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Controlled Incorporation of Water Molecules into Carboxy Hydrogen-Bond Networks: A Designed Approach

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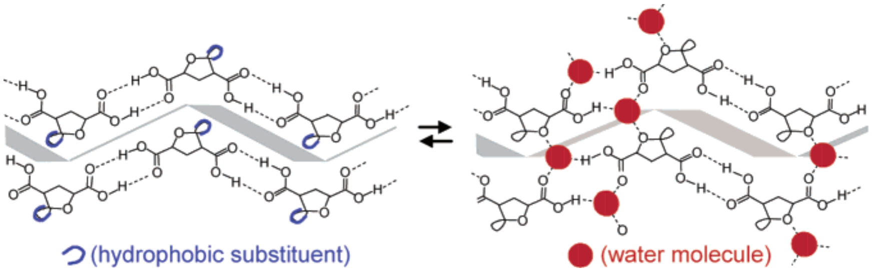
ABSTRACT



The incorporation of water molecules into the hydrogen-bonded pattern of condensed organic materials implies an unfavorable entropic tradeoff resulting from water ordering. Here we show for a family of diacids of general structure (±)-1 that extended chains of anhydrous or hydrated structures can be prepared by controlling the steric factors that lead to the closest packing of individual components.

Here we show for a family of diacids of general structure (±)-**1** (Figure 1) that extended chains of anhydrous or hydrated structures can be selectively prepared in the solid state by controlling the steric factors that lead to the closest packing of individual components.[1] Our strategy was to construct robust H-bonded arrays by using molecular descriptors with unbalanced H-bond donor/acceptor ratios that might redress the d/a imbalance by inclusion of molecules of water.[2]

Carboxy groups commonly self-associate by a packing mode where two carboxy groups link them across an inversion center through two O−H···O═C hydrogen bonds leading to the formation of cyclic dimers.[3] This array should link (±)-**1** carboxy groups to one another giving a centrosymmetric H-bonding pattern forming chains with alternating distribution of enantiomers (Scheme 1, I). Since H-bonded organic structures form reversibly and exhibit slow kinetics for nucleation and crystal growth,[4] both anhydrous

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(1) (a) Eisenberg, D.; Kauzmann, W. *The Structure and Properties of Water*; Oxford University Press: New York, 1969. (b) Robinson, G. W.; Zhu, S.-B.; Singh, S.; Evans, M. W. *Water in Biology, Chemistry, and Physics*; World Scientific: Singapore, 1996. (c) Pratt, R. L. *Chem. Rev.* **2002**, *102*, 2627−2853.

(2) Increases in the number of hydrogen-bond acceptor groups with respect to the donor groups increase the proportion of organic compounds that crystallizes as hydrates: Desiraju, G. R. *Chem. Commun.* **1991**, 426−429.

(3) For some representative examples, see: (a) Ermer, O. *J. Am. Chem. Soc.* **1988**, *110*, 3747−3754. (b) Zhao, X.; Chang, Y.; Fowler, F. W.; Lauher, J. W. *J. Am. Chem. Soc.* **1990**, *112*, 6627−6634. (c) Asthon, P. R.; Collins, A. N.; Fyfe, M. C. T.; Menzer, S.; Stoddart, J. F.; Williams, D. J. *Angew. Chem., Int. Ed.* **1997**, *36*, 735−739. (d) Holy, P.; Zavada, J.; Cisarova, I.; Podlaha, J. *Angew. Chem., Int. Ed.* **1999**, *38*, 381−383. (e) Bernstein, J.; Davey, R. J.; Henck, J.-O. *Angew. Chem., Int. Ed.* **1999**, *38*, 3441−3461. (f) Kobayashi, K.; Shikahara, T.; Horn, E.; Furukawa, N. *Tetrahedron Lett.* **2000**, *41*, 89−93. (g) Jetti, R. K. R.; Xue, F.; Mak, T. C. N.; Nangia, A. *J. Chem. Soc., Perkin Trans. 2* **2000**, 1223−1232. (h) Thalladi, V. R.; Nüsse, M.; Boese, R. *J. Am. Chem. Soc.* **2000**, *122*, 9227−9236.

