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Sterically Hindered Aromatic Tethered Carboxylic Acids: What is the Critical Length of the Tether for Adoption of Centrosymmetric Dimer Synthon?

Jarugu Narasimha Moorthy* and Palani Natarajan

Department of Chemistry, Indian Institute of Technology, Kanpur 208016, India

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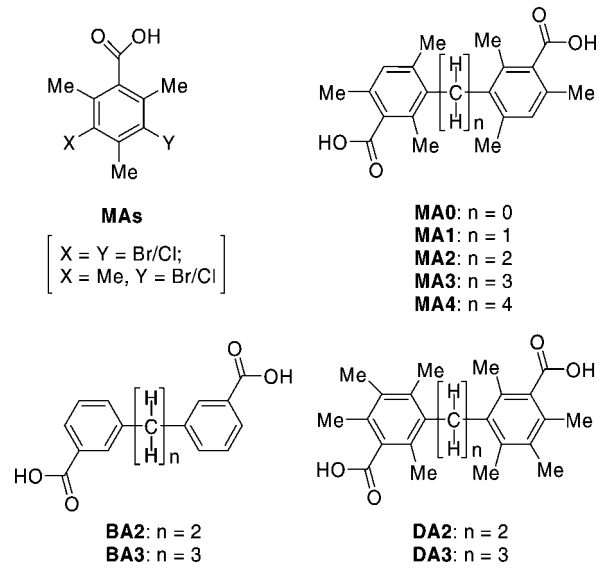
ABSTRACT: The synthesis and X-ray structural investigations of sterically hindered aromatic tethered carboxylic acids have been carried out to examine the extent to which the tether modifies the molecular structures and the occurrence of strong O−H···O hydrogen bond-mediated synthons of the carboxyl groups. The diacids based on mesitylene- and isodurene carboxylic acids (**MA2** and **DA2**) containing a C_2-tether were found to exhibit pseudopolymorphism/solvatomorphism. Whereas a C_3-tethered dimesitoic acid **MA3** crystallized only in the presence of 2,4,6-collidine as a guest, the isodurene analogue **DA3** resisted crystallization. The adoption of the centrosymmetric dimer motif was observed for the butylene-tethered dimesitoic acid **MA4**. The situation appears to be a little relaxed for unhindered diacids such that a C_3-tether is sufficient for adoption of the centrosymmetric dimer synthon in the crystal lattice, as revealed by the crystal structure of 1,3-bis(*m*-carboxyphenyl)propane, **BA3**. The topological changes, that is, skewed (for odd) and extended (for even), imparted by the tether appear to render the close packing with simultaneous exploitation of the strong O−H···O hydrogen bonds difficult even for diacids with a C_2-tether. Thus, for short chain lengths, the tether typically behaves like a functional group, which perturbs the molecular association based on O−H···O hydrogen bonds of the otherwise strongly interacting carboxyl groups.

Introduction

The strength as well as the directionality associated with O/N−H···O/N hydrogen bonds confer some predictability as to the ways/patterns in which the functional groups such as carboxylic acids, amides, etc. undergo association.[1] Insofar as the carboxylic acids as a class of functional group compounds is concerned, a dimer synthon is found in >90% of the compounds that contain no competing donors or acceptors, as revealed by CSD analyses.[2] Indeed, the carboxylic acid dimer motif has been elegantly exploited since the emergence of molecular self-assembly; the formation of a hexagonal rosette structure from trimesic acid[3] and a 3-dimensional diamondoid structure from adamantane tetracarboxylic acid[4] constitute prototype examples of self-assembly based on carboxyl groups. Intriguingly, the alternative catemeric motif is found in only ca. 6% of the structures,[5] despite the fact that the number of hydrogen bonds in both dimeric and catemeric motifs is 2. While the inexplicable preponderance for the occurrence of the dimer motif in the crystal structures of carboxylic acids continues to be an enigma,[2c] Desiraju and co-workers have recently shown that the catemeric motif becomes favored in the crystal packing of a family of phenylpropiolic acids[2c] and cubanecarboxylic acids, in which an ancillary C−H···O hydrogen bond augments adoption of the catemeric motif.[5,6] Be this as it may, the knowledge as to the robustness of synthons and also of factors that might obviate the occurrence of the latter is crucial for engineering target solid materials with a predesired molecular organization.[7] In our laboratories, we have found that sterically hindered aromatic carboxylic acids represent rather *sensitive* systems from the point of view of molecular self-assembly.[8] While the dimer motif is indeed observed in some hindered benzoic acids, for example, pentamethylbenzoic acid, a complete departure from the dimer motif is observed when a weakly interacting halogen group is substituted at a *meta* position of the carboxyl group.[8a] We have shown that 3-halo- and 3,5-dihalomesitoic acids (**MA**s, Chart 1) undergo helical self-assembly in what appears to be a scenario in which the weakly interacting groups decisively control the molecular association based on strongly interacting groups;[8a] in fact, a similar situation prevails for the class of sterically hindered amides.[9] In continuation of these investigations, we found that the conjoined and sterically hindered dicarboxylic acid **MA0** did not adopt dimer motif, but exhibited unusual crystal packing in which a unique planar hexameric water was found to be entrapped in the crystal lattice via hydrogen bonding.[8b] As a logical extension of these studies, we recently inquired into the self-assembly of a sterically hindered diacid separated by a methylene spacer, that is, bis(3-carboxymesityl)methane **MA1**.[8c] Notably, the diarylmethane dicarboxylic acid **MA1** did not crystallize by exploiting the hydrogen bonds of the carboxyl groups, but exhibited pseudopoly-

Chart 1



* To whom correspondence should be addressed. E-mail: moorthy@iitk.ac.in.

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morphism/solvatomorphism[10] suggesting that the tether affects the self-assembly of diacids based on the dimeric/catemeric motif. This led us to the present investigation in which we wished to seek answer for the question: what number of carbon-tether would suffice to ensure adoption of the preponderant dimer motif in the crystal structures of sterically hindered diacids? We have synthesized sterically hindered dimesitoic acids **MA2**-**MA4** and diisodurene carboxylic acids **DA2**,**DA3** as well as unhindered dibenzoic acids **BA2**, **BA3**, shown in Chart 1, and carried out structural investigations.

