Host–Guest Chemistry

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Control of Differential Inclusion Complexation in the Solid State by Seed Crystals**

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Simple phenol and naphthol derivatives include various guest compounds through host–guest hydrogen bonds to produce crystalline inclusion complexes.[1] As these inclusion complexation processes occur selectively, separation of isomers and enantiomers can be carried out upon complexation.[2] Of these phenol and naphthol derivatives, 2,2′-dihydroxy-1,1′-binaphthyl (**1**) is the most interesting host compound because of its axel-asymmetric structure. As optically active **1** precisely recognizes the chirality of the guest molecule it includes, enantiomeric separation of the guest can be

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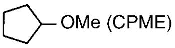
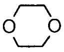
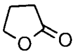
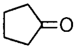
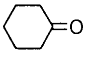
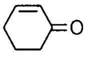
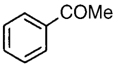
performed easily.[3] However, inclusion complexation of guest compounds with racemic **1** has not been extensively studied to date. Herein, we report that differential inclusion complexation between racemic host **1** and simple gaseous guests in the solid state can be controlled by a seed crystal. We also report that inclusion complexation of **1** with gaseous guests in the solid state occurs only in the presence of a seed crystal.

First, inclusion complexes were prepared by recrystallization of **1** from the liquid guests indicated in Table 1. Four types of inclusion patterns are possible according to the host/guest ratio, namely, with 1:2, 1:1, 2:3, and 3:1 stoichiometries. Interestingly, Et_2O formed two types of inclusion complexes with host/guest ratios of 1:2 and 3:1. The 1:2 complex, **2**, loses Et_2O at a relatively lower temperature (40–61 °C) than the 3:1 complex **3** does (87–108 °C). X-ray crystal structural studies showed that **2** has a loose structure (Figure 1), whereas **3** has a more compact and rigid structure (Figure 2). In complex **2**, Et_2O probably evaporates easily through the channel shown in Figure 1. In complex **3**, however, the molecule of Et_2O is trapped tightly, surrounded by three host molecules.

Table 1: Properties of inclusion complexes of **1** with various liquid guests.

Guest	Host/guest ratio[a]	Decomposition temperature [°C]	$\tilde{\nu}$OH [cm^{-1}][b]
Et_2O	3:1	87–108	3419, 3459, 3489
Et_2O	1:2	40–61	3198
 OMe (CPME)	1:2	37–74	3198
THF	2:3	48–106	3173, 3519
	2:3	61–116	3248
MeOAc	3:1	83–108	3403, 3463, 3491
EtOAc	3:1	75–105	3413, 3464, 3490
	1:2	87–128	3366
$Me_2C{=}O$	1:1	70–98	3036, 3404
	1:1	79–107	3321, 3419
	1:1	87–117	3264, 3417
	1:2	94–121	3199
	1:2	97–141	3198

[a] The ratio was determined by ^{1}H NMR spectroscopy and thermogravimetric analysis. [b] IR spectra were measured using the ATR (attenuated total reflectance) method.

Interestingly, **2** and **3** could also be prepared by recrystallization of **1** (0.2 g) from 3 and 5 mL of Et_2O to give **3** and **2**, respectively (Scheme 1). The more stable complex **3** ($(\mathbf{1})_3{\cdot}Et_2O$) formed preferentially when the complexation was performed rapidly from a concentrated solution. When the complexation was performed slowly from a diluted solution, the less stable **2** ($\mathbf{1}{\cdot}(Et_2O)_2$) crystallized out. This is the first example of differential inclusion complexation by controlling the concentration of the solution, although differential complexations by controlling the temperature[3] or the type of solvent used for crystallization[4] have also been reported. However, when **1** (0.2 g) was recrystallized from an intermediate volume of Et_2O (4 mL), either **2** or **3** formed

