博士論文

Host-Guest Chemistry in Porous Crystals

（細孔性結晶内でのホスト−ゲスト化学）

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Contents

Chapter 1 General Introduction 1

1.1 Solution state host–guest chemistry 2

1.2 Crystalline state hosts 6

1.3 Overview of this thesis 11

1.4 Reference 13

Chapter 2 Synthesis of a Porous Crystal Consisting of the Structure of Solution Host Molecules and Guest Inclusion Ability 18

2.1 Introduction 19

2.2 Synthesis of a porous crystal 22

2.3 Guest inclusion into porous crystals 26

2.4 Summary 36

2.5 Experimental sections 37

2.6 Reference 56

Chapter 3 Reactions of Guest Molecules in Porous Crystals 57

3.1 Introduction 58

3.2 Bimolecular acylation reaction in porous crystals 62

3.3 Oxidation reaction by host–guest interaction in porous crystals 66

3.4 Reaction of cyclobutenedione and bisketene in both solution state host molecule and porous crystals 68

3.5 Summary 73

3.6 Experimental sections 74

3.7 Reference 100

Chapter 4 Fullerenes Inclusion into Huge Pores in Porous Crystals 102

4.1 Introduction 103

4.2 Fullerene inclusion into porous crystals 104

4.3 Fullerene separation by inclusion into porous crystals 107

4.4 TTF and C_{60} inclusion into porous crystals 110

4.5 Summary 111

4.4 Experimental sections 112

4.5 Reference.....121

Chapter 5 Porous Microcrystals for Evaluation of Host–Guest Interactions as Stationary Phase of HPLC Column 123

5.1 Introduction 124

5.2 Synthesis of porous microcrystals.....126

5.3 HPLC column using porous microcrystals by host–guest interaction 129

5.4 Summary 131

5.5 Experimental sections 132

5.6 Reference.....142

Chapter 6 Absolute Structure Determination of Guest Molecules by Porous Crystals with Chiral Environment 144

6.1 Introduction 145

6.2 Synthesis of porous crystals with chiral environment.....147

6.3 Absolute structure determination of guest molecules 150

6.4 Summary 159

6.5 Experimental sections 160

6.6 References 172

Chapter 7 Summary and Perspective 174

List of Publications.....177

Acknowledgment 179

CHAPTER 1

General Introduction

Host–guest chemistry[1] is defined as "the field of chemistry consisting of syntheses and applications of highly structured molecular complexes formed by recognition and incorporation of the matched guest by the host molecule having a designed cavity" by Cram who got the novel prize in 1987. Until now, many kinds of artificial host compounds were synthesized and applied to guest inclusion, chemical reactions, catalysts and separation of molecules in solution state. Rich chemistry has been developed in solution state host–guest chemistry.

On the other hand, crystalline state hosts were well studied such as zeolite, metal organic framework (MOF)[2,3] and porous coordination polymer (PCP)[2,4] mainly for gas absorption by activation of the cavity and high pressure. Guest inclusion into crystalline state hosts like solution state hosts is relative rare because high-efficient guest inclusion into crystalline state hosts is tough work without using the system of "nature abhors a vacuum".

From this aspect, host–guest chemistry in crystalline state like rich chemistry of solution state host–guest chemistry is very attractive and fascinating.

Before moving on to describe the results, the background around this research is described in this introductory chapter. In the first section 1.1., solution state host–guest chemistry are briefly introduced. Not only efficient guest inclusion but also rich chemistry based on guest inclusion was performed. Then crystalline state hosts are overviewed in the section 1.2. Finally, the purpose of this thesis is declared with an outline of following chapters based on the background discussed above.

1.1. Solution state host–guest chemistry

1.1.1. Typical examples of solution state host molecules

Solution state host molecules have been studied for more than 100 years. Cyclodextrin (Fig. 1.1.(a)), which is D-glucose connected cyclic molecule, was firstly isolated in 1891 by Villiers[5,6] and identified, further investigated by Schardinger.[5,7] Formation of iodine adducts reported in 1911[5,8] seems to be first report of guest inclusion into cyclodextrin. Then the crystal structure was partially reported in 1959[9,10] and fully reported in 1965.[9,11] This host molecule can include small organic molecules inside and was applied to asymmetric resolution of mandelic acid esters,[12] hydrolysis of phenyl esters[13] about 50 years ago and used in the fields of food chemistry, medicinal chemistry and cosmetic chemistry at the present day. Another typical example of solution state host molecules is crown ether (Fig. 1.1.(b)), which is macrocyclic ether molecule firstly reported in 1967 by Pedersen[14] and inclusion of metal ions was also reported in same paper. Inclusion ability for metal cations was depended on the pore size of crown ether. Furthermore, this molecule was applied to organic synthesis, ion separation, ionophore and chiral resolution.[1] Calixarene (Fig. 1.1.(c)) is a cyclic oligomer synthesized from phenol and aldehyde. This molecule can bind small organic molecules[15] and used as skeletons of organic host molecules.[16] Other analogues were reported such as resorcinarene,[17] calixpyrrole,[18] cavitand[19] and carcerand.[20] Cucurbituril derivatives (Fig. 1.1.(d)), which are macromolecule consisted of glicoluril monomers and methylene linkers, was firstly synthesized in 1905[21] but full characterization was reported in 1981.[22] Guest inclusion properties are changed by number of glicouril.[23,24] Cucurbit[5]uril can bind small guest like protons, metal ions and ammonium ions and cucurbit[6]uril can include guests such as Xe, benzene and THF. Cucurbit[7]uril is slightly larger than cucurbit[5]uril and cucurbit[6]uril, therefore it can include organic molecules like adamantine derivatives, naphthalene and *o*-carborane.

Various kinds of host molecules were designed and synthesized. But easily synthesized host molecules can only include small ions and small solvent molecules and host molecules, which have large cavity enough to include large molecules, are synthetically complicate and difficult in this stage.

Figure 1.1. Structures of (a) cyclodextrin, (b) crown ether, (c) calixarene and (d) cucurbituril.

1.1.2. Solution state host molecules by self-assembly

In 1990s, several kinds of host molecules by self-assembly were reported for construction of large cavity in host molecules. Relatively weak bonds like hydrogen bonds and coordination bonds were mainly used as driving forces of syntheses of host molecules. Host molecules are automatically synthesized by just mixing of pieces of hosts. Synthetic difficulties were overcome by using self-assembly systems.

Representative examples of host molecules by hydrogen bond are capsule structure hosts (Fig. 1.2.) reported by Rebek, Jr. and co-workers.[25-27] Several sizes of capsules were synthesized as dimer structures only by change the monomers. In these capsule host molecules, encapsulation of benzanilide in unfavoered Z conformation,[28] encapsulation of alkanes in helical conformation,[29] acceleration of Diels–Alder reaction[30] and catalytic Diels–Alder reaction of benzoquinone and thiophene dioxide derivative[31] were performed.

Figure 1.2. Structures of Rebek's capsules.

Self-assembly of organic ligands and metal ions by coordination bonds gave many types of host molecules. Raymond and co-workers reported tetrahedral anionic host molecule (Fig. 1.3.(a)) synthesized from catechol ligand and metal ion.[32] This anionic host stabilized reactive cationic species by encapsulation[33] and produced activation of C–H bond by trapping of iridium complex,[34] catalytic reactions of cationic 3-aza-Cope rearrangement[35] and hydrolysis of orthoformate in basic conditions.[36] Fujita and co-workers reported octahedral cationic cage host molecule (Fig. 1.3.(b)) prepared from tridentate triazine ligand and *cis* position capped palladium ion.[37] This molecular host showed not only guest inclusion such as stable hydrophobic dimers,[38] neutral guest molecules[39] and polyfluorinated compounds,[40] but also some chemical reactions such as unusual photochemical dimerizations[41-43], catalytic Knoevenagel condensation[44] and organometallic reactions[45,46] in the host cage. Recently, Nitschke and co-workers reported tetrahedral cage host molecule[47] (Fig. 1.3.(c)). The cage host showed white phosphorus inclusion[48] and control over Diels–Alder reactivity of guest molecules.[49]

Figure 1.3. Structures of (a) Raymond's cage, (b) Fujita's cage and (c) Nitschke's cage.

Due to large cavities in self-assemble host cages, many kinds of interesting phenomena were discovered not only guest inclusion but also chemical reactions of guest molecules, catalysis and stabilization of unstable molecules. Like these examples, solution state host–guest chemistry have been studied for a long time from the several aspects and showed rich chemistry. It is worth noting that driving forces of guest inclusion are host–guest interaction such as hydrogen bond, π-π interaction, CH-π interaction, hydrophobic effect and charge transfer interaction. The interesting phenomena are based on these weak but important interactions.

In the consideration of crystals of discrete host molecule, it is difficult to include guest molecules into crystals because of tight packing of host molecules prevent guest entrance. Even though some chemical reactions of guest molecules in crystals of discrete host molecule were reported,[50-53] guest inclusion was performed before crystallization. Just crystallization of discrete host molecules cannot realize host–guest chemistry in crystalline state.

1.2. Crystalline state hosts

1.2.1. Early examples of crystalline host

Guest inclusion into crystals has been developed independently of solution state host–guest chemistry. Forming of hydrate from gas or liquid substrates was discovered in early 19th century and another early example is a crystal of urea including alkane molecule reported in 1949.[54] Guest inclusion into zeolite has been studied from long ago and included guest molecules such as acetylene, ammonia and sulfur were analyzed by X-ray crystallography in 1970s.[55-57]

Porous crystals based on coordination bonds have been developed as infinite architectures with repeated structures. In 1959, structure of three-dimensional network complex $[Cu\{(NC)(C_4H_8)(CN)\}_2]NO_3$ was reported.[58] Iwamoto and co-workers reported benzene and aniline clathrates of metal complex hosts.[59] Robson and co-workers reported infinite frameworks consisting of organic ligand and copper ion (Fig. 1.4.(a)) and counter anion exchange of the porous crystal.[60] Fujita and co-workers reported two-dimensional network structure from 4,4'-bipyridine and cadmium ion (Fig. 1.4.(b)) and separation of *o*-dibromobenzene from a mixture of *o*- and *m*-dibromobenzene by crystallization in a solvent of a mixture of *o*- and *m*-dibromobenzene and X-ray structure of *o*-dibromobenzene included in the network structure.[61] In this stage, just the structure of porous crystal was mainly focused on.

Figure 1.4. X-ray structures of (a) Robson's infinite framework (b) Fujita's two-dimensional network including *o*-dibromobenzene molecules.

1.2.2. Gas absorption into porous crystals

Recently, porous crystals, which are called as PCPs and MOFs, have been paid attention as gas absorption materials because they have high porosity, regular structure and robust framework consisting of organic ligands and metal ions. Kitagawa and co-workers reported first gas absorption into porous crystals in 1997.[62] They also achieved observation of oxygen[63] and acetylene molecules[64] (Fig. 1.5.(a)) in porous crystals by MEM (maximum entropy method)/Rietveld method. Yaghi and co-workers reported porous metal organic framework (MOF-5)[65] and X-ray structure of N_2 absorbed in MOF-5 (Fig. 1.5.(b)).[66] They also reported systematic design of pore size and functionality with isoreticular structures by just changing the ligands[67] and absorption of many kinds of gas into MOFs.

Figure 1.5. X-ray structures of (a) acetylene included in PCP and (b) N_2 included in MOF-5.

In the MOFs and PCPs field, gas absorption into porous materials was performed by activation of pores and high pressure of gas. This method is different from the method of guest inclusion in solution state host–guest chemistry.

1.2.3. Inclusion of non-gas guest molecules into porous crystals

Gas molecule is a main target for inclusion into porous crystals but non-gas molecule inclusion into porous crystals was also reported. Yaghi and co-workers reported organic dye molecules,[68] vitamin-B_{12} and protein[69] inclusion into MOFs by immersion of the crystals into guest solution. Inclusions of guest molecules were analyzed by change of the crystal color, Raman spectroscopy and UV-Vis study but only spectroscopic analyses implied small amount guest inclusion.

For the efficient guest inclusion, vapor phase inclusion of organometallic compound guests[70] by activation of cavity and sublimation of guests was reported. Kim and co-workers reported ferrocene inclusion in vapor phase and X-ray structure of ferrocence included MOF-5 (Fig. 1.6.(a)).[71] In this method, large amount of guest molecules enough to analyzed by X-ray crystallography can be included into porous crystals. But origin of guest inclusion is same as gas absorption into porous crystals as mentioned in chapter 1.2.2. and generality of guest molecules was lost due to vapor phase inclusion.

Co-crystallization is also one method of creation of guest-included crystals. For example, the porphyrin derivative included porous crystals were obtained by co-crystallization of the ligand, metal ion and the porphyrin derivative and used as a catalyst mimicking heme enzymes.[72] This co-crystallization method was used in not only the field of porous crystal, but also the field of organic crystal.[73] When co-crystallization method is used, guest molecules cannot be extracted or gotten out from crystals.

Another efficient guest inclusion method is using host–guest interaction. Fujita and co-workers reported aromatic guest compounds inclusion into porous crystal synthesized from ZnI_2 electron-deficient ligand.[74] By guest inclusion, crystal color turned from colorless to yellow, which indicated charge transfer interaction. Furthermore, included guest compound could be observed by X-ray crystallography (Fig. 1.6.(b)) and π-π interaction was observed between the guest and the ligand (Fig. 1.6.(c)). Host–guest interaction is very important for not only guest inclusion in solution state host but also guest inclusion in porous crystals.

Figure 1.6. X-ray structures of (a) ferrocene included in MOF by vapor phase inclusion and (b) tryphenylene (blue color) included in porous crystal. (c) π-π stack of tryphenylene guest and ligand.

1.2.4. Porous crystal with cavity whose shape is solution state host molecule

It seems to be good way for introduction of solution state host into cavity of porous crystal to use host–guest interaction for efficient guest inclusion. Stoddart, Yaghi and co-workers attempted to synthesis of porous crystals by crown ether linked ligand.[75] When the crystals were immersed into a saturated solution of paraquat dication, color of the crystals turned from yellow to red. This color change indicated charge transfer interaction between paraquat dication and crown ether rings. Crown ether linked to framework worked well to include guest molecules.

Another idea is construction of porous crystal with cavity whose shape is solution state host molecule.[76] An early example is combination of square shape host molecules[77] and two dimensional network structure of square shaped cavity[61] as described above. Kim and co-workers reported one dimensional coordination polymer of cucurbituril by complexation of cucurbit[6]uril and rubidium ion (Fig. 1.7.(a)).[78] Complexation of cucurbituril and Rb_2SO_4 in the presence of THF or ethylenediamine caused inclusion of THF or ethylenediamine in the cavity but introduction of guest molecules after making the porous crystals were not mentioned. Yaghi, Stoddart and co-workers reported porous crystals synthesized from cyclodextrin and metal ion (Fig. 1.7.(b)).[79] They attempted organic dye inclusion into cyclodextrin MOF in two approaches. One method was co-crystallization of cyclodextrin ligand, metal ion and organic dye, which gave red colored crystals and inclusion of guest was confirmed by

NMR spectroscopy. The other was immersion of activated crystals into a saturated solution of organic dye, which caused inclusion of guest molecules into porous crystals confirmed by NMR spectroscopy. In both cases, observation of guest molecules by X-ray crystallography was failed so it was not conclusive that cyclodextrin moieties bound guest molecules.

Figure 1.7. X-ray structures of porous crytsals with (a) cucurbituril shaped cavity and (b) cyclodextrin shaped cavity.

Like these examples, just construction of porous crystal with host molecule shaped cavity was achieved but the cavity did not work well for inclusion of guest molecules. It is difficult to include the guest molecules into the porous crystals like solution state host molecules even though they have host molecule shaped cavities. Additionally, it is also hard to obtain the proof of inclusion of guest molecules in host molecule shaped cavity. The field is now developing and new porous crystals, which have guest inclusion ability based on host–guest interactions like solution state host molecules, will give a dramatic improvement of the field.

1.3. Survey of this thesis

Solution state host–guest chemistry has been developed independently of chemistry of porous crystals but host–guest chemistry system in solution state can be applied to chemistry of porous crystals. Concept of this thesis is transfer of solution state host–guest chemistry to crystalline state chemistry for achieving of host–guest chemistry in porous crystals. Not only guest molecules inclusion into porous crystals but also rich chemistry like solution state host–guest chemistry could be realized in porous crystals. Moreover, host–guest chemistry in porous crystals provided a new X-ray crystallographic analysis method without crystallization process, which could not be realized in solution state host–guest chemistry.

In chapter 2, a new porous crystal with cavity whose shape is octahedral host molecule was successfully synthesized. The crystals could include guest molecules by just immersion of the crystals into saturated solutions of guest molecules. X-ray crystallography of the crystal revealed that the crystal had similar guest inclusion ability to solution state host molecule. Furthermore, obtaining X-ray structure of guest molecules in the porous crystals was applied to X-ray crystallography of liquid molecules.

In chapter 3, three kinds of chemical reactions of guest molecules in the pores of porous crystals based on strong guest inclusion were performed. (1) Strong guest inclusion caused bimolecular reaction without leaching of the first substrate. Moreover, steric effect of octahedral cage gave interesting chemoselectivity in the reaction. (2) Oxidation reaction of guest molecules was performed by electron transfer interaction between host framework and guest molecules. (3) Chemical reaction of water sensitive molecules was performed in both solution state host molecules and porous crystals. In solution state host molecules, yield of the product was not so good because of water solvent. On the other hand, yield of the product was good in porous crystals because of avoidance of water.

In chapter 4, inclusion of fullerenes into large pores in porous crystals was attempted. About 35 wt% of fullerenes were included into porous crystals by immersing the crystals into a saturated solution of fullerenes. Furthermore, separation of higher fullerenes by inclusion into porous crystals was carried out.

In chapter 5, microcrystals of porous crystals were synthesized for evaluation of host–guest interactions as stationary phase of HPLC column. Quick mixing of a ligand solution and a metal solution gave microcrystals of the porous crystal. Compounds could be separated with microcrystal packed HPLC column by the difference of strength of host–guest interaction.

In chapter 6, chiral porous crystals with chiral parts were synthesized. By inclusion of chiral guest molecules into the chiral porous crystals, absolute structure determination of chiral guest molecules by comparison with absolute structure of chiral parts in framework of chiral porous crystals was achieved. Moreover, absolute structure determination of chiral compounds from the fractions of analytical HPLC was carried out.

In chapter 7, results and discussions in this thesis were summarized.

Figure 1.8. Concept of this thesis.

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CHAPTER 2

Synthesis of a Porous Crystal Consisting of the Structure of Solution Host Molecules and Guest Inclusion Ability

Abstract: Octahedral cage host molecule in solution has been studied for the impressive inclusion ability of guest molecules. To achieve guest inclusion like solution state host molecules in porous crystals, a porous crystal whose structure was three-dimensional array of octahedral cages was synthesized. The porous crystal showed guest inclusion by just immersing the crystals into a guest solution. X-ray crystallography revealed similar guest inclusion ability of porous crystals to solution state host molecules. Furthermore, Getting the X-ray structures of liquid molecules at room temperature were successfully achieved by inclusion into porous crystals without crystallization process of the liquid guests themselves. The foundation of host–guest chemistry in porous crystals was successfully created.

2.1. Introduction

The octahedral M_6L_4 (M = metal, L = ligand) cage host molecule[1] **2** synthesized from tridentate triazine ligand and *cis* position capped Pd salt shows very strong inclusion ability of guest molecules especially electron-rich molecules due to electron-deficient ligand[2] in solution state (Fig. 2.1.). This electron-deficient ligand and cage shaped cavity seem to be important for inclusion of guest molecules.

Figure 2.1. Octahedral cage host molecule **2** and inclusion of electron-rich molecules into **2**.

For sufficient guest inclusion into a crystalline host, a porous crystal consisting of octahedral cage structure by this electron-deficient ligand is predictably effective. In consideration of the single crystal of cage host **2**, while there are a few reports of photoreaction of guest molecules in single crystals of cage host **2**,[3,4] guest inclusion was performed before crystallization of host cage **2**. Guest inclusion into the single crystal of cage host **2** is impossible because of no doorway for guest molecules and no passage to enter to the cavity (Fig. 2.2.). Crystalline state host–guest chemistry cannot be realized by just crystallization of host cage **2**. Construction of a porous crystal by network of octahedral cages seems to be a good way to realize efficient guest inclusion into crystals.

Figure 2.2. Packing structure of host cage **2**. Packing structure shows no doorway for guest entering.

There is an example of a crystalline complex that has octahedral cage structure by the ligand and copper ion reported by Robson and co-workers in 1996.[5] But there is no cavity for guest inclusion because of its interpenetrated structure (Fig. 2.3).

Figure 2.3. Synthesis of a crystalline complex reported by Robson and co-workers in 1996.[3] The interpenetrated structure is shown in the green part and the orange part.

In this chapter, a porous crystal whose structure is three-dimensional array of octahedral cage host molecules was newly synthesized. The crystal showed no interpenetrated structure and 78% void space. Then guests, especially electron-rich molecules, were included in the cage cavity in the porous crystal. When the guest was tetrathiafulvalene (TTF), the guest-included structure of the porous crystal was compared with that of solution state cage host molecule and it is revealed that the porous crystal has same guest inclusion ability as solution cage host. Finally, this guest inclusion and X-ray structure of guest molecules without crystallization process were applied to X-ray analysis of liquid compound.

2.2. Synthesis of a Porous Crystal

Porous crystal **1** was synthesized from layer diffusion method in a test tube (Fig. 2.4.). As the under layer, a solution of 2,4,6-tris(4-pyridyl)-1,3,5-triazine (**3**) in 1,2-dichlorobenzene and methanol were prepared. Onto this under layer, methanol solution of $Co(NCS)_2$ was slowly added. After standing for 1 week at room temperature, orange crystals **1** were obtained at the glass wall of boundary of two layers in 60% yield.

Figure 2.4. Synthesis of porous crystals **1**.

X-ray crystallography of as-synthesized crystal **1** was performed and the crystal structure revealed that infinite array of octahedral M_6L_4 cage with 6 Co vertices and 4 ligand **3** panels (Fig. 2.5.(a)). The M_6L_4 cage in crystal **1** is quite similar to that of solution state host cage **2**. The neighboring and antipodal Co–Co distances were 13.24 and 18.73 Å, respectively and the respective Pd–Pd distances of 13.01 and 18.62 Å in cage **2**. This structure was not interpenetrated unlike Robson and co-workers report.[5] Therefore, there were cavity in the octahedral cages probably because of overhanging

thiocyanate in the cavity and between these cages but solvent molecules such as 1,2-dichlorobenzene and methanol were not observed in the X-ray structure due to severe disorder of these solvent molecules. From the elemental analysis, 200 1,2-dichlorobenzene and 40 methanol molecules existed per unit cell and this result corresponded to 70% weight loss in thermogravimetoric analysis (Fig. 2.5.(b)). There is space for doorway and passage to enter in crystal cavity between octahedral M_6L_4 cages and there is 78% solvent accessible void in **1** by void calculation program in PLATON.[6]

Figure 2.5. (a) X-ray structure of porous crystal **1**. The structure was composed of three dimensional network structure of M_6L_4 type octahedral cages. (b) TG-DSC spectra of porous crystal **1**. (black line: weight change, red line: differential scanning calorimetry). Conditions: temperature range: from 25 to 300 ºC, heating rate: 5 K/min, nitrogen flow: 30 mL/min.

There are two types of cavities in porous crystal **1** except for M_6L_4 octahedral cage shape cavity (Fig. 2.6.), namely $M_{12}L_8$ cuboctahedral shape cavity and $M_{12}L_{24}$ cuboctahedral shape cavity. The $M_{12}L_8$ cuboctahedral cage is consisting from 8 ligand **3** shares panel ligand **3** and Co vertices with 8 octahedral M_6L_4 cages. The $M_{12}L_{24}$ cuboctahedral cage is defined from 24 edges of ligand **3** and 12 Co vertices. This cage is isostructural with previously reported discrete $M_{12}L_{24}$ spherical complex in solution.[7] Distance of two sulfur atoms exposed to large cuboctahedral cavities is about 1.2 nm. Fullerenes inclusion into the huge cuboctahedral cavity will be discussed in chapter 4.

Figure 2.6. Structures of three kinds of cages.

