Metal–Macrocycle Frameworks: Porous Supramolecular Crystals with Multiple Molecular Receptors on the Pore Surfaces

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1. Introduction
Molecular-sized spaces formed within self-assembled hollow nano-structures, such as capsules, micelles/vesicles, and porous crystals, have attracted considerable attention due to their specific spatial functions for molecular encapsulation, separation, transportation, and transformation. In order to enhance selectivity and efficiency of these spatial functions, it is of significant importance to precisely control the size, shape, and chemical and physical properties of the interior surfaces of the nano-space. In line with this concept, a novel strategy is required for the arrangement of multiple functional groups in an accurately-oriented way at desired positions of the interior surface. However, it has long been a challenge to arrange a variety of molecular recognition sites on the surface in a site-selective manner. To realize this, I envisioned that self-assembly of metallo-macroyclic compounds would provide novel porous crystalline materials with well-defined molecular receptors arising from the macrocyclic cavities on the inner pore surfaces.

In this study, I have synthesized a family of porous crystalline materials, Metal–Macrocycle Frameworks (MMFs), composed of one, two, or four stereoisomers of trinuclear macrocyclic PdII complexes. These MMFs possess nano-sized pores surrounded by a variety of molecular binding pockets on the interior surfaces. The chemical and physical properties of the MMF surface can be adjusted by site-selective, reversible surface modification simply by soaking in a solvent containing organic/inorganic guest molecules. Notably, not only the size and shape of the pore but also the binding modes of guest molecules can be tuned by solvent-induced pseudopolymorphism of the MMFs. Furthermore, asymmetric crystallization of the MMFs was induced by optically-active sugar-derived lactones, generating chirality of the pore and the binding pockets of the MMFs.

2. Synthesis of Metal–Macrocycle Framework 1
A porous Metal–Macrocycle Framework 1 (MMF-1) with five kinds of enantiomeric-paired binding pockets was constructed from a structurally flexible tris-bidentate macrocyclic ligand \( L \) and \( \text{PdCl}_2(\text{CH}_3\text{CN})_2 \). Complexation of ligand \( L \) and 3 equiv. of \( \text{PdCl}_2(\text{CH}_3\text{CN})_2 \) in \( \text{CH}_3\text{CN} \) produces yellow single-crystals in 41% yield which consist of an equal amount of four stereoisomers of neutral trinuclear macrocyclic PdII complexes, \( \text{Pd}_3\text{LCl}_6 \) (Figure 1a). In the two conformational isomers (\( \text{Syn} \) and \( \text{Anti} \)), all the three or two PdII centers, respectively, are located on the same side of the macrocyclic ligand (Figures 1b,c). For each isomer, two helical structures (\( P \) and \( M \)) are induced by intramolecular, circularly-oriented three \( \text{C-H}\cdots\pi \) interactions (Figure 1d). Moreover, each trinuclear PdII macrocyclic complex has a pair of guest binding pockets on their top and bottom faces, head- and tail-Pockets, respectively. In the crystal formed in \( \text{CH}_3\text{CN} \), the four isomers are regularly arranged mainly through \( \text{N-H}\cdots\text{Cl} \) hydrogen bonding and Pd-Pd interactions to construct a rectangular nano-channel structure with the size of \( 1.4 \times 1.9 \text{ nm}^2 \) (Figure 1e). This nano-channel can provide five enantiomerically-paired guest binding pockets on the pore surface.
3. Site-selective guest adsorption to the MMF-1 surface

Adsorption behaviors of small aromatic molecules to the MMF-1 surface were examined for the site-selective surface modification in a noncovalent manner. X-ray diffraction of a single-crystal, which was obtained as the result of the crystal-to-crystal transformation by the soaking of a single crystalline MMF-1 in a 1:1 (v/v) mixed solvent of CH₃CN and benzene at 30 °C for one day, revealed that benzene molecules are included within two sets of binding pockets, (P/M)-Anti-head and (P/M)-Syn-tail Pockets, mainly through C-H--π interactions and van der Waals interactions (82% and 66% occupancies, respectively) (Figure 2a). Residual benzene molecules in the free pore space are highly disordered. Furthermore, other simple aromatic hydrocarbons, such as naphthalene and azulene, show different binding modes from that of benzene, indicating that the adsorption behaviors on the surface depend on the size and/or shape of guest molecules (Figure 2b).

