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# Non-coplanar aromatic carboxylic acids: Unusual conformation-dependent self-assembly and pseudopolymorphism of di(3-carboxymesityl)methane

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#### Abstract

The dicarboxylic acids 3 and 4, i.e., di(3-carboxy-2,4,6-trimethylphenyl)methane and di(3-carboxyphenyl)methane, are created by a methylene tethering of mesitoic acid and benzoic acid, respectively. These diacids may explore two low energy conformations, viz., *syn* and *anti*. Whereas the *syn*-diacid 3 is found to undergo self-assembly in the solid state via a very rare tetrameric motif, the *anti*-diacid 3 is found to exhibit pseudopolymorphism with guest molecules such as DMSO and PhOH–H<sub>2</sub>O. The unusual patterns of assembly and the occurrence of pseudopolymorphism for the *syn* and *anti* conformers, respectively, appear to emanate from an unique structural feature that emerges as a consequence of tethering. It appears that the molecules that contain strongly interacting functional groups in non-coplanar aryl rings will suffer from packing problems, which manifests itself in a new mode of packing and the phenomenon of pseudopolymorphism.

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### 1. Introduction

The ultimate goal of crystal engineering [1,2], which is concerned with the understanding of intermolecular interactions in the context of crystal packing and exploiting such an understanding to design new solids with desired physical and chemical properties, is to be able to predict crystal packing and *synthesize* crystals with predetermined molecular ordering. Although the *supramolecular synthon* approach involving identification of crystals as retrosynthetic targets [2] has led to a tremendous advancement in predictively engineering crystal structures, subtle variation of structural attributes thwart the expected crystal packing based on supposedly robust supramolecular synthons [3]. Thus, there is a need to understand how, when and why the crystal packing may take a departure from the expected organization based on supposedly robust supramolecular synthons.

One of the functional groups that have been extensively explored in the realm of supramolecular chemistry is the carboxylic acid. The COOH group may, in principle, exist in either of the two geometries, viz., syn and anti. Leiserowitz and co-workers [4] comprehensively analyzed various patterns in which the COOH groups assemble in the crystals. Accordingly, two primary patterns in which the acids have been found to self-assemble are the centrosymmetric dimer motif and the polymeric catemer motif (Fig. 1). The Cambridge Structural Database (CSD) has been analyzed from time-to-time to gauge the frequency of occurrence of patterns in which the carboxylic acids are found to associate [5]. In general, the dimer motif has been found to occur in >90% of the acid structures in which other functional groups that potentially compete for hydrogen bonding are absent. The catemer and other patterns that include dimer motifs expanded by solvents, tetramers, a hexamer motif and a helical motif are observed in the remaining

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Fig. 1. Various motifs that are possible for the self-assembly of carboxylic acids.

10% of the structures [5d]. Given that the carboxylic acid serves as one hydrogen bond donor and one hydrogen bond acceptor in both dimeric as well as catemeric motifs, what indeed causes the acids to crystallize with such a bias in favor of the centrosymmetric dimer motif predominantly is intriguing. Understanding of factors that promote adoption of either dimeric or catemeric motif is important in the utilization of carboxyl group as a supramolecular synthon reliably in crystal engineering. Recently, Desiraju et al. showed that ancillary  $C-H\cdots O$  hydrogen bonds support prevalence of the rare *syn-anti* catemeric motif, cf. Fig. 1, in a family of phenylpropiolic acids [5c] and cubanecarb-oxylic acids [6].

