

Development of a chiral host system tunable via changes in a 2₁-column packing structure

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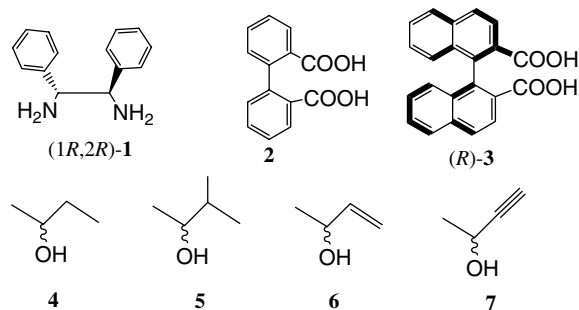
Abstract—A tunable chiral host system was developed by the self-assembly of a chiral 2₁-column structure formed from (1*R*,2*R*)-1,2-diphenylethylenediamine and dicarboxylic acid. This host system can include guest molecules by changing the packing of a chiral 2₁-column enantioselectively.

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Many supramolecular host compounds that include guest molecules have been reported.¹ However, it has been very difficult to modulate the shape and properties of the cavity in these host complexes.² In order to solve this problem, supramolecular host complexes composed of two or three molecules bearing tunable properties have been developed.³ Unfortunately, the cavities of these complexes have been achiral. Although tunable chiral host complexes have been reported, they are composed of one molecule.⁴ Recently, we reported a chiral supramolecular host system composed of an amine and a carboxylic acid derivative. The amine was (1*R*,2*R*)-diphenylethylenediamine [(1*R*,2*R*)-**1**] and the carboxylic acid was either biphenic acid (**2**) or chiral (*R*)-1,1'-binaphthyl-2,2'-dicarboxylic acid [(*R*)-**3**].⁵ Characteristically, these host complexes are formed by the self-assembly of a chiral 2₁-columnar hydrogen- and ionic-bonded network structure lacking strong interactions. In the (1*R*,2*R*)-**1**-(*R*)-**3** system, we found that guest molecules are included by changing the packing of these chiral 2₁-columns. Therefore, we expect

that guest molecules may be included by changing the packing of these chiral 2₁-columns in also the (1*R*,2*R*)-**1**-**2** system. Moreover, it is expected that these (1*R*,2*R*)-**1**-**2** and (1*R*,2*R*)-**1**-(*R*)-**3** systems may recognize a slight difference around an asymmetric center of a guest molecule by the self-assembly of the chiral 2₁-column, too.

In this letter, we report the inclusion and recognition behavior of structurally similar racemic (*rac*) guest molecules by using the (1*R*,2*R*)-**1**-**2** and (1*R*,2*R*)-**1**-(*R*)-**3** systems. The change of the packing style in the composition of the 2₁-columns was studied by X-ray analysis. As guest molecules, four kinds of *rac*-secondary butanol derivatives, 2-butanol (**4**), 3-methyl-2-butanol (**5**), 3-buten-2-ol (**6**) and 3-butyne-2-ol (**7**), were used.



Keywords: Chiral supramolecular complex; 2₁-Column; Molecular recognition; Tunable host complex.

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Inclusion of guest molecules into the (1*R*,2*R*)-1–2 system was attempted by adding (1*R*,2*R*)-1 and 2 to each of the alcohol solutions. Crystals were not obtained from the 3-buten-2-ol solution, but colorless crystals **I–III** were obtained from the 2-butanol, 3-methyl-2-butanol and 3-butyn-2-ol solutions, respectively. X-ray analysis was performed to investigate the inclusion mechanism of these guest molecules. The structures of crystals **I–III** are shown in Figure 1.^{5,6}

X-ray analyses revealed the same stoichiometry for these inclusion crystals, that is, (1*R*,2*R*)-1:2:H₂O:alkyl alcohol = 1:1:1:1. The crystals share a characteristic columnar hydrogen- and ionic-bonded network around the 2₁-axis, which is formed from ammonium hydrogens and carboxylate oxygens. The included water molecules (Fig. 1, indicated in red) link the carboxyl group and

