Bull. Chem. Soc. Jpn., *72*, *1395—1401 (1999)*

Guest-Exchange and Guest-Release via Gas–Solid Contact in Clathrate Crystals Based on 2,5-Bis(9-hydroxyfluoren-9-yl)thieno[3,2-*b*]thiophene as a Host Compound

Koji Kuruma, Hiro-o Nakagawa, Tatsuro Imakubo, and Keiji Kobayashi*

Department of Chemistry, Graduate School of Arts and Sciences, The University of Tokyo,
Komaba, Meguro-ku, Tokyo 153-8902

(Received January 12, 1999)

The host compound 2,5-bis(9-hydroxyfluoren-9-yl)thieno[3,2-*b*]thiophene (**1**) afforded clathrate crystals represented by the formula (**1**)(guest)$_2$ for the guests EtOH, *n*-PrOH, and *i*-PrOH. Their X-ray crystal analyses revealed that the host frameworks are isostructural. The guest molecules, which are embedded in a channel-type of host void, were exchanged with other guest species by vapor contact. Upon exposure of these crystals to methanol vapor, guest elimination was induced to give the guest-free host **1** crystal [β-form, $P\bar{1}$, a = 13.111(4), b = 13.724(3), c = 9.766(3) Å, α = 97.11(2), β = 98.64(3), γ = 64.56(2)°, V = 1565.3(8) Å^3]. The crystal thus obtained is a polymorphic form of the guest-free **1** crystal which is obtained by recrystallization from dichloromethane [α-form, $P2_1/n$, a = 17.403(3), b = 20.654(4), c = 8.695(1) Å, β = 99.73(1)°, V = 3080.4(9) Å^3]. Once the guest molecules have been lost, gas-sorptive enclathration was not accomplished for either of these polymorphic host crystals; host **1** does not act as an apohost.

Considerable interest in crystalline host–guest inclusion complexes, generally designated as clathrate crystals,[1—3] has arisen over the past ten years from the viewpoints of chemical separations, topochemical reactions, or development of new solid materials. Clathrate crystals are usually prepared by recrystallization of host compounds from a solution including guest species or using a guest compound itself as a solvent. The sorptive formation of clathrates via contact with liquid[4] or vapor[5] of guest species has been also demonstrated for some host compounds that have been referred to as apohosts. A relevant example of apohosts is anthracenebisresorcinol host which has been investigated by Aoyama et al.[6] The apohost binds various guests in the same guest–host stoichiometry as in recrystallization. Recently we have demonstrated some novel guest exchange phenomena on gas-solid contact which are significantly different from the inclusion behavior in recrystallization. Thus, exposure of the clathrates to gaseous external guests brought about ternary clathrates as a result of site-selective guest accommodation at two independent guest sites in the host lattice.[7] This result prompted us to investigate clathrate-to-clathrate transformation in the solid-state by gas–solid contact, in particular for the host compounds which provide two independent sites of guest accommodation.

Recently we have explored a series of new host compounds for clathrate crystals, among which 2,5-bis(9-hydroxyfluoren-9-yl)thieno[3,2-*b*]thiophene (**1**)[8—11] was revealed to yield the clathrate crystals incorporating alcohols in a channel-type inclusion lattice.[12] Involvement of the channel seems to be advantageous for guest migration in the solid and hence for long-range cooperative reorganization of the crystal structure. Preliminary results have indicated that the clathrate represented by the formula (**1**)(EtOH)$_2$, enclathrating ethanol in the 1 : 2 host to guest ratio, undergoes guest exchange to afford (**1**)(*n*-PrOH)$_2$ on exposure to *n*-PrOH vapor.[12] Here we describe in detail such transformation of the clathrates induced by gas–solid contact along with the novel occurrence of the polymorphic crystals for guest-free **1** (Chart 1).

Results and Discussion

Isostructural Framework of the Host Molecules in (1)-(*n*-PrOH)$_2$, (1)(*i*-PrOH)$_2$, and (1)(EtOH)$_2$. Recrystallization of **1** from various solvents yielded the clathrate crystals, as given in Table 1. Among those, the host lattices of (**1**)-(*n*-PrOH)$_2$, (**1**)(*i*-PrOH)$_2$, and (**1**)(EtOH)$_2$ are isostructural with each other.[13] The crystal data of these three compounds are listed in Table 2. Their unit cell parameters are similar and the packing motif of the host molecules is analogous, as shown in Figs. 1 and 2. A channel-type of inclusion void is constructed along the *b* axis by the walls of the two crystallographically independent host molecules, in which the two

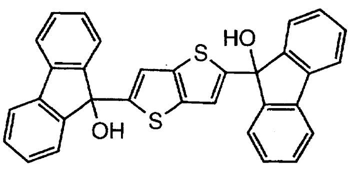

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Chart 1.

