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Helical Self-Assembly of Substituted Benzoic Acids: Influence of Weaker X···X and C−H···X Interactions

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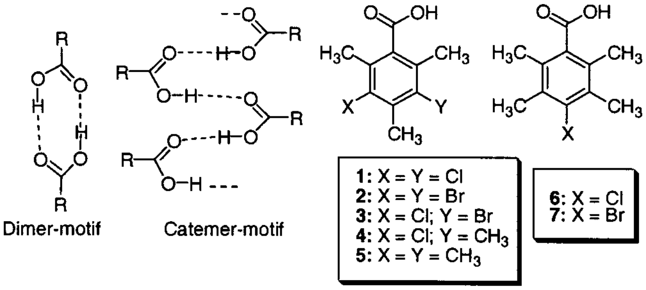
An invaluable approach for the success of crystal engineering,[1] a paradigm for supramolecular synthesis, is the exploitation of the principles of molecular self-assembly.[2] The latter relies heavily on the ability of certain molecular subunits (functional groups) to self-interact in a noncovalent fashion and to conserve a specific and persistent pattern/motif (supramolecular synthon)[1b] that permits predictability as to the overall organization. Among numerous supramolecular synthons, the centrosymmetric dimer motif of carboxylic acids has been exploited successfully in the network design and synthesis.[3] Incidentally, the reliability of the dimer motif in acids is less than what is generally believed. The Cambridge Structural Database analyses have revealed that while 90% of the acids assemble via the dimer motif, 10% of the acids take up three different types of motifs;[4] the catemer motif[5] is observed in 4% of the crystal structures and the dimers expanded by incorporation of solvent molecules are observed in the remaining 6%. Furthermore, the weaker C−H···O and C−H···N interactions have been shown to distort and modify the structures predicted based on dimer-topology of the carboxyl groups in a dramatic way.[6] Therefore, it has been suggested that one must consider the strong[7] and weak hydrogen bonding[8] interactions jointly in the analysis and design of crystal structures.[6] Herein we describe how the weaker C−H···X and X···X interactions mediate the unprecedented helical assembly of sterically encumbered carboxylic acids **1**−**4** via the stronger O−H···O hydrogen bonds.[9]

The X-ray crystal structure analyses of acids **1** and **2** revealed that they are isostructural (tetragonal, I_1/a). The conformation of the carboxyl group in both cases is found to be syn-planar.[5] As one may expect, the plane of the carboxyl group lies almost orthogonal to that of the aromatic ring in both cases (80.4 and 82.1° in **1** and **2**, respectively). Insofar as the hydrogen bonds involving the COOH group are concerned, one observes an unusual helical organization of the molecules along the 4_1-screw axis (Figure 1), linked together by O−H···O hydrogen bonds ($d_{\mathrm{O\cdots O}}$ and $\theta_{\mathrm{O-H\cdots O}}$ are 2.60 Å and 168.8° in **1** and 2.60 Å and 179.0° in **2**). Thus, each coil of the helix contains 4 residues with the distance between the coils corresponding to the unit cell dimension along the *c*-axis, which is ca. 8.60 Å. Further, a closer inspection of the molecular packing revealed that the crystal lattice is stabilized by X···X[10] and C−H···X[11] interactions in addition to the O−H···O hydrogen bonds (Figure 2). Of the two halogens, only one is found to be involved in nonbonded X···X ($d_{\mathrm{Cl\cdots Cl}}(\mathbf{1}) = 3.67$ and $d_{\mathrm{Br\cdots Br}}(\mathbf{2}) = 3.72$ Å) and C−H···X interactions ($d_{\mathrm{H\cdots X}}$ and $\theta_{\mathrm{C-H\cdots X}}$ are 2.83 Å and 147.7° for **1** and 2.99 Å and 141.0° for **2**). Interestingly, the second halogen atom remains a noninteractive “spectator”. It is noteworthy that the unsubstituted *m*-chloro- and *m*-bromobenzoic acids exhibit the standard dimer motif in their crystal structures.[12]

Remarkably, the durene carboxylic acids **6** and **7** are found to be isostructural as are **1** and **2**. These acids exhibit a packing pattern involving both the dimer motif and X···X interactions leading to an organization that is akin to a tape/ribbon (Figure 3). The nonbonded distances for the Cl···Cl and Br···Br in **6** and **7** are 3.56 and 3.87 Å, respectively. In contrast to acids **1** and **2**, no weaker C−H···X interactions are found in **6** and **7**.



1: X = Y = Cl
2: X = Y = Br
3: X = Cl; Y = Br
4: X = Cl; Y = CH3
5: X = Y = CH3

6: X = Cl
7: X = Br

The isostructurality of **1** and **2** and the involvement of only one of the two halogen atoms in the crystal lattice stabilization prompted us to determine the crystal structures of **3**−**5**. Thus, we sought to establish (i) if there exists any obvious preference for one of the two halogens, i.e., Cl and Br, to be involved in the lattice stabilization and (ii) whether the halogen atom at the meta position (with respect to the COOH group) is necessary for the unusual helical assembly observed with acids **1** and **2**.

