A Pseudorotaxane System Containing γ-Cyclodextrin Formed via Chiral Recognition with an Au\textsubscript{6}Ag\textsubscript{3}Cu\textsubscript{3} Molecular Cap

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A Pseudorotaxane System Containing γ-Cyclodextrin Formed via Chiral Recognition with an Au\textsubscript{16}Ag\textsubscript{13}Cu\textsubscript{13} Molecular Cap

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Introduction

Rotaxanes and pseudorotaxanes are well-known supramolecules in which a macrocyclic molecular ring is threaded by a rod-shaped molecular axle, with its terminal position(s) connected to bulky molecular cap(s).\[1] While a variety of macrocyclic molecules have been employed as molecular rings for the creation of rotaxanes and pseudorotaxane architectures,\[2] the use of cyclodextrins (CDs) as molecular rings has been a target of intensive studies in recent decades\[3] because of their versatile molecular recognition abilities\[4] that lead to a wide range of applications, such as molecular motors,\[5] drug delivery,\[6] and hydrogel systems.\[7] Although the evaluation of intermolecular interactions between ring and axle molecules is essential to understand molecular recognition, most previous studies on rotaxanes and pseudorotaxanes containing CDs as a molecular ring have been performed mainly via NMR spectroscopy in solution rather than X-ray crystallography in the solid state.\[8] and reports on the X-ray crystal structures of this class of supramolecules are scarce.\[9] In particular, only one crystal structure containing γ-CD as a molecular ring has been reported\[10] because of the large cavity size of γ-CD, which hinders the formation of effective intermolecular interactions with the axle molecule.

Abstract: Solvent-mediated crystal-to-crystal transformations of \([\text{AuAgCu}_{11} \text{Cu}_{2} \text{O}_{4}(\text{H}_{2}\text{O})_{2}(\text{o-phen})(\text{tdme})]^{2+}\) \(\text{d-[1}(\text{H}_{2}\text{O})_{2}]^{3+}\); \text{pen}^{2+} = \text{penicilliaminate}, \text{tdme} = 1,1,1-tris(diphenylphosphinomethyl)ethane) to form unique supramolecular species are reported. Soaking crystals of \(\text{d-[1}(\text{H}_{2}\text{O})_{2}]^{3+}\) in aqueous Na\text{bdc} (bdc\textsuperscript{2−} = 1,4-benzenedicarboxylate) yielded crystals containing \(\text{d-[1}(\text{bdc})(\text{H}_{2}\text{O})_{2}]^{3+}\) due to the replacement of a terminal aqua ligand in \(\text{d-[1}(\text{bdc})(\text{H}_{2}\text{O})_{2}]^{3+}\) by a monodentate bdc\textsuperscript{2−} ligand. When γ-cyclodextrin (γ-CD) was added to aqueous Na\text{bdc}, \(\text{d-[1}(\text{bdc})(\text{H}_{2}\text{O})_{2}]^{3+}\) was transformed to \(\text{d-[1}(\text{bdc@γ-CD})(\text{H}_{2}\text{O})_{2}]^{3+}\) where a γ-CD ring was threaded by a bdc\textsuperscript{2−} molecule to construct a pseudorotaxane structure. While the use of dicarboxylates with an aliphatic carbon chain instead of bdc\textsuperscript{2−} afforded analogous pseudorotaxanes, such pseudorotaxane species were not formed when crystals of \(\text{AuAgCu}_{11} \text{Cu}_{2} \text{O}_{4}(\text{L-phen})(\text{tdme})]^{3+}\) \(\text{l-[1}(\text{H}_{2}\text{O})_{2}]^{3+}\) enantiomeric to \(\text{d-[1}(\text{H}_{2}\text{O})_{2}]^{3+}\) were soaked in aqueous Na\text{bdc} and γ-CD, affording only crystals containing \(\text{l-[1}(\text{bdc})(\text{H}_{2}\text{O})_{2}]^{3+}\).

Results and Discussion

Here, we report a pseudorotaxane system containing γ-CD as a molecular ring, the structure of which was established by single-crystal X-ray crystallography. This system was prepared from a chiral \(\text{Au}_{16} \text{Ag}_{13} \text{Cu}_{13}\) complex with D-penicilliaminate, \(\text{d-[1}(\text{H}_{2}\text{O})_{2}]^{3+}\) = \([\text{AuAgCu}_{11} \text{Cu}_{2} \text{O}_{4}(\text{D-phen})(\text{tdme})]^{3+}\) \(\text{tdme} = 1,1,1\)-tris(diphenylphosphinomethyl)ethane, \(\text{D-phen} = \text{D-penicilliaminate})^{[11]}\), in combination with dicarboxylate and γ-CD via solvent-mediated crystal-to-crystal transformations (Scheme 1). We found that the γ-CD ring was threaded by a molecular axle of dicarboxylate attached to a molecular cap of an \(\text{Au}_{16} \text{Ag}_{13} \text{Cu}_{13}\) complex in a largely distorted manner such that the smaller opening, rather than the larger opening, unusually interacts with the \(\text{Au}_{16} \text{Ag}_{13} \text{Cu}_{13}\) molecular cap. Notably, the use of the corresponding \(\text{Au}_{16} \text{Ag}_{13} \text{Cu}_{13}\) complex with L-penicilliaminate \(\text{l-[1}(\text{H}_{2}\text{O})_{2}]^{3+}\) did not afford an analogous pseudorotaxane species without including γ-CD in the structure. This is the first example of a structurally characterized pseudorotaxane system prepared via chiral recognition between a γ-CD ring and a chiral molecular cap.
Transformation of D-[1(H2O)3]2+ in aqueous bdc2-

