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ARTICLE

2,6-Dimethylphenol derived H-phosphonate and α-hydroxyphosphonate: Facile synthesis, crystal chemistry, supramolecular association and metal complexation

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Sazzat Hossain,[§] Sandeep K. Gupta[§] and Ramaswamy Murugavel*

Facile synthesis of a H-phosphonate [(ArO)P(O)H(OH)] (**2**) and a α-hydroxyarylphosphonate [(ArO)P(O)(OH)(CMe_2OH)] (**3**) has been achieved throguh the hydrolysis of [(ArO)PCl_2] (**1**) in either toluene or acetone as the solvent, respectively. The dichlorie **1** iteself was synthesiszed from a reaction of ArOH (Ar = 2,6-$Me_2C_6H_3$O) with phosphorous trichloride. The unstable H-phosphonate **1** and the three different crystalline modifications of the aryl α-hydroxyphosphonate **2** (viz., ansolvate, solvate and hydrate) have been crystallized under different crystallization conditions and their molecular structures have been determined by singe crystal X-ray diffraction studies. These fours crystalline forms exhibit either two-dimensional sheet-like polymeric structures or tubular structures with water channels, assisted by supramolecular interactions such as H-bonding, CH-π, etc. Crystallisation of the α-hydroxyarylphosphonate (**3**) from a warm dimethylformamide solution leads to the ready decomposition of the solvent to dimethylammonium cation to yield the salt of **3**, [Me_2NH_2][(ArO)(CMe_2OH)POO)] (**6**). Reactivity of the α-hydroxyarylphosphonate **1** with metal acetates has been investigated and its copper and zinc complexes [M(HL)$_2$(2,2′-bpy)(H_2O)](H_2O) (M = Cu (**7**); Zn(**8**) (HL = [(ArO)P(O)(O)(CMe_2OH)]$^-$) have been isolated and structurally characterized. Mononuclear **7** and **8** form linear polymeric chains assisted by intermolecular H-bonding interactions involving a large number of proton donor and acceptor sites present in these complexes.

Introduction

Organophosphonates are an interesting class of structurally diverse organophosphorous compounds, which possess a very stable C-P bond and are ubiquitous both in materials and biological chemistry. For last several decades, they have been considered as very useful ligands in the field of synthetic inorganic and material chemistry for the synthesis of zeolitic secondary building units, discrete metal complexes, and open frameworks and microporous structures with promising applications.[1] Research on organophosphonates garnered further interest in medicinal and biological chemistry because of their enzyme inhibitor and anti-cancer activity.[2] Apart from the diverse industrial applications of phosphonates themselves, metal-phosphonates also display a multitude of industrial applications in areas such as ion exchange,[3] gas adsorption and separation,[4] proton conductivity,[5] stereoselective catalysis,[6] photochemistry,[7] and chemical reagents in a number of synthetic organic chemistry applications[8]. Many methods have been employed in the literature for the synthesis of phosphonates via the formation of C-P bond such as Abramov, Pudovic, Michaelis-Becker and Michaelis-Arbuzov reactions and the catalytic cross coupling reactions, of which the widely used is Arbuzov reaction.[9] Recently the synthesis of H-phosphonate and α-hydroxyphosphonate has particularly garnered much attention, because as compared to the esters of phosphoric acid, H-phosphonates contain a very reactive *P-H* linkage with rich chemistry which can be transformed into a number of biologically active functional derivatives such as α-aminophosphonic acids, bisphosphonates, nucleoside H-phosphonates, poly(alkylene H-phosphonate)s etc. under mild conditions.[10] Further, analogous to β-amino-α-hydroxyphosphonic acids, α-hydroxyphosphonates also act as inhibitors of enzymes such as renin, HIV protease and polymerase.[11] The synthesis of α-hydroxyphosphonate is usually carried out by the hydrophosphonylation reaction where the electron rich phosphorous compound undergoes nucleophilic addition to the carbonyl carbon.[12] Various reaction conditions and catalysts, both in stoichiometric and non-stoichiometric ratio have been used for carrying out this transformation. Catalysts are usually organic or inorganic bases or acids, although metal catalyst such as Ti(O^iPr)$_4$ and various organometallic lanthanide complexes have also been recently employed for the transformation.[13]

Due to the presence of donor acidic hydroxyl groups and the acceptor P=O moiety, H-phosphonate and α-

§ equal contribution

Department of Chemistry, Indian Institute of Technology Bombay, Mumbai 400 076, India. E-mail: naresh@chem.iitb.ac.in, rmv@chem.iitb.ac.in

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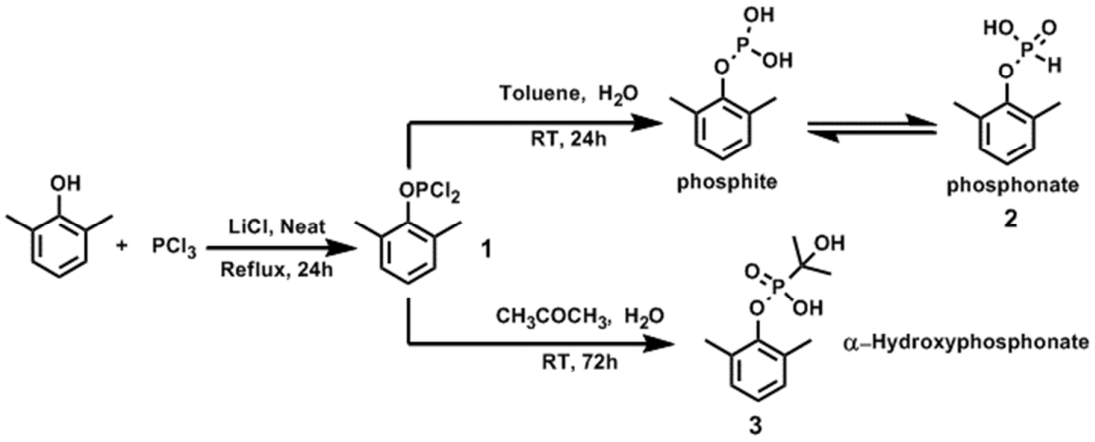


Scheme 1. Synthetic route to H-phosphonate (**2**) and α-hydroxyarylphosphonate (**3**).

hydroxyphosphonate have the ability to exhibit self-association through strong or weak supramolecular interactions such as hydrogen bonds and form aggregates as displayed by tert-butylphosphonic acid in the solid state structures depending on the solvent used for crystallisation.[14] Depending on the nature and donor or acceptor property of the solvent molecule, they participate in different supramolecular interactions with the molecule of interest resulting in the formation of solvates. Further, the intermolecular H-bonds play an important role in stabilizing the organic molecules by forming aggregates as small as dimers to polymers, macrocycles and polymolecular aggregates extending into one, two or three dimensions.[15] These supramolecular interactions are not only important from a structural point of view but they also lead to different crystalline forms depending on various factors such as solvent of crystallisation, temperature, pressure, nature of the constituents units, additives used and impurities present, crystal seed, method of crystallisation etc. giving rise to polymorphism.[16] Recently we reported the pseudo-polymorphism exhibited by 4-amino-2,6-diisopropylphenyl phosphate showing single crystal to single crystal transformation of the porous structures assisted by hydrogen bonds.[17] Polymorphism is an important aspect in the pharmaceutical industry which enables better understanding of the relation between supramolecular structures with the properties displayed by the polymorphs as different polymorphs display different properties as solubility, stability, bioavailability leading to different drug bioactivity of the active pharmaceutical ingredients (APIs).[18]

Further, as organophosph-onates/ates have been widely investigated for the formation of zeolite secondary building units and synthesis of polynuclear complexes of main group, transition and lanthanides metal ions showing varying properties, α-hydroxyphosphonate has the potential to serve as a ligand for synthesizing metal complexes with new structural topologies due to the presence of new functional alcoholic hydroxyl groups.[1,19-21] Also varying the nature of the ketone or aldehyde group used in the synthesis of the ligand can provide variation in the steric effect leading to different topologies.