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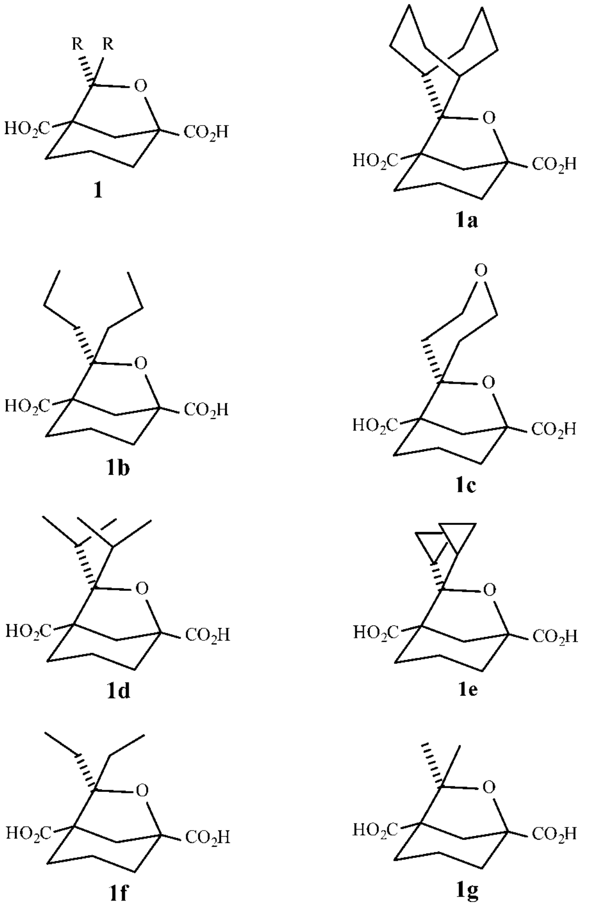
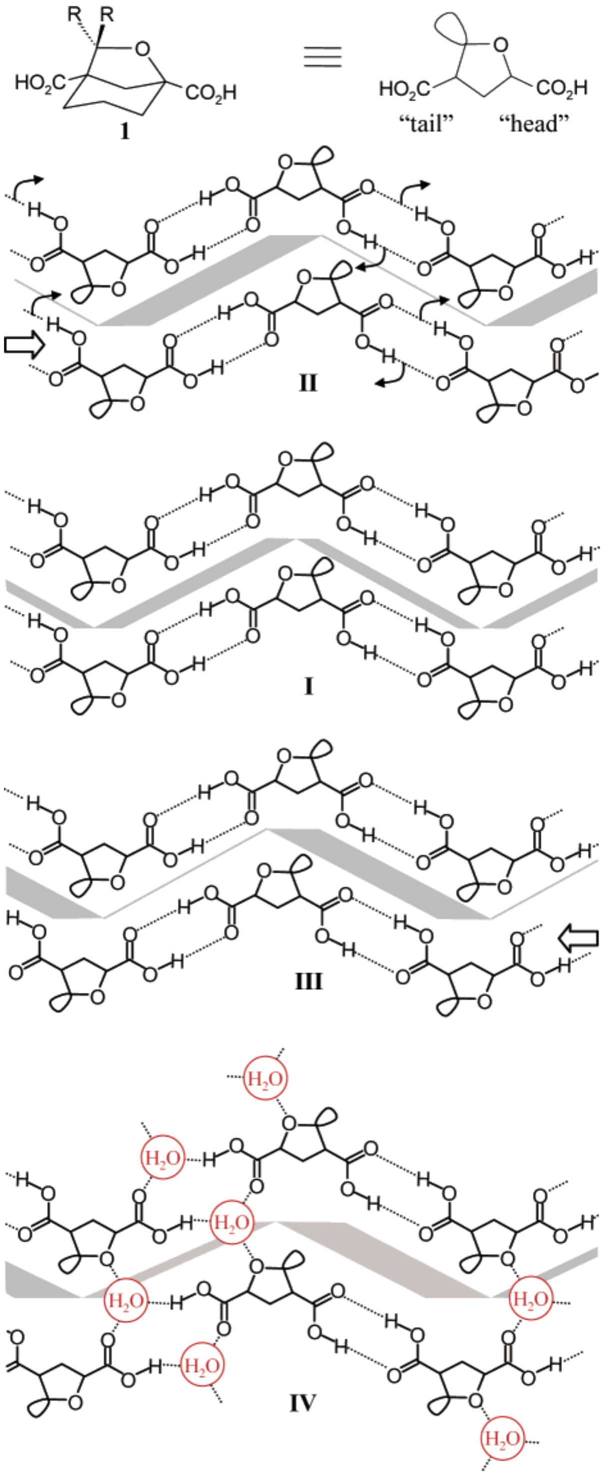


Figure 1. Family of diacids used in this study.

