Drastic Increase in the Flexibility of Open Host Frameworks of a Steroidal Host Compound upon Shortening Its Spacer

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Nordeoxycholic acid (**NDCA**), which has a shorter side chain than the steroidal host compound, deoxycholic acid (**DCA**), forms inclusion crystals with various organic substances at 1:1 or 2:1 host–guest ratios. X-ray crystallographic studies reveal that four types of host frameworks (bilayer, monolayer, tape, and hexagonal) are generated by **NDCA**, in stark contrast to the robust and dominant bilayer frameworks formed from **DCA**, although they have the same functional groups capable of hydrogen bonding. The first three host frameworks are further divided into three, two, and four sub-types by arrangements of the hydrogen-bonded host columns, tapes, or layers, respectively. A total of nine types of open host frameworks are observed depending on the nature of the guest compounds. The sizes of the guest compounds induce isomerization of these host frameworks having molecular cavities, which is rationalized by the range of values of PC_{cavity}, which are ratios of the volumes between the guest compound and the host cavities. Such a drastic increase of flexibility of the open host framework by the slight chemical modification from **DCA** to **NDCA** deserves attention with respect to crystal engineering. Unique 2_1 helical assemblies of **DCA** are linked by the carboxyl group at the side chain to form a robust sheet-like structural motif. In **NDCA**, on the other hand, the linkage between the helices becomes impossible because of the shortening of the side chain's length, which results in destruction of the sheet-like motif to yield renewed molecular voids among the unique 2_1 helical assemblies. These remarkable differences in the flexibility of the open host frameworks provide us with a possible strategy for designing of new host compounds.

Introduction

Host compounds of lattice inclusion compounds usually include a wide range of guest components having various steric dimensions and functional groups.[1] The robust nature of the open host frameworks having one- or two-dimensional host cavities is regarded as an explanation for their versatile inclusion properties. The host−guest ratios decrease upon increasing the size of the guest components. These inclusion properties are similar to those of inorganic host compounds. For example, classical organic host compounds, such as urea,[2] tri-*o*-thymotide (TOT),[3] deoxycholic acid (3α,12α-dihydroxy-5β-cholan-24-oic acid, **DCA**),[4] and helical tubland hosts,[5] display this type of inclusion phenomenon. On the other hand, the flexibility of open host frameworks that are dependent on the nature of their included components has recently attracted much attention toward providing another explanation of their versatile enclathration.[3a,6−12] In this case, the host−guest ratios are usually 1:1, and the steric dimensions and functional groups of the guest components are widely variable and affect the open architectures of the host frameworks. As a result, both the robustness and flexibility of the open host frameworks enable such organic host compounds to include a wide range of the guest compounds. Classification of host compounds by the mechanisms of their wide inclusion abilities should be important for understanding the nature of the host compounds and for the design of useful host frameworks and host cavities.

The preparation of robust host frameworks by structural modification of host compounds has attracted much interest with the respect to the crystal engineering of nanoporous crystalline materials, because they are accessible for the development of host systems having adjustable and predictably shaped host cavities. Indeed, there have been many attempts to control the morphologies of host cavities by modification of host compounds known to form robust frameworks. For instance, changing the spacing units between the functional groups capable of hydrogen bonding has been attempted to control the sizes of host cavities.[13] These strategies have not always been effective, however, and they often yield host frameworks that differ from the original ones, even though they have numerous divergent

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hydrogen bonding sites in their molecular structures.[14] This phenomenon indicates that some of the factors for designing robust host frameworks remain unclear. Therefore, there is a need for a strategy in which the flexibility of open host frameworks can be adjusted so that various host cavities are generated and designed from molecular considerations. In this report, we describe the drastic change that occurs in the flexibility of open host frameworks upon shortening the distance between the hydrogen bonding functional groups of **DCA** by one methylene unit.

DCA is one of the oldest and commercially available host compounds that include a wide range of organic substances.[4] Wieland's discovery of its crystalline inclusion compounds with fatty acids dates back to the early 1910s, and a series of molecular crystalline compounds, called "choleic acids," has been studied extensively. X-ray crystallography revealed that **DCA** forms unique bilayer structures having alternating stacks of hydrophobic and lipophilic layers. The bent molecular shape of **DCA** provides molecular channels, one-dimensional molecular cavities, running through the lipophilic layer. Most organic guest compounds are included in this type of host framework. Such frameworks have been utilized as anisotropic reaction media for photoreactions and polymerizations.[15,16] Only a hydrate crystal gives another structure, namely that of a hexagonal type.[17] Moreover, some derivatives prepared by modification of the side chains, for example, the methyl ester,[18] amides,[19] and sodium salt,[20] have been reported to form similar bilayer structures featuring molecular channels. In particular, alkylammonium salts of **DCA** allow fine-tuning of the host cavities to be controlled by the sizes of the aliphatic portions of the ammonium cations.[21]

The robustness of the bilayer structure of **DCA** is attributed mainly to intermolecular hydrogen bonding between steroidal α-faces (hydrophilic faces). From the nature of the planar asymmetric steroidal skeleton and the facial amphiphilicity, the 2_1 helical tape assembly shown in Figure 1 (a) may be regarded as the dominant assembly.[22] This characteristic assembly is retained by the two hydroxy groups at the C3 and C12 positions. Moreover, as shown in Figure 1 (b), carboxyl groups at the side chain link the neighboring tape assemblies with the one-dimensional hydrogen bond networks to form the robust sheet-like structural motif. This robust sheet-like motif stacks up to generate the same channel-like host cavity as shown in Figure 1 (c). Consideration of the hierarchical scheme in this robust bilayer structure gave us an idea for the design of a new host, based on the strategy of breaking the linkages between the tape assemblies to generate independence in each tape to form new host cavities.

In this report, we describe the crystal structures and inclusion phenomena of 23-nordeoxycholic acid (3α,12α-dihydroxy-5β-23-norcholan-23-oic acid, **NDCA**), which has a shorter side chain, by one methylene unit, between the

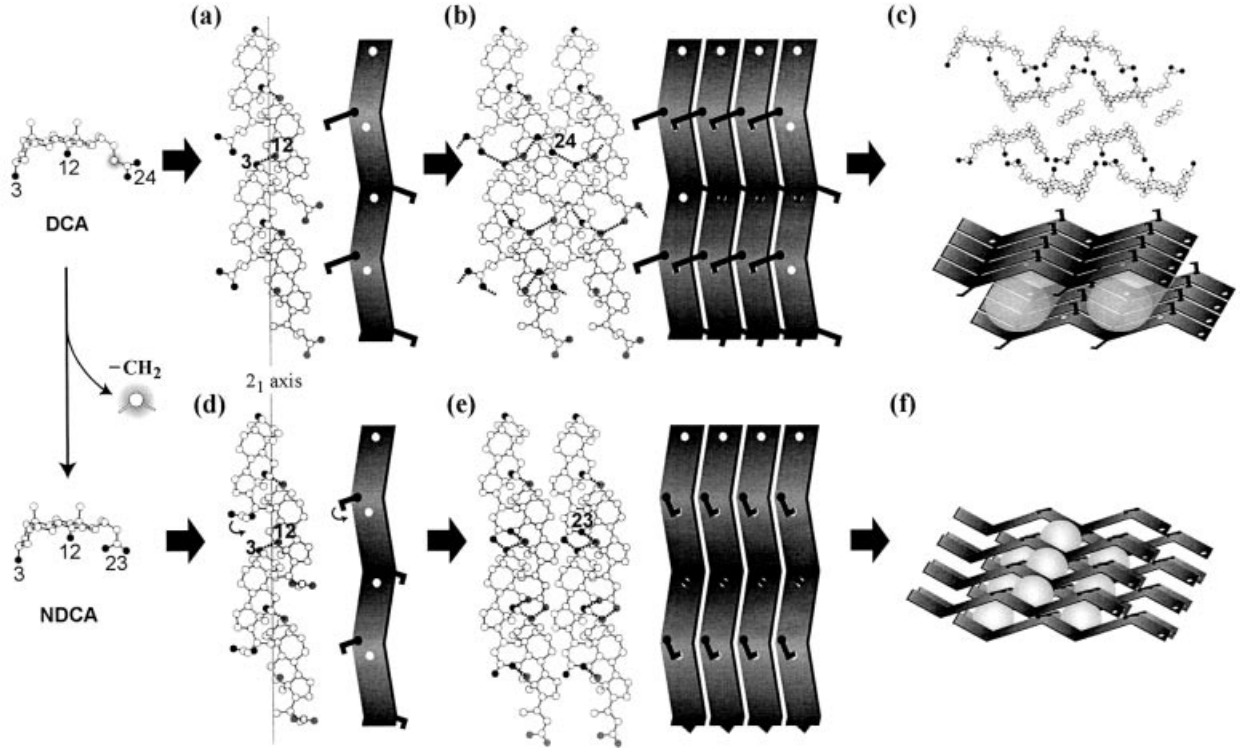
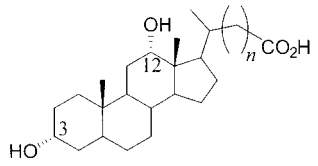


Figure 1. Molecular design of **NDCA** toward changing the flexibility of the host framework; (a) 2_1 helical tape assembly that is hydrogen bonded by two hydroxy groups at the C3 and C12 positions, (b) sheet-like structural motif that is hydrogen bonded by the carboxyl group at the side chain, and (c) host framework accompanying the channel-like host cavities of **DCA**; (d) 2_1 helical tape assembly of **NDCA** having a *gauche* conformation of the side chain; because the side chain is too short to link the tapes, conformational changes of the side chain are expected to form (e) a cyclic hydrogen-bonded network resulting in the independence of each tape; through a diverse range of aggregation modes, (f) various host frameworks should form from the new host cavities



n=1 ; nordeoxycholic acid (**NDCA**)
n=2 ; deoxycholic acid (**DCA**)

steroid rings and the terminal carboxylic acid on the side chain. Because this chemical modification conserves the number of hydrogen bond functional groups, the helical tape assembly should be preserved regardless of the length of the side chain (see d in Figure 1). The shortened side chain, however, is not long enough to link the neighboring tapes. Therefore, it may be possible that the carboxyl group of the side chain becomes hydrogen bonded within the tape through a cyclic hydrogen bond network, which would result in the structural independence of each tape, as shown in Figure 1 (e). As a result, the tape assemblies should stack up without the necessity of the sheet-like structural motif (see f in Figure 1) and so more varieties of host frameworks might be expected to form in the inclusion compounds of **NDCA**.