Solvent resistance of porous crystal **1** was investigated by soaking of **1** into several kinds of solvents. In the case of aromatic solvent such as toluene, xylene, mesitylene and halogenated solvent such as dichloromethane, 1,2-dichloroethane, crystallinity of **1** was maintained. When aprotic polar solvents such as acetonitrile, ethyl acetate, tetrahydrofuran, acetone, DMF, DMSO and protic polar solvent such as methanol, isopropyl alcohol, acetic acid and water were used, crystallinity of **1** got lost and crystals were decomposed. Removing the solvent inside the cavity by evaporation in vacuo caused to decrease the crystallinity due to large porosity of the crystals.

2.3. Guest Inclusion into Porous Crystals

Guest inclusion into porous crystals **1** was performed with in mind the fact that host cage molecule **2** can include electron-rich molecules due to electron-deficient ligand **3**. First target molecule was electron-rich TTF molecule. TTF inclusion was attempted by immersion of **1** into a saturated toluene solution of TTF and crystal color turned from orange to black, which indicated guest inclusion into **1**. From diffuse reflection spectrum of the black crystal, broad charge transfer band was observed at 500–900 nm (Fig. 2.7.). X-ray crystallography of crystal **1** immersed into a TTF solution for 1 week at room temperature was performed. The crystal structure revealed 4 TTF molecules were included in one octahedral M_6L_4 cage shaped cavity (Fig. 2.8.). Each TTF molecule located on ligand **3** with the 3.4~3.6 Å distance, which showed π-π stack of TTF and ligand **3**. In other large cavity, there should be other TTF molecules and solvent molecules from the elemental analysis result but they could not be assigned because of severe disorder. It is worth noting that the space group of TTF included in **1** change to tetragonal $P4_2/mnm$ from original cubic Fm-$3m$ by distorting the cage structure. For example, before the TTF inclusion, antipodal Co–Co distance is 18.73 Å, but after TTF inclusion, antipodal Co–Co distances are 18.32 and 19.03 Å. This lower symmetry of the space group is very important for observation of guest molecules in porous crystals.

Figure 2.7. Diffuse reflectance spectra of porous crystal **1** and TTF inclusion porous crystals.

Figure 2.8. (a) Inclusion of TTF into **1** and pictures of as-synthesized crystals and TTF included crystals. (b) X-ray strcture of TTF included in **1**. (c) Orientation of ligand **3** and TTF.

Inclusion of TTF into solution state host cage **2** was also attempted for the comparison with porous crystal **1**. TTF was suspended in aqueous solution of **2** at room temperature for 1 h and excess TTF was filtrated. Color of solution changed from colorless to black by the charge transfer interaction between TTF and ligand **3** (Fig. 2.9.(a)). TTF inclusion confirmed by upfield-shifted proton signal at around 5.5 ppm derived from included TTF in the ^{1}H NMR spectrum (Fig. 2.9.(b)). Single crystals were obtained by slow evaporation of solvent and X-ray crystallography of TTF included **2** was performed. Crystal structure showed 4 TTF tightly packed in octahedral M_6L_4 cage. Number of included TTF is same in the case of porous crystal **1** and location of TTF is similar to porous crystal **1** case (Fig. 2.10.). These X-ray structures reveal that porous crystal **1** has similar guest inclusion ability to that of host cage **2** in solution.

Figure 2.9. (a) Inclusion of TTF into solution host cage **2**. (b) ^{1}H NMR spectrum (500 MHz, 300 K, $CDCl_3$) of authentic TTF and (c) ^{1}H NMR spectrum (500 MHz, 300 K, D_2O) **2⊃(TTF)$_4$**.

Figure 2.10. Comparison of X-ray structure of TTF included in porous crystal **1** with that of TTF included in solution host cage **2**.

Guest inclusion into crystalline host and X-ray structure can contribute to understand the guest location in the solution host cage. When porous crystals **1** were immersed into a saturated toluene solution of diphenylamine (**4**), crystal color turned red derived from charge transfer interaction between ligand **3** and guest **4**. Broad charge transfer band was observed at 400–750 nm from diffuse reflection spectrum of the red crystal (Fig. 2.11.(a)). X-ray crystallography of the crystal clearly showed 4 guest molecules **4** were included into one M_6L_4 cage (Fig. 2.11.(b)) with π-π stack to ligand **3**. On the other hand, **4** was suspended in aqueous solution of host cage molecule **2** and solution color turned red. ^{1}H NMR unambiguously showed the inclusion of guest **4** into **2**. In the crystallization, however, guest molecule escaped from the cage cavity and X-ray crystallography was not conclusive. In the case of porous crystal **1**, crystallization was not necessary for getting the X-ray structure therefore troublesome problem like guest escape can be avoided. Furthermore, porous crystal **1** shows similar guest inclusion to that of cage **2** hence guest **4** location in host cage **2** can be predicted by the X-ray structure of **4** included into porous crystal **1**.

Figure 2.11. (a) Diffuse reflectance spectra of porous crystal **1** and **4** inclusion porous crystal. (b) X-ray structure of a M_6L_4 cage in porous crystal **1** including **4**.

In the case of guest **4**, guest molecules were observed even in huge $M_{12}L_8$ and $M_{12}L_{24}$ cages (Fig. 2.12.). In $M_{12}L_8$ cage, 6 guests were stacked onto ligand **3** and totally 15 guests were observed. In $M_{12}L_{24}$ cage, disordered 6 guest molecules were observed. In consideration of large thermal ellipsoid of guest molecules in huge $M_{12}L_8$ and $M_{12}L_{24}$ cages, guest molecules in huge cages were not so strongly included compared with those in M_6L_4 cages.

Figure 2.12. X-ray structures of a $M_{12}L_8$ cage and $M_{12}L_{24}$ cage in **1** including **4**.

Another electron-rich 2,2'-bithophene (**5**) can be observed in porous crystal **1** by X-ray crystallography. Inclusion of **5** was performed in the same way of TTF. By X-ray analysis of **5** included into **1**, 4 guest molecules **5** were observed in one M_6L_4 cage (Fig. 2.13.) with stacking of guest molecules on ligand **3**.

Figure 2.13. X-ray structure of **5** included in porous crystal **1**.

2-adamantanone (**6**) could be included in porous crystal **1** and observed by X-ray crystallography (Fig. 2.14.) while **6** is not aromatic molecule. Inclusion method was same as TTF inclusion case. 4 molecules of guest **6** were observed in octahedral M_6L_4 cage and hydrogen bonds were observed between guest molecules. Furthermore, 12 guest molecules were observed in $M_{12}L_{24}$ cage with hydrogen bonds between guest **6** and hydrogen of ligand **3**. On the other hand, no guest was observed in $M_{12}L_8$ cage.

Figure 2.14. X-ray structure of **6** included in **1**.

Additionally, these included guest molecules could be removed from porous crystals **1** by only soaking the crystals into flesh toluene. Color change due to guest inclusion returned to orange color and crystallinity was maintained.

In the thought of the guest molecules in the X-ray structure of the guests included in porous crystal **1**, X-ray structure of the guest molecules can be obtained without crystallization process of the guest itself. This phenomenon is applied to liquid compound whose crystallization is difficult. One drop of diphenylmethane (**7**) was added to one crystal of **1**. After 2 days at room temperature, X-ray crystallography was carried out. X-ray structure showed the 4 guests **7** in the M_6L_4 cage (Fig. 2.15.(a)) and the guests stacked with ligand **3**. Structure of **7** was clearly observed by just immersion of **1** into **7**.

Other guest molecules without aromatic rings for interaction to ligand **3** were attempted. One crystal of **1** was soaked into one drop of cyclohexanone (**8**) and allowed to stand for 2 d at room temperature. By the X-ray crystallography of the crystal, X-ray structure of 4 guests **8** in the M_6L_4 cage was obtained (Fig. 2.15.(b)). In this case, any specific interactions between guest molecules and the framework were not observed. Relatively large thermal ellipsoid of included guest molecules suggested weak binding of guest molecules in octahedral M_6L_4 cages. Additionally, *t*-BuOH as a guest molecule was performed in the same inclusion method in the case of **7**. X-ray structure of 4 *t*-BuOH molecules in the M_6L_4 cage in porous crystal **1** was obtained (Fig. 2.15.(c)). Guest molecules in the octahedral cages interacted with each other by hydrogen bonds.

Figure 2.15. X-ray structure of (a) **7** included in crystal **1**, (b) **8** included in crystal **1** and (c) *t*-BuOH included in **1**. (Ellipsoids are drawn at the 50% probability.)

In this chapter, X-ray structures of several kinds of guest molecules included in porous crystal **1** were reported but many attempts of X-ray crystallography of guest molecules included in porous crystal **1** were failed. Some patterns about Bravais lattices were found in the examples of success and failure. Bravais lattice of one successful pattern was tetragonal P (finally, tetragonal $P4_2mnm$, $a = b$ = 26~27 Å, c = 36~37 Å). This type was occurred by distortion of the framework by host–guest interaction from cubic to tetragonal. Another pattern of Bravais lattice was cubic F (finally, cubic Fd-3c, $a = b = c$ = 74~75 Å or tetragonal $I4_1/acd$, $a = b$ = 36~38 Å, c = 73~74 Å, NOT cubic Fm-3m, $a = b = c$ = 36~38 Å). In this pattern, guest molecules in large cavities could be observed. Bravais lattice of one pattern of failure was cubic P ($a = b = c$ = 36~38 Å). In this case, not only guest molecules but also framework could not be observed and initial phase could not be determined. Another one was cubic F ($a = b = c$ = 36~38 Å), which was same as as-synthesized unit cell. In this case, guest inclusion amount seemed to be too low or host–guest interaction seem to be too weak to change the framework. Only cyclohexane was determined by decrease symmetry from cubic to monoclinic but only framework was observed in the usual case.

2.4. Summary

The porous crystal with three-dimensional array of octahedral M_6L_4 cages, which were same structure as molecular host cage **2**, was successfully synthesized as orange single crystals. The porous crystal had three kinds of cage: (1) octahedral M_6L_4 cage, (2) cuboctahedral $M_{12}L_8$ cage and (3) cuboctahedral $M_{12}L_{24}$ cage. Several kinds of guest inclusion into porous crystals **1** were performed. TTF inclusion into **1** showed similar guest inclusion ability of **1** to solution state host cage **2**, it indicated host–guest chemistry like host cage **2** could be performed in porous crystal **1**. Furthermore, getting the X-ray structure of guest molecules without crystallization process was applied to X-ray structure of liquid compound. These phenomena acted as a stepping stone to crystalline sponge method, which is new crystallographic analysis method for small amount and non-crystallization compound. The platform for host–guest chemistry in porous crystals could be obtained.

2.5. Experimental sections

Contents

2.5.1. Materials and methods

2.5.2. Synthesis and characterization of porous crystal 1

2.5.3. Guest inclusion into porous crystal 1 and discrete cage 2

2.5.4. Liquid guest inclusion into one crystal of porous crystal 1 on small scale

2.5.1. Materials and methods

Solvents and reagents were purchased from TCI Co., Ltd., WAKO Pure Chemical Industries Ltd., Sigma-Aldrich Co., and Frontier Carbon Co. All the chemicals were used without any further purification. ^{1}H and ^{13}C NMR spectra were recorded on Bruker DRX-500 (500 MHz) and AV-500 (500 MHz) spectrometers. All NMR spectral data were collected at 300 K, and chemical shifts were reported as the delta scale in parts per million (ppm) relative to an external standard tetramethylsilane (δ = 0.00 ppm for ^{1}H and ^{13}C NMR). Microscopic IR spectra were recorded on Varian DIGILAB Scimitar instrument. Analytical HPLC (high performance liquid chromatography) chromatograms were recorded on a JASCO UV-970 spectrometer equipped with a JASCO PU-980 pump. Thermogravimetric analysis was performed on a STA 409 PG/T equipped with a QMS 403C/T (NETZSCH). UV-Vis absorption and diffuse reflectance spectra were recorded on a SHIMADZU UV-3150 spectrometer. Diffuse reflectance spectra were recorded with an integrating sphere and were converted from reflection to absorbance by the Kubelka–Munk method. Elemental analyses were performed on a YANACO MT-6. Single crystal X-ray diffraction data were collected on a BRUKER APEX-II CCD diffractometer equipped with a focusing mirror (MoK$_a$ radiation λ = 0.71073 Å) and a N_2 generator (Japan Thermal Eng. Co., Ltd.).

2.5.2. Synthesis and characterization of porous crystal 1

Synthesis of porous crystal 1. A solution of ligand **3** (6.3 mg, 20 μmol) in 1,2-dichlorobenzene (4.0 mL) and methanol (1.0 mL) was added in a test tube. A methanol solution of $Co(NCS)_2$ (40 mM, 1.0 mL) was carefully added on the solution of ligand **3**. The resulting solution was allowed to stand for 1 week at room temperature. Then, the orange crystals were isolated by filtration to give porous crystal **1** (16.7 mg) in 60% yield based on ligand **3**. (The isolation yield of the crystal is calculated as an averaged value of 5 batches.) Elemental analysis: calculated for $\{[(\mathbf{3})_4(Co(NCS)_2)_3]\bullet 25(1,2\text{-dichlorobenzene})\bullet 5(MeOH)\}_n$; C 49.89, H 3.02, N 7.49; found C 49.60, H 2.92, N 7.43. IR (single crystal, cm^{-1}): 3066(m), 2047(s, NCS st.), 1579(m), 1514(s), 1374(m), 1317(m), 1125(s), 967(m), 901(m), and 650(m). UV-Vis (diffuse reflectance, $BaSO_4$, λ [nm]) 245 and 366.

X-ray crystallographic data for as-synthesized porous crystal 1

Figure S2.1. Crystal structure of porous crystal **1**. (Ellipsoids are drawn at the 50% probability.)

Crystallographic data: $C_{26}H_{16}N_{10}CoS_2$, M_r = 591.56, crystal dimensions 0.35 × 0.31 × 0.26 mm^3, Cubic, space group, *Fm*-3*m*, $a = b = c$ = 37.461(5) Å, V = 52571(12) Å^3, T = 85 K, Z = 24, r_{calcd} = 0.448 g cm^{-3}, 1443 unique reflections out of 1954 with $I > 2\sigma(I)$, 58 parameters, 1.54 < θ < 23.45°, final R factors R_1 = 0.0998 and wR_2 = 0.283 for all data. CCDC deposit number 766604. Residual electron densities in the solvent-accessible void due to disordered solvent molecules were treated with the PLATON SQUEEZE program.[8] Before the treatment of SQUEEZE program; the maximum electron density remained was 3.008, R_1 = 0.03225 and wR_2 = 0.6309 for all data with 1201 unique reflections out of 1954 with $I > 2\sigma(I)$.

2.5.3. Guest inclusion into porous crystal 1 and discrete cage 2

General procedure for single-crystal-to-single-crystal guest encapsulation with porous crystal 1

As-synthesized porous crystal **1** (10 ~ 20 mg) was first washed with toluene (5 mL × 3 times), and then was immersed into a saturated toluene solution (3~5 mL) of guest molecule at room temperature. The progress of encapsulation was monitored by diffuse reflectance spectra or microscopic FT-IR after filtration of crystals.

Inclusion crystal 1⊃(TTF):

Elemental analysis: calculated for $\{[(\mathbf{3})_4(Co(NCS)_2)_3]\bullet 4.5(TTF)\bullet 4(toluene)\bullet H_2O\}_n$; C 51.85, H 3.27, N 13.64; found C 51.92, H 3.55, N 13.88 IR (single crystal, FLUOROLUBE, cm^{-1}): 3066(m), 2049(s, NCS st.), 1579(m), 1514(s), 1371(m), 969(m), 901(m), 803(m), and 646(m). UV-Vis (diffuse reflectance, $BaSO_4$, λ [nm]) 371 and 631.

Inclusion crystal 1⊃(diphenylamine):

Elemental analysis: calculated for $\{[(\mathbf{3})_4(Co(NCS)_2)_3]\bullet 7(diphenylamine)\bullet 3.8(toluene)\bullet 0.25H_2O\}_n$; C 68.36, H 4.74, N 15.64; found C 68.08, H 5.02, N 15.51. IR (single crystal, FLUOROLUBE, cm^{-1}): 3395(m), 3326(m, NH st.), 3044(m), 2048(s, NCS st.), 1594(m), 1503(m), 1416(m), and 1373(m). UV-Vis (diffuse reflectance, $BaSO_4$, λ [nm]) 280 and 490.

Inclusion crystal 1⊃(bithiophene):

Elemental analysis: calculated for $\{[(\mathbf{3})_4(Co(NCS)_2)_3]\bullet 7(bithiophene)\bullet(toluene)\}_n$; C 55.88, H 3.26, N 13.87; found C 55.43, H 3.62, N 13.20. IR (single crystal, FLUOROLUBE, cm^{-1}): 3130(m), 3070(m), 2050(s, NCS st.), 1516(s), 1373(m). UV-Vis (diffuse reflectance, $BaSO_4$, λ [nm]) 495 (sholder).

Inclusion crystal 1⊃(2-adamantanone):

Elemental analysis: calculated for $\{[(\mathbf{3})_4(Co(NCS)_2)_3]\bullet 19(adamanthanone)\bullet 10(toluene)\}_n$; C 73.14, H 7.16, N 7.57; found C 73.17, H 7.07, N 7.83. IR (single crystal, FLUOROLUBE, cm^{-1}): 2917(s), 2855(m), 2054(s, NCS st.), 1719(s, C=O st.), 1520(s), 1377(m).

Figure S2.2. Crystal structure of porous crystal **1** after the inclusion of TTF. (Ellipsoids are drawn at the 50% probability.)

Crystallographic data: $C_{102}H_{64}N_{30}Co_3S_{22}$, M_r = 2592.16, crystal dimensions 0.16 × 0.15 × 0.10 mm^3, Tetragonal, space group, $P4_2/mnm$, $a = b$ = 26.405(4) Å, c = 36.631(5) Å, V = 25540 (6) Å^3, T = 85 K, Z = 4, r_{calcd} = 0.674 g cm^{-3}, 6911 unique reflections out of 11617 with $I > 2\sigma(I)$, 371 parameters, 0.95 < θ < 24.87°, final R factors R_1 = 0.0853 and wR_2 = 0.1476 for all data. CCDC deposit number 766605.

Residual electron densities in the solvent-accessible void due to disordered guest and solvent molecules were treated with the PLATON SQUEEZE program. (Before the treatment of SQUEEZE program; the maximum electron density remained was 1.322, R_1 = 0.2249 and wR_2 = 0.5585.)

Figure S2.3. Crystal structure of porous crystal **1** after the inclusion of diphenylamine. (Ellipsoids are drawn at the 50% probability.)

Crystallographic data: $C_{80}H_{64.5}N_{14.5}CoS_2$, M_r = 1352.01, crystal dimensions 0.37 × 0.34 × 0.31 mm^3, Cubic, space group, *Fd*-3*c*, $a = b = c$ = 74.972(2) Å, V = 421392 (22) Å^3, T = 85 K, Z = 192, r_{calcd} = 1.023 g cm^{-3}, 12747 unique reflections out of 17942 with $I > 2\sigma(I)$, 812 parameters, $0.94 < \theta < 26.35°$, final R factors R_1 = 0.1479 and wR_2 = 0.4544 for all data. CCDC deposit number 766606.

Figure S2.4. Crystal structure of porous crystal **1** in $M_{12}L_8$ and $M_{12}L_{24}$ cage after the inclusion of diphenylamine. (Ellipsoids are drawn at the 50% probability.)

Figure S2.5. Crystal structure of porous crystal **1** after the inclusion of 2,2'-bithiophene. (Guest molecules in the pore are omitted for clarity. Ellipsoids are drawn at the 50% probability.)

Crystallographic data: $C_{94}H_{60}Co_3N_{30}S_{12}$, M_r = 2171.35, crystal dimensions 0.32 × 0.30 × 0.28 mm^3, Tetragonal, space group, $P4_2/mnm$, $a = b$ = 26.580(8) Å, c = 36.273(11) Å, V = 25628(13) Å^3, T = 90(2) K, Z = 4, r_{calcd} = 0.563 g cm^{-3}, 7021 unique reflections out of 9896 with $I > 2\sigma(I)$, 374 parameters, 0.99 < θ < 23.53°, final R factors R_1 = 0.1108 and wR_2 = 0.3295 for all data. CCDC deposit number *unpublished data*.

Figure S2.6. Crystal structure of porous crystal **1** after the inclusion of 2-adamantanone. (Ellipsoids are drawn at the 50% probability.)

one cage

included 2-adamantanone

packing structure

Crystallographic data: $C_{89}H_{94}Co_{1.5}N_{15}O_5S_3$, M_r = 1638.37, crystal dimensions 0.36 × 0.36 × 0.32 mm^3, Tetragonal, space group, $I4_1/acd$, $a = b$ = 37.524(3) Å, c = 73.717(11) Å, V = 103789(19) Å^3, T = 90(2) K, Z = 32, r_{calcd} = 0.839 g cm^{-3}, 22235 unique reflections out of 464176 with $I > 2\sigma(I)$, 1026 parameters, 1.22 < θ < 24.79°, final R factors R_1 = 0.1983 and wR_2 = 0.5611 for all data. CCDC deposit number *unpublished data*.

General procedure for guest encapsulation into discrete cage 2

The cage host **2** was synthesized according to previously reported procedure.[1] To a 20 mM aqueous solution of **2**, an excess amount of guest solid was added, and the resulting suspension was stirred at room temperature for 1 h. Residual solid was removed by filtration, and the filtrate was analyzed by NMR spectroscopy.

TTF included in discrete cage 2⊃(TTF)$_4$

^{1}H NMR (500 MHz, D_2O, 300 K) δ 9.39 (d, J = 6.0 Hz, 24H, pyridine-α), 8.83 (d, J = 6.0 Hz, 24H, pyridine-β), 5.51 (br s, 8H, TTF), 3.20 (s, 24H, N-CH_2-CH_2-N), and 2.79 (s, 72H, N-CH_3). Inclusion of four TTF molecules was confirmed by X-ray crystallographic analysis with a single crystal grown by slow evaporation of water. In solution there exists an equilibrium between **2**⊃(TTF)$_4$ and empty cage. Hence the guest proton signal was observed with an intensity of 8H.[7] ^{13}C NMR (125 MHz, D_2O, 300 K) δ 169.6, 152.4 (pyridine-α), 145.8, 126.5 (pyridine-β), 118.9 (br, TTF *C*-H), 109.8 (br, TTF, center *C*=*C*), 63.2 (N-*C*H$_2$-*C*H$_2$-N), and 50.8 (N-*C*H$_3$). Elemental analysis: calculated for $C_{108}H_{144}N_{48}O_{36}Pd_6$•3(TTF)•11$H_2O$; C 36.55, H 4.33, N 16.24; found C 36.34, H 4.19, N 16.51. (For elemental analysis, inclusion complex was precipitated by distilling water with a rotary evaporator at 40 ºC. During this process, guest TTF was partially escaped from the cage.) IR (single crystal, FLUOROLUBE, cm^{-1}): 3104(m), 3027(m), 2936(m), 1751(w), 1669(m), 1616(m), 1575(m), and 964(m). UV-Vis (H_2O) λ [nm] (ε [cm^{-1}•M^{-1}]): 630 (620).

Diphenylamine included in discrete cage 2⊃(Ph$_2$NH)$_n$

^{1}H NMR (500 MHz, D_2O, 300 K) δ 9.27 (d, J = 5.1 Hz, 24H, pyridine-α), 8.63 (d, J = 5.1 Hz, 24H, pyridine-β), 5.55 (t, J = 7.0 Hz, 6H, diphenylamine *m*-H), 5.27 (t, J = 7.3 Hz, 3H, diphenylamine *p*-H), 4.68 (d, J = 7.0 Hz, 6H, diphenylamine *o*-H), 3.09 (s, 24H, N-CH_2-CH_2-N), and 2.70 (s, 72H, N-CH_3). The NH proton for diphenylamine was not observed due to proton–deuterium exchange. For the same reason noted above, a ratio of host/guest =1 : 1.5 was obtained by integration ratio. ^{13}C NMR (125 MHz, D_2O, 300 K) δ 169.3, 152.4 (pyridine-α), 145.6, 141.9, 128.5 (diphenylamine *m*-C), 121.4 (pyridine-β), 120.7 (diphenylamine *p*-C), 116.7 (diphenylamine *o*-C), 63.3 (N-*C*H$_2$-*C*H$_2$-N), and 50.9 (N-*C*H$_3$). Elemental analysis: calculated for $C_{108}H_{144}N_{48}O_{36}Pd_6$•2($Ph_2NH$)•26$H_2O$; C 38.33, H 5.31, N 16.93; found C 38.18, H 5.19,

N 17.20. IR (single crystal, FLUOROLUBE, cm^{-1}): 3105(m), 3029(m), 2938(m), 1616(m), 1577(m), 1518(w), 1042(w), and 968(m). UV-Vis (H_2O) λ [nm] (ε [cm^{-1}•M^{-1}]): 431 (470).