To further assess the shape- and orientation-selectivities in the guest adsorption, three dibromobenzene isomers were selected as guests. Single-crystal X-ray analyses revealed that adsorption of dibromobenzene isomers is highly shape-selective on the MMF-1 surface (Figures 2c-e). O-isomer is captured in the (P/M)-Syn-tail and (P/M)-Ellipsoidal Pockets (51% and 53%, respectively). On the other hand, m-isomer is trapped in the (P/M)-Syn-tail and (P/M)-Anti-head Pockets (52% and 89%, respectively), and p-isomer is included only in the (P/M)-Ellipsoidal Pockets (68%). It should be noted that every dibromobenzene isomer is oriented without fluctuation as confirmed by electron densities of heavy Br atoms. Subsequently, a solution containing a mixture of m- and p-dibromobenzenes in CH₃CN was used for binary guest arrangement. The crystal structure of MMF-1 including m- and p-isomers shows that two guests are sorted in different binding pockets (Figure 2f). The binding selectivity of the dibromobenzene mixture is completely consistent with those of both individual isomers.

Furthermore, highly diastereoselective guest adsorption was achieved when using optically-active, disubstituted aromatic molecules, (1R)- or (1S)-1-(3-chlorophenyl)ethanol (Figures 2g,h). Single-crystal X-ray diffraction of a single crystal, which was obtained by the soaking of the MMF-1 in a 1:2 (v/v) mixture of CH₃CN and (1R)-isomer at 30 °C for one day, revealed that the guest molecules are encapsulated in one of the enantiomerically-paired binding pockets. As is obvious, the (1S)-isomer is encapsulated into each mirror-image binding pocket. In the electron density map, there is no electron density assignable to the guest molecule in the other enantiomerically-paired binding pockets. This strongly suggests that the resulting diastereoselectivity is substantially high.
4. Direct X-ray observation of a guest exchange process on the MMF-1 surface

In order to study adsorption kinetics of guest molecules on the MMF-1 surface, the time-course X-ray analysis was conducted. Four successive single-crystal X-ray measurements allowed to visualize a guest exchange process at the molecular binding pockets. To make the guest exchange more slowly, the experiment was carried out at $-180$ °C, and the incubation for the guest exchange was conducted at $-40$ °C (Figures 3a,b). The crystal structures of the MMF-1 crystal briefly-immersed into a 1:2 (v/v) mixed solvent of CH$_3$CN and (1R)-1-(3-chloropheny)ethanol at 23 °C for 5 min are shown in Figures 3c-f. Comparative study of the four structures indicated a slow guest exchange process in the (P)-Syn-tail Pocket. Moreover, an intermediate guest adsorption was clearly detected as indicated by arrows. These atomic level observations would provide a new insight into the kinetics of guest adsorption behaviors on the inner crystal surface.

5. Three-dimensionally interconnected pores: MMF-2

The trinuclear macrocyclic Pd$^0$ complex, Pd$_3$LCl$_6$, exhibits solvent-induced pseudopolymorphisms. One of them is MMF-2, which has a different size and shape of pore with different guest binding pockets on the surface from MMF-1. Complexation of ligand L and 3 equiv. of PdCl$_2$(CH$_3$CN)$_2$ in a 1:9 (v/v) mixed solvent of DMSO and CH$_2$Cl$_2$ generates yellow-orange single crystals of rac-MMF-2 composed of only (P/M)-Syn isomers (Figure 4a). The single-crystal X-ray diffraction revealed that rac-MMF-2 crystallizes in a chiral cubic space group, $I2_3$, with a Flack parameter 0.48(5), indicating that rac-MMF-2 exists as a racemic mixed crystal. Namely, a unit cell of the rac-MMF-2 crystal consists of one kind of stereoisomers of Pd$_3$LCl$_6$, either a (P)- or an (M)-Syn isomer, but the rac-MMF-2 as a whole contains an equal amount of both (P)- and (M)-Syn isomers. In rac-MMF-2, (P/M)-Syn isomers interact with each other through N-H---Cl hydrogen bonds (average N-Cl distance, 3.3 Å) and Pd-Pd interactions (Pd-Pd distance, 3.17 Å) to form three-dimensionally connected pores. In addition, rac-MMF-2 has cylindrical nano-spaces with a diameter of 10 Å and a length of 7 Å surrounded by two types of the molecular binding pockets, Syn-head and -tail Pockets (Figure 4b).

