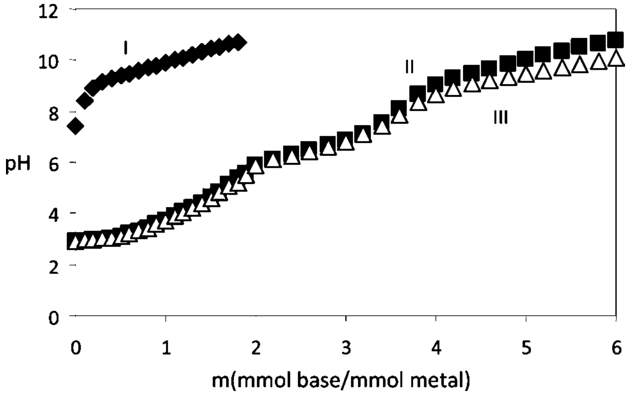


Figure 2. Potentiometric titration curves of Cr(III) complexes of Aha in $0.1\ mol \cdot L^{-1}\ KNO_3$ at 25 °C. I: Aha alone ($T_L = 2.24 \cdot 10^{-3}\ mol \cdot L^{-1}$). II: (1:1) molar ratio of Cr(III) to Aha ($T_{Cr} = T_L = 2.24 \cdot 10^{-3}\ mol \cdot L^{-1}$). III: (1:2) molar ratio of Cr(III) to Aha ($T_{Cr} = 2.24 \cdot 10^{-3}\ mol \cdot L^{-1}$, $T_L = 4.48 \cdot 10^{-3}\ mol \cdot L^{-1}$).

Results and Discussion

Aha Complexes. The potentiometric titration curves of a 1:1 mole ratio of Cr(III)−Aha exhibit an inflection point at m (mmol base/mmol metal) = 2.0 and $m = 4.0$ (Figure 2, curve II). The formation of a CrL^{2+} type complex of Cr(III) with Aha, in the $m = 0.0$ to 2.0 range, may be inferred from the drops in the buffer regions of the titration curves and from the inflection point at $m = 2.0$. Further, the extended hydrolysis of the CrL^{2+} complex between $m = 2.0$ and 4.0 may be proposed from the inflection point at $m = 4.0$. Moreover, continued drops on pH readings after $m = 2.0$ suggest that hydrolysis of a CrL^{2+} type complex is initiated in the system.

The potentiometric titration curves of Cr(III)−Aha in 1:2 mole ratio show, first, inflection points at $m = 2.0$ and, second, inflection at $m = 4.0$ (Figure 2, curves III). As a result, the formation of the CrL^{2+} type complex for different mole ratios was taken into account (Table 1). In all of these titrations, the process of equilibration was slow after the addition of 2 equiv of OH^- per mole of Cr(III), and drifting of pH occurred in the pH = 6.0 to 8.0 range. The occurrence of the $[CrL(OH)]^+$ complex was assumed.

The occurrence of the CrL^{2+} complex was verified by introducing 216 pH values into the BEST computer program, and its formation constant was determined (Table 1).

The existence of the $[CrL(OH)]^+$ complex was considered, and its formation constant was found by introducing 148 pH values measured in all mole ratios (Table 1).

By means of the distribution diagram, the speciation of the major species in the defined pH ranges was obtained. The major species are Cr(III), CrL^{2+}, and $[CrL(OH)]^+$ (Figure 3).

To validate the existence of the CrL^{2+} complex, the stoichiometry of the formed complex was investigated spectroscopically. Solutions of Aha alone, 1:1, and 1:2 mol ratios of Cr(III) and Aha were prepared at pH = 4.5 in a 0.1 M KCl ionic medium since it was noticed that the CrL^{2+} complex ion exists in the pH = 4.0 to 6.0 range; therefore, the spectrum of each Cr(III)−Aha system exhibits the coordination of oxygen atoms as evidenced by charge transfer between these donors and Cr(III) (Figure 4). The conformities of this Cr(III)−Aha system to Beer's law were checked within the chosen concentration range. Job's diagrams were drawn at $\lambda = 240$ nm regardless of their mole ratios for the solution of the Cr(III)−Aha system in which the mole fractions (x_M) of Cr(III) were in the $x_M = (0.00$ to

