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Chain-like assembly of threonine-based cyclophanes through π–π interaction and C–H···O hydrogen bond

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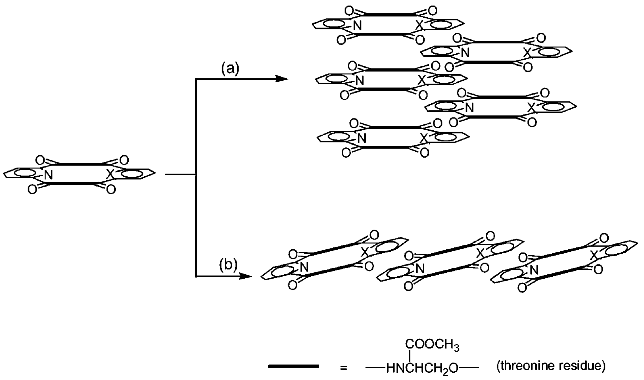
Abstract—In this paper, we described the conversion of tube to chain assembly of threonine-based cyclophanes by variation of the steric demand of molecules. The interesting properties of these cyclophanes in hosting hydroxyl-containing guest molecules through three-centered hydrogen bonding and the C–H···O hydrogen bonds were also reported.

Self-assembly of specific solid structures continues to be a theme of current interest for developing materials with enhanced optical, electrical, or catalytic properties.[1] Although it is still difficult to predict how a particular molecule will pack in the solid state, considerable progress has been achieved in recent years in this respect.[2,3] One popular approach is to incorporate into the molecule of interest a small number of functional groups that can limit the possible orientations of the molecule in space. Also, the well known π–π interaction[4] is widely recognized as an important strategy in self-assembly.[5] Recently, a study on crystal structures of some serine-based cyclophanes showed that the presence of pyridine unit helped in stacking the macrocycles in interdigitating tubular fashion via the π–π interaction between the benzene ring and pyridine ring or the pyridine ring and pyridine ring (Scheme 1a).[6] This stimulated our interest in examining whether a chain-like assembly of π–π stacks (Scheme 1b) can be possibly achieved by certain structural modification. One practical way in this regard is to increase steric demand through variations of molecular structure to prevent vertical columnar stacking. Indeed, a conversion of this type for some hydroxyl acids from layer to channel structure has recently been realized.[7] In the present report, we will disclose our recent findings of an a↔b type conversion of the title compounds.



Scheme 1. Two types of possible stackings of cyclophane involving pyridine/benzene groups through π–π interactions ($X = N$ or CH).

The substrates used in this work contained threonine [$HOCH(CH_3)CH(NH_2)COOH$] unit, which bears an additional β-methyl group in comparison with serine and thus may render an opportunity for examining the structural effect of self-assembly. So two aromatic-bridged threonine-based cyclophanes[8] **1** and **2** (Fig. 1a) were synthesized following a literature procedure[6] and their single crystal structures were determined by the X-ray diffraction. To our expectation, the crystallographic experiments unambiguously confirmed the structural conversion of the solid assembly. In this paper, we will

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Keywords: Self-assembly; Cyclophane; π–π Interaction; C–H···O hydrogen bond.

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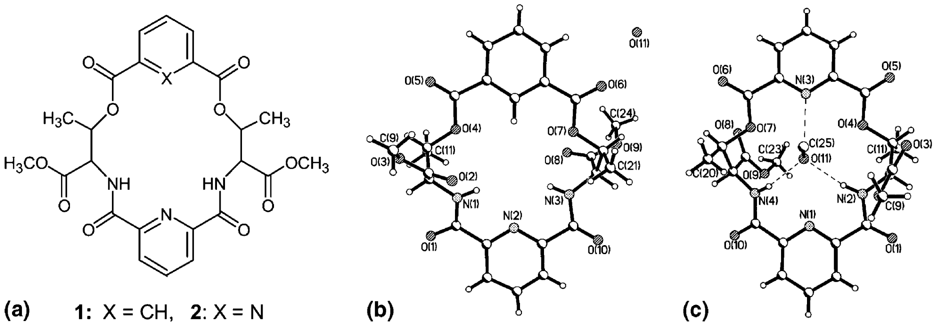

Figure 1. (a) Chemical structures of cyclophane **1** and **2**. (b) X-ray structure of **1**. (c) X-ray structure of **2**. Hydrogen bonds to a methanol molecule are indicated by dashed lines (N(2)···O(11) 2.969 Å, N(2)H···O 2.205 Å, angle 147.9°; N(4)···O(11) 3.334 Å, N(4)H···O 2.483 Å, angle 170.5°; N(3)···O(11) 3.005 Å).

also report their interesting property as host molecules utilizing the three-centered hydrogen bonding to accommodate hydroxyl-containing guest molecules and the formation of water molecular channel driven by both π–π interactions and C–H···O hydrogen bonds.