Results

Synthesis of Diacids. The diacids **MA2** and **DA2** were prepared by reductive dimerization of bromomethymesitylene or bromomethylisodurene in the presence of Mg to afford 1,2-dimesityl/diisodurylethane followed by Friedel−Crafts acylation using $(COCl)_2/AlCl_3$ (Scheme 1); the bromomethyl precursors were, in turn, prepared by bromomethylation of mesitylene/isodurene using paraformaldehyde/HBr. The diacid **BA2** was prepared by catalytic hydrogenation of 1,2-bis(3-bromophenyl)-ethylene and subsequent cyanation and hydrolysis. The starting olefin was synthesized by McMurry coupling of *m*-bromobenzaldehyde. The diacid **BA3** was prepared by following the synthetic route shown in Scheme 1. Accordingly, the dibromochalcone, available from base-catalyzed condensation between *m*-bromobenzaldehyde and *m*-bromoacetophenone, was reduced under H_2 and Pd/C conditions to the corresponding 1,3-di(*m*-bromophenyl)propane derivative. The latter was subjected to cyanation followed by hydrolysis to obtain the diacid **BA3**. An analogous procedure was employed for the synthesis of 1,3-dimesitylpropane starting from acetylmesitylene and mesitaldehyde. 1,3-Dimesitylpropane was subjected to Friedel−Crafts acylation with oxalyl chloride to afford **MA3**. A similar protocol starting from isodurene led to the diacid **DA3**, Scheme 1. The butane-tethered dimesitoic acid **MA4** was synthesized starting from 1,4-dimesitylbutane by direct carboxylation with $(COCl)_2/AlCl_3$ in CS_2. The required 1,4-dimesitylbutane was prepared by catalytic hydrogenation of the precursor 1,4-dimesityl-1,4-dione, which was readily obtained by Friedel−Crafts acylation of mesitylene using $(CH_2COCl)_2/AlCl_3$.

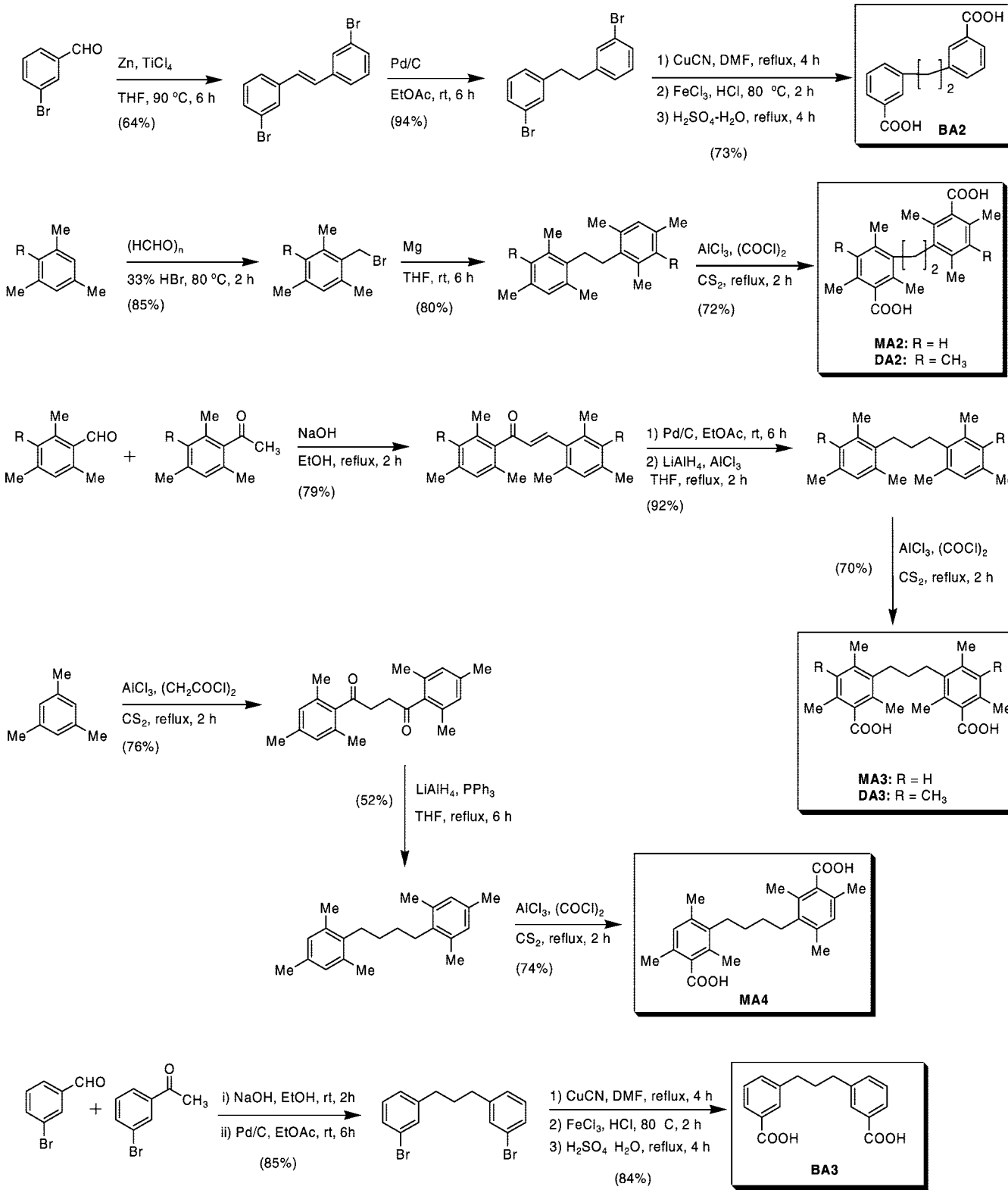
X-ray Crystal Structure Determinations and Crystal Packing Analyses. The crystallization of dibenzoic acids **BA2** and **BA3**, dimesitoic acids **MA2**−**4**, and diisodurene carboxylic acids **DA2** and **DA3** was tried in various solvents and in several combinations of solvents. Further, the crystallization via slow acidification of the solutions of disodium salts in water was also attempted for some of the acids. From a number of crystallization experiments, we were successful in getting the crystals of **BA3** in DMSO, **MA2** in MeOH and DMF, **MA3** in ethyl acetate/collidine, **MA4** in DMF and **DA2** in MeOH. The crystallization of the diacids **BA2** and **DA3** was unsuccessful in a variety of conditions and crystallization procedures. In the following are described the crystal structures of the diacids of each class.

