# Dinuclear Catecholate Helicates: Their Inversion Mechanism

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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 $Fe_2L_3$ 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-$Ga_2(2)_3^{6-}$ anions rather than the heterochiral *meso* or Λ,Δ-$Ga_2(2)_3^{6-}$ species.[13] Triple-stranded helicates containing either the biscatecholamide **2** or the bisterephthalamides **3−6** were obtained by the stoichiometric

## Scheme 1
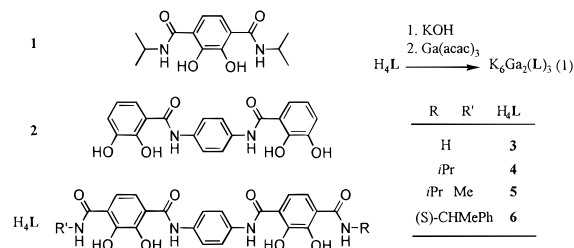


reaction of the doubly deprotonated ligands, $K_2H_2L$,[14] with Ga-$(acac)_3$ or $Fe(acac)_3$ in $CH_3OH$ at room temperature (Scheme 1).[15] Recently, it has been suggested that a *trans* influence in the catecholamide moiety is relevant to the formation of the dinuclear helicates.[12] Our results 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 $Ga_2(L)_3^{6-}$ focused on ligands **3−6**. The CD spectrum of the chiral iron complex $K_6$-$Fe_2(6)_3$ shows a negative Cotton effect at 443 nm, which supports the assignment of homochiral Λ,Λ- and Δ,Δ-configurations of the $Ga_2(L)_3^{6-}$ anions in solution. Final corroboration came from single-crystal X-ray diffraction of complexes, $K_6Ga_2(3)_3$ and $K_6Ga_2(4)_3$, which contain nonchiral ligands.[16] These are racemic mixtures of dinuclear triple helical complexes of $D_3$ molecular symmetry and Λ,Λ- or Δ,Δ-configuration.[17]

At ambient temperature, solutions of $K_6Ga_2(L)_3$, **L = 2, 4,** and **6,** or $(N(CH_3)_4)_6Ga_2(3)_3$ in $CD_3OD$ 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 $Ga_2(4)_3^{6-}$ and $Ga_2(5)_3^{6-}$ was confirmed by the proton resonance splitting of the diastereotopic methyl groups of the isopropyl substituents, which appear as an $A_3B_3X$ system.

Since ligand **5** is unsymmetrical, the complexation reaction (Scheme 1) yields a mixture of *cis*-$K_6Ga_2(5)_3$ and *trans*-$K_6Ga_2$-$(5)_3$ 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 $D_2O$ the spectrum shows the expected four singlets and eight methyl spin doublets in the $NCH_3$ and NCH-$(CH_3)_2$ regions, respectively.[18] Variable-temperature NMR studies in $D_2O$ (p[D] = 12.1) were carried out in order to study both the isomerization and inversion mechanisms.[19] Upon heating, coalescence of the $NCH(CH_3)_2$ resonances was ob-

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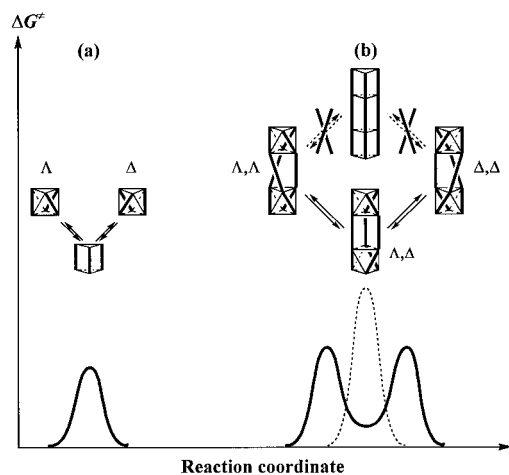(8) Carrano, C. J.; Raymond, K. N. *J. Am. Chem. Soc.* **1978,** *100*, 5371.
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(13) MM2 calculations on the CaChe system showed a 19 kJ $mol^{-1}$ preference of the Λ,Λ-, Δ,Δ-$Ga_2(2)_3^{6-}$ over the *meso* compound Λ,Δ-$Ga_2$-$(2)_3^{6-}$.