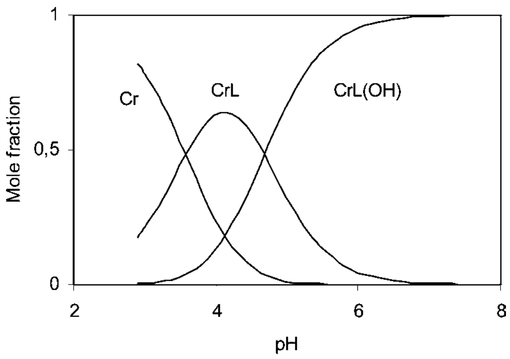


Figure 3. Species distribution curves of the Aha system and Cr(III) ion as a function of $-\log [H^+]$, for a solution initially containing $2.24 \cdot 10^{-3}$ $mol \cdot L^{-1}$ Aha and $2.24 \cdot 10^{-3}$ $mol \cdot L^{-1}$ Cr(III) ion.

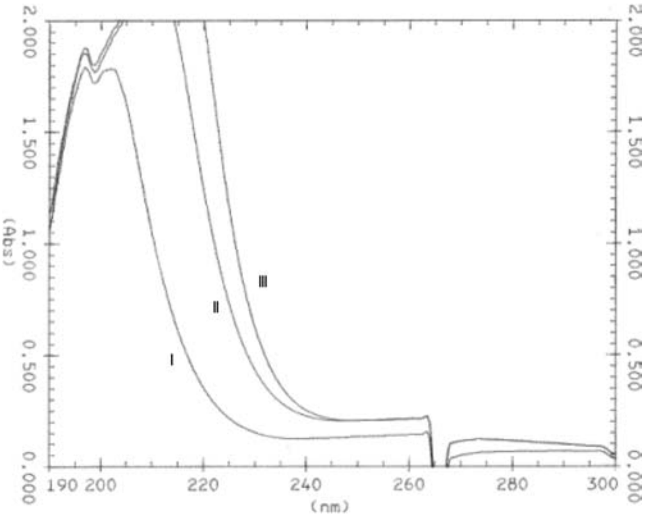


Figure 4. Absorption spectra of Cr(III) complexes of Aha in 0.1 $mol \cdot L^{-1}$ KCl at 25 °C (pH = 4.0). I: Aha alone ($T_L = 1 \cdot 10^{-4}$ $mol \cdot L^{-1}$; $x_M = 0.0$). II: (1:1) Cr(III):Aha ($T_{Cr} = T_L = 1 \cdot 10^{-4}$ $mol \cdot L^{-1}$; $x_M = 0.5$). III: (1:2) Cr(III):Aha ($T_{Cr} = 1 \cdot 10^{-4}$ $mol \cdot L^{-1}$, $T_L = 2 \cdot 10^{-4}$ $mol \cdot L^{-1}$; $x_M = 0.33$).

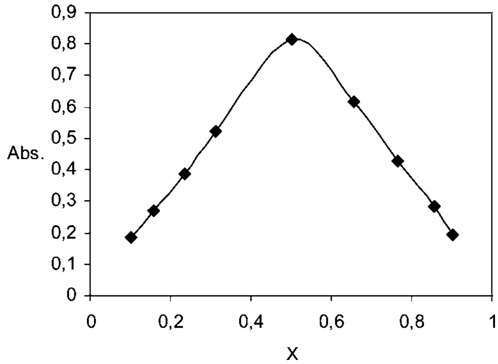


Figure 5. Job's plot for Cr(III)−Aha complexes at $\lambda = 240$ nm and at pH = 4.0.

1.00) range (Figure 5). In a Job's plot, the stoichiometries of the formed complex ion at pH = 4.5 correspond to $x_M = 0.5$, indicating a 1:1 molar ratio of Cr(III) to Aha.