Table 1. Inclusion Properties of Host **1**. The Guest Ratio to a Host Molecule

Guest	Guest/Host	Guest	Guest/Host
MeOH	—	Acetone	2
EtOH	2	Ethyl acetate	2
n-PrOH	2	Diethyl ether	2
i-PrOH	2	Tetrahydrofuran	2
n-BuOH	2	1,4-Dioxane	2
s-BuOH	2/3	Benzene	4/3
i-BuOH	2	Dichloromethane	—
t-BuOH	2	Dimethyl sulfoxide	2
AcOH	—	*N*,*N*-Dimethylformamide	2
PhOH	—	Cyclohexanone	2

independent guest molecules are accommodated.

The molecular shapes are significantly different for *n*-PrOH, *i*-PrOH, and EtOH, which usually results in the formation of topologically and geometrically different frameworks of the host molecules. For example, the inorganic clathrates based on cadmium cyanide have been reported to form the completely different crystals for these isomeric propyl alcohols.[14)] Host **1** changes the packing modes for DMSO and benzene as already reported[9)] and now provides the channel structure for the alcohols. Thus, host **1** is not like zeolite nor any well-known organic host such as urea,[15)] which retains the rigid host lattice independent of the guest species.[16)]

In all the three crystals, the O···O distances between the host molecules are within 2.82 Å, suggesting that the host molecules are linked by the hydrogen bonds. Although the guest molecules have greater thermal motion than their hosts, yielding larger scatter in the bond lengths for the guests, it is suggested that the guest molecules are also involved in hydrogen bonding (Fig. 2).

The two C–O bonds of the host molecule in (**1**)(*n*-PrOH)$_2$ take a *gauche* conformation close to the eclipsed one with respect to the C–S bonds of the thienothiophene ring and hence the intramolecular O···S contacts as short as 3.06 and 2.95 Å are observed in (**1**)(*n*-PrOH)$_2$. It is also the case for (**1**)(*i*-PrOH)$_2$ and (**1**)(EtOH)$_2$. The O···S contacts in (**1**)(*i*-PrOH)$_2$ and (**1**)(EtOH)$_2$ are 3.02 and 2.95 Å, and 3.01 and 2.96 Å, respectively. The guest *i*-PrOH molecules in (**1**)(*i*-PrOH)$_2$ are observed as almost planar molecules, which could be ascribed to dynamic disorder of these guest molecules.[17)]

Guest Exchange via Gas–Solid Contact in Isostructural Host Framework. When inclusion complexes (**1**)(EtOH)$_2$ are exposed to *n*-PrOH vapor, EtOH is gradually replaced by *n*-PrOH. The increase of *n*-PrOH as well as the decrease of EtOH were followed by the NMR integration of the dissolved samples in appropriate intervals. The results are represented in Fig. 3. The guest exchange of (**1**)(EtOH)$_2$ was complete within 120 h. The exchange rate was dependent on crystal sizes. The finely ground sample clearly exchanges more rapidly than the unground crystal under similar conditions. The X-ray powder diffraction pattern remained that of the starting (**1**)(EtOH)$_2$ throughout the exchange process and even after complete guest exchange (Fig. 4).

We have recently discovered the site-selectivity of guest accommodation in two independent guest sites in host–guest–guest ternary clathrate crystals.[7)] For (**1**)(EtOH)$_2$ it is also interesting to see if the guest molecules at one site are preferentially exchanged at the earlier stage of vapor contact and then those at the other site are displaced to complete the exchange. Unfortunately, we could not ascertain if such site preference is involved or not, since appropriate single-crystals corresponding to (**1**)(*n*-PrOH)$_x$(EtOH)$_{2-x}$ for X-ray crystallographic analyses could not be obtained.