Figure S2.7. ^{1}H NMR spectra (500 MHz, 300 K) of authentic (a) diphenylamine in $CDCl_3$, and inclusion complexes (b) **2**⊃$(Ph_2NH)_n$ in D_2O. (Only the spectrum (d) was recorded at 323 K in order to avoid peak overlap.

Figure S2.8. X-ray crystal structure of inclusion complex **2**⊃$(TTF)_4$. (Counter anions are omitted for clarity. Ellipsoids are drawn at the 50% probability.)

Crystallographic data: $C_{132}H_{160}N_{48}O_{36}Pd_6S_{16}$, M_r = 2117.89, crystal dimensions 0.40 × 0.35 × 0.34 mm^3, Tetragonal, space group, $I4_1/a$, $a = b$ = 27.886(4) Å, c = 30.086(4) Å, V = 23396 (6) $Å^3$, T = 85 K, Z = 4, r_{calcd} = 1.177 g cm^{-3}, 9717 unique reflections out of 11763 with $I > 2\sigma(I)$, 544 parameters, $1.00 < \theta < 26.21°$, final R factors R_1 = 0.0535 and wR_2 = 0.1457 for all data. CCDC deposit number 766607. Solvents molecules were not crystallographically well defined and the residual electron densities in the solvent-accessible void were removed from the structure and the data treated with the PLATON SQUEEZE program.

Figure S2.9. Diffuse reflectance spectra in $BaSO_4$ powder of porous crystal **1** and guest inclusion porous crystals (a) TTF and (b) Ph_2NH. UV-Vis absorption spectra of (c) cage host **2** and TTF inclusion host cage (at 0.4 mM in water) and (d) cage host **2** and Ph_2NH inclusion host cage (at 2.0 mM in water). Blue lines show absorption spectra of guest molecules in toluene as references.

2.5.4. Liquid guest inclusion into one crystal of porous crystal 1 on small scale

General procedure for single-crystal-to-single-crystal guest encapsulation with porous crystal 1

On a glass plate, a crystal of **1** (280 × 280 × 200 μm^3) was soaked in a drop of liquid guest (5 μl) at room temperature with the care about not evaporation of liquid guest. After standing for 2 d, the crystal was picked using a protectant and mounted onto the X-ray diffractometer. After collection of the diffraction data, the same crystal was subsequently analyzed by microscopic FT-IR spectroscopy.

Inclusion crystal 1⊃(diphenylmethane):

IR (single crystal, FLUOROLUBE, cm^{-1}): 3062 (m), 3027 (m), 2042 (s, NCS st.), 1600 (m), 1577 (m), 1514 (s), 1509 (s), 1495 (s), 1373 (m).

Inclusion crystal 1⊃(cyclohexanone):

IR (single crystal, FLUOROLUBE, cm^{-1}): 2941(s), 2865(m), 2053(s, NCS st.), 1713(s, C=O st.), 1522(m), 1375(m).

Inclusion crystal 1⊃(*t*-BuOH):

IR (single crystal, FLUOROLUBE, cm^{-1}): 3439(s br, OH st.), 2971(s), 2064(s, NCS st.), 1578(m), 1516(s), 1371(m).

Figure S2.10. Crystal structure of porous crystal **1** after the inclusion of diphenylmethane. (Ellipsoids are drawn at the 50% probability.)

Crystallographic data: $C_{32.5}H_{24}Co_{0.75}N_{7.50}S_{1.5}$, M_r = 611.88, crystal dimensions 0.35 × 0.25 × 0.20 mm^3, Tetragonal, space group, $P4_2/mnm$, $a = b$ = 26.694(3) Å, c = 36.188(9) Å, V = 25787(8) Å^3, T = 90(2) K, Z = 16, r_{calcd} = 0.630 g cm^{-3}, 7503 unique reflections out of 9789 with $I > 2\sigma(I)$, 442 parameters, $0.95 < \theta < 23.36°$, final R factors R_1 = 0.0972 and wR_2 = 0.2896 for all data. CCDC deposit number *unpublished data*.

Figure S2.11. Crystal structure of porous crystal **1** after the inclusion of cyclohexanone. (Ellipsoids are drawn at the 50% probability.)

Crystallographic data: $C_{45}H_{34}N_{15}Co_{1.5}S_3O$, M_r = 985.45, crystal dimensions 0.28 × 0.28 × 0.20 mm^3, Monoclinic, space group, $C2/m$, a = 37.218(6), b = 37.293(6), c = 26.388(5) Å, β = 134.988(2)º, V = 25974(8) Å^3, T = 93 K, Z = 8, 11134 unique reflections out of 23220 with $I > 2\sigma(I)$, 908 parameters, 0.95 < θ < 25.00°, final R factors R_1 = 0.0822 and wR_2 = 0.2430 for all data. CCDC deposit number 910380.

Figure S2.12. Crystal structure of porous crystal **1** after the inclsuion of *t*-BuOH. (Ellipsoids are drawn at the 50% probability.)

Crystallographic data: $C_{20.08}H_{13.44}Co_{0.75}N_{7.50}S_{1.50}O_{0.14}$ M_r = 454.36, crystal dimensions 0.25 × 0.25 × 0.16 mm^3, Tetragonal, space group, $P4_2/mnm$, $a = b$ = 26.520(3) Å, c = 37.519(4) Å, V = 26389(6) Å^3, T = 90(2) K, Z = 16, r_{calcd} = 0.457 g cm^{-3}, 7468 unique reflections out of 1414 with $I > 2\sigma(I)$, 327 parameters, 1.214 < θ < 26.422°, final R factors R_1 = 0.1254 and wR_2 = 0.3745 for all data. CCDC deposit number *unpublished data*.

Residual electron densities in the solvent-accessible void due to disordered guest and solvent molecules were treated with the PLATON SQUEEZE program. (Before the treatment of SQUEEZE program; the maximum electron density remained was 1.124, R_1 = 0.1862 and wR_2 = 0.4630.)

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CHAPTER 3

Reactions of Guest Molecules in Porous Crystals

Abstract: Specific chemical reactions were reported in solution state octahedral M_6L_4 cage molecule. Like reactions in solution state host molecules, several chemical reactions in porous crystals were performed. Bimolecular acylation reaction in porous crystals was successfully carried out without leaching the first substrate. Furthermore, unusual chemoselectivity was observed by steric effect of octahedral M_6L_4 cages. Oxidation reaction of included guest molecules in porous crystals by molecular oxygen caused due to strong host–guest interaction. Additionally, thermal reactions of distorted four-membered ring molecules and subsequently oxidation reactions of water sensitive molecules were carried out in both solution state host molecule and porous crystals. The reactions proceeded efficiently in porous crystals because water solvent was avoided. Unique chemical reactions were successfully achieved in porous crystals.

3.1. Introduction

Reactions of guest molecules in host molecules in solution state have been well studied[1] because of their specificity compared with no host molecule conditions. Especially, in host cage **2**, various kinds of specific reactions were reported. For example, unusual regio- and stereoselective Diels–Alder reaction of anthracene and dienophile gave 1,4 adduct by steric constriction.[2] Not only new regioselectivity but also new reactivity were showed of the Diels–Alder reactions of inert arenes and dienophile in host cage **2**.[3] And unusual oxidation reaction of adamantane in host cage **2** by photoirradiation was also reported.[4]

On the other hand, chemical reactions in porous crystals have been also investigated independently of solution state reactions in host molecules. For example, porous crystals based catalytic reactions[5,6] by incorporated catalysts into frameworks,[7] molecules included in porous crystals[8] and nanoparticles included in porous crystals,[9] reactions of reagents with the substituents introduced into ligands[10] what is called postsynthetic modification and chemical reactions of reagents with incorporated compounds between the ligands[11] in single-crystal-to-single-crystal fashion for observation of unstable chemical species,[12] Dieals–Alder reactions[13] and palladium-mediated reactions[14] were performed.

In this chapter, three types of chemical reactions in porous crystals **1** based on strong guest inclusion were performed. First one was bimolecular acylation in porous crystals (in chapter 3.2.). In consideration of reactions of guest molecules in porous crystals, it is very important to confine the guests to porous crystals for avoiding the guest escape. Especially in the case of bimolecular reaction in porous crystals, first substrate can escape from porous crystals when second substrate is introduced into porous crystals by diffusion of the solution of second substrate. Then inefficient chemical reaction in porous crystals is performed (Fig. 3.1.(a)). Hence guest inclusion ability of **1** is very useful for the reactions in porous crystals in an attempt to avoid the escape of first substrate from porous crystals (Fig. 3.1.(b)). 4-hydroxydiphenylamine (**9**), which is electron-rich molecule, was selected as first substrate and ethyl isocyanate (**10**) was chose as second substrate and acylation was performed in **1**. In addition, chemoselectivity was observed in the reaction by steric effect of octahedral M_6L_4 cages.

Figure 3.1. (a) Image of a bimolecular reaction in a usual porous crystal. (b) Image of a bimolecular reaction in porous crystal **1**.

Second reactions were oxidation reactions using host–guest interactions (in chapter 3.3.). When strong electron-donor molecules were included, not only charge transfer but also electron transfer between guest molecules and host porous crystals were observed because of electron deficient ligand **3**. Due to the strong host–guest interactions, oxidation reaction of guest molecules in porous crystal **1** proceeded by only exposure of the guest included in crystals to air. Concretely speaking, compound **9** was oxidized to **14** by inclusion into **1** and exposure to air.

Figure 3.2. Image of oxidation reaction of **9** in porous crystal **1** using electron transfer from guest molecules to ligand **3**.

Third one was transfer of reactions of guest molecules from solution state host to crystalline state via octahedral M_6L_4 cage using water sensitive molecules (in chapter 3.4.). As described previously, unique and interesting chemical reactions were performed in host cage **2**. But water sensitive compounds cannot be used because water solvent is necessary to include of guest molecules. On the other hand, porous crystal **1** also has octahedral M_6L_4 cage with similar recognition ability to solution state host **2** and guest inclusion is performed in organic solvent therefore water sensitive molecules can be dealt in octahedral M_6L_4 cages by porous crystals **1**. Therefore, thermal ring opening reactions of cyclobutenedione and subsequent oxidation reactions of bisketene,[15] which is water sensitive molecule, were carried out both in solution state host **2** and porous crystal **1**. Especially, 3,4-bis(trimethylsilyl)-3-cyclobutene-1,2 -dione (**15**) was selected as substrate of chemical reactions in porous crystals **1** because of 2,3-bis(trimethylsilyl)-1,3-butadiene-1,4-dione (**16**) is relatively stable enough to

observe by ^{1}H NMR measurement. In no host conditions, air oxidation of bisketene was not clear reaction, namely several kinds of bi-products were obtained.[16] In solution state host **2**, oxidation of bisketene proceeded and almost pure product **17** was obtained in ^{1}H NMR spectrum but yield was not so high because of unidentified precipitate by water solvent . On the other hand, in porous crystal **1**, oxidation of bisketene was performed in good yield (Fig. 3.3.).

Figure 3.3. Ring opening reaction of cyclobutenedione **15** and oxidation of bisketene **16**.

3.2. Bimolecular acylation reaction in porous crystals

For bimolecular reaction, introduction of 4-hydroxydiphenylamine **9** as first substrate was carried out by only immersion of porous crystal **1** into a saturated toluene solution of **9** for 24 h at room temperature. Crystal color turned reddish-black and diffuse reflectance spectrum showed broad charge transfer band at 500–700 nm (Fig. 3.4.(a)). Extraction experiment and thermogravimetric spectrum showed 35 wt% inclusion of guest **9** in porous crystals **1** (Fig. 3.4.(b)). X-ray crystallographic analysis revealed that 4 guest molecules **9** were included in M_6L_4 cage (Fig. 3.5.) and 6 guest molecules **9** in $M_{12}L_8$ cage and 6 guest molecules **9** in $M_{12}L_{24}$ cage, which implied that 40% of **9** in porous crystals was included in M_6L_4 cage and 60% of **9** was included in large cavities (Fig. 3.6.). Each guest molecule **9** in M_6L_4 cage was stacked onto ligand **3** and the OH group located outside of the M_6L_4 cage. In contrast, NH group was covered with panel ligand **3**.

Figure 3.4. (a) Diffuse reflectance spectra of porous crystals **1** and guest-included porous crystals **1⊃9**. (b) TG-DSC curves of guest-included porous crystals **1⊃9**. (heating rate: 5 K/min, nitrogen flow: 30 mL/min.)

Figure 3.5. X-ray structure of **9** included in porous crystal **1**. Guest **9** located in large cavities were omitted for clarify.

Figure 3.6. X-ray structure of **9** included in $M_{12}L_8$ cage and $M_{12}L_{24}$ cage.

Acylation in porous crystals **1** was performed by immersion of guest **9** included in porous crystals into a decane solution of excess amount of ethyl isocyanate **10** as second substrate. After 12 h standing, the crystals were filtrated and decomposed by addition of HCl. The products were extracted by CH_2Cl_2 and analyzed by NMR spectroscopy. From the ^{1}H NMR spectrum, *O*-acylated compound **12** and *N,O*-diacylated compound **13** were formed in 38% and 55% yield, respectively. Totally 93% of guest **9** was

reacted without leaching out (Fig. 3.7.). Furthermore, leaching out of ligand **3** and $Co(NCS)_2$ were not observed and crystallinity of **1** was maintained.

Figure 3.7. Acylation reaction in porous crystal **1**.

In this reaction, unusual chemoselectivity was observed. In porous crystal **1**, *O*-acylated compound **12** and *N,O*-diacylated compound **13** were observed but *N*-acylated compound **11** was not observed. In solution reaction without crystal **1**, mainly *N*-acylated compound **11** was obtained. From these results, in porous crystal **1**, less nucleophilic OH group was reacted preferentially. Even in existing of free NH group, ratio of products was not changed in prolonged 24 h reaction time. From the X-ray structure, it was expected that NH group covered with M_6L_4 cage did not react but OH group located outside the cage reacted preferentially.

To understand the chemoselectivity, the product ratio was traced in the reaction. The ratio of the products was checked by quenching of the reaction at several points and analyzing by ^{1}H NMR measurement (Fig. 3.8.). The product ratio at 0–4 h clearly revealed that *N*-acylated compound **11** was formed at initial stage of this reaction and provided as an intermediate of *N,O*-diacylated compound **13**. The ratio of *O*-acylated compound **12** gradually increased over 8 h. Importantly, *O*-acylated compound **12** was not converted to *N,O*-diacylated compound **13** in the reaction. From these results, it could be concluded that there were two competing reaction pathways in porous crystal **1**: (1) *N*-acylation and subsequent *O*-acylation and (2) *O*-acylation only. From the X-ray structure of **9** included in crystal **1**, pathway (1) occurred in the huge $M_{12}L_8$ and $M_{12}L_{24}$ cages and pathway (2) occurred in M_6L_4 cages because *N*-acylation was provided in M_6L_4 cages by covering of NH group with M_6L_4 cages. And 38% yield of **11** corresponded to the percentage of **9** located in M_6L_4 cage (40%) observed by X-ray crystallography, which implied *O*-acylation occurred in M_6L_4 cage and *N,O*-diacylation occurred in large cavities.

Figure 3.8. Reaction trace about acylation of **9** in crystal **1**.

To confirm the effect of octahedral M_6L_4 cage, this acylation was performed in host cage **2** in solution state. Inclusion of **9** into cage **2** was carried out by suspension of **9** to aqueous solution of **2** and solution color turned to dark-red. Guest inclusion was confirmed by upfield-shift of the guest proton signals in ^{1}H NMR spectrum. The ploton signals of unsubstituted phenyl ring of **9** were shifted more than those of other parts, consistent with the location of **9** in M_6L_4 cage in porous crystal **1**, where NH group was covered and OH was exposed. The solution of **3** included in cage **2** was treated with 5 equivalent of **10** and *O*-acylated product **12** was selectively formed. The product was obtained as precipitated white solid because the product was not good guest for cage **2** (Fig. 3.9.). This result supported the conclusion of prevention of the covered NH group and preferential reaction of the exposed OH group.

Figure 3.9. Acylation reaction in solution state host cage **2**.

3.3. Oxidation reaction by host–guest interaction in porous crystals

Strong charge transfer was observed when electron-rich molecules were included in porous crystal **1**. Furthermore, when TTF included crystal **1** was analyzed by ESR measurement, one signal derived from radical species was observed. In the case of as-synthesized **1**, no ESR signal was observed. These results indicated that not only charge transfer interaction but also electron transfer interaction were occurred by electron-rich guest molecule inclusion into **1**.

ESR measurement of several guest molecules included crystal **1** was attempted and redox potentials of these molecules were investigated. In the case of TTF, **9** or *N*-((4-phenylamino)phenyl)acetoamide, ESR signal was observed but in the case of **4** or **5** no ESR signal was observed. From these results, the regularity was observed, that is to say the guest compound whose redox potential from –0.06 to 0.38 V was ESR active and from 0.46 to 0.93 V was ESR silent (Fig. 3.10.).

Figure 3.10. Relation between ESR signals and oxidation potentials.

Electron transfer interaction in crystals was applied to oxidation reaction of guest molecules. Guest **9** included porous crystals **1** was exposed to air for 1 week at room temperature and included compounds were extracted by immersion of the crystals into dichloromethane. ^{1}H NMR spectrum showed oxidized product **14** was formed in 27% yield. Furthermore, the yield increased to 42% by change the guest inclusion solvent from toluene to trifluoromethylbenzene and temperature to 80 ºC (Fig. 3.11.). In contrast, no oxidation reaction was observed by only exposing compound **9** to air or just mixing with ligand **3** or $Co(NCS)_2$. These results strongly indicated that this oxidation

reaction was carried out by electron transfer interaction between host crystals and guest molecules. Additionally, this 42% yield in the crystalline state reaction was comparable to the percentage of **9** located in M_6L_4 cage (40%) observed by X-ray crystallography, which implied that **9** included strongly in the M_6L_4 cage was oxidized and **9** in the huge cages did not react because **9** in M_6L_4 cage strongly interacted with ligand **3**.

Figure 3.11. Oxidation reaction of **9** in crystal **1** and ^{1}H NMR spectrum (500 MHz, 300 K, $CDCl_3$) of the crude mixture.

3.4. Reactions of cyclobutenedione and bisketene in both solution state host molecule and porous crystals

As described in chapter 3.1., reactions of cyclobutenedione and water sensitive bisketene in both solution state host molecule and porous crystals were performed toward the purpose of transfer of reactions of guest molecules from solution state host to crystalline state. First, thermal ring opening reaction of cyclobutenedione **15** and oxidation of bisketene **16** in solution state host **2** were performed. Cyclobutenedione **15** was suspended to aqueous solution of host cage molecule **2** for 30 min at 45 ºC and excess amount of guest molecules were filtrated. ^{1}H NMR of the aqueous solution showed upfield-shift of the peak of guest molecules at around –1.3 ppm, which showed inclusion of **15** into host cage **2**. After getting the single crystal of **2⊃15** by slow evaporation of water solvent, X-ray crystallography was performed and the crystal structure revealed one guest **15** was included in the octahedral M_6L_4 cage (Fig. 3.12.).

Figure 3.12. X-ray structure of **2⊃15**.

Thermal ring opening reaction and subsequent oxidation were carried out by heating the aqueous solution of **2⊃15** at 100 ºC for 7 h under air. After decomposition of host **2** by addition of HCl, the product was extracted by dichloromethane. ^{1}H NMR of the extracted product showed only one proton signal derived from product **17** except of signals of solvent and TMS (Fig. 3.13.). But yield was only 18% based on starting material **15** and insoluble black precipitation was obtained. The precipitation seemed to be derived from a reaction of bisketene **16** with water at the thought that the product **17** was obtained from **15** via intermediate water sensitive bisketene **16**.

Figure 3.13. ^{1}H NMR spectra (500 MHz, 300 K) of (a) compound **15** (in $CDCl_3$), (b) **2⊃15** (in D_2O) and (c) extract of after heating of aqueous solution of **2⊃15** (in $CDCl_3$).

To confirm of an effect of water solvent, the reactions of just the single crystal of **2⊃15** were performed. Single crystals of **2⊃15** were heated at 100 ºC for 7 h under air and the product was extracted in a same manner as reactions of aqueous solution of **2⊃15**. The yield of **17** was increased to 45% and black insoluble precipitation was not obtained but starting material **15** was remained. The packing model of X-ray structure of **2⊃15** revealed that there is not space enough to enter the oxygen molecules between octahedral cages (Fig. 3.14.).

Figure 3.14. Packing model of X-ray structure of **2⊃15**.

Therefore, the reactions were performed in porous crystal **1** because (1) octahedral M_6L_4 cages in porous crystal **1** showed similar guest inclusion ability to host cage **2**, (2) a solvent used in the case of porous crystal **1** is not water but organic solvent and (3) there is enough space for enter of oxygen molecules due to large $M_{12}L_8$ and $M_{12}L_{24}$ cavity. Inclusion of **15** into porous crystal **1** was carried out by soaking of crystal **1** into a saturated toluene solution of **15** and confirmed by microscopic IR measurement and elemental analysis. Additionally, extraction experiment revealed 33 wt% inclusion of **15** in porous crystal **1**. First, **15** included in crystal **1** was heated at 100 ºC for 2 h under argon atmosphere. In microscopic IR spectrum, the peak derived from bisketene **16** was observed. The product was extracted by immersion of the crystals into dichloromethane and solvent was evaporated. ^{1}H NMR measurement of the product clearly showed bisketene **16** was generated even in porous crystal **1**. Subsequent heating of the crystals at 100 ºC for 2 h under air gave maleic anhydride **17**

in 91% yield (Fig. 3.15.). For the control experiment, compound **15** was heated at 100 ºC for 7 h under air and **17** was obtained in only 14% yield. From these results, it was concluded that effective oxidation reaction was performed in porous crystal **1** by transfer of chemical reactions of guest molecules from solution state host to crystalline state.

Figure 3.15. Thermal reaction of **15** and oxidation reaction of **16** in porous crystals **1** and ^{1}H NMR spectra (500 MHz, 300 K, $CDCl_3$) of extracts.

Thermal ring opening reaction of 3,4-diphenyl-3-cyclobutene-1,2-dione **18** was also performed because formation more unstable 2,3-diphenyl-1,3-butadiene-1,4-dione **19** from **18** was reported.[17] Inclusion of **18** into porous crystal **1** was carried out by immersion of crystal **1** into a saturated mesitylene solution of **18** and confirmed by microscopic IR measurement and elemental analysis. Heating of the crystals at 150 ºC for 12 h under air gave maleic anhydride **20** in 66% yield and another by-product in 8% yield (Fig.3.16.). X-ray crystallography of the by-product clearly showed the by-product was 3,4-diphenyldihydrothiophene-2,5-dione **21**, which contained sulfur atom from thiocyanate in framework, by C–S bond length about 1.79 Å. Only heating of **18** at 150 ºC for 12 h under air gave **20** in 63% yield and **21** was not obtained. The reaction implied porous crystal **1** could be used for sulfur introduction reaction.

Figure 3.16. Thermal reaction of **18** and oxidation reaction of **19** in porous crystals **1**.

3.5. Summary

Three kinds of reactions were performed in porous crystals **1**. Bimolecular reaction in porous crystal **1** was successfully achieved. By strong inclusion of the guests, almost substrates in crystals did not leached out. Furthermore, unusual chemoselectivity was observed by characteristic guest location in octahedral cage. This guest location was applied to proton-coupled electron transfer reaction by another group.[18] Additionally, electron transfer between guest molecules and host framework based on strong host–guest interaction was applied to unusual oxidation reaction by molecular oxygen. And thermal reaction of cyclobutenedione and oxidation of bisketene were attempted in host cage **2** and porous crystals **1**. These reactions proceeded efficiently in porous crystal **1** by avoidance of water solvent. These reactions indicated that reactions based on host–guest interactions in porous crystal **1** have a potential of application to specific or catalytic reaction in porous crystals.

