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Accounts

Inclusion Properties and Solid-State Behavior of Thiophene-Condensed Host Compounds

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A series of new clathrate host molecules, each containing thiophene rings as a rigid and bulky substituent, has been synthesized based on the "wheel and axle"-type of host design. The interest in these hosts is focused on the continuous change in the length of the "axle" part together with their electron-donating ability. Moreover, the tertiary alcohol moiety in the "wheel" part can undergo the substitution reactions in the solid state. Thus, the host : guest ratio and the conformation of the host molecules exhibit novel dependences on the number of the condensed thiophene rings. Guest exchange via gas solid contact has been achieved in the clathrates which provide a channel-type inclusion void. Isostructural and polymorphic transformation of the host lattices has been found upon gas-solid contact. Pseudo-polymorphic change was also observed in guest release. Ternary crystals exhibited novel site-selectivity for random inclusion of two alcohol guests. The donor character of the hosts can afford three-component charge-transfer complexes enclathrating solvent molecules. Cogrinding the host and the acceptor enhanced the solid-state charge transfer interactions, which have been associated with the nucleophilic substitution in the solid state induced by gas-solid contact. These results indicate one future direction for research on crystalline inclusion complexes.

The development of supramolecular chemistry has aroused considerable interest in lattice-assisted inclusion compounds, where the guest fits into the intermolecular spaces created by the packing of the host molecules. The host lattices include three-dimensional extended solids, networks of hydrogen-bonded molecules, and molecular solids in which only van der Waals forces maintain the host structure. These solid-state compounds are also designated as clathrate crystals.[1] Their chemistry has gained importance in material sciences[2] and crystal engineering.[3] A rigid basic framework and bulky substituents are usually required for a host molecule in order to provide suitable cavities in the crystal structure to accommodate guest molecules. A characteristic example is 1,1,6,6-tetraphenyl-2,4-hexadiyne-1,6-diol that has been explored by Toda.[4] The 2,4-hexadiyne part constructs a linear rigid backbone and its two terminal carbons bear bulky phenyl groups. Thus, this host molecule could be regarded as a "wheel and axle"-type structure (Chart 1). The large "wheel" groups at the end of the rigid "axle" act as spacers to prevent the host molecules themselves from packing efficiently in three dimensions, and then create voids for occupation by the guest molecules. Based on such a "wheel and axle" concept, a variety of host compounds have been designed.[5]

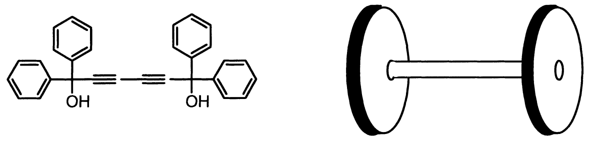


Chart 1. "Wheel and Axle" structure of host 1,1,6,6-tetraphenyl-2,4-hexadiyne-1,6-diol.

Although clathrate crystals are formed under lattice-assisted inclusion of a guest species, incorporation of designed intermolecular interactions between guest and host is useful to bring about versatile complexation properties and solid-state behaviors. In most of the cases, a hydrogen-bonding moiety is used to enhance the process of molecular recognition between host and guest. Incorporation of weak charge-transfer interactions in clathrate crystals is also interesting, since such crystal design is in contrast to the general consensus that charge-transfer complexes are formed from planar donor and acceptor molecules. Raggedness of the molecular structure is disadvantageous for the formation of crystalline charge-transfer complexes, while it is favorable for a host compound to form clathrate crystals. Such molecules would possess versatile complexation properties and solid-state properties to lead to new solid-state materials. In this context, a new host series **1**–**5** and their related host compounds have been designed. Hosts **1**–**5** have thiophene and condensed thiophenes, ***1***–***4*** respectively, as an axle part; they have relatively low ionization energies[6] and could fulfil the requirement for the host compounds noted above (Chart 2).

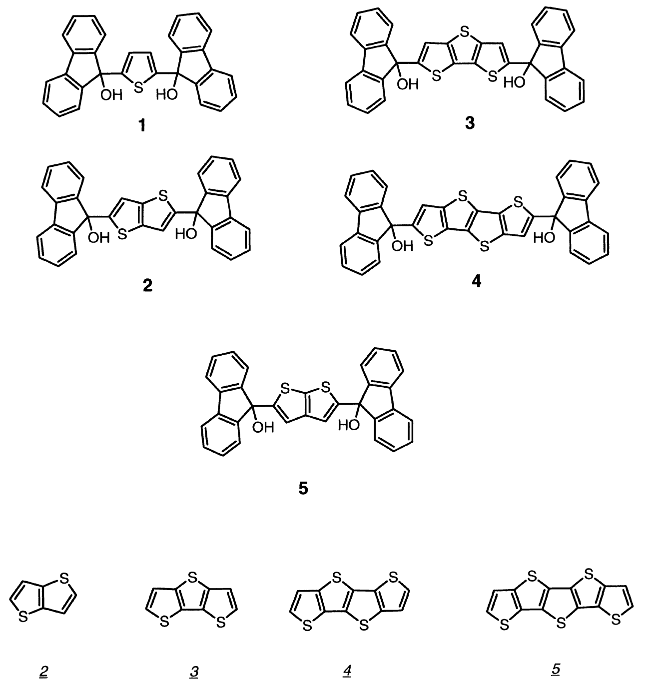


Chart 2.

Another aim in the design of this host series is to induce solid-state reactions in these clathrate crystals. The triphenylmethyl-type *tert*-alcohol moiety at the center of the "wheel" part is expected to have reactivity as the precursor of a carbocation intermediate. Particularly, substitution of the thiophene ring would stabilize a cationic center and promote a reaction via carbocation.[7] Thus, it would be possible to realize solid-state ionic reactions between the host and appropriate guest compounds.

This account overviews characteristic inclusion properties and solid-state behavior of the new host compounds whose design is based on thiophenes. First, we describe inclusion properties as host compounds for crystalline host–guest complexes and then solid-state properties as charge-transfer complexes. Finally, their solid-state reactivity is described, which originates from the involvement of a partial structure of triphenylmethyl-type *tert*-alcohols as a reactive moiety.

Even-Odd Effect in Inclusion Properties

Upon crystallization from various solvents, a series of the new host compounds show broad inclusion properties. In a series of linearly condensed polythiophenes (Table 1), a trend in the host:guest stoichiometry is found: the host compounds with an even number of thiophene rings have a tendency to give the host:guest stoichiometry of 1:2, whereas those with an odd number of thiophene rings tend to give 1:1 stoichiometry. A typical example is the crystal including DMSO as a guest compound; the crystalline complexes (**1**)(DMSO), (**2**)(DMSO)$_2$, (**3**)(DMSO), and (**4**)(DMSO)$_2$ are formed, respectively, from the corresponding host compound.[8]

The most remarkable structural features in the host molecules are in the conformation of the "wheel" part. Two C–OH bonds in the host molecules adopt a *gauche* conformation close to the eclipsed form with respect to the C–S bonds of the terminal thiophene rings. This means that in (**1**)(DMSO) and (**3**)(DMSO), the C–OH groups at both ends of the "axle" are directed to the same side (*syn*), whereas in the host having an even number of thiophene rings, (**2**)(DMSO)$_2$ and (**4**)(DMSO)$_2$, the C–OH groups are directed to sides opposite to each other (*anti*) (Fig. 1).

Table 1. Inclusion Properties of Hosts **1**–**4** and **5**

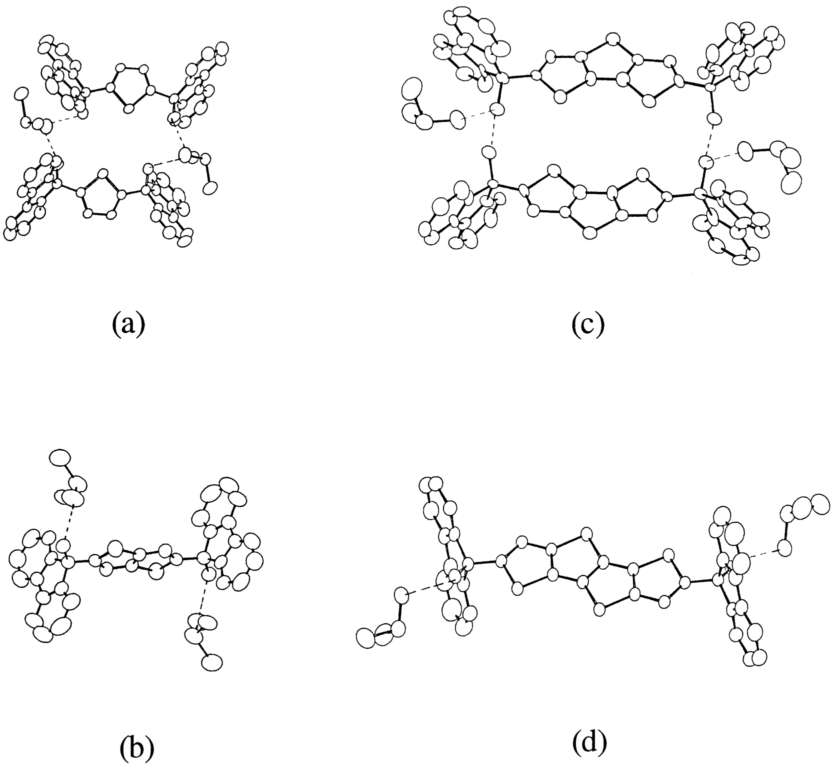
Guest	Host				
	1	**2**	**3**	**4**	**5**
EtOH	0	1:2	1:1	—[a]	2:1
Acetone	0	1:2	1:1	—[a]	4:1
DMSO	1:1	1:2	1:1	1:2	1:2
DMF	1:2	1:2	1:1	0	—
Dioxane	1:1	1:2	1:1	1:2	1:1
Benzene	0	3:4	0	—[a]	1:1

a) Not determined owing to immediate loss of the guest molecules.