Table 2. Crystallographic Data and X-Ray Experimental Detailes for Clathrate Crystals of Host **1**

Compound	(**1**)(*n*-PrOH)$_2$ [a)]	(**1**)(*i*-PrOH)$_2$	β-(**1**)(EtOH)$_2$ [b)]	α-(**1**)(EtOH)$_2$ [a)]
Formula	$(C_{32}H_{20}O_2S_2)(C_3H_8O)_2$	$(C_{32}H_{20}O_2S_2)(C_3H_8O)_2$	$(C_{32}H_{20}O_2S_2)(C_2H_6O)_2$	$(C_{32}H_{20}O_2S_2)(C_2H_6O)_2$
M_w	620.82	620.82	592.78	592.78
Space group	$P\bar{1}$	$P\bar{1}$	$P\bar{1}$	$P2_1/a$
a/Å	13.01(2)	13.275(4)	13.111(4)	17.403(3)
b/Å	13.689(6)	13.796(4)	13.724(3)	20.654(4)
c/Å	10.590(2)	10.384(2)	9.766(3)	8.695(1)
α/°	96.58(3)	97.71(2)	97.11(2)	90
β/°	101.38(4)	100.42(2)	98.64(3)	99.73(1)
γ/°	62.76(5)	62.66(2)	64.56(2)	90
V/Å^3	1643(3)	1658.5(9)	1565.3(8)	3080.4(9)
Z	2	2	2	2
D_c/g cm^{-3}	1.254	1.243	1.258	1.278
Crystal size	0.50×0.20×0.20	0.80×0.30×0.30	0.60×0.40×0.30	0.50×0.40×0.40
2θ range	4—55	4—55	4—50	4—55
N_{obsd}	7540	7943	5025	7809
$N_{\text{ref.}}$ $[\lvert F_o \rvert > 3\sigma(\lvert F_o \rvert)]$	3111	4094	3336	4552
No. of variables refined	398	398	421	380
R value	0.078	0.059	0.057	0.074
R_w value	0.093	0.037	0.060	0.074

a) Ref. 12. b) Ref. 13.