From a recent CSD analyses of solvates, Jacco van de Streek [7] pointed out an observation that the molecules that contain strongly interacting functional groups in non-coplanar aromatic rings, e.g., 1,1'-binaphthyl-2,2'dicarboxylic acid 1 (Chart 1), exhibit more than average tendency to form solvates. We were delighted to recognize that our own discovery of inclusion of a hexameric planar



Chart 1. Structures of the diacids 3 and 4, and their conformations.

water network in the crystal lattice of bimesityl-3,3'-dicarboxylic acid **2**, which we reported some time ago [8], falls in line with this observation. This prompted us to examine the crystal structures of sterically hindered as well as unhindered benzoic acids, viz., bis(3-carboxy-2,4,6-trimethylphenyl)methane **3** and di(3-carboxyphenyl)methane **4**, as the two carboxyaryl rings would be related in these cases by a non-coplanar tetrahedral angle. In addition to exploring the occurrence of solvatomorphism/pseudopolymorphism [9] – crystallization of a given compound with solvents – in these cases, we were also motivated to examine:

- How the tethering with a methylene spacer influences the self-assembly via dimer motif, which is predominantly observed in simple benzoic acids as well as sterically-hindered acids such 2,6-dimethylbenzoic acid (Refcode: DMBNZA10), mesitoic acid (TMBZAC), pentamethylbenzoic acid (TUSOIH), etc.
- The possibility of conformation-dependent crystal packing due to two low-energy *syn* and *anti* conformations that the molecules may exist in (Chart 1).

Herein, we report a rare *tetrameric* assembly of COOH groups in the crystal lattice of solvent-free diacid **3** and its conformation-dependent guest inclusion behavior, i.e., pseudopolymorphism, with DMSO and PhOH– $H_2O$ .

## 2. Experimental

### 2.1. General aspects

Anhydrous tetrahydrofuran (THF) was freshly distilled over sodium prior to use. All other solvents were distilled prior to use. Column chromatography was conducted with silica gel (Acme, Mumbai, 60–120  $\mu$ m mesh). <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on a JEOL-Lambda (400 MHz) spectrometer using CDCl<sub>3</sub> as a solvent. IR spectra were recorded on a Bruker Vector 22 FT-IR spectrophotometer. The melting points were determined with a Perfit Melting point apparatus (India) and are uncorrected. The commercial chemicals were used as received.

The diacid **4**, i.e., bis(3-carboxyphenyl)methane, was prepared by following the reported procedure [10].

# 2.2. Synthesis of bis(3-bromo-2,4,6-trimethylphenyl)methane [11]

To a solution of 8.5 g (48.3 mmol) of NBS and 3.0 g (12 mmol) dimesitylmethane [12] in 50 mL of  $CH_3CN$  was added a catalytic amount of TFA with vigorous stirring. The reaction mixture was allowed to stir for 8 h at room temperature. Subsequently, the solution was concentrated and the organic material was extracted with  $CHCl_3$ . The combined extract was washed with 10% NaOH solution followed by water, dried over anhyd Na<sub>2</sub>SO<sub>4</sub> and the

solvent was removed in vacuo. The pure product was isolated as a colorless solid by silica-gel column chromatography using petroleum ether as an eluent, yield 3.3 g (67%); mp 242–244 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  2.14 (s, 6H), 2.28 (s, 6H), 2.49 (s, 6H), 4.09 (s, 2H), 6.86 (s, 2H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  16.28, 20.14, 21.62, 30.83, 132.19, 136.95, 138.21, 139.16, 142.10.

# 2.3. Preparation of bis(3-cyano-2,4,6-trimethylphenyl) methane

To a solution of 2.6 g (28.0 mmol) of CuCN in 20 mL of DMF was added 3.0 g (7.3 mmol) of bis(3-bromo-2.4.6-trimethylphenyl)methane and the resultant mixture was heated at reflux (150-160 °C) for 6 h. Subsequently, the reaction mixture was cooled to room temperature and a solution of FeCl<sub>3</sub>(4.2 g in 5.0 mL of 2.4 N HCl) was added. The mixture was heated at 70-80 °C for 2 h and cooled. The organic matter was extracted with chloroform, washed with water, dried over anhyd Na<sub>2</sub>SO<sub>4</sub> and the solvent removed in vacuo. The pure product was isolated as a colorless solid by silica-gel column chromatography using CHCl<sub>3</sub> and petroleum ether mixture (20:80) as an eluent, yield 1.7 g (70%); IR (KBr) cm<sup>-1</sup> 2241, 3083; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  2.10 (s, 6H), 2.28 (s, 6H), 2.45 (s, 6H), 4.03 (s, 2H), 6.91 (s, 2H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  19.07, 20.45, 21.35, 31.33, 112.55, 117.86, 130.49, 135.38, 139.94, 140.23, 141.67.