Results and Discussion

Formation of Inclusion Crystals

NDCA includes as many organic guests as **DCA**.[4] Table 1 lists the inclusion complexes of **NDCA**. In contrast to the variable host−guest ratios of **DCA**, most of the inclusion crystals of **NDCA** have 1:1 or 2:1 host−guest ratios, independent of the steric dimensions of the guest compounds. X-ray diffraction (XRD) patterns illustrate that **NDCA** has nine types of host architectures, which are summarized in Table 1. This phenomenon suggests that the versatile inclusion ability can be attributed to structural isomerizations of the open host frameworks. All these complexes were characterized further by X-ray crystallography.

Destruction of a Robust Sheet-Like Structural Motif by Breaking the Linkage between the Helical Assemblies

Chemical modification of **NDCA** from **DCA** completely conserves the number of the hydrogen-bonding functional groups and the steroidal skeleton. Therefore, the characteristic 2_1 helical tape assembly of **DCA** (Figure 1, a) can be adopted regardless of the length of the side chain. When

Table 1. Guest compounds for **NDCA**

Guest	H:G ratio[a]	Host framework[b]	Guest	H:G ratio[a]	Host framework[b]
Methanol	1:1	**H**	Acetone	2:1	**C1**
Ethanol	1:1	**M1**	2-Butanone	2:1	**C1**
1-Propanol	1:1	**M1**	2-Pentanone	2:1	**C1**
2-Propanol	1:1	**M1**	3-Pentanone	2:1	**C1**
2-Methyl-1-propanol	1:1	**M1**	2-Hexanone	GF	**T4**
2-Methyl-2-propanol	1:1	**M2**	2,4-Pentadione	2:1	**C1**
1-Butanol	2:1	**C1**	Cyclohexanone	2:1	**C1**
2-Butanol	1:1	**M1**	Acetophenone	2:1	**C2**
2,2-Dimethyl-1-propanol	1:1	**M2**	2′-Hydroxyacetophenone	1:1	**T1**
2-Methyl-1-butanol	1:1	**M2**	4′-Methylacetophenone	2:1	**C2**
3-Methyl-1-butanol	1:1	**T1**	3′-Methoxyacetophenone	2:1	**T2**
2-Methyl-2-butanol	1:1	**M2**	Propiophenone	GF	**T4**
3-Methyl-1-butanol	1:1	**M2**	1-Acetonaphthone	GF	**T4**
1-Pentanol	2:1	**C1**	1,4-Dioxane	2:1	**C1**
2-Pentanol	2:1	**C1**	Tetrahydrofuran	2:1	**C1**
3-Pentanol	2:1	**C1**	Anisole	1:1	**T1**
2-Ethyl-1-butanol	1:1	**M2**	Ethyl acetate	GF	**T4**
3,3-Dimethyl-1-butanol	1:1	**M2**	Ethyl propionate	GF	T4
2,3-Dimethyl-2-butanol	1:1	**M2**	Methyl benzoate	2:2	**C2**
3,3-Dimethyl-2-butanol	1:1	**M2**	γ-Butyrolactone	2:1	**C1**
2-Methyl-1-pentanol	1:1	**T3**	γ-Valerolactone	2:1	**C1**
3-Methyl-1-pentanol	2:1	**C1**	γ-Heptalactone	2:1	**C1**
4-Methyl-1-pentanol	2:1	**T1**	Acetonitrile	2:1	**C1**
2-Methyl-2-pentanol	1:1	**M2**	Propionitrile	2:1	**C1**
3-Methyl-2-pentanol	1:1	**M2**	Acrylonitrile	2:1	**C1**
4-Methyl-2-pentanol	1:1	**M3**	Benzonitrile	2:1	**C1**
2-Methyl-3-pentanol	1:1	**M2**	Benzene	1:1	**T1**
3-Methyl-3-pentanol	1:1	**M2**	Toluene	1:1	**T1**
1-Hexanol	2:1	**C1**	*o*-Xylene	1:1	**T1**
2-Hexanol	1:1	**M2**	*m*-Xylene	GF	**T4**
3-Hexanol	GF[c]	**C4**	*p*-Xylene	GF	**T4**
1-Nonanol	GF	**C4**			
Benzyl alcohol	1:1	**T1**			

[a] Determined by TG. [b] Determined by XRD, see Exp. Sect. **H**: hexagonal type; **M1**, **M2**, and **M3**: monolayer types; **C1** and **C2**: *C*2-tape types; **T1**, **T2**, **T3**, and **T4**: T types. [c] GF = guest-free crystal.

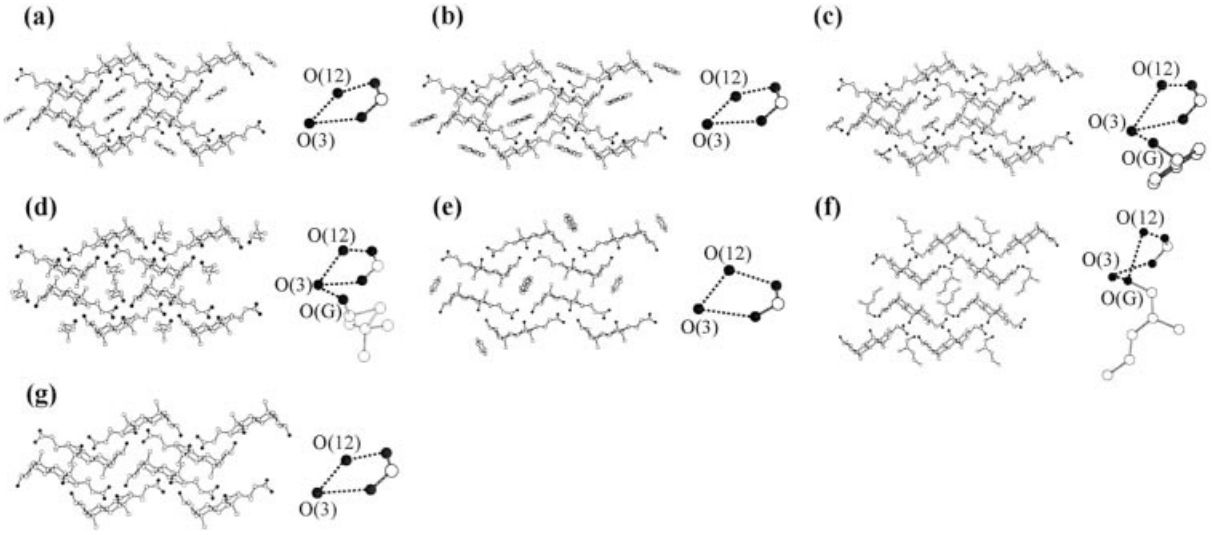


Figure 2. Crystal structures and hydrogen bonding networks of **NDCA** cocrystallized with (a) toluene (1:1), (b) *o*-xylene (1:1), (c) benzyl alcohol (1:1), (d) 3,3-dimethyl-1-butanol (1:1), (e) 3′-methoxyacetophenone (2:1), and (f) 2-methyl-1-pentanol (1:1), and in its (g) guest-free state; hydrogen atoms have been omitted for clarity

NDCA forms the tape assembly, however, the shortened side chain is expected to break the linkage between the tape assemblies, as shown in Figure 1 (e) . Actually, the same tape assembly as **DCA** is observed in some of the inclusion compounds of **NDCA** without any linking between neighboring tapes. Figure 2 depicts the molecular packing diagrams and corresponding hydrogen bond networks of six inclusion crystals and a guest-free crystal of **NDCA**. All of these seven structures are composed of a common tape assembly that aggregates in different ways. Because the side chain is too short to form the one-dimensional hydrogen bond network, as observed for **DCA**, the carboxyl group at the side chain forms a closed cyclic network with the sequence OH(23a)···OH(3)···OH(12)···O(23b), except for 2-methyl-1-pentanol (see f in Figure 1), where the hydroxy group of the guest alcohol is hydrogen-bonded between the OH(3) and OH(12) units.

To form this closed, cyclic hydrogen bond network, conformational changes of the side chain are needed, as shown in Figure 1 (d). The C17−C20−C22−C23 torsion angles for **DCA** and **NDCA** in the inclusion crystals of *o*-xylene are 60° (*gauche*) and 172° (*trans*), respectively. The *gauche* conformation keeps the carboxyl group away from the 2_1 axis (Figure 1, a, b, and d). This orientation of the carboxyl group is suitable for binding to the neighboring tape assembly. On the other hand, the *trans* conformation brings the carboxyl group close to the 2_1 axis to form the cyclic network (Figure 1, e). As we see from Figure 1 (e), the *trans* conformation of **NDCA** is more suitable for the cyclic hydrogen bond network when compared to an imaginary *trans* conformation of **DCA**. In this way, the conformational change induced by the shortened side chain is the rational result based on the formation of the possible hydrogen bonds of the side chain. Consequently, as expected in Figure 1 (f), these closed hydrogen bond networks actually give the tape assemblies independence from the dominance of the robust sheet-like structural motif of **DCA**.

