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Crystal engineering with acid and pyridine heteromeric synthon: neutral and ionic co-crystals†

Ramkinkar Santra, Nayan Ghosh and Kumar Biradha*

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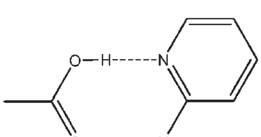
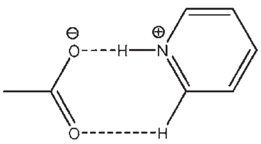
The reaction of trimesic acid (H_3TMA) with 2,6-bis(4-pyridylmethylene)cyclohexanone (1) in MeOH and phenol resulted in a co-crystal $H_3TMA{\cdot}1$ (1 : 1). The crystal structure of this co-crystal was found to contain a triply interpenetrated (6,3) hydrogen bonded network. The repeat of this reaction without PhOH resulted in crystals of an ionic compound which also contains both the components in 1 : 1 ratio. The crystal structure of this ionic solid exhibits a doubly interpenetrated three-dimensional hydrogen bonded network.

The design and synthesis of co-crystals has become very attractive area of research due to the potential applications in pharmaceuticals.[1] In the crystal engineering point of view they are of at most interest due to their versatility to exhibit supramolecular isomers and polymorphs.[2] For any given two chemical partners it is always possible to obtain more than one crystalline solid due to the differences in stoichiometries or supramolecular synthons.[3] The idea of engineering co-crystals serves the purpose of building large solid-state structures without the hassles of covalent synthesis. The synthon that is formed between carboxylic acids and pyridine moieties is one of the most exploited synthon for designing co-crystals.[4] This is a heteromeric synthon and exists in two forms (**I** in co-crystals, **II** in ionic solids), depending on the acidity and basicity of the acid and pyridine functionalities and also on the reaction conditions.

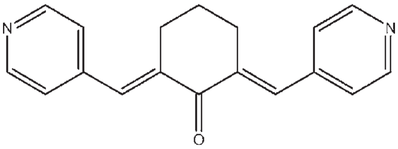


I



II

The α-polymorph of 1,3,5-benzenetricarboxylic acid (trimesic acid, H_3TMA) contains a honeycomb network with huge cavities of dimension 14 × 14 Å.[5] Further, H_3TMA is well known to form several elegant hydrogen bonded networks in various co-crystals and clathrates.[6] The most revealing examples using heteromeric synthon **I** are the co-crystals of H_3TMA with 4,4-bipyridine or 1,2-bis(4-pyridyl)ethane (2 : 3 ratio) which exhibit parallel interpenetrated honeycomb networks.[7] In those cases, the stoichiometry of the molecular components is such that the number of –COOH groups and pyridine groups are equal. Therefore the network constituted is a hexagon with huge cavities of dimension *ca.* 39 × 27 Å. In our present study we have used a chemically reactive spacer, such as 3-pentadienone, between the pyridyl groups. Accordingly the ligand considered for this purpose is 2,6-bis(4-pyridylmethylene)cyclohexanone (**1**). Our studies reveal that molecule **1** has an ability to form a co-crystal as well as an ionic complex with H_3TMA depending on the crystallization conditions. Interestingly the co-crystal and ionic complex have similar stoichiometries of H_3TMA and **1**, but differs from those of Zaworotko and co-workers[7]



