MAGNETIC RESONANCE

IT has become customary to hold a workshop in magnetic resonance each year at Varian Associates in Palo Alto, California. At these workshops new workers are introduced to the principles and practice of nuclear magnetic resonance and electron paramagnetic resonance, while those already experienced in the fields have the opportunity to discuss new developments. This custom has been adopted by the Swiss daughter company, Varian *A.G.*, the second annual workshop of which was recently held at its Research Laboratory in Zurich during September 24–28.

Lectures and laboratory demonstrations in both subjects were offered, the lectures being given in the main building of the University of Zurich while practical work was conducted at Varian's Research Laboratory. The introductory lecture to the first part of the programme—devoted to high-resolution nuclear magnetic resonance—was given by Dr. E. Rogers of Varian Associates, who was one of the Bloch group during the early days of nuclear resonance. Dr. J. N. Shoolery, also of Varian Associates, talked about the theory of nuclear magnetic resonance spectroscopy during the following two lectures, thus providing a foundation for the interpretation by the participants themselves of high-resolution spectra. Further instruction in spectra interpretation and in spectrometer operation was given by Dr. P. von Philipsborn of the University of Zurich, Dr. R. J. Abraham of the University of Liverpool, and Dr. A. Melera of Varian *A.G.* The instrumentation of nuclear resonance spectrometers was discussed by Mr. R. Wenk of Varian *A.G.*, and the course was finished by Dr. Abraham with a lecture about recent applications of proton coupling constants in organic chemistry.

The introductory lecture to electron paramagnetic resonance was given by Dr. A. Horsfield of Varian *A.G.*, and this was followed by a lecture on free radicals in solution by Dr. A. Carrington of the University of Cambridge. Dr. J. Combrisson from the French Atomic Energy Authority at Saclay talked about the applications of double resonance and the Overhausser effect in chemistry. The principles of electron paramagnetic resonance instrumentation were given by Mr. R. Tschudin of Varian *A.G.* An account of oriented free radicals in crystals was given by Dr. A. Horsfield, and Dr. A. Carrington gave a second lecture on transition metal ions and the triplet state as studied by electron resonance. Prof. R. Adams of the University of Kansas, in closing the course, spoke of the use of electron paramagnetic resonance techniques in electrochemistry. Practical work included instruction in the analyses of electron paramagnetic resonance spectra and demonstrations with an electron resonance spectrometer were given.

A total of ninety participants attended the workshop, representing most of the countries in Europe. A ladies' programme was arranged for the wives of the conference members and a workshop dinner was held at one of the old guild-houses of Zurich. It is planned to hold another workshop in magnetic resonance in Zurich in September 1963.

OCTACALCIUM PHOSPHATE AND HYDROXYAPATITE

Crystal Structure of Octacalcium Phosphate

OCTACALCIUM phosphate (OCP), also called tetracalcium hydrogentriphosphate, $Ca_4H(PO_4)_3 \cdot 2{\cdot}5H_2O$, is frequently encountered in systems containing calcium phosphates more basic than dicalcium phosphate[1–4], and it appears to have a significant role in the chemistry of bones, teeth, phosphate fertilizers, and other precipitated calcium phosphates (see following communication). Its existence as a distinct crystalline phase rather than a hydrous 'defective apatite' has been questioned[5,6], but was established by single crystal[7] and powder-diffraction X-ray studies[8]. Its X-ray, optical, and chemical properties indicate[7] that OCP is structurally related to hydroxyapatite (HA), although the two salts are not isostructural, and that OCP is composed of apatitic layers that are parallel to the *b–c* plane and separated by hydrated layers. The structure of OCP, a preliminary account of which is given here, is in accordance with these indications. The method of preparation of OCP is described in the following communication.

The following unit-cell constants of OCP were used in the structure analysis:

$a = 19{\cdot}87$ Å $\alpha = 89° 17'$
$b = 9{\cdot}63$ Å $\beta = 92° 13'$
$c = 6{\cdot}87_5$ Å $\gamma = 108° 57'$
$Z = 2(Ca_8H_2(PO_4)_6 \cdot 5H_2O)$ Space group, $P1$ or $P\bar{1}$

The centrosymmetric space group, $P\bar{1}$, which was assumed in the analysis, was verified by the success of the structure determination. Chemical analyses do not yield constant numbers of waters of hydration, and this uncertainty reflects the ease with which water enters and leaves the OCP lattice. The cell contents listed in the tabulation were used in the final structure refinement which required 172 positional and thermal parameters for the 8 calcium, 6 phosphorus, and 29 oxygen atoms in the asymmetric unit. Eleven scale factors were included also, but the parameters of the 12 unique hydrogens were omitted, so that a total of 183 parameters was used. Altogether, 2,332 independent structure factors were utilized in the refinement; of these, 1,419 were from intensities measured photometrically and 913 from intensities estimated visually. Most of the visually estimated intensities were those of reflexions too weak to be measured photometrically.