In the present study, we report the synthesis of a H-phosphonate and three forms of a α- hydroxyarylphosphonate with solid state structures showing their self-association via supramolecular interactions. The coordination chemistry of the α- hydroxyarylphosphonate has also been investigated.

Results and discussion

Phosphonates 2 and 3: In view of the interesting supramolecular architectures encountered in the solid state structures of molecular systems with free *P-OH* groups and the structural variations produced by the metal complexes depending on the ligand architecture, a arylhydrogenphosphonate, [(ArO)P(O)H(OH)] (**2**) and a α-hydroxyarylphosphonate, [(ArO)P(O)(OH)(CMe_2OH)] (**3**), with active free *P=O*, *–PH, -P-OH* and *–C-OH* groups have been synthesized using a Mannich type condensation procedure.[22] The treatment of 2,6-dimethylphenol with excess phosphorous trichloride under reflux condition using lithium chloride as catalyst yields dichloro(2,6-dimethylphenoxy)phosphine (**1**) as the sole product in a nearly quantitative yield. The product was purified by vacuum distillation under inert atmosphere and used for further reactions. The hydrolysis of the phosphine **1** with two equivalents of water in dry toluene under inert atmosphere leads to the formation of 2,6-dimethylphenyl hydrogen phosphonate **2** via the intermediate formation of 2,6-dimethylphenyl dihydrogen phosphite. However when aqueous acetone was used as the solvent for the hydrolysis of **1**, 2,6-dimethylphenyl hydrogen 2-hydroxypropan-2-yl phosphonate **3** was isolated. The phosphonates **2** and **3** were purified by crystallization from toluene and characterized by both spectroscopic techniques and analytical methods. The solid-state structures of **2** and **3** have been determined using single crystal X-ray diffraction studies.

The presence of a broad peak at 2259 cm^{-1} in the FTIR spectrum of compound **2** clearly indicates the presence of P-OH group whereas the absorption at 2461 cm^{-1} corresponds to the P-H stretching vibration. The characteristic signature for the P=O bond appears at 1179 cm^{-1}, whereas the peaks at 1092 cm^{-1} and 943 cm^{-1} correspond to the symmetric and anti-symmetric P-O-C stretching vibration. The formation of compound **2** is further supported by the presence of a proton

coupled doublet appearing in the ^{31}P NMR spectrum of compound **2** with the peak position at δ 6.52 and 2.06 ppm corresponding to the one bond ^{31}P-^{1}H spin-spin coupling ($^{1}J(^{31}P,^{1}H)$ = 720.1 Hz) (Fig. 1). In the ^{1}H NMR spectrum, the resonance due to the P-*H* proton appears as a doublet due to the one bond P-H coupling at δ 7.75 and 6.31 ppm; the P-O*H* signal appears at δ 11.56 ppm. The compound has further been characterized by the presence of a peak at m/e 187.0518 corresponding to the $[M+1]^{+}$ ion in the ESI-HRMS.

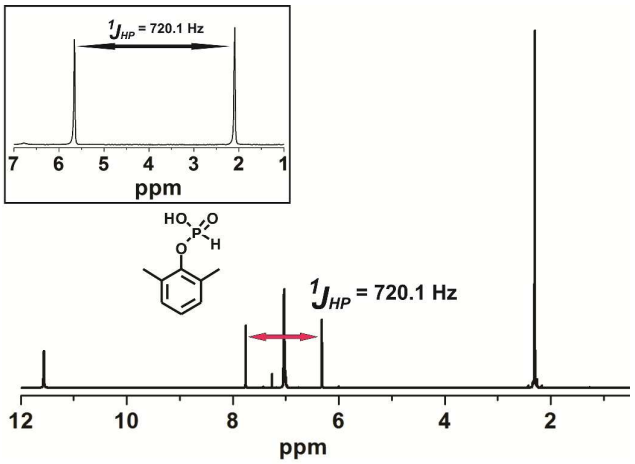
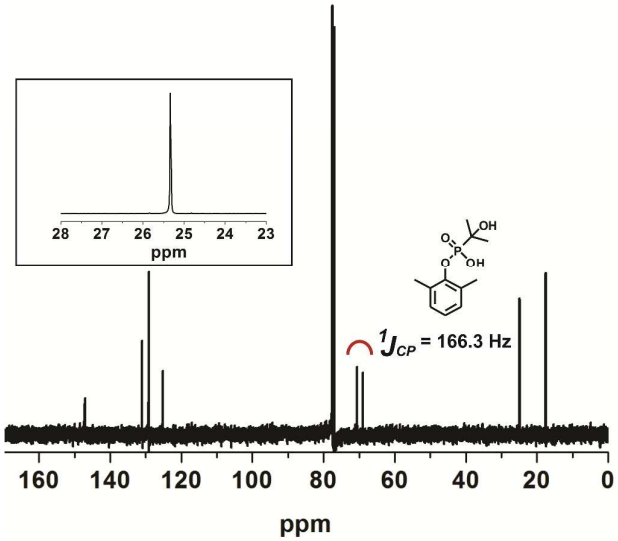


Figure 1. ^{1}H NMR spectrum of compound **2** ($CDCl_3$) showing ($^{1}J(^{31}P,^{1}H)$ coupling; Inset; ^{31}P NMR spectrum of compound ($CDCl_3$).

