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Supramolecular Tilt Chirality Derived from Symmetrical Benzene Molecules: Handedness of the 2_1 Helical Assembly

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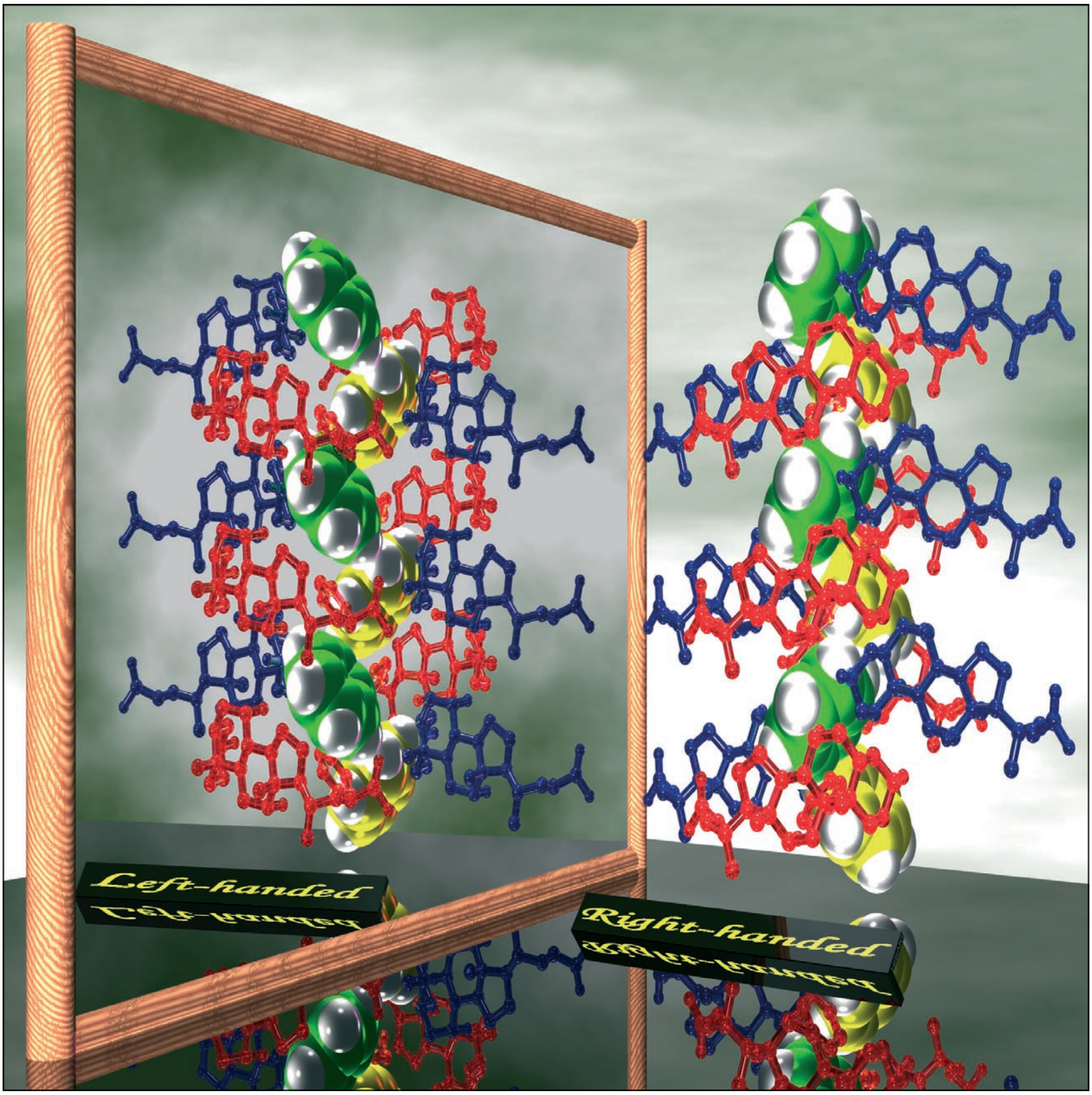

Abstract: Achiral molecules can form aggregates with chirality. This depends on the relative position of the molecules, in other words, the tilt of the molecules (so-called supramolecular tilt chirality). In this paper, we describe supramolecular chirality appearing in a 2_1 column composed of symmetrical benzene molecules, which is formed in the host cavity of inclusion crystals of cholic acid. Moreover, we determined the handedness, that is, right or left, of the 2_1 helical column of benzene on the basis of the molecular tilt. Determination of the 2_1 helical handedness was performed on assemblies of other benzene derivatives in cholic acid crystals and benzene assemblies in other host frameworks selected from the Cambridge Structural Database. Finally, we demonstrated complementarity of the handedness between the 2_1 symmetrical host framework of cholic acid and the benzene column.

Keywords: chirality · crystal engineering · helical structures · host–guest systems · supramolecular chemistry

Introduction

Supramolecular chirality[1] is a remarkably important concept for treating molecular assemblies and self-organized systems. Helical assemblies, in particular, have attracted much attention[2] as they are often found among the most fundamental of the activities of life. Helical assemblies are also seen in organic crystals, and mostly have 2_1 symmetrical structures.[3] In association with this, we focused on the supramolecular chirality of 2_1 helical assemblies composed of the highly symmetrical molecule benzene in the solid state and the determination of the handedness of the helical assemblies.

So far, we have studied inclusion crystals of steroidal and alkaloidal asymmetric compounds such as cholic acid derivatives. We obtained more than three hundred types of inclusion crystals and revealed by X-ray diffraction analysis that these crystals take on various types of host frameworks.[4] To understand how the crystals are constructed from single molecules and how the guest molecules have an effect on the construction of the host frameworks, we developed the hierarchical interpretation process for crystal structures of inclusion compounds of cholic acid, brucine, and cinchona alkaloid.[5] In the hierarchical interpretation process, the key structure is the 2_1 helical assembly formed through noncovalent interactions. As a result, we could logically perform a well-ordered explanation of the crystal structures starting from the steroidal molecular structure. This hierarchical interpretation showed that the diversity of the host framework mainly resulted from the varied arrangements of the inherent 2_1 helices. Later, we tackled the fact that it was necessary for the understanding of the supramolecular chirality of the 2_1 assemblies to determine their helical sense, that is, right- or left-handedness, and to discriminate their enantiomeric isostructures. Although we tried to determine the handedness of the 2_1 helical assemblies, there was no suitable method for doing so due to the characteristics of a 2_1 helix as described later.

