

Dinuclear Catecholate Helicates: Their Inversion Mechanism

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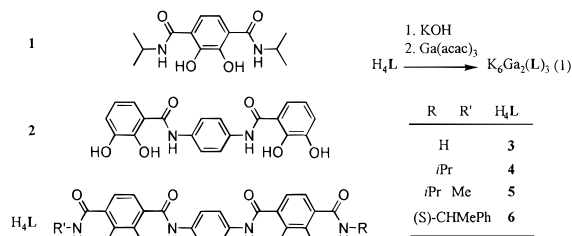
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In coordination chemistry, the simplest supramolecular architecture is the two-metal-center helicate.¹ As a result of a spontaneous, self-assembling process in which ligands wrap around two or more metal centers, helicates can be viewed as simple models of more complex natural structures.² Recently, we have described how the formation of the helical cluster is driven by the geometry of the ligand and the incommensurate coordination numbers of the ligand and metal.³ Perhaps the earliest triple helicate^{4–7} to be characterized, however, is that formed with rhodotorulic acid, the dihydroxamate siderophore produced by the yeast *Rhodotorula pilimanae*. At neutral pH, a complex of Fe₂L₃ stoichiometry is formed and was characterized as an enantiomerically pure Δ -*cis* helicate.^{8,9} Subsequently, we published the X-ray structure of a related synthetic iron(III) trihelicate based on 1,2-hydroxypyridinone binding groups.¹⁰

This paper reports the synthesis, structure, and inversion mechanism of a new class of dinuclear biscatechol triple helicates^{11,12} in which the two coordination centers are coupled such that the chirality at the first metal center (Λ or Δ) is replicated at the second. For the first time, the coupling of the two metal centers of such a system is investigated with respect to the kinetics of inversion, using nuclear magnetic resonance as a probe. The crystal structure and solution reaction dynamics provide a clear picture of how the two coordination sites interact, both in determining the static ground-state geometry and the dynamic transition state for inversion.

Molecular mechanics calculations indicated that the biscatecholamide ligand **2** would form a racemic mixture of the homochiral, Λ, Λ -, Δ, Δ -Ga₂(**2**)₃^{6–} anions rather than the heterochiral *meso* or Λ, Δ -Ga₂(**2**)₃^{6–} species.¹³ Triple-stranded helicates containing either the biscatecholamide **2** or the bisterephthalamides **3–6** were obtained by the stoichiometric

Scheme 1



reaction of the doubly deprotonated ligands, K₂H₂L,¹⁴ with Ga(acac)₃ or Fe(acac)₃ in CH₃OH at room temperature (Scheme 1).¹⁵ Recently, it has been suggested that a *trans* influence in the catecholamide moiety is relevant to the formation of the dinuclear helicates.¹² Our results demonstrate that terephthalamide-based ditopic ligands, which have no potential for a *trans* influence, form helicates equally well.

Attempts to study the structure and mechanism of inversion in dinuclear metallohelicates of the type Ga₂(L)₃^{6–} focused on ligands **3–6**. The CD spectrum of the chiral iron complex K₆-Fe₂(**6**)₃ shows a negative Cotton effect at 443 nm, which supports the assignment of homochiral Λ, Λ - and Δ, Δ -configurations of the Ga₂(L)₃^{6–} anions in solution. Final corroboration came from single-crystal X-ray diffraction of complexes, K₆Ga₂(**3**)₃ and K₆Ga₂(**4**)₃, which contain nonchiral ligands.¹⁶ These are racemic mixtures of dinuclear triple helical complexes of D₃ molecular symmetry and Λ, Λ - or Δ, Δ -configuration.¹⁷

At ambient temperature, solutions of K₆Ga₂(L)₃, L = **2**, **4**, and **6**, or (N(CH₃)₄)₆Ga₂(**3**)₃ in CD₃OD or DMSO-*d*₆ each display one discrete, static set of ¹H NMR resonances which are slightly shifted when compared to the spectra of the free ligands. The chirality at the metal centers of Ga₂(**4**)₃^{6–} and Ga₂(**5**)₃^{6–} was confirmed by the proton resonance splitting of the diastereotopic methyl groups of the isopropyl substituents, which appear as a A₃B₃X system.

