

Preparation and characterization of new hybrid organic/inorganic systems derived from calcium (α -aminoalkyl)-phosphonates and -phosphonocarboxylates

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Abstract

We have studied the phenomenon of calcium complexation by lab synthesized amphiphilic (α -aminoalkyl)-phosphonocarboxylic or -phosphonic acids. The electrical conductivity of aqueous solutions of sodium salts of all these acids was measured versus the volume of a calcium salt solution added. It appeared that calcium complexes are formed in a Ca/P atomic ratio close to 1. Calcium phosphonocarboxylates and calcium phosphonates were also precipitated by mixing aqueous solutions of disodium salts of phosphorus amphiphiles and calcium nitrate solutions. Before chemical analysis, these complexes were calcined to remove the organic part. In the mineralized products, calcium and phosphate were assayed: the Ca/P atomic ratio was equal to 1. X-ray diffraction and IR spectroscopy showed that they are made entirely of β pyrophosphate ($\text{Ca}_2\text{P}_2\text{O}_7$), a result in agreement with previous chemical analysis. The chemical formula of the starting calcium complexes could be written as $\text{CaL}\cdot 2\text{H}_2\text{O}$ (L = ligand). The SEM micrographs of these complexes show plate-like structures. XRD patterns are characteristic of layered structures. These facts suggest that calcium complexes are composed of alternating bimolecular layers of calcium alkylphosphonocarboxylates or calcium alkylphosphonates, the chains being tilted and partially interdigitated.

Keywords: Calcium (α -aminoalkyl)-phosphonates; Calcium (α -aminoalkyl)-phosphonocarboxylates; Conductimetric study; Layered structures

1. Introduction

Metal phosphonates are a rich class of organic/inorganic hybrid materials and have been actively studied in recent years. The fact that the phosphonate group (RPO_3) contains both an inorganic part, which can form part of an inorganic framework, and an organic part, suggests the preparation of novel materials should be possible. The vast majority of these solids are layered and may be modulated by the choice of both organic and inorganic moieties. This modulation can

lead to structural diversity, allowing a wide range of applications such as sorption and ion exchange [1], catalysis [2,3], sensors [4,5] and non-linear optics [4,6,7].

Recently, there has been an interest in the chemistry of calcium phosphonates due to the use of phosphonate-based drugs for diagnosis and therapy of various diseases of bones and for the study of calcium metabolism [8–14]. Bis(phosphonates) are an important class of drugs that have been reported to be active as anticalcification and antiresorption agents and have been used for the treatment of osteoporosis [15]. The usefulness of phosphonates is enhanced by their stability over wide ranges of pH and temperature. Moreover, phosphonates with (P–C) bonds do not hydrolyze in the presence of pyrophosphatase like phosphates and so retain their activity in conditions in which phosphates would be destroyed [16]. Recently, nongeminal bis(phosphonates) with a

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✉ In memory of Dr. Guita Etemad-Moghadam, who directed this work and regrettably passed away on March 2002.

keto group in the α position have been reported to be active as anticalcification and antiresorption agents [17–19]. Furthermore, the calcium coordinating properties of phosphonic acids were examined to arrive at a better understanding of their biological activities (inhibition of metalloenzymes, metabolic regulation, etc.).

In our team, we have synthesized in good yields a series of (α -aminoalkyl)-phosphonocarboxylic and -phosphonic acids [20]. Their fields of application cover chemistry, medicine and agricultural science, due to their various complexing, biological and agrochemical properties [21–23]. We have studied their surfactant properties [24] and their adsorption at the air/water interface on various ion-containing subphases (Na^+ , Ca^{2+} and Mg^{2+}) [25]. The more compact and stable monolayers are formed on the subphase containing calcium ion. This metal presents strong affinity toward phosphorus acids and forms stable dimeric complexes at the interface. Here, we reported the chelating properties of these phosphorus amphiphiles with calcium ion, the characterization of Ca-phosphonocarboxylates and Ca-phosphonates in aqueous solution and in solid state are presented. This study provides an opportunity to produce mixed organic/inorganic systems that could be used to prepare new materials and biomaterials.

