Self-Assembly of Conformationally Rigid Dialcohols (Bis-Benzocyclobutenols): Supramolecular Cyclophanes and Arrays

ARTICLE *in* CRYSTAL GROWTH & DESIGN · SEPTEMBER 2013

Impact Factor: 4.89 · DOI: 10.1021/cg400791a

CRYSTAL GROWTH & DESIGN

Article

pubs.acs.org/crystal

Self-Assembly of Conformationally Rigid Dialcohols (Bis-Benzocyclobutenols): Supramolecular Cyclophanes and Arrays

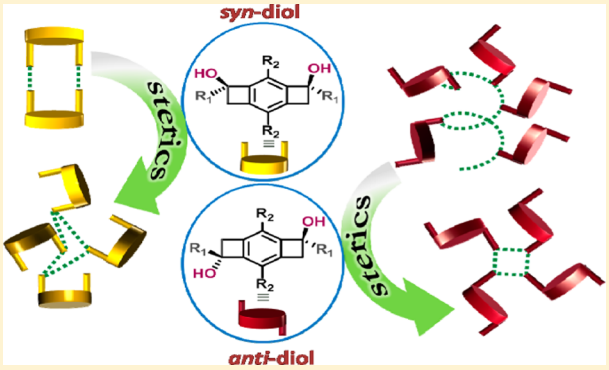
Alankriti Bajpai,[†] Parthasarathy Venkatakrishnan,[†] Susovan Mandal,[†] Subhas Samanta,[†] Paloth Venugopalan,*[,‡] and Jarugu Narasimha Moorthy*[,†]

[†]Department of Chemistry, Indian Institute of Technology, Kanpur 208016, India

[‡]Department of Chemistry, Panjab University, Chandigarh 160014, India

Supporting Information

ABSTRACT: Bis-benzocyclobutenols are synthetically important intermediates, and their structures have been established for the first time. These unique molecular systems allow investigation of the hydrogen bond-mediated aggregation of diols with rigid disposition of the hydroxyl groups on both sides of a flat arene core, namely bis-benzocyclobutene. The *syn*-diols **1a** and **2a** were found to assemble via O−H···O hydrogen bonds between the hydroxyl groups into dimers, which may be termed "supramolecular cyclophanes". However, the analogous diols that are sterically encumbered by ethyl and phenyl groups were found to aggregate via adoption of tetrameric (*syn*-**2c**) or water-expanded dimeric (*syn*-**2b**) supramolecular synthons. The sterically unhindered *anti* diols were found to self-assemble via helical supramolecular synthon in contrast to the sterically encumbered ones; the latter were found to display preference to undergo cyclic tetrameric aggregation. The results thus point to intriguing possibilities in the adoption of supramolecular synthons when a given diol is constrained by the obligation to exploit two or more functional groups of the same kind.



INTRODUCTION

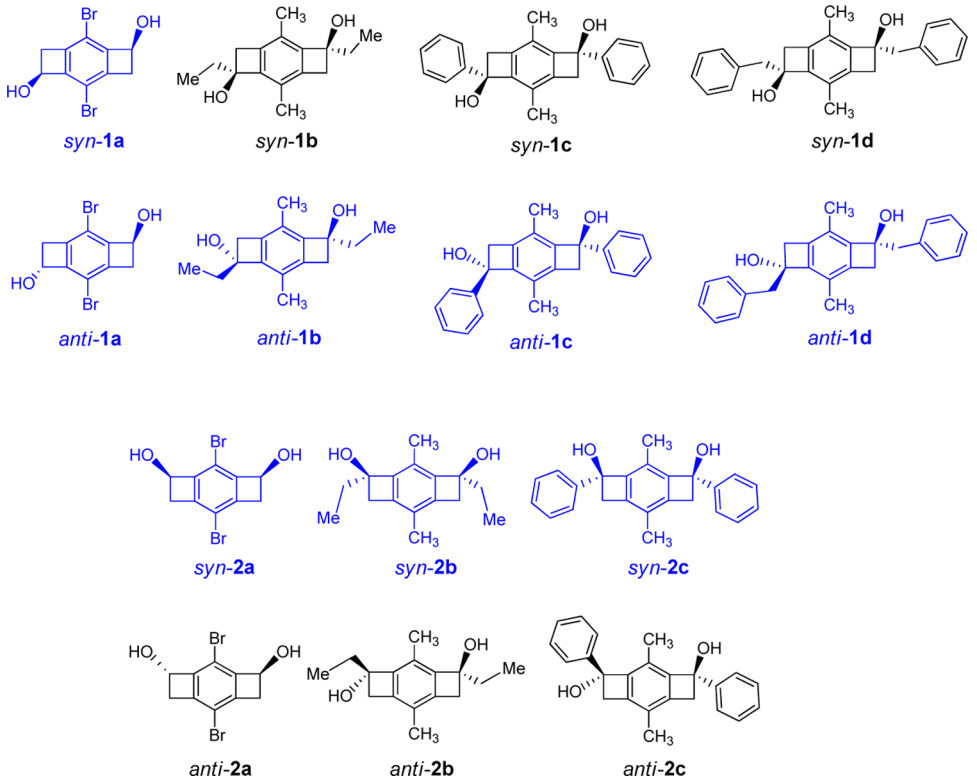
Molecular organization dictates the properties exhibited by solids.[1] Organic solid-state aggregation can be controlled to a large degree by certain groupings of atoms in molecules (functional groups), which interact strongly by noncovalent interactions. The structural subunits that manifest as interaction motifs between molecules/tectons[2] and embody the essence of crystal in terms of molecular recognition are referred to as "supramolecular synthons" (abbreviated as 'SSs' for simplicity in the present context).[3] Exploitation of SSs of functional groups is a meaningful approach to control the molecular organization, that is, crystal engineering.[4] Indeed, it is also a credible strategy for the hitherto insurmountable problem of crystal structure prediction.[5] Tremendous efforts in crystal engineering have led to identification of SSs for virtually every functional group.[3,6] Cambridge Structural Database (CSD)[7] has been a terrific source for learning about different kinds of SSs that one may observe for a given functional group and their relative occurrence statistically.[8] To what degree a given SS of a particular functional group in a given molecule can be observed is something that cannot be readily predicted, although the statistical prevalence of one over the other(s) may guide in crystal engineering. This uncertainty as to the occurrence of a particular SS under all circumstances is primarily due to the fact that the crystal packing occurs, in general, with a trade-off between close packing and maximization of the utilization of intermolecular interactions. Despite this uncertainty, predictability as to the SS reproducibility/robustness for a given molecular system is important in the context of crystal engineering.[9] Incidentally, this information is not much available when the molecule is characterized by not just one kind of functional group but two or more functional groups of the same type or different types! It is known that even the presence of weakly interacting groups overwhelms the molecular organization based on strongly interacting groups.[10]

