Acta Crystallographica Section B
Structural Science
ISSN 0108-7681

Seven hexamethylenetetramine (HMTA) complexes with mono- and dicarboxylic acids: analysis of packing modes of HMTA complexes in the literature

Andreas Lemmerer

Molecular Sciences Institute, School of Chemistry, University of the Witwatersrand, Private Bag 3, Johannesburg, Gauteng 2050, South Africa

Correspondence e-mail: andreas.lemmerer@wits.ac.za

Received 8 December 2010
Accepted 9 February 2011

Dedicated to Professor George Ferguson on the occasion of his 75th birthday.

The crystal structures of seven hexamethylenetetramine (HMTA) complexes, or co-crystals, with carboxylic acid donor molecules are reported to explain the link between the molecular structure of HMTA and the crystal structure of the co-crystals, *i.e.* the dimension and shape of their hydrogen-bonded assembly. A comprehensive and detailed literature survey of HMTA complexes (38), be they neutral co-crystals or salts, with molecules containing carboxylic acid and phenol functional groups reveals that in general two N acceptors are used for strong O—H···N interactions. Owing to the relative arrangement of two of the four N atoms, the most common type of assembly features one-dimensional zigzag chains. Weak interactions of the C—H···N type are formed by N atoms not involved in strong interactions. These chains also form the basis of two-dimensional assemblies. These one- and two-dimensional assemblies feature either two or three functional groups. If only one functional group is on the donor molecule, then wing or V-shaped zero-dimensional assemblies are formed, which can be considered to be the building blocks for one- and two-dimensional assemblies. In general, the HMTA molecules form two-dimensional layers which are stabilized by weak hydrogen bonds. Co-crystals with cyclohexylcarboxylic acid (I), 4-fluorobenzoic acid (II), 4-methylbenzoic acid (III) and cinnamic acid (IV) all feature the V-shaped zero-dimensional assemblies. Co-crystals with *cis*-1,4-cyclohexyldicarboxylic acid (VI) and *trans*-1,4-cyclohexylcarboxylic acid (VII) feature the zigzag chains and can be structurally derived from co-crystal (I). Co-crystal (V), with 4-nitrobenzoic acid, has solvent water included and features hydrogen bonding to all four N atoms of the HMTA molecule.

1. Introduction

By combining two molecules in an attempt to prepare a new chemical entity a number of factors are crucial in determining the success of the outcome. Organic covalent synthesis has made great strides in the past and is now a field of chemistry where the understanding of what makes two molecules or reagents react is at an advanced level. Supramolecular synthesis, which aims to prepare a multi-component molecular complex, is a related process with a history as long as organic synthesis (Stahly, 2009). However, understanding this synthesis is still at an intermediate level where pertinent questions remain unanswered or where theory and knowledge are lacking (Desiraju, 2007). This has not prevented researchers from preparing a large number of these complexes, commonly referred to as co-crystals for simplicity (Bond, 2007; Lemmerer *et al.*, 2008), that are then available to glean trends and information on the intermolecular processes required to create these new crystalline entities in the solid state.

Knowledge of the principles of solid-state packing of single and multiple molecules is vital to understanding co-crystal formation. A large fundamental leap was made through the work of Kitaiigorodski and his principle of close packing of molecules using the bumps and hollows principle. In unimolecular compounds the key to understanding how molecules pack comes from an understanding of the intermolecular interactions that exist between the functional groups on the molecule, as well as the shape of the molecule. The connection between *molecular structure* and *crystal structure* is key (Desiraju, 2010). In these simplest cases the functional groups interacting are uniform and many functional groups have been studied as to their effect on the packing of the molecule as a whole (Leiserowitz, 1976; Leiserowitz & Tuval, 1978; Das & Desiraju, 2006). For example, 1,4-benzoquinone has hydrogen-bonding functional groups in a symmetrical arrangement, and the crystal structure results in a linear ribbon of hydrogen bonds (Desiraju, 1995). Adamantane-1,3,5,7-tetracarboxylic acid has its four functional groups in a tetrahedral arrangement (owing to the molecular shape of the adamantane backbone), and the resulting crystal structure forms a diamondoid network (Ermer, 1988). When it comes to a particular crystal structure shape arising from the molecular structures of two different molecules (containing different yet complimentary functional groups), similar molecular structure and crystal structure linkages can be made. For example, trimesic acid has three carboxylic acids (hydrogen-bond donors) in a trigonal arrangement, and 4,4-bipyridine has a linear arrangement of hydrogen-bond acceptors. The crystal structure of this co-crystal has a hexagonal arrangement resulting from the trigonal shape of one of the component molecules (Desiraju, 1997). When it comes to bimolecular and larger complexes (co-crystals) there are different functional groups that need to be taken into consideration, leading to a greater multitude of possible interaction types, geometries and crystal-packing architectures. Dominant in the intermolecular interactions are hydrogen bonding (Steiner, 2002; Desiraju, 2002; Burrows, 2004), which have been used to create zero- to three-dimensional architectures. One of the most studied combinations of dissimilar functional groups are carboxylic acids and phenols as the hydrogen-bond donor, and *N*-heterocycle-containing molecules as hydrogen-bond acceptors (Lemmerer *et al.*, 2008; Lemmerer *et al.*, 2010; Shattock *et al.*, 2008; Vishweshwar *et al.*, 2003*a*,*b*). In these combinations H acts as a hydrogen-bond donor to the hydrogen-bond acceptor properties of the lone pair on the N atom. Some trends have been categorized in co-crystals made up of molecules containing these functionalities on chemically distinct molecules, such as nicotinamide (Karki *et al.*, 2009; Lemmerer & Bernstein, 2010), isonicotinamide (Aakeröy *et al.*, 2002; Báthori *et al.*, 2011), acridine (Mei & Wolf, 2004) and numerous other pyridine derivatives, and a number of acid- and phenol-containing molecules (Lemmerer *et al.*, 2011). A well known molecule containing the N lone-pair functionality is hexamethylenetetramine, also known as urotropine, abbreviated as hexamine or HMTA/HMT in the literature. To date, no detailed analysis of the intermolecular interactions and packing modes of co-crystals of this simple yet versatile molecule exist, although many articles report similar observations with regard to the flexibility of the molecule to accept one to four hydrogen bonds from different donor molecules (Ghosh *et al.*, 2005; Daka & Wheeler, 2006; Li *et al.*, 2001; Lemmerer, 2011); we refer to the second molecule that contains the COOH or COH functional groups as the donor

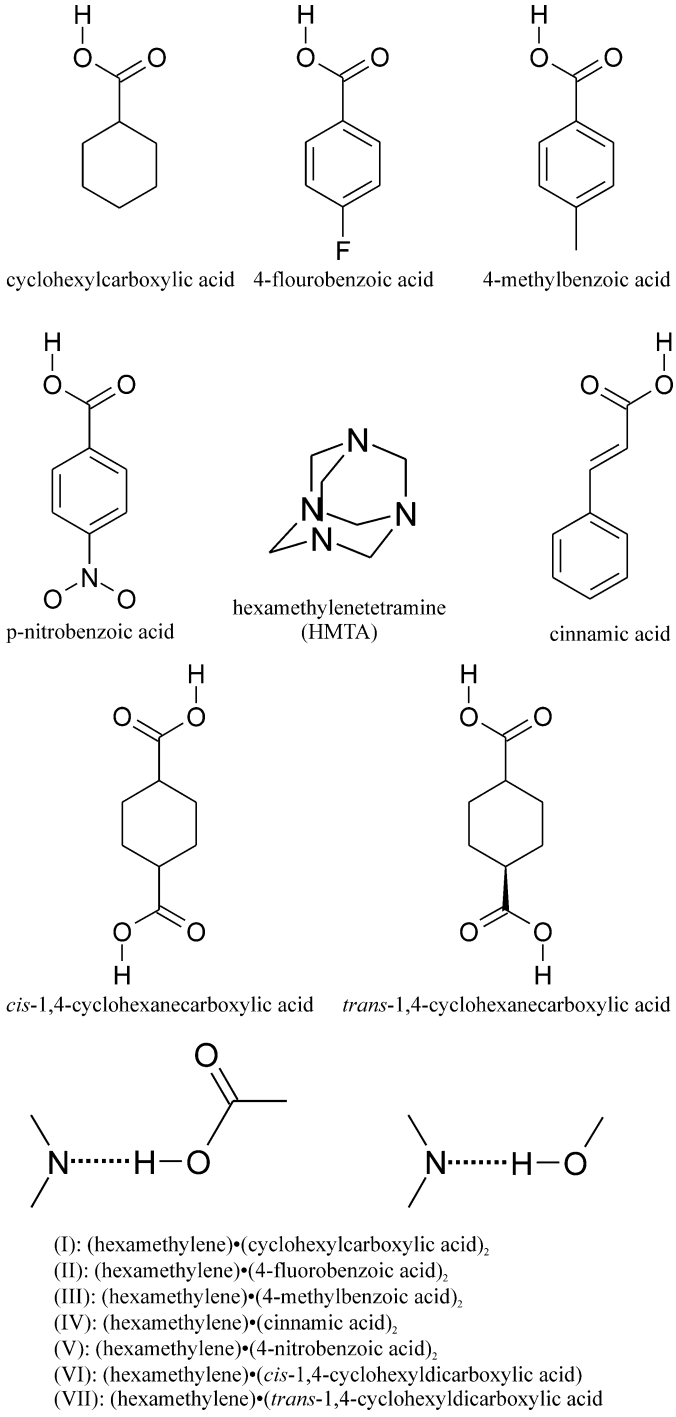

Figure 1
The seven carboxylic acid molecules and HMTA used to make co-crystals (I)–(VII) in this study with the O—H···N hydrogen bonds expected to form in the co-crystals reported in this study and in the literature.

Table 1
Experimental details.

Experiments were carried out at 173 K with Mo $K\alpha$ radiation using a Bruker APEX II CCD area-detector diffractometer. Absorption was corrected for by multi-scan methods, *SADABS* (Sheldrick, 1996).