As another research topic, we studied the generation of supramolecular chirality from achiral molecules on molecular assemblies composed of organic salts: achiral ammonium carboxylates.[6] Although we constructed hydrogen-bonded robust organic layer crystals composed of various ammonium carboxylates, chiral layered crystals were achieved only when 4-methylbenzylamine was employed among the various amines.[7] We naturally wondered why chiral crystals should appear from achiral molecules and, hence, sought the origin of the chirality. We carefully surveyed the literature concerning other chiral systems and noticed that authors mentioned the presence of chiral conformers for the origin of chirality, but did not discuss how the chiral conformers assembled to construct chiral crystals. We concluded that a systematic method is required to interpret the supramolecular chirality of chiral crystal structures. We finally reached the idea that supramolecular chirality in chiral layered crystals is due to parallel stacking of two-dimensional layers, as described in our recent paper.[7]

During our study of the inclusion crystals of natural molecules and chiral crystals from achiral molecules, we came across the fact that even highly symmetrical molecules form assemblies with chirality. Generally, a symmetrical object is naturally achiral; its mirror image is thus identical with the original (Figure 1a). On the other hand, an assembly composed of the two objects can exhibit chirality and can have

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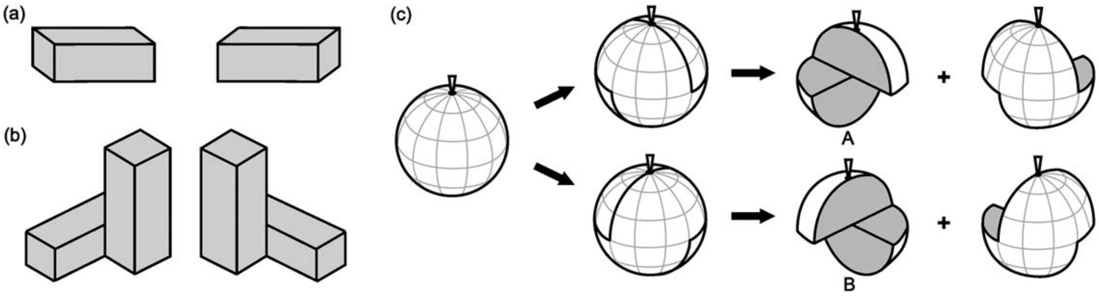


Figure 1. Chirality generated in assemblies composed of symmetrical objects. Mirror-pair image of a) a cuboid, b) an assembly composed of two cuboids, and c) la coupe du roi apples.

the distinguishable enantioisostructures shown in illustrations of polyhedrons[8] and la coupe du roi chiral apples[9] (Figure 1b and c, respectively). These examples are classics and must be well-understood. Indeed, chiral aggregated structures composed of achiral molecules are often reported in solution,[10] in liquid crystals,[11] on films or surfaces,[12] and in crystals.[13] For example, achiral banana-shaped molecules packed in liquid crystals were reported to show chiral structures with a tilt of the molecule.[11] However, to our knowledge, there has not yet been a report discussing such chirality derived from simple, highly symmetrical molecules in the fields of organic and organometallic crystallography. This seems to be due to the practice of crystallography being dominated by mathematical treatments, and intuitive and/or visual viewpoints toward chiral assemblies in crystals have been overlooked. We believe that the establishment of the concept of chirality in simple systems should provide a highly useful approach in the treatment of more-complicated assembly systems with chirality.

Herein, we demonstrate that achiral objects can form chiral 2_1 symmetrical assemblies whose chirality depends on the tilt of the molecules, and determine the handedness of 2_1 helical assemblies of benzene molecules, which form in the host cavity of cholic acid inclusion crystals, on the basis of the molecular tilt. Furthermore, determination of the 2_1 helical handedness is performed on assemblies of other benzene derivatives in cholic acid crystals and benzene assemblies in other host frameworks selected from the Cambridge Structural Database (CSD). Finally, we demonstrate complementarity of the handedness between the assemblies of cholic acid and those of benzene molecules.

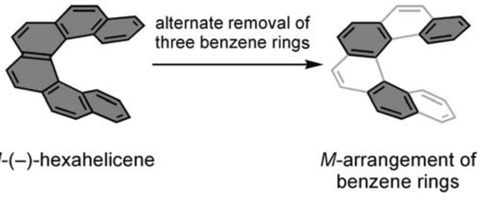
Abstract in Japanese:

アキラルな分子であっても、その集合体はキラリティをもつことがある。このキラリティは分子の相対的位置、換言すれば分子の傾きに依存する。本論文では、コール酸の包接結晶中で見られたベンゼン分子の2_1らせんカラムに現れる超分子キラリティについて明らかにした。さらに分子の傾きをもとに、このらせんカラムのキラリティ（右巻き、左巻き）を定義すると共に、本手法によって、コール酸の包接結晶で見られるその他のベンゼン誘導体、および種々のホストフレームワーク内で観測されるベンゼンの2_1らせんカラムのキラリティを初めて決定した。コール酸の包接結晶中における2_1カラムのキラリティはどのベンゼン誘導体でも一様に右巻きを示すことがわかった。これは、ホストフレームワークが形成する右巻き2_1らせんのキラリティから誘起された結果である。

Results and Discussion

Supramolecular Tilt Chirality on the 2_1 Assemblies of Benzene

Generally, helices are well-known to be asymmetric, and their handedness can be easily distinguished by their appearance. However, a 2_1 helix still remains ambiguous from the viewpoint of its handedness because the 2_1 screw operation includes a 180° rotation and translation, making it impossible to distinguish right- or left-handed rotation.[14] So far, there have been several examples that describe the handedness of 2_1 helical assemblies in crystals. In these cases, noncovalent bonds such as hydrogen bonds[13c,g,15] and coordination bonds[16] were employed for connection between the molecules, thus allowing the determination of the handedness of 2_1 helical assemblies from their appearance. However, in the 2_1 assemblies of benzene molecules, which have highly symmetrical structures and form no directional noncovalent bonds, neither their helicity nor supramolecular chirality have been discussed, although Matsuura and Koshima suggested that an imaginary helical arrangement of three symmetrical benzene molecules may be given by removing three benzene rings from *M*-(−)-hexahelicene (Scheme 1).[13h]



Scheme 1. Helical benzene arrangement inspired by helicene. A helical arrangement of three symmetrical benzene molecules may be given by removing three benzene rings from helicene.

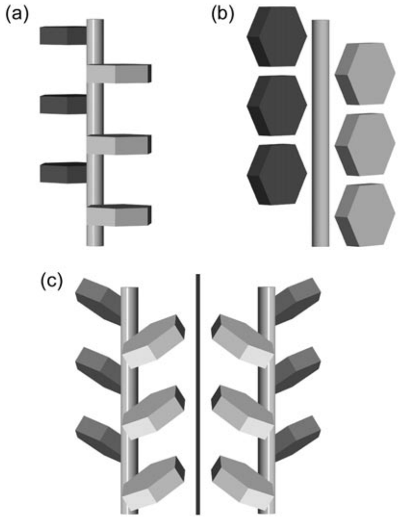


Figure 2. A schematic representation of one-dimensional arrangements of hexagonal objects a) perpendicular to, b) parallel to, and c) tilted from an axis drawn as a pillar. A mirror-image pair of a 2_1 helical arrangement is shown in c).

