Communications to the Editor

Guest-Incorporation in Ternary Clathrate Formation Is Random but Shows Site-Selectivity

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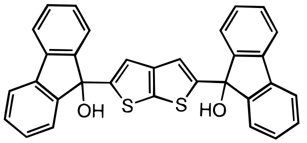
Crystalline inclusion complexes, designated as clathrates,[1] are usually composed of both host and guest species, and their supramolecular design has been extensively investigated.[2] On the other hand, there have been few structural studies of three-component clathrates. In the context of host−guest−guest clathrate chemistry, two guest compounds of similar molecular shape and size may be incorporated with random distribution in the host cavity to form a ternary clathrate. The X-ray crystallographic characterization of such three-component crystalline complexes has attracted little attention, because selective inclusion has been much more of a central problem than random incorporation. We now describe for the first time novel inclusion and guest-exchange behavior in the formation of ternary clathrate crystals.[3]

The host compound 2,5-bis(9-hydroxyfluoren-9-yl)thieno[2,3-*b*]thiophene (**1**)[4] formed a channel-type inclusion cavity on recrystallization from *n*-PrOH and *i*-PrOH to give the clathrates (**1**)(*n*-PrOH)$_2$ and (**1**)(*i*-PrOH)$_2$, respectively, with a 1:2 stoichiometric ratio.



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The difference between the primary and secondary backbone geometries of the two propanol isomers might normally be expected to result in the formation of different clathrate structures.[5] Host **1**, however, forms the isostructural clathrate crystals with the isomeric guests *n*-PrOH and *i*-PrOH.[6] It should be noted here that the host lattice of **1** changes its structure according to the guest compounds and cannot persist in a guest-free state.[7] Thus host **1** resembles neither an inorganic host such as zeolite nor an organic host such as urea.

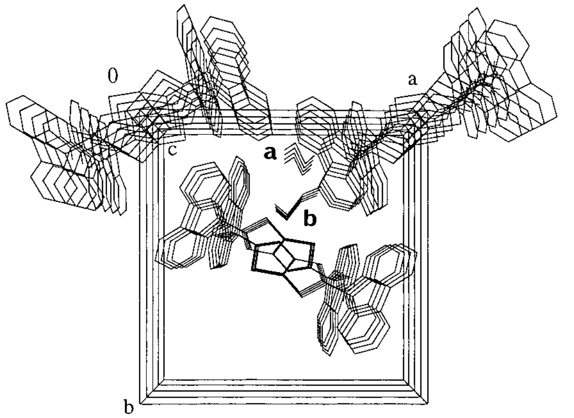

Figure 1. Perspective view of the channel along the *c* axis in **1** (*n*-PrOH)$_2$.

Crystallographically, there are two nonequivalent guest molecules at site **a** and site **b** in the channel along the *c* axis (Figure 1).[8] Each of the hydroxyl groups of the host molecule is linked to a guest molecule by hydrogen bonding. A pair of (host)(guest)$_2$ units dimerizes in a face-to-face manner through hydrogen bonding into a centrosymmetric (host)$_2$(guest)$_4$ unit, forming a cyclic (−OH)$_4$ array of hydrogen bonds.

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(1) (a) *Molecular Inclusion and Molecular Recognition-Clathrates I and II in Topics in Current Chemistry*; Weber, E., Ed.; Springer-Verlag: Berlin-Heidelberg; 1987 and 1988; Vols. 140 and 149. (b) Bishop, R. *Chem. Soc. Rev.* **1996**, 311.

(2) *Crystallography of Supra-molecular Compounds*; Tsoucaris, G., Atwood, J. L., Lipkowski, J., Eds.; Kluwer Academic Publishers: London, 1996.