Based on the differences of the aggregation manners of the characteristic 2_1 helical tape assemblies, these structures are classified into four types, which we name as T1, T2, T3, and T4, respectively. The inclusion crystals of toluene, *o*-xylene, benzyl alcohol, and 3,3-dimethyl-1-butanol are classified as T1 types. The crystals of 3′-methoxyacetophenone, 2-methyl-1-pentanol, and the guest-free host be-

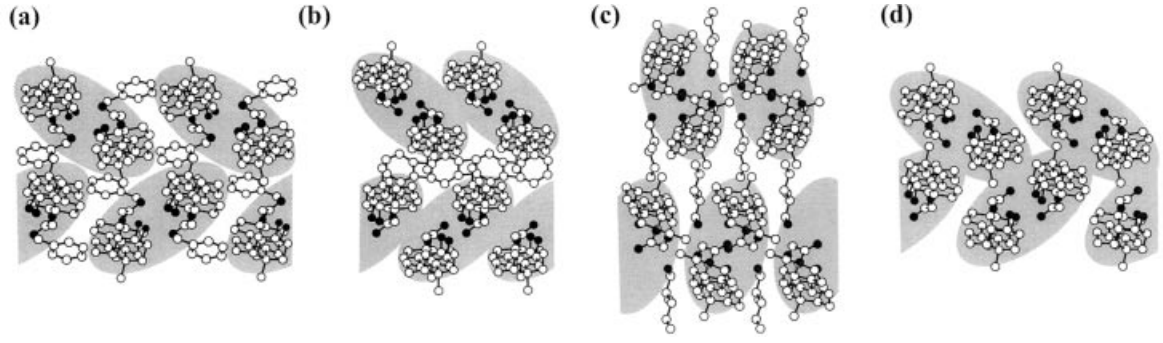


Figure 3. Side views of the four distinct aggregation modes of the common 2_1 helical tape assembly: (a) T1, (b) T2, (c) T3, and (d) T4; the shadowed ellipse represents the characteristic 2_1 helical tape assembly viewed from the axis

long to the T2, T3 and T4 types, respectively. Figure 3 depicts the side views of the four types of frameworks with each of the tapes highlighted in gray. The densest packing of the tapes is observed in the guest-free crystal, T4 (see d in Figure 3). Vertical expansion between the tapes yields the T1-type aggregation manner. Further expansion in a vertical direction produces the T2-type aggregation. T3-type aggregation is the result of extreme horizontal contraction. In this way, the shortening of the side chain actually induces diversity into the aggregation manner of the tape assemblies by intercepting the crucial hydrogen bond network of the robust sheet-like motif of **DCA**.

Furthermore, the diverse aggregation manners of the tape assemblies lead to various host cavities depending on the nature of the guest compounds. Aromatic compounds with relative small substituents, such as benzene, toluene, and benzyl alcohol, are included in the T1 type. In the case of benzyl alcohol, the hydroxy group takes part in the cyclic hydrogen bond network and the phenyl ring is suitable for the steric dimension of the channel. The larger aromatic compounds are included in the T2 type assembly with 2:1 host−guest ratios. The T3 type is a unique host framework that includes only 2-methyl-1-pentanol. The hydroxy group takes part in the hydrogen bond network in the same manner as benzyl alcohol does in the T1 type. Figure 4 displays cross sections of the host cavities. They are all channel-type one-dimensional host cavities having dimensions of 4.6 Å × 7.6 Å (*c* axis) for T1, 4.2 Å × 11.2 Å (*a* axis) for T2, and 7.7 Å × 9.3 Å (*c* axis) for T3. In the case of T3, the thin and flat guest alcohol is enclosed within the much wider and thinner host cavity relative to the other two frameworks. The alkyl group spreads perpendicular to the direction of the channel. The wavy wall of the channel fits the shape of the guest component. Steric complementary and

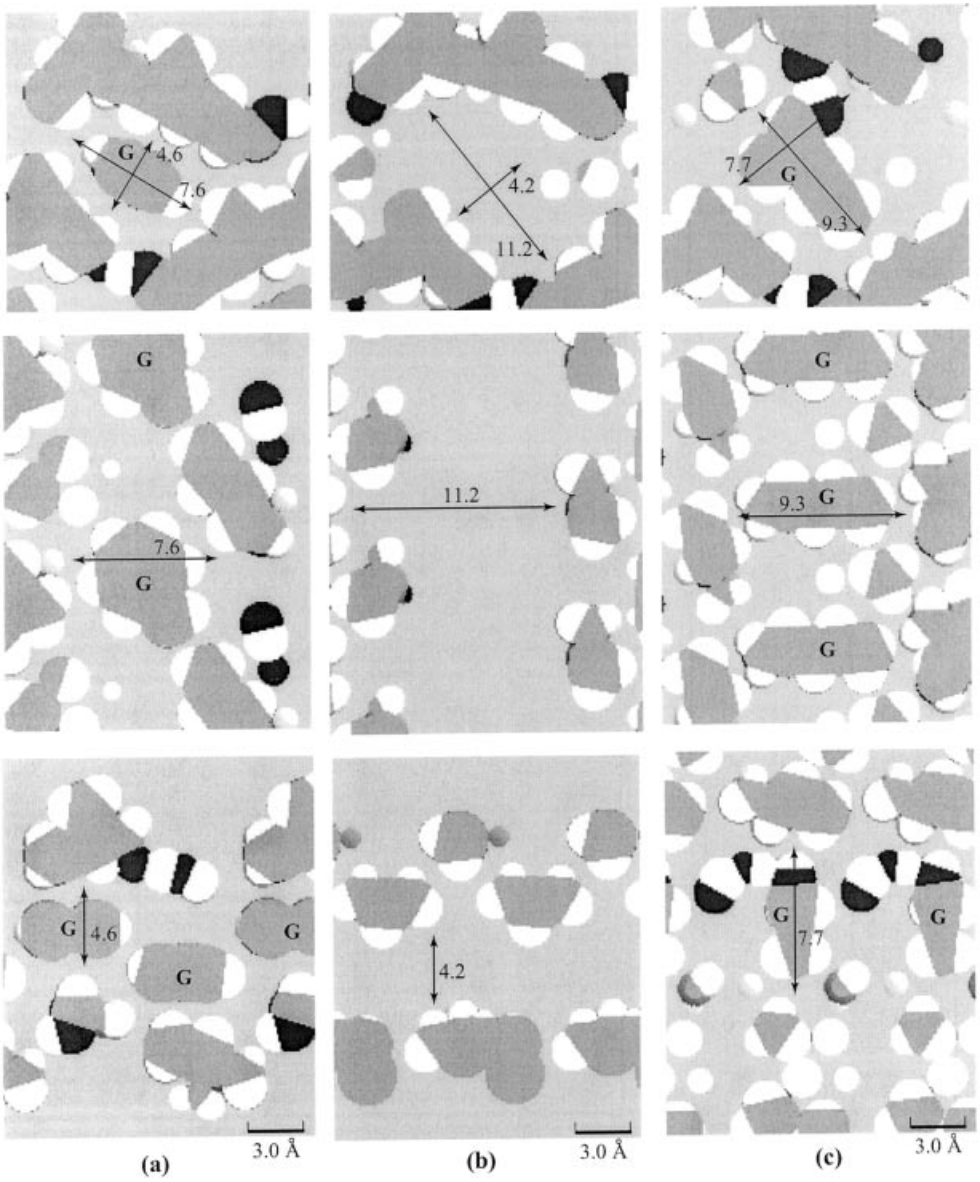


Figure 4. Tomographies of (a) toluene (T1, top *c* axis, middle *b* axis, bottom *a* axis), (b) 3′-methoxyacetophenone (T2, top *a* axis, middle *c* axis, bottom *b* axis), (c) 2-methyl-1-pentanol (T3, top *c* axis, middle *b* axis, bottom *a* axis), respectively

hydrogen bonding contribute to stabilize this T3-type structure. On the other hand, T1 and T2 have the narrow channels (ca. 4.6 and 4.2 Å thicknesses, respectively). These thicknesses are suitable for incorporating phenyl rings, and, thus, benzene and toluene are included. In the T2 type, the wall of the host channel is the most smooth, which enables it to form 2:1 complexes with larger aromatic compounds. Thus, the shortening of the side chain results not only in diversity for the manner in which aggregation of the tape assemblies occurs, but also in the various corresponding host cavities that capture various guest compounds inside.

Diverse Host Frameworks Based on Reconstruction of the Characteristic Tape Assembly

Twenty crystal structures of **NDCA** with various guest compounds, including the seven structures described above, have been solved. The crystallographic parameters are listed in Table 2. Figure 5 depicts molecular packing diagrams and the corresponding hydrogen bond networks of the thirteen structures that are not composed of the 2_1 tape assembly described in Figure 1 (d). These thirteen structures are classified into three major types — monolayer (M), *C*2 tape (C), and hexagonal (H) — based on the hydrogen bonding networks as shown in Figure 6. In the M and C types, each framework is composed of another structural motif that is not a remnant of the structure of **DCA**. Furthermore, from the differences between the aggregation manners of the tape assemblies, the M and C types are divided further into sub-types: M1, M2, M3, C1, and C2. In this way, shortening of the methylene spacer at the side chain produces the three new types of open host frameworks — monolayer, *C*2 tape, and hexagonal — that have not been observed in complexes of **DCA**. This phenomenon also is the result of intercepting the crucial hydrogen bond network of the robust sheet-like motif (see b in Figure 1).

Monolayer (M) Types

Figure 5 (a−f) show the crystal structures and hydrogen bond networks of the M-type structures. The characteristic feature is a columnar monolayer structure. The host molecules stack along the *b* axis mediated by hydrogen bonding between a carboxyl group of one host molecule and two hydroxy groups from another (Figure 7). The host−host hydrogen bonds yield the monolayer column. Guest molecules are incorporated in the cavities between the host columns. The hydroxy group takes part in the linear hydrogen bond network, and the alkyl group is surrounded by the lipophilic faces of the host columns. Therefore, all the guest compounds included in M-type structures are alcohols and the host−guest ratios are 1:1.