The Crystal Structures of Ethylene-Tethered Dimesitoic Acids, MA2 and DA2. The crystals of the diacid **MA2** were grown from its solution in (i) a mixture of methanol/diethyl ether and (ii) DMF. The crystals from MeOH−ether combination were found to include methanol in the crystal lattice, while those grown from DMF were found to include DMF in the crystal lattice, vide infra. The crystals of methanol solvate were found to belong to the monoclinic crystal system (space group: $P2_1/c$). The details of crystal structure determination and refinement are given in Table 1. The asymmetric unit cell contained only half of the diacid **MA2** molecule with the associated methanol solvent molecule such that the stoichiometry between **MA2** and methanol is 1:2. The operation of inversion symmetry leads to the complete diacid molecule in which the carboxyl groups are oriented in an *anti* relationship with respect to each other as shown in Figure 1; it should be noted that all diacids may, in principle, explore two near-energetic *syn* and *anti* conformations. Due to the steric effect of the methyl groups, the carboxyl group is twisted by 68.41° with respect to the plane of the mesityl ring to which it is bonded. The crystal packing of **MA2**·methanol is shown in Figure 2. As can be seen, the hydrogen of the carboxyl group is involved in a strong hydrogen bond with the oxygen atom of methanol (D = 2.56 Å, d = 1.73 Å, $\theta_{O-H\cdots O}$ = 169.4°), while the carbonyl oxygen of the carboxyl group forms a hydrogen bond with the hydroxyl group of another methanol (D = 2.73 Å, d = 1.89 Å, $\theta_{O-H\cdots O}$ = 177.5°). This results in a *rare* solvent-expanded catemer as shown in Figure 2. One observes that the O−H···O hydrogen-bonded catemeric chain is supported by a C−H···π interaction (D = 3.83 Å, d = 2.96 Å, $\theta_{C-H\cdots\pi}$ = 149.3°) between the methyl hydrogen of methanol and the mesityl ring as shown in Figure 2. To establish the precedence of such a motif and to further unravel ways in which the carboxyl group may be approached by a solvent such as methanol, which is a hydrogen bond donor as well as an acceptor, the Cambridge Structural Database (CSD ver. 1.9, 2007) was searched for all carboxylic acids that contain MeOH in their crystal structures. The search with the query "COOH and MeOH" yielded 140 structures in all. While several cases were found in which two methanol molecules were found to expand the dimer motif, we could glean only four instances in which MeOH was found to be involved in the assembly of acids in a manner that it is not an expanded dimeric motif as shown in Figure 3 (ref. codes: JOBXON, VAZKUD, VUSPAA, and WELVOY). The pattern observed for **MA2**·MeOH corresponds to c in Figure 3.

The crystals of the DMF solvate of the **MA2** grown by slow evaporation of its solution in DMF were found to belong to triclinic system (space group: $P\bar{1}$). The crystal structure determination, cf. Table 1, revealed the stoichiometry between **MA2** and DMF to be 1:2. As in the above case, the inversion symmetry operation over half of the molecule and the solvent DMF contained in the asymmetric unit leads to the full structure of the diacid, in which the relative disposition of the carboxyl groups is found to be *anti*, cf. Figure 1. The oxygen atom of the solvent was found to be disordered, and the refinement was accomplished by associating partial occupancies to the two disordered positions; indeed, the carboxyl hydrogen was located at two different positions from the difference Fourier, which suggests that the oxygens of the carboxyl group are also positionally disordered. The carboxyl group is found to be inclined at an angle of 84.94° with respect to the mesityl ring. The crystal packing of **MA2**·DMF is shown in Figure 4. The carboxylic acid group is found to be hydrogen bonded to a DMF molecule via a strong O−H···O hydrogen bond (D = 2.56 Å, d = 1.74 Å, $\theta_{O-H\cdots O}$ = 168.6°).

The diisodurene carboxylic acid with the ethylene spacer, that is, **DA2**, was readily crystallized from its methanol solution by slow evaporation. The X-ray crystal structure analyses, cf. Table 1, revealed the presence of methanol in 1(**DA2**):2(MeOH) stoichiometry. The crystals were found to be isostructural with those of **MA2**·MeOH solvate except for incremental increase in the volume to accommodate additional methyl groups. Thus, the diacid was found to lie on the inversion center and exhibit molecular organization exactly identical to that shown for

Scheme 1. Synthetic Routes for the Preparation of Diacids



MA2·MeOH, cf. Figure 2. The geometrical parameters for the hydrogen bonds between the acid and MeOH are as follows: C(O)OH···O(H)Me: D = 2.57 Å, d = 1.63 Å, $\theta_{O-H\cdots O}$ = 171.3°; and C(OH)O···HOMe: D = 2.71 Å, d = 1.88 Å, $\theta_{O-H\cdots O}$ = 175.2°).

The Crystal Structures of Propylene-Tethered Dimesitoic Acids, MA3 and BA3. The crystals of the diacid **MA3** were obtained by slow evaporation of its solution in EtOAc containing a few drops of 2,4,6-collidine. The block-like crystals were found to be stable such that their ^{1}H NMR and TGA analyses could be readily performed. These analyses revealed the stoichiometry between **MA3** and 2,4,6-collidine to be 1:2. The X-ray analyses showed that the crystals belong to the monoclinic crystal system (space group: *C*2/*c*). The central methylene carbon of the diacid molecule was found to lie on the 2-fold axis of symmetry so that the asymmetric unit comprised only

Table 1. Crystal Data for the Diacids MA2, MA3, MA4, BA3, and DA2

property	**MA2**·MeOH	**MA2**·DMF	**DA2**·MeOH	**BA3**	**MA3**·collidine	**MA4**
chemical formula	$C_{24}H_{34}O_6$	$C_{28}H_{40}N_2O_6$	$C_{26}H_{38}O_6$	$C_{17}H_{16}O_4$	$C_{39}H_{50}N_2O_4$	$C_{24}H_{30}O_4$
formula weight	418.51	500.62	446.56	284.30	610.81	382.48
crystal system	monoclinic	triclinic	monoclinic	monoclinic	monoclinic	orthorhombic
space group	$P2_1/c$ (14)	$P\bar{1}$ (2)	$P2_1/c$ (14)	$C2/c$ (15)	$C2/c$ (15)	$Pbca$ (61)
a, Å	12.058(2)	7.392(2)	12.226(1)	13.498(5)	30.153(4)	13.523(3)
b, Å	8.435(1)	8.955(2)	8.803(1)	5.009(5)	7.946(2)	9.472(2)
c, Å	11.801(2)	11.907(2)	11.602(1)	21.647(5)	16.177(2)	16.254(3)
α, °	90.0	71.00(1)	90.0	90.0	90.0	90.0
β, °	106.28(1)	78.48(1)	105.65(1)	99.93(1)	117.19(1)	90.0
γ, °	90.0	65.83(1)	90.0	90.0	90.0	90.0
volume, Å^3	1152.1(2)	678.0(2)	1202.4(2)	1441.6(2)	3447.8(8)	2082.1(7)
Z	2	1	2	4	4	4
T, K	100	100	100	100	100	100
μ mm^{-1}	0.085	0.086	0.086	0.093	0.075	0.082
F(000)	452	270	484	600	1320	928
reflections collected	6344	4456	6539	4140	8838	12919
unique reflections	2261	3186	2345	1559	3038	2581
reflections with $I < 2\sigma(I)$	1658	2375	2016	1038	3091	1907
ρ_{calc}, g cm^{-3}	1.206	1.226	1.233	1.310	1.177	1.220
goodness-of-fit	1.05	1.09	1.067	1.051	1.058	1.069
final R_1 [$I < 2\sigma(I)$]	0.0622	0.0677	0.0612	0.0584	0.0577	0.0594
final wR_2	0.181	0.130	0.132	0.1475	0.1525	0.167

