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Crystal Habit of a Novel Host-Guest Complex Composed of 1,1,2,2-Tetrakis(4-hydroxyphenyl)ethane and 5-Chloro-2-methyl-4-isothiazolin-3-one

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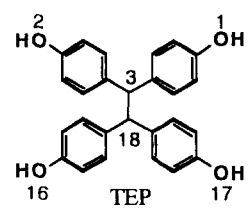
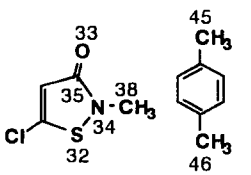
Abstract: *The crystal structure of the inclusion complex of 1,1,2,2-tetrakis(4-hydroxyphenyl)ethane (TEP) with 5-chloro-2-methyl-4-isothiazolin-3-one (CMI) is characterized as layered molecular sheets composed of hydrogen-bonded polyphenol chains. CMI molecules bind to TEP by S•••π electrostatic interaction and by O-H•••O=C hydrogen bonding to form a crystalline complex of TEP•2CMI, which behaves as a unique host with different recognition from TEP.* © 1997 Elsevier Science Ltd.

In various technological fields, especially in selective separation, chemical stabilization, solidification, topochemistry and the like, characteristic host-guest complex crystallinity is favored by material scientists.[2,3] To design crystalline host-guest complexation, molecules that have at least one phenolic hydroxyl group have been studied as host compounds.[2,4] We have previously reported that 1,1,2,2-tetrakis(4-hydroxyphenyl)ethane (TEP) makes a crystalline inclusion complex with various n-donors, and that the branching phenol groups are extremely effective as hydrogen bonding sites to construct such a systematic structure.[5,6] Recently, during the investigation of controlling the release and activity of bioactive materials, we found that TEP includes an industrial biocide, 5-chloro-2-methyl-4-isothiazolin-3-one (CMI)[7], and forms a novel crystalline complex of TEP•2CMI (formal including ratio of TEP and CMI, 1:2). This inclusion complex gradually dissociates into its components in an aqueous environment and is expected to be used as a long-lived biocide.[8] In this paper, we wish to report the crystal structure of the inclusion complex, TEP•2CMI, and its unique properties.



TEP



CMI *p*-xylene

The TEP•2CMI complex was simply formed by crystallization in methanol solution containing TEP and CMI. The crystal structure was established by an X-ray crystallographic study.[9] The TEP•2CMI complex structure is build up with a characteristic pattern of a hydrogen bond network (Figure 1), being different from that of the TEP•methanol complex[6a] previously reported. One TEP molecule bonds to four other TEP molecules by intermolecular hydrogen bonding. The oxygen O(1) [or O(16)] bonds to the oxygen O(17) [or O(2)] on the adjacent TEP molecule as a hydrogen donor [O(1)-O(17) : 2.88 Å] and makes the TEP molecules extend in molecular sheets parallel to the (100) plane with the hydrogen bond network. On the other hand, the oxygen O(17) [or O(2)] of TEP bonds to the carbonyl oxygen O(33) of the CMI [O(17)-O(33) : 2.64 Å] as a hydrogen donor. The shorter distance of 2.64 Å should be explained by some strong interaction between the TEP•2CMI molecular sheets. Two CMI molecules (Ca,Cb), which bind to each sheet by hydrogen bonds, alternately exist by piling up between the two phenol rings (Pa, Pb) of each sheet. These four ring planes (Pa-Cb-Ca-Pb in Figure 1) are almost parallel and the distance

between them is almost equal and *ca.* 3.5 Å. The sulfur S(32) of CMI exists in a certain position between the two phenol rings (Pa, Pc) of the TEP molecule, which is 3.63 and 3.65 Å away from a centroid of each phenol ring and is 4.04 Å away from the nitrogen N(34) of the adjacent CMI molecule. In the ^{13}C NMR spectra in the solid state using the CP/MAS (cross polarization/magic angle spinning) technique (Figure 5a)[10], the strong peak (at 32.05 ppm) assigned to the methyl carbon C(38) of CMI in the spectrum appeared 2.0 ppm downfield relative to free CMI (at 30.0 ppm).[11] From the results of MO calculations (Figure 2), the sulfur atom of CMI possesses a positive charge, and the carbons of the phenol ring and the nitrogen of CMI possess a negative charge.[12] The downfield shift of C(38) could be explained as an electric field effect produced by the S•••N electrostatic interaction between the adjacent CMI molecules. Accordingly, it is considered that there exists S•••π and S•••N electrostatic interactions between the phenol rings of TEP and the sulfurs of CMI, and between the adjacent CMI molecules,[13] which stabilize the characteristic crystal structure of layered molecular sheets.