Th guest DMSO molecules are hydrogen-bonded to the OH groups in the host molecules. In (**2**)(DMSO)$_2$ and (**4**)(DMSO)$_2$, two OH groups adopt an *anti* orientation so that each of the two OH groups of the host molecule is individually hydrogen-bonded to a DMSO molecule, resulting in a host:guest ratio of 1:2. On the other hand, the host composed with an odd number of thiophene rings has two hydroxy groups in *syn* alignment, thereby making a cyclic dimer by face-to-face intermolecular hydrogen bonds. Two guest molecules participate in linking these two host molecules, leading to the 1:1 ratio.

These results demonstrate the interesting even-odd effect in conformational change in the "wheel" part, which depends on the length of the "axle", that is, the number of condensed thiophene rings. Furthermore, the dependence is associated also with the control of the direction of the hydrogen bonds and hence, is responsible for the host:guest stoichiometry. The even-odd effects may be ascribable to two factors. One is the conformational preference of the S–C and C–O bonds due to an attractive electrostatic interaction between the sulfur and oxygen atoms.[9] Computational studies on non-bonded sulfur-oxygen in the thiazole nucleoside have indicated that these contacts are the result of an attractive electrostatic interaction between a positively charged sulfur atom and a negatively charged oxygen.[10] An alternative explanation for the even-odd effect is based on the concept of close molecular packing in the crystalline state. A molecular structure with the inversion center is preferred for close packing. In a series of linearly condensed-polythiophenes, hosts **2** and **4** have inversion centers in their molecular structure, while hosts **3** and **5** are constructed in such structure by making the (host)$_2$(DMSO)$_2$ unit. The molecular symmetry is correlated with the number of the condensed thiophene rings.

It is interesting to note here that the dependency on linear extension of the central spacer, i.e. changing the number of thiophene rings, is also observed in the electronic properties of the mother framework of condensed thiophene compounds 2–5. The longest UV absorption maximum shifts linearly in the order of 5 (357 nm) > 4 (333 nm) > 3 (304 nm) > 2 (280 nm).[11] The ionization energies of a series of condensed


(a) (c)

(b) (d)

Fig. 1. Host-guest arrangements in clathrate crystals of **1**–**4** including DMSO. (a) (**1**)(DMSO), (b) (**2**)(DMSO)$_2$, (c) (**3**)(DMSO), (d) (**4**)(DMSO)$_2$. In the crystals in which crystallographically non-equivalent host-guest units are involved, only one of those is depicted.

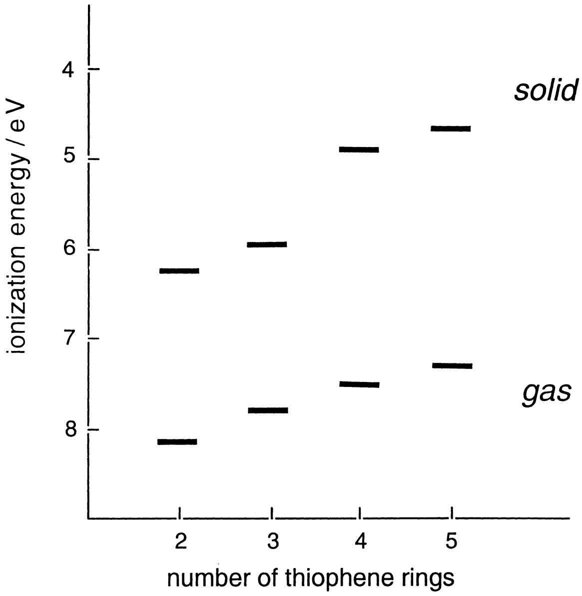


Fig. 2. Ionization energies in the gaseous and solid states for a series of polycondensed thiophenes, *2*–*5*.

thiophenes *2*–*5* in the gas phase are continuously lowered with increase of the number of thiophene rings.[6,12] The ionization energies in the solid state, however, show rather characteristic features (Fig. 2); the threshold ionization energies of *4* and *5* are extremely low as compared to those of other related polycondensed aromatic compounds.[6] These results indicate that in compounds *4* and *5* the difference in the ionization energies for the gaseous and solid states is significant, giving rise to large polarization energies.[13] These results have been interpreted in terms of the intermolecular orbital interactions in the solid state of *4* and *5*. The zig-zag edge constructed of two sulfur atoms are advantageous for interaction with the neighboring molecules in a fastener-like alignment. In fact, the X-ray crystal structures of *4* revealed that the shortest crystallographic axis is 4.03 Å,[14] an extremely short value compared to that for the isoelectronic hydrocarbon, chrysene (5.78 Å).[15] The molecular packing of *4* corresponds to a *β*-structure, which has been proposed for crystal structures of hydrogen-poor polynuclear aromatic compounds.[16]

Isostructural Clathrate Crystals of Isomeric Hosts

Clathrate crystals often afford isostructural host lattices for different guest molecules, since a change in the guest component, usually solvent molecules, causes only slight perturbation of the whole host-guest crystal. For example, 1,1′-binaphthyl-2,2′-dicarboxylic acid forms isostructural 1:2 inclusion complexes with ethanol and 1-propanol.[17] Dioxane, THF, and chloroform are basically different in molecular structure, while they are enclathrated in the common isostructural host framework of 5-methoxysulfadiazine.[18] On the other hand, for different hosts, isostructural crystals have rarely been encountered, even incorporating common guest species. This may be because the crystal lattices depend mainly on the host structure, usually larger in molecular architecture than the guest component, so perturbation of the crystal packing induced by

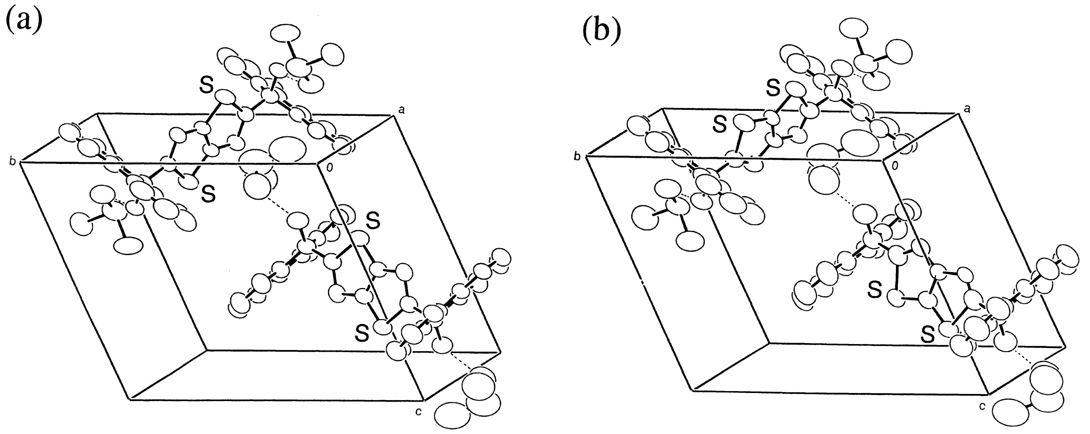


Fig. 3. Packing arrangements of (a) (**2**)$(DMSO)_2$ and (b) (**5**)$(DMSO)_2$. The O···O shows the relation linked by the hydrogen bonding between the hosts and the guest.

the host is more pronounced. Host compounds which are similar in size and shape are expected to give isostructural crystals and to provide a unique opportunity for investigation of the crystal structure-solid properties relationship. Thiourea and selenourea do not crystallize in isostructural form, whereas they afford isostructural clathrate crystals including adamantane as a guest.[19] Perchloro(2,2′-biphenylene)diphenylsilane and -germane form isostructural adducts with two molecules of benzene.[20] In these examples, the host molecules are replaced by homologues with the same group elements. Thus, compound **5** has been designed as an isomeric host of **2**, in which the thieno[3,2-*b*]thiophene ring of **2** is displaced by the thieno[2,3-*b*]thiophene ring.

