One, two, and three methylene phosphonic acid groups (–$CH_2PO_3H_2$) on a mesitylene ring: synthesis, characterization and aspects of supramolecular aggregation†

Ramaswamy Murugavel[*ab] **and Mayank Pratap Singh**[a]

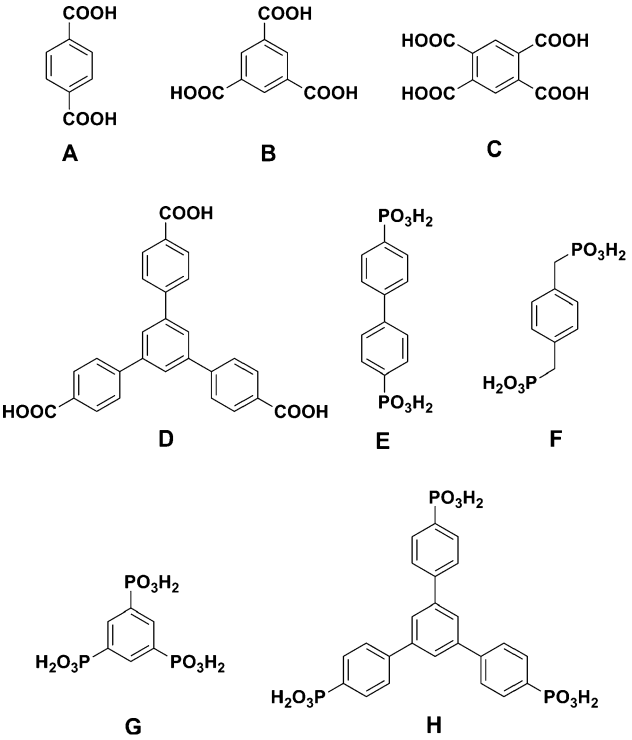
Received (in Victoria, Australia) 19th November 2009, Accepted 17th March 2010
DOI: 10.1039/b9nj00691e

The ease of substitution of –CH_2Br group on the mesitylene ring in a stepwise manner has been exploited to prepare mesitylene mono-, bis-, and tris-methylene phosphonic acids $C_6H_2Me_3(CH_2PO_3H_2)$ (**1**), $C_6HMe_3(CH_2PO_3H_2)_2$ (**2**), and $C_6Me_3(CH_2PO_3H_2)_3$ (**3**) in 80–90% yield, through a Michaelis–Arbuzov reaction followed by acid hydrolysis. Compounds **1–4** have been characterized by analytical and spectroscopic (IR, NMR, and MS) techniques. The X-ray structural investigations on all the three compounds reveal that the central mesitylene ring is a robust platform for hosting multiple methylene phosphonic acid groups. Mesitylene mono-methylene phosphonic acid **1**, which can be considered as the sterically encumbered modification of benzyl phosphonic acid, interestingly associates as a one-dimensional tubular structure through extensive O–H···O hydrogen bonding between adjacent –PO_3H_2 groups, albeit with no such interactions between the tubes due to the highly hydrophobic nature of the surface. The X-ray structure of mesitylene-1,3-diphosphonic acid **2** reveals that the molecules exhibit a *syn*-orientation of the –$CH_2PO_3H_2$, which are involved in extensive P–OH···O hydrogen bonding to result in a two-dimensional layered structure. The presence of three –PO_3H_2 units on the same side of the mesitylene ring in **3** results in a three-dimensional framework solid. The present studies clearly reveal a linear relationship between the dimensionality of the supramolecular structure and the number of phosphonic acid moieties on the mesitylene ring.

Introduction

A major focus in the ever-expanding field of supramolecular chemistry lies in the design of simple molecules in which multiple 'adhesive' functional groups (*e.g.* tectons such as –COOH) are judiciously placed on a rigid central building block (synthons such as aromatic rings).[1–3] An elegant example of such an approach is the demonstration of the formation of the hydrogen-bonded sheet structure of benzene-1,3,5-tricarboxylic acid (trimesic acid), often referred to as a honeycomb or chicken-wire network.[3a] While trimesic acid represents one of the early examples of poly(carboxylic) aromatic acids amenable for supramolecular aggregation, later research showed that several similar compounds with more than one carboxylic function on an aryl ring, such as those shown in Scheme 1 (**A–D**),[4] could be employed for the generation of architectures in the solid-state through extensive hydrogen bonding.

Phosphonic acids have long been known for their ability to bind many metal ions (per acid group) and thus they generate



Scheme 1 Arene-based polyacids used for the preparation of supramolecular assemblies and metal–organic frameworks.

---

[a] *Department of Chemistry, Indian Institute of Technology – Bombay, Powai, Mumbai-400076, India. E-mail: rmv@chem.iitb.ac.in; Fax: +91-22-2572 3480*
[b] *Centre for Research in Nanotechnology and Science, Indian Institute of Technology – Bombay, Powai, Mumbai-400076, India*

† Electronic supplementary information (ESI) available: Details of spectroscopic investigations of compounds **1–3**. CCDC reference numbers 755660–755662. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b9nj00691e

highly polymeric inorganic–organic networks.[5,6] Among these, notable are the layered metal phosphonates discovered in the 1970s, and shown to have interesting applications.[6] This abilities of these groups of compounds was exploited by placing two or more phosphonic acid moieties on a rigid aryl platform, as shown in Scheme 1 (**E–H**).[7] This has been well demonstrated in the case of diphosphonic acids (used to prepare pillared solids) and triphosphinic acids (used to prepare three-dimensional structures).[6] Apart from their use as polydentate ligands,[6] these bis- and tris-phosphonic acids can themselves self-assemble both in solution and in the solid state through extensive (and strong) intra- and intermolecular P–O–H···O–P hydrogen bonds, as in the case of trimesic acid described above.[3a] Notable among such hydrogen-bonded structures of phosphonic acids are 4-methyl-2,6-bis(phosphonomethyl)phenol,[8] *o*-, *m*-, and *p*-fluorobenzylphosphonic acid,[9] (*R*)-1-phenyl-2-carboxyethylphosphonic acid,[10] *rac*-(hydroxy(phenyl)methylene)diphosphonic acid monohydrate, (hydroxy(4-nitrophenyl)methylene)diphosphonic acid,[11] and (4-vinylbenzyl)phosphonic acid,[12] which have been characterized by single-crystal X-ray diffraction studies and shown to have interesting association properties.

As a part of our ongoing studies on metal phosphonates[13] and phosphates[14] in order to achieve new types of supramolecular architectures, we have designed and synthesized three new benzyl phosphonic acids. The aromatic rings in the new acids have been substituted at all six positions by additional alkyl groups to enhance the solubility. Thus, while the 1-, 3-, and 5-positions of the aryl ring have methyl substituents, the 2-, 4-, and 6-positions host a methylene group to which the $–PO_3H_2$ moiety is attached. Unlike compound **H** (Scheme 1), where the mesityl ring and the phosphonate groups are in the same plane, the introduction of the flexible $–CH_2$ linker between the aromatic ring and $–PO_3H_2$ moiety in the present case could lead to different relative dispositions for the phosphonic acids on either side of the central ring. Thus for a given molecule, depending on the relative dispositions of the phosphonic acids moieties (*cis* or *trans*, for example), it is possible to recognize different supramolecular arrays. The present investigation addresses these questions, and reports the strategies used to synthesize these molecules, as well as their spectral characterization and crystal structure determination, to showcase the structural variety these molecules can offer in forming supramolecular arrays.