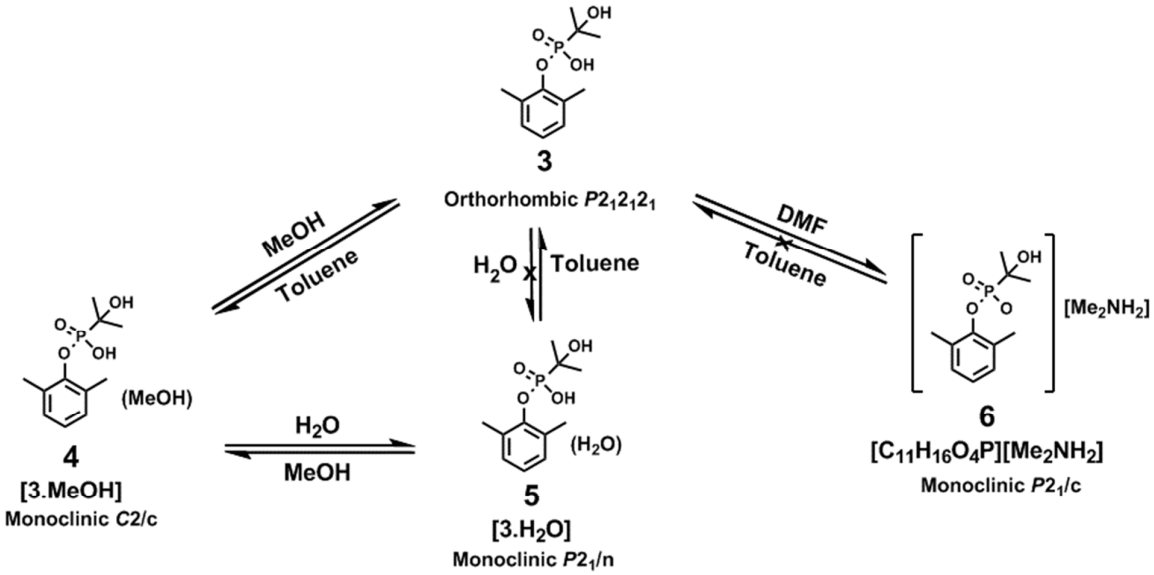
Similar to compound **2**, in the FTIR spectrum of compound **3**, the characteristic signature for the P=O bond appears at 1177 cm^{-1}, whereas the peak at 1094 cm^{-1} and 973 cm^{-1} corresponds to the symmetric and anti-symmetric stretching P-O-C vibrations. Two broad absorptions appearing at 2319 cm^{-1} and 3408 cm^{-1} can be readily assigned to the PO-H and CO-H vibrations in compound **3**, respectively. The presence of a solitary uncouple resonance at δ = 25.6 ppm in the ^{31}P NMR spectrum indicates the formation of the phosphonate **3** as the only product. The position of the various resonances and their relative intensities in the ^{1}H NMR spectrum of **3** are consistent with the molecular composition and structure. The ^{13}C NMR spectrum of **3** further confirms the insertion of acetone across the P-H bond. For example, the carbonyl carbon of the acetone after insertion appears as a doublet at δ 69.8 ($^{1}J_{CP}$ = 166.3 Hz),



confirming the insertion; the ^{13}C spectrum is further consistent with other types of carbon atoms in the molecule (Fig. 2).

Figure 2. ^{13}C NMR spectrum of compound **3** ($CDCl_3$) showing ($^{1}J(^{31}P,^{13}C)$ coupling; Inset; ^{31}P NMR spectrum of compound ($CDCl_3$).

Various crystalline forms of 3: The crude product **3** obtained from the reaction when recrystallized from toluene yields the anhydrate (Scheme 2). This form undergoes a reversible



Scheme 2. Three crystalline (**3**, **4** and **5**) and salt (**6**) forms of α-hydroxyarylphosphonate and their solution transformation.

transformation into the solvate form **4** (3.MeOH) on crystallisation from methanol. Form **4** can be transformed to form **5** (4.H_2O) on crystallisation from water. No single crystal to single crystal transformation was observed in any of the forms by dipping the single crystals of the compound in different solvents unlike our earlier observation in the case 4-amino-2,6-diisopropylphenyl phosphate.[22] Attempts to desolvate forms **4** and **5** under vacuum only yields amorphous powder.

Crystallisation of form **3** from warm DMF solution however yields the dimethylammonium salt of the phosphonate ligand $[Me_2NH_2][(ArO)(CMe_2OH)POO)]$ (**6**), through decomposition of the DMF molecule yielding dimethylammonium cation. The FTIR spectrum of **6** confirms the salt form which shows a sharp peak at 3256 cm^{-1} with a shoulder at 3331 cm^{-1} indicating the presence of NH_2Me_2 ammonium group; absence of any broad peak around the 2300 cm^{-1} region indicates the transfer of the proton from the P-OH group to the $NHMe_2$. The ^1H NMR spectrum is consistent with the integrated intensities of the individual protons from the NH_2Me_2 cation and the phosphonate anion. The ^{31}P NMR spectrum shows a single resonance at δ 21.39 ppm, a shift of 4.2 ppm from the parent neutral form **3**.

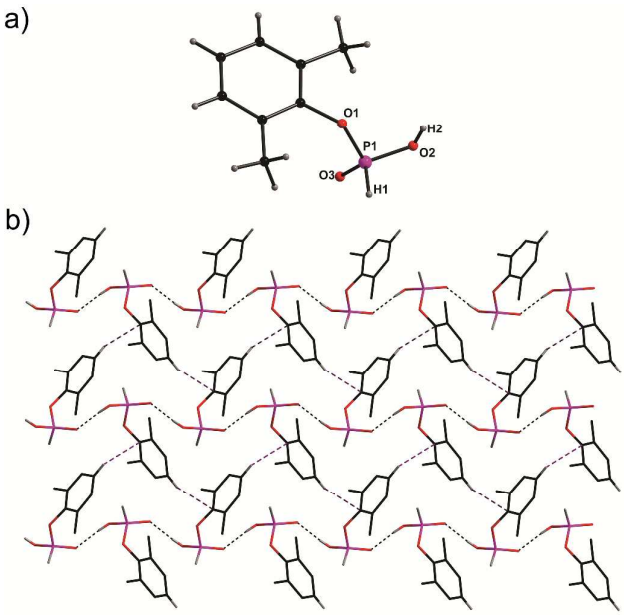


Figure 3. (a) Molecular structure of the arylhydrogenphosphonate (**2**) and (b) two-dimensional sheet like structure formed through supramolecular interactions (selected H-atoms have been omitted for clarity).

Molecular structure of 2: Rectangular crystals of H-phosphonate **2** crystalizes in the orthorhombic space group *P*ca2_1. The compound exists in the more stable pentavalent phosphonate form rather than the trivalent phosphite form. The asymmetric unit contains a single molecule of compound **2** in which the central tetra coordinate phosphorus, which is surrounded by four different substituents, exists in a distorted tetrahedral geometry with the bond angles around it ranging from 102.2(10)° to 112.6(11)°. The P-H bond distance of 1.28(2) Å is comparable to those found in many similar H-phosphonates,[23] although in general P-H distances can vary from 1.000 Å to 1.647 Å in other environments.[24] The three P-O distances in the molecule are 1.579(2), 1.527(2), and 1.469(2) Å correspond to P-O(Ar), P-O(H) and P=O linkages respectively. CCDC search reveals that the crystal structure of compound **2**, is the only free monoester H-phosphonate with free P-OH group whose crystal structure is being reported,[25] while most structural studies on H-phosphonates are of the diesters.[23,24]

The hydroxyl group of the molecule undergoes intermolecular hydrogen bonding with the phosphoryl O3 atom leading to the formation of a linear one-dimensional chain with a C(4) motif[26] (O2-H2...O3#1, 1.79(3) Å, 174(4) °). The C4-H4…C1(π) interactions (2.836 Å, 160.81°) connect this 1D chains into 2D sheets.