In spite of its close similarity in shape and size to **2**, host **5** gave rather a different host-to-guest ratio for each guest (Table 1).[21] Among the guests investigated, *n*-PrOH, *i*-PrOH, and DMSO formed isostructural clathrate crystals for hosts **2** and **5**. The details for the crystals of (**5**)(*n*-PrOH) and (**5**)(*i*-PrOH) are described later. We shall confine our attention here to the DMSO and benzene clathrates. DMSO, which has the ability of strong inter-host-guest interaction using hydrogen bonding, affords isostructural crystals (**2**)$(DMSO)_2$ and (**5**)$(DMSO)_2$.[21] In both crystals, the two OH groups in the host molecules are hydrogen-bonded individually to a DMSO molecule to constitute a trimeric unit of $(host)(guest)_2$ (Fig. 3). Such structure with an inversion center would be favorable also for **5** to crystallize. Thus, the difference in the position of sulfur atoms in **5** is disregarded; the strong hydrogen bonding that constitutes a trimeric unit overcomes the less favorable O···S interaction to bring about an isostructural crystal. On the other hand, benzene, a weakly-interacting guest, affords quite different crystal structures with discrete host : guest ratios: $(\mathbf{2})_3(benzene)_4$ and (**5**)(benzene).[22]

For benzene, a variety of weak host-guest interactions compete in host–guest cocrystallization. Therefore, the crystal structures might be sensitive to even a slight difference in the molecular structure of the isomeric hosts. The electrostatic O···S interactions take effect in the molecular packing for benzene clathrates to result in the formation of different crystals structures. In fact, all the OC–CS bonds of the host molecules in $(\mathbf{2})_3(benzene)_4$ and (**5**)(benzene) crystals adopt a preferential *gauche* conformation with respect to the C–S and C–O bonds.[22]

It should be noted that the crystals of the guest free hosts **2** and **5** are not isostructural with each other. Unfortunately, an appropriate single crystal of **2** for an X-ray crystallographical study could not be obtained. However, the IR spectra and X-ray powder diffraction patterns of **2** and **5** show clear differences, indicating that the position of the sulfur atoms is a rather important factor in determining the crystal structures of the host molecules themselves.

Pseudopolymorphism in Clathrate Crystals

Pseudo-polymorphism is defined for the crystalline forms of a compound (host) that differ in the species or stoichiometry of the included solvents (guest).[23] The former is frequently encountered,[24] while the latter, the existence of two or more crystalline inclusion compounds for the same host and guest, is rare in clathrate crystals.[25] Different host-to-guest stoichiometry would be realized when the host-guest interactions are flexible enough to allow them to be nearly equi-energetic.[26]

The occurrence of two solvated crystalline forms of tri(2-benzo[*b*]thienyl)methyl alcohol (**6**) with acetonitrile as a guest has been found.[27] Compound **6** (Chart 3) yielded two modifications: (**6**)(MeCN) and $(\mathbf{6})_2(MeCN)$. The finding was serendipitous but the formation of each crystal is reproducible. The 1 : 1 clathrate (*α*-form) is obtained by crystallization from a mixed solvent of acetonitrile and ethanol (2 : 1), while the 2 : 1 crystal (*β*-form) is isolated from an acetonitrile solution by slow evaporation of the solvent at room temperature.

The TG trace of the *α*-form shows a stepwise release of the guest; a half of the guest molecules is lost at 80 °C to give the 2 : 1 crystal and the remaining half is lost at 150 °C to afford

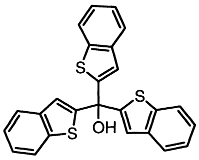


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Chart 3.

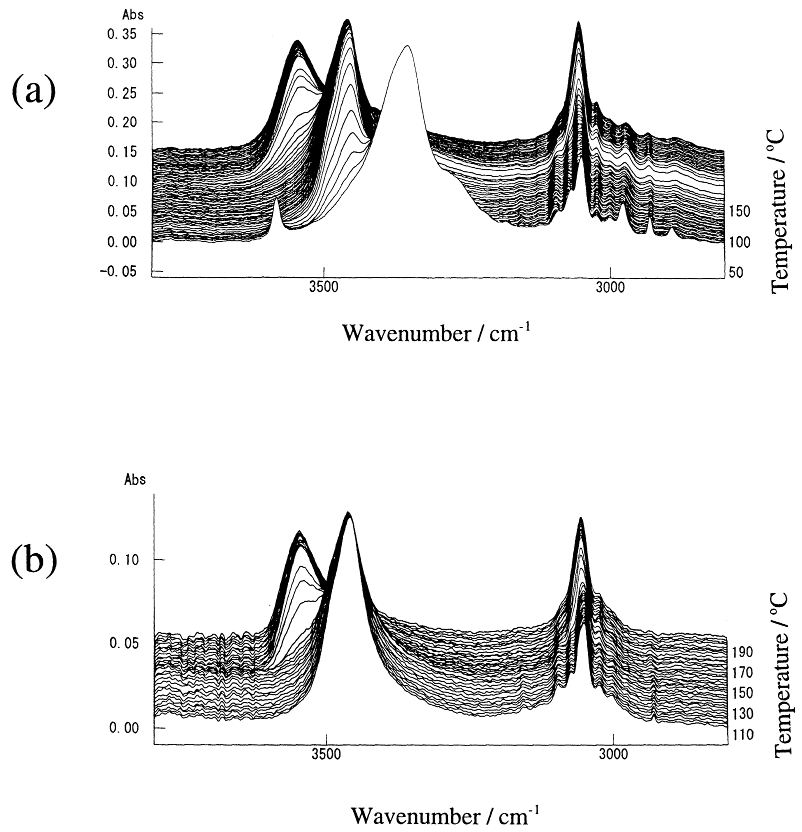


Fig. 4. The temperature-dependent FTIR spectra in the ca. 2700–3700 cm^{-1} region. (a) For (**6**)(MeCN) recorded by upper shift with raising the temperature from 40 to 190 °C. (b) For $(\mathbf{6})_2$(MeCN) recorded by upper shift with raising the temperature from 100 to 190 °C.

the guest-free crystal of **6**. The 2:1 crystals resulting from the α-form were revealed to be the same as the β-form obtained by recrystallization from acetonitrile. The guest-free **6** crystal cannot incorporate MeCN vapor to reproduce the α- or β-form. Thus, the host molecule is not regarded to be an apohost which can undergo sorptive guest incorporation via contact with liquid or gaseous guest.[28,29]

In the variable-temperature FTIR spectroscopy of α-form (Fig. 4), marked spectral changes were observed at 80 °C and 150 °C, corresponding to the transformation to the β-form and the guest-free form, respectively. Thus, the absorption band of OH stretching vibration shifts from 3354 cm^{-1} (α-form) to 3460 cm^{-1} (β-form) and then to 3545 cm^{-1} (guest-free).

The X-ray crystal analysis of the α- and β-crystals revealed that the band at 3354 cm^{-1} is associated with linear-type -OH–NC- hydrogen bonding, while that at 3460 cm^{-1} is associated with a bifurcated hydrogen bond to the CN group by two OH groups of the host molecule (Fig. 5). The former is stronger and the latter is weaker. The band at 3545 cm^{-1} is assigned to the free OH band of **6**. The transformation of the α- to β-form involves the reorganization of the hydrogen bonding. The hydrogen bonding energy of a bifurcated pattern in the β-form could roughly be estimated by DSC measurements to be a half of 17.5 kJ mol^{-1}, that is ca. 9 kJ mol^{-1}. The calorific value should include also the change in packing energies, which are assumed based on the density of the crystals to be endothermic for each desorption step; the density of the crystals increases in the order of the α-form (1.313 g cm^{-3}) $<$ the β-form (1.342 g cm^{-3}) $<$ guest-free **6** (1.379 g cm^{-3}). Thus, the above bonding energy should be modified to be more than 9 kJ mol^{-1}.

The bifurcated hydrogen bond to the C=O group is common,[30] while that to the CN group as described herein is quite rare. Recent investigation using the Cambridge Structural Database (CSD) shows that the C≡N···HO interactions have a strong tendency to linearity.[31] Weak H-donors such as the H–C and H–N groups have been known to participate in bifurcated hydrogen bonds to the N≡C- group as supramolecular synthons.[32]

Guest Exchange via Gas-Solid Contact

Host **2** forms isostructural clathrate crystals for EtOH and *n*-PrOH. In these crystals, $(\mathbf{2})(\mathrm{EtOH})_2$ and $(\mathbf{2})(n\text{-PrOH})_2$, the unit cell parameters are similar and the packing motif of the host molecules is analogous (Fig. 6). A channel-type inclusion void is constructed along the *b*-axis by the walls of the two crystallographically independent host molecules, in which the two independent guest molecules are accommodated.[33] When $(\mathbf{2})(\mathrm{EtOH})_2$ crystals are exposed to *n*-PrOH vapor, EtOH is gradually replaced by *n*-PrOH. The X-ray powder diffraction pattern of $(\mathbf{2})(\mathrm{EtOH})_2$ remains throughout the exchange process and even after complete guest exchange. The reverse exchange process was also accomplished for $(\mathbf{2})(n\text{-PrOH})_2$ using EtOH vapor as an external guest, giving $(\mathbf{2})(\mathrm{EtOH})_2$.