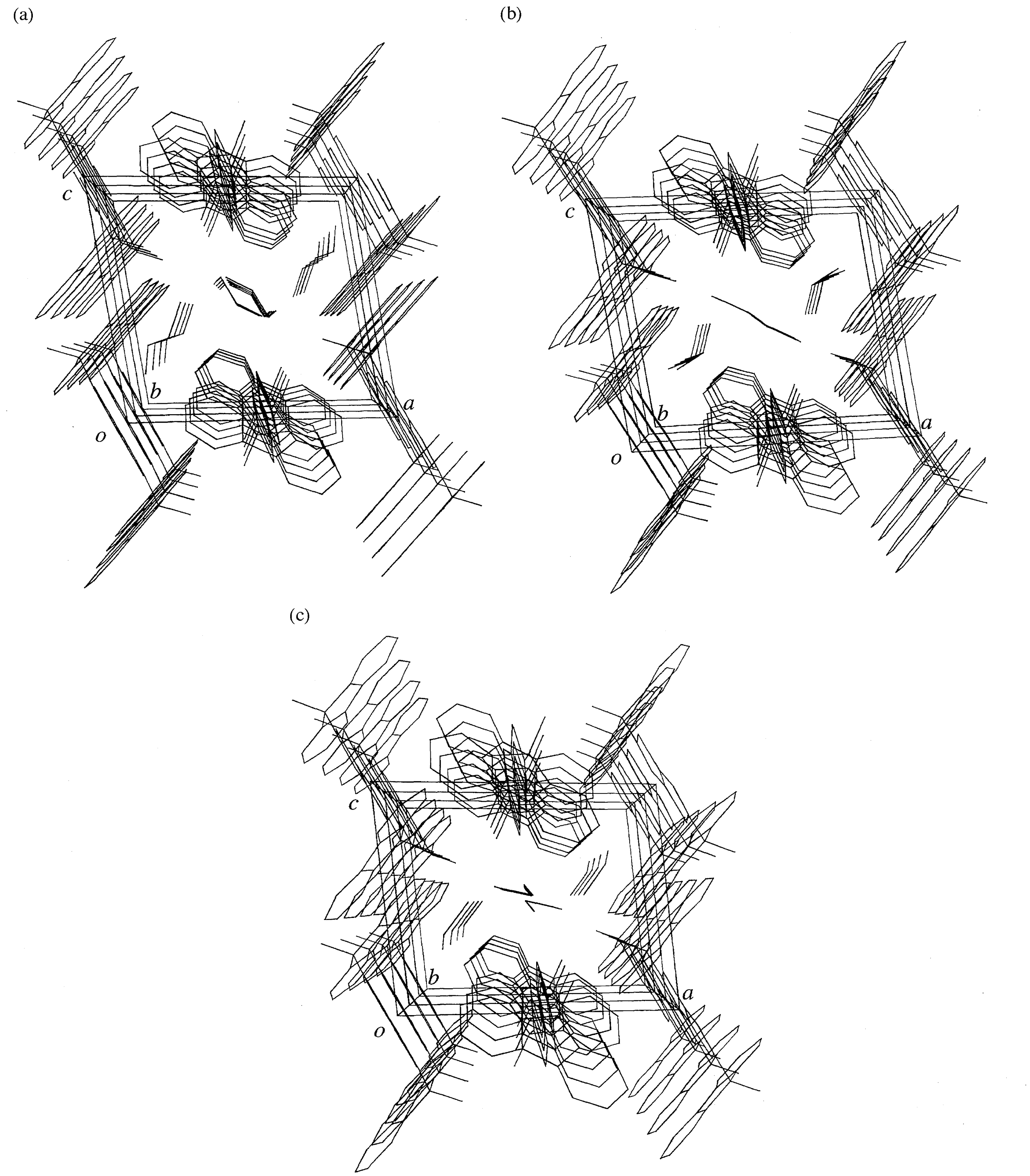

Fig. 1. Crystal structure showing the isostructural inclusion channel viewed along the *b* axis for three clathrate crystals. a) (**1**)(n-PrOH)$_2$; b) (**1**)(i-PrOH)$_2$; c) β-(**1**)(EtOH)$_2$.[13)]

Judging from the time course curve, which exhibits no retardation nor hold at the 1 : 1 guest to guest ratio of (**1**)-(n-PrOH)(EtOH), it seems unlikely that site preference for n-PrOH and EtOH is involved in the guest accommodation. The two guest components should be enclathrated at both sites with random distribution as solid-solution throughout the exchange process.

The reverse exchange process was also accomplished for (**1**)(n-PrOH)$_2$ using EtOH vapor as an external guest to give (**1**)(EtOH)$_2$ (Fig. 3). The similar guest exchange has been also observed for isostructural (**1**)(i-PrOH)$_2$ by the use of n-PrOH or EtOH vapor. On the other hand, gaseous i-PrOH could not induce complete exchange of the guests in (**1**)-(EtOH)$_2$ and (**1**)(n-PrOH)$_2$. The exchange has stopped at

