A coincident spontaneous resolution system for racemic 1,1′-binaphthyl-2,2′-dicarboxylic acid and 1,2-diphenylethylenediamine induced by water†

Yoshitane Imai,*[a] Kakuhiro Kawaguchi,[a] Nobuo Tajima,[b] Tomohiro Sato,[c] Reiko Kuroda[cd] and Yoshio Matsubara*[a]

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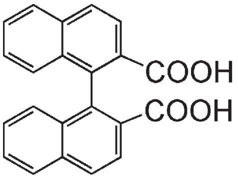
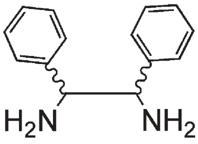
Spontaneously resolvable conglomerate crystals are obtained by combining racemic (*rac*)-1,1′-binaphthyl-2,2′-dicarboxylic acid and *rac*-1,2-diphenylethylenediamine, and this spontaneous resolution system is induced by water which is present in the crystallization solvent.

Many chiral resolution systems have been developed by crystallizing a racemate with an enantiopure derivatizing agent. Spontaneous resolution systems are quite attractive in that no chiral auxiliary is required for resolving racemates.[1] This system with a preferential crystallization method has been successfully applied to the resolution of racemates on an industrial scale. Moreover, it has been reported that conglomerate crystals can be formed by combining two kinds of racemates with an asymmetric center, achieving coincident optical resolution.[2] However, conglomerate crystals of racemic (*rac*)-binaphthyl derivatives with axial chirality are rarely reported.[3]

In this paper, we report the novel coincident spontaneous resolution system of a *rac*-binaphthyl derivative of acid/amine salts induced by water present in the crystallization solvent. As a target *rac*-binaphthyl derivative, we selected *rac*-1,1′-binaphthyl-2,2′-dicarboxylic acid (*rac*-**1**), which is extremely useful as a starting material for the synthesis of chiral materials. As an amine compound, *rac*-1,2-diphenylethylenediamine (*rac*-**2**), an equimolar mixture of (1*R*,2*R*)-**2** and (1*S*,2*S*)-**2**, was used.



(*R*)-, (*S*)-**1**



(1*R*,2*R*)-, (1*S*,2*S*)-**2**

The formation of conglomerate crystals of *rac*-**1** and *rac*-**2** was attempted *via* crystallization from *n*-butanol (*n*-BuOH). A mixture of *rac*-**1** and *rac*-**2** was dissolved in dry *n*-BuOH and left to stand at room temperature under dry atmosphere.[4] After a few days, colorless crystals **I** (16 mg)[5] were obtained. X-Ray analysis was performed to investigate the structure of these crystals, shown in Fig. 1.[6,‡] Unfortunately, crystal **I** is a *rac*-crystal composed of (*R*)-, (*S*)-**1** and (1*R*,2*R*)-, (1*S*,2*S*)-**2**. The stoichiometry of the crystal is (*R*)-**1** : (*S*)-**1** : (1*R*,2*R*)-**2** : (1*S*,2*S*)-**2** : *n*-BuOH = 1 : 1 : 1 : 1 : 4, and the space group is *C*2/*c*. The crystal consists of a columnar supramolecular hydrogen- and ionic-bonded network along the *b* axis (Fig. 1(a)). This column, which has pseudo-centrosymmetry, is composed of (*R*)-, (*S*)-**1** and (1*R*,2*R*)-, (1*S*,2*S*)-**2**. The linkages