	(I)	(II)	(III)	(IV)
Crystal data				
Chemical formula	$C_6H_{12}N_4{\cdot}2C_7H_{12}O_2$	$C_6H_{12}N_4{\cdot}2C_7H_5FO_2$	$C_6H_{12}N_4{\cdot}2C_8H_8O_2$	$C_6H_{12}N_4{\cdot}2C_9H_8O_2$
M_r	396.53	420.42	412.48	436.5
Crystal system, space group	Monoclinic, $P2_1/n$	Monoclinic, $P2_1/n$	Monoclinic, $P2_1/n$	Orthorhombic, $Cmc2_1$
a, b, c (Å)	6.0341 (1), 30.9087 (5), 11.7024 (2)	6.1529 (1), 26.9424 (6), 11.8758 (3)	6.1754 (18), 28.234 (7), 12.154 (3)	30.8030 (6), 9.6904 (2), 7.3655 (1)
β (°)	103.366 (1)	100.553 (1)	99.869 (15)	90
V (Å^3)	2123.45 (6)	1935.40 (7)	2087.8 (9)	2198.55 (7)
Z	4	4	4	4
μ (mm^{-1})	0.09	0.12	0.09	0.09
Crystal size (mm)	0.45 × 0.4 × 0.06	0.5 × 0.5 × 0.24	0.3 × 0.24 × 0.05	0.47 × 0.35 × 0.25
Data collection				
T_{min}, T_{max}	0.96, 0.99	0.95, 0.97	0.97, 0.99	0.96, 0.98
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	37 573, 5102, 3862	30 806, 4670, 4058	10 621, 3866, 1948	10 013, 1452, 1376
R_{int}	0.039	0.025	0.094	0.046
Refinement				
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.050, 0.137, 1.03	0.038, 0.100, 1.01	0.121, 0.366, 1.10	0.031, 0.084, 1.07
No. of reflections	5102	4670	3866	1452
No. of parameters	259	277	273	155
No. of restraints	0	0	0	1
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement	H atoms treated by a mixture of independent and constrained refinement	H-atom parameters constrained	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.39, −0.25	0.22, −0.24	0.87, −0.55	0.19, −0.17

	(V)	(VI)	(VII)
Crystal data			
Chemical formula	$C_6H_{12}N_4{\cdot}2C_7H_5NO_4{\cdot}2H_2O$	$C_8H_{12}O_4{\cdot}C_6H_{12}N_4$	$C_8H_{12}O_4{\cdot}C_6H_{12}N_4$
M_r	510.47	312.37	312.37
Crystal system, space group	Monoclinic, $C2/c$	Monoclinic, $P2_1/m$	Orthorhombic, $Fdd2$
a, b, c (Å)	12.0807 (4), 7.4730 (2), 25.0633 (7)	5.9169 (4), 21.6383 (15), 6.1135 (4)	23.7999 (4), 44.9245 (8), 5.7804 (1)
β (°)	98.909 (1)	108.028 (1)	90
V (Å^3)	2235.39 (11)	744.29 (9)	6180.40 (19)
Z	4	2	16
μ (mm^{-1})	0.12	0.10	0.1
Crystal size (mm)	0.37 × 0.31 × 0.09	0.66 × 0.42 × 0.11	0.36 × 0.31 × 0.12
Data collection			
T_{min}, T_{max}	0.96, 0.98	0.93, 0.98	0.96, 0.98
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	16 252, 2697, 2336	7732, 1834, 1671	18 095, 2054, 1915
R_{int}	0.029	0.021	0.030
Refinement			
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.036, 0.110, 1.01	0.038, 0.101, 1.14	0.033, 0.099, 1.08
No. of reflections	2697	1834	2054
No. of parameters	173	109	205
No. of restraints	3	0	1
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement	H atoms treated by a mixture of independent and constrained refinement	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.33, −0.28	0.38, −0.19	0.22, −0.21

Computer programs used: *APEX*2 (Bruker, 2005), *SAINT-Plus*, *XPREP* (Bruker, 2004), *SHELXS*97, *SHELXL97* (Sheldrick, 2008), *ORTEP*3 (Farrugia, 1997), *DIAMOND* (Brandenburg, 1999), *WinGX* publication routines (Farrugia, 1999), *PLATON* (Spek, 2003).

molecule. The majority of complexes have phenol groups on the donor molecules, with a number of carboxylic acid donor molecules also known (see §3). We aim to sum all the available knowledge of HMTA complexes, including for completeness those that are salts (proton transfer from the donor molecule to the N atom of the HMTA molecule) into a single report.

What has been repeatedly observed is that complexes with this molecule (containing four N atoms in a tetrahedral

Table 2
Summary of co-crystals (I)–(VII).

Co-crystal	Number of N acceptors used	Ratio of C—O to C═O	Dimension of assembly	Average C—N bond of N involved in hydrogen bonding	Average C—N bond of N not involved in hydrogen bonding
(I)	2	1.076 (1) 1.090 (1)	Zero-dimensional	1.477 (4)	1.461 (6)
(II)	2	1.084 (1) 1.091 (1)	Zero-dimensional	1.480 (5)	1.465 (4)
(III)	2	1.094 (7) 1.039 (7)	Zero-dimensional	1.479 (7)	1.462 (6)
(IV)	2	1.089 (2)	Zero-dimensional	1.479 (6)	1.467 (7)
(V)	4	1.093 (1)	One-dimensional chains	1.475 (1)	–
(VI)	2	1.095 (1)	Zigzag chains	1.475 (7)	1.463 (3)
(VII)	2	1.088 (2) 1.089 (2)	Zigzag chains	1.479 (4)	1.467 (5)

environment) seldom show the usage of all four N atoms (MacLean *et al.*, 1999), even when provided with a stoichiometrically exact number of hydrogen-bond donor groups (Coupar, Glidewell & Ferguson, 1997) by using donor molecules with either one, two or three functional groups. This seems to indicate that there is a conflict between satisfying all the hydrogen-bond donors, *i.e.* creating a saturated hydrogen-bonding situation, and creating the most efficient geometric packing (Desiraju, 1995) with geometric factors overriding in the case of HMTA. Most commonly encountered are complexes where two N atoms are used (Zakaria *et al.*, 2003). Some attempts have been successful to make use of all four N atoms (Coupar, Ferguson *et al.*, 1997), and the cited authors have speculated on why their deliberate methodology worked in choosing the correct donor molecule.

To describe how the molecular structure of HMTA affects the crystal structure, and in particular the dimensionality of the assembly of the HMTA complexes, we performed a very detailed analysis of known complexes in the literature, as well as showing further examples of controlling the assembly by preparing seven new co-crystals with carboxylic acid containing donor molecules (see Fig. 1).

2. Experimental

2.1. Synthesis of complexes (I)–(VII)

All reagents and solvents were obtained from Aldrich (except for *cis*- and *trans*-1,4-cyclohexanedicarboxylic acid, obtained from TCI America) and used without further purification. Solutions of the monocarboxylic acids and HMTA (2:1 stoichiometric ratio), and solutions of the dicarboxylic acid molecules and HMTA (1:1 stoichiometric ratio) were prepared in methanol (98%). All co-crystals were obtained by slow evaporation at room temperature under ambient pressure over a number of days. Later, a single experiment was carried out in which crystals were grown from a solution of cyclohexanecarboxylic acid and HMTA in a starting stoichiometric ratio of 4:1.

2.2. Single-crystal X-ray crystallography

All diffraction data were collected on a Bruker Apex II CCD diffractometer (Bruker, 2005) with graphite-monochromated Mo $K\alpha$ radiation (λ = 0.71073 Å) at 173 K using an Oxford Cryostream 700 (Table 1). Data reduction and cell refinement were carried out using *SAINT-PLUS* (Bruker, 2004) and space groups were determined from systematic absences by *XPREP* (Bruker, 2004) and further justified by the refinement results. Empirical absorption corrections were performed on all crystals using *SADABS* (Sheldrick, 1996). In all cases the structures were solved using the *WinGX* suite of programs (Farrugia, 1999) by direct methods using *SHELXS*97 (Sheldrick, 2008), and refined using full-matrix least-squares calculations based on F^2 using *SHELXL*97 (Sheldrick, 2008). All non-H atoms were refined with anisotropic displacement parameters. Finally all the H atoms on C atoms were placed at idealized positions with isotropic displacement parameters relative to those of the heavy atoms to which they are attached [U_{iso}(H) = 1.2U_{eq}(C) or 1.5U_{eq}(C)]. The H atoms on O atoms were located in difference-Fourier maps and refined freely, with isotropic displacement parameters 1.5 times those of the O atom, for all compounds except (III). The H atoms on O atoms in (III) were placed at idealized positions as the crystal quality of (III) was generally very poor and the diffraction pattern featured streaky spot shapes. The structure of (III) has high R factors, and a residual electron density of 0.87 e Å^{-3} at a distance of 0.88 Å from C4.

2.3. Cambridge Structural Database (CSD) search

All CSD searches were carried out using Version 5.31 with the November 2009, February, May and November 2010 updates (Allen, 2002). The search query for HMTA complexes gave 167 hits, which was reduced to 49 after the removal of duplicate entries, molecules with a fourth covalent bond to N atoms (N—O, N—C, excluding N—H), the structure of HMTA itself and any inorganic salts of HMTA, and only including complexes with any C—OH, CO^-, COOH or COO^- functional groups. The filters applied to the search are: three-dimensional coordinates determined, no powder structures, only organics. The *ConQuest* search query file with 167 hits and the CIF file containing the 49 entries in the final list are given in the supplementary material.[1]

[1] Supplementary data for this paper are available from the IUCr electronic archives (Reference: SO5048). Services for accessing these data are described at the back of the journal.

3. Results and discussion

3.1. Crystal structure description

Co-crystals (I)–(VII) are all neutral and feature an N acceptor to hydrogen-bond donor ratio of 1:2, except for co-crystal (V) which has a ratio of 1:4. The decision as to whether a salt or co-crystal was formed was made on the basis of the ratio of the C—O single bond (long) to the C═O double bond length (short), which are listed in Table 2 for all compounds. This criterion has been used previously by Aakeröy *et al.* (2007) and the ratios obtained are in accordance with those of neutral co-crystals. A carboxylate salt would have a lower ratio of about 1.030. The bond distances and angles within the seven co-crystals reported are generally as expected (Allen *et al.*, 1987). When discussing the hydrogen-bonding interactions only the strong hydrogen bonds, of the type O—H···N and O—H···O and charge-assisted N^{+}—H···O^{-} (Braga *et al.*, 1995; Zakaria *et al.*, 2003), will be mentioned. When discussing the arrangements of the HMTA molecules to the donor molecules, weak C—H···N hydrogen bonds to the unused N atoms left over from the strong hydrogen-bonded interactions have also been included, as will become clear in the discussion. Five of the carboxylic acid molecules chosen contain a benzene backbone, as most of the complexes found in the literature are aromatic containing molecules. Two of the seven are on a cyclohexane backbone to monitor conformational factors.

