Ab Initio Studies on Organophosphorus Compounds. Part 3.[1,2] Cationic Calcium Binding to Phosphonate and Phosphinate Monoanions and their Sulfur Analogues

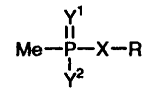
Jari P. Räsänen,[a] Esko Pohjala[b] and Tapani A. Pakkanen*,[a]
[a] *University of Joensuu, Department of Chemistry, PO Box 111, FIN-80101, Joensuu, Finland*
[b] *Leiras Oy, PO Box 33, FIN-33721, Tampere, Finland*

Interactions between cationic calcium and 18 organophosphorus compounds, containing different numbers of oxygen and sulfur atoms, have been studied systematically. All the molecular backbones studied were of the phosphonate or phosphinate type. Molecular structures and calcium orientations through space were calculated by *ab initio* molecular orbital methods with the 3-21G(*) basis set. Different calcium binding sites were found for each molecule. The energetics of the calcium orientations were compared. The results give a quantum chemical reference for experimental studies of many phosphorus-containing biological systems inside living organisms, in which calcium(II) regulates cell functions. Examples of such systems are the bisphosphonate–osteoclast interactions in osteolytic bone diseases.

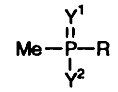
Calcium binding to phosphorus-containing molecules has been found to be very important in the biosphere. Calcium is essential for biological processes. It is a major component of different types of skeletal structures inside many living organisms, and a small amount of calcium is also present in body fluids and soft tissues. This minor amount of Ca^{II} has an important role in maintaining several biochemical processes. It regulates many cell functions, for example neurotransmitter-releasing processes, chemotaxis, exo- and endo-cytosis and many enzymic activities[3] and interactions between bisphosphonate–bone–osteoclasts.[4] Because all the above mentioned reaction mechanisms include some unknown factors, extensive experimental and theoretical research work with phosphorus–calcium systems is still needed. Interactions between some phosphorus-containing compounds and cationic alkaline and alkaline-earth metals have been studied earlier by *ab initio* MO methods.[5–8] With theoretical calculations three different types of binding model have been found for the coordination chemistry of Li^+, Na^+ and PO_3^-. Systems may form monodentate, bidentate or tridentate structures. The $LiPO_3$ and $NaPO_3$ complexes have been studied with 3-21G(*) and 6-31G* basis sets and the preferred coordination for both is bidentate.[5] Interactions between anionic $H_2PO_4^-$ and monovalent Li^+, Na^+, $CH_3NH_2H^+$ or divalent Be^{2+}, Me^{2+} have been calculated.[7,9–11] The interaction energies of Ca^{2+}–carboxy, –carbonyl and –water groups have been studied by *ab initio* molecular orbital methods.[12,13] Nevertheless a very limited number of studies, giving theoretical calculations of interactions between cationic Ca^{2+} and phosphorus-containing compounds, exist.[14–16]

Because some organophosphorus compounds have been used as pharmaceuticals, *e.g.* biphosphonates,[17,19] their reactions with cationic calcium need to be studied. In this study, the binding sites of calcium have been investigated with several monoanionic methylphosphonate, methyl methylphosphonate, methylphosphinate and dimethyl phosphinate compounds and their sulfur analogues. The general structures of the calculated compounds with the main atomic numbering schemes of the molecules are shown below. More data are presented in Fig. 1 and Table 1.

Conformational analyses were performed for all the cases studied. As a result, several different binding sites of calcium and corresponding molecular conformations for each molecule were found. All the observed minimum energy conformations with calcium were fully optimized. Molecular geometries were investigated to find out the substituent effects of oxygen and sulfur. Because the 3-21G(*) basis set was applied to the study of intermolecular interactions, it was important to use counterpoise correction to reduce the error in calculated interaction energies. Solvent effects of the interaction pairs studied have been calculated using the self-consistent reaction field (SCRF) method. SCRF calculations with different solvents and molecules have been studied effectively earlier by Wong *et al.*[20–23] They have reported that a correlated version of Onsagers's formalism will provide a good qualitative understanding of the effect of the electrostatic interaction of the ionic or neutral dipolar species with its surrounding medium.[20–23]



$$\mathrm{Me{-}\overset{\overset{\textstyle Y^1}{\|}}{\underset{\underset{\textstyle Y^2}{|}}{P}}{-}X{-}R}$$



$$\mathrm{Me{-}\overset{\overset{\textstyle Y^1}{\|}}{\underset{\underset{\textstyle Y^2}{|}}{P}}{-}R}$$