The initial structure approximation was derived from Patterson sections, $P(U,V,W)$, at levels $W = 0$, 1/4, and 1/2. Positions in two dimensions for the eight calciums and five of the phosphates were derived mostly from a series of ($hk0$) Fourier projections. The remainder of the structure was determined by a series of three-dimensional Fourier syntheses and least-squares refinements which brought the dis-

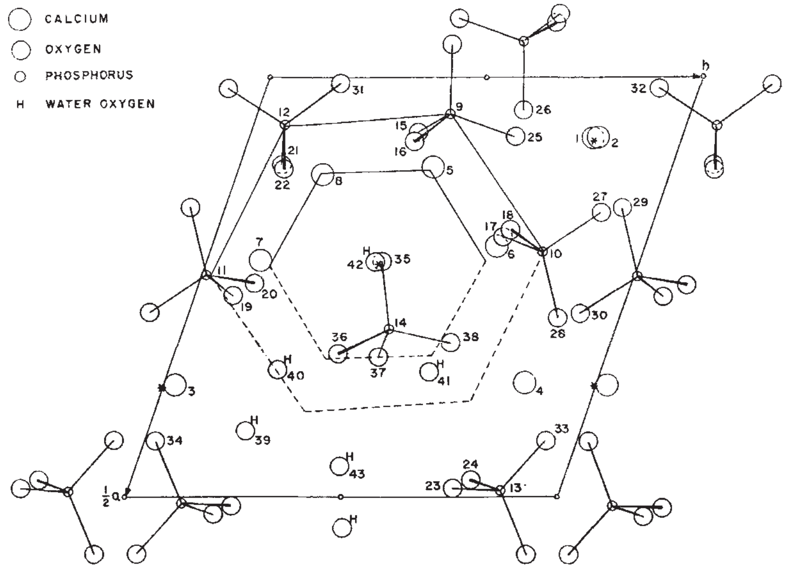

Fig. 1

agreement between the observed and calculated structure factors within 12 per cent. The averages for the estimated standard deviations in the positional parameters are 0·005 Å for the calciums, 0·006 Å for the phosphorus atoms, 0·021 Å for the phosphate oxygens, and 0·045 Å for the water oxygens.

The atomic parameters of OCP are listed in Table 1 and the structure, projected down the *c* axis, is shown in Fig. 1. The numbering of atoms in the figure corresponds with that in Table 1. The corners of the larger hexagon in Fig. 1 are the phosphorus sites as they occur in HA[9], and the corners of the smaller hexagon are the calcium sites. Only four of the sites on each of these hexagons are filled in OCP. The sites of the missing atoms are shown connected by broken lines. Four phosphorus positions of OCP closely match those of HA; but this is less true for the four calciums, particularly Ca(6) and Ca(7). A water molecule, O(41), appears to have replaced a missing calcium. The remaining four calciums of HA comprise two pairs of 'column' calciums. In OCP, one of these pairs, Ca(1) and Ca(2), is in virtually the same position as in HA, in which the two calciums lie one above the other in the position marked by the asterisk. The other pair of column calciums is split in OCP—one, Ca(3), is quite near its HA site as shown by the asterisk, and the other, Ca(4), is shifted by about 1·5 Å parallel to the *b* axis. The structure of OCP is a close copy of that of HA for small values of *x*. In the region where *x* approaches the value 1/4, the dissimilarities become quite apparent, and at larger values of *x* there is no similarity between the two salts. The region defined approximately by $1/4 > x > -1/4$ is referred to as the 'apatite layer'.