half of the molecule and 2,4,6-collidine. Thus, the relative orientation of the carboxyl groups in the molecule is *anti*. Further, due to the freedom of rotation about the C−C σ-bonds of the propane spacer, the molecule may in principle adopt any of the four conformations,[11] that is, tt, tg, gg, and g^-g^+ shown in Figure 1. The conformation that is found for the diacid corresponds to "tt". The crystal packing diagram of the **MA3**·2collidine intercalate is shown in Figure 5. One observes alternating layers of host and guest molecules along the *b*-axis. While the host molecules are organized in a manner that the carboxymesitylene moieties undergo π-stacking, the molecules in the layer of the guests are found in "parallel-displaced" geometries as shown in Figure 5. The COOH groups of the diacid **MA3** form strong hydrogen bonds with collidine molecules via O−H···N intermolecular bonds (D = 2.64 Å, d = 1.84 Å, $\theta_{O-H\cdots O}$ = 166.8°). Clearly, collidine terminates the otherwise possible polymeric propagation of carboxyl groups via dimeric/catemeric motif. The carbonyl oxygen atom of carboxyl group involves in two strong C−H···O hydrogen bonds with the aromatic hydrogen (D = 3.55 Å, d = 2.70 Å, $\theta_{C-H\mu O}$ = 151.6°) and methyl hydrogen (D = 3.54 Å, d = 2.60 Å, $\theta_{C-H\cdots O}$ = 143.2°) of the collidine guest.

The crystals of diacid **BA3** were obtained from its solution in DMSO over a period of 2−3 weeks. The X-ray structure

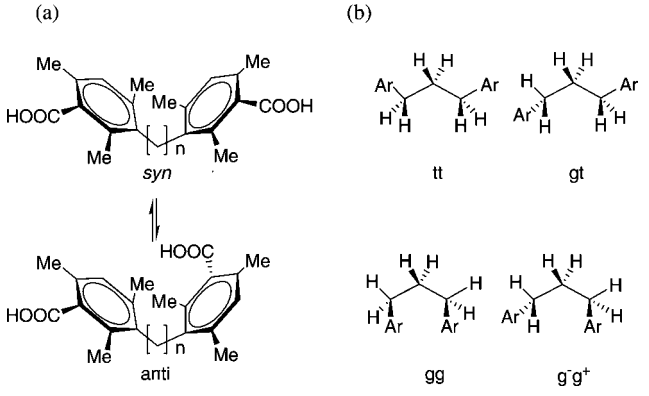


Figure 1. The near-energetic conformations that may be possible for all of the *meta*-substituted diacids (a), and the low-energy conformations of a diarylpropane (b).

determination revealed the absence of any solvent molecule. The crystals were found to correspond to the monoclinic crystal system (space group: $C2/c$), and its molecular center of symmetry was found to coincide with the crystallographic inversion center. The crystal packing is shown in Figure 6. As may be seen, the diacid adopts coiled/twisted conformation and undergoes self-assembly via cyclic dimer motif. The geometrical parameters for the observed O−H···O hydrogen bond are D = 2.62 Å, d = 1.49 Å, $\theta_{O-H\cdots O}$ = 177.7°.

The Crystal Structure of Butylene-Tethered Dimesitoic Acid, MA4. The crystals of diacid **MA4** were obtained by evaporation of its saturated solution in DMSO and DMF. The X-ray diffraction analyses of the crystals grown from the two solvents gave rise to identical cell parameters. The crystals were found to be orthorhombic (space group: *Pbca*). The structure determination and refinement, cf. Table 1, revealed the absence of any solvent molecule in the crystal lattice. The asymmetric unit cell was found to contain a half-component such that the complete molecule is generated by inversion symmetry operation. As a result, the carboxyl groups are related to each other by *anti* geometry, cf. Figure 1. The planes of the carboxyl groups are found to be inclined by an angle of 51.7° with respect to the mesitylene ring. The crystal packing of **MA4** is shown in Figure 6. Remarkably, the carboxyl groups are found to undergo self-assembly via the typical dimer motif of carboxylic acids. Thus, the assembly leads to a one-dimensional zigzag chain via strong O−H···O hydrogen bonds (D = 2.65 Å, d = 1.83 Å, $\theta_{O-H\cdots O}$ = 175.1°).

Discussion

As mentioned at the outset, the emphasis of our investigations was to examine how the length of an aliphatic spacer, whose length is varied from one carbon to four carbons, affects the self-assembly of sterically hindered *meta*-diaromatic carboxylic acids. The motivation for these investigations was the inexplicable and conspicuous absence of the otherwise robust carboxylic acid cyclic and centrosymmetric dimer motif that we noted in simple halogen-substituted mestoic acids, that is, **MA**s[8a] (Chart 1) and in dimesitoic acids **MA0**[8b] and **MA1**.[8c] While **MA0** crystallized as an unusual hydrate,[8b] unique pseudopolymorphism/solvatomorphism was observed in the case of **MA1**;[8c]

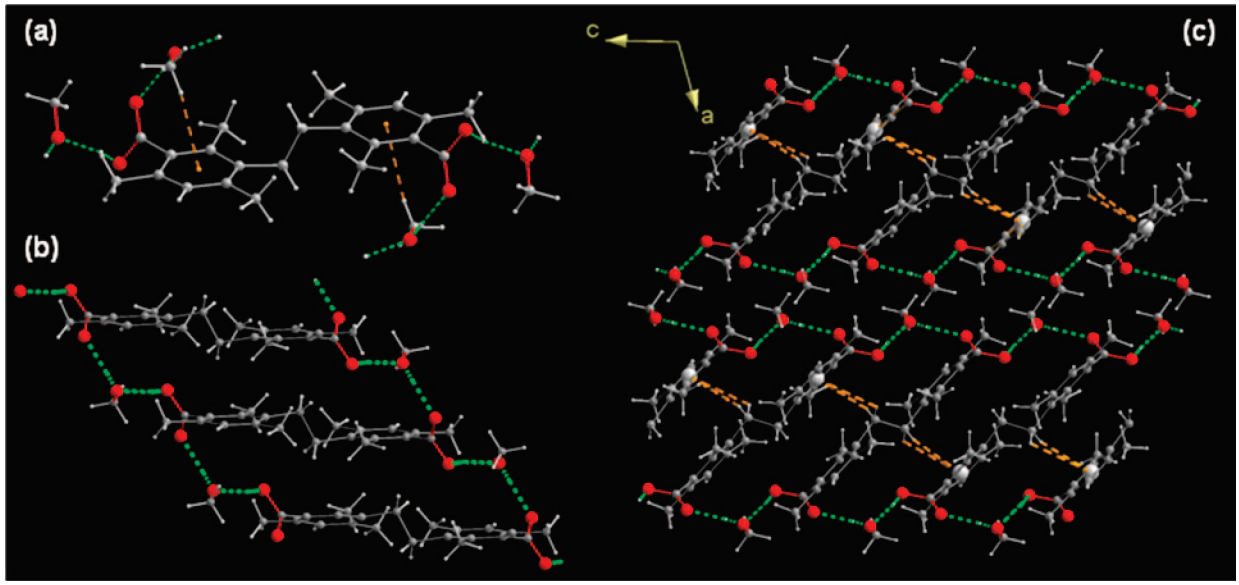


Figure 2. The molecular structure of **MA2**·2MeOH (a), the solvent-expanded catemeric motif of the carboxyl group (b), and the crystal packing of the solvate (c). Notice that the MeOH-assisted strands of the acids are further supported by C−H···π interactions between the mesitylene moieties and the methylene hydrogens of the tether.