Surprisingly, the TEP•2CMI complex exhibits the unique function of selective guest-exchange in aromatic solvents in which it is hardly soluble. When the TEP•2CMI powder was stirred in *p*-xylene for three days at 25 °C followed by filtration, it gave the new molecular complex of TEP•CMI•*p*-xylene (stoichiometric ratio, 1:1:1) (Entry 5 in Table 1), while no exchange was observed in other aromatic solvents (Entries 1, 2, 3 and 4 in Table 1). The selective guest-exchange from CMI to *p*-xylene was also observed in two-component xylene isomer mixtures (Entries 2 and 3 in Table 2). This guest-exchange is very curious because no crystalline complex has been observed between TEP itself and such aromatic hydrocarbons.[5] Actually, TEP•2CMI as a host selectivity recognizes the guest molecule of *p*-xylene to form another crystalline complex. Figure 3 shows the thermal analysis curves of TEP•2CMI and the

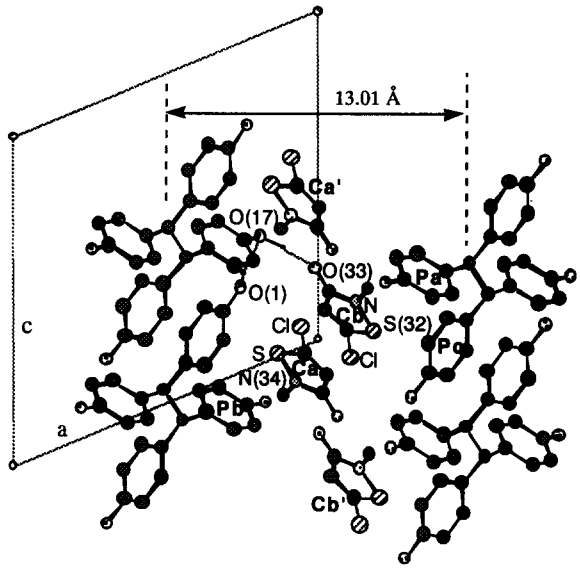


Figure 1 Packing diagram in the crystal of TEP•2CMI viewed along the *b* axis.

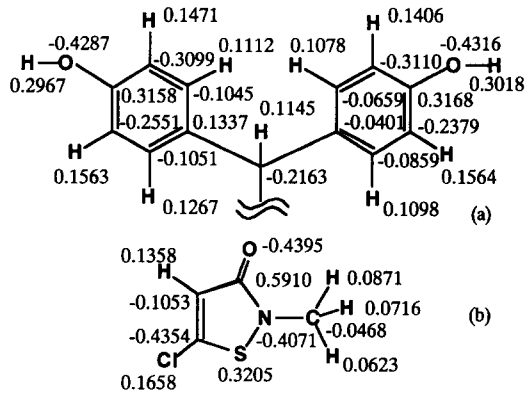


Figure 2 ESP charge of (a) TEP and (b) CMI.

Table 1 Guest-exchange of TEP•2CMI in aromatic solvents

Entry	aromatic solvent	TEP : CMI : solvent molar ratio[a]
1	benzene	1 : 2 : 0 [b]
2	toluene	1 : 2 : 0 [b]
3	*o*-xylene	1 : 2 : 0 [b]
4	*m*-xylene	1 : 2 : 0 [b]
5	*p*-xylene	1 : 1 : 1
6	*p*-xylene	2 : 3 : 1 [c]

a) Determined by NMR integration (in CD_3OD).
b) No exchange.
c) Incompletely exchanged sample formed by stirring for one day at 25 °C.

new complex TEP•CMI•*p*-xylene.[14] The guest-exchanged complex loses two-component guest molecules in two distinct steps. The first step starts at 104 °C and loses the *p*-xylene molecules (Peak A on the DTA curve), while the second step begins at 150 °C in near accordance with the decomposition behavior of TEP•2CMI to release the second guest, CMI (Peak B on the DTA curves). Thereafter, both complexes melt at temperatures from 289 to 329 °C to give rise to the sharper C peak on the DTA curve. From these observations, it is suggested that the TEP - TEP intermolecular interactions as well as the basic TEP molecular sheet structures are almost the same in both crystalline complexes.