2. Materials and methods

2.1. Materials

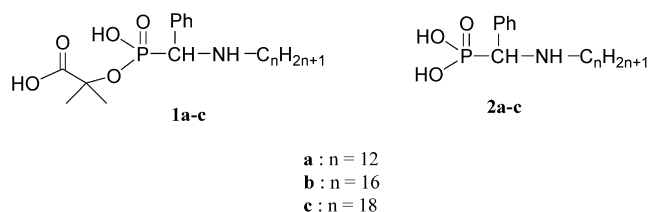
Phosphonic and phosphonocarboxylic acids were synthesized in our laboratory. The calcium nitrate ($\text{Ca}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$) was commercially purchased from Mercks (Purity > 98%).

2.2. Synthesis of surfactants

The synthesis and the characterization of phosphorus amphiphiles, (α -aminoalkyl)-phosphonocarboxylic **1** and -phosphonic **2** acids was already been described in a previous work [20]. The structure of carboxyisobutyl (α -aminoalkyl)-phosphonic acid monoesters **1** and (α -aminoalkyl)-phosphonic acids **2** are shown in Scheme 1.

2.3. Disodium salts of phosphorus acids 1 and 2

Since (α -aminoalkyl)-phosphonocarboxylic **1** and -phosphonic **2** acids are not soluble in water, their sodium salts were prepared using a cation-exchange resin (Amberlite IR120 Na^+ , 2.0 mequiv g^{-1}). The aqueous solution was then freeze-dried to give a white powder. The micellisation parameters of these salts have been described in a previous work and ranging from 0.03 to 1.62 mM [24].



Scheme 1. Structure of (α -amino)-phosphonocarboxylic acids **1a–c** and (α -amino)-phosphonic acids **2a–c**.

2.4. Calcium salts derived from (α -aminoalkyl)-phosphonocarboxylic acids **1** and (α -aminoalkyl)-phosphonic acids **2**

1 equiv. (0.6 mmol) of a solution of calcium nitrate $\text{Ca}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$ (150 mM, pH = 6) in distilled-deionized water was added to 1 equiv. (0.6 mmol) of a solution of disodium salts of (α -aminoalkyl)-phosphonocarboxylic acids **1** or (α -aminoalkyl)-phosphonic acids **2** (15 mM, pH = 8). The Ca-phosphonocarboxylates and Ca-phosphonates precipitated as flocculent solids. The mixture was kept under stirring for 2 h at 25 °C. Samples were then centrifuged, washed with water and dried under vacuum.

2.5. Conductimetric study

This study was carried out on the sodium salts of (α -aminoalkyl)-phosphonocarboxylic **1** and -phosphonic **2** acids (they are soluble in water) in order to examine the interactions between the calcium ions and the anionic heads of these acids **1–2**. To do so, the variation of the ionic conductivity of an aqueous solution of their disodium salts was followed at 25 °C versus the amounts of calcium nitrate solution ($\text{Ca}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$) added. The LF 315-type conductimeter used was from WTW. The conductivity cell was an electrode of the type KLE 315. Its cell constant is 1 cm^{-1} . This conductivity meter has three ranges of sensitivity allowing measurements between 0 and 20 mS. The selected concentrations of phosphorus ligand ranged from 1 to 2.5 mM.

2.6. Analytical methods for calcium complexes

2.6.1. FTIR spectra

FTIR spectra within the range 400–4000 cm^{-1} were recorded with a Perkin–Elmer FTIR 1600 spectrometer from pellets consisting of 1 mg of powder dispersed in 300 mg of KBr.

2.6.2. X-ray diffraction

X-ray diffraction diagrams were obtained with a SEI-FERT XRD 3000 TT diffractometer using the $\text{K}\alpha_1$ radiation of a copper anticathode ($\lambda = 1.5405 \text{ \AA}$).

2.6.3. Scanning electron microscopy (SEM)

The morphology of Ca-phosphonocarboxylates and Ca-phosphonates was examined by SEM on a JEOL Jsm-6400

microscope. The samples were firstly metallized with silver for 2 min in order to avoid the phenomenon of charge accumulation on the surface, which occurs under the electron beam. The samples were then introduced into the apparatus under a vacuum of 10^{-6} mm Hg and observed.