The guest exchange described above takes place while re-

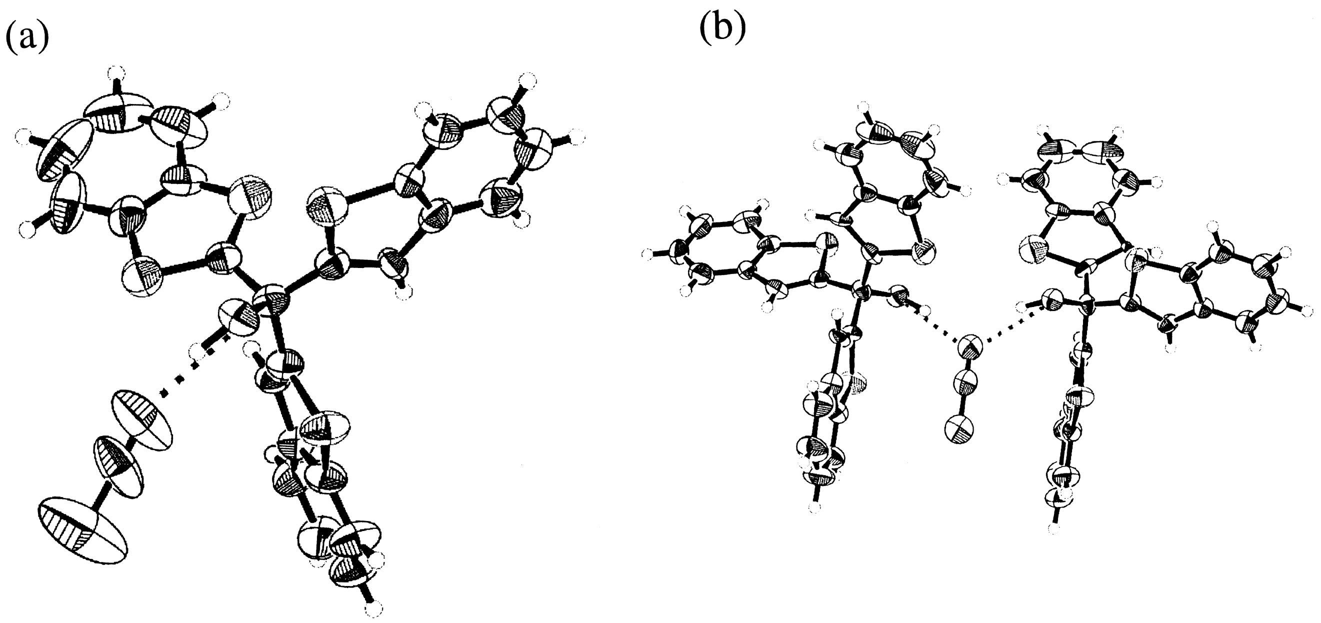


Fig. 5. Host–guest arrangement in pseudopolymorphous clathrates of **6**. (a) (**6**)(MeCN); (b) $(\mathbf{6})_2$(MeCN). The dotted lines indicate the O···O relations linked by the hydrogen bond. An inversion disorder of the ring occurs in one of the benzo[*b*]thiophene rings in (**6**)(MeCN).

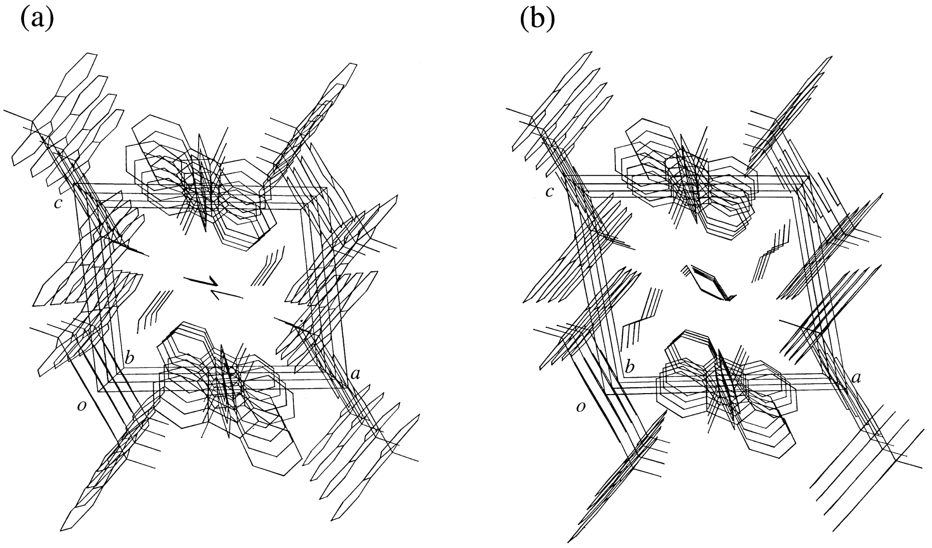


Fig. 6. Crystal structures showing the isostructural inclusion channel viewed along the *b* axis for two clathrate crystals. (a) β-(**2**)$(EtOH)_2$. (b) (**2**)$(n\text{-}PrOH)_2$.

taining the starting channel lattice. More interesting is guest exchange to a different channel structure. Transformation of the crystal lattices induced by guest exchange via gas–solid contact has rarely been reported.[34,35] Such phenomenon has been encountered in a polymorphic crystal of (**2**)$(EtOH)_2$, which crystallizes in space group $P2_1/a$ and also consists of channel-type host cavities (Fig. 7).[33] This crystal is referred to as the α-form of (**2**)$(EtOH)_2$ and the polymorph that is isostructural to the (**2**)$(n\text{-}PrOH)_2$ is referred to as the β-form. The channel structure is different for α- and β- forms. These dimorphic crystals show conformational polymorphism. There are distinct differences in the conformation of the host molecules. In the α-form, the two C–O bonds are in a close *trans* conformation with respect to the C–S bonds of the thiophene rings, whereas those in the β-form are arranged close to the eclipsed forms.

The α-(**2**)$(EtOH)_2$ crystals were exposed to *n*-PrOH vapor. The guest exchange takes place to form (**2**)$(n\text{-}PrOH)_2$ crystals.[36] In the X-ray powder diffraction measurements, the intensity of the peaks corresponding to the starting α-(**2**)$(EtOH)_2$ decreases, while that of the peaks due to (**2**)$(n\text{-}PrOH)_2$ crystals increases, and after the complete exchange the diffraction patterns are converted to that of (**2**)$(n\text{-}PrOH)_2$. This transformation is a crystal-to-crystal transformation, but is not a topologi-

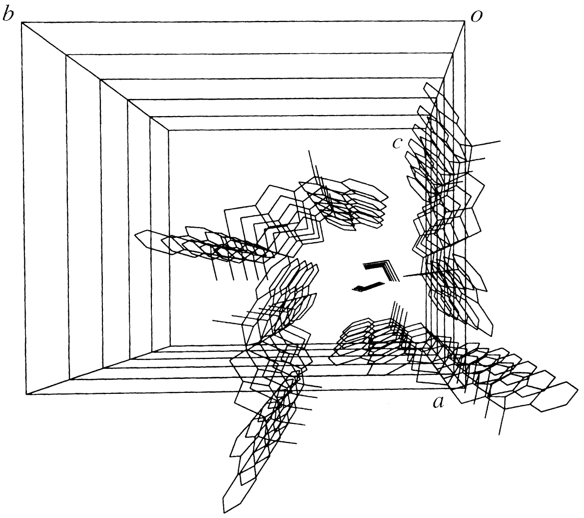


Fig. 7. Crystal structure of α-(**2**)$(EtOH)_2$ showing the inclusion channel viewed along the *c* axis.

cal single crystal-to-single crystal transformation, since a single crystal of α-(**2**)$(EtOH)_2$ disintegrates into micro-crystalline particles of (**2**)$(n\text{-PrOH})_2$ upon the guest exchange.

