Metal-organodiphosphonate chemistry: hydrothermal syntheses and structures of Ca(II)
coordination polymers with xylyldiphosphonate ligands

Valerie Lopez,[#] Tiffany M. Smith Pellizzerri, Matthew D. Lijewski, Karin Ruhlandt* and Jon
Zubieta*

Department of Chemistry, Syracuse University

Syracuse, NY 13244

- # V. Lopez, Synthesis and Characterization of Calcium Arylphosphonate Metal Organic Frameworks, Masters Thesis, Syracuse University, 2014.
- Corresponding authors: Tel: +1 315-443-2547; fax: +1 315-443-4070; E-mail jazubiet@syr.edu (JZ). Tel: +1 315-443-1306; fax: +1 315-443-4070; E-mail kruhland@syr.edu (KR).

Abstract. Hydrothermal reactions of $\text{Ca}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$ and the appropriate xylyldiphosphonic acid provided crystals of $[\text{Ca}(p\text{-C}_8\text{H}_8\text{P}_2\text{O}_6\text{H}_2)(\text{OH}_2)_3]_n$ (1), $[\text{Ca}(m\text{-C}_8\text{H}_8\text{P}_2\text{O}_6\text{H}_2)(\text{OH}_2)_2]_n$ (2), and $[\text{Ca}(o\text{-C}_8\text{H}_8\text{P}_2\text{O}_6\text{H}_2)(\text{OH}_2)]_n$ (3). The juxtaposition of phosphonate donor groups on the xylyl-diphosphonate linkers is a major structural determinant. Thus, the structure of $[\text{Ca}(p\text{-C}_8\text{H}_8\text{P}_2\text{O}_6\text{H}_2)(\text{OH}_2)_3]_n$ (1) is three dimensional, while $[\text{Ca}(m\text{-C}_8\text{H}_8\text{P}_2\text{O}_6\text{H}_2)(\text{OH}_2)_2]_n$ (2) and $[\text{Ca}(o\text{-C}_8\text{H}_8\text{P}_2\text{O}_6\text{H}_2)(\text{OH}_2)]_n$ (3) exhibit reduced dimensionalities, one- and two-dimensional, respectively. The structures exhibit variable coordination numbers, as well as variable numbers of coordinated water molecules. In addition, hydrogen bonding plays an important role in the structural chemistry of these materials.

Keywords: calcium phosphonates, coordination polymers, hydrothermal reactions, x-ray structures.

1.0 Introduction

The function of the human skeleton includes the support of the body, protection of vital organs, and a reservoir of minerals for balanced metabolism. Defects of the skeletal system are induced by traumatic injuries, but can also be age related or the result of pathological degeneration. Beyond middle age, there are several architectural changes in the human bone including a decrease in the bone volume fraction and connectivity density for trabecular bone [1] and a decrease in thickness and an increase in the porosity for cortical bones [2-4]. The overall effect of these architectural changes is that the bone becomes more prone to fractures and other bone diseases like osteoporosis. Although several materials including ceramics and coated metals are effective for short-term treatment [5,6], significant problems arise for long-term therapy, including the lack of mechanical strength and the biocompatibility of the materials [5].

For example, while metal implants provide the strength and stability [7-10], these materials are not bioinert, as illustrated by their propensity for corrosion under ion release, resulting in hydrolysis to form oxides and hydroxides that trigger pH changes in the body [11]. To prolong the life of the implant, the metal is often coated with biocompatible materials such as hydroxyapatite and polyacrylic acid [11-13]. Furthermore, metal implants require invasive surgical procedures and significant recovery times [13]. On the other hand, bioceramics are witnessing increased use as dental and bone implants [14], with applications ranging from artificial teeth and parts for pacemakers to kidney dialysis machines, due to their bioinert, biodegradable and bioactive properties. However, there are significant disadvantages, including considerable wear and tear, as well as noisy movement of parts [15]. Finally, while composite materials have been developed that display desired properties such as mechanical strength, biocompatibility and biodegradability, there is not a single material developed to date that combines all desired properties [16-18].

Alternatively, various drug therapies have been developed to combat bone disease. The most commonly used drugs for the specific case of osteoporosis are bisphosphonates, which have been shown to slow resorption of bone tissue to assist in maintenance or even increase bone density [2]. While the effectiveness of such drugs in the absorption of osteoclast provides the rationale for further development [19], side effects which include, but are not limited to, muscle pain, blood in the urine, dizziness, heartburn, irritation as well as weakness, have also been documented [20].

A unique strategy for bone repair is the use of scaffolds, which degrade or resorb while bearing regenerating tissue [21]. Such scaffolds furnish a structural matrix that fills a defect in the bone to allow cells to adhere while providing a free flow of nutrients and waste [22]. Scaffolds for bone regeneration must be osteoconductive or osteoinductive, that is, they must support bone cell functions or stimulate bone formation [23]. Recent efforts to design scaffolds with appropriate properties have focused on metal organic frameworks (MOFs) with open pore structures with the potential for osteoconductivity [24,25].