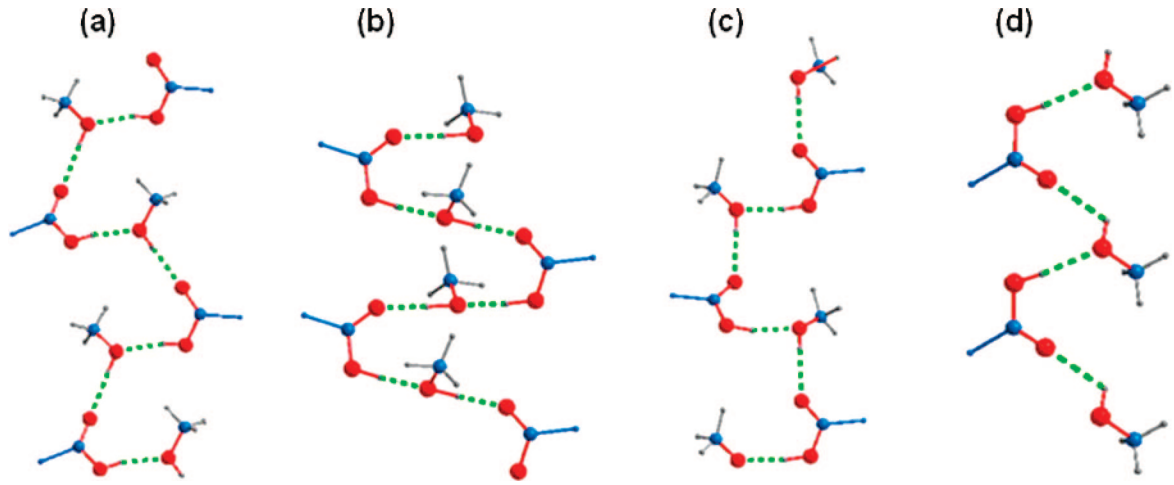


Figure 3. Various ways in which MeOH is found to expand the catemeric motif of carboxylic acids. Refcodes of the structures in which the motifs "a−d" were identified, respectively, are WELVOY, VUSPAA, JOBXON and VAZKUD. Notice that the solvent methanol molecules may approach the carbonyl carbon in three different geometries as in a−c. While the 2_1-screw related carboxyl groups are tied together by MeOH in a−c, the translation-symmetry related molecules are joined together by MeOH in the motif d.

the origin of pseudopolymorphism was attributed to the packing problems of a molecular system that typifies two near orthogonal carboxymesityl rings. It must be noted that the molecules with perpendicular planes exhibit packing difficulties leading to increased propensity for pseudopolymorphism/solvatomorphism, as has been shown recently by Jacco Van de Streek from CSD analyses.[12] In light of these observations, the crystal structure analyses of diacids tethered by ethylene and homologous spacers were deemed important to elucidate the extent which the increase in the length of the tether influences molecular structure and organization in general,[13] and the dimer synthon in particular.

The diacids connected by an ethylene spacer, that is, **MA2** and **DA2**, resisted crystallization in a variety of solvents. The crystals suitable for X-ray studies could be obtained only from MeOH and DMF for **MA2** and from MeOH for **DA2**. In all of these structures, only half of the molecule was found in the asymmetric unit cell with a solvent molecule (MeOH/DMF) such that the ratio between the diacid and the included solvent is 1:2. Evidently, the free acid does not readily crystallize. In the case of the DMF solvate of **MA2**, the solvent simply terminiates the possible hydrogen-bond mediated polymeric propagation of the diacid molecules, Figure 4. In contrast, one observes what may be regarded as a "solvent-expanded catemeric motif" in **MA2**·2MeOH solvate, Figure 3; while the acid hydrogen is bonded to the methanol oxygen, the methanol hydrogen is bonded to the carbonyl oxygen of 2_1-screw-related molecule leading to a novel solvent-expanded polymeric chain. Indeed, the structure of **DA2**·2MeOH is completely isostructural with that of **MA2**·2MeOH. The CSD analyses of the structures of acids in which MeOH is found to be involved in expanding the catemeric motif led to identification of only four structures. Interestingly, these structures, despite being limited in number, reveal intriguing geometries in which the solvent methanol may approach the carbonyl oxygen of the acids. The identified patterns in Figure 3 suggest that the hydrogen atom of methanol

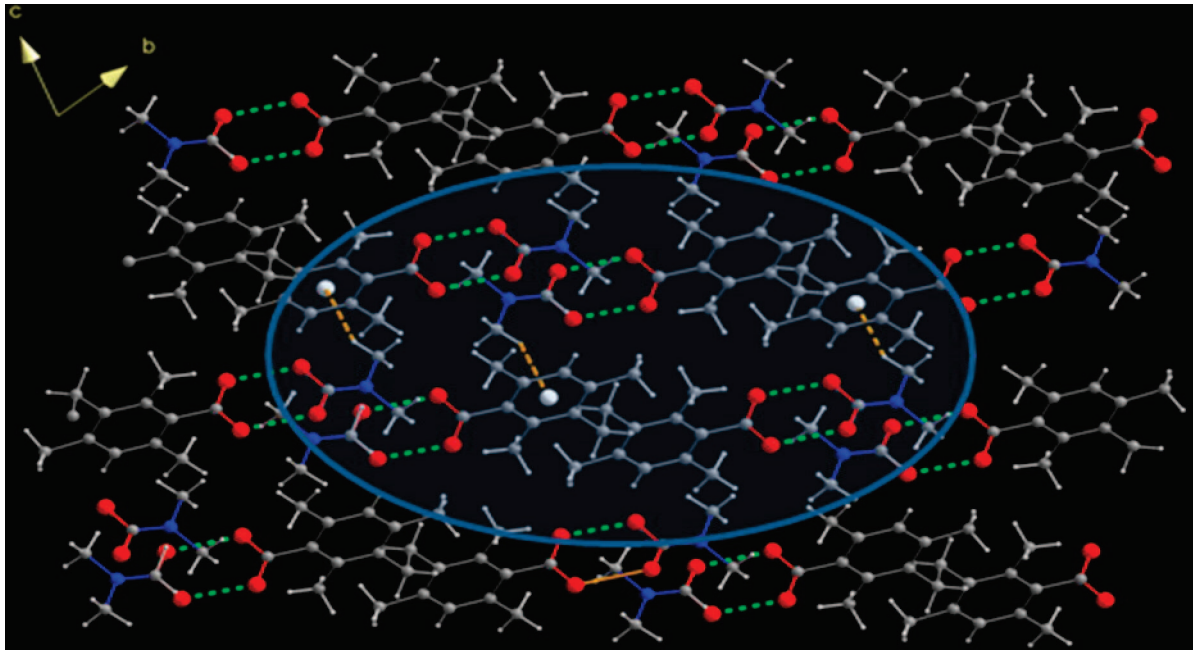


Figure 4. The crystal packing diagram of **MA2**·DMF. The DMF oxygen is disordered over two positions. The C−H···π interaction between the methyl hydrogen of DMF and the arene moiety is shown in the ring.

