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Complete Enantioseparation through Supramolecular Complex Formation between Tris(1,3-diaminopropane)cobalt(III) Phosphate and β-Cyclodextrin, $[Co(tn)_3]PO_4 \cdot \beta$-CDX

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The supramolecular complex $[Co(tn)_3]PO_4 \cdot \beta$-CDX (tn = 1,3-diaminopropane; β-CDX = β-cyclodextrin) was prepared through β-CDX, *rac*-$[Co(tn)_3]Cl_3$, and Na_3PO_4 in a mole ratio of 1:2:2. After one recrystallization process, the circular dichroism spectrum confirmed that complete enantioseparation of $[Co(tn)_3]PO_4$ is achieved in this system. X-ray crystal structure analysis reveals the presence of the only Λ-enantiomer in the unit cell and the head-to-head chiral discrimination structure of this system. Thus, we found that the present diastereomer formation with β-CDX affords the very convenient and effective optical resolution procedure of $[Co(tn)_3]^{3+}$.

Cyclodextrins (CDXs) are cyclic chiral oligomers having α-1,4-linked D-glucose units. Their remarkable including properties have been applied to the enantioseparation of organic compounds of isopropyl methylphosphinate[1] and sulfinyl compounds.[2] Our related investigation includes the optical resolution of metal complexes with long pendant groups by CDXs.[3] Recently, we found that CDXs can function as chiral discriminating agents for large molecules such as metal complexes without alkyl and/or aryl pendant groups.[4] In the isolated supramolecular complex $[Co(en)_3]_2(CO_3)_3 \cdot 2\alpha$-CDX (en = 1,2-diaminoethane), the chiral discriminating force is mainly relevant to the three-dimensional hydrogen-bonding networks. Because this procedure is more widely applicable, we applied it to the optical resolution of $[Co(tn)_3]^{3+}$ (tn = 1,3-diaminopropane) and found a very efficient resolution method using β-CDX.

β-CDX (283.7 mg, 0.25 mmol), *rac*-$[Co(tn)_3]Cl_3$ (193.8 mg, 0.50 mmol), and Na_3PO_4 (190.1 mg, 0.50 mmol) were dissolved in water (20 mL) at room temperature, and ethanol (20 mL) was added to the solution with stirring. The vessel was sealed with a film and kept in a refrigerator. After 1 week, pink-yellow crystals (**1**) were obtained. The crystals easily effloresce in air by losing ethanol molecules. The yield was 40% based on Co^{III}. Elemental analysis indicates that crystal **1** has the composition $[Co(tn)_3]PO_4 \cdot \beta\text{-CDX} \cdot 0.5C_2H_5OH \cdot 22H_2O$.[5] This composition means that β-CDX does not act as an anion but as a neutral molecule. Ethanol is dispensable to the supramolecular composition, and the absence of ethanol led to separate crystallization of the complex and CDX molecules.

The circular dichroism (CD) spectrum was measured for complex **1**. It has been well-known that the presence of oxoanions such as PO_4^{3-} and SeO_3^{2-} strongly affects the CD strength of $[Co(en)_3]^{3+}$ because of ion-pair formation.[6] A similar situation has been reported in the present six-membered chelate ring system containing PO_4^{3-}.[7] The high-energy dominant CD component in the first d−d absorption band considerably decreases with a lowering of the solution's pH, and simultaneously the CD peak positions shift to the shorter-wavelength region. Such changes ceased at a pH of less than 4. Hence, all CD spectra were measured in solutions below pH 4. The original CD peak value $\Delta\varepsilon_{474} = -0.14$ of complex **1** becomes $\Delta\varepsilon_{474} = -0.17$ after one recrystallization process, which corresponds to the pure Λ value reported by Fujita et al.[8] Thus, it turned out that complete enantioseparation is achieved in complex **1**. The opposite enantiomer Δ-$[Co(tn)_3]I_3$ ($\Delta\varepsilon_{474} = +0.16$) was obtained from the original mother filtrate by the addition of an excess amount of NaI. The standard optical resolutions of $[Cr(tn)_3]^{3+}$ [9] and $[Co(tn)_3]^{3+}$ [10] by sodium nitrocamphor as a resolving agent were rather old and complicated, and complete enantioseparation of $[Co(tn)_3]^{3+}$ by column

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(5) Elem anal. Calcd for $[Co(tn)_3](PO_4) \cdot \beta\text{-CDX} \cdot 0.5C_2H_5OH \cdot 22H_2O$ ($C_{52}H_{147}N_6O_{61.5}P_1Co_1$): H, 7.67; C, 32.35; N, 4.35. Found: H, 7.70; C, 32.36; N, 4.33.