2.6.4. Chemical analysis of Ca-phosphonocarboxylates and Ca-phosphonates

These complexes contain organic matter. It was thus necessary to remove it completely before calcium and phosphorus assays. For this, complexes were heated in air progressively ($4\text{ }^{\circ}\text{C}/\text{min}$) from room temperature to $950\text{ }^{\circ}\text{C}$ and maintained at this temperature overnight. The weight loss of the samples, due to loss of organic matter, was measured carefully. Mineralized samples were dissolved in perchloric acid. More precisely, 50 mg of solid were attacked by 2.5 ml of a perchloric acid solution (2 M), and then adjusted to 50 ml. This solution was used to assay calcium and phosphorus.

2.6.5. Calcium

Calcium was assayed by volumetric titration [26]. The sequestering agent is the disodium salt of ethylene diamine tetraacetic acid (EDTA) in the presence of ammonia. The amount of EDTA in excess was determined with a zinc chloride solution. The indicator was eriochrome black. The error on the calcium content is about 0.5% atom.

2.6.6. Phosphorus

Phosphorus was assayed by colorimetry as phosphovanadomolybdenum ($\lambda = 460\text{ nm}$) [27]. Depending on the Ca/P atomic ratio in the mineralized samples, phosphorus can be present as phosphate and condensed phosphate (pyrophosphate, for example). The latter does not react with the vanadomolybdic reagent. For this, it was necessary to hydrolyze the P–O–P bond beforehand. This hydrolysis was carried out at $100\text{ }^{\circ}\text{C}$ in acid medium: a 10 ml aliquot of the assay solution was taken and 5 ml of a perchloric acid solution (12 M) added to it. It was then heated for 1 h. The resulting solution was used for the colorimetric determination as described previously. The error on the phosphorus content is about 0.5% atom.

3. Results and discussion

3.1. Conductimetric study

The conductivity variations of solutions of sodium salts of (α -aminoalkyl)-phosphonocarboxylic **1** and -phosphonic **2** acids versus the number of calcium ions added in regard to the number of moles of phosphonate initially present in the solution, is shown in Fig. 1 (a case of the disodium salt of dodecylphosphonocarboxylic acid **Na-1a**, for example).

Two straight lines of different slopes can be seen. They intersect at a break-point. Before this point, the added Ca^{2+}

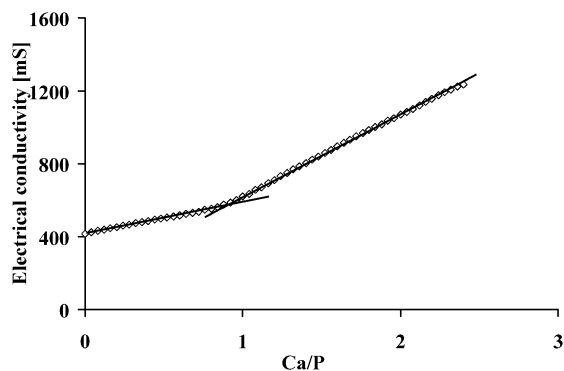


Fig. 1. Plots of electrical conductivity vs Ca/P ratio (number of moles of calcium added/number of moles of phosphonates present) for the disodium salts of dodecylphosphonocarboxylic acid **Na-1a** in aqueous media at $25\text{ }^{\circ}\text{C}$.

Table 1

Atomic Ca/P ratios of calcium complexes derived of **1** and **2** formed in solution and calculated by conductimetric study

C_n	Phosphonocarboxylate		Phosphonate	
	Compound	Ca/P	Compound	Ca/P
12	1a	0.96	2a	0.9
16	1b	0.92	2b	1.02
18	1c	1.05	2c	1

ions react with the phosphorus heads of the surfactant molecules. The slight increase in the ionic conductivity of the solution is thus due to the addition of nitrate ions. Indeed, the calcium complex formed appears as a precipitate and no longer contributes to the conductivity of the solution. After the break-point, a sharp increase in the conductivity of the solution is due to the addition of calcium and nitrate ions and corresponds exactly to the calibration curve obtained with the calcium nitrate solution. Thus, the intersection of the straight lines is the point of equivalence: all the surfactant molecules are bound to calcium ions. The value of the Ca/P ratio at this point, equal to 0.96, indicated that the complex is formed with a calcium/phosphonic acid ratio close to 1, within experimental error.