We are concerned herein with the self-assembly of dialcohols. The early pioneering work of Brock[11] has shown that the aggregation of alcohols occurs via several SSs, namely, polymeric chains, rings, helices, etc. Clearly, the molecular topology that comprises bulk and shape plays a pivotal role in the overall self-assembly, and hence, the kind of SS adopted.[12] A compelling fact with regard to aggregation of alcohols is that they largely undergo helical self-assembly when sterically encumbered;[11,13] we showed recently that simple sterically hindered benzyl alcohols aggregate via helical SS.[9c] In a rather detailed and comprehensive investigation on dialcohols, Bishop and co-workers unraveled the fact that one observes typically two types of patterns, namely staircase ladders and step

Received: May 22, 2013
Revised: September 18, 2013
Published: September 20, 2013

   dx.doi.org/10.1021/cg400791a | *Cryst. Growth Des.* 2013, 13, 4714−4720

Chart 1. Structures BCBs Explored for Self-Assembly[a]



[a]The ones in blue refer to the BCBs for which X-ray structures are determined in the present study.

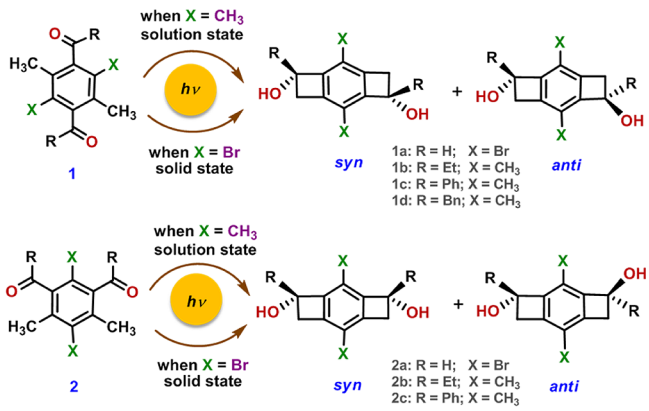
ladders.[14] Incidentally, a variety of supramolecular inclusion host compounds are diols.[15] We were thus motivated to explore the self-assembly of bis-benzocyclobutenols (BCBs, Chart 1), which are benzylic alcohols that are structurally constrained with unique disposition of the hydroxyl groups as in syn and anti diastereomers. In general, benzocyclobutenols are excellent synthetic intermediates and have been tremendously exploited in the synthesis of diverse compounds.[16] In particular, BCBs are relatively less known, and their reactions are virtually unexplored. While these are difficult to be prepared from conventional synthesis, we demonstrated some time ago that one may access them via solid-state diphotocyclization of the conformationally predestined precursor dialdehydes,[17] vide infra.

The objectives in undertaking the present structural studies of BCBs shown in Chart 1 were to (i) establish the structures of these novel synthetic intermediates, (ii) explore the self-assembly of diastereomeric diols that are conformationally predisposed in a unique manner, and (iii) examine how sterics or presence of weakly interacting groups influence the strong O−H···O hydrogen-bonded self-assembly of dialcohols. Herein, we show that the *syn*-diols assemble into supramolecular cyclophanes. The steric bulk is shown to divert association away from the dimer SS and favor adoption of ring SS; of course, the *anti*-diols are found to self-assemble into infinite arrays as one may expect but with the ring motif, when hindered sterically.

RESULTS AND DISCUSSION

The *syn*/*anti* diastereomers of **1a** and **2a** in Chart 1 were obtained by solid-state photolysis of their precursor tere- or isophthalaldehydes, while those of **1b**−**d** and **2b**−**d** were conveniently accessed by solution-state photolysis of their corresponding benzophenones in benzene, cf., Scheme 1.[17] Photolysis led to the formation of diastereomers, which were

Scheme 1. Synthetic Routes for Various Bis-Benzocyclobutenol Derivatives (BCBs)



separated either by recrystallization or by a careful silica-gel column chromatography. All the isomers of BCBs have previously been thoroughly characterized by comprehensive analytical data.[17]

The crystals of the *syn*-**1a**, **2a**-**c**, and *anti*-**1a**−**d** isomers of BCBs (Chart 1) were grown by slow evaporation of their solutions in chloroform or ethyl acetate. Our serious attempts at growing suitable quality crystals of other isomers were in vain; crystallization was attempted in various solvents such as dichloromethane, chloroform, ethyl acetate, methanol, ethanol, and in combinations of solvents such as petroleum ether−ethyl acetate, chloroform−ethyl acetate, chloroform−ethanol, etc.