2.4. Synthesis of bis(3-carbamoyl-2,4,6-trimethylphenyl) methane

A solution of 1.5 g (5.21 mmol) of bis(3-cyano-2,4,6-trimethylphenyl)methane in ca. 5.0 mL of AcOH–H<sub>2</sub>SO<sub>4</sub> (2:1, v/v) was heated at reflux. The progress of the reaction was monitored by TLC analysis. After completion of the reaction (16 h), the reaction mixture was poured into ice-cold water. The product that precipitated out was filtered to obtain bis(3-carbamoyl-2,4,6-trimethylphenyl)methane as a colorless powder, yield 1.4 g (83%), mp >280 °C; IR (KBr) cm<sup>-1</sup> 1647, 3156, 3343; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz)  $\delta$  2.00 (s, 6H), 2.03 (s, 6H), 2.16 (s, 6H) 3.93 (s, 2H), 6.82 (s, 2H), 7.38 (s, 2H), 7.57 (s, 2H); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>,100 MHz)  $\delta$  16.91, 18.74, 20.58, 30.99, 129.57, 130.0, 131.81, 134.84, 135.74, 137.86, 171.98.

# 2.5. Synthesis of bis(3-carboxy-2,4,6-trimethylphenyl) methane

To a suspension of 1.1 g (3.25 mmol) of bis(3-carbamoyl-2,4,6-trimethylphenyl)methane in 10 mL of 60%  $H_2SO_4$  was added 5 mL of TFA with vigorous stirring and heated at 80 °C for ca. 3 h. Subsequently, the solution was concentrated and the organic material was extracted with ethyl acetate. The combined extract was evaporated. The pure product was isolated as a colorless solid by silica-gel column chromatography using ethyl acetate and petroleum ether mixture (50:50) as an eluent; yield 0.9 g (81%); IR (KBr) cm<sup>-1</sup>1691, 3413; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>, 400 MHz)  $\delta$  2.10 (s, 6H), 2.12 (s, 6H), 2.26 (s, 6H) 4.08 (s, 2H), 6.88 (s, 2H); <sup>13</sup>C NMR (DMSO-d<sub>6</sub>,100 MHz)  $\delta$  17.73, 19.34, 21.05, 31.74, 130.83, 131.83, 133.22, 135.22, 136.37, 138.16, 171.64.

#### 2.6. X-ray crystallographic structure determinations

The crystals were mounted in a glass capillary, cooled to 100 K and the intensity data were collected on a Bruker Nonius SMART APEX CCD detector system with Mo

Table 1

The crystal data for diacid **3**-free and its phenol and DMSO pseudopolymorphs

Property	3-Free	3–DMSO	3–PhOH
Chemical formula	$C_{21}H_{24}O_4$	$C_{25}H_{36}O_6S_2$	C27H30O6
Formula weight	340.4	496.66	450.51
Crystal system	Monoclinic	Monoclinic	Orthorhombic
Space group	C2/c	C2/c	Pbca
<i>a</i> (Å)	21.320(3)	33.844(4)	16.574(3)
<i>b</i> (Å)	7.5687(11)	8.8859(10)	11.793(3)
<i>c</i> (Å)	22.508(3)	8.6693(10)	23.350(5)
α (°)	90	90	90
β (°)	100.103(5)	102.720(2)	90
γ (°)	90	90	90
Volume (Å <sup>3</sup> )	3575.8(9)	2543.2(5)	4563.9(17)
Ζ	8	4	8
T (K)	100(2)	100(2)	100(2)
$\mu (\mathrm{mm}^{-1})$	0.086	0.247	0.092
<i>F</i> (000)	1456	1064	1920
Reflections collected	9673	6915	24251
Unique reflections	3487	2491	4448
Reflections with $I > 2\sigma(I)$	2365	2067	3214
$\rho_{\rm calc} ({\rm g}{\rm cm}^{-3})$	1.265	1.297	1.311
Goodness-of-fit	1.022	1.060	1.001
Final $R_1$ [ $I \ge 2\sigma(I)$ ]	0.060	0.048	0.056
Final $wR_2$	0.1336	0.1166	0.1402