Suitable single crystals of the macrocycles **1** and **2** were obtained from aqueous methanol. The solid-state molecular and assembled structures of **1** and **2** were determined by X-ray crystallographic analysis.[9] In the lattice of **1**, a disordered water molecule was found in the crystal lattice (Fig. 1b). Interestingly, in the lattice of **2**, a methanol molecule in hydrogen bonding with N(2)H, N(4)H, and N(3) atoms of **2** was found (Fig. 1c). The hydrogen bonds involved all three hydrogen-bonding sites of methanol hydroxyl, revealing an interesting tripodal recognition motif. Since development of effective artificial receptors for recognition of hydroxyl-containing compounds, such as carbohydrates,[10] is still one of the contemporary challenges in supramolecular chemistry, the present observation in the crystal structure of **2** would likely provide a useful clue for designing new receptors. No obvious intramolecular hydrogen bond was found in **1** and **2** except for the short contacts between pyridine N and adjacent amide NHs (For **1**: N(2)···HN(1), 2.370 Å; N(2)···HN(3), 2.305 Å. For **2**: N(1)···HN(2), 2.376 Å; N(1)···HN(4), 2.398 Å).

Inspection of the crystal structures further revealed that both **1** and **2** assembled into a chain-like supramolecular structure. Macrocycle **1**, containing both pyridine and benzene rings in its backbone, assembled into an extended chain-like structure in a head-to-tail pattern through π–π interactions between pyridine and benzene rings with a ~3.7 Å separation (Fig. 2a). The two aromatic rings of π–π interaction were almost parallel to each other with the dihedral angel of ~4°. Despite a 17° tilt of the pyridine planes of π–π interactions, similar chain-like assembly was also observed in macrocycle **2** (Fig. 3a), which contained repeats of pyridine and threonine units. Two pyridine rings of π–π interaction had a separation of ~3.8 Å.

The observation of the chain-like assemblies of macrocycles **1** and **2**, instead of the interdigitating tubular assemblies for the serine-based cyclophanes as reported in the literature,[6] probably resulted from the presence of the methyl and ester units in their molecular backbones, as both were nearly perpendicular to the molecular plane and oriented in opposite directions (Fig. 1b and c). Therefore, if the molecules were stacked in an interdigitating tubular fashion, the steric hindrance, arising respectively, from the methyl and ester units of the two adjacent molecules in the same column, would prevent the vertical contacts of molecules.

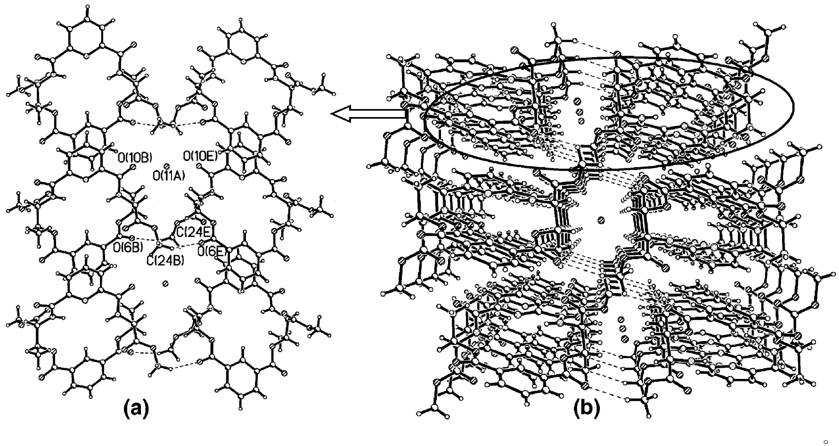

Figure 2. (a) The chains of π–π stacks of **1** are held together by pairs of C–H···O hydrogen bonds (C(24)···O(6) 3.321 Å, C(24)H···O 2.437 Å, angle 153.1°). (b) A 3D representation of channels, which are filled with water molecules.