Blue crystals of D-[1(H2O)3](tfac)3 (tfac = trifluoroacetate), in which D-[1(H2O)3]2+ cations are surrounded by tfac- anions in a 2D layer structure (Figure S1), were prepared according to the procedure described in our recent publication.11,12 When blue crystals of D-[1(H2O)3](tfac)3 with a hexagonal block shape were soaked in an aqueous solution containing Na2bdc (bdc2- = 1,4-benzenedicarboxylate) at room temperature, the original crystals immediately lost its transparency and disappeared with the concomitant formation of a blue-white suspension in a few days, from which blue crystals of D-2 with a thin hexagonal plate shape gradually appeared over two weeks. Completion of the crystal transformation was confirmed by the powder X-ray diffraction of the product, which exhibited a single set of diffractions that are distinct from those of D-[1(H2O)3](tfac)3 (Figure S2).12 The diffuse reflection and circular dichroism spectra of D-2 in the solid state are essentially the same as those of D-[1(H2O)3](tfac)3 (Figure S3),12 indicating the retention of the Au2Ag2Cu3 dodecanuclear structure during the crystal transformation. However, the IR spectrum indicated that the tfac- anions in D-[1(H2O)3](tfac)3 are replaced by bdc2- in D-2 (Figure S4).12 On the basis of these results, together with the X-ray fluorescence and elemental analyses, D-2 was determined to have a chemical formula of [1]bdc3·3nH2O.

The structure of D-2 was determined by single-crystal X-ray diffraction analysis, which revealed the complex cations and bdc2- counteranions in a 1:1 ratio. The complex cation in D-2 contains two trigold(I) metalloligands [Au3(tdme)(D-pen)]3+–[13] spanned by three linear Ag+ and three square-planar Cu+ centers to form a spherical Au2Ag2Cu6 dodecanuclear structure, with its apical positions covered by tdme phenyl groups and its equatorial positions surrounded by three square planar Cu+ centers (Figures 1a and 1b). This structural feature is the same as that of the Au2Ag2Cu6 complex cation in D-[1(H2O)3](tfac)3.11 However, one of the three water molecules coordinated to the three different Cu+ centers in D-[1(H2O)3]2+ is replaced by a monodentate bdc2- ligand with an occupancy of 0.5 in D-2. This implies that D-2 has a 1:1 mixture of D-[1(bdc)(H2O)2]+ and D-[1(H2O)3]2+ as complex cations, corresponding to the chemical formula [1(bdc)3·(H2O)3]·2(bdc). In the D-[1(bdc)(H2O)2]+ cation, a carboxyl group in bdc2- forms an intramolecular NH2···OOC (N···O = 2.64 Å) hydrogen bond with an adjacent amine group in D-pen (Figures 1a and 1b), which appears to sustain the axle structure of bdc2- perpendicular to the square planar Cu+. In the crystal packing structure of D-2, D-[1(bdc)(H2O)2]+ and D-[1(H2O)3]2+ cations form a dimeric assembly through an intramolecular OH···OOC (O···O = 2.83 Å) hydrogen bond (Figure 1c). The dimers are further linked in a 1D chain structure through intermolecular NH2···OH2 (N···O = 2.90 Å) hydrogen bonds (Figure 1d).12

Transformation of D-[1(H2O)3]2+ in aqueous bdc2- and γ-CD

Following the formation of [1(bdc)(H2O)2]+ with a pendent bdc2- axle molecule, crystals of D-[1(H2O)3](tfac)3 were soaked in aqueous Na2bdc containing excess γ-CD to insert the axle molecule of bdc2- into the γ-CD ring. This procedure yielded blue crystals of D-3 via solvent-mediated crystal-to-crystal transformation.14 Again, completion of the crystal transformation from D-[1(H2O)3](tfac)3 to D-3 was proven by the powder X-ray diffraction (Figure S2).12 and the retention of the Au2Ag2Cu6 dodecanuclear structure in the course of the transformation was confirmed by the solid-state diffuse reflection and circular dichroism spectroscopy (Figure S3),12 together with the X-ray fluorescence analysis. The presence of both bdc2- and γ-CD in D-3 was shown by the IR spectroscopy (Figure S4).12