Results and discussion

Synthesis and characterization

To synthesize the three phosphonic acids, a general synthetic procedure was employed. Treatment of 33% HBr in CH_3COOH with mesitylene in different stoichiometric ratios under varying reaction conditions (such as duration and temperature) led to the formation of the respective benzyl bromides in a high yield.[15] The bromomesityl derivatives were subjected to the Michaelis–Arbuzov reaction with triethylphosphite in xylene. The removal of excess xylene and triethylphosphite, followed by the hydrolysis of the product by concentrated hydrochloric acid, resulted in the formation of the respective phosphonic acids **1–3** (Scheme 2). All the three new compounds have been characterized by elemental analysis, IR spectroscopy, NMR spectroscopy (^{1}H and ^{31}P), ESI-MS, diffuse-reflectance UV-vis spectroscopy, and fluorescence spectroscopy. All three compounds yielded satisfactory elemental analysis. In the case of compound **2**, although the single crystals contained lattice ethanol, the vacuum-dried sample did not show the presence of lattice ethanol in the sample. The lattice water present in the single crystals of **3**, however, was retained even after prolonged drying, and hence its elemental analysis corresponds to the formulation as found for the single crystals.

The infrared spectra (recorded as KBr discs) displayed an intense absorption at 2260 for **1**, 2239 for **2**, and 2331 cm^{-1} for **3**, corresponding to the presence of P–OH groups. The ^{31}P NMR spectra recorded in deuterated methanol show a single resonance for all the three samples (δ 28.2 for **1**, 27.14 for **2**, and 22.2 ppm for **3**). The UV-vis spectra in methanol show absorption maxima at 208–212 nm for all three compounds; likewise, there is an emission for each compound at 301–312 nm in the UV region. The solid-state UV spectrum was also studied for all the compounds in the reflectance mode.

ESI-MS studies

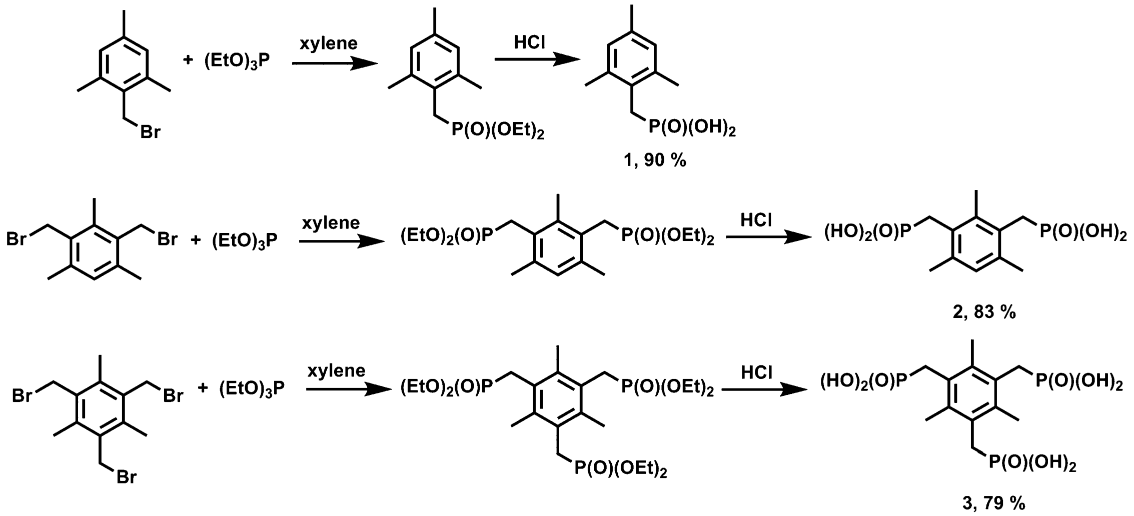
Phosphonic acids, due to the presence of polar hydrophilic $–PO_3H_2$ terminus, are known to aggregate in solution and produce discrete clusters.[16] Hence, the association behavior of all the three acids in the gas phase was examined with the help of ESI-MS studies in methanol under positive ionization mode. Interestingly, the spectra obtained not only exhibit an $(M + 1)^+$ ion peak in each case, but also contain a peak corresponding to the formation of H-bonded aggregates in solution. For example, the mesitylene mono-methylene phosphonic acid **1** displays peaks at *m*/*z* 214, 426, 642, 856 and 1070 corresponding to the aggregates $(M + 1)^+$, $(2M + 1)^+$, $(3M + 1)^+$, $(4M + 1)^+$ and $(5M + 1)^+$, respectively. Similar observations were also observed for **2** (309 $(M + 1)^+$, 616 $(2M + 1)^+$, 924 $(3M + 1)^+$) and **3** (1232 $(4M + 1)^+$. 403 $(M + 1)^+$, 804 $(2M + 1)^+$ and 1206 $(3M + 1)^+$). The spectra are shown in Fig. 1.

Determination of molecular structures

While the ESI-MS studies clearly shed light on the formation of discrete aggregates in the gas phase, we wanted to study this phenomenon further, and to this end the association behavior of these title compounds in the solid-state was explored by single-crystal X-ray diffraction studies (Table 1). The single crystals for all the three acids were grown by slow evaporation of the solvent from an appropriate solution. While the crystallization of products **1** and **3** was straightforward, compound **2** yielded poor-quality single crystals even after several attempts. It was also necessary to add small amounts of aniline to the solution of **2** during crystallization.

Crystal structure of 1

Compound **1** crystallizes in the monoclinic space group $P2_1/c$. The asymmetric part of the unit cell contains one molecule of **1** with no other lattice solvents. While all the methyl groups on



Scheme 2 Synthesis of phosphonic acids using the Michaelis–Arbuzov reaction.

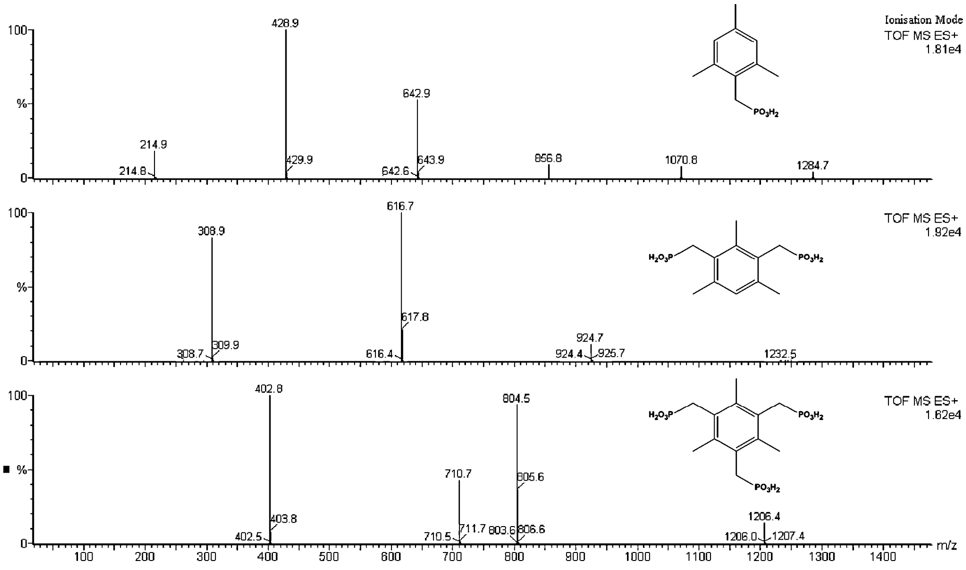


Fig. 1 Mass spectra of **1**, **2**, and **3** (the asterisks represent the aggregated molecular ion peaks).