Scheme 1. Two-Dimensional Schematic Construction of Anhydrous (**I**−**III**) and Hydrated (**IV**) Head-to-Head/Tail-to-Tail Assemblies of Diacid (±)-**1**[a]



[a] Dashed lines represent hydrogen bonds. Gaps between chains are shaded in grey. See text for further details.

and hydrated (if any) states of aggregation should coexist in equilibrium.

The anhydrous assembly I is driven by two important interactions: hydrophobic packing in the vertical direction and hydrogen bonding of carboxy dimers in the horizontal direction. However, this arrangement forces the carboxy dimers of adjacent hydrogen-bonded chains into an unfavorable, repulsive proximity. Naturally, the system becomes unstable and tends to advance to a more stable situation by distancing the carboxy dimers from one another. One way of doing this is to slide the molecules along the chain axis to maintain the carboxy dimers away from one another (Scheme 1, II or III). This offset leads to a situation where the carboxy dimers are separated at one end of the column, whereas at the other end, the carboxy dimers move much closer.

The offset that places the carboxy dimer close to the oxygen of the oxolane rings, shown by III, becomes ideal for the incorporation of water molecules into the H-bonding pattern, the oxolane ring oxygen acting as an H-bond acceptor.[5] This further allows the extension of the H-bonding into the vertical direction, forming a two-dimensional array (IV).[6] However, upkeep of the necessary coplanarity for water incorporation depends on the homologue selected.

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(4) (a) ten Wolde, P. R.; Frenkel, D. *Science* **1997**, *277*, 1975−1978. (b) Talenquer, V.; Oxtoby, D. W. *J. Chem. Phys.* **1998**, *109*, 223−227. (c) Oxtoby, D. W. *Acc. Chem. Res.* **1998**, *31*, 91−97. (d) Lee, W. T.; Salje, E. K. H.; Dove, M. T. *J. Phys.: Condens. Matter* **1999**, *11*, 7385−7410. (e) Yan, S.-T.; Vekilov, P. G. *J. Am. Chem. Soc.* **2001**, *123*, 1080−1089.

Indeed, with homologues that include bulky substituents, offsetting by shifting molecules along the chain axis is not a possibility, since molecules are forced to remain in a sterically repulsive environment. Twisting carboxy groups and oxolane rings out of plane is therefore inevitable for bulky diacids, which prevents any possibility of incorporating water molecules into the H-bonding pattern.

Of the seven molecules studied, **1a**−**g** (Figure 1),[7] the four bulkier homologues (**1a**−**d**) generate structures that do not present incorporation of water into their H-bonding pattern. In structural arrangements **1a**, **1b**, and **1d**, carboxy groups turn out-of-plane with respect to the oxolane ring, forcing the monomers to keep an asymmetrical parallel projection along the chain (Figure 2a).

In diacid **1c**, the carboxylic acid functionality adjacent to the oxolane oxygen atom forms a conventional dimer about an inversion center, but the other carboxylic acid group slips around to the oxygen of the oxane ring, forming a large hydrogen-bonded array about an inversion center. The result is an anhydrous two-dimensional structure, but not one of those expected, although it can be readily envisioned from offset II (curved arrows, Scheme 1). Homologues **1e** and **1f** incorporate molecules of water into their H-bonding patterns, maintaining a symmetrical antiparallel projection of the molecules that extend in a two-dimensional array (Figure 2b). In the smallest homologue studied, **1g**, because the top side of the molecule complements the bottom side, hydration occurred at both the left and right sides of the molecule,[6] extending the H-bonding pattern in a three-dimensional array[8] (Figure 2c).

For the incorporation of water molecules into H-bonding patterns to be effective, the model requires (a) mutual recognition of end groups in a one to one relationship, that is, each group is linked to one other group only, and (b) that molecules stack into columns providing sufficient hydrophobic strength to steer the intergrooving pattern. It is impossible, however, to unmistakably link the behavior of a particular molecule with a predefined (hydrated or anhydrous) crystalline state in advance and its need to be optimized from a family of homologues.

The model results are robust and clearly explain the hydrated or anhydrous H-bonding patterns, on the exclusive basis of the structure of the molecular components. It appears that to maintain hydrated arrays, the volume corresponding to cyclopropyl substituents (**1e**) is within the limit of the maximum allowed. Larger appendages provide anhydrous packing.

