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Strontium–Calcium Hydroxyapatite Solid Solutions Precipitated from Basic, Aqueous Solutions[1]

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Measurements of unit cell dimensions and strontium content have been made on hydroxyapatite preparations that were precipitated from basic, mixed calcium-strontium nitrate solutions and dried at 110°. A complete series of solid solutions is formed with lattice constants varying linearly with composition. However, the precipitation process shows a marked discrimination against strontium and chemically homogeneous solid solutions are obtained only if the ratio of strontium to calcium in the aqueous solution is maintained constant during the precipitation process. The discrimination against strontium decreases with increase in precipitation rate.

Introduction

In a previous paper[2] the formation of a complete solid solution series between strontium and calcium hydroxyapatite was reported. These solid solutions were prepared by precipitation from a basic, aqueous solution at 90° followed by heating the washed precipitate to 950°. Although the X-ray diffraction lines from the heated solid solutions were sharp for all compositions, indicating homogeneous preparations, those from the unheated solid solution precipitates were broad, and in some cases asymmetric. In these unheated samples the line breadth varied with composition, but the solid solution lines were always broader than those from the pure end members prepared in the same way. This line broadening in the unheated precipitates could have been caused by strain accompanying solid solution formation, by a particle size that varied with composition or by chemical heterogeneity in the solid solution precipitate. The latter hypothesis has previously been put forward[2] as the explanation for the line broadening. The purpose of this paper is to report evidence in support of this hypothesis and to show that homogeneous solid solutions can be prepared directly from aqueous solution without the necessity of heat treatment at 950°.

With this purpose in mind preparations were carried out with accurately weighed quantities so that the distribution of Sr and Ca between solid and solution could be quantitatively determined.

Experimental

The solid solutions were prepared by adding an $(NH_4)_2HPO_4$ solution to a boiling solution of $Ca(NO_3)_2$ and $Sr(NO_3)_2$. Both solutions were made basic with ethylenediamine. The materials and the general procedures used for sample preparation, Sr analysis and lattice constant measurement were the same as described in the previous paper.[2] The following modifications of the general preparation procedure were used.

(a) **F Series.**—The phosphate solutions contained about 1 g. $(NH_4)_2HPO_4$ weighed to ± 0.2 mg. in 200 ml. of water to which 9 ml. of ethylenediamine was added. The Ca and Sr concentrations in the $Ca(NO_3)_2$–$Sr(NO_3)_2$ solutions are shown in Table I. The total volume of the Ca–Sr solution was 1700 ml. and this included 3 ml. of ethylenediamine.

(b) **F4$_d$.**—The phosphate and Ca–Sr solutions were the same as in the F4$_c$ preparation (see Table I). However, an attempt was made to keep the amount of Ca and Sr in the solution constant as the precipitation occurred. This was done by adding a Ca–Sr solution from a buret into the original Ca–Sr solution at a rate equal to that of the phosphate addition. The added solution contained 0.09981 g. atoms Ca and 0.009404 g. atoms Sr in 250 ml.

(c) **G Series.**—These preparations were made in the same way as the F series preparations and were used to obtain the lattice constants shown in Fig. 2.

(d) **Recrystallization Experiments.**—Two experiments were performed; one in which a fresh calcium hydroxyapatite precipitate was placed in a concentrated $Sr(NO_3)_2$ solution, and another in which a fresh strontium hydroxyapatite precipitate was placed in a concentrated $Ca(NO_3)_2$ solution. The solutions were made basic with ethylenediamine and kept boiling for about 2 hr. before being washed in the usual manner.

(e) **Precipitation Rate.**—The effect of rate of phosphate addition on precipitate composition was investigated in preparations K2$_a$, K3 and K4, Table II. One gram of $(NH_4)_2HPO_4$ weighed to ±0.2 mg. plus 9 ml. of ethylenediamine in 59 ml. of water was added through a buret to the boiling Ca–Sr solution. The times for phosphate addition were as follows: K2$_a$, 5 sec.; K3, 1 min.; K4, 2 hr.