1

The reaction of H_3TMA with **1** in MeOH and PhOH resulted in 1 : 1 cocrystals (**2**). The asymmetric unit of **2** is constituted by one molecule each of H_3TMA, **1** and MeOH (9% of the crystal volume). The C–O bond lengths of the –COOH groups (1.304(3), 1.204(3); 1.252(3), 1.272(3); 1.308, 1.204(3) Å) indicate that the carboxylic acid groups are not deprotonated. The imbalance between –COOH and pyridine groups (three *vs.* two) was taken care of by the formation of one self-dimer of –COOH groups (O–H···O: 1.64 Å, 2.625(4) Å, 179°). These dimers of H_3TMA moieties are linked by the hetero-dimer **I** (O–H···N: 1.63 Å, 2.606(3) Å, 171°; 1.64 Å, 2.618(3) Å, 173°; C–H···O: 2.65 Å, 3.292(4) Å, 127°; 2.42 Å, 3.163(5) Å, 124°) to form a two-dimensional network containing elliptical cavities of dimension 42.4 × 23.2 Å (Fig. 1(a)). On a whole this network can best be described as a (6,3) or distorted honeycomb network in which each distorted hexagon is formed by six units of H_3TMA and four units of **1**. The two-dimensional layer is corrugated which helps the self interpenetration of the networks in parallel fashion (Fig. 1(b)–(d)). Therefore three of these networks interpenetrate in parallel fashion to form a triple interpenetrated layer with a thickness of 9 Å. It is interesting to note here that Nangia *et al.* reported a similar architecture in the co-crystal of cyclohexane-1,3-*cis*,5-*cis*-tricarboxylic acid and 4,4′-bipyridine.[8]

Department of Chemistry, Indian Institute of Technology, Kharagpur, 721302, India. E-mail: kbiradha@chem.iitkgp.ernet.in; Fax: 91-3222-282252; Tel: 91-3222-283346

† Electronic supplementary information (ESI) available: ORTEP drawings and IR spectra for **2**, **3** and **5** and simplified pictures for the crystal structure of **3**. CCDC reference numbers 682928–682930. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b803280g

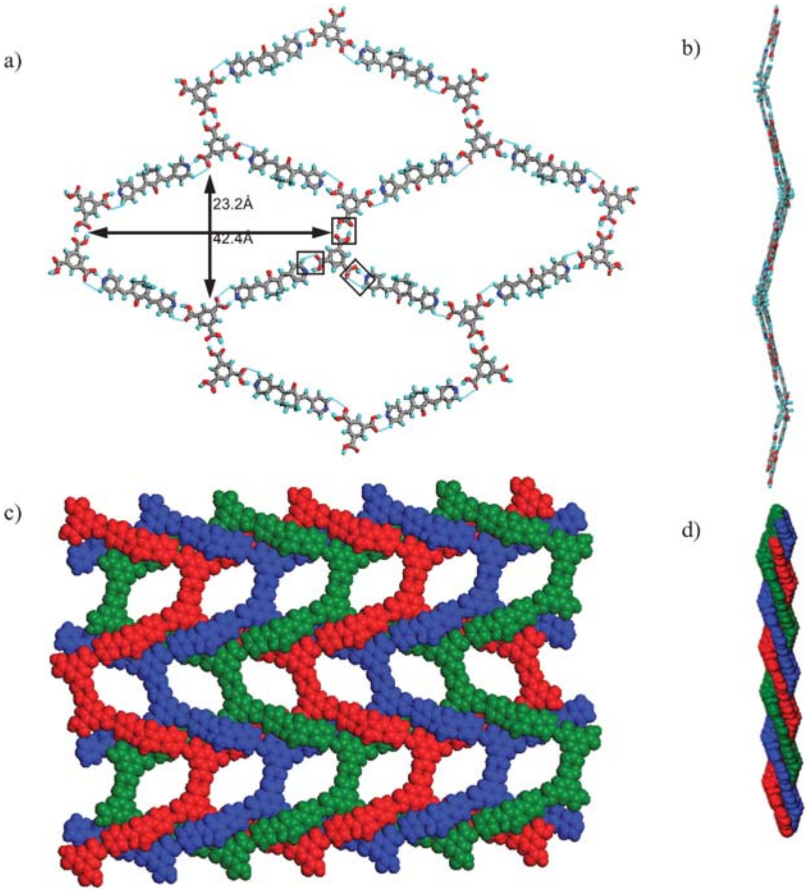


Fig. 1 Illustrations for the crystal structure of **2**: (a) (6,3)-hydrogen bonded network (*ab*-plane), with supramolecular synthons shown in boxes; (b) side view (along *a*-axis) of the layer representing the corrugated nature; (c) space-filling representation of the triple interpenetrated layer (*ab*-plane); (d) side view of the triple interpenetrated layer (along *a*-axis).