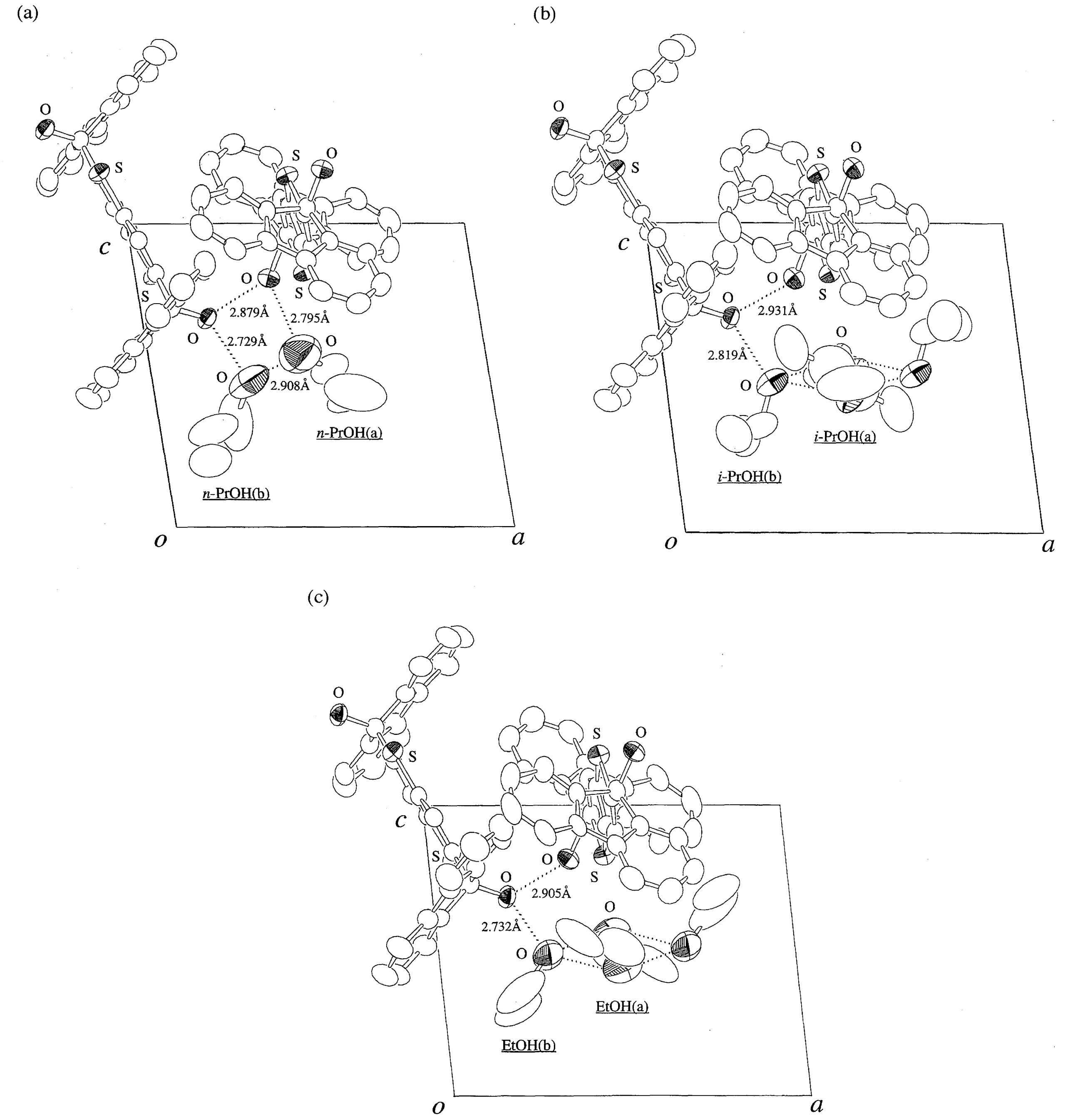

Fig. 2. Packing arrangements of the host and guest molecules. a) (**1**)(n-PrOH)$_2$; b) (**1**)(i-PrOH)$_2$; c) β-(**1**)(EtOH)$_2$.[13] The dotted lines indicate the O···O relations linked by the hydrogen bonds based on the distance of 2.4—3.0 Å as proof of existence of hydrogen bonding.

approximately 25% displacement without leading to the formation of (**1**)(i-PrOH)$_2$ (Fig. 3). These results seem to suggest that, in order to cause the guest exchange in the host lattices of **1**, the external guest should have smaller size than the internal guest. The cell volume decreases in the order (**1**)(i-PrOH)$_2$ [1658 Å^3] > (**1**)(n-PrOH)$_2$ [1643 Å^3] > (**1**)-(EtOH)$_2$ [1565 Å^3], presumably indicating that the channel becomes narrower in this order.

The gas-sorptive formation of clathrate crystals has been found for some host-guest systems.[18] Host **1** does not exhibit such behavior on exposure to guest vapor; the guest-free host **1** cannot incorporate the gaseous external guest. This fact indicates that the guest exchange does not proceed via the guest-free crystals followed by the reorganization at the solid surface to form the clathrates. The displacement may be induced while keeping the channel by continuous removal of the internal guest molecules and insertion of the external guest molecules.[19]

Guest Elimination via Gas–Solid Contact to Give Guest Free Host Crystal. Host **1** afforded no crystalline inclusion