Conductimetric studies of all α -amino phosphorus acids **1a-c** and **2a-c** led to the same results: the presence of an equivalence point corresponding to the formation of calcium complexes for all compounds **1a-c** and **2a-c**. The Ca/P atomic ratio determined from this point, is reported in Table 1. In all cases, their atomic Ca/P ratios are close to 1. Calcium complexes are formed only for a Ca/L ratio equal to 1.

3.2. Studies of calcium complexes derived from phosphonocarboxylic acid **1** and phosphonic acid **2**

Calcium alkyl-phosphonocarboxylate **Ca-1** or -phosphonate **Ca-2** were prepared by combining an aqueous solution of the disodium salts of the phosphorus acid, **1** or **2** with a solution of calcium nitrate (see experimental part). These

Table 2

Atomic Ca/P ratios of calcium salts of phosphorus acids **1** and **2** calculated by chemical analysis

C_n	Phosphonocarboxylate		Phosphonate	
	Compound	Ca/P	Compound	Ca/P
12	Ca-1a	1	Ca-2a	1
16	Ca-1b	0.98	Ca-2b	1.02
18	Ca-1c	1.01	Ca-2c	0.99

calcium complexes were characterized by various conventional techniques.

3.3. Chemical analysis of complexes

Assays of calcium and phosphorus were performed on calcium alkyl-phosphonocarboxylate **Ca-1** and -phosphonate **Ca-2** samples after heating to 950 °C. They allowed the Ca/P atomic ratio to be determined (Table 2). As can be seen in Table 2, all mineralized calcium complexes present a Ca/P atomic ratio close to 1.

3.4. Loss in weight by mineralization at 950 °C

The loss is due firstly to the decomposition of phosphonate into phosphate with loss of organic matter, and on the other hand, to the departure of structural water molecules present in the complexes **Ca-1** and **Ca-2**. All the experimental losses in weight are in agreement with calculated losses in weight assuming that each molecule of complex contains two water molecules ($\text{CaL}\cdot 2\text{H}_2\text{O}$) (Table 3).

3.5. IR spectroscopy

We compared the infrared spectrum of the phosphorus acids, their disodium salts and their calcium complexes. The study shows similar variations for all the calcium phosphonocarboxylates **Ca-1** or phosphonates **Ca-2**. So, we will describe only one example of each type of these calcium phosphorus salts.

The infrared spectra for dodecylphosphonocarboxylic acid **1a**, its disodium salt **Na-1a** and its complex of calcium **Ca-1a** are shown in Fig. 2.

The characteristic infrared bands of the keto group (C=O) of carboxylic acid **1a** occur at 1724 cm^{-1} . The conversion to the disodium salt **Na-1a** is accompanied by a shift of the peak towards lower frequencies ($\Delta\nu = 115 \text{ cm}^{-1}$).

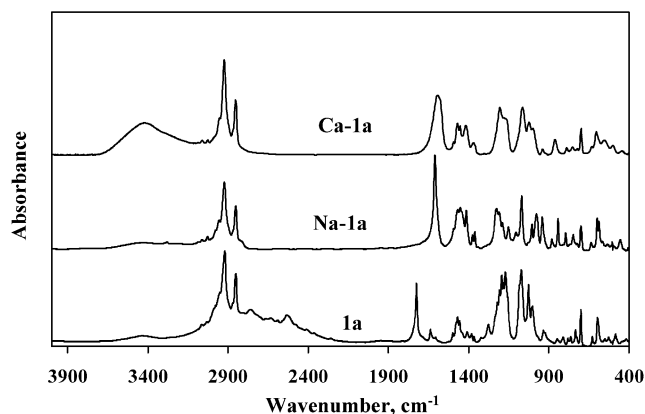


Fig. 2. IR spectra of: (a) phosphonocarboxylic acid **1a**, (b) its disodium salt **Na-1a**, (c) its calcium salt **Ca-1a**.

This indicates the passage to the carboxylate form. Under the effect of binding with the calcium ion, the C=O peak widened and moved 132 cm^{-1} towards lower frequencies. This is explained by the reduction in the double character of C=O group indicating that calcium is coordinated by the oxygen atoms of the carboxylic group. We identified, for free acid **1a** at 1117 cm^{-1} , the characteristic infrared bands (P=O) of the PO_3 group. Two other distinct bands, related to the symmetric and unsymmetric vibrations of the P-OH group, are respectively identified at 1071 and 1025 cm^{-1} .

