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# A new host 2,3,6,7,10,11-hexahydroxy triphenylene which forms chiral inclusion crystalline lattice: X-ray structural study of the chiral crystalline lattice

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ABSTRACT: The title compound was found to form an inclusion complex crystal with various kinds of guests. It was also found that crystalline lattice of some inclusion complex is chiral. By an enantioselective inclusion complexation in the chiral lattice, the racemic guest was resolved. The chiral crystalline lattice was studied by X-ray analysis. Solid-state synthesis of the title host compound is also described. Copyright © 2000 John Wiley & Sons, Ltd.

KEYWORDS: inclusion crystal; chiral crystal; hexahydroxytriphenylene; optical resolution

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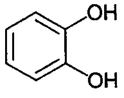
It is known that some achiral molecules are arranged in a chiral form in their own crystals and their solid-state reaction gives chiral products.[1] In the case that achiral molecules cannot arrange in a chiral form in their own crystals, a chiral host molecule assists to arrange these achiral molecules in a chiral form in their host–guest inclusion complex crystal which upon solid-state reaction gives chiral product.[2] We have been looking for an achiral host compound which arranges in a chiral form to form a chiral inclusion crystalline lattice and have finally found that the title achiral compound **2** forms chiral crystalline lattice in which guest molecules are accommodated. X-ray analysis of a chiral 1:3 inclusion compound of **2** with cyclopentanone showed that the chirality is induced by the formation of chiral helix of **2** molecules through their hydrogen bond network.

Although the title compound **2** is important as a material,[3] its most reasonable synthetic method, trimerization of catechol **1** in solution, is not effective. Heating of a solution of **1** in the presence of $FeCl_3$ gives **2** as a brown crystal in 2% yield. This synthetic method is rather complicated and gives colored impure **2** in low yield. Although a convenient trimerization method of catechol dialkyl ether in the presence of $MoCl_5$ in $CH_2Cl_2$ to give hexaalkyl ether of **2** has been reported,[4] its conversion to **2** by an ether bond cleavage is very difficult. We report a simple synthetic method in the solid state which gives colorless **2** in relatively high yield. We also report that **2** shows inclusion ability for various kinds of guest compounds, and that **2** forms achiral inclusion crystalline lattice with some guest molecules. The chiral structure was proven by measurement of CD spectra in Nujol mull and X-ray crystal structure analysis for a 1:3 inclusion complex of **2** with cyclopentanone.

Previously we have reported a simple but very effective synthetic method of 2,2′-dihydroxy-1,1′-binaphthyl by the solid-state coupling reaction of 2-naphthol in the presence of $FeCl_3 \cdot 6H_2O$ under ultrasonic irradiation. We found this solid-state synthetic method is applicable to the trimerization reaction of **1** to **2**. A mixture of powdered **1** and $FeCl_3 \cdot 6H_2O$ was irradiated with ultrasound (28 kHz) for 24 h, and the reaction mixture was worked up to give **2** as brown crystals in 37% yield. The colored product contained quinoid derivatives of **2** and was difficult to purify to get a



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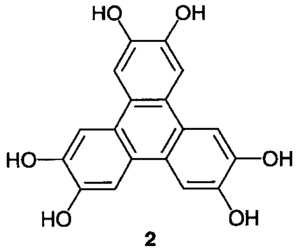

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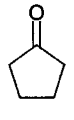

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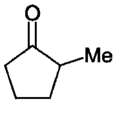

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**Table 1.** Host–guest ratio of inclusion complexes of 2[a]

| Guest | host/guest[b] |
|---|---|
| *n*-PrOH | 1:3 |
| *i*-PrOH | 1:2[c] |
| *n*-BuOH | 1:3 |
| Cyclopentanol | 1:3 |
| Cyclohexanol | 1:2 |
| Acetone | nc |
| Acetonylacetone | 2:3 |
| Cyclopentanone | 1:3[c] |
| Cyclopentanone | 1:4:$H_2O$ |
| Cyclopentenone | 1:3[c] |
| 2-Methylcyclopentanone | 1:3[c] |
| 3-Methylcyclopentanone | 1:3 |
| Cyclohexenone | 1:3[c] |
| Cyclohexanone | 1:3 |
| 2-Methylcyclohexanone | 1:3 |
| 3-Methylcyclohexanone | 1:3 |
| $\gamma$-Butyrolactone | 1:3 |
| THF | 1:2 |
| 1,4-dioxane | 1:2 |
| DMF | 1:2 |

[a] All melting points are unclear.
[b] The ratio was determined by $^1$H-NMR or TG measurement.
[c] Chiral inclusion compound.

colorless sample by usual methods such as recrystallization from the solvent. Purification of **2** by inclusion complexation with a guest compound was developed. For example, recrystallizations of **2** from cyclopentanone **3** gave a **2**·cyclopentanone 1:3 inclusion complex **4** as colorless prisms. Evaporation of the cyclopentanone guest molecules from **4** gave pure **2** as colorless crystals in 16% yield (m.p. 387 °C).