Single-crystal X-ray analysis revealed that D-3 contains complex cations and tfac- anions in a 1:1 ratio. The complex cation has an Au2Ag2Cu6 dodecanuclear structure in D-[1(bdc)(H2O)2]+ with a pendent bdc2- ligand (Figures 2a and 2b), which is essentially the same as that of the D-[1(bdc)(H2O)2]+ cation found in D-2. In D-3, however, the pendent bdc2- is enclosed by a γ-CD ring to form a pseudorotaxane structure in D-[1(bdc@γ-CD)(H2O)2]+, with the smaller opening of the γ-CD ring facing the Au2Ag2Cu6 molecular cap. In pseudorotaxane structures reported to date, a molecular cap is commonly located on the larger opening of the CD ring with secondary hydroxyl groups rather than the smaller opening with primary hydroxyl groups,15 which is a result of the ease of inserting a molecular axle into the larger opening of a CD ring. This is also the case for a pseudorotaxane structure containing γ-CD and fullerene as a molecular ring and a molecular cap, respectively, which is the only pseudorotaxane containing γ-CD that has been structurally characterized to date.16 Thus, D-[1(bdc@γ-CD)(H2O)2]+ is the first example of a structurally characterized pseudorotaxane in which the smaller opening of the CD ring faces a molecular cap. Inspection of the crystal structure of D-3 revealed that two trans carboxyl groups in the [Cu(II-pen)]3+ moiety in the Au2Ag2Cu6 molecular cap form O-H···O (O···O = 2.74 Å, 2.84 Å) hydrogen bonds.

Figure 1. Crystal structure of D-2. Side (a) and top (b) views of the Au2Ag2Cu6 complex cation of D-[1(bdc)(H2O)2]+. (c) Dimeric structure composed of D-[1(bdc)(H2O)2]+ and D-[1(bdc)(H2O)2]+. (d) 1D chain formed via intermolecular NH2···OH2 hydrogen bonds. Colors: red, Au; silver, Ag; blue, Cu; orange, P; yellow, S; pink, O; pale blue, N; gray, C. H atoms are omitted for clarity.
The radii of the γ-CD ellipses in d-3 (r_u and r_b < r_n) are 11.4 Å and 13.0 Å, respectively.

Transformation of d-[1(H,O)3]3+ in aqueous adp2−/sbr2−/sbc2− and γ-CD

To investigate whether a similar pseudorotaxane structure with a distorted γ-CD ring is formed when dicarboxylate anions with an aliphatic carbon chain are used instead of bdc2− with an aromatic benzene ring, crystals of d-[1(H,O)3]3+ were soaked in an aqueous solution containing adipate (adp2−: C6H4(COOO)2), suberate (sbr2−: C6H4(COOO)2), and sebacate (sbc2−: C12H22(COOO)2) in the presence of excess γ-CD, which led to the production of crystals d-4, d-5, and d-6, respectively, via solvent-mediated crystal-to-crystal transformation.†[14] The presence of d-1[12], dicarboxylate, and γ-CD in d-4, d-5, and d-6 was confirmed by the solid-state reflection, circular dichroism, and IR spectroscopy (Figures S7 and S8).†[12] together with the X-ray fluorescence and elemental analyses. Single-crystal X-ray analysis established that d-4, d-5, and d-6 have pseudorotaxane structures very similar to that of d-3, except for the presence of an axle molecule with an aliphatic carbon chain in place of bdc2− in d-3 (Figure 4). Similar to that in d-3, the γ-CD rings in d-4, d-5, and d-6 are largely distorted, forming O···O hydrogen bonds with the Au(I)Ag(I)Cu(I) molecular cap of d-[1(H,O)3]3+ via primary hydroxyl groups of its smaller opening. This indicates that the hydrogen-bonding interaction between the molecular of the pseudorotaxane structure in this system. Contrary to that in d-3,
the noncoordinating carboxyl group of each axle molecule (adp\(^{2-}\), sbc\(^{2-}\) s, sbc\(^{3-}\)) in the crystals of d-4, d-5, and d-6 is hydrogen-bonded with an adjacent pseudorotaxane molecule to form a polyrotaxane-like chain structure (Figure 4d and S9).