Molecular structure 3 and its solvated forms 4 and 5: Compound **3** when crystallized from toluene yields fine needle shaped colourless crystals. The ansolvate form **3** crystallizes in the orthorhombic space group $P2_12_12_1$ with a single molecule in the asymmetric part of the unit cell (Fig. 4). The major structural difference between **2** and **3** is the insertion of acetone molecule in the later compound. Thus the central tetrahedral phosphorus in **3** is surrounded by a carbon and three oxygen atoms is less distorted (107.63(7)-115.73(8)°) that that found in **2**. The P-O(Ar) and P-O(H) bonds are considerably longer (1.593(1) and 1.558(1) Å) in comparison to the same linkages in H-phosphonate **2** (see above).

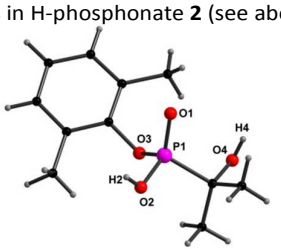


Figure 4. Molecular structure of the anhydrate form of arylhydrogenphosphonate (**3**).

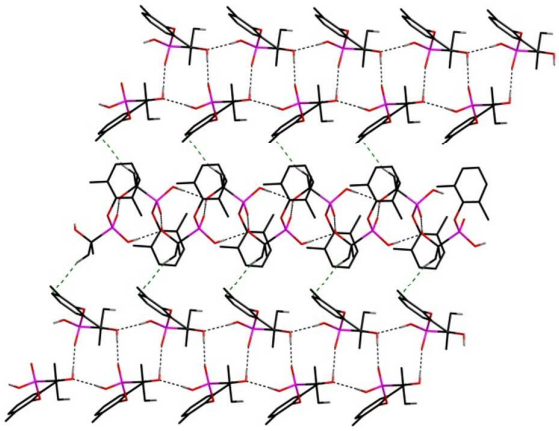


Figure 5. Supramolecular interactions leading to a two-dimensional structure in the anhydrate form (**3**) (selected H-atoms have been omitted for clarity).

Both the hydroxyl groups of the ligand (P-OH and C-OH) are involved in strong intermolecular hydrogen bonding thereby forming an infinite linear chain (O2-H2...O4#1, 1.82(3) Å, 177(3)°; O4-H4...O1#2, 1.80(3) Å, 180(3) °). The two hydroxyl groups form $R^3_3(11)$ motif. Similar to compound **2**, the C11-H11C…C5(π) interactions (2.886 Å, 159.40°) extends the infinite linear chain of phosphonates into a 2D polymeric structure (Fig. 5).

The methanol solvate form **4** (**3**.MeOH) crystalizes in the monoclinic space group *C*2/c with a single phosphonate ligand and a methanol lattice molecule in the asymmetric part of the unit cell (Fig. 6). The structural parameters (bond distances and bond angles) around phosphorus are comparable to those found in the parent compound **3**. The lattice methanol however alters the supramolecular aggregation considerably. The two hydroxyl groups from the phosphonate molecule and the methanol hydroxyl groups are involved in strong hydrogen bonding to form a wave-like polymer with $R^4_4(12)$ and $R^2_4(10)$ motifs (O5-H5A...O1, 1.87(2) Å, 179(2)°; O2-H2...O5#1, 1.59(2) Å, 174(2)°; O4-H4...O1#2, 1.95(2) Å, 171(2)°) (Fig. 7). The wave-like polymer is involved in weak C5-H5...O4 (2.650 Å, 155.53°) interactions, forming a two-dimensional polymeric structure (Fig. 7 & 8).

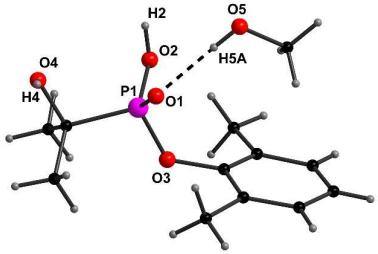


Figure 6. Crystal structure of the methanol solvate form **4** (3.MeOH) showing H-bonding between the donor methanolic –OH group and acceptor P=O group.

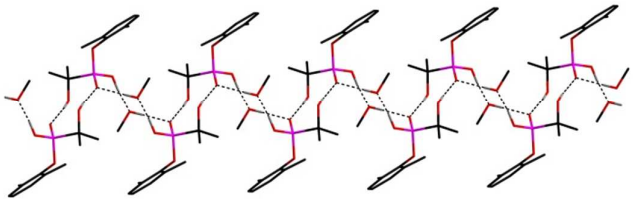


Figure 7. H-bonding interactions resulting in the formation of a wave like polymer in the solvate form **4** (selected H-atoms have been omitted for clarity).

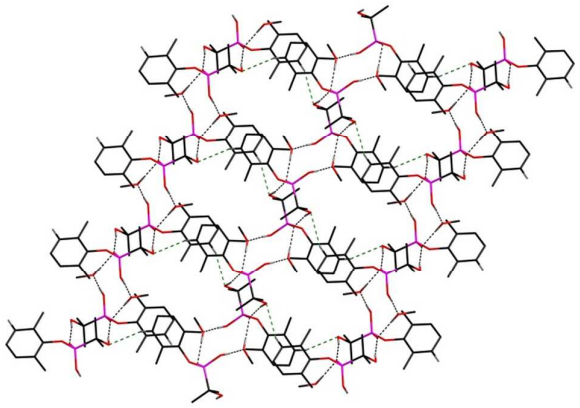


Figure 8. CH-O bonding interactions leading to the formation two-dimensional array of phosphonate ligands in **4** (selected H-atoms have been omitted for clarity).

Single crystal X-ray diffraction study of a thin needle crystal of **5** (monohydrate of **3**) crystallized from water reveals that the compound crystalizes in the monoclinic space group $P2_1/n$. The asymmetric part of the unit cell contains three molecules of the phosphonate **3** along with three water molecules of crystallization. The hydroxyl groups of the phosphonate molecule and the water molecule are involved in extensive hydrogen bonding interactions (Fig. 9 and Table 1) forming a one-dimensional tube like structure with water channels inside the tube (Fig. 10). The tube-like structure has a hydrophilic core with a hydrophobic outer sheath of the aryl rings (Fig. 11).

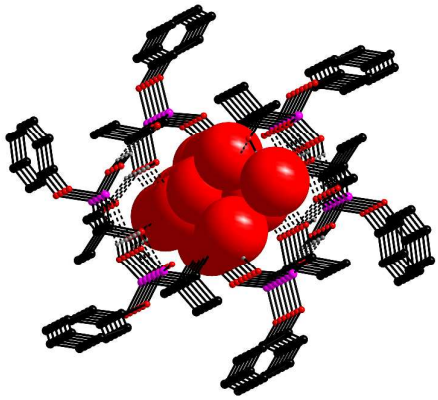


Figure 9. Extensive H-bonding interactions in the hydrate form **5** (selected carbon and H-atoms have been omitted for clarity).

Table 1. Hydrogen bonds for form **5** [Å and °].