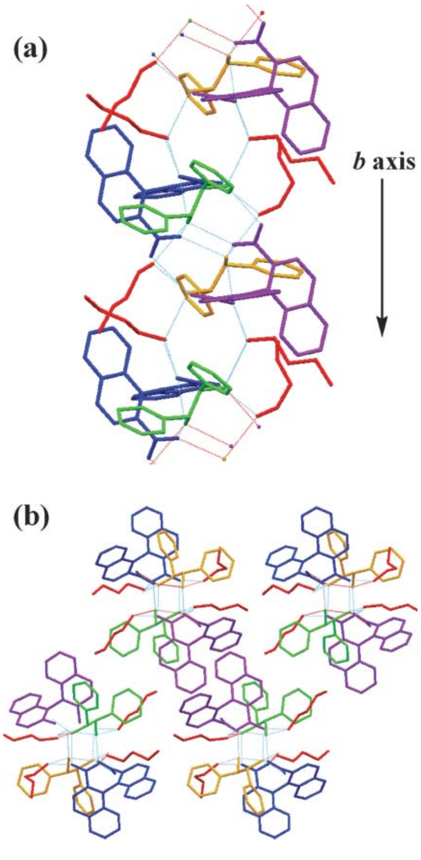


Fig. 1 Crystal structure of complex **I**. (a) Column structure is parallel to the *b* axis. (b) Packing structure observed along the *b* axis.

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[a] *Department of Applied Chemistry, Faculty of Science and Engineering, Kinki University, 3-4-1 Kowakae, Higashi-Osaka, 577-8502, Japan. E-mail: y-imai@apch.kindai.ac.jp; y-matsu@apch.kindai.ac.jp*
[b] *First-Principles Simulation Group, Computational Materials Science Center, NIMS, Sengen, Tsukuba, Ibaraki, 305-0047, Japan*
[c] *JST ERATO-SORST Kuroda Chiromorphology Team, 4-7-6 Komaba, Meguro-ku, Tokyo, 153-0041, Japan*
[d] *Department of Life Sciences, Graduate School of Arts and Sciences, The University of Tokyo, 3-8-1 Komaba, Meguro-ku, Tokyo, 153-8902, Japan*

† Electronic supplementary information (ESI) available: Crystal structure of complex **III**. See DOI: 10.1039/b714226a

consist mainly of ammonium hydrogens, generated from the carboxylic acid anion of **1** and protonation of the amine in **2**. *n*-BuOH molecules (red molecules) link the carboxyl group and the amino group through hydrogen bonds and contribute to the maintenance of the columnar frame.

In order to study the effect of the crystallization solvent, *n*-propanol (*n*-PrOH) and *n*-pentanol (*n*-PenOH) were also used as crystallization solvents. Although good-quality colorless crystals, **II** (15 mg) for *n*-PrOH and **III** (15 mg)[5] for *n*-PenOH, were obtained, they were also *rac*-crystals.[4] The structure of crystal **II** is shown in Fig. 2.[6]‡ The stoichiometry of crystal **II** is (*R*)-**1** : (*S*)-**1** : (1*R*,2*R*)-**2** : (1*S*,2*S*)-**2** : *n*-PrOH = 1 : 1 : 1 : 1 : 4, and the space group is $P\bar{1}$. This crystal also consists of a columnar supramolecular hydrogen- and ionic-bonded network composed of (*R*)-, (*S*)-**1** and (1*R*,2*R*)-, (1*S*,2*S*)-**2** with pseudo-centrosymmetry. *n*-PrOH molecules (red molecules) link the carboxyl group and the amino group through hydrogen bonds and contribute to the maintenance of the columnar frame. In crystal **III**, the stoichiometry is (*R*)-**1** : (*S*)-**1** : (1*R*,2*R*)-**2** : (1*S*,2*S*)-**2** : *n*-PenOH = 1 : 1 : 1 : 1 : 4, and the space group is $P\bar{1}$. The crystal structure of crystal **III** is also formed by self-assembly of a similar column structure composed of **1** and **2**, as in crystal **I** including *n*-BuOH (ESI,† Fig. S1).

