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Communication

Hierarchical Self-Organization and Disorganization of Helical Supramolecular Columns Mediated by H-Bonding and Shape Complementarity

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ABSTRACT: H-bonding, shape complementarity, and quasi-equivalence are widely accepted as some of the most influential molecular recognition events mediating biological and synthetic self-organizations. H-bonds are weaker than ionic but stronger than van der Waals forces. However, the directionality of H-bonds makes them the most powerful among all nonbonding interactions. Here, we selected two taper-shaped self-assembling dendrons, one flexible and one rigid, and equipped them with $-CO_2CH_3$, $-CH_2OH$, and $-COOH$ at their apex. They demonstrated the hierarchical way in which shape-complementarity in the presence of $-CO_2CH_3$ mediated highly ordered helical self-organization for the case of the rigid building block and less ordered helical arrays for the flexible one. Weak H-bonding by $-CH_2OH$ unwound the helix from the rigid dendron, yielding a porous column. Due to its quasi-equivalence, the flexible dendron tolerated better the H-bonding by $-CH_2OH$ self-organizing a different helical column. The rigid and the flexible dendrons yielded only disorganized nonhelical columns in the presence of $-COOH$ at the apex. This balance between rigidity, flexibility, and tolerance or lack of it to diverse H-bonding architectures indicates that mechanistic elucidation of the self-organization process helps endow it with the same building block, both helical organizations approaching biological precision, and disorganized nonhelical arrangements.

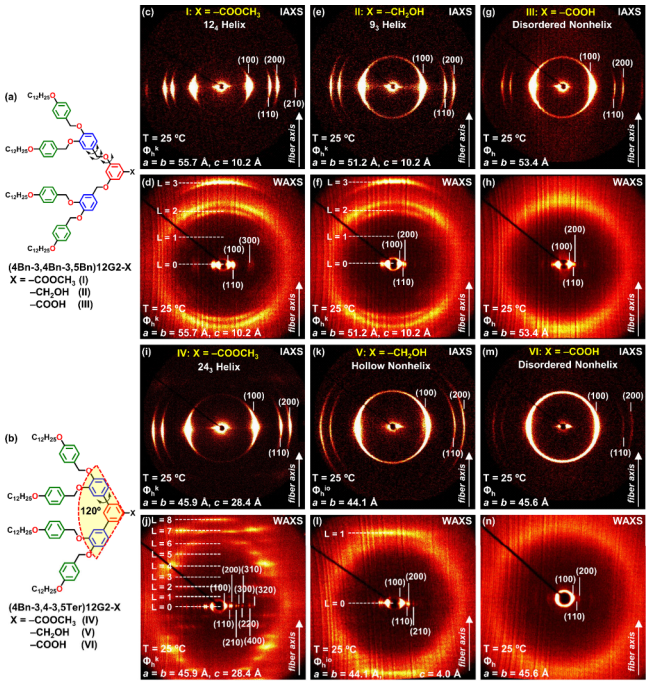

Figure 1. Structures of (4Bn-3,4Bn-3,5Bn)12G2-X (a) and (4Bn-3,4-3,5Ter)12G2-X (b) with X = $-COOCH_3$, $-CH_2OH$, and $-COOH$ groups and oriented fiber intermediate angle X-ray diffraction (IAXS) and wide-angle X-ray diffraction (WAXS) (c−h) for (a) and (i−n) for (b).

The α-helix[1] and the pleated sheet[2] of polypeptide chains, Chargaff's rule of complementary base pairing in DNA,[3] and the double-helix of DNA[4] have been, most probably, the most influential events demonstrating the powerful role of H-bonding during self-organization of biological macromolecules. A similar role was played by the H-bonding of the nylons[5] for synthetic macromolecules. Shape complementarity and quasi-equivalence of rodlike and icosahedral viruses[6a−d] provided the second most influential molecular recognition tool of biological self-organization. In the field of dendrimers, Tomalia defined related structural events as "critical nanoscale design parameters" (CNDPs).[6e,f] The combination of directionality and strength of H-bonds integrated with shape complementarity and quasi-equivalence has impacted also the field of complex synthetic self-organization including that of supramolecular polymers.[7] The merger of shape complementarity and H-bonding has been widely recognized as being dominant molecular recognition concepts in self-organization. However, we are not aware of any report demonstrating that shape complementarity and H-bonding can be as prominent in the disorganization processes as in the self-organization one. Here, we have selected two self-assembling dendrons developed by our laboratory, previously employed to self-organize a diversity

