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Imposition of Chirality in a Dinuclear Triple-Stranded Helicate by Ion Pair Formation[1]

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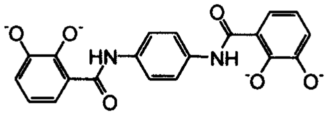
Chirality is a fundamental property intrinsic to many supramolecular systems.[2] Helical assemblies are inherently chiral, regardless of the stereotopic information contained within the individual building blocks.[3−5] Metallo-supramolecular helicates, assembled from achiral ligands and metal centers, form racemic mixtures of clockwise and counterclockwise structures in which all the metal centers are homoconfigurational.[6]

How is chirality in helicates communicated, and can it be controlled through noncovalent forces in solution? Chirality in natural, biological supramolecular systems such as the helical iron complex of rhodotorulic acid, the dihydroxamate siderophore produced by the yeast *Rhodotorula mucilaginosa*, is determined by chiral centers within the individual ligand substituent.[7,8] Likewise, chiral preference in synthetic supramolecular architecture is often introduced by covalently integrating a chiral moiety, such as a carbon stereocenter, into one or more subunits of the complete structure.[9−16] We have previously demonstrated that the incorporation of stereocenters at the extremities of a bis-bidentate catecholate ligand leads to the exclusive formation of one dinuclear triple helicate enantiomer.[17] There are very few systems in which resolution of enantiomers is achieved despite the absence of chiral components within the substructure. The best known abiological example is quartz.[18] An unusual synthetic example reported by Lehn and co-workers[19] is a helicate that spontaneously resolves into two enantiomers upon crystallization.



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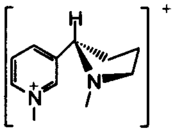

s-nic

Herein we report asymmetric induction with tunable chirality in a discrete dinuclear triple helicate, $[\mathrm{Ga}_2\mathbf{1}_3]^{6-}$ ($\mathrm{H}_4\mathbf{1}$ = *N*,*N*′-bis(2,3-dihydroxybenzoyl)-1,4-phenylenediamine,[20] an *achiral* ligand) by the use of a chiral counterion. The counterion, (*S*)-*N*-methylnicotinium[21] (**s-nic**), is found to have stereospecific interactions with the helicate. Other examples of asymmetric induction to a supramolecular system were reported by Oda et al.[22] and Lacour et al.[23]

There are two key distinctions between this $[\mathrm{Ga}_2\mathbf{1}_3]^{6-}$ helicate system and other reported cases of chiral resolution or determination in metallohelicates. First, the three bis-bidentate ligands that bridge the two octahedral metal centers are achiral. Therefore in the absence of an external stereogenic source, a racemic mixture of helicates is observed. Second, the labile gallium metal centers allow rapid racemization. Similar D_3 symmetric homoconfigurational helicates based on gallium catecholate coordination have been reported to undergo very rapid intramolecular inversion at room temperature.[17,24]

Diffusion of THF into a methanolic solution of $\mathrm{K}_6[\mathrm{Ga}_2\mathbf{1}_3]$ in the presence of excess **s-nic** selectively yields crystals of the $\Lambda\Lambda$ isomer as $\mathrm{K}(\textbf{s-nic})_5[\mathrm{Ga}_2\mathbf{1}_3]$.[25] The crystal structure reveals five cocrystallized **s-nic** ions per helicate (Figure 1). One potassium ion, which coordinates strongly to the catecholate oxygens on the helical caps, remains. The chirality at the metal centers is determined by steric interaction from the flatly anchored pyridinium and the chiral pyrrolidine moiety. Each pyridinyl ring of **s-nic**, with the nitrogen 3.75 Å away from the centroid of the catecholate ring, is in parallel arrangement with the nearest catecholate ring. This conformation suggests strong cation−π interaction between the electron-poor pyridinium ring of **s-nic** (π-acceptor) and the electron-rich catecholate ring of the ligand (π-donor). Each pyrrolidine unit is angled away from the metal

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(25) Monoclinic, $P2_1$, orange, $a = 14.424(3)$ Å, $b = 24.772(5)$ Å, $c = 18.473(4)$ Å, $\beta = 107.88(3)°$, −143 °C, $Z = 2$, $R_1 = 9.35\%$, GOF = 1.519. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Center as supplementary publication no. CCDC 139491. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: +44 1223−336-033; e-mail: deposit@ccdc.cam.ac.uk).

