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Chiral Synthesis of a Mononuclear Nickel(II) Complex Formed from an Achiral Tripodal Amine Ligand: Spontaneous Resolution

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A neutral chiral mononuclear Ni(II) complex *cis*-[Ni(NCS)$_2$(tren)] (**1**) [tren = tris(2-aminoethyl)amine] has been isolated in a reaction of nickel(II) salt with an achiral ligand tren and NH$_4$SCN in a MeOH−H$_2$O (1:1) mixture. The crystal structure of **1** reveals the encapsulation of Ni(II) ions in a facial {NiN$_6$} coordination environment that includes four nitrogen donors from the tetradentate chelate tren and two nitrogen donors from two *cis*-NCS (monodentate) ligands. The chirality of **1** arises from symmetry breaking of the *cis*-(NCS)$_2$-Ni(II) octahedral complex by the tetradentate chelate tren. Compound **1** exhibits both its enantiomers in a DMF solution through a Pfeiffer effect when *l*- and *d*-arabinose are used as environment substances. The particular synthesis, described herein, offers total spontaneous resolution, as is evidenced from crystal structure and circular dichroism spectral studies.

A standard "Inorganic Chemistry" text book describes that a *pure inorganic octahedral complex* can possess chirality and optical activity, when the relevant octahedral complex has at least one chelate ring, as originally discovered by Alfred Werner.[1] A tris-chelate complex [Co(en)$_3$]$^{3+}$ (D_3 symmetry), for example, can be resolved into its enantiomers. The chirality for this tris-chelate arises from the spiral configuration of the chelate ring providing the basis for right (Δ) and left (Λ)-handed notations. The octahedral complex *cis*-[CoCl$_2$(en)$_2$]Cl is also optically active because it has no S$_n$ element of symmetry. An enantiopure form of such a chiral coordination complex is of the utmost importance because of its potential applications in enantioselective synthesis and asymmetric catalysis.[2] The optical resolution of this type of chiral chelate into its pure enantiomers is a difficult task because of their instant racemization due to the labile nature of the chelate ring. An enantiopure chiral coordination complex can be obtained either by enantioselective synthesis using an enantiopure ligand or by a spontaneous resolution upon crystallization of a recemic compound. Spontaneous resolution of a racemic compound, generally, results in a conglomerate, where the two enantiomers (left-handed and right-handed forms) crystallize out separately. Jaques et al.[3] have demonstrated that only less than 10% of the racemates form conglomerates. When a particular synthesis leads to the isolation of only homochiral (one-handed) crystals (totally asymmetric state), that synthesis is called total spontaneous resolution. However, the synthesis, which brings about total spontaneous resolution, yielding only homochiral crystals, is extremely rare and unpredictable a priori since the factors determining the process are less understood.[4] We have chosen a tripodal ligand, namely, tris(2-aminoethyl)amine (tren), and a monodentate ligand (NCS$^-$) to obtain an octahedral coordination complex *cis*-[Ni(NCS)$_2$(tren)] (**1**), which is analogous to the optically active coordination complex *cis*-[CoCl$_2$(en)$_2$]$^{1+}$. We wish to report here a unique synthesis that leads to total spontaneous resolution of the chiral coordination complex *cis*-[Ni(NCS)$_2$(tren)] (**1**). We have also demonstrated the molecular-level chirality (solution optical resolution) by using two pure enantiomers of arabinose through the Pfeiffer effect. How the molecular-level chirality of complex **1** has transformed to a supramolecular-level chiralty, leading to total spontaneous resolution, is an important theme of this report.

The title compound *cis*-[Ni(NCS)$_2$(tren)] (**1**) is isolated by the slow evaporation of an aqueous methanolic solution of Ni(OAc)$_2$·4H$_2$O, the ligand tren, and NH$_4$SCN.[5] Compound

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(5) Synthesis of *cis*-[Ni(NCS)$_2$(tren)] (**1**): Light blue, block-shaped crystals of **1** were obtained from the slow evaporation of a MeOH−H$_2$O (1:1) solution (50 mL) of Ni(OAc)$_2$·4H$_2$O (0.25 g, 1 mmol), tren (0.29 g, 1.98 mmol), and NH$_4$SCN (0.16 g, 2.10 mmol). Yield: 0.112 g (35% based on Ni(OAc)$_2$·4H$_2$O). Anal. calcd for C$_8$H$_{18}$N$_6$S$_2$Ni (**1**): C, 29.92; H, 5.65; N, 26.17. Found: C, 30.09; H, 5.77; N, 26.23. IR (KBr, cm^{-1}): 3305s, 3281s, 2087m, 2075s, 1579s, 1405s. UV−vis (DMF) [λ_{max} /nm (ε/M^{-1}cm^{-1})]: 560 (120), 360 (190), 280 (2320).