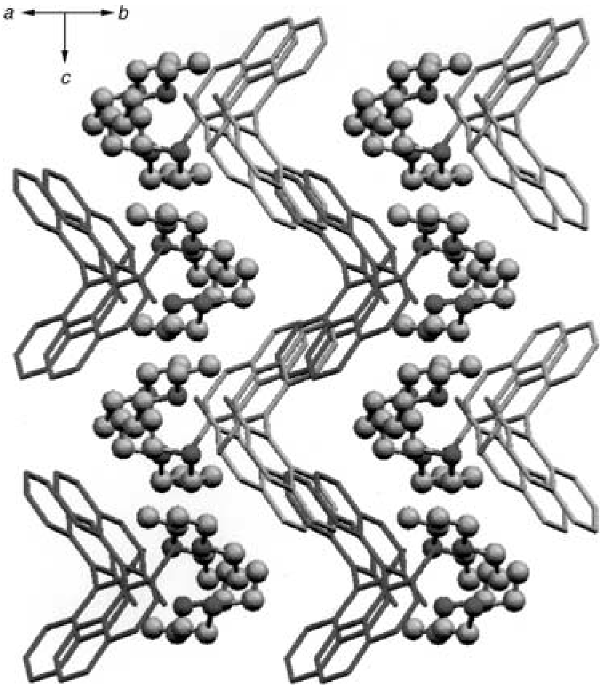


Figure 1. Crystal structure of **2** ($\mathbf{1}{\cdot}(Et_2O)_2$).

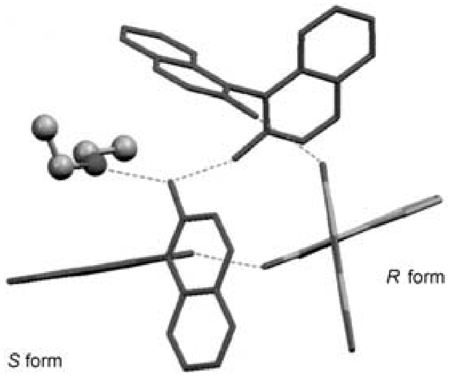
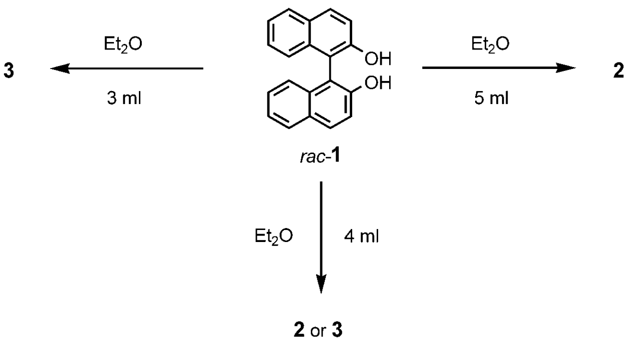


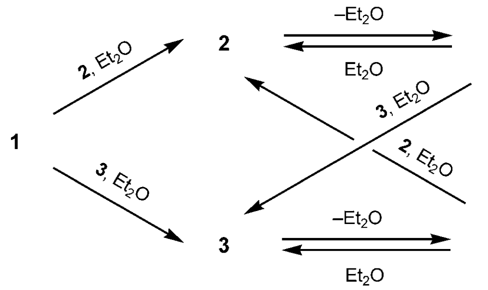
Figure 2. Crystal structure of **3** ($(\mathbf{1})_3{\cdot}Et_2O$).



Scheme 1. Inclusion complexation of host **1** and guest Et_2O by recrystallization of **1** from solutions in Et_2O at different concentrations.

depending on the specific conditions. The pattern of the complexation could be controlled by the seed crystal which formed initially, and this was confirmed by the following seed crystal experiments: Recrystallization of **1** (0.2 g) from 3 and 4 mL of Et_2O by adding one seed crystal of **2** led to formation of **2**; similar recrystallization of **1** (0.2 g) from 3 and 4 mL of Et_2O by adding one seed crystal of **3** led to formation of **3**.