Line Profiles.—A General Electric XRD-3 diffraction unit with 1° beam slit, 0.05° detector slit and CuK$_\alpha$ radiation was used to measure the line profile of the (222) reflection for a number of preparations. Geiger counter readings were taken at fixed angles with a 2% counting error. Corrections for instrumental broadening were derived from measurements on a coarsely crystalline hydroxyapatite by using the Fourier analysis procedure of Stokes.[3]

Results and Discussion

It is reasonable to assume that the ratio, Sr/Ca, in the precipitate forming at any instant is proportional to the Sr/Ca ratio in the solution at that instant. If, in addition, the assumption is made that once a crystallite has formed its rate of solution is negligibly slow with respect to the duration of the precipitation process, then it is possible to apply the method of Doerner and Hoskins[4] and derive a distribution constant λ where

$$\frac{d(\mathrm{Sr})}{dt} \bigg/ \frac{d(\mathrm{Ca})}{dt} = \lambda \frac{(\mathrm{Sr})}{(\mathrm{Ca})} \qquad (1)$$

(Sr) and (Ca) are the amounts of Sr and Ca in solution at any instant. This equation can be integrated over the course of the phosphate addition to give

$$\log \frac{(\mathrm{Sr})_i}{(\mathrm{Sr})_f} = \lambda \log \frac{(\mathrm{Ca})_i}{(\mathrm{Ca})_f} \qquad (2)$$

where subscripts i and f refer to initial and final amounts of Ca and Sr in solution. If our two assumptions are correct, λ should be a constant for all values of $(\mathrm{Sr})_i/(\mathrm{Ca})_i$ as well as for different fractions of initial Sr plus Ca precipitated. The amounts of Sr and Ca and calculated values of λ

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[2] R. L. Collin, THIS JOURNAL, **81**, 5275 (1959).

[3] A. R. Stokes, *Proc. Phys. Soc. (London)*, **61**, 382 (1948).

[4] H. A. Doerner and W. M. Hoskins, THIS JOURNAL, **47**, 662 (1925).

TABLE I

SOLUTION AND SOLID COMPOSITIONS

Sample no.	Initial solution Ca, g. atoms	Initial solution Sr, g. atoms	Solid Sr,[a] atom %	Final solution Ca, g. atoms	Final solution Sr, g. atoms	λ	D
$F1_c$	0.1800	0.0200	1.2	0.1676	0.0198	0.1050	0.1016
F2	.1004	.1000	9.2	.0889	.0988	.0964	.0911
F3	.0600	.1400	19.8	.0499	.1375	.0977	.0898
F4	.0404	.1600	30.8	.0317	.1561	.1008	.0901
$F4_c$	.0100	.0400	41.8	.0027	.0347	.1069	.0552
F5	.0200	.1800	50.2	.0137	.1737	.0950	.0796
F6	.0100	.1900	69.3	.0061	.1812	.0960	.0761
F7	.0040	.1960	86.0	.0022	.1851	.0972	.0735
F8	.0020	.1980	93.6	.0012	.1862	.1185	.0932

[a] $\frac{\text{G. atoms Sr}}{\text{G. atoms Sr} + \text{g. atoms Ca}} \times 100.$

TABLE II

EFFECT OF RATE OF PHOSPHATE ADDITION ON λ

Sample no.	Initial solution Ca, g. atoms	Initial solution Sr, g. atoms	Solid Sr, atom %	Final solution Ca, g. atoms	Final solution Sr, g. atoms	λ	Time PO_4 addn.
$K2_a$	0.0400	0.1607	35.7	0.0318	0.1562	0.125	5 sec.
K3	.0400	.1600	34.9	.0318	.1556	.121	1 min.
K4	.0400	.1600	33.6	.0316	.1558	.114	2 hr.

in the F series preparations, which were designed to test equation 2, are shown in Table I. The values of λ are essentially constant over a wide range of initial solution Sr/Ca ratios and precipitate compositions, only deviating at the ends of the composition range where the value of λ is sensitive to small errors in the analysis of the Sr content of the solid and for $F4_c$ where the value of λ is also subject to a large error because of the low concentrations of Sr and Ca in solution. The average value of λ, with the two end members and $F4_c$ omitted, is 0.0972.