Acids **3** and **4** were found to crystallize in a tetragonal crystal system and exhibit absolute isostructurality with acids **1** and **2**. However, the structure of acid **3** was found to be disordered with respect to the positions of the Cl and Br atoms, suggesting that the two halogens are indiscriminative and contribute equally well to the crystal lattice stabilization. In the crystal structure of **4**,[13] the methyl group at the meta position simply assumes the role of the

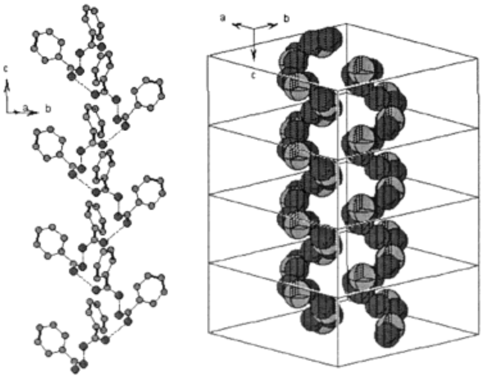


Figure 1. The helical assembly of acid **2** along the 4_1-screw axis. In the left, the hydrogen and Br atoms have been removed for clarity. In the right, only the −COO atoms involved in the hydrogen bonding are shown.

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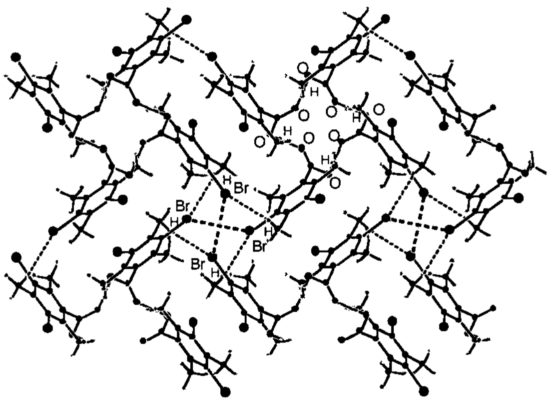

Figure 2. The packing diagram of acid **2** (projection down *c*-axis) showing the Br···Br and C−H···Br short contacts.

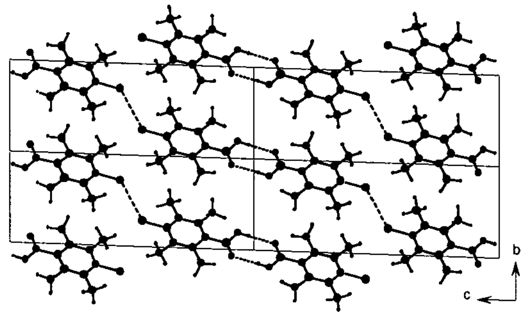

Figure 3. The packing digram of acid **6** showing the Cl···Cl short contacts and the COOH dimer motif.

"spectator" halogen atom in acids **1** and **2**, while the chloro group stabilizes the lattice (Figure 2). In a noteworthy contrast, the pentamethylbenzoic acid **5** crystallizes in the $P2_1/c$ space group and exhibits entirely different crystal packing involving the dimer motif (cf. Supporting Information).

It has been shown that for structures in which the methyl and/or chloro groups participate in *intermolecular interactions characteristic of their own*, the chloro−methyl exchange based on their isosteric relationship cannot be expected.[14] This is precisely what is observed when the "interacting" halogen that is involved in the crystal lattice stabilization (Figures 2 and 3) in **1** and **4** is replaced by an isosteric methyl group as in **5**. The crystal packing changes entirely, emphasizing the importance of the secondary interactions mediated by the halogen atom in the crystal packing. In contrast, the exchange of the "spectator" halogen in **1** by a methyl as in **4** does not result in a similar change of the crystal packing, as they are simply involved in close-packing. As evident from Figures 2 and 3, it is the C−H···X and/or X···X interactions that are responsible for crystal packing in all of the X-substituted acids. The X···X interaction ($d_{X\cdots X}$ = 3.2−4.0 Å for X = Cl and Br) has long been recognized as an attractive and anisotropic one[10c] and has been exploited successfully in solid-state [2+2] cycloadditions.[10d] On the contrary, the C−H···X interaction has been recognized only recently[11] and its applications as applied to stereoselective organic reactions have just begun to unfold.[15] While the operation of X···X interactions in conjunction with the stronger O−H···O hydrogen bonds is well-precedented, e.g. *p*-chloro- and *p*-bromobenzoic acids exhibit packing patterns similar to those of **6** and **7**,[16] the existence of a composite of C−H···X and X···X interactions together with the O−H···O hydrogen bonds as in **1**−**4** is hitherto unknown. This appears to be the reason for the observed paradigm shift in the association of the carboxyl groups in **1**−**4** leading to a 4-fold helical self-assembly via O−H···O hydrogen bonds[17] as compared to that in acids **6** and **7**.

Hydrogen-bonded helices have originated from the work of Hamilton and co-workers.[18a] A variety of helices based on diverse skeletons and interactions are now known.[18] Given the current interest in helices,[18d,e] the present results with simple benzene carboxylic acid derivatives **1**−**4** are remarkable. The X-ray analyses reported herein not only unravel a motif that is unprecedented, but also underscore the role of weaker interactions in modifying the supposedly "robust" supramolecular motif in a decisive manner. A better understanding of the influence of weaker interactions when coupled with stronger O−H···O hydrogen bonds is thus necessary for application of carboxyl groups in supramolecular chemistry in a reliable manner.

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Supporting Information Available: The crystallographic data for all of the acids **1**−**7** and the crystal packing diagram for **5** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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