dx.doi.org/10.1021/cg400791a | *Cryst. Growth Des.* 2013, 13, 4714−4720

Table 1. Crystal Data for Bis-Benzocyclobutenols 1 and 2

compound	*syn*-**1a**	*syn*-**2a**	*syn*-**2b**	*syn*-**2c**	*anti*-**1a**	*anti*-**1b**	*anti*-**1c**	*anti*-**1d**
molecular formula	$C_{10}H_8Br_2O_2$	$C_{10}H_8Br_2O_2$	$C_{16}H_{24}O_3$	$C_{24}H_{22}O_2$	$C_{10}H_8Br_2O_2$	$C_{16}H_{22}O_2$	$C_{24}H_{22}O_2$	$C_{26}H_{26}O_2$
formula weight	319.96	319.96	264.35	342.42	319.96	246.34	342.42	370.47
temperature	100(2)	100(2)	100(2)	100(2)	100(2)	100(2)	100(2)	100(2)
wavelength	0.71073	0.71073	0.71073	0.71073	0.71073	0.71073	0.71073	0.71073
crystal dimensions (mm)	0.13 × 0.11 × 0.09	0.09 × 0.09 × 0.09	0.23 × 0.17 × 0.12	0.19 × 0.18 × 0.13	0.10 × 0.10 × 0.08	0.13 × 0.13 × 0.12	0.18 × 0.16 × 0.12	0.10 × 0.10 × 0.06
crystal system	monoclinic	monoclinic	triclinic	monoclinic	orthorhombic	triclinic	triclinic	tetragonal
space group	*C*2/*c*	$P2_1/n$	$P\bar{1}$	$P2_1/n$	$P2_12_12_1$	$P\bar{1}$	$P\bar{1}$	*P*4/*n*
a (Å)	14.727(3)	11.427(3)	6.519(1)	16.906(1)	7.398(5)	7.940(2)	8.239(2)	14.160(5)
b (Å)	8.144(1)	15.005(6)	10.832(2)	13.332(1)	8.098(2)	8.507(2)	10.647(3)	14.160(5)
c (Å)	16.355(3)	12.378(3)	11.734(2)	16.949(1)	16.350(2)	10.553(3)	11.165(3)	10.639(5)
α (deg)	90.00	90.00	62.66(1)	90.00	90.00	86.88(1)	77.43(1)	90.00
β (deg)	92.46(3)	95.86(2)	81.45(1)	90.21(1)	90.00	85.69(1)	88.54(1)	90.00
γ (deg)	90.00	90.00	78.99(1)	90.00	90.00	79.87(1)	81.52(1)	90.00
volume (Å^3)	1959.8(6)	2111.3(11)	720.8(3)	3820.2(5)	979.5(7)	699.1(3)	945.5(4)	2133.2(15)
Z	8	8	2	8	4	2	2	8
calcd density (mg/m^3)	2.169	2.013	1.218	1.191	2.170	1.170	1.203	1.154
absorption coefficient (mm^{-1})	8.240	7.648	0.082	0.074	8.243	0.075	0.075	0.071
F(000)	1232	1232	288	1456	616	268	364	792
no. of reflections with I > 2σ(*I*)	957	1131	1919	5000	780	1903	2349	1146
goodness-of-fit on F^2	1.033	1.006	1.095	1.018	1.036	1.034	1.068	1.006
final *R* indices [*I*>2σ(*I*)]	R_1 = 0.0536, wR_2 = 0.0893	R_1 = 0.0741, wR_2 = 0.1235	R_1 = 0.0542, wR_2 = 0.1300	R_1 = 0.0454, wR_2 = 0.0965	R_1 = 0.0459, wR_2 = 0.1082	R_1 = 0.0563, wR_2 = 0.1335	R_1 = 0.0559, wR_2 = 0.1481	R_1 = 0.0507, wR_2 = 0.0856
R indices (all data)	R_1 = 0.1140, wR_2 = 0.0989	R_1 = 0.2883, wR_2 = 0.1594	R_1 = 0.0707, wR_2 = 0.1386	R_1 = 0.0613, wR_2 = 0.1004	R_1 = 0.0738, wR_2 = 0.1173	R_1 = 0.0722, wR_2 = 0.1439	R_1 = 0.0771, wR_2 = 0.1583	R_1 = 0.0815, wR_2 = 0.0920

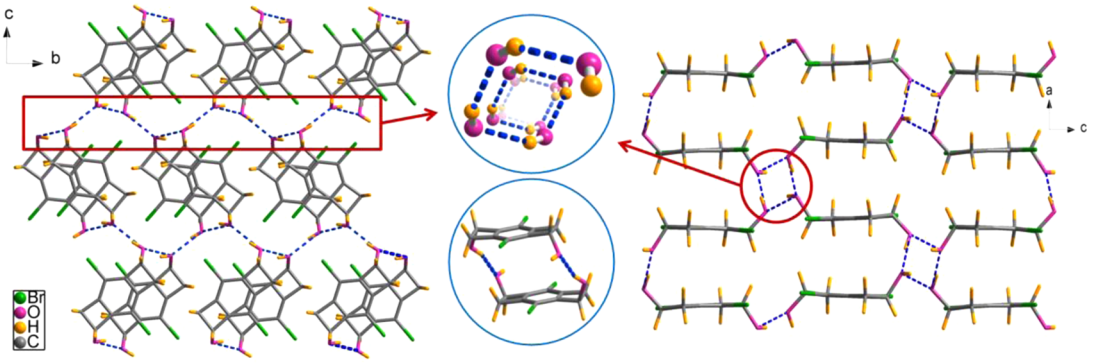


Figure 1. The molecular packing diagrams of *syn*-**1a** (left) and *anti*-**1a** (right) mediated by strong O−H···O hydrogen bonds. The centrosymmetric dimer (supramolecular cyclophane) in *syn*-**1a** held together by two O−H···O hydrogen bonds is shown at the center together with the helical O−H···O hydrogen-bonded SS observed in *anti*-**1a**.