sealed Siemens ceramic diffraction tube ( $\lambda = 0.71073$  Å) and a highly oriented graphite monochromator operating at 50 kV, 30 mA. The lattice parameters and standard deviations were obtained by a least squares fit using 25 frames with 20 s/frame exposures with the Bruker SMART software. The data were processed and reduced using Bruker SAINTPLUS and empirical absorption correction was made using Bruker SADABS. The structure was solved by Direct Methods using SHELXTL package, and refined by the full matrix least-squares based on  $F^2$  using SHELX97 program (Table 1). The hydrogen atoms were located from the difference Fourier for all cases, except for phenol hydrogen and hydrogen atoms of the guest water molecule in 3-PhOH. In this case, the missing hydrogens were not fixed and the refinement was done without hydrogen atoms.

CCDC 658513–658515 contain the supplementary crystallographic data. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033).

#### 3. Results and discussion

The diacid **3** as well as its sterically-unhindered analog **4**, were conveniently synthesized by following the protocol shown in Scheme 1; for **3**, dimesitylmethane was subjected to bromination, cyanation and hydrolysis sequence to afford initially the diamide [13] followed by further hydrolysis to give the diacid **3** (Scheme 1). The diacid **4** was prepared by direct condensation of benzoic acid with *para*-formaldehyde in H<sub>2</sub>SO<sub>4</sub> [10].

The crystallization of diacid 3 was tried in a variety of solvents. While it precipitated out as a powdery material



Scheme 1. Preparation of diacids 3 and 4.

in several of the solvents upon slow evaporation of their solutions, crystals that appeared like shiny chunks grew from the solution of EtOAc–CHCl<sub>3</sub> in the presence of added phenol. In a similar manner, the solution of the acid in DMSO yielded thick blocks upon allowing the solution of **3** in DMSO for a period of 3 weeks. A slow diffusion of HCl vapor into the solution of acid **3** in NaHCO<sub>3</sub> led to square-shaped crystals. While the crystals obtained via diffusion of HCl into the solution of the disodium salt of the diacid **3** were found to be guest free (**3**-Free), those of the crystals grown from DMSO were found to contain two solvent molecules in the crystal lattice (**3**–DMSO). In a similar manner, the crystals that were grown from phenol-contain-

ing solutions of the diacid **3** were found to include one phenol and one adventitious water molecule (**3**–PhOH). The crystal data for the three cases are given in Table 1. Intriguingly, the diacid **4** did not crystallize in a number of crystallization attempts under a variety of conditions.

The diacid 3-free crystallizes in the monoclinic crystal system (C2/c space group) with Z' = 1. In Fig. 2 are shown the molecular structure as well as the crystal packing diagram. As expected, the two carboxyl groups lie almost perpendicular to the planes of the mesitylene rings to which they are connected ( $\theta = 82.68^{\circ}$  and  $80.28^{\circ}$ ). The angle between the planes of the mesitylene rings that are joined by the methylene spacer is 116.3°, and the molecule as a



Fig. 2. The molecular structure of the diacid 3-free (a), dimeric association via two  $O-H \cdots O$  hydrogen bonds (b), further assembly into a tetramer (c) and the overall crystal packing (d).