Since ligand **5** is unsymmetrical, the complexation reaction (Scheme 1) yields a mixture of *cis*-K₆Ga₂(**5**)₃ and *trans*-K₆Ga₂(**5**)₃ isomers. From integration of the respective resonances, the *cis:trans* ratio was determined to be 0.35(1), slightly higher than the value of 0.25 expected for a purely statistical isomer distribution. In D₂O the spectrum shows the expected four singlets and eight methyl spin doublets in the NCH₃ and NCH(CH₃)₂ regions, respectively.¹⁸ Variable-temperature NMR studies in D₂O (p[D] = 12.1) were carried out in order to study both the isomerization and inversion mechanisms.¹⁹ Upon heating, coalescence of the NCH(CH₃)₂ resonances was ob-

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(13) MM2 calculations on the CaChe system showed a 19 kJ mol^{–1} preference of the Λ, Λ -, Δ, Δ -Ga₂(**2**)₃^{6–} over the *meso* compound Λ, Δ -Ga₂(**2**)₃^{6–}.

(14) The ligands H₄L, L = **2–6**, were characterized by elemental analysis, ¹H NMR spectroscopy, and (+)-FABMS; the results are included in the supporting information.

(15) The ¹H NMR, elemental analysis, (+)-FABMS, UV-vis, and CD data of K₆Ga₂(**2**)₃, (N(CH₃)₄)₆Ga₂(**3**)₃, K₆Ga₂(**4**)₃, K₆Ga₂(**5**)₃, K₆Ga₂(**6**)₃, and K₆Fe₂(**6**)₃ are included in the supporting information.

(16) Crystal and refinement data for (N(CH₃)₄)₆Ga₂(**3**)₃·(DMF)₆(H₂O)₄ (pale yellow hexagonal needles grown by ether diffusion into a DMF/H₂O solution of the complex): C₂₁₆H₄₄H₃₂N₄₈O₆₈, fw = 2482.07, hexagonal, P31c, a = 14.283(2) Å, c = 42.966(2) Å, V = 7591(2) Å³, Z = 2, μ(Mo Kα) = 4.20 cm^{–1}, T = 125(1) K, R[I > 2σ(I)] = 0.1189, wR2 = 0.3107. Pale yellow crystals of K₆Ga₂(**4**)₃ (hexagonal plates), grown by vapor diffusion (DMF/diethyl ether), conform to space group P31c, with a = 14.865(2) Å, c = 41.576(8) Å, V = 7591(2) Å³, and Z = 2. The latter crystals tend to lose solvent rapidly. Further details are found in the supporting information.

(17) The observed Ga–O bond lengths and O–Ga–O angles are typical of triscatecholate gallium(III) complexes as are the ligand–metal twist angles (see: Borgias, B. A.; Barclay, S. J.; Raymond, K. N. *J. Coord. Chem.* **1986**, 15, 109.) The intramolecular Ga–Ga distance is 11 Å.

(18) The *cis*-K₆Ga₂(**5**)₃ and *trans*-K₆Ga₂(**5**)₃ isomers are C₃- and C₁-symmetric, respectively. Therefore, a statistical mixture of *cis* and *trans* isomers produces a total of four equally intense methyl resonances (NCH₃ groups) and eight isopropyl spin doublets.

(19) The variable-temperature NMR studies may be found in the supporting information.