For three different crystallization solvents, the obtained crystals were all *rac*-crystals. Therefore, we attempted the formation of a conglomerate crystal, not by changing the crystallization solvent, but by adding an additive to the crystallization solvent. Water, which can form a strong hydrogen bond, was used as the additive. First, crystallization was attempted by using *n*-BuOH with 3% or less moisture, instead of dry *n*-BuOH, at room temperature under air atmosphere.[4] Although the obtained crystals were mainly crystal **I**, a small amount of crystals of **IV** was obtained. The structure of crystal **IV** is shown in Fig. 3.[6]† Although the *R* value of this crystal is unsatisfactory due to the weak diffraction of the sample, the obtained data is sufficient for comparison of the molecular arrangements. In this crystal, although the space group is also $P\bar{1}$, the stoichiometry is (*R*)-**1** : (*S*)-**1** : (1*R*,2*R*)-**2** : (1*S*,2*S*)-**2** : *n*-BuOH : H_2O = 0.5 : 0.5 : 0.5 : 0.5 : 1 : 1. The crystal consists of a columnar supramolecular hydrogen- and ionic-bonded network with pseudo-centrosymmetry along the *a* axis (Fig. 3(a)). This column is also composed of (*R*)-, (*S*)-**1** and (1*R*,2*R*)-, (1*S*,2*S*)-**2**, as in crystal **I**. However, two water molecules (red balls in Fig. 3) link the carboxyl group and the amino group through hydrogen bonds instead of two *n*-BuOH molecules and contribute to the maintenance of the columnar frame.

n-BuOH saturated with water was used next as the crystallization solvent.[4] As a result, crystals of **V**, which are quite different from crystals **I** and **IV**, were obtained. Interestingly, this crystal is a chiral crystal. The space group is $P2_12_12_1$, and water molecules are included with the stoichiometry of (*S*)-**1** : (1*R*,2*R*)-**2** : H_2O = 1 : 1 : 1 (Fig. 4).[7] As a characteristic of the structure, the crystal has a 2_1-helical columnar supramolecular hydrogen- and ionic-bonded network composed of (*S*)-**1** and (1*R*,2*R*)-**2** (Fig. 4(a)). Their linkages are similar to those of crystals **I** and **IV**. The included water molecules (red balls in Fig. 4) link the carboxyl group and the amino group through hydrogen bonds and contribute to the maintenance of the columnar frame. Characteristically, in this

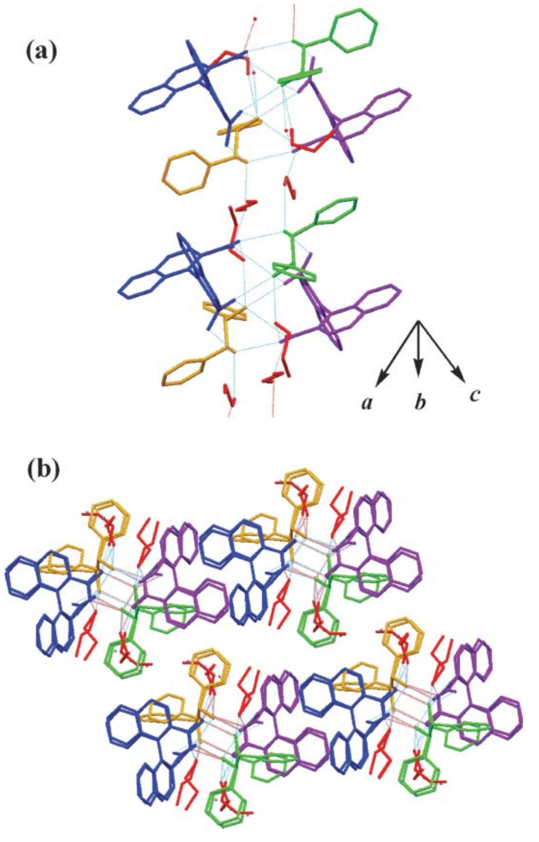

Fig. 2 Crystal structure of complex **II**. (a) Column structure. (b) Packing structure of column structure.

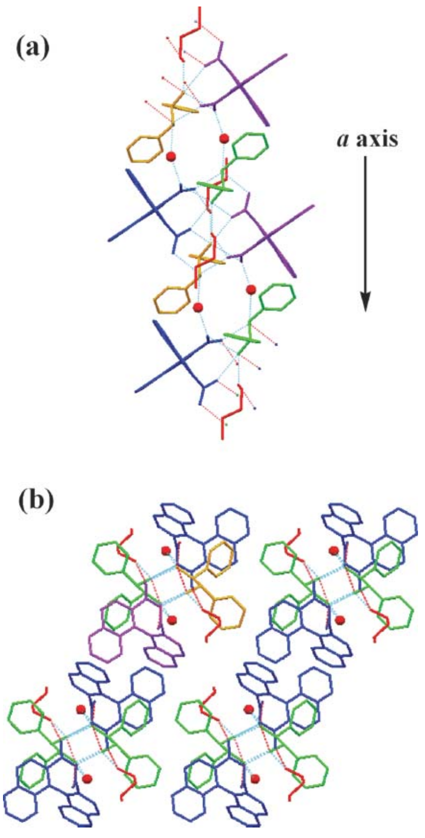

Fig. 3 Crystal structure of complex **IV**. (a) Column structure is parallel to the *a* axis. (b) Packing structure observed along the *a* axis.