the mesitylene ring lie in the plane of the aromatic ring, the solitary $–PO_3H_2$ group is situated above the plane of the ring (as shown in Fig. 2) due to the C–C–P angle of 116.99° at the methylene carbon. The P–C bond length found in **1** (1.758 Å) falls in the range observed for earlier reported alkylphosphonic acids.[8–12] The phosphorus atom exhibits tetrahedral geometry, with the angles varying in the range 107.4 to 114.5°. There are clearly two types of P–O distances in the molecule. While the larger distances (P1–O2 1.545 and P1–O3 1.553 Å) are associated with the P–OH bonds, the shorter one (P1–O1 1.496 Å) corresponds to the P═O phosphoryl moiety. It is pertinent to state that the acidic protons in the molecule were readily located from the difference maps and refined for the convergence of their positional parameters. Thus, in the solid state, clearly both P–O and P═O bonds exist with no significant delocalization of the protons between the three oxygen atoms on the phosphorus.

The presence of P═O and P–OH groups in **1**, like the C═O and C–OH groups in carboxylic acids, leads to an interesting hydrogen-bonded network (Table 3). For example, extensive intermolecular hydrogen bonding between the individual molecules of **1** results in the formation of a ribbon-like structure, as shown in Fig. 3. In this ribbon-like association, two rows of molecules of **1** are arranged in a head-to-head fashion, where the $–PO_3H_2$ groups come together to form a locked zipper-like structure (Fig. 3), and the three oxygen atoms of each phosphonic acid are involved in four different H-bonds (of which only two are unique O1···O2 2.568 Å, O1···O3 2.589 Å). While the phosphoryl oxygen O1 (acceptor) is involved in two hydrogen bonds, the O2 and O3 oxygen atoms (donors) form only one hydrogen bond each. Further, the mesitylene methyl ($Me_3C_6H_2CH_2$) groups on the phosphorus also associate themselves in such a way that the adjacent aryl rings along the ribbon chain are held together by a π–π stacking interaction, as shown in Fig. 3. The distance

Table 1 Crystal data and details of structure refinement for **1–3**

	1	**2**[a]	**3**
Empirical formula	$C_{10}H_{15}O_3P$	$C_{13}H_{24}O_7P_2$	$C_{12}H_{23}O_{10}P_3$
Formula weight	214.19	354.26	420.21
Crystal system	Monoclinic	Orthorhombic	Monoclinic
Space group	$P2_1/c$	$P2_12_12_1$	$P2_1/c$
Temperature (K)	150(2)	150(2)	150(2)
Wavelength (Å)	0.71073	0.71073	0.71073
Unit cell dimensions	a = 14.055(4) Å b = 4.6342(11) Å c = 16.179(4) Å β = 95.38(2)°	a = 13.687(5) Å b = 21.666(5) Å c = 7.258(5) Å —	a = 9.7623(7) Å b = 7.876(2) Å c = 10.4978(8) Å β = 107.936(9)
Volume (Å^3)	1049.2(4)	2152(2)	1743.0(3)
Z	4	4	4
Density (calculated) (Mg m^{-3})	1.356	1.093	1.601
Absorption coefficient (mm^{-3})	0.241	0.225	0.392
F(000)	456	752	880
Crystal size (mm^3)	0.32 × 0.28 × 0.24	0.31 × 0.26 × 0.22	0.40 × 0.37 × 0.31
θ range for data collection	3.03–24.9°	2.96–25.00°	3.06–24.99°
Reflections collected	8445	17 950	5382
Goodness-of-fit on F^2	0.673	0.756	1.136
Final R indices [$I > 2\sigma$(I)]	$R1$ = 0.0566, $wR2$ = 0.1112	$R1$ = 0.0977, $wR2$ = 0.2464	$R1$ = 0.0368, $wR2$ = 0.1009
R indices (all data)	$R1$ = 0.1591, $wR2$ = 0.1255	$R1$ = 0.1866, $wR2$ = 0.2652	$R1$ = 0.0465, $wR2$ = 0.1055
Largest diff. peak and hole (e Å^{-3})	0.310 and −0.312	0.508 and −0.377	0.411 and −0.462

[a] Compound **2** forms very poorly diffracting crystals.

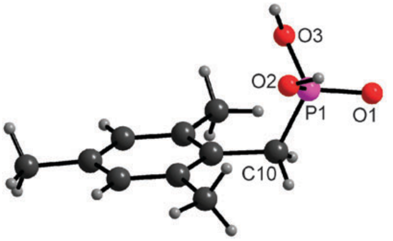


Fig. 2 Molecular structure of **1**.

Table 2 Selected bond lengths (Å) and angles (°) in **1–3**

1			
P(1)–O(1)	1.496(4)	C(1)–C(10)–P(1)	118.6(4)
P(1)–O(2)	1.545(4)	O(1)–P(1)–O(2)	114.5(2)
P(1)–O(3)	1.553(4)	O(1)–P(1)–O(3)	110.5(2)
P(1)–C(10)	1.758(5)	O(2)–P(1)–O(3)	107.4(2)
2			
P(1)–O(1)	1.500(7)	P(2)–O(4)	1.488(7)
P(1)–O(2)	1.523(7)	P(2)–O(5)	1.562(6)
P(1)–O(3)	1.520(6)	P(2)–O(6)	1.493(6)
3			
O(1)–P(1)	1.571(2)	O(2)–P(1)	1.536(2)
O(3)–P(1)	1.501(2)	O(4)–P(2)	1.575(2)
O(5)–P(2)	1.537(2)	O(6)–P(2)	1.490(2)
O(7)–P(3)	1.540(2)	O(8)–P(3)	1.553(2)
O(9)–P(3)	1.502(2)	C(7)–C(1)–P(1)	110.6(2)

between any two adjacent mesitylene rings along the chain was found to be 4.63 Å, suggesting fairly strong π–π interactions between these aromatic rings.