The compounds either crystallized out as fine fibers or fell out as powders. The details of single crystal X-ray diffraction data and refinement for *syn*-**1a**, **2a-c**, and *anti*-**1a−d** are given in Table 1.

The colorless crystals of *syn*-**1a** were found to belong to the monoclinic crystal system with the space group *C*2/*c*. The packing diagram is shown in Figure 1. As one may notice, the hydroxyl groups of BCBs protrude toward the same face of the central benzene ring and involve in hydrogen bonding with their centrosymmetric partners such that one observes the formation of dimers, which may be termed supramolecular cyclophanes. Each dimer is thus a pair of O−H···O hydrogen-bonded BCBs, which is further linked up to the neighboring dimers via additional O−H···O hydrogen bonds leading to chains of dimers along the *b*- and *c*-axes. The dimers are linked up by the helical SS that propagates leading to the formation of two-molecule thick two-dimensional (2D) layers along the *bc* plane down the *a*-axis. It is important to note that one of the bromine atoms in the molecule stabilizes the observed aggregation via a weak C−O···Br halogen bond ($d_{Br\cdots O}$ = 3.22 Å and $\theta_{C-Br\cdots O}$ = 172.7°).

The *anti* diastereomer of **1a** was found to crystallize in the orthorhombic crystal system with the chiral space group of $P2_12_12_1$. The cyclobutene rings in this case are almost planar with respect to the central benzene ring with the hydroxyl groups pointing toward opposite directions. The molecular structure and the packing diagram of *anti*-**1a** are exhibited in Figure 1. Both hydroxyl groups are involved in O−H···O

dx.doi.org/10.1021/cg400791a | *Cryst. Growth Des.* 2013, 13, 4714−4720

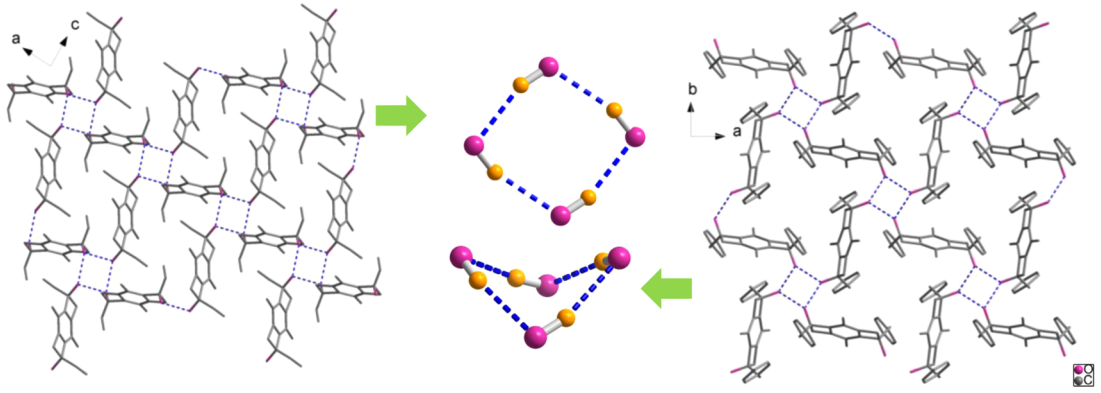


Figure 2. Crystal packing diagrams of *anti*-**1b** (left) and **1d** (right). Planar (**1b**) and puckered (**1d**) tetrameric O—H···O hydrogen bonded SSs that mediate the 2D-layered structures are shown in the middle.

hydrogen-bonded aggregation on either side, resulting in a ladder-type arrangement along the *a* axis. These ladders are further interconnected by strong O—H···O hydrogen bonds in a helical manner leading to a three-dimensional (3D) aggregation.

The *anti* stereoisomer of **1b** was found to crystallize in the triclinic crystal system (space group: $P\bar{1}$). Its asymmetric unit cell was found to consist of two independent molecules, both sitting on the inversion centers, that differ in the orientations of the ethyl groups; in one, the methyl groups of the ethyls are pointed above the bis-benzocyclobutene core, while they are pointed away in the other. The molecular packing diagram of *anti*-**1b** is shown in Figure 2. Interestingly, substitution of the ethyl group in place of hydrogen at the methylene carbon of cyclobutene to which the hydroxyl group is bonded modifies the packing considerably. In this case, the two independent molecules and their centrosymmetrically related pairs assemble via O—H···O hydrogen bonds to form a tetramer.[18] In other words, the SS that one observes is a ring. This tetramer further extends by utilization of the other hydroxyl group in the molecule leading to an infinite tetrameric O—H···O hydrogen bonded 2D network, as shown in Figure 2 (left). The *anti* diastereomer of **1c** is completely analogous to *anti*-**1b** with two independent molecules in the asymmetric unit cell occupying the special positions. As in the case of *anti*-**1b**, they form tetramers and propagate into 2D layers. The crystals of *anti*-**1d**, on the other hand, crystallize in the tetragonal (space group: $P4/n$) crystal system with one molecule in the asymmetric unit cell. In this instance, the molecules exploit the tetrameric ring, which is puckered. The overall packing is otherwise similar to **1b** and **1c**. The increase in steric bulk presumably leads to the SS that is puckered. The crystal packing of **1d** is shown in Figure 2 together with that of **1b**.