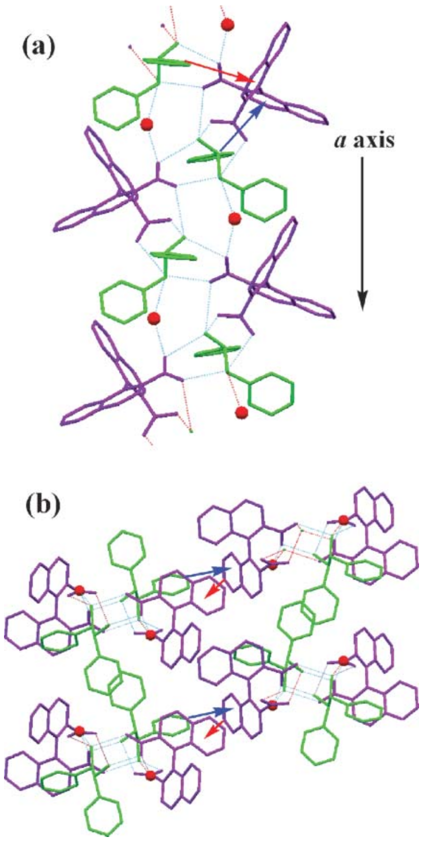

Fig. 4 Crystal structure of complex **V**. (a) Column structure is parallel to the *a* axis. (b) Packing structure observed along the *a* axis. Red and blue arrows show naphthalene–naphthalene edge-to-face and benzene–naphthalene edge-to-face interactions, respectively.

2_1-helical column, a continuous ionic-bonded helical network maintains the column frame. In one batch, chiral crystals with opposite chirality to crystal **V** were obtained.[8] These results suggest that this system can be induced and controlled to form conglomerates by changing the amount of water in the crystallization solvent.

Similarly, when *n*-PrOH including moisture of 30% and *n*-PenOH solution saturated by water were used as crystallization solvents, chiral crystals **V** and crystals with opposite chirality were obtained in all cases as expected. Although pure water was tried as a crystallization solvent, both *rac*-**1** and *rac*-**2** had poor solubility.

In chiral crystal **V**, a continuous ionic-bonded helical network maintains the columnar frame. On the other hand, in *rac*-crystals **I–III**, the ionic-bonded network is not continuous because it is interrupted by the inclusion of *n*-alkyl alcohols. This shows that the 2_1-helical column constructing chiral crystal **V** is stronger than the column of *rac*-crystals **I–III**. That is, the 2_1-helical column structure maintained by water molecules is more easily formed than the column maintained by *n*-alkyl alcohol molecules. Therefore, the 2_1-helical column is formed by using a crystallization solvent saturated by water. Moreover, chiral crystal **V** has naphthalene–naphthalene edge-to-face and benzene–naphthalene edge-to-face interactions (2.49 and 2.66 Å; Fig. 4(b), indicated by red and blue arrows, respectively) between columns. On the other hand, these interactions are not observed in *rac*-crystals **I** and **II**. Although naphthalene–naphthalene edge-to-face interactions between columns (2.82 Å; see ESI,† Fig. S1(b), indicated by red arrows) are also observed in *rac*-crystal **III**, the number and distance of interactions is fewer and longer than that of chiral crystal **V**. It is thought that those interactions cause the self-assembly of the 2_1-helical column with the same helical chirality, forming chiral crystal **V**.