Bha Complexes. In the potentiometric titrations of the Cr(III)−Bha system for a 1:1 mole ratio, inflections were found at $m = 2.0$ and around $m = 4.0$ (Figure 6, curve II). Drift in pH readings occurred at around $m = 2.0$. The stability constants of CrL^{2+} and $CrL(OH)^+$ complexes were determined (Table 1).

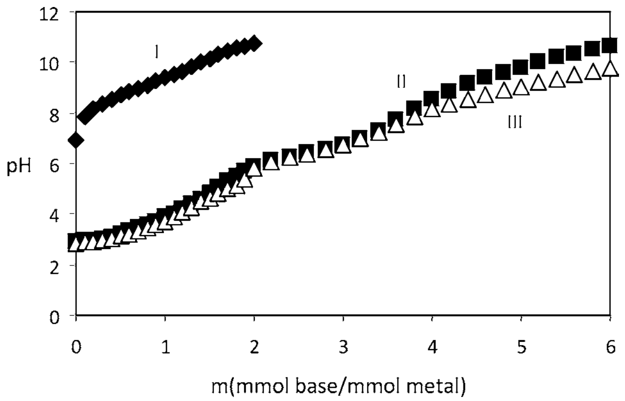


Figure 6. Potentiometric titration curves of Cr(III) complexes of Bha in 0.1 $mol \cdot L^{-1}$ KNO_3 at 25 °C. I: Bha alone ($T_L = 2.24 \cdot 10^{-3}$ $mol \cdot L^{-1}$). II: (1:1) molar ratio of Cr(III) to Bha ($T_{Cr} = T_L = 2.24 \cdot 10^{-3}$ $mol \cdot L^{-1}$). III: (1:2) molar ratio of Cr(III) to Bha ($T_{Cr} = 2.24 \cdot 10^{-3}$ $mol \cdot L^{-1}$, $T_L = 4.48 \cdot 10^{-3}$ $mol \cdot L^{-1}$).

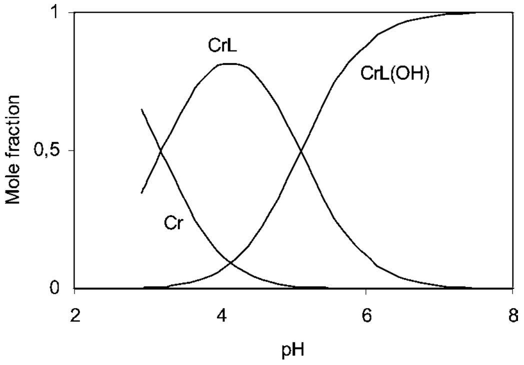


Figure 7. Species distribution curves of the Bha system and Cr(III) ion as a function of $-\log[H^+]$, for a solution initially containing $2.24 \cdot 10^{-3}$ $mol \cdot L^{-1}$ Bha and $2.24 \cdot 10^{-3}$ $mol \cdot L^{-1}$ Cr(III) ion.

The potentiometric titration curves of Cr(III)−Bha in a 1:2 ratio show a first inflection point at $m = 2.0$ and a second inflection at $m = 4.0$ (Figure 6, curves III).

By means of the distribution diagram, the speciation of the major species in the defined pH range was defined. The major species are Cr(III), CrL^{2+}, and $[CrL(OH)]^+$ (Figure 7).

To validate the existence of a CrL^{2+} type complex, the stoichiometry of the formed complex was investigated spectroscopically (Figure 8). Job's diagrams were drawn at $\lambda = 310$ nm regardless of their mole ratios for the solution of the Cr(III)−Bha system in which the mole fractions (x_M) of Cr(III) were in the $x_M = (0.00$ to $1.00)$ range (Figure 9). In the Job's plot, the stoichiometries of the formed complex ion at pH = 4.5 correspond to $x_M = 0.5$, indicating a 1:1 molar ratio of Cr(III) to Bha.