First, we explain that it is in principle possible for hexagonal objects to exhibit chirality in their 2_1 symmetrical assemblies. Figure 2 shows schematically three types of one-dimensional, 2_1 symmetrical assemblies composed of these objects. The objects in Figure 2a and b are aligned perpendicular and parallel to the 2_1 axis, respectively, leading to the existence of a glide plane in the assemblies. As a result, the assemblies in Figure 2a and b are not chiral. In Figure 2c, on the other hand, the objects are tilted from the axis to give an arrangement with no glide plane but a twofold screw axis, indicating the appearance of chirality in the assembly. Therefore, the molecular tilt against the axis is indispensable for the appearance of chirality in the 2_1 symmetrical assembly composed of highly symmetrical benzene. We term such chirality supramolecular tilt chirality.[17] In fact, the tilt chirality of a 2_1 helical assembly of benzene is seen in its inclusion crystals. As a representative example, we show an inclusion crystal of cholic acid with benzene (Figure 3), which belongs to the chiral space group $P2_1$.[18]

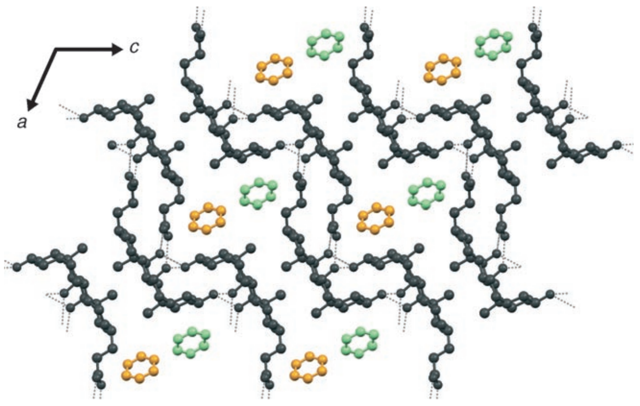


Figure 3. Packing diagram of the crystals of cholic acid including benzene. Hydrogen atoms are omitted for clarity.

In connection with chirality appearing in guest-molecular assemblies in cocrystals, guest molecules often form a 1D column in the host framework, and the guest column exhibits its chirality induced by the chiral host framework. Indeed, Gdaniec, Połoński, and co-workers, for example, reported that achiral aromatic ketones and nitrosamine derivatives are included in the host framework of cholic acid to form 1D columns, and that the guest molecules exhibit CD activity due to their twisted and fixed conformation, which is induced by the chiral host frameworks.[19] However, what we describe herein is the supramolecular chirality of the 2_1 assemblies, not of the single molecules.

Figure 4 shows the 2_1 helical assemblies of benzene actually observed in the host cavity (Figure 4a) and its virtual mirror image (Figure 4b), in which the two types of benzene molecules related by the 2_1 symmetry are colored green and orange. As seen in the side views, the benzene molecules are tilted against the twofold screw axis. In the case of the real image (Figure 4a), for example, the green benzene molecules are inclined to the right, whereas the orange ones are inclined to the left. Owing to this molecular tilt, the assem-

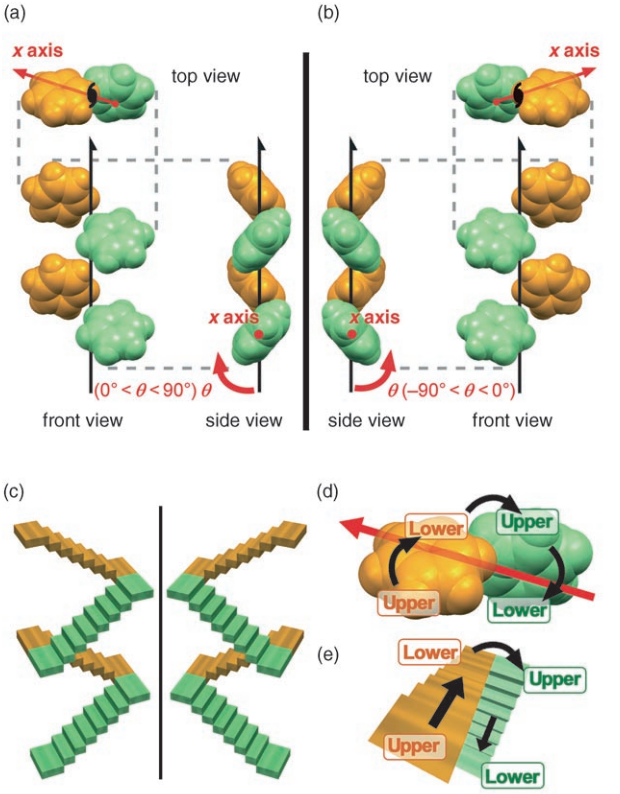


Figure 4. A mirror-image pair of a) real and b) virtual 2_1 helical assemblies of benzene molecules in a cavity composed of cholic acid. Benzene molecules in front of and behind the twofold screw axis are colored green and orange, respectively. The red arrow denotes the x axis originating from the center of the benzene ring and perpendicular to the twofold screw axis. The angle θ denotes a clockwise horizontal rotation around the x axis, which indicates right- ($0° < \theta < 90°$) or left-handedness ($-90° < \theta < 0°$). c) A mirror-image pair of stairs that exhibits 2_1 symmetry. d) and e) Top views of the right-handed assembly of benzene molecules (d) and right-handed stairs (e).

blies exhibit supramolecular tilt chirality, and these two assemblies are an enantiomeric pair.

Definition of Handedness of 2_1 Assemblies of Benzene Molecules

In connection with the handedness of the assemblies, when the 2_1 symmetrical assemblies are viewed from the side in Figure 4a and b, they look like helical stairs (Figure 4c), which plainly exhibit right- and left-hand senses, respectively. Furthermore, the top view of the observed crystal in Figure 4d clearly indicate the *P*-screw form, which is that of the stairs shown in Figure 4e.

To express the handedness clearly, a perpendicular axis *x* originating from the center of the benzene ring is projected to the twofold screw axis, and an angle θ that denotes a horizontal rotation around the *x* axis is defined. If θ is in the range $0° < \theta < 90°$, the helix exhibits right-handedness (Figure 4a); if $-90° < \theta < 0°$, the helix is left-handed (Figure 4b). In this way, the handedness of 2_1 helical assemblies can be determined by the molecular tilt. Other benzene derivatives are also included in the host cavity of cholic acid in a similar fashion.[20–23] The included benzene derivatives and the handedness of their helical columns observed in 46 inclusion crystals are summarized in Table 1, in which all but six of the 2_1 helical arrangements were determined to be right-handed on the basis of the method described above (see below); six benzene derivatives did not form 2_1 helical columns probably owing to a steric effect of the substituents and the existence of another guest molecule. For comparison, we also analyzed the crystal structure of benzene itself. Benzene usually crystallizes with the space group *Pbca*, which does not exhibit 2_1 symmetry.[24] Under certain conditions of high pressure, however, benzene is reported to crystallize with the space group $P2_1/c$.[25] The structure involves a twofold screw axis along the crystallographic *b* axis and benzene molecules in 3D contact with the neighboring molecules in the crystal. Figure 5 shows the *ac* plane in the crystal structure, and benzene molecules related by the 2_1 symmetry are colored orange and green. Benzene molecule A is surrounded by four neighbor molecules B, C, D, and E related by 2_1 symmetry. Therefore, there are four types of 2_1 helical assemblies, A–B, A–C, A–D, and A–E. Assemblies A–B and A–D are assessed to be in right-handed, whereas A–C and A–E are left-handed. In this way, the 2_1 assemblies of benzene molecules give both types of handedness depending

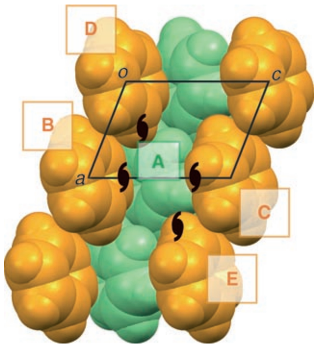


Figure 5. The *ac* plane in the crystal structure of benzene.