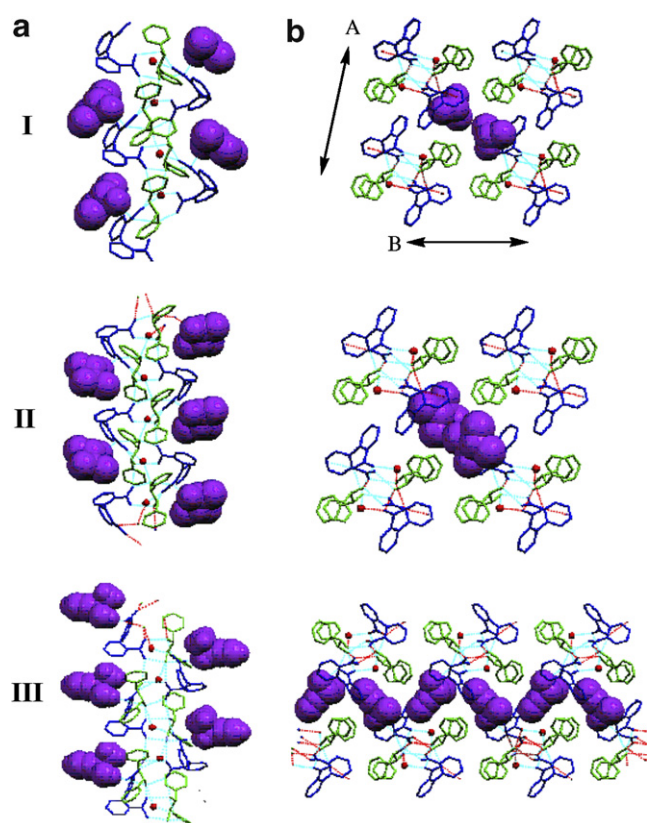


Figure 1. Crystal structures of **I–III**. Water molecules are shown in red and alkyl alcohol molecules in purple. (a) Columnar hydrogen- and ionic-bonded network is parallel to the *b*-axis for crystals **I** and **II** and the *a*-axis for crystal **III**. (b) Views down the *b*-axis for crystals **I** and **II** and down the *a*-axis for crystal **III**.

the amino group through a hydrogen bond and contribute to the maintenance of the columnar frame. Each alkyl alcohol (Fig. 1, indicated in purple) was maintained in the cavity by a hydrogen bond to the carboxyl group. In complexes **I** and **II**, the packing structure of the 2₁-column as well as each 2₁-column structure are common to both. However, as the size of the guest changes from 2-butanol to 3-methyl-2-butanol, the distances between the 2₁-columns [*A* and *B*, Fig. 1b] become longer (from 11.372 to 11.643 Å for *A*) and shorter (from 13.818 to 13.545 Å for *B*). Thus, by slightly changing the packing of the 2₁-columns, the crystal can accommodate structurally different alkyl alcohols. Crystal **III** has completely different cell parameters from those of crystals **I** and **II** (Table 1).

Although each 2₁-column structure in complex **III** is the same as in complexes **I** and **II**, the packing of the 2₁-columns is different [Fig. 1b]. Interestingly, when the packing diagram of this crystal is observed along the *b*-axis, channel-like cavities are seen. This packing style is produced by the rotation of the 2₁-columns around the *b*-axis (Fig. 2), resulting in weaker interactions in the 2₁-column structure. In this channel-like cavity, 3-butyn-2-ol is trapped one-dimensionally along the direction of the cavity.