(3) For recent examples of occurrence of three-component clathrates, see: (a) Dvorak, D.; Zavada, J.; Etter, M. C.; Loehlin, J. H. *J. Org. Chem.* **1992**, *57*, 4839. Caira, M. R.; Coetzee, A.; Koch, K. R.; Nassimbeni, L. R.; Toda, F. *J. Chem. Soc., Perkin Trans. 2* **1996**, 569. (b) Caira, M. R.; Coetzee, A.; Koch, K. R.; Nassimbeni, L. R.; Toda, F. *J. Chem. Soc. Perkin Trans. 2* **1996**, 569. (c) Kawai, Y.; Kunitomo, J.; Ohno, A. *Tetrahedron Lett.* **1996**, *37,* 8905. (d) Kolotuchin, S. V.; Fenlon, E. E.; Wilson, S. R.; Loweth, C. J.; Zimmerman, S. C. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2654. (e) Caira, M. R.; Nassimbeni, L. R.; Scott, J. L. *J. Chem. Soc., Perkin Trans. 2* **1994**, 1403. (f) Weber, E.; Skobridis, K.; Wierig, A.; Barbour, L. J.; Caira, M. R.; Nassimbeni, L. R. *Chem. Ber.* **1993**, *126*, 1141. (g) Barbour, L. J.; Steed, J. W.; Atwood, J. L. *J. Chem. Soc., Perkin Trans. 2* **1995**, 857. (h) Lynch, D. E.; Smith, G.; Byriel, K. A.; Kennard, C. H. L. *J. Chem. Soc., Chem. Commun.* **1992**, 300. (i) Biradha, K.; Edwards, R. E.; Foulds, G. J.; Robinson, W. T.; Desiraju, G. R. *J. Chem. Soc. Chem. Commun.* **1995**, 1705. (j) Brunet, P.; Simard, M.; Wuest, J. D. *J. Am. Chem. Soc.* **1997**, *119*, 2737. (k) Ochiai, K.; Mazaki, Y.; Noshikiori, S.; Kobayashi, K.; Hayashi, S. *J. Chem. Soc., Perkin Trans. 2* **1996**, 1139.

(4) (a) Hayashi, N.; Mazaki, Y.; Kobayashi, K. *J. Chem. Soc., Chem. Commun.* **1994**, 2351. (b) Hayashi, N.; Mazaki, Y.; Kobayashi, K. *J. Org. Chem.* **1995**, *60*, 6342. (c) Mazaki, Y.; Hayashi, N.; Kobayashi, K. *J. Chem. Soc., Chem. Commun.* **1992**, 1381.

(5) For example, a selective inclusion of *i*-PrOH from a mixed solvent of *n*-PrOH and *i*-PrOH has been reported; Suzuki, H. *Tetrahedron Lett.* **1992**, *33*, 6318. Inorganic clathrates form topologically and geometrically different framework for *n*-PrOH and *i*-PrOH: Kim, J.; Whang, D.; Lee, J. I.; Kim, K. *J. Chem. Soc., Chem. Commun.* **1993**, 1400.

(6) For isostructurality of organic crystals, see: Kalman, A.; Parkanyi, L. In *Advances in Molecular Structure Research*; Hargittai, M., Hargittai, I., Eds.; JAI Press Inc.: Greenwich, CT, 1997; p 189.

(7) Among the clathrates obtained from host **1** so far, (**1**)$_2$(MeOH), (**1**)$_2$(EtOH), (**1**)(ethyleneglycol), (**1**)(DMSO)$_2$, (**1**)(benzene), and (**1**)(nitromethane) have been revealed to differ in their X-ray structures. For (**1**)$_2$(EtOH), (**1**)(DMSO)$_2$, and (**1**)(benzene), see ref 4. The other crystal structures will be reported elsewhere in due course.

(8) Crystal data at room temperature with Mo Kα radiation ($\lambda = 0.710\ 69$ Å): **(1)(*n*-PrOH)$_2$** $P2_1/n$, $a = 15.838(1)$, $b = 16.015(3)$, and $c = 13.127(9)$ Å, $\beta = 92.86(0)°$, $V = 3325(2)$ Å^3, $Z = 4$, $\rho_{\mathrm{calcd}} = 1.240$ g cm^{-1}, 3418 reflections of 8249 with $I > 3(\sigma)I$, $R = 0.0656$, $R_W = 0.0737$; **(1)(*i*-PrOH)$_2$** $P2_1/n$, $a = 16.071(2)$, $b = 16.051(4)$, and $c = 13.054(2)$ Å, $\beta = 95.45(2)°$, $V = 3352(1)$ Å^3, $Z = 4$, $\rho_{\mathrm{calcd}} = 1.230$ g cm^{-1}, 3352 reflections of 8400 with $I > 3(\sigma)I$, $R = 0.0952$, $R_W = 0.0895$; **(1)(*n*-PrOH)$_{1.4}$(*i*-PrOH)$_{0.6}$** $P2_1/n$, $a = 15.836(3)$, $b = 15.936(3)$, and $c = 13.194(2)$ Å, $\beta = 93.74(1)°$, $V = 3323(1)$ Å^3, $Z = 4$, $\rho_{\mathrm{calcd}} = 1.240$ g cm^{-1}, 3289 reflections of 8190 with $I > 3(\sigma)I$, $R = 0.0898$, $R_W = 0.0985$; **(1)(*n*-PrOH)$_{0.4}$(*i*-PrOH)$_{1.6}$** $P2_1/n$, $a = 16.004(1)$, $b = 16.005(2)$, $c = 13.116(2)$ Å, $\beta = 95.08(1)°$, $V = 3346(1)$ Å^3, $Z = 4$, $\rho_{\mathrm{calcd}} = 1.232$ g cm^{-1}, 3929 reflections of 8472 with $I > 3(\sigma)I$, $R = 0.0665$, $R_W = 0.0824$; **(1)(*n*-PrOH)(*i*-PrOH)** $P2_1/n$, $a = 15.865(2)$, $b = 15.895(2)$, and $c = 13.225(1)$ Å, $\beta = 94.14(1)°$, $V = 3326(1)$ Å^3, $Z = 4$, $\rho_{\mathrm{calcd}} = 1.240$ g cm^{-1}, 4011 reflections of 8344 with $I > 3(\sigma)I$, $R = 0.0691$, $R_W = 0.0827$. In all analyses, the *i*-PrOH molecules are disordered to give the appearance of a planar framework structure. This disorder along with the large thermal motion of the guest molecules is responsible for the relatively high *R* values. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre.