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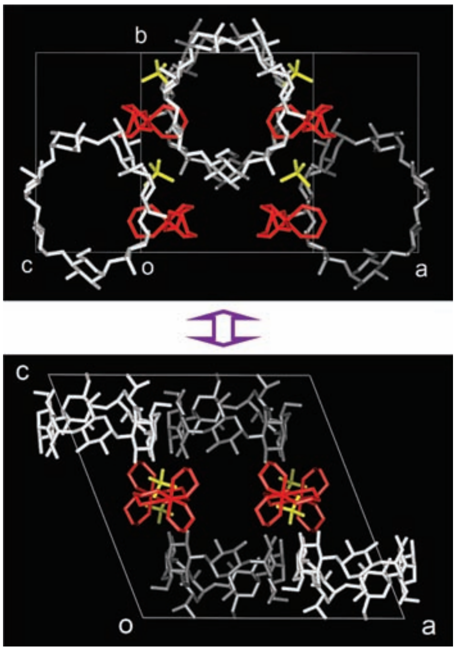

Figure 1. Crystal structures of complex **1**. Color code: red, Λ-$[Co(tn)_3]^{3+}$; yellow, PO_4^{3-}; white, β-CDX.

chromatography was achieved in 1975.[8] Therefore, we claim that the present resolution procedure using β-CDX is very convenient and efficient.

Figure 1 shows the X-ray crystal structure of complex **1**.[11] One unit cell contains four molecules of $[Co(tn)_3]^{3+}$, four molecules of PO_4^{3-}, and four molecules of β-CDX. Because each molecule is related by 2 and 2_1 axes, there is only one crystallographically independent molecule. The crystal structure firmly shows that only the Λ-Co^{III} ion exists in the unit cell, and, hence, complete enantioseparation is realized in complex **1**. Strong hydrogen bonds are formed between $[Co(tn)_3]^{3+}$ and PO_4^{3-}, and the resulting spiral linkage structures grow along the *b* axis. β-CDXs are arranged in the *ab* plane and constitute layer structures. Two adjacent layers are shifted with respect to each other by half a molecule, showing a brick-work pattern. The $[Co(tn)_3]PO_4$ chains exist between the β-CDX layers.

The complex cation $[Co(tn)_3]^{3+}$ has approximately a 3-fold symmetry. The three chelate rings take a chair conformation, but the direction of one chelate ring is opposite to those of the other two rings, as shown in Figure 2. Three crystal structures of $[Co(tn)_3]^{3+}$ have been reported so far: the two structures[12] take the tris(chair) conformation of the same direction, and the remaining structure[13] takes the tris(skew) conformation of the same direction. Hence, this is the first example of the tris(chair) conformation with opposite directions.

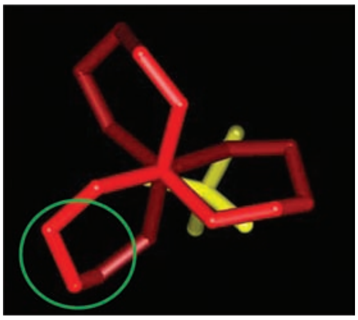

Figure 2. Conformation of Λ-$[Co(tn)_3]^{3+}$ in complex **1**.

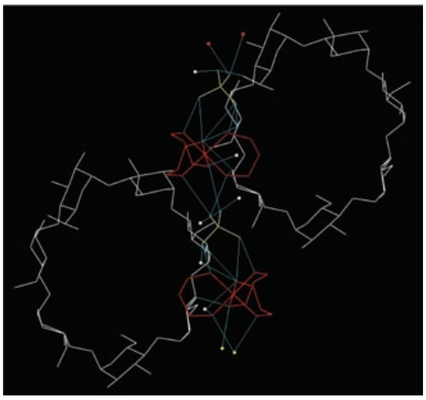

Figure 3. Hydrogen-bonding networks in complex **1**.

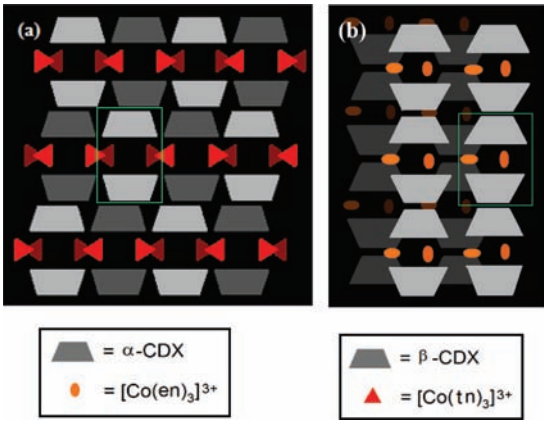

Figure 4. Model description of the crystal packing of complex **1** (a) and $[Co(en)_3]_2(CO_3)_3 \cdot 2\alpha$-CDX (b).