3.6. Experimental sections

Contents

3.6.1. Materials and methods
3.6.2. Synthesis and characterization of 9 inclusion crystal
3.6.3. Crystalline state acylation reaction
3.6.4. Reaction tracing
3.6.5. Control experiment with discrete cage
3.6.6. Oxidation reaction of 9 in porous crystals
3.6.7. Reactions of cyclobutenedione and bisketene in discrete cage
3.6.8. Reactions of cyclobutenedione and bisketene in porous crystal

3.6.1. Materials and methods

^{1}H and ^{13}C NMR spectra were recorded on Bruker DRX-500 (500 MHz) NMR spectrometer or Bruker AVANCE 500 (500 MHz) NMR spectrometer with CP-TCI cryoprobe. All NMR spectral data were collected at 300 K and the chemical shift are reported in parts per million (ppm) relative to an internal standard tetramethylsilane (δ = 0.00 ppm for ^{1}H and ^{13}C NMR) for $CDCl_3$, and to a residual solvent signal for DMSO-d_6 (δ = 2.50 ppm for ^{1}H and 39.52 for ^{13}C NMR). MALDI-TOF MS measurement was performed using a Bruker Autoflex speed. IR measurements for organic compounds were carried out as KBr pellets using a DIGILAB FTS-7000 instrument. The single crystal microscopic FT-IR spectra were recorded on a Varian DIGILAB Scimitar instrument. Thermo gravimetric analysis was performed on a STA 409 PG/T equipped with a QMS 403C/T (NETZSCH). ESR spectra were recorded on a JEOL JMS-RE1X. UV-Vis absorption and diffuse reflectance spectra were recorded on a SHIMADZU UV-3150 spectrometer. Diffuse reflectance spectra were recorded with an integrating sphere and were converted from reflection to absorbance by the Kubelka–Munk method. Elemental analyses were performed on a YANACO MT-6. Single crystal X-ray diffraction data were made using a BRUKER APEX-Ⅱ/CCD diffract meter equipped with a focusing mirror (MoK_{α} radiation λ = 0.71073 Å) and a N_2 generator (Japan Thermal Eng. Co., Ltd.).

4-Hydroxydiphenylamine was purchased from TCI Co. LTD. and used after crystallization with chlorobenzene/petroleum ether. Other solvents and reagents were obtained from commercial suppliers and used without further purification.

3.6.2. Synthesis and characterization of guest inclusion crystal

Inclusion crystal 1⊃9: As-synthesized crystals **1** (*ca*. 300 mg) were first washed with toluene (5 mL × 3 times), and then were immersed into a saturated toluene solution (5 mL) of guest **9** at room temperature under argon atmosphere. After 24 h, inclusion crystal **1⊃9** was isolated by filtration. For elemental analysis, TG-DSC, and extraction experiments, obtained crystals were vacuum dried at 1 mmHg for 20 min at room temperature so that the weight of crystals remains steady.

IR (single crystal, FLUOROLUBE, cm^{-1}): 3326 (m, NH and OH st.), 3061(m), 3029(m), 2361(m), 2332(m), 2056(s, NCS st.), 1653(m), 1598(m), 1517(s), 1375(s). UV-Vis (diffuse reflectance, $BaSO_4$, λ [nm]) 462 and 594 (shoulder). Elemental analysis: calculated for $\{[(\mathbf{3})_4(Co(NCS)_2)_3]\bullet 9(\mathbf{9})\bullet(\text{toluene})\bullet(1,2\text{-dichlorobenzene})\}_n$; C 67.86, H 4.84, N 13.19.; found C 67.58, H 4.94, N 13.12;

Extraction experiment: Inclusion crystal **1⊃9** (175.4 mg) was decomposed with 1.0 M hydrochloric acid (30 mL) and organic guest was extracted with dichloromethane (30 mL × 5 times). The combined organic layer was washed with saturated $NaHCO_3$ aq, dried over Na_2SO_4. After the solvent evaporation, solid **9** (60.6 mg, 34.5 wt%) was obtained. The purity of obtained guest was also confirmed by ^1H NMR spectrum.

Figure S3.1. Crystal structure of porous crystal **1** after the inclusion of 4-hydroxydiphenylamine. (Ellipsoids are drawn at the 50% probability.)

Crystallographic data: $C_{58.65}H_{45.93}N_{12.72}CoS_2O_{2.72}$, M_r = 1095.49, crystal dimensions 0.46 × 0.38 × 0.35 mm^3, Cubic, space group, *Fd*-3*c*, $a = b = c$ = 74.992(3) Å, V = 421737 (28) Å^3, T = 90 (2) K, Z = 192, r_{calcd} = 0.828 g cm^{-3}, 13281 unique reflections out of 15484 with $I > 2\sigma(I)$, 723 parameters, $1.33 < \theta < 25.00°$, final R factors R_1 = 0.1581 and wR_2 = 0.3986 for all data. CCDC deposit number 846614.

3.6.3. Crystalline state acylation reaction

Procedure for bimolecular reaction in porous crystals 1

Inclusion crystals **1⊃9** (140 mg, containing 49 mg (265 μmol) of **9**) was soaked into a decane solution of ethyl isocyanate (**10**) (1.15 M, 4.4 mL) under argon atmosphere and then allowed to stand at room temperature for 12 h. After the immersion, porous crystals **1** were carefully separated from the supernatant by decantation, and subsequently washed with decane (*ca*. 5 mL).

Reaction products in crystals **1** were extracted according to the procedure described above to give a product mixture (74 mg) consisting of compounds **12** (26 mg, 38%) and **13** (48 mg, 55%).

From the combined decane solution, 5.3 mg of the product mixture (**12** : **13** = 55 : 45; *i.e.* total 7% based on **9**) was obtained.

Control experiment in solution

To a toluene solution of 4-hydroxydiphenylamine **9** (2.5 M, 0.1 mL), excess amount of EtNCO **10** was added via syringe pump (flow rate: 0.12 mL/h) over 12 h at room temperature. After additional stirring for 12 h, the reaction was quenched by addition of water. Reaction products were extracted with CH_2Cl_2, the resulting organic phase was dried over Na_2SO_4, and the solvent was removed by evaporation. The residual solid was analyzed by ^{1}H NMR spectroscopy. *N*-acylated product **11** was obtained in 77% yield and diacylated product **13** was obtained in 23% yield.

Characterization of the products

Each product was synthesized in a large scale reaction and isolated by silica gel column chromatography.

Compound 12

R_f = 0.63 (eluent: CH_2Cl_2/MeOH = 20/1). ^{1}H NMR (500 MHz, DMSO, 300 K): δ 8.08 (s, 1H, H_d), 7.60 (t, J = 5.7 Hz, 1H, H_g), 7.21 (t, J = 8.2 Hz, 2H, H_b), 7.03 (t, 4H, H_c, H_e), 6.95 (d, J = 8.2 Hz, 2H, H_f), 6.79 (t, J = 7.6 Hz, 1H, H_a), 3.08 (q, J = 7.0 Hz, 2H, CH_2), 1.07 (t, J = 7.0 Hz, 3H, CH_3). ^{13}C NMR (125 MHz, DMSO, 300 K): δ 155.1, 144.6, 144.3, 140.8, 129.6, 122.9, 119.8, 118.1, 116.6, 35.7, 15.4. IR (KBr, cm^{-1}): 3384(m), 3336(m), 1705(s), 1514(m), 1261(w), 1221(m), 841(w), 745(w), 696(w). Elemental analysis (%); Calculated for $C_{15}H_{16}N_2O_2$; C 70.29, H 6.29, N 10.89 found C 70.03, H 6.49, N 10.72. MS (MALDI-MS) *m/z*, calculated for $C_{15}H_{16}N_2O_2$, 256.30, found 256.00 $[M]^+$.

Compound 13

R_f = 0.41 (eluent: CH_2Cl_2/MeOH = 20/1). ^{1}H NMR (500 MHz, DMSO, 300 K): δ 7.72 (t, J = 5.7 Hz, 1H, H_i), 7.35 (t, J = 7.6 Hz, 2H, H_b), 7.21-7.17 (m, 3H, H_a, H_c, H_g), 7.14 (d, J = 8.2 Hz, 2H, H_g), 7.06 (d, J = 8.2 Hz, 2H, H_h), 6.02 (t, J = 5.7 Hz, 1H, H_d), 3.11-3.07 (m, 4H, H_e, H_j), 1.07 (t, J = 7.0 Hz, 3H, H_k), 0.99 (t, J = 7.0 Hz, 3H, H_f). ^{13}C NMR (125 MHz, DMSO, 300 K): δ 155.8, 154.0, 148.5, 143.4, 140.1, 129.1, 128.1, 127.3, 125.6, 122.2, 35.3, 35.0, 15.4, 14.8. IR (KBr, cm^{-1}): 3401(w), 3308(w), 1729(s), 1654(s), 1500(s), 1329(w), 1258(w), 1211(m), 696(w). Elemental analysis (%); Calculated for $C_{18}H_{21}N_3O_3$; C 66.04, H 6.47, N 12.84; found C 65.92, H 6.47, N 12.71. MS (MALDI-MS) *m/z*, calculated for $C_{18}H_{21}N_3O_3$, 328.39 $[M+H]^+$, 350.37 $[M+Na]^+$, 366.48 $[M+K]^+$, found 328.29 $[M+H]^+$, 350.40 $[M+Na]^+$, 366.23 $[M+K]^+$.

Compound 11

R_f = 0.35 (eluent: CH_2Cl_2/MeOH = 20/1). ^{1}H NMR (500 MHz, DMSO, 300 K): δ 9.53 (s, 1H, *OH*), 7.27 (t, *J* = 8.2 Hz, 2H, H_b), 7.13 (d, *J* = 7.6 Hz, 2H, H_c), 7.08 (t, *J* = 7.6 Hz, 1H, H_a), 7.02 (d, *J* = 8.2 Hz, 2H, H_d), 6.76 (d, *J* = 8.8 Hz, 2H, H_e), 5.76 (t, *J* = 5.7 Hz, 1H, *NH*), 3.05 (q, *J* = 7.0 Hz, 2H, CH_2), 0.97 (t, *J* = 7.0 Hz, 3H, CH_3). ^{13}C NMR (125 MHz, DMSO, 300 K): δ 156.0, 144.2, 133.8, 129.7, 128.6, 126.1, 124.3, 116.1, 34.9, 15.5. IR (KBr, cm^{-1}): 3395(m), 3098(w), 3024(w), 2970(w), 1634(s), 1514(s), 1489(s), 1449(m), 1305(m), 1281(m), 1254(m), 756(w), 692(w). Elemental analysis (%); Calculated for $C_{15}H_{16}N_2O_2$; C 70.29, H 6.29, N 10.93; found C 70.16, H 6.42, N 10.91. MS (MALDI-MS) *m/z*, calculated for $C_{15}H_{16}N_2O_2$, 257.31 $[M+H]^+$, 279.11 $[M+Na]^+$, 295.40 $[M+K]^+$, found 257.47 $[M+H]^+$, 279.43 $[M+Na]^+$, 295.37 $[M+K]^+$.

3.6.4. Reaction tracing

Procedure

For facile and accurate evaluation of the conversion and product ratio in crystal, ethyl isocyanate (**10**) was introduced into the pores by vapor diffusion. Guest-included porous crystals **1⊃9** (20 mg) was placed on a watch glass (3.0 cm in diameter), which was exposed to a vapor of **10** in a paired petri dish (4.5 cm in diameter) containing a solution of ethyl isocyanate (0.5 mL) and toluene (0.5 mL). After standing at room temperature for a certain period of time, the organic compound was extracted from crystals according to the procedure described above to give a product mixture and analyzed by ^{1}H NMR spectroscopy.

The results of independent 18 batches were summarized in the plot of Figure 3.8.

Figure S3.2. The ^{1}H NMR spectra (in DMSO-d_6) of the reaction mixture extracted from crystals of **1** after exposure to EtNCO vapor for 0, 0.5, 1, 3, 6, and 12 h.

3.6.5. Control experiment with discrete cage

Inclusion of guest 9 into discrete cage 2

According to the same procedure in chapter 2, cage host **2** was synthesized in D_2O. To a 20 mM solution of **2**, an excess amount of guest solid **9** (30 mg toward 1 mL of the solution) was added, and the resulting suspension was stirred at room temperature for 1 h. Residual solid was removed by filtration.

9 included in cage **2**

^{1}H NMR (500 MHz, D_2O, 300 K): δ 9.40 (d, J = 6.0 Hz, 24H, pyridine-α), 8.71 (d, J = 6.0 Hz, 24H, pyridine-β), 5.61 (br t, J = 7.3 Hz, 6H, H_b), 5.47 (br d, J = 7.6 Hz, 6H, H_e), 5.11 (br d, J = 7.6 Hz, 6H, H_c), 4.95 (br d, J = 7.6 Hz, 6H, H_d), 4.45 (br t, J = 7.5 Hz, 3H, H_a), 3.22 (s, 24H, N-CH_2-CH_2-N), 2.82 (s, 72H, N-CH_3). The NH proton and OH proton for 4-hydroxydiphenylamine were not observed due to proton-deuterium exchange. The gust signals were assigned based on H-H COSY and NOE spectra. In solution there exists an equilibrium between host-guest complex and empty cage, hence inclusion number n was determined to be ~3 based on the integration ratio. ^{13}C NMR (125 MHz, D_2O, 300 K): δ 168.5, 152.5, 151.9, 145.5, 145.2, 132.8, 127.9, 126.0, 124.8, 118.2, 114.9, 114.7 61.8, 50.4. IR (KBr, cm^{-1}): 3431(m), 3018(w), 2922(w), 1622(w), 1521(s), 1381(s), 1207(w), 1125(w), 1061(m), 1008(w), 955(w), 808(m). UV-Vis (H_2O) λ [nm] (ε [cm^{-1}•M^{-1}]) 461 (240).

Figure S3.3. ^{1}H NMR spectra (500 MHz, 300 K) of (a) 4-hydroxydiphenylamine in $CDCl_3$ and (b) **2⊃9** in D_2O. (* denotes solvent or impurity peaks.)

(Magnification of the guest region)

Figure S3.4. UV-Vis absorption spectra of 4-hydroxydiphenylamine (**9**) in toluene, host cage **2** and inclusion complex **2⊃9** in water.

Acylation reaction between 2⊃9 and EtNCO

To a stirring solution of **2⊃9**, 5 equivalent of EtNCO **10** (based on the guest encapsulated) was added at room temperature. The proton signals of guest **9** on ^{1}H NMR spectrum were disappeared within 1 h concomitantly with precipitation of product **12**.

3.6.6. Oxidation reaction of 9 in porous crystals

Guest inclusion into porous crystals

TTF, *N*-((4-phenylamino)phenyl)acetoamide, **4** or **5** included in porous crystals **1** were prepared as described in chapter 2.5.3. **9** included in porous crystals **1** were prepared as described in chapter 3.6.2.

N-((4-phenylamino)phenyl)acetoamide included in crystal **1**

UV-Vis (diffuse reflectance, $BaSO_4$, λ [nm]) 364 and 572. Elemental analysis calculated for $\{[(\mathbf{3})_4(Co(NCS)_2)_3]\bullet 2.5(N\text{-}[4\text{-}(phenylamino)phenyl]\text{-}acetamide)\bullet 1.5(toluene)\bullet 1,2\text{-}dichlorobenzene\bullet H_2O\}_n$; C 58.84, H 3.85, N 18.54; found C 58.75, H 4.23, N 18.72.

ESR measurement of guests included in porous crystals 1

Figure S3.5. ESR spectra of guests included in porous crystals **1** at 123 K.

Oxidation reaction of 9 in porous crystal 1 under air

4-hydroxydiphenylamine **9** included in porous crystals **1** (140.14 mg) was heated at 80 ºC under air for 1 week. The crystal was immersed in dichloromethane (5 mL) for extraction and supernatant was collected by decantation (repeat 3 times). After removing the solvent by rotary evaporator, **14** was obtained in 42% yield determined by integral ratio of ^{1}H NMR.

Characterization of 4-(phenylimino)cyclohexa-2,5-dienone

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ 7.42 (t, J = 8.0 Hz, 2H, H_b), 7.31 (dd, J = 2.5, 10.3 Hz, 1H, H_d or $H_{d'}$), 7.25 t, J = 7.0 Hz, 1H, H_a), 7.09 (dd, J = 2.5, 10.3 Hz, 1H, H_d or $H_{d'}$), 6.89 (d. J = 7.5 Hz, 2H, H_c), 6.70 (dd, J = 2.5, 10.3 Hz, 1H, H_e or $H_{e'}$), 6.54 (dd, J = 2.5, 10.3 Hz, 1H, H_e or $H_{e'}$). ^{1}H NMR value corresponded to the reported data.[19]

Optimization of inclusion solvent

When **9** was included in porous crystals **1**, several solvents (trifluoromethylbenezene, dichloromethane, toluene, decane) were tried. After inclusion of **9** in these conditions, Oxidation reaction of **9** in crystal **1** was performed. (All yields were determined by integral ratio of ^{1}H NMR)

Figure S3.6. ^{1}H NMR spectra (500 MHz, $CDCl_3$, 300 K) of oxidation reaction of **9** in crystal **1** at room temperature when (a) trifluorobenzene, (b) dichloromethane, (c) toluene, (d) decane was used as inclusion solvent.

Control experiment of oxidation reaction of 9 in the presence of 3 or $Co(NCS)_2$

Ligand **3** (3.0 mg, 0.0096 mmol) or $Co(NCS)_2$ (3.0 mg, 0.017 mmol) was added in a saturated trifluoromethylbenzene solution of **9** (1 mL) and heated at 80 ºC under air for 1 week. After heating, insoluble ligand **3** or $Co(NCS)_2$ was removed by filtration and solvent was removed in vacuo and measured by ^{1}H NMR. In ^{1}H NMR spectra, no peak derived from **14** was observed.

Figure S3.7. ^{1}H NMR spectra (500 MHz, $CDCl_3$, 300 K) of control experiment result in the presence of (a) ligand **3** and (b) $Co(NCS)_2$.

3.6.7. Reactions of cyclobutenedione and bisketene in discrete cage

Synthesis of 2,3-bis(trimetylsilyl)-4,4-dichloro-2-cyclobuteneone

Zinc dust (2.5 g, 38 mmol) in a 50 mL two-neck flask was heated by a heat gun for 5 min with stirring for activation of zinc. After cooling, bis(trimethylsilyl)acetylene (2.4 g, 14 mmol) in 13 mL of ether was added, followed by dropwise addition with stirring of trichloroacetyl chloride (5.5 g, 30 mmol) in 8 mL dimethoxyethane over 1 h at room temperature and the solution was stirred for 3 d. The reaction mixture was filtered through celite, rinsed with hexane, and the filtrate was washed with H_2O and saturated $NaHCO_3$ aqueous solution, dried over Na_2SO_4, and evaporated, and the resulting oil was chromatographed on silica gel (7% EtOAc in hexane, R_f = 0.50) to give the product as yellow oil (3.0 g, 11 mmol) in 76% yield. ^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ 0.42 (s, 9H), 0.28 (s, 9H). This ^{1}H NMR value corresponded to the reported data.[16]

Synthesis of 3,4-bis(trimethylsilyl)-3-cyclobutene-1,2-dione (15)

H_2SO_4 (6 mL) was added to 2,3-bis(trimetylsilyl)-4,4-dichloro-2-cyclobuteneone (2.0 g, 7.1 mmol) at 55 ºC and stirred for 12 min. After the mixture was quenched with ice, extracted three times with ether. The combined ether extracts were washed with saturated $NaHCO_3$ aqueous solution and H_2O, dried over Na_2SO_4, and evaporated. The product was chromatographed on silica gel (hexane: EtOAc = 30: 1, R_f = 0.33) to give **15** (0.47 g, 2.0 mmol) as yellow solid in 29% yield. ^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ 0.37 (s, 18H). ^{13}C NMR (125 MHz, $CDCl_3$, 300 K): δ 217.3, 202.2, -1.41. ^{1}H NMR and ^{13}C NMR values corresponded to the reported data.[16]

Synthesis of 2,3-bis(trimethylsilyl)-1,3-butadiene-1,4-dione (16)

A sample of **13** (1.5 g, 6.6 mmol) in toluene (2 mL) was refluxed under Ar for 1.5 h. After solvent was evaporated, the product **16** (1.5 g, 6.6 mmol) was obtained as yellow oil in 100% yield. ^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ 0.21 (s, 18H). This ^{1}H NMR data corresponded to the reported data.[16]

Synthesis of 2,3-bis(trimethylsilyl)maleic anhydride (17)

To a solution of compound **17** (1.5 g, 6.6 mmol) in $CHCl_3$ (16 mL), Br_2 (1.1 g, 6.6 mmol) was added. After the mixture stirred for 1 h at room temperature, quenched with ice and stirred at room temperature for 17 h. The mixture was extracted with CH_2Cl_2 and washed with with saturated $NaHCO_3$ aqueous solution and H_2O, dried over Na_2SO_4, and evaporated. The product was chromatographed on silica gel (hexane: EtOAc = 20: 1, R_f = 0.32) to give **17** (0.22 g, 0.92 mmol) as colorless solid in 14% yield. ^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ 0.39 (s, 18H). ^{13}C NMR (125 MHz, $CDCl_3$, 300 K): δ 168.6, 161.6, 0.18. ^{1}H NMR and ^{13}C NMR values corresponded to the reported data.[20]

Synthesis of 2,3-diphenyl-4,4-dichloro-2-cyclobuteneone

Zinc dust (5.0 g, 76 mmol) in a 50 mL two-neck flask was heated by a heat gun for 5 min with stirring for activation of zinc. After cooling, diphenylacetylene (5.0 g, 28 mmol) in 25 mL of ether was added, followed by dropwise addition with stirring of trichloroacetyl chloride (10.9 g, 60 mmol) in 15 mL dimethoxyethane over 1 h at room temperature and the solution was stirred for 3 d. The reaction mixture was filtered through celite, rinsed with hexane, and the filtrate was washed with H_2O and saturated $NaHCO_3$ aqueous solution, dried over Na_2SO_4, and evaporated, and the resulting oil was chromatographed on silica gel (hexane: CH_2Cl_2 = 10: 1, R_f = 0.17) to give the product as yellow solid (3.3 g, 11 mmol) in 41% yield. ^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ 8.07 (d, J = 7.5 Hz, 2H), 7.81 (d, J = 7.5 Hz, 2H), 7.61 (t, J = 7.5 Hz, 1H), 7.55 (t, J = 5.0 Hz, 2H), 7.47 (t, J = 5.0 Hz 2H), 7.46 (t, J = 7.5 Hz 1H). This ^{1}H NMR value corresponded to the reported data.[21]

Synthesis of 3,4-diphenyl-3-cyclobutene-1,2-dione (18)

H_2SO_4 (10 mL) was added to 2,3-diphenyl-4,4-dichloro-2-cyclobuteneone (3.0 g, 10.4 mmol) at 85 ºC and stirred for 30 min. After the mixture was quenched with ice, extracted three times with ether. The combined ether extracts were washed with saturated $NaHCO_3$ aqueous solution and H_2O, dried over Na_2SO_4, and evaporated. The product was chromatographed on silica gel (hexane: CH_2Cl_2 = 1: 1, R_f = 0.19) to give **18** (2.3 g, 10.0 mmol) as yellow solid in 97% yield. ^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ 8.09 (d, J = 7.0 Hz, 2H, *o*-H), 7.61 (t, J = 7.5 Hz, 1H, *p*-H), 7.56 (t, J = 7.5 Hz, 2H, *m*-H). ^{1}H NMR value corresponded to the reported data.[22]

X-ray structure

Crystal data for **18**: $C_{16}H_{10}O_2$, M_r = 234.24, crystal dimensions 0.28 × 0.13 × 0.10 mm^3, Monoclinic, space group, $P2_1/c$, a = 3.8216(13), b = 21.298(7) Å, c = 13.992(5) Å, $\alpha = \gamma$ = 90º, β =95.574(4)º, V = 1133.5 (7) Å^3, T = 90 K, Z = 4, r_{calcd} = 1.373 g cm^{-3}, 1942 unique reflections out of 10280 with $I > 2\sigma(I)$, 163 parameters, 1.75 < θ < 24.73°, final R factors R_1 = 0.0335 and wR_2 = 0.1473 for all data. CCDC deposit number *unpublished data*.

Inclusion of 15 into solution host cage 2

Excess amount of **15** (*ca*. 50 mg) was suspended into aqueous solution of host cage **2** (20 mM, 5 mL) and stirred at 45 ºC for 30 min. Excess amount of guest was filtrated.