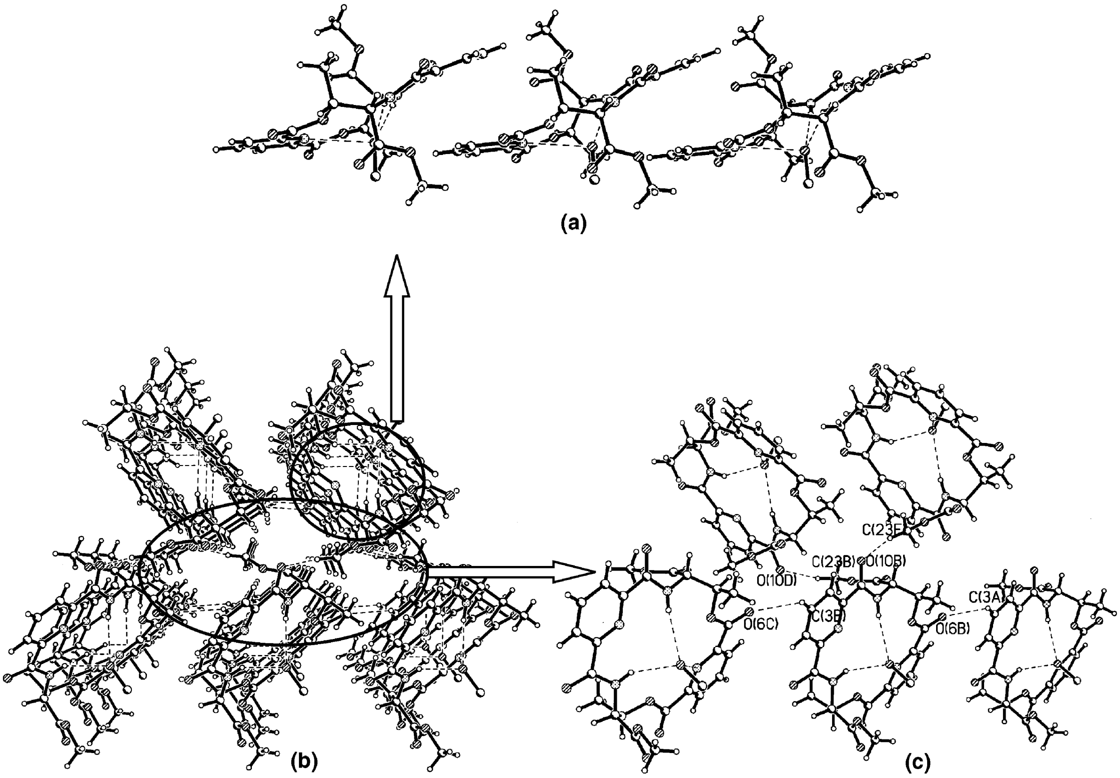

Figure 3. (a) The chain-like structure of π–π stacks of **2**. (b) A 3D view of the stacking. (c) C–H···O hydrogen-bonding interactions (C(3)···O(6) 3.208 Å, C(3)H···O 2.570 Å, angle 126.2°; C(23)···O(10) 3.318 Å, C(23)H···O 2.420 Å, angle 155.2°).

It is noteworthy that these chains of the π–π stacks in macrocycles **1** and **2** were further linked through intermolecular C–H···O hydrogen bonds. The chains of the π–π stacks in **1** were formed in a dimer through a series of similar pair of C–H···O hydrogen bonds, consequently creating the extended tubular structures, which were parallel to the *b* axis in the crystal cell (Fig. 2a and b). The neighboring chain-like dimers are held together only by hydrophobic interactions. Noteworthy is that some disordered water molecules existed in the center of the channels with equal separation of 8.709 Å. The closest contacts to water molecule were found with the two O(10) atoms of the two adjacent molecules, which belonged to the respective chain in the dimer. The three hydrogen-bonding O atoms were exactly in line (angle for O(10)···O(11_w)···O(10): 180°) and the distance of each water molecule with adjacent O(10)s was 2.992 Å. Thus it is reasonable to assume that water molecules are hydrogen bonded to both O(10)s.