Let us now consider the case of *syn*-**2a**, which was found to crystallize in the monoclinic crystal system ($P2_1/n$) with two independent molecules in the asymmetric unit cell. The crystal packing of *syn*-**2a** is shown in Figure 3. As one may expect, the *syn* disposition of the hydroxyl groups should facilitate the formation of supramolecular dimer via two O—H···O hydrogen bonds. Indeed, one observes the formation of supramolecular cyclophane for one of the two independent molecules (A). This dimer of molecule A is hooked up by two molecules of symmetry-related B in an end-capping fashion with a pair of O—H···O hydrogen bonds. The resulting tetramers further interconnect via hydrogen bonds between molecules B to lead to a 2D-layered structure. One observes that the crystal lattice

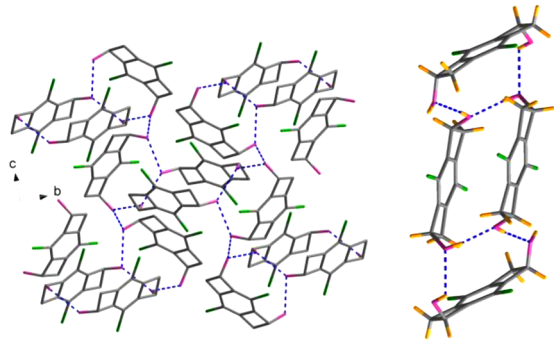


Figure 3. The crystal packing diagram of *syn*-**2a** (left). The dimeric structure that is end-capped by two other molecules to form a tetrameric unit is also shown (right).

in this case is further stabilized by Br···Br type II interaction[19] ($d_{Br\cdots Br}$ = 3.68 Å and $\theta_{C-Br\cdots Br}$ = 99.8°).

The crystals of *syn*-**2b** were found to belong to the triclinic crystal system with the space group $P\bar{1}$. Its asymmetric unit cell was found to contain one molecule each of *syn*-**2b** and water. The ethyl groups attached to the methine carbon are found to exist in different conformations. The hydrogen bonding between hydroxyl groups and the water molecules is found to lead to a water-expanded dimer motif that propagates as a chain down the *b* axis. It is noteworthy that the introduction of ethyl groups in place of hydrogens precludes formation of the supramolecular cyclophane. In contrast, *syn*-**2c** crystallizes in the monoclinic crystal system (space group: $P2_1/n$), with two molecules in the asymmetric unit cell. Four molecules of **BCBs** employ one hydroxyl group each to form a hydrogen-bonded cyclic tetramer. The second hydroxyl group in each generates a similar kind of tetramer in the same direction along the *b* axis. The crystal packing diagram for the dialcohol *syn*-**2c** is also shown in Figure 4. Clearly, the bis-benzylic alcohols that are sterically hindered (i.e., **2b** and **2c**) do not form supramolecular cyclophanes but aggregate via the tetrameric motif, which is expanded by water in the case of **2b**.

Insights Concerning the Self-Assembly of Conformationally-Rigid Dialcohols and Some Generalizations. In general, a variety of SSs such as chains, helices, rings, etc. are adopted by alcohols in their crystals.[11,14,15] Pioneering analyses by Brock et al. have shown that size and shape crucially determine the SS adoption in alcohols.[11] Accordingly, small molecules appear to aggregate as chains, while larger molecules arrange around a screw axis to avoid steric congestion; our

dx.doi.org/10.1021/cg400791a | *Cryst. Growth Des.* 2013, 13, 4714−4720

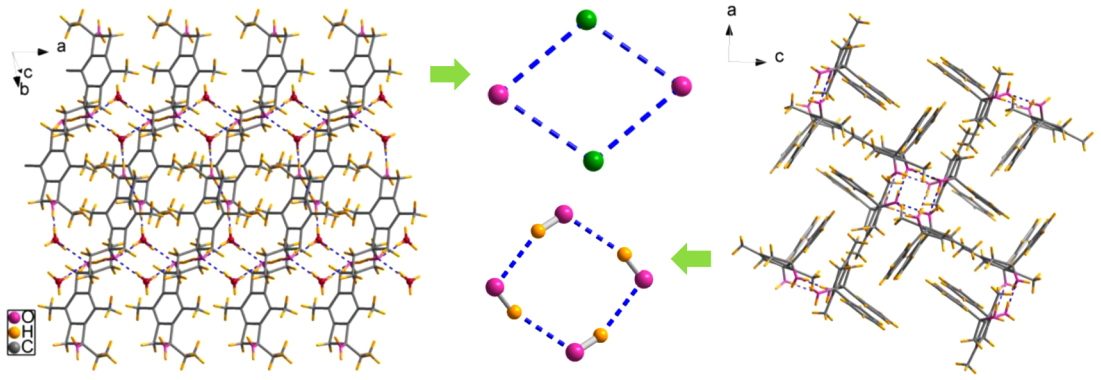


Figure 4. The molecular structure and crystal packing diagram of *syn*-**2b** (left) and **2c** (right). The O−H···O hydrogen-bonded SSs that are involved in the crystal structures are also shown. Notice the involvement of two water molecules (green) in the formation of the ring SS in the case of *syn*-**2b**.

recent work on sterically hindered benzyl alcohols, indeed, led to confirmation of this generalization.[9c] Insofar as dialcohols are concerned, Bishop and co-workers showed that several diols adopt a ladder-type arrangement in what are differentiated as a step ladder and a staircase ladder.[14] In the backdrop of this literature, the investigation of the aggregation of BCBs in Chart 1 deemed compelling to us. As mentioned at the outset, benzocyclobutenols are excellent synthetic intermediates and have been tremendously exploited in the synthesis of diverse compounds.[16] On the other hand, BCBs are relatively less known and their reactions are virtually unexplored. Structurally, they are of two types; in diols **2**, the two hydroxyl groups are toward the same part of the molecular structure, while they are located diagonally about the planar benzocyclobutane structure in diols **1**. Further, depending on relative orientation of the hydroxyl groups, one has access to *syn* and *anti* diasteromers. The unique arrangement of the hydroxyl functionalities allows the self-assembly of diastereoisomers with distinct disposition of the hydroxyl groups to be explored. Additionally, introduction of a substituent such as ethyl/benzyl/phenyl at the α-carbons renders the hydroxyl groups sterically encumbered, such that the influence of steric crowding on the aggregation can be probed in a uniquely substituted set of rigid benzyl alcohols.