Table 1. Helical handedness of 2_1 assemblies composed of benzene derivatives in cholic acid inclusion crystals.

Refcode	Guest	Handedness	Ref.	Refcode	Guest	Handedness	Ref.
BIFQAI01	cyanobenzene	*R*	20a	HURPEP	*n*-hexylbenzene	–[b]	20c
ERIPEA	*m*-xylene	*R*	20b	LAFCAW	aniline	*R*	21a
ERIPUQ	*p*-xylene	*R*	20b	LAFCEA	nitrobenzene	*R*	21a
GUNKOP	toluene	*R*	20a	NOJPOR	acetone, 1,2-dichlorobenzene	–[c,d]	21b
GUNKUV	ethylbenzene	*R*	20a	POZPUP	propiophenone	*R*	19a
GUNLAC	ethylbenzene	*R*	20a	POZQAW	4-fluoropropiophenone	*R*	19a
GUNLEG	phenylacetylene	*R*	20a	PUWREE	*N*-methyl-*N*-nitrosoaniline	*R*	19b
GUNLIK	3-phenyl-1-propene	*R*	20a	PUWROO	*N*-benzyl-*N*-nitrosoaniline	–[e]	19b
GUNLUW	chlorobenzene	*R*	20a	QOQFAD	*N*-chloroaniline	–[a,f]	20d
GUNMAD	bromobenzene	*R*	20a	RABJUV	3-chloroacetophenone	*R*	22c
GUNMEH	iodobenzene	*R*	20a	RABKAC	3-fluoroacetophenone	*R*	22c
GUNMIL	chlorobenzene	*R*	20a	RABKEG	4-fluoroacetophenone	*R*	22c
GUNMOR	bromomethylbenzene	*R*	20a	TEMWOX	*p*-toluidine	*R*	21c
GUNMUX	benzaldehyde	*R*	20a	UMABAL	nitrosobenzene	*R*	23
GUNNAE	phenyl acetate	*R*	20a	VABSOG	acetophenone	*R*	20e
GUNNEI	benzyl formate	*R*	20a	WEYNUJ	benzene	*R*	18
GUNNIM	anisole	*R*[a]	20a	YAZTIC	3-fluoroaniline	*R*[a]	22b
GUNNOS	phenetole	*R*	20a	YOYFIB	*o*-xylene	–[b]	22b
GUNNUY	benzyl methyl ether	*R*	20a	YUNYOV	2-fluorobenzyl alcohol	*R*	22c
GUNPIO	benzyl alcohol	*R*	20a	YUNZAI	4-fluorobenzyl alcohol	*R*	22c
GUNPOU	*N*-methylaniline	*R*	20a	ZUZDON	2-fluoroaniline	*R*	22d
GUNPUA	*N*-ethylaniline	*R*	20a	ZUZDUT	4-fluoroaniline	*R*	22d
HURNUD	*N*-amylbenzene	–[b]	20c	ZUZFAB	3,4-difluoroaniline	*R*	22d

[a] The absolute structure is inverted. However, given the structure of cholic acid, the column of benzene included in the cavity must be right-handed. [b] The isolated 2_1 column does not form due to a steric effect of the substituent. [c] The isolated 2_1 column does not form due to another guest molecule, acetone. [d] NOJPOR belongs to the space group *P*1. [e] The isolated 2_1 column does not form due to bulkiness of the guest molecule. However, two benzene rings in the same guest molecule are located with right-hand sense. [f] QOQFAD belongs to the space group $P2_12_12_1$.

on which assembly is selected, and thus the crystal of benzene belongs to an achiral space group.

Other isolated 2_1 helical assemblies of benzene are found in the literature.[26,27] In these crystals, benzene molecules are included in slits in the host frameworks. Although their handedness and supramolecular chirality have not been described at all, the supramolecular chirality in the 2_1 assembly was successfully determined by our method described above. In Figure 6, the top and side views of seven crystal structures with space group $P2_1/n$ selected from the CSD are shown; the host and benzene molecules are shown in tube and space-filling models, respectively. The benzene molecules in front of and behind the twofold screw axis are shown in white and gray, respectively. Although the crystals with the space group $P2_1/n$ have isolated 2_1 benzene columns of a certain helical handedness, the crystals include both right- and left-handed columns, resulting in achiral whole structures. On the other hand, the top and side views of seven crystal structures with space group $P2_1$ are shown in Figure 7. In these cases, the helical columns in each crystal have identical handedness: the crystals KOSHIJ and GOLBOY include only the right-handed 2_1 columns, whereas the others include only the left-handed ones, resulting in chiral crystal structures with a certain handedness.

Complementarity of the Helical Handedness of the Host Framework and the Guest Assembly

Notably, all of the 2_1 helical arrangements of the benzene derivatives exhibit only the right-hand sense in the cavity of cholic acid inclusion crystals (Table 1). This is a result of the identical chirality of the host frameworks (Figure 8a). In