In the case of disodium salt **Na-1a**, we identified the symmetric and unsymmetric vibration of the anion PO_2^- that occur respectively at 1069 and 977 cm^{-1} . In the case of calcium complex **Ca-1a**, the symmetric vibration of PO_2^- were identified in the region of 1205 and 1170 cm^{-1} . The unsymmetric vibration occurs around 1064 cm^{-1} . The main bands of water molecules occur in the region 3400 cm^{-1} in the case of calcium phosphonocarboxylate **Ca-1a**. We deduce that calcium complexes **Ca-1** are hydrated.

In the case of the free phosphonic acid, we describe the example of phosphonic acid **2a** (Fig. 3).

For acid **2a** we identified characteristic bands (P=O) of the PO_3 group at 1170 cm^{-1} . The P-OH band presents symmetric and unsymmetric vibrations at 1082 and 960 cm^{-1} respectively. In the form of disodium salt **Na-2a**, the two vibrations (symmetric and unsymmetric) at 1101 and 982 cm^{-1} respectively are characteristic of PO_3^{2-} anion. In the case of the calcium complex **Ca-2a**, a large band that occurs at 1080 cm^{-1} characterizes the unsymmetric vibration of the

Table 3

Experimental ratios (final mass of mineralized complexes/initial mass of complexes) and the theoretical ratios calculated for the formulae proposed for complexes $\text{CaL}\cdot 2\text{H}_2\text{O}$

Compound	Phosphonocarboxylate		Compound	Phosphonate	
	m_f/m_i (experimental ratio)	m_t/m_i (theoretical ratio)		m_f/m_i (experimental ratio)	m_t/m_i (theoretical ratio)
Ca-1a	0.249	0.246	Ca-2a	0.294	0.295
Ca-1b	0.21	0.22	Ca-2b	0.262	0.261
Ca-1c	0.218	0.211	Ca-2c	0.25	0.247

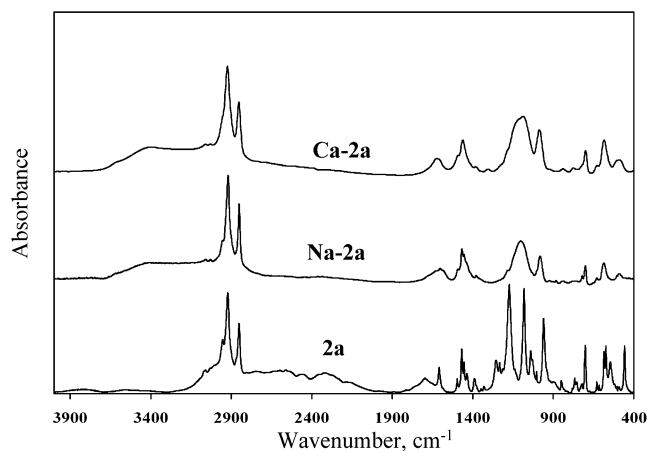


Fig. 3. IR spectra of: (a) phosphonic acid **2a**, (b) its disodium salt **Na-2a**, (c) its calcium salt **Ca-2a**.

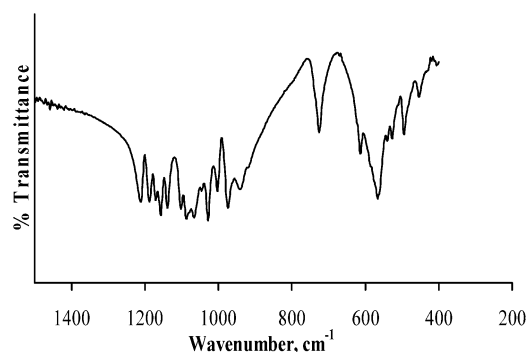


Fig. 4. IR spectra of calcium octadecylphosphonocarboxylate **Ca-1c** after mineralization.

anion PO_3^{2-} . The less intense band at 984 cm^{-1} corresponds to the symmetric vibration of anion PO_3^{2-} . The main bands of water molecules occur in the region 3400 cm^{-1} and at 1616 cm^{-1} . This indicates that the calcium complexes **Ca-2** are hydrated.