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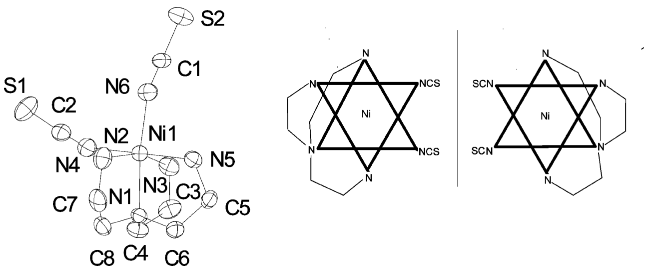

Figure 1. Left: Thermal ellipsoidal plot of *cis*-[Ni(NCS)$_2$(tren)] (**1**). Right: Enantiomeric representations of compound **1**.

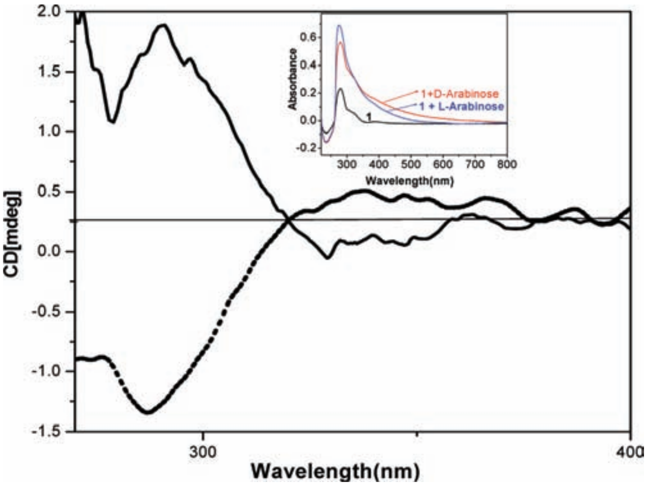

Figure 2. Solid line (—): The CD spectrum of the solution mixture of *d*-arabinose (0.1 g) in 35 mL of a 3.55 × 10^{-3} M DMF solution of compound **1**. Dotted line (•••): The CD spectrum of the solution mixture of *l*-arabinose (0.1 g) in 35 mL of a 3.55 × 10^{-3} M DMF solution of **1**. Inset: Black line: UV−vis spectrum of a 1 × 10^{-4} M DMF solution of compound **1**. Blue line: UV−vis spectrum obtained when 0.05 g of *l*-arabinose was added to 6 mL of a 1 × 10^{-4} M DMF solution of compound **1**. Red line: UV−vis spectrum obtained when 0.05 g of *d*-arabinose was added to 6 mL of a 1 × 10^{-4} M DMF solution of compound **1**.

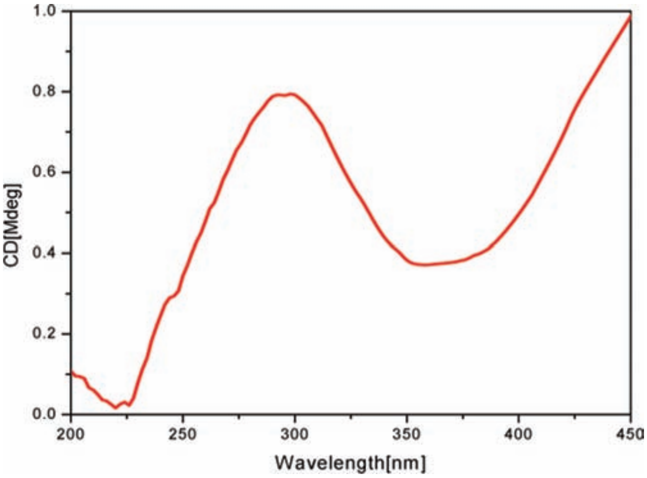

Figure 3. Single-crystal circular dichroism (CD) curve of **1**.