It would be of further interest to compare the structure of **1** with similar alkyl phosphonic acids reported in the literature. Although the parent benzyl phosphonic acid ($C_6H_5CH_2PO_3H_2$)[17] has not yet been structurally characterized, the solid-state structures of *ortho*- and *meta*-fluorobenzylphosphonic acid have been determined by single-crystal X-ray diffraction studies.[9] Both the isomers of fluorobenzylphosphonic acid organize themselves in a supramolecular architecture through weak hydrogen bonding in a pattern that is similar to that found in **1** (*i.e.* head-to-head, but with different orientations of phenyl rings). In case of fluorobenzylphosphonic acids, the adjacent phenyl rings are not involved in the side-on overlap leading to π–π interactions (as in the case of **1**), probably owing to strong F–F repulsions (in order to minimize the F–F repulsions, the adjacent rings in the lattice lie almost perpendicular to each other).[9] Similarly, the 4-vinylphosphonic acid also has weak hydrogen-bonding interactions between the phosphonic acid moieties in a head-to-head fashion, with phenyl rings not participating in any π–π interactions.[9] On the other hand, other aliphatic phosphonic acids organize themselves in a cluster or polymeric form through a weak hydrogen-bonding network. For example, cyclohexylphosphonic

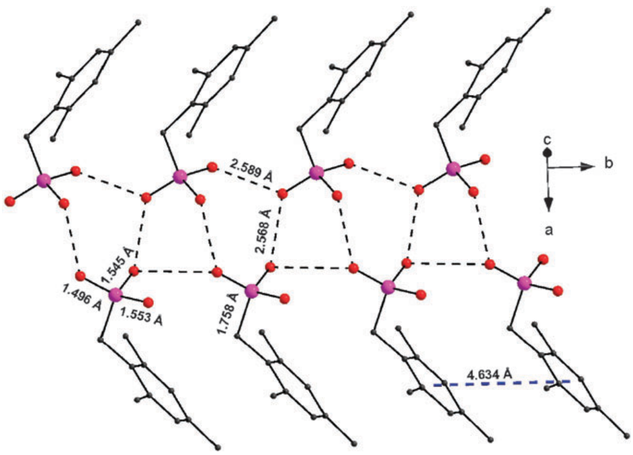


Fig. 3 Tubular association of molecules of **1** in the crystal.

Table 3 Possible O–H$\cdots$O hydrogen bonds in **1–3**

D–H$\cdots$A	**D$\cdots$A (Å)**	**H$\cdots$A (Å)**	**D–H (Å)**	**D–H$\cdots$A (°)**
Compound **1**				
O2–H(2W)$\cdots$O1^{a}	2.564(4)	1.88	0.87	134
O3–H(3W)$\cdots$O1^{b}	2.595(5)	1.77	0.87	156
Compound **2**^{i}				
O(1)$\cdots$O(5)^{c}	2.51(1)	—	—	—
O(2)$\cdots$O(4)^{d}	2.49(1)	—	—	—
O(3)$\cdots$O(6)^{c}	2.52(1)	—	—	—
Compound **3**				
O(5)–H(5)$\cdots$O(10)	2.507(2)	1.72(3)	0.79(3)	172.64(4)
O(2)–H(1)$\cdots$O(9)^{e}	2.511(2)	1.68(3)	0.86(4)	160.72(4)
O(4)–H(4)$\cdots$O(1)^{e}	2.797(3)	1.90(3)	0.92(3)	165.18(3)
O(1)–H(2)$\cdots$O(3)^{e}	2.601(3)	1.95(5)	0.65(5)	171.98(6)
O(8)–H(8)$\cdots$O(3)^{e}	2.614(2)	1.75(3)	0.86(3)	174.34(4)
O(7)–H(7)$\cdots$O(6)^{f}	2.557(2)	1.75(3)	0.84(3)	162.62(3)
O(10)–H(10A)$\cdots$O(6)^{g}	2.707(3)	1.75(5)	0.95(5)	176.60(4)
O(10)–H(10B)$\cdots$O(9)^{h}	2.729(3)	1.86(3)	0.88(3)	171.46(3)

Symmetry of the acceptor atoms:^{a} $2-x, \frac{1}{2}+y, \frac{3}{2}-z$. ^{b} $x, 1+y, z$. ^{c} $x-\frac{1}{2}, \frac{3}{2}-y, 1-z$. ^{d} $x-\frac{1}{2}, \frac{3}{2}-y, -z$. ^{e} $2-x, -y, 1-z$. ^{f} $1+x, \frac{1}{2}-y, \frac{1}{2}+z$. ^{g} $x, \frac{1}{2}-y, z-\frac{1}{2}$. ^{h} $x-1, \frac{1}{2}-y, z-\frac{1}{2}$. ^{i} Hydrogen atoms attached to PO_3 groups were not fixed.

acid[18] forms a zig-zag polymeric chain like structure while *tert*-butylphosphonic acid[16] forms a cluster-like assembly, although a polymeric association is also known.

Crystal structure of 2

Growing single crystals of mesitylene-bis(methylene)phosphonic acid **2** proved far more difficult. In a successful attempt, compound **2** was crystallized by dissolving the white powder of **2** in dimethylformamide and carefully layering the resultant solution with aniline. After two months, colorless prisms of **2** were obtained, which were later found to have crystallized in the orthorhombic non-centrosymmetric $P2_12_12_1$ space group with considerable twinning. The asymmetric part of the unit cell contains one molecule of **2** along with a molecule of ethanol. In the monomeric form of compound **2**, the two methylene phosphonic acid moieties are situated on the same side of the aromatic ring in such a way that the $–PO_3H_2$ groups (*syn*) and the central aromatic ring are perpendicular to each other (Fig. 4). The *cis* arrangement of the two phosphonic acid groups is somewhat surprising due to the fact that in the *anti* arrangement the system could have avoided the steric crowding. However, it appears that the supramolecular structure formation (*vide infra*) is the driving force for the formation of *syn* configuration. These two phosphonic acid arms make slightly different angles at the methylene carbon atoms (C(6)–C(11)–P(1) 115.3°; C(4)–C(9)–P(2) 115.9°) and are almost parallel to each other (Fig. 4) (torsion angle of 3.33° between the two $–PO_3H_2$ arms) (Table 2). The phosphorus atom is in a slightly distorted tetrahedral geometry, with angles of 110 to 113.7°.

The *syn* and parallel orientations of the two $–PO_3H_2$ groups on the mesitylene ring renders an approximate '⊔' shape for **2**, with P–O termini at the open ends. Arranging these '⊔'-shaped objects in the normal and inverted forms alternately with a periodic shift as shown in Fig. 5 (top) leads to the formation of a wavelike hydrogen-bonded one-dimensional chain (Table 3).

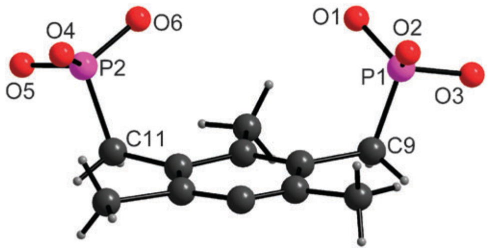


Fig. 4 Molecular structure of **2**.

The three oxygen atoms and two protons on each of the phosphorus termini are further used as 'glue' to connect the one-dimensional wave-like chains to a two-dimensional sheet with the original wave-like surface (Fig. 5). This type of stepwise of aggregation in **2** generated from atomic coordinates is shown in Fig. 6. The schematic representation at the bottom of Fig. 6 further illustrates that the two-dimensional wave-like sheets are stacked in such as way that there is strong aromatic π–π interactions between the mesitylene rings of adjacent layers.

