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Symmetry of Posner's Cluster

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Understanding the fundamental structure of clusters with a Ca/P molar ratio of 1.5 is important because clustering is implicated in the formation process of hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$; HAP), which has a chemical and structural resemblance to bone and tooth minerals.[1,2] The description of the HAP structure was first reported in 1964,[3] and its interpretation in terms of aggregation of $Ca_9(PO_4)_6$ clusters, the so-called Posner's clusters, has been widely used since the publication of the article reported in ref 1. A major step in the understanding of the biomineralization process was done when an amorphous calcium phosphate (ACP) was shown to be the precursor of HAP in vitro in a solution supersaturated as highly as a physiological solution.[4] This ACP has a Ca/P molar ratio of 1.45 ± 0.05[4] and it has been proposed that it consists of roughly spherical $Ca_9(PO_4)_6$ Posner's clusters close-packed to form larger spherical particles with water heals in the interstices.[1] However, this structural model was obtained solely by X-ray radial distribution function analyses[1,3] and there has been much debate regarding the structure of ACP with other structural candidates proposed.[5] Analysis of the ACP through ab initio calculations has not yet been reported, and we have therefore initiated a series of theoretical works on this subject. Due to the low resolution of the experimental data we have studied alternative candidates for ACP such as $Ca_3(PO4)_2$[6] and $Ca_6(PO4)_4$[7] clusters. Posner's cluster appears to be energetically favored in comparison with these alternative candidates.[8] Should Posner's cluster be the correct structural model of ACP, its geometry in this environment remains to be determined. In our first attempt to determine the geometry of Posner's cluster in the ACP environment, we analyzed the geometrical changes encountered while transferring the cluster from the HAP structure to an isolated form.

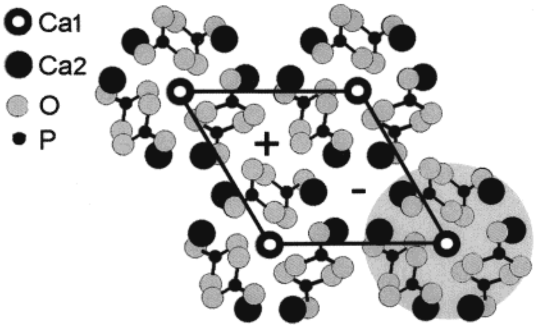

Figure 1. Schematic representation of the hydroxyapatite ($Ca_{10}(PO_4)_6$-$(OH)_2$; HAP) crystal projected on the *ab* plane. Four Posner's clusters $Ca_9(PO_4)_6$ of identical chirality are represented. The rest of the atoms, two OH groups and one Ca atom per unit cell, are incorporated in the voids among the clusters and form positive and negative columns parallel to the *c*-axis. The surface of the unit cell is delimited by black lines. One Posner's cluster is highlighted. Note that the aggregation of three Posner's clusters of identical chirality around the positive column leads to the formation of a supplemental Posner's cluster of opposite chirality. Note also the arrangement of symmetry D_{3d} of six calcium atoms around the negative center which permits minimization of the repulsion among these positively charged calcium atoms and the optimization of their interaction with the negative column.

The Posner's cluster found in the HAP structure has a C_3 symmetry and contains two types of calcium atoms which differ in their coordination and bonding properties. The first type, Ca1, consists of a set of three calcium atoms positioned at $z = 0$, $^1/_2$, and 1 levels on the 3-fold rotation axis parallel to the crystallographic *c*-axis. The second type, Ca2, consists of a set of six calcium atoms positioned three by three on the mirror planes at $z = ^1/_4$ and $^3/_4$ (see Figure 1). The HAP structure contains two distinct $Ca_9(PO_4)_6$ cluster units with different chirality: one is that centering on the Ca1 site at the $z = 0$ level, while the other is that centering on the Ca1 site at the $z = ^1/_2$ level, sharing half of their volumes. They have a noncentrosymmetric C_3 symmetry resulting from the 3-fold rotation axis parallel to the *c*-axis and are mirror images with respect to the mirror planes at $z = ^1/_4$ and $^3/_4$. Therefore, they are right- and left-handed chiral clusters. Using ab initio methods and restricting the discussion to structures containing the C_3 operation of symmetry, the chiral feature of Posner's cluster is shown to disappear when the cluster is isolated. The cluster adopts a centrosymmetric S_6 symmetry. In isolated form, finite size effects alter the geometry of the cluster. In particular, the Ca1 atoms positioned on the 3-fold rotation axis at $z = 0$ and 1 have 6 neighboring oxygen atoms in the HAP structure while they have only 3 neighboring oxygen atoms in isolated form. We have performed the calculations within the restricted Hartree−Fock (HF) and B3LYP schemes using a split valence plus polarization (SVP) basis set quality.[9,10] This basis set quality has been shown to correctly describe the potential energy surfaces (PES) associated with calcium phosphate clusters.[6] Geometrical data and relative energies obtained from the B3LYP scheme have been selected throughout the article.