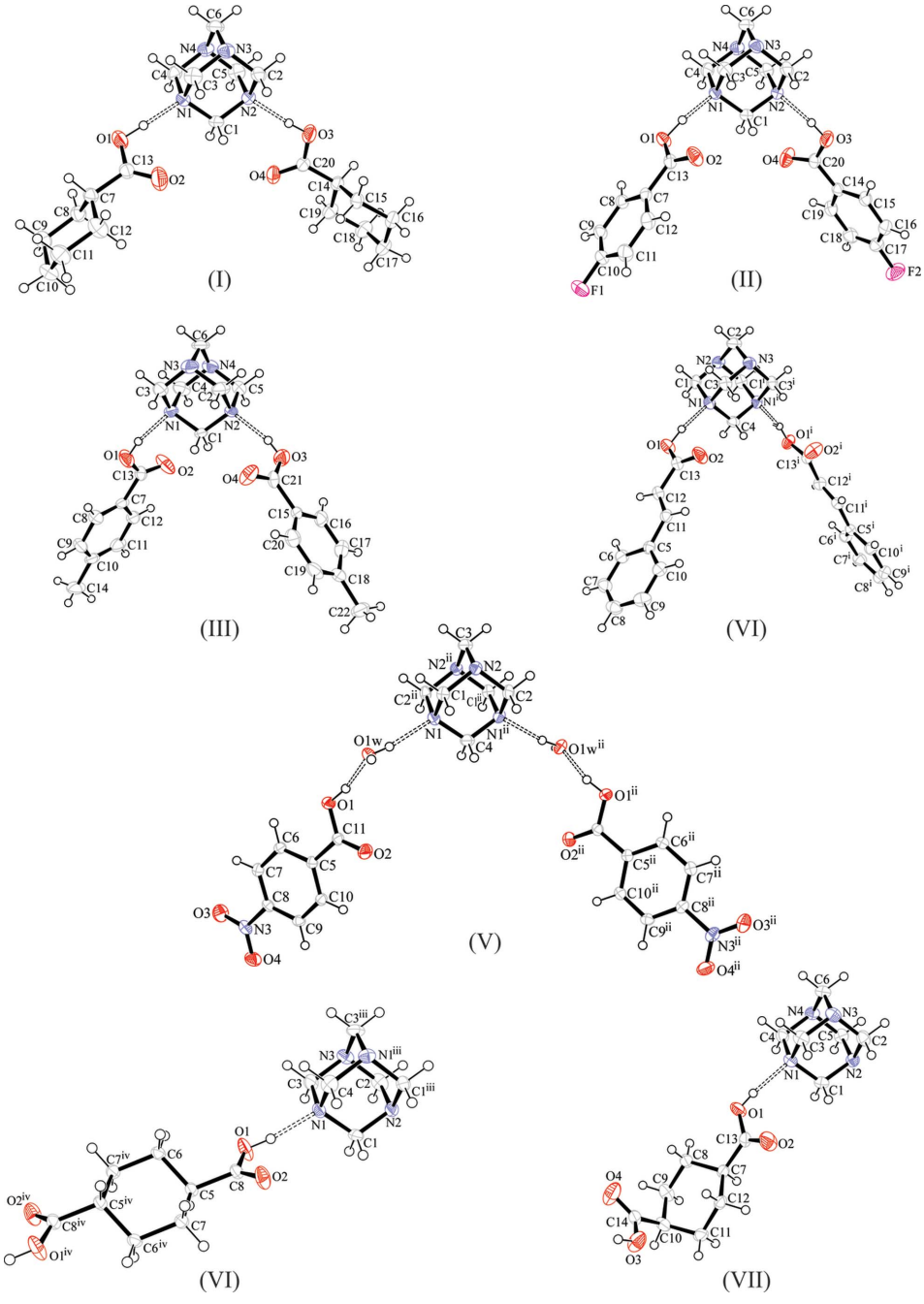

Figure 2
The asymmetric units and numbering scheme of the HMTA co-crystals with seven carboxylic acids. The anisotropic displacement parameters are shown at the 50% probability level. Symmetry codes: (i) $-x, y, z$; (ii) $-x+1, y, -z+\frac{1}{2}$; (iii) $x, -y+\frac{1}{2}, z$; (iv) $-x+2, -y+1, -z+2$.

3.1.1. Isostructural co-crystals with cyclohexylcarboxylic acid (I), 4-fluorobenzoic acid (II) and 4-methylbenzoic acid (III). The contents of the asymmetric units of (I), (II) and (III) are shown in Fig. 2 and clearly resemble each other. The asymmetric unit in each case consists of a single HMTA molecule and two acid molecules, both hydrogen bonding to the HMTA molecule using only two of the four N acceptor atoms. The cell parameters, space group and fractional coordinates show that these three co-crystals are isostructural. Two carboxylic acid molecules hydrogen bonding to a single HMTA molecule create a V-shape supermolecule. This V-shape has previously been described as 'wings' (Mak *et al.*, 1978). These supermolecules then stack head-to-tail along the *c* axis but in parallel directions along the *b* axis (Fig. 3). A number of weaker hydrogen bonds of the type C—H···O, C—H···N and C—H···F are formed between the supermolecules but are not shown in the packing diagrams. These hydrogen bonds are between the unused N acceptor atoms on the HMTA and

the carbonyl O of the acid molecules. The arrangement of the HMTA molecules consists of two-dimensional layers, parallel to the *ac* plane, separated by bilayers of the donor molecules in all three co-crystals. The HMTA layers are stabilized by two C—H···N hydrogen bonds, thus creating a saturated hydrogen-bonding assembly where all four N atoms are used.

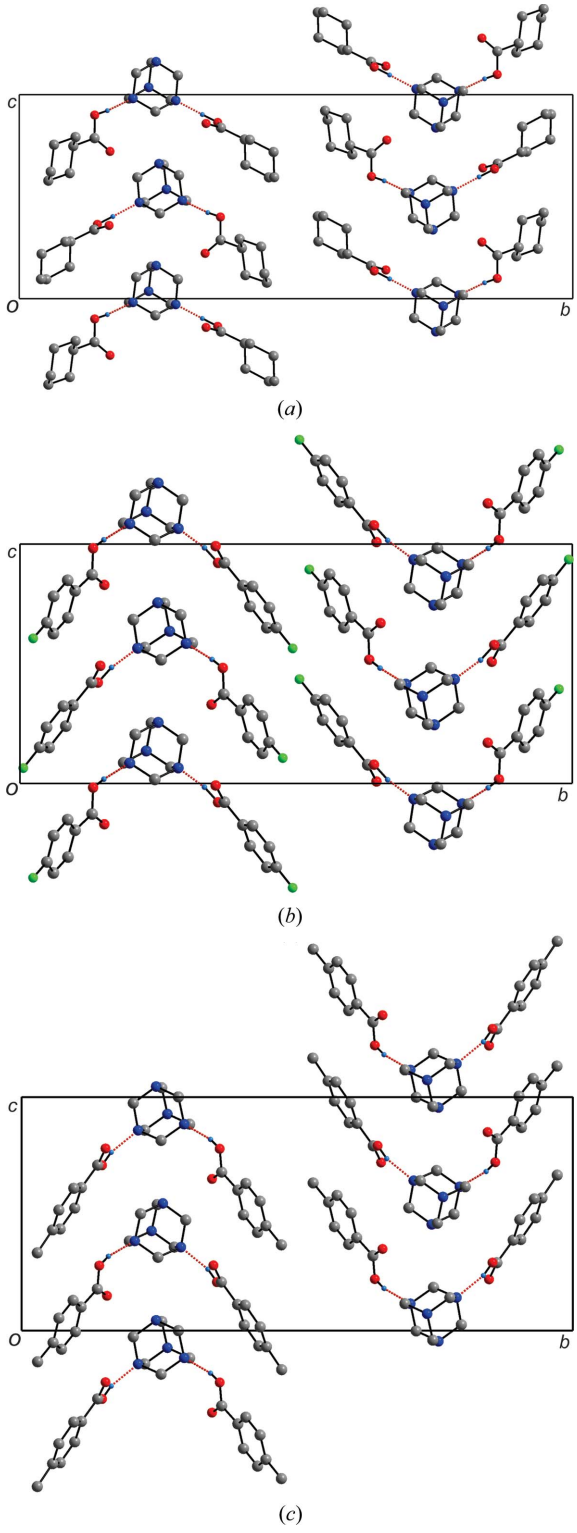

Figure 3
The packing diagrams of a filled unit cell of HMTA co-crystals with (*a*) cyclohexylcarboxylic acid (I), (*b*) 4-fluorobenzoic acid (II) and (*c*) 4-methylbenzoic acid (III). All three co-crystals are isostructural. H atoms not involved in hydrogen bonding are omitted for clarity.

3.1.2. Co-crystal with cinnamic acid (IV). Co-crystal (IV) is not isostructural to the previous three acids and contains half their asymmetric units. The asymmetric unit of (IV) consists of half a HMTA molecule sitting on a mirror plane, and one cinnamic acid molecule on a general position (Fig. 2). The hydrogen bonding is still the same as before, with only two N atoms used for hydrogen-bonding interactions, and the same V-shaped supermolecules are present. The supermolecules stack head-to-tail along the *c* axis, but are stacked in an antiparallel arrangement along the *a* axis (Fig. 4). There are C—H···N hydrogen bonds between HMTA molecules which form a two-dimensional layer in the *bc* plane and are separated by bilayers of donor molecules.

3.1.3. Hydrated co-crystal with 4-nitrobenzoic acid (V). Co-crystal (V) is very different to the previous four co-crystals. This co-crystal contains waters of hydration, resulting in a substantially different set of intermolecular interactions and packing architecture. The water molecules originate from the water residue in the methanol solvent. The asymmetric unit consists of one half HMTA molecule sitting on a twofold axis, as well as one 4-nitrobenzoic acid and one water molecule, both on general positions (Fig. 2). The two H atoms on the water molecule hydrogen bond to two different HMTA molecules such that all four N atoms act as acceptors for the hydrogen-bond donors on water, not just two as in (I)–(IV). Each HMTA molecule is surrounded by a hydration sphere (Fig. 5*a*). The carboxylic acid donor molecules hydrogen bond to the O atom of the water molecule, and not to the N atoms of the HMTA molecule. The HMTA and water molecules form a one-dimensional chain along the *c* axis, and the acid molecules are attached pendent-like to these chains (Fig. 5*b*). Adjacent chains are interdigitated through acid molecules along the *a* axis and the interdigitation is stabilized by π-stacking of the aromatic rings [Cg···Cg centroid separations are 3.5423 (6) and 3.5621 (6) Å]. There are a number of C—H···O hydrogen bonds between HMTA and donor molecules, and between donor molecules themselves. The HMTA molecules form two-

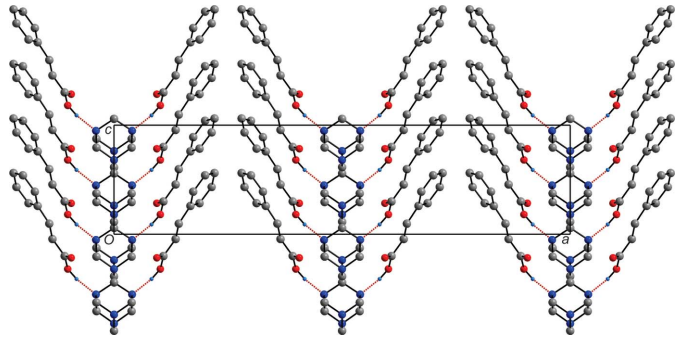

Figure 4
The packing of co-crystal (IV) with cinnamic acid. Note the different relative arrangement of the supermolecules in the *a*-axis direction compared with the *b*-axis direction of co-crystals (I)–(III) in Fig. 3. H atoms not involved in hydrogen bonding are omitted for clarity.

dimensional layers (in the *bc* plane), separated again by bilayers of donor molecules. There are no C—H···N hydrogen bonds between the HMTA molecules.