D-H...A	d(D...A)	<(DHA)
O(14)-H(14A)...O(8)#1	2.971(8)	163.6
O(15)-H(15B)...O(12)#1	2.880(5)	140.1
O(13B)-H(13C)...O(4)	2.828(7)	150.8
O(4)-H(4A)...O(7)	2.848(4)	157(5)
O(2)-H(2)...O(15)#3	2.42(9)	153(10)
O(12)-H(12)...O(13A)	2.879(7)	173(4)
O(12)-H(12)...O(13B)	2.614(6)	143(4)
O(8)-H(8)...O(11)	2.675(4)	164(6)
O(10)-H(10)...O(7)	2.584(3)	161(7)
O(6)-H(6)...O(3)	2.403(4)	169(4)

Symmetry transformations used to generate equivalent atoms:
#1 x,y+1,z #2 x,y-1,z #3 -x+1,-y+1,-z+1

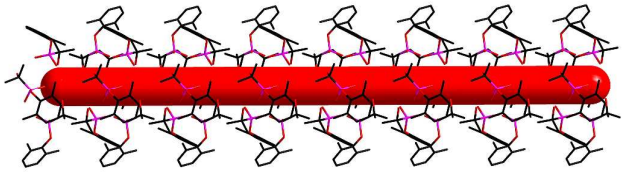


Figure 10. Tubular structure with water channel (red-rod) formed from the extensive H-bonding interactions (selected H-atoms have been omitted for clarity).

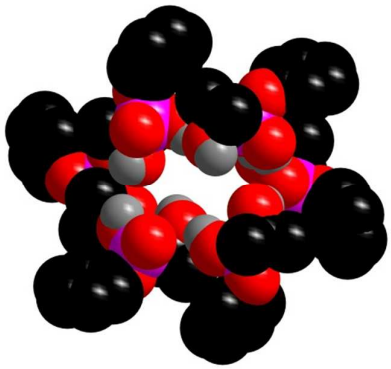


Figure 11. Space fill model showing the outer hydrophobic periphery and the inner void space occupied by the water molecules.

Molecular structure of 6: The dimethyl ammonium salt of the phosphonate ligand **6** crystalizes in the monoclinic space group $P2_1/c$ with one anionic phosphonate ligand and one dimethyl ammonium cation in the asymmetric part of the unit cell (Fig. 12). The negative charge of the phosphonate ligand is delocalized as evident from the P-O distances (P1-O3, 1.502(2) Å; P1-O2, 1.505(1) Å) with the phosphorous atom existing in a distorted tetrahedral geometry with angles varying from 109.73(7)° to 114.54(8)°. The dimethyl ammonium cation along with the phosphoryl hydroxyl group and the alcoholic hydroxyl group are involved in extensive strong hydrogen bonding leading to the formation of a two-dimensional sheet like structure (N1-H1A...O3#1, 1.84(2) Å, 172(2)°; O4-H4...O2#2, 1.85(3) Å, 170(2)°; N1-H1B...O2, 1.83(3) Å, 168(2)°) (Fig. 13). The dimethyl ammonium cation remains embedded between the two layers of the anionic phosphonate ligand.

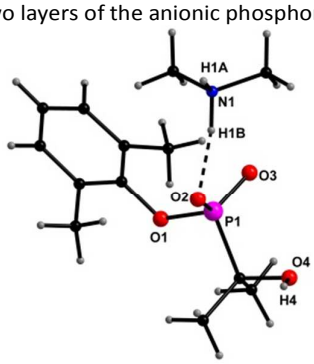


Figure 12. Asymmetric unit of the salt form, $[NH_2Me_2][(ArO)P(O)(O)(CMe_2OH)]$ (**6**).

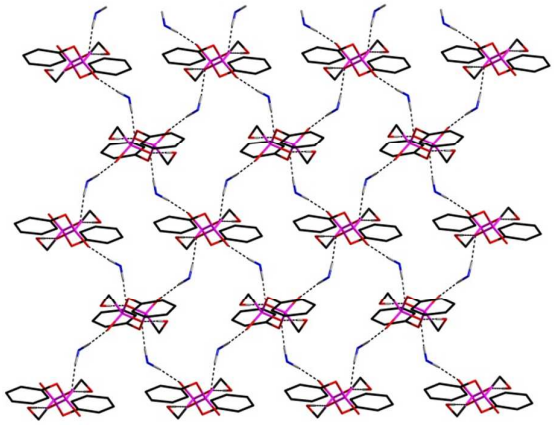
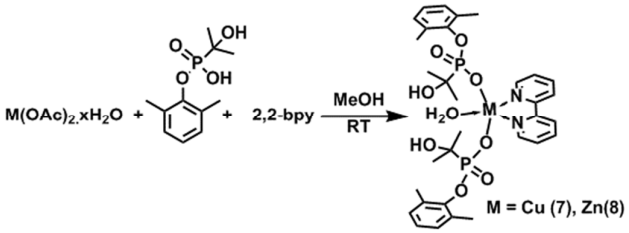


Figure 13. H-bonding interactions leading to the formation 2-dimensional array of anionic phosphonate ligands and dimethylammonium cation in **6** (methyl groups and selected H-atoms have been omitted for clarity).

Metal Reactivity

The presence of an alcoholic $–CMe_2OH$ group in $[(ArO)P(O)(OH)(CMe_2OH)]$ instead of an acidic P-OH as in phosphonate ligands of the type, $[ArP(O)(OH)_2]$ or the phosphate ligands of the type, $[(ArO)P(O)(OH)_2]$ can induce great diversity in the structural topologies seen in the metal complexes formed by them. In order to ascertain this reactivity difference, we have chosen the simple reaction of phosphonic acids with metal acetates and 2,2′-bipyridine yielding dinuclear or tetranuclear metal complexes with metal ions bridged by the phosphonate ligand and the metal ion chelated by the 2,2′-bipyridine, rendering the formation of polymeric structures.[20g,27] Use of bipyridyl ligands in the reaction of copper salts and phosphonate ligands not only impedes the formation of the polymeric architecture but also leads to diverse topologies from structural point of view through the participation of different supramolecular interactions such as H-bonding, π- π interactions etc.[28]

Reaction of hydrated copper and zinc acetate with equimolar amounts of $[(ArO)P(O)(OH)(CMe_2OH)]$ (**3**) in methanol in the presence of 2,2′-bipyridine as the chelating ligand (Scheme 3) yields the mononuclear complexes of the empirical composition, $[M(HL)_2(2,2'\text{-bpy})(H_2O)](H_2O)$ (M = Cu (**7**); Zn (**8**) where HL = $[(ArO)P(O)(O)(CMe_2OH)]^-$).



Scheme 3. Reactivity of α-hydroxyarylphosphonate (**3**) with metal acetates.