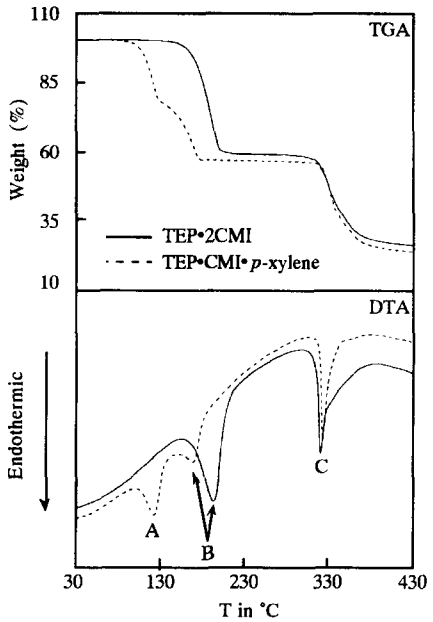


Figure 3 TGA and DTA thermograms for TEP•2CMI and TEP•CMI•*p*-xylene.

Table 2 Guest-exchange of TEP•2CMI in two-component solvent mixtures

Entry	solvent mixture (I / II) a)	TEP : CMI : I : II molar ratio b)
1	*o*-xylene / *m*-xylene	1 : 2 : 0 : 0 c)
2	*o*-xylene / *p*-xylene	1 : 1 : 0 : 1
3	*m*-xylene / *p*-xylene	1 : 1 : 0 : 1

a) Equimolar ratio.
b) Determined by NMR integration (in CD_3OD).
c) No exchange.

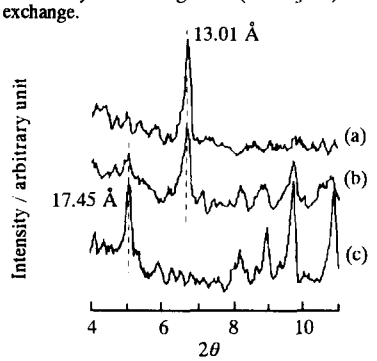


Figure 4. X-ray powder diffraction patterns of (a) TEP•2CMI, (b) incompletely exchanged sample[16] and (c) TEP•CMI•*p*-xylene at 300 K.

The characteristic change of a crystal structure was observed between the TEP•2CMI and TEP•CMI•*p*-xylene complexes. Figure 4 shows the powder X-ray diffraction patterns[15] of the two inclusion complexes of TEP•2CMI, TEP•CMI•*p*-xylene and the incompletely exchanged sample[16] which is regarded as the mixture of the TEP•2CMI and TEP•CMI•*p*-xylene crystals (Entry 6 in Table 1). The peak at $2\theta=6.79°$ (13.01 Å), which denotes the (100) plane spacing of TEP•2CMI (Figure 1), disappeared with the appearance of a new peak at $2\theta=5.06°$ (17.45 Å, about twice the (010) plane spacing of TEP•2CMI) as the guest-exchange progressed. The ^{13}C NMR spectra in the solid state using the CP/MAS technique[10] shows the changing of the environment around CMI (Figure 5). The upfield shift of the methyl carbon C(38) of CMI as the guest- exchange proceeds as shown in the two spectra, b) and c), can be attributed to a break up of the S•••N interaction. The downfield shift