When the above reaction was carried out in the absence of PhOH, this resulted in the crystals of an ionic compound (**3**) which contains H_3TMA and **1** in 1 : 1 stoichiometry. The asymmetric unit of **3** contains one moiety of each component. The C–O bond lengths of H_3TMA (1.203(2), 1.306(2); 1.197(2), 1.310(2); 1.224(2), 1.279(2) Å) indicate that the one of COOH groups is deprotonated. The ionic components of the structure can be described as $[H_2TMA\cdots H\cdots TMAH_2]^{-1}$ (O···H···O: 2.438(2) Å, 180°) and $[\mathbf{1}\cdots H\cdots \mathbf{1}]^{+1}$ (N···H···N: 2.679(2) Å, 180°). In the anionic component the H-atom bonded to two carboxylates lies on an inversion center. These ionic components assemble *via* synthon **I** to form a three-dimensional network in the crystal lattice (Fig. 2). In the network, the anionic part acts as a six-connected node and the cationic part acts as a long spacer with a length of 28.5 Å. Four out of six connections of the anionic part are utilized for self assembling with each other to form a corrugated two-dimensional layer of (4,4)-topology (O–H···O: 1.56 Å, 2.529(2) Å, 166°, Fig. 2(a) and (b)). The remaining two connections of the anionic part are utilized to inter-connect the layers by pyridine groups of the $[\mathbf{1}\cdots H\cdots \mathbf{1}]^{+1}$ unit *via* synthon **I** (O–H···N: 1.67 Å, 2.645(2) Å, 171°; C–H···O: 2.82 Å, 3.465(2) Å, 128°). These layers are separated by each other with a distance of 19.1 Å (*a*-axis length). Two of these three-dimensional networks are interpenetrated to fill the large channels and voids of the network (Fig. 2(c) and (d)).

The reaction of H_3TMA with the 3-pyridyl analogue of **1** (**4**) in MeOH resulted in a precipitate which was dissolved by adding few drops of DMF. Slow evaporation of this solution resulted in co-crystals of **5** with 1 : 2 stoichiometry of H_3TMA and **4**. The asymmetric unit is constituted by two units of **4** and one unit of H_3TMA. One unit of **4** forms a one-dimensional chain with two carboxylic groups of H_3TMA *via* synthon **I** (O–H···N: 1.68 Å, 2.654(2) Å, 172°, C–H···O: 2.38 Å, 3.152(2) Å, 127°) and O–H···N hydrogen bonds (O–H···N: 1.67 Å, 2.642(2) Å, 172°); no auxiliary C–H···O hydrogen bond was formed as the planes of pyridine and –COOH groups are non-planar (47°) (Fig. 3(a)). Only one pyridyl group of the second unit of **4** binds to the third carboxylic group of H_3TMA *via* synthon **I** (O–H···N: 1.72 Å, 2.689(2) Å, 169°; C–H···O: 2.62 Å, 3.256(2) Å, 126°). This type of binding generates a one-dimensional chain containing U-shape cavities which are filled by the interdigitation with neighboring chains (Fig. 3(b)).

Here it is interesting to note that all the three structures are composed of synthon **I**, the ionic synthon **II** was not observed even in ionic solid (**3**). The presence of phenol may solvate the ligand **1** better, due to the high acidity of phenolic O–H group, which results in the neutral compound **2** rather than the ionic