Complexes **7** and **8** have been characterized by both analytical and spectroscopic techniques and their structures

have been established by single crystal X-ray diffraction studies. The FTIR spectrum of both the compounds shows absence of any broad peak around 2300 cm^{-1} region, indicating complete deprotonation of the phosphonate ligand. The characteristic P=O stretching frequency and the symmetric and anti-symmetric M-O-P stretching frequency appears at 1183, 1094 and 898 cm^{-1} for compound **7** and at 1181, 1059 and 899 cm^{-1} for compound **8,** respectively. The ^{1}H NMR spectrum of **8** shows the corresponding resonant peaks for the ligand and the 2,2′-bipyridine whereas the ^{31}P NMR spectrum shows single resonant peak at δ 22.07 ppm, a δ 3.1 ppm upfield shift from the ligand. The thermal decomposition studies have been carried out under nitrogen atmosphere. The complex **8** loses the lattice and coordinated water molecules up to 180 ^{o}C following which a sharp weight loss is observed due to the loss of the organic part of the phosphonate ligand leaving a residue of 52.5 % (theoretical yield, 52.1 %). Further heating to 700 ^{o}C leads to the loss of the 2,2′-bipyridine moiety leaving behind 30.0 weight percent of $Zn(PO_3)_2$ (theoretical yield, 30.1 %). The metaphosphate eliminates P_2O_5 on heating above 800 ^{o}C leaving behind white ZnO as the residue (observed yield, 10.69 %, theoretical yield, 10.95 %). Compound **7** also shows a similar decomposition behaviour leaving black CuO as the residue.

The fact that the nature of the product in these reactions is different from the widely used classical phosphonate/ate ligand and the presence of the free –CMe_2OH groups gives rise to ample scope for further reaction with active metal precursors such as $AlMe_3$, $Ti(O^iPr)_4$, etc. to synthesise active metal catalysts or the design of new magnetically interesting bimetallic systems or frameworks with new structural diversity.

Molecular structure of 7 and 8: The crystals of copper and zinc complexes **7** and **8** were obtained by slow evaporation of the solvent from the reaction mixture at ambient conditions. Single crystal X-ray diffraction study of a thin green needle-like crystal of compound **7** reveals that the complex crystalizes in the monoclinic space group $P2_1/n$. The zinc(II) complex **8** is isomorphous with the copper complex **7**. The asymmetric unit of the unit cell of **7** contains two chemically similar but crystallographically different monomeric copper(II) molecules. Copper ions in these molecules are coordinated to two monoanionic phosphonate ligands, one chelating 2,2′-bipyridine ligand and one water molecule, in addition to two lattice water molecules in the asymmetric unit (Fig. 14). The copper(II) ion adopts distorted trigonal bipyramidal geometry with one nitrogen atom from the bipyridine unit and two oxygen atoms from the phosphonate ligand forming the trigonal plane while the apical positions areoccupied by the other nitrogen atom of the bipyrdine ligand and the coordinated water molecule. The Cu-N distances are Cu1-N1…1.980(4) Å, Cu1-N2…2.023(4) Å, Cu2-N4…1.972(3) Å and Cu2-N3…2.018(4) Å. The average Cu-O(P) and Cu-O(W) distances are 2.0655 Å and 1.9830 Å respectively. The copper complex is involved in both intramolecular and intermolecular hydrogen bonding, forming a wave-like infinite polymeric chain as depicted in Fig. 15. In the zinc complex **8**, the average Zn-N, Zn-O(P) and Zn-O(W) distances are 2.09625, 1.9795 and 2.1215 Å, respectively.

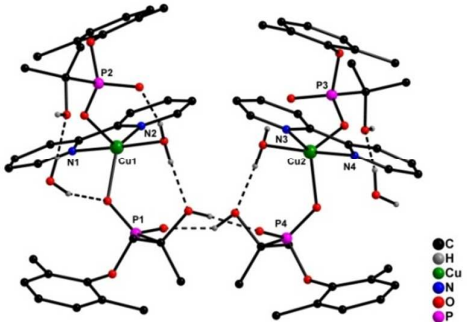


Figure 14. Asymmetric unit of the complex **7** (some hydrogen atoms are omitted for clarity).

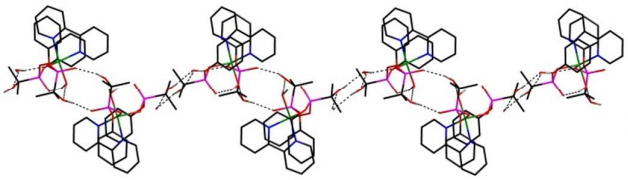


Figure 15. One dimensional wave-like polymer of compound **7**.

Conclusions

The H-phosphonate **2** with active –PH and P-OH group is a versatile precursor for the synthesis of biologically active derivatives to mimic the cytotoxicity displayed by other active phosphonate molecules. The H-phosphonate and the three forms of the α-hydroxyarylphosphonate ligand viz., ansolvate (**3**), solvate (**4**) and hydrate (**5**) show interesting supramolecular interactions leading to polymeric structures with the hydrate form forming a tubular structure with water channels inside the hydrophobic cavity. Compounds such as **5** with water channels are interesting candidates for proton conductivity studies. Further, the metal reactions of α-hydroxyarylphosphonate can lead to great diversity in structures as seen in the simple reaction with metal acetates. The free alcoholic –OH groups can be selectively utilized for further reactions and are promising candidates for forming newer types of heterometallic clusters.

Experimental Section

Materials and methods

The syntheses of compounds **1–3** were carried out under a nitrogen atmosphere using standard Schlenk line techniques. Reaction with metal acetates was performed under aerobic conditions. The melting points were measured in glass capillaries and are reported uncorrected. Infrared spectra were obtained using a Perkin-Elmer Spectrum One FT-IR spectrometer as KBr diluted discs. Microanalyses were performed on a Thermo Finnigan (FLASH EA 1112) microanalyzer. The ^{1}H (Me_4Si internal standard), ^{13}C NMR and ^{31}P (85% H_3PO_4 external standard) NMR spectra were recorded

using a either a Bruker 500 MHz or 400 MHz spectrometer. The ESI MS studies were carried out on Bruker MaXis impact mass spectrometer. Solvents were purified according to standard procedures prior to use.[29] Commercially available starting materials such as 2,6-dimethylphenol (Sigma Aldrich), phosphorous trichloride (Spectrochem), lithium chloride (Sigma Aldrich), copper acetate monohydrate (Merck) and zinc acetate tetrahydrate (Merck) were used as procured.

Synthesis of (ArO)PCl_2 (1) : An oven dried Schlenk flask was charged with 2,6-dimethylphenol (5.25 g, 43.0 mmol) and phosphorus trichloride (10.0 mL, 115.0 mmol) followed by the addition of lithium chloride (0.17 g, 4.0 mmol) as the catalyst under nitrogen atmosphere. The reaction mixture was refluxed for 48 h and then cooled to room temperature. Excess PCl_3 was removed then under vacuum and the resulting colourless liquid was fractionally distilled under reduced pressure. The product as distillate was obtained in nearly quantitative yield and was used as such for further reactions.