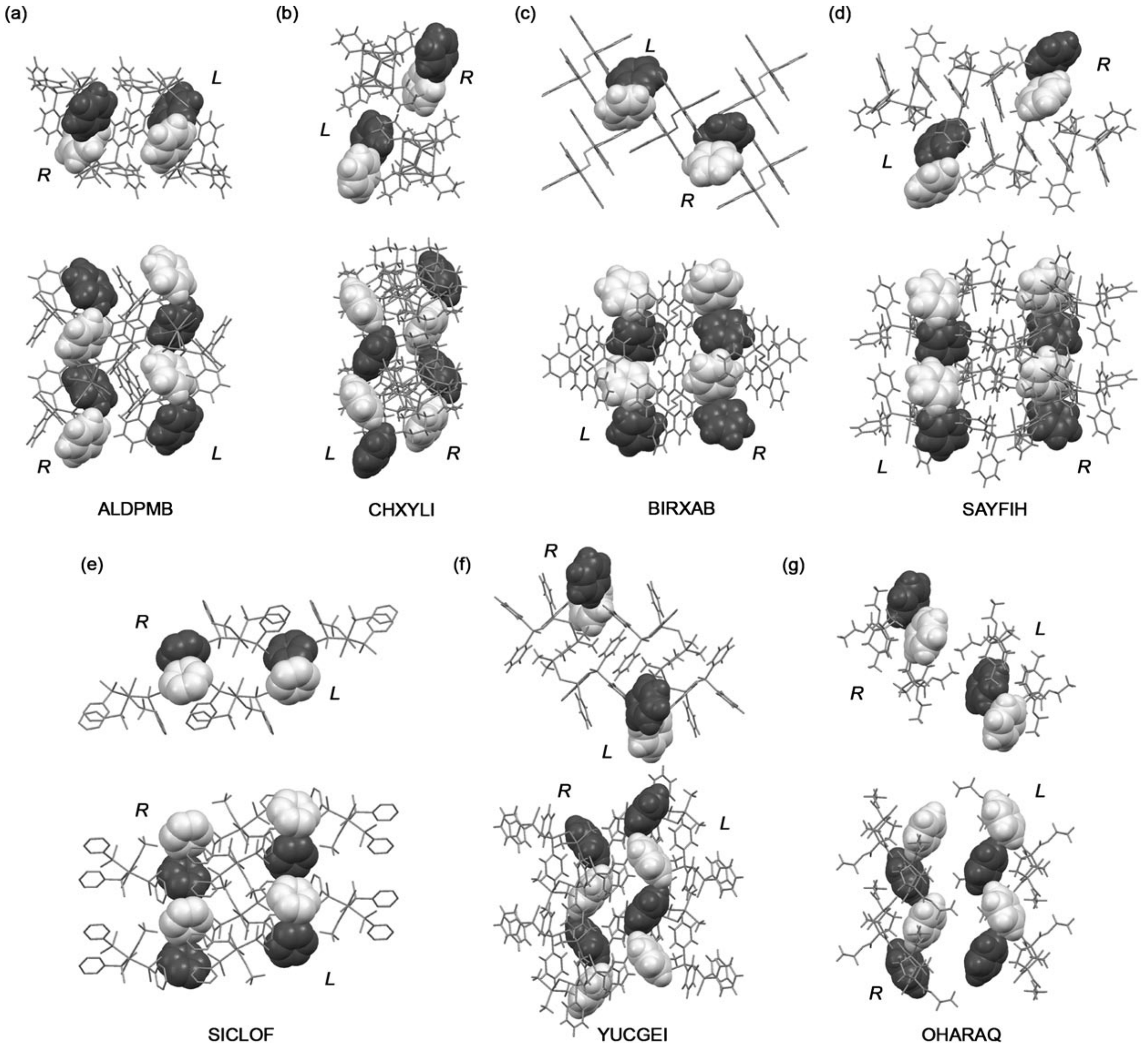


Figure 6. Top and side views of helical columns of benzene of both right- and left-hand sense in the host frameworks of a) $Mo(CO)_4[(C_6H_5)_3P{=}CH{-}CH{=}CH_2]$ (ALDPMB),[26f] b) cyclohexyllithium hexamer (CHXYLI),[26b] c) bis-9-(9-phenyl)fluorenylperoxide (BIRXAB),[26e] d) isoxazol-5-yl iron complex (SAYFIH),[26c] e) $IrMe_2(PMe_2Ph)_3BF$ (SICLOF),[26g] f) $Me_3Sn(SPPh_2)_2N$ (YUCGEI),[26a] g) tricyclic amidal derivative (OHARAQ);[26d] CSD Refcodes are in parentheses. The handedness of the helices is shown by *R* (right) or *L* (left). Benzene molecules in front of and behind the twofold screw axis are shown in white and gray, respectively. The host frameworks are shown as tube models for clarity.