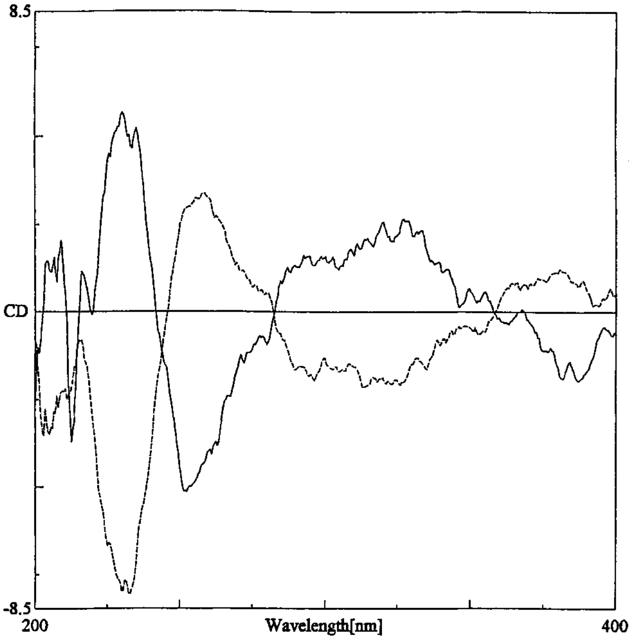

**Figure 2.** CD spectra of two enantiomeric 1:3 inclusion crystals of **2** with 2-cyclopentenone in Nujol mulls

When **2** is recrystallized from usual solvents, inclusion crystals are formed, containing the solvent molecules in host-guest ratios as indicated in Table 1. Of these inclusion crystals, those with achiral guests, such as *i*-PrOH, cyclopentanone, 2-cyclopentenone and 2-cyclohexenone, are found to be chiral by measurement of the CD spectra in Nujol mulls.[5] In each case, one piece of the inclusion crystal showed (+)-Cotton effect and the other piece of crystal showed (−)-Cotton effect, and these two