We also analyzed the calcined powders of these complexes by IR of the powder and we identified for all complexes **Ca-1** and **Ca-2** the presence only of β pyrophosphate ($\text{Ca}_2\text{P}_2\text{O}_7$). The IR spectrum obtained after mineralization of the calcium complex derived from the phosphonocarboxylic acid with 18 atoms of carbon **Ca-1c** is reported in Fig. 4.

The presence of several narrow bands around 1200 cm^{-1} that have the same order of intensity, an intense side peak at 726 cm^{-1} and band at 566 cm^{-1} are characteristic of β pyrophosphate. This phase having a Ca/P atomic ratio equal to 1 is observed for all complexes. These complexes are thus formed with atomic ratios Ca/P = 1 as we confirmed by the chemical analysis.

3.6. Scanning electron microscope (SEM)

The morphology of the calcium alkyl phosphonocarboxylate **Ca-1** and calcium alkyl phosphonate **Ca-2** was studied

with the scanning electron microscope (SEM). Fig. 5 gives the SEM micrograph of some of the calcium phosphorus complexes prepared and shows the formation of large plate-like crystals. The formation of flat crystals suggests layered structures for these complexes.

3.7. X-ray diffraction

We also analyzed the calcined powders of these complexes by XRD of the powder and we identified, for all phosphorus calcium complexes **Ca-1** and **Ca-2**, the presence of only β pyrophosphate ($\text{Ca}_2\text{P}_2\text{O}_7$). This is in agreement with the chemical analysis and IR spectroscopy done for these complexes.

As seen from Fig. 6, the XRD pattern of the starting calcium dodecylphosphonocarboxylate **Ca-1a** shows an intense low angle peak at $\theta = 1.94^\circ$ ($d = 22.7\text{ \AA}$) characteristic of a layered structure.

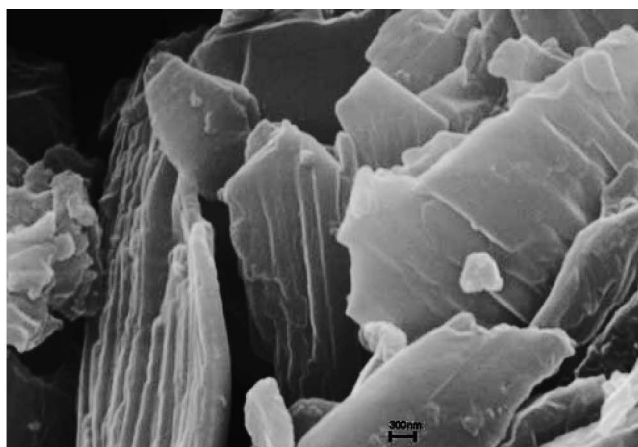
The same XRD pattern is observed for all complexes of calcium **Ca-1** and **Ca-2**. This reveals that calcium alkyl phosphonocarboxylate or phosphonate complexes have a layered structure. The d spacings of these complexes are reported in Table 4.

Firstly, we can observe that d spacing increases with the carbon number of the alkyl groups. Besides, we note that the d spacing is higher for phosphonate complexes **Ca-2** than for phosphonocarboxylate **Ca-1** complexes.

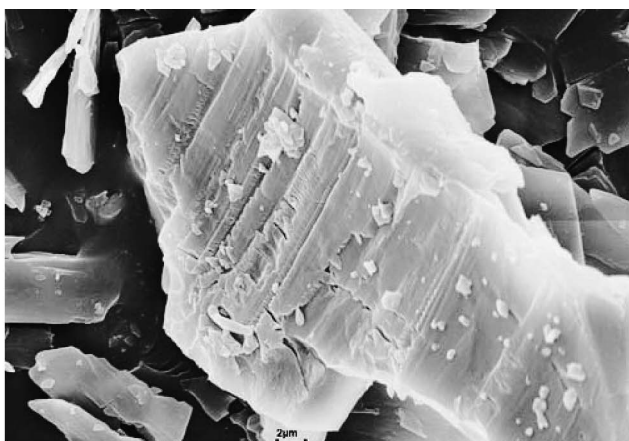
The width of the peaks at half height was measured. It was close to 1° for all calcium phosphonocarboxylates, and only about 0.5° for all calcium phosphonates. This means that there is a difference in the degree of ordering between the two cases.