1 crystallizes in chiral space group $P2_12_12_1$.[6] The thermal ellipsoid plot with the atom labeling scheme is shown in Figure 1, left. The Ni(II) is attached with four N atoms of the tripodal amine and two terminal thiocyanato N atoms. The Ni−N distances are in the range 2.072(6)−2.152(6) Å. The range of angles at the Ni center is 81.1(2)−177.9(2)°. The *cis* alignment of two N-bound thiocyanates [<N4−Ni1−N6 = 91.1(2)] makes the octahedral complex nonsuperimposible with its mirror images. The left- and right-handed enantiomeric forms of *cis*-[Ni(NCS)$_2$(tren)] (**1**) are schematically represented in Figure 1 (right). Both of these enantiomers, present in the solution of *cis*-[Ni(NCS)$_2$(tren)] (**1**) (a racemate), can be realized or optically resolved by using the Pfeiffer effect,[7] an effect in which the displacement of a racemate equilibrium occurs in favor of one enantiomer upon treatment with an enantiopure optically active compound (known as an environment substance). In the present study, we have used *l*-arabinose and *d*-arabinose as environment substances. The circular dichroism (CD) spectra of the compound *cis*-[Ni(NCS)$_2$(tren)] (**1**) enriched by the Pfeiffer effect when *l*- and *d*-arabinose are employed as environment substances in DMF are presented in Figure 2. It can be seen that the CD spectra of *cis*-[Ni(NCS)$_2$(tren)] (**1**) in the presence of *l*- and *d*-arabinose are enantiomeric. A Cotton effect at ca. 340 nm is clearly observed and is associated with the chromophores of the enantiomeric *cis*-[Ni(NCS)$_2$(tren)] (**1**) that have electronic absorption at ca. 280 nm. Absorption spectra of the recemic complex *cis*-[Ni(NCS)$_2$(tren)] (**1**) and that of the racemic complex together with *l*-arabinose and *d*-arabinose (as an environment substance) in DMF solutions are shown in Figure 2 (inset). The spectral feature for the racemate with a sharp absorption at 280 nm changes to broad features on the addition of *l*- and *d*-arabinose (see inset of Figure 2). The Cotton effects at 340 nm correspond to the electronic absorption band (at 280 nm) that has been assigned as charge transfer transitions.[8] When *l*-arabinose is added to the DMF solution of *cis*-[Ni(NCS)$_2$(tren)] (**1**), conversion to the (+)340 enantiomer takes place. On the other hand, the addition of *d*-arabinose shifts the equilibrium to the (−)340 enantiomer (Figure 2). The structural configurations of *l*- and *d*-arabinose, used as environment substances in the present study, are shown in Scheme S2 in the Supporting Information. Once we achieved and realized both enantiomers of *cis*-[Ni(NCS)$_2$(tren)] (**1**) in the solution state through a Pfeiffer effect, we were interested in checking the chirality of isolated compound *cis*-[Ni(NCS)$_2$(tren)] (**1**), obtained by one-pot crystallization.[5] It is remarkable that a single crystal of *cis*-[Ni(NCS)$_2$(tren)] (**1**), obtained in this synthesis, exhibits positive feature in its CD curve (Figure 3). The CD experiment was repeated from several syntheses using the same procedure,[5] and surprisingly, in each case, the crystal shows the positive CD spectra (see section S1 in the Supporting Information). From its crystal structure, it is evident that the pertinent molecule has a Λ conformation (see Figure 1, right, and Figure S1 in

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(6) Crystallographic data for **1**: $C_8H_{18}N_6S_2Ni$, $M = 321.11$, orthorhombic, space group $P2_12_12_1$, $a = 8.646(4)$ Å, $b = 10.852(5)$ Å, $c = 14.704(7)$ Å, $U = 1379.7(11)$ Å^3, $Z = 4$, $D_{\text{calcd}} = 1.546$ g cm^{-3}, $\mu = 1.697$ mm^{-1}, $F(000) = 672$, crystal size = 0.32 × 0.14 × 0.12 mm^3; 10 627 reflections were measured with 2506 unique reflections ($R_{\text{int}} = 0.0299$), of which 2115 ($I > 2\sigma(I)$) were used for the structure solution. Final R1 (wR2) = 0.0250 (0.0613), 154 parameters. The final Fourier difference synthesis showed minimum and maximum peaks of −1.542 and +1.044 e Å^{-3}; Flack parameter = 0.03(2).