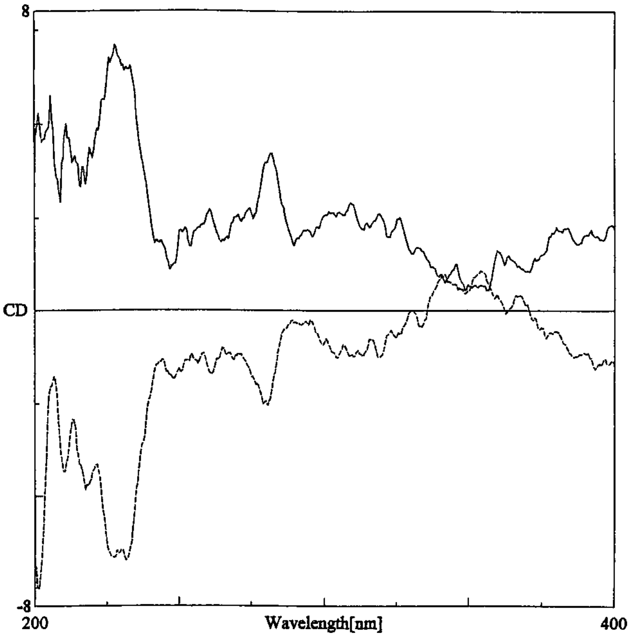

**Figure 1.** CD spectra of two enantiomeric 1:3 inclusion crystals of **2** with cyclopentanone in Nujol mulls

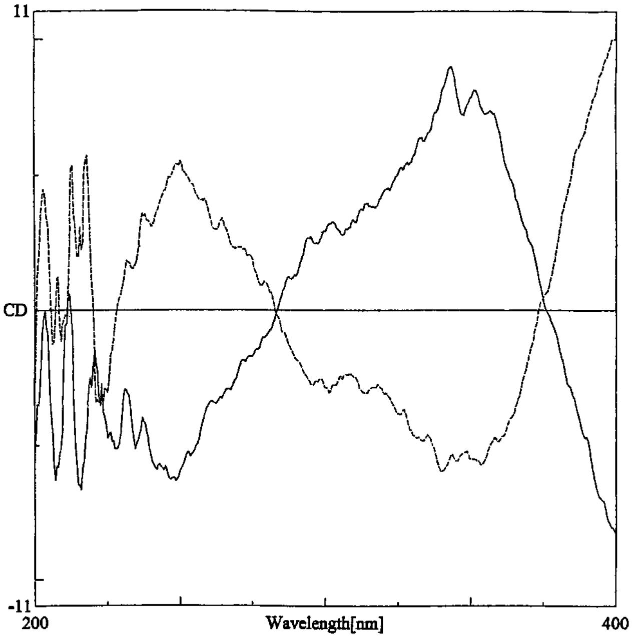

**Figure 3.** CD spectra of two enantiomeric 1:3 inclusion crystals of **2** with 2-cyclohexenone in Nujol mulls

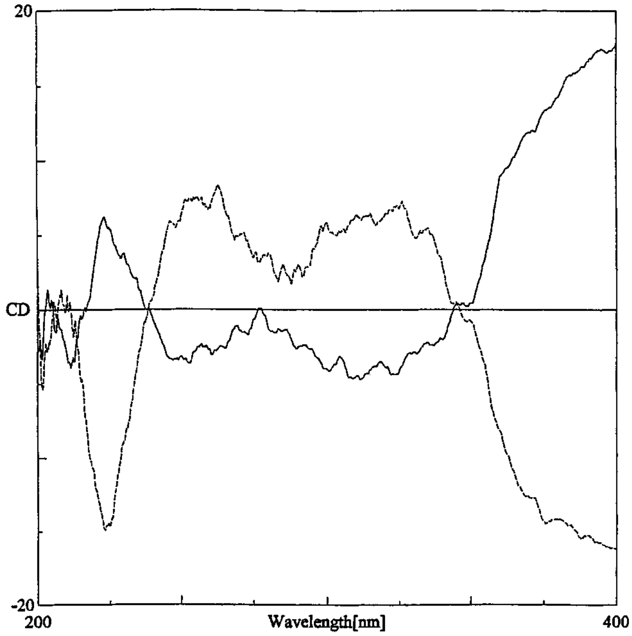

**Figure 4.** CD spectra of two enantiomeric 1:3 inclusion crystals of **2** with 2-methylcyclopentanone in Nujol mulls

showed nicely mirror imaged spectra, as shown in Figs 1–4. It has been well established that chirality in the crystalline state can easily be detected by measurement of CD spectra in Nujol mulls. In order to clarify the reason why achiral host molecules of **2** form chiral crystalline lattice with achiral guest molecules, the X-ray crystal structure of **4** was studied. Interestingly, however, inclusion complex **5** of **2** with cyclopentanone and $H_2O$ in 1:4:1 is achiral. The X-ray crystal structure of **5** was also studied.

Figure 5 illustrates the conformation of **4** with the hydrogen bonding interactions between compound **2** and cyclopentanone. The hydroxyl groups, O3-H, O9-H and O15-H, make intramolecular hydrogen bonds as donors with O4, O10 and O16, respectively. The carbonyl oxygens of cyclopentanones, O21, O31 and O41, act as acceptors in hydrogen bonds from O3-H, O4-H and O9-H, respectively. Thus, O3-H and O9-H are involved in bifurcated hydrogen bonds as shown in Fig. 5. The compound **2** in **4** is roughly flat [within 0.14 (1) Å]. However, the molecule is distorted from the planarity because of the steric repulsion between