The crystals of α-(**2**)$(EtOH)_2$ were found in the early 1990s,[36] while the β-polymorph has been encountered more recently. It is interesting that the previously found α-form crystals have not been found again since the investigation using β-crystals was undertaken. The crystals of α-(**2**)$(EtOH)_2$ should be referred to as a disappearing polymorph.[37]

Guest Release via Gas-Solid Contact

The crystalline complex including MeOH could not be obtained by recrystallization of host **2** from MeOH. Then, one may wonder if the MeOH-inclusion crystals could be obtained by the guest exchange of (**2**)$(EtOH)_2$ or (**2**)$(n\text{-PrOH})_2$ by exposure to MeOH vapor. Actually, the guest exchange was not induced, while the internal guests EtOH or *n*-PrOH were lost and the guest-free host solids were formed in both crystals. The guest-free crystals thus obtained showed X-ray powder diffraction patterns which are evidently different from those of the guest-free host crystal obtained by recrystallization from CH_2Cl_2 (Fig. 8).[33] These observations imply the occurrence of polymorphs in host **2** crystals, one being obtained by recrystallization and the other by the guest release.

The molecular size of MeOH is the smallest in alcohols. The MeOH molecules could enter into the channel by pulling out the internal guest molecules, whereas MeOH would be too small to keep the channel framework provided for EtOH and *n*-PrOH. Then, the host lattices would collapse and be reorganized without enclathration of the MeOH molecules. This is in line with the observation that host **2** afforded no clathrate crystals upon recrystallization from MeOH.

The gas-sorptive formation of clathrate crystals has been found for several host-guest systems.[28,29] The resorcinol host exploited by Aoyama is a relevant example.[29] Host **2** does not exhibit such sorptive guest incorporation on exposure to guest vapor. This fact indicates that the guest exchange noted above does not proceed via guest-free crystals followed by the reorganization at the solid surface via interaction with the external guest. The displacement may be induced while keeping the channel by continuous removal of the internal guest molecules and insertion of the external guest molecules.

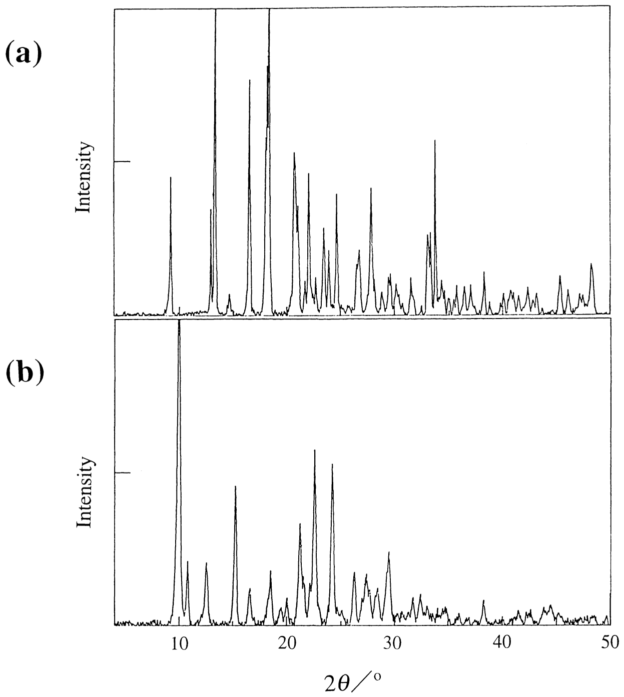
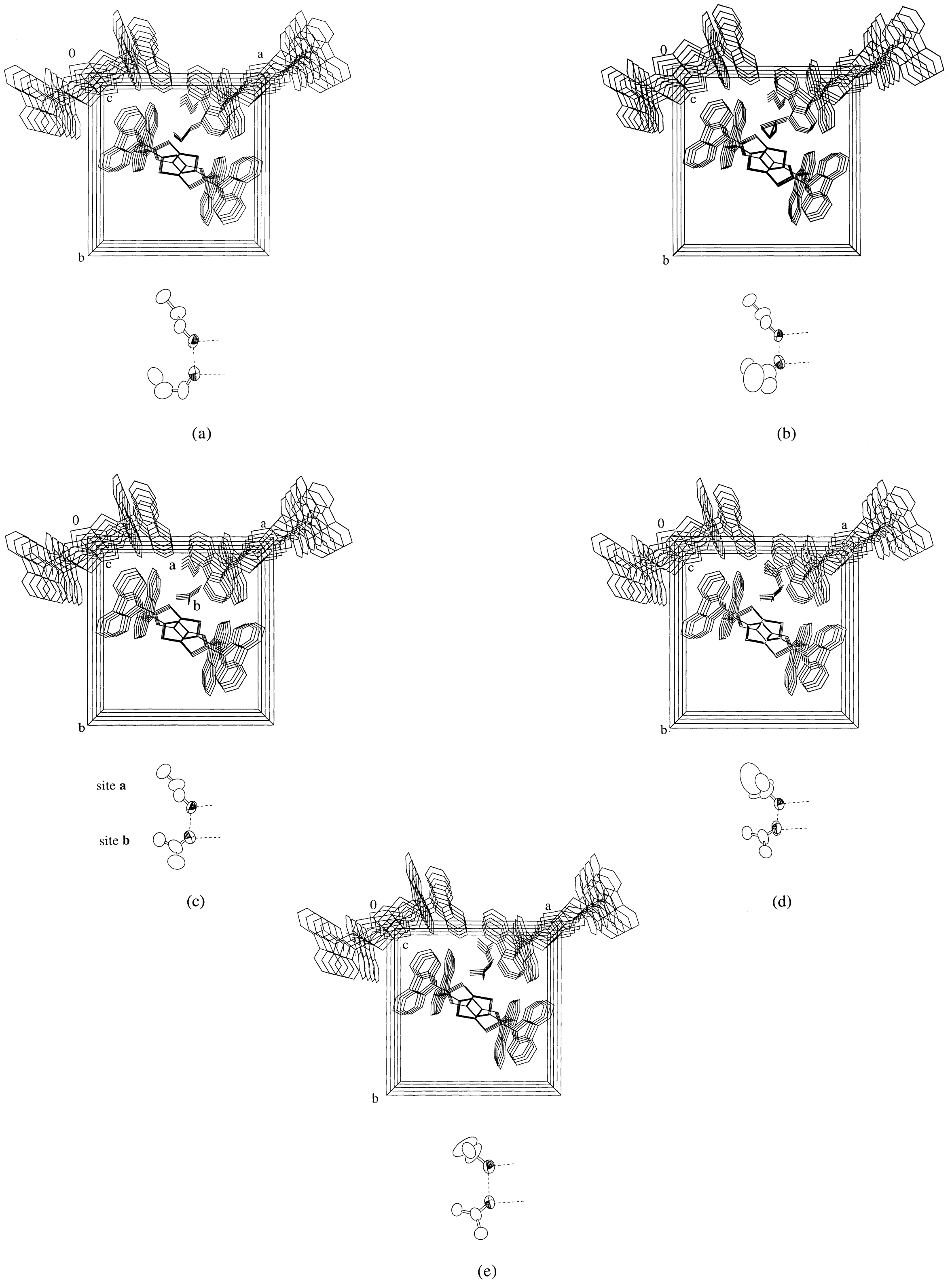


Fig. 8. X-ray powder diffraction patterns for polymorph of guest-free **2**. (a) the crystals obtained by recrystallization of **2** from CH_2Cl_2. (b) the crystals obtained by exposure of β-(**2**)$(EtOH)_2$ to MeOH vapor.

Not Guest-Selective but Site-Selective

Host **5** forms a channel-type inclusion cavity on recrystallization from *n*-PrOH and *i*-PrOH to give the clathrates (**5**)$(n\text{-PrOH})_2$ and (**5**)$(i\text{-PrOH})_2$, respecively.[40] The difference between the backbone geometries of the two isomeric propyl alcohols might normally be expected to result in the formation of different clathrate structures. In fact, a clathrate that has topologically and geometrically different frameworks for *n*-PrOH and *i*-PrOH has been known.[38] Selective inclusion of *i*-PrOH from a mixed solvent of *n*-PrOH and *i*-PrOH has been described.[39] Nevertheless, crystals of (**5**)$(n\text{-PrOH})_2$ and (**5**)$(i\text{-PrOH})_2$ are isostructural. Crystallographically, there are two nonequivalent guest molecules at site ***a*** and site ***b*** in the channel along the *c* axis (Fig. 9). Each of the hydroxy groups of the host molecules is linked to a guest molecule by hydrogen bonding. Taking into consideration that (**5**)$(n\text{-PrOH})_2$ and (**5**)$(i\text{-PrOH})_2$ are isostructural, one can reasonably assume that host **5** shows no guest-selectivity between *n*-PrOH and *i*-PrOH. In fact, guest competition experiments using a mixed solvent of *n*-PrOH and *i*-PrOH revealed that **5** cocrystallizes with the guest alcohols in the same ratio as that of the solution to give three-component clathrates (**5**)$(n\text{-PrOH})_x(i\text{-PrOH})_{2-x}$ in all fractions (x = 0–2) of the guest component.[40] Therefore, one might assume that both guest components are distributed randomly among sites ***a*** and ***b*** like a solid solution in the channel. However, this is not the case (Fig. 9), as seen in the X-ray crystal structures of (**5**)$(n\text{-PrOH})_{1.4}(i\text{-PrOH})_{0.6}$ and (**5**)(*n*-



(a) (b) (c) (d) (e)

Fig. 9. Crystal structures of n-PrOH and i-PrOH inclusion crystals of **5** and guest occupation at site ***a*** and ***b***. The guest molecules are also hydrogen-bonded with the host hydroxy groups (omitted in the figure) to form an O···O four-centered circle made up of two guests and two host molecules. (a) $(\mathbf{5})(n\text{-PrOH})_2$. (b) $(\mathbf{5})(n\text{-PrOH})_{1.4}(i\text{-PrOH})_{0.6}$. (c) $(\mathbf{5})(n\text{-PrOH})(i\text{-PrOH})$. (d) $(\mathbf{5})(n\text{-PrOH})_{0.4}(i\text{-PrOH})_{1.6}$. (e) $(\mathbf{1})(i\text{-PrOH})_2$.