^{1}H NMR (500 MHz, D_2O, 300 K, TMS as external standard): δ 9.37 (d, J = 6.0 Hz, 24H, pyridine-α), 8.82 (d, J = 6.0 Hz, 24H, pyridine-β), 3.21 (s, 24H, N-CH_2-CH_2-N), 2.82 (s, 72H, N-CH_3), -1.31 (s, 18H, SiCH_3). ^{13}C NMR (125 MHz, D_2O, 300 K, TMS as external standard): δ 215.4, 200.9, 168.9, 151.7, 144.9, 125.7, 62.54, 50.14 and -3.88. IR (KBr cm^{-1}): 3414(m), 2923(m), 1763(s, CO st.), 1522(s), 1381(s), 1058(m), 810(m). Elemental analysis: calculated for $C_{108}H_{144}N_{48}O_{36}Pd_6$•(**13**)•22$H_2O$; C 35.86, H 5.25, N 17.01; found C 35.58, H 5.28, N 17.34.

Figure S3.8. X-ray crystal structure of inclusion complex **2⊃15**. (One guest molecule is located between cages. Counter anions are omitted for clarity. Ellipsoids are drawn at the 50% probability.)

Crystallographic data: $C_{126.26}H_{177.40}N_{40}O_{15.57}Pd_6Si_{3.57}$, M_r = 3243.28, crystal dimensions 0.12 × 0.07 × 0.07 mm^3, Monoclinic, space group, *C*2/*c*, a = 45.126(8), b = 27.206(5) Å, c = 38.020(7) Å, $\alpha = \gamma = 90°$, β =105.616(2)°, V = 44954 (14) Å^3, T = 90 K, Z = 8, r_{calcd} = 0.958 g cm^{-3}, 35886 unique reflections out of 193612 with $I > 2\sigma(I)$, 1784 parameters, 1.25 < θ < 24.26°, final R factors R_1 = 0.0923 and wR_2 = 0.2443 for all data. CCDC deposit number *unpublished data*.

Thermal reaction of 2⊃15 under air

The solution of **2⊃15** (20 mM, 5 mL) were heated at 100 ºC for 7 h under air. After decomposition of host cage **2** by addition of aqueous solution of HCl (5 M, 5 mL), the product was extracted by dichloromethane (5 mL × 3 times). Combined organic layer was washed with 10 mL of saturated $NaHCO_3$ aqueous solution and 10 mL of H_2O, dried over Na_2SO_4 and concentrated in vacuo to afford **17** (2.8 mg, 0.012 mmol) as colorless solid in 18% yield.

Thermal reaction of single crystal of 2⊃15 under air

The crystals of **2⊃15** (88.2 mg) were heated at 100 ºC for 7 h under air. After decomposition of host cage **2** by HCl, the product was extracted by dichloromethane and solvent was evaporated. The product was chromatographed on silica gel (hexane: EtOAc = 20: 1, R_f = 0.32) to give **17** (4.3 mg, 0.018 mmol) as colorless solid in 45% yield.

Figure S3.9. Microscopic FT-IR spectra of single crystal of **2⊃15** before heating and after heating.

3.6.8. Reactions of cyclobutenedione and bisketene in porous crystal

Inclusion of 3,4-bis(trimethylsilyl)-3-cyclobutene-1,2-dione (15) in crystal 1

As-synthesized crystals **1** (*ca*. 300 mg) were first washed with toluene (5 mL × 3 times), and then were immersed into a saturated toluene solution (5 mL) of guest **15** at room temperature for 1 day.

From 172.8 mg of inclusion complex **1⊃15**, 56.7 mg of **15** (32.8 wt%) was extracted. IR (single crystal, FLUOROLUBE, cm^{-1}): 3065(m), 2960(m), 2048(s, NCS st.), 1761(s, CO st.), 1513(m), 1372(m). UV-Vis (diffuse reflectance, $BaSO_4$, λ [nm]) 335. Elemental analysis: calculated for $\{[(\mathbf{3})_4(Co(NCS)_2)_3]\bullet 4(\mathbf{15})\bullet 3.5(toluene)\}_n$; C 57.00, H 4.97, N 13.99.; found C 56.84, H 5.12, N 13.79.

Figure S3.10. Microscopic FT-IR spectra of **1** (black) and **1⊃15** (red).

Thermal reaction of 15 in crystal 1

• Under argon atmosphere

The crystals of **1⊃15** (*ca*. 50 mg) were heat heated at 100 ºC for 2 h under argon. The product was extracted by immersion of the crystals into dichloromethane (5 mL × 3 times).

• Under argon atmosphere and air

The crystals of **1⊃15** (104.0 mg, **15**: 34.1 mg, 0.15 mmol) were heated at 100 ºC for 2 h under argon and subsequently heated at 100 ºC for 2 h under air. After decomposing of the crystals by HCl (5 M, 10 mL) , product was extracted three times with dichloromethane (10 mL) and washed with 10 mL of saturated $NaHCO_3$ aqueous solution and 10 mL of H_2O, dried over Na_2SO_4, and evaporated. The product was chromatographed on silica gel (hexane: EtOAc = 20: 1, R_f = 0.32) to give **17** (33.3 mg, 0.14 mmol) as colorless solid in 91% yield.

Figure S3.11. Microscopic FT-IR spectra of **1⊃15** (red), after heating of **1⊃15** under Ar for 2 h (black) and subsequently heating for 2 h under air (blue).

Control experiment of thermal reaction of 15 under air

Toluene solution of **15** (113.2 mg, 0.50 mmol) (2 ml) was heated at 100 ºC for 7 h under air. Solvent was removed by evaporation and measured by ^{1}H NMR. The product was chromatographed on silica gel (hexane: EtOAc = 20: 1, R_f = 0.32) to give **17** (17.0 mg, 0.070 mmol) as colorless solid in 14% yield.

Inclusion of 3,4-diphenyl-3-cyclobutene-1,2-dione (18) in complex 1

As-synthesized crystals **1** (*ca*. 300 mg) were first washed with toluene (5 mL × 3 times), and then were immersed into a saturated toluene solution (5 mL) of guest **18** at room temperature for 1 day.

From 120.1 mg of inclusion complex **1⊃18**, 39.5 mg of **18** (32.9 wt%) was extracted. IR (single crystal, FLUOROLUBE, cm^{-1}): 3066(m), 3030(m), 2054(s, NCS st.), 1780(s, CO st.), 1749(m), 1577(m), 1519(m), 1373(m). Elemental analysis: calculated for $\{[(\mathbf{3})_4(Co(NCS)_2)_3]\bullet 4(\mathbf{18})\bullet 4(toluene)\bullet 0.3(1,2\text{-dichlorobenzene})\}_n$; C 66.05, H 3.91, N 13.45.; found C 65.79, H 4.29, N 13.19.

Figure S3.12. Microscopic FT-IR spectra of **1** (black), **1⊃18** (red).

Thermal reaction of 18 in crystal 1 under air

The crystals of **1⊃18** (101.9 mg **18**: 33.5 mg, 0.14 mmol) were heated at 150 ºC for 12 h under air. After decomposing of the crystals by aqueous solution of HCl (5 M, 10 mL), product was extracted three times with dichloromethane (10 mL) and washed with 10 mL of saturated $NaHCO_3$ aqueous solution and 10 mL of H_2O, dried over Na_2SO_4, and evaporated. The product was chromatographed on silica gel (hexane: EtOAc = 20: 1, R_f = 0.20) to give **20** (23.7 mg, 0.095 mmol) as yellow solid in 66% yield and (hexane: EtOAc = 20: 1, R_f = 0.27) **21** (2.9 mg, 0.011 mmol) as yellow solid in 8% yield.

Characterization of 21

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ 7.37 (t, J = 7.5 Hz, 2H, *p*-H), 7.32 (t, J = 7.5 Hz, 4H, *m*-H), 7.23 (d, J = 7.5 Hz, 4H, *o*-H). ^{13}C NMR (125 MHz, $CDCl_3$, 300 K): δ 191.4, 148.5, 130.3, 130.1, 128.7, 128.5. MS (MALDI-MS) *m/z*, calculated for $C_{16}H_{10}O_2S$, 266.0 $[M]^+$, 279.11, found 265.8 $[M]^+$.

X-ray structure of **21**

Crystal data for **21**: $C_{16}H_{10}O_2S$, M_r = 266.3138, crystal dimensions 0.15 × 0.09 × 0.08 mm^3, Monoclinic, space group, $P2_1/n$, a = 11.2403(10), b = 6.8233(6) Å, c = 16.2067(14) Å, $\alpha = \gamma = 90°$, β =91.8100(10)°, V = 1242.37 (19) Å^3, T = 90 K, Z = 4, r_{calcd} = 1.424 g cm^{-3}, 2095 unique reflections out of 10940 with $I > 2\sigma(I)$, 172 parameters, 2.17 < θ < 24.66°, final R factors R_1 = 0.0279 and wR_2 = 0.1414 for all data. CCDC deposit number *unpublished data*.

Control experiment of thermal reaction of 18 under air

Mesitylene solution of **18** (117.19 mg, 0.50 mmol) (2 ml) was heated at 150 ºC for 12 h under air. Solvent was removed by evaporation and measured by ^{1}H NMR. The product was chromatographed on silica gel (hexane: EtOAc = 20: 1, R_f = 0.20) to give **20** (78.4 mg, 0.31 mmol) as yellow solid in 63% yield.

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CHAPTER 4

Fullerenes Inclusion into Huge Pores in Porous Crystals

Abstract: There are huge cages whose diameters are about 1.2 nm in porous crystal **1**. Therefore, fullerenes (diameter is more than 1 nm) inclusion was performed into porous crystals. Inclusions of C_{60} and C_{70} into porous crystals were carried out by just soaking of crystals into saturated toluene solutions of fullerenes and 35 wt% inclusion of C_{60} and 34 wt% inclusion of C_{70} were achieved. Moreover, preferentially inclusion of C_{70} from mixture of C_{60} and C_{70} was also achieved. Huge pores could be also used effectively for guest inclusion.

4.1. Introduction

The hosts for fullerenes[1] have well studied because of fullerenes interesting nature, which are relatively large size (diameter: C_{60} = 1.03 Å, C_{70} = 1.13 Å), unusual spherical shape and unpolarized chemical nature. First study of designed fullerene hosts was reported in 1992[2] by azacrown compound and many kinds of host molecules in solution state have been reported such as calixarene derivatives,[3-5] aromatic heterocycles,[6-7] TTF based hosts,[8,9] porphyrin based hosts[10,11] and host molecules by self-assembly.[12-14]

On the other hand, fullerenes inclusion into porous crystals is very rare. In 2004, one example of C_{60} inclusion into MOF was reported[15] but trace amount of C_{60} was included and crystal color was slightly turned pale red (Fig. 4.1.). This fullerene inclusion was analyzed by only Raman spectroscopy.

Figure 4.1. A picture of C_{60} included in MOF crystal. Reprinting with permission from ref. 15. Copyright 2004 Nature Publishing Group.

In porous crystal **1**, there are huge cages whose entrance diameter is about 1.2 nm shown in chapter 2. The size of huge pores is favorable for inclusion of fullerenes. In this chapter, fullerenes inclusion into porous crystal **1** was performed. Porous crystal **1** showed inclusion of about 35 wt% of C_{60} and C_{70} and preferentially inclusion of C_{70} from mixture of C_{60} and C_{70}. Furthermore, preferentially inclusion of other higher fullerene derivatives such as C_{76}, C_{78}, C_{82}, C_{84} compared with C_{60} was also achieved.

4.2. Fullerenes inclusion into porous crystals

Inclusion of fullerene C_{60} into porous crystals was attempted by immersing of porous crystals **1** into a saturated solution of fullerenes. First chloroform, toluene and 1,2-dichlorobenzene were used as solvents for inclusion. In the chloroform case, crystal color did not change because of low solubility of C_{60} into chloroform (0.16 mg/mL).[16] When 1,2-dichlorobenzene was used, crystal color turned to pale black, which showed small amount inclusion of C_{60} into **1** because too high solubility of C_{60} into 1,2-dichlorobenzene (27 mg/mL)[16] caused stabilization of C_{60} outside the crystals than inside the crystals. Finally, when toluene (solubility of C_{60}: 2.8 mg/mL)[16] was used as solvent, crystal color turned dark black (Fig. 4.2.(a)), which showed C_{60} inclusion into **1**. From these results, toluene was selected as a suitable solvent for C_{60} inclusion. After immersion of porous crystals into saturated toluene solution at room temperature for 1 week, black crystals were decomposed using HCl aq. and extraction of C_{60} by toluene. After evaporation of solvent, weight of included C_{60} was measured and 29 wt% C_{60} was included in **1**. When inclusion time increased more than 1week, weight of included C_{60} did not change. Next, inclusion temperature was optimized by measurement of inclusion amount of C_{60} in porous crystals. At –20 ºC and 60 ºC, 21 wt% and 35 wt% of C_{60} was included, respectively. At higher temperature than 60 ºC, crystal color turned gray, which indicated decomposition of the crystals. From these results, 35 wt% inclusion of C_{60} was achieved into **1**. From the study of molecular modeling, porous crystal **1** can include C_{60} up to 64 wt% (Fig 4.2.(b)), which implied about half of the large pore was occupied by C_{60}. And 34 wt% of C_{70} was also included in porous crystals **1** in the same conditions of C_{60} inclusion.

Figure 4.2. (a) Pictures of C_{60} included in crystals **1**. (b) Model structure of C_{60} included in crystal **1** (64 wt%).

In the case of fullerene inclusion, strong host–guest interaction was not observed from the diffuse reflectance spectra (Fig. 4.3.). However, retention capacity of porous crystal **1** for fullerene guests was high, namely when fullerene included crystals were soaked into flesh toluene, included fullerenes were gradually extracted to toluene solvent and half-lives of C_{60} included crystal and C_{70} included crystal in toluene were 15 and 25 days, respectively (Fig. 4.4.). X-ray crystallographic analyses of these crystals were performed and framework of the crystal was observed. But unfortunately, included fullerenes were not observed because of low occupancy, severe disorder, shape of guest molecules and high symmetry of host crystals.

Figure 4.3. Solid state diffuse reflectance spectra of fullerene inclusion crystals (a) **1⊃(C_{60})** and (b) **1⊃(C_{70})**.

Figure 4.4. Plots of fullerene extracted from C_{60} or C_{70} included in crystals **1** vs extraction time.

4.3. Fullerenes separation by inclusion into porous crystals

As shown in the difference of half-life in toluene, better inclusion ability for larger C_{70} into porous crystal **1** was observed. Porous crystals **1** were soaked into a toluene solution of C_{60}:C_{70} = 1:1 for 1 week at room temperature and crystals were decomposed and inclusion compounds were extracted. HPLC analysis revealed that the extract contained enriched C_{70} (C_{60}:C_{70} = 21:79) (Fig. 4.5.(b)). Additionally, when fresh porous crystals **1** was soaked into a solution of C_{60}:C_{70} = 21:79 for 1 week at room temperature, moreover enriched C_{70} was extracted (C_{60}:C_{70} = 7:93) (Fig. 4.5.(c)).

Figure 4.5. HPLC chromatogram of (a) C_{60}:C_{70} = 1:1, (b) extract from crystal **1** after immersion of C_{60}:C_{70} = 1:1, (c) extract from crystal **1** after immersion of C_{60}:C_{70} = 21:79.

Furthermore, fullerenes extraction from commercially available fullerene soot produced by Krätschmer–Huffman arc method was attempted. Fullerene soot was put into a thimble filter and dipped into a toluene containing suspended porous crystals. In this system, only fullerenes were extracted to toluene and included into porous crystals. After standing for 1 week at room temperature, included compounds were analyzed in a similar way described above. Fullerene soot contained small amount of C_{70} (C_{60}:C_{70} = 90:10) but after inclusion into porous crystals **1**, C_{70} was enriched (C_{60}:C_{70} = 76:24) (Fig. 4.6.).

Figure 4.6. HPLC chromatogram of (a) simple toluene extract of fullerene soot (r.t. for 1 week) and (b) extract from porous crystal **1** after 1 week immersion in the presence of fullerene soot.

Other higher fullerenes inclusion was also performed. Porous crystals **1** were immersed into a saturated toluene solution of commercially available mixture of higher fullerene derivatives for 1 week at 60 ºC, included fullerenes in crystals were measured in a similar manner to previous one. HPLC chromatogram showed porous crystals **1** preferentially included larger fullerenes and the ratio of C_{76}, C_{78}, C_{82} and C_{84} compared with C_{60} increased by 2.6–2.7 times (Fig. 4.7.).

Figure 4.7. HPLC chromatogram of (a) initial mixture of higher fullerene derivatives and (b) extract from crystal **1** after immersion of higher fullerene derivatives solution.

4.4. TTF and C_{60} inclusion into porous crystals

Inclusion of TTF and C_{60} into porous crystal **1** was attempted to observe electron transfer from TTF to C_{60} via **1**. When the crystals **1** were immersed into a solution of mixture of TTF (20 mM) and C_{60} (saturated), 31 wt% of the guest mixture (TTF:C_{60} = 57:43 analyzed by HPLC) was included (Fig. 4.8.).

Figure 4.8. HPLC chromatogram of (a) TTF:C_{60} = 1:1 solution and (b) extract from TTF and C_{60} inclusion crystal **1**.

ESR analyses of TTF included crystals, C_{60} included crystals, TTF and C_{60} included crystals and co-crystal of TTF and C_{60} were attempted. In the case of C_{60} included crystals and co-crystal of TTF and C_{60}, no ESR signal was observed. In the case of TTF included crystals and TTF and C_{60} included crystals, ESR signals were observed but these results were not conclusive to electron transfer from TTF to C_{60} because of non-orientation organic radicals in crystals. But al least, two kinds of guest inclusion into porous crystal **1** was successfully achieved.

4.5. Summary

Inclusion of C_{60} and C_{70} in 35 wt% and 34 wt% into porous crystal **1** were achieved, respectively. Moreover, preferentially inclusion of C_{70} from 1:1 mixture of C_{60} and C_{70} and preferentially inclusion of C_{70} from commercially available fullerene soot into **1** was achieved. From fullerene soot including higher fullerenes, preferentially inclusion of higher fullerenes compared with C_{60} was also achieved. Even in strong host–guest interaction was not observed, interesting host–guest chemistry in porous crystal could be achieved in huge cages. If much amount of fullerene is included, some interesting phenomena will be observed, for example, X-ray structure of fullerenes in porous crystal, photoreaction of fullerenes in porous crystal for syntheses of new carbon materials.

4.6. Experimental sections

Contents

4.6.1. Materials and methods
4.6.2. Inclusion of fullerenes
4.6.3. Selective inclusion of higher fullerene derivatives

4.6.1. Materials and methods

Solvents and reagents were purchased from TCI Co., Ltd., WAKO Pure Chemical Industries Ltd., Sigma-Aldrich Co., and Frontier Carbon Co. All the chemicals were used without any further purification. Microscopic IR spectra were recorded on Varian DIGILAB Scimitar instrument. Analytical HPLC (high performance liquid chromatography) chromatograms were recorded on a JASCO UV-970 spectrometer equipped with a JASCO PU-980 pump. UV-Vis absorption and diffuse reflectance spectra were recorded on a SHIMADZU UV-3150 spectrometer. Diffuse reflectance spectra were recorded with an integrating sphere and were converted from reflection to absorbance by the Kubelka–Munk method. Elemental analyses were performed on a YANACO MT-6. Single crystal X-ray diffraction data were collected on a BRUKER APEX-II CCD diffractometer equipped with a focusing mirror (MoK$_a$ radiation λ = 0.71073 Å) and a N_2 generator (Japan Thermal Eng. Co., Ltd.).

4.6.2. Inclusion of fullerenes

General procedure for fullerene inclusion into porous crystals 1

As-synthesized crystals **1** (*ca.* 50 mg) were immersed into a saturated toluene solution of fullerene C_{60} or C_{70} (10 mL) at room temperature. The suspension was heated to 60 ºC. After 1 day, the supernatant was removed by decantation, another 10 mL of a saturated fullerene solution was added to the residue, and the resulting suspension was again allowed to stand at 60 ºC. After 1 week with six solution-replacement cycles, the inclusion complex was obtained as black crystals.

Inclusion crystal 1⊃(C_{60}): 39.7 mg of inclusion crystal **1**⊃(C_{60}) was decomposed by addition of HCl, and fullerene C_{60} was extracted with toluene. The combined organic phase was washed and dried over Na_2SO_4, and the solvent was removed in vacuo to give pure C_{60} (14.0 mg, 35 wt %). The purity of extracted C_{60} was confirmed by ^{1}H and ^{13}C NMR spectroscopy and HPLC analysis.

Elemental analysis: found C 73.04, H 2.52, N 12.09; calculated for $\{[(\mathbf{3})_4(Co(NCS)_2)_3]$ •1.68(C_{60})•4(toluene)•0.75(1,2-dichlorobenzene)$\}_n$; C 73.26, H 2.42, N 12.13. IR (single crystal, FLUOROLUBE, cm^{-1}): 3063(m), 2922(w), 2054(s, NCS st.), 1608(m), 1580(m), 1518(s), 1419(m), and 1373(m). UV-Vis (diffuse reflectance, $BaSO_4$, λ [nm]) 339, 605.

Inclusion crystal 1⊃(C_{70}): From 14.5 mg of inclusion complex **1**⊃(C_{70}), 4.9 mg of C_{70} was extracted by the same procedure as above.

Elemental analysis: found C 68.74, H 2.60, N 13.69; calculated for $\{[(\mathbf{3})_4(Co(NCS)_2)_3]$ •1.12(C_{70})•2.25(toluene)•1.3(1,2-dichlorobenzene)$\}_n$; C 68.99, H 2.36, N 13.41;. IR (single crystal, FLUOROLUBE, cm^{-1}): 3066(m), 2922(w), 2068(s, NCS st.), 1610(m), 1579(m), 1388(m), 1039(m), and 963(m). UV-Vis (diffuse reflectance, $BaSO_4$, λ [nm]) 388, 518, 561.

Calculations for an ideally C_{60} close-packed model

Molecular mechanics calculations were carried out using Materials Studio ver. 4.4.0.0 (Accelrys Software Inc.) The coordinate of the framework of porous crystal **1** was generated from its crystal structure (lattice range $-1 < x < 1$, $-1 < y < 1$, $-1 < z < 1$) and used for calculations without symmetry restriction. Geometry optimization (Forcite calculations) was performed by a Smart Algorithm with convergence tolerances of ultra-fine quality: Energy 2.0e–5 kcal/mol; Force 0.001 kcal/mol/Å, and displacement 1.0e–5 Å.

Extraction of fullerenes from inclusion crystals

UV-Vis spectroscopy: Inclusion crystals **1**⊃(C_{60}) or **1**⊃(C_{70}) (3.0 mg) were immersed into 3.0 mL of toluene (spectroscopic grade) in a quartz UV-cell. The resulting suspension was gently stirred at room temperature without crashing crystals. Concentration of the extracted fullerene was measured by absorption spectra of the supernatant. (detection wavelength: 540 nm for C_{60} and 600 nm for C_{70})

4.6.3. Selective inclusion of higher fullerene derivatives

From a C_{60}:C_{70} = 1:1 solution

Porous crystal **1** was immersed into a C_{60}:C_{70} = 1:1 solution (100 mL for 25 mg of the crystal, 0.10 mM each) at room temperature. The inclusion behavior was monitored by HPLC analysis after dissolving the crystal in aqueous hydrochloric acid followed by toluene extraction of fullerene contents. The ratio of C_{60}:C_{70} reached to a constant value after 1 week.

From 39.3 mg of resulting inclusion complex, 3.1 mg of a mixture of C_{60} and C_{70} (HPLC ratio 21:79) was isolated. (*i.e.* 8 wt % inclusion)

From a C_{60}:C_{70} = 21:79 solution

According to the procedure described above, porous crystal **1** was immersed into a toluene solution of fullerenes C_{60} and C_{70} (50 mL, 0.042 and 0.158 mM, respectively).

HPLC measurement conditions:

solvent: toluene/acetonitrile = 7:3

column: Develosil RPFULLERENE (Nomura Chemical Co., Ltd.; inner diameter 4.6 mm × length 250 mm)

detector: UV at 335 nm

flow rate: 1.0 mL/min

From fullerene soot

Fullerene soot (1.0 g) was placed in a thimble filter (ADVANTEC, 20 mm × 90 cm) and the filter was dipped into a suspension of porous crystal **1** (49.2 mg) in toluene (20 mL) as indicated in the below diagram. The extraction system was allowed to stand at room temperature for 1 week. The supernatant and encapsulated fullerenes were analyzed by HPLC in a similar way to the former experiment.