Surprisingly, these seed crystal experiments could also be carried out in the solid state. First, Et_2O (guest)-free hosts **4** and **5** were prepared by evaporation of the guest from **2** and **3**, respectively, by heating at 50 °C under 20 mmHg. Contact of **4** and **5** with Et_2O vapor at room temperature for 12 and 3 h, respectively, gave **2** and **3**, respectively (Scheme 2). These data strongly suggest that **4** and **5** "remember" the original inclusion pattern of **2** and **3**, respectively. Nevertheless, no structural differences between **4** and **5** could be observed by IR spectroscopy or X-ray powder diffraction studies. There is a possibility that **4** and **5** still keep a small amount of Et_2O guest molecules in their inclusion cavities and that these inclusion complex lattices play a role as the seed crystal during complexation in the solid state. When a mixture of powdered **4** and a seed crystal of **3** (2 wt %) was exposed to Et_2O vapor for 3 h, **4** was converted into **3** ($(\mathbf{1})_3{\cdot}Et_2O$) in quantitative yield. By similar contact of a powdered mixture of **5** and a seed crystal of **2** (2 wt %) for 12 h, **5** was converted into **2** ($\mathbf{1}{\cdot}(Et_2O)_2$). Furthermore, contact of a powdered mixture of **1** (98 mg, 0.34 mmol) and **2** (2 mg, 4.6 μmol; 2 wt %, 1.35 mol %) with Et_2O vapor for 12 h gave **2** in quantitative yield (Scheme 2). Similar contact of a powdered mixture of **1** (98 mg, 0.34 mmol) and **3** (2 mg, 2.1 μmol; 2 wt %, 0.62 mol %) with Et_2O vapor for 3 h gave **3** in quantitative yield. However, contact of powdered **1** with Et_2O vapor in the absence of a seed crystal for 72 h did not lead to the formation of any inclusion complexes.



Scheme 2. Seed crystal experiments in the inclusion complexation between solid host **1** and gaseous guest Et_2O.

Seed crystals were also effective for the inclusion complexation of **1** with some other guests. Contact of powdered **1** with gaseous MeOAc and EtOAc for 3 h in the presence of seed crystals of inclusion complexes $(\mathbf{1})_3{\cdot}$MeOAc and $(\mathbf{1})_3{\cdot}$EtOAc, respectively, led to the corresponding inclusion complexes in quantitative yields. Inclusion complexation of **1** and gaseous cyclopentyl methyl ether (CPME) in the presence of a seed crystal of the 1:2 complex $\mathbf{1}{\cdot}(\mathrm{CPME})_2$ for 12 h gave the same inclusion complex as the complex of the seed crystal in quantitative yield. In all of the cases studied, inclusion complexation did not occur in the absence of the seed crystal.

IR spectral data of inclusion complexes of **1** with different guests but at the same host/guest ratio were similar to each other, and the complexes decomposed at similar temperatures (Table 1). The complexes at the same host/guest ratio also have similar solid-state structures. For example, the crystal structures of **2** ($\mathbf{1}{\cdot}(Et_2O)_2$) and the 1:2 complex of **1** with CPME ($\mathbf{1}{\cdot}(\mathrm{CPME})_2$) are very similar, while the crystal structures of **3** ($(\mathbf{1})_3{\cdot}Et_2O$) and the 3:1 complex of **1** with EtOAc[6] ($(\mathbf{1})_3{\cdot}$EtOAc) are also very similar. However, the crystal structure of a 1:2 complex of **1** with 2-cyclohexenone is completely different to that of **2**, and the structures of 2:3 complexes of **1** with THF and 1,4-dioxane are also different.[7]

These data suggest that a crystal of an inclusion complex is effective as a pseudo seed crystal for the formation of a complex at the same host/guest ratio but with a different guest compound (Table 2). For example, contact of powdered **1** with gaseous EtOAc for 3 h in the presence of seed crystal $(\mathbf{1})_3{\cdot}$MeOAc gave the complex $(\mathbf{1})_3{\cdot}$EtOAc, also in a 3:1 host/guest ratio. Similar contact of **1** with gaseous guests in the presence of seed crystals of complexes with host/guest ratios as anticipated in the products indeed gave quantitative yields of inclusion complexes with the same host/guest ratio as those of the seed. These data clearly show the high efficiency of the pseudo seed crystal. However, contact of **1** with gaseous guests in the presence of seed crystals that have a different host/guest ratio from those of the expected product did not afford any inclusion complexes. In the last two examples shown in Table 2, seed crystals $(\mathbf{1})_3{\cdot}$MeOAc and $(\mathbf{1})_3{\cdot}Et_2O$ did not work as seed crystals for the complexation of **1** with CPME, which forms only the 1:2 host/guest complex. In all the cases studied, 3:1 host/guest complexes were formed more easily than those at a 1:2 ratio.

Table 2: Inclusion complexation of powdered **1** and gaseous guests in the presence of a pseudo seed crystal.