Three sub-types of the monolayer type structures are distinguished by the arrangements of the host columns: an alternating overlap type in M1, a parallel type in M2, and a herring-bone type in M3, as shown in Figure 7 (see c−e), respectively. Ethanol, 1-propanol, and 2-methyl-1-propanol are included in the M1 type and 3-methyl-2-butanol and 3,3-dimethyl-1-butanol are included in the M2 type. 4-Methyl-2-pentanol is the only guest compound that is included in the M3 type. **NDCA** changes the host frameworks in response to the sizes and shapes of the alkyl group of the included alcohols.

To estimate the steric dimensions of the host cavities, we analyzed cross-sections of the host cavities, as shown in Figure 8. The steric dimensions are the irregular squares are 4.7 Å × 7.1 Å (viewed down the *c* axis) for M1, 6.9 Å × 7.8 Å (viewed down the *c* axis) for M2, and 8.7 Å × 6.9 Å (viewed down the *b* axis) for M3, respectively. M1 has the narrowest cavity and includes ethanol and propanol. The larger cavity in M2 is able to include a variety of aliphatic alcohols having more than four carbon atoms. M3 has suitable host cavities for more bulky 4-methyl-2-pentanol.

C2 Tape (C) Types

Figure 5 (see g−l) show the crystal structures of C-type aggergates. The most remarkable structural feature is the tape structure formed by hydrogen bonds. In the hydrophilic layer, a cyclic hydrogen bond network involves two hydroxy groups at the 3-position and two carboxylic acid units at the side chain from four different host molecules. This assembly links the host molecules in an anti-parallel manner to yield a corrugated tape (see a in Figure 9). The hydroxy group at the 12-position does not take part in the host−host hydrogen bond network.

In the lipophilic layer, the hydrogen-bonded tapes stack in a parallel manner for C1 (see b in Figure 9) and in a herring-bone manner for C2 (see c in Figure 9) as a result of van der Waals interactions and steric complementary. The parallel arrangement provides small void spaces between the side chains because of the unbalanced molecular structure that consists of a wide steroidal plane and a narrow side chain. The herring-bone arrangement enlarges the host cavity between the tapes. Cross sections of the host cavities in C1 and C2 are shown in Figure 10 (a and b). These cavities have rectangular cavities with dimensions of 8.6 Å × 6.2 Å (*c* axis) and 7.2 Å × 12.0 Å (*b* axis), respectively. In the former type, small, aliphatic, polar organic compounds, such as acetone, 2-butanone, propionitrile, and γ-valerolactone, are included in 2:1 host−guest ratios. In the case of the alcohols as guests, the hydroxy group forms a guest-to-host hydrogen bond. The thickness and width of the host cavities in the C2 type structures only fit aromatic rings (ca. 3.5 Å). This steric fit and the hydrogen bond stabilize the inclusion crystals at 1:1 host−guest ratios. Acetophenone and 4′-methylacetophenone are included in the C2 type. The sizes of the guest compounds isomerize the open host frameworks without changing the nature of the hydrogen bond networks.

Hexagonal (H) Type

The methanol clathrate of **NDCA** forms a hexagonal structure having a 1:1 host−guest ratio. The crystal structure and hydrogen bond network are depicted in Figure 5 (m). The structural feature is the honeycomb arrangement,

Table 2. Crystallographic data of **NDCA**

Guest compound: (monolayer)	Methanol	Ethanol	1-Propanol	2-Methyl-1-propanol	3-Methyl-2-butanol	3,3-Dimethyl-1-butanol	4-Methyl-2-pentanol
Formula	$C_{24}H_{42}O_5$	$C_{26}H_{44}O_5$	$C_{26}H_{46}O_5$	$C_{27}H_{48}O_5$	$C_{28}H_{50}O_5$	$C_{29}H_{52}O_5$	$C_{29}H_{52}O_5$
Molecular mass	410.59	424.62	438.65	452.67	466.70	480.73	480.73
Crystal system	hexagonal	monoclinic	monoclinic	monoclinic	monoclinic	monoclinic	orthorhombic
Space Group	$P6_5$	$P2_1$	$P2_1$	$P2_1$	$C2$	$C2$	$P2_12_12_1$
a (Å)	14.9763(9)	11.247(10)	11.637(8)	11.7891(8)	22.061(1)	22.434(3)	12.385(5)
b (Å)	–	10.303(5)	9.941(7)	9.9351(8)	10.1160(5)	10.154(2)	23.215(4)
c (Å)	17.458(1)	12.059(7)	12.38(2)	12.675(1)	12.6721(7)	12.828(2)	10.224(3)
α (deg)	–	–	–	–	–	–	–
β (deg)	–	117.13(4)	116.93(2)	115.757(4)	94.460(2)	93.963(5)	–
γ (deg)	–	–	–	–	–	–	–
V (Å^3)	3391.0(4)	1243.0(1)	1277.0(1)	1337.1(2)	2819.5(2)	2915.4(7)	2939.0(1)
Z	6	2	2	2	4	4	4
$D_{calcd.}$ (g/cm^3)	1.206	1.134	1.141	1.124	1.099	1.095	1.086
Number of unique reflections	2126	3026	2008	2498	2614	2690	2002
Number of observed reflections	1644	2715	1883	2232	1958	1537	1680
R_1; Rw	0.074; 0.179	0.041; 0.052	0.053; 0.119	0.070; 0.179	0.061; 0.146	0.138; 0.366	0.058; 0.103
GOF	1.47	1.84	1.34	1.64	1.36	1.91	1.27
$2\theta_{max.}$ (deg)	136.4	55.0	50.0	136.5	136.5	136.5	50.0
R/P	6.25	7.05	6.72	7.70	6.36	6.12	5.47
Temperature (°C)	−60	23.0	−72	−60	25	23	−69
Host framework	H	M1	M1	M1	M2	M2	M3

Guest compound	Propionitrile	Acetone	2-Butanone	γ-Valerolactone	Acetophenone	4′-Methyl-acetophenone	Guest-free
Formula	$C_{49}H_{81}O_8N$	$C_{49}H_{82}O_9$	$C_{50}H_{84}O_9$	$C_{51}H_{84}O_{10}$	$C_{54}H_{84}O_9$	$C_{55}H_{86}O_9$	$C_{23}H_{38}O_4$
Molecular mass	812.18	815.18	829.21	857.22	877.25	891.28	378.55
Crystal system	monoclinic	triclinic	triclinic	monoclinic	monoclinic	monoclinic	orthorhombic
Space Group	$P2_1$	$P1$	$P2_1$	$P2_1$	$P2_1$	$P2_1$	$P2_12_12_1$
a (Å)	15.316(10)	10.5710(9)	10.956(1)	15.213(6)	10.876(2)	10.9501(4)	13.4507(9)
b (Å)	7.624(1)	15.269(2)	15.318(2)	7.622(5)	15.2052(9)	15.4233(6)	14.7280(7)
c (Å)	20.479(3)	7.583(3)	7.699(4)	20.885(7)	15.340(2)	15.3023(7)	10.8338(8)
α (deg)	–	92.47(2)	90.01(3)	–	–	–	–
β (deg)	100.309(3)	104.61(2)	110.58(3)	99.14(2)	98.89(1)	98.478(2)	–
γ (deg)	–	80.221(9)	80.695(10)	–	–	–	–
V (Å^3)	2352(1)	1167.1(4)	1191.4(7)	2390(1)	2506.3(5)	2556.1(2)	2146.2(2)
Z	2	1	1	2	2	2	4
$D_{calcd.}$ (g/cm^3)	1.146	1.160	1.156	1.191	1.162	1.158	1.171
Number of unique reflections	3913	3696	3581	4075	4651	4664	2132
Number of observed reflections	3814	3619	3454	3662	4423	3558	2132
R_1; Rw	0.053; 0.152	0.095; 0.220	0.066; 0.179	0.057; 0.124	0.047; 0.108	0.051; 0.115	0.060; 0.149
GOF	1.54	1.04	1.76	1.15	1.09	1.19	1.54
$2\theta_{max.}$ (deg)	50.0	50.1	50.0	51.2	51.3	136.5	136.5
R/P	7.29		6.37	6.66	7.79	6.16	8.70
Temperature (°C)	−64	−64	15	−75	20	23	−70
Host framework	C1	C1	C1	C1	C2	C2	T4

Guest compound	Toluene	*o*-Xylene	Benzyl alcohol	3′-Methoxy-acetophenone	2-Methyl-1-pentanol	3,3-Dimethyl-1-butanol (T type)
Formula	$C_{30}H_{46}O_9$	$C_{32}H_{50}O_4$	$C_{30}H_{46}O_5$	$C_{27.5}H_{42}O_5$	$C_{29}H_{52}O_5$	$C_{29}H_{52}O_5$
Molecular mass	470.69	498.74	486.69	453.64	480.73	480.73
Crystal system	orthorhombic	orthorhombic	orthorhombic	orthorhombic	orthorhombic	orthorhombic
Space Group	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$
a (Å)	14.815(1)	14.950(1)	14.700(3)	15.442(2)	14.1767(5)	14.819(4)
b (Å)	15.833(4)	15.931(1)	16.439(4)	21.071(2)	25.5717(8)	18.036(6)
c (Å)	11.412(1)	11.4388(8)	11.481(5)	7.7443(7)	7.5273(2)	10.869(4)
α (deg)	–	–	–	–	–	–
β (deg)	–	–	–	–	–	–
γ (deg)	–	–	–	–	–	–
V (Å^3)	2676.8(8)	2724.4(4)	2773(1)	2519.9(4)	2728.8(1)	2905(1)
Z	4	4	4	4	4	4
$D_{calcd.}$ (g/cm^3)	1.168	1.216	1.165	1.196	1.170	1.099
Number of unique reflections	2499	2683	3589	2607	2832	3770
Number of observed reflections	2392	2110	1916	2356	2534	1461
R_1; Rw	0.096; 0.277	0.061; 0.159	0.060; 0.051	0.143; 0.339	0.114; 0.279	0.148; 0.350
GOF	1.92	1.27	1.85	3.00	1.42	2.70
$2\theta_{max.}$ (deg)	51.3	136.5	55.0	136.5	136.4	55.0
R/P	9.53	7.79	6.06	9.39	8.23	5.66
Temperature (°C)	−60	−75	25	−75	−75	20
Host framework	T1	T1	T1	T2	T3	T1