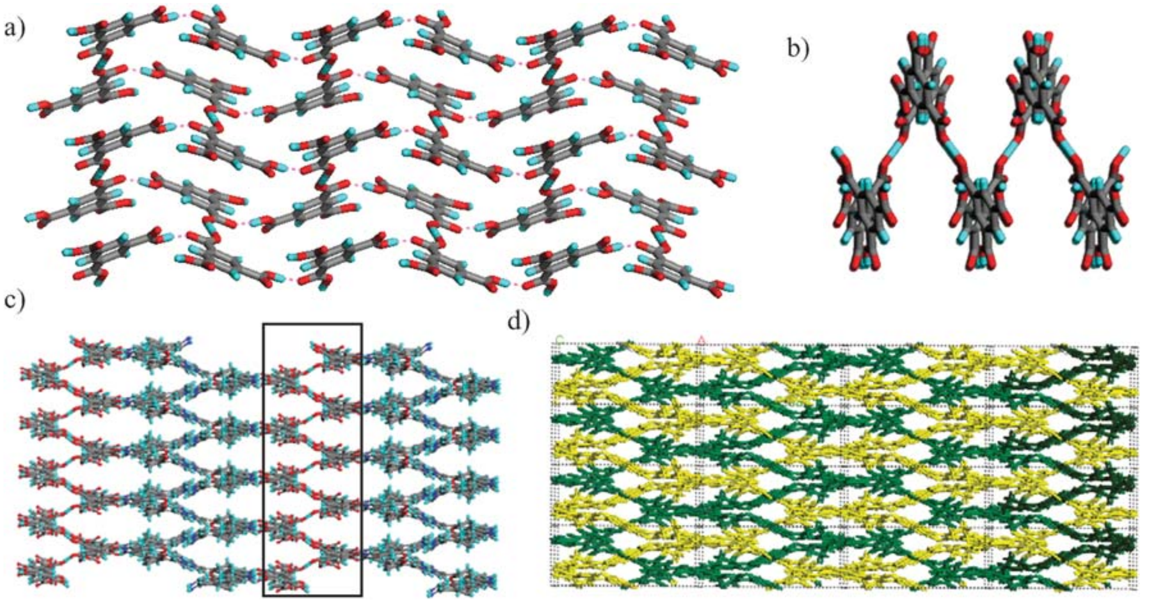


Fig. 2 Illustrations for the crystal structure of **3**. (a) Two-dimensional layer (*bc*-plane) *via* self-assembly of anionic species; (b) side view of the layer (along the *c*-axis); (c) three-dimensional network (*ab*-plane), where the rectangular box represents the trimesate layer; (d) doubly interpenetrated three-dimensional network (*ab*-plane);

compound **3**. The structure exhibited by co-crystal **2** is more predictable than that exhibited by ionic solid **3**. Our results support the recent survey of Aakeröy *et al.* which states that the structural predictability is higher in co-crystals than in ionic solids.[4] The presence of such large cavities in both **2** and **3** indicates the importance of H_3TMA co-crystals in the construction of large hydrogen bonded two- and three-dimensional frameworks similar to those of metal–organic frameworks. Further, it is noteworthy that the two- and three-dimensional networks observed here are interpenetrated in 3-fold and 2-fold manner, respectively. Here it is important to note that the formation of co-crystals **2** and **3** does not show any dependency on the initial ratios of components **1** and H_3TMA in the crystallization solution. The observed ratios of components could be the manifestation of the resultant stable architecture for given components in given conditions. Therefore the results obtained here differ from those of 4,4′-bipyridine and H_3TMA co-crystals. It was also found that the use of a lower amount of phenol than required for **1** leads to the exclusive formation of **2**. Another aspect worth mentioning here is that the double bonds of **1** in the crystal structures of **2**, **3** and **5** do not satisfy the topochemical principle for undergoing solid-state photochemical reaction.[9] We are currently investigating new co-crystals of molecule **1** and its derivatives for the purpose of conducting solid-state photochemical reactions.