Recently, some excellent examples of tubular structure have been reported.[11] Some interesting tubular assemblies of water molecules were also exploited in the aggregates of some small molecules.[12] To the best of our knowledge, the observation reported herein is the first example of the tube-like assembly that is mainly driven by the combination of C–H···O hydrogen bonds and π–π interactions.

The chains of the π–π stacks in **2** were held together by two types of C–H···O hydrogen bonds (Fig. 3c), and there were no solvent-assessable voids in the crystal lattice. A closer-packed lattice than that in **1** was formed as reflected by the higher density (1.346 vs 1.277 g/cm^3).

In summary, the present study reports the formation of a chain-like assembly of the π–π stacks by incorporating steric demands into molecular structure. The self-assembling chains are further held together by intermolecular C–H···O hydrogen bonds. Consequently, macrocycle **1** forms a water-containing tubular structure through C–H···O hydrogen bonds and π–π interactions, and macrocycle **2** forms a closer-packed lattice. In addition, a promising tripodal receptor of **2** for hydroxyl-containing guest molecules is reported. These findings may provide useful clues for determining the types of crystal packing and for studying molecular recognition.

Acknowledgements

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8. Compound **1**: Yield 32%; mp 215–217 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.61 (s, 1H), 8.47 (d, $J = 8.1$ Hz, 2H), 8.44 (d, $J = 10.2$ Hz, 2H), 8.30 (dd, $J = 1.8$, 6.3 Hz, 2H), 8.13 (t, $J = 8.1$ Hz, 1H), 7.61 (t, $J = 10.1$ Hz, 1H), 5.95–5.98 (m, 2H), 5.16 (dd, $J = 1.8$, 9.9 Hz, 2H), 3.72 (s, 6H), 1.55 (d, $J = 6.3$ Hz, 6H); FAB-MS m/z 528 $(M+1)^+$. Compound **2**: Yield 25%; mp 190–192 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.28 (d, $J = 9.6$ Hz, 2H), 8.43 (d, $J = 7.8$ Hz, 2H), 8.38 (d, $J = 7.8$ Hz, 2H), 8.09 (t, $J = 7.8$ Hz, 1H), 8.04 (t, $J = 7.8$ Hz, 1H), 6.00–6.04 (m, 2H), 5.19 (dd, $J = 1.8$, 9.6 Hz, 2H), 3.72 (s, 6H), 1.56 (d, $J = 6.6$ Hz, 6H); FAB-MS m/z 529 $(M+1)^+$.
9. Crystallographic data: for **1**+$0.5H_2O$, empirical formula: $C_{25}H_{25.50}N_3O_{10.25}$, crystal size: 0.20×0.15×0.04, monoclinic, $a = 13.955(3)$ Å, $b = 8.709(2)$ Å, $c = 23.227(6)$ Å, $\alpha = \gamma = 90°$; $\beta = 101.389(6)$, $V = 2767.4(12)$, $T = 293(2)$ K, space group $C2$, $Z = 4$, $d_{calcd} = 1.277$ g/cm^3, $F(000) = 1114$, 5813 reflections measured, 4376 unique ($R_{int} = 0.0323$). The final $R1 = 0.0738(I > 2\sigma)$, 0.1521(all data), $wR2 = 0.1804(I > 2\sigma)$, 0.2166(all data). For **2**+CH_3OH, empirical formula: $C_{25}H_{28}N_4O_{11}$, crystal size: 0.25×0.20×0.15, Monoclinic, $a = 9.222(3)$ Å, $b = 8.635(3)$ Å, $c = 17.724(6)$ Å, $\alpha = \gamma = 90°$; $\beta = 101.436(6)$, $V = 1383.4(8)$, $T = 293(2)$ K, space group $P2(1)$, $Z = 2$, $d_{calcd} = 1.346$ g/cm^3, $F(000) = 588$, 5812 reflections measured, 4297 unique ($R_{int} = 0.0223$). The final $R1 = 0.0501(I > 2\sigma)$, 0.0731(all data), $wR2 = 0.1234(I > 2\sigma)$, 0.1379(all data). Crystallographic data for **1** and **2** have been deposited at the Cambridge Crystallographic Data Centre, reference CCDC 234640 for **1**, CCDC 234641 for **2**.
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