whole assumes the shape of 'V'. Most importantly, the conformation with respect to the carboxyl groups present in two rings is found to be *svn*. The crystal packing in Fig. 2 reveals a rather unusual pattern for the assembly of the carboxyl groups. Whereas the dimer and the catemeric forms are not observed, the centrosymmetricallyrelated acids are found to form a dimer via two O-H···O hydrogen bonds involving both of the two carboxyl groups  $(D = 2.58 \text{ Å}, d = 1.80 \text{ Å} \text{ and } \theta_{O-H\cdots O} = 153.6^{\circ})$ , thereby leaving open one O-H donor and one C=O acceptor for further self-assembly. Two such dimers assemble further via 2 O-H···O bonds (D = 2.68 Å, d = 1.84 Å and  $\theta_{O-}$  $_{H \cdots O} = 171.0$  °), thereby completing a tetrameric motif  $R_4^4(16)$  motif as shown in Fig. 2. The tetrameric assembly is a rare occurrence for carboxylic acids in general. The rigorous CSD analyses carried out recently [5d] show only four cases for which such an assembly has been observed

so far (Ref. codes: BODPEP, CLACET01, EJEQOZ and ETYTAC). It is noteworthy that the tetrameric assembly observed for the diacid **3** constitutes the first instance for any aromatic carboxylic acid in particular.

The crystals of the diacid **3** grown from DMSO were found to include the latter in the crystal lattice. The crystals belonged to monoclinic system (space group: C2/c). The asymmetric unit cell was found to consist of only half of the diacid **3** with associated DMSO solvent molecule, which suggests the stoichiometry between the diacid **3** and DMSO to be 1:2; this relative ratio was also established by <sup>1</sup>H NMR analysis of the crystals dissolved in acetone- $d_6$ . Due to the 2-fold symmetry, the carboxyl groups of the diacid **3** assume *anti* orientation. The crystal packing of the **3**–DMSO lattice inclusion complex is shown in Fig. 3. One may draw a close analogy between the molecular packing in this crystal with that observed in the



Fig. 3. The molecular structure of the diacid **3** with DMSO (a), the solvent-expanded dimer (b) and crystal packing (c). Notice that the diacids form a tape via the intermediacy of DMSO solvent molecules.

guest-free lattice discussed above. Each of the carboxyl groups is found to be hydrogen bonded to the oxygen atom of DMSO via a strong O-H···O hydrogen bond (D = 2.58 Å, d = 1.71 Å and  $\theta_{O-H···O} = 164.4^{\circ}$ ). Two such centrosymmetrically-related pairs assemble via 2 C-H···O hydrogen bonds (D = 3.21 Å, d = 2.31 Å and  $\theta_{C-H···O} = 156.0^{\circ}$ ) to form solvent-expanded dimers that propagate as tapes, Fig. 3.

We have analyzed the crystal structures of carboxylic acids containing DMSO deposited in CSD (ver. 1.9, 2007). There is a variety of ways by which the DMSO is included in the crystal lattices of the carboxylic acids. The modes of DMSO inclusion I–V are schematically shown in Chart 2. The association mode observed in the case of 3–DMSO corresponds to the pattern II. The solvent molecules are firmly bound in the crystal lattice, and the TGA analyses show that solvent molecules begin to escape at ca. 198 °C.

The crystals of **3**–PhOH were found to correspond to orthorhombic crystal system (space group: *Pbca*). The crystal structure shows that the diacid molecules exist in *anti* conformation in this case as well. Further, one molecule of phenol and adventitious water are found to be included in the crystal lattice for each molecule of the diacid. Due to the sterics of the methyl groups at ortho positions, the carboxyl groups are twisted by 82.39° and 70.28° with respect to the mesityl rings to which they are bonded. In Fig. 4 is shown the crystal packing down *a*-axis, which reveals the formation of channels down *a*-axis between the layers of the 'V'-shaped diacids. The guest phenols that are hydrogen bonded to water reside in these channels. A careful analyses shows that the two carboxyl hydrogens of the two acids that are translation-symmetry related are bonded to phenol-water couple via strong O-H···O hydrogen bonds  $(D = 2.54 \text{ Å}, d = 1.73 \text{ Å}, \theta_{O-H\cdots O} = 173.8^{\circ}$  and D = 2.64 Å, d = 1.85 Å,  $\theta_{O-H-O} = 161.2^{\circ}$ ) as shown in Fig. 4. Interestingly, the acceptor carbonyl oxygen atoms of the two carboxyl groups involve in strong C-H···O hydrogen bonds (D = 2.82 Å, d = 1.91 Å,  $\theta_{C-H-O} = 130.5^{\circ}$  and D = 3.22 Å, d = 2.54 Å,  $\theta_{C-H-O} = 130.2^{\circ}$ ) with the b-glide-related another molecule as shown in Fig. 4. The inclusion of phenol by acids is indeed very rare. The CSD analyses reveal only 4 examples of phenol inclusion complexes of carboxylic acids (refcodes: FEYYUE, GOSPOL, JIDWEY01, XIBOUU). We believe that the role of water is also space-filling in addition to bridging the phenol and the carboxyl group of the diacid via hydrogen bonding. Clearly, the molecular topology of the diacid 3 appears to be the sole cause for the observed guest inclusion.

