A New Oligomeric Complex of Cyclic Hydrogenphosphonates with Calcium Perchlorate

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A hybrid organic/inorganic material is obtained with calcium as the structural building block. The structure of this new oligomeric complex was confirmed by a single crystal X-ray diffraction, which shows the bridging position of the calcium ions between four dioxazaphosphocane moieties.

Methylenebisphosphonates, also known as geminal bisphosphonates, are analogues of pyrophosphates and are also characterized by a P−C−P bond. These compounds with various side chains linked to the central carbon atom, like Etidronate® or Clodronate®, have been extensively studied and widely used in treating various diseases of bone and calcium metabolism.[1−3]

Whereas monophosphonates have been reported to be inactive with respect to calcium related disorders,[4] the presence of a potential donor group adjacent to the phosphonate moiety (as in α-acylphosphonates or α-hydroxyiminophosphonates) restores this activity.[5] Despite the large number of bis-phosphonates investigated for their biological activity or even used clinically, structural studies of their calcium complexes are very limited. However, a common feature of the few structural studies reported is that the Ca ion forms bidentate chelates with two oxygen atoms.[6−7]

In this field, we have synthesized, in the past few years, new eight-membered cyclic hydrogenophosphonates named dioxazaphosphocanes. These cyclic and nonionizable phosphodiesters, with two donor groups (carbonyl and phosphoryl) in the same molecule, display interesting complexing properties towards alkaline earth metal cations.[8]

The complexing properties of the dioxazaphosphocane moiety have been demonstrated in the solid state by an X-ray structure determination. It revealed an original polymeric arrangement which is in accordance with the previously claimed stoichiometry and the data obtained by classical physical methods (NMR and IR spectroscopy).

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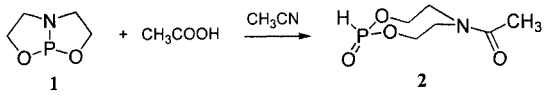
The synthesis of dioxazaphosphocanes, based on the reactivity of a constrained bicyclophosphane, was developed in our laboratory.[9] Scheme 1 shows the synthesis of compound **2**, studied in this paper, which is obtained by an oxidative addition reaction of acetic acid to the bicyclophosphane **1**.[10]



1 **2**

Scheme 1

By a single crystal X ray diffraction analysis, we have recently demonstrated that the dioxazaphosphocane **2** adopts a crown conformation in the solid state.[11] This conformation is retained in solution according to the ^{1}H and ^{13}C NMR spectra, thus meaning that the phosphoryl and carbonyl groups are in favourable positions for complexation.

We have already observed the formation of a well-defined complex from the reaction of dioxazaphosphocane **2** with calcium perchlorate. Comparison of the IR spectra of the free ligand and of the complex shows shifts to lower frequencies for the carbonyl ($\Delta\nu_{C=O}$ = 22 cm^{-1}) and phosphoryl ($\Delta\nu_{P=O}$ = 14 cm^{-1}) stretching vibrations; hence they are both involved in the complexation. Moreover, interaction of the phosphoryl group with calcium was confirmed by ^{31}P NMR spectroscopy ($\Delta\delta^{31}{}_{P}$ = 0.9 ppm; $\Delta^{1}{}_{JPH}$ = 32 Hz). The chemical formula of complex **3** [$CaL_2{\cdot}(ClO_4)_2$ (with L = compound **2**)] is consistent with a 1:2 stoichiometry (one calcium atom for two heterocycles) as determined by elemental analysis, and from these results we previously proposed a sandwich-type structure, with the calcium atom being located between two dioxazaphosphocane moieties.

A single crystal X-ray diffraction analysis of this complex (Figure 1) confirmed that the complexation actually involves the phosphoryl and carbonyl groups.

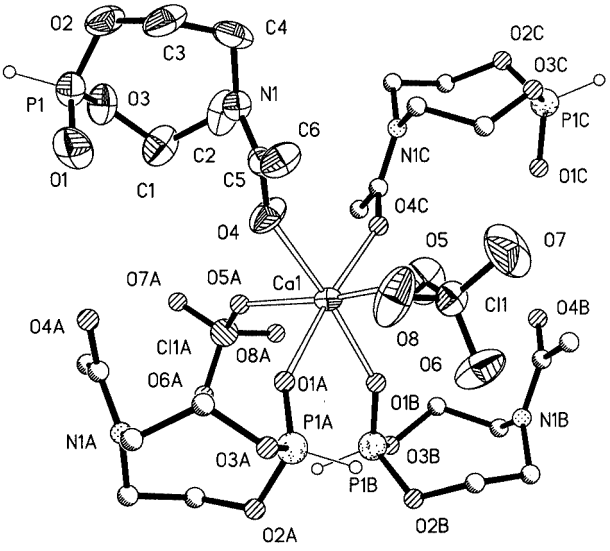


Figure 1. Structure of **3** in the solid state; the asymmetric unit is drawn as a thermal ellipsoid diagram at the 50% probability level; the figure shows the coordination environment of the Ca cation; except for the hydrogen atom bonded to the phosphorus, all others hydrogen atoms have been omitted for clarity; selected bond lengths [Å] and angles [°]: Ca−O1A 2.280(6), Ca−O4 2.281(5), Ca−O5 2.36(4), O1A−Ca−O1B 85.0(4), O1A−Ca−O4 92.5(2), O1A−Ca−O4C 174.3(2), O1A−Ca−O5 91.5(5), O1A−Ca−O5C 92.9(5)

However, calcium is not located between two dioxazaphosphocane moieties, but is bridged between four heterocycles leading to the formation of a one-dimensional polymeric material in which the metal plays the role of a template element. However, and in contrast to the solid state, the sandwich-type structure is not unlikely in solution. It is important to notice that in complex **3** the dioxazaphosphocane moieties retain the crown conformation previously determined for the free ligand.