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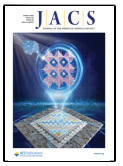

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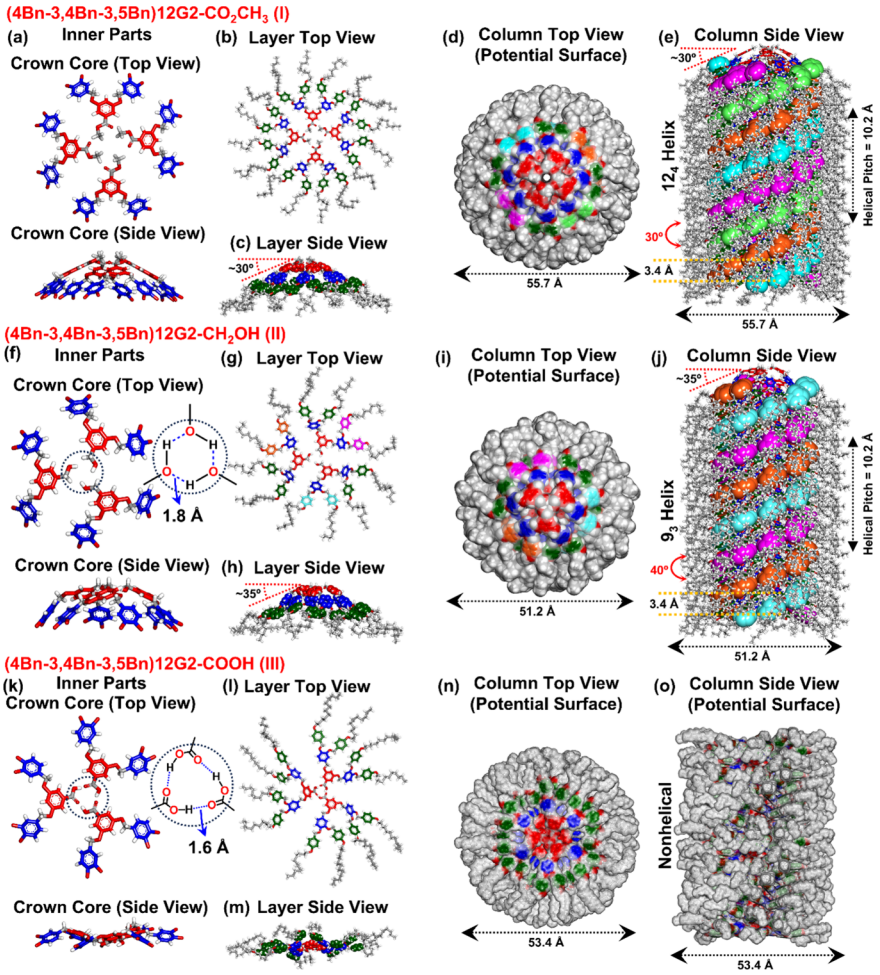

Figure 2. Mechanisms of self-organization and disorganization of (4Bn-3,4Bn-3,5Bn)12G2-X with X = $-COOCH_3$ (**I**) (a,b,c,d,e), $-CH_2OH$ (**II**) (f,g,h,I,j), and −COOH (k,l,m,n,o) (**III**) were obtained by the reconstruction of the oriented fiber X-rays by supramolecular models.