$\text{PrOH})_{0.4}(i\text{-PrOH})_{1.6}$. In $(\mathbf{5})(n\text{-PrOH})_{1.4}(i\text{-PrOH})_{0.6}$, site ***a*** is occupied by the major component, n-PrOH, and site ***b*** is shared with two guests. For $(\mathbf{5})(n\text{-PrOH})_{0.4}(i\text{-PrOH})_{1.6}$, the distribution is opposite to that of $(\mathbf{5})(n\text{-PrOH})_{1.4}(i\text{-PrOH})_{0.6}$; site ***b*** is occupied exclusively by the major guest *i*-PrOH, while site ***a*** is occupied randomly by two guests. Consequently, in the 1:1:1 ternary crystal (**5**)(*n*-PrOH)(*i*-PrOH), each guest lies at its most favorable site.

The majority of the guests in the solution preferentially locate at their most favorable site, leaving the other site open for random distribution. Nevertheless, the guest ratio of the solution is realized through sites ***a*** and ***b***. This unique inclusion phenomenon would be ascribed to the occurrence of multiple inclusion sites which are slightly different in the void cavity for discrimination by two isomeric alcohols.

When inclusion complex (**5**)(*n*-PrOH)$_2$ was exposed to *i*-PrOH vapor, *n*-PrOH was gradually replaced by *i*-PrOH, forming three-component clathrates.[40] Surprisingly, the exchange almost stopped at 50% to form the 1:1:1 ternary clathrate (Fig. 10). Further exchange above 50% was quite slow. Thus, once (**5**)(*n*-PrOH)$_2$ has been formed, no change in the host-to-guest ratio occurs even after 20 days. Similar behavior has been observed for (**5**)(*i*-PrOH)$_2$; upon exposure of (**5**)(*i*-PrOH)$_2$ to gaseous *n*-PrOH, the exchange does not exceed 50%, again giving the 1:1:1 clathrate (**5**)(*n*-PrOH)(*i*-PrOH) (Fig. 11).

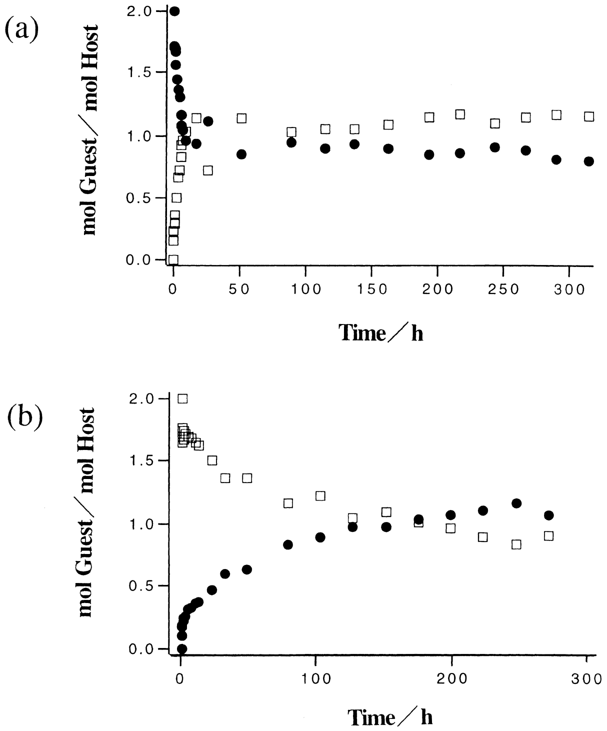


Fig. 10. Time course of guest exchange via gas-solid contact. (a) conversion from (**5**)(*n*-PrOH)$_2$ to (**5**)(*n*-PrOH)(*i*-PrOH). (b) conversion from (**5**)(*i*-PrOH)$_2$ to (**5**)(*n*-PrOH)(*i*-PrOH). ●: fraction of *n*-PrOH. □: fraction of *i*-PrOH.

The inclusion behavior of **5** for *n*-PrOH and *i*-PrOH is thus different for recrystallization from solution and for guest exchange via gas–solid contact. These results again indicate that the guest exchange via gas–solid contact does not result from condensation of the guests on the solid surface, followed by recrystallization of the surface and concomitant enclathration and reorganization.

The unique solid-state phenomena described here seem to be characteristic for ternary clathrates which include two guest species. Little attention has been paid to characterization of three-component crystalline complexes. Host–guest–guest or host–host–guest clathrate expands the region of supramolecular chemistry.[41]

Clathrate Crystals with Charge-Transfer Character

As already noted in the introduction, the host compounds designed in the forgoing investigation are endowed with donor character, even though it is not so strong. In spite of irregular structures as donor species, these compounds afforded crystalline charge-transfer complexes.

When a weak acceptor such as 1,2,4,5-tetracyanobenzene (TCNB) is used for complexation,[42] compound **2** crystallizes including solvent molecules to give a three-component 1:1:1 complex, (**2**)(TCNB)(CH_2Cl_2). In the diffuse-reflectance of (**2**)(TCNB)(CH_2Cl_2) a well-defined intense band is observed at 410 nm, whereas this band is not observed in each component in the solid state. Similarly, **5** forms complex (**5**)(TCNB)(CH_2Cl_2), while the molecular complex derived from **1** has a 2:1 stoichiometry of (**1**)$_2$(TCNB) without enclathration of CH_2Cl_2. Hosts **3** and **4** afford no molecular complexes with TCNB. Host **4** is the most electron-donating among the compounds **1**–**4**. Nevertheless, it gave no complex with TCNB, indicating that the formation of (**1**)$_2$(TCNB), (**2**)(TCNB)(CH_2Cl_2), and (**5**)(TCNB)(CH_2Cl_2) cannot be merely ascribed to charge-transfer complexation. The X-ray crystal structure of (**5**)(TCNB)(CH_2Cl_2) indicates that a –D–A–D–A–D–A- type of mixed stacks is constructed by the face-to-face overlapping of the fluorenyl and the TCNB rings.[42] In (**1**)$_2$(TCNB) crystal, the molecule of **1** is arranged in such a way that one of its fluorenyl rings faces a TCNB molecule and the other faces the fluorenyl ring of the neighboring **1** molecule (Fig. 12) to stack in a –D–A–D–D–A–D- sequence. It should be noted that the polycondensed thiophenes, **2**, **3**, **4**, give no crystalline molecu-

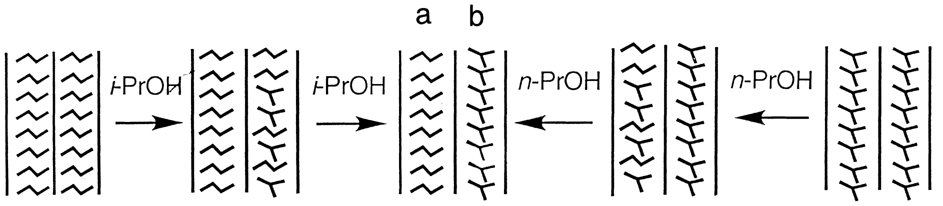


Fig. 11. Schematic representation for the exchange of guest molecules at site ***a*** and ***b*** in a channel constructed in the clathrates of **5**. N-shaped molecules represent *n*-PrOH and Y-shaped molecules represent *i*-PrOH.

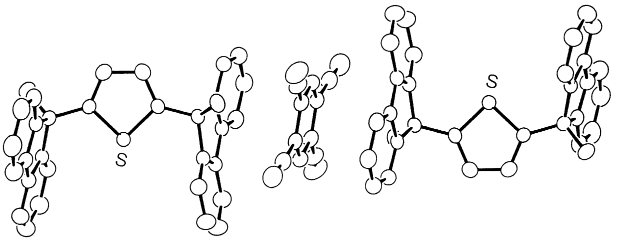


Fig. 12. Perspective view of the trimeric unit in (**1**)$_2$(TCNB).

lar complexes with TCNB despite their molecular planarity.