**Transformation of L-[1(H\(_2\)O)]\(^{3+}\) in aqueous bdc\(^{2-}\) and γ-CD**

Since the molecular cap of d-[1(H\(_2\)O)]\(^{3+}\) is chiral due to the presence of asymmetric D-pen ligands, we next used L-[1(H\(_2\)O)]\(^{(0)}\)(taa)\(_2\) with pen instead of d-[1(H\(_2\)O)]\(^{(0)}\)(taa)\(_2\) with D-pen in the reaction to evaluate the importance of chirality in the formation of the pseudorotaxane structure. Soaking crystals of L-[1(H\(_2\)O)]\(^{(0)}\)(taa)\(_2\) in aqueous Na\(_2\)bdc in the presence of γ-CD under the same conditions yielded crystals of L-2. The diffuse reflection, circular dichroism, and IR spectra in the solid state (Figures S10 and S11), together with the X-ray fluorescence and elemental analyses, indicated that L-2 has a chemical formula of [1(bdc)\(_2\)](H\(_2\)O)\(_3\)\(_3\)(bdc)\(_2\), corresponding to that of d-2 rather than that of d-3, which lacks γ-CD. The crystal structure of L-2 is entirely enantiomeric to that of d-2, as confirmed by single-crystal X-ray analysis (Figure S12). Thus, L-[1(bdc)(H\(_2\)O)]\(^{3+}\) bearing a molecular cap of L-[1(H\(_2\)O)]\(^{3+}\) does not accept a γ-CD ring in the structure. Molecular modeling suggested that steric repulsion, rather than hydrogen-bonding interaction, exists between the primary hydroxyl groups of γ-CD and carboxyl groups of pen ligands when pen ligands in d-[1(bdc)(H\(_2\)O)]\(^{3+}\) are replaced by L-pen (Figure S13). While a number of reports on chiral recognition due to CD have appeared to date, such a structurally established supramolecular system with CD, which shows the formation of a rotxane/pseudorotaxane structure controlled by the chirality of a molecular cap rather than a molecular axle, is unprecedented.

**Conclusion**

In this study, we showed the solvent-mediated crystal-to-crystal transformation of d-[1(H\(_2\)O)]\(^{(0)}\)(taa)\(_2\) to d-[1(bdc)(H\(_2\)O)]\(^{(0)}\)(bdc)\(_2\) in an aqueous solution containing bdc\(^{2-}\) and γ-CD. Single-crystal X-ray crystallography revealed that in d-3, bdc\(^{2-}\) is bound perpendicular to the [Cu\(_{2}\)(pen)]\(^{3+}\) plane of d-[1(H\(_2\)O)]\(^{3+}\) through coordination and hydrogen bonds, and a γ-CD ring is inserted to generate a pseudorotaxane structure. Remarkably, the γ-CD ring is largely distorted, with its smaller ring side facing the [Cu\(_{2}\)(pen)]\(^{3+}\) plane to form intermolecular hydrogen bonds. While an analogous pseudorotaxane structure was also generated by using adp\(^{2-}\), sbc\(^{2-}\) and sbc\(^{3-}\) instead of bdc\(^{2-}\), the employment of L-[1(H\(_2\)O)]\(^{(0)}\)(taa)\(_2\) for the reaction did not accommodate γ-CD in the structure because of the chirality mismatch between the molecular cap of L-[1(H\(_2\)O)]\(^{3+}\) and the γ-CD ring. Thus, we established a novel class of pseudorotaxane systems, in which the unusual inclusion mode and large distortion of γ-CD are induced by an intermolecular interaction with a chiral molecular cap via chiral recognition.

**Crystal Structures**

Deposition Number(s) = <url>https://www.ccdc.cam.ac.uk/services/structures?sid=doi:10.1002/chem.202101XXX〉 2096869 (for d-2), 2096870 (for d-3), 2096871 (for d-4), 2096872 (for d-5), 2096873 (for d-6), 2096874 (for L-2), 2096875 (for d-[1(H\(_2\)O)]\(^{(0)}\)(taa)\(_2\)[Au\(_2\)(Cu\(_{2}\)(bdc)(D-pen)\(_3\)][tmeda]2)].</url> contain the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe <url>http://www.ccdc.cam.ac.uk/structures</url> - Access Structures service</url>.

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**Conflict of interest**

The authors declare no conflict of interest.

**Keywords:** Pseudorotaxane • γ-CD • Multinuclear complex • Chiral recognition • X-ray crystallography


Thirty crystal structures of CD-based rotaxanes/pseudorotaxanes, which were identified by searching with the keywords cyclodextrin, rotaxane or pseudorotaxane, are registered in the September 2020 version of the Cambridge Crystallographic Database (CSD).
Pseudorotaxanes are created from an Au$_6$Ag$_3$Cu$_3$ complex with d-penicillamine combined with dicarboxylate and γ-CD via a solvent-mediated crystal-to-crystal transformation. In the structure, a γ-CD ring is threaded by a dicarboxylate axle such that the smaller opening of γ-CD faces a Au$_6$Ag$_3$Cu$_3$ complex cap in a largely distorted manner. The corresponding complex with l-penicillamine does not accept a γ-CD ring in the structure.