of helical structures and functions,[8] and demonstrated that their complementarity associated with the presence and/or absence of H-bonding can mediate both self-organization and disorganization. The first dendron known formerly as (4-3,4-3,5)12G2-X where X is the functional group attached to its apex is constructed from benzyl ether repeat units.[9] Due to the low rotation barriers around its sp^2-sp^3-sp^3-sp^2 bonds (Figure 1a), the flexible dendron exhibits a tapered shape with an adaptable taper angle enabled by its quasi-equivalence. This building block tolerates a large diversity of aromatic groups in various sequences[10] in its structure, all following the same self-organization principles. In this case, we will use the compound with benzyl ether groups only, and therefore, its structure will be referred to as (4Bn-3,4Bn-3,5Bn)12G2-X (Figure 1a) in order to discriminate it from the second rigid building block. The second self-assembling dendron selected by us[11] has a closely related primary structure based on a *meta*-terphenyl (Ter) combined with benzyl ether repeat units only on its periphery, (4Bn-3,4-3,5Ter)12G2-X (Figure 1b). In the second dendron, the replacement of sp^2-sp^3-sp^3-sp^2 bonds with sp^2-sp^2 maintains its taper shape but transforms the adaptable taper angle of the flexible dendron[12] into a rigid taper angle of 120° (Figure 1b). The structure of the X-group changes, but to a lesser extent, even the rigid taper angle, as will be discussed with examples in a future publication. We would like to specify that the branching points of (4Bn-3,4Bn-3,5Bn)12G2-X are constructed from the renewable plant phenolic acids 3,4-dihydroxybenzoic acid, known also as protocatechuic acid, and 3,5-dihydroxybenzoic acid, known as α-resorcylic acid.[13] The same two phenolic acids were employed in a Ni-catalyzed borylation paired with Ni-catalyzed cross-coupling methodology elaborated in our laboratory[11] to synthesize libraries of *m*-terphenyl phenolic acids[14] including the one employed in the synthesis of (4Bn-3,4-3,5Ter)12G2-X.[11] It should be noted that terphenyls are also natural products.[15] Both dendron structures have $-COOCH_3$, $-CH_2OH$, and −COOH as X groups. Intermediate-angle X-ray scattering (IAXS) and wide-angle X-ray scattering (WAXS) on oriented fiber experiments together with the reconstruction of the molecular models combined with experimental and theoretical densities, according to methodologies elaborated and employed in our laboratory, were utilized for the structural and mechanistic determination of the self-organization obtained from all compounds.

The IAXS (top row in black) and WAXS (bottom row in red) of I, II, III (Figure 1c,d,e,f and g,h) and of IV, V, VI (Figure 1i,j,k,l and m,n) indicate the self-organization and disorganization concept. The IAXS results shown in Figure 1c,d,g and in Figure 1i,k,m demonstrate that regardless of the structure of X, all self-organizations form highly ordered columnar hexagonal crystalline (Φ_h^k), columnar hexagonal with intracolumnar order (Φ_h^{io}), or columnar hexagonal

