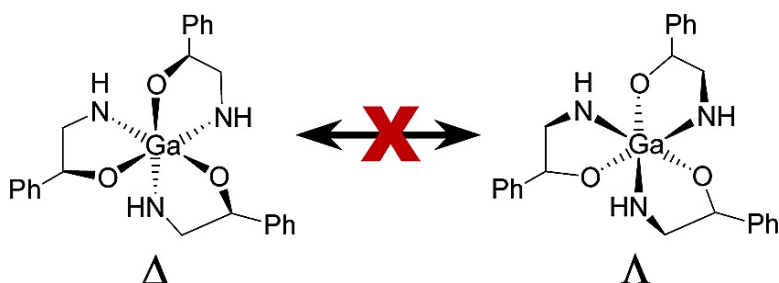Communication

What Should Be Impossible: Resolution of the Mononuclear Gallium Coordination Complex, Tris(benzohydroxamato)gallium(III)

Julia L. Brumaghim, and Kenneth N. Raymond

More About This Article

Additional resources and features associated with this article are available within the HTML version:

- Supporting Information
- Access to high resolution figures
- Links to articles and content related to this article
- Copyright permission to reproduce figures and/or text from this article

View the Full Text HTML

What Should Be Impossible: Resolution of the Mononuclear Gallium Coordination Complex, Tris(benzohydroxamato)gallium(III)[1]

Julia L. Brumaghim and Kenneth N. Raymond*

Department of Chemistry, University of California, Berkeley, California 94720

Received May 8, 2003; E-mail: raymond@socrates.berkeley.edu

Chirality of metal complexes has been of theoretical interest to chemists since the time of Werner[2] and the relative stability of such complexes was explained by Taube's application of crystal field theory.[3] Metal complex chirality also has important practical applications in areas as varied as chiral metal catalysts[4,5] and microbial iron transport.[6-8] Recently, chiral supramolecular clusters have demonstrated that a stable, chiral nanovessel can be prepared by coupling the chiral metal centers that form the vertexes of the cluster.[9] Understanding the stability and racemization mechanisms of chiral metal complexes is essential to rational development of applications based on chiral metal coordination complexes and to enable design of more robust chiral supramolecular assemblies. Very few resolved chiral complexes of labile metals have been reported—they should be impossible. The d^{10} Ga^{3+} ion has no ligand field stabilization and is consequently considered a classic example of a "labile" metal ion. We report here the resolution of simple complexes of this cation.

The hydroxamate functional group $(R(OH)NC(O)R')$ is a common iron-binding motif found in siderophores, small molecules synthesized by bacteria as iron-transport agents. Deprotonation of the $N(OH)$ to give the hydroxamate anion results in a powerful bidentate ligand. When $R = H$, further deprotonation (usually as the metal complex) gives the hydroximate anion $[(O)N=C(O)]^{2-}$.

Octahedral coordination of a metal by three hydroxamate ligands can potentially exist in two geometrical isomers by virtue of the two different donor atoms of the hydroxamate. Each of these *fac* (previously denoted as *cis*) and *mer* (previously denoted as *trans*) geometrical isomers can exist as either Λ or Δ optical isomers. The Δ and Λ isomers for the *fac* geometrical isomers are shown in Figure 1. Although a metal hydroxamate complex can potentially exist as four possible isomers, X-ray crystallography has found only the two *fac* geometrical isomers of the Fe(III)[10] and Ga(III)[11] benzohydroxamate complexes. This *fac* geometry has also been found in the potassium salt of tris(thiobenzohydroximato)chromium-(III)[12] and the isostructural ferric complex.[13] In solution ^1H NMR also shows only one isomer for the Ga complex.

Resolution of the Λ and Δ isomers of the kinetically inert tris-(thiohydroxamato)chromium(III) complex and the tris(thiohydroxamato)chromium(III) and cobalt(III) complexes have been reported.[13] In the related tris(benzohydroxamate)iron(III) complex, the ferric ion is high-spin d^5. Due to the lack of ligand field stabilization, high-spin ferric complexes are generally considered kinetically labile.[14] Despite this lability, the corresponding ferric hydroxamate complexes were also resolved,[15] resulting in the first report of the resolution of a high-spin ferric complex stable in solution under ambient conditions.