A closer look at the types of interactions responsible for the supramolecular 2-D sheet formation reveals that there are three unique hydrogen bonds originating from each molecule of **2** (O1$\cdots$O5 2.52 Å, O2$\cdots$O4 2.49 Å and O3$\cdots$O6 2.52 Å) (Fig. 5). Due to the poor quality of the diffraction data and the absence of any marked difference between the three P–O distances on each of the two phosphonic acid groups, no attempt has been made either to identify the P–OH hydrogen atoms from the difference map or geometrically fix them. Hence, the hydrogen bonding pattern has been derived from D$\cdots$A (O$\cdots$O) distances only. Unlike in **1**, each oxygen atom in **2** is involved in only one hydrogen bond with the neighboring acceptor atom. In the final structure, each molecule of **2** is surrounded by six other neighbors, with the aryl–aryl ring distances varying from 7.258 Å to 11.246 Å.

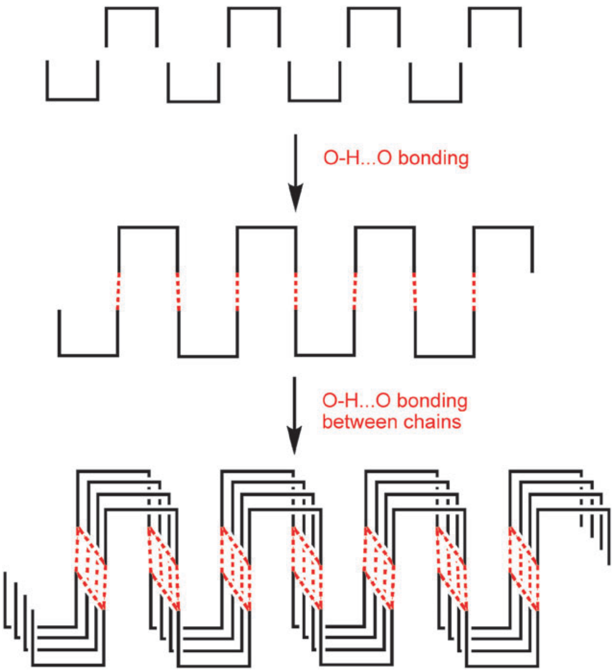


Fig. 5 Schematic representation of the supramolecular assembly in **2**.

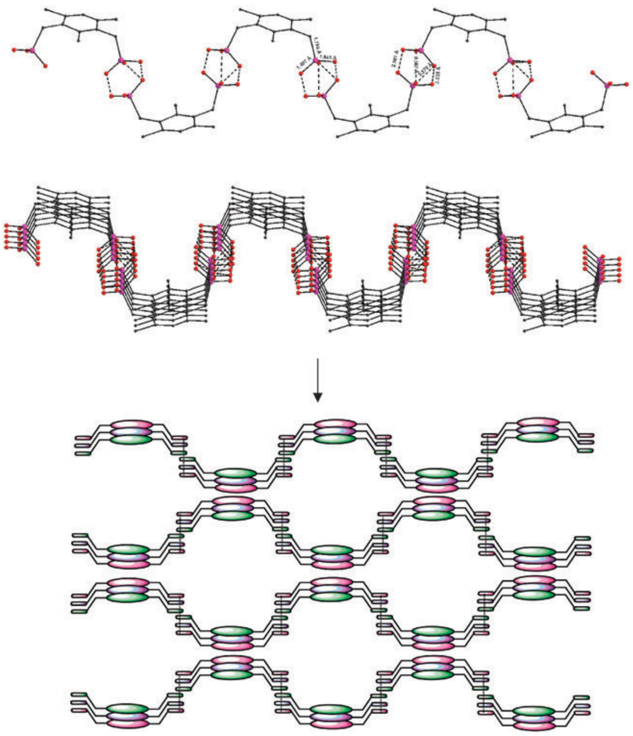


Fig. 6 Evolution of face-on stacked 2-D sheets arrangement in the crystals of **2**.

Crystal structure of 3

Suitable crystals for single-crystal X-ray analysis were grown by dissolving the crude sample of **3** in methanol, carefully layering diethyl ether on it, and keeping the solution at 5 °C. After ten days, well formed crystals started to separate from mother liquor. Compound **3** crystallizes in the monoclinic crystal system in the $P2_1/c$ space group as the monohydrate. The final refined structure is depicted in Fig. 7.

The three $-PO_3H_2$ groups on **3** are placed on the same side of the mesitylene ring, and hence the molecular structure of **3** resembles that of an open bowl (which can also be described as a W-form or *cis–cis–cis* form) (Scheme 3).[19–23] This arrangement, where the functional hydrophobic PO_3H_2 groups constitute the rim of bowl and the aryl ring forms the flat base, is the preferred structural form for a mesitylene ring bearing three $-CH_2X$ groups (X = SO_3H,[19] 1-phenyl-1*H*-tetrazol-5-ylsulfanyl,[20] OH,[21] 2-isopropylphenol,[22] and Br[23]) on the 2-, 4-, and 6-positions of the aryl ring. The tetrahedral C(7)–C(1)–P(1), C(9)–C(3)–P(2), and C(11)–C(5)–P(3) angles (110.64°, 115.10° and 114.30°) at the methylene carbon atoms and the associated torsional angles further testify to the bowl shape of the molecule. In contrast, in the case of 1,3,5-benzene-triphosphonic acid, all the three $-PO_3H_2$ groups and the benzene ring lie in the same plane.[16,18] Further, unlike in the monoacid **1** and the diacid **2**, in **3** there is no effective π–π stacking between the mesitylene rings (the shortest distance between any two adjacent aryl rings is 10.4 Å).

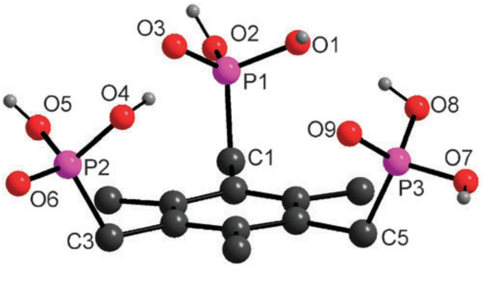
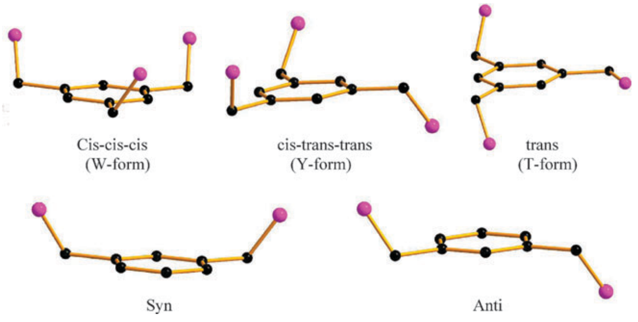


Fig. 7 Molecular structure of **3**.



Scheme 3 Possible conformations for the diacid and triacid.