3.1.4. Isomeric co-crystals with *cis*-1,4-cyclohexanedicarboxylic acid (VI) and *trans*-1,4-cyclohexanedicarboxylic acid (VII). The dicarboxylic acids used to make co-crystals (VI) and (VII) are based on the cyclohexylcarboxylic acid used to make co-crystal (I). There are two isomers: the *cis* isomer has the two carboxylic acid functional groups in equatorial positions, while the *trans* isomer has one equatorial and one axial. The asymmetric unit in (VI) contains one half molecule of HMTA on a mirror plane, and one half *cis*-1,4-cyclohexanecarboxylic acid molecule on a centre of inversion (Fig. 2). Each acid molecule hydrogen bonds to two HMTA molecules and *vice versa*, resulting in a continuous chain of V-shaped supermolecules. The shape of the chain has been previously described as a zigzag chain (Mak *et al.*, 1977) and runs along the *b* axis (Fig. 6*a*). The chains stack in a parallel fashion along the *a* axis. The asymmetric unit of (VII) contains one molecule of HMTA and *trans*-1,4-cyclohexanecarboxylic acid, both on general positions (Fig. 2). The same hydrogen-bonding interactions and similar packing architecture as (VI) are observed (Fig. 6*b*). There are a number of C—H···O and C—H···N interactions between the chains. The HMTA two-dimensional layers are stabilized by two C—H···N hydrogen bonds, and are separated by two-dimensional layers of the donor molecules.

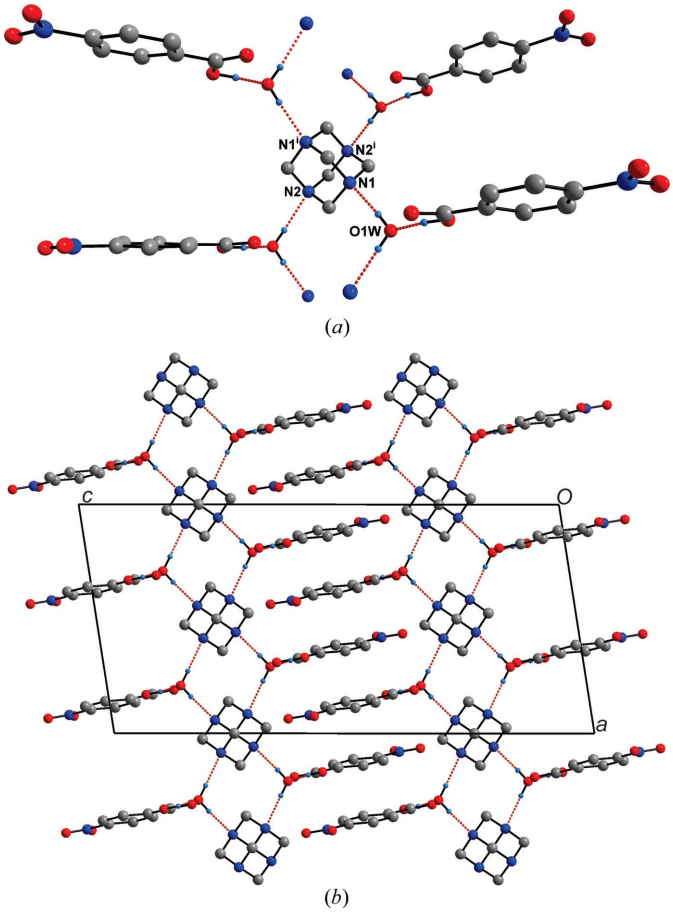

Figure 5
(*a*) The fourfold hydrogen-bonding interactions of the HMTA molecules with four water molecules. Note that the acid molecules have been displaced from their expected hydrogen-bonding interaction to HMTA, and now hydrogen bond to the water molecules instead. (*b*) Packing diagram down the *b* axis, showing the interdigitated chains. H atoms not involved in hydrogen bonding are omitted for clarity. Symmetry codes: (i) $-x+1, y, -z+\frac{1}{2}$.

3.2. Comparison of co-crystals (I)–(VII)

All co-crystals except (V) resulted in complexes that reflected the starting stoichiometric ratio of 1:2 for the two molecules in solution. This is in accordance with the complexes found in the literature, where the ratio of donor to acceptor molecules is predominantly 1:2, even for didonor molecules, which then feature a ratio of 1:1. The hydrogen-bonding interactions are all fairly linear (see Table 3), which is allowed by a lack of any steric constraint around the donor and acceptor functional groups. There is a statistically significant lengthening (taking into account the standard deviations of the averages) of the C—N bond lengths to the N atoms involved in hydrogen bonding (generally N1 or N2) over those that are not (N3 or N4; Table 2). This characteristic has been noted previously by Coupar, Glidewell & Ferguson (1997) and Coupar, Ferguson *et al.* (1997). An experiment was attempted to see if it was possible to saturate the hydrogen bonding on HMTA with the monocarboxylic acid cyclohexanecarboxylic acid to make a 1:4 co-crystal, but this resulted in the same 1:2

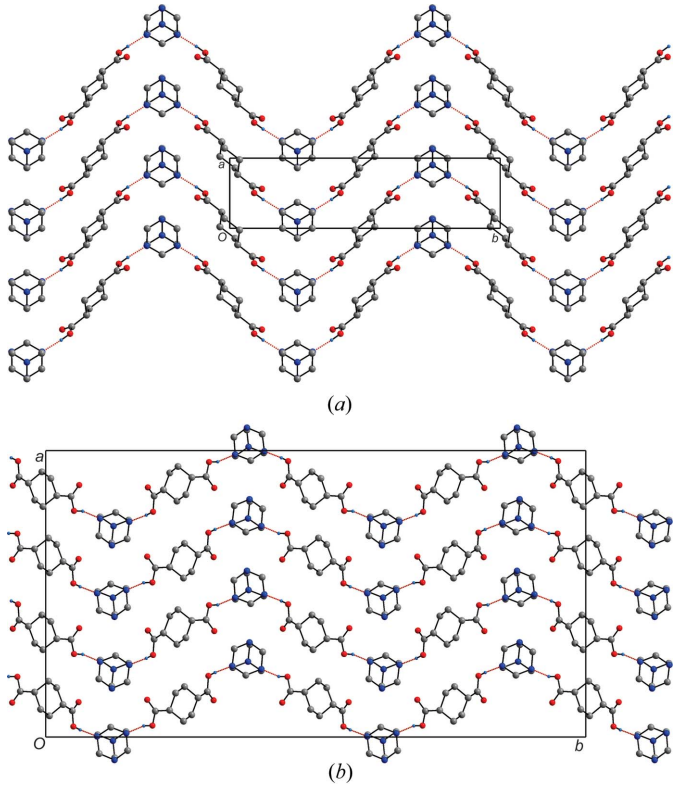

Figure 6
Packing of the zigzag chains of the isomeric co-crystals (*a*) (VI) and (*b*) (VII). H atoms not involved in hydrogen bonding are omitted for clarity.

co-crystal as (I). In all the co-crystals there is a consistent theme throughout with regard to the arrangement of the HMTA molecules. The HMTA molecules all form two-dimensional layers, which are stabilized by two C—H···N hydrogen bonds. Some of these C—H···N hydrogen bonds can be considered to be no more than short contacts (as the distance between C and N is greater than the sum of their van der Waals radii), but are clearly present as intermolecular interactions within the layers formed by the HMTA molecules. This feature will be further assessed in the analysis of the literature structures below.

3.3. Summary of HMTA complexes in the literature

The complexes can be subdivided into the dimensionality of the hydrogen-bonded assemblies formed by the molecules, and will thus be described individually as either zero-, one-, two- or three-dimensional. When describing the dimensionality only the strong interactions, of the type O—H···N, O—H···O and N^+—H···O^-, are considered. The weaker interactions, in particular C—H···N, are taken into consideration when looking at the arrangement of the HMTA molecules relative to the donor molecules, and lead to higher dimensions by joining together the assemblies formed by strong interactions. For completeness, complexes involving H-atom transfer to form salts (seven found) are included, although the vast majority are co-crystals (31 found). Only unique structures are listed (a number of complexes have temperature-dependent phase transitions but the assemblies are unchanged, *e.g.* EKECOM and IJETOG series).

3.3.1. Zero-dimensional assemblies. There are 12 complexes that do not have an extended assembly of hydrogen bonds. Two of them are akin to the V-shaped co-crystals reported in this study, and use the mono-functional donor molecules *m*-cresol (HMTMCR) and resorcinol (RSHMTA02) in a 1:2 ratio, where the HMTA molecule accepts two hydrogen bonds. A further three consist of only one molecule each of HMTA and the donor interacting, *i.e.* the HMTA only accepts one hydrogen bond, as in IDUTUX, VIJTIR and YOLQOF. In YOLQIF the same zero-dimensional assembly is seen, except that a salt has formed and the HMTA cation hydrogen bonds to the anion. The only zero-dimensional assembly that has three hydrogen bonds is HMTTPO10, which has three phenol molecules hydrogen bonding to a central HMTA molecule. Two structures have a zero-dimensional pattern, but involve more than one molecule each of HMTA and the donor. The co-crystal with 1,2-cylohexanediol forms a hydrogen-bonded ring (described as a rhombus by the authors), where two HMTA and two diol molecules interact (IZAXIQ; Fig. 7*a*). A more involved assembly is found in the salt DIBZAQ, which has a HMTA cation hydrogen bonding to the donor (N^+—H···O^-), and a second (neutral) HMTA molecule accepting a hydrogen bond from a neutral 3,5-dinitrobenzoic acid donor (O—H···N) (Fig. 7*b*). These two separate entities are then joined by a common water molecule. In FIFFIK the donor molecule is deprotonated and one of the carboxylate O atoms acts as a twofold acceptor to two water molecules to form a $R_4^2(8)$ ring. This ring has two HMTA cations bonding to the two water molecules. A zero-dimensional assembly resulting from the opposite of the V-shaped motif has two HMTA molecules hydrogen bonding to a central *m*-benzenedicarboxylic acid molecule (MIPVOW). The salt WISNER has the didonor molecule 1,2,4,5-tetracarboxylic acid, where two protons are transferred to two HMTA molecules.