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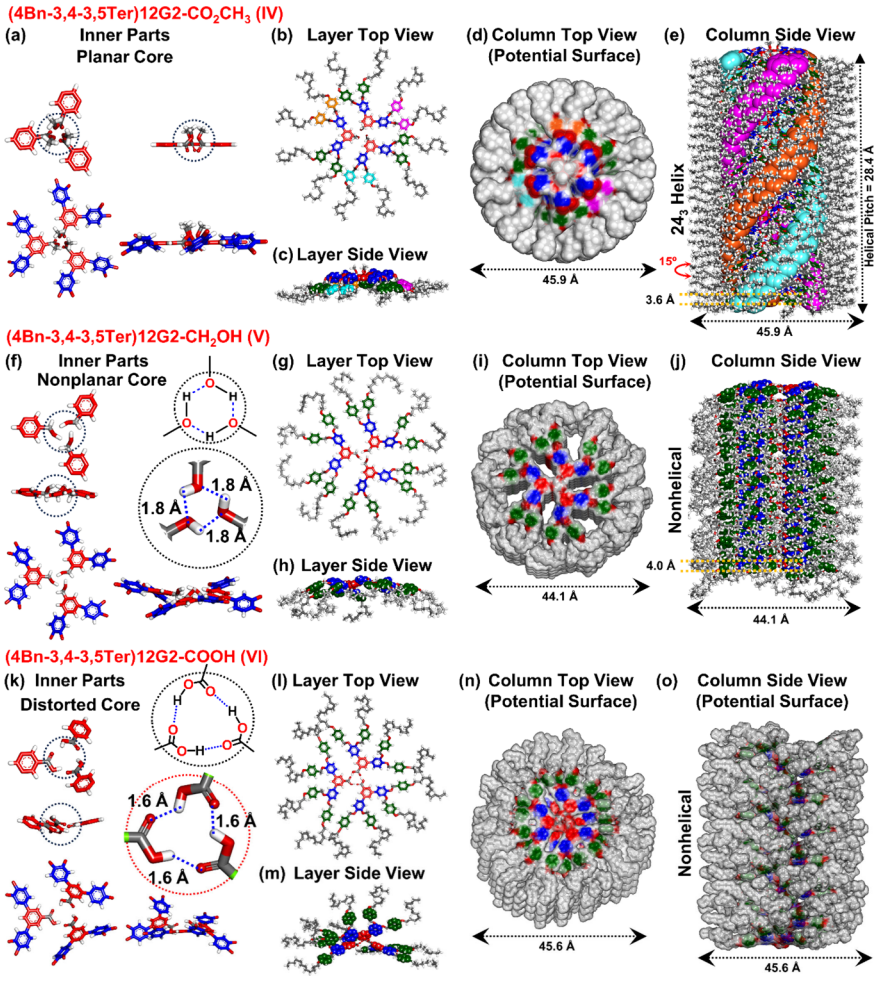

Figure 3. Mechanisms of self-organization and disorganization of (4Bn-3,4-3,5Ter)12G2-X with X = $-COOCH_3$ (**IV**) (a,b,c,d,e), $-CH_2OH$ (**V**) (f,g,h,I,j), and −COOH (**VI**) (k,l,m,n,o) were obtained by the reconstruction of the oriented fiber X-rays by supramolecular models.

disordered liquid crystalline (Φ_h) periodic arrays (Figure S1). The $\Phi_h{}^k$ periodic array is also exhibited by helical polypeptides.[1] However, WAXS results from Figure 1d,f,h and Figure 1j,l,n exhibit contrastingly different diffractograms that are strongly dependent on the structure of X. WAXS of I and II (Figure 1d,f) always show diffractions corresponding to 12/4 and 9/3 helical ordered columnar hexagonal crystal ($\Phi_h{}^k$). Helical self-organization and quasi-equivalence represent universal methodologies employed by biological systems to minimize their free energy.[6c,16]

WAXS of III (Figure 1h) shows X-ray diffraction corresponding to a nonhelical disordered columnar hexagonal periodic array (Φ_h). These results validate that I and II form closely related helical ordered columnar structures even if in the case of I, X = $-COOCH_3$ and in the case of II, X = $-CH_2OH$.