We stress here the novel idea that the two chiral forms of the cluster can be understood as being the clockwise and anticlockwise distortions from the D_{3d} point group symmetry. In the course of the study, this distortion will be of central importance. This distortion leads to the dimerization in atomic distances in the HAP structure, in particular those between consecutive Ca2 atoms present on the circumference of the cluster (see Figure 2), and can be analyzed through a dihedral angle α defined in Figure 2. The Ca2a−Ca2b and Ca2b−Ca2c distances and the angle α are 0.42 nm, 0.58 nm, and 38.4° in the HAP structure in comparison with identical Ca2a−Ca2b and Ca2b−Ca2c distances and an angle α of 60° in a D_{3d} structure.

We studied Posner's cluster starting from the D_{3d} symmetry and gradually reduced the symmetry to lower subgroups. Within the D_{3d} symmetry, we found two different isomers varying in the orientation of the PO_4 groups on the σ_v planes (see Figure 3).

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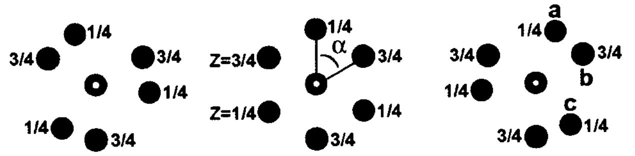

Figure 2. Top view of the nine calcium atoms of Posner's cluster forming a D_{3d} arrangement (center) or two chiral C_3 arrangements (left and right). Note that exactly three Ca1 atoms are present on the C_3 axis. The *z*-height of each calcium atom is specified. α is the dihedral angle defined by the atoms labeled a and b and the C_3 axis. This figure is applied identically for the comparison of the two chiral forms of the D_3 isomer with the centrosymmetric S_6 isomer.

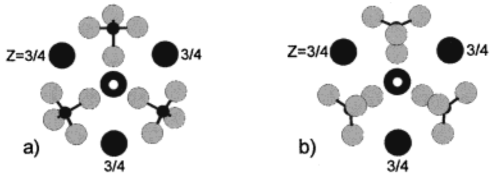

Figure 3. Top view of the two isomers of symmetry D_{3d}. Only the top halves of the clusters are represented. The *z*-height of each calcium atom is specified. The position of the atom forming the lower half is obtained by application of a S_6 operation. Note that 3 Ca2 atoms are present on the C_3 axis, and that the isomers a and b differ in the orientation of PO_4 groups.