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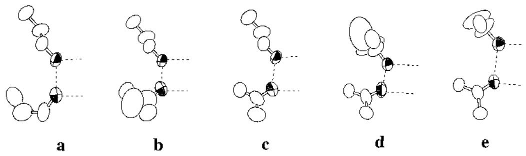

Figure 2. View of the two independent guest molecules showing their relationship linked by hydrogen bonding (indicated by dotted lines). The guest molecules are also hydrogen-bonded with the host hydroxyl groups (omitted in the figure) to form an O···O four-centered circle made up of two guest and two host molecules. All O···O distances are within 2.80 Å: (a) (**1**)(*n*-PrOH)$_2$, (b) (**1**)(*n*-PrOH)$_{1.4}$(*i*-PrOH)$_{0.6}$, (c) (**1**)(*n*-PrOH)(*i*-PrOH), (d) (**1**)(*n*-PrOH)$_{0.4}$(*i*-PrOH)$_{1.6}$, and (e) (**1**)(*i*-PrOH)$_2$.

It is reasonable to assume that the host shows no guest-selectivity between *n*-PrOH and *i*-PrOH, because (**1**)(*n*-PrOH)$_2$ and (**1**)(*i*-PrOH)$_2$ are isostructural. In fact, guest competition experiments using a mixed solvent of *n*-PrOH and *i*-PrOH revealed that **1** cocrystallizes with two guest alcohols in the same ratio as that of the solution to give three-component clathrates (**1**)(*n*-PrOH)$_x$(*i*-PrOH)$_{2-x}$ in all fractions ($x = 0-2$) of the guests component. Therefore, one may 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, as seen in the X-ray crystal structures of (**1**)(*n*-PrOH)$_{1.4}$(*i*-PrOH)$_{0.6}$ and (**1**)(*n*-PrOH)$_{0.4}$(*i*-PrOH)$_{1.6}$ (Figure 2b,d).[8] In (**1**)(*n*-PrOH)$_{1.4}$(*i*-PrOH)$_{0.6}$ site **a** is occupied by the major component, in this case *n*-PrOH, and site **b** is shared with two guests. For (**1**)(*n*-PrOH)$_{0.4}$(*i*-PrOH)$_{1.6}$, the distribution is completely opposite to that of (**1**)(*n*-PrOH)$_{1.4}$(*i*-PrOH)$_{0.6}$: site **b** is occupied exclusively by the major guest *i*-PrOH, while site **b** is occupied randomly by two compounds. Consequently, in the 1:1:1 ternary complex (**1**)(*n*-PrOH)(*i*-PrOH),[8] obtained by recrystallization of **1** from the 1:1 mixture of *n*-PrOH and *i*-PrOH, each guest molecule lies at its most favorable site (Figure 2c).