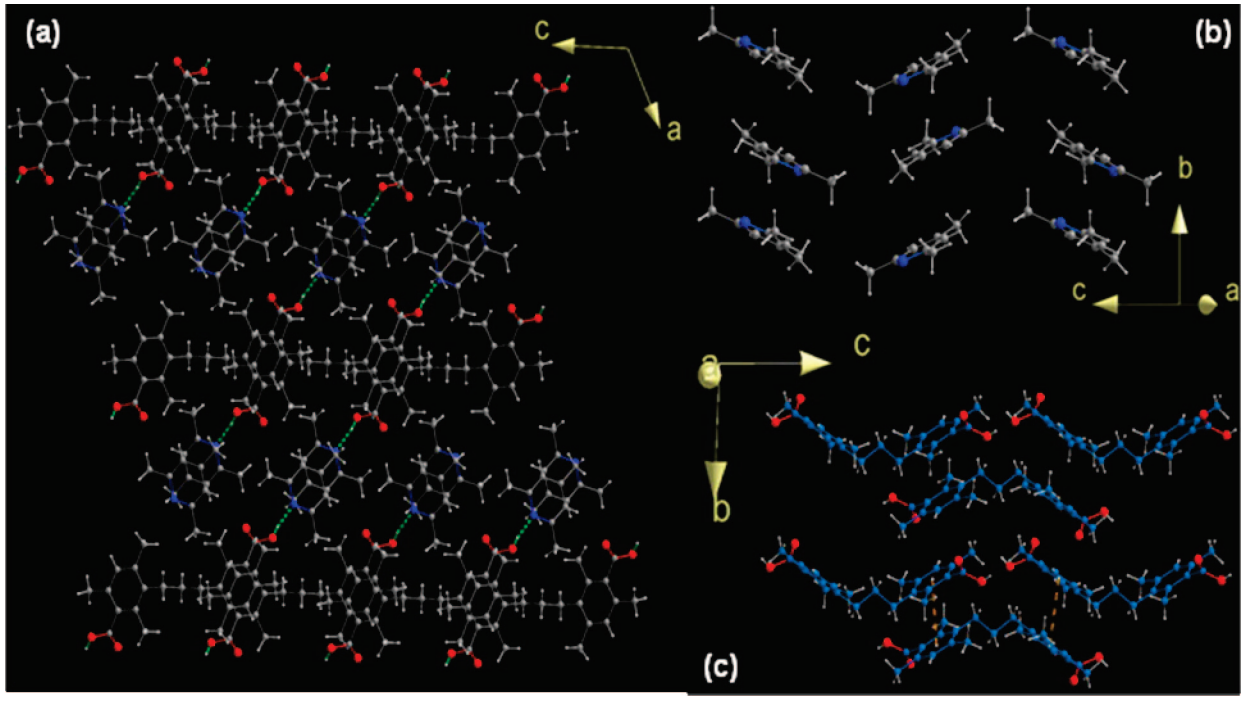


Figure 5. The crystal packing of **MA3**·2 collidine (a), the arrangement of guest molecules alone (b) and the host molecules alone (c).

may lie on the C═O axis or along either side with, of course, different magnitudes of perpendicular displacement from the plane of the carboxyl group; the observed solvent-expanded catemeric motif is quite uncommon, and the pattern observed in **MA2**·2MeOH and **DA2**·2MeOH corresponds to that of c shown in Figure 3. It is noteworthy that the methanol hydrogens are necessarily *syn* to the hydroxyl groups of the acids in MeOH-expanded dimeric synthons. Thus, more detailed investigation of MeOH solvates of carbonyl compounds, e.g., amides, esters, ketones, etc., might offer new insights into various modes of approach of the hydrogen donors.

Our best efforts to obtain the crystals of propylene-tethered dimesitoic acid **MA3** as well as diisodurene carboxylic acid **DA3** were in vain in a range of solvents that do not contain an organic base such as 2,4,6-collidine. In the case of the former, the crystals were obtained only in the presence of an added collidine base. As in the case of **MA2**·2DMF, the collidine molecules form O−H···N hydrogen bonds with the carboxyl hydrogens of the acids leading to discrete complexes.[14] The crystallization of acids in the presence of aromatic bases such as pyridine, lutidine, etc. is also known to lead to the formation of salts via proton transfer from the acid to the base.[15] Of course,

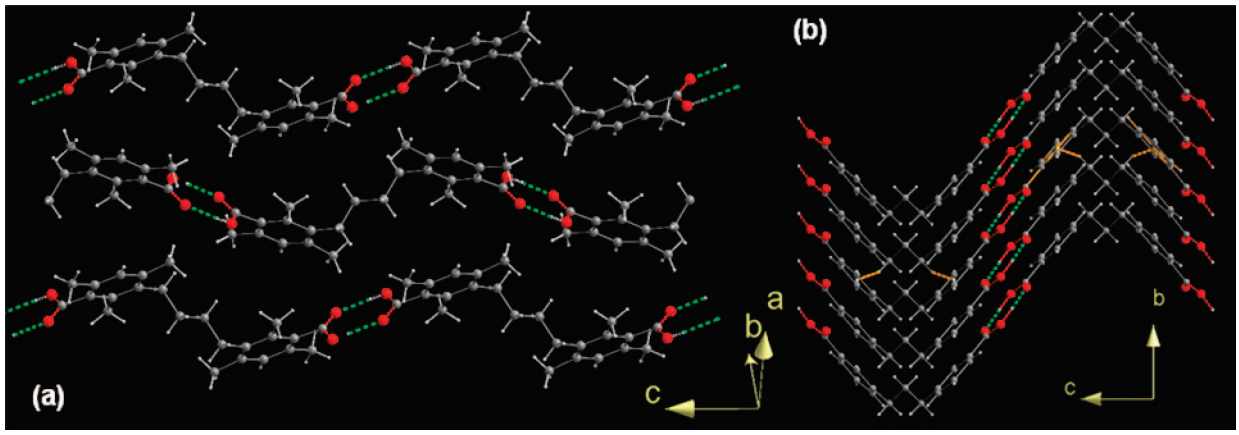


Figure 6. The crystal packing diagrams of diacids **MA4** (a) and **BA3** (b). Observe that the centrosymmetric dimer motif leads to zigzag polymeric chains of the diacids in each case.

the occurrence of proton transfer is subject to a critical difference in pK_a of the acid and the protonated base, that is, ΔpK_a. Recently, Nangia and co-workers have shown based on their studies on the cocrystals of cyclohexane tricarboxylic acids with pyridine that the contact between carboxylic acid and pyridine corresponds to O−H···N interaction for $0 < \Delta pK_a < 3.75$, and ionic character, that is, N^+−H···O, for $\Delta pK_a > 3.75$.[16] In the present instance, the ΔpK_a value is calculated to be ca. 4.0 based on the reported pK_a's of 3.48 and 7.48 for mesitoic acid[17] and protonated pyridinium salt,[18] respectively; of course, mesitoic acid is presumed to be equal to a half component of the molecule. The salt formation is not observed according to the above criterion. Presumably, the crystal packing environment affects the acidity, as has been pointed out by Nangia et al.,[16] in addition to the conformational influence (skewed geometry of the diacid) to preclude complete proton transfer.