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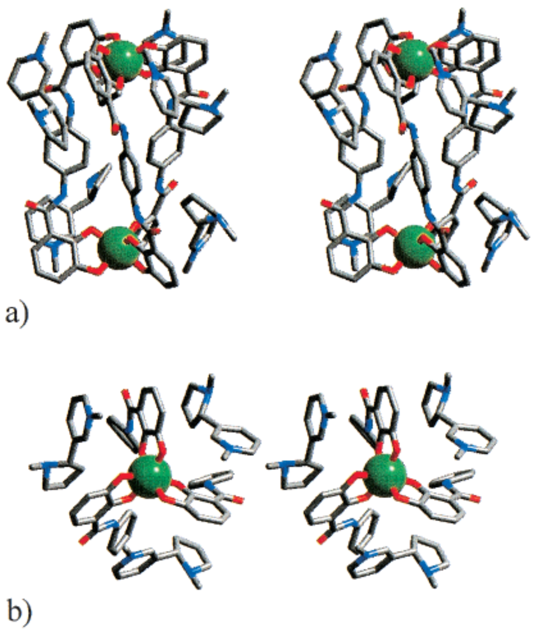

Figure 1. Stereo projections of the X-ray crystal structure of K(**s-nic**)$_5$-[Ga$_2$**1**$_3$]. Green sphere: Ga. (a) The potassium ion at the bottom of the helicate is omitted from view. (b) Only the top metal center is shown.

center and tilted toward the middle of the helicate in a twist direction prescribed by the carbon stereocenter. Each catecholate ring is sandwiched between a pyridinium on one side and a pyrrolidine on the other side from an adjacent molecule of **s-nic**. Significantly, the approximate 109° angle between the pyridinium and the pyrrolidine planes allows for good spatial fit into the void defined by two adjacent catecholate rings spaced 120° apart.

The absolute configuration of the bulk crystalline sample of $\Lambda\Lambda$-K(**s-nic**)$_5$[Ga$_2$**1**$_3$] was confirmed by a solid state CD spectrum.[17,26] Enantiomerically enriched K(**s-nic**)$_5$[Ga$_2$**1**$_3$] crystals showed no CD signals when dissolved in both unbuffered and buffered (carbonate, pH 9.5) aqueous solutions. (We have previously reported rapid racemization rates for similar helicate species in aqueous environment.[17]) However, an equilibrated millimolar methanolic solution does exhibit enantiomeric excess of the $\Lambda\Lambda$ helicate as determined by CD polarimetry. In solution, the chiral induction effect relies on tight ion pairing between the helicate and the enantiopure **s-nic**. The higher dielectric constant of water versus methanol allows formation of a strong hydration sphere around the charged helicates and **s-nic**, and thus decreases the extent of ion pairing in aqueous solutions. Since intermolecular communication of stereo information requires specific steric interactions between the ions, weaker solvation by methanol leads to observable chiral induction in solution.

As further evidence for the necessity of very specific interactions between the helicate and **s-nic**, no enantiomeric excess was observed when **s-nic** was added to a 0.01 M solution of mononuclear K$_3$Ga(**L**)$_3$ (**L** = 2,3-dihydroxy-4-(isopropylcarbamoyl)benzene) in methanol. This result suggests that catecholate pairing interaction with **s-nic** pyridinium ring alone is not sufficient to induce chirality. Rather, in addition to these strong cation$-\pi$ interactions, steric interactions between the **s-nic** pyrrolidine and the aromatic rings linking the two helicate metal centers, as well as synergy resulting from mechanical coupling at both metal centers, all contribute to chiral induction in the helicate.