The majority of the guests in the solution have a priority for location at their most favorable site, leaving the other site open for random distribution. Nevertheless, the guests ratio of the solution is realized through sites **a** and **b**. This unique inclusion phenomenon is associated with the occurrence of multiple inclusion sites which are slightly different in the void cavity for discrimination by two isomeric alcohols.[9]

When inclusion complex (**1**)(*n*-PrOH)$_2$ was exposed to *i*-PrOH vapor, *n*-PrOH was gradually replaced with *i*-PrOH, forming three-component clathrates. The increase of *i*-PrOH and the decrease of *n*-PrOH were followed by NMR integrations of the dissolved samples at appropriate intervals. The most surprising finding was that the exchange almost stopped at 50% to form the 1:1:1 ternary clathrate (Figure 3). Further exchange above 50% was quite slow. Thus, once (**1**)(*n*-PrOH)(*i*-PrOH) has been formed, no change in the host-to-guest ratio occurs even after 20 days.[10] Similar behavior has also been observed for (**1**)(*i*-PrOH)$_2$; upon exposure of clathrate (**1**)(*i*-PrOH)$_2$ to gaseous *n*-PrOH, the exchange does not exceed 50%, again forming the 1:1:1 clathrate, (**1**)(*n*-PrOH)(*i*-PrOH).

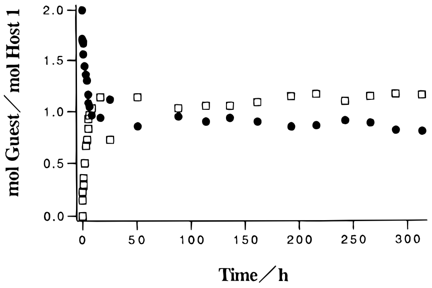

Figure 3. Time course of guest exchange via gas−solid contact resulting in conversion from (**1**)(*n*-PrOH)$_2$ to (**1**)(*n*-PrOH)(*i*-PrOH): fraction of *n*-PrOH (●); fraction of *i*-PrOH (□).

The differing inclusion behavior in recrystallization and gas−solid contact indicates that the guest exchange in 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.[11] The displacement in the channel could be induced by continuous removal of the internal guest molecules and insertion of the external guest molecule. The gaseous external guest expels the same guest species that is located in an uncomfortable site but cannot extrude the counterpart that is already embedded at its comfortable site.

In summary, ternary clathrates represented as (**1**)(*n*-PrOH)$_x$(*i*-PrOH)$_{2-x}$ show novel phenomena in cocrystallization and guest exchange behavior, which are not shown in two-component clathrates. Further investigation on random inclusion may well reveal that these phenomena are universal and fundamental, leading to a better understanding of the sorptive mechanism and selectivity of clathrate formation.

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Supporting Information Available: Tables of atomic coordinates, isotropic and anisotropic displacement coefficients, and bond lengths and angles and torsion angles for (**1**)(*n*-PrOH)$_2$, (**1**)(*n*-PrOH)$_{1.4}$(*i*-PrOH)$_{0.6}$, (**1**)(*n*-PrOH)(*i*-PrOH), (**1**)(*n*-PrOH)$_{0.4}$(*i*-PrOH)$_{1.6}$, (**1**)(*i*-PrOH)$_2$ (62 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

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(9) At site **a** the guest *n*-PrOH molecule adopts a *trans* conformation, while at site **b** the molecule is in a *gauche* conformation and exhibits larger thermal motion than the molecule at site **a**. Thus, site **a** is considered to be a restricted and closely packed environment for *n*-PrOH. On the other hand, the *i*-PrOH molecule exhibits less thermal motion at site **b**, which is considered to be preferred over site **a** for the *i*-PrOH molecule.

(10) For a single crystal of (**1**)(*n*-PrOH)$_2$ about 0.5 × 0.3 × 0.3 mm in size, the complete displacement to form the 1:1:1 clathrate has been accomplished in 1 month at room temperature during which the crystal appeared not to collapse or to become opaque, reminiscent of a single-crystal-to-single-crystal transformation. Unfortunately, despite our intensive efforts, the quality of crystals produced by the guest exchange was inadequate to permit a single-crystal X-ray diffraction study. However, the X-ray powder diffraction measurements and solid-state CP MAS NMR spectra indicated that the host lattice of (**1**)(*n*-PrOH)$_2$ is retained throughout the guest exchange process.

(11) For rearrangement of the crystal lattice induced by guest exchange via gas−solid contact, see: (a) Shibakami, M.; Tamura, M.; Sekiya, A. *J. Am. Chem. Soc.* **1995**, *117*, 4499. (b) Abrahams, B. F.; Hardie, M. J.; Hoskins, B. F.; Robson, R.; Williams, G. A. *J. Am. Chem. Soc.* **1992**, *114*, 10641. (c) Hayashi, N.; Mazaki, Y.; Kobayashi, K. *Adv. Mater.* **1994**, *6*, 654.