The complexation behavior of the host, comprising of (1*R*,2*R*)-1 and (*R*)-3 was investigated in a similar manner. (1*R*,2*R*)-1 and (*R*)-3 were dissolved in solutions of each of the four *rac*-butanol derivatives to form inclusion complexes. In this case, crystals were not obtained from the 3-butyn-2-ol solution, but colorless crystals **IV–VI** were obtained from the 2-butanol, 3-methyl-2-butanol and 3-buten-2-ol solutions, respectively. X-ray analysis was performed to investigate the inclusion mechanism of the guest molecules. The structures and crystal data of crystals **IV–VI** are shown in Figure 3 and Table 2.^{5,7}

X-ray analyses revealed the same stoichiometry of these inclusion crystals, that is, (1*R*,2*R*)-1:(*R*)-3:H₂O:alkyl alcohol = 1:1:1:1, with the same *P*2₁2₁ space group. These crystals share a characteristic columnar hydrogen- and ionic-bonded network around the 2₁-axis formed by the carboxyl and amino groups, as in crystals **I–III**. The included water molecules (Fig. 3, indicated in red) link the carboxyl group and the amino group through a hydrogen bond and contribute to the maintenance of the columnar frame. Each alkyl alcohol (Fig. 3, indicated in purple) was maintained in the cavity by a

Table 1. Comparison of crystal data for crystals **I–III**

Complex	I	II	III
Chemical formula	C ₁₄ H ₁₈ N ₂ ·C ₁₄ H ₈ O ₄ ·C ₄ H ₁₀ O·H ₂ O	C ₁₄ H ₁₈ N ₂ ·C ₁₄ H ₈ O ₄ ·C ₅ H ₁₂ O·H ₂ O	C ₁₄ H ₁₈ N ₂ ·C ₁₄ H ₈ O ₄ ·C ₄ H ₆ O·H ₂ O
Cell setting	Monoclinic	Monoclinic	Orthorhombic
Space group	<i>P</i> 2 ₁	<i>P</i> 2 ₁	<i>P</i> 2 ₁ 2 ₁ 2 ₁
<i>a</i> (Å)	11.3720(8)	11.643(3)	9.4027(4)
<i>b</i> (Å)	9.4378(7)	9.420(2)	13.3768(6)
<i>c</i> (Å)	13.8177(10)	13.545(3)	23.2133(11)
<i>V</i> (Å ³)	1469.66(18)	1471.6(5)	2919.7(2)
<i>Z</i>	2	2	4

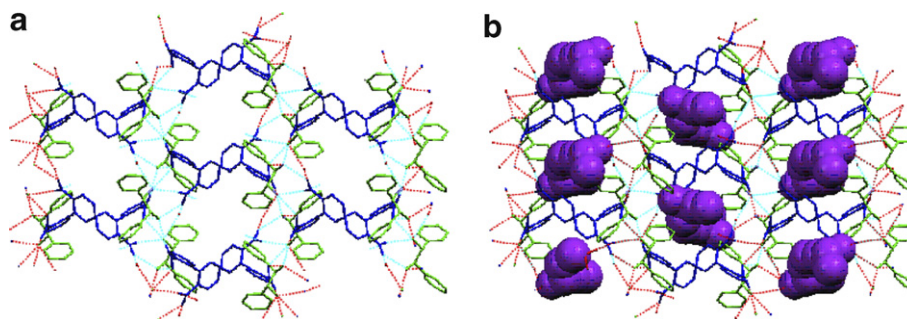


Figure 2. Packing structure of complex III observed along the *b*-axis: (a) without 3-butyn-2-ol; (b) with 3-butyn-2-ol.