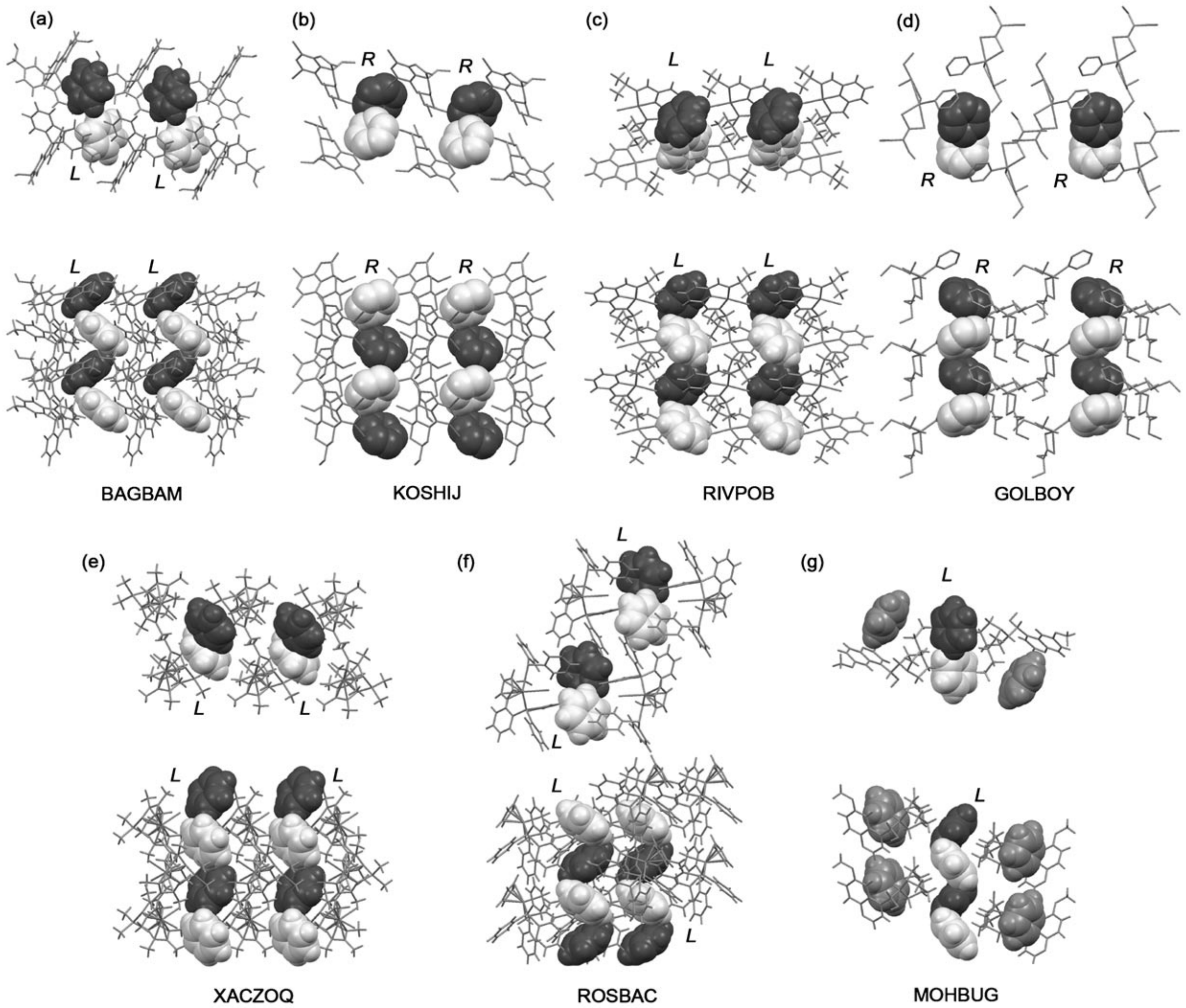


Figure 7. Top and side views of helical columns of benzene of identical handedness in the host frameworks of a) spirobifluorene derivative (BAGBAM),[27c] b) metylergoline derivative (KOSHIJ),[27a] c) $RhCl(2,6\text{-}(C(Me){=}N\textit{i}Pr)_2C_5H_3N)$ (RIVPOB),[27f] d) bis(diethyldithiocarbamato-S,S′) pyridine zinc(II) (GOLBOY),[27g] e) $[Me_2Si(C_5Me_4)_2]MoCl_2$ (XACZOQ),[27e] f) (S)-$[(\eta^5\text{-}C_5H_5)Re(NO)(PPh_3)(CH_2PPh_2)]$ (ROSBAC),[27b] and g) dihydroquinine derivative (MOHBUG);[27d] CSD Refcodes are in parentheses. The handedness of the helices is shown by *R* (right) or *L* (left). Benzene molecules in front of and behind the twofold screw axis are shown in white and gray, respectively. The host frameworks are shown as tube models for clarity.

these systems, multiple intermolecular hydrogen bonding of the cholic acid molecules construct 2_1 helical assemblies with right-handedness, which is determined on the basis of the molecular tilt of cholic acid,[28] leading to a right-handed host cavity. Figure 8b shows the cross-section of the cavity cut by a plane parallel to the twofold screw axis and involving the center of the left-tilting orange benzene molecules in Figure 4a.[29] The cross-section clearly shows that the benzene molecules colored yellow fit the cavity surrounded by the cholic acid molecules. The same situation is observed in the cross-section involving right-tilting benzene molecules and the corresponding cavity. As a result, the whole host cavity also has a right-handed 2_1 symmetry. Therefore, a complementary relationship between the 2_1 helical assemblies of benzene and the surrounding host framework is clearly observed, from which the appearance of the identical supramolecular chirality in the assemblies of benzene molecules is derived. This relationship is expressed by the well-known Fischer lock-and-key principle proposed in 1894.[30] However, the important point here is the direction in which the key should be rotated, right or left. Thus, we emphasize that the relationship here can be illustrated by a right-handed bolt and nut as shown in Figure 8c.

Conclusions

In this study, we focused on the arrangements of benzene molecules in inclusion crystals and demonstrated the appearance of supramolecular chirality in benzene molecules. In the field of supramolecular chemistry established by Lehn,[1a] the 2_1 assembly composed of symmetrical benzene molecules described herein must be one of the simplest and most fundamental that exhibits supramolecular chirality. Furthermore, we determined the handedness of the 2_1 helical columns of benzene and its derivatives in the host frame-

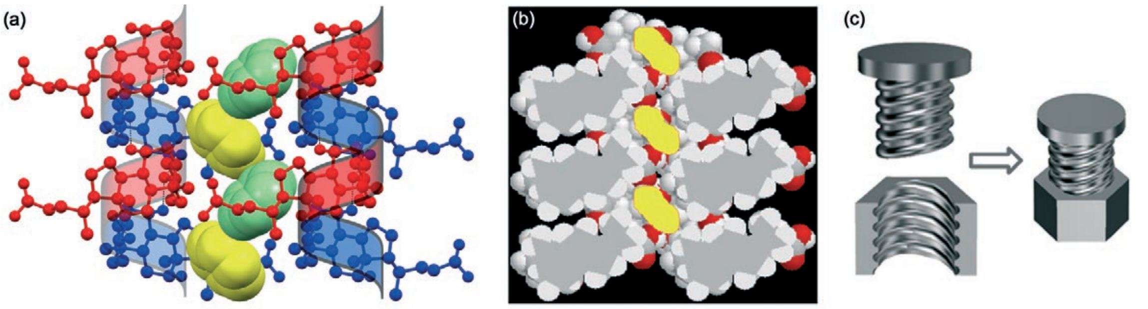


Figure 8. a) Partial structure of benzene inclusion crystal of cholic acid with illustration of helical ribbons. Cholic acid and benzene molecules are drawn with ball-and-stick and space-filling models, respectively. b) Cross-section of the cavity along the twofold screw axis. The cutting plane is set in the center of the yellow benzene molecule behind the 2_1 axis in Figure 4a. The benzene molecules are colored yellow. c) A right-handed bolt and nut, which represent the relationship between included benzene and the assembly of cholic acid molecules.

works of cholic acid and others. The determination of the handedness was successfully performed on the basis of the molecular tilt of benzene.

According to Motherwell and co-workers, more than 52000 organic crystals in the CSD exhibit 2_1 symmetric helical structures.[31] To understand the supramolecular chirality of 2_1 symmetrical assemblies, further investigation in terms of the helical sense and expansion of the method of determining helical handedness to a wide range of systems are now proceeding in our laboratory.

Acknowledgements

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[1] a) J.-M. Lehn, *Supramolecular Chemisty: Concepts and Perspectives*, VCH, Weinheim, **1995**; b) J. W. Steed, J. L. Atwood, *Supramolecular Chemistry*, Wiley-VCH, Weinheim, **2000**; c) L. Perez-García, D. B. Amabilino, *Chem. Soc. Rev.* **2002**, *31*, 342–356; d) M. A. Mateos-Timoneda, M. Crego-Calama, D. N. Reinhoudt, *Chem. Soc. Rev.* **2004**, *33*, 363–372; e) *Supramolecular Chirality* in *Top. Curr. Chem.*, *Vol. 265* (Eds.: M. Crego-Calama, D. N. Reinhoudt), Springer, Berlin, **2006**.

[2] a) J. H. K. K. Hirschberg, L. Brunsveld, A. Ramzi, J. A. J. M. Vekemans, R. P. Sijbesma, E. W. Meijer, *Nature* **2000**, *407*, 167–170; b) T. Nakano, Y. Okamoto, *Chem. Rev.* **2001**, *101*, 4013–4038; c) H. Fenniri, B.-L. Deng, A. E. Ribbe, *J. Am. Chem. Soc.* **2002**, *124*, 11064–11072; d) V. Percec, M. Glodde, T. K. Bera, Y. Miura, I. Shiyanovskaya, K. D. Singer, V. S. K. Balagurusamy, P. A. Heiney, I. Schnell, A. Rapp, H.-W. Spiess, S. D. Hudson, H. Duan, *Nature* **2002**, *419*, 384–387; e) H. Katagiri, T. Miyagawa, Y. Furusho, E. Yashima, *Angew. Chem.* **2006**, *118*, 1773–1776; *Angew. Chem. Int. Ed.* **2006**, *45*, 1741–1744.

[3] A. I. Kitaigorodskii, *Molecular Crystals and Molecules*, Academic Press, London, **1973**.