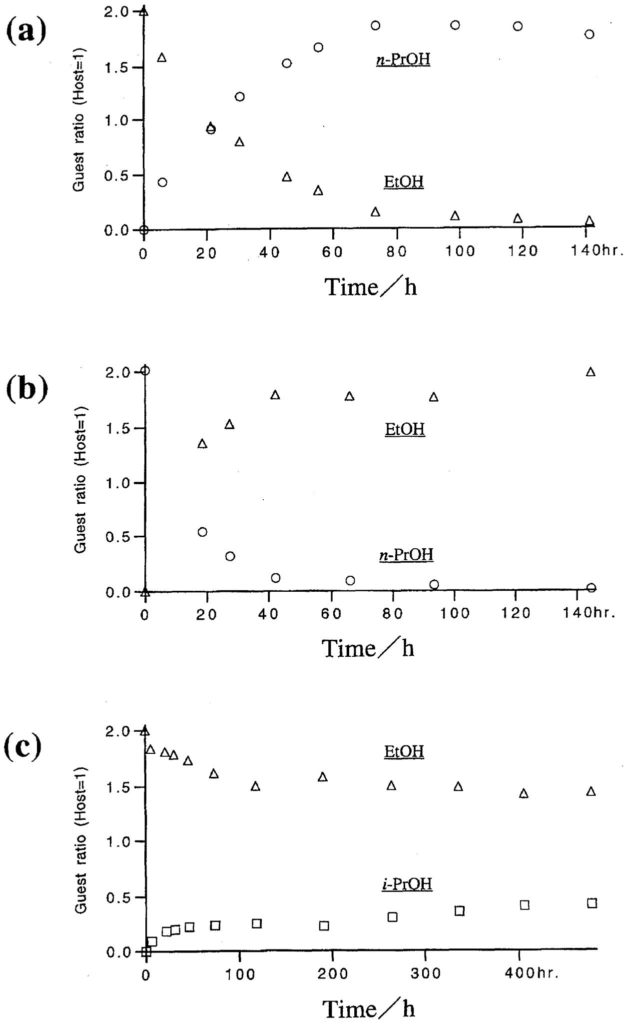

Fig. 3. Time-course of guest exchange via gas-solid contact; a) *β*-(**1**)(EtOH)$_2$ exposed to *n*-PrOH vapor; b) (**1**)(*n*-PrOH)$_2$ exposed to EtOH vapor; c) *β*-(**1**)(EtOH)$_2$ exposed to *i*-PrOH vapor.

complexes in recrystallization from methanol. Then, to see if the clathrate crystals with these guests could be obtained by the guest exchange by gas–solid contact, the three isomorphic crystals (**1**)(EtOH)$_2$, (**1**)(*n*-PrOH)$_2$, and (**1**)(*i*-PrOH)$_2$ were exposed to methanol vapor as an external guest. The guest exchange could not be induced, while the internal guests were lost and the guest-free host solids were formed in all the cases. The guest-free crystal obtained by the contact with methanol vapor showed the X-ray powder diffraction pattern depicted in Fig. 5. This pattern is evidently different from that of the guest-free host crystal which is obtained by recrystallization from dichloromethane (Fig. 5). These observations imply the occurrence of polymorphs in host **1** crystals; one (*α*-**1**) is formed by recrystallization from CH$_2$Cl$_2$ and the other (*β*-**1**) is by contact of the clathrates with methanol vapor. The X-ray crystal structure of *α*-**1** has already been determined.[12] On the other hand, an X-ray crystal analysis of *β*-**1** was not successful in spite of our intensive efforts because of poor reflection data. However, the difference in the crystal structure of *α*-**1** and *β*-**1** is evident; the melting point of *α*-**1** is 220 °C, while *β*-**1** melts at 200 °C. Polymorph *α*-**1** shows a sharp absorption band in IR spectrum ascribable to the free OH group at 3510 cm^{-1}, while *β*-**1** has a broad OH band at lower wavenumber at 3270 cm^{-1}, indicating that intermolecular hydrogen bonding is involved in *β*-**1** but not

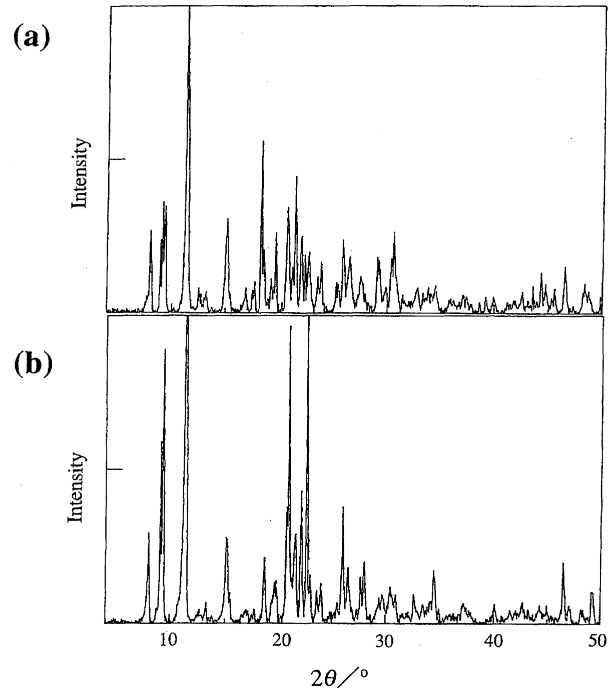

Fig. 4. X-Ray powder diffraction patterns of *β*-(**1**)(EtOH)$_2$; a) before exposure to *n*-PrOH vapor; b) after complete exchange with *n*-PrOH.