R = H or Me
Y^1, Y^2, X = O or S

Computational Methods

To study interactions between the metal ion and the phosphorus compounds, Hartree–Fock SCF-MO calculations were performed with GAUSSIAN 90 and 92 programs[24,25] on SGI 4D/35 and Indigo R4000/Elan computers. Molecular backbone geometries were optimized with 3-21G(*) and 6-31G* basis sets as in our earlier work.[1,2] Through-space interactions of calcium with phosphonates and phosphinates were calculated with the 3-21G(*) basis set. The split valence basis set for calcium was taken from the work of Dobbs and Hehre,[26] in which the 3-21G(*) basis set was formed from the 3-21G basis by the addition of a set of single d-type Gaussian functions. For normal and hypervalent compounds the 3-21G(*) basis set has been found to predict geometrical results that are in good agreement with experimental values and the values of the higher levels of theoretical calculations.[26–29] The 3-21G(*) basis set level has been used lately with calcium–malonate interactions.[30] The basis set superposition error (BSSE) between calcium and molecular backbone orbitals was calculated for all the compounds studied. Estimations of the effects of aqueous solvation have been performed using the SCRF method of GAUSSIAN 92.[25]

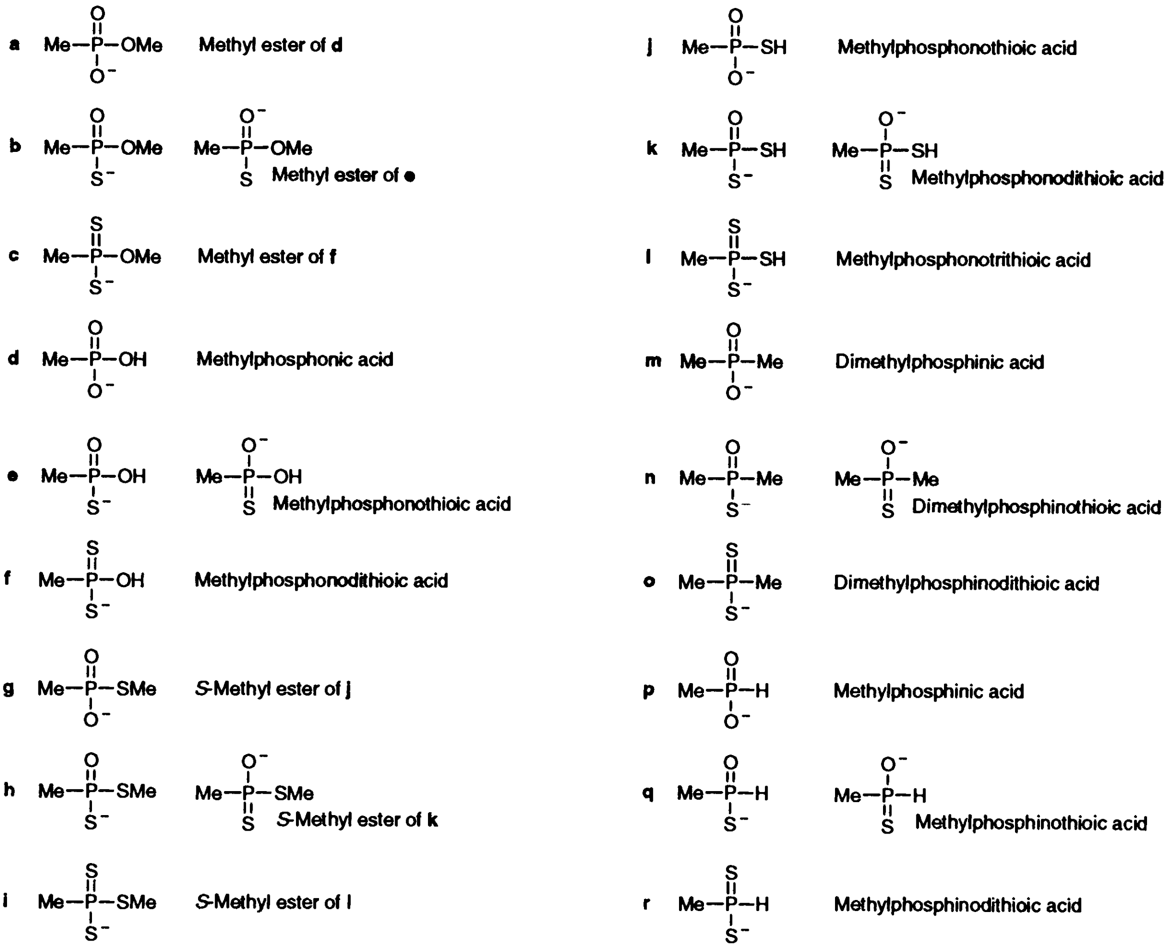


Fig. 1 Structural formulae of the compounds studied. Interactions with Ca^{2+} were calculated for all the monoanions presented.

Results and Discussion

The optimized anionic phosphonate structures **a**-**l** without calcium have X-P-C angles from 96 to 102°.[1,2] Compounds **a**-**l** have P-O and P-S bond lengths in the ranges of 148-149 and 197-199 pm, respectively.[1,2] Experimental values for single P-O and double P=O bonds are 156/145 pm and for the corresponding sulfur analogues, 210/192 pm.[29,31] The value of the free P-O bond length in earlier work was 147 pm for the free monoanion of dimethyl phosphate (or DMP^-) with 3-21G(*) up to 6-31 + G* basis sets.[15,31] Teraishi *et al.* have reported an r[P-O] value of 152 pm with the MP2/6-31 + G* level.[32] *Ab initio* MO studies for $CH_3CH_2P(S)Cl_2$ have predicted the P=S bond to be 190 pm.