Replacement of Fe(III) with Ga(III) to give the tris(benzohydroxamate)gallium(III) complex (1) gives a diamagnetic d^{10} compound which also has no ligand field stabilization. Usually Ga(III) is approximately twice as labile as Fe(III), with a water exchange rate for the aqua ion of 403 s^{-1} compared to 160 s^{-1} for Fe(III).[16]
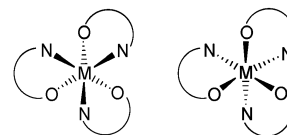

Figure 1. Λ-fac (left) and Δ-fac (right) geometries of tris(benzohydroxamato) complexes.
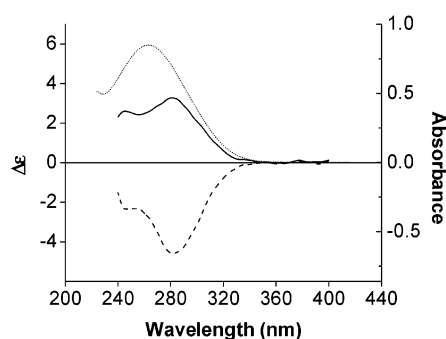

Figure 2. UV-vis (⋯) and circular dichroism spectra for the Λ (—) and Δ (- - -) isomers of **1** in chloroform.

Despite this greater lability, resolution of racemic **1** into its Λ and Δ optical isomers has been achieved. Although optically active gallium compounds have been synthesized in the solid state[17] and as part of self-assembled supramolecular structures,[18] this is the first reported resolution of a mononuclear gallium complex.

Compound **1** was prepared from gallium nitrate and sodium benzohydroxamate.[11] The Λ and Δ optical isomers were deprotonated to form the hydroximato complex followed by precipitation of the desired isomer with Λ- or Δ-[Co(en)_3]I_3 (en = ethylenediamine) and reprotonation, using a modification of the procedure reported by Abu-Dari.[15,19] Despite the greater lability expected of complex **1** as compared to that of the analogous iron complex, the resolved isomers of **1** do not racemize in aprotic solvents.

The absorption and circular dichroism spectra of **1** in chloroform are shown in Figure 2.[20] Assignment of a Δ configuration to the isomer of **1** which shows a band with a negative Cotton effect at 280 nm and a shoulder at 244 nm[21] is based on the assignment of the corresponding tris(benzohydroxamato)iron(III) complex.[15] The spectra of Δ- and Λ-**1** are different from those of the resolved iron complexes, since gallium is only stable in the 3+ oxidation state and therefore lack the metal-to-ligand charge-transfer bands seen for the analogous iron complexes at 355 and 460 nm. Thus, the observed bands at 280 and 244 nm for the gallium complex are due to ligand transitions. Both the resolved gallium and iron benzohydroxamate complexes show remarkable stability in solution. The resolved Λ- and Δ-isomers of the tris(benzohydroxamato)-iron(III) complex show no loss of optical activity in chloroform or other aprotic solvents over a one-month period. Similarly, the optical activity of Λ- or Δ-**1** in solution shows no loss of signal intensity

over a one-week period in aprotic solvents such as chloroform or THF. However, the resolved iron and gallium complexes racemize immediately in protic solvents. This unusual stability to racemization in aprotic solvents as well as similar racemization behavior in protic solvents suggests a similar racemization mechanism for the two complexes. The resolved iron benzohydroxamate complexes are more stable to racemization than the corresponding gallium complexes; addition of 70% methanol to chloroform solutions of the iron complexes causes complete racemization, while addition of 50% methanol to chloroform solutions of the gallium complexes causes complete racemization.[22]

Although crystal structures have provided structural information for benzohydroxamate complexes, interconversion of Δ and Λ and/ or *fac* and *mer* isomers in solution has not been examined. While the paramagnetism of Fe(III) complexes hinders study by NMR spectroscopy, studying the diamagnetic gallium analogues circumvents this difficulty. This technique has previously been used to investigate the isomerization of gallium tris(catecholate) complexes,[23] as well as gallium complexes of ferrichrome analogues. Detailed studies of the racemization behavior of these complexes will soon be reported.[22]

In summary, despite the greater lability and ligand exchange rate of Ga(III) over Fe(III), resolution of the Δ and Λ optical isomers of **1** has been accomplished. Optical activity of these resolved gallium complexes indicates they have unprecedented solution stability. While there may be practical applications of this unusual behavior, we regard the most significant result to be the surprise of these findings and our altered understanding of a classical topic in coordination chemistry.

References

(1) Paper #72 in the series "Coordination Chemistry of Microbial Iron Transport Proteins". For the previous paper, see: Goetz, D. H. H., M. A.; Borregaard, N.; Bluhm, M. E.; Raymond, K. N.; Strong, R. K. *Mol. Cell* **2002**, *10*, 1033–1043.