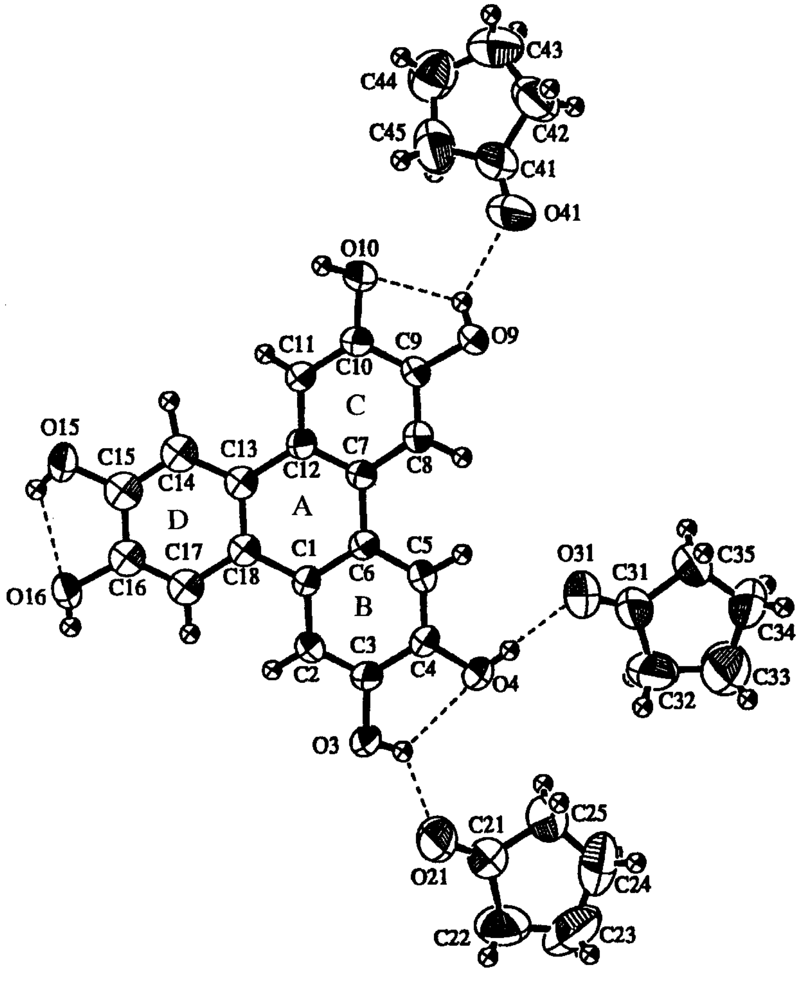

**Figure 5.** Perspective plot of complex (**4**) showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level except for hydrogen atoms

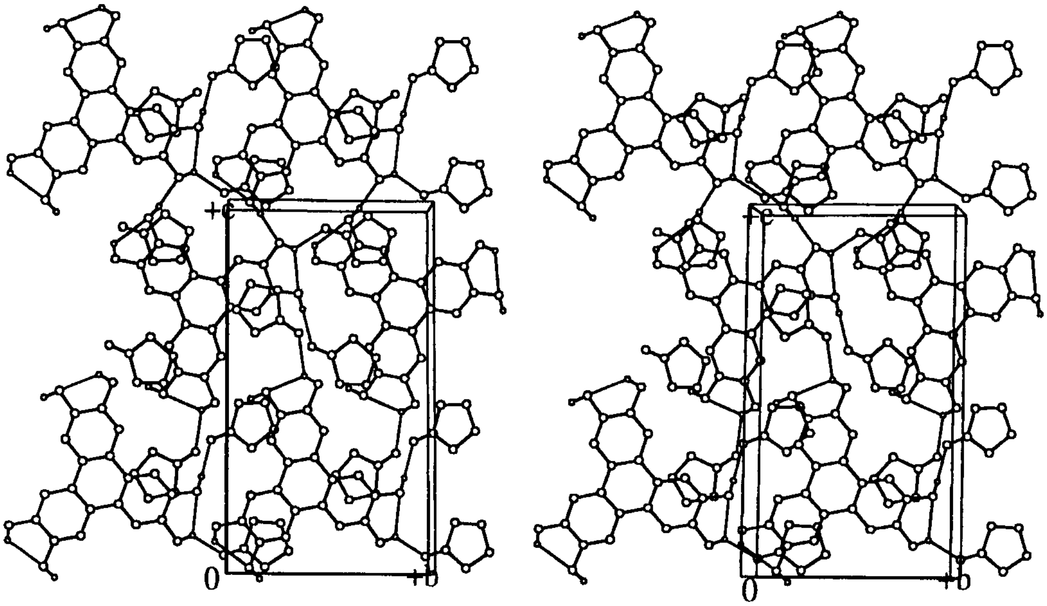

**Figure 6.** Molecular packing and hydrogen bonding of complex (**4**) viewed down the *a*-axis. The hydrogen bonds are shown by thin lines