Figure 3 shows the hydrogen-bonding network in complex **1**. The blue lines show hydrogen bonds of less than 3.2 Å. The special role of PO_4^{3-} ions is inferred to mediate mutual interactions between $[Co(tn)_3]^{3+}$ and β-CDX, and the resulting hydrogen-bonding networks among $[Co(tn)_3]^{3+}$, PO_4^{3-}, and β-CDX will stabilize the supramolecular complex.

In crystals containing CDX molecules, three packing types (cage-type, channel-type, and layer-type) are known so far. In the cage-type structure, CDX molecules are arranged in a herringbone fashion and both ends of the cavity are closed by adjacent molecules to create an isolated "cage". The channel-type structure is formed by the linear stacking of CDX, which has an infinite cylindrical channel. The related complex

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(11) (a) The single crystals of **1** suitable for X-ray analysis were obtained by recrystallization from a water–ethanol solution. It contains some molecules of ethanol, but the ethanol molecules are disordered and did not locate anywhere. (b) Crystal data for complex **1**: $C_{51}H_{144}N_6O_{61}P_1Co_1$, M_r = 1907.61, 0.40 × 0.30 × 0.25 mm, T = 200(1) K, monoclinic, $C2$ (No. 5), Z = 4, a = 24.3083 (4) Å, b = 17.4823(4) Å, c = 24.2872(4) Å, β = 111.4100(7)°, V = 9609.0(3) Å^3, μ = 2.99 cm^{-1}, $F(000)$ = 4088, ρ_{calcd} = 1.319 g cm^{-3}, $2\theta_{max}$ = 55.0°. A total of 120 oscillation images were collected. Of the 51 944 reflections collected, 21 332 were unique (R_{int} = 0.014). Final R1 = 0.0508 for 21 332 reflections with $I > 2\sigma(I)$ (1061 parameters) and wR = 0.1527 for all reflections.

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$[Co(en)_3]_2(CO_3)_3 \cdot 2\alpha$-CDX belongs to a head-to-head mode of the channel-type. In the layer-type packing structure, CDXs are arranged in a plane to make molecular layers. The present complex **1** belongs to this layer-type structure, as described above.

Two supramolecular complexes of $[Co(tn)_3]PO_4 \cdot \beta$-CDX and $[Co(en)_3]_2(CO_3)_3 \cdot 2\alpha$-CDX adopt the different CDX packing structures. However, we noticed that both complexes have a common chiral discrimination structure (green area), as shown in Figure 4a,b; both complexes adopt the head-to-head CDX packing mode, where each of the primary hydroxyl group faces meets together and each of the secondary hydroxyl group faces also meets together. The Co^{III} ions exist only in the intervals between two secondary hydroxyl group faces. It is reasonable to consider that chiral discrimination is more preferable at the secondary hydroxyl group face than at the primary hydroxyl group face because the former has twice as many hydroxyl groups as the latter. In fact, the coordination[14] and/or strong interaction[15] between metal ions and CDXs have been reported at the secondary hydroxyl group side. In $[Mg(H_2O)_6]Cl_2 \cdot 0.5\beta$-CDX, CDXs adopt the head-to-tail packing mode and $[Mg(H_2O)_6]^{2+}$ ions exist in all CDX intervals between the primary hydroxyl group face and the secondary hydroxyl group face.[16] This may be an example of a low-quality discriminating structure. Thus, we conclude that the head-to-head mode is more advantageous than the head-to-tail one in view of chiral recognition.

Many other counterions such as Cl^-, I^-, NO_3^-, ClO_4^-, $CH_3CO_2^-$, SO_3^{2-}, SO_4^{2-}, CO_3^{2-}, ClO_4^-, and $C_2O_4^{2-}$ instead of PO_4^{3-} were attempted. Only the carbonate ion CO_3^{2-} gave similar supramolecular complex $[Co(tn)_3]_2(CO_3)_3 \cdot \beta$-CDX.[17] These results mean that the supramolecular complex formation is very dependent upon counteranions. Because PO_4^{3-} and CO_3^{2-} ions are tri- and divalent anions, respectively, and have high pK_a values, they can contribute to strong hydrogen bonds. The special roles of PO_4^{3-} and CO_3^{2-} ions are inferred to mediate mutual interactions between $[Co(tn)_3]^{3+}$ and β-CDX, and the resulting hydrogen-bonding networks among $[Co(tn)_3]^{3+}$, counteranions, and β-CDX will stabilize the supramolecular complex.

Supporting Information Available: Experimental procedures, X-ray crystallography of complex **1**, and CD spectral measurement. This material is available free of charge via the Internet at http://pubs.acs.org.

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