Moreover, rac-MMF-2 can capture small organic molecules such as benzene and cyclohexane. Single-crystal X-ray analysis of a crystal, which was obtained after the soaking of crystalline MMF-2 in a 1:1 (v/v) mixed solvent of benzene and CH$_2$Cl$_2$, revealed that benzene molecules are adsorbed to both Syn-head and -tail Pockets mainly through C-H---Cl hydrogen bonding and C-H---π interactions (Figure 4c). For uptake experiments with cyclohexane, only a Syn-head Pocket captures cyclohexane but with low occupancy of 17%. So in competition experiments, a selective uptake behavior of benzene over cyclohexane was observed for the rac-MMF-2. The crystals of rac-MMF-2 were soaked into a CH$_2$Cl$_2$ solution of benzene and cyclohexane (1.0 M each) for one day at 30 °C, and then digested in
DMSO-d$_6$/DCl-D$_2$O. The $^1$H NMR spectrum of the resulting mixture indicated that molar ratio of benzene and cyclohexane trapped in the MMF-2 pores is 90:10, namely the selectivity of benzene uptake over cyclohexane is 9. Thus, the crystal structures and $^1$H NMR spectroscopy suggest that MMF-2 exhibits a high capability of molecular separation through the nano-space surrounded by the molecular binding pockets.

6. Asymmetric crystallization of MMF-2 with optically-active lactones

Asymmetric crystallization of MMF-2 was achieved by chirality induction using optically-active sugar-derived lactones (Figure 5). Crystallization of Pd$_3$LCl$_6$ in a 1:9 (v/v) mixed solvent of DMSO and CH$_2$Cl$_2$ in the presence of 30 equiv. of D-glucono-1,5-lactone or 70 equiv. of D-glucurono-6,3-lactone produced homochiral MMF-2 crystals, P-MMF-2 or M-MMF-2, respectively. The single-crystal structures of P- and M-MMF-2 show that their unit cell structures are completely the same as that of rac-MMF-2 and no chiral lactones as the asymmetric induction reagents were therefore included in the crystals. Importantly, the Flack parameters of P- and M-MMF-2 are 0.07(9) and 0.06(7), respectively, indicating high asymmetric induction. Thus, the optically-active lactones have influence not on the crystal structures, but on the asymmetric induction of the MMF-2 crystals. The resulting chiral spaces could be applied for catalytic asymmetric reactions.

7. Other pseudopolymorphisms of MMF; MMF-3 and MMF-4

The trinuclear Pd$^{II}$ complexes show further solvent-induced pseudopolymorphisms to form two other types, MMF-3 and MMF-4 from a 1:9 (v/v) mixed solvent of DMSO and CHCl$_3$ (Figure 6a). These two different porous MMF crystals composed of (P/M)-Syn isomers are simultaneously formed as concomitant polymorphs from a 1:9 (v/v) mixed DMSO-CHCl$_3$ solution containing ligand L and 3 equiv. of PdCl$_2$(CH$_3$CN)$_2$. The crystal habit and packing structure of MMF-3 are similar to those of rac-MMF-2. However, MMF-3 crystallizes in an achiral cubic space group, I43d, and contains both (P)- and (M)-Syn isomers in a unit cell. For MMF-4 whose unit cell also consists of both (P)- and (M)-Syn isomers, the packing structure is completely different from that of rac-MMF-2 and MMF-3 (Figure 6b). In MMF-4, (P)- and (M)-Syn isomers alternately are aligned in a head-to-tail manner along the c axis (Figure 6c). Furthermore, these columns of the (P/M)-Syn isomers make a hexagonal array in the packing structure to form a one-dimensional hexagonal nano-channel structure with a diameter of 1.2 nm.

8. Conclusion

To develop functional supramolecular spaces, I have constructed a family of Metal–Macrocycle Frameworks from trinuclear macrocyclic Pd$^{II}$ complexes as the building blocks. The resulting self-assembled crystalline compounds have a variety of molecular binding pockets on their inner pore surfaces. Using these binding pockets, site-selective, reversible surface modification has been achieved with small aromatic organic molecules. Furthermore, the size and shape of the MMF pores and the types and chirality of the binding pockets on the surfaces can be controlled by solvent-induced pseudopolymorphisms and asymmetric crystallization in the presence of optically-active lactones. Such supramolecular, multi-functional spaces formed in MMF would show space-specific functions, such as molecular separation, highly efficient asymmetric catalytic reactions, and polymer formation.