From a commercially available mixture of higher fullerene derivatives

A mixture of higher fullerenes was purchased from Frontier Carbon Co. (nanom gold), and used as received.

Inclusion crystal was synthesized by immersion of porous crystal **1** (100 mg) in a saturated toluene solution of higher fullerene (10 mL) at 60 ºC.

Figure S4.1. Summarized graph of the higher fullerene inclusion.

Inclusion of TTF and fullerene C_{60} in complex 1

Crystal **1** (*ca*. 100 mg) was immersed into toluene solution (3 ml) of C_{60} (saturated) and TTF (20 mM) at 60 ºC. Toluene solution of C_{60} (saturated) and TTF (20 mM) was replaced every 1 day for 1 week and TTF and C_{60} included in crystal **1** was obtained.

From 56.6 mg of inclusion crystal **1**⊃(TTF, C_{60}), 17.7 mg of TTF and C_{60} (31.3 wt%, TTF: 8.6 wt% and C_{60}: 22.7 wt% from HPLC) was extracted.

Figure S4.2. ESR spectra of (a) TTF included porous crystal and (b) TTF and C_{60} included porous crystal.

Synthesis of co-crystal of TTF and C_{60}

Chlorobenzene solution (2 mL) of TTF (32.7 mg, 0.16 mmol) and C_{60} (saturated) in vial glass (for 5 mL) was putted in hexane (3 mL) in larger vial glass (for 20 mL). After 3 d, co-crystal of TTF and C_{60} (4.4 mg, 2.7% (average of 6 batches)) as black crystal was obtained.

Elemental analysis calculated for {1.1(C_{60})•(TTF)•0.2(hexane)}; C 86.68, H 0.68; found C 86.66, H 0.83.

X-ray crystallographic analysis

Crystallographic data: $C_{33}H_2S_2$, M_r = 924.97, crystal dimensions 0.22 × 0.17 × 0.15 mm^3, triclinic, *P-1*, a = 9.824(3), b = 9.965(3), c = 10.201(6) Å, α = 94.818(4), β = 97.202(4), γ = 116.658(3), V = 874.3(6) $Å^3$, Z = 2, T = 90(2) K, r_{calcd} = 1.757 g cm^{-3}, 3278 unique reflections out of 3601 with $I > 2\sigma(I)$, 316 parameters, 2.038 < θ < 26.725°, final R factors R_1 = 0.0649 and wR_2 = 0.1701 for all data. CCDC deposit number *unpublished* data.

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CHAPTER 5

Porous Microcrystals for Evaluation of Host–Guest Interactions as Stationary Phase of HPLC Column

Abstract: Evaluation of host–guest interactions is valuable for investigation of guest inclusion. To apply the porous crystal **1** for column chromatography for evaluation of host–guest interactions, microcrystals of **1** were synthesized. The microcrystals showed almost same amount guest inclusion as single crystal **1**, which indicated microcrystals had same structure as single crystal **1**. The microcrystals packed column separated compounds depended on the electronic nature of compounds. In the case of separation of titanocene compounds, the titanocene compound included in octahedral M_6L_4 cages shown in X-ray crystallography had long retention time, which indicated separation of compounds were performed by host–guest interaction based on solution state host–guest chemistry.

5.1. Introduction

Evaluation of host–guest interactions is important for presumptions of whether guest molecules can be included or not into a host, amount of inclusion of guest molecules and consideration for practical use. Easy and conventional way for guest screening is affinity column chromatography[1-3] but there is a possibility of failure to immobilize a host and loss of the function of a host by immobilization.

Porous crystal **1** has similar guest recognition ability to host cage **2** whose strength of guest accommodation depended on the electron nature of the guest because ligand **3** interacted with the guest by charge transfer or π-π interaction. Furthermore, included guest molecules could be extracted from porous crystals **1** shown in chapter 2. These unique characters of **1** are appropriate for stationary phase of packed column of HPLC and are applicable to evaluation of host–guest interactions.

Porous crystals were applied as new materials in chromatography[4,5] for the last years. First application of MOFs as a packing material was reported in 2006[6] for the separation of alkane mixtures in gas phase. The application of porous crystals in chromatography in liquid phase firstly reported in 2007[7] for the separation of xylene isomers. Porous crystals contained columns separated several types of compounds such as branched alkane,[8] alkylaromatics,[9] enantiomers[10] and fullerenes.[11,12] But previous examples were not focused on host–guest interaction like a porous crystal **1** whose host–guest interactions based on host cage **2** in solution state.

In the consideration of application of porous crystal **1** to stationary phase of HPLC column, however, single crystal **1** is not so good for stationary phase of HPLC column from the aspects of amount and packing into a column. Single crystal **1** was obtained only about 17 mg per 1 test tube, which is insufficient for packing into a column. Shape of single crystal **1** is cubic about 0.5 mm on a side, which is too big to pack. Good sample is microcrystals of porous crystal in large scale synthesis. Actually, only a few examples of large scale synthesis of microcrystals are reported.[13,14] Some conditions are important for the large scale synthesis; (1) to obtain the substrate easily (2) mild reaction conditions (3) no troublesome by-product and work-up. Porous crystal **1** meets the requirements for large scale synthesis.

In this chapter, at the beginning, microcrystals of porous crystal **1** were synthesized for packed column by quick mixing of solution of ligand and metal salt in 50 g scale.

Then the microcrystals were packed to a column and separations of several compounds were performed with host–guest interaction. These retention times of compounds are consistent with strength of host–guest interactions.

5.2. Synthesis of porous microcrystals and guest inclusion

Addition of methanol solution of $Co(NCS)_2$ (40 mM, 100 mL) quickly to 1,2-dichlorobenzene/methanol solution of ligand **3** (4.0 mM, 500 mL) and subsequent vigorous stirring for 30 s provided 2.6 g of orange microcrystals **22** in 60% yield. On the other hand, slow addition of methanol solution of $Co(NCS)_2$ (40 mM, 5 mL) by syringe pump at a rate of 2.5 mL/h to 1,2-dichlorobenzene/methanol solution of ligand **3** (4.0 mM, 20 mL) with stirring gave pale pink powder, which was not microcrystal **22**. These results mentioned that quick mixing of solutions of ligand **3** and $Co(NCS)_2$ was very important for synthesis of microcrystal **22**.

Synthesis of microcrystal **22** in large scale was attempted. Addition of methanol solution of $Co(NCS)_2$ (40 mM, 1.8 L) quickly (< 10 s) to 1,2-dichlorobenzene /methanol solution of ligand **3** (4.0 mM, 9.0 L) and subsequent vigorous stirring for 30 s provided 52 g of orange microcrystals **22** in 62% yield. According to the powder X-ray measurement of **22**, powder X-ray pattern of **22** was consistent with that of single crystal **1** (Fig. 5.1.). From the result, porous microcrystals **22** with networked cage structure were obtained.

Figure 5.1. PXRD patterns of microcrystal **22** and single crystal **1**.

The median grain size of microcrystals **22** was measured to be X_{50} = 25 μm by laser diffraction analysis (Fig. 5.2.(a)) and was smaller than that of single crystal **1** (X_{50} = 0.52 mm) (Fig. 5.2.(b)). SEM measurement revealed the cuboctahedral shape of **22** with an average diameter of *ca.* 25 μm.

Figure 5.2. (a) Laser light-scattering size distribution analysis of microcrystals **22**. (b) Size distribution histogram of single crystals **1**, obtained from microscopic measurement of 193 crystals.

To check and compare of the guest inclusion ability, TTF and C_{60} inclusion into **22** were carried out (Fig. 5.3.). When microcrystals **22** (70 mg) were soaked into a saturated toluene solution of TTF (4 mL), the color of microcrystals rapidly turned black, which implied TTF inclusion into **22**. The diffuse reflectance spectrum of the black microcrystals was almost same as that of TTF included single crystal **1**. The inclusion TTF amount in **22** was determined to be 33 wt% by extraction experiment and

elemental analysis, which corresponded to that in single crystal **1** (30 wt%). C_{60} inclusion into **22** was performed in a similar way and 35 wt% of C_{60} inclusion into **22** was measured, which also matches the amount of C_{60} inclusion into single crystal **1** (35 wt%). It was concluded that guest inclusion ability of microcrystals **22** was comparable to that of single crystals **1**.

Figure 5.3. Pictures of of (a) as-synthesized, (b) TTF included and (c) C_{60} included microcrystal **22** and single crystal **1**.

The small size of microcrystals **22** contributed the faster inclusion of TTF than single crystals **1**. The inclusion amount of TTF into microcrystals **22** was 23 wt% by 1 min immersion, whereas only 15 wt% inclusion was measured in the case of single crystal **1** at the same time period. Although TTF inclusion reached to maximum amount for 1 h in both microcrystal and single crystal cases, particular difference of guest inclusion amount was observed in initial 1min because of large surface area of microcrystals.

5.3. HPLC column using porous microcrystals by host–guest interaction

To apply of fine grain size and guest inclusion ability of microcrystals **22**, packed column of microcrystals **22** was prepared. The separation of the mixture of three aldehyde compounds, 2-naphthylaldehyde (**23**), 5-formyl-2,2′-bithiophene (**24**), and formyltetrathiafulvalene (**25**) was performed (Fig. 5.4.). The three compounds were eluted and the retention times were 4.7, 7.9 and 17.9 min, respectively. The order of elution corresponded to the order of the strength of electron-donating character of π-conjugated rings of three compounds. These results indicate the separation of three compounds was achieved using host–guest interaction (charge transfer of π-π interactions between ligand **3** and three compounds).

Figure 5.4. HPLC chromatogram of aldehyde compounds with microcrystal **22** packed column.

To search the effect of the bulkiness of the guests, retention times of three titanocene compounds **26-28** were measured (Fig. 5.5.). In previous report,[15,16] it was reported that ruthenium complex with cyclopentadienyl (Cp) or indenyl ligands can be included in host cage **2** but pentamethylcyclopentadienyl (Cp*) ligand is too bulky to be included in host cage **2**. Cp*-titanocene **26** was eluted from microcrystals **22** packed column faster than **27** and **28** even though there are no big difference in electron-donating characters. Cp-titanocene **28** showed the longest retention time, which indicates **28** is most favorable guest for octahedral cage. The size and electronic nature of guests affects the retention times of guests.

Figure 5.5. HPLC chromatogram of titanocene compounds with microcrystal **22** packed column.

For further investigation, titanocene compounds **26-28** included in single crystals **1** analyzed by ICP measurement and X-ray crystallography. Titanocene **26-28** compounds inclusion crystals were prepared by immersion of single crystals **1** into saturated toluene solutions of titanocene compounds. As expected above, Cp-titanocene **28** showed the highest guest inclusion number by ICP measurement (7.6 molecules/cage unit). In the case of other compounds **26** and **27** was also confirmed by ICP analysis, but inclusion numbers were smaller (3.0 molecules/cage unit in the case of **26** and 3.0 molecules/cage in the case of **27**). X-ray structure analysis of Cp-titanocene **28** included in crystal **1** revealed one **28** was included in M_6L_4 cage and rather disorderd **28** located around the portals (Fig. 5.6.). Two Cp rings of **28** in the M_6L_4 cage favorably stacked onto ligand **3**, which indicated strong host–guest interaction whereas other guests were trapped weakly. In the case of **26** and **27**, X-ray analyses were not successful because of disorder and low occupancy of guest molecules due to weaker host–guest interaction compared with **28**.

Figure 5.6. X-ray structure of Cp-titanocene **28** included in crystal **1**.

5.4. Summary

Microcrystals **22** were successfully synthesized by quick mixing of ligand and metal salt solution in 50 g scale. Microcrystals **22** could include almost same amount of guest molecules as single crystal **1** and faster inclusion compared with crystal **1** because of high surface area of microcrystals. Microcrystals **22** packed column showed good separation of compounds depended on electron-donating nature of guest molecules, which indicated separation of the compounds by host–guest interaction. Unlike other porous crystals column, the host–guest chemistry of porous crystals based on solution state host cage **2** could be applied to HPLC column system.

5.5. Experimental sections

Contents

5.5.1. Materials and methods

5.5.2. Preparation of microcrystals

5.5.3. Guest inclusion experiments

5.5.4. Microcrystal based HPLC column

5.5.1. Materials and methods

Solvents and reagents were purchased from TCI Co., Ltd., WAKO Pure Chemical Industries Ltd., and Sigma-Aldrich Co. Deuterated solvents were acquired from Cambridge Isotope Laboratories, Inc. All the chemicals were used without any further purification. Bis(pentamethylcyclopentadienyl)dimethyl titanium (**26**),[17] Bis(indenyl)dimethyl titanium (**27**),[18] and Bis(cyclopentadienyl)dimethyl titanium (**28**)[19] were prepared according to the reported procedure. H and ^{13}C NMR spectra were recorded on Bruker DRX-500 (500 MHz) and AV-500 (500 MHz) spectrometers. All NMR spectral data were collected at 300 K, and chemical shifts were reported as the delta scale in parts per million (ppm) relative to an external standard tetramethylsilane (δ = 0.00 ppm for ^{1}H and ^{13}C NMR). Analytical HPLC (high performance liquid chromatography) chromatograms were recorded on a JASCO UV-970 spectrometer equipped with a JASCO PU-980 pump. UV-Vis absorption and diffuse reflectance spectra were recorded on a SHIMADZU UV-3150 spectrometer. Diffuse reflectance spectra were recorded with an integrating sphere and were converted from reflection to absorbance by the Kubelka–Munk method. Elemental analyses were performed on Exeter Analytical, Inc. CE-440F CHN/O/S Elemental Analyzer. Inductively coupled plasma (ICP) analyses were performed on a Thermo Scientific iCAP 6300. ATR-IR spectra were measured on a DIGILAB FTS-7000 instrument with SPECAC golden gate single reflection diamond ATR accessory. Laser light-scattering size distribution analyses were performed in toluene solution under sonication by Sympatec HELOS&RODOS. Scanning Electron Microscope was recorded on JEOL JSM-7000F. PXRD patterns were recorded on a RIGAKU RINT2200 diffractometer using Cu-Kα radiation (λ = 1.5406 Å) with the sample protected from dryness using a protectant (paraton-N). Single crystal X-ray diffraction data were collected on a BRUKER APEX-II CCD rotating anode diffractometer equipped with focusing mirrors with MoK_{α} (λ = 0.71073 Å) radiation under cryogenic conditions, which are controlled with a cryostat system equipped with a N_2 generator (Japan Thermal Eng. Co., Ltd.).

5.5.2. Preparation of microcrystals

Synthesis of microcrystals:

A solution of ligand **3** (630 mg, 2.0 mmol) in *o*-dichlorobenzene (400 ml) and methanol (100 ml) was placed in a 500 ml flask and stirred at 600 rpm. A methanol solution of $Co(NCS)_2$ (40 mM, 100 ml) was poured into the ligand solution within 10 s, after which orange microcrystals formed in 30 s. The suspension was further stirred for 15 min and then was allowed to stand for 15 min. Supernatant was removed by decantation and microcrystalline powder was washed three times as follows: 100 ml of *o*-dichlorobenzene was added, and the mixture was allowed to stand for 30 min, and then supernatant was removed by decantation. After the washing, the powder was isolated by filtration to give microcrystals **22** (2.63 g) in 60% yield based on ligand **3**. Elemental analysis: calculated for $([(\mathbf{3})_4(Co(NCS)_2)_3]\bullet 47(o\text{-dichlorobenzene}))_n$, C 49.78, H 2.74, N 4.76; found C 49.49, H 2.87, N 4.84. IR (ATR, cm^{-1}): 2054(s, NCS st.), 1515(s), 1456(s), 1435(m), 1373(m), 1316(m), 1127(m), 1062(m), 1033(s), 808(s), 746(s), 651(m). UV-Vis (diffuse reflectance, $BaSO_4$, λ [nm]) 367.

The reaction scale can be readily scaled up to 50 g scale. A solution of ligand **3** (11.34 g, 36.3 mmol) in *o*-dichlorobenzene (7.2 L) and methanol (1.8 L) was placed in a 10 L beaker and stirred at 1400 rpm. A methanol solution of $Co(NCS)_2$ (40 mM, 1.8 L) was poured into the beaker within 10 s, after which orange microcrystals formed in 30 s. The suspension was further stirred for 3 min and then was allowed to stand for 15 min. Supernatant was removed by decantation and microcrystalline powder was washed three times as follows: 1 L of *o*-dichlorobenzene was added, and the mixture was allowed to stand for 30 min, and then supernatant was removed by decantation. After the washing, the powder was isolated by filtration to give **22** (52.45 g) in 62% yield based on ligand **3**. Elemental analysis: calculated for $([(\mathbf{3})_4(Co(NCS)_2)_3]\bullet 51(o\text{-dichlorobenzene}))_n$, C 49.65, H 2.47, N 4.83; found C 49.76, H 2.74, N 4.61.

Figure S5.1. Comparison of ATR-IR spectra of (red) microcrystals **22** and (black) single crystals **1**.

Figure S5.2. A picture of microcrystals **22** obtained in 50 g scale synthesis.

Figure S5.3. SEM images of microcrystals **22** after C_{60} inclusion and OsO_4 stained. (a) Overview and (b) Magnified picture. To avoid evaporation of solvent in crystal, C_{60} was included in microcrystal **22**.

5.5.3. Guest inclusion experiments

General procedure for solvent exchange of microcrystals 22: As-synthesized microcrystals **22** (ca. 50 mg) was immersed into 20 mL of *o*-dichlorobenzene. The supernatant was removed by decantation and 20 mL of cosolvent (*o*-dichlorobenzene/toluene = 9/1) was added, and the mixture was allowed to stand for 1 h. This protocol was repeated, changing the ratio of *o*-dichlorobenzene and toluene in cosolvent from 7/3, 5/5, 3/7, 1/9, to 10/0 in sequence. The resulting crystal was directly used without isolation.

Inclusion complex 22•(TTF):
70 mg of solvent exchanged microcrystal **22** was immersed into 4 mL of TTF saturated toluene solution at room temperature for 60 min, which was collected by filtration to afford **22**·(TTF). The content of TTF was measured by extraction experiment as follows: 32.8 mg of inclusion microcrystal **22**·(TTF) was decomposed with 10 mL of 5 M HCl aq. The mixture was extracted three times with 10 mL of toluene. Organic layer was combined and washed with 10 mL of saturated $NaHCO_3$ aqueous solution and 10 mL of H_2O, dried over Na_2SO_4, concentrated in vacuo to afford 9.3 mg of TTF. The content of TTF was calculated to be 33.2 wt%. Elemental analysis: calculated for $([(\mathbf{3})_4(Co(NCS)_2)_3]\bullet\ 4(TTF))_n$, C 47.26, H 2.49, N 16.21; found C 47.15, H 2.09, N 16.02.; IR (ATR, cm^{-1}): 2052(s, NCS st.), 1514(s), 1456(s), 1435(m), 1373(s), 1315(m), 1126(m), 1060(m), 1034(s), 802(s), 748(s), 652(m). UV-Vis (diffuse reflectance, $BaSO_4$, λ [nm]) 396 and 615.

Figure S5.4. Comparison of ATR-IR spectra of (blue) microcrystals **22**·(TTF) and (red) single crystals **1**•(TTF).

Inclusion complex 22·C_{60}:

70 mg of solvent exchanged microcrystal **22** was immersed into 10 mL of a saturated toluene solution of C_{60} at room temperature for 7 days, which was collected by filtration to afford the guest encapsulated powder **22**•C_{60}. The content of C_{60} was measured by same procedure as TTF case. From 77.0 mg of inclusion microcrystal **22**·C_{60}, 27.0 mg of C_{60} was extracted (35.1 wt%).

Elemental analysis: calculated for $([(\mathbf{3})_4(Co(NCS)_2)_3]\bullet(C_{60}))_n$, C 49.65, H 2.47, N 4.83; found C 49.76, H 2.74, N 4.61.; IR (ATR, cm^{-1}): 2038(s, NCS st.), 1515(s), 1454(m), 1371(s), 1315(m), 1061(m), 1034(m), 802(s), 750(m), 650(s). UV-Vis (diffuse reflectance, $BaSO_4$, λ [nm]) 342 and 464.

Figure S5.5. Comparison of ATR-IR spectra of (blue) microcrystals **22**•C_{60} and (red) large single crystals **1**•C_{60}.

Comparison of inclusion rate between microcrystals 22 and single crystals 1:

30–50 mg of toluene inclusion microcrystalline powder **22** or single crystal **1** was immersed in toluene solution (4 mL) of TTF (100 mM) for 1, 3, 5, 60 min, respectively. The inclusion microcrystal was filtrated and dried under reduced pressure. The content of TTF was measured by extraction experiment as described above.

Figure S5.6. Inclusion rate of TTF with (blue) microcrystals **22** and (black) single crystals **1**.

General procedure for preparation of titanocene-inclusion single crystals:
5-20 mg of single crystals **1** were immersed in a saturated toluene solution of titanocene derivative (4 mL) for 24 h. The inclusion porous crystal **1•(26–28)** was isolated by filtration.

Inclusion complex 1•26:
ICP data (in 5 M HNO_3): concentration ratio (ppm/ppm) Co/Ti = 0.65/0.83 (corresponding to 3.0 molecules of **26** per a M_6L_4 cage); IR (single crystal, cm^{-1}) 2045 (s, NCS st.), 1773(m), 1613(m), 1577(m), 1514(s), 1465(s), 1376(s), 1318(s), 1213(s), 1165(m), 1061(s), 1014(s), 816(s), 742(m).

Inclusion complex 1•27:
ICP data (in 5 M HNO_3): concentration ratio (ppm/ppm) Co/Ti = 5.92/7.22 (corresponding to 3.0 molecules of **27** per a M_6L_4 cage); IR (single crystal, cm^{-1}) 2057(s), 2037(s), 1966(m), 1864 (m), 1731 (m), 1613 (s), 1578 (s), 1530(s), 1462(s), 1382(s), 1318(s), 1262(m), 1213(s), 1163(m), 1061(s), 1014(s), 871(s), 829(s), 729(s).

Inclusion complex 1•28:
ICP data (in 5 M HNO_3): concentration ratio (ppm/ppm) Co/Ti = 1.86/3.84 (corresponding to 7.6 molecules of **28** per a M_6L_4 cage); Elemental analysis: calculated for $\{[(\mathbf{3})_4(Co(NCS)_2)_3]\bullet\ 8(\mathbf{28})\bullet\ 6.5(toluene)\}_n$, C 65.28, H 5.69, N 10.40; found C 65.19, H 5.63, N 10.00. IR (single crystal, cm^{-1}): 2048(s, NCS st.), 1814(s), 1728(m), 1613(m), 1580(s), 1530(s), 1443(s), 1415(m), 1382(s), 1319(s), 1262(m), 1213(s), 1163(m), 1061(s), 1015(s), 871(m), 834(m) 729(m).

5.5.4. Microcrystal based HPLC column

HPLC column preparation and experiments:

HPLC columns (6010-stainless column W 1/4×4.0×150, GL Science Inc.) were packed with 2 wt% slurry of microcrystalline powder **22** in toluene using a slurry HPLC packer (6010−61200). The columns were allowed to settle with anhydrous toluene at a flow rate of 10.0 ml/min under 1300 psi for 2 h. HPLC experiments were performed at a flow rate of 1.0 mL/min with 5 μm solution of analyses, and UV adsorption was monitored.

DFT calculations

Density functional theory (DFT) calculations were carried out with Gaussian03 package using Becke's three-parameter exchange-correlation energy combined with the Lee–Yang–Parr correlation functional, B3LYP.[20-23] Generic basis sets 6-31G were used for the calculation.

Figure S5.7.. HOMO orbitals of **23**–**25** and LUMO orbital of **3**.

X-ray crystallographic data

Figure S5.8. X-ray crystal structure of inclusion complex **1•28**. (Ellipsoids are drawn at the 50% probability.)