Our sustained efforts with the crystallization of other *syn* diastereomers of **1** with the exception of **1a** and *anti* diastereoisomers of **2** were not fruitful. Clearly, lack of crystallization points to the influence of rigid disposition of the hydroxyl groups, which seemingly suffer from the flexibility required for aggregation via O−H···O hydrogen bonding. Presumably, the latter in these isomers leads to a loose crystal packing, which indeed should be a source of guest inclusion. Unfortunately, our efforts with a variety of solvents did not lead to inclusion crystals that could be studied by X-ray diffraction. Otherwise, the limited, yet meaningful set of dialcohols for which the structure have been determined are quite useful in delineating certain insights concerning the self-assembly of conformationally predisposed dialcohols. As revealed by the X-ray determined crystal structures, the BCBs are flat, planar, and conformationally rigid systems with hydroxyl groups protruding either on the same face (*syn*) or on the opposite faces (*anti*) of the central benzene ring. The crystal packing analyses of *syn*-**1a**, *anti*-**1a**−**d**, and *syn*-**2a**−**c** reveal that the dialcohols self-assemble in all cases by exploiting O−H···O hydrogen bonds; the distances of O−H···O hydrogen bonds (d) fall in the range of 1.9−2.1 Å with the corresponding O···O distances (D) in the range of 2.72−2.84 Å. The angular parameters (θs) for O−H···O hydrogen bonds are almost close to linearity (i.e., 152−175°), cf., Table 2.

Table 2. Geometrical Parameters for the O−H···O Hydrogen Bonds Observed in the Crystals of Bis-Benzocyclobutenols

compound	$d_{O\cdots O}$ (Å)	$\theta_{O-H\cdots O}$ (°)	$d_{O-H\cdots O}$ (Å)
syn-**1a**	2.84	158.8	2.06
	2.74	152.3	1.98
syn-**2a**	2.77	166.8	1.97
	2.74	169.5	1.93
syn-**2b**	2.77	175.4	1.85
	2.77	171.0	1.82
syn-**2c**	2.72	–	–
	2.73		
	2.74		
	2.75		
anti-**1a**	2.74	158.2	1.96
	2.81	158.9	2.03
anti-**1b**	2.74	161.5	1.93
	2.75	161.5	1.94
anti-**1c**	2.77	161.2	1.99
	2.74	153.8	1.98
anti-**1d**	2.73	162.2	1.94

With just two structures available for the *syn* isomers of diols that are sterically unhindered (i.e., **1a** and **2a**), it strikingly emerges that in both of these compounds the O−H···O hydrogen-bonded assembly does lead to the anticipated supramolecular cyclophane geometry; while both the molecules in the asymmetric unit cell in *syn*-**1a** are found to be associated as dimers, this association is found for at least one of two different molecules present in the asymmetric unit cell of *syn*-**2a**. However, when the hydrogen at α-carbon of the hydroxyl group is replaced by an ethyl to phenyl group (e.g., *syn*-**2b** and **2c**), the packing pattern deviates in an unusual manner. Whereas the tetramer is observed in the case of *syn*-**2b** via involvement of two hydroxyl groups from two diol molecules and two water molecules, the tetramer is generated in the case of *syn*-**2c** by four hydroxyl groups from four diol molecules.

Although the *anti*-diol of **1a** forms a dimer linked up by only one O−H···O hydrogen bond, the *anti* orientation of the hydroxyl groups facilitate a zigzag ladder-like assembly. The hydroxyl groups form a 2_1 helix along the b axis. In contrast, introduction of sterics at the benzylic sites of the BCBs leads to tetrameric association with a cyclic square (ring) SS in all **1b**−

dx.doi.org/10.1021/cg400791a | *Cryst. Growth Des.* 2013, 13, 4714−4720

d; the increase in steric bulk manifests in slight distortion of the O−H···O hydrogen-bonded SS in *anti*-**1d**. The tetrameric motifs are extended in all directions by BCB units as linkers. Clearly, the steric crowding around the hydroxyl moiety facilitates the tetrameric assembly of BCBs with fixed disposition of hydroxyl functionalities. This feature is different from what is observed with simple sterically hindered benzyl alcohols for which helical SS is observed.[9c]

Insofar as the influence of weakly interacting groups such as Br is concerned, we find that in the case of both diastereomers of **1a**, the observed helical SS is augmented by O···Br interactions. All O···Br contacts are directed toward the helical SSs and thus support the central helical H-bonded core. In the case of *syn*-**2a**, Br···Br contacts are observed, which also aid in the stabilization of the overall assembly. These auxiliary interactions merely stabilize the existing O−H···O hydrogen-bonding pattern.