As mentioned at the outset, the motivation to analyze the self-assembly of diacids **3** and **4** was to explore if the non-coplanar aromatic dicarboxylic acids exhibit increased propensity for guest inclusion. Although molecules tend to pack as closely as possible in the crystals, strong and specific directional interactions may lead to open networks depending on the fashion in which the interactions are predestined in the molecular building blocks. Due to two strong and directional hydrogen bonds, the dimer motif of carboxyl groups has been exploited reliably in molecular tectonics to create open-framework structures in which the guest molecules occupy the void spaces. For example, the



Chart 2. Various patterns in which the dimer motif of carboxyl groups is expanded by DMSO solvent molecules.



Fig. 4. The mode of assembly of the carboxyl groups of 3 with lattice included phenol and water (top). The crystal packing of 3-PhOH down *b*-axis (bottom). The included phenol and water oxygen are shown in a space-filling model. It is noteworthy that the association of acids with water leads to channels down *a*-axis, within which the guest phenols are located.

2-dimensional trimesic acid [14] and related derivatives [5a] and hexakis(p-carboxyphenyl)benzene [15] and 3-dimensional 1,1'-binaphthyl-2,2'-dicarboxylic acid [16] and spirobifluorene-2,2',7,7'-tetracarboxylic acid [17] crystallize with inclusion of guest molecules in the networks of the acids assembled by the dimer motif. Indeed, Nangia and coworkers [18] exploited the dimer motif to develop hostguest inclusion compounds. However, the trade-off between close-packing and exploitation of strong-hydrogen bonding interactions appears to be one of the reasons for the observation of structures in which neither of the dimeric and catemeric motifs of carboxylic acid is observed. For example, tetrakis(*p*-carboxyphenyl)methane [19] crystallizes with inclusion of toluene and DMSO, and the carboxyl groups are found to be bonded to DMSO solvent. Similarly, 3,3',5,5'-tetrakis(p-carboxyphenyl)bimesityl, reported by us [20], also crystallizes with DMSO bonded to the carboxyl group.

For exploitation of carboxylic acids in the molecular self-assembly, it is important to understand the factors that influence adoption of a particular motif, i.e. dimeric or catemeric. As mentioned earlier, Desiraju et al. recently showed that the rare catemeric motif predominates in a unique class of arylpropiolic acids, in which auxiliary C-H...O hydrogen bonds augment the catemeric motif [5c,5d]. Clearly, the structural attributes play an important and decisive role in the determination of ultimate crystal packing and the observation of a particular packing/binding motif. We sought to investigate this aspect also in the conformationally-flexible diarylmethane dicarboxylic acids 3 and 4, which may in principle exhibit two extreme lowenergy conformations, i.e., syn and anti, cf. Chart 1. Insofar as the diacid **3** is concerned, the rigidity of the carboxyl groups due to steric hindrance from the ortho methyl groups imposes barrier on the directionality for the selfassembly via carboxyl groups. Hence, the diacid 3 may

be considered as a rigid 'V'-shaped module with freedom for rotation of each of the carboxymesityl rings as a whole with respect to the central methylene carbon. The rotation of one of the carboxymesityl ring with respect to the other leads to two low-energy conformations, i.e., *syn* and *anti*. Thus, the diacid **3** offers the opportunity to analyze conformation-dependent crystal packing behavior in addition to exploring the influence of structural attributes involving non-coplanar aryl rings on the solid-state self assembly of dicarboxylic acids. The diacid **4**, the sterically-unhindered analog of **3**, may also explore the two extreme conformations, but the carboxyl groups in this case are not posed with any barrier to lie in the plane of the phenyl rings.