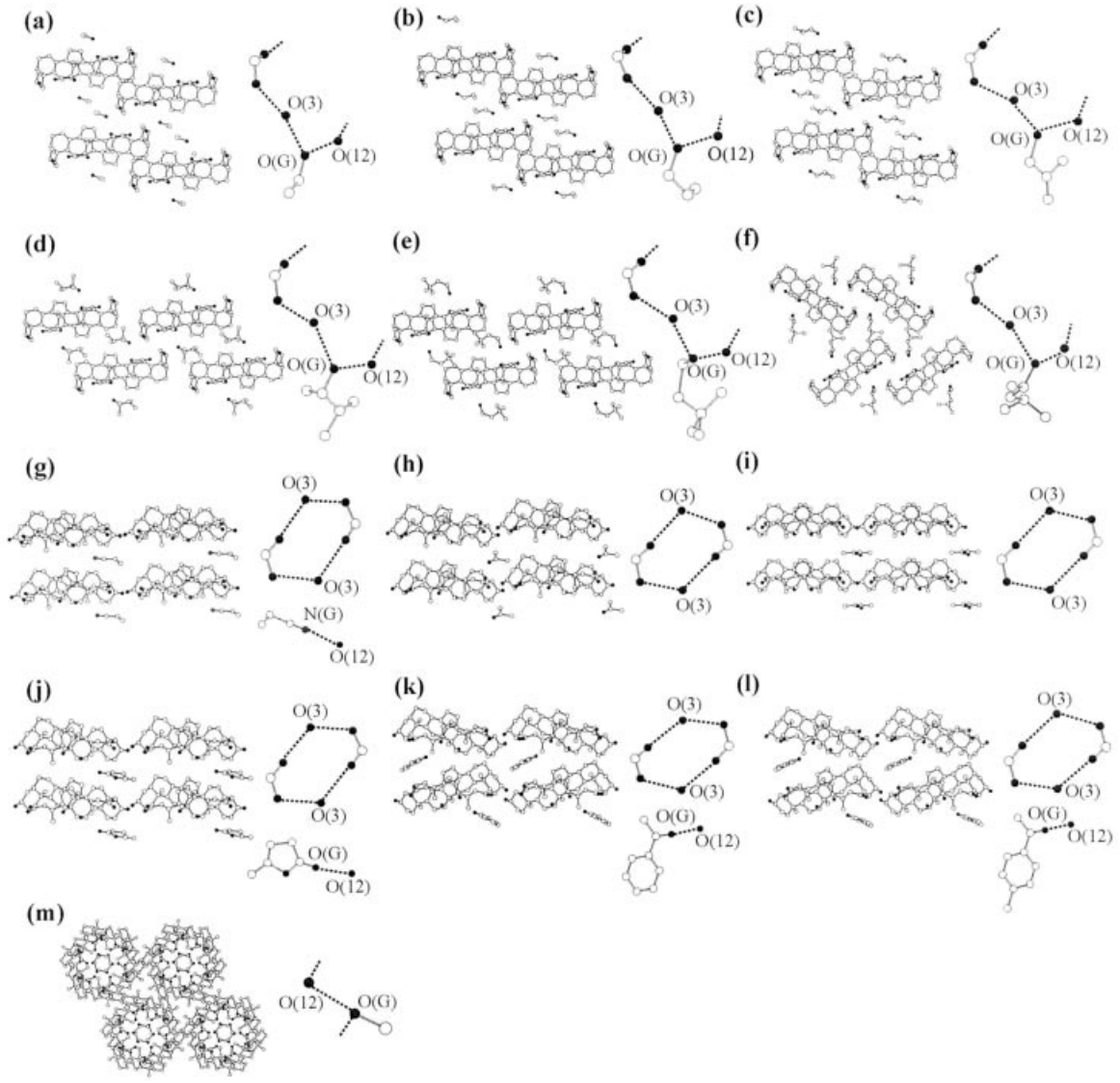


Figure 5. Crystal structures and hydrogen bond networks of **NDCA** cocrystallized with (a) ethanol (1:1), (b) 1-propanol (1:1), (c) 2-methyl-1-propanol (1:1), (d) 3-methyl-2-butanol (1:1), (e) 3,3-dimethyl-1-butanol (1:1), (f) 4-methyl-2-pentanol (1:1), (g) propionitrile (2:1), (h) acetone (2:1), (i) 2-butanone (2:1), (j) γ-valerolactone (2:1), (k) acetophenone (2:1), (l) 4′-methylacetophenone (2:1), and (m) methanol (1:1); hydrogen atoms have been omitted for clarity

in which the host compounds are arranged along a sixfold screw axis. The columns have a hydrophilic core and a lipophilic surface, as shown in Figure 11. In the hydrophilic core, complicated one-dimensional hydrogen bond networks occur between the host and guest compounds. The methanol guest molecule is included in the core. The resulting lipophilic columns assemble by van der Waals interactions.

Isomerization of Host Frameworks by Functional Groups for Major Types

To understand how the host frameworks adapt to the guest components, we characterized the host frameworks of all inclusion crystals by XRD. The major three types of host frameworks depend on the nature of the functional groups of the guest compounds and, in particular, on their hydrogen bonding properties. Firstly, aliphatic alcohols that mostly act as hydrogen bond donors and hydrogen bond acceptors are included in the M-type structures. The resulting helical hydrogen bond networks involve two host−guest hydrogen bonds, which causes stable inclusion crystals to form. When the shapes and sizes of the alkyl parts are not suitable for the M types, the host frameworks isomerize to other types, for example, methanol gives the H type and 2-methyl-1-pentanol gives the T3 type. Secondly, since ketones and nitriles have hydrogen bond acceptors, they tend to be included in the C-type structures. The host frameworks are constructed of a cyclic hydrogen bond network involving the two hydroxy groups at the 3-position and the two carboxylic acid units at the side chain. The hydroxy group at the 12-position is free from the construc-

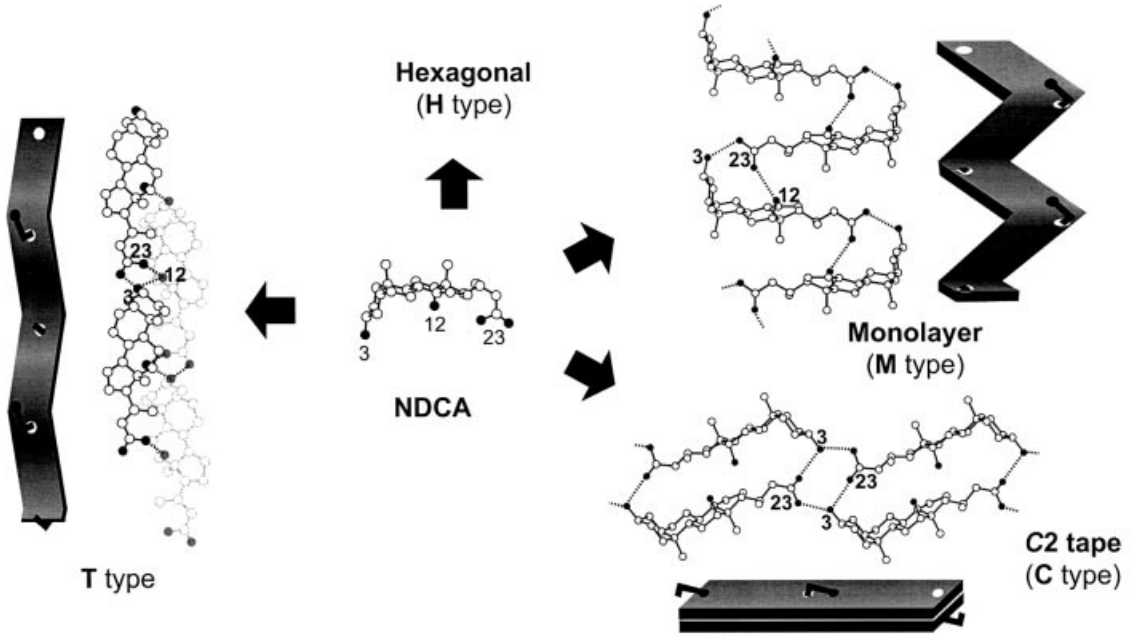


Figure 6. Four distinct structural motifs of **NDCA**; three structural motifs, the M, C, and H types, are retained from the different hydrogen bond networks of **DCA**, but the T type is not