[33] Eighteen anionic phosphorus compounds **a**-**r** (Fig. 1) were selected from previous studies[1,2] for a detailed calcium binding analysis. Interatomic distances and calculated energies of the oxygen and sulfur compounds studied are shown in Table 1. The conformational analyses were performed in steps: (1) rigid conformational analysis; (2) partially optimized conformational analysis and (3) geometry optimization.

(1) *Rigid Conformational Analysis.*—In the first stage a rigid conformational analysis was performed. The study with the series of single point calculations was made to produce preferred calcium orientations around the molecular backbone. The Ca-Y bond length was parametrized to be 210 pm.[14] The Ca-Y-P bond angle was rotated between values 80 and 90 and 100°. The Ca-Y-P-C torsional angle was rotated 360° in steps of 30° (Fig. 2). All the other molecular parameters were fixed. If Y^1 and Y^2 are different atom types, then both were used to define the torsional rotations of the metal ion. Energy diagrams for all molecules give minimum energy conformations in Ca-Y-P-C torsional angle ranges, 60-90 and 210-240°. In addition, the third energy minimum of some compounds is about 180°. All energy curves predict a global minimum near 240° as shown in Fig. 3. In that preferred orientation, calcium was near the axis that bisects the Y^1-P-Y^2 angle.

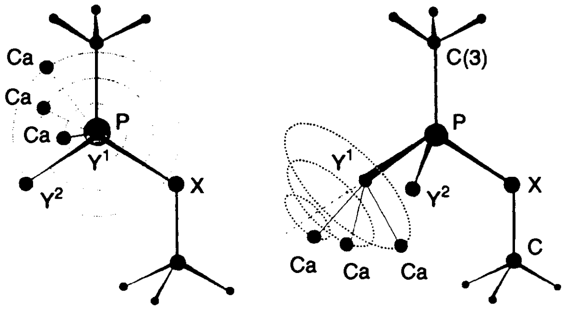


Fig. 2 The main principle of the conformational analysis. Analysis was made by rotating the Ca-Y(1/2)-P-C(3) torsional angle with steps of 30°. X, Y^1 and Y^2 are oxygen or sulfur atoms.

(2) *Partially Optimized Conformational Analysis.*—In the second stage, four compounds (**a**, **b**, **d** and **e**) were selected for a detailed partially optimized conformational analysis. In this procedure all the molecular parameters except the rotatable Ca-Y-P-C torsional angle were optimized free. Calculated relative energy curves of the analysis are shown in Fig. 4. In this figure, the curves for structures **a** and **d** are 1 and 4, respectively. Structures **b** and **e** each have two curves, because calcium binding to the Y atom (oxygen or sulfur) was studied separately with respect to Ca-O-P-C and Ca-S-P-C torsional angles.