Calcium phosphonate structures have been reported in the literature [28–32]. However, calcium complexes with long phosphonate chains remain limited and were described as stacked bilayers [29,33]. Most of the reported metal phosphonate structures contain two-dimensional sheets of metal ions joined to the PO_3 groups in such a way that the organic moieties are arrayed above and below the plane of the layer. These layers are therefore effectively phosphonate sandwiches with the metal ion in the middle: $\text{R-PO}_3\text{-M-O}_3\text{P-R}$. This general motif occurs for di-, tri- and tetra-valent metals, aliphatic and aromatic R groups, dibasic and monobasic phosphonates, and anhydrous and hydrated compounds. We found structures similar to Langmuir–Blodgett films. Indeed, these films also have layered structures and are considered as hybrid “organic/inorganic” structures [34].

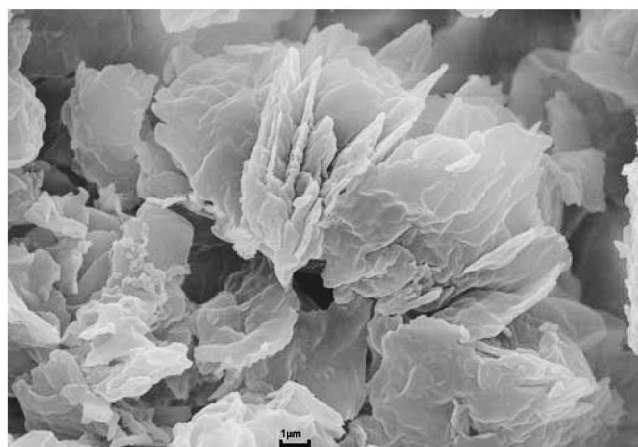
In the present case, the Ca/P stoichiometry is 1, the d spacing of the calcium phosphorus complexes can be regarded as the thickness of the bilayer, made up of organic part (alkyl groups) and inorganic part (calcium ion, phosphonates or phosphonocarboxylates and water). The double layers are held together by electrostatic attractions between calcium ion, phosphonates or phosphonocarboxylates anions and water molecules, while the organic domains interact via van der Waals force. The d spacing found for these com-



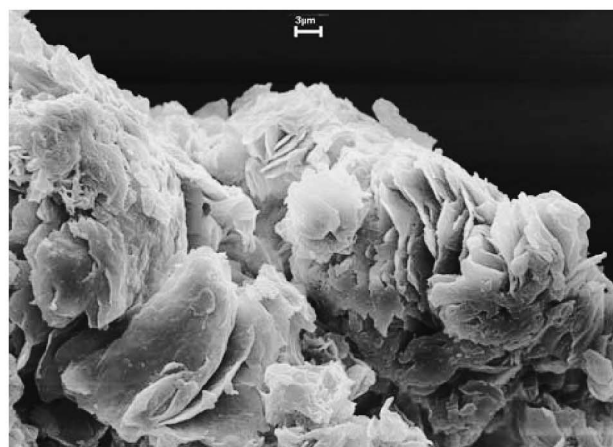
(a)



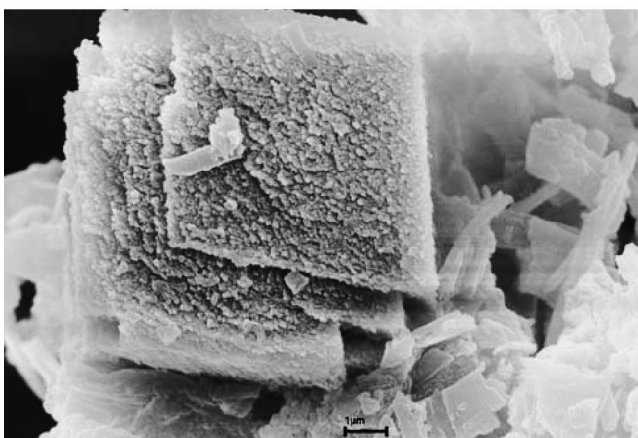
(b)