The design of an appropriate MOF scaffold requires the appropriate metal and multipodal ligand to act as the nodes and linkers of the framework, respectively [26]. Since calcium whose MOF chemistry remains largely unexplored is a key component of bones and teeth [27], this was an appropriate choice of metal node for the construction of the scaffolds. In view of their efficacy in therapy for osteoporosis, bisphosphonates were chosen as the dipodal ligand linkers for the construction of the frameworks. The family of α , ω -alkyldiphosphonates has been extensively studied and shown to typically form three-dimensional frameworks, characterized as “pillared layer” materials whose interlamellar separations may be modified by variations of tether lengths [28-30]. In contrast, xylyldiphosphonate ligands [31-36] have not been extensively studied although structural diversity can be developed for complexes with M(II) sites by exploiting the readily available ligand isomers, 1,2-, 1,3- and 1,4-xylyldiphosphonate. As part of our continuing investigations of the structural chemistry of bisphosphonate materials [37-39], we report the syntheses and structures of three Ca(II)-xylyldiphosphonate compounds, $[\text{Ca}(p\text{-C}_8\text{H}_8\text{P}_2\text{O}_6\text{H}_2)(\text{OH}_2)_3]_n$ (1), $[\text{Ca}(m\text{-C}_8\text{H}_8\text{P}_2\text{O}_6\text{H}_2)(\text{OH}_2)_2]_n$ (2), and $[\text{Ca}(o\text{-C}_8\text{H}_8\text{P}_2\text{O}_6\text{H}_2)(\text{OH}_2)]_n$ (3).

2. Experimental Section

2.1 General Procedures. All chemicals were used as obtained without further purification with the exception of p-xylene diphosphonic acid, ortho-xylene diphosphonic acid and meta-xylene diphosphonic acid which were synthesized in a similar fashion to the literature method [40] using the respective dibromide starting materials. $\text{Ca}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$ was purchased from Sigma-Aldrich. All syntheses were carried out in 23-mL poly(tetrafluoroethylene)-lined stainless steel containers under autogenous pressure. The pH values of the solutions were measured prior to

and after heating using pHDrion vivid 1-11® pH paper. Water was distilled above 3.0MΩ in-house using a Barnstead Model 525 Biopure Distilled Water Center.

2.2 Synthesis of $[Ca(p-C_8H_8P_2O_6H_2)(OH_2)_3]_n$ (1). A solution of $Ca(NO_3)_2 \cdot 4H_2O$ (0.121g, 0.50 mmol) and p-xylene-diphosphonic acid (0.084g, 0.30mmol), and H_2O (4mL, 220mmol) in the mole ratio 1.0:0.60:440 was stirred briefly before heating to 150°C for 72 hours. The initial and final pH values were 3 and 4, respectively. Colorless blocks suitable for X-ray diffraction were isolated 5% yield. IR (KBr pellet, cm^{-1}): 3445(m), 2391(w), 1635(s), 1384(s), 1262(w), 1155(w), 1124(m), 1014(w), 937(m), 842(w), 823(m), 804(w), 722(m), 557(m), 490(m), 438(m).

2.3 Synthesis of $[Ca(m-C_8H_8P_2O_6H_2)(OH_2)_2]_n$ (2).

A solution of $Ca(NO_3)_2 \cdot 4H_2O$ (0.089g, 0.40mmol) and the appropriate xylene-diphosphonic acid (0.082g, 0.30mmol), triethylamine (0.034g, 0.34mmol) and H_2O (5mL, 280mmol) in the mole ratio 1.0:0.75:0.85:700 was stirred briefly before heating to 150°C for 72 hours in a PTFE-lined pressure vessel of 12 mL capacity. The initial and final pH values were 6 and 6, respectively. Colorless blocks suitable for X-ray diffraction were isolated in 10 % yield. IR (KBr pellet, cm^{-1}): 3466(m), 2343(w), 1636(s), 1384(s), 1259(w), 1155(w), 1124(m), 1012(m), 936(m), 556(m), 441(m).

2.4 Synthesis of $[Ca(o-C_8H_8P_2O_6H_2)(OH_2)]_n$ (3).

A solution of $Ca(NO_3)_2 \cdot 4H_2O$ (0.079g, 0.30mmol) and 1,2-xylene-diphosphonic acid (0.081g, 0.30mmol), triethylamine (0.034g, 0.34mmol) and H_2O (4mL, 220mmol) in the mole ratio 1.0:1.0:1.13:733 was stirred briefly before heating to 150°C for 10 days in a PTFE-lined pressure vessel of 12 mL capacity. The initial and final pH values were 6 and 6, respectively. The vessel was allowed to slowly cool to room temperature and a yellow liquid with a small amount of colorless crystalline and white solids were recovered. The crystalline solid was collected by filtration and separated from the powder (yield: 5%). IR (KBr pellet, cm^{-1}): 3428(s), 1638(s), 1384(s), 1262(w), 1085(w), 948(w), 824(w), 658(m), 519(m).