If, contrary to our above hypotheses, the solid crystallites were able to redissolve after formation or if in any way the entire crystallite were to come to equilibrium with the final solution, then one would expect the ratio $D = \frac{(\text{Sr})_s}{(\text{Ca})_s} \Big/ \frac{(\text{Sr})_f}{(\text{Ca})_f}$, where subscript s refers to the solid and subscript f to the final solution, to be a constant. Values of D are also listed in Table I, and it is apparent that they vary widely.

Once a value for λ has been determined it is possible to examine the X-ray line profiles given by the precipitates and test the assumption that the observed line width is a combination of two parts, (a) an intrinsic line width independent of composition and arising from small particle size or strain and (b) a part arising from the inhomogeneous nature of the precipitate whose composition is changing according to (1) as precipitation occurs.

Following the general convolution approach of Stokes,[3] we can write an expression for the observed line profile, $h(\epsilon)$, in terms of the convolution of $f(\epsilon)$ the intrinsic line profile, and $g(\epsilon)$ the weight function arising from the inhomogeneous nature of the precipitate. Fourier transform theory tells us that

$$h(\epsilon) = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{\infty} G(\zeta) \cdot F(\zeta) e^{-2\pi i \epsilon \zeta} \, d\zeta \qquad (3)$$

where $G(\zeta)$ is the Fourier transform of $g(\epsilon)$ and $F(\zeta)$ is the Fourier transform of $f(\epsilon)$. $F(\zeta)$ was calculated from the observed line profile of pure calcium hydroxyapatite prepared by the same method as the solid solution and dried at 110°. $G(\zeta)$ was evaluated graphically using $\lambda = 0.1$ to determine the composition spread and using the lattice parameters obtained from the solid solutions heated to 950°[2] to calculate the corresponding spread in lattice parameters. A correction factor was also introduced into $G(\zeta)$ to take account of the increase in scattered intensity as Sr replaces Ca in the structure.

Figure 1 shows the observed (222) profiles from calcium hydroxyapatite heated to 950°, calcium hydroxyapatite dried at 110°, and solid solution $F4_c$ (41.8 atom % Sr). The calculated line profile for $F4_c$ is shown also. The observed and calculated curves agree well, and this supports the assumption that the line broadening can be divided into two parts. The intrinsic line broadening of the pure calcium hydroxyapatite corresponds to a crystallite diameter of 300 Å.

One further test can be made. A homogeneous solid solution should result by starting with a solution of composition $F4_c$ and adding Ca and Sr as precipitation occurs so that the amounts of Sr and Ca in solution remain constant. The rate at which Sr and Ca must be added was calculated using $\lambda = 0.094$, and a solid solution precipitate, $F4_d$, with a line profile slightly sharper than for pure calcium hydroxyapatite was obtained (Fig. 1).

All the above results indicate that extensive recrystallization is not occurring, at least after a few minutes from the time of precipitate formation. In further support of this is the observation that when freshly prepared precipitates of calcium or strontium hydroxyapatite were placed in contact with a solution of the opposite cation there was little pickup revealed by fluorescence analysis or by lattice constant measurement on the precipitate heated to 950°. In the case of Sr hydroxyapatite placed in a Ca solution, there was no indication of Ca pickup (less than 2 atom % Ca), and in the case of Ca hydroxyapatite ex-