Table 3
N—H···N and O—H···O hydrogen-bonding details for co-crystals (I)–(VII).

Excludes C—H···O and C—H···N hydrogen bonds.

D—H···*A*	*D*—H (Å)	H···*A* (Å)	*D*···*A* (Å)	*D*—H···*A* (°)
(I)				
O1—H1···N1	0.97 (3)	1.70 (3)	2.6684 (17)	177 (2)
O3—H3···N2	0.87 (3)	1.81 (3)	2.6771 (17)	174 (2)
(II)				
O1—H1···N1	1.01 (2)	1.60 (2)	2.6046 (12)	170 (2)
O3—H3···N2	0.91 (2)	1.75 (2)	2.6556 (13)	173 (2)
(III)				
O1—H1···N1	0.84	1.83	2.654 (6)	166
O3—H3···N2	0.84	1.80	2.620 (6)	164
(IV)				
O1—H1···N1	0.95 (3)	1.71 (3)	2.6496 (18)	168 (2)
(V)				
O1—H1···O1*W*	0.933 (15)	1.616 (15)	2.5373 (11)	168 (1)
O1*W*—H1*W*···N1	0.838 (8)	1.986 (9)	2.8148 (11)	170 (1)
O1*W*—H2*W*···N2^{i}	0.849 (9)	2.014 (9)	2.8465 (11)	166 (1)
(VI)				
O1—H1···N1	0.90 (2)	1.79 (2)	2.6859 (12)	173 (2)
(VII)				
O1—H1···N1	0.81 (4)	1.87 (3)	2.6732 (19)	171 (3)
O3—H3···N2	0.81 (3)	1.90 (4)	2.677 (2)	161 (3)

Symmetry codes: (i) $-x+\frac{3}{2}, y+\frac{1}{2}, -z+\frac{1}{2}$.

3.3.2. One-dimensional assemblies. Complexes involving either neutral or charged species are the most likely to form one-dimensional assemblies. There are 18 listed in Table 4, with 13 of them forming one-dimensional zigzag chains very similar to those described for co-crystals (VI) and (VII). Most of the donor molecules are bifunctional, having either two phenol groups, two carboxylic acids or one of each functional group. One forms chains through a water molecule (BUQQAF04), whereas another one involves molecules having three phenol groups (RAWDEY). In RAWDEY the third phenol bonds to a pendant HMTA molecule using a discrete hydrogen bond. The remaining 13 complexes have one-dimensional zigzag chains that are very similar to each other. They are most commonly encountered in the dicarboxylic acids, such as in undecanedioic acid (EKECOM01; Fig. 7*c*), pimelic acid (IJETOG), adipic acid (MIPVEM), decanedioc acid (YEJKON), azelaic acid (FITTQI) and the half deprotonated suberate anion (TIPWAQ01). Diphenols that feature this assembly are methyl-3,5-dihydroxybenzoate (FEQXEF), hydroquinone (HMTHQU), 4,4′-dithiophenol

(RAWCOH), 4,4′-sulfonyldiphenol (RAWCUN) and 4,4′-isopropylidenediphenol (RAWDAU). 4-Hydroxybenzoic acid is the only mixed functional group co-crystal found (FEQXIF). All of these 13 complexes have two hydrogen bonds to the HMTA molecule/cation. Other one-dimensional assemblies consist of either conjoined rhombi (similar to IZAXIQ) as in CERXIH (using 1,2-dihydroxybenzene; Fig. 7*d*) and co-crystal (V) (Fig. 5), or rhombi connected into a zigzag chain by a third phenol group such as in 1,3,5-trihydroxybenzene (RAWDIC; Fig. 7*e*). In salt complexes more involved one-dimensional assemblies are formed with water molecules (MEVXIU01 and MIPVAI).

3.3.3. Two-dimensional assemblies. The two-dimensional assemblies are most frequently extensions of the one-dimensional zigzag chains seen in the one-dimensional assemblies. By having two intersecting chains using all four N atoms on the HMTA molecule, two-dimensional assemblies, described as nets, are obtained that ultimately can be described as being built up from hydrogen-bonded rings. BOQBEO has $R_8^8(44)$ rings using 2,2′-biphenol (Fig. 7*f*) and HUSWIB has $R_8^8(48)$ rings using (1*R*,2*S*)-camphoric acid, and both use all four N atoms. In contrast similar nets are observed in RUWJOI, which has $R_6^6(48)$ rings, but only uses three N atoms on the HMTA molecule. This is compensated for by the tridonor molecule 1,1,1-tris(4-hydroxyphenyl)amine. The previous two structures were didonor molecules. A different way of generating two-dimensional assemblies is by joining one-dimensional zigzag chains by O—H···O hydrogen bonds. ROKQIR has three phenol groups, two of which hydrogen bond to two N atoms of the HMTA molecule and the third hydrogen bonds to a phenol group on adjacent chains, *i.e.* crosslinking across the zigzag chains. Other two-dimensional assemblies rely on the donor molecules hydrogen bonding to each other using other functional groups or solvent molecules that are then linked by the HMTA molecules. IHERIW forms rings of six molecules (two water and four donor) with the phenol groups and water molecules hydrogen bonding to the nitro groups on the donor molecules. Three of these rings then hydrogen bond to a central HMTA molecule. GUTSIX, which is a salt, has one of the three carboxylic acid groups deprotonated. Hydrogen bonding between the neutral carboxylic acid and charged carboxylate groups creates a two-dimensional network, which has cavities filled by two HMTA cations, which hydrogen bond to the inward pointing carboxylate groups. An elegant assembly is seen in the co-crystal HIRZIF, which has a tridonor phenol molecule. Each donor molecule forms three hydrogen bonds to three HMTA molecules and each HMTA molecule accepts three hydrogen bonds from three donor molecules. This creates a two-dimensional pattern of '*pear-shaped rings*', which stack above each other in a space-filling manner (Fig. 7*g*).

3.3.4. Three-dimensional assemblies. To the best of our knowledge, only one co-crystal can be considered to form a three-dimensional assembly

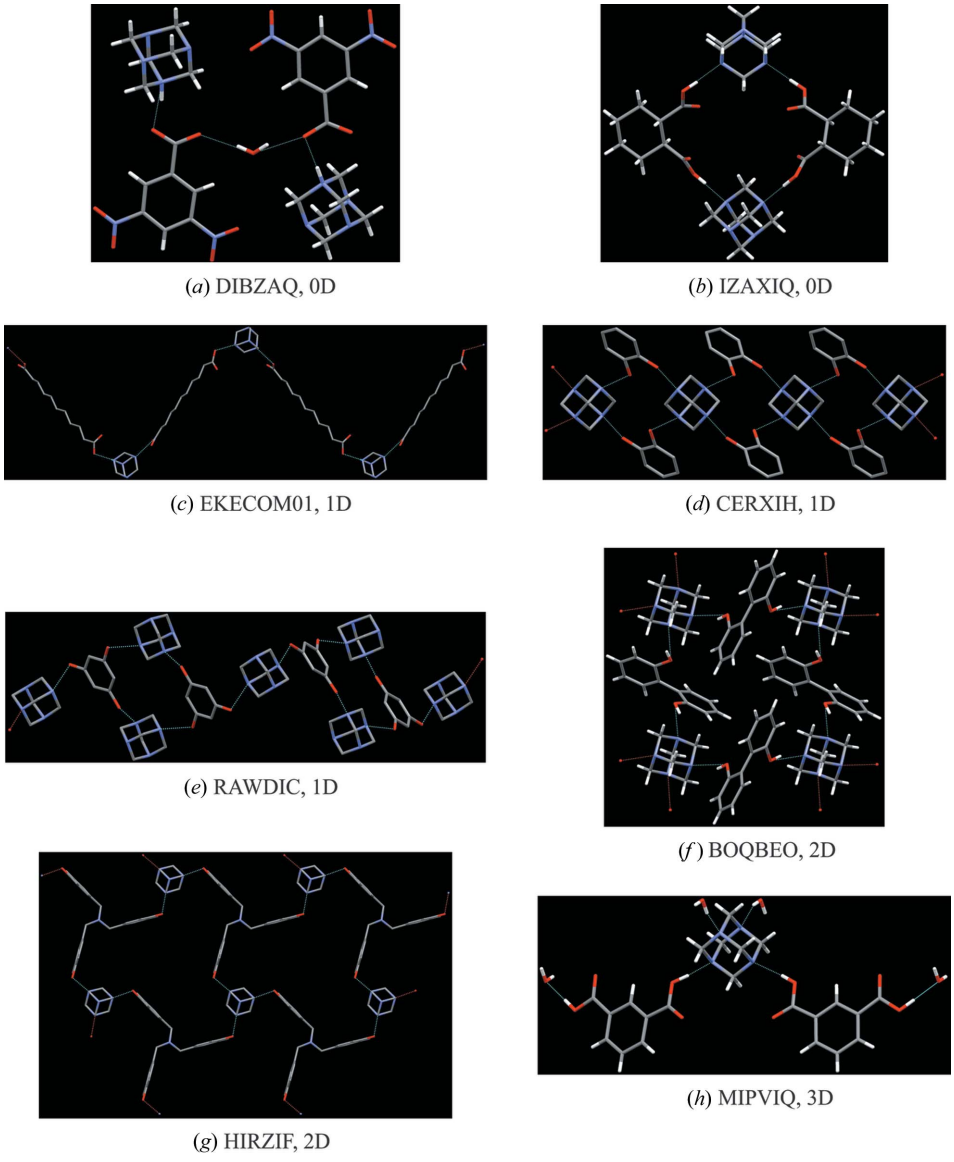

Figure 7
Selected packing diagrams of the different hydrogen-bonded assemblies encountered in the literature for HMTA complexes. H atoms are omitted for clarity in some diagrams.

Table 4
Summary of HMTA complexes in the literature.

Complexes that are salts are indicated, the remainder are co-crystals.