Conclusion

Over the acidic pH range, the binding of these HL ligands to Cr(III) in a 1:1 mole ratio takes place, presumably via (O^-, O^-) sites, and ML^{2+} type complexes are formed.

At near neutral pH values, $CrL(OH)^+$ type hydroxo complexes are also formed by hydrolytic equilibria, and their formation constants were also calculated.

The stoichiometries of the formed complexes were defined from application of the spectroscopic continuous variation method; the occurrences of the CrL^{2+} type complexes were verified.

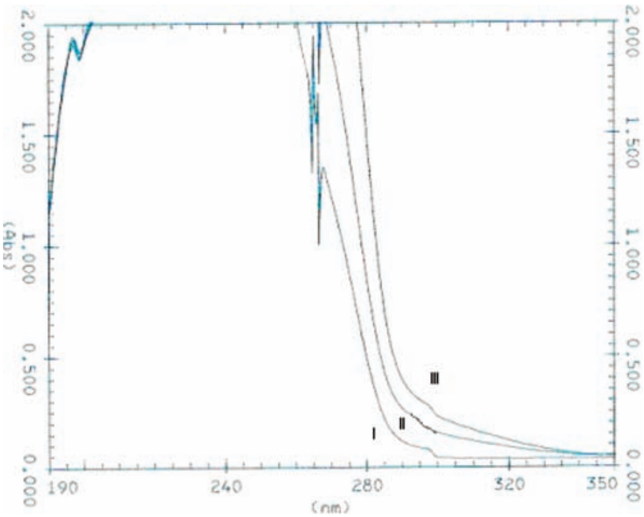


Figure 8. Absorption spectra of Cr(III) complexes of Bha in 0.1 mol·L^{-1} KCl at 25 °C (pH = 4.0). I: Bha alone ($T_L = 1 \cdot 10^{-4}$ mol·L^{-1}; $x_M = 0.0$). II: (1:1) Cr(III):Bha ($T_{Cr} = T_L = 1 \cdot 10^{-4}$ mol·L^{-1}; $x_M = 0.5$). III: (1:2) Cr(III):Bha ($T_{Cr} = 1 \cdot 10^{-4}$ mol·L^{-1}, $T_L = 2 \cdot 10^{-4}$ mol·L^{-1}; $x_M = 0.33$).

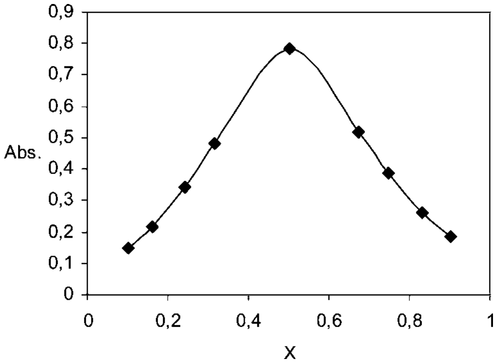


Figure 9. Job's plot for Cr(III)−Bha complexes at $\lambda = 310$ nm and at pH = 4.0.

Aha forms a more stable complex with the chromium(III) ion than Bha. This result is in agreement with the overall basicity of the ligands.

On the other hand, the behavior of the chromium(III) ion toward hydroxamic acids could also be compared with hydroxamic acid complexes of the oxovanadium(IV) and Fe(III) ions. V(III) is a d^2 ion; Cr(III) is a d^3 ion; and Fe(III) in high spin complexes is a d^5 ion. They have ionic radii of 0.78 Å, 0.76 Å, and 0.79 Å, respectively,[1] for a coordination number six. The VO^{2+} ion is formed by rapid oxidation of V(III) in air. These three transition metal ions form strong complexes with hydroxamic acids. The stabilities of complexes of HL type ligands with VO^{2+}, Cr(III), and Fe(III) aqua ions increase in the order CrL < VOL < FeL (VOL: $\beta_{Aha} = 8.69$, $\beta_{Bha} = 8.43$; FeL: $\beta_{Aha} = 11.35$, $\beta_{Bha} = 11.25$).[32]

Acknowledgment

The instruments used in this research were supplied by the Alexander Von Humbold Foundation, to whom the authors wish to express their sincere thanks.