Replacing the H-bonding generated from $-CH_2OH$ with H-bonding obtained from −COOH disassembles the 12/4 helix by unwinding it into a nonhelical column (compare Figure 1f and h). This demonstrates, as will be discussed mechanistically in Figure 2, that the adaptable taper angle of (4-Bn-3,4Bn-3,5Bn)12G2-X tolerates X = $-COOCH_3$ and X = $-CH_2OH$ to mediate helical columns but does not tolerate X = −COOH. WAXS of IV, V, and VI are shown in Figure 1j, l, and n. The contrast between the diffractograms generated with a rigid taper angle containing different X groups is much higher than in the case of the self-organizations obtained from the building blocks with adaptable taper angle. WAXS of IV containing X = $-COOCH_3$ exhibits a 24/3 triple-helix. WAXS of V containing X = $-CH_2OH$ and of VI containing X = −COOH (Figure 1l,n) demonstrated the unwinding of the 24/3 triple-helix of IV and generation of disorganized nonhelical columns. What is the mechanism of these self-organizations and disorganizations mediated by shape complementarity and H-bonding? Figure 2 outlines the mechanism of self-organization of the building blocks with adaptable taper angle I (Figure 2a,b,c,d,e), II (Figure 2f,g,h,i,j), and III (Figure 2k,l,m,n,o) containing X = $-COOCH_3$, $-CH_2OH$, and −COOH. The adaptability of the taper angle permits the self-organization of helical columns in the case of both I and II. A 12/4 helix with a helical pitch of 10.2 Å and diameter of 55.7 Å was obtained for the case of I (Figure 2a−e), while a 9/3 helix with a helical pitch of 10.2 Å and a diameter of 51.2 Å was generated in the case of II (Figure 2f,g,h,i,j). A nonhelical column was attained in the case of III (Figure 2k,l,m,n,o). The different structures of the H-bonding architectures are responsible for these self-organization and disorganization processes. These self-organization and disorganization processes mediated by shape complementarity and H-bonding are more dramatically observed for the case of the building block with a rigid taper angle (Figure 3). Compound IV with X = $-COOCH_3$ self-organized a highly ordered helical hexagonal crystalline columnar periodic array

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(Φ_h^k) that was already reported (Figure 3a,b,c,d,e).[11] The apex of the terphenyl containing X = $-COOCH_3$ exhibits planar phenyl groups (Figure 1a). This process allows three tapered building blocks to form the cross-section of a column (Figure 3b,d) that will rotate around the long axis of the column to fill the space and generate a 24/3 triple-helix column (Figure 3e). Replacing X = $-COOCH_3$ with $-CH_2OH$ transforms IV into V, which due to directional H-bonding averting the planar arrangement of the phenyl groups in the center of the column (Figure 3f). The cross-section layer of the column continues to contain three building blocks which, due to their nonplanar arrangement, cannot rotate around the column axis and, instead of a helical conformation, generates a disorganized nonhelical column with intracolumnar order (Φ_h^{io}) containing multiple pores (Figure 3i,j). Replacing X = $-CH_2OH$ with X = $-COOH$ transforms V into VI, which has a different H-bonding directionality when three building blocks generate the cross-section of the column (Figure 3k,l,m). The resulting supramolecular column is completely disorganized and self-organizes into nonhelical liquid crystals (Φ_h) (Figure 3n,o).

In conclusion, these results demonstrated that taper-shaped rigid and flexible self-assembling dendrons self-organize highly ordered helical columns in the presence of X = $-CO_2CH_3$, which does not provide any H-bonding at their apex. Replacing X = $-CO_2CH_3$ with X = $-CH_2OH$ at their apex unwinds the helical structure self-organized from the rigid dendron, providing a porous column. The same structural transformation mediated a different helical self-organization of the flexible quasi-equivalent dendron. Adding X = $-COOH$ at the apex creates disorganized nonhelical columns for both the rigid and flexible dendrons. These data indicate that not only the strength of the H-bond but also the directionality of the weak H-bonds together with the flexibility of the shape complementary building blocks are important in mediating self-organization and disorganization. Interestingly and unexpectedly, both the rigid and the flexible dendrons self-organized the highest ordered helical column in the absence of H-bonding functional groups at their apex. Most importantly, the hierarchical processes involving H-bonding strength, directionality, and shape complementarity combined with rigidity, flexibility, and quasi-equivalence must be completely elucidated before biological precision can be enacted in any synthetic self-organization. This is very important because the kinetics and thermodynamics of tapered, conical, and crown-like dendrons are completely different during their self-organization processes, as briefly already discussed in a previous publication.[16f] These experiments have definitively demonstrated that, as in the case of viral capsids,[6] shape complementarity can be the dominant factor in the self-organization of synthetic complex helical systems. Additional developments based on the concepts elaborated here are being used to construct unprecedented supramolecular architectures, which will be reported soon.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/jacs.4c10958.

Methods for synthesis and structural analysis by XRD (PDF)

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Author Contributions

The manuscript was written through the contributions of all authors. All authors have given approval to the final version of the manuscript.

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Notes

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