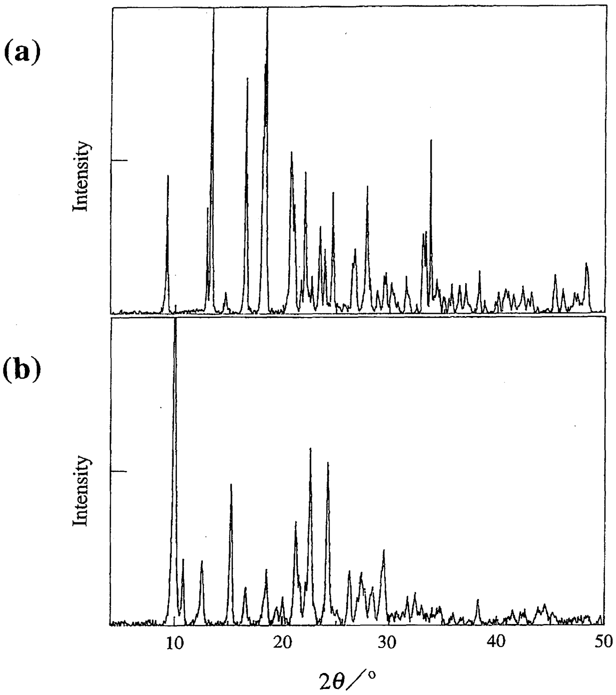

Fig. 5. X-Ray powder diffraction patterns for guest-free host **1**. a) *α*-form obtained by recrystallization of **1** from CH$_2$Cl$_2$; b) *β*-form obtained by exposure to MeOH vapor.

in *α*-**1**. Indeed, an X-ray crystal analysis of *α*-**1** has shown that the molecules are not linked by hydrogen bonds.[12]

Methanol is the smallest alcohol in molecular size. Therefore, the internal guests, EtOH, *n*-PrOH, or *i*-PrOH could be replaced with MeOH, whereas methanol would be too small to keep the channel framework provided for these three alcohols. Then, the host lattices would collapse and be reorganized without methanol molecules. This is in line with the observation that host **1** affords no clathrate crystals when recrystallized from methanol.

Polymorphic Crystals of (1)(EtOH)$_2$. In crystalline host guest inclusion complexes, the variation of host–guest interactions in addition to host–host and guest–guest ones tends to cause different host to guest ratios for given host and guest compounds rather than polymorphs of common host to guest compositions. The former are sometimes erroneously designated as polymorphs in pharmaceutical chemistry.[20] Weber uses the term pseudo-polymorphism for the *polymorph of solvation difference*.[21]

It should be noted that clathrate (**1**)(EtOH)$_2$ described in this work is a polymorphic crystal different from the previously reported one.[12] Hereafter, the crystal found in this work is referred to as *β*-(**1**)(EtOH)$_2$ and the previous one as *α*-(**1**)(EtOH)$_2$. As noted already, the host framework of newly found *β*-(**1**)(EtOH)$_2$ is isostructural with those of (**1**)(*n*-PrOH)$_2$ and (**1**)(*i*-PrOH)$_2$ crystals (Fig. 1), while *α*-(**1**)(EtOH)$_2$ shows a different channel structure (Fig. 6). The crystal data of *α*-(**1**)(EtOH)$_2$ are listed in Table 2 along with those of *β*-(**1**)(EtOH)$_2$. In both crystals the guest EtOH molecules are accommodated in a channel-type of inclusion lattice (Figs. 1 and 6).

There are discrete differences in the conformation of the host molecules between the two crystals. In *α*-(**1**)(EtOH)$_2$ the two C–O bonds are closely in a *trans* conformation with respect to the C–S bonds of the thiophene rings (dihedral angles of the CS–CO bond: 161° and 168°), whereas those in *β*-(**1**)(EtOH)$_2$ are arranged close to eclipsed forms (dihedral angles: 37° and 42°). Conformational polymorphism is an important subject of research and has been extensively investigated for monocomponent crystals.[22] The clathrate (**1**)(EtOH)$_2$ provides a novel example of the conformational polymorphism in two-component molecular crystals, which seems to be rather rare.