Literature Cited

(1) Cotton, F. A.; Wilkinson, G.; Murillo, C. A.; Bochmann, M. *Advanced Inorganic Chemistry*, 6th ed.; John Wiley Interscience: New York, 1999.

(2) Drljaca, A.; Spiccia, L. Early stages of the hydrolysis of chromium(III) in aqueous solution. *Polyhedron* **1996**, *15*, 2875–2886.

(3) Stefanowicz, T.; Napieralska-Zagosda, S. Investigations of chromium(III) ion hydrolysis equilibrium as a function of time. *Pol. J. Chem.* **1992**, *66*, 835–845.

(4) Mertz, W.; Schwarz, K. Chromium(III) and the glucose tolerance factor. *Arch. Biochem. Biophys.* **1959**, *85*, 292–295.

(5) Galuszka, G.; Cieslak-Golonka, M.; Wojciechowska, A. Synthetic models for the glucose tolerance factor: the spectroscopic characterization and toxicity studies of monomeric and dimeric Cr(III) species. *Polyhedron* **1998**, *21*, 3785–3794.

(6) Vincent, J. B. The bioinorganic chemistry of chromium(III). *Polyhedron* **2001**, *20*, 1–26.

(7) Birus, M.; Budimir, A.; Gabricevic, M. Complexation of beryllium(II) with hydroxamic acids in aqueous medium; spectrophotometric determination of stability constants. *J. Inorg. Biochem.* **1999**, *75* (2), 85–91.

(8) Buglyo, P.; Potari, N. Study of the interaction between oxovanadium(IV) and hydroxamic acids. *Polyhedron* **2005**, *24* (7), 837–845.

(9) Khalil, M. M.; Fazary, A. E. Potentiometric studies on binary and ternary complexes of di- and trivalent metal ions involving some hydroxamic acids, amino acids, and nucleic acid components. *Monatsh. Chem.* **2004**, *135*, 1455–1474.

(10) Gez, S.; Luxenhofer, R.; Levina, A.; Codd, R.; Lay, P. A. Chromium(V) complexes of hydroxamic acids: formation, structures, and reactivities. *Inorg. Chem.* **2005**, *44*, 2934–2943.

(11) Miller, M. Syntheses and therapeutic potential of hydroxamic acid based siderophores and analogs. *Chem. Rev.* **1989**, *89*, 1563–1579.

(12) Muri, E. M. F.; Nieto, M. J.; Sindelar, R. D.; Williamson, J. S. Hydroxamic acids as pharmacological agents. *Curr. Med. Chem.* **2002**, *9*, 1631–1653.

(13) Kurzak, B.; Kozlowski, H.; Farkas, E. Hydroxamic and aminohydroxamic acids and their complexes with metal ions. *Coord. Chem. Rev.* **1992**, *114*, 169–200.

(14) Abu-Dari, K.; Ekstrand, J. D.; Freyberg, D. P.; Raymond, K. N. Coordination chemistry of microbial iron transport compounds. *Inorg. Chem.* **1979**, *18*, 108–112.

(15) Rudzka, K.; Arif, A. M.; Berreau, L. M. Chemistry of a Ni(II) acetohydroxamic acid complex: formation, reactivity with water, and attempted preparation of zinc and cobalt analogues. *Inorg. Chem.* **2005**, *44*, 7234–7242.

(16) Glorius, M.; Moll, H.; Geipel, G.; Bernhard, G. Complexation of uranium(VI) with aromatic acids such as hydroxamic and benzoic acid investigated by TRLFS. *J. Rad. Nucl. Chem.* **2008**, *277* (2), 371–377.

(17) Farkas, E.; Kozma, E.; Petho, M.; Herlihy, K. M.; Micera, G. Equilibrium studies on copper(II)- and iron(III)-monohydroxamates. *Polyhedron* **1998**, *17* (19), 3331–3342.