Ca^{2+} generally accepts a coordination number of eight or nine,[12] and its coordination shell is either full, or completed with one molecule of solvent (e.g. H_2O, CH_3CN, THF). A coordination number of six, while less common, leads to well-defined octahedral complexes.[13] This latter arrangement is found in antibiotics like Benastatine A[14] or Griseocheline.[15] In complex **3** the calcium atom is coordinated to six oxygen atoms, four from four different dioxazaphosphocane moieties and two from perchlorate anions. The charge neutrality of the complex is maintained by perchlorate anions located on both parts of the mean plane formed by the other complexing oxygen atoms from two carbonyl groups and two phosphoryl groups for each calcium ion. The Ca−O distances are in the range 2.37−2.26 Å and there are no other Ca−O contacts less than 3.2 Å to indicate any additional coordination of Ca.

The most prominent common structural feature is the arrangement of the $[CaL_2]\cdot(ClO_4)_2$ units (L = dioxazaphosphocane **2**) in polymeric chains, where the metal centers are connected by bridging dioxazaphosphocane groups (Figure 2).

An examination of Ca/dioxazaphosphocane complex formation under physiological conditions is in progress, because in many biomineralizing systems organized organic assemblies serve as inductive templates for mediating the nucleation and growth of inorganic crystals.

Experimental Section

3: $[Ca(ClO_4)_2\cdot 6H_2O]$ (0.37 g, 1.08 mmol) in MeCN (30 mL) was added to a solution of dioxazaphosphocane **2** (0.42 g, 2.17 mmol) in MeCN (50 mL). The mixture was stirred at room temperature for 10 min. Slow evaporation of the solvent produced colorless crystals of **3** (0.48 g, 70%). ^{31}P NMR (80.96 MHz, CH_3CN, 298 K): $\delta = 8.8$ ($^1J_{PH} = 760$ Hz) ppm. $C_{12}H_{24}CaCl_2N_2O_{16}P_2$ (624.98): calcd. C 23.04, H 3.84, N 4.48; found C 23.13, H 3.65, N 4.49.

Crystal Data for 3: $C_{12}H_{24}CaCl_2N_2O_{16}P_2$, $M = 625.25$, monoclinic, $C2/c$, $a = 15.067(5)$ Å, $b = 12.271(4)$ Å, $c = 13.564(4)$ Å, $\beta = 94.792(6)°$, $V = 2499.2(13)$ Å^3, $Z = 4$, $\rho_c = 1.662$ Mg m^{-3}, $F(000) = 1288$, $\lambda = 0.71073$ Å, $T = 193(2)$ K, μ(Mo-K_α) = 0.669 mm^{-1}, crystal size 0.2 × 0.2 × 0.05 mm, $2.14° < \Theta < 23.25°$, 4459 reflections (1761 independent with $R_{int} = 0.0638$) were collected at low temperatures with an oil-coated shock-cooled crystal on a Bruker-AXS CCD 1000 diffractometer. The structure was solved by direct methods (SHELXS-97)[16] and 209 parameters were refined using the least-squares method on F^2.[17] All non-hydrogen atoms were refined anisotropically. The hydrogen atoms of the molecules were idealized geometrically and refined using a riding model. The hydrogen atom bonded to the phosphorus atom was located by a difference Fourier procedure. A disorder of the ClO_4 anion was refined anisotropically with the help of 202 ADP and distance restraints. Largest electron density residue: 0.599 e·Å^{-3}, R_1 [for $I > 2\sigma(I)$] = 0.0711 and $wR_2 = 0.1795$ (all data) with $R_1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$ and $wR_2 = [\Sigma w(F_o^2 - F_c^2)^2/\Sigma w(F_o^2)^2]^{0.5}$.

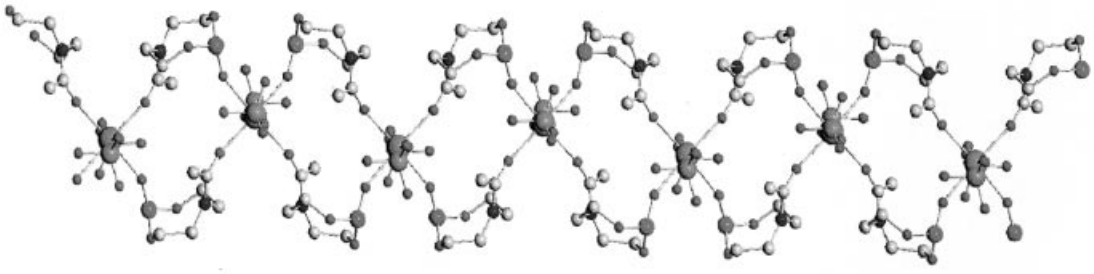


Figure 2. Ball-and-stick view showing the polymeric nature of **3**

CCDC-178965 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) +44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

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