CONCLUSIONS

We have established the crystal structures of synthetically important bis-benzocyclobutenols (BCBs) for the first time. These diols represent unique systems with rigid disposition of hydroxyl groups on both sides of the flat bis-benzocyclobutene core. The self-assembly of these diols via strong O−H···O hydrogen bonding has been examined in a small, yet meaningful set of compounds. The *syn*-diols **1a** and **2a** are found to assemble into the expected dimeric structures that may be termed supramolecular cyclophanes. However, the dialcohols that are rendered sterically encumbered by ethyl and phenyl groups are found to deviate in that they aggregate via adoption of tetrameric (*syn*-**2c**) and water-expanded dimeric supramolecular synthons (*syn*-**2b**). The *anti* dialcohols that are sterically not hindered were found to aggregate via helical SS in contrast to the sterically encumbered ones; the latter were found to display preference to undergo cyclic tetrameric aggregation. Given that sterically hindered benzyl monoalcohols have been found to assemble via the 4_1-screw helix, the observed tetrameric cyclic square (ring) SS in dialcohols points to a shift in the SS adoption. The results thus point to intriguing possibilities in SS adoption when a given molecule is constrained by the obligation to aggregate via two or more functional groups of the same kind or of different kinds.

EXPERIMENTAL SECTION

X-ray Crystal Structure Determinations. Good quality single crystals for X-ray analysis were obtained by slow evaporation of their solutions in organic solvents such as chloroform, ethyl acetate, methanol, ethanol, etc. The intensity data were collected on a Bruker Nonius SMART APEX CCD detector system and processed with SAINTPLUS. Empirical absorption correction was made using Bruker SADABS. The structure was solved in each case by Direct Methods using SHELXTL and refined by the full matrix least-squares method based on F^2 using SHELX97.[20] All the nonhydrogen atoms were refined anisotropically. The hydrogen atoms were included in their idealized positions with fixed isotropic U values and were allowed to ride with their respective nonhydrogen atoms. The crystal data and details of refinement are included in Table 1. The small size of the crystals and weak reflection data precluded a better *R* value for all data in the case of *syn*-**2a**.

ASSOCIATED CONTENT

Supporting Information

CIF files. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Authors

*venugopalanp@yahoo.com.
*moorthy@iitk.ac.in.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

J.N.M. thankfully acknowledges generous financial support from DST (SERB), India. A.B. and S.M. are grateful to CSIR for senior research fellowships.

REFERENCES

(1) (a) Desiraju, G. R. *Crystal Engineering: The Design of Organic Solids*; Elsevier: Amsterdam, 1989. (b) Nangia, A.; Desiraju, G. R. *Top. Curr. Chem.* **1998**, *198*, 57. (c) *Crystal Engineering: From Molecules and Crystals to Materials*; Braga, D., Orpan, A. G., Eds.; NATO ASI Series; Kluwer: Dordecht, The Netherlands, 1999. (d) *Frontiers in Crystal Engineering*; Tiekink, E. R. T., Vittal, J. J., Eds.; Wiley: Chichester, West Sussex, England, 2006. (e) Bradshaw, D.; Claridge, J. B.; Cussen, E. J.; Prior, T. J.; Rosseinsky, M. *Acc. Chem. Res.* **2005**, *38*, 273.

(2) (a) Wang, X.; Simard, M.; Wuest, J. D. *J. Am. Chem. Soc.* **1994**, *116*, 12119. (b) Brunet, P.; Simard, M.; Wuest, J. D. *J. Am. Chem. Soc.* **1997**, *119*, 2737.

(3) Desiraju, G. R. *Angew. Chem., Int. Ed.* **1995**, *34*, 2311.

(4) (a) Etter, M. C. *Acc. Chem. Res.* **1990**, *23*, 120. (b) Whitesides, G. M.; Simanek, E. E.; Mathias, J. P.; Seto, C. T.; Chin, D. N.; Mammen, M.; Gordon, D. M. *Acc. Chem. Res.* **1995**, *28*, 37. (c) Moulton, B.; Zaworotko, M. J. *Chem. Rev.* **2001**, *101*, 1629. (d) Hosseini, M. W. *Acc. Chem. Res.* **2005**, *38*, 313. (e) Desiraju, G. R. *Angew. Chem., Int. Ed.* **2007**, *46*, 8342.

(5) (a) Gavezzotti, A. *Acc. Chem. Res.* **1994**, *27*, 309. (b) Dunitz, J. D. *Chem. Commun.* **2003**, 545. (c) For recent remarkable success with CSP, see: Neumann, M. A.; Leusen, F. J. J.; Kendrick, J. *Angew. Chem., Int. Ed.* **2008**, *47*, 2427.

(6) (a) Desiraju, G. R. *Chem. Commun.* **1997**, 1475. (b) Steiner, T. *Angew. Chem., Int. Ed.* **2002**, *41*, 48. (c) Shattock, T. R.; Arora, K. K.; Vishweshwar, P.; Zaworotko, M. J. *Cryst. Growth Des.* **2008**, *8*, 4533. (d) Sarma, B.; Sanphui, P.; Nangia, A. *Cryst. Growth Des.* **2010**, *10*, 2388. (e) Clarke, H. D.; Arora, K. K.; Bass, H.; Kavuru, P.; Ong, T. T.; Pujari, T.; Wojtas, L.; Zaworotko, M. J. *Cryst. Growth Des.* **2010**, *10*, 2152. (f) Kavuru, P.; Aboarayes, D.; Arora, K. K.; Clarke, H. D.; Kennedy, A.; Marshall, L.; Ong, T. T.; Perman, J.; Pujari, T.; Wojtas, Ł.; Zaworotko, M. J. *Cryst. Growth Des.* **2010**, *10*, 3568. (g) Ivasenko, O.; Perepichka, D. F. *Chem. Soc. Rev.* **2011**, *40*, 191. (h) Dunitz, J. D.; Gavezzotti, A. *Cryst. Growth Des.* **2012**, *12*, 5873.

(7) Allen, F. H. *Acta Crystallogr.* **2002**, *B58*, 380.