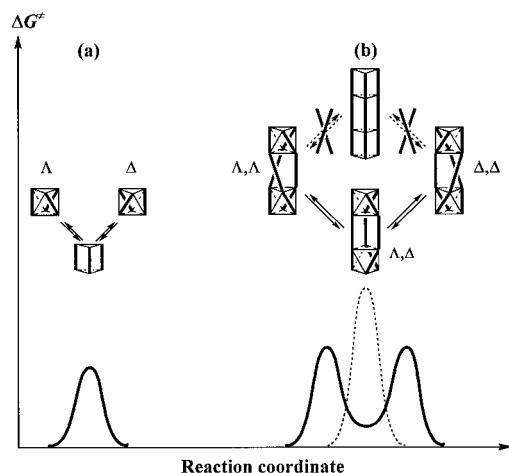


Figure 1. Stereochemical courses and potential energy diagrams for intramolecular inversion of (a) the mononuclear complex $\text{Ga}(\mathbf{1})_3^{3-}$ and (b) the $\Lambda, \Lambda\text{-Ga}_2(\mathbf{4})_3^{6-}$ and $\Delta, \Delta\text{-Ga}_2(\mathbf{4})_3^{6-}$ dinuclear complexes involving the heterochiral $\Lambda, \Delta\text{-Ga}_2(\mathbf{4})_3^{6-}$ complex as an intermediate (solid lines). Inversion with an hypothetical, concerted twisting of both metal centers is indicated by a dashed line: $\Delta G^\ddagger(\text{Ga}_2(\mathbf{4})_3^{6-}) = 2 \Delta G^\ddagger(\text{Ga}(\mathbf{1})_3^{3-})$.

served for both *cis*- $\text{Ga}_2(\mathbf{5})_3^{6-}$ and *trans*- $\text{Ga}_2(\mathbf{5})_3^{6-}$. The discrete exchange pattern of the NCH_3 resonances indicates that both isomers invert independently and without *cis*–*trans* isomerization under these conditions.

Similarly, in $\text{Ga}_2(\mathbf{4})_3^{6-}$ the two diastereotopic $\text{NCH}(\text{CH}_3)_2$ resonances broaden, pass through a coalescence point at $T_c = 390$ K, and eventually resolve into a single doublet. In the presence of excess ligand and up to 425 K, no ligand exchange was observed. These results confirm that the collapse of the methyl doublets is due to intramolecular inversion. The activation parameters for this process were derived from an Eyring plot of the first-order rate constants calculated by line shape analysis.²⁰ Consistent with an intramolecular mechanism, these parameters are not solvent dependent: $\Delta G^\ddagger_{298} = 80(2)$ kJ mol⁻¹, $\Delta H^\ddagger = 75(1)$ kJ mol⁻¹, and $\Delta S^\ddagger = -15(5)$ J mol⁻¹ K⁻¹ in $\text{DMSO-}d_6$; $\Delta G^\ddagger_{298} = 79(2)$ kJ mol⁻¹, $\Delta H^\ddagger = 75(1)$ kJ mol⁻¹, and $\Delta S^\ddagger = -12(6)$ J mol⁻¹ K⁻¹ in D_2O at $\text{p}[\text{D}] = 12.1$.

We have recently investigated the inversion of the mononuclear helicate precursor, $\text{K}_3\text{Ga}(\mathbf{1})_3$.²¹ Above $\text{p}[\text{D}] = 9$, that inversion is intramolecular and proceeds through a Bailar twist,²² with an activation barrier of 67.4(9) kJ mol⁻¹. Compared to the mononuclear complex, the free energy inversion barrier for $\text{K}_6\text{Ga}_2(\mathbf{4})_3$ in $\text{DMSO-}d_6$ or D_2O solutions ($\text{p}[\text{D}] = 12.1$) is only 1.2 times higher.

Two limiting cases for coupling of the two metal centers and their chirality can be considered: for weak coupling the barrier should remain essentially unchanged, whereas for very strong coupling the two centers must move through the trigonal-prismatic transition state simultaneously (Figure 1). In such a case, the activation barrier would be expected to be effectively twice the barrier for inversion of the mononuclear complex. The kinetic data show a weak coupling of both metal centers. Thus we conclude that inversion of the Λ, Λ - and $\Delta, \Delta\text{-Ga}_2(\mathbf{L})_3^{6-}$ helicates involves the heterochiral $\Lambda, \Delta\text{-Ga}_2(\mathbf{L})_3^{6-}$ anion as an intermediate, which is produced by a single twist event along the reaction pathway, as indicated in Figure 1.