Table 1 Selected interatomic distances between calcium and the phosphonate or phosphinate backbone. Total energies and the relative energies of different conformations and BSSE corrections.

	Substituent				Distance (pm)						E_{rel} [d]/kJ mol^{-1}		
	X	Y[1]	Y[2]		r(Ca–X)	r(Ca–Y[1])	r(Ca–Y[2])	E_{tot} [a]/au	E_{int} [b]/ kJ mol^{-1}	E_{BSSE} [c]/ kJ mol^{-1}	E_R	E_{SCRF}	E_{R+BSSE}
a	O	O	O	min 1	403	224	224	−1314.710 18	−1376.7	120.2	0.0	0.0	0.0
				min 2	230	216	395	−1314.687 28	−1316.6	104.0	60.1	17.3	43.9
b	O	O	S	min 1	426	219	283	−1635.901 04	−1295.4	77.8	0.0	0.0	0.0
				min 2	254	225	303	−1635.890 63	−1268.1	87.0	27.3	52.5	36.5
				min 3	226	413	272	−1635.859 49	−1186.4	59.3	109.1	60.9	90.6
c	O	S	S	min 1	456	278	278	−1957.077 25	−1189.3	34.2	0.0	0.0	0.0
				min 2	243	289	296	−1957.074 92	−1183.2	54.3	6.1	24.6	26.3
d	O	O	O	min 1	387	224	225	−1275.896 51	−1372.5	120.5	0.0		0.0
				min 2	406	224	224	−1275.895 27	−1369.2	119.4	3.3		2.2
				min 3	229	216	395	−1275.874 31	−1314.2	110.3	58.3		48.1
e	O	O	S	min 1	424	219	285	−1597.085 74	−1281.3	78.9	0.0		0.0
				min 2	410	220	284	−1597.084 04	−1276.9	80.0	4.5		5.6
				min 3	250	225	307	−1597.076 09	−1256.0	91.0	25.3		37.4
f	O	S	S	min 1	239	293	296	−1918.260 61	−1174.8	58.5	0.0		0.0
				min 2	457	279	279	−1918.260 54	−1174.6	34.3	0.2		−24.1
g	S	O	O	min 1	419	225	225	−1635.899 41	−1330.0	107.9	0.0	0.0	0.0
h	S	O	S	min 1	441	219	285	−1957.092 20	−1260.7	74.7	0.0	0.0	0.0
				min 2	443	220	284	−1957.091 77	−1259.5	73.6	1.1	−7.7	0.0
i	S	S	S	min 1	466	279	279	−2278.275 44	−1174.1	32.9	0.0	0.0	0.0
				min 2	502	278	279	−2278 273 51	−1169.1	32.8	5.1	−11.6	5.0
j	S	O	O	min 1	421	226	225	−1597.076 00	−1319.4	108.8	0.0		0.0
				min 2	421	225	226	−1597.076 00	−1319.4	108.7	0.0		−0.1
k	S	O	S	min 1	445	220	285	−1918.268 55	−1248.7	73.6	0.0		0.0
l	S	S	S	min 1	468	279	279	−2239.451 06	−1155.4	32.5	0.0		0.0
m	—	O	O	min 1	—	224	224	−1240.234 66	−1393.8	116.0	0.0	0.0	0.0
n	—	O	S	min 1	—	219	283	−1561.428 29	−1308.0	77.6	0.0	0.0	0.0
o	—	S	S	min 1	—	278	278	−1882.611 74	−1204.3	34.1	0.0	0.0	0.0
p	—	O	O	min 1				unstable					
q	—	O	S	min 1				unstable					
r	—	S	S	min 1	—	280	280	−1843.767 01	−1181.2	33.3	0.0		0.0

[a] E_{tot} = total energy of the compounds calculated with the 3-21G(*) basis set. [b] E_{int} = interaction energy between calcium and the phosphonate or phosphinate backbone. [c] E_{BSSE} = the amount of BSSE correction. [d] E_R = relative energies for different compounds. E_{SCRF} = relative energies of SCRF calculations for different compounds. E_{R+BSSE} = relative energies for different compounds with BSSE corrections.