In solution, an equilibrium between the free nicotinium and the $\Delta\Delta$ and $\Lambda\Lambda$ helicate isomers has been modeled.

$$\begin{tikzcd} \Lambda\Lambda \;+ n1\ \textbf{s-nic} \arrow[r, shift left, "K_\Lambda"] \arrow[d, shift left] & \Lambda\Lambda\cdots(\textbf{s-nic})_{n1} \arrow[l, shift left] \\ \Delta\Delta \;+ n2\ \textbf{s-nic} \arrow[r, shift left, "K_\Delta"] \arrow[u, shift left] & \Delta\Delta\cdots(\textbf{s-nic})_{n2} \arrow[l, shift left] \end{tikzcd}$$

The initial racemic solution has equal concentrations of the $\Lambda\Lambda$ and $\Delta\Delta$ complexes, i.e., $[\Lambda\Lambda]/[\Delta\Delta] = 1$. When **s-nic** is present, an enantiomeric excess is observed because **s-nic** binds to the $\Lambda\Lambda$ isomer more extensively and more strongly than to the $\Delta\Delta$ isomer; $m = n_1 - n_2 > 0$ and K_Λ is greater than K_Δ.

$$\frac{K_\Lambda}{K_\Delta} = \frac{[\Lambda\Lambda\cdots(\textbf{s-nic})]}{[\Delta\Delta\cdots(\textbf{s-nic})]}[\textbf{s-nic}]^{m} \quad m = n1 - n2$$

The observable equilibrium derived from the CD experiment gives the net Δ versus Λ concentrations. The enantiomeric excess was measured as a function of **s-nic** concentration given a constant helicate concentration (shown in Supporting Information).[27] Analyzing the data according to the equations

$$\log\frac{1+\mathrm{ee}}{1-\mathrm{ee}} = m\log[\textbf{s-nic}] + \log\frac{K_\Lambda}{K_\Delta}$$

$$\frac{[\Lambda]}{[\Delta]} = \frac{1+\mathrm{ee}}{1-\mathrm{ee}} \qquad \mathrm{ee} = \frac{[\Lambda\Lambda]-[\Delta\Delta]}{[\Lambda\Lambda]+[\Delta\Delta]}$$

reveals that the binding affinity of **s-nic** for the $\Lambda\Lambda$ helicate is about 6 times stronger ($\log K_\Lambda/K_\Delta = 3.6 \pm 0.2$) than the affinity for the $\Delta\Delta$ helicate at 0.56 mmol of **s-nic**. Further evidence for specific tight ion interaction in solution includes VT NMR spectroscopy data showing that the protons in close proximity to the cation$-\pi$ and van der Waals contact sites exhibit an unusually large chemical shift dependence on temperature. Also, 2-dimensional NOESY experiments indicate good correlation between proton interactions in methanol and their spatial proximity in the solid state.

In summary, we have demonstrated a way of generating and controlling dynamic chirality in a helicate system composed of achiral subunits. Greater understanding of chirality in relevant supramolecular assemblies should facilitate the design of new chiral systems composed of labile components with precise and dynamic control of chirality.

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Supporting Information Available: X-ray structural information for K(**s-nic**)$_5$[Ga$_2$**1**$_3$] (CIF). Solid state CD and UV$-$vis spectra. Figure for cation$-\pi$ interaction. Log$-$log graph of ee as a function of [**s-nic**]. This information is available free of charge via the Internet at http://pubs.acs.org.

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(26) Since helicate racemization occurs in solution, enantiomeric excess of the bulk crystalline sample was determined in the solid state.

(27) Instrumentation: UV$-$vis spectra were recorded using a HP 8453 spectrometer. Solution and solid state CD spectra were recorded with a JASCO 500C spectropolarimeter. Solid state CD spectra: A crystalline sample of K(**s-nic**)$_5$[Ga$_2$**1**$_3$] was ground with KBr and pressed into an orange transparent disk (thickness = 0.8 mm). The disk was scanned at four perpendicular orientations in order to eliminate the linear dichroism component by averaging the spectra. Solution CD spectra: methanolic solutions of the pure helicate K$_6$[Ga$_2$**1**$_3$] and nicotinium **s-nic** were freshly prepared. Samples of different stoichiometry and concentration were prepared from stock solutions and allowed to equilibrate for a minimum of 30 min.