Complexation with tetracyanoquinodimethane (TCNQ) was achieved by using butyronitrile as solvent. Compound **2** forms again a 1:1:1 three-component crystal, (**2**)(TCNQ)(C_3H_7-CN).[43] The donor and acceptor molecules are aligned in a –D–A–D–A- sequence by face-to-face stacking of the fluorenyl ring and TCNQ ring. The solvent molecules are entrapped in the lattice provided by the donor and acceptor molecules. TetrafluoroTCNQ (F_4TCNQ), which is a stronger acceptor than TCNQ, forms complex (**2**)(F_4TCNQ)(C_3H_7CN). The X-ray crystal analysis revealed that the crystal structure is isostructural with that of (**2**)(TCNQ)(C_3H_7CN).[43]

When **3** was recrystallized together with dichlorodicyano-*p*-benzoquinone (DDQ) from dichloromethane, a three-component complex comprised of the 2:1:1 stoichiometry of **3**:DDQ:H_2O was isolated as dark-greenish crystals.[44] The molecules **3** make a cage-like dimeric unit, in which both the dithienothiophene and the fluorenyl planes face outside the dimeric block.[45] The dimeric units are aligned in a rather rarely encountered –D–D–A–D–D–A- stacking column along the a axis (Fig. 13).[46] Even though a mixed stack is seen along the a axis, along the c axis the dimeric donor molecules are aligned in a face-to-face stack of the fluorenyl π-planes. Thus, a segregated columnar stack is realized, even in the charge-transfer complex composed of the donor molecule bearing bulky and rotation-free fluorenyl substituents. The inner C=C bond of moiety **3** is obviously longer than that of the neutral one, indicating that charge transfer is induced in the crystals.

As the ionization energy of fluorene (IP = 7.89 eV) is lower than that of thieno[3,2-*b*]thiophene (IP = 8.10 eV), the overlap with the acceptor molecules is accomplished at the fluorenyl rings. As seen above, crystallization of a donor-acceptor system that consists of ragged-shaped molecules requires the lattice-assisted inclusion of solvent molecules as the third component for crystallization. Host **5** enclathrates a stable organic free radical 4-amino-2,2,6,6-tetramehylpiperidin-1-oxyl (ATEMPO) together with solvent molecules to afford (**5**)(ATEMPO)$_2$(dioxane)$_2$.[47] These crystals exhibit antiferromagnetic spin interactions below 4 K. On the other hand, clathrate crystals derived from host **2**, (**2**)(ATEMPO)$_2$, are paramagnetic down to liquid-helium temperature. The crystals of (**5**)(ATEMPO)$_2$(dioxane)$_2$ and (**2**)(ATEMPO)$_2$ include a common guest compound ATEMPO, whereas those show different magnetic properties in the solid state. This study suggests a potential importance of ternary clathrate crystals to explore new molecular solids.

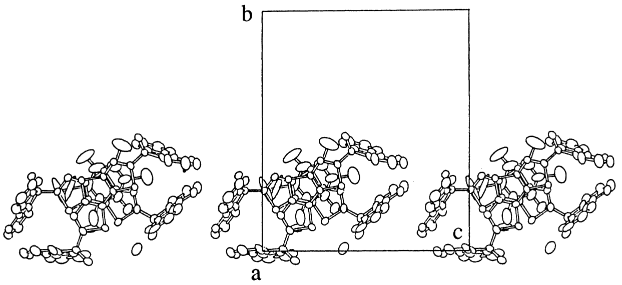


Fig. 13. Crystal structure of (**3**)$_2$(DDQ)(H_2O) showing a columnar stack of host **3** molecules along the *c* axis.

Charge-Transfer Interaction Induced by Cogrinding Donor and Acceptor

It has been demonstrated that two-component crystalline complexes are formed simply by grinding together two separate crystalline phases. Some hydrogen-bonded complexes[48] and host-guest clathrate crystals[49] should be considered as examples. It is also the case for charge-transfer complexes: complexation is accomplished not only by recrystallization of the donor and acceptor components from solutions, but also by cogrinding the solid donor and acceptor species.[50] The solids obtained by cogrinding TTF and TCNQ exhibit high electrical conductivity of similar magnitude to that found in the TTF-TCNQ complex obtained by recrystallization.[51] In this case, both TTF and TCNQ are planar molecules. Then, is it also possible for non-planar donor compounds to induce charge-transfer complexation by solid-state cogrinding with acceptors ?

Alcohol **2** and TCNQ were coground in a mortar with a pestle to give a dark-green solid.[52,53] When the coground solids were dissolved in acetonitrile, the dark color disappeared immediately, and TCNQ and alcohol **2** were recovered quantitatively. The solids resulting from cogrinding exhibited absorption at 534 nm, which is identical to that observed in crystalline charge transfer complex (**2**)(TCNQ)(C_3H_7CN) obtained by recrystallization from butyronitrile (C_3H_7CN). It is of interest that the X-ray powder diffraction intensities decrease significantly with cogrinding, indicating that the crystalline phase of both starting components collapses and the charge-transfer cocrystalline phase is not constructed.

By grinding a mixture of donor and acceptor species in the solid state, imperfections containing unpaired electron spins can be introduced. Thus, it has been known that the ESR signal appears in the powder sample obtained by grinding a mixture of perylene and bromanil.[54] A similar phenomenon has been observed for non-planar compounds: upon cogrinding with TCNQ or DDQ in a mortar with a pestle, compound **2** gives rise to amorphous solids which involve a radical ionic species, as probed by UV/vis and ESR spectra.[52,53] For molecules with irregular shape such as **2**, periodic packing to form crystals of charge-transfer complexes would be unfavorable and such molecules rather take random orientation in the coground solids. However, the solid-state grinding would force the molecules closer together by collapsing the original lattice structure and hence would permit charge-transfer at the interface of the donor and acceptor to allow location of unpaired electrons.

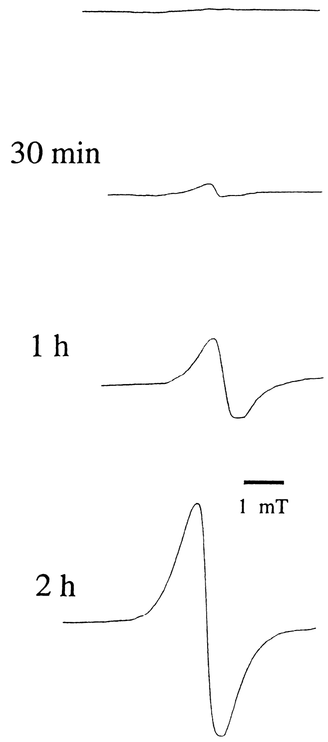


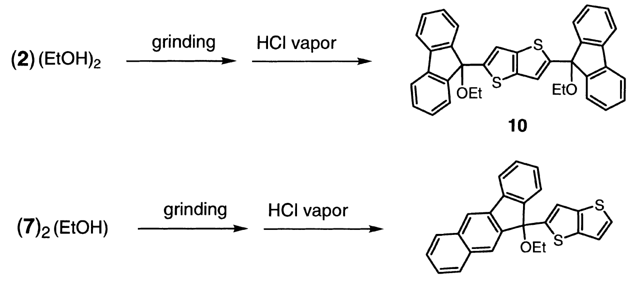
Fig. 14. Enhancement of the ESR signal with grinding (**2**)(TCNQ)(C_3H_7CN) crystals. At the outset (top) there are no signals.

The above observation is in line with the following experiments reported by Matsunaga.[55] When 2,4,6-trinitrodiphenylamines are melted and then quickly cooled, the resulting super-cooled melt shows a deeper color than that in the crystalline state, indicating that charge-transfer interactions are enhanced. For example, 3′-methoxy-2,4,6-trinitrodiphenylamine is yellow in the crystalline state, while it is reddish-orange in the molten and super-cooled state. Even when the molecular packing in the crystalline state is unfavorable for the intermolecular charge-transfer interactions, contact between the two moieties may be allowed by the disorder introduced by melting.

Then, it is interesting to see if there is any effect of grinding on crystalline charge-transfer complexes in which the donor and acceptor molecules are already periodically aligned. When the homogeneous (**2**)(TCNQ)(C_3H_7CN) crystals were ground in a mortar, the ESR signals were enhanced (Fig. 14).[43] The ground solids again result in collapse of crystallinity as probed by X-ray powder diffraction measurements. These observations indicate that the electron transfer is promoted by grinding and that enhanced electron spins are trapped in imperfection sites. As described in the next section, the spin enhancement is associated with the reactivity of solids induced by gas-solid contact.

Solid-State Reactions of the Clathrates

We planned to realize the solid-state ionic reactions between the host and guest species. Ionic reactions are usually carried out by dissolving the substrate in solvent. If ionic reactions could be achieved in the solid state, we could avoid the expense of solvents and the processes would have ecological and economical value.[56]



Scheme 1.