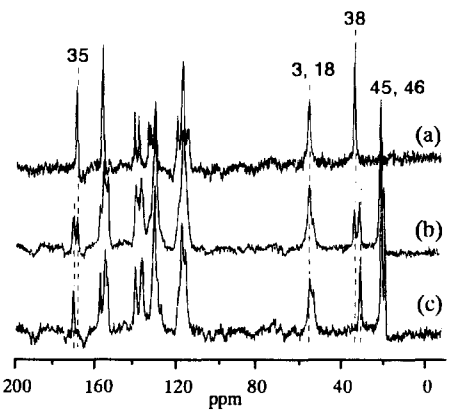


Figure 5. ^{13}C CP/MAS NMR spectra of (a) TEP•CMI, (b) incompletely exchanged sample[16] and (c) TEP•CMI•*p*-xylene at 300 K.

of the carbonyl carbon C(35) may be ascribed to the optimization of the hydrogen bonding interaction between the phenolic hydroxyl group of the TEP molecule and the CMI molecule by the disappearance of the S•••N interaction. All CMI molecules included in the resulting TEP•CMI•*p*-xylene are crystallographically equivalent as shown in the spectrum c). From these observations, it is considered that one of the CMI moieties stacked between the two phenol rings of the TEP•2CMI complex is exchanged by *p*-xylene moieties to form the TEP•CMI•*p*-xylene crystal structure, the unit cell of which is about twice as large the TEP•2CMI crystal along the *b* axis. Also, if the Ca and Cb' CMIs in Figure 1, and the Ca' and Cb CMIs of adjacent moieties along the *b* axis are exchanged by *p*-xylene, the structure would correspond with the analytical data. The selective CMI - *p*-xylene exchange might be explained by the good fit of the *p*-xylene molecule in the lattice void in the layered structure of the host complex.

In conclusion, host complex construction was proposed as a convenient method to get another new inclusion host with different functions without synthesizing a new compound host itself. We believe that the host TEP, which can form various polymorphic crystals with characteristic guests due to the branched hydrogen bonding sites, has great potential for the future design of molecular crystals with unique functions such as an intelligent recognition property.

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9. *Crystal data* for TEP•2CMI: asymmetric unit $C_{17}H_{15}NO_3SCl$, M = 348.50 (1/2 molecule), monoclinic, space group $P2_1/c$, a = 14.016(5), b = 9.064(3), c = 13.702(5) Å, β = 111.87(3) degree, V = 1616(1) Å^3, Z = 4, Dx = 1.43 g/cm^3, Crystal Size = 0.3×0.3×0.2 mm^3, Colorless plate, Linear absorption coefficient = 32.80 /cm (Cu Kα).
   Intensity data were measured at room temperature on a Mac Science MXC 18 4-circle diffractometer using Cu-Kα (λ = 1.54178 Å) radiation. max h,k,l 10, 10, 13. 3112 reflections measured, 2695 unique, 2603 were used in the analysis. The Mac Science Crystan-G program was used. Direct method, full-matrix least-squares refinement with all atoms. Hydrogen atom positions were calculated by difference Fourier synthesis. Final residuals R = 0.061, Rw = 0.110.
10. The ^{13}C CP/MAS NMR spectra were obtained on a Brucker AMX400 FT NMR spectrometer at a carbon frequency of 100.6 MHz with a sample spinning speed of 3.5 KHz. Spinning side bands have been eliminated from the spectrum by the TOSS method. Chemical shifts are given relative to an external Me_4Si standard, with glycine as a secondary standard (carboxyl carbon signal at 176.03 ppm).
11. CMI: $^{\delta}C$ (100 MHz, CDCl3) 30.0, 114.6, 145.5, and 167.1.
12. ESP (electrostatic potential) charge of CMI and TEP was calculated with MNDO using MOPAC Ver.6. The coordinates of the heavy atoms were taken from the crystal structure of TEP•2CMI. The positions of the hydrogens are optimized with PM3.
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14. Differential Thermal Analysis (DTA) and Thermal Gravimetric Analysis (TGA) were carried out using a Seiko TG/DTA 320 apparatus with a SSC/5200 thermal controller. Thermal analysis was carried out at a ramp rate of 20 °C/min. During the run, nitrogen was passed through the cell at 200 ml/min.
15. X-ray diffraction measurements by Cu-Kα beam were done using a Rigaku GEIGER FLEX RAD-2A operated at a 40 Kv, 20 mA condition.
16. The incompletely exchanged sample was formed by stirring the TEP•2CMI powder in *p*-xylene for one day at 25 °C.

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