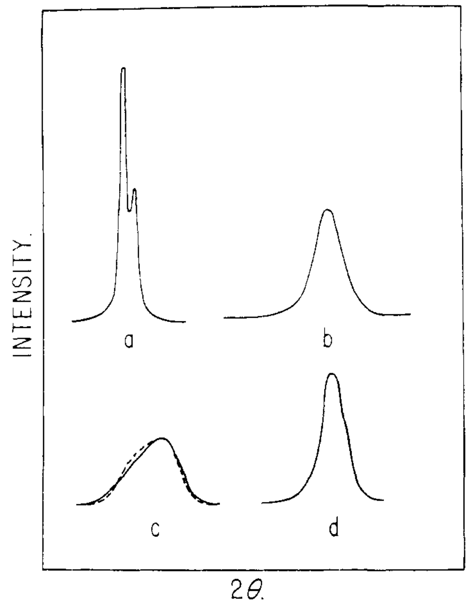

Fig. 1.—X-Ray diffraction profiles of the (222) line; intensity *vs.* scattering angle (2θ): (a) calcium hydroxyapatite heated to 950°, (b) calcium hydroxyapatite dried at 110°, (c) solid solution preparation $F4_c$ with calculated profile dashed, and (d) solid solution preparation $F4_d$. All curves have been normalized to give equal areas under the curves.

posed to a Sr solution, the precipitate picked up only 2 atom % Sr.

The lattice constants of the G series preparations are shown in Fig. 2. Within the probable errors of lattice constant and composition measurements the lattice constants vary linearly with composition over the entire range. Although these preparations were not strictly homogeneous the initial amounts of Ca plus Sr were large enough so that the change in composition of the solution during the precipitation process was not too great. No differences in line widths were noticed on rough ratemeter traces of the various samples.

As Doerner and Hoskins[4] have shown in connection with the Ra–$BaSO_4$ system, the value of λ is quite sensitive to the method of preparation. Specifically, λ depends on the rate of the precipitation. Under the conditions necessary for the derivation of (2) and if the addition of phosphate is sufficiently fast and the concentration of cations in solution sufficiently low with respect to phosphate concentration, the precipitation reaction would remove all the cations from solution in the immediate neighborhood of the phosphate. That is, with a large local excess of phosphate all the cations, Sr and Ca, in the neighborhood would be incorporated into the precipitate; there would be no discrimination and λ would be unity. Also, if phosphate is added in stoichiometric excess, essentially all the Sr and Ca would be precipitated ($(Sr)_f$ and $(Ca)_f$ in (2) would approach zero) and again λ would be unity.

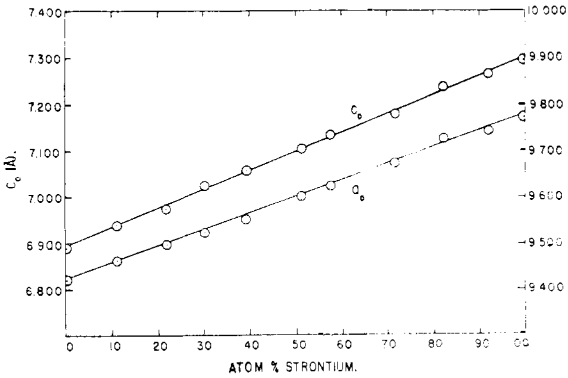

Fig. 2.—Lattice constants of solid solutions *vs.* atom % strontium.

The results of experiments designed to show the effect of rate of phosphate addition on λ are given in Table II. Although the change in λ is not great, it does increase as the rate of phosphate addition increases. Also, the effect of increasing the concentration of the phosphate solution can be seen by comparing the value of λ for K4 with the average value of λ for the F series. The phosphate solution used for K4 was four times as concentrated as were those used in the F series and the λ value is appreciably higher. These results are in agreement with theoretical expectations as well as with the work of Doerner and Hoskins[4] and others.[5]

Summary.—Homogeneous solid solutions with lattice constants varying linearly with composition over the entire Ca–Sr hydroxyapatite range can be precipitated from solution if the Sr/Ca ratio of the solution is held constant during the precipitation. The precipitates prepared in these experiments give an X-ray line broadening that corresponds to a particle diameter around 300 Å. and this line broadening is no greater for the solid solutions than for the pure end members.

Under the conditions of our experiments there is a marked discrimination against Sr in the precipitation process which does not change with solid solution composition, at least between 1 and 86 atoms % Sr. In agreement with theory, the magnitude of this discrimination is decreased by increasing the rate of precipitation.

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(5) L. Gordon, M. L. Salutsky and H. H. Willard, "Precipitation from Homogeneous Solution," John Wiley and Sons, Inc., New York, N. Y., 1959, p. 107.