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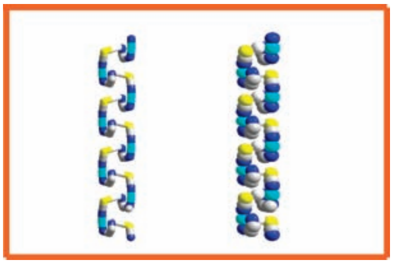

Figure 4. Wire-frame (left) and space-filling (right) representations of the helical structure in compound **1**. Color code: Ni, cyan; S, yellow; C, light grey; N, blue; H, white.

section S4 of the Supporting Information). Thus, the left-handed conformation (Λ) is responsible for the observation of a positive CD spectrum (Figure 3). In order to analyze total spontaneous resolution for this Λ enantiomer of compound **1** crystals, that is, whether all of the individual crystals have the same handedness (100% "e.e.") in this present one-pot synthesis,[5] we performed numerous CD studies on single crystals, isolated in this synthetic procedure.[5] Accordingly, we did many single-crystal CD measurements to see, for example, how many out of 10 single crystals have the same chirality (a statistical analysis) from many repetitive syntheses (but using the same procedure as described in ref 5). In a typical experiment of 10 single crystals, all 10 crystals exhibited positive features in their respective CD spectra. We performed five similar CD experiments, each with 10 single crystals obtained from different repetitive syntheses. The average data out of these experiments help us to conclude that 100% of the crystals isolated from this synthesis have the same chirality (section S1, Supporting Information).

We have analyzed intermolecular interactions in the crystal structure to correlate supramolecular interactions with crystal chirality.[9] The minute structural changes at the molecular level can induce the dramatic changes beyond the pertinent molecule affecting the equilibrium between racemates and conglomerates. We found that this total spontaneous resolution, resulting in a totally asymmetric macroscopic state of crystals of *cis*-[Ni(NCS)$_2$(tren)] (**1**), occurs through the formation of supramolecular homochiral helices, as shown in Figure 4. The helices are formed through N−H···S hydrogen-bonding interactions (N−H from the tren ligand and S from the NCS$^-$ ligand). Remarkably, only one-handed helices of each kind are stabilized, inducing asymmetry into the relevant crystal. The helix propagates through the crystallographic *b* axis. One full turn of the helix has a pitch distance of 10.85 Å and contains two molecules of the mononuclear nickel complex. The path of the helix can be traced by following the H bonds counter-clockwise around the 2-fold screw axis of the helix. Here, the local chirality of the enantiopure molecule ensures the supramolecular chirality, leading to the formation of only left-handed helices at the supramolecular level throughout the crystal lattice. The absolute configuration for the enantiopure complex molecule was successfully determined by refining the Flack parameter.[10]

In conclusion, we have described here a unique systhesis that leads to total spontaneous resolution of a chiral molecule, *cis*-[Ni(NCS)$_2$(tren)] (**1**), which is obtained from achiral components. We have also demonstrated the molecular-level chirality by using the Pfeiffer effect. Still, we could not have isolated or crystallized the other enantiomer, which would display a negative CD curve. Work is in progress in this direction. To the best of our knowledge, this is an intriguing example of a simple octahedral complex that exhibits total spontaneous resolution.

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Supporting Information Available: Single-crystal CD spectra from different synthesis slots and a table of crystal data and structure refinement for *cis*-[Ni(NCS)$_2$(tren)] (**1**). A table of bond distances and angles for compound **1**, structural drawing, and electronic spectra. X-ray crystallographic file in CIF format for compound **1**. This material is available free of charge via the Internet at http://pubs.acs.org.

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