The presence of six P–OH protons and three P=O groups on the rim of the bowl-shaped **3** leads to an extensive association of the molecules through a H-bonding network. The construction of the final observed supramolecular structure in **3** is shown in Fig. 8. The polar heads at the rim of two molecules of **3** come face-to-face, as shown in Fig. 8b, to form a dimeric structure, in which all six phosphonic acid groups interact with each other through short O–H···O hydrogen bonds. These dimeric structures are connected to each other by the lattice water molecules as well as additional O–H···O interactions involving phosphonic acid moieties, leading to successive formation of a 1-D polymeric chain (Fig. 8c), a two-dimensional sheet (Fig. 8d) and finally a three-dimensional framework structure (Fig. 8e). In the entire structure, the adjacent molecules of **3** are inverted with respect to each other so that the polar groups can aggregate together by hydrogen-bonding interactions, whereas the non-polar aromatic rings can stack one over other with the aid of π-interactions. The structure of **3** consists of seven unique hydrogen bonds, five of which involve phosphoric moieties alone as donor and acceptors. The lattice water takes part in the additional two hydrogen bonds. One can thus conclude that the preference for the bowl-shaped *cis*,*cis*,*cis*-conformation for **3** (the W-form) over the other isomeric forms depicted in Scheme 3 is primarily due to the ability of the triacid to engage itself in the maximum number of supramolecular interactions in this conformation (thirteen hydrogen bonds emanating from each molecule of **3** and three hydrogen bonds emanating from each lattice water molecule) (Table 3).

Conclusions

We have shown in this contribution that even a simple aromatic hydrocarbon such as mesitylene can be used a platform for hosting multiple phosphonic acid groups through a series of simple organic transformations (Scheme 1). The mono-, di-, and trimethylene bromides on the mesitylene readily undergo Michaelis–Arbuzov reactions to yield the respective phosphonate esters in high yields, and the acid hydrolysis yields the free phosphonic acids in each case.

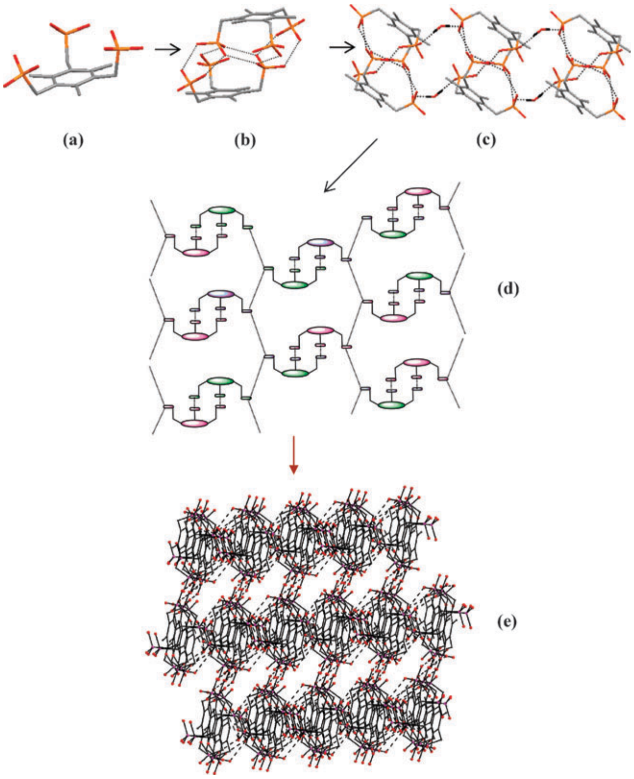


Fig. 8 Evolution of the 3-D supramolecular structure in **3**.

Despite difficulties, it was possible to isolate the mono-, di-, and triphosphonic acids as single crystals. The structure determination in the solid-state for all the three derivatives has revealed valuable information regarding the conformational preferences of these molecules, as well as their ability to associate in the solid state to form supramolecular structural motifs. Interestingly, when only one –$CH_2PO_3H_2$ group is present on the aryl ring, a one dimensional tubular aggregation of molecules of **1** is observed. The presence of two –$CH_2PO_3H_2$ groups in **2** leads to the expansion of the structural motif to the second dimension, yielding a wave-like association. The bowl-shaped molecule **3**, which contains three –$CH_2PO_3H_2$ groups on the aryl ring, maximizes the number of H-bonding interactions in the system and yields a perfect three-dimensional supramolecular structure. Thus, the present study clearly shows a direct correlation between the dimensionality and the number of acid groups present. Finally, apart from the interest in these molecules as supramolecular synthons to construct new structural motifs, the presence of a large number of acidic protons makes them ideal candidates as ligands in metal phosphonate chemistry to realize newer cages and layered solids. We are currently investigating these aspects.

Experimental section

Instruments and methods

All the starting materials and the products were found to be stable towards moisture and air. Hence, no specific precautions were taken to rigorously exclude air during the manipulation of the compounds. Solvents were purified by employing conventional procedures and were distilled prior to their use.[24] Commercially available starting materials such as 33% HBr in acetic acid (Spectrochem), paraformaldehyde (S.d. Fine), Xylene (S.d. Fine), mesitylene (Aldrich) and triethylphosphite (Aldrich) were used as received. Mono-(bromomethyl)mesitylene, di(bromomethyl)mesitylene and tri(bromomethyl)mesitylene) were synthesized using a previously described literature method.[15] The conversion of bromo derivatives to the corresponding diethyl phosphonate esters was carried out as described previously by a Michaelis–Arbuzov reaction involving the alkyl bromide and triethyl phosphite.[25]

Infrared spectra were obtained on a Perkin Elmer Spectrum One FT-IR spectrometer as KBr diluted discs. The ^1H and ^{31}P NMR spectra were recorded on a Varian 300 and 400 MHz instrument using Me_4Si as an internal reference for the ^1H NMR spectra. The melting points were measured in glass capillaries and are reported uncorrected. The ESI mass spectra were recorded on Micromass Q-Tof spectrometer. Microanalyses were performed on a Thermo Finnigan (FLASH EA 1112) microanalyzer. UV-vis spectra (both in solid and solution) were obtained on a Shimadzu UV-260 spectrophotometer and the fluorescence spectral measurements were carried out on a Perkin Elmer LS-55 luminescence spectrometer.

Synthesis of mesityl-1-methylenephosphonic acid (1)

Mesityl-1-methylene-bis(ethylphosphonate) was heated under reflux in excess concentrated hydrochloric acid for 24 h. During this time a white powder started to precipitate, which was filtered off, and washed with cold water followed by petroleum ether, and air-dried. Recrystallization from methanol and diffusion with dichloromethane resulted in colorless crystals. Yield 90%. M.p. >250 °C. Anal. Calcd. for $C_{10}H_{15}O_3P$: C, 56.07; H, 7.06. Found: C, 56.30; H, 7.08. Selected IR frequencies (as KBr diluted disc): 3416(s), 2922(s), 2660 (w), 1614(s), 1259(s), 1046(s), 859(s), 581(m), 489(s). m/z = 215.0 $(M + 1)^+$. ^1H NMR (400 MHz, δ/ppm, MeOH-d_4): 6.72 (s, 2H, Ar–H), 3.1 (d, 2H, –CH_2–PO_3H_2, J = 21.84 Hz), 2.25 (s, 6H, Ar–CH_3), 3.5 (s, 3H, Ar–CH_3). ^{31}P NMR (400 MHz, δ/ppm, MeOH-d_4): 28.20. UV-vis (methanol, ε/nm): 208.6 (20 860). DR-UV: 276.5, 471.7. Fluorescence (nm): 212.6 ($\lambda_{\text{excitation}}$), 301.3 ($\lambda_{\text{emission}}$).