hydrogens on carbon atoms at peri-positions. The rings B and C are bent down and up from the central ring A, and the ring D is twisted against the ring A with the dihedral angles of C5–C6–C7–C8 = −2.8(6)°, C11–C12–C13–C14 = 2.2(6)°, and C2–C1–C18–C17 = 2.4(5)°. The three joint bonds which link the catechol molecules and the central benzene ring are lengthened by about 0.064 Å compared with the other bonds of the ring A in order to reduce the steric repulsion between the hydrogen atoms: C6–C7 = 1.469(5), C12–C13 = 1.477(5), C1–C18 = 1.469(5), C1–C6 = 1.406(5), C7–C12 = 1.411(6) and C13–C18 = 1.407(5) Å. The molecular packing and the hydrogen bonding scheme of **4** are shown in Fig. 6. There are two major hydrogen bond sequences. One comprises an infinite chain: ---O9-H---O10-H---O9-H--- with an additional O9-H---O41. The other system consists of a five-link finite chain: O15-H---O16-H---O3H---O4-H---O31 with an additional O3-H---O21. The intermolecular hydrogen bonds, O10-H---O9 and O16-H---O3, link the host molecules (2) around the $2_1$ screw axes passing through $x = 0$ and $z = 1/2$, and $x = -1/2$ and $z = 0$ (or 1), respectively, indicating that the molecules **2** are connected by two-dimensional hydrogen bond networks. These networks are parallel to the (1 0 −1) plane and cyclopentanone molecules occupy the space between these networks.

Figure 7 illustrates the conformation of **5** with the hydrogen bonding interactions between the compound **2**, and four cyclopentanones and a water molecule. The hydroxyl groups, O3-H, O9-H and O15-H, make intramolecular hydrogen bonds as donors with O4, O10 and O16, similarly to those shown in Fig. 5. The O3-H, O4-H and O16-H act as hydrogen bonding donors to interact with the carbonyl oxygens, O21, O31 and O51, respectively. The water molecule (O1) acts as an acceptor and a donor to bridge O9-H and O41. The compound **2** in **5** shows slightly larger distortion than that observed in **4** with the maximum deviation of 0.267 Å from the mean plane. The rings B′ and D′ are bent up and down from the central ring A′, and the ring C′ is twisted against the ring A with the dihedral angles of C5–C6–C7–C8 = 7.6(5)°, C11–C12–C13–C14 = 3.2(4)°, and C2–C1–C18–C17 = −5.1(5)°. The three joint bonds between the catechol moieties and the central benzene ring are lengthened by about 0.055 Å compared with the other three bonds of the ring A in order to reduce the steric repulsion between hydrogens on carbon atoms at peri-positions: C6–C7 = 1.465(4), C12–C13 = 1.464(4), C1–C18 =1.466(4), C1–C6 = 1.412(4), C7–C12 = 1.404(6) and C13–C18 = 1.413(4) Å.

The molecular packing and the hydrogen bonding scheme of **5** is shown in Fig. 8. There are two major hydrogen bond sequences. One comprises a finite chain: O10-H---O3-H---O4-H---O31 with a branched hydrogen bond, O3-H---O21. The other system consists of a five-link cyclic system: O15-H---O9-H---O1-H---O51---H-O16---H-O15 with a branch, O3-H---O21. The hydroxyl groups, O3-H and O15-H are included in the bifurcated hydrogen bonds. The O9-H was judged not to be included in the intramolecular hydrogen bond with O10 because of the long O---H distance [2.47(4) Å] and the large deviation from the linearity of O-H---O [102(4)°], although there should be a weak interaction between O9-H and O10.

The intermolecular hydrogen bond, O15-H---O9, links the host molecules (**2**) along the *b*-axis, to form a chiral arrangement of **2** along the $2_1$ screw axes. This helical arrangement of **2** is connected to the other helical one of