Let us first consider the behavior of the diacid 3. What is noteworthy is the fact that the molecules adopt syn conformation in the solvent-free modification of the diacid of 3, while they explore anti conformation in DMSO and in the presence of phenol. Neither of the dimeric and catemeric motifs is observed for the self-assembly of 3 in 3-free, but a very rare tetrameric association is found, cf. Fig. 2. As mentioned earlier, this pattern is known for only four instances so far. Is it the steric hindrance that prohibits adoption of dimeric/catemeric motifs? There are several instances of sterically-hindered acids that include 2,6-dimethylbenzoic acid, mesitoic acid, pentamethylbenzoic acid, etc. for which the dimer motif is observed. It is known that steric factors may influence the adoption of catemeric motif in favor of the dimer motif [4,5c]. Thus, the reason why the latter is not observed in 3-free should be traceable to the tethering of two such acids by a methylene carbon, which evidently changes the shape of the molecule from a planar constituent mesitoic acid to a more complex 'V'-shaped rigid structure. We believe that sterically-hindered dicarboxylic acids are very sensitive to adopting the dimeric motif such that a simple perturbation by way of electronic factors or structural variation of the kind such as tethering in 3 may result in altogether new and rare pattern of assembly; we have previously shown that dibromo/ dichloro-substitution of mesitylene carboxylic acid leads to helical self-assembly [3]. Presumably, the close-packing of the diacid 3 in its syn and anti conformations via dimeric/catemeric motif is difficult because of the tethering such that the rare tetrameric assembly as shown in Fig. 1 emerges ultimately as the final outcome. We were not successful in identifying any other guest-free modification in which the relative disposition of carboxyl groups is *anti*. However, it is this conformation that is found in the pseudopolymorphs of the diacid 3 with DMSO and PhOH-H<sub>2</sub>O. This shows that the *anti*-diacid presumably cannot undergo close packing except with appropriate guest molecules. It is noteworthy that the guest species in both DMSO and PhOH are directly hydrogen bonded to the carboxyl groups of the diacid 3.

Strangely, we could not obtain the crystals of the diacid 4 from a number of crystallization attempts in a variety of solvents that include EtOAc, MeOH, dioxane, CHCl<sub>3</sub>, NO<sub>2</sub>C<sub>6</sub>H<sub>5</sub>, CH<sub>3</sub>CN, etc. and mixed solvent systems. It

appears that the earlier attempts to obtain crystals were also in vain, which is reflected from the structure determination using powder XRD data (Ref. code: BZPHCC). This further attests to the difficulty in the crystal growth of simple methylene-tethered carboxylic acids, which assume a complex enough shape to pose severe problems with crystallization.

# 4. Conclusions

We have examined the solid-state self-assembly of a sterically-hindred methylene-tethered dicarboxylic acid 3. which may explore two extreme and low-energy conformations, viz., svn and anti. The molecular topology in conjunction with steric hindrance appear to divert the syn-diacid 3 from adopting the otherwise prevalent dimer motif in favor of a very rare tetrameric association. The same attributes appear to impart guest-binding propensity to the diacid molecules in their anti conformations resulting in the occurrence of pseudopolymorphism with DMSO and PhOH-H<sub>2</sub>O. Given that the carboxyl group is one of the important functional groups that is exploited in crystal engineering, the conformation-dependent crystal packing and observation of pesudopolymorphism for the diacid 3 in its syn and anti conformation suggest that the sterically-hindered acids are highly susceptible to exhibiting variations in association modes. The fact that simple unhindered dicarboxylic acid 4 does not crystallize in various attempts bears out the influence of structural changes through methylene tethering on the self-assembly of aromatic carboxylic acids.

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