Crystallographic data: $C_{240.02}H_{209.42}N_{60}Co_6S_{12}Ti_{7.08}$, Mr = 5023.58, crystal dimensions 0.05 x 0.05 x 0.05 mm^3, Tetragonal, space group, *I4/m, a* = 26.554(5) Å, *b* = 26.554(5) Å, *c* = 37.523(7) Å, *V* = 26458(11) $Å^3$, *T* = 90 K, *Z* = 2, r_{calcd} = 0.631 g cm^{-3}, 108572 unique reflections out of 10375 with I > 2σ(*I*), 552 parameters, 1.084 < θ < 23.815º, final *R* factors R_1 = 0.2051, wR_2 = 0.5084 for all data. CCDC deposit number 1030780.

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CHAPTER 6

Absolute Structure Determination of Guest Molecules by Chiral Porous Crystals

Abstract: Absolute structure of a chiral compound should be determined with caution and one of the trustworthy methods is combination of Bijvoet and relative method by X-ray crystallography. For the absolute structure determination of a chiral compound, novel porous crystals were designed and synthesized. Absolute structure of a chiral compound was performed from X-ray structures of a chiral compound included in porous crystals. Absolute structure of a chiral compound could be compared with chiral parts whose absolute structure was already known. Furthermore, absolute structure determinations of chiral compounds were achieved from fraction of analytical HPLC in microgram scale.

6.1. Introduction

Absolute structure determination[1] of a chiral molecule is one of the tough works for structure determination. There are two main types of methods of absolute structure determination: (1) non-empirical method such as Bijvoet method[2] using anomalous scattering of heavy atoms in X-ray crystallography, exciton chirality method in CD measurement[3] and molecular orbital calculation of CD[4] or VCD[5,6] spectra and (2) relative method, which means compared with internal standard such as comparison with X-ray structure of chiral parts whose absolute structure is already known and Mosher's method[7-9] in NMR spectroscopy. One of the most trustable methods of absolutes structure determination is combination of Bijvoet method and relative method in X-ray crystallography.

In chapter 2, X-ray structure of guest molecules could be obtained without crystallization process by inclusion of guest molecules into porous crystals. This phenomenon was used for new crystal-free X-ray analysis method what is called crystalline sponge method and reported by also other groups.[10,11] In this time, the unique technique motivated me to consideration of application to absolute structure determination. If porous crystals have chiral parts whose absolute structure is already determined, absolute structure determination of chiral guest molecules included into porous crystals can be performed by Bijvoet method and relative method compared with chiral parts in framework of porous crystals.

For the synthesis of chiral porous crystals, previously reported modular synthesis method of porous crystals[12] was used (Fig. 6.1.(a)). By complaxation of ligand **3** and ZnI_2 in the presence of triphenylene derivatives, porous crystals introduced triphenylene derivatives by stacking structure with ligand **3** could be obtained. For example, hydroxyl group, amino group, nitro group, formyl group,[13] azide group[14] and so on incorporated porous crystals were reported. Therefore triphenylene derivatives with chiral parts, that is chiral dioxolane moieties (Fig. 6.1.(b)) that can be synthesized from reported aldehyde moiety was newly designed and used for syntheses of chiral porous crystals.

Figure 6.1. (a) Modular synthesis of porous crystals. (b) Chiral triphenylene derivatives used for the synthesis of chiral porous crystals.

In this chapter, novel porous crystals with chiral parts introduced into the frameworks were synthesized. Chiral molecules included in the porous crystals and absolute structure determinations of the guests were achieved by Bijvoet and relative method. In the case of inclusion of each enantiomer, guest locations in the pores were different, which indicates the porous crystals have chiral environment. Furthermore, combination of this method with HPLC separation was achieved.

6.2. Synthesis of porous crystals with chiral environment

Chiral porous crystal (*S*,*S*)-**30** was synthesized in a similar fashion reported previously.[9] In a test tube, methanol as buffer and methanol solution of ZnI_2 were layered onto nitrobenzene/methanol solution of ligand **3** and chiral triphenyrene derivative (*S*,*S*)-**29**. After standing 1 week at room temperature, yellow needle crystals were obtained in 34% yield (Fig. 6.2.). Elemental analysis showed the composition formula of the crystals was $\{[(\mathbf{3})_2(ZnI_2)_3\bullet(S,S)\text{-}\mathbf{29}]\bullet(\text{solvent})_x\}_n$ for as-synthesized (*S*,*S*)-**30**. X-ray crystallography of as-synthesized (*S*,*S*)-**30** did not go well because of severe disorder of chiral dioxolane moieties but framework and triphenylene derived from (*S*,*S*)-**29** could be observed. For inclusion of the guest molecules, solvent replacement was performed from nitrobenzene to cyclohexane by immersing the crystals in cyclohexane for 1 week at room temperature. Solvent replacement was confirmed by elemental analysis and microscopic IR measurement.

Figure 6.2. Synthesis of porous crystal (*S*,*S*)-**30**.

After solvent exchange from nitrobenzene to cyclohexane, X-ray crystallography of the crystal (*S*,*S*)-**30** could be successfully performed and it was revealed that the crystal had quadrangle 1D channel pore (*ca.* 7×4 Å^2) and triangle 1D channel pore (*ca.* 7×5 Å^2). Introduction of triphenylene derivative (*S*,*S*)-**29** into the framework was observed in a stacking structure with ligand **3** and chrial dioxolane parts were exposed to 1D channel pores (Fig. 6.3.(a)). The space group of the structure was orthorhombic $P2_12_12_1$, which indicated this structure was chiral. Flack parameter[15] of the structure 0.057(11) is low enough for determination of absolute structure. Instead of (*S*,*S*)-**29**, enantiomer (*R*,*R*)-**29** was used in a synthesis of the porous crystal, which gave yellow needle crystals (*R*,*R*)-**30** (Fig. 6.3.(b)).

Figure 6.3. X-ray structures of (a) (*S*,*S*)-**30** and (b) (*R*,*R*)-**30**.

The origin of chirality was investigated from the X-ray structure of (*R*,*R*)-**30**. There were two non-equivalent (*R*,*R*)-**29** in crystal structure of (*R*,*R*)-**30** and short contacts between (*R*,*R*)-**29** and framework of (*R*,*R*)-**30** could be observed (Fig. 6.4.). Due to these short contacts, ligand **3** were rotated and distorted, which propagated all of the framework of (*R*,*R*)-**30**. Gathering of these partial chiralities could cause entire chirality of the crystal structure.

Figure 6.4. Locations of two non-equivalent (*R*,*R*)-**29** in (*R*,*R*)-**30** and short contacts between (*R*,*R*)-**29** and framework of (*R*,*R*)-**30** shown in red dash lines.

6.3. Absolute structure determination of guest molecules

Absolute structure determinations of chiral guest molecules were performed by inclusion of guests into (*S*,*S*)-**30** or (*R*,*R*)-**30**. Guest inclusion procedure was sane as previously reported one.[16] One crystal of (*S*,*S*)-**30** and cyclohexane (45 μL)/CH_2Cl_2 (5 μL) solution of dimethyl L-(+)-tartrate (**31**) (10 μg) were added into a vial with a cap and a needle for slow evaporation of solvent and allowed to stand for 2 d at 50 ºC. X-ray crystallography of the crystal showed guests **31** located in the pore of (*S*,*S*)-**30** (Fig. 6.5.). Absolute structure of guest **31** was determined as (2*R*,3*R*) configuration by not only Frack parameter (0.108(3)) but also comparison with chiral dioxolane parts of (*S*,*S*)-**29** whose absolute structure was already known.

Figure 6.5. X-ray structure of **31** included in (*S*,*S*)-**30**. Framework, chiral parts and guest molecules are shown in gray, green and blue, respectively. One guest molecule is shown as thermal ellipsoid (50% probability).

A pair of enantiomers inclusion into chiral porous crystals (*S*,*S*)-**30** and (*R*,*R*)-**30** revealed that these crystals had chiral environment and could distinguish chiral molecules. (–)-menthone ((–)-**32**) was included into (*S*,*S*)-**30** by immersion of a crystal (*S*,*S*)-**30** into liquid guest (–)-**32** (50 μL) for 1 week at room temperature. By X-ray analysis of the crystal, guest (–)-**32** was observed in the triangle pore and absolute structure of (–)-**32** could be determined as (1*R*,4*S*) configuration by Bijvoet method (Flack parameter = 0.088(5)) and comparison with chiral parts (Fig. 6.6.(a)). Next, (+)-menthone ((+)-**32**) was included into (*R*,*R*)-**30** in the same method as (–)-**32** inclusion into (*S*,*S*)-**30**. X-ray crystallography of the crystal showed (+)-**32** was included in pores of (*R*,*R*)-**30** and absolute structure of the guest could be determined as (1*S*,4*R*) configuration (Fig. 6.6.(b)). And comparison of the structure of (–)-**32** in (*S*,*S*)-**30** with (+)-**32** in (*R*,*R*)-**30** showed that these structures are mirror image, namely these are in an enantiomeric relationship. Then inclusion of (+)-**32** into (*S*,*S*)-**30** was attempted. X-ray crystallography of the crystal revealed that guest (+)-**32** located in the triangle pore but different location and orientation from the case of guest (–)-**32** inclusion into (*S*,*S*)-**30** (Fig. 6.6.(c)). The result indicated that structure of (–)-**32** included in (*S*,*S*)-**30** and structure of (+)-**32** included in (*S*,*S*)-**30** are in a diastereomeric relationship and could distinguish chiral molecules. Additionally, guest (–)-**32** was included into (*R*,*R*)-**30**. X-ray crystallographic analysis of (–)-**32** included into crystal (*R*,*R*)-**30** was also performed and it was revealed that structure of (–)-**32** included in (*R*,*R*)-**30** and structure of (+)-**32** included in (*S*,*S*)-**30** are mirror images. These results strongly suggested that (*S*,*S*)-**30** and (*R*,*R*)-**30** have chiral environment.

Figure 6.6. X-ray structures of (a) (–)-**32** included in (*S*,*S*)-**30**, (b) (+)-**32** included in (*R*,*R*)-**30**, (c) (+)-**32** included in (*S*,*S*)-**30**, (d) (–)-**32** included in (*R*,*R*)-**30**. Guest molecules are shown as thermal ellipsoid (50% probability).

From the X-ray structures of (–)-**32** in (*S*,*S*)-**30** and (+)-**32** in (*S*,*S*)-**30**, difference of interactions between guest molecules and frameworks were observed. In the case of (–)-**32**, short contacts and hydrogen bond between the guest and the chiral part in (*S*,*S*)-**29** were observed (Fig. 6.7.(a)), which indicated that (–)-**32** was recognized by the interactions. On the other hand, in the case of (+)-**32**, interactions between the guest and ligand **3** by CH-π interaction and iodine by hydrogen bond were observed, which meant (+)-**32** was recognized by chiral framework in (*S*,*S*)-**30**.

Figure 6.7. Interactions between guest molecules and frameworks in X-ray structures of (a) (–)-**32** included in (*S*,*S*)-**30** and (b) (+)-**32** included in (*S*,*S*)-**30**.

(*R*)-4-Chloromethyl-2,2-dimethyl-1,3-dioxolane (**34**) was included in (*S*,*S*)-**30** by immersion of the crystal into liquid guest **34** for 2 days at room temperature. X-ray crystallography showed inclusion of **34** in the quadrangle pores in the crystal (Fig. 6.8.(a)). In spite of same dioxolane structure of guest molecule as (*S*,*S*)-**29**, guest molecules **34** did not interact with (*S*,*S*)-**29** but interact with framework of the crystal by hydrogen bonds (Fig. 6.8.(b)). Guest **34** was recognized by chiral framework in (*S*,*S*)-**30**.

Figure 6.8. (a) X-ray structure of **34** included in (*S*,*S*)-**30**. Guest molecule is shown as thermal ellipsoid (50% probability). (b) Interactions between guest molecule and framework of crystal (*S*,*S*)-**30**. Hydrogen bonds are shown in red dash lines.

(*R*)-1,3-Dimethylpyrrolidine-2,5-dione (**35**) was also included in (*R*,*R*)-**30** by immersion of **35** into liquid guest **35** for 1 week at room temperature. X-ray analysis of the crystal revealed guest molecules **35** were located in triangle pores in the crystal (Fig. 6.9. (a)). In the X-ray structure, hydrogen bond and CH-π interactions were observed between guest and host framework. Interestingly, guest structure was not observed using (*S*,*S*)-**30**, which indicated not matching of the guest structure with (*S*,*S*)-**30**.

Figure 6.9. (a) X-ray structure of **35** included in (*R*,*R*)-**30**. Guest molecule is shown as thermal ellipsoid (50% probability). (b) Interactions between guest molecule and framework of crystal (*R*,*R*)-**30**.

Absolute structure determination of a chiral compound was performed using the compound in the fraction of a racemic mixture in HPLC analysis. Racemic mixture of 2-bromo-1-phenylethanol (**36**) was obtained the reduction of phenacyl bromide. In the chiral HPLC chart of compound **36** (100 μg), two fractions derived from two enantiomeric isomers were observed at 11.7 and 12.3 min, respectively (Fig. 6.10.). Each fraction could not be identified as *R* isomer or *S* isomer.

Figure 6.10. HPLC chromatogram of racemic mixture **36**.

Then first fraction was collected to the vial and solvent was evaporated. In the first trial, one crystal of (*R*,*R*)-**30**, cyclohexane (45 μL) and 1,2-dichloroethane (5 μL) were added in the vial. The vial with a cap and a needle was allowed to stand for 2 d at 50 ºC for guest inclusion. X-ray crystallography of the crystal was attempted but low occupancy (33%) guest molecules was observed in pores of the crystal, which indicated combination of crystal (*R*,*R*)-**30** and first fraction was not so good. In the second trial, (*S*,*S*)-**30** was used instead of (*R*,*R*)-**30**. X-ray crystallography of the crystal showed guests (100% occupancy) in the pores and absolute structure of the compound was determined as *R* configuration (Fig. 6.11.(a)). Additionally, second fraction was also investigated by using crystal (*R*,*R*)-**30** because of an enantiomeric relationship between *R* isomer in (*S*,*S*)-**30** and *S* isomer in (*R*,*R*)-**30**. Absolute structure of the chiral compound in the second fraction was clearly showed as *S*

configuration by X-ray analysis of guest (100% occupancy) included crystal (Fig. 6.11.(b)). Absolute structure determination by porous crystals was applied to combination with HPLC analysis.

Figure 6.11. X-ray structures of (a) first fraction included in (*S*,*S*)-**30** and (b) second fraction included in (*R*,*R*)-**30**. Guest molecules are shown as thermal ellipsoid (50% probability).

Difference of guest occupancy between first fraction in (*R*,*R*)-**30** and second fraction in (*R*,*R*)-**30** was investigated from X-ray structures. In the case of first fraction in (*R*,*R*)-**30**, only π-π stack between guest and framework was observed. On the other hand, in the case of second fraction in (*R*,*R*)-**30**, three hydrogen bonds were observed between guest and framework. Difference of these interactions between guest molecules and host framework strongly affected the occupancy of guest molecules in porous crystals.

Figure 6.12. Guest location in X-ray structures of (a) first fraction included in (*R*,*R*)-**30** and (b) second fraction included in (*R*,*R*)-**30**.

Finally, guest inclusion from racemic mixture into (*S*,*S*)-**30** was attempted. One crystal of (*S*,*S*)-**30**, 45 μL of cyclohexane and 5 μL of 1,2-dichloroethane solution of **35** (1 mg/1 mL) were added in a micro vial with a needle. The vial was allowed to stand for 2 days at 50 ºC and solvent was slowly evaporated. X-ray crystallographic analysis showed *R* isomers of **36** were included in (*S*,*S*)-**30**. This result was matched with the result of inclusion of *R* isomer in 100% occupancy into (*S*,*S*)-**30**. And the result indicates that there is a possibility of preferentially inclusion of an enantiomer from racemic mixture or a minor enantiomer in high enantiomeric excess mixture. Absolute structure determination by the chiral porous crystals should be performed from enantiomeric pure sample.

6.4. Summary

Two kinds of porous crystals with chiral environment by introduction of chiral triphenylene derivatives were successfully synthesized. Subsequently inclusion of chiral guest molecules were performed and absolute structure determination of the guest molecules were achieved with Bijvoet method and relative method compared with chiral parts introduced into the framework. Enantiomers inclusion into the porous crystals revealed the porous crystals had chiral environment in the pores. Additionally, absolute structure determination of chiral compounds from HPLC fractions in microgram scale. The porous crystals have possibility to be one of the most reliable methods of absolute structure determination.

6.5. Experimental sections

Contents

6.5.1. Materials and methods

6.5.2. Synthesis and characterization of chiral porous crystals and guest inclusion

6.5.3. Chiral guest inclusion into chiral porous crystals

6.5.4. Combination with chiral HPLC

6.5.1. Materials and methods

^{1}H and ^{13}C NMR spectra were recorded on Bruker DRX-500 (500 MHz) NMR spectrometer or Bruker AVANCE 500 (500 MHz) NMR spectrometer with CP-TCI cryoprobe. All NMR spectral data were collected at 300 K and the chemical shift are reported in parts per million (ppm) relative to an internal standard tetramethylsilane (δ = 0.00 ppm for ^{1}H and ^{13}C NMR) for $CDCl_3$. IR measurements for organic compounds were carried out using a JASCO FT/IR-6700 instrument. The single crystal microscopic FT-IR spectra were recorded on a Varian DIGILAB Scimitar instrument. GC-MS spectra were obtained on an Agilent 5973 inert Mass selective Detector equipped with a 6890N Network GC system and an EI source. Elemental analyses were performed on a YANACO MT-6. Single crystal X-ray diffraction data were made using a BRUKER APEX-II/CCD diffract meter equipped with a focusing mirror (MoK_α radiation λ= 0.71073 Å) and a N_2 generator (Japan Thermal Eng. Co., Ltd.) or Rigaku XtaLAB P200 diffractometer equipped with a PILATUS200K detector using multi-layer mirror (MoK_α radiation λ= 0.71073 Å). Analytical HPLC (high performance liquid chromatography) chromatograms were recorded on a JASCO MD-2018 photodiode array detecter equipped with a JASCO PU-2089 pump, JASCO AS-2059 sampler, JASCO CO-2060 column thermostat and ADVANTEC CHF 122SC fraction collecter.

Solvents and reagents were purchased from TCI Co., Ltd., WAKO Pure Chemical Industries Ltd., and Sigma-Aldrich Co. Deuterated solvents were acquired from Cambridge Isotope Laboratories, Inc. All the chemicals were used without any further purification. (*R*)-1,3-Dimethylpyrrolidine-2,5-dione[17] and 2-bromo-1-phenylethanol[18] were prepared according to the reported procedure. Screw-top microvial (Osaka chemical, cat. No. 11090620), screw cap with septum seal (Osaka chemincal, cat. No. 53951-09FB) and syringe needle (TERUMO, cat. No. NN-2116R) were used for guest inclusion into porous crystals.

6.5.2. Synthesis and characterization of chiral porous crystals and guest inclusion

Preparation of (4*S*,5*S*)-4,5-dimethyl-2-(triphenylen-2-yl)-1,3-dioxolane (*S*,*S*)-29

To a solution of triphenylene-2-carbaldehyde (1.00 g, 3.90 mmol) and (*S*,*S*)-(+)-2,3-butanediol (0.5 mL, 5.5 mmol) in toluene (25 mL) was added *p*-toluenesulfonic acid monohydrate (10 mg, 0.058 mmol). The resulting solution was heated under reflux with Dean-Stark trap for overnight. The reaction mixture solution was washed with saturated aqueous solution of $NaHCO_3$, and brine and dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by chromatography on silicagel (eluent: CH_2Cl_2/*n*-hexane = 1/1, R_f = 0.32) to afford the title compound (1.07 g, 84%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ 8.76 (s, 1H, triphenylene-H), 8.71-8.65 (m, 5H, triphenylene-*H*), 7.79 (dd, *J* = 8.5 Hz, 1.5 Hz, 1H, triphenylene-*H*), 7.68-7.66 (m, 4H, triphenylene-*H*), 6.22 (s, 1H, H^a), 3.96-3.89 (m 2H, H^b), 1.46 (d, *J* = 6.0 Hz, 3H, H^c), 1.40 (d, *J* = 6.0 Hz, 3H, $H^{c'}$). ^{13}C NMR (125 MHz, $CDCl_3$, 300 K): δ 137.4 (Cq), 130.4 (Cq), 130.0 (Cq), 129.9 (Cq), 129.8 (Cq), 129.7 (Cq), 129.6 (Cq), 127.4 (2×CH), 127.2 (2×CH), 125.2 (CH), 123.6 (CH), 123.5 (2×CH), 123.3 (2×CH), 121.5 (CH), 102.8 (CH^a), 80.6 (CH^b), 78.9 (CH^b), 17.3 (CH_3^c), 17.1 ($CH_3^{c'}$). IR (ATR, cm^{-1}): 1426(m), 1375(m), 1084(s), 752(s), 721(s). Elemental analysis (%); Calculated for $C_{23}H_{20}O_2$; C 84.12, H 6.14. found C 84.01, H 6.18. MS (EI-MS) *m/z*, calculated for $C_{23}H_{20}O_2$, 328.15, found 328 $[M]^+$.

Preparation of (4*R*,5*R*)-4,5-dimethyl-2-(triphenylen-2-yl)-1,3-dioxolane (*R*,*R*)-29

The procedure is the same as the above. Starting from triphenylene-2-carbaldehyde (1.00 g, 3.90 mmol) and (*R*,*R*)-(–)-2,3-butanediol (0.5 mL, 5.5 mmol) to get the title compound (1.01 g, 79%). ^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ 8.76 (s, 1H, triphenylene-H), 8.71-8.65 (m, 5H, triphenylene-*H*), 7.79 (dd, *J* = 8.5 Hz, 1.5 Hz, 1H, triphenylene-*H*), 7.68-7.66 (m, 4H, triphenylene-*H*), 6.22 (s, 1H, H^a), 3.96-3.89 (m 2H, H^b), 1.47 (d, *J* = 6.0 Hz, 3H, H^c), 1.41 (d, *J* = 6.0 Hz, 3H, $H^{c'}$). ^{13}C NMR (125 MHz,

$CDCl_3$, 300 K): δ 137.5 (Cq), 130.4 (Cq), 130.0 (Cq), 129.9 (Cq), 129.8 (Cq), 129.7 (Cq), 129.6 (Cq), 127.4 (2×CH), 127.3 (2×CH), 125.2 (CH), 123.7 (CH), 123.6 (2×CH), 123.4 (CH), 123.3 (CH), 121.6 (CH), 102.8 (CH^a), 80.6 (CH^b), 78.9 (CH^b), 17.3 (CH_3^c), 17.1 ($CH_3^{c'}$). IR (ATR, cm^{-1}): 1426(m), 1375(m), 1085(s), 752(s), 721(s). Elemental analysis (%); Calculated for $C_{23}H_{20}O_2$; C 84.12, H 6.14. found C 84.29, H 6.39. MS (EI-MS) *m/z*, calculated for $C_{23}H_{20}O_2$, 328.15, found 328 $[M]^+$.

Synthesis of (*S*,*S*) chiral porous crystal

On a solution of 2,4,6-tri(4-pyridyl)-1,3,5-triazine **3** (6.3 mg, 0.02 mmol) and (4*S*,5*S*)-4,5-dimethyl-2-(triphenylen-2-yl)-1,3-dioxolane (32.8 mg, 0.1 mmol) in a mixture of nitrobenzene (4 mL) and methanol (1 mL), methanol (0.5 mL) was layered as buffer layer and then solution of ZnI_2 (9.6 mg, 0.03 mmol) in methanol (0.5 mL). The solution was allowed to stand for 1 week. Resulting yellow crystals were collected and washed with nitrobenzene to give the complex in 34% (8.7 mg, averaged of 5 batches) based on ligand **3**.

IR (single crystal, FLUOROLUBE, cm^{-1}): 3069(m), 2972(m), 2861(m), 1620(s), 1577(s), 1512(s), 1478(m), 1376(s), 1345(s, NO, st.). Elemental analysis (%); Calculated for $\{[(\mathbf{3})_2(ZnI_2)_3\bullet(S,S)\text{-}\mathbf{29}]\bullet 5(PhNO_2)(MeOH)\}_n$; C 42.25, H 2.88, N 9.31. found C 42.10 H 2.78, N 9.38.

Synthesis of (*R*,*R*) chiral porous crystal

The procedure is the same as the above. Starting from 2,4,6-tri(4-pyridyl)-1,3,5-triazine **3** (6.3 mg, 0.02 mmol), (4*R*,5*R*)-4,5-dimethyl-2-(triphenylen-2-yl)-1,3-dioxolane (32.8 mg, 0.1 mmol) and ZnI_2 (9.6 mg, 0.03 mmol) to give get the complex in 37% (9.0 mg, averaged of 5 batches).