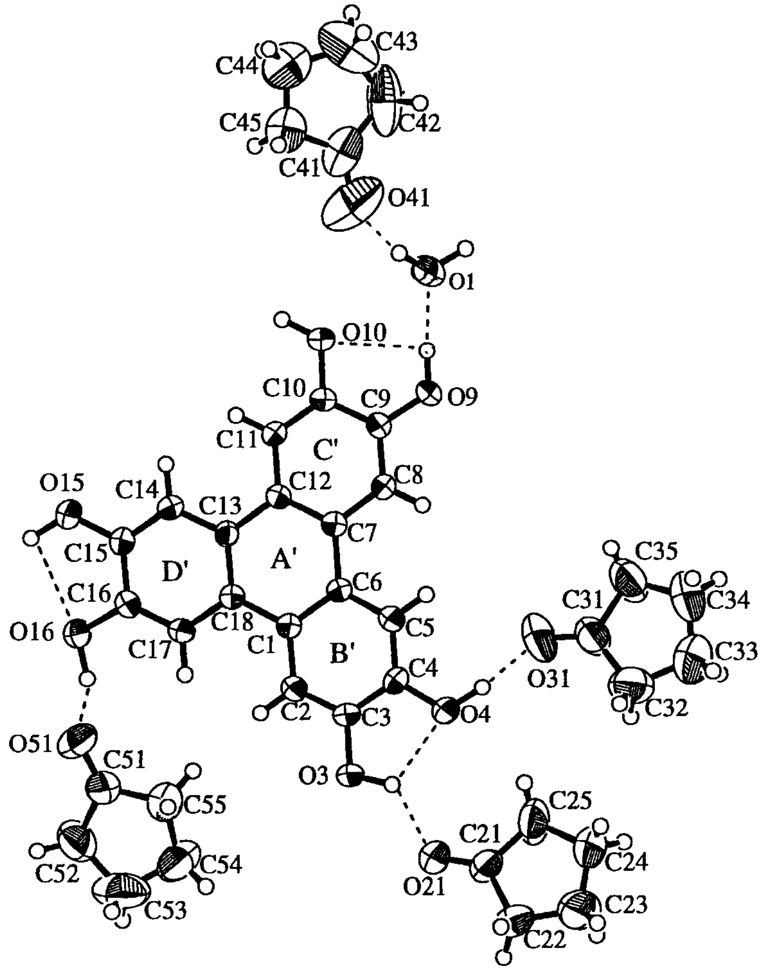

**Figure 7.** Perspective plot of complex (**5**) showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level except for hydrogen atoms

the opposite chirality through the hydrogen bond, O10-H---O3, to give an achiral hydrogen bond networks in two-dimension. These networks are parallel to the *bc* plane and cyclopentanone molecules occupy the space between these networks similarly to that found in complex **4**.

In solution, the host molecules might make three intramolecular hydrogen bonds for entropy reasons and interact with as many guests (cyclopentanone) as possible to make transient complexes like that shown in Figs 5 and 7. When the concentration of the solution goes up, the host molecules can interact with other hosts by using the free O-H groups formed by releasing cyclopentanones to expand the hydrogen bond network. The network will be reasonably planar since the molecule **2** and cyclopentanone are approximately planar. The right-handed and left-handed short helices are formed at equal weight. It seems that the alternative arrangements of right- and left-handed helixes are energetically favorable in **5**, while there are two ways: one is stacking of the networks with the same chirality to form a chiral crystal, and the other is the alternative stacking of the networks with the opposite chirality. In the inclusion complex of **4**, the two-dimensional networks of same chirality stack with a larger van der Waal stabilization than those of opposite chirality.

We cannot see the reason why the inclusion complex between the molecules **2** and cyclopentanones gives the optically resolved crystal (**4**) on the one hand and the achiral crystal (**5**) on the other. However, there are some interesting features in these crystals. The predominant factor to determine the molecular arrangements is extensive hydrogen bonds in the crystal. The hosts (**2**) and guests (cyclopentanone and water in **5**) which are hydrogen bonded in a two-dimensional way, roughly arrange in one plane. In the crystal **4**, the molecules on the plane are related only by $2_1$ screw axes, indicating that this plane is chiral, while in the crystal **5**, the molecules are related by $2_1$ screw axes and center of symmetries, resulting in the achiral plane. The planes just stack one by one to make a chiral crystal in **4** and an achiral crystal in **5**.

When a racemic guest compound is accommodated enantioselectively in the chiral crystalline lattice formed