(8) (a) Gavezzotti, A.; Filippini, G. *J. Am. Chem. Soc.* **1995**, *117*, 12299. (b) Nangia, A. *CrystEngComm* **2002**, *4*, 93. (c) Hofmann, D. W. M.; Kuleshova, L. N.; Antipin, M. Y. *Cryst. Growth Des.* **2004**, *4*, 1395.

(9) (a) Hofmann, D. W. M.; Kuleshova, L. N.; Antipin, M. Y. *Cryst. Growth Des.* **2004**, *4*, 1395. (b) Banerjee, R.; Mondal, R.; Howard, J. A. K.; Desiraju, G. R. *Cryst. Growth Des.* **2006**, *6*, 999. (c) Moorthy, J. N.; Mandal, S.; Venugopalan, P. *Cryst. Growth Des.* **2012**, *12*, 2942.

(10) (a) Desiraju, G. R.; Murty, B. N.; Kishan, K. V. R. *Chem. Mater.* **1990**, *2*, 447. (b) Kuduva, S. S.; Craig, D. C.; Nangia, A.; Desiraju, G. R. *J. Am. Chem. Soc.* **1999**, *121*, 1936. (c) Moorthy, J. N.; Natarajan, R.; Mal, P.; Venugopalan, P. *J. Am. Chem. Soc.* **2002**, *124*, 6530.

(11) Brock, C. P.; Duncan, L. L. *Chem. Mater.* **1994**, *6*, 1307.

(12) For example, steric control on the self-assembly of *N,N′*-dialkylthioureas, see: Custelcean, R.; Gorbunova, M. G.; Bonnesen, P. V. *Chem.−Eur. J.* **2005**, *11*, 1459.

(13) (a) Taylor, R.; Macrae, C. F. *Acta Crystallogr.* **2001**, *B57*, 815. (b) Fraile, A. G.; Morris, D. G.; Martinez, A. G.; Cerero, S. D. L. M.; Muir, K. W.; Ryder, K. S.; Vilar, E. T. *Org. Biomol. Chem.* **2003**, *1*, 700.

(14) Nguyen, V. T.; Ahn, P. D.; Bishop, R.; Scudder, M. L.; Craig, D. C. *Eur. J. Org. Chem.* **2001**, 4489.
(15) (a) Design of Organic Solids; Weber, E., Ed.; *Topics in Current Chemistry*; Springer: Berlin, 1998; Vol. *198*. (b) Ung, A. T.; Gizachew, D.; Bishop, R.; Scudder, M. L.; Dance, I. G.; Craig, D. C. *J. Am. Chem. Soc.* **1995**, *117*, 8745. (c) Caira, M. R.; Coetzee, A.; Nassimbeni, L. R.; Weber, E.; Wierig, A. *J. Chem. Soc., Perkin Trans. II* **1995**, 281. (d) Caira, M. R.; Coetzee, A.; Nassimbeni, L. R.; Weber, E.; Wierig, A. *J. Chem. Soc., Perkin Trans. II* **1997**, 237. (e) Bishop, R.; Craig, D. C.; Nguyen, V. T.; Scudder, M. L. *Aust. J. Chem.* **2001**, *54*, 637. (f) Yue, W.; Bishop, R.; Craig, D. C.; Scudder, M. L. *CrystEngComm* **2002**, *4*, 591. (g) Bishop, R. *Acc. Chem. Res.* **2009**, *42*, 67. (h) Skobridis, K.; Paraskevopoulos, G.; Theodorou, V.; Seichter, W.; Weber, E. *Cryst. Growth Des.* **2011**, *11*, 5275.
(16) (a) Macdonald, D. I.; Durst, T. *J. Org. Chem.* **1988**, *53*, 3663. (b) Fitzgerald, J. J.; Drysdale, N. E.; Olofson, R. A. *J. Org. Chem.* **1992**, *57*, 7122. (c) Fitzgerald, J. J.; Pagano, A. R.; Sakoda, V. M.; Olofson, R. A. *J. Org. Chem.* **1994**, *59*, 4117. (d) Zhang, X.; Foote, C. S. *J. Org. Chem.* **1994**, *59*, 5235. (e) Hamura, T.; Suzuki, T.; Matsomoto, T.; Suzuki, K. *Angew. Chem., Int. Ed.* **2006**, *45*, 6294. (f) Shaw, S. *Synth. Commun.* **2007**, *37*, 4183. (g) Chtchemelinine, A.; Rosa, D.; Orellana, A. *J. Org. Chem.* **2011**, *76*, 9157.
(17) (a) Moorthy, J. N.; Venkatakrishnan, P.; Mal, P.; Venugopalan, P. *J. Org. Chem.* **2003**, *68*, 327. (b) Moorthy, J. N.; Samanta, S. *ARKIVOC*; Scholarly Publishing Office: Gainesville, FL, 2007; Vol. *8*, p 324.
(18) Hawkins, S. C.; Scudder, M. L.; Craig, D. C.; Rae, A. D.; Abdul Raof, R. B.; Bishop, R.; Dance, I. G. *J. Chem. Soc., Perkin Trans. 2* **1990**, 855.
(19) (a) Ramasubbu, N.; Parthasarthy, R.; Murray-Rust, P. *J. Am. Chem. Soc.* **1986**, *108*, 4308. (b) Desiraju, G. R.; Parthasarthy, R. *J. Am. Chem. Soc.* **1989**, *111*, 8725. (c) Bui, T. T. T.; Dahaoui, S.; Lecomte, C.; Desiraju, G. R.; Espinosa, E. *Angew. Chem., Int. Ed.* **2009**, *48*, 3838.
(20) Sheldrick, G. M. *SHELX-97, Program for the Solution and Refinement of Crystal Structures*; University of Göttingen: Göttingen, Germany, 1997.