CSD refcode	Donor molecules	Input ratio (HMTA: donor) and observed ratio	Number of O—H···N or N^+—H···O^- hydrogen bonds per HMTA	Number of C—H···N hydrogen bonds per HMTA†	No. of functional groups on donors	Packing of HMTA and donor molecules	Hydrogen-bonding pattern, dimension, description	Ref.
Zero-dimensional assemblies								
(1) DIBZAQ (salt)‡	3,5-Dinitrobenzoate, water	1:1 resulting in 2:2:1	1	2	1 and 2	Two-dimensional layer of HMTA alternating with two-dimensional layer of donor	Discrete, zero-dimensional	(*a*)
(2) HMTMCR	*m*-Cresol	1:2 resulting in 1:2	2	Note 1	1	Two-dimensional layer of HMTA alternating with two-dimensional bilayer of donor	Discrete, zero-dimensional, V-shape	(*b*)
(3) HMTTPO10	Phenol	1:1 resulting in 1:3	3	1	1	One-dimensional channel of HMTA surrounded by six donors	Discrete, zero-dimensional	(*c*)
(4) IDUTUX	2,2,3,3-Tetramethylcyclopropane carboxylic acid	1:1 resulting in 1:1	1	3	1	Two-dimensional bilayer of HMTA alternating with a two-dimensional bilayer of donor	Discrete, zero-dimensional	(*d*)
(5) IZAXIQ	1,2-Cyclohexane dicarboxylic acid	1:1 resulting in 1:1	2	2	2	Two-dimensional layer of HMTA alternating with two-dimensional bilayer of donor	Ring, zero-dimensional, rhombus	(*e*)
(6) FIFFIK (salt)	5-nitrosalicylate, water	1:1 resulting in 1:1:1	1	3	2 and 2	Two-dimensional bilayer of HMTA alternating with two-dimensional bilayer of acid	$R_4^2(8)$ ring with water and carboxylate, pendant HMTA cation bond to water	(*f*)
(7) MIPVOW	*m*-Benzenedicarboxylic acid	1:1 resulting in 2:1	1	3	2	One-dimensional channel of two donor molecules surrounded by ten HMTA	Discrete, zero-dimensional	(*g*)
(8) RSHMTA02	Resorcinol	1:1 resulting in 1:1	2	2	2	Two-dimensional layer of HMTA alternating with two-dimensional layer of donor	Discrete, zero-dimensional, V-shape	(*h*)
(9) VIJTIR	Phenylacetic acid	1:1 resulting in 1:1	1	3	1	One-dimensional channel of four HMTA surrounded by eight donors	Discrete, zero-dimensional	(*i*)
(10) WISNER (salt)	Benzene-1,2,4,5-tetracarboxylic acid	2:1, 1:1 and 1:2 resulting in 2:1	1	3	4	One-dimensional channel of donor surrounded by four HMTA	Discrete, zero-dimensional	(*j*)
(11) YOLQIZ	2,4,6-Trinitrophenolate	1:1 resulting in 1:1	1	3	1	Two-dimensional bilayer of HMTA alternating with two-dimensional bilayer of donor	Discrete, zero-dimensional	(*k*)
(12) YOLQOF	4-Hydroxy-3-methoxybenzaldehyde	1:1 resulting in 1:1	1	3	1	Two-dimensional bilayer of HMTA alternating with two-dimensional bilayer of donor	Discrete, zero-dimensional	(*l*)

Table 4 (continued)

CSD refcode	Donor molecules	Input ratio (HMTA: donor) and observed ratio	Number of O—H···N or N^+—H···O^- hydrogen bonds per HMTA	Number of C—H···N hydrogen bonds per HMTA†	No. of functional groups on donors	Packing of HMTA and donor molecules	Hydrogen-bonding pattern, dimension, description	Ref.
One-dimensional assemblies								
(13) BUQQAF04	4-Nitrophenol, water	1:1 or 1:2 resulting in 1:2:1	3	1	1 and 2	Two-dimensional layer of HMTA alternating with two-dimensional layer of donor	Zigzag chains using water molecule, one-dimensional, donor is pendant to chains and bonds to either HMTA or water molecules	(*m*)
(14) CERXIH	1,2-Dihydroxybenzene	1:2 resulting in 1:2	4	0	2	Two-dimensional layer of HMTA alternating with two-dimensional bilayer of donor	Ring, one-dimensional, joined rhombii	(*n*)
(15) EKECOM01	Undecanoic acid	1:1 resulting in 1:1	2	2	2	Two-dimensional layer of HMTA alternating with two-dimensional layer of donor	Zigzag chains, one-dimensional	(*o*)
(16) FEQXEF	Methyl-3,5-dihydroxybenzoate	1:1 resulting in 1:1	2	2	2	Two-dimensional layer of HMTA alternating with two-dimensional layer of donor	Zigzag chains, one-dimensional	(*p*)
(17) FEQXIJ	4-Hydroxybenzoic acid	1:1 resulting in 1:1	2	2	2	Two-dimensional layer of HMTA alternating with two-dimensional layer of donor	Zigzag chains, one-dimensional	(*p*)
(18) FITTQI (salt)‡	Azelaic acid	1:1 resulting in 1:1	2	2	2	Two-dimensional layer of HMTA alternating with two-dimensional layer of donor	Zigzag chains, one-dimensional	(*q*)
(19) HMTHQU	Hydroquinone	1:1 resulting in 1:1	2	2	2	Two-dimensional layer of HMTA alternating with two-dimensional layer of donor	Zigzag chains, one-dimensional	(*r*)
(20) IJETOG	Pimelic acid	1:1 resulting in 1:1	2	2	2	Two-dimensional layer of HMTA alternating with two-dimensional layer of donor	Zigzag chains, one-dimensional	(*s*)
(21) MEVXIU01 (salt)	2,4-Dinitrobenzoate, water	1:1 resulting in 1:1:1	1	3	1 and 2	Two-dimensional bilayer of HMTA alternating with two-dimensional bilayer of donor	Chain of water and anion, pendant HMTA cation bonds to anion	(*t*)
(22) MIPVAI (salt)	2,2-Dithiosalicyclic acid, water	1:1 resulting in 2:2:1	2	1	2 and 2	One-dimensional channel of HMTA surrounded by donor	Two chains of donor molecules, chains are connected by water molecules, HMTA is pendant to the two chains, one-dimensional	(*g*)
(23) MIPVEM	Adipic acid	1:1 resulting in 1:1	2	2	2	Two-dimensional layer of HMTA alternating with two-dimensional layer of donor	Zigzag chains, one-dimensional	(*g*)

Table 4 (continued)

CSD refcode	Donor molecules	Input ratio (HMTA: donor) and observed ratio	Number of O—H···N or N^+—H···O^- hydrogen bonds per HMTA	Number of C—H···N hydrogen bonds per HMTA†	No. of functional groups on donors	Packing of HMTA and donor molecules	Hydrogen-bonding pattern, dimension, description	Ref.
(24) RAWCOH	4,4′-Dithiophenol	1:1, 1:2, 1:4 all resulting in 1:1	2	2	2	Two-dimensional layer of HMTA alternating with two-dimensional layer of donor	Zigzag chains, one-dimensional	(*u*)
(25) RAWCUN	4,4′-Sulfonyldiphenol	1:1, 1:2, 1:4 all resulting in 1:1	2	2	2	Two-dimensional layer of HMTA alternating with two-dimensional layer of donor	Zigzag chains, one-dimensional	(*u*)
(26) RAWDAU	4,4′-Isopropylidenediphenol	1:1, 1:2, 1:4 all resulting in 1:1	2	2	2	Two-dimensional corrugated layer of HMTA with two-dimensional layer of donor	Zigzag chains, one-dimensional	(*u*)
(27) RAWDEY	1,1,1-Tris(4-hydroxyphenyl)ethane	1:1, 1:2, 1:4 all resulting in 2:1	2 and 1	2 and 3	3	Two-dimensional corrugated layer of HMTA with two-dimensional layer of donor	Zigzag chains, one-dimensional and pendant HMTA to donor	(*u*)
(28) RAWDIC	1,3,5-Trihydroxybenzene	1:1, 1:2, 1:4 all resulting in 3:2	2	2	3	One-dimensional channel of two donor molecules surrounded by eight HMTA	Zigzag chains of joined rhombus, one-dimensional	(*u*)
(29) TIPWAQ01 (salt)‡	Suberate	1:1 resulting in 1:1	2	2	2	Two-dimensional layer of HMTA alternating with two-dimensional layer of donor	Zigzag chains, one-dimensional	(*v*)
(30) YEJKON	Decanedioc acid	1:1 resulting in 1:1	2	2	2	Two-dimensional layer of HMTA alternating with two-dimensional layer of donor	Zigzag chains, one-dimensional	(*w*)
Two-dimensional assemblies								
(31) BOQBEO	2,2-Biphenol	1:1 resulting in 1:2	4	0	2	One-dimensional channels of HMTA surrounded by four donors	Zigzag chains forming rings $R_8^8(44)$, two-dimensional	(*x*)
(32) GUTSIX (salt)	Cycylohexane-1,3,5-tricarboxylic acid	1:1 resulting in 1:1	1	2	3	One-dimensional channel of two HMTA molecules surrounded by eight donors	Network of donor anions, HMTA pendant, two-dimensional	(*y*)
(33) HIFZIF	Tris(4-hydroxy-3,5-dimethylbenzyl)-amine	1:1 resulting in 1:1	3	1	3	One-dimensional channel of HMTA surrounded by three donors	Zigzag chains forming 'pear-shaped' rings, two-dimensional	(*z*)
(34) HUSWIB	(1*R*,3*S*)-camphoric acid	1:2 resulting in 1:2	4	0	2	Two-dimensional layer of HMTA alternating with two-dimensional bilayer of donor	Zigzag chains forming $R_8^8(44)$ rings, two-dimensional	(*aa*)
(35) IHERIW	4-Nitrobenzene-1,2-diol hydrate	1:2 resulting in 1:2:1	3	1	2 and 2	Two-dimensional layer of HMTA alternating with two-dimensional layer of donor	A number of rings (see text), two-dimensional	(*bb*)

Table 4 (continued)

CSD refcode	Donor molecules	Input ratio (HMTA: donor) and observed ratio	Number of O—H···N or N^+—H···O^- hydrogen bonds per HMTA	Number of C—H···N hydrogen bonds per HMTA†	No. of functional groups on donors	Packing of HMTA and donor molecules	Hydrogen-bonding pattern, dimension, description	Ref.
(36) ROKQIR	1,1,3-Tris(2-methyl-4-hydroxy-5-*tert*-butylphenyl)butane	1:1 resulting in 1:1	2	2	3	One-dimensional channel of HMTA surrounded by four donors	Zigzag chains joined by a chain of alcohol hydrogen bonds, two-dimensional	(*cc*)
(37) RUWJOI	1,1,1-Tris(4-hydroxyphenyl)amine	1:1, 1:2, 1:4 all resulting in 1:1	3	1	3	Two-dimensional layer of HMTA alternating with two-dimensional bilayer of donor	Zigzag chains form ring, two-dimensional	(*dd*)
Three-dimensional assemblies								
(38) MIPVIQ	*m*-Benzenedicarboxylic acid, water	1:1 resulting in 1:1:1	4	0	2 and 2	One-dimensional channel of HMTA surrounded by donor	Zigzag chain using water, zigzag chain using acid, crosslinked by water, three-dimensional	(*g*)