(14) The ligands $H_4L$, **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 $K_6Ga_2(2)_3$, $(N(CH_3)_4)_6Ga_2(3)_3$, $K_6Ga_2(4)_3$, $K_6Ga_2(5)_3$, $K_6Ga_2(6)_3$, and $K_6Fe_2(6)_3$ are included in the supporting information.
(16) Crystal and refinement data for $(N(CH_3)_4)_6Ga_2(3)_3 \cdot (DMF)_6(H_2O)_4$ (pale yellow hexagonal needles grown by ether diffusion into a DMF/$H_2O$ solution of the complex): $C_{216}Ga_4H_{328}N_{48}O_{68}$, fw = 2482.07, hexagonal, $P\bar{3}1c$, $a = 14.283(2)$ Å, $c = 42.966(2)$ Å, $V = 7591(2)$ Å$^3$, $Z = 2$, $\mu$(Mo Kα) = 4.20 $cm^{-1}$, $T = 125(1)$ K, R[$I > 2\sigma(I)$] = 0.1189, wR2 = 0.3107. Pale yellow crystals of $K_6Ga_2(4)_3$ (hexagonal plates), grown by vapor diffusion (DMF/diethyl either), conform to space group $P\bar{3}1c$, with $a = 14.865(2)$ Å, $c = 41.576(8)$ Å, $V = 7591(2)$ Å$^3$, 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*-$K_6Ga_2(5)_3$ and *trans*-$K_6Ga_2(5)_3$ isomers are $C_3$- and $C_1$-symmetric, respectively. Therefore, a statistical mixture of *cis* and *trans* isomers produces a total of four equally intense methyl resonances ($NCH_3$ 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 $Ga(1)_3^{3-}$ and (b) the $\Lambda,\Lambda$-$Ga_2(4)_3^{6-}$ and $\Delta,\Delta$-$Ga_2(4)_3^{6-}$ dinuclear complexes involving the heterochiral $\Lambda,\Delta$-$Ga_2(4)_3^{6-}$ complex as an intermediate (solid lines). Inversion with an hypothetical, concerted twisting of both metal centers is indicated by a dashed line: $\Delta G^{\ddagger}(Ga_2(4)_3^{6-}) = 2\ \Delta G^{\ddagger}(Ga(1)_3^{3-})$.

served for both *cis*-$Ga_2(5)_3^{6-}$ and *trans*-$Ga_2(5)_3^{6-}$. 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 $Ga_2(4)_3^{6-}$ the two diastereotopic $NCH(CH_3)_2$ 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 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 p[D] = 12.1.

We have recently investigated the inversion of the mononuclear helicate precursor, $K_3Ga(1)_3$.[21] Above p[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 $K_6Ga_2(4)_3$ in DMSO-$d_6$ or $D_2O$ solutions (p[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 $\Lambda,\Lambda$- and $\Delta,\Delta$-$Ga_2(L)_3^{6-}$ helicates involves the heterochiral $\Lambda,\Delta$-$Ga_2(L)_3^{6-}$ anion as an intermediate, which is produced by a single twist event along the reaction pathway, as indicated in Figure 1.

At lower p[D] in $D_2O$ a second mechanism becomes dominant. A first-order dependence on [D$^+$] was observed for the inversion reaction of the mononuclear triscatecholate $K_3$-$Ga(1)_3$ complex, which was proposed to involve the singly protonated metal complex.[21] For the dinuclear $K_6Ga_2(4)_3$ complex, this dependence is cleanly second-order below p[D] = 7, with an experimental rate equation $k = k_0 + k_1[D^+]^2$ ($k_0 = 0.08(1)$ 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 $K_6Ga(4)_3$ 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 p[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 $Ga_2(L)_3^{6-}$ 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 $\Lambda,\Delta$-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 [D$^+$] for the proton-dependent reaction since both metal centers must be protonated, and simultaneously invert, to interchange the $\Lambda,\Lambda$- to $\Delta,\Delta$-helicate configuration.

**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 param-eters, hydrogen coordinates and isotropic displacement parameters, and observed and calculated structure factors for $(N(CH_3)_4)_6Ga_2(3)_3\cdot(DMF)_6$-$(H_2O)_4$; visible absorption and CD spectra of $K_6Fe_2(6)_3$ in $CH_3OH$ and variable-temperature $^1H$ NMR spectra of $K_6Ga_2(4)_3$ in DMSO-$d_6$ and of $K_6Ga_2(5)_3$ in $D_2O$; p[D]-dependence of the inversion rate for $K_3Ga(1)_3$ and $K_6Ga_2(4)_3$ (14 pages). See any current masthead page for ordering and Internet access instructions.

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