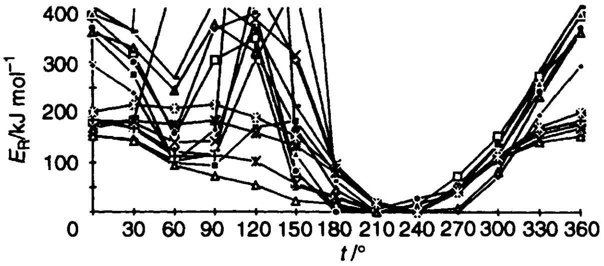


Fig. 3 Rigid conformational analysis with single-point calculations after every 30° rotational step of defined Ca–Y(1/2)–P–C(3) torsional angle. Curves are the calculated relative energies for all compounds with H_3C–P–X–CH_3 and H_3C–P–CH_3 backbones. The preferred range is around 240°.

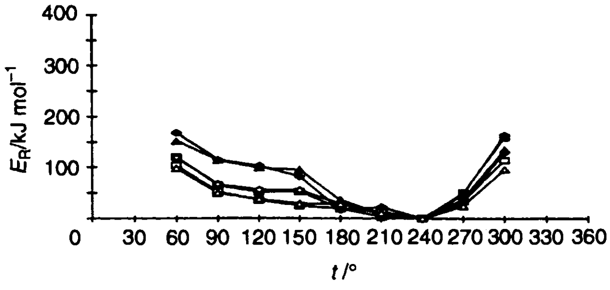


Fig. 4 Partially optimized conformational analysis, in which after every 30° increment all other parameters have been relaxed. Compounds studied were **a**, **b**, **d**, **e**. The preferred range is around 240° as in Fig. 3. Curves 1 (■) and 4 (◇) belong to the **a** and **d** molecules, respectively. Curves 2 (□) and 3 (◆) are for **b** and 5 (▲) and 6 (△) are for **e**. In molecules **b** and **e** both Ca–O–P–C and Ca–S–P–C sides (Y[1] = O and Y[2] = S) have been studied.

Curves 2 and 3 belong to structure **b** and the corresponding series 5 and 6 to structure **e**. The energy results (shown in Fig. 4) are in good agreement with the previously discussed rigid model calculations (shown in Fig. 3) where a Ca–Y–P–C torsional angle near to 240 °C is preferred for calcium binding.

(3) *Geometry Optimization of Calcium Complexes.*—Three different calcium orientations were selected for each molecule as starting-points of geometry optimization. The selection was based on the number of energy curve minima in the above-discussed conformational analysis. If the curves predict only two energy minima for the compound, the third value of the torsional angle of 180 ° was included in the calculations. Full optimization was made for selected calcium binding models. As a result, several different bidentate and tridentate calcium orientations were found for the molecules studied. The optimized parameters of calcium binding are presented in Table 1.

After adding the interaction to the calculated molecular system, the average values of the X–P–C angle are 105° for structures **a**–**f** (X = oxygen) and 108° for **g**–**l** (X = sulfur), respectively. Calculated O–C and S–C bond lengths are 147 and 183 pm, respectively. Because of the calcium interaction, the P–O and P–S bond lengths are somewhat longer than those observed without calcium. The global minimum energy conformations of the phosphonate molecules **a**–**f** (X = oxygen)

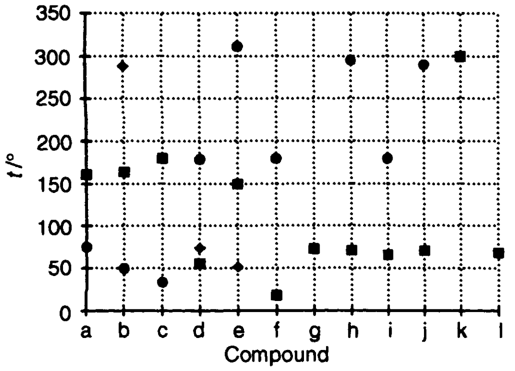


Fig. 5 Calculated ranges of the torsional R–X–P–C angles of the molecular backbone for compounds **a**–**l** (R = H or CH_3). Data points give all the observed conformational minima for each system. Molecules **a**–**c** and **d**–**f** have –O–CH_3 and –O–H tails. Corresponding compounds **g**–i and **j**–**l** have –S–CH_3 and –S–H tails.