Table 1. ATOMIC POSITIONS OF OCTACALCIUM PHOSPHATE

Atom number	Parameter *x*	*y*	*z*
Ca(1)	0·0717	0·7929	0·0048
Ca(2)	0·0702	0·8055	0·5029
Ca(3)	0·3660	0·0246	0·0226
Ca(4)	0·3628	0·8339	0·5313
Ca(5)	0·1071	0·4490	0·7617
Ca(6)	0·2016	0·6600	0·2745
Ca(7)	0·2178	0·1250	0·7697
Ca(8)	0·1153	0·2006	0·2606
P(9)	0·0431	0·4473	0·2576
P(10)	0·2073	0·7703	0·7749
P(11)	0·2348	0·0096	0·2736
P(12)	0·0562	0·0708	0·7577
P(13)	0·4922	0·8646	0·2668
P(14)	0·3001	0·4748	0·2455
O(15)	0·0638	0·3836	0·0744
O(16)	0·0751	0·3835	0·4312
O(17)	0·1897	0·6638	0·5986
O(18)	0·1812	0·6769	0·9556
O(19)	0·2589	0·0867	0·0798
O(20)	0·2452	0·1271	0·4356
O(21)	0·1031	0·0981	0·5766
O(22)	0·1072	0·1030	0·9404
O(23)	0·4891	0·7499	0·1045
O(24)	0·4803	0·7856	0·4661
O(25)	0·0693	0·6141	0·2600
O(26)	0·0386	0·6095	0·7360
O(27)	0·1600	0·8727	0·7506
O(28)	0·2852	0·8573	0·7889
O(29)	0·1547	0·9172	0·2606
O(30)	0·2803	0·9085	0·3103
O(31)	0·0075	0·1677	0·7543
O(32)	0·0133	0·9075	0·7606
O(33)	0·4317	0·9276	0·2311
O(34)	0·4332	0·0284	0·7404
O(35)	0·2187	0·4045	0·2111
O(36)	0·3272	0·3791	0·3976
O(37)	0·3335	0·4730	0·0520
O(38)	0·3153	0·6280	0·3236
O(39)	0·4212	0·2259	0·2577
O(40)	0·3481	0·2501	0·8202
O(41)	0·3506	0·6046	0·7244
O(42)	0·2205	0·3886	0·7743
O(43)	0·4618	0·4718	0·6508

Of the remaining two phosphate ions, the one near the lower edge of the figure, P(13), ties the apatite layers together, and the other, P(14), lies in the region which in HA is occupied by the two 'hexagonal' calcium atoms which are missing in OCP. One of the oxygen atoms, O(35), of P(14) lies in the centre of the hexagon and occupies an OH^- site of HA. The other OH^- site of HA is occupied in OCP by a water molecule, O(42). Where the symbols for the phosphate oxygen, O(35), and the water molecule, O(42), overlap in Fig. 1, the asterisk depicts both the centre of the two hexagons and the OH^- sites of HA. The region bounded by the non-apatitic phosphates P(13) and P(14) is an irregular channel filled with waters of hydration. The portion of the cell defined approximately by $3/4 > x > 1/4$ is referred to as the 'water layer'.

The water molecule, O(43), shown as the pair nearest the symmetry centres at $x = y = 1/2$, appeared in the Fourier section with about one-half the electron density of the other oxygen atoms, and its temperature factor became abnormally large in the least-squares refinement. This is taken to indicate that this site was incompletely occupied in the crystal on which the X-ray intensity measurements were made.

Its layer-type structure and the similarity of part of its structure to that of HA are reflected in the chemical and physical properties of OCP (following communication). The close correspondence between the atomic positions in the apatite layer of OCP and those of HA indicates that epitaxial overgrowths of one compound on the other are very likely. The water layer, which occupies almost half the OCP unit cell, rules out consideration of OCP as a 'defect apatite' and makes formation of true solid solutions of the two compounds highly unlikely. Formation of lamellar mixed crystals of the two compounds, as described in the following communication, is more probable.

The channel in the water layer explains both the ease with which OCP loses water and the difficulty of establishing a definite degree of hydration. The formula for OCP used here is based on the assumption that the partially filled water site for O(43) is completely filled in the ideal compound. There is sufficient room at the site for a water molecule, where it is co-ordinated to eight oxygens by distances less than 3·5 Å. Complete loss of water from this site would yield the formula $Ca_4H(PO_4)_3.2H_2O$, which is sometimes given[3,4] for OCP. There is no space in the unit cell large enough to accommodate another water molecule, and it appears that earlier indications[7,8] of more than 2·5 moles of water are in error. Hayek *et al.*[3] found that two samples of OCP dried for a short time at 100° C contained 2·5 moles of water, indicating that drying at this temperature removes non-essential water without much loss of water from the lattice. In view of these results, the formula $Ca_8H_2(PO_4)_6.5H_2O$ would be a better designation for OCP because it avoids fractional moles of hydration, it represents the asymmetric unit, and it is consistent with the common name.

The asymmetric unit of OCP contains two non-water protons which may form interphosphate hydrogen bonds. One such hydrogen bond is indicated by a distance of 2·47 Å between oxygens O(20) and O(36). This hydrogen presumably contributes to the weak 2,400 cm^{-1} infra-red absorption reported for OCP (ref. 10) and for 'calcium-deficient' apatites[11]. The other interphosphate oxygen-to-oxygen distances are greater than 2·9 Å, and a second interphosphate hydrogen bond cannot be located definitely on the basis of the present information.