It is thus apparent that the crystallization of diacids **MA2**, **MA3**, **DA2**, and **DA3** does not *readily* occur in a range of solvents that we attempted without inclusion of solvent molecules in their crystal lattices, which suggests the difficulty associated with favorable packing that simultaneously exploits the hydrogen bonds of the carboxyl groups. Presumably, the ethylene and propylene tethers do not permit the molecules from striking a tradeoff between the packing and utilization of hydrogen bonds. In other words, the behavior of the diacids **MA0** through **MA3** attests to the fact that the monomeric carboxymesitylene/isodurene moieties lose their identity when tethered, and exhibit pseudopolymorphism/solvatomorphism; indeed, the unique steric hindrance and *meta* location of the carboxyl groups give rise to novel modes of guest binding, as has been observed for **MA0**[8b] and **MA1**[8c] reported earlier, and also for **MA2** and **DA2** of present study. That these monomeric carboxyarenes regain their freedom and adopt the dimer motif is revealed by the crystal structure of **MA4**; the dimer motif leads to a polymeric zigzag chain as expected, Figure 6. Thus, it may be reckoned that for sterically hindered and tethered dimesitoic acids, a C_4-tether liberates the dimer motif, while a tether up to C_3 drastically disturbs both synthons of the carboxyl group, that is, dimeric and catemeric. This situation seems to be rather relaxed for analogous sterically unhindered diacids, viz., tethered *m*-benzoic acids, as is revealed by the structure of **BA3**. In this instance, the carboxyl groups are found to be associated in the centrosymmetric dimer motif, Figure 6. It should be noted that the structures of **BA2** could not be grown, while the structure of **BA1** appears to be yet unkown.[19] Given that all of the *m*-diacids investigated herein may undergo free rotation about C−C sigma bonds of the tether, the extrema of which represent two near-energetic *syn* and *anti* conformations (Figure 1), and further that the carboxyl group as a plane may also have some flexibility to orient with respect to the mesitylene ring to which it is bonded, one may infer that the pseudopolymorphism/solvatomorphism observed for C_2-tethered diacids is presumably due to the conformational flexibility. We contend that the conformational flexibility is unlikely to be a reason, as the C_4-tethered diacid **MA4** crystallizes readily. In general, conformationally flexible molecules tend to adopt most stable conformations in their crystal lattices.[20] From this point of view, C_2-and C_3-tethered diacids are expected, respectively, to be *staggered* and *skewed* in their lowest energy conformations, which is what is observed in the crystal lattices of **MA2**, **DA2**, **MA3** and **DA3**.

Insofar as the tethering is considered, it is noteworthy that the phenomenon of alternation in the physical property such as melting point is well-known in diacids,[21] aminophenols,[22] dithiols, etc.[23] separated by a tether of odd and even number of carbons. In fact, the alternation of melting points in alkanes with odd and even number of carbons was recognized as early as 1877.[21a] Incisive studies by Boese and co-workers[21b] on aliphatic diacids have revealed that the twisted geometries of diacids with a tether of an odd number of carbons permit less efficient molecular packing as compared to those of the diacids with a tether of even number of carbons. Accordingly, the structures of all the propylene-tethered diacids, that is, **MA3** and **BA3**, are skewed, as mentioned above, while those of the ethylene- and butylene-tethered ones are extended. The skewed geometry does not appear to permit ready crystallization without incorporation of guest molecules as in the case of C_1- and C_3-tethered sterically hindered mesitoic acids.[8c] The reason for a similar propensity in the case of C_2-tethered diacids, that is, **MA2** and **DA2**, should be explicable from the freedom that the molecules apparently lose to pack efficiently by exploiting the O−H···O hydrogen bonded synthons of the carboxyl group.

The length of the tether plays a crucial role in a variety of functions such as charge transport phenomenon in biological systems,[24] energy-transfer in photochemical processes,[25] self-assembly in monolayers,[26] mechanisms of molecular sensors,[27] coordination polymerizations,[28] etc. Our results with sterically hindered diacids demonstrate the fact that the tether behaves as an equivalent of a functional group, which may modify the structure and hence the interaction vectors to cause the prediction

of molecular organization difficult even for acids that predominantly adopt dimer motif.

Conclusions

We have carried out syntheses and structural investigations of a broad set of tethered sterically hindered aromatic acids, whose self-assembly in the solid state is sensitive to simple structural changes. While neither of the robust O−H···O hydrogen-bonded centrosymmetric dimer and catemer synthons was observed for C_2- and C_3-tethered mesitoic- and isodurenecarboxylic acids, it is found that they exhibit increased propensity toward psuedopolymorphism/solvatomorphism and crystallize as solvates of MeOH/DMF/2,4,6-collidine; the crystal structures of MeOH solvates in conjunction with CSD analyses offer more insights into the ways in which the hydrogen bonding solvents may approach the carboxyl group. The C_4-tether appears to suffice for each of the acid moieties to independently exhibit the preponderant centrosymmetric dimer synthon. The situation appears to be a little relaxed for unhindered diacids such that the C_3-tether as in **BA3** is sufficient for adoption of centrosymmetric dimer synthon in the crystal lattice. The topological changes, that is, skewed (for odd) and extended (for even), imparted by the tether appear to render the close packing with simultaneous exploitation of strong O−H···O hydrogen bonds difficult even for diacids with a C_2-tether. Thus, for short chain lengths, the tether typically behaves like a functional group, which perturbs the molecular association based on O−H···O hydrogen bonds of otherwise strongly interacting carboxyl groups.

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Supporting Information Available: The details of synthesis, spectral reproductions of all synthetic intermediates and the final diacids, TGA scan for **MA3**·2collidine complex, details of X-ray structure determinations and cif files for all the structures determined. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) (a) Desiraju, G. R. *Crystal Engineering: The Design of Organic Solids*; Elsevier: Amsterdam, 1989. (b) Desiraju, G. R. *Angew. Chem. Int. Ed.* **1995**, *34*, 2311. (c) Leiserowitz, L. *Acta Crystallogr.* **1976**, *B32*, 775. (d) Etter, M. C. *Acc. Chem. Res.* **1990**, *23*, 120. (e) Jeffrey, G. A. *An Introduction to Hydrogen Bonding*; Oxford University Press: New York, 1997. (f) MacDonald, J. C.; Whitesides, G. M. *Chem. Rev.* **1994**, *94*, 2383. (g) Lawrence, D. S.; Jiang, T.; Levett, M. *Chem. Rev.* **1995**, *95*, 2229.