Guest in seed crystal (**1**/guest ratio)	Gaseous guest	Reaction time [h]	Guest in product (**1**/guest ratio)
MeOAc (3:1)	EtOAc	3	EtOAc (3:1)
MeOAc (3:1)	Et_2O	3	Et_2O (3:1)
EtOAc (3:1)	MeOAc	3	MeOAc (3:1)
EtOAc (3:1)	Et_2O	3	Et_2O (3:1)
Et_2O (3:1)	MeOAc	3	MeOAc (3:1)
Et_2O (1:2)	CPME	12	CPME (1:2)
CPME (1:2)	Et_2O	12	Et_2O (1:2)
MeOAc (3:1)	CPME	12	–
Et_2O (3:1)	CPME	12	–

The efficient role of the seed crystal for inclusion complexation in the solid state is fascinating and has not been reported until now. As far as we are aware, only one report of a seed crystal experiment has been described in which the transformation among three polymorphs of chlorampnenicol palmitate in the solid state proceeded two times faster in the presence of a seed crystal.[8] The present findings on the role of seed crystals will become useful in many scientific fields and will give various hints to develop new technologies.

Although the mechanism of the role of seed crystals is interesting, it is not easy to clarify. However, as it has been established that molecules in a crystal move quite easily in the solid state,[9] easy movement of gaseous molecules into the crystal is understandable. Surprisingly, host **1** which has a helical structure with a twofold symmetry axis[10] is converted efficiently into a sheet structure in **2** and a cyclic structure in **3** in the solid state upon contact with Et_2O vapor in the presence of a seed crystal.

Experimental Section

Crystal data for $\mathbf{1}\cdot(Et_2O)_2$ (**2**): $C_{28}H_{34}O_4$, $M_r = 434.55$, monoclinic, $\beta = 108.86(2)°$, $a = 11.659(7)$, $b = 9.757(6)$, $c = 11.886(7)$ Å, $V = 1279.4(13)$ Å^3, $T = 293$ K, space group Pn, $Z = 2$, $\lambda(Cu_{K\alpha}) = 1.54$ Å; for 1835 observed reflections, the final R (on F) $= 0.0798$ and wR (on F^2) $= 0.2306$ for $I > 2\sigma(I)$.

Crystal data for $(\mathbf{1})_3\cdot Et_2O$ (**3**): $C_{64}H_{52}O_7$, $M_r = 933.11$, triclinic, $\alpha = 83.395(5)$, $\beta = 80.977(5)$, $\gamma = 77.516(5)°$, $a = 10.403(2)$, $b = 10.790(2)$, $c = 22.282(4)$ Å, $V = 2403.1(8)$ Å^3, $T = 173.1$ K, space group $P\bar{1}$, $Z = 2$, $\lambda(Mo_{K\alpha}) = 0.71$ Å; for 7107 observed reflections, the final R (on F) $= 0.0510$ and wR (on F^2) $= 0.1250$ for $I > 2\sigma(I)$.

Crystal data for $\mathbf{1}\cdot(CPME)_2$: $C_{16}H_{19}O_2$, $M_r = 243.31$, monoclinic, $\beta = 118.84(2)°$, $a = 22.957(15)$, $b = 9.811(7)$, $c = 13.998(9)$ Å, $V = 2762(3)$ Å^3, $T = 293$ K, space group $C2/c$, $Z = 8$, $\lambda(Cu_{K\alpha}) = 1.54$ Å; for 1960 observed reflections, the final R (on F) $= 0.0767$ and wR (on F^2) $= 0.2065$ for $I > 2\sigma(I)$.

Crystal data for $\mathbf{1}\cdot$(2-cyclohexen-1-one)$_2$: $C_{26}H_{22}O_3$, $M_r = 382.44$, monoclinic, $\beta = 91.371(16)°$, $a = 13.598(9)$, $b = 10.488(6)$, $c = 17.895(11)$ Å, $V = 2551(3)$ Å^3, $T = 293$ K, space group $P2_1/n$, $Z = 4$, $\lambda(Cu_{K\alpha}) = 1.54$ Å; for 3605 observed reflections the final R (on F) $= 0.1130$ and wR (on F^2) $= 0.2123$ for $I > 2\sigma(I)$.

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Keywords: crystal growth · host–guest systems · inclusion compounds · solid-state reactions

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