(18) Santos, J. M.; Carvalho, S.; Paniago, E. B.; Duarte, H. A. Potentiometric, spectrophotometric and density functional study of the interaction of N-hydroxyacetamide with oxovanadium(IV): the influence of ligand to the V(IV)/V(V) oxi-reduction reaction. *J. Inorg. Biochem.* **2003**, *95* (1), 14–24.

(19) Khalil, M. M.; El-Deeb, M. M.; Mahmoud, R. K. Equilibrium studies of binary systems involving lanthanide and actinide metal ions and some selected aliphatic and aromatic monohydroxamic acids. *J. Chem. Eng. Data* **2007**, *52*, 1571–1579.

(20) O'Brien, E. C.; Farkas, E.; Gil, M. J.; Fitzgerald, D.; Castineras, A.; Nolan, K. B. Metal complexes of salicylhydroxamic acid (H_2Sha), anthranilic hydroxamic acid and benzohydroxamic acid. *J. Inorg. Biochem.* **2000**, *79* (1−4), 47–51.

(21) Farkas, E.; Csoka, H. Solution equilibrium studies on metal complexes of 2,3-dihydroxy-phenylalanine-hydroxamic acid (Dopaha) and models: catecholate versus hydroxamate coordination in iron(III)-, aluminium(III)- and molybdenum(VI)-Dopaha complexes. *J. Inorg. Biochem.* **2002**, *89*, 219–226.

(22) Aksoy, M. S.; Özer, U. Potentiometric and spectroscopic studies with chromium(III) complexes of hydroxysalicylic acid derivatives in aqueous solution. *Turk. J. Chem.* **2003**, *27* (6), 667–673.

(23) Aksoy, M. S.; Özer, U. Equilibrium studies on chromium(III) complexes of salicylic acid and salicylic acid derivatives in aqueous solution. *Chem. Pharm. Bull.* **2004**, *52* (11), 1280–1284.

(24) Aksoy, M. S.; Aydın, R.; Türkel, N.; Özer, U. Formation constants of chromium(III), scandium(III) and yttrium (III) complexes of some hydroxynaphthoic acids. *Chem. Pharm. Bull.* **2005**, *53* (5), 471–475.

(25) Aksoy, M. S. Complexes of chromium(III) with 2,3-dihydroxynaphthalene-6-sulfonic acid and 4,5-dihydroxynaphthalene-2,7-disulfonic acid in aqueous solution. *Chem. Pharm. Bull.* **2008**, *56* (6), 771−774.

(26) Aksoy, M. S. Formation constants of chromium(III) complexes with 8-hydroxyquinoline and 8-hydroxyquinoline-5-sulfonic acid. *Asian J. Chem.* **2009**, *21* (7), 5189–5198.

(27) Gran, G. Determination of the equivalent point in potentiometric titrations. *Acta Chem. Scand.* **1956**, *29*, 599.

(28) Schwarzenbach, G.; Flaschka, A. *Complexometric Titrations*; Chauser Press: New York, 1969.

(29) Irving, H. M.; Miles, M. G.; Pettit, L. D. A study of some problems in determining the stoicheiometric proton dissociation constants of complexes by potentiometric titrations using a glass electrode. *Anal. Chim. Acta* **1967**, *38*, 475–488.

(30) Beck, M. T.; Nagypàl, I. *Chemistry of Complex Equilibria*; John Wiley: New York, 1990.

(31) Martell, A. E.; Motekaitis, R. J. *Determination and Use of Stability Constants*; VCH publishers: New York, 1989.

(32) Martell, A. E.; Smith, R. M.; Motekaitis, R. J. *Critically Selected Stability Constants of Metal Complexes Database Version 4.0*; NIST Standard Reference Data: Gaithersburg USA, 1997.

(33) Smith, R. M.; Martell, A. E. *Critical Stability Constants*; Plenum Press: New York, 1989; Vols. 3, 5, 6.

Received for review September 27, 2009. Accepted January 15, 2010.

JE900780N