2.5 X-ray Crystallography. Crystallographic data for all compounds were collected at low temperature (90K) on a Bruker KAPPA APEX DUO diffractometer equipped with an APEX II CCD system using Mo-K α radiation ($\lambda = 0.71073 \text{ \AA}$) [41,42]. The data were corrected for Lorentz and polarization effects [43], and adsorption corrections were made using SADABS [45]. The structures were solved by direct methods, and refinements were made using the SHELXTL [46] crystallographic software. After first locating all of the nonhydrogen atoms from the initial solution of each structure, the models were refined against F^2 using first isotropic and then anisotropic thermal displacement parameters until the final value of $\Delta/\sigma_{\text{max}}$ was less than 0.001. Hydrogen atoms were introduced in calculated positions and refined isotropically. Neutral atom scattering coefficients and anomalous dispersion corrections were taken from the *International Tables*, Vol. C. Crystallographic details for the structures of **1-3** are summarized in **Table 1**. Selected bond lengths and angles are provided in **Tables 2-6**. Full tables of bond lengths and angles for the structures are given in the supplementary materials. Images of the crystal structures were generated using CrystalMaker® [47].

2.6 Thermal gravimetric Analyses. TGA data for compound **1** were collected on a Q500 V6.7 Build 203 Thermogravimetric Analyzer. A 5.3370 mg sample of the compound was loaded on a platinum pan to perform the analysis. Purified nitrogen gas was introduced with a balance purge rate of 40 mL/min and a sample purge rate of 60 mL/min. The temperature was ramped at 10°C per minute until a final temperature of 700°C was reached. For compounds **2** and **3**, the analyses were performed on a TGA Q50 V20.13 Build 39 Thermogravimetric Analyzer. The sample loadings were 0.6420 mg and 0.2440 mg of compound for **2** and **3**, respectively. Purified nitrogen gas was used with a balance purge rate of 40 mL/min and a sample purge rate of 60 mL/min. The temperature was ramped at 10°C per minute until a final temperature of 800°C was reached.

3. Results and Discussion

3.1 Syntheses.

Hydrothermal methods have been applied for decades to the synthesis of zeolites and metal phosphates [48,49] and have been extended more recently to the routine synthesis of metal oxides and organic-inorganic composite materials [50-53]. Reactions are typically carried out in

water at 120-250 °C under autogenous pressure, and product composition depends on a number of critical conditions, including pH of the medium, temperature and hence pressure, the presence of structure-directing cations, and the use of mineralizers. Hydrothermal methods have been exploited for decades in the preparation of metal-diphosphonate materials with pillared layer structures, such as that of the prototypical pillared layer compound $[\text{Cu}_2(\text{H}_2\text{O})_2(1,4\text{-O}_3\text{PC}_8\text{H}_8\text{PO}_3)]$ [39].

Compound **1** was obtained at 150°C by hydrothermal reaction of $\text{Ca}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$ with [1,4-phenylenebis(methylene)]bis-phosphonic acid in water. While compound **2** and **3** were obtained under similar conditions as compound **1**, triethylamine was added to the solution to increase the solution pH to 6. Reactions carried out over a wide range of temperatures (80-200°C) showed that the reactants remain partially soluble below 135°C but decompose above 200°C, with an optimal temperature of approximately 150°C.

The infrared spectra of the compounds a broad peak in the 3420-3460 cm^{-1} range attributed to $\nu(\text{O-H})$ from coordinated water molecules. The compounds also exhibit a series of medium to strong bands in the 1100 to 1650 cm^{-1} region associated with $\nu(\text{P-O})$ of the phosphonate ligands.

The TGA for compound **1** displays an initial weight loss totaling 15% in three steps between 80 °C and 200 °C attributed to the loss of the coordinated water molecules. There is a plateau of stability between 200 °C and 350 °C, followed by a weight loss of 5%. Subsequently, the weight remains constant to 650 °C, whereupon ligand dissociation occurs. Compound **2** shows a similar pattern of early weight loss, i. e., ca. 15% in three steps between 50 °C and 200 °C due to the loss of coordinated water. In this case, the material is stable to 600 °C, whereupon the phosphonate ligand begins to dissociate. In contrast, compound **3** exhibits a sharp loss of ca. 30% weight between 180 °C and 200 °C, followed by a gradual weight loss of 45% over the 200 °C to 800 °C range. In all cases, the amorphous gray residue is most likely a calcium oxide-phosphate mixture.

3.2 Descriptions of the Structures of this Study.

As shown in Figure 1, the structure of $[\text{Ca}(p\text{-C}_8\text{H}_8\text{P}_2\text{O}_6\text{H}_2)(\text{OH}_2)_3]_n$ (**1**) is three-dimensional. The connectivity is best described in terms of a subunit of chains of seven

coordinate Ca(II) sites linked through bidentate, bridging phosphonate ligands in the O,O'-bridging mode, running parallel to the c-axis (Figure 2). Each of these chains is connected through the xylyl linkers of the ligands to four adjacent chains to provide the three-dimensional connectivity.