At lower $\text{p}[\text{D}]$ in D_2O a second mechanism becomes dominant. A first-order dependence on $[\text{D}^+]$ was observed for the inversion reaction of the mononuclear triscatecholate $\text{K}_3\text{-Ga}(\mathbf{1})_3$ complex, which was proposed to involve the singly protonated metal complex.²¹ For the dinuclear $\text{K}_6\text{Ga}_2(\mathbf{4})_3$ complex, this dependence is cleanly second-order below $\text{p}[\text{D}] = 7$, with an experimental rate equation $k = k_0 + k_1[\text{D}^+]^2$ ($k_0 = 0.08(1)$ s⁻¹ and $k_1 = 2.7(3) \times 10^{12}$ M⁻² s⁻¹ at 298 K). This constitutes a remarkable confirmation of the mechanism outlined in Figure 1. Inversion of one center, which occurs rapidly because of the single protonation, does not change the overall chirality owing to the higher energy of the heterochiral intermediate and its consequent short lifetime (Figure 1). Only when the second metal center is also protonated can the overall inversion of the helicate occur. In the absence of mechanical coupling of the metal centers only a single proton dependence would be expected because the *meso* intermediate would have the same energy as the homochiral anions and consequently a long lifetime.

The activation parameters for the proton-independent and proton-assisted inversion pathways of $\text{K}_6\text{Ga}(\mathbf{4})_3$ are respectively: $\Delta G^\ddagger_{298} = 79(2)$ kJ mol⁻¹, $\Delta H^\ddagger = 78(1)$ kJ mol⁻¹, $\Delta S^\ddagger = -5(2)$ J mol⁻¹ K⁻¹ (in good agreement with the one obtained at $\text{p}[\text{D}] = 12.1$) and $\Delta G^\ddagger_{298} = 1.7(1)$ kJ mol⁻¹, $\Delta H^\ddagger = 45(1)$ kJ mol⁻¹, $\Delta S^\ddagger = 145(6)$ J mol⁻¹ K⁻¹. The apparent activation parameters for the proton-dependent reactions are measures of the free energy of the protonation reaction itself, plus the free energy of activation for inversion of the protonated complex. Since it is expected that the enthalpy of protonation will be negative and the entropy of protonation positive, the relatively small activation enthalpy and the apparently high activation entropy must be interpreted with this in view.

In conclusion, it is found that the inversion of dinuclear $\text{Ga}_2(\mathbf{L})_3^{6-}$ complexes occurs by an intramolecular mechanism that does not lead to *cis*–*trans* isomerization but rather to individual twisting of both metal centers. For the first time, the effective coupling of the coordination sites in the helicate complex have been studied by investigating the kinetics of this process. While the heterochiral Λ, Δ -complexes are high enough in energy not to be seen in measurable concentration, they represent a low enough energy intermediate so that the transition state effectively involves twisting of only one metal center. The consequence for the proton-independent reaction is that the activation barrier is essentially that of the mononuclear complex. Most remarkably, this also leads to a clean second-order dependence on $[\text{D}^+]$ for the proton-dependent reaction since both metal centers must be protonated, and simultaneously invert, to interchange the Λ, Λ - to Δ, Δ -helicate configuration.

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Supporting Information Available: Characterization data for ligands and complexes; structure, tables of crystal data and structure refinement, atomic coordinates and equivalent isotropic displacement parameters, bond lengths and angles, anisotropic displacement parameters, hydrogen coordinates and isotropic displacement parameters, and observed and calculated structure factors for $(\text{N}(\text{CH}_3)_4)_6\text{Ga}_2(\mathbf{3})_3 \cdot (\text{DMF})_6 \cdot (\text{H}_2\text{O})_4$; visible absorption and CD spectra of $\text{K}_6\text{Fe}_2(\mathbf{6})_3$ in CH_3OH and variable-temperature ¹H NMR spectra of $\text{K}_6\text{Ga}_2(\mathbf{4})_3$ in $\text{DMSO-}d_6$ and of $\text{K}_6\text{Ga}_2(\mathbf{5})_3$ in D_2O ; $\text{p}[\text{D}]$ -dependence of the inversion rate for $\text{K}_3\text{Ga}(\mathbf{1})_3$ and $\text{K}_6\text{Ga}_2(\mathbf{4})_3$ (14 pages). See any current masthead page for ordering and Internet access instructions.

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