(2) (a) Kolotuchin, S. V.; Felon, E. E.; Wilson, S. R.; Loweth, C. J.; Zimmerman, S. C. *Angew. Chem., Int. Ed.* **1995**, *34*, 2654. (b) Steiner, T. *Acta Crystallogr.* **2001**, *B57*, 103. (c) Das, D.; Desiraju, G. R. *Chem. Asian J.* **2006**, *1*, 231. (d) Allen, F. H.; Motherwell, W. D. S.; Raithby, P. R.; Shields, G. P.; Taylor, R. *New J. Chem.* **1999**, 25.

(3) Herbstein, F. H. *Comprehensive Supramolecular Chemistry*; Macnicol, D. D., Toda, F., Bishop, R., Eds.; Pergamon: Oxford, UK, 1996; Vol. 6, pp 61−83..

(4) Ermer, O. *J. Am. Chem. Soc.* **1988**, *110*, 3747.

(5) Kuduva, S. S.; Craig, D. C.; Nangia, A.; Desiraju, G. R. *J. Am. Chem. Soc.* **1999**, *121*, 1936.

(6) For an organic magnetic material based on catemeric-assembly, see. (a) Maspoch, D.; Domingo, N.; Ruiz-Molina, D.; Wurst, K.; Vaughan, G.; Tejada, J.; Rovira, C.; Veciana, J. *Angew. Chem., Int. Ed.* **2004**, *43*, 1828.

(7) (a) Holy, P.; Zavada, J.; Cisarova, I.; Podlaha, J. *Angew. Chem., Int. Ed.* **1999**, *38*, 381. (b) Kobayashi, K.; Shkahara, T.; Horn, E.; Furukawa, N. *Tetrahedron Lett.* **2000**, *41*, 89. (c) Zhou, H.; Dang, H.; Ji-Hyun, Yi.; Nanci, A.; Rochefort, A.; Wuest, J. D. *J. Am. Chem. Soc.* **2007**, *129*, 13774.

(8) (a) Moorthy, J. N.; Natarajan, R.; Mal, P.; Venugopalan, P. *J. Am. Chem. Soc.* **2002**, *124*, 6530. (b) Moorthy, J. N.; Natarajan, R.; Venugopalan, P. *Angew. Chem., Int. Ed.* **2002**, *41*, 3417. (c) Moorthy, J. N.; Natarajan, P. *J. Mol. Struct.* **2007**,

(9) Moorthy, J. N.; Singhal, N.; Natarajan, P.; Savitha, G. Unpublished results.

(10) There is a lot of controversy associated with the usage of the word "pseudopolymorphism", see. (a) Desiraju, G. *Cryst. Growth Des.* **2004**, *4*, 1089. (b) Seddon, K. R. *Cryst. Growth Des.* **2004**, *4*, 1087. (c) Nangia, A. *Cryst. Growth Des.* **2006**, *6*, 2.

(11) East, A. L. L.; Aguero, P. C.; Liu, H.; Judge, R. H.; Lim, E. C. *J. Phys. Chem. A.* **2000**, *104*, 1456.

(12) Van de Streek, J. *CrystEngComm* **2007**, *9*, 350.

(13) Rehm, T.; Schmuck, C. *Chem. Commun.* **2008**, 801.

(14) Foces, F. C.; Saiz, A. L. L.; Lorente, P.; Golubev, N. S.; Limbach, H. H. *Acta Crystallogr.* **1999**, *C55*, 377.

(15) (a) Aakeroy, C. B.; Beatty, A. M.; Helfrich, B. A. *J. Am. Chem. Soc.* **2002**, *124*, 14425. (b) Aakeroy, C. B.; Desper, J.; Urbina, J. *CrystEngComm* **2005**, *7*, 193.

(16) (a) Bhogala, B. R.; Basavoju, S.; Nangia, A. *CrystEngComm* **2005**, *7*, 551. (b) Bhogala, B. R.; Basavoju, S.; Nangia, A. *Cryst. Growth Des.* **2005**, *5*, 1683.

(17) Brown, H. C.; Braude, E. A.; Nachod, F. C. *Determination of Organic Structure by Physical Methods*; Academic Press: New York, 1995.

(18) Bruice, T. C.; Zipplies, M. F.; Lee, W. A. *Proc. Natl. Acad. Sci. U. S. A.* **1986**, *83*, 4646.

(19) The CSD (April 1998 version) search yielded the refcode: BZPHCC, for which the coordinates are unavailable.

(20) A lot of organic photochemical reactions in the solid state are rationalized based on this notion, see. (a) Scheffer, J. R.; Garcia-Garibay, M.; Nalamasu, O. *Org. Photochem.* **1987**, *8*, 249. (b) Garcia-Garibay, M. A. *Acc. Chem. Res.* **2003**, *36*, 491.

(21) (a) Bayer, A. *Ber. Chem. Ges.* **1877**, *10*, 1286. (b) Thalladi, V. R.; Nusse, M.; Boese, R. *J. Am. Chem. Soc.* **2000**, *122*, 9227.

(22) Vangala, V. R.; Bhogala, B. R.; Dey, A.; Desiraju, G. R.; Broder, C. K.; Smith, P. S.; Mondal, R.; Howard, J. A. K.; Wilson, C. C. *J. Am. Chem. Soc.* **2003**, *125*, 14495.

(23) (a) Thalladi, V. R.; Boese, R. *New J. Chem.* **2000**, *24*, 579. (b) Thalladi, V. R.; Boese, R.; Weiss, H. C. *J. Am. Chem. Soc.* **2000**, *122*, 1186. (c) Thalladi, V. R.; Boese, R.; Weiss, H. C. *Angew. Chem., Int. Ed.* **2000**, *39*, 918. (d) Boses, R.; Weiss, H. C.; Blaser, D. *Angew. Chem., Int. Ed.* **1999**, *38*, 988.

(24) Drummond, T. G.; Hill, M. G.; Barton, J. K. *J. Am. Chem. Soc.* **2004**, *126*, 15010.

(25) Klan, P.; Wagner, P. J. *J. Am. Chem. Soc.* **1998**, *120*, 2198.

(26) Spori, D. M.; Venkataraman, N. V.; Tosatti, S. G. P.; Durmaz, F.; Spencer, N. D.; Zurcher, S. *Langmuir* **2007**, *23*, 8053.

(27) For example, see. (a) Secor, K. E.; Glass, T. E. *Org. Lett.* **2004**, *6*, 3727.

(28) (a) Tabellion, F. M.; Seidel, S. R.; Arif, A. M.; Stang, P. J. *J. Am. Chem. Soc.* **2001**, *123*, 11982. (b) Ouellette, W.; Koo, B. K.; Burkholder, E.; Golub, V.; Connor, C. J. O.; Zubieta, J. *J. Chem. Soc., Dalton Trans.* **2004**, 1527.

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