The Ca(II) coordination sphere is defined by four phosphonate oxygen donors from four xylyl-diphosphonate ligands and three aqua ligands, producing a distorted pentagonal bipyramidal geometry. The equatorial plane is defined by the three aqua ligands and two of the phosphonate oxygen donors while the axial positions are occupied by the remaining two phosphonate oxygens. Each terminus of the xylyldiphosphonate ligands bridges two Ca sites and projects a protonated, pendant P-O(H) group. The P-O bond lengths unambiguously identify the pendant group as the protonation site: the coordinated units exhibit P-O bond lengths of 1.509(2) Å and 1.517(2) Å, while the uncoordinated unit has a P-O distance of 1.572(2) Å, consistent with a P-O(H) group.

It is noteworthy that an important structural feature of **1** is hydrogen bonding. The hydrogen and oxygen atom of the non-coordinating P-O(H) groups are involved in hydrogen bonding with distances of 2.605(1) Å and 2.538 Å and O-H...O angles of 156.71° and 174.55°. The calcium bound water molecules are also involved in hydrogen bonding at a distance of 2.786 Å and an angle of 169.26° (Figure 3). The lengths and geometry of the hydrogen bond interactions are similar to reported values for moderate hydrogen bonding interactions [6]. Selected hydrogen bonding interactions are summarized in Table 3.

The structural consequences of replacing the 1,4-xylyldiphosphonate ligand of **1** with the 1,3-xylyldiphosphonate of **2** are dramatic, as shown in Figure 4. The covalent connectivity is now one-dimensional with the ribbons running parallel to the crystallographic b-axis. The chains are constructed from seven coordinate Ca(II) nodes linked by both μ^2, η^2 - and μ^2, η^3 -PO₃H groups. Each calcium center bonds to five phosphonate oxygen donors from four phosphonate groups and to two aqua ligands. The geometry at the calcium atoms is distorted pentagonal bipyramidal, with the pentagonal plane occupied by the aqua ligands and three phosphonate oxygens and the axial positions defined by two phosphonate oxygen atoms. The two phosphonate termini of the ligands adopt distinct coordination modes with one in the common O,

O'-bridging mode and the second chelating to one Ca site and bridging to a second metal site through one of the chelating oxygen atoms.

Once again, the protonation sites of the phosphonate ligands are revealed by the P-O distances; however, the identity of one site is rather unusual. Within the O, O'-bridging ligand, the pendant, uncoordinated oxygen is protonated with a P-O distance of 1.579(1) Å compared to distances of 1.496(1) and 1.526(1) Å for the coordinated oxygen atoms which is similar to that observed for compound 1. However, the P-O distance of 1.581(1) Å for the other -PO₃H site, compared to distances of 1.509 (1) and 1.509(1) Å for a coordinated site and a pendant site, identifies a terminally coordinated oxygen atom as the protonated site, rather than the pendant P-O group.

Hydrogen bonding plays a major role in expanding the structure into two dimensions (Figure 5 and Table 5). The hydrogen atoms of the P-O(H) groups are involved in hydrogen bonding with the aqua ligands of neighboring units at distances of 2.510 Å and angles of 174.25°. Additionally, there are interactions at distances of 2.553 and 3.088 Å between the protonated phosphonate oxygen donors and other phosphonate oxygens.

Once again, the juxtaposition of -PO₃H groups on the xylyldiphosphonate ligand is a major structural determinant, as illustrated in the two-dimensional structure of [Ca(*o*-C₈H₈P₂O₆H₂)(OH₂)]_n (3), shown in Figures 6 and 7. The layer structure is constructed of a chain substructure (Figure 8) linked to adjacent chains through one of the ligand termini. The Ca centers exhibit six coordination, distorted from the idealized octahedral and trigonal prismatic limits. Each calcium site coordinates to five oxygen donors from five different -PO₃H groups, associated with three different 1,2-xylyl-diphosphonate ligands. The chain substructure exhibits two distinct heterocyclic ring structures: one is the common eight-membered [P-O-Ca-O-P-O-Ca-O-] ring associated with the doubly O, O'-bridged [Ca₂(RPO₃H)₂] groupings, while the second is a simple [Ca₂O₂] tetranuclear ring. These ring alternate in propagating the chain substructure.

The two dimensional connectivity is accomplished through one terminus of the xylyldiphosphonate ligand which serves to link adjacent chains. In this manner, there are two distinct -PO₃H environments. The first is associated with a single chain and assumes the

common O, O'-bridging role; the second, in contrast, directs a single phosphonate oxygen to the chain as a bridging ligand between adjacent calcium sites, while a second oxygen donor is directed to a metal site of an adjacent chain.