Synthesis of [(ArO)P(O)(H)(OH)] (2): (ArO)PCl_2 (4.46 g, 20 mmol) obtained in the above step was dissolved in dry toluene at room temperature and then slowly cooled to -20 ^{o}C using an ice-salt mixture. The solution was then hydrolysed by the drop wise addition of two equivalent of distilled water. The solution was then stirred overnight at room temperature. Evaporation of the toluene led to a viscous liquid. It was then washed with petroleum ether (60^{o}-80^{o}C) several times when the product was obtained as white powder. M.p: 38-39 ^{o}C. Yield: 3.10 g (83 %). FTIR (as KBr diluted disc, cm^{-1}): 3421(br), 2953 (w), 2923 (m), 2861 (w), 2461 (w), 2284 (w), 2159 (br), 1650(br), 1478(vs), 1380 (m), 1268(s), 1223(vs), 1179(vs), 1093(s), 1027(vs), 994(vs), 942(vs), 870(m), 767(s), 567(m), 503(s). ^{1}HNMR ($CDCl_3$, 500 MHz) δ: 11.01 (br, 1H, *P-OH*), 7.75-6.31 (d, $^{1}J_{HP}$ = 720.1 Hz, 1H, *PH*), 7.02 (m, *Ar-H*, 3H), 2.29 (s, *Ar-CH_3*, 6H) ppm. ^{31}P NMR ($CDCl_3$, 202.46 MHz) δ: 5.64, 2.09 ppm ($^{1}J_{PH}$ = 718.7 Hz). ^{13}C ($CDCl_3$, 125.75 MHz) δ: 147.3, 130.3, 129.2, 125.6, 17.3 ppm. ESI-HRMS m/z = 187.0518 $[M+1]^{+}$.

Synthesis of [(ArO)P(O)(OH)(CMe_2OH)](3): (ArO)PCl_2 (4.46 g, 20 mmol) obtained in the first step was dissolved in acetone (100 mL) at room temperature. Two equivalent of water was then added dropwise resulting in the evolution of hydrogen chloride gas. The reaction mixture was stirred for three days at room temperature. The solvent was then removed under vacuum and the viscous liquid obtained was triturated with petroleum ether (60 ^{o} - 80 ^{o}C) to obtain the desired product as off white powder. M.p: 141-142 ^{o}C. Yield: 0.81 g (16.5 %). Anal. Calcd. For $C_{11}H_{17}O_4P$; C, 54.10; H, 7.02; Found, C, 53.62; H, 6.96. FTIR (as KBr diluted disc ,cm^{-1}): 3431(br), 3067 (m), 2993 (w), 2932 (w), 2853 (w), 2807 (w), 2319(br), 1628(br), 1471(s), 1380 (w), 1258(s), 1177(vs), 1162 (vs), 1094(s), 973 (vs), 925 (vs), 850(m), 780(m), 770 (m), 497 (m). ^{1}HNMR ($CDCl_3$, 400 MHz) δ: 6.96 (m, *Ar-H*, 3H), 5.84 (br, *P-OH*), 2.27 (s, *Ar-CH_3*, 6H), 1.50 (s, *Aliphatic CH_3*, 3H), 1.46 (s, *Aliphatic CH_3*, 3H) ppm. ^{31}P NMR ($CDCl_3$, 202.46 MHz) δ: 25.32 ppm. ^{13}C ($CDCl_3$, 100.6 MHz) δ: 147.2, 131.0, 129.1, 125.2, 70.6-69.0 (d, $^{1}J_{CP}$ = 166.3 Hz), 24.9, 17.5 ppm. ESI-MS m/z = 245.09 $[M+1]^{+}$.

Synthesis of [NH_2Me_2][(ArO)P(O)(O)(CMe_2OH)] (**6**): Compound **3** (0.025 g, 1 mmol) was dissolved in warm dimethylformamide (1.0 mL) in a sample vial (5.0 mL). Block shaped colourless crystals were obtained after a week. M.p: 190-191 ^{o}C. Yield: 0.002 g (67 %, based on **3**). Anal. Calcd. For $C_{13}H_{24}NO_4P$; C, 53.97; H, 8.36, N, 4.84; Found, C, 53.42; H, 7.96, N, 4.70. FTIR (as KBr diluted disc ,cm^{-1}): 3411(m), 3331(m), 3257 (s), 3015 (w), 2984 (w), 2965 (w), 2934 (w), 2740(m), 2473 (s), 1626 (w), 1469 (s), 1430 (w), 1264 (m), 1191 (vs), 1174 (vs), 1152 (vs), 1091 (s), 1059 (vs), 1028 (m), 963 (w), 934 (m), 892 (vs), 769 (s), 741 (s), 693 (m), 565(m), 528 (m), 506(m). ^{1}HNMR (CD_3OD, 400 MHz) δ: 6.87 (d, *Ar-$C^{3,5}H$*, $^{3}J_{HH}$ = 7.4 Hz, 2H), 6.75 (t, *Ar-$C^{4}H$*, $^{3}J_{HH}$ = 7.4 Hz, 1H), 2.42 (d, *N-CH_3*, $^{3}J_{HH}$ = 1.3 Hz, 6H), 2.34 (s, *Ar-CH_3*, 6H), 1.47 (s, *Aliphatic CH_3*, 3H), 1.44 (s, *Aliphatic CH_3*, 3H) ppm . ^{31}P NMR (CD_3OD, 162.0 MHz) δ: 21.39 ppm. ^{13}C (CD_3OD, 125.75 MHz) δ: 151.1, 132.7, 129.7, 124.5, 71.9- 70.55 (d, $^{1}J_{CP}$ = 165.9 Hz), 35.3, 26.8, 18.7 ppm. ESI-MS m/z = 290.14 $[M+1]^{+}$.

Synthesis of [Cu$(HL)_2$(bpy)(MeOH)].2H_2O (7): To a solution of copper acetate monohydrate (0.05 g, 0.25 mmol) in methanol (10 mL) was added **3** (0.122 g, 0.5 mmol) and the solution was stirred for 10 minutes followed by the addition of solid 2,2'-bipyridine (0.040 g,0.25 mmol). The reaction mixture was then stirred for 2 h at room temperature and filtered. The clear green filtrate was then kept for crystallisation at ambient conditions. Long needle shaped green crystals were obtained after two weeks. M.p: 170-172 ^{o}C. Yield: 0.121 g (65 %, based on **3**). Anal. Calcd. For $C_{64}H_{88}Cu_2N_4O_{20}P_4$; C, 51.78; H, 5.98; N, 3.77; Found, C, 51.88; H, 5.78; N, 3.86. FTIR (as KBr diluted disc, cm^{1}) : 3433 (br), 2966 (w), 2925 (w), 1638 (m), 1610 (s), 1602 (s), 1497 (m), 1474 (s), 1448 (s), 1381 (m), 1265 (s), 1183 (vs), 1159 (vs), 1094 (s), 1055 (vs), 1033 (vs), 954 (m), 898 (vs), 854 (w), 770 (vs), 739 (s), 732 m), 668 (m), 566 (m), 525 (m), 504(m).