They correspond to an energy of 0.0 and −10.0 kcal/mol. We formed the distortions of geometry of these two isomers by calculating isomers corresponding to all the subgroups of the D_{3d} point group containing a C_3 axis. The first distortion is obtained by conserving the symmetry operation σ_v forming the group C_{3v}. Taking the two D_{3d} isomers as initial geometries, we obtained, after optimization of geometry, a single isomer located on the PES between the two D_{3d} isomers. In this isomer, 3 PO_4 groups are organized in a manner similar to those of the D_{3d} isomer corresponding to Figure 3a and 3 PO_4 groups are organized in a manner similar to those of the D_{3d} isomer corresponding to Figure 3b. The energy associated with this isomer is −80.5 kcal/mol. The second distortion is obtained by conserving the symmetry operation C_2 forming the group D_3. Taking the two D_{3d} isomers as initial geometries, we obtained a single isomer located on the PES between the two D_{3d} isomers. This distortion is similar to the one seen in the HAP structure and leads to dimerization of the atomic distances of consecutive Ca2 atoms on the circumference of the cluster (see Figure 2). This leads to the appearance of two chiral forms for this D_3 isomer, which correspond to an energy of −121.5 kcal/mol. A third distortion is obtained by conserving the rotary-reflection axis to form the S_6 group. We obtained a single isomer which corresponds to an energy of −132.5 kcal/mol. The two D_3 chiral clusters can be described as clockwise and anticlockwise distortions of this S_6 isomer (see Figure 2). In the D_3 isomer, the optimized values for the Ca2a−Ca2b and Ca2b−Ca2c distances and for the angle α are 0.373 nm 0.393 nm, and 52.5°, respectively. The chemical interpretation of the energy stabilization in the S_6 isomer in comparison with the D_3 chiral forms is that the S_6 isomer has the distinct feature of preserving the arrangement of symmetry D_{3d} of the six neighboring oxygen atoms around the central calcium atom. This minimizes the repulsion between the negatively charged oxygen atoms and optimizes their interaction with the positively charged calcium atom. Figure 4 shows the arrangement of atoms in the S_6 isomer. A partial configuration interaction procedure within the HF orbitals has been attempted for the S_6 and D_3 isomers. As previously reported,[11] the electron correlation contributions to the electronic energy are large. Nonetheless, this does not significantly change the energy difference between the S_6 and D_3 isomers (see Supporting Information). Allowing the simultaneous occurrence of all these distortions leads to the point group C_3. Starting from the atomic position of the HAP crystal, the optimization of the geometry of Posner's cluster conducted within the C_3 group leads to the S_6 isomer. This shows that Posner's cluster can reach this isomer without being trapped in a higher energy minimum. The increase in symmetry could be obtained even while conducting the calculation within the C_3 group because this group is a subgroup of the S_6 symmetry group. Considering a starting geometry of symmetry C_i, which is the second subgroup of the S_6 symmetry group, leads to the identical result, i.e., the convergence to the S_6 isomer. From vibrational frequency calculations performed at the HF level, the D_3 and S_6 isomers were found to correspond to energy minima with a zero-point vibrational energy of 81.0 and 81.1 kcal/mol, respectively. In contrast, the C_{3v} isomer does not correspond to an energy minimum. Distorting its geometry according to the normal modes associated with imaginary frequency enables us to define two starting geometries of C_3 symmetry, which lead, after geometry optimization, to the S_6 and D_3 isomers. The D_{3d} isomers do not correspond to energy minima. This could be anticiped because we have obtained the C_{3v}, D_3, and S_6 isomers by restarting the calculations, with lower symmetry constraints, from the D_{3d} optimized geometries.

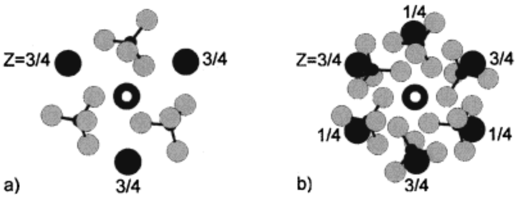

Figure 4. Top view of the isomer of symmetry S_6: (a) top half of the cluster and (b) full cluster. The *z*-height of each calcium atom is specified. Note the arrangement of symmetry D_{3d} of six oxygen atoms around the central positively charged calcium atom.

The chirality of Posner's cluster in the HAP structure arises from the geometrical distortion analyzed in Figure 2. The chemical interpretation of this distortion in the HAP is that it optimizes the 6 Ca2 positions around the OH negative column, forming an arrangement of symmetry D_{3d} (see Figure 1). This minimizes the repulsion between the positively charged calcium atoms and optimizes their interaction with the negatively charged column. We have optimized the geometry of a system composed of one Posner's cluster surrounded by three OH^- groups fixed at the position of the HAP negatively charged columns (see Figure 1S). The presence of OH^- induced the geometrical distortion analyzed in Figure 2. In aqueous or ACP environments this geometrical distortion is unexpected because structural orders similar to the HAP negatively charged columns are not likely to exist. Similarly, this distortion does not stabilize Posner's cluster in an isolated form. We are currently performing ab initio calculations to verify the existence of Posner's cluster in an aqueous solution. The attempt of this computational challenge is motivated by the recent demonstration of the presence of calcium phosphate clusters in an aqueous solution with dimensions similar to those of Posner's cluster.[12]

Because of the lack of precise experimental data, it has been a common practice to represent Posner's cluster in an ACP environment by its geometry observed in the HAP structure.[1,12] We have demonstrated that the structure of Posner's cluster in isolated form is notably different from that in a HAP environment. In particular, the chirality feature of Posner's cluster found in the HAP environment is suggested to disappear in a isolated form and in aqueous solution. Based on our findings, we recommend the reconsideration of any structural assertion related to Posner's cluster in the actual structural model of ACP and in the cluster growth model of the HAP crystal.[12]

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Supporting Information Available: Tables with HF, B3LYP, MP2, and CISD energies; HF and B3LYP optimized geometries; the optimized geometry of $Ca_9(PO_4)_6(OH^-)_3$ (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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