Once again, the phosphonate termini are in the singly deprotonated mode $\text{-PO}_3\text{H}$. The protonation sites are clearly identified by the P-O distances, with the protonated oxygen atoms having P-O distances of 1.570(6) Å and 1.559(6) Å, while the average of other P-O distances is 1.483(7) Å. The protonation sites are the common uncoordinated, pendant oxygen atoms.

4.0 Conclusions

Hydrothermal methods have been used to prepare a series of coordination polymers of the general type $\text{M(II)/xylyldiphosphonate}$. The structures reveal that the geometry of the xylyldiphosphonate ligand is a dominant structural determinant. Thus, while the 1,4-xylyldiphosphonate ligand in $[\text{Ca}(p\text{-C}_8\text{H}_8\text{P}_2\text{O}_6\text{H}_2)(\text{OH}_2)_3]_n$ (1) allows expansion of the structure into three dimensions, presumably reflecting the spatial accommodation allowed by the donor group juxtapositioning, when the *meta* and *ortho* derivatives are used in $[\text{Ca}(m\text{-C}_8\text{H}_8\text{P}_2\text{O}_6\text{H}_2)(\text{OH}_2)_2]_n$ (2) and $[\text{Ca}(o\text{-C}_8\text{H}_8\text{P}_2\text{O}_6\text{H}_2)(\text{OH}_2)]_n$ (3) one and two dimensional structures, respectively, are observed. The dimensionality of these latter two structures is not readily predictable based on geometric considerations alone.

Other curious features of the structures are the variabilities in coordination number and in the number of coordinated water molecules. Thus, compounds 1 and 2 exhibit distorted seven coordination while 3 is six coordinate. The number of coordinated water molecules for the series is three, two and one for compounds 1, 2 and 3, respectively.

The relative ease of synthesis and the stability of these compounds suggests that they may have potential for treatment of bone disease. We are currently investigating their stabilities and toxicities in osteoblast cells and their potential for stimulating bone mineralization.

Acknowledgement. This work was funded by a grant from the National Science Foundation (CHE-0907787). We also acknowledge support for the IGERT program through NSF Grant No. DGE-1068780.

Appendix A. Supplementary data

Additional material available from the Cambridge Crystallographic Data Centre, CCDC No. CCDC 1418295-1418297, comprises the final atomic coordinates for all atoms, thermal parameters, and a complete listing of bond distances and angles, for compounds **1-3**, respectively. Copies of this information may be obtained free of charge on application to The Director, 12 Union Road, Cambridge, CB2 2EZ, UK, fax: +44 1223 336 033, e-mail: data_request@ccdc.cam.ac.uk or <http://www.ccdc.cam.ac.uk>.

Supplementary data associated with this article can be found in the online version, at . The supplementary data consists of ORTEP views of the structures (Figures **S1-S3**), infrared spectra in Figures **S4-S6**, and TGA profiles in Figures **S7-S9**.

References

- [1] H. Chen, S. Shoumura, S. Emura, Y. Bunai, Osteoporosis Int. 19 (2008) 1473.
- [2] H. Ritzel, M. Amling, M. Posl, M. Hahn, G. Delling, Bone and Miner 12 (1997) 89.
- [3] H. Brockstedt, J. Bollerslev, F. Melsen, L. Mosekilde, Bone 18 (1996) 6.
- [4] C. Nyssen Behets, P. Y.Duchesne, A. Dhem, Gerontology 43 (1997) 316.
- [5] L. L. Hench, J. Am. Ceram. Soc. 74 (1991) 1487.
- [6] S. Dorozhkin, J. Mater. Sci. 44 (2009) 2343.
- [7] G. Wang, M. Xu, X. Tian, C. Gong, Hanjie Xuebao 32 (2011) 45.
- [8] T. Kokubo, H.-M. Kim, M. Kawashita, Biomaterials 24 (2003) 2161.
- [9] A. Bansiddhi, T.D. Sargeant, S. I. Stupp, D.C. Dunand, Acta Biomaterialia 4 (2008) 773.

- [10] Y. Cai, S. Zhang, X. Zeng, D. Sun J. Mater. Sci.: Mater. Med. 22 (2011) 1633.
- [11] E. De Giglio, D. Cafagna, M. A. Ricci, L. Sabbatini, S. Cometa, C. Ferretti, M. Mattioli-Belmonte, J. Bioactive and Compatible Polymers 25 (2010) 374.
- [12] M. Roy, V. K. Balla, S. Bose, A. Bandyopadhyay, Adv. Eng. Mater. 12 (2010) B637.
- [13] A. J. Wirth, J. Goldhahn, C. Flaig, P. Arbenz, R. Müller, G. H. van Lenthe, Bone 49 (2011) 473.
- [14] G.P. Jayaswal, S.P. Dange, A.N. Khalikar., J Indian Prosthodont. Soc. 10 (2010) 8.
- [15] P. Taddei, S. Affatato, C. Fagnano, A. Toni, J. Mater. Sci. 41 (2006) 399.
- [16] S. Dorozhkin, J. Mater. Sci. 44 (2009) 2343.
- [17] D. Tadic, M. Epple, Biomaterials 25 (2004) 987.
- [18] S. Dorozhkin, Materials 2 (2009) 1975.
- [19] S. Cremers, S. Papapoulos, Bone 49 (2011) 42.
- [20] Mc. McKague. D. Jorgenson. K. A. Buxton, Can. Fam. Physician. 56 (2010) 1015.
- [21] Z.G, Z. Jin, T. Cao, Biomed Mater 3 (2008) 22001.
- [22] D. Zacher, R. Schmid, C. Wöll, R.A. Fischer, Angew. Chem. Int. Ed. 50 (2011) 176.
- [23] A.K. Cheetham, C.N.R. Rao, R.K. Feller, Chem. Commun. (2006) 4780.