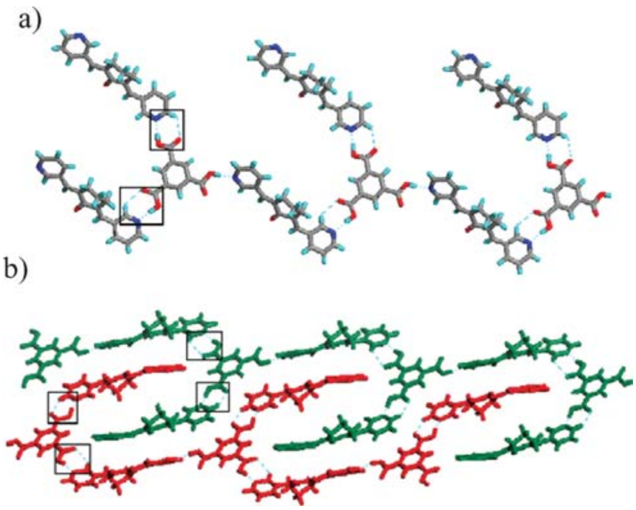


Fig. 3 Illustrations for the crystal structure of co-crystal **5**. (a) One-dimensional network, (b) interdigitation of two one-dimensional chains; rectangular boxes represent synthon **I**.

Experimental

Compounds **1** and **4** were synthesized by the Aldol condensation reaction of cyclohexanone with the corresponding pyridine aldehydes.

Crystallization of 2

A 1 : 1 mixture of **1** and H_3TMA were dissolved in a mixed solvent of methanol and phenol (5 : 1 ratio) and kept at room temperature for slow evaporation. After 4–5 days yellow square rod shaped crystals formed in 60–70% yield; mp 295–300 °C.

Crystallization of 3

A 1 : 1 mixture of **1** and H_3TMA was dissolved in methanol and left at room temperature. After 10–12 h yellow hexagonal platelike crystals were obtained in 80–90% yield; mp 295–300 °C.

Crystallization of 5

A 2 : 1 mixture of **4** and H_3TMA was dissolved in methanol and DMF. The solution was left for slow evaporation at room temperature. After 2–3 days light yellow rod shaped crystals were obtained in 60–70% yield; mp 240 °C.

X-Ray crystallography

The single-crystal data for **2**, **3** and **5** were collected on a Bruker-APEX-2 X-ray diffractometer equipped with graphite-monochromated Mo-Kα radiation (λ = 0.71073 Å) by the hemisphere method. The structures were solved by direct methods and refined by least-squares methods on F^2 using SHELX-97.[10] Non-hydrogen atoms were refined anisotropically and hydrogen atoms attached to C-atoms were fixed at calculated positions and refined using a riding model. The hydrogen atoms of –COOH groups are located and refined. The atoms corresponding to solvent methanol in the crystal structure of **2** shown higher thermal motions and therefore the Platon squeeze option was used in the final refinement.[11]

Crystal data for 2. $C_{27}H_{22}N_2O_7$, monoclinic, space group *C*2/*c*; a = 23.612(2), b = 15.0618(12), c = 17.8456(15) Å, β = 128.492(2), V = 4967.5(7) Å^3, Z = 8; D_c = 1.301 g cm^{-3}, 2963 reflections out of 6426 unique reflections with $I > 2\sigma(I)$, $1.74 < \theta < 28.74°$; final R-factors: R_1 = 0.0637, wR_2 = 0.1565.

Crystal data for 3. $C_{54}H_{44}N_4O_{14}$, monoclinic, space group $P2_1/c$; a = 19.1296(7), b = 7.7639(3), c = 15.7687(6) Å, β = 98.138(1), V = 2318.4(2) Å^3, Z = 2; D_c = 1.394 g cm^{-3}, 3965 reflections out of 6721 unique reflections with $I > 2\sigma(I)$, $2.15 < \theta < 30.13°$; final R-factors: R_1 = 0.0504, wR_2 = 0.1690.

Crystal data for 5. Monoclinic, space group $P2_1/n$; a = 6.6119(8), b = 19.013(2), c = 30.150(4) Å, β = 92.300(4), V = 3787.2(8) Å^3, Z = 4; D_c = 1.338 g cm^{-3}, 5851 reflections out of 8612 unique reflections with $I > 2\sigma(I)$, $1.27 < \theta < 27.50°$; final R-factors: R_1 = 0.0507, wR_2 = 0.1718.

Acknowledgements

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