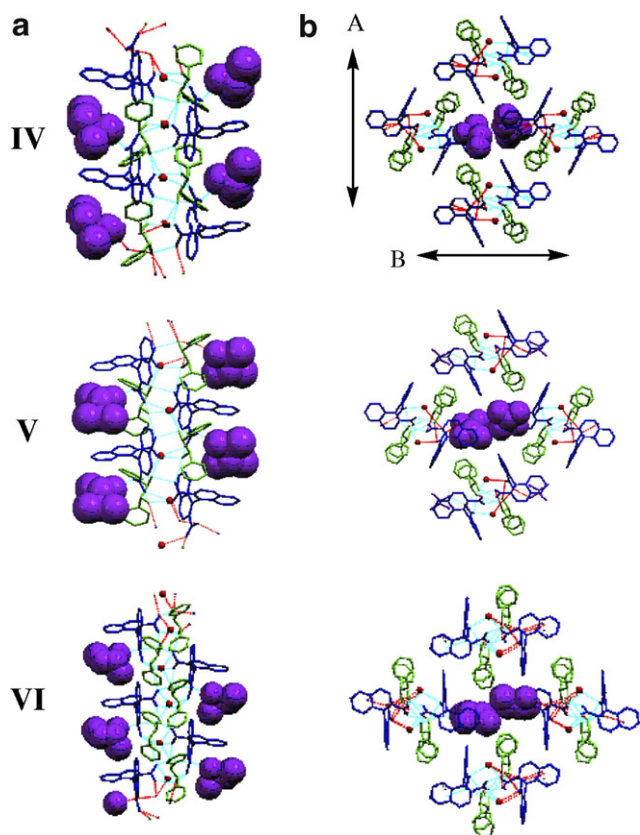


Figure 3. Crystal structures of IV–VI. Water molecules are shown in red and alkyl alcohol molecules in purple. (a) Columnar hydrogen- and ionic-bonded network is parallel to the *a*-axis. (b) Views down the *a*-axis.

hydrogen bond to the carboxyl group. In complexes IV and V, the packing style of the 2_1 -columns as well as each 2_1 -column structure are common to both. How-

ever, as the guest structure changes from 2-butanol to 3-methyl-2-butanol, the distances between the 2_1 -columns [*A* and *B*, Fig. 3b] become longer (from 19.596 to 19.982 Å for *A*, and from 18.443 to 18.950 Å for *B*). Thus, by slightly changing the packing of the 2_1 -columns, these structurally different alcohols can be accommodated, as in the biphenic acid crystal.

In complex VI, the packing of the 2_1 -columns is different from that in crystals IV and V. When the packing diagrams of crystals IV and V are observed along the *a*-axis, it is seen that one naphthol ring of the binaphthol molecule lies vertically between the 2_1 -columns. On the other hand, in complex VI, one naphthol ring of the binaphthol molecule is parallel along the *b*-axis. Also in this complex, the 2_1 -columns are rotated around the *a*-axis to include the 3-butyn-2-ol molecules. These results suggest that this supramolecular host system may be versatile enough to accommodate many kinds of guest molecules by dynamically changing the packing mode of the 2_1 -columns according to the guest molecule structure.

Because these host complexes are chiral, they can include guest alcohols enantioselectively. The optical purity of the guest alcohol in the crystal was determined with good reproducibility by GC analysis using a Chiral-DEX CB capillary column. As expected in the (1*R*,2*R*)-1–2 system, the enantioselectivity depends on the guest structure. 91% ee was achieved for (*S*)-2-butanol and 52% ee for (*R*)-3-butyn-2-ol. Although Figure 1 shows only the spacefilling view of the major alcohol, electron density corresponding to the minor alcohol is observed as a disorder in the same cavity. Unfortunately, when *rac*-3-methyl-2-butanol was used as a guest alcohol, enantiomeric excess was not observed (~0% ee). In complexes I and III, the included major alcohol is

Table 2. Comparison of crystal data for crystals IV–VI

Complex	IV	V	VI
Chemical formula	C ₁₄ H ₁₈ N ₂ ·C ₂₂ H ₁₂ O ₄ ·C ₄ H ₁₀ O·H ₂ O	C ₁₄ H ₁₈ N ₂ ·C ₂₂ H ₁₂ O ₄ ·C ₅ H ₁₂ O·H ₂ O	C ₁₄ H ₁₈ N ₂ ·C ₂₂ H ₁₂ O ₄ ·C ₄ H ₈ O·H ₂ O
Cell setting	Orthorhombic	Orthorhombic	Orthorhombic
Space group	<i>P</i> 2 ₁ 2 ₁ 2	<i>P</i> 2 ₁ 2 ₁ 2 ₁	<i>P</i> 2 ₁ 2 ₁ 2 ₁
<i>a</i> (Å)	9.5831(6)	9.5068(6)	9.5166(8)
<i>b</i> (Å)	18.4429(12)	18.9504(11)	18.1389(15)
<i>c</i> (Å)	19.5963(12)	19.9816(12)	19.3955(16)
<i>V</i> (Å ³)	3463.5(4)	3599.8(4)	3348.1(5)
<i>Z</i>	4	4	4