- [24] B. Chen, S. Ma, F. Zapata, F.R. Fronczek, E.B. Lobkovsky, H.-C. Zhou, *Inorg. Chem.* 46 (2007) 1233.
- [25] C. Schmidt, A.A. Ignatius, L.E. Claes, *J Biomed Mater Res.* 54 (2001) 209.
- [26] H. Furukawa, K.E. Cordova, M. O’Keeffe, O.M. Yaghi, *Science* 341 (2013) 974.
- [27] C.M. Weaver, *Curr Osteoporos. Rep.* 12 (2014) 211.
- [28] A. Clearfield, *Prog. Inorg. Chem.* 47 (1998) 371.
- [29] A. Clearfield, *Dalton Trans.* (2008) 6089.
- [30] A. Clearfield, K.D. Demadis, eds., *Metal Phosphonate Chemistry from Synthesis to Applications*, Royal Society of Chemistry, Cambridge, UK (2012).
- [31] D.M. Poojary, B. Zhang, A. Clearfield, *Chem. Mater.* 11 (1999) 421.
- [32] D.I. Arnold, X. Ouyang, A. Clearfield, *Chem. Mater.* 14 (2002) 2020.
- [33] D.M. Poorjary, B. Zhang, A. Clearfield, *J. Am. Chem. Soc.* 119 (1997) 12550.
- [34] D.M. Poorjary, B. Zhang, P. Bellinghausen, A. Clearfield, *Inorg. Chem.* 35 (1996) 4942.
- [34] D. Knog, J. Zn, J. McBee, A. Clearfield, *Inorg. Chem.* 45 (2006) 977.
- [35] D. Kong, Y. Li, J.H. Ross, R.A. Clearfield, *Chem. Commun.* (2003) 1720.
- [36] M.M. Gomez-Alcantura, A. Cabeza, M. Martinez-Lara, M.A.G. Aranda, R. Suau, N. Bhuvanesh, A. Clearfield, *Inorg. Chem.* 43 (2004) 5283.
- [37] T.M. Smith, D. Symester, K. Perrin, J. Vargas, M. Tichenor, C.J. O’Connor, J. Zubieta, *Inorg. Chim. Acta* 402 (2013) 46.
- [38] T.M. Smith, K. Perkins, D. Symester, S.R. Freund, J. Vargas, L. Spinu, J. Zubieta, *CrystEngComm.* 16 (2014) 191.
- [39] T.M. Smith, L. Strauskulage, K.A. Perrin, D. Symester, S.R. Freund, J. Vargas, L. Spinu, J. Zubieta, *Inorg. Chim. Acta* 411 (2014) 134.

- [40] D.I. Arnold, X. Ouyang, A. Clearfield, Chem. Mater. 14 (2002) 2020.
- [41] APEX2, Data Collection Software, version 2011.8-0, Bruker-AXS Inc., Madison, WI, (2011).
- [42] SMART, Data Collection Software, version 5.630, Bruker-AXS Inc., Madison, WI, (1997-2002).
- [43] SAINT plus, Data Reduction Software, version 6.45A, Bruker-AXS Inc., Madison, WI, (1997-2002).
- [44] G.M. Sheldrick, SADABS, University of Göttingen (1996).
- [45] SHELXTL PC, version 6.12, Bruker-AXS Inc., Madison, WI (2002).
- [46] CrystalMaker®: a crystal and molecular structures program. CrystalMaker Software Ltd., Oxford, England (www.crystallmaker.com).
- [47] R.M. Barrer, Hydrothermal Chemistry of Zeolites, Academic Press, London (1982).
- [48] A.N. Lobachev, G.D. Archand, Crystallization Processes Under Hydrothermal Conditions, Consultants Bureau, New York (1973).
- [49] M.S. Whittingham, Curr. Opin. Solid State Mater. Sci. 1 (1996) 227.
- [50] R.A. Laudise, Chem. Eng. News 65 (1987) 30.
- [51] J. Gopalakrishnan Chem. Mater. 7 (1995) 1265.
- [52] J. Zubietta, Solid-State Methods, Hydrothermal. In Comprehensive Coordination Chemistry II; J.A. McCleverty, T.J. Meyer, Elsevier Science: New York 1 (2004) 697-709.
- [53] T. Steiner, Angew. Chem. Int. Ed. 41 (2002) 48.