(*a*) Fun *et al.* (2007); (*b*) Mak *et al.* (1978); (*c*) Jordan & Mak (1970); (*d*) Feng *et al.* (2006); (*e*) Venkatraman *et al.* (2004); (*f*) Smith *et al.* (2005); (*g*) Li *et al.* (2001); (*h*) Ng *et al.* (2002); (*i*) Mak *et al.* (1986); (*j*) Lough *et al.* (2000); (*k*) Usman *et al.* (2002*a*); (*l*) Usman *et al.* (2002*b*); (*m*) Ng (2008); (*n*) Daka & Wheeler (2006); (*o*) Pinheiro *et al.* (2003); (*p*) Ghosh *et al.* (2005); (*q*) Hostettler *et al.* (1999); (*r*) Mak *et al.* (1977); (*s*) Gardon *et al.* (2003); (*t*) Rosli *et al.* (2006); (*u*) Coupar, Glidewell & Ferguson (1997); (*v*) Gaillard *et al.* (1996); (*w*) Gardon *et al.* (2001); (*x*) MacLean *et al.* (1999); (*y*) Shan *et al.* (2003); (*z*) de Bruyn *et al.* (1996); (*aa*) Zakaria *et al.* (2003); (*bb*) Chantrapromma *et al.* (2002); (*cc*) Meehan *et al.* (1997); (*dd*) Coupar, Ferguson *et al.* (1997). † The criteria for locating C—H···N contacts was up to 0.5 Å larger than the sum of the van der Waals radii. Note 1: No H atoms in the CIF file. ‡ These complexes have both carboxylic acids and carboylate groups.

using only strong O—H···N hydrogen bonds. MIPVIQ is a hydrated co-crystal using *m*-benzenedicarboxylic acid and water. A central HMTA molecule accepts two hydrogen bonds from two acid molecules and two hydrogen bonds from two water molecules (Fig. 7*h*). The acid molecules further hydrogen bond to the water molecules. Repeating this sequence generates the three-dimensional assembly.

3.4. General observations on HMTA complexes

The nature and geometry of the HMTA molecule allow for a number of different kinds of hydrogen-bonded assemblies, depending on the stoichiometry and the number and type of functional groups on the donor molecules. A total of 38 complexes have been described in the literature previously. Of those, the vast majority are with didonor molecules (22). Complexes with monodonor, tridonor and tetradonors are found less frequently; their numbers are nine, six and one. The number of N atoms used as acceptors in strong interactions follows a similar trend; complexes using two N atoms are found 19 times. For one, three and four N atoms used, the numbers are 11, four and five. The correlation between didonors and diacceptors is seen in the ratios of the two molecules observed in the crystal structures; 16 crystal structures have a 1:1 ratio. The dominant hydrogen-bonded assembly involves the zigzag chains seen in 1:1 complexes with didonor molecules and using two N atoms. Even when all four N atoms are used, the assembly either remains one-dimensional with some other shape or becomes two-dimensional by forming rings. The didonor molecules generally have the two functional groups on opposite ends of the molecule, and this predisposes the formation of the chains. Zero-dimensional assemblies are typically formed by either monodonor molecules or didonor molecules where the two functional groups are in close proximity. There are exceptions to these generalizations and only by performing a truly systematic study of didonor molecules with different relative positions of their functional groups can more accurate conclusions be drawn. Two-dimensional assemblies have generally been formed with tridonor molecules [exceptions are 2,2′-biphenol, (1*R*,2*S*)-camphoric acid and 4-nitrobenzene-1,2-diol]. Interestingly, the three-dimensional assembly observed has two didonor molecules, one of them water. Perhaps the key to forming three-dimensional assemblies lies in using smaller donor molecules.

Significantly, a pattern that emerges from the literature review and analysis is that the HMTA molecules overwhelmingly arrange themselves into two-dimensional layers or two-dimensional bilayers, which are generally mimicked by the two-dimensional layering of the donor molecules. 27 out of the 38 complexes feature some sort of layering of the HMTA molecules, and the remaining ten have the HMTA molecules arranged in a one-dimensional pattern, often surrounded by the donor molecules to form a channel architecture. Even though the focus in the literature review was on the strong interactions, Table 4 shows that in almost every instance (33 times) the unused N atoms are involved in weak interactions of the C—H···N type. These weak interactions are featured between the HMTA molecules and hence are a vital cog in the

Table 5
HMTA complexes using iodine halogen bonding only.

CSD refcode	Acceptor molecule and ratio of acceptor to HMTA	Number of halogen atoms per acceptor molecule	Number of halogen-bonding interactions per HMTA molecule	Dimension of halogen-bonded assembly	Packing of HMTA and donor molecules	Ref.
(1) HEXAIF10	Iodoform (1:1)	3	3	Three-dimensional	Two-dimensional layer of HMTA alternating with two-dimensional layer of donor	(*a*)
(2) HMTNTI	Tri-iodo-nitrogen and iodine (1:1:1)	3 and 2	4	Three-dimensional	One-dimensional channel of HMTA surrounded by four donors	(*b*)
(3) HXMIOD	Iodine (2:1)	2	2	Three-dimensional	One-dimensional channel of HMTA surrounded by six donors	(*c*)
(4) HXMTDI	Iodine (1:1)	2	2	Zigzag chains	Two-dimensional layer of HMTA alternating with two-dimensional layer of donor	(*c*)
(5) QIHCIT	1,4-Diiodobenzene (1:1)	2	2	Zigzag chains	Two-dimensional layer of HMTA alternating with two-dimensional layer of donor	(*d*)
(6) QIHCOZ01	1,4-Diiodofluorobenzene (1:1)	2	2	Zigzag chains	Two-dimensional layer of HMTA alternating with two-dimensional layer of donor	(*e*)
(7) QIHCUF	Tetraiodoethylene (1:1)	2	2	Zigzag chains	Two-dimensional layer of HMTA alternating with two-dimensional layer of donor	(*d*)
(8) YUYNUB	Iodine (3:1)	2	3	Zero-dimensional	Isolated HMTA surrounded by donor	(*f*)

References: (*a*) Dahl & Hassel (1970); (*b*) Pritzkow (1974); (*c*) Pritzkow (1975); (*d*) Walsh *et al.* (2001); (*e*) Bolte (2003); (*f*) Tebbe & Nagel (1995).

two-dimensional assembly of the HMTA. In this regard, one can consider the HMTA molecule to always make use of all four of its acceptor atoms, even though the proportion of strong interactions generally seems to favour only two N atoms and the remainder of the N atoms are completed by weak interactions. A caveat needs to be added to this statement in that when examining the weak interactions, considerable leeway was allowed in the distance criteria for the C—H···N interactions, being sometimes up to 0.5 Å greater than the sum of the van der Waals radii. The three instances that do not make use of all four N atoms are found in the salt complexes DIBZAQ, MIPVAI and GUTSIX.

The hydrogen-bonding motifs shown by co-crystals (I)–(VII) in this study are characteristic for the assemblies shown in general for the previous HMTA complexes. Co-crystals (I)–(III) all have zero-dimensional assemblies in terms of the motif created by the hydrogen bonding of HMTA with the donor molecules. All of them have a V-shape (by virtue of the molecular shape of the HMTA molecule) and only have two donor molecules for every HMTA molecule. These V-shaped entities consisting of three molecules will be referred to as the building block to forming one-dimensional assemblies. These V-shaped trimers, as found in (I), can be extended to a one-dimensional hydrogen-bonded assembly by adding the same donor functionality (carboxylic acid) to the donor molecules, which then join up the V-shaped trimers to form one-dimensional zigzag chains, as found in co-crystals (VI) and (VII). Again, the zigzag shape comes from the tetrahedral arrangement of the N donors and is truly the dominant hydrogen-bonded assembly. The molecular structure of the donor molecules is hence also crucial in determining the crystal structure, as the monodonor cyclohexylcarboxylic acid in (I) becomes a didonor molecule in (VI) and (VII), and hence forms one-dimensional assemblies. The shape of the one-dimensional assembly is derived from the molecular shape of the acceptor HMTA molecule. An interesting result is co-crystal (V), which is only the fifth known structure that makes use of all four N donors in strong interactions. The original aim was to make another zero-dimensional V-shaped assembly like in co-crystals (I)–(IV) using the same crystallization procedure; however, water was incorporated into the crystal structure and displaced the donor molecule from its role as hydrogen-bond donor to the HMTA molecule. The water hydrogen bonds equally to all four N acceptors. In comparison, the hexahydrate of HMTA only makes use of three N atoms (Mak, 1965). Nonetheless, all seven co-crystals display the same two-dimensional layering of HMTA molecules, which are stabilized by the weaker interactions.

3.5. Note on other HMTA complexes in the literature

There are complexes that make use of halogen bonding as another important intermolecular interaction, and complexes using halogen atoms (acting as Lewis acids) have been made

with HMTA (acting as a Lewis base). In these complexes HMTA acts as the donor molecule (donating electron pairs) and the molecule with the halogen atom as the lone-pair acceptor. Owing to the tetrahedral arrangement of the N atoms, the possibility exists to make diamondoid networks with molecules that also have four halogen atoms in a tetrahedral arrangement. Two such complexes with this specific three-dimensional assembly are (HMTA)·(1,3,5,7-tetrabromoadamantane)$_2$ (PIZDUX) and (HMTA)·(1,3,5,7-tetrabromoadamantane)·(tetrabromomethane) (PIZFAF) (Reddy *et al.*, 1994). Neutral complexes with iodine as the halogen atom on the donor molecule are more common as it has the greatest polarization of the halogen atoms (Präseng *et al.*, 2009; Forni *et al.*, 2004). These complexes have also been investigated to make zero-, one- and three-dimensional assemblies (see Table 5). The majority of exclusively halogen-bonded complexes have two halogen bonds per HMTA molecule, with two cases of three and one case of four also observed. The shape of the one-dimensional assemblies is very similar to the zigzag chains of HMTA complexes with carboxylic acids or phenols described above (Lemmerer, 2011); as well as the two-dimensional layering of the HMTA molecules.