In conclusion, by combining *rac*-**1** with *rac*-**2**, the novel spontaneous resolution system of *rac*-**1** was developed. In this system, both *rac*-**1** and *rac*-**2** can be enantioselectively resolved at the same time. Moreover, the formation of conglomarate crystals is induced by the presence of water in the crystallization solvent. This work is expected to be useful in coincidently obtaining chiral **1** and **2** on an industrial scale and designing new types of spontaneous resolution systems.

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Notes and references

‡ *Crystallographic data*: For **I**: $2C_{14}H_{18}N_2{\cdot}2C_{22}H_{12}O_4{\cdot}4C_4H_{10}O$, M = 1405.72, monoclinic, space group *C*2/*c*, a = 55.014(3), b = 11.3600(1), c = 27.971(2) Å, β = 119.229(1)°, U = 15255(2) Å^3, Z = 8, D_c = 1.224 g cm^{-3}, μ(Mo-Kα) = 0.081 mm^{-1}, 46044 reflections measured, 17465 unique, final $R(F^2)$ = 0.0786 using 9136 reflections with $I > 2.0\sigma(I)$, R(all data) = 0.1584, T = 120(2) K. CCDC 659150. For **II**: $2C_{14}H_{18}N_2{\cdot}2C_{22}H_{12}O_4{\cdot}4C_3H_8O$, M = 1349.62, triclinic, space group $P\bar{1}$, a = 14.094(1), b = 16.039(1), c = 16.595(1) Å, α = 100.747(1), β = 98.764(1), γ = 96.318(1)°, U = 3605.0(4) Å^3, Z = 2, D_c = 1.243 g cm^{-3}, μ(Mo-Kα) = 0.083 mm^{-1}, 32076 reflections measured, 16190 unique, final $R(F^2)$ = 0.0779 using 11639 reflections with $I > 2.0\sigma(I)$, R(all data) = 0.1075, T = 120(2) K. CCDC 659152. For III: $C_{14}H_{18}N_2{\cdot}C_{22}H_{12}O_4{\cdot}2C_5H_{12}O$, M = 730.91, triclinic, space group $P\bar{1}$, a = 11.361(1), b = 14.185(1), c = 14.231(1) Å, α = 115.435(1), β = 102.599(1), γ = 90.983(1)°, U = 2005.2(2) Å^3, Z = 2, D_c = 1.211 g cm^{-3}, μ(Mo-Kα) = 0.079 mm^{-1}, 17817 reflections measured, 9005 unique, final $R(F^2)$ = 0.0536 using 6635 reflections with $I > 2.0\sigma(I)$, R(all data) = 0.0788, T = 120(2) K. CCDC 652859. For **IV**: $C_{14}H_{18}N_2{\cdot}C_{22}H_{12}O_4{\cdot}C_4H_{10}O{\cdot}H_2O$, M = 646.76, triclinic, space group $P\bar{1}$, a = 11.374(3), b = 13.900(3), c = 13.903(3) Å, α = 111.011(4), β = 99.866(4), γ = 113.279(4)°, U = 1754.7(7) Å^3, Z = 2, D_c = 1.224 g cm^{-3}, μ(Mo-Kα) = 0.082 mm^{-1}, 14899 reflections measured, 7691 unique, final $R(F^2)$ = 0.1350 using 3874 reflections with $I > 2.0\sigma(I)$, R(all data) = 0.2361, T = 120(2) K. CCDC 659151. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b714226a

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4 A mixture of (*R*)-**1** (8 mg, 0.024 mmol), (*S*)-**1** (8 mg, 0.024 mmol), (1*R*,2*R*)-**2** (5 mg, 0.024 mmol), and (1*S*,2*S*)-**2** (5 mg, 0.024 mmol) were dissolved in *n*-alkyl alcohol (2 mL) and left to stand at room temperature. After a few days, several colorless crystals were produced.

5 This weight is the total crop of obtained crystals in one batch.

6 (*R*)-**1**, (*S*)-**1**, (1*R*,2*R*)-**2** and (1*S*,2*S*)-**2** molecules are shown by blue, purple, green and orange molecules, respectively. Included *n*-alkyl alcohol is shown in red.

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8 The weight which is the total crop of obtained both chiral crystals in one batch is 18 mg.