Synthesis of [Zn$(HL)_2$(bipy)(MeOH)].2H_2O (8): To a solution of zinc acetate tetrahydrate (0.055 g, 0.25 mmol) in methanol (10 mL) was added **3** (0.122 g, 0.5 mmol) and the solution was stirred for 10 minutes followed by the addition of solid 2,2'-bipyridine (0.040 g,0.25 mmol). The reaction mixture was then stirred for 2 h at room temperature and filtered. The clear colourless filtrate was then kept for crystallisation at ambient conditions. Long needle shaped colourless crystals were obtained after ten days. M.p: 181-182 ^{o}C. Yield: 0.135 g (72 %, based on **3**). Anal. Calcd. For $C_{64}H_{88}Zn_2N_4O_{20}P_4$; C, 51.65; H, 5.96; N, 3.76; Found, C, 51.64; H, 5.71; N, 3.69. FTIR (as KBr diluted disc, cm^{1}) : 3398 (br), 2967 (w), 2925 (w), 1607 (w), 1599 (w), 1476 (m), 1445 (s), 1383 (w), 1265 (w), 1181 (vs), 1094(s), 1059 (s), 1039 (s), 1026 (m), 954 (w), 899 (s), 854 (w), 771 (s), 739 (m), 565 (w), 522 (w), 502(2). ^{1}HNMR (CD_3OD, 500 MHz) δ: 8.52 (m, *Ar(bpy)-H^{6}*, 2H), 8.26 (m, *Ar(bpy)-H^{3}*, 2H), 8.15 (m, *Ar(bpy)-H^{5}*, 2H), 7.61 (m, *Ar(bpy)-H^{4}*, 2H), 6.5 (m, *Ar(P)-H,* 6H), 2.08 (s, *Ar-CH_3*, 12H), 1.56 (s, *Aliphatic CH_3*, 6H), 1.53 (s,

Aliphatic CH_3, 6H) ppm . ^{31}P NMR (CD_3OD, 162.0 MHz) δ: 21.95 ppm. ^{13}C (CD_3OD, 125.75 MHz) δ: 150.2, 142.3, 131.9, 129.5, 127.8, 124.9, 123.3, 72.1-70.7 (d, $^1J_{CP}$ = 168.5 Hz), 26.6, 18.5 ppm.

X-ray crystallography

Suitable single crystals of each of the compounds were selected and mounted on a Rigaku Saturn 724+ ccd diffractometer using Paratone for unit cell determination and three dimensional intensity data collection. Data integration and indexing was carried out using Rigaku suite of programs CrystalClear and CrystalStructure.[30] The structures were solved using direct methods (SIR-92).[31] Structure refinement and geometrical calculations were carried out using programs in the WinGX module.[32] The final structure refinement was carried out using full least square methods on F^2 using SHELXL-2012.[33] Some spurious residual electron density peaks in compound **7** and **8** could not be modelled. Data quality in case of compound **8** is poor due to poor X-ray diffraction quality of thin needle like crystal. Details of crystal data and structure refinement are given in Table 2.

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Notes and references

‡ Footnotes relating to the main text should appear here. These might include comments relevant to but not central to the matter under discussion, limited experimental and spectral data, and crystallographic data.

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Table 2. Crystal data and refinement details for compounds **1**–**8**

Compound	**2**	**3**	**4**	**5**	**6**	**7**	**8**
Empirical formula	$C_8H_{11}O_3P$	$C_{11}H_{17}O_4P$	$C_{12}H_{21}O_5P$	$C_{11}H_{19}O_5P$	$C_{13}H_{24}NO_4P$	$C_{32}H_{44}N_2O_{10}P_2Cu$	$C_{32}H_{44}N_2O_{10}P_2Zn$
Formula weight	186.14	244.21	276.26	262.23	289.3	742.17	744
Temperature	150(2) K	150(2) K	150(2) K	150(2) K	100(2) K	150(2) K	150(2) K
Crystal system	Orthorhombic	Orthorhombic	Monoclinic	Monoclinic	Monoclinic	Monoclinic	Monoclinic
Space group	$Pca2_1$	$P2_12_12_1$	$C2/c$	$P2_1/n$	$P2_1/c$	$P2_1/n$	$P2_1/n$
a (Å)	14.265(5)	6.1259(12)	21.412(5)	17.986(3)	12.989(5)	16.269(4)	16.398(6)
b (Å)	7.246(2)	13.308(3)	7.5902(15)	7.8722(11)	9.027(4)	24.011(6)	23.992(8)
c (Å)	8.860(3)	14.863(3)	18.474(4)	28.879(4)	14.006(5)	18.920(5)	18.942(7)
α (°)	90	90	90	90	90	90	90
β (°)	90	90	105.450(4)	92.107(3)	111.738(5)	112.875(4)	112.576(5)
γ (°)	90	90	90	90°	90	90	90
Volume ($Å^3$)	915.8(5)	1211.7(4)	2893.9(11)	4086.2(11)	1525.4(10)	6810(3)	6881(4)
Z	4	4	8	12	4	8	8
Density (mgm^{-3})	1.350	1.339	1.268	1.279	1.260	1.448	1.436
Abs. coeff. (mm^{-1})	0.265	0.224	0.200	0.209	0.190	0.794	0.865
Reflections collected	6730	9190	10609	22808	9896	26387	50366
Independent reflections	1582 [R(int) = 0.0229]	2255 [R(int) = 0.0166]	2678 [R(int) = 0.0224]	7332 [R(int) = 0.0221]	2836 [R(int) = 0.0388]	12393 [R(int) = 0.0398]	12415 [R(int) = 0.0799]
Completeness to 2θ	99.80%	99.20%	99.40%	98.90%	99.80%	98.00%	99.60%
Data / restraints / parameters	1582 / 1 / 119	2255 / 0 / 213	2678 / 0 / 192	7332 / 8 / 506	2836 / 0 / 190	12393 / 2 / 881	12415 / 0 / 869
GooF (F^2)	1.063	1.072	1.041	1.06	1.104	1.161	1.188
Final R indices [I>2sigma(I)]	R1 = 0.0247, wR2 = 0.0586	R1 = 0.0197, wR2 = 0.0523	R1 = 0.0322, wR2 = 0.0866	R1 = 0.0603, wR2 = 0.1618	R1 = 0.0420, wR2 = 0.0901	R1 = 0.0755, wR2 = 0.1572	R1 = 0.1009, wR2 = 0.2710
R indices (all data)	R1 = 0.0249, wR2 = 0.0587	R1 = 0.0197, wR2 = 0.0524	R1 = 0.0329, wR2 = 0.0872	R1 = 0.0632, wR2 = 0.1645	R1 = 0.0465, wR2 = 0.0928	R1 = 0.0872, wR2 = 0.1646	R1 = 0.1115, wR2 = 0.2885

2,6-Dimethylphenol derived H-phosphonate and α-hydroxyphosphonate: Facile synthesis, crystal chemistry, supramolecular association and metal complexation

Sazzat Hossain, Sandeep K. Gupta and Ramaswamy Murugavel*

Table of Contents

H-phosphonate and α-hydroxyarylphosphonate with active *P-H*, *P-OH* groups have been synthesized from 2,6-dimethylphenol and their aggregation behaviour assisted by different supramolecular interactions have been investigated.