4. Conclusion

Designing hydrogen-bonded assemblies using two or more different molecules depends on what the molecules have to offer in terms of hydrogen-bonding functionality, the number and type of interactions it can undergo, as well as the shape of the molecule and the relative positions of the functional groups. The hydrogen-bonding interactions of carboxylic acid and phenol groups with the lone pair of N atoms is now a well established robust interaction and is used throughout the complexes surveyed in the literature, and the seven new co-crystals reported here. Most of the complexes, be they salt or co-crystal, use only two of the N atoms on the HMTA molecule to connect the donor with HMTA in strong interactions. Owing to the tetrahedral geometry and the relative position of any two N atoms (*the molecular structure*), one-dimensional chains are commonly featured in the complexes, and have a zigzag shape when using bifunctional donor molecules (*the crystal structure*). In summary, however, it is clear that all N donors are used in both strong and weak interactions, the latter in assembling the HMTA molecules into two-dimensional layers.

The University of the Witwatersrand and the Molecular Sciences Institute are thanked for providing the infrastructure and financial support for this work. Professor Demetrius C. Levendis is thanked for valuable comments regarding the preparation of this manuscript. The reviewers for this manuscript are thanked for providing additional insights which have been incorporated into the discussion.

References

Aakeröy, C. B., Beatty, A. M. & Helfrich, B. A. (2002). *J. Am. Chem. Soc.* **124**, 14425–14432.
Aakeröy, C. B., Fasulo, M. E. & Desper, J. (2007). *Mol. Pharm.* **4**, 317–322.
Allen, F. H. (2002). *Acta Cryst.* B**58**, 380–388.
Allen, F. H., Kennard, O., Watson, D. G., Brenner, L., Orpen, A. G. & Taylor, R. (1987). *J. Chem. Soc. Perkin Trans. 2*, pp. S1–19.
Báthori, N. B., Lemmerer, A., Venter, G. A., Bourne, S. A. & Caira, M. R. (2011). *Cryst. Growth Des.* **11**, 75–87.
Bolte, M. (2003). Private communication (refcode QIHCOZ01). CCDC, Cambridge, England.
Bond, A. D. (2007). *CrystEngComm*, **9**, 833–834.
Braga, D., Grepionio, F., Biradha, K., Pedireddi, V. R. & Desiraju, G. (1995). *J. Am. Chem. Soc.* **117**, 3156–3166.
Brandenburg, K. (1999). *DIAMOND*, Version 2.1e. Crystal Impact GbR, Bonn, Germany.
Bruker (2004). *SAINT-Plus*, Version 7.12. Bruker AXS Inc., Madison, Wisconsin, USA.
Bruker (2005). *APEX*2, Version 1.27. Bruker AXS Inc., Madison, Wisconsin, USA.
Bruyn, P. J. de, Gable, R. W., Potter, A. C. & Solomon, D. H. (1996). *Acta Cryst.* C**52**, 466–468.
Burrows, A. D. (2004). *Struct. Bond.* **108**, 55–96.
Bussien Gaillard, V., Paciorek, W., Schenk, K. & Chapuis, G. (1996). *Acta Cryst.* B**52**, 1036–1047.
Chantrapromma, S., Usman, A., Fun, H.-K., Poh, B.-L. & Karalai, C. (2002). *Acta Cryst.* C**58**, o675–o677.
Coupar, P. I., Ferguson, G., Glidewell, C. & Meehan, P. R. (1997). *Acta Cryst.* C**53**, 1978–1980.
Coupar, P. I., Glidewell, C. & Ferguson, G. (1997). *Acta Cryst.* B**53**, 521–533.
Dahl, T. & Hassel, O. (1970). *Acta Chem. Scand.* **24**, 377–383.
Daka, P. & Wheeler, K. A. (2006). *Acta Cryst.* E**62**, o5477–o5479.
Das, D. & Desiraju, G. R. (2006). *Chem. Asian J.* **1–2**, 231–244.
Desiraju, G. R. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 2311–2327.
Desiraju, G. R. (1997). *Curr. Opin. Solid State Mater. Sci.* **2**, 451–454.
Desiraju, G. R. (2002). *Acc. Chem. Res.* **35**, 565–573.
Desiraju, G. R. (2007). *Angew. Chem. Int. Ed.* **46**, 2–17.
Desiraju, G. R. (2010). *J. Chem. Sci.* **122**, 667–675.
Ermer, O. (1988). *J. Am. Chem. Soc.* **110**, 3747–3754.
Farrugia, L. J. (1997). *J. Appl. Cryst.* **30**, 565.
Farrugia, L. J. (1999). *J. Appl. Cryst.* **32**, 837–838.
Feng, H., Zhang, H.-M., Tu, B. & Jin, Z.-M. (2006). *Acta Cryst.* E**62**, o3122–o3123.
Forni, A., Metrangelo, P., Pilati, T. & Resnati, G. (2004). *Cryst. Growth Des.* **4**, 291–295.
Fun, H.-K., Rosli, M. M., Lee, B.-S., Ong, L.-H. & Chantrapromma, S. (2007). *J. Mol. Struct.* **837**, 132–141.
Gardon, M., Pinheiro, C. B. & Chapuis, G. (2003). *Acta Cryst.* B**59**, 527–536.
Gardon, M., Schönleber, A., Chapuis, G., Hostettler, M. & Bonin, M. (2001). *Acta Cryst.* C**57**, 936–938.
Ghosh, K., Datta, M., Fröhlich, R. & Ganguly, N. C. (2005). *J. Mol. Struct.* **737**, 201–206.
Hostettler, M., Birkedal, H., Gardon, M., Chapuis, G., Schwarzenbach, D. & Bonin, M. (1999). *Acta Cryst.* B**55**, 448–458.
Jordan, T. H. & Mak, T. C. W. (1970). *J. Chem. Phys.* **52**, 3790–3794.
Karki, S., Friščič, T. & Jones, W. (2009). *CrystEngComm*, **11**, 470–481.
Leiserowitz, L. (1976). *Acta Cryst.* B**32**, 775–802.
Leiserowitz, L. & Tuval, M. (1978). *Acta Cryst.* B**34**, 1230–1247.
Lemmerer, A. (2011). *Z. Kristallogr.* **226**, doi: 10.1524/zkri.2011.1375.
Lemmerer, A., Adsmond, D. & Bernstein, J. (2011). *Cryst. Growth Des.* Submitted for publication.
Lemmerer, A., Báthori, N. B. & Bourne, S. A. (2008). *Acta Cryst.* B**64**, 780–790.
Lemmerer, A. & Bernstein, J. (2010). *CrystEngComm*, **12**, 2029–2033.

Lemmerer, A., Bernstein, J. & Kahlenberg, V. (2010). *CrystEngComm*, **12**, 2856–2864.
Li, W., Zhang, J.-P., Tong, M.-L. & Chen, X.-M. (2001). *Aust. J. Chem.* **54**, 213–217.
Lough, A. J., Wheatley, P. S., Ferguson, G. & Glidewell, C. (2000). *Acta Cryst.* B**56**, 261–272.
MacLean, E. J., Glidewell, C., Ferguson, G., Gregson, R. M. & Lough, A. J. (1999). *Acta Cryst.* C**55**, 1867–1870.
Mak, T. C. W. (1965). *J. Chem. Phys.* **43**, 2799–2805.
Mak, T. C. W., Tse, C.-S., Chong, Y.-H. & Mok, F.-C. (1977). *Acta Cryst.* B**33**, 2980–2982.
Mak, T. C. W., Xiaoming, C., Kailiang, S., Jiaxing, Y. & Chaode, Z. (1986). *J. Crystallogr. Spectrosc. Res.* **16**, 639–646.
Mak, T. C. W., Yu, W.-H. & Lam, Y.-S. (1978). *Acta Cryst.* B**34**, 2061–2063.
Meehan, P. R., Gregson, R. M., Glidewell, C. & Ferguson, G. (1997). *Acta Cryst.* C**53**, 1637–1640.
Mei, X. & Wolf, C. (2004). *Cryst. Growth Des.* **7**, 1099–1103.
Ng, S. W. (2008). *Acta Cryst.* E**64**, o2195.
Ng, S. W., Naumov, P., Ibrahim, A. R., Fun, H.-K., Chantrapromma, S., Wojciechowski, G., Brzezinski, B. & Hanna, J. V. (2002). *J. Mol. Struct.* **609**, 89–95.
Pinheiro, C. B., Gardon, M. & Chapuis, G. (2003). *Acta Cryst.* B**59**, 416–427.
Präseng, C., Whitwood, A. C. & Bruce, D. W. (2009). *Cryst. Growth Des.* **9**, 5319–5326.
Pritzkow, H. (1974). *Z. Anorg. Allg. Chem.* **409**, 237–247.
Pritzkow, H. (1975). *Acta Cryst.* B**31**, 1589–1593.
Reddy, D. S., Craig, D. C. & Desiraju, G. R. (1994). *J. Chem. Soc. Chem. Commun.* pp. 1457–1458.
Rosli, M. M., Fun, H.-K., Lee, B. S., Ruanwas, P. & Chantrapromma, S. (2006). *Acta Cryst.* E**62**, o3296–o3298.
Shan, N., Bond, A. D. & Jones, W. (2003). *New J. Chem.* **27**, 365–371.
Shattock, T. R., Arora, K. K., Vishweshwar, P. & Zaworotko, M. J. (2008). *Cryst. Growth Des.* **8**, 4533–4545.
Sheldrick, G. M. (1996). *SADABS*. University of Göttingen, Germany.
Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.
Smith, G., Hartono, A. W., Wermuth, U. D., Healy, P. C., White, J. M. & Rae, D. (2005). *Aust. J. Chem.* **58**, 47–52.
Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.
Stahly, G. P. (2009). *Cryst. Growth Des.* **9**, 4212–4229.
Steiner, T. (2002). *Angew. Chem. Int. Ed.* **41**, 48–76.
Tebbe, K.-F. & Nagel, K. (1995). *Acta Cryst.* C**51**, 1388–1390.
Usman, A., Chantrapromma, S., Fun, H.-K., Poh, B.-L. & Karalai, C. (2002*a*). *Acta Cryst.* C**58**, o46–o47.
Usman, A., Chantrapromma, S., Fun, H.-K., Poh, B.-L. & Karalai, C. (2002*b*). *Acta Cryst.* C**58**, o48–o50.
Venkatraman, R., Ray, P. C. & Fronczek, F. R. (2004). *Acta Cryst.* C**60**, o633–o635.
Vishweshwar, P., Nangia, A. & Lynch, V. M. (2003*a*). *Cryst. Growth Des.* **3**, 783–790.
Vishweshwar, P., Nangia, A. & Lynch, V. M. (2003*b*). *CrystEngComm*, **5**, 164–168.
Walsh, R. B., Padgett, C. W., Metrangelo, P., Resnati, G., Hanks, T. W. & Pennington, W. T. (2001). *Cryst. Growth Des.* **1**, 165–175.
Zakaria, C. M., Ferguson, G., Lough, A. J. & Glidewell, C. (2003). *Acta Cryst.* B**59**, 118–131.