(2) Werner, A. Z. *Anorg. Chem.* **1883**, *3*, 267–330 (in translated and annotated form in Kauffman, G. B. *Classics in Coordination Chemistry*; Dover Publications: New York, 1968).

(3) Taube, H. *Chem. Rev.* **1952**, *50*, 69–126.

(4) Maruoka, K. *Pure Appl. Chem.* **2002**, *74*, 123–128.

(5) Aspinall, H. C. *Chem. Rev.* **2002**, *102*, 1807–1850.

(6) Raymond, K. N.; Dertz, E. A. In *Iron Transport in Bacteria: Molecular Genetics, Biochemistry, Microbial Pathogenesis and Ecology*; Payne, S., Crosa, J., Eds.; ASM Press: Washington, DC, 2003. In press.

(7) Neilands, J. B. *J. Biol. Chem.* **1995**, *270*, 26723–26726.

(8) Müller, G.; Matzanke, B. F.; Raymond, K. N. *J. Bacteriol.* **1984**, *160*, 313–318.

(9) Ziegler, M.; Davis, A. V.; Johnson, D. J.; Raymond, K. N. *Angew. Chem., Int. Ed.* **2003**, *42*, 665–668.

(10) Lindner, V. H. J.; Göttlicher, S. *Acta Crystallogr., Sect. B* **1969**, *25*, 832–842.

(11) Borgias, B. A.; Barclay, S. J.; Raymond, K. N. *J. Coord. Chem.* **1986**, *15*, 109–123.

(12) Abu-Dari, K.; Freyberg, D. P.; Raymond, K. N. *Inorg. Chem.* **1979**, *18*, 2427–2433.

(13) Abu-Dari, K.; Raymond, K. N. *Inorg. Chem.* **1977**, *16*, 807–812.

(14) Basolo, F.; Pearson, R. G. *Mechanisms of Inorganic Reactions*; 2nd ed.; Wiley: New York, 1967.

(15) Abu-Dari, K.; Raymond, K. N. *J. Am. Chem. Soc.* **1977**, *99*, 2003–2005.

(16) Hugi-Cleary, D.; Helm, L.; Merbach, A. E. *J. Am. Chem. Soc.* **1987**, *109*, 4444–4450.

(17) Stalder, S. M.; Wilkinson, A. P. *Chem. Mater.* **1997**, *9*, 2168–2173.

(18) Terpin, A. J.; Ziegler, M.; Johnson, D. J.; Raymond, K. N. *Angew. Chem., Int. Ed.* **2001**, *40*, 157–160.

(19) Resolution of **1** was carried out in glassware soaked overnight in HCl to remove any iron contamination. A racemic mixture of **1** (0.50 g) was dissolved in water (15 mL), and NaOH (1 mL, 2.5 M) was added to form the tris(hydroximato) complex. This solution was cooled in an ice bath, and a [Δ-Co(en)$_3$]I$_3$ solution (0.325 g in 15 mL water) was added dropwise. The solution was then stirred for 5 min, the pH was decreased to 8–9, and methanol (30 mL) was added to precipitate the double salt. The resulting white precipitate was filtered and added to a separatory funnel containing a solution of water (50 mL), sodium acetate (5 g), and acetic acid (5 mL of 0.1 M). Chloroform was added, and the resolved Λ-**1** was separated (1 × 30 mL, 1 × 10 mL). The chloroform fractions were combined, dried over magnesium sulfate, filtered, and evaporated in vacuo to give a white solid. Yield of Λ-**1**: 0.20 g (80%). The Δ isomer of **1** was prepared using the same method, substituting [Λ-Co(en)$_3$]I$_3$ for Δ.

(20) UV–vis spectra were obtained on a Hewlett-Packard B542A diode array spectrometer. Circular dichroism spectra were measured on a Jasco 810 spectropolarimeter using 1 × 10^{-5} M solutions.

(21) The Δ isomer of tris(benzohydroxamato)iron(III) has a negative Cotton band at 256 nm.

(22) Brumaghim, J. L.; Dertz, E. A.; Davis, A. V.; Raymond, K. N. Manuscript in preparation.

(23) Kersting, B.; Telford, J. R.; Meyer, M.; Raymond, K. N. *J. Am. Chem. Soc.* **1996**, *118*, 5712–5721.

(24) Dayan, I.; Libman, J.; Agi, Y.; Shanzer, A. *Inorg. Chem.* **1993**, *32*, 1467–1475.

JA0360283