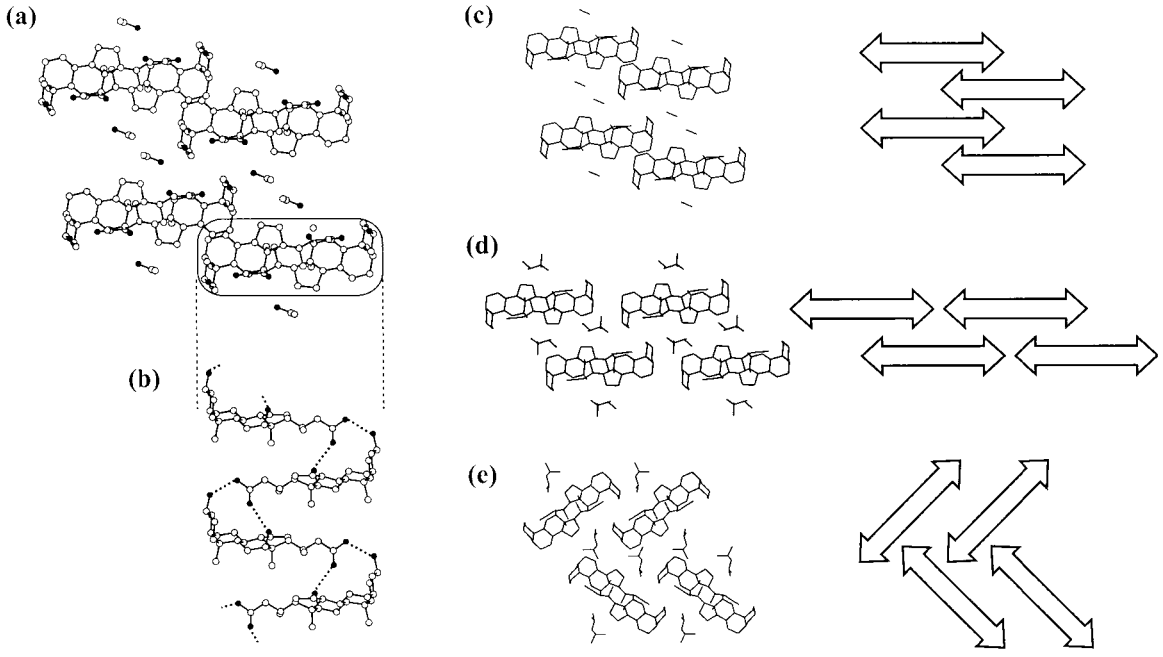


Figure 7. Schematic representations of monolayer (M) types; (a) crystal structure of **NDCA** cocrystallized with ethanol (1:1), viewed from the crystallographic *b* axis, and (b) side view of the monolayer column; (c) ethanol, M1; (d) 3-methyl-2-butanol, M2; (e) 4-methyl-2-pentanol, M3; respectively

tion of the host framework and, thus, is utilized as a hydrogen bond to "hook" the guest compounds. Finally, aromatic compounds are included in the T-type structures. They have a large host cavity and thin void spaces, which are suitable only to bind phenyl rings. The guest compounds having hydrogen bond acceptors form the C2-type frameworks. Host-to-guest hydrogen bonding plays an essential role for formation of this type of structure. Therefore, aromatic ketones and esters, such as acetophenone and methyl benzoate, are included in the C2 type. The absence of hydrogen bond acceptors or donors in the guest molecules results in the formation of T1-type structures. Benzene, toluene, and *o*-xylene belong to this type of structure. In the case of benzyl alcohol, the hydroxy group takes part in the cyclic hydrogen bond network in the T1 type of structure.

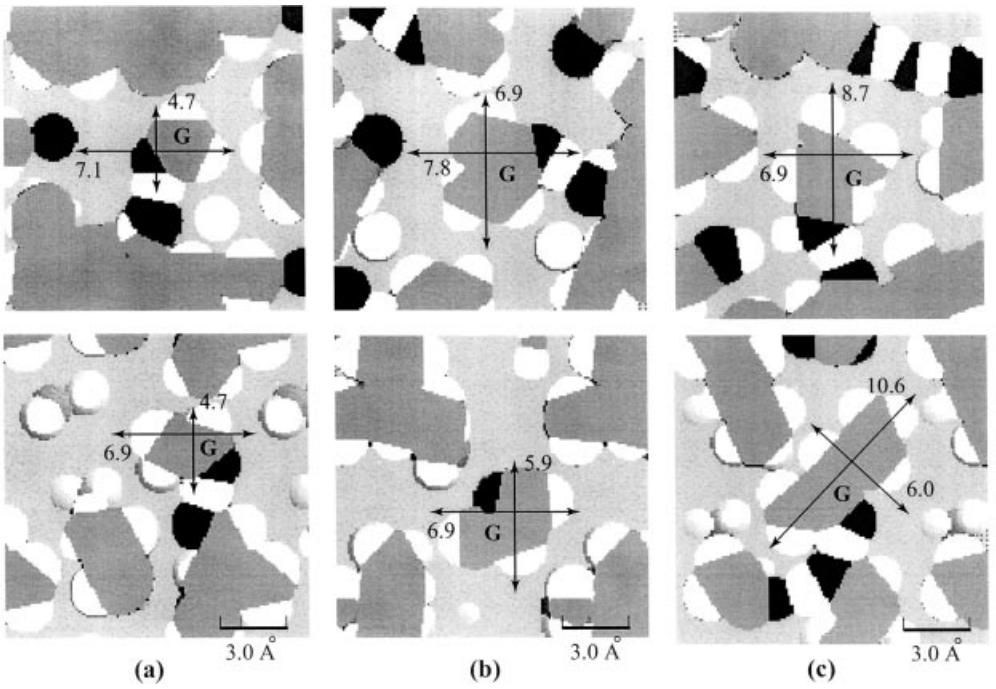


Figure 8. Tomographics of **NDCA** cocrystallized with (a) ethanol (M1, top *b* axis, bottom *c* axis), (b) 3-methyl-2-butanol (M2, top *b* axis, bottom *c* axis), and (c) 4-methyl-2-pentanol (M3, top *c* axis, bottom *a* axis)

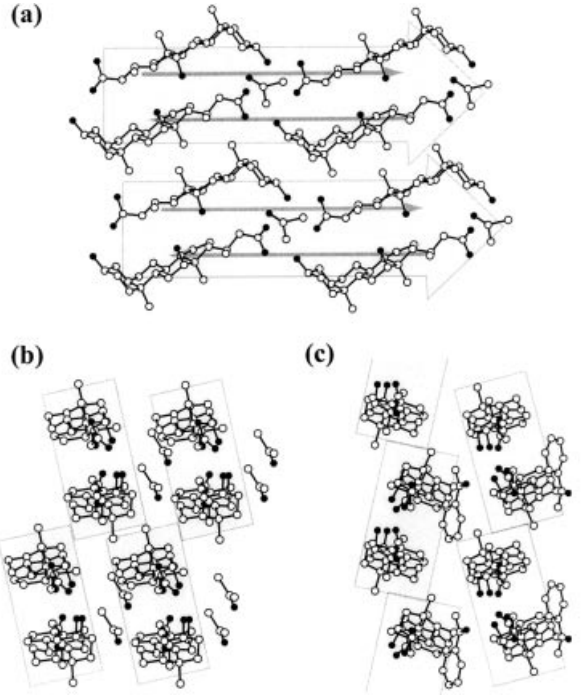


Figure 9. Schematic representations of *C*2 tape (C) types; (a) crystal structure of **NDCA** cocrystallized with acetone (2:1), viewed from crystallographic *c* axis [(b) a side view of tapes(C1)], and with (c) acetophenone (C2 viewed from crystallographic *c* axis)

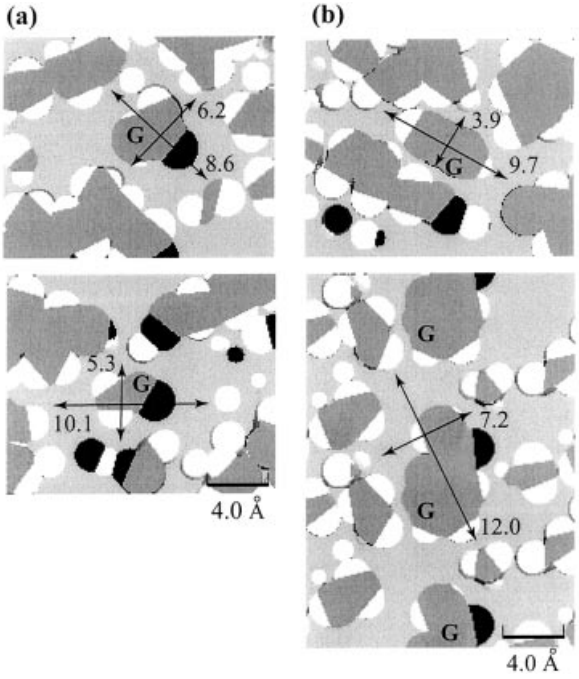


Figure 10. Tomographies of **NDCA** cocrystallized with (a) acetone (C1, top *c* axis bottom *a* axis) and (b) acetophenone (T2, top *a* axis, bottom *b* axis)

Isomerization of Host Frameworks by Size for Minor Types

To clarify the importance that the steric dimensions of the guest compounds have on the isomerization of the host frameworks, we calculated the packing coefficients of the host cavities (PC_{cavity}), which are volume ratios of the host cavities relative to the included guest compounds, as a parameter to define the steric fit between them.[11] Table 3 summarizes the parameters of all the examined inclusion crystals and the values of PC_{cavity} are plotted against the vol-

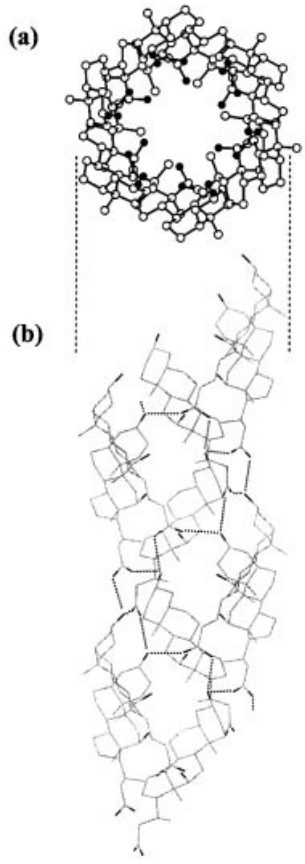


Figure 11. (a) Crystal structure of **NDCA** cocrystallized with methanol (1:1; H types), viewed from crystallographic *c* axis, and (b) a side view of the columns

umes of the guest compounds in Figure 12; these values lie in the range 0.38−0.74. In a series of the guest compounds of the M, C, and T types, the smaller guest compounds are included in the smaller M1-, C1-, and T1-type structures and the larger guests form the larger M2, C2, and T2 types. The boundaries of the guest volumes between them are 100, 110, and 130 Å^3 for the M, C, and T types, respectively. Exceeding the upper limits of the guest volumes gives rise to changes in the host frameworks by transforming the manner of aggregation , such as the monolayer column, tape, and layer structural motifs. These results indicate that the functional groups of the guest compounds play a primary role for formation of the major host frameworks and that the steric dimensions affect the formation of the minor host frameworks. The guest compounds having much different steric dimensions form unique host frameworks, such as M3 and T3.