The great variety in the anion–cation combinations which form apatite-type structures indicates that a high degree of stability is associated with this atomic arrangement. OCP appears to be the first-established compound with this arrangement in a layer-type structure, and it is noteworthy that this structural feature persists even though it is present in only about one-half of the unit cell. Arnold[1] and Carlström[5] suggested that OCP is a hydrated, layer-type modification of HA. Their views that the layers are formed simply by replacement of calcium ions by hydronium ions and that the layers are normal to the *c* axis were not borne out by the structure determination.

The two most common habits of HA (following communication) are such that the forms (100) could be the major contributors to the surface area of the crystals. Since the layers of OCP also are parallel to the 100 face, the structure of the water layer may prove to be a useful model for describing the interface between the apatite crystal and the aqueous phase.

The two-dimensional phase of this work was done at the University of Amsterdam on a grant from the Rockefeller Foundation, Agriculture, with advice of Prof. Caroline H. MacGillavry of the Laboratory for Inorganic Chemistry. Mr. Abraham Krouger of the Netherlands Organization for Pure Scientific Research (Z.W.O.) prepared the films from which the intensity data were collected.

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Crystallographic and Chemical Relations between Octacalcium Phosphate and Hydroxyapatite

MANY investigators[1,5,6,12–16] have observed that precipitated calcium phosphates that give apatitic X-ray patterns often have mole ratios Ca : P less than that of hydroxyapatite (HA), $Ca_5(PO_4)_3OH$. Most of these investigators have advanced explanations for this apparent anomaly, none of which is entirely satisfactory. On the basis of a recent determination (preceding communication) of the structure of octacalcium phosphate (OCP), $Ca_4H(PO_4)_3{\cdot}2{\cdot}5H_2O$, we offer another explanation which is consistent with the crystal structures of these two calcium phosphates. We have suggested[7] that HA and OCP form crystalline interlayered or lamellar mixtures analogous in this respect to clays. Such intra-crystalline mixtures not only account for apatitic precipitates with ratios Ca : P less than that in HA, but also explain observed chemical and physical properties of precipitated basic calcium phosphates.

We have obtained further evidence in support of this explanation from X-ray and petrographic investigations of basic calcium phosphates the mole ratios of Ca : P of which ranged from 1·33, that in OCP, to 1·67, that in HA, and of products obtained from OCP by dehydration in air, hydrolysis in boiling water, and treatment with fluoride solutions. Many of the alteration processes were observed with single-crystal X-ray techniques. The basic calcium phosphates were prepared in several ways, including titrations of phosphate solutions with solutions of calcium salts, ammoniation of acidic calcium phosphate solutions, hydrolysis of dicalcium phosphate, and diffusion of solutions of calcium acetate and sodium phosphate. The temperatures of the preparations ranged from 20° to 100° C.

The crystals used in the single-crystal X-ray studies were prepared by diffusion at 50°–60° C of 0·5 M sodium phosphate solution into a 0·5 M calcium chloride solution. Both solutions were also 0·5 M in sodium acetate, as was the barrier solution; all were adjusted to *p*H 8. The optical properties of some of the crystals showed that they had partially hydrolysed.

The optical properties of OCP were measured on crystals that were prepared by slow hydrolysis at 40° C of dicalcium phosphate in 0·5 M sodium acetate solution[7].

OCP crystallizes as thin (100) blades of triclinic : pinacoidal symmetry. The blades are elongated along *c* and modified by the set {010} and the terminating set {011}. Contact twinning with (100) as the twin plane was commonly observed optically. Single-crystal X-ray patterns commonly revealed twinning with *c* as the twin axis, and this is probably the polysynthetic twinning observed optically. In both modes of twinning the (100) is the composition plane.

The crystals are biaxial (−) with a $2V$ of 50°–55° (calc. 54°). The refractive indexes measured by the immersion method at 25° C are $N_\alpha = 1{\cdot}576$, $N_\beta = 1{\cdot}583$, and $N_\gamma = 1{\cdot}585$. The optic plane is inclined to the (100), where its trace on that face is at 78° relative to *c* in acute α. The acute bisectrix lies in the quadrant defined by *a*, *-b*, *-c*. One optic axis is roughly normal to (100), which accounts for the very low birefringence of crystals in their preferred orientation. Dispersion $(r > v)$ is very weak. The specific gravity obtained by the sink–float method is