Table 1. Summary of Crystallographic Data for the Structures of This Study.

Compound	<u>[Ca(p-C₈H₈P₂O₆H₂)(OH₂)₃]_n</u> (1)	<u>[Ca(m-C₈H₈P₂O₆H₂)(OH₂)₂]_n</u> (2)	<u>[Ca(o-C₈H₈P₂O₆H₂)(OH₂)₁]_n</u> (3)
Empirical formula	C ₈ H ₁₈ CaO ₉ P ₂	C ₈ H ₁₂ CaP ₂ O ₇	C ₈ H ₁₂ CaP ₂ O ₇
Formula weight	360.24	322.2	322.2
Crystal system	Monoclinic	Monoclinic	Monoclinic
Space group	C2/c	P2 ₁ /c	C2/c
T (K)	90(2)	90(2)	90(2)
a, Å	22.623(3)	12.6090(12)	14.652(7)
b, Å	7.07029(8)	7.6048(7)	6.766(3)
c, Å	9.0974(11)	13.1373(12)	24.840(11)
β	103.848(2)	93.7700(10)	91.863(6)
Volume (Å ³)	1413.4(3)	1257.0(2)	2461.3(19)
Z	4	4	8
Calculated density (g/cm ⁻³)	1.693	1.687	1.706
Absorption coefficient (mm ⁻¹)	0.709	0.775	0.791
2θ range	1.85 to 28.39°	1.62 to 27.36°	1.640 to 26.87°
Unique reflections	1915	2977	1422
Total reflections	10082	12683	2035
Goodness-of-fit on <i>F</i> ²	0.879	0.825	0.879
R ₁ , wR ₂ (all data)	R ₁ = 0.0257, wR ₂ = 0.0978	R ₁ = 0.0366, wR ₂ = 0.1033	R ₁ = 0.1129, wR ₂ = 0.2286
R ₁ , wR ₂ (Final)	R ₁ = 0.0239, wR ₂ = 0.0935	R ₁ = 0.0305, wR ₂ = 0.0956	R ₁ = 0.0789, wR ₂ = 0.2102

Mo K_α(λ=0.71073Å). R₁= Σ/|F_o|-|F_c|/Σ|F_d; wR₂ = [Σ_w(F_o²-F₂²)²/Σ_w(F_o²)²]^{1/2}

Table 2. Selected bond lengths (Å) and angles (°) for **1**.

			168.62(8)
Ca(1)-O(1)	2.3486(15)	O(1)-Ca(1)-O(1)#	
Ca(1)-O(2)	2.4764(17)	O(1)-Ca(1)-O(2)	88.83(5)
Ca(1)-O(4)	2.4148(18)	O(1)-Ca(1)-O(4)	84.15(6)
Ca(1)-O(5)	2.434(3)	O(1)-Ca(1)-O(5)	95.69(4)
		O(4)-Ca(1)-O(5)	68.78(4)
P(1)-O(1)	1.5086(16)	O(2)-Ca(1)-O(4)	73.79(5)
P(1)-O(2)	1.5168(16)	O(4)-Ca(1)-O(4)#	137.55(8)
P(1)-O(6)	1.5724(16)	O(2)-Ca(1)-O(2)#	76.90(8)

Symmetry transformations used to generate equivalent atoms:

#1 -x+2,y,-z+3/2   #2 -x+2,-y+1,-z+2   #3 -x+3/2,-y+3/2,-z+2

Table 3. Selected hydrogen bonding distances (Å) and angles (°) for **1**.

D-H...A	<DHA	d(D...A)
O4-H7...O1	169.26	2.786
O4-H1...O6	156.71	2.753
O5-H2...O2	161.64	3.108
O5-H2...O1	130.33	3.072
O5-H3...O1	138.14	3.072
O6-H8...O2	174.55	2.538

Table 4. Selected bond lengths (Å) and angles (°) for **2**

Ca(1)-O(2)	2.5547(14),	O(4)-Ca(1)-O(7)	167.44(5)
	2.3410(13)	O(4)-Ca(1)-O(2)#1	89.53(5)
Ca(1)-O(3)	2.4633(14),	O(7)-Ca(1)-O(2)#1	99.66(5)
	2.493(1)		
Ca(1)-O(5)	2.506(1)		
Ca(1)-O(4)	2.2785(13)	O(4)-Ca(1)-O(3)#2	88.26(5)
Ca(1)-O(7)	2.3408(13)	O(7)-Ca(1)-O(3)#2	100.27(5)
P(1)-O(2)	1.5095(13)	O(2)#1-Ca(1)-O(3)#2	89.50(5)
P(1)-O(6)	1.5092(13)	O(4)-Ca(1)-O(2)	90.98(5)
P(1)-O (5)	1.5808(13)	O(7)-Ca(1)-O(2)	83.75(5)
P(2)-O(4)	1.4963(13)	O(2)#1-Ca(1)-O(2)	157.73(4)
P(2)-O(7)	1.5258(13)	O(3)#2-Ca(1)-O(2)	68.27(5)
P(2)-O(1)	1.5794(13)		

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,y-1/2,-z+1/2   #2 -x+1,y+1/2,-z+1/2

Table 5. Selected hydrogen bonding distances (Å) and angles (°) for **2**.