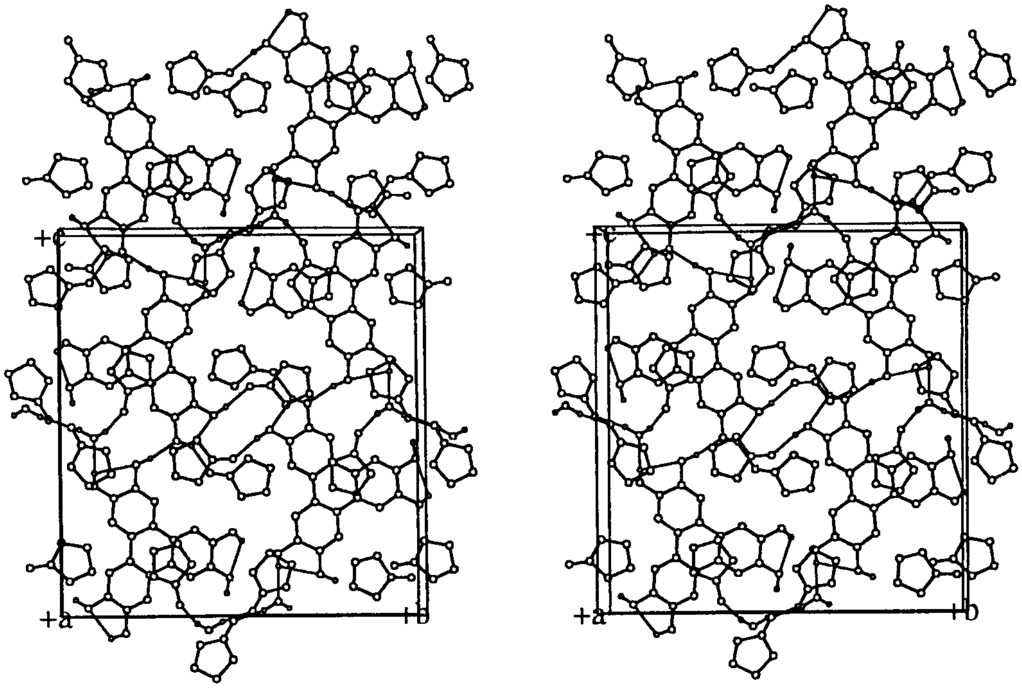

**Figure 8.** Molecular packing and hydrogen bonding of complex (**5**) viewed down the *a*-axis. The hydrogen bonds are shown by thin lines

by the chiral arrangement of the achiral host **2**, optical resolution without using any chiral source becomes possible. Recrystallization of **2** from 2-methylcyclopentanone **6** gave their 1:3 inclusion crystals. One piece of the crystal showed (+)-Cotton effect at around 300 nm in the solid state CD spectrum, and the other piece of crystal showed (−)-Cotton effect at the same region (Fig. 4). Heating of the former and latter crystals *in vacuo* gave (+)-**6** of 34% ee and (−)-**6** of 37% ee, respectively by distillation. It is clear that chiral recognition of **6** occurs in the chiral crystalline lattice formed by a chiral arrangement of the achiral **2** molecules. However, in the inclusion crystalline lattice of **2** with 2- and 3-methylcyclohexanone, the **2** molecules are not arranged in chiral form and these racemic guests are not resolved (Table 1).

## EXPERIMENTAL

### Synthesis of 2,3,6,7,10,11-hexahydroxytriphenylene (2) in the solid state

A mixture of finely powdered catecol (**1** 20 g, 0.182 mol) and FeCl$_3$6H$_2$O (196.8 g, 0.728 mol) was irradiated by ultrasound for 24 h. The reaction mixture was washed with dilute HCl and water, and the dried product was extracted with hot cyclopentanone to give crude **2** (10 g, 51% yield). Recrystallization of the crude **2** from cyclopentanone gave a 1:1 inclusion complex of **2** with cyclopentanone (7.2 g) from which pure **2** (m.p. 387 °C, 4 g, 20% yield) was obtained by evaporation of the guest compound. $\nu$OH:2485 and 3425 cm$^{-1}$; $^1$H NMR (CDCl$_3$): $\delta$ 7.7 (s, OH, 6H) and 8.7 (s, Ar, 6H). Found: C, 66.67; H, 3.54%. Calculated for C$_{18}$H$_{12}$O$_6$: C, 66.67%, H, 3.73%.

### Preparation of inclusion complexes of 2 with guest compounds

Inclusion complex was prepared by recrystallization of **2** from the guest compound. For example, recrystallization of **2** from cyclopentanone gave a 1:3 complex of **2** with the guest as colorless prisms in a quantitative yield. $\nu$OH:3270 cm$^{-1}$, $\nu$C=O 1620 cm$^{-1}$; $^1$H NMR: $\delta$ 2.0 (m, CH$_2$, 12H), 2.2 (m, CH$_2$, 12H), 7.7 (s, OH, 6H) and 8.7 (s, Ar. 6H). Found: C, 68.75; H, 6.34%. Calculated for C$_{33}$H$_{36}$O$_9$: C, 68.74%, H, 6.29%. By the same procedure, inclusion complexes indicated in Table 1 were prepared. All complexes did not show a clear melting point. The host:guest ratio was determined by $^1$H NMR or TG measurement. By measurement of CD spectra of the inclusion crystals in Nujol mulls, it was determined whether the inclusion crystal is chiral or not. These data are shown in Table 1.