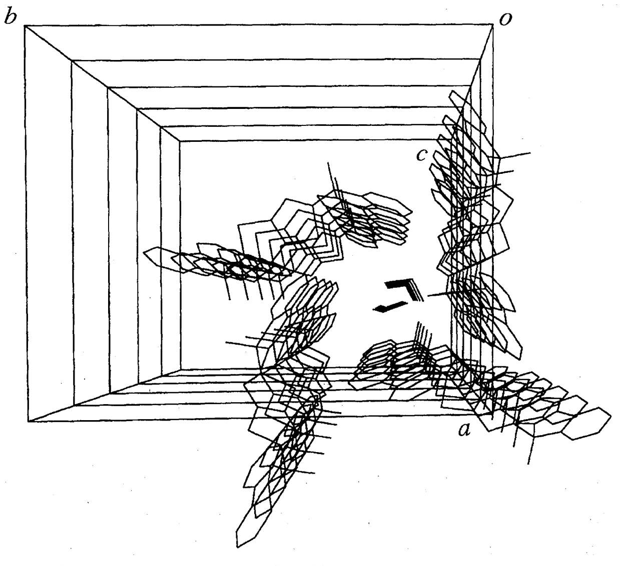

Fig. 6. Crystal structure of *α*-(**1**)(EtOH)$_2$ showing the inclusion channel viewed along the *c* axis.

The polymorphic crystals of (**1**)(EtOH)$_2$ exhibited differing thermal properties in the differential scanning calorimetry (DSC) measurements. The crystal of *α*-form loses the guest molecules at 84 °C, while the new form, *β*-(**1**)(EtOH)$_2$, loses those at 73 °C, indicating that the guest molecules in the *α*-form are strongly incorporated in the host lattice as compared to those of *β*-(**1**)(EtOH)$_2$. It is interesting to note that we have never obtained the previously found *α*-(**1**)(EtOH)$_2$ crystals again, after we encountered *β*-(**1**)(EtOH)$_2$ crystals.[23]

Experimental

Complexation. The host compound **1** was prepared according to the procedure described in a previous paper.[10] Crystalline inclusion complexes were grown by slow evaporation of the solvent from a solution of **1** dissolved in a minimum amount of the respective solvent. The host : guest ratios were determined by means of the ^{1}H NMR integrations and/or X-ray analyses.

Guest Exchange. The powdered clathrate crystals were placed in a vial without a cap and then kept in a small closed chamber, in the bottom of which a shallow pool of the external guest alcohol was maintained to ensure constant vapor pressure. In appropriate intervals, the portion of the solid was taken out, dried in air, and analyzed by NMR spectroscopy.

X-Ray Crystallographic Studies. Intensity data of (**1**)(*i*-PrOH)$_2$ and *β*-(**1**)(EtOH)$_2$ were collected on a Rigaku AFC-5S diffractometer using Mo K*α* radiation (λ = 0.710690 Å) at room temperature. The crystal structure of (**1**)(*i*-PrOH)$_2$ was solved by direct methods using SIR92 program[24] and refined using the teXsan crystallographic software package of Molecular Structure Co. The crystal structure of *β*-(**1**)(EtOH)$_2$ was solved by direct methods using SIR-88 program[25] and the refinement was carried out using the teXsan program. All non-H atoms were refined anisotropically. For both crystals the H-atoms were fixed geometrically and not refined. Crystallographic informations are presented in Table 2. The complete $F_o - F_c$ data are deposited as Document No. 72020 at the Office of the Editor of Bull. Chem. Soc. Jpn. The X-ray crystallographic analyses of (**1**)(*n*-PrOH)$_2$ and *α*-(**1**)(EtOH)$_2$ have already been reported.[12] As references for polymorphism and isostructurality, their crystal data are also listed in Table 2.

X-Ray Powder Diffraction. The X-ray diffraction analysis was conducted on a Rigaku RAD-C X-ray diffractometer with monochromatic Cu *Kα* radiation (λ = 1.5418 Å).

Differential Scanning Calorimetry (DSC). The DSC traces were recorded on a Seiko SSC-5200 differential scanning calorimeter with a scanning rate of 5 deg min^{-1} from 40—230 °C.

The present work was supported by Grants-in-Aid for Scientific Research Nos. 08640673 and 09874122 from the Ministry of Education, Science, Sports and Culture.

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