Polymorphism of Inclusion Crystals

The host molecules change their host frameworks to fit the guest molecules. Some guest compounds, however, yield polymorphic crystals. For example, crystals from 3,3-dimethyl-1-butanol inclusion have both T-type (T1) (Figure 2, d) and monolayer-type (M2) structures (Figure 5, e), depending on the recrystallization temperature. The former is a low-temperature polymorph at 303 K and the latter a high-temperature one at 293 K. These structures have identical host−guest combinations as well as identical host−guest ratios. This pair is an example of polymorphism in a two-component system.[23] Moreover, this guest com-

Table 3. Packing coefficients of the selected crystalline inclusion compounds

Guest	No. of guest molecules in the unit cell	Molecular volume [Å^3]	V_{cavity} [a] [Å^3]	PC_{cavity} [b] [%]	Host framework
Methanol	6	38.9	357.1	65.4	**H**
Ethanol	2	55.6	208.2	53.4	**M1**
1-Propanol	2	73.1	243.2	60.1	**M1**
2-Methyl-1-propanol	2	90.3	308.6	58.5	**M1**
3-Methyl-2-butanol	4	107.2	1122	38.2	**M2**
3,3-Dimethyl-1-butanol	4	124.6	1039	48.0	**M2**
4-Methyl-2-pentanol	4	124.7	880.6	56.6	**M3**
Propionitrile	2	64.9	319.1	40.7	**C1**
Acetone	1	66.3	162.2	40.9	**C1**
2-Butanone	1	83.5	177.3	47.1	**C1**
γ-Valerolactone	2	100.4	330.7	60.7	**C1**
Acetophenone	2	120.9	454.0	53.3	**C2**
4′-Methylacetophenone	2	131.7	471.8	55.8	**C2**
Toluene	4	100.8	623.3	64.7	**T1**
o-Xylene	4	117.5	672.0	70.0	**T1**
Benzyl alcohol	4	110.7	659.2	67.2	**T1**
3′-Methoxyacetophenone	4	138.3	523.2	52.9	**T2**
2-Methyl-1-pentanol	4	126.0	683.4	73.8	**T3**

[a] V_{cavity} is the volume of the unit cell calculated using a 0.7-Å-radius probe. [b] PC_{cavity} = (guest volume) × (number of guest molecule in unit cell)/V_{cavity} × 100.

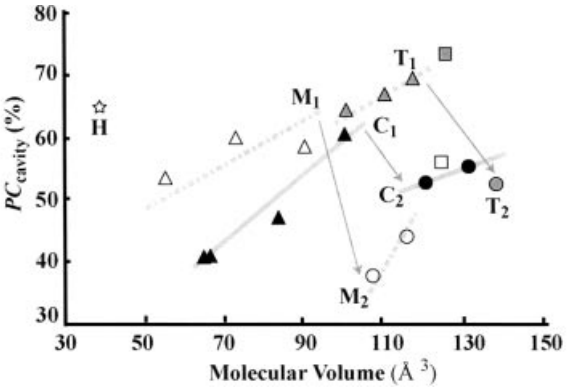


Figure 12. (a) PC_{cavity} profiles of **NDCA**: H (open asterisk,), M1 (open triangles), C1 (filled triangles, black), T1 (filled triangles, grey), M2 (open circles), C2 (filled circles, black), T2 (filled circles, grey), M3(rectangles), and T3 (filled cubes).

pound has size and shape that is complementary to both the T1 and M2 types of host frameworks (Figure 12).

Conclusion

We have demonstrated the inclusion abilities and crystal structures of **NDCA**, a compound whose side chain is shorter than that of the parent **DCA**. The shortening of this side chain extends the diversity of the aggregation manner from the 2_1 helical tape assembly inherent in the steroidal skeleton of **DCA**. This molecular design was based on a strategy of breaking the linkage between the tape assemblies to generate the independence of each tape. Actually, the tape assembly of **NDCA** possesses flexibility beyond the dominance of the robust sheet-like structural motif of **DCA**. As the result, various host cavities are produced, depending on the nature of the guests, through diverse arrangements of the tape assemblies. Furthermore, this definitive chemical modification, which brings about the destruction of the robust sheet-like motif, also induces the fundamental reconstruction of the inherent 2_1 helical tape assembly to form other distinct structural motifs in responce to the functional groups and volume of the guest compounds. In this way, the results from this rational molecular design can be regarded as one of the applicable strategies for adjusting the robustness of structural motifs and host cavities.

Experimental Section

General: All solvents and chemicals were of reagent-grade quality; they were purchased commercially and used without further purification. The host 3α,12α-dehydroxy-5β-23-norcholan-23-oic acid (**NDCA**) was prepared from **DCA** by degradation of the side chain.[24] Infrared spectra were recorded with a JASCO IR-Report-100 or JESCO IR-810 spectrometer. Differential thermal analysis (DTA), and thermal gravimetry (TG), were performed on a Rigaku TAS100 system and Thermoplus TG-8120; the compound (ca.10 mg) was analyzed from 300 to 510 K at a heating rate of 5 K·min^{-1}. X-ray powder diffraction (XRD) patterns were measured using a Rigaku RINT-2000 with Cu-K_α radiation at room temperature.

Preparations of Inclusion Crystals: Preparation of inclusion crystals usually involves recrystallization from organic substances. A typical procedure involves dissolving **NDCA** (40 mg) in a guest solvent (0.8 mL) with heating at its boiling point. The solution is cooled to room temperature until crystals begin to form. The crystals are collected and dried on the filter paper. Weight losses observed during TGA and the 2θ angles (with relative intensity in parentheses) observed by XRD are summarized as follows:

Guest-Free: XRD: 14.280 (14), 15.280 (97), 16.200 (40), 16.440 (100), 19.460 (18).

Water: TGA: 4.1% weight loss. XRD: 11.700 (43), 12.740 (18), 13.540 (26), 14.400 (73), 17.860 (100), 18.600 (96), 20.560 (56).

Methanol: TGA: 8.0% weight loss. XRD: 11.640 (64), 15.380 (55), 16.820 (50), 17.900 (37), 18.560 (100), 20.560 (53).

Ethanol: TGA: 7.1% weight loss. XRD: 8.060 (14), 8.500 (100), 12.040 (26), 15.420 (23), 17.640 (17), 19.040 (15).

1-Propanol: TGA: 13.7% weight loss. XRD: 8.440 (73), 8.660 (44), 12.040 (53), 15.280 (60), 17.500 (100), 19.040 (44).

2-Propanol: TGA: 15.3% weight loss. XRD: 8.200 (73), 8.420 (41), 12.020 (45), 14.820 (49), 17.260 (100), 17.260 (56), 19.500 (40).

2-Methyl-1-propanol: TGA: 15.1% weight loss. XRD: 11.920 (68), 12.260 (73), 13.200 (40), 17.200 (100), 22.160 (20).

2-Methyl-2-propanol: TGA: 16.4% weight loss. XRD: 7.760 (28), 8.300 (57), 11.760 (100), 13.860 (55), 16.620 (84), 17.660 (21), 18.440 (23).

1-Butanol: TGA: 8.6% weight loss. XRD: 11.060 (20), 12.060 (20), 12.180 (20) 17.400 (100).

2-Butanol: TGA: 15.2% weight loss. XRD: 8.300 (100), 11.980 (39), 14.740 (52), 17.120 (56), 18.140 (19).

2,2-Dimethyl-1-propanol: TGA: 19.4% weight loss. XRD: 7.600 (9), 8.760 (9), 9.520 (9), 12.000 (8), 16.520 (10), 17.240 (100), 17.540 (12), 19.920 (33).

2-Methyl-1-butanol: TGA: 18.5% weight loss. XRD: 7.420 (28), 7.580 (100), 10.640 (26), 10.800 (37), 16.520 (49), 17.420 (66).

3-Methyl-1-butanol: TGA: 19.0% weight loss. XRD: 7.780 (26), 11.060 (18), 12.080 (35), 12.800 (59),12.960 (78), 14.100 (100), 15.780 (45), 17.580 (38), 18.360 (70), 20.660 (41).

2-Methyl-2-butanol: TGA: 19.2% weight loss. XRD: 7.980 (100), 9.580 (21), 10.860 (35), 16.740 (59), 17.540 (36), 17.920 (27).

3-Methyl-2-butanol: TGA: 17.7% weight loss. XRD: 7.900 (100), 7.920 (99), 10.780 (50), 10.940 (96), 16.640 (69), 16.760 (88), 17.140 (36), 17.340 (37), 17.920 (58), 20.480 (36).

1-Pentanol: TGA: 11.3% weight loss. XRD: 12.060 (100), 17.120 (61), 17.280 (34), 17.480 (28), 18.660 (18).