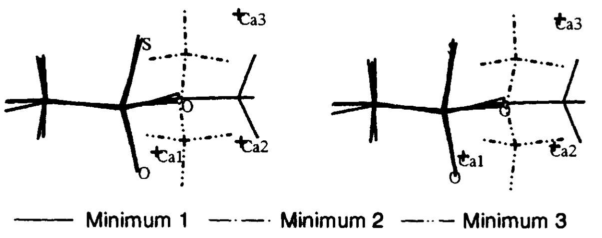


Fig. 6 Three calculated conformational minima of compound **b**. Different calcium binding sites are labelled in the order of preference Ca1, Ca2 and Ca3. The methyl group is turned as far as possible from calcium.

studied have an average P–X distance of 157 pm. If Y^1 and Y^2 are oxygen atoms, bond lengths P–Y^1 P–Y^2 have average values of 153 pm. If Y^1 and Y^2 are sulfur atoms, the same bonds have values of 201 pm. The second and third minimum energy conformations have P–X bonds about 10 pm longer than the first minima. There are no significant changes in P–Y^1 and P–Y^2 bond lengths in different conformations of the molecules with X = O. In experimental studies on the crystal structure of the $CaCl_2MDP$,[33] the average value given for r[P–O] is 152 pm.[33] The previous experimental value [33] is in good agreement with above discussed calculated theoretical results of this study. In the present study the global minimum energy conformations, values of 129–131 and 121–125° are reported for the R–O–P angle, with R = CH_3 and R = H, respectively. If all the calculated conformations of each structure with the R–O–P angle are taken into consideration, the range of variation is 117–131°.

In the phosphonate molecules **g**–**l** (X = sulfur), the average bond length of P–X is 206 pm, while that of both P–Y^1 and P–Y^2 (Y^1 and Y^2 = sulfur) is 203 pm. If Y^1 and Y^2 are oxygen atoms, the same bonds have values of 154 pm. There are no significant changes in P–X, P–Y^1 and P–Y^2 bonds in different conformations of the structures. The values of the molecular backbone bond angles R–S–P are 100–102 and ~97° for minimum energy conformations, with R = CH_3 and R = H, respectively. If all calculated conformations of molecules with R–S–P are considered, the range is 97–102°. In general the R–S–P angles have been found to be smaller than the corresponding R–O–P angles. Compounds **a**–**l** have several conformations with different orientations of the –X–R tail. Collected values of the R–X–P–C torsional angles are presented in Fig. 5. Three different ranges of angles were found for the torsion angles discussed above. Firstly, the R–X–P–C backbone is about 160°. Secondly, there are two bent torsions ~55 and ~300°. The torsional angle of the tail depends mainly on the proportion of oxygen and sulfur atoms in the molecular backbones. In general, the –X–R tail is oriented to the opposite side of the calcium.

Phosphinate structures **m**–**o** have an eclipsed orientation of methyl groups, and compound **r** has staggered hydrogen and methyl groups. The calculated average values of the Ca–O and Ca–S distances are similar to the corresponding phosphonate–calcium systems. The C–P–C angles in the **m**–**o** compounds changes in the range of 106–107° and in **r**, the H–P–C angle has a value of 105°. According to calculations, structures **p** and **q** were unstable with the 3-21G(*) level.