Synthesis of mesityl-1,3-bis(methylenephosphonic acid) (2)

Mesityl-1,3-bis(methylene-bis(ethylphosphonate)) was boiled with aqueous concentrated hydrochloric acid for 15 h under reflux. During this period a white solid separated out, and this was filtered off, washed with water, and air-dried. A small fraction of the compound was recrystallized from dimethylformamide. Yield 83%. M.p. >240 °C. Anal. Calcd. for $C_{11}H_{18}O_6P_2$: C, 42.87; H, 5.89. Found: C, 42.21; H, 5.12. Selected IR frequencies (as KBr diluted disc): 3419(s), 2239(s), 1540(s), 1452(s), 1232(s), 1052(s), 931(s), 804(s), 720(s), 620(s), 544(s). m/z = 309.0 $(M + 1)^+$. ^1H NMR (400 MHz, δ/ppm, MeOH-d_4): 7.0 (s, 1H, Ar–H), 3.3 (d, 4H, –CH_2–PO_3H_2, J = 21.84 Hz), 2.36 (s, 3H, Ar–CH_3), 2.31 (s, 3H, Ar–CH_3). ^{31}P NMR (400 MHz, δ/ppm, MeOH-d_4): 27.14. UV-vis (methanol, ε/nm): 212 (21 200). DR-UV: 274.8, 461.8. Fluorescence (nm): 271.5 ($\lambda_{\text{excitation}}$), 312.4 ($\lambda_{\text{emission}}$).

Synthesis of mesityl-1,3,5-tris(methylenephosphonic acid) (3)

A mixture of phosphonate ester and excess concentrated hydrochloric acid was heated under reflux for 30 h, and the solution cooled to room temperature. Removal of solvent under vacuum resulted in an off-white solid, which was recrystallized from methanol by layering of diethyl ether. Colorless crystals formed after 5 days, and these were collected by filtration and washed with cooled methanol. Yield 79%. M.p. >280 °C. Anal. Calcd. for $C_{12}H_{21}O_9P_3$: C, 35.83; H, 5.26. Found: C, 34.35; H, 5.25. Selected IR frequencies (as KBr diluted disc): 3300(s), 2331(s), 1421(s), 1262(s), 1190(s), 1137(s), 993(s), 958(s), 747(s), 520(s), 552(s). m/z = 403.0 $(M + 1)^+$. ^1H NMR (400 MHz, δ/ppm, DMSO-d_6): 3.26 (d, 6H, $-CH_2-PO_3H_2$, J = 21.06 Hz), 2.51 (s, 9H, Ar–CH_3). ^{31}P NMR (400 MHz, δ/ppm, DMSO-d_6): 22.2. UV-vis (methanol, ε/nm): 208.4 (208 400). DR-UV: 278.6, 513.7. Fluorescence (nm): 213.2 ($\lambda_{excitation}$), 308 ($\lambda_{emission}$).

Single-crystal X-ray diffraction studies

Intensity data for **1–3** were collected on an Oxford Xcalibur CCD diffractometer operating at 150 K. All calculations were carried out using the programs in WinGX module.[26] The structure was solved in each case by direct methods (SIR-92).[27] The final refinement of the structure was carried out using full least-squares methods on F^2 using SHELXL-97.[28] The hydrogen atoms in case of **1** and **2** were placed in geometrically calculated positions (obtaining the torsional angles from electron density) and were refined using a riding model. No attempts were made fix the hydrogen atoms attached to oxygen atoms in **2** due to the poor quality of the data and the inability to distinguish P=O from P–OH groups on P1 and P2. In the case of **3**, all the hydrogen atoms attached to carbon atoms were fixed as above. However, the hydrogen atoms attached to oxygen centres in **3** were located from the difference maps and refined with individual isotropic displacement parameters.

In the case of **2**, the quality of the data obtained was very poor (even with repeated data collection from different crystals) which was due to the poor quality of the single crystals themselves. Hence the refinement of the structure of **2** did not converge to low R or wR_2 values. Selected crystal data are presented in Table 1 and detailed crystallographic data for all the structures are provided in the ESI†.

Acknowledgements

This work was supported by DST, New Delhi. M.P.S. thanks UGC, New Delhi, for a research fellowship. We thank the DST-funded National Single Crystal Diffraction Facility at IIT-Bombay for the diffraction data and the SAIF, IIT-Bombay for the spectral data.

References

1 (*a*) G. R. Desiraju, *Crystal Engineering: The Design of Organic Solids*, Elsevier, Amsterdam, 1989; (*b*) F. Vogtle, *Supramolecular Chemistry*, Wiley, Chichester, 1991; (*c*) J.-M. Lehn, *Supramolecular Chemistry: Concepts and Perspectives*, VCH, New York, 1995.

2 (*a*) N. L. Rosi, J. Eckert, M. Eddaoudi, D. T. Vodak, J. Kim, M. OKeeffe and O. M. Yaghi, *Science*, 2003, **300**, 1127; (*b*) J. Yang, J.-F. Ma, Y.-Y. Liu, J.-C. Ma and S. R. Batten, *Cryst. Growth Des.*, 2008, **8**, 4383; (*c*) A. Comotti, S. Bracco, P. Sozzani, S. Horike, R. Matsuda, J. Chen, M. Takata, Y. Kubota and S. Kitagawa, *J. Am. Chem. Soc.*, 2008, **130**, 13664; (*d*) E. Dugan, Z. Wang, M. Okamura, A. Medina and S. M. Cohen, *Chem. Commun.*, 2008, 3366.

3 (*a*) F. H. Herbstein and M. Kapon, *Acta Crystallogr., Sect. B: Struct. Crystallogr. Cryst. Chem.*, 1979, **35**, 1614; (*b*) O. Ermer, *J. Am. Chem. Soc.*, 1988, **110**, 3747; (*c*) S. V. Kolotuchin, E. E. Fenlon, S. R. Wilson, C. J. Loweth and S. C. Zimmerman, *Angew. Chem., Int. Ed. Engl.*, 1996, **34**, 2654; (*d*) K. Biradha, D. Dennis, V. A. MacKinnon, C. V. K. Sharma and M. J. Zaworotko, *J. Am. Chem. Soc.*, 1998, **120**, 11894; (*e*) S. V. Kolotuchin, P. A. Thiessen, E. E. Fenlon, S. R. Wilson, C. J. Loweth and S. C. Zimmerman, *Chem. Eur. J.*, 1999, **5**, 2537; (*f*) S. E. Dale, M. R. J. Elsegood and S. J. Richards, *Chem. Commun.*, 2004, 1278.

4 (*a*) Y. Ogata, M. Tsuchida and A. Muramot, *J. Am. Chem. Soc.*, 1957, **79**, 6005; (*b*) K. Tsugunori, K. Kiyoshi, M. Sadayuki and S. Nobuyuki, *Chem. Lett.*, 1986, **3**, 299; (*c*) S. B. Choi, M. J. Seo, M. Cho, Y. Kim, M. K. Jin, D.-Y. Jung, J.-S. Choi, W.-S. Ahn, J. L. C. Rowsell and J. Kim, *Cryst. Growth Des.*, 2007, **7**, 2290.