IR (single crystal, FLUOROLUBE, cm^{-1}): 3063(m), 2974(m), 2870(m), 1616(s), 1578(s), 1523(s), 1423(m), 1375(s), 1348(s NO, st.). Elemental analysis (%); Calculated for $\{[(\mathbf{3})_2(ZnI_2)_3\bullet(R,R)\text{-}\mathbf{29}]\bullet 4(PhNO_2)(MeOH)\}_n$; C 41.43, H 2.81, N 9.20. found C 41.19 H 2.78, N 9.03.

Solvent replacement of the chiral crystal

The initial nitrobenzene guest was exchanged for cyclohexane in advance of guest inclusion by immersing the crystals in cyclohexane (*ca*. 10 mg/10 ml) at room temperature for 1 week.

Cyclohexane included in (*S*,*S*) chiral crystal

IR (single crystal, FLUOROLUBE, cm^{-1}): 3055(m), 2924(s), 2849(s), 1616(s), 1576(s), 1508(s), 1448(m), 1423(m), 1375(s). Elemental analysis (%); Calculated for $\{[(\mathbf{3})_2(ZnI_2)_3\bullet(S,S)\text{-}\mathbf{29}]\bullet 2.5(\text{cyclohexane})\}_n$; C 41.90, H 3.52, N 7.92. found C 41.68 H 3.63, N 7.90. Crystallographic data: $C_{145.69}H_{143.38}I_{12}N_{24}O_4Zn_6$, M_r = 4209.54, crystal dimensions 0.15 × 0.10 × 0.10 mm^3, Orthorhombic, space group, $P2_12_12_1$, a = 13.7047(6) Å, b = 27.5239(9) Å, c = 45.7839(19) Å, V = 17270.0(12) $Å^3$, T = 93 K, Z = 4, r_{calcd} = 1.619 g cm^{-3}, 36814 unique reflections out of 119360 with $I > 2\sigma(I)$, 1372 parameters, 3.006 < θ < 27.478°, final R factors R_1 = 0.0581 and wR_2 = 0.1785 for all data. CCDC deposit number *unpublished data*.

Cyclohexane included in (*R*,*R*) chiral crystal

IR (single crystal, FLUOROLUBE, cm^{-1}): 3053(m), 2927(s), 2850(s), 1616(s), 1577(s), 1514(s), 1448(m), 1424(m), 1374(s). Elemental analysis (%); Calculated for $\{[(\mathbf{3})_2(ZnI_2)_3\bullet(R,R)\text{-}\mathbf{29}]\bullet 2.8(\text{cyclohexane})\}_n$; C 42.42, H 3.64, N 7.83. found C 42.20 H 3.70, N 7.59. Crystallographic data: $C_{123.62}H_{98.25}I_{12}N_{24}O_4Zn_6$, M_r = 3899.02, crystal dimensions 0.09 × 0.07 × 0.06 mm^3, Orthorhombic, space group, $P2_12_12_1$, a = 13.732 (3) Å, b = 27.786(7) Å, c = 45.873(11) Å, V = 17504(7) $Å^3$, T = 90 K, Z = 4, r_{calcd} = 1.480 g cm^{-3}, 35828 unique reflections out of 191530 with $I > 2\sigma(I)$, 1276 parameters, 0.857 < θ < 26.397°, final R factors R_1 = 0.0770 and wR_2 = 0.2420 for all data. CCDC deposit number *unpublished data*.

6.5.3. Chiral guest inclusion into chiral porous crystals

General procedure of guest inclusion into chiral crystal

Liquid guest (50 μL) was added to one chiral porous crystal (*S*,*S* or *R*,*R*) in a micro vial. After standing for 1 week at room temperature, the crystal was picked using a protectant and mounted onto X-ray diffractmeter. After measurement of single crystal X-ray diffraction, same crystal subsequently used for microscopic IR measurement. For elemental analysis, 1 mL liquid guest and c.a. 10 mg crystals were used.

Dimethyl (L)-(+)-tartrate included in (*S*,*S*) chiral crystal

Dimethyl (L)-(+)-tartrate (10 μg), cyclohexane (45 μL) and dichloromethane (5 μL) was added to one (*S*,*S*) chiral porous crystal in a micro vial with a needle. After standing for 2 days at 50 ºC for slow evaporation of solvent, the crystal was picked using a protectant and mounted onto X-ray diffractmeter. After measurement of single crystal X-ray diffraction, same crystal subsequently used for microscopic IR measurement. For elemental analysis, 1 mg guest and c.a. 10 mg crystals were used.

IR (single crystal, FLUOROLUBE, cm^{-1}): 3520(m), 2926(m), 1746(s, C=O, st.), 1618(s), 1578(s), 1518(s), 1424(s), 1376(s). Calculated for $\{[(\mathbf{3})_2(ZnI_2)_3\bullet(S,S)\text{-}\mathbf{29}]\bullet 2.5(\text{dimethyl (L)-(+)-tartrate})\bullet 0.8(\text{cyclohexane})\}_n$; C 39.06, H 3.27, N 6.94. found C 38.83, H 3.41, N 7.04. Crystallographic data: $C_{148}H_{138}I_{12}N_{24}O_{34}Zn_6$, M_r = 4711.84, crystal dimensions 0.09 × 0.07 × 0.07 mm^3, Orthorhombic, space group, $P2_12_12_1$, a = 13.9105(13) Å, b = 28.652(3) Å, c = 44.885(4) Å, V = 17889(3) $Å^3$, T = 90 K, Z = 4, r_{calcd} = 1.749 g cm^{-3}, 42426 unique reflections out of 211409 with $I > 2\sigma(I)$, 2073 parameters, $0.843 < \theta < 27.941°$, final R factors R_1 = 0.0652 and wR_2 = 0.2237 for all data. CCDC deposit number *unpublished data*.

(–)-menthone included in (*S*,*S*) chiral crystal

(–)-menthone (50 μL) was added to one (*S*,*S*) chiral porous crystal in a micro vial. After standing for 1 week at room temperature, the crystal was picked using a protectant and mounted onto X-ray diffractmeter. After measurement of single crystal X-ray

diffraction, same crystal subsequently used for microscopic IR measurement. For elemental analysis, 1 mL liquid guest and c.a. 10 mg crystals were used.

IR (single crystal, FLUOROLUBE, cm^{-1}): 3054(m), 2955(m), 2927(m), 2850(m), 1706(s, C=O, st.), 1616(s), 1578(s), 1516(s), 1449(s), 1375(s), 1313(m). Elemental analysis (%); Calculated for $\{[(\mathbf{3})_2(ZnI_2)_3\bullet(S,S)\text{-}\mathbf{29}]\bullet 3.7((-)\text{-menthone})\}_n$; C 46.47, H 4.49, N 6.77. found C 46.20 H 4.71, N 6.91. Crystallographic data: $C_{145}H_{136.60}I_{12}N_{24}O_{6.70}Zn_6$, M_r = 4237.59, crystal dimensions 0.20 × 0.10 × 0.07 mm^3, Orthorhombic, space group, $P2_12_12_1$, a = 13.9817(12) Å, b = 28.988(2) Å, c = 44.391(4) Å, V = 17992(3) $Å^3$, T = 90 K, Z = 4, r_{calcd} = 1.581 g cm^{-3}, 30817 unique reflections out of 169636 with $I > 2\sigma(I)$, 1780 parameters, 1.155 < θ < 24.754°, final R factors R_1 = 0.0714 and wR_2 = 0.1962 for all data. CCDC deposit number *unpublished data*.

(+)-menthone included in (*R*,*R*) chiral crystal

The guest inclusion, X-ray measurement, IR measurement and elemental analysis procedure is the same as the above. (+)-menthone (50 μL) was added to one (*R*,*R*) chiral porous crystal in a micro vial for 1week at room temperature.

IR (single crystal, FLUOROLUBE, cm^{-1}): 3053(m), 2955(m), 2927(m), 2871(m), 1702(s, C=O, st.), 1614(s), 1577(s), 1513(s), 1424(s), 1373(s), 1312(m). Calculated for $\{[(\mathbf{3})_2(ZnI_2)_3\bullet(R,R)\text{-}\mathbf{29}]\bullet 4.5((+)\text{-menthone})\}_n$; C 47.60, H 4.75, N 6.53. found C 47.36 H 5.05, N 6.34. Crystallographic data: $C_{123}H_{97}I_{12}N_{24}O_{4.5}Zn_6$, M_r = 3898.26, crystal dimensions 0.20 × 0.10 × 0.07 mm^3, Orthorhombic, space group, $P2_12_12_1$, a = 13.960(3) Å, b = 28.823(6) Å, c = 44.262(8) Å, V = 17810(6) $Å^3$, T = 90 K, Z = 4, r_{calcd} = 1.454 g cm^{-3}, 36566 unique reflections out of 189819 with $I > 2\sigma(I)$, 1577 parameters, 1.160 < θ < 26.415°, final R factors R_1 = 0.0849 and wR_2 = 0.2528 for all data. CCDC deposit number *unpublished data*.

(+)-menthone included in (*S*,*S*) chiral crystal

The guest inclusion, X-ray measurement, IR measurement and elemental analysis procedure is the same as the above. (+)-menthone (50 μL) was added to one (*S*,*S*)

chiral porous crystal in a micro vial for 1week at room temperature.

IR (single crystal, FLUOROLUBE, cm^{-1}): 3053(m), 2953(m), 2926(m), 2868(m), 1702(s, C=O, st.), 1619(s), 1577(s), 1516(s), 1423(s), 1376(s), 1314(m). Calculated for $\{[(\mathbf{3})_2(ZnI_2)_3\bullet(S,S)\text{-}\mathbf{29}]\bullet 3.5((+)\text{-menthone})\}_n$; C 46.07, H 4.40, N 6.86. found C 45.88 H 4.48, N 6.77. Crystallographic data: $C_{123}H_{97}I_{12}N_{24}O_{4.5}Zn_6$, M_r = 3898.26, crystal dimensions 0.20 × 0.10 × 0.07 mm^3, Orthorhombic, space group, $P2_12_12_1$, a = 13.9571(17) Å, b = 28.803 (4) Å, c = 44.464(6) Å, V = 17875(4) $Å^3$, T = 90 K, Z = 4, r_{calcd} = 1.449 g cm^{-3}, 36668 unique reflections out of 191674 with $I > 2\sigma(I)$, 1780 parameters, 1.414 < θ < 26.406°, final R factors R_1 = 0.0762 and wR_2 = 0.2467 for all data. CCDC deposit number *unpublished data*.

(–)-menthone included in (*R*,*R*) chiral crystal

The guest inclusion, X-ray measurement, IR measurement and elemental analysis procedure is the same as the above. (–)-menthone (50 μL) was added to one (*R*,*R*) chiral porous crystal in a micro vial for 1week at room temperature.

IR (single crystal, FLUOROLUBE, cm^{-1}): 3055(m), 2957(m), 2928(m), 2869(m), 1703(s, C=O, st.), 1616(s), 1577(s), 1503(s), 1423(s), 1372(s), 1313(m). Elemental analysis (%); Calculated for $\{[(\mathbf{3})_2(ZnI_2)_3\bullet(R,R)\text{-}\mathbf{29}]\bullet 3((-)\text{-menthone})\}_n$; C 45.04, H 4.16, N 7.08. found C 44.82 H 4.32, N 6.80. Crystallographic data: $C_{123}H_{97}I_{12}N_{24}O_{4.5}Zn_6$, M_r = 3898.26, crystal dimensions 0.13 × 0.10 × 0.07 mm^3, Orthorhombic, space group, $P2_12_12_1$, a = 13.9507(16) Å, b = 28.809 (3) Å, c = 44.682(5) Å, V = 17958(4) $Å^3$, T = 90 K, Z = 4, r_{calcd} = 1.187 g cm^{-3}, 30621 unique reflections out of 168766 with $I > 2\sigma(I)$, 1576 parameters, 1.153 < θ < 24.710°, final R factors R_1 = 0.0740 and wR_2 = 0.2328 for all data. CCDC deposit number *unpublished data*.

(*R*)-4-Chloromethyl-2,2-dimethyl-1,3-dioxolane included in (*S*,*S*) chiral crystal

(*R*)-4-Chloromethyl-2,2-dimethyl-1,3-dioxolane (50 μL) was added to one (*S*,*S*) chiral porous crystal in a micro vial. After standing for 2 days at room temperature, the crystal was picked using a protectant and mounted onto X-ray diffractmeter. After

measurement of single crystal X-ray diffraction, same crystal subsequently used for microscopic IR measurement.

IR (single crystal, FLUOROLUBE, cm^{-1}): 3063(m), 2933(m), 1643(m), 1612(m), 1577(m), 1509(s), 1425(m), 1373(s). Crystallographic data: $C_{124}H_{99}ClI_{12}N_{24}O_6Zn_6$, M_r = 3971.74, crystal dimensions 0.15 × 0.13 × 0.12 mm^3, Orthorhombic, space group, $P2_12_12_1$, a = 13.9417(11) Å, b = 28.646(2) Å, c = 44.615(4) Å, V = 17818(2) $Å^3$, T = 90 K, Z = 4, r_{calcd} = 1.481 g cm^{-3}, 36555 unique reflections out of 191225 with $I > 2\sigma(I)$, 1639 parameters, 1.157 < θ < 26.413°, final R factors R_1 = 0.0706 and wR_2 = 0.2318 for all data. CCDC deposit number *unpublished data*.

(*R*)-1,3-Dimethylpyrrolidine-2,5-dione included in (*R*,*R*) chiral crystal

(*R*)- 1,3-Dimethylpyrrolidine-2,5-dione (50 μL) was added to one (*R*,*R*) chiral porous crystal in a micro vial. After standing for 1 week at room temperature, the crystal was picked using a protectant and mounted onto X-ray diffractmeter. After measurement of single crystal X-ray diffraction, same crystal subsequently used for microscopic IR measurement.

IR (single crystal, FLUOROLUBE, cm^{-1}): 3059(m), 2973(m), 2931(m) 1775(s, C=O, st.), 1694(s, C=O, st.), 1618(s), 1578(m), 1513(s), 1426(m), 1378(s). Crystallographic data: $C_{121.60}H_{93.40}I_{12}N_{24}O_6Zn_6$, M_r = 3897.42, crystal dimensions 0.15 × 0.10 × 0.10 mm^3, Orthorhombic, space group, $P2_12_12_1$, a = 13.989(2) Å, b = 28.651(4) Å, c = 44.397(6) Å, V = 17795(4) $Å^3$, T = 90 K, Z = 4, r_{calcd} = 1.455 g cm^{-3}, 33889 unique reflections out of 179789 with $I > 2\sigma(I)$, 1559 parameters, 1.494 < θ < 25.731°, final R factors R_1 = 0.0690 and wR_2 = 0.2302 for all data. CCDC deposit number *unpublished data*.

6.5.4. Combination with chiral HPLC

The racemic mixture of 2-bromo-1-phenylethanol was dissolved in *n*-hexane/CH_2Cl_2 = 9/1 (100 μg/20 μL) and separated by analytical HPLC. Two fractions eluted at 11.7 and 12.3 min were collected in a separate vial. After evaporation of the solvent in vacuo, one chiral porous crystal was added into the vial with cyclohexane (45 μL) and 1,2-dichloroethane (5 μL). Incubation of the samples was performed at 50 ºC for 1 week.

HPLC measurement conditions:
solvent: *n*-hexane/ethanol = 99:1
column: CHIRALPAK IC (Nomura Chemical Co., Ltd.; inner diameter 4.6 mm × length 250 mm)
detector: UV at 254 nm
flow rate: 1.0 mL/min

(*R*)-2-bromo-1-phenylethanol (1st fraction) included in (*S*,*S*) chiral crystal

IR (single crystal, FLUOROLUBE, cm^{-1}): 3481(m, OH, st.), 3056(m), 2968(m), 2927(m), 1619(s), 1576(s), 1522(s), 1508(s), 1374(s). Crystallographic data: $C_{137.32}H_{109.74}Br_{2.42}I_{12}N_{24}O_{6.42}Zn_6$, M_r =4306.75, crystal dimensions 0.12 × 0.12 × 0.08 mm^3, Orthorhombic, space group, $P2_12_12_1$, a = 13.9239(19) Å, b = 28.645(4) Å, c = 44.185(6) Å, V = 17623(4) $Å^3$, T = 90 K, Z = 4, r_{calcd} = 1.623 g cm^{-3}, 35962 unique reflections out of 129151 with $I > 2\sigma(I)$, 1748 parameters, 3.011 < θ < 27.465°, final R factors R_1 = 0.0730 and wR_2 = 0.2361 for all data. CCDC deposit number *unpublished data*.

(*S*)-2-bromo-1-phenylethanol (2nd fraction) included in (*R*,*R*) chiral crystal

IR (single crystal, FLUOROLUBE, cm^{-1}): 3481(m, OH, st.), 3055(m), 2970(m), 2926(m), 1619(s), 1577(s), 1521(s), 1508(s), 1375(s). Crystallographic data: $C_{129.82}H_{101.30}Br_{1.48}I_{12}N_{24}O_{5.48}Zn_6$, M_r =4118.23, crystal dimensions 0.10 × 0.08 × 0.08

mm^3, Orthorhombic, space group, $P2_12_12_1$, a = 13.8958(3) Å, b = 28.6671(7) Å, c = 43.9979(11) Å, V = 17526.7(7) $Å^3$, T = 90 K, Z = 4, r_{calcd} = 1.561 g cm^{-3}, 38762 unique reflections out of 202157 with $I > 2\sigma(I)$, 1748 parameters, $3.017 < \theta < 27.586°$, final R factors R_1 = 0.0832 and wR_2 = 0.2755 for all data. CCDC deposit number *unpublished data*.

Inclusion from racemic mixture of 2-bromo-1-phenylethanol into (*S*,*S*) chiral crystal

2-bromo-1-phenylethanol (10 μg), cyclohexane (45 μL) and 1,2-dichloroethane (5 μL) was added to one (*S*,*S*) chiral porous crystal in a micro vial with a needle. After standing for 2 days at 50 ºC for slow evaporation of solvent, the crystal was picked using a protectant and mounted onto X-ray diffractmeter. After measurement of single crystal X-ray diffraction, same crystal subsequently used for microscopic IR measurement.

IR (single crystal, FLUOROLUBE, cm^{-1}): 3474(m, OH, st.), 3061(m), 2971(m), 2930(m), 1619(s), 1576(s), 1521(s), 1507(s), 1374(s). Crystallographic data: $C_{130.18}H_{101.70}Br_{1.52}I_{12}N_{24}O_{5.52}Zn_6$, M_r =4127.13, crystal dimensions 0.08 × 0.07 × 0.07 mm^3, Orthorhombic, space group, $P2_12_12_1$, a = 13.908(3) Å, b = 28.821(5) Å, c = 44.102(8) Å, V = 17678(6) $Å^3$, T = 90 K, Z = 4, r_{calcd} = 1.551 g cm^{-3}, 36087 unique reflections out of 193292 with $I > 2\sigma(I)$, 1659 parameters, 0.844 < θ < 26.379º, final R factors R_1 = 0.0890 and wR_2 = 0.2792 for all data. CCDC deposit number *unpublished data*.

Figure S6.1. X-ray structures of guest in (*R*,*R*)-**30** from racemic mixture of **36**. Guest molecule is shown as thermal ellipsoid (50% probability).

6.6. References

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CHAPTER 7

Summary and Perspective

In this doctorial thesis, host–guest chemistry was studied in porous crystals based on solution state host–guest chemistry. Rich chemistry was developed in porous crystals like solution state host–guest chemistry.

In the chapter 2, novel porous crystal whose structure is three-dimensional array of octahedral M_6L_4 cage was synthesized. Electron-rich guest molecules were included strongly due to the electron-deficient ligand. X-ray structure of guest molecules included in porous crystal revealed the porous crystal had similar guest inclusion ability to solution host cage molecule. Furthermore, this guest inclusion was applied to obtain X-ray structures of liquid molecules.

In the chapter 3, chemical reactions were carried out in porous crystals. Bimolecular reaction in porous crystals was achieved without leaching out of the first substrate by strong inclusion of the first substrate in the octahedral M_6L_4 cages. Furthermore, strong host–guest interaction caused oxidation reaction of guest molecules by molecular oxygen in porous crystals. Moreover, reactions of unique four-membered ring molecule and oxidation reaction of water sensitive bisketene were performed in both solution state octahedral cage host and porous crystals. In porous crystal, the reactions proceeded efficiently because of avoidance of water.

In the chapter 4, fullerenes inclusion into huge pores was attempted. Immersion of porous crystals into a toluene solution of C_{60} caused color change of the crystals from orange to black and 35 wt% inclusion of C_{60} was achieved. Separation of C_{70} from solution mixture of C_{60} and C_{70} was also performed by inclusion of fullerenes into porous crystals.

In the chapter 5, the microcrystal of the porous crystal were synthesized for

evaluation of host–guest interaction as stationary phase of HPLC column. The microcrystals showed same guest inclusion ability as single crystals. The microcrystals packed column showed separation of guest molecules based on host–guest interaction between electron-rich compounds and octahedral cages.

In the chapter 6, synthesis of chiral porous crystals and absolute structure determination of guest molecules by relative method were achieved. Complexation of triazine ligand and ZnI_2 in the presence of chiral triphenylene gave porous crystals with chiral parts in the framework. Inclusion of chiral molecules into chiral porous crystals and absolute structure determination of chiral guest by comparison with chiral part whose absolute structure was already known were carried out.

Through these chapters, host–guest chemistry in solution could be transferred to crystalline state. Not only inclusion of guests into porous crystals but also chemical reactions in porous crystals, application to HPLC column and absolute structure determination were achieved. There is a possibility for porous crystals to be used as solid materials or heterogeneous catalysts by strong inclusion of homogeneous catalysts. Moreover, there is another possibility that is application to analytical method for X-ray crystallography. In this thesis chapter 2, X-ray structures of liquid molecules were obtained but X-ray structure of not only liquid molecules but also tiny amount molecules were obtained by inclusion of porous crystals.[1,2] Valuable usage of porous crystals were discovered, however, kinds of porous crystals are limited and too high nucleophilicity molecules, hydrophilic molecules and too large molecules cannot be analyzed by porous crystals used now. By solution of these problems, this application of porous crystals will be really usable method using the feature of porous 'crystals'. Actually, new porous crystals are now investigating for large guest molecules and hydrophilic guest molecules.

The chemistry of porous crystals about not only guest inclusion and chemical reactions in crystals but also newborn X-ray crystallographic method gave new aspects in chemistry. In all chemistry in this thesis, host–guest interactions based on weak interactions showed very important work. Rich and interesting chemistry will be discovered by the valuable interactions.

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List of Publications

1. "Networked Molecular Cages as Crystalline Sponges for Fullerenes and Other Guests"
   Yasuhide Inokuma, Tatsuhiko Arai, Makoto Fujita
   Nat. Chem. **2010**, *2*, 780–783.
   [Chapter 2,4]

2. "Bimolecular Reaction via the Successful Introduction of Two Substrates into the Crystals of Networked Molecular Cages"
   Yasuhide Inokuma, Nodoka Kojima, Tatsuhiko Arai, Makoto Fujita
   J. Am. Chem. Soc. **2011**, *133*, 19691–19693.
   [Chapter 3]

3. "Networked-Cage Microcrystals for Evaluation of Host-Guest Interactions"
   Shohei Matsuzaki, Tatsuhiko Arai, Koki Ikemoto, Yasuhide Inokuma, Makoto Fujita
   J. Am. Chem. Soc. **2014**, *136*, 17899–17901.
   [Chapter 5]

[Other publications]

1. "X-ray analysis on the nanogram to microgram scale using porous complexes"
   Yasuhide Inokuma, Shota Yoshioka, Junko Ariyoshi, Tatsuhiko. Arai, Yuki Hitora, Kentaro Takada, Shigeki Matsunaga, Kari Rissanen, Makoto Fujita
   Nature **2013**, *495*, 461–466.

2. "Preparation and Guest-Uptake Protocol for a Porous Complex Useful for 'Crystal-Free' Crystallography"
   Yasuhide Inokuma, Shota Yoshioka, Junko Ariyoshi, Tatsuhiko Arai, Makoto Fujita
   Nat. Protoc. **2014**, *9*, 246-252.

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