2-Pentanol: TGA: 9.4% weight loss. XRD: 7.140 (100), 7.620 (68), 10.760 (24), 16.500 (27), 17.160 (30), 17.660 (24).

3-Pentanol: TGA: 10.2% weight loss. XRD: 12.080 (100), 13.120 (45), 17.280 (80), 18.840 (26), 22.000 (23).

2-Ethyl-1-butanol: TGA: 20.5% weight loss. XRD: 7.620 (71), 8.720 (26), 11.020 (29), 12.560 (67), 13.940 (96), 15.900 (28), 16.080 (27), 17.720 (100), 20.540 (54).

3,3-Dimethyl-1-butanol: TGA: 20.6% weight loss. XRD: 7.780 (57), 8.720 (25), 9.380 (29), 10.000 (24), 10.680 (62), 11.500 (36), 11.780 (50), 14.600 (30), 16.480 (100), 16.900 (43), 17.280 (44), 17.640 (37), 19.500 (28).

2,3-Dimethyl-2-butanol: TGA: 22.7% weight loss. XRD: 7.920 (59), 10.760 (40), 11.560 (37), 16.600 (100).

3,3-Dimethyl-2-butanol: TGA: 21.4% weight loss. XRD: 7.680 (100), 9.300 (18), 10.740 (34), 14.420 (26), 16.340 (63), 17.180 (51).

2-Methyl-1-pentanol: TGA: 21.3% weight loss. XRD: 6.920 (39), 9.200 (19), 13.540 (34), 13.800 (38), 15.000 (98), 18.220 (33), 21.240 (100).

3-Methyl-1-pentanol: TGA: 12.0% weight loss. XRD: 10.700 (26), 11.920 (100), 13.020 (37), 16.980 (81), 18.280 (31).

4-Methyl-1-pentanol: TGA: 11.2% weight loss. XRD: 8.740 (44), 11.620 (50), 12.820 (31), 16.640 (40), 16.880 (42), 20.720 (37), 21.320 (40), 26.500 (100).

2-Methyl-2-pentanol: TGA: 21.9% weight loss. XRD: 7.700 (76), 7.880 (100), 10.720 (37), 14.800 (41), 16.600 (38), 17.460 (34), 21.520 (35).

3-Methyl-2-pentanol: TGA: 22.0% weight loss. XRD: 7.680 (100), 10.780 (31), 11.840 (21), 16.420 (48), 17.120 (29), 17.600 (36).

4-Methyl-2-pentanol: TGA: 20.3% weight loss. XRD: 7.440 (100), 10.2608 (14), 13.300 (23), 14.100 (12), 15.820 (30), 17.000 (19), 20.800 (22), 23.900 (17).

2-Methyl-3-pentanol: TGA: 21.8% weight loss. XRD: 8.000 (100), 10.680 (13), 15.900 (12), 16.600 (28), 17.860 (19), 20.520 (10).

3-Methyl-3-pentanol: TGA: 21.0% weight loss. XRD: 7.880 (100), 9.380 (21), 10.680 (28), 11.620 (35), 14.680 (33), 16.220 (66), 16.460 (57), 17.140 (35), 17.680 (35).

1-Hexanol: TGA: 11.5% weight loss. XRD: 12.080 (87), 13.160 (37), 17.340 (100).

2-Hexanol: TGA: 20.8% weight loss. XRD: 7.580 (100), 10.980 (49), 11.560 (20), 15.800 (24), 17.200 (63), 17.580 (37).

3-Hexanol: Guest-free crystal.

1-Nonanol: Guest-free crystal.

Ethylene glycol: Water.

1,4-Butandiol: Water.

Benzyl alcohol: TGA: 21.5% weight loss. XRD: 8.740 (20), 10.800 (21), 12.880 (100), 14.200 (61), 16.240 (35), 18.560 (100).

Acetone: TGA: 9.9% weight loss. XRD: 8.580 (29), 16.020 (100), 16.600 (10), 17.300 (10).

2-Butanone: TGA: 8.9% weight loss. XRD: 8.460 (94), 9.300 (68), 11.880 (45), 12.460 (45), 16.080 (81), 16.720 (79), 17.380 (89), 18.140 (100).

2-Pentanone: XRD: 11.700 (28), 12.060 (93), 13.120 (32), 17.200 (100), 18.700 (21).

3-Pentanone: TGA: 10.1% weight loss. XRD: 11.880 (100), 12.960 (18), 17.060 (45), 18.640 (11).

2-Hexanone: Guest-free crystal.

2,4-Pentadione: TGA: 10.2% weight loss. XRD: 11.880 (81), 12.260 (100), 13.020 (27), 13.160 (25), 14.180 (46), 16.720 (61), 17.420 (50), 18.480 (58), 22.680 (36).

Cyclohexanone: TGA: 11.8% weight loss. XRD: 11.900 (61), 12.360 (100), 13.160 (43), 16.660 (19), 17.200 (76), 17.700 (18), 22.960 (32).

Acetophenone: TGA: 12.6% weight loss. XRD: 11.460 (100), 14.080 (55), 16.320 (11), 16.460 (14), 19.140 (19).

2′-Hydroxyacetophenone: TGA: 27.8% weight loss. XRD: 10.560 (14), 13.100 (31), 14.340 (16), 15.460 (20), 17.680 (25), 18.660 (100), 21.320 (41).

4′-Methylacetophenone: TGA: 13.5% weight loss. XRD: 10.080 (31), 11.360 (77), 13.780 (39), 14.000 (58), 16.240 (100), 17.500 (64), 17.740 (41).

3′-Methoxyacetophenone: TGA: 15.3% weight loss. XRD: 10.040 (25), 13.720 (24), 14.040 (100), 15.180 (36), 16.700 (40), 17.660 (35), 17.840 (40), 21.040 (17).

Propiophenone: Guest-free crystal.

1-Acetonaphthone: Guest-free crystal.

1,4-Dioxane: TGA: 7.4% weight loss. XRD: 11.620 (29), 14.380 (39), 16.880 (51), 17.860 (35), 18.560 (100).

Tetrahydrofuran: TGA: 9.5% weight loss. XRD: 12.040 (70), 12.460 (87), 13.300 (40), 16.920 (7), 17.380 (100), 18.460 (14).

Anisole: TGA: 19.2% weight loss. XRD: 11.120 (45), 11.720 (41), 13.340 (73), 14.680 (75), 15.220 (77), 16.440 (100), 19.320 (78), 21.980 (64).

Ethyl Acetate: Guest-free crystal.

Methyl Propionate: Water.

Ethyl Propionate: Guest-free crystal.

Methyl Benzoate: TGA: 15.2% weight loss. XRD: 11.560 (100), 14.040 (38), 15.920 (36), 16.180 (11), 19.160 (11).

γ-Butyrolactone: TGA: 9.0% weight loss. XRD: 9.620 (24), 11.820 (38), 12.460 (100), 13.150 (33), 17.160 (77).

γ-Valerolactone: TGA: 11.3% weight loss. XRD: 12.220 (82), 13.280 (24), 14.240 (23), 17.120 (100), 17.500 (23), 18.780 (23).

γ-Heptalactone: TGA: 13.5% weight loss. XRD: 8.740 (35), 10.460 (37), 11.820 (68), 12.640 (43), 16.700 (100).

Acetonitrile: TGA: 7.9% weight loss. XRD: 12.140 (100), 13.180 (11), 17.300 (37), 17.560 (12).

Propionitrile: TGA: 7.1% weight loss. XRD: 12.020 (100), 12.140 (99), 13.100 (28), 17.220 (92).

Acrylonitrile: TGA: 7.2% weight loss. XRD: 12.320 (57), 13.280 (25), 17.420 (100), 19.260 (10).

Benzonitrile: TGA: 10.7% weight loss. XRD: 11.720 (32), 15.560 (100), 16.440 (29), 16.880 (33).

Benzene: TGA: 14.5% weight loss. XRD: 11.200 (8), 13.360 (28), 13.520 (100), 13.660 (46), 14.880 (52), 19.320 (36).

Toluene: TGA: 17.0% weight loss. XRD: 10.020 (16), 11.840 (65), 14.780 (64), 15.080 (62), 15.600 (42), 16.140 (100), 19.200 (29).

***o*-Xylene:** TGA: 21.7% weight loss. XRD: 10.880 (23), 11.060 (22), 13.320 (76), 14.560 (38), 15.440 (37), 19.040 (100), 21.620 (38).

***m*-Xylene:** Guest-free crystal.

***p*-Xylene:** Guest-free crystal.

X-ray Structural Analysis: Single-crystal X-ray diffraction data for the inclusion crystals of NDCA were collected with a Rigaku RAXIS-RAPID 2D area detector, a Rigaku RAXIS-IV 2D area detector, or a Rigaku AFC-7R diffractometer. The diffractometers use graphite-monochromatized Cu-K_α or Mo-K_α radiations. Diffraction data were corrected for absorption using the software package.[25] Direct methods (SHELX-86, SIR-88 and SIR-92) were employed for the solution of the structure. All non-hydrogen atoms were refined anisotropically based on F^2. Hydrogen atoms of the host were fixed in calculated positions using thermal parameters based on the corresponding C atoms [U(H) = 1.2−1.5U_{eq}(C)]. The crystallographic data are given in Table 2. CCDC-219167 to -219186 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

Molecular Graphics and Calculations: Cross sections of host channels were depicted using MODRASTE.[26] The atomic radii of hydrogen, carbon, and oxygen atoms in the cross-sectional views are 1.20, 1.60, and 1.45 Å, respectively. The volumes of the host cavities were calculated from the atomic coordination by using the Free Volume program[27] in the Cerius^2 (version 4.0) software package.[28] The volumes of the host cavities were calculated by using a 0.7-Å-radius probe, and the following values were adopted for the atomic radii: hydrogen: 1.20 Å, carbon: 1.70 Å, and oxygen: 1.60 Å.

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