maintained in the 2₁-column by both a hydrogen bond to a hydroxyl group and CH– π interactions (3.1 and 3.4 Å, respectively) between the alkyl chain of the alcohol and the benzene ring of the biphenic acid. This CH– π interaction does not function well in complex **II**, therefore, enantiomeric excess is not observed. Moreover, in complexes **I** and **III**, the absolute configuration of the included major alcohol is different. This is caused by the difference in the packing style of the 2₁-column.

In the (1*R*,2*R*)-**1**–(*R*)-**3** system, the enantioselectivity of the guest alcohol in the crystal greatly depends on the guest structure, giving 21% ee, 43% ee and 27% ee for (*S*)-2-butanol, (*S*)-3-methyl-2-butanol and (*R*)-3-buten-2-ol, respectively. Figure 3 also shows only the spacefilling view of the included major alcohol, and electron density corresponding to the minor alcohol is observed as disorder in the same cavity. Compared with complexes **IV** (or **V**) and **VI**, the absolute configuration of the included alcohol is different. The difference in the packing style of the 2₁-column causes selectivity for a particular absolute configuration of the included alcohol. The enantiomeric excess is good as the enantioselectivity of *rac*-alkyl alcohol. These results show that this host system can recognize slight differences around an asymmetric center of a guest molecule by self-assembly of the chiral 2₁-column.

In conclusion, a two-component chiral host system consisting of amine and carboxylic acid derivatives can include guest molecules by changing the packing of the chiral 2₁-columns by recognizing a slight difference of the guest molecules. These chiral cavities may also be used as an asymmetric reaction field in the future.

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6. (a) Crystallographic data of **II**: C₁₄H₁₈N₂·C₁₄H₈O₄·C₅H₁₂O·H₂O, *M* = 560.67, monoclinic, space group *P*2₁, *a* = 11.643(3), *b* = 9.420(2), *c* = 13.545(3) Å, *U* = 1471.6(5) Å³, *Z* = 2, *D*_c = 1.265 g cm⁻³, μ (Mo K α) = 0.087 mm⁻¹, 10897 reflections measured, 6415 unique, final *R*(*F*²) = 0.0705 using 3443 reflections with *I* > 2.0 σ (*I*), *R*(all data) = 0.1078, *T* = 100 K. CCDC 616579; (b) Crystallographic data of **III**: C₁₄H₁₈N₂·C₁₄H₈O₄·C₄H₆O·H₂O, *M* = 542.61, orthorhombic, space group *P*2₁2₁2₁, *a* = 9.4027(4), *b* = 13.3768(6), *c* = 23.2133(11) Å, *U* = 2919.7(2) Å³, *Z* = 4, *D*_c = 1.234 g cm⁻³, μ (Mo K α) = 0.085 mm⁻¹, 21828 reflections measured, 7260 unique, final *R*(*F*²) = 0.0500 using 6551 reflections with *I* > 2.0 σ (*I*), *R*(all data) = 0.0543, *T* = 100 K. CCDC 616580.
7. Crystallographic data of **VI**: C₁₄H₁₈N₂·C₂₂H₁₂O₄·C₄H₈O·H₂O, *M* = 644.74, orthorhombic, space group *P*2₁2₁2₁, *a* = 9.5166(8), *b* = 18.1389(15), *c* = 19.3955(16) Å, *U* = 3348.1(5) Å³, *Z* = 4, *D*_c = 1.279 g cm⁻³, μ (Mo K α) = 0.086 mm⁻¹, 20923 reflections measured, 7662 unique, final *R*(*F*²) = 0.0592 using 6280 reflections with *I* > 2.0 σ (*I*), *R*(all data) = 0.0765, *T* = 100 K. CCDC 616581.