5 (*a*) K. Maeda, *Microporous Mesoporous Mater.*, 2004, **73**, 47; (*b*) J. M. Taylor, A. Mahmoudkhani and G. K. H. Shimizu, *Angew. Chem., Int. Ed.*, 2007, **46**, 795; (*c*) R. C. Finn, E. Burkholder and J. Zubieta, *Chem. Commun.*, 2001, 1852; (*d*) P. Yin, L.-M. Zheng, S. Gaob and X.-Q. Xina, *Chem. Commun.*, 2001, 2346; (*e*) D. Kong, Y. Li, J. H. Ross Jr and A. Clearfield, *Chem. Commun.*, 2003, 1720.

6 (*a*) A. Clearfield, Metal Phosphonate Chemistry, *Progress in Inorganic Chemistry*, ed. K. D. Karlin, John Wiley & Sons, New York, 1998, vol. 47, pp. 371–510 and references therein; (*b*) G. Alberti, in *Comprehensive Supramolecular Chemistry*, ed. J. M. Lehn, Pergamon-Elsevier Science, Oxford, UK, 1996, vol. 7; (*c*) G. Cao, H. Hong and T. E. Mallouk, *Acc. Chem. Res.*, 1992, **25**, 420; (*d*) A. Clearfield, *Inorganic Ion Exchange Material*, CRC press, Boca Raton, Florida, 1982; (*e*) G. Alberti, *Acc. Chem. Res.*, 1978, **11**, 163; (*f*) J. D. Wand, A. Clearfield and G.-J. Peng, *Mater. Chem. Phys.*, 1993, **35**, 208; (*g*) F. Fredoueil, D. Massiot, P. Janvier, F. Gingl, M. Bujoli-Doeuff, M. Evain and A. Clearfield, *Inorg. Chem.*, 1999, **38**, 1831; (*h*) G. Cao, V. M. Lynch and L. N. Yacullo, *Chem. Mater.*, 1993, **7**, 583.

7 (*a*) G. Próchniak, J. Zon, M. Daszkiewicz, A. Pietraszko and A. Videnova-Adrabinska, *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.*, 2007, **63**(7), o434; (*b*) S. Konar, J. Zon, A. V. Prosvirin, K. R. Dunbar and A. Clearfield, *Inorg. Chem.*, 2007, **46**, 5229; (*c*) D. Kong, J. Zon, J. McBee and A. Clearfield, *Inorg. Chem.*, 2006, **45**, 977; (*d*) J. Beckmann, R. Ruttinger and T. Schwich, *Cryst. Growth Des.*, 2008, **8**, 3271.

8 G. Ferguson, J. F. Gallagher, W. Vogt, J. Phillips and G. J. B. Williams, *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.*, 1993, **49**, 1024.

9 K. J. Langley, P. J. Squattrito, F. Adani and E. Montoneri, *Inorg. Chim. Acta*, 1996, **253**, 77.

10 S. Gardner, M. Motevalli, K. Shastri, A. C. Sullivan and P. B. Wyatt, *New J. Chem.*, 2002, **26**, 433.

11 M. Lecouvey, C. Barbey, A. Navaza, A. Neuman and T. Prange, *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.*, 2002, **58**, o521.

12 R. Frantz, J.-O. Durand, F. Carre, G. F. Lanneau, J. L. Bideau, B. Alonso and D. Massiot, *Chem. Eur. J.*, 2003, **9**, 770.

13 (*a*) R. Murugavel and S. Shanmugan, *Chem. Commun.*, 2007, 1257; (*b*) R. Murugavel and S. Shanmugan, *Dalton Trans.*, 2008, 5358; (*c*) R. Murugavel and M. P. Singh, *Inorg. Chem.*, 2006, **45**, 9154.

14 (*a*) R. Murugavel and S. Kuppuswamy, *Angew. Chem., Int. Ed.*, 2006, **45**, 7022; (*b*) R. Murugavel, S. Kuppuswamy, R. Boomishankar and A. Steiner, *Angew. Chem., Int. Ed.*, 2006, **45**, 5536; (*c*) R. Murugavel and S. Kuppuswamy, *Chem. Eur. J.*, 2008, **14**, 3869; (*d*) R. Murugavel, S. Shanmugan and S. Kuppuswamy, *Eur. J. Inorg. Chem.*, 2008, 1508; (*e*) R. Murugavel and S. Shanmugan, *Organometallics*, 2008, **27**, 2784; (*f*) R. Murugavel, S. Kuppuswamy and S. Randoll, *Inorg. Chem.*, 2008, **47**, 6028; (*g*) R. Murugavel and S. Kuppuswamy, *Inorg. Chem.*, 2008, **47**, 7686.

15 A. W. Made and R. H. Made, *J. Org. Chem.*, 1993, **58**, 1262.

16 M. Mehring, M. Schurmann and R. Ludwig, *Chem. Eur. J.*, 2003, **9**, 837.
17 N. Gauvry and J. Mortier, *Synthesis*, 2001, 553.
18 K. Merz and A. Knuefer, *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.*, 2002, **58**, o187.
19 S. A. Dalrymple, M. Parvez and G. K. H. Shimizu, *Chem. Commun.*, 2001, 2672.
20 W. Wei, P. N. Ning and Z. Bing, *Acta Crystallogr., Sect. E: Struct. Rep. Online*, 2006, **62**, o603.
21 W. Bell, P. I. Coupar, G. Ferguson and C. Glidewell, *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.*, 1996, **52**, 2520.
22 D. Oezlem, I. Samil, A. Nesuhi, K. Cihan and A. Erbil, *Acta Crystallogr., Sect. E: Struct. Rep. Online*, 2005, **61**, o1724.
23 P. Murray, C. Willans, M. W. Bredenkamp and J.-A. Gertenbach, *Acta Crystallogr., Sect. E: Struct. Rep. Online*, 2006, **63**, o224.
24 *Vogel's Textbook of Practical Organic Chemistry*, Langman Group, Essex, Harlow, UK, 5th edn, 1989.
25 (*a*) G. Tchani, G. Baziard-Mouysset, S. Younes, J. Bellan, M. Payard, J. L. Stigliani, G. Grassy, R. Bonnafous and J. Tisne-Versailles, *Eur. J. Med. Chem.*, 1992, **27**, 845; (*b*) M. Ranasinghe, P. Murphy, Z. Lu, S. D. Huang, R. J. Twieg and T. Goodson III, *Chem. Phys. Lett.*, 2004, **383**, 411; (*c*) J. Fawcett, A. W. G. Platt and S. Vickers, *Polyhedron*, 2003, **22**, 1431; (*d*) N. A. Caplan, C. I. Pogson, D. J. Hayes and G. M. Blackburn, *J. Chem. Soc., Perkin Trans. 1*, 2000, 421.
26 WinGXL. J. Farrugia, *J. Appl. Crystallogr.*, 1999, **32**, 837.
27 A. Altomare, G. Cascarano, C. Giacovazzo and Z. Gualardi, *J. Appl. Crystallogr.*, 1993, **26**, 343.
28 G. M. Sheldrick, *SHELXL-97 Program for Structure Refinement*, University of Göttingen, Germany, 1997.