[4] For examples, see: a) M. Miyata, M. Shibakami, S. Chirachanchai, K. Takemoto, N. Kasai, K. Miki, *Nature* **1990**, *343*, 446–447; b) K. Sada, M. Sugahara, K. Kato, M. Miyata, *J. Am. Chem. Soc.* **2001**, *123*, 4386–4392; c) K. Kato, M. Sugahara, N. Tohnai, K. Sada, M. Miyata, *Cryst. Growth Des.* **2004**, *4*, 263–272; d) K. Nakano, K. Sada, K. Nakagawa, K. Aburaya, N. Yoswathananont, N. Tohnai, M. Miyata, *Chem. Eur. J.* **2005**, *11*, 1725–1733; for reviews, see; e) M. Miyata, K. Sada in *Comprehensive Supramolecular Chemistry*, *Vol. 6* (Eds.: D. D. MacNicol, F. Toda, R. Bishop), Pergamon, Oxford, **1996**, pp. 147–176; f) M. Miyata, K. Sada, N. Yoswathananont in *Encyclopedia of Supramolecular Chemistry*, *Vol. 1* (Eds.: by J. L. Atwood and J. W. Steed), Marcel Dekker, New York, **2004**, pp. 441–451.

[5] a) T. Watabe, K. Kobayashi, K. Kato, K. Sada, M. Miyata, *Mol. Cryst. Liq. Cryst.* **2005**, *440*, 117–124; b) K. Kato, N. Tohnai, M. Miyata, *Mol. Cryst. Liq. Cryst.* **2005**, *440*, 125–132; c) T. Watabe, D. Yoshikawa, I. Hisaki, N. Tohnai, M. Miyata, *Chem. Lett.* **2006**, *35*, 806–807; d) T. Watabe, K. Kobayashi, I. Hisaki, N. Tohnai, M. Miyata, *Bull. Chem. Soc. Jpn.* **2007**, in press.

[6] For examples, see: a) A. Matsumoto, T. Odani, K. Sada, M. Miyata K. Tashiro, *Nature* **2000**, *405*, 328–330; b) A. Matsumoto, K. Sada, K. Tashiro, M. Miyata, T. Tsubouchi, T. Tanaka, T. Odani, S. Nagahama, T. Tanaka, K. Inoue, S. Saragai, S. Nakamoto, *Angew. Chem.* **2002**, *114*, 2612–2615; *Angew. Chem. Int. Ed.* **2002**, *41*, 2502–2505; c) K. Sada, K. Inoue, T. Tanaka, A. Tanaka, A. Epergyes, S. Nagahama, A. Matsumoto, M. Miyata, *J. Am. Chem. Soc.* **2004**, *126*, 1764–1771.

[7] A. Tanaka, K. Inoue, I. Hisaki, N. Tohnai, M. Miyata, A. Matsumoto, *Angew. Chem.* **2006**, *118*, 4248–4251; *Angew. Chem. Int. Ed.* **2006**, *45*, 4142–4245.

[8] M. Gardner, *The New Ambidextrous Universe*, W. H. Freeman and Co., New York, **1999**, pp. 152.

[9] In 1983, Anet, Mislow, and co-workers reported that combination of two homochiral molecules gives an achiral product, citing la coupe du roi as an example. On the other hand, the chiral enantiopair of la coupe du roi apples A and B in Figure 1c can be regarded as assemblies composed of two pieces of an achiral quartered apple; see: F. A. L. Anet, S. S. Miura, J. Siegel, K. Mislow, *J. Am. Chem. Soc.* **1983**, *105*, 1419–1426.

[10] For examples, see: a) U. DeRossi, S. Dahne, S. C. J. Meskers, H. P. J. M. Dekkers, *Angew. Chem.* **1996**, *108*, 827–830; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 760–763; b) J. M. Ribó, J. Crusats, F. Sagués, J. Claret, R. Rubires, *Science* **2001**, *292*, 2063–2066.

[11] For examples, see: a) D. R. Link, G. Natale, R. Shao, J. E. MacIennan, N. A. Clark, E. Körblova, D. M. Walba, *Science* **1997**, *278*, 1924–1927; b) T. Sekine, T. Niori, J. Watanabe, T. Furukawa, S. W. Choi, H. Takezoe, *J. Mater. Chem.* **1997**, *7*, 1307–1309.

[12] For examples, see: a) S. De Feyter, F. C. De Schryver, *Chem. Soc. Rev.* **2003**, *32*, 139–150; b) T. Yamaguchi, T. Kimura, H. Matsuda, T. Aida, *Angew. Chem.* **2004**, *116*, 6510–6515; *Angew. Chem. Int. Ed.* **2004**, *43*, 6350–6355; c) A. M. Berg, D. L. Patrick, *Angew. Chem.* **2005**, *117*, 1855–1857; *Angew. Chem. Int. Ed.* **2005**, *44*, 1821–1823; d) F. Vidal, E. Delvigne, S. Stepanow, N. Lin, J. V. Barth, K. Kern, *J. Am. Chem. Soc.* **2005**, *127*, 10101–10106.

[13] For examples, see: a) K. A. Hirsch, S. R. Wilson, J. S. Moore, *Chem. Eur. J.* **1997**, *3*, 765–771; b) M. P. Lightfoot, F. S. Mair, R. G. Pritchard, J. E. Warren, *Chem. Commun.* **1999**, 1945–1946; c) T. B. Norsten, R. McDonald, N. R. Branda, *Chem. Commun.* **1999**, 719–720; d) B. Gong, C. Zheng, H. Zeng, J. Zhu, *J. Am. Chem. Soc.* **1999**, *121*, 9766–9767; e) K. Tanaka, D. Fujimoto, T. Oeser, H. Irngartinger, F. Toda, *Chem. Commun.* **2000**, 413–414; f) I. Azumaya, D. Uchida, T. Kato, A. Yokoyama, A. Tanatani, H. Takayanagi, T. Yokozawa, *Angew. Chem.* **2004**, *116*, 1384–1387; *Angew. Chem. Int. Ed.* **2004**, *43*, 1360–1363; g) S. Jayanty, T. P. Radhakrishnan, *Chem. Eur. J.* **2004**, *10*, 2661–2667; h) T. Matsuura, H. Koshima, *J. Photochem. Photobiol. C* **2005**, *6*, 7–24; i) H. Neukirch, E. Guido, R. Liantonio, P. Metrangolo, T. Pilati, G. Resnati, *Chem. Commun.* **2005**, 1534–1536.

[14] *International Tables for Crystallography*, *Vol. A*, *Space-Group Symmetry*, (Ed.: T. Hahn,), Kluwer Academic Publishers, London, **1983**.

[15] a) N. S. Begum, C. R. Girija, G. Nagendrappa, *CrystEngComm* **2004**, *6*, 116–119; b) H. Koshima, H. Kawanishi, M. Nagano, H. Yu, M. Shiro, T. Hosoya, H. Uekusa, Y. Ohashi, *J. Org. Chem.* **2005**, *70*, 4490–4497.