### Optical resolution of 2-methylcyclopentanone by inclusion complexation with 2

Recrystallization of **2** from 2-methylcyclopentanone (**6**) gave their 1:3 inclusion complex crystals (**7**). Heating of one piece of the crystal which shows a (+)-Cotton effect in the region of 300 nm *in vacuo* gave (+)-**6** of 34% ee $[\alpha]_D + 17.2°$ (*c* 0.06, MeOH) by distillation. Heating of the other piece of crystal which shows a (−)-Cotton effect in the region of 300 nm *in vacuo* gave (−)-**6** of 37% ee $[\alpha]_D -18.5°$ (*c* 0.07, MeOH).

## Crystallographic studies

The X-ray data were collected on a Rigaku AFC7R four-circle diffractometer, using $\omega/2\theta$ scan mode. All calculations were performed with the crystallographic software package teXsan (Molecular Structure Corporation, 1985, 1992). The structure was solved by direct methods[6] and subsequent Fourier recycling,[7] and refined by full-matrix least-squares refinement against $|F|$, with all hydrogen atoms fixed at the calculated positions except hydroxy hydrogens for **4**. No absorption corrections were applied. Full X-ray data for compounds **4** and **5** are available from the epoc website at http://www.wiley.com/epoc/

Crystal data for **4**: $C_{18}H_{12}O_6 \cdot 3C_5H_8O$, monoclinic, space group $P2_1$, Mo$K\alpha$ radiation, $2\theta$max = 50°, $a = 7.986(3)$, $b = 10.161(2)$, $c = 18.554(2)$ Å, $\beta = 99.84(1)°$, $V = 1483.5(5)$ Å$^3$. $Dc = 1.291$ g cm$^{-3}$, μ = 0.94 cm$^{-1}$, 2708 independent intensities, 2175 observed $[l > 1.00\sigma\ (l)]$, $T = 296$ K, weighting scheme = $1/[\sigma^2\ (Fo)^2 + (0.025)^2\ Fo^2]^{-1}$, $R = 0.058$, $R_w = 0.075$, GOF = 2.08, maximum residual electron density 0.33 e Å$^{-3}$.

Crystal data for **5**: $C_{18}H_{12}O_6 \cdot 4C_5H_8O \cdot H_2O$, monoclinic, space group $P2_1/c$, Mo$K\alpha$ radiation, $a = 7.603(7)$, $b = 20.937(3)$, $c = 22.245(3)$ Å, $\beta = 91.85(3)°$, $V = 3539(3)$ Å$^3$, $Dc = 1.274$ g cm$^{-3}$, μ = 0.93 cm$^{-1}$, $2\theta$ max = 50°, 6423 independent intensities, 3930 observed $[l > 1.00\sigma\ (l)]$, $T = 296$ K, weighting scheme = $1/[\sigma^2\ (Fo)^2 + (0.03)^2\ Fo^2]^{-1}$, $R = 0.071$, $R_w = 0.082$, GOF = 1.74, maximum residual electron density 0.19 e Å$^{-3}$.

## REFERENCES

1. F. Toda, H. Miyamoto, H. Koshima and Z. Urbanczyk-Lipkowska, *J. Org. Chem.*, **62**, 9261 (1997).
2. F. Toda, *Synlett*, 303 (1993); F. Toda, *Acc. Chem. Res.*, **28**, 480 (1995).
3. S. Chandrasekhar, *Liq. Cryst.*, **14,** 3 (1993).
4. S. Kumar and M. Manickam, *J. Chem. Soc., Chem. Commun.*, 1615 (1997).
5. F. Toda, H. Miyamoto, S. Kikuchi, R. Kuroda and F. Nagami, *J. Am. Chem. Soc.*, **118**, 11315 (1996); F. Toda, H. Miyamoto and K. Knemoto, *J. Am. Chem. Soc.*, **61**, 6490 (1996).
6. G. M. Sheldrick *Crystallographic Computing 3* (Eds G. M. Sheldrick C. Kruger Goddard) Oxford University Press, Oxford, 175 (1985).
7. P. T. Beurskens, G. Admiraal, G. Beurskens, W. P. Bosman, R. de Gelder, R. Israel, J. M. M. Smits, The DIRDIF-94 program system, Technical Report of the Crystallography Laboratory, University of Nijmegen, The Netherlands, 1994.