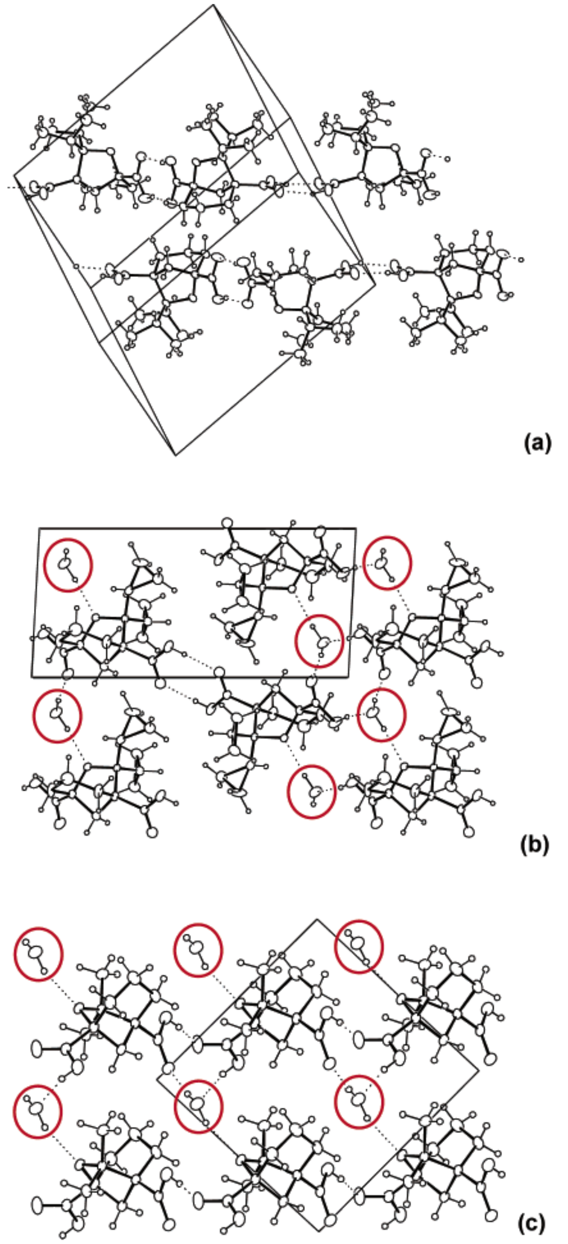

Figure 2. (a) Crystal packing of compound (±)-**1d**: two independent molecules and related translational molecules are linked in a head-to-head/tail-to-tail fashion forming a one-dimensional homochiral array. (b) Crystal packing of compound (±)-**1e**·H_2O: a two-dimensional array maintains one carboxy dimer, while the carboxylic acid function adjacent to the oxolane oxygen is engaged in hydrogen bonds with water molecules. (c) Crystal packing of diacid (±)-**1g**·H_2O: the three-dimensional array involves a head-to-tail/tail-to-head molecular arrangement where both carboxylic acid functions are H-bonded to water molecules.[6,8] Water molecules are encircled in red.

In conclusion, whereas inclusion of water molecules by a solid matrix is a well-known phenomenon, the cause of such

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(5) Because in a cyclic carboxylic acid dimer there is repulsion and destabilization from short O···H and H···H contact across the ring, increasing the ring size by incorporation of ordered water molecules maintaining the centrosymmetry of the H-bonding pattern will be a stabilizing factor in that structure.

(6) Since in Scheme 1 we have considered the more favorable head-to-head/tail-to-tail arrangement, water can only be ordered with the participation of the oxolane oxygen in the head-to-head carboxy acid pattern. However, the head-to-tail arrangement cannot be excluded. In this latter case, hydration should occur by distribution of water molecules among both (head-to-tail and tail-to-head) carboxy dimer patterns.

(7) Crystals of all compounds were grown under identical conditions using a previously water-saturated mixture of carbon tetrachloride/*n*-hexane as a solvent.

(8) Another significant effect of carboxy group twisting that we ought to consider is that, since the two alternating carboxy dimers along the chain are in almost perpendicular planes, ordering water molecules along both dimers extends the H-bonding in two further directions, giving a three-dimensional array.

a process is poorly understood.[1] The data presented above demonstrate that steric matching of remote hydrophobic substituents is an effective tool for controlled incorporation of water molecules into the hydrogen-bonded pattern of condensed organic materials. Although the extension of this concept as the necessary and sufficient motif for hydration remains to be explored, the capacity for directed aggregation demonstrated here represents a significant step in the programmed association of water into noncovalent H-bonded complexes and should permit the design of more complex assemblies.

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Supporting Information Available: Spectroscopic and analytical data, crystal packing diagrams for all compounds (**1a**−**g**), and X-ray crystallographic data for **1a**−**g** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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