[16] a) T. Ezuhara, K. Endo, Y. Aoyama, *J. Am. Chem. Soc.* **1999**, *121*, 3279–3283; b) F. M. Tabellion, S. R. Seidel, A. M. Arif, P. J. Stang, *Angew. Chem.* **2001**, *113*, 1577–1580; *Angew. Chem. Int. Ed.* **2001**, *40*, 1529–1532; c) M. Kondo, M. Miyazawa, Y. Irie, R. Shinagawa, T. Horiba, A. Nakamura, T. Naito, K. Maeda, S. Utsuno, F. Uchida, *Chem. Commun.* **2002**, 2156–2157; d) E.-Q. Gao, Y.-F. Yue, S.-Q. Bai, Z. He, C.-H. Yan, *J. Am. Chem. Soc.* **2004**, *126*, 1419–1429.

[17] a) I. Hisaki, T. Watabe, Y. Kogami, N. Tohnai, M. Miyata, *Chem. Lett.* **2006**, *35*, 1274–1275; b) T. Watabe, I. Hisaki, N. Tohnai, M. Miyata, *Chem. Lett.* **2007**, in press.

[18] K. Nakano, K. Sada, M. Miyata, *Chem. Lett.* **1994**, 137–140.

[19] a) M. Gdaniec, T. Połoński, *J. Am. Chem. Soc.* **1998**, *120*, 7353–7354; b) M. Szyrszyng, E. Nowak, M. Gdaniec, M. J. Milewska, A. Herman, T. Połoński, *J. Org. Chem.* **2001**, *66*, 7380–7384.

[20] a) K. Nakano, K. Sada, Y. Kurozumi, M. Miyata, *Chem. Eur. J.* **2001**, *7*, 209–220; b) K. Nakano, E. Mochizuki, N. Yasui, K. Morioka, Y. Yamauchi, N. Kanehisa, Y. Kai, N. Yoswathananont, N. Tohnai, K. Sada, M. Miyata, *Eur. J. Org. Chem.* **2003**, 2428–2436; c) N. Yoswathananont, K. Sada, M. Miyata, S. Akita, K. Nakano, *Org. Biomol. Chem.* **2003**, *1*, 210–214; d) N. Yoswathananont, S. Chirachanchai, K. Tashiro, K. Nakano, K. Sada, M. Miyata, *CrystEngComm* **2001**, *3*, 74–77; e) K. Miki, A. Masui, N. Kasai, M. Miyata, M. Shibakami, K. Takemoto, *J. Am. Chem. Soc.* **1988**, *110*, 6594–6596.

[21] a) M. R. Caira, L. R. Nassimbeni, J. L. Scott, *J. Chem. Soc. Chem. Commun.* **1993**, *612*–614; b) J. L. Scott , *Supramol. Chem.* **1996**, *7*, 201–207; c) J. L. Scott, *J. Chem. Crystallogr.* **1996**, *26*, 185–189.

[22] a) M. Shibakami, M. Tamura, A. Sekiya, *J. Inclusion Phenom. Mol. Recognit. Chem.* **1995**, *22*, 155–168; b) M. Shibakami, A. Sekiya, *J. Chem. Soc. Chem. Commun.* **1994**, 429–430; c) M. Shibakami, M. Tamura, A. Sekiya, *J. Am. Chem. Soc.* **1995**, *117*, 4499–4505; d) M. Shibakami, M. Tamura, A. Sekiya, *J. Inclusion Phenom. Mol. Recognit. Chem.* **1995**, *22*, 299–311.

[23] M. Gdaniec, T. Bytner, M. Szyrszyng, T. Połoński, *J. Inclusion Phenom. Macrocyclic Chem.* **2001**, *40*, 243–247.

[24] R. W. G. Wyckoff, *Crystal Structures*, *Vol. 6*, *The Structure of Benzene Derivatives*, *Vol. 1*, Wiley, New York, **1969**.

[25] G. J. Piermarini, A. D. Mighell, C. E. Weir, S. Block, *Science* **1969**, *165*, 1250–1255.

[26] a) I. W. Bassi, R. Scordamaglia, *J. Organomet. Chem.* **1973**, *51*, 273–280; b) R. Zerger, W. Rhine, G. Stucky, *J. Am. Chem. Soc.* **1974**, *96*, 6048–6055; c) T. Pilati, M. Simonetta, S. Quici, *Cryst. Struct. Commun.* **1982**, *11*, 1027–1032; d) V. N. Kalinin, T. V. Rozantseva, P. V. Petrovskii, A. S. Batsanov, Y. T. Struchkov, *J. Organomet. Chem.* **1989**, *372*, 287–293; e) E. G. Lundquist, K. Folting, J. C. Huffman, K. G. Caulton, *Organometallics* **1990**, *9*, 2254–2261; f) K. C. Molloy, M. F. Mahon, I. Haiduc, C. Silvestru, *Polyhedron* **1995**, *14*, 1169–1171; g) R. B. Grossman, K. Hattori, S. Parkin, B. O. Patrick, M. A. Varner, *J. Am. Chem. Soc.* **2002**, *124*, 13686–13687.

[27] a) K. Neupert-Laves, M. Dobler, *Helv. Chim. Acta* **1981**, *64*, 1653–1662; b) K. Seifert, N. M. Phuong, B. R. Vincent, *Helv. Chim. Acta* **1992**, *75*, 288–293; c) H. F. Haarman, J. M. Ernsting, M. Kranenburg, H. Kooijman, N. Veldman, A. L. Spek, P. W. N. M. van Leeuwen, K. Vrieze, *Organometallics* **1997**, *16*, 887–900; d) A. V. Ivanov, M. Kritikos, A. Lund, O. N. Antsutkin, T. A. Rodnina, *Zh. Neorg. Khim.* **1998**, *43*, 1482–1490; e) D. Churchill, J. H. Shin, T. Hascall, J. M. Hahn, B. M. Bridgewater, G. Parkin, *Organometallics* **1999**, *18*, 2403–2406; f) K. Kromm, B. D. Zwick, O. Meyer, F. Hampel, J. A. Gladysz, *Chem. Eur. J.* **2001**, *7*, 2015–2027; g) T. Borowiak, G. Dutkiewicz, J. Thiel, *Z. Naturforsch.* **2002**, *B57*, 586–592.

[28] a) K. Kato, K. Inoue, N. Tohnai, M. Miyata, *J. Inclusion Phenom. Macrocyclic Chem.* **2004**, *48*, 61–67; b) T. Watabe, K. Kato, N. Tohnai, M. Miyata in *Structure and Dynamics in Macromolecular Systems with Specific Interactions* (Eds.: K. Adachi, T. Sato), Osaka University Press, Osaka, **2005**, pp. 157–167.

[29] The cross-section was prepared by the plugin software MDL-Chime.

[30] *The Lock-and-Key Principle: Perspectives in Supramolecular Chemistry*, *Vol. 1*, (Ed.: J.-P. Behr), John Wiley & Sons Inc., New York, **1994**.

[31] J. W. Yao, J. C. Cole, E. Pidcock, F. H. Allen, J. A. K. Howard, W. D. S. Motherwell, *Acta Crystallogr. Sect. B* **2002**, *58*, 640–646.

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