Energetically, the most stable conformations for compounds **a**–**r** have been reached, when the metal cation is in the Y^1–P–Y^2 plane and bisects the angle (Y^1–P–Y^2). When atoms Y^1 nd Y^2 are of the same type, a very symmetrical orientation of the cation towards the molecular backbone exists (*e.g.* Table 1, structure **a**, minimum 1). When the compound has atoms Y^1 = oxygen and Y^2 = sulfur, the preferred binding of the cation is in the same plane, but more turned towards the sector of the oxygen side (*e.g.* Fig. 6, structure **b**, minimum 1, where r[Ca–Y^1] = 219 and r[Ca–Y^2] = 283 pm). Average calculated internuclear distances for the calcium–oxygen and calcium–sulfur pairs are 222.8 and 280.8 pm, respectively. In experimental studies on the crystal structure of calcium dichloromethylenediphosphonate ($CaCl_2MDP$),[34] the value given for the Ca ··· O distance is 236 pm.[34] For the same compound, the theoretically calculated value of the Ca ··· O distance with the 3-21G(*) level has been predicted to be 214 pm.[14] The molecular backbones with the –X–CH_3 (**a**–**c**, **g**–**i**) and the –X–H (**d**–**f**, **j**–**l**) tails have similar distances between Ca and X atoms. The differences between the distances change from 1 to 16 pm, and the greatest value is reached when Y^1, Y^2 and X are all oxygens. When the amount of sulfur in the molecular backbone increases, the distance differences between similar molecular pairs with –X–CH_3 and –X–H tails decrease. In comparing the effects of the hydrogen and methyl groups, one should note that the electron donating nature of a methyl group is greater than that of hydrogen. The methyl group pushes the electron density towards X (X = O or S), resulting in a decreasing interaction and an increasing distance between the calcium and the X atom. The calcium–sulfur distances have been found to be about 65–66 pm greater than those of calcium–oxygen. Both the electronegativity and the radii of the oxygen and sulfur atoms influence the calcium orientation. Calcium distances as a function of the Y^1, Y^2 and X atoms are presented in Table 1. In the **a**–**f** and **g**–**l** series the Mulliken charges follow this trend, as the charge on phosphorus decreases, the amount on sulfur increases. For example, with compounds **a**–**c** Mulliken charges of 1.7, 1.5 and 1.1, respectively were calculated for the phosphorus atom.

The second type of energy minimum for the bidentate structures has been reached when the metal cation is in the Y^1–P–X or Y^2–P–X plane and bisects previously defined angles (*e.g.* Table 1, structure **a**, minimum 2 and Fig. 6, structure **b**, minimum 3, where r[Ca–X] = 226 and r[Ca–Y^2] = 272 pm). In general, calcium has more freedom to select a binding site on, above or below that plane, than it had in the case of the most stable conformations. Calcium prefers to interact with an oxygen, when a choice of space orientation sectors between the oxygen or sulfur side of molecules exists. The third type of energy minimum was found to be a tridentate system, in which the calcium is on the top of a trigonal pyramid, based on atoms Y^1, Y^2 and X (*e.g.* Table 1, structures: **b**, **c** minimum 2 and **f** minimum 1). An example of tridentate binding is presented in Fig. 6: structure **b** minimum 2, where the internuclear distances from Ca to X, Y^1, Y^2 are 254, 225 and 303 pm, respectively.

Phosphinate-type structures **p** and **q** were found to be unstable when the basis set at the 3-21G(*) level was used. All the other calculated structures, **a**–**o** and **r**, have one or more energetically stable conformations. In general, interaction energies follow this trend: when the amount of sulfur increases in the molecular backbone, the interaction energy decreases. Structure **a** (minimum 1) with three oxygen atoms and an -O-CH_3 tail, has an interaction energy of -1377 kJ mol^{-1}. When the same molecular backbone has three sulfur atoms, structure **i** (minimum 1), the corresponding value is -1174 kJ mol^{-1}. The relative energies of the different conformations were calculated for all the compounds studied. In phosphonate structures **a**–**f**, where X = oxygen, clear differences of relative energies between the conformations are shown. Energy variations depend on both the calcium binding sites and the -X–R tail orientations with respect to the molecular backbone. Relative energy differences stem mainly from the calcium binding site. When different conformations of the same structure are compared, the relative energy effect of the -X–R tail orientation is approximately ~5 kJ mol^{-1}. If the calcium binding site *versus* the molecular backbone changes, then the conformational relative energies change in the range 24–54 kJ mol^{-1}. Differences between relative conformational energies almost disappear with the **g**–**l** systems, where the binding position of the calcium is almost stable and only the orientation of the -X–R tail changes. Calculated phosphinates **m**–**r** have only one energy minimum for each compound.