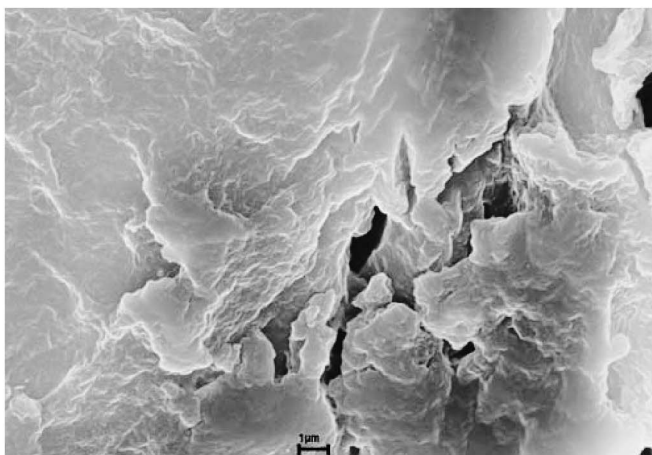
(c)



(d)



(e)



(f)

Fig. 5. SEM micrograph for calcium complexes of phosphorus acids **1** and **2** showing the layered structures: (a) and (b) **Ca-1a**; (c) and (d) **Ca-1b**; (e) **Ca-2a**; (f) **Ca-2c**.

plexes is close to the length of these complexes of calcium **Ca-1** and **Ca-2** estimated by molecular modeling studies. Consequently, the alkyl chains have a tilt angle with respect to the normal of the metal ion plane. We estimated the tilt an-

gle to be around 50° to 60° . In fact, the literature reports calcium complexes where the molecules form a tilt angle compared to the normal with the layers. The Langmuir-Blodgett films prepared starting from the calcium octade-

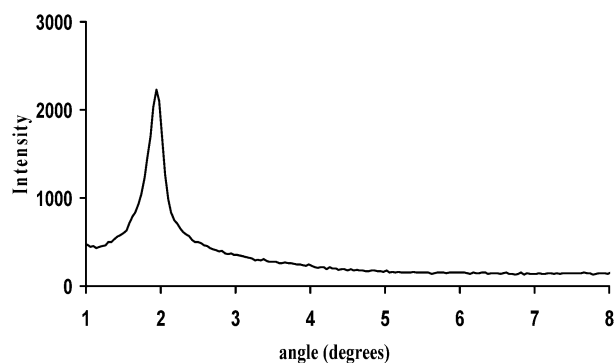


Fig. 6. XRD patterns of calcium dodecylphosphonocarboxylate **Ca-1a** ($\lambda = 1.5405 \text{ \AA}$).

Table 4

d spacing of layered structure of complexes **Ca-1** and **Ca-2** calculated from XRD peaks

C_n	Phosphonocarboxylate		Phosphonate	
	Compound	d (\AA)	Compound	d (\AA)
12	Ca-1a	22.7	Ca-2a	24.8
16	Ca-1b	24.6	Ca-2b	26.6
18	Ca-1c	30.4	Ca-2c	31

cylphosphonates have a layered structure. The alkyl chains tilt at an angle of 42° compared to the normal [34]. In the same way, the angle which the calcium alkyl phosphonates $\text{Ca}(\text{O}_3\text{PC}_n\text{H}_{2n+1})$ ($n > 5$) form compared to the normal is estimated at 60° [28b].

The tilted alkyl chains of the complexes **Ca-1** and **Ca-2** are also interdigitated. We can note that for calcium phosphonocarboxylates **Ca-1**, when the width of the peaks at half height greater, the distance between two atoms of phosphorus is also greater so the alkyl chains of calcium phosphonocarboxylates **Ca-1** should be able to intercalate easily.

4. Conclusion

In this work we present new organic/inorganic systems derived from calcium alkyl phosphonocarboxylates and calcium alkyl phosphonates. These complexes are prepared by combining an aqueous solution of disodium salts of the phosphorus acids and a solution of calcium nitrate. In aqueous media, a conductimetric study showed that complexes are formed with atomic ratios $\text{Ca}/\text{P} = 1$. In the solid state, we characterized the calcium complexes by conventional techniques: chemical analysis, IR, XRD and SEM. Calcium alkyl-phosphonocarboxylates and -phosphonates have a layered structure. The chemical formula of these complexes was $\text{CaL}\cdot 2\text{H}_2\text{O}$. It consists of alternating layers. The alkyl group forms the organic moieties. Calcium ion, phosphonocarboxylates or phosphonates and molecules of water form the inorganic moieties. These new Ca-phosphonocarboxylates and Ca-phosphonates could present

potential applications in the domains of materials and biomaterials.

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