D-H...A	<DHA	d(D...A)
O(1)-H2p...O(6)	174.25	2.510
O3w-H2w...O(1)	159.59	2.807
O3-H2w...O(5)	115.45	2.988
O3-H1w...O(6)	175.71	2.695
O5-H3p...O(7)	177.56	2.553
O5-H3p...O(1)	112.10	3.088

Table 6. Selected bond lengths (Å) and angles (°) for **3**.

Ca1-O10	2.285(9)	O4-Ca1-O6	144.80(18)
Ca1-O4	2.338(5)	O1-Ca1-O6	119.9(2)
Ca1-O1	2.342(5)	O4-Ca1-O2	78.29(16)
Ca1-O2	2.327(5)	O1-Ca1-O2	138.5(2)
Ca1-O6	2.362(5)	O2-Ca1-O2	72.76(18)
Ca1-O2	2.403(5)	O6-Ca1-O2	88.56(18)
Ca1-O10	3.005(9)	O4-Ca1-O6	144.80(18)
P1-O10	1.472(9)	O1-Ca1-O6	119.9(2)
P1-O2	1.487(5)	O10-Ca1-O4	84.8(3)
P1-O3	1.570(6)	O10-Ca1-O1	84.9(3) .
P1-C4	1.783(7)	O4-Ca1-O1	89.97(17)
P2-O4	1.476(5)	O10-Ca1-O2	149.0(3)
P2-O1	1.497(5)	O4-Ca1-O2	122.58(19)
P2-O5	1.559(6)	O1-Ca1-O2	81.11(19)
P2-C7	1.787(7)		

Figure Captions

Figure 1. A ball and stick representation of the three dimensional structure of $[\text{Ca}(\text{p-C}_8\text{H}_8\text{P}_2\text{O}_6\text{H}_2)(\text{OH}_2)_3]_n$ (1), viewed normal to the ab plane. Atom labeling scheme: calcium, green; phosphorus, purple; oxygen, red; carbon, gray. This scheme is used throughout the figures.

Figure 2. A view of the one dimensional $\{\text{Ca}(\text{RPO}_3\text{H})_2(\text{H}_2\text{O})_3\}_n$ substructure of 1, running parallel to the c -axis.

Figure 3. A representation of the H-bonding scheme of 1; the bonds are shown as dashed blue lines.

Figure 4. A ball and stick representation of the one-dimensional structure of $[\text{Ca}(\text{m-C}_8\text{H}_8\text{P}_2\text{O}_6\text{H}_2)(\text{OH}_2)_3]_n$ (2); the chains run parallel to the b -axis.

Figure 5. A view of the H-bonding for 2.

Figure 6. A view of the two dimensional structure of $[\text{Ca}(\text{o-C}_8\text{H}_8\text{P}_2\text{O}_6\text{H}_2)(\text{OH}_2)_2]_n$ (3), viewed normal to the ac -plane.

Figure 7. A view of a layer of 3 in the ab -plane.

Figure 8. Ball and stick representation of the one-dimensional $\{\text{Ca}(\text{HO}_3\text{PC}_8\text{H}_8\text{PO}_3\text{H})(\text{H}_2\text{O})\}_n$ substructure of 3.

Figure 1.

Figure 2.

Figure 3.

Figure 4.

Figure 5.

Figure 6.

Figure 7.

Figure 8.

Metal-organodiphosphonate chemistry: hydrothermal syntheses and structures Ca(II)
coordination polymers with xylyldiphosphonate ligands

Valerie Lopez, Tiffany M. Smith, Matthew D. Lijewski, Karin Ruhlandt and Jon Zubieta

Graphical Abstract. Hydrothermal reactions were exploited in the syntheses of three Ca(II)-organodiphosphonate materials: the three-dimensional $[\text{Ca}(\text{p-C}_8\text{H}_8\text{P}_2\text{O}_6\text{H}_2)(\text{OH}_2)_3]_n$ (1), the one-dimensional $[\text{Ca}(\text{m-C}_8\text{H}_8\text{P}_2\text{O}_6\text{H}_2)(\text{OH}_2)_2]_n$ (2), and the two-dimensional $[\text{Ca}(\text{o-C}_8\text{H}_8\text{P}_2\text{O}_6\text{H}_2)(\text{OH}_2)]_n$ (3). A view of the structure of compound 1 is shown.