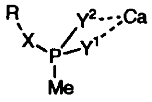
The influence of the basis set superposition error (BSSE) was calculated for all compounds **a**–**r** studied. The range of the energy correction change is 3–9%. In earlier theoretical work the BSSE, calculated at the 3-21G level for interactions between $H_2PO_4^-$ and Na^+, was 18%. The correlation correction with the previous anion and Li^+ and Mg^{2+} cations was below 5%.[7] The BSSE corrections calculated at the minimum basis set level for a Ca^{2+} and malonate or formate ligand system were 15–28%.[35] The split valence basis sets have been found to predict better results.[36] The calculated BSSE corrections for the compounds of this study seem to be in good agreement with earlier theoretical results. The highest and lowest values of the BSSE correction for compounds **a**–**r** studied are 121 and 33 kJ mol^{-1}, respectively. With the phosphonate compounds the general order of the energy minima between different conformations with the same backbone remains unchanged in spite of the inclusion of the BSSE correction. The only difference is structure **f**, in which the standard energy calculation predicts the tridentate coordination to be the most stable. When the BSSE correction is taken into account, the same bidentate form is the preferred global minimum, which was the commonly found interaction mode in the other systems studied. The variation ranges of the BSSE corrections are the same in the dimethyl phosphinate **m**–**o** compounds. In the case of methyl phosphinate **p**–**r** type compounds, only the disulfur system **r** has a stable interaction model with calcium and a BSSE correction of about 3%. Dioxygen **p** and oxygen–sulfur **q** systems were unstable with calcium. Generally, with phosphonate and phosphinate compounds, the BSSE correction has the highest value when the molecular backbone includes the maximum amount of oxygen atoms. The trend of the correlation correction is the same with -X–H and -X–CH_3 type phosphonate structures.

Solvent effects for the compounds studied have been calculated with the SCRF method.[25] In this procedure the dipole of the molecule will induce a dipole in the medium, which will interact with the molecular dipole to lead to net stabilization. SCRF energies were calculated using a single point method with the 3-21G(*) basis set for all conformations found for compounds **a**–**c**, **g**–**i**, **m**, **n** and **o**. Relative energies of different conformations are presented in Table 1. The solute was placed in a spherical cavity immersed in a continuous water medium. The relative permittivity used was $\varepsilon = 78.54$ (298 K).[37] Molecular volume calculations with 3-21G(*) level were used to produce solute radius for the compounds studied.

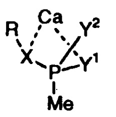
Reaction field results agree with the general order of energy minimum of conformations especially in the case of calcium binding sites. Although water as medium changes the order of minima of compounds **h** and **i**, the calcium orientation will stay unchanged in these structures and only the methyl group turns from one side of the molecule to the other side. The SCRF had a very small influence on the Mulliken populations of the molecules studied. Because the calculated reaction field depends on the molecular dipole and polarizability, it is obvious that the SCRF model can produce only a crude model for water as media for the calcium–molecule pairs studied. The reaction field model of interaction energies between spherical cationic calcium and anionic phosphorus compounds is quite unrealistic, because the Ca^{2+} ion will not be affected by a reaction field since it has no dipole moment. It is a fact that Ca–water interactions are a very important part of the presented interaction studies and they should be taken care of effectively. In spite of this, calculated qualitative gas phase models can be used as starting points for further studies between calcium–water–phosphorus compounds.

Conclusions

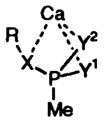
In this study interactions between several organophosphorus compounds of phosphonate and phosphinate type and calcium ion were calculated. Molecular structures were optimized with the 3-21G(*) basis set. Energy values were corrected by BSSE. Solvent effects were studied by SCRF methods. Different calcium binding sites were found for each compound. In the preferred model of binding, bidentate coordination, the position of the calcium was defined by the Y^1–P–Y^2 plane, and the axis that bisects the angle (Y^1–P–Y^2). Other minima were found to be of the bidentate and tridentate type, in which the atom X takes part in calcium interactions. In other words, the position of calcium was defined by *e.g.* the Y^1–P–X plane, and the axis that bisects the angle (Y′–P–X). In the tridentate model calcium, Y^1, Y^2 and X were all in the interaction distance. Calculated different calcium binding types are shown below, where the bidentate 1 complex is the global minimum (or minimum 1) whereas the bidentate 2 and tridentate forms are higher energy conformations.



Bidentate 1



Bidentate 2



Tridentate

R = H or Me

Y^1, Y^2, X = O or S

If oxygen and sulfur compete for calcium binding, the cation locates preferentially closer to oxygen than to sulfur. Average distances Ca–O and Ca–S were 223 and 281 pm, respectively. It seems the reported theoretical results provide a suitable basis for further molecular orbital studies on calcium interactions in biological systems.

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