The (**2**)(EtOH)$_2$ crystals were exposed to HCl gas in a desiccator at room temperature for 3 h. After working up using a dilute aqueous NaOH solution, the products were analyzed by means of NMR to show that the corresponding ether **10** was formed in 38% yield (Scheme 1). Throughout the exposure procedure there was no sign of wetting or melting. This reaction was designated as "solid-state solvolysis," since nucleophilic substitution reactions by ethanol are achieved while retaining the solid-state, without dissolving the substrate in ethanol.

Similar solid-state solvolyses were observed in clathrates of host **7** and **8** (Chart 4) including alcohols as guests. Th racemic forms of **7** and **8** afforded crystalline inclusion complexes represented by formulas (**7**)$_2$(MeOH), (**7**)$_2$(EeOH), (**8**)(*i*-PrOH), and (**8**)(*n*-PrOH). When exposed to HCl vapor, these solid powders afforded the corresponding alkyl ethers in 22, 34, 35, and 76% yields, respectively.[53,43] Unfortunately, optically pure **7** and **8** afforded no crystalline inclusion complexes with alcohols, probably, due to lack of an inversion center in the molecule and thereby inefficiency for close packing. Therefore, the stereochemistry of the solid-state nucleophilic substitution reactions is not disclosed yet.[58]

It is interesting to note that solid-state photolysis of (**2**)(EtOH)$_2$ resulted also in a substitution reaction to give **10** in 21% yield along with the monoether in 43% (Scheme 1).[57] The solid-state formation of **10** is conclusive, since the mass spectra of the irradiated solids exhibit, prior to work-up procedure, the molecular ion peaks ascribed to **10**. Such "solid-state photosolvolysis" was also observed in (**5**)$_2$(EtOH) crystals.

In the above noted solid-state solvolysis the catalyst is intro-

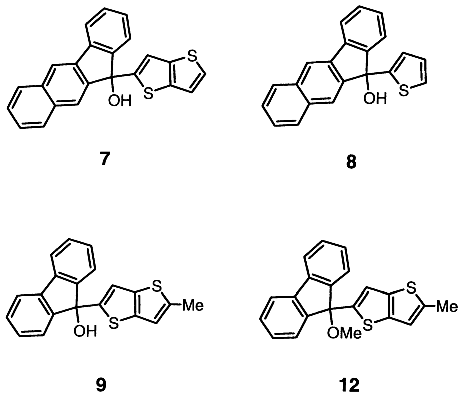
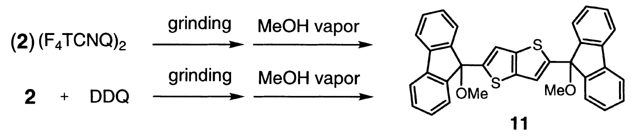


Chart 4.



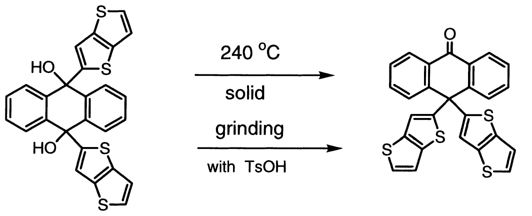
Scheme 2.

duced as an external gaseous component. It is rather difficult to obtain the clathrates including an acid component as guest, because the hosts are quite labile on recrystallization from acidic solutions. Thus, instead of clathrates including an acid in solids, the crystals bearing a charge-transfer nature were utilized. As described already, host **2** forms three-component crystals, (**2**)(F_4TCNQ)(C_3H_7CN). On grinding the homogeneous crystals of this (**2**)(F_4TCNQ)(C_3H_7CN) followed by contact with MeOH vapor, we obtained the methoxy-substituted product **11** in over 90% yield (Scheme 2). No products originating from F_4TCNQ were detected and F_4TCNQ was recovered quantitatively. Similarly, the substitution was induced in (**2**)$(DDQ)_2$ to give **11** by grinding, followed by contact with methanol vapor.[52,53]

It has been confirmed that charge-transfer interactions are induced by cogrinding the donor and acceptor compounds. So the coground solids of the host and acceptor species, instead of the ground powder of the homogeneous charge-transfer crystals, were exposed to alcohol vapor. Thus, on cogrinding with F_4TCNQ followed by exposure to vapor of methanol, compound **2** afforded **11**. Similar gas-solid reactions take place by cogrinding of **2** with DDQ followed by exposure to methanol to give diether **11** in 25% together with monoether in 35% yield. Compound **9** undergoes an analogous methoxy substitution to give **12** in 45% yield. In all cases, the solid-state was maintained throughout the procedure of grinding and exposure.

The mechanism proposed is that a radical cation is generated in the coground solids via charge-transfer interaction and collapses to generate a proton.[53] The proton thus produced in the solid state acts as a catalyst. This mechanistic interpretation is deduced from ESR, UV, CV, and electrochemical oxidation in solution. A key observation for this mechanism is obtained by using methoxy-substituted derivative **12**: the solid-state solvolysis cannot be induced on the coground solids of **12** and DDQ followed by exposure to ethanol vapor. It is evident that the hydroxy group in the host compound plays an essential role for the promotion of the solid state solvolysis. The acidity of alcohol radical cations is significantly enhanced.[59] The acid generation is propagated upon contact of the carbocation with methanol vapor. The crystals of (**2**)(TCNQ)(C_3H_7CN), which is isostructural with (**2**)(F_4TCNQ)(C_3H_7CN), afforded no substitution. The acceptor ability of F_4TCNQ is stronger than that of TCNQ, generating radical cation species to promote the substitution reactions.[43]

Host compounds **13** and **14**, which are *cis* and *trans* isomers respectively, could be used for investigation of the stereochemical aspects of the solid-state substitution reactions. Unfortunately, these hosts gave no clathrates incorporating alcohols or acceptor species, while a novel thermally induced rearrangement was found in these hosts themselves. Thus, a vinylogous pinacol rearrangement, involving an intramolecular 1,4-migration of the bulky thienothienyl substituent and a marked change in the crystal structures, was thermally induced in the solid state for **13** and **14**. When heated to a temperature over 180–240 °C, these crystals were transformed quantitatively, with accompanying dehydration, to crystals of anthrone derivative **15** without wetting or melting (Scheme 3).[60]



13 **14**
cis *trans*

15

Scheme 3.

The intramolecular nature of the rearrangement was ascertained based on the product distribution from the reaction of the mixed crystals of **14** and its isomer, which bears isomeric thieno[3,2-*b*]thiophene and thieno[2,3-*b*]thiophene rings. The 1,4-pinacol type rearrangements were also induced, along *cis–trans* isomerization, by cogrinding the diol with *p*-toluenesulfonic acid in a mortar at room temperature.[60]

Concluding Remarks

The inclusion properties of a new series of thiophene-condensed hosts and their solid-state behaviors have been summarized. A variety of solid-state phenomena that are rather unexpected were found. One may wonder if the initial intention of the molecular design has been fulfilled. Some results are as expected, but some results are much more promising.

A variety of crystalline three-component complexes were encountered, which are formed via cooperative effect including lattice-assisted clathration, charge-transfer interaction, and hydrogen-bonding. Host–guest–guest or host–host–guest ternary clathrate chemistry should be an impetus for future research. The channel structures for guest inclusion are frequently realized for these host series. It is not easy to assess what is essentially responsible for such channel voids. The incorporation of two planar walls, one the fluorenyl ring, and the other the thienothiophene ring, is effective for the occurrence of channels. Through this work, polymorphism and isostructural crystals of the host-guest binary system have been found. These phenomena should be important to expand the field of crystal engineering likewise as isomerisms at the molecular level. The host compounds herein have revealed the fundamental solid-state phenomena that are universal to lead to a better understanding of the sorptive mechanism and selectivity of clatharate formation.

Some general accounts suggest the following:

(1) Incorporation of polycondensed thiophene rings exhibits consecutive change in the molecular structure of host compounds and can manipulate or tune the inclusion properties to some extent as seen in an even-odd effect.

(2) In the ternary clathrates, the guest inclusion is random but site-selective. The guest exchange in a channel occurs while retaining the channel without collapse and reorganiza-

tion at the solid surface via gas-solid contact.

(3) The occurrence of pseudopolymorphism is ascribed to the difference in the magnitude of the intermolecular interactions, which is also associated with the direction of hydrogen-bonding. The bifurcated hydrogen bonding to the CN group was found.

(4) The incorporation of charge-transfer interactions is a unique approach to induce the solid-state two-component reactions.

(5) The solid-state reactions induced by grinding tend to result in amorphous states.

(6) Insight into the implication of solid-state grinding is deduced; the solid-state cogrinding forces the component molecules to come closer together and to permit a stronger contact than in the periodically arranged crystalline state. Also, increase in imperfections in the solids would be favorable for localization of electron spins.

(7) The solvolysis retaining the solid state could be induced in clathrates by gas–solid contact.

The future of this field is intimately connected with the progress and the discovery of new strategies for crystalline inclusion formation and the deeper understanding of the crystal engineering.

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